

# Spectroscopy: Principles, Theory, Techniques and Applications

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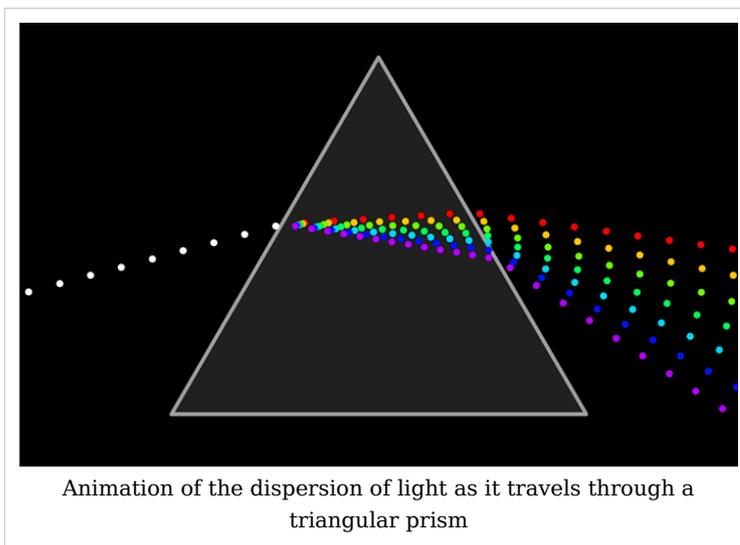
# Spectroscopy-An Introduction

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## Spectroscopy

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**Spectroscopy** was originally the study of the interaction between radiation and matter as a function of wavelength ( $\lambda$ ). In fact, historically <sup>[1]</sup>, spectroscopy referred to the use of visible light dispersed according to its wavelength, e.g. by a prism. Later the concept was expanded greatly to comprise any measurement of a quantity as function of either wavelength or frequency. Thus it also can refer to a response to an alternating field or varying frequency ( $\nu$ ). A further extension of the scope of the definition added energy ( $E$ ) as a variable, once the very close relationship  $E = h\nu$  for photons was realized ( $h$  is the Planck constant). A plot of the response as a function of wavelength—or more commonly frequency—is referred to as a spectrum; see also spectral linewidth.



**Spectrometry** is the spectroscopic technique used to assess the concentration or amount of a given species. In those cases, the instrument that performs such measurements is a spectrometer or spectrograph.

Spectroscopy/spectrometry is often used in physical and analytical chemistry for the identification of substances through the spectrum emitted from or absorbed by them.

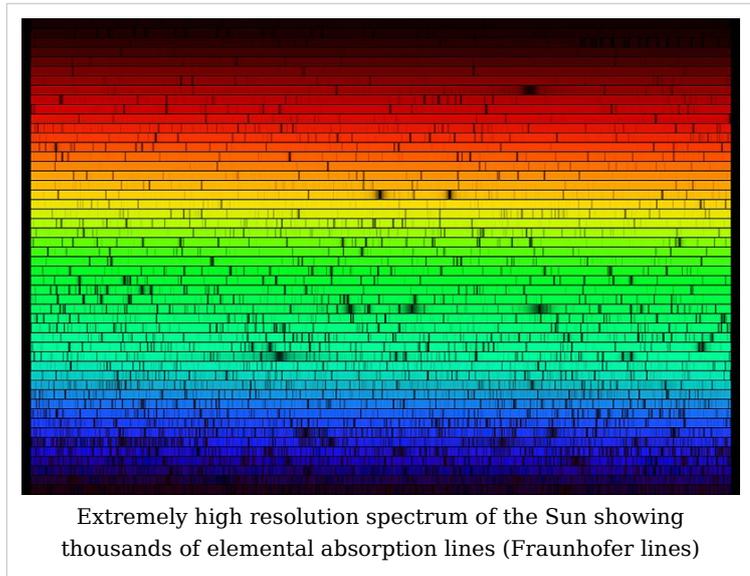
Spectroscopy/spectrometry is also heavily used in astronomy and remote sensing. Most large telescopes have spectrometers, which are used either to measure the chemical composition and physical properties of astronomical objects or to measure their velocities from the Doppler shift of their spectral lines.

## Classification of methods

### Nature of excitation measured

The type of spectroscopy depends on the physical quantity measured. Normally, the quantity that is measured is an intensity, either of energy absorbed or produced.

- Electromagnetic spectroscopy involves interactions of matter with electromagnetic radiation, such as light.
- → Electron spectroscopy involves interactions with electron beams. Auger spectroscopy involves inducing the Auger effect with an electron beam. In this case the measurement typically involves the kinetic energy of the electron as variable.
- Mass spectrometry involves the interaction of charged species with magnetic and/or electric fields, giving rise to a mass spectrum. The term "mass spectroscopy" is deprecated, for the technique is primarily a form of measurement, though it does produce a spectrum for observation. This spectrum has the mass  $m$  as variable, but the measurement is essentially one of the kinetic energy of the particle.
- Acoustic spectroscopy involves the frequency of sound.
- Dielectric spectroscopy involves the frequency of an external electrical field
- Mechanical spectroscopy involves the frequency of an external mechanical stress, e.g. a torsion applied to a piece of material.



### Measurement process

Most spectroscopic methods are differentiated as either atomic or molecular based on whether or not they apply to atoms or molecules. Along with that distinction, they can be classified on the nature of their interaction:

- Absorption spectroscopy uses the range of the electromagnetic spectra in which a substance absorbs. This includes → atomic absorption spectroscopy and various molecular techniques, such as infrared spectroscopy in that region and nuclear magnetic resonance (NMR) spectroscopy in the radio region.
- Emission spectroscopy uses the range of electromagnetic spectra in which a substance radiates (emits). The substance first must absorb energy. This energy can be from a variety of sources, which determines the name of the subsequent emission, like luminescence. Molecular luminescence techniques include spectrofluorimetry.
- Scattering spectroscopy measures the amount of light that a substance scatters at certain wavelengths, incident angles, and polarization angles. The scattering process is much faster than the absorption/emission process. One of the most useful applications of light scattering spectroscopy is → Raman spectroscopy.

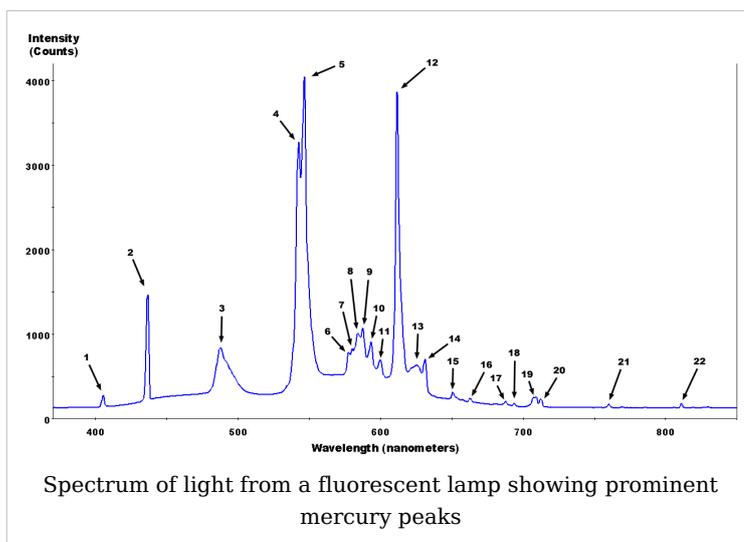
## Common types

### Absorption

Absorption spectroscopy is a technique in which the power of a beam of light measured before and after interaction with a sample is compared. When performed with tunable diode laser, it is often referred to as Tunable diode laser absorption spectroscopy (TDLAS). It is also often combined with a modulation technique, most often wavelength modulation spectrometry (WMS) and occasionally frequency modulation spectrometry (FMS) in order to reduce the noise in the system.

### Fluorescence

Fluorescence spectroscopy uses higher energy photons to excite a sample, which will then emit lower energy photons. This technique has become popular for its biochemical and medical applications, and can be used for confocal microscopy, fluorescence resonance energy transfer, and fluorescence lifetime imaging.



### X-ray

When X-rays of sufficient frequency (energy) interact with a substance, inner shell electrons in the atom are excited to outer empty orbitals, or they may be removed completely, ionizing the atom. The inner shell "hole" will then be filled by electrons from outer orbitals. The energy available in this de-excitation process is emitted as radiation (fluorescence) or will remove other less-bound electrons from the atom (Auger effect). The absorption or emission frequencies (energies) are characteristic of the specific atom. In addition, for a specific atom small frequency (energy) variations occur which are characteristic of the chemical bonding. With a suitable apparatus, these characteristic X-ray frequencies or Auger electron energies can be measured. X-ray absorption and emission spectroscopy is used in chemistry and material sciences to determine elemental composition and chemical bonding.

X-ray crystallography is a scattering process; crystalline materials scatter X-rays at well-defined angles. If the wavelength of the incident X-rays is known, this allows calculation of the distances between planes of atoms within the crystal. The intensities of the scattered X-rays give information about the atomic positions and allow the arrangement of the atoms within the crystal structure to be calculated.

## Flame

Liquid solution samples are aspirated into a burner or nebulizer/burner combination, desolvated, atomized, and sometimes excited to a higher energy electronic state. The use of a flame during analysis requires fuel and oxidant, typically in the form of gases. Common fuel gases used are acetylene (ethyne) or hydrogen. Common oxidant gases used are oxygen, air, or nitrous oxide. These methods are often capable of analyzing metallic element analytes in the part per million, billion, or possibly lower concentration ranges. Light detectors are needed to detect light with the analysis information coming from the flame.

- **Atomic Emission Spectroscopy** - This method uses flame excitation; atoms are excited from the heat of the flame to emit light. This method commonly uses a total consumption burner with a round burning outlet. A higher temperature flame than atomic absorption spectroscopy (AA) is typically used to produce excitation of analyte atoms. Since analyte atoms are excited by the heat of the flame, no special elemental lamps to shine into the flame are needed. A high resolution polychromator can be used to produce an emission intensity vs. wavelength spectrum over a range of wavelengths showing multiple element excitation lines, meaning multiple elements can be detected in one run. Alternatively, a monochromator can be set at one wavelength to concentrate on analysis of a single element at a certain emission line. Plasma emission spectroscopy is a more modern version of this method. See Flame emission spectroscopy for more details.
- → **Atomic absorption spectroscopy** (often called AA) - This method commonly uses a pre-burner nebulizer (or nebulizing chamber) to create a sample mist and a slot-shaped burner which gives a longer pathlength flame. The temperature of the flame is low enough that the flame itself does not excite sample atoms from their ground state. The nebulizer and flame are used to desolvate and atomize the sample, but the excitation of the analyte atoms is done by the use of lamps shining through the flame at various wavelengths for each type of analyte. In AA, the amount of light absorbed after going through the flame determines the amount of analyte in the sample. A graphite furnace for heating the sample to desolvate and atomize is commonly used for greater sensitivity. The graphite furnace method can also analyze some solid or slurry samples. Because of its good sensitivity and selectivity, it is still a commonly used method of analysis for certain trace elements in aqueous (and other liquid) samples.
- **Atomic Fluorescence Spectroscopy** - This method commonly uses a burner with a round burning outlet. The flame is used to solvate and atomize the sample, but a lamp shines light at a specific wavelength into the flame to excite the analyte atoms in the flame. The atoms of certain elements can then fluoresce emitting light in a different direction. The intensity of this fluorescing light is used for quantifying the amount of analyte element in the sample. A graphite furnace can also be used for atomic fluorescence spectroscopy. This method is not as commonly used as atomic absorption or plasma emission spectroscopy.

**Plasma Emission Spectroscopy** In some ways similar to flame atomic emission spectroscopy, it has largely replaced it.

- Direct-current plasma (DCP)

A direct-current plasma (DCP) is created by an electrical discharge between two electrodes. A plasma support gas is necessary, and Ar is common. Samples can be deposited on one of the electrodes, or if conducting can make up one electrode.

- Glow discharge-optical emission spectrometry (GD-OES)
- Inductively coupled plasma-atomic emission spectrometry (ICP-AES)
- Laser Induced Breakdown Spectroscopy (LIBS) (LIBS), also called Laser-induced plasma spectrometry (LIPS)
- Microwave-induced plasma (MIP)

**Spark or arc (emission) spectroscopy** - is used for the analysis of metallic elements in solid samples. For non-conductive materials, a sample is ground with graphite powder to make it conductive. In traditional arc spectroscopy methods, a sample of the solid was commonly ground up and destroyed during analysis. An electric arc or spark is passed through the sample, heating the sample to a high temperature to excite the atoms in it. The excited analyte atoms glow emitting light at various wavelengths which could be detected by common spectroscopic methods. Since the conditions producing the arc emission typically are not controlled quantitatively, the analysis for the elements is qualitative. Nowadays, the spark sources with controlled discharges under an argon atmosphere allow that this method can be considered eminently quantitative, and its use is widely expanded worldwide through production control laboratories of foundries and steel mills.

## Visible

Many atoms emit or absorb visible light. In order to obtain a fine line spectrum, the atoms must be in a gas phase. This means that the substance has to be vaporised. The spectrum is studied in absorption or emission. Visible absorption spectroscopy is often combined with UV absorption spectroscopy in UV/Vis spectroscopy. Although this form may be uncommon as the human eye is a similar indicator, it still proves useful when distinguishing colours.

## Ultraviolet

All atoms absorb in the Ultraviolet (UV) region because these photons are energetic enough to excite outer electrons. If the frequency is high enough, photoionization takes place. UV spectroscopy is also used in quantifying protein and DNA concentration as well as the ratio of protein to DNA concentration in a solution. Several amino acids usually found in protein, such as tryptophan, absorb light in the 280 nm range and DNA absorbs light in the 260 nm range. For this reason, the ratio of 260/280 nm absorbance is a good general indicator of the relative purity of a solution in terms of these two macromolecules. Reasonable estimates of protein or DNA concentration can also be made this way using Beer's law.

## Infrared

Infrared spectroscopy offers the possibility to measure different types of inter atomic bond vibrations at different frequencies. Especially in organic chemistry the analysis of IR absorption spectra shows what type of bonds are present in the sample. It is also an important method for analysing polymers and constituents like fillers, pigments and plasticizers.

## Near Infrared (NIR)

The near infrared NIR range, immediately beyond the visible wavelength range, is especially important for practical applications because of the much greater penetration depth of NIR radiation into the sample than in the case of mid IR spectroscopy range. This

allows also large samples to be measured in each scan by → NIR spectroscopy, and is currently employed for many practical applications such as: rapid grain analysis, medical diagnosis pharmaceuticals/medicines<sup>[2]</sup>, biotechnology, genomics analysis, proteomic analysis, interactomics research, inline textile monitoring, food analysis and chemical imaging/hyperspectral imaging of intact organisms<sup>[3] [4] [5]</sup>, plastics, textiles, insect detection, forensic lab application, crime detection, various military applications, and so on.

## Raman

Raman spectroscopy uses the inelastic scattering of light to analyse vibrational and rotational modes of molecules. The resulting 'fingerprints' are an aid to analysis.

## Coherent anti-Stokes Raman spectroscopy (CARS)

→ CARS is a recent technique that has high sensitivity and powerful applications for *in vivo* spectroscopy and imaging<sup>[6]</sup>.

## Nuclear magnetic resonance

Nuclear magnetic resonance spectroscopy analyzes the magnetic properties of certain atomic nuclei to determine different electronic local environments of hydrogen, carbon, or other atoms in an organic compound or other compound. This is used to help determine the structure of the compound.

## Photoemission

## Mössbauer

Transmission or conversion-electron (CEMS) modes of Mössbauer spectroscopy probe the properties of specific isotope nuclei in different atomic environments by analyzing the resonant absorption of characteristic energy gamma-rays known as the Mössbauer effect.

## Other types

- Acoustic spectroscopy
- Auger Spectroscopy

A method used to study surfaces of materials on a micro-scale. It is often used in connection with electron microscopy.

- Cavity ring down spectroscopy
- Circular Dichroism spectroscopy
- Dielectric spectroscopy
- Force spectroscopy
- → Fourier transform spectroscopy

An efficient method for processing spectra data obtained using interferometers. Nearly all infrared spectroscopy (Such as FTIR) and Nuclear Magnetic Resonance (→ NMR) spectroscopy are based on Fourier transforms.

- → Fourier transform infrared spectroscopy (FTIR)
- → Hadron spectroscopy

Studies the energy/mass spectrum of hadrons according to spin, parity, and other particle properties. Baryon spectroscopy and meson spectroscopy are both types of

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hadron spectroscopy.

- Inelastic electron tunnelling spectroscopy (IETS)  
Uses the changes in current due to inelastic electron-vibration interaction at specific energies which can also measure optically forbidden transitions.
- Inelastic neutron scattering  
Like Raman spectroscopy, but with neutrons instead of photons.
- Mechanical spectroscopy  
Involves interactions with macroscopic vibrations, such as phonons. An example is acoustic spectroscopy, involving sound waves.
- → Neutron spin echo spectroscopy  
Measures internal dynamics in proteins and other soft matter systems
- → Nuclear magnetic resonance (NMR)
- Photoacoustic spectroscopy  
Measures the sound waves produced upon the absorption of radiation.
- Photothermal spectroscopy  
Measures heat evolved upon absorption of radiation.
- Raman optical activity spectroscopy  
Exploits Raman scattering and optical activity effects to reveal detailed information on chiral centers in molecules.
- → Terahertz spectroscopy  
Uses wavelengths above infrared spectroscopy and below microwave or millimeter wave measurements.
- → Time-resolved spectroscopy  
Spectroscopy of matter in situations where the properties are changing with time.
- Thermal infrared spectroscopy  
Measures thermal radiation emitted from materials and surfaces and is used to determine the type of bonds present in a sample as well as their lattice environment. The techniques are widely used by organic chemists, mineralogists, and planetary scientists.

## Background subtraction

Background subtraction is a term typically used in spectroscopy when one explains the process of acquiring a background radiation level (or ambient radiation level) and then makes an algorithmic adjustment to the data to obtain qualitative information about any deviations from the background, even when they are an order of magnitude less decipherable than the background itself.

Background subtraction can effect a number of statistical calculations (Continuum, Compton, Bremsstrahlung) leading to improved overall system performance.

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## References Cited

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- [2] J. Dubois, G. Sando, E. N. Lewis, Near-Infrared Chemical Imaging, A Valuable Tool for the Pharmaceutical Industry, G.I.T. Laboratory Journal Europe, No. 1-2, 2007
- [3] [http://www.malvern.com/LabEng/products/sdi/bibliography/sdi\\_bibliography.htm](http://www.malvern.com/LabEng/products/sdi/bibliography/sdi_bibliography.htm) E. N. Lewis, E. Lee and L. H. Kidder, Combining Imaging and Spectroscopy: Solving Problems with Near-Infrared Chemical Imaging. Microscopy Today, Volume 12, No. 6, 11/2004.
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- [6] C.L. Evans and X.S. Xie.2008. Coherent Anti-Stokes Raman Scattering Microscopy: Chemical Imaging for Biology and Medicine., doi:10.1146/annurev.anchem.1.031207.112754 *Annual Review of Analytical Chemistry*, 1: 883-909.

## See also

- Absorption cross section
- Astronomical spectroscopy
- Atomic spectroscopy
- → Nuclear magnetic resonance
- → 2D-FT NMRI and Spectroscopy
- → Near infrared spectroscopy
- Coherent spectroscopy
- Cold vapour atomic fluorescence spectroscopy
- Deep-level transient spectroscopy
- → EPR spectroscopy
- Gamma spectroscopy
- Metamerism (color)
- Rigid rotor
- Rotational spectroscopy
- Saturated spectroscopy
- Scanning tunneling spectroscopy
- Scattering theory
- Spectral power distributions
- Spectral reflectance
- Spectrophotometry
- Spectroscopic notation
- Spectrum analysis
- → Vibrational spectroscopy
- Vibrational circular dichroism spectroscopy
- Joseph von Fraunhofer
- Robert Bunsen
- Gustav Kirchhoff

## External links

- Spectroscopy links (<http://www.dmoz.org//Science/Physics/Optics/Spectroscopy//>) at the Open Directory Project
  - Amateur spectroscopy links (<http://www.dmoz.org//Science/Astronomy/Amateur/Spectroscopy//>) at the Open Directory Project
  - History of Spectroscopy ([http://www.cofc.edu/~deavorj/521/History of Spectroscopy.htm](http://www.cofc.edu/~deavorj/521/History%20of%20Spectroscopy.htm))
  - Chemometric Analysis for Spectroscopy (<http://www.laboratoryequipment.com/article-chemometric-analysis-for-spectroscopy.aspx>)
  - The Science of Spectroscopy (<http://www.scienceofspectroscopy.info>) - supported by NASA, includes OpenSpectrum, a Wiki-based learning tool for spectroscopy that anyone can edit
  - A Short Study of the Characteristics of two Lab Spectroscopes (<http://ioannis.virtualcomposer2000.com/spectroscope/>)
  - NIST government spectroscopy data (<http://physics.nist.gov/Pubs/AtSpec/index.html>)
  - Potentiodynamic Electrochemical Impedance Spectroscopy (<http://www.abc.chemistry.bsu.by/vi/>)
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# Spectroscopy Theory

## Quantum mechanics

**Quantum mechanics** is a set of principles underlying the most fundamental known description of all physical systems at the submicroscopic scale (at the atomic level). Notable among these principles are both a dual wave-like and particle-like behavior of matter and radiation, and prediction of probabilities in situations where classical physics predicts certainties. Classical physics can be derived as a good *approximation* to quantum physics, typically in circumstances with large numbers of particles. Thus quantum phenomena are particularly relevant in systems whose dimensions are close to the atomic scale, such as molecules, atoms, electrons, protons and other subatomic particles. Exceptions exist for certain systems which exhibit quantum mechanical effects on macroscopic scale; superfluidity is one well-known example. Quantum theory provides accurate descriptions for many previously unexplained phenomena such as black body radiation and stable electron orbits. It has also given insight into the workings of many different biological systems, including smell receptors and protein structures.<sup>[1]</sup>

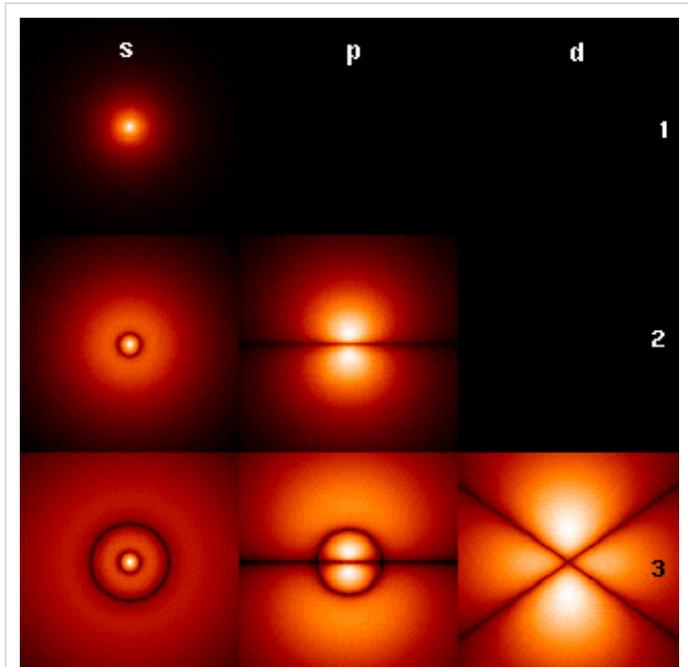


Fig. 1: Probability densities corresponding to the wavefunctions of an electron in a hydrogen atom possessing definite energy (increasing downward:  $n = 1, 2, 3, \dots$ ) and angular momentum (increasing across:  $s, p, d, \dots$ ). Brighter areas correspond to higher probability density in a position measurement. Wavefunctions like these are directly comparable to Chladni's figures of acoustic modes of vibration in classical physics and are indeed modes of oscillation as well: they possess a sharp energy and thus a keen frequency. The angular momentum and energy are quantized, and only take on discrete values like those shown (as is the case for resonant frequencies in acoustics).

### Overview

The word *quantum* is Latin for "how great" or "how much."<sup>[2]</sup> In quantum mechanics, it refers to a discrete unit that quantum theory assigns to certain physical quantities, such as the energy of an atom at rest (see Figure 1, at right). The discovery that waves have discrete energy packets (called quanta) that behave in a manner similar to particles led to the branch of physics that deals with atomic and subatomic systems which we today call quantum mechanics. It is the underlying mathematical framework of many fields of physics

and chemistry, including condensed matter physics, solid-state physics, atomic physics, molecular physics, computational chemistry, quantum chemistry, particle physics, and nuclear physics. The foundations of quantum mechanics were established during the first half of the twentieth century by Werner Heisenberg, Max Planck, Louis de Broglie, Albert Einstein, Niels Bohr, Erwin Schrödinger, Max Born, John von Neumann, Paul Dirac, Wolfgang Pauli, William Hamilton, David Hilbert, and others.<sup>[3]</sup> Some fundamental aspects of the theory are still actively studied.<sup>[4]</sup>

Quantum mechanics is essential to understand the behavior of systems at atomic length scales and smaller. For example, if classical mechanics governed the workings of an atom, electrons would rapidly travel towards and collide with the nucleus, making stable atoms impossible. However, in the natural world the electrons normally remain in an uncertain, non-deterministic "smeared" (wave-particle wave function) orbital path around or "thru" the nucleus, defying classical electromagnetism.<sup>[5]</sup>

Quantum mechanics was initially developed to provide a better explanation of the atom, especially the spectra of light emitted by different atomic species. The quantum theory of the atom was developed as an explanation for the electron's staying in its orbital, which could not be explained by Newton's laws of motion and by Maxwell's laws of classical electromagnetism.<sup>[6]</sup>

In the formalism of quantum mechanics, the state of a system at a given time is described by a complex wave function (sometimes referred to as orbitals in the case of atomic electrons), and more generally, elements of a complex vector space.<sup>[7]</sup> This abstract mathematical object allows for the calculation of probabilities of outcomes of concrete experiments. For example, it allows one to compute the probability of finding an electron in a particular region around the nucleus at a particular time. Contrary to classical mechanics, one can never make simultaneous predictions of conjugate variables, such as position and momentum, with arbitrary accuracy. For instance, electrons may be considered to be located somewhere within a region of space, but with their exact positions being unknown. Contours of constant probability, often referred to as "clouds" may be drawn around the nucleus of an atom to conceptualize where the electron might be located with the most probability. Heisenberg's uncertainty principle quantifies the inability to precisely locate the particle given its conjugate.<sup>[8]</sup>

The other exemplar that led to quantum mechanics was the study of electromagnetic waves such as light. When it was found in 1900 by Max Planck that the energy of waves could be described as consisting of small packets or quanta, Albert Einstein exploited this idea to show that an electromagnetic wave such as light could be described by a particle called the photon with a discrete energy dependent on its frequency. This led to a theory of unity between subatomic particles and electromagnetic waves called wave-particle duality in which particles and waves were neither one nor the other, but had certain properties of both. While quantum mechanics describes the world of the very small, it also is needed to explain certain "macroscopic quantum systems" such as superconductors and superfluids.<sup>[9]</sup>

Broadly speaking, quantum mechanics incorporates four classes of phenomena that classical physics cannot account for: (I) the quantization (discretization) of certain physical quantities, (II) wave-particle duality, (III) the uncertainty principle, and (IV) quantum entanglement. Each of these phenomena is described in detail in subsequent sections.<sup>[10]</sup>

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## History

The **history of quantum mechanics**<sup>[11]</sup> began essentially with the 1838 discovery of cathode rays by Michael Faraday, the 1859 statement of the black body radiation problem by Gustav Kirchhoff, the 1877 suggestion by Ludwig Boltzmann that the energy states of a physical system could be discrete, and the 1900 quantum hypothesis by Max Planck that any energy is radiated and absorbed in quantities divisible by discrete 'energy elements',  $E$ , such that each of these energy elements is proportional to the frequency  $\nu$  with which they each individually radiate energy, as defined by the following formula:

$$E = h\nu = \hbar\omega$$

where  $h$  is Planck's Action Constant. Planck insisted<sup>[12]</sup> that this was simply an aspect of the processes of absorption and emission of radiation and had nothing to do with the physical reality of the radiation itself. However, this did not explain the photoelectric effect (1839), i.e. that shining light on certain materials can function to eject electrons from the material. In 1905, basing his work on Planck's quantum hypothesis, Albert Einstein<sup>[13]</sup> postulated that light itself consists of individual quanta. These later came to be called photons (1926). From Einstein's simple postulation was born a flurry of debating, theorizing and testing, and thus, the entire field of quantum physics...

## Quantum mechanics and classical physics

Predictions of quantum mechanics have been verified experimentally to a very high degree of accuracy. Thus, the current logic of correspondence principle between classical and quantum mechanics is that all objects obey laws of quantum mechanics, and classical mechanics is just a quantum mechanics of large systems (or a statistical quantum mechanics of a large collection of particles). Laws of classical mechanics thus follow from laws of quantum mechanics at the limit of large systems or large quantum numbers.<sup>[14]</sup>

The main differences between classical and quantum theories have already been mentioned above in the remarks on the Einstein-Podolsky-Rosen paradox. Essentially the difference boils down to the statement that quantum mechanics is coherent (addition of *amplitudes*), whereas classical theories are incoherent (addition of *intensities*). Thus, such quantities as *coherence lengths* and *coherence times* come into play. For microscopic bodies the extension of the system is certainly much smaller than the coherence length; for macroscopic bodies one expects that it should be the other way round.

This is in accordance with the following observations:

Many "macroscopic" properties of "classic" systems are direct consequences of quantum behavior of its parts. For example, stability of bulk matter (which consists of atoms and molecules which would quickly collapse under electric forces alone), rigidity of this matter, mechanical, thermal, chemical, optical and magnetic properties of this matter—they are all results of interaction of electric charges under the rules of quantum mechanics.

While the seemingly exotic behavior of matter posited by quantum mechanics and relativity theory become more apparent when dealing with extremely fast-moving or extremely tiny particles, the laws of classical "Newtonian" physics still remain accurate in predicting the behavior of surrounding ("large") objects—of the order of the size of large molecules and bigger—at velocities much smaller than the velocity of light.

## Theory

There are numerous mathematically equivalent formulations of quantum mechanics. One of the oldest and most commonly used formulations is the transformation theory proposed by Cambridge theoretical physicist Paul Dirac, which unifies and generalizes the two earliest formulations of quantum mechanics, matrix mechanics (invented by Werner Heisenberg)<sup>[15]</sup> and wave mechanics (invented by Erwin Schrödinger).

In this formulation, the instantaneous state of a quantum system encodes the probabilities of its measurable properties, or "observables". Examples of observables include energy, position, momentum, and angular momentum. Observables can be either continuous (e.g., the position of a particle) or discrete (e.g., the energy of an electron bound to a hydrogen atom).

Generally, quantum mechanics does not assign definite values to observables. Instead, it makes predictions about probability distributions; that is, the probability of obtaining each of the possible outcomes from measuring an observable. Oftentimes these results are skewed by many causes, such as dense probability clouds or quantum state nuclear attraction. Much of the time, these small anomalies are attributed to different causes such as quantum dislocation. Naturally, these probabilities will depend on the quantum state at the instant of the measurement. When the probability amplitudes of four or more quantum nodes are similar, it is called a quantum parallelism. There are, however, certain states that are associated with a definite value of a particular observable. These are known as "eigenstates" of the observable ("eigen" can be roughly translated from German as inherent or as a characteristic). In the everyday world, it is natural and intuitive to think of everything being in an eigenstate of every observable. Everything appears to have a definite position, a definite momentum, and a definite time of occurrence. However, quantum mechanics does not pinpoint the exact values for the position or momentum of a certain particle in a given space in a finite time; rather, it only provides a range of probabilities of where that particle might be. Therefore, it became necessary to use different words for (a) the state of something having an *uncertainty relation* and (b) a state that has a *definite* value. The latter is called the "eigenstate" of the property being measured.

For example, consider a free particle. In quantum mechanics, there is wave-particle duality so the properties of the particle can be described as a wave. Therefore, its quantum state can be represented as a wave, of arbitrary shape and extending over all of space, called a wave function. The position and momentum of the particle are observables. The Uncertainty Principle of quantum mechanics states that both the position and the momentum cannot simultaneously be known with infinite precision at the same time. However, one can measure just the position alone of a moving free particle creating an eigenstate of position with a wavefunction that is very large at a particular position  $x$ , and almost zero everywhere else. If one performs a position measurement on such a wavefunction, the result  $x$  will be obtained with almost 100% probability. In other words, the position of the free particle will almost be known. This is called an eigenstate of position (mathematically more precise: a *generalized eigenstate (eigendistribution)* ). If the particle is in an eigenstate of position then its momentum is completely unknown. An eigenstate of momentum, on the other hand, has the form of a plane wave. It can be shown that the wavelength is equal to  $h/p$ , where  $h$  is Planck's constant and  $p$  is the momentum of the eigenstate. If the particle is in an eigenstate of momentum then its position is completely

blurred out.

Usually, a system will not be in an eigenstate of whatever observable we are interested in. However, if one measures the observable, the wavefunction will instantaneously be an eigenstate (or generalized eigenstate) of that observable. This process is known as wavefunction collapse. It involves expanding the system under study to include the measurement device, so that a detailed quantum calculation would no longer be feasible and a classical description must be used. If one knows the corresponding wave function at the instant before the measurement, one will be able to compute the probability of collapsing into each of the possible eigenstates. For example, the free particle in the previous example will usually have a wavefunction that is a wave packet centered around some mean position  $x_0$ , neither an eigenstate of position nor of momentum. When one measures the position of the particle, it is impossible to predict with certainty the result that we will obtain. It is probable, but not certain, that it will be near  $x_0$ , where the amplitude of the wave function is large. After the measurement is performed, having obtained some result  $x$ , the wave function collapses into a position eigenstate centered at  $x$ .

Wave functions can change as time progresses. An equation known as the Schrödinger equation describes how wave functions change in time, a role similar to Newton's second law in classical mechanics. The Schrödinger equation, applied to the aforementioned example of the free particle, predicts that the center of a wave packet will move through space at a constant velocity, like a classical particle with no forces acting on it. However, the wave packet will also spread out as time progresses, which means that the position becomes more uncertain. This also has the effect of turning position eigenstates (which can be thought of as infinitely sharp wave packets) into broadened wave packets that are no longer position eigenstates.

Some wave functions produce probability distributions that are constant in time. Many systems that are treated dynamically in classical mechanics are described by such "static" wave functions. For example, a single electron in an unexcited atom is pictured classically as a particle moving in a circular trajectory around the atomic nucleus, whereas in quantum mechanics it is described by a static, spherically symmetric wavefunction surrounding the nucleus (Fig. 1). (Note that only the lowest angular momentum states, labeled  $s$ , are spherically symmetric).

The time evolution of wave functions is deterministic in the sense that, given a wavefunction at an initial time, it makes a definite prediction of what the wavefunction will be at any later time. During a measurement, the change of the wavefunction into another one is not deterministic, but rather unpredictable, i.e., random.

The probabilistic nature of quantum mechanics thus stems from the act of measurement. This is one of the most difficult aspects of quantum systems to understand. It was the central topic in the famous Bohr-Einstein debates, in which the two scientists attempted to clarify these fundamental principles by way of thought experiments. In the decades after the formulation of quantum mechanics, the question of what constitutes a "measurement" has been extensively studied. Interpretations of quantum mechanics have been formulated to do away with the concept of "wavefunction collapse"; see, for example, the relative state interpretation. The basic idea is that when a quantum system interacts with a measuring apparatus, their respective wavefunctions become entangled, so that the original quantum system ceases to exist as an independent entity. For details, see the article on measurement in quantum mechanics.

## Mathematical formulation

In the mathematically rigorous formulation of quantum mechanics, developed by Paul Dirac<sup>[16]</sup> and John von Neumann<sup>[17]</sup>, the possible states of a quantum mechanical system are represented by unit vectors (called "state vectors") residing in a complex separable Hilbert space (variously called the "state space" or the "associated Hilbert space" of the system) well defined up to a complex number of norm 1 (the phase factor). In other words, the possible states are points in the projectivization of a Hilbert space, usually called the complex projective space. The exact nature of this Hilbert space is dependent on the system; for example, the state space for position and momentum states is the space of square-integrable functions, while the state space for the spin of a single proton is just the product of two complex planes. Each observable is represented by a maximally-Hermitian (precisely: by a self-adjoint) linear operator acting on the state space. Each eigenstate of an observable corresponds to an eigenvector of the operator, and the associated eigenvalue corresponds to the value of the observable in that eigenstate. If the operator's spectrum is discrete, the observable can only attain those discrete eigenvalues.

The time evolution of a quantum state is described by the Schrödinger equation, in which the Hamiltonian, the operator corresponding to the total energy of the system, generates time evolution.

The inner product between two state vectors is a complex number known as a probability amplitude. During a measurement, the probability that a system collapses from a given initial state to a particular eigenstate is given by the square of the absolute value of the probability amplitudes between the initial and final states. The possible results of a measurement are the eigenvalues of the operator - which explains the choice of *Hermitian* operators, for which all the eigenvalues are real. We can find the probability distribution of an observable in a given state by computing the spectral decomposition of the corresponding operator. Heisenberg's uncertainty principle is represented by the statement that the operators corresponding to certain observables do not commute.

The Schrödinger equation acts on the entire probability amplitude, not merely its absolute value. Whereas the absolute value of the probability amplitude encodes information about probabilities, its phase encodes information about the interference between quantum states. This gives rise to the wave-like behavior of quantum states.

It turns out that analytic solutions of Schrödinger's equation are only available for a small number of model Hamiltonians, of which the quantum harmonic oscillator, the particle in a box, the hydrogen molecular ion and the hydrogen atom are the most important representatives. Even the helium atom, which contains just one more electron than hydrogen, defies all attempts at a fully analytic treatment. There exist several techniques for generating approximate solutions. For instance, in the method known as perturbation theory one uses the analytic results for a simple quantum mechanical model to generate results for a more complicated model related to the simple model by, for example, the addition of a weak potential energy. Another method is the "semi-classical equation of motion" approach, which applies to systems for which quantum mechanics produces weak deviations from classical behavior. The deviations can be calculated based on the classical motion. This approach is important for the field of quantum chaos.

An alternative formulation of quantum mechanics is Feynman's path integral formulation, in which a quantum-mechanical amplitude is considered as a sum over histories between initial and final states; this is the quantum-mechanical counterpart of action principles in

classical mechanics.

## Interactions with other scientific theories

The fundamental rules of quantum mechanics are very deep. They assert that the state space of a system is a Hilbert space and the observables are Hermitian operators acting on that space, but do not tell us which Hilbert space or which operators, or if it even exists. These must be chosen appropriately in order to obtain a quantitative description of a quantum system. An important guide for making these choices is the correspondence principle, which states that the predictions of quantum mechanics reduce to those of classical physics when a system moves to higher energies or equivalently, larger quantum numbers. In other words, classic mechanics is simply a quantum mechanics of large systems. This "high energy" limit is known as the *classical* or *correspondence limit*. One can therefore start from an established classical model of a particular system, and attempt to guess the underlying quantum model that gives rise to the classical model in the correspondence limit.



Unsolved problems in physics: *In the correspondence limit of **quantum mechanics**: Is there a preferred interpretation of quantum mechanics? How does the quantum description of reality, which includes elements such as the "superposition of states" and "wavefunction collapse", give rise to the reality we perceive?*

When quantum mechanics was originally formulated, it was applied to models whose correspondence limit was non-relativistic classical mechanics. For instance, the well-known model of the quantum harmonic oscillator uses an explicitly non-relativistic expression for the kinetic energy of the oscillator, and is thus a quantum version of the classical harmonic oscillator.

Early attempts to merge quantum mechanics with special relativity involved the replacement of the Schrödinger equation with a covariant equation such as the Klein-Gordon equation or the Dirac equation. While these theories were successful in explaining many experimental results, they had certain unsatisfactory qualities stemming from their neglect of the relativistic creation and annihilation of particles. A fully relativistic quantum theory required the development of → quantum field theory, which applies quantization to a field rather than a fixed set of particles. The first complete quantum field theory, quantum electrodynamics, provides a fully quantum description of the electromagnetic interaction.

The full apparatus of quantum field theory is often unnecessary for describing electrodynamic systems. A simpler approach, one employed since the inception of quantum mechanics, is to treat charged particles as quantum mechanical objects being acted on by a classical electromagnetic field. For example, the elementary quantum model of the hydrogen atom describes the electric field of the hydrogen atom using a classical  $-\frac{e^2}{4\pi\epsilon_0} \frac{1}{r}$  Coulomb potential. This "semi-classical" approach fails if quantum fluctuations in the electromagnetic field play an important role, such as in the emission of photons by charged particles.

Quantum field theories for the strong nuclear force and the weak nuclear force have been developed. The quantum field theory of the strong nuclear force is called quantum chromodynamics, and describes the interactions of the subnuclear particles: quarks and

gluons. The weak nuclear force and the electromagnetic force were unified, in their quantized forms, into a single quantum field theory known as electroweak theory, by the physicists Abdus Salam, Sheldon Glashow and Steven Weinberg.

It has proven difficult to construct quantum models of gravity, the remaining fundamental force. Semi-classical approximations are workable, and have led to predictions such as Hawking radiation. However, the formulation of a complete theory of quantum gravity is hindered by apparent incompatibilities between general relativity, the most accurate theory of gravity currently known, and some of the fundamental assumptions of quantum theory. The resolution of these incompatibilities is an area of active research, and theories such as string theory are among the possible candidates for a future theory of quantum gravity.

## Example

The particle in a 1-dimensional potential energy box is the most simple example where restraints lead to the quantization of energy levels. The box is defined as zero potential energy inside a certain interval and infinite everywhere outside that interval. For the 1-dimensional case in the  $x$  direction, the time-independent Schrödinger equation can be written as:<sup>[18]</sup>

$$-\frac{\hbar^2}{2m} \frac{d^2\psi}{dx^2} = E\psi.$$

The general solutions are:

$$\psi = Ae^{ikx} + Be^{-ikx} \quad E = \frac{\hbar^2 k^2}{2m}$$

or

$$\psi = C \sin kx + D \cos kx \text{ (by Euler's formula).}$$

The presence of the walls of the box restricts the acceptable solutions of the wavefunction. At each wall:

$$\psi = 0 \text{ at } x = 0, x = L.$$

Consider  $x = 0$

- $\sin 0 = 0$ ,  $\cos 0 = 1$ . To satisfy  $\psi=0$  the  $\cos$  term has to be removed. Hence  $D = 0$ .

Now consider:  $\psi=C \sin kx$

- at  $x = L$ ,  $\psi=C \sin kL=0$
- If  $C = 0$  then  $\psi=0$  for all  $x$ . This would conflict with the Born interpretation
- therefore  $\sin kL = 0$  must be satisfied, yielding the condition.

$$kL = n\pi \quad n = 1, 2, 3, 4, 5, \dots$$

In this situation,  $n$  must be an integer showing the quantization of the energy levels.

## Relativity and quantum mechanics

The modern world of physics is founded on the two tested and demonstrably sound theories of general relativity and quantum mechanics —theories which appear to contradict one another. The defining postulates of both Einstein's theory of relativity and quantum theory are indisputably supported by rigorous and repeated empirical evidence. However, while they do not directly contradict each other theoretically (at least with regard to primary claims), they are resistant to being incorporated within one cohesive model.

Einstein himself is well known for rejecting some of the claims of quantum mechanics. While clearly inventive in this field, he did not accept the more philosophical consequences and interpretations of quantum mechanics, such as the lack of deterministic causality and the assertion that a single subatomic particle can occupy numerous areas of space at one time. He also was the first to notice some of the apparently exotic consequences of entanglement and used them to formulate the Einstein-Podolsky-Rosen paradox, in the hope of showing that quantum mechanics had unacceptable implications. This was 1935, but in 1964 it was shown by John Bell (see Bell inequality) that Einstein's assumption was correct, but had to be completed by *hidden variables* and thus based on wrong philosophical assumptions. According to the paper of J. Bell and the Copenhagen interpretation (the common interpretation of quantum mechanics by physicists for decades), and contrary to Einstein's ideas, quantum mechanics was

- neither a "realistic" theory (since quantum measurements do not *state* pre-existing properties, but rather they *prepare* properties)
- nor a *local* theory (essentially not, because the state vector  $|\psi\rangle$  determines simultaneously the probability amplitudes at all sites,  $|\psi\rangle \rightarrow \psi(\mathbf{r}), \forall \mathbf{r}$ ).

The Einstein-Podolsky-Rosen paradox shows in any case that there exist experiments by which one can measure the state of one particle and instantaneously change the state of its entangled partner, although the two particles can be an arbitrary distance apart; however, this effect does not violate causality, since no transfer of information happens. These experiments are the basis of some of the most topical applications of the theory, quantum cryptography, which works well, although at small distances of typically  $\leq 1000$  km, being on the market since 2004.

There do exist quantum theories which incorporate *special* relativity—for example, quantum electrodynamics (QED), which is currently the most accurately tested physical theory <sup>[19]</sup>—and these lie at the very heart of modern particle physics. Gravity is negligible in many areas of particle physics, so that unification between general relativity and quantum mechanics is not an urgent issue in those applications. However, the lack of a correct theory of quantum gravity is an important issue in cosmology.

## Attempts at a unified theory

Inconsistencies arise when one tries to join the quantum laws with general relativity, a more elaborate description of spacetime which incorporates gravitation. Resolving these inconsistencies has been a major goal of twentieth- and twenty-first-century physics. Many prominent physicists, including Stephen Hawking, have labored in the attempt to discover a "Grand Unification Theory" that combines not only different models of subatomic physics, but also derives the universe's four forces—the strong force, electromagnetism, weak force, and gravity—from a single force or phenomenon. Leading the charge in this field is Edward Witten, a physicist that formulated the groundbreaking M-theory which is an attempt at describing the supersymmetrical based string theory.

## Applications

Quantum mechanics has had enormous success in explaining many of the features of our world. The individual behaviour of the subatomic particles that make up all forms of matter—electrons, protons, neutrons, photons and others—can often only be satisfactorily described using quantum mechanics. Quantum mechanics has strongly influenced string theory, a candidate for a theory of everything (see reductionism) and the multiverse hypothesis. It is also related to statistical mechanics.

Quantum mechanics is important for understanding how individual atoms combine covalently to form chemicals or molecules. The application of quantum mechanics to chemistry is known as quantum chemistry. (Relativistic) quantum mechanics can in principle mathematically describe most of chemistry. Quantum mechanics can provide quantitative insight into ionic and covalent bonding processes by explicitly showing which molecules are energetically favorable to which others, and by approximately how much. Most of the calculations performed in computational chemistry rely on quantum mechanics.

Much of modern technology operates at a scale where quantum effects are significant. Examples include the laser, the transistor, the electron microscope, and magnetic resonance imaging. The study of semiconductors led to the invention of the diode and the transistor, which are indispensable for modern electronics.

Researchers are currently seeking robust methods of directly manipulating quantum states. Efforts are being made to develop quantum cryptography, which will allow guaranteed secure transmission of information. A more distant goal is the development of → quantum computers, which are expected to perform certain computational tasks exponentially faster than classical computers. Another active research topic is quantum teleportation, which deals with techniques to transmit quantum states over arbitrary distances.

In many devices, even the simple light switch, quantum tunneling is vital, as otherwise the electrons in the electric current could not penetrate the potential barrier made up, in the case of the light switch, of a layer of oxide. Flash memory chips found in USB drives also use quantum tunneling to erase their memory cells.

## Philosophical consequences

Since its inception, the many counter-intuitive results of quantum mechanics have provoked strong philosophical debate and many interpretations. Even fundamental issues such as Max Born's basic rules concerning probability amplitudes and probability distributions took decades to be appreciated.

The Copenhagen interpretation, due largely to the Danish theoretical physicist Niels Bohr, is the interpretation of quantum mechanics most widely accepted amongst physicists. According to it, the probabilistic nature of quantum mechanics predictions cannot be explained in terms of some other deterministic theory, and does not simply reflect our limited knowledge. Quantum mechanics provides probabilistic results because the physical universe is itself probabilistic rather than deterministic.

Albert Einstein, himself one of the founders of quantum theory, disliked this loss of determinism in measurement (this dislike is the source of his famous quote, "God does not play dice with the universe."). Einstein held that there should be a local hidden variable theory underlying quantum mechanics and that, consequently, the present theory was incomplete. He produced a series of objections to the theory, the most famous of which has

become known as the EPR paradox. John Bell showed that the EPR paradox led to experimentally testable differences between quantum mechanics and local realistic theories. Experiments have been performed confirming the accuracy of quantum mechanics, thus demonstrating that the physical world cannot be described by local realistic theories.

The *Bohr-Einstein debates* provide a vibrant critique of the Copenhagen Interpretation from an epistemological point of view.

The Everett many-worlds interpretation, formulated in 1956, holds that all the possibilities described by quantum theory simultaneously occur in a "multiverse" composed of mostly independent parallel universes. This is not accomplished by introducing some new axiom to quantum mechanics, but on the contrary by *removing* the axiom of the collapse of the wave packet: All the possible consistent states of the measured system and the measuring apparatus (including the observer) are present in a *real* physical (not just formally mathematical, as in other interpretations) quantum superposition. (Such a superposition of consistent state combinations of different systems is called an entangled state.) While the multiverse is deterministic, we perceive non-deterministic behavior governed by probabilities, because we can observe only the universe, i.e. the consistent state contribution to the mentioned superposition, we inhabit. Everett's interpretation is perfectly consistent with John Bell's experiments and makes them intuitively understandable. However, according to the theory of quantum decoherence, the parallel universes will never be accessible to us. This inaccessibility can be understood as follows: once a measurement is done, the measured system becomes entangled with both the physicist who measured it and a huge number of other particles, some of which are photons flying away towards the other end of the universe; in order to prove that the wave function did not collapse one would have to bring all these particles back and measure them again, together with the system that was measured originally. This is completely impractical, but even if one could theoretically do this, it would destroy any evidence that the original measurement took place (including the physicist's memory).

## See also

- Combinatorics and physics
  - Copenhagen interpretation
  - Correspondence rules
  - Fine-structure constant
  - Interpretation of quantum mechanics
  - Introduction to quantum mechanics
  - Many-worlds interpretation
  - Measurement in quantum mechanics
  - Measurement problem
  - Photon dynamics in the double-slit experiment
  - Photon polarization
  - Quantum chemistry
  - Quantum chromodynamics
  - → Quantum computers
  - Quantum decoherence
  - Quantum electrochemistry
-

- Quantum electronics
- → Quantum field theory
- Quantum information
- Quantum mind
- Quantum optics
- Quantum pseudo-telepathy
- Quantum thermodynamics
- Quantum triviality
- Quantum Zeno effect
- Quasi-set theory
- Relation between Schrödinger's equation and the path integral formulation of quantum mechanics
- Schrödinger's cat
- Theoretical and experimental justification for the Schrödinger equation
- Theoretical chemistry

## Notes

- [1] [http://discovermagazine.com/2009/feb/13-is-quantum-mechanics-controlling-your-thoughts/article\\_view?b\\_start:int=1&-C](http://discovermagazine.com/2009/feb/13-is-quantum-mechanics-controlling-your-thoughts/article_view?b_start:int=1&-C)
- [2] <http://www.merriam-webster.com/dictionary/quantum>
- [3] <http://mooni.fccj.org/~ethall/quantum/quant.htm>
- [4] Compare the list of conferences presented here <http://ysfine.com>.
- [5] [http://www.geocities.com/mik\\_malm/quantmech.html](http://www.geocities.com/mik_malm/quantmech.html)
- [6] <http://www.statemaster.com/encyclopedia/Quantum-mechanics>
- [7] [http://books.google.com/books?id=gCfvWx6vuzUC&pg=PA52&lpg=PA52&dq=quantum+mechanics+electron's+complex+vector+space&source=bl&ots=TIZnJa-\\_rV&sig=RIXob6U1WvgifRp\\_g8la1-ibm84&hl=en&ei=1mYfSvaOFpLKtgf5vujsAw&sa=X&oi=book\\_result&ct=result&resnum=3](http://books.google.com/books?id=gCfvWx6vuzUC&pg=PA52&lpg=PA52&dq=quantum+mechanics+electron's+complex+vector+space&source=bl&ots=TIZnJa-_rV&sig=RIXob6U1WvgifRp_g8la1-ibm84&hl=en&ei=1mYfSvaOFpLKtgf5vujsAw&sa=X&oi=book_result&ct=result&resnum=3)
- [8] <http://www.aip.org/history/heisenberg/p08a.htm>
- [9] <http://www.crystalinks.com/quantumechanics.html>
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- [13] A. Einstein, *Über einen die Erzeugung und Verwandlung des Lichtes betreffenden heuristischen Gesichtspunkt (On a heuristic point of view concerning the production and transformation of light)*, *Annalen der Physik* **17** (1905) 132-148 (reprinted in *The collected papers of Albert Einstein*, John Stachel, editor, Princeton University Press, 1989, Vol. 2, pp. 149-166, in German; see also *Einstein's early work on the quantum hypothesis*, *ibid.* pp. 134-148).
- [14] <http://www.scribd.com/doc/5998949/Quantum-mechanics-course-iwhatisquantummechanics>
- [15] Especially since Werner Heisenberg was awarded the Nobel Prize in Physics in 1932 for the creation of quantum mechanics, the role of Max Born has been obfuscated. A 2005 biography of Born details his role as the creator of the matrix formulation of quantum mechanics. This was recognized in a paper by Heisenberg, in 1940, honoring Max Planck. See: Nancy Thorndike Greenspan, "The End of the Certain World: The Life and Science of Max Born" (Basic Books, 2005), pp. 124 - 128, and 285 - 286.
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- [18] Derivation of particle in a box, [chemistry.tidalswan.com](http://chemistry.tidalswan.com) ([http://chemistry.tidalswan.com/index.php?title=Quantum\\_Mechanics](http://chemistry.tidalswan.com/index.php?title=Quantum_Mechanics))
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## External links

### General

- The Modern Revolution in Physics ([http://www.lightandmatter.com/html\\_books/6mr/ch01/ch01.html](http://www.lightandmatter.com/html_books/6mr/ch01/ch01.html)) - an online textbook
- J. O'Connor and E. F. Robertson: A history of quantum mechanics ([http://www-history.mcs.st-andrews.ac.uk/history/HistTopics/The\\_Quantum\\_age\\_begins.html](http://www-history.mcs.st-andrews.ac.uk/history/HistTopics/The_Quantum_age_begins.html))
- Introduction to Quantum Theory at Quantiki ([http://www.quantiki.org/wiki/index.php/Introduction\\_to\\_Quantum\\_Theory](http://www.quantiki.org/wiki/index.php/Introduction_to_Quantum_Theory))
- Quantum Physics Made Relatively Simple (<http://bethe.cornell.edu/>): three video lectures by Hans Bethe
- H is for h-bar (<http://www.nonlocal.com/hbar/>)
- Quantum Mechanics Books Collection (<http://www.freebookcentre.net/Physics/Quantum-Mechanics-Books.html>): Collection of free books

### Course material

- MIT OpenCourseWare: Chemistry (<http://ocw.mit.edu/OcwWeb/Chemistry/index.htm>). See 5.61 (<http://ocw.mit.edu/OcwWeb/Chemistry/5-61Fall-2004/CourseHome/index.htm>), 5.73 (<http://ocw.mit.edu/OcwWeb/Chemistry/5-73Fall-2005/CourseHome/index.htm>), and 5.74 (<http://ocw.mit.edu/OcwWeb/Chemistry/5-74Spring-2005/CourseHome/index.htm>)
- MIT OpenCourseWare: Physics (<http://ocw.mit.edu/OcwWeb/Physics/index.htm>). See 8.04 (<http://ocw.mit.edu/OcwWeb/Physics/8-04Spring-2006/CourseHome/index.htm>), 8.05 (<http://ocw.mit.edu/OcwWeb/Physics/8-05Fall-2004/CourseHome/index.htm>), and 8.06 (<http://ocw.mit.edu/OcwWeb/Physics/8-06Spring-2005/CourseHome/index.htm>)
- 5½ Examples in Quantum Mechanics (<http://www.physics.csbsju.edu/QM/>)
- Imperial College Quantum Mechanics Course to Download (<http://www.imperial.ac.uk/quantuminformation/qi/tutorials>)
- Spark Notes - Quantum Physics (<http://www.sparknotes.com/testprep/books/sat2/physics/chapter19section3.rhtml>)
- Doron Cohen: Lecture notes in Quantum Mechanics (comprehensive, with advanced topics) (<http://arxiv.org/abs/quant-ph/0605180>)
- Quantum Physics Online : interactive introduction to quantum mechanics (RS applets) (<http://www.quantum-physics.polytechnique.fr>)
- Experiments to the foundations of quantum physics with single photons (<http://www.quantumlab.de>)

### FAQs

- Many-worlds or relative-state interpretation (<http://www.hedweb.com/manworld.htm>)
- Measurement in Quantum mechanics (<http://www.mtnmath.com/faq/meas-qm.html>)

### Media

- Everything you wanted to know about the quantum world (<http://www.newscientist.com/channel/fundamentals/quantum-world>) — archive of articles from *New Scientist* magazine.
- Quantum Physics Research ([http://www.sciencedaily.com/news/matter\\_energy/quantum\\_physics/](http://www.sciencedaily.com/news/matter_energy/quantum_physics/)) from Science Daily

- "Quantum Trickery: Testing Einstein's Strangest Theory" (<http://www.nytimes.com/2005/12/27/science/27eins.html?ex=1293339600&en=caf5d835203c3500&ei=5090>). The New York Times. December 27, 2005. <http://www.nytimes.com/2005/12/27/science/27eins.html?ex=1293339600&en=caf5d835203c3500&ei=5090>.

### Philosophy

- Quantum Mechanics (<http://plato.stanford.edu/entries/qm>) entry in the *Stanford Encyclopedia of Philosophy* by Jenann Ismael
- David Mermin on the future directions of physics (<http://www.physicstoday.org/pt/vol-54/iss-2/p11.html>)

## Quantum field theory

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**Quantum field theory** or **QFT**<sup>[1]</sup> provides a theoretical framework for constructing → quantum mechanical models of systems classically described by fields or of many-body systems. It is widely used in particle physics and condensed matter physics. Most theories in modern particle physics, including the Standard Model of elementary particles and their interactions, are formulated as relativistic quantum field theories. In condensed matter physics, quantum field theories are used in many circumstances, especially those where the number of particles is allowed to fluctuate—for example, in the BCS theory of superconductivity.

In quantum field theory (QFT) the forces between particles are mediated by other particles. The electromagnetic force between two electrons is caused by an exchange of photons. Intermediate vector bosons mediate the weak force and gluons mediate the strong force. There is currently no complete quantum theory of the remaining fundamental force, gravity, but many of the proposed theories postulate the existence of a graviton particle which mediates it. These force-carrying particles are virtual particles and, by definition, cannot be detected while carrying the force, because such detection will imply that the force is not being carried.

In QFT photons are not thought of as 'little billiard balls', they are considered to be field quanta - necessarily chunked ripples in a field that 'look like' particles. Fermions, like the electron, can also be described as ripples in a field, where each kind of fermion has its own field. In summary, the classical visualisation of "everything is particles and fields", in quantum field theory, resolves into "everything is particles", which then resolves into "everything is fields". In the end, particles are regarded as excited states of a field (field quanta).

### History

Quantum field theory originated in the 1920s from the problem of creating a → quantum mechanical theory of the electromagnetic field. In 1926, Max Born, Pascual Jordan, and Werner Heisenberg constructed such a theory by expressing the field's internal degrees of freedom as an infinite set of harmonic oscillators and by employing the usual procedure for quantizing those oscillators (canonical quantization). This theory assumed that no electric charges or currents were present and today would be called a free field theory. The first reasonably complete theory of quantum electrodynamics, which included both the electromagnetic field and electrically charged matter (specifically, electrons) as quantum

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mechanical objects, was created by Paul Dirac in 1927. This quantum field theory could be used to model important processes such as the emission of a photon by an electron dropping into a quantum state of lower energy, a process in which the *number of particles changes* — one atom in the initial state becomes an atom plus a photon in the final state. It is now understood that the ability to describe such processes is one of the most important features of quantum field theory.

It was evident from the beginning that a proper quantum treatment of the electromagnetic field had to somehow incorporate Einstein's relativity theory, which had after all grown out of the study of classical electromagnetism. This need to *put together relativity and quantum mechanics* was the second major motivation in the development of quantum field theory. Pascual Jordan and Wolfgang Pauli showed in 1928 that quantum fields could be made to behave in the way predicted by special relativity during coordinate transformations (specifically, they showed that the field commutators were Lorentz invariant), and in 1933 Niels Bohr and Leon Rosenfeld showed that this result could be interpreted as a limitation on the ability to measure fields at space-like separations, exactly as required by relativity. A further boost for quantum field theory came with the discovery of the Dirac equation, a single-particle equation obeying both relativity and quantum mechanics, when it was shown that several of its undesirable properties (such as negative-energy states) could be eliminated by reformulating the Dirac equation as a quantum field theory. This work was performed by Wendell Furry, Robert Oppenheimer, Vladimir Fock, and others.

The third thread in the development of quantum field theory was the need to *handle the statistics of many-particle systems* consistently and with ease. In 1927, Jordan tried to extend the canonical quantization of fields to the many-body wavefunctions of identical particles, a procedure that is sometimes called second quantization. In 1928, Jordan and Eugene Wigner found that the quantum field describing electrons, or other fermions, had to be expanded using anti-commuting creation and annihilation operators due to the Pauli exclusion principle. This thread of development was incorporated into many-body theory, and strongly influenced condensed matter physics and nuclear physics.

Despite its early successes, quantum field theory was plagued by several serious theoretical difficulties. Many seemingly-innocuous physical quantities, such as the energy shift of electron states due to the presence of the electromagnetic field, gave infinity — a nonsensical result — when computed using quantum field theory. This "divergence problem" was solved during the 1940s by Bethe, Tomonaga, Schwinger, Feynman, and Dyson, through the procedure known as renormalization. This phase of development culminated with the construction of the modern theory of quantum electrodynamics (QED). Beginning in the 1950s with the work of Yang and Mills, QED was generalized to a class of quantum field theories known as gauge theories. The 1960s and 1970s saw the formulation of a gauge theory now known as the Standard Model of particle physics, which describes all known elementary particles and the interactions between them. The weak interaction part of the standard model was formulated by Sheldon Glashow, with the Higgs mechanism added by Steven Weinberg and Abdus Salam. The theory was shown to be renormalizable and hence consistent by Gerardus 't Hooft and Martinus Veltman.

Also during the 1970s, parallel developments in the study of phase transitions in condensed matter physics led Leo Kadanoff, Michael Fisher and Kenneth Wilson (extending work of Ernst Stueckelberg, Andre Peterman, Murray Gell-Mann and Francis Low) to a set of ideas and methods known as the renormalization group. By providing a better physical

understanding of the renormalization procedure invented in the 1940s, the renormalization group sparked what has been called the "grand synthesis" of theoretical physics, uniting the quantum field theoretical techniques used in particle physics and condensed matter physics into a single theoretical framework.

The study of quantum field theory is alive and flourishing, as are applications of this method to many physical problems. It remains one of the most vital areas of theoretical physics today, providing a common language to many branches of physics.

## Principles of quantum field theory

### Classical fields and quantum fields

→ Quantum mechanics, in its most general formulation, is a theory of abstract operators (observables) acting on an abstract state space (Hilbert space), where the observables represent physically-observable quantities and the state space represents the possible states of the system under study. Furthermore, each observable corresponds, in a technical sense, to the classical idea of a degree of freedom. For instance, the fundamental observables associated with the motion of a single quantum mechanical particle are the position and momentum operators  $\hat{x}$  and  $\hat{p}$ . Ordinary quantum mechanics deals with systems such as this, which possess a small set of degrees of freedom.

(It is important to note, at this point, that this article does not use the word "particle" in the context of wave-particle duality. In quantum field theory, "particle" is a generic term for any discrete quantum mechanical entity, such as an electron, which can behave like classical particles or classical waves under different experimental conditions.)

A **quantum field** is a quantum mechanical system containing a large, and possibly infinite, number of degrees of freedom. This is not as exotic a situation as one might think. A classical field contains a set of degrees of freedom at each point of space; for instance, the classical electromagnetic field defines two vectors — the electric field and the magnetic field — that can in principle take on distinct values for each position  $r$ . When the field *as a whole* is considered as a quantum mechanical system, its observables form an infinite (in fact uncountable) set, because  $r$  is continuous.

Furthermore, the degrees of freedom in a quantum field are arranged in "repeated" sets. For example, the degrees of freedom in an electromagnetic field can be grouped according to the position  $r$ , with exactly two vectors for each  $r$ . Note that  $r$  is an ordinary number that "indexes" the observables; it is not to be confused with the position operator  $\hat{x}$  encountered in ordinary quantum mechanics, which is an observable. (Thus, ordinary quantum mechanics is sometimes referred to as "zero-dimensional quantum field theory", because it contains only a single set of observables.) It is also important to note that there is nothing special about  $r$  because, as it turns out, there is generally more than one way of indexing the degrees of freedom in the field.

In the following sections, we will show how these ideas can be used to construct a quantum mechanical theory with the desired properties. We will begin by discussing single-particle quantum mechanics and the associated theory of many-particle quantum mechanics. Then, by finding a way to index the degrees of freedom in the many-particle problem, we will construct a quantum field and study its implications.

## Single-particle and many-particle quantum mechanics

In ordinary quantum mechanics, the time-dependent one-dimensional Schrödinger equation describing the time evolution of the quantum state of a single non-relativistic particle is

$$\left[ \frac{-\hbar^2}{2m} \frac{\partial^2}{\partial x^2} + V(\mathbf{x}) \right] |\psi(t)\rangle = i\hbar \frac{\partial}{\partial t} |\psi(t)\rangle,$$

where  $m$  is the particle's mass,  $V$  is the applied potential, and  $|\psi\rangle$  denotes the quantum state (we are using bra-ket notation).

We wish to consider how this problem generalizes to  $N$  particles. There are two motivations for studying the many-particle problem. The first is a straightforward need in condensed matter physics, where typically the number of particles is on the order of Avogadro's number ( $6.0221415 \times 10^{23}$ ). The second motivation for the many-particle problem arises from particle physics and the desire to incorporate the effects of special relativity. If one attempts to include the relativistic rest energy into the above equation, the result is either the Klein-Gordon equation or the Dirac equation. However, these equations have many unsatisfactory qualities; for instance, they possess energy eigenvalues which extend to  $-\infty$ , so that there seems to be no easy definition of a ground state. It turns out that such inconsistencies arise from neglecting the possibility of dynamically creating or destroying particles, which is a crucial aspect of relativity. Einstein's famous mass-energy relation predicts that sufficiently massive particles can decay into several lighter particles, and sufficiently energetic particles can combine to form massive particles. For example, an electron and a positron can annihilate each other to create photons. Thus, a consistent relativistic quantum theory must be formulated as a many-particle theory.

Furthermore, we will assume that the  $N$  particles are indistinguishable. As described in the article on identical particles, this implies that the state of the entire system must be either symmetric (bosons) or antisymmetric (fermions) when the coordinates of its constituent particles are exchanged. These multi-particle states are rather complicated to write. For example, the general quantum state of a system of  $N$  bosons is written as

$$|\phi_1 \cdots \phi_N\rangle = \sqrt{\frac{\prod_j N_j!}{N!}} \sum_{p \in S_N} |\phi_{p(1)}\rangle \cdots |\phi_{p(N)}\rangle,$$

where  $|\phi_i\rangle$  are the single-particle states,  $N_j$  is the number of particles occupying state  $j$ , and the sum is taken over all possible permutations  $p$  acting on  $N$  elements. In general, this is a sum of  $N!$  ( $N$  factorial) distinct terms, which quickly becomes unmanageable as  $N$  increases. The way to simplify this problem is to turn it into a quantum field theory.

## Second quantization

In this section, we will describe a method for constructing a quantum field theory called **second quantization**. This basically involves choosing a way to index the quantum mechanical degrees of freedom in the space of multiple identical-particle states. It is based on the Hamiltonian formulation of quantum mechanics; several other approaches exist, such as the Feynman path integral<sup>[2]</sup>, which uses a Lagrangian formulation. For an overview, see the article on quantization.

## Second quantization of bosons

For simplicity, we will first discuss second quantization for bosons, which form perfectly symmetric quantum states. Let us denote the mutually orthogonal single-particle states by  $|\phi_1\rangle, |\phi_2\rangle, |\phi_3\rangle$ , and so on. For example, the 3-particle state with one particle in state  $|\phi_1\rangle$  and two in state  $|\phi_2\rangle$  is

$$\frac{1}{\sqrt{3}} [|\phi_1\rangle|\phi_2\rangle|\phi_2\rangle + |\phi_2\rangle|\phi_1\rangle|\phi_2\rangle + |\phi_2\rangle|\phi_2\rangle|\phi_1\rangle].$$

The first step in second quantization is to express such quantum states in terms of **occupation numbers**, by listing the number of particles occupying each of the single-particle states  $|\phi_1\rangle, |\phi_2\rangle$ , etc. This is simply another way of labelling the states. For instance, the above 3-particle state is denoted as

$$|1, 2, 0, 0, 0, \dots\rangle.$$

The next step is to expand the  $N$ -particle state space to include the state spaces for all possible values of  $N$ . This extended state space, known as a Fock space, is composed of the state space of a system with no particles (the so-called vacuum state), plus the state space of a 1-particle system, plus the state space of a 2-particle system, and so forth. It is easy to see that there is a one-to-one correspondence between the occupation number representation and valid boson states in the Fock space.

At this point, the quantum mechanical system has become a quantum field in the sense we described above. The field's elementary degrees of freedom are the occupation numbers, and each occupation number is indexed by a number  $j \dots$ , indicating which of the single-particle states  $|\phi_1\rangle, |\phi_2\rangle, \dots, |\phi_j\rangle \dots$  it refers to.

The properties of this quantum field can be explored by defining creation and annihilation operators, which add and subtract particles. They are analogous to "ladder operators" in the quantum harmonic oscillator problem, which added and subtracted energy quanta. However, these operators literally create and annihilate particles of a given quantum state. The bosonic annihilation operator  $a_2$  and creation operator  $a_2^\dagger$  have the following effects:

$$a_2|N_1, N_2, N_3, \dots\rangle = \sqrt{N_2} |N_1, (N_2 - 1), N_3, \dots\rangle,$$

$$a_2^\dagger|N_1, N_2, N_3, \dots\rangle = \sqrt{N_2 + 1} |N_1, (N_2 + 1), N_3, \dots\rangle.$$

It can be shown that these are operators in the usual quantum mechanical sense, i.e. linear operators acting on the Fock space. Furthermore, they are indeed Hermitian conjugates, which justifies the way we have written them. They can be shown to obey the commutation relation

$$[a_i, a_j] = 0 \quad , \quad [a_i^\dagger, a_j^\dagger] = 0 \quad , \quad [a_i, a_j^\dagger] = \delta_{ij},$$

where  $\delta$  stands for the Kronecker delta. These are precisely the relations obeyed by the ladder operators for an infinite set of independent quantum harmonic oscillators, one for each single-particle state. Adding or removing bosons from each state is therefore analogous to exciting or de-exciting a quantum of energy in a harmonic oscillator.

The Hamiltonian of the quantum field (which, through the Schrödinger equation, determines its dynamics) can be written in terms of creation and annihilation operators. For instance, the Hamiltonian of a field of free (non-interacting) bosons is

$$H = \sum_k E_k a_k^\dagger a_k,$$

where  $E_k$  is the energy of the  $k$ -th single-particle energy eigenstate. Note that

$$a_k^\dagger a_k |\dots, N_k, \dots\rangle = N_k |\dots, N_k, \dots\rangle.$$

### Second quantization of fermions

It turns out that a different definition of creation and annihilation must be used for describing fermions. According to the Pauli exclusion principle, fermions cannot share quantum states, so their occupation numbers  $N_i$  can only take on the value 0 or 1. The fermionic annihilation operators  $c$  and creation operators  $c^\dagger$  are defined by

$$\begin{aligned} c_j |N_1, N_2, \dots, N_j = 0, \dots\rangle &= 0 \\ c_j |N_1, N_2, \dots, N_j = 1, \dots\rangle &= (-1)^{(N_1 + \dots + N_{j-1})} |N_1, N_2, \dots, N_j = 0, \dots\rangle \\ c_j^\dagger |N_1, N_2, \dots, N_j = 0, \dots\rangle &= (-1)^{(N_1 + \dots + N_{j-1})} |N_1, N_2, \dots, N_j = 1, \dots\rangle \\ c_j^\dagger |N_1, N_2, \dots, N_j = 1, \dots\rangle &= 0 \end{aligned}$$

These obey an anticommutation relation:

$$\{c_i, c_j\} = 0 \quad , \quad \{c_i^\dagger, c_j^\dagger\} = 0 \quad , \quad \{c_i, c_j^\dagger\} = \delta_{ij}$$

One may notice from this that applying a fermionic creation operator twice gives zero, so it is impossible for the particles to share single-particle states, in accordance with the exclusion principle.

### Field operators

We have previously mentioned that there can be more than one way of indexing the degrees of freedom in a quantum field. Second quantization indexes the field by enumerating the single-particle quantum states. However, as we have discussed, it is more natural to think about a "field", such as the electromagnetic field, as a set of degrees of freedom indexed by position.

To this end, we can define *field operators* that create or destroy a particle at a particular point in space. In particle physics, these operators turn out to be more convenient to work with, because they make it easier to formulate theories that satisfy the demands of relativity.

Single-particle states are usually enumerated in terms of their momenta (as in the particle in a box problem.) We can construct field operators by applying the Fourier transform to the creation and annihilation operators for these states. For example, the bosonic field annihilation operator  $\phi(\mathbf{r})$  is

$$\phi(\mathbf{r}) \stackrel{\text{def}}{=} \sum_j e^{i\mathbf{k}_j \cdot \mathbf{r}} a_j$$

The bosonic field operators obey the commutation relation

$$[\phi(\mathbf{r}), \phi(\mathbf{r}')] = 0 \quad , \quad [\phi^\dagger(\mathbf{r}), \phi^\dagger(\mathbf{r}')] = 0 \quad , \quad [\phi(\mathbf{r}), \phi^\dagger(\mathbf{r}')] = \delta^3(\mathbf{r} - \mathbf{r}')$$

where  $\delta(x)$  stands for the Dirac delta function. As before, the fermionic relations are the same, with the commutators replaced by anticommutators.

It should be emphasized that the field operator is *not* the same thing as a single-particle wavefunction. The former is an operator acting on the Fock space, and the latter is just a scalar field. However, they are closely related, and are indeed commonly denoted with the same symbol. If we have a Hamiltonian with a space representation, say

$$H = -\frac{\hbar^2}{2m} \sum_i \nabla_i^2 + \sum_{i < j} U(|\mathbf{r}_i - \mathbf{r}_j|)$$

where the indices  $i$  and  $j$  run over all particles, then the field theory Hamiltonian is

$$H = -\frac{\hbar^2}{2m} \int d^3r \phi^\dagger(\mathbf{r}) \nabla^2 \phi(\mathbf{r}) + \int d^3r \int d^3r' \phi^\dagger(\mathbf{r}) \phi^\dagger(\mathbf{r}') U(|\mathbf{r} - \mathbf{r}'|) \phi(\mathbf{r}') \phi(\mathbf{r})$$

This looks remarkably like an expression for the expectation value of the energy, with  $\phi$  playing the role of the wavefunction. This relationship between the field operators and wavefunctions makes it very easy to formulate field theories starting from space-projected Hamiltonians.

## Implications of quantum field theory

### Unification of fields and particles

The "second quantization" procedure that we have outlined in the previous section takes a set of single-particle quantum states as a starting point. Sometimes, it is impossible to define such single-particle states, and one must proceed directly to quantum field theory. For example, a quantum theory of the electromagnetic field *must* be a quantum field theory, because it is impossible (for various reasons) to define a wavefunction for a single photon. In such situations, the quantum field theory can be constructed by examining the mechanical properties of the classical field and guessing the corresponding quantum theory. The quantum field theories obtained in this way have the same properties as those obtained using second quantization, such as well-defined creation and annihilation operators obeying commutation or anticommutation relations.

Quantum field theory thus provides a unified framework for describing "field-like" objects (such as the electromagnetic field, whose excitations are photons) and "particle-like" objects (such as electrons, which are treated as excitations of an underlying electron field).

### Physical meaning of particle indistinguishability

The second quantization procedure relies crucially on the particles being identical. We would not have been able to construct a quantum field theory from a distinguishable many-particle system, because there would have been no way of separating and indexing the degrees of freedom.

Many physicists prefer to take the converse interpretation, which is that *quantum field theory explains what identical particles are*. In ordinary quantum mechanics, there is not much theoretical motivation for using symmetric (bosonic) or antisymmetric (fermionic) states, and the need for such states is simply regarded as an empirical fact. From the point of view of quantum field theory, particles are identical if and only if they are excitations of the same underlying quantum field. Thus, the question "why are all electrons identical?" arises from mistakenly regarding individual electrons as fundamental objects, when in fact it is only the electron field that is fundamental.

### Particle conservation and non-conservation

During second quantization, we started with a Hamiltonian and state space describing a fixed number of particles ( $N$ ), and ended with a Hamiltonian and state space for an arbitrary number of particles. Of course, in many common situations  $N$  is an important and perfectly well-defined quantity, e.g. if we are describing a gas of atoms sealed in a box. From the point of view of quantum field theory, such situations are described by quantum states that are eigenstates of the number operator  $\hat{N}$ , which measures the total number of particles present. As with any quantum mechanical observable,  $\hat{N}$  is conserved if it

commutes with the Hamiltonian. In that case, the quantum state is trapped in the  $N$ -particle subspace of the total Fock space, and the situation could equally well be described by ordinary  $N$ -particle quantum mechanics.

For example, we can see that the free-boson Hamiltonian described above conserves particle number. Whenever the Hamiltonian operates on a state, each particle destroyed by an annihilation operator  $a_k$  is immediately put back by the creation operator  $a_k^\dagger$ .

On the other hand, it is possible, and indeed common, to encounter quantum states that are *not* eigenstates of  $\hat{N}$ , which do not have well-defined particle numbers. Such states are difficult or impossible to handle using ordinary quantum mechanics, but they can be easily described in quantum field theory as quantum superpositions of states having different values of  $N$ . For example, suppose we have a bosonic field whose particles can be created or destroyed by interactions with a fermionic field. The Hamiltonian of the combined system would be given by the Hamiltonians of the free boson and free fermion fields, plus a "potential energy" term such as

$$H_I = \sum_{k,q} V_q (a_q + a_{-q}^\dagger) c_{k+q}^\dagger c_k,$$

where  $a_k^\dagger$  and  $a_k$  denotes the bosonic creation and annihilation operators,  $c_k^\dagger$  and  $c_k$  denotes the fermionic creation and annihilation operators, and  $V_q$  is a parameter that describes the strength of the interaction. This "interaction term" describes processes in which a fermion in state  $k$  either absorbs or emits a boson, thereby being kicked into a different eigenstate  $k+q$ . (In fact, this type of Hamiltonian is used to describe interaction between conduction electrons and phonons in metals. The interaction between electrons and photons is treated in a similar way, but is a little more complicated because the role of spin must be taken into account.) One thing to notice here is that even if we start out with a fixed number of bosons, we will typically end up with a superposition of states with different numbers of bosons at later times. The number of fermions, however, is conserved in this case.

In condensed matter physics, states with ill-defined particle numbers are particularly important for describing the various superfluids. Many of the defining characteristics of a superfluid arise from the notion that its quantum state is a superposition of states with different particle numbers.

## Axiomatic approaches

The preceding description of quantum field theory follows the spirit in which most physicists approach the subject. However, it is not mathematically rigorous. Over the past several decades, there have been many attempts to put quantum field theory on a firm mathematical footing by formulating a set of axioms for it. These attempts fall into two broad classes.

The first class of axioms, first proposed during the 1950s, include the Wightman, Osterwalder-Schrader, and Haag-Kastler systems. They attempted to formalize the physicists' notion of an "operator-valued field" within the context of functional analysis, and enjoyed limited success. It was possible to prove that any quantum field theory satisfying these axioms satisfied certain general theorems, such as the spin-statistics theorem and the CPT theorem. Unfortunately, it proved extraordinarily difficult to show that any realistic field theory, including the Standard Model, satisfied these axioms. Most of the theories that could be treated with these analytic axioms were physically trivial, being restricted to

low-dimensions and lacking interesting dynamics. The construction of theories satisfying one of these sets of axioms falls in the field of constructive quantum field theory. Important work was done in this area in the 1970s by Segal, Glimm, Jaffe and others.

During the 1980s, a second set of axioms based on geometric ideas was proposed. This line of investigation, which restricts its attention to a particular class of quantum field theories known as topological quantum field theories, is associated most closely with Michael Atiyah and Graeme Segal, and was notably expanded upon by Edward Witten, Richard Borcherds, and Maxim Kontsevich. However, most physically-relevant quantum field theories, such as the Standard Model, are not topological quantum field theories; the quantum field theory of the fractional quantum Hall effect is a notable exception. The main impact of axiomatic topological quantum field theory has been on mathematics, with important applications in representation theory, algebraic topology, and differential geometry.

Finding the proper axioms for quantum field theory is still an open and difficult problem in mathematics. One of the Millennium Prize Problems—proving the existence of a mass gap in Yang-Mills theory—is linked to this issue.

## Phenomena associated with quantum field theory

In the previous part of the article, we described the most general properties of quantum field theories. Some of the quantum field theories studied in various fields of theoretical physics possess additional special properties, such as renormalizability, gauge symmetry, and supersymmetry. These are described in the following sections.

### Renormalization

Early in the history of quantum field theory, it was found that many seemingly innocuous calculations, such as the perturbative shift in the energy of an electron due to the presence of the electromagnetic field, give infinite results. The reason is that the perturbation theory for the shift in an energy involves a sum over all other energy levels, and there are infinitely many levels at short distances which each give a finite contribution.

Many of these problems are related to failures in classical electrodynamics that were identified but unsolved in the 19th century, and they basically stem from the fact that many of the supposedly "intrinsic" properties of an electron are tied to the electromagnetic field which it carries around with it. The energy carried by a single electron—its self energy—is not simply the bare value, but also includes the energy contained in its electromagnetic field, its attendant cloud of photons. The energy in a field of a spherical source diverges in both classical and quantum mechanics, but as discovered by Weisskopf, in quantum mechanics the divergence is much milder, going only as the logarithm of the radius of the sphere.

The solution to the problem, presciently suggested by Stueckelberg, independently by Bethe after the crucial experiment by Lamb, implemented at one loop by Schwinger, and systematically extended to all loops by Feynman and Dyson, with converging work by Tomonaga in isolated postwar Japan, is called renormalization. The technique of renormalization recognizes that the problem is essentially purely mathematical, that extremely short distances are at fault. In order to define a theory on a continuum, first place a cutoff on the fields, by postulating that quanta cannot have energies above some extremely high value. This has the effect of replacing continuous space by a structure where very short wavelengths do not exist, as on a lattice. Lattices break rotational

symmetry, and one of the crucial contributions made by Feynman, Pauli and Villars, and modernized by 't Hooft and Veltman, is a symmetry preserving cutoff for perturbation theory. There is no known symmetrical cutoff outside of perturbation theory, so for rigorous or numerical work people often use an actual lattice.

The rule is that one computes physical quantities in terms of the observable parameters such as the physical mass, not the bare parameters such as the bare mass. The main point is not that of getting finite quantities (any regularization procedure does that), but to eliminate the regularization parameters by a suitable addition of counterterms to the original Lagrangian. The main requirements on the counterterms are a) Locality (polynomials in the fields and their derivatives) and b) Finiteness (number of monomials in the Lagrangian that remain finite after the introduction of all the necessary counterterms). The reason for (b) is that each new counterterm leaves behind a free parameter of the theory (like physical mass). There is no way such a parameter can be fixed other than by its experimental value, so one gets not a single theory but a family of theories parameterized by as many free parameters as the counterterms added to the Lagrangian. Since a theory with an infinite number of free parameters has virtually no predictive power the finiteness of the number of counterterms is required.

On a lattice, every quantity is finite but depends on the spacing. When taking the limit of zero spacing, we make sure that the physically-observable quantities like the observed electron mass stay fixed, which means that the constants in the Lagrangian defining the theory depend on the spacing. Hopefully, by allowing the constants to vary with the lattice spacing, all the results at long distances become insensitive to the lattice, defining a continuum limit.

The renormalization procedure only works for a certain class of quantum field theories, called **renormalizable quantum field theories**. A theory is **perturbatively renormalizable** when the constants in the Lagrangian only diverge at worst as logarithms of the lattice spacing for very short spacings. The continuum limit is then well defined in perturbation theory, and even if it is not fully well defined non-perturbatively, the problems only show up at distance scales which are exponentially small in the inverse coupling for weak couplings. The Standard Model of particle physics is perturbatively renormalizable, and so are its component theories (quantum electrodynamics/electroweak theory and quantum chromodynamics). Of the three components, quantum electrodynamics is believed to not have a continuum limit, while the asymptotically free SU(2) and SU(3) weak hypercharge and strong color interactions are nonperturbatively well defined.

The renormalization group describes how renormalizable theories emerge as the long distance low-energy effective field theory for any given high-energy theory. Because of this, renormalizable theories are insensitive to the precise nature of the underlying high-energy short-distance phenomena. This is a blessing because it allows physicists to formulate low energy theories without knowing the details of high energy phenomenon. It is also a curse, because once a renormalizable theory like the standard model is found to work, it gives very few clues to higher energy processes. The only way high energy processes can be seen in the standard model is when they allow otherwise forbidden events, or if they predict quantitative relations between the coupling constants.

## Gauge freedom

A gauge theory is a theory that admits a symmetry with a local parameter. For example, in every  $\rightarrow$  quantum theory the global phase of the wave function is arbitrary and does not represent something physical. Consequently, the theory is invariant under a global change of phases (adding a constant to the phase of all wave functions, everywhere); this is a global symmetry. In quantum electrodynamics, the theory is also invariant under a *local* change of phase, that is - one may shift the phase of all wave functions so that the shift may be different at every point in space-time. This is a *local* symmetry. However, in order for a well-defined derivative operator to exist, one must introduce a new field, the gauge field, which also transforms in order for the local change of variables (the phase in our example) not to affect the derivative. In quantum electrodynamics this gauge field is the electromagnetic field. The change of local gauge of variables is termed gauge transformation.

In quantum field theory the excitations of fields represent particles. The particle associated with excitations of the gauge field is the gauge boson, which is the photon in the case of quantum electrodynamics.

The degrees of freedom in quantum field theory are local fluctuations of the fields. The existence of a gauge symmetry reduces the number of degrees of freedom, simply because some fluctuations of the fields can be transformed to zero by gauge transformations, so they are equivalent to having no fluctuations at all, and they therefore have no physical meaning. Such fluctuations are usually called "non-physical degrees of freedom" or *gauge artifacts*; usually some of them have a negative norm, making them inadequate for a consistent theory. Therefore, if a classical field theory has a gauge symmetry, then its quantized version (i.e. the corresponding quantum field theory) will have this symmetry as well. In other words, a gauge symmetry cannot have a quantum anomaly. If a gauge symmetry is anomalous (i.e. not kept in the quantum theory) then the theory is non-consistent: for example, in quantum electrodynamics, had there been a gauge anomaly, this would require the appearance of photons with longitudinal polarization and polarization in the time direction, the latter having a negative norm, rendering the theory inconsistent; another possibility would be for these photons to appear only in intermediate processes but not in the final products of any interaction, making the theory non unitary and again inconsistent (see optical theorem).

In general, the gauge transformations of a theory consist several different transformations, which may not be commutative. These transformations are together described by a mathematical object known as a gauge group. Infinitesimal gauge transformations are the gauge group generators. Therefore the number of gauge bosons is the group dimension (i.e. number of generators forming a basis).

All the fundamental interactions in nature are described by gauge theories. These are:

- Quantum electrodynamics, whose gauge transformation is a local change of phase, so that the gauge group is  $U(1)$ . The gauge boson is the photon.
- Quantum chromodynamics, whose gauge group is  $SU(3)$ . The gauge bosons are eight gluons.
- The electroweak Theory, whose gauge group is  $U(1) \times SU(2)$  (a direct product of  $U(1)$  and  $SU(2)$ ).
- Gravity, whose classical theory is general relativity, admits the equivalence principle which is a form of gauge symmetry.

## Supersymmetry

Supersymmetry assumes that every fundamental fermion has a superpartner that is a boson and vice versa. It was introduced in order to solve the so-called Hierarchy Problem, that is, to explain why particles not protected by any symmetry (like the Higgs boson) do not receive radiative corrections to its mass driving it to the larger scales (GUT, Planck...). It was soon realized that supersymmetry has other interesting properties: its gauged version is an extension of general relativity (Supergravity), and it is a key ingredient for the consistency of string theory.

The way supersymmetry protects the hierarchies is the following: since for every particle there is a superpartner with the same mass, any loop in a radiative correction is cancelled by the loop corresponding to its superpartner, rendering the theory UV finite.

Since no superpartners have yet been observed, if supersymmetry exists it must be broken (through a so-called soft term, which breaks supersymmetry without ruining its helpful features). The simplest models of this breaking require that the energy of the superpartners not be too high; in these cases, supersymmetry is expected to be observed by experiments at the Large Hadron Collider.

## See also

- List of quantum field theories
  - Feynman path integral
  - Quantum chromodynamics
  - Quantum electrodynamics
  - Quantum flavordynamics
  - Quantum geometrodynamics
  - Quantum hydrodynamics
  - Quantum magnetodynamics
  - Quantum triviality
  - Schwinger-Dyson equation
  - Relation between Schrödinger's equation and the path integral formulation of quantum mechanics
  - Relationship between string theory and quantum field theory
  - Abraham-Lorentz force
  - Photon polarization
  - Theoretical and experimental justification for the Schrödinger equation
  - Invariance mechanics
  - Green-Kubo relations
  - Green's function (many-body theory)
  - Common integrals in quantum field theory
-

## Notes

- [1] Weinberg, S. *Quantum Field Theory*, Vols. I to III, 2000, Cambridge University Press: Cambridge, UK.
- [2] Abraham Pais, *Inward Bound: Of Matter and Forces in the Physical World* ISBN 0198519974. Pais recounts how his astonishment at the rapidity with which Feynman could calculate using his method. Feynman's method is now part of the standard methods for physicists.

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- Srednicki, Mark ; *Quantum Field Theory* (<http://gabriel.physics.ucsb.edu/~mark/qft.html>)
- Kuhlmann, Meinard ; *Quantum Field Theory* (<http://plato.stanford.edu/entries/quantum-field-theory/>), Stanford Encyclopedia of Philosophy
- Quantum field theory textbooks: a list with links to amazon.com (<http://motls.blogspot.com/2006/01/qft-didactics.html>)
- Pedagogic Aids to Quantum Field Theory (<http://quantumfieldtheory.info>). Click on the link "Introduction" for a simplified introduction to QFT suitable for someone familiar with quantum mechanics.

# Algebraic quantum field theory

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1. REDIRECT → Local quantum field theory

## Local quantum field theory

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The **Haag-Kastler** axiomatic framework for → quantum field theory, named after Rudolf Haag and Daniel Kastler, is an application to *local* quantum physics of C\*-algebra theory. It is therefore also known as **Algebraic Quantum Field Theory (AQFT)**. The axioms are stated in terms of an algebra given for every open set in Minkowski space, and mappings between those.

Let **Mink** be the category of open subsets of Minkowski space  $M$  with inclusion maps as morphisms. We are given a covariant functor  $\mathcal{A}$  from **Mink** to **uC\*alg**, the category of unital C\* algebras, such that every morphism in **Mink** maps to a monomorphism in **uC\*alg** (*isotony*).

The Poincaré group acts continuously on **Mink**. There exists a pullback of this action, which is continuous in the norm topology of  $\mathcal{A}(M)$  (Poincaré covariance).

Minkowski space has a causal structure. If an open set  $V$  lies in the causal complement of an open set  $U$ , then the image of the maps

$$\mathcal{A}(i_{U,U \cup V})$$

and

$$\mathcal{A}(i_{V,U \cup V})$$

commute (spacelike commutativity). If  $\bar{U}$  is the causal completion of an open set  $U$ , then  $\mathcal{A}(i_{U,\bar{U}})$  is an isomorphism (primitive causality).

A state with respect to a C\*-algebra is a positive linear functional over it with unit norm. If we have a state over  $\mathcal{A}(M)$ , we can take the "partial trace" to get states associated with  $\mathcal{A}(U)$  for each open set via the net monomorphism. It's easy to show the states over the open sets form a presheaf structure.

According to the GNS construction, for each state, we can associate a Hilbert space representation of  $\mathcal{A}(M)$ . Pure states correspond to irreducible representations and mixed states correspond to reducible representations. Each irreducible (up to equivalence) is called a superselection sector. We assume there is a pure state called the vacuum such that the Hilbert space associated with it is a unitary representation of the Poincaré group compatible with the Poincaré covariance of the net such that if we look at the Poincaré algebra, the spectrum with respect to energy-momentum (corresponding to spacetime translations) lies on and in the positive light cone. This is the vacuum sector.

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## External links

- Local Quantum Physics Crossroads <sup>[1]</sup> - A network of scientists working on Local Quantum Physics
- Algebraic Quantum Field Theory <sup>[2]</sup> - AQFT resources at the University of Hamburg

## Suggested reading

- Haag, Rudolf (1992). *Local Quantum Physics: Fields, Particles, Algebras*. Springer.

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[1] <http://www.lqp.uni-goettingen.de/>

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# Algebraic logic

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In mathematical logic, **algebraic logic** formalizes logic using the methods of abstract algebra.

## Algebras as models of logics

Algebraic logic treats algebraic structures, often bounded lattices, as models (interpretations) of certain logics, making logic a branch of order theory.

In algebraic logic:

- Variables are tacitly universally quantified over some universe of discourse. There are no existentially quantified variables or open formulas;
- Terms are built up from variables using primitive and defined operations. There are no connectives;
- Formulas, built from terms in the usual way, can be equated if they are logically equivalent. To express a tautology, equate a formula with a truth value;
- The rules of proof are the substitution of equals for equals, and uniform replacement. Modus ponens remains valid, but is seldom employed.

In the table below, the left column contains one or more logical or mathematical systems, and the algebraic structure which are its models are shown on the right in the same row. Some of these structures are either Boolean algebras or proper extensions thereof. Modal and other nonclassical logics are typically modeled by what are called "Boolean algebras with operators."

Algebraic formalisms going beyond first-order logic in at least some respects include:

- Combinatory logic, having the expressive power of set theory;
- Relation algebra, arguably the paradigmatic algebraic logic, can express Peano arithmetic and most axiomatic set theories, including the canonical ZFC.

logical system	its models
Classical sentential logic	Lindenbaum-Tarski algebra Two-element Boolean algebra
Intuitionistic propositional logic	Heyting algebra
Łukasiewicz logic	MV-algebra

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Modal logic K	Modal algebra
Lewis's S4	Interior algebra
Lewis's S5; Monadic predicate logic	Monadic Boolean algebra
First-order logic	Cylindric algebra Polyadic algebra Predicate functor logic
Set theory	Combinatory logic Relation algebra

## History

On the history of algebraic logic before World War II, see Brady (2000) and Grattan-Guinness (2000) and their ample references. On the postwar history, see Maddux (1991) and Quine (1976).

*Algebraic logic* has at least two meanings:

- The study of Boolean algebra, begun by George Boole, and of relation algebra, begun by Augustus DeMorgan, extended by Charles Sanders Peirce, and taking definitive form in the work of Ernst Schröder;
- Abstract algebraic logic, a branch of contemporary mathematical logic.

Perhaps surprisingly, algebraic logic is the oldest approach to formal logic, arguably beginning with a number of memoranda Leibniz wrote in the 1680s, some of which were published in the 19th century and translated into English by Clarence Lewis in 1918. But nearly all of Leibniz's known work on algebraic logic was published only in 1903, after Louis Couturat discovered it in Leibniz's Nachlass. Parkinson (1966) and Loemker (1969) translated selections from Couturat's volume into English.

Brady (2000) discusses the rich historical connections between algebraic logic and model theory. The founders of model theory, Ernst Schroder and Leopold Loewenheim, were logicians in the algebraic tradition. Alfred Tarski, the founder of set theoretic model theory as a major branch of contemporary mathematical logic, also:

- Co-discovered Lindenbaum-Tarski algebra;
- Invented cylindric algebra;
- Wrote the 1940 paper that revived relation algebra, and that can be seen as the starting point of abstract algebraic logic.

Modern mathematical logic began in 1847, with two pamphlets whose respective authors were Augustus DeMorgan and George Boole. They, and later C.S. Peirce, Hugh MacColl, Frege, Peano, Bertrand Russell, and A. N. Whitehead all shared Leibniz's dream of combining symbolic logic, mathematics, and philosophy. Relation algebra is arguably the culmination of Leibniz's approach to logic. With the exception of some writings by Leopold Loewenheim and Thoralf Skolem, algebraic logic went into eclipse soon after the 1910-13 publication of *Principia Mathematica*, not to revive until Tarski's 1940 reexposition of relation algebra.

Leibniz had no influence on the rise of algebraic logic because his logical writings were little studied before the Parkinson and Loemker translations. Our present understanding of Leibniz the logician stems mainly from the work of Wolfgang Lenzen, summarized in Lenzen (2004).<sup>[1]</sup> To see how present-day work in logic and metaphysics can draw inspiration from, and shed light on, Leibniz's thought, see Zalta (2000).<sup>[2]</sup>

## See also

- Abstract algebraic logic
- Algebraic structure
- Boolean algebra (logic)
- Boolean algebra (structure)
- Cylindric algebra
- Lindenbaum-Tarski algebra
- Mathematical logic
- Model theory
- Monadic Boolean algebra
- Predicate functor logic
- Relation algebra
- Universal algebra

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## External links

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# Quantum logic

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In  $\rightarrow$  quantum mechanics, **quantum logic** is a set of rules for reasoning about propositions which takes the principles of quantum theory into account. This research area and its name originated in the 1936 paper by Garrett Birkhoff and John von Neumann, who were attempting to reconcile the apparent inconsistency of classical boolean logic with the facts concerning the measurement of complementary variables in quantum mechanics, such as position and momentum.

Quantum logic can be formulated either as a modified version of propositional logic or as a non-commutative and non-associative many-valued (MV) logic<sup>[1] [2] [3] [4] [5]</sup>. It has some properties which clearly distinguish it from classical logic, most notably, the failure of the distributive law of propositional logic:

$$p \text{ and } (q \text{ or } r) = (p \text{ and } q) \text{ or } (p \text{ and } r),$$

where the symbols  $p$ ,  $q$  and  $r$  are propositional variables. To illustrate why the distributive law fails, consider a particle moving on a line and let

$p$  = "the particle is moving to the right"

$q$  = "the particle is in the interval  $[-1,1]$ "

$r$  = "the particle is not in the interval  $[-1,1]$ "

then the proposition " $q$  or  $r$ " is true, so

$$p \text{ and } (q \text{ or } r) = p$$

On the other hand, the propositions " $p$  and  $q$ " and " $p$  and  $r$ " are both false, since they assert tighter restrictions on simultaneous values of position and momentum than is allowed by the uncertainty principle. So,

$$(p \text{ and } q) \text{ or } (p \text{ and } r) = \text{false}$$

Thus the distributive law fails.

Quantum logic has been proposed as the correct logic for propositional inference generally, most notably by the philosopher Hilary Putnam, at least at one point in his career. This thesis was an important ingredient in Putnam's paper *Is Logic Empirical?* in which he analysed the epistemological status of the rules of propositional logic. Putnam attributes the idea that anomalies associated to quantum measurements originate with anomalies in the logic of physics itself to the physicist David Finkelstein. It should be noted, however, that this idea had been around for some time and had been revived several years earlier by George Mackey's work on group representations and symmetry.

The more common view regarding quantum logic, however, is that it provides a formalism for relating observables, system preparation filters and states. In this view, the quantum logic approach resembles more closely the C\*-algebraic approach to quantum mechanics; in fact with some minor technical assumptions it can be subsumed by it. The similarities of the quantum logic formalism to a system of deductive logic may then be regarded more as a curiosity than as a fact of fundamental philosophical importance.

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## Introduction

In his classic treatise *Mathematical Foundations of Quantum Mechanics*, John von Neumann noted that projections on a Hilbert space can be viewed as propositions about physical observables. The set of principles for manipulating these quantum propositions was called *quantum logic* by von Neumann and Birkhoff. In his book (also called *Mathematical Foundations of Quantum Mechanics*) G. Mackey attempted to provide a set of axioms for this propositional system as an orthocomplemented lattice. Mackey viewed elements of this set as potential *yes or no questions* an observer might ask about the state of a physical system, questions that would be settled by some measurement. Moreover Mackey defined a physical observable in terms of these basic questions. Mackey's axiom system is somewhat unsatisfactory though, since it assumes that the partially ordered set is actually given as the orthocomplemented closed subspace lattice of a separable Hilbert space. Piron, Ludwig and others have attempted to give axiomatizations which do not require such explicit relations to the lattice of subspaces.

The remainder of this article assumes the reader is familiar with the spectral theory of self-adjoint operators on a Hilbert space. However, the main ideas can be understood using the finite-dimensional spectral theorem.

## Projections as propositions

The so-called *Hamiltonian* formulations of classical mechanics have three ingredients: *states*, *observables* and *dynamics*. In the simplest case of a single particle moving in  $\mathbf{R}^3$ , the state space is the position-momentum space  $\mathbf{R}^6$ . We will merely note here that an observable is some real-valued function  $f$  on the state space. Examples of observables are position, momentum or energy of a particle. For classical systems, the value  $f(x)$ , that is the value of  $f$  for some particular system state  $x$ , is obtained by a process of measurement of  $f$ . The propositions concerning a classical system are generated from basic statements of the form

- Measurement of  $f$  yields a value in the interval  $[a, b]$  for some real numbers  $a, b$ .

It follows easily from this characterization of propositions in classical systems that the corresponding logic is identical to that of some Boolean algebra of subsets of the state space. By logic in this context we mean the rules that relate set operations and ordering relations, such as de Morgan's laws. These are analogous to the rules relating boolean conjunctives and material implication in classical propositional logic. For technical reasons, we will also assume that the algebra of subsets of the state space is that of all Borel sets. The set of propositions is ordered by the natural ordering of sets and has a complementation operation. In terms of observables, the complement of the proposition  $\{f \geq a\}$  is  $\{f < a\}$ .

We summarize these remarks as follows:

- The proposition system of a classical system is a lattice with a distinguished *orthocomplementation* operation: The lattice operations of *meet* and *join* are respectively set intersection and set union. The orthocomplementation operation is set complement. Moreover this lattice is *sequentially complete*, in the sense that any sequence  $\{E_i\}_i$  of elements of the lattice has a least upper bound, specifically the set-theoretic union:

$$\text{LUB}(\{E_i\}) = \bigcup_{i=1}^{\infty} E_i.$$

In the Hilbert space formulation of quantum mechanics as presented by von Neumann, a physical observable is represented by some (possibly unbounded) densely-defined self-adjoint operator  $A$  on a Hilbert space  $H$ .  $A$  has a spectral decomposition, which is a projection-valued measure  $E$  defined on the Borel subsets of  $\mathbf{R}$ . In particular, for any bounded Borel function  $f$ , the following equation holds:

$$f(A) = \int_{\mathbf{R}} f(\lambda) dE(\lambda).$$

In case  $f$  is the indicator function of an interval  $[a, b]$ , the operator  $f(A)$  is a self-adjoint projection, and can be interpreted as the quantum analogue of the classical proposition

- Measurement of  $A$  yields a value in the interval  $[a, b]$ .

## The propositional lattice of a quantum mechanical system

This suggests the following quantum mechanical replacement for the orthocomplemented lattice of propositions in classical mechanics. This is essentially Mackey's *Axiom VII*:

- The orthocomplemented lattice  $Q$  of propositions of a quantum mechanical system is the lattice of closed subspaces of a complex Hilbert space  $H$  where orthocomplementation of  $V$  is the orthogonal complement  $V^\perp$ .

$Q$  is also sequentially complete: any pairwise disjoint sequence  $\{V_i\}_i$  of elements of  $Q$  has a least upper bound. Here disjointness of  $W_1$  and  $W_2$  means  $W_2$  is a subspace of  $W_1^\perp$ . The least upper bound of  $\{V_i\}_i$  is the closed internal direct sum.

Henceforth we identify elements of  $Q$  with self-adjoint projections on the Hilbert space  $H$ .

The structure of  $Q$  immediately points to a difference with the partial order structure of a classical proposition system. In the classical case, given a proposition  $p$ , the equations

$$\begin{aligned} I &= p \vee q \\ 0 &= p \wedge q \end{aligned}$$

have exactly one solution, namely the set-theoretic complement of  $p$ . In these equations  $I$  refers to the atomic proposition which is identically true and  $0$  the atomic proposition which is identically false. In the case of the lattice of projections there are infinitely many solutions to the above equations.

Having made these preliminary remarks, we turn everything around and attempt to define observables within the projection lattice framework and using this definition establish the correspondence between self-adjoint operators and observables : A *Mackey observable* is a countably additive homomorphism from the orthocomplemented lattice of the Borel subsets of  $\mathbf{R}$  to  $Q$ . To say the mapping  $\varphi$  is a countably additive homomorphism means that for any sequence  $\{S_i\}_i$  of pairwise disjoint Borel subsets of  $\mathbf{R}$ ,  $\{\varphi(S_i)\}_i$  are pairwise orthogonal projections and

$$\varphi\left(\bigcup_{i=1}^{\infty} S_i\right) = \sum_{i=1}^{\infty} \varphi(S_i).$$

**Theorem.** There is a bijective correspondence between Mackey observables and densely-defined self-adjoint operators on  $H$ .

This is the content of the spectral theorem as stated in terms of spectral measures.

## Statistical structure

Imagine a forensics lab which has some apparatus to measure the speed of a bullet fired from a gun. Under carefully controlled conditions of temperature, humidity, pressure and so on the same gun is fired repeatedly and speed measurements taken. This produces some distribution of speeds. Though we will not get exactly the same value for each individual measurement, for each cluster of measurements, we would expect the experiment to lead to the same distribution of speeds. In particular, we can expect to assign probability distributions to propositions such as  $\{a \leq \text{speed} \leq b\}$ . This leads naturally to propose that under controlled conditions of preparation, the measurement of a classical system can be described by a probability measure on the state space. This same statistical structure is also present in quantum mechanics.

A *quantum probability measure* is a function  $P$  defined on  $Q$  with values in  $[0,1]$  such that  $P(0)=0$ ,  $P(I)=1$  and if  $\{E_i\}_i$  is a sequence of pairwise orthogonal elements of  $Q$  then

$$P\left(\sum_{i=1}^{\infty} E_i\right) = \sum_{i=1}^{\infty} P(E_i).$$

The following highly non-trivial theorem is due to Andrew Gleason:

**Theorem.** Suppose  $H$  is a separable Hilbert space of complex dimension at least 3. Then for any quantum probability measure on  $Q$  there exists a unique trace class operator  $S$  such that

$$P(E) = \text{Tr}(SE)$$

for any self-adjoint projection  $E$ .

The operator  $S$  is necessarily non-negative (that is all eigenvalues are non-negative) and of trace 1. Such an operator is often called a *density operator*.

Physicists commonly regard a density operator as being represented by a (possibly infinite) density matrix relative to some orthonormal basis.

For more information on statistics of quantum systems, see quantum statistical mechanics.

## Automorphisms

An *automorphism* of  $Q$  is a bijective mapping  $\alpha:Q \rightarrow Q$  which preserves the orthocomplemented structure of  $Q$ , that is

$$\alpha\left(\sum_{i=1}^{\infty} E_i\right) = \sum_{i=1}^{\infty} \alpha(E_i)$$

for any sequence  $\{E_i\}_i$  of pairwise orthogonal self-adjoint projections. Note that this property implies monotonicity of  $\alpha$ . If  $P$  is a quantum probability measure on  $Q$ , then  $E \rightarrow \alpha(E)$  is also a quantum probability measure on  $Q$ . By the Gleason theorem characterizing quantum probability measures quoted above, any automorphism  $\alpha$  induces a mapping  $\alpha^*$  on the density operators by the following formula:

$$\text{Tr}(\alpha^*(S)E) = \text{Tr}(S\alpha(E)).$$

The mapping  $\alpha^*$  is bijective and preserves convex combinations of density operators. This means

$$\alpha^*(r_1S_1 + r_2S_2) = r_1\alpha^*(S_1) + r_2\alpha^*(S_2)$$

whenever  $1 = r_1 + r_2$  and  $r_1, r_2$  are non-negative real numbers. Now we use a theorem of Richard Kadison:

**Theorem.** Suppose  $\beta$  is a bijective map from density operators to density operators which is convexity preserving. Then there is an operator  $U$  on the Hilbert space which is either linear or conjugate-linear, preserves the inner product and is such that

$$\beta(S) = USU^*$$

for every density operator  $S$ . In the first case we say  $U$  is unitary, in the second case  $U$  is anti-unitary.

**Remark.** This note is included for technical accuracy only, and should not concern most readers. The result quoted above is not directly stated in Kadison's paper, but can be reduced to it by noting first that  $\beta$  extends to a positive trace preserving map on the trace class operators, then applying duality and finally applying a result of Kadison's paper.

The operator  $U$  is not quite unique; if  $r$  is a complex scalar of modulus 1, then  $rU$  will be unitary or anti-unitary if  $U$  is and will implement the same automorphism. In fact, this is the only ambiguity possible.

It follows that automorphisms of  $Q$  are in bijective correspondence to unitary or anti-unitary operators modulo multiplication by scalars of modulus 1. Moreover, we can regard automorphisms in two equivalent ways: as operating on states (represented as density operators) or as operating on  $Q$ .

## Non-relativistic dynamics

In non-relativistic physical systems, there is no ambiguity in referring to time evolution since there is a global time parameter. Moreover an isolated quantum system evolves in a deterministic way: if the system is in a state  $S$  at time  $t$  then at time  $s > t$ , the system is in a state  $F_{s,t}(S)$ . Moreover, we assume

- The dependence is reversible: The operators  $F_{s,t}$  are bijective.
- The dependence is homogeneous:  $F_{s,t} = F_{s-t,0}$ .
- The dependence is convexity preserving: That is, each  $F_{s,t}(S)$  is convexity preserving.
- The dependence is weakly continuous: The mapping  $\mathbf{R} \rightarrow \mathbf{R}$  given by  $t \rightarrow \text{Tr}(F_{s,t}(S)E)$  is continuous for every  $E$  in  $Q$ .

By Kadison's theorem, there is a 1-parameter family of unitary or anti-unitary operators  $\{U_t\}_t$  such that

$$F_{s,t}(S) = U_{s-t} S U_{s-t}^*$$

In fact,

**Theorem.** Under the above assumptions, there is a strongly continuous 1-parameter group of unitary operators  $\{U_t\}_t$  such that the above equation holds.

Note that it easily follows from uniqueness from Kadison's theorem that

$$U_{t+s} = \sigma(t,s) U_t U_s$$

where  $\sigma(t,s)$  has modulus 1. Now the square of an anti-unitary is a unitary, so that all the  $U_t$  are unitary. The remainder of the argument shows that  $\sigma(t,s)$  can be chosen to be 1 (by modifying each  $U_t$  by a scalar of modulus 1.)

## Pure states

A convex combinations of statistical states  $S_1$  and  $S_2$  is a state of the form  $S = p_1 S_1 + p_2 S_2$  where  $p_1, p_2$  are non-negative and  $p_1 + p_2 = 1$ . Considering the statistical state of system as specified by lab conditions used for its preparation, the convex combination  $S$  can be regarded as the state formed in the following way: toss a biased coin with outcome probabilities  $p_1, p_2$  and depending on outcome choose system prepared to  $S_1$  or  $S_2$

Density operators form a convex set. The convex set of density operators has extreme points; these are the density operators given by a projection onto a one-dimensional space. To see that any extreme point is such a projection, note that by the spectral theorem  $S$  can be represented by a diagonal matrix; since  $S$  is non-negative all the entries are non-negative and since  $S$  has trace 1, the diagonal entries must add up to 1. Now if it happens that the diagonal matrix has more than one non-zero entry it is clear that we can express it as a convex combination of other density operators.

The extreme points of the set of density operators are called pure states. If  $S$  is the projection on the 1-dimensional space generated by a vector  $\psi$  of norm 1 then

$$\text{Tr}(SE) = \langle E\psi|\psi\rangle$$

for any  $E$  in  $Q$ . In physics jargon, if

$$S = |\psi\rangle\langle\psi|,$$

where  $\psi$  has norm 1, then

$$\text{Tr}(SE) = \langle\psi|E|\psi\rangle.$$

Thus pure states can be identified with *rays* in the Hilbert space  $H$ .

## The measurement process

Consider a quantum mechanical system with lattice  $Q$  which is in some statistical state given by a density operator  $S$ . This essentially means an ensemble of systems specified by a repeatable lab preparation process. The result of a cluster of measurements intended to determine the truth value of proposition  $E$ , is just as in the classical case, a probability distribution of truth values **T** and **F**. Say the probabilities are  $p$  for **T** and  $q = 1 - p$  for **F**. By the previous section  $p = \text{Tr}(SE)$  and  $q = \text{Tr}(S(I-E))$ .

Perhaps the most fundamental difference between classical and quantum systems is the following: regardless of what process is used to determine  $E$  immediately after the measurement the system will be in one of two statistical states:

- If the result of the measurement is **T**

$$\frac{1}{\text{Tr}(ES)}ESE.$$

- If the result of the measurement is **F**

$$\frac{1}{\text{Tr}((I-E)S)}(I-E)S(I-E).$$

(We leave to the reader the handling of the degenerate cases in which the denominators may be 0.) We now form the convex combination of these two ensembles using the relative frequencies  $p$  and  $q$ . We thus obtain the result that the measurement process applied to a statistical ensemble in state  $S$  yields another ensemble in statistical state:

$$M_E(S) = ESE + (I-E)S(I-E).$$

We see that a pure ensemble becomes a mixed ensemble after measurement. Measurement, as described above, is a special case of quantum operations.

## Limitations

Quantum logic derived from propositional logic provides a satisfactory foundation for a theory of reversible quantum processes. Examples of such processes are the covariance transformations relating two frames of reference, such as change of time parameter or the transformations of special relativity. Quantum logic also provides a satisfactory understanding of density matrices. Quantum logic can be stretched to account for some kinds of measurement processes corresponding to answering yes-no questions about the state of a quantum system. However, for more general kinds of measurement operations (that is quantum operations), a more complete theory of filtering processes is necessary. Such an approach is provided by the consistent histories formalism. On the other hand, quantum logics derived from MV-logic extend its range of applicability to irreversible quantum processes and/or 'open' quantum systems.

In any case, these quantum logic formalisms must be generalized in order to deal with super-geometry (which is needed to handle Fermi-fields) and non-commutative geometry (which is needed in string theory and quantum gravity theory). Both of these theories use a partial algebra with an "integral" or "trace". The elements of the partial algebra are not observables; instead the "trace" yields "greens functions" which generate scattering amplitudes. One thus obtains a local S-matrix theory (see D. Edwards).

Since around 1978 the Flato school ( see F. Bayen ) has been developing an alternative to the quantum logics approach called deformation quantization (see Weyl quantization ).

In 2004, Prakash Panangaden described how to capture the kinematics of quantum causal evolution using System BV, a deep inference logic originally developed for use in structural proof theory.[6] Alessio Guglielmi, Lutz Straßburger, and Richard Blute have also done work in this area.[7]

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## See also

- Mathematical formulation of quantum mechanics
- Multi-valued logic
- Quasi-set theory
- HPO formalism (An approach to temporal quantum logic)
- → Quantum field theory

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## External links

- Stanford Encyclopedia of Philosophy entry on Quantum Logic and Probability Theory (<http://plato.stanford.edu/entries/qt-quantlog/>)

# Quantum computer

A **quantum computer** is a device for computation that makes direct use of quantum mechanical phenomena, such as superposition and entanglement, to perform operations on data. The basic principle behind quantum computation is that quantum properties can be used to represent data and perform operations on these data.<sup>[1]</sup>

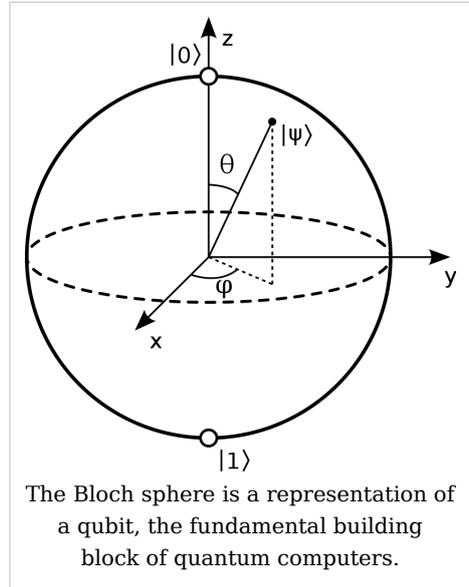
Although quantum computing is still in its infancy, experiments have been carried out in which quantum computational operations were executed on a very small number of qubits (**quantum binary digits**). Both practical and theoretical research continues with interest, and many national government and military funding agencies support quantum computing research to develop quantum computers for both civilian and national security purposes, such as cryptanalysis.<sup>[2]</sup>

If large-scale quantum computers can be built, they will be able to solve certain problems much faster than any of our current classical computers (for example Shor's algorithm). Quantum computers are different from other computers such as DNA computers and traditional computers based on transistors. Some computing architectures such as optical computers<sup>[3]</sup> may use classical superposition of electromagnetic waves. Without some specifically quantum mechanical resources such as entanglement, it is conjectured that an exponential advantage over classical computers is not possible.<sup>[4]</sup>

## Basis

A classical computer has a memory made up of bits, where each bit holds either a one or a zero. A quantum computer maintains a sequence of qubits. A single qubit can hold a one, a zero, or, crucially, any quantum superposition of these; moreover, a pair of qubits can be in any quantum superposition of 4 states, and three qubits in any superposition of 8. In general a quantum computer with  $n$  qubits can be in an arbitrary superposition of up to  $2^n$  different states simultaneously (this compares to a normal computer that can only be in *one* of these  $2^n$  states at any one time). A quantum computer operates by manipulating those qubits with a fixed sequence of quantum logic gates. The sequence of gates to be applied is called a *quantum algorithm*.

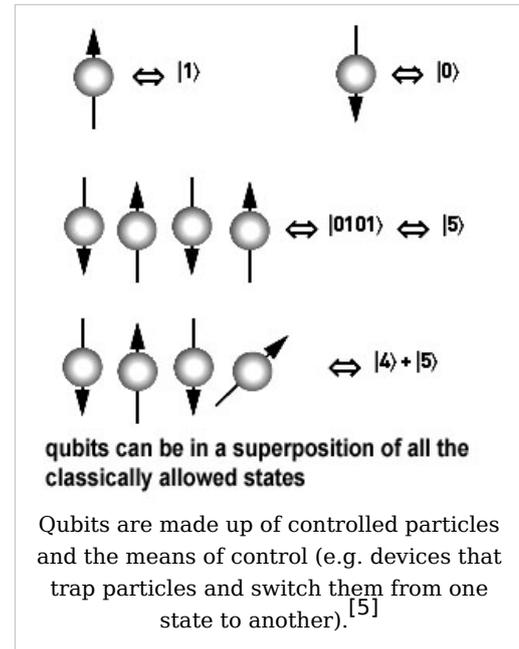
An example of an implementation of qubits for a quantum computer could start with the use of particles with two spin states: "down" and "up" (typically written  $|\downarrow\rangle$  and  $|\uparrow\rangle$ , or  $|0\rangle$  and  $|1\rangle$ ). But in fact any system possessing an observable quantity  $A$  which is *conserved* under time evolution and such that  $A$  has at least two discrete and sufficiently spaced consecutive eigenvalues, is a suitable candidate for implementing a qubit. This is true



because any such system can be mapped onto an effective spin-1/2 system.

## Bits vs. qubits

Consider first a classical computer that operates on a three-bit register. The state of the computer at any time is a probability distribution over the  $2^3 = 8$  different three-bit strings 000, 001, ..., 111. If it is a deterministic computer, then it is in exactly one of these states with probability 1. However, if it is a probabilistic computer, then it may have a chance in being in a number of different states. We can describe this probabilistic state by eight nonnegative numbers  $a, b, c, d, e, f, g, h$  (where  $a =$  probability computer is in state 000,  $b =$  probability computer is in state 001, etc.). There is a restriction that these probabilities sum to 1.



The state of a three-qubit quantum computer is similarly described by an eight-dimensional vector  $(a, b, c, d, e, f, g, h)$ , called a wavefunction. However, instead of adding to one, the sum of the *squares* of the coefficient magnitudes,  $|a|^2 + |b|^2 + \dots + |h|^2$ , must equal one. Moreover, the coefficients are complex numbers. Since states are represented by complex wavefunctions, two states being added together will undergo interference. This is a key difference between quantum computing and probabilistic classical computing.<sup>[6]</sup>

If you measure the three qubits, then you will observe a three-bit string. The probability of measuring a string will equal the squared magnitude of that string's coefficients (using our example, probability that we read state as 000 =  $|a|^2$ , probability that we read state as 001 =  $|b|^2$ , etc.). Thus a measurement of the quantum state with coefficients  $(a, b, \dots, h)$  gives the classical probability distribution  $(|a|^2, |b|^2, \dots, |h|^2)$ . We say that the quantum state "collapses" to a classical state.

Note that an eight-dimensional vector can be specified in many different ways, depending on what basis you choose for the space. The basis of three-bit strings 000, 001, ..., 111 is known as the computational basis, and is often convenient, but other bases of unit-length, orthogonal vectors can also be used. Ket notation is often used to make explicit the choice of basis. For example, the state  $(a, b, c, d, e, f, g, h)$  in the computational basis can be written as  $a|000\rangle + b|001\rangle + c|010\rangle + d|011\rangle + e|100\rangle + f|101\rangle + g|110\rangle + h|111\rangle$ , where, e.g.,  $|010\rangle = (0, 0, 1, 0, 0, 0, 0, 0)$ . The computational basis for a single qubit (two dimensions) is  $|0\rangle = (1, 0)$ ,  $|1\rangle = (0, 1)$ , but another common basis is the Hadamard basis of  $|+\rangle = \frac{1}{\sqrt{2}}(1, 1)$  and  $|-\rangle = \frac{1}{\sqrt{2}}(1, -1)$ .

Note that although recording a classical state of  $n$  bits, a  $2^n$ -dimensional probability distribution, requires an exponential number of real numbers, practically we can always think of the system as being exactly one of the  $n$ -bit strings—we just don't know which one. Quantum mechanically, this is not the case, and all  $2^n$  complex coefficients need to be kept

track of to see how the quantum system evolves. For example, a 300-qubit quantum computer has a state described by  $2^{300}$  (approximately  $10^{90}$ ) complex numbers, more than the number of atoms in the observable universe.

## Operation

While a classical three-bit state and a quantum three-qubit state are both eight-dimensional vectors, they are manipulated quite differently for classical or quantum computation, respectively. For computing in either case, the system must be initialized, for example into the all-zeros string,  $|000\rangle$ , corresponding to the vector  $(1,0,0,0,0,0,0,0)$ . In classical randomized computation, the system evolves according to the application of stochastic matrices, which preserve that the probabilities add up to one (i.e., preserve the L1 norm). In quantum computation, on the other hand, allowed operations are unitary matrices, which are effectively rotations (they preserve that the sum of the squares add up to one, the Euclidean or L2 norm). (Exactly what unitaries can be applied depend on the physics of the quantum device.) Consequently, since rotations can be undone by rotating backward, quantum computations are reversible. (Technically, quantum operations can be probabilistic combinations of unitaries, so quantum computation really does generalize classical computation. See quantum circuit for a more precise formulation.)

Finally, upon termination of the algorithm, the result needs to be read off. In the case of a classical computer, we *sample* from the probability distribution on the three-bit register to obtain one definite three-bit string, say 000. Quantum mechanically, we *measure* the three-qubit state, which is equivalent to collapsing the quantum state down to a classical distribution (with the coefficients in the classical state being the squared magnitudes of the coefficients for the quantum state, as described above) followed by sampling from that distribution. Note that this destroys the original quantum state. Many algorithms will only give the correct answer with a certain probability, however by repeatedly initializing, running and measuring the quantum computer, the probability of getting the correct answer can be increased.

For more details on the sequences of operations used for various algorithms, see universal quantum computer, Shor's algorithm, Grover's algorithm, Deutsch-Jozsa algorithm, quantum Fourier transform, quantum gate, quantum adiabatic algorithm and quantum error correction.

## Potential

Integer factorization is believed to be computationally infeasible with an ordinary computer for large integers that are the product of only a few prime numbers (e.g., products of two 300-digit primes).<sup>[7]</sup> By comparison, a quantum computer could efficiently solve this problem using Shor's algorithm to find its factors. This ability would allow a quantum computer to "break" many of the cryptographic systems in use today, in the sense that there would be a polynomial time (in the number of digits of the integer) algorithm for solving the problem. In particular, most of the popular public key ciphers are based on the difficulty of factoring integers (or the related discrete logarithm problem which can also be solved by Shor's algorithm), including forms of RSA. These are used to protect secure Web pages, encrypted email, and many other types of data. Breaking these would have significant ramifications for electronic privacy and security. The only way to increase the security of an algorithm like RSA would be to increase the key size and hope that an

adversary does not have the resources to build and use a powerful enough quantum computer.

A way out of this dilemma would be to use some kind of quantum cryptography. There are also some digital signature schemes that are believed to be secure against quantum computers. See for instance Lamport signatures.

Besides factorization and discrete logarithms, quantum algorithms offering a more than polynomial speedup over the best known classical algorithm have been found for several problems,<sup>[8]</sup> including the simulation of quantum physical processes from chemistry and solid state physics, the approximation of Jones polynomials, and solving Pell's equation. No mathematical proof has been found that shows that an equally fast classical algorithm cannot be discovered, although this is considered unlikely. For some problems, quantum computers offer a polynomial speedup. The most well-known example of this is *quantum database search*, which can be solved by Grover's algorithm using quadratically fewer queries to the database than are required by classical algorithms. In this case the advantage is provable. Several other examples of provable quantum speedups for query problems have subsequently been discovered, such as for finding collisions in two-to-one functions and evaluating NAND trees.

Consider a problem that has these four properties:

1. The only way to solve it is to guess answers repeatedly and check them,
2. There are  $n$  possible answers to check,
3. Every possible answer takes the same amount of time to check, and
4. There are no clues about which answers might be better: generating possibilities randomly is just as good as checking them in some special order.

An example of this is a password cracker that attempts to guess the password for an encrypted file (assuming that the password has a maximum possible length).

For problems with all four properties, the time for a quantum computer to solve this will be proportional to the square root of  $n$ . That can be a very large speedup, reducing some problems from years to seconds. It can be used to attack symmetric ciphers such as Triple DES and AES by attempting to guess the secret key. Regardless of whether any of these problems can be shown to have an advantage on a quantum computer, they nonetheless will always have the advantage of being an excellent tool for studying quantum mechanical interactions, which of itself is an enormous value to the scientific community.

Grover's algorithm can also be used to obtain a quadratic speed-up [over a brute-force search] for a class of problems known as NP-complete.

Since chemistry and nanotechnology rely on understanding quantum systems, and such systems are impossible to simulate in an efficient manner classically, many believe quantum simulation will be one of the most important applications of quantum computing.<sup>[9]</sup>

There are a number of practical difficulties in building a quantum computer, and thus far quantum computers have only solved trivial problems. David DiVincenzo, of IBM, listed the following requirements for a practical quantum computer:<sup>[10]</sup>

- scalable physically to increase the number of qubits;
  - qubits can be initialized to arbitrary values;
  - quantum gates faster than decoherence time;
  - universal gate set;
  - qubits can be read easily.
-

## Quantum decoherence

One of the greatest challenges is controlling or removing decoherence. This usually means isolating the system from its environment as the slightest interaction with the external world would cause the system to decohere. This effect is irreversible, as it is non-unitary, and is usually something that should be avoided, if not highly controlled. Decoherence times for candidate systems, in particular the transverse relaxation time  $T_2$  (for  $\rightarrow$  NMR and MRI technology, also called the *dephasing time*), typically range between nanoseconds and seconds at low temperature.<sup>[6]</sup>

These issues are more difficult for optical approaches as the timescales are orders of magnitude lower and an often cited approach to overcoming them is optical pulse shaping. Error rates are typically proportional to the ratio of operating time to decoherence time, hence any operation must be completed much more quickly than the decoherence time.

If the error rate is small enough, it is thought to be possible to use quantum error correction, which corrects errors due to decoherence, thereby allowing the total calculation time to be longer than the decoherence time. An often cited figure for required error rate in each gate is  $10^{-4}$ . This implies that each gate must be able to perform its task 10,000 times faster than the decoherence time of the system.

Meeting this scalability condition is possible for a wide range of systems. However, the use of error correction brings with it the cost of a greatly increased number of required qubits. The number required to factor integers using Shor's algorithm is still polynomial, and thought to be between  $L$  and  $L^2$ , where  $L$  is the number of bits in the number to be factored; error correction algorithms would inflate this figure by an additional factor of  $L$ . For a 1000-bit number, this implies a need for about  $10^4$  qubits without error correction.<sup>[11]</sup> With error correction, the figure would rise to about  $10^7$  qubits. Note that computation time is about  $L^2$  or about  $10^7$  steps and on 1 MHz, about 10 seconds.

A very different approach to the stability-decoherence problem is to create a topological quantum computer with anyons, quasi-particles used as threads and relying on braid theory to form stable logic gates.<sup>[12] [13]</sup>

## Candidates

There are a number of quantum computing candidates, among those:

- Superconductor-based quantum computers (including SQUID-based quantum computers)<sup>[14]</sup>
- Trapped ion quantum computer
- Optical lattices
- Topological quantum computer
- Quantum dot on surface (e.g. the Loss-DiVincenzo quantum computer)
- $\rightarrow$  Nuclear magnetic resonance on molecules in solution (liquid NMR)
- Solid state NMR Kane quantum computers
- Electrons on helium quantum computers
- Cavity quantum electrodynamics (CQED)
- Molecular magnet
- Fullerene-based ESR quantum computer
- Optic-based quantum computers (Quantum optics)
- Diamond-based quantum computer<sup>[15] [16] [17]</sup>

- Bose-Einstein condensate-based quantum computer<sup>[18]</sup>
- Transistor-based quantum computer - string quantum computers with entrainment of positive holes using an electrostatic trap
- Spin-based quantum computer
- Adiabatic quantum computation<sup>[19]</sup>
- Rare-earth-metal-ion-doped inorganic crystal based quantum computers<sup>[20] [21]</sup>

The large number of candidates shows explicitly that the topic, in spite of rapid progress, is still in its infancy. But at the same time there is also a vast amount of flexibility.

In 2005, researchers at the University of Michigan built a semiconductor chip which functioned as an ion trap. Such devices, produced by standard lithography techniques, may point the way to scalable quantum computing tools.<sup>[22]</sup> An improved version was made in 2006.

## Quantum computing in computational complexity theory

This section surveys what is currently known mathematically about the power of quantum computers. It describes the known results from computational complexity theory and the theory of computation dealing with quantum computers.

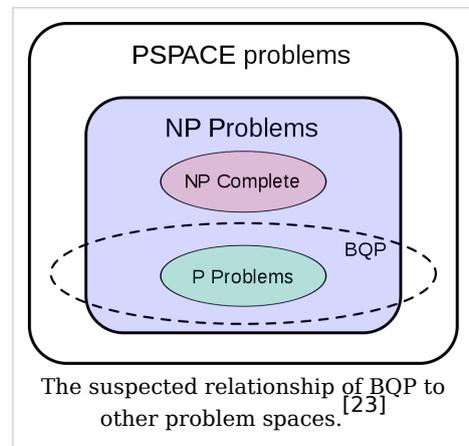
The class of problems that can be efficiently solved by quantum computers is called **BQP**, for "bounded error, quantum, polynomial time". Quantum computers only run **probabilistic** algorithms, so **BQP** on quantum computers is the counterpart of **BPP** on classical computers. It is defined as the set of problems solvable with a polynomial-time algorithm, whose probability of error is bounded away from one quarter.<sup>[23]</sup> A quantum computer is said to "solve" a problem if, for every instance, its answer will be right with high probability. If that solution runs in polynomial time, then that problem is in **BQP**.

**BQP** is contained in the complexity class  $\#P$  (or more precisely in the associated class of decision problems  $P^{\#P}$ ),<sup>[24]</sup> which is a subclass of PSPACE.

**BQP** is suspected to be disjoint from NP-complete and a strict superset of **P**, but that is not known. Both integer factorization and discrete log are in **BQP**. Both of these problems are **NP** problems suspected to be outside **BPP**, and hence outside **P**. Both are suspected to not be NP-complete. There is a common misconception that quantum computers can solve NP-complete problems in polynomial time. That is not known to be true, and is generally suspected to be false.<sup>[24]</sup>

Quantum gates may be viewed as linear transformations. Daniel S. Abrams and Seth Lloyd have shown that if *nonlinear* transformations are permitted, then NP-complete problems could be solved in polynomial time. It could even do so for  $\#P$ -complete problems. They do not believe that such a machine is possible.

Although quantum computers may be faster than classical computers, those described above can't solve any problems that classical computers can't solve, given enough time and memory (however, those amounts might be practically infeasible). A Turing machine can simulate these quantum computers, so such a quantum computer could never solve an



undecidable problem like the halting problem. The existence of "standard" quantum computers does not disprove the Church–Turing thesis.<sup>[23]</sup>

## See also

- List of emerging technologies
- Quantum bus
- Timeline of quantum computing
- Chemical computer
- DNA computer
- Decoherence by transposons in evolution
- Mathematical biology
- Molecular computer

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## External links

- jQuantum: Java quantum circuit simulator (<http://jquantum.sourceforge.net/jQuantumApplet.html>)
  - QCAD: Quantum circuit emulator (<http://www.phys.cs.is.nagoya-u.ac.jp/~watanabe/qcad/index.html>)
  - C++ Quantum Library (<https://gna.org/projects/quantumlibrary>)
  - Haskell Library for Quantum computations (<http://hackage.haskell.org/cgi-bin/hackage-scripts/package/quantum-arrow>)
  - Video Lectures by David Deutsch ([http://www.quiprocone.org/Protected/DD\\_lectures.htm](http://www.quiprocone.org/Protected/DD_lectures.htm))
  - Quasi quantum computer. (<http://x-machines.comoj.com/hyper-electromagnetics/index.html>)
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# Techniques and Applications

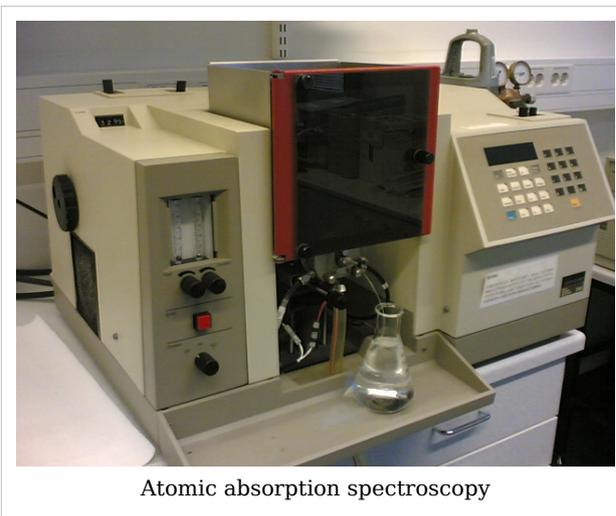
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## Atomic absorption spectroscopy

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In analytical chemistry, **atomic absorption spectroscopy** is a technique for determining the concentration of a particular metal element in a sample.<sup>[1]</sup> The technique can be used to analyze the concentration of over 70 different metals in a solution.

Although atomic absorption spectroscopy dates to the nineteenth century, the modern form was largely developed during the 1950s by a team of Australian chemists. They were led by Alan Walsh and worked at the CSIRO (Commonwealth Science and Industry Research Organisation) Division of Chemical Physics in Melbourne, Australia.<sup>[2]</sup>



Atomic absorption spectroscopy

### Principles

The technique makes use of absorption spectrometry to assess the concentration of an analyte in a sample. It relies therefore heavily on Beer-Lambert law.

In short, the electrons of the atoms in the atomizer can be promoted to higher orbitals for a short amount of time by absorbing a set quantity of energy (i.e. light of a given wavelength). This amount of energy (or wavelength) is specific to a particular electron transition in a particular element, and in general, each wavelength corresponds to only one element. This gives the technique its elemental selectivity.

As the quantity of energy (the power) put into the flame is known, and the quantity remaining at the other side (at the detector) can be measured, it is possible, from Beer-Lambert law, to calculate how many of these transitions took place, and thus get a signal that is proportional to the concentration of the element being measured.

## Instrumentation

In order to analyze a sample for its atomic constituents, it has to be atomized. The sample should then be illuminated by light. The light transmitted is finally measured by a detector. In order to reduce the effect of emission from the atomizer (e.g. the black body radiation) or the environment, a spectrometer is normally used between the atomizer and the detector.

### Types of Atomizer

The technique typically makes use of a flame to atomize the sample,<sup>[3]</sup> but other atomizers such as a graphite furnace<sup>[4]</sup> or plasmas, primarily inductively coupled plasmas, are also used.<sup>[5]</sup>

When a flame is used it is laterally long (usually 10 cm) and not deep. The height of the flame above the burner head can be controlled by adjusting the flow of the fuel mixture. A beam of light passes through this flame at its longest axis (the lateral axis) and hits a detector.

### Analysis of liquids

A liquid sample is normally turned into an atomic gas in three steps:

1. Desolvation (Drying) - the liquid solvent is evaporated, and the dry sample remains
2. Vaporization (Ashing) - the solid sample vaporises to a gas
3. Atomization - the compounds making up the sample are broken into free atoms.

## Radiation Sources

The radiation source chosen has a spectral width narrower than that of the atomic transitions.

### Hollow cathode lamps

Hollow cathode lamps are the most common radiation source in atomic absorption spectroscopy. Inside the lamp, filled with argon or neon gas, is a cylindrical metal cathode containing the metal for excitation, and an anode. When a high voltage is applied across the anode and cathode, gas particles are ionized. As voltage is increased, gaseous ions acquire enough energy to eject metal atoms from the cathode. Some of these atoms are in an excited states and emit light with the frequency characteristic to the metal<sup>[6]</sup>. Many modern hollow cathode lamps are selective for several metals.

### Diode lasers

Atomic absorption spectroscopy can also be performed by lasers, primarily diode lasers because of their good properties for laser absorption spectrometry.<sup>[7]</sup> The technique is then either referred to as diode laser atomic absorption spectrometry (DLAAS or DLAS),<sup>[8]</sup> or, since wavelength modulation most often is employed, wavelength modulation absorption spectrometry.

## Background Correction methods

The narrow bandwidth of hollow cathode lamps make spectral overlap rare. That is, it is unlikely that an absorption line from one element will overlap with another. Molecular emission is much broader, so it is more likely that some molecular absorption band will overlap with an atomic line. This can result in artificially high absorption and an improperly high calculation for the concentration in the solution. Three methods are typically used to correct for this:

- Zeeman correction - A magnetic field is used to split the atomic line into two sidebands (see Zeeman effect). These sidebands are close enough to the original wavelength to still overlap with molecular bands, but are far enough not to overlap with the atomic bands. The absorption in the presence and absence of a magnetic field can be compared, the difference being the atomic absorption of interest.
- Smith-Hieftje correction (invented by Stanley B. Smith and Gary M. Hieftje) - The hollow cathode lamp is pulsed with high current, causing a larger atom population and self-absorption during the pulses. This self-absorption causes a broadening of the line and a reduction of the line intensity at the original wavelength.<sup>[9]</sup>
- Deuterium lamp correction - In this case, a separate source (a deuterium lamp) with broad emission is used to measure the background emission. The use of a separate lamp makes this method the least accurate, but its relative simplicity (and the fact that it is the oldest of the three) makes it the most commonly used method.

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## See also

- Beer-Lambert law
- Laser absorption spectrometry
- JAAS Journal of Analytical Atomic Spectrometry

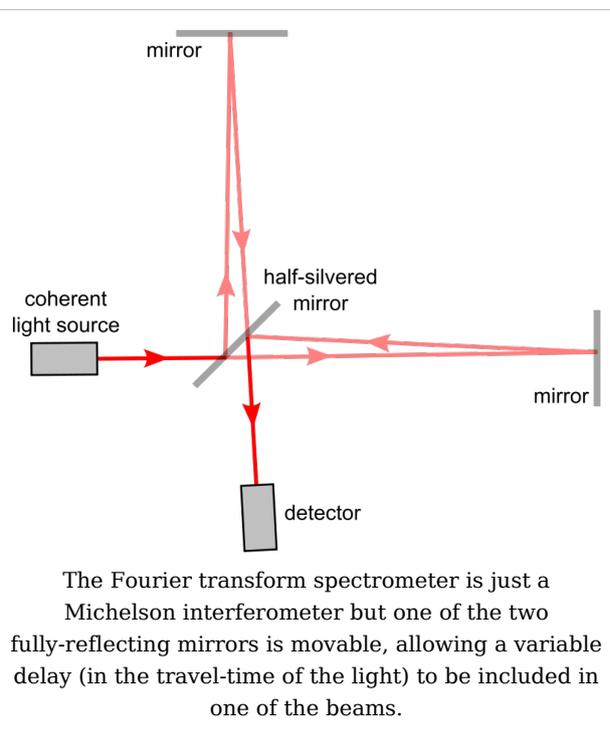
# Fourier transform spectroscopy

**Fourier transform spectroscopy** is a measurement technique whereby spectra are collected based on measurements of the temporal coherence of a radiative source, using time-domain measurements of the electromagnetic radiation or other type of radiation. It can be applied to a variety of types of spectroscopy including optical spectroscopy, infrared spectroscopy (FT IR, FT-NIRS), → Fourier transform (FT) nuclear magnetic resonance<sup>[1]</sup>, mass spectrometry and → electron spin resonance spectroscopy. There are several methods for measuring the temporal coherence of the light, including the continuous wave *Michelson* or *Fourier transform* spectrometer and the pulsed Fourier transform spectrograph (which is more sensitive and has a much shorter sampling time than conventional spectroscopic techniques, but is only applicable in a laboratory environment).

## Continuous wave *Michelson* or *Fourier transform* spectrograph

The Michelson spectrograph is similar to the instrument used in the Michelson-Morley experiment. Light from the source is split into two beams by a half-silvered mirror, one is reflected off a fixed mirror and one off a moving mirror which introduces a time delay -- the Fourier transform spectrometer is just a Michelson interferometer with a movable mirror. The beams interfere, allowing the temporal coherence of the light to be measured at each different time delay setting, effectively converting the time domain into a spatial coordinate. By making measurements of the signal at many discrete positions of the moving mirror, the spectrum can be reconstructed using a Fourier transform of the temporal coherence of the light. Michelson

spectrographs are capable of very high spectral resolution observations of very bright sources. The Michelson or Fourier transform spectrograph was popular for infra-red applications at a time when infra-red astronomy only had single pixel detectors. Imaging Michelson spectrometers are a possibility, but in general have been supplanted by imaging Fabry-Perot instruments which are easier to construct.



## Pulsed *Fourier transform* spectrometer

A pulsed *Fourier transform* spectrometer does not employ transmittance techniques. In the most general description of pulsed FT spectrometry, a sample is exposed to an energizing event which causes a periodic response. The frequency of the periodic response, as governed by the field conditions in the spectrometer, is indicative of the measured properties of the analyte.

### Examples of Pulsed *Fourier transform* spectrometry

In magnetic spectroscopy (EPR, NMR), an RF pulse in a strong ambient magnetic field is used as the energizing event. This turns the magnetic particles at an angle to the ambient field, resulting in gyration. The gyrating spins then induce a periodic current in a detector coil. Each spin exhibits a characteristic frequency of gyration (relative to the field strength) which reveals information about the analyte.

In FT-mass spectrometry, the energizing event is the injection of the charged sample into the strong electromagnetic field of a cyclotron. These particles travel in circles, inducing a current in a fixed coil on one point in their circle. Each traveling particle exhibits a characteristic cyclotron frequency-field ratio revealing the masses in the sample.

### The Free Induction Decay

Pulsed FT spectrometry gives the advantage of requiring a single, time-dependent measurement which can easily deconvolute a set of similar but distinct signals. The resulting composite signal, is called a *free induction decay*, because typically the signal will decay due to inhomogeneities in sample frequency, or simply unrecoverable loss of signal due to entropic loss of the property being measured.

### Fellgett Advantage

One of the most important advantages of Fourier transform spectroscopy was shown by P.B. Fellgett, an early advocate of the method. The Fellgett advantage, also known as the multiplex principle, states that a multiplex spectrometer such as the Fourier transform spectroscopy will produce a gain of the order of the square root of  $m$  in the signal-to-noise ratio of the resulting spectrum, when compared with an equivalent scanning monochromator, where  $m$  is the number of elements comprising the resulting spectrum when the measurement noise is dominated by detector noise.

### Converting spectra from time domain to frequency domain

$$S(t) = \int_{-\infty}^{\infty} I(\nu) e^{-i\nu 2\pi t} d\nu$$

The sum is performed over all contributing frequencies to give a signal  $S(t)$  in the time domain.

$$I(\nu) = 2\text{Re} \int_{-\infty}^{\infty} S(t) e^{2i\pi\nu t} dt$$

gives non-zero value when  $S(t)$  contains a component that matches the oscillating function. Remember that

$$e^{ix} = \cos x + i \sin x$$

## See also

- Applied spectroscopy
- → 2D-FT NMRI and Spectroscopy
- Forensic chemistry
- Forensic polymer engineering
- → nuclear magnetic resonance
- Infra-red spectroscopy

## References and notes

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## Further reading

- Ellis, D.I. and Goodacre, R. (2006). "Metabolic fingerprinting in disease diagnosis: biomedical applications of infrared and Raman spectroscopy". *The Analyst* **131**: 875-885. doi: 10.1039/b602376m (<http://dx.doi.org/10.1039/b602376m>).

## External links

- Description of how a Fourier transform spectrometer works (<http://scienceworld.wolfram.com/physics/FourierTransformSpectrometer.html>)
- The Michelson or Fourier transform spectrograph (<http://www.astro.livjm.ac.uk/courses/phys362/notes/>)
- Internet Journal of Vibrational Spectroscopy - How FTIR works (<http://www.ijvs.com/volume5/edition5/section1.html#Feature>)
- Fourier Transform Spectroscopy Topical Meeting and Tabletop Exhibit (<http://www.osa.org/meetings/topicalmeetings/fts/default.aspx>)

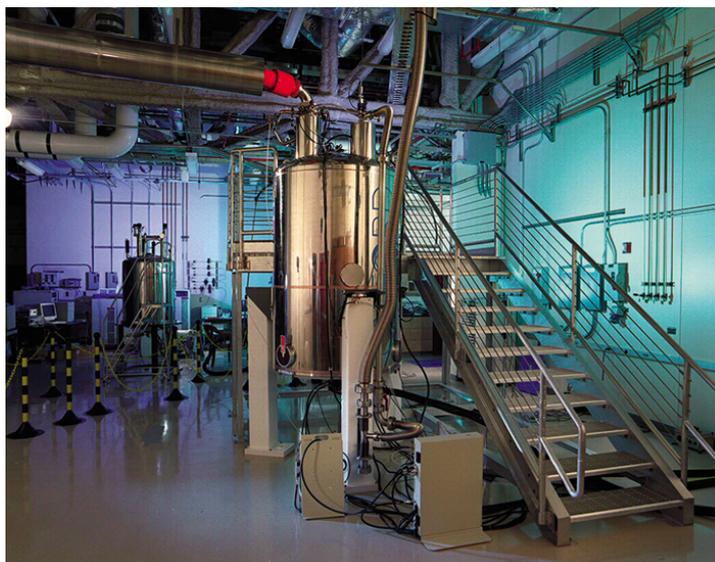
# Nuclear magnetic resonance

**Nuclear magnetic resonance (NMR)** is the name given to a physical resonance phenomenon involving the observation of specific  $\rightarrow$  quantum mechanical magnetic properties of an atomic nucleus in the presence of an applied, external magnetic field. Many scientific techniques exploit NMR phenomena to study molecular physics, crystals and non-crystalline materials through NMR spectroscopy. NMR is also routinely used in advanced medical imaging techniques, such as in magnetic resonance imaging (MRI).

All nuclei that contain odd numbers of nucleons have an intrinsic magnetic moment and angular momentum, in other words a spin  $> 0$ . The most commonly studied nuclei are  $^1\text{H}$  (the most NMR-sensitive isotope after the radioactive  $^3\text{H}$ ) and  $^{13}\text{C}$ , although nuclei from isotopes of many other elements (e.g.  $^2\text{H}$ ,  $^{10}\text{B}$ ,  $^{11}\text{B}$ ,  $^{14}\text{N}$ ,  $^{15}\text{N}$ ,  $^{17}\text{O}$ ,  $^{19}\text{F}$ ,  $^{23}\text{Na}$ ,  $^{29}\text{Si}$ ,  $^{31}\text{P}$ ,  $^{35}\text{Cl}$ ,  $^{113}\text{Cd}$ ,  $^{195}\text{Pt}$ ) are studied by high-field NMR spectroscopy as well.

A key feature of NMR is that the resonance frequency of a particular substance is directly proportional to the strength of the applied magnetic field. It is this feature that is exploited in imaging techniques; if a sample is placed in a non-uniform magnetic field then the resonance frequencies of the sample's nuclei depend on where

in the field they are located. Since the resolution of the imaging techniques depends on how big the gradient of the field is, many efforts are made to develop more powerful magnets,



Pacific Northwest National Laboratory's high magnetic field (800 MHz, 18.8 T) NMR spectrometer being loaded with a sample.



900MHz, 21.2 T NMR Magnet at HWB-NMR, Birmingham, UK being loaded with a sample

often using superconductors. The effectiveness of NMR can also be improved using hyperpolarization, and/or using two-dimensional, three-dimensional and higher dimension multi-frequency techniques.

The principle of NMR usually involves two sequential steps:

- The alignment (polarization) of the magnetic nuclear spins in an applied, constant magnetic field  $\mathbf{H}_0$ .
- The perturbation of this alignment of the nuclear spins by employing an electro-magnetic, usually radio frequency (RF) pulse. The required perturbing frequency is dependent upon the static magnetic field ( $\mathbf{H}_0$ ) and the nuclei of observation.

The two fields are usually chosen to be perpendicular to each other as this maximises the NMR signal strength. The resulting response by the total magnetization ( $\mathbf{M}$ ) of the nuclear spins is the phenomenon that is exploited in NMR spectroscopy and magnetic resonance imaging. Both use intense applied magnetic fields ( $\mathbf{H}_0$ ) in order to achieve dispersion and very high stability to deliver spectral resolution, the details of which are described by chemical shifts, the Zeeman effect, and Knight shifts (in metals).

NMR phenomena are also utilized in low-field NMR, NMR spectroscopy and MRI in the Earth's magnetic field (referred to as Earth's field NMR), and in several types of magnetometers.

## History

### Discovery

Nuclear magnetic resonance was first described and measured in molecular beams by Isidor Rabi in 1938.<sup>[1]</sup> Eight years later, in 1946, Felix Bloch and Edward Mills Purcell refined the technique for use on liquids and solids, for which they shared the Nobel Prize in physics in 1952.

Purcell had worked on the development and radar applications during World War II at Massachusetts Institute of Technology's Radiation Laboratory. His work during that project on the production and detection of RF energy, and on the absorption of such RF energy by matter, preceded his discovery of NMR.

They noticed that magnetic nuclei, like  $^1\text{H}$  and  $^{31}\text{P}$ , could absorb RF energy when placed in a magnetic field of a strength specific to the identity of the nuclei. When this absorption occurs, the nucleus is described as being *in resonance*. Different atomic nuclei within a molecule resonate at different (radio) frequencies for the same magnetic field strength. The observation of such magnetic resonance frequencies of the nuclei present in a molecule allows any trained user to discover essential, chemical and structural information about the molecule.

The development of nuclear magnetic resonance as a technique of analytical chemistry and biochemistry parallels the development of electromagnetic technology and its introduction into civilian use.

## Theory of nuclear magnetic resonance

### Nuclear spin and magnets

All nucleons, that is neutrons and protons, composing any atomic nucleus, have the intrinsic quantum property of spin. The overall spin of the nucleus is determined by the spin quantum number  $S$ . If the number of both the protons and neutrons in a given isotope are even then  $S = 0$ , i.e. there is no overall spin; just as electrons pair up in atomic orbitals, so do even numbers of protons or even numbers of neutrons (which are also spin- $1/2$  particles and hence fermions) pair up giving zero overall spin. Interestingly, however, a proton and neutron will have lower energy when their spins are parallel, **not anti-parallel**, as this parallel spin alignment does not infringe upon the Pauli principle, but instead has to do with the quark fine structure of these two nucleons. Therefore, the spin ground state for the deuteron (the deuterium nucleus, or the  $^2\text{H}$  isotope of hydrogen) --that has only a proton and a neutron-- corresponds to a spin value of **1**, *not of zero*; the single, isolated deuteron is therefore exhibiting an NMR absorption spectrum characteristic of a quadrupolar nucleus of spin **1**, which in the 'rigid' state at very low temperatures is a characteristic ('Pake') *doublet*, (not a singlet as for a single, isolated  $^1\text{H}$ , or any other isolated fermion or dipolar nucleus of spin  $1/2$ ). On the other hand, because of the Pauli principle, the (radioactive) tritium isotope has to have a pair of anti-parallel spin neutrons (of total spin zero for the neutron spin couple), plus a proton of spin  $1/2$ ; therefore, the character of the tritium nucleus ('triton') is again magnetic dipolar, *not quadrupolar*-- like its non-radioactive deuteron neighbor, and the tritium nucleus total spin value is again  $1/2$ , just like for the simpler, abundant hydrogen isotope,  $^1\text{H}$  nucleus (the *proton*). The NMR absorption (radio) frequency for tritium is however slightly higher for tritium than that of  $^1\text{H}$  because the tritium nucleus has a slightly higher gyromagnetic ratio than  $^1\text{H}$ . In many other cases of *non-radioactive* nuclei, the overall spin is also non-zero. For example, the  $^{27}\text{Al}$  nucleus has an overall spin value  $S = 5/2$ .

A non-zero spin is thus always associated with a non-zero magnetic moment ( $\mu$ ) via the relation  $\mu = gS$ , where  $g$  is the gyromagnetic ratio. It is this magnetic moment that allows the observation of NMR absorption spectra caused by transitions between nuclear spin levels. Most radioactive nuclei (with some rare exceptions) that have both even numbers of protons and even numbers of neutrons, also have zero nuclear magnetic moments--and also have zero magnetic dipole and quadrupole moments; therefore, such radioactive isotopes do not exhibit any NMR absorption spectra. Thus,  $^{14}\text{C}$ ,  $^{32}\text{P}$ , and  $^{36}\text{Cl}$  are examples of radioactive nuclear isotopes that have no NMR absorption, whereas  $^{13}\text{C}$ ,  $^{31}\text{P}$ ,  $^{35}\text{Cl}$  and  $^{37}\text{Cl}$  are stable nuclear isotopes that do exhibit NMR absorption spectra; the last two nuclei are quadrupolar nuclei whereas the preceding two nuclei ( $^{13}\text{C}$  and  $^{31}\text{P}$ ) are dipolar ones.

→ Electron spin resonance (ESR) is a related technique which detects transitions between electron spin levels instead of nuclear ones. The basic principles are similar; however, the instrumentation, data analysis and detailed theory are significantly different. Moreover, there is a much smaller number of molecules and materials with unpaired electron spins that exhibit ESR (or electron paramagnetic resonance (EPR)) absorption than those that have NMR absorption spectra. Significantly also, is the much greater sensitivity of ESR and EPR in comparison with NMR. Furthermore, ferromagnetic materials and thin films may exhibit 'very unusual', highly resolved ferromagnetic resonance (FMR) spectra, or ferromagnetic spin wave resonance (FSWR) excitations in non-crystalline solids such as ferromagnetic metallic glasses, well beyond the common single-transitions of most routine

NMR, FMR and EPR studies.<sup>[2] [3]</sup>

## Values of spin angular momentum

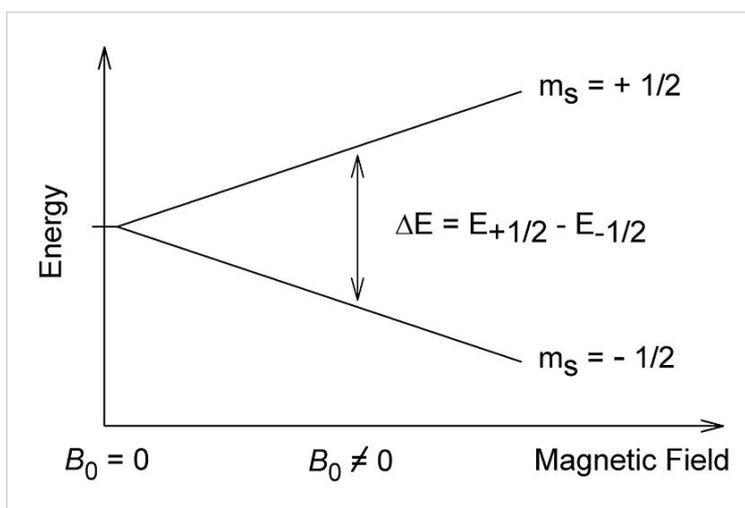
The angular momentum associated with nuclear spin is quantized. This means both that the magnitude of angular momentum is quantized (i.e.  $S$  can only take on a restricted range of values), and also that the orientation of the associated angular momentum is quantized. The associated quantum number is known as the magnetic quantum number,  $m$ , and can take values from  $+S$  to  $-S$ , in integer steps. Hence for any given nucleus, there is a total of  $2S + 1$  angular momentum states.

The z-component of the angular momentum vector ( $\mathbf{S}$ ) is therefore  $S_z = m\hbar$ , where  $\hbar$  is the reduced Planck constant. The z-component of the magnetic moment is simply:

$$\mu_z = gS_z = gm\hbar$$

## Spin behavior in a magnetic field

Consider nuclei which have a spin of one-half, like  $^1\text{H}$ ,  $^{13}\text{C}$  or  $^{19}\text{F}$ . The nucleus has two possible spin states:  $m = 1/2$  or  $m = -1/2$  (also referred to as spin-up and spin-down, or sometimes  $\alpha$  and  $\beta$  spin states, respectively). These states are degenerate, i.e. they have the same energy. Hence the number of atoms in these two states will be approximately equal at thermal equilibrium.



If a nucleus is placed in a magnetic field, however, the interaction between the nuclear magnetic moment and the external magnetic field mean the two states no longer have the same energy. The energy of a magnetic moment  $\boldsymbol{\mu}$  when in a magnetic field  $\mathbf{B}_0$  is given by:

$$E = -\boldsymbol{\mu} \cdot \mathbf{B}_0 = -\mu_z B_0 \cos \theta .$$

Usually  $\mathbf{B}_0$  is chosen to be aligned along the z axis, therefore  $\cos\theta=1$ :

$$E = -\mu_z B_0 ,$$

or alternatively:

$$E = -gm\hbar B_0 .$$

As a result the different nuclear spin states have different energies in a non-zero magnetic field. In hand-waving terms, we can talk about the two spin states of a spin  $1/2$  as being *aligned* either with or against the magnetic field. If  $g$  is positive (true for most isotopes) then  $m = 1/2$  is the lower energy state.

The energy difference between the two states is:

$$\Delta E = g\hbar B_0 ,$$

and this difference results in a small population bias toward the lower energy state.

### Magnetic resonance by nuclei

Resonant absorption by nuclear spins will occur only when electromagnetic radiation of the correct frequency (e.g., equaling the Larmor precession rate) is being applied to match the energy difference between the nuclear spin levels in a constant magnetic field of the appropriate strength. The energy of an absorbed photon is then  $E = h\nu_0$ , where  $\nu_0$  is the resonance radiofrequency that has to match (that is, it has to be equal to) the Larmor precession frequency  $\nu_L$  of the nuclear magnetization in the constant magnetic field  $\mathbf{H}_0$ . Hence, a magnetic resonance absorption will only occur when  $\Delta E = h\nu_0$ , which is when  $\nu_0 = gB_0/(2\pi)$ . Such magnetic resonance frequencies typically correspond to the radio frequency (or RF) range of the electromagnetic spectrum for magnetic fields up to  $\sim 20$  T. It is this magnetic resonant absorption which is detected in NMR.

### Nuclear shielding

It might appear from the above that all nuclei of the same nuclide (and hence the same  $g$ ) would resonate at the same frequency. This is not the case. The most important perturbation of the NMR frequency for applications of NMR is the 'shielding' effect of the surrounding electrons. In general, this electronic shielding reduces the magnetic field *at the nucleus* (which is what determines the NMR frequency).

As a result the energy gap is reduced, and the frequency required to achieve resonance is also reduced. This shift in the NMR frequency due to the electrons' molecular orbital coupling to the external magnetic field is called chemical shift, and it explains why NMR is able to probe the chemical structure of molecules which depends on the electron density distribution in the corresponding molecular orbitals. If a nucleus in a specific chemical group is shielded to a higher degree by a higher electron density of its surrounding molecular orbital, then its NMR frequency will be shifted "upfield" (that is, a lower chemical shift), whereas if it is less shielded by such surrounding electron density, then its NMR frequency will be shifted "downfield" (that is, a higher chemical shift).

Unless the local symmetry of such molecular orbitals is very high (leading to "isotropic" shift), the shielding effect will depend on the orientation of the molecule with respect to the external field ( $\mathbf{H}_0$ ). In solid-state NMR spectroscopy, magic angle spinning is required to average out this orientation dependence in order to obtain values close to the average chemical shifts. This is unnecessary in conventional NMR investigations of molecules, since rapid molecular tumbling averages out the chemical shift anisotropy (CSA). In this case, the term "average" chemical shift (ACS) is used.

### Relaxation

The process called population relaxation refers to nuclei that return to the thermodynamic state in the magnet. This process is also called  $T_1$ , "spin-lattice" or "longitudinal magnetic" relaxation, where  $T_1$  refers to the mean time for an individual nucleus to return to its thermal equilibrium state of the spins. Once the nuclear spin population is relaxed, it can be probed again, since it is in the initial, equilibrium (mixed) state.

The precessing nuclei can also fall out of alignment with each other (returning the net magnetization vector to a non-precessing field) and stop producing a signal. This is called  $T_2$  or *transverse relaxation*. Because of the difference in the actual relaxation mechanisms involved (for example, inter-molecular vs. intra-molecular magnetic dipole-dipole interactions),  $T_1$  is always longer than  $T_2$  (that is, slower spin-lattice relaxation, for

example because of smaller dipole-dipole interaction effects). In practice, the value of  $T_2^*$  which is the actually observed decay time of the observed NMR signal, or free induction decay, (to  $1/e$  of the initial amplitude immediately after the resonant RF pulse)-- also depends on the static magnetic field inhomogeneity, which is quite significant. (There is also a smaller but significant contribution to the observed FID shortening from the RF inhomogeneity of the resonant pulse). In the corresponding FT-NMR spectrum-- meaning the Fourier transform of the free induction decay--the  $T_2^*$  time is inversely related to the width of the NMR signal in frequency units. Thus, a nucleus with a long  $T_2$  relaxation time gives rise to a very sharp NMR peak in the FT-NMR spectrum for a very homogeneous ("well-shimmed") static magnetic field, whereas nuclei with shorter  $T_2$  values give rise to broad FT-NMR peaks even when the magnet is shimmed well. Both  $T_1$  and  $T_2$  depend on the rate of molecular motions as well as the gyromagnetic ratios of both the resonating and their strongly interacting, next-neighbor nuclei that are not at resonance.

## NMR spectroscopy

NMR spectroscopy is one of the principal techniques used to obtain physical, chemical, electronic and structural information about molecules due to either the chemical shift Zeeman effect, or the Knight shift effect, or a combination of both, on the resonant frequencies of the nuclei present in the sample. It is a powerful technique that can provide detailed information on the topology, dynamics and three-dimensional structure of molecules in solution and the solid state. Thus, structural and dynamic information is obtainable (with or without "magic angle" spinning (MAS)) from NMR studies of quadrupolar nuclei (that is, those nuclei with spin  $S > 1/2$ ) even in the presence of magnetic dipole-dipole interaction broadening (or simply, dipolar broadening) which is always much smaller than the quadrupolar interaction strength because it is a magnetic vs. an electric interaction effect.

Additional structural and chemical information may be obtained by performing double-quantum NMR experiments for quadrupolar nuclei such as  $^2\text{H}$ . Also, nuclear magnetic resonance is one of the techniques that has been used to design quantum automata, and also build elementary  $\rightarrow$  quantum computers.<sup>[4] [5]</sup>

## Continuous wave (CW) spectroscopy

In its first few decades, nuclear magnetic resonance spectrometers used a technique known as continuous-wave spectroscopy (CW spectroscopy). Although NMR spectra could be, and have been, obtained using a fixed magnetic field and sweeping the frequency of the electromagnetic radiation, this more typically involved using a fixed frequency source and varying the current (and hence magnetic field) in an electromagnet to observe the resonant absorption signals. This is the origin of the anachronistic, but still common, "high" and "low" field terminology for low frequency and high frequency regions respectively of the NMR spectrum.

CW spectroscopy is inefficient in comparison to Fourier techniques (see below) as it probes the NMR response at individual frequencies in succession. As the NMR signal is intrinsically weak, the observed spectra suffer from a poor signal-to-noise ratio. This can be mitigated by signal averaging i.e. adding the spectra from repeated measurements. While the NMR signal is constant between scans and so adds linearly, the random noise adds more slowly—as the square-root of the number of spectra (see Random walk). Hence the

overall ratio of the signal to the noise increases as the square-root of the number of spectra measured.

### Fourier transform spectroscopy

Most applications of NMR involve full NMR spectra, that is, the intensity of the NMR signal as a function of frequency. Early attempts to acquire the NMR spectrum more efficiently than simple CW methods involved irradiating simultaneously with more than one frequency. It was soon realized, however, that a simpler solution was to use short pulses of radio-frequency (centered at the middle of the NMR spectrum). In simple terms, a short square pulse of a given "carrier" frequency "contains" a range of frequencies centered about the carrier frequency, with the range of excitation (bandwidth) being inversely proportional to the pulse duration (the Fourier transform (FT) of an approximate square wave contains contributions from all the frequencies in the neighborhood of the principal frequency). The restricted range of the NMR frequencies made it relatively easy to use short (millisecond to microsecond) radiofrequency (RF) pulses to excite the entire NMR spectrum.

Applying such a pulse to a set of nuclear spins simultaneously excites all the single-quantum NMR transitions. In terms of the net magnetization vector, this corresponds to tilting the magnetization vector away from its equilibrium position (aligned along the external magnetic field). The out-of-equilibrium magnetization vector precesses about the external magnetic field vector at the NMR frequency of the spins. This oscillating magnetization vector induces a current in a nearby pickup coil, creating an electrical signal oscillating at the NMR frequency. This signal is known as the free induction decay (FID) and contains the vector-sum of the NMR responses from all the excited spins. In order to obtain the frequency-domain NMR spectrum (NMR absorption intensity vs. NMR frequency) this time-domain signal (intensity vs. time) must be FTed. Fortunately the development of FT NMR coincided with the development of digital computers and Fast Fourier Transform algorithms.

Richard R. Ernst was one of the pioneers of pulse (FT) NMR and won a Nobel Prize in chemistry in 1991 for his work on FT NMR and his development of multi-dimensional NMR (see below).

### Multi-dimensional NMR Spectroscopy

The use of pulses of different shapes, frequencies and durations in specifically-designed patterns or *pulse sequences* allows the spectroscopist to extract many different types of information about the molecule. Multi-dimensional nuclear magnetic resonance spectroscopy is a kind of FT NMR in which there are at least two pulses and, as the experiment is repeated, the pulse sequence is varied. In *multidimensional nuclear magnetic resonance* there will be a sequence of pulses and, at least, one variable time period. In three dimensions, two time sequences will be varied. In four dimensions, three will be varied.

There are many such experiments. In one, these time intervals allow (amongst other things) magnetization transfer between nuclei and, therefore, the detection of the kinds of nuclear-nuclear interactions that allowed for the magnetization transfer. Interactions that can be detected are usually classified into two kinds. There are *through-bond* interactions and *through-space* interactions, the latter usually being a consequence of the nuclear

Overhauser effect. Experiments of the nuclear Overhauser variety may be employed to establish distances between atoms, as for example by  $\rightarrow$  2D-FT NMR of molecules in solution.

Although the fundamental concept of  $\rightarrow$  2D-FT NMR was proposed by Professor Jean Jeener from the Free University of Brussels at an International Conference, this idea was largely developed by Richard Ernst who won the 1991 Nobel prize in Chemistry for his work in FT NMR, including multi-dimensional FT NMR, and especially  $\rightarrow$  2D-FT NMR of small molecules.<sup>[6]</sup> Multi-dimensional FT NMR experiments were then further developed into powerful methodologies for studying biomolecules in solution, in particular for the determination of the structure of biopolymers such as proteins or even small nucleic acids.<sup>[7]</sup>

Kurt Wüthrich shared (with John B. Fenn) in 2002 the Nobel Prize in Chemistry for his work in protein FT NMR in solution.

### **Solid-state NMR spectroscopy**

This technique complements biopolymer X-ray crystallography in that it is frequently applicable to biomolecules in a liquid or liquid crystal phase, whereas crystallography, as the name implies, is performed on molecules in a solid phase. Though nuclear magnetic resonance is used to study solids, extensive atomic-level biomolecular structural detail is especially challenging to obtain in the solid state. There is little signal averaging by thermal motion in the solid state, where most molecules can only undergo restricted vibrations and rotations at room temperature, each in a slightly different electronic environment, therefore exhibiting a different NMR absorption peak. Such a variation in the electronic environment of the resonating nuclei results in a blurring of the observed spectra--which is often only a broad Gaussian band for non-quadrupolar spins in a solid-- thus making the interpretation of such "dipolar" and "chemical shift anisotropy" (CSA) broadened spectra either very difficult or impossible.

Professor Raymond Andrew at Nottingham University in UK pioneered the development of high-resolution solid-state nuclear magnetic resonance. He was the first to report the introduction of the MAS (magic angle sample spinning; MASS) technique that allowed him to achieve spectral resolution in solids sufficient to distinguish between chemical groups with either different chemical shifts or distinct Knight shifts. In MASS, the sample is spun at several kilohertz around an axis that makes the so-called magic angle  $\theta_m$  (which is  $\sim 54.74^\circ$ , where  $\cos^2\theta_m = 1/3$ , or  $3\cos^2\theta_m - 1 = 0$ ) with respect to the direction of the static magnetic field  $\mathbf{H}_0$ ; as a result of such magic angle sample spinning, the chemical shift anisotropy bands are averaged to their corresponding average (isotropic) chemical shift values. The above expression involving  $\cos^2\theta_m$  has its origin in a calculation that predicts the magnetic dipolar interaction effects to cancel out for the specific value of  $\theta_m$  called the magic angle. One notes that correct alignment of the sample rotation axis as close as possible to  $\theta_m$  is essential for cancelling out the dipolar interactions whose strength for angles sufficiently far from  $\theta_m$  is usually greater than  $\sim 10$  kHz for C-H bonds in solids, for example, and it is thus greater than their CSA values.

A concept developed by Sven Hartmann and Erwin Hahn was utilized in transferring magnetization from protons to less sensitive nuclei (popularly known as cross-polarization) by M.G. Gibby, Alex Pines and John S. Waugh. Then, Jake Schaefer and Ed Stejskal demonstrated also the powerful use of cross-polarization under MASS conditions which is

now routinely employed to detect low-abundance and low-sensitivity nuclei.

## Sensitivity

Because the intensity of nuclear magnetic resonance signals and, hence, the sensitivity of the technique depends on the strength of the magnetic field the technique has also advanced over the decades with the development of more powerful magnets. Advances made in audio-visual technology have also improved the signal-generation and processing capabilities of newer machines.

As noted above, the sensitivity of nuclear magnetic resonance signals is also dependent on the presence of a magnetically-susceptible nuclide and, therefore, either on the natural abundance of such nuclides or on the ability of the experimentalist to artificially enrich the molecules, under study, with such nuclides. The most abundant naturally-occurring isotopes of hydrogen and phosphorus (for example) are both magnetically susceptible and readily useful for nuclear magnetic resonance spectroscopy. In contrast, carbon and nitrogen have useful isotopes but which occur only in very low natural abundance.

Other limitations on sensitivity arise from the quantum-mechanical nature of the phenomenon. For quantum states separated by energy equivalent to radio frequencies, thermal energy from the environment causes the populations of the states to be close to equal. Since incoming radiation is equally likely to cause stimulated emission (a transition from the upper to the lower state) as absorption, the NMR effect depends on an excess of nuclei in the lower states. Several factors can reduce sensitivity, including

- Increasing temperature, which evens out the population of states. Conversely, low temperature NMR can sometimes yield better results than room-temperature NMR, providing the sample remains liquid.
- Saturation of the sample with energy applied at the resonant radiofrequency. This manifests in both CW and pulsed NMR; in the first, CW, case this happens by using too much continuous power that keeps the upper spin levels completely populated; in the second case, saturation occurs by pulsing too frequently --without allowing time for the nuclei to return to thermal equilibrium through spin-lattice relaxation. For nuclei such as  $^{29}\text{Si}$  this is a serious practical problem as the relaxation time is measured in seconds; for protons in "pure" ice, or  $^{19}\text{F}$  in high-purity (undoped) LiF crystals the spin-lattice relaxation time can be on the order of an hour or longer. The use of shorter RF pulses that tip the magnetization by less than  $90^\circ$  can partially solve the problem by allowing spectral acquisition without the complete loss of NMR signal.
- Non-magnetic effects, such as electric-quadrupole coupling of spin-1 and spin- $\frac{3}{2}$  nuclei with their local environment, which broaden and weaken absorption peaks.  $^{14}\text{N}$ , an abundant spin-1 nucleus, is difficult to study for this reason. High resolution NMR instead probes molecules using the rarer  $^{15}\text{N}$  isotope, which has spin- $\frac{1}{2}$ .

## Isotopes

Many chemical elements can be used for NMR analysis.<sup>[8]</sup>

### Commonly used nuclei:

- $^1\text{H}$ , the most commonly used, very useful. Highly abundant, the most sensitive nucleus apart from tritium ( $^3\text{H}$ ) which is not commonly used as it is unstable and radioactive. Narrow chemical shift with sharp signals. In particular, the  $^1\text{H}$  signal is used in magnetic resonance imaging.
- $^2\text{H}$ , commonly used in the form of deuterated solvents to avoid interference of solvents in measurement of  $^1\text{H}$ . Also used in determining the behavior of lipids in lipid membranes and other solids or liquid crystals as it is a relatively non-perturbing label which can selectively replace  $^1\text{H}$ .
- $^3\text{He}$ , very sensitive. Low percentage in natural helium, has to be enriched. Used mainly in studies of endohedral fullerenes.
- $^{10}\text{B}$ , lower sensitivity than  $^{11}\text{B}$ . Quartz tubes must be used as borosilicate glass interferes with measurement.
- $^{11}\text{B}$ , more sensitive than  $^{10}\text{B}$ , yields sharper signals. Quartz tubes must be used as borosilicate glass interferes with measurement.
- $^{13}\text{C}$ , commonly used. There is a low percentage in natural carbon, therefore spectrum acquisition on unlabelled takes a long time. Frequently used for labeling of compounds in synthetic and metabolic studies. Has low sensitivity and wide chemical shift, yields sharp signals. Low percentage makes it useful by preventing spin-spin couplings and makes the spectrum appear less crowded. Slow relaxation means that spectra are not integrable unless long acquisition times are used.
- $^{14}\text{N}$ , medium sensitivity nucleus with wide chemical shift. Its large quadrupole moment interferes in acquisition of high resolution spectra, limiting usefulness to smaller molecules and functional groups with a high degree of symmetry such as the headgroups of lipids.
- $^{15}\text{N}$ , relatively commonly used. Can be used for labeling compounds. Nucleus very insensitive but yields sharp signals. Low percentage in natural nitrogen together with low sensitivity requires high concentrations or expensive isotope enrichment.
- $^{17}\text{O}$ , low sensitivity and very low natural abundance. Used in metabolic and biochemical studies.
- $^{19}\text{F}$ , relatively commonly measured. Sensitive, yields sharp signals, has wide chemical shift.
- $^{31}\text{P}$ , 100% of natural phosphorus. Medium sensitivity, wide chemical shift range, yields sharp lines. Used in biochemical studies.
- $^{35}\text{Cl}$  and  $^{37}\text{Cl}$ , broad signal.  $^{35}\text{Cl}$  significantly more sensitive, preferred over  $^{37}\text{Cl}$  despite its slightly broader signal. Organic chlorides yield very broad signals, its use is limited to inorganic and ionic chlorides and very small organic molecules.
- $^{43}\text{Ca}$ , used in biochemistry to study calcium binding to DNA, proteins, etc. Moderately sensitive, very low natural abundance.
- $^{195}\text{Pt}$ , used in studies of catalysts and complexes.

**Other nuclei** (usually used in the studies of their complexes and chemical binding, or to detect presence of the element):

- $^6\text{Li}$ ,  $^7\text{Li}$
- $^9\text{Be}$

- $^{19}\text{F}$
- $^{21}\text{Ne}$
- $^{23}\text{Na}$
- $^{25}\text{Mg}$
- $^{27}\text{Al}$
- $^{29}\text{Si}$
- $^{31}\text{P}$
- $^{33}\text{S}$
- $^{39}\text{K}$ ,  $^{40}\text{K}$ ,  $^{41}\text{K}$
- $^{45}\text{Sc}$
- $^{47}\text{Ti}$ ,  $^{49}\text{Ti}$
- $^{50}\text{V}$ ,  $^{51}\text{V}$
- $^{53}\text{Cr}$
- $^{53}\text{Mn}$
- $^{57}\text{Fe}$
- $^{59}\text{Co}$
- $^{61}\text{Ni}$
- $^{63}\text{Cu}$ ,  $^{65}\text{Cu}$
- $^{67}\text{Zn}$
- $^{69}\text{Ga}$ ,  $^{71}\text{Ga}$
- $^{73}\text{Ge}$
- $^{77}\text{Se}$
- $^{81}\text{Br}$
- $^{87}\text{Rb}$
- $^{87}\text{Sr}$
- $^{95}\text{Mo}$
- $^{109}\text{Ag}$
- $^{113}\text{Cd}$
- $^{125}\text{Te}$
- $^{127}\text{I}$
- $^{133}\text{Cs}$
- $^{135}\text{Ba}$ ,  $^{137}\text{Ba}$
- $^{139}\text{La}$
- $^{183}\text{W}$
- $^{199}\text{Hg}$

## Applications

### Medicine

The use of nuclear magnetic resonance best known to the general public is magnetic resonance imaging for medical diagnosis and MR Microscopy in research settings, however, it is also widely used in chemical studies, notably in NMR spectroscopy such as proton NMR, carbon-13 NMR, deuterium NMR and phosphorus-31 NMR. Biochemical information can also be obtained from living tissue (e.g. human brain tumours) with the technique known as in vivo magnetic resonance spectroscopy or chemical shift NMR Microscopy.

These studies are possible because nuclei are surrounded by orbiting electrons, which are also spinning charged particles such as magnets and, so, will partially shield the nuclei. The

amount of shielding depends on the exact local environment. For example, a hydrogen bonded to an oxygen will be shielded differently than a hydrogen bonded to a carbon atom. In addition, two hydrogen nuclei can interact via a process known as spin-spin coupling, if they are on the same molecule, which will split the lines of the spectra in a recognizable way.

## Chemistry

By studying the peaks of nuclear magnetic resonance spectra, chemists can determine the structure of many compounds. It can be a very selective technique, distinguishing among many atoms within a molecule or collection of molecules of the same type but which differ only in terms of their local chemical environment. See the articles on carbon-13 NMR and proton NMR for detailed discussions.

By studying  $T_2^*$  information, a chemist can determine the identity of a compound by comparing the observed nuclear precession frequencies to known frequencies. Further structural data can be elucidated by observing *spin-spin coupling*, a process by which the precession frequency of a nucleus can be influenced by the magnetization transfer from nearby nuclei. Spin-spin coupling is most commonly observed in NMR involving common isotopes, such as Hydrogen-1 ( $^1\text{H}$  NMR).

Because the nuclear magnetic resonance *timescale* is rather slow, compared to other spectroscopic methods, changing the temperature of a  $T_2^*$  experiment can also give information about fast reactions, such as the Cope rearrangement or about structural dynamics, such as ring-flipping in cyclohexane. At low enough temperatures, a distinction can be made between the axial and equatorial hydrogens in cyclohexane.

An example of nuclear magnetic resonance being used in the determination of a structure is that of buckminsterfullerene (often called "buckyballs", composition  $\text{C}_{60}$ ). This now famous form of carbon has 60 carbon atoms forming a sphere. The carbon atoms are all in identical environments and so should see the same internal H field. Unfortunately, buckminsterfullerene contains no hydrogen and so  $^{13}\text{C}$  nuclear magnetic resonance has to be used.  $^{13}\text{C}$  spectra require longer acquisition times since carbon-13 is not the common isotope of carbon (unlike hydrogen, where  $^1\text{H}$  is the common isotope). However, in 1990 the spectrum was obtained by R. Taylor and co-workers at the University of Sussex and was found to contain a single peak, confirming the unusual structure of buckminsterfullerene.<sup>[9]</sup>

## Non-destructive testing

Nuclear magnetic resonance is extremely useful for analyzing samples non-destructively. Radio waves and static magnetic fields easily penetrate many types of matter and anything that is not inherently ferromagnetic. For example, various expensive biological samples, such as nucleic acids, including RNA and DNA, or proteins, can be studied using nuclear magnetic resonance for weeks or months before using destructive biochemical experiments. This also makes nuclear magnetic resonance a good choice for analyzing dangerous samples.

## Data acquisition in the petroleum industry

Another use for nuclear magnetic resonance is data acquisition in the petroleum industry for petroleum and natural gas exploration and recovery. A borehole is drilled into rock and sedimentary strata into which nuclear magnetic resonance logging equipment is lowered. Nuclear magnetic resonance analysis of these boreholes is used to measure rock porosity, estimate permeability from pore size distribution and identify pore fluids (water, oil and gas). These instruments are typically low field NMR spectrometers.

## Process control

NMR has now entered the arena of real-time process control and process optimization in oil refineries and petrochemical plants. Two different types of NMR analysis are utilized to provide real time analysis of feeds and products in order to control and optimize unit operations. Time-domain NMR (TD-NMR) spectrometers operating at low field (2–20 MHz for  $^1\text{H}$ ) yield free induction decay data that can be used to determine absolute hydrogen content values, rheological information, and component composition. These spectrometers are used in mining, polymer production, cosmetics and food manufacturing as well as coal analysis. High resolution FT-NMR spectrometers operating in the 60 MHz range with shielded permanent magnet systems yield high resolution  $^1\text{H}$  NMR spectra of refinery and petrochemical streams. The variation observed in these spectra with changing physical and chemical properties is modelled utilizing chemometrics to yield predictions on unknown samples. The prediction results are provided to control systems via analogue or digital outputs from the spectrometer.

## Earth's field NMR

In the Earth's magnetic field, NMR frequencies are in the audio frequency range. EFNMR is typically stimulated by applying a relatively strong dc magnetic field pulse to the sample and, following the pulse, analysing the resulting low frequency alternating magnetic field that occurs in the Earth's magnetic field due to free induction decay (FID). These effects are exploited in some types of magnetometers, EFNMR spectrometers, and MRI imagers. Their inexpensive portable nature makes these instruments valuable for field use and for teaching the principles of NMR and MRI.

## Quantum computing

**NMR quantum computing** uses the spin states of molecules as qubits. NMR differs from other implementations of quantum computers in that it uses an ensemble of systems, in this case molecules. The ensemble is initialized to be the thermal equilibrium state (see quantum statistical mechanics).

## Magnetometers

Various magnetometers use NMR effects to measure magnetic fields, including proton precession magnetometers (PPM) (also known as proton magnetometers), and Overhauser magnetometers. See also Earth's field NMR.

## Makers of NMR equipment

Major NMR instrument makers include Oxford Instruments, Bruker, SpinLock SRL, General Electric, JEOL, Kimble Chase, Philips, Siemens AG, Varian, Inc. and SpinCore Technologies, Inc.

## See also

- Carbon-13 NMR
  - Chemical shift
  - → 2D-FT NMRI and Spectroscopy
  - Dynamic Nuclear Polarisation (DNP)
  - Earth's field NMR (EFNMR)
  - Electromagnetism
  - Electron spin/paramagnetic resonance
  - Ferromagnetic resonance
  - Free induction decay (FID)
  - Gyromagnetic ratio
  - Hyperpolarization
  - In vivo magnetic resonance spectroscopy (MRS)
  - J-coupling
  - Larmor equation (Not to be confused with Larmor formula).
  - Larmor precession
  - Low field NMR
  - Magic angle spinning
  - Magnetic resonance imaging (MRI)
  - Magnetometer
  - NMR spectra database
  - NMR spectroscopy
  - NMR Microscopy
  - Nuclear quadrupole resonance (NQR)
  - Overhauser magnetometer
  - Protein dynamics
  - Protein NMR
  - Proton NMR
  - Proton precession magnetometer (PPM)
  - Proton magnetometer
  - Rabi cycle
  - Relaxometry
  - Relaxation (NMR)
  - Solid-state NMR
  - Stark effect
  - Zeeman effect
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## Notes

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## External links

- NMR/MRI tutorial (<http://www.cis.rit.edu/htbooks/nmr/inside.htm>)
- Richard Ernst, NL - Developer of Multidimensional NMR techniques (<http://www.vega.org.uk/video/programme/21>) Freeview video provided by the Vega Science Trust.
- 2D-FT NMR , MR--Imaging and related Nobel awards (<http://planetphysics.org/encyclopedia/2DFTImaging.html>) Illustrated applications of 2D-FT NMR and MR-Imaging.
- 'An Interview with Kurt Wuthrich' (<http://www.vega.org.uk/video/programme/115>) Freeview video by the Vega Science Trust (Wüthrich was awarded a Nobel Prize in

- Chemistry in 2002 "for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution").
- *Acronyms, Abbreviations and Initialisms - Nuclear Magnetic Resonance* (<http://abbreviations.oxid.ro/Academic-and-Science/Nuclear-Magnetic-Resonance/>)
  - A free interactive simulation of NMR principles (<http://vam.anest.ufl.edu/forensic/nmr.html>)
  - Bionmr.com - discussion of NMR applications in biological systems (<http://www.bionmr.com>)
  - NMR Wiki (<http://www.nmrwiki.org>) Open NMR,EPR,MRI web project
  - The International Society of Magnetic Resonance (<http://www.ismar.org>)
  - AUREMOL (Universitaet Regensburg) (<http://www.auremol.de>)
  - NMR processing software from ACD/Labs (<http://www.acdlabs.com/>) for 1D ([http://www.acdlabs.com/products/spec\\_lab/exp\\_spectra/nmr/](http://www.acdlabs.com/products/spec_lab/exp_spectra/nmr/)) and 2D ([http://www.acdlabs.com/products/spec\\_lab/exp\\_spectra/2d\\_nmr/](http://www.acdlabs.com/products/spec_lab/exp_spectra/2d_nmr/)) NMR spectra. DB interface available.
  - NMR Prediction software ACD/NMR Predictors ([http://www.acdlabs.com/products/spec\\_lab/predict\\_nmr/](http://www.acdlabs.com/products/spec_lab/predict_nmr/))
  - Automated elucidation of chemical structures ACD/Structure Elucidator ([http://www.acdlabs.com/products/spec\\_lab/complex\\_tasks/str\\_elucidator/](http://www.acdlabs.com/products/spec_lab/complex_tasks/str_elucidator/))
  - NMR simulation software QSim (<http://www.bpc.lu.se/QSim>)
  - Free software for simulation of spin coupled multiplets and DNMR spectra WINDNMR-Pro (<http://www.chem.wisc.edu/areas/reich/plt/windnmr.htm>)
  - NMR processing software NMRPipe (<http://spin.niddk.nih.gov/bax/software/NMRPipe>)
  - BMRB (<http://www.bmrb.wisc.edu/>) BioMagResBank - A repository for experimental data from NMR spectroscopy of proteins, peptides, nucleic acids and small biomolecules.
  - RMN (<http://www.grandinetti.org/Software/RMN>) - An NMR data processing program for the Macintosh.
  - Applications of Time-Domain NMR in Process Control ([http://www.process-nmr.com/time\\_domain\\_process\\_nmr\\_spectrom.htm](http://www.process-nmr.com/time_domain_process_nmr_spectrom.htm))
  - Applications of High Resolution FT-NMR in Real-Time Process Control (<http://www.process-nmr.com/process.htm>)
  - Introduction to Process NMR (<http://www.process-nmr.com/pdfs/Edwards EAS-2007 Intro 11-14-07.pdf>)
  - NMR and Diesel Manufacturing (<http://www.process-nmr.com/pdfs/Giammatteo EAS 2007.pdf>)
  - HWB-NMR (<http://nmr.bham.ac.uk>) Henry Wellcome Building for Biomolecular NMR, Birmingham, UK.
  - CARA (<http://www.nmr.ch/>) - Computer Aided Resonance Assignment, freeware, developed at the group of Prof. Kurt Wüthrich
  - CCPN (<http://www.ccpn.ac.uk/>) - The Collaborative Computing Project for NMR, based at the University of Cambridge, UK
  - Vanderbilt Structural Biology (<http://structbio.vanderbilt.edu>) General site for structural biology at Vanderbilt University. NMR, x-ray crystallography, and computational biology all included.
  - Janocchio (<http://janocchio.sourceforge.net>) Conformation-dependent coupling and NOE prediction for small molecules.
-

- Earth's field NMR (EFNMR) ([http://www.teachspin.com/instruments/earths\\_field\\_NMR/index.shtml](http://www.teachspin.com/instruments/earths_field_NMR/index.shtml))
- Animation of NMR spin  $\frac{1}{2}$  precession (<http://www.chem.queensu.ca/FACILITIES/NMR/nmr/webcourse/precess.htm>)
- Article on helium scarcity and potential effects on NMR and MRI communities (<http://www.ebyte.it/stan/blog.html#08Feb29>)
- CERMAX - CEntro de Ressonancia Magnetica Antonio Xavier (<http://cermax.itqb.unl.pt>)

## 2D-FT NMRI and Spectroscopy

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**2D-FT Nuclear magnetic resonance imaging (2D-FT NMRI)**, or **Two-dimensional Fourier transform nuclear magnetic resonance imaging (NMRI)**, is primarily a non—invasive imaging technique most commonly used in biomedical research and medical radiology/nuclear medicine/MRI to visualize structures and functions of the living systems and single cells. For example it can provides fairly detailed images of a human body in any selected cross-sectional plane, such as longitudinal, transversal, sagittal, etc. The basic NMR phenomenon or physical principle<sup>[1]</sup> is essentially the same in N(MRI), → nuclear magnetic resonance/→ FT (NMR) spectroscopy, topical NMR, or even in Electron Spin Resonance /EPR; however, the details are significantly different at present for EPR, as only in the early days of NMR the static magnetic field was scanned for obtaining spectra, as it is still the case in many EPR or ESR spectrometers. NMRI, on the other hand, often utilizes a linear magnetic field gradient to obtain an image that combines the visualization of molecular structure and dynamics. It is this dynamic aspect of NMRI, as well as its highest sensitivity for the  $^1\text{H}$  nucleus that distinguishes it very dramatically from X-ray CAT scanning that 'misses' hydrogens because of their very low X-ray scattering factor.

Thus, NMRI provides much greater contrast especially for the different soft tissues of the body than computed tomography (CT) as its most sensitive option observes the nuclear spin distribution and dynamics of highly mobile molecules that contain the naturally abundant, stable hydrogen isotope  $^1\text{H}$  as in plasma water molecules, blood, disolved metabolites and fats. This approach makes it most useful in cardiovascular, oncological (cancer), neurological (brain), musculoskeletal, and cartilage imaging. Unlike CT, it uses no ionizing radiation, and also unlike nuclear imaging it does not employ any radioactive isotopes. Some of the first MRI images reported were published in 1973<sup>[2]</sup> and the first study performed on a human took place on July 3, 1977.<sup>[3]</sup> Earlier papers were also published by Sir Peter Mansfield<sup>[4]</sup> in UK (Nobel Laureate in 2003), and R. Damadian in the USA<sup>[5]</sup>, (together with an approved patent for 'fonar', or magnetic imaging). The detailed physical theory of NMRI was published by Peter Mansfield in 1973<sup>[6]</sup>. Unpublished 'high-resolution' (50 micron resolution) images of other living systems, such as hydrated wheat grains, were also obtained and communicated in UK in 1977-1979, and were subsequently confirmed by articles published in *Nature* by Peter Callaghan.

## NMR Principle

Certain nuclei such as  $^1\text{H}$  nuclei, or 'fermions' have spin-1/2, because there are two spin states, referred to as "up" and "down" states. The nuclear magnetic resonance absorption phenomenon occurs when samples containing such nuclear spins are placed in a static magnetic field and a very short radiofrequency pulse is applied with a center, or carrier, frequency matching that of the transition between the up and down states of the spin-1/2  $^1\text{H}$  nuclei that were polarized by the static magnetic field. [7] Very low field schemes have also been recently reported. [8]



Advanced 4.7 T clinical diagnostics and biomedical research NMR Imaging instrument.

## Chemical Shifts

NMR is a very useful family of techniques for chemical and biochemical research because of the chemical shift; this effect consists in a frequency shift of the nuclear magnetic resonance for specific chemical groups or atoms as a result of the partial shielding of the corresponding nuclei from the applied, static external magnetic field by the electron orbitals (or molecular orbitals) surrounding such nuclei present in the chemical groups. Thus, the higher the electron density surrounding a specific nucleus the larger the chemical shift will be. The resulting magnetic field at the nucleus is thus lower than the applied external magnetic field and the resonance frequencies observed as a result of such shielding are lower than the value that would be observed in the absence of any electronic orbital shielding. Furthermore, in order to obtain a chemical shift value independent of the strength of the applied magnetic field and allow for the direct comparison of spectra obtained at different magnetic field values, the chemical shift is defined by the ratio of the strength of the local magnetic field value at the observed (electron orbital-shielded) nucleus by the external magnetic field strength,  $H_{loc}/H_0$ . The first NMR observations of the chemical shift, with the correct physical chemistry interpretation, were reported for  $^{19}\text{F}$  containing compounds in the early 1950s by Herbert S. Gutowsky and Charles P. Slichter from the University of Illinois at Urbana (USA).

A related effect in metals is called the Knight shift, which is due only to the conduction electrons. Such conduction electrons present in metals induce an "additional" local field at the nuclear site, due to the spin re-orientation of the conduction electrons in the presence of the applied (constant), external magnetic field. This is only broadly 'similar' to the chemical shift in either solutions or diamagnetic solids.

## NMR Imaging Principles

A number of methods have been devised for combining magnetic field gradients and radiofrequency pulsed excitation to obtain an image. Two major methods involve either 2D-FT or 3D-FT<sup>[9]</sup> reconstruction from projections, somewhat similar to Computed Tomography, with the exception of the image interpretation that in the former case must include dynamic and relaxation/contrast enhancement information as well. Other schemes involve building the NMR image either point-by-point or line-by-line. Some schemes use instead gradients in the rf field rather than in the static magnetic field. The majority of NMR images routinely obtained are either by the Two-Dimensional Fourier Transform (2D-FT) technique<sup>[10]</sup> (with slice selection), or by the Three-Dimensional Fourier Transform (3D-FT) techniques that are however much more time consuming at present. 2D-FT NMRI is sometime called in common parlance a "spin-warp". An NMR image corresponds to a spectrum consisting of a number of 'spatial frequencies' at different locations in the sample investigated, or in a patient.<sup>[11]</sup> A two-dimensional Fourier transformation of such a "real" image may be considered as a representation of such "real waves" by a matrix of spatial frequencies known as the k-space. We shall see next in some mathematical detail how the 2D-FT computation works to obtain 2D-FT NMR images.

## Two-dimensional Fourier transform imaging and spectroscopy

A two-dimensional Fourier transform (2D-FT) is computed numerically or carried out in two stages, both involving 'standard', one-dimensional Fourier transforms. However, the second stage Fourier transform is not the inverse Fourier transform (which would result in the original function that was transformed at the first stage), but a Fourier transform in a second variable—which is 'shifted' in value—relative to that involved in the result of the first Fourier transform. Such 2D-FT analysis is a very powerful method for both NMRI and two-dimensional  $\rightarrow$  nuclear magnetic resonance spectroscopy (2D-FT NMRS)<sup>[12]</sup> that allows the three-dimensional reconstruction of polymer and biopolymer structures at atomic resolution.<sup>[13]</sup> for molecular weights (Mw) of dissolved biopolymers in aqueous solutions (for example) up to about 50,000 Mw. For larger biopolymers or polymers, more complex methods have been developed to obtain limited structural resolution needed for partial 3D-reconstructions of higher molecular structures, e.g. for up 900,000 Mw or even oriented microcrystals in aqueous suspensions or single crystals; such methods have also been reported for *in vivo* 2D-FT NMR spectroscopic studies of algae, bacteria, yeast and certain mammalian cells, including human ones. The 2D-FT method is also widely utilized in optical spectroscopy, such as *2D-FT NIR hyperspectral imaging* (2D-FT NIR-HS), or in MRI imaging for research and clinical, diagnostic applications in Medicine. In the latter case, 2D-FT  $\rightarrow$  NIR-HS has recently allowed the identification of single, malignant cancer cells surrounded by healthy human breast tissue at about 1 micron resolution, well-beyond the resolution obtainable by 2D-FT NMRI for such systems in the limited time available for such diagnostic investigations (and also in magnetic fields up to the FDA approved magnetic field strength  $H_0$  of 4.7 T, as shown in the top image of the state-of-the-art NMRI instrument). A more precise mathematical definition of the 'double' (2D) Fourier transform involved in both 2D NMRI and 2D-FT NMRS is specified next, and a precise example follows this generally accepted definition.

## 2D-FT Definition

A 2D-FT, or two-dimensional Fourier transform, is a standard Fourier transformation of a function of two variables,  $\mathbf{f}(x_1, x_2)$ , carried first in the first variable  $x_1$ , followed by the Fourier transform in the second variable  $x_2$  of the resulting function  $\mathbf{F}(s_1, s_2)$ . Note that in the case of both 2D-FT NMRI and 2D-FT NMRS the two independent variables in this definition are in the time domain, whereas the results of the two successive Fourier transforms have, of course, frequencies as the independent variable in the NMRS, and ultimately spatial coordinates for both 2D NMRI and 2D-FT NMRS following computer structural reconstructions based on special algorithms that are different from FT or 2D-FT. Moreover, such structural algorithms are different for 2D NMRI and 2D-FT NMRS: in the former case they involve macroscopic, or anatomical structure determination, whereas in the latter case of 2D-FT NMRS the atomic structure reconstruction algorithms are based on the quantum theory of a microphysical (quantum) process such as nuclear Overhauser enhancement NOE, or specific magnetic dipole-dipole interactions<sup>[14]</sup> between neighbor nuclei.

### Example 1

A 2D Fourier transformation and phase correction is applied to a set of 2D NMR (FID) signals:  $\mathbf{s}(t_1, t_2)$  yielding a real 2D-FT NMR 'spectrum' (collection of 1D FT-NMR spectra) represented by a matrix  $\mathbf{S}$  whose elements are

$$\mathbf{S}(\nu_1, \nu_2) = \text{Re} \int \int \cos(\nu_1 t_1) \exp(-i\nu_2 t_2) s(t_1, t_2) dt_1 dt_2$$

where  $\nu_1$  and  $\nu_2$  denote the discrete indirect double-quantum and single-quantum(detection) axes, respectively, in the 2D NMR experiments. Next, the covariance matrix is calculated in the frequency domain according to the following equation

$$\mathbf{C}(\nu'_2, \nu_2) = \mathbf{S}^T \mathbf{S} = \sum_{\nu_1} [S(\nu_1, \nu'_2) S(\nu_1, \nu_2)], \quad \text{with } \nu_2, \nu'_2 \text{ taking all possible}$$

single-quantum frequency values and with the summation carried out over all discrete, double quantum frequencies  $\nu_1$ .

### Example 2

Atomic Structure from 2D-FT STEM Images<sup>[15]</sup> of electron distributions in a high-temperature cuprate superconductor 'paracrystal' reveal both the domains (or 'location') and the local symmetry of the 'pseudo-gap' in the electron-pair correlation band responsible for the high-temperature superconductivity effect (obtained at Cornell University). So far there have been three Nobel prizes awarded for 2D-FT NMR/MRI during 1992-2003, and an additional, earlier Nobel prize for 2D-FT of X-ray data ('CAT scans'); recently the advanced possibilities of 2D-FT techniques in Chemistry, Physiology and Medicine<sup>[16]</sup> received very significant recognition.<sup>[17]</sup>

## Brief explanation of NMRI diagnostic uses in Pathology

As an example, a diseased tissue such as a malign tumor, can be detected by 2D-FT NMRI because the hydrogen nuclei of molecules in different tissues return to their equilibrium spin state at different relaxation rates, and also because of the manner in which a malign tumor spreads and grows rapidly along the blood vessels adjacent to the tumor, also inducing further vascularization to occur. By changing the pulse delays in the RF pulse

sequence employed, and/or the RF pulse sequence itself, one may obtain a 'relaxation—based contrast', or contrast enhancement between different types of body tissue, such as normal vs. diseased tissue cells for example. Excluded from such diagnostic observations by NMRI are all patients with ferromagnetic metal implants, (e.g., cochlear implants), and all cardiac pacemaker patients who cannot undergo any NMRI scan because of the very intense magnetic and RF fields employed in NMRI which would strongly interfere with the correct functioning of such pacemakers. It is, however, conceivable that future developments may also include along with the NMRI diagnostic treatments with special techniques involving applied magnetic fields and very high frequency RF. Already, surgery with special tools is being experimented on in the presence of NMR imaging of subjects. Thus, NMRI is used to image almost every part of the body, and is especially useful for diagnosis in neurological conditions, disorders of the muscles and joints, for evaluating tumors, such as in lung or skin cancers, abnormalities in the heart (especially in children with hereditary disorders), blood vessels, CAD, atherosclerosis and cardiac infarcts <sup>[18]</sup> (courtesy of Dr. Robert R. Edelman)

## See also

- Nuclear magnetic resonance (NMR)
  - Edward Mills Purcell
  - Felix Bloch
  - Medical imaging
  - Paul C. Lauterbur
  - Magnetic resonance microscopy
  - Peter Mansfield
  - Computed tomography (CT)
  - Solid-state NMR
  - Knight shift
  - John Hasbrouck Van Vleck
  - Chemical shift
  - Herbert S. Gutowsky
  - John S. Waugh
  - Charles Pence Slichter
  - Protein nuclear magnetic resonance spectroscopy
  - Kurt Wüthrich
  - Nuclear Overhauser effect
  - Fourier transform spectroscopy(FTS)
  - Jean Jeneer
  - Richard R. Ernst
  - Relaxation
  - Earth's field NMR (EFNMR)
  - Robinson oscillator
  - FT-NIRS (NIR)
  - Magnetic resonance elastography
-

## Footnotes

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pmid=9990066.

## External links

- Cardiac Infarct or "heart attack" Imaged in Real Time by 2D-FT NMRI ([http://www.mr-tip.com/exam\\_gifs/cardiac\\_infarct\\_short\\_axis\\_cine\\_6.gif](http://www.mr-tip.com/exam_gifs/cardiac_infarct_short_axis_cine_6.gif))
- Interactive Flash Animation on MRI (<http://www.e-mri.org>) - *Online Magnetic Resonance Imaging physics and technique course*
- Herbert S. Gutowsky
- Jiri Jonas and Charles P. Slichter: NMR Memoires at NAS about Herbert Sander Gutowsky; NAS = National Academy of Sciences, USA, (<http://books.nap.edu/html/biomems/hgutowsky.pdf>)
- 3D Animation Movie about MRI Exam (<http://www.patienceys.com/MRI/>)
- International Society for Magnetic Resonance in Medicine (<http://www.ismrm.org>)
- Danger of objects flying into the scanner ([http://www.simplyphysics.com/flying\\_objects.html](http://www.simplyphysics.com/flying_objects.html))

## Related Wikipedia websites

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- → Fourier transform spectroscopy
- → FT-NIRS
- Chemical imaging
- Magnetic resonance elastography
- → Nuclear magnetic resonance (NMR)
- Chemical shift
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- Robinson oscillator
- Earth's field NMR (EFNMR)
- Rabi cycle

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# Electron spin resonance

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1. redirect electron paramagnetic resonance

## Fluorescence spectroscopy

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**Fluorescence spectroscopy** aka fluorometry or spectrofluorometry, is a type of electromagnetic spectroscopy which analyzes fluorescence from a sample. It involves using a beam of light, usually ultraviolet light, that excites the electrons in molecules of certain compounds and causes them to emit light of a lower energy, typically, but not necessarily, visible light. A complementary technique is absorption spectroscopy.

Devices that measure fluorescence are called fluorometers or fluorimeters.

### Theory

Molecules have various states referred to as energy levels. Fluorescence spectroscopy is primarily concerned with electronic and vibrational states. Generally, the species being examined will have a ground electronic state (a low energy state) of interest, and an excited electronic state of higher energy. Within each of these electronic states are various vibrational states.

In fluorescence spectroscopy, the species is first excited, by absorbing a photon, from its ground electronic state to one of the various vibrational states in the excited electronic state. Collisions with other molecules cause the excited molecule to lose vibrational energy until it reaches the lowest vibrational state of the excited electronic state.

The molecule then drops down to one of the various vibrational levels of the ground electronic state again, emitting a photon in the process. As molecules may drop down into any of several vibrational levels in the ground state, the emitted photons will have different energies, and thus frequencies. Therefore, by analysing the different frequencies of light emitted in fluorescent spectroscopy, along with their relative intensities, the structure of the different vibrational levels can be determined.

In a typical experiment, the different frequencies of fluorescent light emitted by a sample are measured, holding the excitation light at a constant wavelength. This is called an *emission spectrum*. An *excitation spectrum* is measured by recording a number of emission spectra using different wavelengths of excitation light.

## Instrumentation

Two general types of instruments exist:

- Filter fluorometers use filters to isolate the incident light and fluorescent light.
- Spectrofluorometers use diffraction grating monochromators to isolate the incident light and fluorescent light.

Both types utilize the following scheme:

The light from an excitation source passes through a filter or monochromator, and strikes the sample.

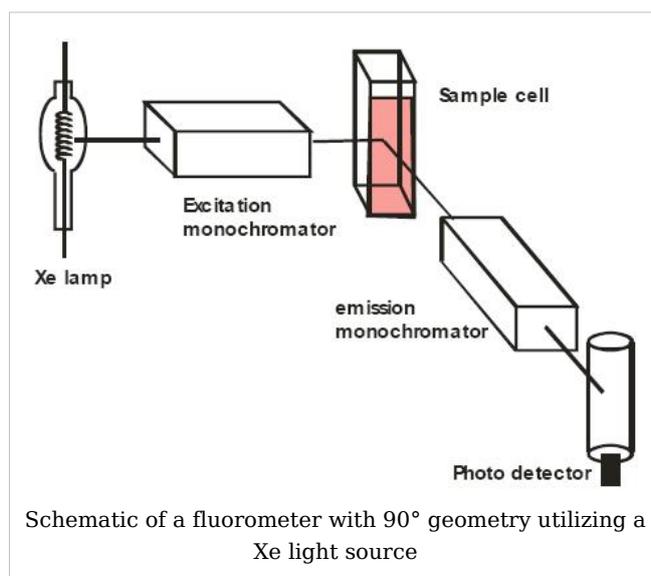
A proportion of the incident light is absorbed by the sample, and some of the molecules in the sample fluoresce. The fluorescent light is emitted in all directions. Some of this fluorescent light

passes through a second filter or monochromator and reaches a detector, which is usually placed at  $90^\circ$  to the incident light beam to minimize the risk of transmitted or reflected incident light reaching the detector.

Various light sources may be used as excitation sources, including lasers, photodiodes, and lamps; xenon arcs and mercury-vapor lamps in particular. A laser only emits light of high irradiance at a very narrow wavelength interval, typically under 0.01 nm, which makes an excitation monochromator or filter unnecessary. The disadvantage of this method is that the wavelength of a laser cannot be changed by much. A mercury vapor lamp is a line lamp, meaning it emits light near peak wavelengths. By contrast, a xenon arc has a continuous emission spectrum with nearly constant intensity in the range from 300-800 nm and a sufficient irradiance for measurements down to just above 200 nm.

Filters and/or monochromators may be used in fluorimeters. A monochromator transmits light of an adjustable wavelength with an adjustable tolerance. The most common type of monochromator utilizes a diffraction grating, that is, collimated light illuminates a grating and exits with a different angle depending on the wavelength. The monochromator can then be adjusted to select which wavelengths to transmit. For allowing anisotropy measurements the addition of two polarization filters are necessary: One after the excitation monochromator or filter, and one before the emission monochromator or filter.

As mentioned before, the fluorescence is most often measured at a  $90^\circ$  angle relative to the excitation light. This geometry is used instead of placing the sensor at the line of the excitation light at a  $180^\circ$  angle in order to avoid interference of the transmitted excitation light. No monochromator is perfect and it will transmit some stray light, that is, light with other wavelengths than the targeted. An ideal monochromator would only transmit light in the specified range and have a high wavelength-independent transmission. When measuring at a  $90^\circ$  angle, only the light scattered by the sample causes stray light. This results in a better signal-to-noise ratio, and lowers the detection limit by approximately a factor 10000<sup>[1]</sup>, when compared to the  $180^\circ$  geometry. Furthermore, the fluorescence can also be measured from the front, which is often done for turbid or opaque samples<sup>[2]</sup>.



The detector can either be single-channeled or multichanneled. The single-channeled detector can only detect the intensity of one wavelength at a time, while the multichanneled detects the intensity at all wavelengths simultaneously, making the emission monochromator or filter unnecessary. The different types of detectors have both advantages and disadvantages.

The most versatile fluorimeters with dual monochromators and a continuous excitation light source can record both an excitation spectrum and a fluorescence spectrum. When measuring fluorescence spectra, the wavelength of the excitation light is kept constant, preferably at a wavelength of high absorption, and the emission monochromator scans the spectrum. For measuring excitation spectra, the wavelength passing through the emission filter or monochromator is kept constant and the excitation monochromator is scanning. The excitation spectrum generally is identical to the absorption spectrum as the fluorescence intensity is proportional to the absorption. <sup>[3]</sup>

## Analysis of data

At low concentrations the fluorescence intensity will generally be proportional to the concentration of the fluorophore.

Unlike in UV/visible spectroscopy, 'standard', device independent spectra are not easily attained, however. Several factors influence and distort the spectra, and corrections are necessary to attain 'true', i.e. machine-independent, spectra. The different types of distortions will here be classified as being either instrument- or sample-related. Firstly, the distortion arising from the instrument is discussed. As a start, the light source intensity and wavelength characteristics varies over time during each experiment and between each experiment. Furthermore, no lamp has a constant intensity at all wavelengths. To correct this, a beam splitter can be applied after the excitation monochromator or filter to direct a portion of the light to a reference detector.

Additionally, the transmission efficiency of monochromators and filters must be taken into account. These may also change over time. The transmission efficiency of the monochromator also varies depending on wavelength. This is the reason that an optional reference detector should be placed after the excitation monochromator or filter. The percentage of the fluorescence picked up by the detector is also dependent upon the system. Furthermore, the detector quantum efficiency, that is, the percentage of photons detected, varies between different detectors, with wavelength and with time, as the detector inevitably deteriorates.

Correction of all these instrumental factors for getting a 'standard' spectrum is a tedious process, which is only applied in practice when it is strictly necessary. This is the case when measuring the quantum yield or when finding the wavelength with the highest emission intensity for instance.

As mentioned earlier, distortions arise from the sample as well. Therefore some aspects of the sample must be taken into account too. Firstly, photodecomposition may decrease the intensity of fluorescence over time. Scattering of light must also be taken into account. The most significant types of scattering in this context are Rayleigh and Raman scattering. Light scattered by Rayleigh scattering has the same wavelength as the incident light, whereas in Raman scattering the scattered light changes wavelength usually to longer wavelengths. Raman scattering is the result of a virtual electronic state induced by the excitation light. From this virtual state, the molecules may relax back to a vibrational level

other than the vibrational ground state <sup>[4]</sup>. In fluorescence spectra, it is always seen at a constant wavenumber difference relative to the excitation wavenumber e.g. the peak appears at a wavenumber  $3600\text{ cm}^{-1}$  lower than the excitation light in water.

Other aspects to consider are the inner filter effects. These include reabsorption. Reabsorption happens because another molecule or part of a macromolecule absorbs at the wavelengths at which the fluorophore emits radiation. If this is the case, some or all of the photons emitted by the fluorophore may be absorbed again. Another inner filter effect occurs because of high concentrations of absorbing molecules, including the fluorophore. The result is that the intensity of the excitation light is not constant throughout the solution. Resultingly, only a small percentage of the excitation light reaches the fluorophores that are visible for the detection system. The inner filter effects change the spectrum and intensity of the emitted light and they must therefore be considered when analysing the emission spectrum of fluorescent light. <sup>[5]</sup> <sup>[6]</sup>

## Tryptophan Fluorescence

Tryptophan is an important intrinsic fluorescent probe (amino acid), which can be used to estimate the nature of microenvironment of the tryptophan. When performing experiments with denaturants, surfactants or other amphiphilic molecules, the microenvironment of the tryptophan might change. For example, if a protein containing a single tryptophan in its 'hydrophobic' core is denatured with increasing temperature, a red-shift emission spectrum will appear. This is due to the exposure of the tryptophan to an aqueous environment as opposed to a hydrophobic protein interior. In contrast, the addition of a surfactant to a protein which contains a tryptophan which is exposed to the aqueous solvent will cause a blue shifted emission spectrum if the tryptophan is embedded in the surfactant vesicle or micelle <sup>[7]</sup>. Proteins that lack tryptophan may be coupled to a fluorophore.

At 295 nm, the tryptophan emission spectrum is dominant over the weaker tyrosine and phenylalanine fluorescence.

## Applications

Fluorescence spectroscopy is used in, among others, biochemical, medical, and chemical research fields for analyzing organic compounds. There has also been a report of its use in differentiating malignant, bashful skin tumors from benign.

Fluorescence can also be used to redirect photons, see fluorescent solar collector

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# Fluorescence correlation spectroscopy

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**Fluorescence correlation spectroscopy (FCS)** is a common technique used by physicists, chemists, and biologists to experimentally characterize the dynamics of fluorescent species (e.g. single fluorescent dye molecules in nanostructured materials, autofluorescent proteins in living cells, etc.). Although the name indicates a specific link to fluorescence, the method is used today also for exploring other forms of luminescence (like reflections, luminescence from gold-beads or quantum dots or phosphorescent species). The "spectroscopy" in the name is not readily found as in common usage a spectrum is generally understood to be a frequency spectrum. The autocorrelation is a genuine form of spectrum, however: It is the time-spectrum generated from the power spectrum (via inverse fourier transform).

Commonly, FCS is employed in the context of optical microscopy, in particular confocal or two photon microscopy. In these techniques light is focused on a sample and the measured fluorescence intensity fluctuations (due to diffusion, physical or chemical reactions, aggregation, etc.) are analyzed using the temporal autocorrelation. Because the measured property is essentially related to the magnitude and/or the amount of fluctuations, there is an optimum measurement regime at the level when individual species enter or exit the observation volume (or turn on and off in the volume). When too many entities are measured at the same time the overall fluctuations are small in comparison to the total signal and may not be resolvable - in the other direction, if the individual fluctuation-events are too sparse in time, one measurement may take prohibitively too long. FCS is in a way the fluorescent counterpart to dynamic light scattering, which uses coherent light scattering, instead of (incoherent) fluorescence.

When an appropriate model is known, FCS can be used to obtain quantitative information such as

- diffusion coefficients
- hydrodynamic radii
- average concentrations
- kinetic chemical reaction rates
- singlet-triplet dynamics

Because fluorescent markers come in a variety of colors and can be specifically bound to a particular molecule (e.g. proteins, polymers, metal-complexes, etc.), it is possible to study the behavior of individual molecules (in rapid succession in composite solutions). With the development of sensitive detectors such as avalanche photodiodes the detection of the fluorescence signal coming from individual molecules in highly dilute samples has become practical. With this emerged the possibility to conduct FCS experiments in a wide variety of specimens, ranging from materials science to biology. The advent of engineered cells with genetically tagged proteins (like green fluorescent protein) has made FCS a common tool for studying molecular dynamics in living cells.

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## History

Signal-correlation techniques have first been experimentally applied to fluorescence in 1972 by Magde, Elson, and Webb<sup>[1]</sup>, who are therefore commonly credited as the "inventors" of FCS. The technique was further developed in a group of papers by these and other authors soon after, establishing the theoretical foundations and types of applications.<sup>[2] [3] [4]</sup> See Thompson (1991)<sup>[5]</sup> for a review of that period.

Beginning in 1993<sup>[6]</sup>, a number of improvements in the measurement techniques--notably using confocal microscopy, and then two photon microscopy--to better define the measurement volume and reject background greatly improved the signal-to-noise and allowed single molecule sensitivity.<sup>[7] [8]</sup> Since then, there has been a renewed interest in FCS, and as of August 2007 there has been over 3,000 papers using FCS found in Web of Science. See Krichevsky and Bonnet<sup>[9]</sup> for a recent review. In addition, there has been a flurry of activity extending FCS in various ways, for instance to laser scanning and spinning disk confocal microscopy (from a stationary, single point measurement), in using cross-correlation (FCCS) between two fluorescent channels instead of autocorrelation, and in using Förster Resonance Energy Transfer (FRET) instead of fluorescence.

## Typical FCS setup

The typical FCS setup consists of a laser line (wavelengths ranging typically from 405 - 633 nm (cw), and from 690 - 1100 nm (pulsed)), which is reflected into a microscope objective by a dichroic mirror. The laser beam is focused in the sample, which contains fluorescent particles (molecules) in such high dilution, that only few are within the focal spot (usually 1 - 100 molecules in one fL). When the particles cross the focal volume, they fluoresce. This light is collected by the same objective and, because it is red-shifted with respect to the excitation light it passes the dichroic reaching a detector, typically a photomultiplier tube or avalanche photodiode detector. The resulting electronic signal can be stored either directly as an intensity versus time trace to be analyzed at a later point, or, computed to generate the autocorrelation directly (which requires special acquisition cards). The FCS curve by itself only represents a time-spectrum. Conclusions on physical phenomena have to be extracted from there with appropriate models. The parameters of interest are found after fitting the autocorrelation curve to modeled functional forms.<sup>[10]</sup> The setup is shown in Figure 1.

## The Measurement Volume

The measurement volume is a convolution of illumination (excitation) and detection geometries, which result from the optical elements involved. The resulting volume is described mathematically by the point spread function (or PSF), it is essentially the image of a point source. The PSF is often described as an ellipsoid (with unsharp boundaries) of few hundred nanometers in focus diameter, and almost one micrometre along the optical axis. The shape varies significantly (and has a large impact on the resulting FCS curves) depending on the quality of the optical elements (it is crucial to avoid astigmatism and to check the real shape of the PSF on the instrument). In the case of confocal microscopy, and for small pinholes (around one Airy unit), the PSF is well approximated by Gaussians:

$$PSF(r, z) = I_0 e^{-2r^2/\omega_x^2} e^{-2z^2/\omega_z^2}$$

where  $I_0$  is the peak intensity,  $r$  and  $z$  are radial and axial position, and  $\omega_{xy}$  and  $\omega_z$  are the radial and axial radii, and  $\omega_z > \omega_{xy}$ . This Gaussian form is assumed in deriving the functional form of the autocorrelation.

Typically  $\omega_{xy}$  is 200-300 nm, and  $\omega_z$  is **2-6** times larger.<sup>[11]</sup> One common way of calibrating the measurement volume parameters is to perform FCS on a species with known diffusion coefficient and concentration (see below). Diffusion coefficients for common fluorophores in water are given in a later section.

The Gaussian approximation works to varying degrees depending on the optical details, and corrections can sometimes be applied to offset the errors in approximation.<sup>[12]</sup>

## Autocorrelation Function

The (temporal) autocorrelation function is the correlation of a time series with itself shifted by time  $\tau$ , as a function of  $\tau$ :

$$G(\tau) = \frac{\langle \delta I(t) \delta I(t + \tau) \rangle}{\langle I(t) \rangle^2} = \frac{\langle I(t) I(t + \tau) \rangle}{\langle I(t) \rangle^2} - 1$$

where  $\delta I(t) = I(t) - \langle I(t) \rangle$  is the deviation from the mean intensity. The normalization (denominator) here is the most commonly used for FCS, because then the correlation at  $\tau = 0$ ,  $G(0)$ , is related to the average number of particles in the measurement volume.

## Interpreting the Autocorrelation Function

To extract quantities of interest, the autocorrelation data can be fitted, typically using a nonlinear least squares algorithm. The fit's functional form depends on the type of dynamics (and the optical geometry in question).

### Normal Diffusion

The fluorescent particles used in FCS are small and thus experience thermal motions in solution. The simplest FCS experiment is thus normal 3D diffusion, for which the autocorrelation is:

$$G(\tau) = G(0) \frac{1}{(1 + (\tau/\tau_D))(1 + a^{-2}(\tau/\tau_D))^{1/2}} + G(\infty)$$

where  $a = \omega_z/\omega_{xy}$  is the ratio of axial to radial  $e^{-2}$  radii of the measurement volume, and  $\tau_D$  is the characteristic residence time. This form was derived assuming a Gaussian measurement volume. Typically, the fit would have three free parameters-- $G(0)$ ,  $G(\infty)$ , and  $\tau_D$ --from which the diffusion coefficient and fluorophore concentration can be obtained. With the normalization used in the previous section,  $G(0)$  gives the mean number of diffusers in the volume  $\langle N \rangle$ , or equivalently--with knowledge of the observation volume size--the mean concentration:

$$G(0) = \frac{1}{\langle N \rangle} = \frac{1}{V_{eff} \langle C \rangle},$$

where the effective volume is found from integrating the Gaussian form of the measurement volume and is given by:

$$V_{eff} = \pi^{3/2} \omega_{xy}^2 \omega_z.$$

$\tau_D$  gives the diffusion coefficient:  $D = \omega_{xy}^2 / 4\tau_D$ .

## Anomalous diffusion

If the diffusing particles are hindered by obstacles or pushed by a force (molecular motors, flow, etc.) the dynamics is often not sufficiently well-described by the normal diffusion model, where the mean squared displacement (MSD) grows linearly with time. Instead the diffusion may be better described as anomalous diffusion, where the temporal dependence of the MSD is non-linear as in the power-law:

$$MSD = 6D_a t^\alpha$$

where  $D_a$  is an anomalous diffusion coefficient. "Anomalous diffusion" commonly refers only to this very generic model, and not the many other possibilities that might be described as anomalous. Also, a power law is, in a strict sense, the expected form only for a narrow range of rigorously defined systems, for instance when the distribution of obstacles is fractal. Nonetheless a power law can be a useful approximation for a wider range of systems.

The FCS autocorrelation function for anomalous diffusion is:

$$G(\tau) = G(0) \frac{1}{(1 + (\tau/\tau_D)^\alpha)(1 + a^{-2}(\tau/\tau_D)^\alpha)^{1/2}} + G(\infty),$$

where the anomalous exponent  $\alpha$  is the same as above, and becomes a free parameter in the fitting.

Using FCS, the anomalous exponent has been shown to be an indication of the degree of molecular crowding (it is less than one and smaller for greater degrees of crowding)<sup>[13]</sup>.

## Polydisperse diffusion

If there are diffusing particles with different sizes (diffusion coefficients), it is common to fit to a function that is the sum of single component forms:

$$G(\tau) = G(0) \sum_i \frac{\alpha_i}{(1 + (\tau/\tau_{D,i})) (1 + a^{-2}(\tau/\tau_{D,i}))^{1/2}} + G(\infty)$$

where the sum is over the number different sizes of particle, indexed by  $i$ , and  $\alpha_i$  gives the weighting, which is related to the quantum yield and concentration of each type. This introduces new parameters, which makes the fitting more difficult as a higher dimensional space must be searched. Nonlinear least square fitting typically becomes unstable with even a small number of  $\tau_{D,i}$ s. A more robust fitting scheme, especially useful for polydisperse samples, is the Maximum Entropy Method<sup>[14]</sup>.

## Diffusion with flow

With diffusion together with a uniform flow with velocity  $v$  in the lateral direction, the autocorrelation is<sup>[15]</sup>:

$$G(\tau) = G(0) \frac{1}{(1 + (\tau/\tau_D))(1 + a^{-2}(\tau/\tau_D))^{1/2}} \times \exp[-(\tau/\tau_v)^2 \times \frac{1}{1 + \tau/\tau_D}] + G(\infty)$$

where  $\tau_v = \omega_{xy}/v$  is the average residence time if there is only a flow (no diffusion).

## Chemical relaxation

A wide range of possible FCS experiments involve chemical reactions that continually fluctuate from equilibrium because of thermal motions (and then "relax"). In contrast to diffusion, which is also a relaxation process, the fluctuations cause changes between states of different energies. One very simple system showing chemical relaxation would be a stationary binding site in the measurement volume, where particles only produce signal when bound (e.g. by FRET, or if the diffusion time is much faster than the sampling interval). In this case the autocorrelation is:

$$G(\tau) = G(0) \exp(-\tau/\tau_B) + G(\infty)$$

where

$$\tau_B = (k_{on} + k_{off})^{-1}$$

is the relaxation time and depends on the reaction kinetics (on and off rates), and:

$$G(0) = \frac{1}{\langle N \rangle} \frac{k_{on}}{k_{off}} = \frac{1}{\langle N \rangle} K$$

is related to the equilibrium constant  $K$ .

Most systems with chemical relaxation also show measureable diffusion as well, and the autocorrelation function will depend on the details of the system. If the diffusion and chemical reaction are decoupled, the combined autocorrelation is the product of the chemical and diffusive autocorrelations.

## Triplet State Correction

The autocorrelations above assume that the fluctuations are not due to changes in the fluorescent properties of the particles. However, for the majority of (bio)organic fluorophores--e.g. green fluorescent protein, rhodamine, Cy3 and Alexa Fluor dyes--some fraction of illuminated particles are excited to a triplet state (or other non-radiative decaying states) and then do not emit photons for a characteristic relaxation time  $\tau_F$ . Typically  $\tau_F$  is on the order of microseconds, which is usually smaller than the dynamics of interest (e.g.  $\tau_D$ ) but large enough to be measured. A multiplicative term is added to the autocorrelation account for the triplet state. For normal diffusion:

$$G(\tau) = G(0) \frac{1 - F + F e^{-\tau/\tau_F}}{1 - F} \frac{1}{(1 + (\tau/\tau_{D,i})) (1 + a^{-2}(\tau/\tau_{D,i}))^{1/2}} + G(\infty)$$

where  $F$  is the fraction of particles that have entered the triplet state and  $\tau_F$  is the corresponding triplet state relaxation time. If the dynamics of interest are much slower than the triplet state relaxation, the short time component of the autocorrelation can simply be truncated and the triplet term is unnecessary.

## Common fluorescent probes

The fluorescent species used in FCS is typically a biomolecule of interest that has been tagged with a fluorophore (using immunohistochemistry for instance), or is a naked fluorophore that is used to probe some environment of interest (e.g. the cytoskeleton of a cell). The following table gives diffusion coefficients of some common fluorophores in water at room temperature, and their excitation wavelengths.

Fluorescent dye	$D$ ( $\times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ )	Excitation wavelength (nm)	Reference

Rhodamine 6G	2.8, 3.0, 4.14 ± 0.05 @ 25.00 °C	514	[16], [17], [18]
Rhodamine 110	2.7	488	[19]
Tetramethyl rhodamine	2.6	543	
Cy3	2.8	543	
Cy5	2.5, 3.7 ± 0.15 @ 25.00 °C	633	[20], [21]
carboxyfluorescein	3.2	488	
Alexa-488	1.96	488	[22]
Atto655-maleimide	4.07 ± 0.1 @ 25.00 °C	663	[23]
Atto655-carboxylicacid	4.26 ± 0.08 @ 25.00 °C	663	[24]
2', 7'-difluorofluorescein (Oregon Green488)	4.11 ± 0.06 @ 25.00 °C	498	[25]

## Variations of FCS

FCS almost always refers to the single point, single channel, temporal autocorrelation measurement, although the term "fluorescence correlation spectroscopy" out of its historical scientific context implies no such restriction. FCS has been extended in a number of variations by different researchers, with each extension generating another name (usually an acronym).

## Fluorescence Cross-Correlation Spectroscopy (FCCS)

FCS is sometimes used to study molecular interactions using differences in diffusion times (e.g. the product of an association reaction will be larger and thus have larger diffusion times than the reactants individually); however, FCS is relatively insensitive to molecular mass as can be seen from the following equation relating molecular mass to the diffusion time of globular particles (e.g. proteins):

$$\tau_D = \frac{3\pi\omega_{xy}^2\eta}{2kT}(M)^{1/3}$$

where  $\eta$  is the viscosity of the sample and  $M$  is the molecular mass of the fluorescent species. In practice, the diffusion times need to be sufficiently different--a factor of at least **1.6**--which means the molecular masses must differ by a factor of **4**.<sup>[26]</sup> Dual color fluorescence cross-correlation spectroscopy (FCCS) measures interactions by cross-correlating two or more fluorescent channels (one channel for each reactant), which distinguishes interactions more sensitively than FCS, particularly when the mass change in the reaction is small.

## Two-and three-photon FCS excitation

Several advantages in both spatial resolution and minimizing photodamage/photobleaching in organic and/or biological samples are obtained by two-photon or three-photon excitation FCS<sup>[27] [28] [29] [30] [31]</sup>.

## FRET-FCS

Another FCS based approach to studying molecular interactions uses fluorescence resonance energy transfer (FRET) instead of fluorescence, and is called FRET-FCS.<sup>[32]</sup> With FRET, there are two types of probes, as with FCCS; however, there is only one channel and light is only detected when the two probes are very close--close enough to ensure an interaction. The FRET signal is weaker than with fluorescence, but has the advantage that there is only signal during a reaction (aside from autofluorescence).

## Image Correlation Spectroscopy (ICS)

When the motion is slow (in biology, for example, diffusion in a membrane), getting adequate statistics from a single-point FCS experiment may take a prohibitively long time. More data can be obtained by performing the experiment in multiple spatial points in parallel, using a laser scanning confocal microscope. This approach has been called Image Correlation Spectroscopy (ICS)<sup>[33]</sup>. The measurements can then be averaged together.

Another variation of ICS performs a spatial autocorrelation on images, which gives information about the concentration of particles<sup>[34]</sup>. The correlation is then averaged in time.

A natural extension of the temporal and spatial correlation versions is spatio-temporal ICS (STICS)<sup>[35]</sup>. In STICS there is no explicit averaging in space or time (only the averaging inherent in correlation). In systems with non-isotropic motion (e.g. directed flow, asymmetric diffusion), STICS can extract the directional information. A variation that is closely related to STICS (by the Fourier transform) is k-space Image Correlation Spectroscopy (kICS).<sup>[36]</sup>

There are cross-correlation versions of ICS as well.<sup>[33]</sup>

## Scanning FCS variations

Some variations of FCS are only applicable to serial scanning laser microscopes. Image Correlation Spectroscopy and its variations all were implemented on a scanning confocal or scanning two photon microscope, but transfer to other microscopes, like a spinning disk confocal microscope. Raster ICS (RICS)<sup>[37]</sup>, and position sensitive FCS (PSFCS)<sup>[38]</sup> incorporate the time delay between parts of the image scan into the analysis. Also, low dimensional scans (e.g. a circular ring)<sup>[39]</sup>--only possible on a scanning system--can access time scales between single point and full image measurements. Scanning path has also been made to adaptively follow particles.<sup>[40]</sup>

## Spinning disk FCS, and spatial mapping

Any of the image correlation spectroscopy methods can also be performed on a spinning disk confocal microscope, which in practice can obtain faster imaging speeds compared to a laser scanning confocal microscope. This approach has recently been applied to diffusion in a spatially varying complex environment, producing a pixel resolution map of diffusion coefficient.<sup>[41]</sup> The spatial mapping of diffusion with FCS has subsequently been extended to TIRF system.<sup>[42]</sup> Spatial mapping of dynamics using correlation techniques had been applied before, but only at sparse points<sup>[43]</sup> or at coarse resolution<sup>[35]</sup>.

## Total internal reflection FCS

Total internal reflection fluorescence (TIRF) is a microscopy approach that is only sensitive to a thin layer near the surface of a coverslip, which greatly minimizes background fluorescence. FCS has been extended to that type of microscope, and is called TIR-FCS<sup>[44]</sup>. Because the fluorescence intensity in TIRF falls off exponentially with distance from the coverslip (instead of as a Gaussian with a confocal), the autocorrelation function is different.

## Other fluorescent dynamical approaches

There are two main non-correlation alternatives to FCS that are widely used to study the dynamics of fluorescent species.

## Fluorescence recovery after photobleaching (FRAP)

In FRAP, a region is briefly exposed to intense light, irrecoverably photobleaching fluorophores, and the fluorescence recovery due to diffusion of nearby (non-bleached) fluorophores is imaged. A primary advantage of FRAP over FCS is the ease of interpreting qualitative experiments common in cell biology. Differences between cell lines, or regions of a cell, or before and after application of drug, can often be characterized by simple inspection of movies. FCS experiments require a level of processing and are more sensitive to potentially confounding influences like: rotational diffusion, vibrations, photobleaching, dependence on illumination and fluorescence color, inadequate statistics, etc. It is much easier to change the measurement volume in FRAP, which allows greater control. In practice, the volumes are typically larger than in FCS. While FRAP experiments are typically more qualitative, some researchers are studying FRAP quantitatively and including binding dynamics.<sup>[45]</sup> A disadvantage of FRAP in cell biology is the free radical perturbation of the cell caused by the photobleaching. It is also less versatile, as it cannot measure concentration or rotational diffusion, or co-localization. FRAP requires a significantly higher concentration of fluorophores than FCS.

## Particle tracking

In particle tracking, the trajectories of a set of particles are measured, typically by applying particle tracking algorithms to movies.<sup>[46]</sup> Particle tracking has the advantage that all the dynamical information is maintained in the measurement, unlike FCS where correlation averages the dynamics to a single smooth curve. The advantage is apparent in systems showing complex diffusion, where directly computing the mean squared displacement allows straightforward comparison to normal or power law diffusion. To apply particle tracking, the particles have to be distinguishable and thus at lower concentration than

required of FCS. Also, particle tracking is more sensitive to noise, which can sometimes affect the results unpredictably.

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## See also

- Confocal microscopy
- Fluorescence cross-correlation spectroscopy
- FRET
- Dynamic light scattering
- Diffusion coefficient

## External links

- Single-molecule spectroscopic methods (<http://dx.doi.org/10.1016/j.sbi.2004.09.004>)
- FCS Classroom (<http://www.fcsxpert.com/classroom>)

# Fourier transform infrared spectroscopy

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1. REDIRECT Infrared spectroscopy#Fourier transform infrared spectroscopy

This is a redirect from a topic, name or term that *does not have its own article*, to an article *section* which covers the subject.

This template automatically categorizes pages to Category:Redirects to sections

### See also/use when more appropriate

- `{{R to list entry}}` and Category:Redirects to list entries
  - `{{R to anchors}}` and Category:Redirects to embedded anchors
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# Near infrared spectroscopy

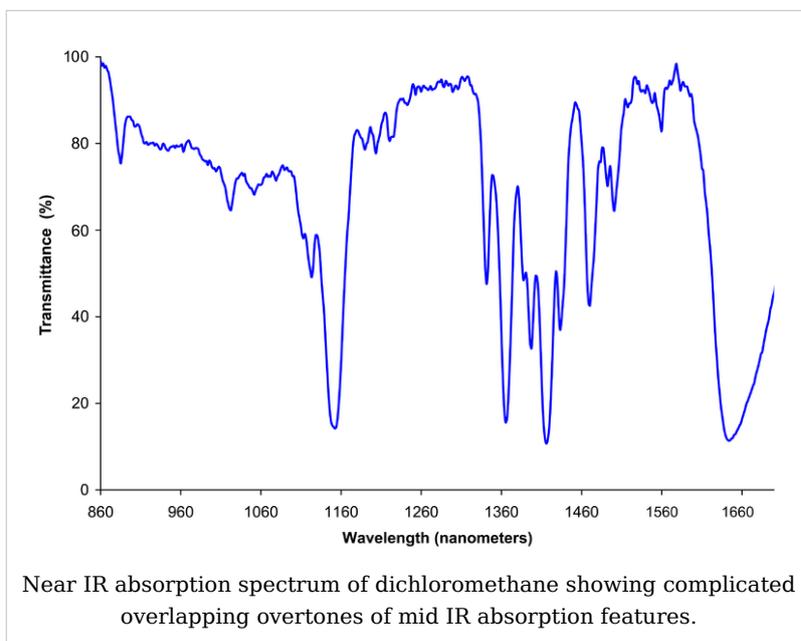
## Near infrared spectroscopy

(NIRS) is a spectroscopic method which uses the near infrared region of the electromagnetic spectrum (from about 800 nm to 2500 nm). Typical applications include pharmaceutical, medical diagnostics (including blood sugar and oximetry), food and agrochemical quality control, as well as combustion research.

## Theory

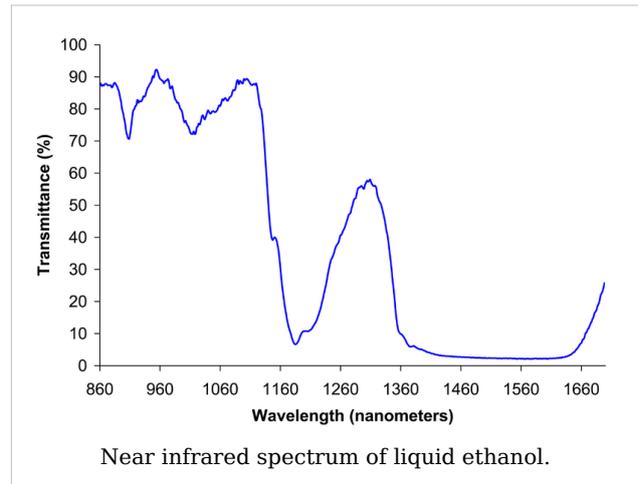
Near infrared spectroscopy is based on molecular overtone and combination vibrations. Such transitions are forbidden by the selection rules of  $\rightarrow$  quantum mechanics. As a result, the molar absorptivity in the near IR region is typically quite small. One advantage is that NIR can typically penetrate much farther into a sample than mid infrared radiation. Near infrared spectroscopy is therefore not a particularly sensitive technique, but it can be very useful in probing bulk material with little or no sample preparation.

The molecular overtone and combination bands seen in the near IR are typically very broad, leading to complex spectra; it can be difficult to assign specific features to specific chemical components. Multivariate (multiple wavelength) calibration techniques (e.g., principal components analysis or partial least squares) are often employed to extract the desired chemical information. Careful development of a set of calibration samples and application of multivariate calibration techniques is essential for near infrared analytical methods.



## History

The discovery of near-infrared energy is ascribed to Herschel in the 19th century, but the first industrial application began in the 1950s. In the first applications, NIRS was used only as an add-on unit to other optical devices that used other wavelengths such as ultraviolet (UV), visible (Vis), or mid-infrared (MIR) spectrometers. In the 1980s, a single unit, stand-alone NIRS system was made available, but the application of NIRS was focused more on chemical analysis. With the introduction of light-fiber optics in the mid 80s and the monochromator-detector developments in early nineties, NIRS became a more powerful tool for scientific research.



Near infrared spectrum of liquid ethanol.

This optical method can be used in a number of fields of science including physics, physiology, or medicine. It was only in the last few decades that NIRS began to be used as a medical tool for monitoring patients.

## Medical uses

Medical applications of NIRS center on the non-invasive measurement of the amount and oxygen content of hemoglobin.

NIRS can be used for non-invasive assessment of brain function through the intact skull in human subjects by detecting changes in blood hemoglobin concentrations associated with neural activity, e.g. in branches of Cognitive psychology as a partial replacement for fMRI techniques. NIRS can be used on infants, where fMRI cannot (at least in the United States), and NIRS is much more portable than fMRI machines, even wireless instrumentation is available, which enables investigations in freely moving subjects<sup>[1]</sup>). However, NIRS cannot fully replace fMRI because it can only be used to scan cortical tissue, where fMRI can be used to measure activation throughout the brain.

The application in functional mapping of the human cortex is called optical topography (OT), near infrared imaging (NIRI) or functional NIRS (fNIRS). The term optical tomography is used for three-dimensional NIRS. The terms NIRS, NIRI and OT are often used interchangeably, but they have some distinctions. The most important difference between NIRS and OT/NIRI is that OT/NIRI is mainly used to detect changes in optical properties of tissue simultaneously from multiple measurement points and display the results in the form of a map or image over a specific area, whereas NIRS provides quantitative data in absolute terms on up to a few specific points. The latter is also used to investigate other tissues such as e.g. muscle, breast, and tumors.

By employing several wavelengths and time resolved (frequency or time domain) and/or spatially resolved methods blood flow, volume<sup>[2]</sup> and oxygenation can be quantified. These measurements are a form of oximetry. Applications of oximetry by NIRS methods include the detection of illnesses which affect the blood circulation (e.g. peripheral vascular disease), the detection and assessment of breast tumors, and the optimization of training in

sports medicine.

NIRS is starting to be used in pediatric critical care, to help deal with cardiac surgery post-op. Indeed, NIRS is able to measure venous oxygen saturation (SVO<sub>2</sub>), which is determined by the cardiac output, as well as other parameters (FiO<sub>2</sub>, hemoglobin, oxygen uptake). Therefore, following the NIRS gives critical care physicians a notion of the cardiac output. NIRS is liked by patients, because it is non-invasive, painless and uses non-ionizing radiation.

The instrumental development of NIRS/NIRI/OT has proceeded tremendously during the last years and in particular in terms of quantification, imaging and miniaturisation<sup>[3]</sup>.

## Industrial Uses

As opposed to NIRS used in optical topography, general NIRS used in chemical assays does not provide imaging by mapping. For example, a clinical CO<sub>2</sub> analyzer requires reference techniques and calibration routines to be able to get accurate CO<sub>2</sub> content change. In this case, calibration is performed by adjusting the zero control of the sample being tested after purposefully supplying 0% CO<sub>2</sub> or another known amount of CO<sub>2</sub> in the sample. Normal compressed gas from distributors contains about 95% O<sub>2</sub> and 5% CO<sub>2</sub> which can also be used to adjust %CO<sub>2</sub> meter reading to be exactly 5% at initial calibration.

## Instrumentation

Instrumentation for near-IR (NIR) spectroscopy is partially similar to instruments for the visible and mid-IR ranges. There is a source, a detector, and a dispersive element (such as a prism, or more commonly a diffraction grating) to allow the intensity at different wavelengths to be recorded. → Fourier transform NIR instruments using an interferometer are also common, especially for wavelengths above ~1000 nm. Depending on the sample, the spectrum can be measured in either in reflection or transmission.

Common incandescent or quartz halogen light bulbs are most often used as broadband sources of near infrared radiation for analytical applications. Light-emitting diodes (LEDs) are also used; they offer greater lifetime and spectral stability and reduced power requirements.<sup>[4]</sup>

The type of detector used depends primarily on the range of wavelengths to be measured. Silicon-based CCDs are suitable for the shorter end of the NIR range, but are not sufficiently sensitive over most of the range. InGaAs and PbS devices are more suitable. In certain diode array (DA) NIRS instruments, both silicon-based and InGaAs detectors are employed in the same instrument. Such instruments can record both visible and NIR spectra 'simultaneously'.

Instruments intended for chemical imaging in the NIR may use a 2D array detector with a acousto-optic tunable filter. Multiple images may be recorded sequentially at different narrow wavelength bands.<sup>[5]</sup>

Many commercial instruments for UV/vis spectroscopy are capable of recording spectra in the NIR range (to perhaps ~900 nm). In the same way, the range of some mid-IR instruments may extend into the NIR. In these instruments the detector used for the NIR wavelengths is often the same detector used for the instrument's "main" range of interest.

## Applications

The primary application of NIRS to the human body uses the fact that the transmission and absorption of NIR light in human body tissues contains information about hemoglobin concentration changes. When a specific area of the brain is activated, the localized blood volume in that area changes quickly. Optical imaging can measure the location and activity of specific regions of the brain by continuously monitoring blood hemoglobin levels through the determination of optical absorption coefficients.

Typical applications of NIR spectroscopy include the analysis of foodstuffs, pharmaceuticals, combustion products and a major branch of astronomical spectroscopy.

### Astronomical spectroscopy

Near-infrared → spectroscopy is used in astronomy for studying the atmospheres of cool stars where molecules can form. The vibrational and rotational signatures of molecules such as titanium oxide, cyanide and carbon monoxide can be seen in this wavelength range and can give a clue towards the star's spectral type. It is additionally used for studying molecules in other astronomical contexts, such as in molecular clouds where new stars are formed. The astronomical phenomenon known as reddening means that near-infrared wavelengths are less affected by dust in the interstellar medium, such that regions inaccessible by optical spectroscopy can be studied in the near-infrared. Since dust and gas are strongly associated, these dusty regions are exactly those where infrared spectroscopy is most useful. The near-infrared spectra of very young stars provide important information about their ages and masses, which is important for understanding star formation in general.

### Remote monitoring

Techniques have been developed for NIR spectroscopic imaging. These have been used for a wide range of uses, including the remote investigation of plants and soils. Data can be collected from instruments on airplanes or satellites to assess ground cover and soil chemistry.

### Medical uses

See above

### Particle measurement

NIR is often used in particle sizing in a range of different fields, including studying pharmaceutical and agricultural powders.

### See also

- fNIR
  - → Fourier transform spectroscopy
  - → FT-NIRS
  - Infrared spectroscopy
  - → Vibrational spectroscopy
  - Rotational spectroscopy
  - → Spectroscopy
-

- Chemical Imaging

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# Vibrational spectroscopy

1. redirect Molecular vibration

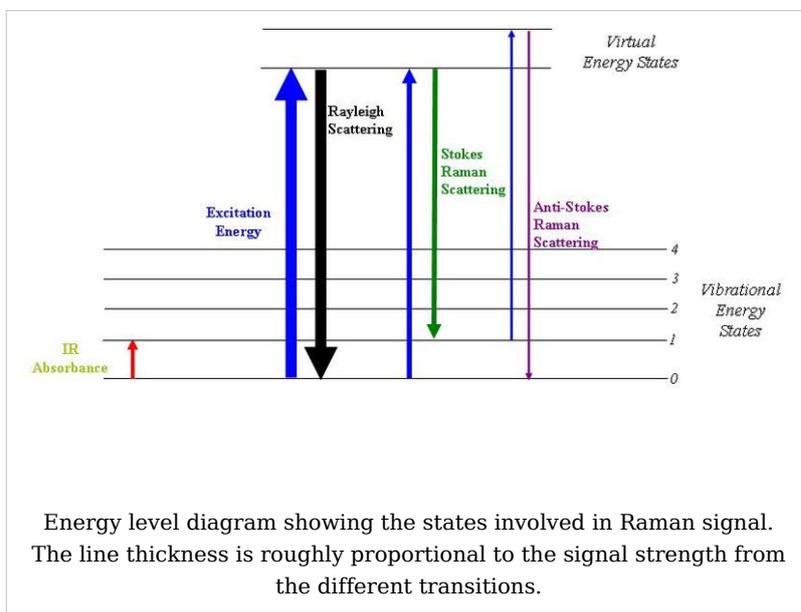
## Raman spectroscopy

### Raman spectroscopy

(pronounced: [rə.mən] S—, named after C. V. Raman) is a → spectroscopic technique used in condensed matter physics and chemistry to study vibrational, rotational, and other low-frequency modes in a system.<sup>[1]</sup> It relies on inelastic scattering, or Raman scattering, of monochromatic light, usually from a laser in the visible, near infrared, or near ultraviolet range. The laser light interacts with phonons or other excitations

in the system, resulting in the energy of the laser photons being shifted up or down. The shift in energy gives information about the phonon modes in the system. Infrared spectroscopy yields similar, but complementary, information.

Typically, a sample is illuminated with a laser beam. Light from the illuminated spot is collected with a lens and sent through a monochromator. Wavelengths close to the laser line, due to elastic Rayleigh scattering, are filtered out while the rest of the collected light is dispersed onto a detector.



Spontaneous Raman scattering is typically very weak, and as a result the main difficulty of Raman spectroscopy is separating the weak inelastically scattered light from the intense Rayleigh scattered laser light. Historically, Raman spectrometers used holographic diffraction gratings and multiple dispersion stages to achieve a high degree of laser rejection. In the past, PMTs were the detectors of choice for dispersive Raman setups, which resulted in long acquisition times. However, modern instrumentation almost universally employs notch or edge filters for laser rejection and spectrographs (either axial transmissive (AT), Czerny-Turner (CT) monochromator) or FT (Fourier transform spectroscopy based), and CCD detectors.

There are a number of advanced types of Raman spectroscopy, including surface-enhanced Raman, tip-enhanced Raman, polarised Raman, stimulated Raman (analogous to stimulated emission), transmission Raman, spatially-offset Raman, and hyper Raman.

## Basic theory

The Raman effect occurs when light impinges upon a molecule and interacts with the electron cloud and the bonds of that molecule. The incident photon excites the molecule into a virtual state. For the spontaneous Raman effect, the molecule will be excited from the ground state to a virtual energy state, and relax into a vibrational excited state. Two series of lines exist around this central vibrational transition. They correspond to the complimentary rotational transition. Anti-stokes lines correspond to rotational relaxation whereas Stokes-Lines correspond to rotational excitation.

A change in the molecular polarization potential — or amount of deformation of the electron cloud — with respect to the vibrational coordinate is required for the molecule to exhibit the Raman effect. The amount of the polarizability change will determine the Raman scattering intensity, whereas the Raman shift is equal to the vibrational level that is involved.

## History

Although the inelastic scattering of light was predicted by Smekal in 1923, it was not until 1928 that it was observed in practice. The Raman effect was named after one of its discoverers, the Indian scientist Sir C. V. Raman who observed the effect by means of sunlight (1928, together with K. S. Krishnan and independently by Grigory Landsberg and Leonid Mandelstam).<sup>[1]</sup> Raman won the Nobel Prize in Physics in 1930 for this discovery accomplished using sunlight, a narrow band photographic filter to create monochromatic light and a "crossed" filter to block this monochromatic light. He found that light of changed frequency passed through the "crossed" filter.

Systematic pioneering theory of the Raman effect was developed by Czechoslovak physicist George Placzek between 1930 and 1934.<sup>[2]</sup> The mercury arc became the principal light source, first with photographic detection and then with spectrophotometric detection. Currently lasers are used as light sources.

## Applications

Raman spectroscopy is commonly used in chemistry, since vibrational information is specific for the chemical bonds in molecules. It therefore provides a fingerprint by which the molecule can be identified. For instance, the vibrational frequencies of SiO, Si<sub>2</sub>O<sub>2</sub>, and Si<sub>3</sub>O<sub>3</sub> were identified and assigned on the basis of normal coordinate analyses using infrared and Raman spectra.<sup>[3]</sup> The fingerprint region of organic molecules is in the (wavenumber) range 500-2000 cm<sup>-1</sup>. Another way that the technique is used is to study changes in chemical bonding, e.g., when a substrate is added to an enzyme.

Raman gas analyzers have many practical applications. For instance, they are used in medicine for real-time monitoring of anaesthetic and respiratory gas mixtures during surgery.

In solid state physics, spontaneous Raman spectroscopy is used to, among other things, characterize materials, measure temperature, and find the crystallographic orientation of a sample. As with single molecules, a given solid material has characteristic phonon modes that can help an experimenter identify it. In addition, Raman spectroscopy can be used to observe other low frequency excitations of the solid, such as plasmons, magnons, and superconducting gap excitations. The spontaneous Raman signal gives information on the population of a given phonon mode in the ratio between the Stokes (downshifted) intensity and anti-Stokes (upshifted) intensity.

Raman scattering by an anisotropic crystal gives information on the crystal orientation. The polarization of the Raman scattered light with respect to the crystal and the polarization of the laser light can be used to find the orientation of the crystal, if the crystal structure (specifically, its point group) is known.

Raman active fibers, such as aramid and carbon, have vibrational modes that show a shift in Raman frequency with applied stress. Polypropylene fibers also exhibit similar shifts. The radial breathing mode is a commonly used technique to evaluate the diameter of carbon nanotubes. In nanotechnology, a Raman microscope can be used to analyze nanowires to better understand the composition of the structures.

Spatially Offset Raman Spectroscopy (SORS), which is less sensitive to surface layers than conventional Raman, can be used to discover counterfeit drugs without opening their internal packaging, and for non-invasive monitoring of biological tissue.<sup>[4]</sup> Raman spectroscopy can be used to investigate the chemical composition of historical documents such as the Book of Kells and contribute to knowledge of the social and economic conditions at the time the documents were produced.<sup>[5]</sup> This is especially helpful because Raman spectroscopy offers a non-invasive way to determine the best course of preservation or conservation treatment for such materials.

Raman spectroscopy is being investigated as a means to detect explosives for airport security.<sup>[6]</sup>

## Microspectroscopy

Raman spectroscopy offers several advantages for microscopic analysis. Since it is a scattering technique, specimens do not need to be fixed or sectioned. Raman spectra can be collected from a very small volume (< 1 μm in diameter); these spectra allow the identification of species present in that volume. Water does not generally interfere with Raman spectral analysis. Thus, Raman spectroscopy is suitable for the microscopic

examination of minerals, materials such as polymers and ceramics, cells and proteins. A Raman microscope begins with a standard optical microscope, and adds an excitation laser, a monochromator, and a sensitive detector (such as a charge-coupled device (CCD), or photomultiplier tube (PMT)). → FT-Raman has also been used with microscopes.

In *direct imaging*, the whole field of view is examined for scattering over a small range of wavenumbers (Raman shifts). For instance, a wavenumber characteristic for cholesterol could be used to record the distribution of cholesterol within a cell culture.

The other approach is *hyperspectral imaging* or *chemical imaging*, in which thousands of Raman spectra are acquired from all over the field of view. The data can then be used to generate images showing the location and amount of different components. Taking the cell culture example, a hyperspectral image could show the distribution of cholesterol, as well as proteins, nucleic acids, and fatty acids. Sophisticated signal- and image-processing techniques can be used to ignore the presence of water, culture media, buffers, and other interferents.

Raman microscopy, and in particular confocal microscopy, has very high spatial resolution. For example, the lateral and depth resolutions were 250 nm and 1.7  $\mu\text{m}$ , respectively, using a confocal Raman microspectrometer with the 632.8 nm line from a He-Ne laser with a pinhole of 100  $\mu\text{m}$  diameter. Since the objective lenses of microscopes focus the laser beam to several micrometres in diameter, the resulting photon flux is much higher than achieved in conventional Raman setups. This has the added benefit of enhanced fluorescence quenching. However, the high photon flux can also cause sample degradation, and for this reason some setups require a thermally conducting substrate (which acts as a heat sink) in order to mitigate this process.

By using Raman microspectroscopy, *in vivo* time- and space-resolved Raman spectra of microscopic regions of samples can be measured. As a result, the fluorescence of water, media, and buffers can be removed. Consequently *in vivo* time- and space-resolved Raman spectroscopy is suitable to examine proteins, cells and organs.

Raman microscopy for biological and medical specimens generally uses near-infrared (NIR) lasers (785 nm diodes and 1064 nm Nd:YAG are especially common). This reduces the risk of damaging the specimen by applying higher energy wavelengths. However, the intensity of NIR Raman is low (owing to the  $\omega^{-4}$  dependence of Raman scattering intensity), and most detectors required very long collection times. Recently, more sensitive detectors have become available, making the technique better suited to general use. Raman microscopy of inorganic specimens, such as rocks and ceramics and polymers, can use a broader range of excitation wavelengths.<sup>[7]</sup>

## Polarized analysis

The polarization of the Raman scattered light also contains useful information. This property can be measured using (plane) polarized laser excitation and a polarization analyzer. Spectra acquired with the analyzer set at both perpendicular and parallel to the excitation plane can be used to calculate the depolarization ratio. Study of the technique is pedagogically useful in teaching the connections between group theory, symmetry, Raman activity and peaks in the corresponding Raman spectra.

The spectral information arising from this analysis gives insight into molecular orientation and vibrational symmetry. In essence, it allows the user to obtain valuable information relating to the molecular shape, for example in synthetic chemistry or polymorph analysis.

It is often used to understand macromolecular orientation in crystal lattices, liquid crystals or polymer samples.<sup>[8]</sup>

## Variations

Several variations of Raman spectroscopy have been developed. The usual purpose is to enhance the sensitivity (e.g., surface-enhanced Raman), to improve the spatial resolution (Raman microscopy), or to acquire very specific information (resonance Raman).

- **Surface Enhanced Raman Spectroscopy (SERS)** - Normally done in a silver or gold colloid or a substrate containing silver or gold. Surface plasmons of silver and gold are excited by the laser, resulting in an increase in the electric fields surrounding the metal. Given that Raman intensities are proportional to the electric field, there is large increase in the measured signal (by up to  $10^{11}$ ). This effect was originally observed by Martin Fleischmann but the prevailing explanation was proposed by Van Duyne in 1977.<sup>[9]</sup>
- **Resonance Raman spectroscopy** - The excitation wavelength is matched to an electronic transition of the molecule or crystal, so that vibrational modes associated with the excited electronic state are greatly enhanced. This is useful for studying large molecules such as polypeptides, which might show hundreds of bands in "conventional" Raman spectra. It is also useful for associating normal modes with their observed frequency shifts.<sup>[10]</sup>
- **Surface Enhanced Resonance Raman Spectroscopy (SERRS)** - A combination of SERS and resonance Raman spectroscopy which uses proximity to a surface to increase Raman intensity, and excitation wavelength matched to the maximum absorbance of the molecule being analysed.
- **Hyper Raman** - A non-linear effect in which the vibrational modes interact with the second harmonic of the excitation beam. This requires very high power, but allows the observation of vibrational modes which are normally "silent". It frequently relies on SERS-type enhancement to boost the sensitivity.<sup>[11]</sup>
- **Spontaneous Raman Spectroscopy** - Used to study the temperature dependence of the Raman spectra of molecules.
- **Optical Tweezers Raman Spectroscopy (OTRS)** - Used to study individual particles, and even biochemical processes in single cells trapped by optical tweezers.
- **Stimulated Raman Spectroscopy** - A two color pulse transfers the population from ground to a rovibrationally excited state, if the difference in energy corresponds to an allowed Raman transition. Two photon UV ionization, applied after the population transfer but before relaxation, allows the intra-molecular or inter-molecular Raman spectrum of a gas or molecular cluster (indeed, a given conformation of molecular cluster) to be collected. This is a useful molecular dynamics technique.
- **Spatially Offset Raman Spectroscopy (SORS)** - The Raman scatter is collected from regions laterally offset away from the excitation laser spot, leading to significantly lower contributions from the surface layer than with traditional Raman spectroscopy.<sup>[12]</sup>
- → **Coherent anti-Stokes Raman spectroscopy (CARS)** - Two laser beams are used to generate a coherent anti-Stokes frequency beam, which can be enhanced by resonance.
- **Raman optical activity (ROA)** - Measures vibrational optical activity by means of a small difference in the intensity of Raman scattering from chiral molecules in right- and left-circularly polarized incident light or, equivalently, a small circularly polarized component in the scattered light.<sup>[13]</sup>

- **Transmission Raman** - Allows probing of a significant bulk of a turbid material, such as powders, capsules, living tissue, etc. It was largely ignored following investigations in the late 1960s<sup>[14]</sup> but was rediscovered in 2006 as a means of rapid assay of pharmaceutical dosage forms.<sup>[15]</sup> There are also medical diagnostic applications.<sup>[16]</sup>
- **Inverse Raman spectroscopy.**
- **Tip-Enhanced Raman Spectroscopy (TERS)** - Uses a silver or gold tip to enhance the Raman signals of molecules situated in its vicinity. The spatial resolution is approximately the size of the tip apex (20-30 nm). TERS has been shown to have sensitivity down to the single molecule level.

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## External links

- Chemical Imaging Without Dyeing (<http://witec.de/en/download/Raman/ImagingMicroscopy04.pdf>) - Chemical Imaging Without Dyeing
- An introduction to Raman spectroscopy (<http://www.jobinyvon.com/Raman/Tutorial-Intro>)
- Raman Fundamentals 'What is Raman Spectroscopy?' (<http://www.andor.com/chemistry/?app=64>)
- DoITPoMS Teaching and Learning Package - Raman Spectroscopy (<http://www.doitpoms.ac.uk/tlplib/raman/index.php>) - an introduction, aimed at undergraduate level
- Raman Spectroscopy Tutorial ([http://161.58.205.25/Raman\\_Spectroscopy/rtr-ramantutorial.php?ss=800](http://161.58.205.25/Raman_Spectroscopy/rtr-ramantutorial.php?ss=800)) - A detailed explanation of Raman Spectroscopy including Resonance-Enhanced Raman Scattering and Surface-Enhanced Raman Scattering.
- The Science Show, ABC Radio National (<http://www.abc.net.au/rn/science/ss/stories/s1581469.htm>) - Interview with Scientist on NASA funded project to build Raman Spectrometer for the 2009 Mars mission: a cellular phone size device to detect almost any substance known, with commercial <USD\$5000 commercial spin-off, prototyped by June 2006.
- Raman spectroscopy for medical diagnosis ([http://pubs.acs.org/subscribe/journals/ancham/79/i11/pdf/0607feature\\_griffiths.pdf](http://pubs.acs.org/subscribe/journals/ancham/79/i11/pdf/0607feature_griffiths.pdf)) from the June 1, 2007 issue of *Analytical Chemistry* (<http://pubs3.acs.org/acs/journals/toc.page?incoden=ancham&indecade=0&involume=79&inissue=11>)

# Coherent anti-Stokes Raman spectroscopy

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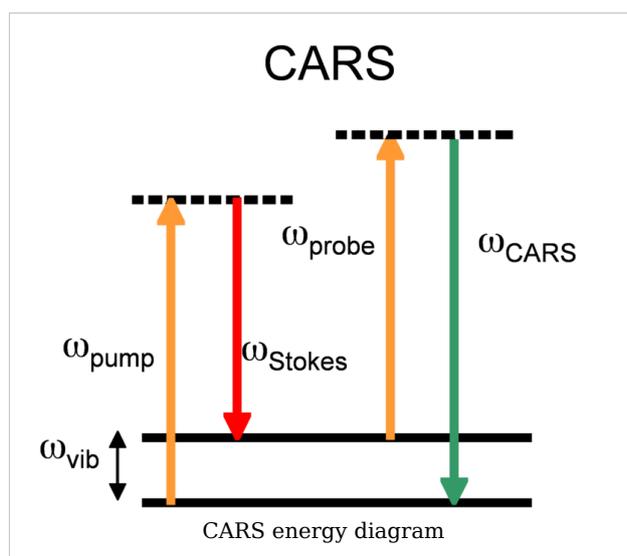
**Coherent anti-Stokes Raman spectroscopy**, also called Coherent anti-Stokes Raman scattering spectroscopy (CARS), is a form of → spectroscopy used primarily in chemistry, physics and related fields. It is sensitive to the same vibrational signatures of molecules as seen in → Raman spectroscopy, typically the nuclear vibrations of chemical bonds. Unlike Raman spectroscopy, CARS employs multiple photons to address the molecular vibrations, and produces a signal in which the emitted waves are coherent with one another. As a result, CARS is orders of magnitude stronger than spontaneous Raman emission. CARS is a third-order nonlinear optical process involving three laser beams: a pump beam of frequency  $\omega_p$ , a Stokes beam of frequency  $\omega_s$  and a probe beam at frequency  $\omega_{pr}$ . These beams interact with the sample and generate a coherent optical signal at the anti-Stokes frequency ( $\omega_p - \omega_s + \omega_{pr}$ ). The latter is resonantly enhanced when the frequency difference between the pump and the Stokes beams ( $\omega_p - \omega_s$ ) coincides with the frequency of a Raman resonance, which is the basis of the technique's intrinsic vibrational contrast mechanism.<sup>[1]</sup>  
[2]

## History

The acronym CARS, which invokes a seemingly inadvertent relation to automobiles, is actually closely related to the birth story of the technique. In 1965, a paper was published by two researchers of the Scientific Laboratory at the Ford Motor Company, P. D. Maker and R. W. Terhune, in which the CARS phenomenon was reported for the first time.<sup>[3]</sup> Maker and Terhune used a pulsed ruby laser to investigate the third order response of several materials. They first passed the ruby beam of frequency  $\omega$  through a Raman shifter to create a second beam at  $\omega - \omega_v$ , and then directed the two beams simultaneously onto the sample. When the pulses from both beams overlapped in space and time, the Ford researchers observed a signal at  $\omega + \omega_v$ , which is the blue-shifted CARS signal. They also demonstrated that the signal increases significantly when the difference frequency  $\omega_v$  between the incident beams matches a Raman frequency of sample. Maker and Terhune called their technique simply 'three wave mixing experiments'. The name coherent anti-Stokes Raman spectroscopy was assigned almost ten years later, by Begley et al. at Stanford University in 1974.<sup>[4]</sup> Since then, this vibrationally sensitive nonlinear optical technique is commonly known as CARS.

## Principle

The CARS process can be physically explained by using either a classical oscillator model or by using a  $\rightarrow$  quantum mechanical model that incorporates the energy levels of the molecule. Classically, the Raman active vibrator is modeled as a (damped) harmonic oscillator with a characteristic frequency of  $\omega_v$ . In CARS, this oscillator is not driven by a single optical wave, but by the difference frequency ( $\omega_p - \omega_s$ ) between the pump and the Stokes beams instead. This driving mechanism is similar to hearing the low combination tone when striking two different high tone piano keys: your ear is



sensitive to the difference frequency of the high tones. Similarly, the Raman oscillator is susceptible to the difference frequency of two optical waves. When the difference frequency  $\omega_p - \omega_s$  approaches  $\omega_v$ , the oscillator is driven very efficiently. On a molecular level, this implies that the electron cloud surrounding the chemical bond is vigorously oscillating with the frequency  $\omega_p - \omega_s$ . These electron motions alter the optical properties of the sample, i.e. there is a periodic modulation of the refractive index of the material. This periodic modulation can be probed by a third laser beam, the probe beam. When the probe beam is propagating through the periodically altered medium, it acquires the same modulation. Part of the probe, originally at  $\omega_{pr}$  will now get modified to  $\omega_{pr} + \omega_p - \omega_s$ , which is the observed anti-Stokes emission. Under certain beam geometries, the anti-Stokes emission may diffract away from the probe beam, and can be detected in a separate direction.

While intuitive, this classical picture does not take into account the quantum mechanical energy levels of the molecule. Quantum mechanically, the CARS process can be understood as follows. Our molecule is initially in the ground state, the lowest energy state of the molecule. The pump beam excites the molecule to a virtual state. A virtual state is not an eigenstate of the molecule, rather it exhibits an infinitely short lifetime, and thus the molecule cannot remain in this state. If a Stokes beam is simultaneously present along with the pump, the virtual state can be used as an instantaneous gateway to address a vibrational eigenstate of the molecule. The joint action of the pump and the Stokes has effectively established a coupling between the ground state and the vibrationally excited state of the molecule. The molecule is now in two states at the same time: it resides in a coherent superposition of states. This coherence between the states can be probed by the probe beam, which promotes the system to a virtual state. Again, the molecule cannot stay in the virtual state and will fall back instantaneously to the ground state under the emission of a photon at the anti-Stokes frequency. The molecule is no longer in a superposition, as it resides again in one state, the ground state. In the quantum mechanical model, no energy is deposited in the molecule during the CARS process. Instead, the molecule acts like a medium for converting the frequencies of the three incoming waves into a CARS signal (a parametric process). There are, however, related coherent Raman processes that occur simultaneously which do deposit energy into the molecule.

## Comparison to Raman spectroscopy

CARS is often compared to Raman spectroscopy as both techniques probe the same Raman active modes. Raman can be done using a single CW laser whereas CARS requires (generally) two pulsed laser sources. The Raman signal is detected on the red side of the incoming radiation where it might have to compete with other fluorescent processes. The CARS signal is detected on the blue side, which is free from fluorescence, but it comes with a non-resonant contribution. The differences between the signals from Raman and CARS (there are many variants of both techniques) stems largely from the fact that Raman relies on a spontaneous transition whereas CARS relies on a coherently driven transition. The total Raman signal collected from a sample is the incoherent addition of the signal from individual molecules. It is therefore linear in the concentration of those molecules and the signal is emitted in all directions. The total CARS signal comes from a coherent addition of the signal from individual molecules. For the coherent addition to be additive, phase-matching must be fulfilled. For tight focusing conditions this is generally not a restriction. Once phase-matching is fulfilled the signal amplitude grows linear with distance so that the power grows quadratically. This signal forms a collimated beam that is therefore easily collected. The fact that the CARS signal is quadratic in the distance makes it quadratic with respect to the concentration and therefore especially sensitive to the majority constituent. The total CARS signal also contains an inherent non-resonant background. This non-resonant signal can be considered as the result of (several) far off-resonance transitions that also add coherently. The resonant amplitude contains a phase shift of  $\pi$  over the resonance whereas the non-resonant part does not. The spectral line shape of the CARS intensity therefore resembles a Fano-profile which is shifted with respect to the Raman signal. To compare the spectra from multi-component compounds, the (resonant) CARS spectral amplitude should be compared to the Raman spectral intensity.

Theoretically Raman spectroscopy and CARS spectroscopy are equally sensitive as they use the same molecular transitions. However, given the limits on input power (damage

threshold) and detector noise (integration time), the signal from a single transition can be collected much faster in practical situation (a factor of  $10^5$ ) using CARS. Imaging of known substances (known spectra) is therefore often done using CARS. Given the fact that CARS is a higher order nonlinear process, the CARS signal from a single molecule is larger than the Raman signal from a single molecule for a sufficiently high driving intensity. However at very low concentrations, the advantages of the coherent addition for CARS signal reduces and the presence of the incoherent background becomes an increasing problem.

Since CARS is such a nonlinear process there are not really any 'typical' experimental numbers. One example is given below under the explicit warning that just changing the pulse duration by one order of magnitude changes the CARS signal by three orders of magnitude. The comparison should only be used as an indication of the order of magnitude of the signals. 200 mW average power input (CW for the Raman), in a 0.9NA objective with a center wavelength around 800 nm, constitutes a power density of  $26 \text{ MW/cm}^2$  (focal length = 1.5 micrometre, focal volume =  $1.16 \text{ micrometre}^3$ , photon energy =  $2.31 \cdot 10^{-19} \text{ J}$  or 1.44 eV). The Raman cross section for the vibration of the aromatic ring in Toluene around  $1000 \text{ cm}^{-1}$  is on the order of  $10^{-29} \text{ cm}^2/\text{molecule}\cdot\text{steradian}$ . Therefore the Raman signal is around  $26 \cdot 10^{-22} \text{ W/molecule}\cdot\text{steradian}$  or  $3.3 \cdot 10^{-21} \text{ W/molecule}$  (over  $4\text{Pi}$ ). That is 0.014 photon/sec\*molecule. The density of Toluene =  $0.8668 \cdot 10^3 \text{ kg/m}^3$ , Molecular mass =  $92.14 \cdot 10^{-3} \text{ kg/mol}$ . Therefore the focal volume ( $\sim 1$  cubic micrometre) contains  $6 \cdot 10^9$  molecules. Those molecules together generate a Raman signal in the order of  $2 \cdot 10^{-11} \text{ W}$  (20pW) or roughly one hundred million photons/sec (over a  $4\text{Pi}$  solid angle). A CARS experiment with similar parameters (150 mW at 1064 nm, 200 mW at 803.5 nm, 15ps pulses at 80Mhz repetition frequency, same objective lens) yields roughly  $17.5 \cdot 10^{-6} \text{ W}$  (on the  $3000 \text{ cm}^{-1}$  line, which has 1/3 of the strength and roughly 3 times the width). This CARS power is roughly  $10^6$  higher than the Raman but since there are  $6 \cdot 10^9$  molecules, the signal per molecule from CARS is only  $4 \cdot 10^{-25} \text{ W/molecule}\cdot\text{sec}$  or  $1.7 \cdot 10^{-6}$  photons/molecule\*sec. If we allow for two factors of three (line strength and line width) than the spontaneous Raman signal per molecule still exceeds the CARS per molecule by a more than two orders of magnitude. The coherent addition of the CARS signal from the molecules however yields a total signal that is much higher than the Raman.

The sensitivity in many CARS experiments is not limited by the detection of CARS photons but rather by the distinction between the resonant and non-resonant part of the CARS signal.

## Applications

CARS is used for species selective microscopy and combustion diagnostics. The first exploits the selectivity of vibrational spectroscopy whereas the latter is aimed at temperature measurements; the CARS signal is temperature dependent. The strength of the signal scales with the difference in the ground state population and the vibrationally excited state population. Since the population of states follows the temperature dependent Bose-Einstein Distribution, the CARS signal carries an intrinsic temperature dependence as well. This temperature dependence makes CARS a popular technique for monitoring the temperature of hot gases and flames.

## See also

- Coherent Stokes Raman spectroscopy
- → Raman spectroscopy
- Four-wave mixing

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# Time-resolved spectroscopy

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In physics and physical chemistry, **time-resolved spectroscopy** is the study of dynamic processes in materials or chemical compounds by means of → spectroscopic techniques. Most often, processes are studied that occur after illumination of a material, but in principle, the technique can be applied to any process which leads to a change in properties of a material. With the help of pulsed lasers, it is possible to study processes which occur on time scales as short as  $10^{-14}$  seconds. The rest of the article discusses different types of time-resolved spectroscopy.

## Transient-absorption spectroscopy

Transient-absorption spectroscopy is an extension of absorption spectroscopy. Here, the absorbance at a particular wavelength or range of wavelengths of a sample is measured as a function of time after excitation by a flash of light. In a typical experiment, both the light for excitation ('pump') and the light for measuring the absorbance ('probe') are generated by a pulsed laser. If the process under study is slow, then the time resolution can be obtained with a continuous (i.e., not pulsed) probe beam and repeated conventional spectrophotometric techniques.

Examples of processes that can be studied:

- Optical gain spectroscopy of semiconductor laser materials.
  - Chemical reactions that are initiated by light (or 'photoinduced chemical reactions');
  - The transfer of excitation energy between molecules, parts of molecules, or molecules and their environment;
  - The behaviour of electrons that are freed from a molecule or crystalline material.
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## Other multiple-pulse techniques

Transient spectroscopy as discussed above is a technique that involves two pulses. There are many more techniques that employ two or more pulses, such as:

- Photon echoes.
- Four-wave mixing (involves three laser pulses)

The interpretation of experimental data from these techniques is usually much more complicated than in transient-absorption spectroscopy.

→ Nuclear magnetic resonance and → electron spin resonance are often implemented with multiple-pulse techniques, though with radio waves and micro waves instead of visible light.

## Time-resolved infrared spectroscopy

Time-resolved infrared (TRIR) spectroscopy also employs a two-pulse, "pump-probe" methodology. The pump pulse is typically in the UV region and is often generated by a high-powered Nd:YAG laser whilst the probe beam is in the infrared region. This technique currently operates down to the picosecond time regime and surpasses transient absorption and emission spectroscopy by providing *structural* information on the excited-state kinetics of both dark and emissive states.

## Time-resolved fluorescence spectroscopy

Time-resolved fluorescence spectroscopy is an extension of → fluorescence spectroscopy. Here, the fluorescence of a sample is monitored as a function of time after excitation by a flash of light. The time resolution can be obtained in a number of ways, depending on the required sensitivity and time resolution:

- With fast detection electronics (nanoseconds and slower);
  - With a streak camera (picoseconds and slower);
  - With optical gating (femtoseconds-nanoseconds) - a short laser pulse acts as a gate for the detection of fluorescence light; only fluorescence light that arrives at the detector at the same time as the gate pulse is detected. This technique has the best time resolution, but the efficiency is rather low. An extension of this optical gating technique is to use a "Kerr gate", which allows the scattered → Raman signal to be collected before the (slower) fluorescence signal overwhelms it. This technique can greatly improve the signal:noise ratio of Raman spectra.
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# Terahertz spectroscopy

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**Terahertz frequency radiation for spectroscopy** is typically generated in one of three ways:

- time domain terahertz spectroscopy (TDS), using ultrashort laser pulses
- photomixing, mixing two radiation sources to generate their difference frequency
- → Fourier transform spectroscopy, using a blackbody radiation source

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## X-ray spectroscopy

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**X-ray spectroscopy** is a gathering name for several → spectroscopic techniques for determining the electronic structure of materials by using x-ray excitation.

### X-ray emission spectroscopy

Karl Manne Georg Siegbahn from Uppsala, Sweden (Nobel Prize 1924), who painstakingly produced numerous diamond-ruled glass diffraction gratings for his spectrometers, was one of the pioneers in developing **X-ray emission spectroscopy** (also called X-ray fluorescence spectroscopy). He measured the X-ray wavelengths of many elements to high precision, using high-energy electrons as excitation source.

Intense and wavelength-tunable X-rays are now typically generated with synchrotrons. In a material, the X-rays may suffer an energy loss compared to the incoming beam. This energy loss of the re-emerging beam reflects an internal excitation of the atomic system, an X-ray analogue to the well-known → Raman spectroscopy that is widely used in the optical region.

In the x-ray region there is sufficient energy to probe changes in the electronic state (transitions between orbitals; this is in contrast with the optical region, where the energy loss is often due to changes in the state of the rotational or vibrational degrees of freedom). For instance, in the ultra soft X-ray region (below about 1 keV), crystal field excitations give rise to the energy loss.

We may think of the photon-in-photon-out process as a scattering event. When the x-ray energy corresponds to the binding energy of a core level electron this scattering process is resonantly enhanced by many orders of magnitude. This type of X-ray emission spectroscopy is often referred to as **resonant inelastic x-ray scattering (RIXS)**.

Due to the wide separation of orbital energies of the core levels, it is possible to select a certain atom of interest. The small spatial extent of core level orbitals forces the RIXS process to reflect the electronic structure in close vicinity of the chosen atom. Thus RIXS experiments give valuable information about the local electronic structure of complex systems, and theoretical calculations are relatively simple to perform.

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## Instrumentation

There exist several efficient designs for analyzing an x-ray emission spectrum in the ultra soft X-ray region. The figure of merit for such instruments is the spectral throughput, i.e. the product of detected intensity and spectral resolving power. Usually, it is possible to change the parameters within a certain range while keeping their product constant.

### Grating spectrometers

Typically, the X-rays emerging from a sample must pass a source-defining slit, then optical elements (mirrors and/or gratings) disperse them by diffraction according to their wavelength and, finally, a detector is placed at their focal points.

### Spherical grating mounts

Henry Augustus Rowland (1848-1901) devised an instrument that allowed the use of a single optical element that combines diffraction and focusing: a spherical grating. Reflectivity of X-rays is low regardless of the used material and therefore grazing incidence upon the grating is necessary. X-ray beams impinging on a smooth surface at a few degrees glancing angle of incidence undergo external total reflection which is taken advantage of to enhance the instrumental efficiency substantially.

Denote by  $R$  the radius of a spherical grating. Imagine a circle with half the radius  $R$  tangent to the center of the grating surface. This small circle is called the **Rowland circle**. If the entrance slit is anywhere on this circle, then a beam passing the slit and striking the grating will be split into a specularly reflected beam, and beams of all diffraction orders, that come into focus at certain points on the same circle.

### Plane grating mounts

Similar as in optical spectrometers, a plane grating spectrometer first needs optics that turns the divergent rays emitted by the x-ray source into a parallel beam. This may be achieved by using a parabolic mirror. The parallel rays emerging from this mirror strike a plane grating (with constant groove distance) at the same angle and are diffracted according to their wavelength. A second parabolic mirror then collects the diffracted rays at a certain angle and creates an image on a detector. A spectrum within a certain wavelength range can be recorded simultaneously by using a 2-dimensional position sensitive detector such as a microchannel photomultiplier plate or an x-ray sensitive CCD chip (film plates are also possible to use).

### Interferometers

Instead of using the concept of multiple beam interference that gratings produce, one may simply let two rays interfere. By recording the intensity of two such co-linearly at some fixed point and changing their relative phase one obtains an intensity spectrum as a function of path length difference. One can show that this is equivalent to a Fourier transformed spectrum as a function of frequency. The highest recordable frequency of such a spectrum is dependent on the minimum step size chosen in the scan and the frequency resolution (i.e. how well a certain wave can be defined in terms of its frequency) depends on the maximum path length difference achieved. The latter feature allows a much more compact design for achieving high resolution than for a grating spectrometer because x-ray wavelengths are small compared to attainable pathlength differences.

## Other types of X-ray spectroscopy

- X-ray absorption spectroscopy
- X-ray magnetic circular dichroism

# Electron spectroscopy

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**Electron → spectroscopy** is an analytical technique to study the electronic structure and its dynamics in atoms and molecules. In general an excitation source such as x-rays, electrons, or synchrotron radiation will eject an electron from an inner-shell orbital of an atom. Detecting photoelectrons that are ejected by x-rays is called x-ray photoelectron spectroscopy (XPS) or electron spectroscopy for chemical analysis (ESCA). Detecting electrons that are ejected from higher orbitals to conserve energy during electron transitions is called Auger electron spectroscopy (AES).

Experimental applications include high-resolution measurements on the intensity and angular distributions of emitted electrons as well as on the total and partial ion yields. Ejected electrons can escape only from a depth of approximately 3 nanometers or less, making electron spectroscopy most useful to study surfaces of solid materials. Depth profiling is accomplished by combining an electron spectroscopy with a sputtering source that removes surface layers.

Synchrotron radiation research work has been carried out at the MAX Laboratory in Lund, Sweden, Elettra Storage Ring in Trieste, Italy, and at ALS in Berkeley, CA.

## Sources

- The University of Adelaide, Australia <sup>[1]</sup>
- The University of Oulu, Finland <sup>[2]</sup>
- Journal of Electron Spectroscopy and Related Phenomena <sup>[3]</sup>

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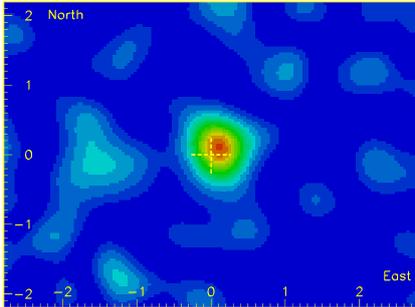
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[3] [http://www.elsevier.com/wps/find/journaldescription.cws\\_home/500848/description#description](http://www.elsevier.com/wps/find/journaldescription.cws_home/500848/description#description)

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# Muon

<i><b>Muon</b></i>	
	
The Moon's cosmic ray shadow, as seen in secondary muons detected 700m below ground, at the Soudan II detector.	
<b>Composition:</b>	Elementary particle
<b>Family:</b>	Fermion
<b>Group:</b>	Lepton
<b>Generation:</b>	Second
<b>Interaction:</b>	Gravity, Electromagnetic, Weak
<b>Antiparticle:</b>	$\mu^+$ (Antimuon)
<b>Theorized:</b>	—
<b>Discovered:</b>	Carl D. Anderson (1936)
<b>Symbol(s):</b>	$\mu^-$
<b>Mass:</b>	$\{105.658369(9) \text{ MeV}/c^2$
<b>Mean lifetime:</b>	$2.19703(4) \times 10^{-6} \text{ s}^{[1]}$
<b>Electric charge:</b>	$-1 e$
<b>Color charge:</b>	None
<b>Spin:</b>	$\frac{1}{2}$

The **muon** (from the Greek letter mu ( $\mu$ ) used to represent it) is an elementary particle similar to the electron, with negative electric charge and a spin of  $\frac{1}{2}$ . Together with the electron, the tauon, and the three neutrinos, it is classified as a lepton. It is the subatomic particle with the second longest mean lifetime (2.2  $\mu\text{s}$ ), behind the neutron ( $\sim 15$  min). Like all elementary particles, the muon has corresponding antiparticle of opposite charge but equal mass and spin: the **antimuon** (also called a *positive muon*). Muons are denoted by  $\mu^-$  and antimuons by  $\mu^+$ . Muons were sometimes referred to as **mu mesons** in the past, even though they are not classified as mesons by modern particle physicists (*see History*).

Muons have a mass of  $105.7 \text{ MeV}/c^2$ , which is about 200 times the mass of the electrons. Since their interactions are very similar to those of the electron, a muon can be thought of as a much heavier version of the electron. Due to their greater mass, muons do not emit as much bremsstrahlung radiation; consequently, they are highly penetrating, much more so than electrons.

As with the case of the other charged leptons, the muon has an associated muon neutrino. Muon neutrinos are denoted by  $\nu_\mu$ .

## History

Muons were discovered by Carl D. Anderson in 1936 while he studied cosmic radiation. He had noticed particles that curved in a manner distinct from that of electrons and other known particles, when passed through a magnetic field. In particular, these new particles were negatively charged but curved to a smaller degree than electrons, but more sharply than protons, for particles of the same velocity. It was assumed that the magnitude of their negative electric charge was equal to that of the electron, and so to account for the difference in curvature, it was supposed that these particles were of intermediate mass (lying somewhere between that of an electron and that of a proton). The discovery of the muon seemed so incongruous and surprising at the time that Nobel laureate I. I. Rabi famously quipped, "Who ordered that?"

For this reason, Anderson initially called the new particle a *mesotron*, adopting the prefix *meso-* from the Greek word for "mid-". Shortly thereafter, additional particles of intermediate mass were discovered, and the more general term *meson* was adopted to refer to any such particle. Faced with the need to differentiate between different types of mesons, the mesotron was in 1947 renamed the *mu meson* (with the Greek letter  $\mu$  (*mu*) used to approximate the sound of the Latin letter *m*).

However, it was soon found that the mu meson significantly differed from other mesons; for example, its decay products included a neutrino and an antineutrino, rather than just one or the other, as was observed in other mesons. Other mesons were eventually understood to be hadrons—that is, particles made of quarks—and thus subject to the residual strong force. In the quark model, a *meson* is composed of exactly two quarks (a quark and antiquark), unlike baryons which are composed of three quarks. Mu mesons, however, were found to be fundamental particles (leptons) like electrons, with no quark structure. Thus, mu mesons were not mesons at all (in the new sense and use of the term *meson*), and so the term *mu meson* was abandoned, and replaced with the modern term *muon*.

## Muon sources

Antimatter
<b>Overview</b>
<b>Annihilation</b>
<b>Devices</b> <ul style="list-style-type: none"> <li>• Particle accelerator</li> <li>• Penning trap</li> </ul>
<b>Antiparticles</b> <ul style="list-style-type: none"> <li>• Positron</li> <li>• Antiproton</li> <li>• Antineutron</li> </ul>
<b>Uses</b> <ul style="list-style-type: none"> <li>• Positron emission tomography</li> <li>• Fuel</li> <li>• Weaponry</li> </ul>

**Bodies**

- ALPHA Collaboration
- ATHENA
- ATRAP
- CERN

**People**

- Paul Dirac
- Carl David Anderson
- Andrei Sakharov

**edit** [2]

Since the production of muons requires an available center of momentum frame energy of over 105 MeV, neither ordinary radioactive decay events nor nuclear fission and fusion events (such as those occurring in nuclear reactors and nuclear weapons) are energetic enough to produce muons. Only nuclear fission produces single-nuclear-event energies in this range, but due to conservation constraints, muons are not produced.

On earth, all naturally occurring muons are apparently created by cosmic rays, which consist mostly of protons, many arriving from deep space at very high energy.

About 10,000 muons reach every square meter of the earth's surface a minute; these charged particles form as by-products of cosmic rays colliding with molecules in the upper atmosphere. Traveling at relativistic speeds, muons can penetrate tens of meters into rocks and other matter before attenuating as a result of absorption or deflection by other atoms.

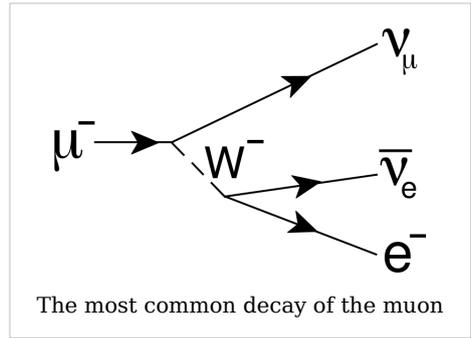
—Mark Wolverton, *science writer, Scientific American magazine, September 2007, page 26 "Muons for Peace"*<sup>[3]</sup>

When a cosmic ray proton impacts atomic nuclei of air atoms in the upper atmosphere, pions are created. These decay within a relatively short distance (meters) into muons (the pion's preferred decay product), and neutrinos. The muons from these high energy cosmic rays, generally continuing essentially in the same direction as the original proton, do so at very high velocities. Although their lifetime *without* relativistic effects would allow a half-survival distance of only about 0.66 km at most, the time dilation effect of special relativity allows cosmic ray secondary muons to survive the flight to the earth's surface. Indeed, since muons are unusually penetrative of ordinary matter, like neutrinos, they are also detectable deep underground and underwater, where they form a major part of the natural background ionizing radiation. Like cosmic rays, as noted, this secondary muon radiation is also directional. See the illustration above of the moon's cosmic ray shadow, detected when 700 m of soil and rock filters secondary radiation, but allows enough muons to form a crude image of the moon, in a directional detector.

The same nuclear reaction described above (i.e., hadron-hadron impacts to produce pion beams, which then quickly decay to muon beams over short distances) is used by particle physicists to produce muon beams, such as the beam used for the muon g-2 <sup>[4]</sup> gyromagnetic ratio experiment (see link below). In naturally-produced muons, the very high-energy protons to begin the process are thought to originate from acceleration by electromagnetic fields over long distances between stars or galaxies, in a manner somewhat analogous to the mechanism of proton acceleration used in laboratory particle accelerators.

## Muon decay

Muons are unstable elementary particles and are heavier than electrons and neutrinos but lighter than all other matter particles. They decay via the weak interaction to an electron, two neutrinos and possibly other particles with a net charge of zero. Nearly all of the time, they decay into an electron, an electron-antineutrino, and a muon-neutrino. Antimuons decay to a positron, an electron-neutrino, and a muon-antineutrino:



$$\mu^- \rightarrow e^- + \bar{\nu}_e + \nu_\mu, \quad \mu^+ \rightarrow e^+ + \nu_e + \bar{\nu}_\mu.$$

The mean lifetime of the (positive) muon is  $2.197\,019 \pm 0.000\,021 \mu\text{s}^{[5]}$ . The equality of the muon and anti-muon lifetimes has been established to better than one part in  $10^4$ .

The tree-level muon decay width is

$$\Gamma = \frac{G_F^2 m_\mu^5}{192\pi^3} I\left(\frac{m_e^2}{m_\mu^2}\right), \text{ where } I(x) = 1 - 8x + 12x^2 \ln\left(\frac{1}{x}\right) + 8x^3 - x^4.$$

A photon or electron-positron pair is also present in the decay products about 1.4% of the time.

The decay distributions of the electron in muon decays have been parametrized using the so-called Michel parameters. The values of these four parameters are predicted unambiguously in the Standard Model of particle physics, thus muon decays represent an excellent laboratory to test the space-time structure of the weak interaction. No deviation from the Standard Model predictions has yet been found.

Certain neutrino-less decay modes are kinematically allowed but forbidden in the Standard Model. Examples, forbidden by lepton flavour conservation, are

$$\mu^- \rightarrow e^- + \gamma \text{ and } \mu^- \rightarrow e^- + e^+ + e^-.$$

Observation of such decay modes would constitute clear evidence for physics beyond the Standard Model (BSM). Upper limits for the branching fractions of such decay modes are in the range  $10^{-11}$  to  $10^{-12}$ .

## Muonic atoms

The muon was the first elementary particle discovered that does not appear in ordinary atoms. Negative muons can, however, form muonic atoms by replacing an electron in ordinary atoms. Muonic atoms are much smaller than typical atoms because the larger mass of the muon gives it a smaller ground-state wavefunction than the electron.

A positive muon, when stopped in ordinary matter, can also bind an electron and form an exotic atom known as muonium (Mu) atom, in which the muon acts as the nucleus. The positive muon, in this context, can be considered a pseudo-isotope of hydrogen with one ninth of the mass of the proton. Because the reduced mass of muonium, and hence its Bohr radius, is very close to that of hydrogen, this short-lived "atom" behaves chemically — to a first approximation — like hydrogen, deuterium and tritium.

## Anomalous magnetic dipole moment

The anomalous magnetic dipole moment is the difference between the experimentally observed value of the magnetic dipole moment and the theoretical value predicted by the Dirac equation. The measurement and prediction of this value is very important in the precision tests of QED (quantum electrodynamics). The E821 experiment <sup>[6]</sup> at Brookhaven National Laboratory (BNL) studied the precession of muon and anti-muon in a constant external magnetic field as they circulated in a confining storage ring. The E821 Experiment reported the following average value (from the July 2007 review by Particle Data Group) <sup>[7]</sup>

$$a = \frac{g - 2}{2} = 0.00116592080(54)(33)$$

where the first errors are statistical and the second systematic.

The difference between the g-factors of the muon and the electron is due to their difference in mass. Because of the muon's larger mass, contributions to the theoretical calculation of its anomalous magnetic dipole moment from Standard Model weak interactions and from contributions involving hadrons are important at the current level of precision, whereas these effects are not important for the electron. The muon's anomalous magnetic dipole moment is also sensitive to contributions from new physics beyond the Standard Model, such as supersymmetry. For this reason, the muon's anomalous magnetic moment is normally used as a probe for new physics beyond the Standard Model rather than as a test of QED (Phys.Lett. B649, 173 (2007) <sup>[8]</sup>).

## See also

- Muonium
- Muon spin spectroscopy
- Muon-catalyzed fusion
- List of particles

## References

- [1] W.-M. Yao et al. (Particle Data Group), J. Phys. G 33, 1 (2006)
- [2] <http://en.wikipedia.org/w/index.php?title=Template:Antimatter&action=edit>
- [3] Wolverton, Mark (September 2007), " Muons for Peace: New way to spot hidden nukes gets ready to debut (<http://www.sciam.com/article.cfm?id=muons-for-peace>)", *Scientific American* (Scientific American, Inc.) **297** (3): 26-28, , retrieved on 2008-08-01 *Note: only first two paragraphs available on-line*
- [4] <http://www.bnl.gov/bnlweb/pubaf/pr/2002/bnlpr073002.htm>
- [5] (<http://arxiv.org/abs/0704.1981v1>)
- [6] <http://www.g-2.bnl.gov/>
- [7] [http://pdg.lbl.gov/2007/reviews/g-2\\_s004219.pdf](http://pdg.lbl.gov/2007/reviews/g-2_s004219.pdf)
- [8] <http://arxiv.org/abs/hep-ph/0611102>
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- J.C. Street and E.C. Stevenson, "New Evidence for the Existence of a Particle of Mass Intermediate Between the Proton and Electron", Phys. Rev. 52, 1003-1004 (1937). Full text available in ([http://prola.aps.org/pdf/PR/v52/i9/p1003\\_1"PDF"](http://prola.aps.org/pdf/PR/v52/i9/p1003_1)).
- Serway & Faughn, *College Physics, Fourth Edition* (Fort Worth TX: Saunders, 1995) page 841
- Emanuel Derman, *My Life As A Quant* (Hoboken, NJ: Wiley, 2004) pp. 58-62.

- Marc Knecht ; *The Anomalous Magnetic Moments of the Electron and the Muon*, Poincaré Seminar (Paris, Oct. 12, 2002), published in : Duplantier, Bertrand; Rivasseau, Vincent (Eds.) ; *Poincaré Seminar 2002*, Progress in Mathematical Physics 30, Birkhäuser (2003) [ISBN 3-7643-0579-7]. Full text available in *PostScript* (<http://parthe.lpthe.jussieu.fr/poincare/textes/octobre2002/Knecht.ps>).

## External links

- Muon anomalous magnetic moment and supersymmetry (<http://antwrp.gsfc.nasa.gov/apod/ap050828.html>)
- g-2 (muon anomalous magnetic moment) experiment (<http://www.g-2.bnl.gov/>)
- muLan (Measurement of the Positive Muon Lifetime) experiment (<http://www.npl.uiuc.edu/exp/mulan/>)
- The Review of Particle Physics (<http://pdg.lbl.gov/>)
- The TRIUMF Weak Interaction Symmetry Test (<http://twist.triumf.ca/>)

# Ionization cooling

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## Physical Principle

**Ionization cooling** is a process by which the beam emittance of a beam of particles may be reduced <sup>[1]</sup>. In ionization cooling, particles are passed through some material. The momentum of the particles is reduced as they ionize atomic electrons in the material. Thus the normalised beam emittance is reduced. By re-accelerating the beam, for example in an RF cavity, the longitudinal momentum may be restored without replacing transverse momentum. Thus overall the angular spread and hence the geometric emittance in the beam will be reduced.

Ionization cooling can be spoiled by stochastic physical processes. Multiple Coulomb scattering in muons as well as nuclear scattering in protons and ions can reduce the cooling or even lead to net heating transverse to the direction of beam motion. In addition, energy straggling can cause heating parallel to the direction of beam motion.

## Muon Cooling

The primary use of ionization cooling is envisaged to be for cooling of muon beams. This is because ionization cooling is the only technique that works on the timescale of the muon lifetime. Ionization cooling channels have been designed for use in a Neutrino Factory and a Muon Collider. Muon ionization cooling is expected to be demonstrated for the first time by the Proof of Principle International Muon Ionization Cooling Experiment. Other PoP muon ionization cooling experiments have been devised.

## Other Particles

Ionization cooling has also been proposed for use in low energy ion beams and proton beams.

## References

- [1] G.I. Budker, in: Proceedings of 15th International Conference on High Energy Physics, Kiev, 1970 A.N. Skrinsky, Intersecting storage rings at Novosibirsk, in: Proceedings of Morges Seminar, 1971 Report CERN/D.PH II/YGC/mng

# ISIS neutron source

**ISIS** is a world leading pulsed neutron and  $\rightarrow$  muon source. It is situated at the Rutherford Appleton Laboratory in Oxfordshire, United Kingdom and is part of the Science and Technology Facilities Council. It uses the techniques muon spectroscopy and neutron scattering to probe the structure and dynamics of condensed matter on a microscopic scale ranging from the subatomic to the macromolecular.

Hundreds of experiments are performed annually at ISIS by visiting researchers from around the world, in diverse science areas including physics, chemistry, materials engineering, earth sciences, biology and archaeology.

## Neutrons and muons

Neutrons are uncharged constituents of atoms and penetrate materials well, deflecting only from the nuclei of atoms. The statistical accumulation of deflected neutrons at different positions beyond the sample can be used to find the structure of a material, and the loss or gain of energy by neutrons can reveal the dynamic behaviour of parts of a sample, for example diffusive processes in solids. At ISIS the neutrons are created by accelerating 'bunches' of protons in a synchrotron, then colliding these with a heavy tantalum metal target, under a constant cooling load to dissipate the heat from the 160 kW proton beam. The tantalum atoms slough off neutrons, and these are channelled through guides, or beamlines, to about 20 instruments, individually optimised for the study of different types of matter. The target



ISIS experimental hall for Target Station 1

station and most of the instruments are set in a large hall. The penetrating neutrons are a dangerous form of radiation so the target and beamlines are heavily shielded with concrete. ISIS produces  $\rightarrow$  muons by colliding a fraction of the proton beam with a graphite target, producing pions which decay rapidly into muons, delivered in a spin-polarised beam to sample stations.

## Science at ISIS

ISIS is administered and operated by the Science and Technology Facilities Council (previously CCLRC). Experimental time is open to academic users from funding countries and is applied for through a twice-yearly 'call for proposals'. Research allocation, or 'beam-time', is allotted to



Another view of the ISIS experimental hall for Target Station 1

applicants via a peer-review process. Users and their parent institutions do not pay for the running costs of the facility, which are as much as £11,000 per instrument per day. Their transport and living costs are also refunded whilst carrying out the experiment. Most users stay in Ridgeway House, a hotel near the site, or at Cosener's House, an STFC-run conference centre in Abingdon. Over 600 experiments by 1600 users are completed every year.

A large number of support staff operate the facility, aid users, and carry out research, the control room is staffed 24 hours a day, every day of the year. Instrument scientists oversee the running of each instrument and liaise with users, and other divisions provide sample environment, data analysis and computing expertise, maintain the accelerator, and run education programmes.

Among the important and pioneering work carried out was the discovery of the structure of high-temperature superconductors and the solid phase of buckminsterfullerene.

Construction for a second target station started in 2003, and the first neutrons were delivered to the target on December 14 2007<sup>[1]</sup>. It will use low-energy neutrons to study soft condensed matter, biological systems, advanced composites and  $\rightarrow$  nanomaterials. To supply the extra protons for this, the accelerator is being upgraded.

## History and background of ISIS

The source was approved in 1977 for the RAL site on the Harwell campus and recycled components from earlier UK science programmes including the accelerator hall which had previously been occupied by the Nimrod accelerator. The first beam was produced in 1984, and the facility was formally opened by the then Prime Minister Margaret Thatcher in October 1985.<sup>[2]</sup>

The name ISIS is not an acronym: it refers to the Ancient Egyptian goddess and the local name for the River Thames. The name was selected for the official opening of the facility in 1985, prior to this it was known as the SNS, or Spallation Neutron Source. The name was considered appropriate as Isis was a goddess who could restore life to the dead, and ISIS made use of equipment previously constructed for the Nimrod and Nina accelerators<sup>[3]</sup>.

## External links

- ISIS facility <sup>[4]</sup>
- ISIS Second Target Station <sup>[5]</sup>
- The Science and Technology Facilities Council <sup>[6]</sup>

## References

- [1] ISIS Second Target Station Project (<http://ts-2.isis.rl.ac.uk/>)
- [2] Linacs at the Rutherford Appleton Laboratory (<http://epubs.cclrc.ac.uk/bitstream/692/linacplahistory.pdf>)
- [3] Explanation of the name of ISIS (<http://www.isis.rl.ac.uk/aboutisis/index.htm>)
- [4] <http://www.isis.rl.ac.uk/>
- [5] <http://ts-2.isis.rl.ac.uk/>
- [6] <http://www.stfc.ac.uk>

Geographical coordinates: 51°34'18"N 1°19'12"W

# Neutron spin echo

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**Neutron spin echo** spectroscopy is an inelastic neutron scattering technique invented by Ferenc Mezei in the 1970's, and developed in collaboration with John Hayter. In recognition of this work and in other areas, Mezei was awarded the first Walter Haelg Prize <sup>[1]</sup> in 1999.

The spin-echo spectrometer possesses an extremely high energy resolution (roughly one part in 100,000). Additionally, it measures the density-density correlation (or intermediate scattering function)  $F(Q,t)$  as a function of momentum transfer  $Q$  and time. Other neutron scattering techniques measure the dynamic structure factor, which then must be converted to  $F(Q,t)$  by a Fourier transform, which is difficult in practice. Because of these advantages over other neutron scattering techniques, NSE is an ideal method to observe <sup>[2]</sup> internal dynamic modes in materials such as a polymer blend, alkane chain, or microemulsion. The extraordinary power of NSE spectrometry was further demonstrated recently <sup>[3]</sup> by the direct observation of coupled internal protein domain dynamics in the protein Taq polymerase, allowing the visualization of protein nanomachinery in motion.

## Technical details

The technique of neutron spin echo exploits the neutron's intrinsic angular momentum, or spin, to access extremely high-resolution inelastic scattering windows.

The core of a neutron spin echo instrument is a *symmetric* field integral around the sample position, and a spin flipper (or the sample itself) to reverse the spin direction, so that any loss in polarisation at the detector position can be directly attributed to inelastic scattering processes in the sample.

Because of the interference of the wavevectors associated with the spin up and spin down quantum states of the neutron, the measured neutron polarisation is proportional to the sample's correlation function *in real time*. This makes it a very useful and intuitive technique for the high-resolution study of low-energy excitations in materials.

In soft matter research the structure of macromolecular objects is often investigated by small angle neutron scattering, SANS. The exchange of hydrogen with deuterium in some of the molecules creates scattering contrast between even equal chemical species. The SANS diffraction pattern --if interpreted in real space-- corresponds to a snapshot picture of the

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molecular arrangement. Neutron spin echo instruments can analyze the inelastic broadening of the SANS intensity and thereby analyze the motion of the macromolecular objects. A coarse analogy would be a photo with a certain opening time instead of the SANS like snapshot. The opening time corresponds to the Fourier time which depends on the setting of the NSE spectrometer, it is proportional to the magnetic field (integral) and to the third power of the neutron wavelength. Values up to several hundreds of nanoseconds are available. Note that the spatial resolution of the scattering experiment is in the nanometer range, which means that a time range of e.g. 100ns corresponds to effective molecular motion velocities of  $1 \text{ nm}/100\text{ns} = 1\text{cm/s}$ . This may be compared to the typical neutron velocity of 200..1000 m/s used in these type of experiments.

## References

- [1] [http://neutron.neutron-eu.net/n\\_ensa/Prize](http://neutron.neutron-eu.net/n_ensa/Prize)
- [2] B. Farago (2006). "Neutron spin echo study of well organized soft matter systems". *Physica B: Condensed matter* **385-386**: 688-691. doi: 10.1016/j.physb.2006.05.292 (<http://dx.doi.org/10.1016/j.physb.2006.05.292>).
- [3] Bu Z, Biehl R, Monkenbusch M, Richter D, Callaway DJE (2005). "Coupled protein domain motion in Taq polymerase revealed by neutron spin-echo spectroscopy.". *Proc Natl Acad Sci U S A* **102** (49): 17646-17651. doi: 10.1073/pnas.0503388102 (<http://dx.doi.org/10.1073/pnas.0503388102>). PMID 16306270.

## Existing Spectrometers

- IN11 (<http://www.ill.eu/in11/>) (Institut Laue-Langevin, ILL (<http://www.ill.fr>), Grenoble, France)
- IN15 (<http://www.ill.eu/in15/>) (Institut Laue-Langevin, ILL (<http://www.ill.fr>), Grenoble, France)
- J-NSE (Juelich Centre for Neutron Science JCNS (<http://www.jcns.info>), Juelich, Germany, hosted by FRMII (<http://wwwnew.frm2.tum.de>), Munich (Garching), Germany)
- NG5-NSE ( NIST CNRF (<http://www.ncnr.nist.gov>), Gaithersburg, USA)
- V5/SPAN ( Hahn-Meitner Institut (<http://www.hmi.de>), Berlin, Germany)
- C2-2 ( ISSP (<http://www.issp.u-tokyo.ac.jp>), Tokai, Japan)

## See also

- neutron scattering
- neutron resonance spin echo
- Biological small-angle scattering
- Soft matter
- NMR
- Protein domain
- Larmor precession
- SAXS

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# Hadron spectroscopy

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**Hadron spectroscopy** is the subfield of particle physics that studies the masses and decays of hadrons. Hadron spectroscopy is also an important part of the new nuclear physics. The properties of hadrons are a consequence of a theory called quantum chromodynamics (QCD).

QCD predicts that quarks and antiquarks bind into particles called mesons. Another type of hadron is called a baryon, that is made of three quarks. There is good experimental evidence for both mesons and baryons. Potentially QCD also has bound states of just gluons called glueballs. One of the goals of the field of hadronic spectroscopy is to find experimental evidence for exotic mesons, tetraquarks, molecules of hadrons, and glueballs.

An important part of the field of hadronic spectroscopy are the attempts to solve QCD. The properties of hadrons require the solution of QCD in the strong coupling regime, where perturbative techniques based on Feynman diagrams do not work. There are several approaches to trying to solve QCD to compute the masses of hadrons:

- Quark models <sup>[1]</sup>
- Lattice QCD
- Effective field theory
- sum rules <sup>[2]</sup>

## Experimental facilities

- Jefferson Lab <sup>[3]</sup> in the US.
- J-PARC <sup>[4]</sup> in Japan.
- GSI <sup>[5]</sup> Darmstadt Germany.

## References

- Article on Key Issues in Hadronic Physics <sup>[6]</sup>
- Review of the quark model in PDG <sup>[7]</sup>

## References

[1] <http://pdg.lbl.gov/2007/reviews/quarkmodrpp.pdf>

[2] <http://uk.arxiv.org/abs/hep-ph/0010175>

[3] <http://www.jlab.org/>

[4] [http://j-parc.jp/NuclPart/index\\_e.html](http://j-parc.jp/NuclPart/index_e.html)

[5] <http://www.gsi.de/>

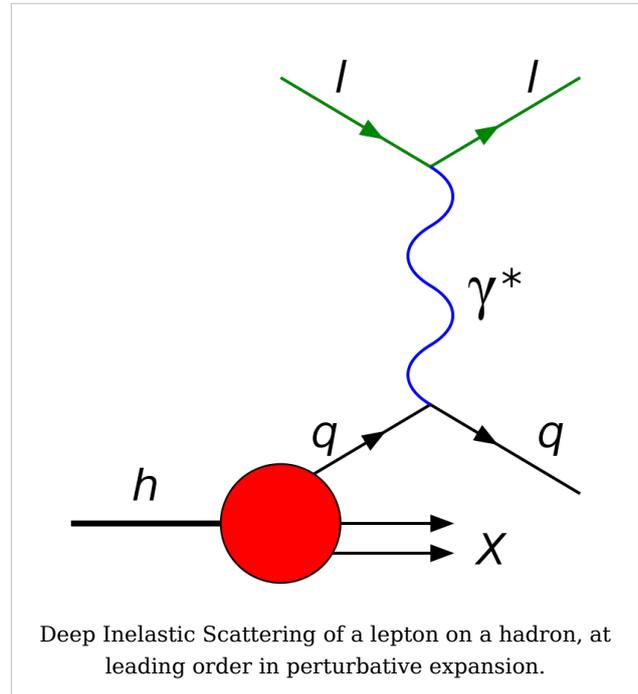
[6] <http://uk.arxiv.org/abs/hep-ph/0012238>

[7] <http://pdg.lbl.gov/2007/reviews/quarkmodrpp.pdf>

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# Deep inelastic scattering

**Deep inelastic scattering** is the name given to a process used to probe the insides of hadrons (particularly the baryons, such as protons and neutrons), using electrons, muons and neutrinos. It provided the first convincing evidence of the reality of quarks, which up until that point had been considered by many to be a purely mathematical phenomenon. It is a relatively new process, first attempted in the 1960s and 1970s. It is conceptually similar to Rutherford Scattering, but with important differences. The reason why this type of scattering is described as "deep" and "inelastic" is discussed at the Oxford University page.<sup>[1]</sup>



## Quarks

The Standard Model of physics, particularly given the work of Murray Gell-Mann in the 1960s, had been successful in uniting much of the previously disparate concepts in particle physics into one, relatively straightforward, scheme. In essence, there were three types of particles.

- The leptons, which were light (as in not particularly massive) particles such as electrons, neutrinos and their antiparticles. They have integer charge
- The bosons, which were particles that exchange forces. These ranged from the massless, easy-to-detect photon (the carrier of the electro-magnetic force) to the exotic (though still massless) gluons that carry the strong nuclear force
- The quarks, which were massive particles that carried fractional charges. They are the "building blocks" of the hadrons. They are also the only particles to be affected by the strong interaction

The leptons had been detected since 1897, when J. J. Thomson had shown that electric current is a flow of electrons. Some bosons were being routinely detected, although the  $W^+$ ,  $W^-$  and  $Z^0$  particles of the electroweak force were only categorically seen in the early 1980s, and gluons were only firmly pinned down at DESY in Hamburg at about the same time. Quarks, however, were still elusive.

## The Experiments

Drawing on Rutherford's groundbreaking experiments in the early years of the Twentieth century, ideas for detecting quarks were formulated. Rutherford had proven that atoms had a small, massive, charged nucleus at their centre by firing alpha particles at atoms in gold. Most had gone through with little or no deviation, but a few were deflected through large angles or came right back. This suggested that atoms had internal structure, and a lot of

empty space.

In order to enter baryons (where quarks were theoretically to be found), a small, penetrating (ie easily accelerated; in reality this meant charged) and easily produced particle needed to be found. Electrons were considered ideal for the role, and in a series of remarkable technological and engineering leaps, electrons were fired as tiny bullets at protons and neutrons in nuclei. As an added bonus, the electrostatic attraction of the positively charged nucleus and the negatively charged electron increased the speed. Later experiments were conducted with muons, but the same principles apply.

The collision absorbs some kinetic energy, and as such it is inelastic (this compares to Rutherford scattering which is elastic, with no loss of kinetic energy, taking into account recoils of the nuclei). The electron emerges from the nucleus, and its trajectory and velocity can be detected.

Analysis of the results led to the following conclusions:

- The hadrons do have internal structure
- In baryons, there are three points of deflection (i.e. baryons consist of three quarks)
- In mesons, there are two points of deflection (i.e. mesons consist of a quark and an anti-quark. The reason they do not consist of two quarks is to do with their colour; see the quark article for more explanation)
- Quarks appear to be point charges, as electrons appear to be, with the fractional charges suggested by the Standard Model

The experiments were important because, not only did they confirm the physical reality of quarks but also proved again that the Standard Model was the correct avenue of research for particle physicists to pursue.

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# Nanotechnology

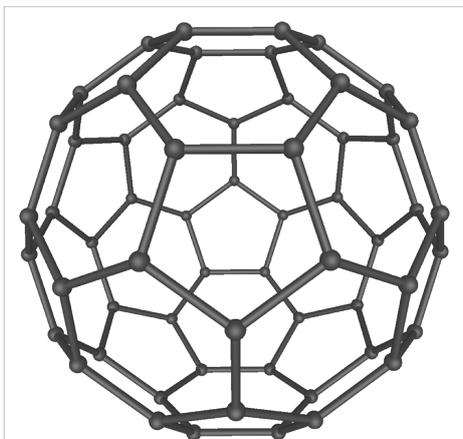
Part of a series of articles on → <b>Nanotechnology</b>
History Implications Applications Regulation Organizations In fiction and popular culture List of topics
<b><i>Subfields and related fields</i></b>
<b>Nanomaterials</b> Fullerenes Carbon nanotubes Nanoparticles
<b>Nanomedicine</b> Nanotoxicology Nanosensor
<b>Molecular self-assembly</b> Self-assembled monolayer Supramolecular assembly DNA nanotechnology
<b>Nanoelectronics</b> Molecular electronics Nanocircuitry Nanolithography Nanoionics
<b>Scanning probe microscopy</b> Atomic force microscope Scanning tunneling microscope
<b>Molecular nanotechnology</b> Molecular assembler Nanorobotics Mechanosynthesis

**Nanotechnology**, shortened to "**Nanotech**", is the study of the control of matter on an atomic and molecular scale. Generally nanotechnology deals with structures of the size 100 nanometers or smaller, and involves developing materials or devices within that size. Nanotechnology is very diverse, ranging from novel extensions of conventional device physics, to completely new approaches based upon molecular self-assembly, to developing new materials with dimensions on the nanoscale, even to speculation on whether we can directly control matter on the atomic scale.

There has been much debate on the future of implications of nanotechnology. Nanotechnology has the potential to create many new materials and devices with wide-ranging applications, such as in medicine, electronics, and energy production. On the other hand, nanotechnology raises many of the same issues as with any introduction of new technology, including concerns about the toxicity and environmental impact of nanomaterials <sup>[1]</sup>, and their potential effects on global economics, as well as speculation

about various doomsday scenarios. These concerns have led to a debate among advocacy groups and governments on whether special regulation of nanotechnology is warranted.

## Origins



Buckminsterfullerene  $C_{60}$ , also known as the buckyball, is the simplest of the carbon structures known as fullerenes. Members of the fullerene family are a major subject of research falling under the nanotechnology umbrella.

The first use of the concepts in 'nano-technology' (but pre-dating use of that name) was in "There's Plenty of Room at the Bottom," a talk given by physicist Richard Feynman at an American Physical Society meeting at Caltech on December 29, 1959. Feynman described a process by which the ability to manipulate individual atoms and molecules might be developed, using one set of precise tools to build and operate another proportionally smaller set, so on down to the needed scale. In the course of this, he noted, scaling issues would arise from the changing magnitude of various physical phenomena: gravity would become less important, surface tension and Van der Waals attraction would become more important, etc. This basic idea appears plausible, and exponential assembly enhances it with parallelism to produce a useful quantity of end products. The term "nanotechnology" was defined by

Tokyo Science University Professor Norio Taniguchi in a 1974 paper<sup>[2]</sup> as follows: "'Nano-technology' mainly consists of the processing of, separation, consolidation, and deformation of materials by one atom or by one molecule." In the 1980s the basic idea of this definition was explored in much more depth by Dr. K. Eric Drexler, who promoted the technological significance of nano-scale phenomena and devices through speeches and the books *Engines of Creation: The Coming Era of Nanotechnology* (1986) and *Nanosystems: Molecular Machinery, Manufacturing, and Computation*,<sup>[3]</sup> and so the term acquired its current sense. *Engines of Creation: The Coming Era of Nanotechnology* is considered the first book on the topic of nanotechnology. Nanotechnology and nanoscience got started in the early 1980s with two major developments; the birth of cluster science and the invention of the scanning tunneling microscope (STM). This development led to the discovery of fullerenes in 1985 and carbon nanotubes a few years later. In another development, the synthesis and properties of semiconductor nanocrystals was studied; this led to a fast increasing number of metal oxide nanoparticles of quantum dots. The atomic force microscope was invented six years after the STM was invented. In 2000, the United States National Nanotechnology Initiative was founded to coordinate Federal nanotechnology research and development.

## Fundamental concepts

One nanometer (nm) is one billionth, or  $10^{-9}$ , of a meter. By comparison, typical carbon-carbon bond lengths, or the spacing between these atoms in a molecule, are in the range 0.12-0.15 nm, and a DNA double-helix has a diameter around 2 nm. On the other hand, the smallest cellular life-forms, the bacteria of the genus *Mycoplasma*, are around 200 nm in length.

To put that scale in another context, the comparative size of a nanometer to a meter is the same as that of a marble to the size of the earth.<sup>[4]</sup> Or another way of putting it: a nanometer is the amount a man's beard grows in the time it takes him to raise the razor to his face.<sup>[4]</sup>

Two main approaches are used in nanotechnology. In the "bottom-up" approach, materials and devices are built from molecular components which assemble themselves chemically by principles of molecular recognition. In the "top-down" approach, nano-objects are constructed from larger entities without atomic-level control.<sup>[5]</sup>

### **Larger to smaller: a materials perspective**

A number of physical phenomena become pronounced as the size of the system decreases. These include statistical mechanical effects, as well as → quantum mechanical effects, for example the "quantum size effect" where the electronic properties of solids are altered with great reductions in particle size. This effect does not come into play by going from macro to micro dimensions. However, it becomes dominant when the nanometer size range is reached. Additionally, a number of physical (mechanical, electrical, optical, etc.) properties change when compared to macroscopic systems. One example is the increase in surface area to volume ratio altering mechanical, thermal and catalytic properties of materials. Diffusion and reactions at nanoscale, nanostructures materials and nanodevices with fast ion transport are generally referred to nanoionics. Novel *mechanical* properties of nanosystems are of interest in the nanomechanics research. The catalytic activity of nanomaterials also opens potential risks in their interaction with biomaterials.<sup>[6]</sup>

For example, if you take aluminum and cut it in half, it is still aluminum. But if you keep cutting aluminum in half until it has dimensions on the nano scale, it becomes highly reactive. This is because the molecular structure was changed.

Materials reduced to the nanoscale can show different properties compared to what they exhibit on a macroscale, enabling unique applications. For instance, opaque substances become transparent (copper); stable materials turn combustible (aluminum); solids turn into liquids at room temperature (gold); insulators become conductors (silicon). A material such as gold, which is chemically inert at normal scales, can serve as a potent chemical catalyst at nanoscales. Much of the fascination with nanotechnology stems from these quantum and surface phenomena that matter exhibits at the nanoscale.<sup>[7]</sup>

### **Simple to complex: a molecular perspective**

Modern synthetic chemistry has reached the point where it is possible to prepare small molecules to almost any structure. These methods are used today to produce a wide variety of useful chemicals such as pharmaceuticals or commercial polymers. This ability raises the question of extending this kind of control to the next-larger level, seeking methods to assemble these single molecules into supramolecular assemblies consisting of many molecules arranged in a well defined manner.

These approaches utilize the concepts of molecular self-assembly and/or supramolecular chemistry to automatically arrange themselves into some useful conformation through a bottom-up approach. The concept of molecular recognition is especially important: molecules can be designed so that a specific conformation or arrangement is favored due to non-covalent intermolecular forces. The Watson-Crick basepairing rules are a direct result of this, as is the specificity of an enzyme being targeted to a single substrate, or the specific

folding of the protein itself. Thus, two or more components can be designed to be complementary and mutually attractive so that they make a more complex and useful whole.

Such bottom-up approaches should be able to produce devices in parallel and much cheaper than top-down methods, but could potentially be overwhelmed as the size and complexity of the desired assembly increases. Most useful structures require complex and thermodynamically unlikely arrangements of atoms. Nevertheless, there are many examples of self-assembly based on molecular recognition in biology, most notably Watson-Crick basepairing and enzyme-substrate interactions. The challenge for nanotechnology is whether these principles can be used to engineer novel constructs in addition to natural ones.

### **Molecular nanotechnology: a long-term view**

Molecular nanotechnology, sometimes called molecular manufacturing, is a term given to the concept of engineered nanosystems (nanoscale machines) operating on the molecular scale. It is especially associated with the concept of a molecular assembler, a machine that can produce a desired structure or device atom-by-atom using the principles of mechanosynthesis. Manufacturing in the context of productive nanosystems is not related to, and should be clearly distinguished from, the conventional technologies used to manufacture nanomaterials such as carbon nanotubes and nanoparticles.

When the term "nanotechnology" was independently coined and popularized by Eric Drexler (who at the time was unaware of an earlier usage by Norio Taniguchi) it referred to a future manufacturing technology based on molecular machine systems. The premise was that molecular scale biological analogies of traditional machine components demonstrated molecular machines were possible: by the countless examples found in biology, it is known that sophisticated, stochastically optimised biological machines can be produced..

It is hoped that developments in nanotechnology will make possible their construction by some other means, perhaps using biomimetic principles. However, Drexler and other researchers<sup>[8]</sup> have proposed that advanced nanotechnology, although perhaps initially implemented by biomimetic means, ultimately could be based on mechanical engineering principles, namely, a manufacturing technology based on the mechanical functionality of these components (such as gears, bearings, motors, and structural members) that would enable programmable, positional assembly to atomic specification (PNAS-1981<sup>[9]</sup>). The physics and engineering performance of exemplar designs were analyzed in Drexler's book *Nanosystems*.

In general it is very difficult to assemble devices on the atomic scale, as all one has to position atoms are other atoms of comparable size and stickiness. Another view, put forth by Carlo Montemagno,<sup>[10]</sup> is that future nanosystems will be hybrids of silicon technology and biological molecular machines. Yet another view, put forward by the late Richard Smalley, is that mechanosynthesis is impossible due to the difficulties in mechanically manipulating individual molecules.

This led to an exchange of letters in the ACS publication *Chemical & Engineering News* in 2003.<sup>[11]</sup> Though biology clearly demonstrates that molecular machine systems are possible, non-biological molecular machines are today only in their infancy. Leaders in research on non-biological molecular machines are Dr. Alex Zettl and his colleagues at Lawrence Berkeley Laboratories and UC Berkeley. They have constructed at least three

distinct molecular devices whose motion is controlled from the desktop with changing voltage: a nanotube nanomotor, a molecular actuator <sup>[12]</sup>, and a nanoelectromechanical relaxation oscillator <sup>[13]</sup>.

An experiment indicating that positional molecular assembly is possible was performed by Ho and Lee at Cornell University in 1999. They used a scanning tunneling microscope to move an individual carbon monoxide molecule (CO) to an individual iron atom (Fe) sitting on a flat silver crystal, and chemically bound the CO to the Fe by applying a voltage.

## Current research

### Nanomaterials

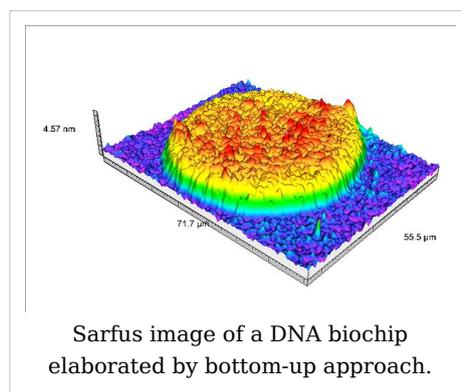
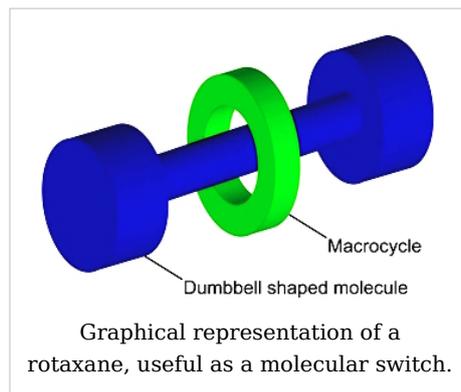
This includes subfields which develop or study materials having unique properties arising from their nanoscale dimensions. <sup>[15]</sup>

- **Interface and Colloid Science** has given rise to many materials which may be useful in nanotechnology, such as carbon nanotubes and other fullerenes, and various nanoparticles and nanorods.
- Nanoscale materials can also be used for **bulk applications**; most present commercial applications of nanotechnology are of this flavor.
- Progress has been made in using these materials for medical applications; see **Nanomedicine**.
- Nanoscale materials are sometimes used in solar cells which combats the cost of traditional Silicon solar cells

### Bottom-up approaches

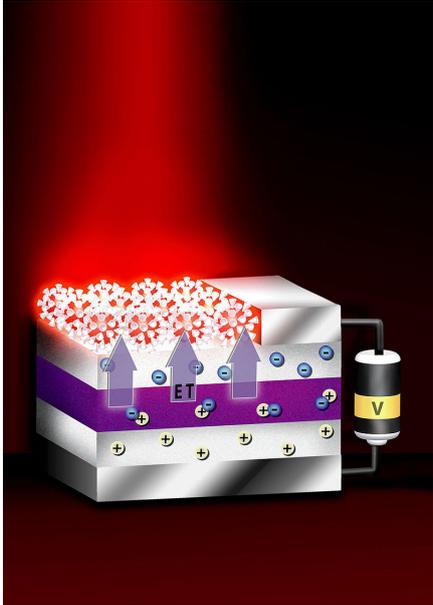
These seek to arrange smaller components into more complex assemblies.

- **DNA nanotechnology** utilizes the specificity of Watson-Crick basepairing to construct well-defined structures out of DNA and other nucleic acids.
- Approaches from the field of "classical" chemical synthesis also aim at designing molecules with well-defined shape (e.g. bis-peptides <sup>[16]</sup> ).
- More generally, **molecular self-assembly** seeks to use concepts of supramolecular chemistry, and molecular recognition in particular, to cause single-molecule components to automatically arrange themselves into some useful conformation.



## Top-down approaches

These seek to create smaller devices by using larger ones to direct their assembly.

- Many technologies descended from conventional **solid-state silicon methods** for fabricating microprocessors are now capable of creating features smaller than 100 nm, falling under the definition of nanotechnology. Giant magnetoresistance-based hard drives already on the market fit this description,<sup>[17]</sup> as do atomic layer deposition (ALD) techniques. Peter Grünberg and Albert Fert received the Nobel Prize in Physics for their discovery of Giant magnetoresistance and contributions to the field of spintronics in 2007.<sup>[18]</sup>
  - Solid-state techniques can also be used to create devices known as **nanoelectromechanical systems** or NEMS, which are related to microelectromechanical systems or MEMS.
- 

This device transfers energy from nano-thin layers of quantum wells to nanocrystals above them, causing the nanocrystals to emit visible light.<sup>[14]</sup>
- Atomic force microscope tips can be used as a nanoscale "write head" to deposit a chemical upon a surface in a desired pattern in a process called **dip pen nanolithography**. This fits into the larger subfield of nanolithography.
  - Focused ion beams can directly remove material, or even deposit material when suitable pre-cursor gasses are applied at the same time. For example, this technique is used routinely to create sub-100 nm sections of material for analysis in Transmission electron microscopy.

## Functional approaches

These seek to develop components of a desired functionality without regard to how they might be assembled.

- **Molecular electronics** seeks to develop molecules with useful electronic properties. These could then be used as single-molecule components in a nanoelectronic device.<sup>[19]</sup> For an example see rotaxane.
- Synthetic chemical methods can also be used to create what forensics call **synthetic molecular motors**, such as in a so-called nanocar.

## Speculative

These subfields seek to anticipate what inventions nanotechnology might yield, or attempt to propose an agenda along which inquiry might progress. These often take a big-picture view of nanotechnology, with more emphasis on its societal implications than the details of how such inventions could actually be created.

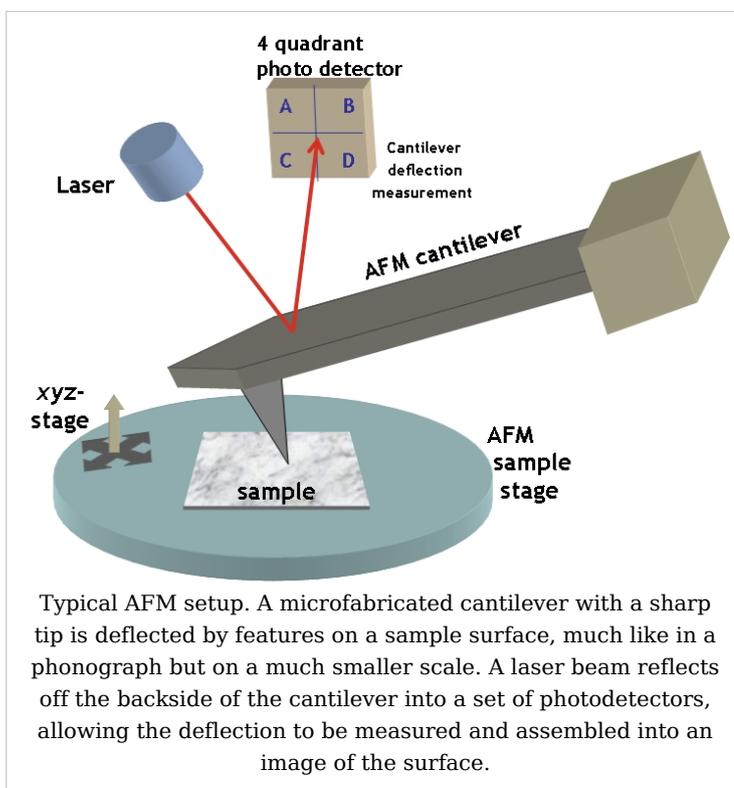
- **Molecular nanotechnology** is a proposed approach which involves manipulating single molecules in finely controlled, deterministic ways. This is more theoretical than the other subfields and is beyond current capabilities.
- **Nanorobotics** centers on self-sufficient machines of some functionality operating at the nanoscale. There are hopes for applying nanorobots in medicine<sup>[20] [21] [22]</sup>, but it may not be easy to do such a thing because of several drawbacks of such devices.<sup>[23]</sup> Nevertheless, progress on innovative materials and methodologies has been demonstrated with some patents granted about new nanomanufacturing devices for future commercial applications, which also progressively helps in the development towards nanorobots with the use of embedded nanobioelectronics concept.<sup>[24] [25]</sup>
- **Programmable matter** based on artificial atoms seeks to design materials whose properties can be easily, reversibly and externally controlled.
- Due to the popularity and media exposure of the term nanotechnology, the words **picotechnology** and **femtototechnology** have been coined in analogy to it, although these are only used rarely and informally.

## Tools and techniques

The first observations and size measurements of nano-particles were made during the first decade of the 20th century. They are mostly associated with the name of Zsigmondy who made detailed studies of gold sols and other nanomaterials with sizes down to 10 nm and less. He published a book in 1914.<sup>[26]</sup> He used ultramicroscope that employs a *dark field* method for seeing particles with sizes much less than light wavelength.

There are traditional techniques developed during 20th century in Interface and Colloid Science for characterizing nanomaterials. These are widely used for *first generation* passive nanomaterials specified in the next section.

These methods include several different techniques for characterizing particle size distribution. This characterization is imperative because many materials that are expected



to be nano-sized are actually aggregated in solutions. Some of methods are based on light scattering. Other apply ultrasound, such as ultrasound attenuation spectroscopy for testing concentrated nano-dispersions and microemulsions.<sup>[27]</sup>

There is also a group of traditional techniques for characterizing surface charge or zeta potential of nano-particles in solutions. This information is required for proper system stabilization, preventing its aggregation or flocculation. These methods include microelectrophoresis, electrophoretic light scattering and electroacoustics. The last one, for instance colloid vibration current method is suitable for characterizing concentrated systems.

Next group of nanotechnological techniques include those used for fabrication of nanowires, those used in semiconductor fabrication such as deep ultraviolet lithography, electron beam lithography, focused ion beam machining, nanoimprint lithography, atomic layer deposition, and molecular vapor deposition, and further including molecular self-assembly techniques such as those employing di-block copolymers. However, all of these techniques preceded the nanotech era, and are extensions in the development of scientific advancements rather than techniques which were devised with the sole purpose of creating nanotechnology and which were results of nanotechnology research.

There are several important modern developments. The atomic force microscope (AFM) and the Scanning Tunneling Microscope (STM) are two early versions of scanning probes that launched nanotechnology. There are other types of scanning probe microscopy, all flowing from the ideas of the scanning confocal microscope developed by Marvin Minsky in 1961 and the scanning acoustic microscope (SAM) developed by Calvin Quate and coworkers in the 1970s, that made it possible to see structures at the nanoscale. The tip of a scanning probe can also be used to manipulate nanostructures (a process called positional assembly). Feature-oriented scanning-positioning methodology suggested by Rostislav Lapshin appears to be a promising way to implement these nanomanipulations in automatic mode. However, this is still a slow process because of low scanning velocity of the microscope. Various techniques of nanolithography such as dip pen nanolithography, electron beam lithography or nanoimprint lithography were also developed. Lithography is a top-down fabrication technique where a bulk material is reduced in size to nanoscale pattern.

The top-down approach anticipates nanodevices that must be built piece by piece in stages, much as manufactured items are made. Scanning probe microscopy is an important technique both for characterization and synthesis of nanomaterials. Atomic force microscopes and scanning tunneling microscopes can be used to look at surfaces and to move atoms around. By designing different tips for these microscopes, they can be used for carving out structures on surfaces and to help guide self-assembling structures. By using, for example, feature-oriented scanning-positioning approach, atoms can be moved around on a surface with scanning probe microscopy techniques. At present, it is expensive and time-consuming for mass production but very suitable for laboratory experimentation.

In contrast, bottom-up techniques build or grow larger structures atom by atom or molecule by molecule. These techniques include chemical synthesis, self-assembly and positional assembly. Another variation of the bottom-up approach is molecular beam epitaxy or MBE. Researchers at Bell Telephone Laboratories like John R. Arthur, Alfred Y. Cho, and Art C. Gossard developed and implemented MBE as a research tool in the late 1960s and 1970s. Samples made by MBE were key to the discovery of the fractional quantum Hall effect for which the 1998 Nobel Prize in Physics was awarded. MBE allows scientists to lay down

atomically-precise layers of atoms and, in the process, build up complex structures. Important for research on semiconductors, MBE is also widely used to make samples and devices for the newly emerging field of spintronics.<sup>[28]</sup>

Newer techniques such as Dual Polarisation Interferometry are enabling scientists to measure quantitatively the molecular interactions that take place at the nano-scale.

However, new therapeutic products, based on responsive nanomaterials, such as the ultradeformable, stress-sensitive Transfersome vesicles, are under development and already approved for human use in some countries.

## Applications

As of August 21, 2008, the Project on Emerging Nanotechnologies estimates that over 800 manufacturer-identified nanotech products are publicly available, with new ones hitting the market at a pace of 3-4 per week.<sup>[29]</sup> The project lists all of the products in a publicly accessible online inventory<sup>[30]</sup>. Most applications are limited to the use of "first generation" passive nanomaterials which includes titanium dioxide in sunscreen, cosmetics and some food products; Carbon allotropes used to produce gecko tape; silver in food packaging, clothing, disinfectants and household appliances; zinc oxide in sunscreens and cosmetics, surface coatings, paints and outdoor furniture varnishes; and cerium oxide as a fuel catalyst.<sup>[31]</sup>

The National Science Foundation (a major distributor for nanotechnology research in the United States) funded researcher David Berube to study the field of nanotechnology. His findings are published in the monograph *Nano-Hype: The Truth Behind the Nanotechnology Buzz*. This published study (with a foreword by [Anwar Mikhail], Senior Advisor for Nanotechnology at the National Science Foundation) concludes that much of what is sold as "nanotechnology" is in fact a recasting of straightforward materials science, which is leading to a "nanotech industry built solely on selling nanotubes, nanowires, and the like" which will "end up with a few suppliers selling low margin products in huge volumes." Further applications which require actual manipulation or arrangement of nanoscale components await further research. Though technologies branded with the term 'nano' are sometimes little related to and fall far short of the most ambitious and transformative technological goals of the sort in molecular manufacturing proposals, the term still connotes such ideas. According to Berube, there may be a danger that a "nano bubble" will form, or is forming already, from the use of the term by scientists and entrepreneurs to garner funding, regardless of interest in the transformative possibilities of more ambitious and far-sighted work.

Nano-membranes have been produced that are portable and easily-cleaned systems that purify, detoxify and desalinate water meaning that third-world countries could get clean water, solving many water related health issues.

## Implications

Due to the far-ranging claims that have been made about potential applications of nanotechnology, a number of serious concerns have been raised about what effects these will have on our society if realized, and what action if any is appropriate to mitigate these risks.

There are possible dangers that arise with the development of nanotechnology. The Center for Responsible Nanotechnology suggests that new developments could result, among other things, in untraceable weapons of mass destruction, networked cameras for use by the government, and weapons developments fast enough to destabilize arms races ("Nanotechnology Basics").

One area of concern is the effect that industrial-scale manufacturing and use of nanomaterials would have on human health and the environment, as suggested by nanotoxicology research. Groups such as the Center for Responsible Nanotechnology have advocated that nanotechnology should be specially regulated by governments for these reasons. Others counter that overregulation would stifle scientific research and the development of innovations which could greatly benefit mankind.

Other experts, including director of the Woodrow Wilson Center's Project on Emerging Nanotechnologies David Rejeski, have testified<sup>[32]</sup> that successful commercialization depends on adequate oversight, risk research strategy, and public engagement. Berkeley, California is currently the only city in the United States to regulate nanotechnology;<sup>[33]</sup> Cambridge, Massachusetts in 2008 considered enacting a similar law,<sup>[34]</sup> but ultimately rejected this.<sup>[35]</sup>

## Health and environmental concerns

Some of the recently developed nanoparticle products may have unintended consequences. Researchers have discovered that silver nanoparticles used in socks to reduce foot odor are being released in the wash with possible negative consequences.<sup>[36]</sup> Silver nanoparticles, which are bacteriostatic, may then destroy beneficial bacteria which are important for breaking down organic matter in waste treatment plants or farms.<sup>[37]</sup>

A study at the University of Rochester found that when rats breathed in nanoparticles, the particles settled in the brain and lungs, which led to significant increases in biomarkers for inflammation and stress response.<sup>[38]</sup>

A major study published more recently in *Nature Nanotechnology* suggests some forms of carbon nanotubes - a poster child for the "nanotechnology revolution" - could be as harmful as asbestos if inhaled in sufficient quantities. Anthony Seaton of the Institute of Occupational Medicine in Edinburgh, Scotland, who contributed to the article on carbon nanotubes said "We know that some of them probably have the potential to cause mesothelioma. So those sorts of materials need to be handled very carefully."<sup>[39]</sup> In the absence of specific nano-regulation forthcoming from governments, Paul and Lyons (2008) have called for an exclusion of engineered nanoparticles from organic food.<sup>[40]</sup>

## Regulation

Calls for tighter regulation of nanotechnology have occurred alongside a growing debate related to the human health and safety risks associated with nanotechnology. Furthermore, there is significant debate about who is responsible for the regulation of nanotechnology. While some non-nanotechnology specific regulatory agencies currently cover some products and processes (to varying degrees) - by "bolting on" nanotechnology to existing regulations - there are clear gaps in these regimes.<sup>[41]</sup> In "Nanotechnology Oversight: An Agenda for the Next Administration,"<sup>[42]</sup> former EPA deputy administrator J. Clarence (Terry) Davies lays out a clear regulatory roadmap for the next presidential administration and describes the immediate and longer term steps necessary to deal with the current shortcomings of nanotechnology oversight.

Stake holders concerned by the lack of a meats to cook and eat with a side of nanoparticles and nanotubes have drawn diagrams with bovine spongiform encephalopathy ('mad cow's disease), thalidomide, genetically modified food,<sup>[43]</sup> nuclear energy, reproductive technologies, biotechnology, and asbestosis. Dr. Andrew Maynard, chief science advisor to the Woodrow Wilson Center's Project on Emerging Nanotechnologies, concludes (among others) that there is insufficient funding for human health and safety research, and as a result there is currently limited understanding of the human health and safety risks associated with nanotechnology.<sup>[44]</sup>

The Royal Society report<sup>[45]</sup> identified a risk of nanoparticles or nanotubes being released during disposal, destruction and recycling, and recommended that "manufacturers of products that fall under extended producer responsibility regimes such as end-of-life regulations publish procedures outlining how these materials will be managed to minimize possible human and environmental exposure" (p.xiii). Reflecting the challenges for ensuring responsible life cycle regulation, the Institute for Food and Agricultural Standards<sup>[46]</sup> has proposed standards for nanotechnology research and development should be integrated across consumer, worker and environmental standards. They also propose that NGOs and other citizen groups play a meaningful role in the development of these standards.

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- " Nanotechnology 101 (<http://www.nanotechproject.org/topics/nano101/>)" from the Project on Emerging Nanotechnologies. (<http://www.nanotechproject.org/topics/nano101/>)
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## External links

- What is Nanotechnology? (<http://www.vega.org.uk/video/programme/3>) (A Vega/BBC/OU Video Discussion).
  - Nanotec Expo (<http://www.nanotecexpo.com.br/english>) - Fair and Congress Latin American of Nanotechnology
  - Nanotechnology (<http://www.dmoz.org/Science/Technology/Nanotechnology/>) at the Open Directory Project
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# Protein-protein interaction

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**Protein-protein interactions** involve not only the direct-contact association of protein molecules but also longer range interactions through the electrolyte, aqueous solution medium surrounding neighbor hydrated proteins over distances from less than one nanometer to distances of several tens of nanometers. Furthermore, such protein-protein interactions are thermodynamically linked functions<sup>[1]</sup> of dynamically bound ions and water that exchange rapidly with the surrounding solution by comparison with the molecular tumbling rate (or correlation times) of the interacting proteins. Protein associations are also studied from the perspectives of biochemistry, quantum chemistry, molecular dynamics, signal transduction and other metabolic or genetic/epigenetic networks. Indeed, protein-protein interactions are at the core of the entire Interactomics system of any living cell.

The interactions between proteins are important for very numerous—if not all—biological functions. For example, signals from the exterior of a cell are mediated to the inside of that cell by protein-protein interactions of the signaling molecules. This process, called signal transduction, plays a fundamental role in many biological processes and in many diseases (e.g. cancers). Proteins might interact for a long time to form part of a protein complex, a protein may be carrying another protein (for example, from cytoplasm to nucleus or vice versa in the case of the nuclear pore importins), or a protein may interact briefly with another protein just to modify it (for example, a protein kinase will add a phosphate to a target protein). This modification of proteins can itself change protein-protein interactions. For example, some proteins with SH2 domains only bind to other proteins when they are phosphorylated on the amino acid tyrosine while bromodomains specifically recognise acetylated lysines. In conclusion, protein-protein interactions are of central importance for virtually every process in a living cell. Information about these interactions improves our understanding of diseases and can provide the basis for new therapeutic approaches.

## Methods to investigate protein-protein interactions

### Biochemical methods

As protein-protein interactions are so important there are a multitude of methods to detect them. Each of the approaches has its own strengths and weaknesses, especially with regard to the sensitivity and specificity of the method. A high sensitivity means that many of the interactions that occur in reality are detected by the screen. A high specificity indicates that most of the interactions detected by the screen are also occurring in reality.

- Co-immunoprecipitation is considered to be the gold standard assay for protein-protein interactions, especially when it is performed with endogenous (not overexpressed and not tagged) proteins. The protein of interest is isolated with a specific antibody. Interaction partners which stick to this protein are subsequently identified by western blotting. Interactions detected by this approach are considered to be real. However, this method can only verify interactions between suspected interaction partners. Thus, it is not a screening approach. A note of caution also is that immunoprecipitation experiments reveal direct and indirect interactions. Thus, positive results may indicate that two proteins interact directly or may interact via a bridging protein.
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- Bimolecular Fluorescence Complementation (BiFC) is a new technique in observing the interactions of proteins. Combining with other new techniques, this method can be used to screen protein-protein interactions and their modulators <sup>[2]</sup>.
  - Affinity electrophoresis as used for estimation of binding constants, as for instance in lectin affinity electrophoresis or characterization of molecules with specific features like glycan content or ligand binding.
  - Pull-down assays are a common variation of immunoprecipitation and immunoelectrophoresis and are used identically, although this approach is more amenable to an initial screen for interacting proteins.
  - Label transfer can be used for screening or confirmation of protein interactions and can provide information about the interface where the interaction takes place. Label transfer can also detect weak or transient interactions that are difficult to capture using other *in vitro* detection strategies. In a label transfer reaction, a known protein is tagged with a detectable label. The label is then passed to an interacting protein, which can then be identified by the presence of the label.
  - The yeast two-hybrid screen investigates the interaction between artificial fusion proteins inside the nucleus of yeast. This approach can identify binding partners of a protein in an unbiased manner. However, the method has a notorious high false-positive rate which makes it necessary to verify the identified interactions by co-immunoprecipitation.
  - *In-vivo* crosslinking of protein complexes using photo-reactive amino acid analogs was introduced in 2005 by researchers from the Max Planck Institute <sup>[3]</sup> In this method, cells are grown with photoreactive diazirine analogs to leucine and methionine, which are incorporated into proteins. Upon exposure to ultraviolet light, the diazirines are activated and bind to interacting proteins that are within a few angstroms of the photo-reactive amino acid analog.
  - Tandem affinity purification (TAP) method allows high throughput identification of protein interactions. In contrast to Y2H approach accuracy of the method can be compared to those of small-scale experiments (Collins et al., 2007) and the interactions are detected within the correct cellular environment as by co-immunoprecipitation. However, the TAP tag method requires two successive steps of protein purification and consequently it can not readily detect transient protein-protein interactions. Recent genome-wide TAP experiments were performed by Krogan et al., 2006 and Gavin et al., 2006 providing updated protein interaction data for yeast organism.
  - Chemical crosslinking is often used to "fix" protein interactions in place before trying to isolate/identify interacting proteins. Common crosslinkers for this application include the non-cleavable NHS-ester crosslinker, *bis*-sulfosuccinimidyl suberate (BS3); a cleavable version of BS3, dithiobis(sulfosuccinimidyl propionate) (DTSSP); and the imidoester crosslinker dimethyl dithiobispropionimidate (DTBP) that is popular for fixing interactions in ChIP assays.
  - Chemical crosslinking followed by high mass MALDI mass spectrometry can be used to analyze intact protein interactions in place before trying to isolate/identify interacting proteins. This method detects interactions among non-tagged proteins and is available from CovalX.
  - SPINE (Strep-protein interaction experiment) <sup>[4]</sup> uses a combination of reversible crosslinking with formaldehyde and an incorporation of an affinity tag to detect interaction partners *in vivo*.
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- Quantitative immunoprecipitation combined with knock-down (QUICK) relies on co-immunoprecipitation, quantitative mass spectrometry (SILAC) and RNA interference (RNAi). This method detects interactions among endogenous non-tagged proteins<sup>[5]</sup>. Thus, it has the same high confidence as co-immunoprecipitation. However, this method also depends on the availability of suitable antibodies.

### Physical/Biophysical and Theoretical methods

- Dual Polarisation Interferometry (DPI) can be used to measure protein-protein interactions. DPI provides real-time, high-resolution measurements of molecular size, density and mass. While tagging is not necessary, one of the protein species must be immobilized on the surface of a waveguide.
- Static Light scattering (SLS) measures changes in the Rayleigh scattering of protein complexes in solution and can non-destructively characterize both weak and strong interactions without tagging or immobilization of the protein. The measurement consists of mixing a series of aliquots of different concentrations or compositions with the analyte, measuring the effect of the changes in light scattering as a result of the interaction, and fitting the correlated light scattering changes with concentration to a model. Weak, non-specific interactions are typically characterized via the second virial coefficient. This type of analysis can determine the equilibrium association constant for associated complexes.<sup>[6]</sup> Additional light scattering methods for protein activity determination were previously developed by Timasheff. More recent Dynamic Light scattering (DLS) methods for proteins were reported by H. Chou that are also applicable at high protein concentrations and in protein gels; DLS may thus also be applicable for *in vivo* cytoplasmic observations of various protein-protein interactions.
- Surface plasmon resonance can be used to measure protein-protein interaction.
- With → Fluorescence correlation spectroscopy, one protein is labeled with a fluorescent dye and the other is left unlabeled. The two proteins are then mixed and the data outputs the fraction of the labeled protein that is unbound and bound to the other protein, allowing you to get a measure of  $K_D$  and binding affinity. You can also take time-course measurements to characterize binding kinetics. FCS also tells you the size of the formed complexes so you can measure the stoichiometry of binding. A more powerful method is [[fluorescence cross-correlation spectroscopy (FCCS) that employs double labeling techniques and cross-correlation resulting in vastly improved signal-to-noise ratios over FCS. Furthermore, the two-photon and three-photon excitation practically eliminates photobleaching effects and provide ultra-fast recording of FCCS or FCS data.
- Fluorescence resonance energy transfer (FRET) is a common technique when observing the interactions of only two different proteins<sup>[7]</sup>.
- Protein activity determination by NMR multi-nuclear relaxation measurements, or → 2D-FT NMR spectroscopy in solutions, combined with nonlinear regression analysis of NMR relaxation or 2D-FT spectroscopy data sets. Whereas the concept of water activity is widely known and utilized in the applied biosciences, its complement--the protein activity which quantitates protein-protein interactions-- is much less familiar to bioscientists as it is more difficult to determine in dilute solutions of proteins; protein activity is also much harder to determine for concentrated protein solutions when protein aggregation, not merely transient protein association, is often the dominant process<sup>[8]</sup>.
- Theoretical modeling of protein-protein interactions involves a detailed physical chemistry/thermodynamic understanding of several effects involved, such as

intermolecular forces, ion-binding, proton fluctuations and proton exchange. The theory of thermodynamically linked functions is one such example in which ion-binding and protein-protein interactions are treated as linked processes; this treatment is especially important for proteins that have enzymatic activity which depends on cofactor ions dynamically bound at the enzyme active site, as for example, in the case of oxygen-evolving enzyme system (OES) in photosynthetic biosystems where the oxygen molecule binding is linked to the chloride anion binding as well as the linked state transition of the manganese ions present at the active site in Photosystem II(PSII). Another example of thermodynamically linked functions of ions and protein activity is that of divalent calcium and magnesium cations to myosin in mechanical energy transduction in muscle. Last-but-not least, chloride ion and oxygen binding to hemoglobin (from several mammalian sources, including human) is a very well-known example of such thermodynamically linked functions for which a detailed and precise theory has been already developed.

- Molecular dynamics (MD) computations of protein-protein interactions.
- Protein-protein docking, the prediction of protein-protein interactions based only on the three-dimensional protein structures from X-ray diffraction of protein crystals might not be satisfactory.<sup>[9] [10]</sup>

## Network visualization of protein-protein interactions

Visualization of protein-protein interaction networks is a popular application of scientific visualization techniques. Although protein interaction diagrams are common in textbooks, diagrams of whole cell protein interaction networks were not as common since the level of complexity made them difficult to generate. One example of a manually produced molecular interaction map is Kurt Kohn's 1999 map of cell cycle control.<sup>[11]</sup> Drawing on Kohn's map, in 2000 Schwikowski, Uetz, and Fields published a paper on protein-protein interactions in yeast, linking together 1,548 interacting proteins determined by two-hybrid testing. They used a force-directed (Sugiyama) graph drawing algorithm to automatically generate an image of their network.<sup>[12] [13] [14]</sup>

An experimental view of Kurt Kohn's 1999 map gmap <sup>[15]</sup>. Image was merged via gimp 2.2.17 and then uploaded to maplib.net

## See also

- Interactomics
- Signal transduction
- Biophysical techniques
- Biochemistry methods
- Genomics
- Complex systems biology
- Complex systems
- Immunoprecipitation
- Protein-protein interaction prediction
- Protein-protein interaction screening
- BioGRID, a public repository for protein and genetic interactions
- Database of Interacting Proteins (DIP)
- NCIBI National Center for Integrative Biomedical Informatics

- Biotechnology
- Protein nuclear magnetic resonance spectroscopy
- → 2D-FT NMR and Spectroscopy
- → Fluorescence correlation spectroscopy
- Fluorescence cross-correlation spectroscopy
- Light scattering
- ConsensusPathDB

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- National Center for Integrative Biomedical Informatics (NCIBI) (<http://portal.ncibi.org/gateway/>)
  - Proteins and Enzymes ([http://www.dmoz.org/Science/Biology/Biochemistry\\_and\\_Molecular\\_Biology/Biomolecules/Proteins\\_and\\_Enzymes/](http://www.dmoz.org/Science/Biology/Biochemistry_and_Molecular_Biology/Biomolecules/Proteins_and_Enzymes/)) at the Open Directory Project
  - FLIM Applications (<http://www.nikoninstruments.com/infocenter.php?n=FLIM>) FLIM is also often used in microspectroscopic/ chemical imaging, or microscopic, studies to monitor spatial and temporal protein-protein interactions, properties of membranes and interactions with nucleic acids in living cells.
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