The Nobel Prize in Chemistry

Compiled by Hikmet Geckil
Department of Molecular Biology and Genetics
Inonu University

The Nobel Prize in Chemistry 2009 was awarded jointly to Venkatraman Ramakrishnan, Thomas A. Steitz and Ada E. Yonath ***"for studies of the structure and function of the ribosome"***.

The Nobel Prize in Chemistry 2008 was awarded jointly to Osamu Shimomura, Martin Chalfie and Roger Y. Tsien ***"for the discovery and development of the green fluorescent protein, GFP"***.

The Nobel Prize in Chemistry 2007 was awarded to Gerhard Ertl ***"for his studies of chemical processes on solid surfaces"***.

The Nobel Prize in Chemistry 2006 was awarded to Roger D. Kornberg ***"for his studies of the molecular basis of eukaryotic transcription"***.

[redacted]

The Nobel Prize in Chemistry 2004 was awarded jointly to Aaron Ciechanover, Avram Hershko and Irwin Rose ***"for the discovery of ubiquitin-mediated protein degradation"***.

The Nobel Prize in Chemistry 2003 was awarded ***"for discoveries concerning channels in cell membranes"*** jointly with one half to Peter Agre ***"for the discovery of water channels"*** and with one half to Roderick MacKinnon ***"for structural and mechanistic studies of ion channels"***.

The Nobel Prize in Chemistry 2002 was awarded ***"for the development of methods for identification and structure analyses of biological macromolecules"*** with one half jointly to John B. Fenn and Koichi Tanaka ***"for their development of soft desorption ionisation methods for mass spectrometric analyses of biological macromolecules"*** and the other half to Kurt Wüthrich ***"for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution"***.

The Nobel Prize in Chemistry 2001 was divided, one half jointly to William S. Knowles and Ryoji

The Nobel Prize in Chemistry 2000 was awarded jointly to Alan J. Heeger, Alan G. MacDiarmid and Hideki Shirakawa ***"for the discovery and development of conductive polymers"***.

The Nobel Prize in Chemistry 1999 was awarded to Ahmed Zewail ***"for his studies of the transition states of chemical reactions using femtosecond spectroscopy"***.

The Nobel Prize in Chemistry 1998 was divided equally between Walter Kohn ***"for his development of the density-functional theory"*** and John A. Pople ***"for his development of computational methods in quantum chemistry"***.

The Nobel Prize in Chemistry 1997 was divided, one half jointly to Paul D. Boyer and John E. Walker ***"for their elucidation of the enzymatic mechanism underlying the synthesis of adenosine triphosphate (ATP)"*** and the other half to Jens C. Skou ***"for the first discovery of an ion-transporting enzyme, Na+, K+ -ATPase"***.

The Nobel Prize in Chemistry 1993 was awarded ***"for contributions to the developments of methods within DNA-based chemistry"*** jointly with one half to Kary B. Mullis ***"for his invention of the polymerase chain reaction (PCR) method"***and with one half to Michael Smith ***"for his fundamental contributions to the establishment of oligonucleotide-based, site-directed mutagenesis and its development for protein studies"***.

The Nobel Prize in Chemistry 1991 was awarded to Richard R. Ernst ***"for his contributions to the development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy"***.

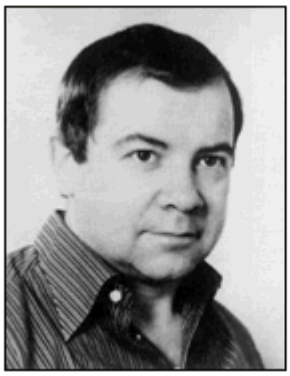
The Nobel Prize in Chemistry 1989 was awarded jointly to Sidney Altman and Thomas R. Cech ***"for their discovery of catalytic properties of RNA"***

The Nobel Prize in Chemistry 1988 was awarded jointly to Johann Deisenhofer, Robert Huber and

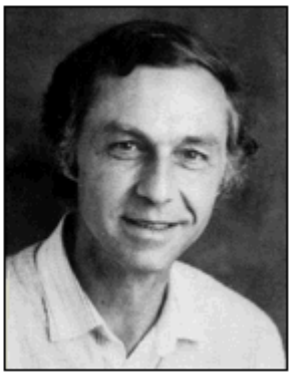
BACK

The Nobel Prize in Chemistry 1988

The Royal Swedish Academy of Sciences has awarded
this year's Nobel Prize in Chemistry to



Dr **Johann Deisenhofer**
University of Texas
Southwestern Medical
Center, Dallas, USA



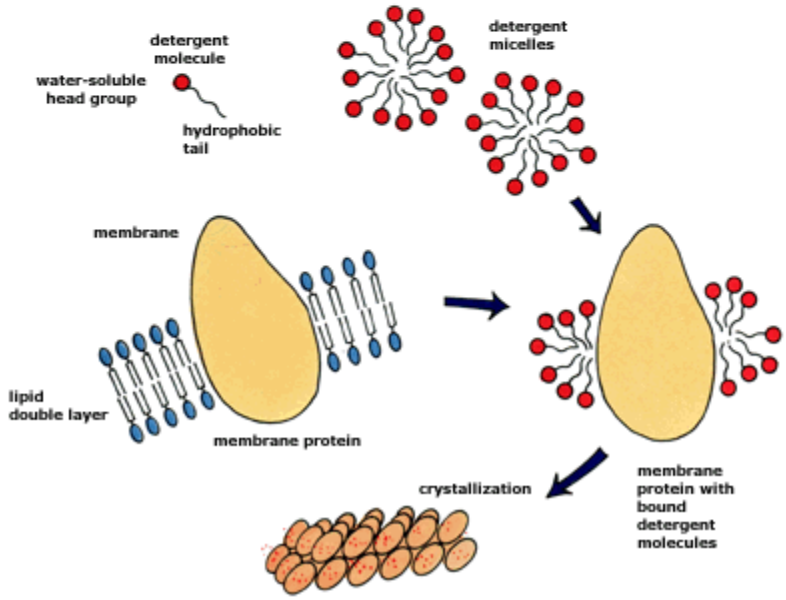
Professor **Robert Huber**
Max-Planck-Institut
für Biochemie,
Martinsried, FRG

Dr **Hartmut Michel**
Max-Planck-Institut
für Biophysik,
Frankfurt/Main, FRG

for the determination of the three-dimensional structure
of a photosynthetic reaction center.

The first crystals of membrane proteins

An important step in biochemical research was taken in 1980 when **Hartmut Michel** managed to crystallize a membrane protein (bacteriorhodopsin) after having solubilized the lipid bilayer of the membrane with a detergent. Detergents, which are structurally similar to membrane lipids, form micelles in water. They bind to membrane proteins with their fatty, hydrophobic tails creating an environment which mimics that in the membrane. Michel found a method to crystallize such protein-detergent complexes. Two years later a definitive breakthrough took place as Michel **succeeded in crystallizing the reaction center from the photosynthetic bacterium** *Rhodopseudomonas viridis*.



The structure of a photosynthetic reaction center

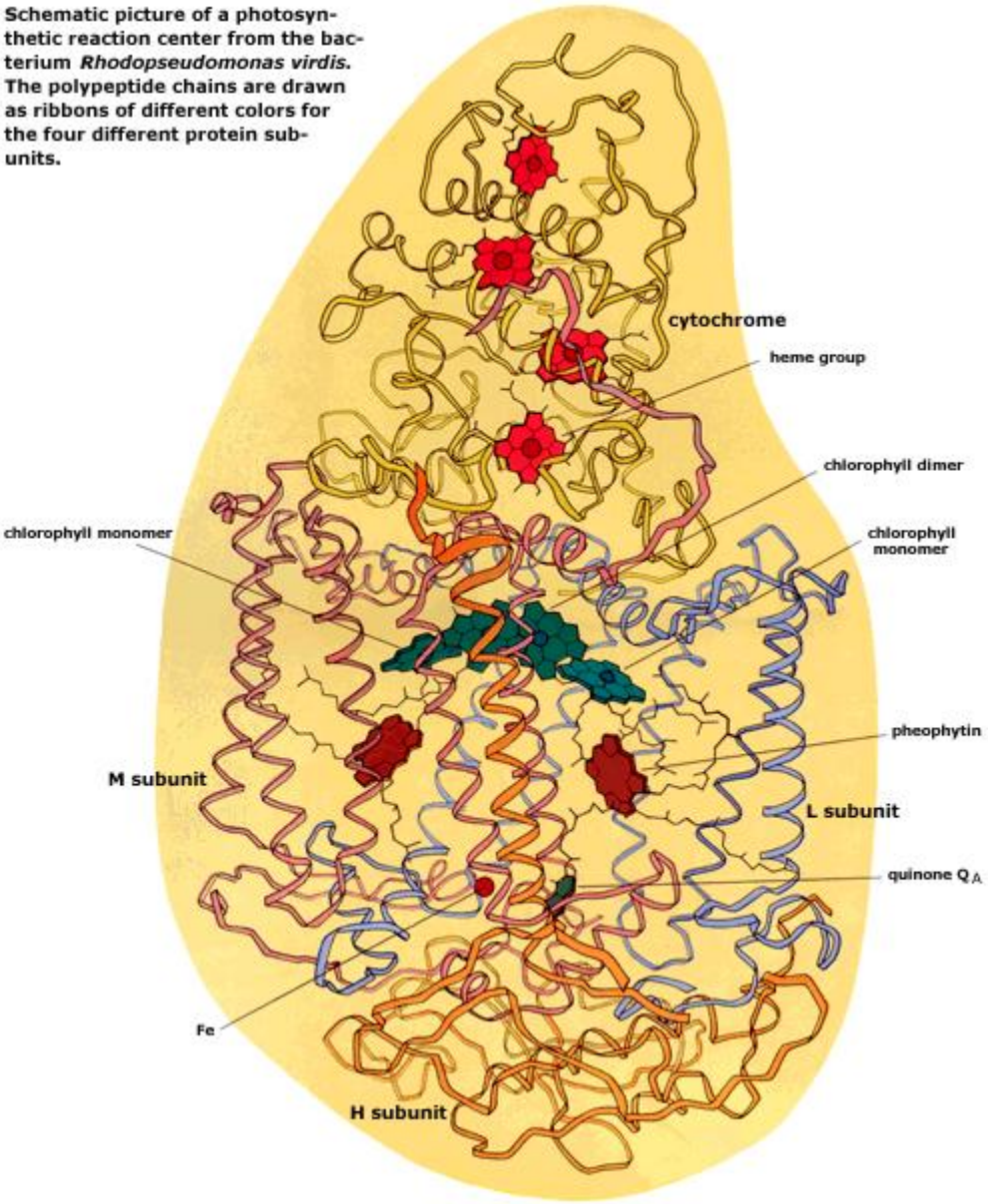
In 1984, after having analyzed the X-ray diffraction pattern from the reaction center crystals, **Johann Deisenhofer**, **Robert Huber** and **Hartmut Michel** could present the **3-dimensional structure** of the reaction center, the first high-resolution structure of a membrane protein and also the most complex molecular structure which had been solved.

The reaction center is composed of four protein subunits. Two of these, the L and M subunits, each form five membrane-spanning helices. The structure shows the precise arrangement in the L and M subunits of the photochemically active groups – two chlorophyll molecules forming a dimer, two monomeric chlorophylls, two pheophytin molecules (these lack the central magnesium ion of chlorophyll), one quinone molecule, called Q_A (a second quinone molecule, Q_B, is lost during the preparation of the reaction center) and one iron ion (Fe). The L and M subunits and their chromophores are related by a twofold symmetry axis that passes through the chlorophyll dimer and the iron.

A third subunit, H, without active groups and located on the membrane inner surface, is anchored to the membrane by a protein helix.

The remaining subunit, a cytochrome with four heme groups (related to the blood pigment hemoglobin), binds at the outer surface of the membrane.

Schematic picture of a photosynthetic reaction center from the bacterium *Rhodopseudomonas virdis*. The polypeptide chains are drawn as ribbons of different colors for the four different protein subunits.



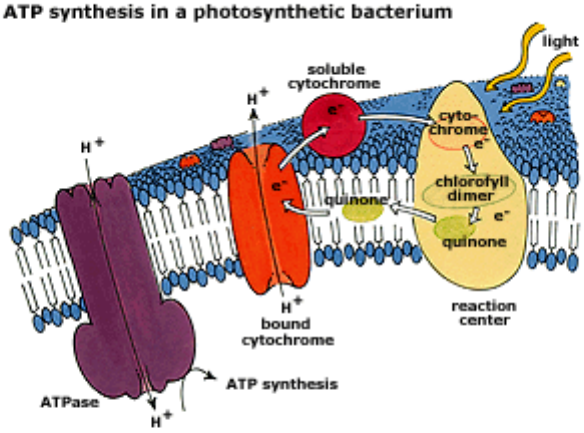
Photosynthesis: Chemical energy from light

Life on earth is dependent on **photosynthesis**, the process in which solar light is converted into chemical energy and stored as carbohydrates. The carbohydrates are, finally, degraded to carbon dioxide and water in the cell respiration in a reaction requiring molecular oxygen. The liberated energy is utilized to power the life processes. In photosynthesis, the carbon dioxide and water are used to resynthesize carbohydrate, while molecular oxygen is released into the atmosphere as a waste product. Thus, not only is present life on earth largely a result of photosynthesis but so is the air we all breathe.

Photosynthesis and respiration are based on the transfer of electrons between donor and acceptor molecules bound to biological membranes – sheet-like structures composed of lipids and proteins which surround the cells and their inner compartments. The photosynthetic reactions in plants take place in the inner membranes of the chloroplasts, the organelles which contain the chlorophyll. Some bacteria have a simpler form of photosynthesis, to some extent similar to that in plants but without the ability to form oxygen.

In all types of photosynthesis, the light energy absorbed by chlorophyll is transferred to membrane-bound protein-pigment complexes, known as reaction centers. In these complexes the light energy initiates electron-transfer reactions which are coupled to the translocation of hydrogen ions across the membrane. The resulting pH gradient is utilized by another membrane-bound protein, ATPase, to synthesize ATP, a compound used as a fuel in energy-demanding biological processes. In cell respiration, too, electron transport is coupled to proton translocation and ATP synthesis.

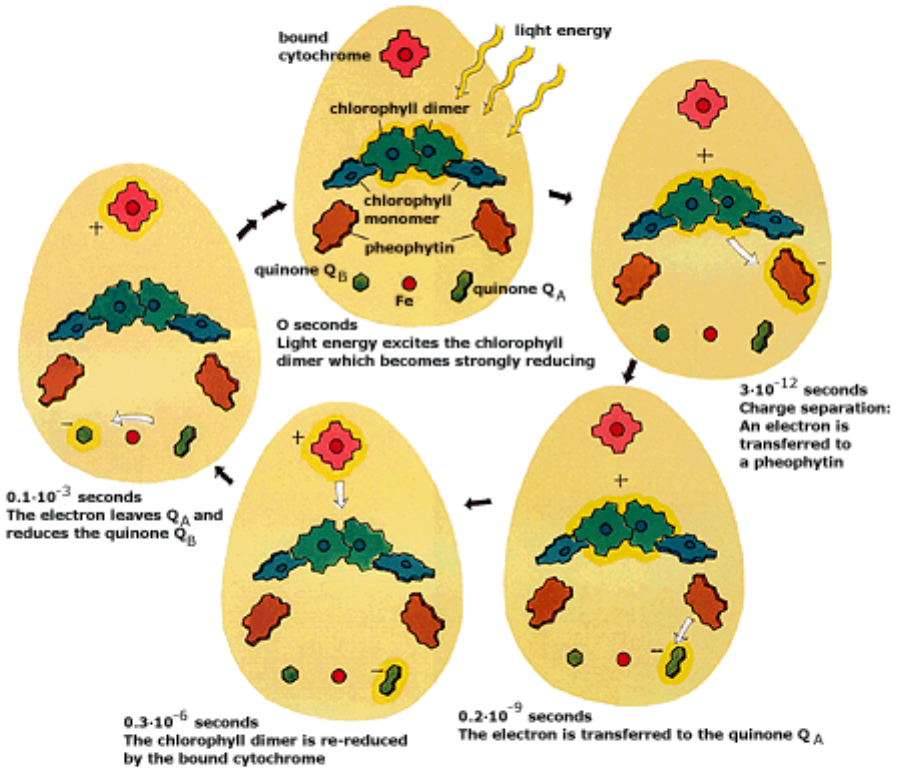
Light-induced electron transport and ATP synthesis in a photosynthetic bacterium



Our knowledge about photosynthesis, respiration and other membrane-associated processes is limited due to the lack of information about the molecular organization of the **membrane proteins** involved, a problem which derives from **difficulties in crystallizing** these proteins. The crystals are used for the determination of the 3-dimensional structure of the proteins by X-ray diffraction, a technique in which X-rays are analyzed after being scattered by the molecules in a crystal.

A closeup of a photosynthetic primary reaction

The 3-dimensional structure of the reaction center and earlier kinetic and spectroscopic results have provided a detailed picture of the primary photosynthetic reactions.



The reactions illustrated above are repeated when another light quantum is absorbed except that this time the Q_B-molecule is reduced to hydroquinone. The hydroquinone leaves the reaction center and is replaced by a new Q_B-molecule from the membrane. The electrons eventually return to the reaction center (to the cytochrome) via other electron carriers. Details in the protein environment around chlorophyll and pheophytin explain why only the right half (the L-subunit branch) of the reaction center is active.

Highlights in photosynthesis research

1771	Joseph Priestley, England, discovers that plants can "purify" air that has been "burned out" by a candle.
1779	Jan Ingenhousz, The Netherlands, demonstrates that the plant in Priestley's experiment is dependent on light and its green parts.
1782-1804	Several researchers show that carbon dioxide and water are stored as organic matter by plants.
1845	Robert Mayer, Germany, points out that plants store solar energy in organic matter.
ca 1915	Richard Willstätter, Germany, (Nobel Prize 1915) suggests that chlorophyll plays an active role in plants.
ca 1930	Cornelis van Niel, USA, proposes that photosynthesis is based on oxidation-reduction reactions and that the primary reaction is a photolysis of water followed by oxygen evolution.
1932	Robert Emerson and William Arnold, USA, conclude that several hundred chlorophyll molecules cooperate in photosynthesis.
1939	Robert Hill, England, demonstrates that photolysis of water and carbon dioxide fixation are separate processes.
1940	Hans Fischer, Germany, solves the chemical structure of chlorophyll. (Nobel Prize 1930 for his investigations of hemes and chlorophyll.)
1954	Melvin Calvin, USA, (Nobel Prize 1961) and coworkers unravel the reactions of carbon dioxide fixation.
1954	Daniel Arnon, USA, discovers light-dependent synthesis of ATP (photophosphorylation).
1960-1961	Robert Hill and Fay Bendall, England, and independently Louis Duysens, The Netherlands, show how two separate photosystems cooperate in plants.
1968	William Parson, USA, confirms Duysens' hypothesis (1956) that chlorophyll is oxidized in the primary reaction of photosynthesis.
1984	**Johann Deisenhofer, Robert Huber** and **Hartmut Michel**, The Federal Republic of Germany, solve the structure of a photosynthetic reaction center from a bacterium.

Perspective

The achievements by Deisenhofer, Huber and Michel that were recognized with the 1988 Nobel Prize in chemistry signify breakthroughs in several fields of research:

Photosynthesis:
- The knowledge about the location of the photochemically active groups in the reaction center has resulted in a deeper understanding of the mechanism of the primary reaction in photosynthetic organisms.
- The structural analogies with plants will facilitate the development of new, selective herbicides which affect the function of the reaction center.

Electron transport:
- For the first time it is shown how the electron-carrying groups are organized spatially in a biological system. This gives a possibility to investigate current theories of electron transfer.

The structure of membrane proteins:
- One will now be able to make better predictions of the structures of other membrane proteins from their amino acid sequence.

Crystallization of membrane proteins:
- Michel's crystallization method can be applied to other membrane proteins.

Membrane proteins participate in many important biological processes:
- Ion pumps and channels regulate the ionic balance of the cell and participate in biological energy conversions, signal transmission in the nervous system and in muscle activity.
- Carriers of substances into and out of the cell.
- Cell surface receptors for hormones and signal substances. Confer cell identity and participate in immunological reactions.
- Convert light to nerve signals in the eye.

Further reading

Scientific American, (1987) Vol 256:6, 42-48.

Trends in Biochemical Sciences, (1987) 12, 321-326.

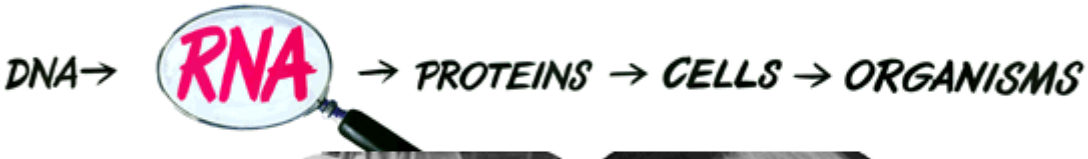
Nature (1985) 318, 618-624.

The Royal Swedish Academy of Sciences, Information about the Nobel Prize in Chemistry 1988 (press release).

BACK

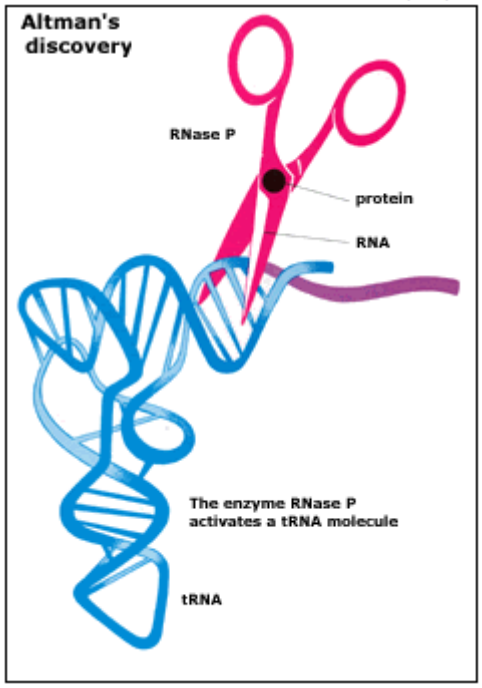
The Nobel Prize in Chemistry 1989

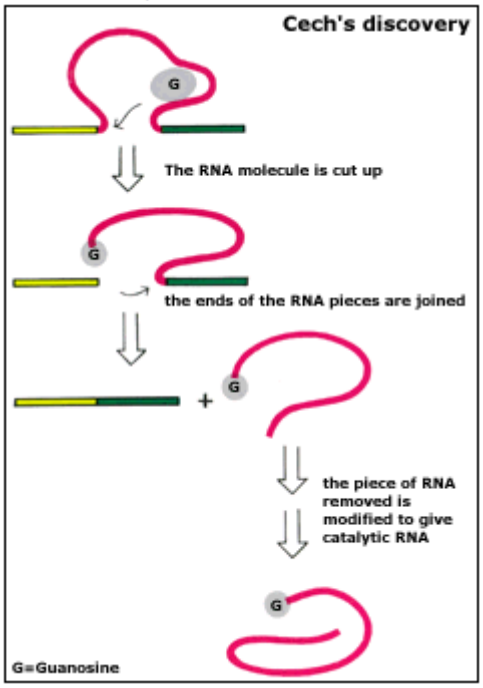
The Royal Swedish Academy of Sciences has awarded this year's Nobel Prize in Chemistry jointly to
Sidney Altman and **Thomas R. Cech**
for their discovery of catalytic properties of RNA



Sidney Altman
Yale University
New Haven, CT, USA

Thomas R. Cech
University of Colorado
at Boulder, USA





The chemistry of life and its central dogma

The genetic information flows from the DNA in our genetic material via RNA to proteins, which in turn construct cells with different functions. This principle is called the **central dogma** of the chemistry of life. It was previously believed that the nucleic acids DNA and RNA serve solely as carriers of the genetic information, whereas proteins in the form of enzymes catalyze the chemical processes of life. The chemist's perspective on genetic information (heredity) and function (biocatalysis) in living cells has changed through the discovery by Sidney Altman and Thomas Cech that **the ribonucleic acid RNA can also function as an enzyme**.

RNA molecules consist of long strands of alternating carbohydrate and phosphate molecules. To each carbohydrate is attached one of the four nitrogen-containing bases: **A**denine, **C**ytosine, **G**uanine and **U**racil. These bases constitute the chemical "letters" in the genetic code which determines the compositions of proteins. Each word in this code contains three of these letters, which can be combined in many different ways, e.g., UCA, CGG, ACU. Each word corresponds to one of the twenty different amino acids found in proteins. The cell has developed a sophisticated molecular machinery which can read the words of the genetic code along the RNA strand and join amino acids together in the order required to construct a protein with a specific function.

The code words in an RNA molecule originate from a DNA molecule. All of our hereditary traits are programmed into the DNA molecules. Most RNA molecules, in contrast, contain information about only one of the cell's many components. For example, one RNA molecule may contain information concerning the pigment in an individual's eyes, while another contains information about insulin. In general, one RNA molecule contains the information from one gene.

Enzymes – biological catalysts

Normally chemical reactions do not proceed spontaneously, but require the help of a **catalyst**.

A catalyst accelerates a chemical reaction without itself being changed. For example, the reaction of hydrogen with oxygen to produce water requires the addition of the metal platinum. These days we encounter the concept of a catalyst most often in connection with technology for cleaning up the exhaust fumes from our automobiles, where platinum and rhodium catalyze the breakdown of polluting nitrogen oxides.

Chemical reactions within living cells must also be catalyzed. Biological catalysts are called enzymes. There is, for instance, an enzyme in our saliva which converts starch to a simple sugar, which is used by the cell to produce energy, and another enzyme which degrades the excess lactic acid produced when we overexert ourselves. All green plants contain enzymes which convert carbon dioxide in the air to nutritious carbohydrates such as sugar and starch. **Without enzymes life would not be possible!**

Enzymes are highly selective. Among the thousands of different compounds in a cell, an enzyme can recognize the right molecule (substrate) and transform it into a new product. This property arises from the special three-dimensional structure of each enzyme. One can compare an enzyme and its substrate with a lock and its key.

Enzymes are very effective catalysts. A chemical reaction might require several months to reach completion without a catalyst, but only a few seconds with the help of an enzyme. Since the enzyme remains unchanged, one enzyme molecule can catalyze the transformation of millions of substrate molecules.

Up until the beginning of the 1980's, all enzymes were thought to be proteins. **We now know that proteins do not have a monopoly on biocatalysis. RNA molecules can also function as enzymes.**

Ribonucleic acid (RNA) – the biomolecule which can do it all

Sidney Altman and **Thomas Cech** have independently studied how the genetic code is transferred from DNA to RNA. They knew, however, that part of the genetic information is not required and must be removed from RNA before the RNA molecule can be utilized by the cell. While searching for the catalysts of RNA maturation, Altman and Cech discovered that these enzymes were composed of catalytic RNA, and not of protein.

Sidney Altman studied the enzyme RNase P, which is found in e.g. intestinal bacteria. RNase P activates a special kind of RNA molecule called tRNA (transfer RNA) by removing a portion which is unnecessary for its function. The enzyme RNase P has the unusual property of containing not only a protein molecule, but an RNA molecule as well. Surprisingly Altman demonstrated that it is the **RNA molecule which acts as a biocatalyst**.

Thomas Cech studied an RNA molecule from the primitive unicellular animal *Tetrahymena*. He discovered that an unnecessary piece of RNA is removed from the middle of this molecule and that the loose ends thus formed are then joined together. It created a sensation when he showed that the RNA molecule itself catalyzes this reaction. The portion of the RNA molecule which is removed modifies itself subsequently so that it can function, among other things, as an RNA-synthesizing enzyme. This means that **catalytic RNA can also make new RNA**.

The work of both Altman and Cech indicates that the catalytic capacities of RNA molecules are intimately dependent on their three-dimensional structures, as is the case with enzyme proteins.

RNA and of origin of life

Which was the first biological molecule on earth? How could life have arisen at all if the DNA molecules of the genetic material could only multiply and be deciphered with the help of enzyme proteins, whereas proteins can only be built up with genetic information from DNA. Which came first, the chicken or the egg?

By the discovery of catalytic RNA the Nobel laureates have shown that neither the chicken nor the egg came first. RNA molecules can possess all the properties required of the original biomolecule: **They can be both genetic material and enzymes at the same time.**

The history of biocatalysis

1835	The Swede Jöns Jacob **Berzelius** describes a catalyst as a substance which can breathe life into slumbering chemical reactions.
1868	Friedrich **Miescher**, Switzerland isolates nucleic acids from white blood cells obtained from discarded bandages.
1877	Wilhelm **Kuhne**, Germany introduces the term "enzyme" and distinguishes between enzymes and bacteria.
1893	Wilhelm **Ostwald**, Latvia classifies enzymes as catalysts.
1926	James **Sumner**, USA (Nobel Prize 1946) crystallizes the enzyme urease and demonstrates that it is a protein.
1940	Torbjörn **Caspersson**, Sweden and Jean **Brachet**, Belgium predict that ribonucleic acids (RNA) are required in order for the cell to make proteins.
1940	George **Beadle*** and Edward **Tatum***, USA advance the hypothesis "one gene – one enzyme". * Nobel Prize 1958.
1944	Oswald **Avery** and coworkers in the United States demonstrate that the genetic material is composed of deoxyribonucleic acid (DNA).
1953	James **Watson***, USA and Francis **Crick***, England demonstrate that the DNA molecule is composed of a double helix. * Nobel Prize 1962.
1960	Francis **Crick** and Sydney **Brenner**, England and François **Jacob*** and Jaques **Monod***, France propose how RNA is used in order for cells to make proteins using information from DNA. * Nobel Prize 1965.
1961-65	Work in the United States by Marshall **Nirenberg***, Johann **Matthaei**, Gobind **Khorana***, Severo **Ochoa** (Nobel Prize 1959) and their coworkers leads the way to the deciphering of the genetic code. * Nobel Prize 1968.
1977	It is demonstrated in several laboratories that RNA molecules must often be cut and rejoined before they can be used, e.g., to make proteins.
1982	Thomas **Cech** (Nobel Prize 1989) discovers that an RNA molecule can cut itself and rejoin the loose ends without the presence of an enzyme protein.
1983	Sidney **Altman** (Nobel Prize 1989) shows that an RNA molecule can possess all the properties of an enzyme.

What happens next?

The discovery of **catalytic RNA**, also called **ribozyme**, has been of great importance to both research and industry.

An important catalyst: In addition to cutting and rejoining RNA, catalytic RNA probably plays a major role in many biological processes. Life processes often require intimate cooperation between proteins and RNA. In the future researchers will probably find that RNA rather than protein-enzymes plays the leading role in many of these processes.

Three-dimensional structure: There are clear indications that catalytic RNA possesses a specific three-dimensional structure in the same manner as enzyme proteins. As soon as scientists have described this structure, it will be easier to understand the chemical reaction mechanism for catalytic RNA.

Custom-designed ribozyme: Catalytic RNA is a new and powerful tool for gene technology. In the mail-house catalogues used by researchers one can find "canned ribozyme" - custom-designed enzymes which cut or join RNA molecules with high precision.

Medical drugs: Within biotechnology and medicine there are obvious applications for catalytic RNA. For example, genetically engineered plants can become virus resistant by producing a ribozyme which can cut and destroy the genetic material of the virus. One can also custom-design ribozymes which can search out infectious viruses and render them harmless. It might even become possible at some future date to cure hereditary diseases with the help of ribozymes.

Further reading

Scientific American (1986) Vol 255, 76-84.

Trends in Biochemical Sciences (1989) Vol 11, 515-518.

Journal of the American Medical Association (1988) Vol 260, 3030-3034.

Advances in Enzymology (1989) Vol 62, 1-36.

The Royal Swedish Academy of Sciences, Information about the Nobel Prize in Chemistry 1989 (press release).

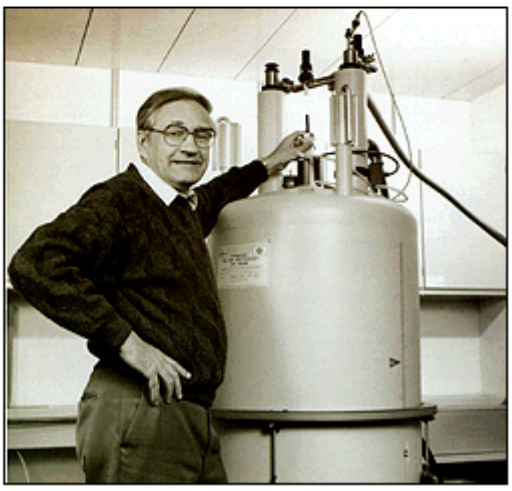
BACK

The Nobel Prize in Chemistry 1991

The Royal Swedish Academy of Sciences has awarded this year's Nobel Prize in Chemistry to

Richard R. Ernst
ETH, Zürich, Switzerland

for his contributions to the development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy.



Richard R. Ernst's revolutionary development of the methodology of nuclear magnetic resonance spectroscopy has transformed NMR into maybe the most important instrumental technique within chemistry today. Ernst has contributed more than anybody else to this development by the discoveries of Fourier-transform NMR and two-dimensional (2D) NMR.

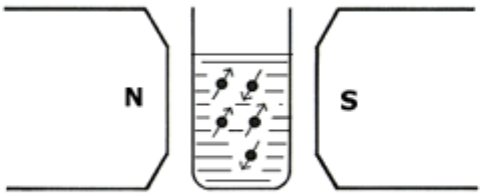
NMR spectroscopy

Spectroscopy deals with the interactions between electromagnetic radiation and matter. How the matter is influenced depends on the wavelength or frequency of the radiation. Scientists use spectroscopy to derive the properties of matter at the molecular level. Nuclear magnetic resonance (NMR) is a special branch of spectroscopy, exploiting the magnetic properties of atomic nuclei. NMR was discovered 1945 in USA by Bloch and Purcell (Nobel Prize in physics 1952).

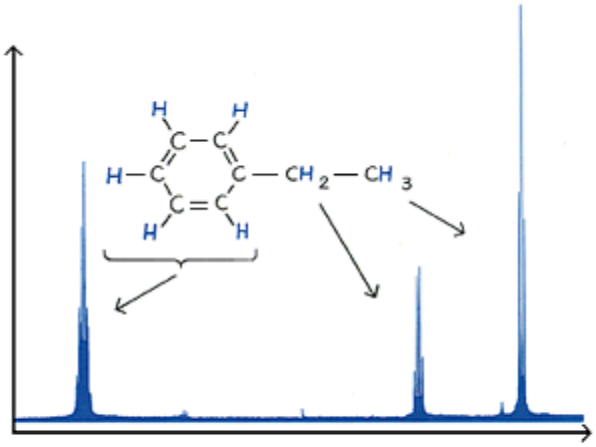
The method functions as follows: A substance is placed in a magnetic field. Some atomic nuclei (e.g. protons, nuclei of hydrogen atoms) then behave like microscopic compass needles, called nuclear spins.

Each nuclear spin orientation corresponds to a different energy level. The spins may jump between the levels when the sample is exposed to radio waves whose frequency exactly matches the energy spacing. This is called resonance. One way of measuring the energy level spacings is to change the irradiation frequency slowly. At resonance, the spins flip and an electric signal is induced. The strength of the signal is plotted as a function of frequency in a diagram, the NMR spectrum.

Around 1950, it was discovered that the nuclear resonance frequencies depended not only on the nature of the atomic nuclei, but also on their chemical environment. The utility of NMR in chemistry soon became obvious: The signals could be used to determine the number and type of chemical groups in a compound. A difficulty in the early days was however the relatively low sensitivity of the NMR method - it was only possible to study rather concentrated solutions of fairly small molecules.



According to the laws of modern physics, the nuclear spins can be oriented in only a few ways with respect to the magnetic field.



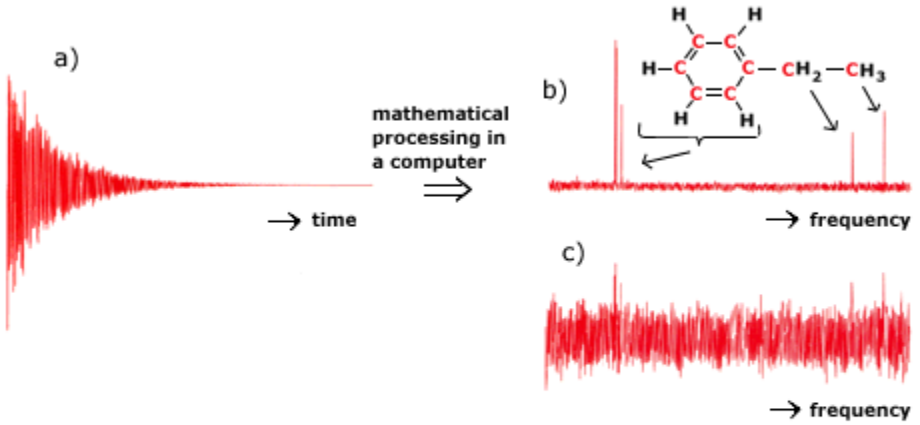
A proton NMR spectrum of a solution containing a simple organic compound, ethyl benzene. Each group of signals corresponds to protons in a different part of the molecule.

Fourier-transform NMR

A major breakthrough occurred in 1966. Richard R. Ernst then discovered (together with Weston A. Anderson, USA) that the sensitivity of NMR spectra could be increased dramatically if the slow frequency sweep was replaced by short, intense radiofrequency pulses. The pulses cause a signal to be emitted by the nuclei. This signal is measured as a function of time after the pulse. It cannot be interpreted directly. Ernst discovered, however, that it was possible to extract the resonance frequencies from such a signal and to convert the signal into a NMR spectrum by a mathematical operation (Fourier* transformation, FT). This is performed rapidly in a computer. The whole process can be compared with stretching both arms over a piano and pushing all the keys at the same time. All the tones are there, but they are difficult to distinguish. A computer can discern the different tones (frequencies).

Ernst's discovery is the basis of modern NMR spectroscopy, called FT NMR. It leads to a tenfold, and sometimes 100-fold increase in sensitivity since the pulse response contains information on all resonance frequencies at the same time. During the same time needed to record a single conventional spectrum, the FT experiment can be repeated many times and the results summed by a computer. FT NMR makes it possible to study small amounts of material as well as chemically interesting isotopes of low natural abundance.

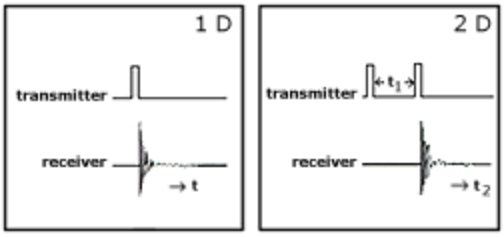
* Fourier was a French mathematician, who lived 200 years ago.



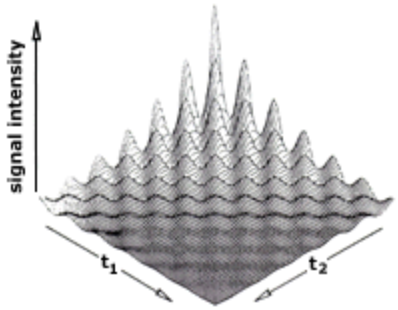
The diagram a) shows a NMR signal from carbon-13 nuclei (which only occur in 1% of all the carbon atoms in nature) in ethyl benzene solution, obtained with the pulse technique by accumulating the response of the nuclear spins to two hundred pulses. The total experiment time was 20 minutes. After Fourier transformation, one obtains the carbon-13 NMR spectrum in the diagram b). If the experiment was performed with the old technique, in the same time one would only manage to perform a single sweep and the spectrum would look like the diagram c).

Two-dimensional NMR

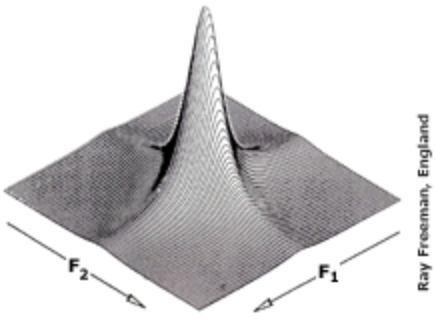
Another important development during the 1960s and the 1970s were new magnet designs, based on superconducting materials. They gave higher and more stable magnetic fields leading to spectra with much better sensitivity and resolution. More complex systems could be studied. In order to move to very complicated molecules, however, the next breakthrough was necessary. Inspired by a Belgian scientist Jean Jeener, Ernst and coworkers developed 1975 two-dimensional (2D) FT NMR which introduced many entirely new possibilities.



The diagram illustrates the time course of the one-dimensional (1D) FT NMR method and the 2D FT NMR. In 1D NMR, the nuclear spins are exposed to a pulse, after which a signal is detected in the receiver as a function of time t after the pulse. In 2D NMR, the nuclear spins are subjected to two (or more) pulses, with a time interval t_1. After the second pulse, the signal is acquired in the same way as in 1D NMR, though here we call the time variable t_2. After this, one returns to the beginning of the experiment and repeats it with other values of t_1.

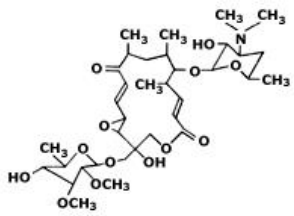


The change of t_1 modfies the signal measured during t_2. This provides a two-dimensional table containing the signal intensity as a function of both t_1 and t_2. After Fourier transformation with respect to both these time variables, one obtains a two-dimensional frequency spectrum in the form of a map showing the dependence of the signal intensity on two frequency variables, denoted F_1 and F_2.

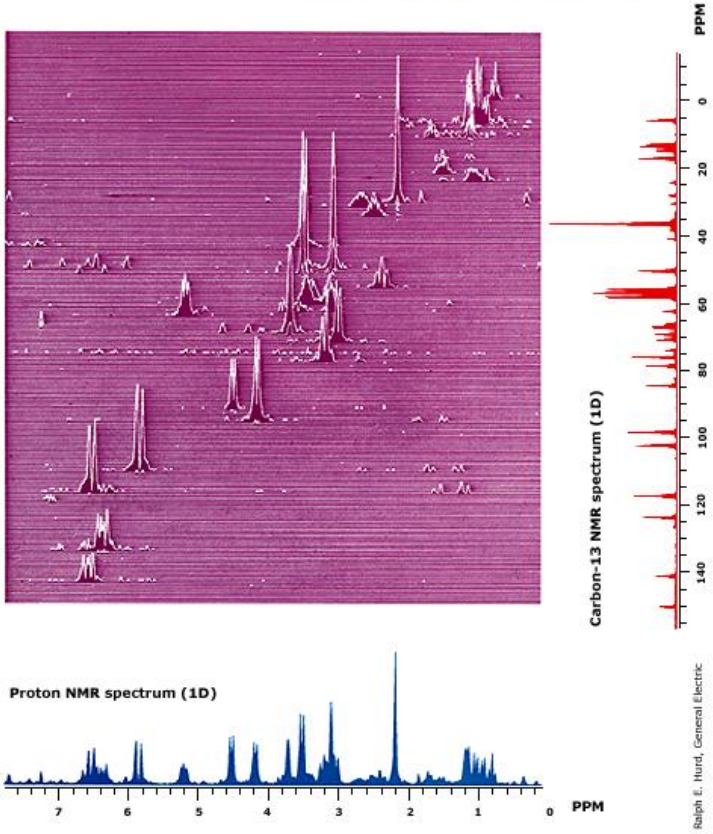


Applications

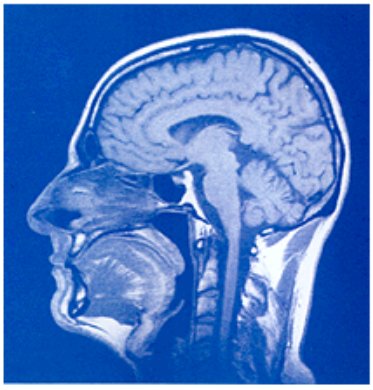
NMR spectroscopy is today used within practically all branches of chemistry, at universities as well as industrial laboratories. A typical NMR investigation combines several types of 1D, 2D (the two-pulse sequence of the 2D NMR method can be modified in many ways, resulting in hundreds of different types of 2D NMR experiments) and sometimes even 3D or 4D experiments. The accumulated information provides often a detailed picture of the molecular structure. The complete three-dimensional structure of many proteins and other biological macromolecules in solution has been determined in this way. NMR is also used to study interactions between different molecules (e.g. enzyme – substrate, soap – water), to study molecular motions in liquids and polymers, to obtain information about rates of certain reactions and much more.



A correlation spectrum for a complicated organic molecule. The two frequency axes correspond to the resonance frequencies of protons and carbon-13. The occurrence of a signal at a certain spot means that the carbon atom which corresponds to the "latitude" in the map is directly bonded to the proton whose resonance frequency is given by the "longitude". The one-dimensional proton and carbon-13 spectra are shown below and on the side of the map.



The NMR technique is also used in medical diagnosis. The magnetic resonance imaging (MRI) instruments that are in use in many hospitals today are NMR instruments of a special kind.



A so-called MR image helps the physicians look into the body. The picture is created by exposing the subject to magnetic field gradients, which make the magnetic field slightly different at different locations in the patient's head. The picture has been taken using a technique based upon Ernst's 2D FT method.

Further reading

Journal of Chemical Education, Sept and Oct 1989, April and May 1990

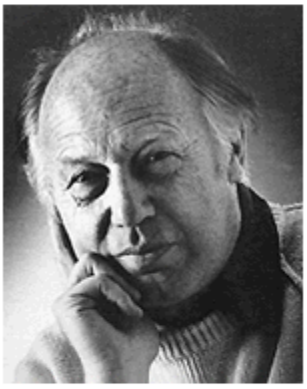
Chemistry in Britain, April 1991

Information on the 1991 Nobel Prize in Chemistry (Press release), The Royal Swedish Academy of Sciences

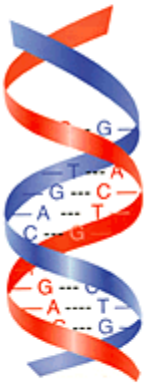
BACK

The Nobel Prize in Chemistry 1993

The Royal Swedish Academy of Sciences awards this year's Nobel Prize in Chemistry to



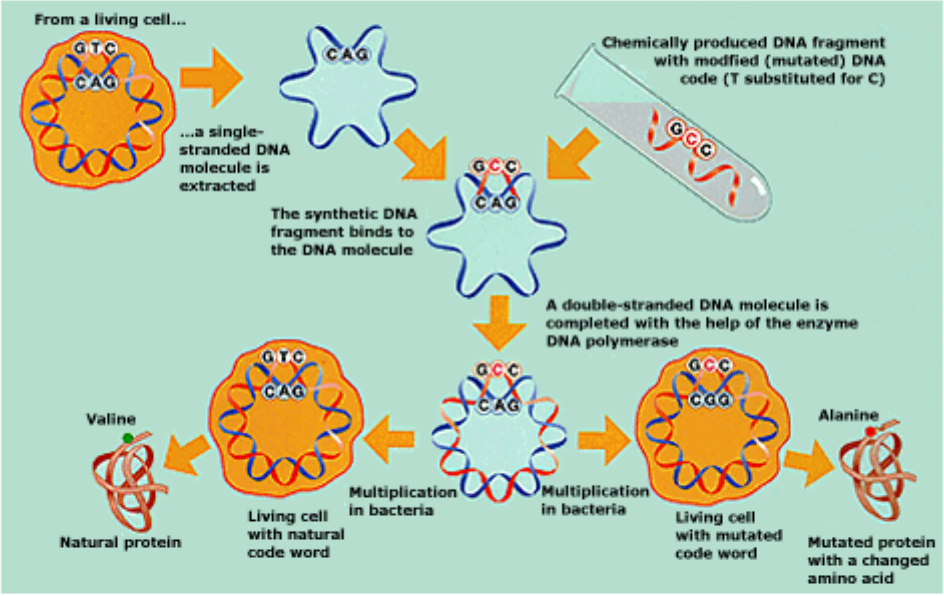
Michael Smith
Canada, for his fundamental contributions to the establishment of oligonucleotide-based, site-directed mutagenesis and its development for protein studies



Kary B. Mullis
USA, for his invention of the polymerase chain reaction (PCR) method

Site-directed mutagenesis reprograms DNA

Using site-directed mutagenesis the information in the genetic material can be changed. A synthetic DNA fragment is used as a tool for changing one particular code word in the DNA molecule. This reprogrammed DNA molecule can direct the synthesis of a protein with an exchanged amino acid. **Michael Smith's** method has become one of biotechnology's most important instruments.

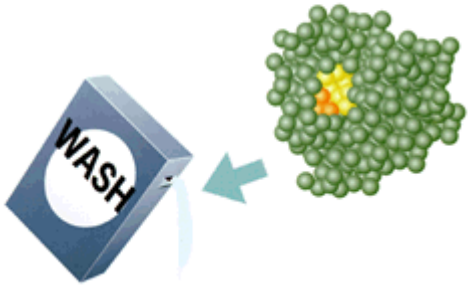


With Smith's site-directed mutagenesis the researchers can study in detail how proteins function and how they interact with other biological molecules. Site-directed mutagenesis can be used, for example, to systematically change amino acids in enzymes, in order to better understand the function of these important biocatalysts. The researchers can also analyse how a protein is folded into its biologically active three-dimensional structure. The method can also be used to study the complex cellular regulation of the genes and to increase our understanding of the mechanism behind genetic and infectious diseases, including cancer.

Protein design

Tailor-made proteins

Enzymes can now be adapted for different industrial processes. Researchers can exploit new strategies for developing pharmaceuticals. Attempts are being made by modifying plant proteins to develop strains which can utilize atmospheric carbon dioxide more efficiently during photosynthesis.

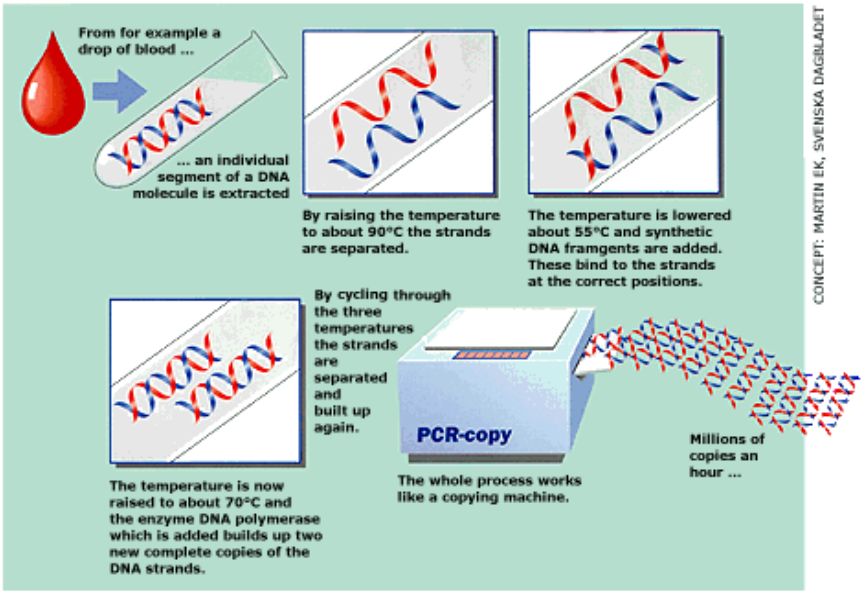


With **protein design**, it has for example been possible to improve the stability of an enzyme which is an important component of detergents, by specifically changing an amino acid (orange) close to the catalytic region (yellow). The enzyme can thereby survive the chemicals also needed to make our clothes clean.

Polymerase Chain Reaction

The PCR method – a copying machine for DNA molecules

DNA molecules can be mass-produced from incredibly small amounts of material with PCR. **Kary Mullis**' discovery allows the chemist to mimic the cell's own natural DNA replication process in a test tube. It has now become much easier to characterise and compare the genetic material from different individuals and organisms.



The PCR method already of great use

In Mullis's method, gene technology has gained a new tool. The sequencing of DNA, for example in the HUGO (Human Genome Organization) project, which aims to determine each individual DNA code in the human genetic material, has been dramatically simplified. There are already many medical applications. Since very small quantities of foreign DNA can be detected, the diagnosis and analysis of, for example, viruses (such as HIV) in clinical samples can be done very rapidly.

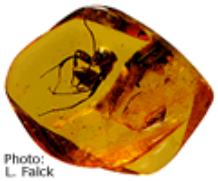
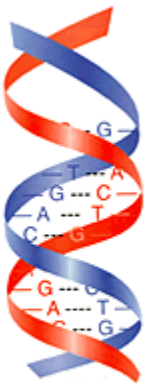


Photo:
L. Falck

DNA from fossil remains can be mass-produced by PCR. Researchers have succeeded in amplifying genetic material from insects trapped in amber that have been extinct for more than 20 million years.

In PCR the police have a new and very reliable fingerprinting method, since the DNA content can be analysed from a single drop of blood or a single hair found at the site of a crime.



The DNA molecule copies itself when cells divide. The double helix is then untwisted and forms two single strands which can be duplicated with the help of the enzyme DNA polymerase. Since A on one strand always corresponds to T on the other and G corresponds to C, two identical new DNA molecules are formed. If there is a misprint of one letter, a mutation occurs which is most often deleterious to the cell.

DNA and the genetic code

The blueprint of life is programmed into the genetic material and would, for a human being, fill at least a million typed pages. What kind of molecule is it that can store so much information inside each and every living cell, even though the cell is often not more than a hundredth of a millimetre across?

We know that DNA (deoxyribonucleic acid) is the carrier of our hereditary characteristics and that it is based on two strands twisted about one another forming a double helix. The strands consist of alternating carbohydrate and phosphate molecules. On each carbohydrate sits one of the four nitrogenous molecules **A**denine, **C**ytosine, **G**uanine and **T**hymine. A DNA strand can thus be compared with a long sentence (sequence) of code words, where each word consists of three letters that can be combined in many different ways, e.g. CAG, ACT.

Each code word can be read by components inside the cell and translated into one of the twenty amino acids that build proteins. The three-dimensional structure, and hence the function, of the proteins is determined by the order in which the different amino acids are linked together according to the genetic code.

Proteins are the cell's most important tools. In function as enzymes they maintain all the reactions needed for supporting life.

Landmarks in the history of gene technology

1868	**F. Miescher**, Switzerland, first isolates nucleic acid from biological material.
1940	G. Beadle* and E. Tatum, USA, put forward the "one gene – one enzyme" hypothesis. (*1958)
1944	**O. Avery**, USA, shows that genetic material does not consist of proteins but of deoxyribonucleic acid (DNA).
1953	J. Watson*, USA, and F. Crick*, UK, show that the DNA molecule consists of a double helix, thus making one of the most important discoveries of this century. (*1962)
1956	A. Kornberg*, USA, discovers the enzyme DNA polymerase, which is needed for copying DNA. (*1959)
1957	A. Todd*, UK, receives the Nobel Prize in Chemistry for synthesis DNA's building blocks. Later G. Khorana and his coworkers in the USA develop these chemical methods further and, for the first time (1970), synthesise a biologically active gene.
1961-65	Work by M. Nirenberg*, **J. Matthei**, G. Khorana*, S. Ochoa and their co-workers in the USA leads to an understanding of the genetic code. (*1969)
1961-69	W. Arber*, Switzerland, D. Nathans* and H. Smith*, USA, discover restriction enzymes, which can cleave DNA molecules in a predetermined way and can hence function as important tools in gene technology. (*1978)
1972	P. Berg*, USA, lays the foundation of recombinant-DNA technology. (*1980)
1975-77	W. Gilbert*, USA, and F. Sanger*, UK, develop methods for determining the sequence of DNA. (*1980)
1978	**Michael Smith***, Canada, and his co-workers manage to induce a site-directed mutation in a bacteriophage DNA molecule.
1982	**Michael Smith*** together with **A. Fehrst** and **G. Winter**, UK, manages to produce large quantities of an enzyme in which, using site-directed mutagenesis, one pre-determined amino acid is exchanged for another. (*1993)
1985	The PCR method developed by **Kary B. Mullis***, USA, for mass-copying of DNA is presented for the first time. (*1993)

*Nobel Prize

Further reading

"The unusual origin of the polymerase chain reaction". Scientific American (1990). Vol. 262:4, 56-61.

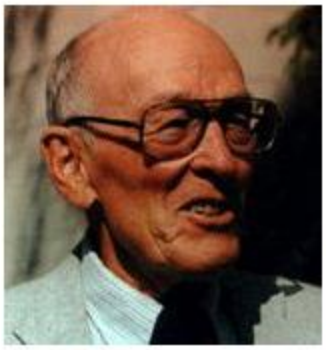
Current Opinion in Biotechnology – Protein Engineering (1993). Vol. 4.

The Royal Swedish Academy of Sciences, Information about the Nobel Prize in Chemistry, 1993 (press release).

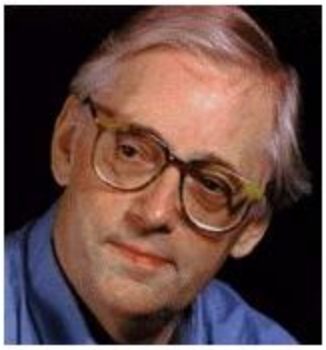
BACK

The Nobel Prize in Chemistry 1997

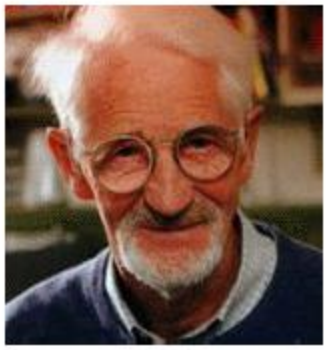
The Royal Swedish Academy of Sciences has awarded the 1997 Nobel Prize in Chemistry with one half to **Paul D. Boyer** and **John E. Walker** for their elucidation of the enzymatic mechanism underlying the synthesis of adenosine triphosphate (ATP); and with one half to **Jens C. Skou,** for the first discovery of an ion-transporting enzyme, Na^+, K^+-ATPase.



Paul D. Boyer
University of California
Los Angeles, U S A



John E. Walker
Medical Research Council
Laboratory of Molecular Biology
Cambridge, United Kingdom



Jens C. Skou
Aarhus University
Denmark

Life's energy currency, ATP

All living organisms, from bacteria, fungi, spinach and worms to crocodiles and humans, use ATP for energy conversion.

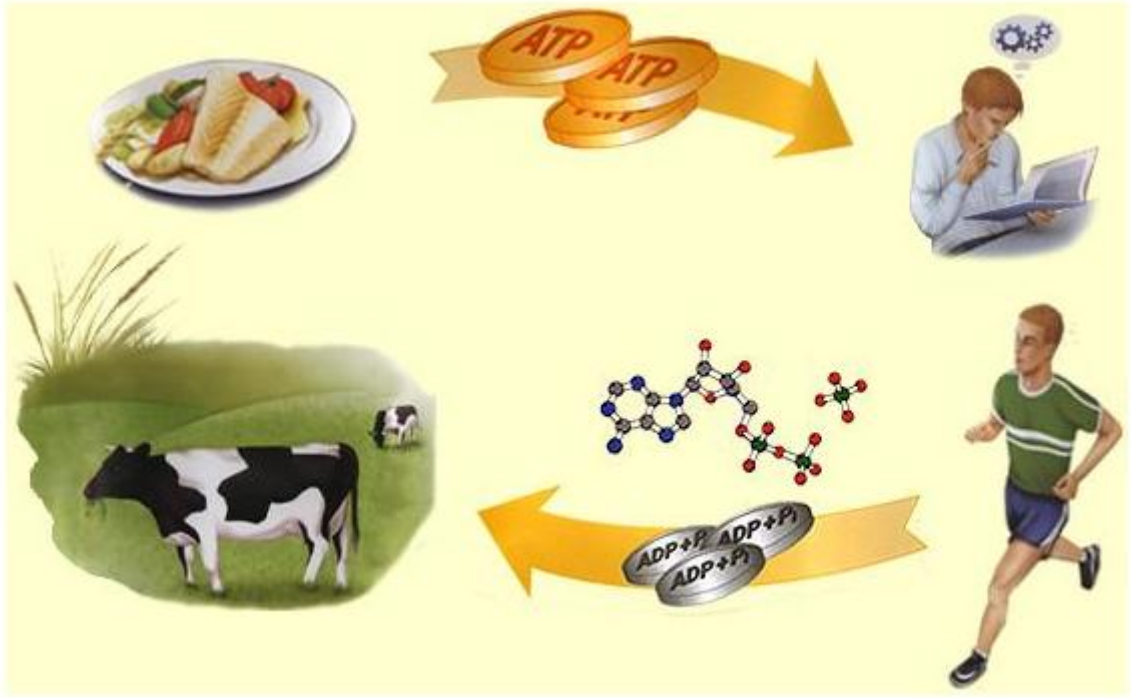
Originally, the energy comes from the sun.

Plants capture it during photosynthesis and convert it to chemical energy as ATP. Using this energy, plants produce carbohydrates, fats and proteins which are eaten by animals and human beings.

In metabolism, the food is broken down and the energy released is used to make ATP.

Energy is interconverted between various forms. Compare this with the idea of different currencies, only one of which is accepted at a time. ATP is an energy currency.

The universal energy transporter



Adenosine triphosphate (ATP) is built up of adenosine and three phosphate groups. The removal of the terminal phosphate group from ATP produces adenosine diphosphate (ADP).

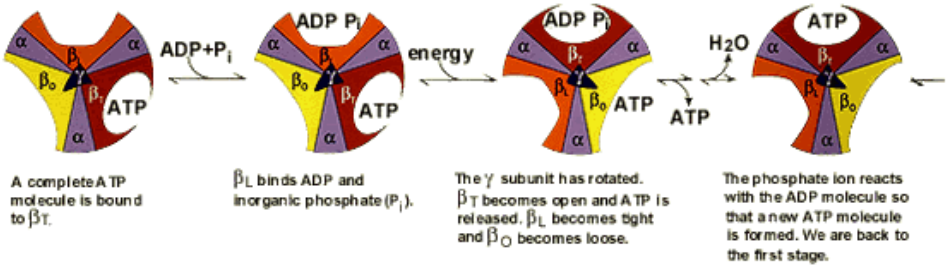
Every day an adult converts a quantity of ATP corresponding to at least half his or her body weight, and nearly a ton during a day of hard work.

Paul D. Boyer and **John E. Walker** have shown how the enzyme ATP synthase makes ATP. ATP synthase is found in chloroplast and mitochondrial membranes and in the cytoplasmic membrane of bacteria. A difference in hydrogen ion concentration across the membrane drives the enzyme to synthesise ATP.

"The Binding Change Mechanism"

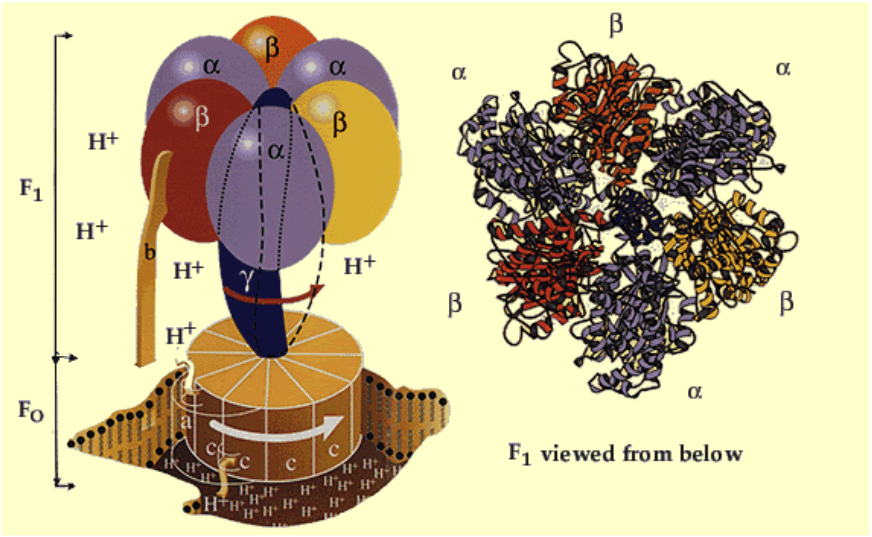
Using chemical methods Paul Boyer proposed that ATP synthase is like a cylinder with alternating alpha and beta subunits. An asymmetrical gamma subunit in the middle of the cylinder causes changes in the structure of the beta subunits when it rotates (100 r.p.s.). He termed these structures open ($beta_O$), loose ($beta_L$) and tight ($beta_T$).

Four stages in ATP synthesis



A molecular machine is discovered

John Walker crystallised the enzyme to study its details. He established that Boyer's proposal for how ATP synthesis takes place, the "molecular machine", was correct.



ATP synthase

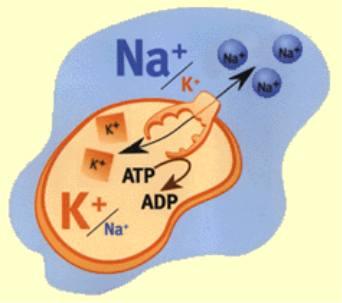
The enzyme consists of an F_O part bound in the membrane and a projecting F_1 part. The F_1 part is known in detail, while less is known about the F_O part.

The F_O part consists of three different protein molecules (subunits a, b and c). When hydrogen ions flow through the membrane via a disc of c subunits, the disc is compelled to rotate. The gamma subunit in the F_1 part is fixed to the disc and therefore rotates with it. The alpha and beta subunits in the F_1 part, however, cannot rotate because they are locked in a fixed position by the b subunit, which is anchored to subunit a in the membrane.

As the gamma subunit functions as an assymmetrical axle, the beta subunits are compelled to undergo the structural changes described in the figures above.

Jens C. Skou was the first to describe an ion pump - an enzyme that gives directed transport of ions through a cell membrane: a fundamental mechanism in every living cell. The existence of several similar ion pumps has since been demonstrated.

The first ion pump discovered



Ion composition outside the cell differs from that inside. When e.g. a nerve is stimulated Na^+ flows into the cell. The electrical potential arising across the membrane causes the nerve impulse to propagate itself along the nerve. The normal state is restored when Na^+ has been pumped out and K^+ pumped in.

Jens Skou discovered Na^+, K^+-ATPase - an enzyme that maintains the balance of sodium (Na^+) and potassium (K^+) ions in cells. Within cells, the concentration of Na^+ ions is lower, and that of K^+ ions higher, than in the surrounding fluid.

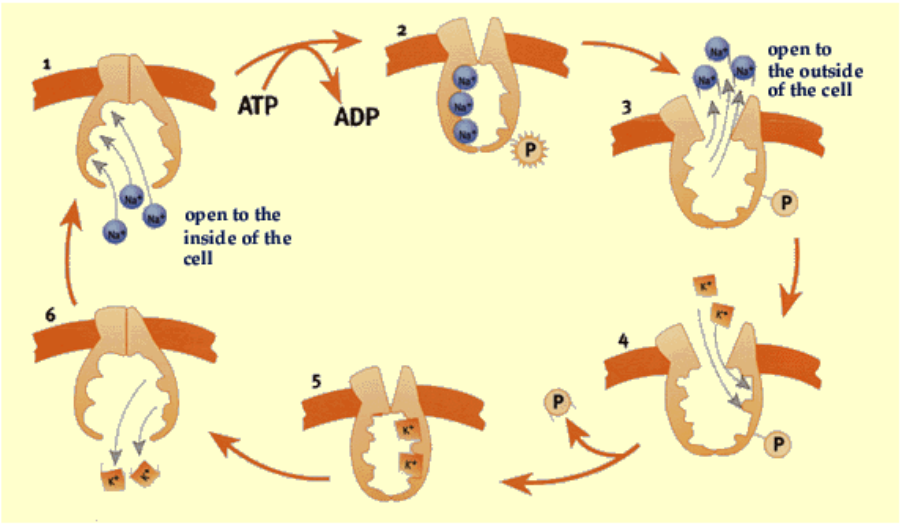
Na^+, K^+-ATPase and other ion pumps must work all the time in our body. If they were to stop, our cells would swell up, and might even burst, and we would rapidly lose consciousness. A great deal of energy is needed to drive ion pumps - in humans, about 1/3 of the ATP that the body produces.

Na^+, K^+-ATPase cycles between two states - open to the inside or the outside of the cell

The enzyme opens up towards the inside of the cell and exposes binding sites for three Na^+ ions.

When the ions are bound, an ATP molecule binds to the enzyme and one of its phosphate groups is transferred.

The enzyme changes shape, opening towards the outside and the Na^+ ions are released. Now binding sites for two K^+ ions are exposed.



When K^+ ions have been pumped into the cell the enzyme returns to its original state, ready to receive new Na^+ ions.

When the K^+ ions are bound, the phosphate group is released.

Ion pumps and pharmaceuticals

Ion pumps are affected by chemical substances. *Digitalis* plants contain a substance that inhibits Na^+, K^+-ATPase which results in an accumulation of sodium ions in cells. Used as a pharmaceutical, it causes reinforced heart muscle activity. Modern medicines against stomach ulcers suppress the activity of an ion pump that creates an acidic environment in the stomach.

History

ATP first discovered in 1929

ATP was first discovered by the German chemist Karl Lohmann. Its structure is established some years later. In 1948 Alexander Todd (UK) synthesises ATP chemically.

Vladimir Engelhart (Russia) notes in 1935 that muscle contractions require ATP. Between 1939 and 1941 Fritz Lipmann (USA) shows that ATP is the main bearer of chemical energy in the cell. He coins the phrase "energy-rich phosphate bonds".

ATP synthase

1937 - Herman Kalckar (Denmark) establishes that ATP synthase is linked with cell respiration.

1961 - The American Ephraim Racker isolates the F_1 part of the ATP synthase.

1961 - Peter Mitchell (UK) shows that cell respiration leads to differing concentrations of hydrogen ions (pH) inside and outside the mitochondrial membrane (the chemiosmotic hypothesis).

1964 - Paul D. Boyer proposes that ATP is synthesised through structural changes in the ATP synthase enzyme.

1973 - Boyer discovers that the step in ATP synthesis which requires energy is the release of ATP and the binding of ADP together with P_i ("The Binding Change Mechanism").

1981 - John E. Walker determines the DNA sequence of the genes encoding the proteins in ATP synthase.

1994 - The structure of the F_1 part of the ATP synthase is determined by Walker and co-workers.

1996-1997 - The hypothesis that parts of ATP synthase rotate during the synthesis and hydrolysis of ATP is demonstrated chemically (Richard Cross, USA), spectroscopically (Wolfgang Junge, Germany) and microscopically (Masasuke Yoshida, Japan).

The Na^+, K^+-ATPase ion pump

1950's - British researchers Richard Keynes and Alan Hodgkin note:

- that Na^+ flows into the cell upon nerve stimulation
- that Na^+ is probably transported out of the cell when ATP is consumed
- that Na^+ transport from the cell can be inhibited by inhibiting ATP synthesis.

1957 - Jens C. Skou finds an ATPase that is activated by sodium and potassium ions. This is the first ion pump to be discovered.

1961 → Other ion pumps requiring ATP are discovered.

BACK

The Nobel Prize in Chemistry 1998

The Royal Swedish Academy of Sciences has awarded the 1998 Nobel Prize in Chemistry in the area of quantum chemistry to **Walter Kohn** for his development of the density-functional theory and to **John A. Pople** for his development of computational methods for use in quantum chemistry.

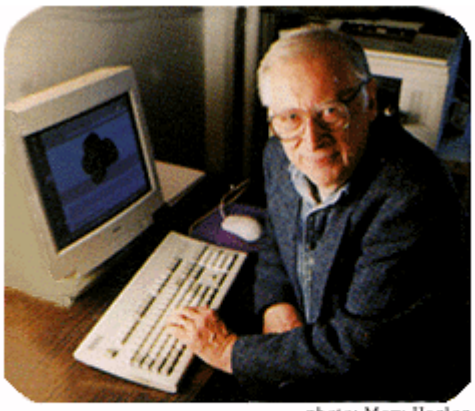


photo: Mary Hanlon

John A Pople
Northwestern University, Evanston, Illinois, U S A

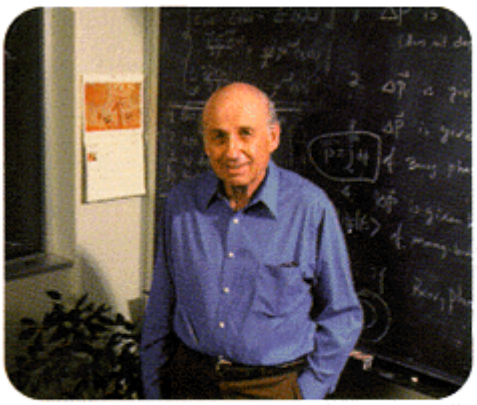


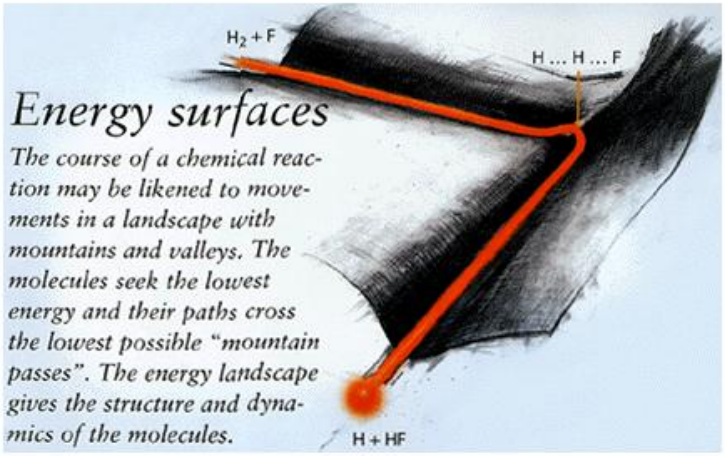
photo: Dave Folks

Walter Kohn
University of California at Santa Barbara, USA

Chemistry with computers $\hat{H}\Psi = E\Psi$

Chemistry is not only test tubes and chemicals. In quantum chemistry, quantum mechanics is used to *compute* the properties of molecules and their interaction. This year's laureates have made it possible to use the complex equations of quantum mechanics to study molecules and chemical processes with the help of computers.

$H_2 \rightarrow H + HF$

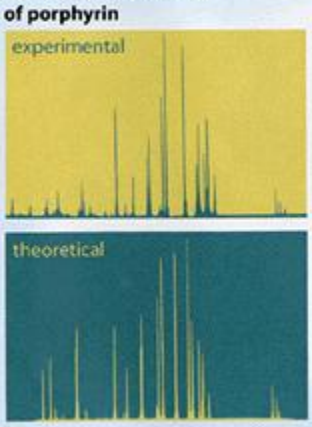


Energy surfaces

The course of a chemical reaction may be likened to movements in a landscape with mountains and valleys. The molecules seek the lowest energy and their paths cross the lowest possible "mountain passes". The energy landscape gives the structure and dynamics of the molecules.

Spectra

The infrared spectrum of porphyrin

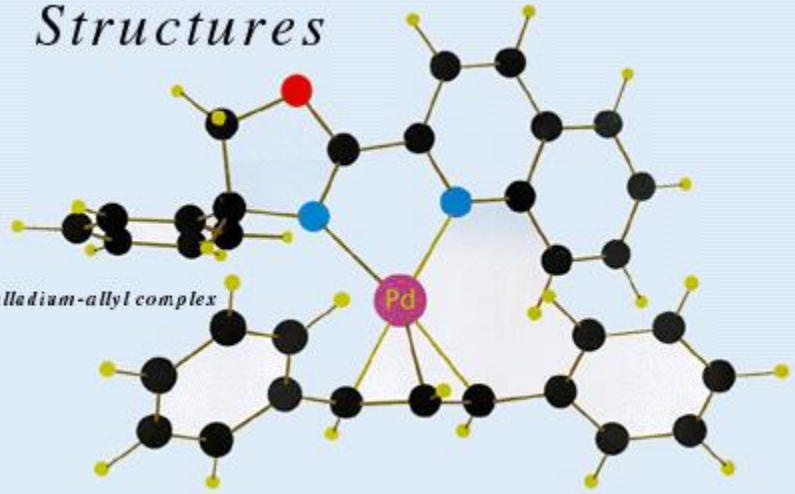


Porphyrin is part of, e.g., chlorophyll and haemoglobin.

The properties of molecules can be studied using different types of spectra. The experimentally measured spectrum of the porphyrin molecule may be interpreted on the basis of a spectrum computed with quantum chemistry.

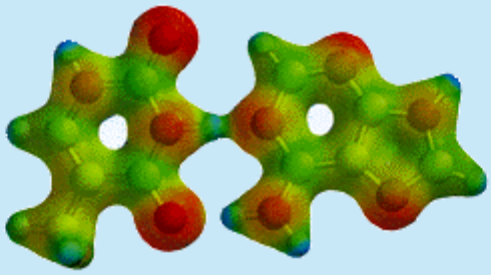
Structures

The three-dimensional structure of molecules can be accurately determined using quantum-chemical methods. One application of this is the development of new catalysts to generate very specific products such as drugs and plastics.



Palladium-allyl complex

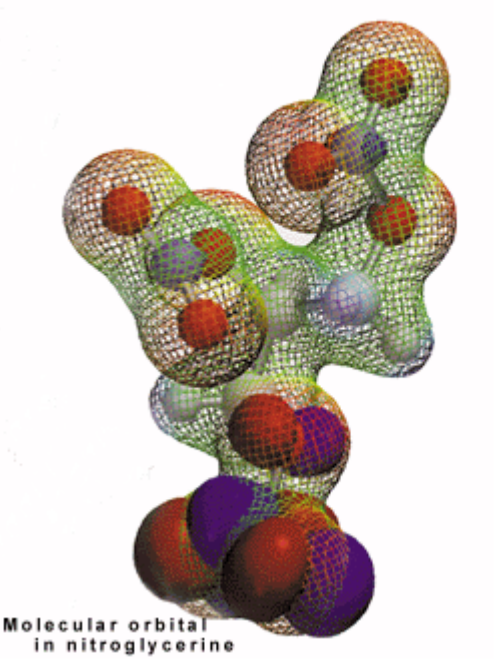
Charge distributions



Charge distributions in molecules can be computed with quantum-chemical methods. Excess of electrons (red in the illustration) in one molecule is drawn to a more positively charged portion of another molecule (blue). In this way the base pairs bind DNA together.

Wave-function methods

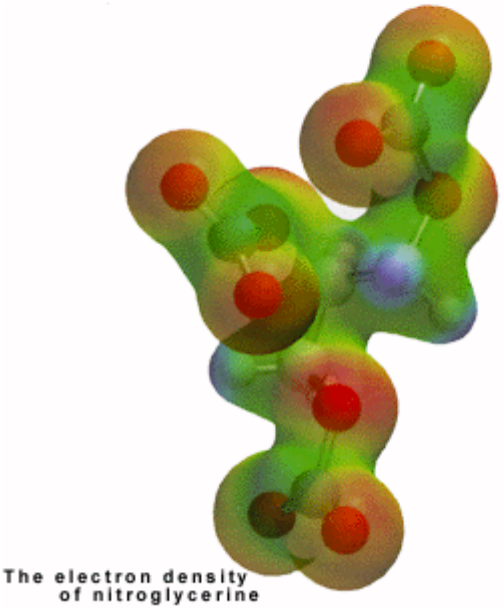
John A. Pople has developed computational methods in chemistry. These are based on different descriptions of the wave function in the Schrödinger equation. He has created a theoretical model chemistry in which a series of increasingly refined approximations systematically approaches the exact solution to the quantum-mechanical equations. In this way it has become possible to control the accuracy of the calculations. The methods were made available to researchers through the GAUSSIAN computer program, today used for quantum-chemical computation within all areas of chemistry.



Molecular orbital in nitroglycerine

Density methods

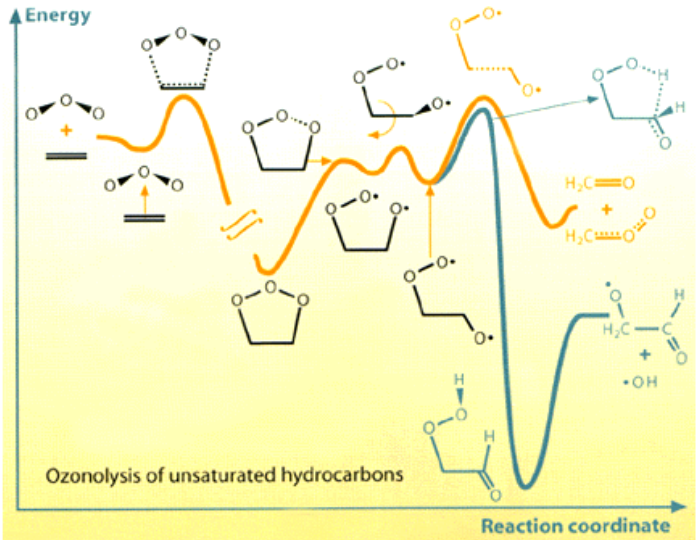
Walter Kohn showed in 1964-65 that the energy of a quantum-mechanical system is uniquely determined by its electron density. This quantity is more easily handled than the complicated wave function in the Schrödinger equation. Kohn also provided a method which made it possible to set up equations whose solutions give the system's electron density and energy. This method, called density functional theory, has become widely used in chemistry since, because of its simplicity, it can be applied to fairly large molecules.



The electron density of nitroglycerine

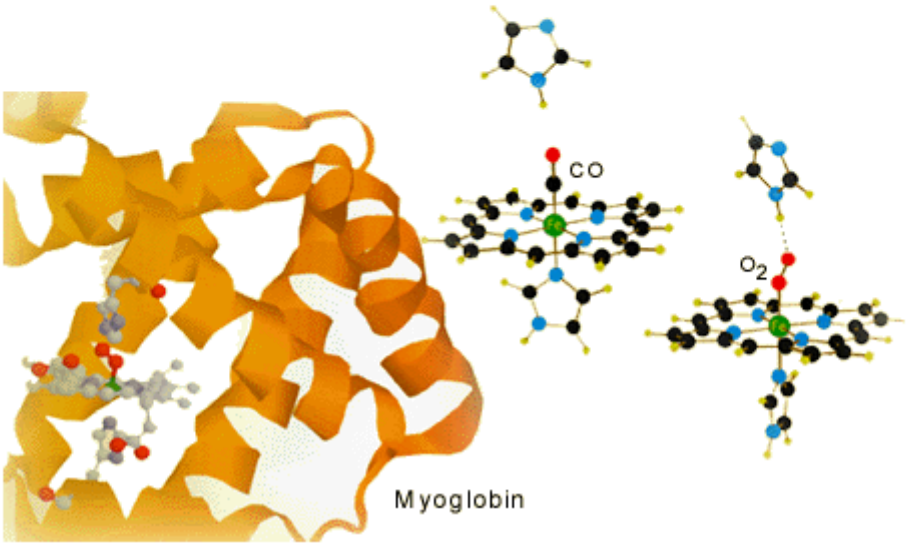
Applications in organic chemistry...

The mechanisms of chemical reactions can be studied with quantum-chemical methods. The Schrödinger equation gives an energy for each molecular structure. The energy curve for a given reaction path, which passes through different intermediate states (minima) and transition states (maxima), shows whether that particular mechanism is possible. The diagram shows possible mechanisms for how ozone, O_3, may react with unsaturated hydrocarbons so that dangerous free radicals are formed.



... and in biochemistry

By selecting a limited number of atoms (20-60) from the active site of an enzyme, bonding and reaction mechanisms can be studied with quantum-chemcial methods. The surrounding protein is described with simpler methods. The model below shows a possible mechanism of how myoglobin in muscles protects itself agains carbon monoxide poisoning. Using hydrogen bonding to one of the amino acids in the protein, oxygen can overcome the competition from the dangerous carbon monoxide.



Further reading

Information on the 1998 Nobel Prize in Chemistry (press release), The Royal Swedish Academy of Sciences

Theoretical Chemistry Expands and Diversifies Across Chemical Disciplines, by E.K. Wilson, *Chemical & Engineering News, August 19, 1996*

Computational Chemistry Impact, by J.H. Krieger, *Chemical and Engineering News*, May 12, 1997

Ab Initio Molecular Orbital Theory, by W.H. Hehre, L. Radom, P.v.R. Schleyer and J.A. Pople, *John Wiley & Sons, New York, 1986*

Density-Functional Theory of Atoms and Molecules, by R.G. Parr and W. Yang, *Oxford Science, Oxford, 1989*

Encyclopedia of Computational Chemistry (ed. Paul v. R. Schleyer), *John Wiley & Sons, New York, 1998*

The Nobel Prize in Chemistry 1999

BACK

The Royal Swedish Academy of Sciences has awarded the 1999 Nobel Prize in Chemistry to Professor Ahmed H. Zewail for his studies of transition states of chemical reactions by femtosecond spectroscopy.

Zewail – King of Femtoland

Ahmed H. Zewail was born near Alexandria in Egypt. He has now been working for many years at Caltech, Pasadena, USA, where he directs a large Laser Femtochemistry laboratory, called Femtoland. He is also Director of the Laboratory for Molecular Sciences (LMS).

Ahmed Zewail receives the 1999 Nobel Prize in Chemistry for being the first to reveal the decisive moments of a chemical reaction – the moments when chemical bonds are broken and formed.

Zewail's technique uses what can be thought of as the world's fastest camera. The "shutter speed" of such a camera must be extremely high since molecules are very small (about 10^{-9}m) and move extremely rapidly (1 000 m/s). To obtain a sharp "image" of the molecules in the course of a chemical reaction requires a femtosecond (10^{-15}s) shutter speed.

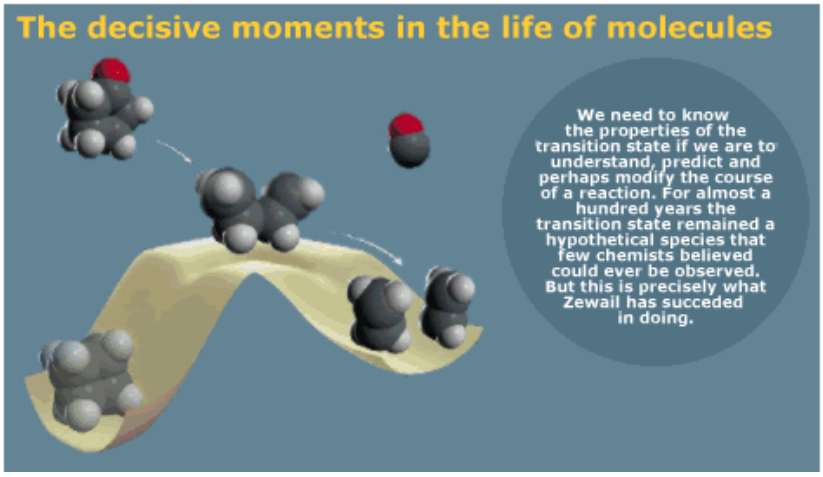
1 ms	1 millisecond = 0.001 s = 10^{-3} s
1 µs	1 microsecond = 0.000 001 s = 10^{-6} s
1 ns	1 nanosecond = 0.000 000 001 s = 10^{-9} s
1 ps	1 picosecond = 0.000 000 000 001 s = 10^{-12} s
1 fs	1 femtosecond = 0.000 000 000 000 001 s = 10^{-15} s

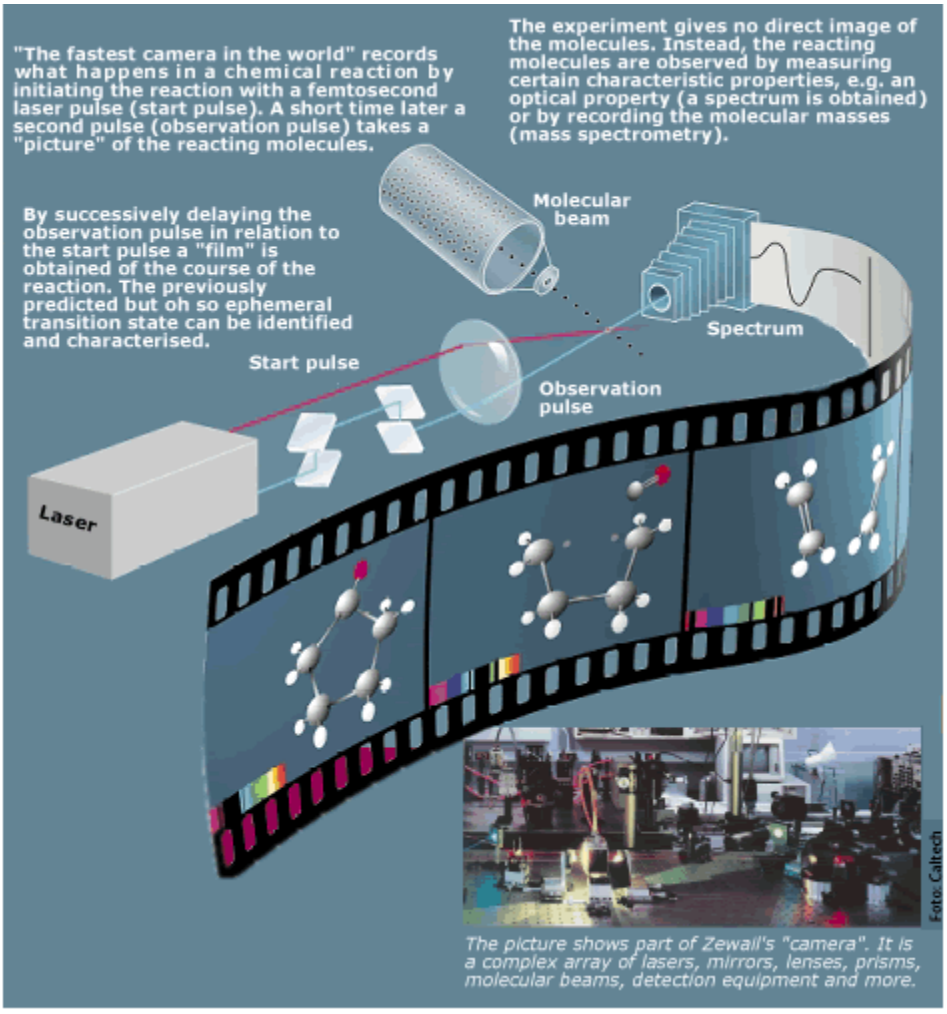
In one second light travels from the earth to the moon, while in one femtosecond it travels a fraction of a human hair's-breadth.

A chemical reaction - up hill and down dale

Like everything in nature, molecules strive to reach the lowest possible energy state. This makes it practical to describe reactions using energy surfaces. A molecule on an energy surface tries, like a child in a water-slide, to reach the lowest point. You need enough speed (high energy) to get up over the crest.

The picture below shows the ring opening of a cyclo-butane molecule to form two ethylene molecules. Zewail studied this reaction by exciting cyclopentanone molecules with a femtosecond pulse. He could show that this reaction occurs via a transition state living a few hundred femtoseconds. This experiment settled an old argument over whether the reaction takes place in one step with simultaneous breaking of both bonds or in two steps, one bond breaking before the other.

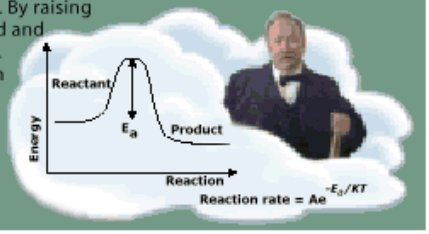




In 1878 the photographer Muybridge was able to capture movement with the fastest camera of the time. His series of pictures once settled a $ 25 000 bet. The wager was about whether a galloping horse at any time has all four hooves off the ground.

The Arrhenius Legacy

The Swedish chemist Svante Arrhenius (Nobel Prize 1903) was interested in how the rate of a chemical reaction varies with temperature. He concluded that there must exist an intermediate in the transformation from reactants to products. Later, this intermediate came to be known as the *transition state*. Imagine this state as the highest point on an energy surface, the crest of a hill over which the reacting molecules must pass to form products. By raising the temperature, more energy is added and more molecules can get over the crest. Arrhenius related the rate of a reaction to the height of the energy barrier (E_a) and to the temperature (T).



Towards ever-shorter times

1889	Arrhenius predicts the existence of transition states in chemical reactions.
1920s	Mixing experiments give information on the *milli*second time-scale.
1949	Flash photolysis is introduced and makes it possible to study chemical reactions without the reactants needing to be mixed. The method is based on the fact that light can initiate chemical reactions (photochemistry). The *micro*second time-scale is reached.
1960	The laser is invented and rapidly makes the *nano*- and *pico*second time-scales available. Milli- to picosecond time-scales give valuable information on chemical reactions, but direct molecular motion is still impossible to observe.
1987	Zewail's first *femto*chemistry experiments.
1999	Guinness Book of Records gives duration of shortest reported light pulse as 4.5 femtoseconds.

Towards the future with femtochemistry

Some research applications of femtochemistry:

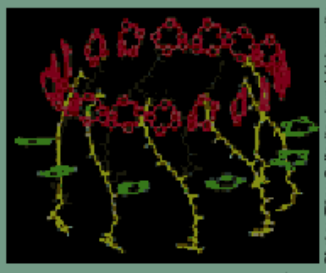


Photo: Tõnu Pullerits, Lund University

Photosynthetic pigment molecules for collection of the sun's light energy.

Biology
The processes of photosynthesis in which light energy is converted to chemical energy are being studied in detail with femtochemistry methods. Knowledge gained can be used for developing processes and materials for artificial photosynthesis.

Materials science
Future electronics will be based on light-driven processes since this allows faster components of greater capacities. Femto-chemistry methods are already being used to study materials for tomorrow's electronics.

Chemistry
Being able to control chemical reactions is the chemist's dream! Knowledge from femtochemistry experiments affords opportunities for doing this and can lead to chemicals with unique new properties.

Medicine
Femtochemistry methods can be used for studying photochemical reactions used in medicine, e.g. for photodynamic cancer therapy.

Further reading

Information of the 1999 Nobel Prize in Chemistry (press release): The Royal Swedish Academy of Sciences

The Femtoland web page: www.its.caltech.edu/~femto

The Birth of Molecules, A.H. Zewail, Scientific American, Vol. 262, Dec. 1990, pp.40-46

Laser Femtochemistry, A.H. Zewail, Science, Vol. 242 (1988), pp. 1645-1653

Femtochemistry: Recent progress in studies of Dynamics and Control of Reactions and their Transition States, A.H. Zewail, J. Phys. Chem. (Centennial Issue), Vol. 100 (1996) 12701-12

Femtochemistry: Ultrafast Dynamics of the Chemical Bond, Vol 1-2, A.H. Zewail. World Scientific 1994 pp.915, ISBN 9810219407

Femtosecond Chemistry, Vol 1-2, Eds. J. Manz, L. Wöste. VCH 1995 pp. 916, ISBN 3-527-29062-1

Femtochemistry and Femtobiology: Ultrafast Reaction Dynamics at Atomic-Scale Resolution, Nobel Symposium 101.Ed.V. Sundström.World Scientific, Singapore 1997. ISBN 1-86094-039-0

The World's Fastest Camera, V.K. Jain. The World and I, October 1995, pp. 156-163

Freezing Time - in a Femtosecond, J.S. Baskin and A.H. Zewail, Science Spectra, Issue 14 (1998) pp. 62-71

Ten years of Femtochemistry: Time Resolution of Physical, Chemical and Biological Dynamics, A.W. Castleman and V. Sundström (eds.), J. Phys. Chem. - Special Issue (1998), pp. 4021.

BACK

The Nobel Prize in Chemistry 2000

The Royal Swedish Academy of Sciences has awarded the Nobel Prize in Chemistry for 2000 jointly to **Alan J. Heeger, Alan G. MacDiarmid** and **Hideki Shirakawa** "for the discovery and development of conductive polymers".

Alan G. MacDiarmid
Professor at the University of Pennsylvania, Philadelphia, USA.

Hideki Shirakawa
Professor Emeritus, University of Tsukuba, Japan.

Alan J. Heeger
Professor at the University of California at Santa Barbara, USA.

Electrically conductive plastic

Alan Heeger, Alan MacDiarmid and Hideki Shirakawa have been awarded the Nobel Prize in Chemistry for showing how plastic can be made to conduct electric current. This surprising discovery has radically altered our view of plastic as a material. Conductive polymers today constitute a growing research field of great significance to chemists and physicists alike.

Plastics that imitate metals

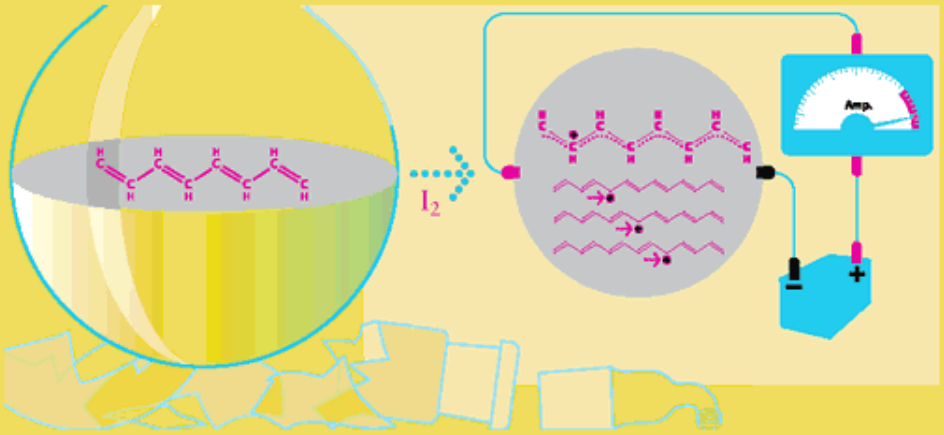
Plastics are *polymers*, molecules formed of many identical units bound to each other like pearls in a necklace. For a polymer to be electrically conductive it must "imitate" a metal – the electrons in the bonds must be freely mobile and not bound fast to the atoms. One condition for this is that the polymer consists of alternate single and double bonds, termed conjugated double bonds. *Polyacetylene* is the simplest possible conjugated polymer. It is obtained by polymerisation of acetylene, shown to the left.

A surprise with a silver lining…

At the beginning of the 1970s Shirakawa was studying the polymerisation of acetylene. In his reaction vessel polyacetylene appeared in the form of an unremarkable black powder. On one occasion a visiting researcher accidentally added *one thousand times* more catalyst than usual. Imagine the researchers' surprise when a beautiful silvery film formed on the surface of the liquid in the vessel. The obvious question was: "If the plastic film shines like a metal, can it conduct electricity, too?"

… and a Nobel medal in gold

Although the polyacetylene film shone like silver, it was not an electrical conductor. Could it perhaps be modified in some way? In the mid-1970s the three Laureates began co-operating to investigate this and results were quick to come. When they caused the films to react with iodine vapour, the conductivity increased by as much as ten million times – a discovery that was eventually to give them a Nobel Prize in Chemistry.

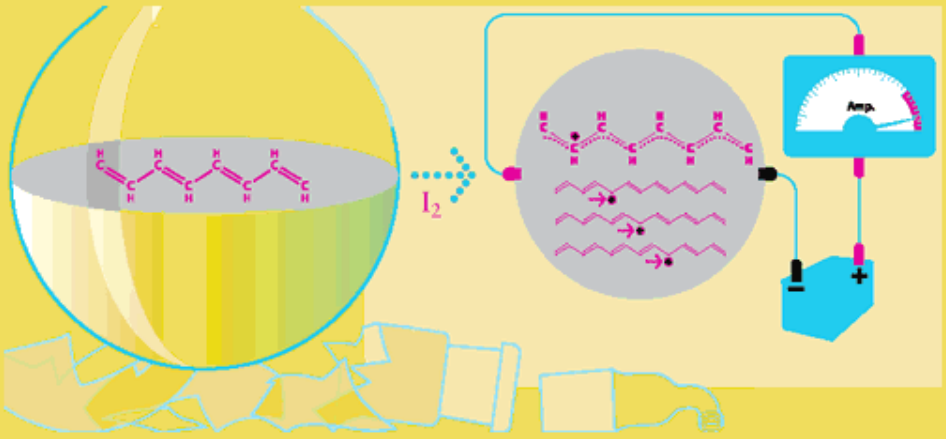


Oxidation with iodine causes the electrons to be jerked out of the polymer, leaving "holes" in the form of positive charges that can move along the chain.

Doping raises molecule performance

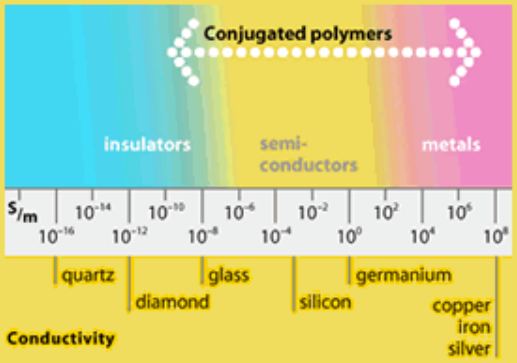
By analogy with semiconductor technology one speaks of *doping* the polymer when it is subjected to oxidation with iodine vapour. The more electrons are removed, the higher the degree of doping and the greater the conductivity.

While polyacetylene can be persuaded to conduct current as well as many metals do, this material is unfortunately no good for practical use. Its conductivity drops rapidly in contact with air. This has led to the development of more stable, conjugated polymers, e.g. polypyrrol, polyaniline and polytiophene.



Brilliant applications

The exciting idea of combining the mouldability and low weight of plastics with the conductivity of metals has prompted intensive development. Since the conductivity can be varied over a very broad area, from poor semi-conductors to metallic-level conductivity, many commercial uses present themselves. Batteries, condensers, anti-static materials and anti-corrosion substances are some examples.



Light-emitting diodes

Just now the most intensive development is aimed at conjugated polymers in their un-doped, semiconductive state. This is because it was discovered ten years ago that some conjugated polymers exhibit electro-luminescence, they glow when a voltages passes through them.

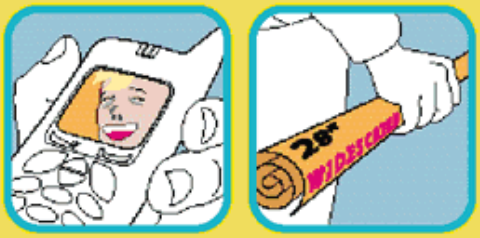
Many applications are predicted for luminescent plastic. We shall soon be seeing the first practical use in light displays in mobile telephones and on information boards. In a few years flat TV screens in luminescent plastic may have become a reality.

By varying the molecular structure, light of different colours can be obtained.

Solar cells

The process giving rise to electro-luminescence can also be "run backwards". Absorption of light creates positive and negative charges that are picked up by the electrodes, providing an electric current. This is the principle of the solar cell.

The advantage of plastic is that large, flexible surfaces can be made relatively easily and cheaply. Solar cell plastic could be spread out over large areas and give us environmental friendly electricity in the not-too-distant future.



Further reading

Information on the Nobel Prize in Chemistry 2000 (press release, information for the public, advanced information, suggested web links to institutions and companies etc), The Royal Swedish Academy of Sciences

Conductive Polymers – Information (advanced) on the Nobel Prize 2000, The Royal Swedish Academy of Sciences

Conductive Polymers, M.G.Kanatzidis, *Chem. Eng. News 3, p. 36, 1990.*

Plastic Electronics, D. de Leeuw, *Physics World, p. 31, March 1999.*

How far will circuits shrink?, R.E. Gleason, *Science Spectra 20, 2000,* p. 32.

The Nobel Prize in Chemistry 2001 BACK

The prize is being awarded to


William S. Knowles


Ryoji Noyori


K. Barry Sharpless

Photos: PRB

This year's Nobel Prize in Chemistry is about molecules that exist in two forms that are mirror images of each other. Often it is important to produce only one of these forms because the molecules, despite being so similar, have quite different functions, in our cells, for example.

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry for 2001 for the development of catalytic asymmetric synthesis, with one half jointly to William S. Knowles and Ryoji Noyori "for their work on chirally catalysed hydrogenation reactions" and the other half to K. Barry Sharpless "for his work on chirally catalysed oxidation reactions".

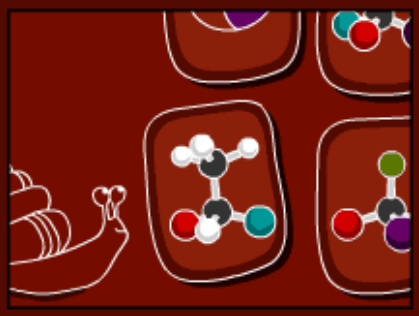
Contents:

Based on materials from the 2001 Nobel Poster for Chemistry

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

The Nobel Prize in Chemistry 2001 BACK

Nature is chiral



Play a game about chiral pairs GO

You need **Flash 5** to play the game.

The word chiral derives from the Greek word ceir (cheir), meaning hand. Our hands are chiral - the right hand is a mirror image of the left - as are most of life's molecules such as (R)-alanine and (S)-alanine, which are mirror images of each other.

In our cells we find only one form of this amino acid, (S)-alanine. The same is true for enzymes, antibodies, hormones and DNA.

Contents:

Based on materials from the 2001 Nobel Poster for Chemistry.

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

What is catalytic asymmetric synthesis?

(*R*)-alanine
R refers to the Latin word rectus, meaning right.

(*S*)-alanine
S refers to the Latin word sinister, meaning left.

When alanine is produced in a laboratory under normal conditions, a mixture is obtained, half of which consists of (*R*)-alanine and half of (*S*)-alanine.

In an *asymmetric synthesis* an *excess* of one of these forms is produced. To achieve this, in a *catalytic* way - that is, with the aid of a molecule that speeds up the reaction without being consumed itself - is what this year's Nobel Laureate's have accomplished.

Since the cells' actors are chiral, many pharmaceutical drugs also have to be chiral. Thus a flourishing pharmaceutical industry has grown up in the wake of the Laureates' achievements.

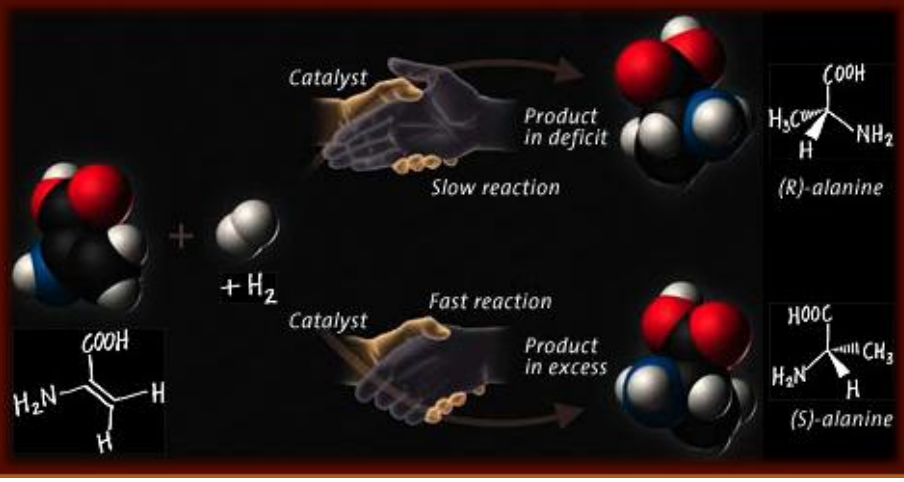
Based on materials from the 2001 Nobel Poster for Chemistry.

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

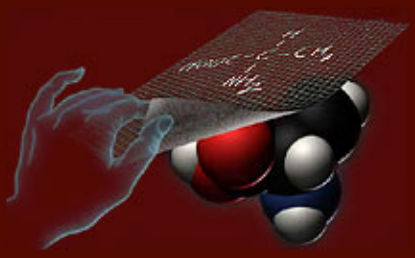
The Nobel Prize in Chemistry 2001 BACK

How does a chiral molecule function?

The substances used as the starting point for these syntheses are in general *not* chiral. The trick is to make the product chiral. This is done using a chiral catalyst molecule. Suppose we compare this molecule with a left hand. A left hand will make a better match in a handshake with another left hand (one of the two emerging product forms) than with a right hand (the other form of the product). Thus a chiral catalyst can control production of the desired chiral product.



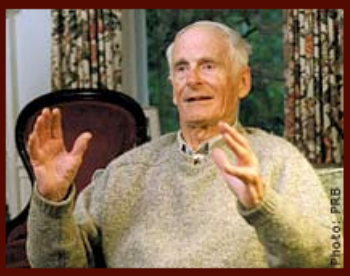
Chemistry becomes three-dimensional



This year's Nobel Prize has its roots in research carried out by the first Nobel Laureate in Chemistry, J. H. van 't Hoff. In 1874 he and J.-A. le Bel proposed the revolutionary hypothesis that molecules are three-dimensional and that they can therefore occur in two forms that are mirror images of each other. Their theory was considered ridiculous, because molecules were thought of as being two-dimensional at that time.

van 't Hoff (Nobel Prize 1901) was one of the first to realize that molecules are three-dimensional.

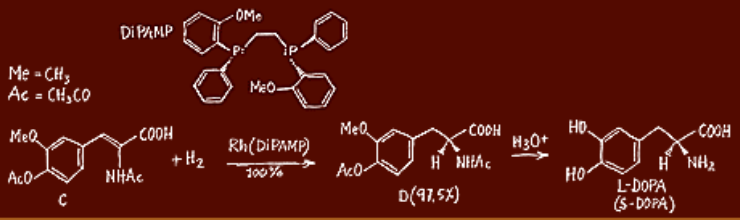
Pioneering work



William S. Knowles
St Louis, Missouri, USA

In 1968 **William S. Knowles** discovered that the metal rhodium can be used in a chiral molecule to catalyse asymmetric *hydrogenation reactions*. Hydrogenation is the addition of hydrogen atoms in H_2 to the carbon atoms in a double bond.

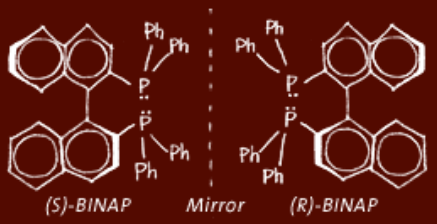
Knowles quickly developed an industrial synthesis of the amino acid L-DOPA, which has proved to be useful in the treatment of Parkinson's disease. This was the first industrial catalytic asymmetric synthesis. It has been followed by many others.



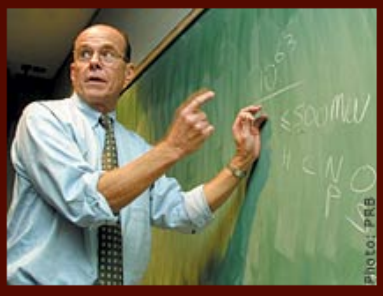
General hydrogenations

Ryoji Noyori
Nagoya University, Chikusa,
Nagoya, Japan

Ryoji Noyori realised the need for more selective catalysts with broader applications. Among the catalysts he has developed is Ru-BINAP, which is used for the synthesis of (*R*)-1,2-propandiol in the production of an antibiotic, levofloxacin. Noyori's catalysts are widely used for the synthesis of fine chemicals and pharmaceutical products as well as new advanced materials.

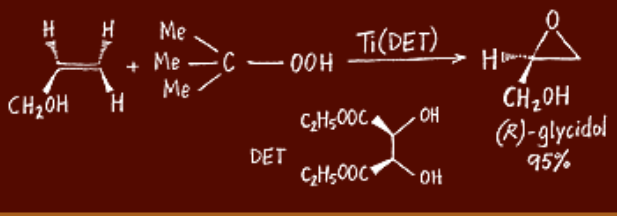


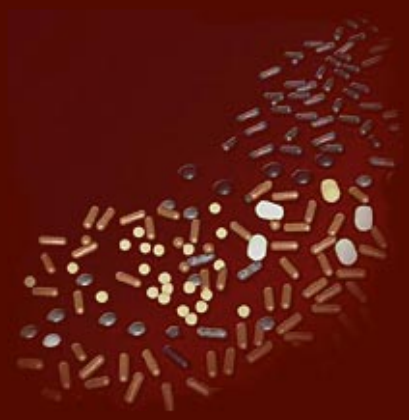
Chirally catalysed oxidations



K. Barry Sharpless
The Scripps Research Institute, La Jolla,
California, USA

Parallel with the advances in chirally catalysed hydrogenation reactions, **Barry Sharpless** has developed corresponding chiral catalysts for other important reactions, *oxidation reactions*. He has made several important discoveries, such as for chirally catalysed epoxidation, which utilises titanium in a chiral molecule. Epoxides are useful intermediate products for various types of synthesis, including the production of drugs for reducing blood pressure.





Further reading

Information on the Nobel Prize in Chemistry 2001, www.nobelprize.org/chemistry/laureates/2001/public.html

The Age of the Molecule, N. Hall, Ed., *Royal Society of Chemistry, London, 1999*

Classics in Total Synthesis, K.C. Nicolaou and E.J. Sorensen, *VCH, Weinheim, 1996*

Asymmetric Catalysis in Organic Synthesis, R. Noyori, *John Wiley and Sons, Inc., NY, 1994*

Stereochemistry of Organic Compounds, E.L. Eliel and S.H. Wilen, *John Wiley and Sons, Inc., NY, 1994*

The Nobel Prize in Chemistry 2002

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry for 2002 "for the development of methods for identification and structure analyses of biological macromolecules" with one half jointly to John B. Fenn and Koichi Tanaka "for their development of soft desorption ionisation methods for mass spectrometric analyses of biological macromolecules" and the other half to Kurt Wüthrich "for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution"

BACK

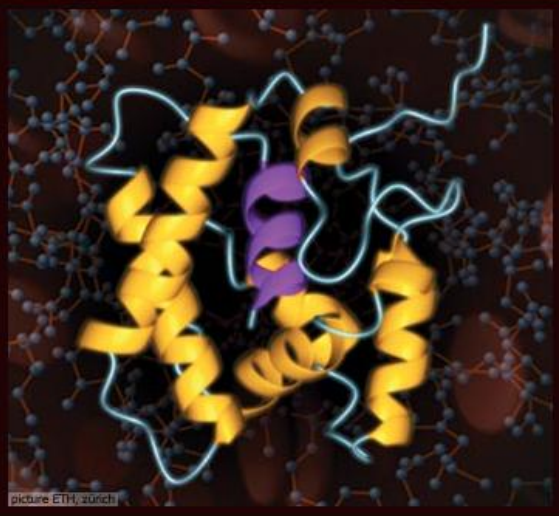
Proteins in close-up

Living cells consist of myriads of molecules. The large molecules, which include the proteins, interact with one another and with other molecules in a never-resting molecular machinery. How can we understand what is happening inside the cell? One important step is to develop tools to "see" with, and this is what this year's Nobel Laureates in Chemistry have done.


John B. Fenn


Koichi Tanaka


Kurt Wüthrich



Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

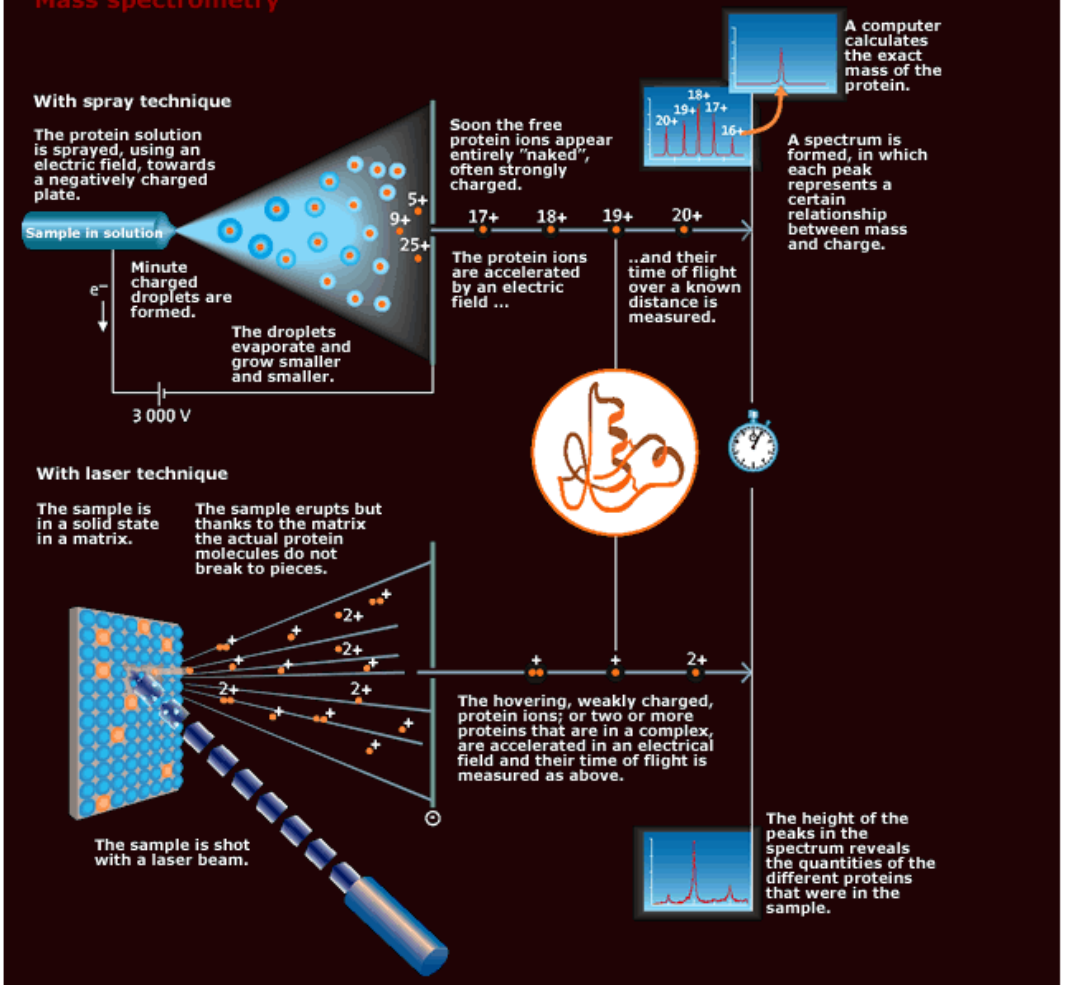
Mass spectrometry:
Of course proteins can fly!

With mass spectrometry we can now quickly identify a substance in a sample by accurately determining its molecular mass. Mass spectrometry is a very widely used method for small and medium-sized molecules. John B. Fenn and Koichi Tanaka showed, in different ways, that macromolecules could also be studied. The trick was to get the proteins to fly, or as John Fenn himself said, to give "wings to molecular elephants".

John B. Fenn is the chemist who invented the electrospray method. Today it is used in laboratories all over the world. Fenn has worked mainly as Professor of Chemistry at Yale University, USA, and at Virginia Commonwealth University, USA.

Koichi Tanaka worked as a research engineer at Shimadzu Corp. in Kyoto, Japan when he was telephoned by the Royal Swedish Academy of Sciences in Stockholm: you have been awarded the Nobel Prize! Tanaka's idea was to use the energy from laser light, ingeniously transferred to the proteins, to get them to let go of one another and hover freely. It worked!

Mass spectrometry



NMR:

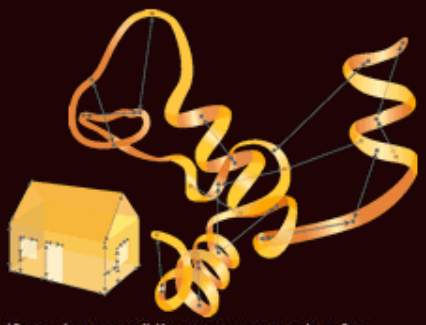
To understand, we need to see

With NMR the three-dimensional structure of different substances can be studied. Unlike the alternative method, X-ray crystallography, NMR can be applied to molecules in solution. This is a great advantage since the natural environment of the protein is the living cell.

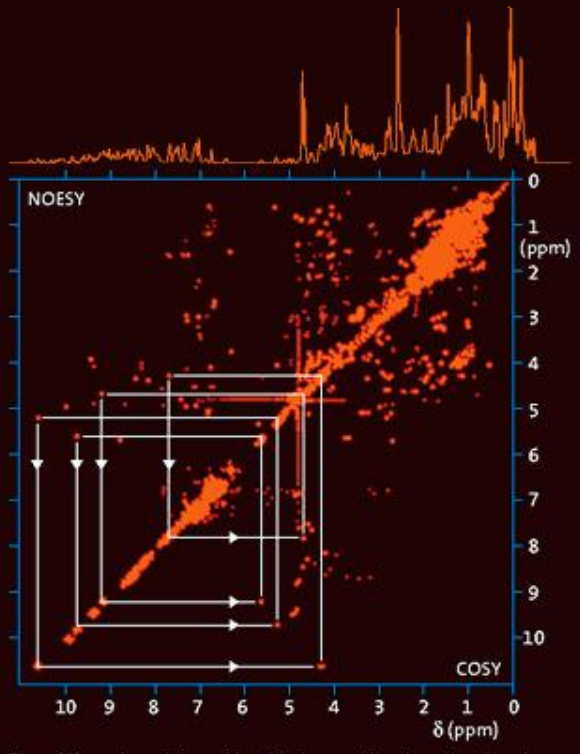
In NMR the sample is placed in a strong magnetic field. Pulses of radio waves are beamed into the sample, the atoms of which "answer" by emitting new radio waves. The result is a spectrum in which each atomic nucleus causes one or more peaks. This is because the magnetic field around each atom is affected by its neighbouring atoms. A large protein gives rise to a very complicated spectrum with numerous peaks.

Many peaks in the spectrum – no problem!

Kurt Wüthrich had an idea for how to find out which peaks correspond to which atoms. His method is called *sequential assignment*. It involves starting with a signal from a known atomic nucleus and then finding the nucleus in the peptide chain that is signalling that it is a neighbour of the first. Wüthrich matched each signal successively with its atom. With a similar method, which senses the distance between nuclei, he then determined a large number of pairwise distances in the protein, which gave the three-dimensional structure of that protein.



If one knows all the measurements of a house one can draw a three-dimensional picture of that house. In the same way, by measuring a vast number of short distances in a protein, it is possible to create a three-dimensional picture of that protein.



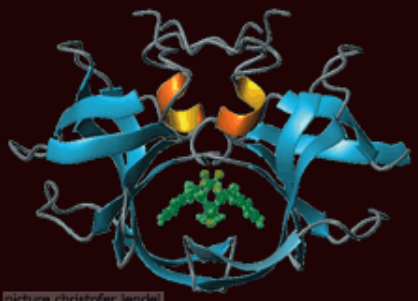
The different nuclei are identified one after the other in a two-dimensional NMR spectrum, here in a composite diagram in which one can navigate between 'cross-peaks' that signal atom proximity.

Kurt Wüthrich preparing a protein solution in an NMR tube. His measurement gives a three-dimensional picture of the protein structure in solution. Wüthrich works at ETH in Zürich, Switzerland and at the Scripps Research Institute, La Jolla, USA.

From early diagnosis to new medicines

Mass spectrometry and NMR have been around for a long time, but the ability to use them on molecules as large as proteins was something most scientists considered impossible. This year's Nobel prize Laureates showed that it could in fact be done! Their methods quickly turned out to be outstanding and have been further developed by other researchers to increase our understanding of the complicated life processes. To understand, we need to see - this year's Nobel prize has given us sharper sight.

Mass spectrometry has recently been reported as a successful method for early diagnosis of malaria. Different forms of cancer, such as breast, prostate and ovarian cancer, can also be discovered much earlier than with present-day methods.



picture christofer lendel

NMR is used in the pharmaceutical industry for determining the structure of proteins and other macromolecules that can be of interest as target molecules for new drugs. It is also possible to find out what small molecules bind to a given protein, thus making them into candidates for new drugs. The picture shows HIV protease with a molecule (in green) that blocks its function.

The Nobel Prize in Chemistry 2002 BACK

Further reading

Information on the Nobel Prize in Chemistry 2002: http://nobelprize.org

Mass Spectrometry:

Electrospray Ionization Mass Spectrometry by Richard B. Cole (ed.), John Wiley & Sons, Jan 15, 1997

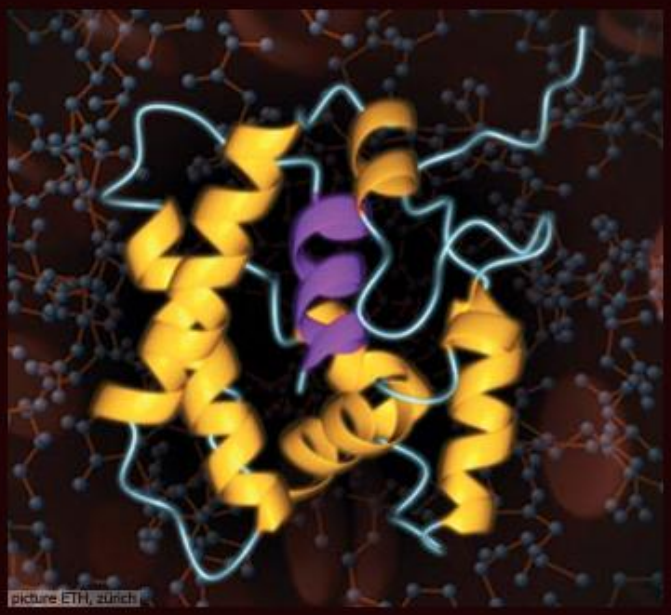
Mass Spectrometry of Proteins and Peptides. Methods in Molecular Biology by J.r. Chapman (ed.), Humana Press, 2000

NMR:

NMR of proteins and nucleic acids by K. Wüthrich and A. Wiley, Interscience publication, John Wiley & Sons, 1986

The way to NMR structures of proteins by K. Wüthrich, Nature Struct. Biol. 8 2001 p. 923-925

NMR in drug discovery by M. Pellacchia, D. Sem and K. Wüthrich, Nature Rev. Drug Discovery 1 2002 p. 211-219



picture ETH, zürich

The Nobel Prize in Chemistry 2003

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry for 2003 "for discoveries concerning channels in cell membranes", with one half of the prize to Peter Agre "for the discovery of water channels" and one half of the prize to Roderick MacKinnon "for structural and mechanistic studies of ion channels".

BACK

Unravelling the secrets of cell channels

Salt and water are important actors in the chemistry of life. Life on earth, and our own lives, originated in salt water – in the oceans and in the womb. Yet only fairly recently have we understood how water molecules and salt ions are transported in and out through the cell walls.

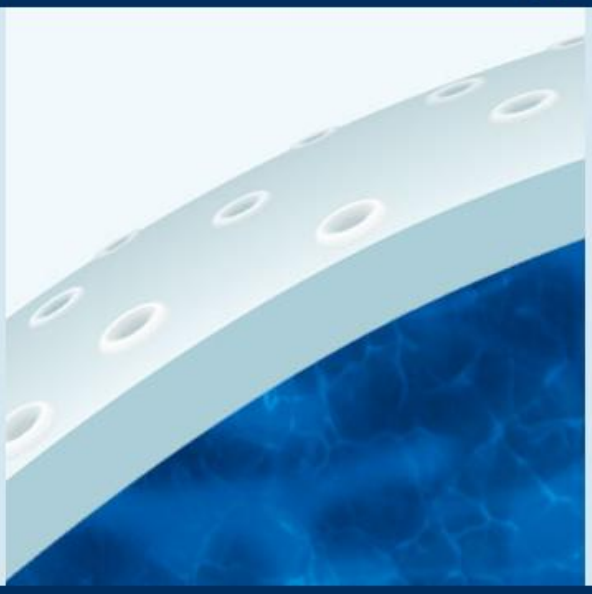


Photo: Keith Weller

Peter Agre

Photo: Arnold Adler
The Rockefeller University

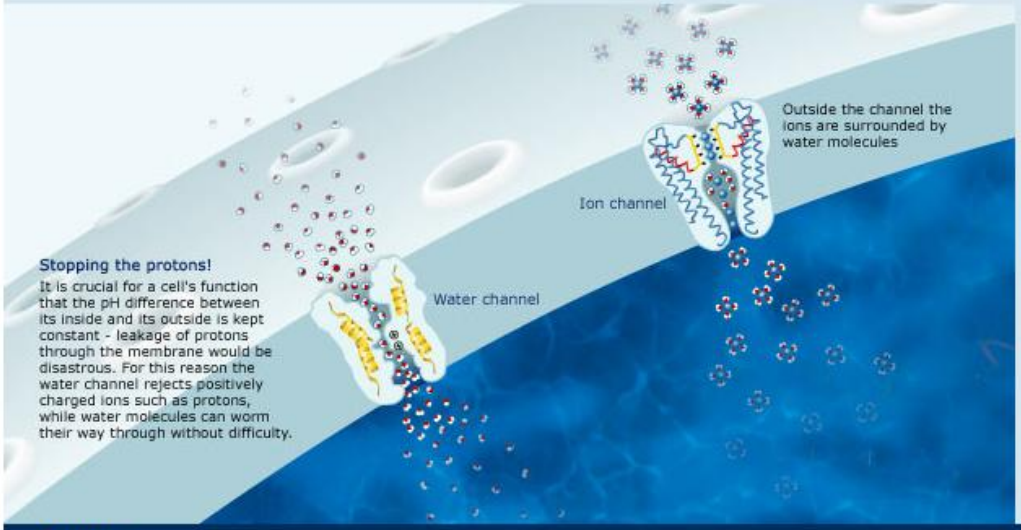
Roderick MacKinnon

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Nobelprize.org
The Official Web Site of the Nobel Prize

The cell's contact with the outer world

The wall that separates a cell from its surroundings - the membrane - is not an impermeable shell. It is pierced through by various sorts of channel. The channels consist of proteins, each with its own function.



Stopping the protons!
It is crucial for a cell's function that the pH difference between its inside and its outside is kept constant - leakage of protons through the membrane would be disastrous. For this reason the water channel rejects positively charged ions such as protons, while water molecules can worm their way through without difficulty.

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

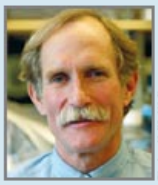
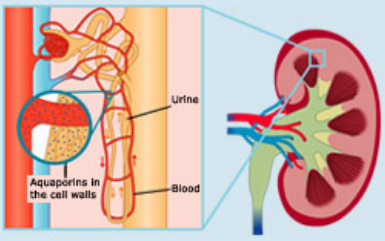


Photo: Keith Weller

Peter Agre
Peter Agre is Professor of Biological Chemistry and Professor of Medicine at Johns Hopkins School of Medicine in Baltimore, USA.

Water channels:
The cell leaks like a sieve

How does water actually pass through the cell membrane? The answer eluded researchers for over a hundred years. It was Peter Agre who finally unravelled the secret. By a happy chance he found the protein that is needed for water to pass in and out. He had discovered the elusive water channel.



The world's most efficient recycling plant

In twenty-four hours, the human kidney produces about 170 litres of primary urine. Fortunately most of this is recovered thanks to a series of cunning mechanisms so that finally only about one litre of urine leaves the body during this time. This recycling machinery consists chiefly of aquaporins - tens of thousands of millions in a single kidney.

The decisive experiment

In 1992 Peter Agre conducted an elegant experiment in which he kept, in water, frog oocytes into which he had introduced a membrane protein called CHIP28. After some minutes the cells containing the protein had swollen up, while the others were unaffected. Obviously, the CHIP28 protein was needed for the cell to be able to let water in - the first water channel was discovered. Agre renamed the protein aquaporin, "water pore". Eight years later and jointly with other research teams he presented the first high-resolution images of the three-dimensional structure of this protein.

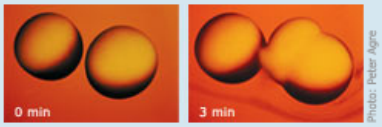


Photo: Peter Agre

Peter Agre's decisive experiment showed that only those cells that contain aquaporin (to the right in the pictures) can absorb water and swell up.

Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2003 BACK


Photo: Arnold Adler, The Rockefeller University

Roderick MacKinnon
Roderick MacKinnon is Professor of Molecular Neurobiology and Biophysics at The Rockefeller University in New York, USA.

Ion channels:
Tiny molecular machines

In 1998 Roderick MacKinnon for the first time determined at high resolution the structure of an ion channel. As so often in biochemistry, form and function are intimately connected. By showing what the protein looked like at the atomic level, he also realised how it functions.

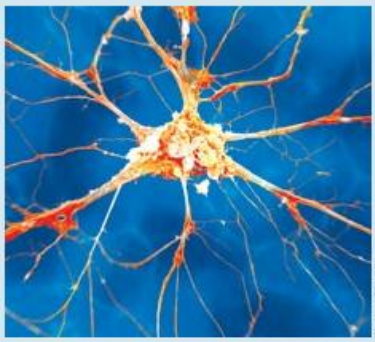
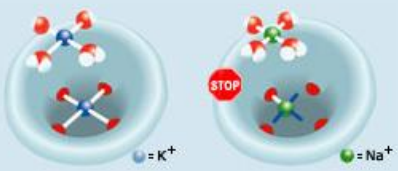


Photo: SPL/TBL

Ion channels play an important role in how nerves function. When for example a signal propagates itself from the brain to the muscles it is all about an interplay of chemical signals and ion currents in the nerve cells. The picture represents a nerve cell.

Only the potassium ions pass through

How can the channel let potassium ions pass but not, for example, sodium ions? The oxygen atoms in the ion filter form an environment which precisely mimics that of the potassium ion outside the filter where it is surrounded by water molecules. So the potassium ion can slip out of its "water coat" and pass through the filter without noticeable resistance.



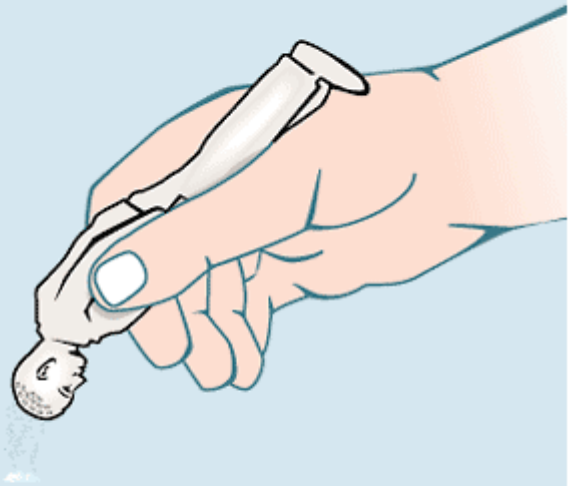
The sodium ion, which is smaller than the potassium ion, draws water molecules more closely to itself and is too small to fit snugly between the oxygen atoms in the ion filter. Sodium ions therefore remain in the water outside the channel.

The Nobel Prize in Chemistry 2003

BACK

Cells signal with salt!

As you read this brief text enormous numbers of ion channels are opening and closing in your brain, of the order of 1,000,000,000,000,000 (10^{15}). The amount of ions moving in the channels during this time would correspond to a pinch of salt. One wonders how much salt a good book would take.



Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2003

BACK

Earlier Nobel Laureates of great importance in the development leading up to this year's award:

1901 » 1909 » 1963 » 1991 » 1997 » 2003

1901 van't Hoff receives the Nobel Prize in Chemistry for his work on chemical thermodynamics and osmotic pressure.

1909 Ostwald receives the Nobel Prize in Chemistry. As early as 1890 he suggested that the electrical signals measured in living tissue could be caused by ion currents passing through the cell membrane.

1963 Eccles, Hodgkin and Huxley receive the Nobel Prize in Physiology or Medicine for their discoveries concerning ion mechanisms in nerve cell membranes.

1991 Neher and Sakmann awarded the Nobel Prize in Physiology or Medicine for their discoveries concerning the function of single ion channels in cells.

1997 Nobel Prize in Chemistry awarded to Boyer and Walker for explaining the function of the membrane protein that produces ATP, and to Skou for his discovery of the sodium-potassium pump.

2003 Agre and MacKinnon awarded this year's Nobel Prize for discoveries concerning channels in the cell membrane.

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Further Reading

Information on the Nobel Prize in Chemistry 2003

WATER CHANNELS

Appearance of water channels in Xenopus oocytes expressing red cell CHIP28 protein by G.M. Preston, T.P. Carroll, W.B. Guggino, and P. Agre, Science 256 (1992), p. 385-387

Molecular Mechanisms for Human Diseases by P. Agre and D. Kozono, FEBS Lett. 555 (2003), p. 72-78

ION CHANNELS

The structure of the potassium channel: Molecular basis of K+ conduction and selectivity by D.A. Doyle, J.M. Cabral, R.A. Pfuetzner, A. Kuo, J.M. Gulbis, S.L. Cohen, B.T. Chait and R. MacKinnon, Science 280 (1998), p. 69-77

Potassium Channels by R. MacKinnon, FEBS Lett. 555 (2003), p. 62-65

Contents:
| Introduction | The cell's contact | Water channels | Ion channels | Cells signal with salt | Timeline | **Further reading** | Credits |

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Proteins that are marked for hacking into small pieces

It has long been clear how proteins are built up in the cell. But the opposite, how they are broken down, was long thought to be less exciting to study. This year's Nobel Laureates, Aaron Ciechanover, Avram Hershko and Irwin Rose, went against the stream and, at the beginning of the 1980s, discovered one of the cell's most important control mechanisms, controlled protein degradation.

Irwin Rose
College of Medicine, University of California, Irvine, USA

Avram Hershko
Rappaport Institute, Technion – Israel Institute of Technology Haifa, Israel

Aaron Ciechanover
Rappaport Institute, Technion – Israel Institute of Technology Haifa, Israel

The discovery was made at the beginning of the 1980s at the Fox Chase Cancer Center in Philadelphia, USA, jointly by the three scientists.

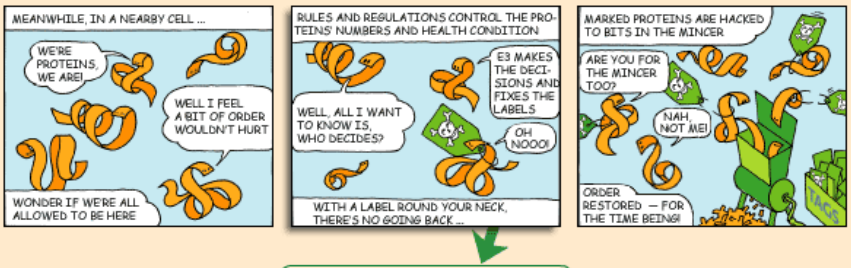
Contents:

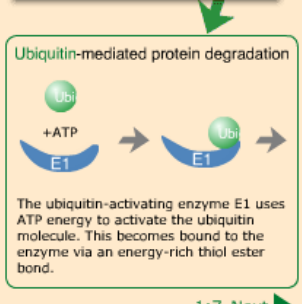
Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

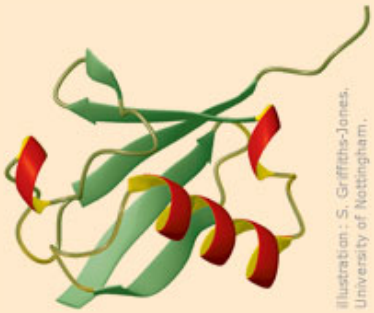
Nobelprize.org
The Official Web Site of the Nobel Prize

The Cell - a teeming mini-workshop

In the cell, proteins are being built up and broken down all the time. For everything to function optimally, the cell also has an integral checkpoint where the composition of various proteins is controlled. Unlike in the spontaneous protein breakdown that food undergoes in our intestines, breaking down proteins inside cells requires energy. This was long a research mystery. Thanks to this year's Nobel Laureates, however, we know that this form of breakdown is an extremely detailed control process in which the protein to be destroyed is marked with a special "label". This happens through a series of chemical reactions, as shown below.







Ubiquitin

This is what the actual label looks like. It consists of a short polypeptide chain, a small protein that is so common in the cells of different organisms that it was early named ubiquitin, from the Latin *ubique,* 'everywhere'. This protein is not broken down in the proteasome but can be used again and again.

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2004 BACK

Proteins are life's building-blocks

In the tiniest intestinal bacteria, in roses and toadstools, in mice and men - in all living cells - proteins answer for both form and function. Naturally, research into proteins is therefore of the greatest interest, particularly for chemists wishing to know how things function at molecular level.

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Copyright © Nobel Media AB 2011

What proteins are marked?

Surprisingly many of the proteins created in the cell are faulty from the start. They must be broken down and rebuilt since they can damage the organism. But perhaps the most important reason for a cell to get rid of a protein is that in this way the cell can control a given chemical reaction. By quickly destroying a protein that has a special function, the cell gets the same result as when one turns off a switch. When the proteins have been hacked to pieces, the cell can use their amino acids to synthesize other proteins. When protein degradation does not function correctly, we can become ill.

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2004 BACK

Prevents self-polination

Did you know that roses are bisexual? Most plants are like this - they're *hermaphrodites*. With such an arrangement, one wonders what prevents plants from fertilising themselves. In fact, ubiquitin-mediated protein breakdown is involved: the plant recognises and rejects its own pollen! The exact mechanism is not yet fully clear, but enzyme E3 has been found and when a proteasome inhibitor has been added, the rejection has been noticeably impaired.

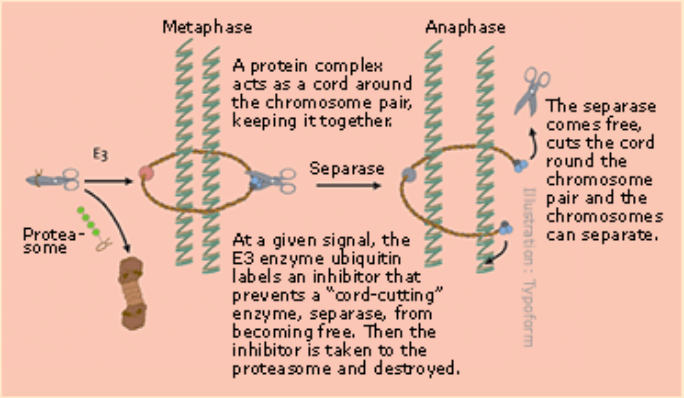
Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Copyright © Nobel Media AB 2011

The most common reason for miscarriage is an error when the mother's and the father's chromosomes are to be separated in the formation of sex cells. Ubiquitin-marking plays an important role here. The picture shows a calf embryo.

How are sex cells formed?

The formation of sex cells, *meiosis,* like normal cell separation, *mitosis,* has many points of contact with the subject of this year's Nobel Prize. A certain E3 enzyme is responsible, among other things, for separating the chromosomes.



Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2004 BACK

Further Reading

Information on the Nobel Prize in Chemistry 2004

Scientific American nr 1/2001

- The Road to the Proteasome
- The Ubiquitin System

Ciechanover et al. Proc. Natl. Acad. Sci. USA, 77, 1365-1368, 1980

Hershko et al. Proc. Natl. Acad. Sci. USA, 77, 1783-1786, 1980

Web Adapted Version of the Nobel Poster from the Royal Swedish Academy of Sciences

Copyright © Nobel Media AB 2011

Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2006

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry for 2006 to Roger D. Kornberg "for his studies of the molecular basis of eukaryotic transcription".

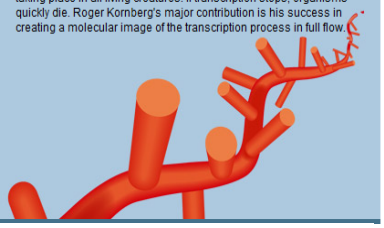
BACK

Roger D. Kornberg
Professor at Stanford University School of Medicine, USA. Born in 1947.

Roger Kornberg surrounded by some of his current co-workers shortly after the announcement of the award of the Nobel Prize in Chemistry for 2006. In his hands he is holding the model of RNA polymerase that resulted from his work.

The DNA-reader in our cells

Before our bodies can make use of the information stored in the genes, the relevant parts of the DNA-molecule must first be copied. The copy – messenger RNA – is used as a blueprint in creating the proteins that in their turn construct the structure and functions of the body. The copying process is called transcription and is continually taking place in all living creatures. If transcription stops, organisms quickly die. Roger Kornberg's major contribution is his success in creating a molecular image of the transcription process in full flow.



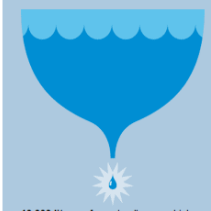
Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2006

BACK

Yeast and human beings

Eukaryotes are organisms whose cells have well-defined nuclei. All green plants, fungi and mammals belong to this group. Roger Kornberg has developed a system of using yeast fungi to study transcription. Yeast cells are similar enough to human cells for the results to apply to us as well.



10.000 litres of yeast culture – which corresponds to **150 kg** of yeast – was used to finally produce **2 g** of pure RNA-polymerase.

Contents:
| Introduction: The DNA-reader in our cells | **Yeast and human beings** | Taking pictures of molecules | The future | Timeline | Further reading | Credits |
Nobel Poster from the Royal Swedish Academy of Sciences, web adapted by Nobel Web

Nobelprize.org
The Official Web Site of the Nobel Prize

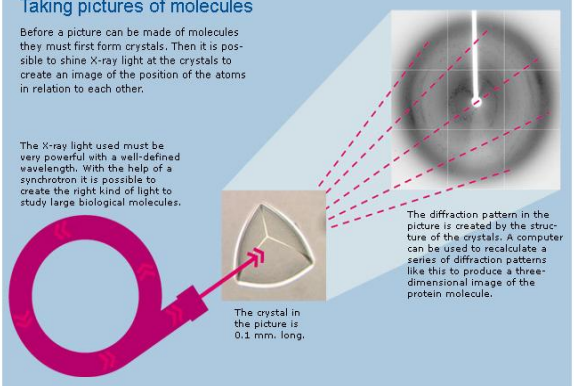
The Nobel Prize in Chemistry 2006

BACK

Taking pictures of molecules

Before a picture can be made of molecules they must first form crystals. Then it is possible to shine X-ray light at the crystals to create an image of the position of the atoms in relation to each other.

The X-ray light used must be very powerful with a well-defined wavelength. With the help of a synchrotron it is possible to create the right kind of light to study large biological molecules.



The diffraction pattern in the picture is created by the structure of the crystals. A computer can be used to recalculate a series of diffraction patterns like this to produce a three-dimensional image of the protein molecule.

The crystal in the picture is 0.1 mm. long.

Contents:
| Introduction: The DNA-reader in our cells | Yeast and human beings | **Taking pictures of molecules** | The future | Timeline | Further reading | Credits |
Nobel Poster from the Royal Swedish Academy of Sciences, web adapted by Nobel Web

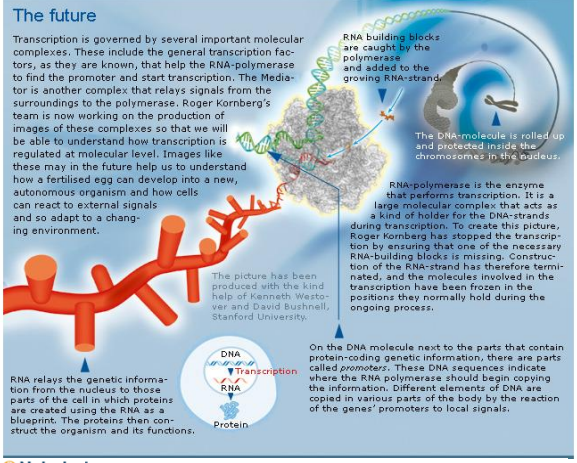
Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2006

BACK

The future

Transcription is governed by several important molecular complexes. These include the general transcription factors, as they are known, that help the RNA-polymerase to find the promoter and start transcription. The Mediator is another complex that relays signals from the surroundings to the polymerase. Roger Kornberg's team is now working on the production of images of these complexes so that we will be able to understand how transcription is regulated at molecular level. Images like these may in the future help us to understand how a fertilised egg can develop into a new, autonomous organism and how cells can react to external signals and so adapt to a changing environment.



Nobelprize.org
The Official Web Site of the Nobel Prize

The Nobel Prize in Chemistry 2006

BACK

1959 1962 1965 1968 1982 1993

1959 Ochoa and Kornberg awarded the Nobel Prize in Physiology or Medicine for the biological synthesis of RNA and DNA.

1962 Crick, Watson and Wilkins awarded the Nobel Prize in Physiology or Medicine for discovery of the double helix.

1965 Jacob, Lwoff and Monod awarded the Nobel Prize in Physiology or Medicine for genetic control of enzyme and virus synthesis.

1968 Khorana, Nirenberg and Holley awarded the Nobel Prize in Physiology or Medicine for the genetic code.

1982 Klug awarded the Nobel Prize in Chemistry for crystallographic electron microscopy of nucleic acid-protein complexes.

1993 Roberts and Sharp awarded the Nobel Prize in Physiology or Medicine for split genes.

Contents:
| Introduction: The DNA-reader in our cells | Yeast and human beings | Taking pictures of molecules | The future | **Timeline** | Further reading | Credits |
Nobel Poster from the Royal Swedish Academy of Sciences, web adapted by Nobel Web

The Nobel Prize in Chemistry 2006

BACK

Further reading

Scientific articles:

- Structural basis of transcription: An RNA polymerase II elongation complex at 3.3 Å resolution, by A. L. Gnatt, P. Cramer, J. Fu, D. A. Bushnell and R. D. Kornberg, *Science 292, p. 1876-1882 (2001)*
- Structural basis of transcription: An RNA polymerase II – TFIIB cocrystal at 4.5 angstroms, by D. A. Bushnell, K. D. Westover, R. E. Davis and R. D. Kornberg, *Science 303, p. 983-988 (2004)*
- Structural basis of eucaryotic gene transcription, by H. Boeger, D. A. Bushnell, R. Davis, J. Griesenbeck, Y. Lorch, J. S. Strattan, K. D. Westover and R. D. Kornberg, *FEBS Lett. 579, p. 899-903 (2005)*

Link:

- Animation of the transcription: The Dolan DNA learning center – genes in education (Media showcase, Transcription: DNA codes for mRNA, 3D animation) »

Contents:
| Introduction: The DNA-reader in our cells | Yeast and human beings | Taking pictures of molecules | The future | Timeline | **Further reading** | Credits |
Nobel Poster from the Royal Swedish Academy of Sciences, web adapted by Nobel Web

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry for 2007 to Gerhard Ertl "for his studies of chemical processes on solid surfaces".

BACK

Photo: Wolfram Däumel, Fritz-Haber-Institut der Max-Planck-Gesellschaft

Molecules on surfaces

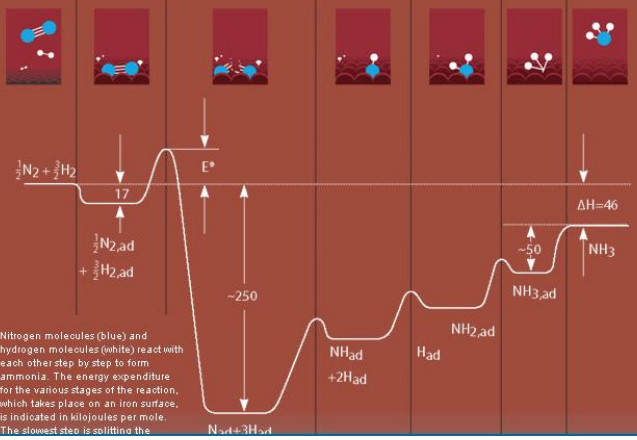
Chemical reactions on solid surfaces are very important in our everyday lives but difficult to study. Ever since the 1960s Gerhard Ertl has been using advanced vacuum techniques to make systematic studies of surface reactions which have enabled him to demonstrate methods of obtaining reliable results in this important and challenging research field.

Gerhard Ertl
Born in 1936 in Bad Cannstadt, Germany. PhD in Physical Chemistry in 1965 from Technische Universität München, Germany. Professor Emeritus, Fritz-Haber-Institut der Max-Planck-Gesellschaft, Berlin, Germany.

Ertl has laid the foundation of a scientific discipline through his enormously systematic and thorough studies. He has often returned to the same problem in surface chemistry decade after decade in order to use new experimental methods to obtain answers to questions posed earlier. His ability to describe in detail how an experiment is to be designed and interpreted has helped him to provide the methodological platform for an entirely new area of research.

Nitrogen becomes artificial fertilizer

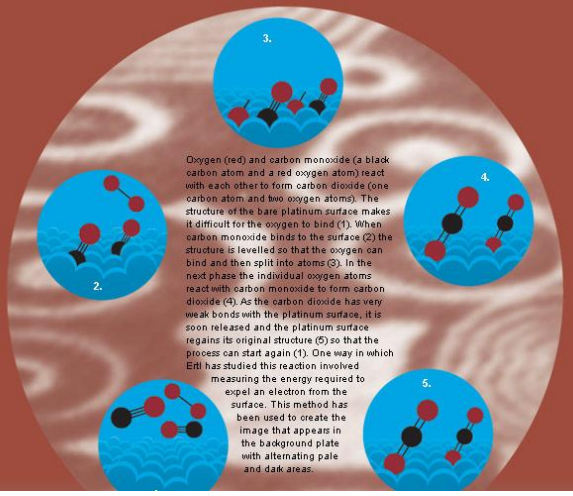
In the Haber-Bosch process nitrogen is extracted from the air to form ammonia. This is an important stage in the production of artificial fertilizers and the process won Fritz Haber the 1918 Nobel Prize in Chemistry. Even though the chemical process has been known for a long time, thanks to Ertl's work we now understand how it functions. The reaction can only take place on a catalytic surface of iron. The surface provides support to enable the atoms in the nitrogen molecules to release their bonds so that they can bind to hydrogen and form ammonia. Ertl has studied the reaction with the help of several different spectroscopic methods and put the different results together to form the complete picture.



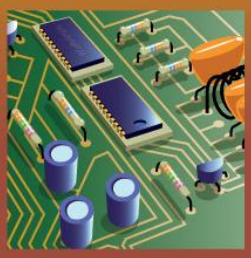
Nitrogen molecules (blue) and hydrogen molecules (white) react with each other step by step to form ammonia. The energy expenditure for the various stages of the reaction, which takes place on an iron surface, is indicated in kilojoules per mole. The slowest step is splitting the

Clean exhaust

In the catalysts of cars poisonous carbon monoxide reacts with oxygen to form carbon dioxide before the exhaust is emitted. This reaction takes place on a surface of platinum, for instance. Ertl has shown that the reaction is considerably more complicated than could be expected and in this way demonstrated the strength of his own methodology in surface chemistry. The speed of the reaction varies depending on how much of the surface is covered by carbon monoxide or by oxygen. Sometimes this gives rise to a chaotic process. The circular patterns in the background plate show fields that alternate between being rich in oxygen (dark) and short of oxygen (pale). During the course of the reaction these change constantly.



Oxygen (red) and carbon monoxide (a black carbon atom and a red oxygen atom) react with each other to form carbon dioxide (one carbon atom and two oxygen atoms). The structure of the bare platinum surface makes it difficult for the oxygen to bind (1). When carbon monoxide binds to the surface (2) the structure is levelled so that the oxygen can bind and then split into atoms (3). In the next phase the individual oxygen atoms react with carbon monoxide to form carbon dioxide (4). As the carbon dioxide has very weak bonds with the platinum surface, it is soon released and the platinum surface regains its original structure (5) so that the process can start again (1). One way in which Ertl has studied this reaction involved measuring the energy required to expel an electron from the surface. This method has been used to create the image that appears in the background plate with alternating pale and dark areas.

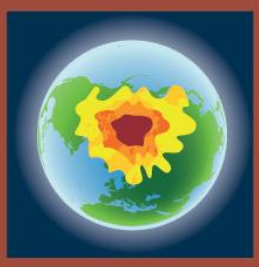


Electronics

It is thanks to the semi-conductor industry that development of the new vacuum techniques required for advanced surface chemistry had already begun in the 1950s. When electronic components are assembled knowledge of surface chemistry is important.

The ozone hole

The ozone layer is damaged by reactions on the surfaces of small ice crystals in the stratosphere, for instance when freon from air conditioners splits ozone molecules.



Corrosion

Rust occurs when oxygen reacts with an iron surface. This is an example of how a surface is ruined by corrosion. Ertl's work helps us to understand corrosion, and this is important in preventing accidents in everything from nuclear power to civil aviation.

1918 1932 1956 1992

1918 Fritz Haber awarded Nobel Prize in Chemistry for the Haber-Bosch process.

1932 Irving Langmuir awarded the first Nobel Prize for general surface chemistry.

1956 Cyril Hinshelwood awarded the Nobel Prize in Chemistry, among other things for the Langmuir-Hinshelwood mechanism for surface reactions.

1992 Ilya Prigogine awarded the Nobel Prize in Chemistry for having described dynamic dissipative structures, chaotic reactions and non-reversible thermodynamics.

Nobel Poster from the Royal Swedish Academy of Sciences, web adapted by Nobel Web AB.

Further reading

More information on the Nobel Prize in Chemistry for 2007 can be found at:

- The Royal Swedish Academy of Sciences
- Nobelprize.org »
- The Nobel Museum

- Oscillatory Kinetics in Heterogeneous Catalysis, R. Imbihl, G. Ertl, *Chemical Review 1995(95) 697–733*
- Primary Steps in Catalytic Synthesis of Ammonia, G. Ertl, *Journal of Vacuum Science and Technology A 1(2) 1247–1253 (1983)*
- Elementarschritte bei der heterogenen Katalyse, G. Ertl, *Angewandte Chemie 102(11) 1258–1266 (1990)*
- Elementarprozesse an Gas-Metall-Grenzflächen, G. Ertl, *Angewandte Chemie* 88(13) 423–433 *(1976)*

Link

- Fritz-Haber-Institut der Max-Planck-Gesellschaft
www.fhi-berlin.mpg.de/surfmag/arts.htm

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry for 2008 jointly to **Martin Chalfie**, **Osamu Shimomura** and **Roger Y. Tsien**, "for the discovery and development of the green fluorescent protein, gfp".

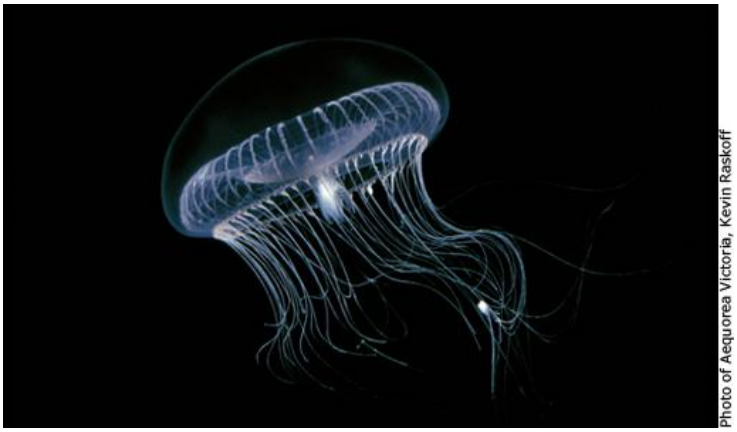


Photo of Aequorea Victoria, Kevin Raskoff

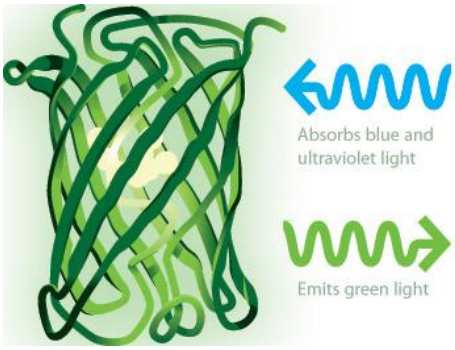
Lessons from the jellyfish's green light

Off the west coast of North America, floats the jellyfish Aequorea victoria. In its light-emitting organs resides the green fluorescent protein, GFP, which glows intensely under ultraviolet light. GFP now revolutionizes the life sciences, and the scientists responsible for its development have been awarded this year's Nobel Prize in Chemistry. The green light enables scientists to track, amongst other things, how cancer tumours form new blood vessels, how Alzheimer's disease kills brain neurons and how HIV infected cells produce new viruses.

An unexpected catch for Shimomura

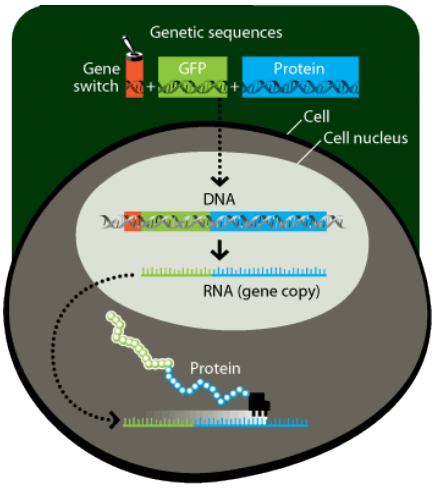
© Osamu Shimomura Originally published in "A Glow in the Dark"

Throughout the summers of the 1960s, Osamu Shimomura (rearmost in the picture above), his family and various assistants, caught tens of thousands of jellyfish in the Pacific Ocean. From the edge, which emit green light when the jellyfish is agitated, Shimomura isolated a protein. Surprisingly, that protein did not shine in green. It was blue. Shimomura assumed that additional proteins were involved, and indeed found one more. It was not luminescent, but did glow bright green under the light of an ultraviolet lamp.



A green guiding star for biosciences

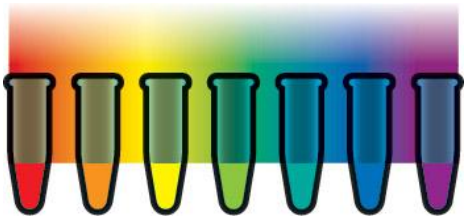
Today, scientists use GFP to understand the function of cells and proteins in living creatures. Proteins are the chemical tools of life – they control most of what happens within a living cell. Every human being functions thanks to the well-oiled machinery of thousands of proteins, like haemoglobin, antibodies and insulin. If something malfunctions, illness and disease often follows. Therefore it is fundamental for the biosciences to map out the role of various proteins. Using DNA-technology, scientists connect GFP to interesting, but otherwise invisible, proteins. GFP functions like a little lantern, which is activated by ultraviolet light. The green glow helps scientists track these proteins in the body.



From Gene to Protein:

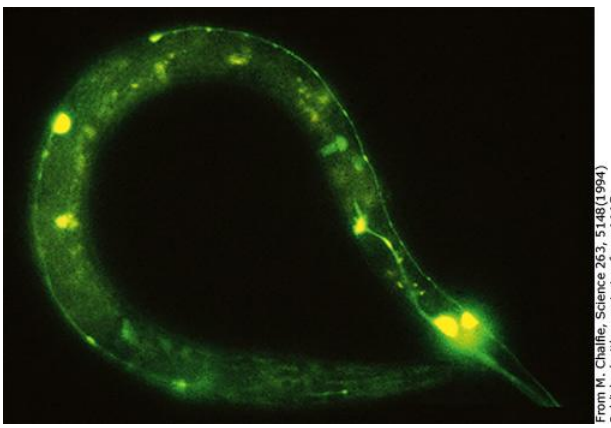
Tsien creates a palette with all the colours of the rainbow

During the 1990s Roger Tsien explored and changed GFP. His playful research resulted in proteins that glowed cyan, blue and yellow. However, he did not manage to produce any red colours. Red light penetrates skin and other biological tissue more easily, and so is especially useful for research.



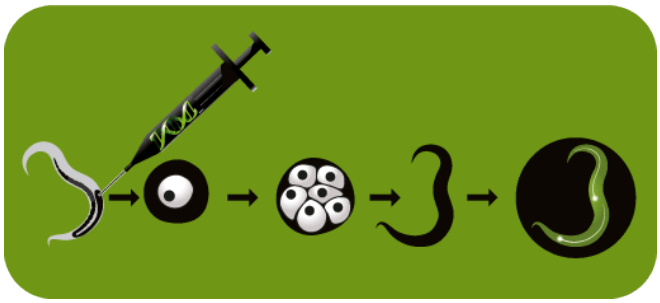
In 1999, Russian scientists isolated a red fluorescent protein, DsRED, from a coral. This protein was larger and more cumbersome than GFP. Tsien, however, managed to decrease the size of DsRED. From DsRED, Tsien also developed proteins with mouth-watering names like mPlum, mCherry, mStrawberry, mOrange and mCitrine.

A brilliant experiment by Chalfie

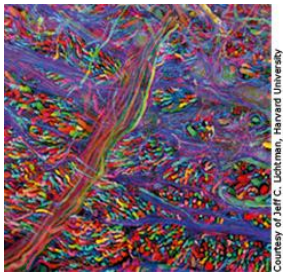


From M. Chalfie, Science 263, 5148 (1994)
Published with permission from AAAS

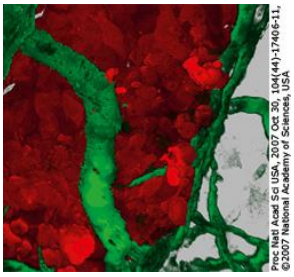
When Martin Chalfie first heard about GFP in 1988, he was delighted. He realised that GFP could possibly be used to colour cells and proteins. If that was the case, it would revolutionize the biosciences. The picture above shows Chalfie's successful experiment. The touch receptor neurons of the millimetre-sized roundworm Caenorhabditis elegans fluoresces green. We can see the round bodies and the long slender projection of the nerve cells.



How cells become green
Chalfie positioned the GFP-gene behind a promoter (a gene switch), which is active in the touch receptor neurons of the round worm. He injected the gene construct into the gonads of a mature worm. The worm is a hermaphrodite and fertilizes itself. The GFP gene is passed onto the eggs that the worm lays. The eggs divide, forming new individuals. The GFP-gene is then present in all cells of the new generation of roundworms, but only the touch receptor neurons will produce GFP. When they fill up with GFP, they start to glow green under ultraviolet light.



The brainbow
Scientists have used three fluorescent proteins in cyan, yellow and red – colours similar to those used by a computer printer – to colour the brain of a mouse. Different neurons randomly produce different amounts of the proteins. We can distinguish single neurons interlaced within the dense network.



Tumour surrounded by nourishing blood vessels
Scientists have coloured a breast cancer tumour with DsRED and the surrounding blood vessels with GFP. In this experiment, scientists discovered two proteins which help breast cancer cells spread. If scientists can neutralize these proteins, they might also be able to stop the cells from breaking away from the tumour area.

Martin Chalfie
US citizen. Born 1947 in Chicago, IL, USA. Professor of Biological Sciences at Columbia University, New York, NY, USA.

Osamu Shimomura
Japanese citizen. Born 1928 in Kyoto, Japan. Professor Emeritus at Marine Biological Laboratory (MBL), Woods Hole, MA, USA, and Boston University Medical School, MA, USA.

Roger Y. Tsien
US citizen. Born 1952 in New York, NY, USA. Professor and Investigator at Howard Hughes Medical Institute, University of California, San Diego, La Jolla, CA, USA.

Further reading

More information about the Nobel Prize in Chemistry for 2008 can be found on:*www.kva.se*, *http://nobelprize.org*, *www.nobelmuseet.se*

Pieribone, V. and Gruber, D.F. (2005) **Aglow in the Dark**, The Belknap Press, Harvard University Press, 2005

Zimmer, M. (2005) **Glowing Genes**, Prometheus Books

Shimomura, O. (2005) **The discovery of aequorin and green fluorescent protein**, *Journal of Microscopy*, 217 3-15

Shaner, N.C. et al (2008) **Improving the photostability of bright monomeric orange and red fluorescent proteins**, *Nature Methods*, 5 545-551

Movie showing a cell producing GFP-tagged HIV particles:*www.nature.com/nature/journal/v454/n7201/suppinfo/nature06998.html*

Website describing the GFP-revolution: *http://www.conncoll.edu/ccacad/zimmer/GFP-ww/GFP-1.htm*

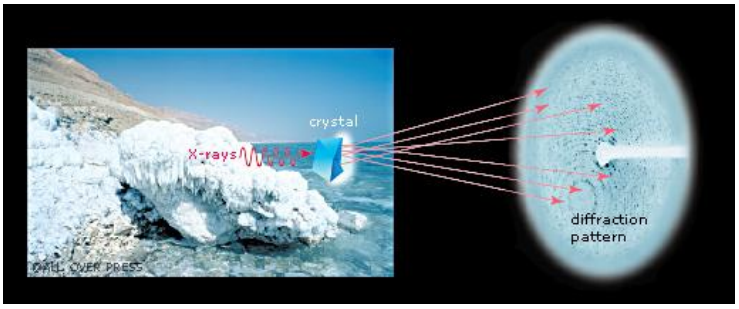
The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry for 2009 jointly to **Venkatraman Ramakrishnan**, **Thomas A. Steitz** and **Ada E. Yonath**, "*for studies of the structure and function of the ribosome*".

How the DNA code becomes life

At the beginning of the twentieth century, the chemical foundations of life were mysterious. Today we know how many of the most important processes function, all the way down to the atomic level. The 2009 Nobel Prize in Chemistry is awarded for the detailed mapping of the ribosome – the cell's own protein factory. Proteins build and control life at the chemical level. As ribosomes are crucial for life, they are also a major target for new antibiotics.

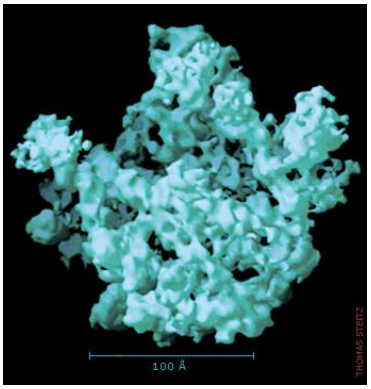
Tough organisms from extreme environments

The story of the 2009 Nobel Prize in Chemistry begins in hot springs and in the Dead Sea. Ada Yonath used micro-organisms from these extreme environments to isolate robust ribosomes. Her goal was to make the ribosomes crystallize, like salt in a solution crystallizes when the water evaporates. After many years of trial and error, Ada Yonath managed to generate well organized crystals with millions of ribosomes assembled into regular patterns.



The crystal reveals the secrets of the ribosome

Ada Yonath sent X-rays through ribosome crystals. When the rays hit the crystal's atoms they are scattered, making millions of dots on a CCD detector. This method is called X-ray crystallography. By analysing the pattern of the dots, researchers can determine the positions of the hundreds of thousands of atoms in the ribosome. However, scientists also needed to know the "phase angle" for each and every dot. This mathematical information is related to the location of the atoms in the crystal. In 1998, Thomas Steitz managed to solve the phase problem and the first crystal structure of the ribosome's large subunit was published.



The blurred picture gets sharper

The first structure of the large subunit was like a dim photograph. Researchers quickly improved the sharpness of the image, and during August and September 2000, each one of the Nobel Laureates published a crystal structure with a resolution that allowed the positions of single atoms to be determined.

The Ribosome – a complex structure

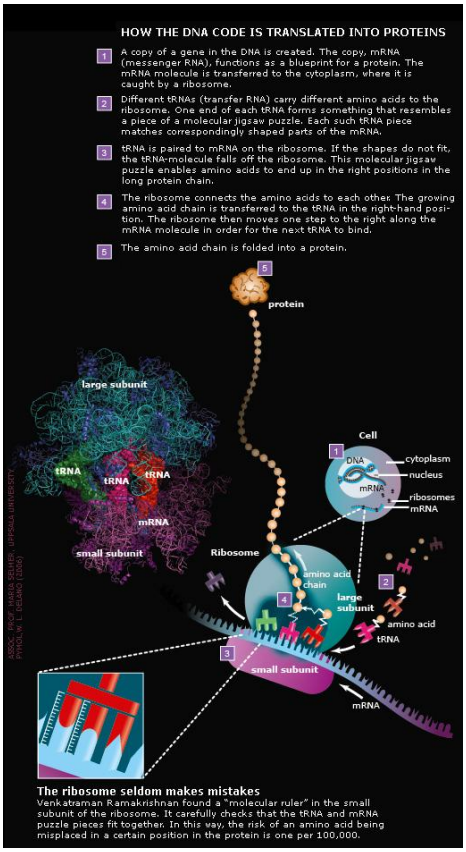
The human body is built from approximately one hundred thousand billion cells. Each cell contains thousands of ribosomes, which are composed of a small and a large subunit. The subunits are built from rRNA-molecules, constructed from nucleotides, and proteins, made from amino acids. Nucleotides and amino acids, in turn, are built from atoms. In all, a ribosome is built from hundreds of thousands of atoms.

The ribosome connects about ten amino acids per second

Thomas Steitz has taken snapshots of different steps in the chemical reaction where amino acids are connected. The reaction is catalysed by the large subunit. Thanks to work of Thomas Steitz, scientists now know which atoms in the ribosome are involved in the various reaction steps.

Proteins control life

In the human body there are tens of thousands of proteins that build and control life at the chemical level. Examples of proteins are oxygen-transporting haemoglobin, hormones such as insulin and the antibodies of the immune system. Proteins are built from 20 different kinds of amino acids which are linked together in long chains. A protein chain can consist of anything from ten to tens of thousands of amino acids.



Ribosome structures will save lives

All three Nobel Laureates have generated structures showing exactly where different antibiotics attack bacterial ribosomes. Some antibiotics inhibit the monitoring mechanism of the molecular ruler (see illustration above), others hinder the formation of the connection between amino acids or block the tunnel through which the emerging protein chain leaves the ribosome. The exact knowledge of where antibiotics bind to the ribosome helps scientists develop new and more efficient drugs. This is expected to save many human lives in the future.

Venkatraman Ramakrishnan
US citizen. Born in 1952 in Chidambaram, Tamil Nadu, India. Senior Scientist and Group Leader at Structural Studies Division, MRC Laboratory of Molecular Biology, Cambridge, UK.

Thomas A. Steitz
US citizen. Born in 1940 in Milwaukee, WI, USA. Sterling Professor of Molecular Biophysics and Biochemistry and Howard Hughes Medical Institute Investigator, both at Yale University, CT, USA.

Ada E. Yonath
Israeli citizen. Born in 1939 in Jerusalem, Israel. Martin S. and Helen Kimmel Professor of Structural Biology and Director of Helen & Milton A. Kimmelman Center for Biomolecular Structure & Assembly, both at Weizmann Institute of Science, Rehovot, Israel.