University of East Anglia

Як навчити ядерні спіни танцювати?

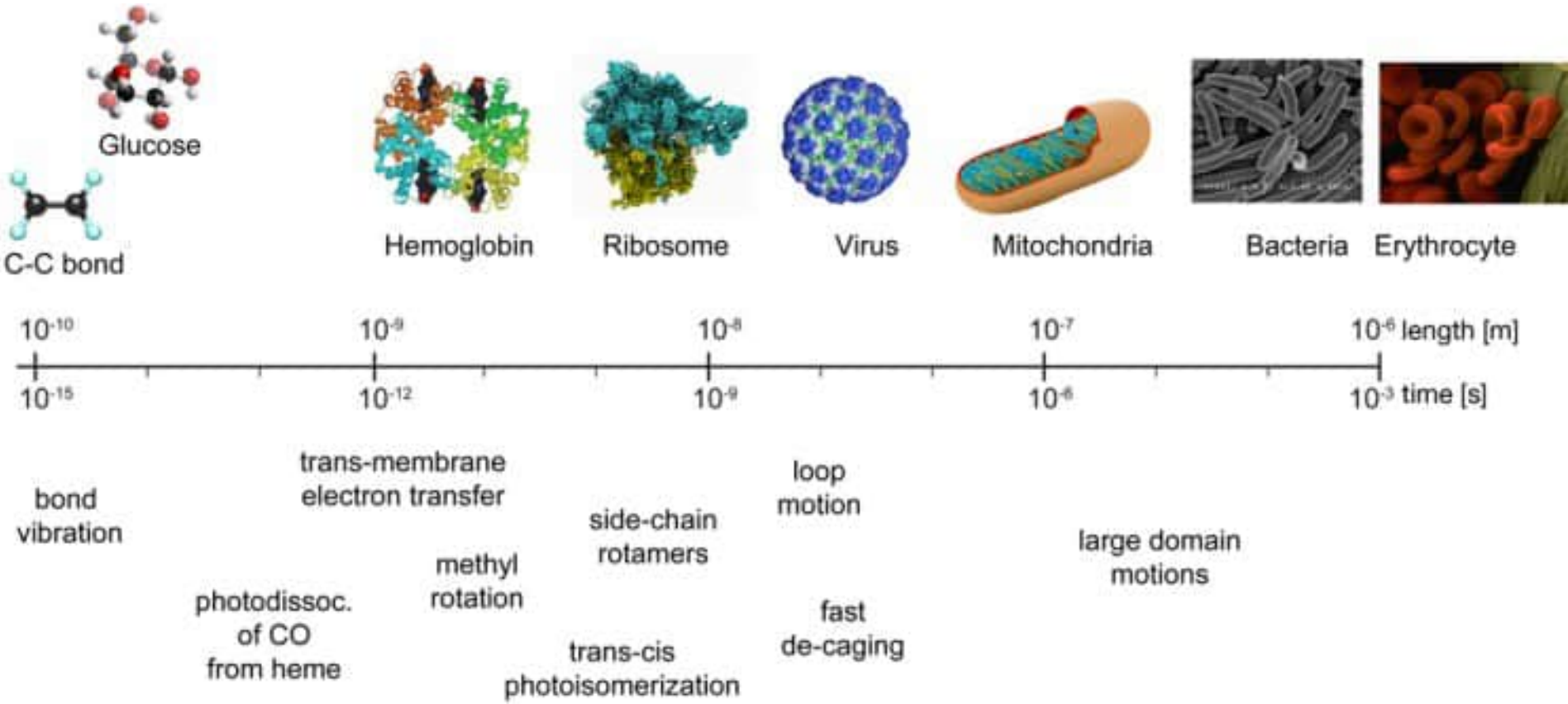
Making nuclear spins dance

Yaroslav Khimyak

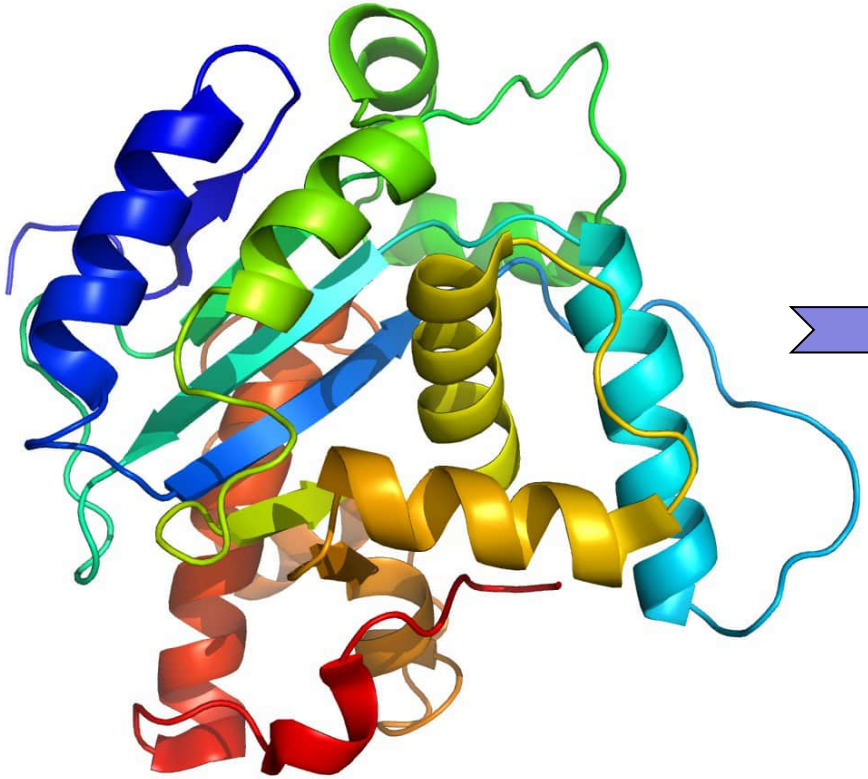
Professor in NMR spectroscopy
Head of Pharmaceutical Materials and Soft Matter
University of East Anglia

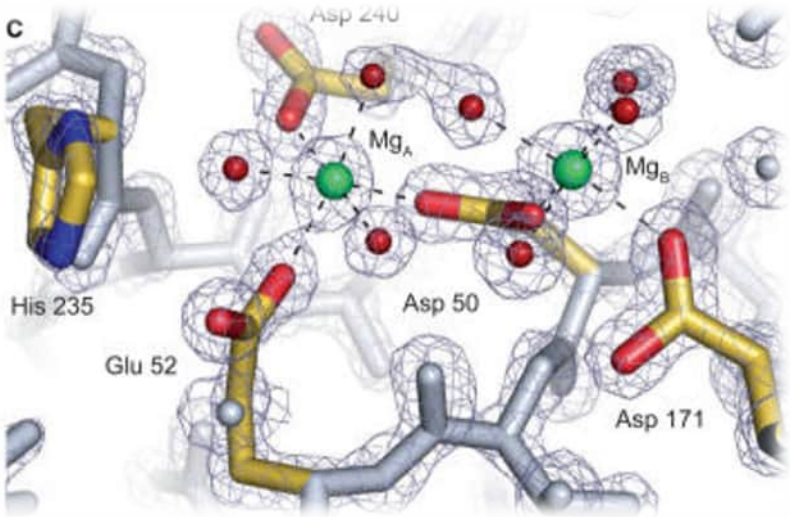
PATRIAE DECORI CIVIBUS EDUCANDIS

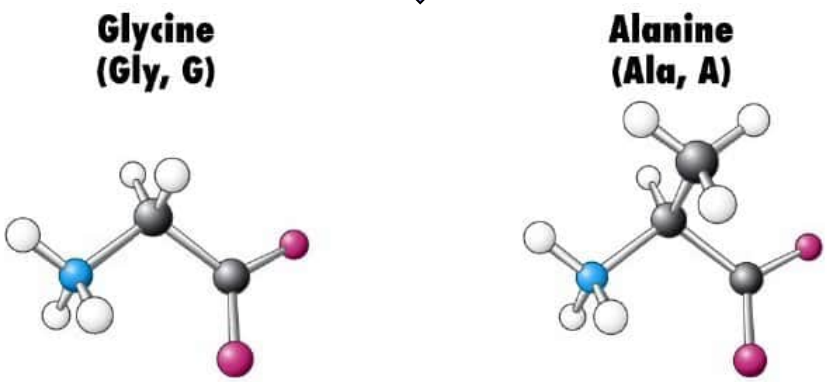
Структура ти динаміка на різних рівнях часу та довжини



Від молекул до атомів



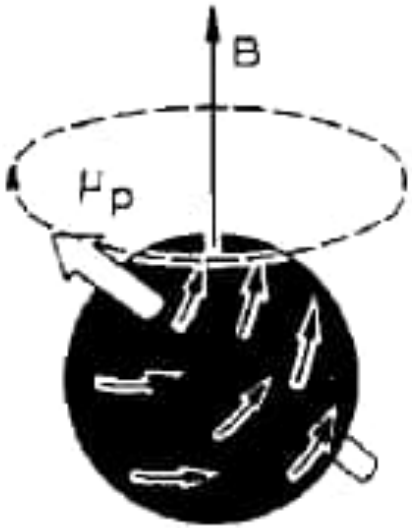




Crystal structure of the S. pombe Pop2p deadenylase subunit, A. T. Jonstrup et al. Nucleic Acids Res. 2007;35(9):3153-64.

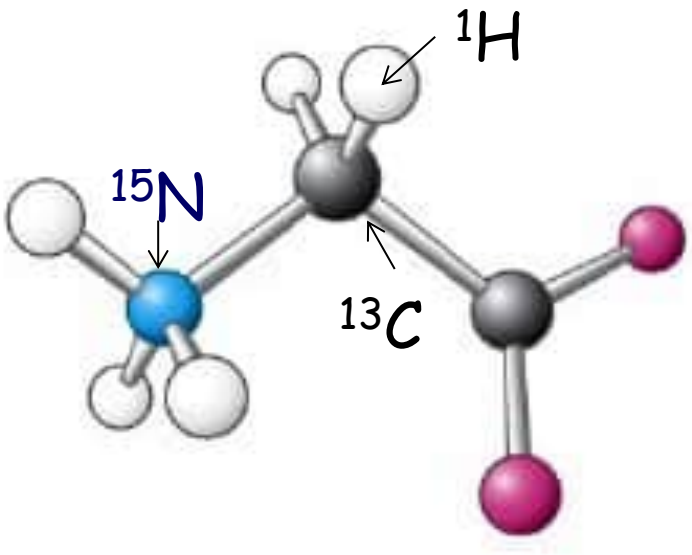
Молекули складаються з ядерних спінів

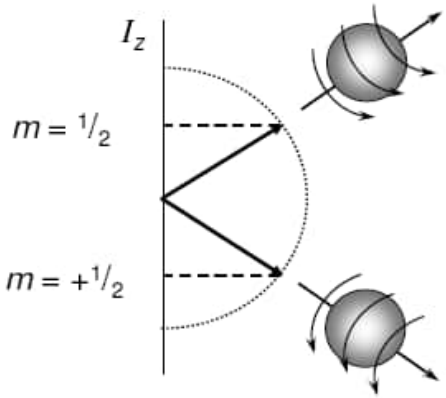
Proton spin precession



$$\mu_p = \frac{e\hbar}{2Mc} \times 2.79$$

$$\omega_{ps} = \frac{2\mu_p B}{\hbar} = \gamma_p B$$



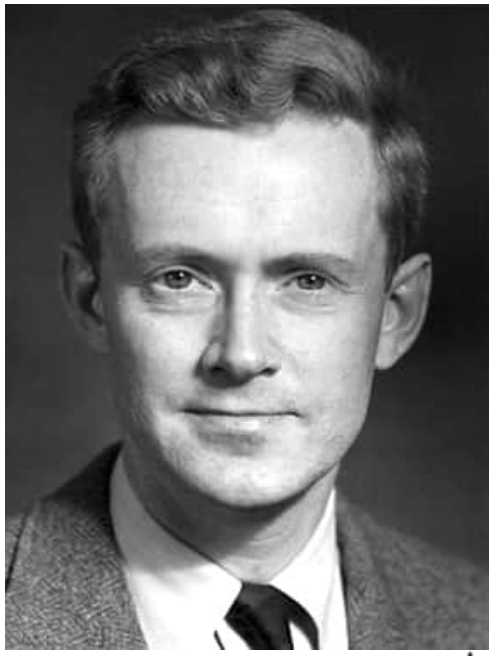


$I = 1/2$ (^{1}H, ^{13}C, ^{19}F, ^{31}P...)

$m = 1/2, -1/2$

Edward M. Purcell,
Research in nuclear magnetism,
Nobel prize in Physics, 1952

Ядерний магнетизм: Nobel Prize in Physics, 1952



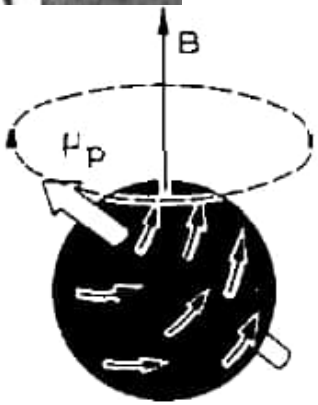
EDWARD M. PURCELL

Research in nuclear magnetism

Nobel Lecture, December 11, 1952

Professor Bloch has told you how one can detect the precession of the magnetic nuclei in a drop of water. Commonplace as such experiments have become in our laboratories, I have not yet lost a feeling of wonder, and of delight, that this delicate motion should reside in all the ordinary things around us, revealing itself only to him who looks for it. I remember, in the winter of our first experiments, just seven years ago, looking on snow with new eyes. There the snow lay around my doorstep - great heaps of protons quietly precessing in the earth's magnetic field. To see the world for a moment as something rich and strange is the private reward of many a discovery. But I am afraid it has little bearing on the sober question we must, as physicists, ask ourselves: What can we learn from all this about the structure of matter? It is my privilege to tell you now of some of the things that can be learned.

Proton spin precession



$$\mu_p = \frac{e\hbar}{2Mc} \times 2.79$$

$$\omega_{ps} = \frac{2\mu_p B}{\hbar} = \gamma_p B$$

Ядерний магнетизм: Nobel Prize in Physics, 1952

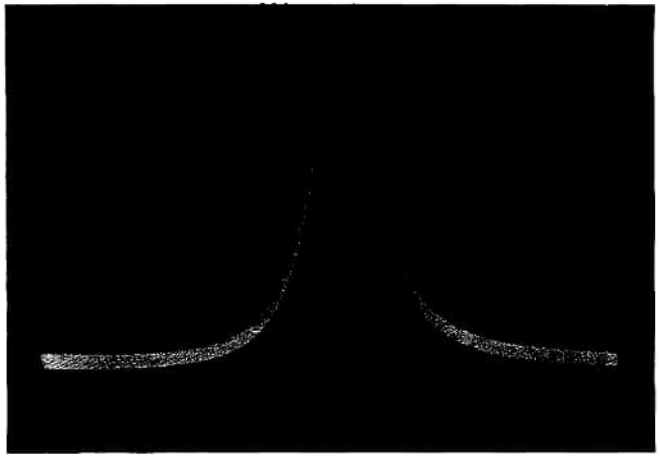


Fig. 3. A resonance line of protons in water, containing $MnSO_4$ as a paramagnetic catalyst and obtained from the phase component of the nuclear induction signal which corresponds to absorption. The photograph is that of the trace on a cathode-ray oscillograph with the *vertical deflection* arising from the rectified and amplified signal, and the *horizontal deflection* corresponding to different values of the constant field.

FELIX BLOCH

The principle of nuclear induction

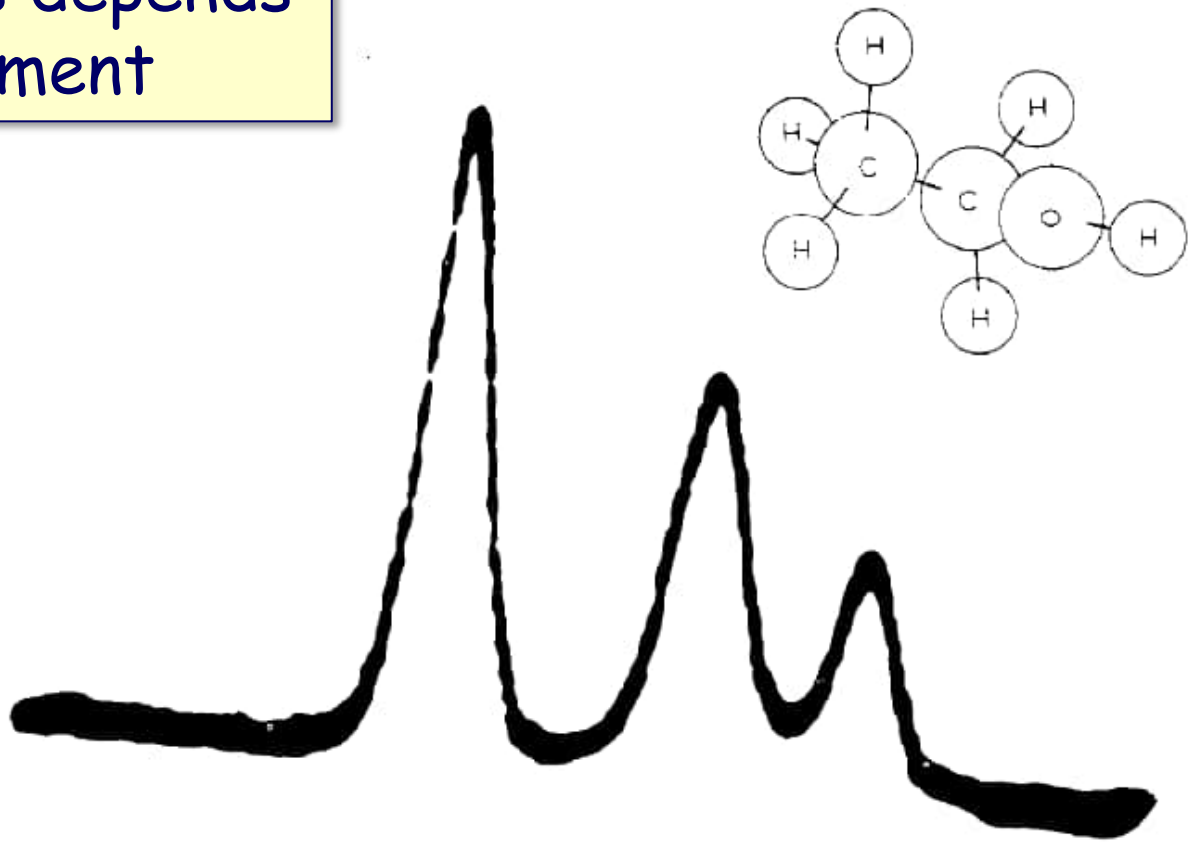
Nobel Lecture, December 11, 1952

It is a tribute to the inherent harmony and the organic growth of our branch of science that every advance in physics is largely due to the developments that preceded it. The discovery for which Purcell and I have received the honor of the Nobel Prize award for the year 1952 is a typical example of this situation, and before describing the principle I shall therefore present an outline of its long and distinguished background.

Both the method and the object go back ultimately to spectroscopy, a field to which modern physics owes so much in other respects. Among the various aspects of this field there are two which are of particular importance here: the Zeeman effect for introducing magnetic fields as an essential element of spectroscopy, and the hyperfine structure of spectral lines for revealing the existence of nuclear moments. The correct interpretation of hyperfine structures was first given in 1924 by Pauli[1], who proposed that atomic nuclei may possess an intrinsic angular momentum (spin) and, parallel to its orientation, a magnetic moment. The energy of interaction of this

Не лише розрізняння ^{1}H від ^{13}C

Energy of transitions depends on electronic environment



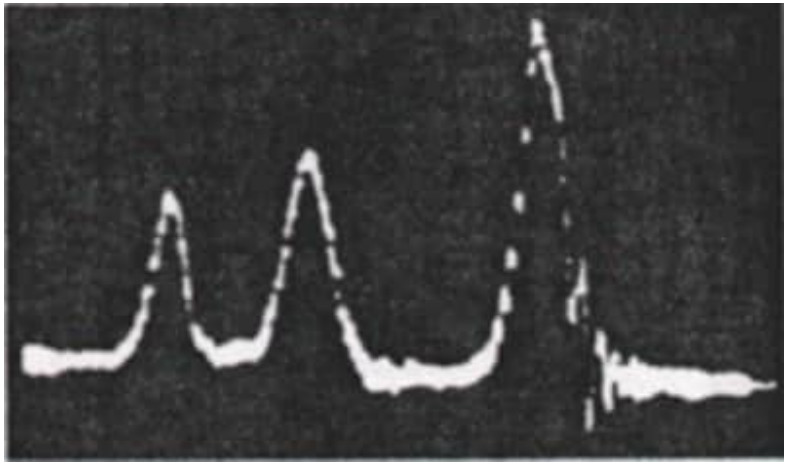
Edward Purcell , *Research in nuclear magnetism*

Felix Bloch, *The principle of nuclear induction*
Nobel prize in Physics 1952

The proton resonance in ethyl alcohol, observed with high resolution. The three lines arise from the CH_3 hydrogens, from the CH_2 hydrogens, and from the OH hydrogen, respectively.

Спектрометер Ядерного Магнітного Резонансу: початки

HR-60 NMR spectrometer (1958). First commercial machine taking full advantage of shimming, sample spinning and



1951. ^{1}H NMR spectrum of ethanol *measured by Purcell's group using a home built instrument*

Спектрометер Ядерного Магнітного Резонансу: початки

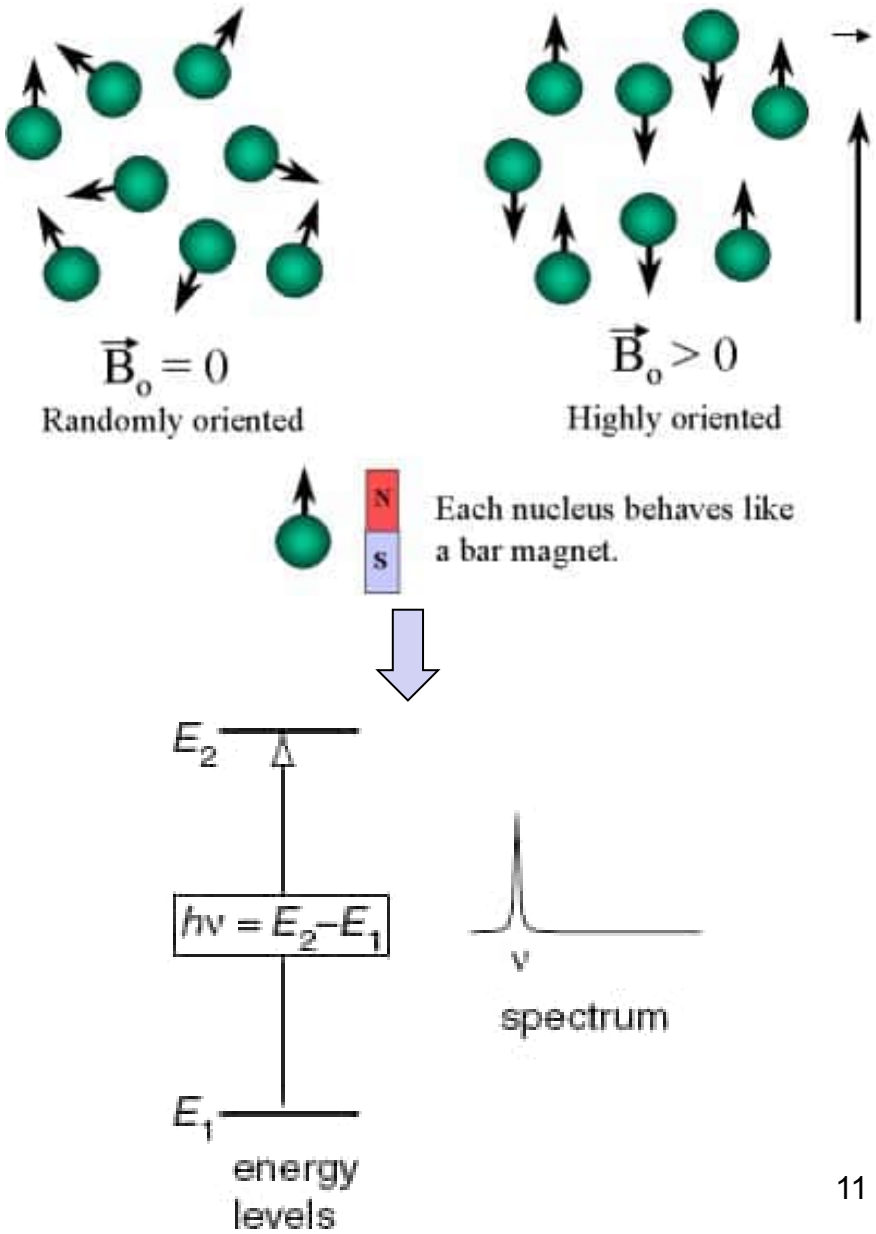
amusing note taped to an archived A-60 at the Chemical Heritage Foundation in Philadelphia:

WARNING: THIS MACHINE SUBJECT TO BREAKDOWNS DURING PERIODS OF CRITICAL NEEDS.

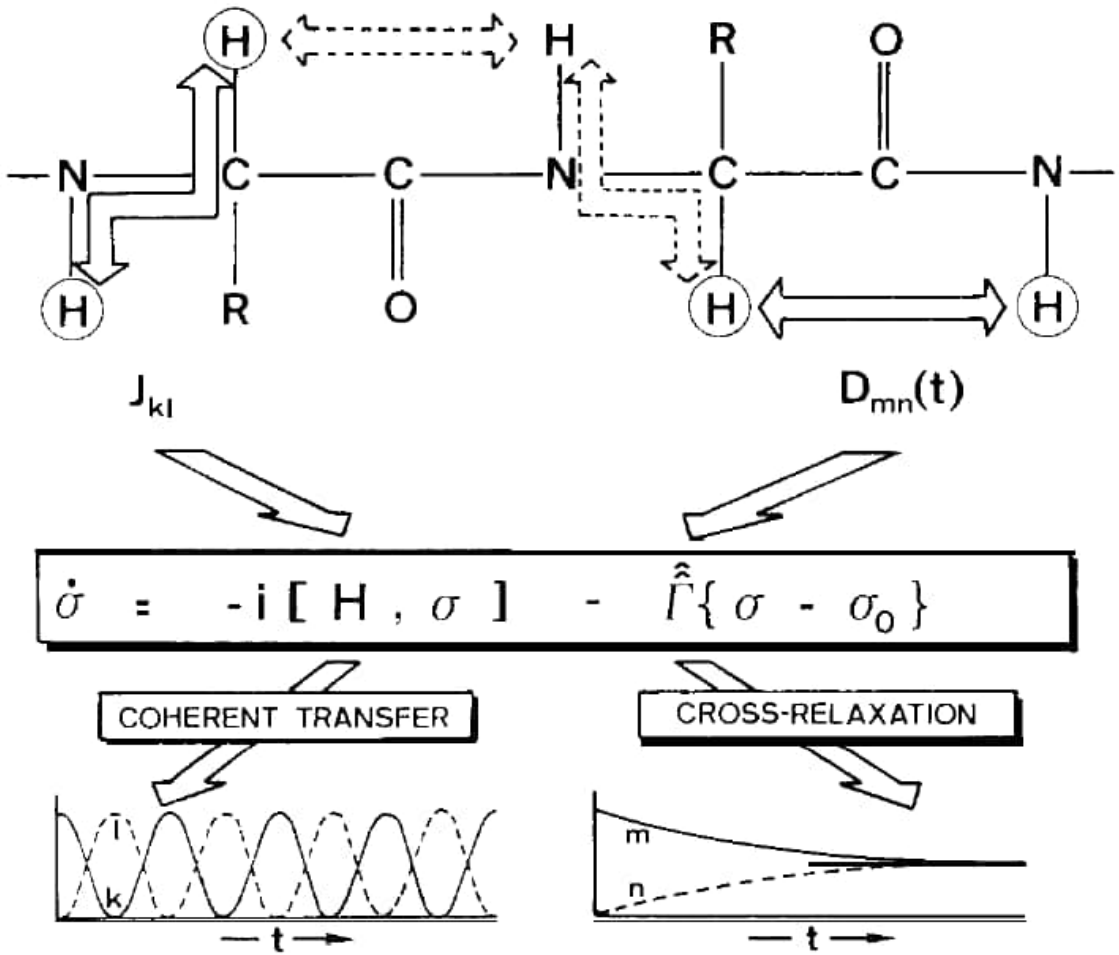
A special circuit in the machine called a "CRISIS DETECTOR" senses the operator's emotional state in terms of how desperate he or she is to use the machine. The "CRISIS DETECTOR" then creates a malfunction proportional to the desperation of the operator. Threatening the machine with violence only aggravates the situation. Likewise, attempts to use any other machine may cause it to malfunction too--they belong to the same union.

KEEP COOL AND SAY NICE THINGS TO THE MACHINE: NOTHING ELSE SEEMS TO WORK.

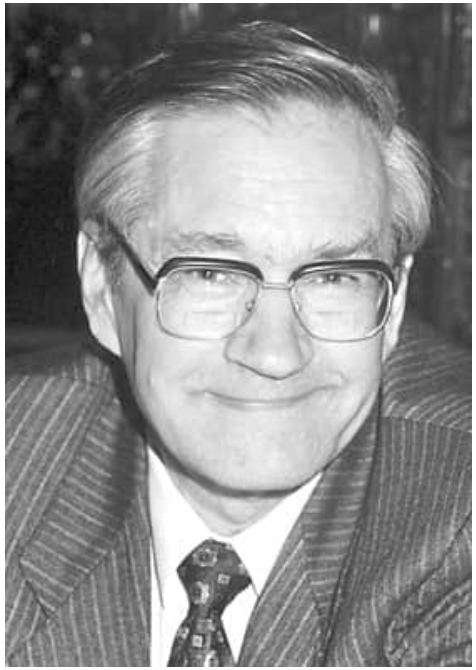
Ядерні спіни : як можна спостерігати енергетичні переходи



Спін в молекулі ніколи не буває наодинці

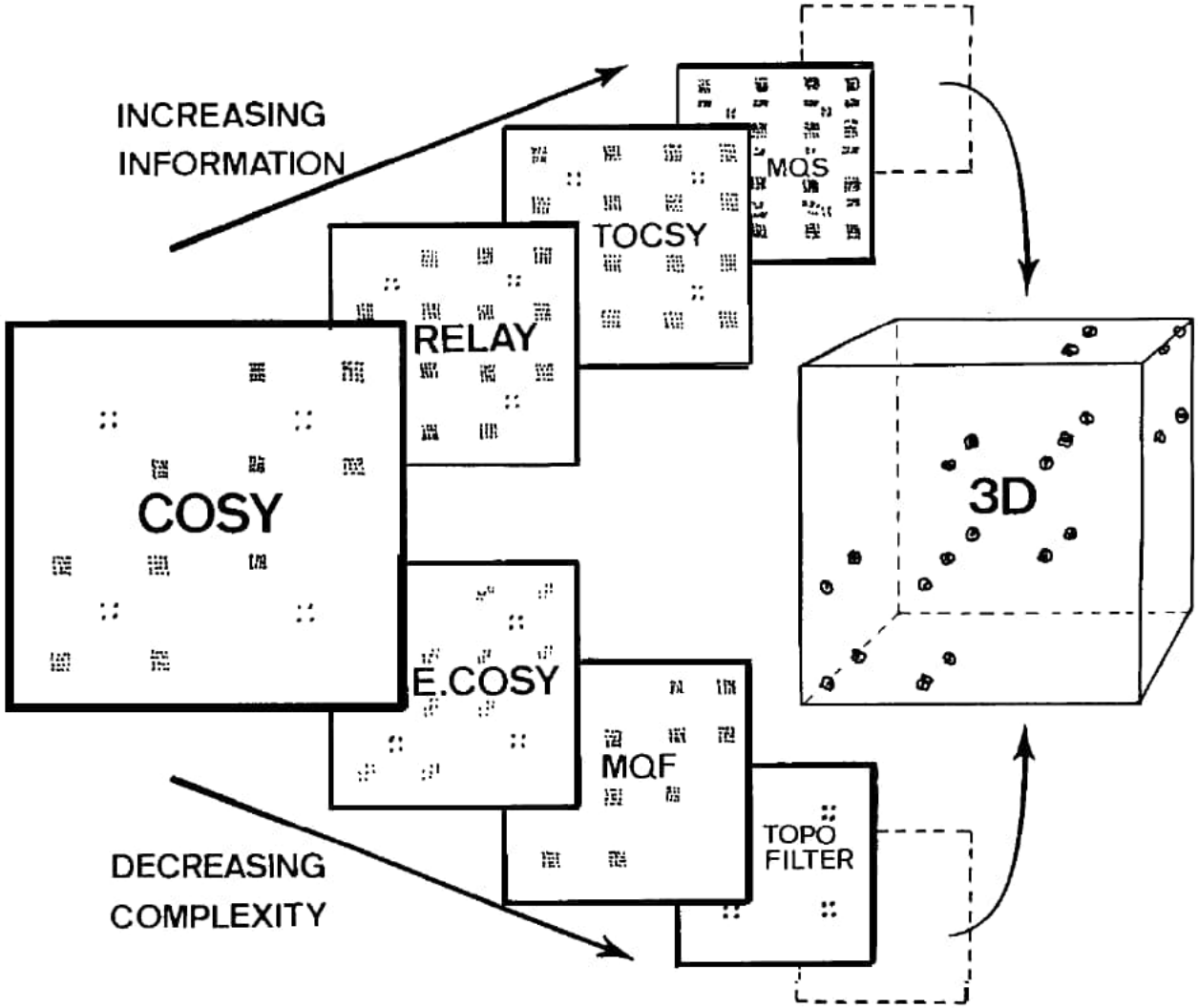


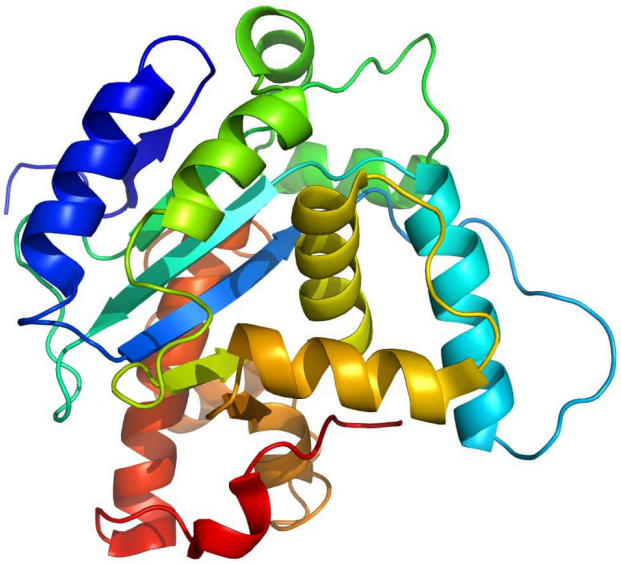
Richard Ernst, *Nuclear Magnetic Resonance Fourier Transform Spectroscopy*, Nobel Prize in Chemistry, 1991



The two pair interactions relevant in NMR: Through bond interaction: coherent transfer of spin order; Through space interaction D causes multiexponential cross relaxation

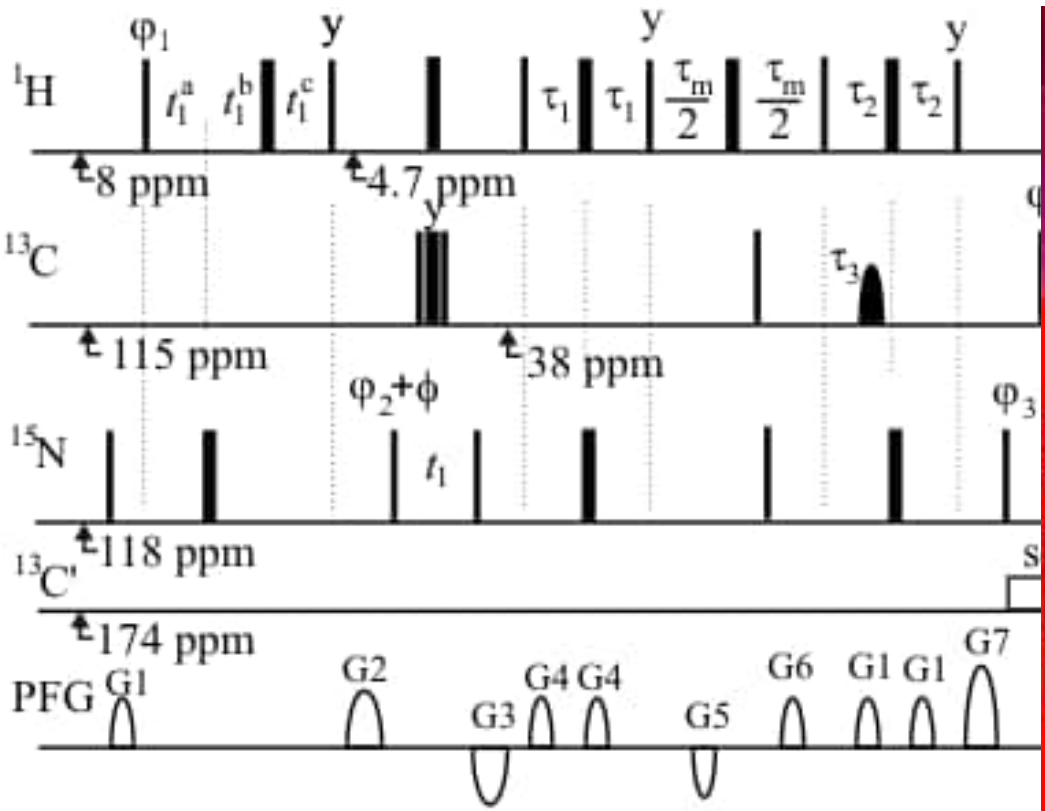
Повне вирішення структури молживе за допомогою ЯМР

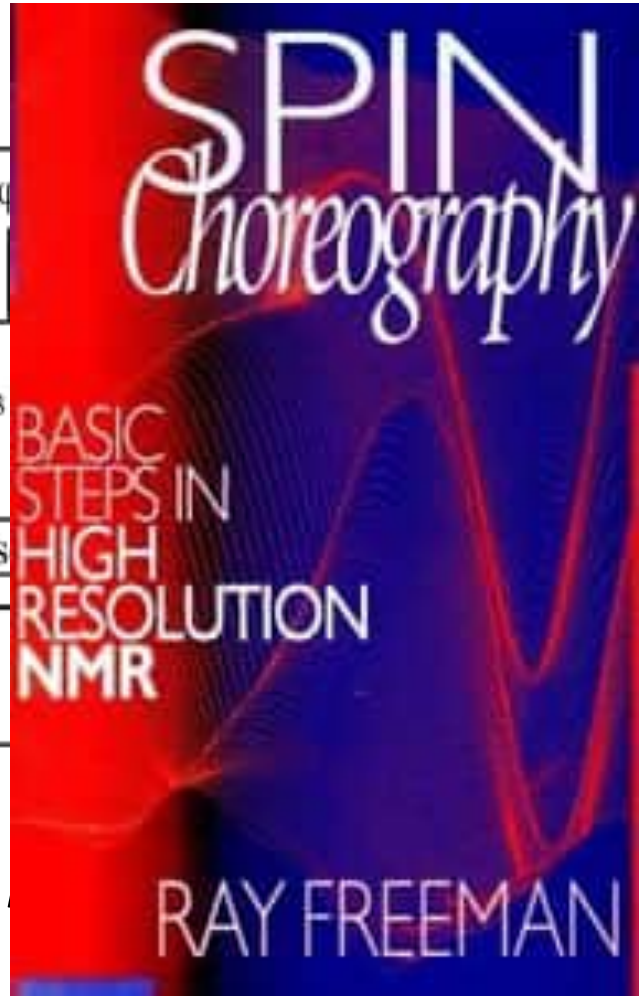




Електромагнітні пульси: як примусити спіни танцювати

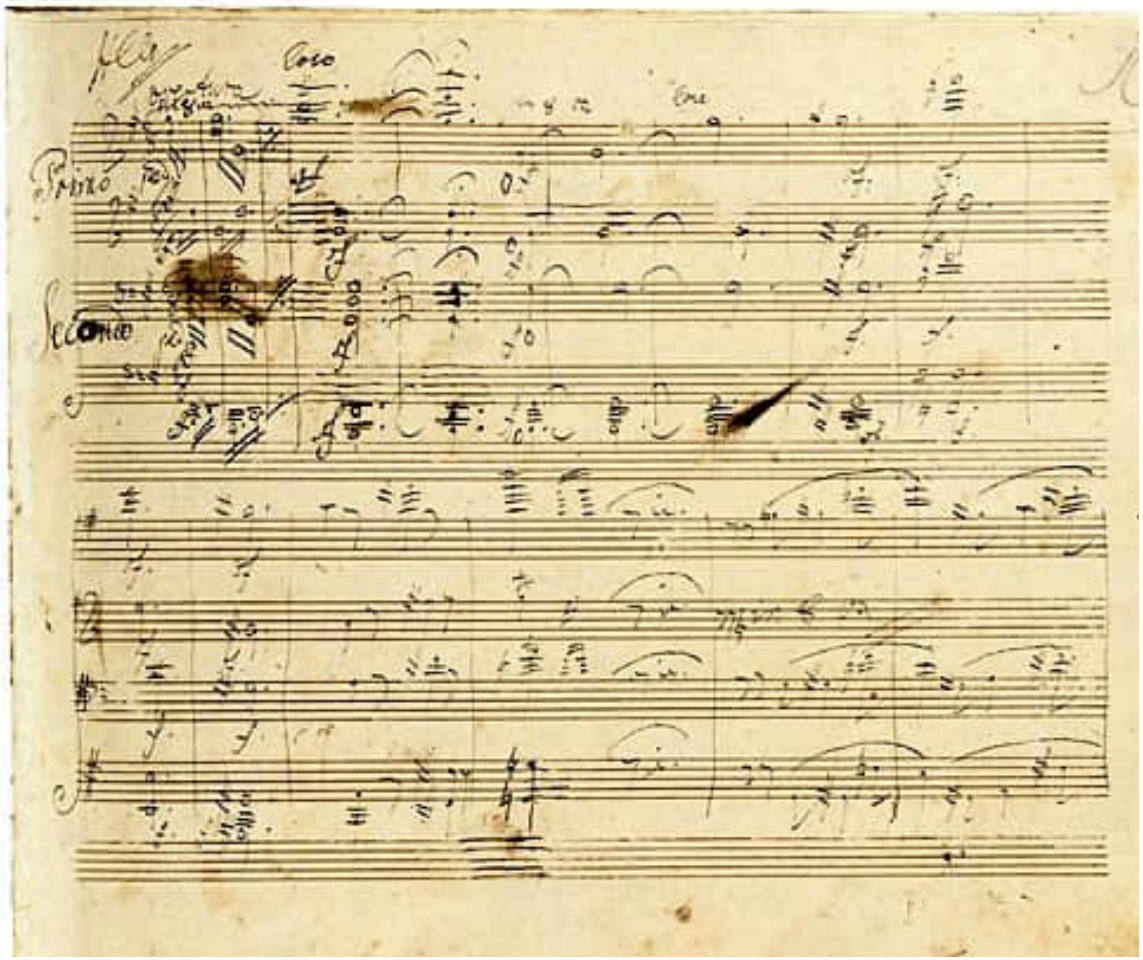
Nuclear spins can be manipulated in concerted fashion using rf pulses: selecting interactions to be observed





A version of gradient filtered NOESY

Спінова Хореографія



Beethoven,
String Quartet op. 131

A 4-channel experiment?

R. Ernst: *"I am not aware of any other field of science outside of magnetic resonance that offers so much freedom and opportunities for a creative mind to invent and explore new experimental schemes that can be fruitfully applied in a variety of disciplines… The practical importance of NMR is enormous and can justify many of the playful activities of an addicted spectroscopist"*.

Ядерна Магнітна Томографія: Nobel Prize in Medicine 2003

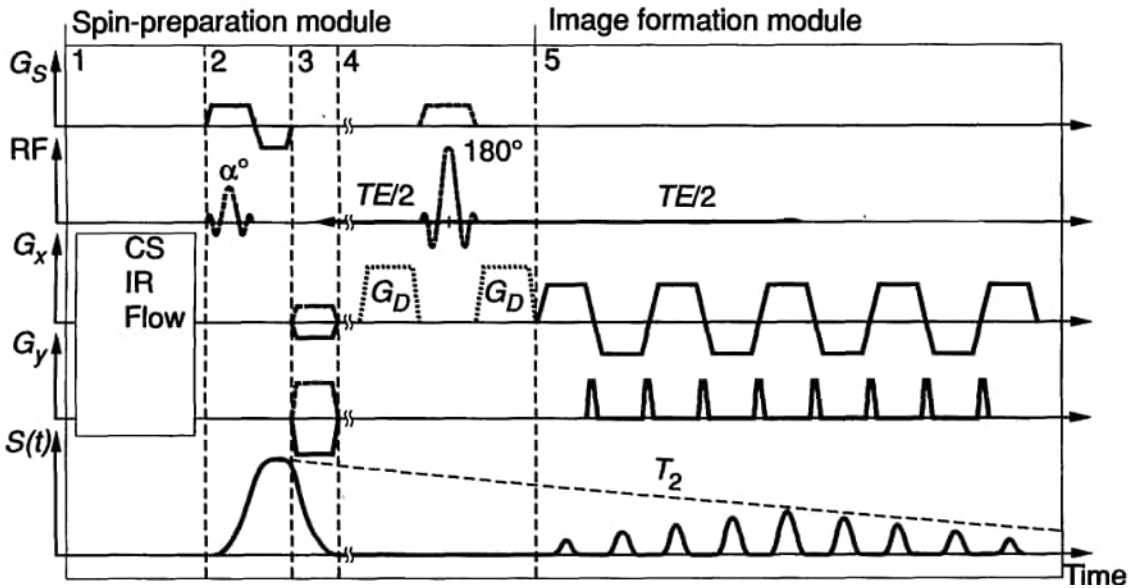
SNAP-SHOT MRI

Nobel Lecture, December 8, 2003

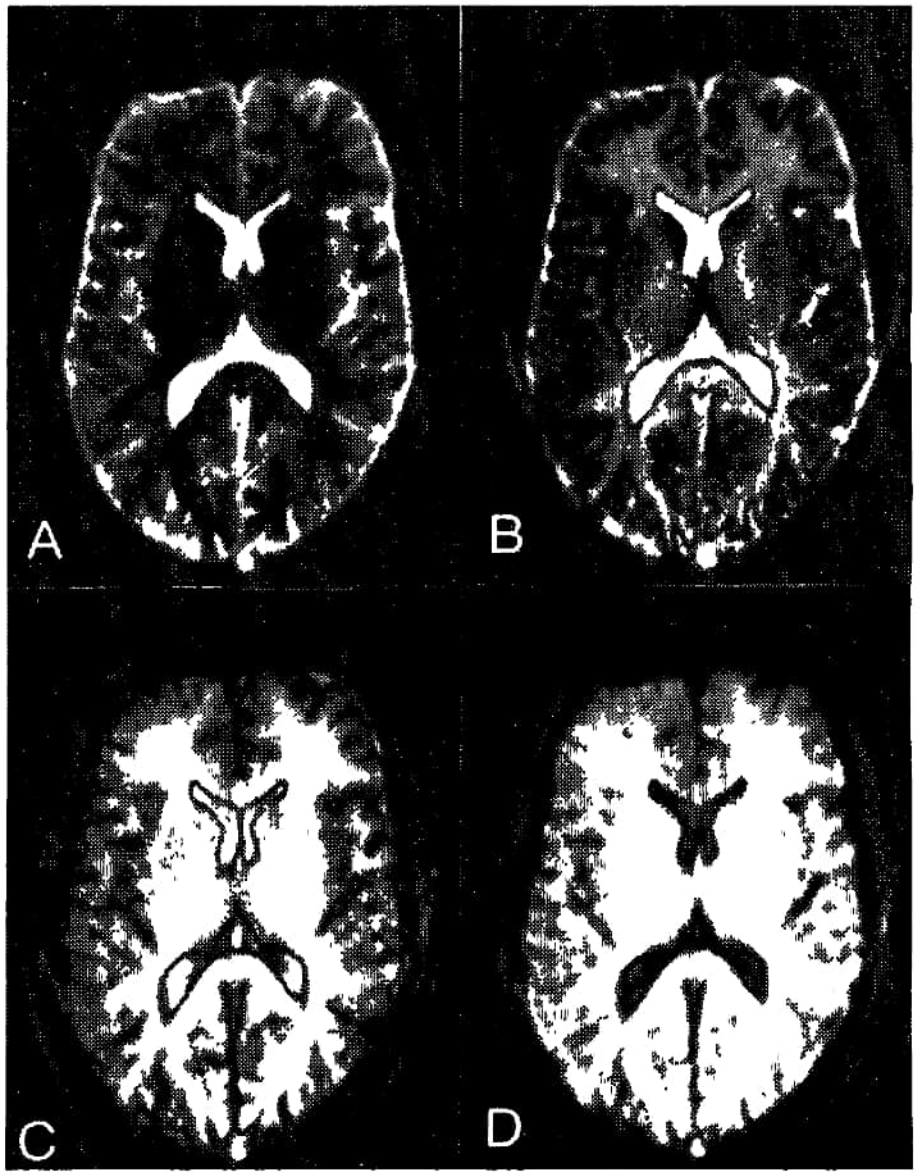
by

PETER MANSFIELD

Sir Peter Mansfield Magnetic Resonance Centre, Department of Physics and Astronomy, University of Nottingham, Nottingham, NG7 2RD, U.K.

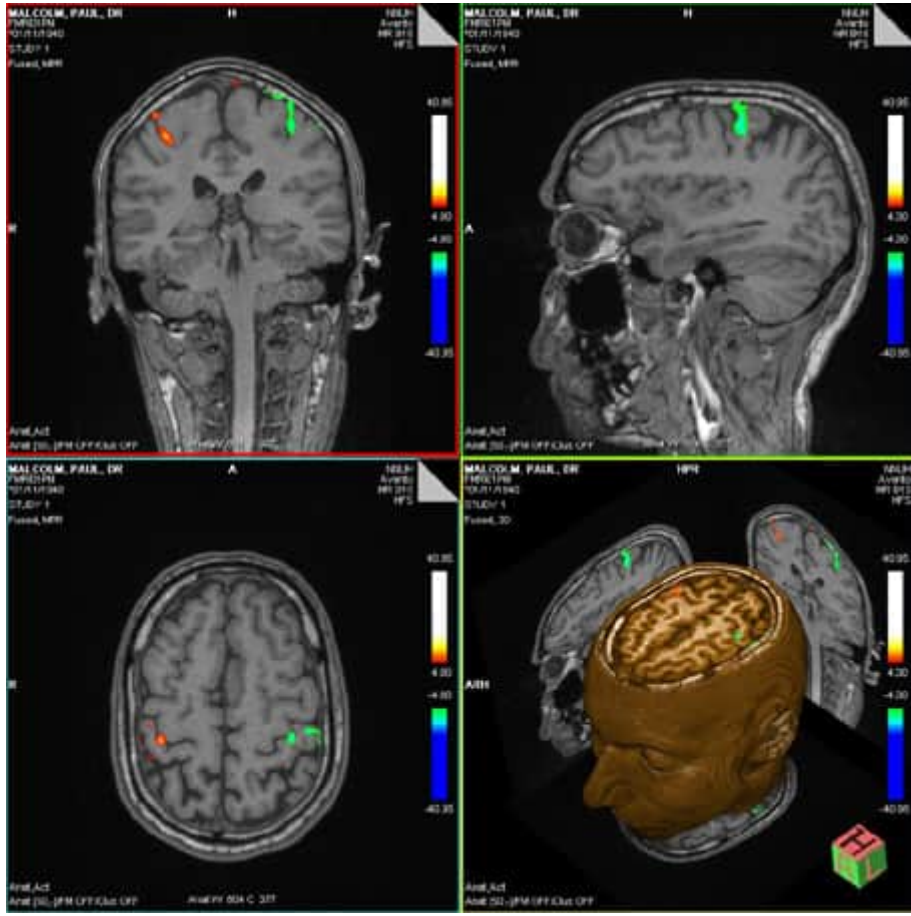


Ядерна Магнітна Томографія



Stehling,
Turner,
Mansfield,
Science, 1991,
453

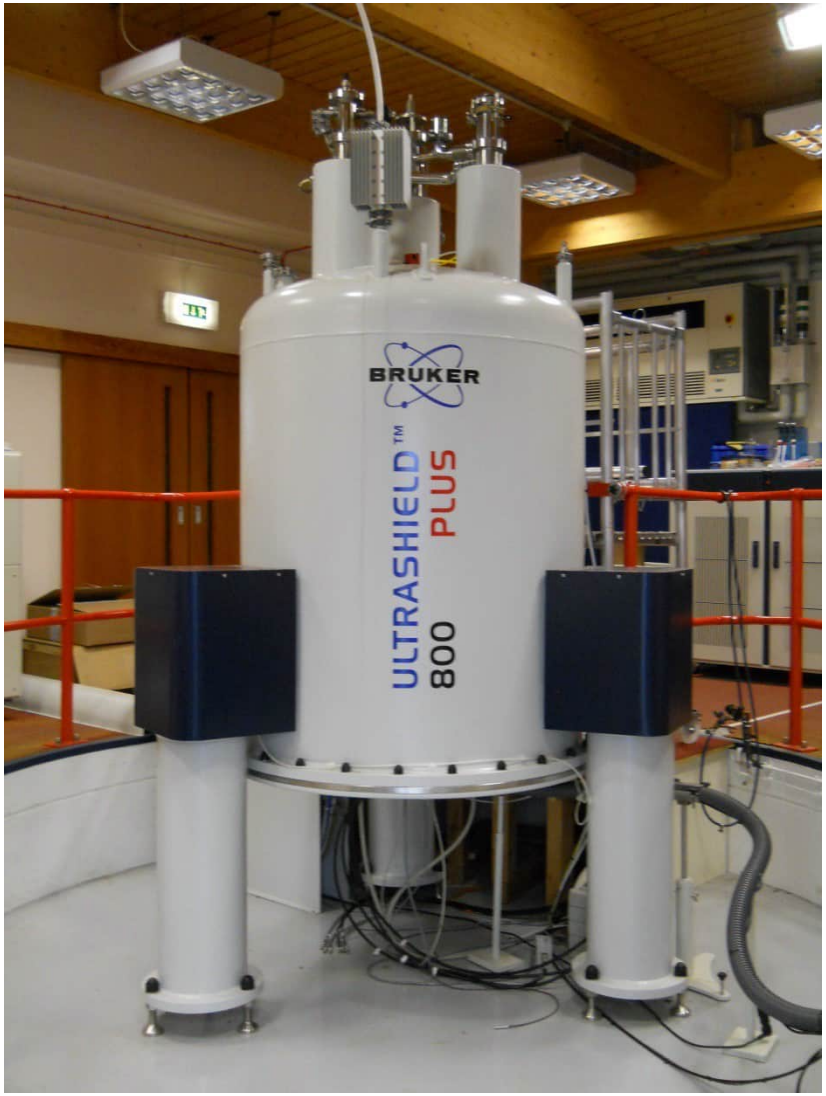
MRI in Norwich



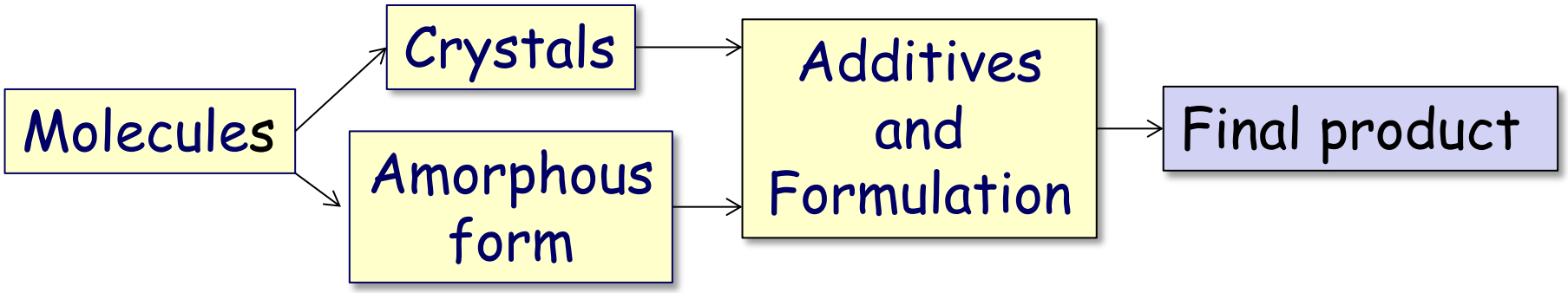
Ядерний Магнітний Резонанс в Норвічі

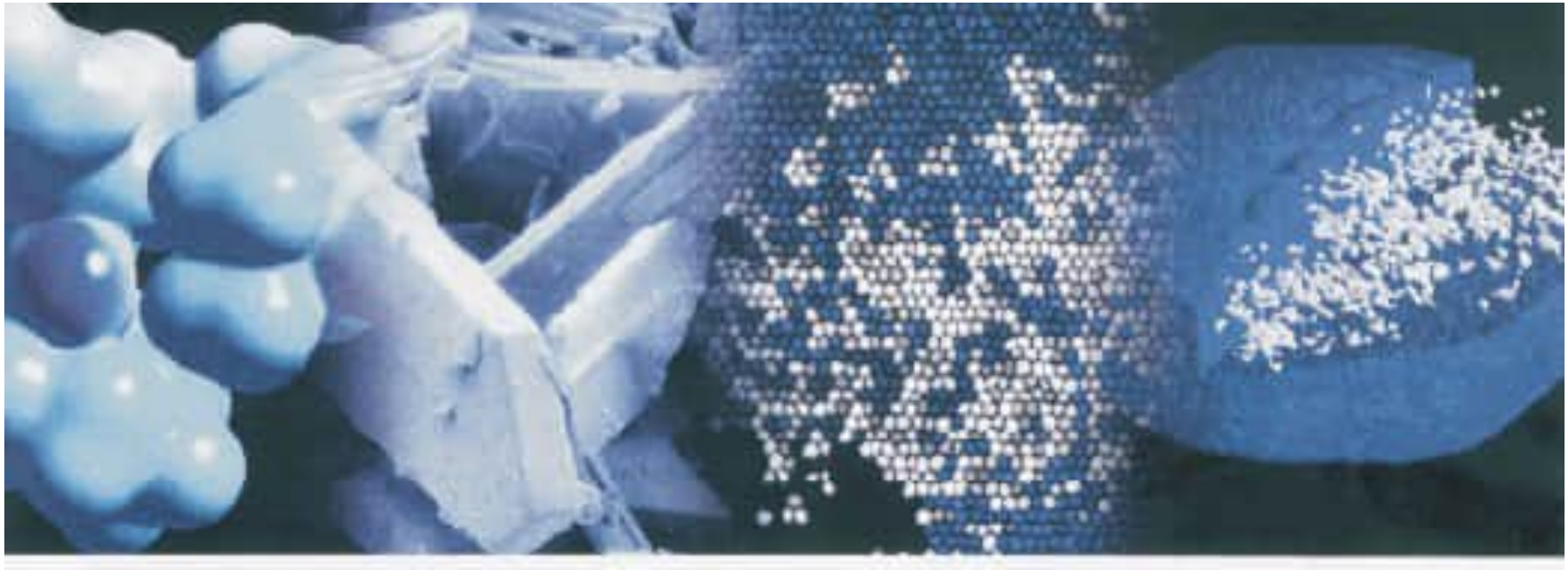
NMR in UEA: state of art facility

Suite of solution and solid-state NMR spectrometers and gel state capability at different fields



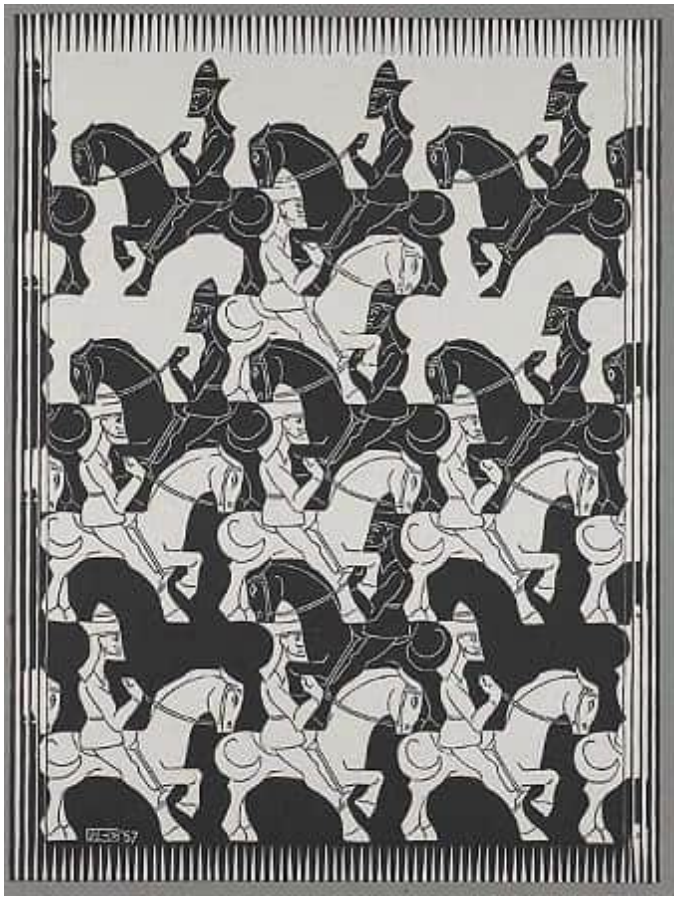
Контроль за процесом огранізації молекуп





How confident are we in predicting the prevalent structure?

Порядок чи Невпорядкування



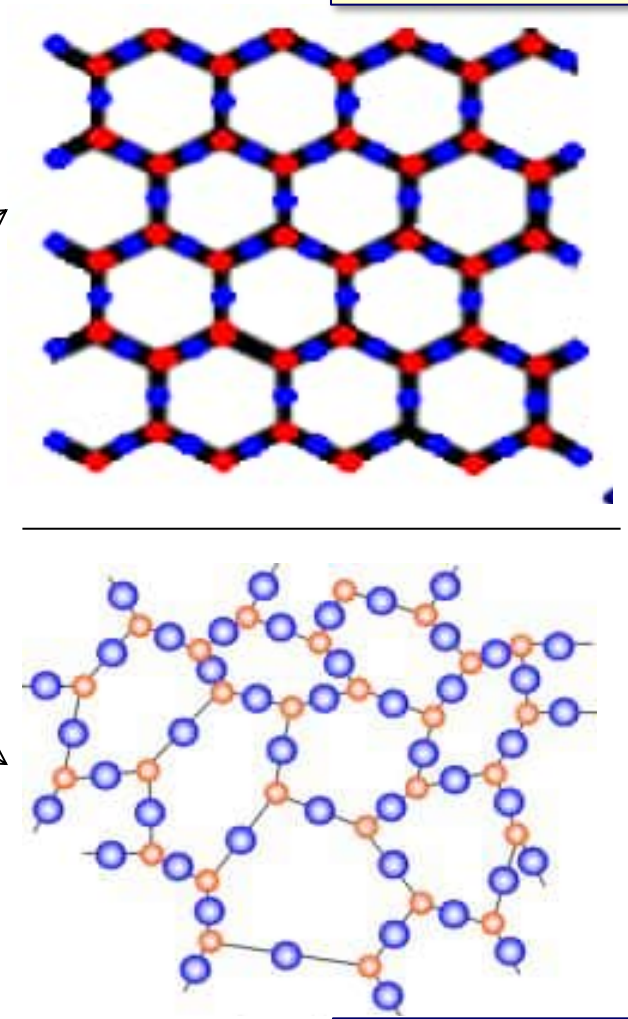
M. Escher: "*Order is repetition of units. Chaos is multiplicity without rhythm.*"

Jackson Pollock: "*The modern artist... is working and expressing an inner world - in other words - expressing the energy, the motion, and other inner forces*"

Self-assembly of Materials

Crystalline Solids

Molecular building blocks

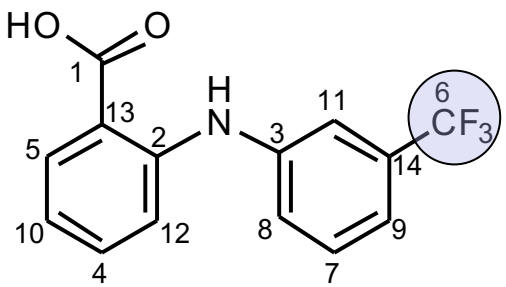


Amorphous Solids

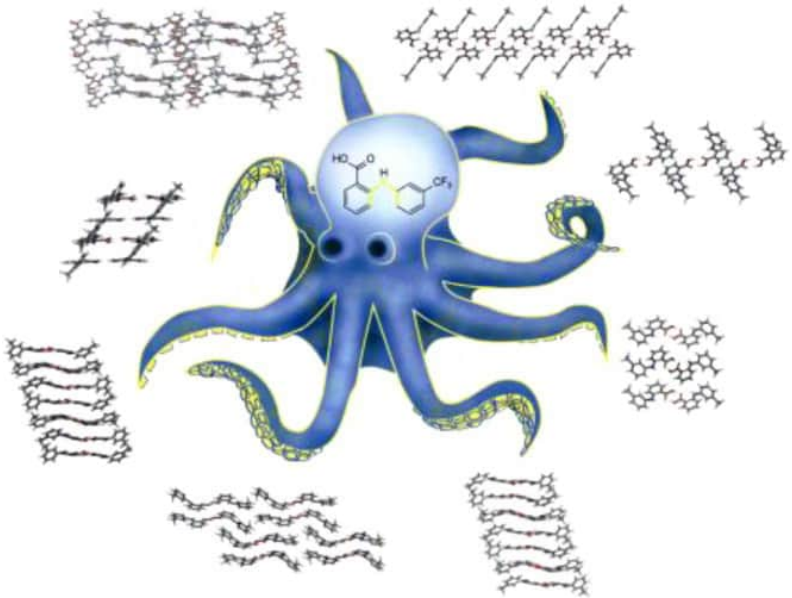
Контроль за кристалами в порах носіїв

Extremely unstable in amorphous state

Recrystallises from the melt upon cooling

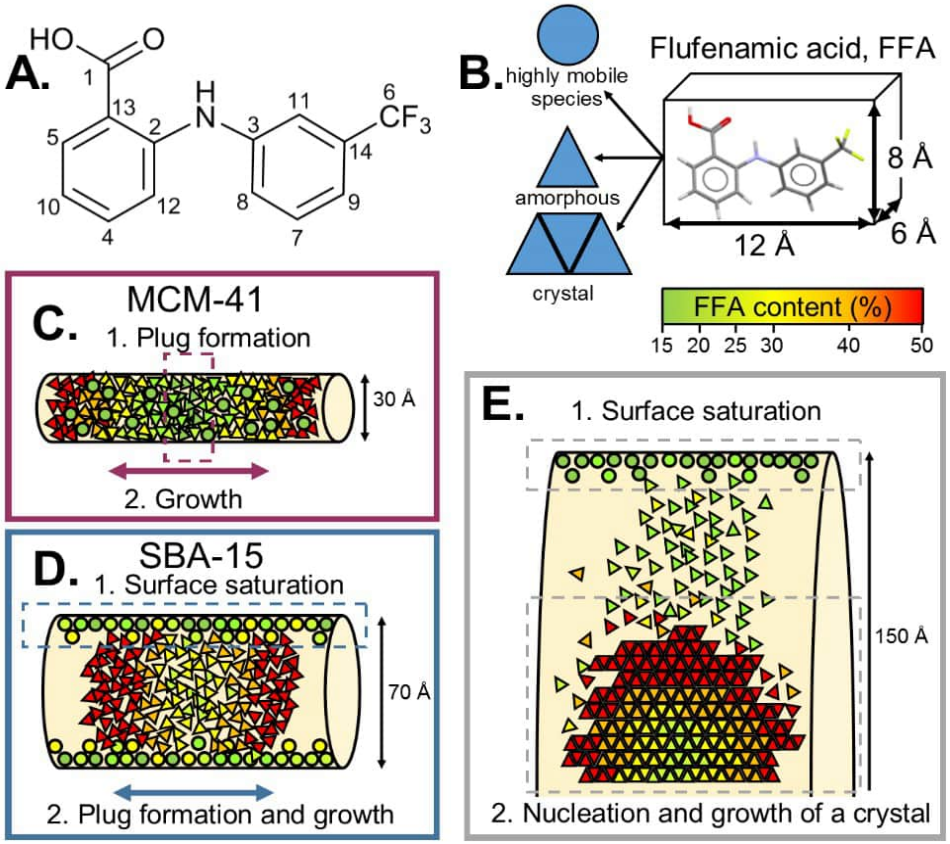


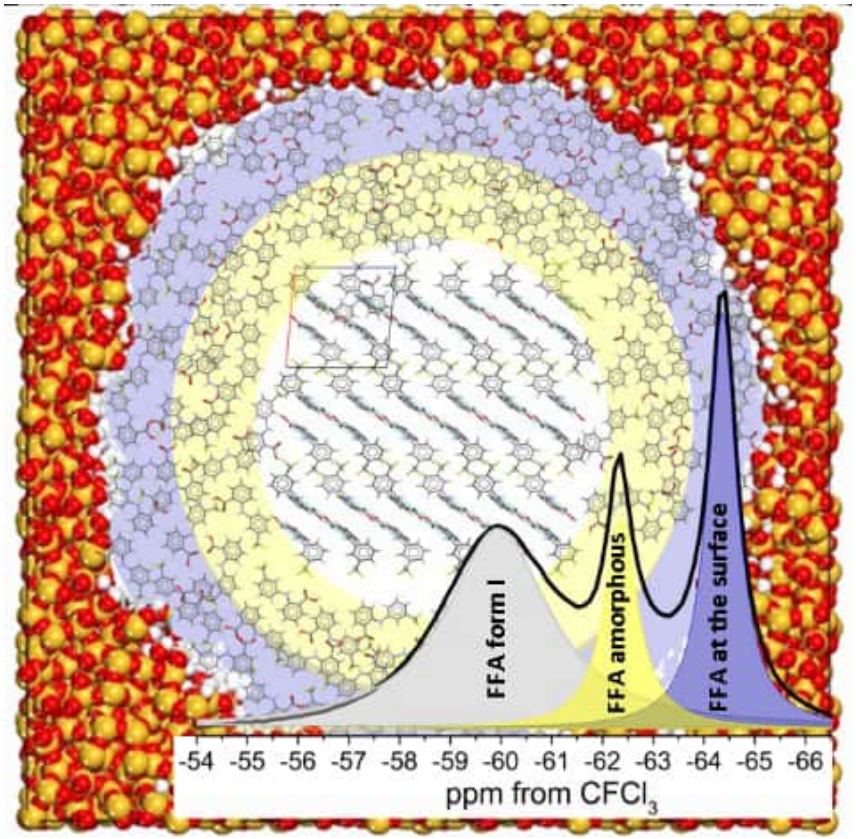
Properties	Flufenamic acid
Molecular weight	281.23
Glass transition temperature (°C)	16.85
Melting point (°C)	134.5 – Form I
Molecular volume (Å^3)	211.53
Number of polymorphs	9



K. P. Nartowski, L. Hawarden, Y. Z. Khimyak *et al*.
Angew. Chem, Int. Ed., **2016**, 55, 8904

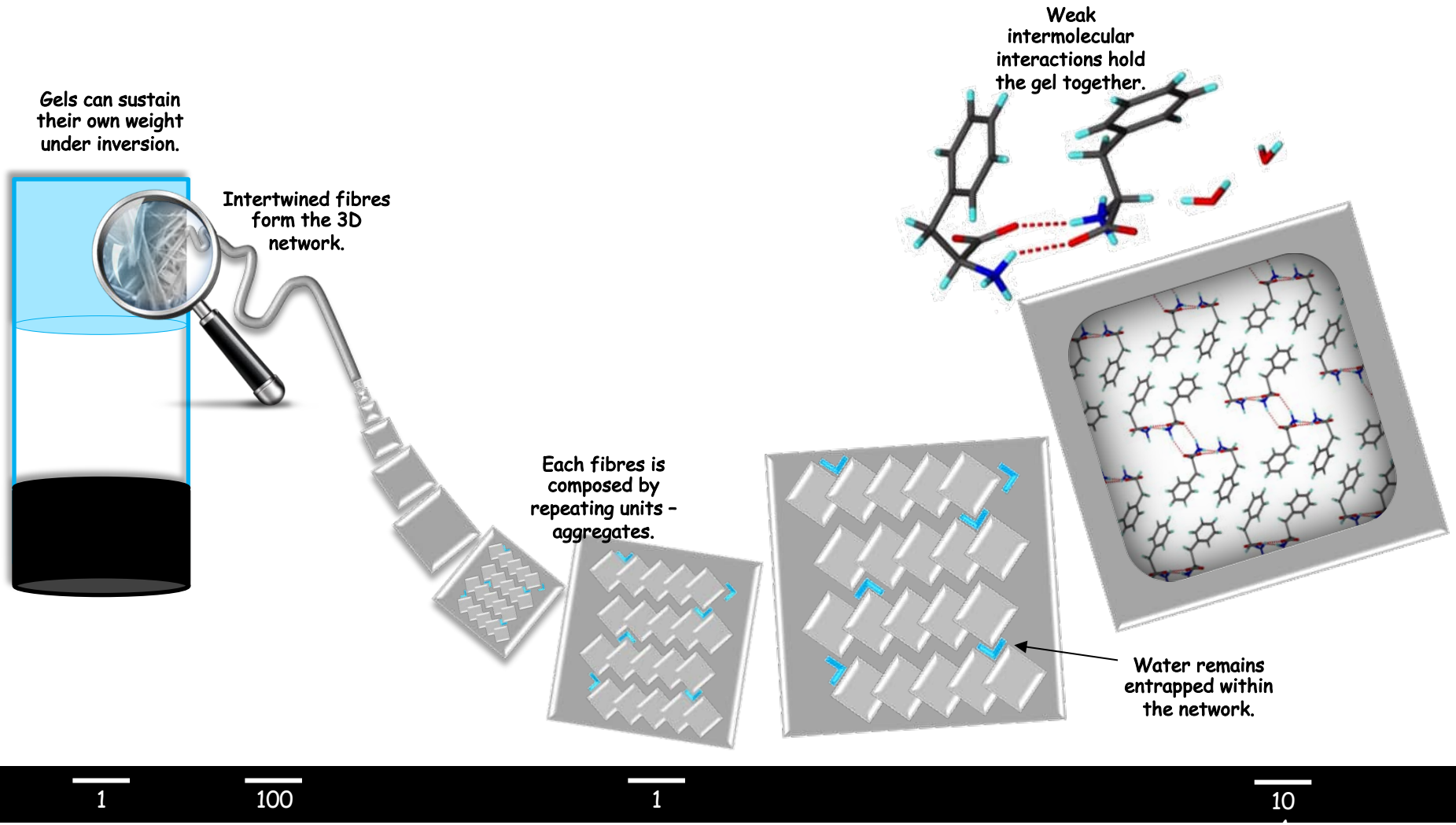
Контроль за кристалами в порах носіїв



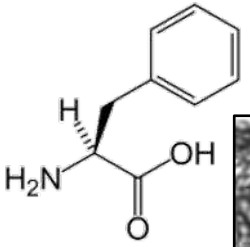


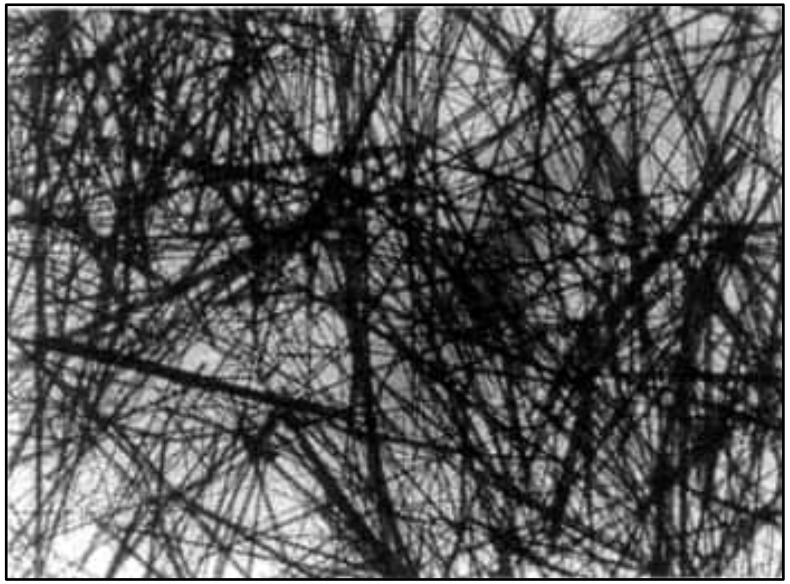
K. P. Nartowski, L. Hawarden, Y. Z. Khimyak *et al*. *Angew. Chem, Int. Ed.*, **2016**, 55, 8904

Дослідження коллоїдів та гелів



Гель-кристалізація фенілаланіну

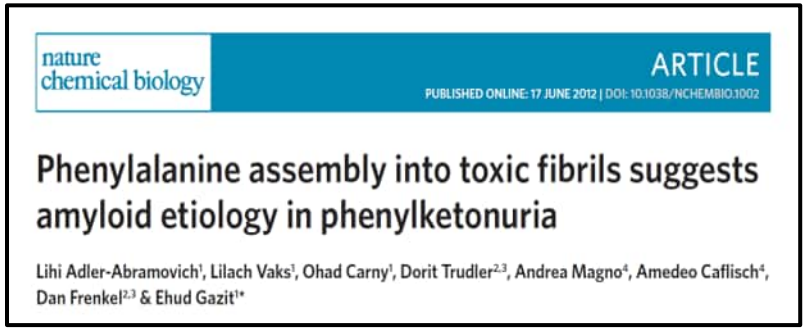




Gel-crystals of *L*-Phe (optical microscope)

Hsu, W.-P.; Koo, K.-K.; Myerson, A. S. *Chem. Eng. Commun.* **2002**, *189*, 1079–1090

2012


nature chemical biology

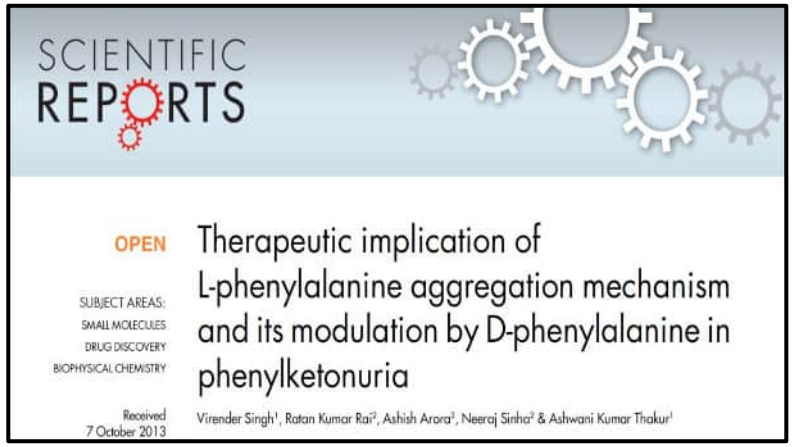
ARTICLE

PUBLISHED ONLINE: 17 JUNE 2012 | DOI: 10.1038/NCHEMBIO.1002

Phenylalanine assembly into toxic fibrils suggests amyloid etiology in phenylketonuria

Lihi Adler-Abramovich[1], Lilach Vaks[1], Ohad Carny[1], Dorit Trudler[2,3], Andrea Magno[4], Amedeo Caflisch[4], Dan Frenkel[2,3] & Ehud Gazit[1*]

2013


SCIENTIFIC REPORTS

OPEN

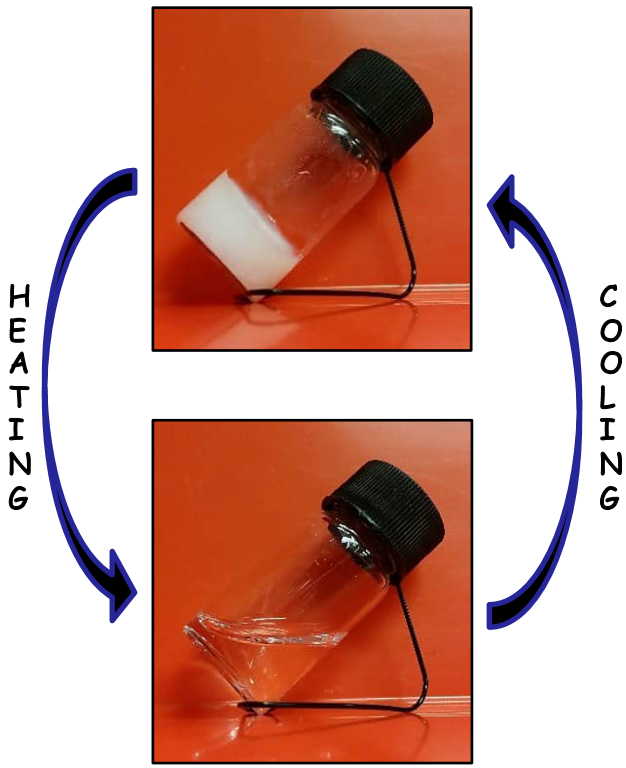
Therapeutic implication of L-phenylalanine aggregation mechanism and its modulation by D-phenylalanine in phenylketonuria

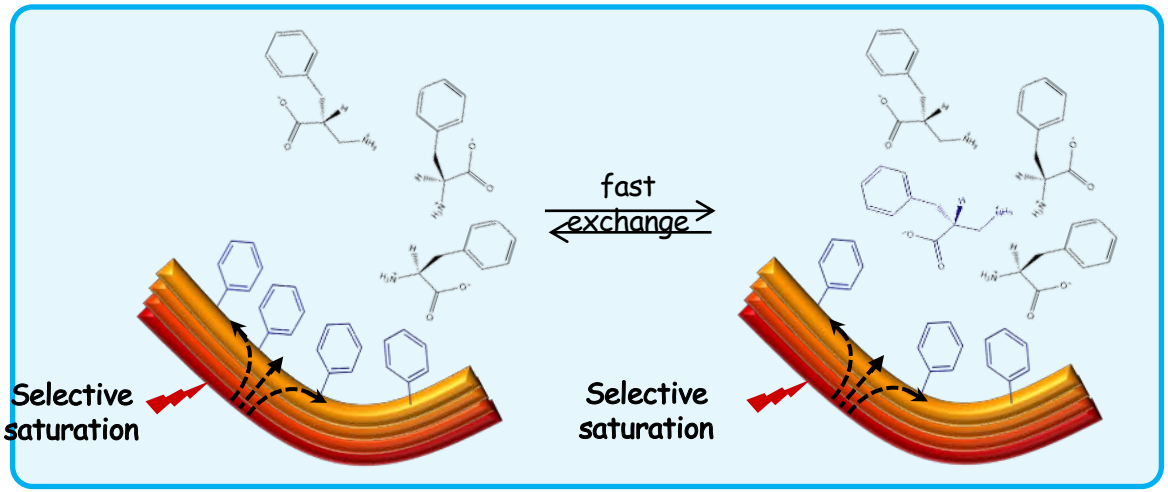
SUBJECT AREAS:
SMALL MOLECULES
DRUG DISCOVERY
BIOPHYSICAL CHEMISTRY

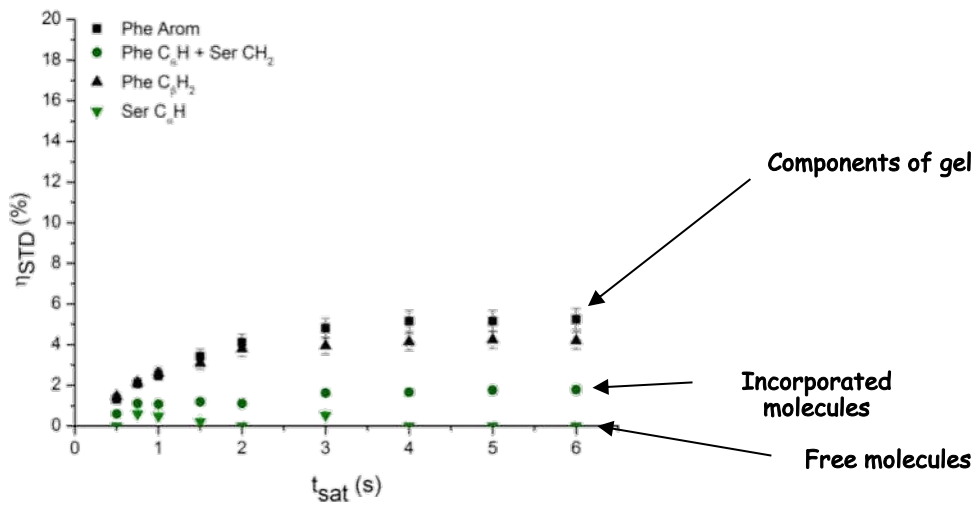
Received
7 October 2013

Virender Singh[1], Ratan Kumar Rai[2], Ashish Arora[3], Neeraj Sinha[2] & Ashwani Kumar Thakur[1]

Дослідження міжмолекулярних взаємодій в колоїдних системах



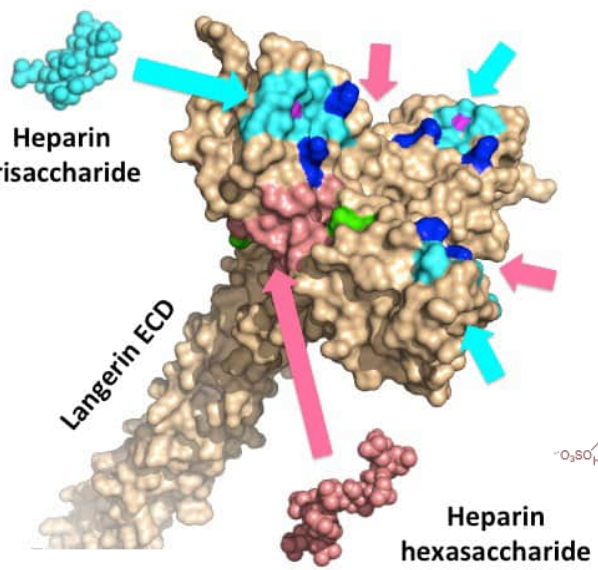




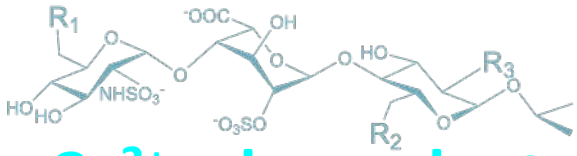
S. M. Ramalhete, *et al*.
Chem. Eur. J, **2017**, 23, 8014-8024

Дослідження бар’єру для інфекції СНІДу : **“Langerin Receptor”**

Langerin “recognizes” heparin molecule in two different ways DEPENDING ON THE SIZE of the heparin molecule

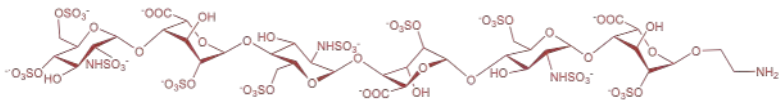


Small Heparin Molecules



Ca^{2+} - dependent

Large Heparin Molecules



Ca^{2+} - independent

Muñoz-García, J. C.; Chabrol, E.; Vivès, R. R.; Thomas, A.; de Paz, J. L.; Rojo, J.; Imberty, A.; Fieschi, F.; Nieto, P. M.; Angulo, J. *J. Am. Chem. Soc.* **2015**, *137*, 4100.

ALL SCIENCE IS INTERDISCIPLINARY – FROM MAGNETIC MOMENTS TO MOLECULES TO MEN

Nobel Lecture, December 8, 2003

by

PAUL C. LAUTERBUR

Biomedical Magnetic Resonance Laboratory, University of Illinois, Urbana, IL 61801, USA.

The title is not a tribute to some trendy hybrid field, but an introduction to a lecture on a Nobel Prize for Physiology or Medicine that is shared by a chemist and a physicist.

Few events could illustrate more clearly the blending both at the boundaries, and sometimes through the bodies, of our disciplines. For that is what they are, disciplines, not natural categories with rigid boundaries to be defended against intrusions, but guides to instruction and efficient administration.

Historically, the record is clear. Chemistry, for example, was cobbled together from mystical alchemy, metallurgy, physics, mineralogy, medicine, and cookery, eliminating incompatibilities as it evolved and consolidated into a more-or-less unified discipline. Physics has been formed, and enriched, by contributions from astronomy, mechanics, mathematics, chemistry, and other sciences. We have recently observed the rationalization of much of biology by chemistry, with the help of physics.

University of East Anglia: Norwich

Acknowledgements

UK high-field solid-state NMR facility

EPSRC
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UNITED KINGDOM

NMR in UEA: early days

First NMR spectrometer: Late 1950s

Varian 40 MHz spectrometer

Chairman of NMR DG

Ken Packer (1995-1997)

Robin Harris

Chairman NMRDG 1978-1981