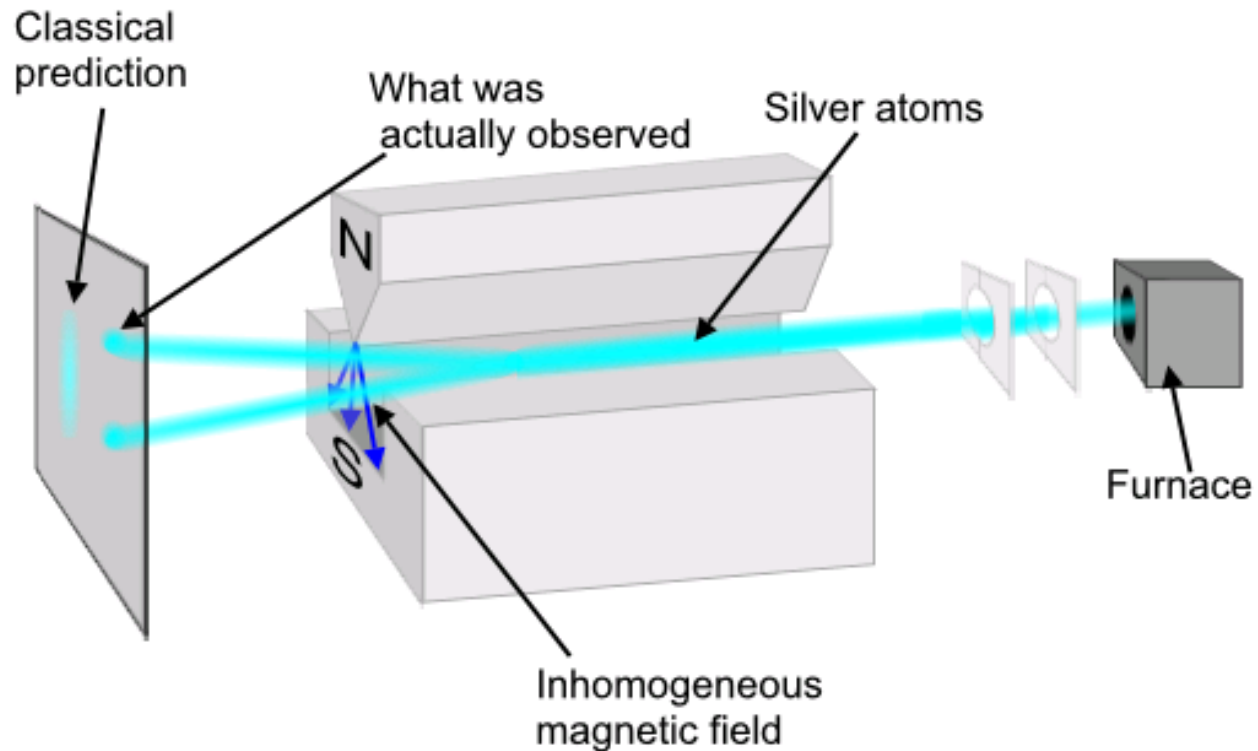


# **Structure Determination Using NMR**

“Basic One- and Two-Dimensional NMR Spectroscopy,”  
H. Friebolin,  
5th Ed.,  
VCH, 2010  
(ISBN 3527327827)



# Stern-Gerlach experiment





## Otto Stern

### **Discovered the Proton's Magnetic Moment**

Electrons and atoms can be regarded as rotating charges giving rise to a magnetic field. In a 1922 experiment, Otto Stern and Walter Gerlach sent a beam of silver atoms through an inhomogeneous magnetic field.

According to classical physics, the beam should have spread out to a distribution but instead, two distinct beams were observed. The result was in accordance with quantum physics: electrons and atoms occupy only certain states of energy and movement. Angular momentum was shown to be quantised.

# The Nobel Prize in Physics 1944



**Isidor Isaac Rabi**

1899-1989

**The Nobel Prize in Physics 1944**  
was awarded to Isidor Isaac  
Rabi "*for his resonance method  
for recording the magnetic  
properties of atomic nuclei*".

# The Nobel Prize in Physics 1952



Felix Bloch



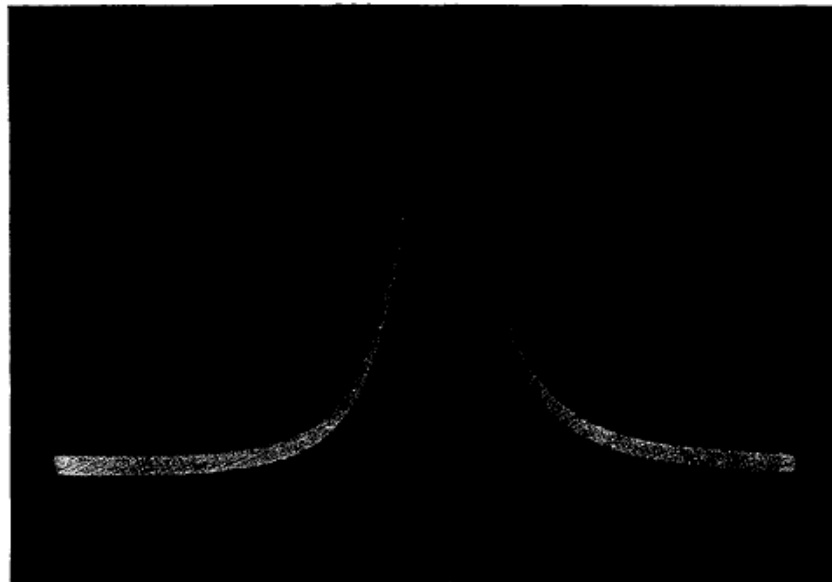
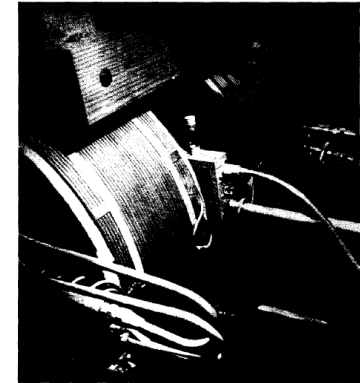
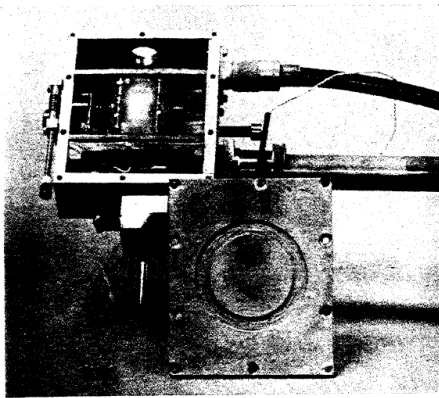
Edward Mills Purcell

**The Nobel Prize in Physics 1952 was awarded jointly to Felix Bloch and Edward Mills Purcell "for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"**

FELIX BLOCH

# The principle of nuclear induction

*Nobel Lecture, December 11, 1952*



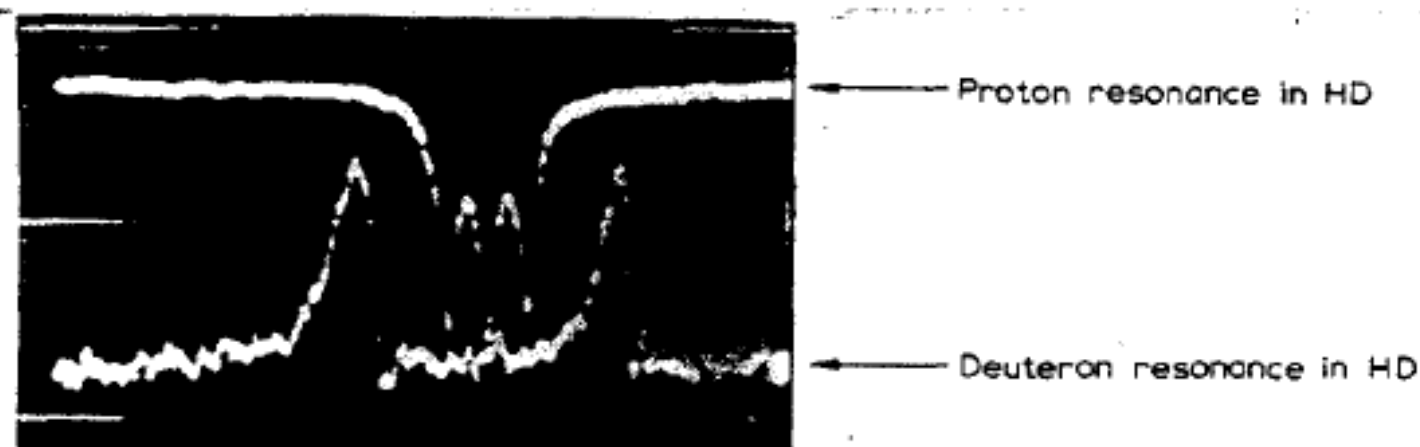
EDWARD M. PURCELL

## Research in nuclear magnetism

*Nobel Lecture, December 11, 1952*

Let us begin with the most direct application of nuclear induction methods, the measurement of nuclear magnetic moments. The basis for this is the resonance condition

$$f = \frac{\mu H_0}{Ih}$$



$$\frac{\mu(^2\text{H})}{\mu(^1\text{H})} = 0.307012189 \pm 30$$

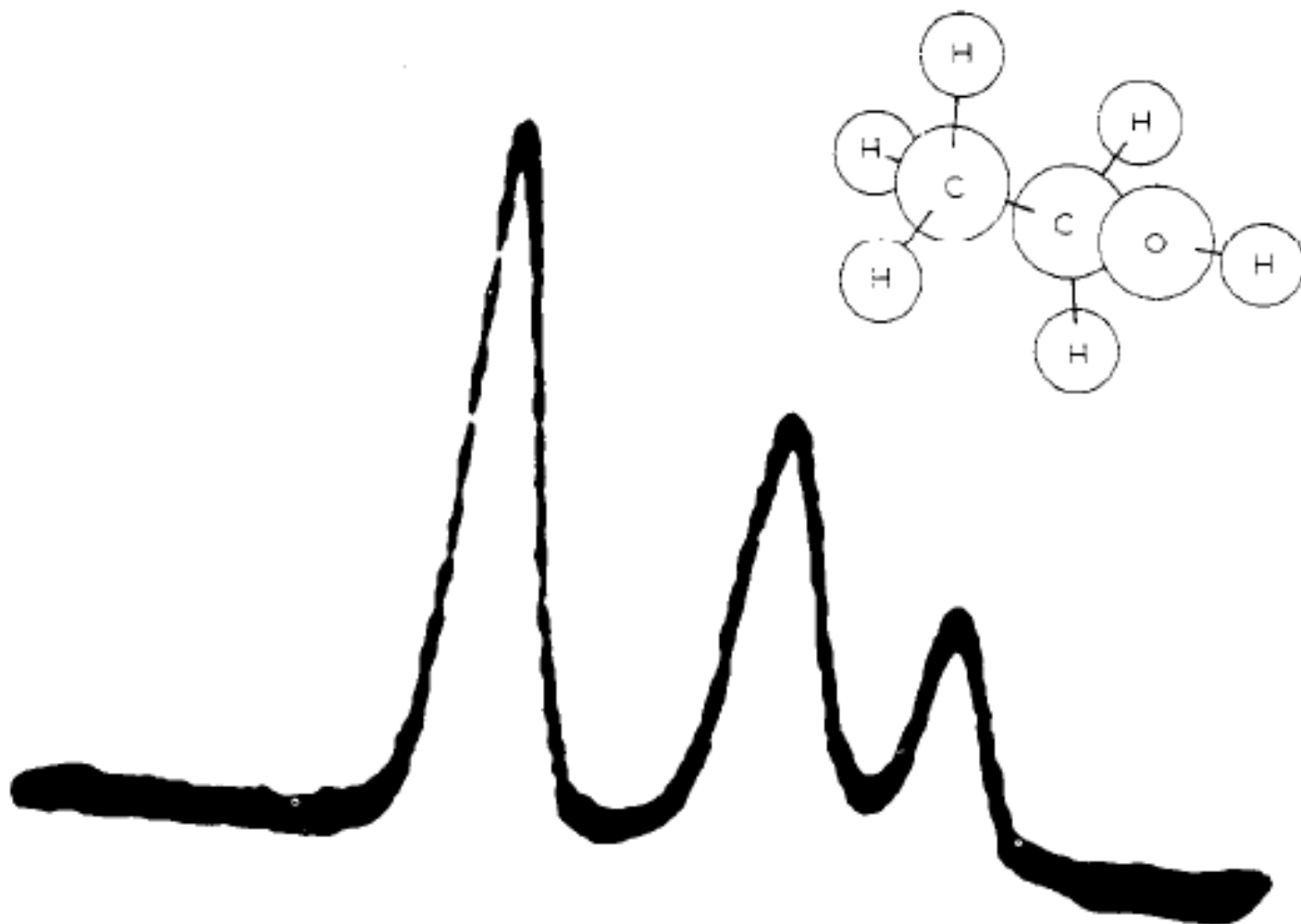


Fig. 6. The proton resonance in ethyl alcohol, observed with high resolution. The three lines arise from the CH<sub>3</sub>hydrogens, from the CH<sub>2</sub>hydrogens, and from the OH hydrogen, respectively.



## The Nobel Prize in Chemistry 1991



**Richard R. Ernst**

**Born:** 14 August 1933, Winterthur, Switzerland

**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"***

# NUCLEAR MAGNETIC RESONANCE FOURIER TRANSFORM SPECTROSCOPY

Nobel Lecture, December 9, 1992

by

RICHARD R. ERNST

Laboratorium für Physikalische Chemie, Eidgenössische Technische Hochschule, ETH-Zentrum 8092 Zurich, Switzerland

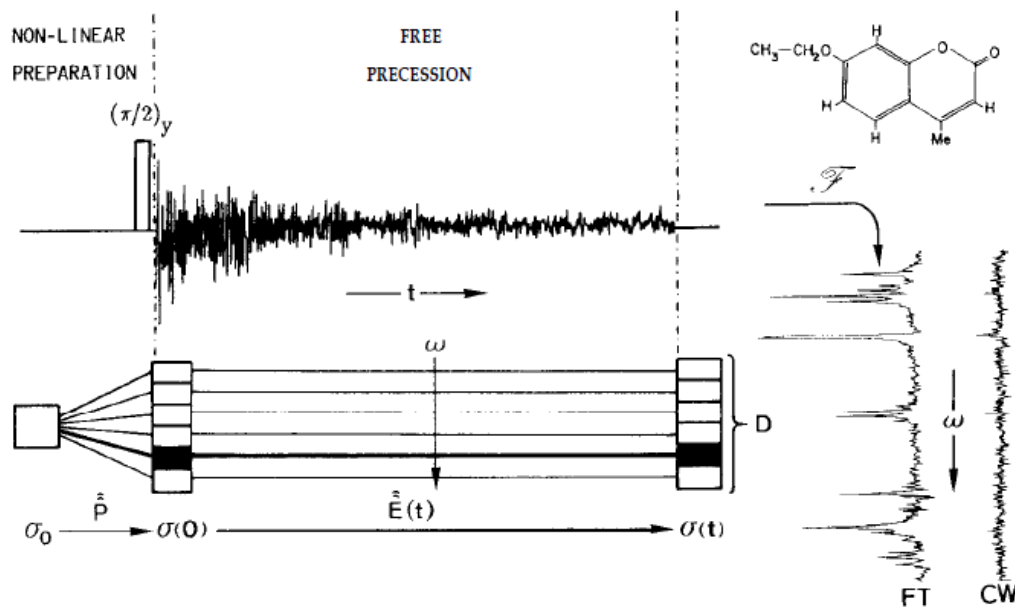


Figure 1. Schematic representation of pulse Fourier transform spectroscopy by the example of 60MHz proton resonance of 7-ethoxy-4-methyl-coumarin (22). An initial  $(\pi/2)_y$  pulse, represented by the rotation superoperator  $P$ , excites from the equilibrium state  $\sigma_0$  transverse magnetization  $\sigma(0)$ . Free precession of all coherences in parallel under the evolution superoperator  $E(t)$  leads to the final state  $\sigma(t)$ . Detection with the detection operator  $D$  produces the shown FID (sum of 500 scans) which, after Fourier transformation, produces the spectrum FT. For comparison, a continuous wave spectrum CW is shown that has been recorded in the same total time of 500 s under identical conditions.

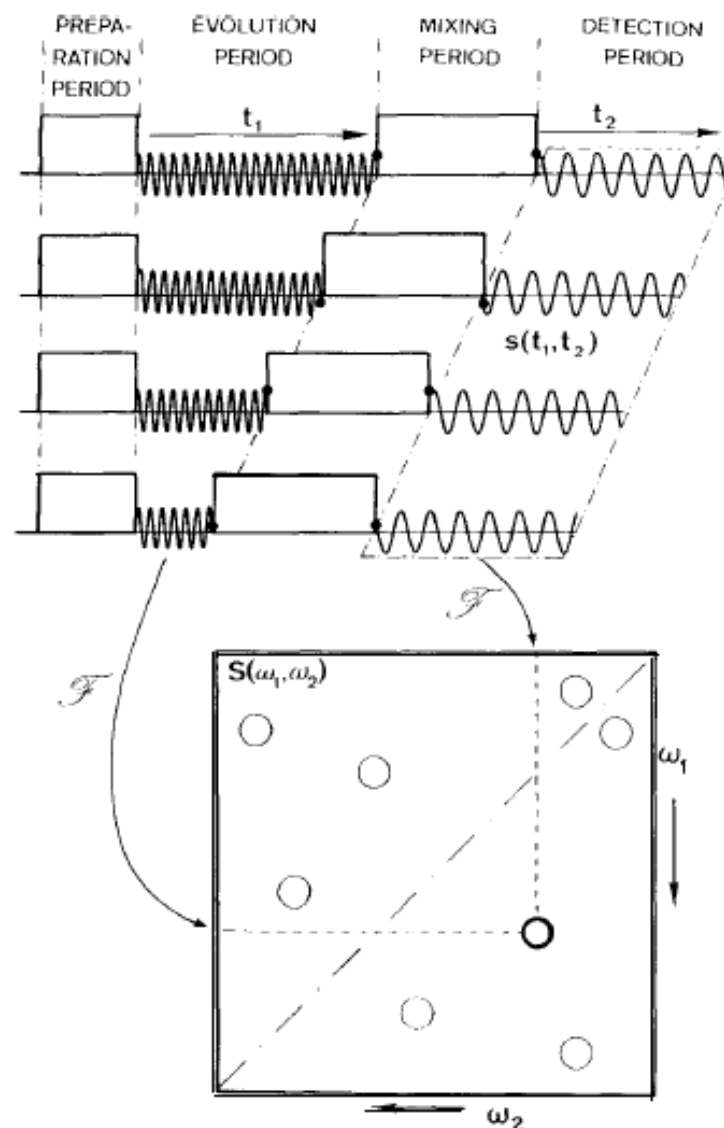


Figure 7. General 2D experiment consisting of a preparation, an evolution, a mixing, and a detection period. The duration  $t$ , of the evolution period is varied systematically from experiment to experiment. The resulting signal  $s(t_1, t_2) \propto \langle D \rangle(t_1, t_2)$  is Fourier-transformed in two dimensions to produce the 2D spectrum  $S(\omega_1, \omega_2)$ .

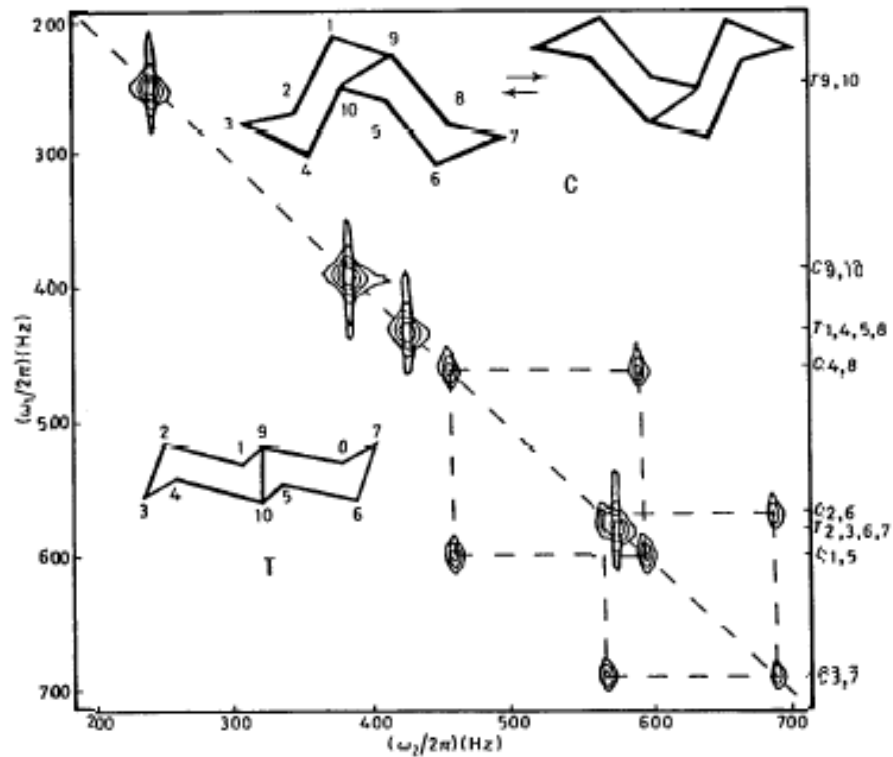
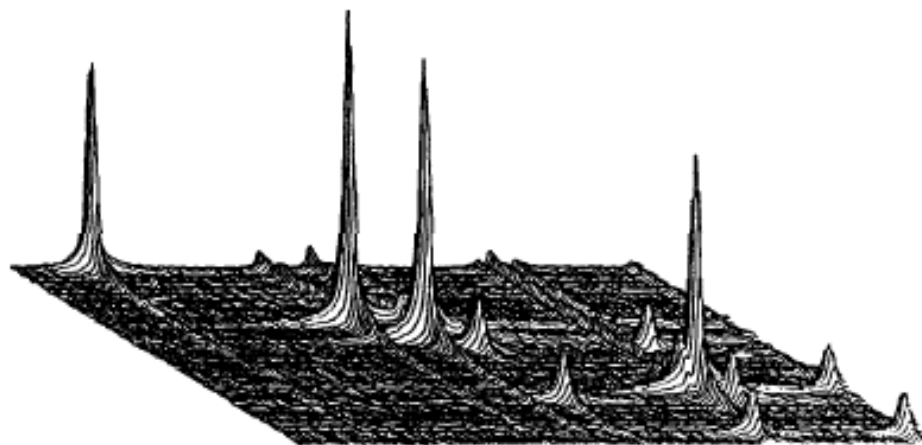


Figure 12. 2D  $^{13}\text{C}$  chemical exchange spectrum (EXSY) of a mixture of cis- and trans-decalin recorded at 22.5 MHz and 241K (76). A stacked plot and a contour representation are given with the assignment of the peaks.

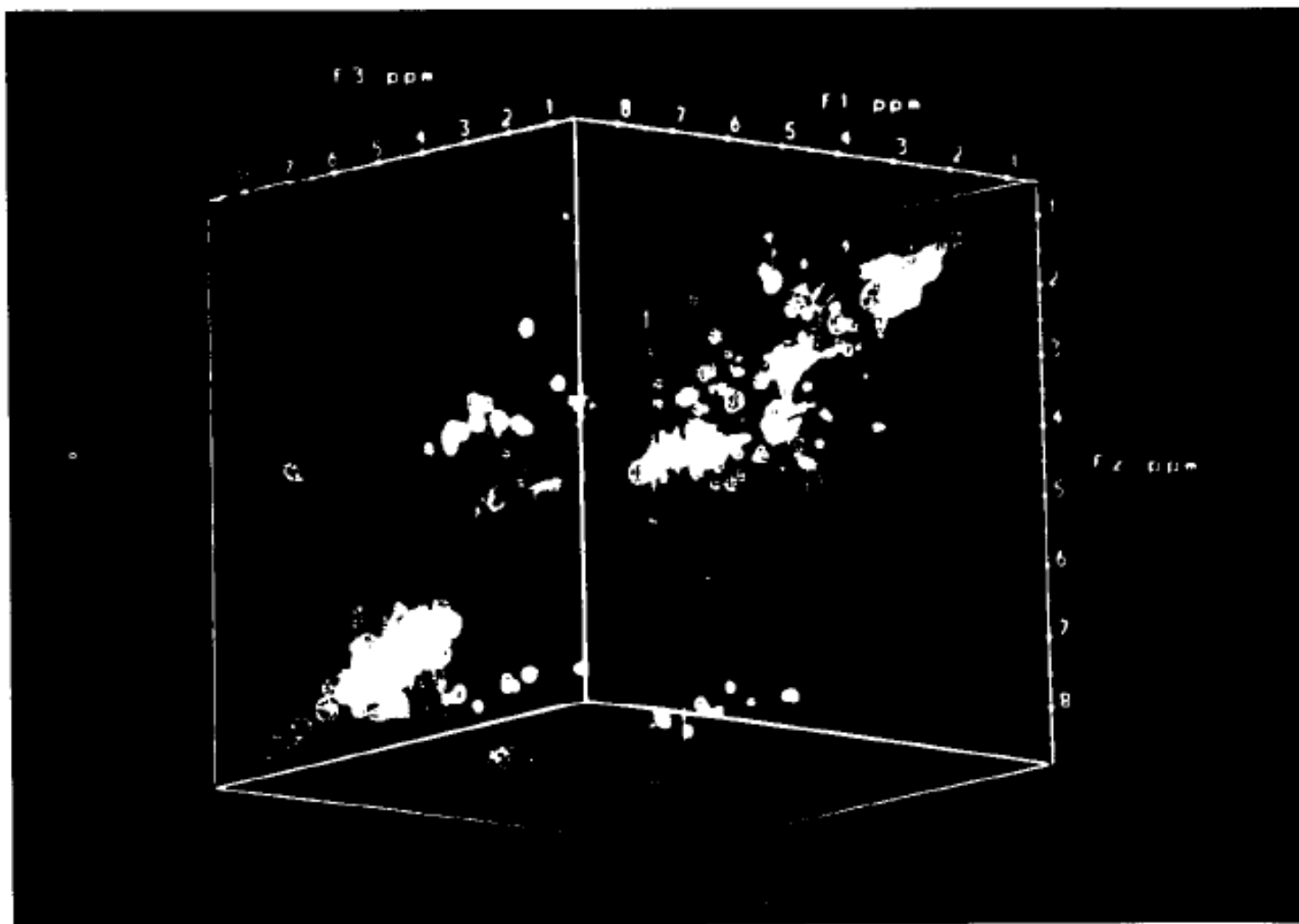


Figure 22. 3D view of a 300 MHz 3D homonuclear ROESY-TOCSY spectrum of buserilin in DMSO-d<sub>6</sub>, photographed from a picture system (116).

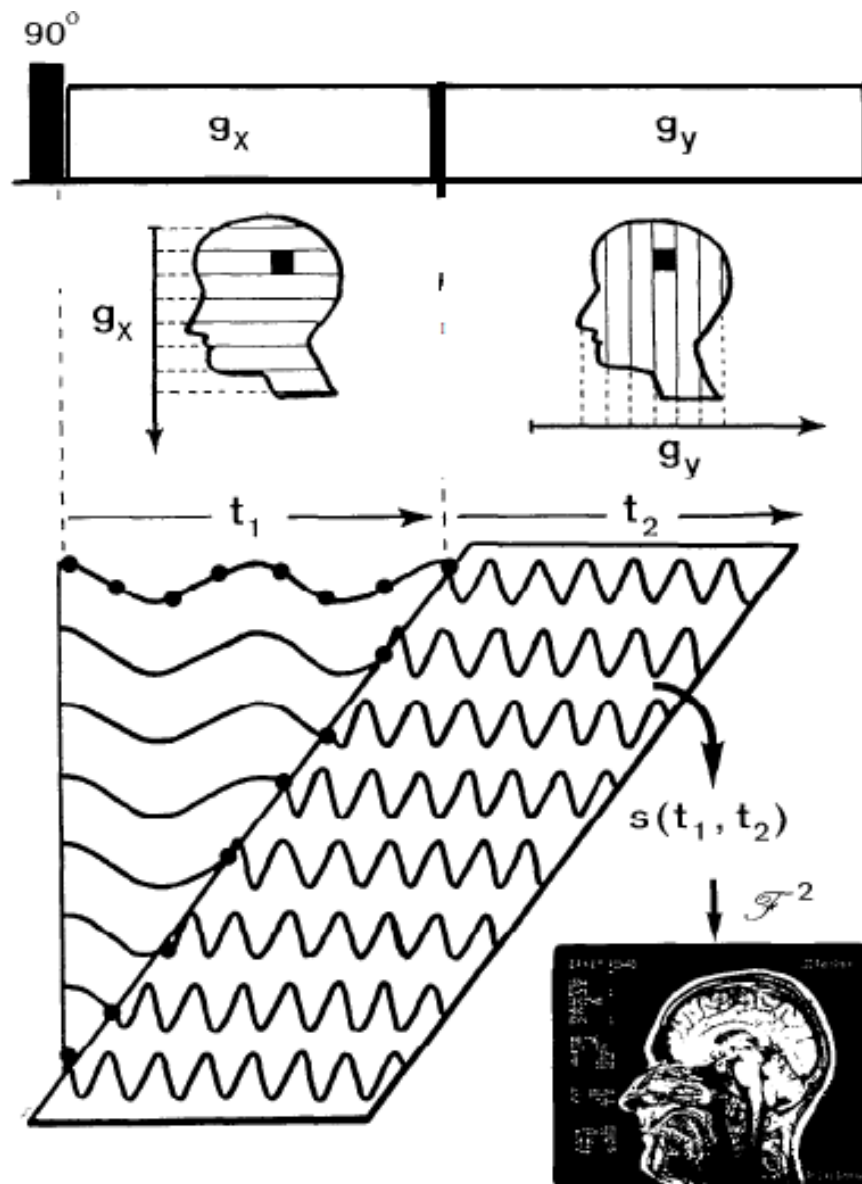


Figure 28. Schematic representation of Fourier NMR imaging, here shown in two dimensions. Two orthogonal gradients are applied during the  $t_1$  and  $t_2$  periods of a 2D experiment. A 2D Fourier transformation of the data set  $s(t_1, t_2)$  produces a 2D image of the investigated subject (R.R.E.).

## The Nobel Prize in Chemistry 2002



John B. Fenn



Koichi Tanaka



Kurt Wüthrich

**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".**

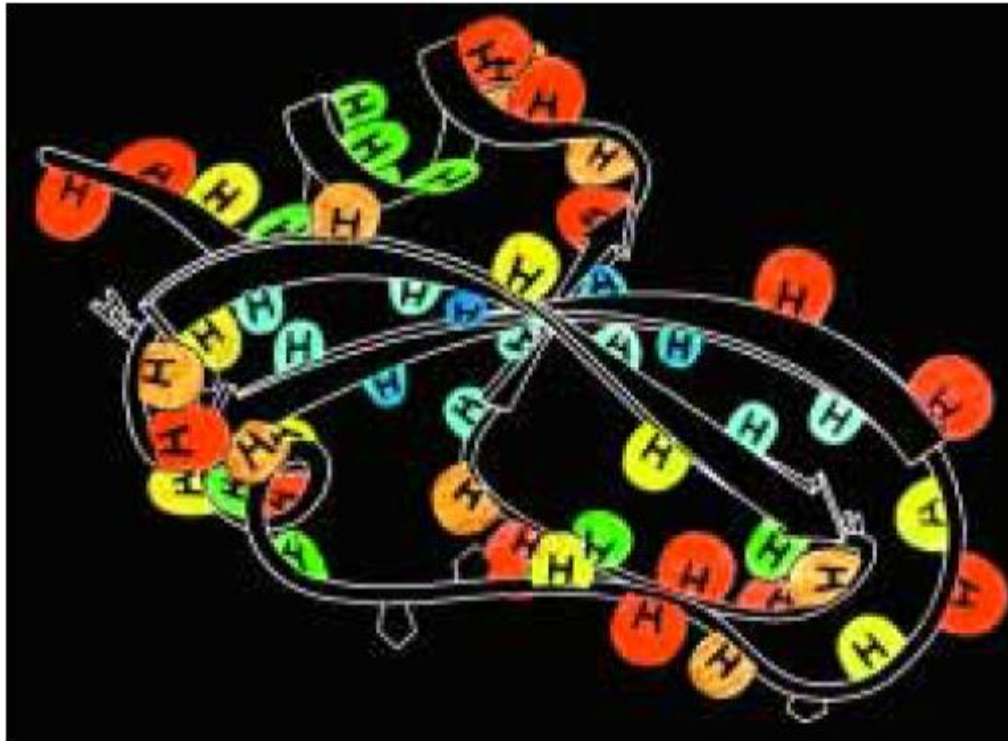
# NMR STUDIES OF STRUCTURE AND FUNCTION OF BIOLOGICAL MACROMOLECULES

Nobel Lecture, December 8, 2002

by

KURT WÜTHRICH

Eidgenössische Technische Hochschule Zürich, CH-8093 Zürich, Switzerland, and The Scripps Research Institute, 10550 N. Torrey Pines Rd., La Jolla, CA 92037, USA.



*Figure 21.* Complete sequence-specific resonance assignments for BPTI obtained using 2D NMR experiments (34). Assigned residues are identified by coloured patches covering their amide protons. (The colour code indicates variable amide proton exchange rates; drawing by Jane Richardson, 1982).



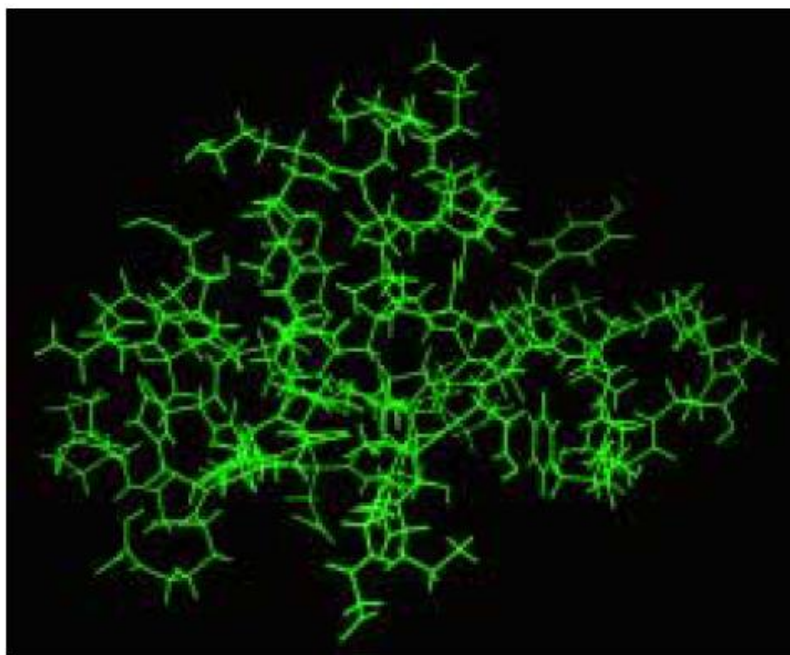


Figure 25. NMR structure of BUSI IIA (43).

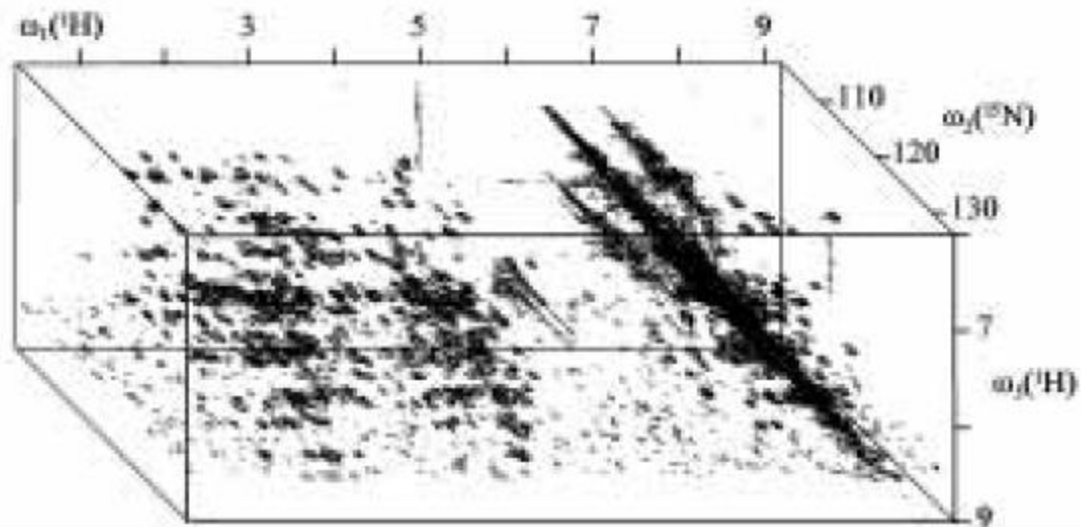


Figure 26. Three-dimensional (3D)  $^{15}\text{N}$ -resolved  $[\text{}^1\text{H}, \text{}^1\text{H}]$ -NOESY spectrum (600 MHz,  $28^\circ\text{C}$ ,  $\text{H}_2\text{O}$ -solution) of the DNA-binding domain of the P22 c2 repressor ( $M \approx 10000$ , uniformly  $^{15}\text{N}$ -labeled).

## Students, Research associates, Technical staff 1970–2002

Werner Hündemann	Nilsu Lotfi	Felix Siroo	Daniel Schuster	Berthold von Freyberg	Gerrard Frank	Jocelyne Flass
Jean-Paul Mervill	Kunihiko Nagayama	Dominique Marlot	Manuel Güseer	Edvards Lepins	Walter Siller	Luigi Giamberini
Andri Mazon	Kathrin J. Parkins	Six R. F. Zuidenweg	Denis D. Rademé	Johanna Blatter	Kristianita Fernandis	Regina Vold
Regula M. Keller	Stephen L. Gordon	Franciska Quentessutti	Francesco Riva	Miguel S. Gil	Rosemarie Hug	Reto Hone
Jan Götz	Lothi Rutt	Arthur Paroli	Hideyuki Hirayama	John F. O'Donnell	Cybil Arnet	Dangshan Lee
Rudolf Baumann	Andreas Dulle	Kenneth R. Mills	Daniel Reusser	Barbara Leising	Richard Blak	Koba Akelahwi
Bernard Dorsey	Daniel Flood	Timothy Nivali	Bernard Ts. Farnet S.	John H. Susswetter	Francisco Lopez-Garcia	Christophe A. Lysek
Jill Hochmann	Werner A. Braun	Michael P. Williamson	Christoph Weber	Toshioji Masuda	Martin Wahl	Sushra Banerjee
Christopher Gschwend	Hansrich Rader	Paula Y. Watnick	Hui Dingxin	Martin Sponck	Jifan Wu	Christoph Hillig
Kasper Eiler	Albert Eugster	Marin Hasler	Peter Ganten	Waltero Anzuch-Barris	Ralf Gasser	Stefan Hurney
Robert Heisel	Gerthard Weber	Daniel Hausman	Francesco Avella	Peter Laglerich	Wenjun Liu	Richard L. J. Keller
Gabriele Kutz	Christoph Briner	Peter Schultze	Takuo Eki	Christian Bortone	Michael Salzer	Giampaolo Parda
Jolan M. Tangirala	Chik Brown	Hans Widmer	Leonard P. M. O'Brien	Valter Cellach	Alexander G. Sobol	Lark Under
Andreas Garbel	Adela Chorosowich	Walter Lauth	Barbara Mazzanti	Stigi Moringo	Fred F. Dandinger	Beat Wigger
Antoinette Schwaninger	Markus Meier	Sabine Ekin	Craig D. Eccles	Jan Johannes	Chih-yen King	Toung Emswary-Ekharjari
Kurt Goller	Subodhaya Ramaprasad	Reto Maroni	Yanping Chen	Gregg Siegel	Bayden Bennett	Christian Scherr
Harald Wagner	Subashini Go	Walter J. Chazin	Dario Neri	Oliver Scholl	Yves-Laurent Viallet	Francesca Florio
Arno Buntl	Shika Go	Michael H. Frey	Hervé Darbon	Wilhelm Scheibel	Ralph Zahn	Pascal Battersdorf
Maurice Desobry	Johannes Scheffler	Wolfgang Denk	Hugo Amacker	Gabriel Hänggi	Michel Hochuli	Sonora Hemmerlin
Peter Sahr	Markus Schmidiger	Sean Hyberts	Wolfgang Kessel	Reto Kersch	Shin-ichi Taka	Vibert Estève Moya
Aaron J. Gibson	Hans Sassi	Stefried Dilling	Ivan Vranesic	Hilario Kordeck	Oliver Ulrich	Valmir Padel
Miguel Linares	Wayne S. Steinwand	Alan D. Kline	Kandata V. R. Chary	Marsal Origer	Jörg Probst	Hart A. Boker
Antonio De Marco	And Kuehn	Alexander M. Lehnerdt	Daniel Braun	Ralph Gaurke	Tian Y. Tang	Holger Toller
Hans-Ulrich Gremlich	Yvonne Hansler	Gustavo Mantelero	Geert Wuyver	Ralph Götts	Thorsten Lohrs	Alvar Godean
Wolfgang Meier	Sachio H. Yamaki	Charles Wynne	Fabrizio Badano	Serge Abbramo	Christine von Salzenberger	Lucas Hone
Larry S. Brown	Sören Huber	Thomas Schaubert	Martin Bos	Mauro Palleuchio	Roberto Fattorusso	Sebastian Hiler
Reto Richard	Fred Stücki	Phonchai Smit	Marie-Paule Saville	Giovanni Ferencik-Estraben	Hans-Joachim Dreier	Ida Aebi
Alexandra S. Frey	Ole Telenius	Green Wong	Agostino Fedu	Christian Mumenthaler	Richard Wüster	Yvonne Auerli
Christopher Bösch	Martin Schäfer	Bruck Wengeler	Joseph Verdrell	Oliver Zerbe	Martin Gahr	Daniel Pérez
Vincent Vill	Stefanien Masure	Wolfram Müller	Thomas A. Szeperski	Silke-Hilke Fritzsche	Samira Zangger	Martina Wüthrich
Lee Sze-Hing	Kong-Hung Lee	Luigi Jorrig	Kurt Bernli	Hideo Imai	Torsten Hemmerlin	Sabine Allen
Jürgen Lütjens	Ramkrishna Misra	Bernardo Celsis	Gian Spillmann	Oliver Christenberger	Kai Schree	Gabriele Ann
Peter Bachmann	Alexandra Antoniou	Rolf Gruber	Jonathan M. Moore	Ralf Bruchhals		

Figure 36. My collaborators at the ETH Zürich from 1970 to 2002.

## The Nobel Prize in Physiology or Medicine 2003



**Paul C. Lauterbur**



**Sir Peter Mansfield**

**The Nobel Prize in Physiology or Medicine 2003 was awarded jointly to Paul C. Lauterbur and Sir Peter Mansfield *"for their discoveries concerning magnetic resonance imaging"***

# 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.

That evening, over dinner, it occurred to me that, as the frequencies of NMR signals depended on the local magnetic field, there might be a general way to locate them in a non-uniform magnetic field. I knew, however, that a static field could not have a unique value in each location in three dimensions, but that a complex shape could be represented by an expansion in a set of functions such as those provided by the correction, or “shim” fields, available on NMR machines to cancel unwanted magnetic field non-uniformities, term by term, with linear gradients, quadratic ones, etc. Could this be the an-

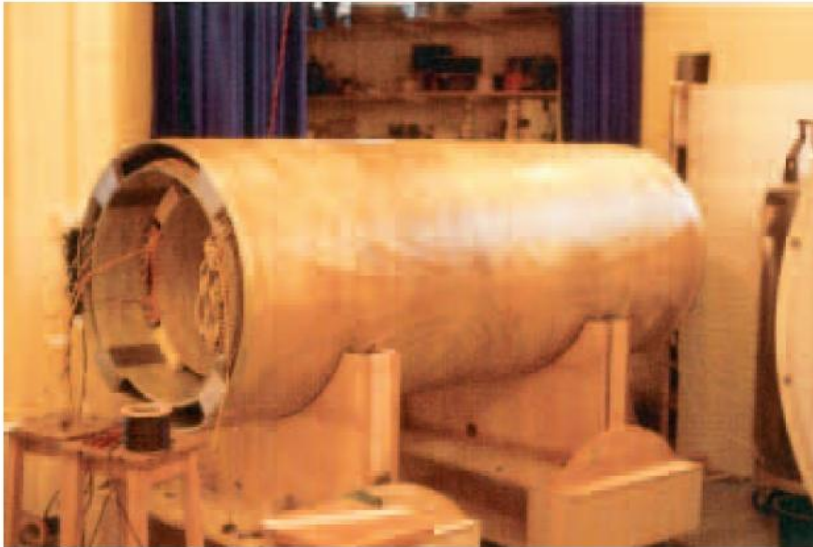
# SNAP-SHOT MRI

Nobel Lecture, December 8, 2003

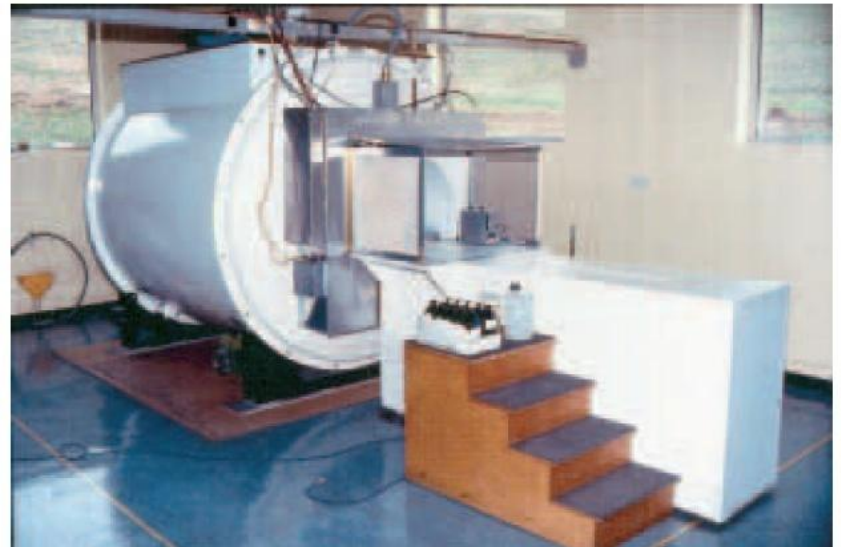
by

PETER MANSFIELD

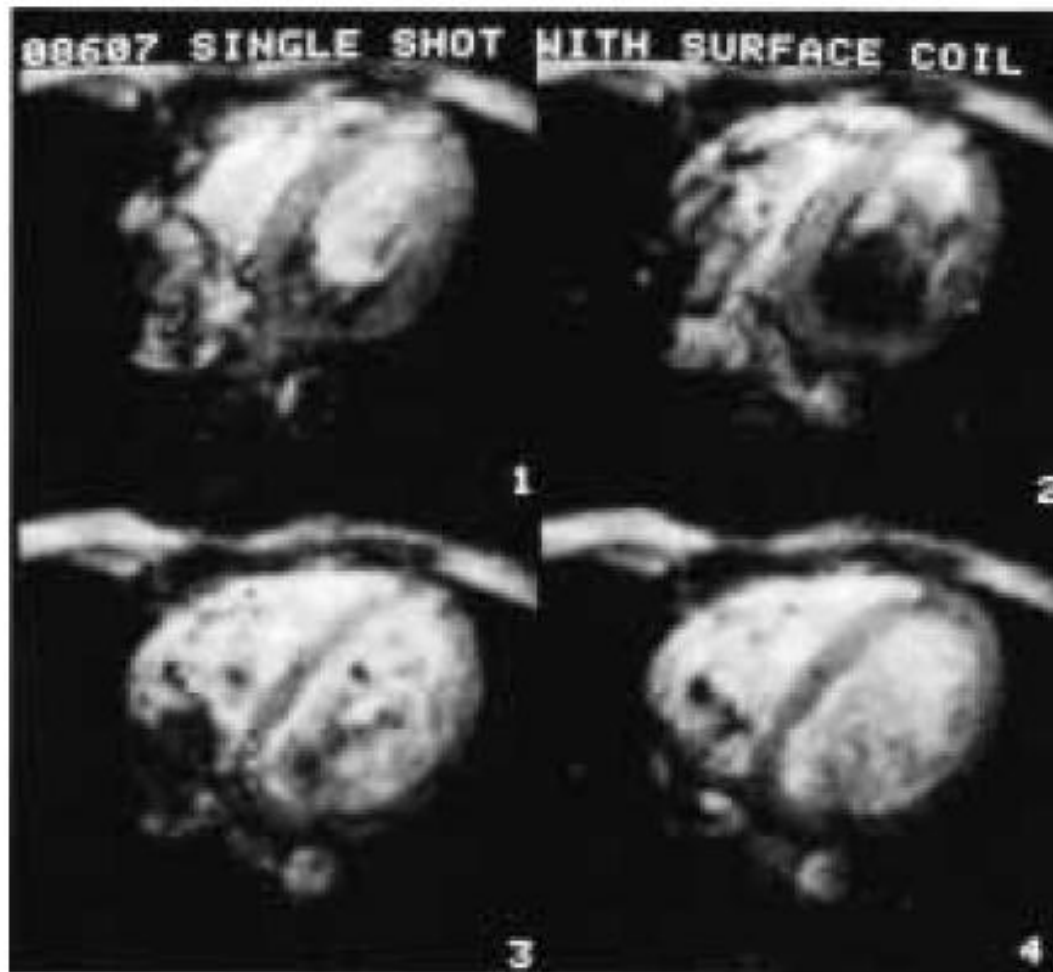
Sir Peter Mansfield Magnetic Resonance Centre, Department of Physics  
and Astronomy, University of Nottingham, Nottingham, NG7 2RD, U.K.



*Figure 2.* Photograph of a doubly screened active magnetic shielded gradient coil set for insertion in the super-conductive magnet of Figure 1.



*Figure 1.* Photograph of home built magnetic resonance imager based on a 0.5 T super-conductive magnet.



*Figure 5.* Snap-shot EPI images through the heart obtained with use of a surface coil. (1) Transection during systole shows left ventricular myocardial wall thickening. (2) Rapid ventricular filling in late systole. (3, 4) Transections obtained during diastole show thinner myocardial walls. The spatial resolution of these images is less than 2 mm. (Reproduced with permission from M J Stehling *et al.*, *RADIOLOGY*, 170: 257-263, (1989).)