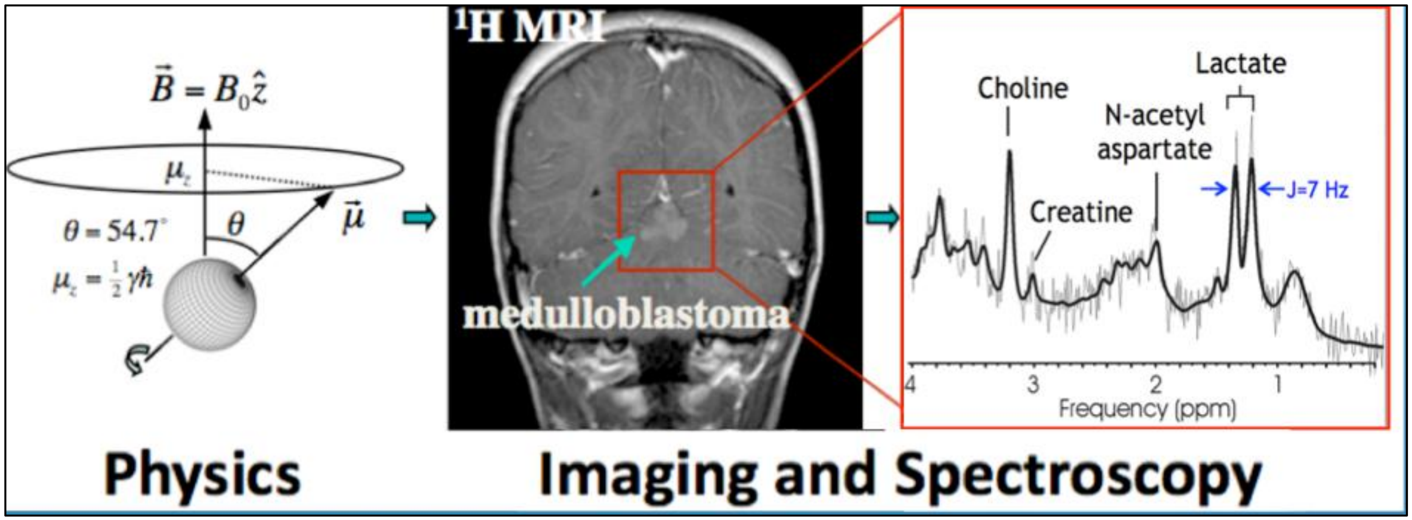
Rad 226a/BioE 226a

Winter 2018-2019

In Vivo MR: Spin Physics and Spectroscopy



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Limitations of Non-interacting Classical Model

- Relaxation
  - Tissue T_1, T_2, and $T_{1\rho}$
  - Anisotropic tissues
- Nuclei other than ^1H
- Chemical exchange effects
- Molecules more complicated than water

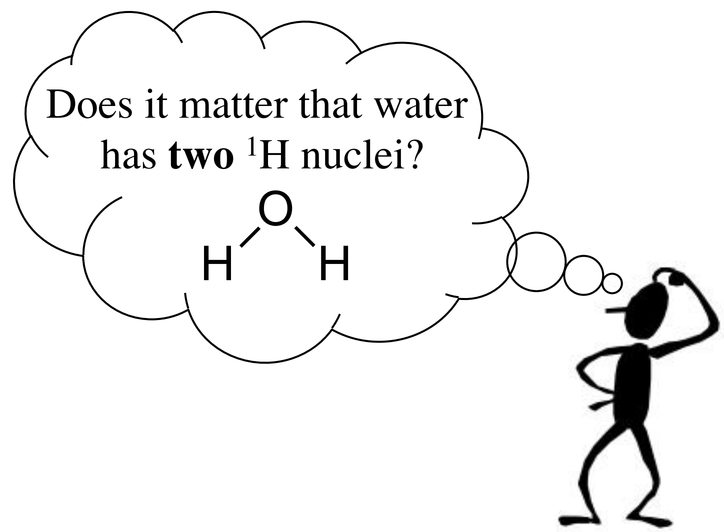
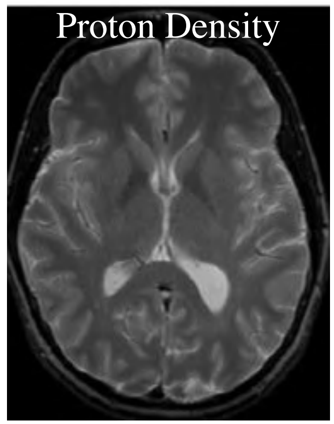
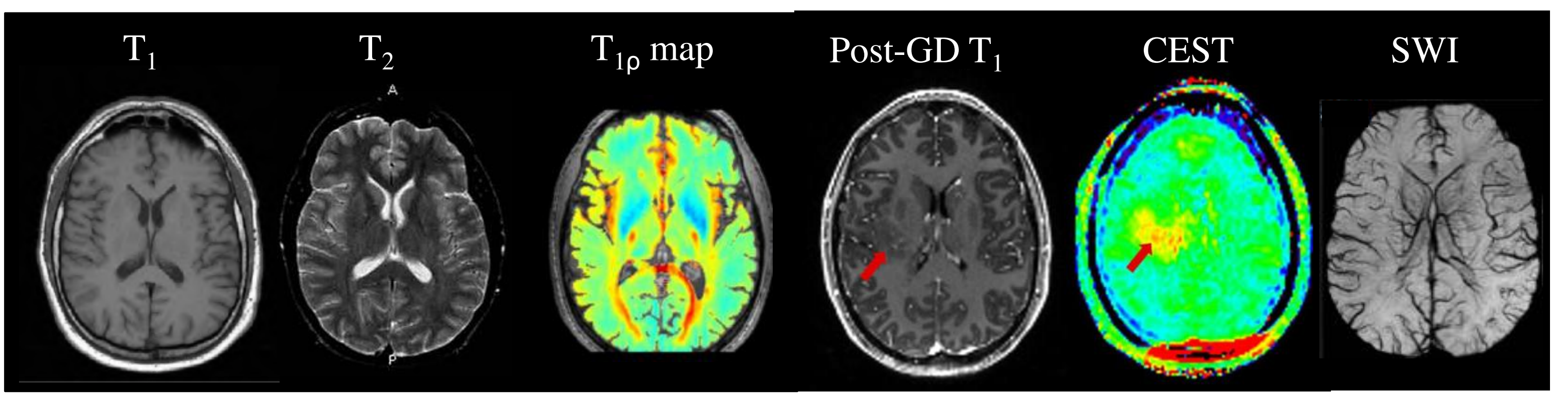


Image Contrast

- Clinical MRI primarily images water. Why do different tissues exhibit different MRI contrast? Are difference solely due to water content?





Lecture #1
Introduction

- Topics
  - Administrative details
  - Course Overview and Motivation
  - Some interesting *in vivo* MR phenomena
- Handouts and Reading Assignments
  - Biographies: Rabi, Purcell, Bloch

Course Administration

- Lectures
  - Tues, Thurs 3:00-4:20 pm, Lucas Learning Center P-069
  - 3 units
- TA
  - ??
- Office Hours
  - To be determined, Office: Lucas Center PS061
  - or by arrangement with instructor (email: spielman@stanford.edu)
- Web site
  - http://web.stanford.edu/class/rad226a/
  - Lecture notes, homework assignments, other handouts (pdf files)

Course Materials

- Recommended Texts
  - F. van de Ven, *Multidimensional NMR in Liquids*, Wiley-VCH, New York, 1995.
  - R. de Graaf, *In Vivo NMR Spectroscopy, 2nd Edition*, Wiley & Sons, Chichester, UK, 2007
- Additional references (not required, but very useful!)

MRI ⇒ • D. Nishimura, *Principles of Magnetic Resonance Imaging*, EE369b notes

Physics ⇒ • M. Levitt, Spin Dynamics, Wiley, Chichester. UK, 2001

QM ⇒ • D. Miller, Quantum Mechanics for Scientists and Engineers, Cambridge Univ. Press, 2008.

Physics ⇒ • C. Slichter, Principles of Magnetic Resonance, Springer, Berlin, 1996.

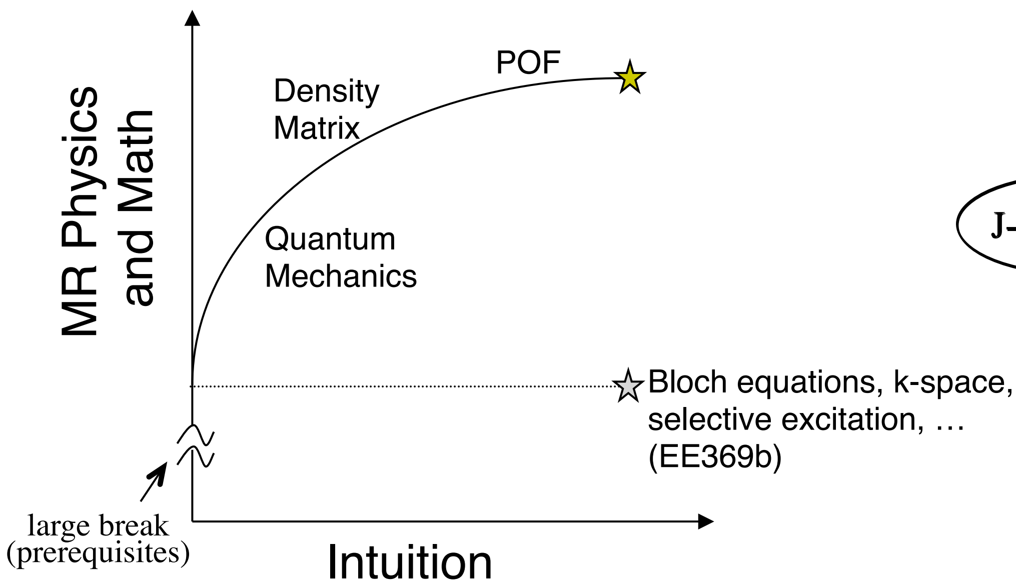
Assignments and Grading

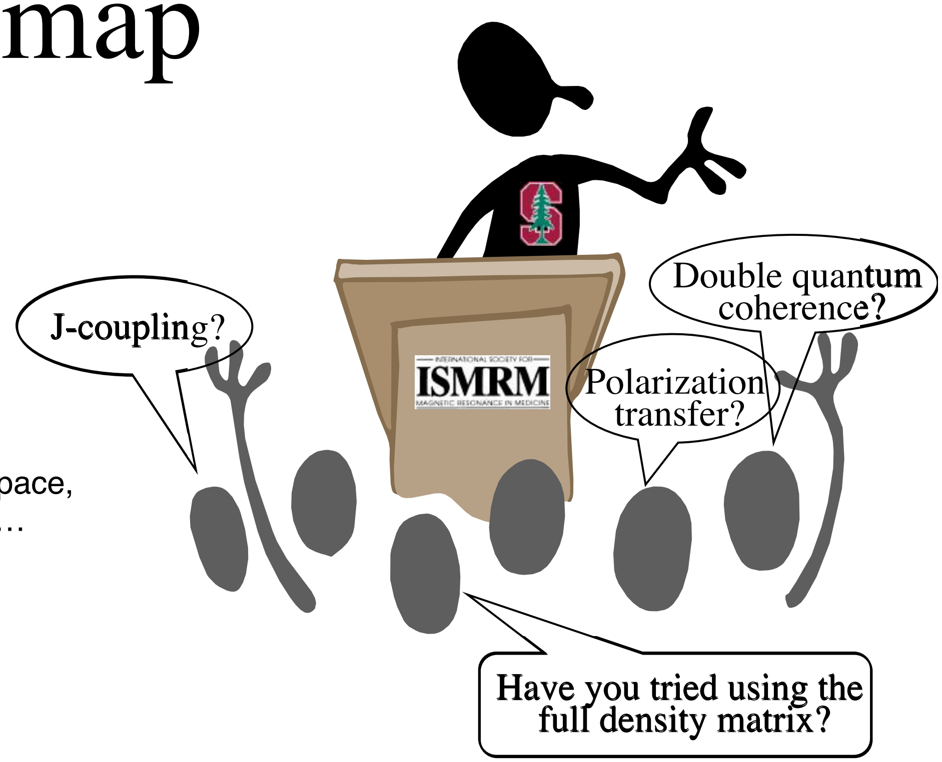
- Weekly problem sets (90%)
- Class participation (10%)
- No Midterm or Final

Overview

- Main Themes:
  - Classical vector model of MRI/MRS doesn’t fully explain many important *in vivo* processes, particularly those involving interactions among spins.
  - Nuclear-nuclear interactions
  - Nuclear-electron interactions
  - We’ll discuss the physics and engineering principles of these phenomena with examples from current research topics and clinical applications.
- Prerequisites
  - EE369b or familiarity with MRI (i.e. Rf pulses, gradients, pulse sequence diagrams, k-space)
  - Working knowledge of linear algebra

Roadmap



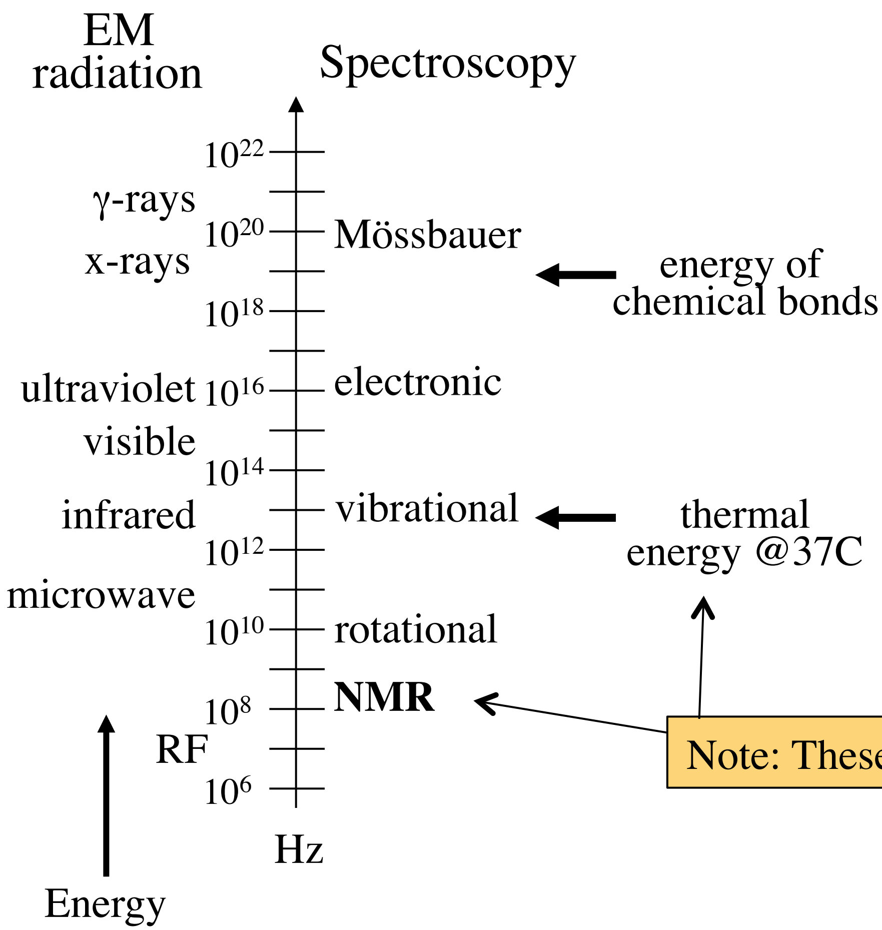


Topics

1. Introduction and Review (2 weeks)
2. Quantum mechanics for NMR (2 week)
3. Density Matrix (1 week)
4. Product Operator Formulism (1.5 weeks)
5. ^{1}H MRS (1.5 weeks)
6. Decoupling (stealth lead-in to relaxation theory) (1 week)

Spectroscopy

- In general, spectroscopy is the study of materials via interactions with electromagnetic fields



Note: These differ by several orders of magnitude!

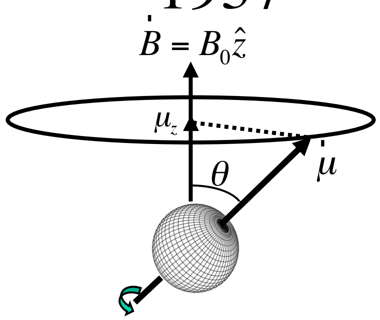
NMR and Molecular Spies

While molecules are too small to observe directly, magnetic nuclei make ideal probes:

- Very sensitive to the local magnetic fields
- Interact extremely weakly with their environment permitting virtually perturbation-free measurements
- Spatially localized

NMR: A Short History

Discovery of NMR
1937



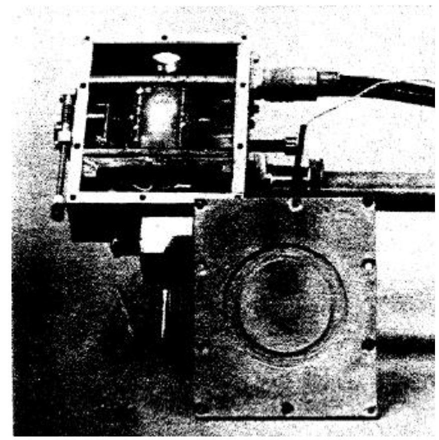
$$\theta = 54.7^\circ,\ I = \tfrac{1}{2},\ m = \tfrac{1}{2}$$

$$\mu_z = \tfrac{1}{2}\gamma\hbar,\ |\vec{\mu}| = \tfrac{\sqrt{3}}{2}\gamma\hbar$$

I.I. Rabi

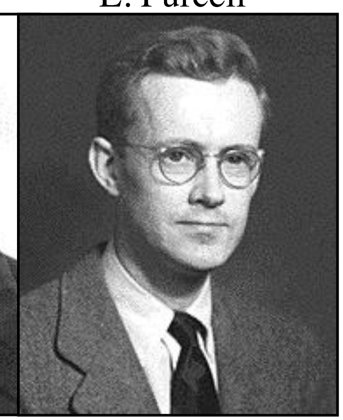
Nobel Prize Physics
1944

NMR in Condensed Matter
1945



F. Bloch

E. Purcell

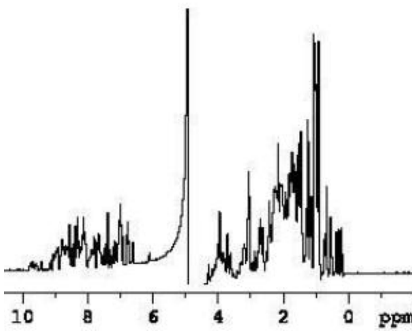


Nobel Prize Physics 1952

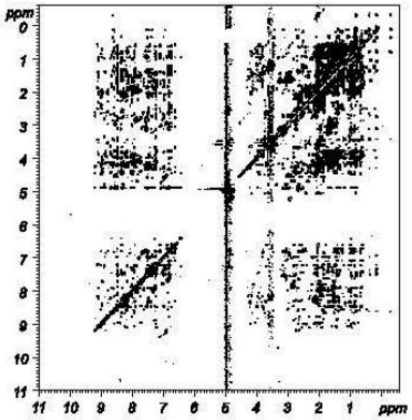
NMR: A Short History

FT-NMR, 2D Spectroscopy
1966-1970s

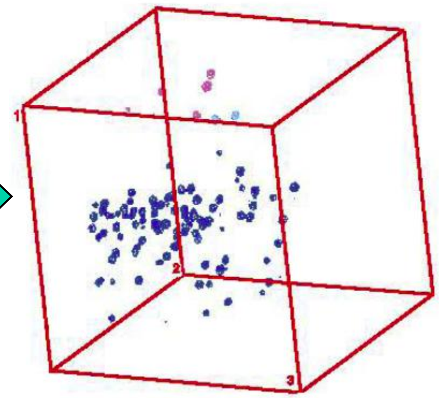
Determining 3D structures of biological macromolecules
1980s



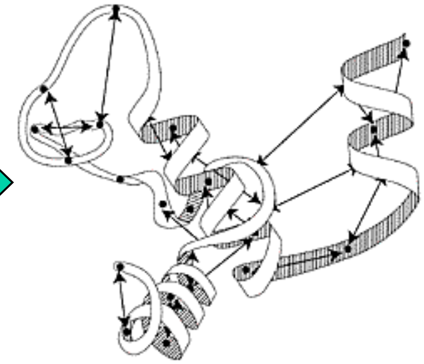
1D Spectrum



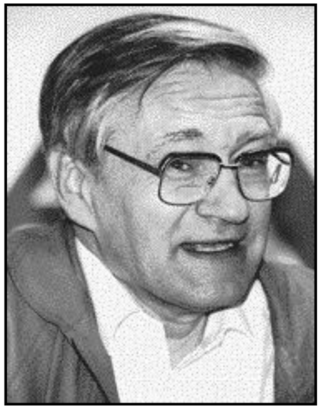
2D Spectrum



3D Spectrum



R. Ernst



Nobel Prize Chemistry
1991

K. Wüthrich

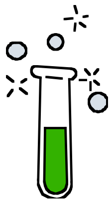
Nobel Prize Chemistry
2002

NMR in the Chemistry Laboratory

- Types of NMR spectroscopy experiments
  - – High resolution studies of liquids ← most relevant for in vivo studies
  - – Solid state NMR (e.g. magic angle spinning)
  - – Studies of substances (or nuclei) with broad resonance lines
- Types of Questions
  - – What is it?
  - – What is the structure?
    - bonding connectivity
    - spatial connectivity
    - molecular conformation
  - – What are the dynamics?

SMRL

In Vivo MRS/MRI



pure liquid — tissue — crystalline solid

- Complex mixture of stuff – water, lipids, metabolites, etc
- Physiological processes

P. Lauterbur

P. Mansfield

Nobel Prize: Medicine 2003

- Types of Questions
  - Where is it?
  - How much?
  - What are the dynamics?
    relaxation times
    chemical processes

MRI

- Standard analysis based on a water signal made up of many independent (non-interacting) nuclei + phenomenological T_1 and T_2 relaxation times.
- Leads to very powerful approaches (e.g. k-space) that adequately explain the bulk of MRI techniques and applications.

Limitations of Non-interacting Classical Model

- Relaxation
  - Tissue T_1, T_2, and $T_{1\rho}$
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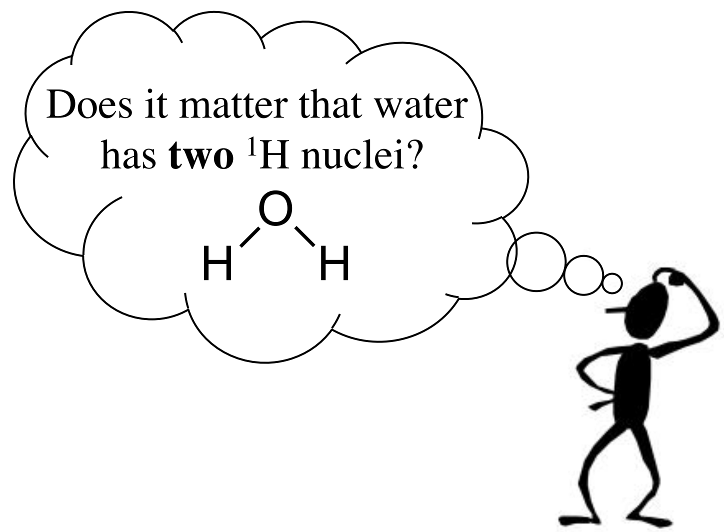
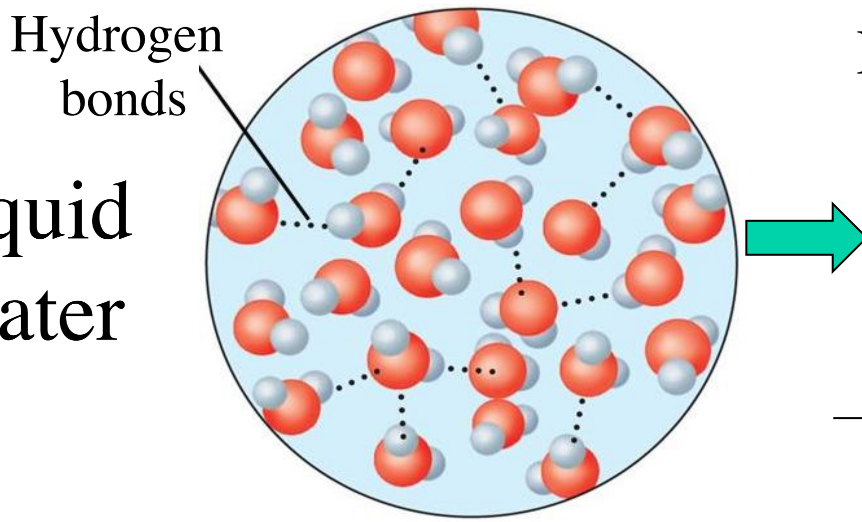
- Nuclei other than ^1H
- Chemical exchange effects
- Molecules more complicated than water

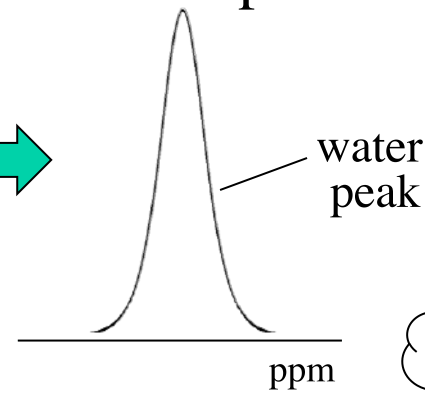


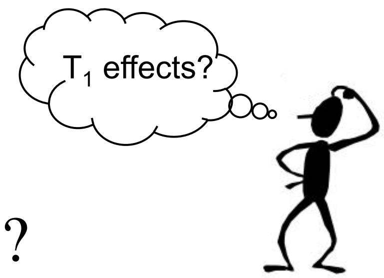
Example: Temperature effects

Liquid water



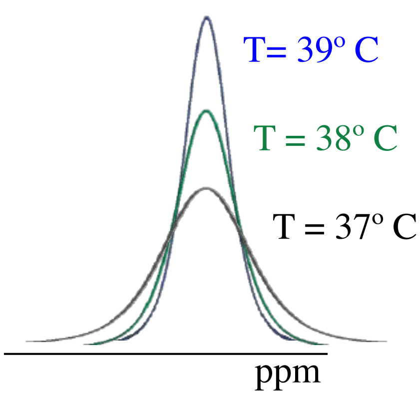
NMR Spectrum



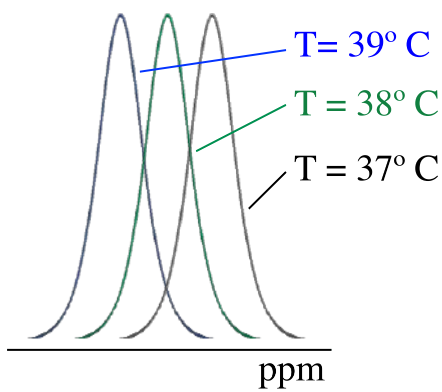


Which is the correct model for the effect of temperature?

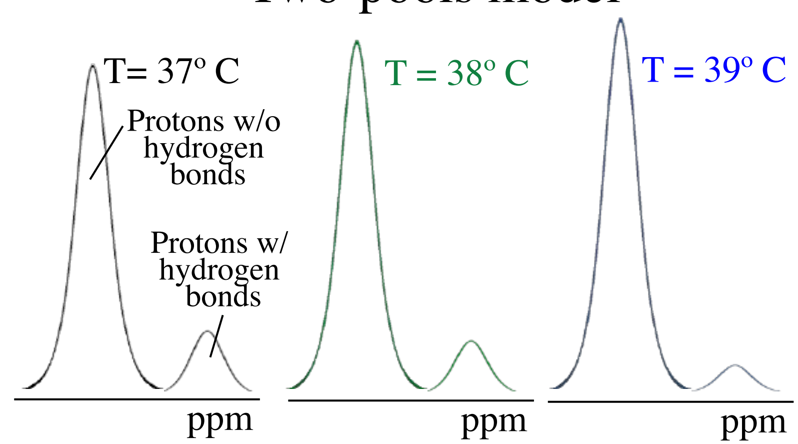
"T_2 model"



"Chemical shift model"

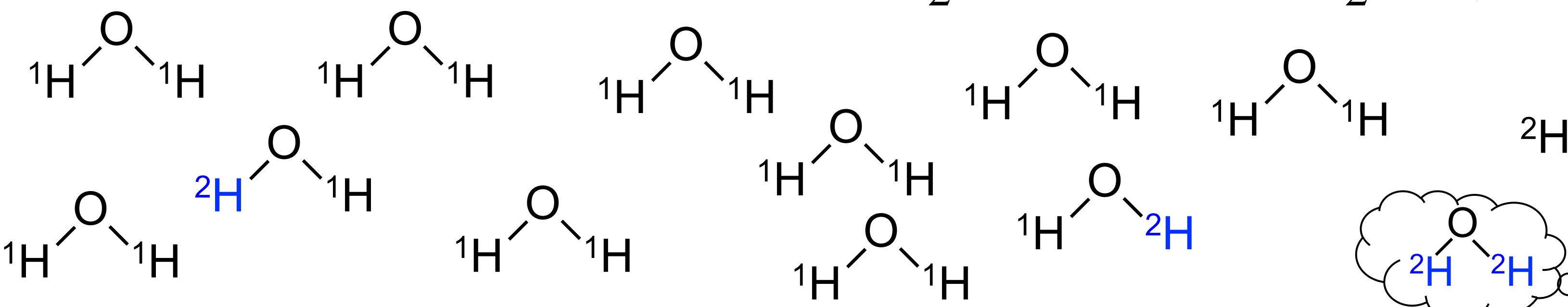


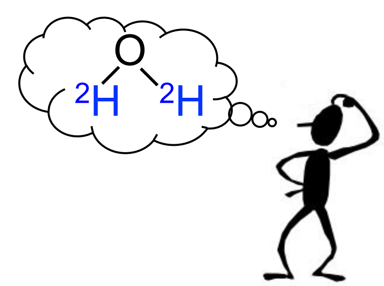
"Two-pools model"



Example: Water, water, water

- Consider a mixture with 5% D_2O and 95% H_2O ($D = {}^2H$)

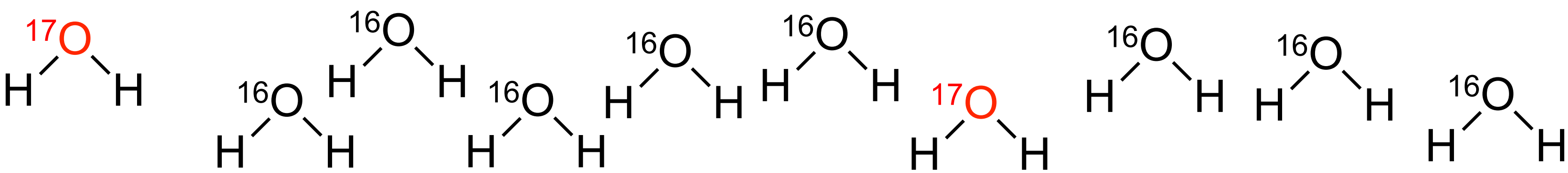




Why is $T_{1,D} << T_{1,H}$? What about $T_{2,D}$ vs $T_{2,H}$?

What if the solution in injected in vivo?

- Consider a mixture with 5% $H_2{}^{17}O$ and 95% $H_2{}^{16}O$

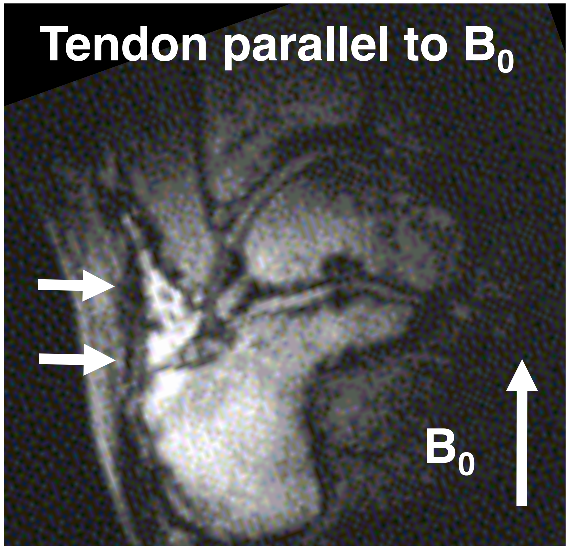


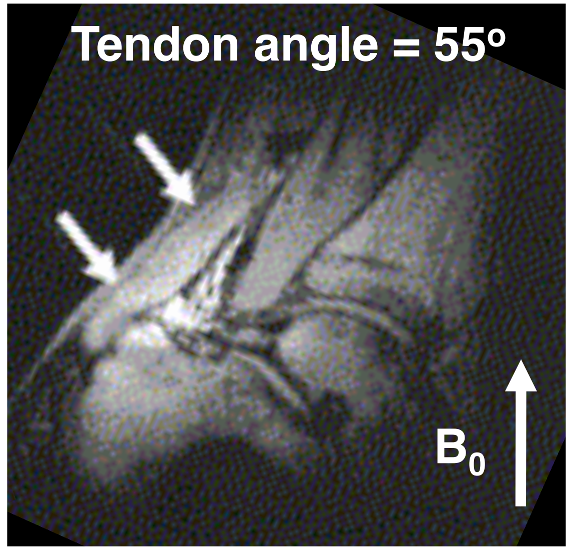
Why is the proton T_2 for this mixture < T_2 for a pure $H_2{}^{16}O$ sample?

What about T_1?

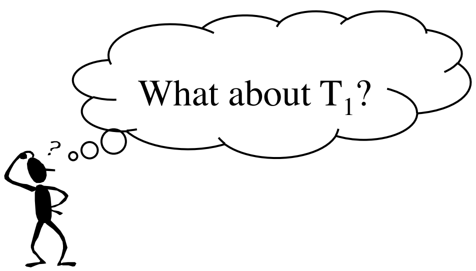
Example: Tendon Imaging

- T_2 of tendons is strongly dependent on the angular orientation with respect to B_0: magic angle = 54.7°

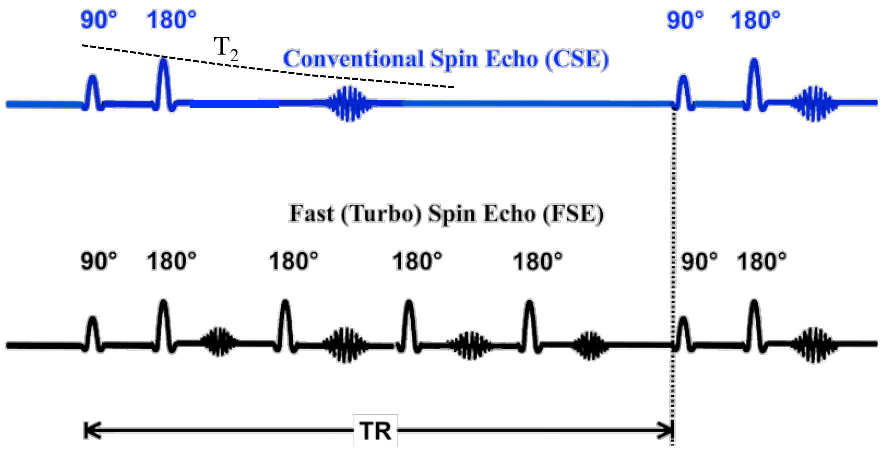




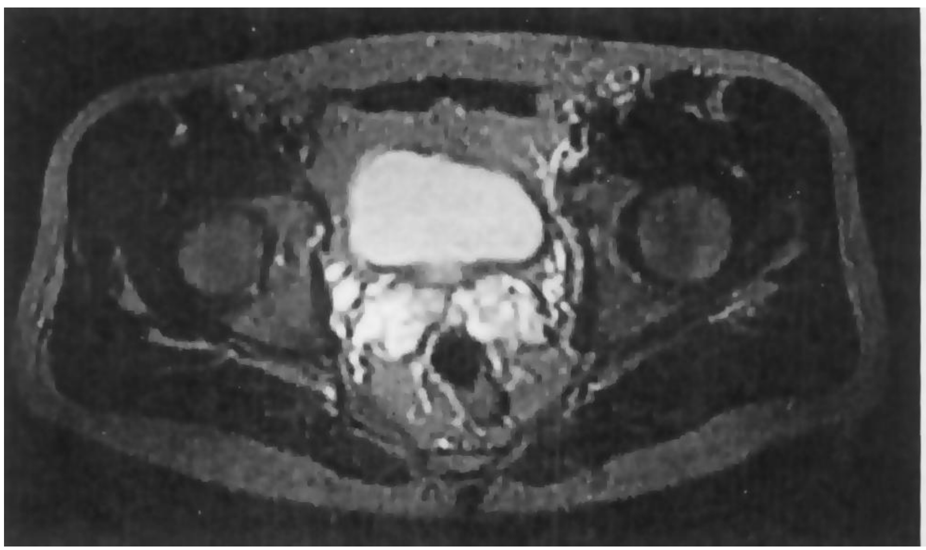
acute Achilles tendon rupture: 3D GRE, TR/TE=21/7 ms

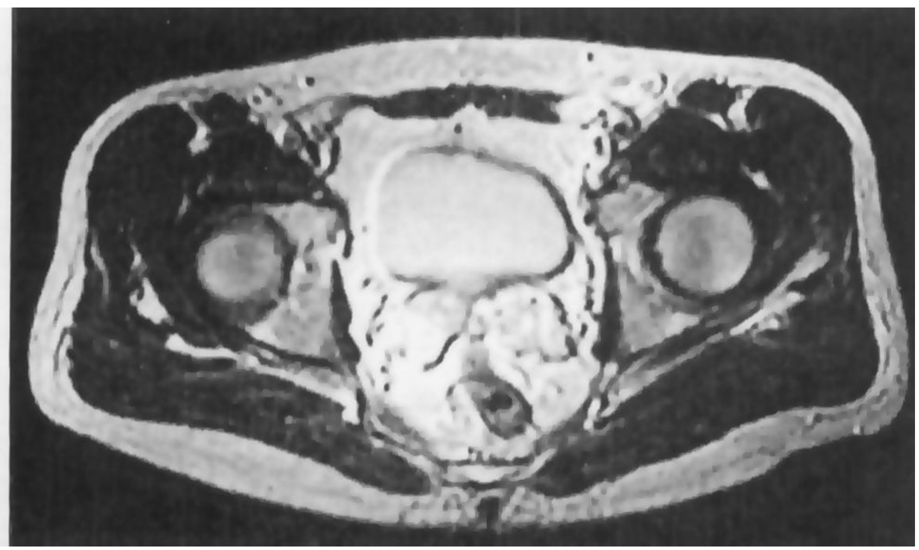


Example: Fast Spin Echo



- Why is fat bright on FSE images?

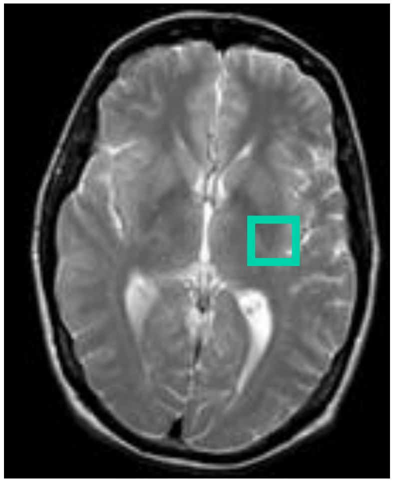


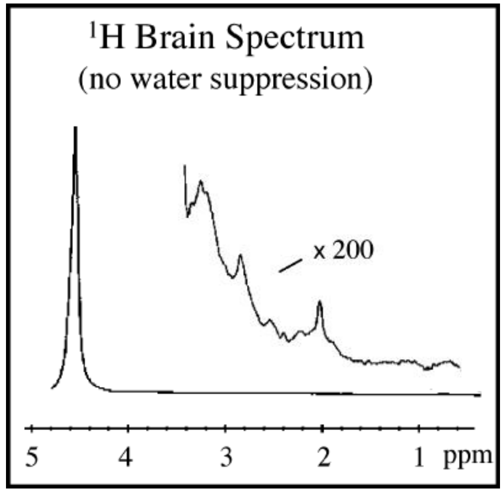


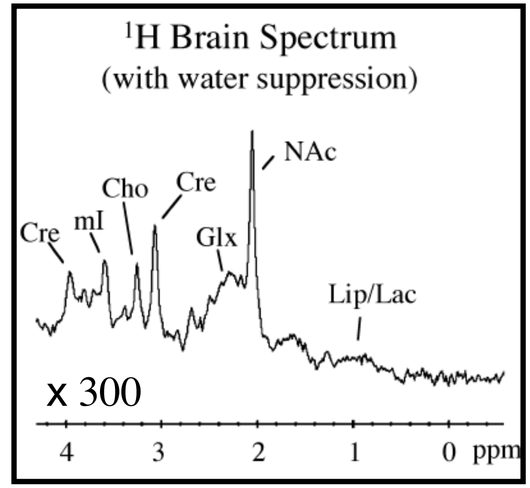
Conventional Spin Echo
TR/TE=2500/80 ms

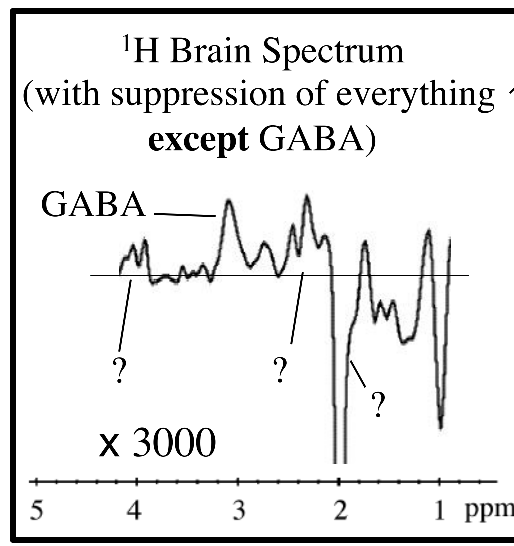
Fast Spin Echo
TR/TE=2500/80 ms, ETL = 8

Example: γ-aminobutyric acid (GABA)







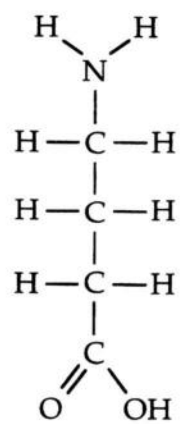


How?

- Why?

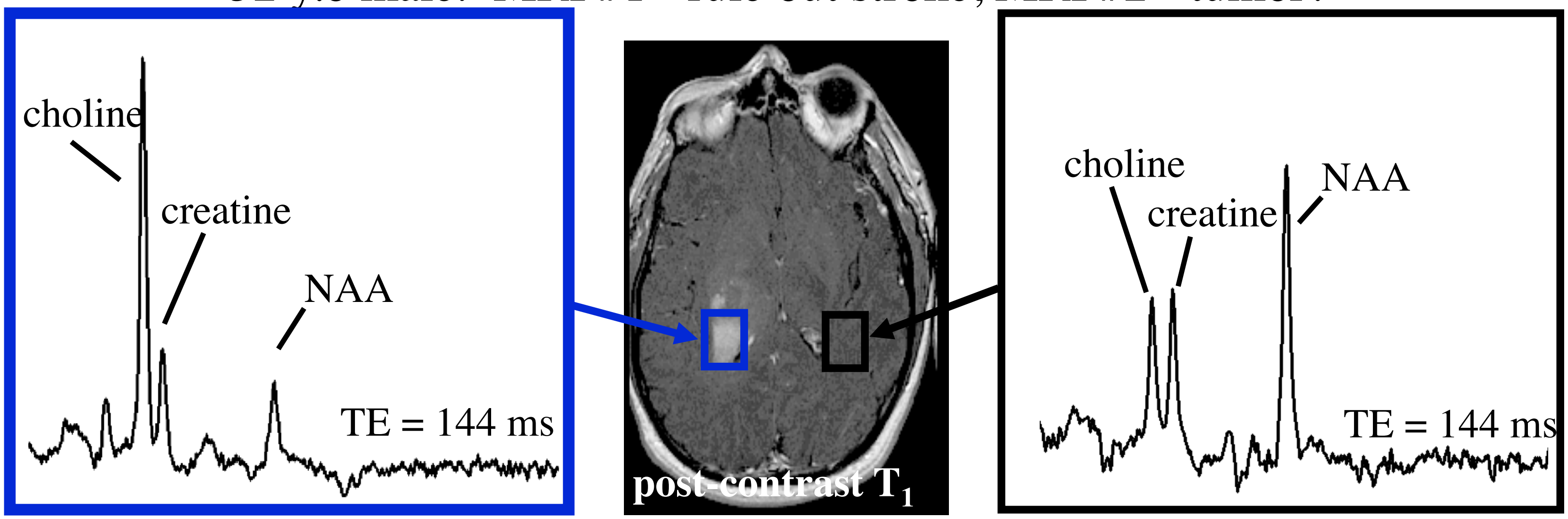
GABA/glutamate are the major excitatory/inhibitory neurotransmitters in the human brain, and are of particular interest for conditions such as autism, for which an excitatory/inhibitory imbalance is hypothesized.

GABA

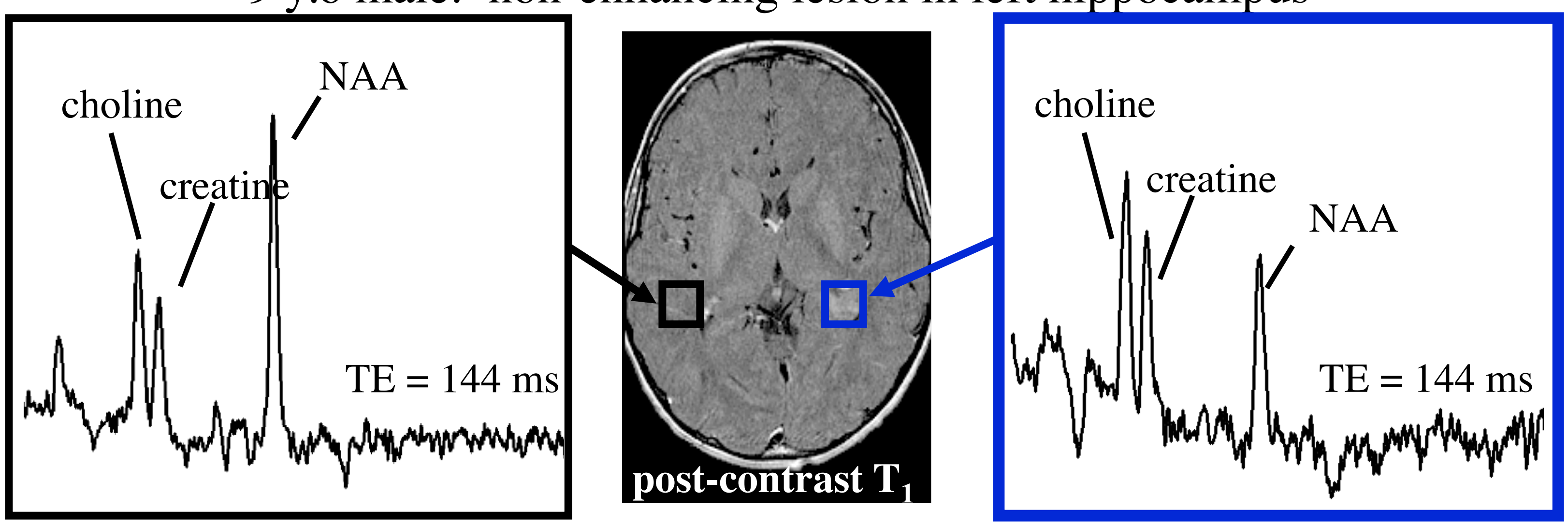


Example: Brain tumors

52 y.o male: MRI #1 - rule out stroke, MRI #2 - tumor?



9 y.o male: non-enhancing lesion in left hippocampus



Next lecture:
Review of Classical MR

Biography: Isidor Isaac Rabi

(born July 29, 1898, Rymanów, Austria-Hungary [now in Poland]—died Jan. 11, l988, New York, N.Y., U.S.) American physicist who was awarded the Nobel Prize for Physics in 1944 for his invention (in 1937) of the atomic and molecular beam magnetic resonance method of observing atomic spectra. Rabi's parents settled in New York City in 1899. After earning a bachelor's degree in chemistry at Cornell University in 1919, Rabi switched to physics and received his Ph.D. from Columbia University in 1927. He did postgraduate work in Europe and then joined the faculty of Columbia University in 1929, becoming professor of physics in 1937. From 1940 to 1945 Rabi was a leader of the group of scientists at the Massachusetts Institute of Technology, Cambridge, who helped in the development of radar. He was a member of the General Advisory Committee of the Atomic Energy Commission from 1946 to 1956 and succeeded J. Robert Oppenheimer as its chairman from 1952 to 1956. He originated the concept of the CERN international laboratory for high-energy physics in Geneva, Switz., and he was one of the founders of the Brookhaven National Laboratory, Upton, N.Y. He also built up one of the world's finest physics departments at Columbia University, one which was to produce several Nobel Prize–winning physicists. Rabi's most important scientific work was his development (in the 1930s) of a method for measuring the magnetic properties of atoms, atomic nuclei, and molecules. The method is based on measuring the spin of the protons in the atom's core, a phenomenon known as nuclear magnetic moments. With the application of his magnetic resonance method, several mechanical and magnetic properties, as well as the shape, of an atomic nucleus can be deduced. The precise measurements yielded by this method made possible such subsequent applications as the atomic clock, the maser, and the laser, as well as the nuclear magnetic resonance imaging used in diagnostic medicine. Rabi's method provided the central technique for virtually all molecular and atomic beam experimentation.

Biography: Felix Bloch

(born Oct. 23, 1905, Zürich, Switz.—died Sept. 10, 1983, Zürich) Swiss-born American physicist who shared (with E.M. Purcell) the Nobel Prize for Physics in 1952 for developing the nuclear magnetic resonance method of measuring the magnetic field of atomic nuclei. Bloch's doctoral dissertation (University of Leipzig, 1928) promulgated a quantum theory of solids that provided the basis for understanding electrical conduction. Bloch taught at the University of Leipzig until 1933; when Adolf Hitler came to power he emigrated to the United States and was naturalized in 1939. After joining the faculty of Stanford University, Palo Alto, Calif., in 1934, he proposed a method for splitting a beam of neutrons into two components that corresponded to the two possible orientations of a neutron in a magnetic field. In 1939, using this method, he and Luis Alvarez (winner of the Nobel Prize for Physics in 1968) measured the magnetic moment of the neutron (a property of its magnetic field). Bloch worked on atomic energy at Los Alamos, N.M., and radar countermeasures at Harvard University during World War II. Bloch returned to Stanford in 1945 to develop, with physicists W.W. Hansen and M.E. Packard, the principle of nuclear magnetic resonance, which helped establish the relationship between nuclear magnetic fields and the crystalline and magnetic properties of various materials. It later became useful in determining the composition and structure of molecules. Nuclear magnetic resonance techniques have become increasingly important in diagnostic medicine. Bloch was the first director general of the European Organization for Nuclear Research (1954–55; CERN).

Biography: Edward Mills Purcell

(born Aug. 30, 1912, Taylorville, Ill., U.S.—died March 7, 1997, Cambridge, Mass.) American physicist who shared, with Felix Bloch of the United States, the Nobel Prize for Physics in 1952 for his independent discovery (1946) of nuclear magnetic resonance in liquids and in solids. Nuclear magnetic resonance (NMR) has become widely used to study the molecular structure of pure materials and the composition of mixtures.During World War II Purcell headed a group studying radar problems at the Radiation Laboratory of the Massachusetts Institute of Technology, Cambridge. In 1946 he developed his NMR detection method, which was extremely accurate and a major improvement over the atomic-beam method devised by the American physicist Isidor I. Rabi.Purcell became professor of physics at Harvard University in 1949 and in 1952 detected the 21-centimetre-wavelength radiation emitted by neutral atomic hydrogen in interstellar space. Such radio waves had been predicted by the Dutch astronomer H.C. van de Hulst in 1944, and their study enabled astronomers to determine the distribution and location of hydrogen clouds in galaxies and to measure the rotation of the Milky Way. In 1960 Purcell became Gerhard Gade professor at Harvard, and in 1980 he became professor emeritus. The same year he received the National Medal of Science.