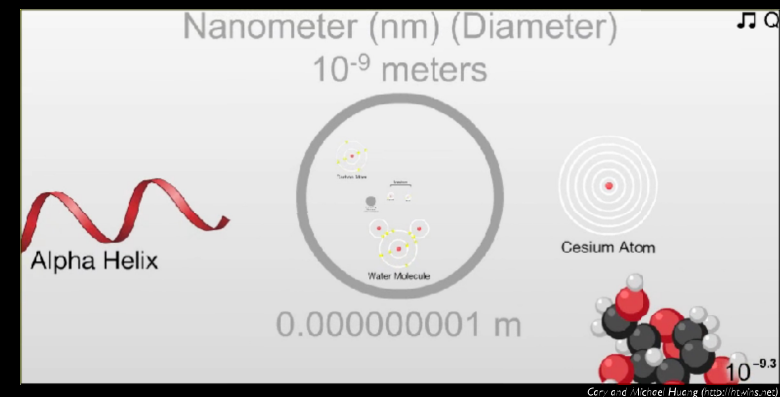


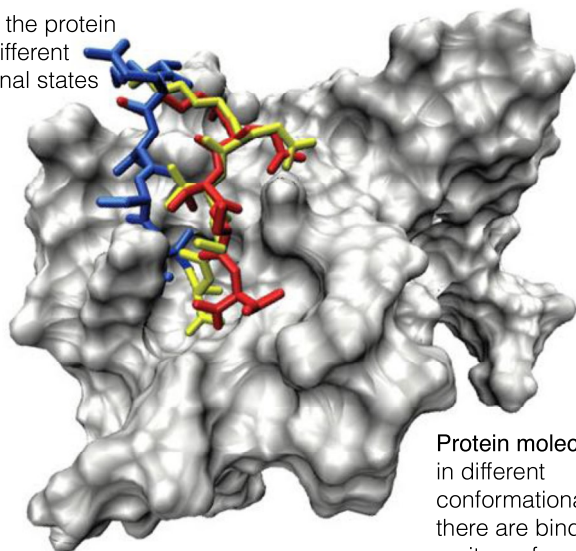
STRUCTURE AND DYNAMICS OF BIOMOLECULAR SYSTEMS

MIKLÓS KELLERMAYER



Structure

Small molecule
(ligand):
may bind to the protein
surface in different
conformational states



Protein molecule:
in different
conformational states;
there are binding sites
on its surface

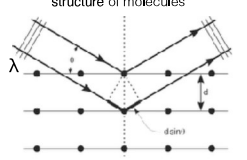
Dynamics



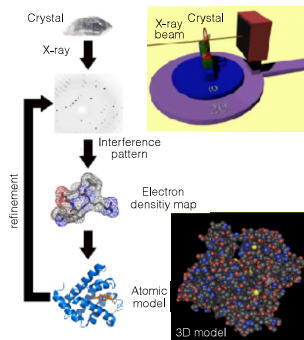
Molecules are in constant rapid motion. In complex molecules (e.g., proteins) the hierarchy of different dynamic modes (e.g., vibration, rotation) results in extremely complex motions. Certain global motions are related to function of the molecule (e.g., domain rotation in a motor protein).

X-ray crystallography

Provides atomic-resolution structure of molecules



Condition of constructive interference: path-length difference is an integer multiple of wavelength (10-200 pm):

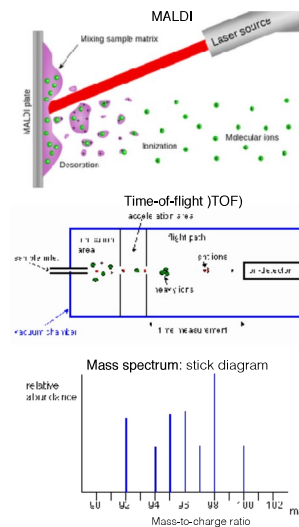
$$2d \sin \theta = n\lambda$$


Mass spectrometry

Provides chemical fingerprint of mixtures based on mass

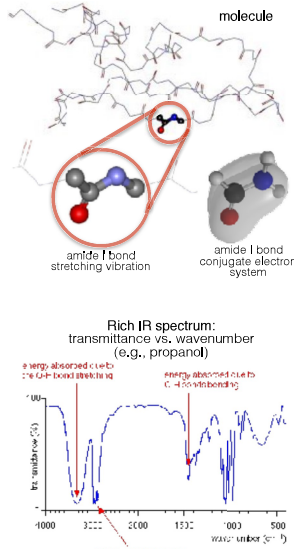
Steps:

1. Ionization (electron, electrospray, MALDI)
2. Mass measurement (magnetic, quadrupole, TOF)
3. Detection (relative quantities)



IR spectroscopy

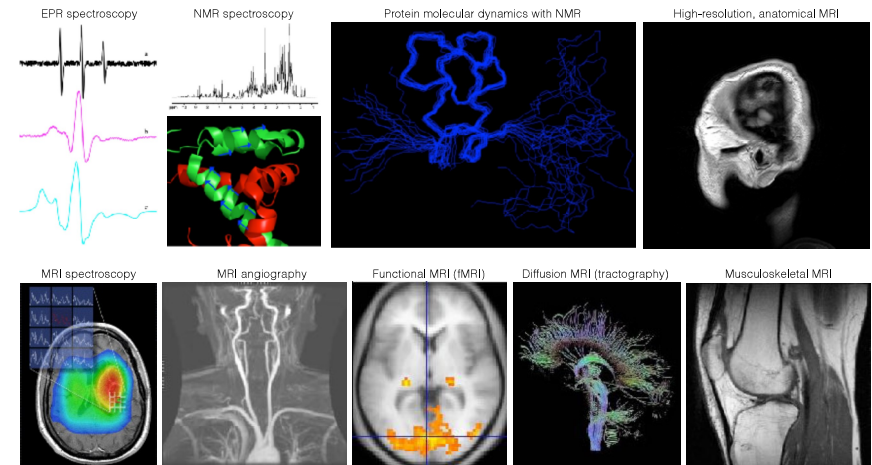
Provides information about chemical composition and vibrational/rotational dynamics



Radio spectroscopies

Revolutionized physics, chemistry, biology and medicine

- Electronspin resonance (ESR, electron paramagnetic resonance - EPR)
- Nuclear Magnetic Resonance (NMR, MRI)



Atomic, molecular systems may behave as elementary magnets

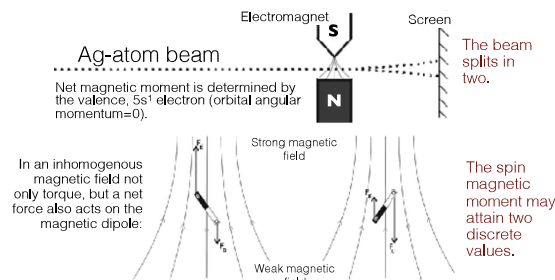
Stern-Gerlach experiment (1922)



Otto Stern (1888-1969)



Walther Gerlach (1889-1979)



Nuclear magnetic resonance, (NMR) Nobel-prize, 1952



Isidor Rabi (1898-1988)



Felix Bloch (1905-1983)

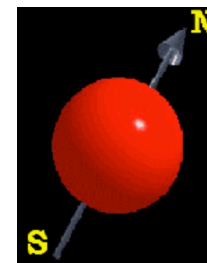


Edward Mills Purcell (1912-1997)

Magnetic resonance: resonance-absorption of electromagnetic energy by a material placed in magnetic field.

Systems with net spin: elementary magnets

- Elementary particles (p, n, e) have their own *spin*.
- Depending on the number of elementary particles and organizational principles (e.g., Pauli principle), *net spin* emerges within the system.
- Atomic nucleus: odd mass number - half nuclear spin (¹H, ¹³C, ¹⁵N, ¹⁹F, ³¹P); even mass number, odd atomic number - whole nuclear spin; even mass and atomic number - zero nuclear spin.
- Electron: net electron spin within a molecular system containing a stable unpaired electron (e.g., free radicals).
- Because of *charge* and *net spin*, *magnetic moment* emerges.



Nuclear magnetic moment:

$$M_N = \gamma_N L$$

γ_N = gyromagnetic ratio (ratio of magnetic moment and angular momentum).
 L = nuclear spin ($L = \sqrt{i(i+1)}\hbar$), i = spin quantum number.

Magnetic moment of the electron:

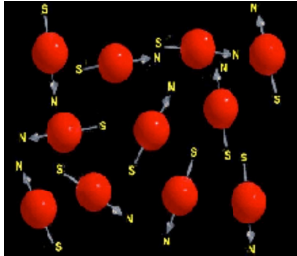
$$M_e = -g\mu_B \sqrt{S(S+1)}$$

g = electron's g-factor (dimensionless number that describes the relationship between magnetic moment and gyromagnetic ratio)

μ_B = Bohr's magneton (unit of the electron's magnetic moment)

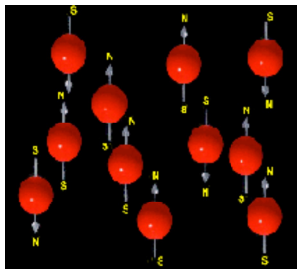
S = spin quantum number

In external magnetic field the elementary magnets orient

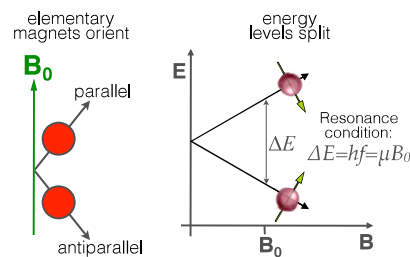


In absence of magnetic field:
random orientation of elementary magnets

Paramagnetism: magnetism emerging in external magnetic field (caused by the orientation of magnetic dipoles).

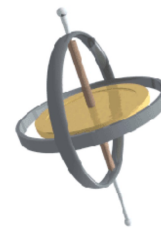


In magnetic field:

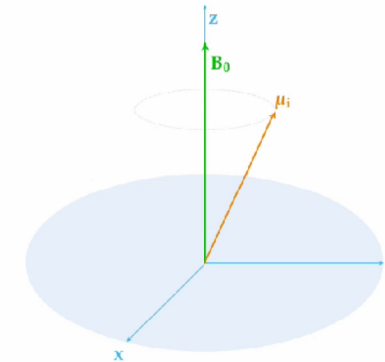


Oriented elementary magnets do precessional motion

Top, gyroscope



Precession



Precession of an elementary magnetic moment (μ_i) in magnetic field (B_0) within a reference xyz space

Precession or Larmor frequency:

$$\omega_0 = \gamma B_0$$

$$f_{Larmor} = \frac{\gamma}{2\pi} B_0$$

Resonance condition:

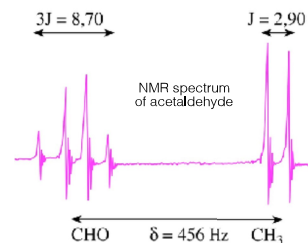
$$\Delta E = \frac{h\omega_0}{2\pi}$$



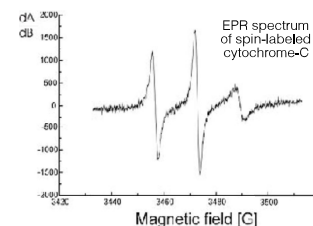
Felix Bloch, 1946

NMR and EPR spectroscopy

- NMR spectrum: intensity of absorbed electromagnetic radiation as a function of frequency.
- The area under the "NMR-line" is proportional to the number of absorbing atomic nuclei.
- The electron cloud distorts the local magnetic field, therefore the frequency condition is shifted: "chemical shift". Chemical structure determination is possible.

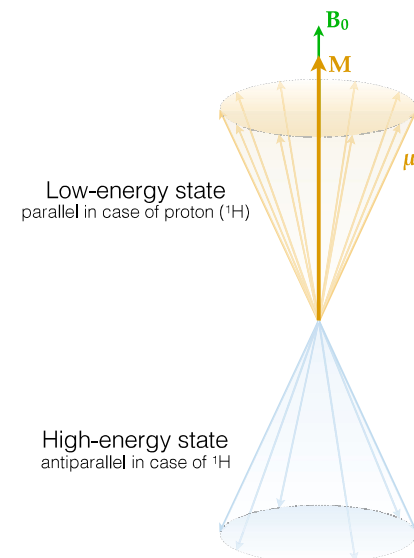


- EPR spectrum: intensity of electromagnetic radiation as a function of magnetic field.
- Magnetic field is lower, but radiation frequencies are greater (microwave) than in NMR.
- Spin-labeling: attachment of a chemical containing a stable unpaired electron.
- Dynamics of rotational motion can be measured up to the 10^{-4} - 10^{-2} s time range.



Net (macroscopic) magnetization

Due to spin access in different energy states



B_0 = magnetic field

M = net magnetization (vectorial quantity, sum of elementary vectors μ_i)

Ratio of low- and high-energy spin populations is determined by the Boltzmann distribution:

$$\frac{N_{antiparallel}}{N_{parallel}} = e^{-\frac{\Delta E}{k_B T}}$$

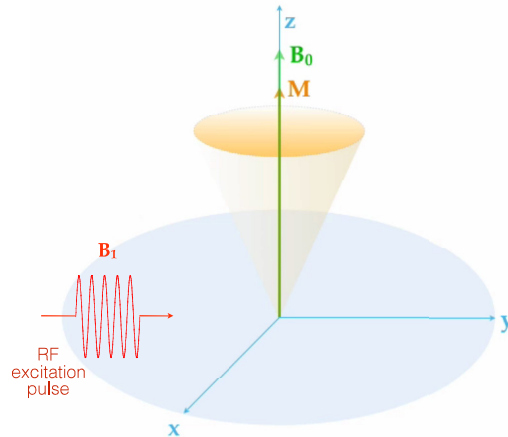
N.B.: magnetic field in MRI is 20-50-thousand times as strong as the earth's magnetic field.

Excitation

Excitation process: the net magnetization vector (M) is tilted from its oriented state into the xy -plane (transverse plane)
Condition: resonance condition, Larmor frequency

B_0 = magnetic field
 M = net magnetization
 B_1 = irradiated radio frequency wave

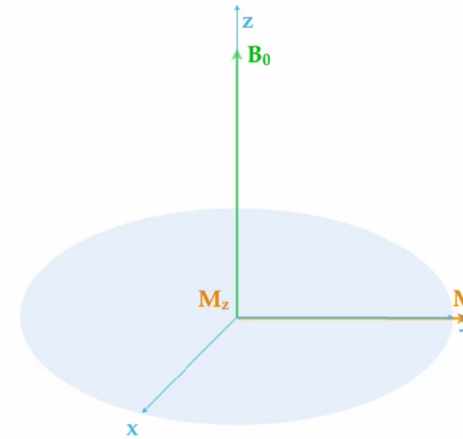
Frequency of excitational electromagnetic radiation used in MRI:
radio frequency



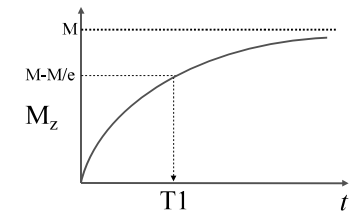
Spin-lattice relaxation

T1 or longitudinal relaxation

T1 relaxation process: return (relaxation) of the z -axis vectorial component of M (M_z) towards the direction of the external magnetic field



M_z : z -axis vectorial component of M



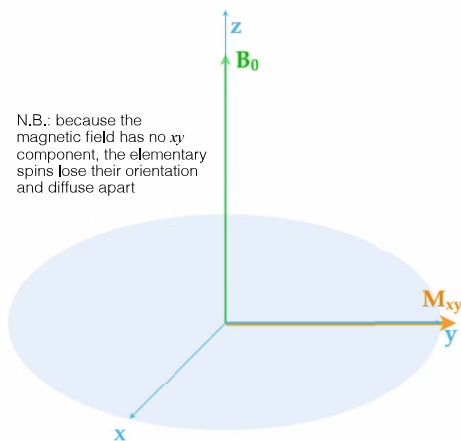
T1 relaxation time:
depends on interaction
between elementary magnet (proton)
and its environment (lattice)

Spin-spin relaxation

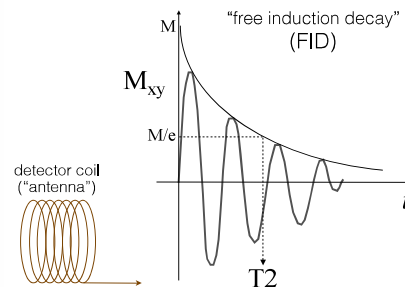
T2 or transverse relaxation

T2 relaxation process: diffusion (spreading) of the elementary magnetic moments (μ_i) resulting in the decay of the transverse(xy)-plane vectorial component of M (M_{xy})

N.B.: because the magnetic field has no xy component, the elementary spins lose their orientation and diffuse apart

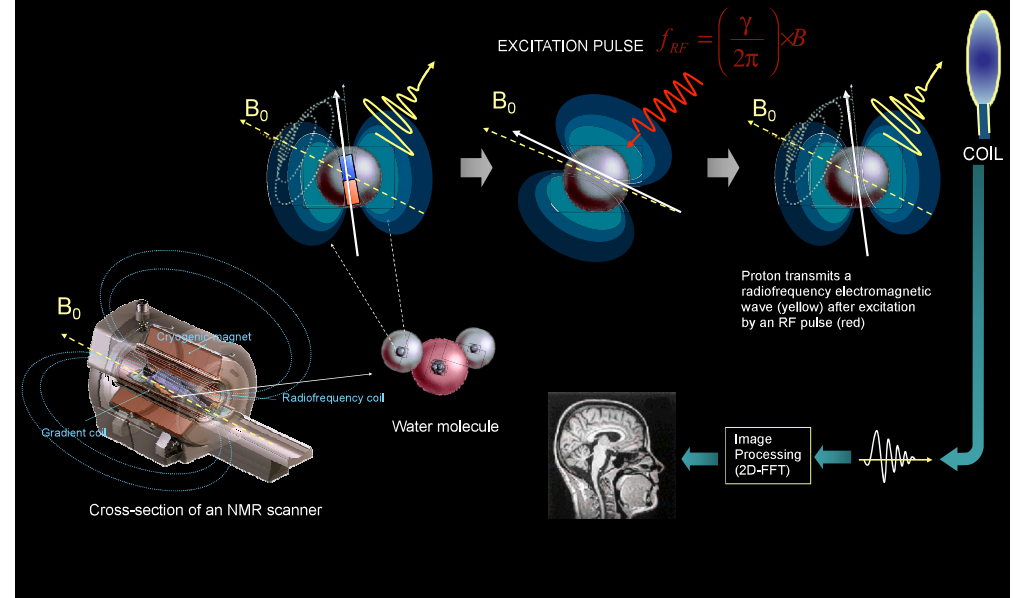


M_{xy} : xy -plane vectorial component of M

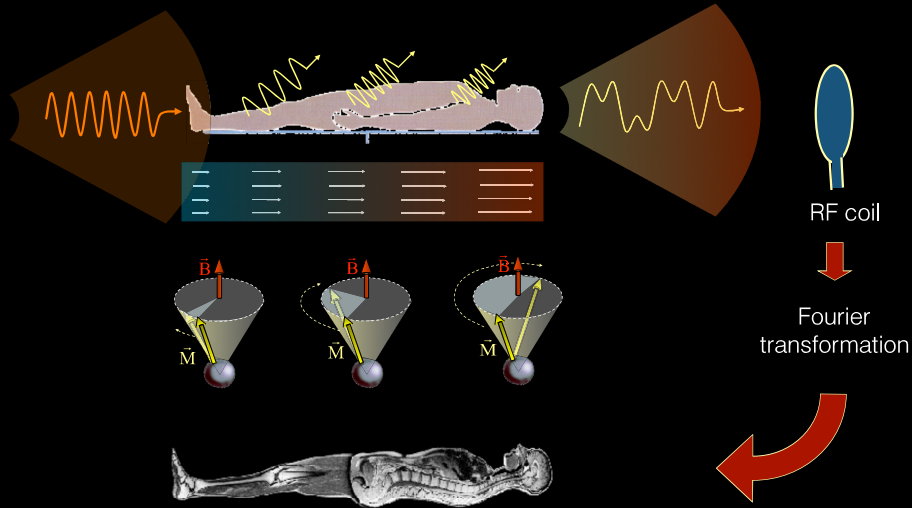


T2 relaxation time:
depends on interaction between
elementary magnets (spins, protons);
process occurs in the transverse (xy) plane

MRI: the human body is macroscopically magnetized

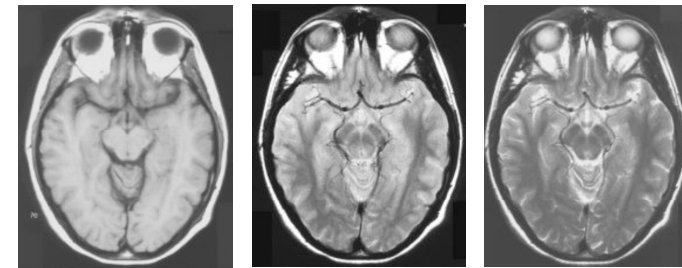
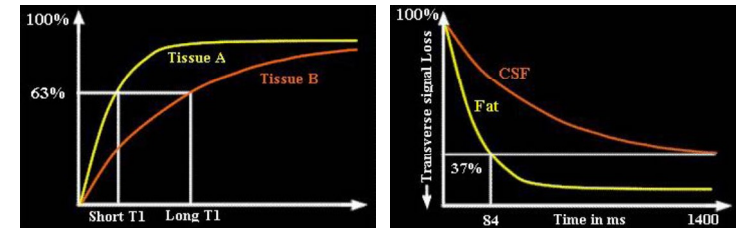


MRI: spatial coding and image reconstruction based on the resonance condition (B_0 -dependent ω)

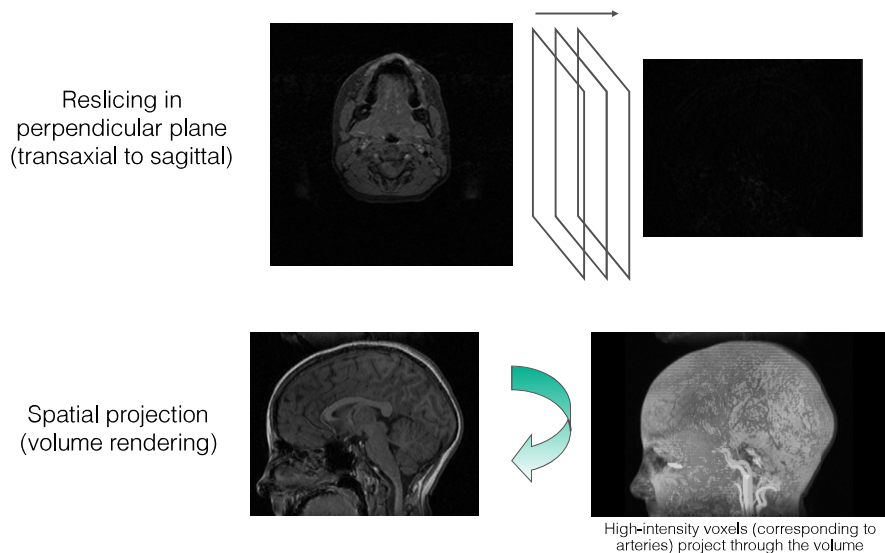


MRI imaging

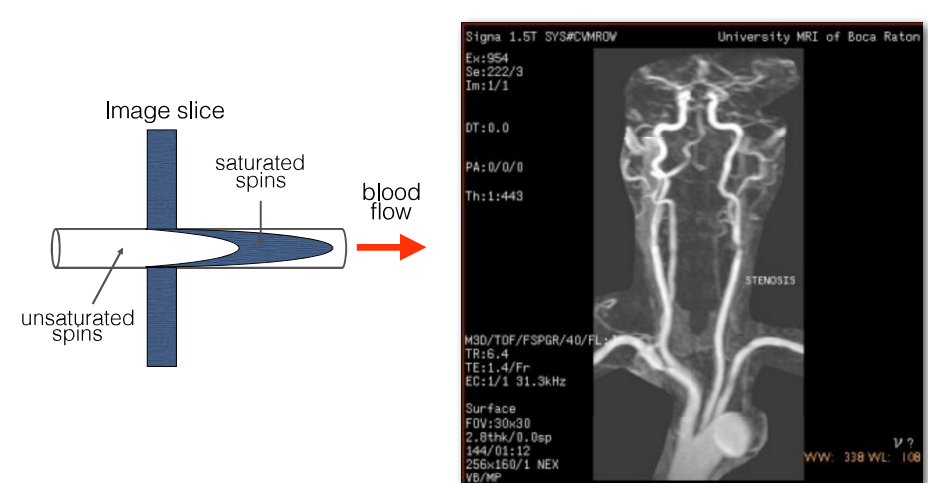
Color contrast based on spin density and relaxation times



MRI: 3D information

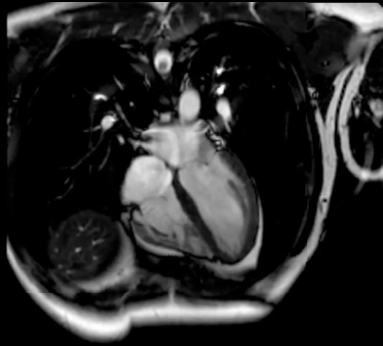


MRI is more than anatomical imaging:
Non-invasive angiography



MRI is more than anatomical imaging

Time-resolved imaging



Blood flow across the cardiac chambers



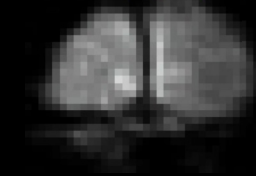
Opening and closing of aorta valve

MRI is more than anatomical imaging

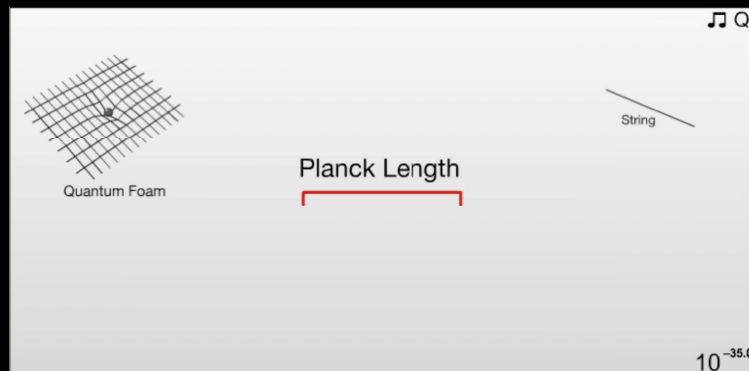
Functional MRI (fMRI)

High time resolution images recorded synchronously with physiological processes

Light pulse ON
Light pulse OFF



Effect of light pulses on visual cortex



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