



DE LA RECHERCHE À L'INDUSTRIE

Cryomagnetism for Neuroscience

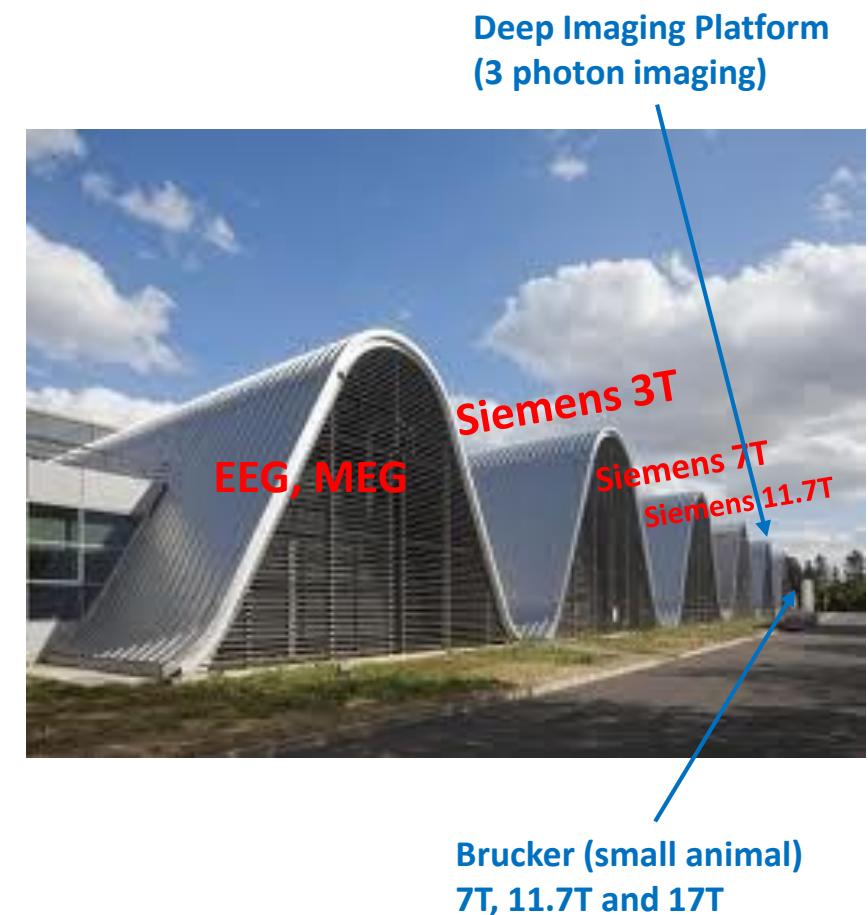
September 30, 2019

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Neuroscience ...

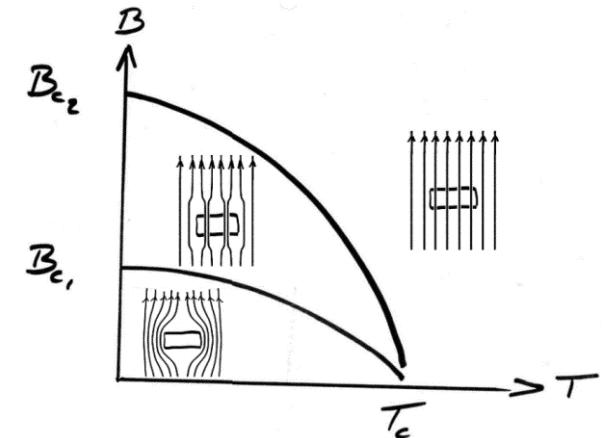
- ▶ Study of the nervous system, in particular the brain
- ▶ The broad(ening) scope of neuroscience
 - Biological basis of learning, memory, behavior, perception, and consciousness (cognitive neuroscience)
 - Brain development
 - Brain diseases (clinical neuroscience)
 - Fundamental properties of biological neuronal networks (Computational neuroscience -> Artificial intelligence)
- ▶ The progress in neuroscience is tightly linked with the developement of technologies to explore the brain in vivo.



Supraconductivity and cryomagnetism ...

► Create intense magnetic fields

- Nuclear magnetic resonance applications
- Magnetic Resonance Imaging



► Create devices that are very sensitive to magnetic fluxes

- Recording the electrical activity of the brain (source of transient magnetic fields in the femtoTesla range)

... « avenue » for a non-invasive and multimodal exploration of the brain

► Magnetic Resonance Imaging

- The nuclear Zeeman effect
- MRI instrumentation & principles
- MRI for neurosciences
- The ultra-high-field MRI perspective

► MagnetoEncephalography

- The (electro)magnetic activity of the brain
- FemtoTesla magnetic flux detection with SQUIDS
- The MEG instrumentation
- MEG in neuroscience

► Conclusions

► Magnetic Resonance Imaging

- The nuclear Zeeman effect
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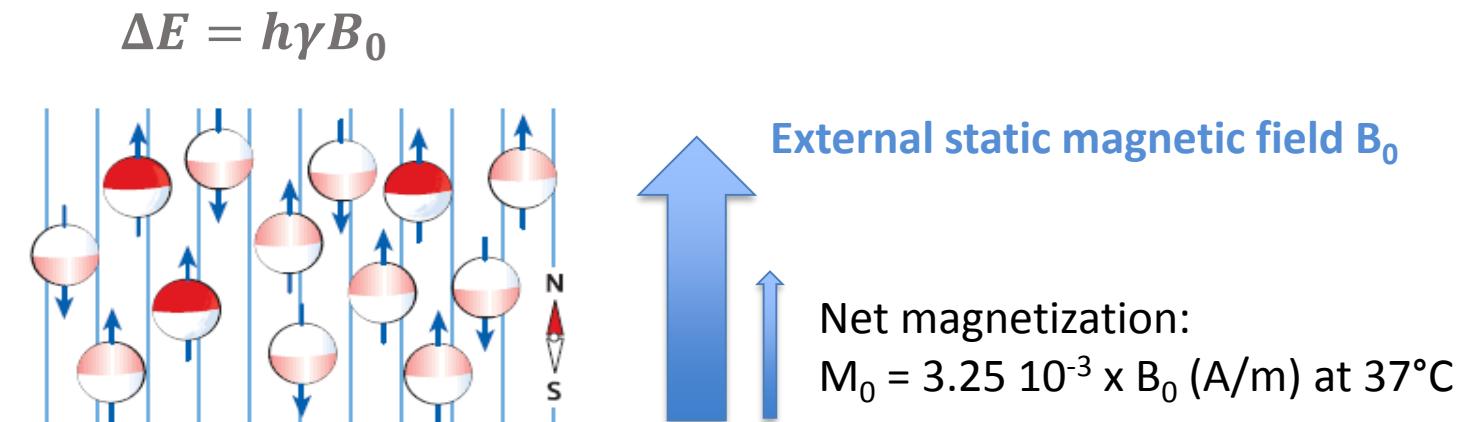
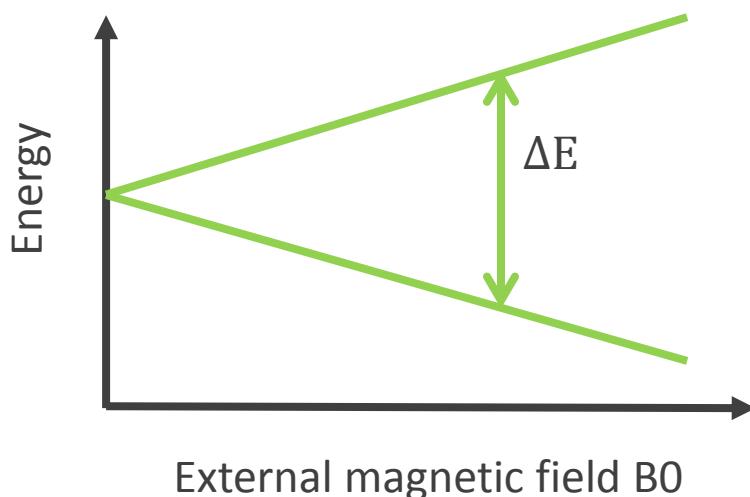
► MagnetoEncephalography

- The (electro)magnetic activity of the brain
- FemtoTesla magnetic flux detection with SQUIDS
- The MEG instrumentation
- MEG in neuroscience

► Conclusions

The nuclear Zeeman effect

- ▶ The proton is **spin $\frac{1}{2}$ particle**. It has a quantified angular momentum and an associated **magnetic moment** ($1.41 \cdot 10^{-26}$ Joule per Tesla).
- ▶ Without external magnetic field, this nuclear magnetism is not observable.
- ▶ With **an external magnetic field B_0** (Tesla), an excess of proton with a spin oriented parallel to B_0 appears.
- ▶ In Quantum mechanics words, the energy gap between a spin « parallel » and a spin « anti-parallel » to the magnetic field is ($\gamma = 42.58$ MHz/Tesla is the gyromagnetic ratio of the proton)



$$\Delta E = h\gamma B_0$$

External static magnetic field B_0

Net magnetization:
 $M_0 = 3.25 \cdot 10^{-3} \times B_0$ (A/m) at 37°C

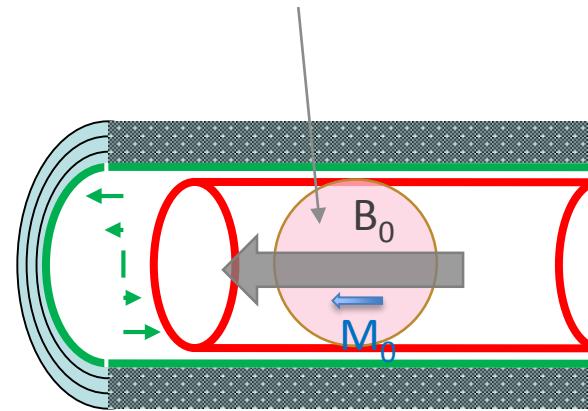
Magnetic Resonance Imaging (MRI) scanner

A clinical (1.5 Tesla) MRI scanner

- Returns a volume image (3D-image) of the magnetization.



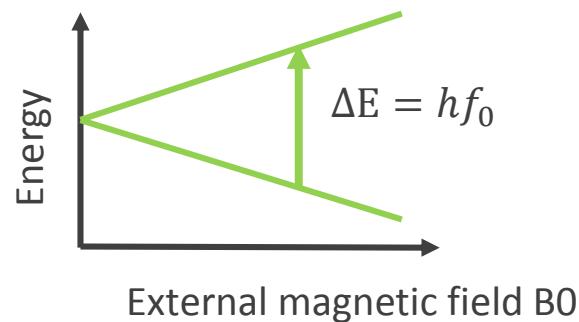
Sample containing protons (human body)



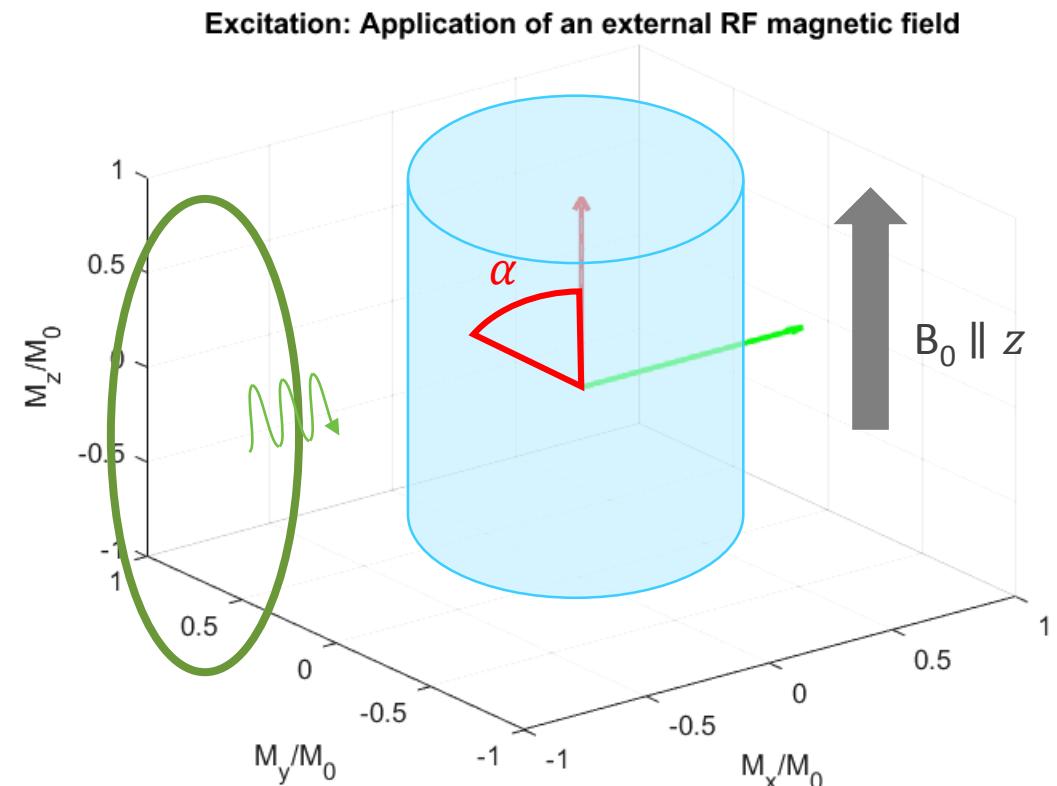
- Superconducting magnet
(high static field)
 - RF coil(s) for
spin excitation & signal detection
 - Gradient
coils (imaging)

Nuclear magnetic resonance

- ▶ Apply a RF current ($f_0 = \frac{\Delta E}{h} = \gamma B_0$) to a coil placed next to the sample

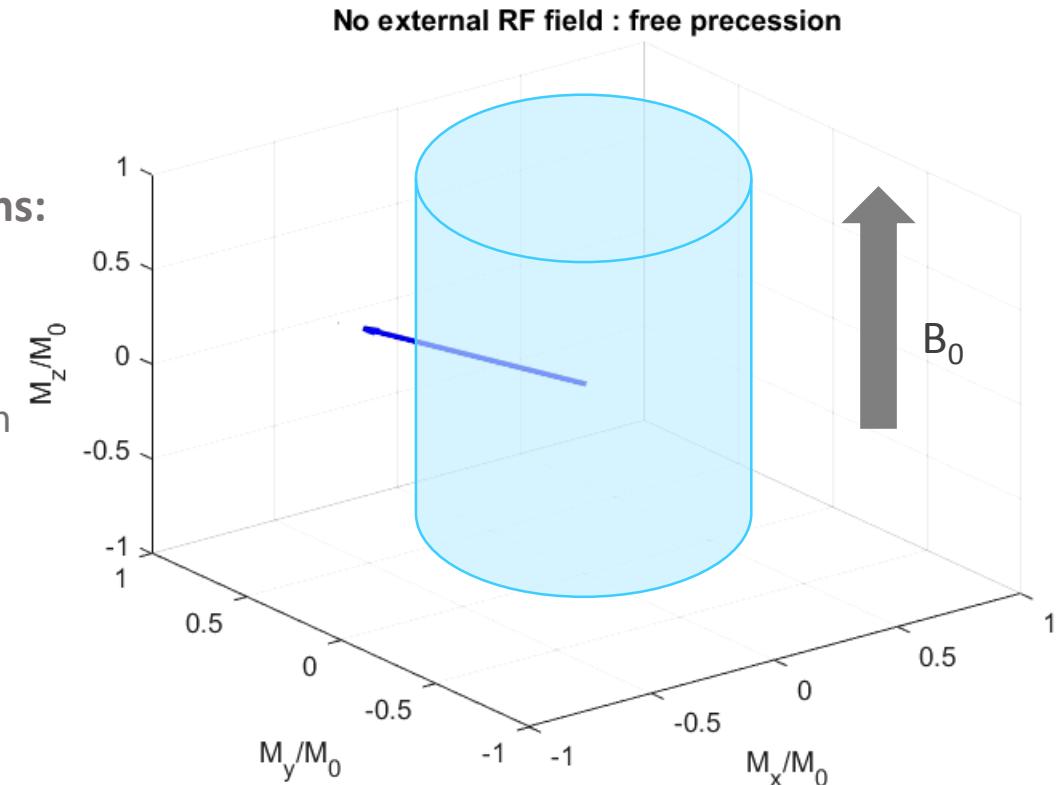
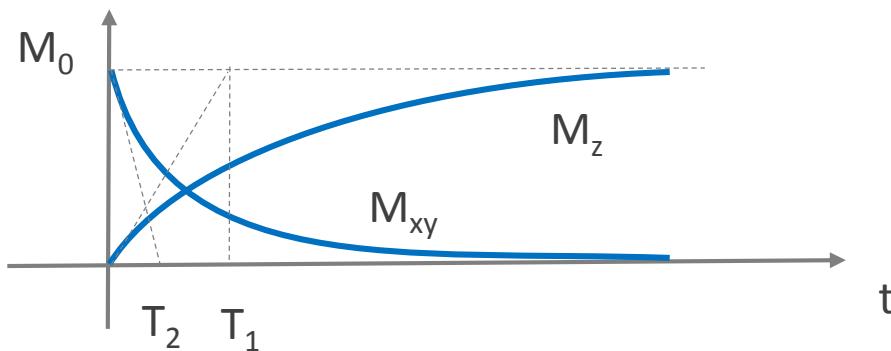


- ▶ (At $B_0 = 1$ Tesla, $f_0 = 42.58$ MHz)
- ▶ Rotating transversal magnetic field B_1 (Tesla)
- ▶ Magnetization is flipped from the z-axis (direction of B_0 by convention) by an angle (α) that grows over time



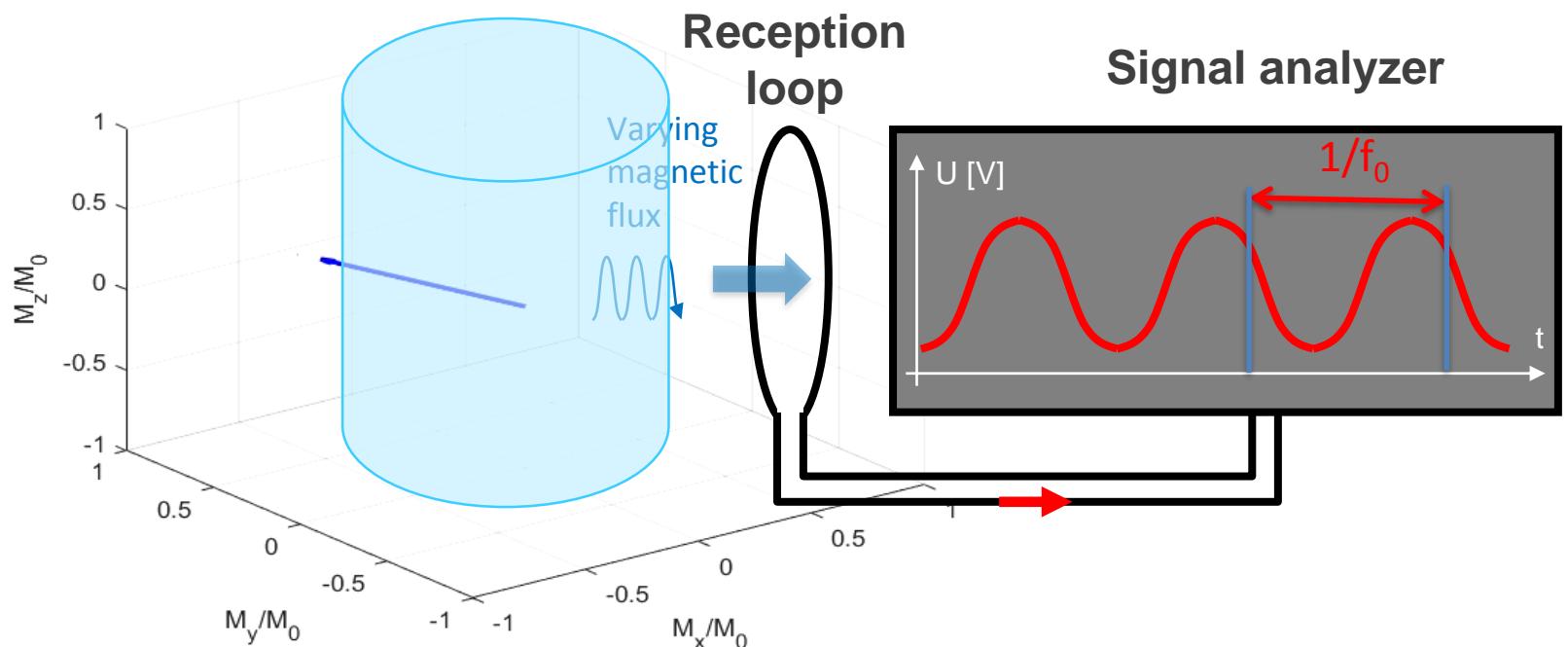
Nuclear magnetic resonance

- ▶ “Switch off” the radio-frequency excitation
- ▶ Magnetization rotates about the z-axis (free precession)
- ▶ Due to molecular motion & interaction between spins:
 - Energy transfer to the lattice
 - $|M_z|$ regrows exponentially (constant T_1 , spin-lattice relaxation time)
 - $|M_{xy}|$ decays exponentially (constant $T_2 < T_1$, spin-spin relaxation time)



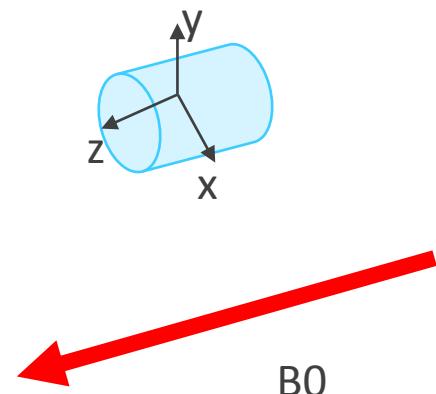
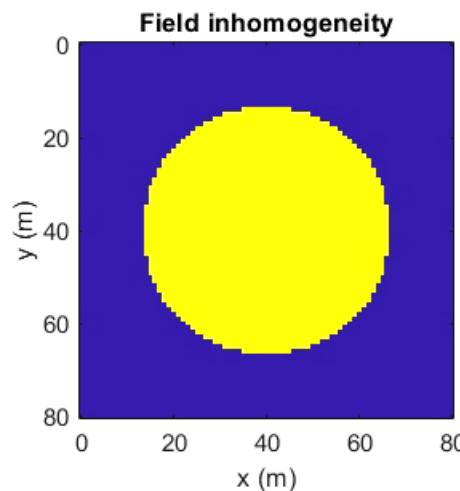
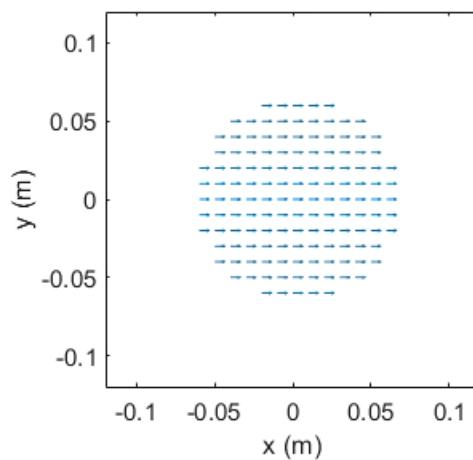
Signal detection

- ▶ Use (by reciprocity) the RF coil for signal reception
- ▶ During free precession, the rotating magnetization is the source a a secondary electromagnetic wave
- ▶ Varying magnetic flux through the reception loop
- ▶ Generation of a measurable voltage across the NRM detection loop

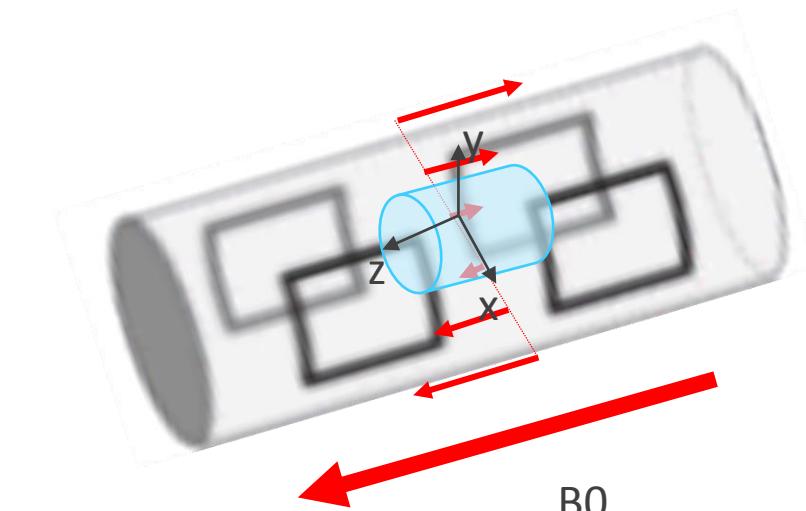
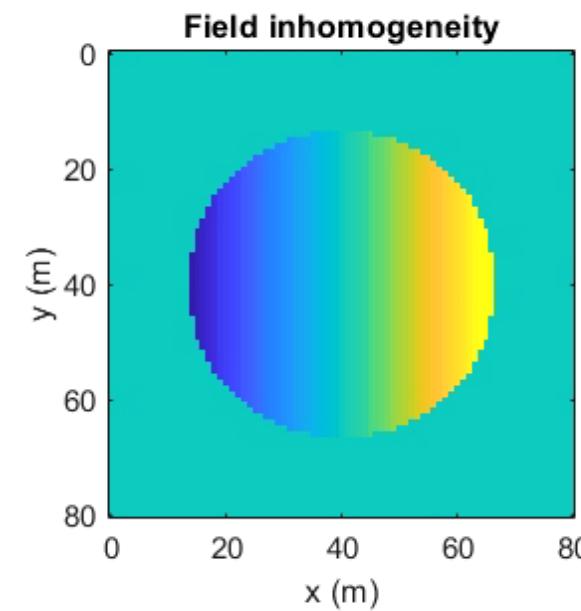
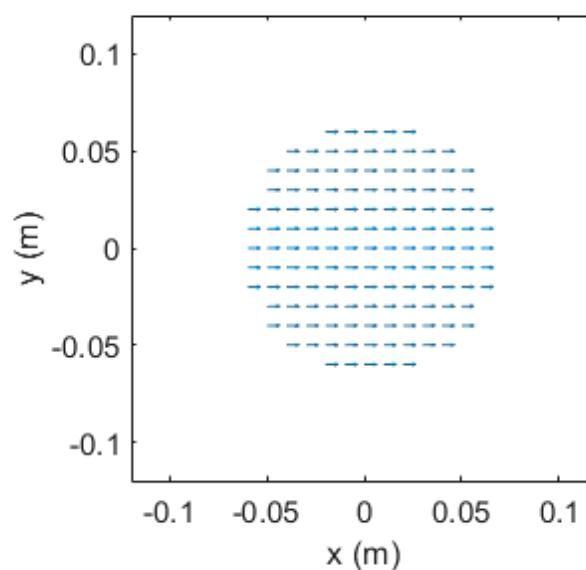


Uniform magnetic field : no spatial information

Magnetization
in the body
after 90° pulse

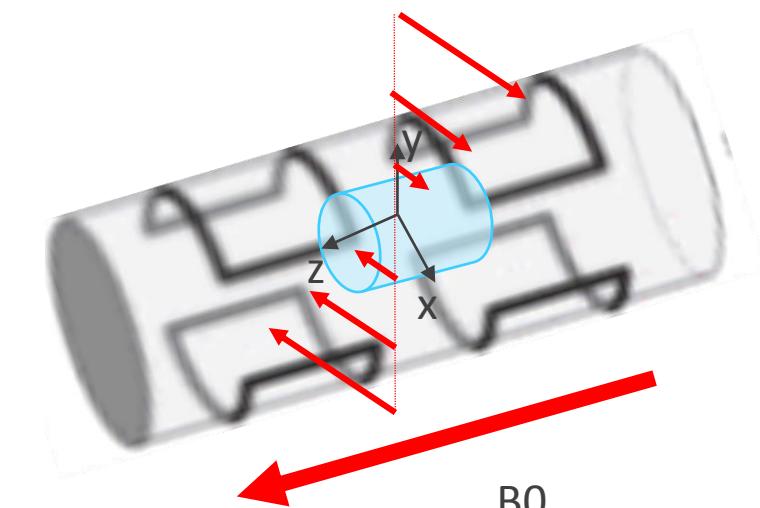
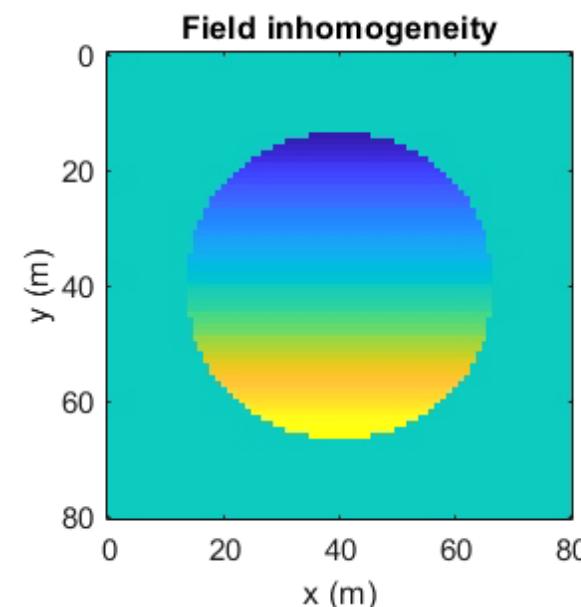
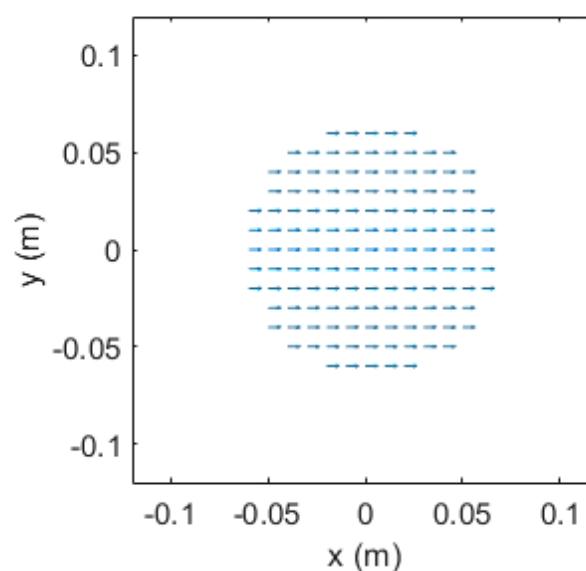


Magnetic field gradient coils : create a linear static field variations



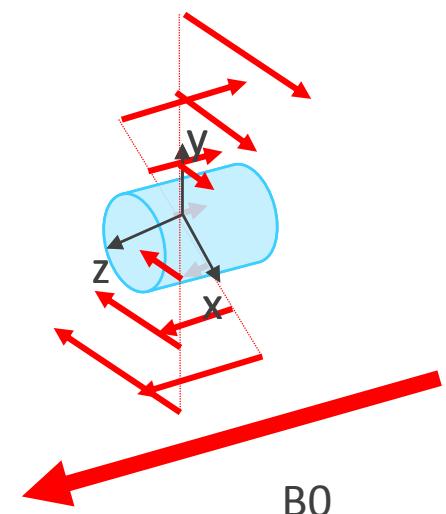
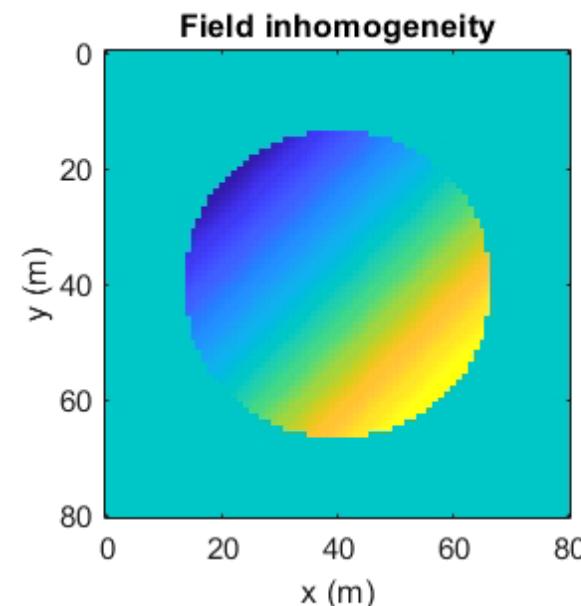
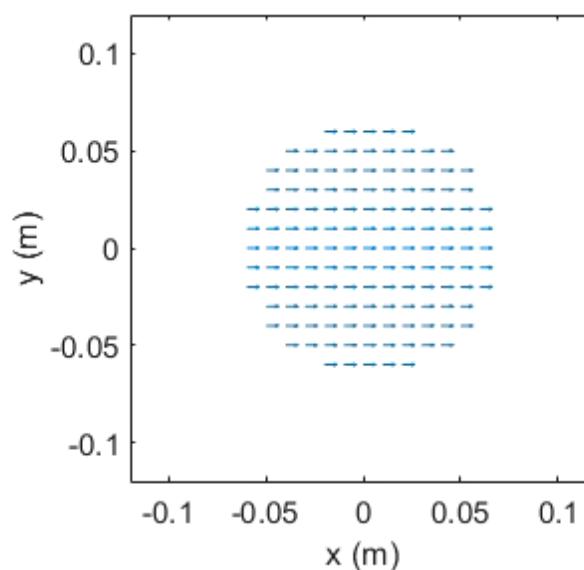
Spatial information in « x »

Magnetic field gradient coils : create a linear static field variations



Spatial information in « y »

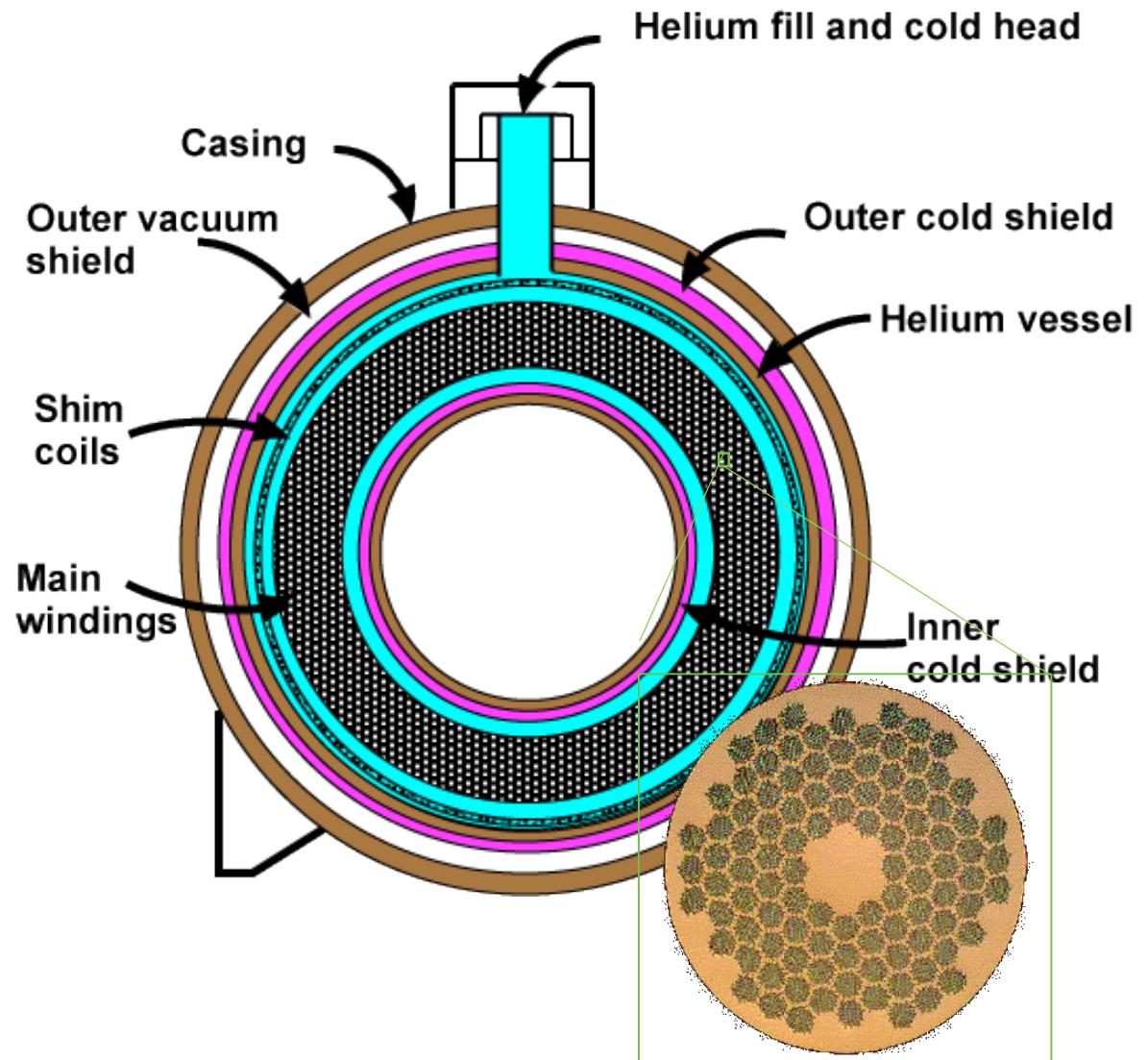
Magnetic field gradient coils : create a linear static field variations



Create enough signal to reconstruct the spatial distribution of the magnetization

Superconducting magnet

- ▶ Electromagnet made from coils of superconducting wire
- ▶ No electrical resistance in the coil's winding
- ▶ Critical temperature (T_c): temperature above which the wire loses its supraconductivity
- ▶ Cooled to cryogenic temperature $< T_c$
- ▶ Material mostly used in MRI superconducting magnets: NbTi
 - $T_c = 10^\circ\text{K}$
 - Suitable for building up to $\sim 11 \text{ T}$ -magnets
- ▶ Coil winding
 - Tens to hundreds of tiny filaments of superconductor (30 – 200 μm thick) in a copper matrix



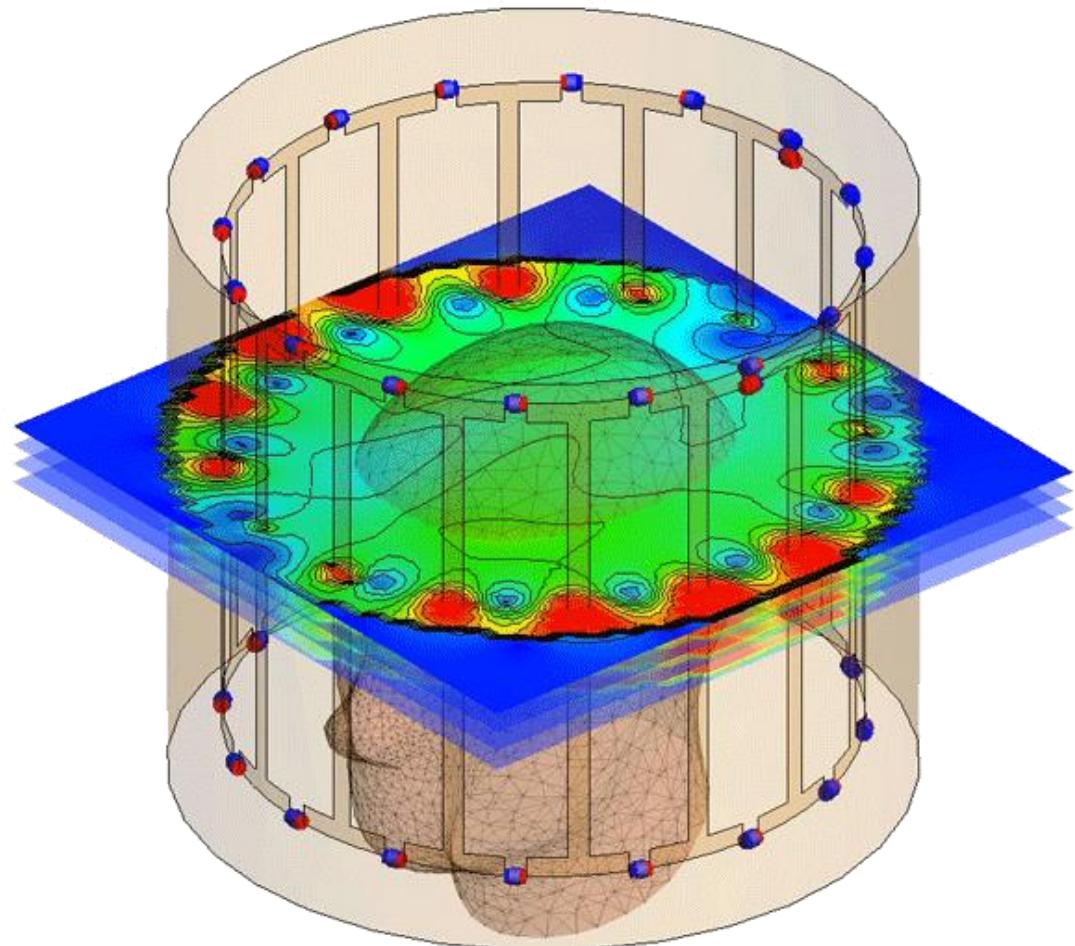
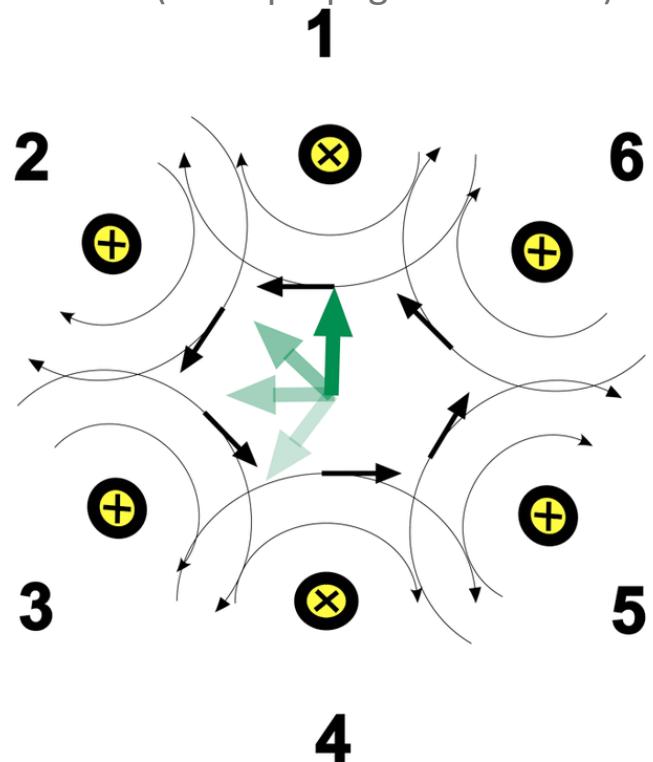
Why privilege superconducting magnets over resistive magnets ?

- ▶ **No power consumption, not heat production**
- ▶ **Excellent temporal stability (less than 1 ppm per hour)**
- ▶ **Excellent field homogeneity (typically less than 0.5 ppm across a sphere of 40 cm of diameter)**
- ▶ **But**
 - field is always « on », need to observe stringent safety rules
 - Care must be taken to minimize magnet-gradient interactions (risk of quench)

RF coil for head imaging

► The « birdcage » design

- Excellent RF field characteristics at frequency below 100 MHz
- Not suitable above \sim 200 MHz (wave propagation effects)

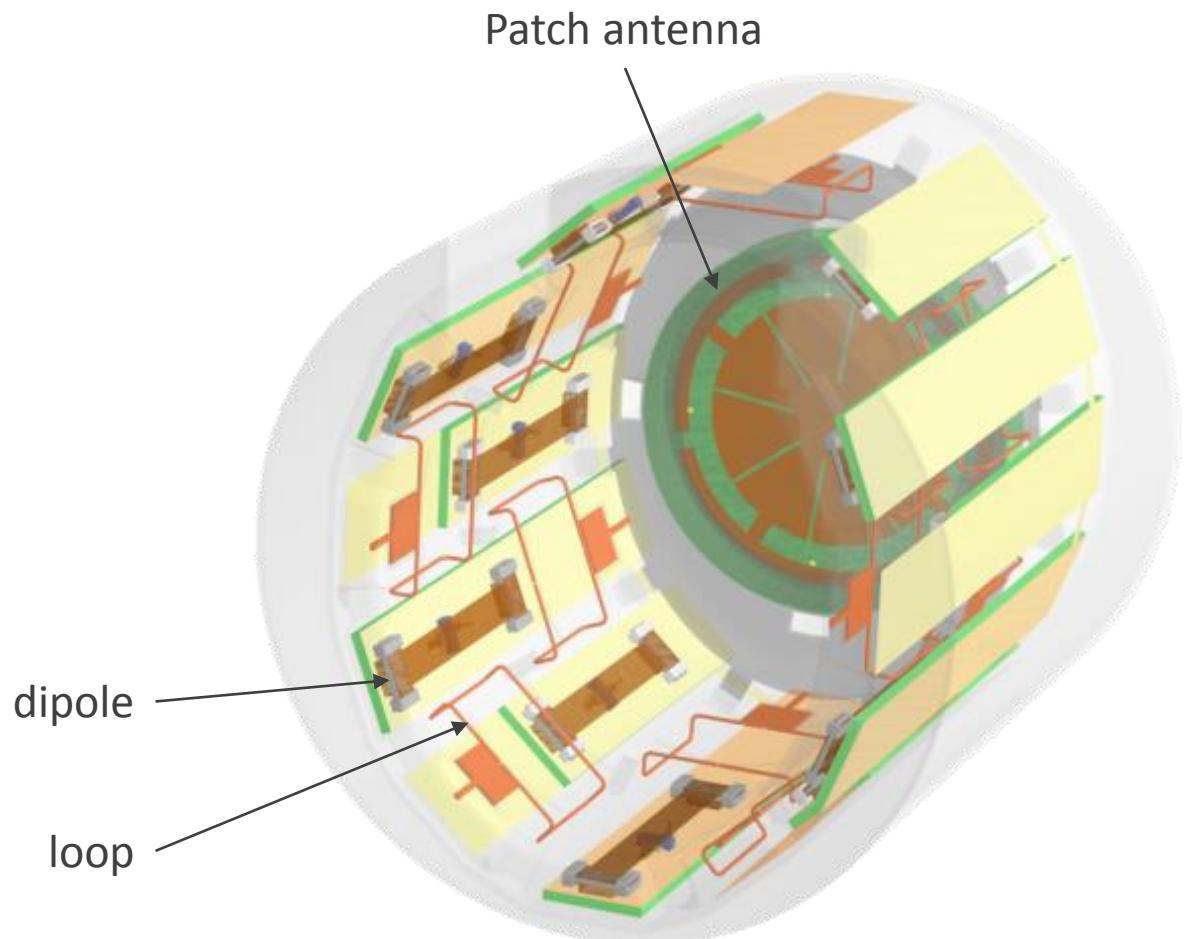


Head coil for 7 Tesla MRI

- ▶ Array of RF loops and/or dipoles



Home-build 8TX-22RX



CAD model of the home-build 8TX-22RX

courtesy of Alexis Amadon & Michel Luong

Signal & noise sources in an NMR experiments

► NMR signal

$$S \propto M_0 \times \frac{d}{dt}(\Phi_{\text{NMR}}) \propto (\gamma B_0)^2 = f_0^2$$

► Noise

- Internal coil noise

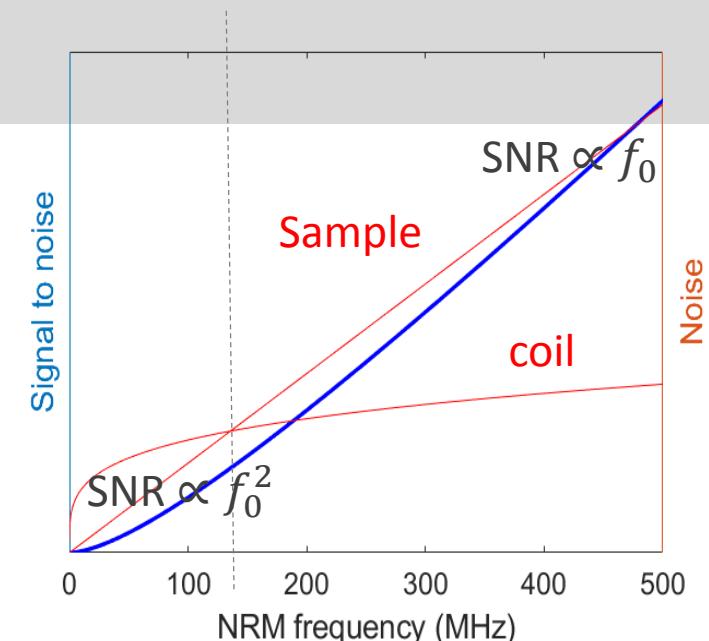
$$\langle N_C^2 \rangle = 4k_B R_C T_C \propto f_0^{1/2}$$

- (Magnetically coupled) sample noise associated with the conductivity of the sample (σ)

$$\langle N_S^2 \rangle = 4k_B R_S T_S \propto \sigma f_0^2$$

► Signal to noise Ratio

$$\frac{S}{\sqrt{\langle N_C^2 \rangle + \langle N_S^2 \rangle}} \propto (f_0)^P, \text{ where } 1 \leq P \leq 2$$

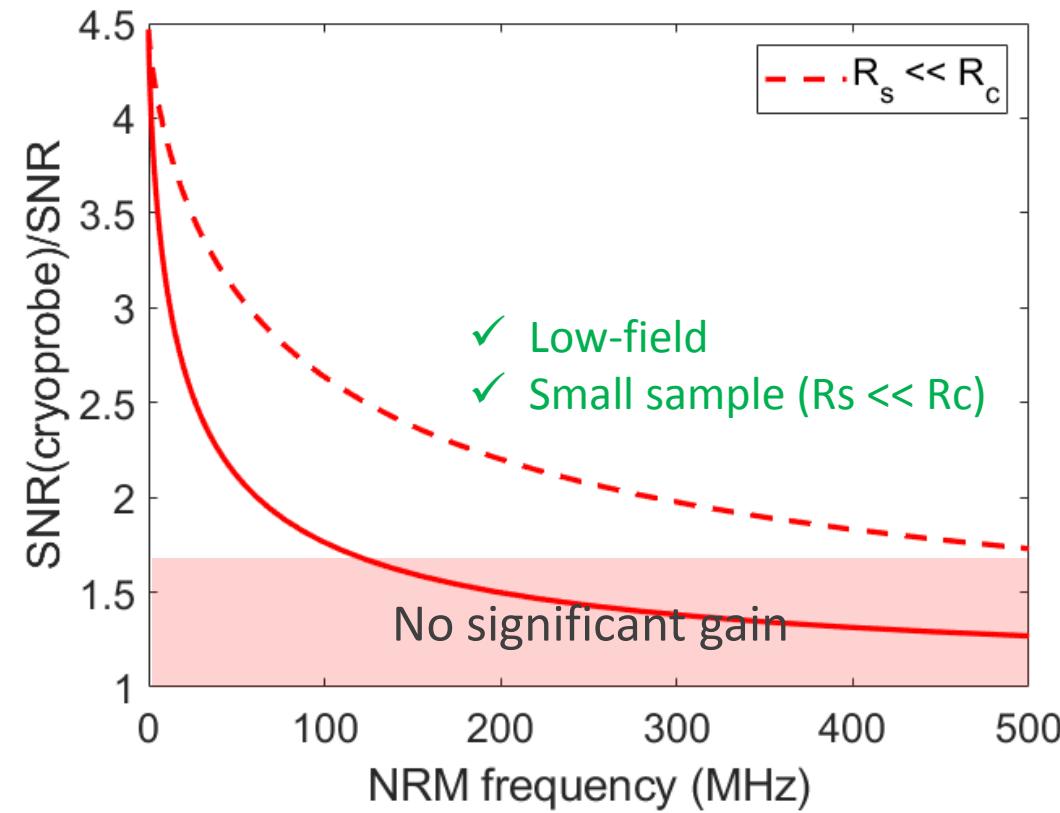


Hoult and Richards, "The signal-to-noise ratio of the nuclear magnetic resonance experiment," *JMR*, vol. 24, no. 1, pp. 71–85, 1976.

Hoult and Lauterbur, "The sensitivity of the zeugmatographic experiment involving human samples," *JMR*, vol. 34, no. 2, pp. 425–433, 1979.

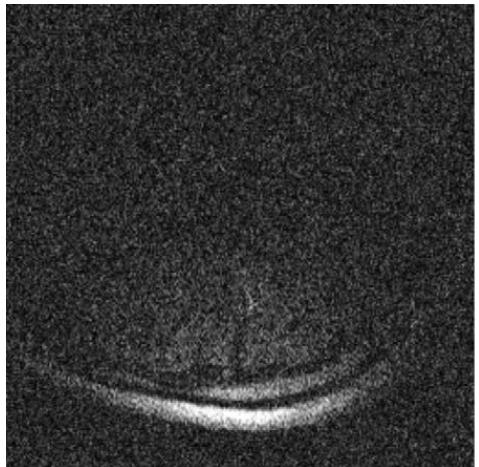
Superconducting NMR probes ?

$$\overline{S} = \sqrt{\langle N_C \rangle + \langle N_S^2 \rangle}$$

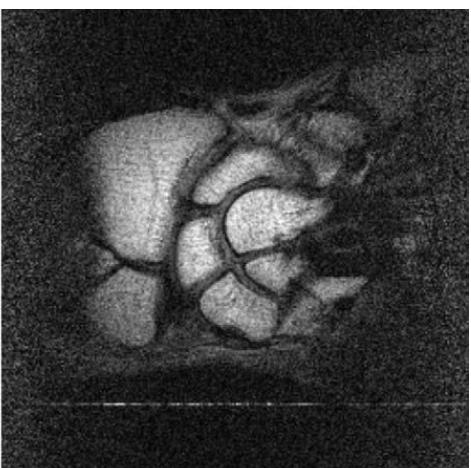
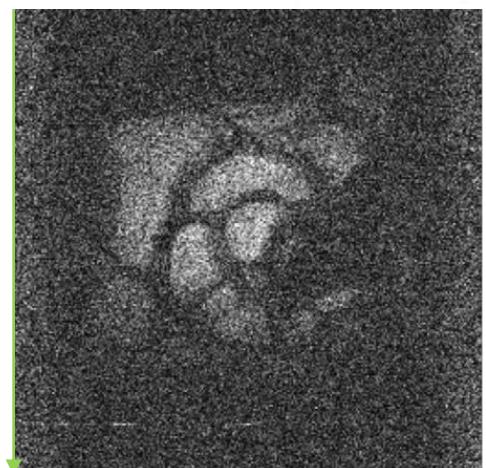
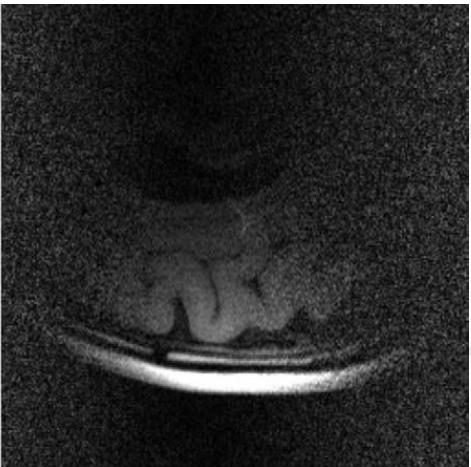


The use of high temperature superconducting (HTS) RF probes

Silver @ 273K



HTS @ 77K



► HTS coil ($T_c > 77K$). YBCO coil onto R-Al₂O₃.^[2]

► **0.2 T MRI (2D Spin-Echo sequence, TA 5:42 min) of the brain (top) / wrist (left) with HTS surface coil (17 mm radius) and a silver-equivalent design. SNR gain = ×6-7.^[1]**

[1] Darrasse and Ginefri, "Perspectives with cryogenic RF probes in biomedical MRI," *Biochimie*, vol. 85, no. 9, pp. 915–937, Sep. 2003.

[2] [Cheong et al. "A high temperature superconducting imaging coil for low-field MRI," *CMR Part B*, vol. 37B, no. 2, pp. 56–64, 2010.

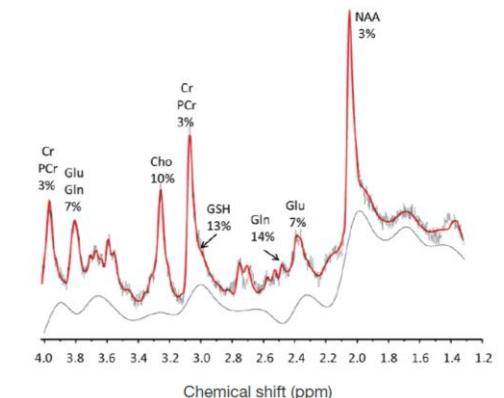
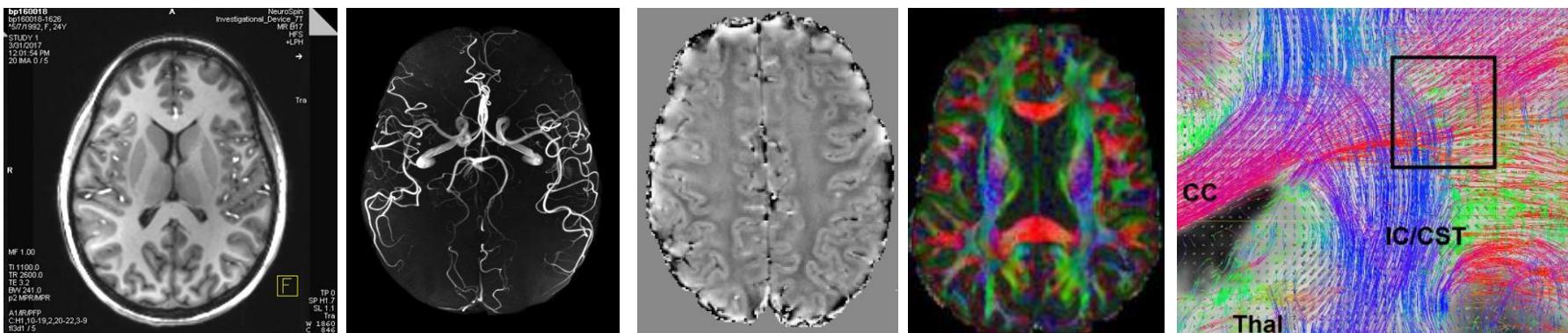


NMR offers a large variety of contrast mechanisms

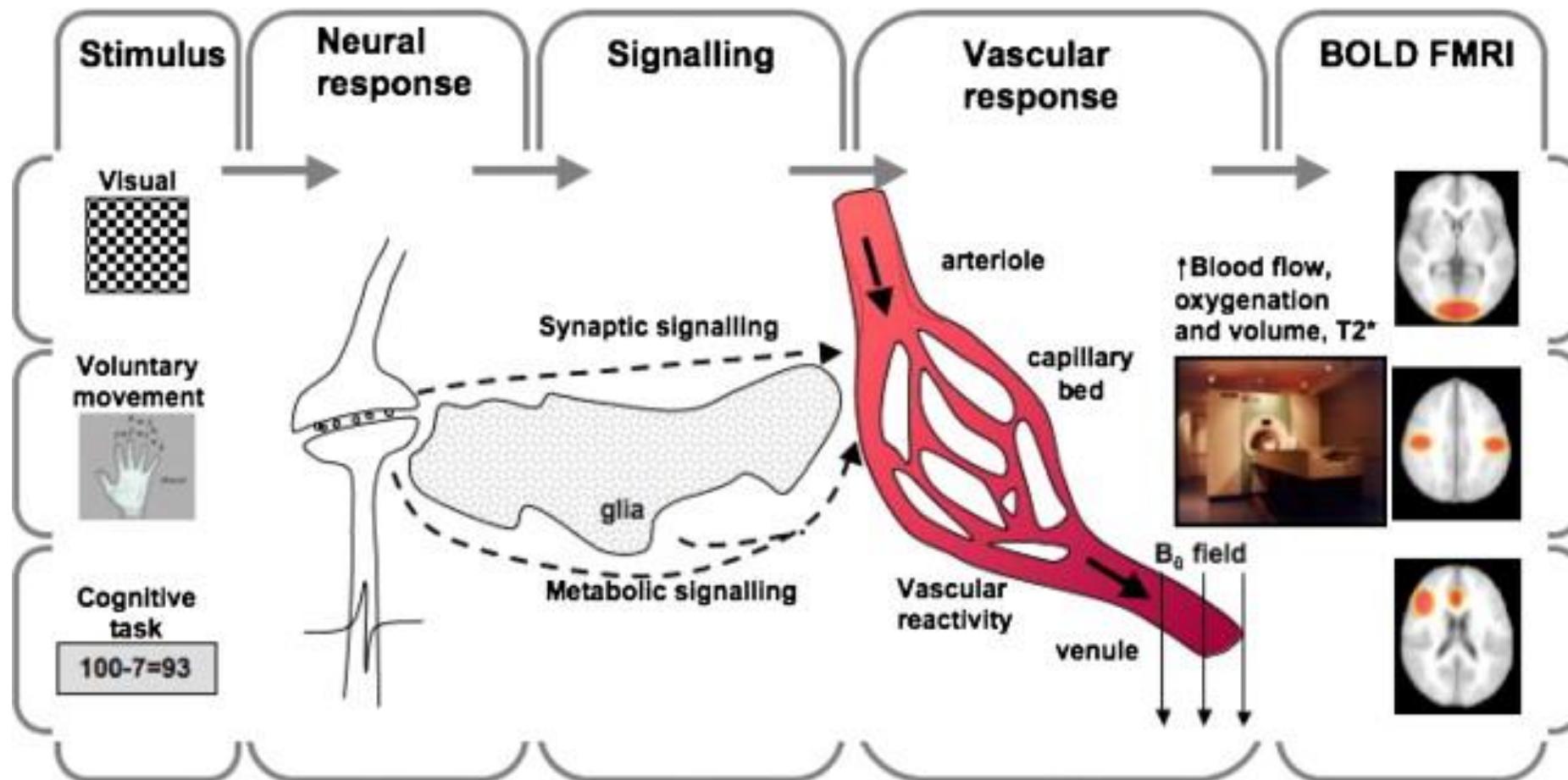
- ▶ relaxation effect (spin-lattice, spin-spin)
- ▶ self-diffusion of the water molecule
- ▶ magnetic susceptibility
- ▶ chemical shift
- ▶ macroscopic flow
- ▶ Blood Oxygenation Level Dependent contrast



- ▶ Anatomical imaging
- ▶ Cerebral blood flow
- ▶ Mean Diffusivity, Diffusion Tensor, tractography ...
- ▶ MR Spectroscopy (identify ~20 brain metabolites)
- ▶ Functionnal MRI

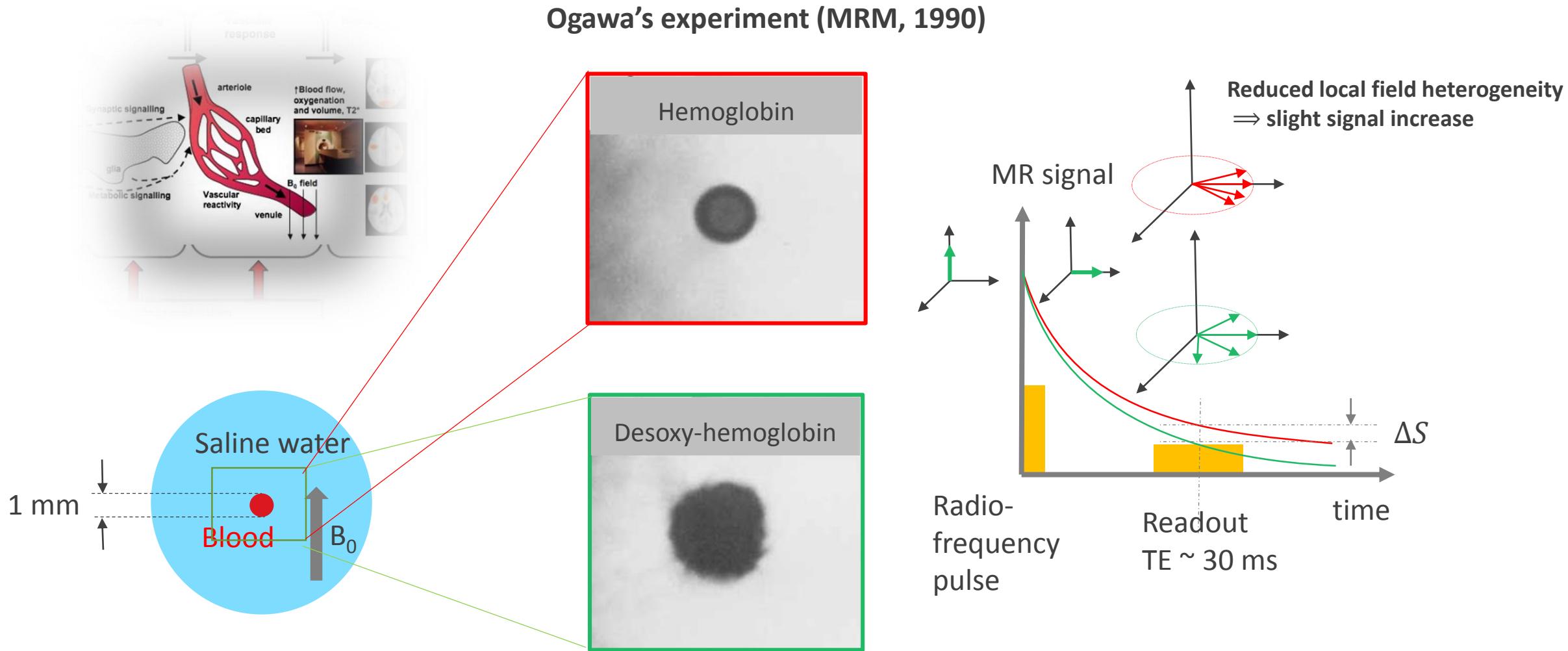


Functional MRI: The blood oxygenation level dependent MRI signal



<http://jonlieffmd.com/blog/complexity-in-searching-for-the-neural-code>

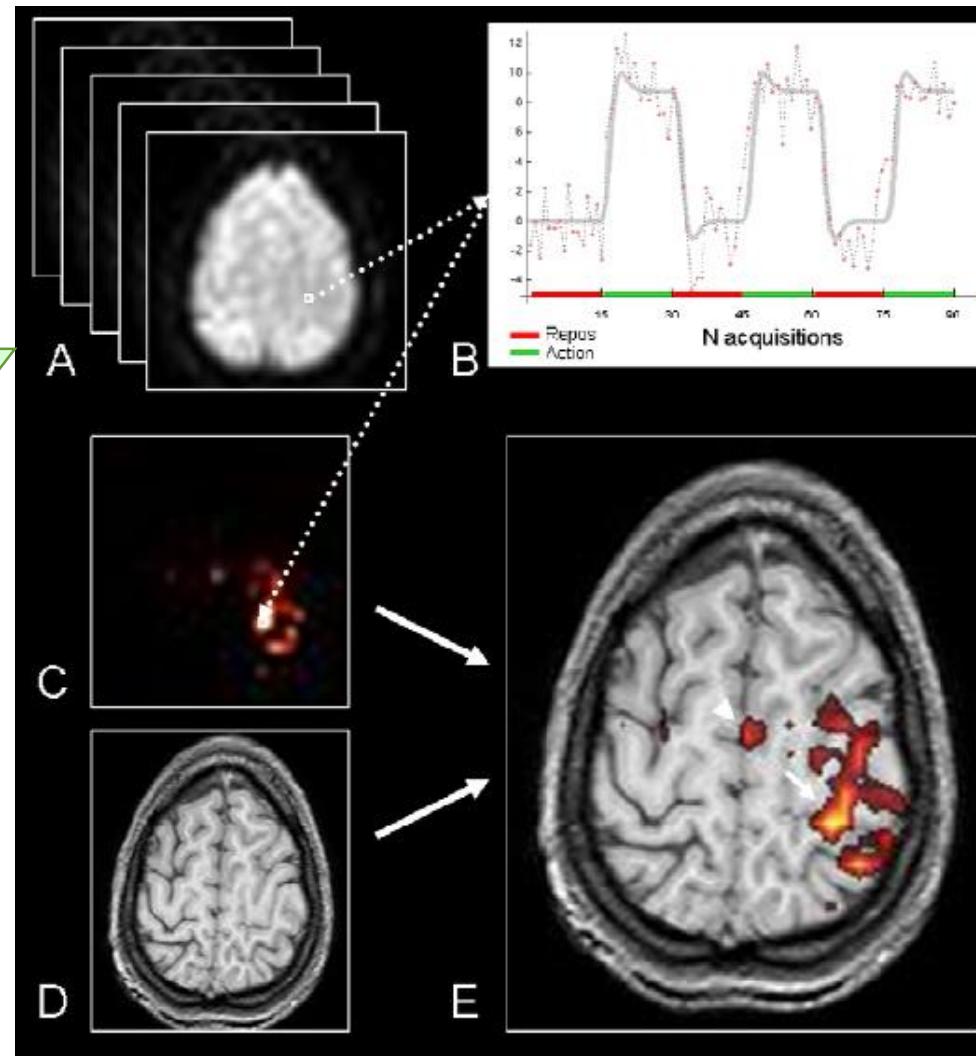
Functional MRI: The blood oxygenation level dependent MRI signal



Ogawa et al. "Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields," *Magn. Reson. Med.*, vol. 14, no. 1, pp. 68–78, Apr. 1990.

Stimulus**Voluntary movement****Cognitive task**

$$100-7=93$$



- ▶ Time series of MR images
- ▶ Time course of the MR signal in a given voxel
- ▶ Significance map of a task-evoked BOLD signal
- ▶ Anatomical MR image
- ▶ « Brain activation » map overlaid on the anatomical image

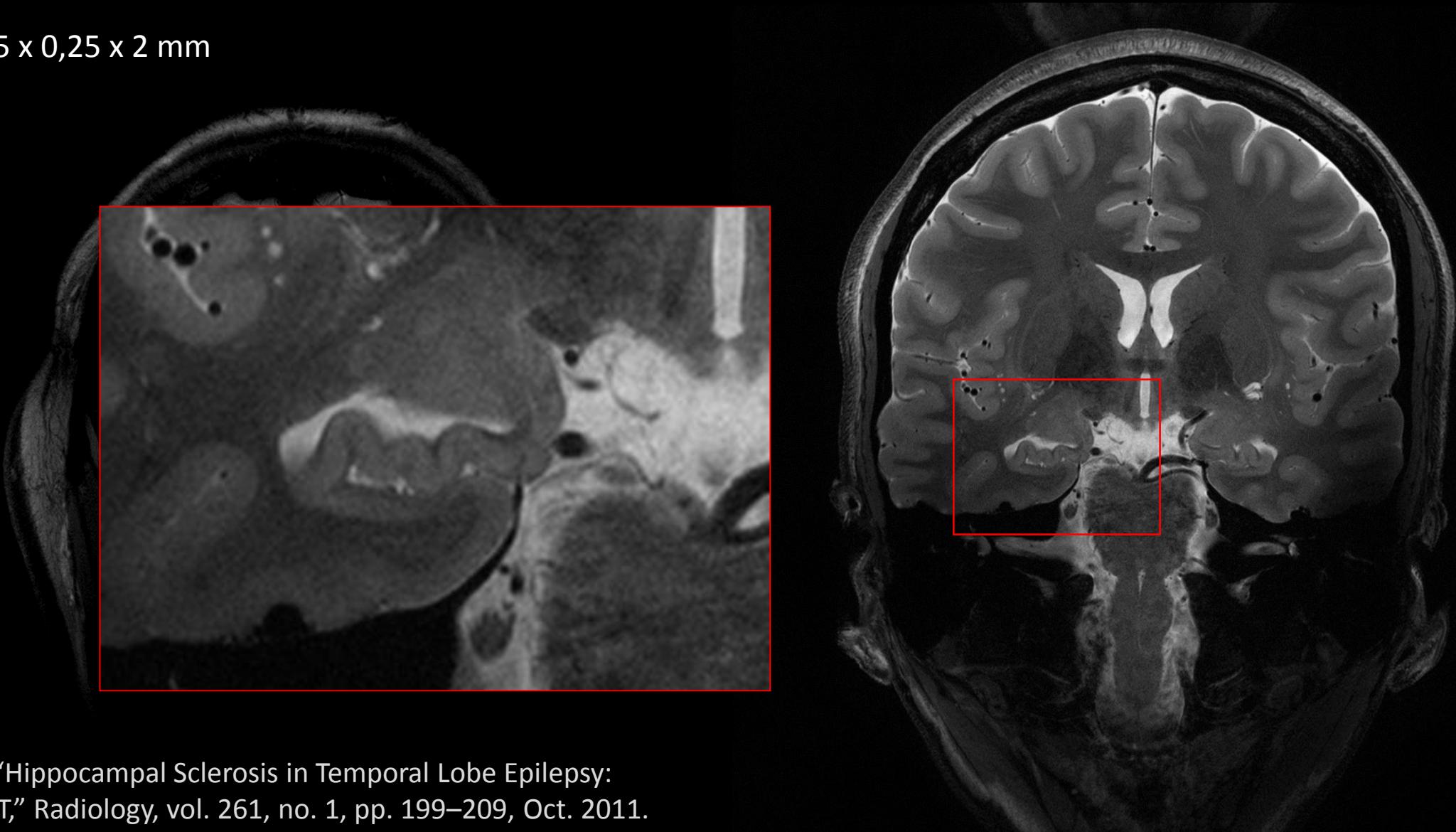
A. Krainik et al., "L'imagerie par résonance magnétique cérébrale fonctionnelle en pratique clinique," Journal de Radiologie, vol. 87, no. 6, pp. 607–617, 2006.

- ▶ **SNR grows supralinearly with B₀**
 - Increase spatial or temporal resolution
- ▶ **Enhanced chemical shift**
 - Applications in **MR spectroscopy & Chemical shift imaging**
- ▶ **Enhance magnetic susceptibility contrast**
 - Blood oxygenation level dependent (BOLD) contrast enhanced -> potential for **functional MRI studies**
- ▶ **Non-proton (Sodium, Phosphorus ...) MRI**

High-resolution turbo-spin echo acquisition at 7 Tesla

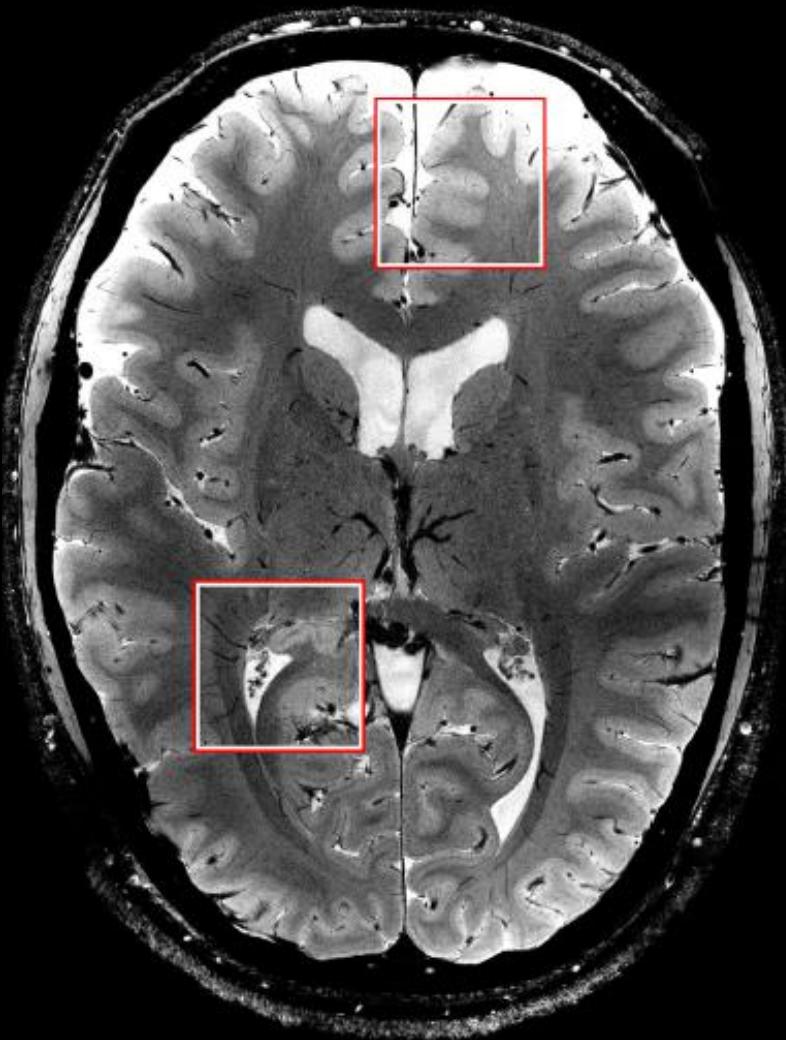
Voxel size 0,25 x 0,25 x 2 mm

TA 20 min

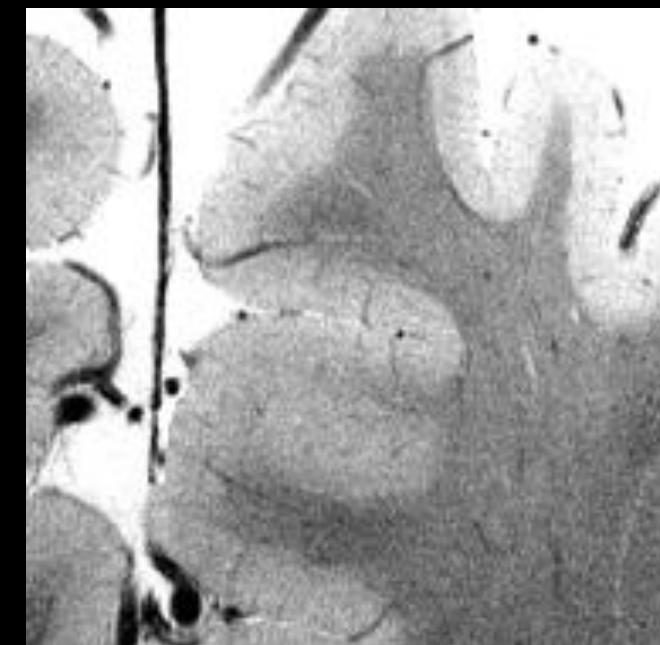
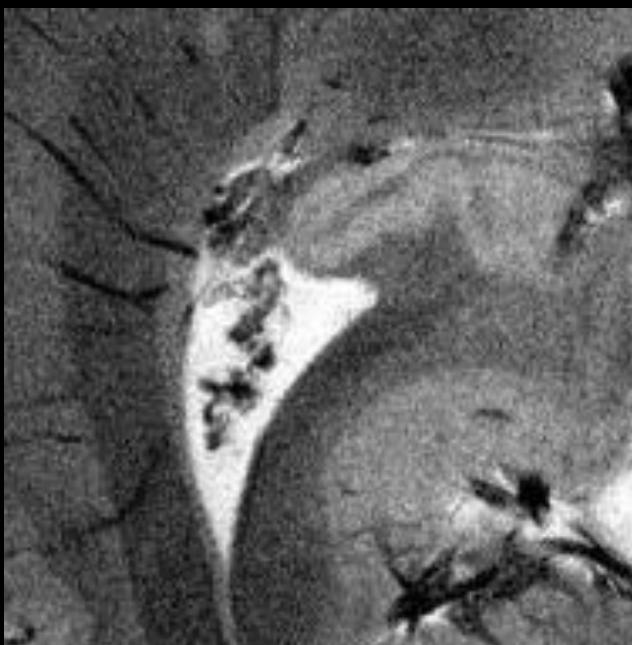


Henry et al., "Hippocampal Sclerosis in Temporal Lobe Epilepsy: Findings at 7 T," Radiology, vol. 261, no. 1, pp. 199–209, Oct. 2011.

High-resolution susceptibility-weighted acquisition of the brain at 7T

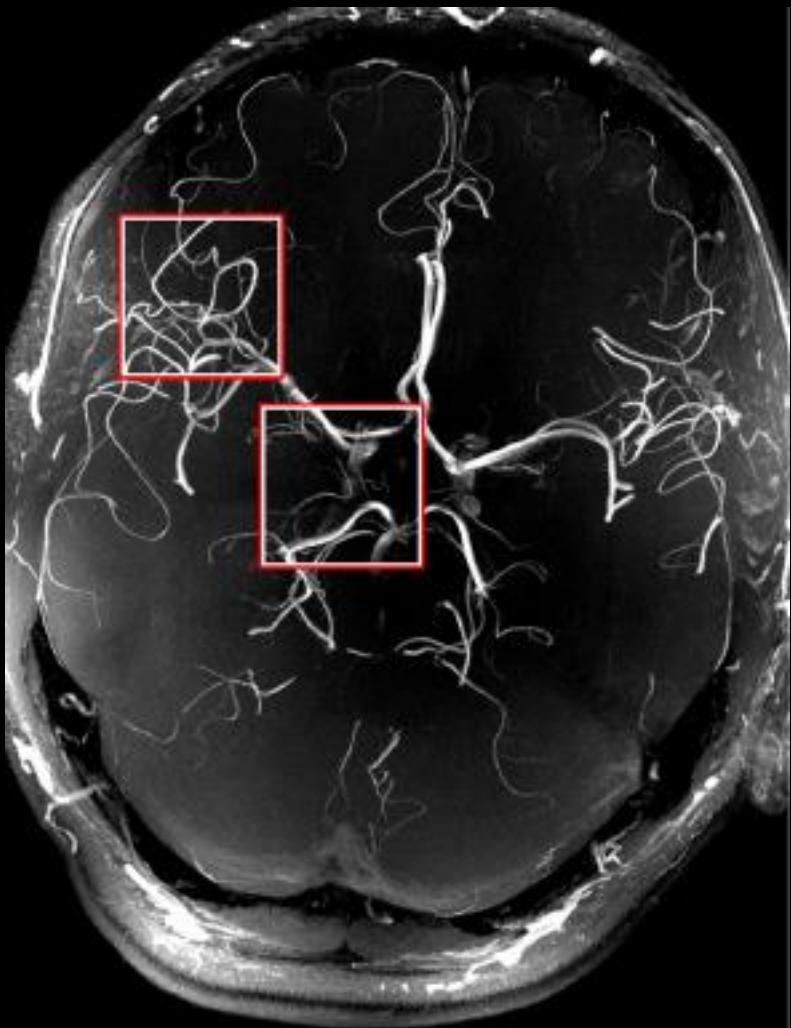


- Voxel size $0.12 \times 0.12 \times 0.6$ mm
- 2 acquisitions of 11:20 each
- Prospective motion correction

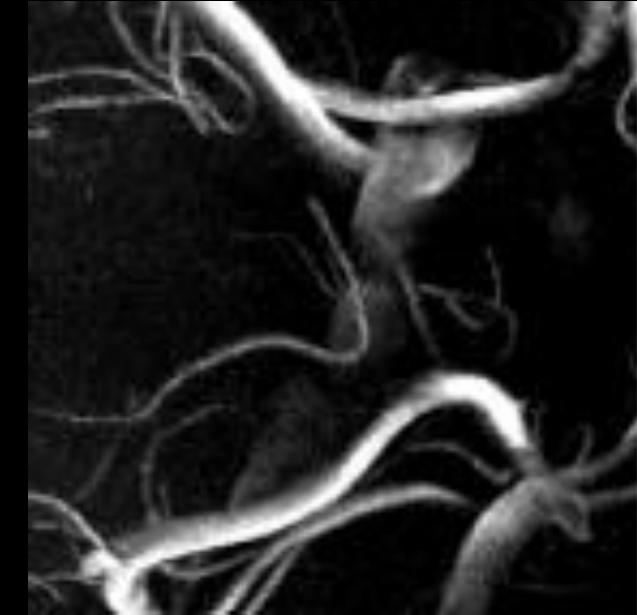
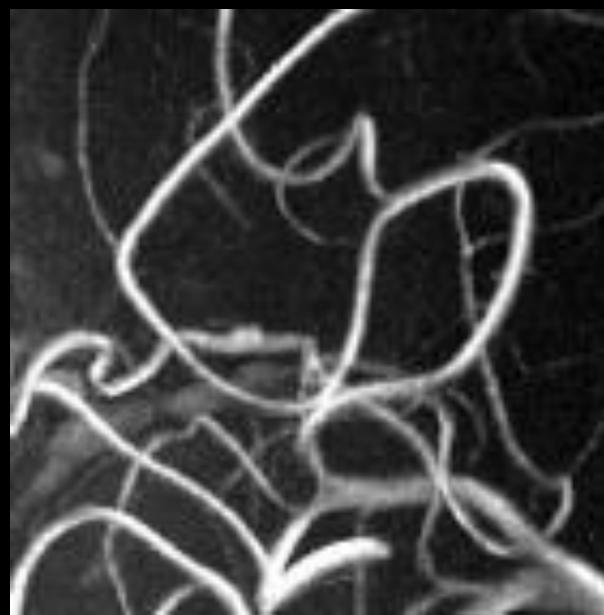


Stucht et al. “Highest Resolution In Vivo Human Brain MRI Using Prospective Motion Correction,” PLOS ONE, vol. 10, no. 7, p. e0133921, Jul. 2015.

High-resolution « Time of flight » acquisition of the brain at 7 Tesla



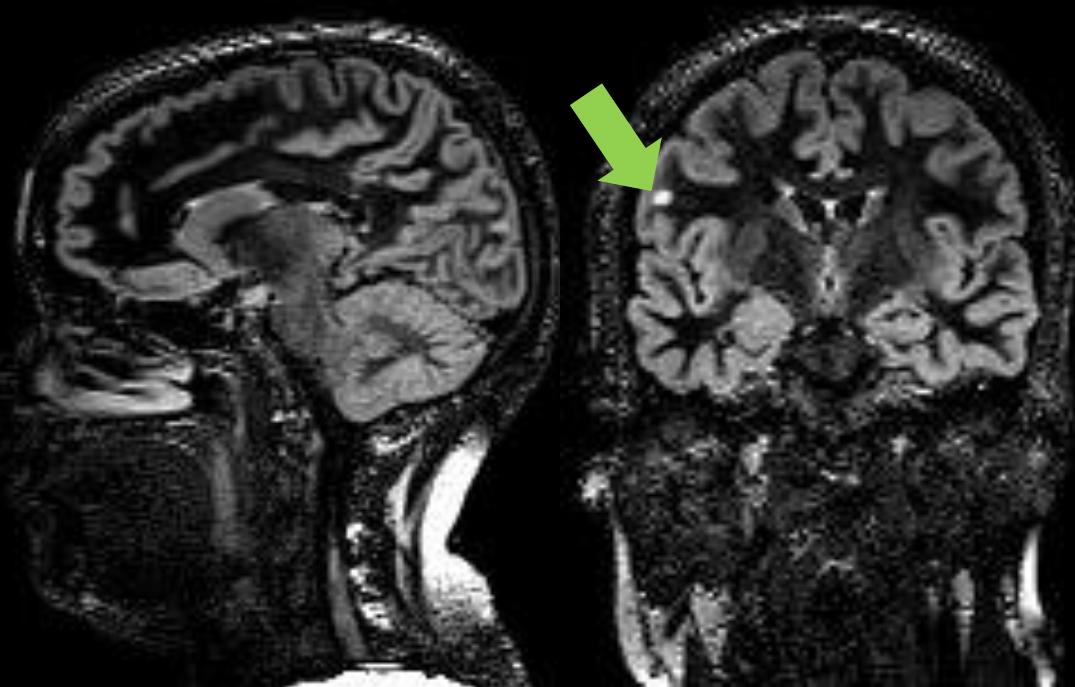
- Voxel size $0.2 \times 0.2 \times 0.2$ mm
- 2 acquisitions of 28 min each
- Prospective motion correction



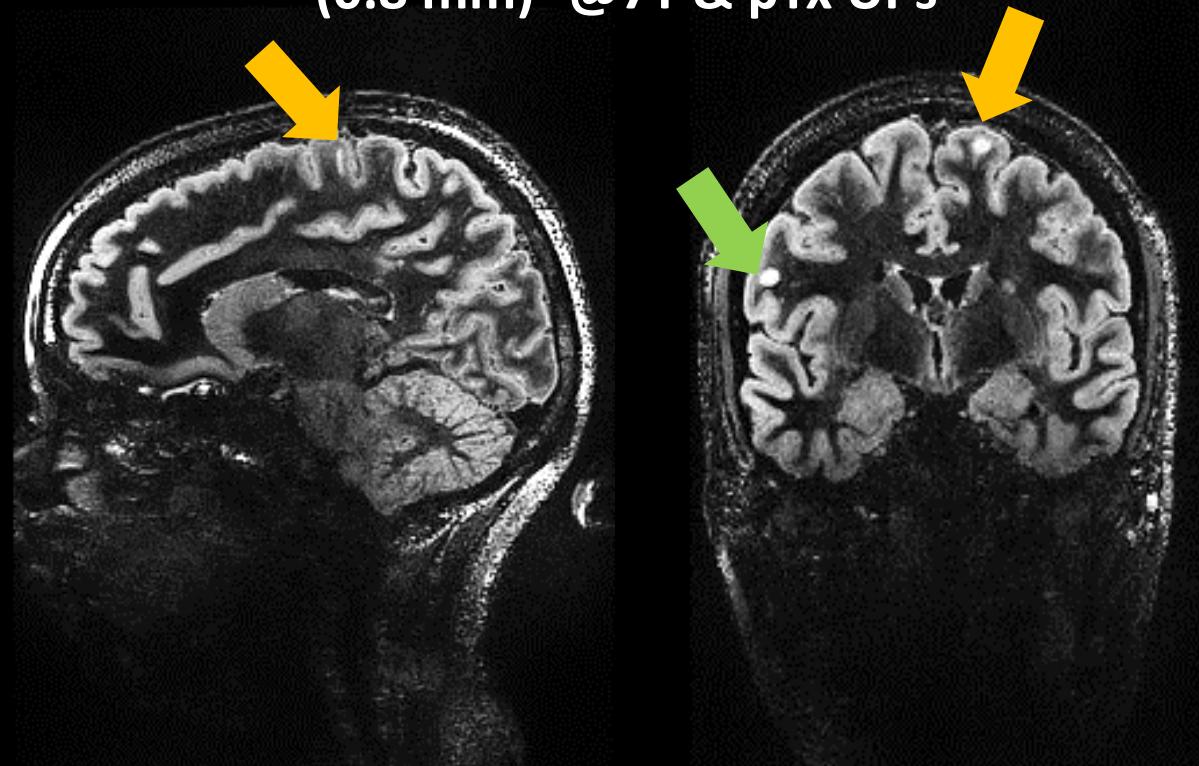
Stucht et al. “Highest Resolution In Vivo Human Brain MRI Using Prospective Motion Correction,” PLOS ONE, vol. 10, no. 7, p. e0133921, Jul. 2015.

Lesion identification in a multiple-sclerosis patient

$(1.3 \text{ mm})^3 @3\text{T}$



$(0.8 \text{ mm})^3 @7\text{T} \& \text{pTx UPs}$



courtesy of Emilie Poirion

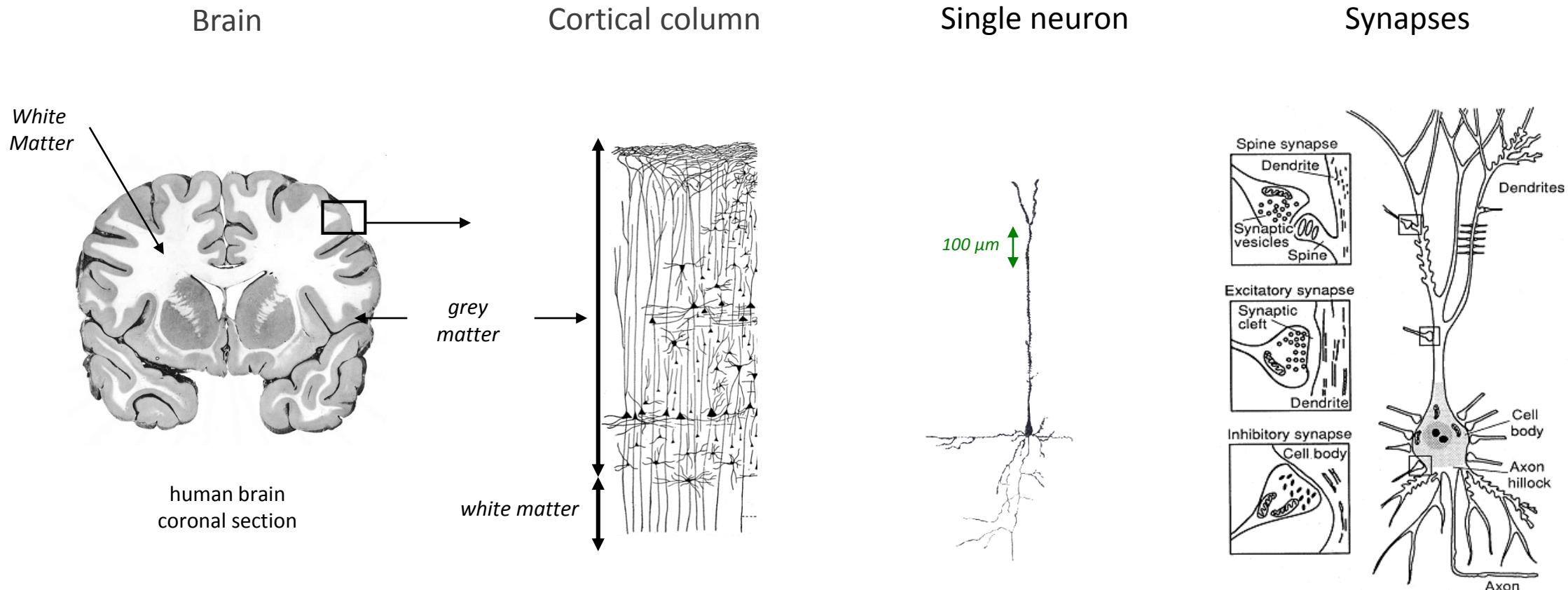
► Magnetic Resonance Imaging

- The nuclear Zeeman effect
- MRI instrumentation & principles
- Application for neurosciences
- The race towards ultra-high-field MRI

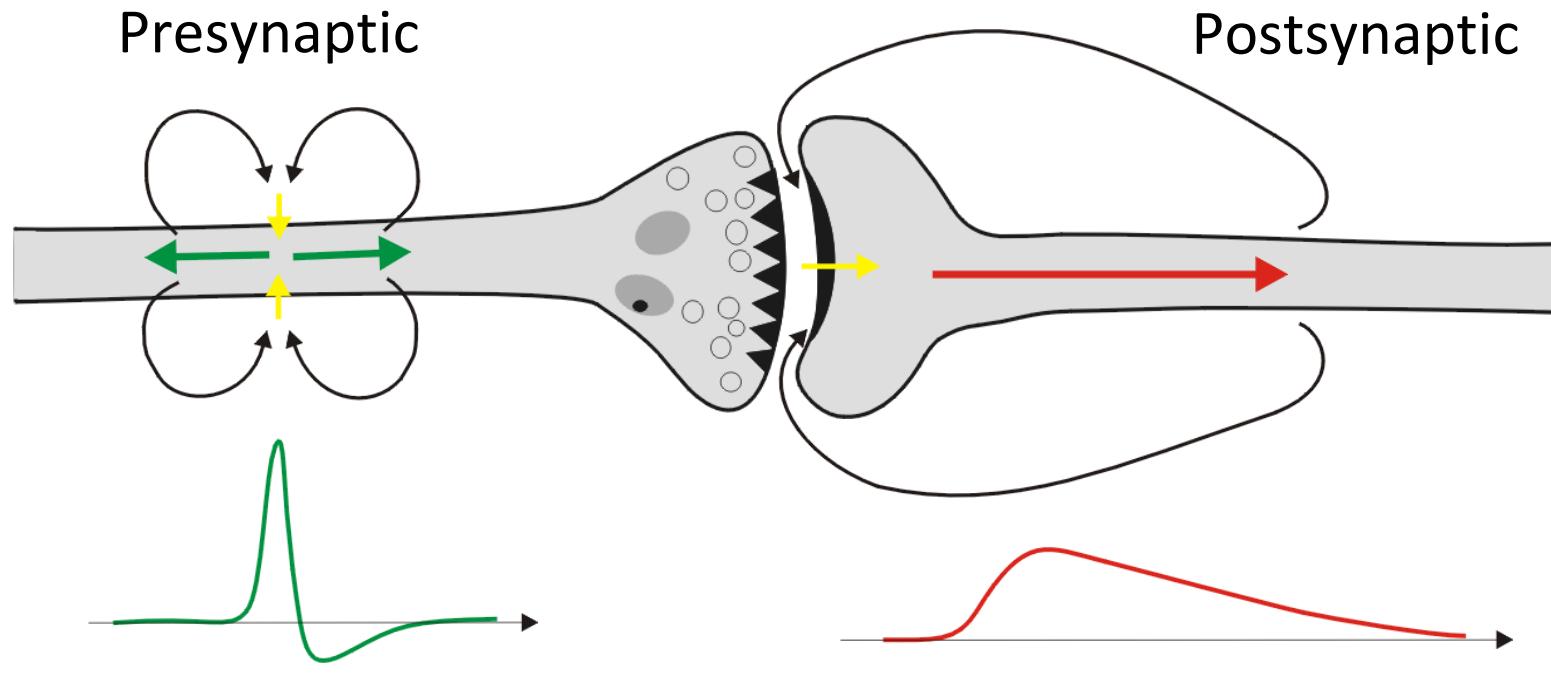
► MagnetoEncephalography

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- The MEG instrumentation
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► Conclusions



courtesy of Lauri Parkonen

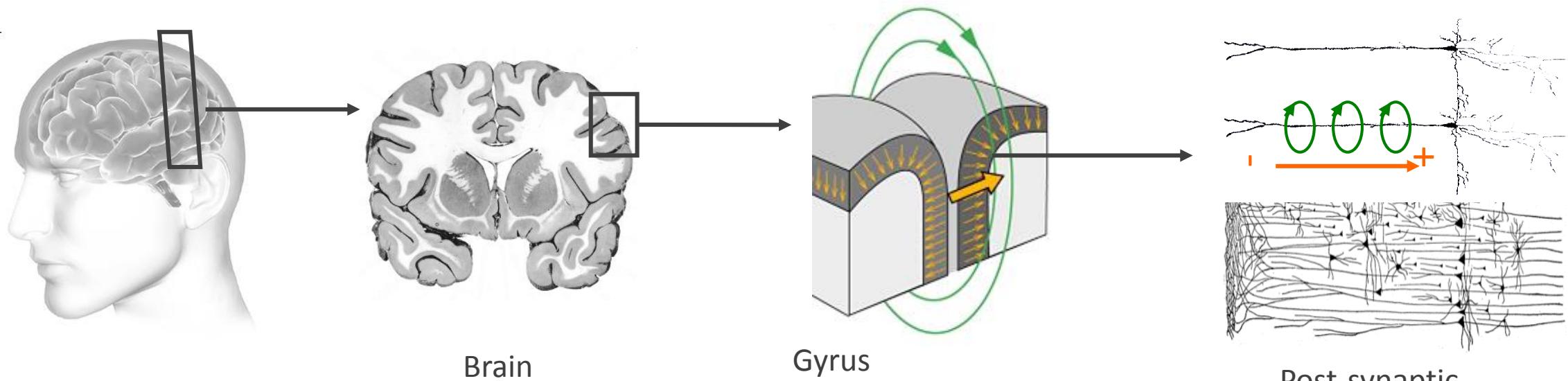


Action potentials

Postsynaptic currents:
**the main source of
MEG&EEG!**

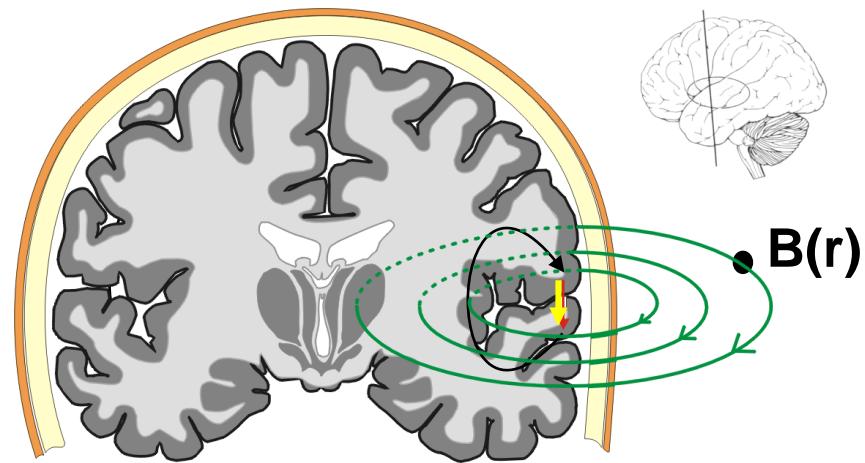
courtesy of Lauri Parkonen

The basis of the MEG signal



MEG benefit over ElectroEncephalography:

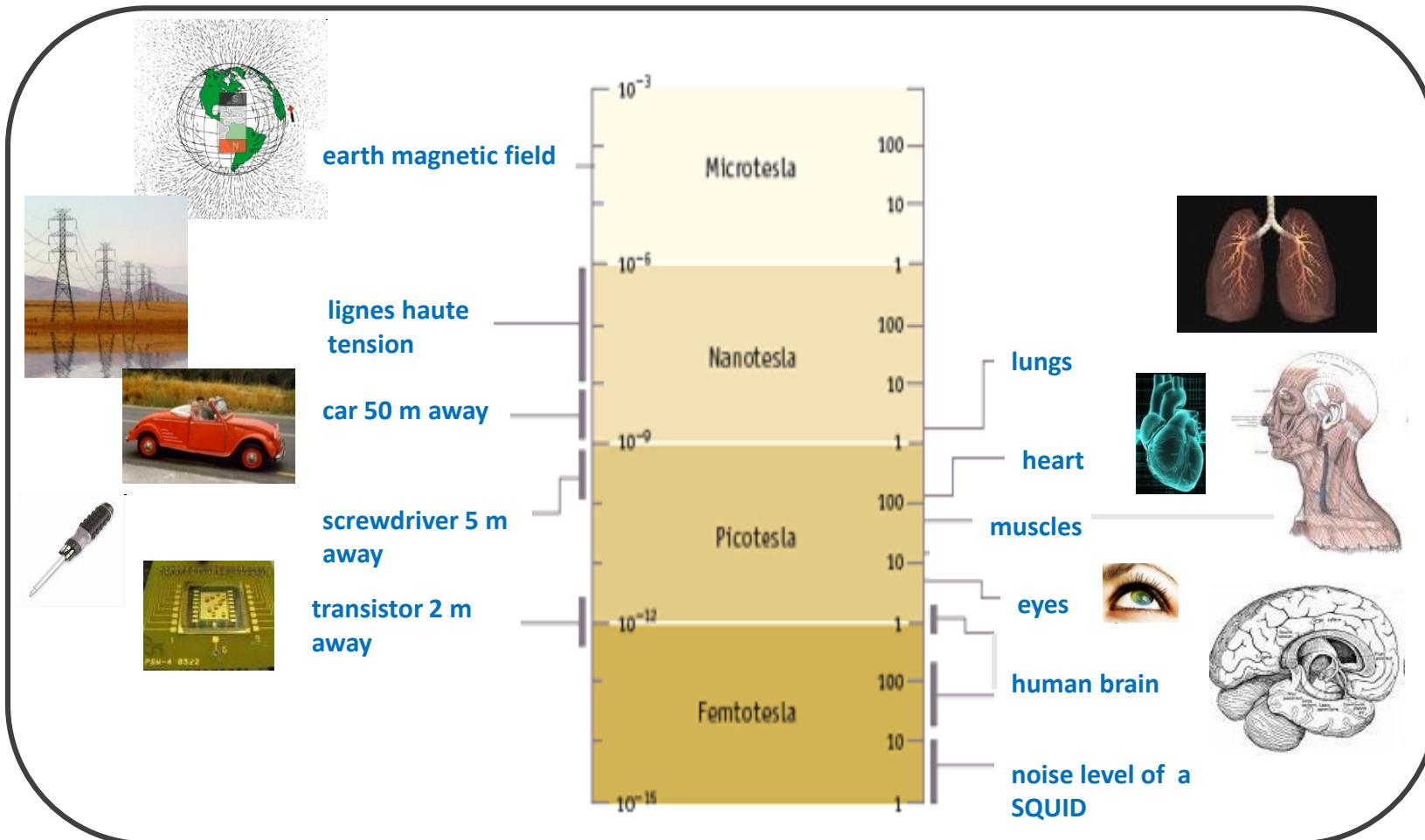
- Whereas the electrical brain signals are distorted and attenuated by the skull, scalp etc, the magnetic field is NOT.
- This makes source localization an easier task with MEG.



courtesy of Lauri Parkonen

Signals of interest in a MEG experiment

Magnetic field associated with brain activity : 10^{-12} to 10^{-13} Tesla (femtoTesla range)

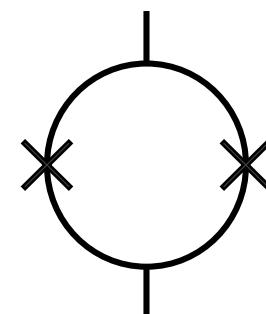
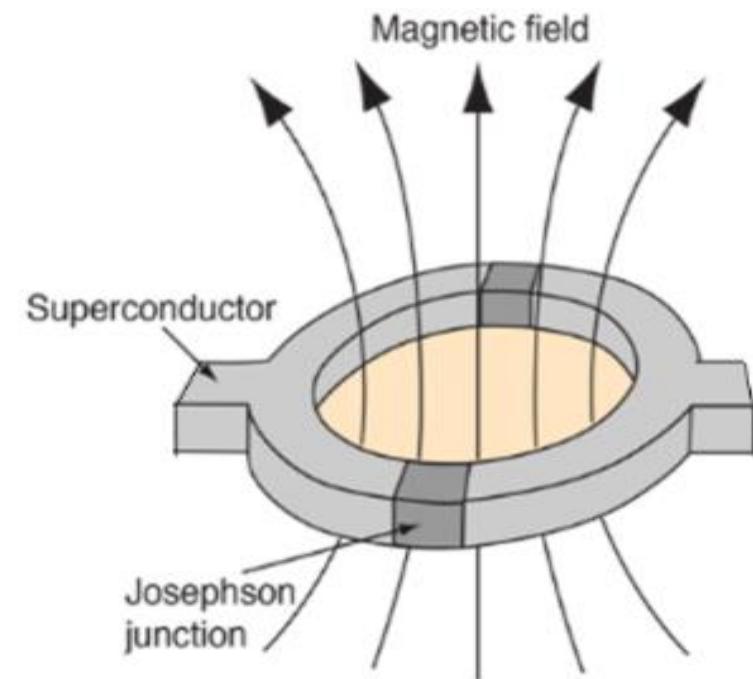


Detection of magnetic fluxes in the femtoTesla range ?

The superconducting QUantum Interference Device (SQUID)

- ▶ Two superconductors separated by parallel Josephson junctions (thin insulating layers)
- ▶ A small electric current can flow across the junctions without developing a voltage across them (“tunnel” effect). Valid until the current exceed the ‘critical current’ (maximum supercurrent).
- ▶ A SQUID allows measuring magnetic field flux changes of the order of one flux quantum:

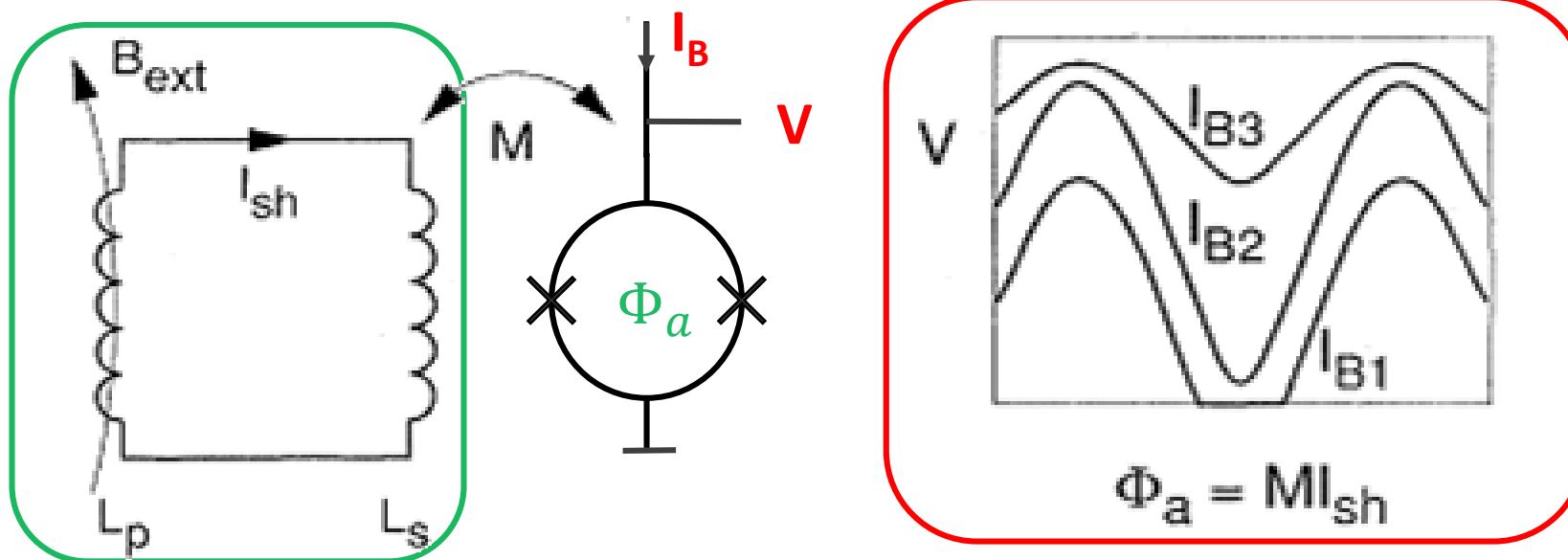
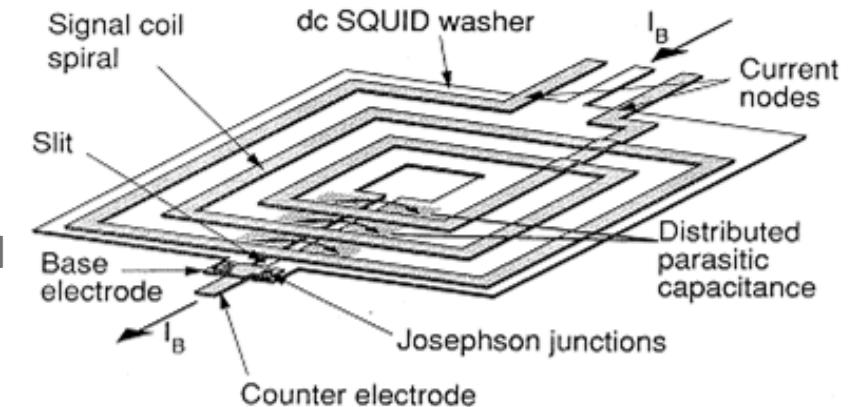
$$\Phi_0 = \frac{h}{2e} = 2,0678 \times 10^{-15} \text{ T.m}^2$$



Schematic representation of the SQUID

Magnetic fluxes detection with Superconducting QUantum Interference Device (SQUIDS)

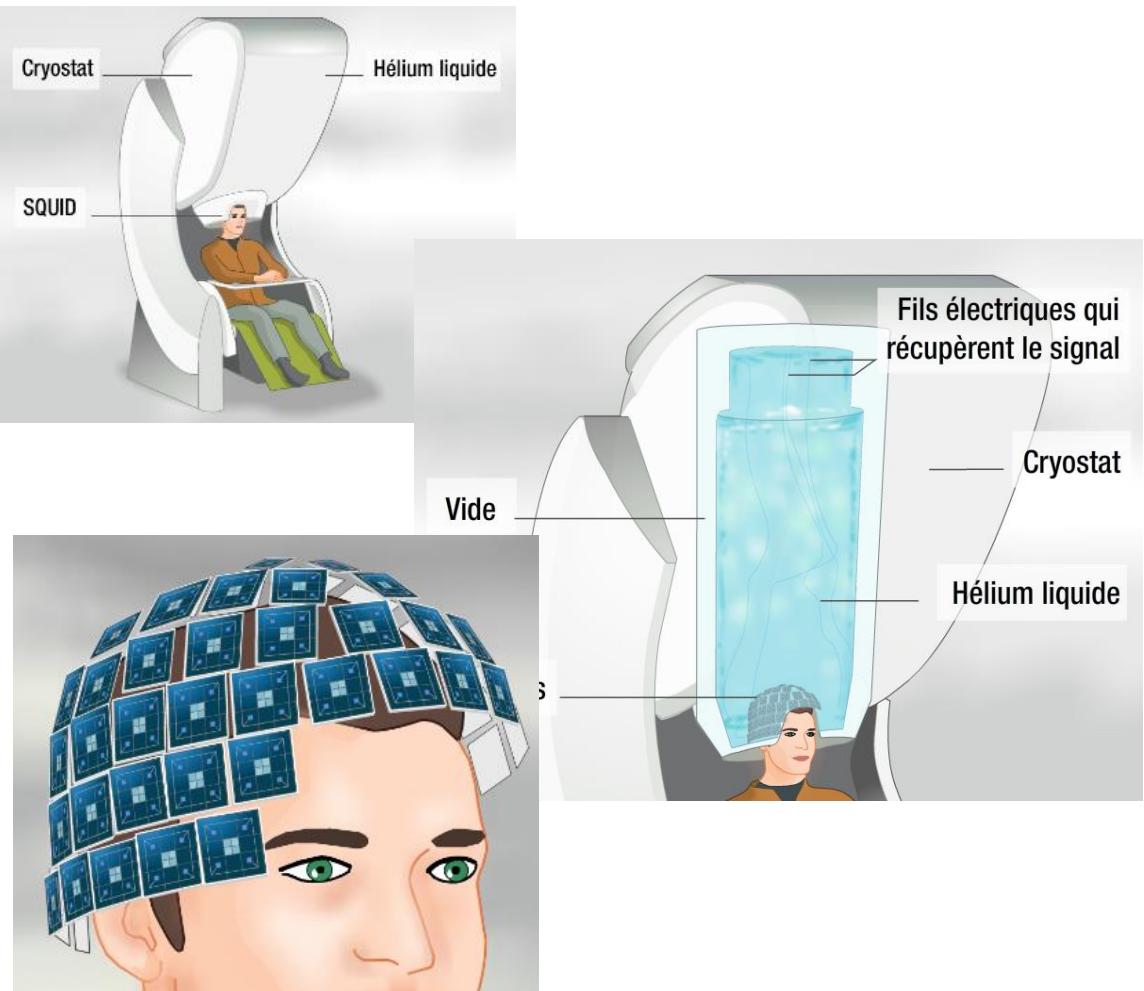
- ▶ The external magnetic signal is coupled to the SQUID using a superconducting **flux transformer**.
- ▶ Magnetic field flux couple to the SQUID = Φ_a
- ▶ Apply a bias current (I_B) across the SQUID just above twice the critical current of the Josephson junctions
- ▶ **Measured voltage varies with Φ_a**



adapted from [1]

[1] Hämäläinen et al. "Magnetoencephalography---theory, instrumentation, and applications to noninvasive studies of the working human brain" *Rev. Mod. Phys.*, vol. 65, no. 2, pp. 413–497, Apr. 1993.

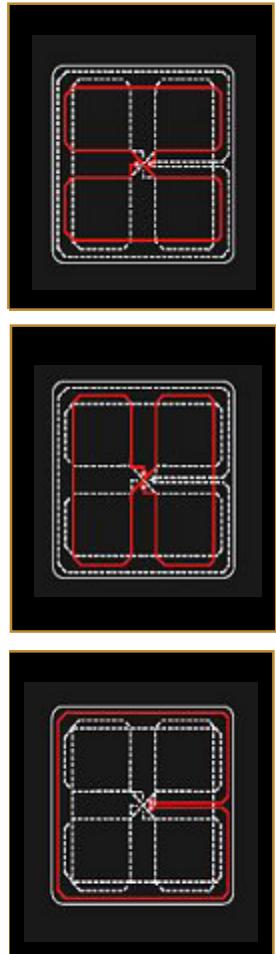
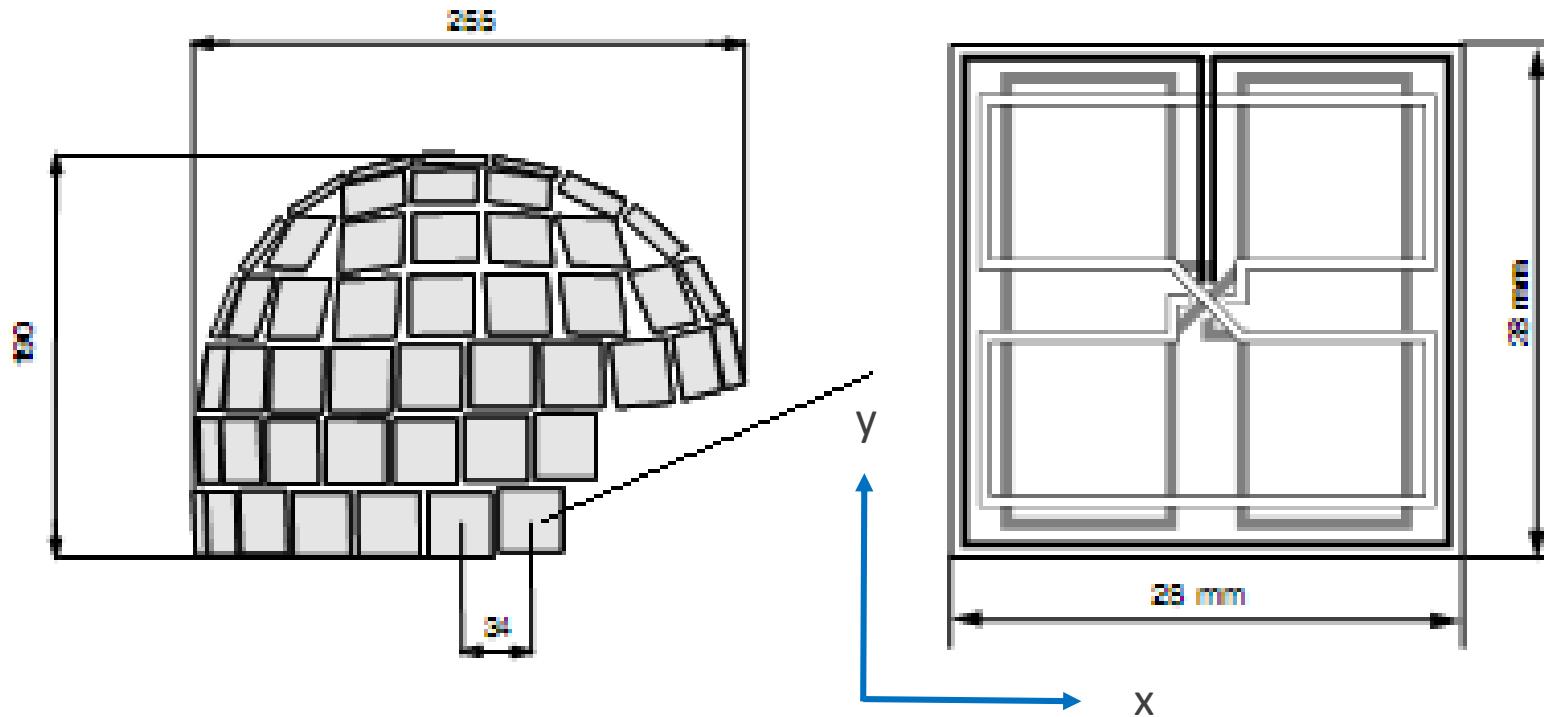
- ▶ SQUIDs operate at a T° below the critical T° of the superconductor (LTS)
- ▶ Bathed in the MEG dewar filled with liquid He ($T^\circ=4K$)
- ▶ 102 sensors elements covering the entire head.
- ▶ To avoid any parasitic magnetic field sources, the MEG system is in a magnetically shielded room



http://joliot.cea.fr/drj/joliot/Pages/Plateformes_et_infrastructures/plateformes-institut/imagerie-in-vivo/Imageurs-cliniques.aspx?Type=Chapitre&numero=4

► Each sensor element is sensitive to three orthogonal field components:

- Normal field component of the magnetic field (B_z)
- Two gradient components of B_z ($\Delta B_z / \Delta x$ & $\Delta B_z / \Delta y$)



MEG installation at Neurospin (Elekta system)

Projection screen
(visual stimuli display;
instructions for the task)

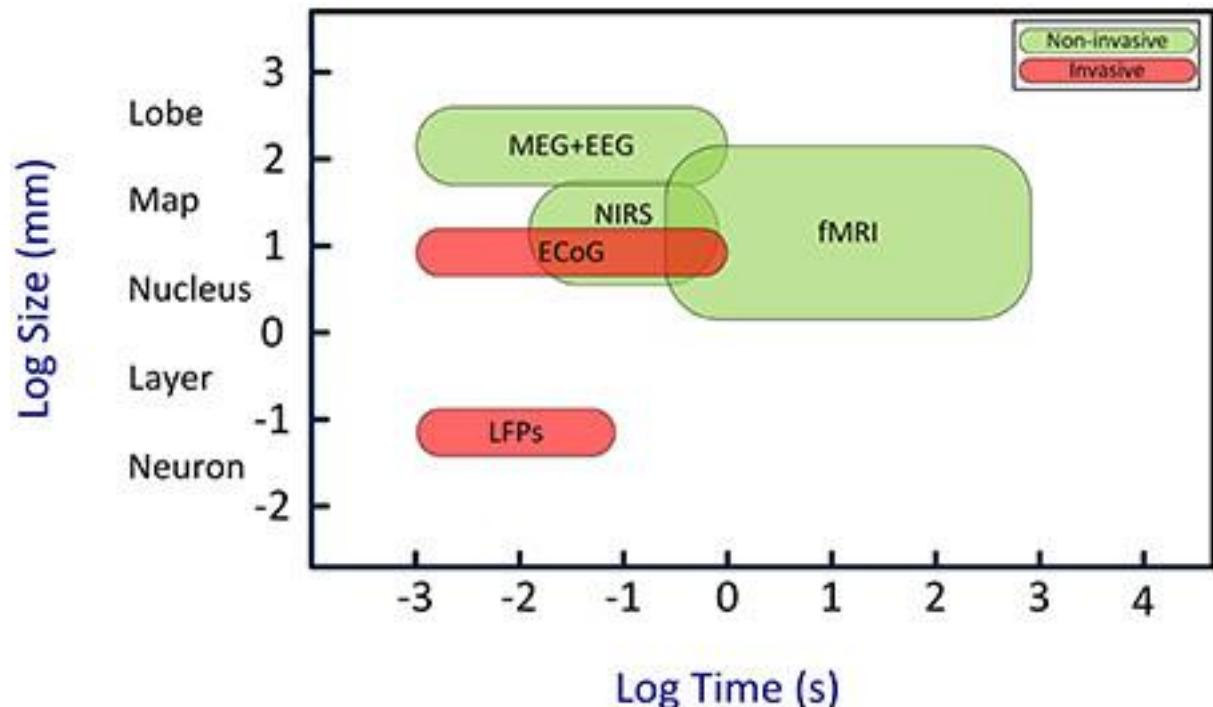


MEG dewar
(~80 liters of liquid He)

Shielded room to prevent parasitic external magnetic field sources

Mapping brain activity

- ▶ Excellent temporal resolution (ms range)
⇒ Rich information on brain dynamics
- ▶ Established methods for source localisation
⇒ spatial resolution \approx cm. But decreases with distance from the sensors.
- ▶ Great potential for studying the large-scale dynamics of brain activity
- ▶ Neuroscience of language, consciousness
- ▶ Resting-state brain research
- ▶ Clinical neuroscience:
 - Epilepsy
 - Autism spectrum disorders
 - Movement disorders

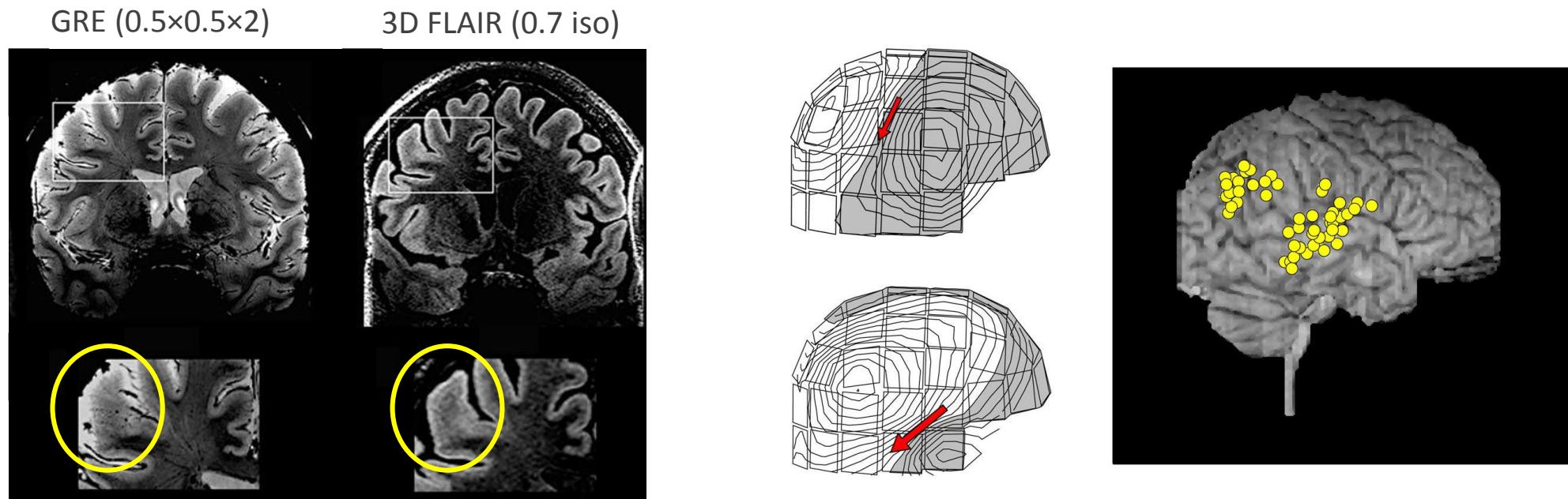


NIRS = near-infrared spectroscopy
fMRI = functional MRI;

ECoG = electro-corticogram;
LFPs = local field potentials

Where MRI and MEG, potentially, can improve patient pre-therapeutic work up

- ▶ 7T MRI with high resolution (< 1 mm): Detect signs of focal cortical dysplasia [1]
- ▶ MEG : detection & localisation of epileptic spikes (here identification of epileptogenic regions in the right hemisphere) [2]



[1] Ciantis *et al.*, “7T MRI in focal epilepsy with unrevealing conventional field strength imaging,” *Epilepsia*, vol. 57, no. 3, pp. 445–454, 2016.

[2] Lounasmaa and Seppä, “SQUIDS in Neuro- and Cardiomagnetism,” *Journal of Low Temperature Physics*, vol. 135, no. 5–6, pp. 295–335, 2004.

► Magnetic Resonance Imaging

- The nuclear Zeeman effect
- MRI instrumentation & principles
- Application for neurosciences
- The race towards ultra-high-field MRI

► MagnetoEncephalography

- The (electro)magnetic activity of the brain
- FemtoTesla magnetic flux detection with SQUIDS
- The MEG instrumentation
- MEG in neuroscience

► Conclusions

- ▶ The progress in neurosciences is tightly linked with the development of brain exploration techniques, among which MRI and MEG
- ▶ High performance MRI machines (high field, stability, homogeneity, high NMR sensitivity, ...) benefit greatly from the progress made in cryomagnetism
- ▶ High quality SQUIDs and superconducting flux transformers has made MEG a key technology to study large scale dynamics of brain activity
- ▶ We have shown the potential of ultra-high field (UHF) MRI to explore the brain better and faster
- ▶ But UHF MRI raises a great challenge when it comes to the development of $B_0 > 7T$ whole body scanner (ISEULT project)

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► **Thanks for your attention.**