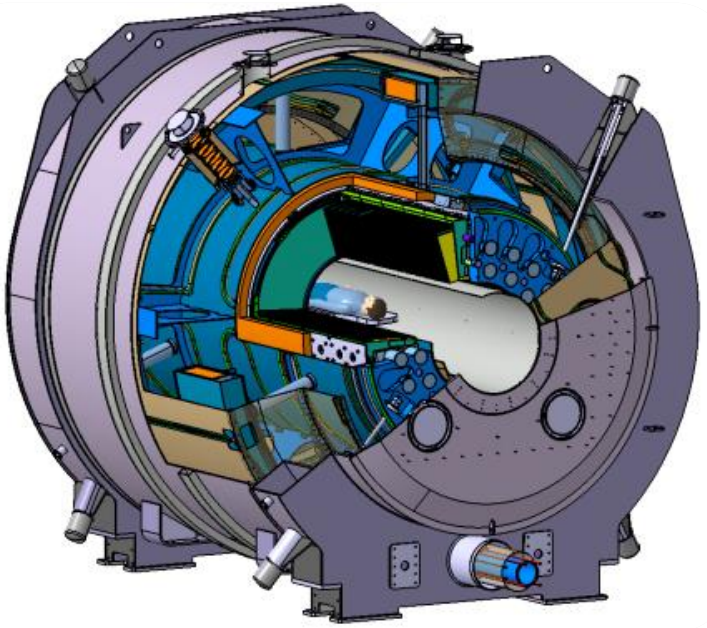
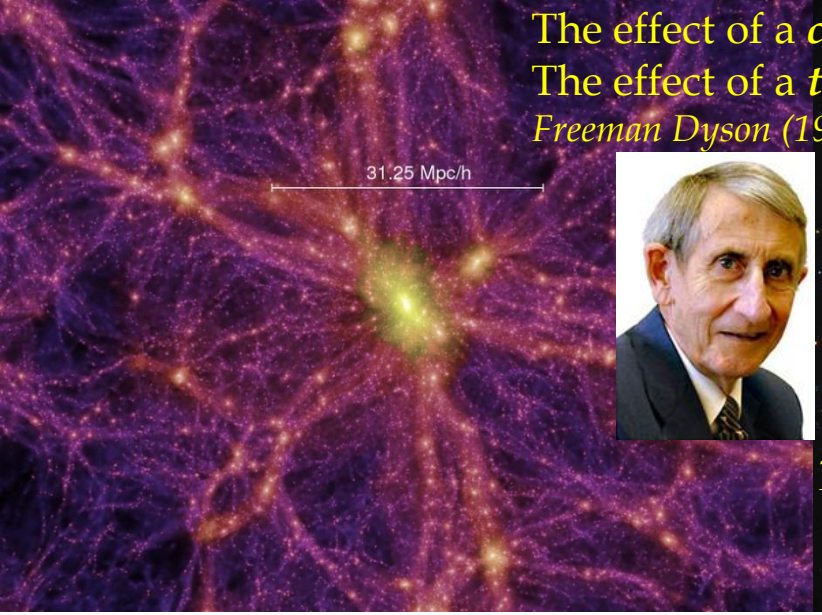
Exploring the Human Brain with Ultra-high Field MRI:
Perspectives from the Iseult Project



Denis Le Bihan
Founding Director, NeuroSpin
Founder and former Strategic Pilot, Iseult Project

IEEE-CSC, ESAS and CSSJ SUPERCONDUCTIVITY NEWS FORUM (global edition), October 2023.
Plenary presentation given at MT-28 2023, Sept. 14, 2023, Aix-en-Provence, France

The effect of a ***concept-driven revolution*** is to *explain* old things in new ways.
The effect of a ***tool-driven revolution*** is to *discover* **new things that have to be explained**.
Freeman Dyson (1997) Imagined Worlds Havard University Press



1998: Supernovae Ia → Accelerated univers expansion
(Riess, Perlmutter, Schmidt 2011 Nobel Prize)
➢ **Dark Energy (~73% of universe content)**

First black hole « image »
Event Horizon Telescope (EHT)
Ultimate proof of the General Relativity Theory

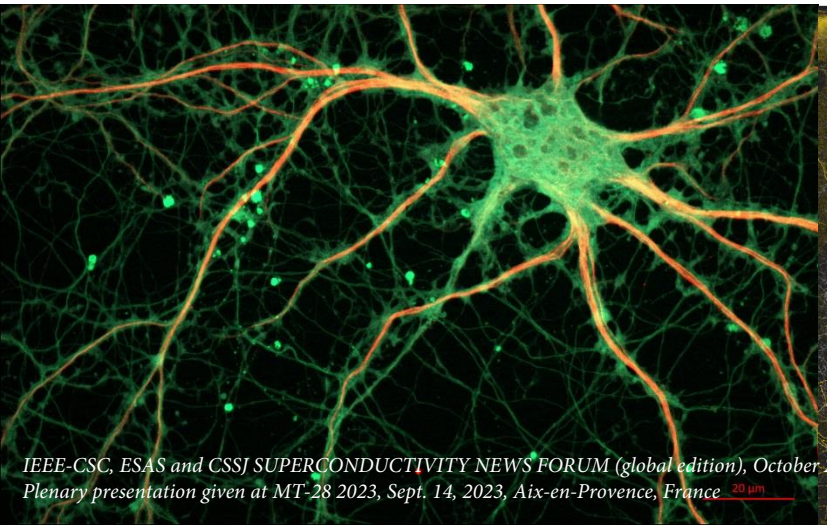
ESO's Very Large Telescope (VLT)

Our *galaxy*: 10^{11} (visible) stars
***Matter, antimatter, dark matter* (and energy)**

Electromagnetism, Relativity
Gauge theories
Quantum Standard Model, ΛCDM model

Our *brain*: 10^{11} (estimated) neurons
***grey matter* and *white matter* (and energy)**

Neural code of consciousness?



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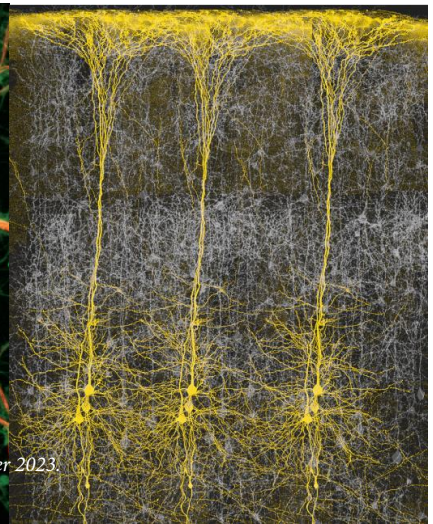
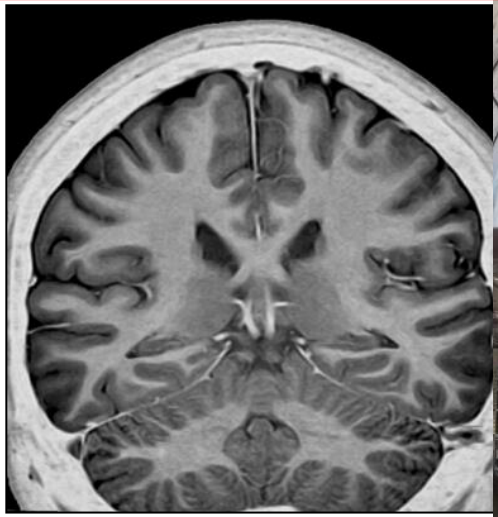
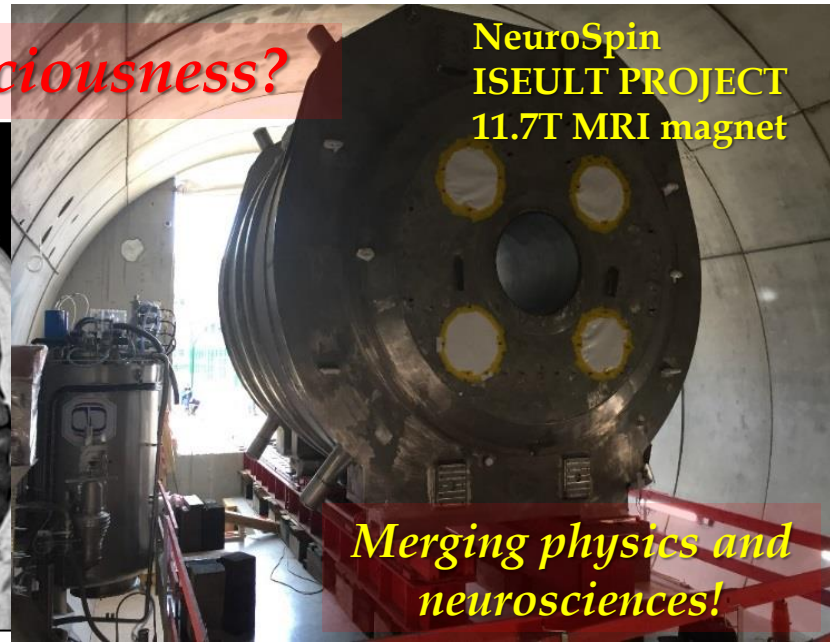


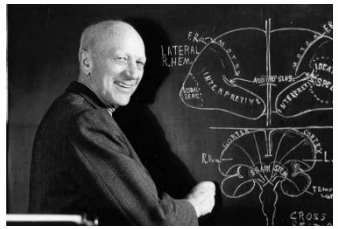




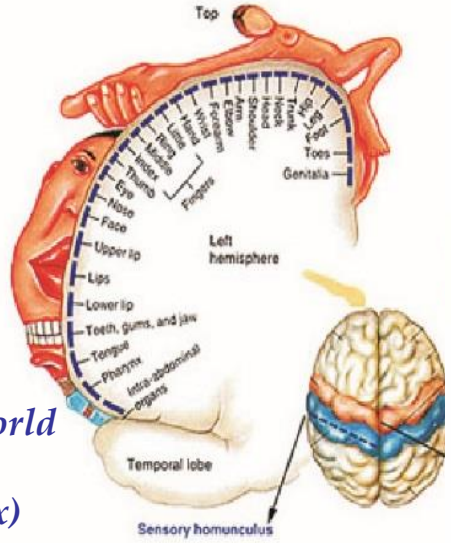
NeuroSpin
ISEULT PROJECT
11.7T MRI magnet

Merging physics and neurosciences!

THE BRAIN *MULTISCALE* FUNCTIONAL ARCHITECTURE

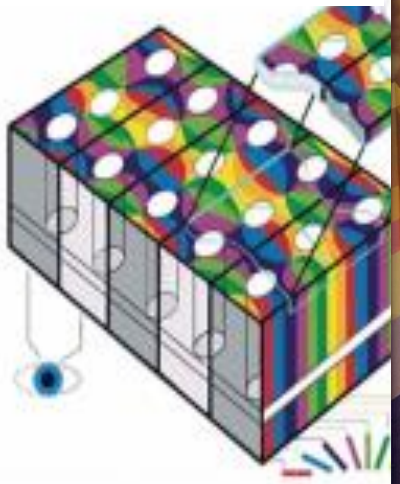


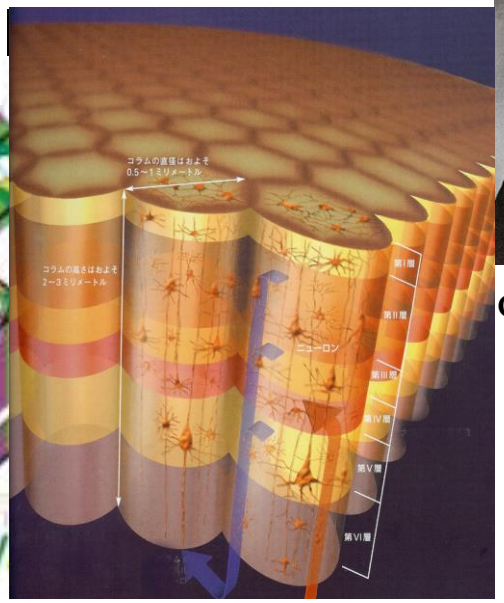
Penfield
1950

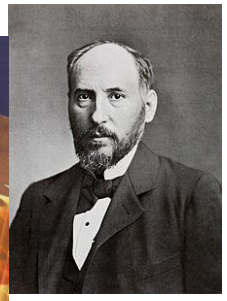


Projection of the world and body along the brain surface (cortex)

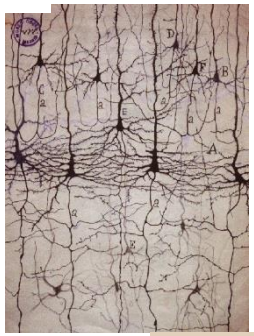
Hubel & Wiesel
1959 (Nobel Prize 1981)

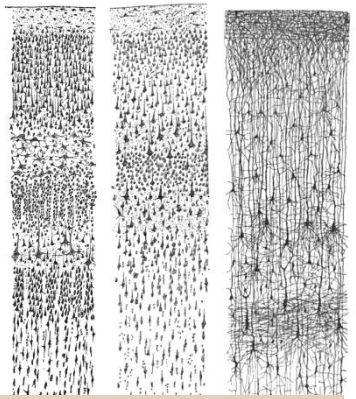




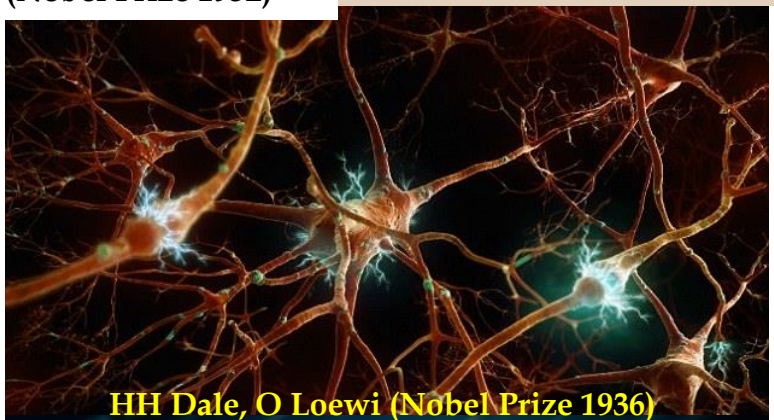


Cajal (Nobel Prize 1906)
Sherrington
(Nobel Prize 1932)

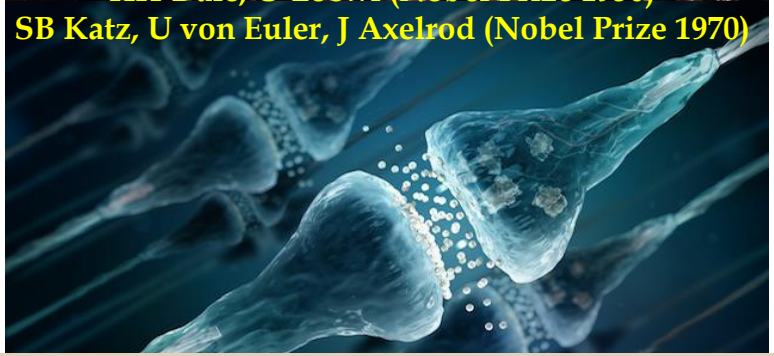




MICROSCOPIC
Neurons and synapses

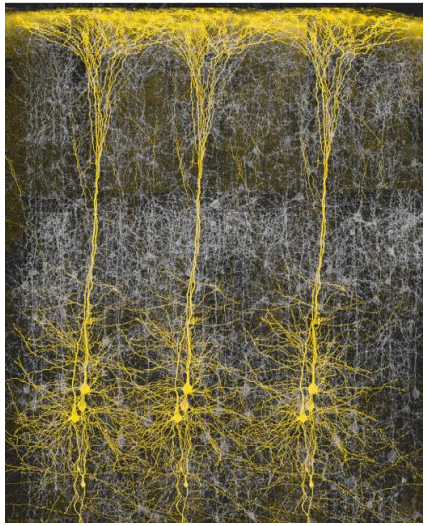


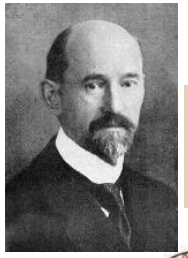
HH Dale, O Loewi (Nobel Prize 1936)
SB Katz, U von Euler, J Axelrod (Nobel Prize 1970)



CELLULAR & MOLECULAR
Neurotransmitters, Synaptic transmission

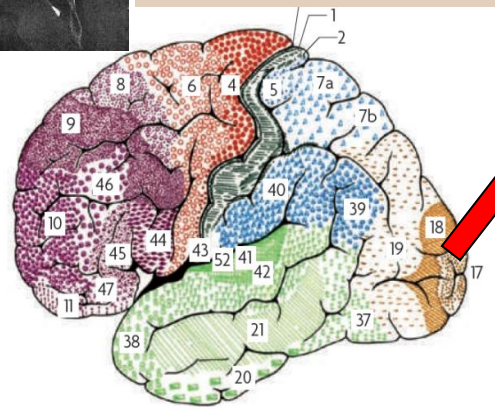
MESOSCOPIC
Column and layers





Brodmann
1908

MACROSCOPIC
regions and 'topies'



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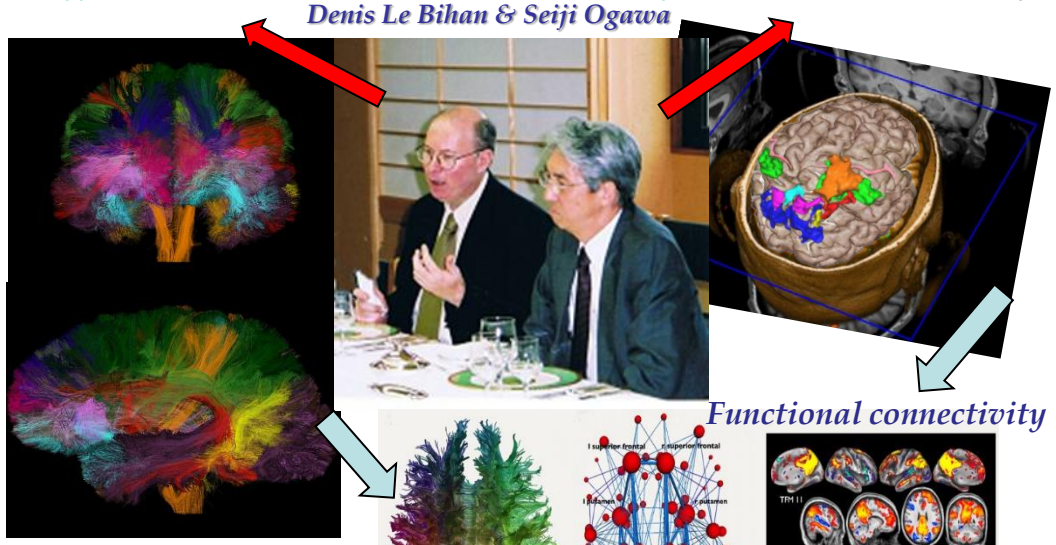
THE BRAIN CONNECTOME

Brain connexions
(Diffusion MRI & DTI)

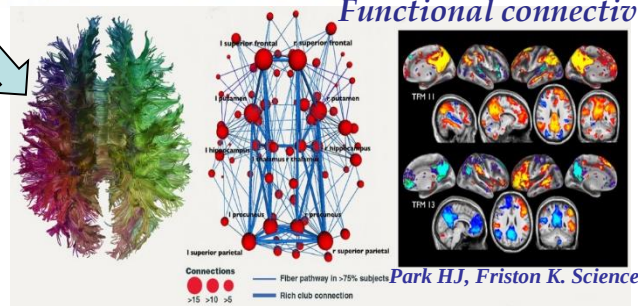
Brain at work
(functional MRI or fMRI)

Denis Le Bihan & Seiji Ogawa

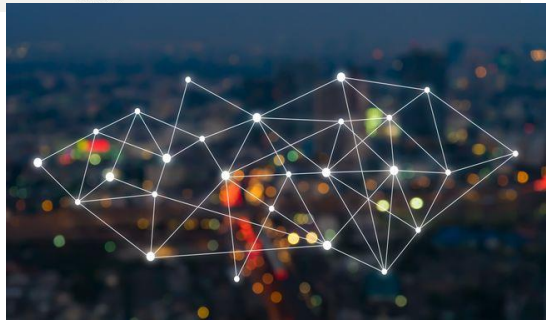


Functional connectivity

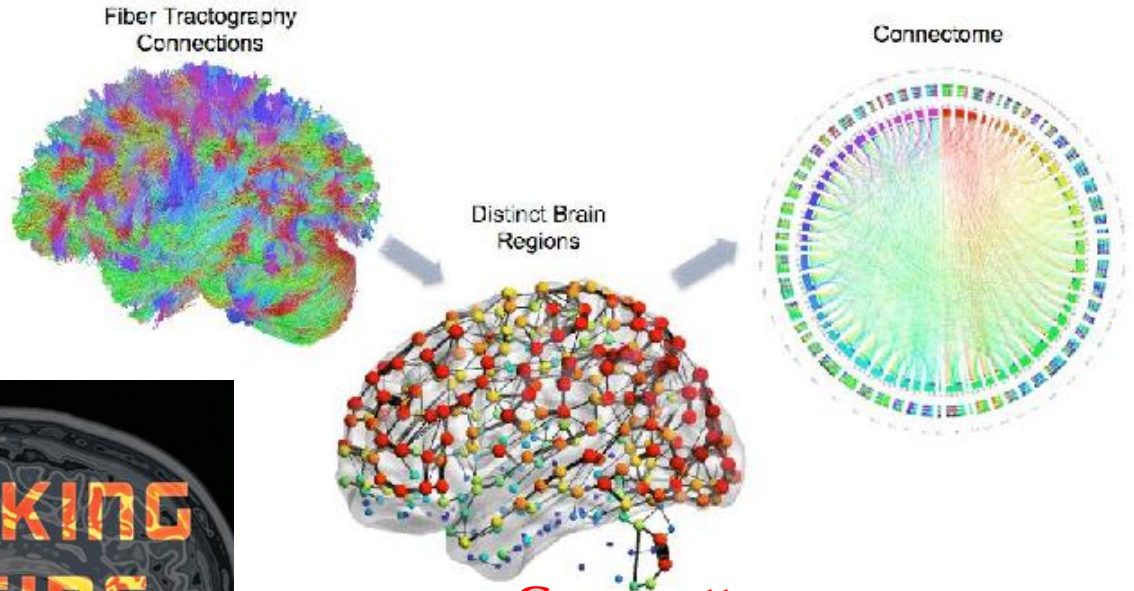
Wired connectivity



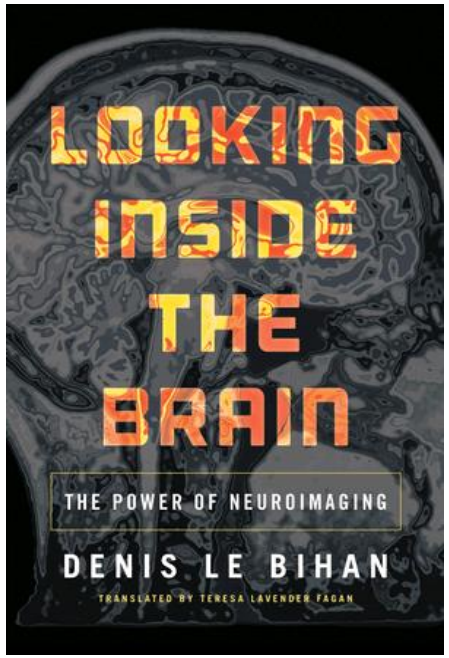
Park HJ, Friston K. Science 2013



White matter:
Brain *temporal* segregation



Gray matter:
Brain *spatial* segregation



The importance of white matter has been overlooked!

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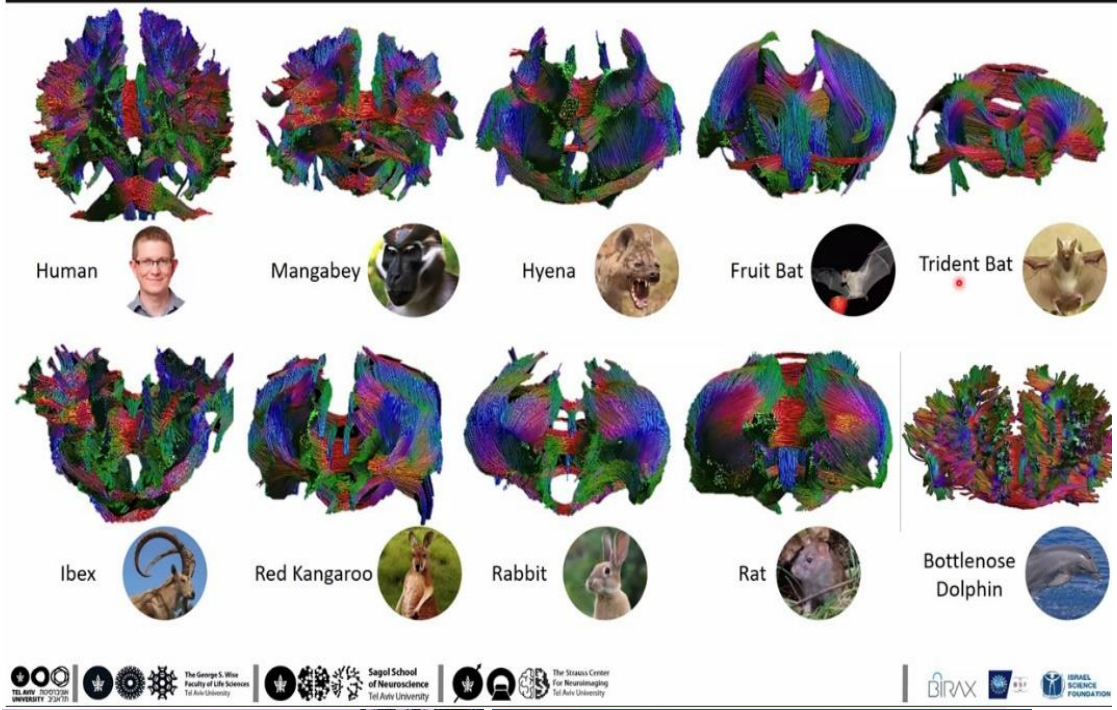
THE BRAIN CONNECTOME

Brain connexions (Diffusion MRI & DTI)

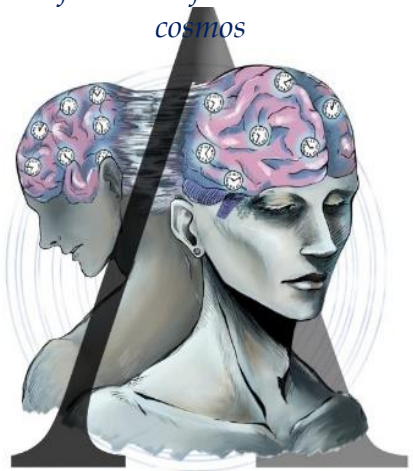


Brain at work (functional MRI or fMRI)

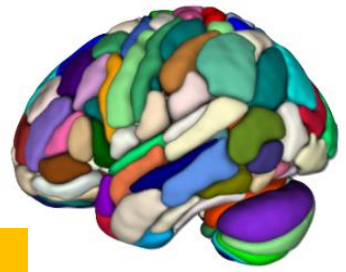
DENIS LE BIHAN

Einstein's Error

At the frontiers of the brain and the cosmos

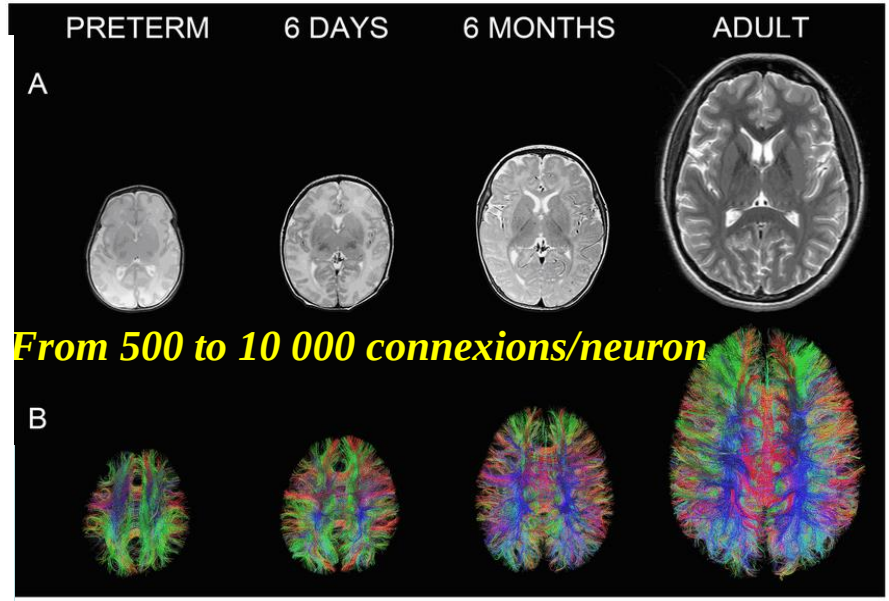


Odile Jacob

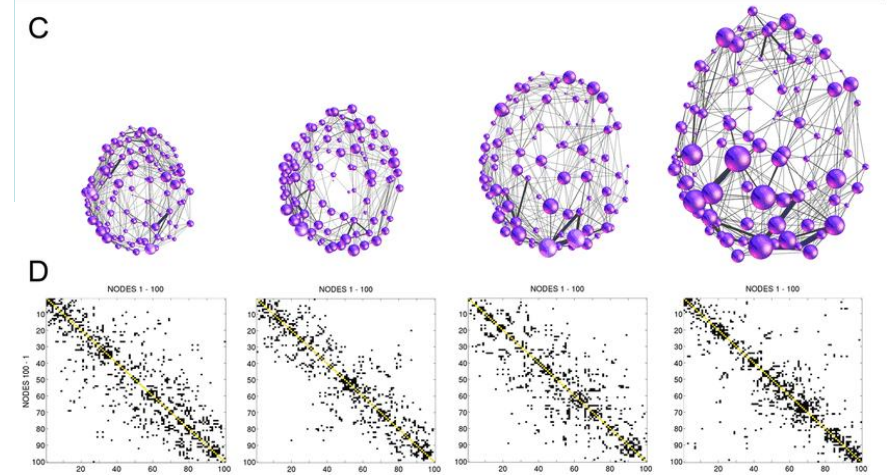


Fan et al. Human Brainnetome Atlas Cerebral Cortex 2016

Gray matter: Brain *spatial* segregation



From 500 to 10 000 connexions/neuron



White matter: Brain *temporal* segregation

A Brain Connectome Relativistic Spacetime

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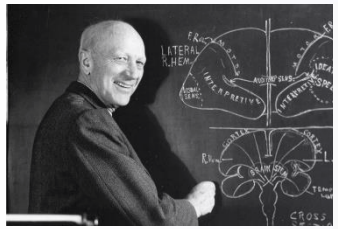
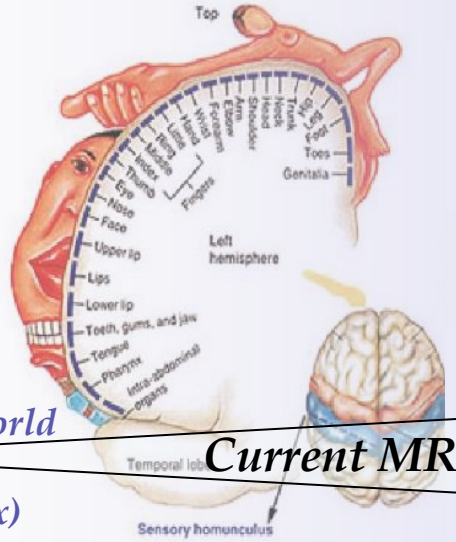
THE LIMITS OF (human) NEUROIMAGING



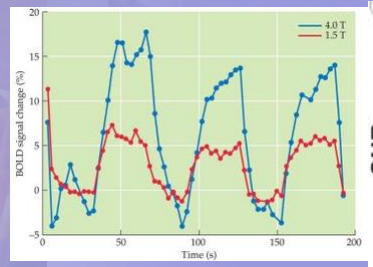
Penfield
1950

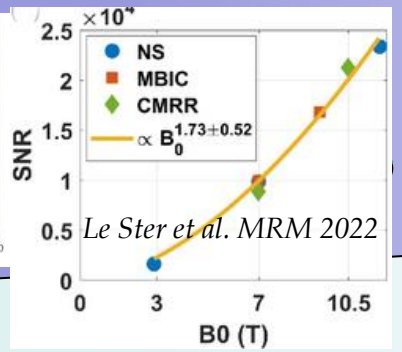


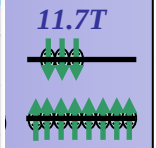
Hubel & Wiesel
1959 (Nobel Prize 1981)

MRI signal (spatial/temporal resolution)

$Mo \approx \gamma B_o / kT$



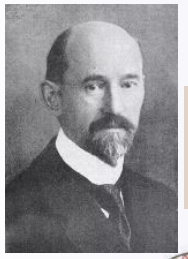




Projection of the world and body along the brain surface (cortex)

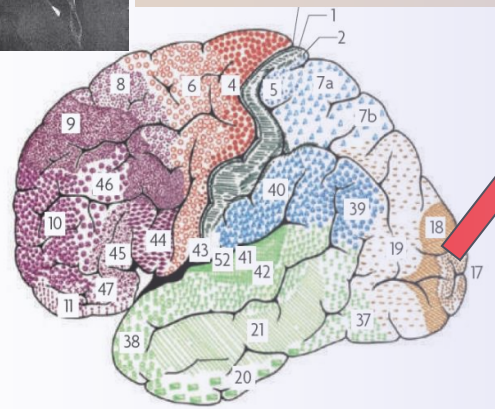
Current MRI « luminosity » (<7 teslas)

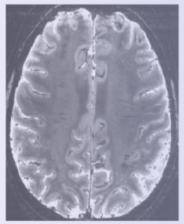
Future MRI « luminosity » (>10 teslas)



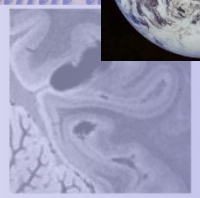
Brodmann
1908

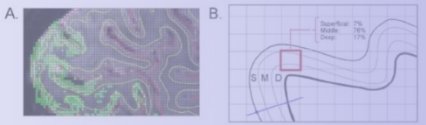
MACROSCOPIC regions and 'topies'





MESOS Column a





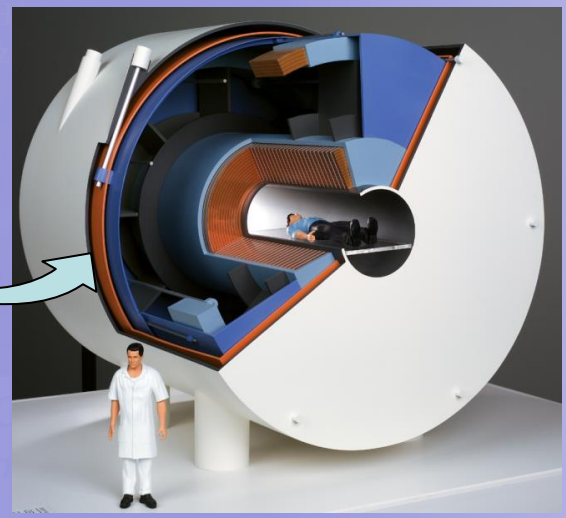
Selective Activation of the Deep Layers of the Human Primary Visual Cortex by Top-Down Feedbacks. Kok et al. Current Biology 2016

Hodgkin & Huxley
1952 (Nobel Prize 1963)

0.00005 teslas

× 223 000

The Iseult Project
11.7 teslas MRI



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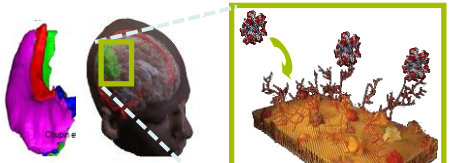
CONCEIVE: The Iseult Project (genesis phase 2001-2004)

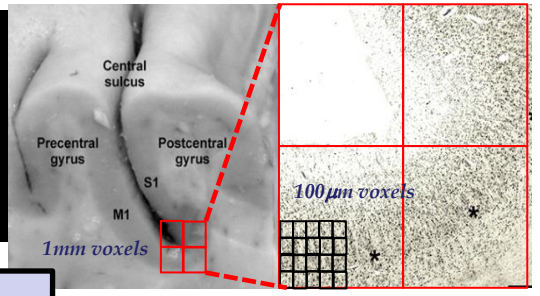
2001
- 3T : ≈ 100 installed systems
- 1x 7T (USA) + 2 orders (USA, J)

→ *11.7T at CEA?*

Roy Gordon (Vice president, Bruker):
« You are mad » (RSNA, Chicago, Nov 27, 2001)



Alzheimer disease
Molecular imaging



Mesoscale cortex architecture

Better see…

…to better understand

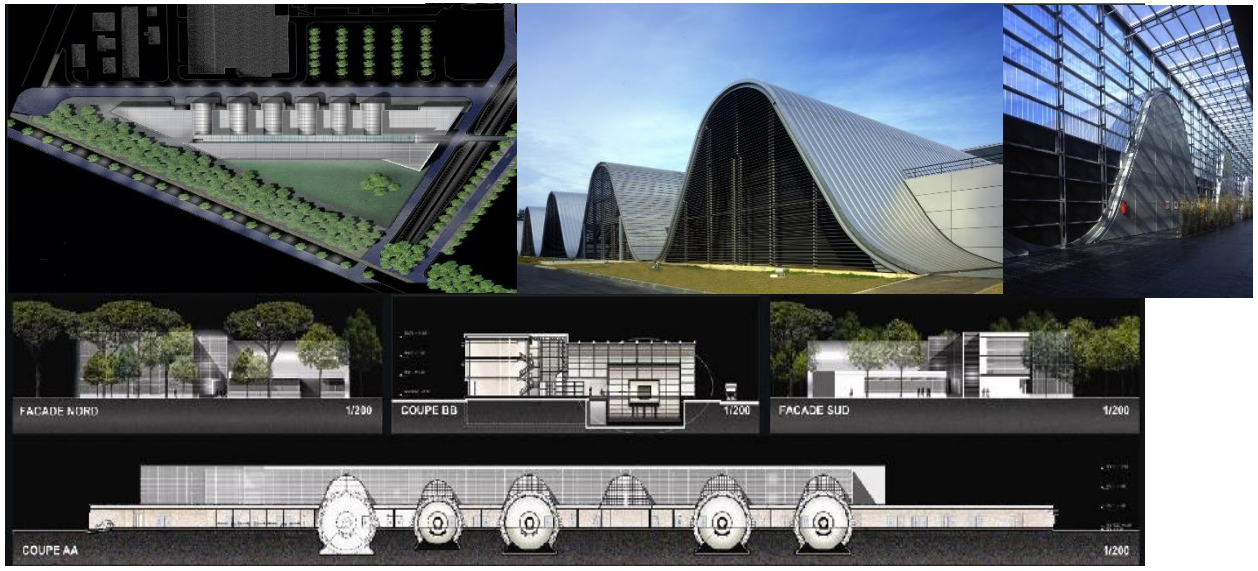
… and discover

Tomorrow: *Mesoscale* brain functional architecture (~100µm)
- ***In vivo*, non invasively**
- ***In the Human* Brain**
- ***Over the whole* brain**

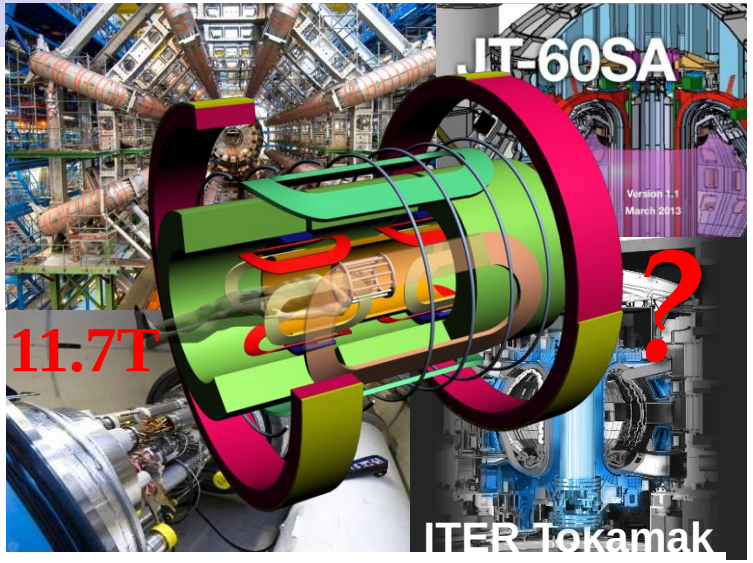
Neural Code ?
Connectome Spacetime?

Uncharted territory

NeuroSpin *Claude Vasconi*



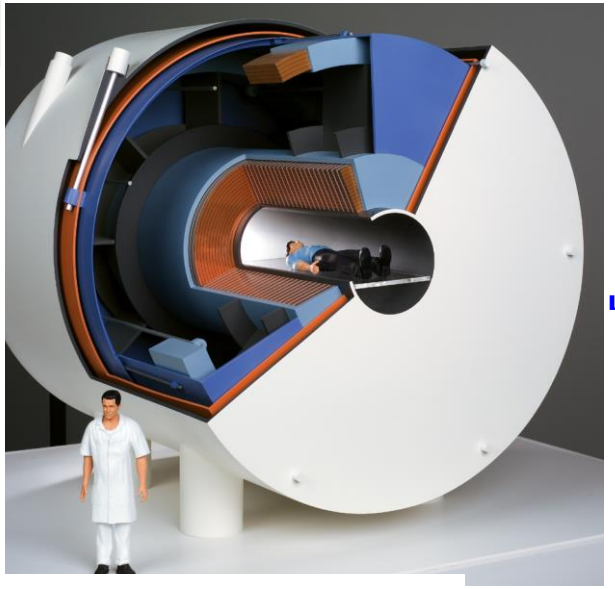
ULTRA-HIGH FIELD MRI

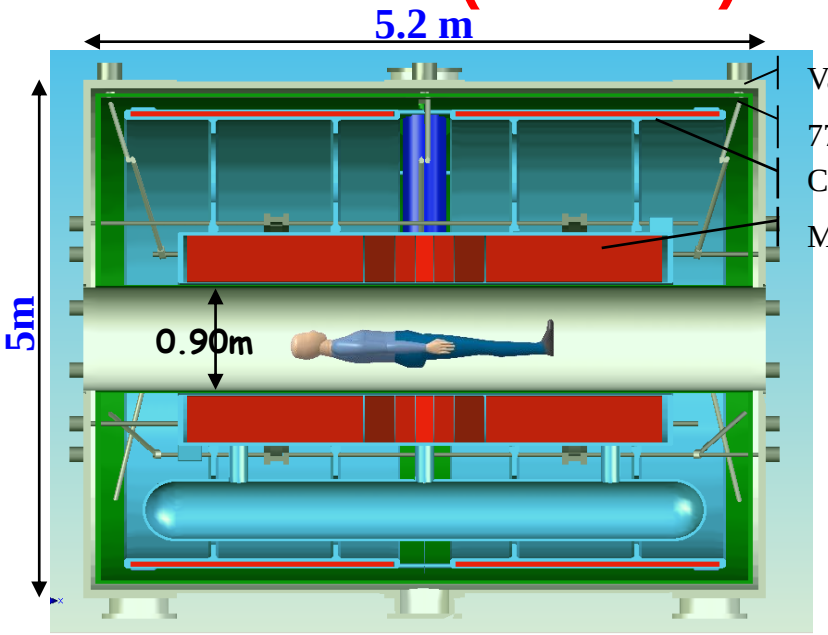


CEA acclaimed Know-How
From High Energy & Particle physics
…. to Nuclear Fusion

DESIGN: CEA/Irfu design for NeuroSpin 900mm bore 11.74T (500MHz) magnet

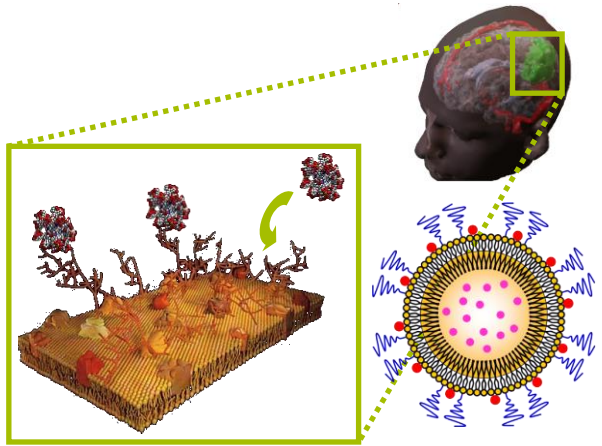
	France (ISEULT)	Allemagne (INUMAC)
Partenaires industriels	ALSTOM Guerbet Contrast for Life	BRUKER SIEMENS
Partenaires académiques	Direction des Sciences du Vivant Direction des Sciences de la Matière	Université de Fribourg
Soutien financier partiel d'agences publiques	oséo	Bundesministerium für Bildung und Forschung

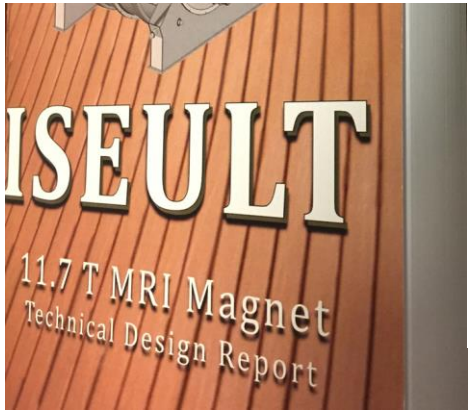




FINANCING: 2004-2008

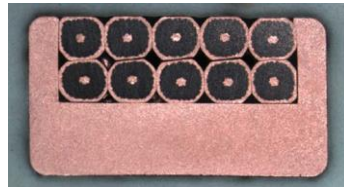
French-German industrial partnership to develop *High Field Molecular Imaging* financed half by the partners and half by the French Industrial Innovation Agency (Oséo/BPI) and the German BMBF
(President Chirac & Chancelor Schroder, April 30, 2004)





CERN magnet design: groundbreaking for MRI

- **900mm** internal diameter
- wetted **double pancakes** in **superfluid He**: **1.8K** (**-271°C**) pressured He II bath connected to a **cryoplant**
- main magnet coil superconducting wire: **multistrand**, **69t NbTi (182 km)**, 9.2x4.9mm² section
- nominal current: **1483 amp** in **driven-mode** (***external power supply***)
- stored energy: **338 MJ**
- overall weight: **132 tons**
- **actively shielded** (*to reduce the fringe field*)



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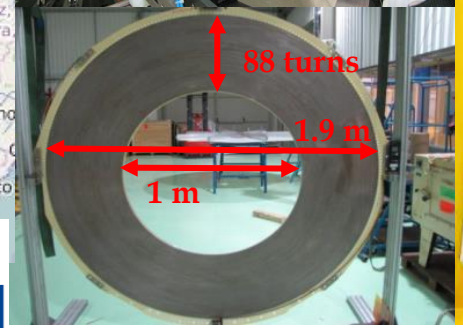
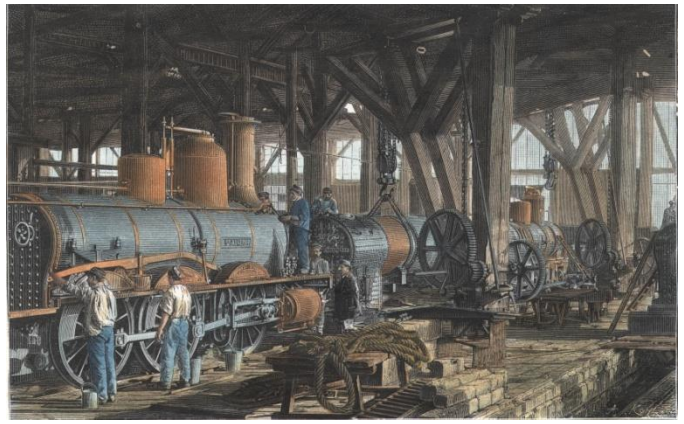
Plenary presentation given at MT-28 2023, Sept. 14, 2023, Aix-en-Provence, France

BUILD … 2008-2017

Dedicated manufacturing processes were made
to build and assemble the pancakes (CEA/Alstom-GE)





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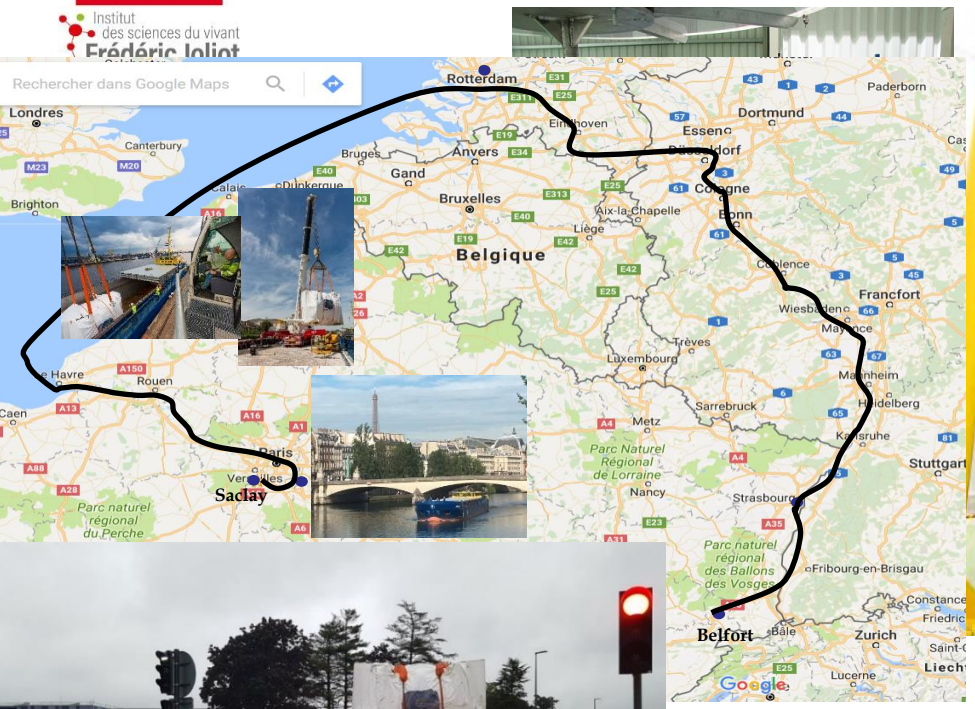

Institut des sciences du vivant Frédéric Joliot

CEA - Saclay

10.55T @ July 4th, 2019

11.72T @ July 19, 2019

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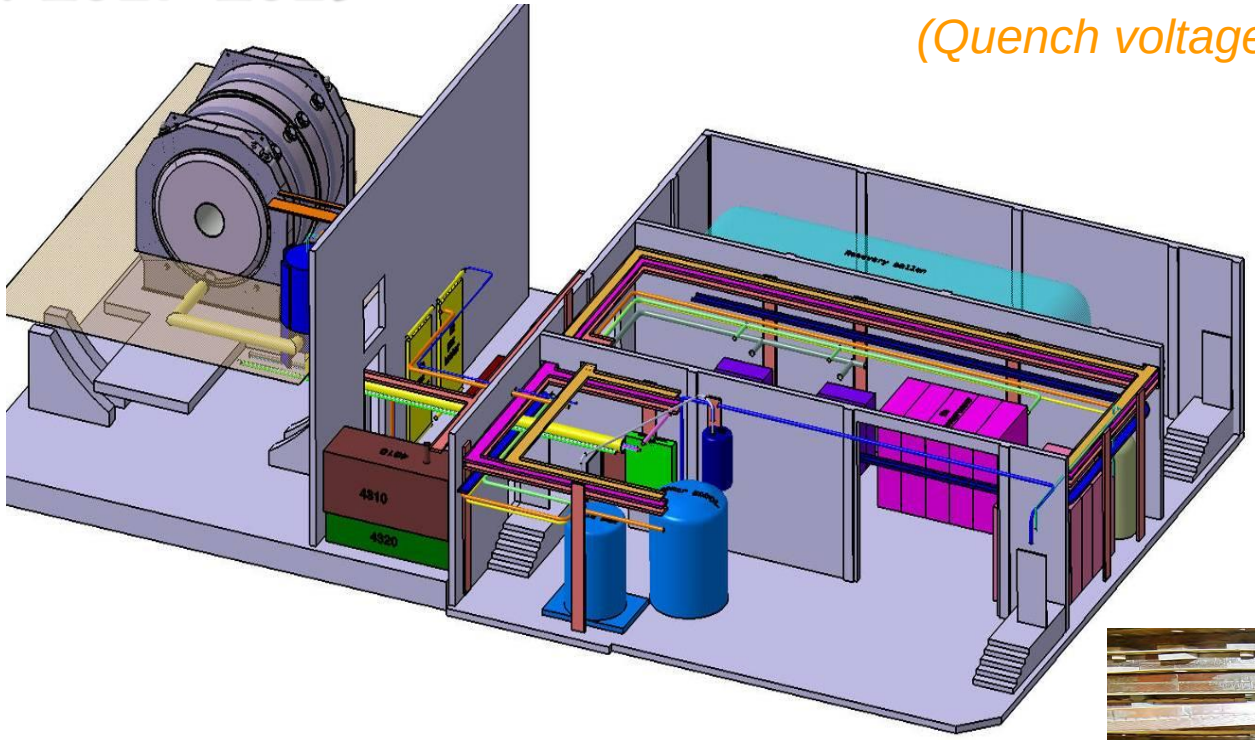
INSTALL …

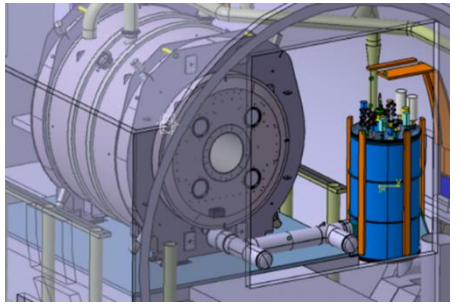
General cryogenic layout for NeuroSpin 11.7T MRI system

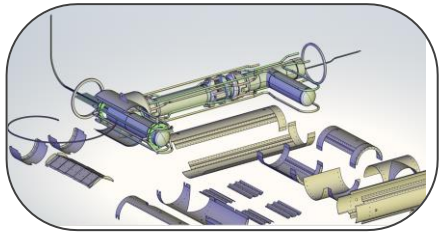
… 2017-2019

- Quench protection: *external dump resistor*.

(Quench voltage to ground 2000 V)





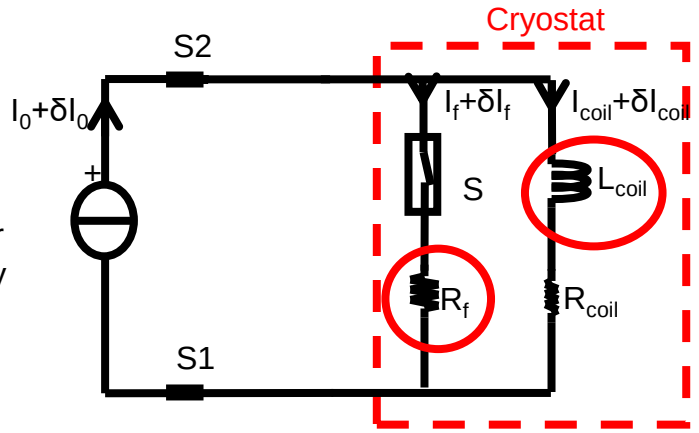


Cryogenic satellite (-271°C) and cryoline (caloduc)

Magnet in *driven* mode (external power supply)

- Stability circuit (current limitator).

Active Magnet Safety System inspired from detector magnet protection (dump resistor)



Power supply

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INSTALL …

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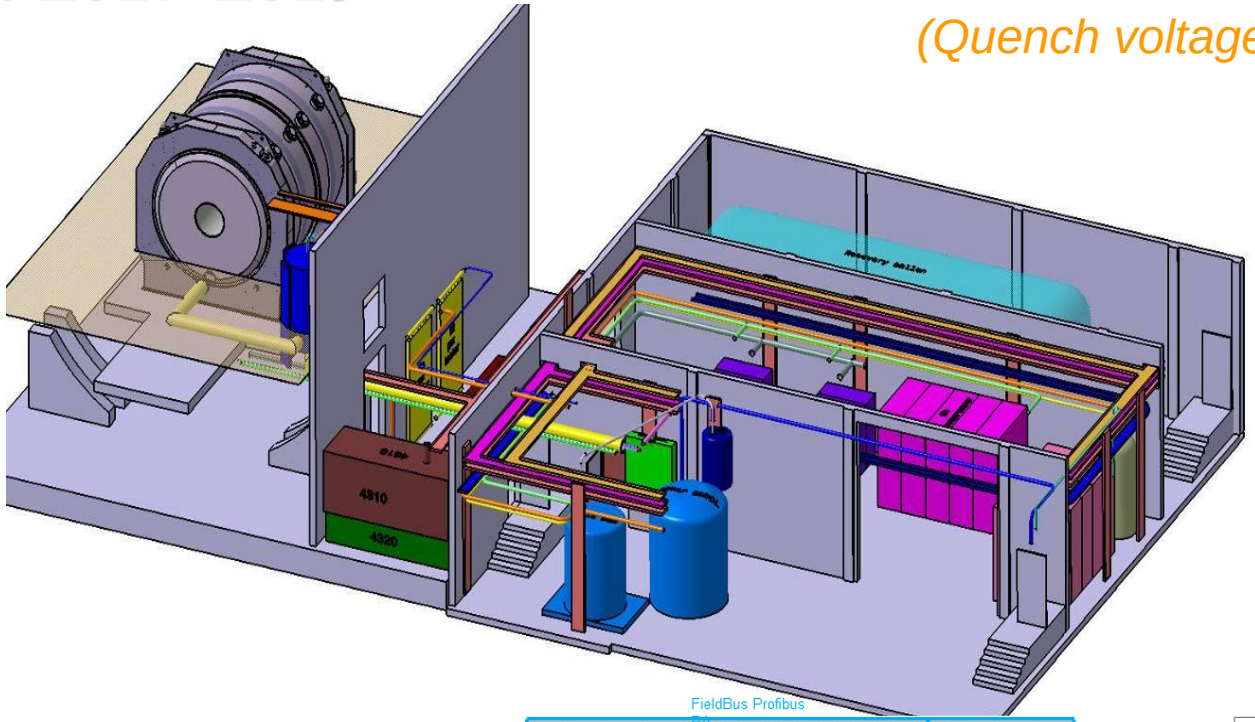

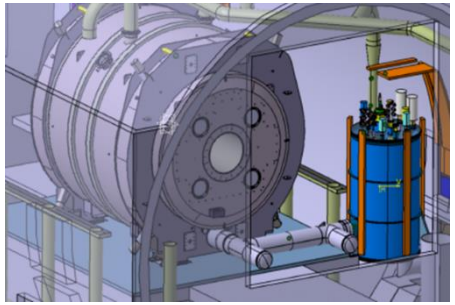

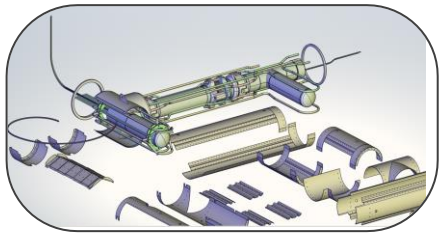

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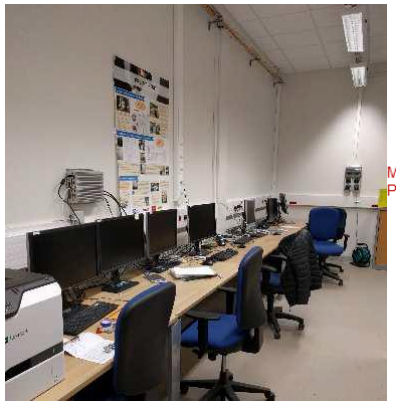
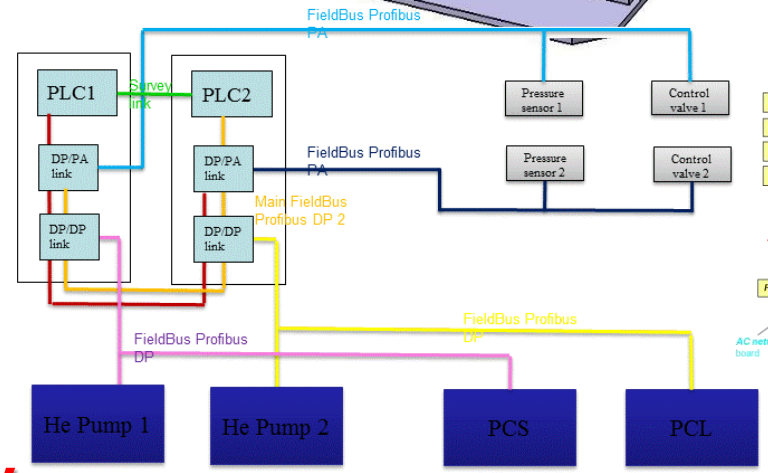
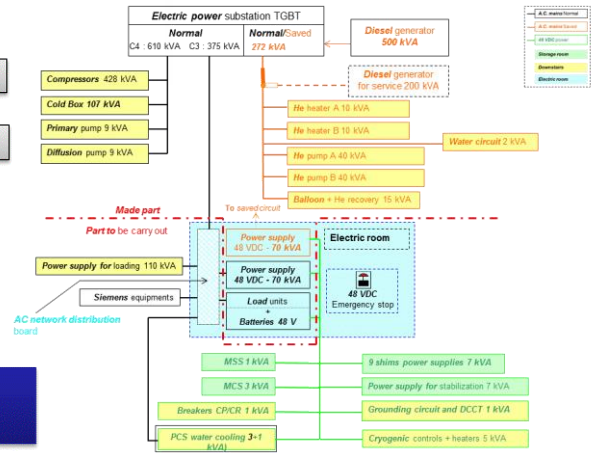
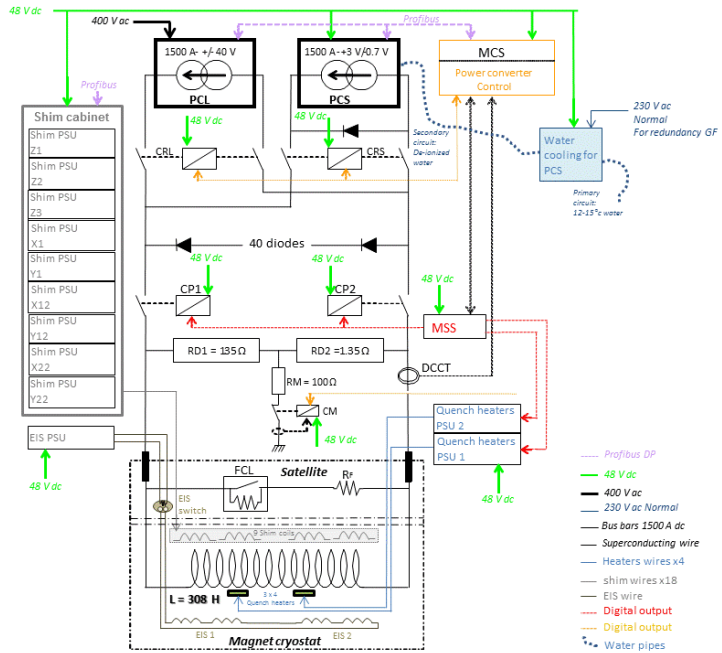


Main FieldBus Profibus DP 1







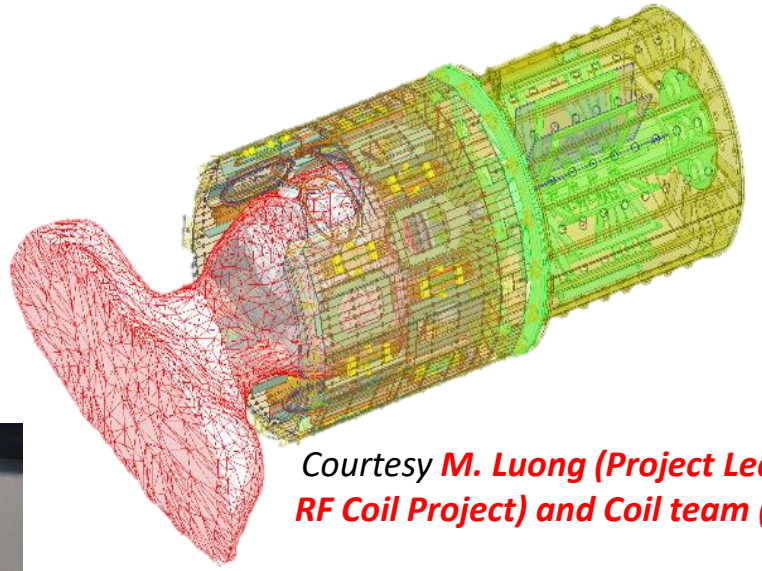
High availability

(24/24, 7/7, >10years, including French holidays, strikes, virus, war, etc.)

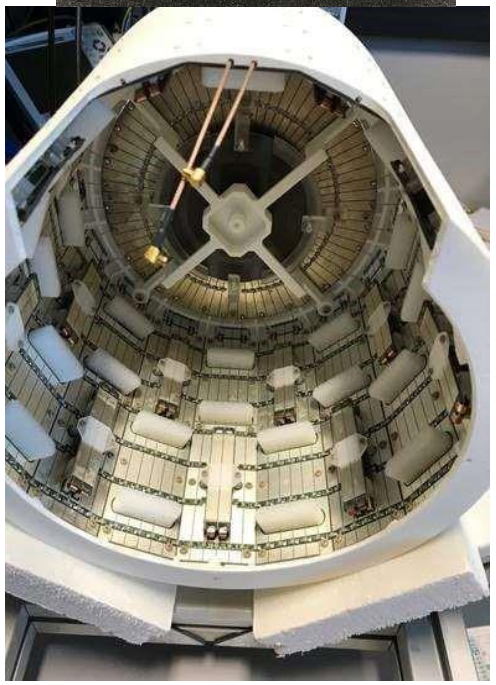
MRI IS NOT ONLY A MAGNET!

New RF coil designs & metamaterials

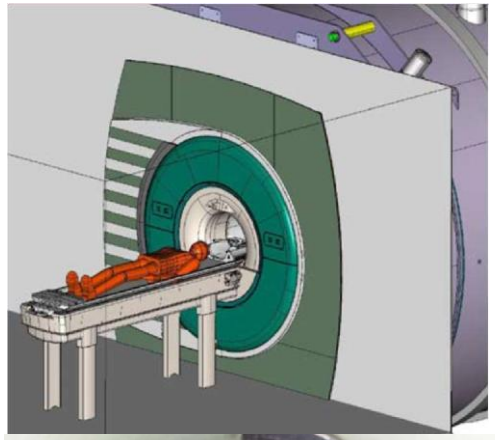
8Tx/32Rx 11.7T humain brain coil

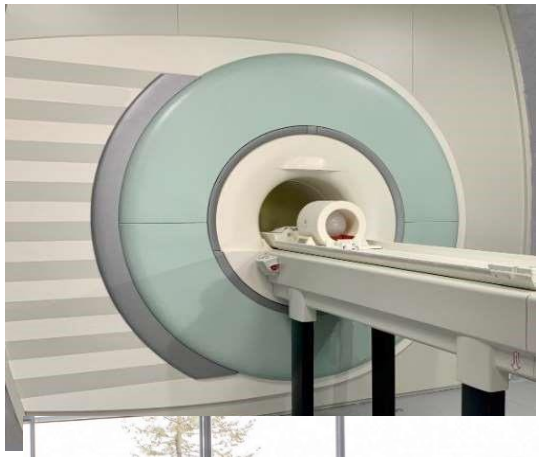


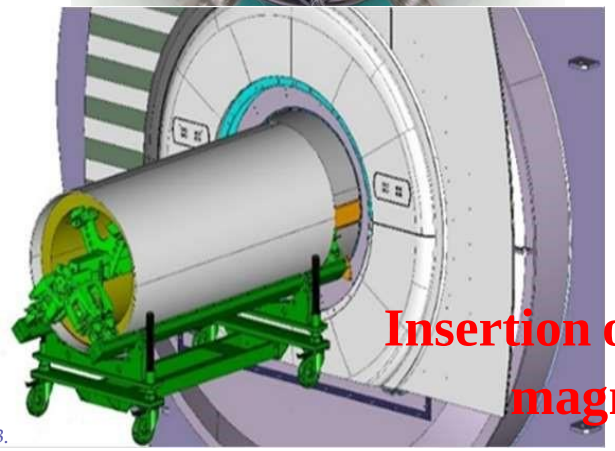
*Courtesy **M. Luong (Project Leader, 11.7T RF Coil Project) and Coil team (Irfu/Joliot)***

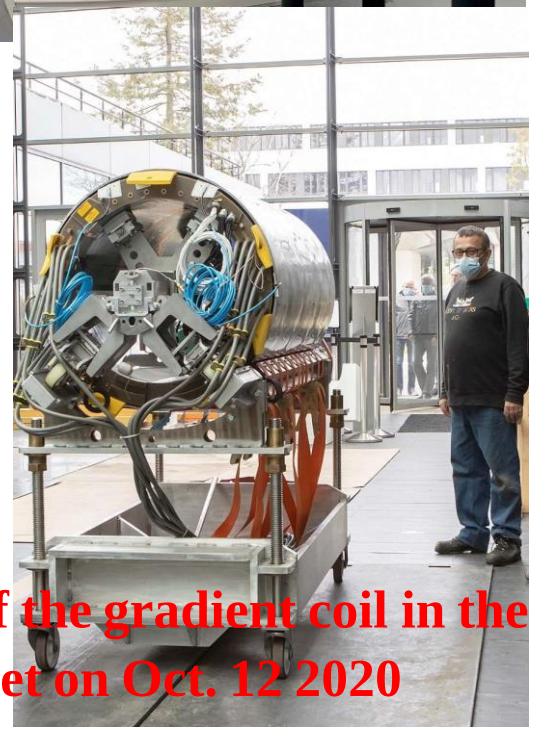


… SIEMENS equipment integration
(gradient coil, bed, electronics & console)









Insertion of the gradient coil in the magnet on Oct. 12 2020

IEEE-CSC, ESAS and CSSJ SUPERCONDUCTIVITY NEWS FORUM (global edition), October 2023.
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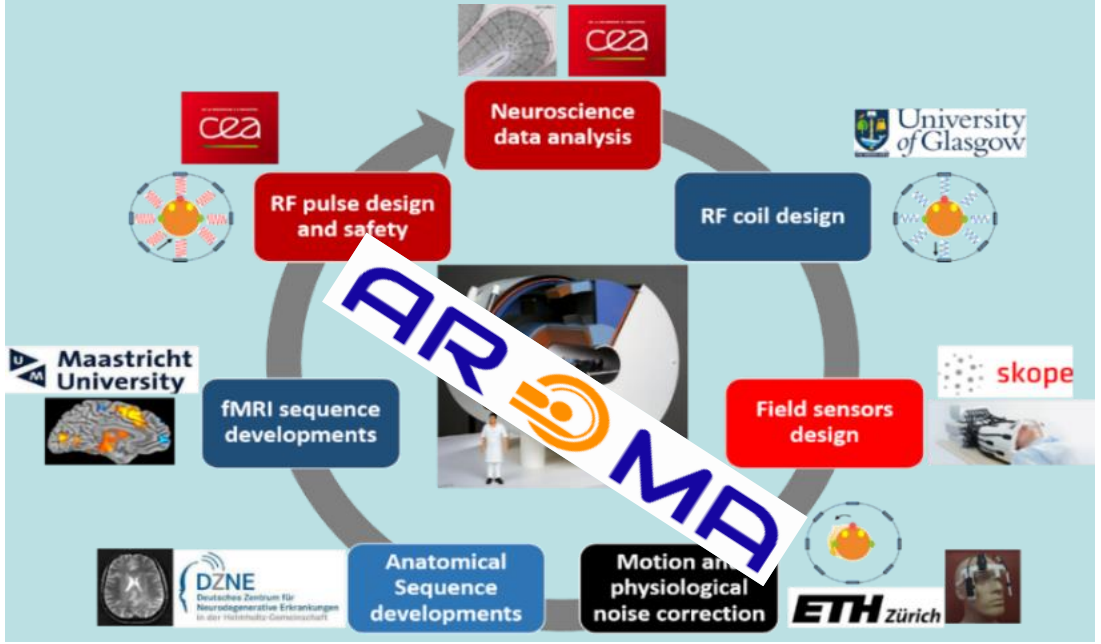
MRI IS NOT ONLY A MAGNET!

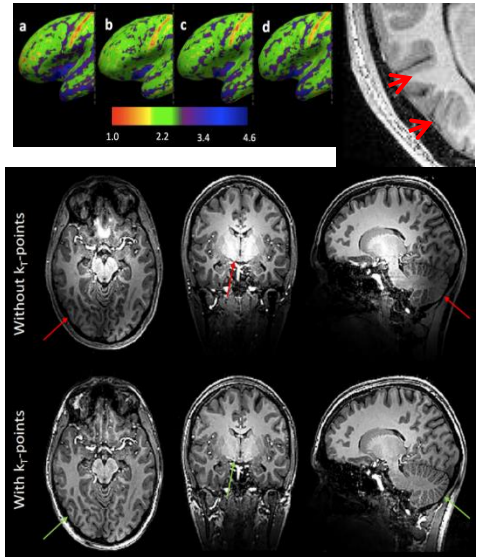
AROMA FET-OPEN (3.6M€) (N. Boulant, PI, 2021 – 2026)

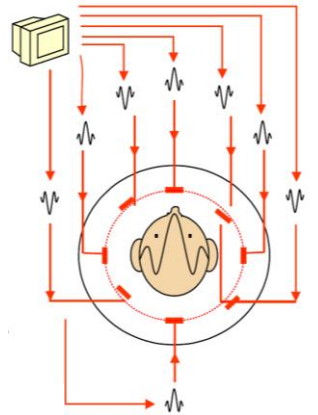
Accurate, Reliable and Optimized functional MAgnetic resonance imaging at unprecedented field strength for unique exploration of the human brain.



New signal spatial encoding strategies (*Parallel Transmission, kT points, universal pulses*)

A. Amadon, N. Boulant

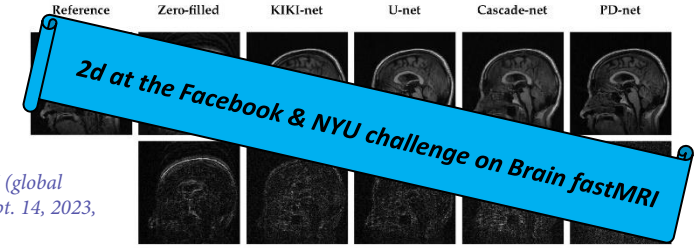


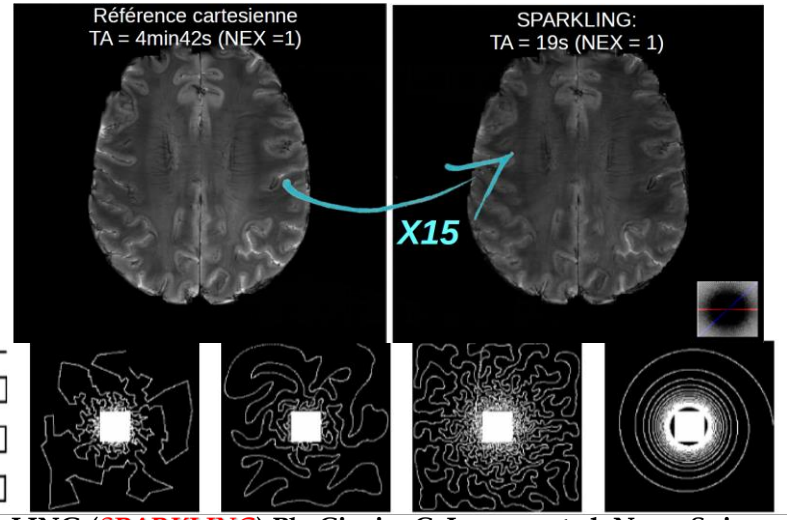


- Tomi-Tricot, Amadon A et al. (2018)
- M. Cloos, N. Boulant, M. Luong, G. Ferrand, E. Giacomini, M.-F. Hang, D. Le Bihan, and A. Amadon, NeuroImage 62:2140-50 (2012).

Acquisition and Image Reconstruction/Processing have become completely intermingled (*Machine Learning, Compress sensing*)

P. Ciuciu, CEA/INRIA





Prospective SPARse K-space sampLING (*SPARKLING*) Ph. Ciuciu, C. Lazarus et al. NeuroSpin

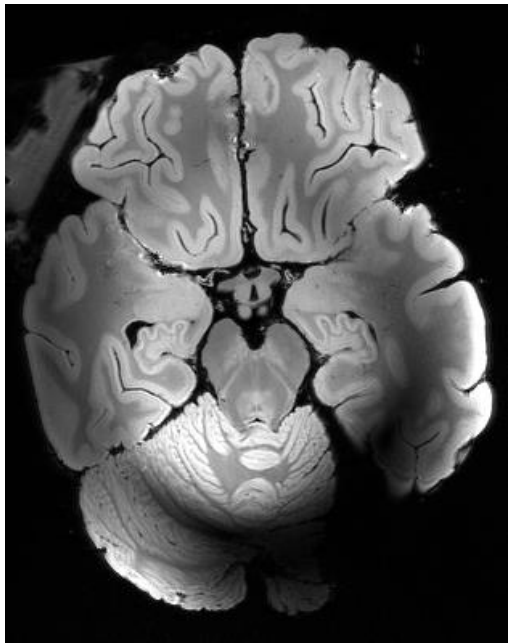
The very first images…(October 2021)

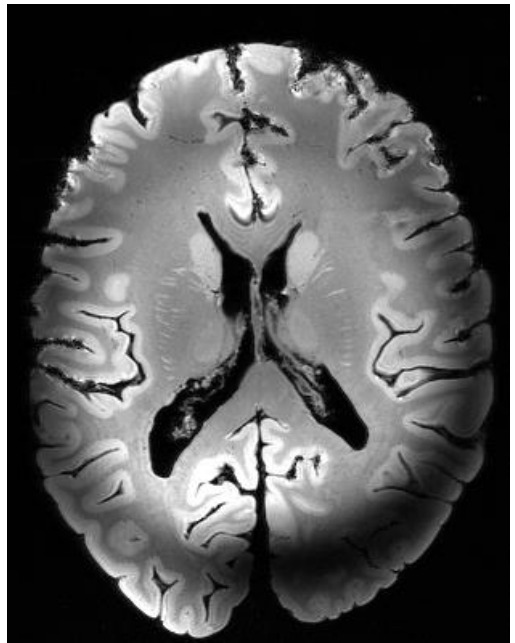
Courtesy N. Boulant, C. Lerman, L. Quettier & Museum National d'Histoire Naturelle, ICM (Mathieu Santin), Paris

BREAKING NEWS!

ACQUISITION OF THE FIRST IMAGES IN NORMAL VOLUNTEERS IN PROGRESS AT NEUROSPIN!!!

Results will be shown by the end of 2023…





ISEULT PROJECT: An inspiring MRI magnet

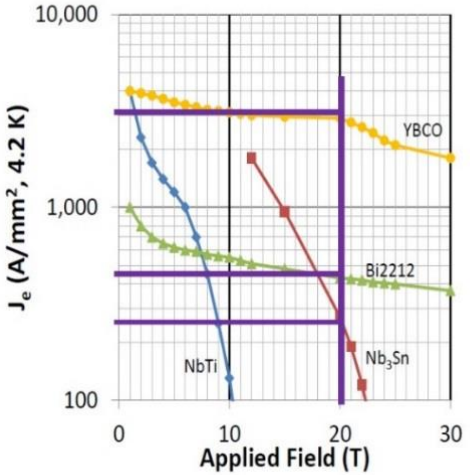
2001
- 3T : ≈ 100 installed systems
- 1x 7T (USA) + 2 orders (USA, J)

→ *11.7T at CEA?*

Roy Gordon (Vice president, Bruker):
« You are mad » (RSNA, Chicago, Nov 27, 2001)

2023: ***Madness has been contagious (no vaccine so far)***
- **11.7T operational @ NeuroSpin**
- 3T : ≈ 7000 installed systems
- 7T : ≈ 100 installed systems
- 1x 8T & 6x 9.4T (USA, Germany, NL, China)
- **1 x 10,5T Minneapolis**
- **3 head-only 11.7T systems: USA (NIH), Korea, (+Nottingham/UK project)**
- **3 projects @14T**: Germany, Chiba, **Nijmegen** (NL)
- **USA : 20T? (Boston, Stanford)**

Superconducting Materials for Magnets

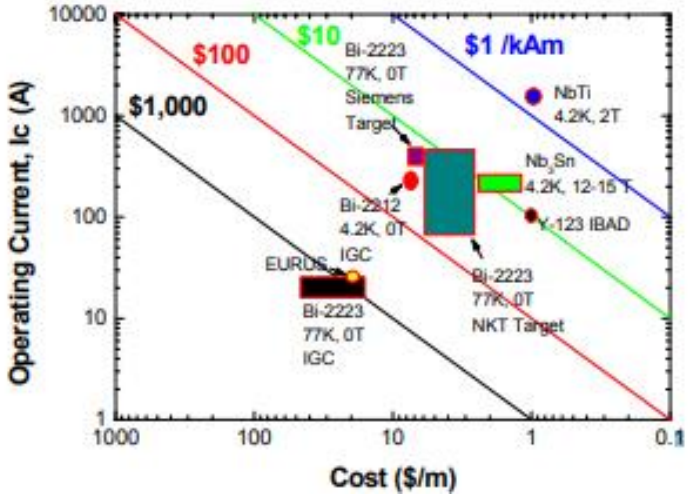


The High-Temperature Superconductors (HTS) YBCO, Bi2212, Bi2223 will superconduct at fields >100T.

For 30 T SC, HTS is required.

At 4 K, extremely high combinations of field and current-density attained!

For 20 T MRI, HTS will likely be preferred over Nb_3Sn.



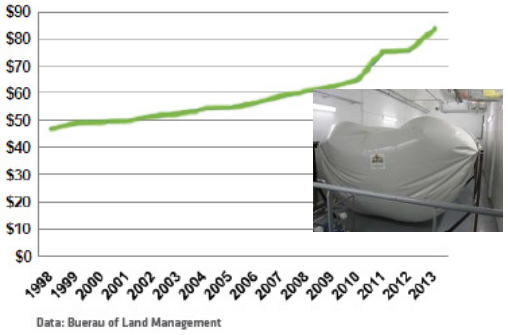
= f($$$)!

Nuclear magnetization
Mo ≈ $\gamma B_o/kT$

The liquid helium crisis (MRI)

World Helium Resources	
Country	Billion Cubic Metres
United States	20.6
Qatar	10.1
Algeria	8.2
Russia	6.8
Canada	2.0
China	1.1

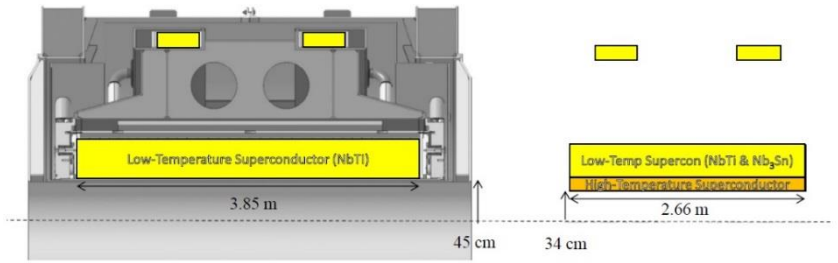
The values above are estimated helium resources from the USGS Mineral Commodity Summary



Perspective on 20 T MRI Magnet

11.75 T, 90 cm Whole-Body
Under Construction, due 2014 (Iseult)

20 T, 68 cm Head-Only
Preliminary Concept

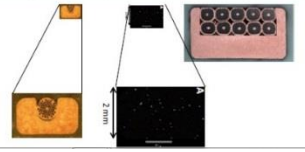


Parameter	Iseult	MagLab 20 T Concept
Conductor Mass (Ton)	65	~35
Stored Energy (MJ)	338	~350
Current Density (A/mm²)	26.4	~40
Magnet Design	CEA	MagLab

HTS + high-strength materials at 4 K operate at high field and current-density resulting in compact magnets.

MRI Magnet Conductor Design

	3 T, 90 cm	21 T, 10 cm	11.74 T, 90 cm (Iseult)	14 T, 68 cm (proposed)
Superconductor	NbTi	Nb_3Sn	NbTi	Nb_3Sn
# of strands	1	1	10	100
Current (Amps)	~300	285	1,500	10,000
Reinforcement	Cu	Steel	Cu	Steel
Strength (MPa)	>250	1,400	>250	1,400
Stiffness (GPa)	110	200	110	200
Stabilizer	Cu	Cu	He	He
C_p (mJ/cc/K)	1	1	552	552
Protection	Cu	Cu	Cu	Cu
J_{cu} (A/mm²)	~280	~230	~70	~250



1,400 / 250 = 5.6 > 3.14

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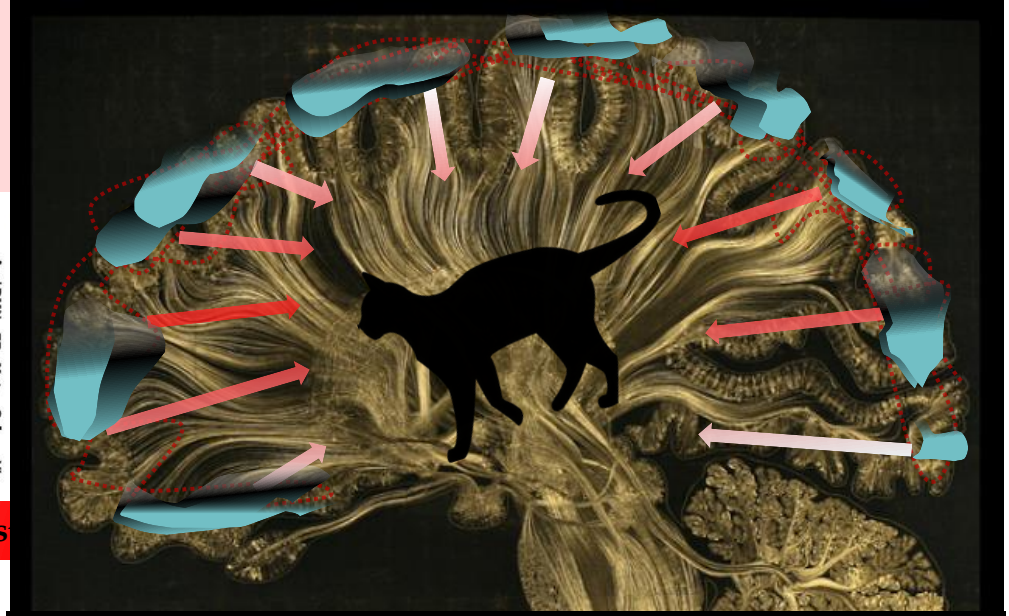
Courtesy M. Bird, National High Magnetic Field Lab, Florida State U

Consciousness in the CONNECTOME RELATIVISTIC SPACETIME

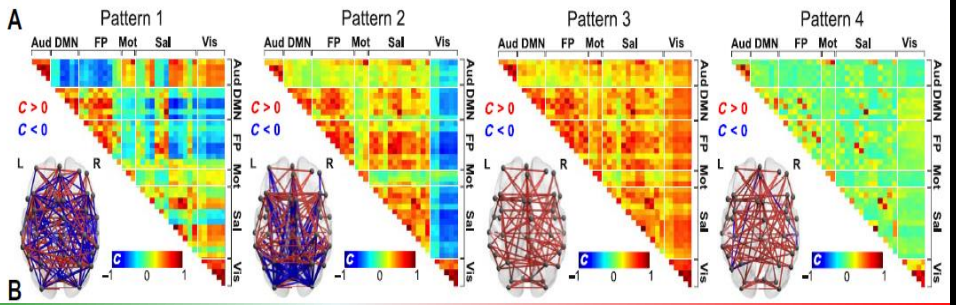


SCIENCE ADVANCES | RESEARCH ARTICLE

COGNITIVE NEUROSCIENCE

Human consciousness is supported by dynamic complex patterns of brain signal coordination

A. Demertzi[1,2,3,a†], E. Tagliazucchi[3,4,a†], S. Dehaene[5,6], G. Deco[7,8], P. Barttfeld[9‡], F. Raimondo[1,2,3,10,11,12], C. Martial[1], D. Fernández-Espejo[13,14,15], B. Rohaut[2,3,16], H. U. Voss[17], N. D. Schiff[18], A. M. Owen[15], S. Laureys[1], L. Naccache[2,3], J. D. Sitt[2,3,a‡]



Conscious state

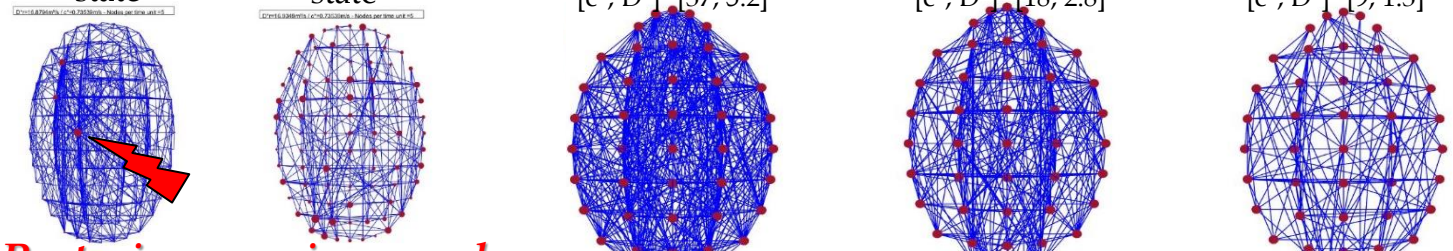
Vegetative state

Healthy controls | Vegetative unresponsive | Minimally conscious s

[c*, D*]=[37, 5.2]

[c*, D*]=[18, 2.8]

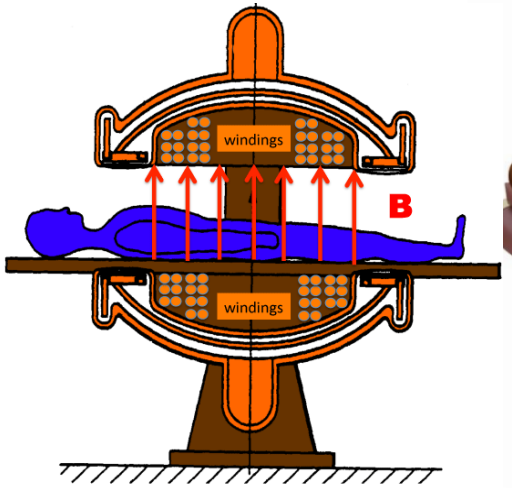
[c*, D*]=[9, 1.3]



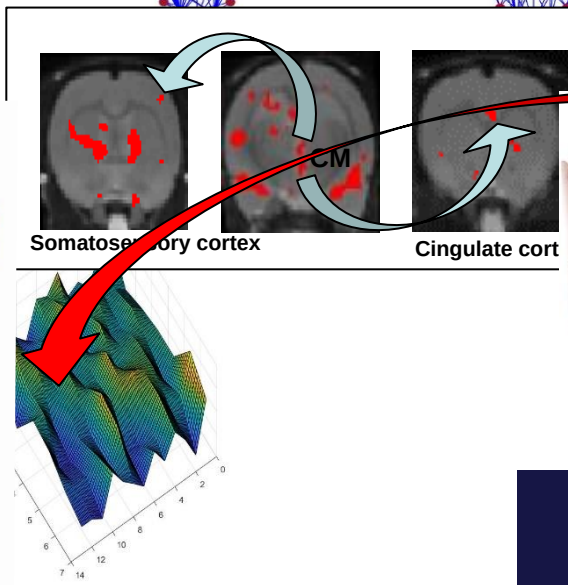
Restoring consciousness by restoring spacetime curvature?

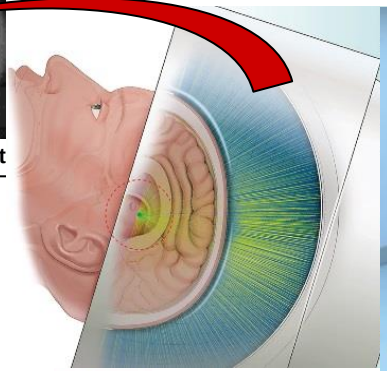
Emergence of consciousness along a 5th dimension from the 4D connectome spacetime (*hologram*) as gravity emerges in 5 dimensions from a 4D univers spacetime (aka Maldacena AdS/CFT 1998)

Awaking out of a vegetative state?



FlatBedMRI?



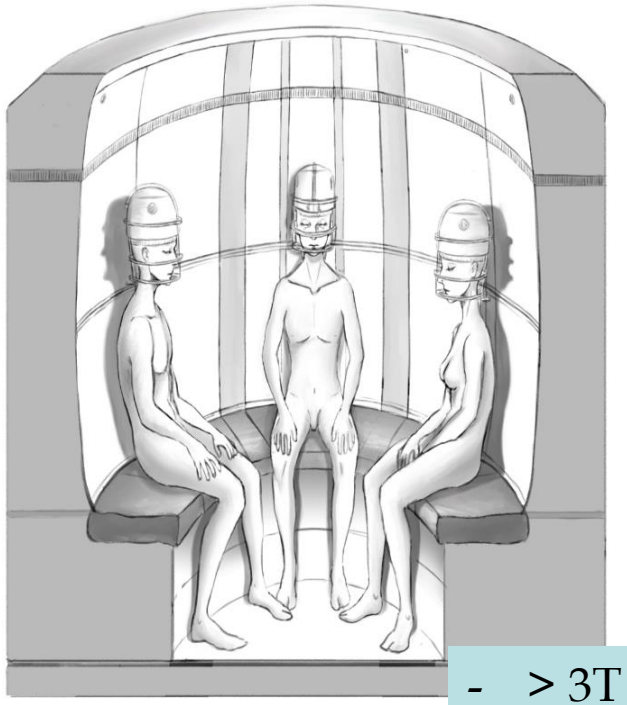


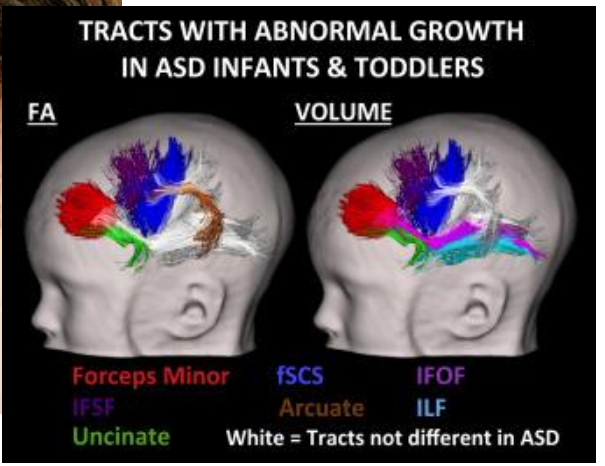
Phased-array Focused Ultrasound System (FUS)

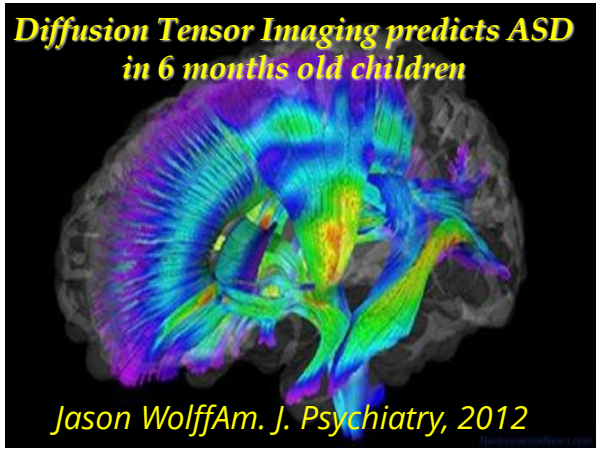
Okazaki, Japan

LARGE MAGNETS FOR « SOCIAL SCIENCES »

Division of
Cerebral Integration
Sadato Laboratory







- > 3T vertical magnet, **> 2-3m internal diameter**
- 2 or 3 « sweep spots » with high field homogeneity (0.05ppm/20cm pk2pk)
- Stability 0.05ppm/h long term, 10^{-4}ppm/10min short term
- Multiple gradient sets (80mT/m) and RF coils
- Head contention (motion artifacts)

Clinical need
Market

REVIEW article
Front. Oncol., 21 February 2023
Sec. Breast Cancer
Volume 13 - 2023 |
https://doi.org/10.3389/fonc.2023.993540

This article is part of the Research Topic
Precision Medical Imaging for Cancer Diagnosis and Treatment
View all 13 Articles ›

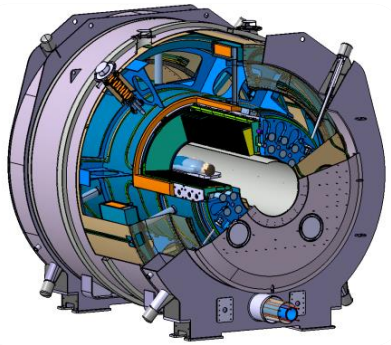
The road to breast cancer screening with diffusion MRI

Mami Iima[1,2] and Denis Le Bihan[3]*

[1] Department of Diagnostic Imaging and Nuclear Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan
[2] Department of Clinical Innovative Medicine, Institute for Advancement of Clinical and Translational Science, Kyoto University Hospital, Kyoto, Japan
[3] NeuroSpin, Joliot Institute, Department of Fundamental Research, Commissariat á l'Energie Atomique (CEA)-Saclay, Gif-sur-Yvette, France

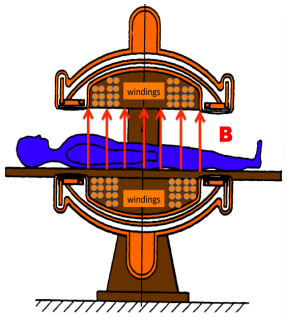
Breast cancer screening

Small & Cheap



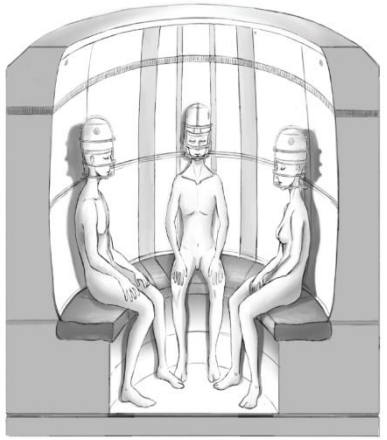
High Bo

>14T brain MRI



FlatBedMRI

Open design



Social magnet

Large size

Science

They did not know it was impossible, so they made it. Mark Twain

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Superconductor Science and Technology
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Topical Review

Human brain MRI at 500 MHz, scientific perspectives and technological challenges

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Commissioning Completion of the Iseult Whole Body 11.7 T MRI System

Lionel Quettier, Guy Aubert, Jean Belorgey, Christophe Berriaud, Philippe Bredy, Guillaume Dilasser, Olivier Dubois, Graham Gilgrass, Quentin Guihard, Vincent Jannot, Francois-Paul Juster, Herve Lannou, Frederic Molinié, Francois Nunio, Arnaud Roger, Thierry Schild, Loris Scola, Armand Sinanna, Vadim Stepanov, and Pierre Vedrine

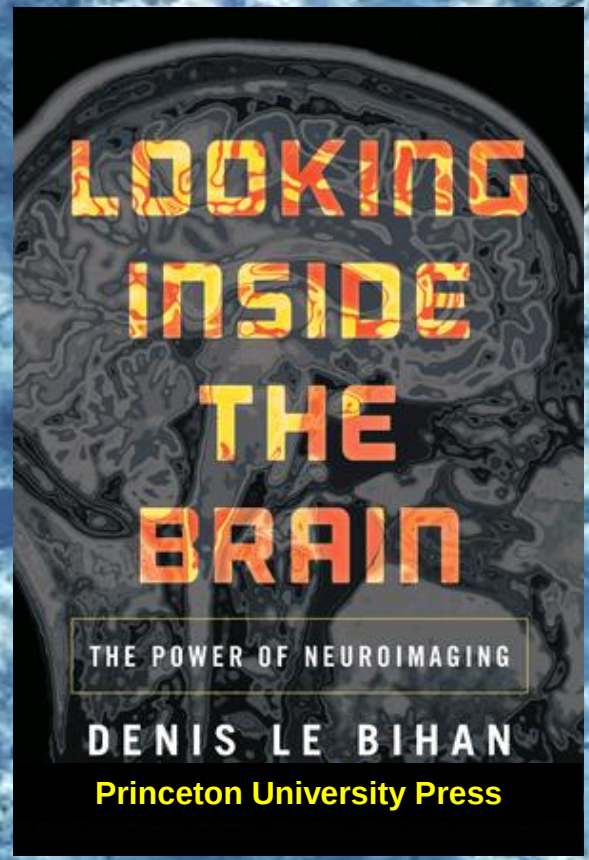
(Invited Paper)

NeuroSpin ISEULT 11.7T WB MRI magnet

First 11.7T Whole-Body MRI magnet
Human Brain Explorer

DENIS LE BIHAN
Einstein's Error
At the frontiers of the brain and the cosmos

Odile Jacob



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