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
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 Harvard University Press

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**Our galaxy**: $10^{11}$ (visible) stars

- Matter, antimatter, dark matter (and energy)

**Our brain**: $10^{11}$ (estimated) neurons

- Grey matter and white matter (and energy)

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**1998: Supernovae Ia $\rightarrow$ Accelerated univers expansion**

(Riess, Perlmutter, Schmidt 2011 Nobel Prize)

- Dark Energy ($\sim 73\%$ of universe content)

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**Electromagnetism, Relativity**

- **Gauge theories**

- Quantum Standard Model, ΛCDM model

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**Neural code of consciousness?**

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**First black hole « image »**

Event Horizon Telescope (EHT) Ultimate proof of the General Relativity Theory

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**NeuroSpin**

ISEULT PROJECT

11.7T MRI magnet

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Merging physics and neurosciences!
THE BRAIN MULTISCALE FUNCTIONAL ARCHITECTURE

**MACROSCOPIC**
Regions and ‘topies’

- **Brodmann** 1908
- **Penfield** 1950

**MESOSCOPIC**
Column and layers

- **Hubel & Wiesel** 1959 (Nobel Prize 1981)

**MICROSCOPIC**
Neurons and synapses

- **Cajal** (Nobel Prize 1906)
- **Sherrington** (Nobel Prize 1932)
- **HH Dale, O Loewi** (Nobel Prize 1936)
- **SB Katz, U von Euler, J Axelrod** (Nobel Prize 1970)

**CELLULAR & MOLECULAR**
Neurotransmitters, Synaptic transmission

Plenary presentation given at MT-28 2023, Sept. 14, 2023, Aix-en-Provence, France**
The importance of white matter has been overlooked!

**White matter:** Brain temporal segregation

**Gray matter:** Brain spatial segregation

**Brain at work:**
( functional MRI or fMRI)

**Brain connexions:**
(Diffusion MRI & DTI)

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**Looking Inside the Brain**

Denis Le Bihan

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**The BRAIN CONNECTOME**

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The importance of white matter has been overlooked!

White matter:
Brains spatial segregation

Gray matter:
Brains temporal segregation

From 500 to 10 000 connexions/neuron
Hodgkin & Huxley 1952 (Nobel Prize 1963)

Broca 1863

Cajal (Nobel Prize 1906)

Sherrington (Nobel Prize 1932)

Penfield 1950

Brodmann 1908

MOLECULAR Neurotransmitters, Synaptic transmission

MACROSCOPIC regions and ‘topies’

Current MRI « luminosity » (<7 teslas)

Future MRI « luminosity » (>10 teslas)

Hodgkin & Huxley 1952 (Nobel Prize 1963)

Hubel & Wiesel 1959 (Nobel Prize 1981)

MRI signal (spatial/temporal resolution) $\text{Mo} \approx \gamma B_0 / kT$

$11.7T$

The Iseult Project

11.7 teslas MRI

$0.00005$ teslas

$\times 223,000$

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

D. Le Bihan

2001
- 3T : \approx 100 installed systems
- 1x 7T (USA) + 2 orders (USA, J)
\rightarrow 11.7T at CEA?

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

Better see…
...to better understand

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

ULTRA-HIGH FIELD MRI

NeuroSpin Claude Vasconi

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

MACRO
MESO
MICRO

1000 millimeters
MESI

Unchartered territory

Alzheimer disease
Molecular imaging

1mm voxels

Mesoscale cortex architecture

Notations:
- MACRO: 1000 millimeters
- MESO: ~100μm
- MICRO: 0.000001 millimeters

Neural Code ?
Connectome Spacetime?
DESIGN: CEA/Irfu design for NeuroSpin 900mm bore 11.74T (500MHz) magnet

- 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)

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

Plenary presentation given at MT-28 2023, Sept. 14, 2023, Aix-en-Provence, France
Dedicated manufacturing processes were made to build and assemble the pancakes (CEA/Alstom-GE)
Dedicated manufacturing processes were made to build and assemble the pancakes (CEA/Alstom-GE).
General cryogenic layout for NeuroSpin 11.7T MRI system

Quench protection: external dump resistor.

(Quench voltage to ground 2000 V)

Magnet in driven mode (external power supply)

Stability circuit (current limitator).

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General cryogenic layout for NeuroSpin 11.7T MRI system

- Quench protection: external dump resistor.
  (Quench voltage to ground 2000 V)

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

High availability
(24/24, 7/7, >10 years, including French holidays, strikes, virus, war, etc.)
New RF coil designs & metamaterials

8Tx/32Rx 11.7T human brain coil

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

MRI IS NOT ONLY A MAGNET!

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

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

Plenary presentation given at MT-28 2023, Sept. 14, 2023, Aix-en-Provence, France
New signal spatial encoding strategies
(Parallel Transmission, kT points, universal pulses)
A. Amadon, N. Boulant

- Tomi-Tricot, Amadon A et al. (2018)

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.

Acquisition and Image Reconstruction/Processing have become completely intermingled (Machine Learning, Compress sensing)
P. Ciuciu, CEA/INRIA


MRI IS NOT ONLY A MAGNET!

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

2d at the Facebook & NYU challenge on Brain fastMRI
The very first images... (October 2021)

BREAKING NEWS!

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

Results will be shown by the end of 2023...

Courtesy N. Boulant, C. Lerman, L. Quettier & Museum National d’Histoire Naturelle, ICM (Mathieu Santin), Paris
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)
- 1x 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)

The liquid helium crisis (MRI)

World Helium Resources

<table>
<thead>
<tr>
<th>Country</th>
<th>Billion Cubic Metres</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>20.6</td>
</tr>
<tr>
<td>Qatar</td>
<td>10.1</td>
</tr>
<tr>
<td>Algeria</td>
<td>8.2</td>
</tr>
<tr>
<td>Russia</td>
<td>6.8</td>
</tr>
<tr>
<td>Canada</td>
<td>2.3</td>
</tr>
<tr>
<td>China</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Trends above are estimated helium resources from the US/Gemini Community Summary

Nuclear magnetization
Mo ≈ γB₀/kT

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Consciousness in the CONNECTOME RELATIVISTIC SPACETIME

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

Awaking out of a vegetative state?

FlatBedMRI?

Conscious state

Vegetative state

Restoring consciousness by restoring spacetime curvature?

Consciousness is supported by dynamic complex patterns of brain signal coordination

Healthy controls | Vegetative unresponsive | Minimally conscious state

$\{c^*, D^*\} = \{37, 5.2\}$

$\{c^*, D^*\} = \{18, 2.8\}$

$\{c^*, D^*\} = \{9, 1.3\}$

Abe Y, Tsurugizawa T, Le Bihan D, 2017, PlosBiology

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, 10⁻⁴ppm/10min short term
- Multiple gradient sets (80mT/m) and RF coils
- Head contention (motion artifacts)
Clinical need
Market
Science

Clinical need
Market

Clinical need
Market

Clinical need
Market
Science

Clinical need
Market
Science

Clinical need
Market
Science

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Market
Science

Clinical need
Market
Science
They did not know it was impossible, so they made it. — Mark Twain