NEUROSPIN: EXPLORING THE BRAIN WITH ULTRA-HIGH FIELD MRI
- Executive summary -
by D. Le Bihan, Director

Activity since opening

The understanding of **how the human brain works** has considerable potential, not only for health care (addressing the expenses of managing neurological and psychiatric patients or simply aging populations) but also for improving human cognition in general (through improved teaching methods, communication between individuals, development of human-machine interfaces, etc.). The goal of **NeuroSpin** is to **explore the brain at spatial and temporal scales** which may give access to **the neural code**, by **pushing the current limits of brain imaging, from mouse to man, as far as possible with ultra high magnetic field (UHF) Magnetic Resonance Imaging and Spectroscopy**. Results are expected to impact not only European health care, but also industry, artificial intelligence, social sciences and the humanities.

Neurospin was opened on January 1st 2007 as a shared facility dedicated to neuroscience. Neurospin is a component of the Biomedical Imaging Institute ("I2BM") of Life Science Direction at CEA. It is headed by Denis Le Bihan, a Member of the French Academy of Sciences and is comprised of five laboratories: NMR methodological research for imaging and spectroscopy (Vincent Lebon), Neurocomputing (Jean-François Mangin), Clinical research (Lucie Hertz-Pannier), Cognitive neuroimaging (Stanislas Dehaene) and Preclinical research (Marc Dhenain). The NeuroSpin platform has nearly 11000 m² of laboratories, offices, technical facilities, and seminar space. This platform consists of both a clinical facility for hosting normal human participants and patients, including children, with 8 beds, test/examination rooms, a nursing facility, mock scanner and an ICU (for studies of consciousness), as well as a preclinical facility for small animals and primates (including trained primates). NeuroSpin also houses several laboratories (electronics, chemistry, biology, histology, etc.).

Benefiting from CEA expertise in magnet and NMR technology, NeuroSpin is being equipped with unique MRI systems operating at very high magnetic field strengths **not yet available elsewhere in the world,** as well as related tools and an advanced computer platform. The imaging equipment presently consists of **3T** and **7T** whole-body MRI systems (the first 7T MRI scanner installed France), and NeuroSpin is also in charge of the MRI park of MIRCen (small bore **7T** MRI system) and SHFJ (clinical **1.5T** system). Future equipment includes a **17T** small-bore horizontal magnet in 2009 and a **11.7T** whole-body (90cm) system to be delivered in 2012, both of which will be world premiers for such systems. In addition there is a 306-channel **MEG** system and several **EEG** systems. For post-processing, Neurospin is equipped with BrainVisa software for image visualization, structural image processing tools, fMRI data analysis tools, and a 150-terabyte data archiving system.

Interfacing researchers with many different backgrounds, NeuroSpin co-ordinates research, provides a network of skills and an optimization of methods, not only within I²BM but also nationally. The first 18 months have been mainly dedicated to organizing research and platform activities. NeuroSpin staff (so far about 50 permanent researchers, technical and administration staff, 30 post-doctoral fellows and graduate students and 30 temporary collaborators) create a wide, strong multidisciplinary environment (mathematics, physics, computer sciences, signal and image processing, neurosciences, neuropsychology, neurology, brain development, molecular imaging, functional genomics, etc.) and work to develop **innovative tools and methodologies** and to apply them to neurobiology in general, from neurogenetics and neurophysiology to cognitive neurosciences and clinical neurology.

However, beside resident researcher teams (from CEA, INSERM, INRIA), ***NeuroSpin*** has been conceived as an ***open, shared facility*** designed to welcome international teams of researchers (public institutions and industry) on a temporary basis (weeks to months), giving them the opportunity to carry out their own studies. This concept, as used for years in the physics community (accelerators, synchrotrons, etc.), has proven very successful, allowing teams to share expensive or rare equipment they could not access on an individual basis. Currently, several researchers from Europe, Asia and USA are working at NeuroSpin. ANR, PHRC, foundations, EU and NIH grants have been obtained (some still pending), and collaboration agreements with exchange of researchers are implemented with the University of Kyoto and Tokyo, as well as the National Yang-Ming University of Taiwan and the National Research Council of Canada. NeuroSpin is also a founding member of ***EATRIS***, a European network of Infrastructures within EU ESFRI framework.

Ongoing research programs (2007-2011)

NeuroSpin projects address either methodological developments or neuroscience and clinical applications. Those projects, coordinated by JB Poline, have been set up within overall mid/long term ***scientific programs***. These rely on the various expertises within the different laboratories and resources of NeuroSpin:

- ***Pushing the limits of MRI*** (*V. Lebon, D. Le Bihan, C. Wiggins, F. Lethimonnier*): The goal of this program is obtain higher spatial and temporal resolution by utilising UHF MRI, and to reach at least one order of magnitude compared to conventional approaches. In humans at 11.7T the target is the '*mesoscale'*, clusters of thousands of neurons, while at 17.6T in animals MRI microscopy could reach the neuron level. To do so, new acquisition schemes must be devised to take into account the change in electromagnetic regimen imposed by ultra-high frequencies (heavily parallel excitation and transmission, reconstruction, dedicated radiofrequency pulses and coil arrays,…). Another component of this program is to investigate contrast mechanisms (such as the relationship between molecular diffusion and tissue physiology) and to explore new avenues to generate contrast using dedicated tracers, along the ***Iseult*** program (see below). Additionally, at UHF spectroscopic techniques allow detection and mapping of non-hydrogen nuclei (e.g. ^{31}P, ^{23}Na, ^{13}C, ^{17}O) and biologically relevant molecules (physiology, metabolism, neurotransmission). This part is carried out across NeuroSpin and MIRCen.

- ***Multiscale brain functional architectur***e *(J.F. Mangin, C. Poupon)*: Current neuroimaging approaches in humans remain at a macroscopic scale (millions of neurons), while invasive recordings in animals explore very small ensembles of neurons. This large gap must be bridged to understand how the brain works. Interaction and synergy exist between all levels and a realistic model of the brain must take this into account. UHF MRI will allow the *mesoscale* to be investigated, but, considering the whole brain, huge data sets containing information on anatomy, connexions, function, metabolism,… will be generated. Furthermore, comparison across individuals and across species are necessary, adding to the complexity and the size of the databases to be analysed. This program aims to produce the mathematical concepts, computer algorithms and visualization tools to explore those scales in a common frame of reference.

- ***Genetics and phenotypic variability in brain anatomy and function*** (*JB Poline*, *B. Thirion*): The goal is to clarify the relationship between genes present and/or expressed in the brain and cognitive phenotypes, examined through behavior and imaging (anatomy and function). Beside advanced imaging methods this program requires the build-up, storage and processing of very large databases, as well as suitable statistical analysis methods. This program is also embedded in an ambitious European Project (*Imagen*) aimed at better understanding the genetic and neural basis of drug addiction in teenagers. This program will also explore variability in brain anatomical and functional phenotypes across individuals.

- ***Brain development and plasticity*** **(***G. Dehaene-Lambertz, L. Hertz-Pannier, C. Wu*): This program attempts to understand how humans acquire cognitive skills, as well as how pathologies, such as epilepsy, may impact brain development. With advanced imaging and dedicated processing techniques it becomes possible to detect on a individual basis features linked to anatomical and functional brain maturation, in infants, babies and even foetuses. Animal models will also be investigated, especially the interaction between gene expression and environment at early phases of brain development and to investigate the mechanisms involved in brain plasticity, whether in the normal or lesioned brain.

- ***Cognitive codes*** (*S. Dehaene, A. Kleinschmidt, C. Pallier, Ph. Ciuciu*): This program aims at defining the neural architecture involved in information processing within the human brain, and how information (especially that specific to man kind: words, sentences, numbers,…) is encoded at different levels along brain regions. An important goal is to understand how circuits present in non-human primates are reused to engage in new activities, such as written language from visual pattern recognition areas or number manipulation from spatially mapped parietal areas. Correlations with studies in awake primates will thus also be an important part of this program. With a knowledge of the brain 'encoding' processes it will become possible to 'read' mental representations from imaging signals using learning techniques (eg, Support Vector Machines). Another important component is ***brain dynamics -*** the temporal features of the brain signals generated by brain function and cognitive processes. Multimodality is then an important requirement, as fast MRI signals collected at UHF must be integrated to those obtained by MEG or EEG. Advanced statistical processing methods are under development to decode temporal information from those signals.

- ***Translational research for neurological and psychiatric disorders*** (*L. Hertz-Pannier, D. Le Bihan, M. Dhenain*) This program bridges the gap between basic research and clinical applications. The preclinical component of this program (***molecular imaging***) aims at developing animal models of human brain disorders, such as Alzheimer's disease, and investigates new strategies to help detect the occurrence of the diseases at a very early stage with the benefit of UHF MRI (microscopy, specific tracers or contrast agents). New therapy approaches are also evaluated. This component extents across NeuroSpin and MIRCen and involves many other partners, especially in industry (Guerbet in ***Iseult*** consortium, Sanofi in ***Transal***, Servier, …). The clinical component evaluates UHF MRI for clinical care (neurodegenerative diseases, brain tumors, …). A significant part is dedicated to pediatrics (epilepsy, genetic disorders, …). The clinical component depends on links with regional care centers, particularly the Salpêtrière Hospital with a large cohort project on Alzheimer patients. Finally, investigation of potential effects of UHF on biological tissues, using animal models, aims to establish safety guidelines for human subjects.

Finally**,** NeuroSpin is also a major partner of the ***Iseult*** program (*D. Le Bihan, F. Lethimonnier*), an ambitious French-German endeavor to develop and explore the potential of UHF MRI for life sciences in general. This 215M€ program relies on the participation of partners in industry (Guerbet, Siemens, Bruker, Alstom) and academia (University of Freiburg, CEA Life Science and Matter Science Divisions) with partial support from public agencies (Oéso in France, BMBF in Germany). The program is in charge of building the world first whole-body 11.7T MRI system, and to develop tracers (^{19}F labeled compounds, lanthanide chelates, USPIOs, CEST complexes,…) customized for UHF MRI, targeted to brain tumors, Alzheimer disease and stroke.

In conclusion, Neurospin is NOT as such a center or neurosciences or biology, nor of a center of MRI physics. Such centers already exist at other sites in the world. Our objective is different: *we wish to join together on the same location the methodological and neurobiological players so that they develop, in synergy, the tools and the models which will enable them to better understand the working of the human brain in normal and deficient conditions*. The results of this project should impact clinical, artificial intelligence, social sciences and industrial fields. A point which must be emphasized is that the equipment, methodologies, and human resources needed for imaging humans are mostly the same as those used on animals. That is the reason why the grouping of teams around a state-of-the-art imaging facility, dedicated to both human and animal studies, appears as an ideal solution, both from a scientific and biomedical as well as economic points of view. This concept, which we are trying bring to life between NeuroSpin and MIRCen within I²BM, is now adopted in many developed nations, who are anxious to optimize the return from very heavy investments, whether they are public or private.