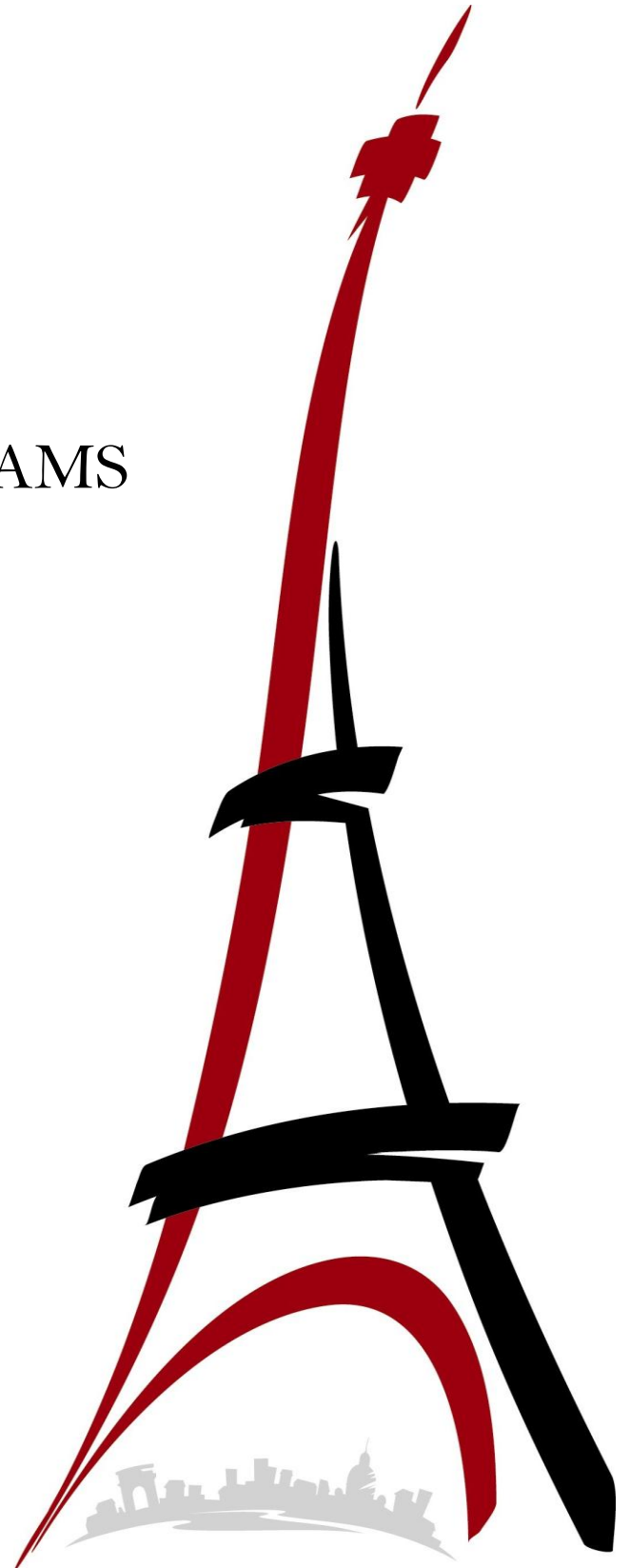




ENP  
PARTICIPATING TEAMS  
*BY CENTERS*  
*November 2011*



## Centre De Neurosciences des Saints-Pères -

### Institut Interdisciplinaire des Sciences du Vivant

*11 research groups*

AUDINAT Etienne's team [Interactions Neurone-Glie](#) UMR 8154

BRUNEL Nicolas' team [Stochastic dynamics of single spiking neurons , Synchronization properties of large networks& Persistent activity, multistability and working memory in network models](#) UMR 8119

CHARPAK Serge's team [From sensory processing to functional hyperaemia](#) UMR 8154

EMILIANI Valentina's team [Wavefront-engineering microscopy](#) UMR 8154

HANSEL David's team [Cerebral Dynamics](#) UMR 8119

MAIER Marc / MC INTYRE Joe's team [Multi-sensory control of the upper limb](#) UMR 8194

MAMASSIAN Pascal's team [Vision](#) UMR 8158

MARTY Alain's team [Laboratory of brain physiology](#) UMR 8118

OGDEN David's team [Photolysis of caged neurotransmitters for experiments in neuronal tissue](#) UMR 8118

OHEIM Martin / ROPERT's team [Biophysics of gliotransmitter release](#) UMR 8154

ZYTNIKI Daniel's team [Spinal physiology and physiopathology](#) UMR 8119

## Faculte des Sciences Pharmaceutiques Paris - Descartes

*1 research group*

AUBOURG Patrick / CARTIER Natalie's team [Biotherapies of Degenerative and Proliferative Diseases of the Nervous System](#) UMR S 745

## Institut de la Vision

*5 research groups*

CHEDOTAL' Alain s team: [Role of axon guidance molecules](#) FVE

LÉVEILLARD Thierry's team: [Implication of RdCVF in maintaining cone photoreceptors and its application for the treatment of photoreceptor degenerations](#) FVE

LIVET Jean's team : [Development of neuronal circuits](#) FVE

PICAUD Serge's team: [Retinal information processing : pharmacology and pathology](#) FVE

SAHEL José-Alain's team: [Systemic biology and translational therapeutics for vision](#) FVE

## Campus de Jussieu - UPMC - Quai Saint Bernard - IFR 83

### 9 research groups

**PMSNC:** Physiopathologie des Maladies du Système Nerveux central

**UMR 7102:** Neurobiologie des Processus Adaptatifs

CABOCHE Jocelyne's team [Neuronal signaling and gene regulation](#) PMSNC

EL MESTIKAWI Salah's team [Normal and pathological Glutamatergic systems](#) PMSNC

FAURE Philippe's team [Neurophysiology and Behavior](#) UMR 7102

GIROS Bruno's team [Physiopathology of psychiatric diseases](#) PMSNC

LAMBOLEZ Bertrand / CAULI Bruno's team [Cortical Network & Neurovascular Coupling](#) UMR 7102

MARIANI Jean's team [Development and aging of the nervous system](#) UMR 7102

RONDI-REIG Laure's team [Navigation, Memory and Aging](#) UMR 7102

SCHNEIDER-MAUNOURY Sylvie's team [Brain patterning and morphogenesis in vertebrates](#) IFR 83

TREMBLEAU Alain's team [Development and plasticity of neural networks](#) UMR 7102

## CRICM & ICM

### 19 research groups

BACCI Alberto's team [Cellular Physiology of Cortical Microcircuits](#)

BARON van EVERCOOREN Anne / NAIT OUMESMAR Brahim's team

[Molecular and cellular approaches of myelin repair](#)

BRICE Alexis' team [Molecular basis, physiopathology and treatment of neurodegenerative diseases](#)

DELATTRE Jean-Yves' team [Experimental neuro-oncology](#)

DUBOIS Bruno's team [Cognition, neuroimaging and brain disorders](#)

DUYCKAERTS Charles / HAIK Stéphane's team [Alzheimer's diseases and Prion Diseases](#)

FONTAINE Bertrand's team [Genetics and mechanisms of membrane excitability disorders and multiple sclerosis](#)

HIRSCH Etienne's team [Experimental therapeutics of neurodegeneration](#)

KABASHI Edor's team [Treatment of Amyotrophic Lateral Sclerosis : From Genetics to Zebrafish](#)

LE GUERN Eric's team [Genetics of diseases of the peripheral nervous system and epilepsy](#)

LUBETZKI Catherine's team [Myelination and remyelination](#)

MALLAT Michel [Role of microglia in development and neurodegenerative diseases](#)

MILES Richard's team [Cortex & Epilepsy](#)

PESSIGLIONE Mathias's team [Motivation, Brain and Behavior](#)

THOMAS Jean-Léon's team [Oligodendrocyte development and Neurovascular Interactions](#)

VIDAILHET Marie's team [Movement disorders and basal ganglia: physiopathology and experimental therapeutics](#)

WYART Claire's team [Optogenetic dissection of spinal circuits](#)

YELNIK Jérôme / MALLET Luc's team [Behavior, Emotion and Basal Ganglia](#)

(*CENIR: Le Centre de NeuroImagerie de Recherche*) :

LEHERICY Stéphane's team [Centre for NeuroImaging Research](#)

## Institut Mondor de Recherche Biomédicale

*2 research groups*

BACHOUD-LEVI Anne Catherine's team [Interventional neuropsychology](#)

LEBOYER Marion's team [Psychiatry genetic](#)

## Institut Jacques Monod

*2 research group*

GALLI Thierry's team [Membrane traffic in neuronal and epithelial morphogenesis](#)

PIERANI Alessandra's team [Genetics and Development of the Cerebral Cortex](#)

## Institut du Fer à Moulin

*7 research groups*

FRANCIS Fiona's team [Cytoskeleton and pathology of neuronal migration](#) *Avenir*

GASPAR Patricia's team [Neurotransmission in neural circuit formation](#)

GIRAULT Jean-Antoine / HERVE Denis' team [Neurotransmission and signaling](#)

GROSZER Matthias' team [Molecular and cellular mechanisms of cortical development](#) *Avenir*

MAMELI Manuel's team [Synapses in the pathophysiology of reward](#)

PONCER Jean-Christophe's team [Plasticity in Cortical Networks and Epilepsy](#)

*Avenir*

SOBEL André's team [Intracellular Signal Relay and Integration](#)

## INSEAD - Fontainebleau

*1 research group*

PLASSMAN Hilke's team [Decision Neuroscience Group](#)

## Centre Des Neurosciences Paris Sud - Orsay

*2 research groups*

LAROCHE Serge's team [Cellular and Molecular Mechanisms of Plasticity and Memory](#)

GRANON Sylvie's team [Neurobiology of decision making](#)

## **IMNC - Imagerie et Modélisation en Neurobiologie et Cancérologie**

*1 research group*

GURDEN Hirc's team [Metabolism, Imaging and Olfaction IMNC](#)

## **MIRCent - Laboratoire des Maladies en Neurobiologie et Cancérologie**

*3 research groups*

BONVENTO Gilles [Cell-cell interactions in neurodegenerative diseases](#)

HANTRAYE Philippe's team [Preclinical therapeutics for neurodegenerative diseases](#)

MARTINOT Jean-Luc / ZILBOVICIUS Monica's team [Brain Imaging & Developmental Psychiatry](#)

## **INAF - Institut National Alfred Fessard**

*8 research groups*

### **NEUROBIOLOGY AND DEVELOPPEMENT**

BALLY CUIF Laure's team [Zebrafish Neurogenetics \(ZEN\)](#)

FORTIN Gilles' team [Neurobiology intégrative of the brainstem to the embryo](#)

PERRON Muriel's team [Stem cells & Neurogenesis in the Retina](#)

ROUYER François' team [Molecular genetics of circadian rhythms](#)

VERNIER Philippe's team [Development and evolution of neurotransmission](#)

### **UNITE DE NEUROSCIENCES : INFORMATION ET COMPLEXITE (UNIC)**

DESTEXHE Alain's team [Oscillatory and stochastic dynamics in thalamo-cortical networks](#)

FREGNAC Yves' team [Cognisciences: Synaptic integration and functional plasticity in primary visual cortex](#)

SHULZ Daniel's team [Neural Processing, Neuromodulation and sensory plasticity](#)

## **NEUROSPIN**

*4 research groups*

LEBIHAN Denis' team [Brain imaging](#)

MANGIN Jean-Francois [Computer-assisted neuroimaging laboratory \(LNAO\)](#)

DEHAENE Stanislas' team [Cognitive neuroimaging laboratory](#)

DEHAENE LAMBERTZ Ghislaine's team [Developmental Neuroimaging](#)

## Centre Hospitalier Sainte-Anne

*3 research groups*

CHNEIWEISS Hervé's team [Glial Plasticity and brain tumors](#)

HAMON Michel's team [Neuropsychopharmacology](#)

KREBS Marie-Odile/ JAY Thérèse's team [Pathophysiology of Psychiatric disorders](#)

SIMONNEAU Michel's team [Functional genomics & psychiatric diseases](#)

## Institut de Recherche Biomedicale - Cochin

*1 research group*

CHELLY Jamel's team [Genetics and physiopathology of neurodevelopmental disorders](#)

## ENS - Ecole Normale Supérieure

*5 research groups*

1\* Group for Neuronal theory

2\*Frontal lobe functions group

CHRISTOPHE Anne's team [Cognitive Science and Psycholinguistics Laboratory](#) 1\*

GIRAUD Anne-Lyse's team [Auditory Language Group](#) 1\*

GUTKIN Boris / DENEVE Sophie's team [Group for neural theory](#) 2\*

KOECHLIN Etienne's team [Cognitive neuroscience](#) 2\*

(*IBENS: Institut de Biologie de l'ENS*) :

SPASSKY Nathalie' team [Functions of ventricular cilia during neurogenesis](#)

## Institut Pasteur

*6 research groups*

BOURGERON Thomas' team [Human genetics and cognitive functions](#)

DI GREGORIO David's team [Unite of Dynamic Neuronal Imaging](#)

CORRINGER Pierre-Jean [Channel-receptors G5 group](#)

LLEDO Pierre-Marie's team [Perception and Memory](#)

MASKOS Uwe's team [Integrative Neurobiology of Cholinergic Systems](#)

PETIT christine's team [Genetics and Physiology of Hearing](#) (Collaborative team Institut de la Vision: [Retinal physiopathology of joint audition and vision losses: Usher's syndrome and other syndromes](#)).

## Collège De France

### 10 research groups

**LPPA:** Laboratoire de Physiologie de la perception et de l'action.

BERTHOZ Alain's team [Physiology of perception and action](#) LPPA

GIAUME Christian's team [Junctional communication and interaction between neuronal and glial networks](#)

FLEISCHMANN Alexander's team [Neural Circuits and Behavior](#)

PROCHIANTZ Alain's team [Development & Neuropharmacology](#)

ROUACH Nathalie's team [Neuroglial Interactions in Cerebral Physiopathology](#)

SELIMI Fekrije's team [Mice, Molecules and Synapse formation](#)

VENANCE Laurent's team [Dynamic and Pathophysiology of Neuronal Networks](#)

WIENER Sidney's team [Neural bases Spatial memory and navigation](#) LPPA

ZUGARO Michael's team [Brain Rhythms and Neural Coding of Memory](#) LPPA

DROULEZ Jacques' team [Active Perception and Probabilistic Approach](#) LPPA

**FVE Team:** *Fondation Voir et Entendre* research groups

**AVENIR:**

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**INAF** Institut National Alfred Fessard

**ENS** Ecole Normale Supérieure

**INSERM** Institut National de la Santé et de la Recherche Médicale

**UPMC** Université Pierre et Marie Curie

**MIRGen** Molecular Imaging Research Center

**CHU** Centre Hospitalier Universitaire

**CRICM** Centre de Recherche du Cerveau et de la Moelle

**UNIC** Unité de Neurosciences, Information & Complexité

**IMNC** Imagerie et modélisation en Neurobiologie et Cancérologie

**PMSNC:** Physiopathologie des Maladies du Système Nerveux central

**IFR 83:** Institut de Biologie intégrative

**IBENS:** Institut de Biologie de l'ENS

**LPPA:** Laboratoire de Physiologie de la perception et de l'action.

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**CENTRE DES NEUROSCIENCES DES SAINTS PERES**

*12 research groups*

# Neuron-Glia Interactions

Etienne AUDINAT

CNRS - INSERM - Université Paris Descartes (UMR 8154)

## ■ Team overview

Our research focuses on the interactions between neurons and glial cells in the central nervous system of rodents. Glial cells are engaged in bi-directional interactions with neurons and contribute actively to the modulation of neuronal network activities. Three main research programs structure the current activity of the team. The first one concerns the astrocytic control of neuronal activity.

We have demonstrated that astrocytes synchronize the activity of neuron ensembles by releasing glutamate and GABA. We currently study whether these two gliotransmitters are released by a single or by different populations of astrocytes. The second project is on the functional analysis of NG2-expressing glial cells.

This project supervised by Maria Cecilia Angulo aims at understanding how synaptic activity influences the fate of NG2 cells. Finally, we also study the functional properties of microglial cells in different physiological and pathological conditions to understand how these immune resident cells interact with neurones.

## ■ Website

[www.biomedicale.univ-paris5.fr](http://www.biomedicale.univ-paris5.fr)

# Stochastic dynamics of single spiking neurons, Synchronization properties of large networks & Persistent activity, multistability and working memory in network models

Nicolas BRUNEL

CNRS - Univ. Paris Descartes (UMR 8119)

## ■ Team overview

We use theoretical approaches from statistical physics and dynamical systems theory to understand the behavior of single neurons or large networks of neurons, in collaboration with neurophysiologists.

We have recently focused our research on models of motoneurons, the dynamics of neocortical networks, of cerebellum, and basal ganglia

## ■ Website

[www.neurophys.biomedicale.univ-paris5.fr](http://www.neurophys.biomedicale.univ-paris5.fr)

# Imaging and neurovascular physiology of the olfactory bulb

Serge CHARPAK

UPD - INSERM - CNRS (UMR 8154)

## ■ Team overview

The objective of the team is to investigate several aspects of glomerular neurophysiology in the rodent, combining electrophysiological recording and two-photon imaging, both in vivo and in vitro.

We investigate functional hyperaemia by addressing the differential roles of neurones and astrocytes during odor stimulation.

Because we are convinced that blood flow regulation cannot be understood without determining precisely which neuronal networks are mobilised, we also study intrinsic and synaptic properties of glomerular neurones.

Finally, we maintain an activity in technological developments, by constructing improved two-photon microscopes and testing new optical probes reporting neuronal activity and oxygen consumption.

## ■ Website

[www.biomedicale.univ-paris5.fr/neurophysiologie](http://www.biomedicale.univ-paris5.fr/neurophysiologie)

# Wavefront-engineering microscopy

Valentina EMILIANI

INSERM – CNRS – Université Paris Descartes (UMR 8154)

## ■ Team overview

This research team is dedicated to the development of optical techniques based on wave front engineering microscopy.

Traditional optical systems modify excitation light patterns through the use of lenses, diaphragms, curved mirrors, gratings, or optical fibers. They are typically limited to the generation of simple patterns (generally of circular symmetry) which are relatively difficult to change during the course of an experiment. In contrast the use of active optical elements such as micro-mirror and optical membrane devices, acousto-optical or nematic liquid crystals displays permits laser light to be dynamically redistributed by modulation of its phase or amplitude.

The active nature of these devices allows illumination patterns to be rapidly and conveniently adapted to experimental needs and greatly widens the types of experiments and studies that can be performed on biological systems. The interest of this team is to develop advanced methods for wave front engineering and to exploit the potentiality of wave front engineering microscopy in the field of neuroscience.

The team activity is organized in three research lines:

1. Spatiotemporal control of neuronal activity by holographic photoactivation patterns
2. Super resolution microscopy (STED)
3. Microendoscopy for deep imaging.

## ■ Website

[www.biomedicale.univ-paris5.fr](http://www.biomedicale.univ-paris5.fr)

# Cerebral Dynamics

David HANSEL

CNRS - Université Paris Descartes (UMR 8119)

## ■ Team overview

Our research concerns the neural dynamics in cerebral cortex, cerebellum and basal basal ganglia. We investigate the mechanisms underlying the emergence of functional properties of neurons, persistent activity and decision making as well as the emergence of synchrony in relation with the physiology and the physiopathology of the central nervous system.

Our approach combines theory (methods borrowed from statistical mechanics, dynamical system theory, numerical simulations) and experiments (electrophysiology in-vitro, morphology and anatomy) in the framework of interdisciplinary collaborations between the theoreticians and the neurophysiologists within the team.

We also cooperate with experimentalists from other laboratories on projects which involve electrophysiology in-vivo in cat and behaving monkeys.

## ■ Website

[www.neurophys.biomedicale.univ-paris5.fr](http://www.neurophys.biomedicale.univ-paris5.fr)

# Multi-sensory control of the upper limb

Septembre 2011

Marc MAIER / Joe Mc INTYRE

CNRS - Université Paris Descartes - Université Paris Diderot (UMR 8194)

## ■ Team overview

We investigate 3 principal topics:

- the control of the dynamic properties of the arm
- multi-articular coordination and redundancy of the arm and of the hand
- multisensory integration during reach, grasp and object manipulation

We combine complementary experimental and theoretical approaches:

- Behavioral studies (movement analysis) in patients and healthy subjects
- Brain imaging in patients and healthy subjects
- Modeling of the CNS using artificial neural networks (ANNs)
- Validation of the models by neurorobotics.

## ■ Bibliography

- McIntyre J, Tagliabue M.

Necessity is the mother of invention: reconstructing missing sensory information in multiple, concurrent reference frames for eye-hand coordination.

**J Neurosci** 2011 31(4):1397-409.

- Lindberg P, Feydy A, Maier MA. White matter organization in cervical spinal cord relates differently to age and control of grip force in healthy subjects.

**J Neurosci** 2010 30(11):4102-4109.

- Le Séac'h AB, Senot P, McIntyre J. Egocentric and allocentric reference frames for catching a falling object. **Exp Brain Res** 2010 201(4):653-62.

- McIntyre J and Lipshits M.

Central processes amplify and transform anisotropies of the visual system in a test of visual-haptic coordination. **J Neurosci** 2008 28: 1246 – 1261.

- Zollo L, Eskiizmirli S, Teti G, Laschi C, Burnod Y, Guglielmelli E, Maier MA.

An anthropomorphic robotic platform for progressive and adaptive sensorimotor learning.

**Advanced Robotics**, 2008, 22 : 91-118.

## ■ Website

[www.biomedicale.univ-paris5.fr](http://www.biomedicale.univ-paris5.fr)

■ **Contact** CNRS UMR 8194, Université Paris Descartes, 45 rue des Saints-Pères, 75270 Paris

T + 33 (0) 1 42 86 43 70 / 33 15 - [marc.maier@parisdescartes.fr](mailto:marc.maier@parisdescartes.fr) / [joe.mcintyre@parisdescartes.fr](mailto:joe.mcintyre@parisdescartes.fr)

## Vision

Pascal MAMASSIAN

CNRS - Université Paris Descartes (UMR 8158)

### ■ Team overview

The vision team of the Laboratoire Psychologie de la Perception has research interests in all aspects of visual perception. Its expertise covers visual attention, visual awareness and perceptual decisions, sensorimotor coupling, 3D perception, and the interaction of vision with the other senses.

It relies on experimental methods issued from psychophysics, neuroimager, patient studies, and modelling. Specific research topics include motion perception, colour modelling, visual attention, three-dimensional perception from multiple cues, cross-modal interactions, eye-movements, perception-action interactions, intention-based vs. reflexive actions, and time perception.

### ■ Website

<http://lpp.psychu.univ-paris5.fr>

## Laboratory of brain physiology

Alain MARTY

CNRS - Univ. Paris Descartes - Univ. Paris Diderot (UMR 8118)

### ■ Team overview

This team employs a multidisciplinary approach including physical methods (optics), mathematical methods (statistical treatment of data and modelling) as well as chemical methods (synthesis of new compounds). It develops new techniques to study intercellular communication in the brain tissue.

Currents lines of research concern the role of internal calcium stores in pre- and postsynaptic signalling; the functional implication of endogenous calcium buffers in presynaptic calcium signalling; the role of ionotropic presynaptic receptors in the regulation of the firing pattern and of the release probability.

### ■ Website

[www.biomedicale.univ-paris5.fr](http://www.biomedicale.univ-paris5.fr)

# Photolysis of Caged Neurotransmitters for Experiments in Neuronal Tissue

Septembre 2010

David OGDEN

CNRS - Université Paris Descartes (UMR 8118)

## ■ Team overview

Photolytic release of the neurotransmitters glutamate or GABA from 'caged' precursors is potentially a way of overcoming the diffusional barriers that prevent exogenous activation of synaptic receptors in neurones on physiological spatial and time scales.

The development of caged neurotransmitters and other caged ligands for use in neuroscience requires strong collaborations with chemists, photochemists and photonics specialists.

A long-standing collaboration with the laboratory of John Corrie at the MRC-National Institute for Medical Research in London has introduced new caged neurotransmitters for use in synaptic physiology which are stable, fast and physiologically inert. Optical and chemical improvements are continually being made to implement spatial localization (on a sub-micron scale) with both near-UV or two-photon excitation.

This approach will be used to study functional properties of synaptic channels in situ, the distribution of neurotransmitter receptors in different neuronal compartments and changes in receptor properties that occur during short term and long term plasticity.

## ■ Bibliography

Huberfeld G, Menendez de la Prida L, Pallud J, Cohen I, Le Van Quyen M, Adam C, Clémenceau S, Baulac M & Miles R. (2011) Glutamatergic preictal discharges emerge at the transition to seizure in the human epileptic temporal lobe. **Nature Neurosci.** 14: 627-34.

Bazelot M, Dinocourt C, Cohen I & Miles R (2010) Inhibitory field potentials in the CA3 region of rat hippocampus.

**J Physiology** 588: 2077-90.

Motti D, Le Duigou C, Eugene E, Chemaly N, Wittner L, Lazarevic D, Krmac H, Marstrand T, Valen E, Sanges R, Stupka E, Sandelin A, Cherubini E, Gustincich S & Miles R (2010) Gene expression analysis of the emergence of epileptiform activity after focal injection of kainic acid into mouse hippocampus.

**European J Neuroscience** 32: 1364-79.

Wittner L, Huberfeld G, Clémenceau S, Erőss L, Dezamis E, Entz L, Ulbert I, Baulac M, Freund TF, Maglóczy Zs & Miles R. (2009) The epileptic human hippocampal CA2 region generates spontaneous interictal like activity in vitro. *Brain* 132: 3032-46.

Eugene E, Delpiel C, Baulac S, Baulac M, Fritschy JM, LeGuern E, Miles R & Poncer JC (2007) Synaptic and non-synaptic effects of GABRG2 mutations linked to human epileptic syndromes.

**J Neurosci** 27: 14108-16.

## ■ Website

[www.chups.jussieu.fr](http://www.chups.jussieu.fr)

## ■ Contact

CNRS UMR 8118 Physiologie Cerebral, Université Paris Descartes, 45 Rue des Saints Pères, 75006 Paris T + 33 (0) 1 42 86 38 04  
[david.ogden@parisdescartes.fr](mailto:david.ogden@parisdescartes.fr)

# Biophysics of gliotransmitter release

Septembre 2011

Martin OHEIM / Nicole ROPERT

CNRS - INSERM (UMR 8154)

## ■ Team overview

The team benefits from a double expertise in neurobiology and optical physics. Nicole Ropert, specialist in synaptic transmission and patch-clamp electrophysiological techniques, and Martin Oheim, expert in the development of new microscopies and quantitative live-cell imaging, successfully combined their expertise to study astrocyte-astrocyte interactions.

Recent work in vitro includes the demonstration of Ca<sup>2+</sup>-dependent lysosomal release from astrocytes (Li et al, 2008) and the identification of an anion-channel mediated Ca<sup>2+</sup>-dependent pathway of glutamate release, using advanced optogenetic tools (Li et al, submitted). The ongoing work includes studying the role of SNARE proteins in the membrane trafficking in astrocytes.

In order to study gliotransmission in physiological and pathological conditions, the team is currently developing new adeno-associated viral (AAV) constructs to stimulate Ca<sup>2+</sup> elevation using light-gated channels in astrocytes in vivo. Using a combination of calcium imaging, electrophysiology, as well as two-photon microscopy, the team will study the effect of light-gated astrocytic activity on the release of neuro-active and vaso-active gliotransmitters, and their impact on the astrocyte-to-astrocyte and astrocyte-to-neuron communication.

Using TIRF and STED microscopy, the team identifies the organelles and cellular compartments as well as the molecular mechanisms governing different forms of release (vesicular and non-vesicular) by astrocytes. Specific Technologies available Primary cultures, acute brain slices, patch-clamp, electrophysiology, video microscopy, calcium imaging, optogenetic, adeno-associated viral (AAV) constructs, immunolabelling, two-photon excitation fluorescence microscopy, total internal reflection fluorescence (TIRF) microscopy, and stimulated emission depletion (STED) fluorescence microscopy.

## ■ Bibliography

- Ducros M, Van't Hoff M, Evrard A, Seebacher C, Schmidt EM, Charpak S, Oheim M. Efficient large core fiber-based detection for multi-channel two-photon fluorescence microscopy and spectral unmixing.

**J Neurosci Methods.** 2011 Jun 15;198(2):172-80.

- Li D, Héroult K, Oheim M, Ropert, N. FM dyes enter via a store-operated calcium channel and modify calcium signaling of cultured astrocytes..

**Proc Natl Acad Sci U S A.,** 2009 106(51): 21960-65.

- Evrard A, Ropert N. Early development of the thalamic inhibitory feedback loop in the primary somatosensory system of the newborn mice.

**J Neurosci,** 2009 29(31):9930-40.

- Li D, Ropert N, Koulakoff A, Giaume C, Oheim M Lysosomes are the major vesicular compartment undergoing Ca<sup>2+</sup>-regulated exocytosis from cortical astrocytes.

**J Neurosci** 2008 28:7648-7658.

- Nadrigny F, Li D, Kemnitz K, Ropert N, Koulakoff A, Rudolph S, Vitali M, Giaume C, Kirchhoff F, Oheim M Systematic colocalization errors between acridine orange and EGFP in astrocyte vesicular organelles. 2007

**Biophys J** 93:969-980

## ■ Website

[www.biomedicale.univ-paris5.fr](http://www.biomedicale.univ-paris5.fr)

## ■ Contact

INSERM U603, CNRS UMR8154, Université Paris Descartes, Lab Neurophysiology and New Microscopies, Centre des Saint Pères, 45 rue des Saints Pères, 75006 Paris

T + 33 (0) 1 42 86 42 22 (N. Ropert) / T + 33 (0) 1 42 86 42 22 (M. Oheim)

Nicole Ropert [nicole.ropert@parisdescartes.fr](mailto:nicole.ropert@parisdescartes.fr) - Martin Oheim [martin.oheim@parisdescartes.fr](mailto:martin.oheim@parisdescartes.fr)

# Laboratory of Neurophysics and Physiology

Daniel ZYTNICKI

CNRS - Université Paris Descartes (UMR 8119)

## ■ Team overview

We are investigating in mutant mice, models of degenerative motoneuron diseases such as the amyotrophic lateral sclerosis and the spinal muscular atrophy, the electrical membrane properties of spinal motoneurons.

Our goal is to elucidate which electrical properties are affected and how they dysfunction can contribute to the degeneration of motoneurons.

To this aim we developed a new preparation that allows us to make stable intracellular recordings of motoneurons in anesthetized mice just before the degeneration starts. In addition, patch clamp recordings of motoneurons in spinal slices of neonate mice allow us to study earlier alterations of the membrane properties. Theoretical researches are carried out in close combination with experimental work and allow us to understand how the changes in membrane properties modify the motoneuron excitability and produce a pathological discharge pattern.

## ■ Website

[www.neurophys.biomedicale.univ-paris5.fr](http://www.neurophys.biomedicale.univ-paris5.fr)

**FACULTE DES SCIENCES PHARMACEUTIQUES PARIS**

**DESCARTES**

*1 research group*

# Biotherapies of Degenerative and Proliferative Diseases of the Nervous System

Aubourg Patrick and Cartier Nathalie

Univ. Paris Descartes - INSERM (UMR s 745)

## ■ Team overview

The specific research areas of this UMR745 team involves the development of new therapeutic strategies that can be implemented in clinics and that concerns more specifically two genetic white matter diseases of the CNS (adrenoleukodystrophy, ALD; and metachromatic leukodystrophy, MLD), Alzheimer disease (AD) and type 1 neurofibromatosis (NF1).

1) The first approach relies upon hematopoietic stem cell (HSCs) gene therapy with lentiviral vector for CNS disease. Brain microglia are derived from myelo-monocytic precursors that exit the bone marrow, cross the blood-brain-barrier and differentiate into microglia.

2) The second approach relies upon the intracerebral delivery of therapeutic genes through viral vector, in particular adeno-associated virus vector (AAV).

3) We are exploring new targets of brain cholesterol homeostasis that is involved in the pathogenesis of Alzheimer disease (AD), particularly the production of amyloid A $\beta$  peptides.

4) Lastly, we are developing a live-cell screening platform to identify new therapeutic targets for NF1 patients who develop untreatable plexiform neurofibromas or neurofibrosarcomas.

## ■ Website

<http://app.parisdescartes.fr>

**INSTITUT DE LA VISION**

*5 research groups*

# Role of axon guidance molecules

Septembre 2011

[Alain CHEDOTAL](#)

INSERM – UPMC - FVE Team

## ■ Team overview

Nervous systems are composed of a network of synaptic connections among excitable cells. This network develops as axons extend from presynaptic neurons and grow often long distances to reach their correct postsynaptic partners. Neuronal migration and myelination are also key processes for the formation and stabilisation of neuronal connections. For years, neurobiologists have tried to uncover the mechanisms controlling axon guidance.

It was found that these are highly conserved between neurons and during evolution. It was also shown that axonal connections are plastic and can be modified during normal physiological processes and in pathological conditions. There is mounting evidence suggesting that axon guidance errors occurring during development, are responsible for neurological deficits in particular in the visual system.

One example comes from a recent work that has shown that human patients suffering of a rare syndrome named HGPPS (horizontal gaze palsy with progressive scoliosis) have an atrophied abducens nucleus (VI), are unable to move their eyes laterally and develop a strong scoliosis. All HGPPS patients bear mutations in the ROBO3 gene. One of our goal is to understand the function of Robo3 in the oculomotor system.

The discovery of neural stem cells in the adult brain was a major finding of the recent years. In many models of lesion of the nervous system, neural stem cells can be derived from their usual migration pathway to integrate the injured region. We are characterizing new molecules controlling neural stem cell development and physiology and determine their ability to promote the regenerative potential of neural on stem cells. These studies could lead to the development of new therapeutic tools to stimulate stem cell migration and differentiation in the visual system.

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**Nature Neuroscience** 11:440-449.

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# Implication of Rdcvf In Maintaining Cone Photoreceptors And Its Application For The Treatment Of Photoreceptor Degenerations

[Thierry LEVEILLARD](#)

INSERM - CNRS - UPMC

FVE Team

## ■ Team overview

The identification of one of the mechanisms leading to a vision loss in patients suffering from inherited degenerative retinal disorders reveals a novel family of signaling genes involved in the regulation of trophic interactions and response to oxidative stress. It represents a potential therapy for these currently untreatable diseases.

The Rod-derived Cone Viability Factor is encoded by the Nucleoredoxin-like-1 gene and the *Nxn1*<sup>-/-</sup> mouse experiences a progressive loss of photoreceptor cells.

This gene encodes for a trophic protein whose role is to maintain the function and consequently the viability of cone photoreceptors. Interestingly, it also encodes by differential splicing for a second protein product that has the characteristics of thioredoxin-like enzyme and protects the photoreceptors and more specifically its interacting protein partner, the TAU protein, against oxidative damage. This novel signaling pathway potentially links environmental insults to an endogenous neuroprotective response.

## ■ Website

[www.vision-research.eu](http://www.vision-research.eu)

## Neuronal circuit development

[Jean LIVET](#)  
UPMC – INSERM  
FVE Team

### ■ Team overview

The aim of our research is to study neuronal circuit development in the mouse, focusing on two stages: i) the establishment of neuronal network architecture during an early phase of development; ii) the reorganization of these networks during late postnatal development. We study those phenomena both at the molecular and cellular level.

Our approach relies on transgenic mice expressing fluorescent proteins, which allow one to visualize neurons and their processes by fluorescence microscopy. In particular, we use a novel imaging technique called Brainbow, which drives the combinatorial expression of distinct colors of fluorescent proteins in neurons. Using this multicolor labelling, multiple neurons in a circuit can be visualized simultaneously.

We initially apply this strategy to a model circuit, the auditory circuit devoted to sound localization. We use it to study the architecture and development of this circuit in combination with classic molecular approaches. In parallel and in collaboration with other teams, we are transposing the Brainbow technique to other cell types, such as the oligodendrocytes myelinating central axons. We also attempt to develop new technique to label mouse neuronal circuits.

■ **Website** [www.fondave.org](http://www.fondave.org)

## Retinal information processing: pharmacology and pathologies

[Serge PICAUD](#)  
INSERM- CNRS - CHNO des Quinze-vingts  
FVE Team

### ■ Team overview

Our lab studies the cellular and molecular mechanisms underlying retinal information processing. For instance, considering contrast enhancement at the photoreceptor terminals, which remains a matter of controversy, we have revisited the GABA hypothesis. Although this hypothesis first proposed in lower vertebrates was declined in the mammalian retina, we have demonstrated the presence of an unconventional GABAergic neurone and GABA receptor expression in cone photoreceptors.

We also investigate how physiological mechanisms can interfere into pathological processes like the irreversible visual field constriction produced in epileptic patients by a blocker of the GABA degrading enzyme. We found that this first line drug for the treatment of infantile spasms or West syndrome, cause taurine deficiency leading to retinal phototoxicity.

Recent studies have focussed on brain machine interfaces with artificial biological neuronal networks in vitro and retinal prostheses in vivo aiming at restoring vision in blind patients.

■ **Website**  
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## Translational research

[José - Alain SAHEL](#)

INSERM - CNRS - UPMC - CHNO Quinze-Vingts  
FVE Team

### ■ Team overview

Our team focuses on translational research, that is, the bidirectional transfert of models and techniques between humans and experimental models.

We thus aim at establishing and validating experimental models of humans diseases, to apply in vivo examination techniques to the experimental retina, and in return to develop clinical application of experimental therapeutics.

Our main interest concern photoreceptor degeneration and vascular diseases. We also developed techniques for in vivo examination at the rodent retina.

### ■ Website

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**CAMPUS DE JUSSIEU - UPMC - QUAI SAINT BERNARD**  
*9 research groups*

# Neuronal signaling and gene regulation

Jocelyne CABOCHE

CNRS – INSERM – UPMC

## ■ Team overview

Our team research is the analysis of MAP kinase signaling pathways in neuroadaptive processes that underlie neuronal plasticity and/or apoptosis. More specifically, we analyse the mechanisms of intracellular trafficking of these signalling pathways, from the membrane to the nucleus, as well as their role in gene regulation. Two thematic areas are developed 1) Role of ERK signalling in long term neuronal adaptation and mnemonic processes: application to toxicomania and Alzheimer's disease. 2) Neurodegeneration and Huntington's disease.

1) Long term neuronal adaptation requires gene regulation. We study more specifically the role of CREB and Elk-1 transcription factors in these processes. We have demonstrated

- The key role of these transcription factors in relation with ERK activation.
- The intracellular mechanisms that govern nuclear translocation of ERK in relation with receptor endocytosis, and cytoskeleton.

Role of ERK signalling in epigenetic responses.

2) Huntington's disease (HD) is a neurodegenerative disease due to expansion of a CAG repeat in the Huntingtin protein. We study intracellular mechanisms that are implicated in neurodegeneration of striatal neurons in HD, more specifically

- The role of cJun-Nterminal Kinase (JNK) et Mitogen Stress Activated Kinase (MSK) in HD.
- The role of DA in striatal vulnerability in HD.

## ■ Website

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# Normal and Pathological Glutamatergic Systems

Septembre 2011

Salah EL MESTIKAWY

INSERM – UPMC – CNRS

## ■ Team overview

Glutamate is the major neurotransmitter of CNS. Before its exocytotic release in the synaptic cleft, glutamate is loaded into synaptic vesicles by three transporters named VGLUT1-3. In the rodent brain, VGLUT1-3 are distributed in three complementary glutamatergic systems showing little overlap. VGLUT1 is essentially cortical, VGLUT2 subcortical and VGLUT3 is present in neurons using other transmitters than glutamate (cholinergic interneurons from the striatum, GABAergic interneurons from the hippocampus and cortex and serotonergic neurons). The three VGLUTs are the first available specific markers of glutamatergic neurons and terminals. These proton-dependent carriers share a high degree of structural and functional homology.

The strength of synaptic transmission is controlled both at the pre- and post-synaptic levels. Vesicular glutamate transporters play an essential role in glutamatergic transmission. Indeed, recent studies have documented that the concentration of vesicular transporters directly impacts on the strength of synaptic transmission.

Our main goal aims at characterizing functionally the three VGLUTs in normal or pathological conditions.

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## Neurophysiology and behaviour

[Philippe FAURE](#)

CNRS – UPMC  
ATIP Team

### ■ Team overview

Dopamine (DA) projections from the midbrain (including ventral tegmental area - VTA and substantia nigra - SN) to striatum and frontal cortex play a major role in behavioral actions controlled by reward and in the formation of habits. The dopaminergic system is also involved in drug addiction.

We are interested in the nicotinic modulation of the dopaminergic system, with ii) the identification of relevant nicotinic acetylcholine receptor (nAChR) in this modulation ii) their role in the organization of behavior and iii) on cellular and behavioural event that occurred during and after repeated exposure to nicotine.

### ■ Website

<http://npa.upmc.fr>

## Psychiatry and neurobiology

[Bruno GIROS](#)

INSERM -UPMC

### ■ Team overview

Our team carries out preclinical studies to better understand psychiatric diseases and to discover innovating therapies. We develop animal models, characterize and study synaptic targets which play a role in neurotransmission (mostly neurotransmitters transporters).

This work is also carried out in humans including studies of genetics of autism and mental retardation, and anatomical approaches.

### ■ Website

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# Cortical Network and Neurovascular Coupling

Septembre 2011

Bertrand LAMBOLEZ / Bruno CAULI

CNRS – UPMC

## ■ Team overview

The team "Cortical network and Neurovascular Coupling" studies neuronal circuits and their relationships with the glio-vascular network in the cerebral cortex. Our previous work has advanced our knowledge of neocortical neuronal types, of their sensitivity to afferent signals, of their places in the functional architecture of intracortical peptidergic transmission, and of their differential roles in neurovascular coupling. Our achievements in real-time imaging of genetically-encoded probes and the development of optogenetics provide us with means of studying the physiology of the cortical neuro-glio-vascular network at the cellular and multicellular levels.

Our current projects focus on **-1-** the cellular mechanisms responsible for the modulation of neuronal ensemble dynamics by acetylcholine, monoamines and neuropeptides **-2-** the respective contribution of neurons and astrocytes to neurovascular coupling, **-3-** feedback loops that determine the interdependence of neuronal activity and energy supply. Most of these experiments are performed on neocortical slices using a combination of patch-clamp, single cell RT-PCR (scPCR), imaging and optogenetics.

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## Development and aging of the nervous system

Jean MARIANI

CNRS - UPMC

### ■ Team overview

In our team a first theme of research is about the mechanisms involved in several late steps of the nervous system development (synaptogenesis, dendritic differentiation and neuronal death) and especially the regressive ones such as synapse elimination and neuronal death) that are present during development as well as in various neurodegenerative diseases. To analyse the network of genes involved we use genetically modified mice, but also postlesional models that are analysed by a pluridisciplinary approach with cellular, molecular, electrophysiological and behavioral techniques. An important issue of these studies is to determine how these genic regulations could be also involved in the normal or pathological aging.

A second theme indeed of our studies is about the aging of the nervous system: we especially study some of the elementary mechanisms involved in most of the neurodegenerative diseases : excitotoxicity, oxydative stress, inflammation.. that altogether can lead to several types of neuronal death (apoptosis , autophagy ...).

### ■ Website

<http://npa.snv.jussieu.fr/eq>

## Navigation, memory and aging

Laure RONDI-REIG

CNRS – UPMC

### ■ Team overview

We aim to understand the neural bases of navigation and spatial memory and the possible causes of their progressive impairment during aging. Our research is divided in two complementary research topics

1) functional interaction between the different memory systems during information encoding and strategies selection during tasks of spatial navigation

2) interaction impairment between these memory systems and possible mechanisms of compensation during normal and pathological aging.

We are particularly interested in functional loops involving interaction or competition between hippocampal and striatal memory systems or those involving the cerebellum (cerebello-thalamo-cortical loop). We do also study possible interaction between the cerebellar system involved in the motor control of action and the hippocampal system involved in mental representation of the environment during a task of spatial memory.

### ■ Website

<http://npa.upmc.fr/eq/equipe>

# Brain patterning and morphogenesis in vertebrates

Septembre 2011

Sylvie SCHNEIDER-MAUNOURY

CNRS - FVE Team

## ■ Team overview

Our group is interested in the molecular and cellular mechanisms underlying brain morphogenesis in vertebrates, and in understanding how these mechanisms are perturbed in human diseases.

To investigate these processes, we take advantage of two complementary model organisms, the mouse and the zebrafish. We have three main research axes.

- 1) We study the gene regulatory hierarchies involved in the early subdivision of the neural plate, the future central nervous system, during gastrulation.
- 2) We investigate the function of primary cilia in brain morphogenesis. Specifically, we study the Rpgrip1L gene, which codes for a protein localized at the ciliary transition zone and whose mutations have been identified in two human ciliopathies, Joubert and Meckel syndromes.
- 3) We have demonstrated the presence of axonal transport of mRNAs in zebrafish embryos and we currently study its mechanisms and functions.

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# Development and plasticity of neural networks

Alain TREMBLEAU

INSERM – CNRS – UPMC

## ■ Team overview

Our group studies the local translation of mRNA and its role in the development and plasticity of neural networks. This work is performed on the adult mouse olfactory system, a model characterized by a continuous neurogenesis making it easy to manipulate. Our two main objectives are :

1) to analyse the local translation of mRNAs in axons and its role in controlling the olfactory map formation ;

2) to characterize the local translation of dendritic mRNAs and its role in dendritogenesis, spinogenesis and synaptogenesis.

Our studies are mainly performed in vivo and ex vivo, using genetically manipulated mice as well as viral vectors. Our project addresses fundamental issues and molecular mechanisms involved in neurodevelopmental pathologies like Fragile X mental retardation. Key works: adult neurogenesis, local translation, olfactory system, axon guidance, dendritogenesis, synaptogenesis.

## ■ Website

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**CRICM & ICM CHU PITIE SALPETRIERE**

*19 research groups*

# Cellular Physiology of Cortical Microcircuits

Septembre 2011

[Alberto BACCI](#)

AP-HP - CNRS - UPMC - INSERM - Institut du Cerveau et de la Moelle épinière -  
Univ. Pierre et Marie Curie - Univ. Paris 6

## ■ Team overview

In the cerebral cortex the constant computation of incoming sensory information is dynamically integrated to provide a coherent representation of the world and generate highly sophisticated cognitive functions. Cortical circuits are made of different neuron types connecting one another through a staggering number of synaptic connections that are responsible for the propagation of information between neurons. The result is the generation of complex functional networks, whose specific activities often produce a wide range of synchronous rhythms, believed to provide the computational substrate for different aspects of cognition. In this context, a tight balance between excitation and inhibition is fundamental for correct brain functioning, as serious neurological and psychiatric diseases can develop when this equilibrium is altered.

Among all cell types, inhibitory cortical neurons (also known as interneurons, which use GABA as neurotransmitter) are highly heterogeneous. In particular, we are focused on (i) how different types of neurons of the cerebral cortex connect one another; (ii) how specific cell types produce different forms of synaptic transmission and plasticity; and (iii) how specific synaptic properties contribute generating various forms of network oscillations. Indeed, GABAergic neurotransmission is fundamental for integrating and filtering incoming information as well as for dictating postsynaptic neuronal spike timing, therefore providing a tight temporal code used by each neuron, or ensemble of neurons, to perform sophisticated computational operations. Altogether, results of these experiments will lead to a better understanding of GABAergic interneuron regulation of neocortical excitability, relevant to both normal and pathological cortical function.

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## **Molecular and cellular approaches of myelin repair**

### [Anne BARON VAN-EVERCOOREN / Brahim NAIT OUMESMAR](#)

INSERM – UPMC

#### ■ **Team overview**

The team is based on two PIs, Anne Baron-Van Evercooren and Brahim Nait Oumesmar, who share a common interest in understanding how remyelination proceeds and how it can be promoted with a strong emphasis on remyelinating cells and animal models of demyelination. They have, however, their independent lines of investigations. Brahim Nait Oumesmar focuses on the transcriptional regulation of CNS myelination and remyelination and Anne Baron-Van Evercooren on cellular mechanisms of CNS myelination with a special focus on stem cells and their role in the repair process.

Our goal is dual: unravel some of the cellular mechanisms involved in the process of remyelination and develop strategies promoting myelin repair.

#### ■ **Website**

[www.cricm.upmc.fr](http://www.cricm.upmc.fr)

## **Molecular basis, physiopathology and treatment of neurodegenerative diseases**

[Alexis BRICE](#)

CNRS - INSERM - UPMC

#### ■ **Team overview**

The research is focused on molecular bases and physiopathology of different neurodegenerative disorders. The methods used are mapping and identification of susceptibility factors and genes responsible for these disorders (Parkinson's and Alzheimer's diseases, frontotemporal dementias, cerebellar ataxias and spastic paraplegias, dystonias). The Genetic progresses allow to establish the relative frequency of each gene, their mutational spectrum, phenotype-genotype correlations and to identify biomarkers thank to the biological material, including neuropathology and precise phenotypical data, collected throughout national and international networks.

Physiopathological mechanisms are approached by characterization of cell and animal models (mice, drosophila and zebrafish) for different diseases (Parkinson's disease, cerebellar ataxias and spastic paraplegias).

These models are used for elucidating physiopathological mechanisms, identifying modifier genes and for testing new therapeutical approaches.

#### ■ **Website**

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## Experimental neuro-oncology

Jean-Yves DELATTRE

INSERM - UPMC

### ■ Team overview

- 1) Clinical-molecular classification of glial tumors
- 2) Identification of genes involved in glioma oncogenesis
- 3) Study of the role of epigenetic alterations in the chemoresistance of gliomas

### ■ Website

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## Cognition, neuroimaging and brain disorders

Bruno DUBOIS

INSERM – UPMC

### ■ Team overview

The major aim of our team is to better understand the neural bases of the main cognitive and behavioural functions in humans, such as spatial attention, executive functions, working memory and the relationships between motivational, emotional and cognitive processes, and their dysfunctions in patients with either focal (vascular or surgical) or degenerative (Alzheimer's disease, fronto-temporal dementia, Parkinson's disease) brain lesions. Our approach is multidisciplinary, based on :

- 1) functional MRI in normal subjects and in patients with brain lesions;
- 2) clinico-neuroimaging correlations (AnaCOM method that we have developed ; tracking of white-matter fibers with diffusion MRI - overTRACK method that we have developed);
- 3) a close collaboration with the department of Neurosurgery (for the study of functions assessed during surgery in awaked patients) and with the Stroke Center (for the data base of the Center of Cognitive Anatomy – CAC).

### ■ Website

[www.cricm.upmc.fr](http://www.cricm.upmc.fr)

# Alzheimer's and Prion diseases

Charles DUYCKAERTS / Stéphane HAIK

INSERM – UPMC – CNRS

## ■ Team overview

We have interest in dementia characterized by the accumulation of amyloid proteins and neurodegeneration.

Modulation of A-beta secretion by cholesterol may have therapeutic implications. We are studying the lipid content of senile plaques using mass spectrometry. We investigate changes in A-beta secretion, APP endocytosis/trafficking and endosome morphology following cholesterol changes. We use Down syndrome models for the search of early markers of Alzheimer disease.

We have identified early markers of neuronal dysfunction in transgenic animals. We inject oligomers of A-beta in mouse brains to study early events of neurodegeneration.

Prions exist as multiple strains that differentiate by the patterns of neurodegeneration they produce. Molecular basis of human strain diversity and properties remains enigmatic and, beyond the prion field, may be relevant to other proteinopathies. They are studied by taking advantage of our expertise in human prion disorders and models recently set up in the team including primary neurons and genetic models in *C.Elegans*. Search for anti-prion molecules and studies on the relationship between PrP, tau and A-beta are in progress.

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# Genetics of multiple sclerosis and muscle excitability disorders

Septembre 2011

Bertrand FONTAINE

INSERM – UPMC – CNRS

## ■ Team overview

Our team has the particularity to be multithematic, being interested in 3 main research topics. Our first aim (PI: S NICOLE and D HANTAI) is to study human disorders with abnormal membrane excitability including muscle channelopathies, congenital myasthenic syndromes and related congenital disorders (peripheral nerve hyperexcitability, thermosensitive neuropathy, alternating hemiplegia of childhood). Part of the research is translational and aims at providing clinical, neurophysiological and molecular characterisations to patients in order to facilitate diagnosis. The other part is more fundamental and is aimed to investigate pathophysiological mechanisms using in vitro and in vivo expression models of the diseases.

The second project (PI: C Delarasse) deciphers the role of factors that might affect the course of Alzheimer's disease (AD) such as the neuroinflammatory processes and the function of the non-amyloidogenic pathway. Our research focuses on the role of the purinergic receptor P2X7R which is upregulated around lesions in AD patients and involved in these pathways.

Our last works lie on the genetics of multiple sclerosis. Our current research is based on the recent identification of 52 genetics factors of susceptibility of multiple sclerosis through a genome wide association study performed by an international consortium (IMSGC). One of our studies concerns the role of genetic interactions between genes coding for adhesion molecules in the development of the disease. The others projects aim to determine the fine localization and the nature of known susceptibility variants by "exom" studies and using evaluation of the genetic burden of patients or group of patients identified by a specific course of the disease.

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# Experimental therapeutics of neurodegeneration

Septembre 2011

Etienne HIRSCH

INSERM – UPMC

## ■ Team overview

Our project is driven by two major complementary objectives:

- 1) to characterize the mechanisms involved in the progression of nerve cell death in neurodegenerative disorders and especially Parkinson's disease (PD);
- 2) to identify functional alterations underlying key clinical symptoms in these disorders. To that aim, we concentrate on the populations of dopaminergic (DA) and cholinergic neurons that are preferentially affected in PD. Our hope is to identify therapeutic targets to slow the progression of neuronal loss and to alleviate symptoms originating from non-DA lesions which represent two major unmet needs for patients suffering from PD. The main targets analyzed are oxidative stress, the role of calcium homeostasis, electrical activity and neuroinflammatory processes.

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# Treatment of Amyotrophic Lateral Sclerosis: From Genetics to Zebrafish -

Septembre 2011

[Edor KABASHI](#)

AP-HP - CNRS - UPMC - INSERM - Institut du Cerveau et de la Moelle épinière - Univ. Pierre et Marie Curie - Univ. Paris 6

## ■ Team overview

Our research team recently appointed at the Brain and Spinal Cord Institute will serve to close the gap between clinical and basic research in neuroscience. We will functionally characterize genetic variants for neurodegenerative diseases and develop models using these mutations. Further, we will use these models to identify and validate compounds with neuroprotective properties. Thus, our research will serve as a ring between clinical and basic research and we hope it will advance both these fields of neuroscience.

Revolutionary advances in human genetic studies allow rapid and efficient exome sequencing for patients affected by a variety of health-related disorders. However, a large number of data is generated that is difficult to analyze. Our team has used extensively zebrafish as a vertebrate model par excellence to characterize genes involved in ALS and other motor neuron diseases. Further, we will use the technological advances in zebrafish genetics, as we plan to generate transgenic lines for common genes involved in these disorders. These models will serve to better understand mechanisms of disease, identify partners of these mutant genes as well as to perform chemical screens for compounds that can rescue disease-related phenotype.

To perform these chemical screens, our group is developing tools to perform automated assays of zebrafish placed in multiwell plates where zebrafish larva are treated with specific chemical compounds. Video recording and analysis of the motor behavior is performed to identify compounds that significantly modulate swimming activity. These assays permit to identify compounds that could reverse neurodegenerative processes thus opening exciting avenues for clinical research. Compounds that are identified in these screens and validated in other models could propose efficient therapies for patients affected by these increasingly common neurological diseases.

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# Genetics of diseases of the peripheral nervous system and epilepsy

Éric LE GUERN

INSERM– UPMC

## ■ Team overview

Our group is interested in the genetics and the physiopathology of epilepsy, peripheral neuropathies and motor neuropathies.

These pathologies can affect the central as well as the peripheral nervous system and all affect the neuronal excitability and conduction. At the clinical level, electrophysiological studies (electroencephalography or electromyography) are essential to classify these pathologies.

We have therefore established close collaborations with neurology but also neurophysiology departments. Our studies focus on the monogenetic forms of these diseases, which constitute useful models for discovering key proteins and pathways that play a role in the development, function or maintenance of the affected neurones and are involved in the physiopathology of the disease. Common pathways regulating ion homeostasis and cell excitability, involving ion channel and neurotransmitter receptors, might be implicated in both epilepsy and motor neuronopathies (ie, amyotrophy lateral sclerosis (ALS))

We will use the same strategy in all of our projects:

- 1- Identification and phenotyping of families;
- 2- Localisation and identification of genes using standard genetical approaches (exclusion of known loci and genes, genome wide screens, candidate gene analysis);
- 3- Analysis of mutational spectrum and phenotype-genotype correlations;
- 4- Studies of the functional consequences of mutations at cellular, tissue and animal levels.

Our group has extensive experience in linkage analysis, including the use of new genomic approaches such as SNPs microarrays. During the last 3 years, our group has developed molecular and cellular tools to study the functional consequences of the mutations (cell biology, proteomic, RNA interference ...).

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# Mechanisms of myelination and remyelination in the central nervous system

Catherine LUBETZKI

INSERM – UPMC

## ■ Team overview

Our project is focused on central nervous system myelination and remyelination, with the following questions: what are the cellular and molecular actors of myelination and are they similar in the remyelination process? Why do some multiple sclerosis lesions remyelinate whereas others remain chronically demyelinated? Is it possible to image myelination and repair?

Combining experimental approaches, in vitro and in vivo, we develop 3 complementary projects :

- 1) Role of neuron-glia interactions on myelination and remyelination, notably in nodal and perinodal domains formation
- 2) Influence of guidance molecules, such as semaphorins, on oligodendrocyte progenitors recruitment towards the demyelinated lesion, hence on myelin repair capacity.
- 3) development of a PET-scan tool (collaboration with CEA) to image demyelination and remyelination, in experimental models then in multiple sclerosis patients.

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# Role of microglia in development and neurodegenerative diseases

Septembre 2011

[Michel MALLAT](#)

INSERM - UPMC - CNRS

## ■ Team overview

Our research focuses on the role of microglia and mechanisms that determine microglial recruitment during normal development or in neurodegenerative diseases. We have found that microglia express two distinct NADPH oxidases, Nox1 and Nox2, that promote microglial capacities to produce cytokines and neurotoxic reactive oxygen species, which trigger neuronal damage in neuroinflammatory lesions. Our current projects, investigate the role of microglial Nox during normal development and in neurodegenerative diseases such as Alzheimer's disease (AD) focusing on neurotoxic signaling generated in animal models of AD.

We have also shown that in mouse models of Amyotrophic Lateral Sclerosis (ALS), the most common motor neuron disease in the adult, the cells in the environment of motor neurons were participating to the disease, especially microglial cells/ macrophages. In addition, microglial cells/ macrophages were important in the symptomatic phase of the disease, which is the one to target in a disease of mainly sporadic etiology like ALS. Our current work focuses on the different pathways implicated in motor neuron- microglia/ macrophages interactions in order to uncover alternative ways to slow down the progression of motor neuron degeneration and ALS disease in mouse models

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# Biotechnology and biotherapy

Jacques MALLET

CNRS - UPMC

## ■ Team overview

The main objectives of the team concern (i) the identification of genes implicated in the pre-disposition to Bipolar Disorder (BD) and schizophrenia (SZ), (ii) their functional validation as therapeutic targets, and (iii) the development of animal models for innovative approaches to the treatment of these diseases. These studies integrate genetic analysis in isolated populations (Sardinia, Palestine, South Africa...) following standardized criteria, high output genome screening and innovative approaches in functional genomics and systems biology in order to identify the vulnerability genes and to develop new animal models for psychiatric diseases.

For the animal models the team takes advantage of modern gene transfer technology (e.g. integrative and non-integrative lentiviral vectors). In particular, vectors containing non-immunogenic regulatory systems are developed which allow regulation of RNA interference and transgene expression by small inducer molecules. These vectors will be prerequisite for the generation of new animal models for the treatment of mental disorders.

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# Cortex & epilepsy

Septembre 2011

Richard MILES

INSERM – UPMC

## ■ Team overview

We study the physiology and anatomy of the hippocampus and how it contributes to normal function and pathological malfunction of this brain region. One special interest concerns mechanisms for the generation of epileptiform activities by tissue from the temporal lobe of patients with pharmacoresistant epilepsies.

Synchronous brain activities are associated with many phenomena from rhythmic motor actions to information coding associated with specific cognitive behaviours. Pathologically synchronous firing generated in different brain areas is the hallmark of many epileptic syndromes. Understanding how synchronous neuronal activity is generated requires knowledge of the control of neuronal excitability, of synaptic communication between neurons and of patterns of neuronal connectivity. We try to link data and concepts from the cellular and synaptic levels with measurements of population activities.

We have defined the role of distinct Ca channel subtypes (Scheuber et al, 2004) and the TI-VAMP vesicular protein (Scheuber et al, 2006) in pre-synaptic function and studied how EPSP-spike coupling controls the precision of action potential generation in CA1 pyramidal cells. We have examined the emergence of synchrony induced by disinhibition (Cohen et al, 2006), shown that a threshold firing frequency must be exceeded to initiate a synchronous event (Prida et al, 2006) and studied the pacemaker role of the CA3a region in this activity (Wittner & Miles, 2007). A defect in chloride homeostasis, which may underly the generation of an interictal-like activity, has been identified in the subiculum of tissue from patients with temporal lobe epilepsies (Cohen et al, 2002). The synaptic and trafficking defects associated with mutations in the gamma two subunit of the GABAA receptor associated with the GEFS+ syndrome has been defined (Eugene et al submitted). We are improving imaging techniques for pre- and post-operative patient evaluation notably with the diffusion tensor technique (Thivard et al, 2005).

Our projects include: (1) functional effects of lamination defects associated with epileptic syndromes; (2) involvement of newly generated or de-differentiated neurones in the construction of an epileptic brain; (3) precision on the basis of EEG / field potential signals used to define neuronal synchrony; (4) mechanisms for the transition to seizure in tissue from patients with temporal lobe epilepsies (5) studies on the role of TTX-resistant Na-channels and the Na / K - ATPase in the subiculum; and (6) definition of pathways for seizure spread from the subiculum to the entorhinal cortex in patients.

Cortex, Hippocampus, Epilepsie, in vitro, Physiologie, Anatomie, Pathologie. Tissue epileptique humain. Dcx, KA. Presubiculum, EEG, Synapse, Circuit.

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# Motivation, Brain and Behavior

[Mathias PESSIGLIONE](#)

UPMC - CNRS - INSERM

## ■ Team overview

My research aims at understanding the determinants of behavior (why we do what we do), in both normal and pathological conditions. To this aim I combine concepts and methods from different scientific fields: neuroscience, psychology, economics and computational modeling. Fundamental interest is elucidating the brain mechanisms that translate beliefs and expectations into particular behaviors. Clinical application is developing therapeutics for a variety of psychiatric and neurological diseases in which motivation is deficient, excessive or deviant.

## ■ Website

<http://sites.google.com/site/motivationbrainbehavior>

# Oligodendrocyte development and neurovascular interactions

Septembre 2011

Jean-Léon THOMAS / Bernard ZALC

INSERM -UPMC

## ■ Team overview

One aspect of our research is the study of oligodendroglial cell development in the embryonic brain, especially the specification and migration of oligodendrocyte precursors (OPs). In addition, since the development of the central nervous system depends on constant interactions between neural cells and the cerebral vascular network, our studies extend to the neurovascular interactions occurring in the neurogenic niches and the white matter of the normal brain, as well as in the context of neural pathologies such as Multiple Sclerosis (MS) and gliomas.

The development of oligodendroglial cells in the embryonic brain has been extensively studied by our team over the last ten years. Specification and migration of oligodendrocyte precursors (OPs) have been investigated: i) the localization of production sites for OPs in the mouse and chick; ii) the diversity of populations of OPs in the embryonic brain; iii) the migratory pathways of OPs in the embryonic brain and their monofocal ventral origin in the embryonic forebrain; iv) the identification of molecules produced by the environment of OPs which control their migration, such as the axonal growth factors netrin-1, semaphorins 3A, 3F and the ephrinBs.

They are also developing new research on the neurovascular interactions, based on the finding that the lymphatic endothelial cell growth factor VEGF-C is also expressed by neural cells and provides a trophic support to neural progenitor cells during brain development. More recently, we have reported the direct action of VEGFR-3, the specific receptor of VEGF-C, in murine adult neural stem cells.

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# Movement disorders and basal ganglia: physiopathology and experimental therapeutics

Septembre 2011

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# Optogenetic dissection of spinal circuits

Septembre 2011

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## ■ Team overview

*Affiliated in September 2010 to the ENP network.*

Neurobiologists have been describing the anatomy of different types of cells in the spinal cord for decades. They have proposed that spinal neurons constitute a central pattern generator underlying the rhythmic bursting activity needed for locomotion. How specific cell types are recruited to generate specific locomotor pattern (with different speed, direction and gating), is still unknown. By developing light gated channels to remotely control (activate or inhibit) neurons in genetically identified neurons in an awake behaving animals (also called “optogenetics”), we can probe the role of specific neurons in underlying locomotor behaviors. Our team has developed optogenetic tools in vivo and has applied these tools to tackle a long-standing question: the function of cerebrospinal fluid contacting neurons (CSFNs) in the spinal cord of Vertebrates. We demonstrated that CSFNs were able to trigger specifically slow locomotion at early stage of development. Now our team aims at reconstructing the circuit of slow swimming involved in the CSFNs mediated response, and more generally dissect the underlying circuits dynamically forming the central pattern generator within the spinal circuitry, recruited to form complex patterns of locomotion.

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# Behavior, Emotion and Basal Ganglia

[Jérôme YELNIK / Luc MALLET](#)

UPMC - CNRS - INSERM

## ■ Team overview

The scientific core of our research program is to study the exact nature of the processing that the basal ganglia (BG) apply to cortical information with three perspectives:

- 1) improve our fundamental knowledge of the cerebral mechanisms of information processing;
- 2) better understand the pathophysiology of human diseases which are related to BG dysfunction; and
- 3) develop innovative treatments for neuropsychiatric refractory disorders notably by means of the deep brain stimulation (DBS) functional neurosurgery.

This research is based on a confrontation between phenomenological and psychopathological studies of disturbances involving the BG and the electrophysiological, neuroimaging and anatomical studies of these structures.

This research program is carried out in patients with Parkinson Disease, Tourette Syndrome, Obsessive Compulsive Disorder, Depression, Cocaine Dependence. Changes in the neuronal activity of BG and related cortical areas provoked by emotional or cognitive processing are examined by using dedicated experiments by means of electrophysiology and neuroimaging techniques. Precise anatomical localization of both electrophysiological and imaging data are performed using a validated 3D deformable atlas, allowing to model the circuits implicated and their interactions in these processes.

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**Center for Neuroimaging Research (CENIR):  
Magnetic resonance imaging platform for clinical neuroscience  
research in human**

[Stéphane LEHERICY](#)

UPMC

■ **Team overview**

Structural and functional brain mapping in the normal and pathological brain:

- Functional and anatomical organization of the normal human brain
- Study of the neuronal basis of cognition, behaviour and aging
- Pathophysiology and diagnosis of neurological and psychiatric diseases
- Functional and anatomical imaging of neurodegenerative diseases, Alzheimer's disease
- Diffusion tensor imaging in the normal and pathological brain.

■ **Website**

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**INSTITUT MONDOR DE RECHERCHE BIOMEDICALE**  
*2 research groups*

## Interventional neuropsychology

[Anne-Catherine BACHOUD-LEVI](#)

Inserm – ENS – Université Paris-Est Créteil – APHP

### ■ Team overview

Our team is built at the interface between basic research in cognition and clinical research in brain therapies. We address two questions:

- 1) the bases of specifically human cognitive functions (language and social cognition), and the role of the striatum in such functions;
- 2) the relation between brain reconstruction and functional reconstruction (rehabilitation and grafting).

Because Huntington's Disease is predominantly characterized by a neural degeneration targeting the striatum, we used it as a model both for striatal lesion and for cell therapy and neuroprotection. We combine large scale studies in cell therapy and basic research in cognition. This specificity enables us for the first time to use intracerebral grafting as a model of plasticity in human beings and to integrate therapeutics in basic research in cognition.

In addition, we develop cognitive programs in language and social cognition within the Département d'Etudes Cognitives (ENS) and transfer them to brain pathology.

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# Psychiatry and genetics

[Marion LEBOYER](#)

INSERM - Université Paris-Est Créteil

## ■ Team overview

Our research efforts have contributed to a better identification of relevant phenotype for genetic studies, particularly on the field of bipolar disorder, schizophrenia, suicide, autism, OCD and pharmaco-genetic studies.

Being principal investigator of national and international groups, she has been able to produce prominent findings such as identification in autism of the first mutations in neuroligins (NLGN-3 and NLGN-4).

On top of classical linkage and association studies, her main research contributions have been to more precisely identify relevant phenotypes for psychiatric genetic using two strategies :

1) "candidate symptom" identification among affected subjects allowing the identification of homogenous and more genetic subforms such as early onset bipolar disorder and

2) clinical, biochemical, cognitive and electrophysiological "endophenotypes" among non-affected relatives.

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**INSTITUT JACQUES MONOD**

*2 research groups*

## Membrane traffic in neuronal and epithelial morphogenesis

[Thierry GALLI](#)

INSERM - CNRS - Université Paris Diderot  
AVENIR Team

### ■ Team overview

The aim of our team is to understand the molecular and cellular mechanisms of membrane trafficking and cell-cell adhesion in neuronal and epithelial morphogenesis. We are particularly focused on tetanus neurotoxin-sensitive and insensitive exocytosis in axonal outgrowth and epithelial cell migration. We study the function of the vesicular SNARE proteins cellubrevin, synaptobrevin, and TI-VAMP, and two cell-cell adhesion molecules: vezatin and L1-CAM.

### ■ Website

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## Genetics and development of the Cerebral Cortex

[Alessandra PIERANI](#)

Univ. Paris Diderot - CNRS  
FVE Team

### ■ Team overview

The neocortex represents the brain structure that has been subjected to a major expansion in its relative size and complexity during mammalian evolution. Cognitive functions depend on the accurate construction of complex neural circuits which begin early during development through a precise orchestration between proliferation of progenitors, spatio-temporal generation of distinct cell types and control of their migration and settling position. Growing evidence supports the notion that the aetiology of numerous neurological and psychiatric illnesses has to be found in alterations of developmental processes.

The aim of our team is to understand the molecular mechanisms which coordinate growth and spatial patterning in the developing cerebral cortex. In particular, we study how Dbx1+ progenitors at the borders of the pallium have contributed to neocortical evolution. Using mouse genetics we have shown that these progenitors give rise to highly migratory cells which will distribute over long distances from their generation site and which will be present only for a transient period during development. We demonstrated that the presence of Dbx1-derived transient neurons is crucial for cortical development and for the establishment of functional cortical networks. Dbx1-derived Cajal-Retzius subtypes in layer I and transient neurons of the cortical plate are involved in tangential (early regionalization and formation of cortical areas) and radial growth of the neocortex, respectively, by controlling cortical progenitors divisions in a non-cell-autonomous manner, and therefore acting as “mobile signaling units”.

Our work points towards a novel general strategy for long-range patterning in large structures, in addition to passive diffusion of morphogens, via migration of signaling cells. By coupling studies on the role of transient neurons in mice and primates we aim at bridging developmental neuroscience with evolution and pathology in humans.

### ■ Website

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**INSTITUT DU FER A MOULIN**

*7 research groups*

# Cytoskeleton and pathology of neuronal migration

Fiona FRANCIS

INSERM – UPMC

AVENIR Team

## ■ Team overview

Childhood epilepsies (often associated with mental retardation) are caused by perturbations of cerebral development, in particular neuronal migration abnormalities giving rise to an abnormal position and function of cells, termed 'heterotopic'.

We have previously shown that mutations in the genes coding for cytoskeletal associated proteins are major causes of migration abnormalities. We aim to better characterize genetic, molecular and pathophysiological mechanisms associated with heterotopic disorders using mouse models.

Our first objective is to clone a gene responsible for band heterotopia in the mouse, which mimics the phenotype observed in human patients. Our second objective will be to understand the molecular mechanisms underlying migration abnormalities due to Dcx and Tuba1a deficiency, two genes previously shown to be mutated in cortical malformations associated with mental retardation and drug-resistant epilepsy. Biochemical and cell biological studies will allow us to better understand how mutation of these cytoskeletal associated proteins perturbs migration.

Our third objective will be to evaluate the functional consequences of abnormal neuron position with respect to epilepsy susceptibility and cognitive deficits. The abnormal connectivity and activity of heterotopic neurons will be analyzed in different heterotopia animal models.

We believe that the abnormal integration of heterotopic cells in neuronal networks, combined with interneuron abnormalities, are responsible for the epilepsy and cognitive deficits observed in these disorders.

These combined studies will allow us to characterize the genetic and cellular perturbations giving rise to cortical neuron migration abnormalities. Our results are likely to provide new insights into the study of certain epilepsies and cognitive deficits of neurodevelopmental origin.

## ■ Website

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## Developmental role of neurotransmitters

[Patricia GASPAR](#)

INSERM – UPMC

### ■ Team overview

My laboratory has focused on the role monoamines on sensory map development.

Major discoveries of the team have concerned the identification of the role of serotonin on the construction of sensory maps, and the characterization of the molecules involved in these effects.

This lead to the identification of transient cellular targets for the effects of serotonin agonists, in particular SSRI antidepressants in the developing brain, whose activation can have lasting consequences on brain wiring and behaviour. More recently the team discovered an interesting interaction between neuronal activity and axon guidance mechanisms that appears mediated by calcium sensitive adenylate cyclases.

Our current projects involve :

- 1) The identification of molecular and cellular targets downstream of neural activity for sensory map formation ;
- 2) the study of the development of the vertebrate serotonin system focusing on the heterogeneity of serotonin cell groups and developmental mechanisms that underlie anxiety phenotypes.

Our lab is currently funded by ANR, European community, INSERM, University Pierre et Marie Curie.

### ■ Website

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# Neurotransmission and signaling

## Jean - Antoine GIRAULT / Denis HERVE

INSERM - UPMC

### ■ Team overview

Our goal is to identify signaling mechanisms that underlie brain plasticity leading to long-lasting behavioral alterations.

Our major model of study is the striatum that plays a crucial role in the control of movements, motivated behaviors, formation of habits, and procedural memory. The striatum is involved in several neurological and psychiatric diseases including Parkinson disease and addiction.

Dopamine controls the acute function of striatal neurons and their long-lasting plasticity, thus contributing to reinforcement learning. Drugs of abuse divert these processes by directly increasing dopamine transmission. Similar mechanisms are involved in side effects of L-DOPA in Parkinsonian patients.

We study signaling pathways controlled by dopamine, glutamate, endocannabinoids and other neurotransmitters, which involve G proteins, protein kinases, phosphatases and gene expression. We attempt to identify the role of these pathways in simple behaviors and to identify assemblies of neurons in which they are activated.

We also investigate other signaling pathways including non-receptor tyrosine kinases of the FAK family. Finally, the group of Laurence Goutebroze studies the molecular bases of interactions between axons and myelinating glial cells.

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# Molecular and cellular mechanisms of cortical development

[Mathias GROSZER](#)

INSERM - UPMC

AVENIR Team - Chair of Excellence

## ■ Team overview

Neuropsychiatric disorders such as autism and schizophrenia spectrum disorders are frequently the result of abnormal brain development.

The current nosologies of these disorders (DSM-IV TR and V, ICD-10) are based on clinical observations due to their complex genetic underpinnings and the lack of biological markers. The problems in psychiatric genetics appear to become approachable with the advent of new whole genome technologies, which promise to facilitate the identification of relevant common and rare genetic variants.

However the ultimate goal, classification and treatment of mental disorders rooted in pathophysiological understanding, requires the identification of molecular pathways and neural circuits involved. Withinin this context

our research exploits rare monogenetic forms of human neurodevelopmental disorders which closely relate to endophenotypes of complex neuropsychiatric diseases.

A mainstay of our research is the generation and analysis of animal models with the aim to identify common molecular pathways and neuronal circuits relevant for the genetic stratification of individuals with neuropsychiatric disorders potentially crossing classical clinical boundaries.

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# Synapses in the pathophysiology of reward

Septembre 2011

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ENP Chair of excellence

## ■ Team overview

The general interest of the lab is to dissect the neuronal circuits implicated in reward learning and to understand how drugs co-opt these connections.

Goal directed actions, aimed to obtain a reward, motivate our behaviors and influence our decisions. Midbrain dopamine neurons activity and therefore dopamine release are enhanced by external cues predicting a reward. Lateral habenula (LHb) neurons play a central role in this regulation since they instruct dopamine neurons during reward learning.

A dysfunction in the output signal from the lateral habenula can be therefore at the basis of dysregulated dopamine signal and underlying neuropsychiatric disorders characterized by an abnormal reward signal (i.e. drug addiction).

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# Plasticity in cortical networks and epilepsy

Septembre 2011

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AVENIR Team

## ■ Team overview

Cortical GABAergic interneurons play a critical role in shaping the activity of neuronal ensembles. In particular, in the hippocampus, GABA signaling is involved in the maintenance of rhythmic population activities associated with various behavioral states and cognitive tasks. However, even a partial reduction in GABAergic transmission leads to an anomalous synchronization of neuronal activity and the emergence of epileptiform discharges.

Our objective is to identify the alterations of GABAergic networks responsible for the initiation and maintenance of epileptiform activities in the hippocampal network. Specifically, we combine cellular electrophysiology and molecular imaging techniques to examine:

- the functional impact of human mutations affecting GABA signaling and associated with idiopathic generalized epileptic syndromes,
- the long term changes in hippocampal GABAergic circuits initiated by a period of epileptiform activity,
- the perturbations of chloride homeostasis induced in several pathological conditions, and their long term effects on synaptic transmission in cortical networks.

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# Intracellular signal relay and integration

[André SOBEL](#)

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## ■ Team overview

Cell morphogenesis, functional differentiation, integrity and plasticity within the nervous tissue are controlled by contacts and interactions of cells with their environment, followed by the relay and integration of resulting intracellular signals. We focus our research more particularly on the actions of these signals on the actin and tubulin cytoskeletons.

**Theme 1** concerns the characterization of the roles and mechanisms of action as well as the regulation of intracellular stathmin family phosphoproteins, whereas

**Theme 2** concerns the study of the formation, roles and mechanisms of action of adhesion complexes involving cadherins.

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**INSEAD**  
*1 research group*

## Decision Neuroscience Group

[Hilke PLASSMANN](#)

ENS - INSERM

### ■ Team overview

Hilke's primary research areas are decision-making in the intersection of neuroscience, psychology and economics.

In recent and current research projects she investigates the influence of cognitive concepts on the consumption experience, satiation for different rewards, and the neural basis of different decision-making related value signals, and ways to alter/self-control/regulate these signals

### ■ Website

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**CENTRE DES NEUROSCIENCES PARIS-SUD 11**  
**ORSAY**  
*2 research groups*

# Cellular and Molecular Mechanisms of Plasticity and Memory

Septembre 2011

[Serge LAROCHE](#)

CNRS – Université Paris-Sud 11

## ■ Team overview

Research in the team focuses on the cellular and molecular mechanisms of learning and memory and on identifying mechanisms responsible for memory dysfunction in brain pathologies.

Our objective is to identify in different structures of the brain such as the hippocampus and cortex the cellular and molecular mechanisms underlying brain of plasticity, to characterize their role in the formation of memories and identify networks and brain structures within which these changes occur during the laying down of memories.

Our approach, from genes to function, leads to both the identification of cellular and synaptic changes linked to learning and to the functional characterisation of the role of signalling cascades, transcription factors, and the regulation of genes and proteins underlying different phases of plasticity and forms of memory. The research projects cover different facets of plasticity and memory, ranging from synaptic mechanisms to neurogenesis, complemented by the analysis of the cellular and molecular mechanisms of memory dysfunction associated with pathologies of genetic origin such as mental retardation or neurodegenerative diseases such as Alzheimer's disease. In these animal models, we explore the potential of genetic, pharmacological or behavioural therapies. The research is based on multidisciplinary approaches including cellular and molecular biology, biochemistry, functional neuroanatomy and imaging, pharmacology, in vivo electrophysiology and behavioural analyses of learning and memory in rats and genetically modified mice.

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# Neurobiology of decision making

Septembre 2011

[Sylvie GRANON](#)

CNRS / Université Paris Sud

## ■ Team overview

Our current projects are aimed at finding the different modulators of flexible behaviours and identifying the neural bases underlying this modularity. They involve the different members of the team:

1. We will identify the role of the neuronal nicotinic receptors (nAChRs) in the modulation of neurotransmitter release in the prefrontal cortex. (Project of Renata Dos-Santos Coura).

It is known that the prefrontal cortex (PFC) receives dopaminergic projection from the ventral tegmental area but also noradrenergic projection from the locus coeruleus, cholinergic projections from the nucleus basalis magnocellularis and serotonergic projection from the dorsal raphe nucleus. It may therefore be of major interest to establish how the nAChRs participate in the integration of the different neurotransmitters on PFC functions.

2. Identification of the neural partners of the prelimbic prefrontal cortex in flexible behaviors. (Project of Jonathan Chabout).

Another important –and controversial- issue in flexible behaviours regards the neurobiological source of the decision switch when conflict between different alternatives exists. This conflict may concern the response selection, the decision to make or the motivation to satisfy (hence, the value of different motivations in competition). The role of the anterior cingulate in conflict at the decision stage, and not at the motor selection stage, has recently been shown in humans, whereas the ventral and dorsolateral PFC and ventral striatum would encode the valence of different behavioural outcomes in a decision-making task. In rodents, the ability to switch task –but not motivation- and to inhibit previously reinforced behaviour has been shown to depend on the orbitofrontal integrity. Thus, even if the circuits involving the different subareas of the PFC and the striatum are certainly crucial to estimate the reinforcement value and response selection, it is not known how the brain circuit exactly allows an appropriate switch between motivations.

3. Relationship between flexible behaviour and impulsive/compulsive traits. (Project of Pierre Serreau)

The last major issue for appropriate decision-making in changing situations or contingencies, is the ability to disengage from one current action, i.e. to inhibit previously reinforced behaviours. This aspect consists in the appropriate control of impulsive/compulsive behaviours. In pathological states, inflexible behaviours have been associated with some other behavioural traits, such as impulsivity, to which some neurobiological markers have been recently associated in humans and in rodents. We will shortly design a task for measuring mice compulsivity in order to test this trait in b2KO mice. We will also study whether some neurobiological markers, like D2/D3 receptors expression, correlate with impulsivity/compulsivity traits.

4. Role of emotions in flexible behaviours (Project of Anne Nosjean).

The relationship between the amygdala and the PFC has not been studied regarding flexible behaviours. We will thoroughly investigate the anatomical and functional PFC-amygdala connections in WT and b2KO mice in behaviours affected by stress.

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**IMNC (Imagerie et Modélisation en Neurobiologie et Cancérologie)**  
*1 research group*

# Metabolism, Imaging and Olfaction (MIO)

Septembre 2011

Hirac GURDEN

CNRS - Université Paris Sud - Université Paris Diderot

## ■ Team overview

What are the mechanisms underlying sensory plasticity in the adult brain? Since olfaction is the main sensory modality in rodents, we study how the olfactory system encodes and processes sensory information. We focus on the rodent's olfactory bulb (OB), which is the structure supporting the first step of odor coding in the brain.

Our experiments include: i/ wide-field high resolution optical imaging of endogenous signals to record spatial maps of olfactory glomeruli activity, ii/ oscillatory activities detected in the local field potentials and emerging from mitral to granule cell interactions, and iii/ behavioral tasks.

To date, we have shown the importance of neuro-astrocytic crosstalk in olfactory maps as well as local energy metabolism and oscillatory activities. We are currently studying spatial and temporal dynamics of OB activities in different nutritional states and during learning using chronic optical chambers, and recording electrodes implanted in situ.

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In Vivo Detection of Excitotoxicity by Manganese-Enhanced MRI : Comparison with Physiological Stimulation.

**Magnetic Research in Medicine (MRM)** \* co-authors.

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**MIRCEN - Laboratoire des Maladies en  
Neurobiologie et Cancérologie**  
*2 research group*

# Cell-cell interactions in neurodegenerative diseases

Septembre 2011

Gilles BONVENTO

CEA - Inserm

## ■ Team overview

Our research focuses on the interactions between neurons and astrocytes, at the fundamental level but also in the context of neurodegenerative diseases in which glial cells display an activated phenotype that is not yet characterized at the functional level. These glial cells play an important role in brain function, particularly in energy metabolism, a function impaired in most neurodegenerative diseases (Alzheimer, Huntington and Parkinson).

Our recent work shows that astrocytes activated by a cytokine (CNTF) effectively protect neurons from energy deficits (Escartin et al., 2006, 2007). One main objective is to develop new therapeutic approaches that target astrocytes and not only neurons, in particular through the use of new viral vectors (Colin et al., 2009). A pre-clinical trial of gene therapy in primates and of clinical phase I in humans is underway with a lentivirus encoding the CNTF. Our current projects seek to determine (1) the functional consequences of astrocyte activation (2) the role of astrocytes in the pathogenesis of Huntington's disease, (3) the factors that contribute to the vulnerability of striatal neurons in Huntington's disease and (4) the metabolic status of selectively affected cells in Alzheimer disease. Experimental approaches include the use of viral vectors in vivo and in vitro and measurements of functional indexes using molecular, biochemical, anatomical, electrophysiological and imaging tools.

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# Neurodegenerative diseases

[Philippe HANTRAYE](#)

CEA - CNRS - Université Paris-Sud 11

## ■ Team overview

The research themes of this research unit are mainly concerned with the study of neurodegenerative diseases and particularly Parkinson's, Huntington's, Alzheimer's diseases and to a less extent prion diseases. The URA CEA CNRS 2210 unit contributes to various research axes of the RTRA :

- theme 6 (origins of imaging signals) of axe 1 "development, plasticity and aging"
- theme 2 (cell therapies and neurotrophic factors) and theme 6 (origins of imaging signals) of axe 2 "cerebral basis of cognitive functions ;
- theme 1 (genetic and environmental mechanisms of neurodegeneration and inflammation, theme 5 (animal models) and theme 6 (new therapeutic strategies) of axe 3 "gene-environment interactions as the origin of neurodegenerative diseases and psychiatric disorders

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# Brain Imaging & Developmental Psychiatry

Septembre 2011

Jean-Luc MARTINOT / Monica ZILBOVICIUS

INSERM – CEA – Université Paris-Sud 11

## ■ Team overview

Cerebral development, imaging and psychopathology.

The first axis of research is to characterize psychiatric disorders linked to brain development, using anatomical and functional neuroimaging.

Patient groups with psychiatric disorders beginning in the early decades of life, are studied at complementary periods: childhood, adolescence, adulthood. Searching for anatomical and functional changes of the brain in a few selected psychiatric syndromes. Autism, schizophrenia and addiction are examples of psychiatric conditions for research in neuroimaging. The comparison with addiction disorders provides a thorough characterization of the detected variations. Neuroimaging and psychiatric treatments.

The second research axis is to identify the brain sites of action of psychotropic drugs and monitoring treatment effects. We search for relationship between response to treatment and anatomical or functional brain specificities.

Psychopharmaceutics./ Transcranial magnetic stimulation./ Drugs of addiction.

Three imaging techniques were adapted to explore the brain of subjects with various mental disorders:

- 1 / MRI (Magnetic Resonance Imaging) for brain morphology
- 2 / functional MRI (fMRI) for brain function,
- 3 / PET (Positron Emission Tomography) for neurochemistry.

The researches of the Unit 1000 INSERM-CEA are performed on CEA platforms, Service Hospitalier Frédéric Joliot and Neurospin. The unit includes two sub-sites, one in the department of Paediatric Radiology of the Necker Hospital, the other one in the Solenn House, adolescents' house, Cochin Hospital.

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**INSTITUT NATIONAL ALFRED FESSARD & NEUROSPIN**  
*8 research groups*

**NEUROBIOLOGY AND DEVELOPPEMENT**

*5 research groups*

# Zebrafish Neurogenetics (ZEN)

Septembre 2011

Laure BALLY-CUIF

CNRS

ENP Chair of excellence

## ■ Team overview

The central nervous system (CNS) of vertebrates is a complex arrangement of neurons and glial cells that underlie brain physiology and animal behavior. These cells are set-up in defined numbers at specific locations from neural progenitors or Neural Stem Cells (NSCs), largely during early stages of life. In addition, the maintenance of NSCs in the brain until adulthood is a general phenomenon, likely crucial to late adaptation events. Indeed, defects in adult neurogenesis have been correlated with neurodegenerative and mood-related disorders, and also occur during ageing. Within this context, the large-frame perspective of our research program is to understand the molecular integration of NSC biology with the ultimate aspect of brain function: the determination of behavior.

To this aim, we focus both on the molecular mechanisms underlying NSC fate during development and adulthood, and on basic features of adult neurogenesis and its impact on behavioral modulation. Our model is the zebrafish, *Danio rerio*, where adult NSCs are abundant, which stands as an excellent comparative vertebrate model to the mouse, and where we recently identified NSC factors that we can now use as starting point towards dissecting NSC genetic cascades. In addition, we developed assays measuring emotional and cognitive behavior in this species.

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# Neurobiology integrative of the brainstem to the embryo

[Gilles FORTIN](#)

Univ. Paris-Sud 11 - CNRS

## ■ Team overview

Development of respiratory oscillators in the embryo.

## ■ Bibliography

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04, Ile-de-France Sud 25, Physiologie moléculaire et intégrative.

# Stem Cells and Neurogenesis in the Retina

Septembre 2011

Muriel PERRON

CNRS

## ■ Team overview

Our group is interested in mechanisms sustaining development of the nervous system and adult neurogenesis, with the retina as our principal model. The retina is indeed a model system for developmental neurobiologists, essentially because of its laminated structure with a limited number of neuron types and its accessibility.

Our key questions are : How proliferation and fate of neural precursors are controlled during embryonic retinogenesis ? What are the molecular mechanisms sustaining neural stem cell activity at post-embryonic stages ? How retinal stem cells participate in the repair of damaged retina ?

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# Molecular genetics of circadian rhythms

[François ROUYER](#)

CNRS

## ■ Team overview

Our group works on the circadian clock that controls the rest-activity rhythms in the drosophila brain. We have three main research lines:

- Neuronal bases of the brain clock: role of the different neuronal oscillators and organization of the network, light and temperature synchronization pathways (inputs), transmission of the circadian information in the brain (outputs)
- Differentiation of the clock neurons and building of the circadian function during brain development
- Molecular bases of the circadian oscillator: post-translational control of clock proteins (phosphorylation, ubiquitination, degradation) and search for new clock components through genetical and molecular approaches.

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# Development and evolution of neurotransmission

[Philippe VERNIER](#)

CNRS - Université Paris-Sud 11

## ■ Team overview

Researches in the laboratory concern many fundamental aspects of brain development and evolution. The researches aim at better understand how the brains of different species develop during embryogenesis, how they are structured and organized as functional systems. Cellular and molecular mechanisms of morphogenesis (hypothalamus, thalamus and pallium, optic tectum) and differentiation (cholinergic and dopaminergic neurons) of the nervous system are compared in several model animals (ascidians, amphioxus, lampreys, zebrafish, medakafish, astyanax, *Xenopus*, chicken, and mice), in order to identify fundamental principles of neural development and differentiation. A special emphasis is given to the study of fundamental aspects of neural stem cells, including embryonic stem cells of the CNS and the neural crest. Implications for some human diseases are also studied.

Lab members have published more than 70 original papers and reviews during these last four years, many of them journals in journals with high impact factor. Researchers also actively participate in the dissemination of scientific information to public.

## ■ Bibliography

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**UNITE DES NEUROSCIENCES**  
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*4 research groups*

# Computational neuroscience

[Alain DESTEXHE](#)

CNRS

## ■ Team overview

Integrative properties of neocortical neurons in high-conductance states.

In awake animals, neurons of cerebral cortex are in a "high-conductance" (HC) state, characterized by a sustained, irregular and very noisy spike discharges.

Neurons have very special integrative properties during such states, in particular regarding the integration of excitatory and inhibitory inputs. Studying this complex integrative dynamics requires a tight association between in vivo, in vitro and computational techniques. HC states are measured intracellularly in vivo in anesthetized animals, and these measurements are then integrated into computational models to recreate such states numerically.

These models are then used in "dynamic-clamp" in vitro experiments, in which computational models interact directly with living neurons recorded intracellularly.

This back-and-forth dynamics between techniques in vivo, in vitro and in computo allows us to re-create HC states in vitro and benefit from this preparation to reconstruct the transfer ("input-output") function of the neuron during HC states. This information is necessary to understand the dynamics of information processing during active states of cerebral cortex.

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# Cogniscience Synaptic integration and functional plasticity in primary visual cortex

[Yves FREGNAC](#)

CNRS

## ■ Team overview

Functional intracellular and synaptic imaging of visual cortical receptive fields, optical imaging of cortical network dynamics, supervised models of Hebbian plasticity during development and adulthood, and the psychophysical correlates of perceptual binding processes in primary cortical areas.

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# Sensory Processing, Neuromodulation and Plasticity

Septembre 2010

Daniel SHULZ

CNRS

## ■ Team overview

Using the barrel cortex of the rat as a system model, our research is centered on the study of neuronal processes responsible for the coding of sensory information and perception, as well as their regulation through the interaction of the animal with the environment. We are interested in the propagation and integration of neuronal information in the primary somatosensory cortex and the emergence of collective properties in response to spatially distributed stimuli on the receptor surface.

In addition, we study the functional and synaptic adaptation of the cortical neuronal network described by Hebbian and non-Hebbian plasticity algorithms. We include in this research, the study of permissive factors linked to the attentional and behavioral state of the animal which are mediated by ascending neuromodulatory systems.

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**NEUROSPIN**  
*4 research groups*

## Brain imaging

Septembre 2011

Denis LE BIHAN

CEA

### ■ Team overview

The goal of Neurospin is to push the current limits of brain imaging, from the mouse to man, as far as possible with very high magnetic field Nuclear Magnetic Resonance (NMR). NMR imaging (MRI) can be used to observe deep organs totally non-invasively. The more intense the magnetic field, the greater the sensitivity, allowing more details to be seen. Benefiting from CEA know-how in the conception of magnets and NMR, Neurospin technical platform is equipped with unrivalled NMR imaging tools.

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# Computer-assisted neuroimaging laboratory (LNAO)

Jean-François MANGIN

CEA

## ■ Team overview

LNAO is a lab of Neurospin, a brain research center focusing on high field magnetic resonance imaging. The lab is in charge of research and development in brain image analysis. The lab hosts fellows from various institutions, including CEA, INSERM and INRIA.

LNAO objective is twofold.

1. The first axis is related to the imaging platform. The lab is in charge of the software platform dedicated to the analysis of the images produced by the scanners of Neurospin. This environment is based on BrainVISA, a federative software framework dedicated to neuroimaging. In this context, the lab is providing user support but also expertise in image analysis during the planing of new neuroscience projects. The core of our methodological research programs aims at keeping the highest expertise in domains like computer vision or Bayesian inference applied to various neuroimaging modalities.

2. The second research axis targets neuroimaging applications in neurosciences. These projects are related to the transverse research programs of Neurospin, namely

- Molecular imaging.
- Brain development.
- Genetics and neuroimaging.
- Multiscale architecture of the brain.
- Cognitive neuroscience.
- Diagnosis of cerebral diseases.

We can be the principal investigators of these research projects or develop them in close collaboration with neuroscientists inside or outside Neurospin.

We can be the principal investigators of these research projects or develop them in close collaboration with neuroscientists inside or outside Neurospin.

## ■ Website

<http://lnao.fr>

# Developmental Neuroimaging

Septembre 2010

[Ghislaine DEHAENE - LAMBERTZ](#)

INSERM - CEA - Université Paris-Sud 11- Collège de France

## ■ Team overview

To understand how complex cognitive functions have emerged in humans, we need to examine their beginnings in human infants. Our team is working along two axes. On one hand we aimed to obtain a functional description of the networks involved at the beginning of life in complex cognitive functions such as language, visual recognition of conspecifics, number perception. On the other hand, we developed methodological tools to improve the study of the fast structural development present at this period of life. Our team is one of the few in the world who is able to combine MRI and EEG to obtain both structural and functional descriptions of the human brain at the beginning of life in order to decipher the initial bias in human brain organization that give rise to human complexity.

More recently, we are addressing the effect of culture and schooling and we are studying the impact of learning to read on brain organization.

Our goals are both fundamental, but also societal. Development should be better understood in order to help the relatively high percentage of children facing developmental disorders, such as dyslexia, dyscalculia, autism but also suffering from brain lesions related to preterm birth, anoxia... Remember that for example only 78.7% of French young adults are correctly mastering reading (from journées d'appel à la défense 2006).

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# Cognitive neuroimaging

Septembre 2011

Stanislas DEHAENE

INSERM – CEA – Université Paris-Sud 11

## ■ Team overview

Study of fine-grained cognitive representations and processes underlying cognition and perception; of contrast between conscious and non-conscious operations, to identify signatures of conscious level processing.

Analyze the impact of education on the adult brain organization for reading and arithmetic.

Study the development of language and consciousness in human infants and young children and human adult architecture for sentence-level processing of language.

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**CENTRE HOSPITALIER SAINTE ANNE**  
*3 research groups*

# Glial Plasticity and brain tumors

[Hervé CHNEIWEISS](#)

INSERM – Université Paris Descartes – Hôpital Saint-Anne

## ■ Team overview

Gliomas are the most frequent primitive brain tumors and remain of poor prognosis due to a lack of effective treatment. Understanding their physiopathology is made difficult by a high level of morphological variability, cellular heterogeneity, and the variability in clinical evolution of patients bearing tumors of similar histological aspect.

Isolation from adult glioma of cancer cells with stem and mesenchymal properties (TIC), has led to the proposal that a minor fraction of the total tumor cell population endowed with stable stem-like properties accounts for the development and the therapeutic resistance of the tumor.

Our own work showed that conversion of mature astrocytes into functional progenitors induced by a single change in their environment sensitizes them to cancerous transformation. We further found that TICs derived from adult and pediatric gliomas, can be induced to lose and re-gain their stem-like properties in response to serum addition to the culture medium. We identified mi-RNA whose expression depends on extracellular signals, and that are involved in the control of these oscillations in the phenotype of TICs.

This plasticity in the phenotype of TICs leads us to challenge the assumption that TICs constitute a cell population with stable intrinsic properties, distinct from the other tumor cells present in gliomas. We postulate that within gliomas, cancerous “stemness” is a functional state that can be acquired by any tumor cell under microenvironment-induced epigenetic modifications. Cycles of gain and loss of the stem-like state would hence be the motor of the tumor development and of its therapeutic resistance.

## ■ Website

<http://cpn.paris5.inserm.fr>

# Neuropsychopharmacology

Michel HAMON

INSERM - UPMC

## ■ Team overview

Molecular, cellular and functional studies of serotonergic (5-HT) neurotransmission in the central nervous system of rodents (rat, mouse, including transgenic animals):

1 - Molecular mechanisms of dendritic/axonal addressing and regulation (desensitization, internalization, mRNA editing, etc) of 5-HT receptors expressed in central neurons;

2 - Development and characterization (behavioural investigations; neuroanatomical, neurogenesis quantification, neurochemical and electrophysiological studies) of preclinical models of psychiatric disorders (depression, addictions), neurological disorders (neuropathic pain, sleep disorders) and comorbid somatic dysfunctions (cardiovascular dysregulations in neuropsychiatric diseases) associated with alterations in central serotonergic neurotransmission;

3 - Development of novel pharmacological treatments for these disorders;

4 - Studies of central effects of psychotropic drugs (antidepressants, anxiolytics, addictive drugs, etc).

## ■ Website:

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# Pathophysiology of psychiatric disorders

Septembre 2010

Thérèse JAY / Marie - Odile KREBS

INSERM – Paris Descartes

## ■ Team overview

Mental illnesses (psychotic, mood disorders) have a major impact on public health. Our research programs aim at better understanding their aetiology and specific pathophysiology in order to facilitate early detection and the development of effective stage-specific intervention strategies. We have 3 complementary interests:

(1) Emotional dysfunctions and frontal limbic networks We explore the influence of emotional contingents (amygdala), the interplay between cannabinoid, dopamine, GABA and glutamate on the dynamics of neuronal plasticity in frontal limbic networks in different physiological conditions and its adaptation to pathological situations and study the influence of therapeutics influence (chemical or not) on plasticity.

(2) Development, genes and environment in psychosis. We study the potential role of candidate genes involved in cortical development and their deficiencies in relation to dysconnectivity

(3) Cannabis and maturation of the adolescent brain. Interactions between development, brain maturation and environment (cannabis or/and stress) are explored using models previously validated in rats (antimitotic MAM prenatal exposure, stress, cannabinoid peripubertal exposure) at the behavioral and molecular level. The same interactions are studied in Humans, in particular during psychosis transition. Our programs combine projects in both human (from gene and cellular model to cognitive functions and brain imaging) and animals. This interchange between basic animal models and human pathophysiology should help to foster development of innovative preventive strategies or treatments and to identify biomarkers predicting the onset and the outcome of these disorders.

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## Functional Genomics & psychiatric diseases

[Michel SIMONNEAU](#)

Univ. Paris Descartes - INSERM

### ■ Team overview

The goal of our group is to identify and investigate the genetic architecture of complex psychiatric and neurodegenerative diseases and the impact of identified variants on synaptic function and its plasticity. This work is important because of the number of persons affected by each of these diseases is close to 1%. For schizophrenia, ~1% of the adult population is affected, representing about 24 million people worldwide. For Autism Spectrum Disorders (ASDs), the Center for Disease Control and Prevention (CDC) reports approximately 9 per 1,000 children in USA. For Late Onset Alzheimer Disease (LOAD), LOAD is predicted to affect 1 in 85 people globally by 2050.

With Tel-Aviv University colleagues, we developed bioinformatics methods of mining Genome Wide Association Studies (GWAS) data. We found that GWAS SZ-related genes interact in a functional network that directly impact dendritic spine morphological plasticity [Loe-Mie et al., HMG, 2010]. We previously found that a similar network was involved in SWI/SNF remodeling by REST/NRSF [Lepagnol-Bestel et al., HMG, 2009].

Using a multidisciplinary research approach we are investigating the phenotypic effects of susceptibility genes using both in vitro and in vivo transgenic mice. To date we have established that certain risk variants contribute to particular subcellular phenotypes. SLC25A12 and MARK1 gene common variants that we found to be associated to ASDs impact dendritic trafficking and dendritic spine plasticity [Lepagnol-Bestel et al., Molecular Psychiatry, 2008; Maussion et al., HMG, 2008].

We identified rare variants that can be causal of ASDs such as copy number variations of AUTS2. We found that AUTS2 encodes a protein located in dendritic spines. In dendritic spines, this protein is a regulator of a E3 ubiquitin ligase specific for AKT2. We were able to rescue the abnormal phenotype by increasing AKT2 in dendritic spines [Lepagnol-Bestel et al., Nature Neuroscience, in revision].

### ■ Bibliography

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**INSTITUT COCHIN**

*1 research group*

# Genetics and physiopathology of neurodevelopmental disorders

[Jamel CHELLY](#)

CNRS –INSERM – Université Paris Descartes

## ■ Team overview

Research activities of our team relate to the study of human genetic diseases and in particular the identification of genes involved in a heterogeneous group of disorders associated with cognitive deficit and learning disabilities. These disorders are also called mental retardation (MR) and are defined by a global deficit of cognitive functions and IQ < 70.

This low level of the IQ is either the only defining clinical features without apparent anomaly of the development of the SNC, or associated with cortical dysgeneses and/or brain malformations.

In order to contribute into the understanding of molecular and cellular processes underlying cognitive deficit and neurodevelopmental disorders, we are developing in continuation with these genetic studies functional investigations that include generation and analyses of animal models deficient for the genes shown to be involved in these disorders.

Current functional investigations are focused on OPHN1, IL1RAPL, DCX and members of the tubulin family, dysfunction of which was shown to be responsible for mental retardation with or without brain cortical dysgeneses.

## ■ Website

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**ECOLE NORMALE SUPERIEURE**

*5 research groups*

## Molecular basis, physiopathology and treatment of neurodegenerative diseases

[Anne CHRISTOPHE](#)

CNRS - INSERM - UPMC

### ■ Team overview

The LSCP conducts interdisciplinary research on the psychological mechanisms underlying acquisition and processing of the language faculty as well as other high level cognitive functions (consciousness, social cognition). Our projects are grouped into 5 themes:

- The sound structure of language (early acquisition, processing and degradation of phonological processing)
- Sentence comprehension (early acquisition and processing of sentences: prosodic, grammatical and pragmatic aspects)
- Development of social cognition (acquisition and processing of moral intuitions and judgments)
- Attention and consciousness (acquisition and processing of conscious and unconscious processes, metacognition and introspection).
- Genetics and developmental disorders (behavioral, neuroscientific and genetic studies of dyslexia and autism).

### ■ Website

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## Auditory Language Group

Anne-Lise GIRAUD

INSERM - CNRS - ENS

### ■ Team overview

Physiology and dysfunctions of speech communication.

Our primary interest is in the neurophysiology of speech perception.

We use PET, fMRI, EEG, MEG, sEEG and computation modelling to understand the basic mechanisms of speech perception in healthy humans and their dysfunction in patients with linguistic communication disorders. The pathologies we are interested in are deafness, auditory rehabilitation by cochlear implants, dyslexia and autism.

Our experimental research is carried out at CENIR (Hopital de la Salpetriere, Paris), Neurospin (Gif sur Yvette) and CERMEP (Lyon). The Team is currently funded by Inserm, CNRS, European Research Council (ERC), Agence Nationale pour la Recherche (ANR), Fondation pour la Recherche Medicale(FRM), and Advanced Bionics.

### ■ Website

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## Group for Neural Theory

### Boris GUTKIN / Sophie DENEVE

ENS

#### ■ Team overview

The goal of the GNT is to understand the basis of information processing in the brain by identifying links between collective neural dynamics and function. Research in the group comprises a broad spectrum of different topics in Computational Neuroscience, including network models of working memory, drug addiction models, probabilistic inference, feature integration, and statistical learning in neuronal architectures, spike-based learning algorithms, and mean-field analysis of recurrent networks, modeling of short-term plasticity in synaptic transmission and dynamics of GABA neurotransmission.

The work is based on methods from computational neuroscience, mathematics, statistics, computer science and physics: e.g. dynamical systems, Bayesian statistics, machine learning, statistical data analysis, stochastic differential equations, compartmental modelling, and mean field methods.

The interns will have a opportunity to take part in a wide range of research projects within the sub-teams of the three PIs: Boris Gutkin, Christian Machens and Sophie Deneve. The Group for Neural Theory has been founded in 2005 as a part of the Département d'Etudes Cognitives (DEC) at Ecole Normale Supérieure (ENS). The group is now part of the Laboratoire de Neurosciences Cognitives (LNC, INSERM Unité 960) within the DEC at the ENS.

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Sophie Denève [sophie.deneve@ens.fr](mailto:sophie.deneve@ens.fr)

# Cognitive neuroscience

Étienne KOEHLIN

INSERM – ENS

## ■ Team overview

The cognitive neuroscience lab conducts researches to understand the neural bases of Action and related cognitive processes along several dimensions: motor, linguistic, social and intentional.

We especially study the brain functional architecture and neuronal computations underlying these processes using modern brain imaging techniques (IRMf, EEG-MEG), experimental psychology techniques and mathematical/ computational modeling.

■ **Website** [www.koechlin.ens.fr](http://www.koechlin.ens.fr)

**INSTITUT DE BIOLOGIE DE L'ENS**

## Functions of ventricular cilia during neurogenesis

[Nathalie SPASSKY](#)

ENS

### ■ Team overview

My group studies the biology of neural stem cells. Recently we first contributed to the demonstration that coordinated beating of ependymal cilia in the adult mouse brain is required for proper migration of neuroblasts towards the olfactory bulb (Sawamoto et al., 2006). Second, we have studied an early population of cells characterized by the expression of the *plp/dm-20* gene.

We have shown that neurogenesis and gliogenesis occur sequentially in the embryonic diencephalon from restricted progenitors (Delaunay et al., 2008).

We have also demonstrated that neural stem cells display a primary cilium in contact with the cerebral ventricles which serves as an antenna to regulate their proliferation in response to sonic hedgehog in both the cerebellum and hippocampus (Han et al., 2008 ; Spassky et al., 2008).

Our goal is thus to decipher the molecular and cellular signals regulating the proliferation and differentiation of neural stem cells in normal and pathological brain development.

### ■ Website

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**INSTITUT PASTEUR**

*6 research groups*

# Human genetics and cognitive functions

[Thomas BOURGERON](#)

CNRS – Institut Pasteur - Université Paris Diderot

## ■ Team overview

Our group explores the genetic contribution to human cognitive functions by studying the genetic susceptibility to psychiatric conditions such as autism spectrum disorders (ASD) or obsessive-compulsive disorders (OCD). Using a genetic approach, we have characterized several candidate genes (FAM8A1, KIF13A, GRIK2, NLGNs, PCDHX/Y) and identified mutations associated with ASD (NLGN3, NLGN4 and SHANK3).

Our main results consist in the identification of a synaptic pathway, sensitive to gene dosage, and associated with ASD.

ASD is diagnosed on the basis of three behaviorally altered domains, namely social deficits, impaired language and communication, stereotyped and repetitive behavior. In the vast majority of the individuals, the origin of the disorder is still unknown. During these last years, our group and others have contributed to a better characterization of the genetic bases of ASD. Several genes are now associated with the condition (Figure), providing a better view of the complex pathways contributing to this condition (anomalies in the number and shape of the synapses, imbalance in excitation/inhibition, increased cell number, high serotonin level).

Based on these results, our project aims now to combine our genetic approach to cell biology and brain imaging, to better characterize, at different integrated levels, the contribution of these genes in the development of language and communication in humans. This knowledge should also shed light on the origin of our ability to communicate, a complex process influenced by genetic/epigenetic factors and the environment.

## ■ Website

[www.pasteur.fr](http://www.pasteur.fr)

# Dynamic Neuronal Imaging

[David DI GREGORIO](#)

CNRS - Université Paris Descartes  
ATIP Team

## ■ Team overview

My team is focused on the study of synaptic function and plasticity, which is fundamental to our understanding of neuronal processing and thought to underlie learning and memory in the central nervous system.

The study of single synapses enables us to define the cell biological mechanisms that control synaptic behaviour.

To overcome the methodological limitations in studying single synapses, we have developed new optical methods that provide submicron spatial resolution and submillisecond temporal resolution.

The aim of our work is to use confocal optical detection of fluorescence molecules and diffraction-limited uncaging of bioactive compounds, in combination with electrophysiological recordings, in order to probe the function of single synaptic contacts within brain slices.

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## Channel-receptors G5 Group

Septembre 2011

Pierre-Jean CORRINGER

CNRS - Institut Pasteur

### ■ Team overview

Nicotinic acetylcholine, GABAA and glycine receptors from the pentameric ligand-gated ion channel (pLGIC) superfamily are key players of the neuronal communication in the brain and are the target of important classes of therapeutic (anti-smoking, anti-Parkinson, anti-Alzheimer compounds, anxiolytics, general anesthetics) and addictive (nicotine, alcohol) drugs. Understanding the functioning of these allosteric proteins and the mechanisms of action of active drugs requires combining atomic-resolution structural studies with functional investigation.

To this aim, we currently use the bacterial pLGIC homolog GLIC, discovered by our group in 2005-2007, as a prototypic receptor of the whole family. Since the creation of our G5 "Channel-Receptors" group in January 2008, we showed, in collaboration with the crystallographer Marc Delarue, that GLIC allows combining both X-ray crystallographic and electrophysiological approaches in parallel.

We were the first to solve the X-ray structure of a pLGIC in an open conformation, and to propose an atomic-scale mechanism for the global reorganization underlying channel gating. In parallel, we solved the structure of the isolated extracellular domain of GLIC in an unexpected hexameric form. We also identified at high resolution the modulatory binding site for general anesthetics on the full 3D structure, by combining X-ray crystallography, whole cell and single channel electrophysiology and molecular dynamics simulations. This provides the principles of the mechanism of action of general anesthetics on GABAA receptors, that are their principal target in humans.

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# Perception and memory

Septembre 2011

Pierre-Marie LLEDO

CNRS – Institut Pasteur

## ■ Team overview

General theme: Epigenetic regulation of neuronal networks and memory

Central topic: Adult plasticity of neuronal networks

System model: The olfactory bulb for its adult neurogenesis

Research topics:

- Functional consequences of adult neurogenesis
- Diversity of adult neural stem cells
- Role of learning in olfactory preferences and aversions
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# Genetics and Physiology of Hearing

[Christine PETIT](#)

INSERM - Institut Pasteur - Collège de France - UPMC  
FVE Team

## ■ Team overview

Our research projects have two tightly linked goals:

(i) to decipher the cellular and molecular mechanisms that underlie the development of the auditory system and the way it processes acoustic signals; the lab is mainly focused on the mechanotransduction (MET) process and the fascinating synaptic properties of the auditory sensory cells as well as the way their auditory afferent neurons operate. A focus on the auditory central system is also developed; and:

(ii) to identify the genes causative for deafness in humans, early- and late-onset forms, as well as forms including retinal defects (Usher syndrome), to elucidate the corresponding pathogenic pathways as well as to search for therapeutic tools based on the gathered knowledge.

Genes causative for some twenty monogenic deafness forms have been identified in C. Petit's laboratory. These proteins are key components of the auditory MET machinery, the sensory cell synapse and the auditory nerves.

r physiology and pathophysiology of the peripheral auditory system through multidisciplinary analyses (morphological, biochemical, in vivo and ex vivo electrophysiology and behavior analyses) of mouse models for human deafness is a major focus of the lab. Because these models also allow unraveling new physiological properties of the hearing system, much effort is devoted to this research field.

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# Integrative neurobiology of cholinergic systems

[Uwe MASKOS / Jean-Pierre CHANGEUX](#)

CNRS - Institut Pasteur

## ■ Team overview

Our research aims to investigate at multiple levels the molecular mechanisms and neuronal circuits underlying executive function and nicotine re-inforcement in a simple animal model. The system chosen is the mouse that lends itself to a large variety of approaches, from genetic manipulations and molecular pharmacology to brain imaging and behaviour.

The ultimate goal is to develop a molecular neurobiology of cognitive functions using a novel molecular genetic strategy: the stereotaxic injection in defined brain regions of lentiviral vectors to stably express defined genes. The method has already been successfully used to restore executive functions and nicotine re-inforcement in the mouse (Maskos et al., Nature, 2005) following re-expression of functional nicotinic acetylcholine receptors (nAChRs) in the VTA of nAChR KO mice. It will be further exploited to differentially express genes in defined categories of neurons, e.g. dopaminergic vs. GABAergic, but also to inactivate genes using the expression of siRNAs. The lentiviral strategy will also be extended to the rat brain and to the construction of genetically modified mice and rats (GMMs and GMRs) by infection of early embryos with lentiviral vectors.

Indeed, many advanced behavioural tests cannot be applied to the mouse, but have given a wealth of information on rat behaviour. This approach can even be potentially applied to non-human primates. nAChRs are known to regulate brain functions such as learning and memory, reward processes and addiction, together with anxiety, central processing of pain, selective attention, sleep and wakefulness. Moreover, nAChRs are implicated in a variety of pathologies, like ADHD, Alzheimer, Tourette, possibly autism, and also ageing. The program will aim at the understanding of the role of defined species of nAChR in the neuronal circuits underlying executive function and nicotine addiction in wild-type and genetically modified organisms. It will include the comparative evaluation of the role of the diverse brain areas and centers engaged in these functions in the mouse, including cortical areas like the prefrontal cortex, primary and secondary sensory areas, the nucleus accumbens, the VTA or the amygdala together with a detailed dissection of the neuromodulatory systems and signal transduction processes under nAChR control.

Combined with the latest developments in functional Magnetic Resonance Imaging (fMRI) and novel fibre-optic deep-brain imaging technology, the cellular and anatomical bases of the underlying brain circuits will be further explored. These data will motivate the development and test of theoretical models (such as the global neuronal workspace) aimed to define the neural processes that underlie generation of cognitive behaviours and their executive control. In particular, a coherent computational network will be built that defines the pathways and processes by which nicotine modifies executive and motivational processes.

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**INSTITUT PASTEUR**

*10 research groups*

# Physiology of perception and action

[Alain BERTHOZ](#)

CNRS - Collège de France (LLPA)

## ■ Team overview

The laboratory of Physiology of perception and the action is a multi-field regrouping teams of which the common goal is better to include/understand the bases neurales perception, action, but also of other cognitive functions like the attention and the memory. Methodologies employed are very varied but with each problem corresponds one or more theoretical and experimental approaches.

One of the originalities of the laboratory is to study these various functions on various levels, of the neuron to the behavior, in the animal and the man. We also work in collaboration with hospitals in order to study these functions among patients and to possibly contribute to the development of methods of diagnostic and rehabilitation.

Lastly, we work with the industrial partners for profitable exchanges of informations and techniques. The laboratory is a mixed unit of research CNRS installed in the buildings of the pulpit of physiology of the perception and the action of the College of France (titular Pr A. Berthoz). It profits from a support from the National Center of Space Studies (CNES) and many national and international co-operations.

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# Junctional communication and interaction between neuronal and glial networks

[Christian GIAUME](#)

INSERM

## ■ Team overview

The main focus of our projects concerns the network organization of glial cells, in particular astrocytes, as the result of their high expression level of connexins, the gap junction proteins.

These projects are considered in the context of the interactions between astrocytes and neurons as well as at the gliovascular interface. Indeed, it is now recognized that astrocytes interact dynamically with neurons and can modify their activity and survival, but so far such interactions are only considered as contributed by individual cells.

Our strategy is to study these interactions at a more integrated level as the result of interactions between neuronal circuits and astroglial networks. As astrocytes “endfeet” surround blood vessels and express a large number of connexins at their contacts, we are also interested in understanding their role at the gliovascular interface and the blood brain barrier.

Our research also covers pathological situations, as there is evidence indicating that neuroglial interactions contribute to epileptic-like activities in neurons.

Finally, we are also interested in a transgenic animal model of Alzheimer’s disease (APP/PS1) in which we have observed that the expression of the two astrocytic connexins is upregulated at the level of amyloid plaques.

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# Neural Circuits and Behavior

Septembre 2011

Alexander FLEISCHMAN

UPMC - INSERM - Univ. Paris 6 - CNRS - Collège de France

## ■ Team overview

My laboratory is interested in the functional properties of neural circuits underlying odor perception. We use a combination of molecular genetic, in vivo imaging and behavioral approaches in mice to understand the logic of odor coding in higher olfactory centers in the cortex.

Odor perception involves the recognition of odorants in the periphery and central mechanisms in the brain that allow the discrimination of odors and appropriate behavioral responses. Odorants are recognized by odorant receptors, expressed in olfactory sensory neurons in the nose. Odors activate subsets of sensory neurons and result in sparse and spatially invariant pattern of glomerular activity in the olfactory bulb, the first processing center of olfactory information in the brain. Information encoded by glomerular activity is then transmitted to higher olfactory centers in the cortex, which are thought to link odor representations to appropriate behavioral responses.

Central to understanding olfactory processing is the elucidation of the functional properties of the underlying neural circuits. In an effort to address this fundamental problem in sensory biology, we have altered the patterns of neural activity evoked by odors, by generating transgenic mice in which 95% of all sensory neurons express the same receptor. Two-photon imaging and behavioral analyses of these transgenic mice suggest a model of olfactory processing in which the recognition of patterns of neural activity, or contrast, is critical for odor detection. To test this model, we exploit a set of defined genetic perturbations in transgenic mice, which alter the expression of odorant receptor genes.

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# Development & Neuropharmacology

Septembre 2010

Alain PROCHIANTZ

CNRS - Collège de France - ENS

## ■ Team overview

Our group has contributed to the new finding that homeoproteins can transfer between cells and have direct non-cell autonomous activities. Homeodomains contain sequences that allow for nuclear export, cellular secretion and subsequent internalization. The mechanisms involved in secretion and internalization are atypical and have been studied in collaboration with Alain Joliot and colleagues, also at ENS. It is in the context of the latter studies that a peptide, called "Penetratin", was designed that can be used to address hydrophilic cargoes into the cell interior, in vitro and in vivo.

Beyond such biotechnological applications, homeoprotein intercellular transfer offers a mode of signal transduction with physiological and developmental implications. We have recently investigated three functions. A first function is the role of homeoprotein intercellular transfer in the formation of compartments within the neuroepithelium. For example, blocking Pax6 passage blocks the early development of the eye anlagen, leading to a small eye or no eye phenotype.

A second function is axonal guidance. Our group has shown, in collaboration with that of Christine Holt (Cambridge, UK), how Engrailed homeoprotein is a guiding cue for retinal ganglion cell axons. A third function, analyzed in collaboration with Takao Hensch (Riken-Tokyo, Japan and Harvard University, Cambridge, USA) is the role of Otx2 transfer in the opening/closure of the critical period in the binocular visual system. Finally, we have started to study the putative role of homeoproteins in specific diseases. A new finding is that Engrailed-1 is a survival factor for adult midbrain dopaminergic neurons.

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# Neuroglial Interactions in Cerebral Physiopathology

Septembre 2011

[Nathalie ROUACH](#)

UPMC - INSERM - Univ. Paris 6 - CNRS - Collège de France

## ■ Team overview

The main goal of our group is to determine whether and how astrocytes play an active and direct role in information processing. We want to unravel the molecular modalities and functional outcomes of neuroglial interactions in physiological and pathological conditions. More precisely, we want to understand how neurons and glia communicate in various regimes of activity and determine the outcome of disrupting their communication on neuronal functions, including their excitability, synaptic transmission, plasticity and synchronization. To overcome the present conceptual and experimental difficulties in the field of neuroglial interactions, we have developed a challenging novel interdisciplinary approach combining electrophysiology, imaging, molecular biology, biochemistry, mathematical modeling and new pharmacological strategies and molecular tools targeted to astrocytes, which permit to analyze and act selectively on populations of astrocytes.

Indeed, a particularly original aspect of our research in this field consists in using tools targeting specifically astrocytes: either pharmacological tools, delivered intracellularly in single astrocytes through a patch pipette and then diffusing in the gap-junction mediated network, or molecular tools, such as knockout mice for astrocytic proteins, as well as more recently, novel engineered lentiviral vectors targeting specifically astrocytes (collaboration with N. Déglon/C. Escartin, MIRCen). Using this multidisciplinary and innovative strategy, our goal is to decipher the specific role of key astroglial properties, such as calcium signaling, membrane currents, as well as connexin and pannexin-mediated transmission in basal synaptic activity, synaptic plasticity, synchronous physiological and pathological (epilepsy) activities.

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# Mice, Molecules and Synapse Formation

Septembre 2011

Fekrije SELIMI

INSERM - CNRS - Collège de France  
ATIP Team

## ■ Team overview

The brain is composed of many different types of neuronal populations that form functional networks by establishing specific synapses. Any disturbance in the process leading to the development of these networks can contribute to neurological diseases such as autism or schizophrenia. This complex process involves both target recognition, through a putative “molecular code”, and activity-dependent stabilization/elimination of synapses. Our scientific goal is to provide new insights on the formation of functional neural networks in vivo, in particular through identification of the genes and proteins controlling synapse specificity. In the past few years, we have developed the synaptic protein profiling approach, which enables, for the first time, the purification of a specific type of synapse from the mouse brain and identification of its protein content. The recently described bacTRAP approach allows gene expression studies in specific neuronal populations in mice. Combining these two innovative strategies and applying them to the study of the olivo-cerebellar network, the specific aims of my project are to:

- 1) perform the first comparison of the protein content of two types of synapses made on the same neuronal target, to identify the proteins characterizing the putative “molecular synaptic code”;
- 2) study the function of the genes identified in our analysis and their potential contribution to brain diseases, by performing a systematic analysis of their function using expression knockdown.

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# Dynamic and pathophysiology of neuronal networks

Septembre 2011

Laurent VENANCE

INSERM - Collège de France

## ■ Team overview

Our research is focused on encoding learning and memory in the basal ganglia, a set of subcortical nuclei implicated in the adaptive control of behavior. Reciprocally connected with the cerebral cortex and the limbic system, the basal ganglia participate to the detection of environmental cues and to the selection of appropriate actions based on motivation and expectancy of reward.

The pathological dysfunction of basal ganglia leads to major motor and cognitive disorders (Parkinson's disease, OCDs Tourette's syndrome, addiction...) for which no fully satisfying treatments are available yet. We study various aspects of the dynamic organization and synaptic interactions underlying the dynamic properties of the basal ganglia network and the changes of these properties in animal models of human pathologies. We are using a multidisciplinary approach combining electrophysiology (in vitro multi-patch-clamp and in vivo recordings), fast-cyclic voltammetry, 2-photon imaging, single-cell RT-PCR and immunohistochemistry, using in vitro and in vivo model. The complementary conceptual and technical expertise of the members of the team together with the collaborations we already established with groups of mathematicians, molecular biologists, clinicians and pharmaceutical industry allow us to investigate the normal and pathological functions of the basal ganglia at the different levels of complexity of the neuronal network.

- 1) The neuronal dynamics and synaptic plasticity (STDP) within the basal ganglia and cortical networks.
- 2) The neuron-glia crosstalk: we analyze the contribution of neurotransmitter uptake by astrocytes on corticostriatal information processing.
- 3) The physiology and pathophysiology of motor and cognitive properties link to dopamine and endocannabinoids.

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# Spatial memory and navigation

Septembre 2011

[Sidney WIENER](#)

CNRS - Collège de France (LLPA)

## ■ Team overview

Our current and future research will continue to target neuronal mechanisms of integration of multisensorial information from the environment and internal signals (such as emotions) as well as the elaboration, memorization and recall of spatial representations. The goal of our studies is to better understand the neural bases of cognitive processes necessary for an animal to survive in its environment, and their relations to adaptive behaviours and learned and remembered associations. Our research axes are also extending to study the genetic bases of representations of the environment, and we will continue to develop new approaches to study and analyse ensemble neuronal activity and brain oscillations in the freely moving animal.

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# Laboratory of Neurophysics and Physiology

Septembre 2011

Michel ZUGARO

Collège de France - CNRS (LLPA)

## ■ Team overview

To study the brain mechanisms of spatial memory in rats, we record the activity of large neuronal ensembles as rats perform learning tasks in various mazes, and during subsequent sleep when memory is consolidated. Our general approach consists in recording and dynamically perturbing the activity of brain networks to understand how they operate. Our studies combine animal behavior, neurophysiology, signal processing and data analysis.

'Place' cells in the hippocampus code for the position of the animal in space. As a rat moves along a given trajectory, place cells are activated one after the other, in sequence. We investigate the role of theta, a prominent hippocampal oscillation (~ 8 Hz), in the formation of these place cell sequences. Subsequently, during slow wave sleep, place cells spontaneously reactivate during fast oscillations (~ 200 Hz) known as 'ripples', replaying trajectories experienced during wake – as if the rat were dreaming that it explores its environment. We study the role of ripples in transferring information to neocortical zones for long term storage.

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# Probabilistic approach and active perception Neuronal Imaging

Septembre 2011

Jacques DROULEZ

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## ■ Team overview

We are interested in three dimensional object perception. More specifically, our research focuses on the way the set of sensory-motor information is integrated by the brain to elaborate a coherent representation of objects and of their geometrical properties. Our working hypothesis is that perception - in particular the visual perception - cannot be understood in isolation; the perception is always guided and modified by subject's action. As a consequence, we are also investigating several aspects of motor control and action planning. These studies give us insight on how perception, i.e. representations extracted from sensory-motor information, can be pertinent for action. Our methods include psychophysical experiments, brain functional imagery, modelling and simulation works performed in collaboration with robotics labs.

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