LabEx BRAIN

Bordeaux Region Aquitaine Initiative for Neuroscience

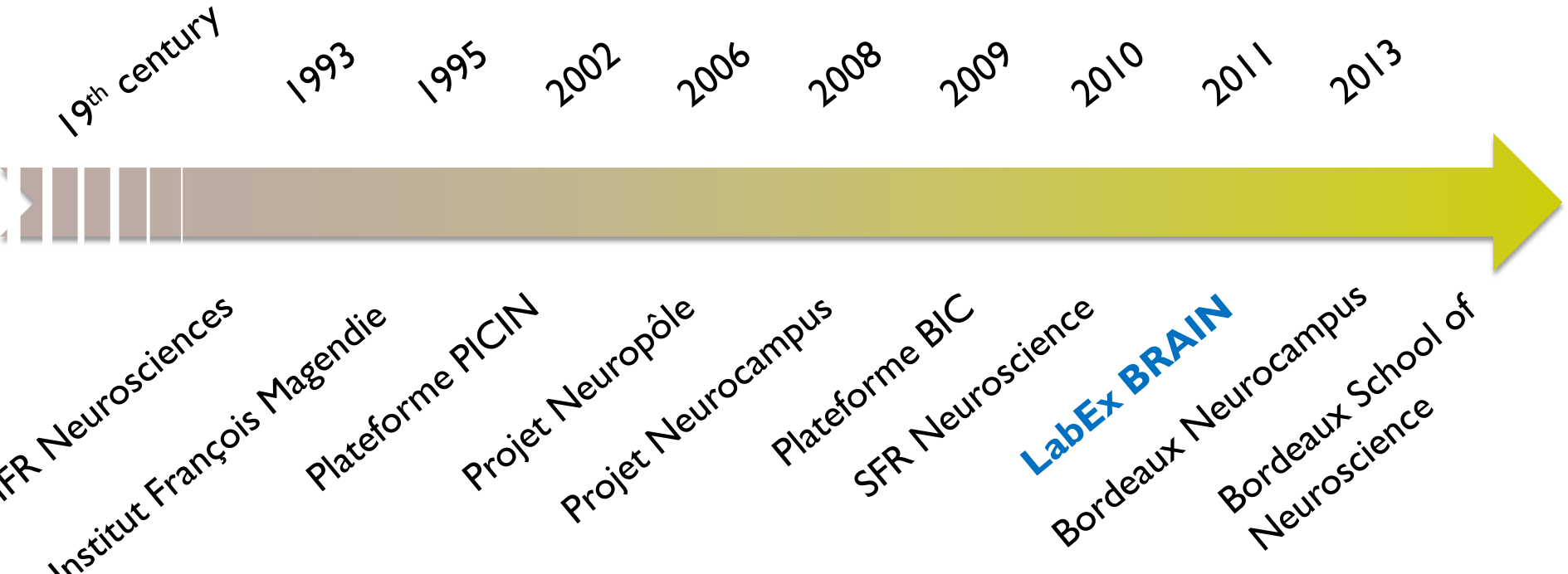
From molecules to behaviour for understanding brain function and its pathologies

Daniel Choquet

The different phases of Neuroscience in Bordeaux

Directors:

- Michel Le Moal (1995-1998)
- Jean François Dartigues (1998-1999)
- Dominique Poulain (1999-2002)
- Bernard Bioulac (2002-2009)
- Christophe Mulle (2009-2010)
- Jean Marc Orgogozo (2011→)



Strength of Bordeaux

- A long past history in neuroscience research
- International recognitions in the fields of:
  - Cell biology of neurons
  - Addiction
  - Motor and sleep disorders
  - Imaging and behavior analysis
- Strong and recurrent support from local and national institutions:
  - The Neurocampus project: 75 M€ from the Regional council to build 10.000 m² of new lab space and new teams
  - The BRAIN project and other infrastructure grants: 33 M€ from the "investissement d'avenir" for transversal projects and core facilities.

Bordeaux Neurocampus

Imaging, chemistry, cell biology and synapse physiology

Network physiology, Plasticity, behavior and addiction

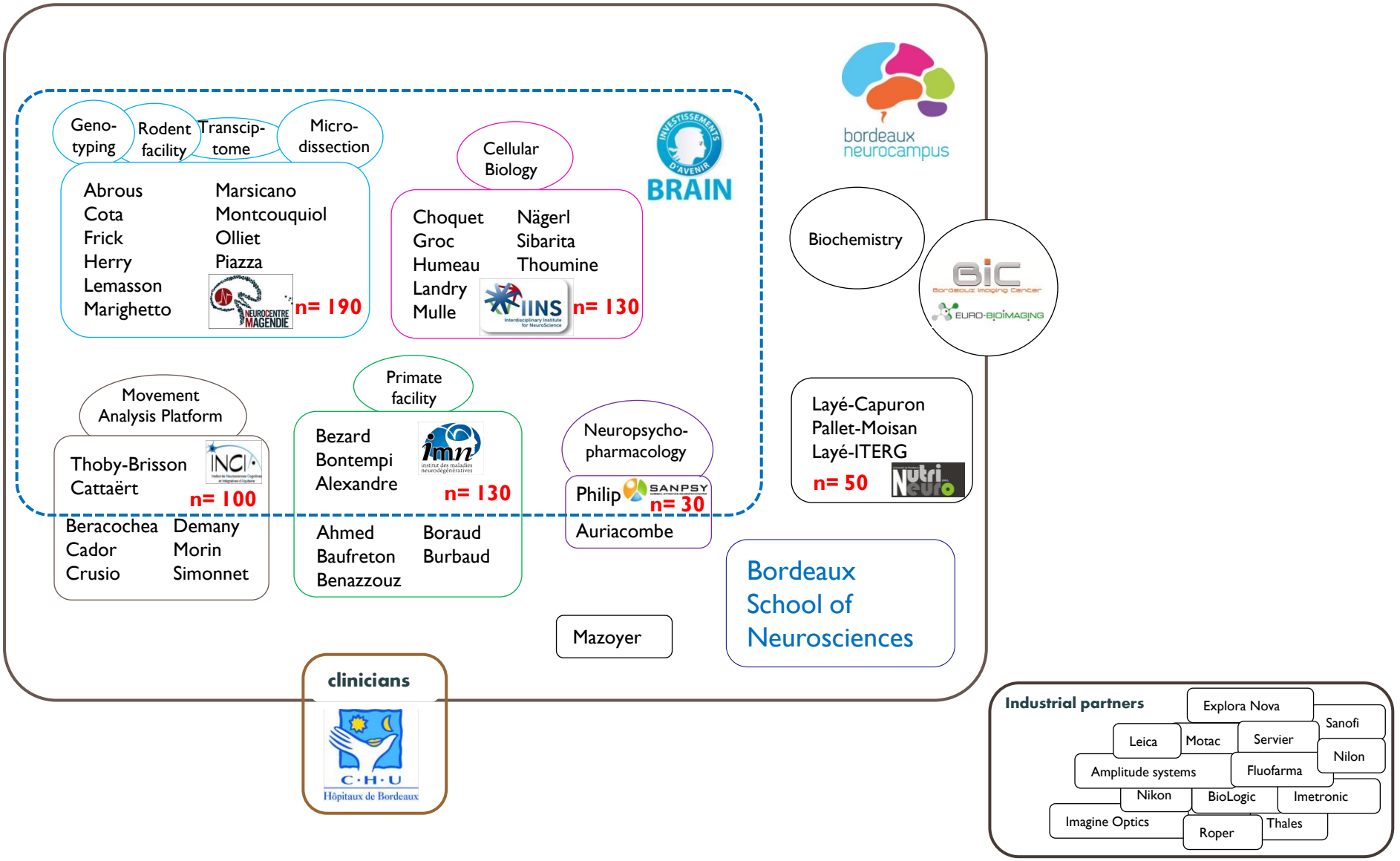
Integrated physiology, motor diseases, primate physiology and behavior, clinical research

Motor physiology and addiction

Neuroscience of nutrition

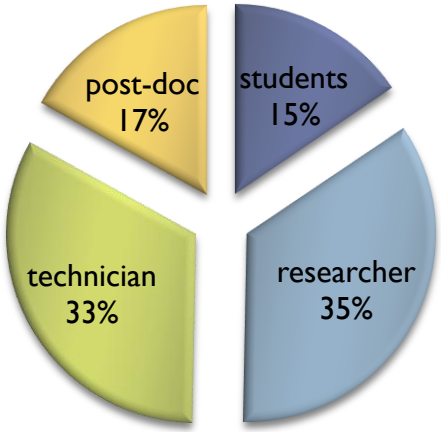
Clinical research of motor, sleep and attention disorders

BRAIN perimeter



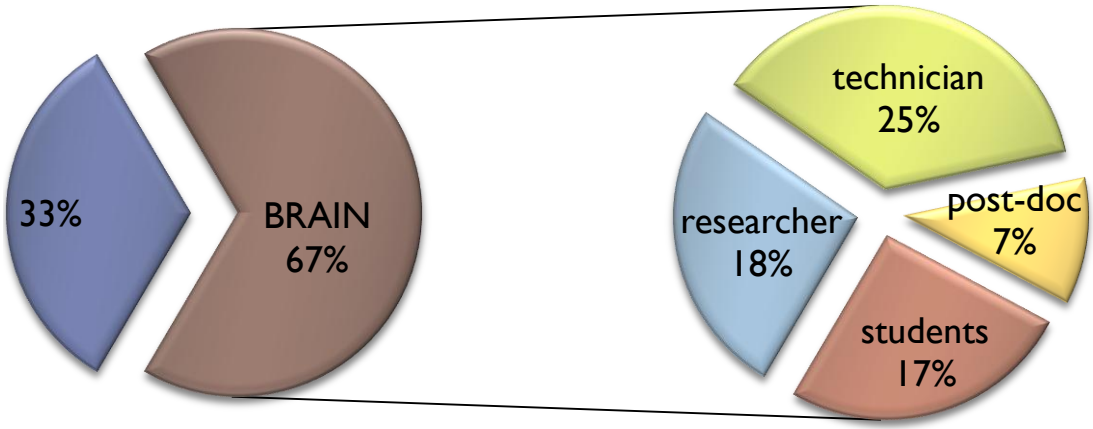
Breakdown per category

bordeaux neurocampus



- 650 members
- 45 teams
- 6 Departments
- From basic to clinical research
- 6 Nation-wide core facilities

INVESTISSEMENTS D'AVENIR
BRAIN



- 400 members
- 24 teams
- 5 Departments

Neurocampus Bordeaux: a new ambition

3 research centers in the same location

- 45 M€, 10 000 m² new laboratories, 2000 m² renovation

Start-up packages for new teams and equipment

- 20 M€ to promote external growth

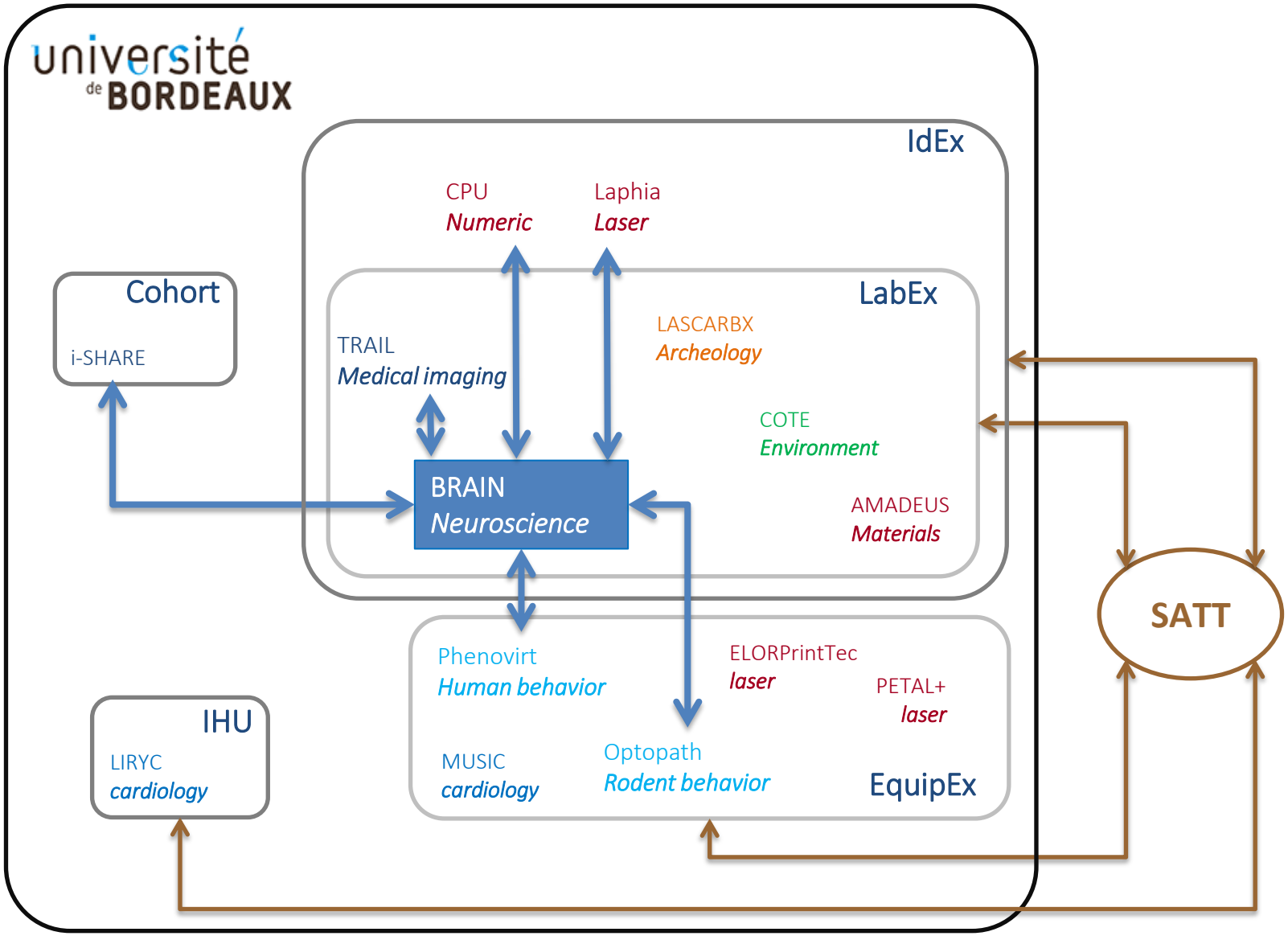
Technological and knowledge transfer

- 300 m² for start-up, 500 m² for Bordeaux Neuroscience School

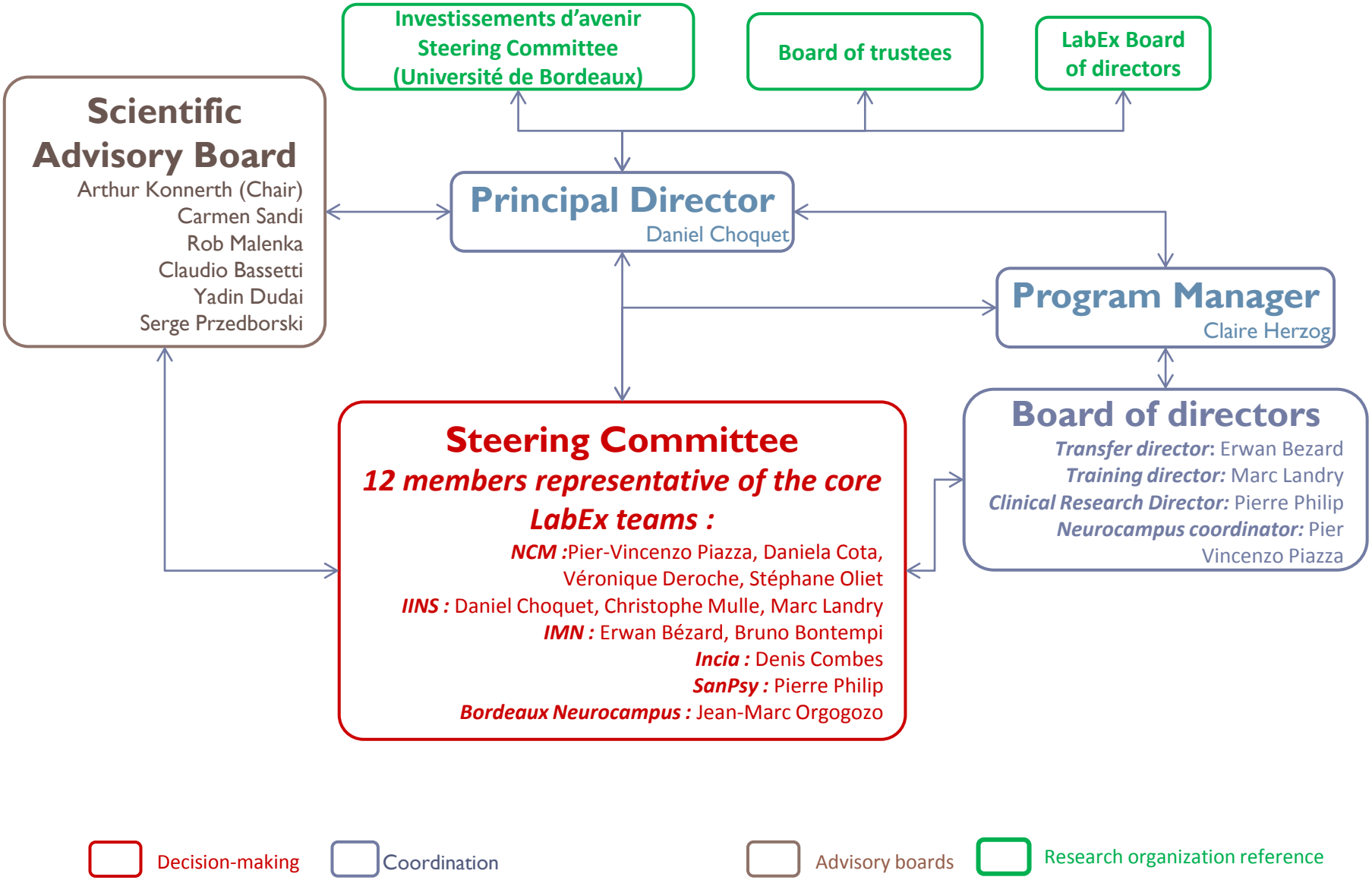
Attractivity of Bordeaux Neurocampus

- 9 new teams created from 2007:
  - Daniela Cota (INSERM)
  - Andreas Frick (INSERM)
  - Giovanni Marsicano (INSERM)
  - Mireille Montcouquiol (INSERM)
  - Valentin Nägerl (CNRS)
  - Jean-Baptiste Sibarita (CNRS)
  - Yann Humeau (CNRS)
  - Frédéric Alexandre (CNRS)
  - Cyril Herry (INSERM)

Insertion within the Excellence Initiative Bordeaux



Governance


Investissements d'avenir
Steering Committee
(Université de Bordeaux)
Board of trustees
LabEx Board
of directors
Scientific
Advisory Board
Arthur Konnerth (Chair)
Carmen Sandi
Rob Malenka
Claudio Bassetti
Yadin Dudai
Serge Przedborski
Principal Director
Daniel Choquet
Program Manager
Claire Herzog
Board of directors
Transfer director: Erwan Bezard
Training director: Marc Landry
Clinical Research Director: Pierre Philip
Neurocampus coordinator: Pier Vincenzo Piazza
Steering Committee
12 members representative of the core LabEx teams :
NCM :Pier-Vincenzo Piazza, Daniela Cota, Véronique Deroche, Stéphane Oliet
IINS : Daniel Choquet, Christophe Mulle, Marc Landry
IMN : Erwan Bézard, Bruno Bontempi
Incia : Denis Combes
SanPsy : Pierre Philip
Bordeaux Neurocampus : Jean-Marc Orgogozo
Decision-making
Coordination
Advisory boards
Research organization reference

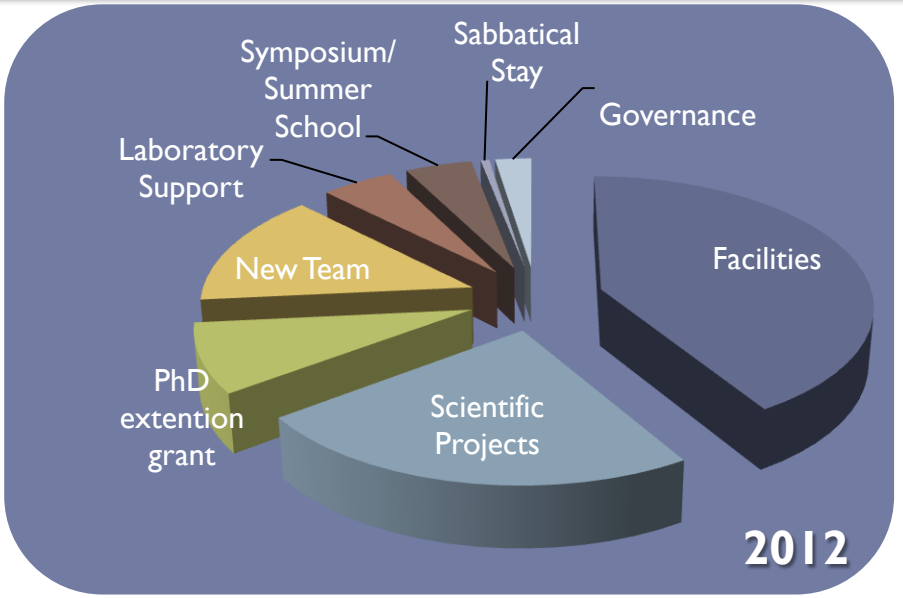
Activities

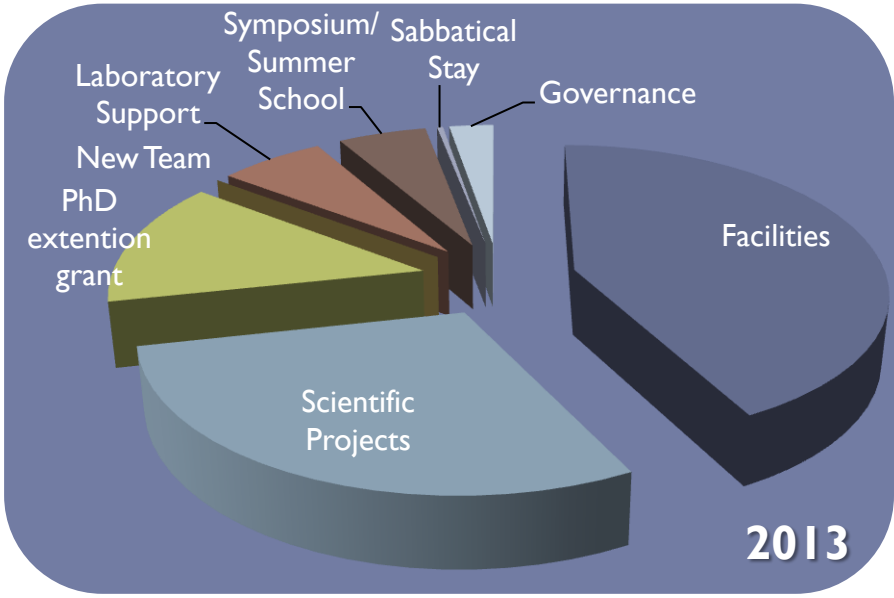
Total of the LabEx BRAIN : 20 M€

Research:
- Facilities
- Scientific projects
- Laboratory running costs

Training:
- phD extention grant
- Summer School
- Bordeaux School of Neuroscience

Attractivity, Dissemination & Transfer:
- Sabbatical stay
- New Teams
- Symposium, public outreach
- Mission to industrials





General process

Steering Committee Votes yearly:
- Main actions
- Calendar
- Budget breakdown

Launching Call for Proposals:
- Scientific projects
- PhD extension grants
- Other grants (meetings, sabbatical…)

Evaluation and Selection by the steering Committee

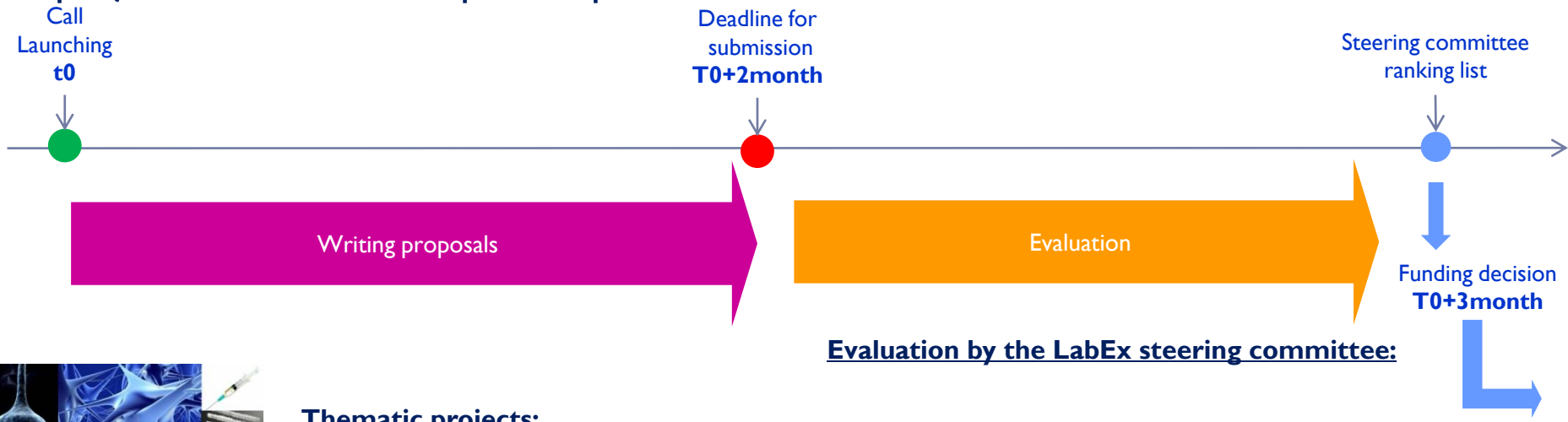
Vote the support for:
- Core Facilities Support
- Laboratory Support
- Bordeaux School of Neuroscience

Funding to the laboratories

Scientific projects: principles

- To promote inter-institutes collaborations
- To re-inforce existing research or to develop audacious and innovative projects
- Rapid, efficient and transparent process

570k€/year



Evaluation by the LabEx steering committee:

Thematic projects:
- validation by axis coordinators
- PI belongs to the LabEx
- Up to 95k€/axis/year

- 26 projects submitted, 14 funded
- 54 % success rate

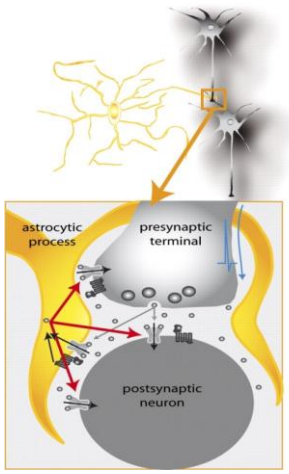
Open call projects:
- Any neuroscience topics
- PI belongs or not to the LabEx
- From 30 to 65k€/project/year

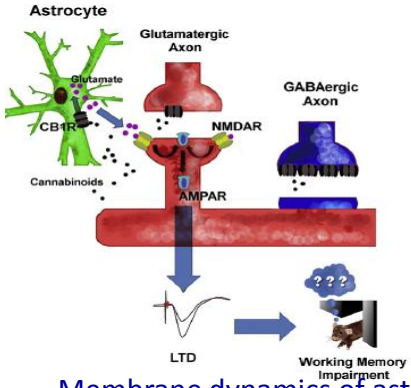
Subproject 1. Patho-Dyn-Syn

Mechanisms and patho-physiological consequences of the dynamic organization of synapses

- 95k€/year
- Coordinators: V. Nägerl and S. Oliet
- 13 participating teams, 1 associated team
- **Understanding of the dynamic processes at synapses underlying brain plasticity utilizing cutting edge dynamic imaging and physiological techniques**

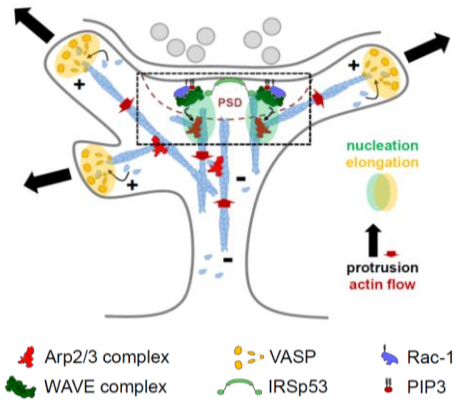
Morpho-functional plasticity of the tripartite synapse
*Marsicano (**Addiction**), Nägerl (**Imaging**), Oliet (**Physiology**)*

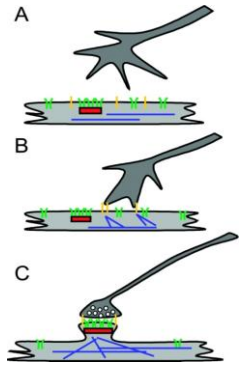




Membrane dynamics of astrocytic glutamate transporter and its functional impact on synaptic functions
*Groc **(imaging),** Oliet **(Physiology)***

Impact of Planar Polarity on shaping neurons and synapses
*Montcouquiol/ Sans (**cellular biology**), Thoumine/ Giannone (**cell biophysics**)*



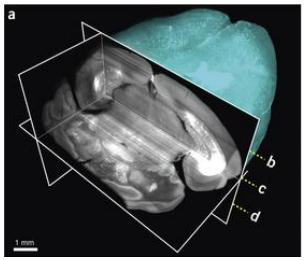


Chem. Rev. **2008**

Subproject 2. Ipsynet

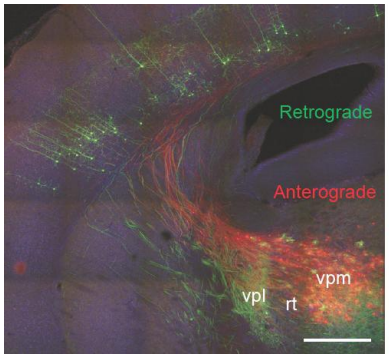
Integrative physiology of synapses and neural networks

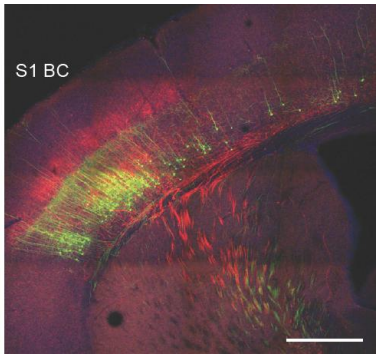
- 95k€/year
- Coordinators: C.Mulle, J.Simmers (TBR)
- 10 participating teams, 4 associated teams
- **Providing a comprehensive understanding of the design and functional dynamics of selected neural circuits**



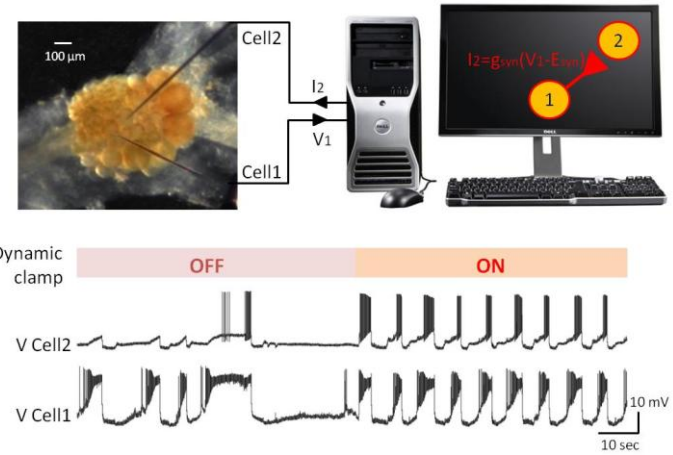
Unraveling the anatomical wiring diagram to understand the physiology and pathophysiology of the hippocampus and neocortex

*Mulle (**hippocampal circuits**), Frick (**viral tracing methods**)*





New Ultramicroscope bought by the BIC



Programing support for hybrid systems applications
Simmers (electrophysiology), Lemasson (neuro-interface technologies), Cattaert (modeling)

Subproject 3: MAD

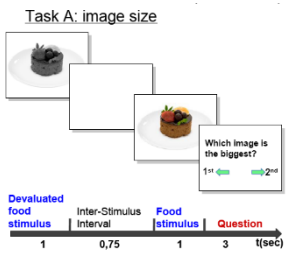
Molecular Basis of the Transition to Addiction

- 95k€/year
- Coordinators: P.V. Piazza, V. Deroche
- 11 participating teams,
- **Identifying the biological basis of the "addiction prone" phenotype that in some drug users triggers the transition to true addiction characterized by a loss of control of drug intake.**

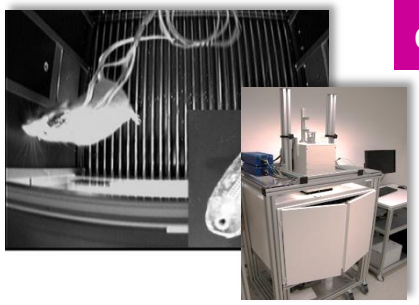
Psychobehavioural characterization of addiction

Mesures of motivational and hedonic states in humans *(Philip, **clinical**, Cota **physiology**) and in rats (Cador, **behavior**).*

Alterations in learning strategies associated with drug addiction *(Deroche /David, **behavior,** Piazza, **psychopharmacology**)*



Characterization of neuronal circuits involved in addiction

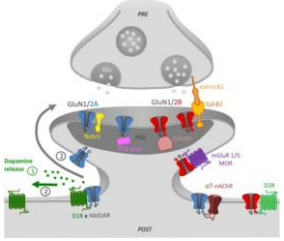


Specifying the brain circuits involved in pathological incentive responses and the loss of control over drug taking during the development of addiction *(Deroche **behavior,** Herry **optogenetic**)*

Probing the role of dedicated valuation neuronal circuits in the development of pathological decision making in addiction individuals (Ahmed **behavior**)

Characterization of molecular pathways involved in vulnerability to drug addiction

Montcouquiol/Sans (**biochemistry**), Groc (**imaging**)



Subproject 4. IThera-AMC

Transversal pathophysiology and innovative therapeutics for Aging, Memory and Cognition

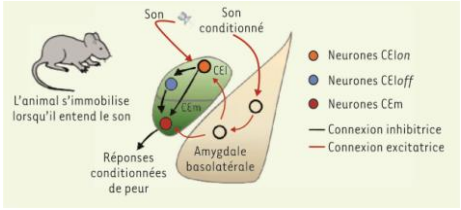
- 95k€/year
- Coordinators: B. Bontempi, J.M. Orgogozo
- 8 participating teams, 9 associated teams
- **Phenotyping relevant memory and cognition disorders associated with ageing in a multi-dimensional way in order to propose innovative therapeutics based on these categorizations.**

DIPPAL: Early diagnosis and pleotherapy of Alzheimer Disease

*Orgogozo, Philip (**clinical**), Bezard (**physiopathology**)*

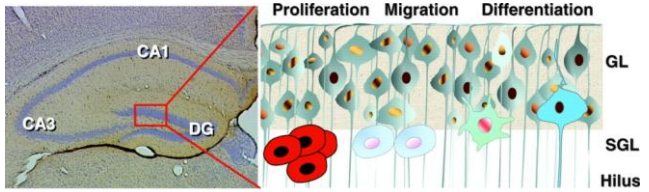
Functional contribution of newly born neurons to the formation of remote memories during normal aging

*Abrous (**neurogenesis**), Bontempi (**memory**)*



Translational study of the cerebral substrates involved in pathological fear recovery

*Herry (**optogenetics**); Bonnet (**medical imaging**)*



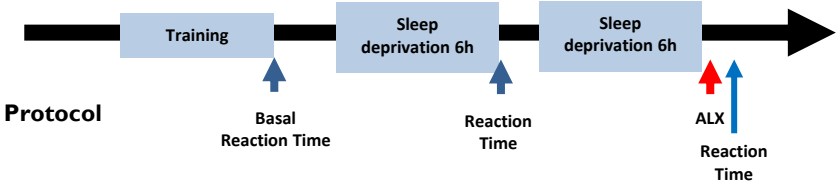
Subproject 5. ITHERA-MSA

Transversal pathophysiology and innovative therapeutics for Motor, Sleep and Attention disorders

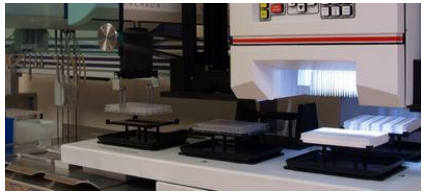
- 95k€/year
- Coordinators: E. Bézard, P. Philip
- 7 participating teams, 8 associated teams
- **Phenotyping relevant motor, sleep and attention disorders in a multi-dimensional way in order to propose innovative therapeutics based on these categorizations.**

Sleep, Cognition and Alzheimer
*Philip (**clinical**)*

Does the orexin system contribute to individual differences in sleep deprivation-induced changes in neurobehavioral function?
*Philip (**clinical, sleep**), Layé (**pre-clinical, behavior/molecular &cellular biology**)*



Establisment of a biological ressources collection
*Meissner (**MSA patients recruitment**); Philip (**clinical tests**)*



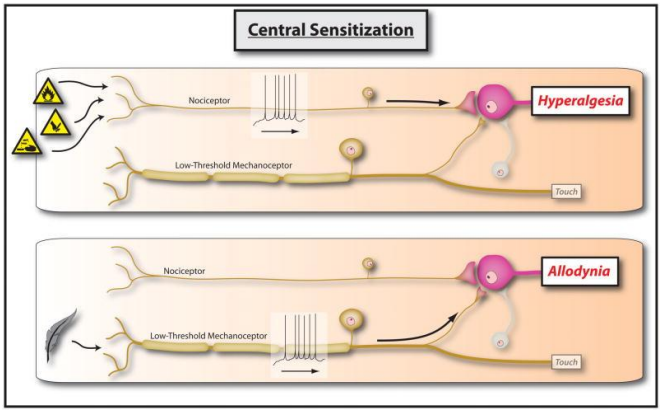
Study of miRNA expression pattern as diagnostic and prognostic biomarker in Amyotrophic Lateral Sclerosis
*Favereaux **(miRNA screening) ;** Le Masson **(clinical)***

Non thematic projects

- 163k€/year
- All Bordeaux Neurocampus teams (46)
- **All the scientific topics aiming at improving our knowledge in neuroscience**

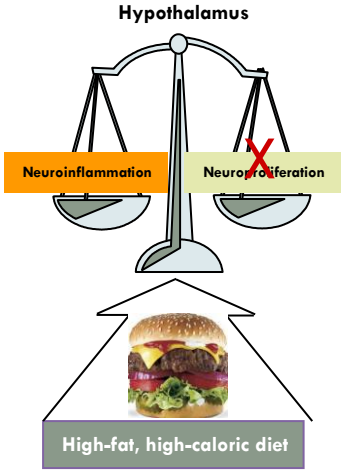
Deciphering the mechanisms of central pain sensitization in vivo using innovative heat-shock local deletion of the L-type calcium channel Cav1.2 gene in the mouse lumbar bulge

*Baudet (**pain**); Fossat (**neuronal network**); Quesson (**imaging**)*



Thermo-sensitive nanoparticules as a carrier of bioactive peptide against pain sensitization

*Landry (**pain**); Heroguez **(nanoparticules**); Petry (**neuroinflammation)***



Relative contribution of the hypothalamic proliferative and neuroinflammatory responses to the obese phenotype

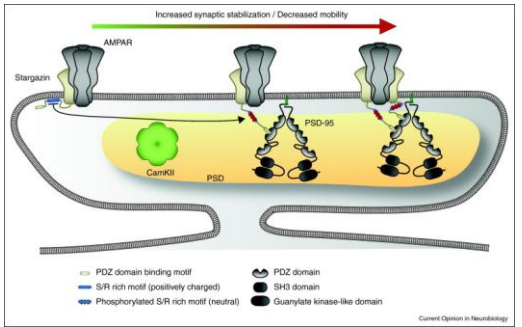
*Cota (**in vivo model**); Abrous (**neuroanatomy**); Layé (**molecular&biochemical studies**)*

The impact of structural changes in axons on information transfert in CA3 neurons: a combined computational and nanoscale imaging study

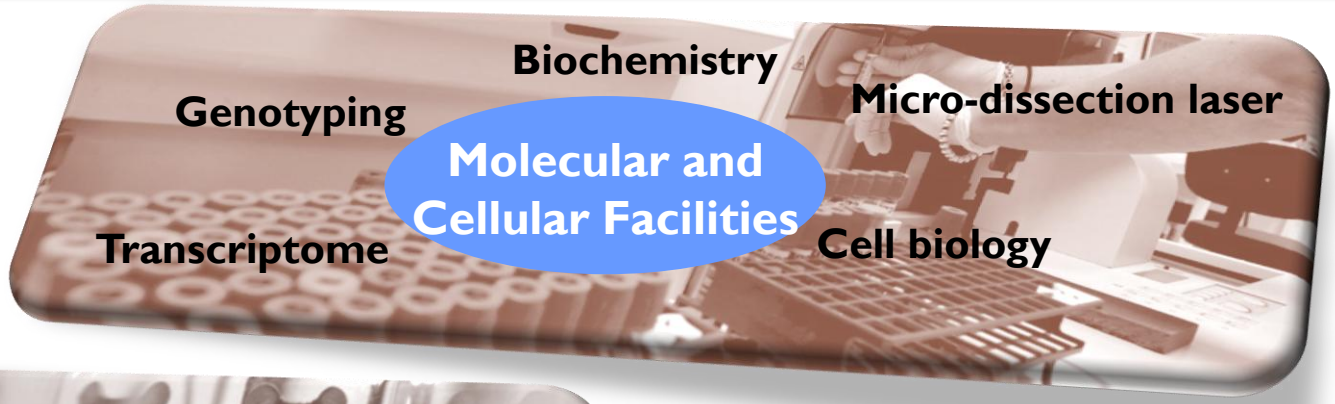
*Cattaert **(neuron simulation);** Nagerl **(imaging)***

Determining the mode of binding of PSD-95 tandem PDZ domains

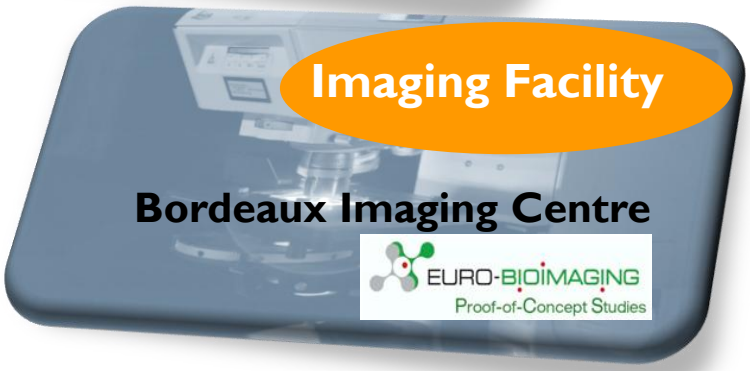
*Sainlos (**synthetic ligands**); Mackereth (**NMR spectroscopy**)*



Facilities over the first 2 years



900k€/year



Open to all Bordeaux Neurocampus
Decrease access costs from 30 to 50 %

PhD Extention Grant

250k€/year

- A scholarship offered to complete Ph.D thesis, either before or after defense
- **Rapid process:** 1.5 month from call launching and funding decision
- **Fair evaluation:** independent evaluation by all the steering committee members, except when the candidate is from a member's institute and final selection in plenary session

2012: 14 submitted, 5 selected
2013: 28 submitted, 8 selected

Open to all Bordeaux Neurocampus teams

Symposium/Summer School

100k€/year

5-10 symposium supported each year
1 summer school

100-400 international attendants

2/3 international speaker

Impact on Publications

- **120** publications in 2013 (Labex Teams)
- 35 papers in journal IF>7, included 14 papers in journals IF>10
- Miles stones publication in
  - **Addiction**

    Discovery of a negative feedback loop protecting the brain from cannabis intoxication. This could open an unforeseen approach for the treatment of cannabis. **Science 2014**
  - **Synapse morphology**

    Discovery of a novel structural mechanism by which neurons can rapidly tune their synapses in response to stimulation. **Nature Neuroscience 2014**
  - **Psychiatric disorders**

    Persistent fear behavior, which is at the core of psychiatric conditions such as anxiety disorders, might be finely regulated at the level of specific prefrontal inhibitory circuits. **Nature 2013**

Ripple effect

In 2013 (Labex teams):

- **3M€** additional grants obtained as co-funds for the 22 scientific projects:
  - 4 ANR, 1PHRC, 2FRM, 2 FFAS, 1 mexican post-doc grant

- Total of co-funds obtained: >**10M€**

SWOT: 1- Strengths-Weaknesses

Strengths

Integration:

- Increased intra-LabEx collaborations : from 10 (2012) to 25 (2013) co-Publications
- New collaborations between basic and clinical teams
- Speeding up Bordeaux Neurocampus dynamic

Attractiveness:

- 45 post-doc, international 50%
- 16 symposia in Bordeaux each year, 100-400 international attendees, 2/3 international speaker

Excellence:

- Facilitated access to high-end facilities
- Success of the PhD extension grant

Weaknesses

- No creation of new teams
- Multiple communication action, lack of a global strategy
- Multiple governance authorities in Bordeaux Neurocampus
- No international PhD program
- No specific transfer program

SWOT: 2- Opportunities, Threats

Opportunities

- Increase capacity: the Neurocampus Project: 75 M€ (delivery in 2016)
  - To build 10 000 m² of new lab space
  - To rationalize animal facilities and the imaging center
- Bordeaux School of Neuroscience, opening 2015
  - Unique hands on training center in Europe,
  - Partnership with IBRO and FENS
- BIC as a European level facility
- IdEx support for inter-labEx collaborations and attractiveness program
- CPER
- Investment fund

Threats:

- Decrease in local and national support
- Unbalanced focus on applied research from governing bodies

Strategy-1

Depending on SAB, pursue successful programs and steer towards more call for projects

- Non thematic call for projects, phD extension grants, facilities, symposium

Reinforce the potential and KETs by attracting New Teams:

- Packages to attract 6-8 new and/or emerging team:
- 1,8 M€ from LabEx BRAIN (+7 M€ Neurocampus)
- Excellence first, and trying to fill gaps (e.g. In vivo imaging, Development, model organisms, clinical research, Physical chemistry, Biosensors)
- Reinforce the ripple effect of BRAIN and adapt its perimeter to the evolution of the community

Reinforce innovative and transversal projects

- Stimulate multidisciplinary inter labex programs with Laphia, CPU, TRAIL: e.g. ExtraBrain
- Develop new facilities (Protein production, Stem cells, Optopath/phenovirt)
- Stimulate Translational programs by increasing clinician – basic scientist contacts

Strategy-2

Increase European visibility and training:

- The Bordeaux School of Neuroscience and BIC
- Increase presence at carreer fairs
- Reinforce links with patient associations, Identify representative icones
- Lobby for improved governing bodies awareness on neuroscience

Attract new funds

- Develop a strategy for better communication and fund raising
- Reinforce access to European funds
- Structure interactions with venture capital