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Neuroscience :
Frontier science of the XXI century

The House of Parliament
Ulaanbaatar, September 24, 2018

- Discoveries about the Brain : some milestones
- The importance of basic research
- What is coming up in Neuroscience
- Translational Research
- Innovation
- International Collaboration :
  IBRO

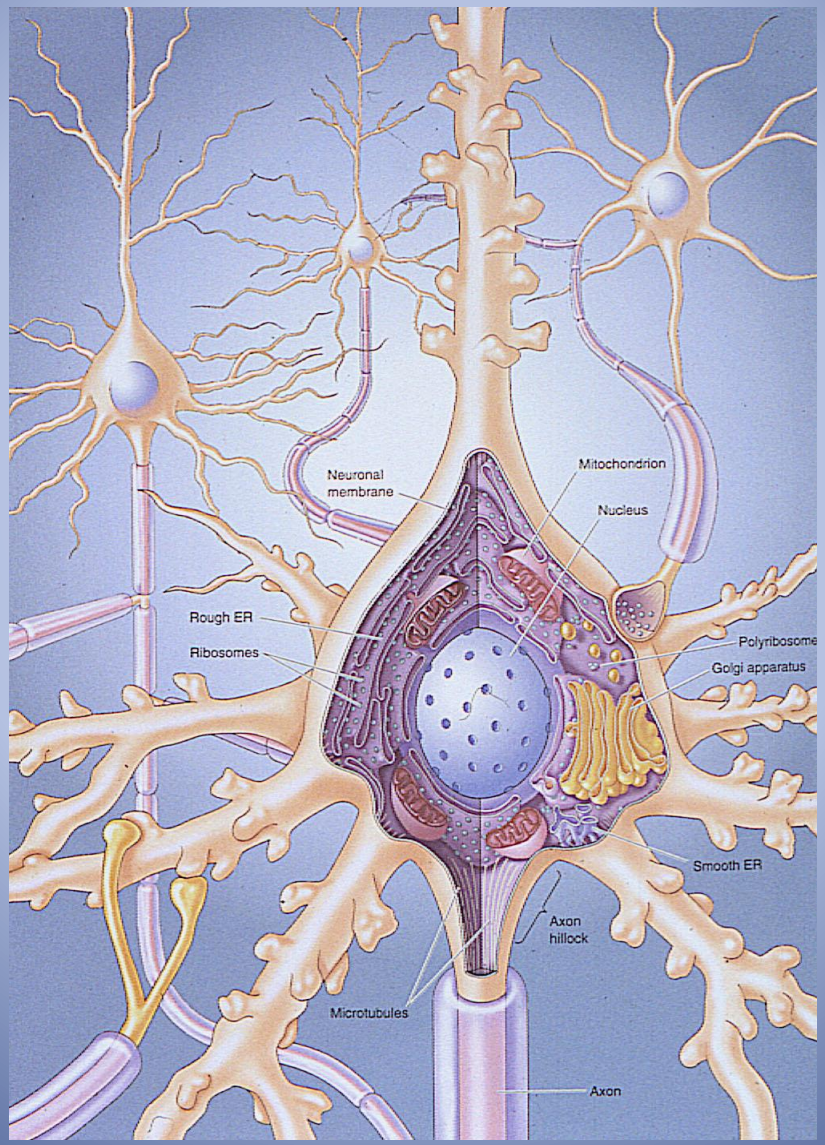
100 billion neurons !

that communicate through

1000’000’000’000’000

synapses!

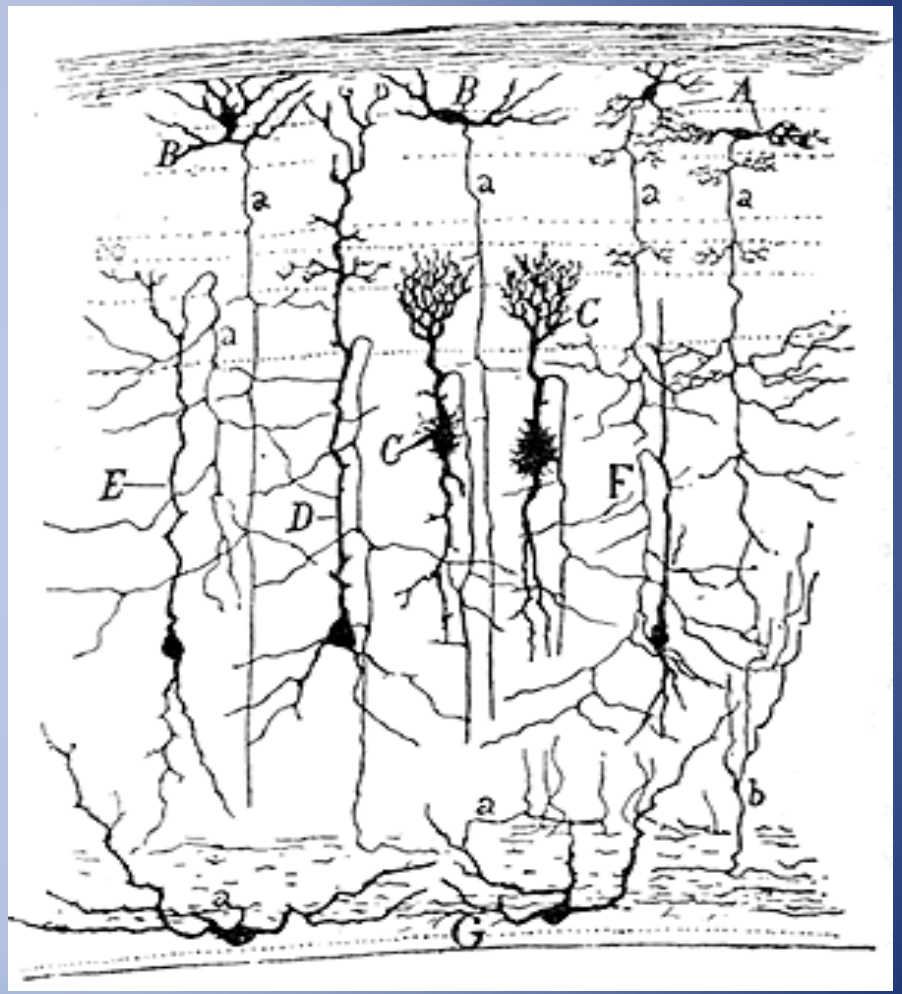
Neurons


Neuronal membrane
Mitochondrion
Nucleus
Rough ER
Ribosomes
Polyribosome
Golgi apparatus
Smooth ER
Axon hillock
Microtubules
Axon

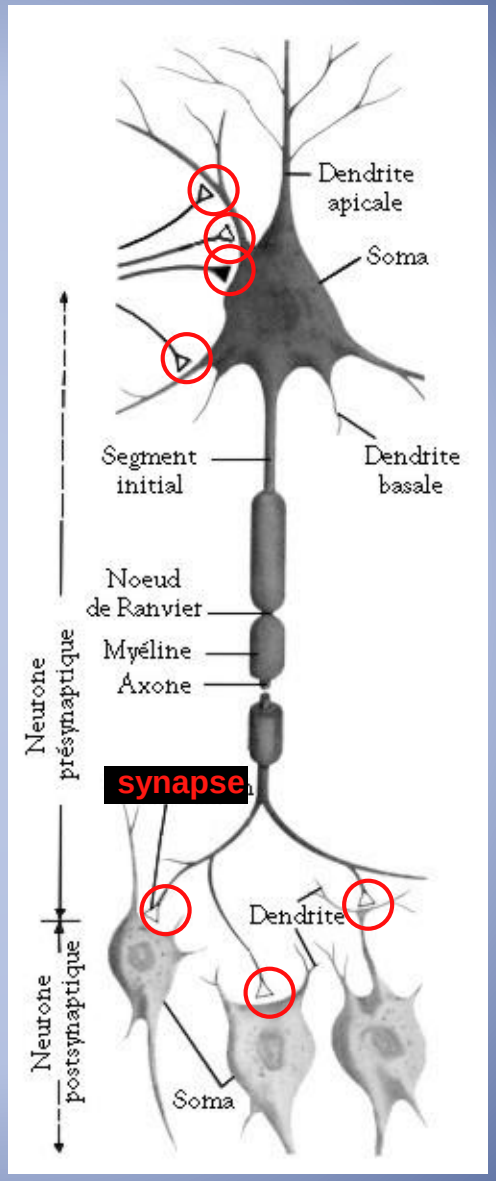
The butterflies of the soul

Santiago Ramon-y-Cajal
(1852 – 1934) Nobel Laureate in 1906

« Like the entomologist in search of colored butterflies,
my attention has chased in the garden of the gray matter, cells with delicate and elegant shapes, the mysterious butterflies of the soul, whose beating of wings may possibly one day reveal to us the secrets of the mind ».



Ramon y Cajal S.: Recuerdos de mi vida: Historia de mi labor cientifica. Alianza Editorial, Madrid, p.98-99, 1984

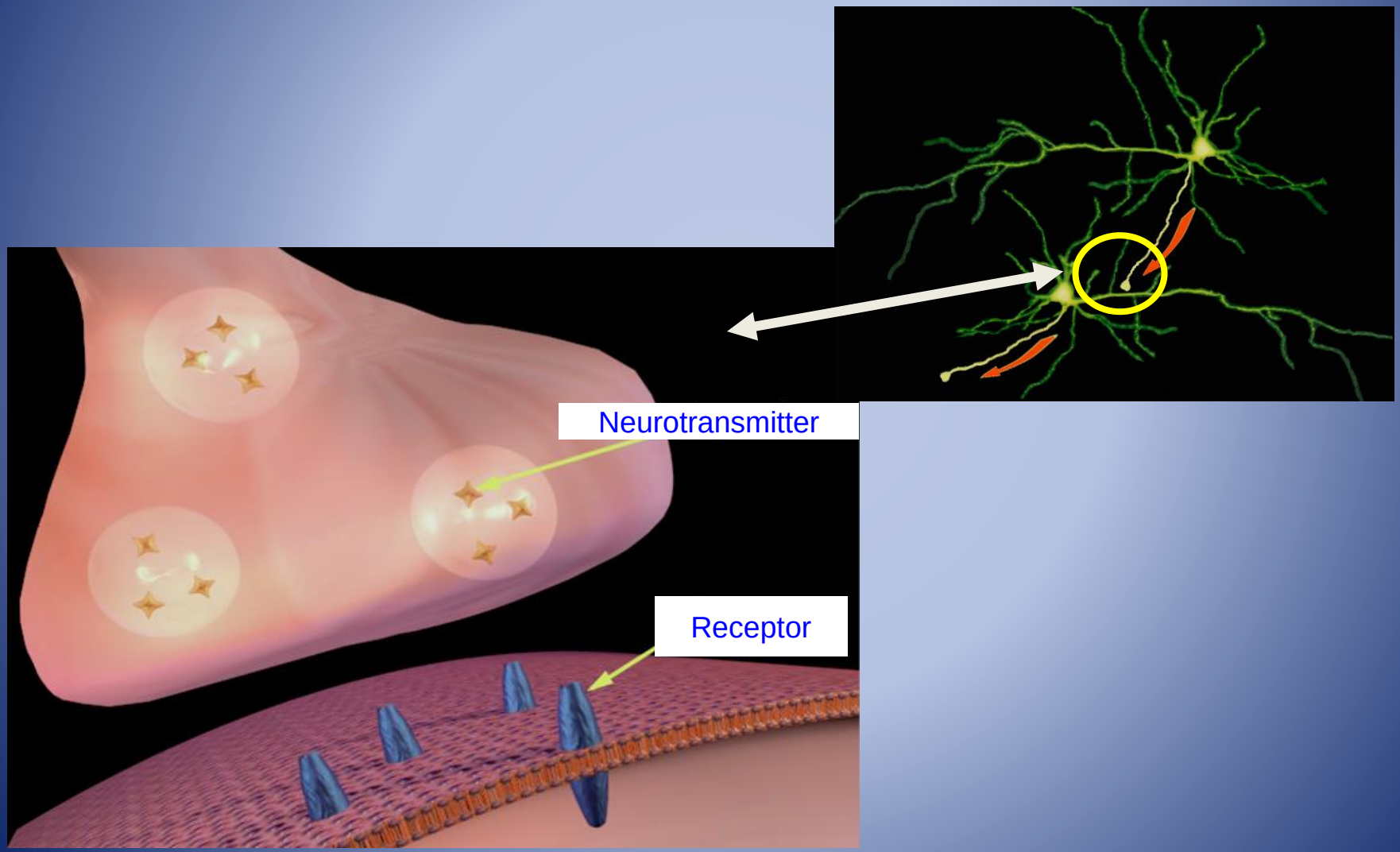


nerve impulse

A single neuron can receive up to 10'000 synapses

10^{15} synapses (1000'000'000'000'000)

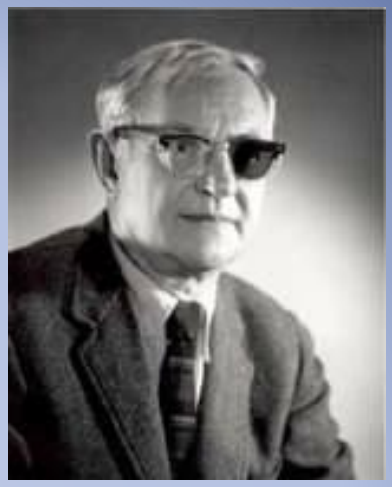
Neuron and Synapse



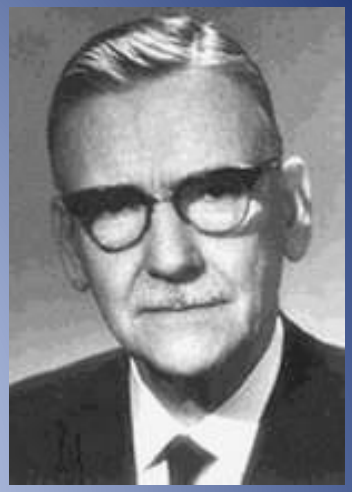
Neuronal signaling

Nobel Laureates 1970

Berand Katz

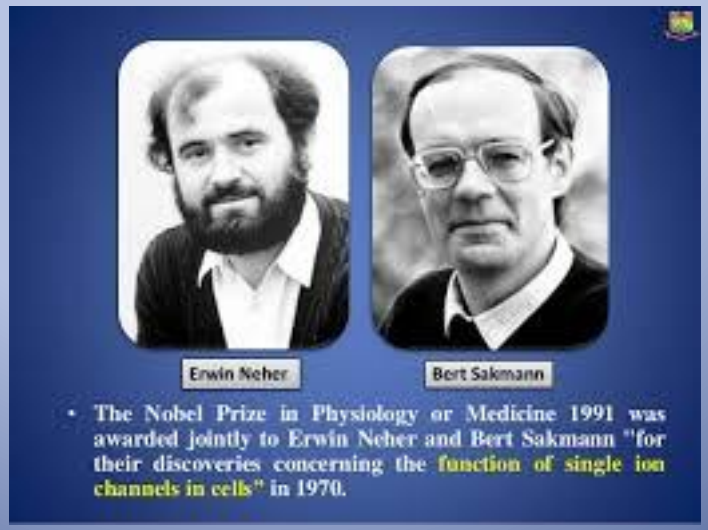


Julius Axelrod

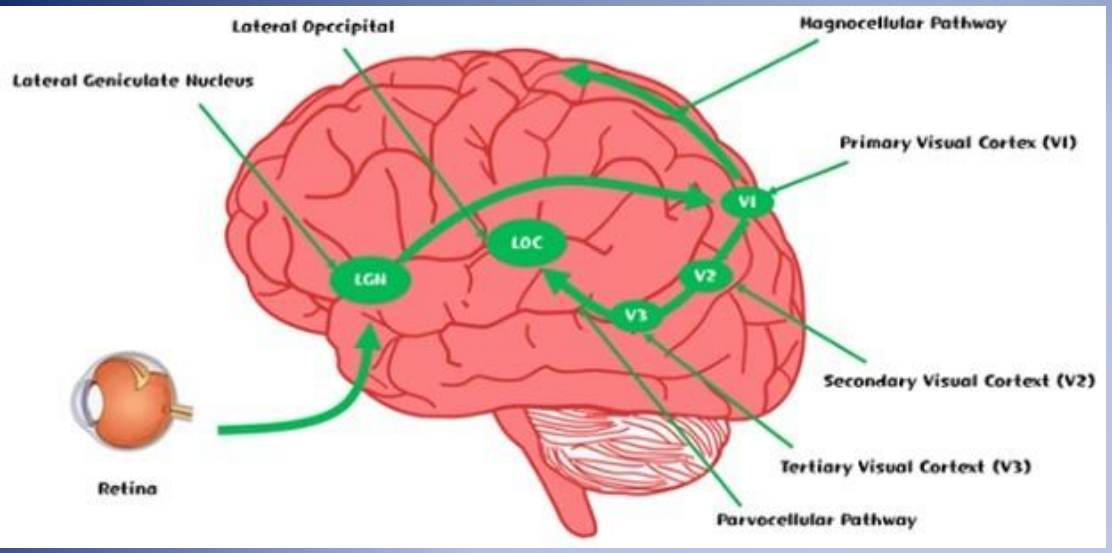


Ulf von Euler

Nobel Laureates 1991

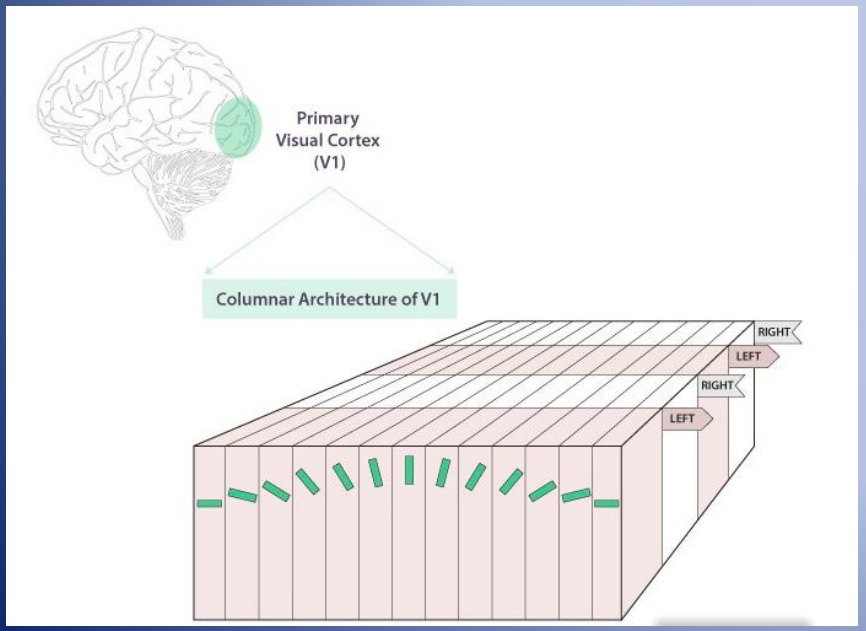


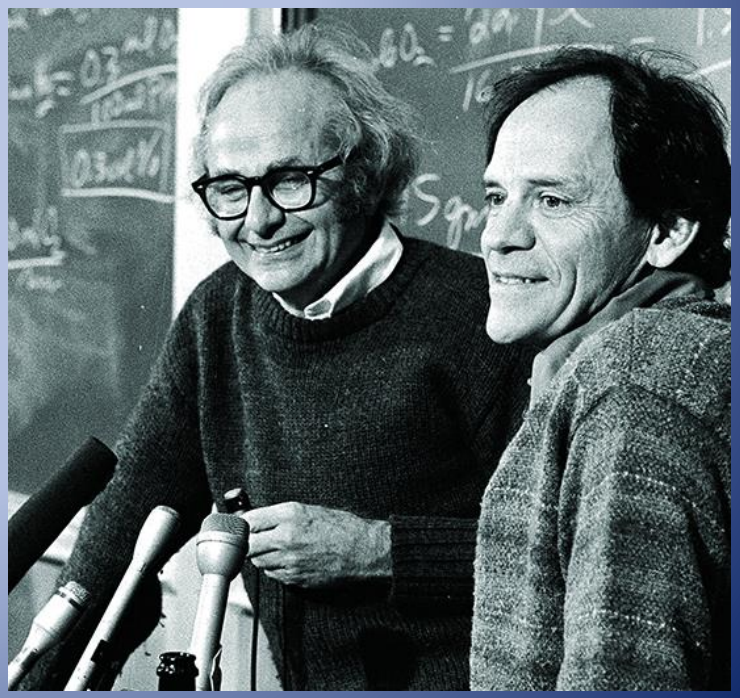
The visual system



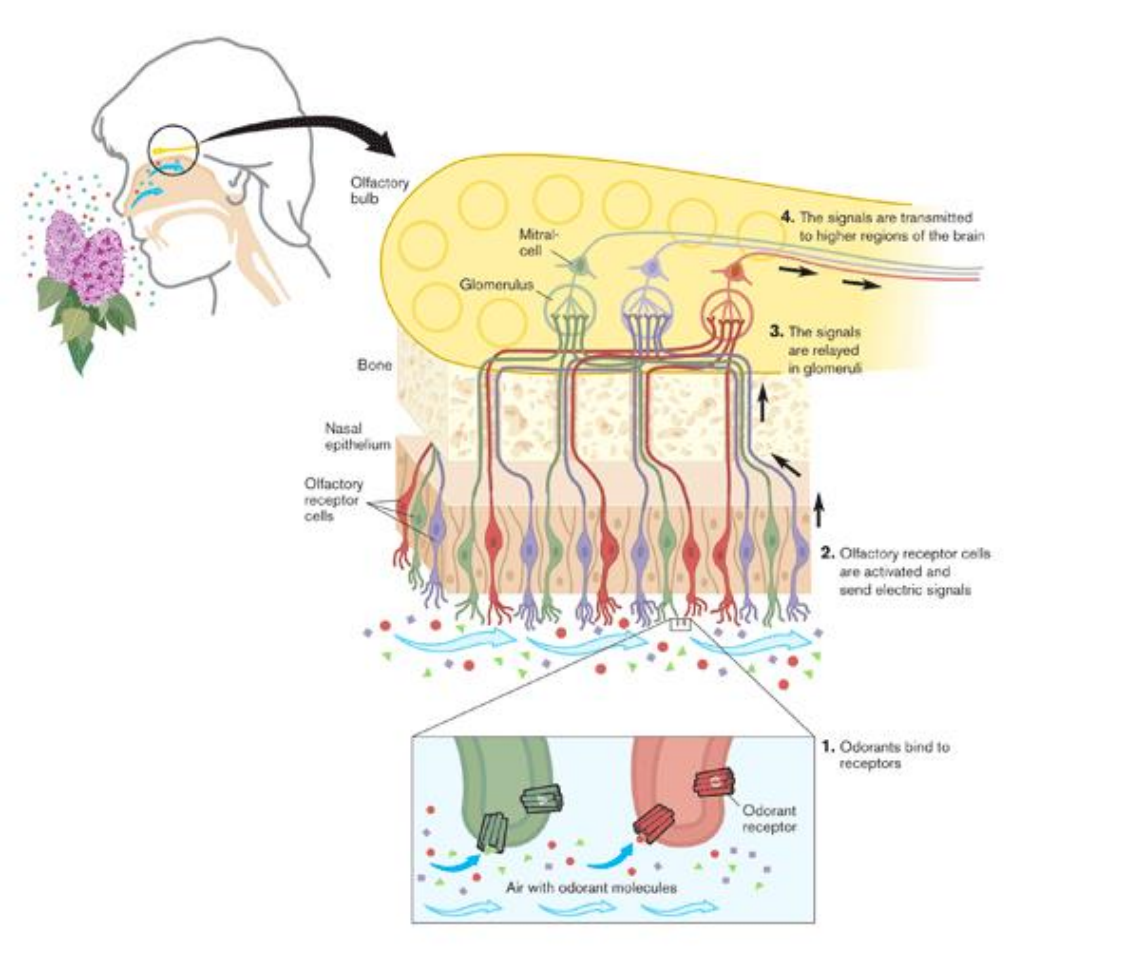
Nobel Laureates in 1981

David Hubel **Torsten Wiesel**

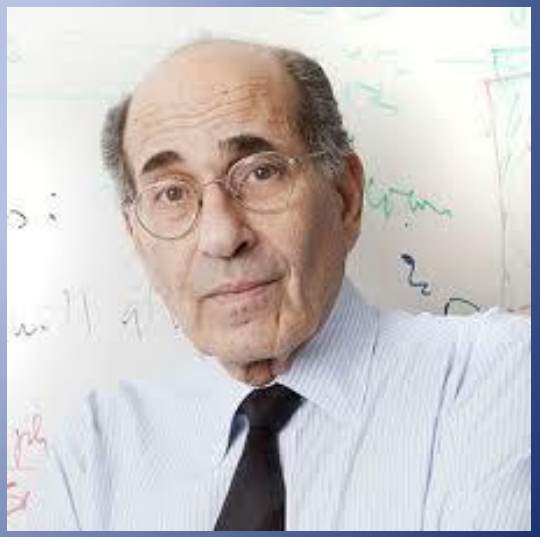




The olfactory system



Linda Buck

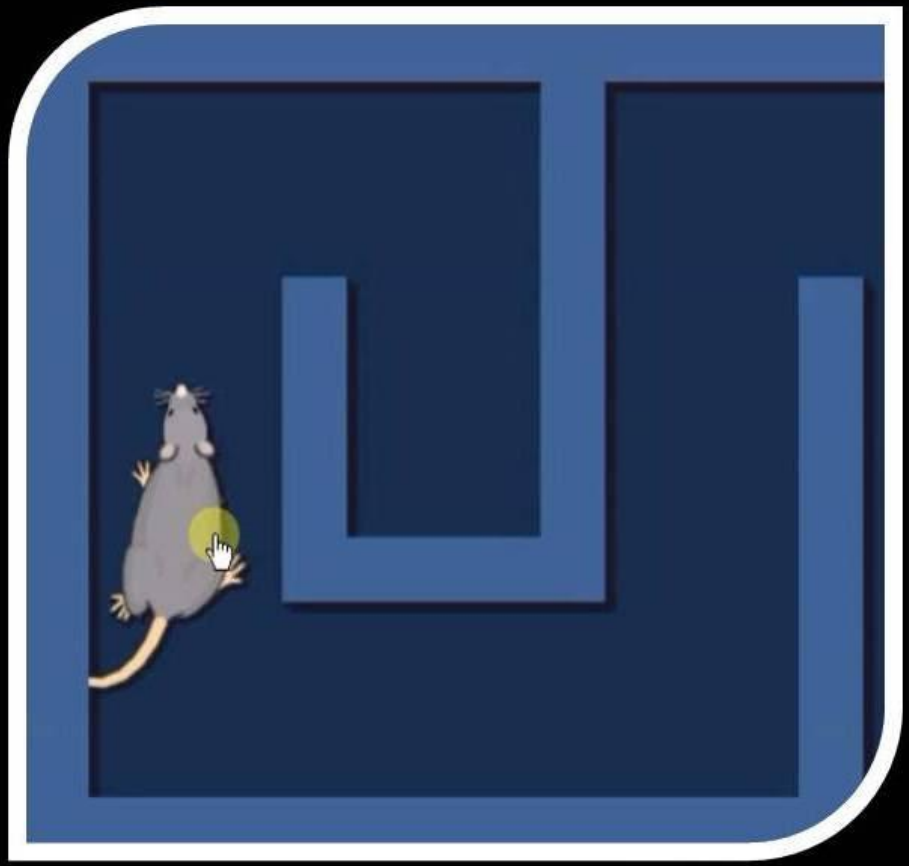


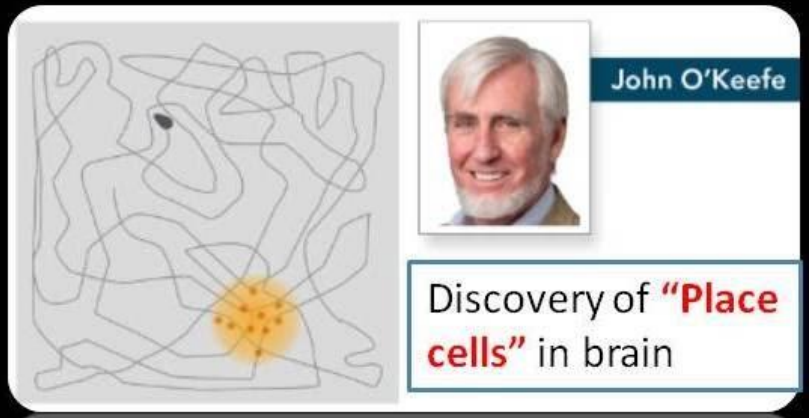
Richard Axel

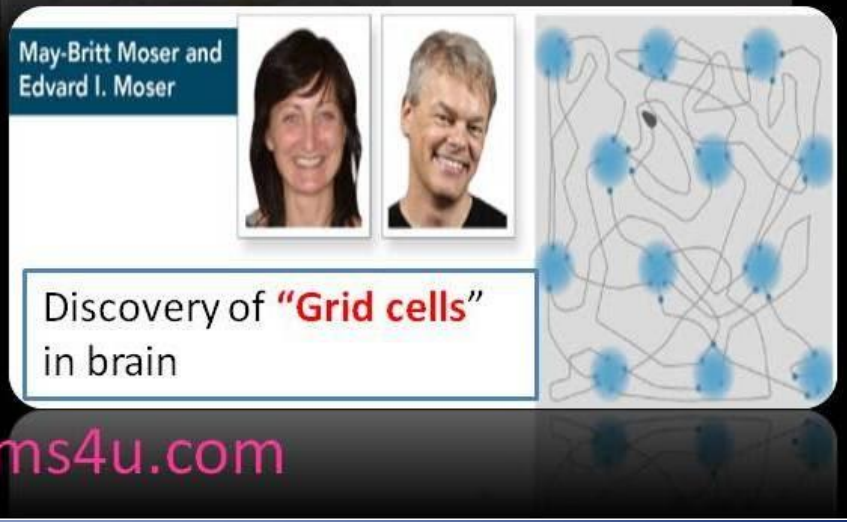
Nobel Laureates in 2004

Nobel Prize in Physiology and Medicine 2014

How we navigate & How we recollect places? What are Place cells and Grid Cells in Brain?







The neuronal networks of our brain are not rigid :
experience modifies them throughout life

Brain plasticity

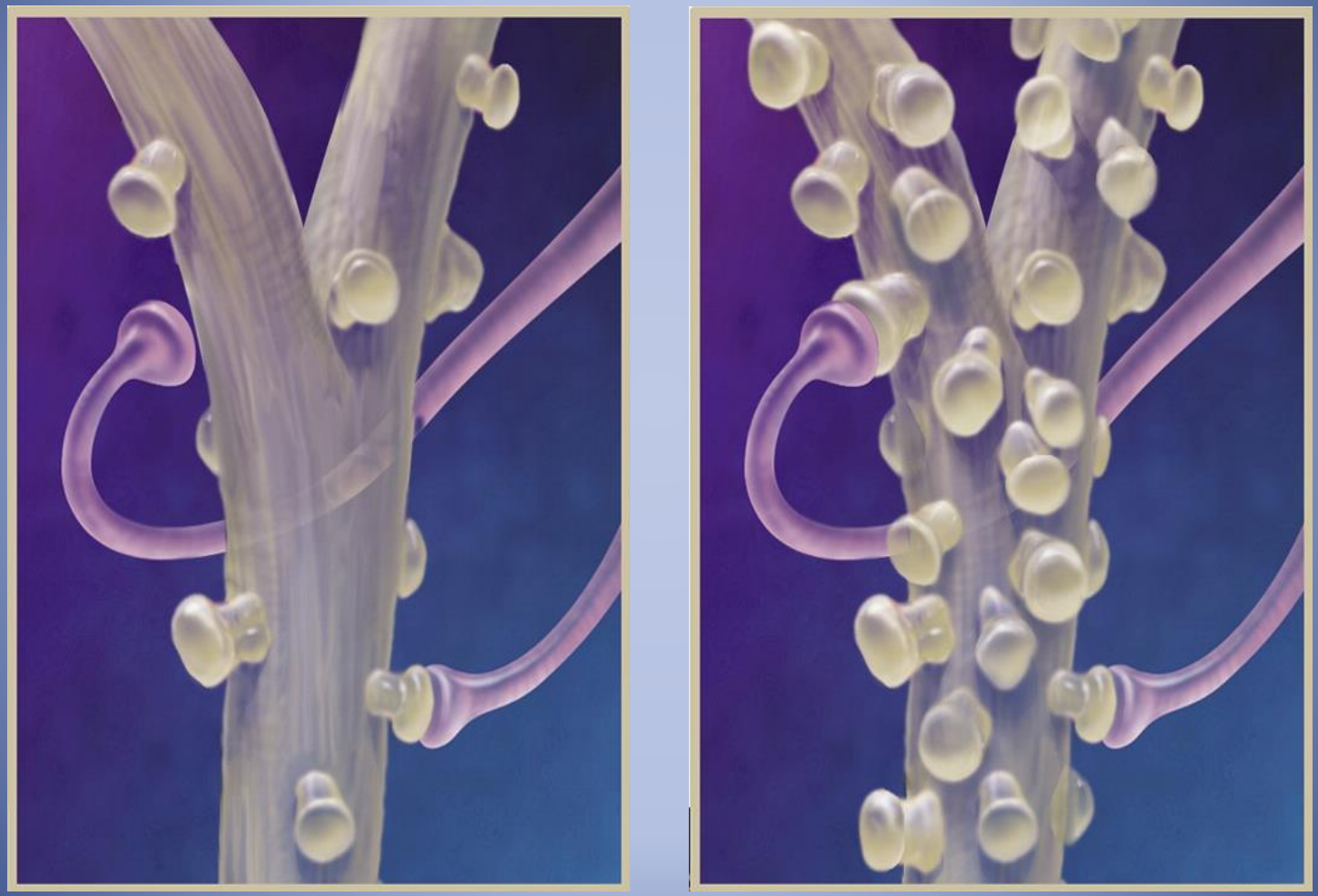
Brain plasticity

The capacity that the brain has to be modified by experience

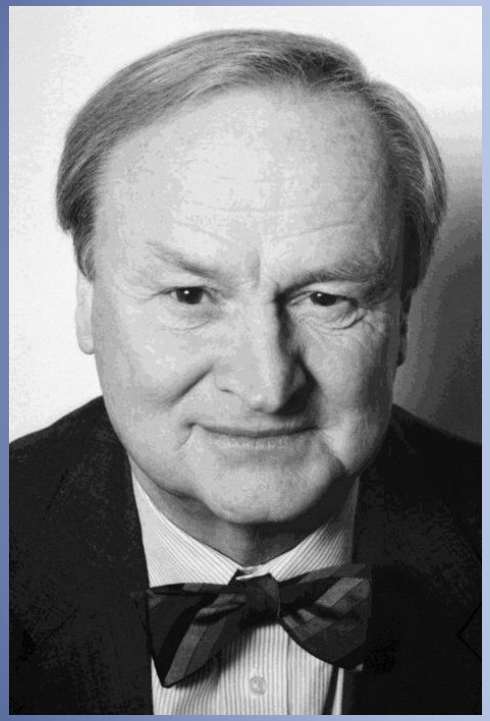
« Synaptic plasticity » - at the basis if the mechanisms of learning and memory

- *variation in the number and architecture of synapses*
- *variation in the synaptic efficacy*

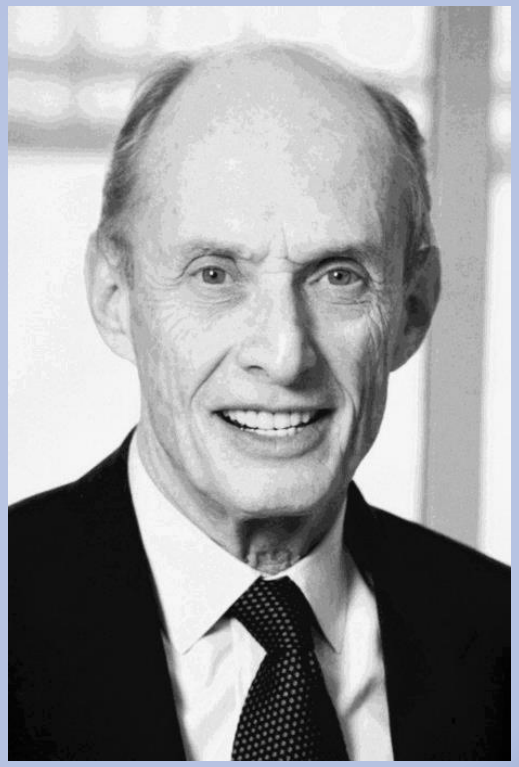
New synaptic connections are formed



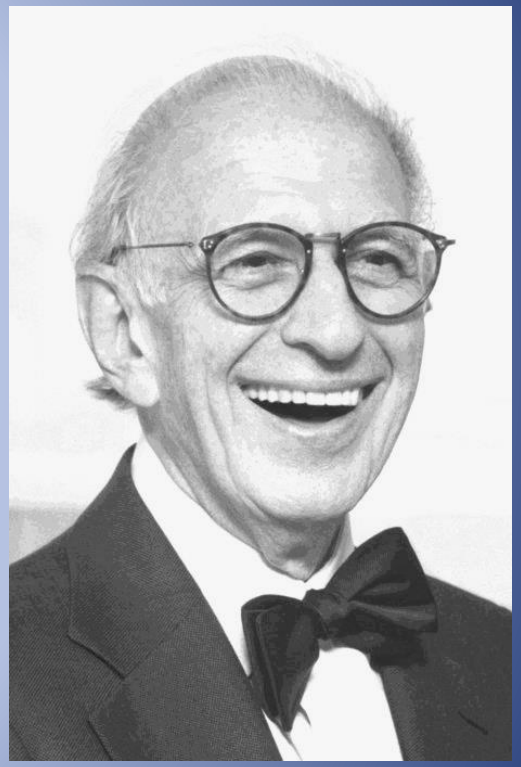
Neuronal signaling and plasticity



Arvid Carlsson



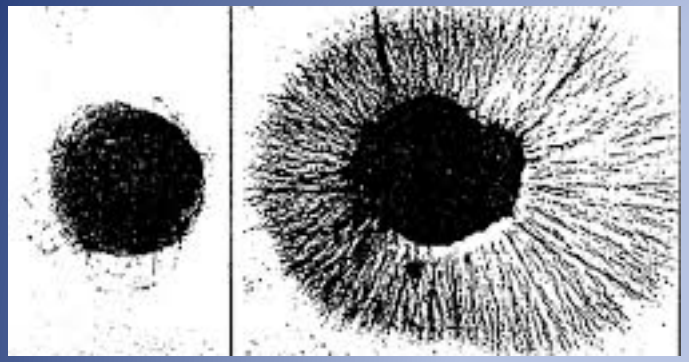
Paul Greengard



Eric Kandel

Nobel Laureates 2000

Factors that are necessary for development, plasticity and neuroprotection



Discovery of Nerve Growth Factor

Rita Levi-Montalcini

Nobel Laureates in 1986

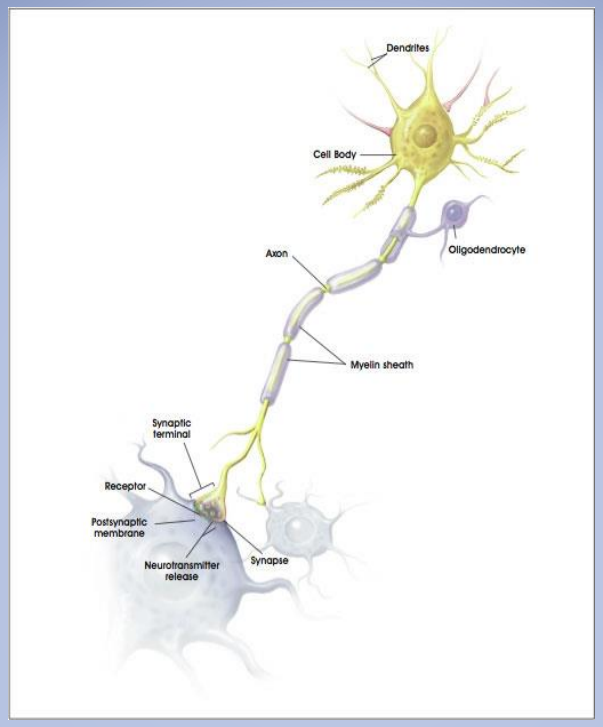
Stanley Cohen

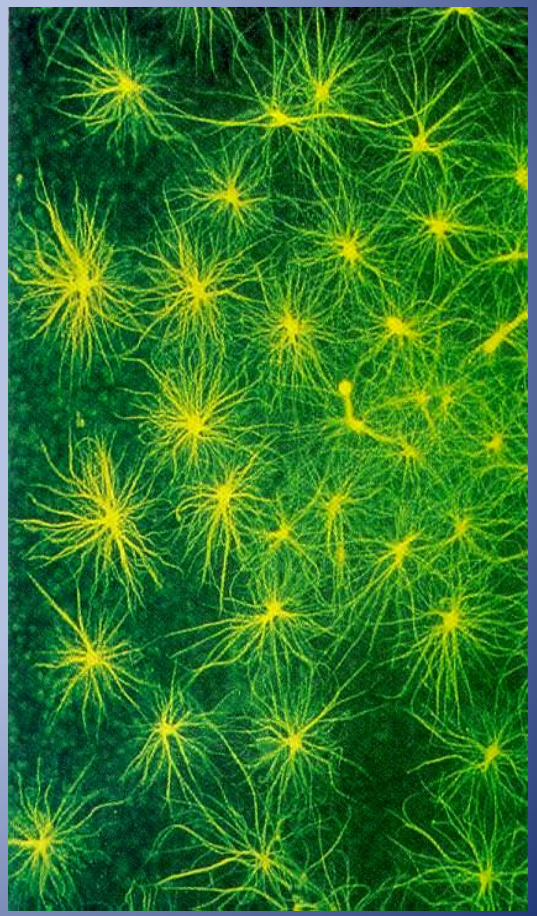
… but there are not only neurons in our brain

… the “other half of the brain” is made by glial cells

Glia : “glue” ?

Rudolf Carl Virchow
(1821 – 1902)

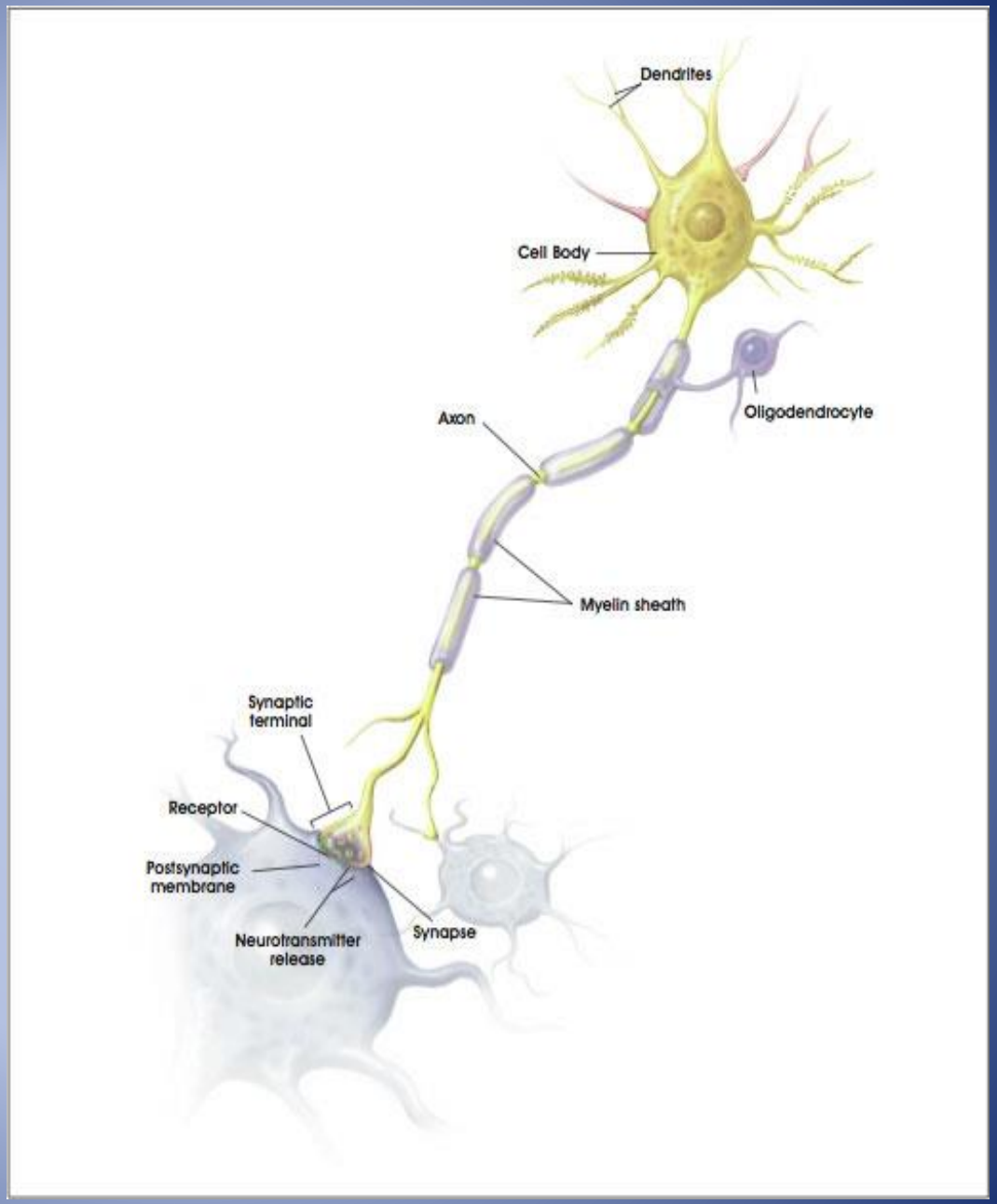




Oligodendrocytes :

Increase speed of nerve inpulse

Multiple sclerosis

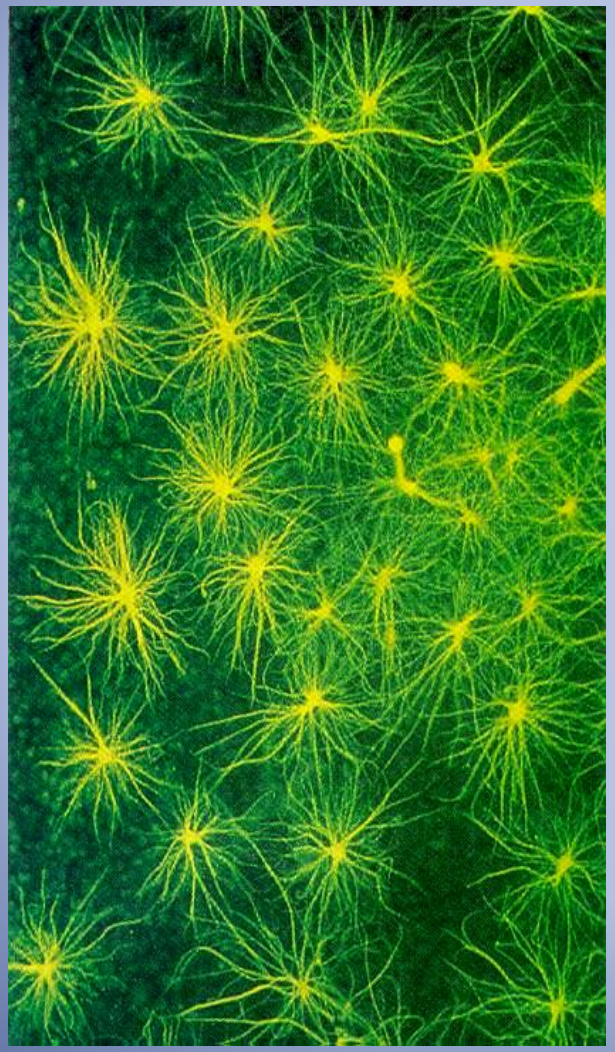


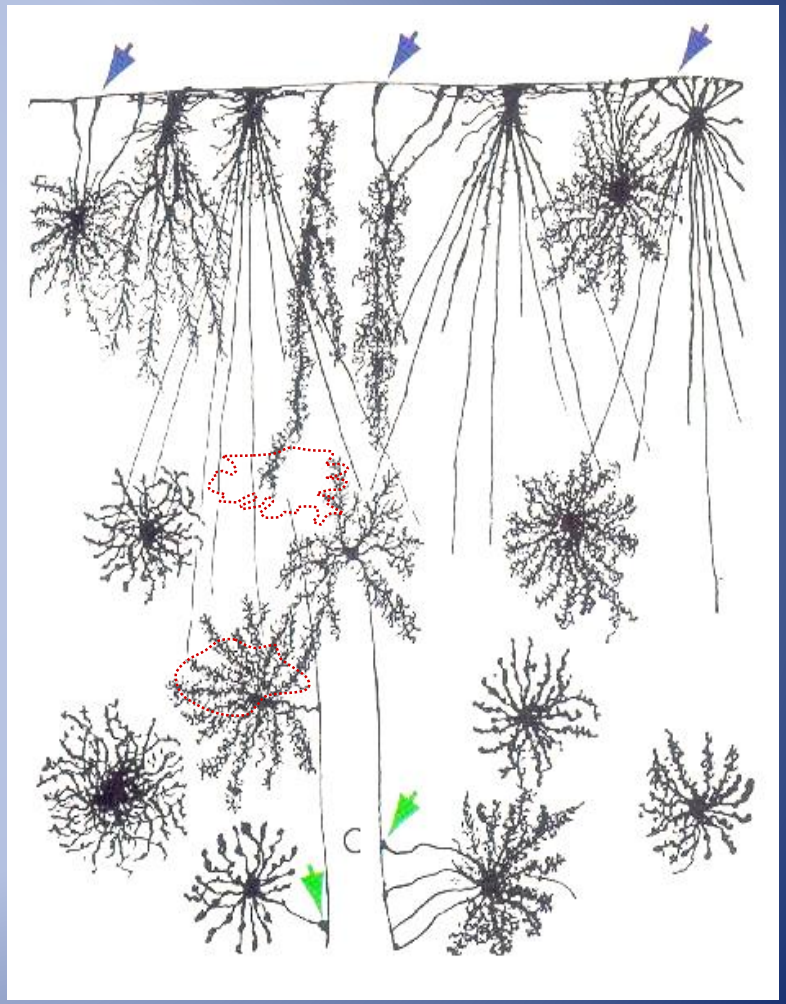
Astrocytes

Provide energy to neurons

Memory

Neurodegenerative diseases





One can see
"the brain at work"

Brain Imaging

The brain is the organ in the body that consumes more energy

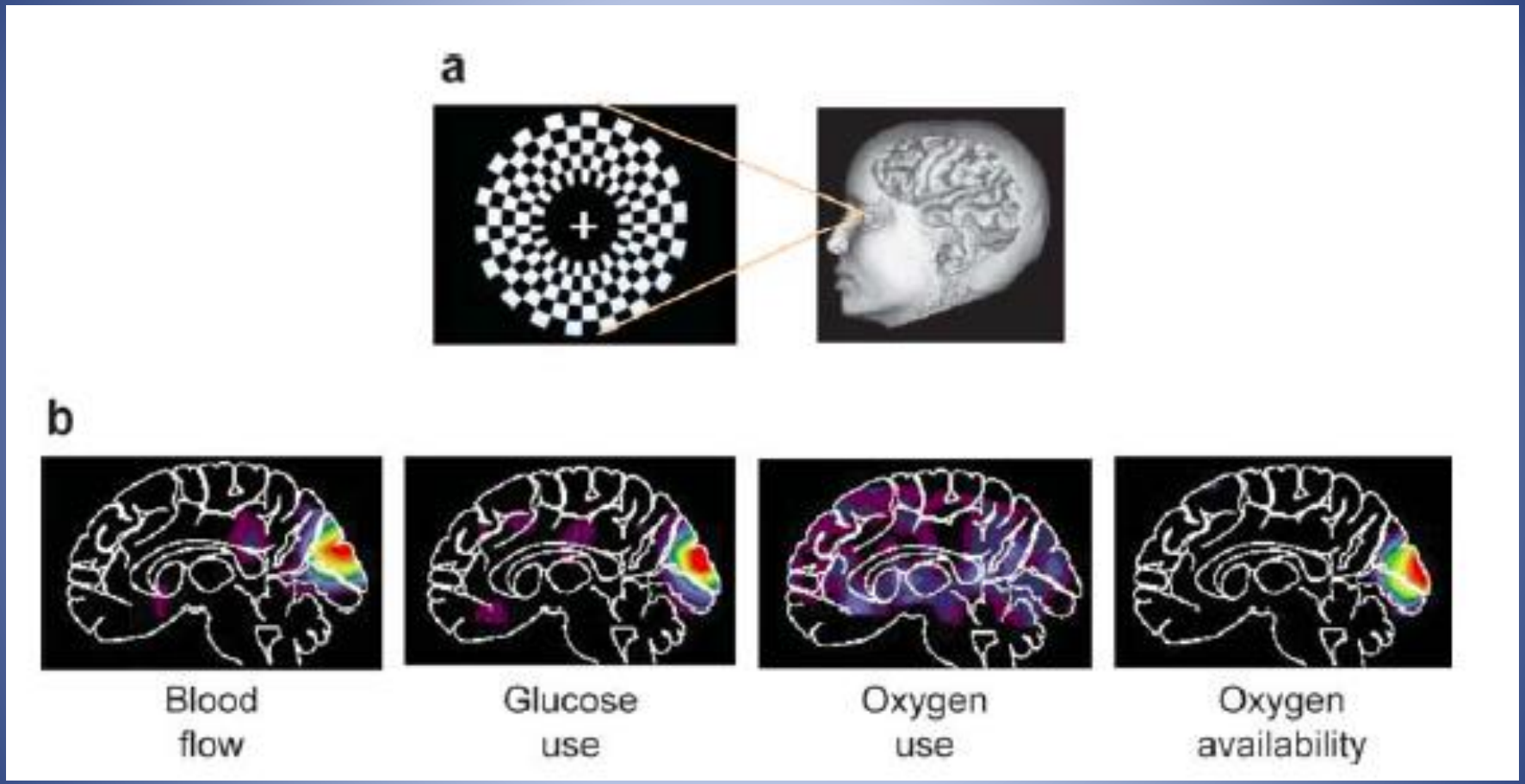
- *2% of the total body mass*

but

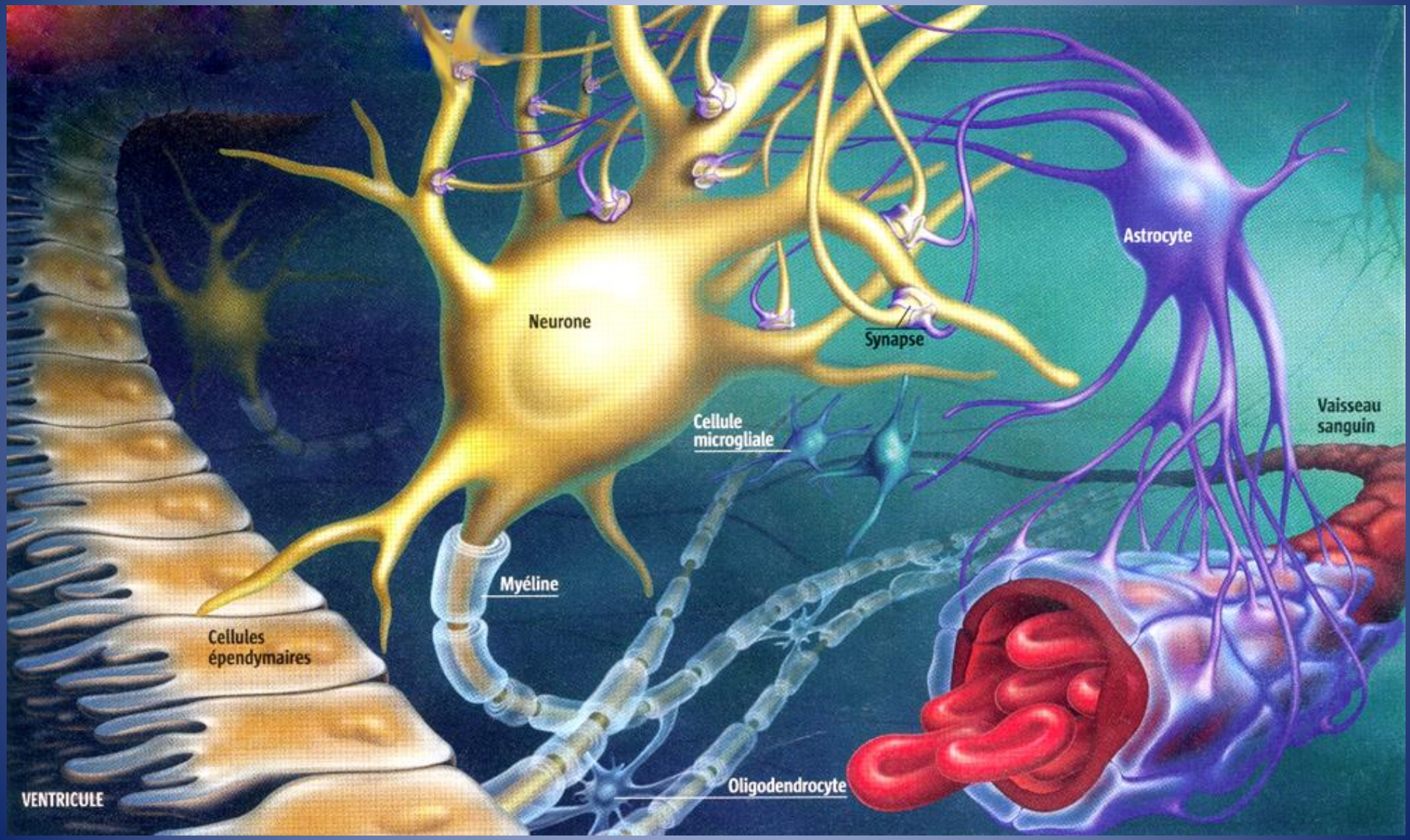
- *20% of energy consumption*

Energetically very efficient:
20 Watt

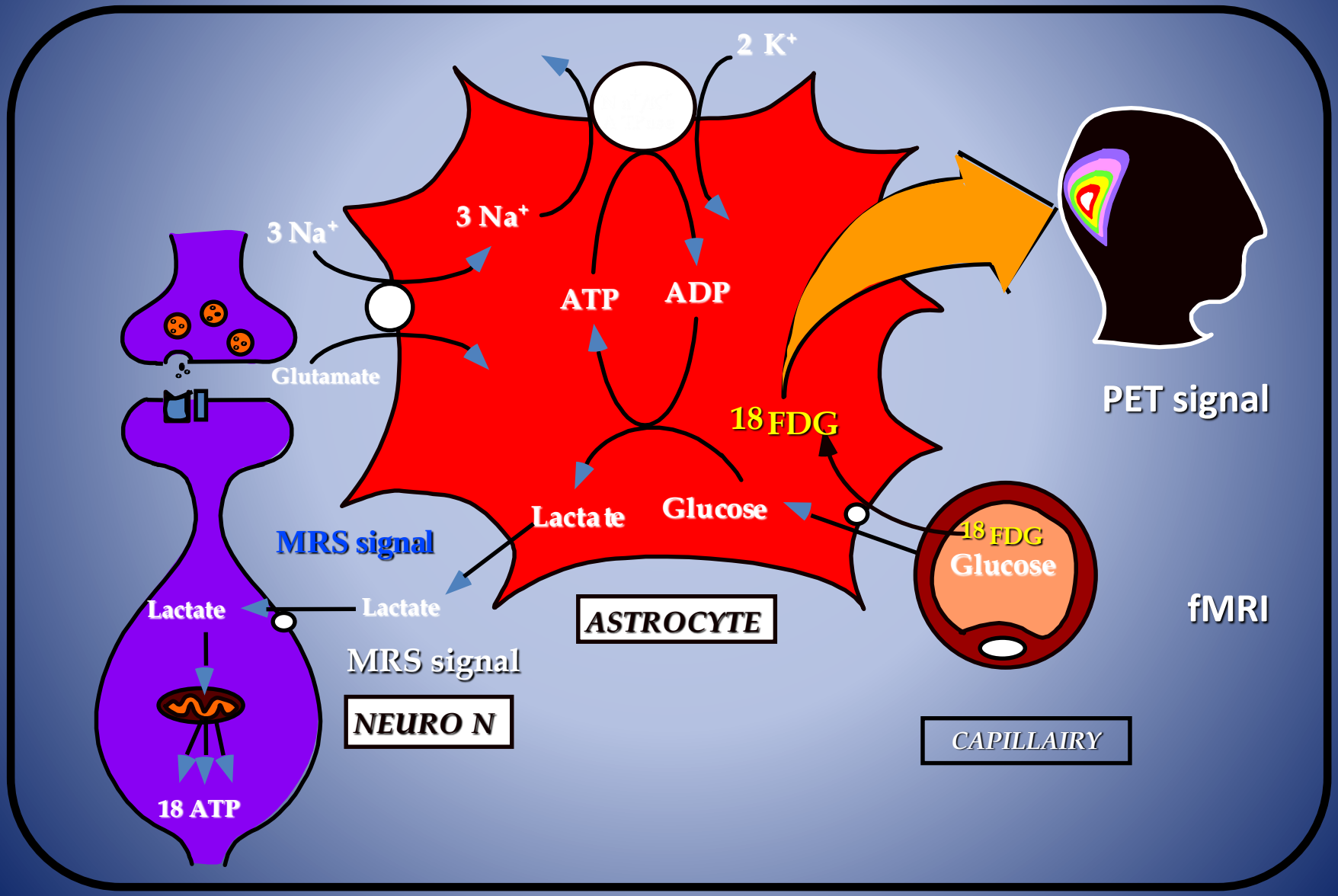
Functional Brain imaging : visual system



A dialogue between cells



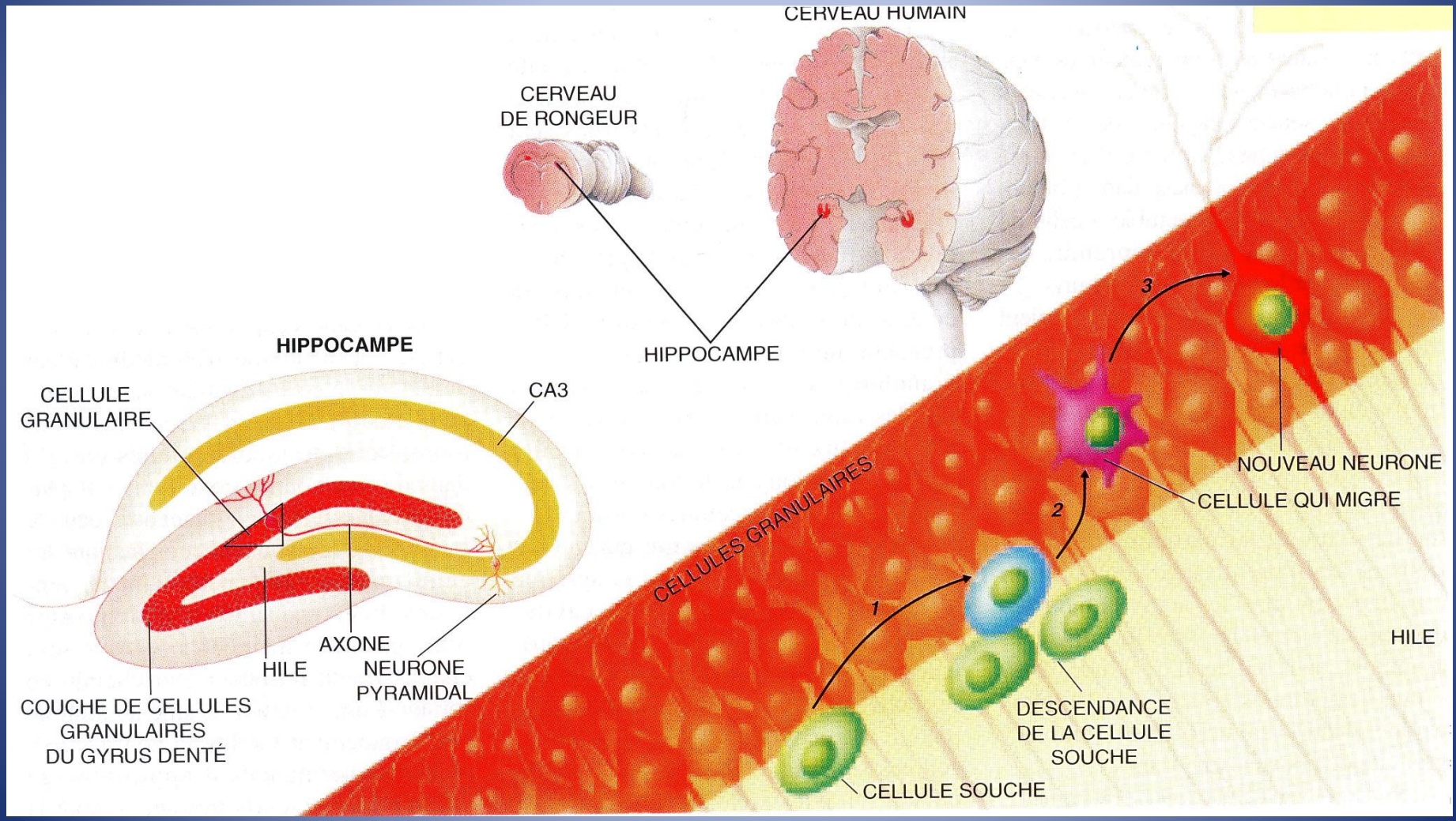
Role of astrocytes in the production of the signals detected by functional brain imaging



Our brain produces new neurons throughout life :

neurogenesis

Neurogenesis



Modulation of neurogenesis

Factors that stimulate neurogenesis

ØN eurotrophic Factors (BDNF)

Factors that inhibit neurogenesis

ØStress

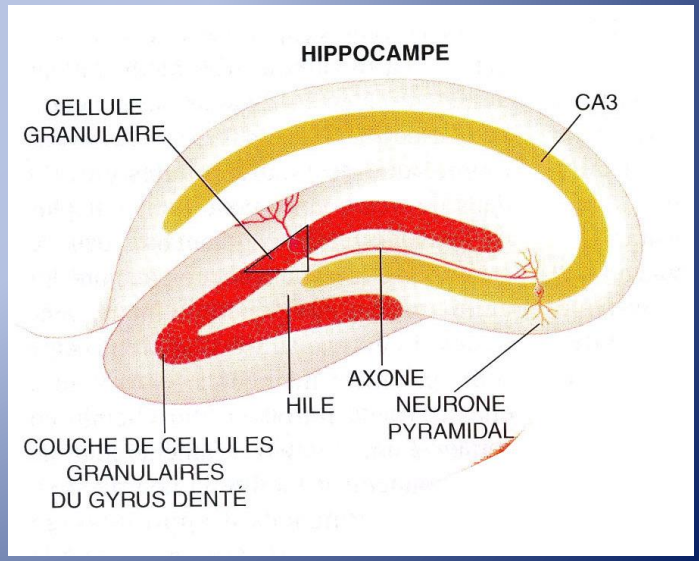
ØGlucocorticoids

Behavioral factors stimulating neurogenesis

ØVaried environnement

ØExercice

ØLearning



- Discoveries about the Brain : some milestones
- The importance of basic research
- What is coming up in Neuroscience
- Translational Research
- Innovation
- International Collaboration :
  IBRO

- Basic research is necessary to advance basic knowledge about the brain and needs to be supported

- Several of the milestones discoveries have also a practical impact :

- Psychopharmacology
- Alzheimer's and Parkinson's disease
- Multiple sclerosis
- Epilepsy
- Neuroprotection

- Discoveries about the Brain : some milestones
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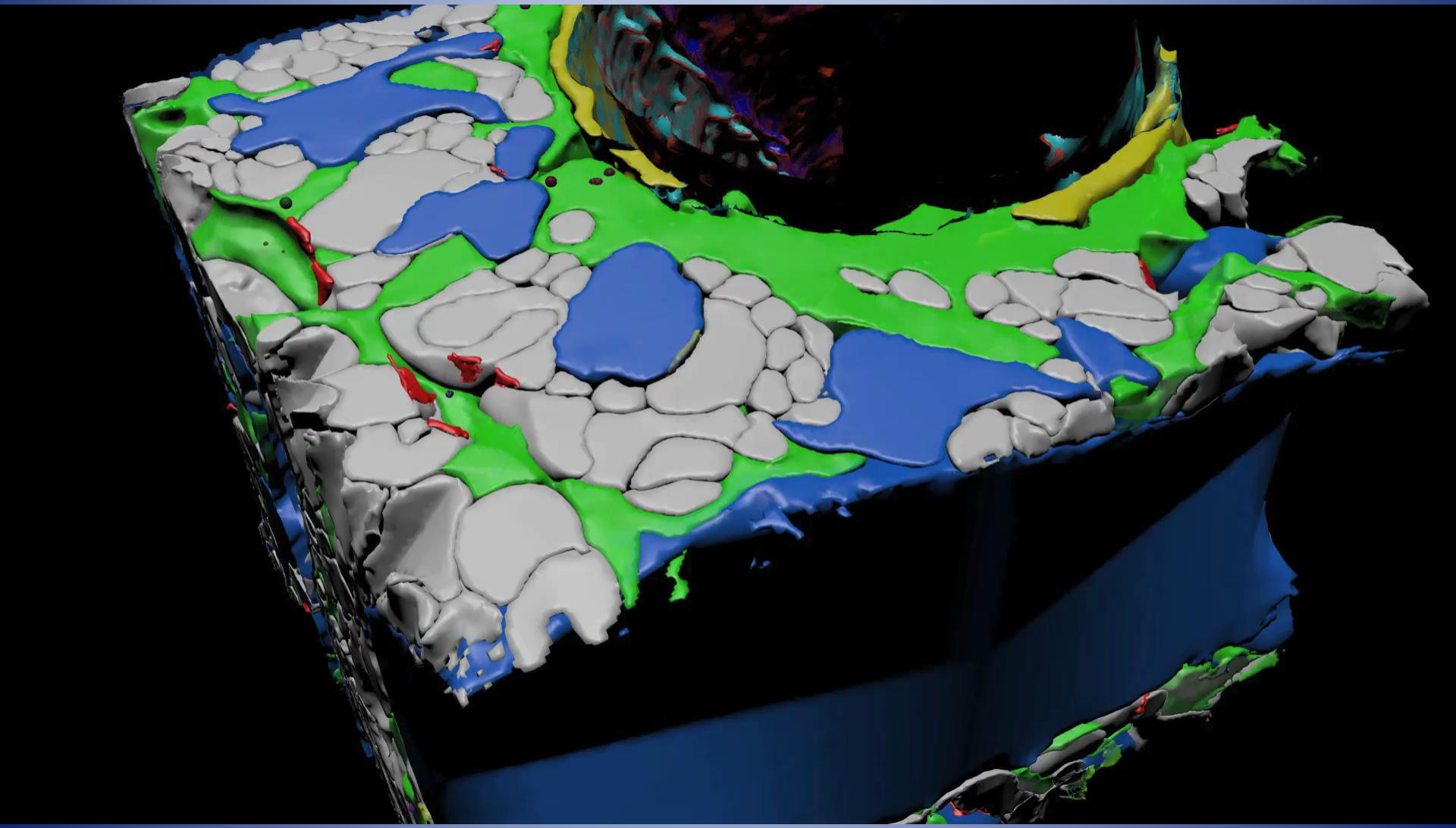
New technologies to visualize brain cells and to navigate inside the brain

Analysis in a 3D Virtual Reality environment

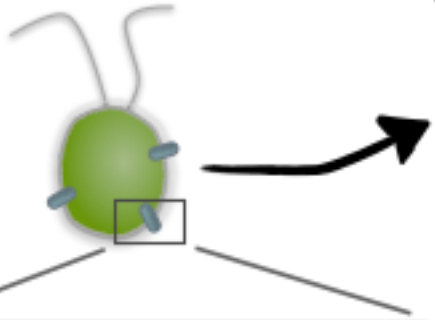


New technologies to activate specific neuronal circuits :

Optogenetics

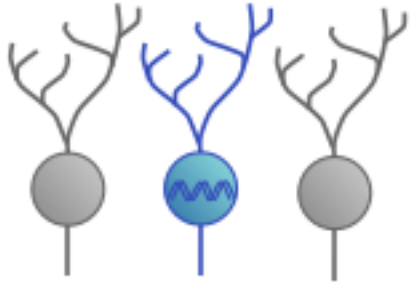
How optogenetics works

A light-sensitive protein from algae



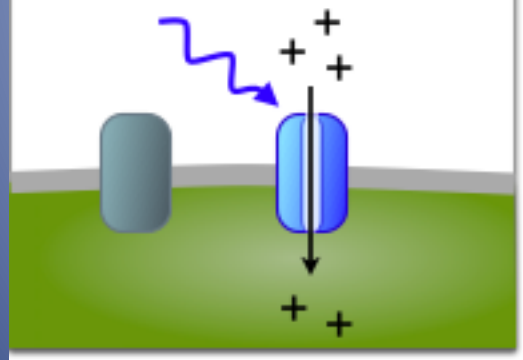
Take the gene for this protein...

... and insert the DNA into specific neurons in the brain

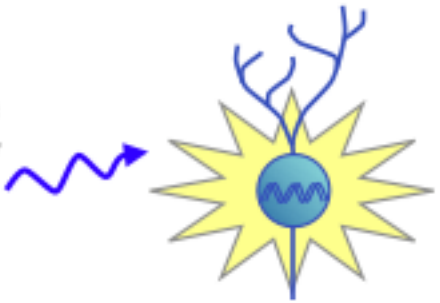


Neurons communicate by "**firing**." This is an electrical signal created by opening & closing ion channels.

This protein is an ion channel that opens in response to **blue light**



So now you can cause neurons to fire just by flashing **blue light!**

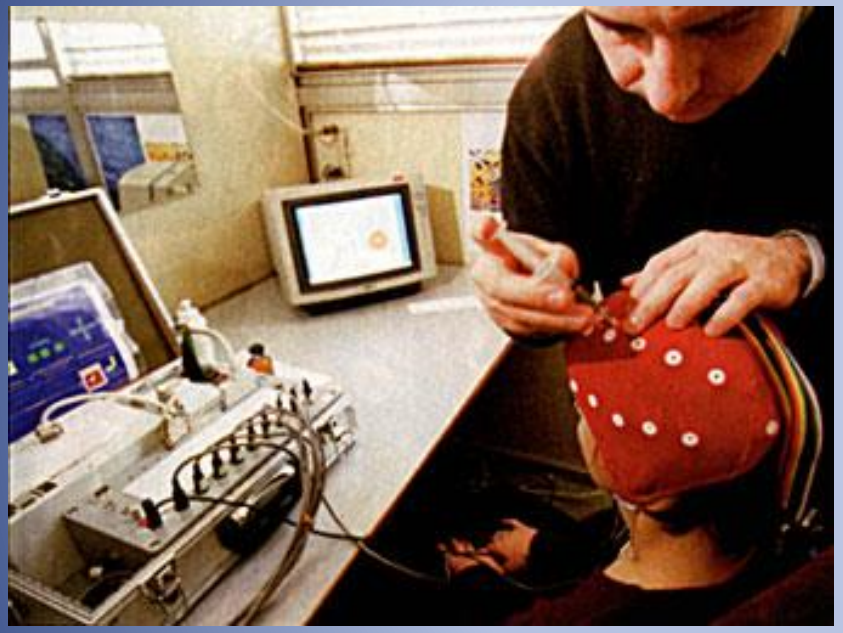


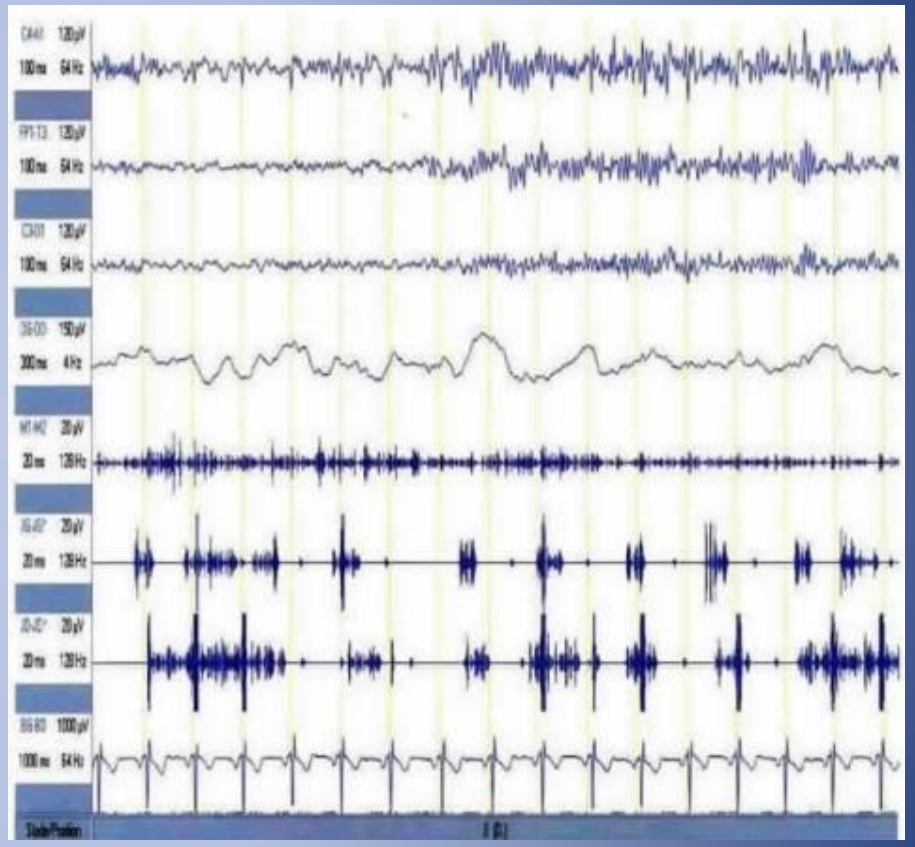
With the right combination of neurons, you can activate an entire brain circuit to control specific behaviors (like movement)

Brain Computer Interfaces

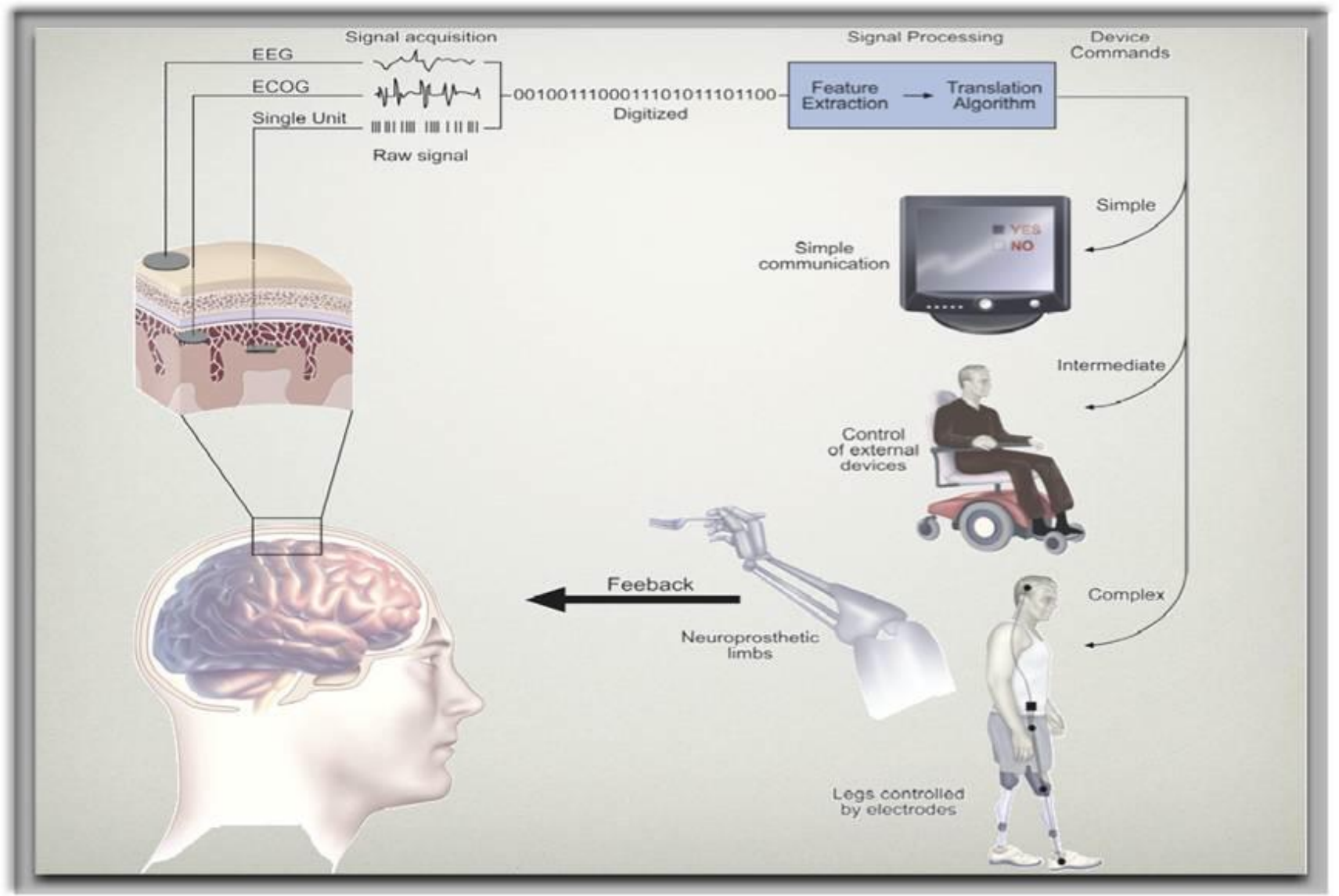
Our brain can direct devices from a distance

Detect the electrical activity of the brain….

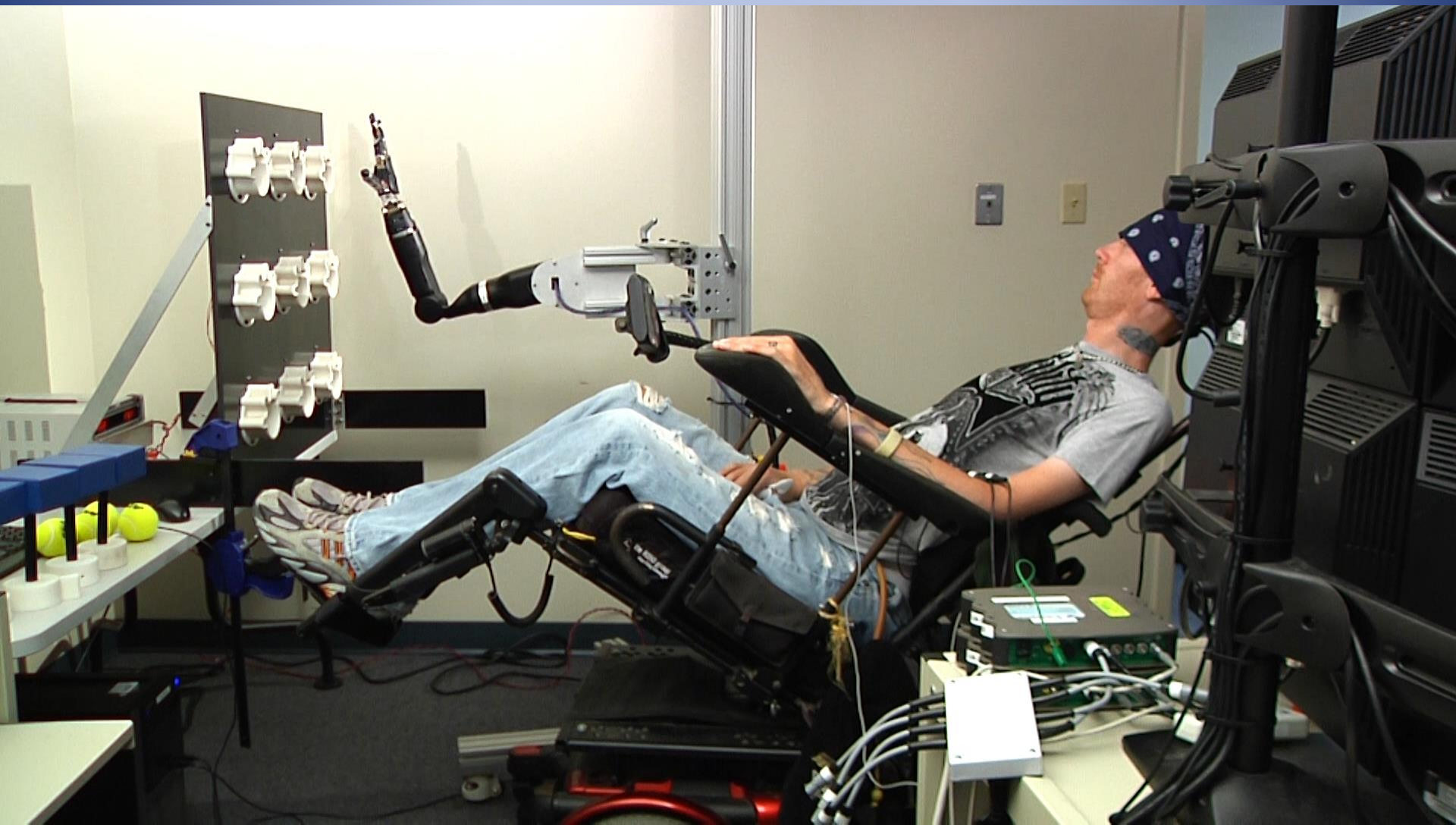




… digitize signals and transmit them to an actuator



brain/computer interface



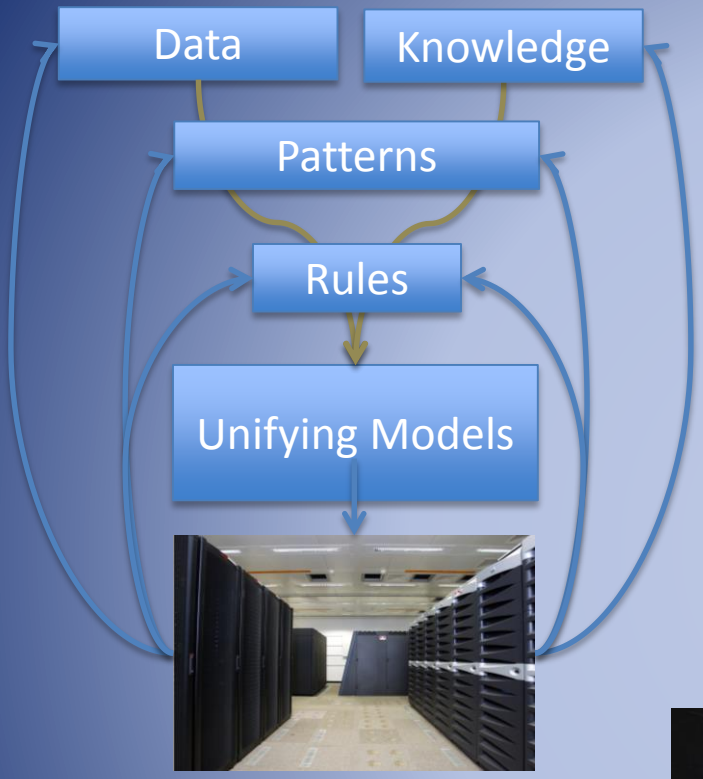
The next challenge:

brain modeling

HBP

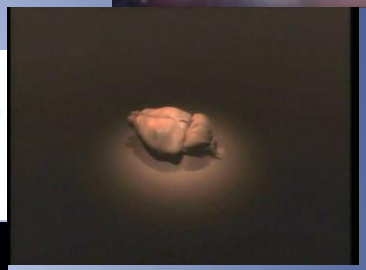
The Human Brain Project

Simulation Based Brain Research



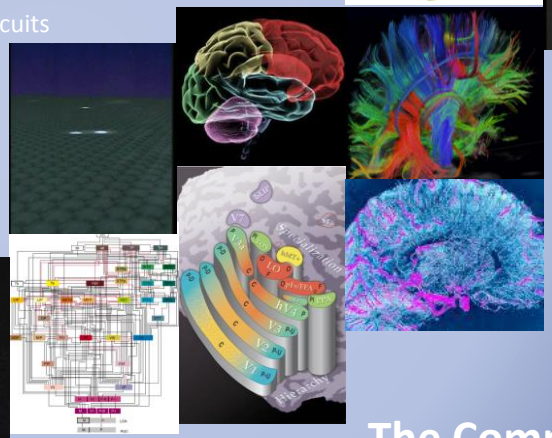
Cognition

Whole brain

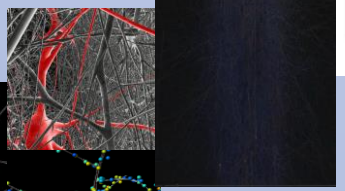


macrocircuits

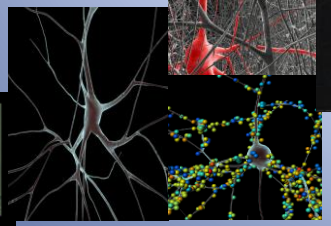
mesocircuits



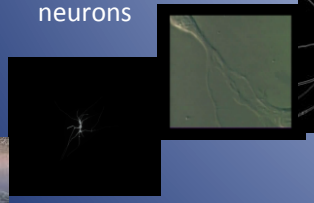
microcircuits



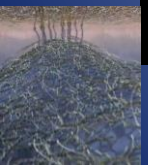
synapses



neurons



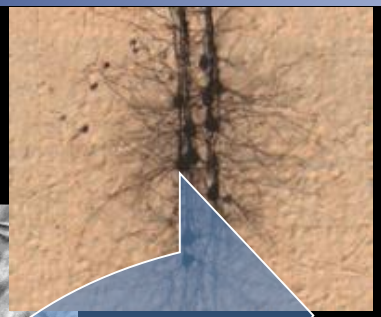
molecules

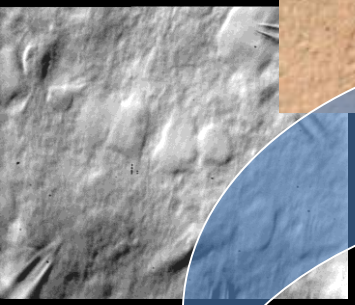


The Computing Challenges

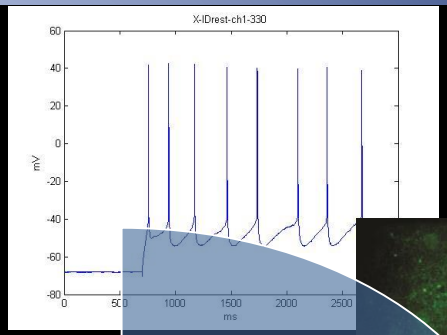
- ✓Data: **Pattern extraction & rules derivation**
- ✓Building: **Constraint-based programming**
- ✓Simulation: **Multi-scale engines**
- ✓Visualization: **Visual supercomputing**
- ✓Analysis: **Interactive supercomputing**
- ✓Virtualization: **In-silico biology**

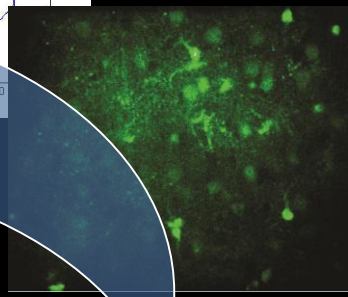
Simulation-based Research

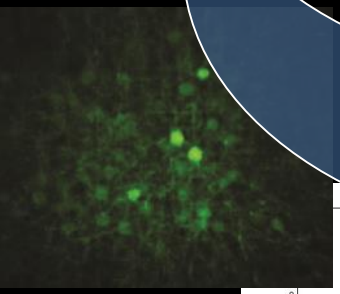




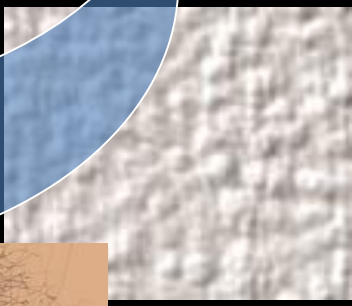
Experiment

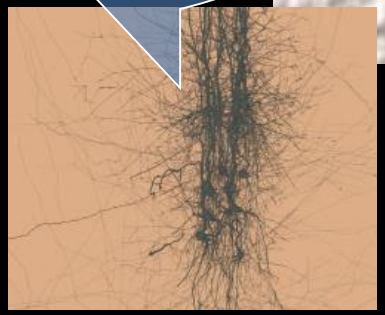


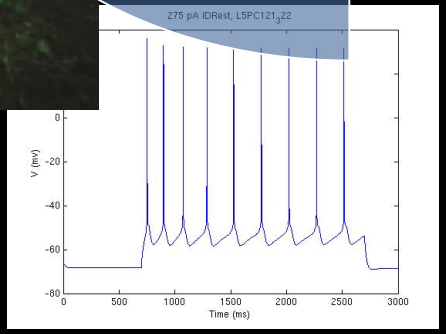




Simulation







- Discoveries about the Brain : some milestones
- The importance of basic research
- What is coming up in Neuroscience
- Translational Research
- Innovation
- International Collaboration :
  IBRO

The (Economic) Burden of Brain Diseases

- About 1/3 of the European population affected by brain-related disorders
- Cost in 2010 for Europe, > € 800 Billion/yr
- Costs are higher than for Cancer, Diabetes & Cardiovascular diseases combined!

Gustavsson, A., et al., Cost of disorders of the brain in Europe 2010, Eur. Neuropsychopharmacol. (2011)

European Brain Council, J Olesen et al., European Journal of Neurology 2012

National Center for Competence in Research

NCCR SYNAPSY

THE SYNAPTIC BASES OF MENTAL DISEASES

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
UNIL | Université de Lausanne
UNIVERSITÉ DE GENÈVE
FNSNF Fonds national suisse Schweizerischer Nationalfonds Fondo nazionale svizzero Swiss National Science Foundation
FMI Friedrich Miescher Institute for Biomedical Research
UNI BASEL
CHUV Centre hospitalier universitaire vaudois
HUG Hôpitaux Universitaires Genève

What are the NCCRs ?

- **In 2001 the Swiss National Science Foundation launched the National Centres of Competence in Research (NCCR).**

- **The main goal of the currently 26 NCCRs is the promotion of scientific excellence in areas of major strategic importance for the future of Swiss research, economy and society.**

The NCCR Synapsy

Competitive call : 60 applications, 8 funded

1.1.2010 – 30.9.2018 : 34 MCHF

Renewed for Phase 3 (2018 – 2022)

162 members

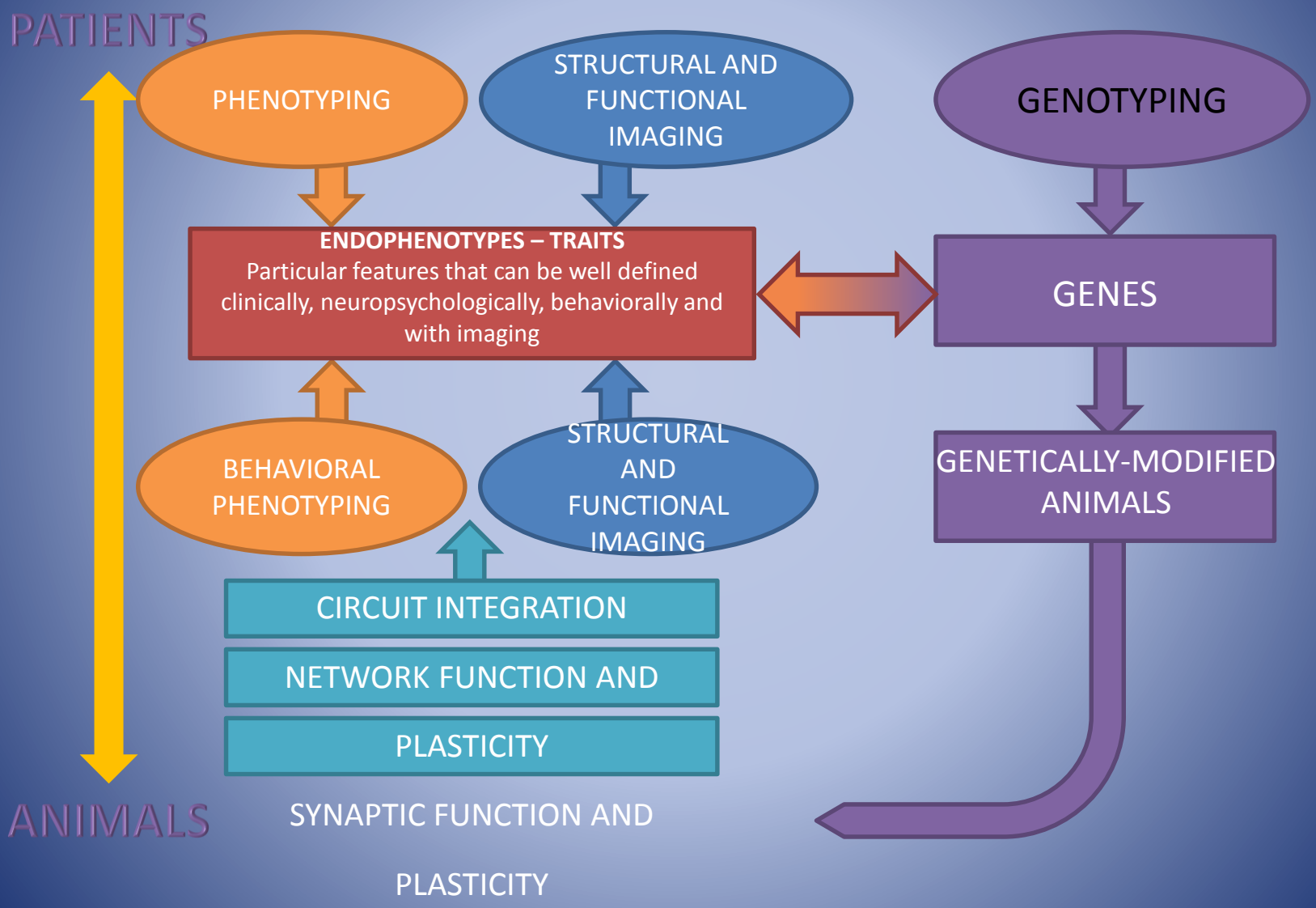
31 project leaders

Main Aims of NCCR Synapsy

- **Establish a strong collaboration between basic neuroscientists and clinicians through well integrated research project based on clinical cohorts.**

- **Introduce a neuroscience culture in the Departments of Psychiatry with aim of training promising young clinicians to promote the emergence of a new generation of psychiatrists motivated by an academic career.**

Strategic Guiding Principles



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Brain ageing, mental health and innovation for healthcare

- the challenges of innovation in the domain of neurology and mental health are becoming a serious healthcare issue worldwide

- furthermore with the ageing of the population issues about brain ageing and brain health are becoming more acute

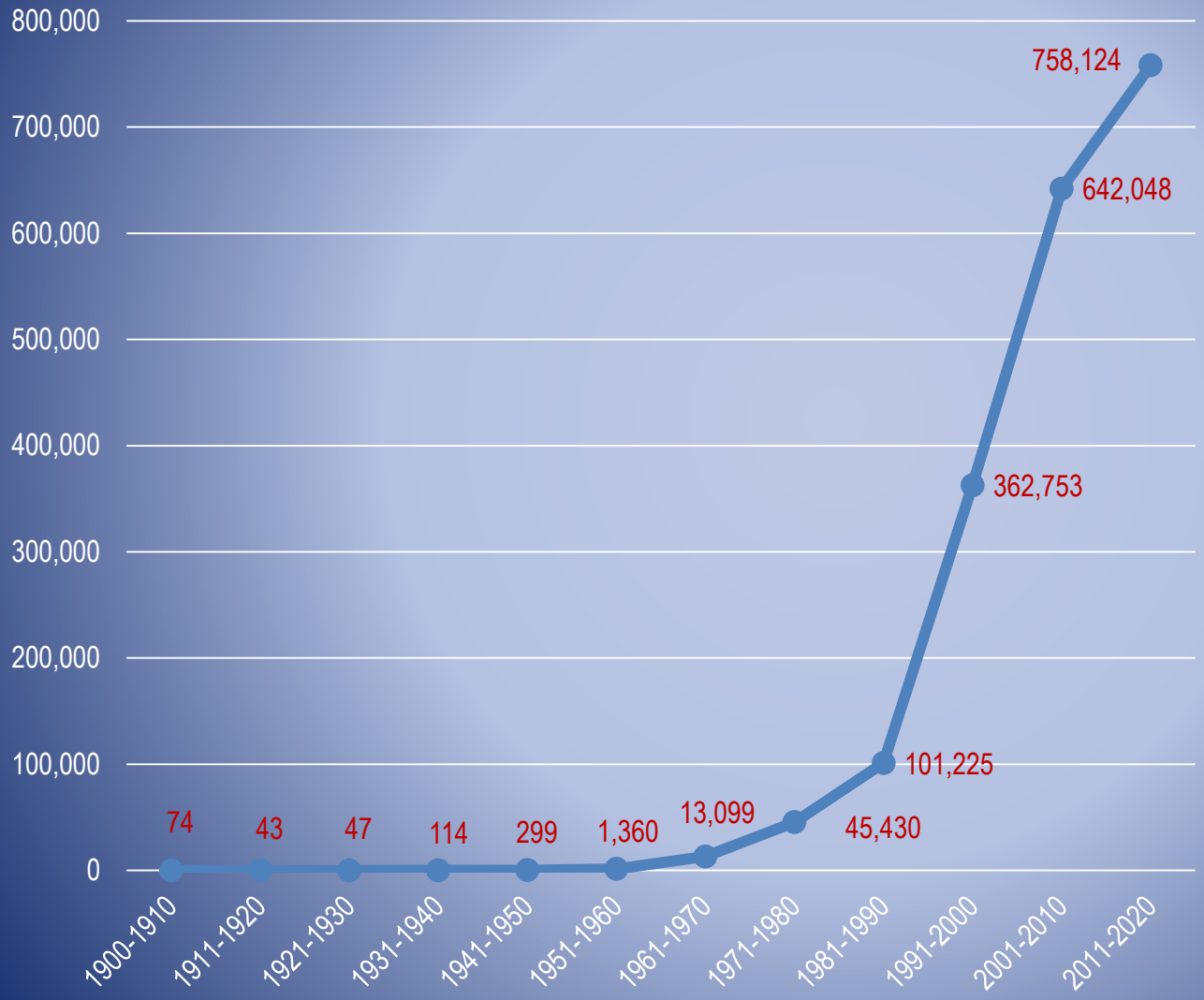
Today's challenges

Brain diseases

- → The lack of efficient treatments for many diseases
- → The rising cost of drug development
- → The divestiture of pharma research
- → The economic burden (> 800 billion/year € for Europe)

EPFL slides, Courtesy P. Aebischer

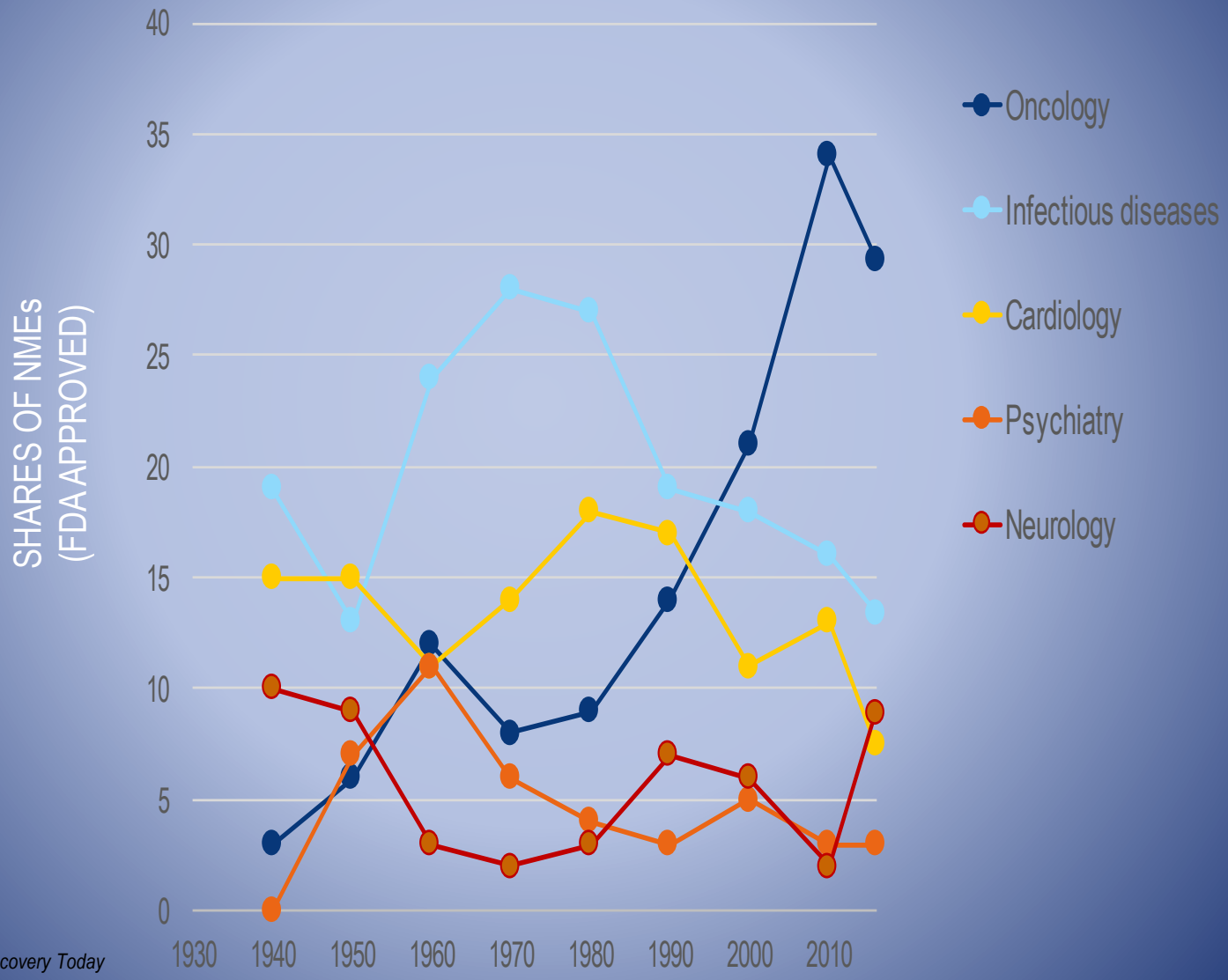
The rise of neuroscience scientific articles



Number of publications in Web of Science® with *neuron* as topic

(2011-2020 extrapolated from 2011-2015)

Low Shares of New Molecular Entities for Neurology



Redrawn and adapted from Drug Discovery Today November 2014

Uniqueness of neurosciences

- → Natural electrical engineering interface
- → Potential of virtual reality tools
- → Powerful functional imaging techniques (MRI, PET, MEG, etc.)
- → Optogenetics tools to study behavior
- → Efficient viral vectors for gene transfer studies (AAV, lenti etc.)
- → Numerous “omics” tools: genomics, proteomics, metabolomics etc.
- → Role of nutritional approaches for prevention

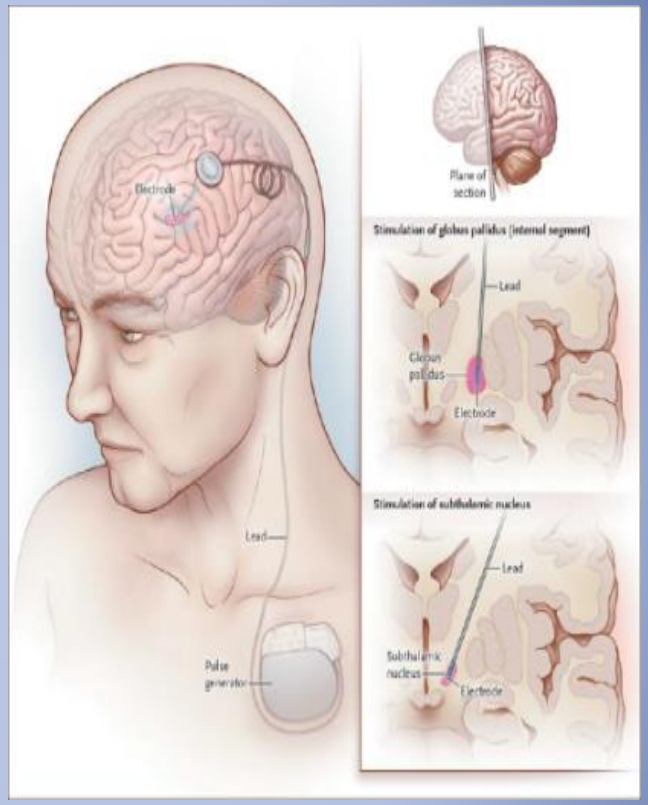
A major neuroscience success: Deep Brain Stimulation DBS

FDA approval:

- 1997 : Essential tremor
- 2002 : Parkinson's disease
- 2003 : Dystonia
- Under evaluation:

depression

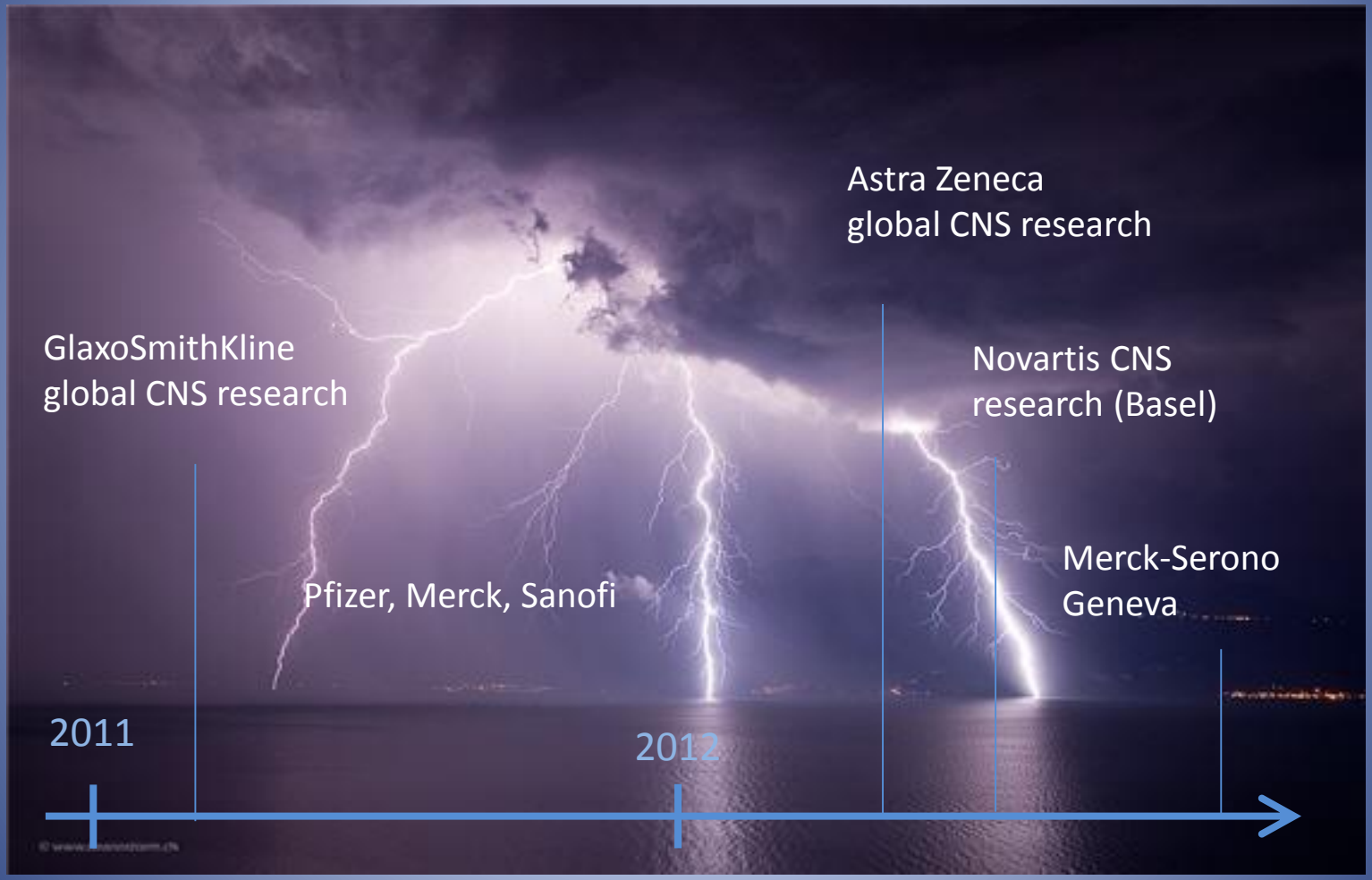
→ More than 100'000 patients treated worldwide



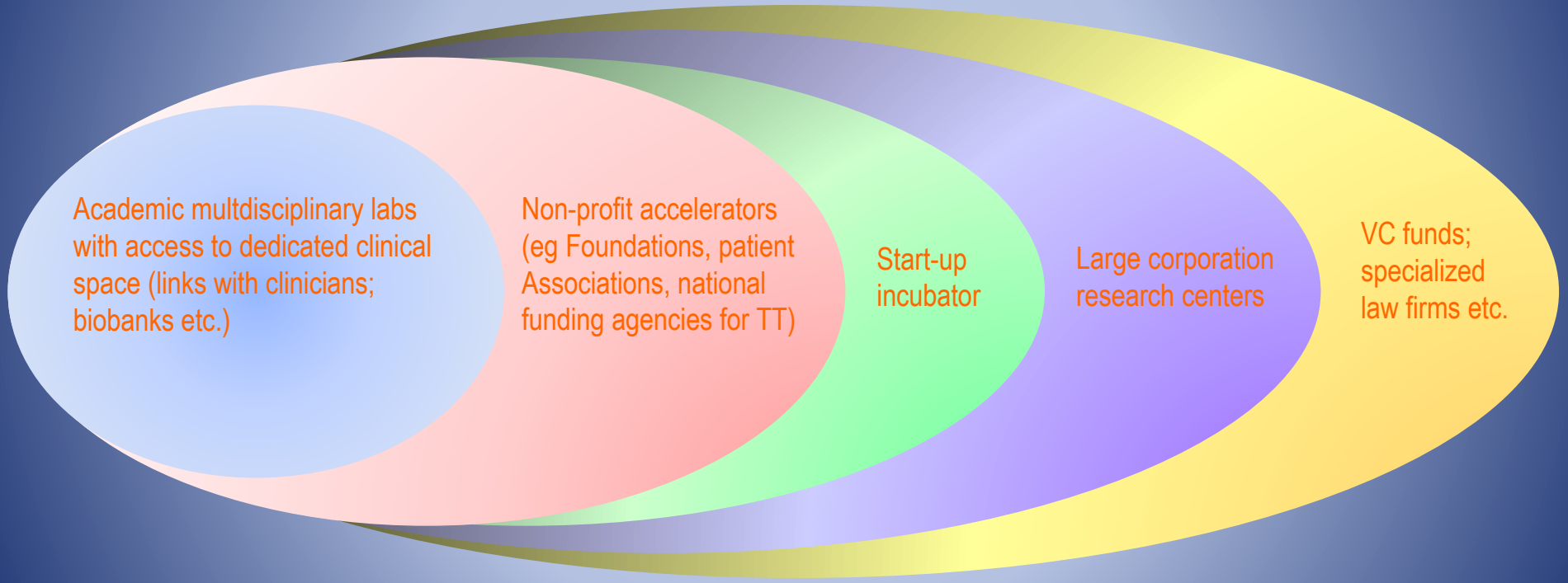
Alim Louis Benabid

Okun MS et al., N Engl J Med 367;16 2012

Set backs in CNS phrama industry

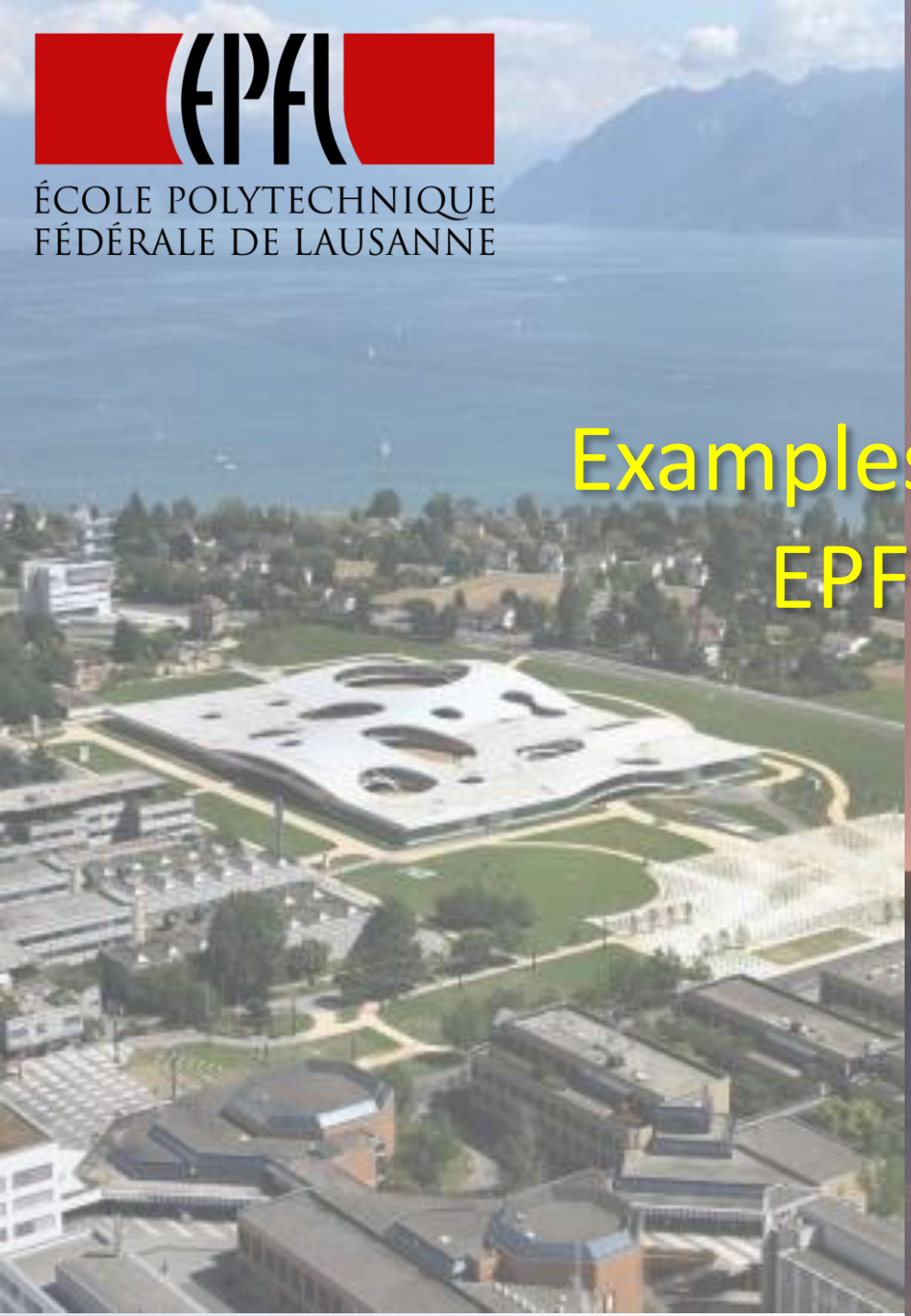


How to create an ecosystem for neurotranslation?



ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

Examples from EPFL

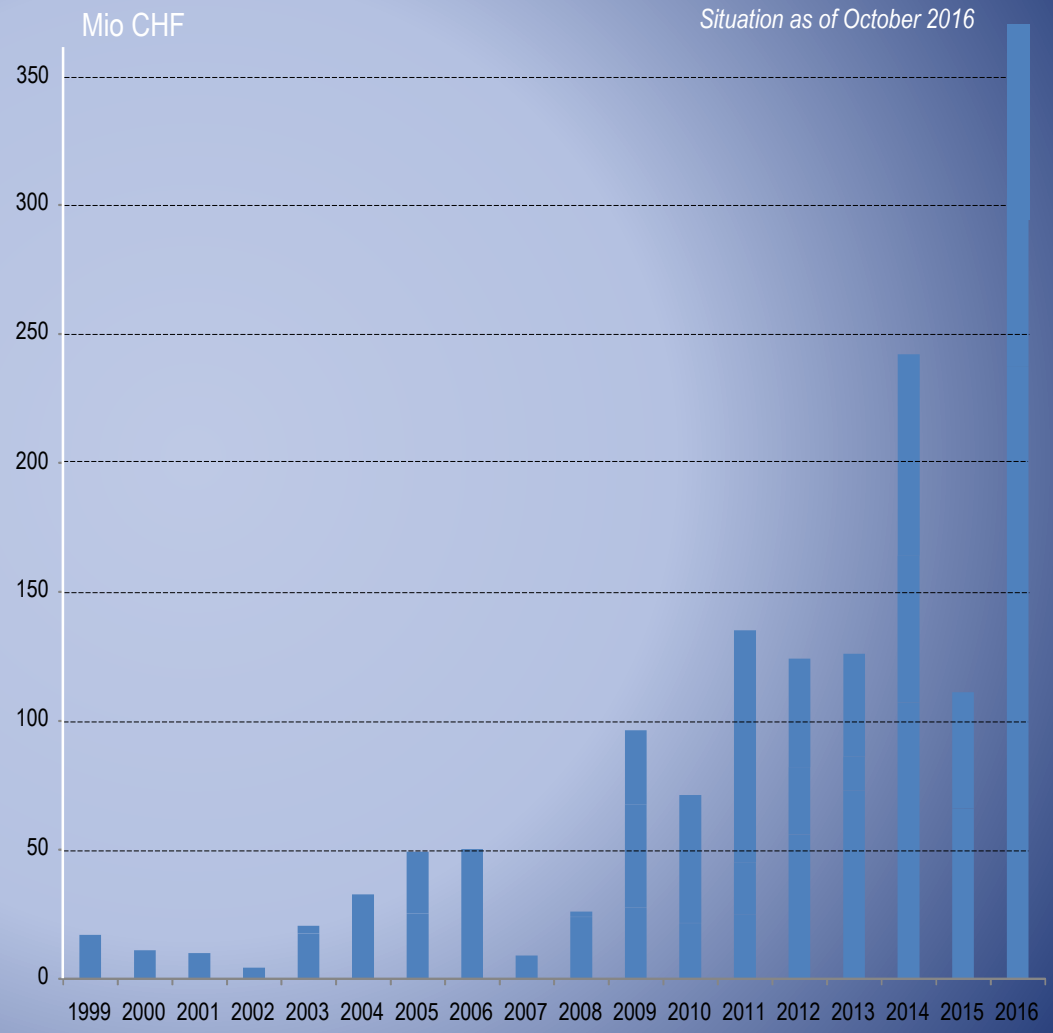


VC funding of EPFL start-up

2016

> 15 start-up

> 350 MCHF of VC funding



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campus biotech

GliaPharm

Target glia to cure neurons

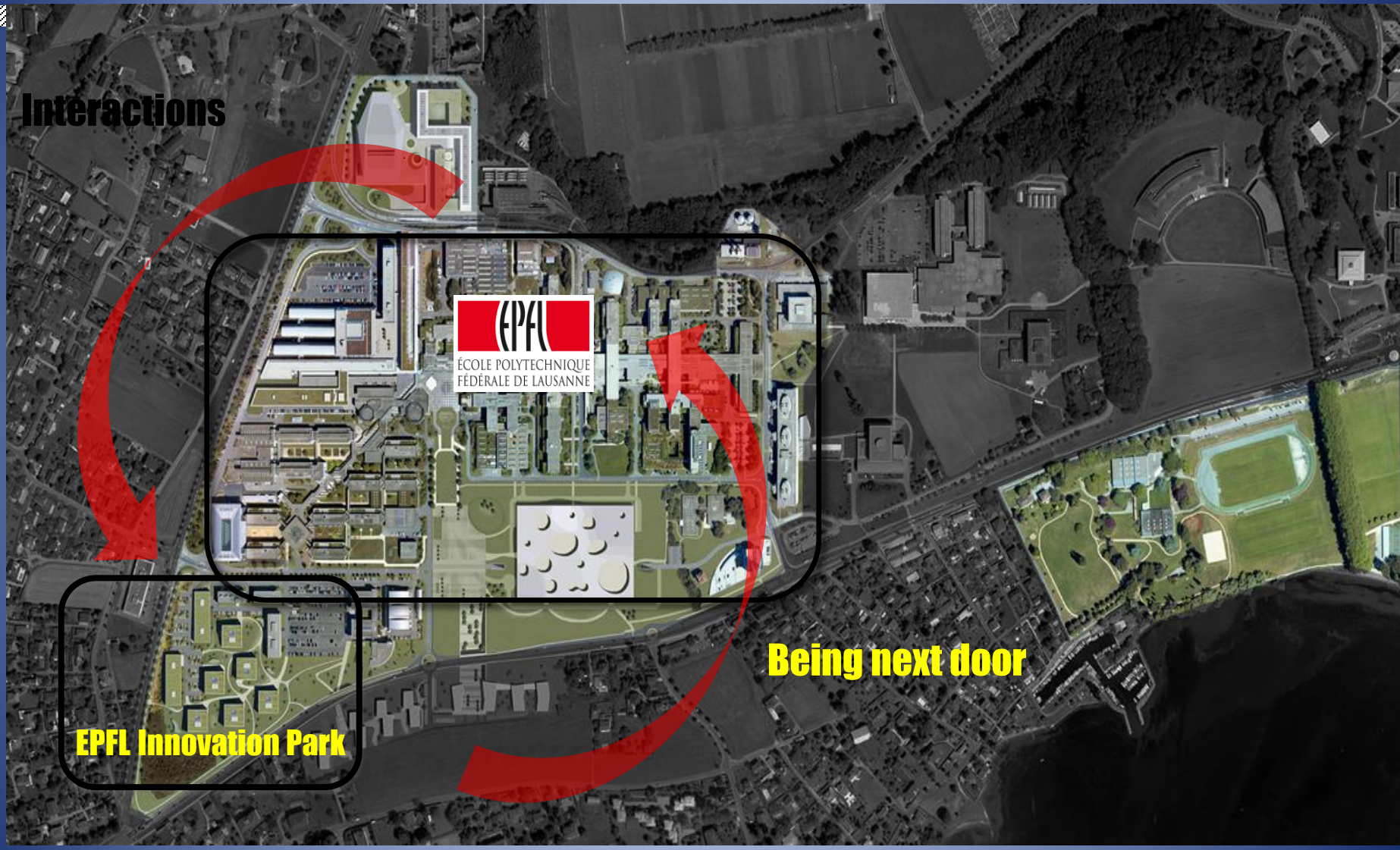
Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Commission for Technology and Innovation CTI

Sylvain Lengacher

Charles Finsterwald

Model of the EPFL Innovation Park



Main points for Reflection

- Brain ageing and mental health represent major human and economic challenges
- Despite remarkable progress in understanding brain function, still considerable knowledge to be acquired about brain function for the development of novel therapies
- Alarmingly big pharma have largely disinvested from neuroscience research, with the possible exception of Alzheimer's disease
- Need for governments to keep supporting in research and that academia continues its progress
- Need to think of different ways to develop private and public partnerships
- Need to develop new business models of collaboration between academia, its innovation activty (start ups) and industry
- Need to create a novel environment for translational research in neuroscience

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  IBRO

INTERNATIONAL BRAIN

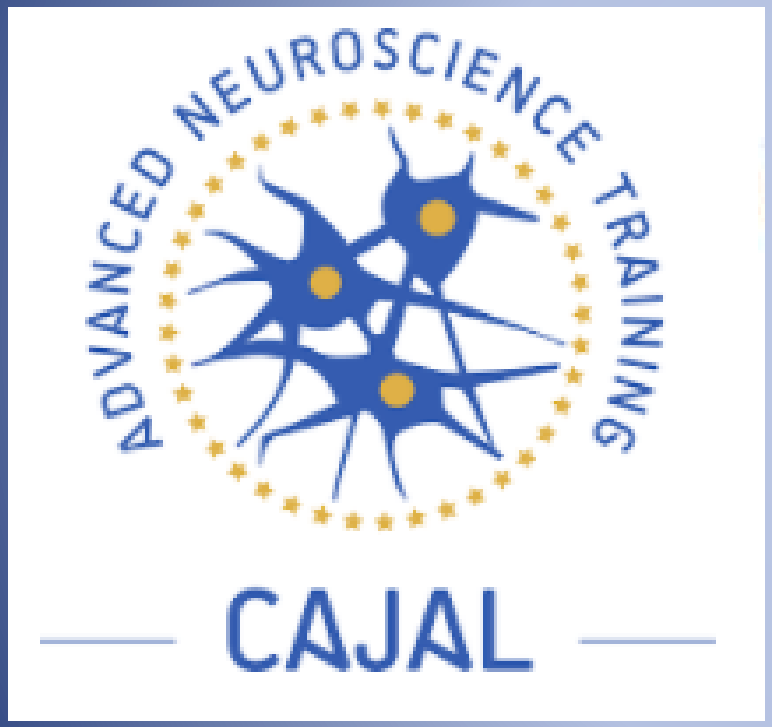
RESEARCH ORGANIZATION

www.ibro.org

Fellowships

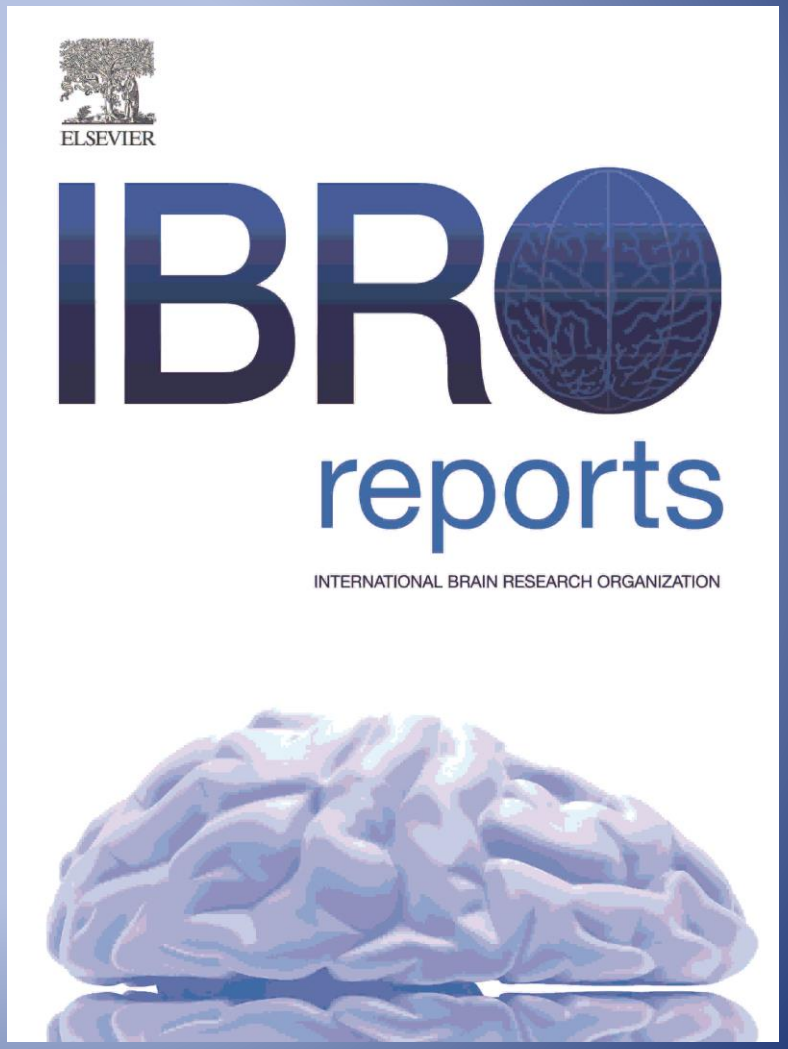
- **Research Fellowships**
- **Return Home Fellowships**

Permanent Training Centers



INTERNATIONAL BRAIN IBRO RESEARCH ORGANIZATION

IBRO JOURNALS



Travel Grants

- International Travel Grants
- IBRO-SfN Travel Grants
- FENS Forum/Regional Meeting Travel Grants
- IBRO World Congress Travel Grants
- Regional Travel Grants

Asia/Pacific Regional Committee (IBRO-APRC)

Bong-Kiun Kaang (Chair, 2018)
Seoul National University
Seoul, Korea

Melinda Fitzgerald (2016)
Curtin University and
Perron Institute
Western Australia

Shigang He (2014)
Chinese Academy of Sciences
Shanghai, China

Nancy Ip (2014)
Hong Kong University of
Science & Technology
Kowloon, Hong Kong

Tadashi Isa (2016)
Kyoto University
Kyoto, Japan

Battuvshin Lkhagvasuren (2018)
Mongolian National University
of Medical Sciences
Ulaanbaatar, Mongolia

Cheah Pike-See (2016)
Universiti Putra Malaysia
Puchong, Selangor, Malaysia

Shubha Tole (2010)
Tata Institute of Fundamental
Research
Mumbai, India

INTERNATIONAL BRAIN IBRO RESEARCH ORGANIZATION

Asia/Pacific Regional Funding

- **Exchange Fellowships**
- **Travel and Short Stay Grants**
- **Advanced Neuroscience Schools**
- **Lecturer Exchange Program**
- **Diversity Grants**
- **Global Advocacy Seed Grants**

INTERNATIONAL BRAIN IBRO RESEARCH ORGANIZATION

MNUMS Mongolian National University of Medical Sciences 1942

MONGOLIAN NEUROSCIENCE SOCIETY

IBRO-APRC Associate School 2018

School on Basic Techniques in Neuroscience — The 1st Ulaanbaatar School

Ulaanbaatar, Mongolia
17-22 SEPTEMBER, 2018

Assets and Challenges for Mongolian Neuroscience

- **A dynamic and motivated National Neuroscience Society**
- **Clinical capacity in neurology, psychiatry, psychology**
- **A few research research groups that could act as nucleation centers**
- **Importance of long term support**
- **Develop training of young scientists**
- **Establish programs that strengthen the collaborations between basic scientists and clinicians**
- **Identify specific “niches” of research where Mongolian neuroscience could have an hedge**