Master of Science in

Computational Biology

Nice Sophia Antipolis University, France

http://cbb.unice.fr

Coordinators

E. De Maria and T. Papadopoulo

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Auron
ST ETIENNE DE TINEE
MONT MOUNIER
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Las Donnas
CÎME NÈGRE
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UBAC DE BLAINON
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1820
CIME D'AURON
AURON 1600
D. 39

November 12, 2030
Dr House meets his patient Bill

- Bill Krivitz suffers from knee arthritis… Severe pain and reduced flexion
- Dr House first looks for a medication?
  - Sequences Bill's genome and tracks deficient genes
  - Seeks drugs fixing the protein which malfunctions
- Dr House and Bill agree on surgery
  - Design of a patient specific prothesis: pre-op simultations
  - Computer monitored physiotherapy
- Epilogue: Bill run the Boston Marathon

Our future: Computational biology

- Computational biology is an emerging interdisciplinary field that applies the techniques of computer science, applied mathematics and statistics to address biological problems.

- The main focus lies on developing mathematical modeling and computational simulation techniques.

- Computational biology addresses scientific research topics with their theoretical and experimental questions without a laboratory.

Let’s start today!

Explore the functional organization of humans

Master of Science in

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One-year course for students interested in a truly **inter-disciplinary learning experience** in the field of computational biology given by experts, **outstanding Professors and Researchers**.

Teaching language: English

Scholarships available

Message from…
a Computer Scientist and Mathematician

Olivier Faugeras,*member of the French Academy of Sciences, INRIA Research Director and team leader of the INRIA-NeuroMathComp project team*

Biology, and neuroscience in particular, has not yet benefited as much as physics from the "unreasonable effectiveness of mathematics", to quote the physicist and Nobel prize winner Eugene Wigner (1960). *This is probably because most of the relevant mathematical theories, such as the theory of bifurcations in dynamical systems or stochastic calculus, have only been developed in the second part of the 20th century and are not taught in our engineering schools and departments even at the Masters level.* ***One of the exciting goals of this new Master is to face this challenge and bring our students up to speed so that they are able to apply these modern mathematical tools to real biological problems.***

What is the scientific goal of this Master?

Focus on the human being

- From different perspectives
  - understanding and modeling functional aspects
  - interpreting biomedical signals for various devices

- At different scales
  - from molecules to organs and the whole organism

- Two main directions
  - Modeling biological functions: from molecules to networks and organs
  - From biomedical signal analysis to computational neuroscience

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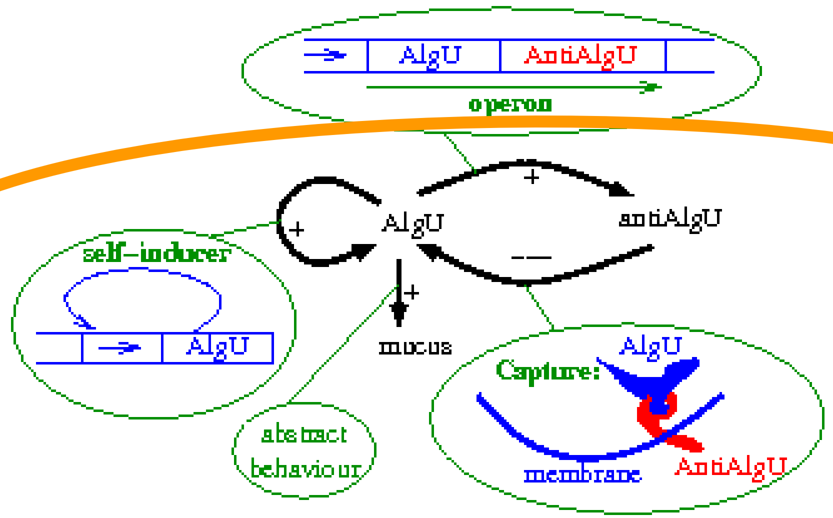
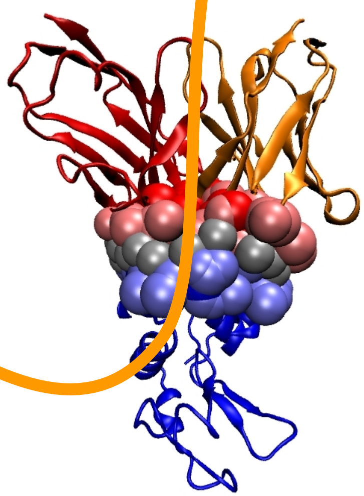
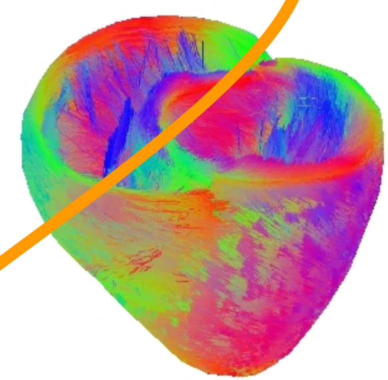
Modeling biological functions: from molecules to networks and organs



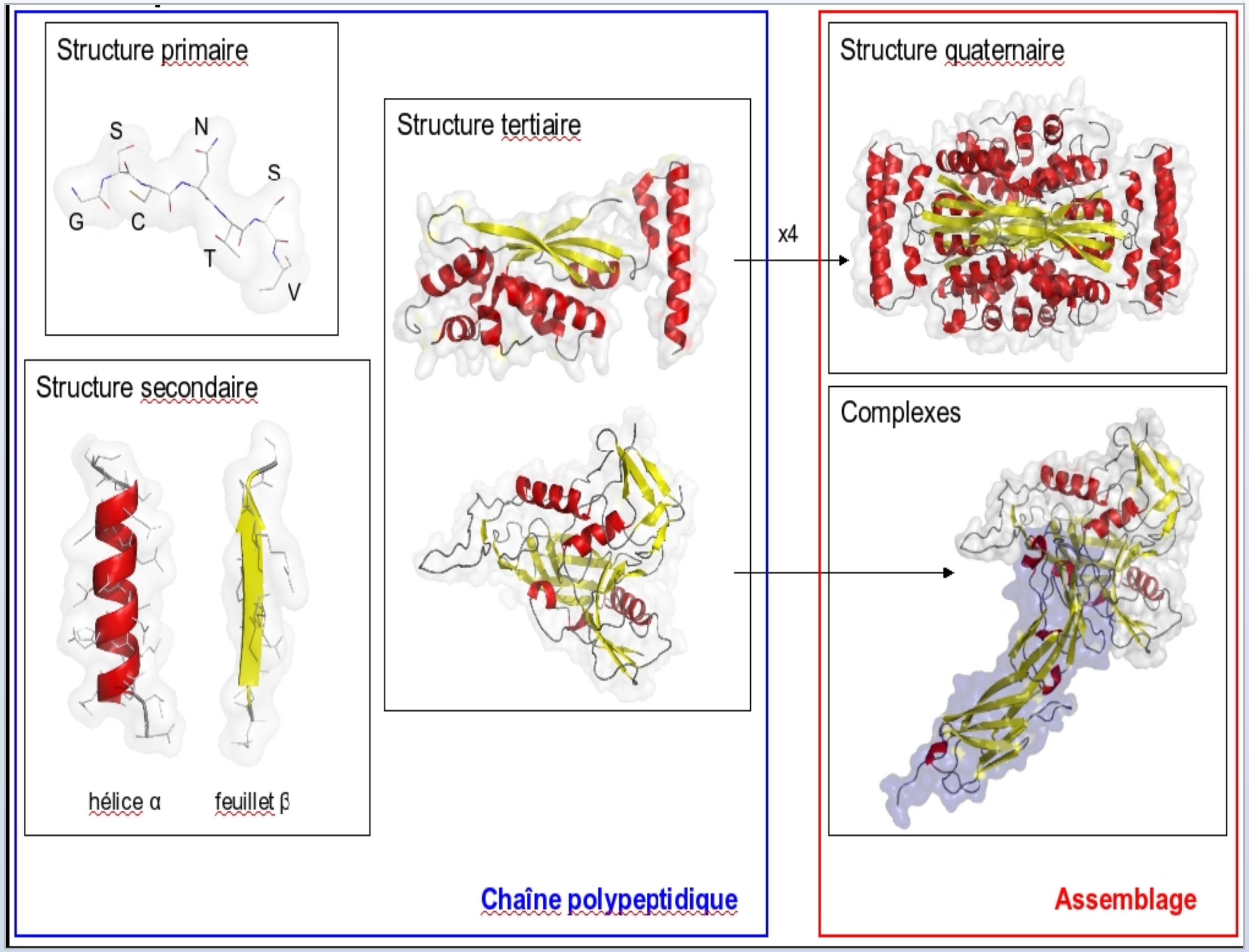




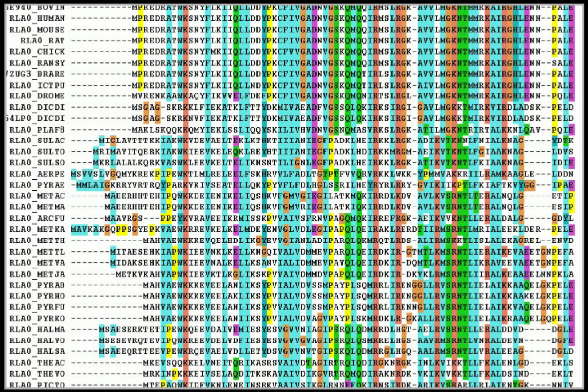
What is a protein?

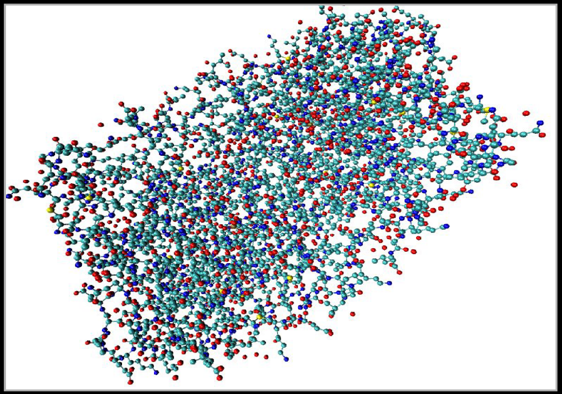
Importance of non-covalent interactions

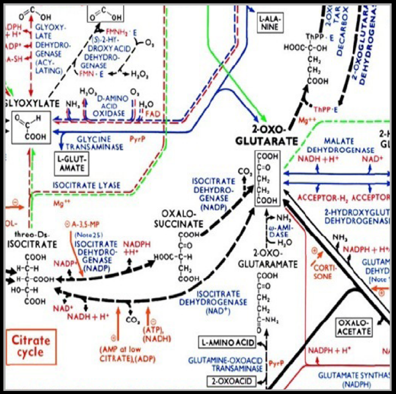
- Primary to quaternary structure



Explore the functional organization of humans







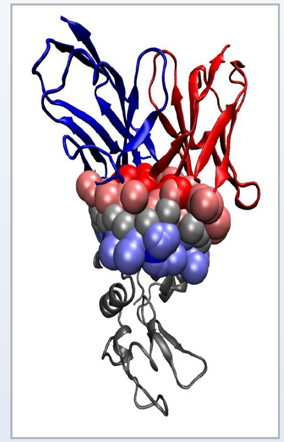
alignments, phylogenies

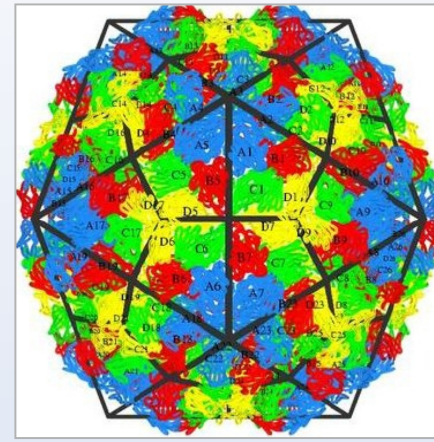
structure-to-function paradigm

functional Behavior of systems

Algorithmic problems in computational structural biology; Understanding proteins and protein interactions

F. Cazals and J. Bernauer (INRIA-ABS)

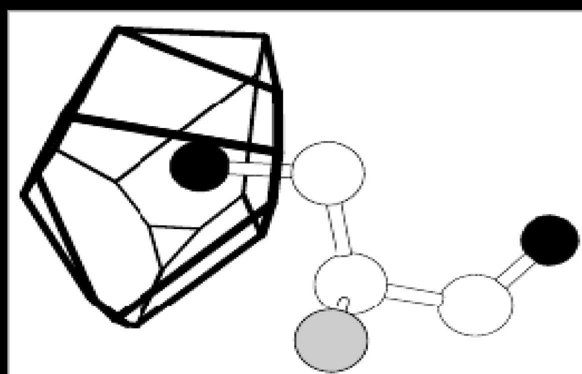


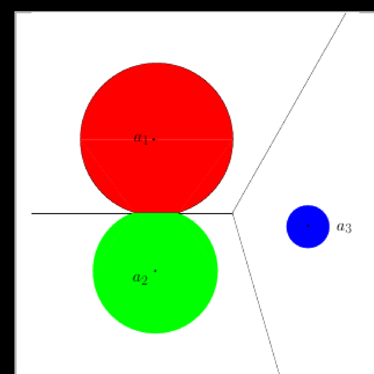


- Protein complexes are ubiquitous
  - Stability and specificity of macro-molecular complexes?
  - Prediction ? (with little/no structural information)
- Structural information is scarce:
  - # non redundant gene sequences 100 # structures
- Computer science perspective: improving the prediction of complexes
  - How does bio-physics constrain macro-molecular geometry?
  - How does one integrate suitable parameters into learning procedures?

Ref: Janin, Bahadur, Chakrabarti; Quart. reviews of biophysics; 2008

Explore the functional organization of humans

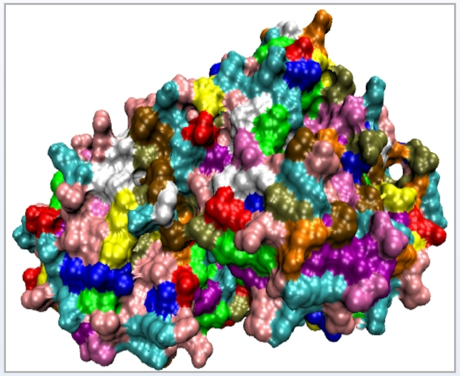




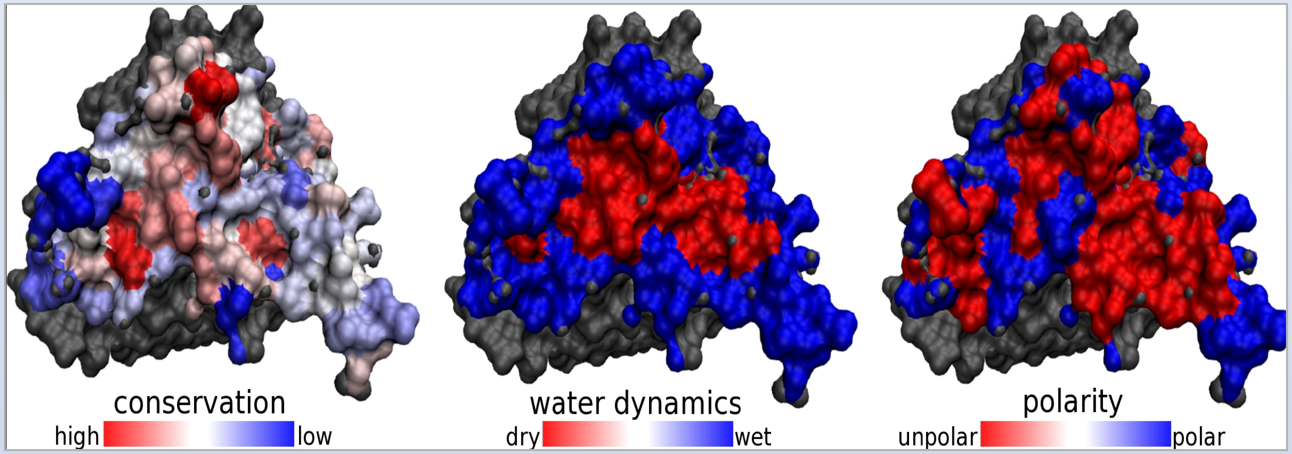
$$a+b\sqrt{\gamma_1}+c\sqrt{\gamma_2}+d\sqrt{\gamma_1\gamma_2}$$

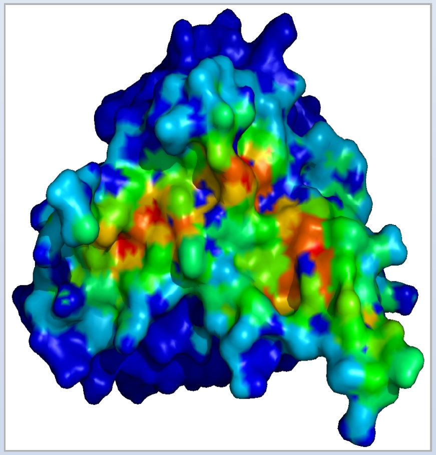
$$\gamma_1\neq\gamma_2$$

Mining Protein - Protein Interfaces



- What are the key residues at a protein interface?
  - Experiments: directed mutagenesis
  - Evolution: conservation
  - (Geometric) modeling
- Strategy developed: discrete interface parameterization
- Conservation dryness, polarity vs geometry



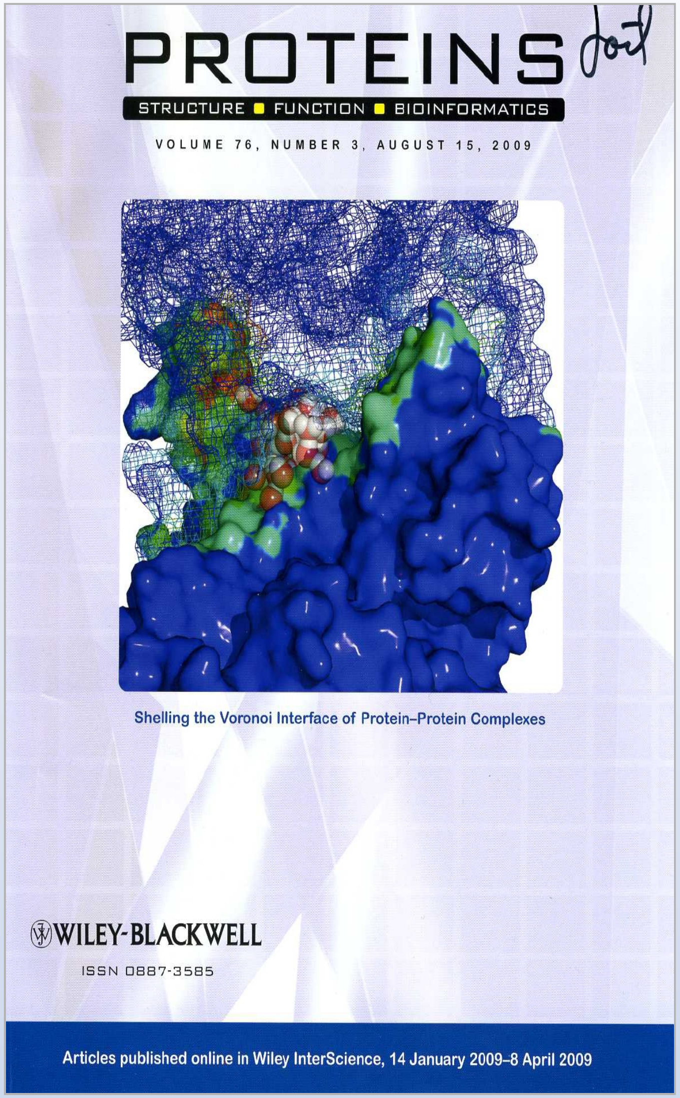


Mining Protein - Protein Interfaces

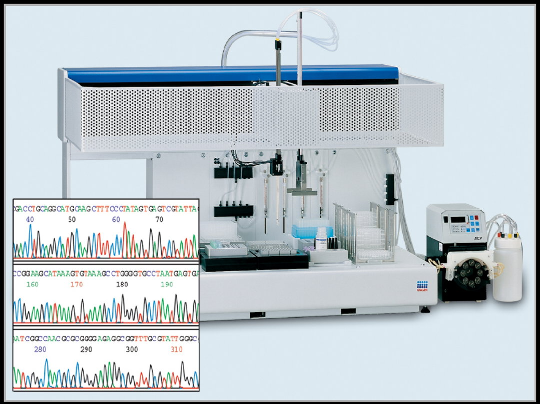
- Assessment: statements from global → per-complex
  - Improved description of biophysical properties

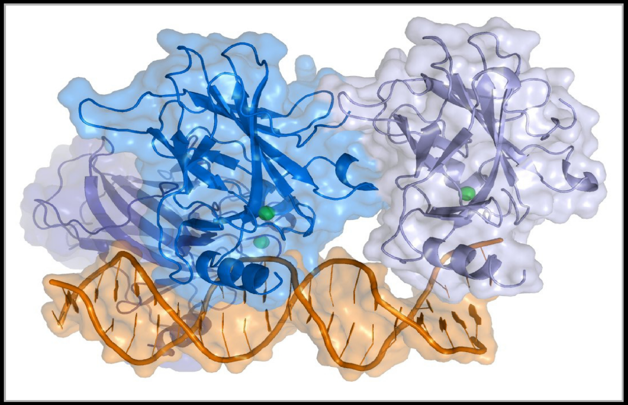
- **Related open questions**
  - the packing properties of atoms,
  - rigidity of molecular domains,
  - percolation of water molecules (cf Fields medal of W Werner)

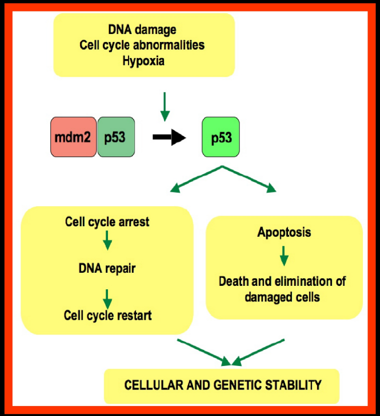
- Experiments and applications:
  - protein engineering,
  - medicine: modulating protein interactions



Explore the functional organization of humans







mutation or deletion of p53 gene

apoptosis; genetic stability; inhibition of angiogenis

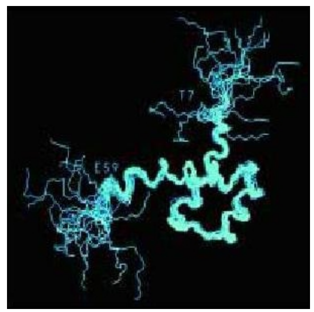
Methodological Perspective: From Molecules to Networks

- Modeling in Structural Biology and Systems Biology

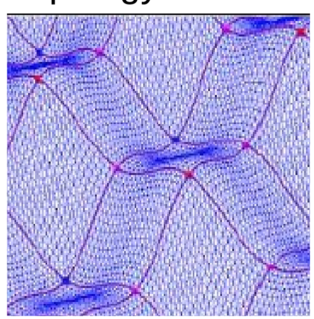
Biochemistry

Biophysics

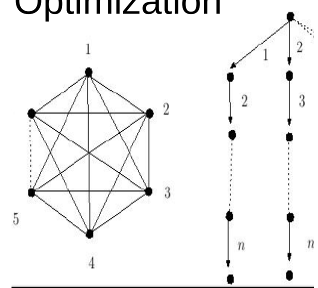
Geometry



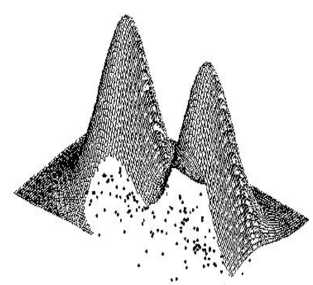
Topology



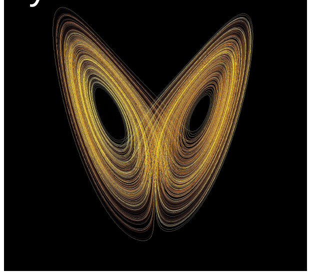
Combinatorics
Optimization



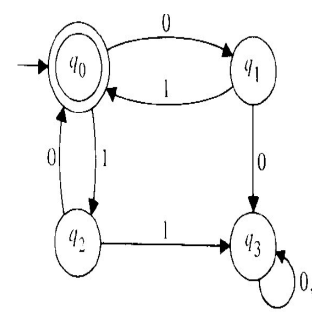
Statistics



Dynamical
Systems



CS

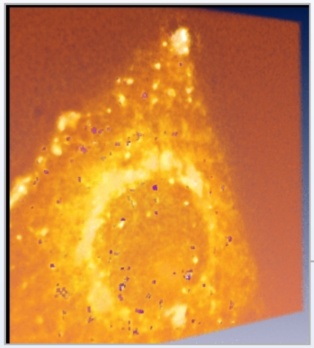


F. Cazals et. Al. course

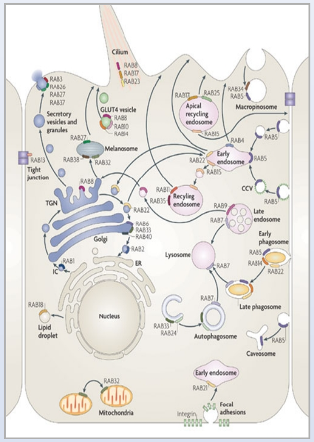
G. Bernot et. Al. course

Investigations Across Scales

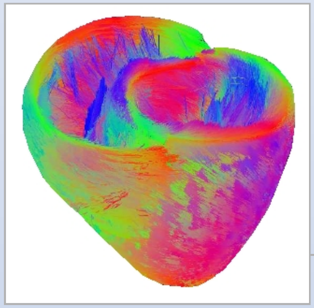
- Deconvolution and denoising for confocal microscopy
  J. Zerubia (INRIA-Ariana) and Laure Blanc-Feraud (CNRS-Ariana)
  - Variational or Markovian models.
  - Wavelets and Wavelet packets



Tracking moving protein complexes by confocal microscopy



- Computational Anatomy and Physiology of the Human Body
  X. Pennec, H. Delingette, G. Malandain and N. Ayache (INRIA-Asclepios)
  - Mathematical methods needed to perform statistics on anatomical objects, with a specific focus on image registration and atlases.
  - Main applications are in medicine and biology: understand the basic processes leading to the apparition of pathology, to model its probable evolution and to plan, simulate, and monitor its therapy



Statistical model of fibers in the heart (here the mean orientation) determined from 9 DTI images of canine hearts.

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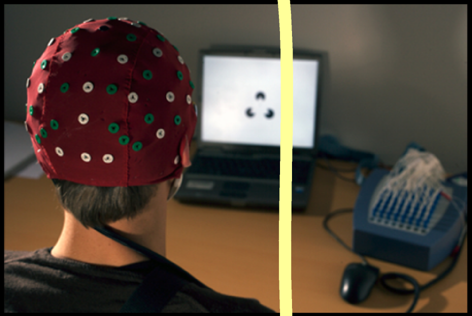
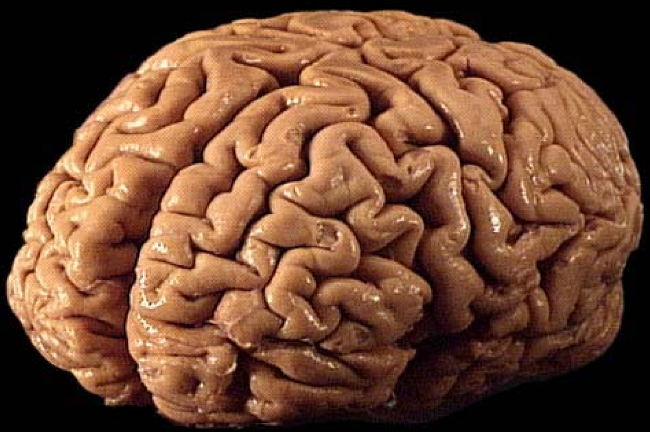
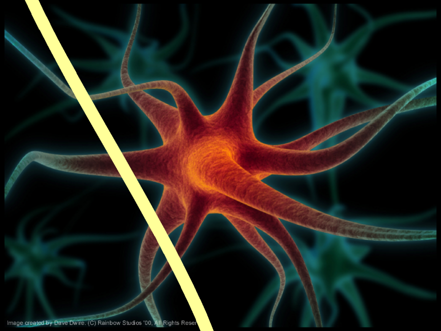
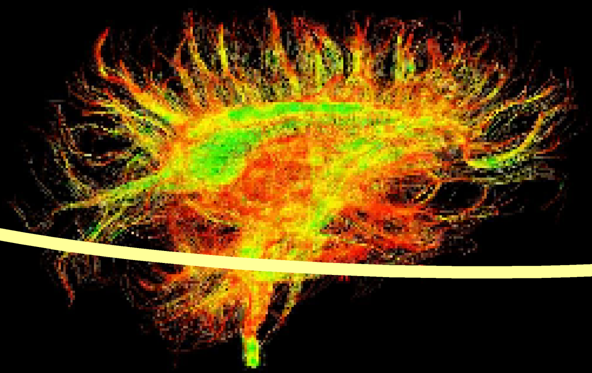
From biomedical signal analysis to computational neuroscience



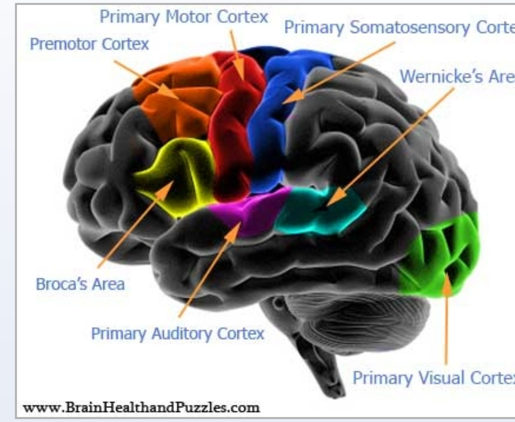


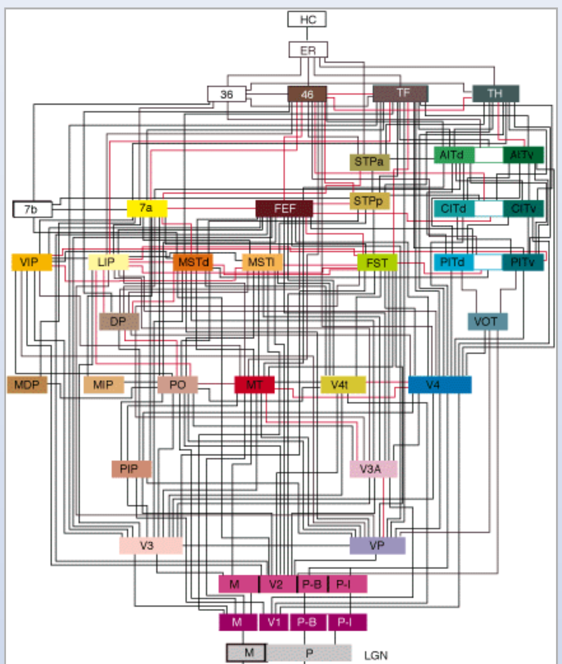




How your brain works?

- **The nervous system** is characterized by the parallel interaction on many sub-systems
  - What are the roles of the different cortical areas?
  - How are they organized?
  - How to measure their activities?
  - How to model the brain?





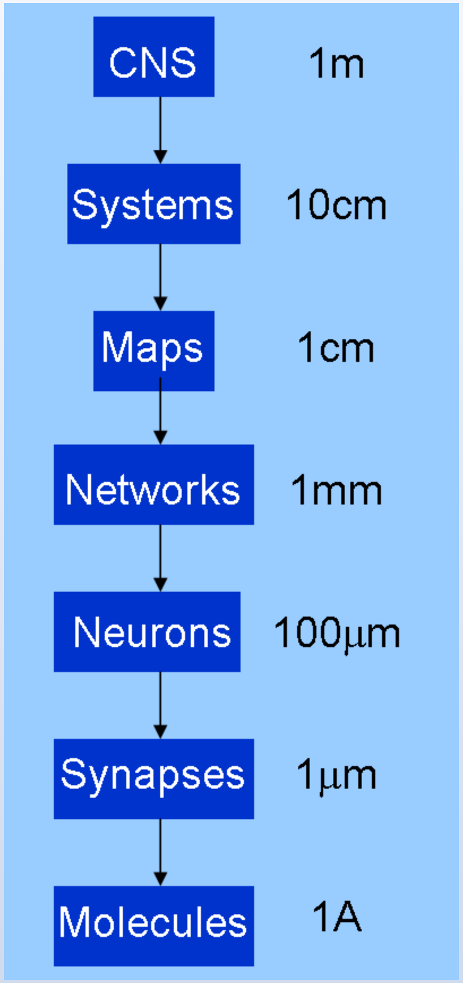
Van essen etal

Last minute: add video here

Scale

- **Several courses** focus on brain
  - at different scales
  - from different perspectives
    - interpreting biomedical signals for various devices
    - understanding and modeling functional aspects
- Depending on the **scale**:
  - different mathematical tools are needed to model brain activity or functional principles
  - different means of observation exist to analyse its activity

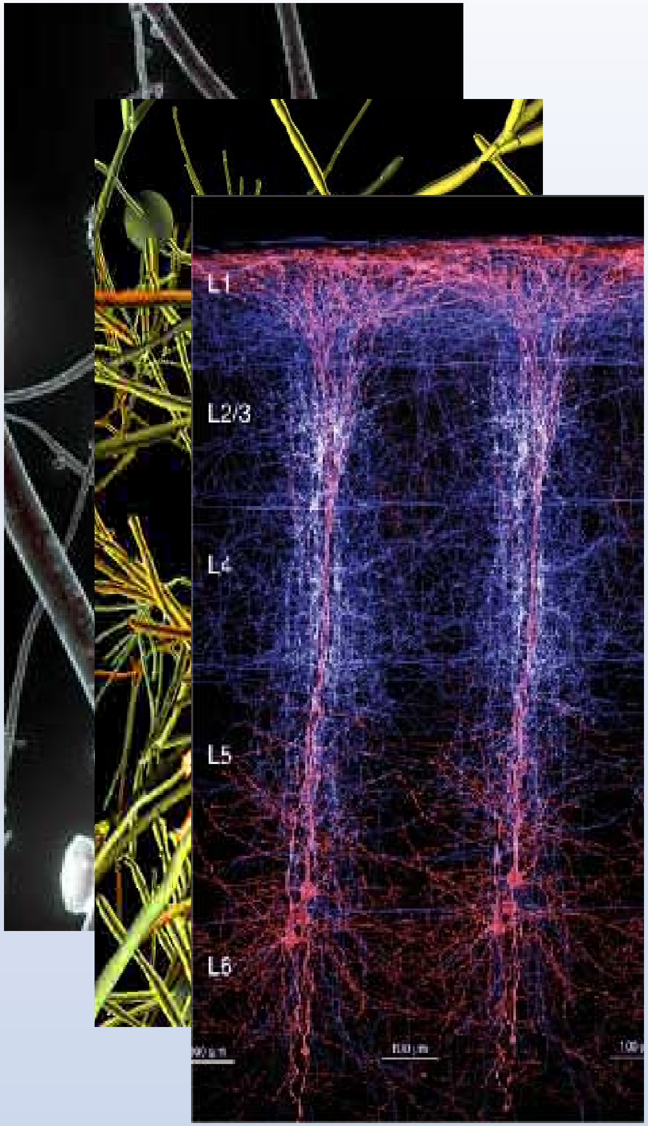
The state of each subsystem at a given **scale** is permanently **evolving** in space and time.



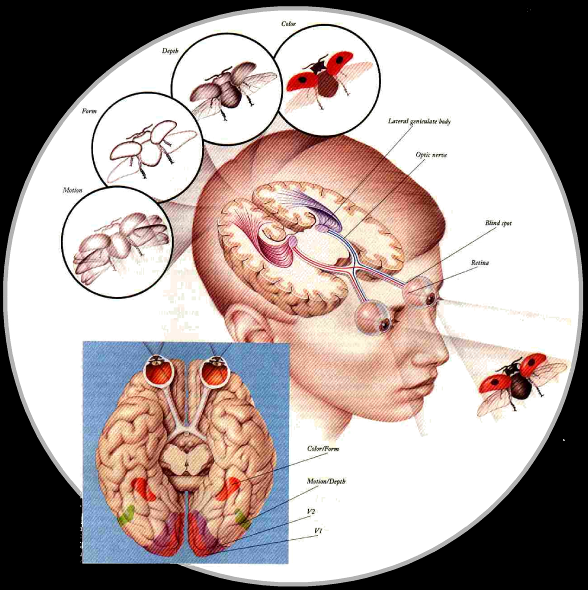
Neuron dynamics

Bruno Cessac and Olivier Faugeras (INRIA, EPI Neuromathcomp)

- **Neurons and synapses**: analysis of neuron dynamics using methods from dynamical systems theory (stability, bifurcations, asymptotic dynamics).
- **Neuronal networks**: Dynamical evolution is characterized by non-linear systems with a large number of degree of freedom. What about the statistics of spike trains?
- **Neural masses**: At a mesoscopic scale the neuronal substrate can represented by a continuum where points represent neuronal populations.



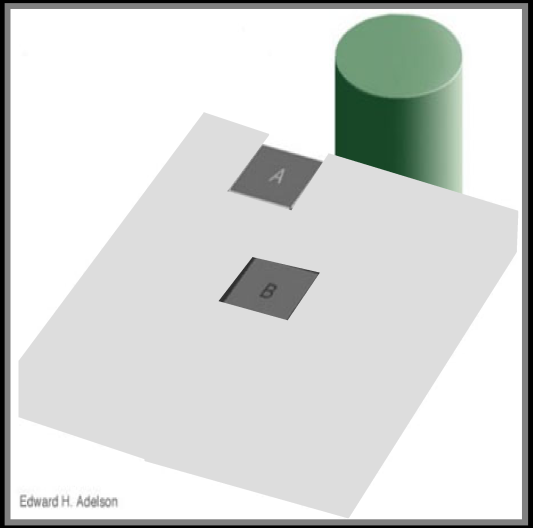
Neuron dynamics also reveals a lot concerning our system behavior! And for example, our **visual system**!

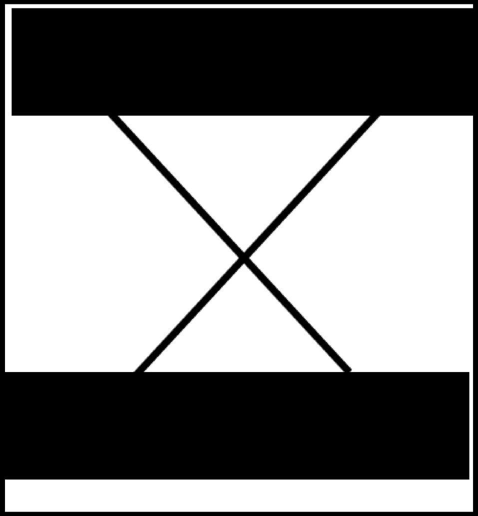


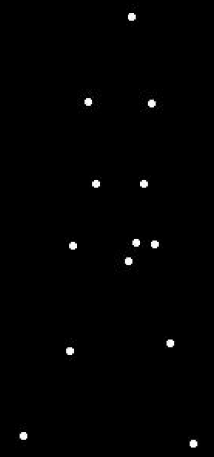
Color
Depth
Form
Motion
Lateral geniculate body
Optic nerve
Blind spot
Retina
Color/Form
Motion/Depth
V2
V1

perception

Explore the functional organization of humans







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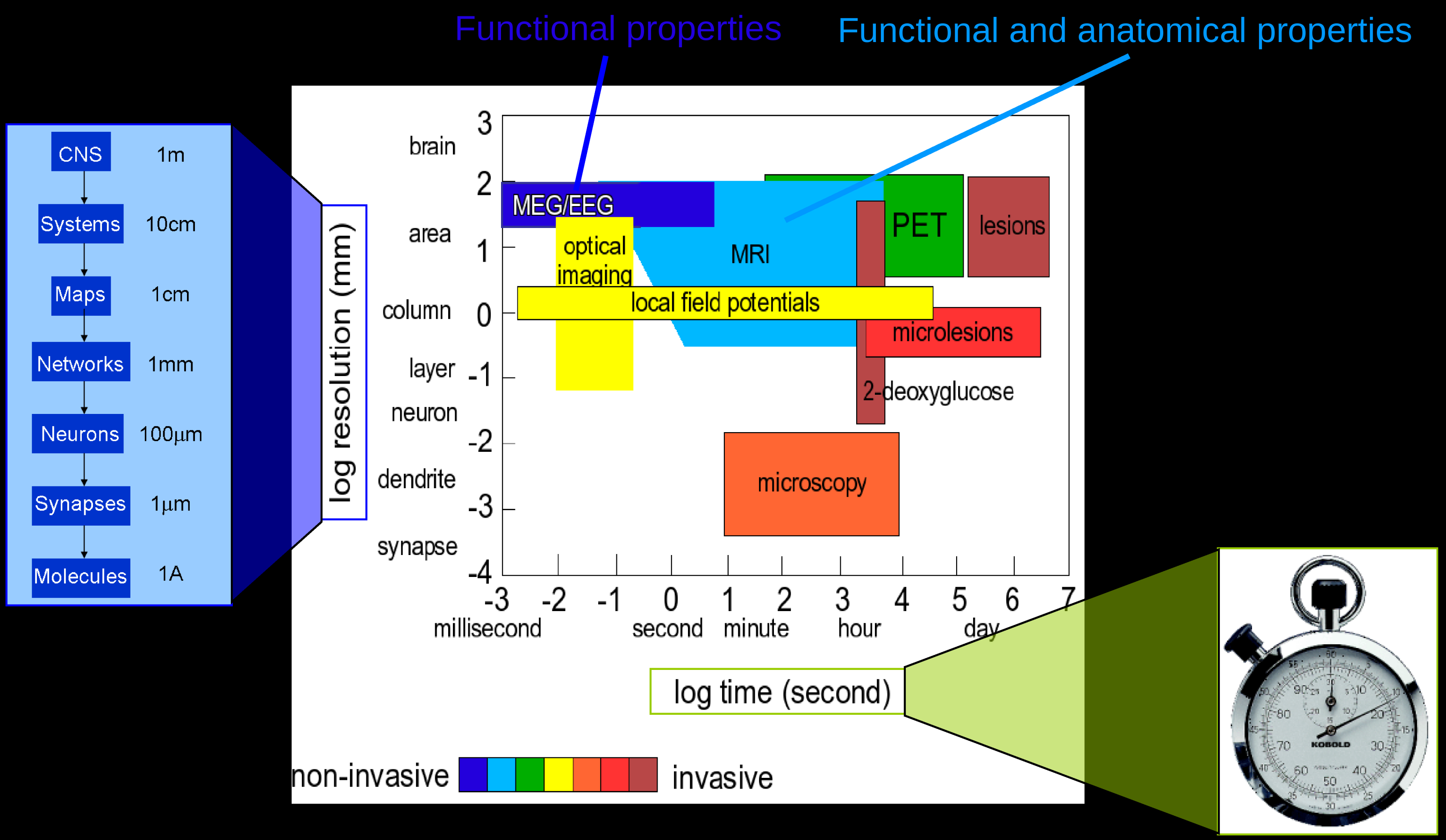

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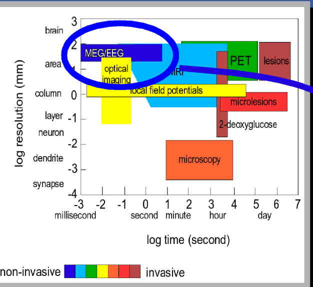
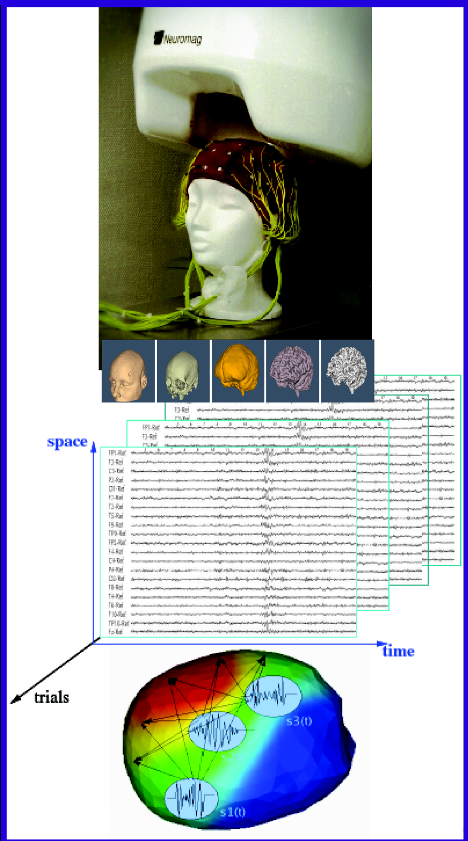


MEG/EEG



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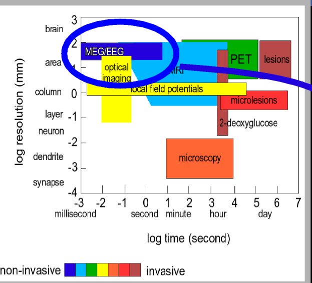

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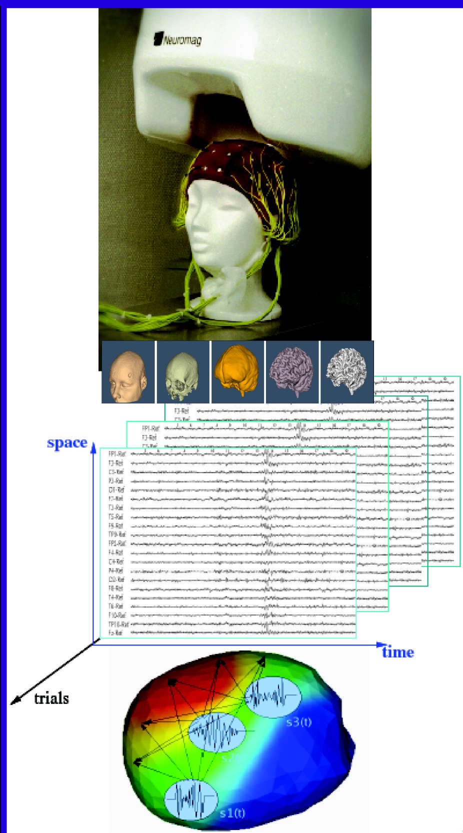
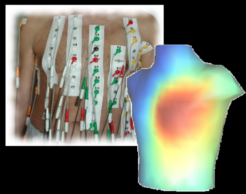
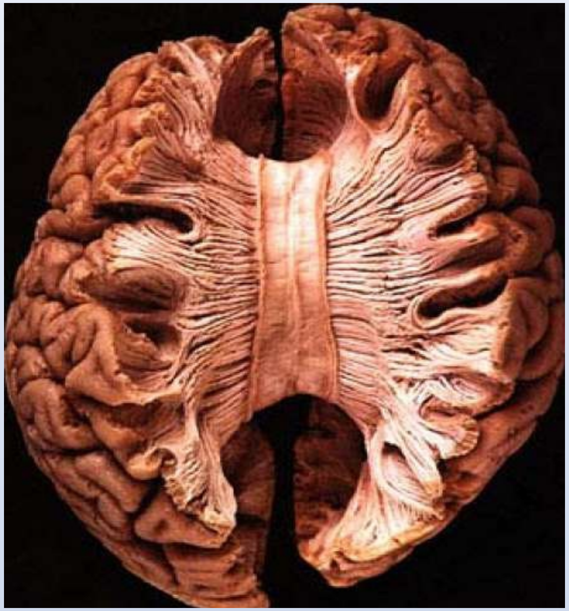


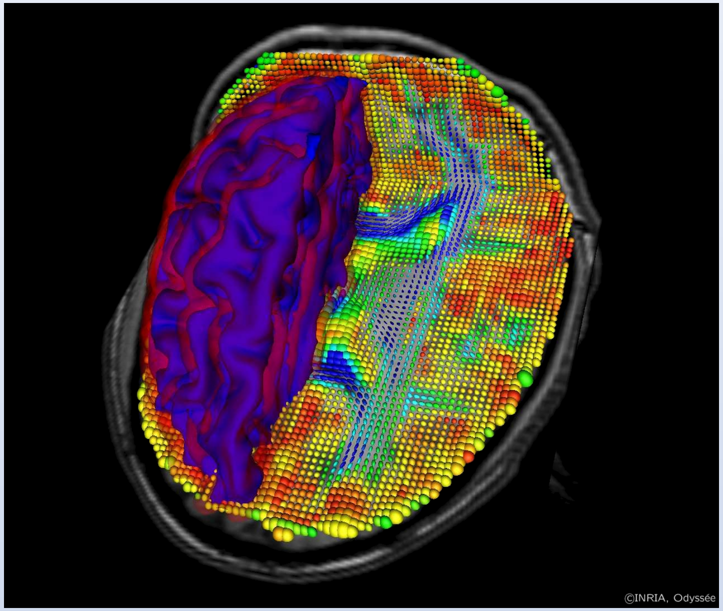


Variational methods and geometric flows for brain imaging

R. Deriche (INRIA-Odyssee)

- Diffusion MRI: From water diffusion to the architecture of cerebral white matter
  - A recent non-invasive method
  - Subvoxel spatial precision (voxel = 1mm^3, sensitivity to diffusion phenomenom = μm → axon fiber bundles)





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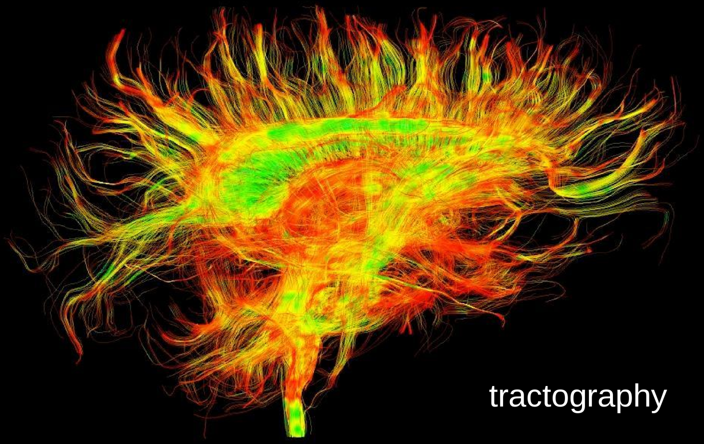
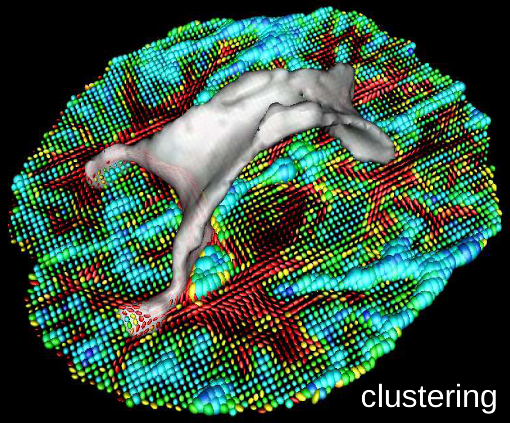


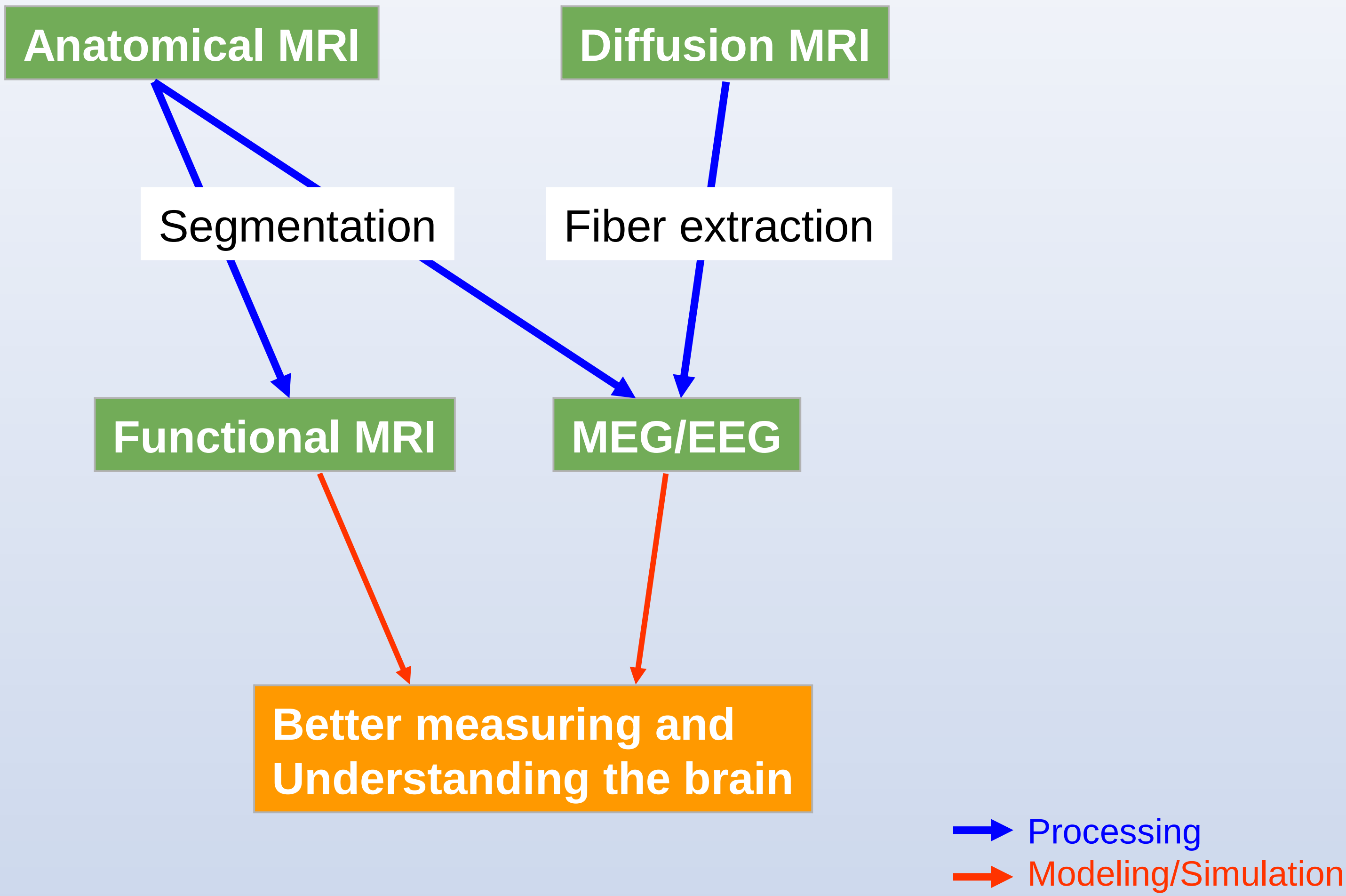
tractography



clustering

Measuring brain activity

- These sensors are complementary



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- To conclude…

With this Master…

- **You** will have a truly inter-disciplinary learning experience in the challenging field of computational biology given by experts, outstanding Professors and Researchers.

- **You** will be in a wide scientific park of approximately 1300 corporations and 30.000 jobs in R&D, mainly focusing on information technology, multimedia, medicine and bio-technologies.

- **You** will have access to a wide network of contacts helping you to find the best opportunities for your internship, *PhD or industrial position.*

Master of Science in

Computational Biology

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http://cbb.unice.fr

November, – April
First round of applications

Begining of May
Notification of acceptance for the first round

May – June
Second round of applications

End of June
Notification of acceptance for the second round

Scholarships available