April 2016 – INFN enters the Human Brain Project leading the WaveScalES consortium

cortical slow waves and impulse responses: matching experimental measures vs. large scale simulations

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WaveScalES coordinator

the APE lab - INFN Roma

Brain Research: Scientific and Translational

Novel experimental techniques permit a quantitative exploration of the Brain Architecture

Understanding the Brain, at different levels of abstraction. Since ever, one of the greatest intellectual ambitions.

A quantitative approach is emerging.

Europe, brain disorders and trauma cost: 798 billion € /year

Increasing, due to the progressive population aging

Possible therapies from better understanding

Computational Neuroscience: an Emerging Quantitative Discipline

INFN

Human Brain Project

Novel Brain Experimental Techniques, multi-modal High Spatial and Temporal Definition

Simulations on Massive Parallel Computers, Robots, Neuromorphic platforms

Computational Neuroscience: a kingdom for physics

Theoretical Models: Long-Range and Short Range Connectome (architecture of connections), Dynamic laws for Neuron Membrane Potential and Currents and Synaptic Plasticity (learning), Consciousness Theories

The Human Brain Project - Intro

- Planned European fund. 500 MEuro, Oct 2013 – 2023
  - Original Consortium: 112 research institutes
  - Ramp up phase: Oct 2013 – March 2016

- Spring 2015 (also in response to criticism during first-years ramp-up phase):
  - Competitive call for new scientific proposals/partners (evaluation by external reviewers)
    - INFN leads the WaveScalES proposal, 4 proposals selected among 57 submitted
  - HBP Commitment: before 2018 define transformation into legal entity
    - National Stakeholders board – will be proportional to national investments
    - **National /Regional Partnering Projects**
    - Scientific Board (presently, 13 + 10 members)
  - Periodic (bi-annual) plan revision, new competitive calls, additional partners

- First HBP operational phase, April 2016-March 2018
  - WaveScalES starts April 2016, 1 MEuro/year, if good results, until 2023
  - 5 senior INFN research positions funded by WaveScalES
  - Discussion of next “WaveScalES HBP budget” in 2018

Slow Waves and Perturbations

- During deep-sleep and anesthesia the cortex moves in a low-complexity mode:
  - Collective oscillations, ~ @ 1Hz, between two states:
    - Down state: neurons nearly silent (firing @ few Hz)
    - Up state: neurons active (firing @ tens of Hz) for a few hundreds ms, then inhibition switch the system to the down-state
  - Local oscillation phase -> slow-waves moving on the cortical surface (planar, spirals, ...)
- Perturbative approach:
  - Localized spatio-temporal impulse
  - Measure the impulse response
  - Quantification of consciousness potential and damages in disease/trauma, forecast of emergence from coma

References:

About the proposal of measurable observables about consciousness and integration/differentiation and macro/scale connectivity

- ❑ Casali et al., (2013) "A Theoretically Based Index of Consciousness Independent of Sensory Processing and Behavior" Science Translational Medicine
- ❑ G. Deco, G. Tononi, et al., (2015) "Rethinking segregation and integration: contributions of whole-brain modelling" Nature Reviews Neuroscience

About Consciousness: example of system of axiomes / postulates focusing on a balance of integration and differentiation

- ❑ G. Tononi (2015) "Integrated Information Theory" Scholarpedia
- ❑ G. Tononi and C. Koch (2015) "Consciousness: here, there and everywhere" Philos. Trans.
- ❑ **Supporting mathematical framework**
  - ❑ Balduzzi, Tononi (2009) "Integrated Information in Discrete Dynamical Systems: Motivation and Theoretical Framework" PLoS Computational Biology
  - ❑ Balduzzi, Tononi (2009) "Qualia: The Geometry of Integrated Information"

About meso-scale cortical connectivity models

- ❑ Schnepel P, et al. (2015) "Physiology and impact of horizontal connections in rat neocortex" Cerebral Cortex
- ❑ T.C. Potjans and M. Diesmann (2014) "The Cell-Type Specific Cortical Microcircuit: Relating Structure and Activity in a Full-Scale Spiking Network Model", Cerebral Cortex

About pioneering large scale modeling experiments of the thalamo-cortical system

- ❑ Modha, S. D., & al., (2011) "Cognitive Computing", Communications of the ACM,
- ❑ E. M. Izhikevich, G. M. Edelman, (2008) "Large-scale model of mammalian thalamocortical systems" PNAS

About Slow Waves

- ❑ Destexhe, A., & Contreras, D. (2011)." The Fine Structure of Slow-Wave Sleep Oscillations: from Single Neurons to Large Networks." Sleep and Anesthesia
- ❑ Timofeev, I., & Chauvette, S. (2011). "Thalamocortical Oscillations: Local Control of EEG Slow Waves." Current Topics in Medicinal Chemistry,

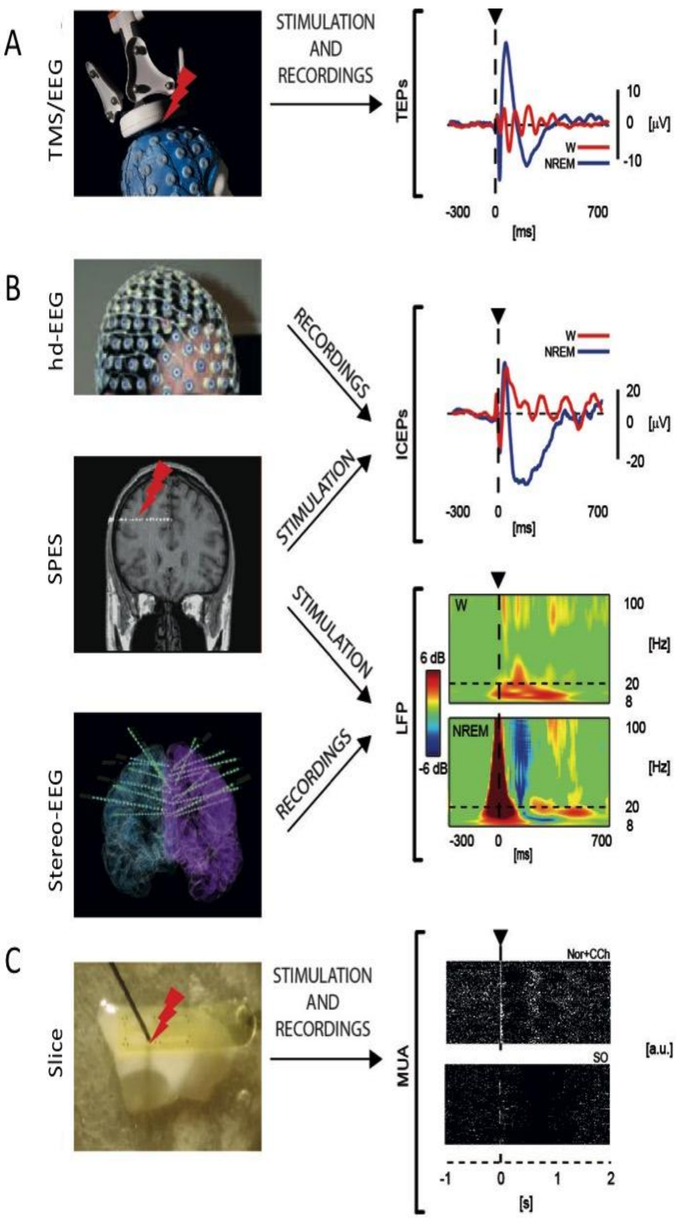
About DPSNN, the large scale neural simulator developed by the APE lab of INFN in cooperation with ISS

- ❑ P.S. Paolucci, et al., (2015) "Dynamic Many-process Applications on Many-tile Embedded Systems and HPC Clusters: the EURETILE programming environment and execution platforms", Journal of Systems Architecture
- ❑ P.S. Paolucci, et al. (2015) "Impact of exponential long range and Gaussian short range lateral connectivity on the distributed simulation of neural networks including up to 30 billion synapses " arXiv:1512.05264
- ❑ P.S. Paolucci, et al.. (2013) "Distributed simulation of polychronous and plastic spiking neural networks: strong and weak scaling of a representative mini-application benchmark executed on a small-scale commodity cluster". arXiv:1310.8478
- ❑ M. Mattia, P. Del Giudice (2000) "Efficient Event-Driven Simulation of Large Networks of Spiking Neurons and Dynamical Synapses. Neural Computation"

WaveScalES in HBP - Summary

- Experimental WaveScalES partners (will) measure brain Slow Waves during deep-sleep and anaesthesia, and during the transition to consciousness, including:
  - non invasive techniques on human: high-def. electro-encephalographic response to trans-cranial magnetic stimulations
  - electro-physiological response to in-vitro/in-vivo opto-pharmacologic stimulation of murine models
- INFN in WaveScalES – mainly in collab. with ISS Roma
  - large scale parallel/distributed simulation of Slow Waves and perturbation responses

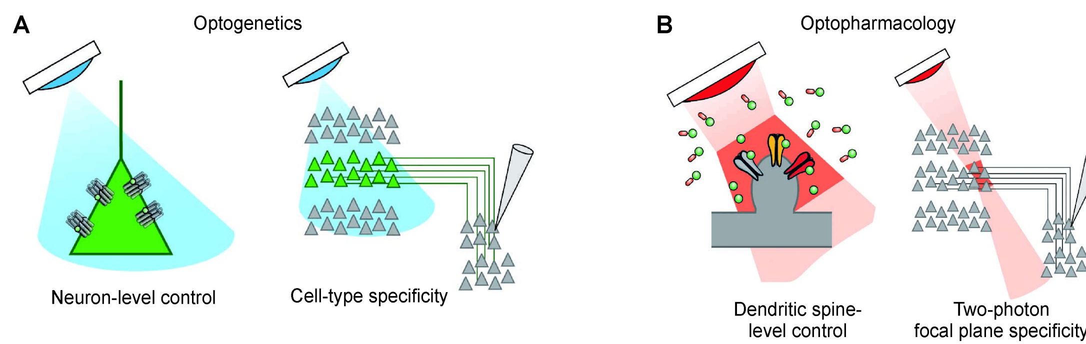
WaveScalES measures: from the human bedside downto the murine slice.



TMS/EEG to assess the changes in cortical connectivity and complexity in physiological and pathological conditions;

Intracortical single-pulse electrical stimulations (SPES) and stereo-EEG recordings in combination with scalp hd-EEG to link slow-wave dynamics to overall network connectivity and complexity.

Electrical / optical stimulations / recordings in brain (slices) to study the effects of (opto)-pharmacological manipulations on bistability, connectivity and complexity.

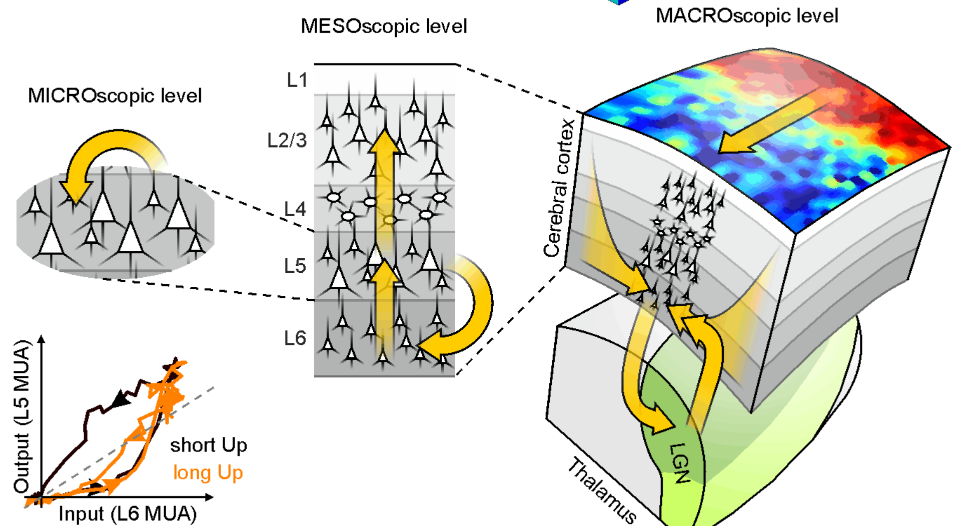


WaveScalES: Research Tasks

Understand multiscale brain exploiting Slow-Wave Activity (SWA) as a Rosetta stone. Five Tasks:

1. Slow-wave activity changes during sleep/anesthesia (leader: ISS Roma: Mattia, Del Giudice)
2. Slow-wave and complexity: from the micro-scale to the bedside (leader: UniMi: Massimini)
3. Slow-wave activity in murine transgenic models of neurological disease
4. Modulation of slow-wave activity with opto-pharmacology
5. Slow wave simulation platforms (leader: INFN)

Human Brain Project



INFN (with ISS): Large-scale spiking simulations (hundreds of billions synapses) distributed over (tens of) thousands of MPI processes, including columnar, areal and inter-areal connectivity models.

Computational objectives: match, explain and predict experimental observations. Improve simulators / HPC interconnects

Pier Stanislao Paolucci – parallel computing CV

- Since 1984, member of APE massive parallel comp. lab, INFN Roma led by Nicola Cabibbo, Giorgio Parisi
- Inventor/developer of parallelization algorithms, parallel hardware architectures, system software tools, applied to:
  - QCD, multidim. FFT, meteorology (cubed-sphere), synthetic aperture radar, oil exploration, acoustic arrays, digital signal processing, multi-processor systems-on-chip, …, large scale neural networks

- 2010-2015 Coordinator, European FP7 Project EURETILE, 5M€
- 2006-2009 Coordinator, European FP6 Project SHAPES, 9M€
- 2000-2010 Chief Technical Officer, Atmel Roma design center (NASDAQ: ATML), 4 year tech. tranf. detachment, then part-time researcher until 2010, then back to INFN (full-time researcher)
  - US patent 6,766,439, US patent 7,437,540
  - 2000-2006 Coordinator, Eureka Project DIAM,
- 1997-2000 Principal Investigator, ESPRIT European proj. mAgic-FPU

WaveScalES partners/key-persons

Human Brain Project

1) INFN, Istituto Nazionale di Fisica Nucleare, APE Parallel Computing Lab, Roma, Italy

Pier Stanislao Paolucci 

Piero Vicini 

2) Consorci Institut d´Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain – **Murine electro-physiology**

Maria Victoria Sanchez-Vives 

Julia Weinert 

3) Università degli Studi di Milano, Italy – **Measures in humans**

Marcello Massimini 

Mario Rosanova 

4) Fundació Institut de Bioenginyeria de Catalunya, Spain – **optopharmacological perturbations**

Pau Gorostiza 

Miquel Bosch 

5) Istituto Superiore di Sanità, Italy – **theoretical models**

Maurizio Mattia 

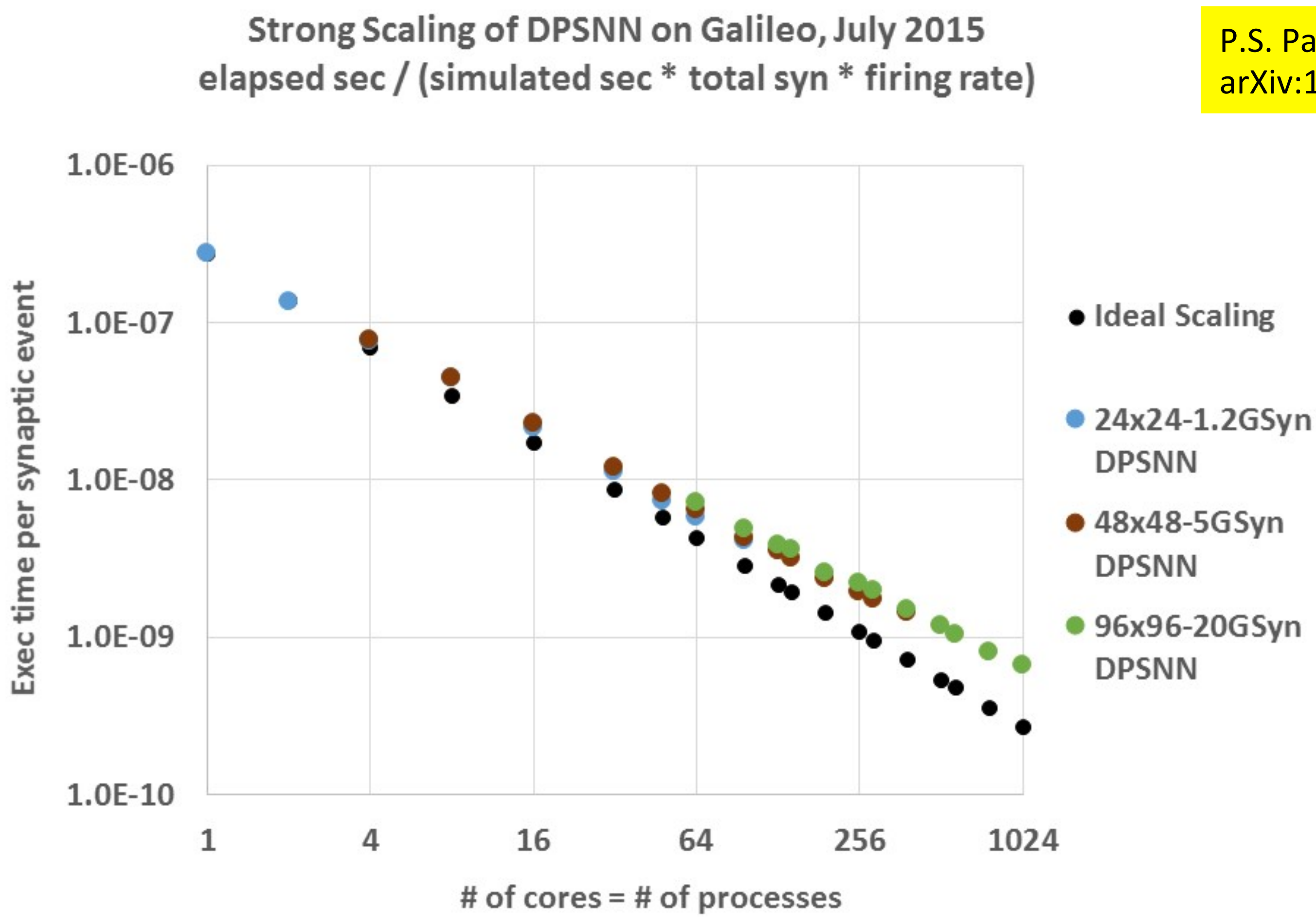
Paolo Del Giudice 

Development of Distributed Plastic Spiking Neural Net Simulator in INFN-

- INFN coordinated EURETILE(2010 - 2015) FP7 project
    - Investigation of future generations of distributed/parallel computers
    - Focus on software/hardware scalability on many core systems
    - Start of DPSNN-STDP code development as a source of requirements and architectural inspiration for extreme parallel computing
- The brain consumes < 50 W computations. A high abstraction simulator of its computations would require >> 50 MW on present generation HPC
- INFN third party of ISS Roma in CORTICONIC (2013 – 2016) FP7 project
    - Identify computational principles of the cerebral cortex
    - First comparison with in-vivo/in-vitro experimental results
    - DPSNN improved for CORTICONIC simulations (support of more realistic biological models) importing models from ISS Perseo scalar simulator
- DPSNN simulator key benchmark in EXANEST (2016-2018) FET Project (INFN, Piero Vicini) – good overlap and development potential for APE lab

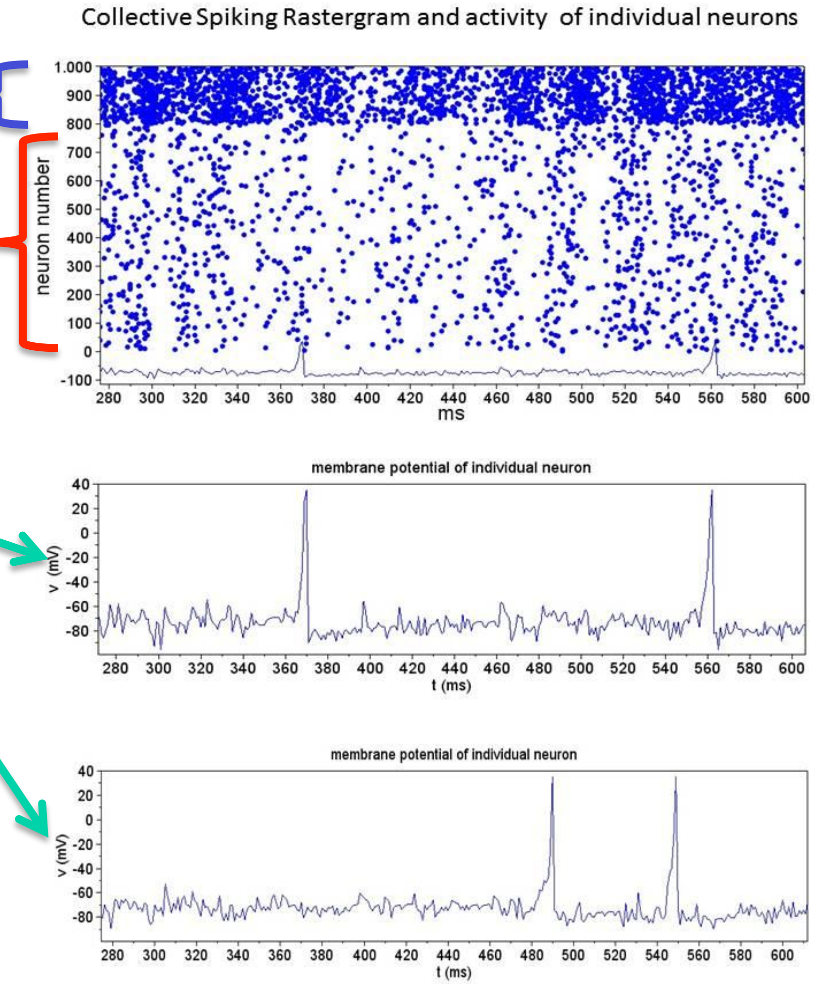
Strong Scaling of our simulator, measured up to 1024 cores, 20 Gsynapses

P.S. Paolucci, et. al (2015)
arXiv:1512.05264



(very small scale example of) neural net simulation

- 200 inhibitory neurons
- 800 excitatory neurons
- Time resolution: 1ms
  - (horizontal axis)
- Each dot in the rastergram represents an individual spike
- The evolution of the membrane potential of individual neurons is simulated
- The evolution of individual synaptic strength is computed (not shown in the picture)
- individual synaptic delays are taken into account
- Individual connections and neural types can be programmed



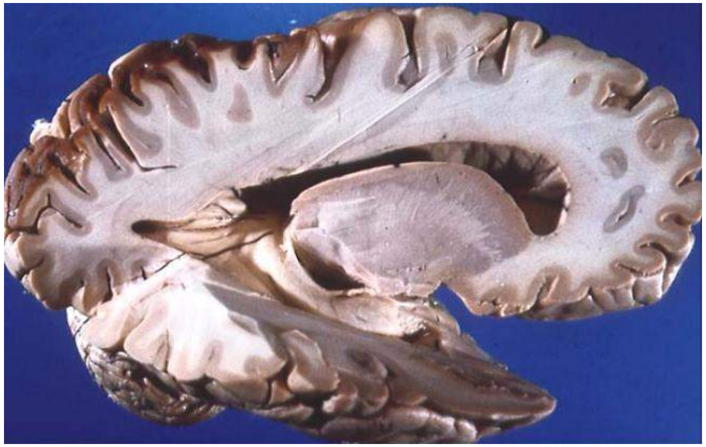
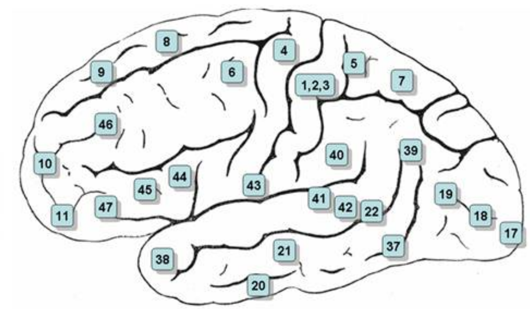


Image: John A Beal CC-BY license. 2005 Louisiana State Univ.

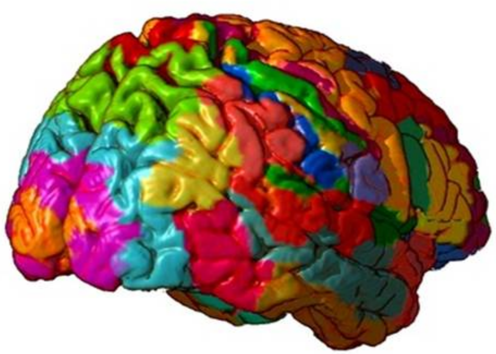
Examples of recent experimental development: White Matter Long Range Connectome

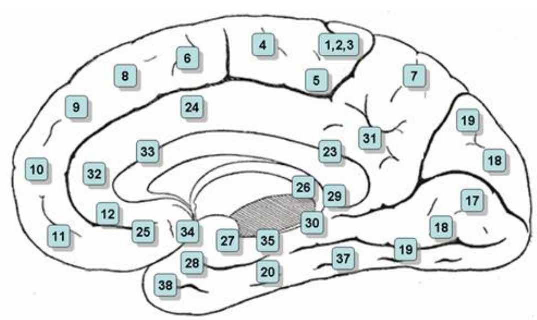
Human Brain Project

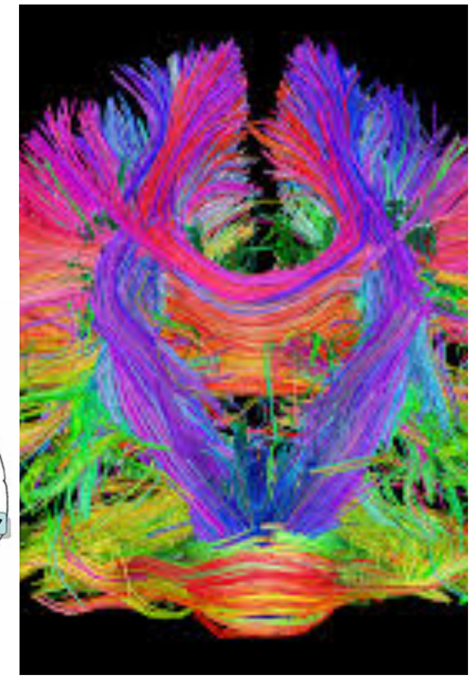


Year 1909 - Brodmann Cortical Areas Defined

Ȼ(2009) Mark Dow







Year 2015 – White matter mapping, DTI - fiber tractography

Experimental techniques… an ample room for INFN contributions

A few examples of novel (last ten years) techniques that are transforming brain research in a quantitative discipline:

- Connectome by DTI-Fiber tractography: measure of the (probability of) long-range connections among brain areas (white matter…)
- opto-genetic/opto-pharmacology: real-time visualization of neuro-synaptic activity and short-range connection (probability)
- High definition Electro Encephalography and Multi-unit Electrode Arrays: hundreds of electro-physiological acquisition/stimulation channels
- Functional Magnetic Resonance Imaging (areas vs. tasks correlation)
- Measure of synaptic STDP (Spiking Time Dependent Plasticity): understanding time-dependent causal/anti-causal learning and temporal arrow
- Computationally efficient models of neural activity/spiking (20 arithmetic operations / (neuron * simulated ms); Parallel/distributed computing
- Quantitative Complexity/Consciousness Indexes/Theories

- …ample room for improvement, e.g. number of acquisition channels, spatial / temporal resolution, (and capacity to manage large teams of researchers
- **Possible INFN contribution on experimental methods**

INFN APE lab

Team (10 people):

- (staff, Roma 1):
  - Piero Vicini, Pier Stanislao Paolucci, Alessandro Lonardo
- (art. 36, Roma 2):
  - Roberto Ammendola
- (Temporary positions, mainly funded by European Projects, Roma 1)
  - Andrea Biagioni, Ottorino Frezza, Francesca Lo Cicero, Michele Martinelli, Elena Pastorelli, Francesco Simula
  - **Long term brain research would benefit from a long term perspective for research personnel. Investment in know-how (personnel) should be secured**

- Created in 1984 by Nicola Cabibbo & Giorgio Parisi
- Since then research & development of parallelization algorithms, system software and hardware architectures for numerical simulations /digital signal processing / HPC
- Several technological / industrial spin-off

Conclusions

- Brain: emergence of a quantitative discipline, scientific and translational impact
- Novel experimental methodologies, Multi-scale Theories, Computational Neuroscience
- WaveScalES in Human Brain Project
  - Combines experiments, theory and simulations
  - **Several opportunities for INFN to be explored…also about the experimental measures/treatment techniques**
  - **Long term brain research in INFN will benefit from a long term perspective. Investment in know-how (INFN research personnel) should be secured. Adequate computational resources needed. Investment (from overhead, in kind and support of national projects) will be key to play a key role in the HBP national stakeholders board.**
  - **Opportunity for Regional/National HBP Partnering Projects**
  - Strong collaboration with ISS (Del Giudice, Mattia), Brain Simulation a key benchmark also in EXANEST FET Project (INFN, Vicini) future interconnects/ storage, strategic overlap exists
  - Didactic/employment opportunity: complex system numerical/theoretical physics