WaveScalES Experiment, in the

Human Brain Project

Simulation of cortical waves using large scale networks of spiking neurons interconnected by plastic synapses

The WaveScalES experiment in the Human Brain Project

Pier Stanislao Paolucci

Coordinator of the WaveScalES consortium

For the APE parallel/distributed computing lab - INFN Roma

Brain Research: Scientific and Translational

WaveScalES Experiment, in the Human Brain Project

Novel experimental techniques permit a quantitative exploration of the Brain Architecture at micro-, meso- and macro scale

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

WaveScalES Experiment, in the Human Brain Project

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

Simulations on Massive Parallel Computers, Robots, Neuromorphic platforms

Computational Neuroscience

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

The Human Brain. A simplistic view. Grey Matter, White Matter, Areas, Columns, Layers

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- About **100 Giga NEURONS** (cells) in a human brain
- about **10000 SYNAPSES (connections) per NEURON**
- Synapses placed on the **AXONAL arborization** of each neuron
- Each neuron receives inputs from synapses touching its **SOMA and DENDRITIC arborization**
- **GRAY MATTER**: neurons and short range connections
- **WHITE MATTER**: long range connections

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

Top-down cortical architecture hierarchy:

- There are **(about a hundred of) AREA**s
- Each area: a bidimensional grid of **CORTICAL COLUMNS** (typical grid step: about hundred micron)
- about **6 LAYERS** in a typical cortical column

Investigating the brain architecture.
A long journey

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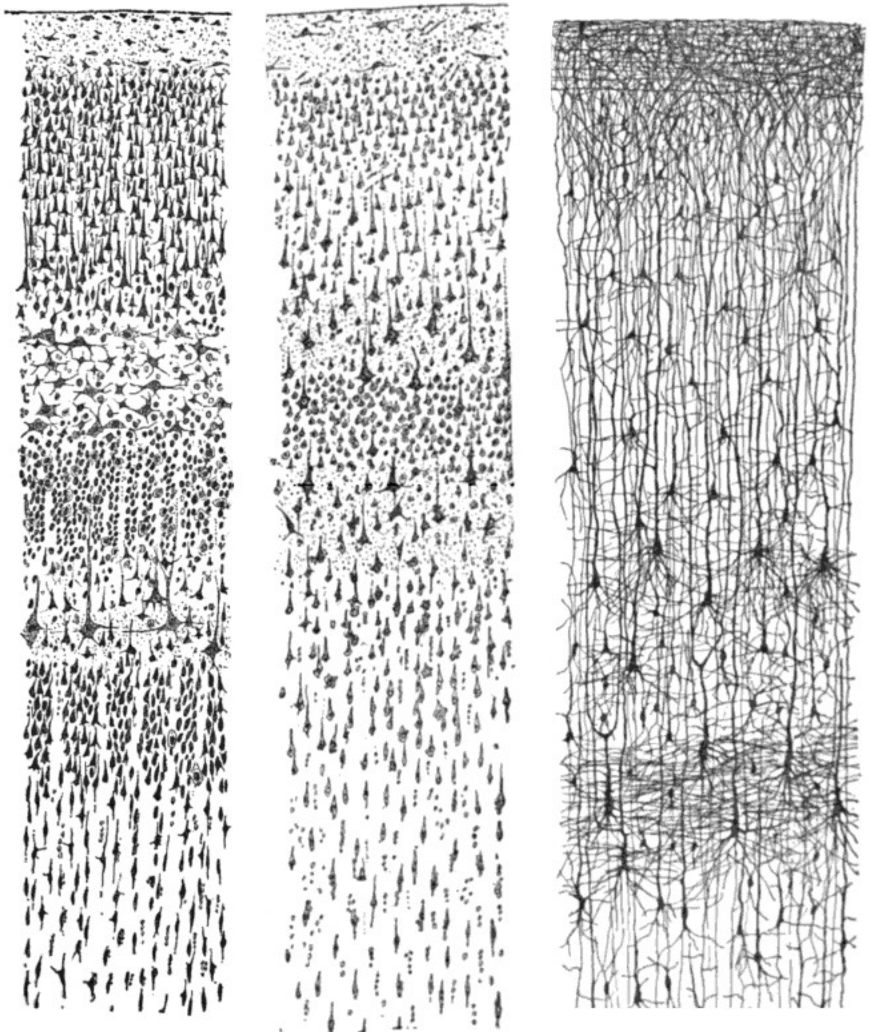
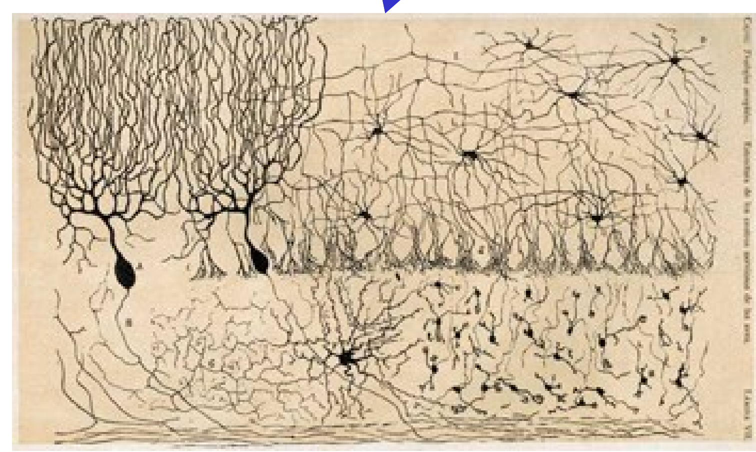


Ramon y Cajal (1899)
Comparative study of
Human Sensory Areas

Ramon y Cajal (1905)
Chick Cerebellum



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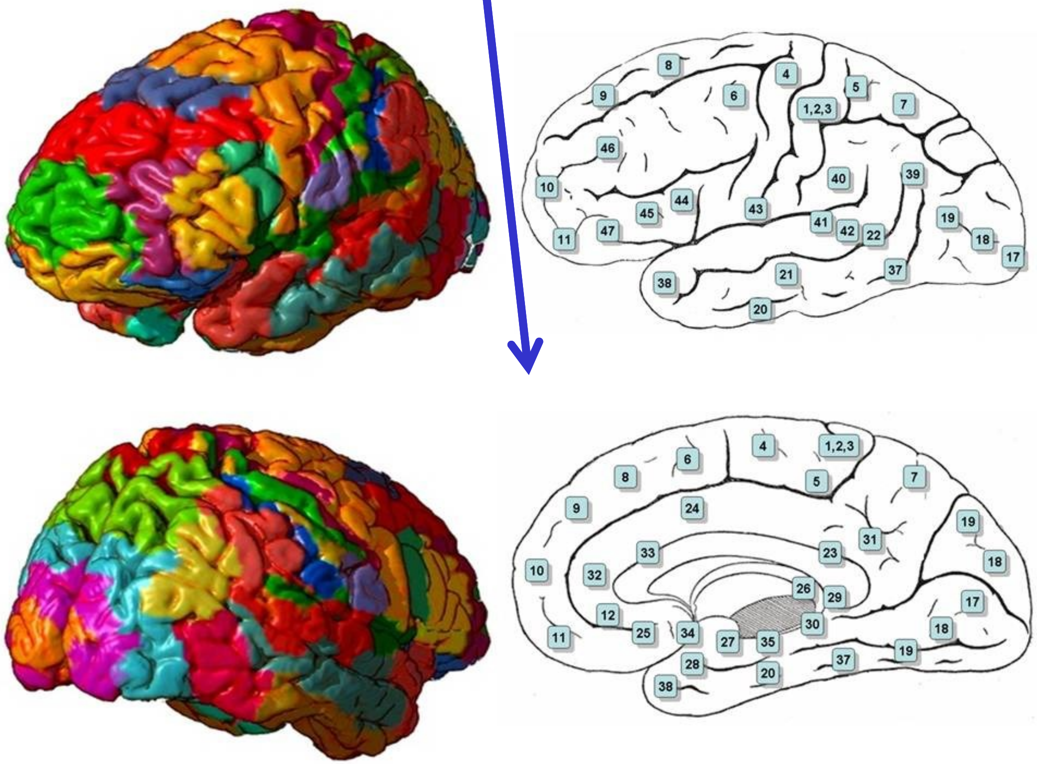
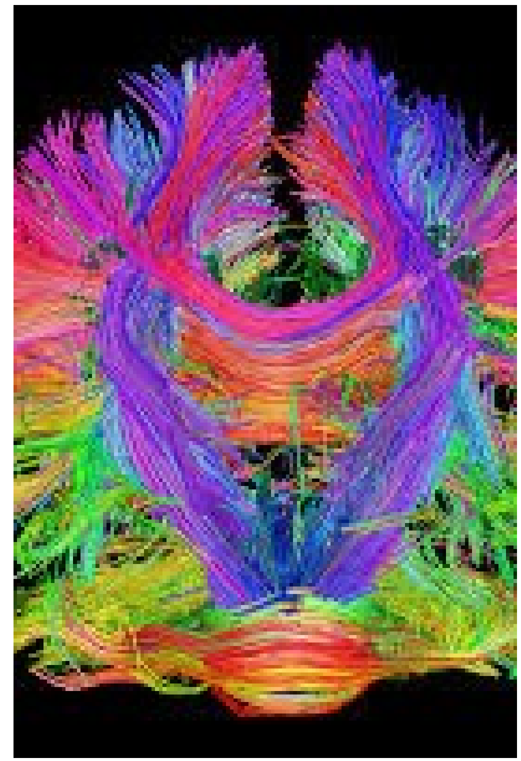
Year 1909 – Definition of Brodmann Cortical Areas





Example of recent experimental development: White Matter Long Range Connectome

Year 2015 – White matter mapping, DTI - fiber tractography

Spiking activity of individual neurons observed in a Zebra Fish Larva

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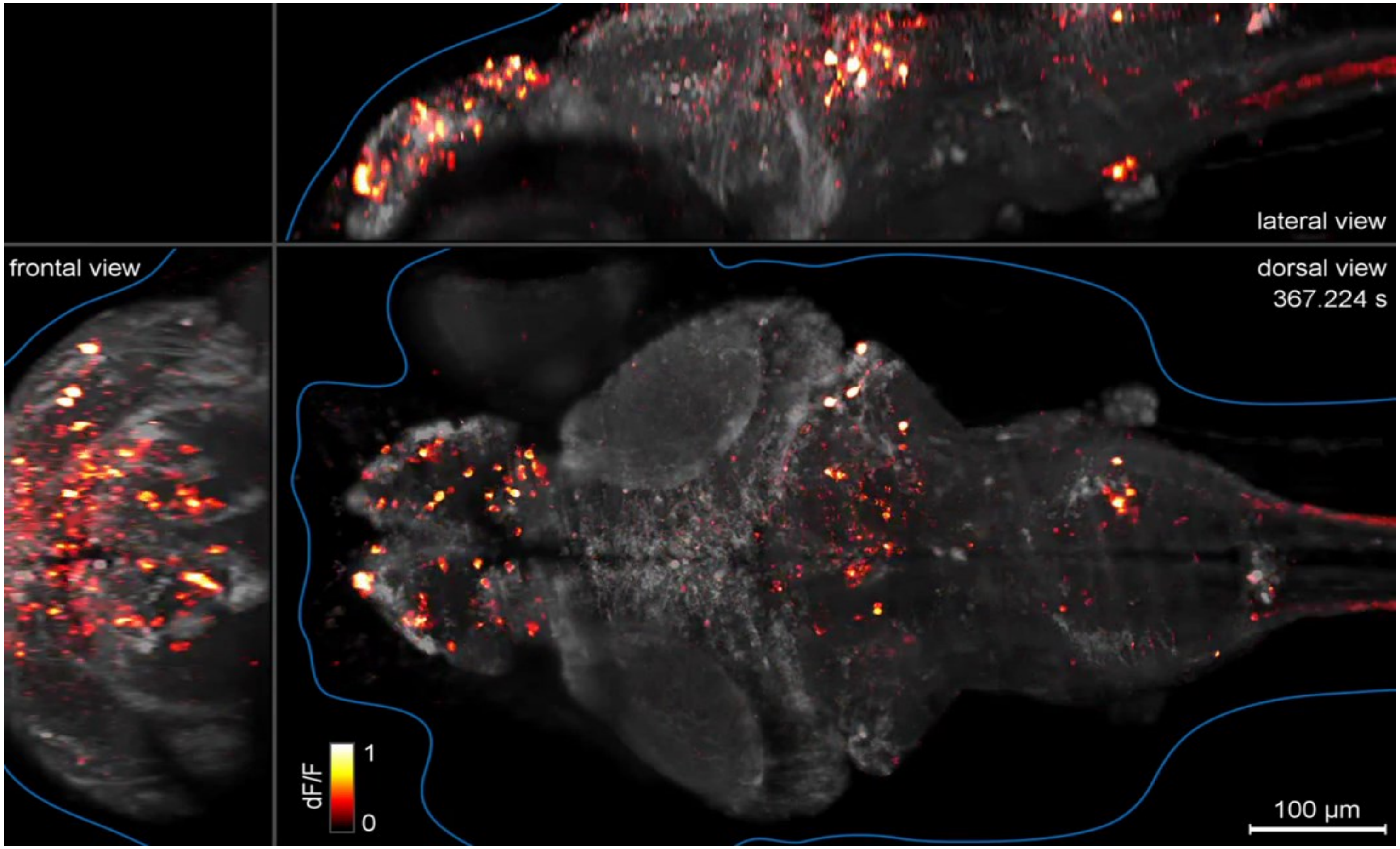

Misha B Ahrens, Philipp J Keller, «Whole-brain functional imaging at cellular resolution using light-sheet microscopy», Nature Methods, 18 March 2013, DOI:10.1038/NMETH.2434 Howard Hughes Medical Institute, 3D recording of temporal spiking activity of ~100 000 neurons. Note: the effective time resolution is still only ~1 s.

Minimal scale example of simulation produced by the simulator DPSNN of INFN APE lab (it can simulate tens of G synapses)

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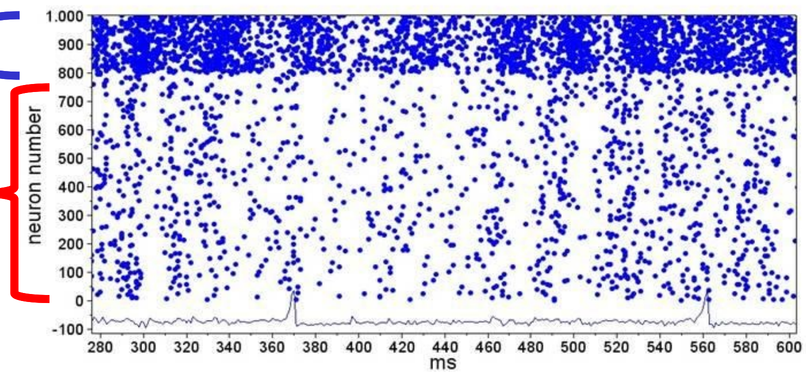
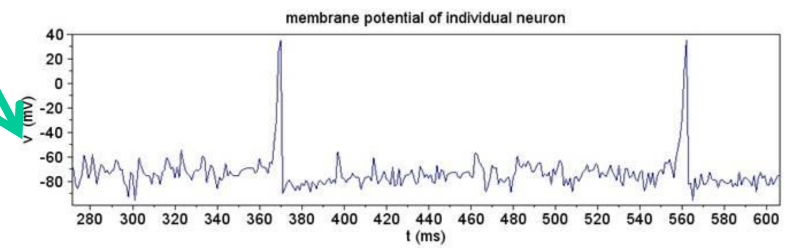
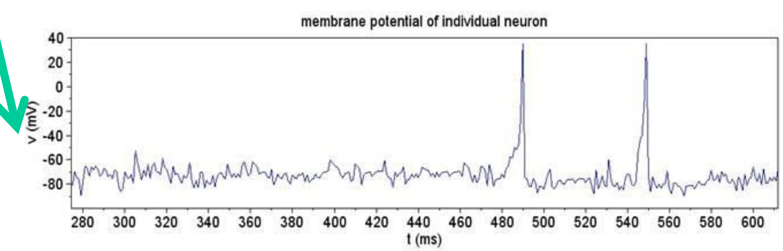
- 200 inhibitory neurons
- 800 excitatory neurons
- Each dot in the rastergram represents an individual neuron spike
- The evolution of the membrane potential of individual neurons is simulated
- About 1M synapses in this simulation
- The evolution of individual synaptic strength is computed (not shown in the picture)
- individual synaptic delays are taken into account
- Individual connections and neural types can be programmed

Collective Spiking Rastergram and activity of individual neurons







WaveScalES Experiment, in the Human Brain Project

The Human Brain Project - Intro

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

- Second half 2015
  - 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 started April 2016
  - 1 MEuro/year, if good results, until 2023

WaveScalES Experiment, in the

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Slow Waves and Perturbations

- During deep-sleep and anaesthesia the cortex moves in a low-complexity mode:
  - Collective oscillations, ~ @ 0.1 – 4 Hz, 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

WaveScalES Experiment, in the

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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
partners / topics / key persons

WaveScalES Experiment, in the Human Brain Project

1. INFN, Istituto Nazionale di Fisica Nucleare, APE **Parallel/Distributed Computing** Lab, Roma, Italy
2. Consorci Institut d´Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain – **Murine electro-physiology**
3. Università degli Studi di Milano, Italy – **Measures in humans**
4. Fundació Institut de Bioenginyeria de Catalunya, Spain – **Optopharmacological Perturbations**
5. Istituto Superiore di Sanità, Italy – **Theoretical Models**

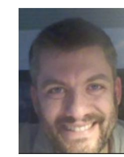
Pier Stanislao Paolucci

Piero Vicini


Maria Victoria Sanchez-Vives

Julia Weinert


Marcello Massimini

Mario Rosanova


Pau Gorostiza

Miquel Bosch

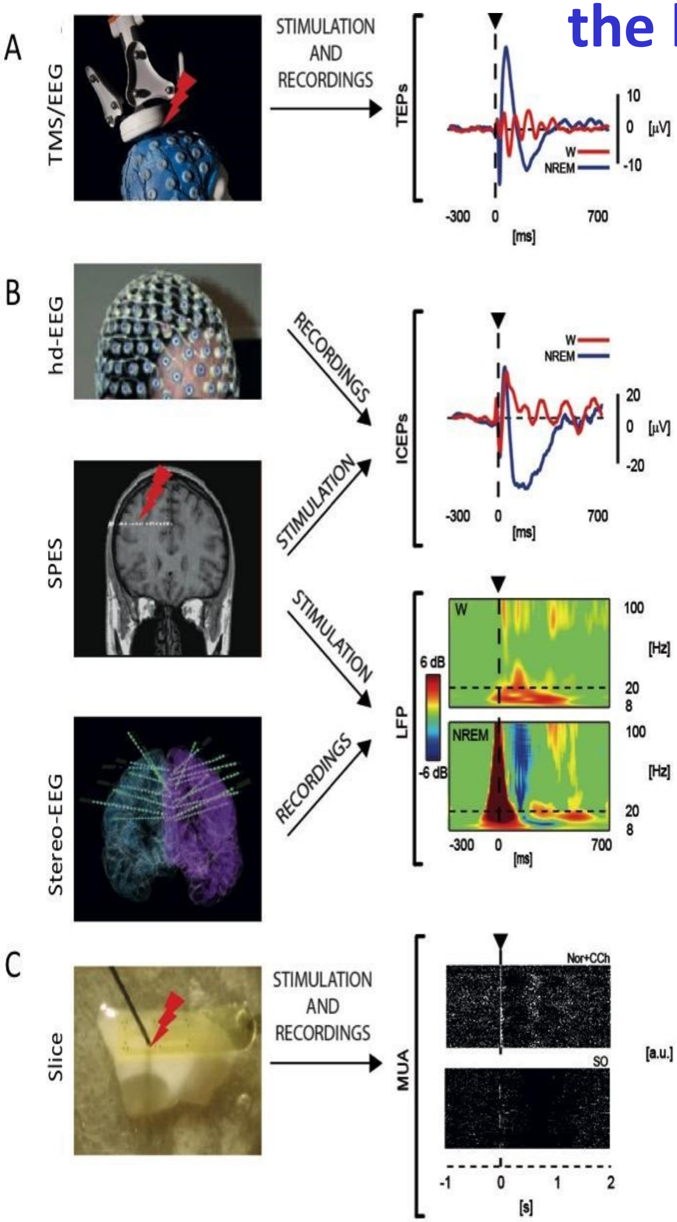

Maurizio Mattia

Paolo Del Giudice


WaveScalES measures: from the human bedside down to the murine slice.

WaveScalES Experiment, in the

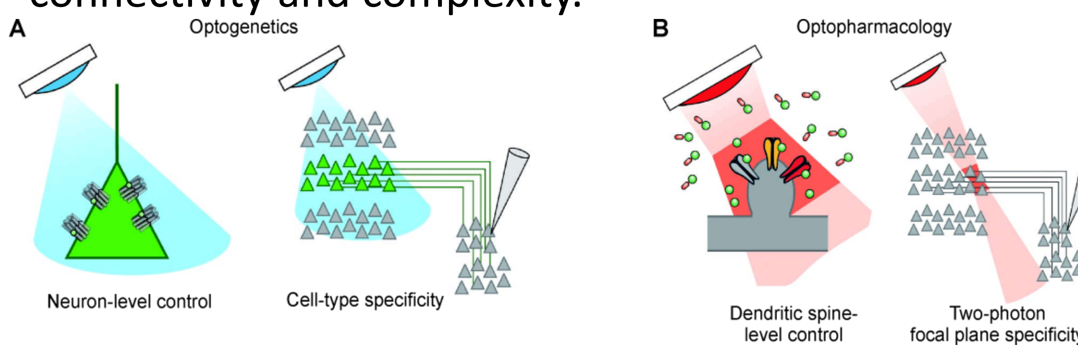
Human Brain Project



TMS/EEG to assess pathological changes in cortical communication and complexity induced by sleep-like bistability;

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.

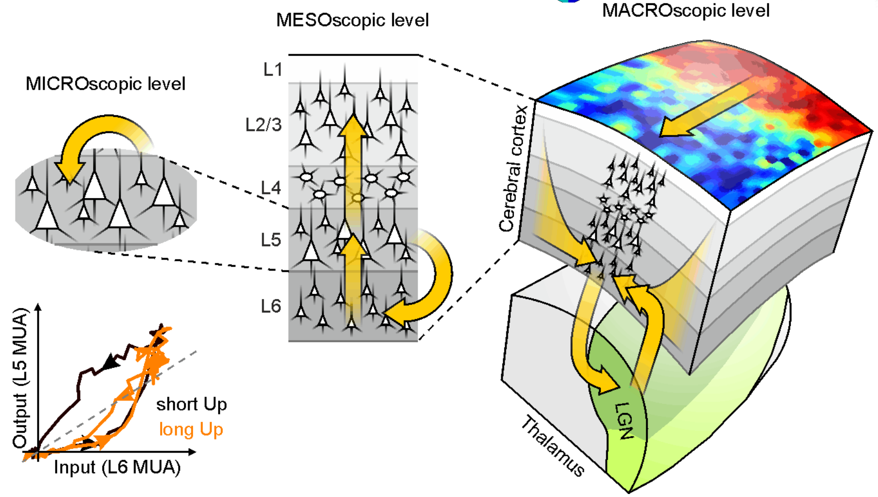
Electrical / optical stimulations / recordings in brain (slices) to study the effects of (opto)-pharmacological manipulations on bistability, connectivity and complexity.



WaveScalES: Research Tasks

Understand multiscale brain exploiting Slow-Wave Activity (SWA).
Five Tasks:

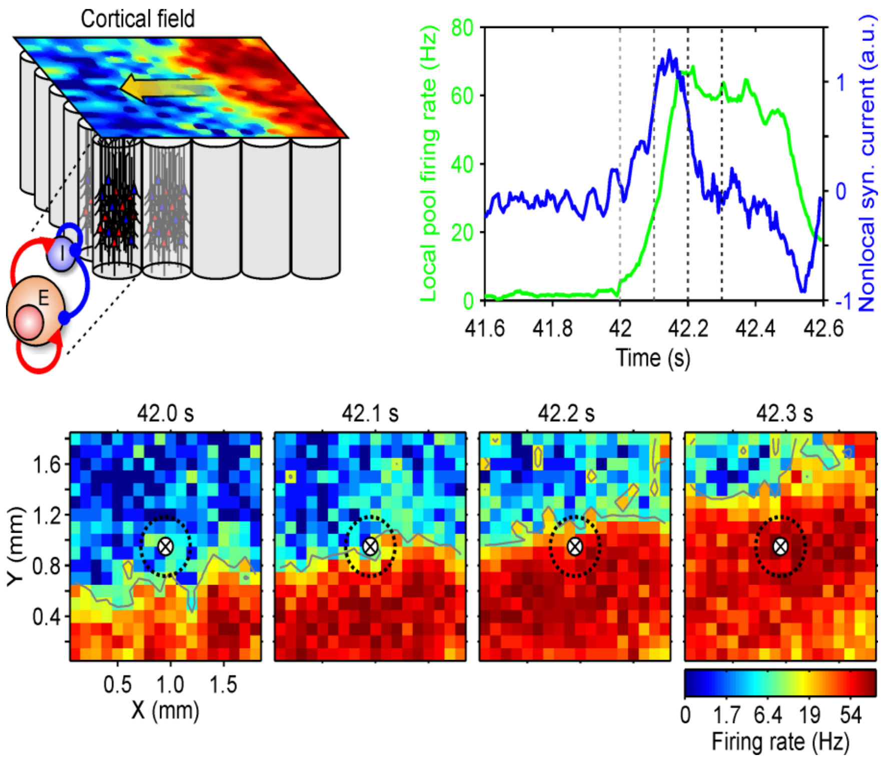
1. Slow-wave activity changes during sleep/anesthesia (ISS)
2. Slow-wave and complexity: from the micro-scale to the bedside (UniMi)
3. Slow-wave activity in murine transgenic models of neurological disease (IDIBAPS)
4. Modulation of slow-wave activity with opto-pharmacology (IBEC)
5. Slow wave simulation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



INFN (with ISS): Large-scale spiking simulations (up to hundreds of billions synapses) distributed over (up to 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

Example of simulation produced using the INFN simulator DPSNN in cooperation with ISS (Paolo Del Giudice, Maurizio Mattia)

WaveScalES Experiment, in the Human Brain Project



Simulation of a large field of cortical columns (pixels of the bottom snapshots), each composed of 2500 excitatory and inhibitory leaky IF neurons. Top, firing rate of the central column (green) of the cortical field and the net synaptic input it receives from neighbouring columns (blue): local vs global contribution. Simulations performed within CORTICONIC project (ISS/INFN) with a total of 10^6 cells and 10^9 synapses.

WaveScalES Experiment, in the Human Brain Project

Network of point-like spiking neurons with plastic synapses

- The Brain is a hierarchical complex system with a multi-scale spatial and temporal architecture
- It can be analyzed, modeled and simulated at several different level of abstraction
- The modeling and simulations presented in this talk are at an intermediate level of abstraction: network of point-like spiking neurons with plastic synapses.
- Spiking networks: an attempt to capture both a few key aspects of the biological architecture and to reproduce the computational properties of large scale networks of neurons, still maintaining some biological plausibility
- **1 hour talk: I had to introduce brutal approximations all-over this presentation**

Synapses matter most, not neurons …

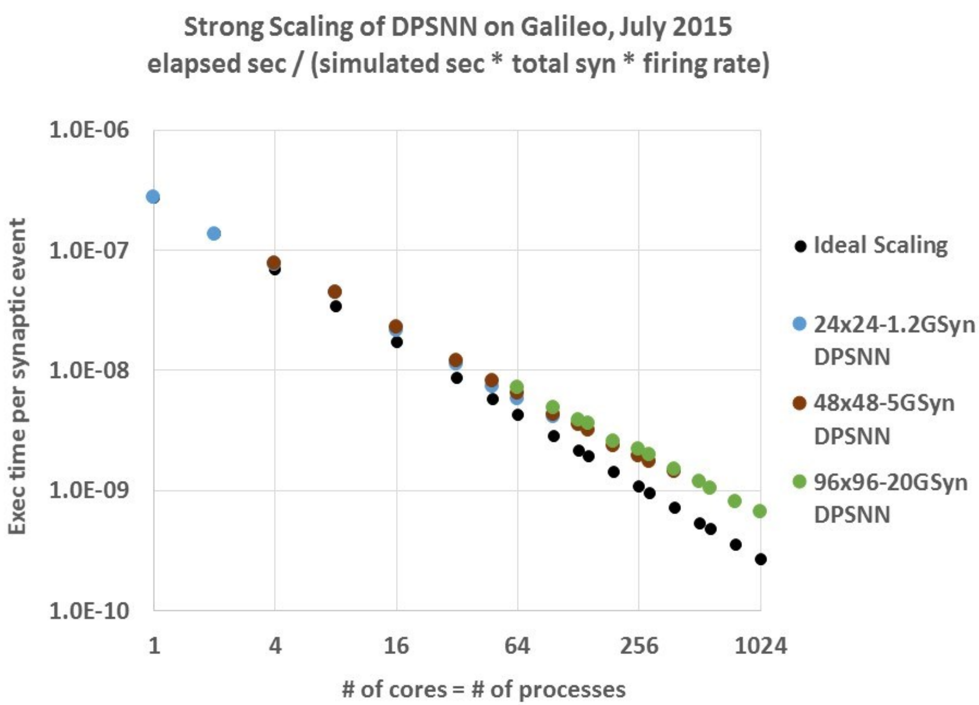
- N:=neurons, M:=mean number of synapses/neuron, f:=mean firing rate (spikes per second per neuron), s:=seconds to be simulated, b:=bytes per synapses
- For every neuron, thousands of synapses (M>1000)
- Every time a neuron spikes, events are triggered on all the synapses on its axonal arborization
  - **A key software and hardware issue for parallelization is the efficient delivery of the spiking messages to synapses**
  - The computational cost of a simulation grows with the total number of synaptic events N*M*f*s.
- Execution times can be normalized dividing them by N*M*f*s to get an execution time per synaptic event
- Memory consumption is dominated by the storage of the synaptic database: N*M*b

DPSNN: Simulation platform parallelized for efficiency on thousand processing cores

WaveScalES Experiment, in the

Human Brain Project

Scaling to 1024 software processes and hardware cores of the distributed simulation of a spiking neural network including up to 20G synapses ***arXiv:1511.09325 (2015)*** E. Pastorelli, P.S. Paolucci et al. (the APE lab) (in collaboration with ISS, Del Giudice, Mattia)



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 (2015)*** E. Pastorelli, P.S. Paolucci et al. (the APE lab) (in collaboration with ISS, Del Giudice, Mattia)

For an introduction to DPSNN see also:

P.S. Paolucci, et al., (2015) Journal of Systems Architecture, "… EURETILE …"
P.S. Paolucci, et al., (2013) arXiv:1310.8478

WaveScalES Experiment, in the

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Pier Stanislao Paolucci – parallel computing CV

- Since 1984, member of APE massive parallel comp. lab, INFN Roma
- 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

- 2016-… Coordinator, WaveScalES experiment in the Human Brain Project
- 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 Experiment, in the

INFN APE lab

Human Brain Project

- ❑ 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
- ❑ Developed several generations of parallel computing systems (APE, APE100, APEmille, APEnext) based on custom VLSI processor and custom interconnects
- ❑ Several technological / industrial spin-off

Team (14 people) in Roma:

- ❑ 4 research staff persons
- ❑ 10 temporary research positions on external funds
- ❑ **Researchers to be recruited in INFN for WaveScalES (call deadline 24 June 2016, colloquium on 18 July, start October 1st) on large-simulation techniques and models for neuro-science**

WaveScalES Experiment, in the

Development of Distributed Plastic Spiking Neural Net Simulator in INFN

Human Brain Project

- INFN Roma APE Lab 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 code development** as a source of requirements and architectural inspiration for extreme parallel computing
- 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 (Paolo Del Giudice, Maurizio Mattia)
- DPSNN simulator **key benchmark** in **EXANEST (2016-2018)** FET Project (INFN, Piero Vicini)
- DPSNN will be further improved in the **HBP WaveScalES experiment**

Main + and - points of our DPSNN simulation engine compared to standard platforms

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- Limited flexibility / configurability of models of neurons, synapses, connectivity
- Difficult maintenance
- DPSNN not a platform for the general neuroscientist. Requires the support of the developer
- **Standard platforms exist and are constantly improving: e.g. NEST, NEURON**
- Fast distributed network initialization
- Mixed time-driven (axonal messages between software processes) and event-driven (synaptic dynamic) scheme **->** high temporal resolution on individual synaptic event AND good scalability on high number of MPI processes
- Highly application specific – dirty down to the essential – no bells and whistles -> speed / scalability potential
- Easy, essential benchmark kernel for hardware architectures

The paradigmatic biological neuron. In spiking-net simulations neurons are much simpler

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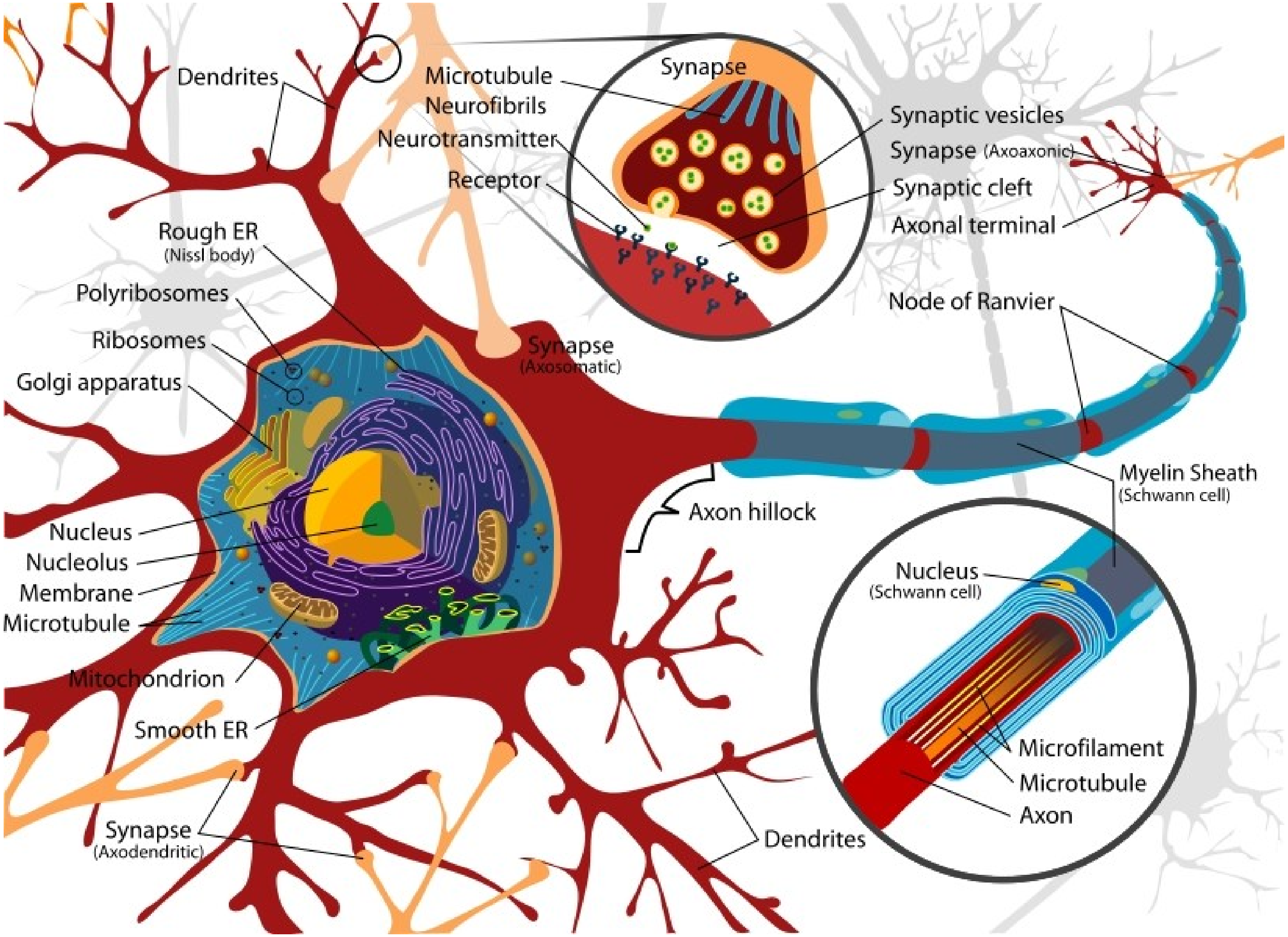
Human Brain Project



Ȼ (2007) Mariana Luiz Villareal

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Simplified model of computational state…

- The membrane of a neuron: a double-lipidic insulator crossed by ionic channels and ionic-pumps, (simplified model, a capacitor in parallel to several voltage generators with variable conductances)

- **Membrane potential and computational state.** The computational state of each neuron is expressed mainly by the electric potential across its membrane.
  - **Polarized state.** Most of the time, the membrane potential fluctuates at about -65 mV. When polarized, **no signals are transmitted to other neurons**
  - **SPIKE.** Mainly as a consequence of synaptic signals, the neuron membrane can emit a **SPIKE**: in about 1ms the neuron first depolarizes to about +30mV and then returns to its polarized state, typically with an hyperpolarization and a spiking refractory period of a few ms
  - **For each SPIKE, an electric signal is transmitted to all synapses through the axonal arborization (an active signal regeneration system)**

… and Memory model

- **Long-term memories** can be stored in the highly sparse graph of its connections (synapses), by the weights of the synapses (i.e. the quantity of current injected in target neurons when synapses are activated by a spike) and by the delay introduced by each axosynaptic connection.
- **Short-term memories (and recalled memories)** can also by represented by the reverberant computational activity of groups of neurons on a moving time window
- **Memory of Darwinian evolution mainly sculpted in the architecture probabilistic description**

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A computational representation of the neuro-synaptic system

- **State of the systems and of the current computation**:
  - a few state variables ***Vi(t), Ui(t),*** … for each of the neuron **1=1..N** (constant parameters ***Ai, Bi****,* … specify the neural kinds)
  - Each neuron projects (a mean of) M synapses towards other neurons and the
- **Long term memories represented by:**
  - ***Wij(t)***, a sparse synaptic connection matrix (**N>>M**).
  - ***Dij***, propagation delay of the spike along the axonal arborization tree
  - … other info about the characteristics of the synapses
- **Micro-, Meso- and Macro-scale description of the architecture:**
  - Probabilistically modulated description of the composition of layers and columns (neural populations) and of the intra-columnar connections (intra-columnar connection probabilities, probability of weights, of propagation delays)
  - Distance dependent laws for inter-columnar connections, delays
  - Matrices of Inter-areal connection probabilies
- **Random number generation everywhere** (probabilistic modulation network generation, simulation of external events and noise)

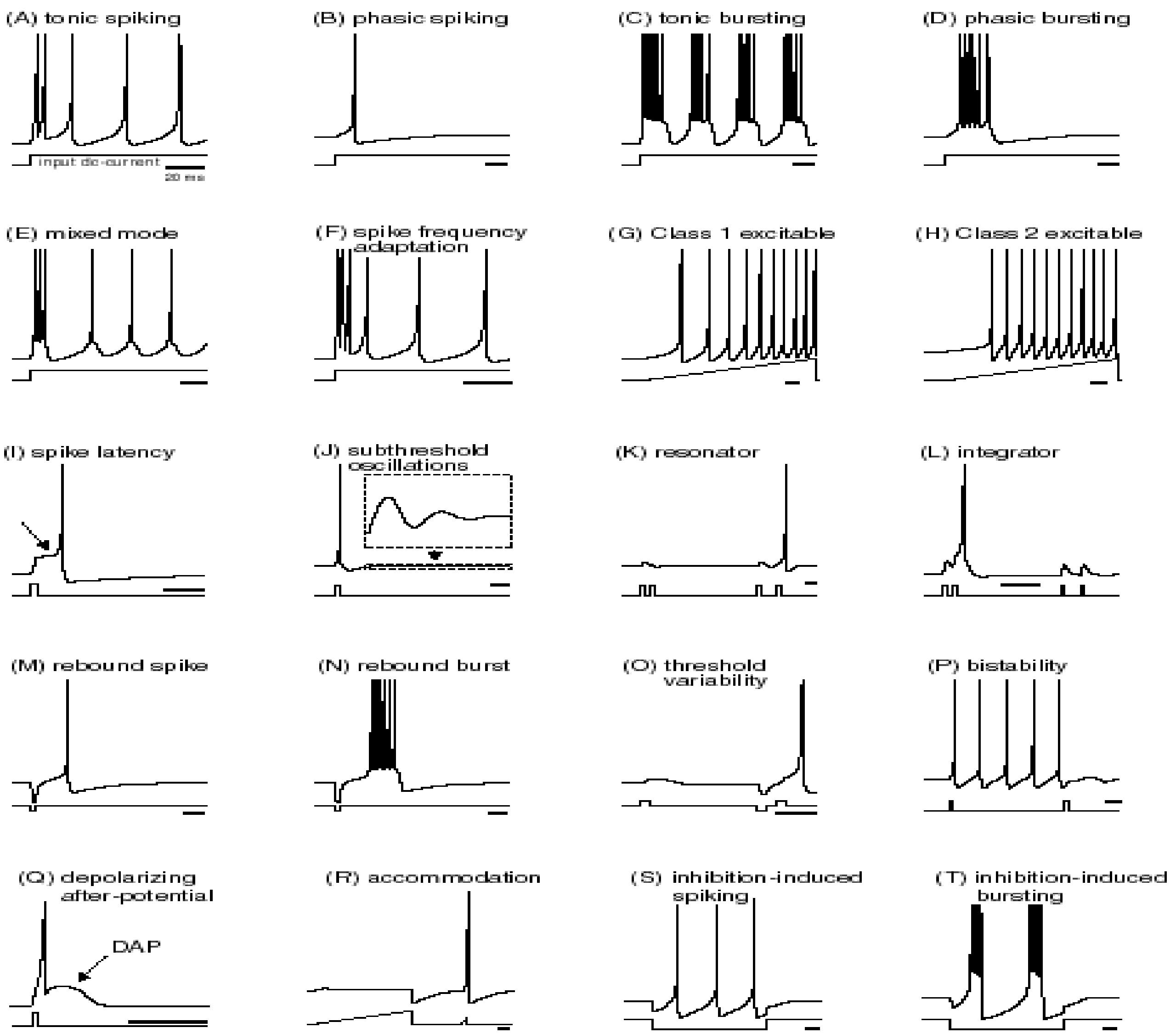
Example of simplified neural dynamics. NOT the one used in WaveScalES as first choice. Two variables: Membrane potential *v* and recovery current **u**

$$
\begin{cases}
if\ v(t) < v_{peak} \quad then & \begin{cases} \dot{v} = 0.04\,v^2 + 5v + 140 - u + I \\ \dot{u} = a(bv - c) \end{cases} \\
if\ v(t) \geq v_{peak} \quad then & \begin{cases} v(t + \Delta t) = c \\ u(t + \Delta t) = u(t) + d \end{cases}
\end{cases}
$$

Where:

- ***v* (t)** is the neural membrane potential. This is the key observable;
  - we say that when ***v*** reaches $\mathbf{v_{peak}}$ a "neural spike" happened;
- **I(t)** is the potential change generated by the sum of all synapses incoming to the neuron.
  - Incoming currents are present if spikes arrived form presynaptic neurons;
- **u(t)** is an auxiliary variable (the recovery current bringing back v to equilibrium);
- **a, b, c, d** are four parameters, constant for each neuron,
  - by varying them the same equations model captures the behaviour of all type of known neural types.

Izhikevich, Eugene M. Simple Model of Spiking Neurons.
IEEE Transactions on Neural Networks, Vol. 14, No. 6, November 2003.



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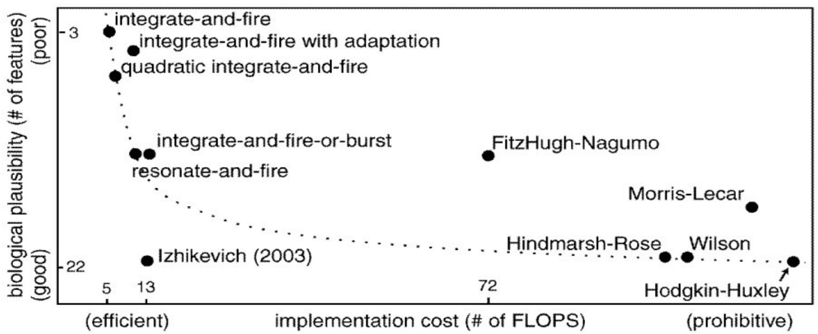
Several tens of types of neurons exist in a brain. They produce in output different spiking behaviours for the same synaptic input

Summary of the neurocomputational properties of biological spiking neurons. Each horizontal bar corresponds to 20 ms. Upper curve: membrane potential. Lower curve: injected current. Picture reproduced with original author's permission (see www.Izhikevich.com)



Models	biophysically meaningful	tonic spiking	phasic spiking	tonic bursting	phasic bursting	mixed mode	spike frequency adaptation	class 1 excitable	class 2 excitable	spike latency	subthreshold oscillations	resonator	integrator	rebound spike	rebound burst	threshold variability	bistability	DAP	accommodation	inhibition-induced spiking	inhibition-induced bursting	chaos	# of FLOPS
integrate-and-fire	-	+	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	5
integrate-and-fire with adapt.	-	+	-	-	-	-	+	+	-	-	-	-	+	-	-	-	-	+	-	-	-	-	10
integrate-and-fire-or-burst	-	+	+		+	-	+	+	-	-	-	-	+	+	+	-	+	+	-	-	-		13
resonate-and-fire	-	+	+	-	-	-	-	+	+	-	+	+	+	+	-	-	+	+	+	-	-	+	10
quadratic integrate-and-fire	-	+	-	-	-	-	-	+	-	+	-	-	+	-	-	+	+	-	-	-	-	-	7
Izhikevich (2003)	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	13
FitzHugh-Nagumo	-	+	+	-		-	-	+	-	+	+	+	-	+	-	+	+	-	+	+	-	-	72
Hindmarsh-Rose	-	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	120
Morris-Lecar	+	+	+	-		-	-	+	+	+	+	+	+	+		+	+	-	+	+	-	-	600
Wilson	-	+	+	+			+	+	+	+	+	+	+	+	+	+		+	+				180
Hodgkin-Huxley	+	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	1200

WaveScalES Experiment, in the Human Brain Project

Floating-point operations per simulated integration step of a list of simplified neural models using time-driven integration schemes

Izhikevich, Eugene M. Which Model to use for cortical spiking neurons? *IEEE Transaction on Neural Networks, 15, no. 5 1063-1070 (2004).*

WaveScalES Experiment, in the Human Brain Project

Example of Synaptic Learning Dynamic: STDP: Spike Timing Dependent Plasticity Song et Al. (2000) formulation.

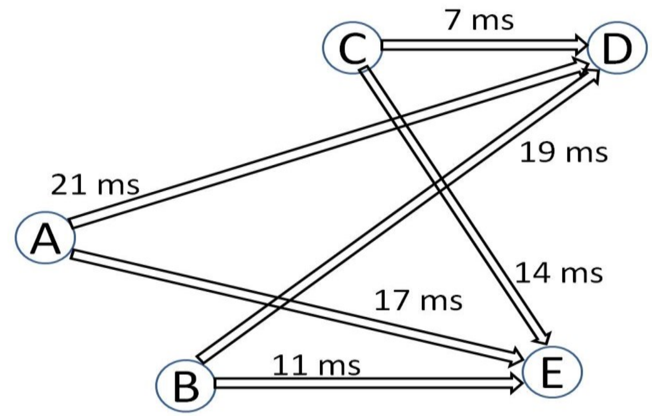
Capturing causal and anti-causal relation between two connected neurons:

- the synapse is maximally potentiated if the delay introduced by the axon causes a delivery of the axonal signal to the target neuron just before the post-synaptic spike.

- The synapse is maximally depressed if the signal arrives just late.

$$t = t_{post} - t_{pre} - d_{axon} \quad \begin{cases} if \; t \geq 0 & \Delta W_{pre,post} = A_+ e^{-\frac{t}{\tau +}} \\ if \; t < 0 & \Delta W_{pre,post} = A_- e^{\frac{t}{\tau -}} \end{cases}$$

Axonal delays could even create the representation for memories of precise temporal sequences of spikes.



If:

- neuron A spikes at a certain time t_0,
- neuron B spikes two ms after,
- and C sends at t_0 +14 ms,

3 spikes would reach simultaneously neuron D.
This could trigger a spike on D at t_0 +21 ms.

The network would be recognizing this temporal activation sequence of A, B, C and D.

A different temporal spiking sequence of the same set of neurons

- A spiking at $t_{0,}$
- C at t_0 +3 ms and
- B at t_0 +6 ms)

could trigger a spike on neuron E at time t_0 +17 ms

Distribution of the same problem (a grid of 64 neural columns) on 4, 64 or 256 software processes

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A sample grid of 64=8x8 neural columns.

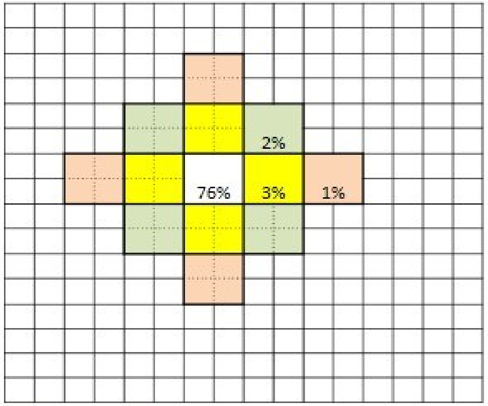
Excitatory neurons projects 76% of their synapses toward neurons located in the same column, 3% to first neighboring columns, 2% to second neighbours and 1% to third neighbours.

Strong scaling measures: a,b,c) are examples of distribution of a grid composed of 64 neural columns over a varying number of software processes and computational cores.

One computational core can host one or more software processes

The number of software processes assigned to each computational core has been changed during the strong scaling measure.

a) 64 neural columns on 64 sw processes - The number of software processes is equal to the number of neural columns.



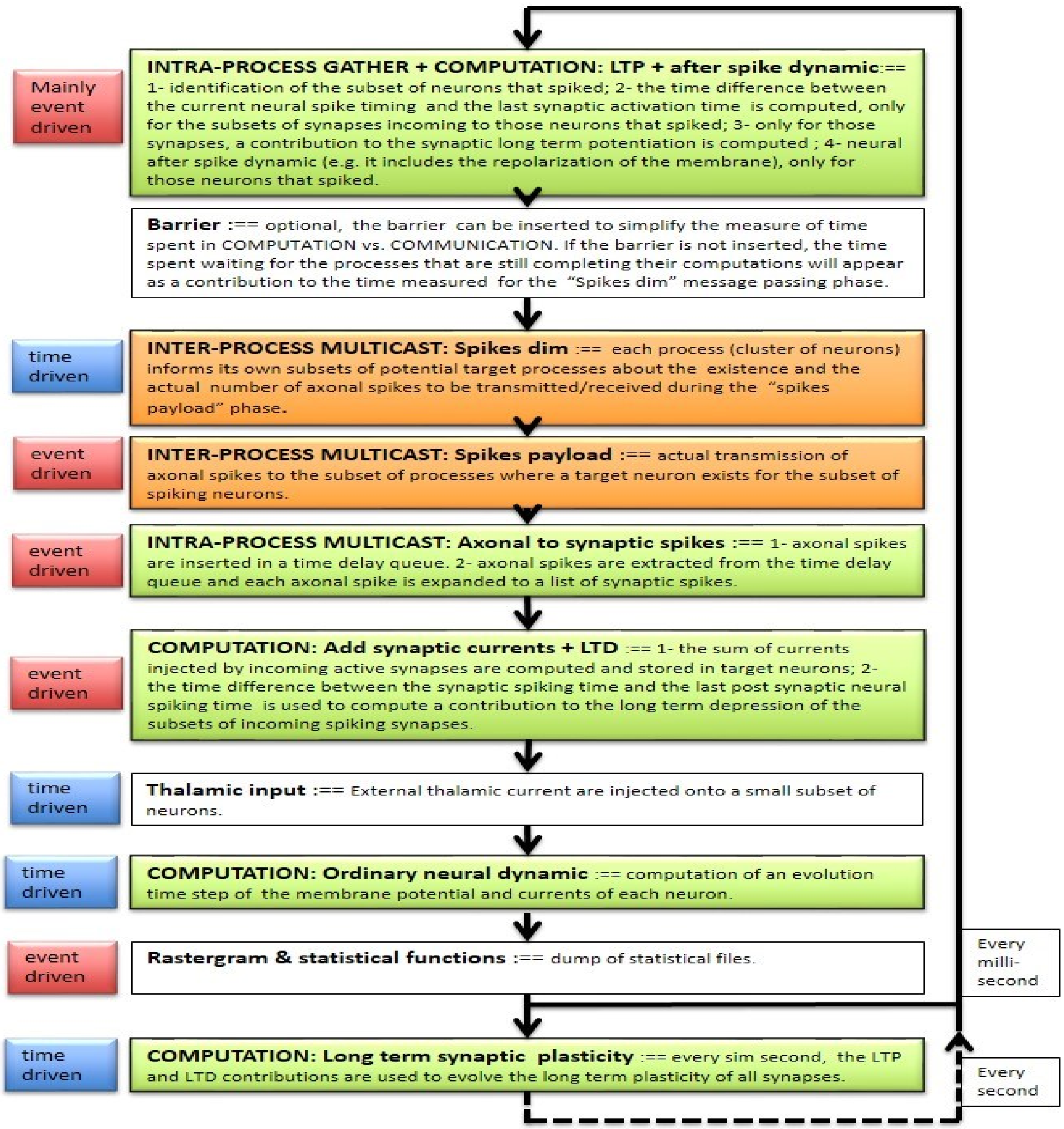
b) 64 neural columns on 256 sw processes - Each neural column is distributed among four software processes.

c) 64 neural columns on 4 sw processes - In this case, 16 neural columns are managed by each software process.

The simulation of the same grid of neural columns produces identical results on all distributions.

WaveScalES Experiment, in the

Human Brain Project



Orange Blocks: MPI communications

Green Blocks: Local Processing

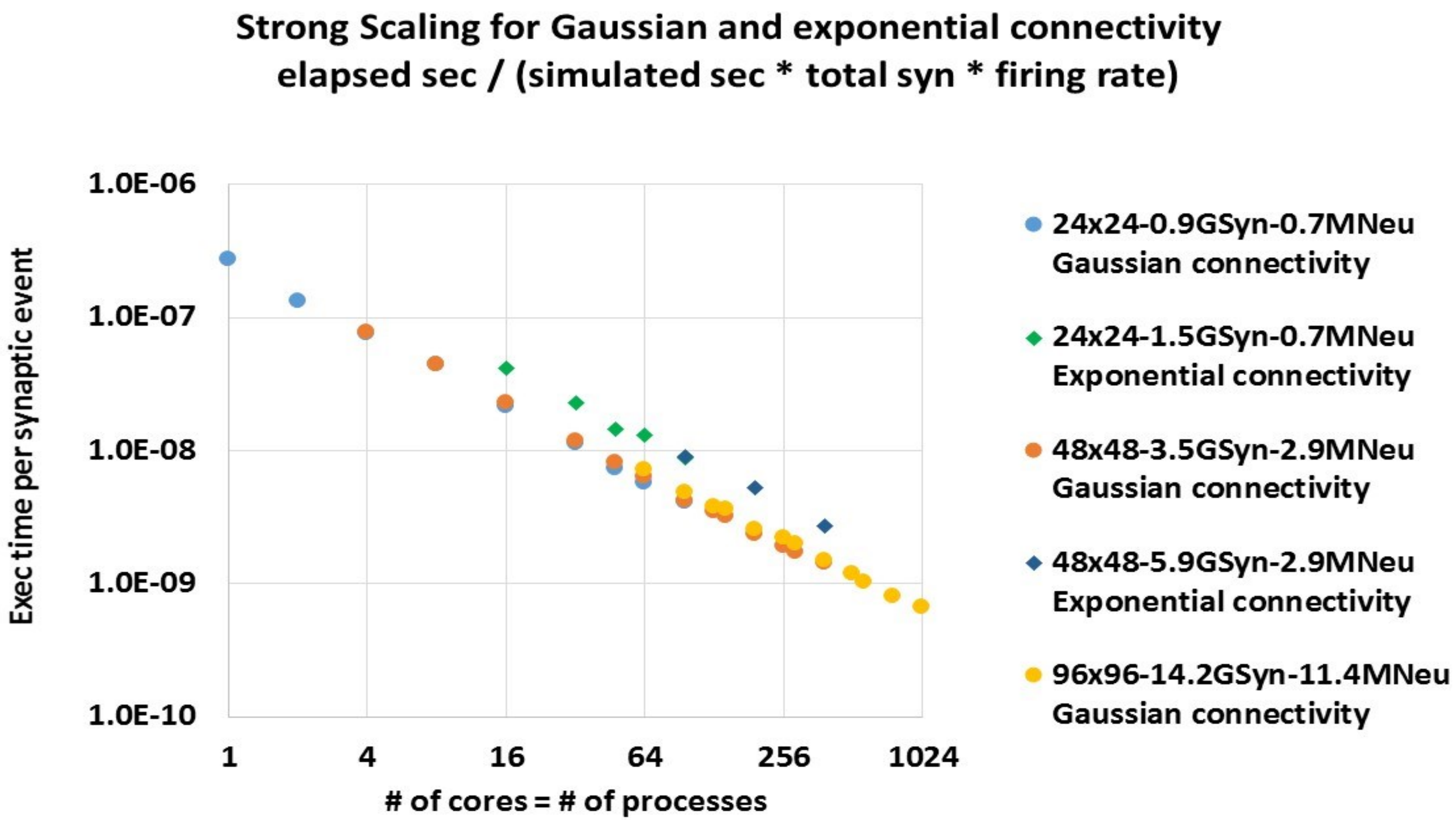
Red labels: Event Driven

Blue labels: Time Driven

Strong scaling (fixed problem sizes, increasing hardware cores) for Long-range (exp –x/L) and short-range (Gaussian –x^2/(2L^2)) connection probabilities

WaveScalES Experiment, in the

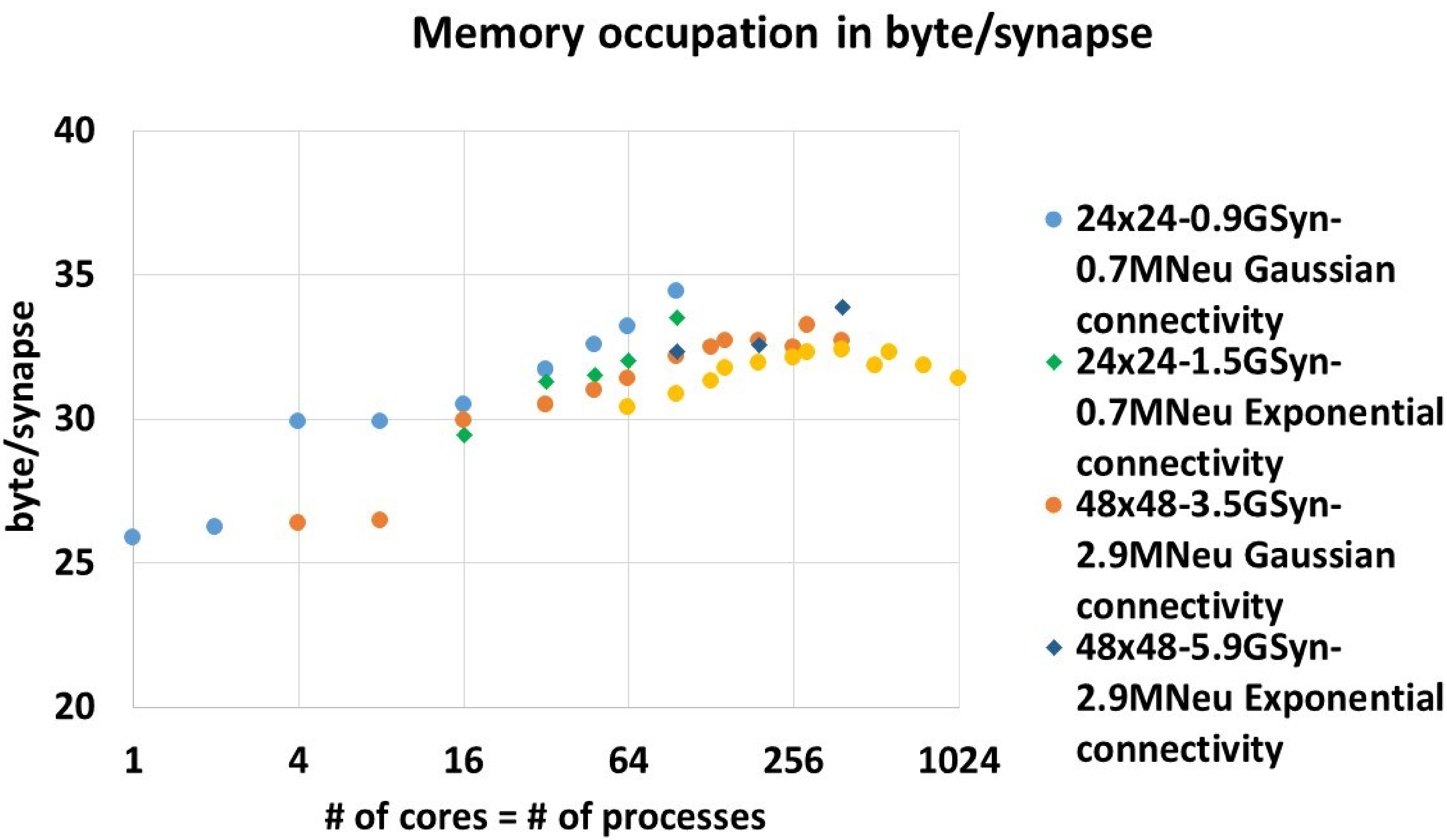
Human Brain Project



Memory consumption (no plasticity case)

WaveScalES Experiment, in the

Human Brain Project



Human Brain Project

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WaveScalES Experiment, in the

Human Brain Project

Conclusions

- **Brain research**: emergence of a quantitative discipline, with scientific and translational impact
  → **Computational Neuroscience**: novel experimental methodologies and massive parallel simulations for multi-scale theoretical models
- **WaveScalES** in the Human Brain Project coordinated by INFN Roma, APE Lab
  - Combines experiments, theory and simulations
    - INFN effort for **large scale simulations** of spiking neural networks
- **Brain simulation** as a **key benchmark** for future interconnects architectures (EXANEST FET Project, INFN Roma, APE Lab)
- **Researchers to be recruited in INFN for WaveScalES (call deadline 24 June 2016, colloquium on 18 July, start October 1st) on large-simulation techniques and models for neuro-science**