Human Brain Project
modeling the brain

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HBP
The Human Brain Project
www.humanbrainproject.eu

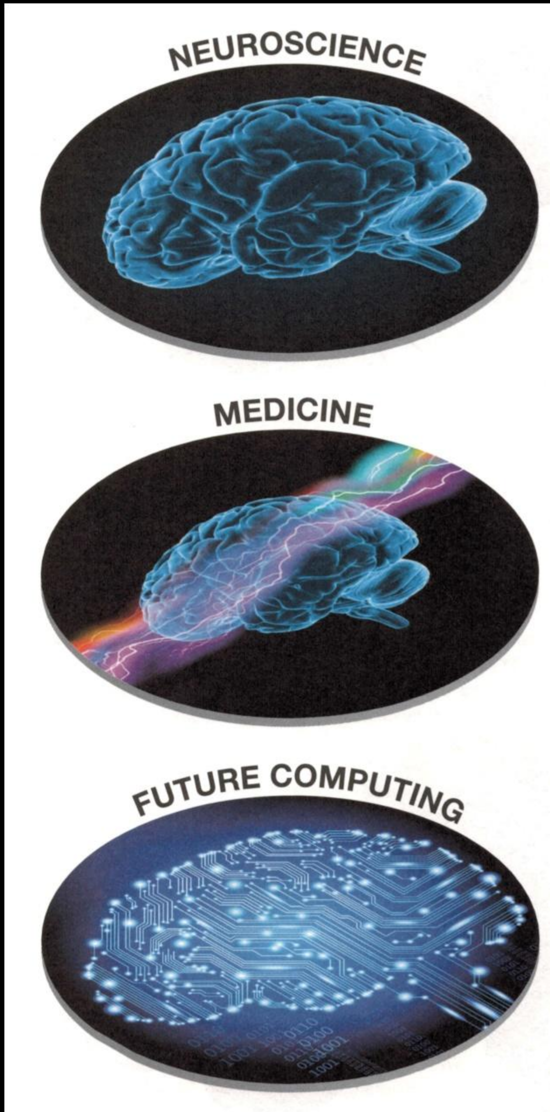
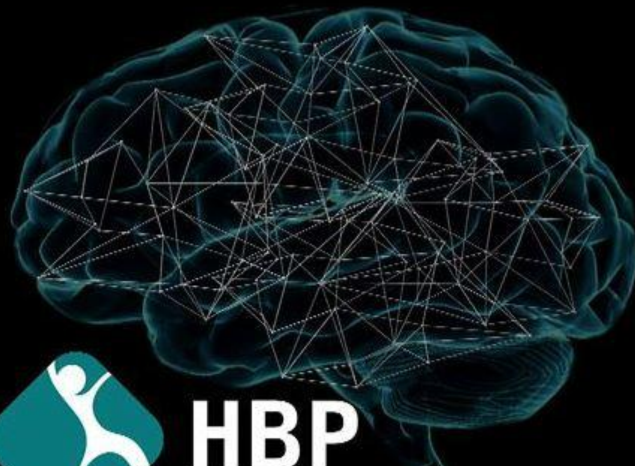


Figure 2: HBP research areas



HBP

The Human Brain Project

www.humanbrainproject.eu

about 300 / 500 millions people

About 800 billions Euros

Impact of brain disorders in Europe

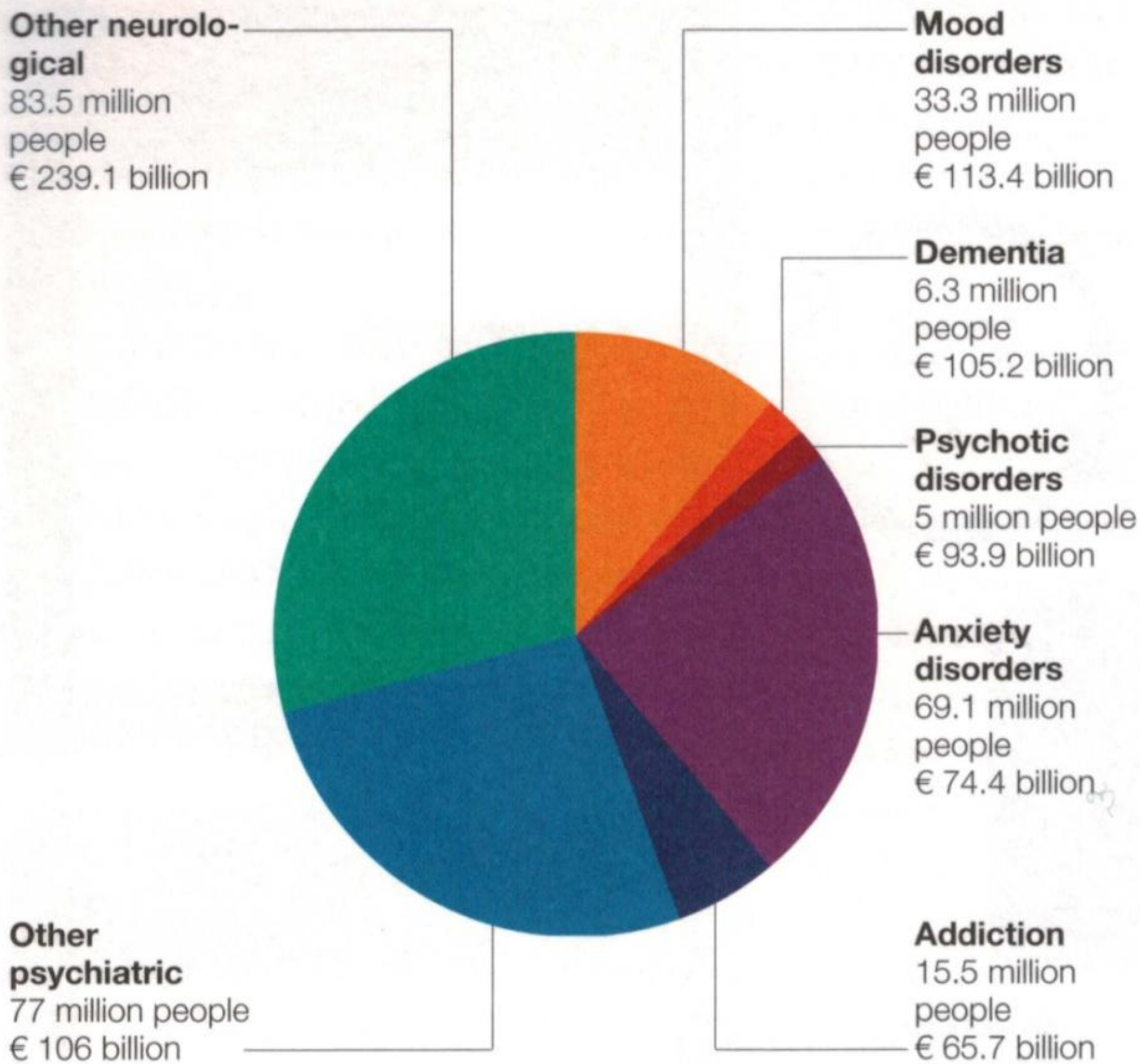


Figure 51: Prevalence and cost of brain disorders (calculated from data in [1])

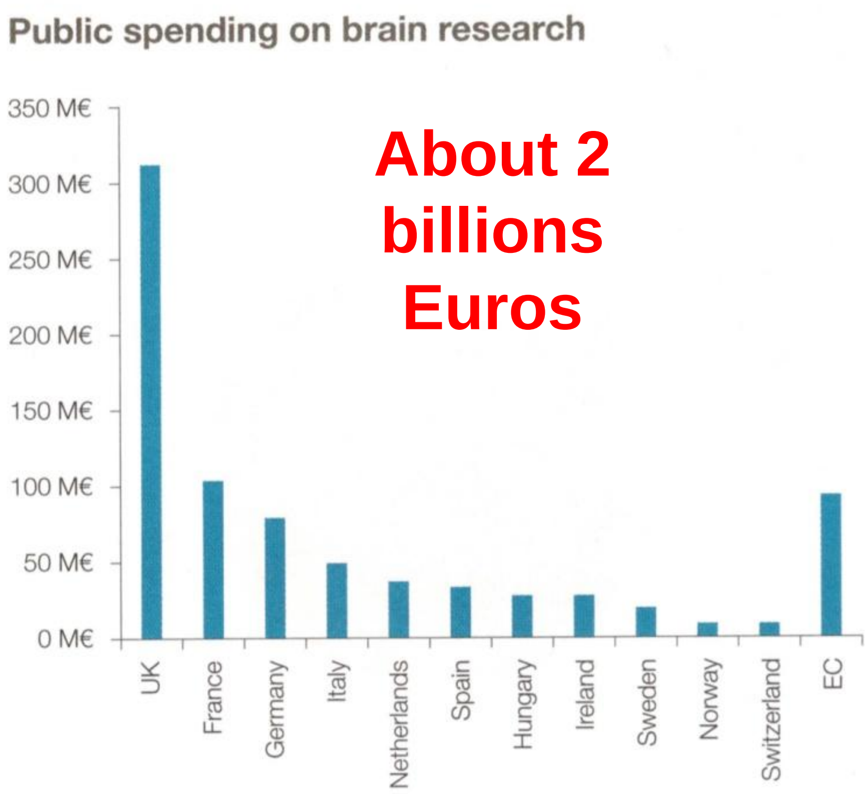


Figure 44: Public spending on brain research by country (2005) [1]

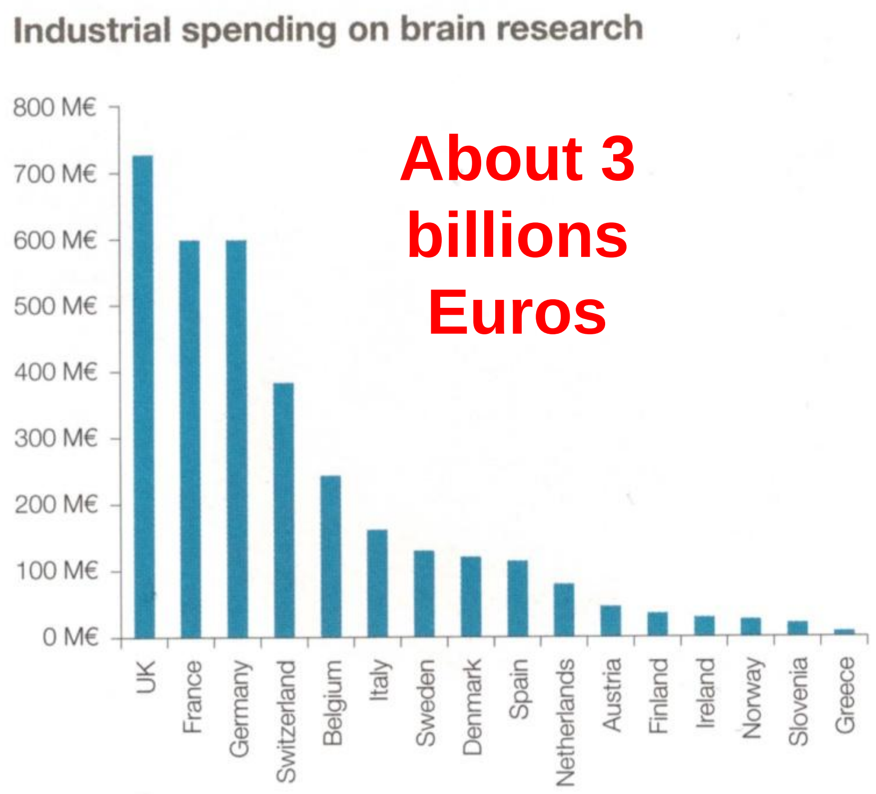
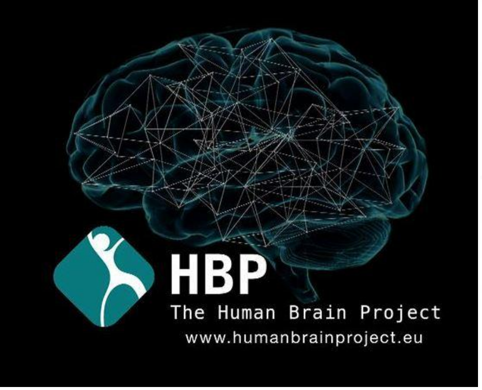


Figure 45: Industrial spending on brain research by country (2005) [1]



87 laboratories

1.2 billion Euros

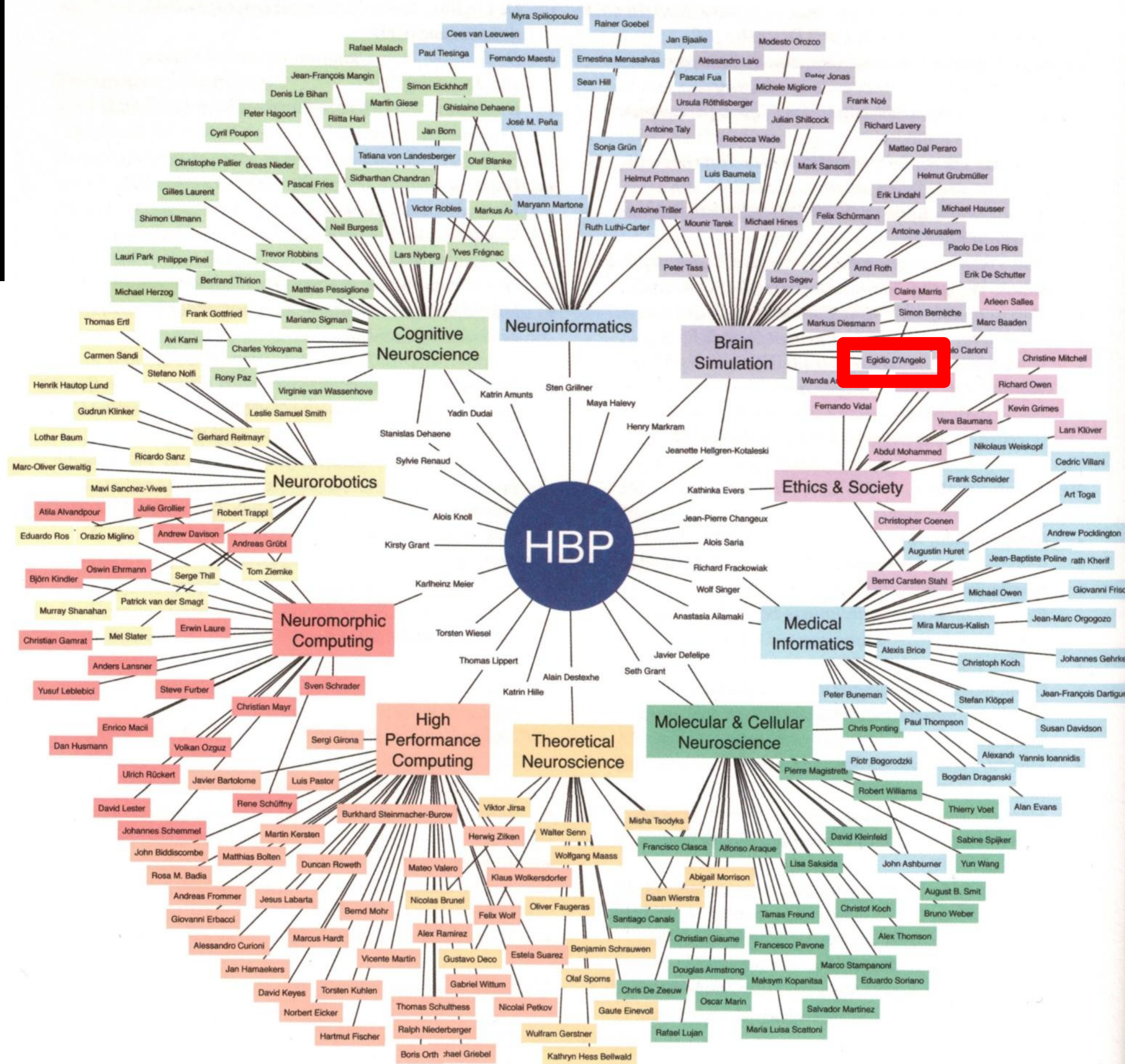


Figure 38: Scientists identified to participate in the HBP. The scientists listed have agreed to participate in the HBP, if it is approved as a FET Flagship

HBP
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Initial HBP Consortium

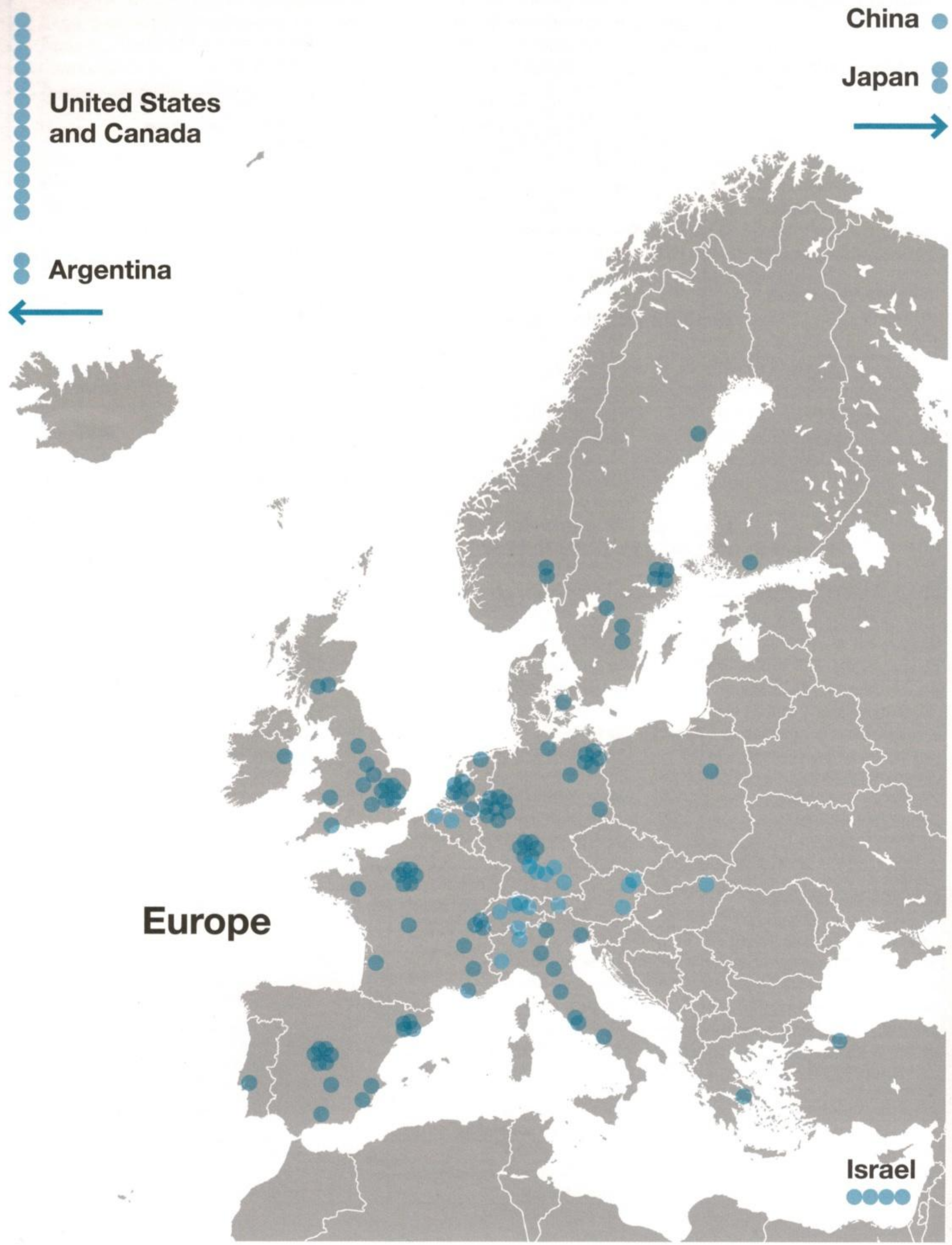


Figure 40: Research institutions identified to participate in the HBP, if approved as a FET Flagship Project

Researchers by division

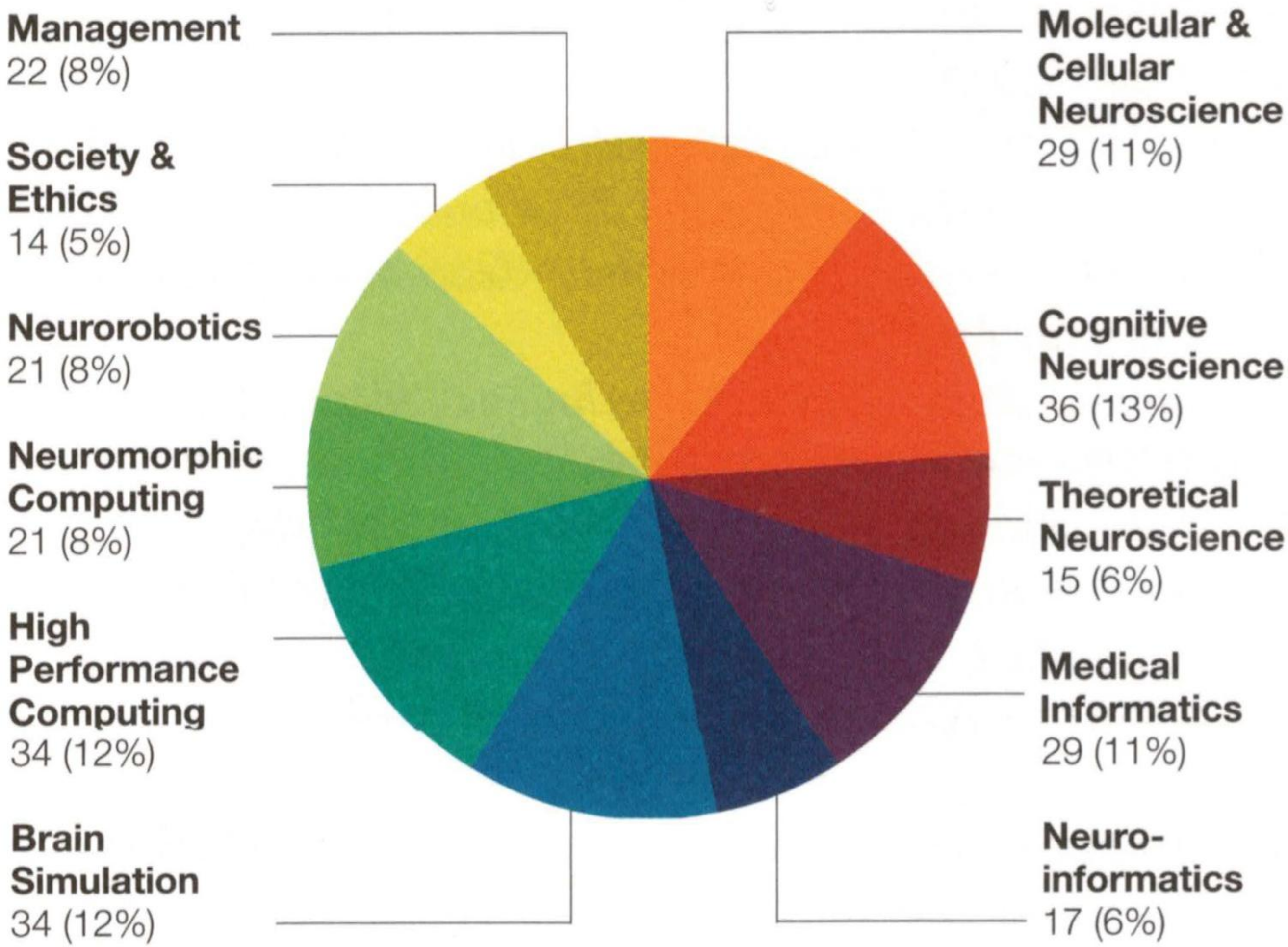
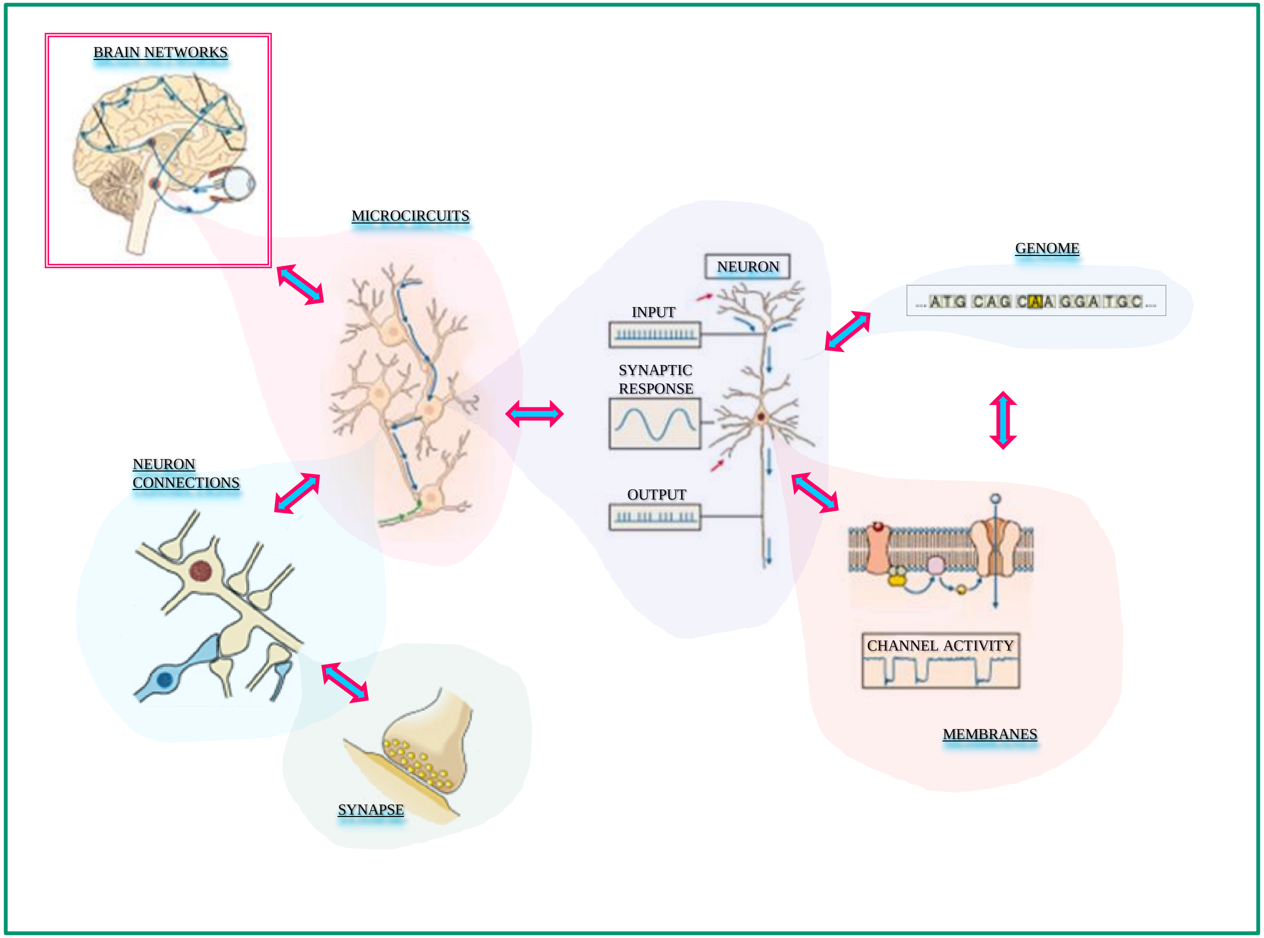
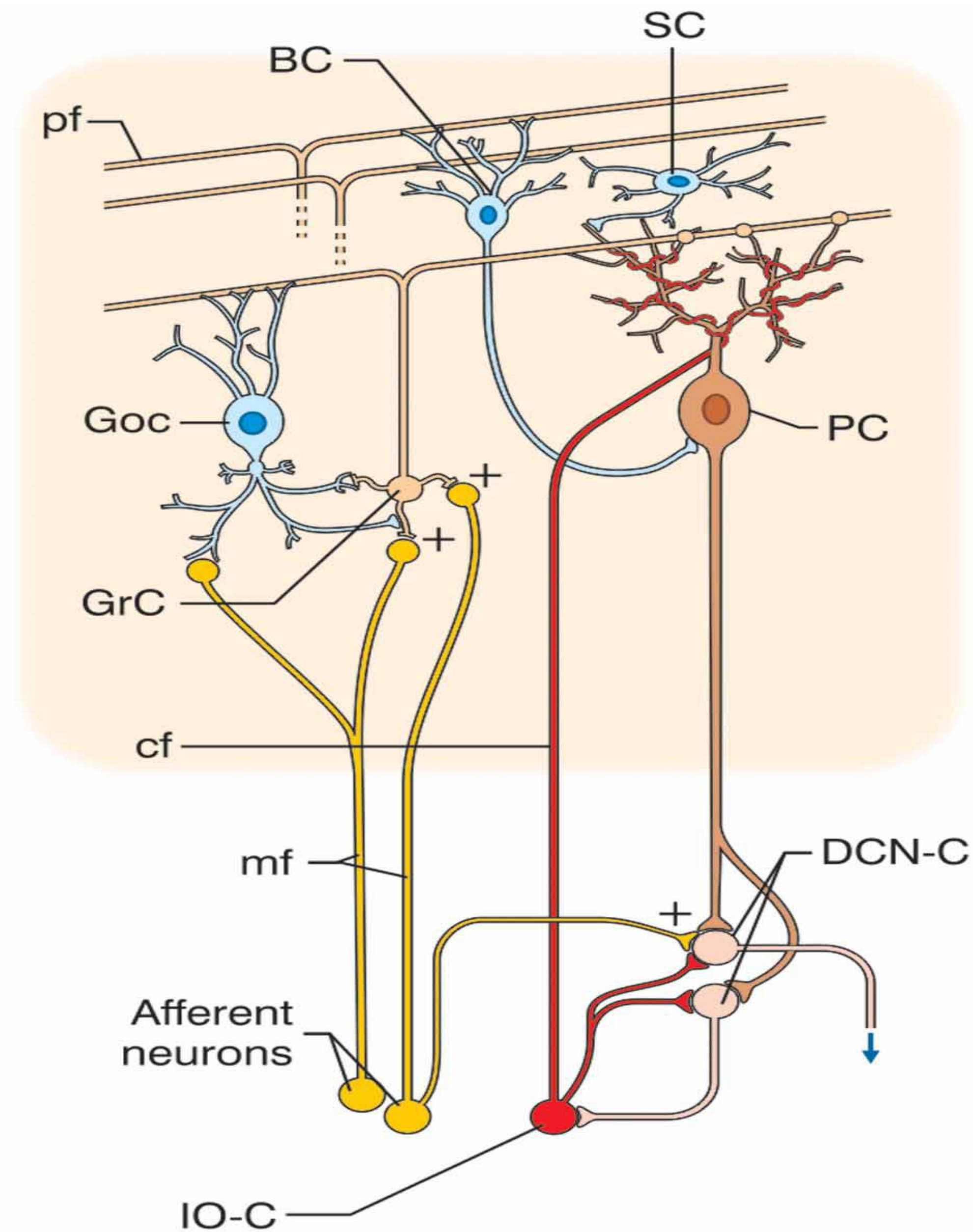


Figure 39: Distribution of researchers by division. Numbers do not include researchers expected to join the project through open calls

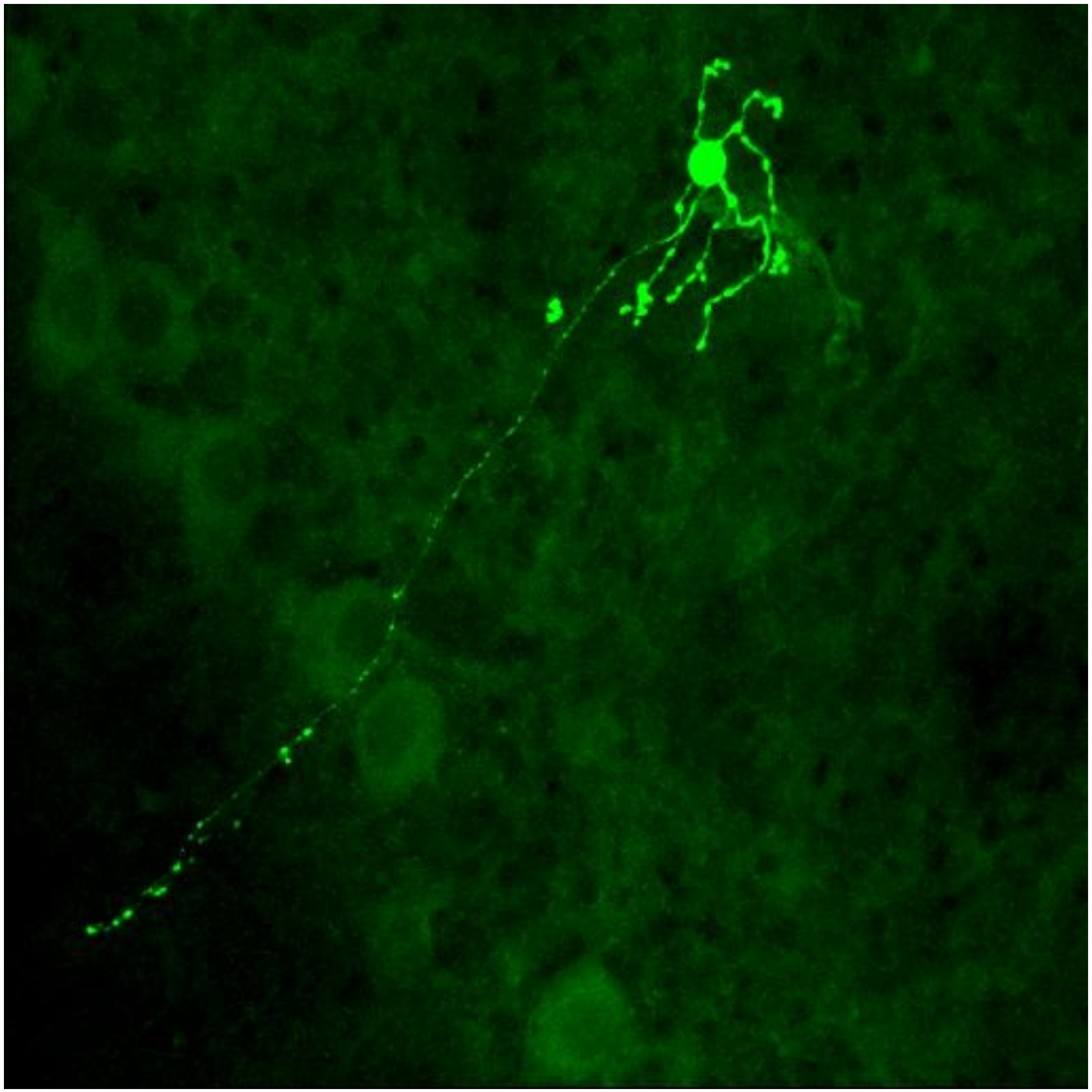
(1)
The "multi-level" organization of the brain

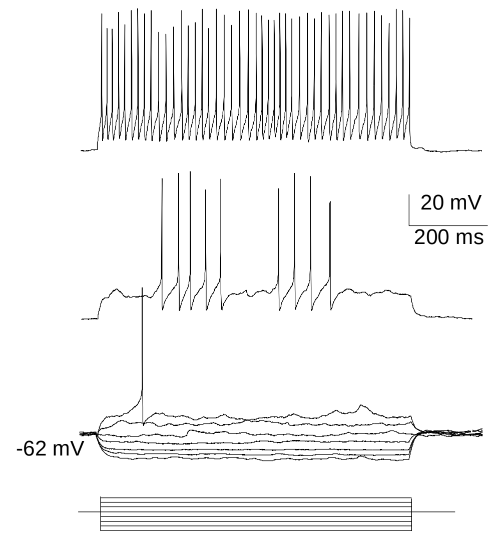


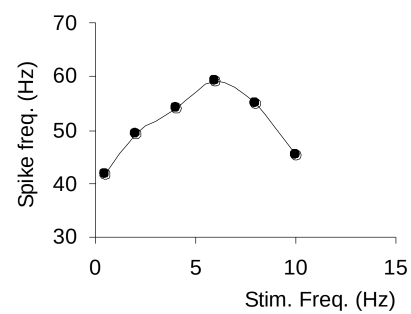
The cerebellar network



Neurons generate complex patterns of action potentials (granule cell)

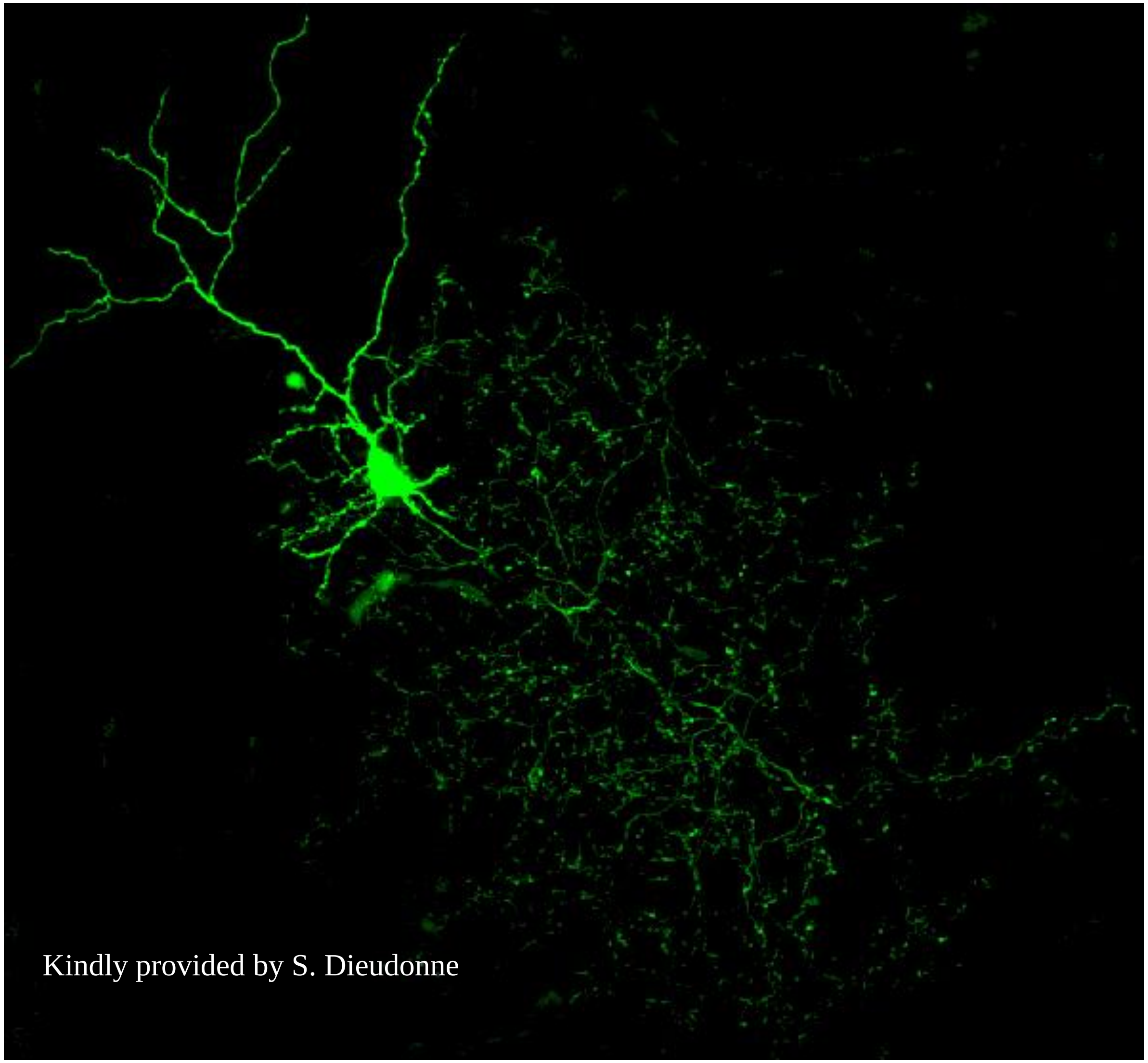


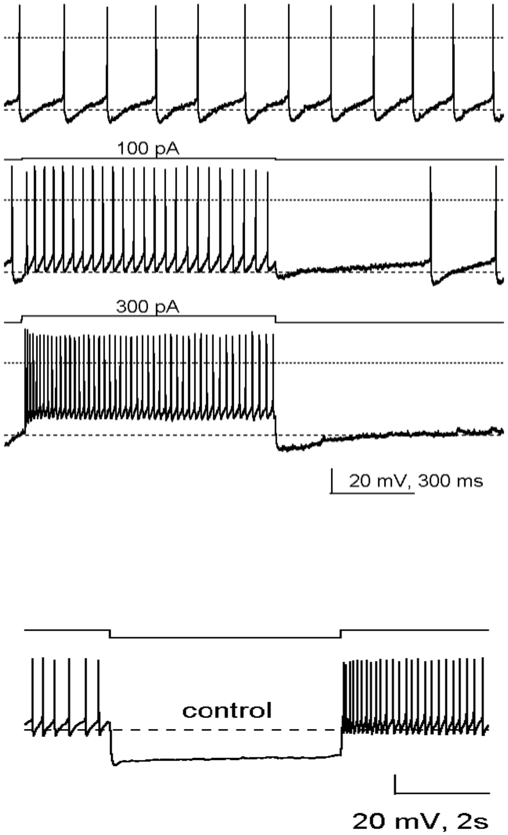




D’Angelo et al., 1995, 1998, 2001

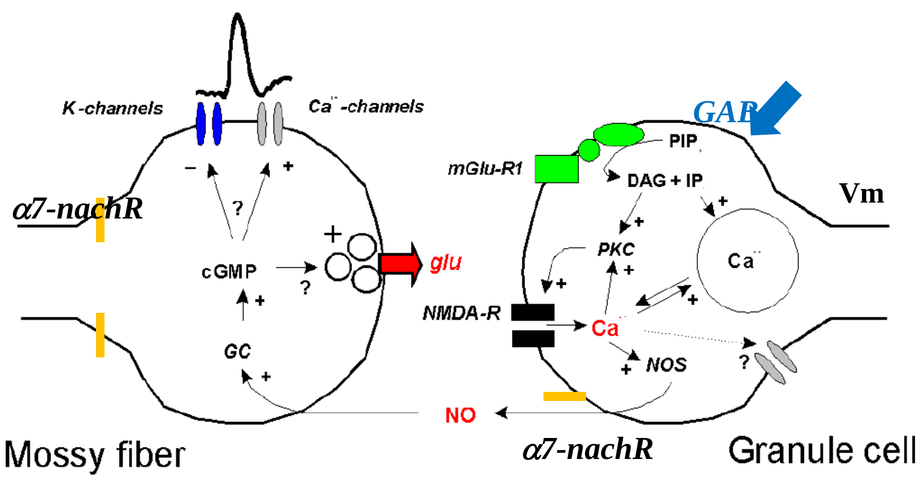
Neurons generate complex patterns of action potentials (Golgi cell)

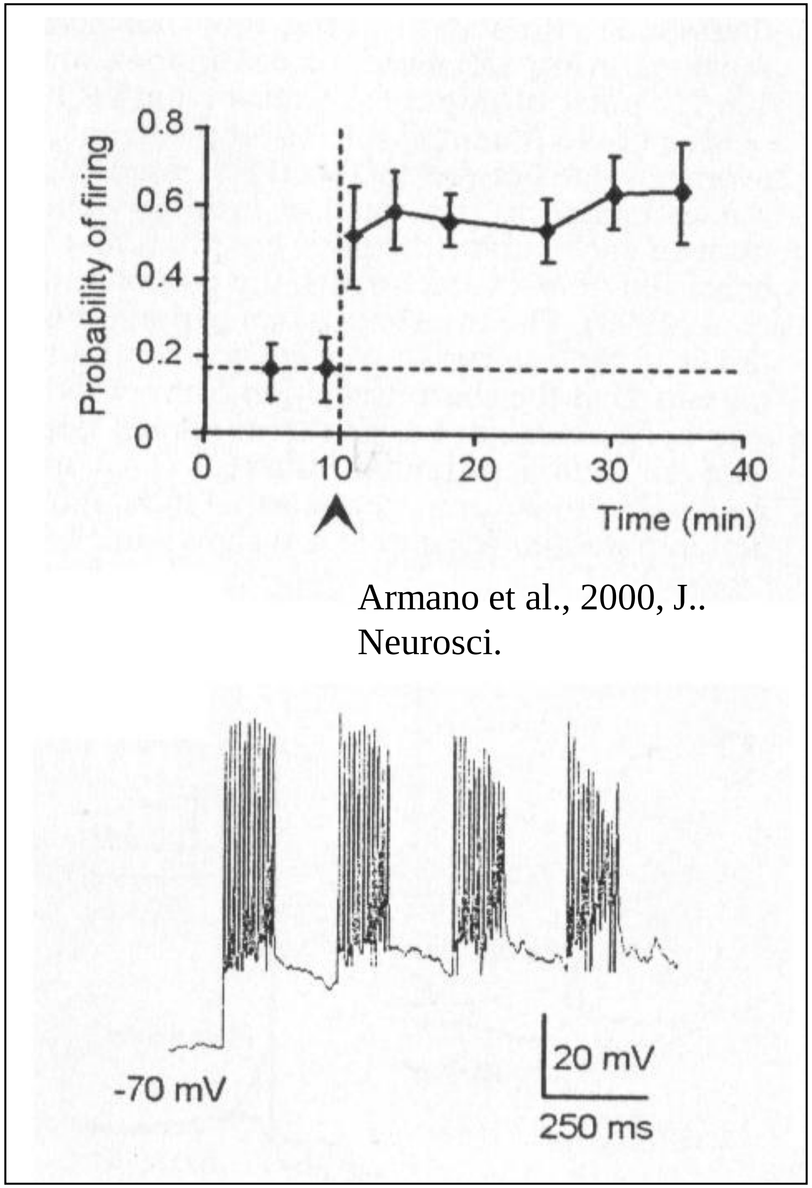




Forti et al., 2006.

Neurons communicate through the synapses and store memory as long-term synaptic plasticity (LTP/LTD)

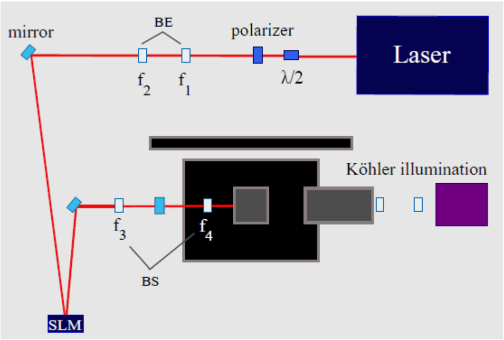


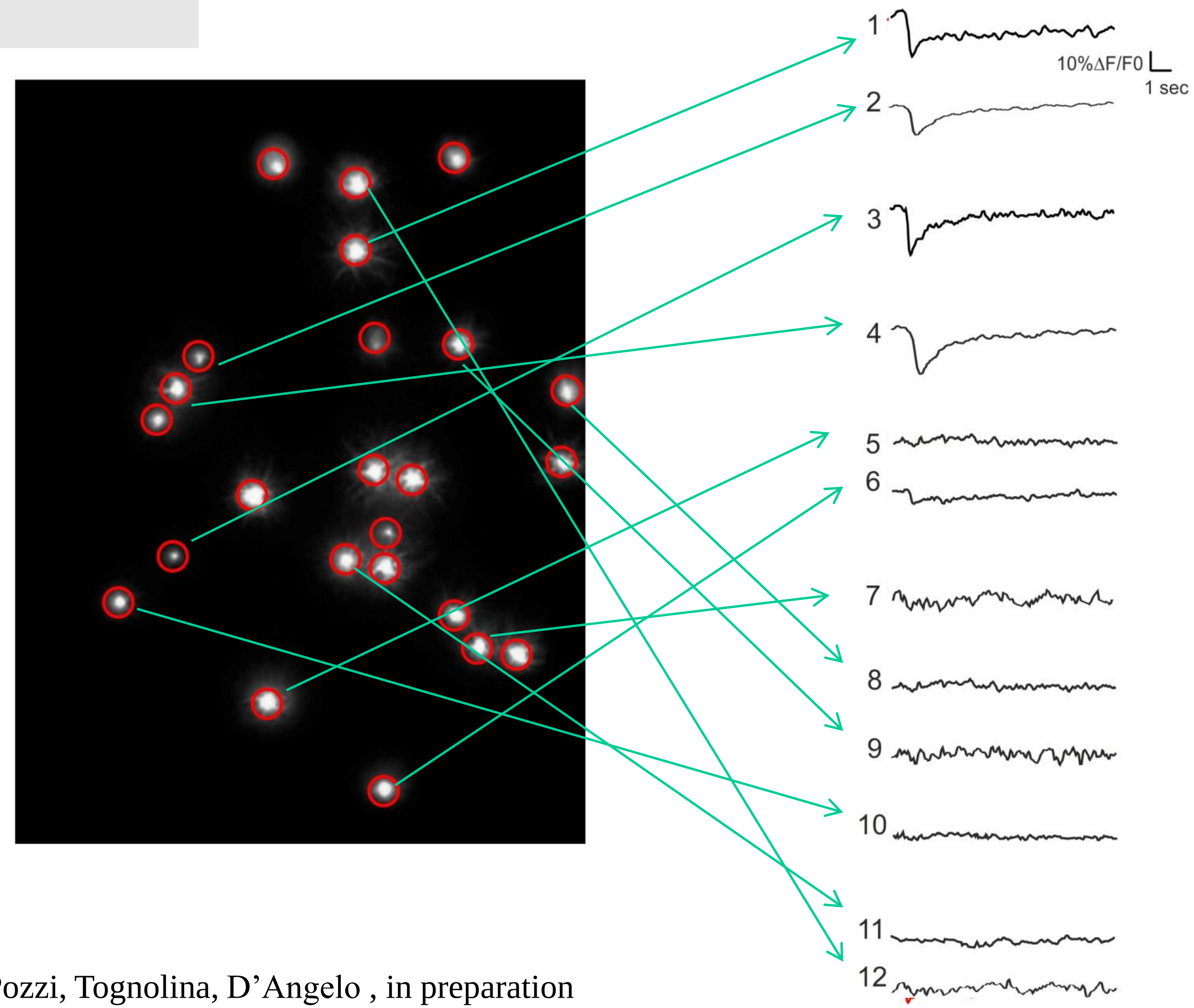


Armano et al., 2000, J.. Neurosci.

D'Angelo et al., 1999;Armano et al., 2000; Maffei et a., 2002,2003; Sola et al., 2004; D'errico et al., 2008; Roggeri et al., 2008; D'Angelo et al., 2013

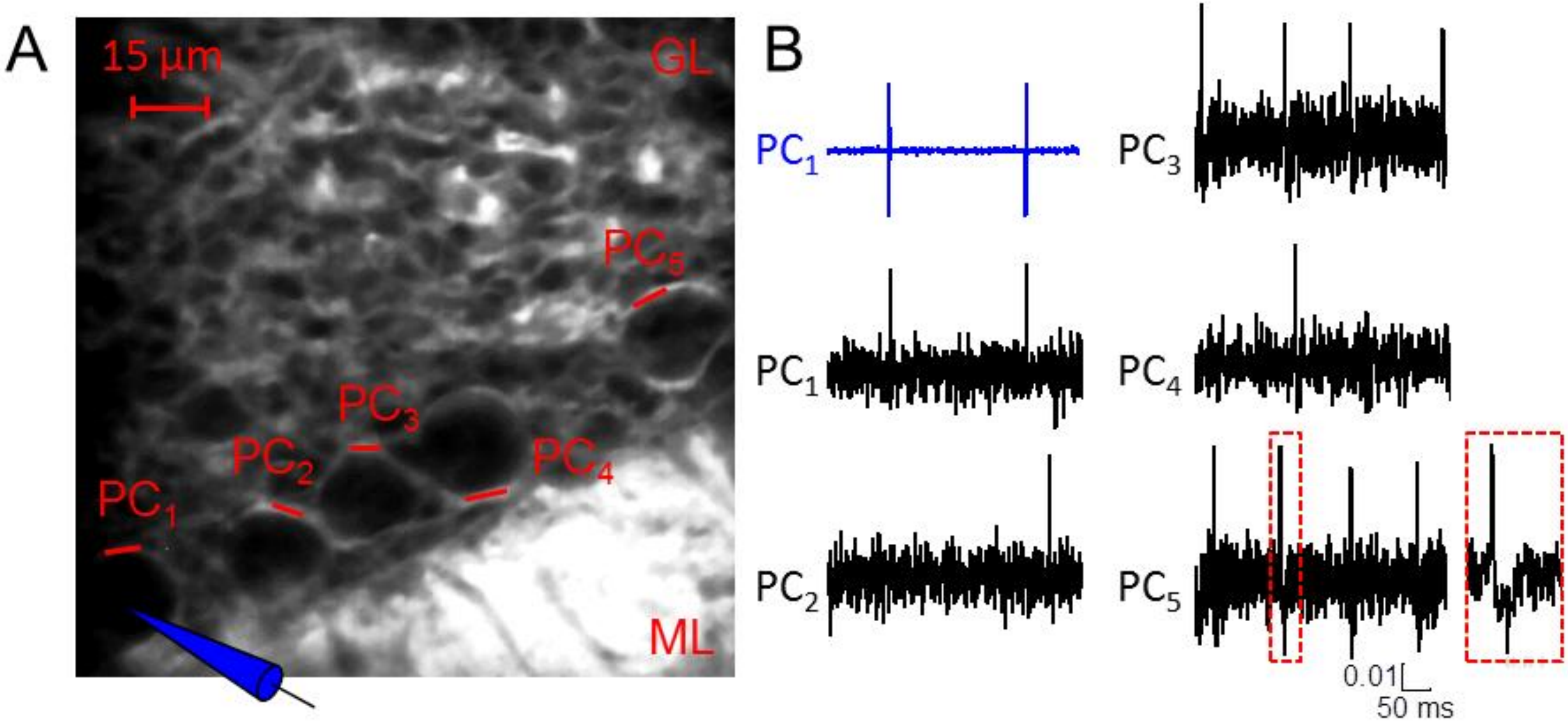
Multiple neurons discharge together





Gandolfi, Mapelli, Pozzi, Tognolina, D’Angelo , in preparation

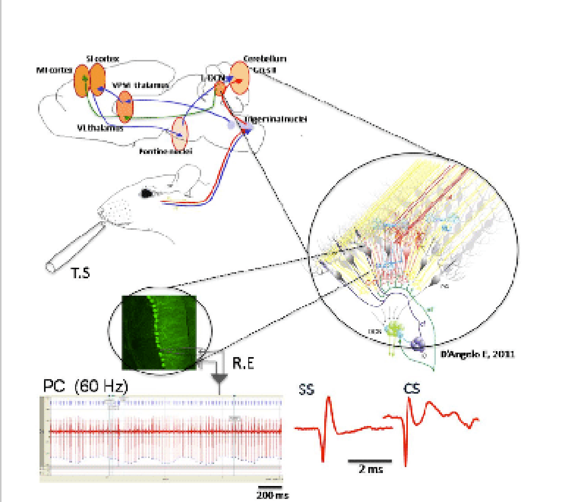
Multi-unit recording of spontaneous activity

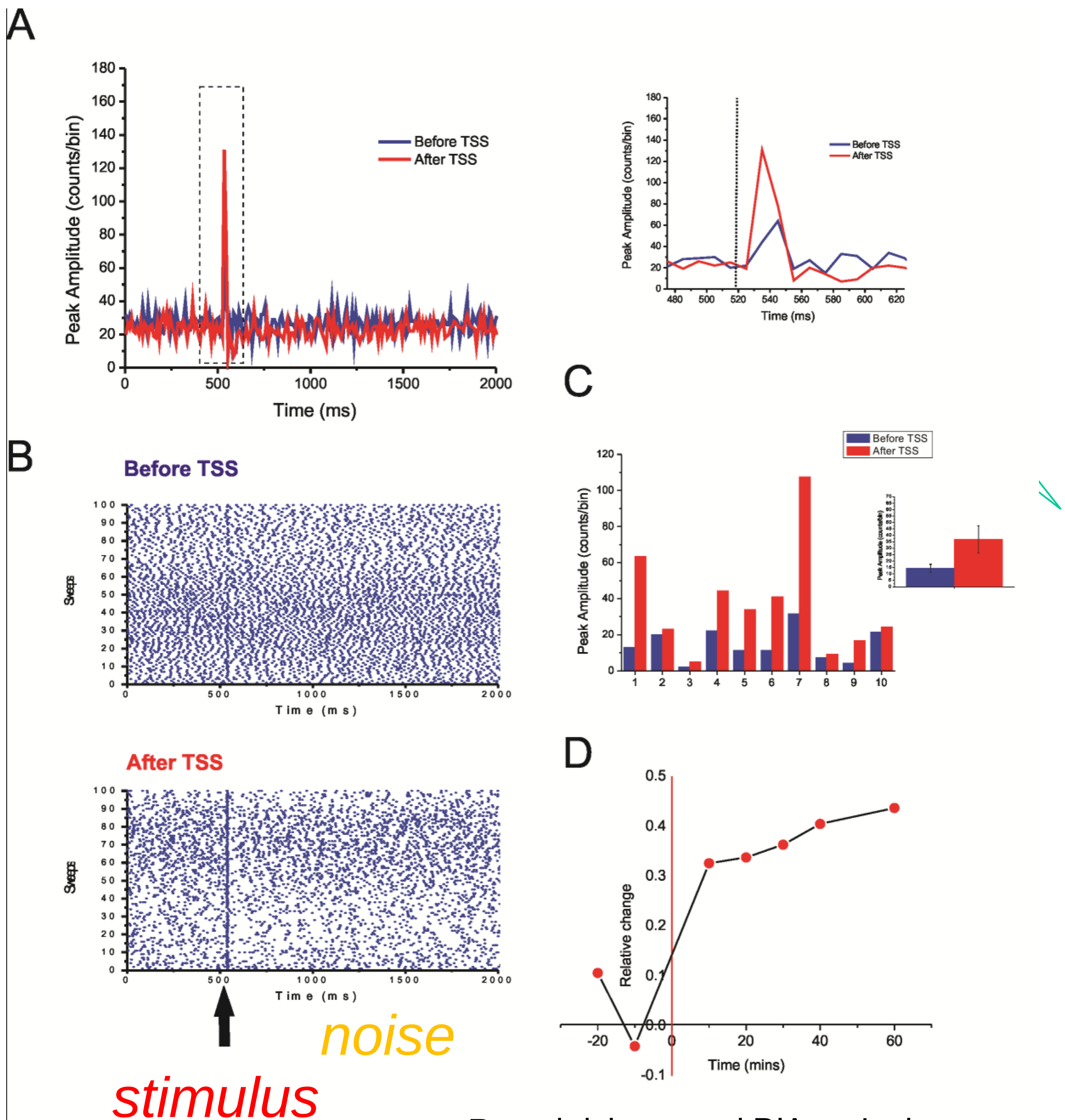


We found that we are able to detect action potential in real time with a **signal to noise around 7** in five neurons simultaneously. Simultaneous optical and electrical recording from cell one shows the high fidelity of the optical measurement. This data shows how this technique can be used to investigate neuronal synchronization opening promising perspective in understanding the computational rule of the brain.

P. Yan, C. Acker, WL. Zhou, P. Lee, C. Bollensdorff, A. Negrean, J. Lotti, L. Sacconi, S. D. Antic, P. Kohl, H. D. Mansvelder, F. S. Pavone, and L. M. Loew, Palette of fluorinated voltage sensitive hemicyanine dyes, Proc Natl Acad Sci U S A, (2102).

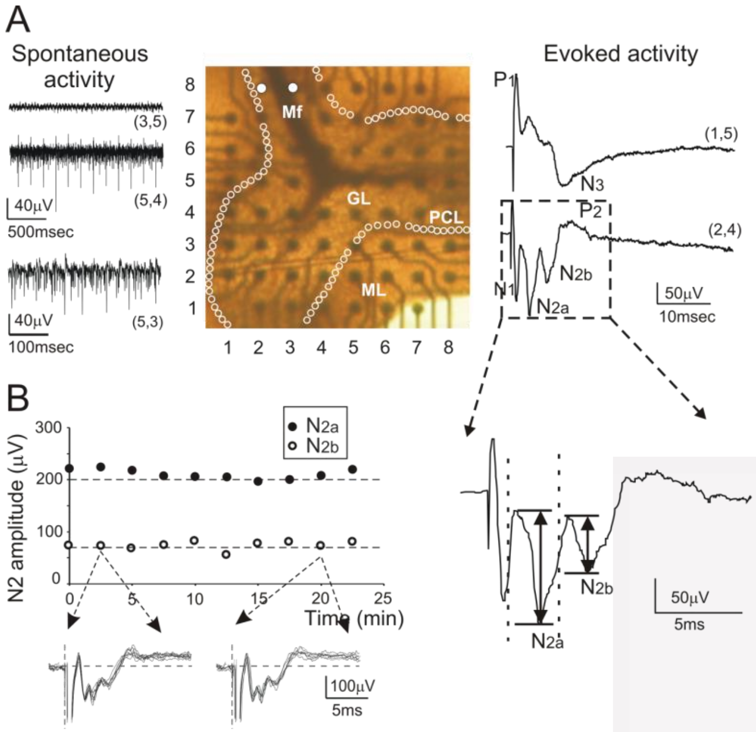
Neuron discharge is probabilistic

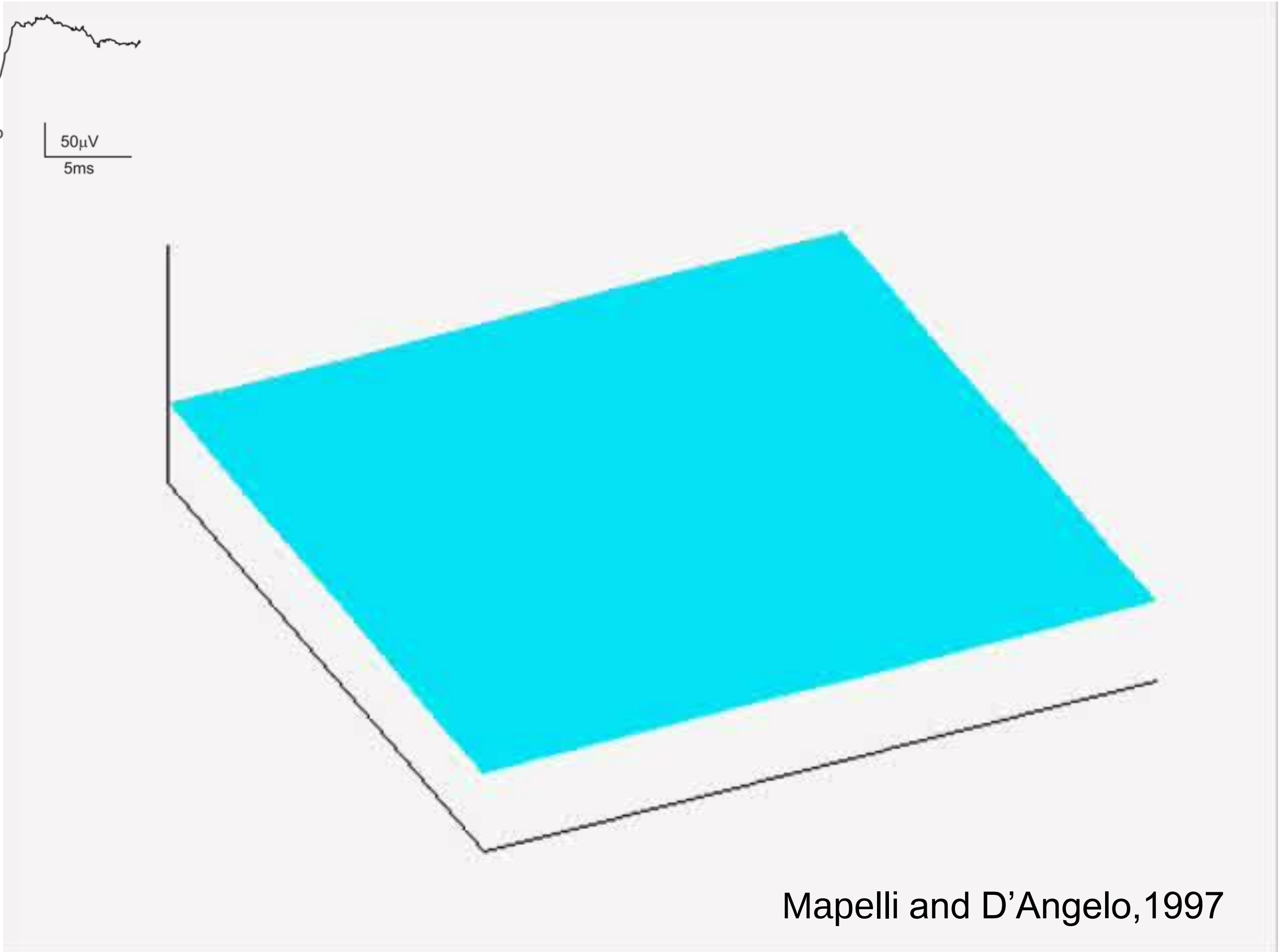




Ramakrishnan and D'Angelo, in preparation

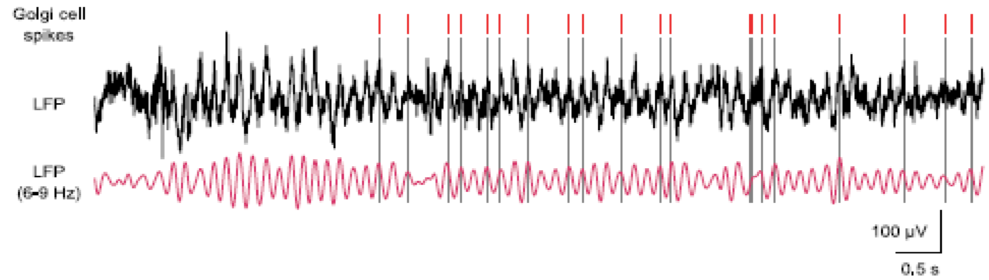
Neural circuits show complex spatio-temporal dynamics





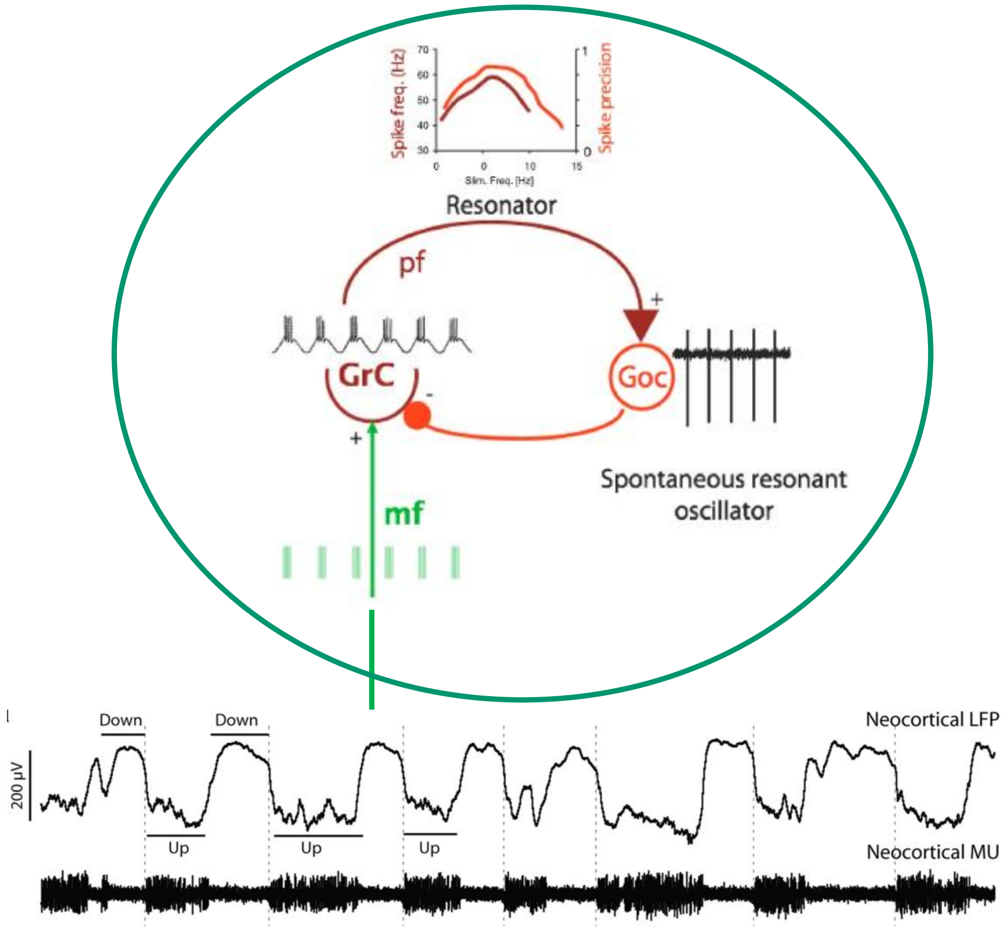
Mapelli and D'Angelo,1997

Neural circuits show resonance and oscillation

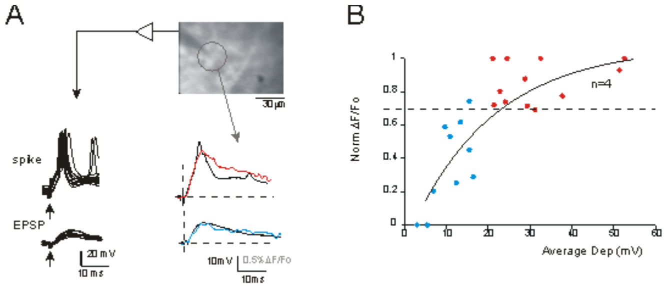


Tuned resonant receiver: granular layer

Oscillating transmitter: Cortico-thalamic system

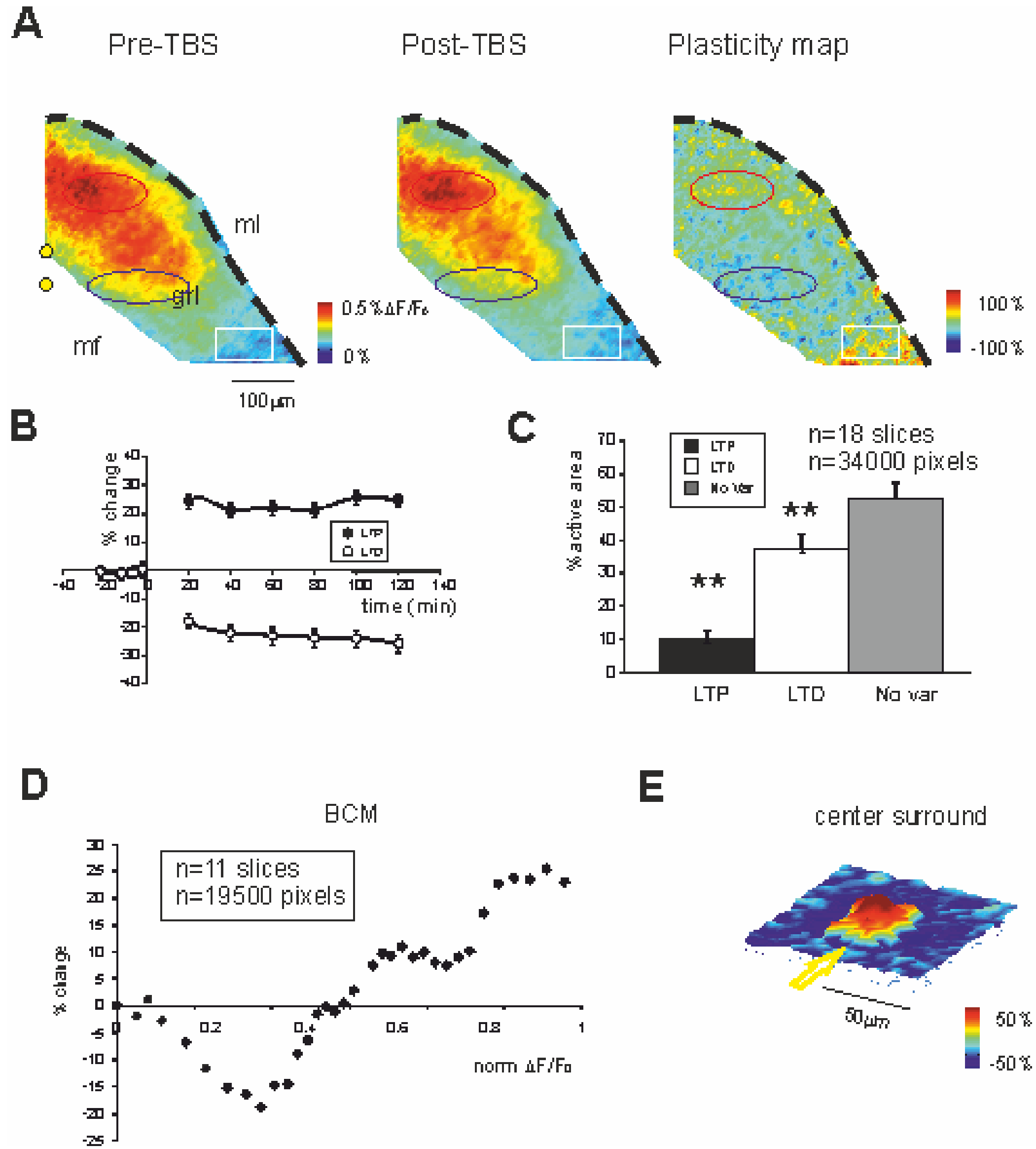


Gandolfi et al., 2013; D’Angelo et al 2013



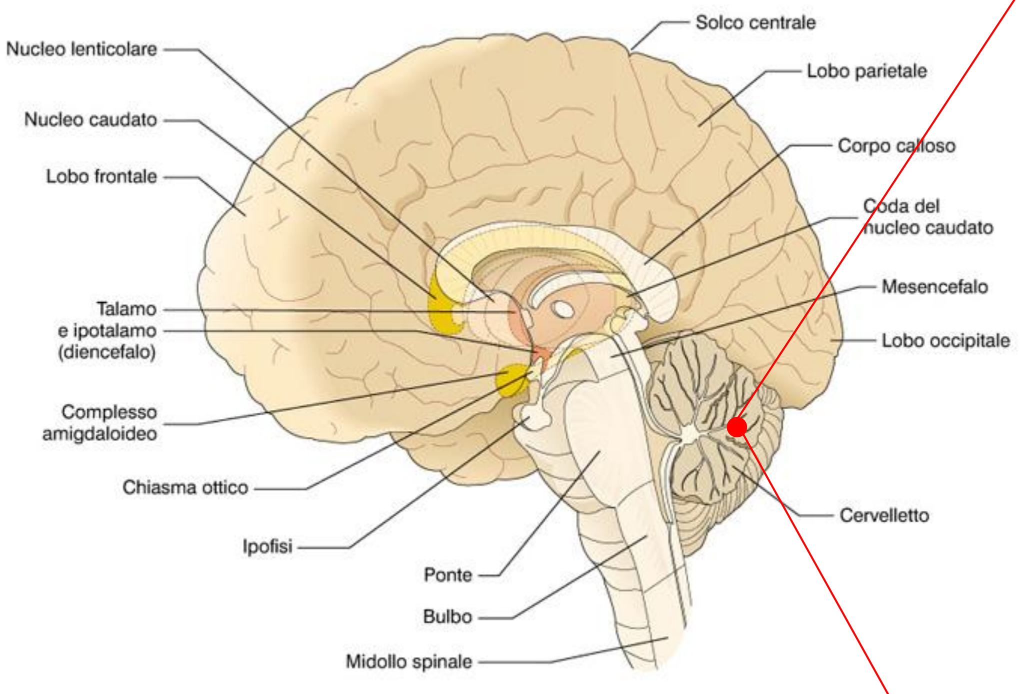
Mapelli et al., 2010 a,b

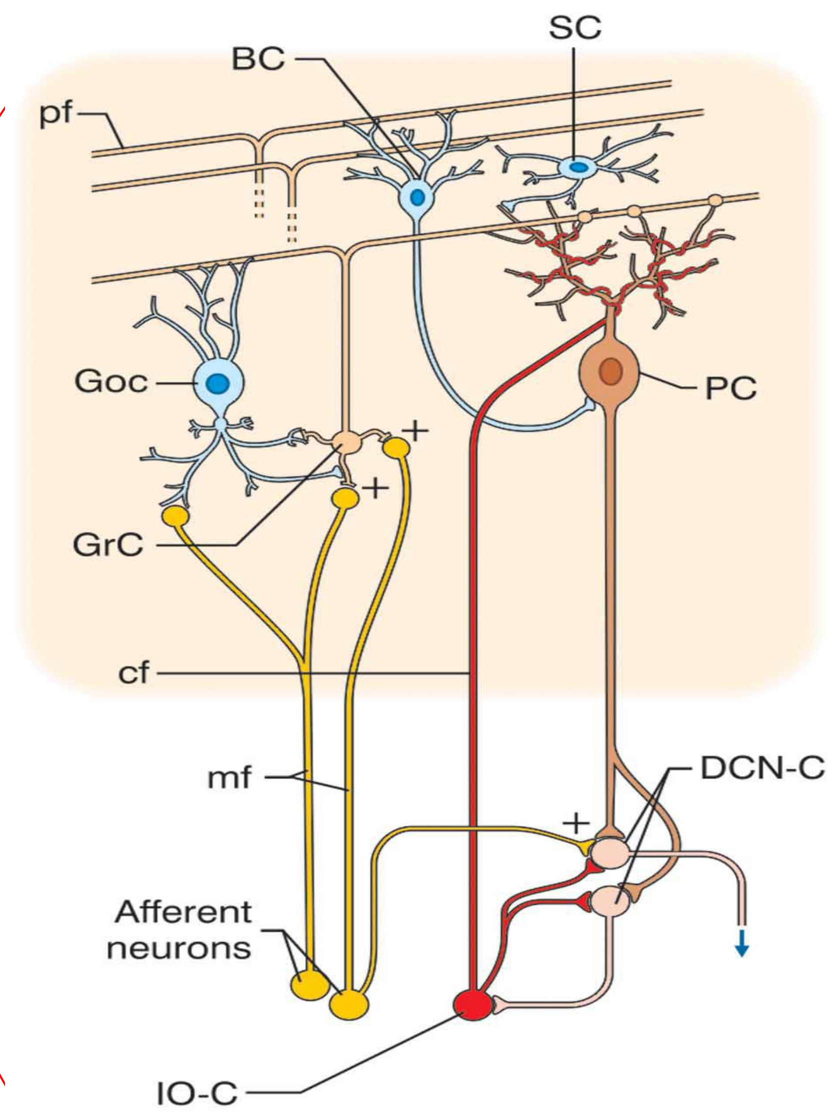
Neural circuit responses are tolopogically organized



Gandolfi, Mapelli, Solinas, D'Angelo , in preparation

Neural circuits have complex architecture

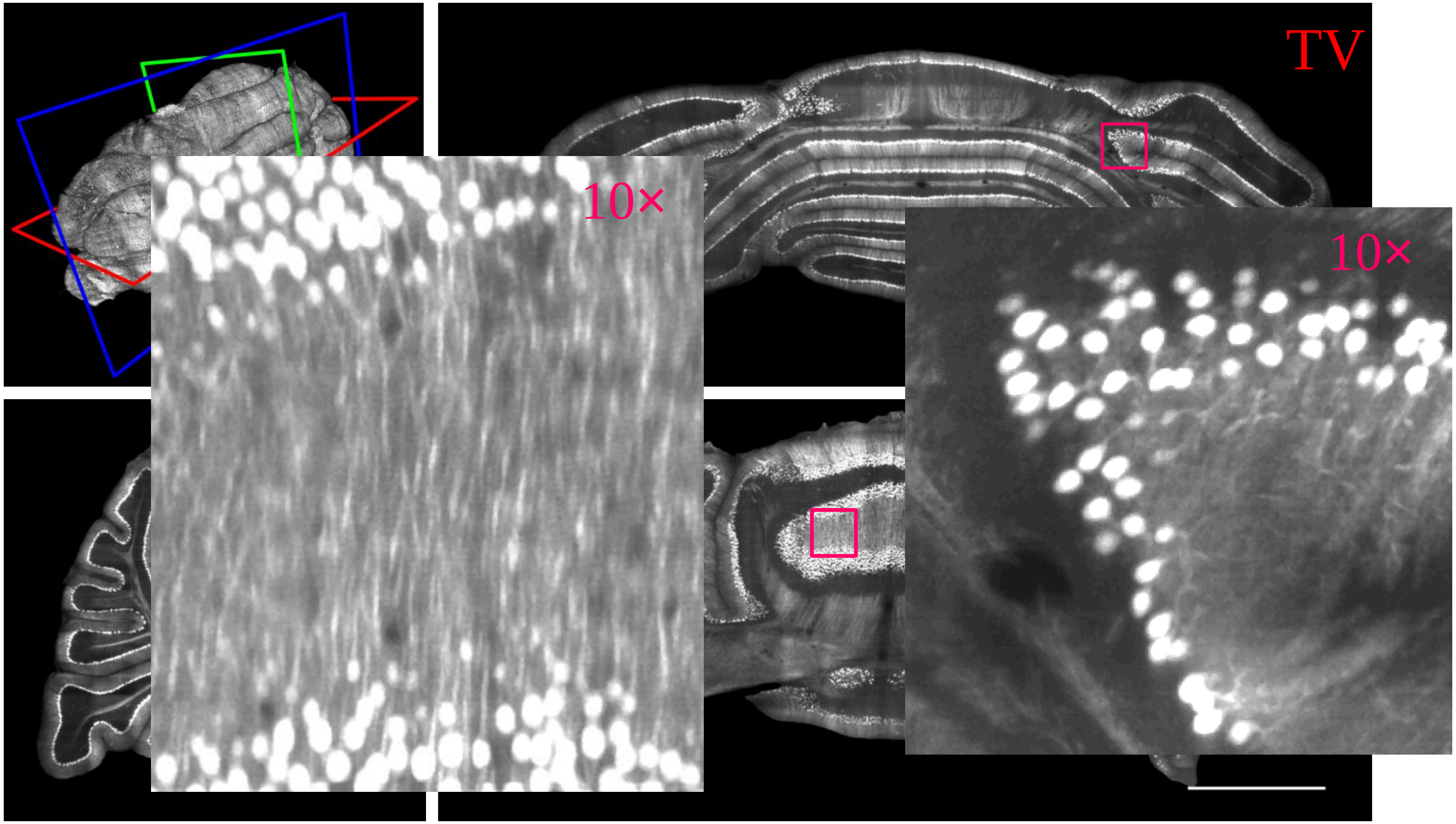




10^{12} neuroni

10^{15} sinapsi

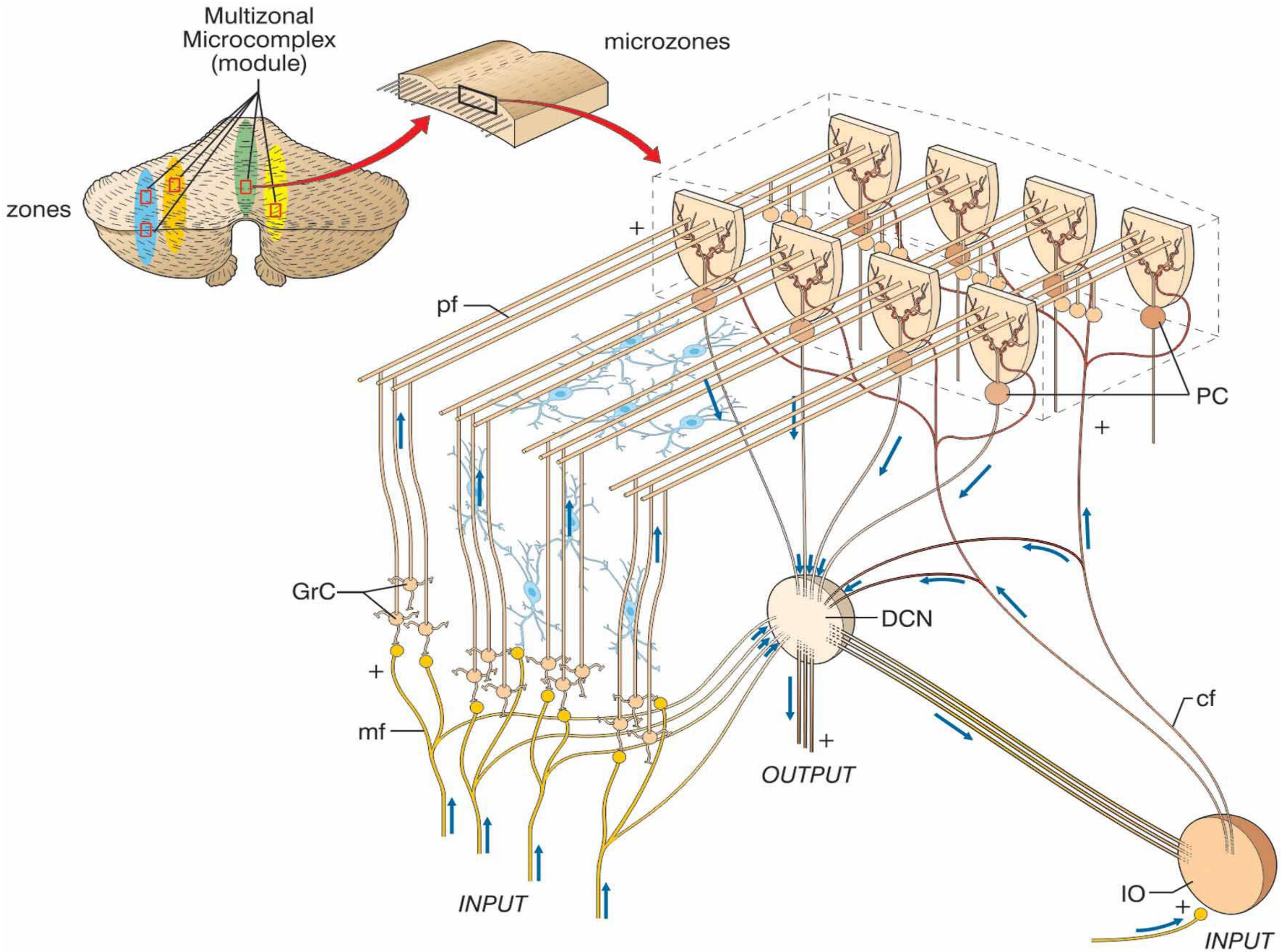
Whole brain imaging



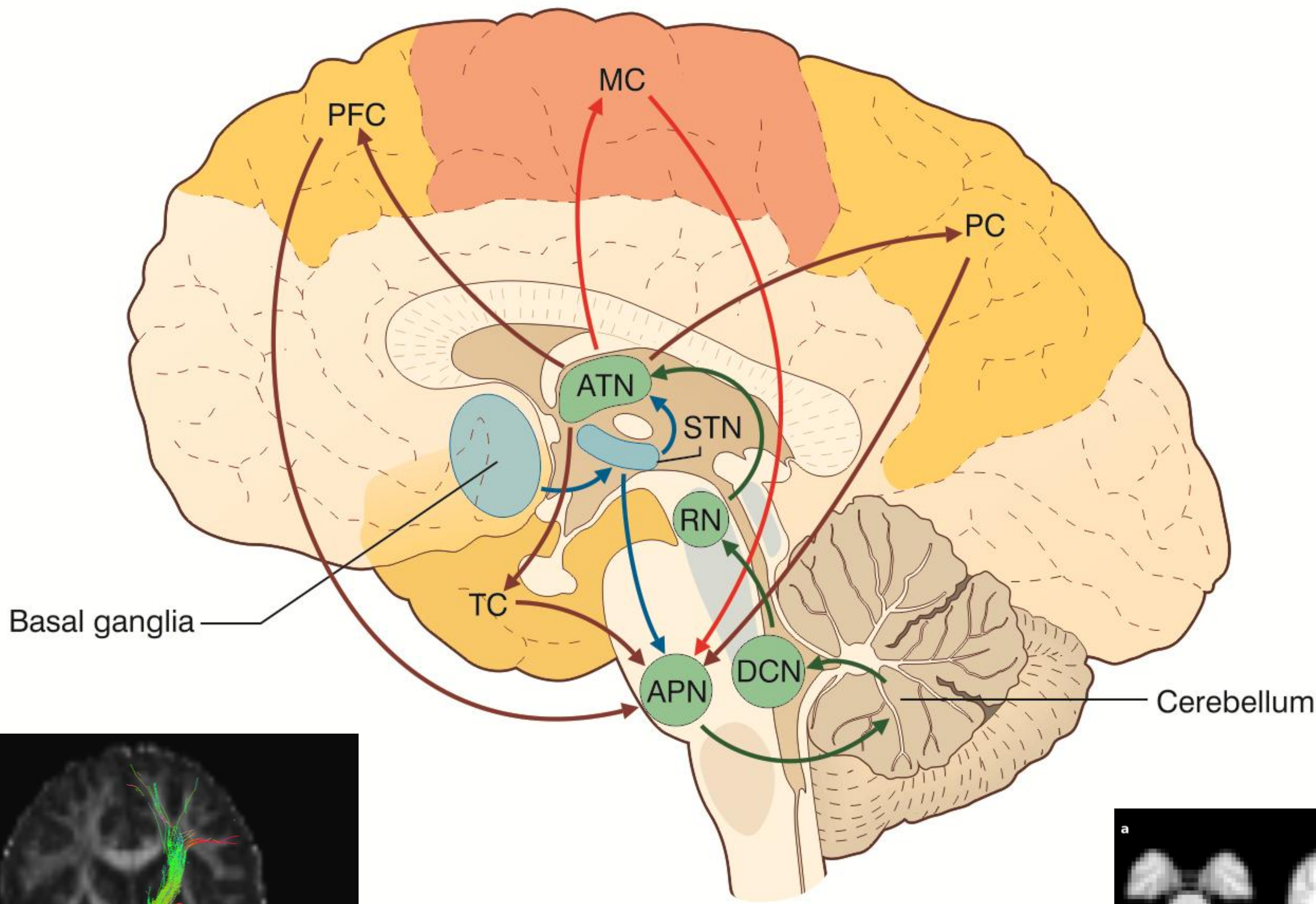
Cerebellum from a P10 L7-GFP mouse cleared in BABB

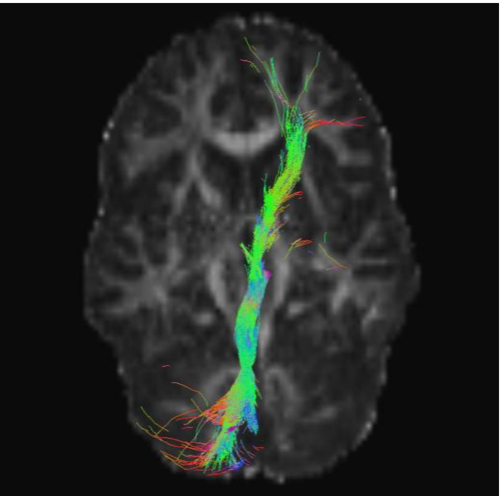
Total volume 73 mm³, voxel size 0.8 × 0.8 × 1 μm³, acquisition time ≈ 24 h (1.3 MegaVoxels/s)
Scale bars: 1 mm.

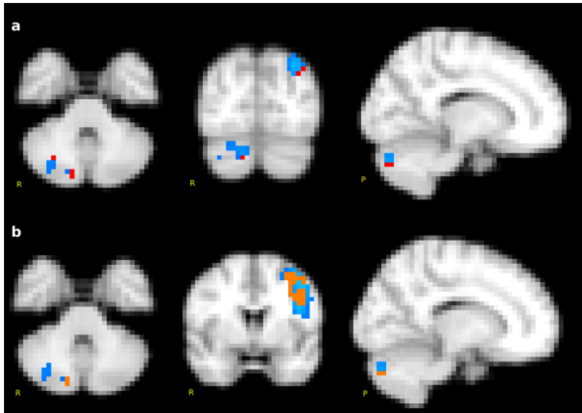
Neural circuits have modular organization



Long-range connections





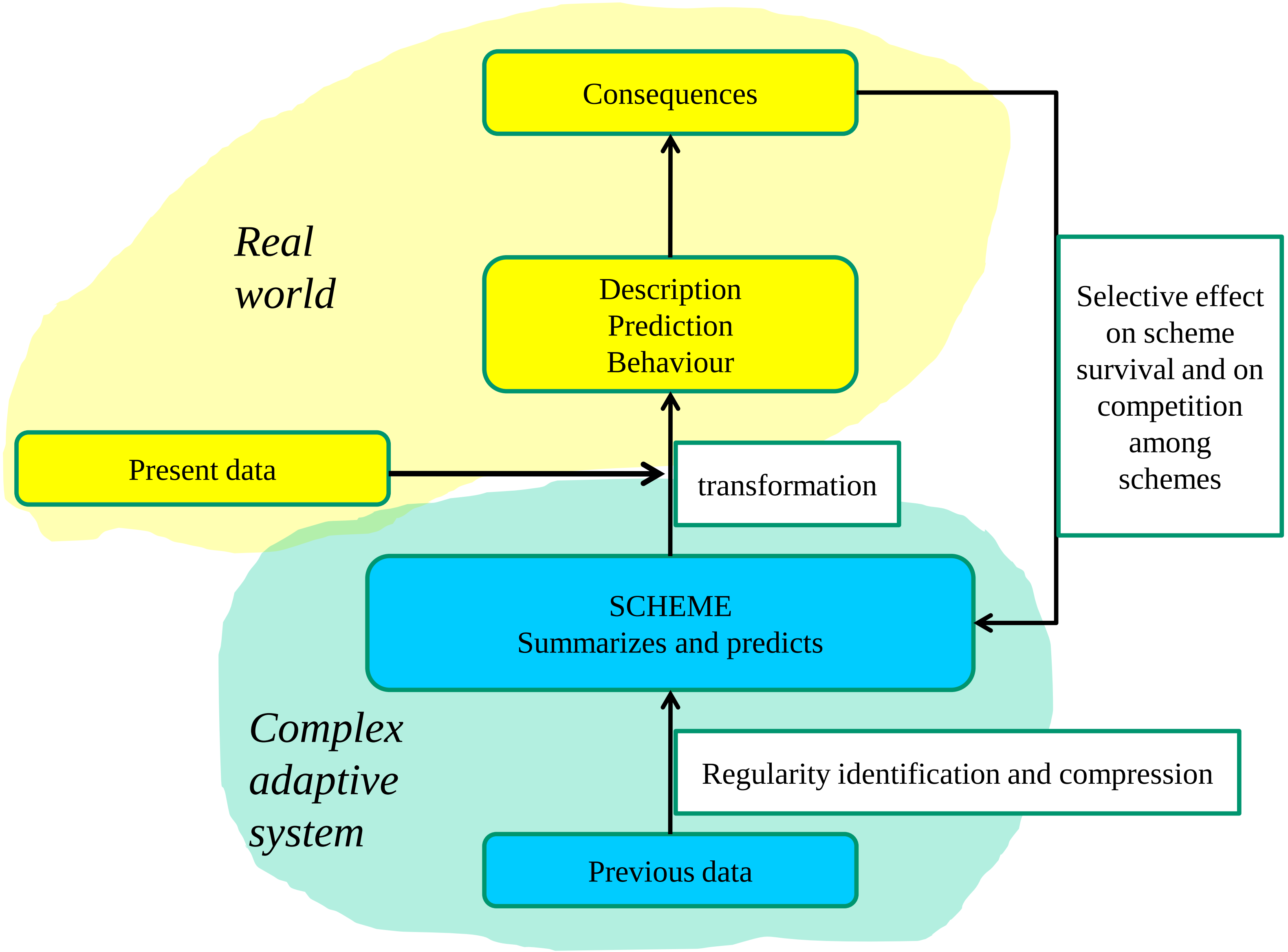


Paelsi et , submitted

Castellazzi et al., submitted

The brain is a

"complex adaptive system"



In summary, beyond general molecular and cellular properties, the brain cannot be investigated as the other tissues

- Is organized in meta-levels
- Has extreme structural and functional complexity
- Operates as a *complex adaptive system*
- Shows emergent properties like behavior and consciousness
- The output is often hard to quantify
- Requires multidisciplinary analysis (Neuroscience)
- Extended implications for medicine, engineering, phylosophy, ethics, society

Moreover, brain function does not compare well to computers

Brain vs. computer:

- Slow (≅100 Hz vs. ≅0.1-1 GHz)
- Imprecise (10^9 less than a CPU)

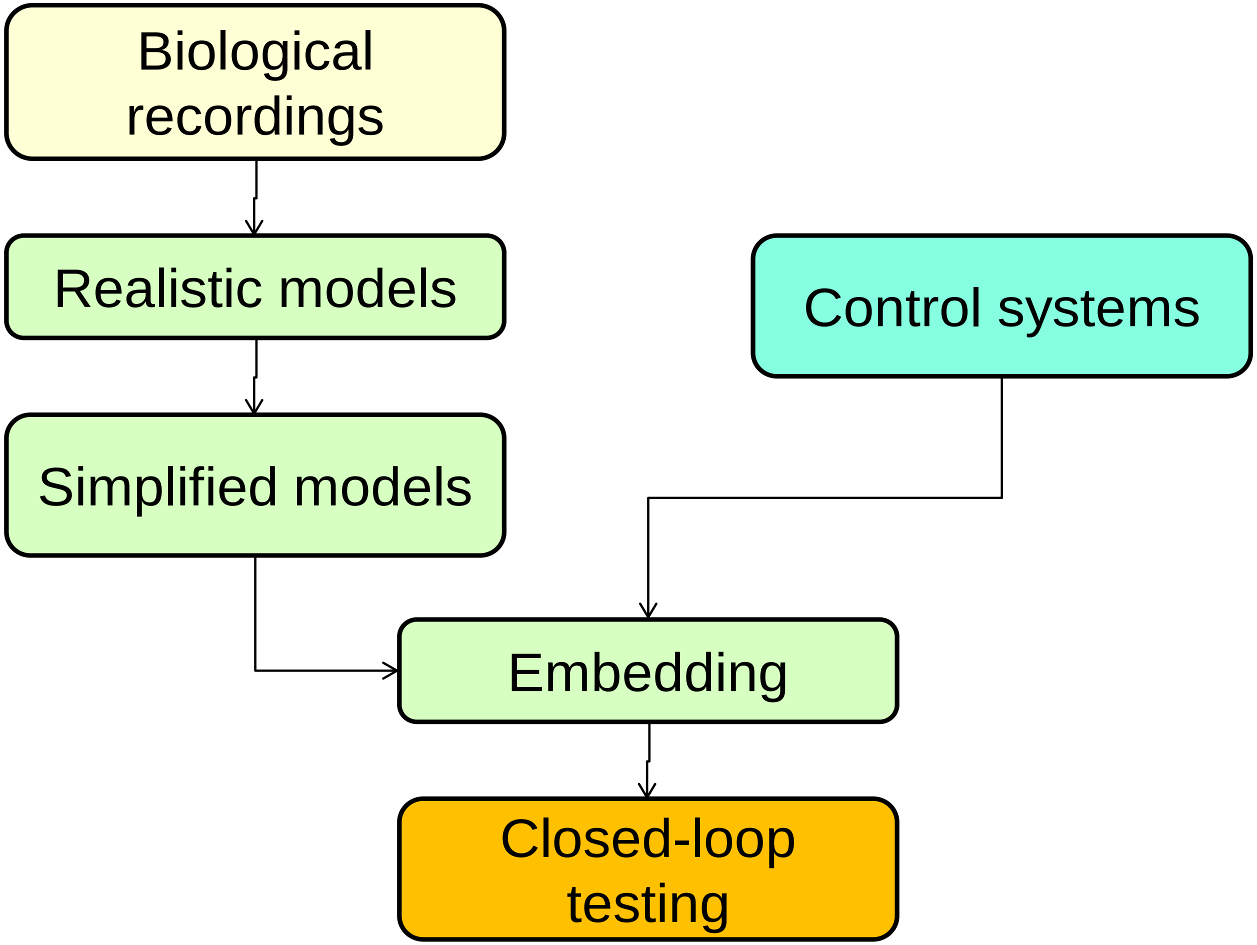
•However, the brain can operate in real time identifying a face among thousands in just 100 ms, a performance out of reach for the most powerful computer.

•Poorly sensitive to hardware break-down (graceful degradation)

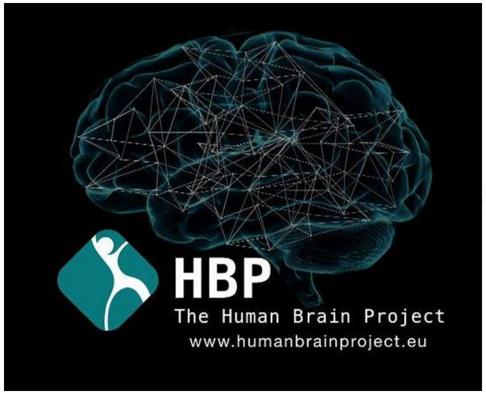
•Self-repairs and modifies with learning (plasticity)

- Has a parallel and hierarchic organization
- Memory and computation exploit the same structural elements
- Elaborates about 10^{18} synapse operations/sec

(2)
The "bottom-up" modeling strategy



D'Angelo et al., , 2013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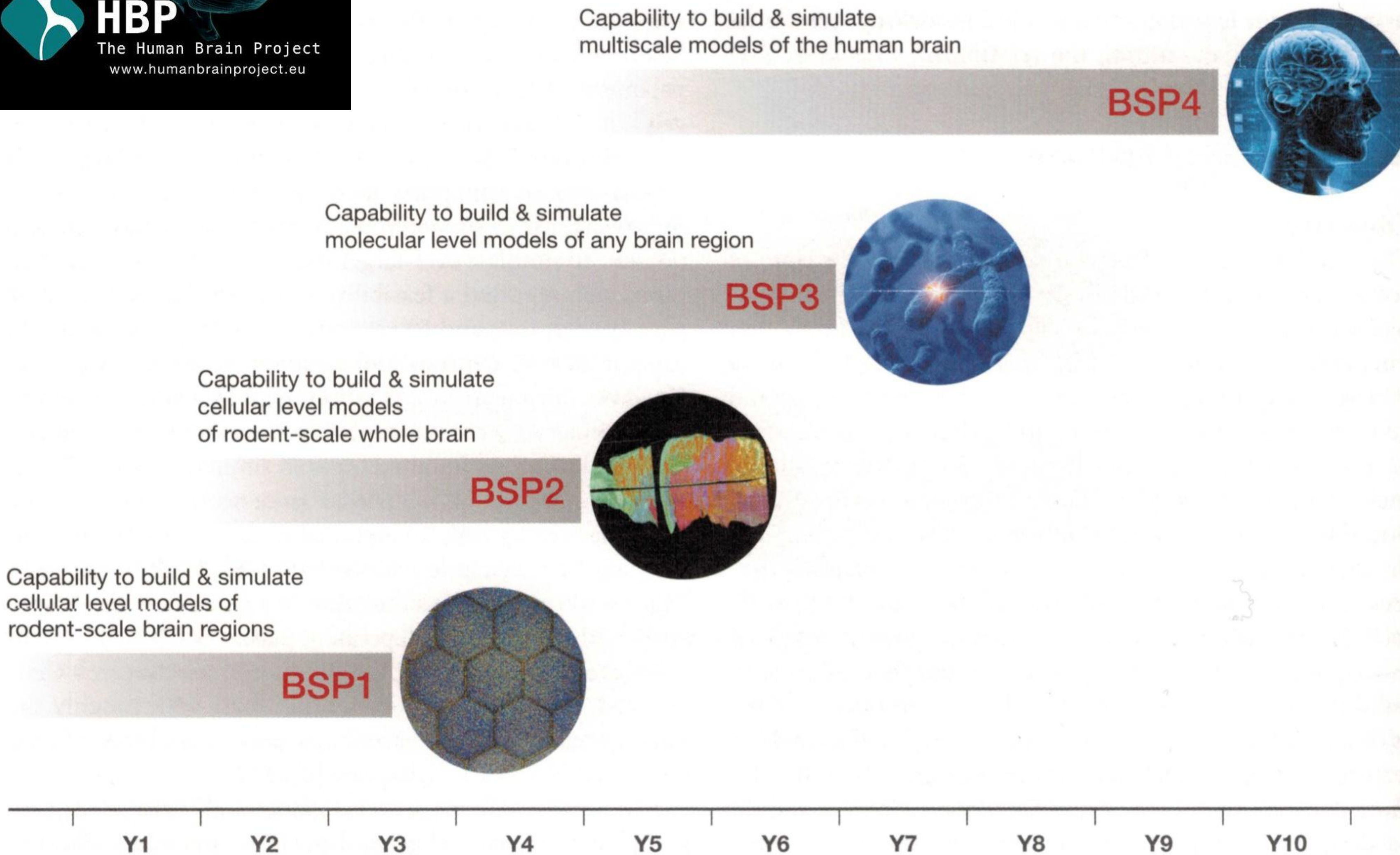
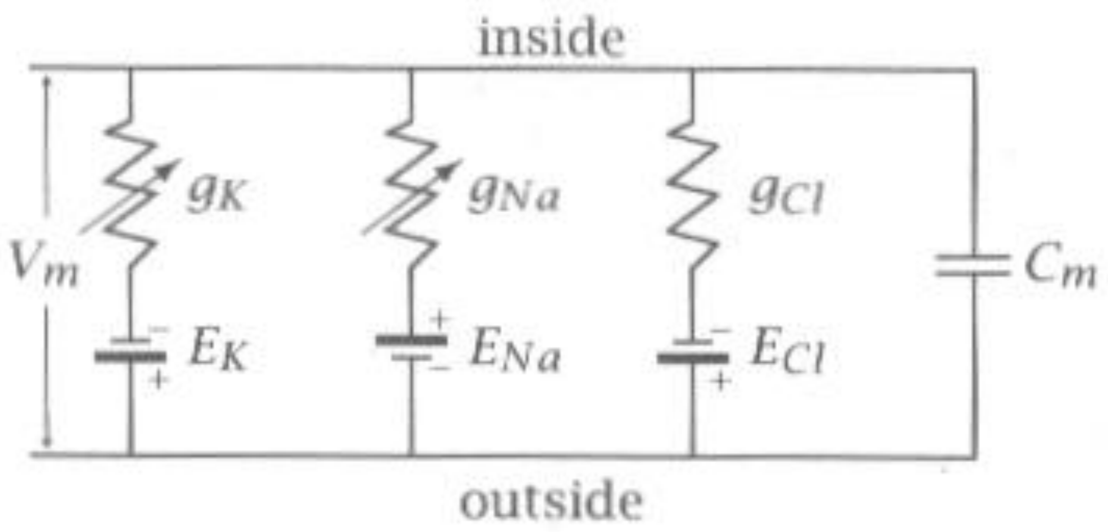

Capability to build & simulate
multiscale models of the human brain
BSP4
Capability to build & simulate
molecular level models of any brain region
BSP3
Capability to build & simulate
cellular level models
of rodent-scale whole brain
BSP2
Capability to build & simulate
cellular level models of
rodent-scale brain regions
BSP1
Y1
Y2
Y3
Y4
Y5
Y6
Y7
Y8
Y9
Y10

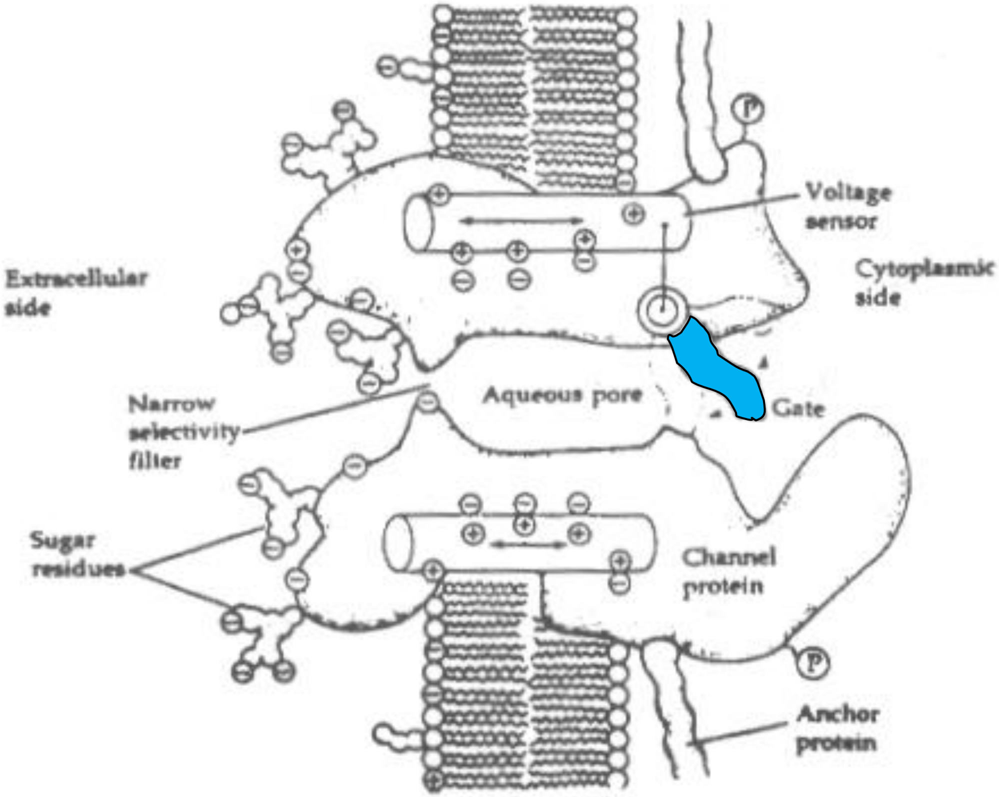
The membrane equation



$$I = I_c + I_K + I_{Na} + I_{Cl}$$

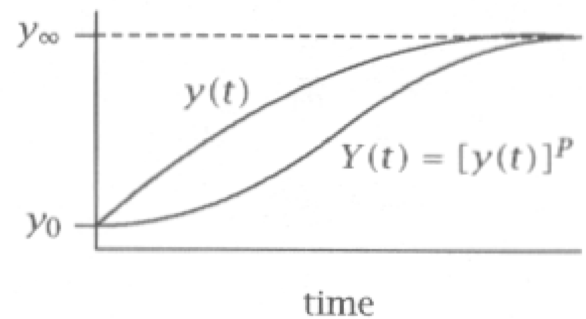
$$I = C\frac{dV}{dt} + g_k(V - E_K) + g_{Na}(V - E_{Na}) + g_{Cl}(V - E_{Cl})$$

The "gating" of ionic channels



$$\mathbf{a} \underset{\alpha}{\overset{\beta}{\rightleftarrows}} \mathbf{b}$$

$y \qquad (1\text{-}y)$



tempo-dipendenza

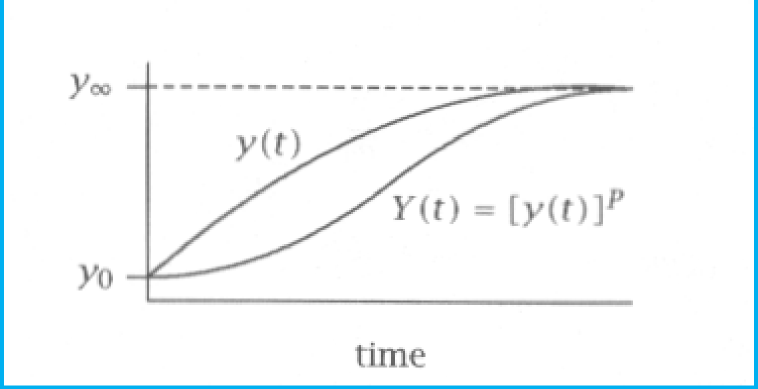
cinetica di primo ordine

$$\frac{dy}{dt} = \alpha(1-y) - \beta y$$

$$y = y_\infty - \left[(y_\infty - y_0)e^{-t/\tau_y}\right]$$

$$\tau_y = \frac{1}{\alpha + \beta}$$

$$y_\infty = \frac{\alpha}{\alpha + \beta}$$



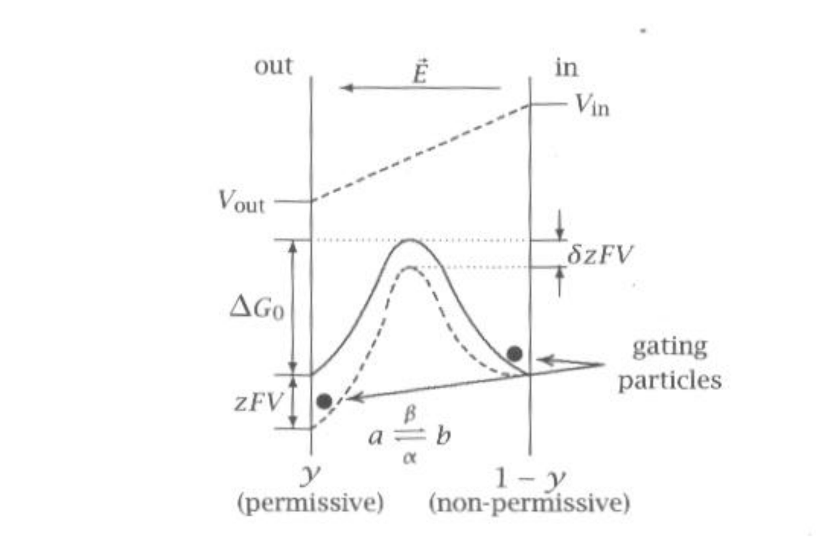
voltaggio-dipendenza

$$\alpha(V) = \alpha_0 e^{\delta VzF/RT}$$

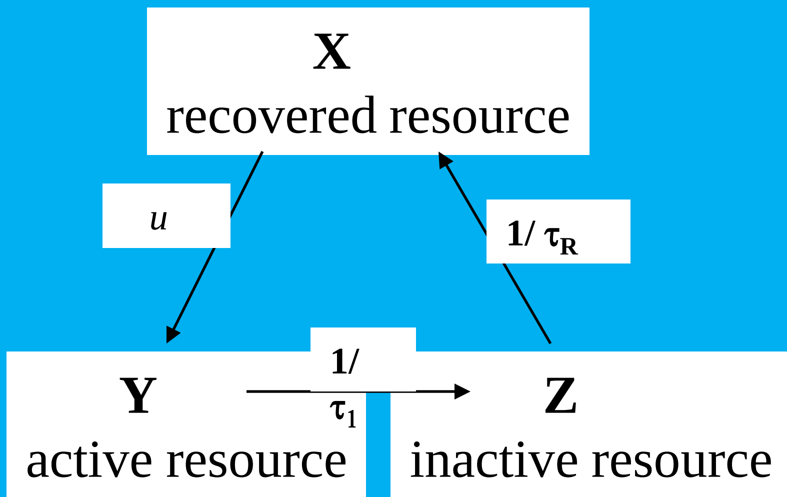
$$\beta(V) = \beta_0 e^{-(1-\delta)VzF/RT}$$

$$\alpha_0 = Ae^{-\Delta G0/RT}$$

$$\beta_0 = Be^{-\Delta G0/RT}$$



Dinamiche presinaptiche di rilascio del neurotrasmettitore



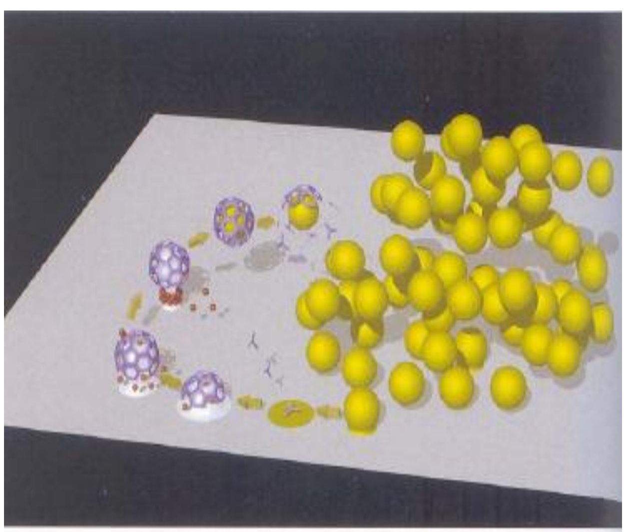
$$\frac{dx}{dt} = \frac{z}{\tau_{REC}} - u \cdot x \cdot \delta(t - t_{SPIKE})$$

$$\frac{dy}{dt} = -\frac{y}{\tau_1} + u \cdot x \cdot \delta(t - t_{SPIKE})$$

$$\frac{dz}{dt} = \frac{y}{\tau_1} - \frac{z}{\tau_{REC}}$$

$$\frac{du}{dt} = -\frac{u}{\tau_{FACIL}} + U \cdot (1-u) \cdot \delta(t - t_{SPIKE})$$

* From Tsodysk and Markram(1998)



U   initial release probability
$t_1 \leftrightarrow$ is supposed to be fast *
$t_r \leftrightarrow$ recovery from depression
$t_f \leftrightarrow$ facilitation

Modelling HH-style

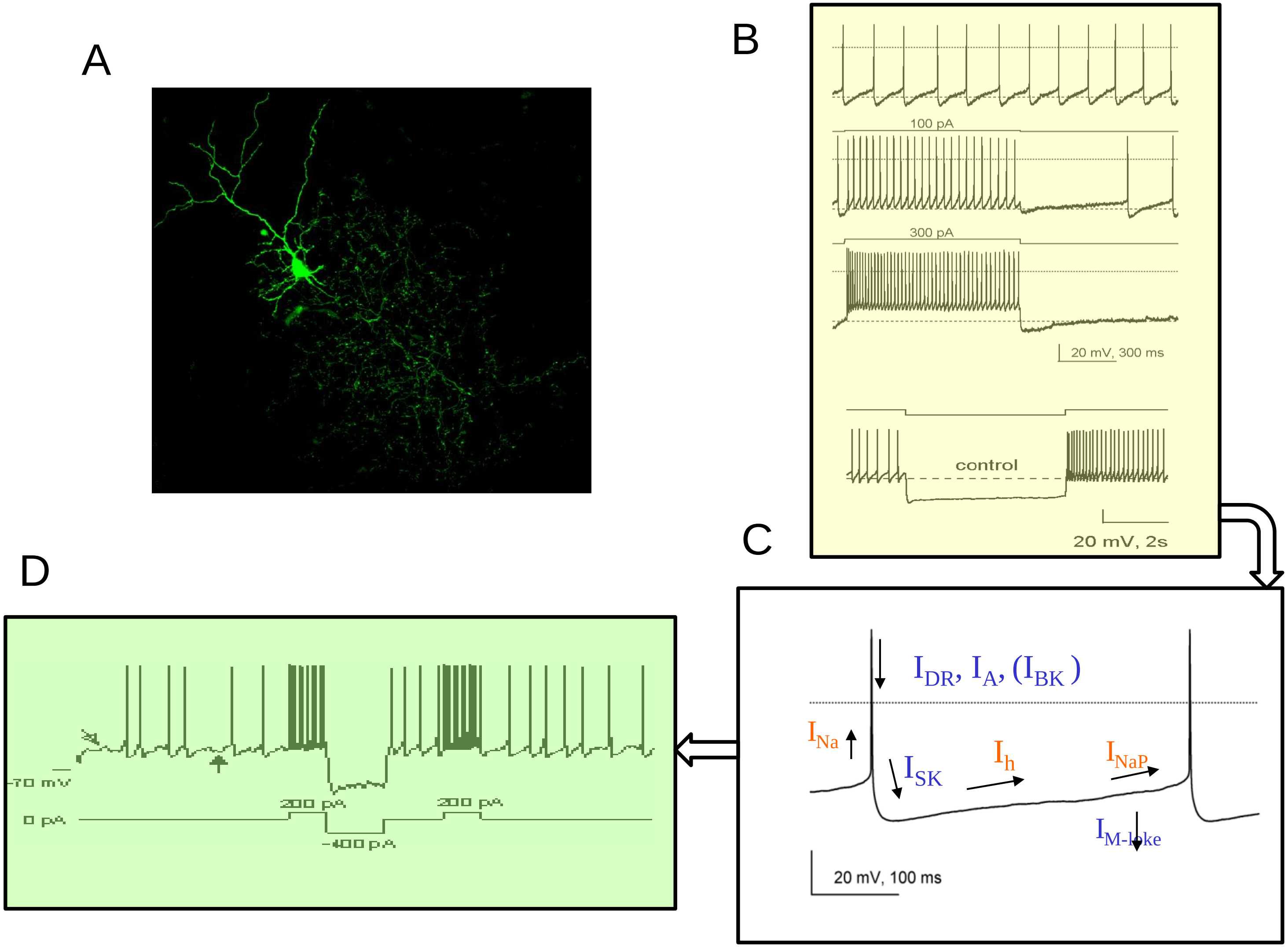
$$\begin{cases} \dfrac{dV}{dt} = \dfrac{1}{\tau_m}\left(V - \dfrac{\sum_i g_i (V - E_i)}{g_{tot}}\right) & \text{dove } \tau_m = R_m / g_{tot} \\ \dfrac{dy_i}{dt} = \alpha_i - (\alpha_i + \beta_i) y_i \end{cases}$$

$$g_i = g_i^{\max} y_{i-att}^{n} y_{i-inatt}^{m}$$

$$\alpha_i, \beta_i = f(V, t)$$

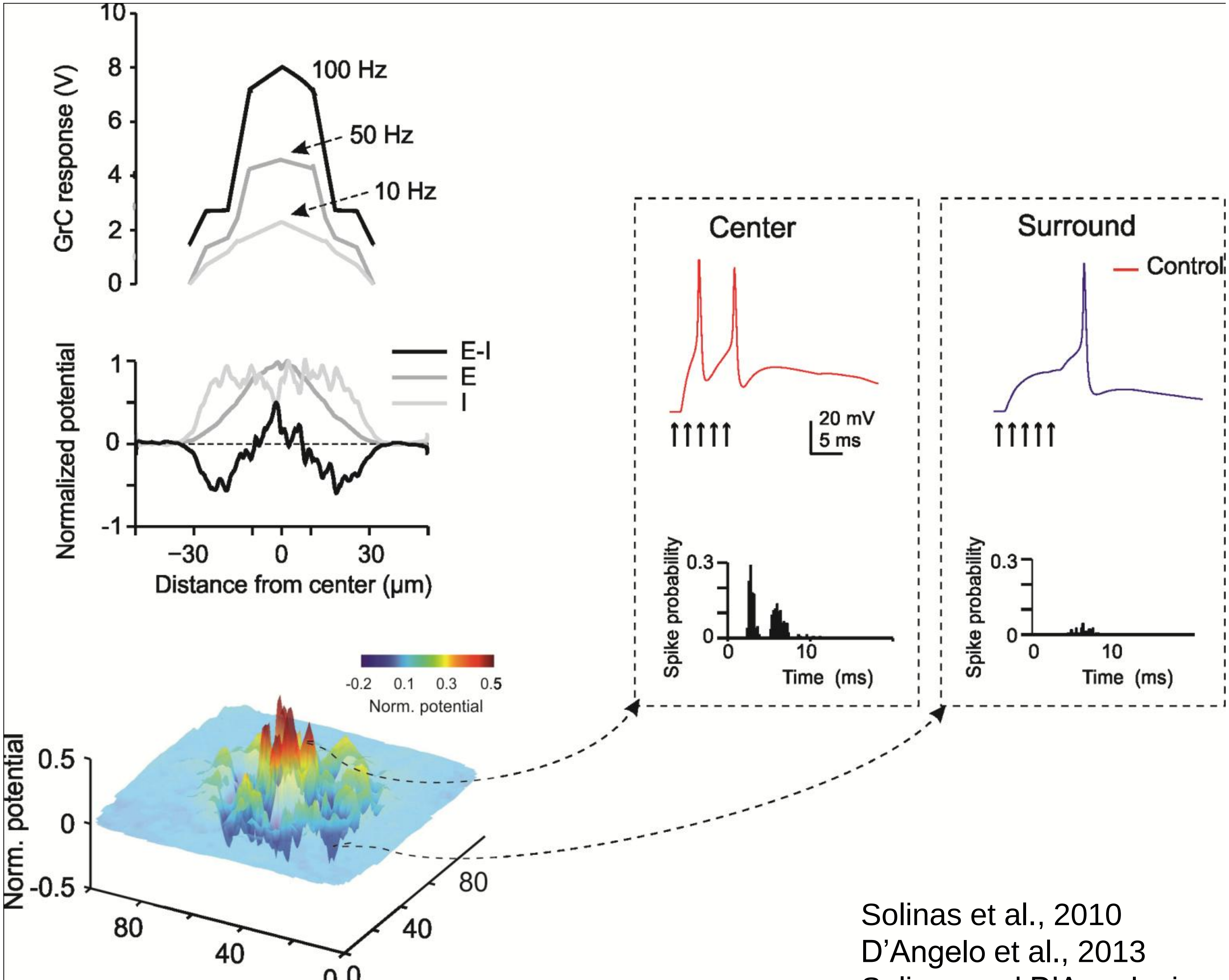
Soluzione con metodi di integrazione numerica

Single cell modeling



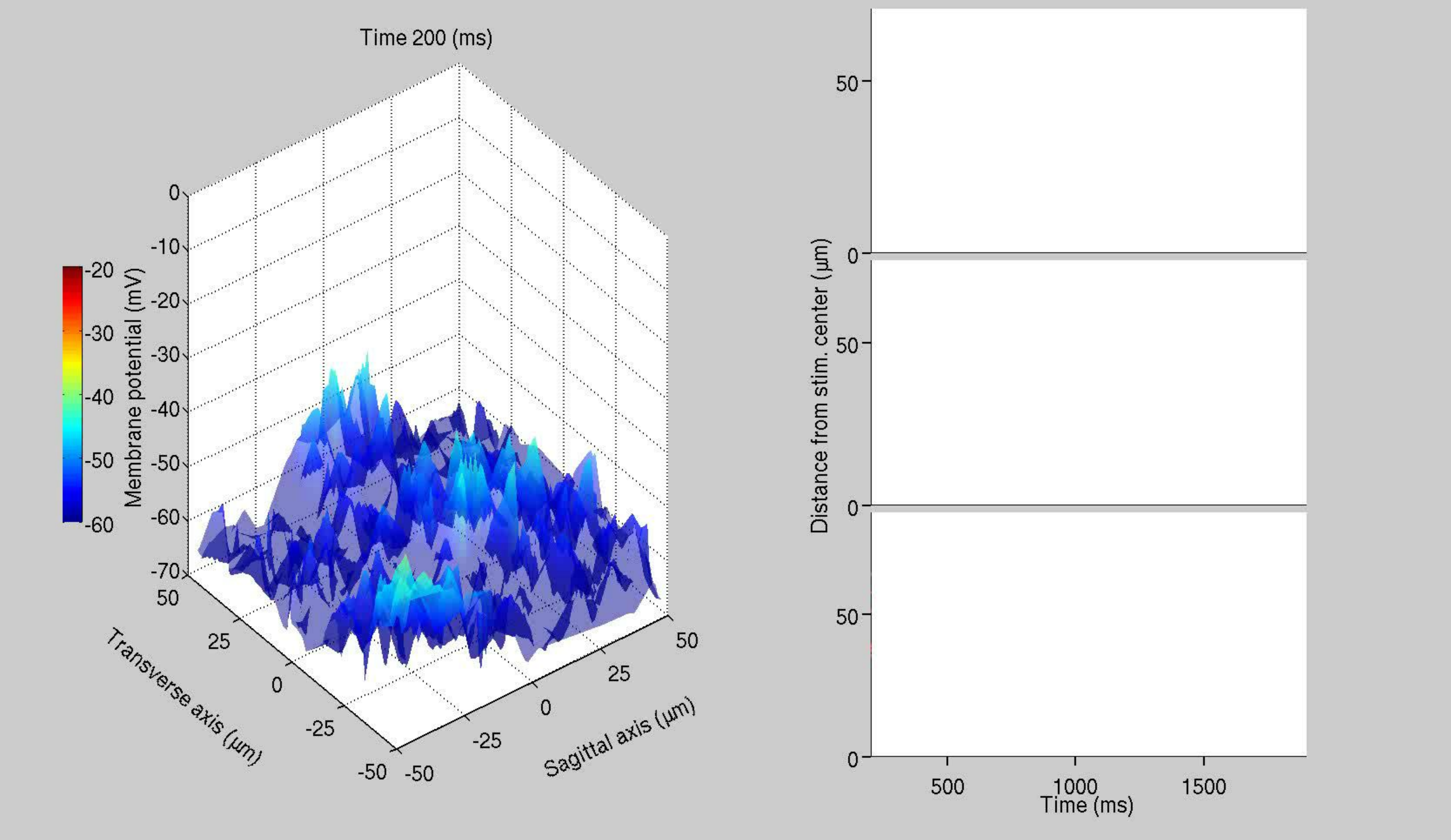
D’Angelo et al., , 2013

Prediction of functional states

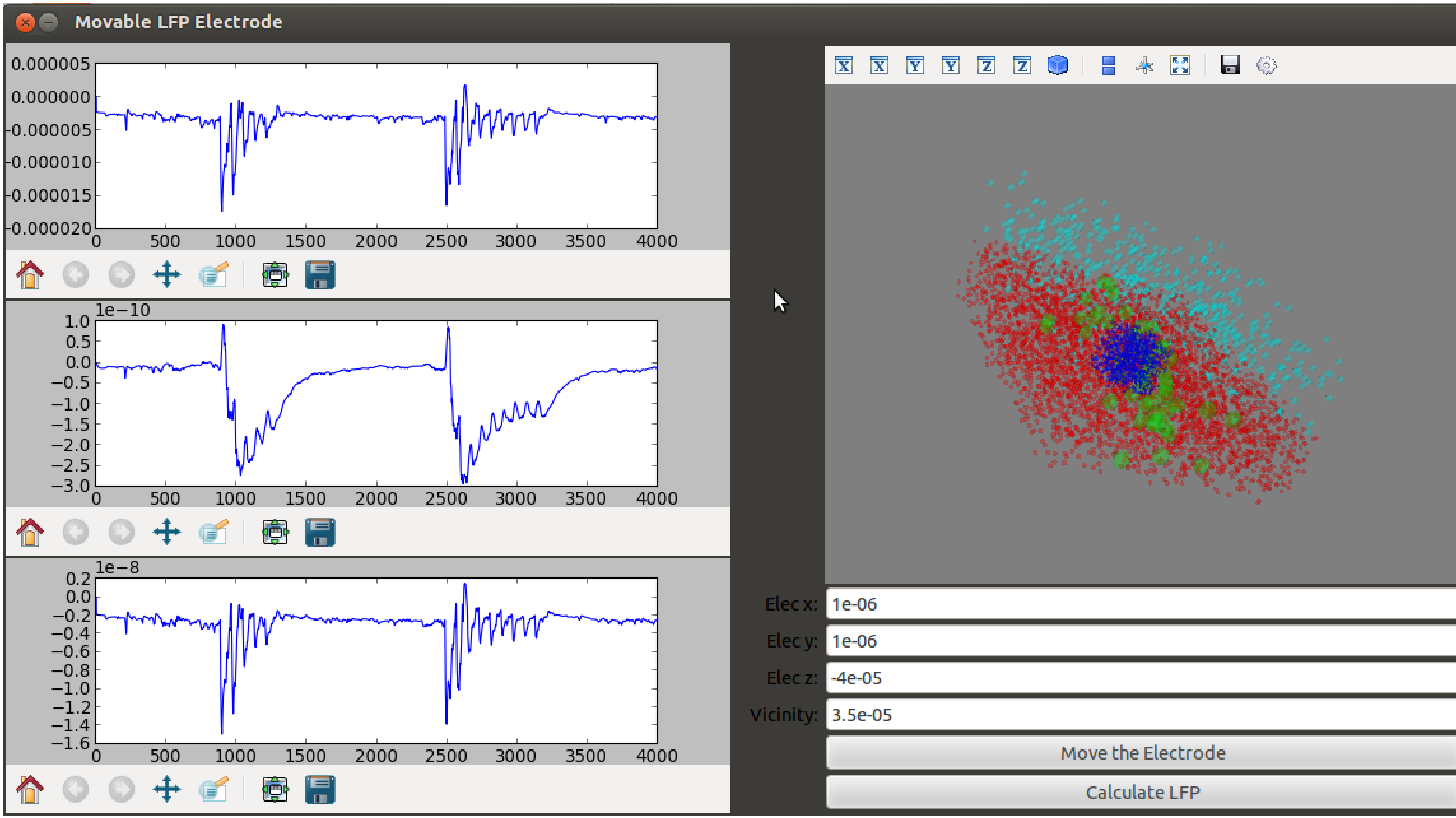


Solinas et al., 2010
D'Angelo et al., 2013
Solinas and D'Angelo, in preparation

Neural circuit modeling



➢ Prediction of LFP generation ….

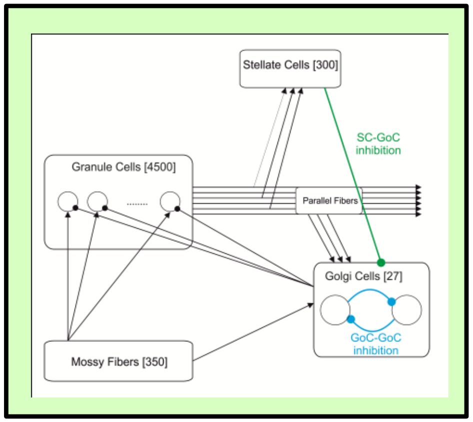


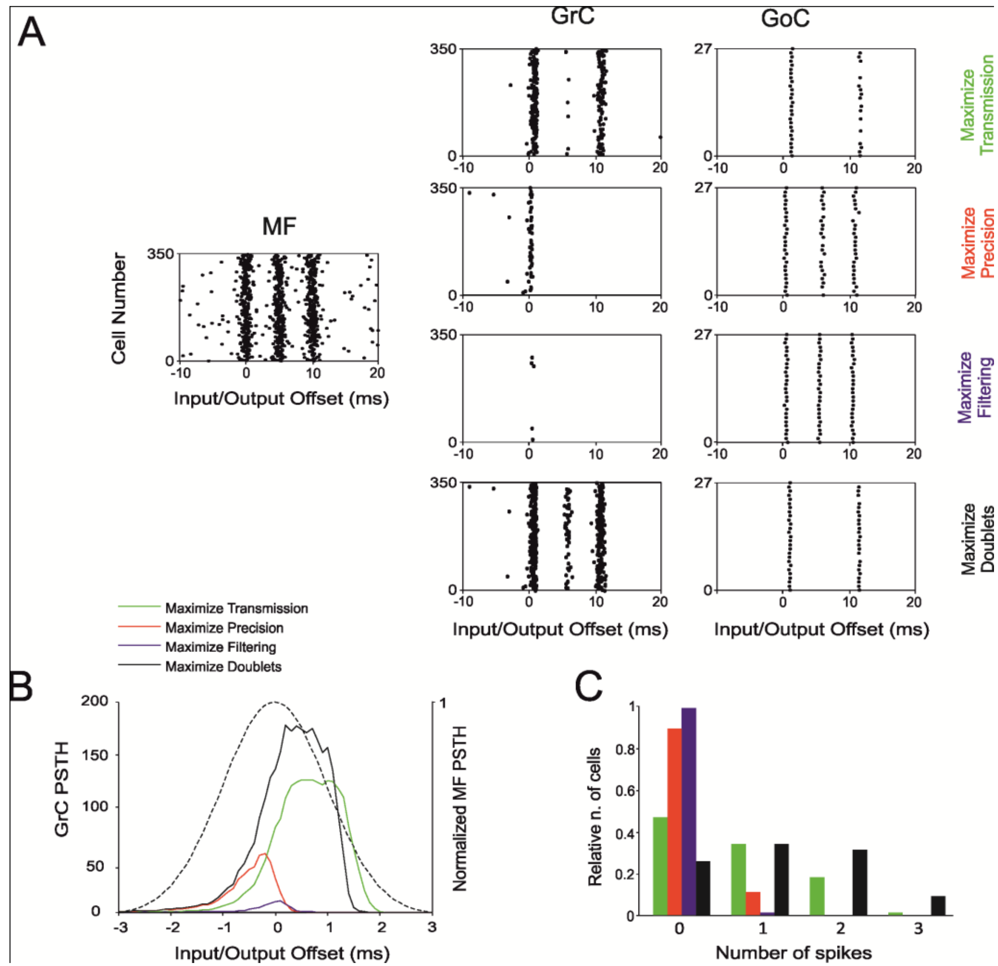
Diwakar, Solinas, D'Angelo et al., in preparation

(3)
Network models in closed-loop simulations

Unreaveling the relationship between single neuron properties and ensamble brain activity

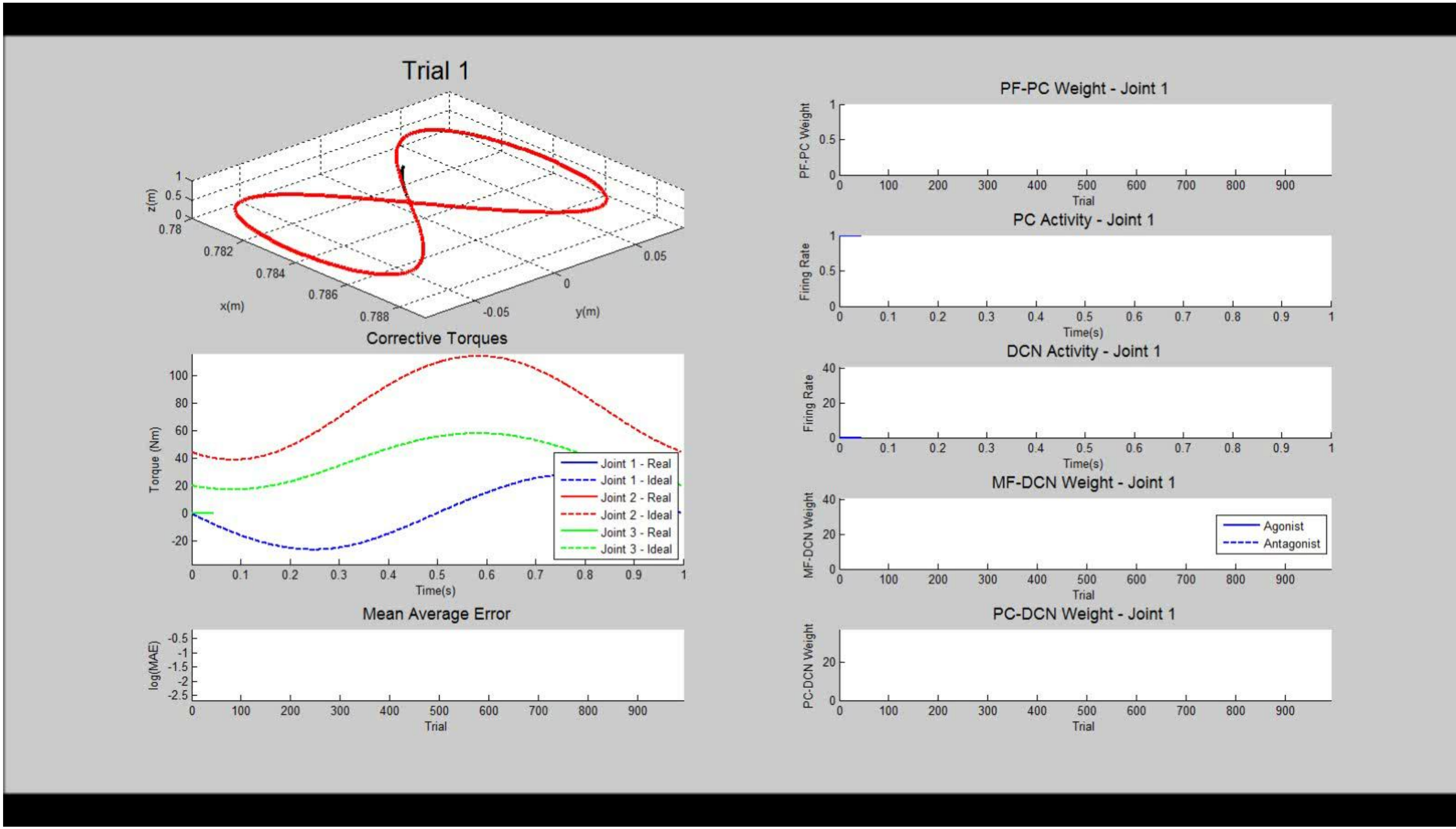
Simplified real-time spiking model of the granular layer network





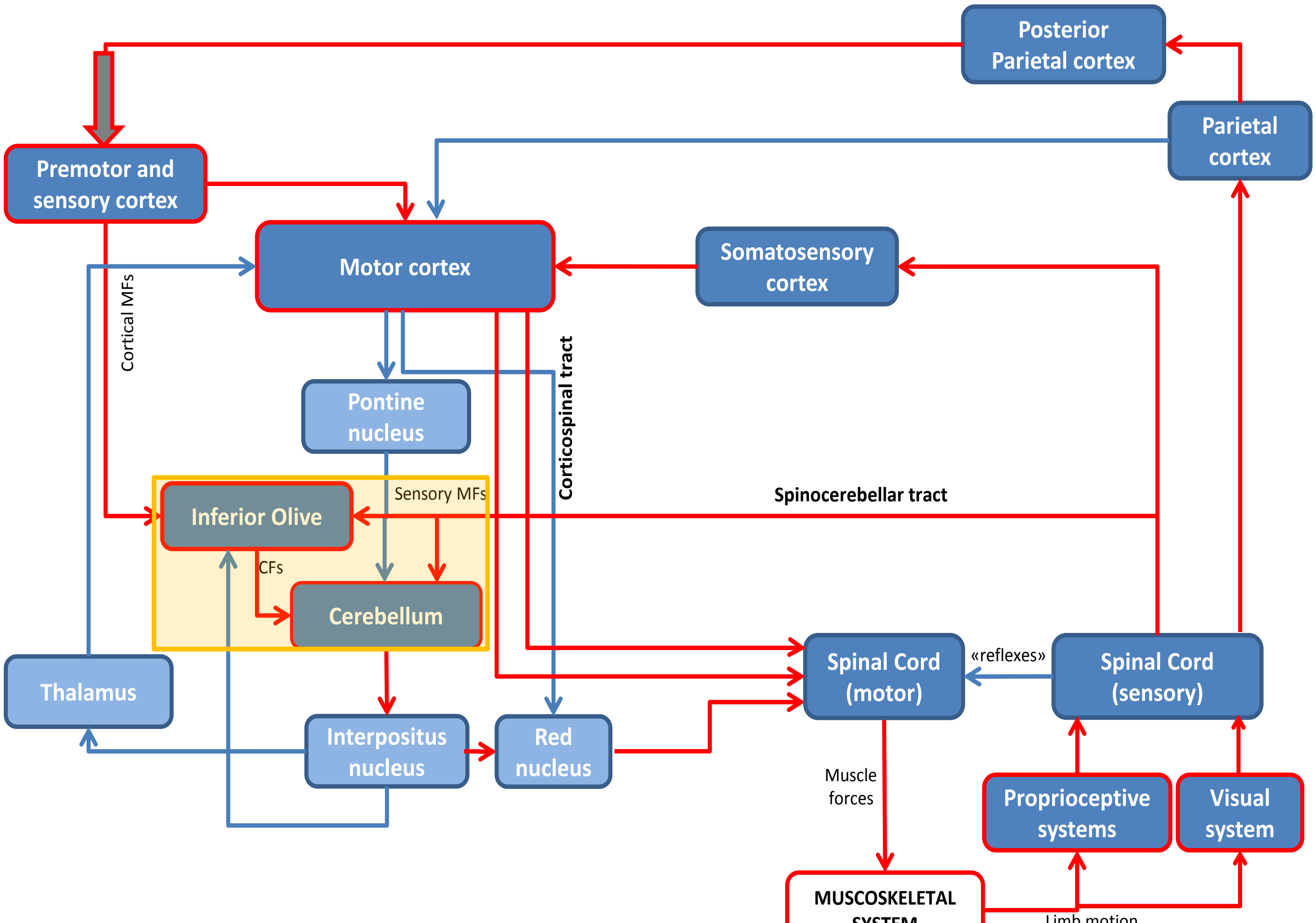
Garrido et al., , 2013

Adaptive learning in a robotic simulator incorporating the cerebellar network and synaptic learning rules



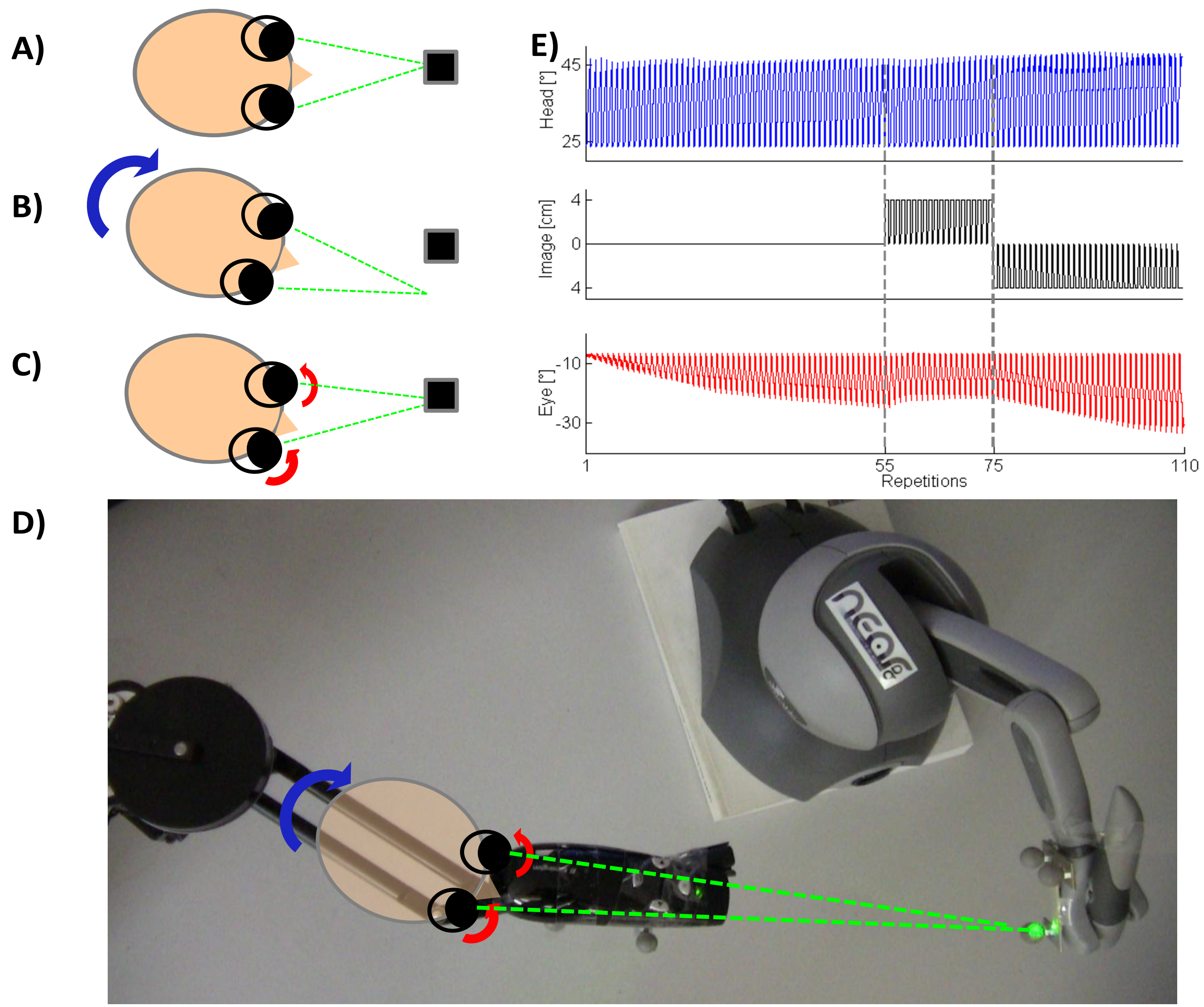
Garrido et al., , 2013

Distributed neuromotor control system embedding the cerebellum model



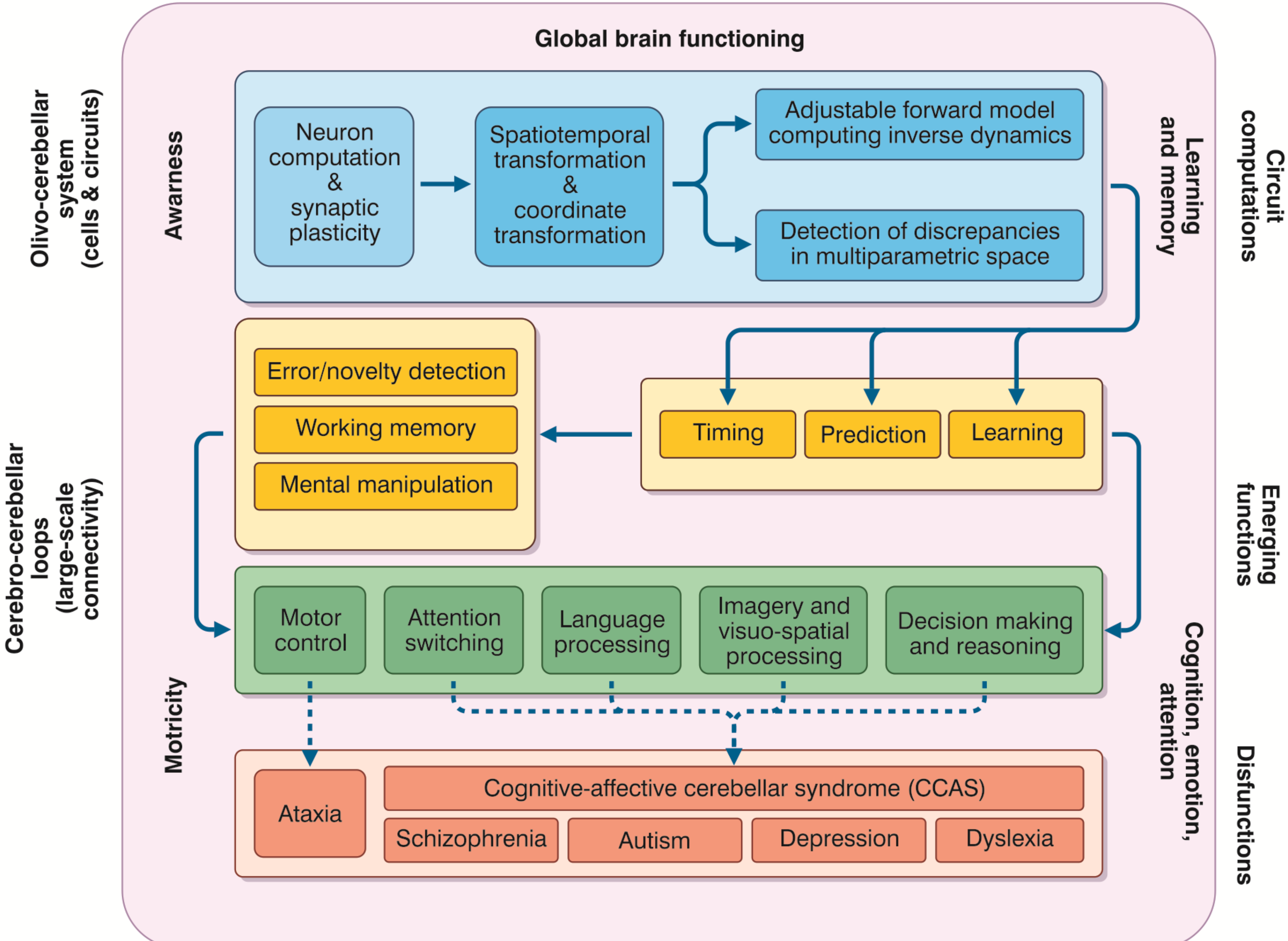
Casellato et al., , 2013

Control system with the cerebellar model running in a real-time robotic platform



Casellato et al., , 2013

Multi-level organization and neurological diseases



Casali and D'Angelo, 2013

(3)
Conclusions

- Large-scale realistic models of brain circuits can be constructed and tested

- These models can help explaining how low-level connect to high-level brain functions

- These models can be applied to computational and robotic control

- These models can foster biomedical research and applications in the clinical sector.

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