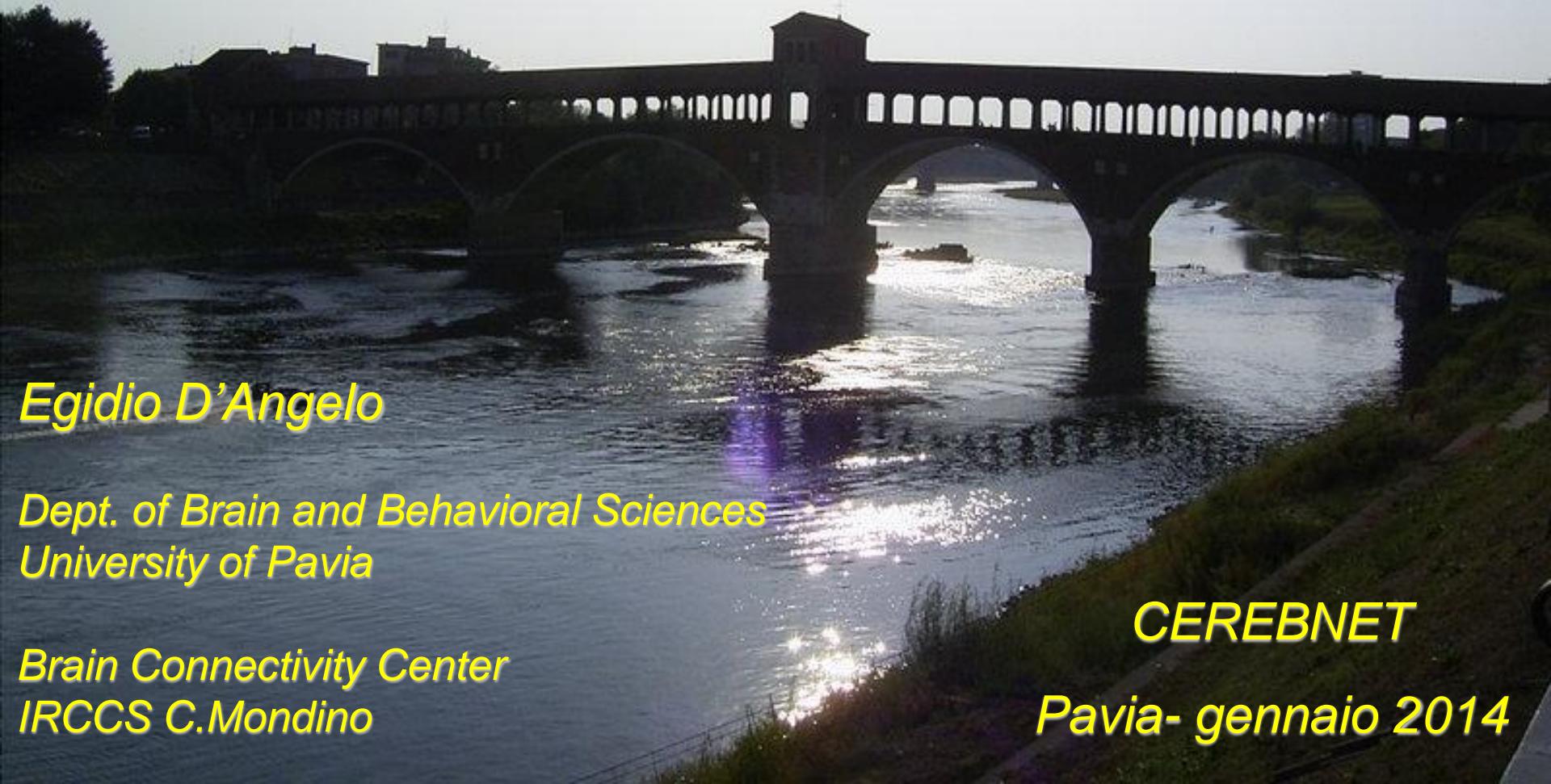


From cellular biophysics to spiking networks for robotic control



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Alessandra Pedrocchi

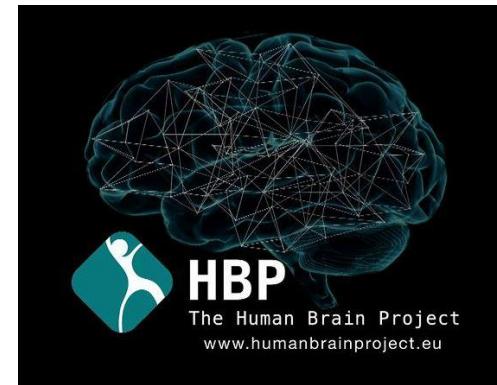
Neuroengineering Lab, Politecnico di Milano

Eduardo Ros

Neurocomputation Lab, University of Granda

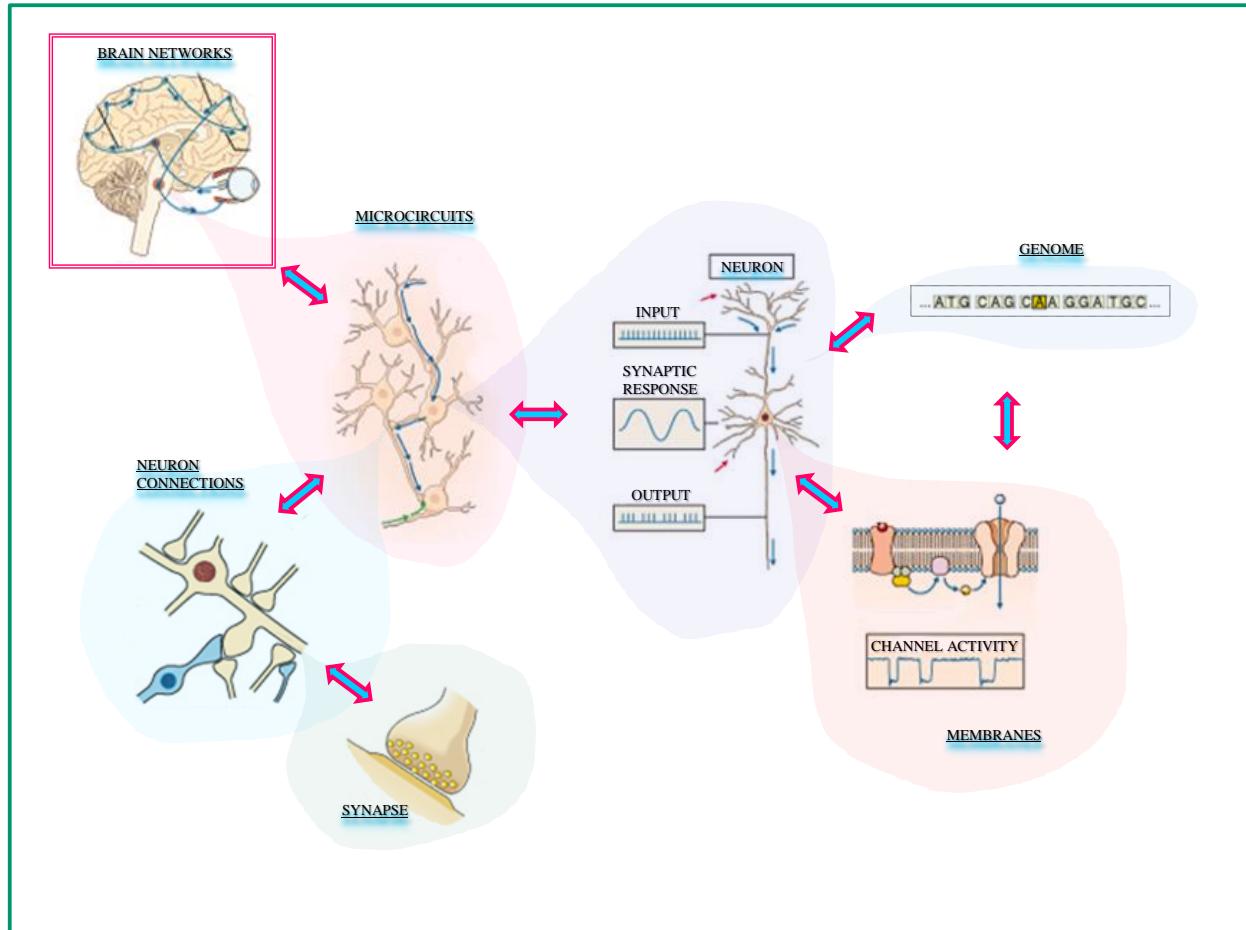
Giacomo Koch

TMS Lab, Clinica Santa Lucia, Rome

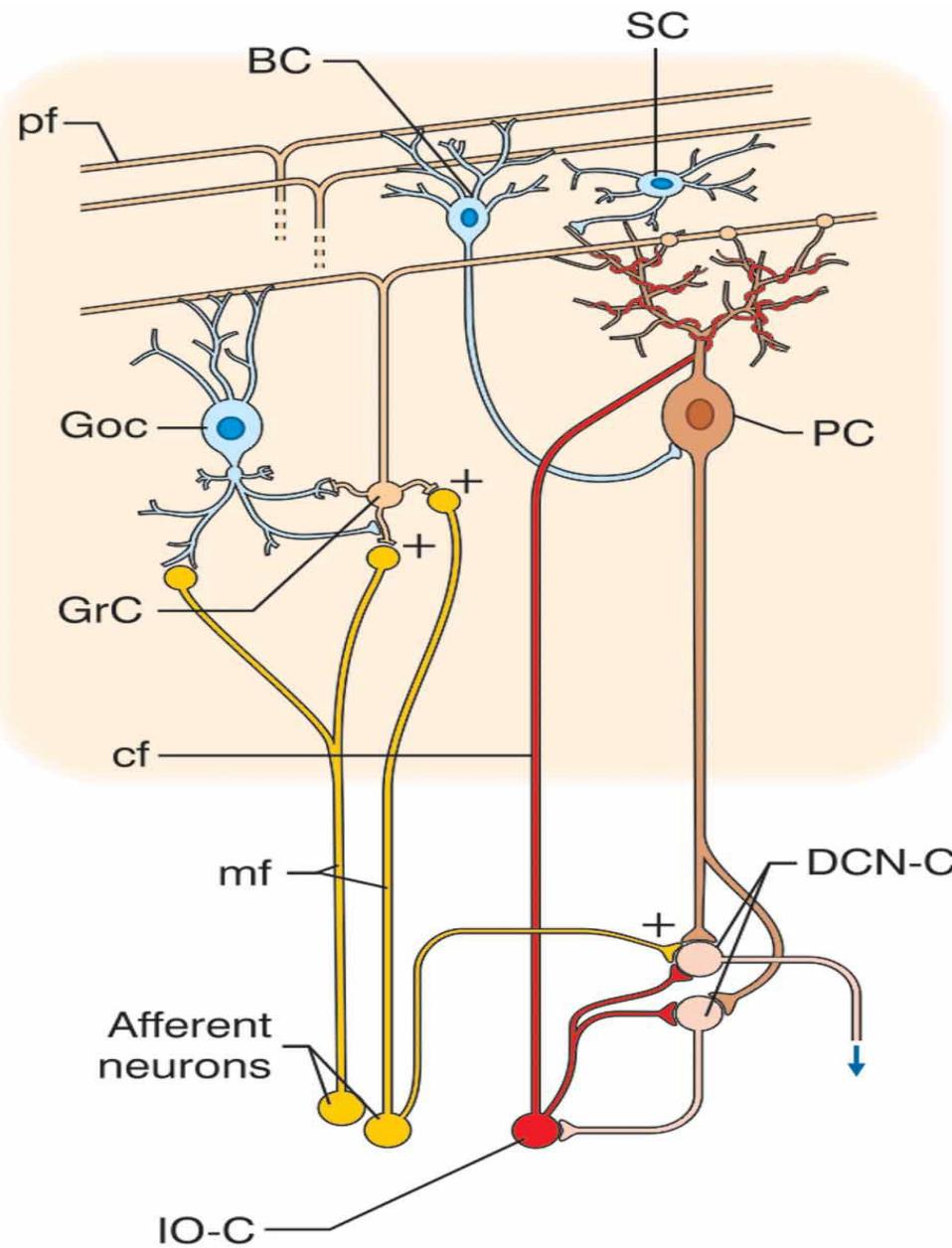


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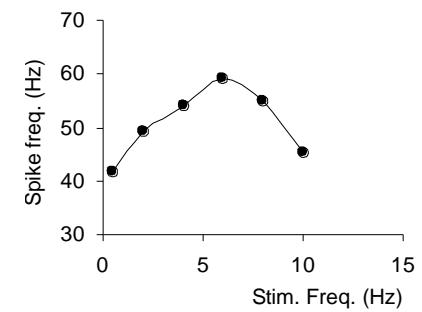
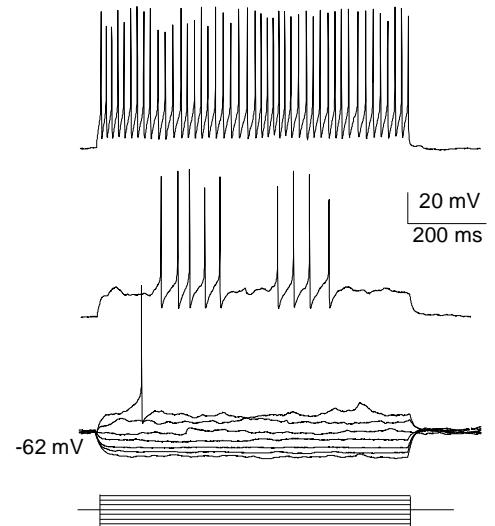
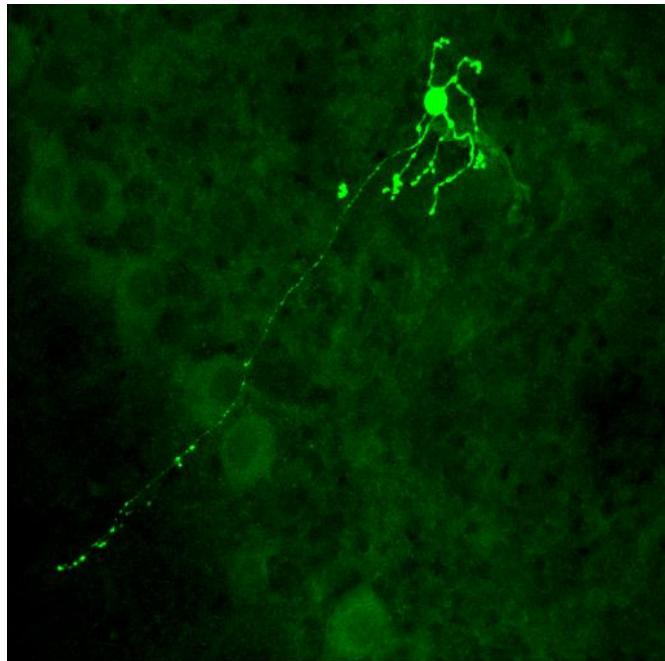
The “multi-level” organization of the brain



The cerebellar network

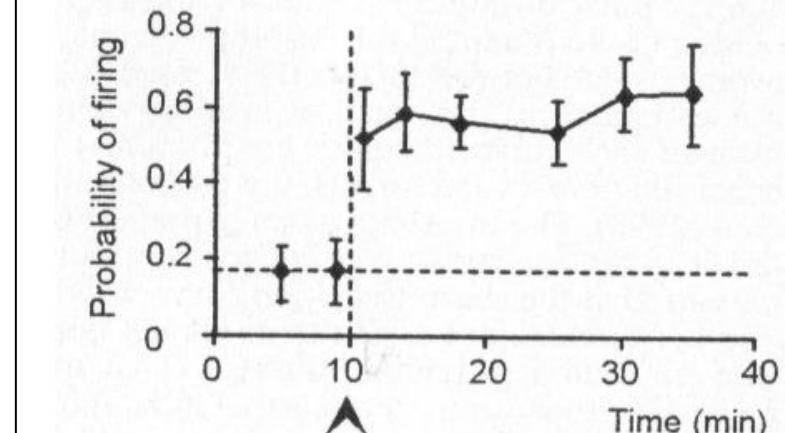
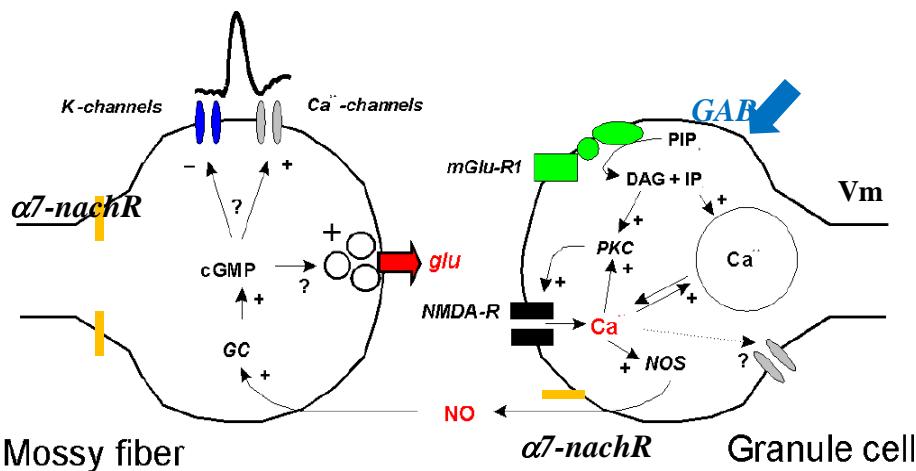


Neurons generate complex patterns of action potentials

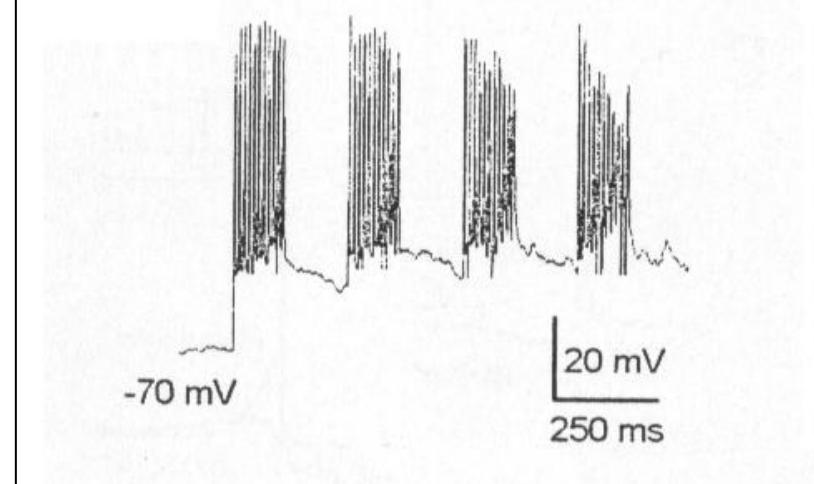


D'Angelo et al., 1995, 1998, 2001

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



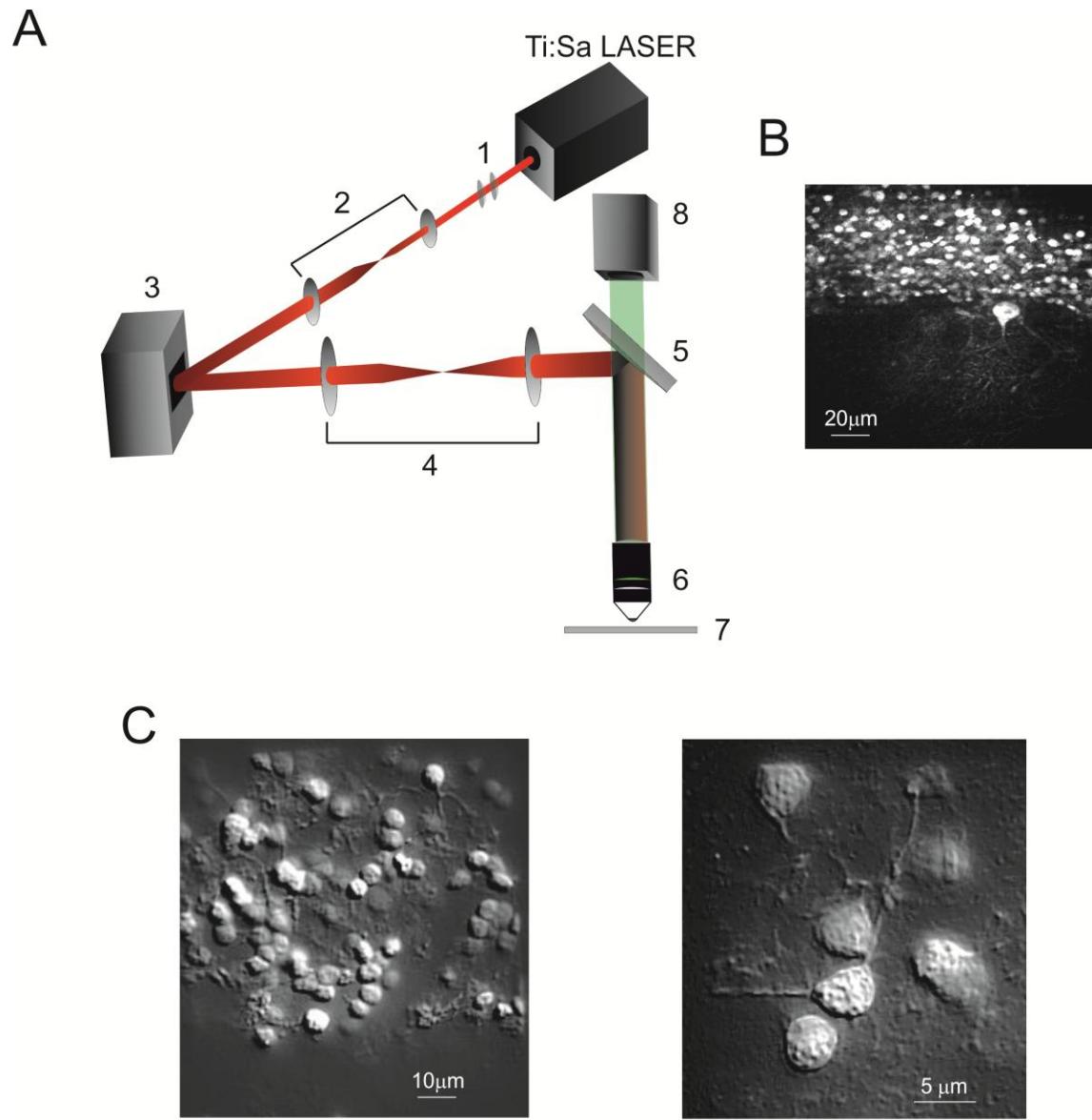
Armano et al., 2000, J.. Neurosci.

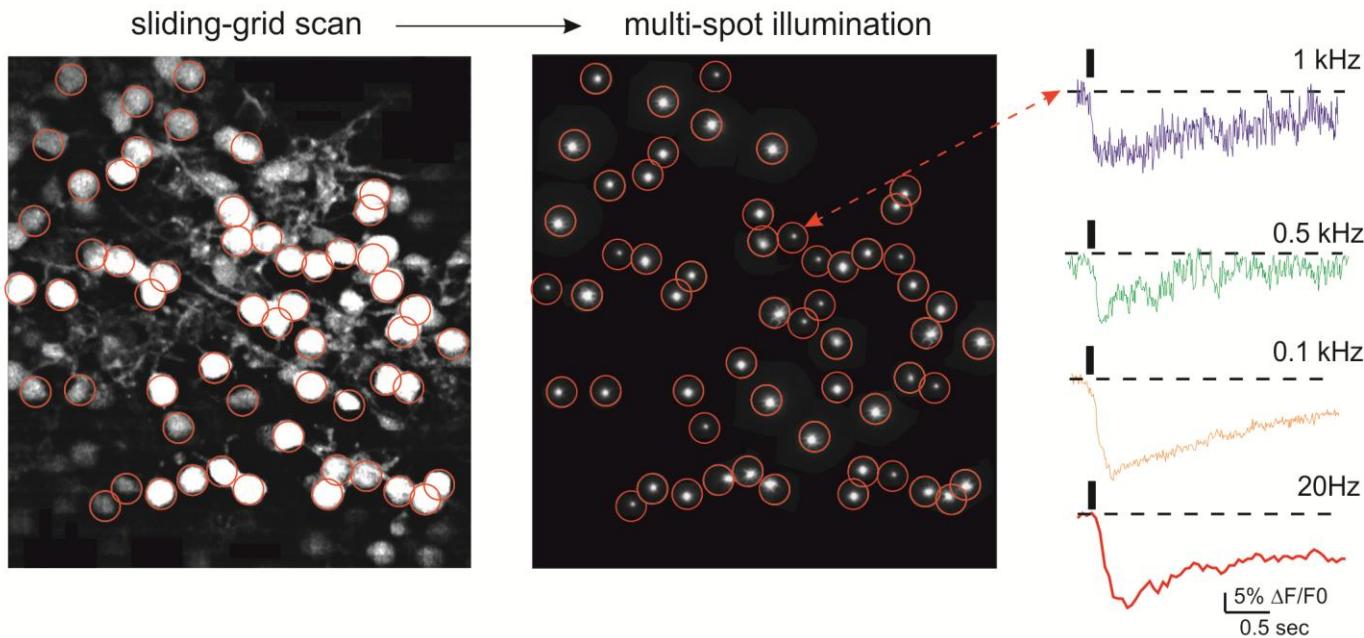
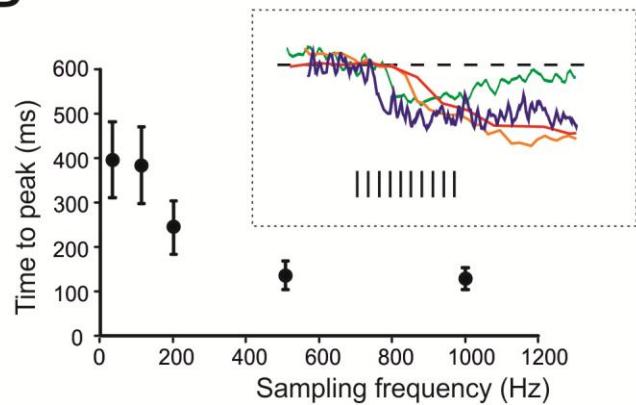
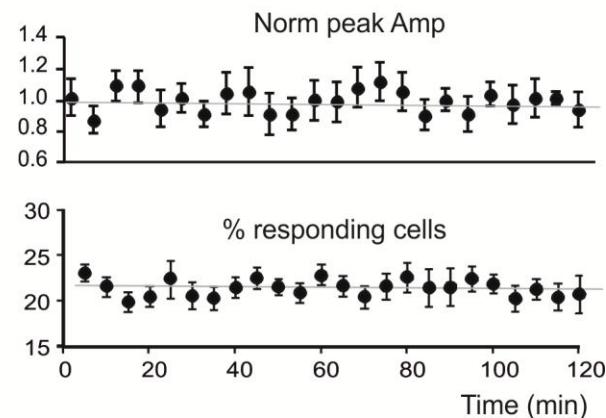


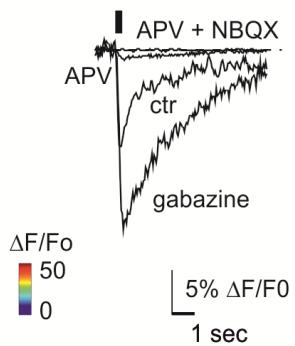
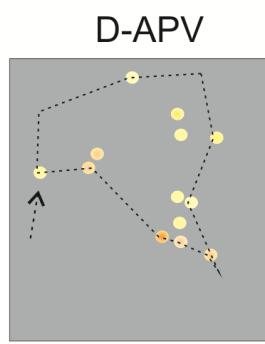
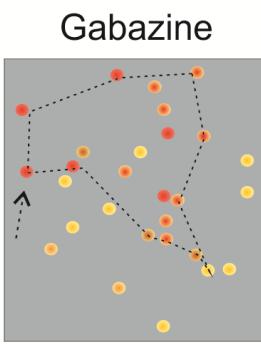
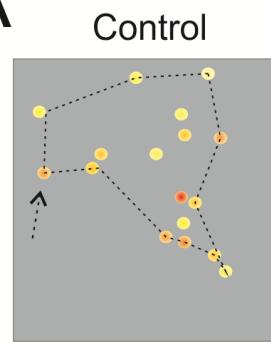
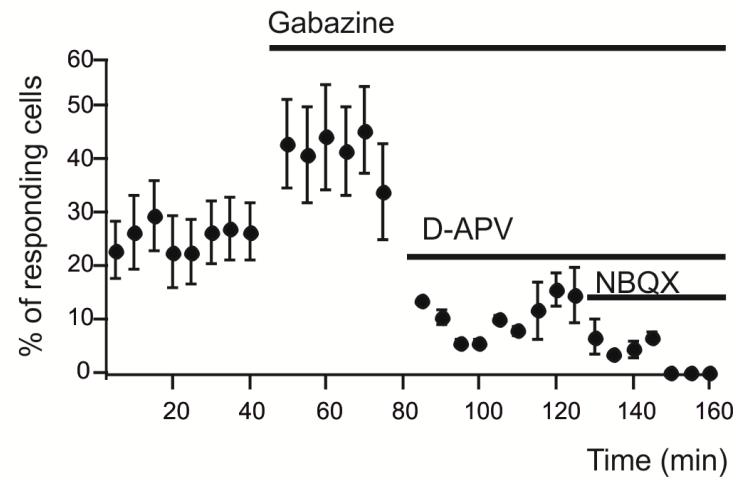
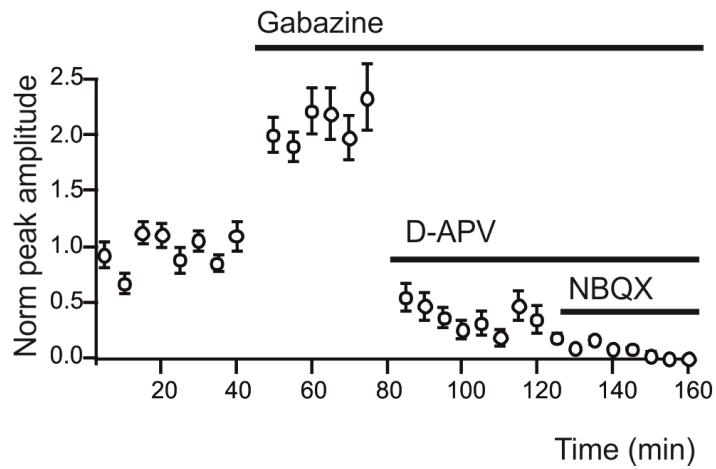
D'Angelo et al., 1999; Armano et al., 2000; Maffei et al., 2002, 2003; Sola et al., 2004; D'errico et al., 2008; Roggeri et al., 2008; D'Angelo et al., 2013

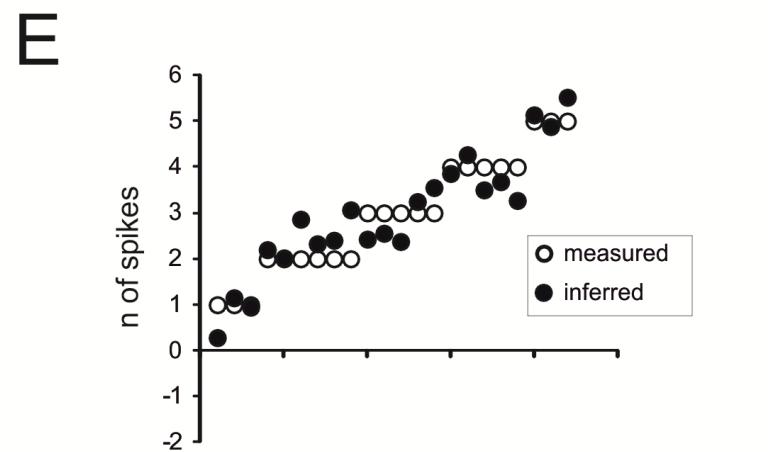
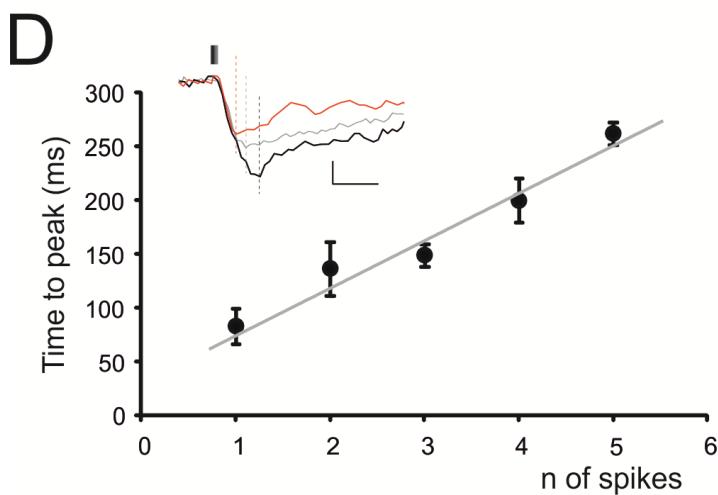
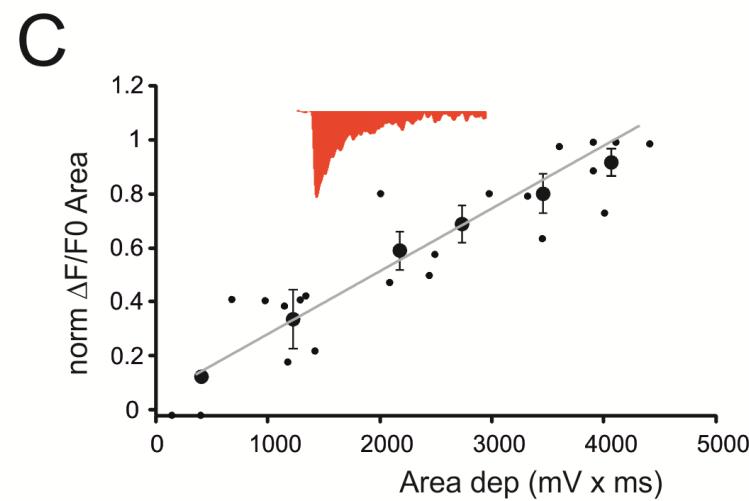
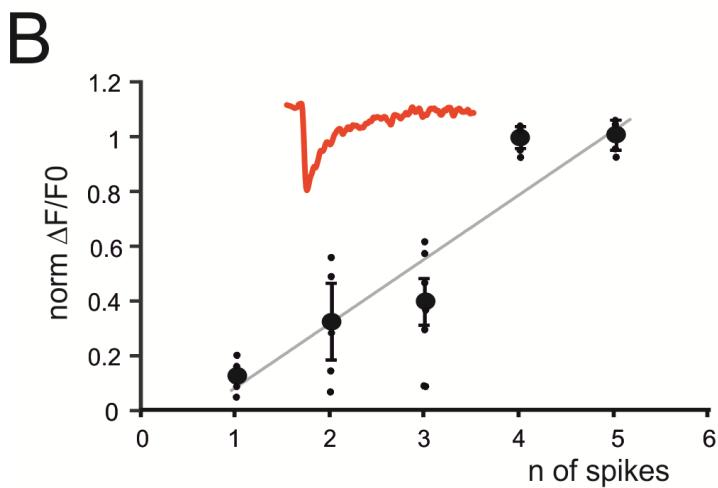
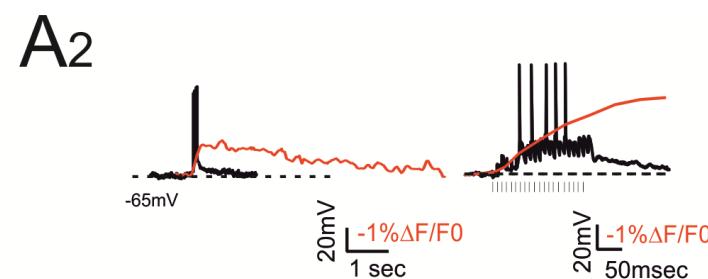
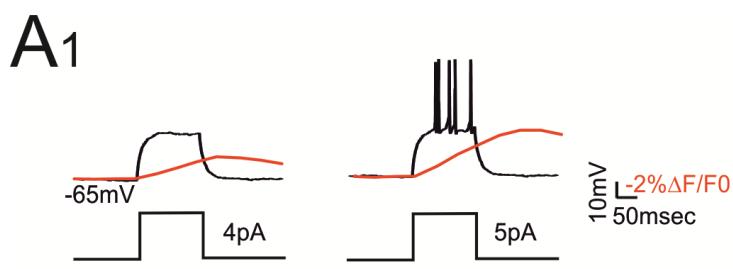
Multiple neurons discharge together

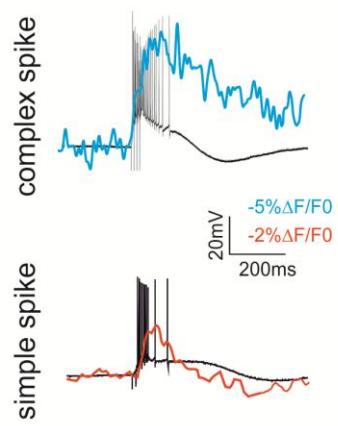
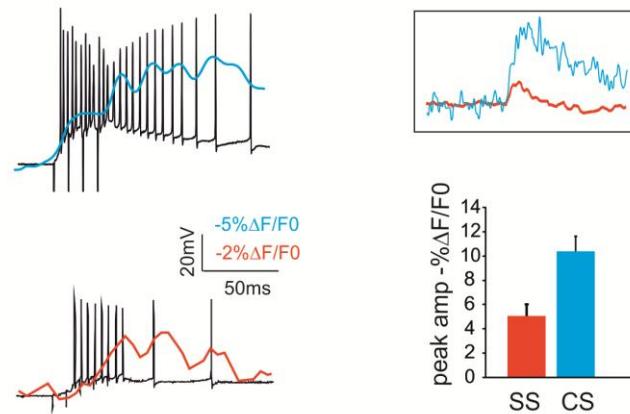
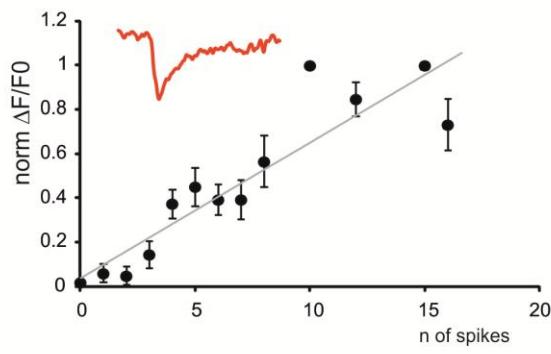
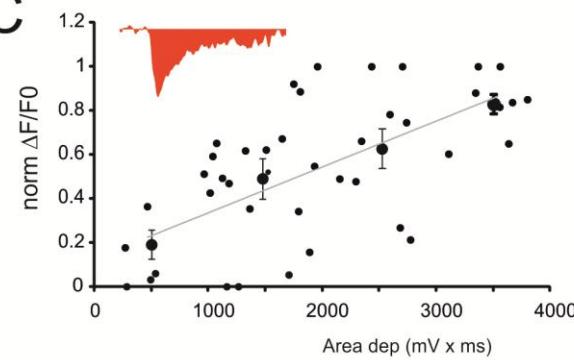
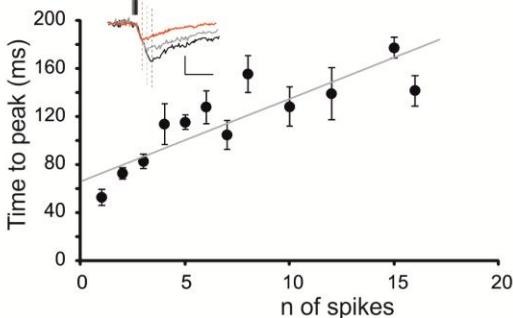
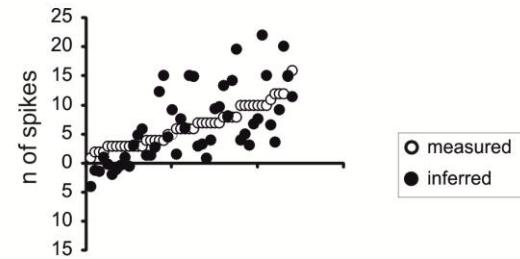
SLM-2PM

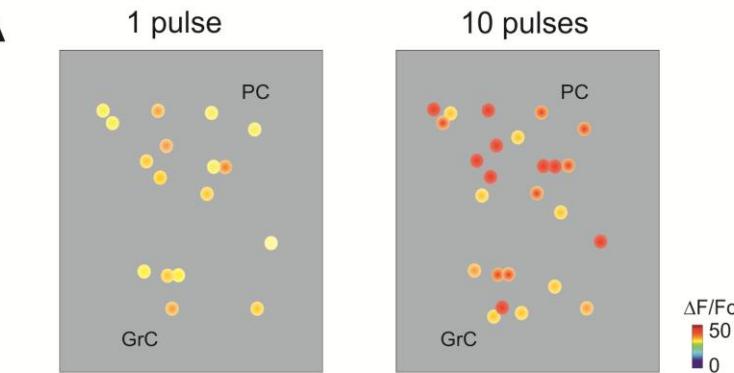
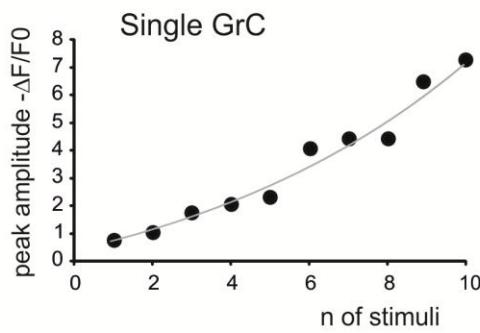
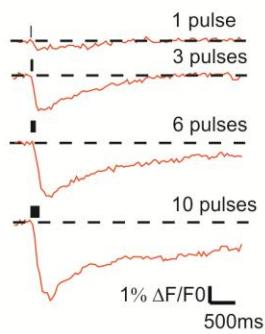
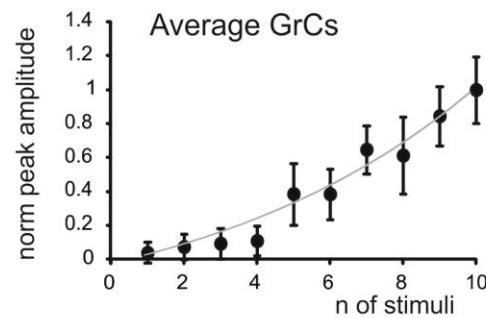
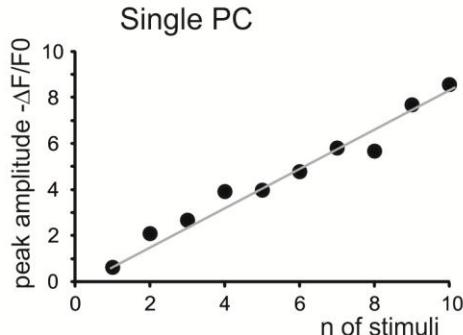
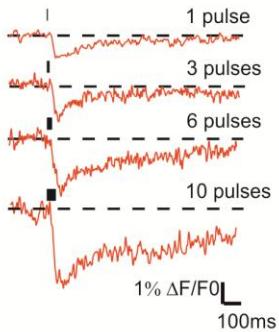
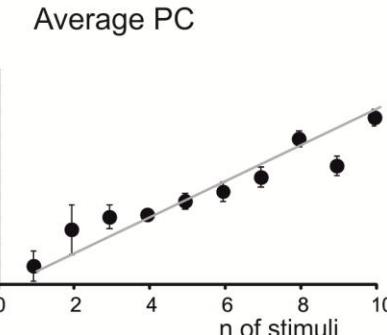


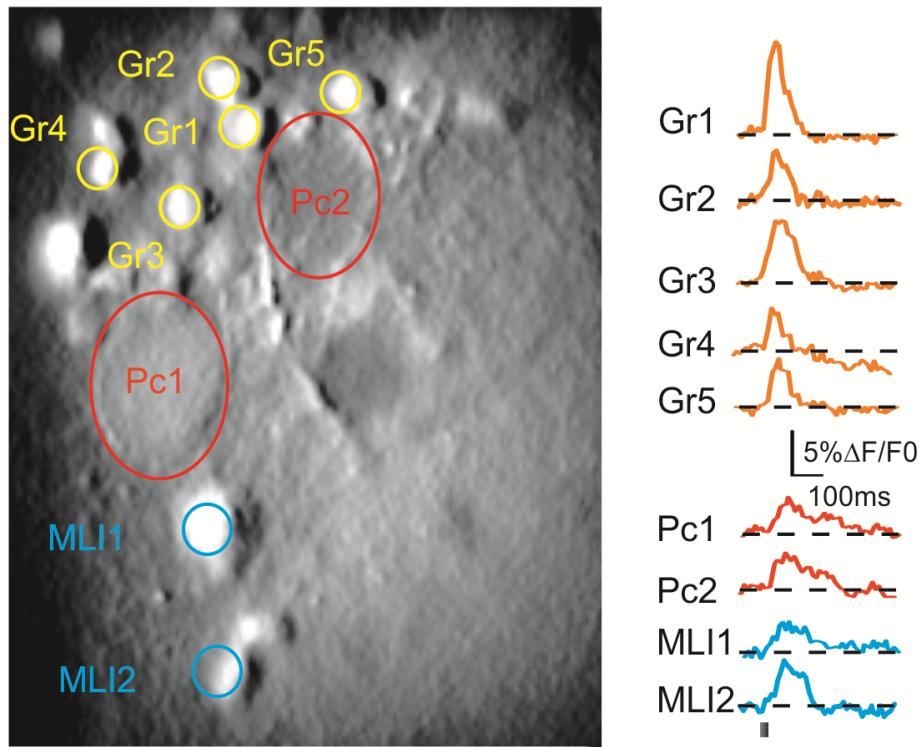
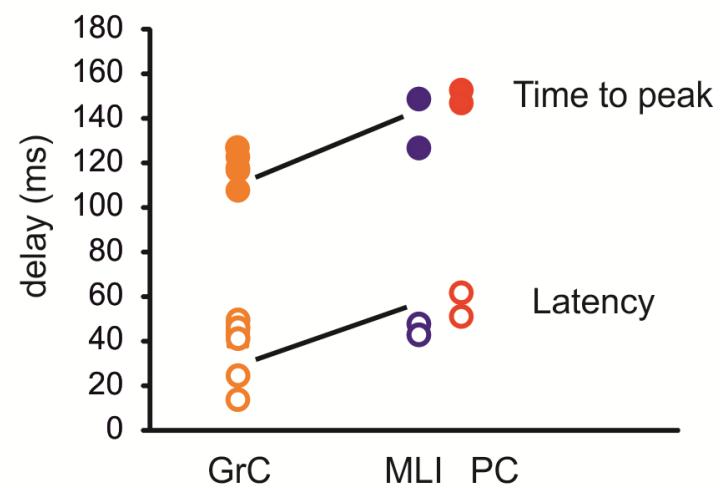
A**B****C**

A**B**



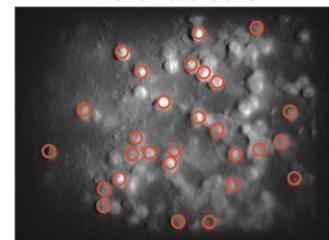
A1**A2****B****C****D****E**

A**B1****B2****C1****C2**

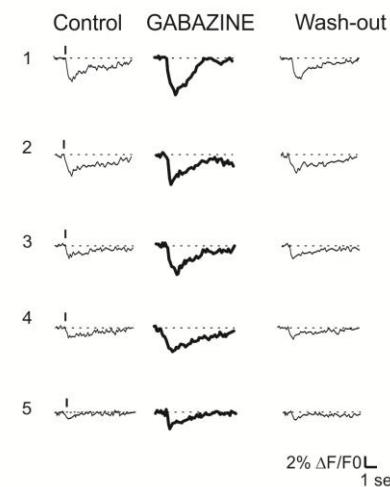
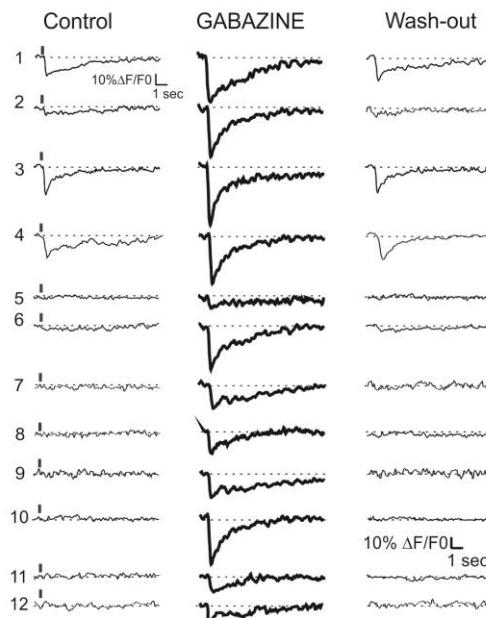
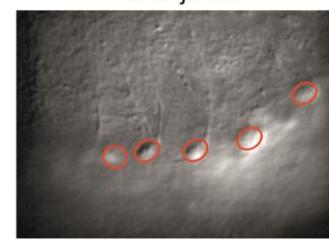
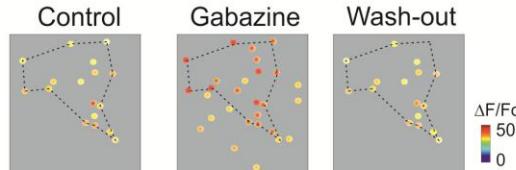
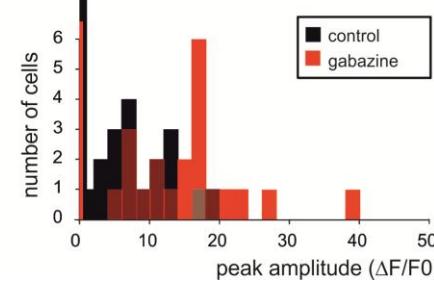
A**B**

A1

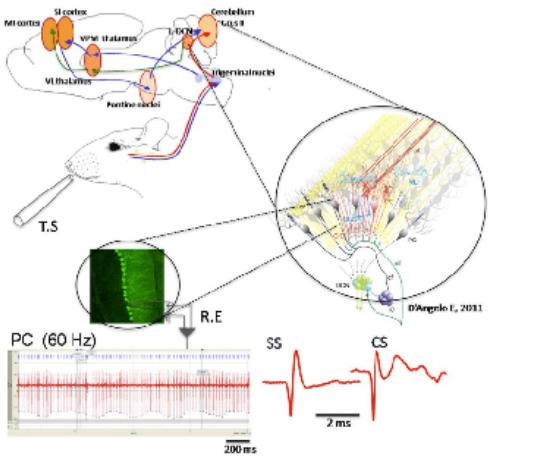
Granule cells

**A2**

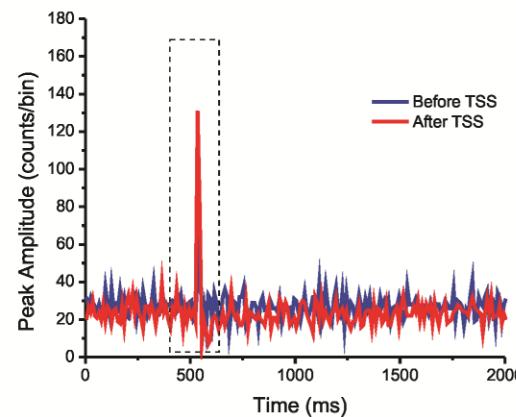
Purkinje cell

**C****B**

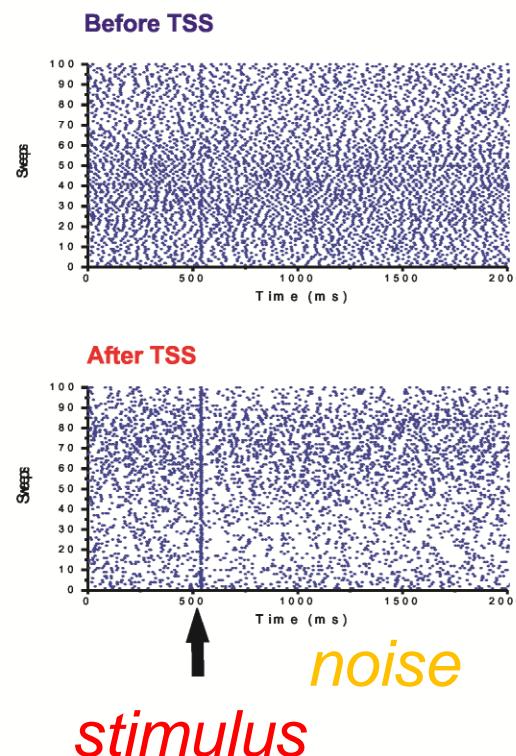
Neuron discharge is probabilistic



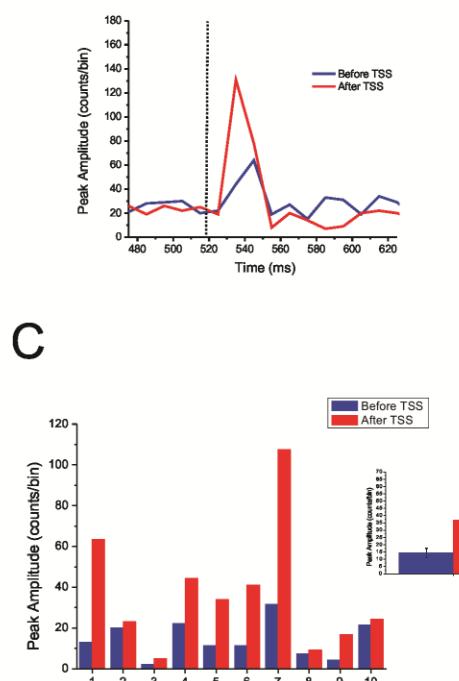
A



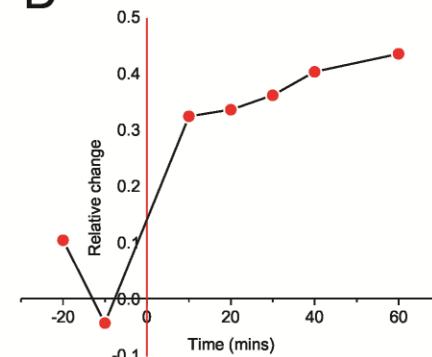
B



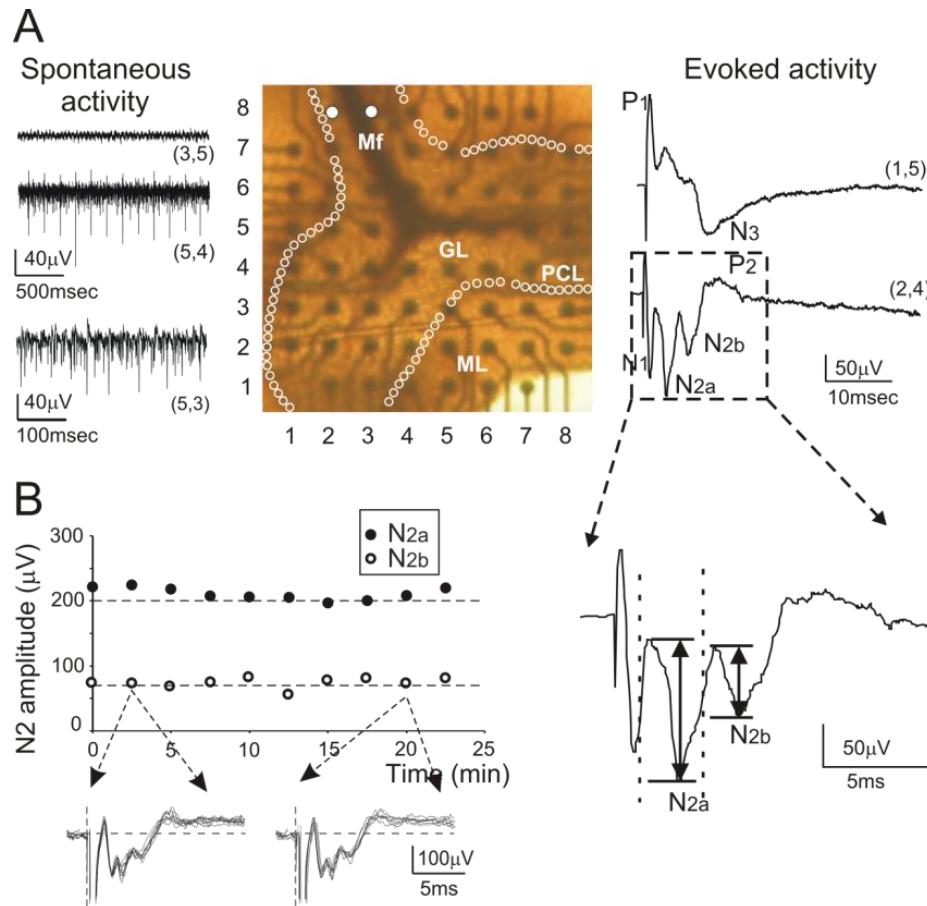
C



D



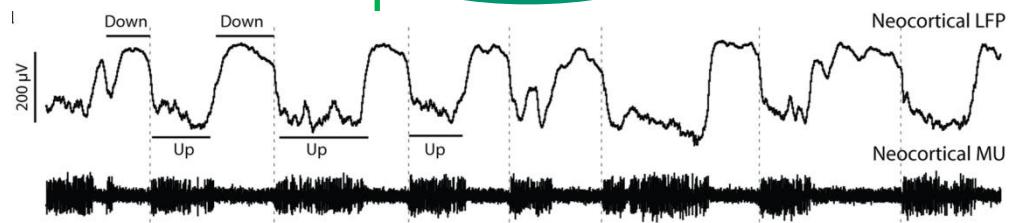
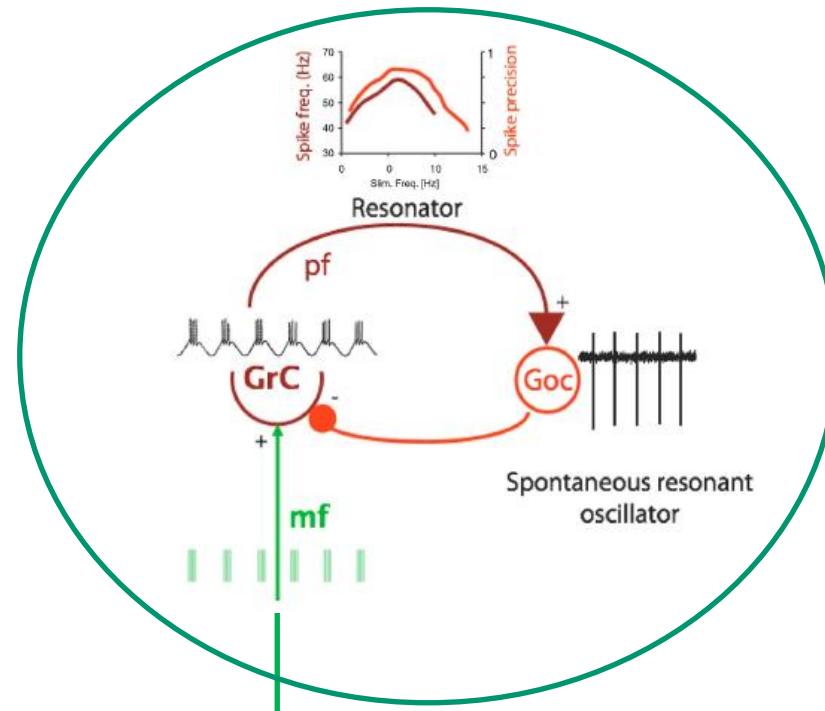
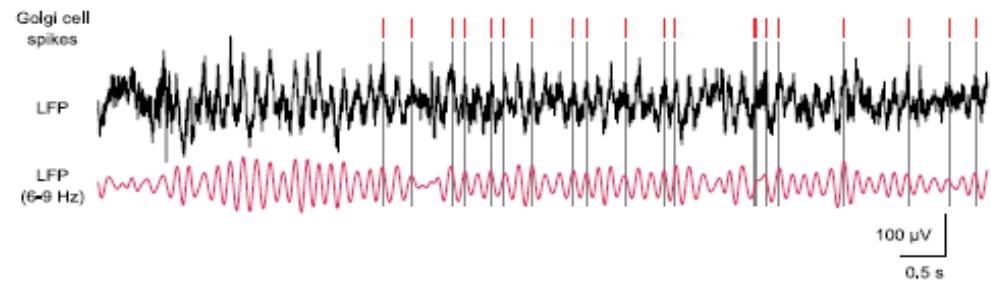
Neural circuits show complex spatio-temporal dynamics

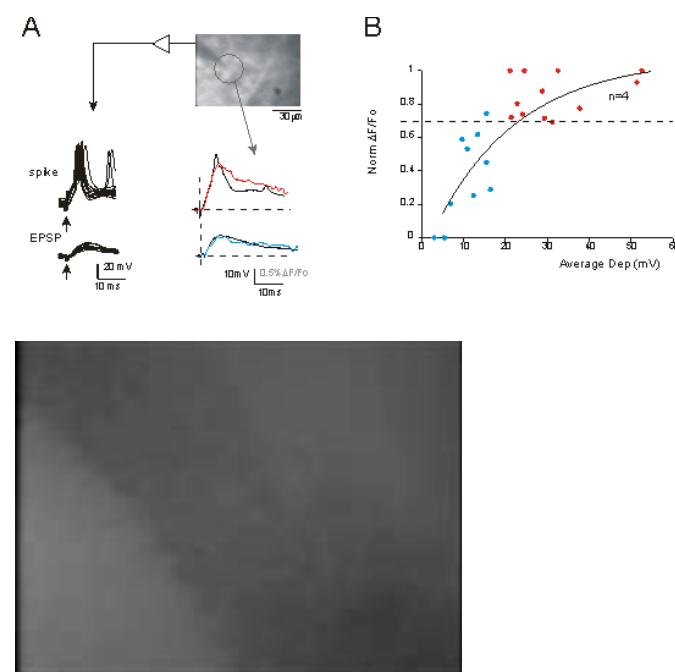


Neural circuits show resonance and oscillation

Tuned resonant receiver:
granular layer

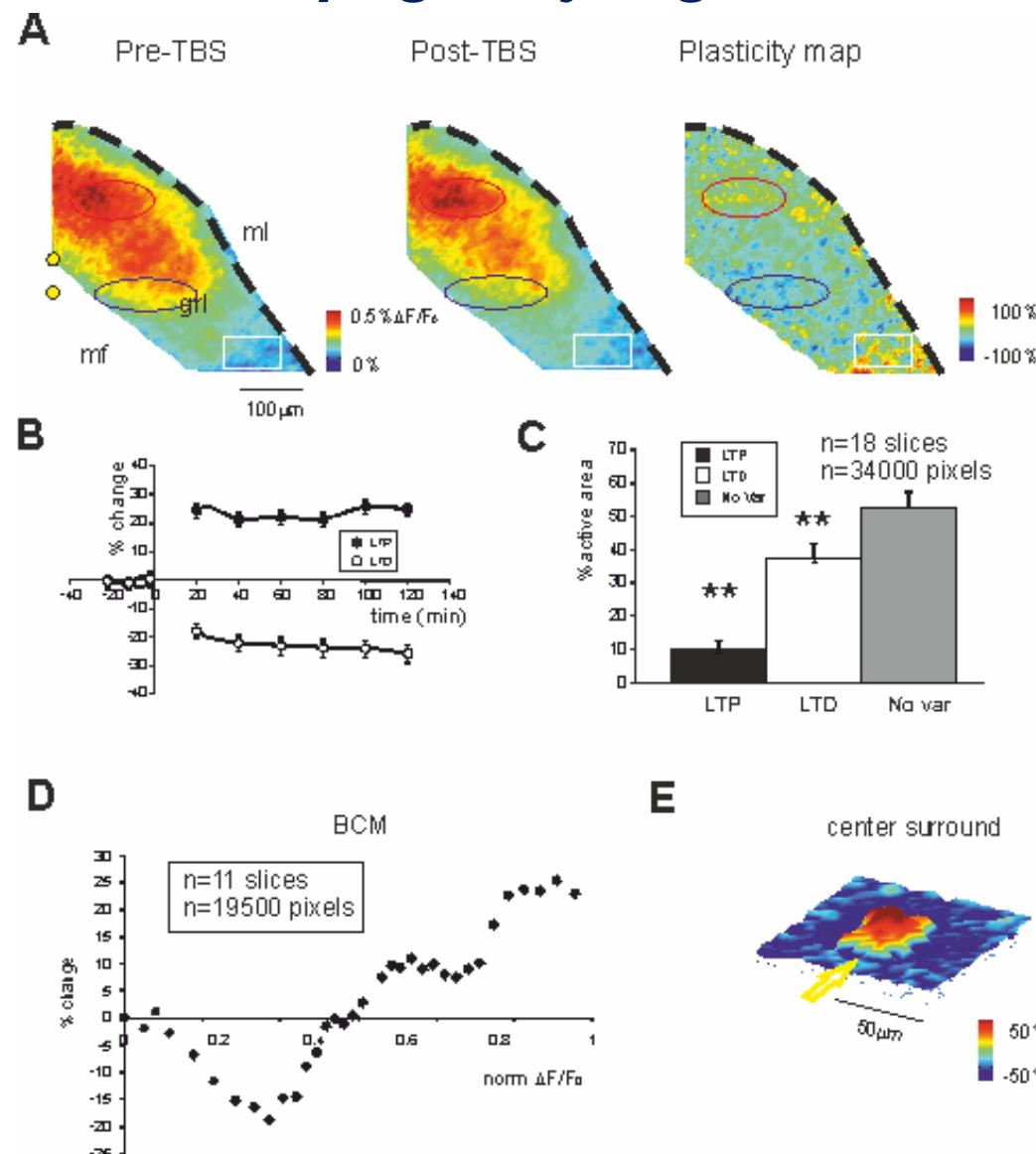
Oscillating transmitter:
Cortico-thalamic system



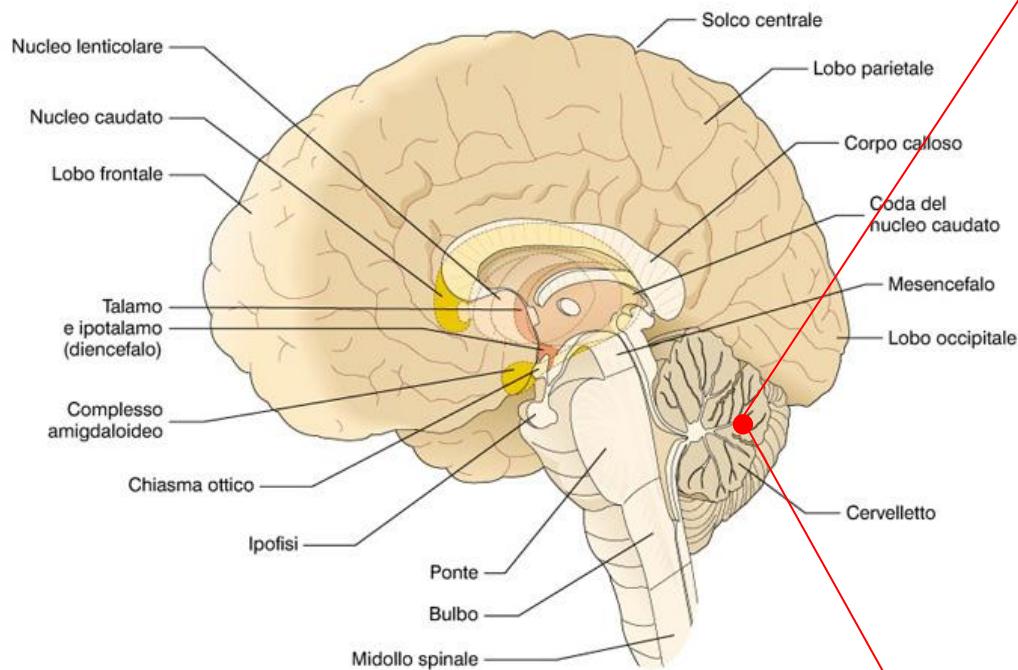


Mapelli et al., 2010 a,b

Neural circuit responses are topologically organized



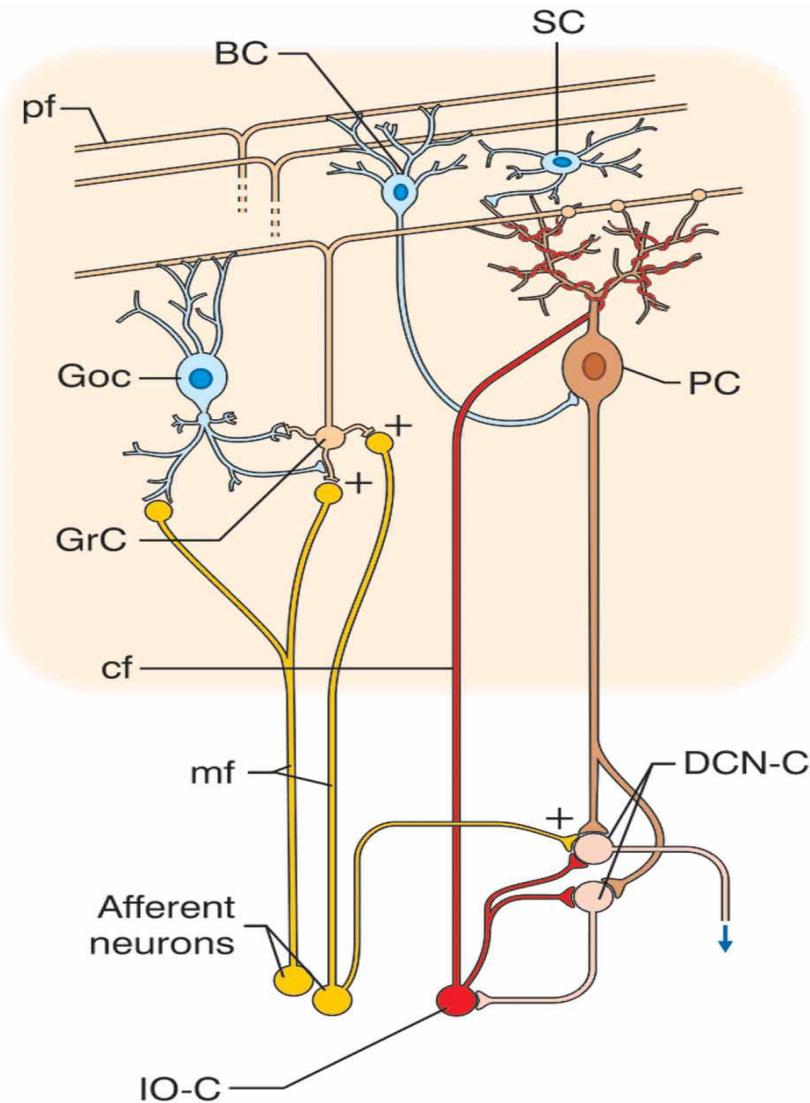
Neural circuits have complex architecture



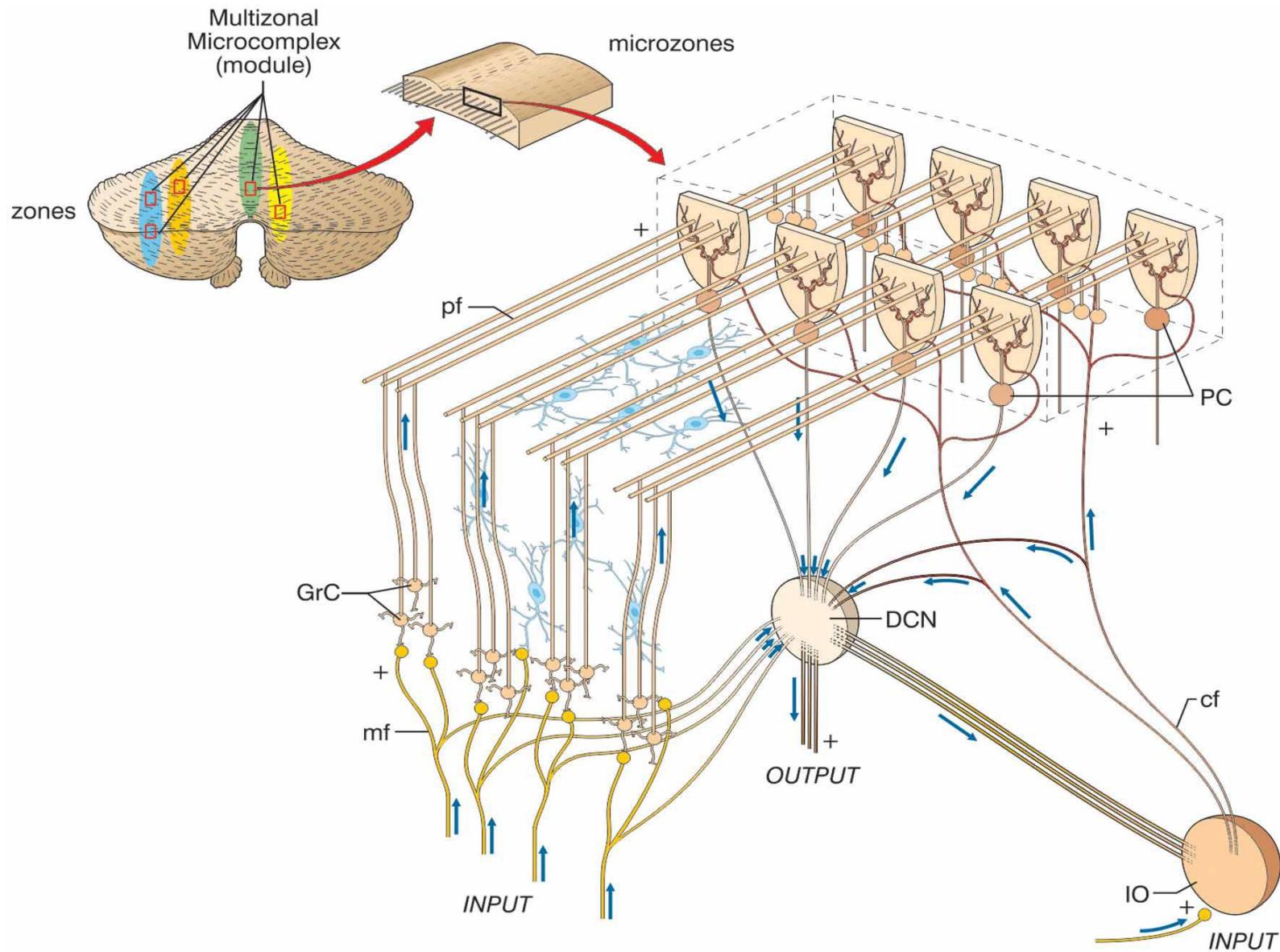
© 2006 edi.ermes milano

10^{12} neuroni

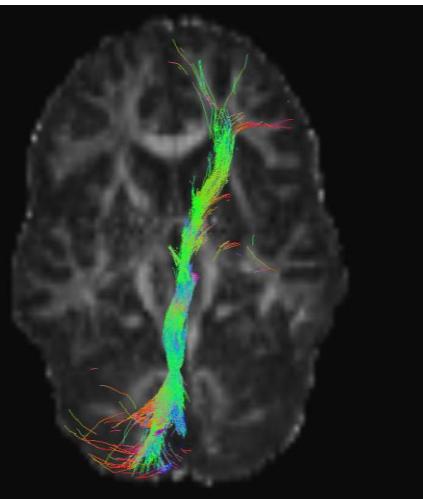
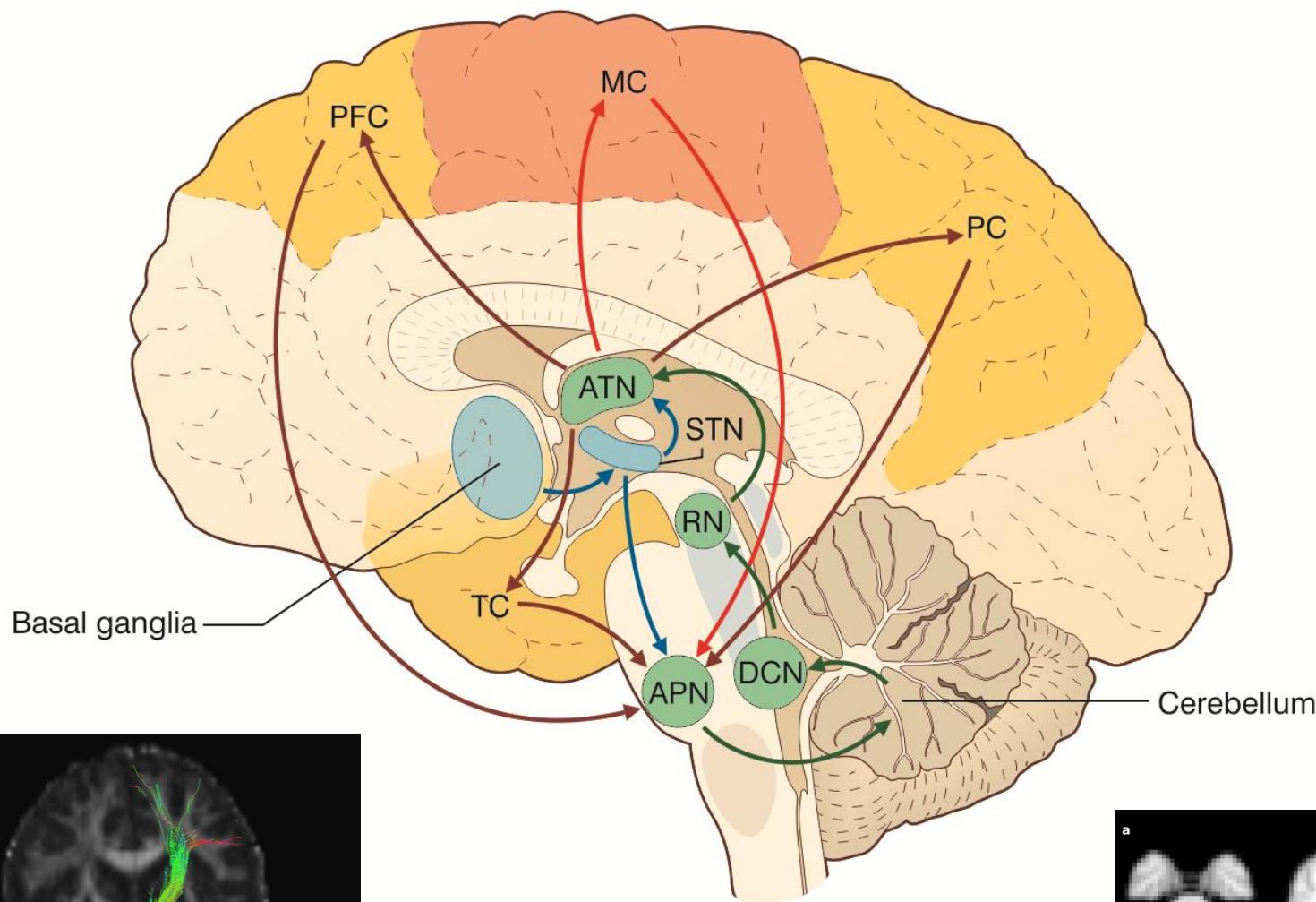
10^{15} sinapsi



Neural circuits have modular organization

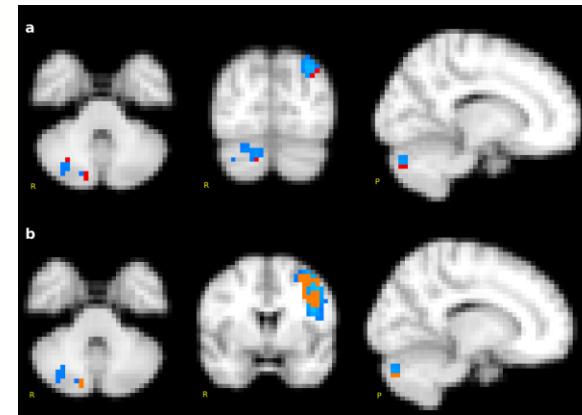


Long-range connections

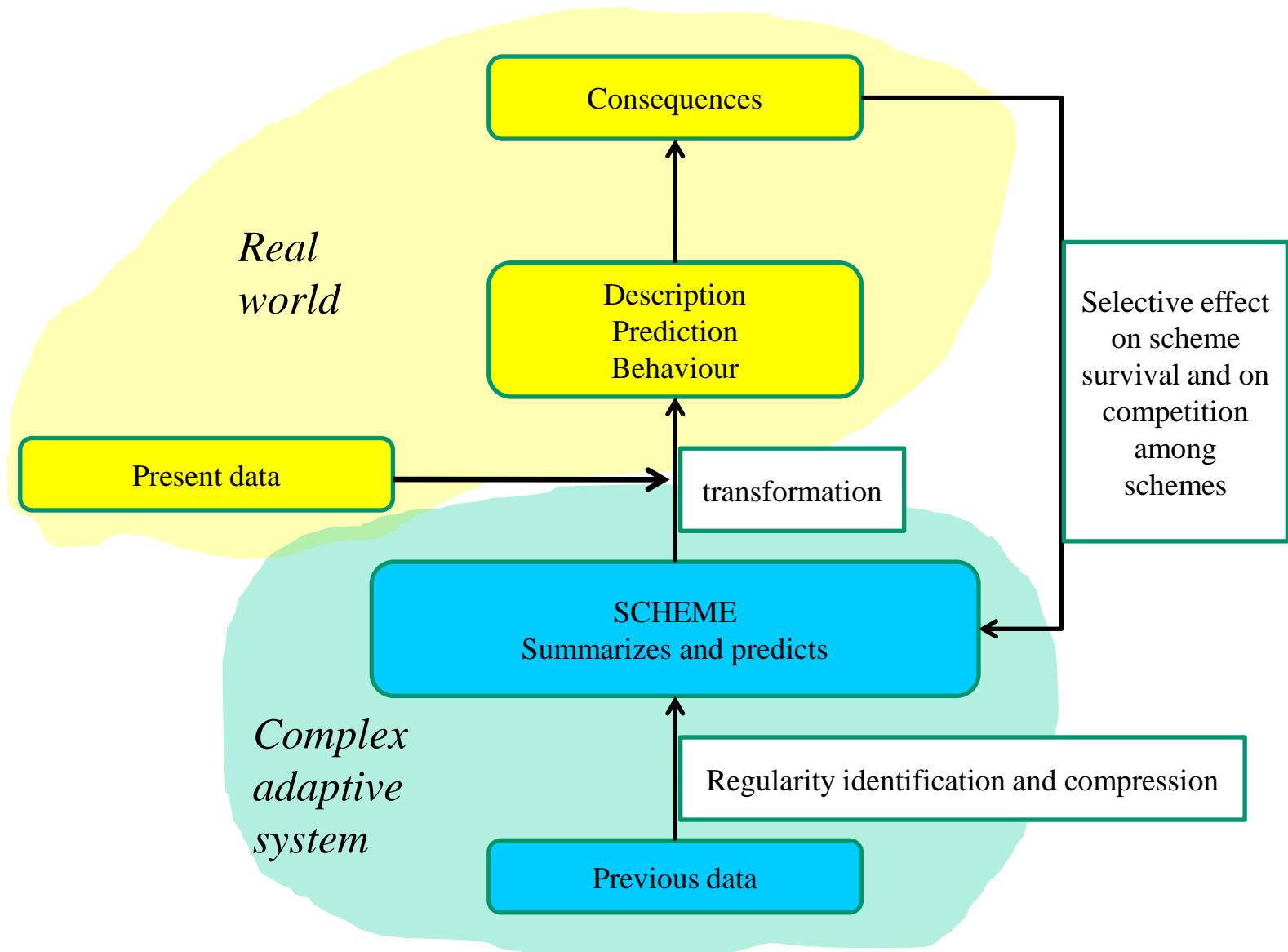


Paelsi et al., submitted

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

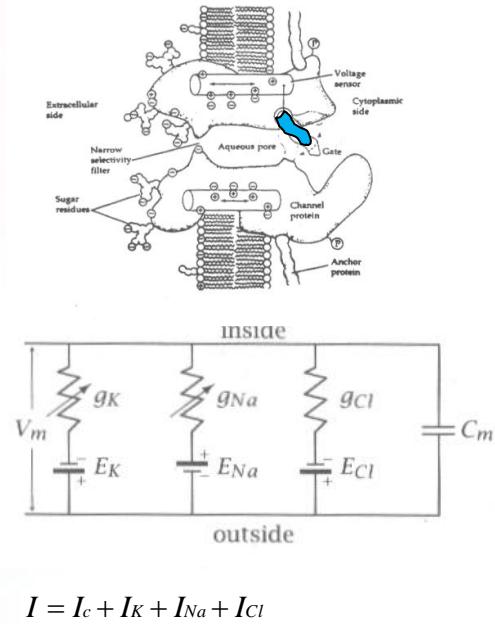
- Is organized in meta-levels
- Has extreme structural and functional complexity
- Operates as a *complex adaptive system*
- Shows emergent properties like behavior and consciousness
 - The output is often hard to quantify
 - Requires multidisciplinary analysis (Neuroscience)
- Extended implications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

Moreover, brain function does not compare well to computers

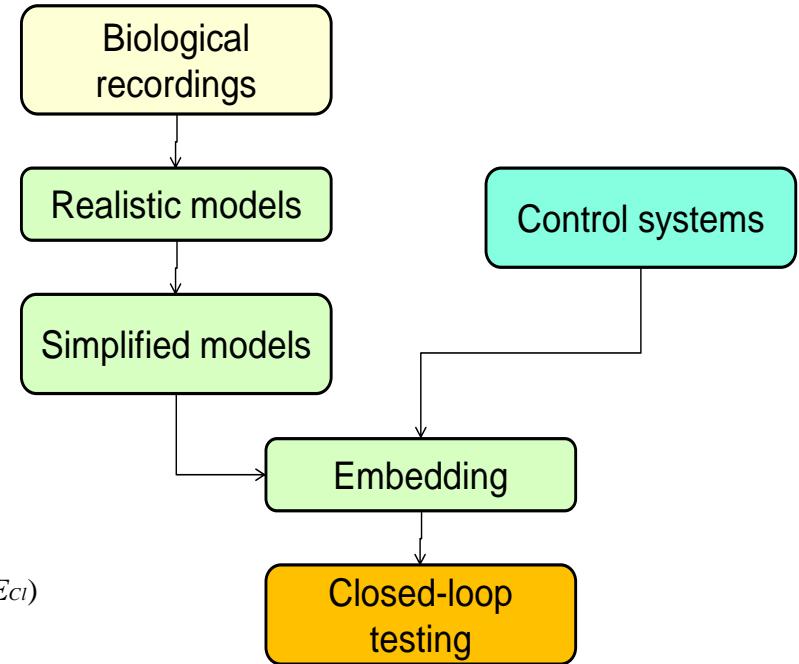
Brain vs. computer:

- Slow (≈ 100 Hz vs. $\approx 0.1\text{-}1$ 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 hierachic organization
- Memory and computation exploit the same structural elements
- Elaborates about 10^{18} synapse operations/sec

The “bottom-up” modeling strategy



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



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

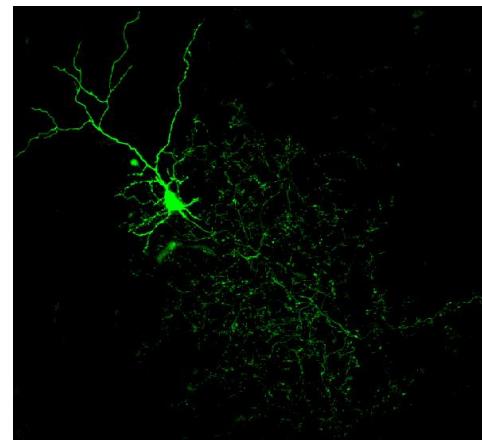
$$g_i = g_i^{\max} y_{i-att}^n y_{i-inatt}^m$$

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

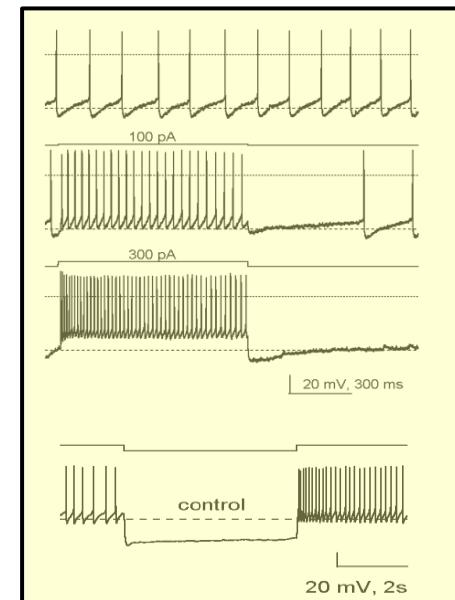
D'Angelo et al., , 2013

Electrophysiology and imaging →

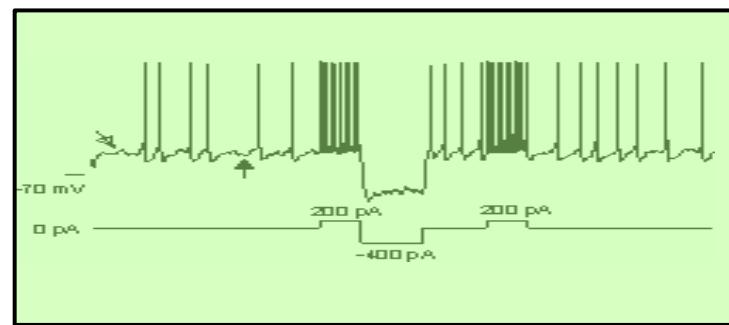
A



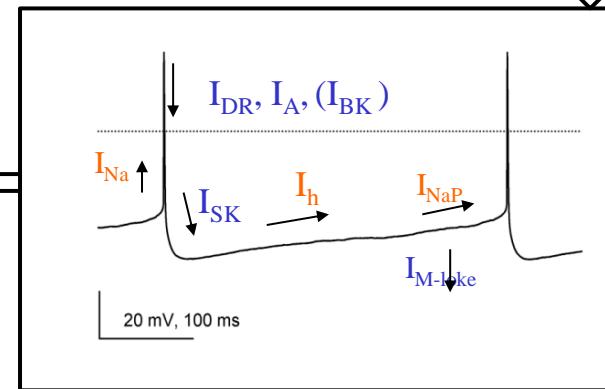
B



D



C



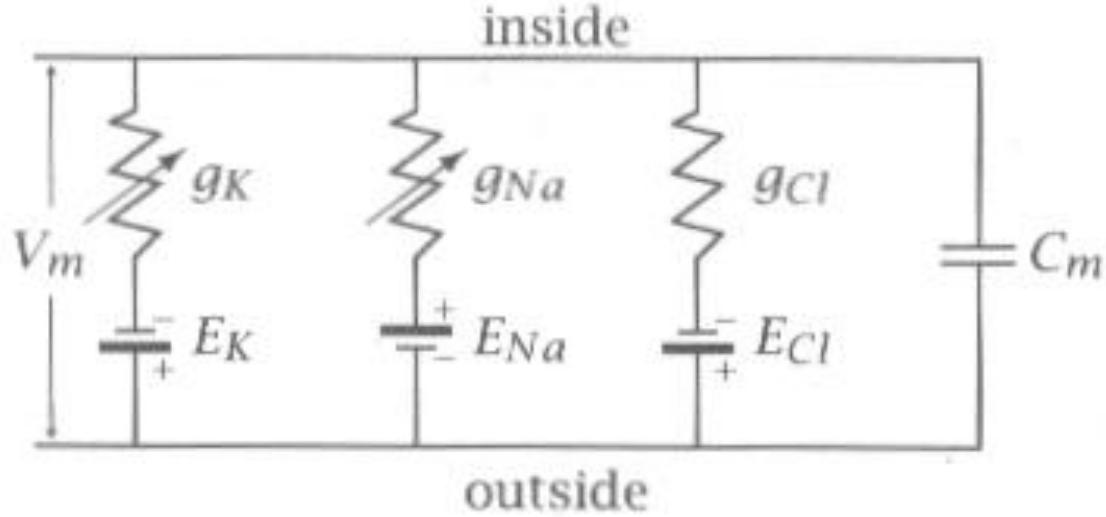
validation in vivo

←

reconstruction in vitro

→ PYTHON-NEURON modeling →

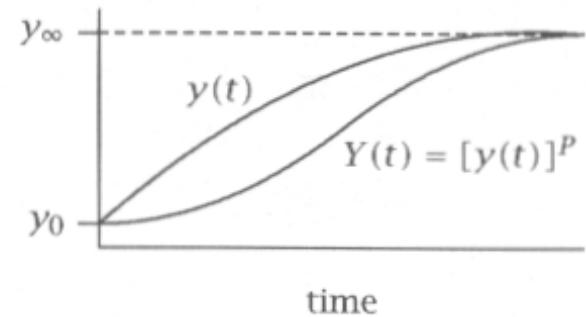
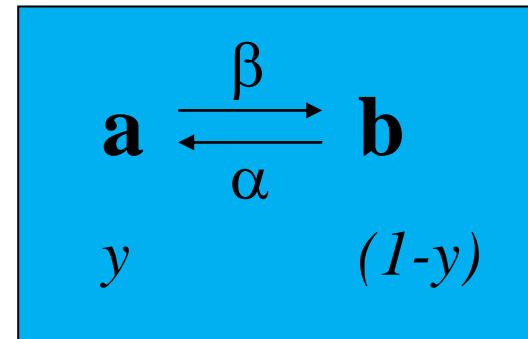
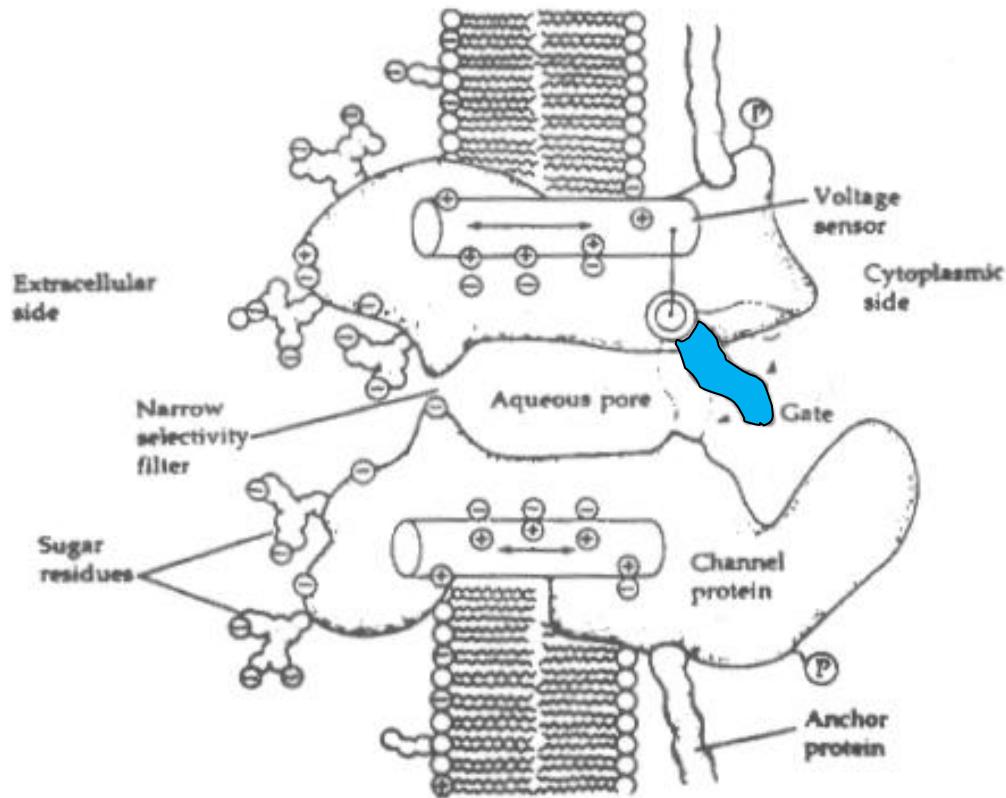
The membrane equation



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

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

The “gating” of ionic channels



tempo-dipendenza

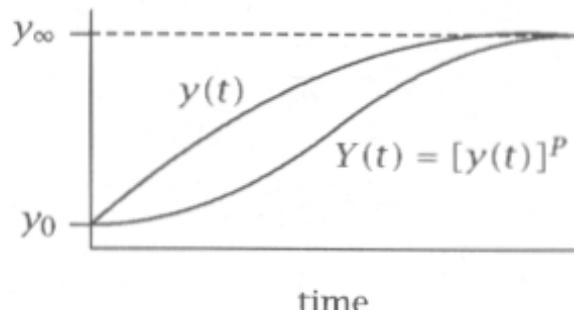
cinetica di primo ordine

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

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

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

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



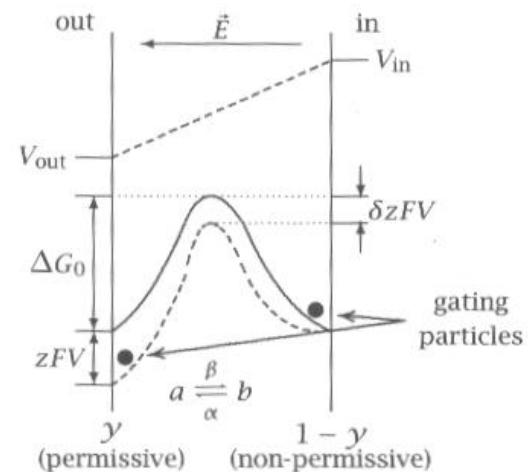
voltaggio-dipendenza

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

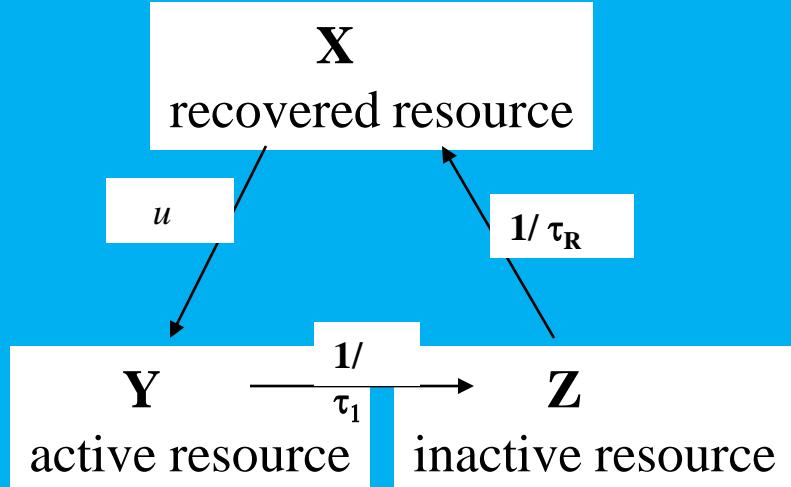
$$\beta(V) = \beta_0 e^{-(1-\delta)V z F / RT}$$

$$\alpha_0 = A e^{-\Delta G_0 / RT}$$

$$\beta_0 = B e^{-\Delta G_0 / RT}$$



Dinamiche presinaptiche di rilascio del neurotrasmettore



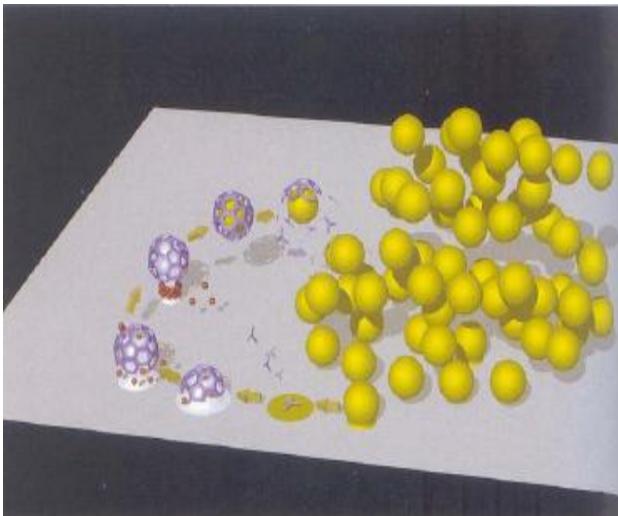
$$\frac{dx}{dt} = \frac{z}{\tau_{REC}} - u \cdot x \cdot \delta(t - t_{SPIKE})$$

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

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

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

* 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

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

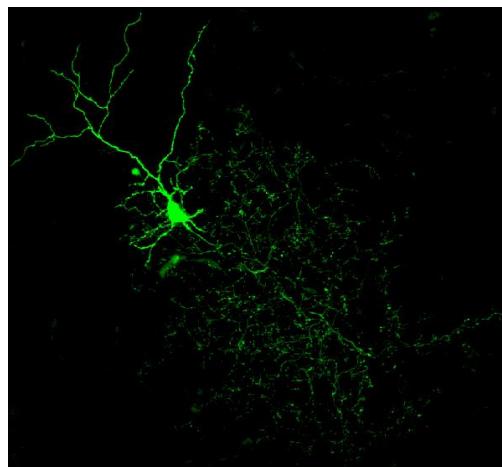
$$g_i = g_i^{\max} y_{i-att}^n y_{i-inatt}^m$$

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

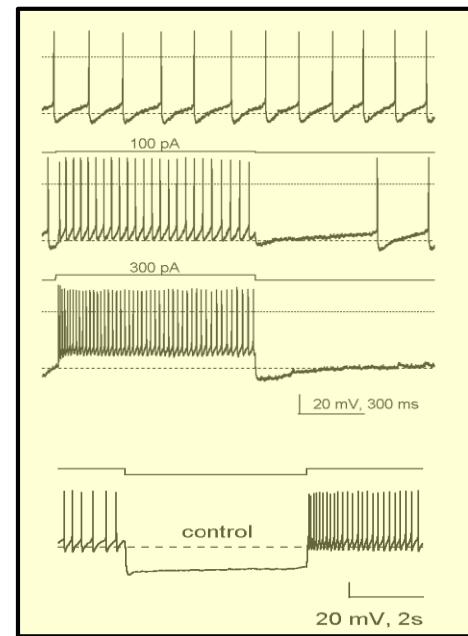
Soluzione con metodi di integrazione numerica

Single cell modeling

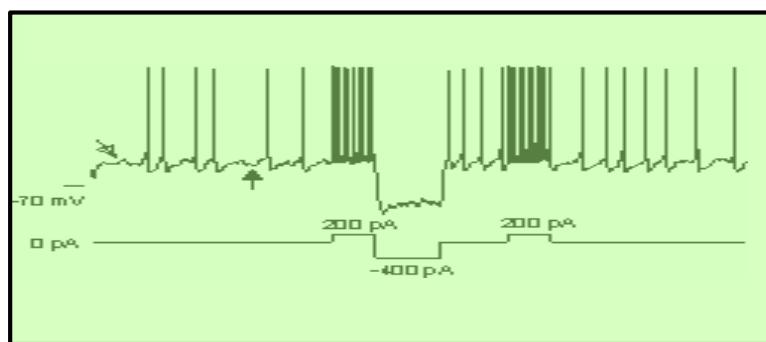
A



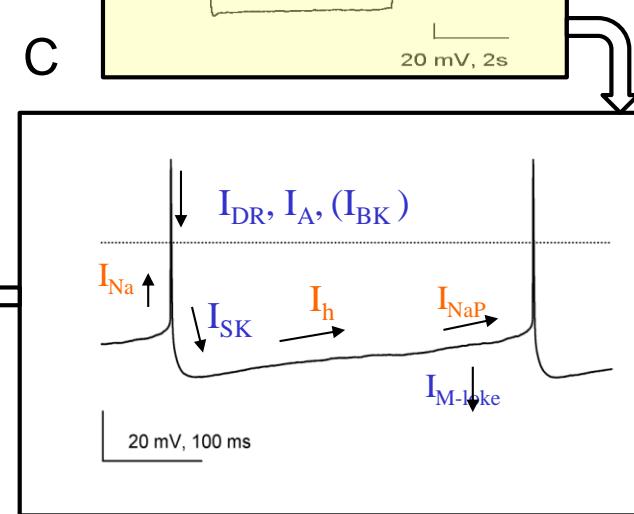
B



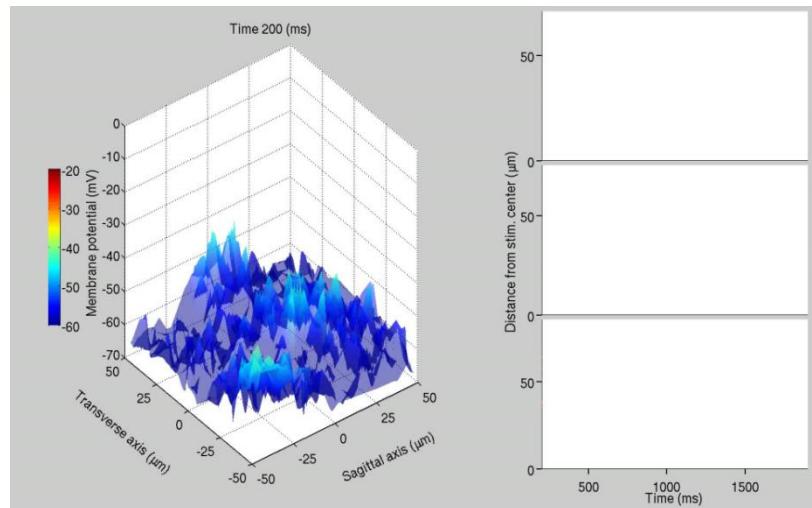
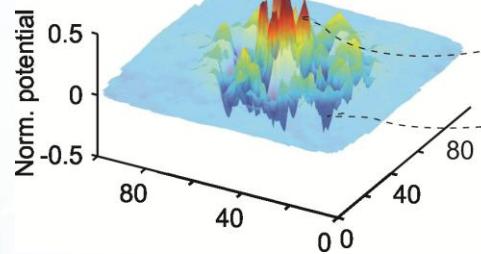
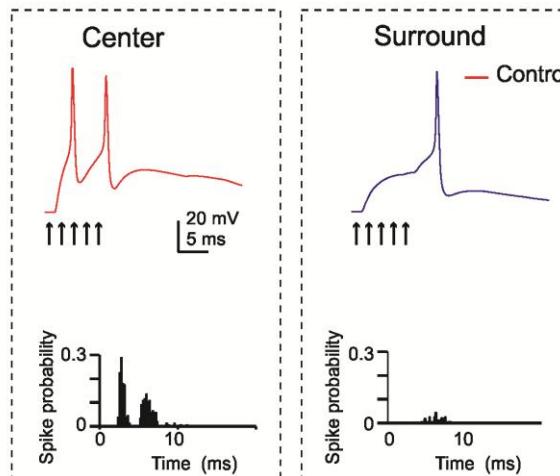
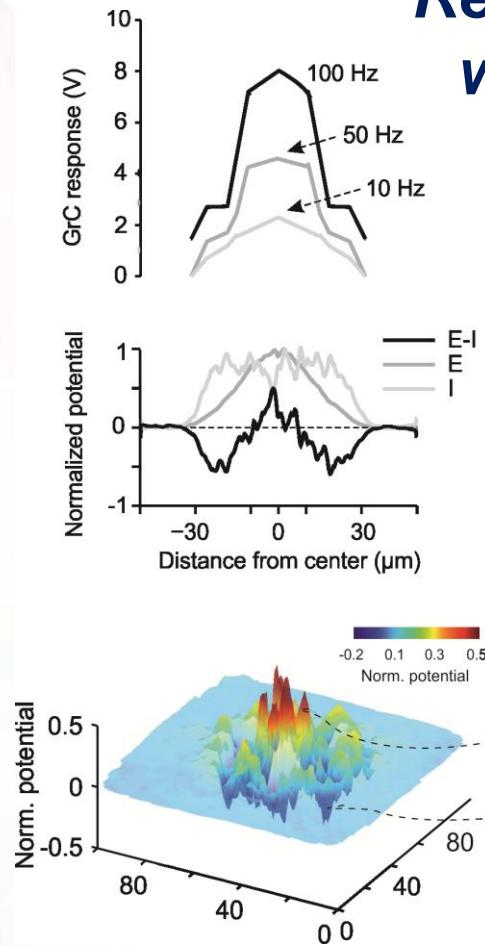
D



C



Reproduction of 4D activity patterns with detailed microcircuit models



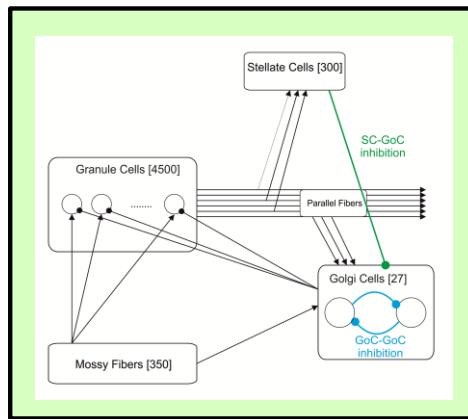
Solinas and D'Angelo 2010

(3)

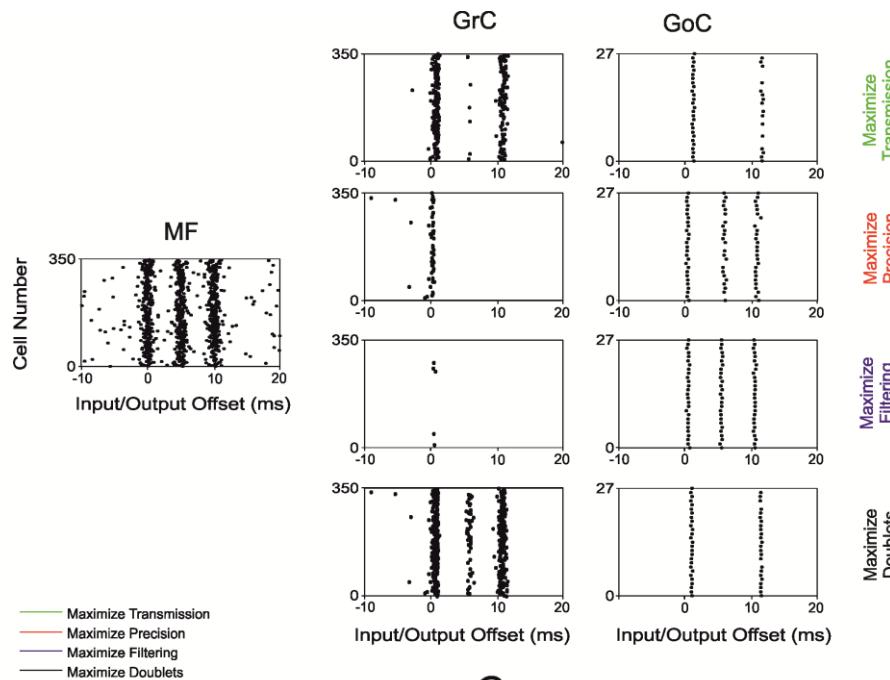
Network models in closed-loop simulations

Unraveling the relationship between single neuron properties and ensemble brain activity

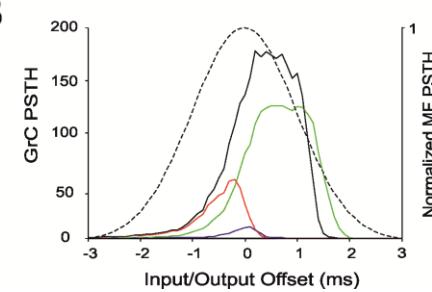
Simplified real-time spiking model of the granular layer network



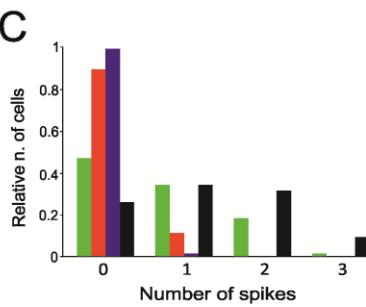
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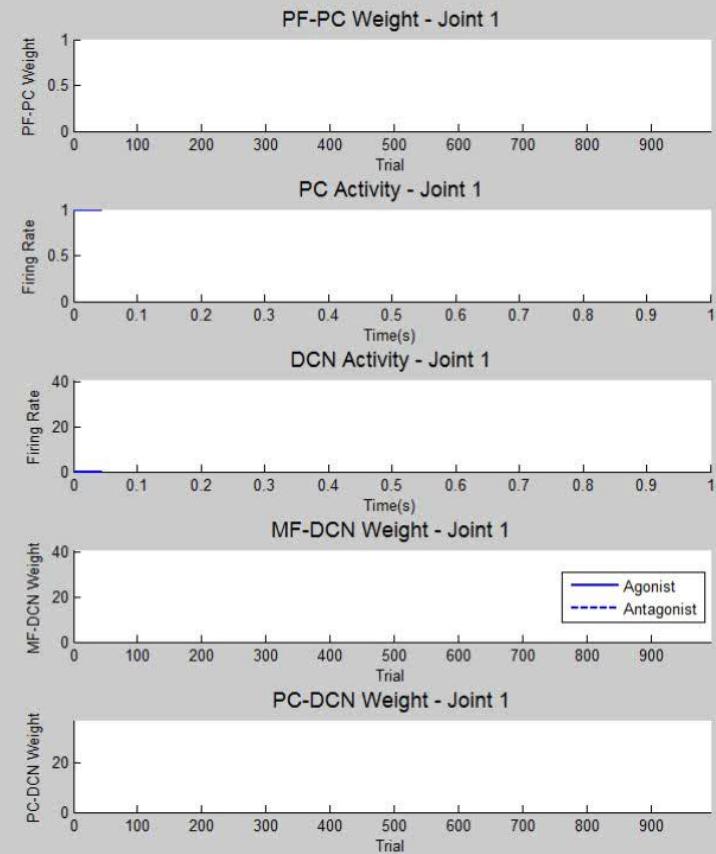
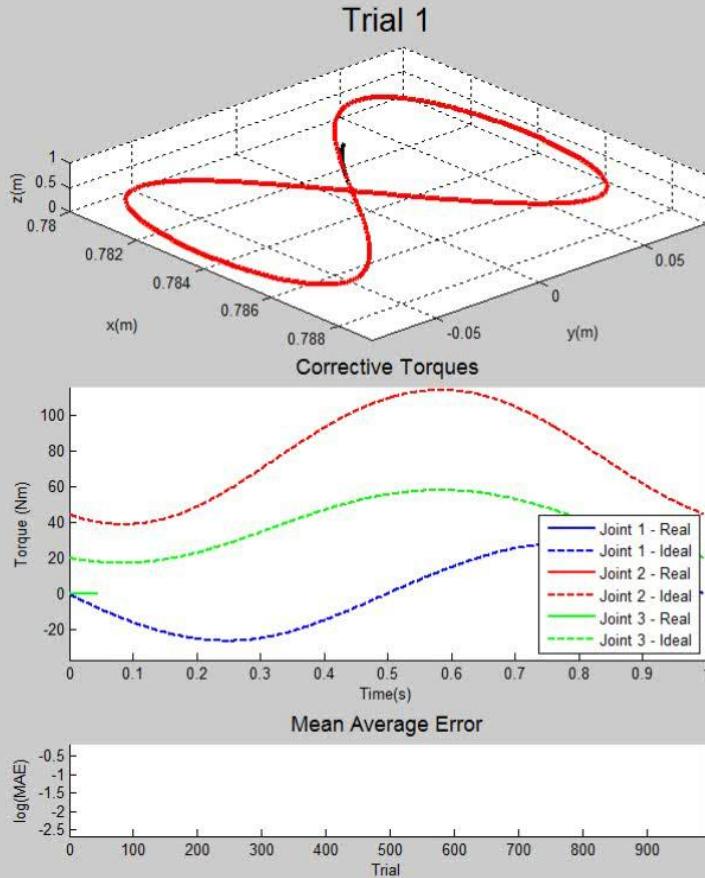
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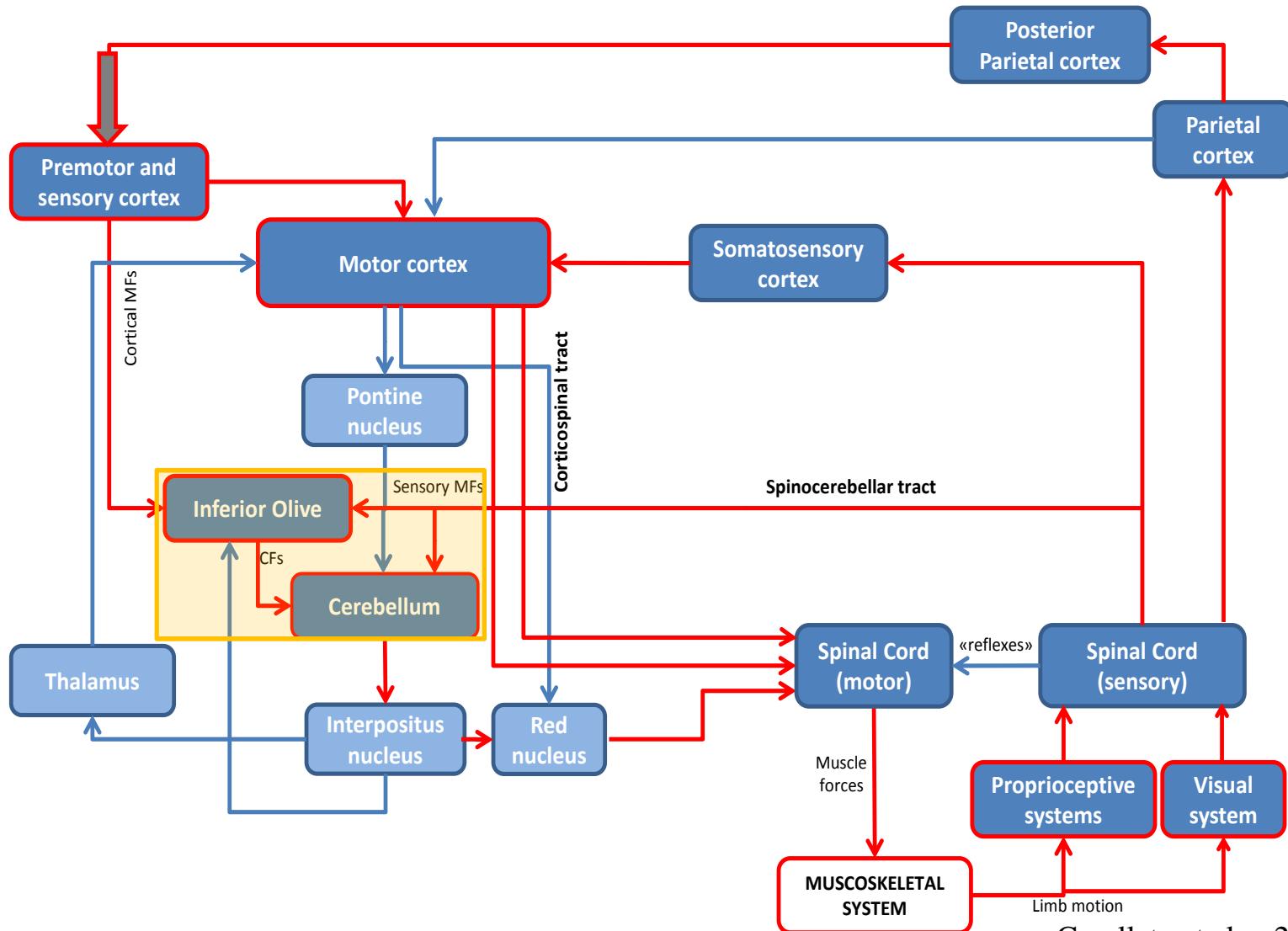
C



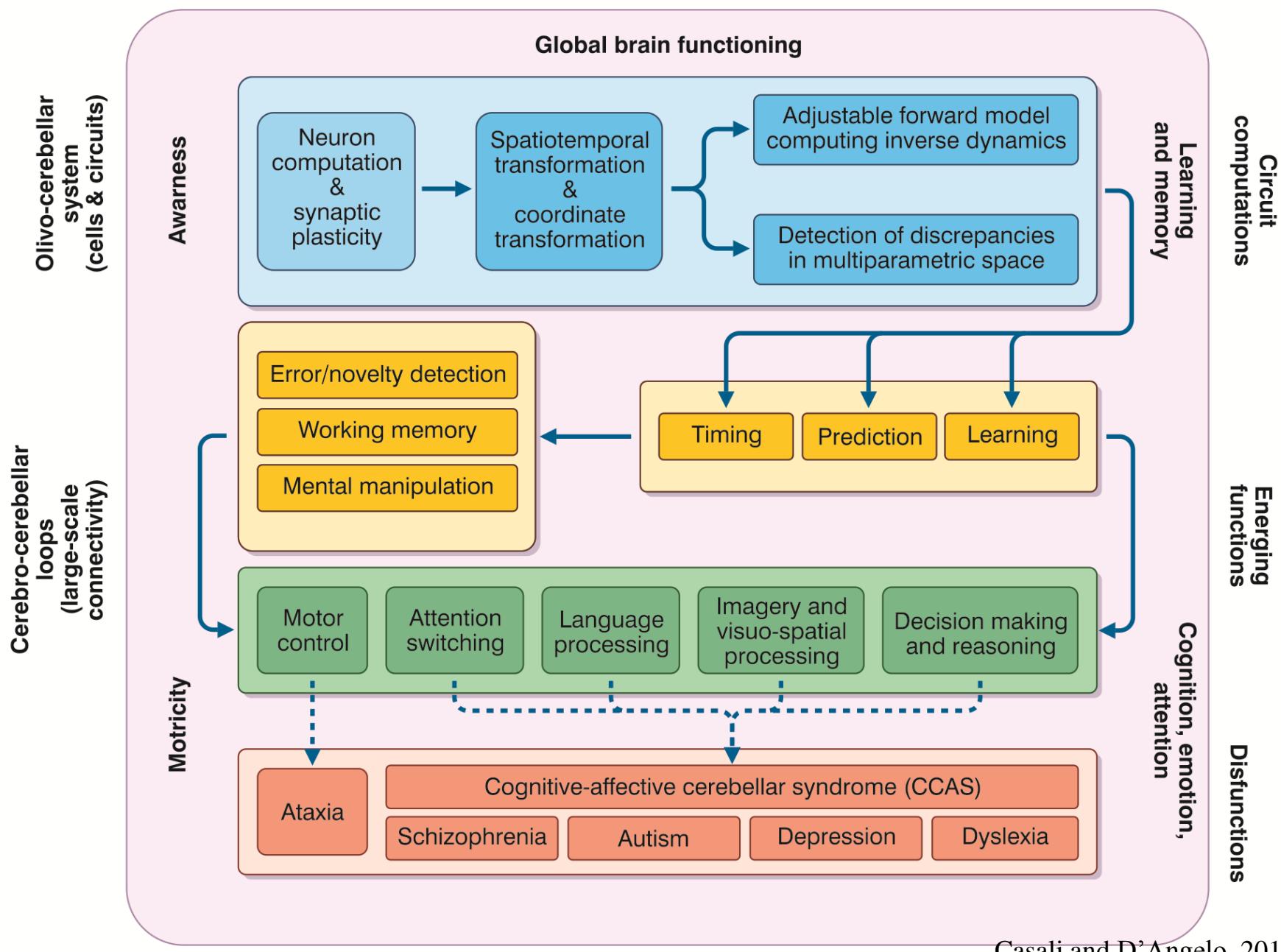
Adaptive learning in a robotic simulator incorporating the cerebellar network and synaptic learning rules



Distributed neuromotor control system embedding the cerebellum model



Multi-level organization and neurological diseases



(3) *Conclusions*

- Large-scale realistic models of brain circuits can be constructed and tested
- These models can help explaining how low-level connections connect to high-level brain functions
- These models can be applied to computational and robotic control
- These models can foster biomdeocal research and applications in the clinical sector.

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