Dinamiche multiscala delle onde lente cerebrali: teoria ed esperimento

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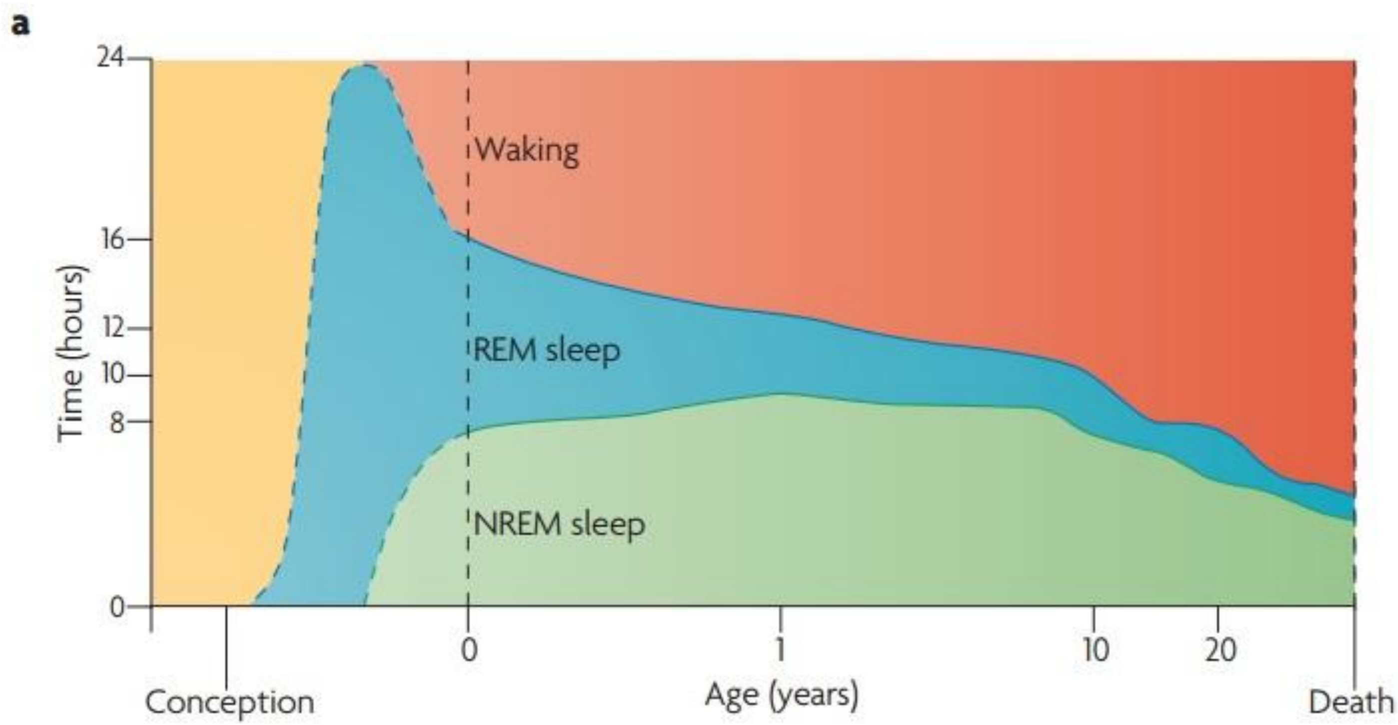
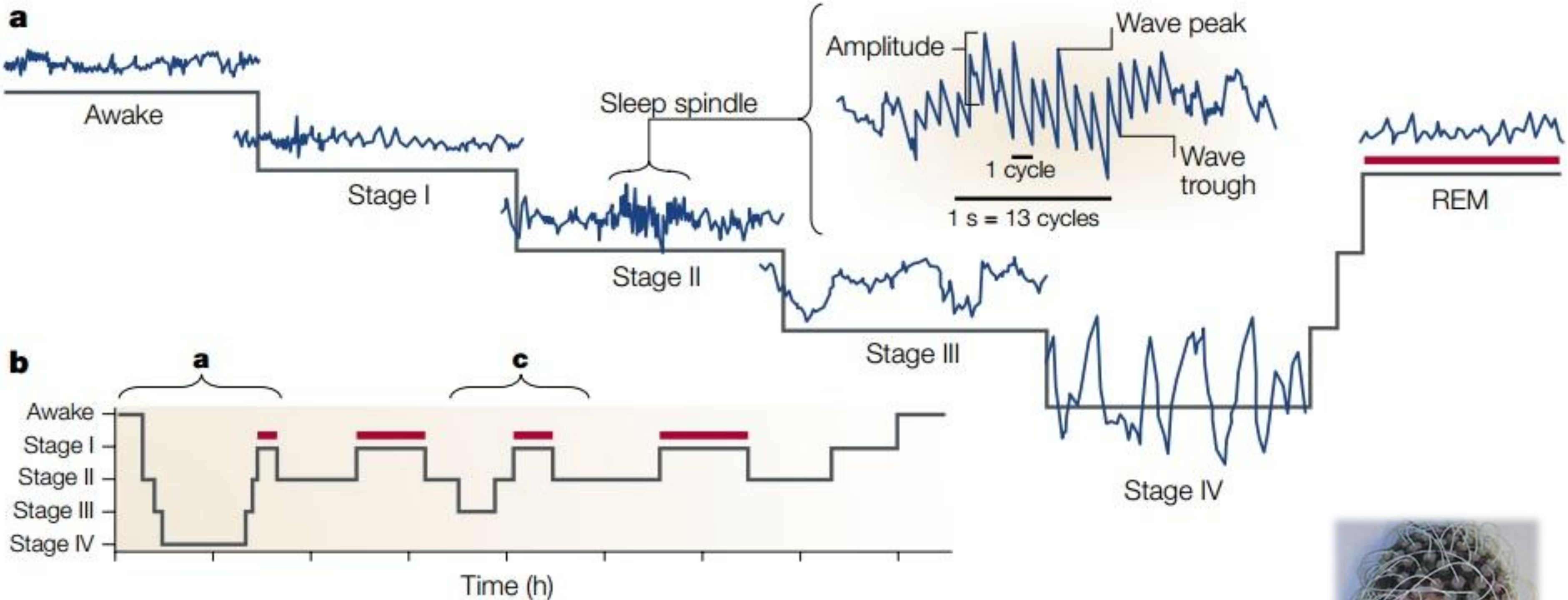
Sleep is a fundamental need

Sleep is a large part of our life



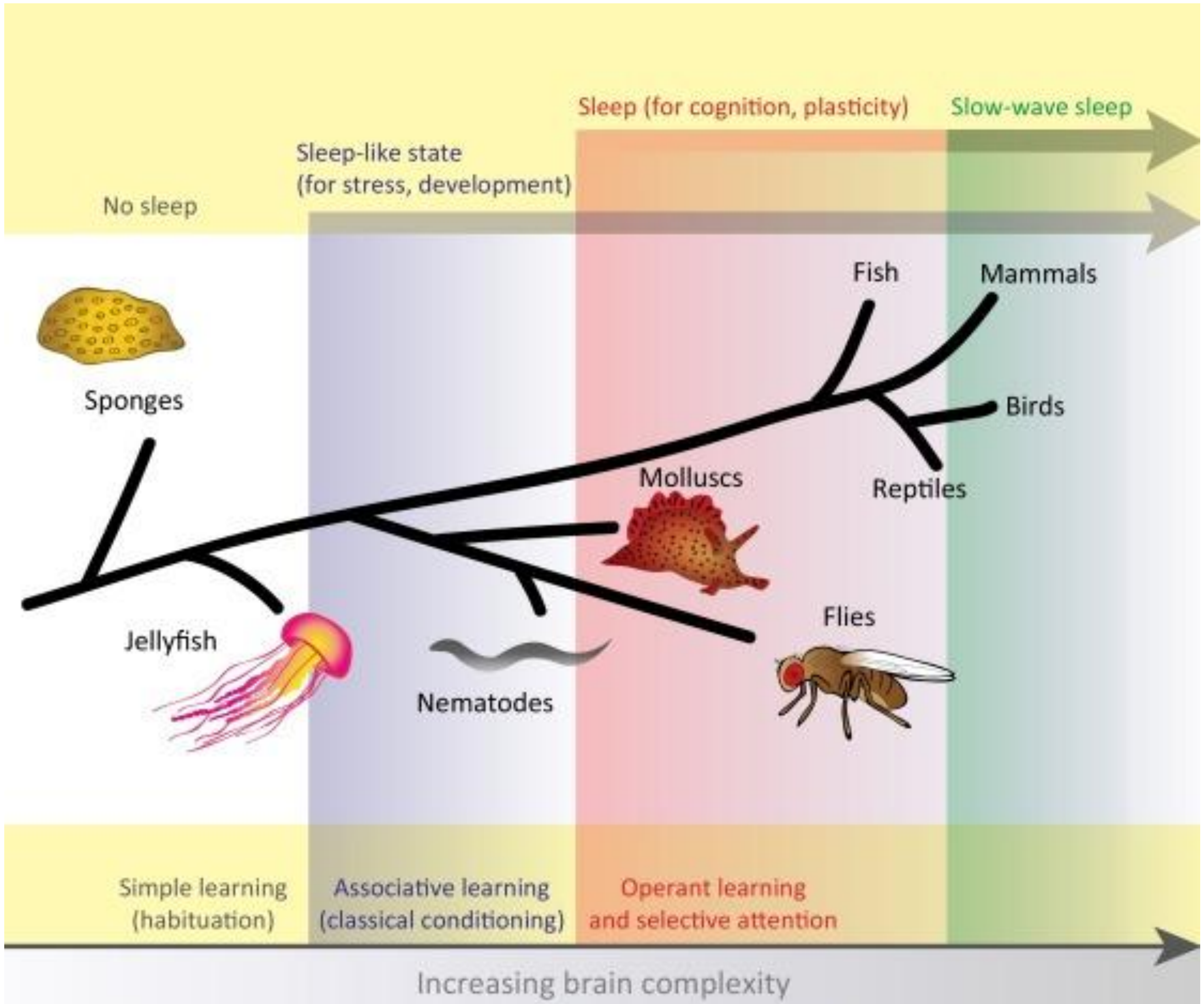
Hobson, *Nat Rev Neurosci,* 2009

Sleep science basics



Pace-Schott & Hobson, *Nat Rev Neurosci,* 2002

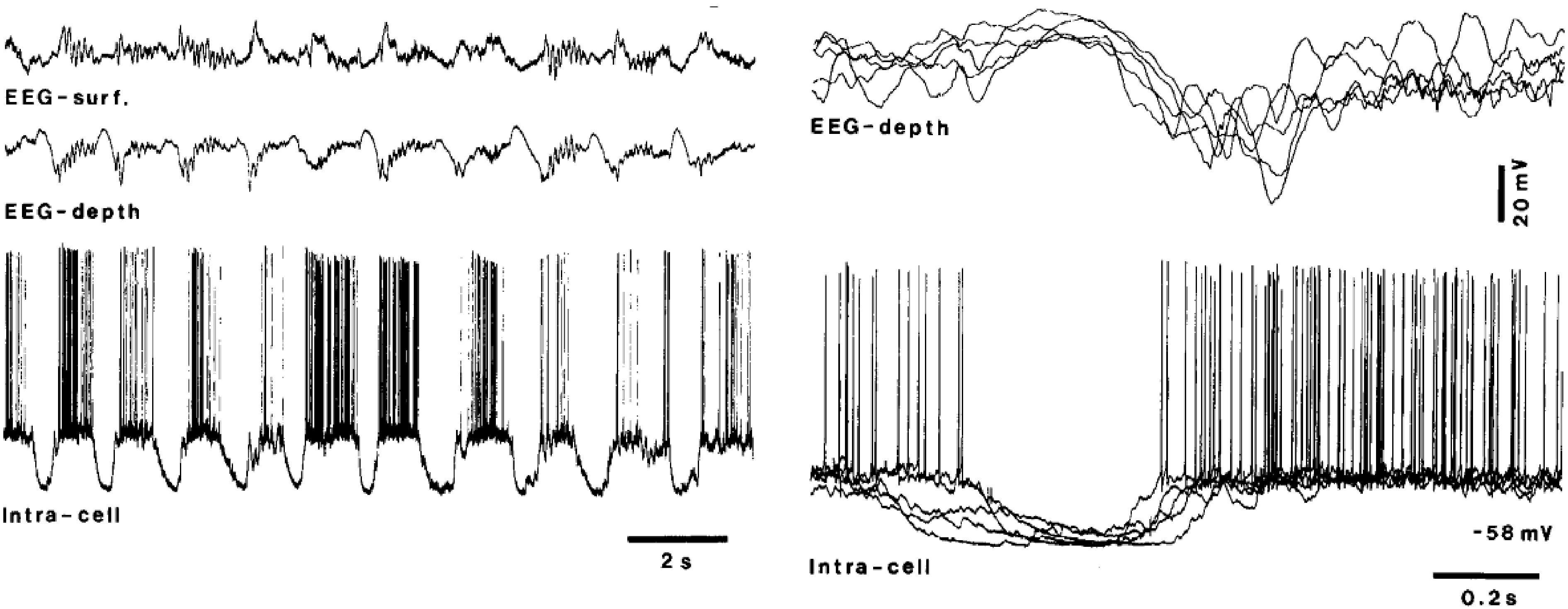
Slow-wave sleep as a default mode



Kirszenblat & van Swinderen, *Trends Neurosci*, 2015

Slow Up/Down oscillations (SO)

Cat Motor Cortex

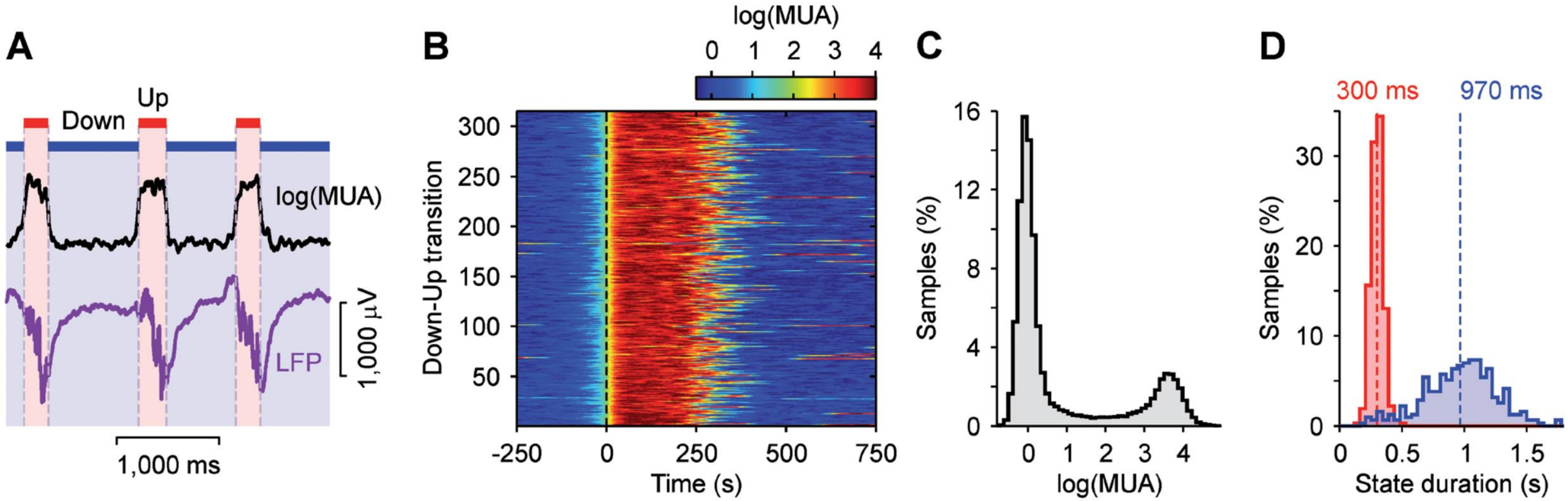


Contreras and Steriade, *J Neurosci*, 1995

- Up (high firing)/Down (quiescent) oscillations (< 1Hz) can be observed in mammals during deep sleep stages and under anesthesia.

Slow Up/Down oscillations (SO)

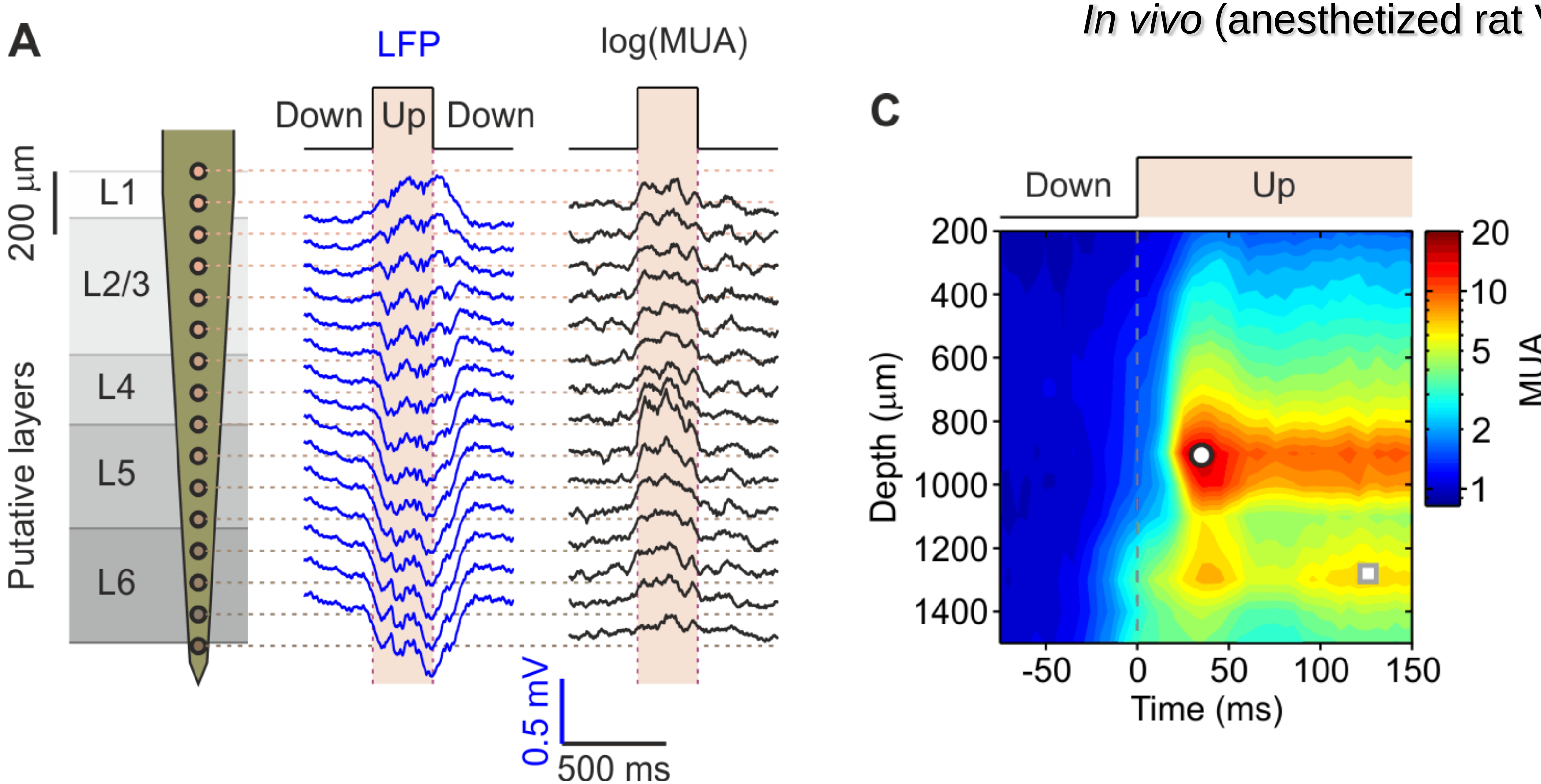
@ M.V. Sanchez-Vives' lab, Barcelona, Spain



- *In vivo* extracellular recordings from visual cortex (V1) of anesthetized (ketamine/medetomidine) rats (adult male Wistar).
- Up and Down state onsets can be reliably singled out inspecting multi-unit activity (MUA, the spiking activity of the neuronal pool nearby the electrode tip).
- The distribution of residence times in Up and Down states are relatively narrow.

Columnar organization of SWA

In vivo (anesthetized rat V1)

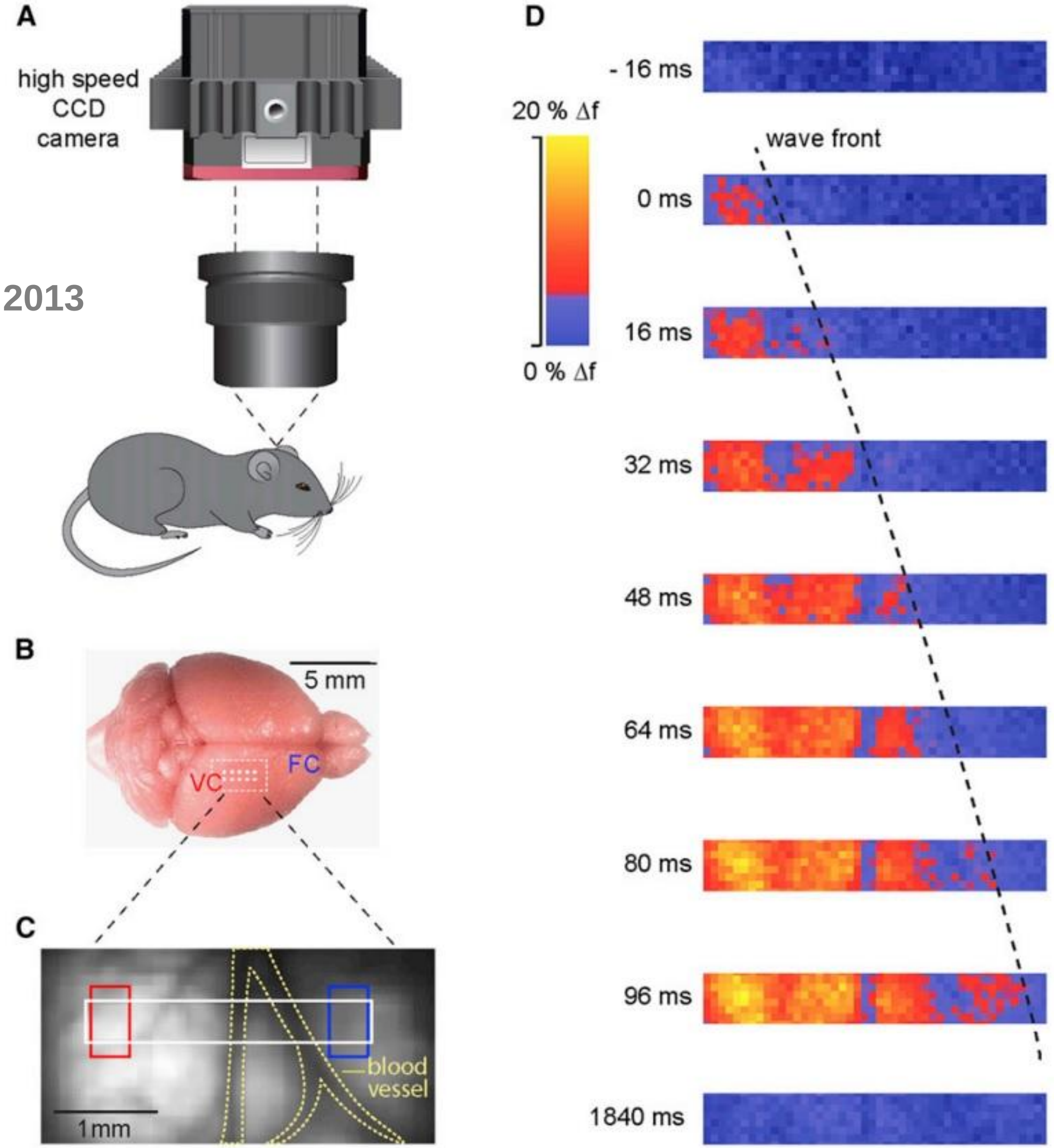


Mattia, Perez-Zabalza, Tort-Colet & Sanchez-Vives, *submitted*

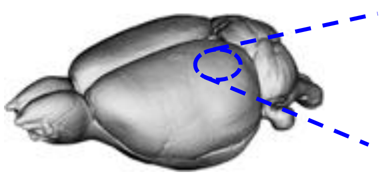
- Down-to-Up transitions initiate in deep layers, successively spreading towards the more superficial ones.

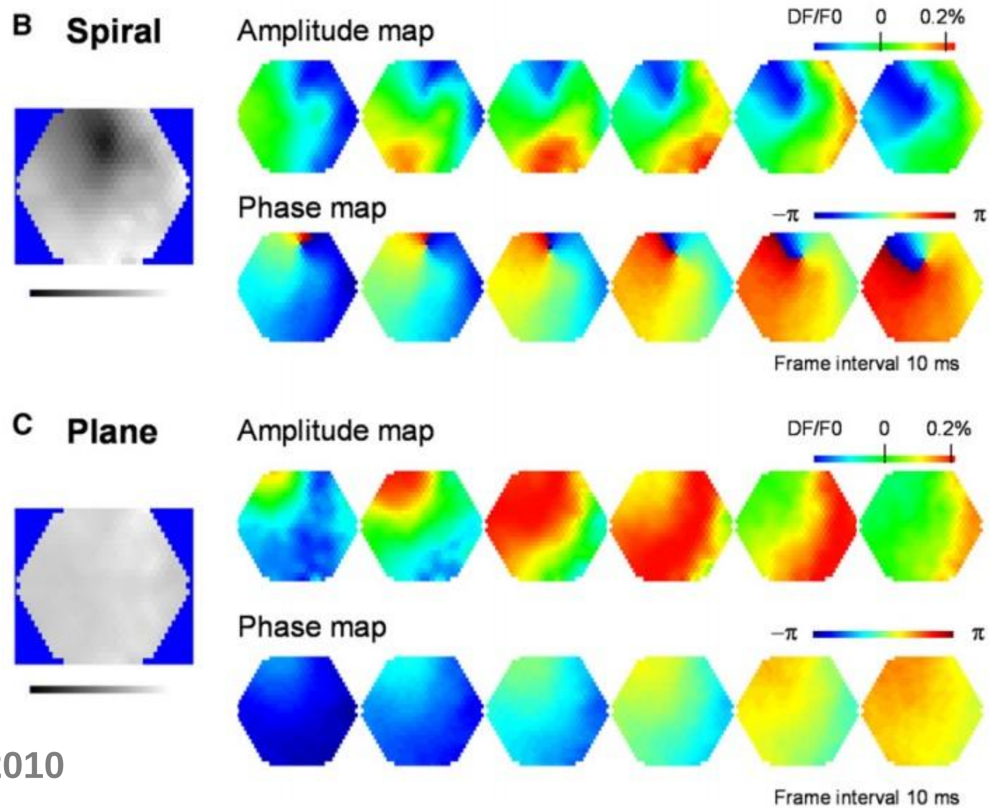
Macroscopic activation waves during SWA

Stroh et al., *Neuron*, 2013

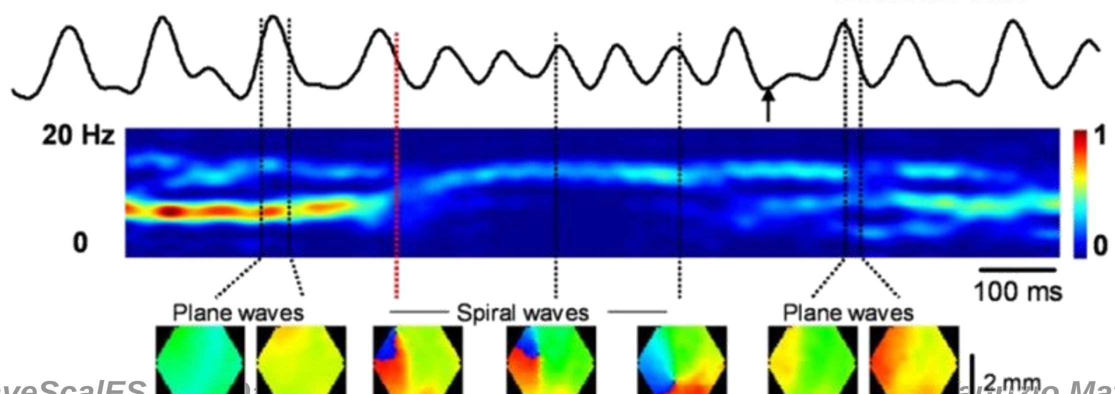


Different spatiotemporal patterns

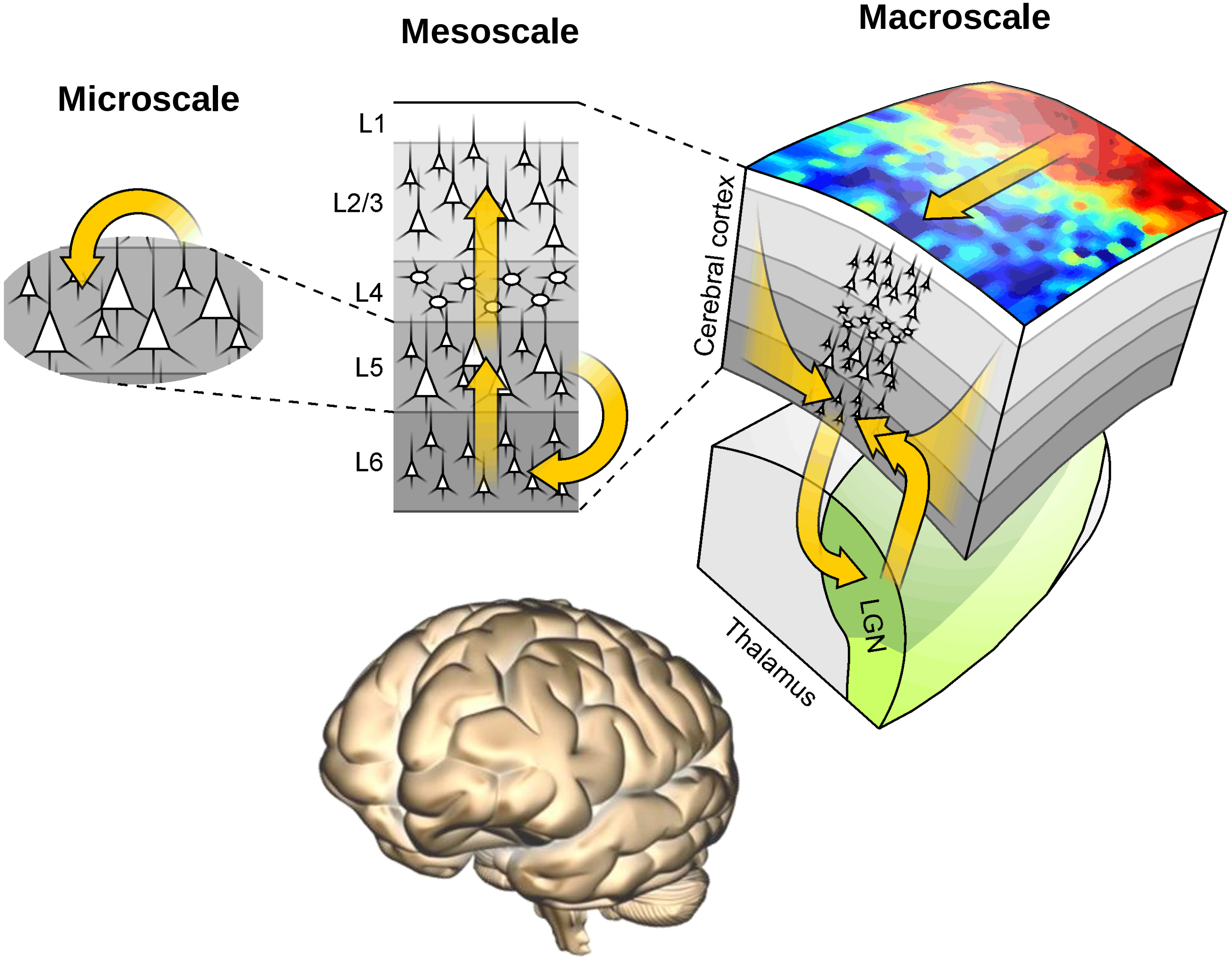




Huang et al., *Neuron,* 2010



SWA → Multiscale organization of the brain

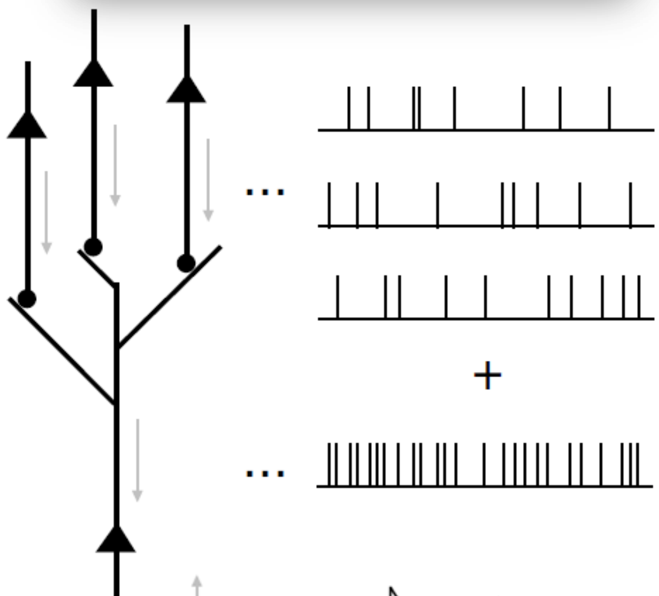


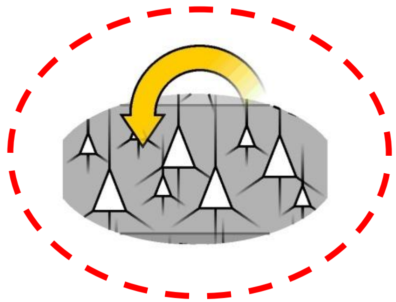
A theoretical "microscopic" description which reduces the dimensionality of the problem is needed to bridge together quantitatively mesoscopic and macroscopic scales.

From single neuron to population dynamics

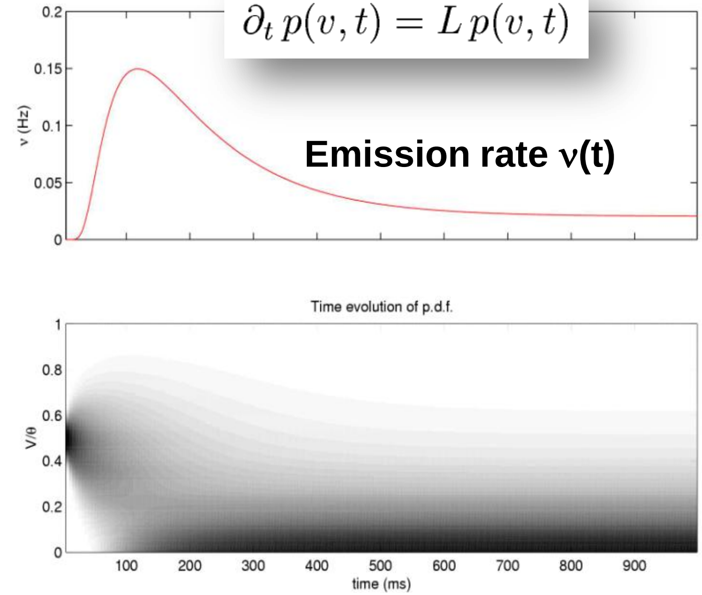
The theoretical hinge: a homogeneous network of generic Integrate-and-Fire (IF).

$$\dot{V}_i(t) = f(V_i) + \sum_{j=1}^{C} J_{ij} \sum_k \delta(t - t_k^{(j)} - \delta)$$



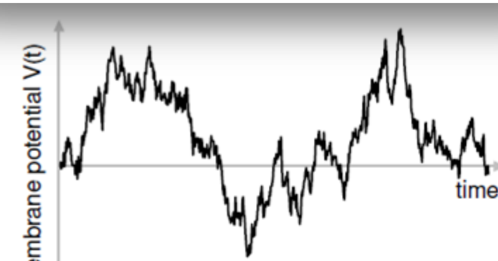


$$\partial_t\, p(v,t) = L\, p(v,t)$$



Diffusion approximation

$$\dot{V}_i(t) = f(V_i) + \mu(V_i,t) + \sigma(V_i,t)\Gamma(t)$$



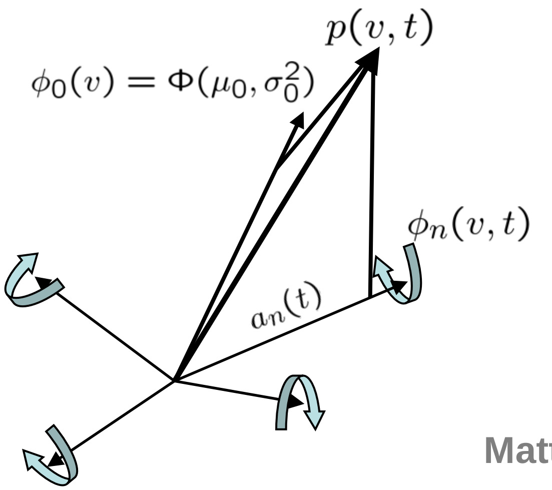
Mean-field approximation

Towards a low-dimensional dynamics…

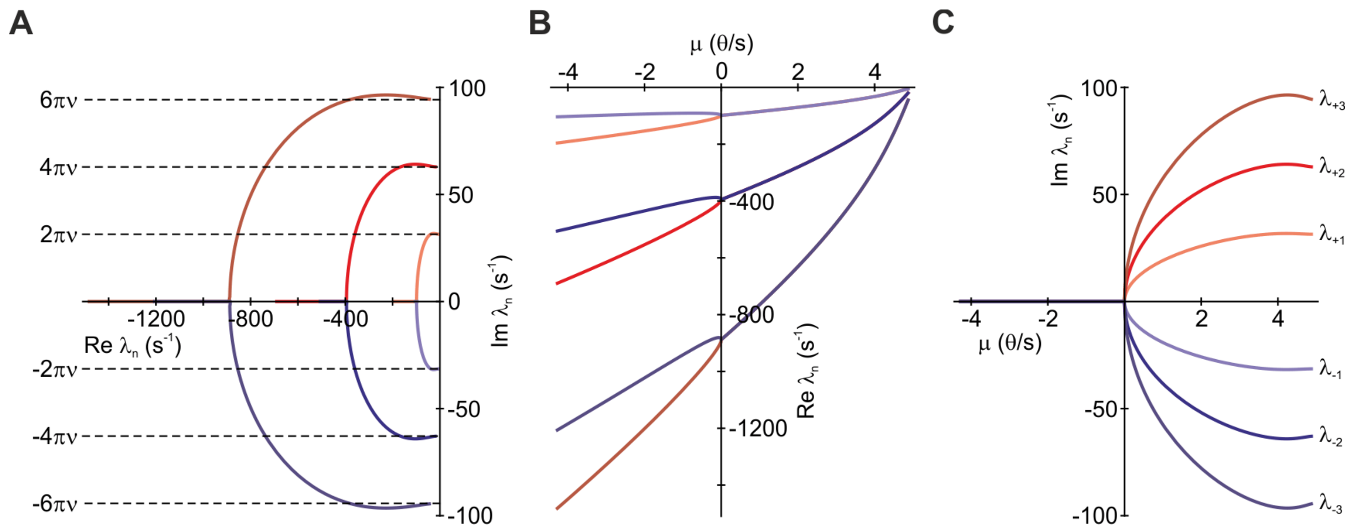
Spectral expansion of the Fokker-Planck equation yields to an effective $\nu(t)$ dynamics.

$$L\,|\phi_n\rangle = \lambda_n(t)\,|\phi_n\rangle$$

$$|p\rangle = \sum_n a_n |\phi_n\rangle$$

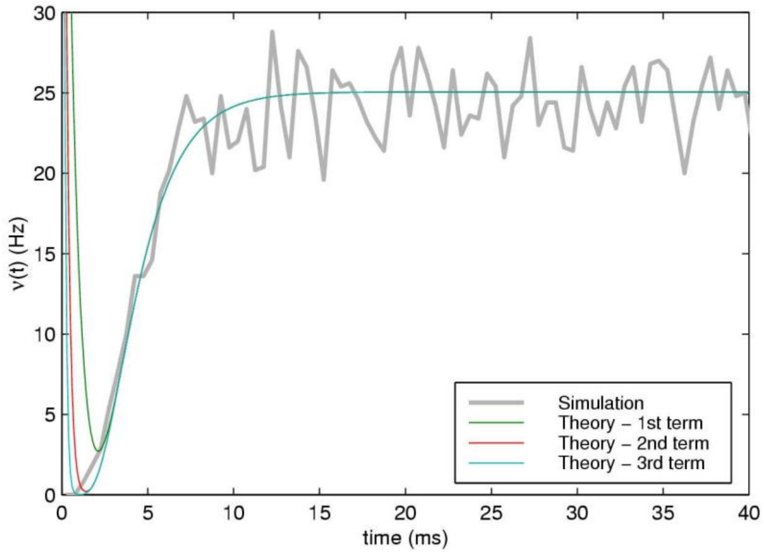


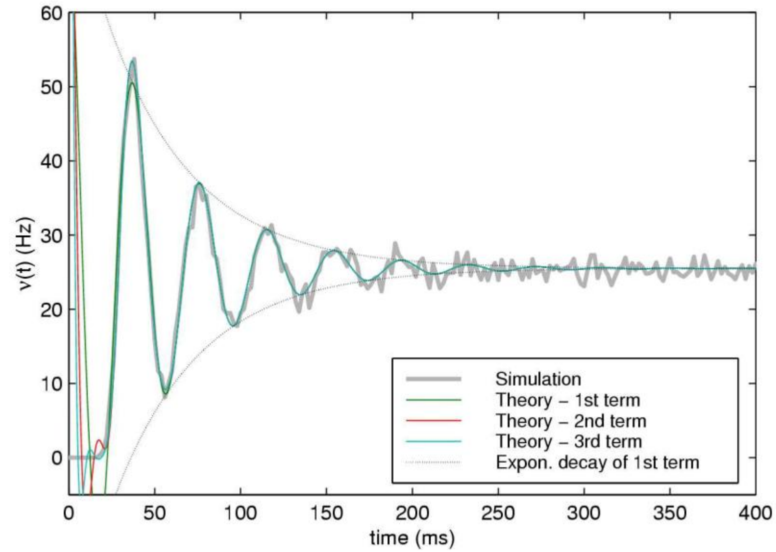
Knight, *Neural Comput*, 2000
Mattia & Del Giudice, *Phys Rev E, 2002*

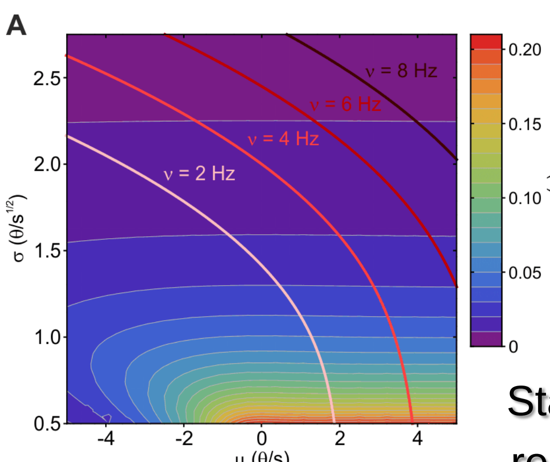


… a low-D Wilson-Cowan equation

A $\nu(t)$ dynamics in which only few modes with slowest eigenvalues are included.



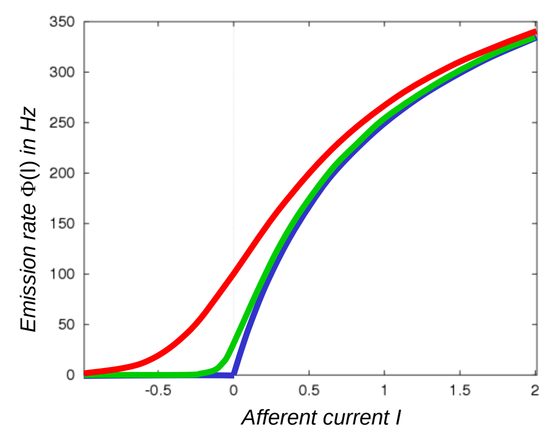




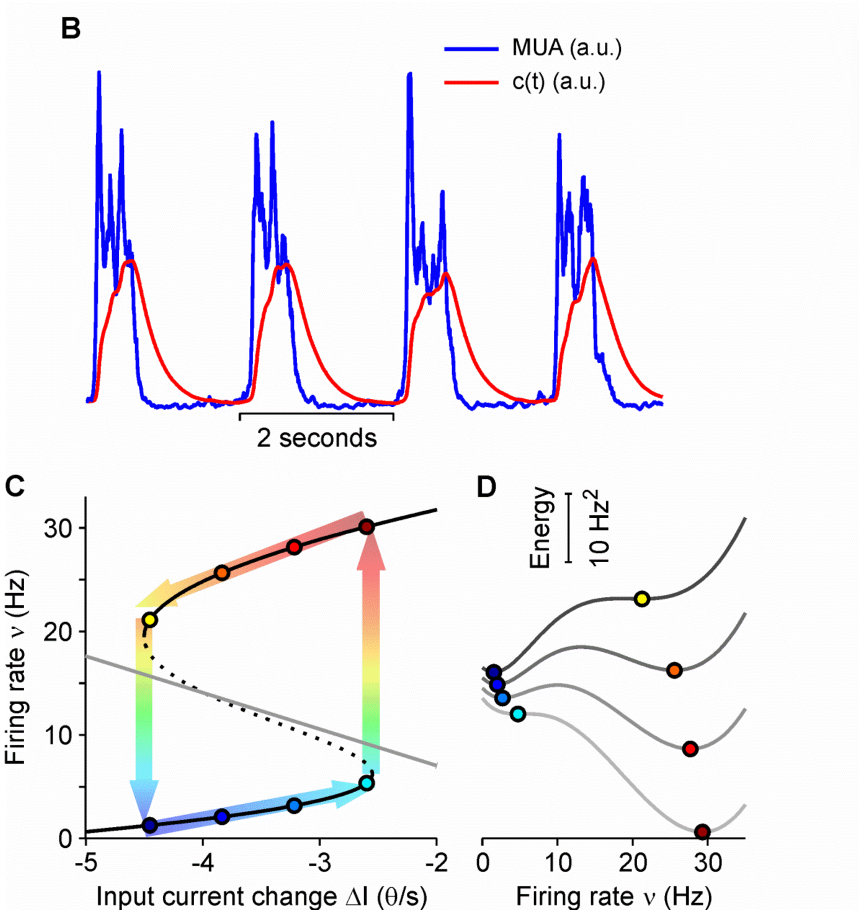
$$\tau(\nu_N)\frac{d\nu}{dt} = \Phi(\nu_N) - \nu + F_N$$

State-dependent relaxation time τ

Current-to-rate gain function Φ



Additional negative feedback to have SO



$$\Delta I = -g \cdot c$$

$$\dot{\nu} = \frac{\Phi(c,\nu) - \nu}{\tau_\nu(c,\nu)}$$

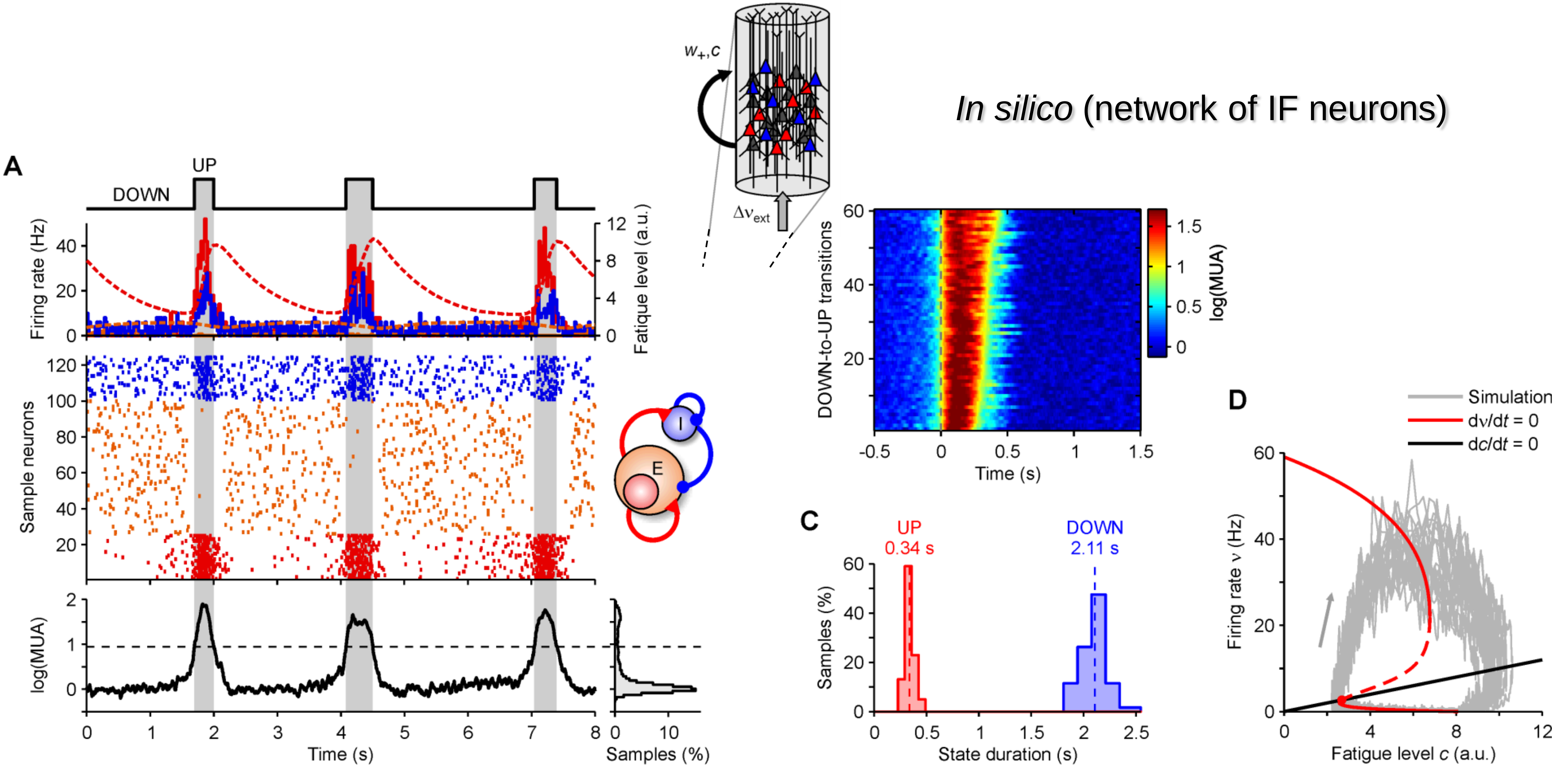
$$\dot{c} = -\frac{c}{\tau_c} + \nu$$

- An activity-dependent fatigue variable c provides an inhibitory feedback.
- The effective energy landscape is shaped by c, making Up and Down states progressively unstable.
- The network behaves like a relaxation oscillator. This is the typical theoretical modeling of SO.

Gigante et al., *Phys Rev Lett* 2007
Mattia & Sanchez-Vives, *Cogn Neurodyn* 2012

Reproducing SO *in silico*

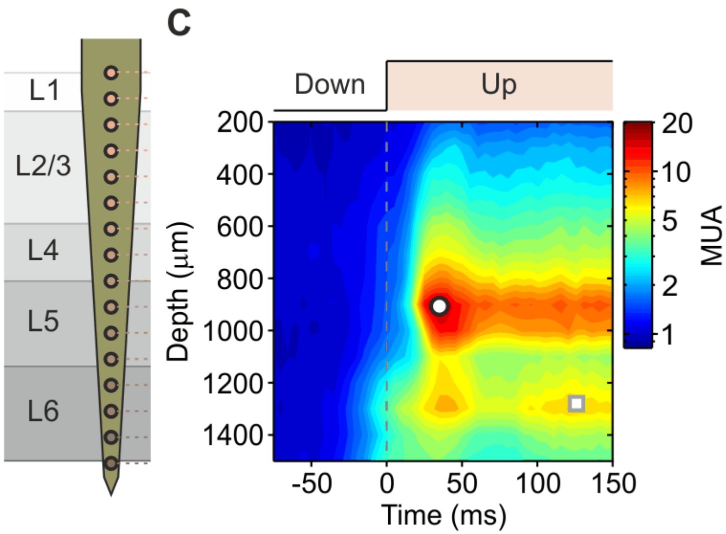
In silico (network of IF neurons)

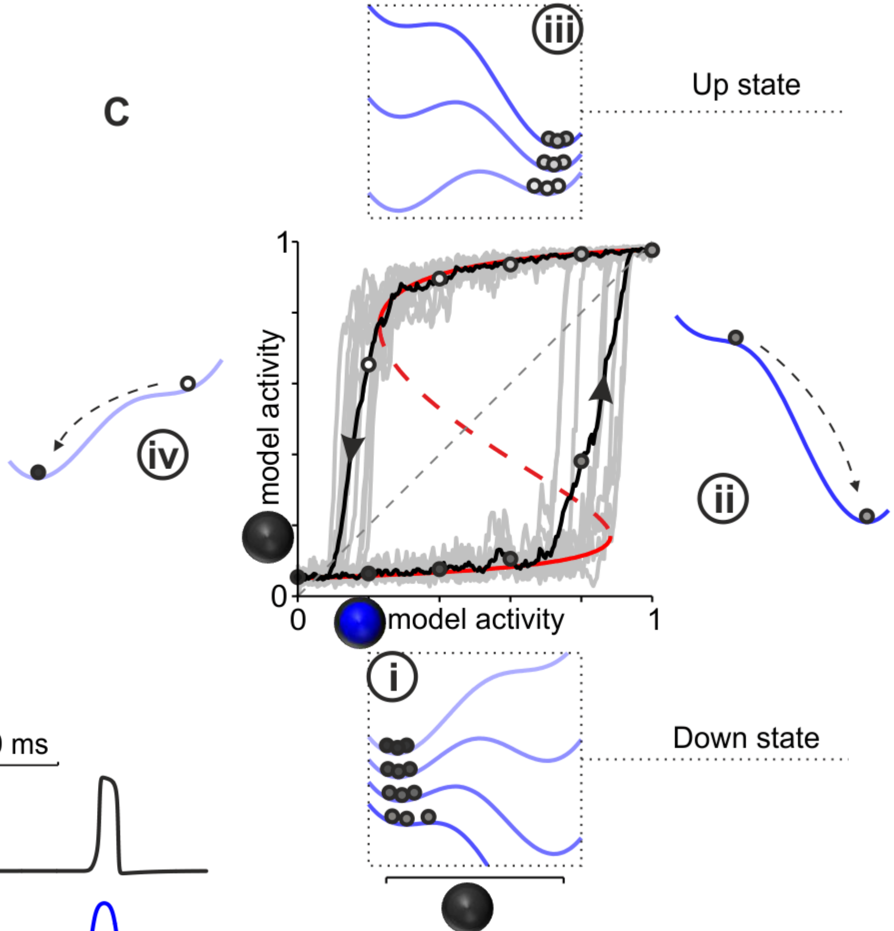


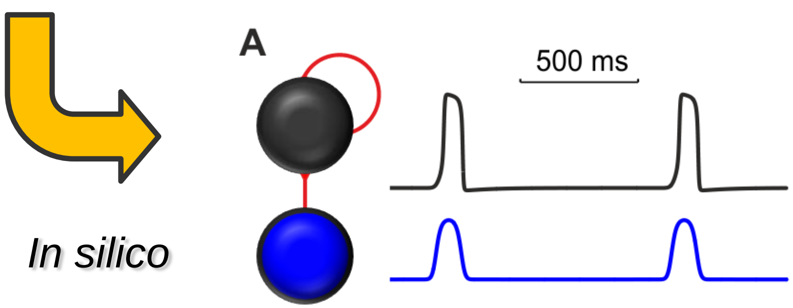
Bazhenov et al., *J Neurosci* 2002; Compte et al., *J Neurophysiol* 2003; Hill & Tononi, *J Neurophysiol* 2005; Destexhe, *J Comput Neurosci* 2009; Mattia & Sanchez-Vives, *Cogn Neurodyn* 2012; D'Andola, Wienert, Mattia & Sanchez-Vives, *in preparation*

Probing bistability underlying *in vivo* SO

In vivo (anesthetized rat V1)





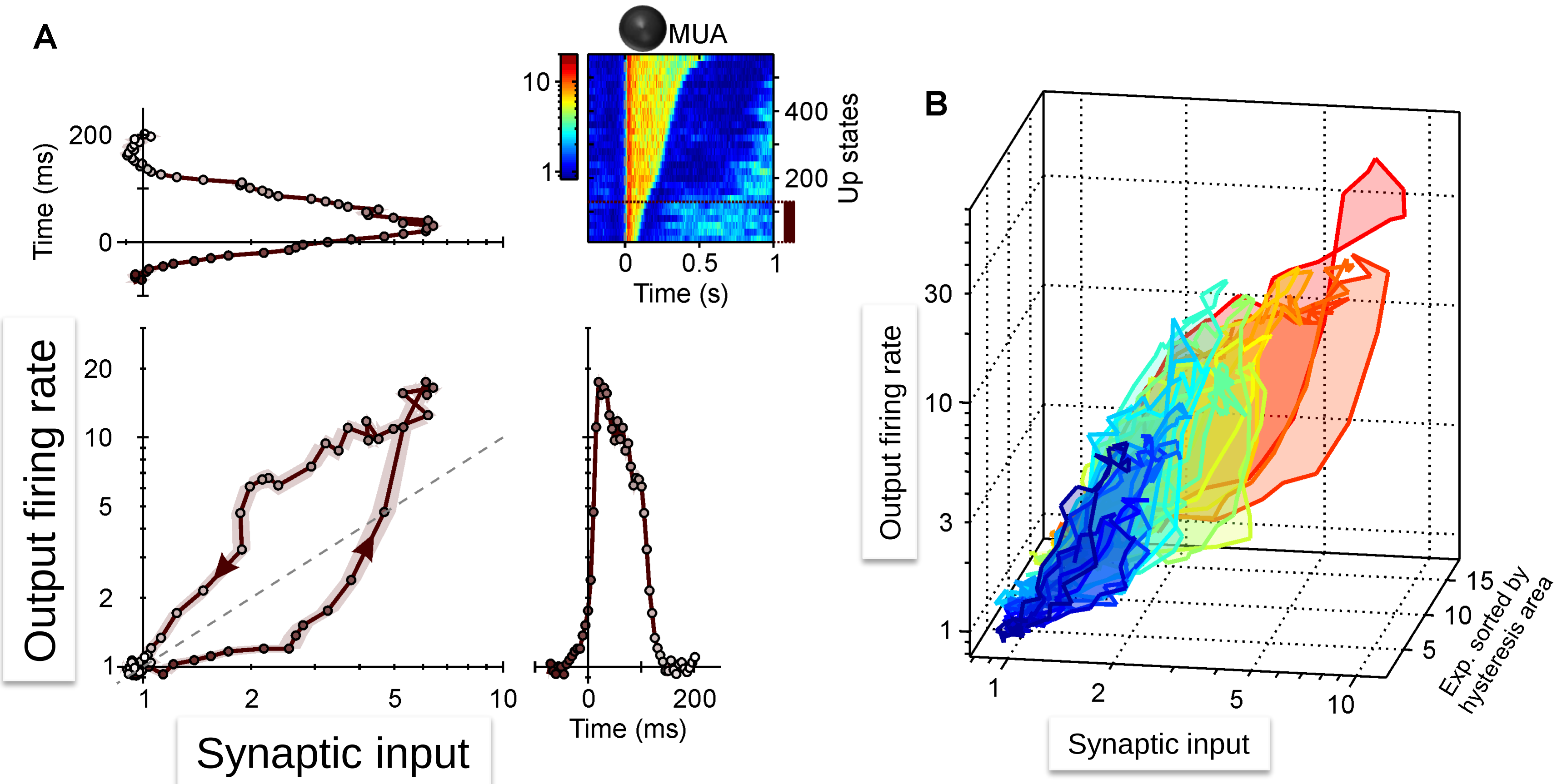


Mattia, Perez-Zabalza, Tort-Colet & Sanchez-Vives, *submitted*

- Hysteresis can be the sign left by a bistable dynamical system, where both Up and Down states are temporarily coexistent stable states.

Hysteresis in L5 cortical modules

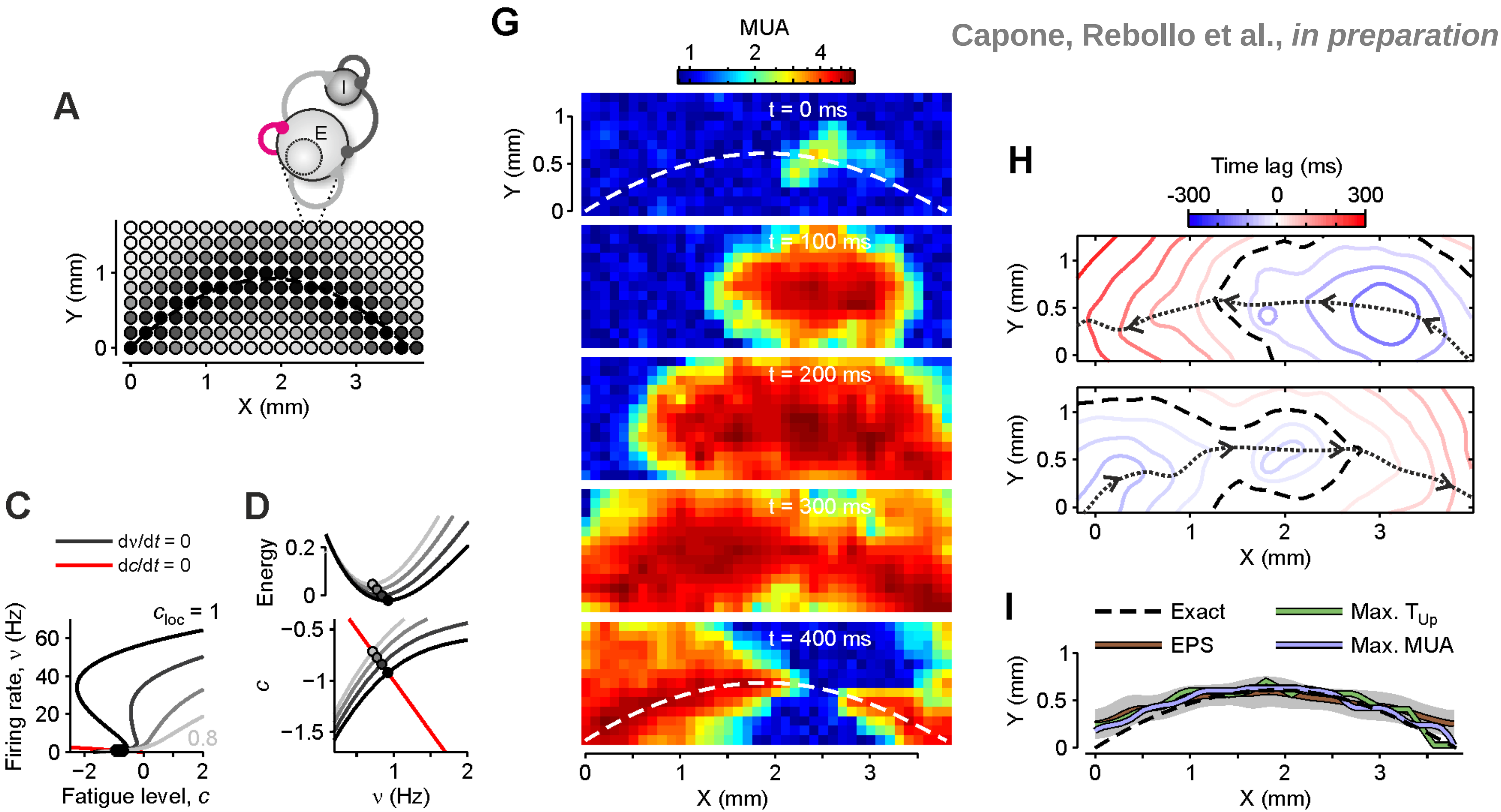
In vivo (rat V1)



- Considering the MUA in deep layers as input activity to the more active module, a history dependent dynamics can be highlighted: responses to the same input can be different.

SWA on *in silico* large-scale neural fields

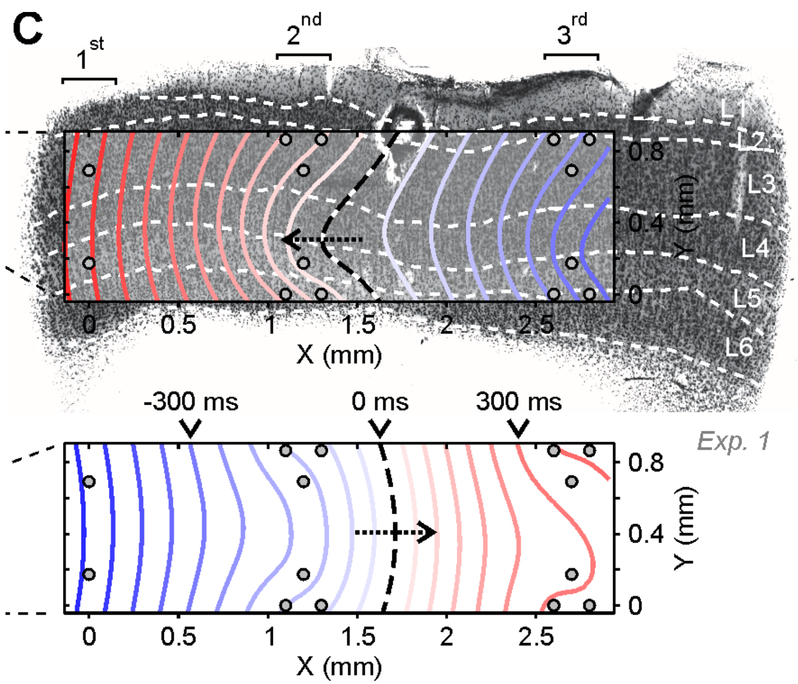
Capone, Rebollo et al., *in preparation*

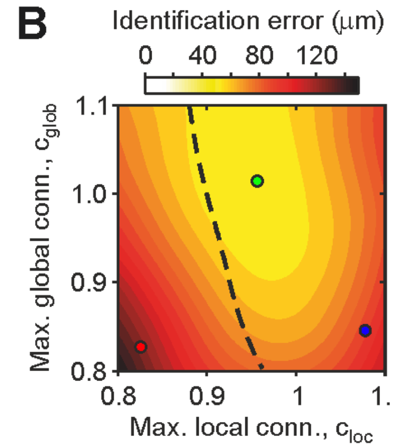


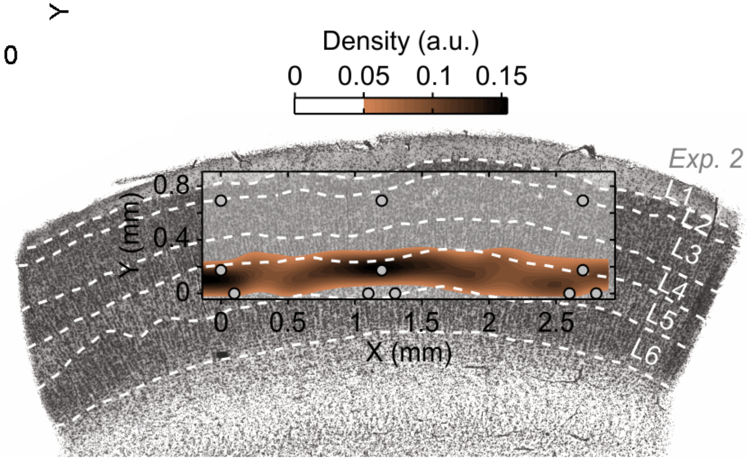
$$\tau \frac{\partial u(x,t)}{dt} = -u(x,t) + \int_{-\infty}^{+\infty} w(y)\Phi[u(x-y,t)]dy$$

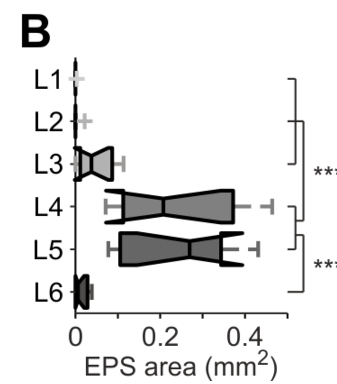
Cortical structure from *in vitro* SWA

Capone, Rebollo et al., *in preparation*



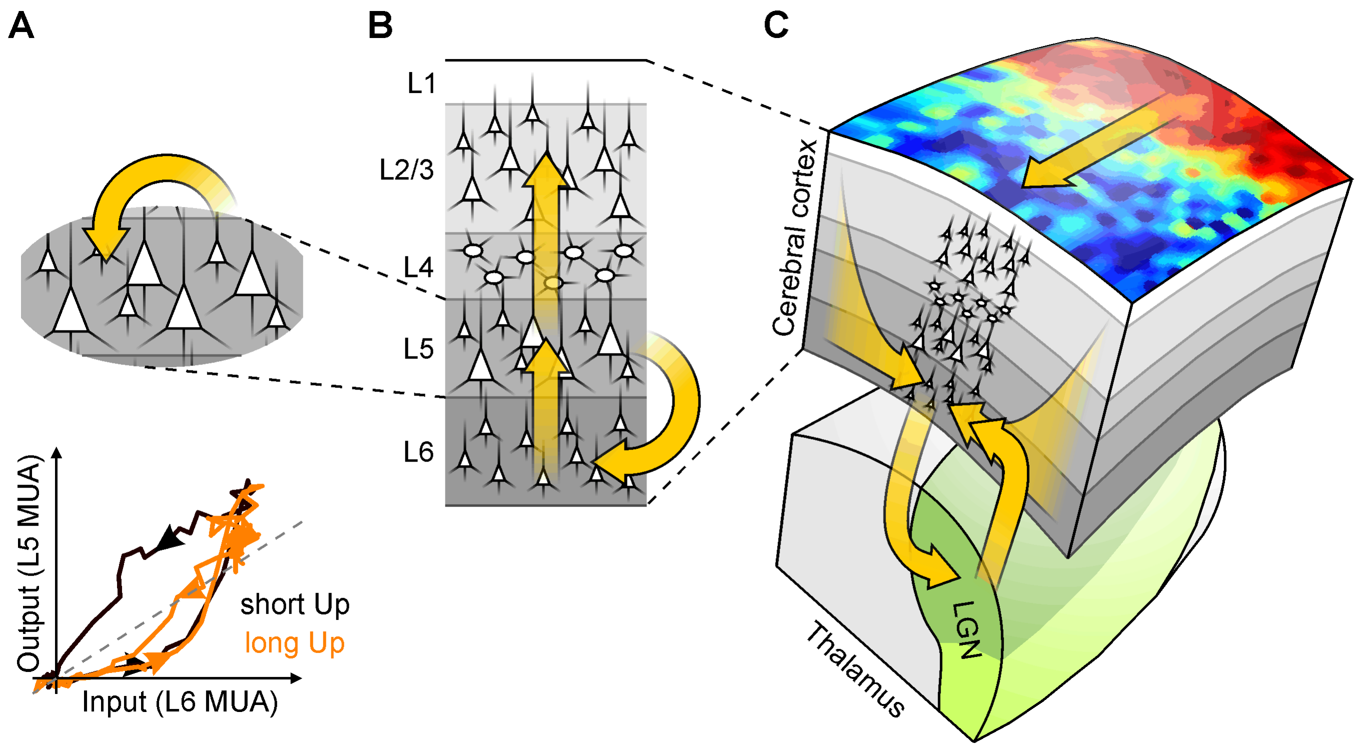






In vitro (ferret cortical slices)

Conclusions and outlooks



- SWA as a default mode which allow to constrain quantitative brain models implemented in in large scale simulations.
- SWA as a reference to investigate differences between normal and pathological brain, and between animal species.
- Sleep-wake brain state transitions: an open window on the computational primitives expressed by neuronal networks.

In collaboration with…

- **Maria V. Sanchez-Vives**
  Nuria Tort-Colet
  Maria Perez-Zabalza
  Beatriz Rebollo
  - *IDIBAPS, Barcelona (Spain)*
- **Alberto Muñoz-Cespédes**
  - *Complutense Univ. of Madrid (Spain)*
- **Cristiano Capone**
  - *PhD @ Sapienza Univ. of Rome & ISS, Rome (Italy)*
- **Paolo Del Giudice**
  Guido Gigante
  - *ISS, Rome (Italy)*

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Looking for post-docs…

- <u>Period</u>: Spring 2016 – Spring 2018 (two years) in Rome
- <u>Background</u>: physics/mathematics/engineering, programming skills for *in vivo* data analysis (Matlab) and/or large-scale spiking neuron network simulations
- <u>Project</u>: WaveScalES – workpackage of the renewed “cognitive and systems neuroscience” subproject of HBP
- <u>Aim</u>: Understanding multiscale dynamics of slow-wave activity from deep anesthesia to wakefulness

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Human Brain Project