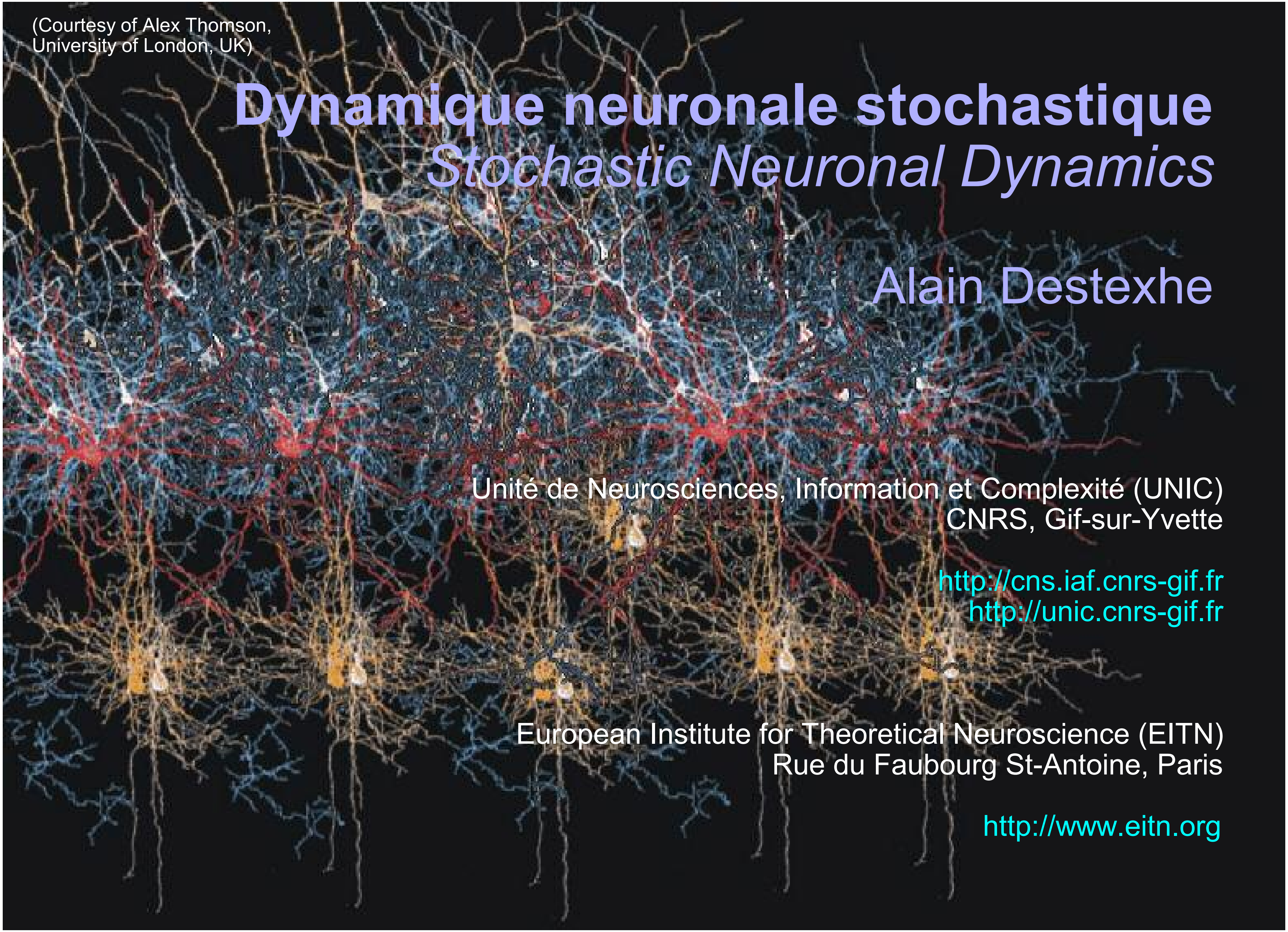


(Courtesy of Alex Thomson,
University of London, UK)

Dynamique neuronale stochastique
Stochastic Neuronal Dynamics

Alain Destexhe

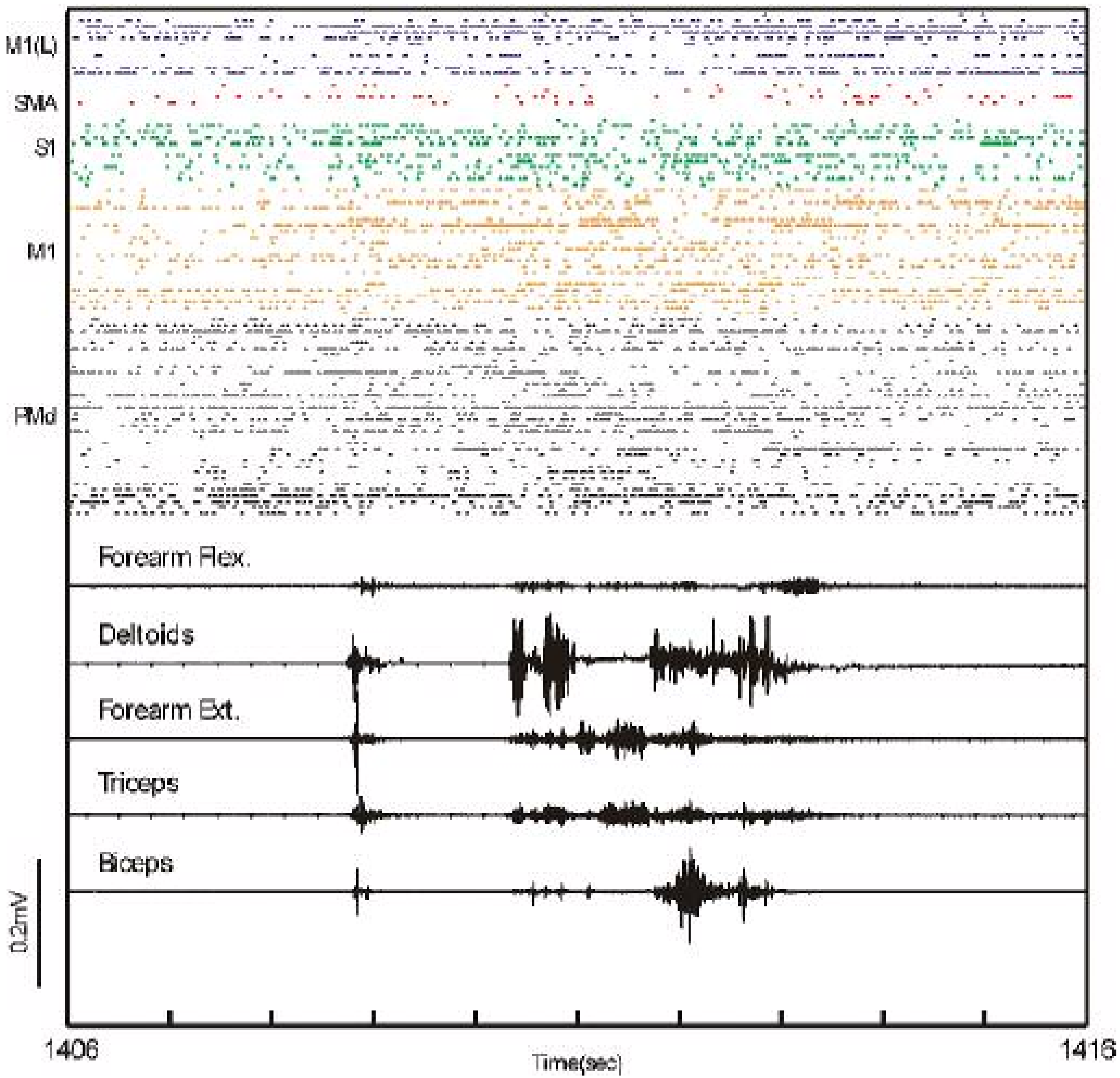
Unité de Neurosciences, Information et Complexité (UNIC)
CNRS, Gif-sur-Yvette

http://cns.iaf.cnrs-gif.fr
http://unic.cnrs-gif.fr

European Institute for Theoretical Neuroscience (EITN)
Rue du Faubourg St-Antoine, Paris

http://www.eitn.org

Complex and seemingly stochastic patterns of neuronal discharge

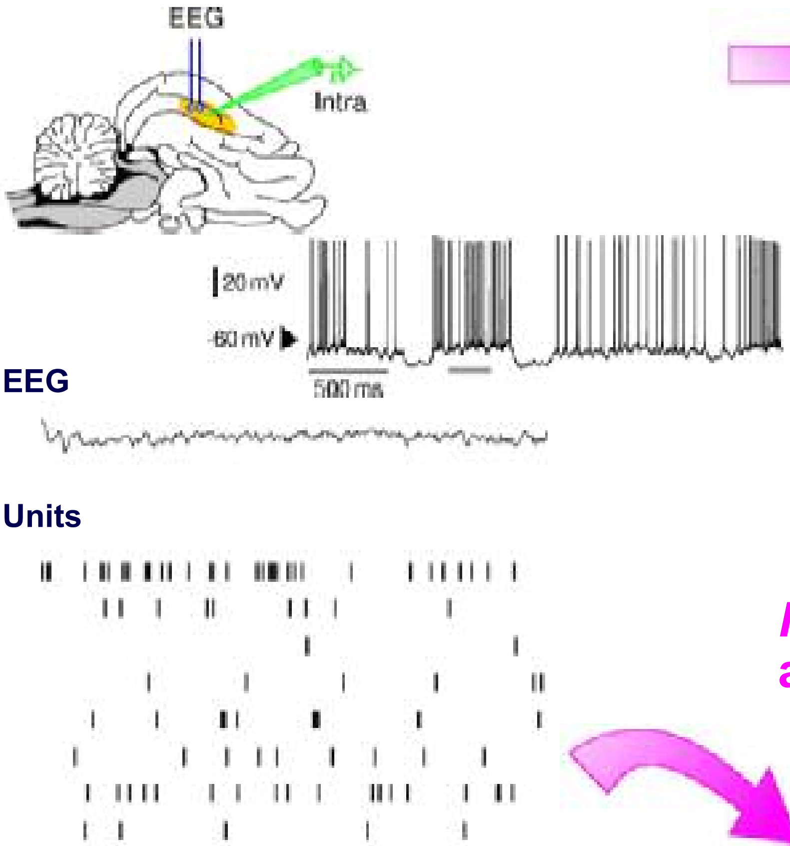


Ensemble activity in the cortex of a behaving rhesus monkey

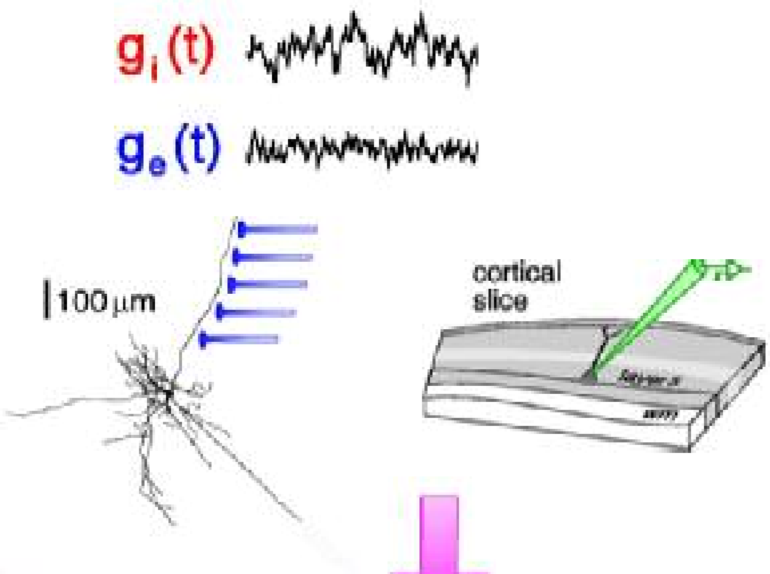
Wessberg
Crist & Nicolelis
(2002)

Multiscale analysis

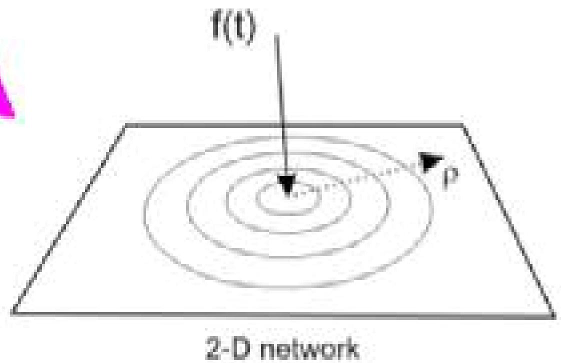
Characterization of “noisy” network activity in vivo: *High-conductance states*

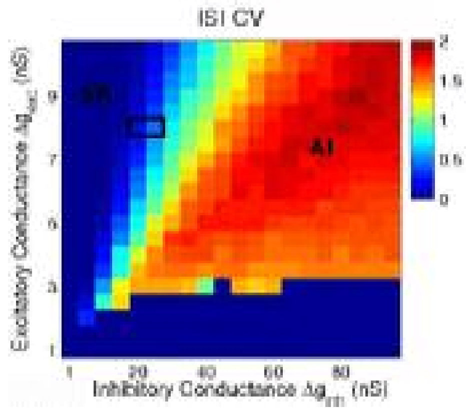


Integrative properties of single neurons during *High-Conductance states*



***High-conductance states* at the network level**



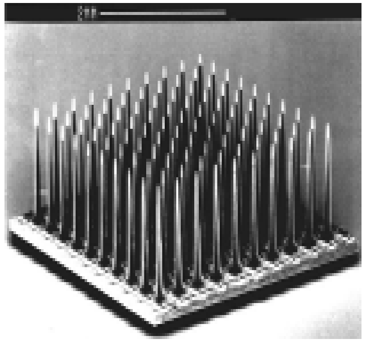


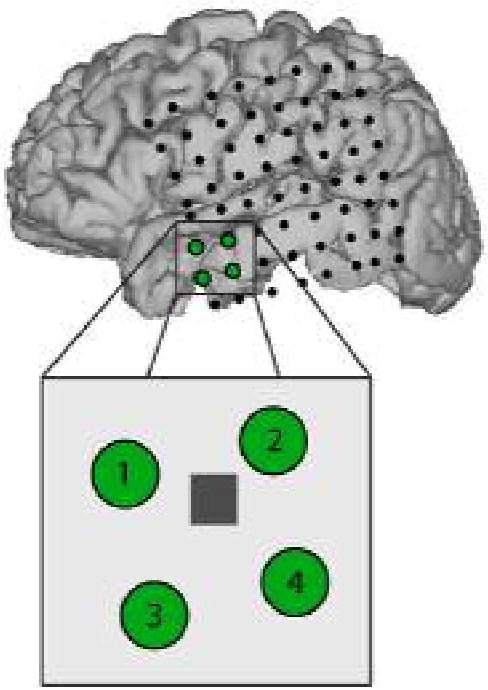
How stochastic is neuronal activity in the awake brain ?

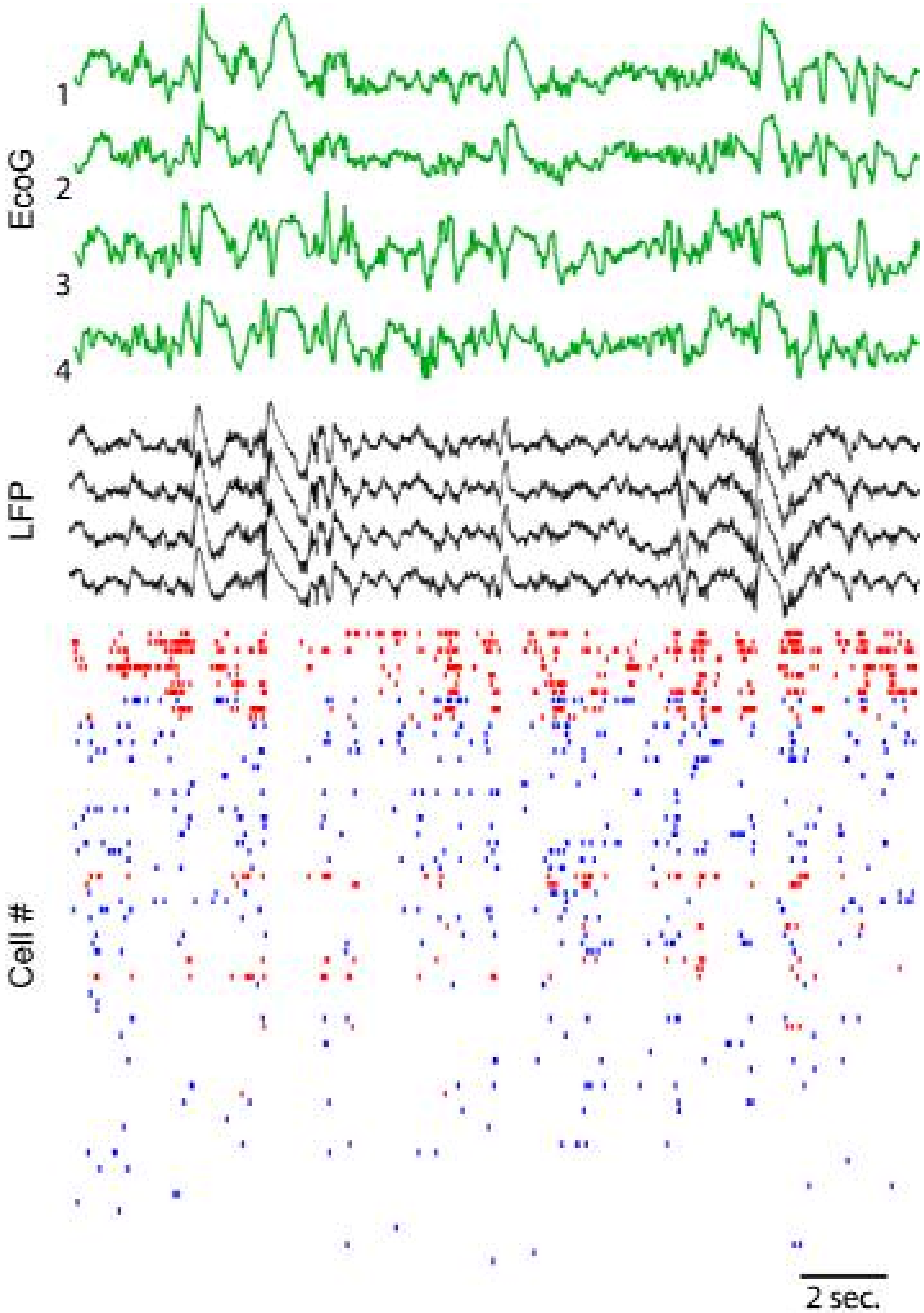
What type of dynamics does it follow ?

Human ensemble recordings

Utah-array recordings in humans

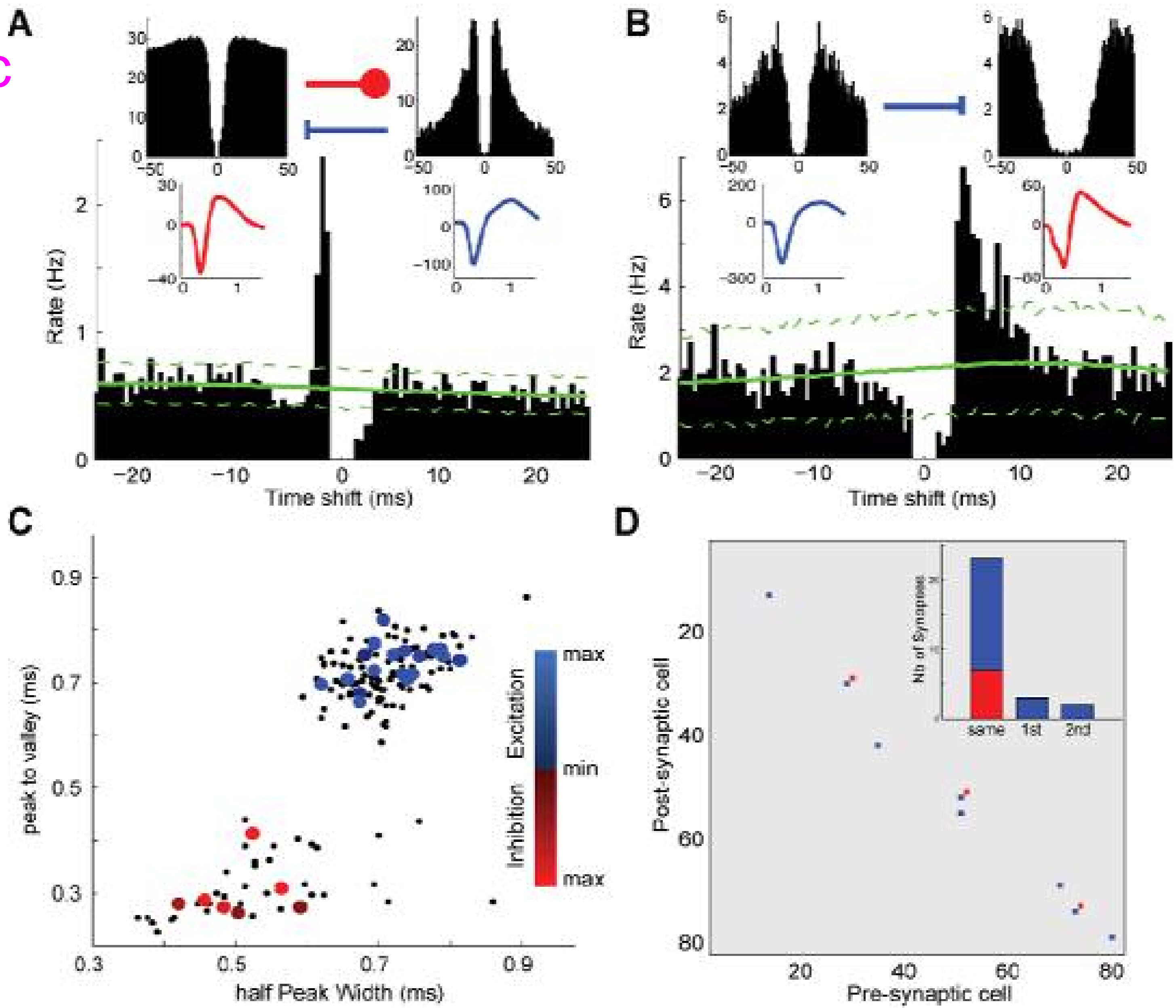






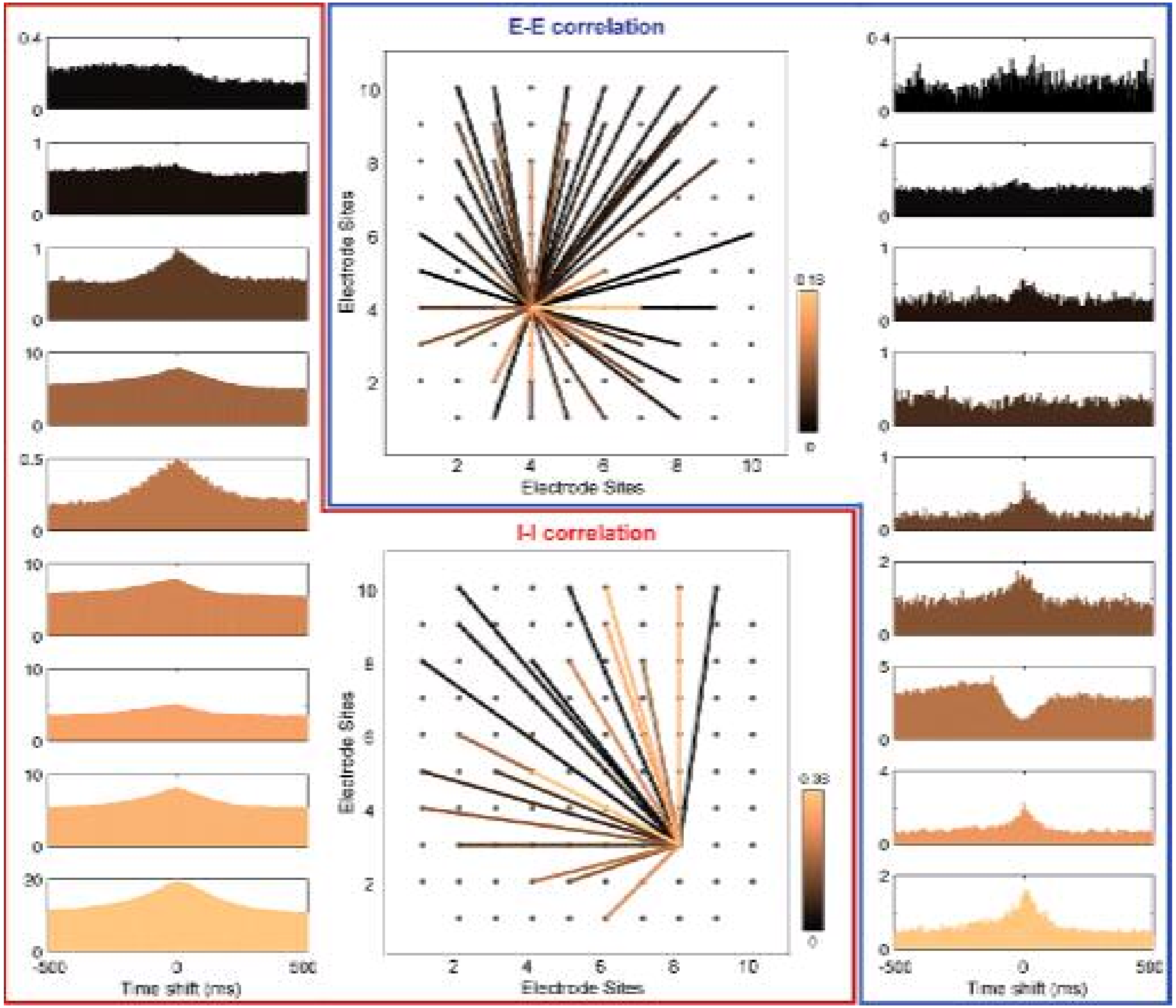
Peyrache et al, *PNAS*, 2012

RS/FS cells monosynaptic connections



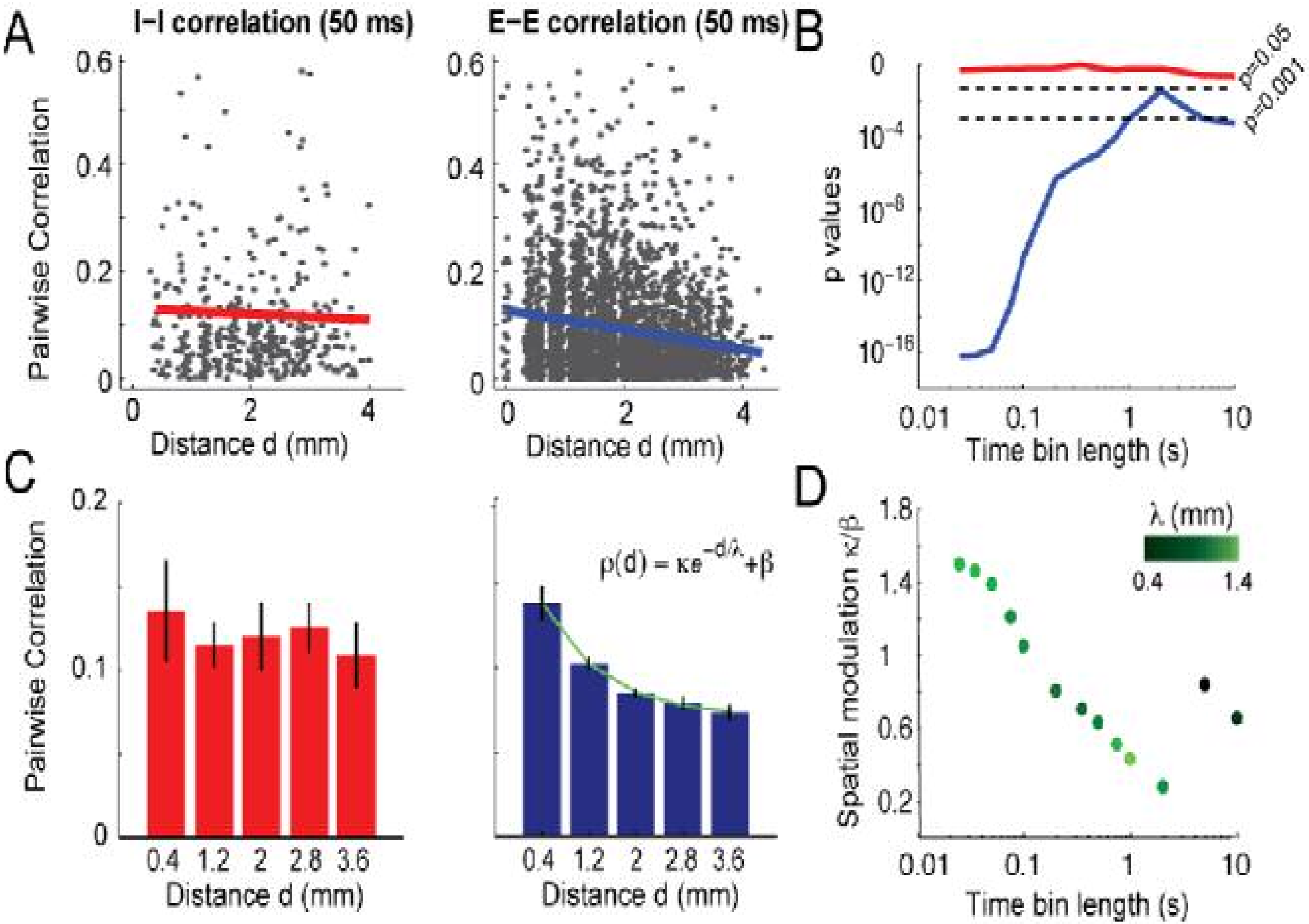
Peyrache et al, *PNAS*, 2012

RS/FS correlations



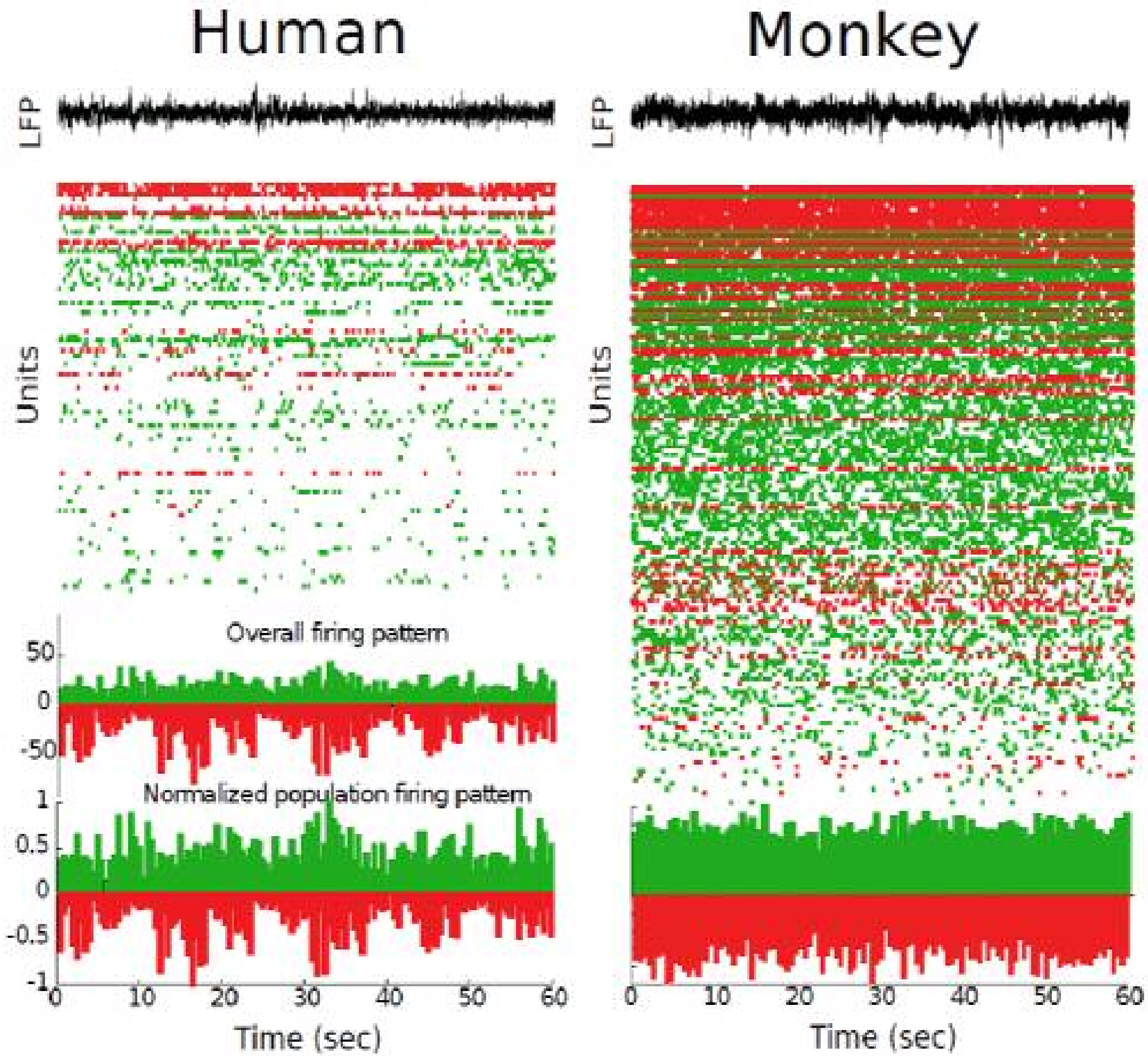
Peyrache et al, *PNAS*, 2012

RS/FS correlations



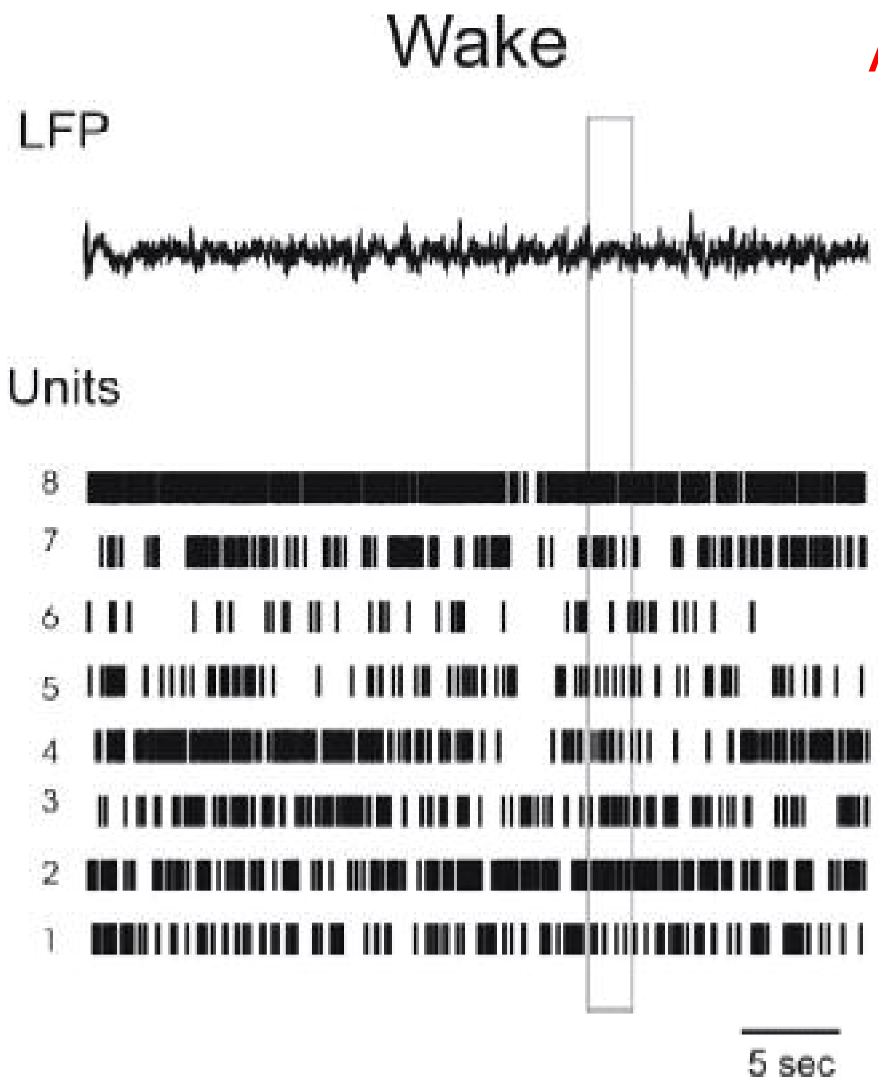
Peyrache et al, *PNAS*, 2012

Irregular activity (awake subjects)

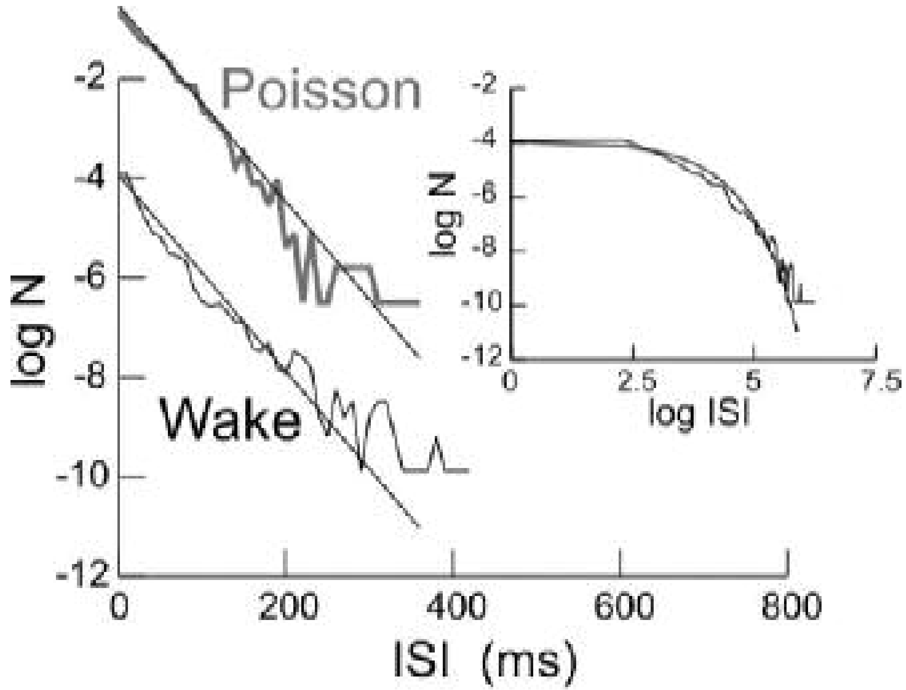


Dehghani et al., *Nature Sci Rep* 2016

Multiunit extracellular recordings in awake cats

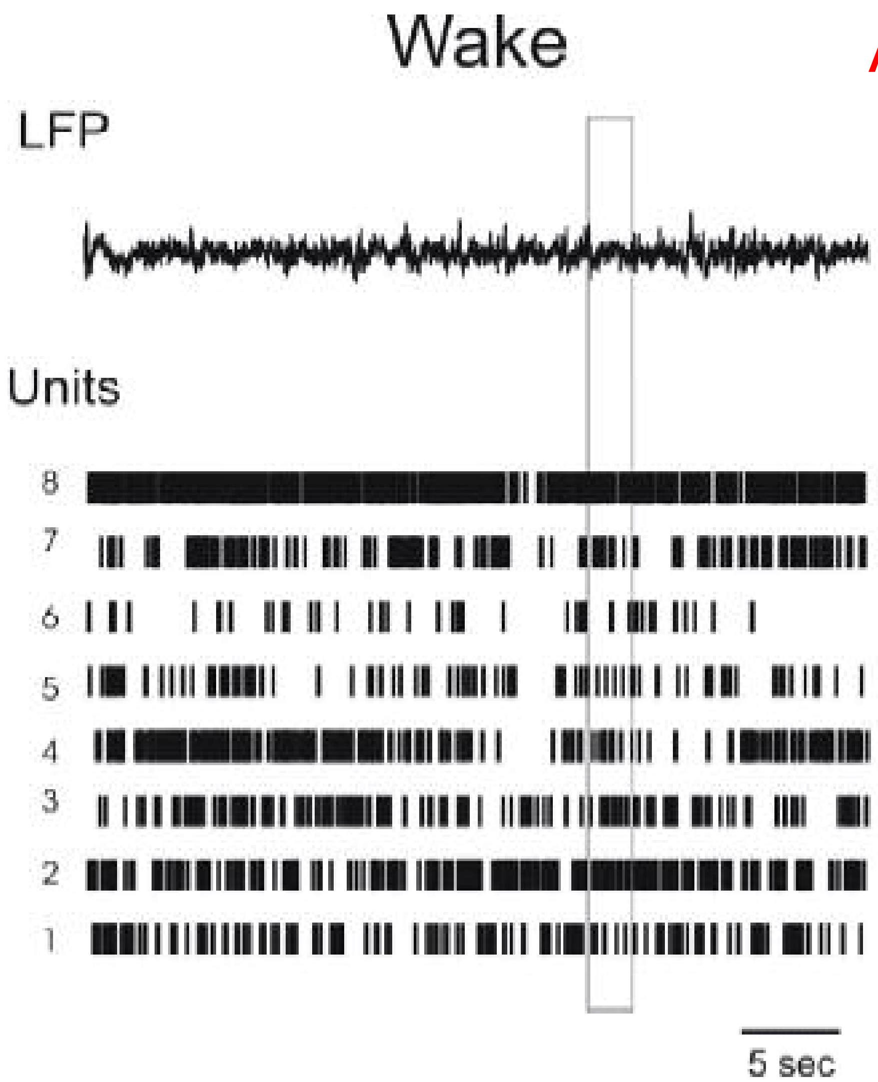


Apparent stochastic dynamics!

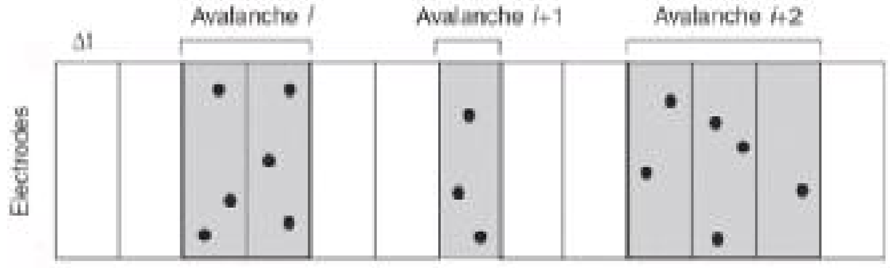


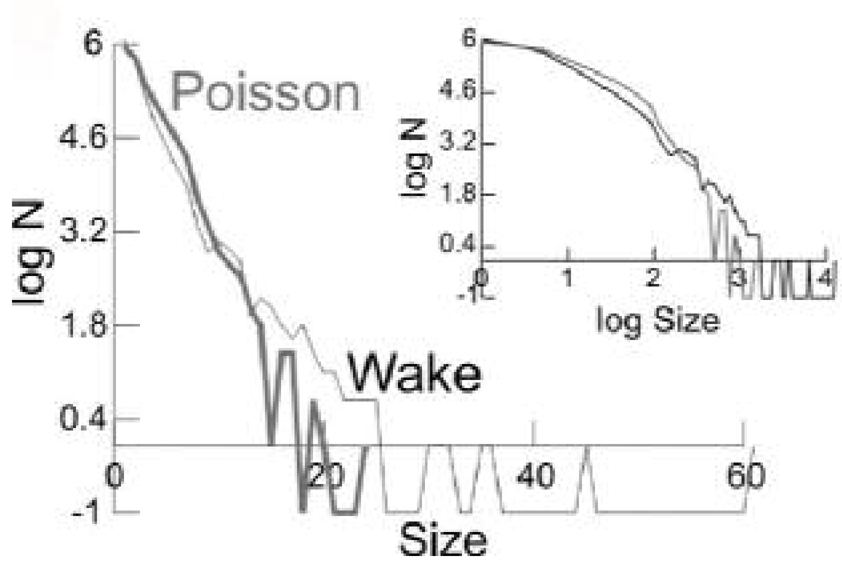
Softky & Koch, *J Neurosci.* 1993
Bedard et al., *Phys Rev Lett* 2006

Multiunit extracellular recordings in awake cats



Apparent stochastic dynamics!

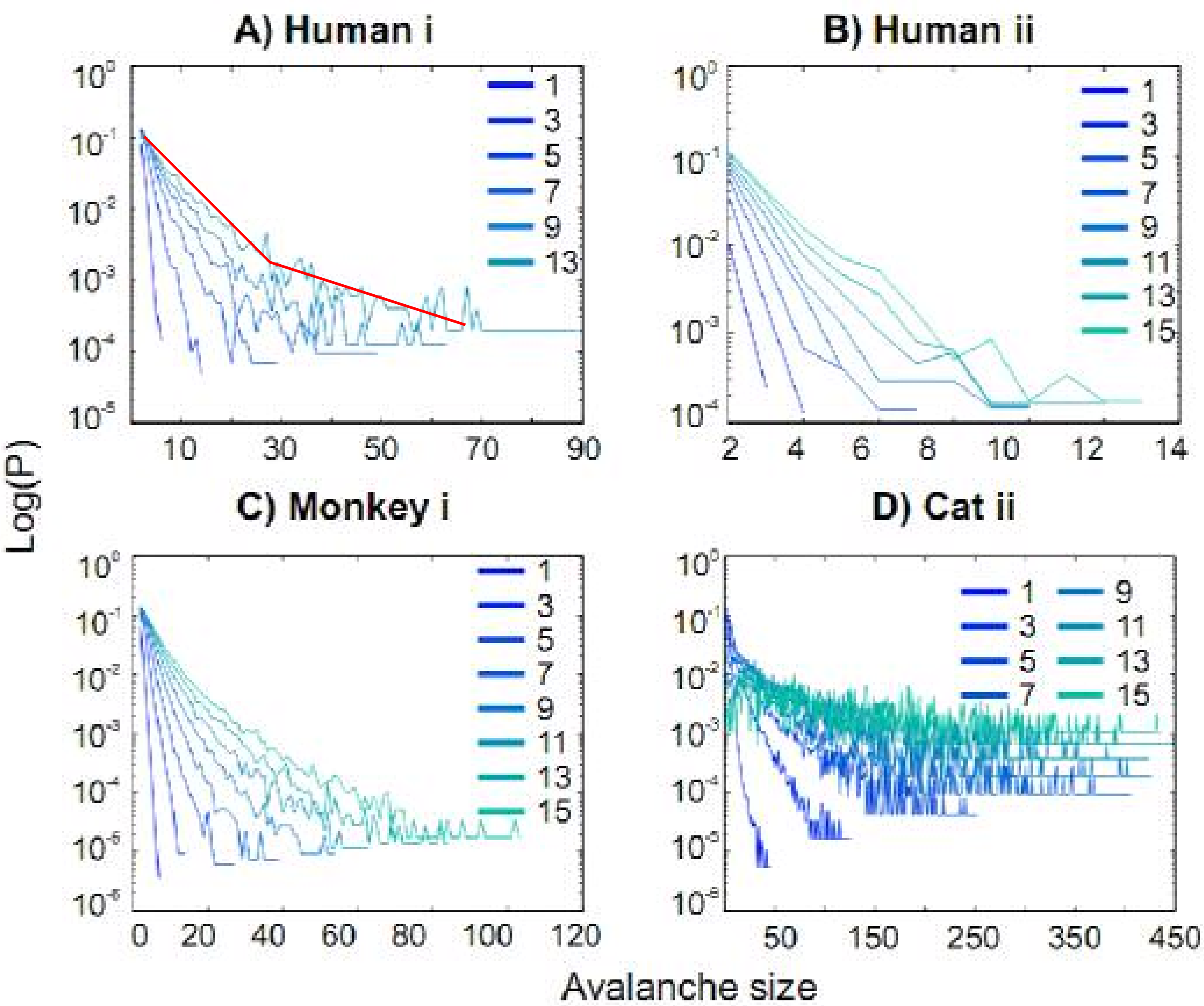




Bedard et al., *Phys Rev Lett* 2006

Avalanche analysis from human neurons

Avalanche analysis in wakefulness (log-linear)

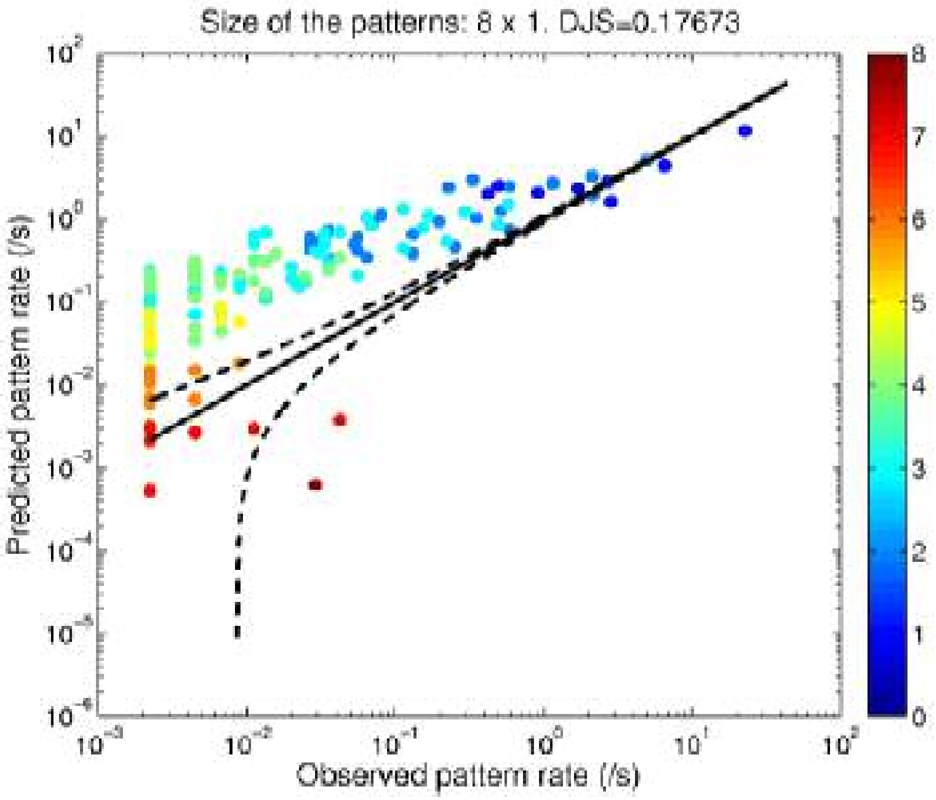


Dehghani et al, *Frontiers Physiol.* 2012

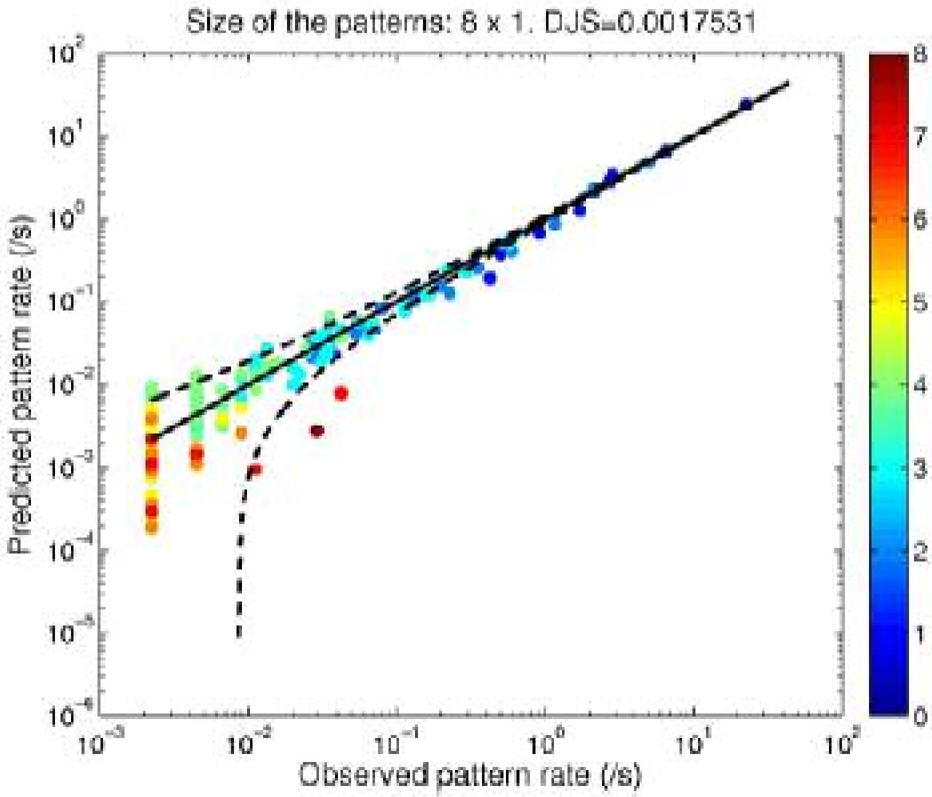
Multiunit extracellular recordings in awake cats

Statistics of spike patterns in cat parietal cortex

Uncorrelated



Correlated

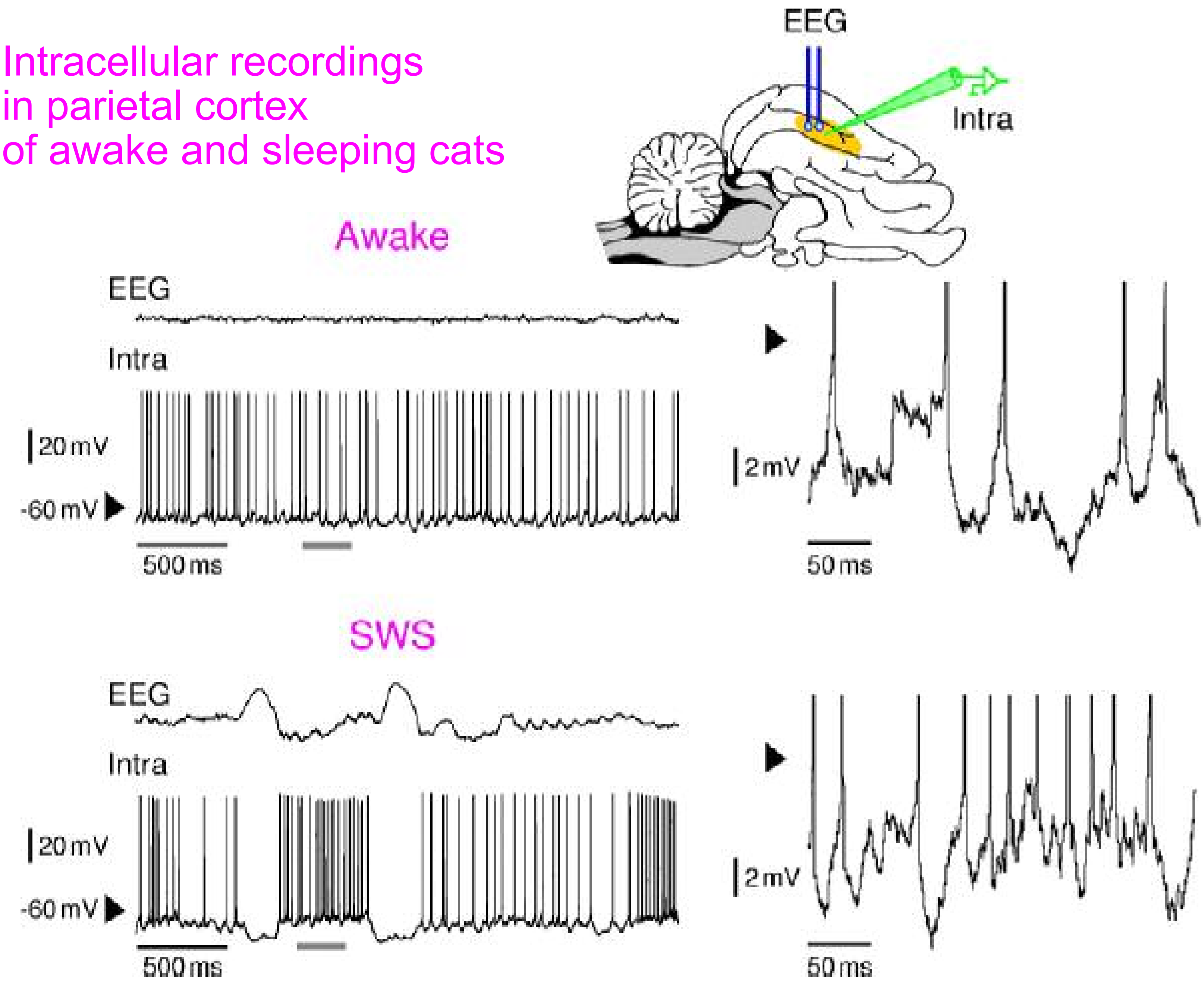


Marre et al.
Physical Review Letters, 2009

High-conductance states
at the cellular level

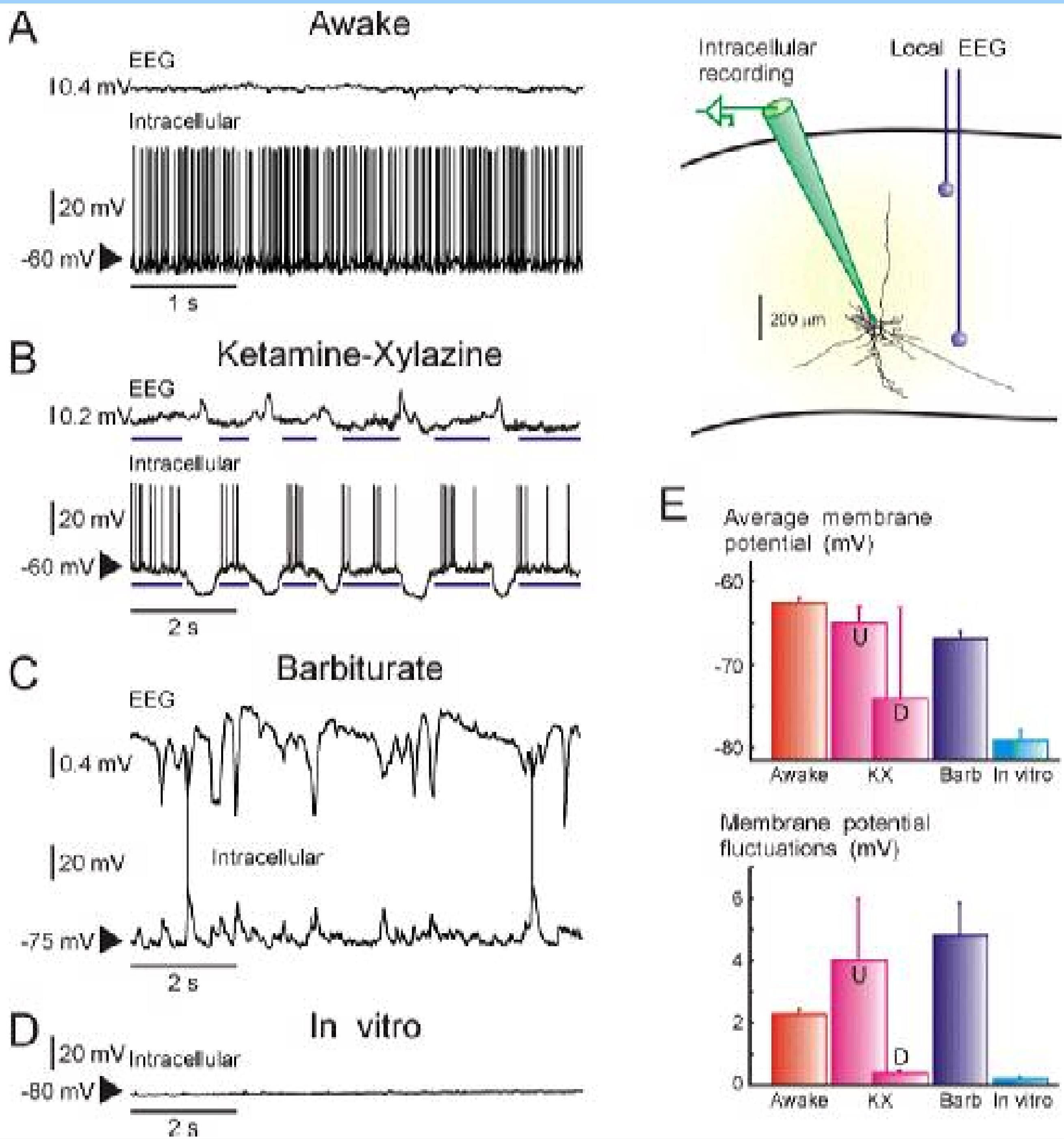
Intracellular characterization of network activity *in vivo*

Intracellular recordings
in parietal cortex
of awake and sleeping cats



(Courtesy of Igor Timofeev, Laval University, Canada)

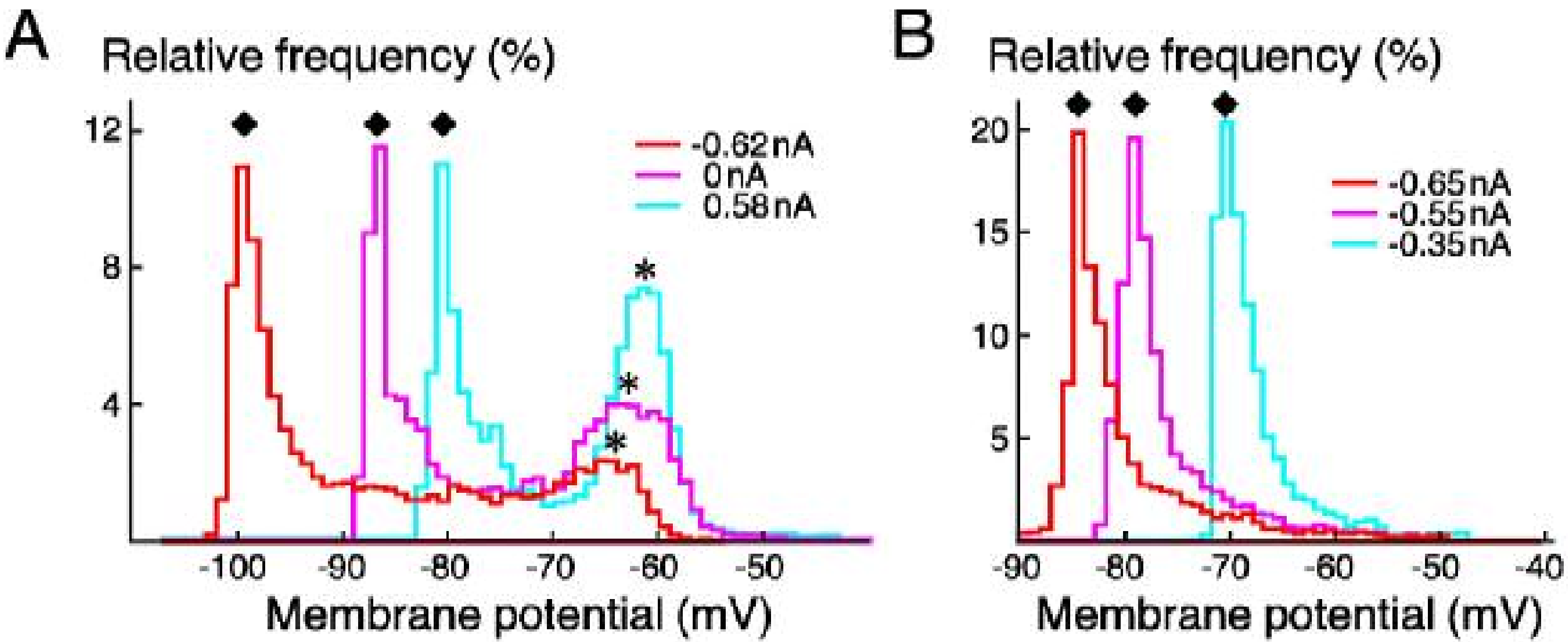
Synaptic "noise" in vivo



Intracellular recordings in parietal cortex in different brain states

Pare et al. *J Neurophysiol*. 1998
Steriade et al. *J Neurophysiol*. 2001
Destexhe et al. *Nature Reviews Neurosci.* 2003

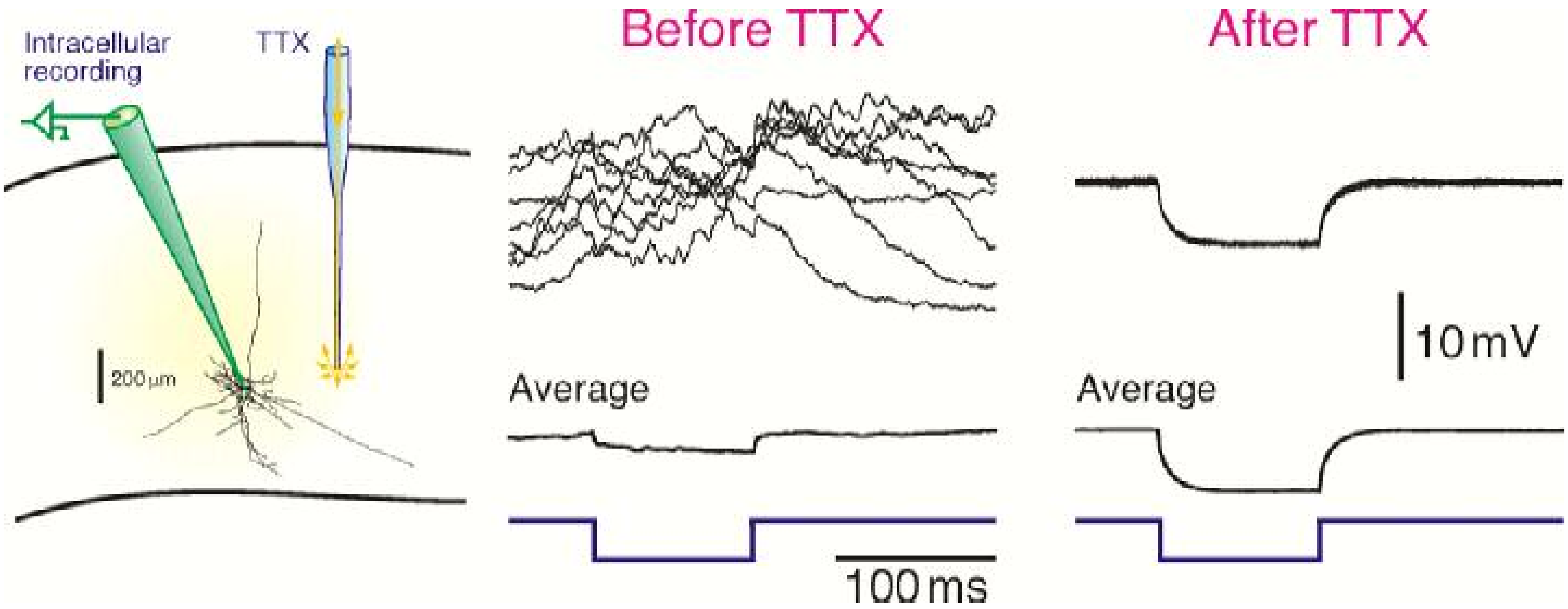
Conductance measurements in vivo



Paré et al., *J. Neurophysiol.* 1998
Destexhe et al., *Nature Reviews Neurosci.* 2003

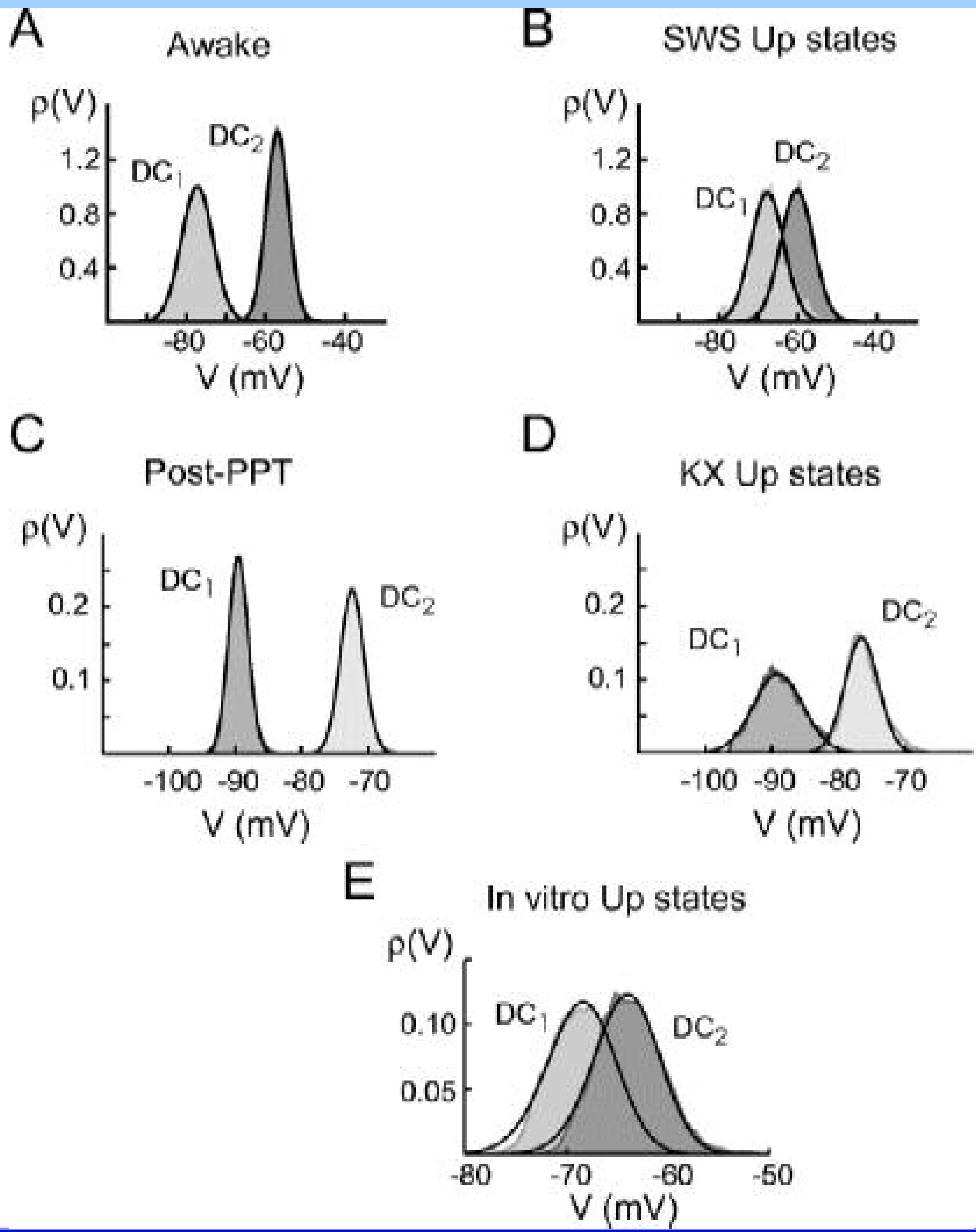
Characterization of up-states *in vivo* by TTX microdialysis

Microperfusion of TTX in cat parietal cortex
under ketamine-xylazine anesthesia



Paré et al., *J. Neurophysiol.* 1998
Destexhe et al., *Nature Reviews Neurosci.* 2003

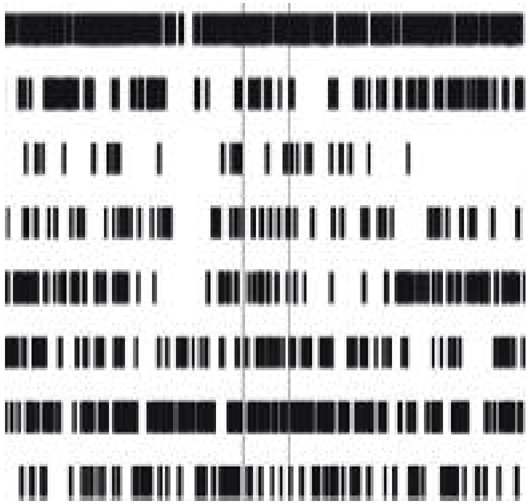
Characterization of up-states *in vivo*



Vm distributions
in different network states

Destexhe & Rudolph
Neuronal Noise, 2012

Rudolph et al.
J. Neurophysiol 2005
J. Neurosci. 2007

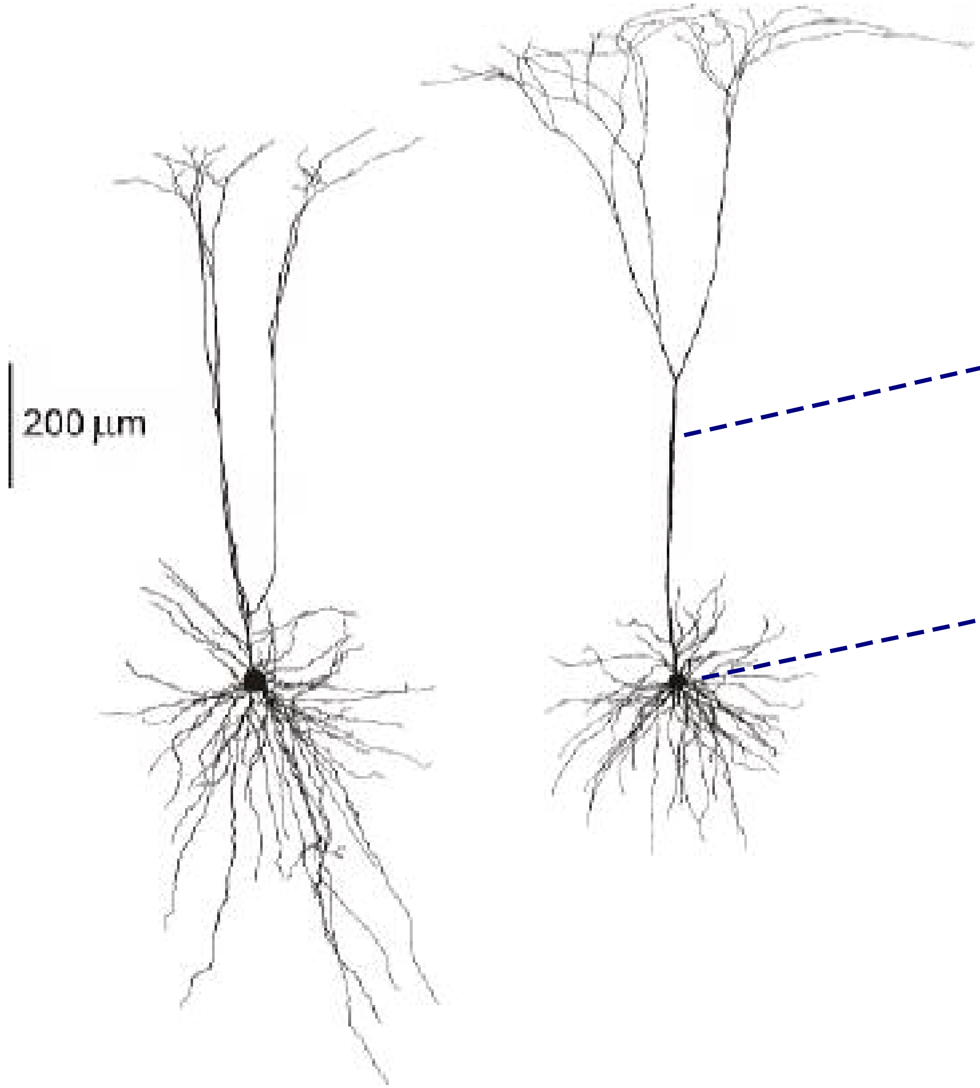


Summary of measurements of neuronal activity in awake animals

- Synaptic activity is intense and noisy, essentially Gaussian distributed (both for Vm and conductances)
- Responsible for a "high-conductance state" (3 to 5-fold larger than resting conductance)
- Statistics of neuronal activity is very close to Poisson processes

Modeling high-conductance states in cortical neurons

Reconstructed neocortical pyramidal neurons with synaptic densities estimated from morphological measurements



Total synapses:
16% inhibitory
84% excitatory

Spine density:
(dendrites > 40 µm from soma)
0.6 spines per μm^2

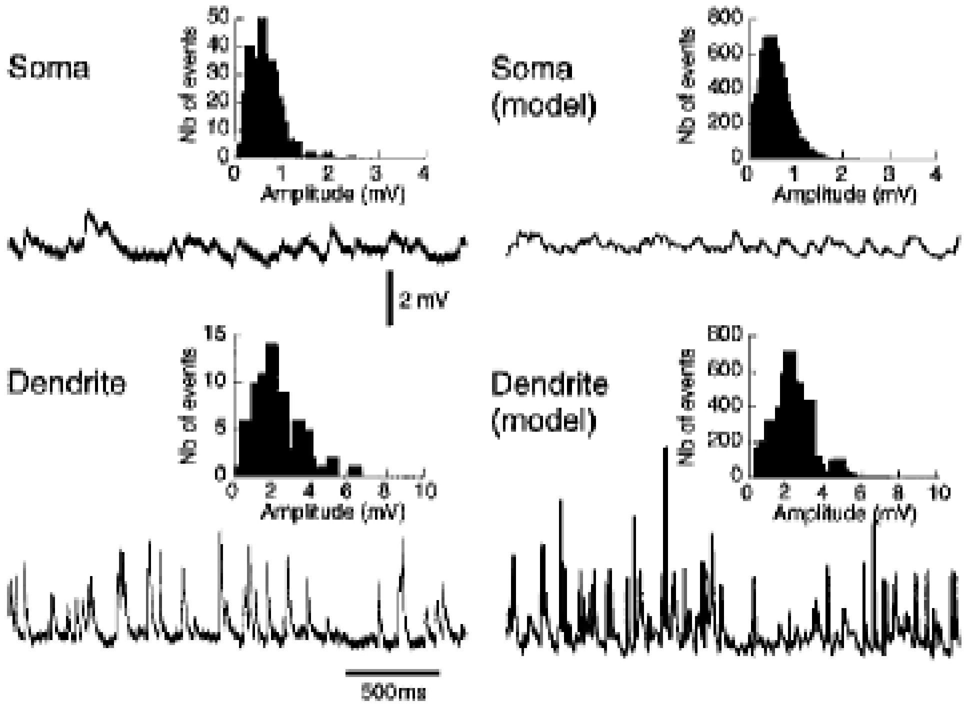
GABAergic synapses on the soma:
10.6 ± 3.7 per 100 μm^2

Total GABAergic synapses:
7% on soma
93% in dendrites

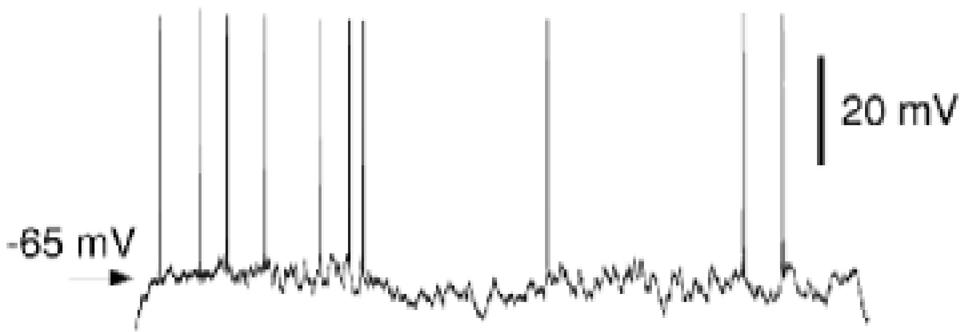
DeFelipe & Fariñas, *Prog. Neurobiol.* (1992);
Larkman, *Comp. Neurol.* (1991)

Estimation of the release parameters of SBA

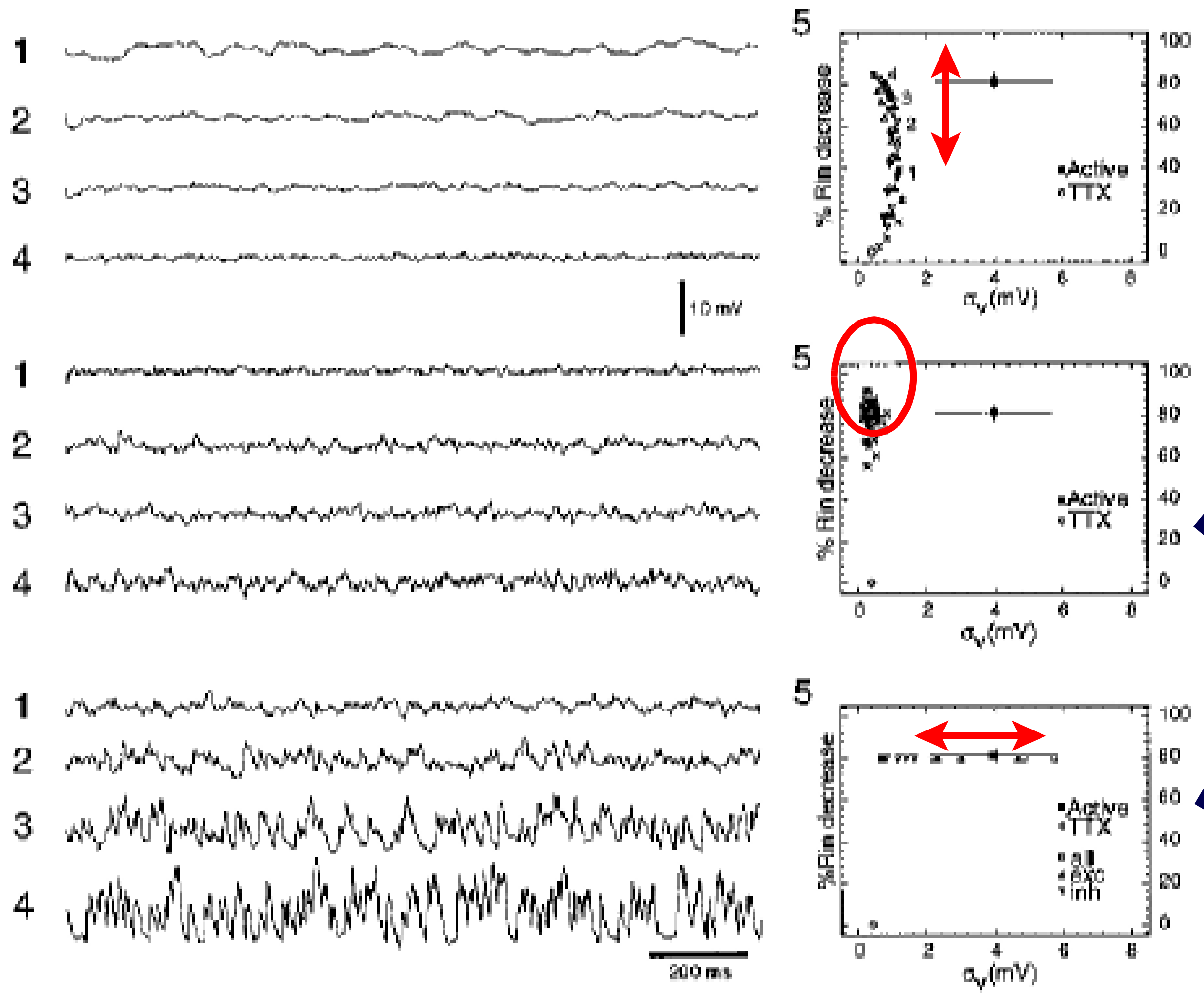
1. Calibration of the model to miniature synaptic events recorded intracellularly *in vivo*



2. Adjustment of release rates to active states recorded intracellularly *in vivo* => Rin, <Vm>, σ_V



Single-cell models of high-conductance states



Constraining release parameters of the model to simulate periods of intense synaptic activity

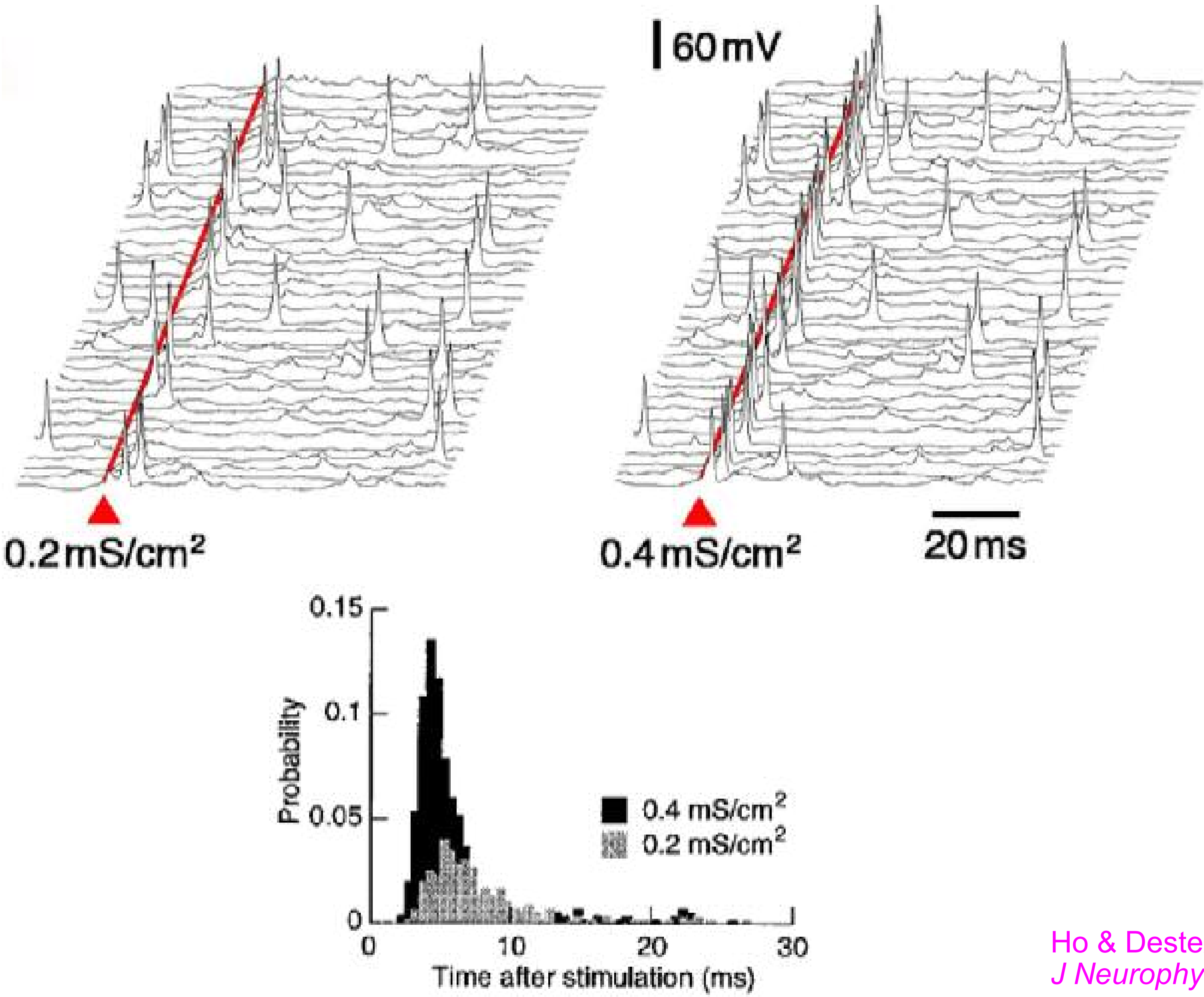
Change in release frequency can account for the experimentally observed R_{in} decrease but not for the standard deviation of V_m

Several combinations of conductance and release frequencies could yield correct R_{in} decrease but failed to reproduce σ_V

Introducing a correlation between release events led to correct R_{in} and σ_V

What are the consequences of high-conductance states on neuronal integrative properties ?

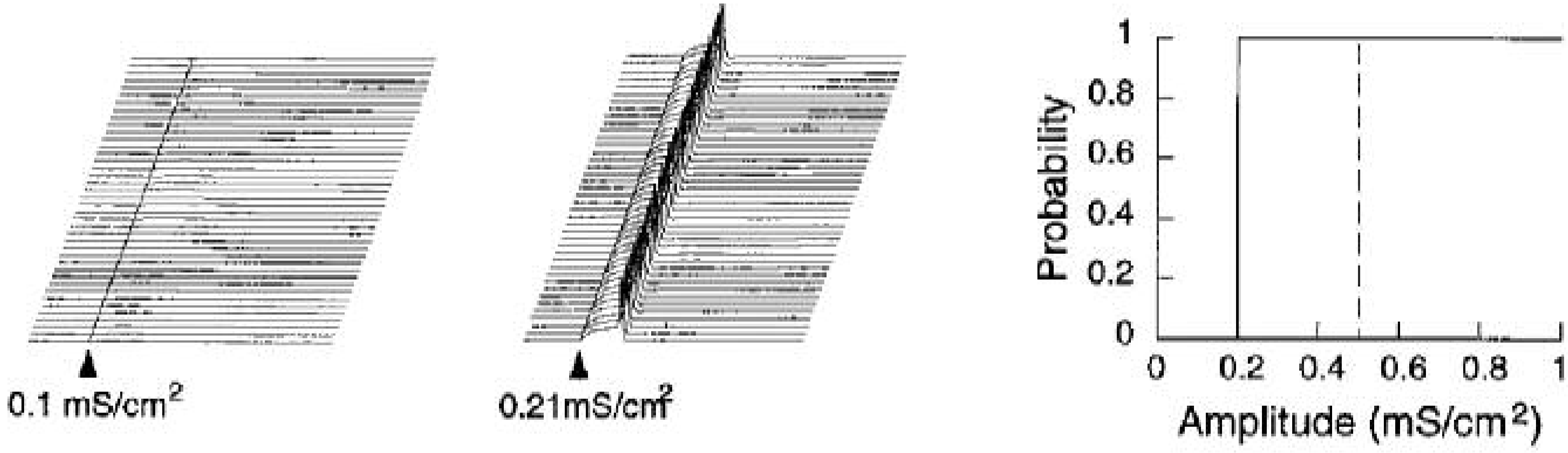
Consequence 1: neurons are probabilistic devices



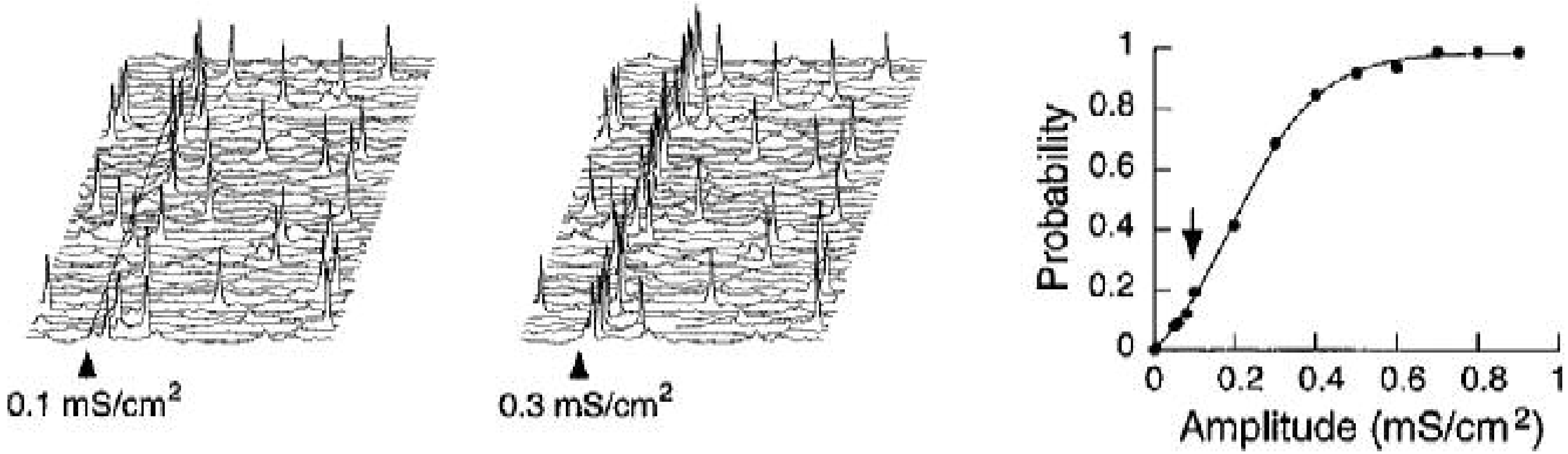
Ho & Destexhe,
J Neurophysiol. 2000

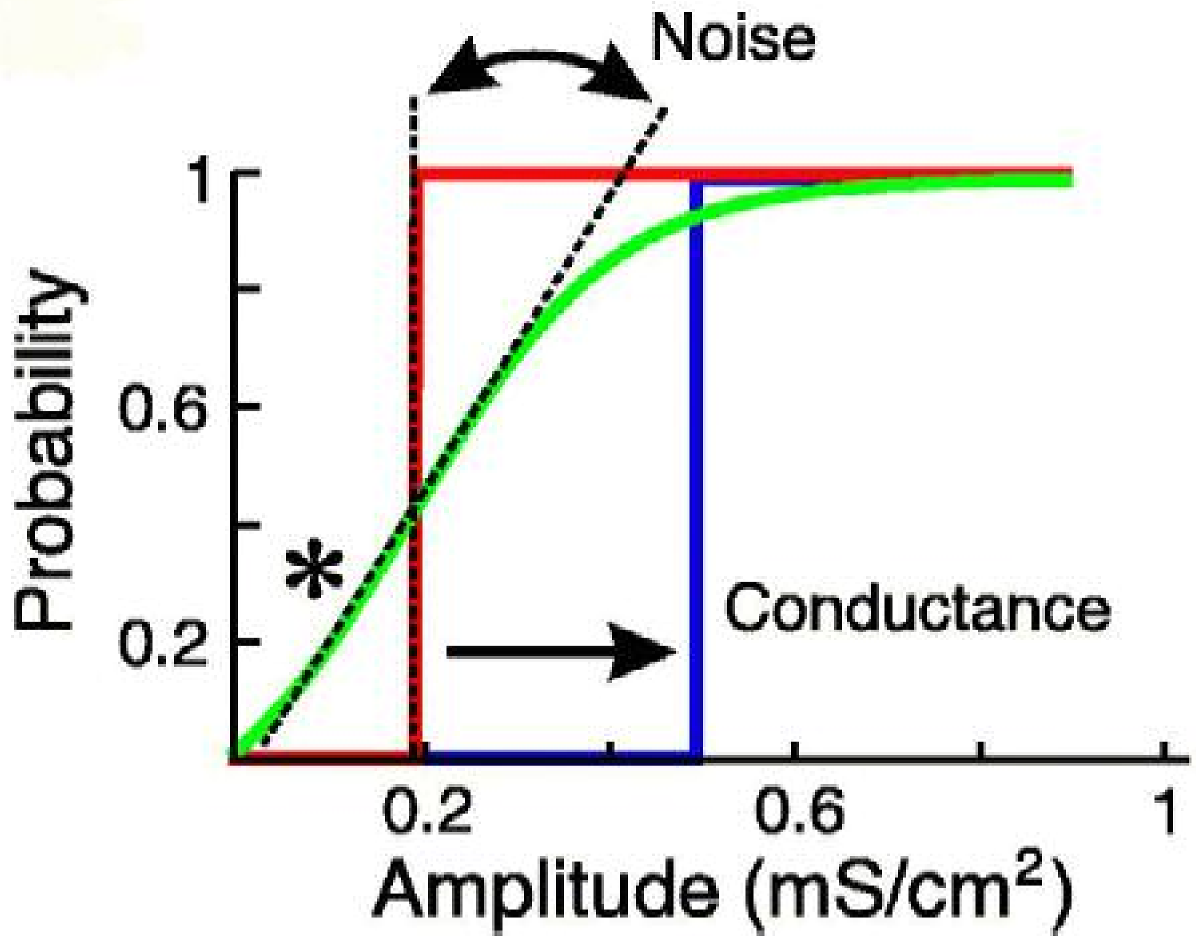
Consequence 2: Enhanced responsiveness

Quiescent



High-conductance noise

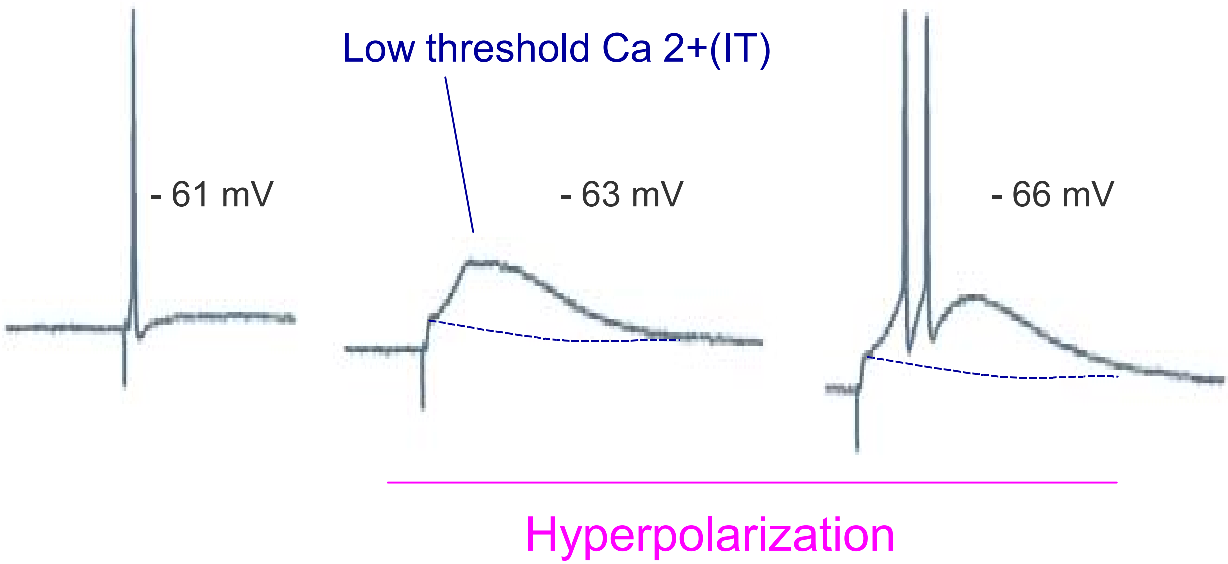



Noise
1
0.6
0.2
Probability
*
Conductance
0.2
0.6
1
Amplitude (mS/cm2)

Dynamic-clamp

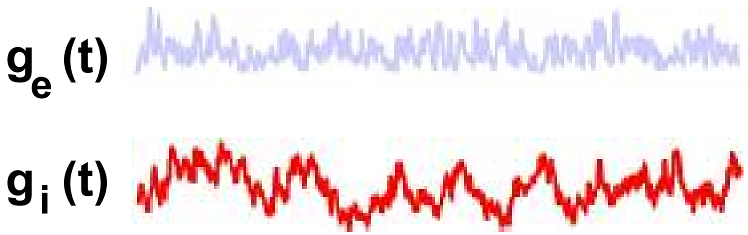
Consequence 5: noise modulates intrinsic properties

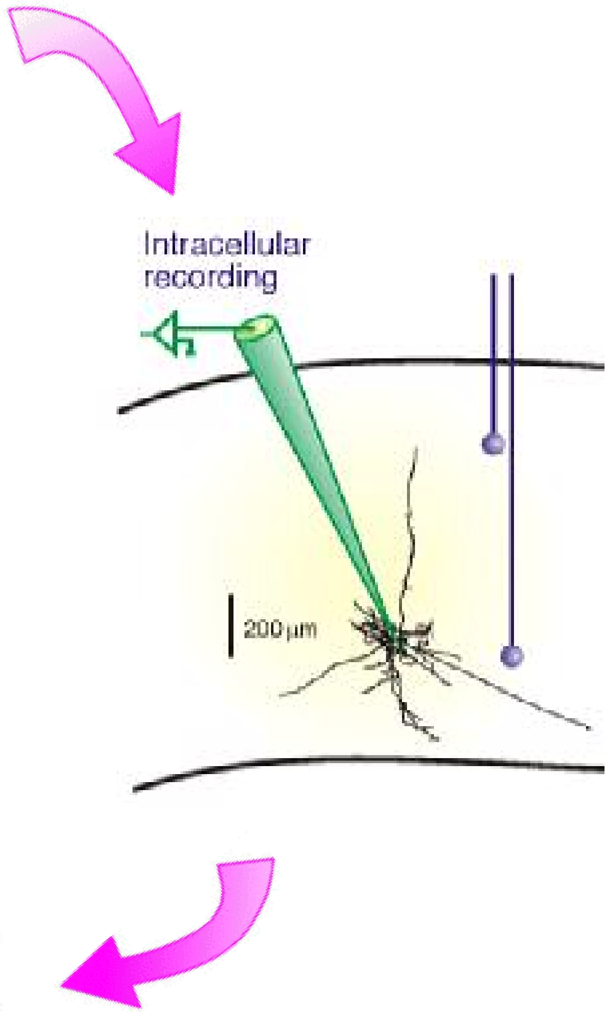
The non-linear properties of thalamocortical cells



Wolfart et al., *Nature Neurosci*, 2005

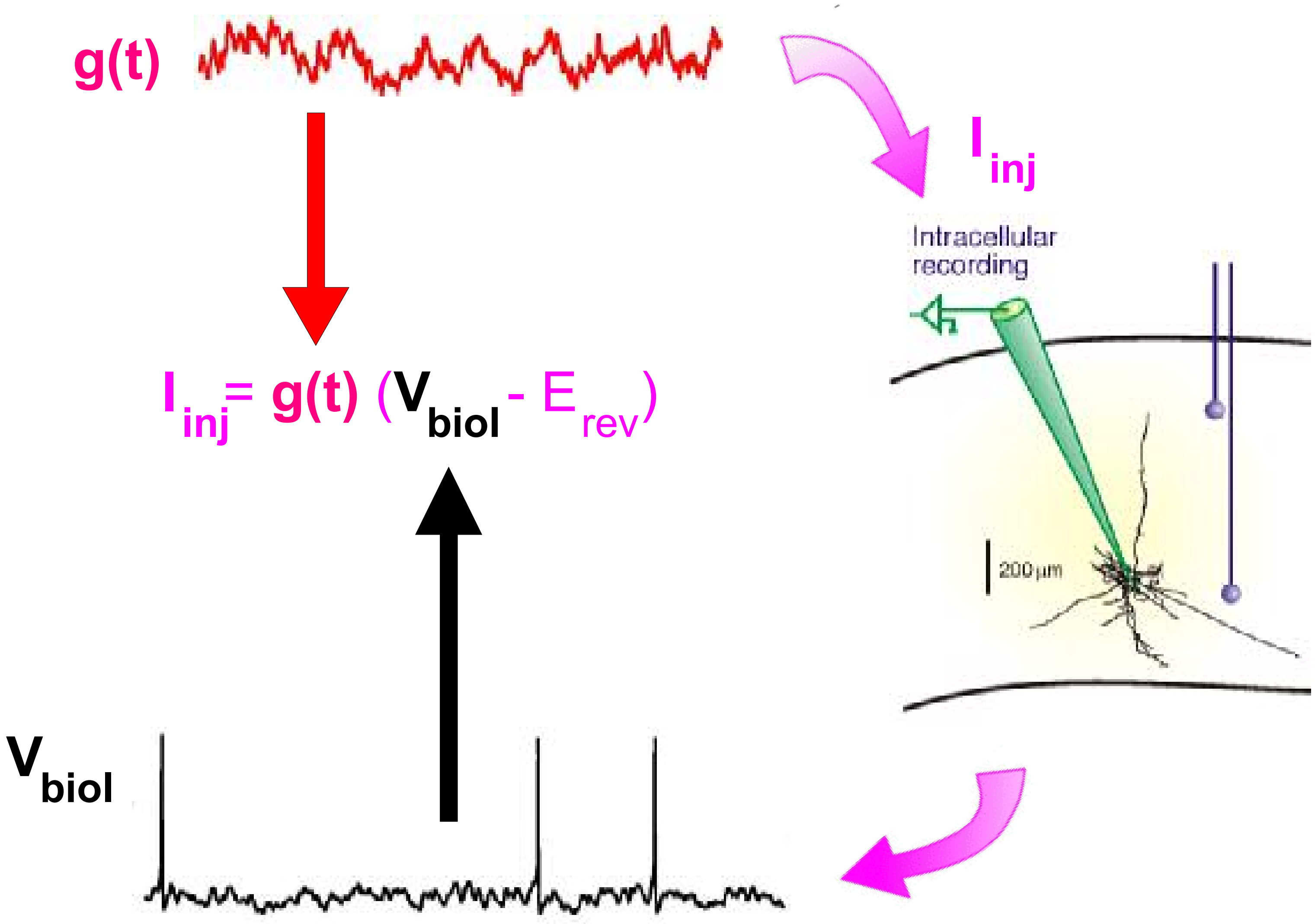
Interaction between Models and Living Cells





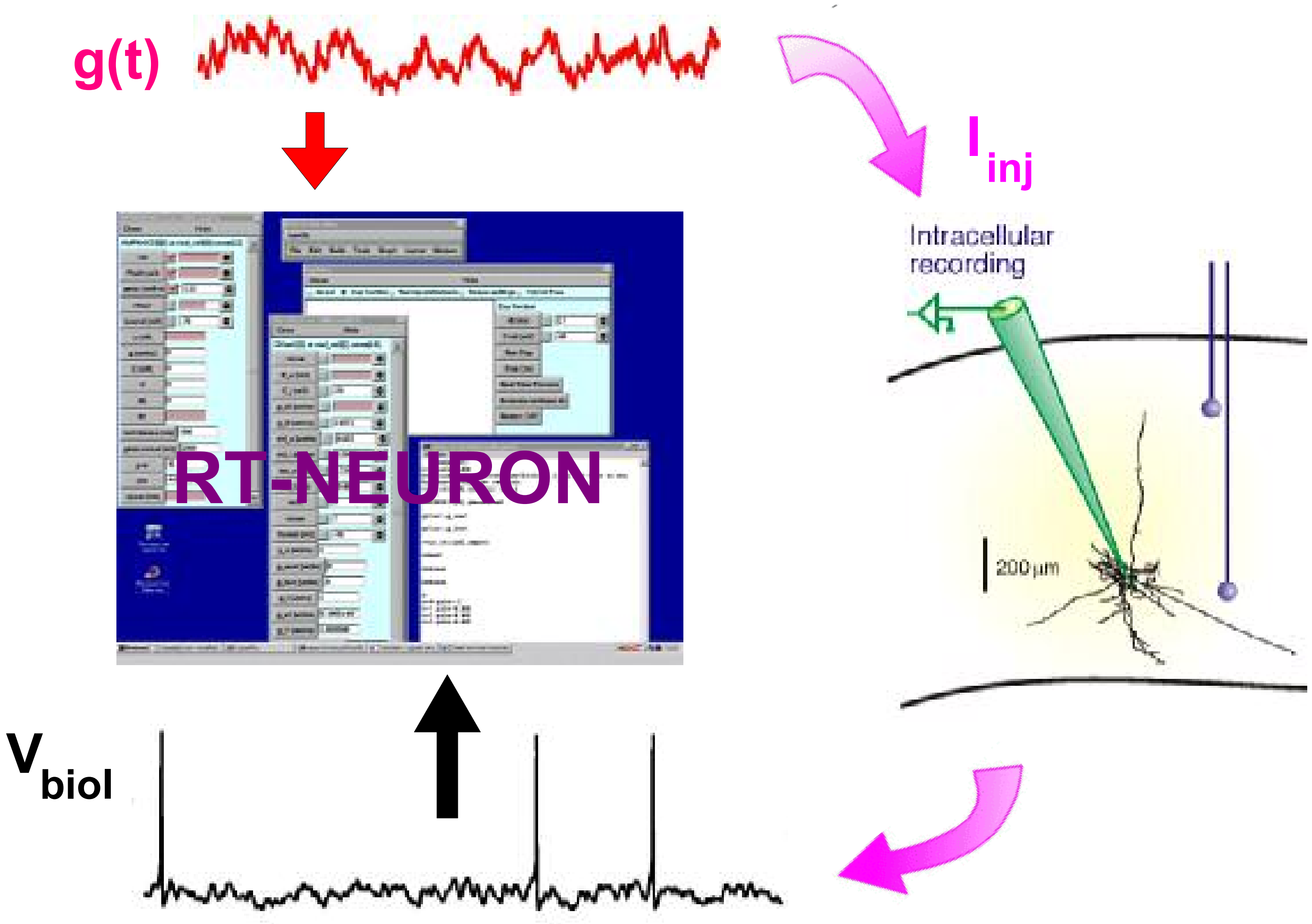
"Controlling synaptic noise": Real-time injection of stochastic synaptic conductances (dynamic-clamp)

The Dynamic-clamp



Robinson & Kawai, 1993
Sharp et al., 1993

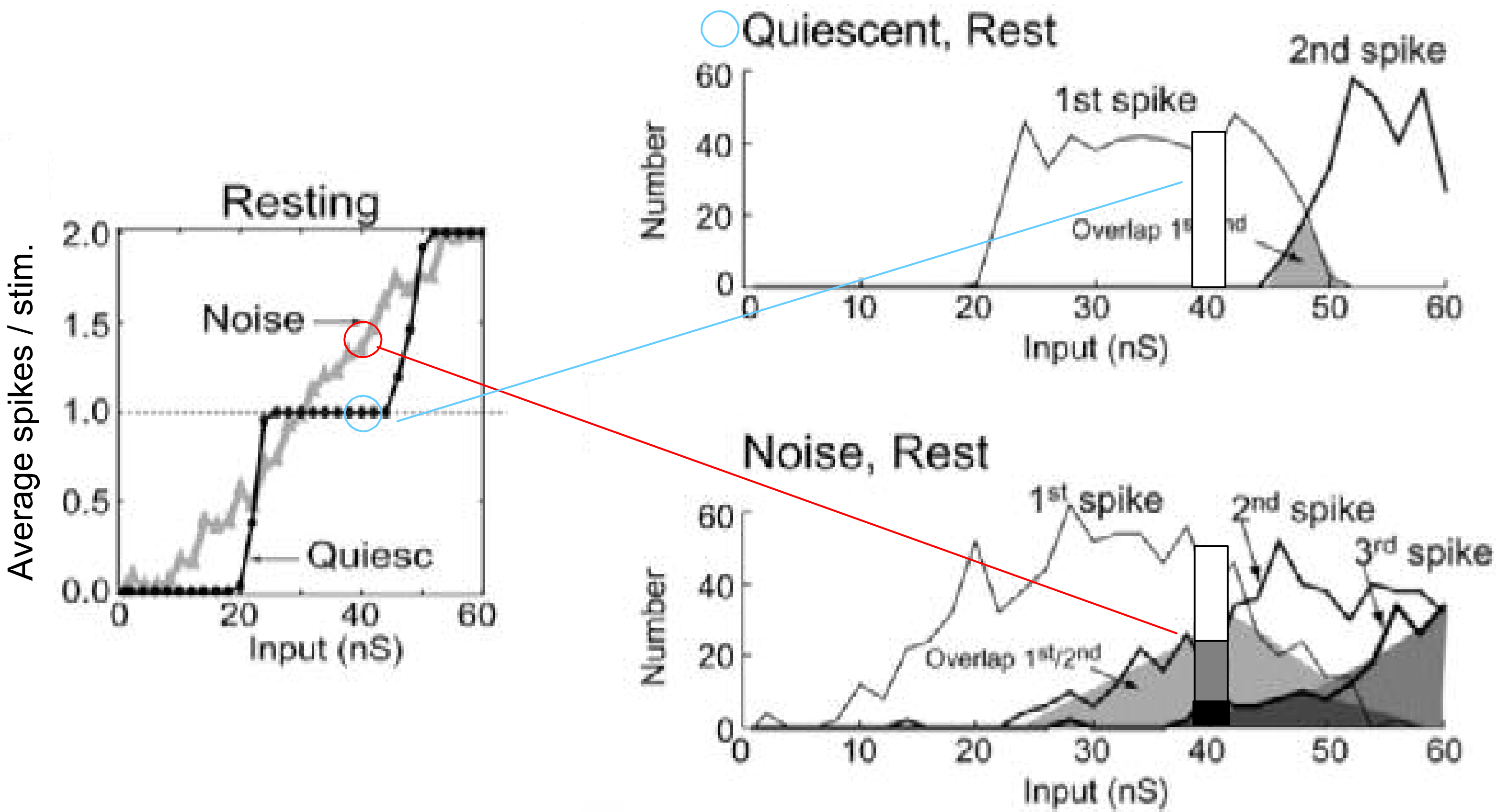
The Dynamic-clamp



RT-NEURON is developed by
Gwen LeMasson, University of Bordeaux

Effect of synaptic noise on intrinsic properties

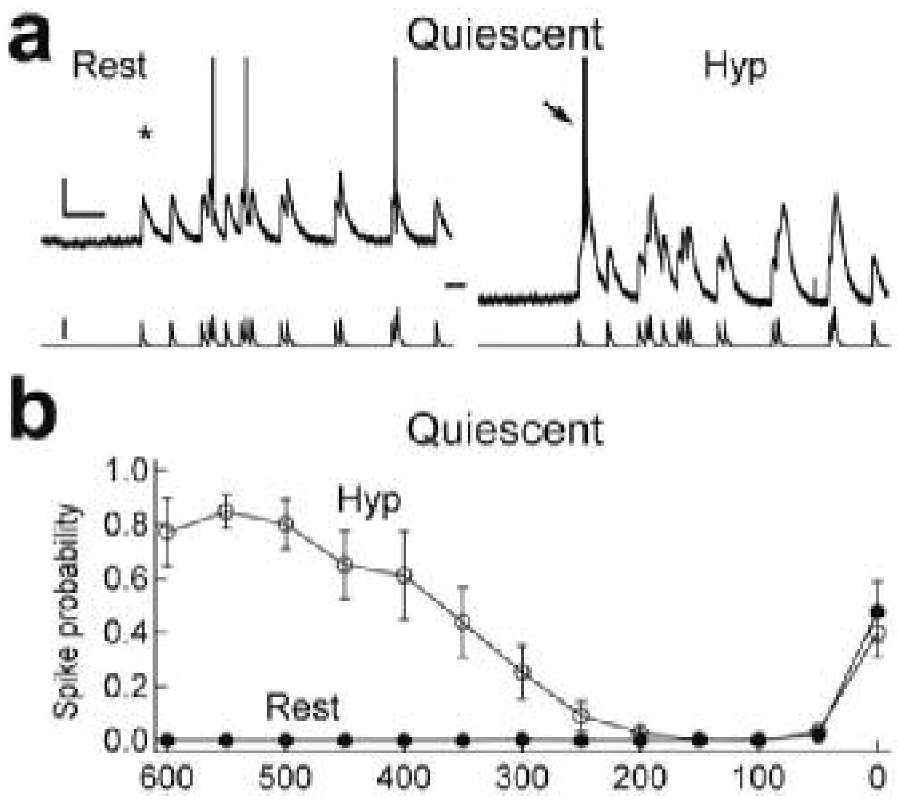
Synaptic background activity mixes single spike
and burst responses in thalamocortical cells



Wolfart et al., *Nature Neurosci*, 2005

Effect of synaptic noise on intrinsic properties

Equalization of spike probabilities

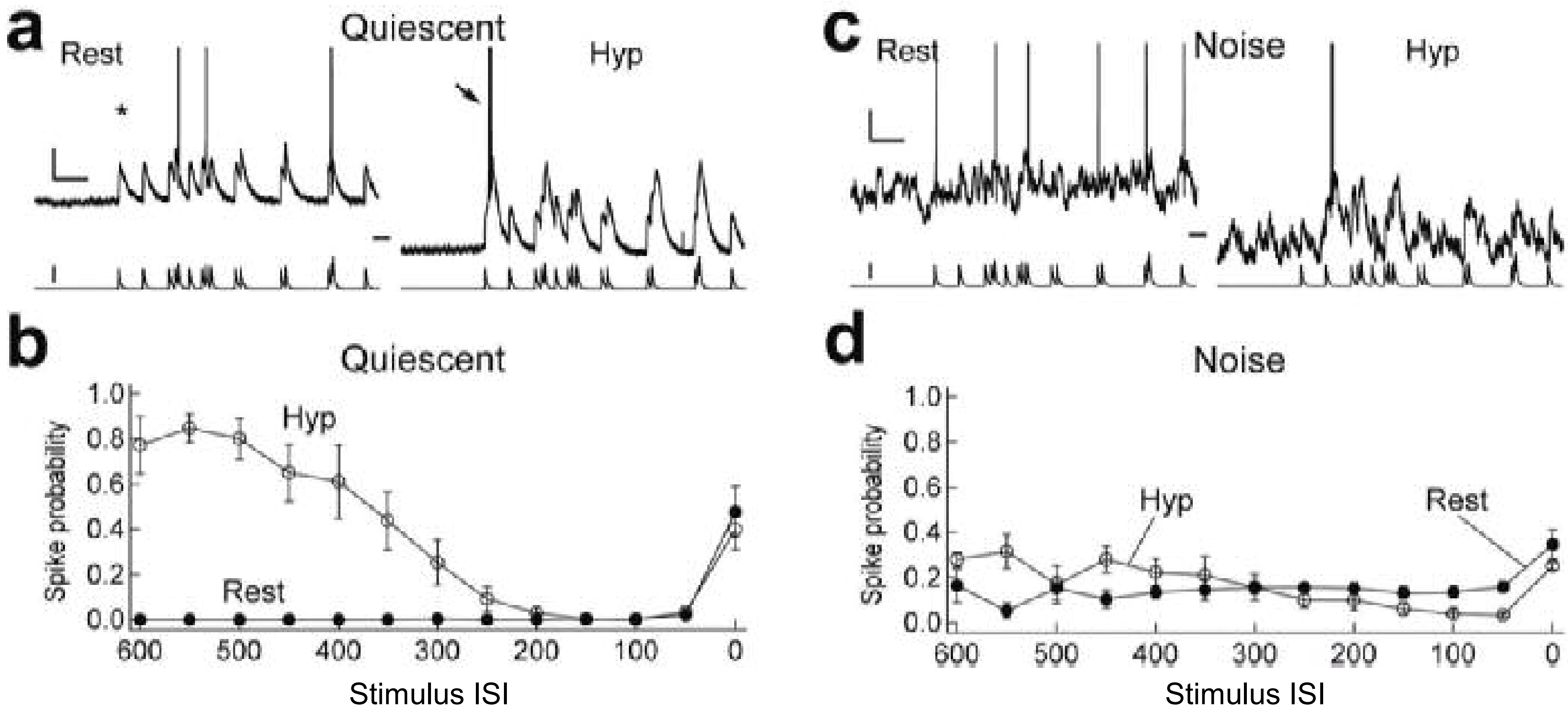


Stimulus ISI

Wolfart et al., *Nature Neurosci*, 2005

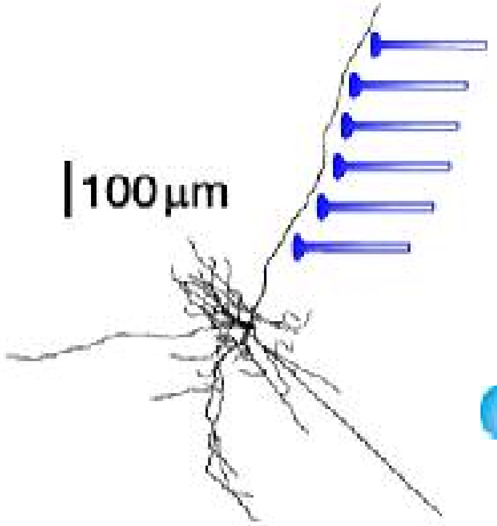
Effect of synaptic noise on intrinsic properties

Equalization of spike probabilities



Wolfart et al., *Nature Neurosci*, 2005

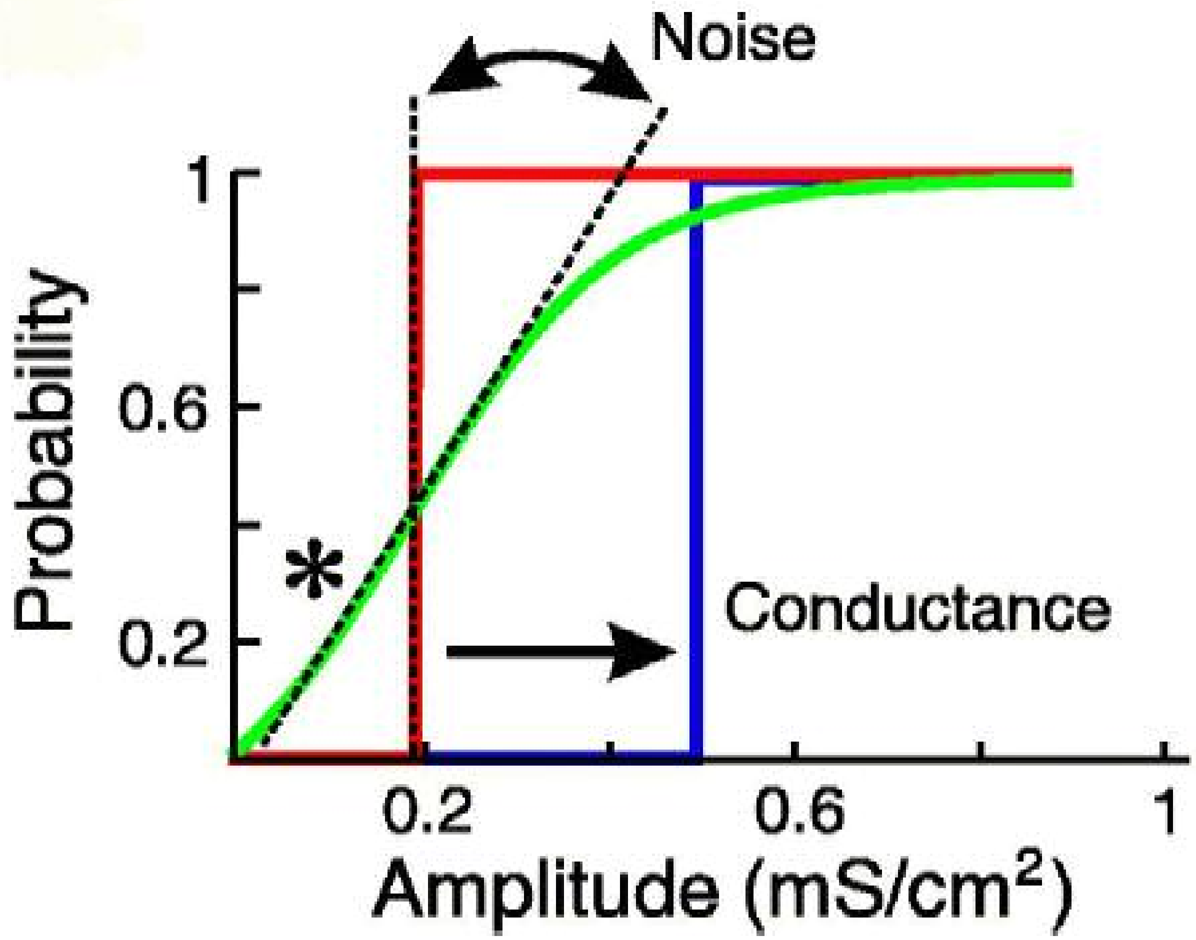
Consequences on integrative properties



Conclusions

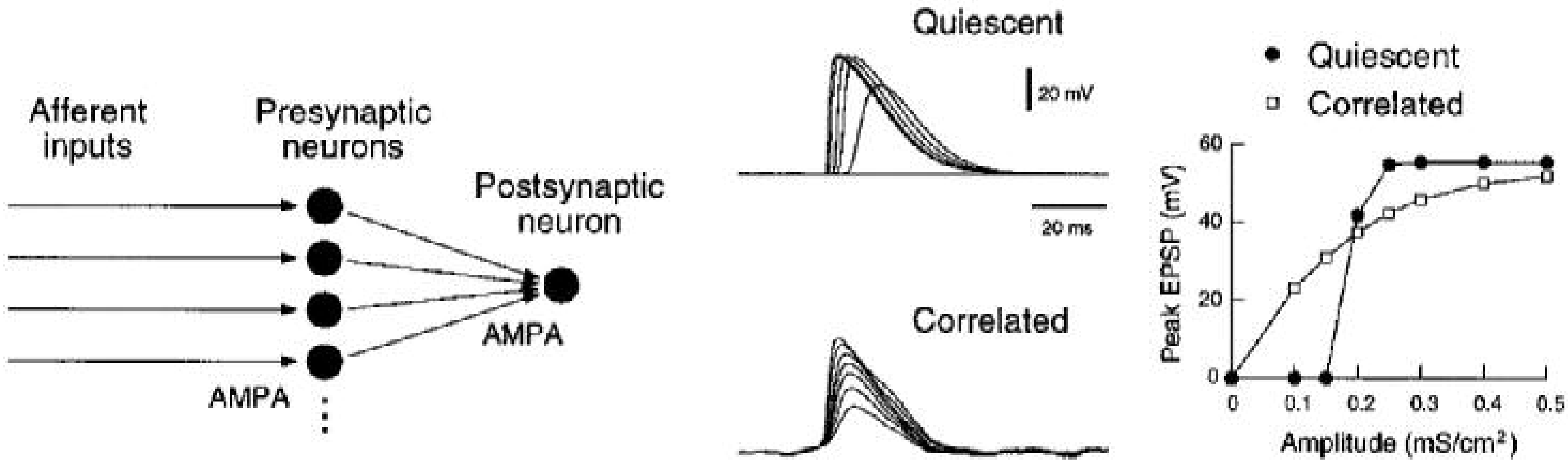
- Central neurons are probabilistic devices due to the presence of synaptic noise
- Enhanced responsiveness (small inputs give a non-zero probability of response)
  Confirmed experimentally by dynamic-clamp
- Equalization of synaptic efficacies (probability of axonal spike initiation is weakly location dependent)
- Sharper temporal processing
- Intrinsic properties are different in the presence of synaptic noise (ie, under in vivo conditions...)

Enhanced responsiveness at the network level ?


Noise
1
0.6
0.2
Probability
*
Conductance
0.2
0.6
1
Amplitude (mS/cm2)

Enhanced responsiveness at the network level

Synaptic background activity enhances the detection of synaptic inputs at the network level



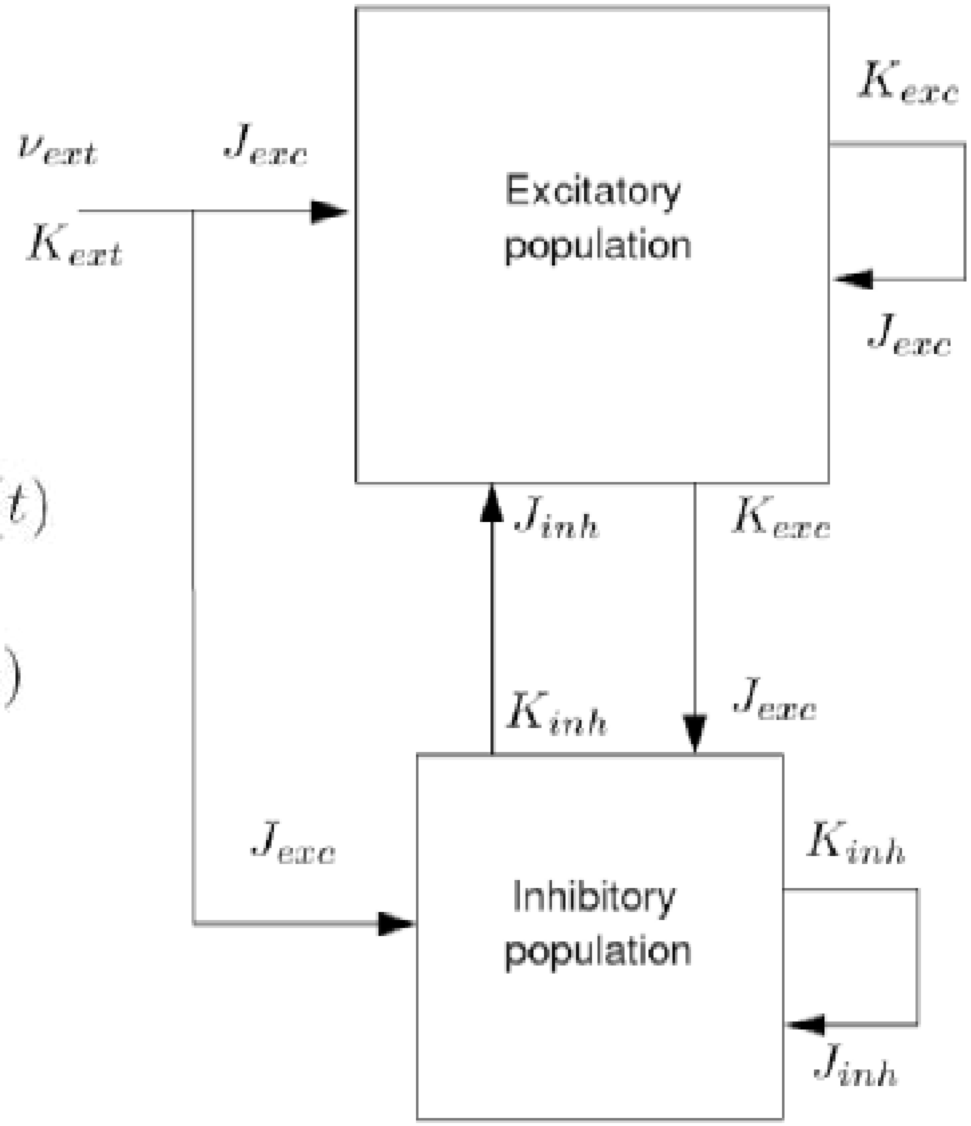
Ho & Destexhe,
J Neurophysiol. 2000

Network models of self-sustained irregular states

Networks of IF neurons

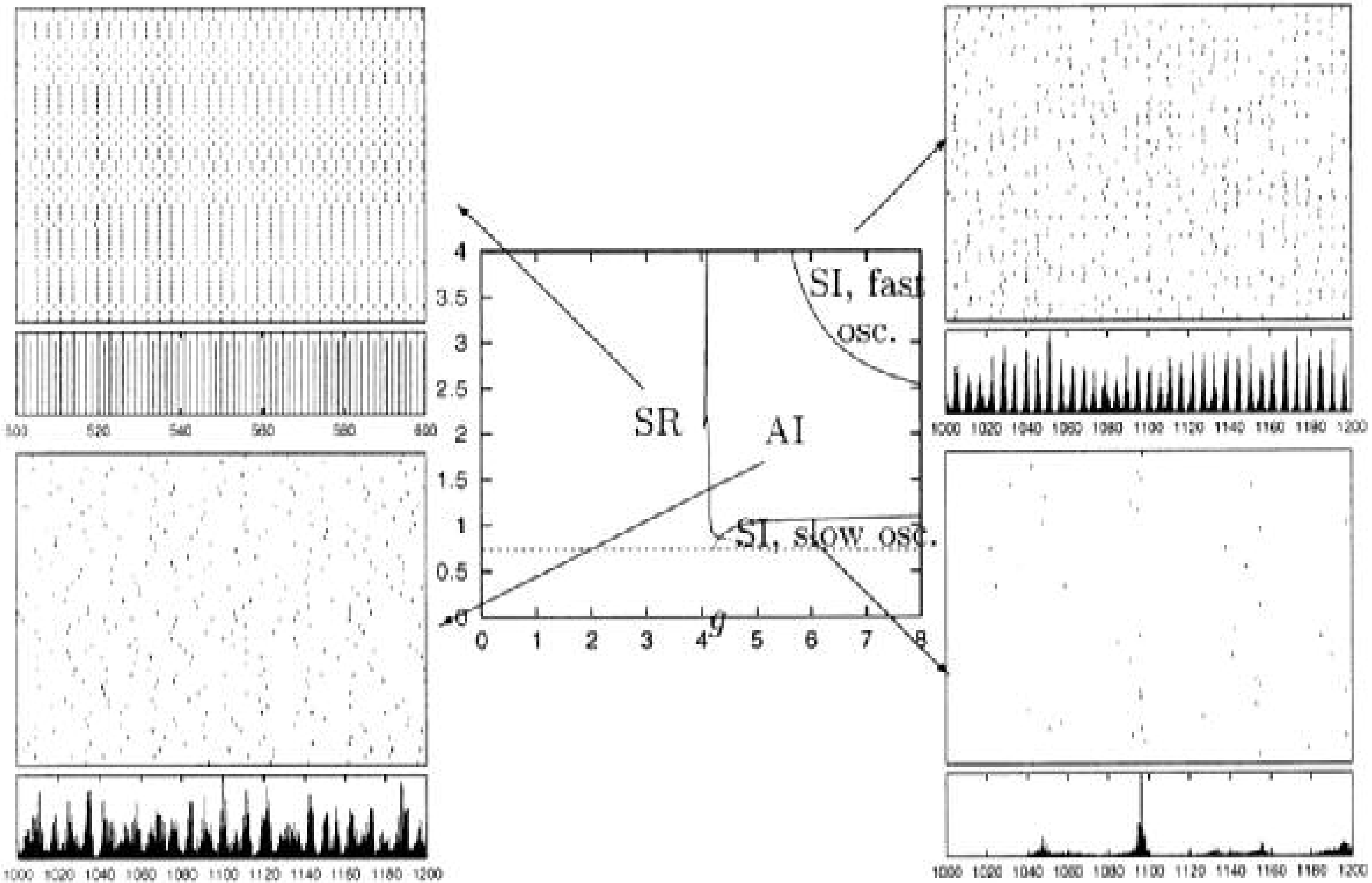
$$C_m \frac{dV_i}{dt} = -g_L(V_i - E_L) + S(t)$$

$$- \sum_j g_{ji}(t)(V_i - E_j)$$



Network models of asynchronous irregular states

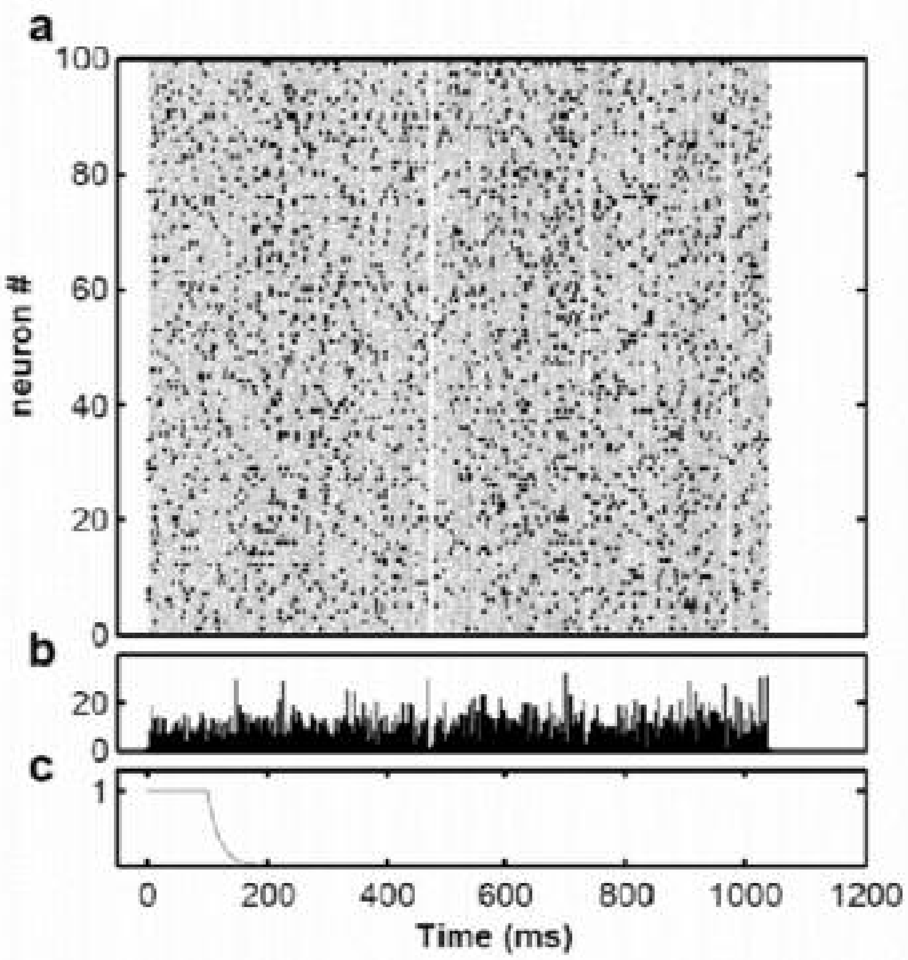
Networks of IF neurons



Brunel, *J Physiol Paris*, 2000

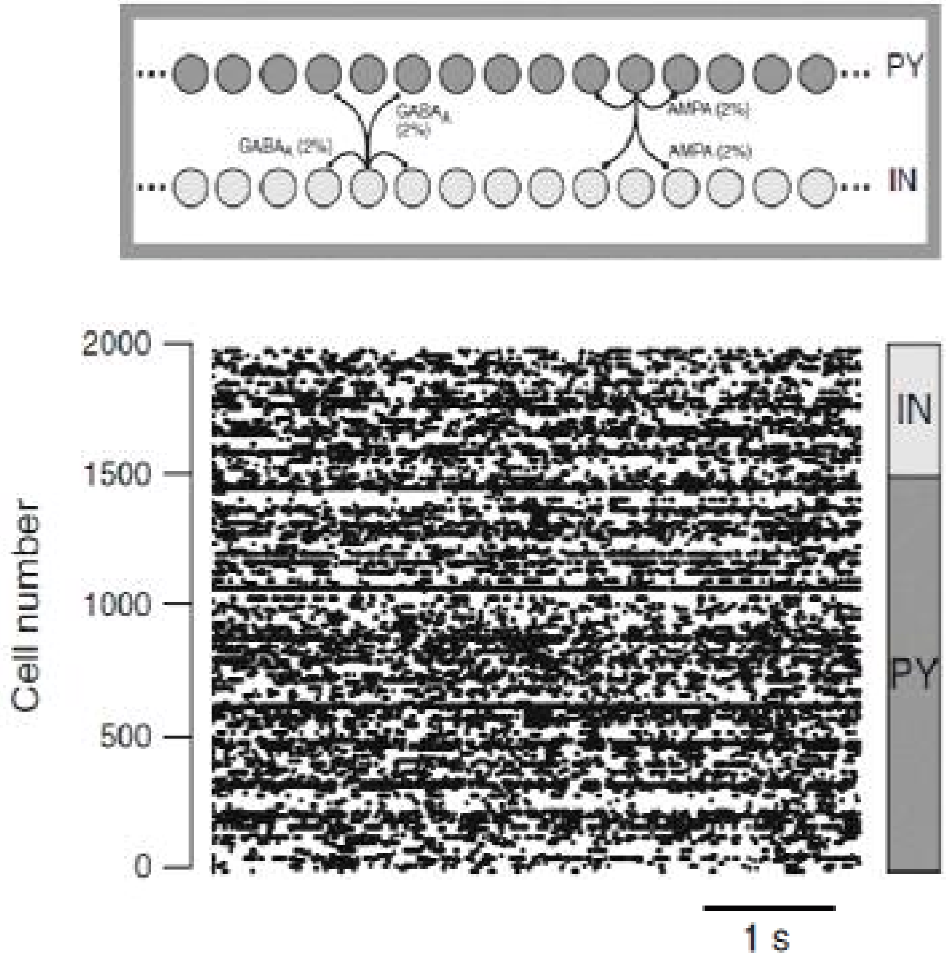
Self-sustained asynchronous irregular states

Networks of
IF neurons
(conductance-based)



Kumar et al.
Neural Computation 2008

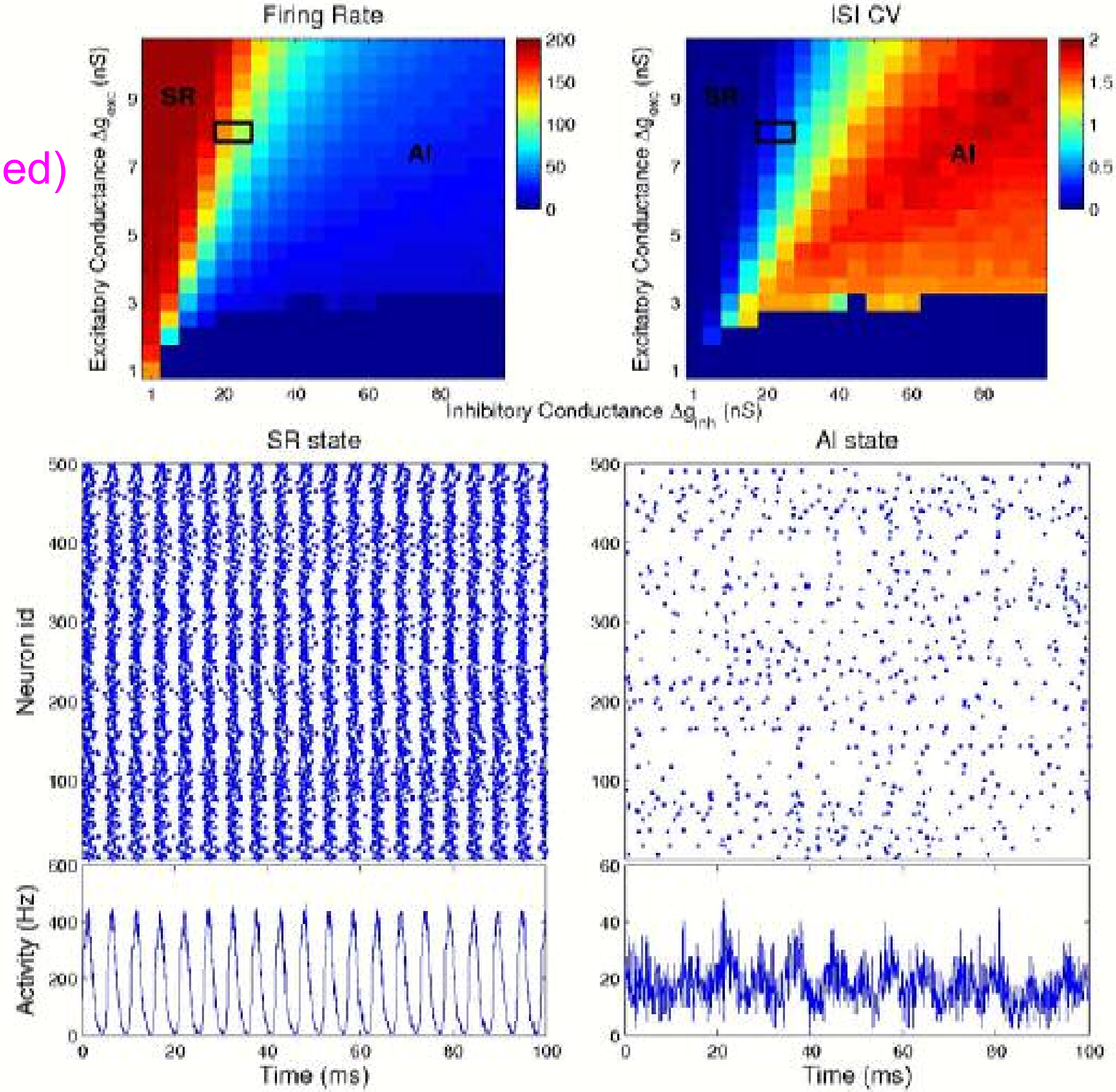
Networks of Adaptive
Exponential (AdEx)
IF neurons
(conductance-based)



Destexhe, *JCNS* 2009

Self-sustained asynchronous irregular states

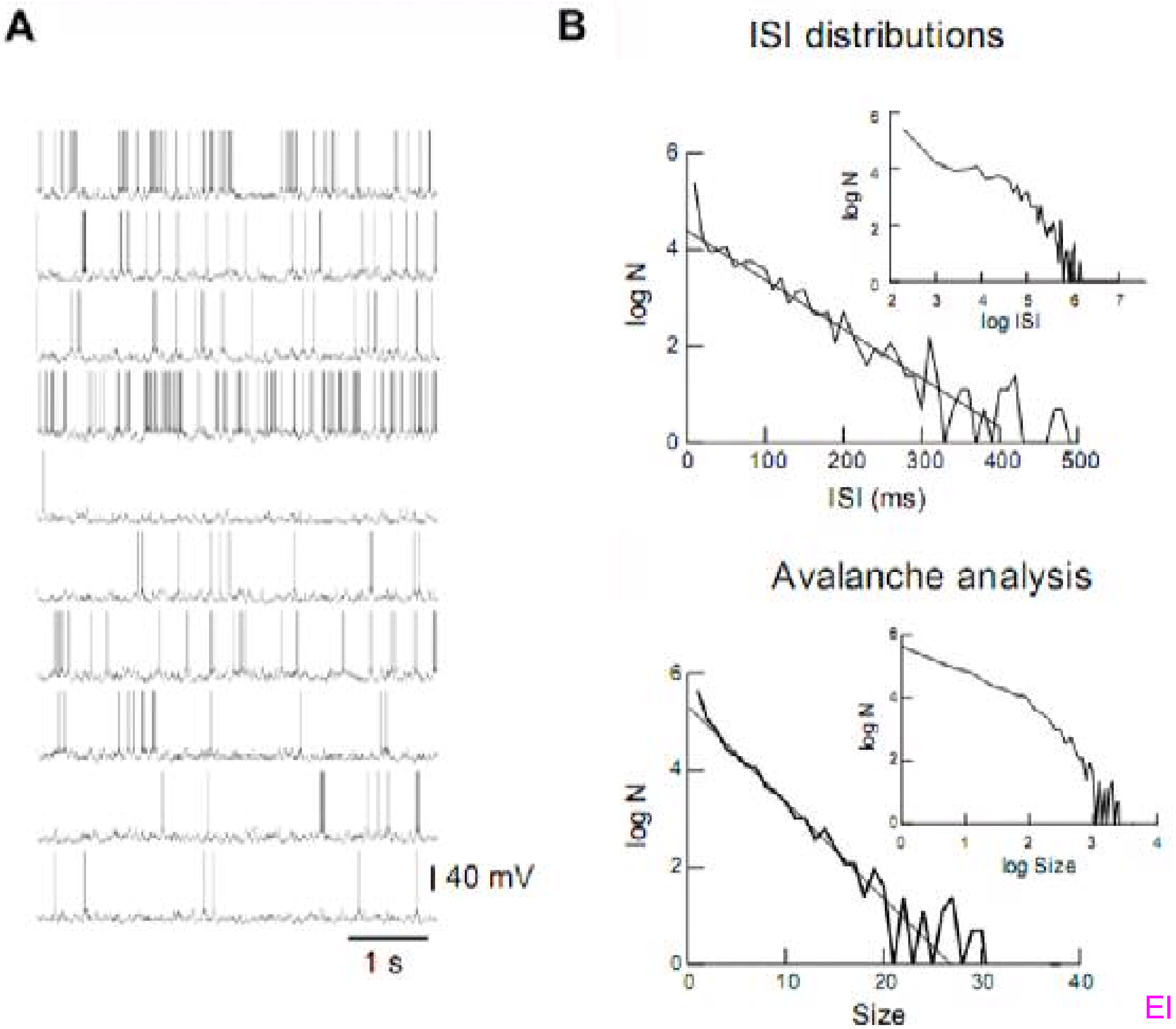
Networks of
IF neurons
(conductance-based)



Vogels & Abbott,
J Neurosci 2005

El Boustani & Destexhe,
Neural Computation 2009

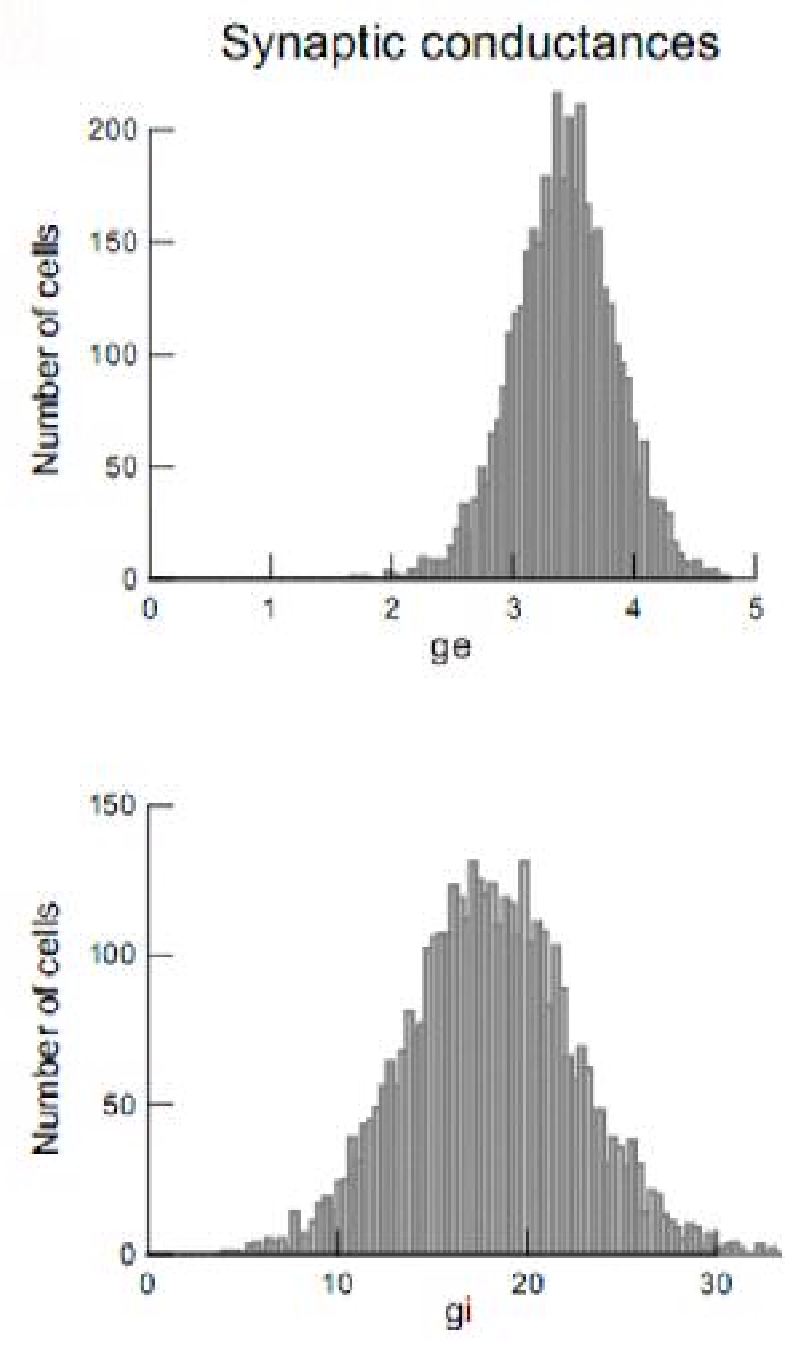
Analysis of AI states



El Boustani et al., *J Physiol Paris*, 2007

Analysis of AI states

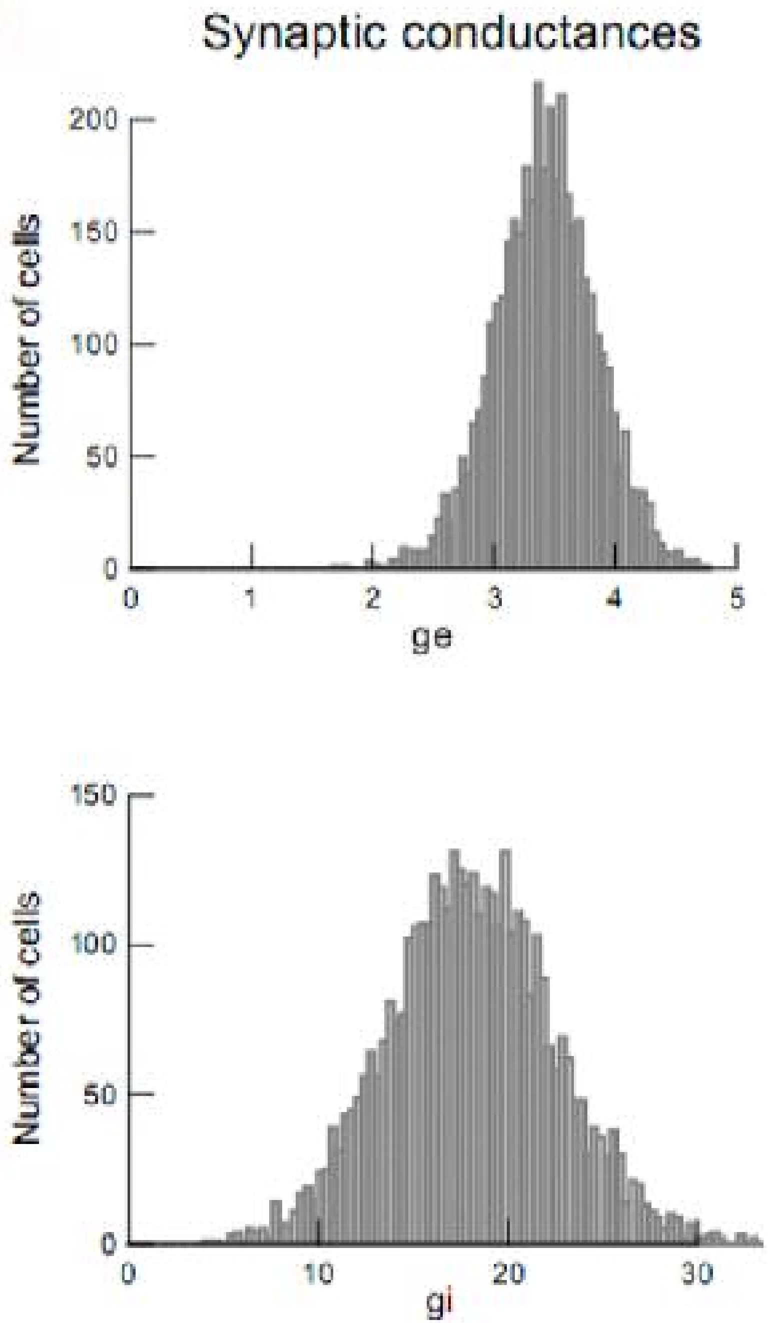
Conductance distributions in the Vogels-Abbott (2005) model



El Boustani et al., *J Physiol Paris*, 2007

Analysis of AI states

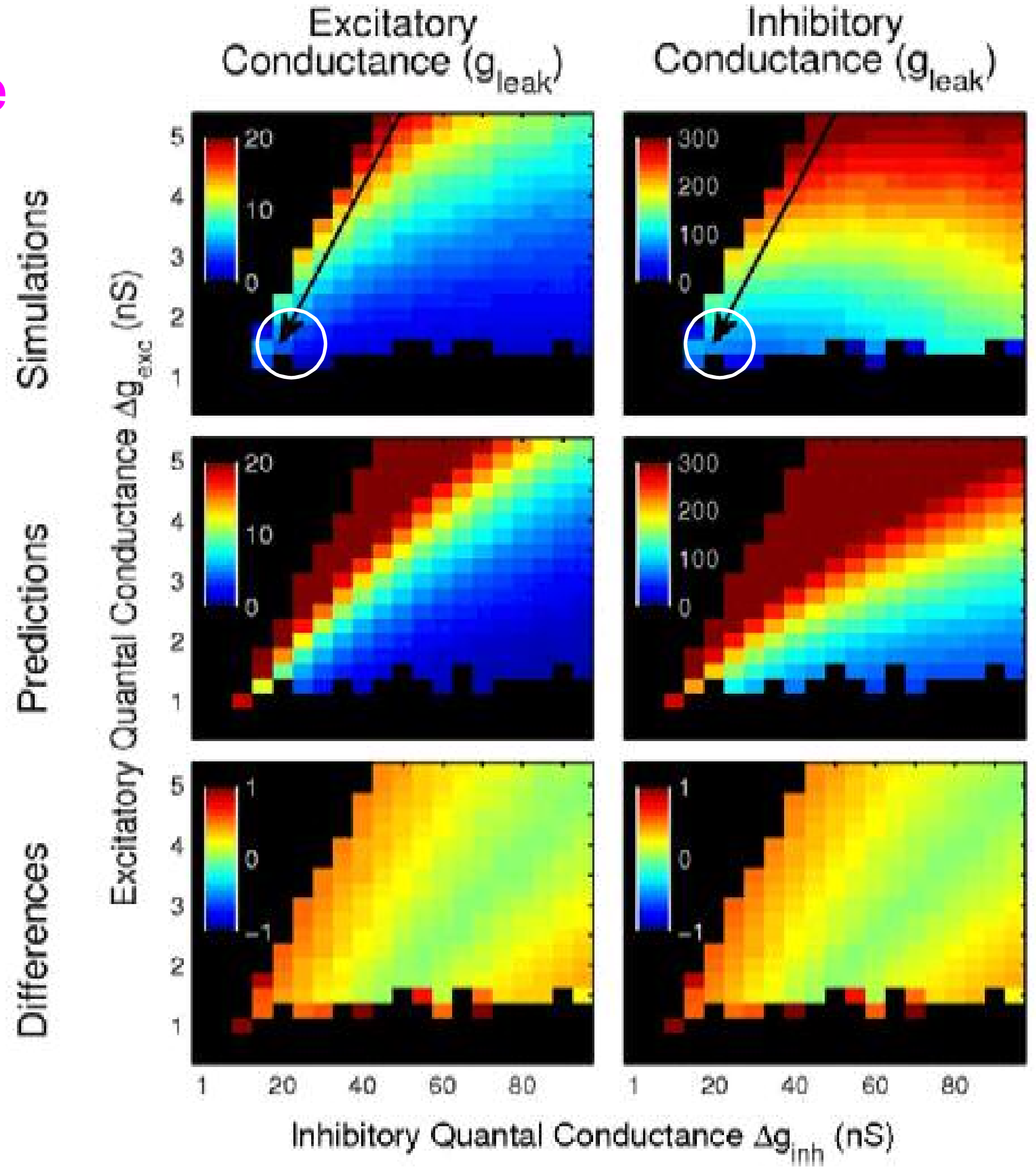
Conductance distributions in the Vogels-Abbott (2005) model



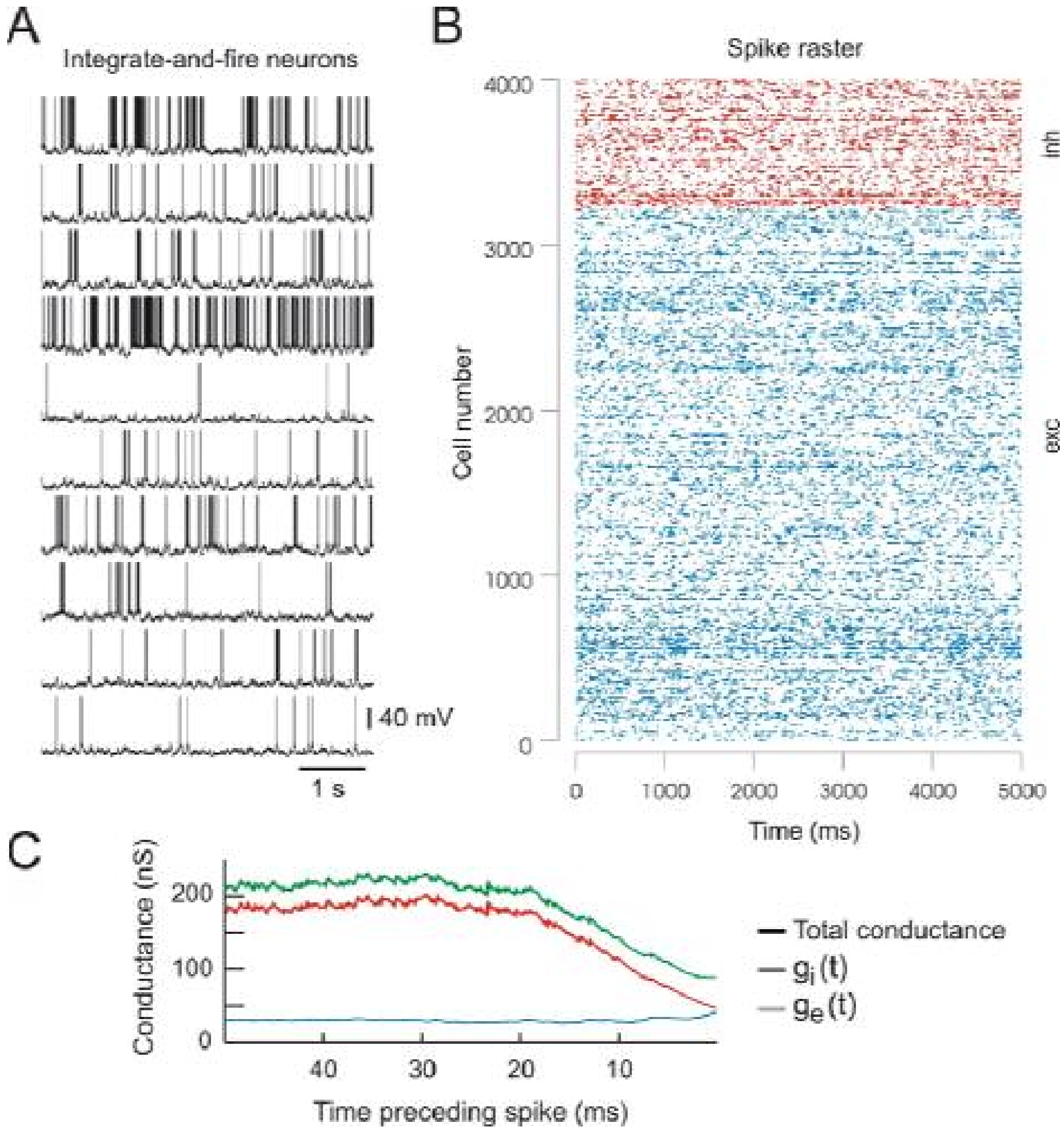
20 times too many!

El Boustani et al., *J Physiol Paris*, 2007

Conductance maps

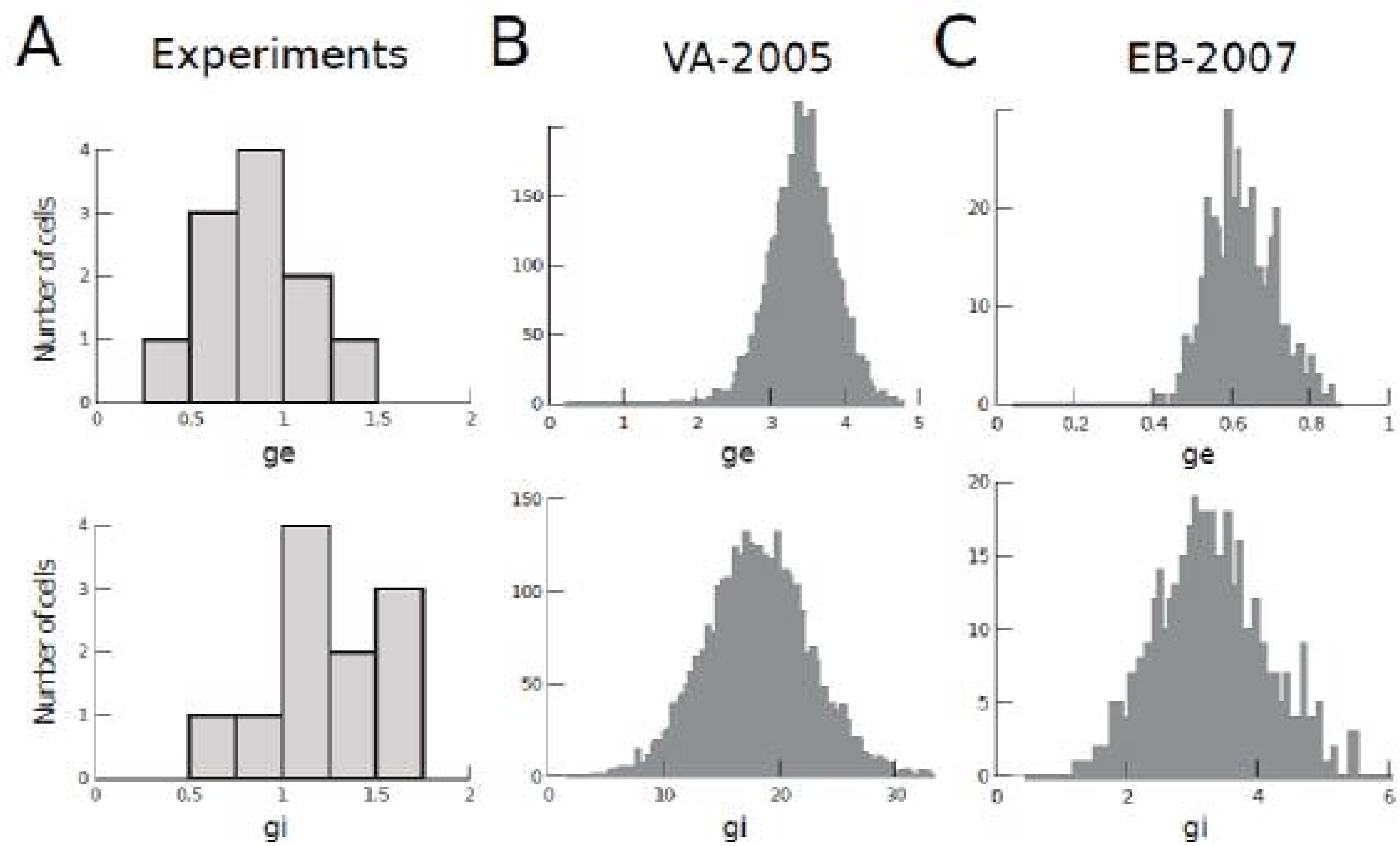


Analysis of AI states

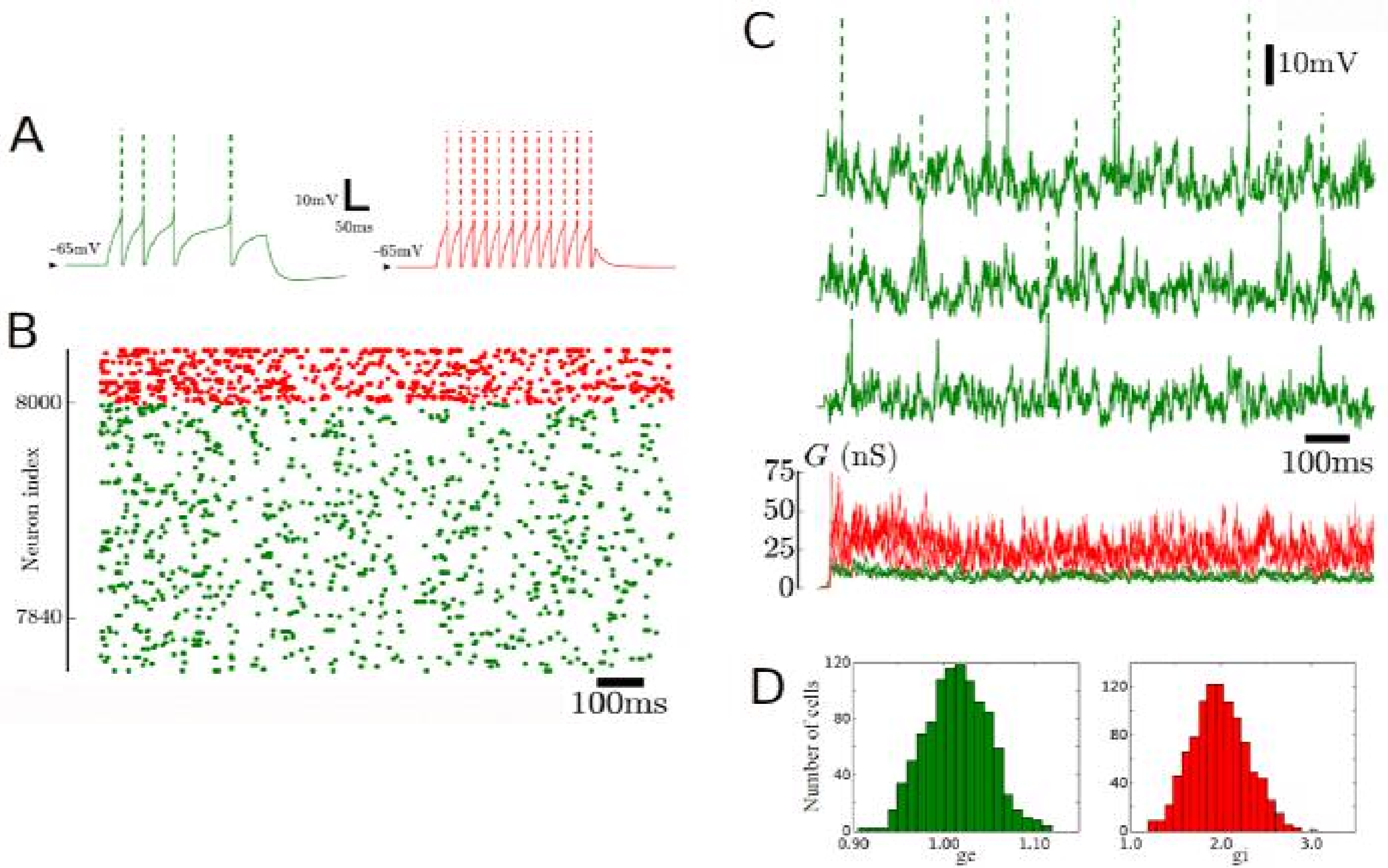


El Boustani et al., *J Physiol Paris*, 2007

Comparison

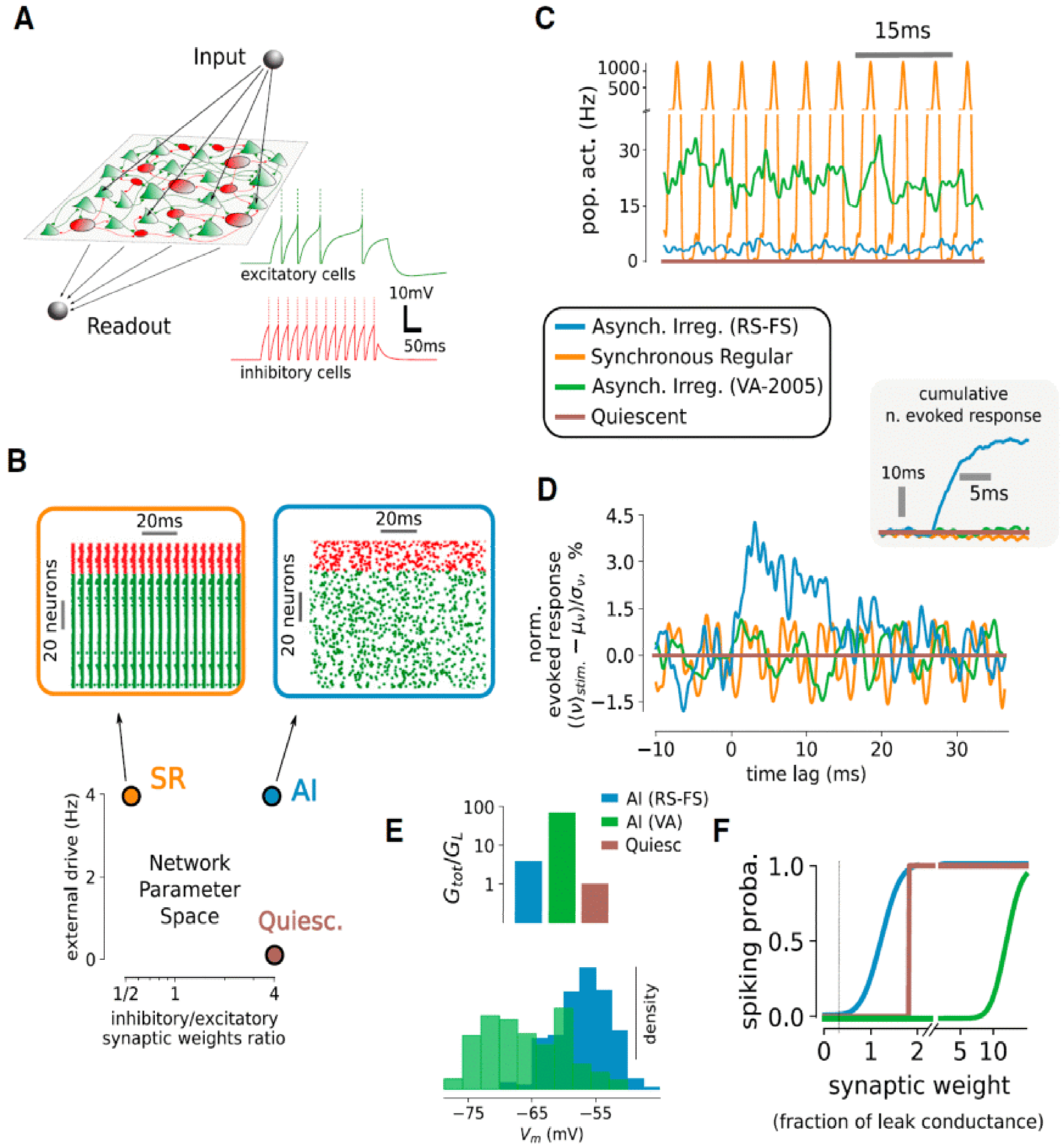

A
Experiments
B
VA-2005
C
EB-2007
Number of cells
ge
gi
Number of cells
ge
gi
ge
gi

Network responsiveness



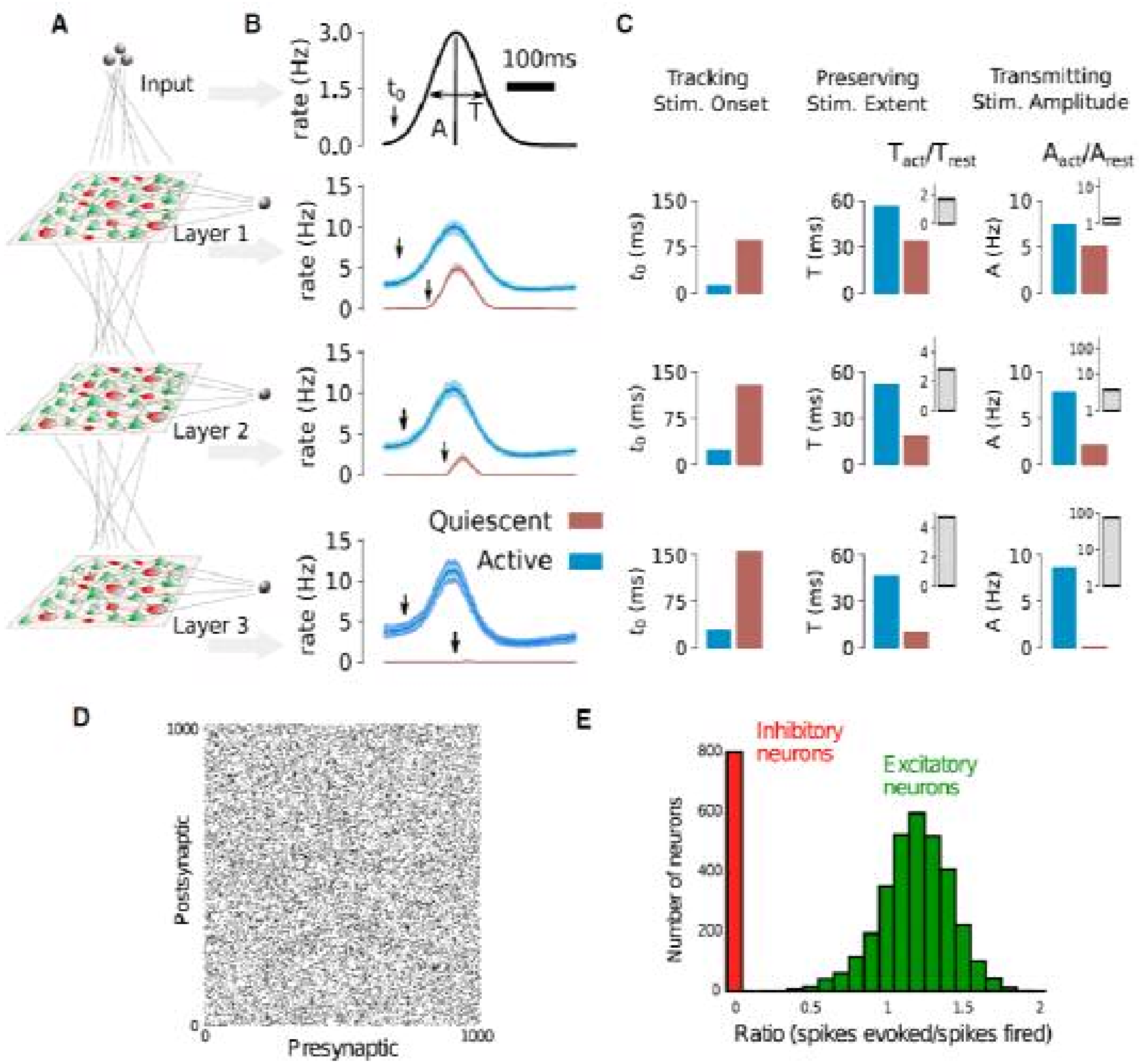
Girones & Destexhe,
arXiv 2016

Network responsiveness



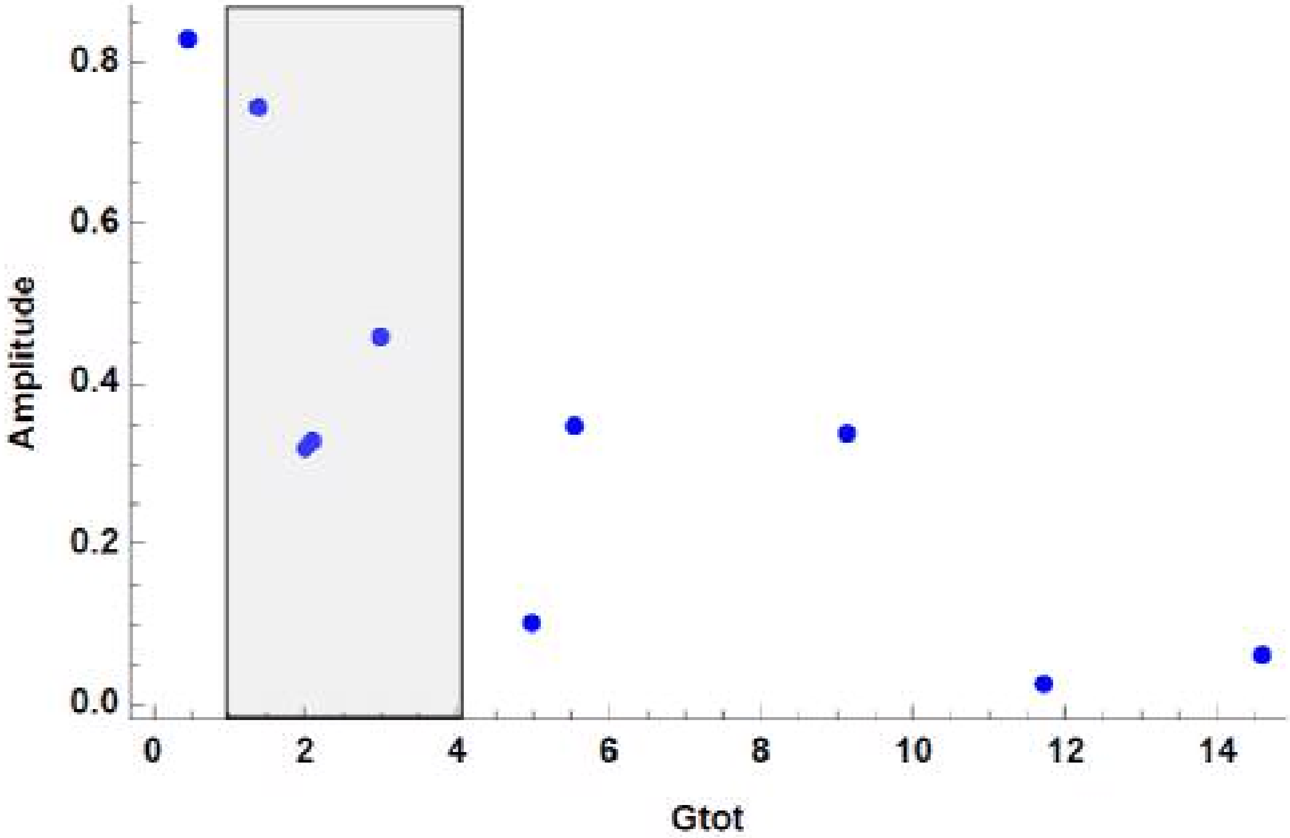
Zerlaut & Destexhe
Neuron 2017

Network responsiveness



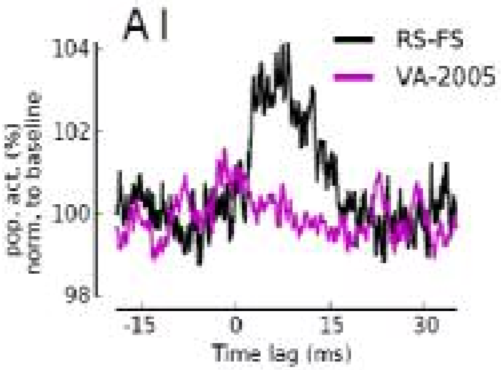
Zerlaut & Destexhe
Neuron 2017

Network responsiveness



Girones & Destexhe,
arXiv 2016

Consequences on integrative properties



Conclusions

- Enhanced responsiveness can be found at the network level...
- ... but only if neurons are in a conductance state consistent with experiments

Thanks to the team...

Michelle Rudolph

Zuzanna Piwkowska

Martin Pospischil

Adrien Peyrache

Claude Bedard

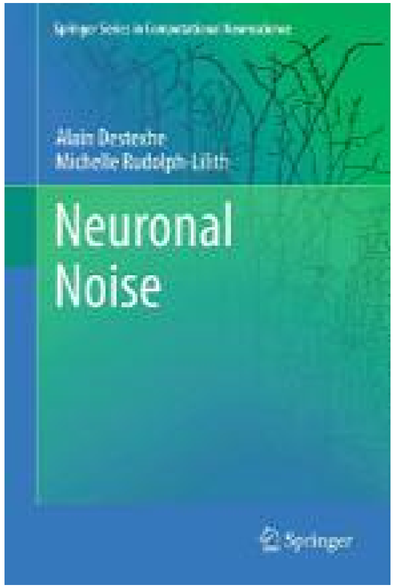
Sami El Boustani

Thierry Bal

Nima Dehghani

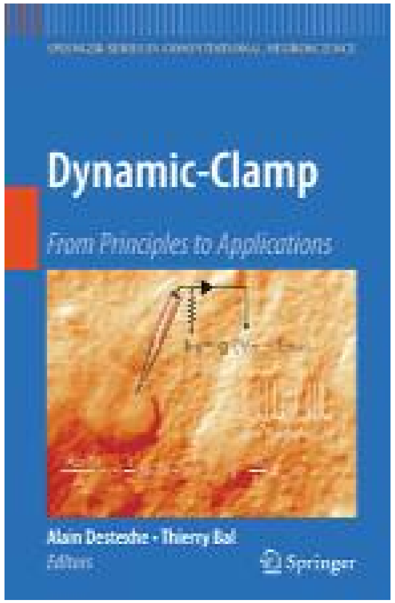
http://cns.iaf.cnrs-gif.fr

Reading material



Review articles:

- *Scholarpedia* article on "High-conductance states" (open access; many articles available, such as "dynamic-clamp", "neuronal noise", etc)
- Destexhe et al. The high-conductance state of neocortical neurons in vivo, *Nature Reviews Neuroscience*, 2003.



Books:

- Dayan & Abbott, *Theoretical Neuroscience (MIT Press, 2001)*
- Koch, *Biophysics of Computation (Oxford UP, 1999)*
- Destexhe & Rudolph, *Neuronal Noise* (Springer, 2012)
- Destexhe & Bal (Eds), *Dynamic Clamp* (Springer, 2009)