# Michael Breakspear

@drbreaky


I respectively acknowledge the Awabakal people, the traditional custodians of the land on which we live and work in Newcastle

# Modelling large-scale neural activity in brain disorders

a human (Roland Goecke)

Humans are inherently dynamic machines, engaged in active action-perception with complex scenes and others

Positioned, embodied, metabolically hungry, social, …

# Modelling large-scale neural activity in brain disorders

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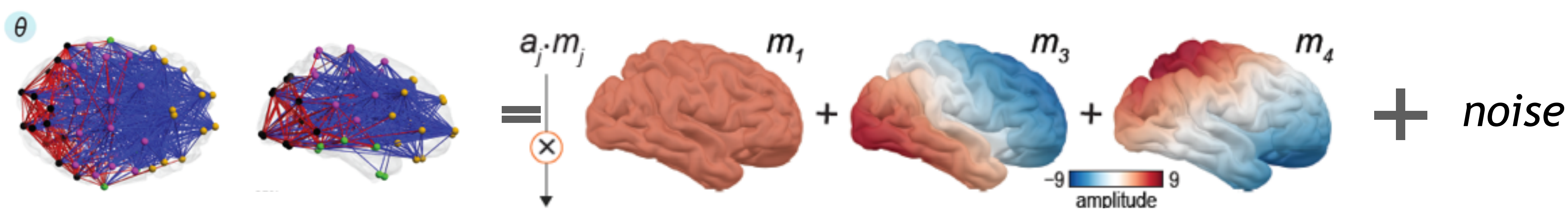


I: Population models : Basic principles

II: Nodes and neural masses

III: Neural fields + modes

IV: A few comments

# I: Population models : Basic principles

The origin of spikes in single neurons was essentially solved by the Nobel-prize winning Hodgkin–Huxley model developed in the 1950s.

$$C\frac{dV}{dt} = g_{Na}m_\infty(V)(V - V_{Na}) + g_K n(V)(V - V_K) + g_L(V - V_L) + I,$$
$$\frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n}.$$

where,

$$m_\infty(V) = \frac{m_{\max}}{1 + \exp[(V_m - V)/\sigma_m]},$$
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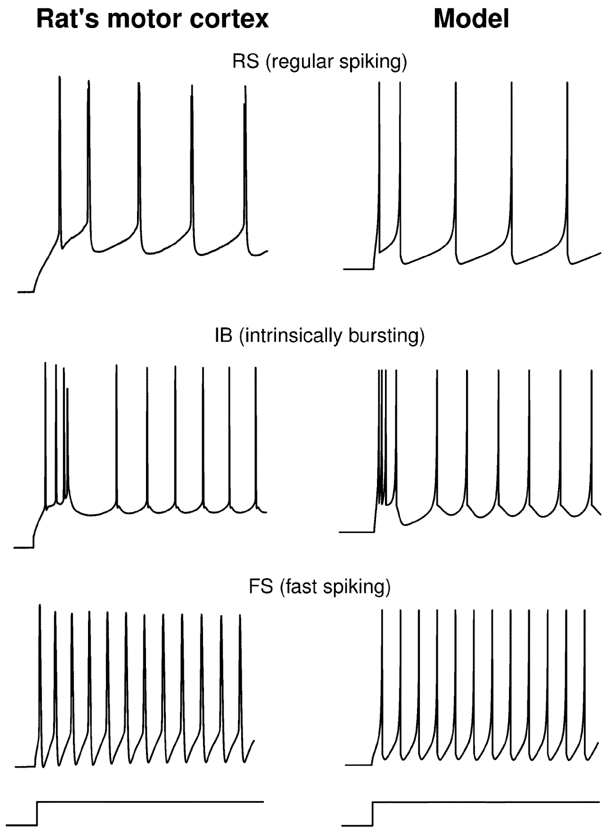



Izhikevich 2004

Drawing directly from detailed neurophysiological recordings of the squid giant axon, this model ascribes the origin of spikes to the interaction of fast depolarizing and slow hyperpolarizing currents, expressed in precise mathematical form

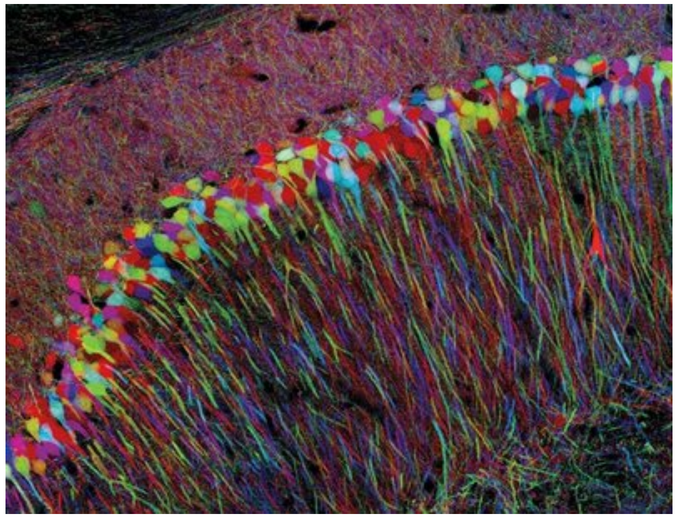
This (Nobel prize winning) success generated decades of spike-based theories of brain computation

# I: Population models : Basic principles

But individual neutrons are buried within circuits of thousands of neurons which are themselves immersed in functional subsystems and large-scale brain networks

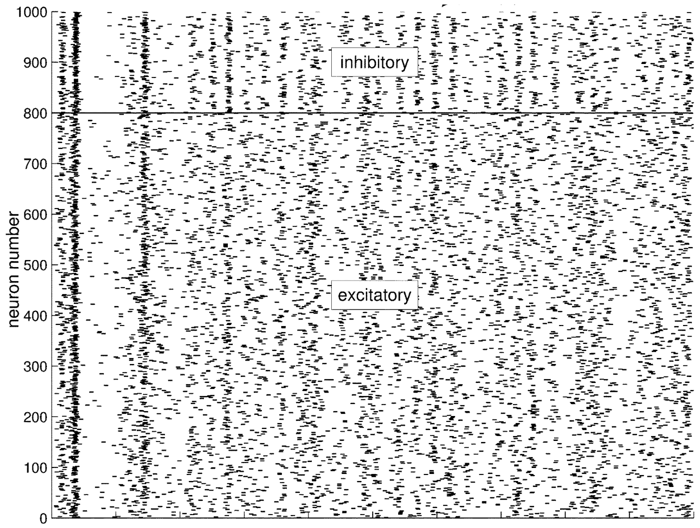
# I: Population models : Basic principles

Local neural population



"Spike raster"

(individual states)

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Breakspear (2017) *Nature Neuroscience*

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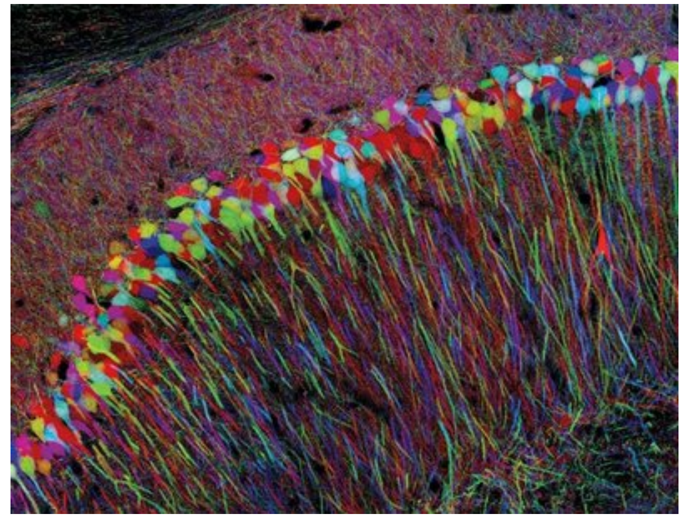

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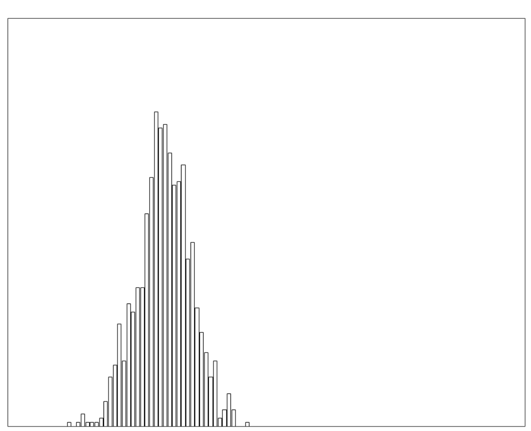
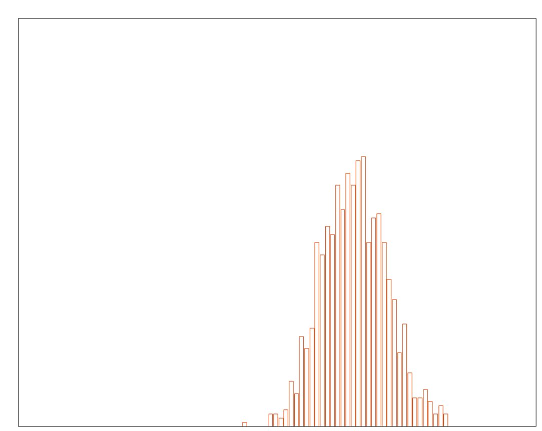
Empirical histogram





Breakspear (2017) *Nature Neuroscience*

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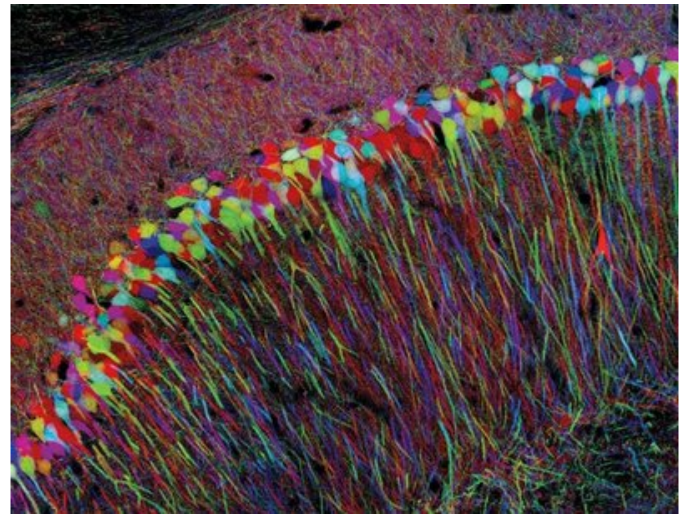

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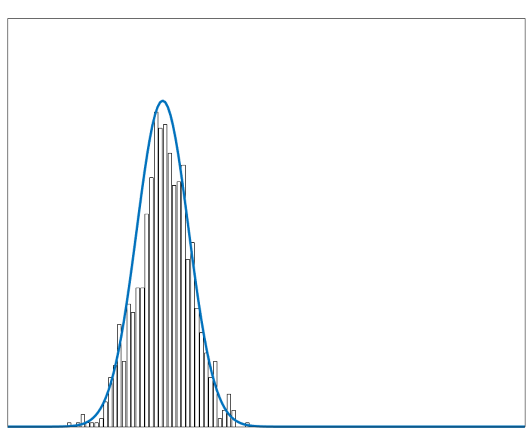
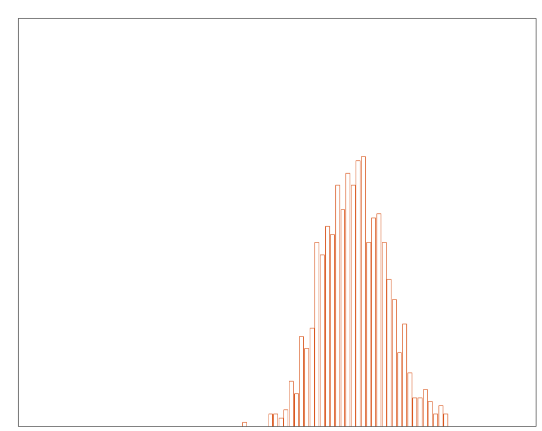
Mean field approximation





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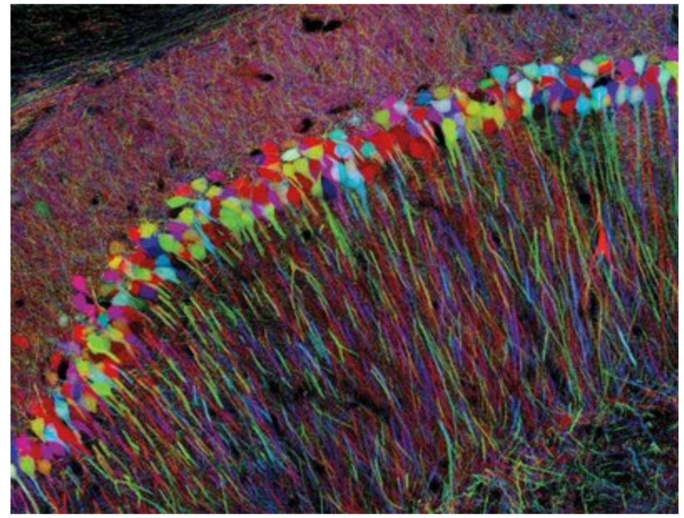

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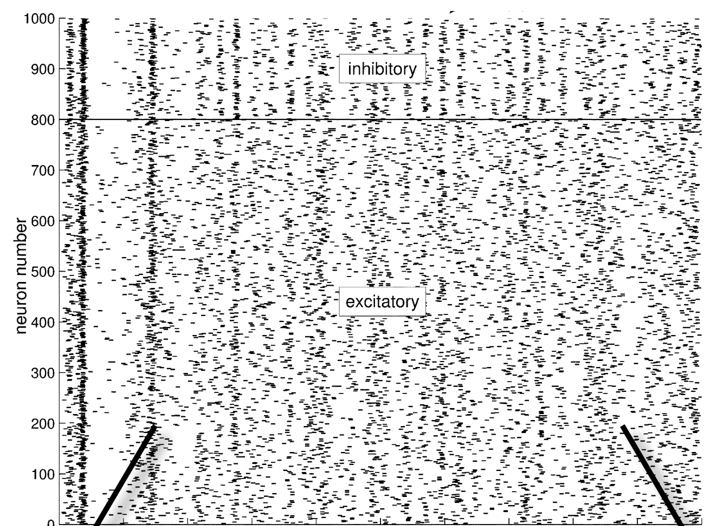


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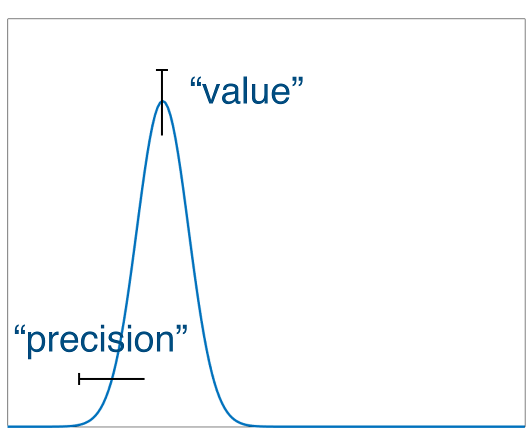


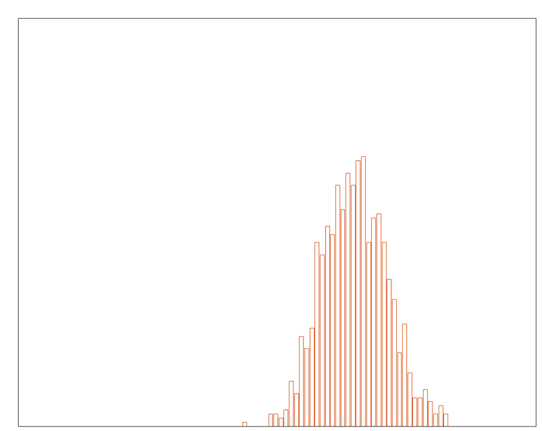

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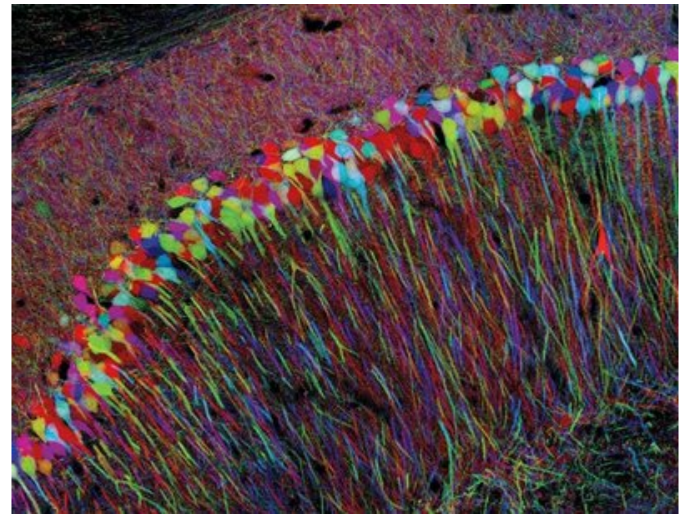
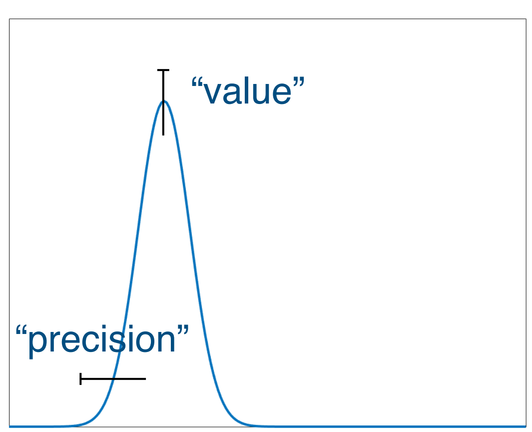


“Spike raster”

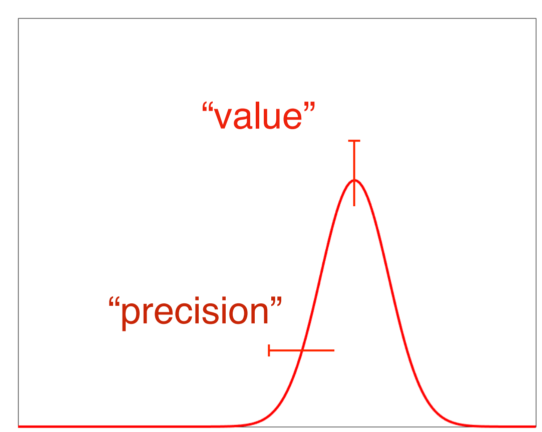
(individual states)


Same approach used widely in physics - e.g. magnetism, super-conductors, LCDs, queueing, swarming

Mean field approximation




$$\frac{\partial \rho}{\partial t} = D\frac{\partial^2 \rho}{\partial \theta^2} - \frac{\partial}{\partial \theta}(v\rho),$$




Forward temporal evolution

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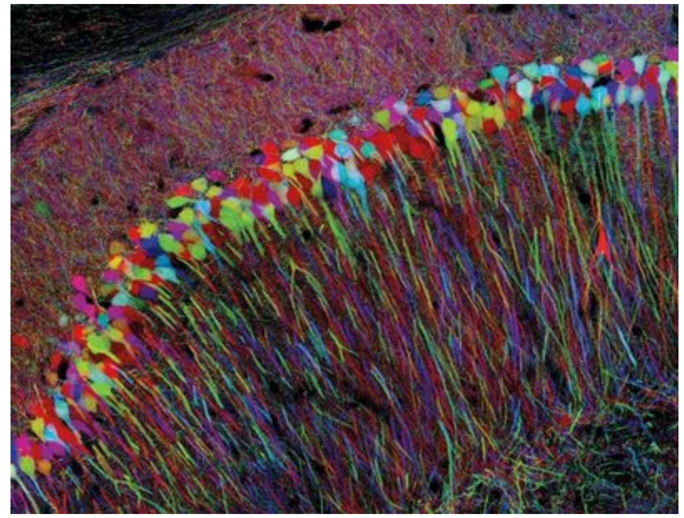

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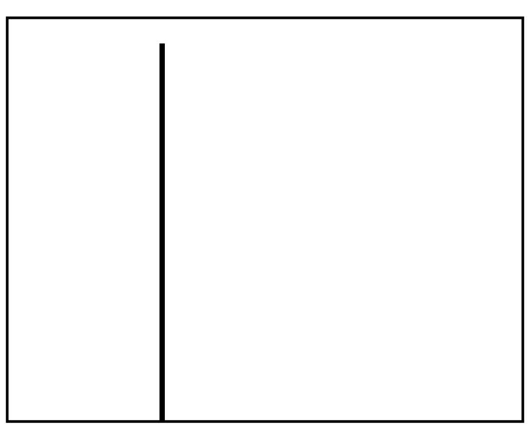
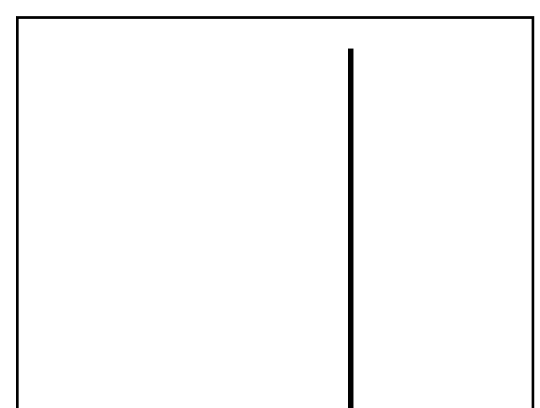
Neural mass approximation



$$\frac{d\mathbf{X}}{dt} = f(\mathbf{X}) + I$$

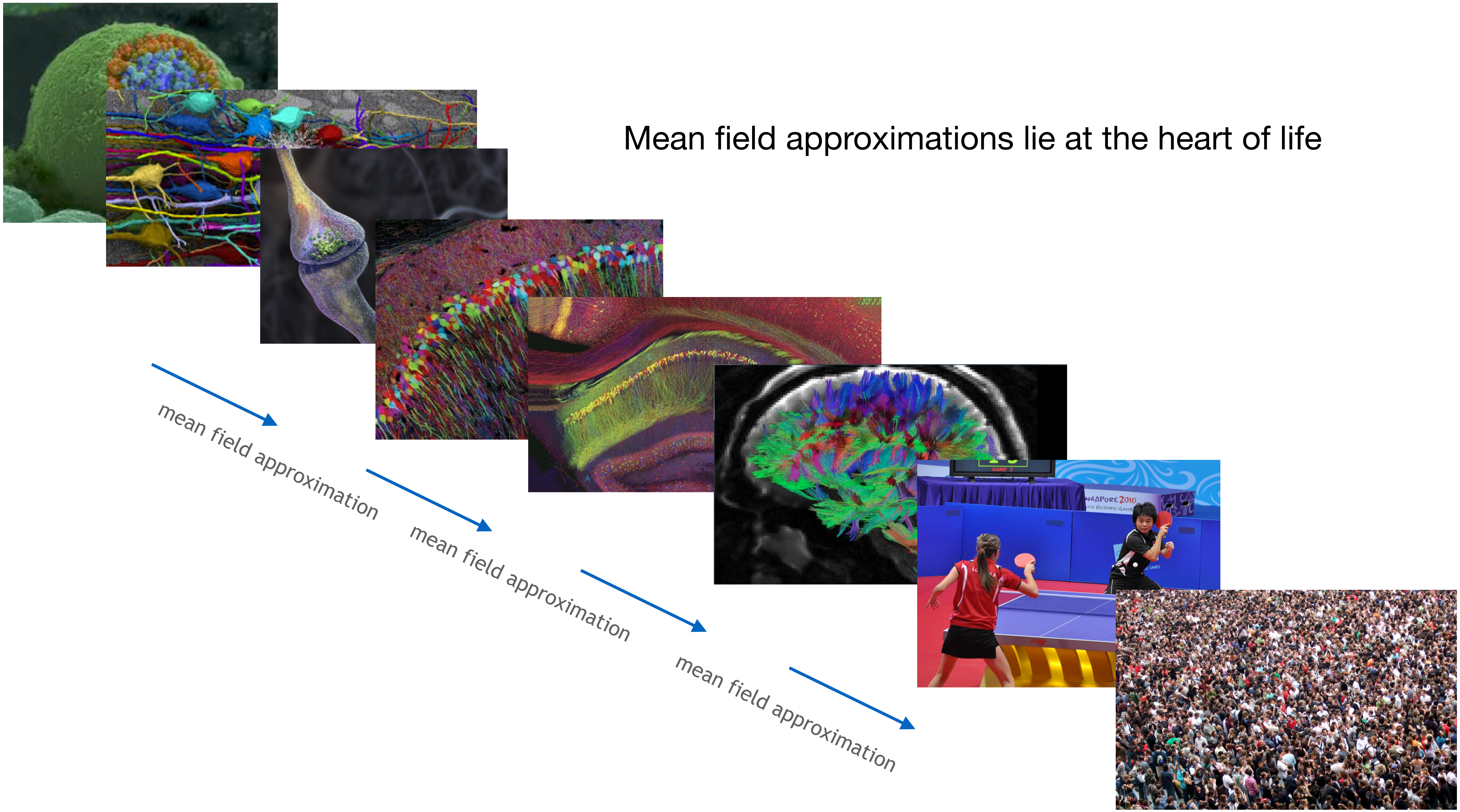


Forward temporal evolution

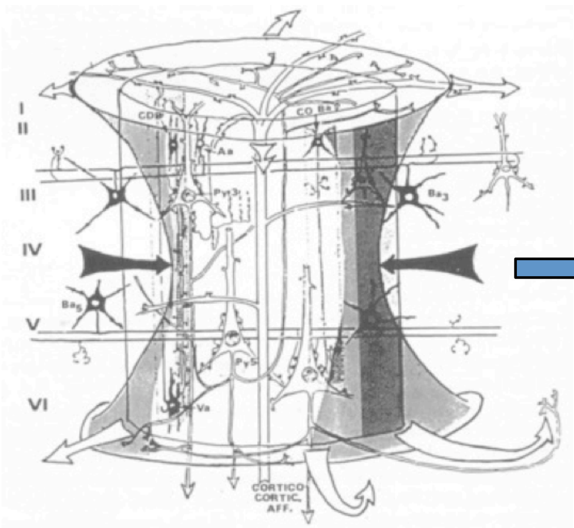
Breakspear M (2017) *Nature Neuroscience*

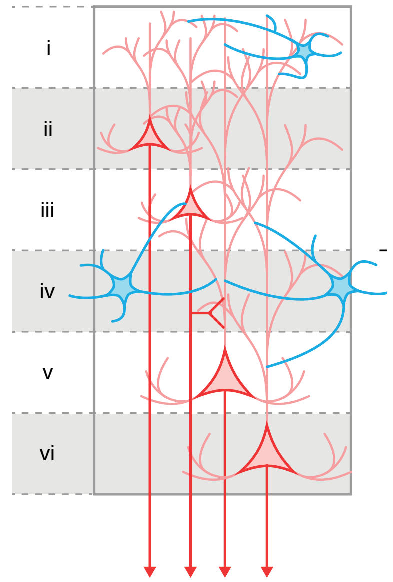
# I: Population models : Basic principles

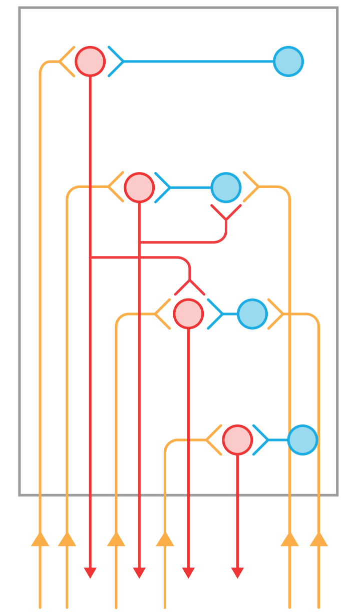
Mean field approximations lie at the heart of life

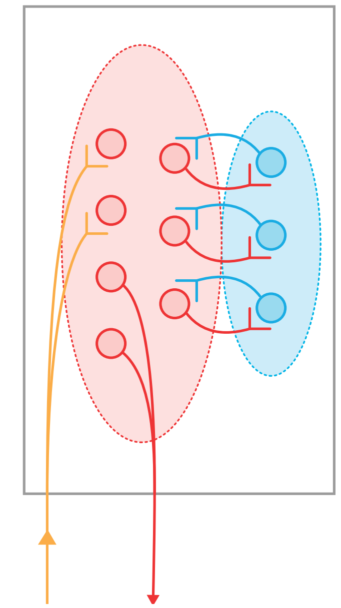


# I: Population models : Basic principles





Complex neural histology
(e.g. cortical column)

Detailed multi
compartment spiking
neural model
(e.g. HBP)

Simple spiking neural
circuit model
(e.g. Brian, neuron,
SpikeNET)

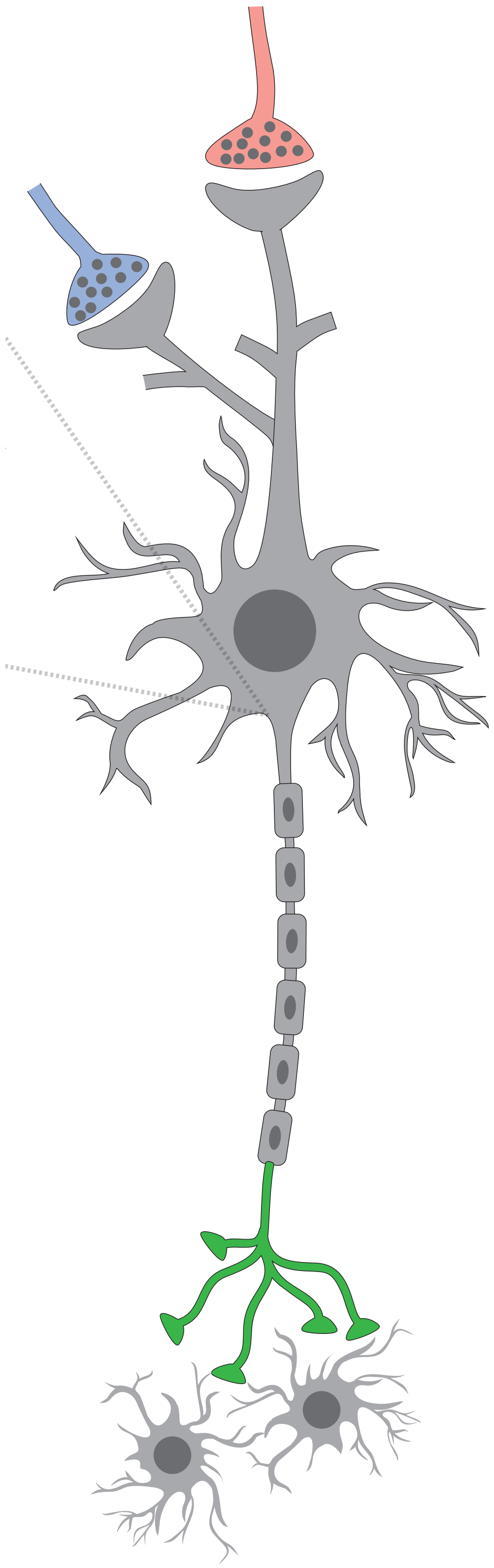
Lumped neural mass
model
(e.g. TVB, BDT)

Mathematical “mean field” dimension reduction

Enslaving principle

Haken (1982) *Synergetik*

# I: Population models : Basic principles



## Conductance based single neuron model

$$C\frac{dV}{dt} = g_{Na}m_\infty(V)(V - V_{Na}) + g_K n(V)(V - V_K) + g_L(V - V_L) + I,$$
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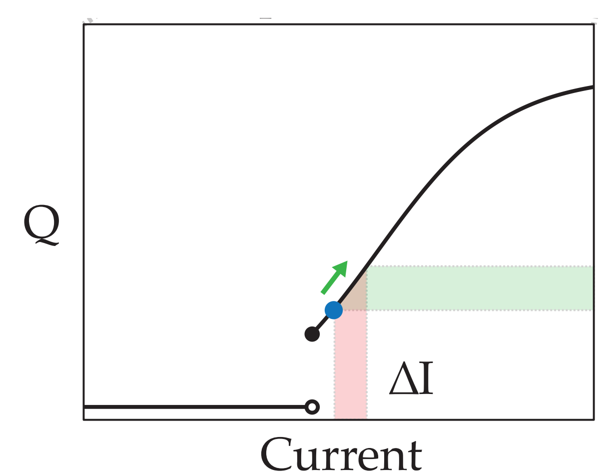
## Bifurcation analysis of input current <-> firing rate (Q)

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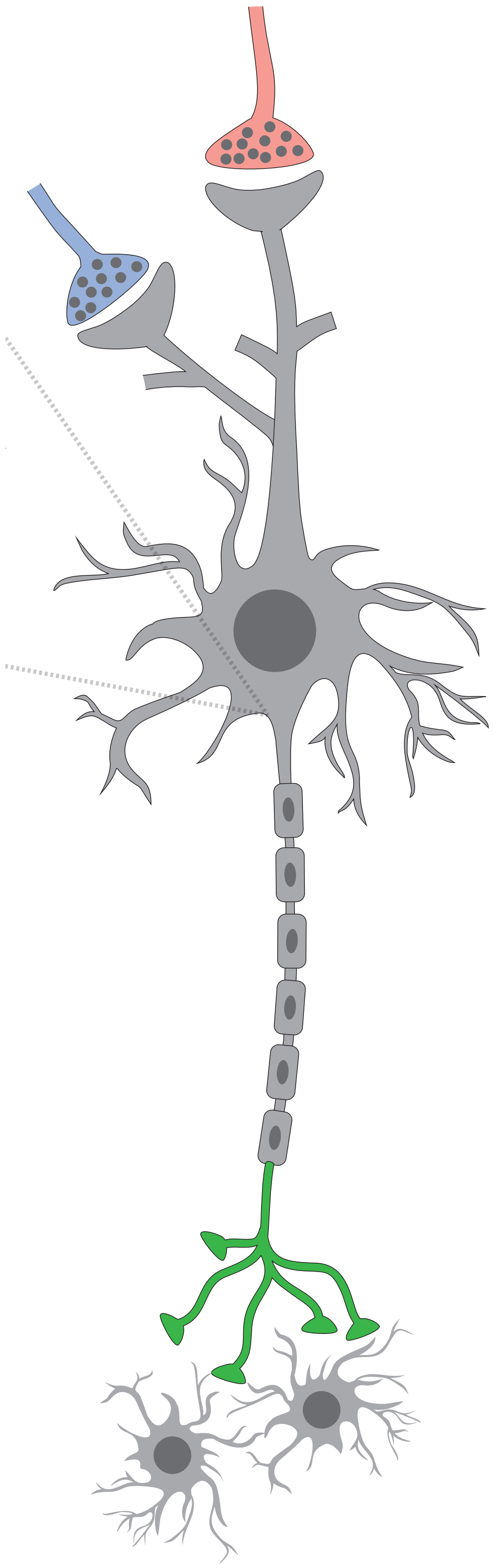
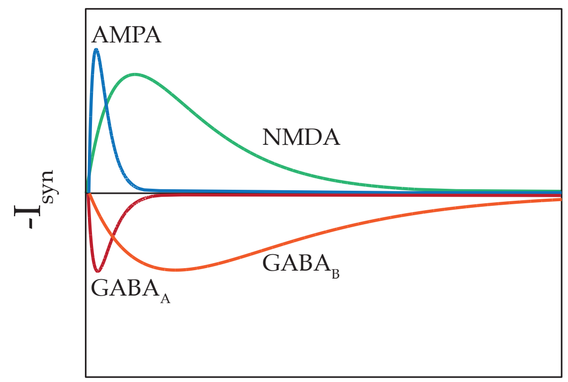
# I: Population models : Basic principles



Add EPSP/IPSP input currents

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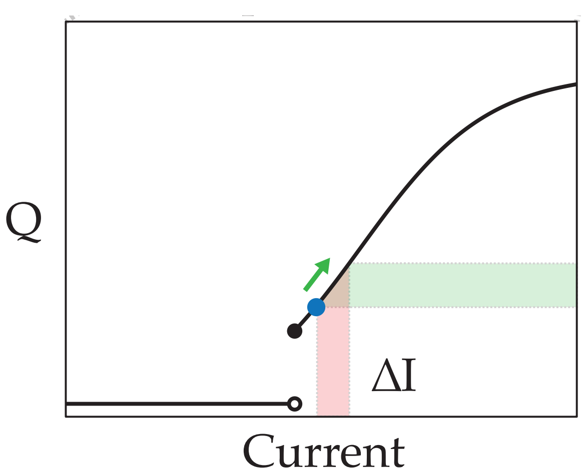


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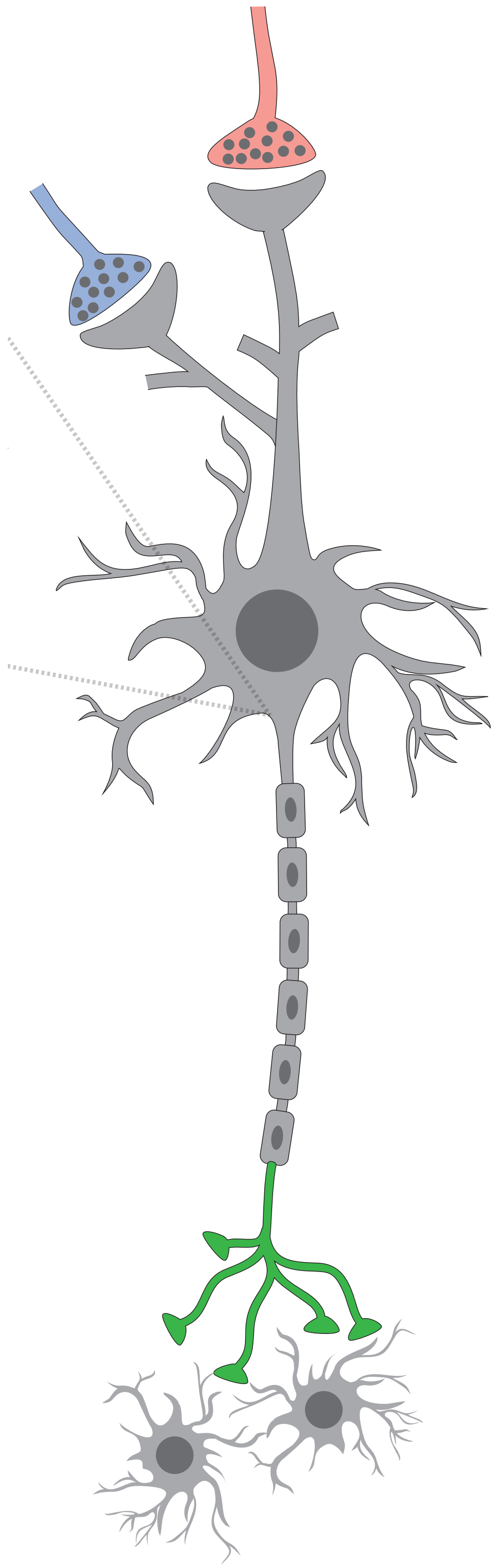

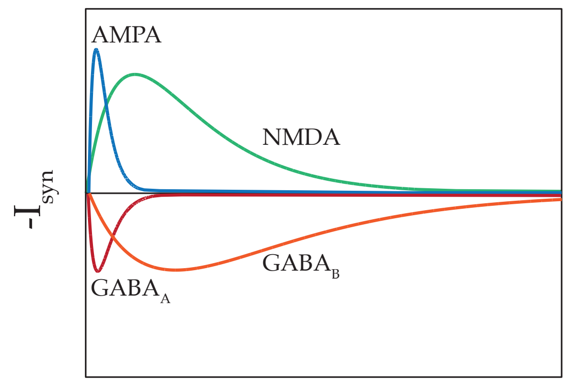


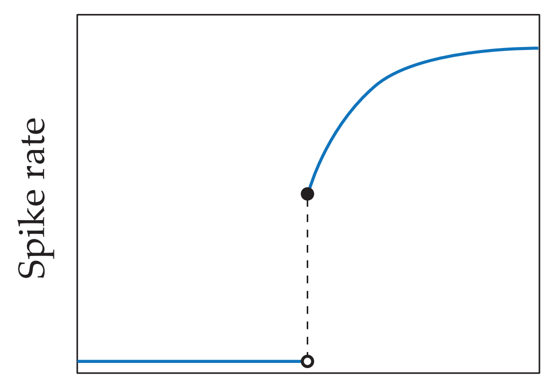


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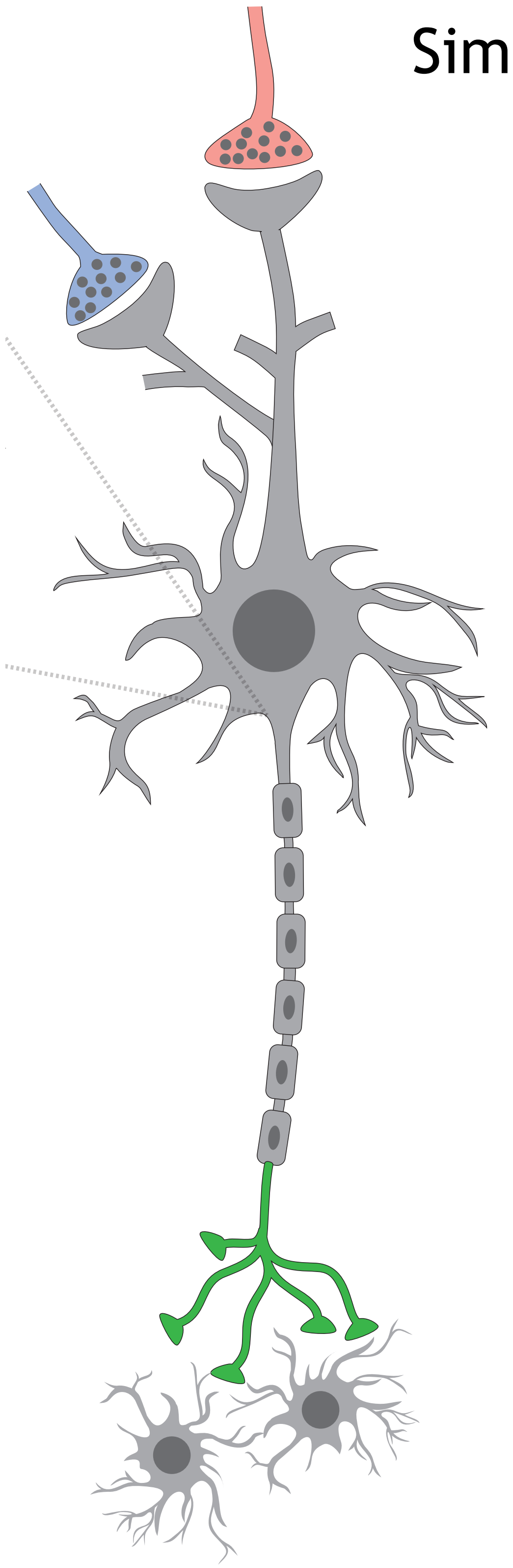
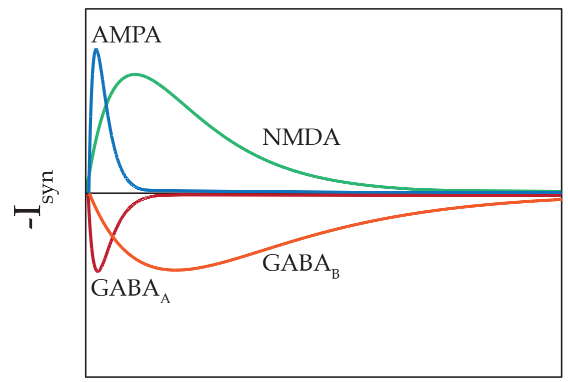
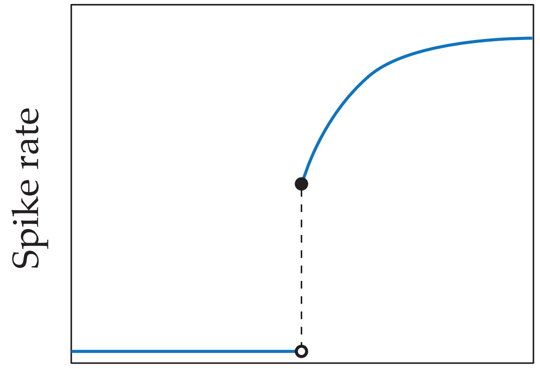
# I: Population models : Basic principles



## Simplified current-based single neuron model




Single neuron response

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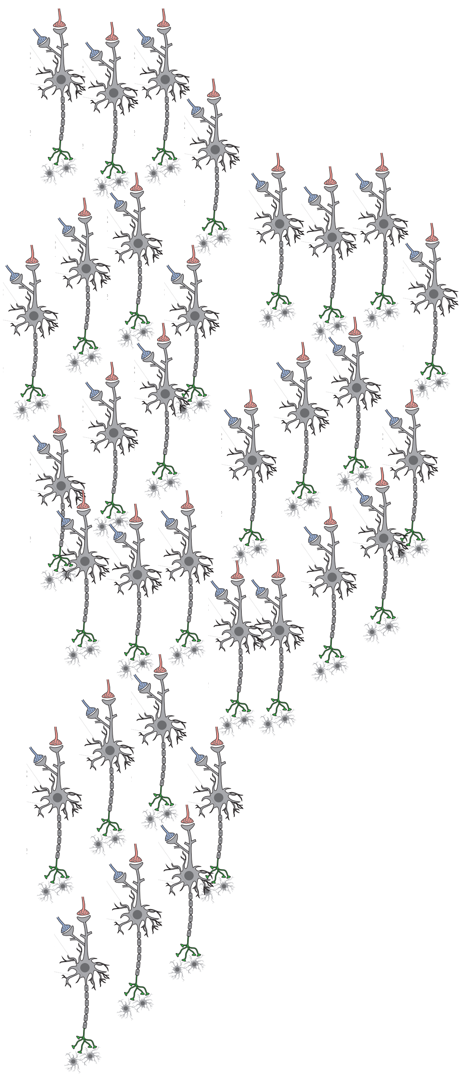
# I: Population models : Basic principles

Detailed conductance-based many-neuron model



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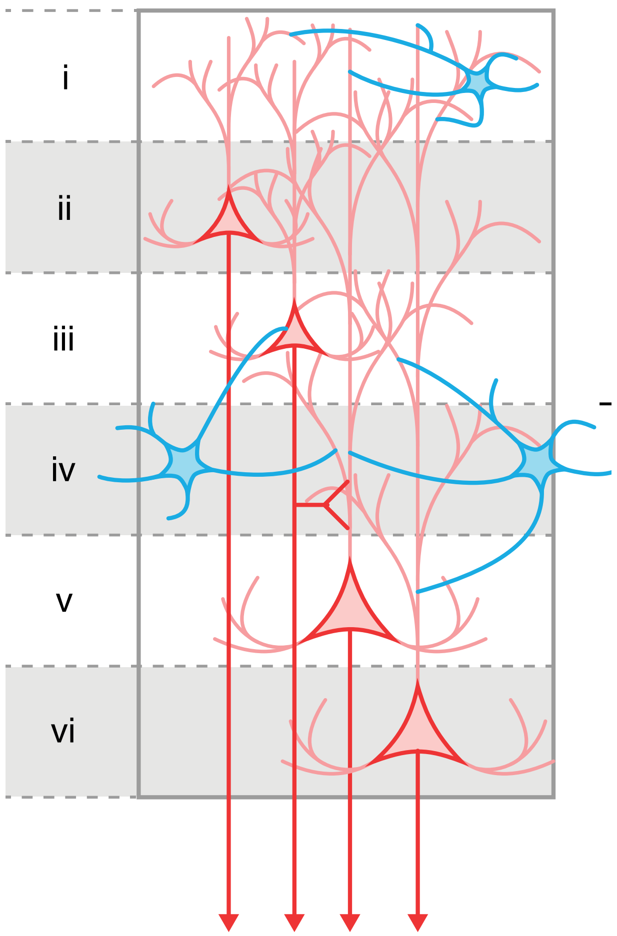
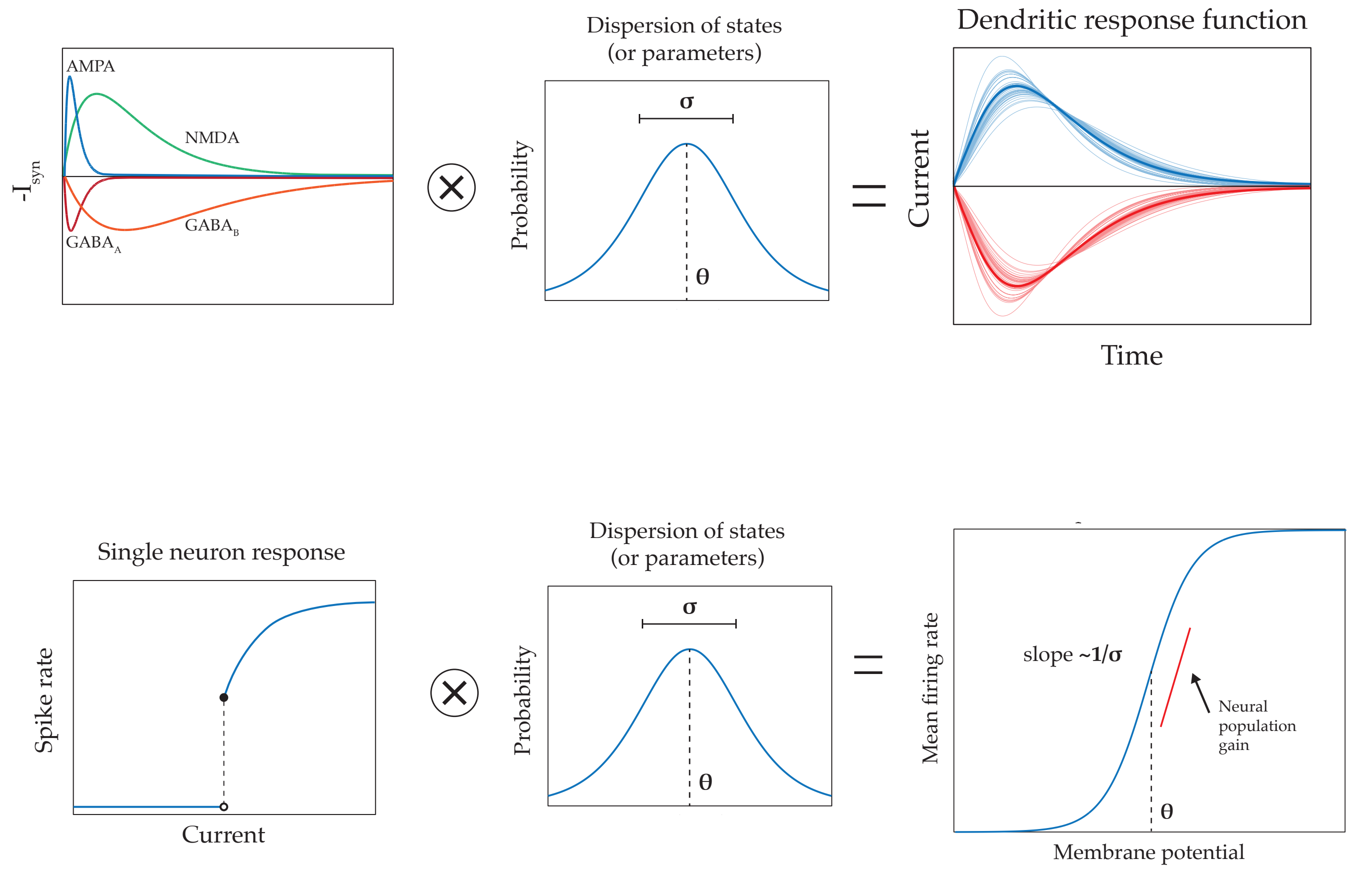
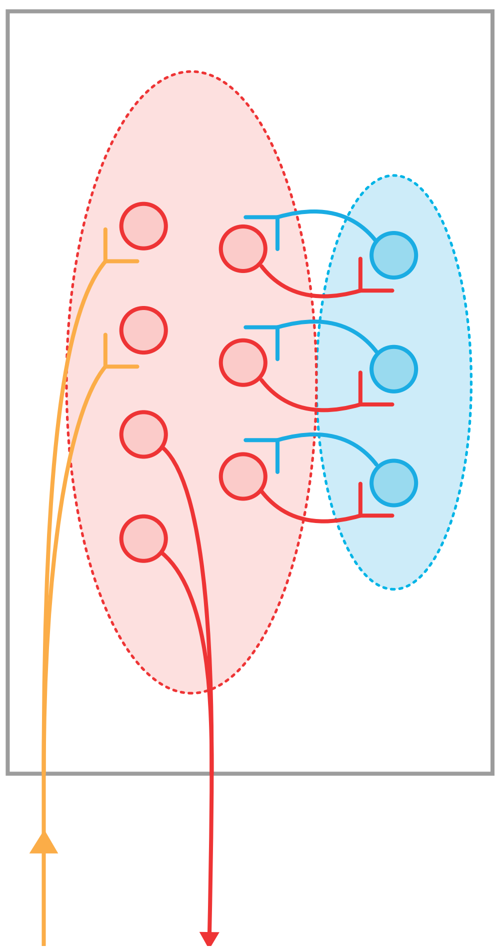
# I: Population models : Basic principles

Simplified current-based single many-neuron model

Neural mass model



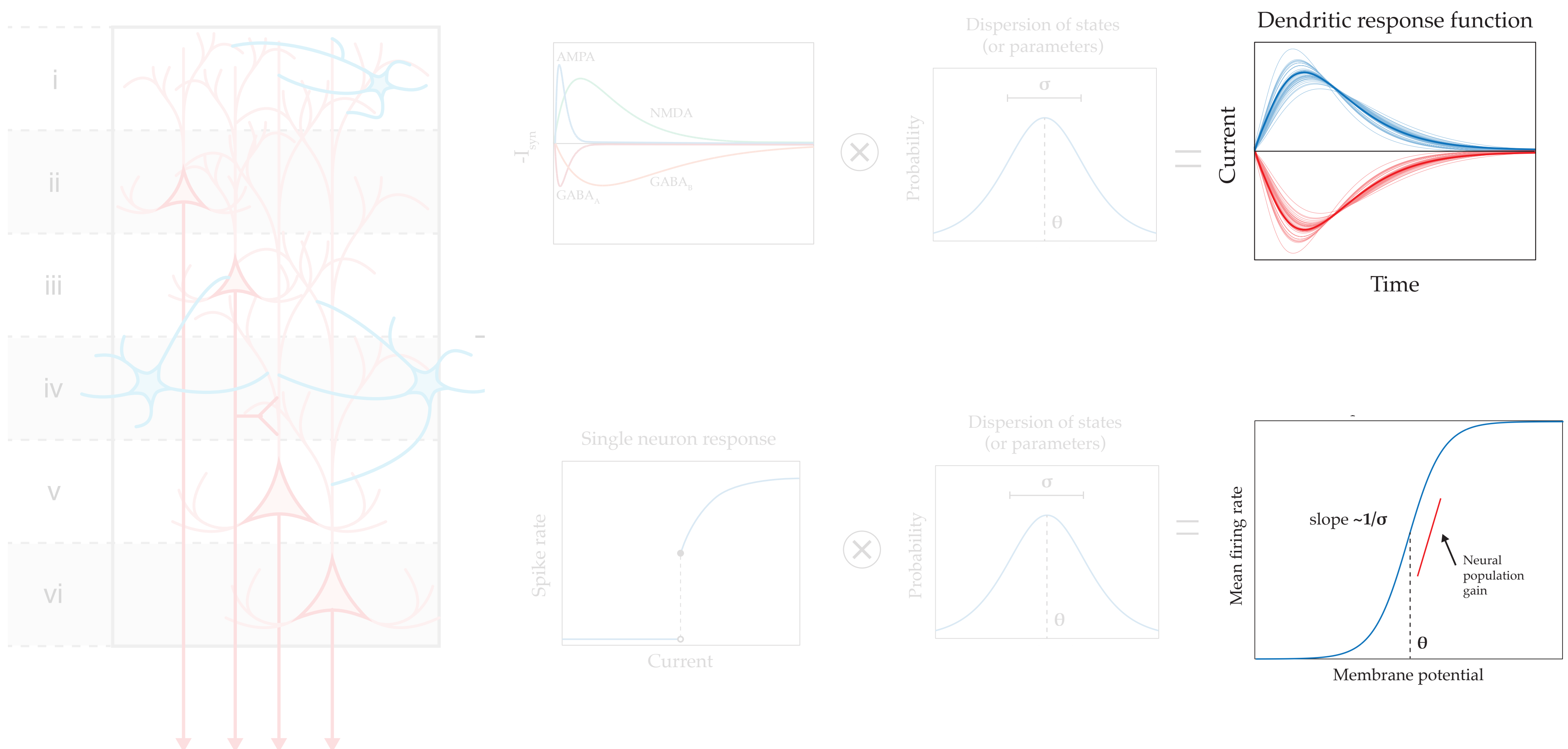



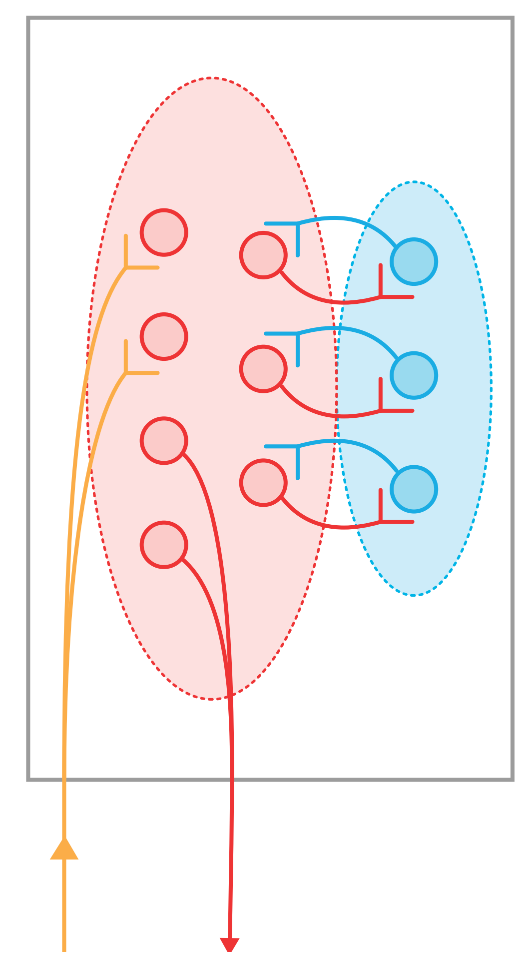
Mac Shine, Eli Muller

# I: Population models : Basic principles

## Simplified current-based single many-neuron model

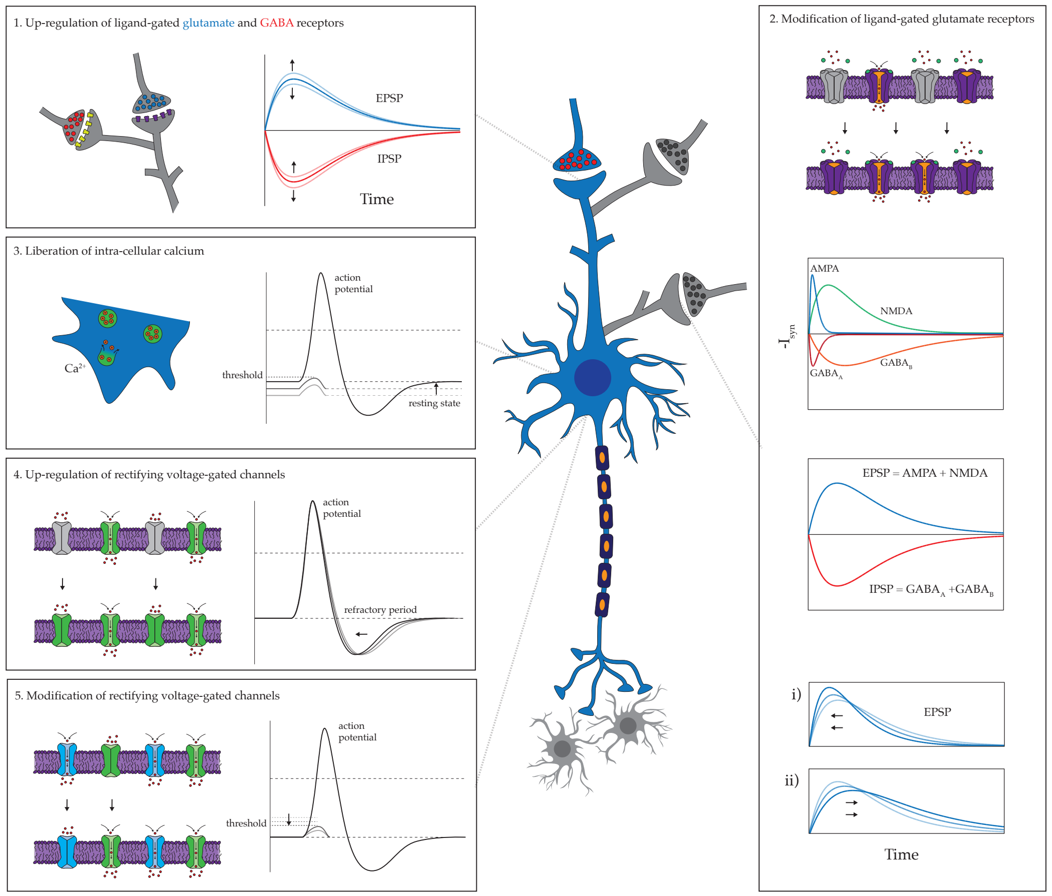
## Neural mass model



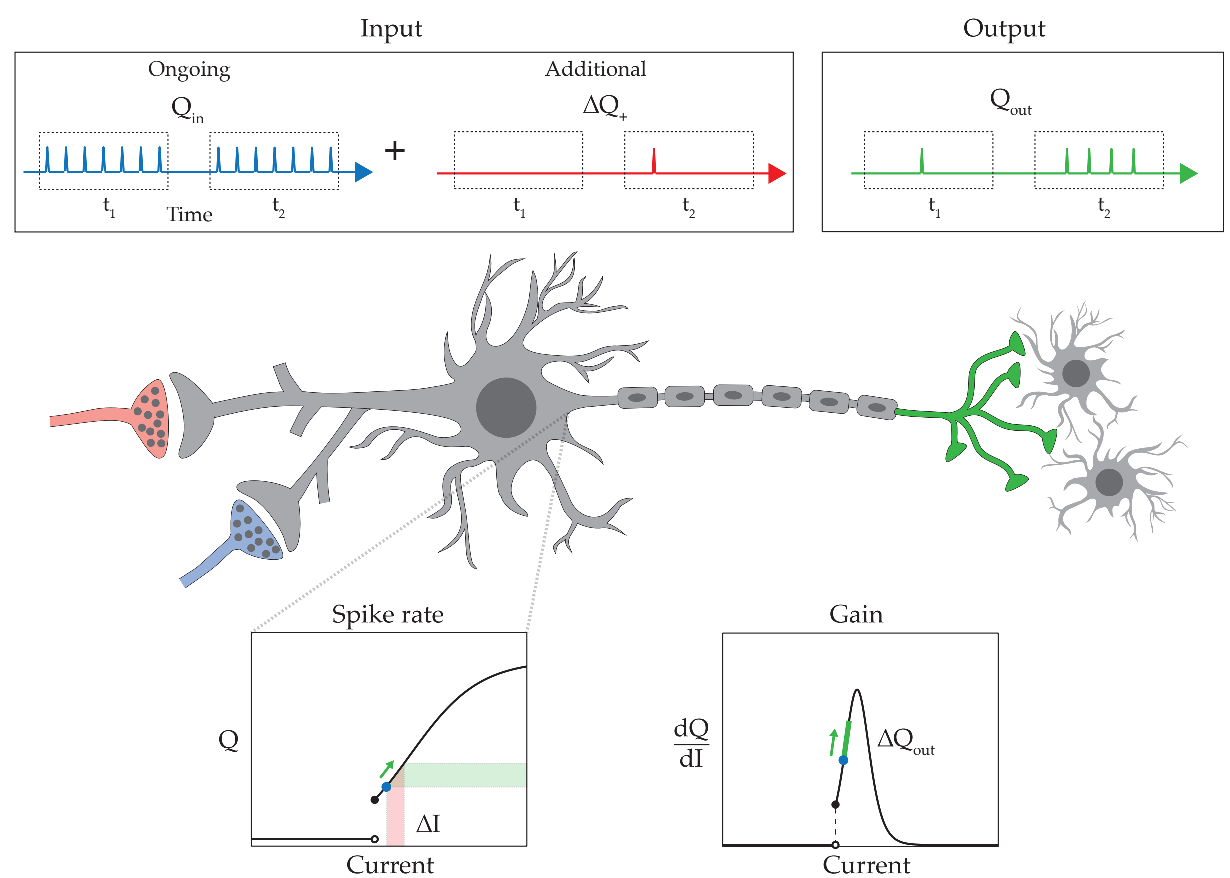



Mac Shine, Eli Muller

# I: Population models : Basic principles




The properties of neutrons are not fixed but are plastic, under the influence of ascending neuromodulatory systems



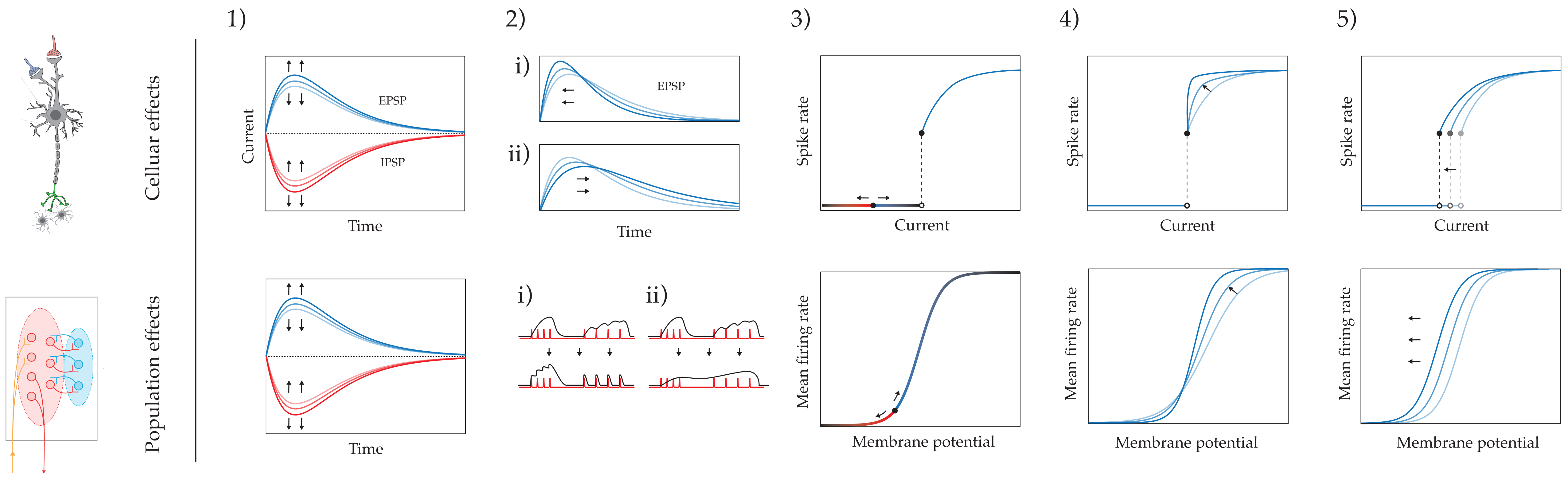

The gain (input-output) of a neutron is also state-dependent so that the response of a neutron to a spike train can be modulated by other inputs

(cf Stephan et al. 2006)

Mac Shine, Eli Muller

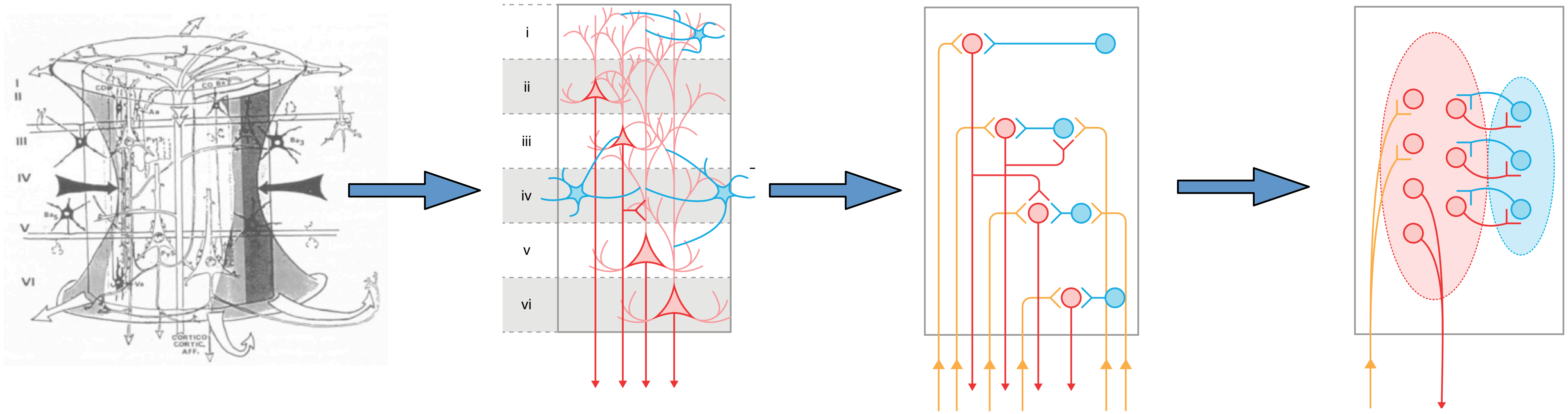
# I: Population models : Basic principles

There are mean field effects for all of these mechanisms of single cell neuroplasticity and state-dependent gain modulation




Mac Shine, Eli Muller

# I: Population models : Basic principles



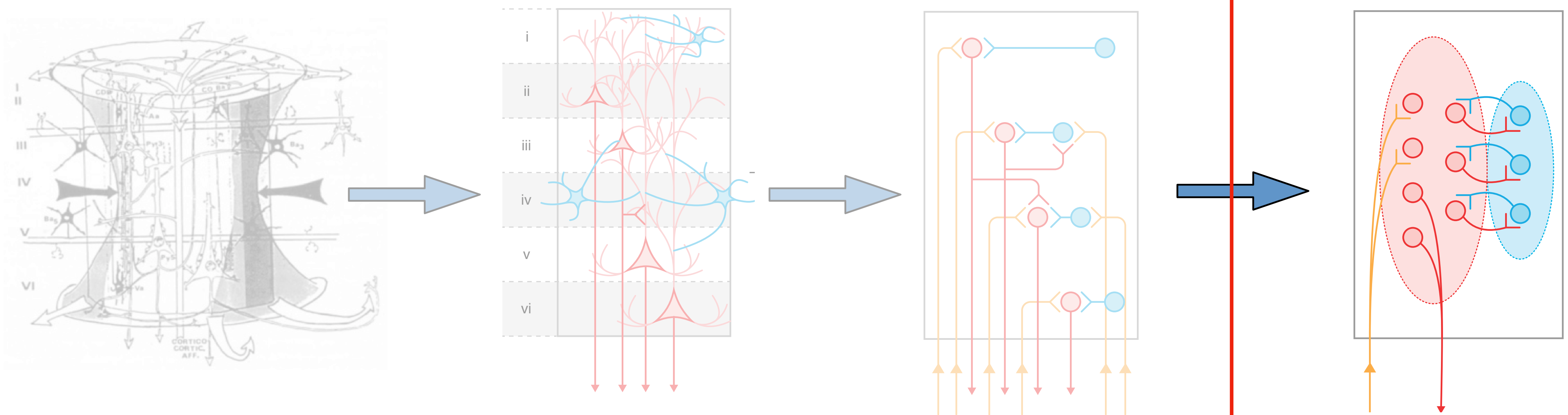

Complex neural histology
(e.g. cortical column)

Detailed multi
compartment spiking
neural model
(e.g. HBP)

Simple spiking neural
circuit model
(e.g. Brian, neuron,
SpikeNET)

Lumped neural mass
model
(e.g. TVB, BDT)

# I: Population models : Basic principles

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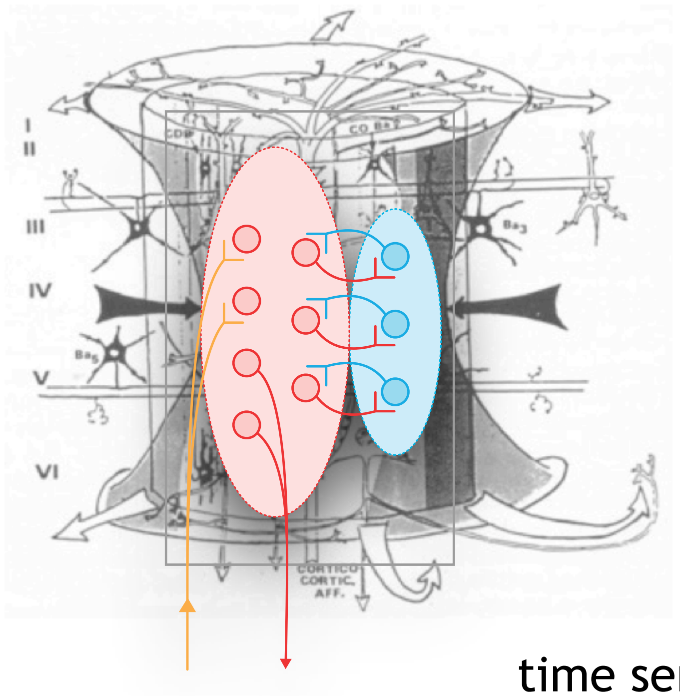
(e.g. TVB, BDT)

Neural mass and neural field models begin with
local lumped (mean field) population models

Freeman (1975) *Biol. Cybernetics*

# II: Nodes and neural masses

## Neural mass model



local “centre of mass” (average states over small area)

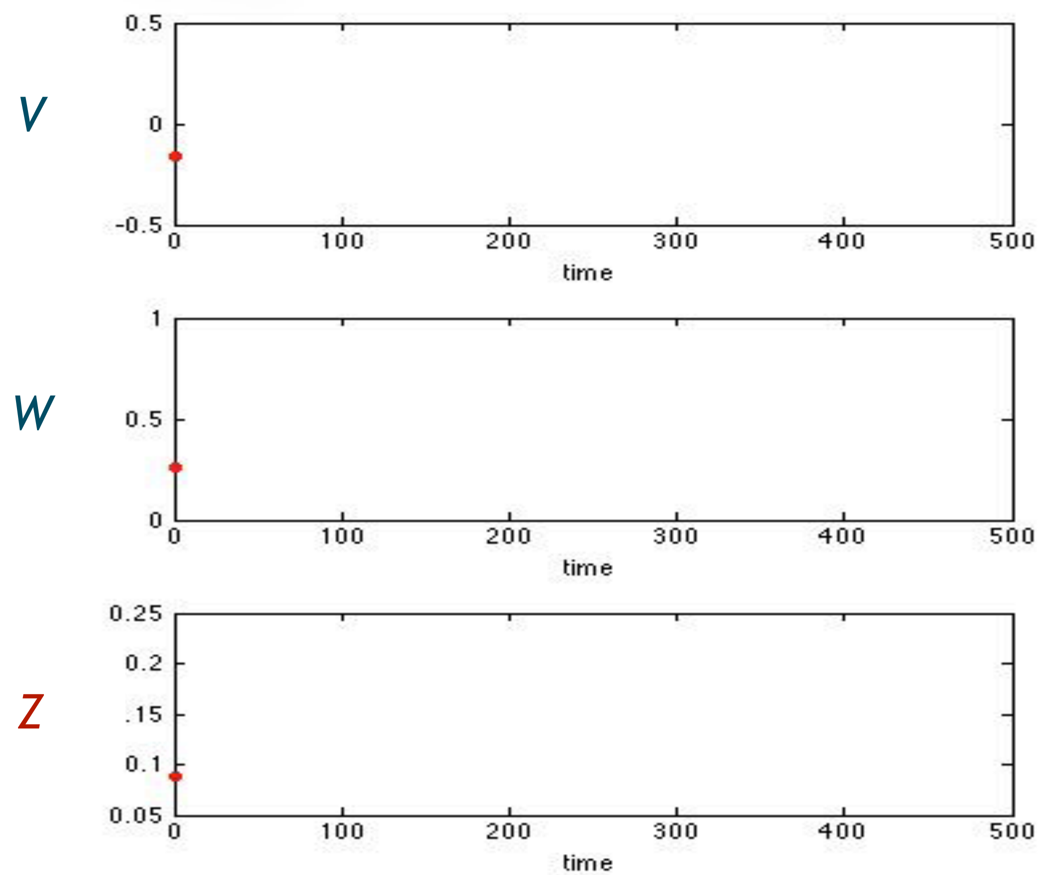
$$\frac{d\mathbf{X}}{dt} = f(\mathbf{X}) + I \qquad \mathbf{X} = \begin{cases} V & \text{pyramidal membrane potential} \\ W & \text{potassium channel conductance} \\ Z & \text{inhibitory membrane potential} \end{cases}$$

(fast)

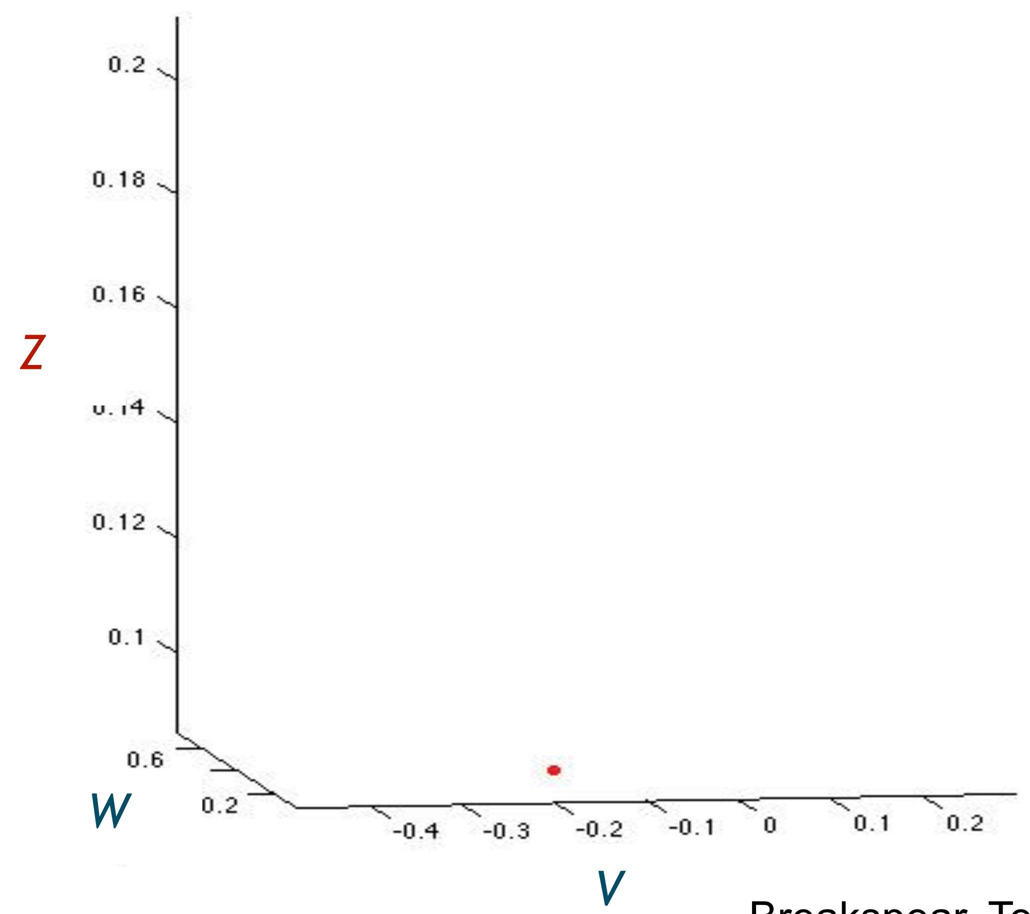
(slow)

“chaos”

time series



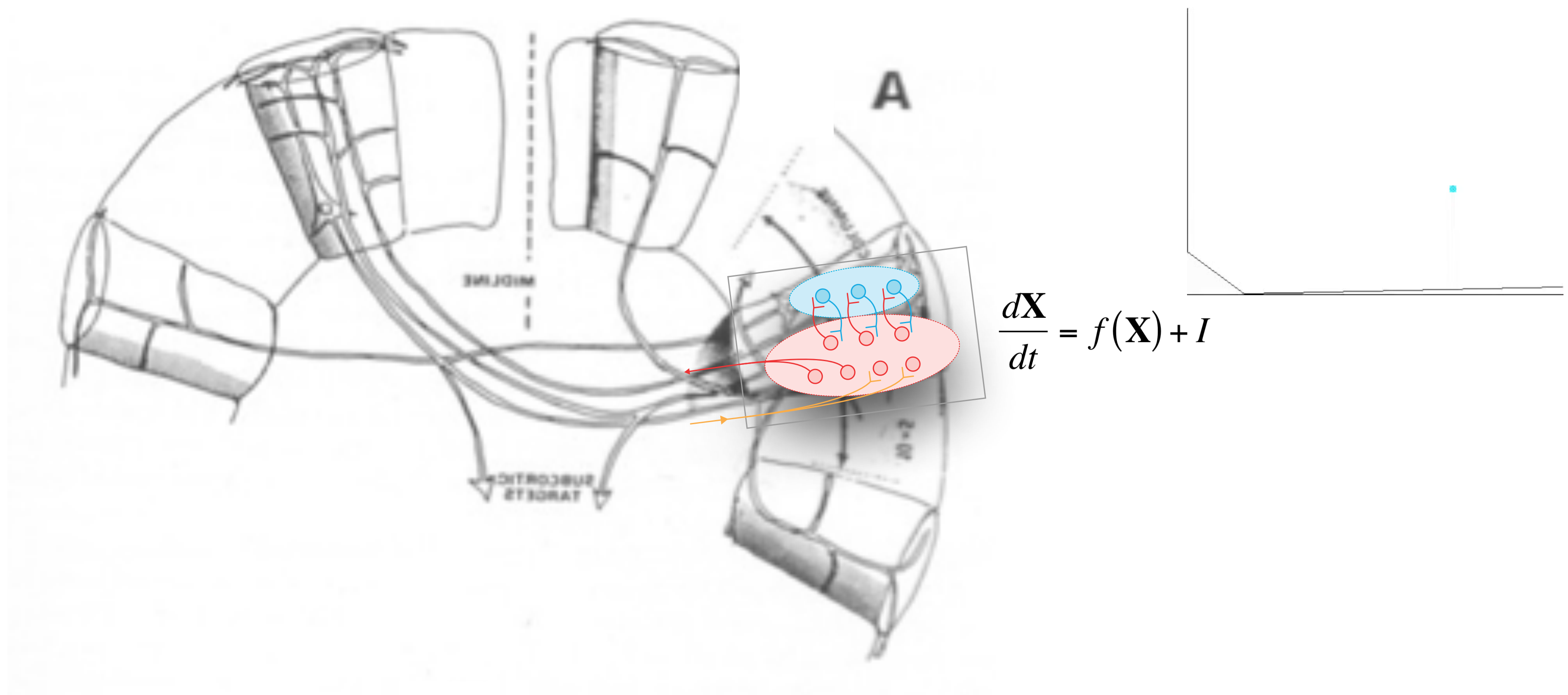

phase portrait




Breakspear, Terry, Friston (2003)

# II: Nodes and neural masses

In neural mass models, a local neural mass model is placed at each of the brain's "nodes"




$$\frac{d\mathbf{X}}{dt} = f(\mathbf{X}) + I$$

Roberts *et al* (2019) *Nature Communications*

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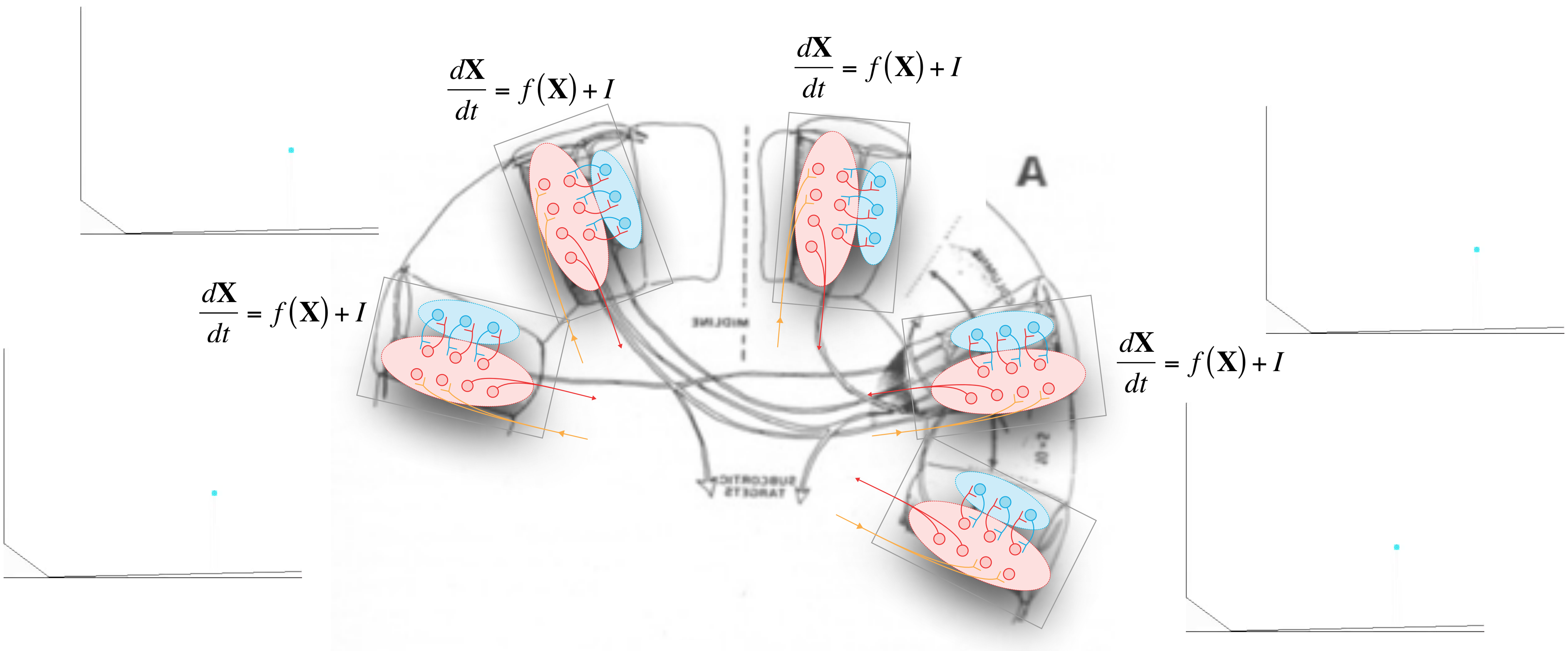


Roberts *et al* (2019) *Nature Communications*

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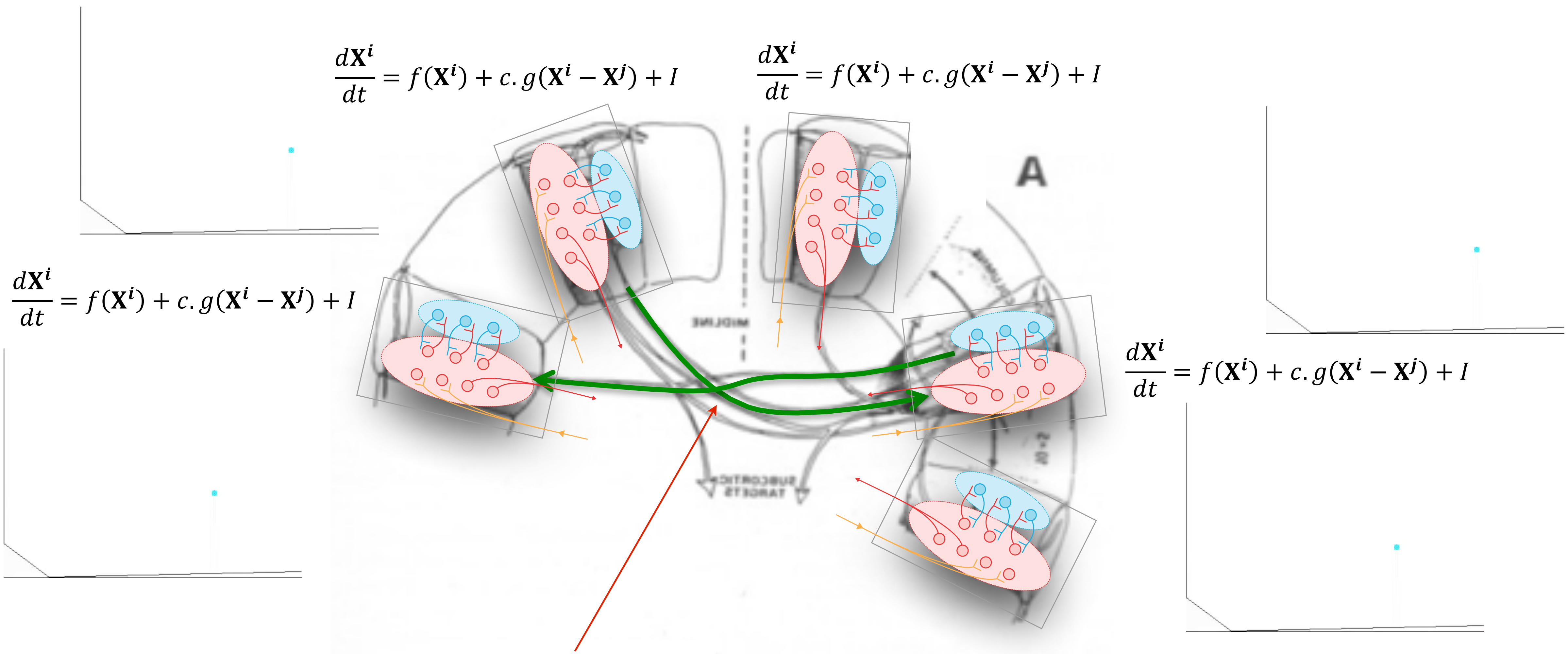
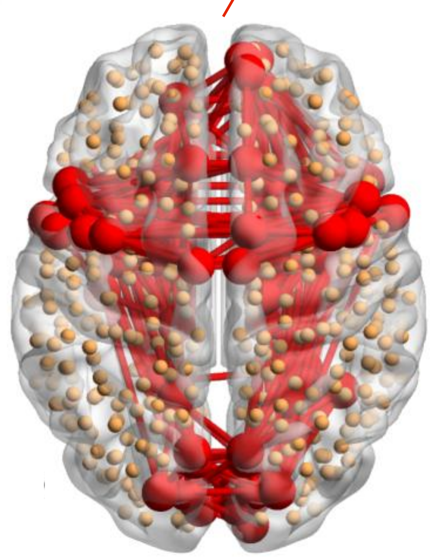



... let them influence each other through the connectome



Roberts *et al* (2019) *Nature Communications*

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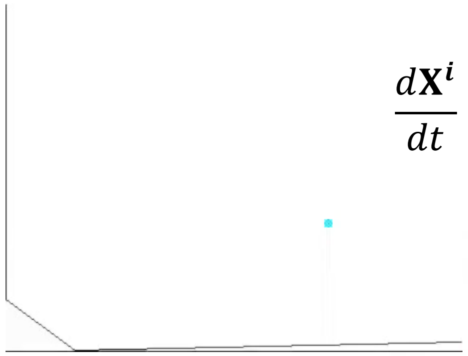

$$\frac{d\mathbf{X}^i}{dt} = f(\mathbf{X}^i) + c.\,g(\mathbf{X}^i - \mathbf{X}^j) + I$$

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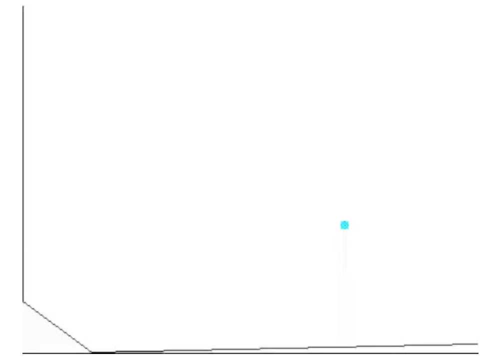

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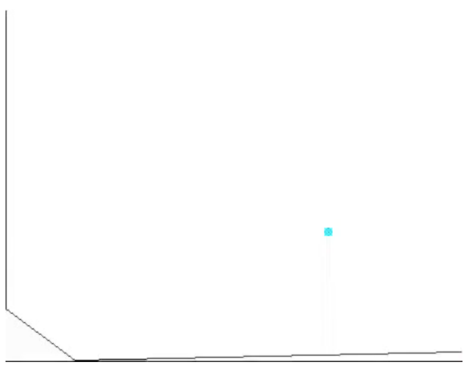

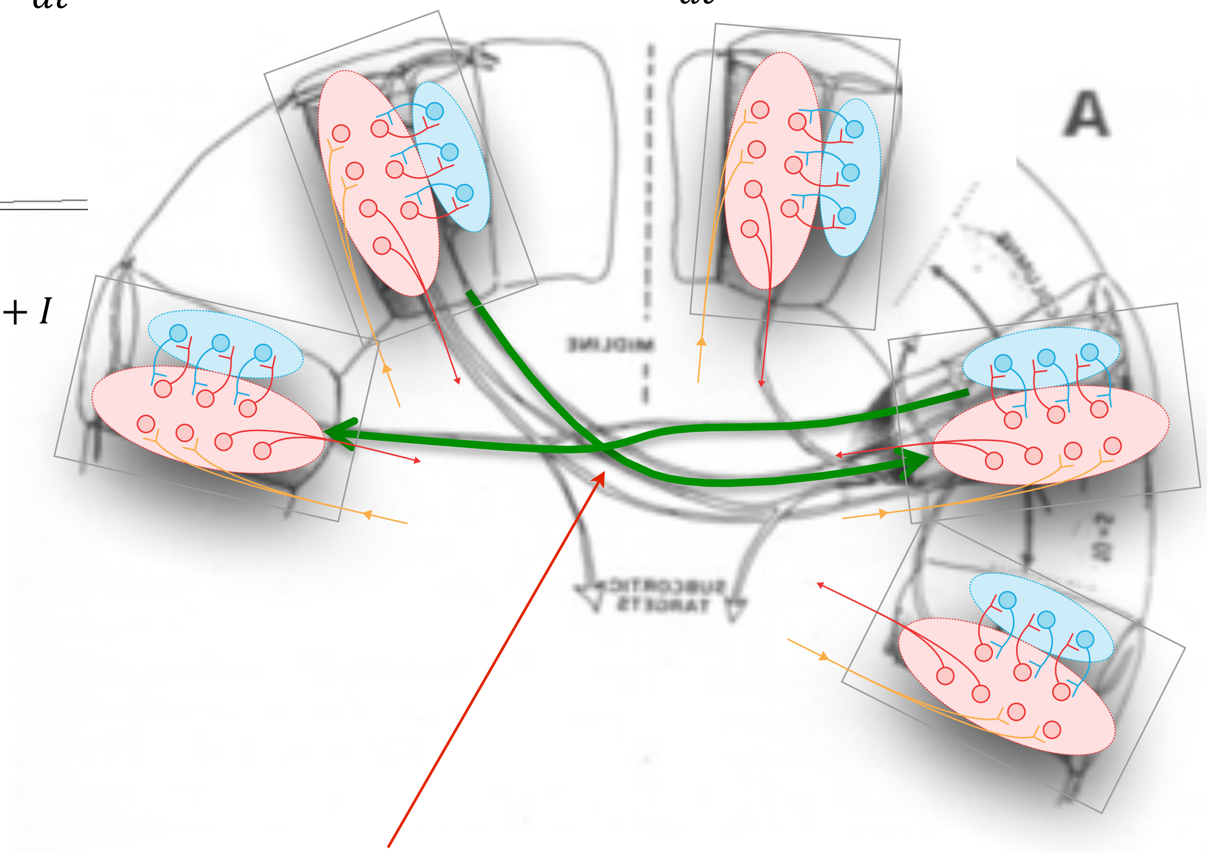


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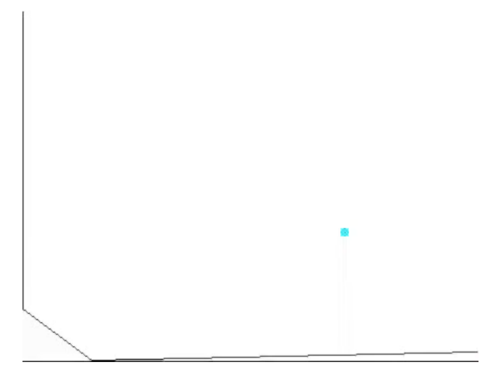
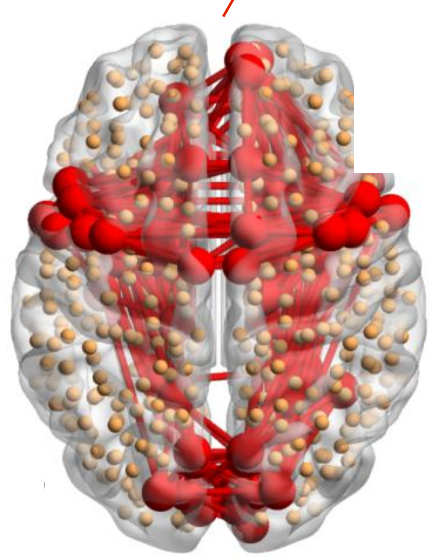
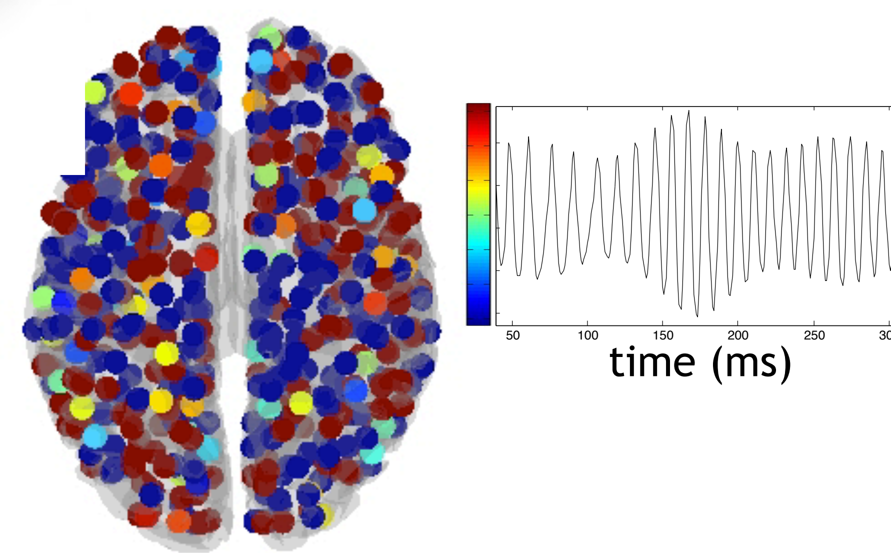


... let them influence each other through the connectome



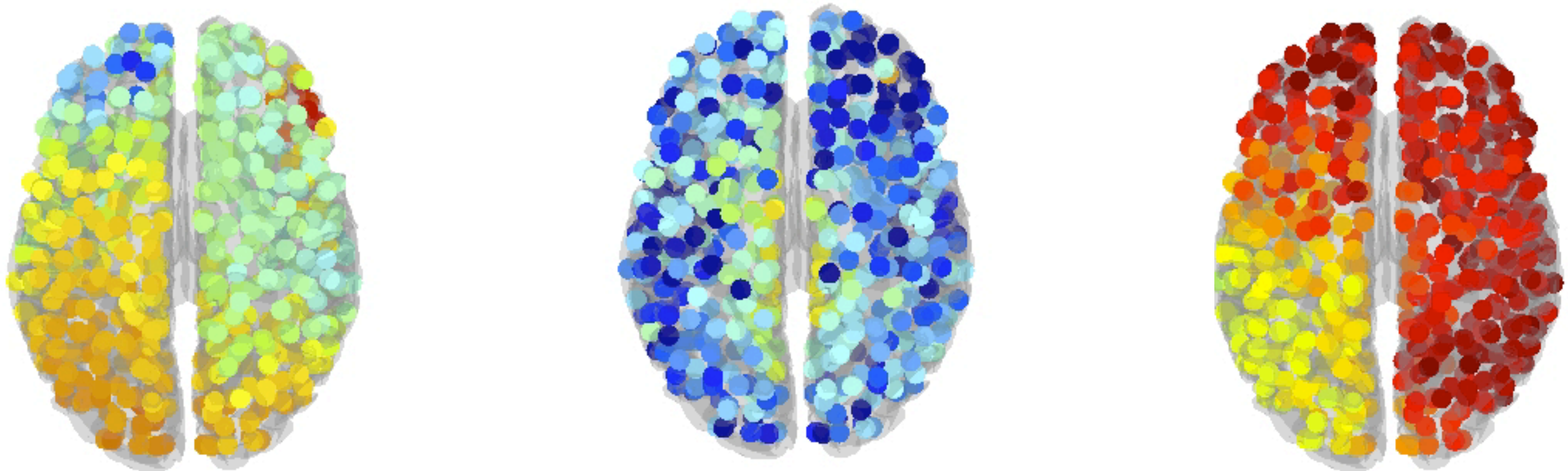
... and see what happens



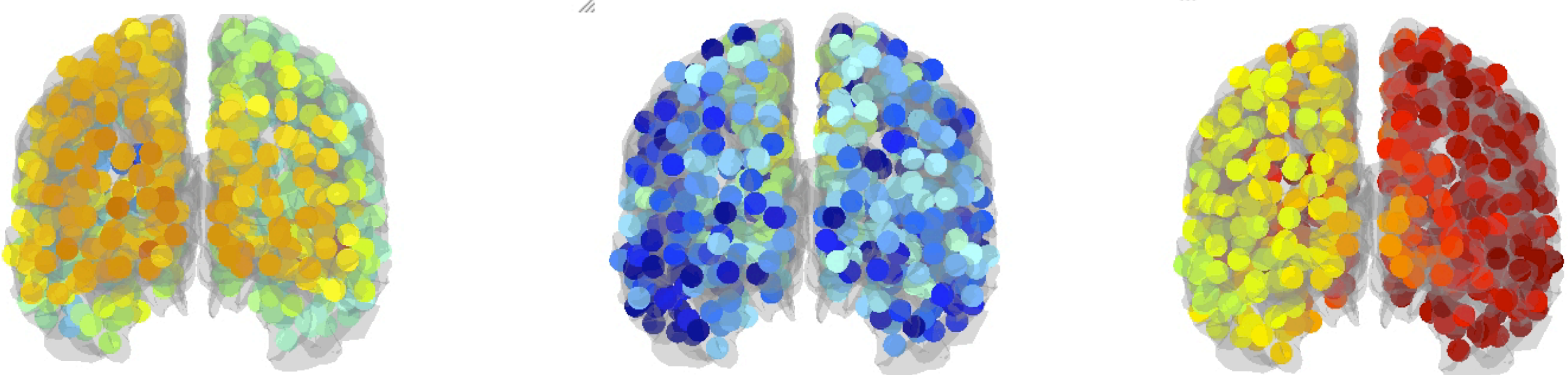

Roberts *et al* (2019) *Nature Communications*

## II: Nodes and neural masses

Strong coupling through the connectome leads to a variety of spatiotemporal patterns



Rotating waves Breathers Travelling waves



# II: Nodes and neural masses

Waves have recently been observed in a broad spectrum of functional neuroscience data, across species, functions, areas, data modalities

BRIEF COMMUNICATIONS

Traveling waves of activity in primary visual cortex during binocular rivalry

Sang-Hun Lee[1,3], Randolph Blake[2] & David J Heeger[1]

VOLUME 8 | NUMBER 1 | JANUAR

nature neuroscience

**Propagating waves mediate information transfer in the motor cortex**

Doug Rubino[1], Kay A Robbins[2] & Nicholas G Hatsopoulos[1]

Neuron

Article

**Reverberation of Recent Visual Experience in Spontaneous Cortical Waves**

Feng Han,[1,4] Natalia Caporale,[2,4] and Yang Dan[1,2,3,*]

nature COMMUNICATIONS

ARTICLE

Received 24 Sep 2013 | Accepted 17 Mar 2014 | Published 28 Apr 2014 DOI: 10.1038/ncomms4675 OPEN

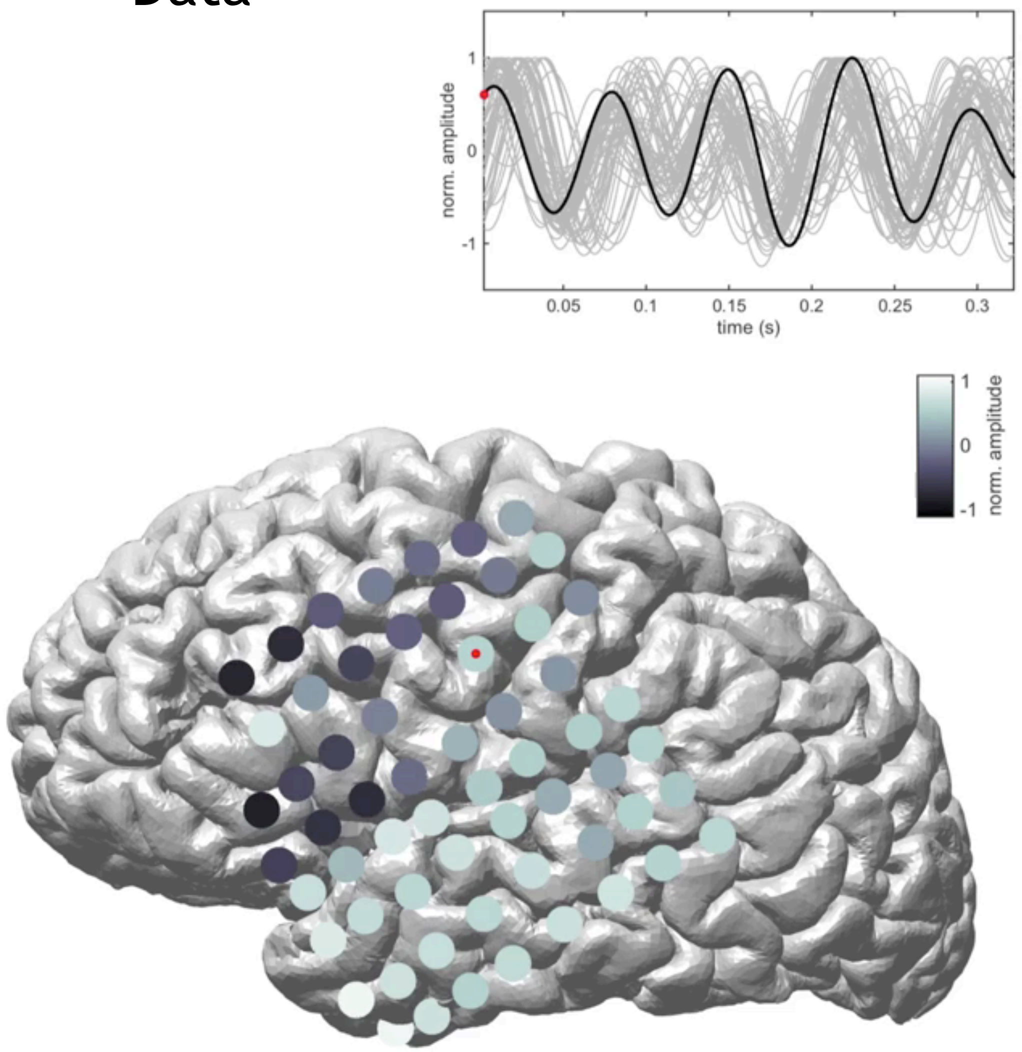
The stimulus-evoked population response in visual cortex of awake monkey is a propagating wave

Lyle Muller[1,*], Alexandre Reynaud[2,*], Frédéric Chavane[2] & Alain Destexhe[1]

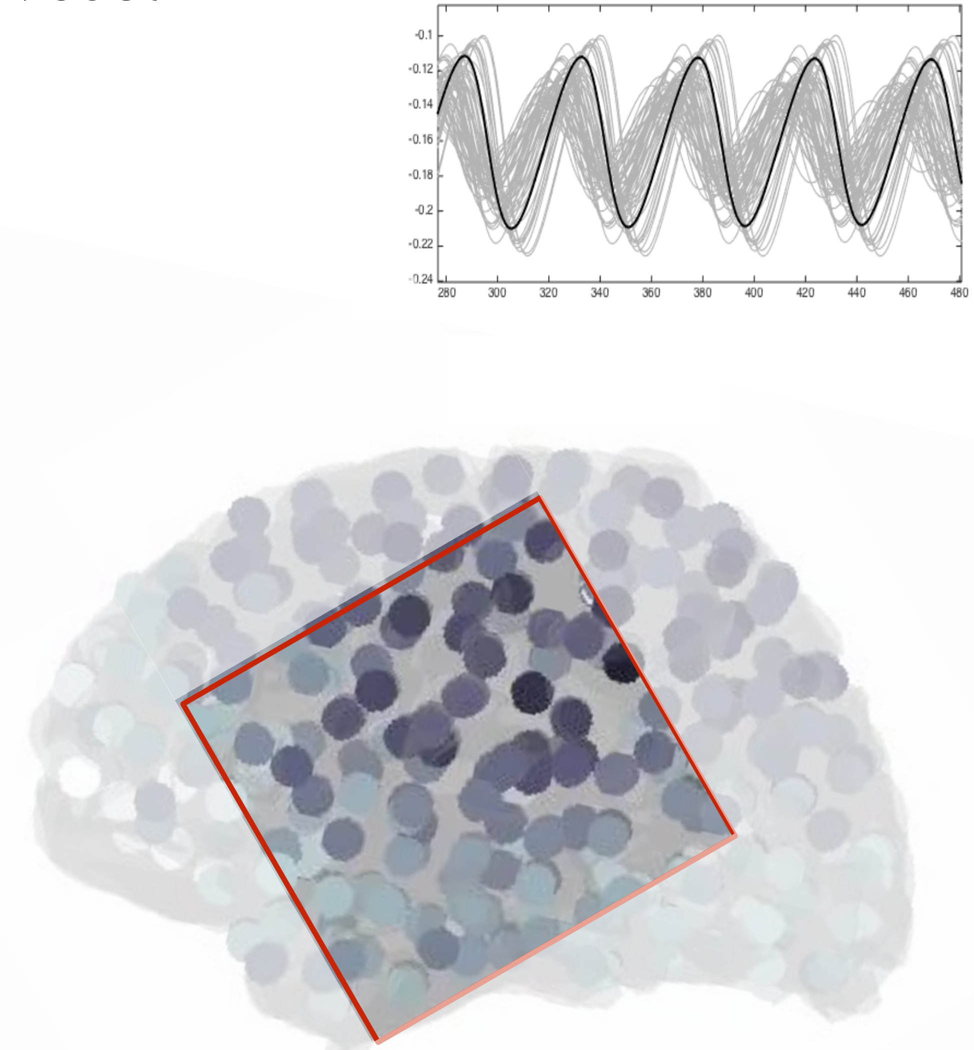
# II: Nodes and neural masses

Interestingly, these predictions bear close relationship with waves in recently acquired human spindles waves during sleep

Data




Model




eLIFE
elifesciences.org

**Rotating waves during human sleep spindles organize global patterns of activity that repeat precisely through the night**

**Lyle Muller[1], Giovanni Piantoni[2], Dominik Koller[1], Sydney S Cash[2], Eric Halgren[3,4], Terrence J Sejnowski[1]***

nature COMMUNICATIONS

ARTICLE

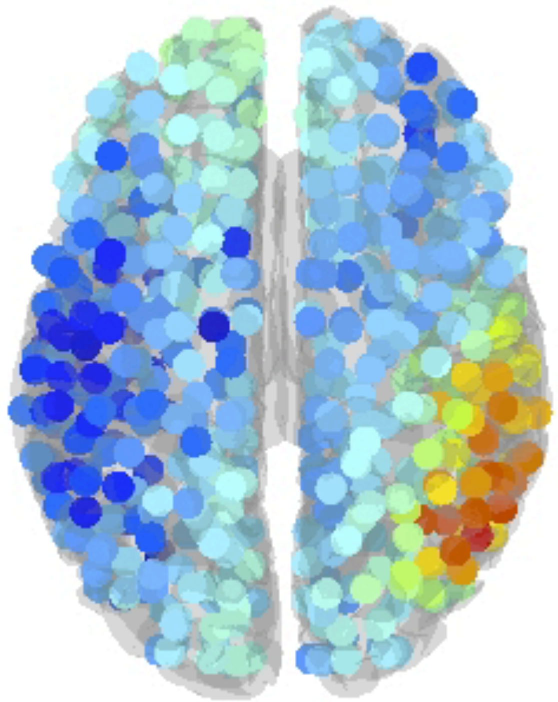
https://doi.org/10.1038/s41467-019-08999-0 OPEN

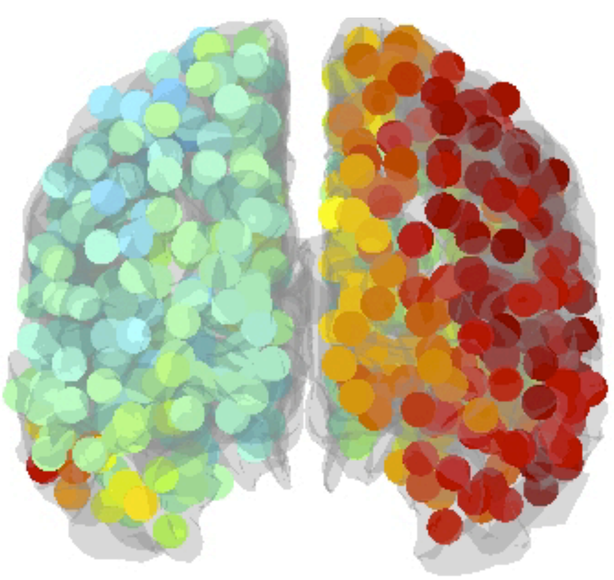
Metastable brain waves

James A. Roberts[1,2], Leonardo L. Gollo[1,2], Romesh G. Abeysuriya[3], Gloria Roberts[4,5], Philip B. Mitchell[4,5], Mark W. Woolrich[3] & Michael Breakspear[1,2,6,7]

# II: Nodes and neural masses

These dynamics spontaneously cycle through distinct spatiotemporal patterns





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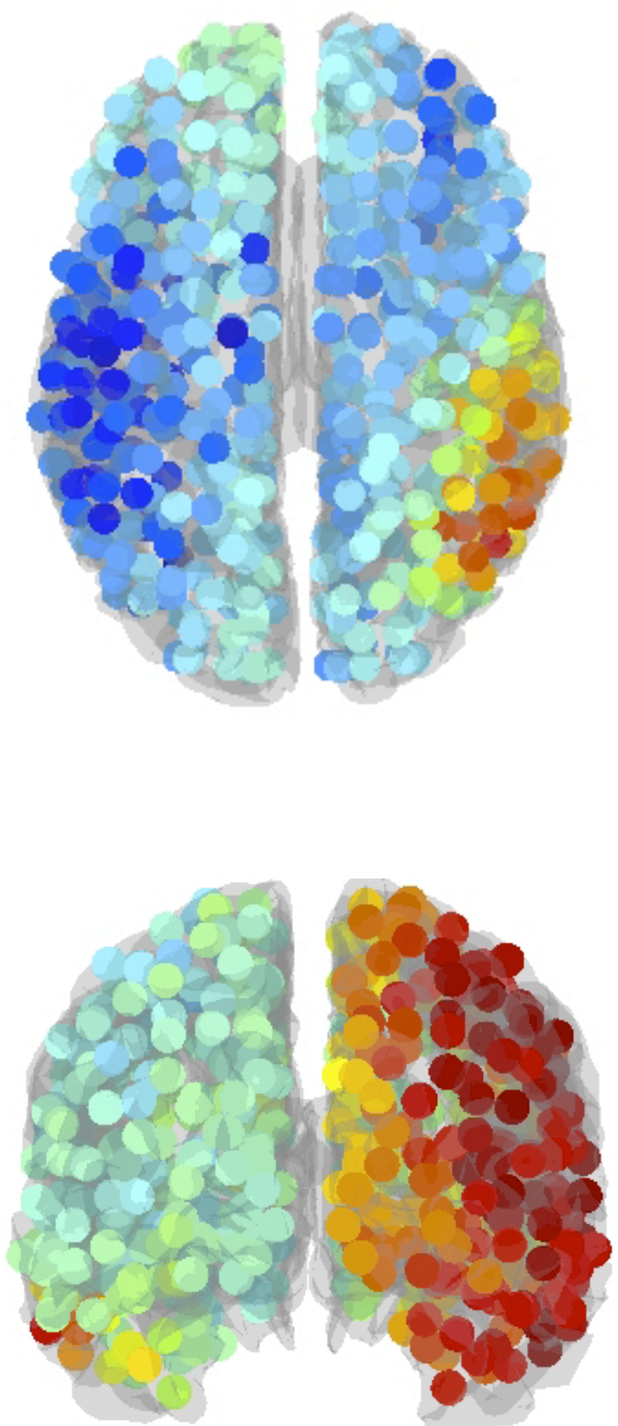
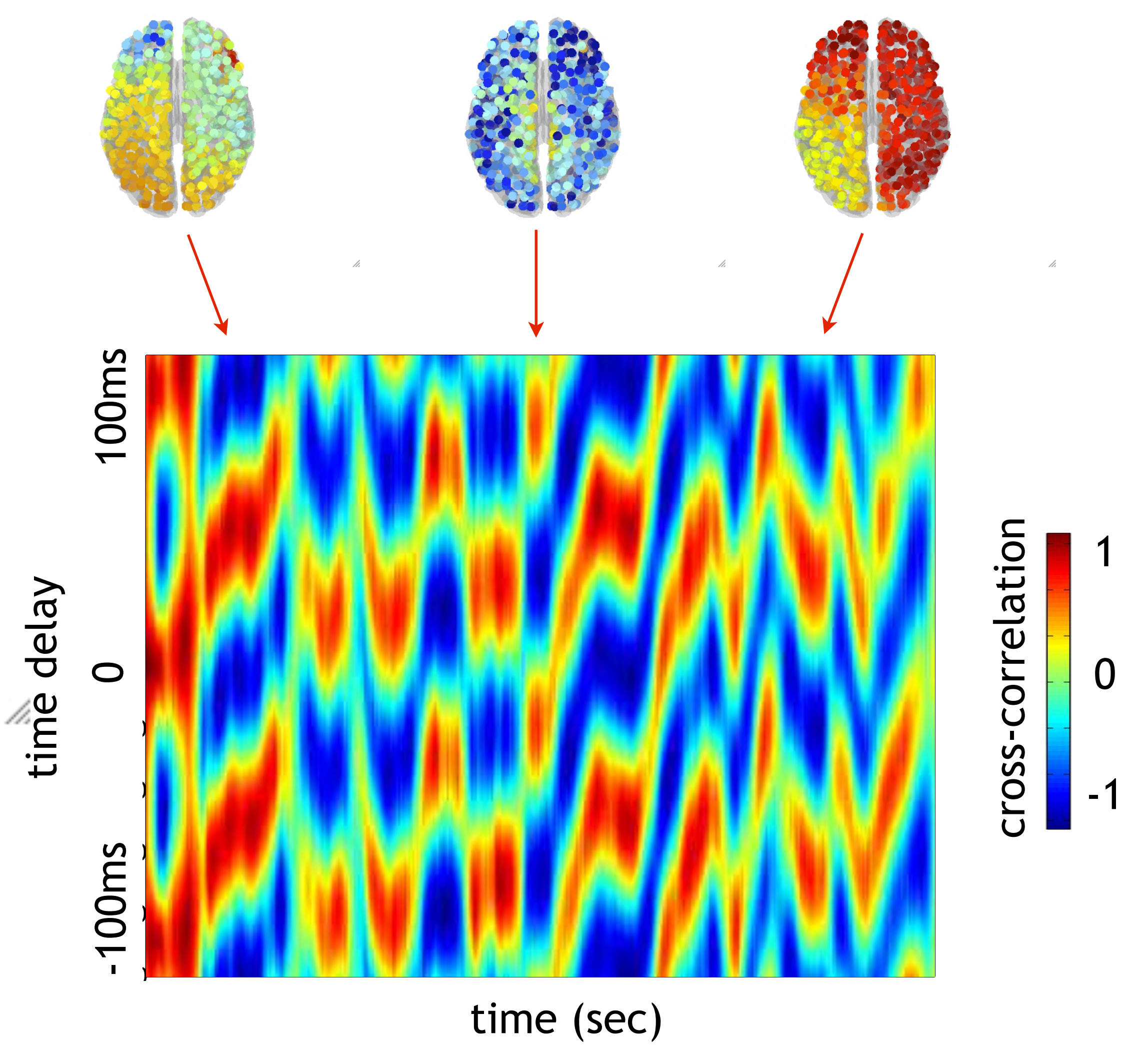


Each pattern is associated with a distinct "whole brain" correlation structure



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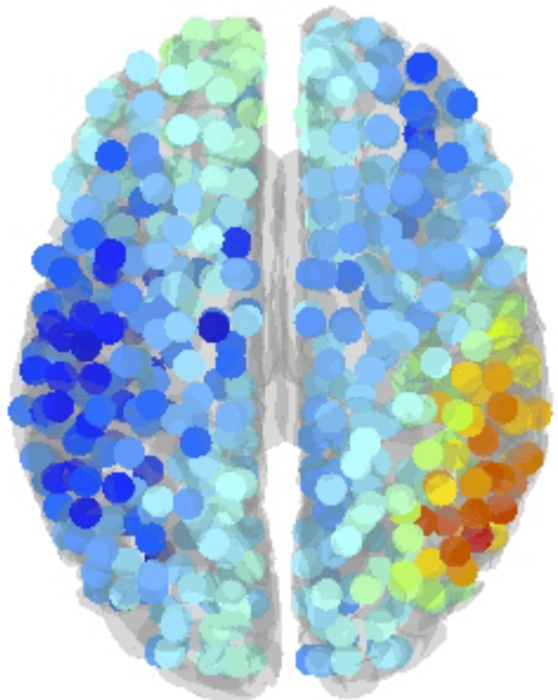

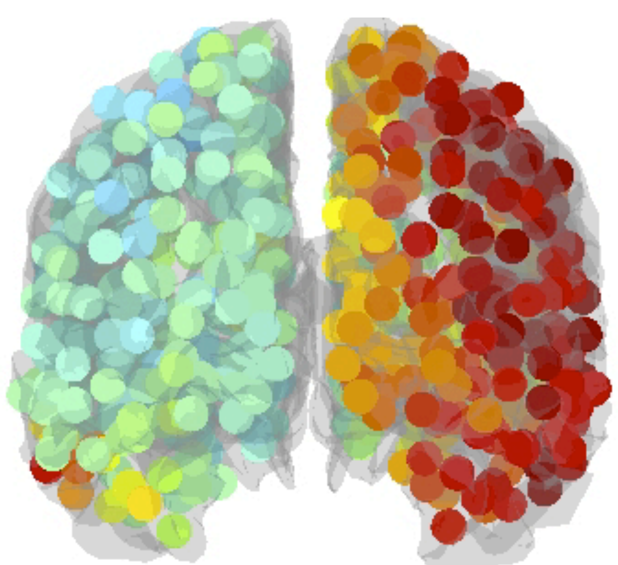

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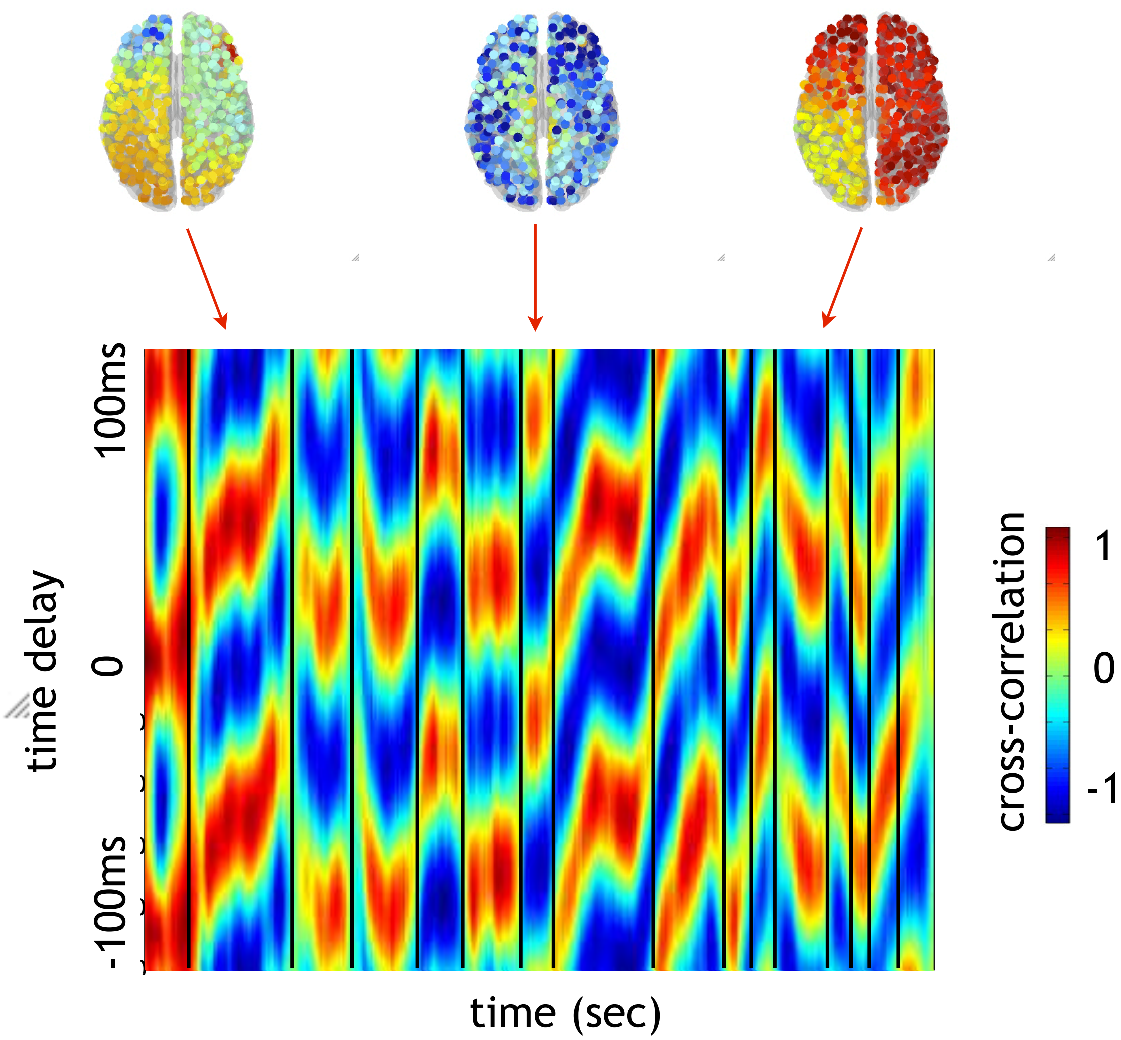
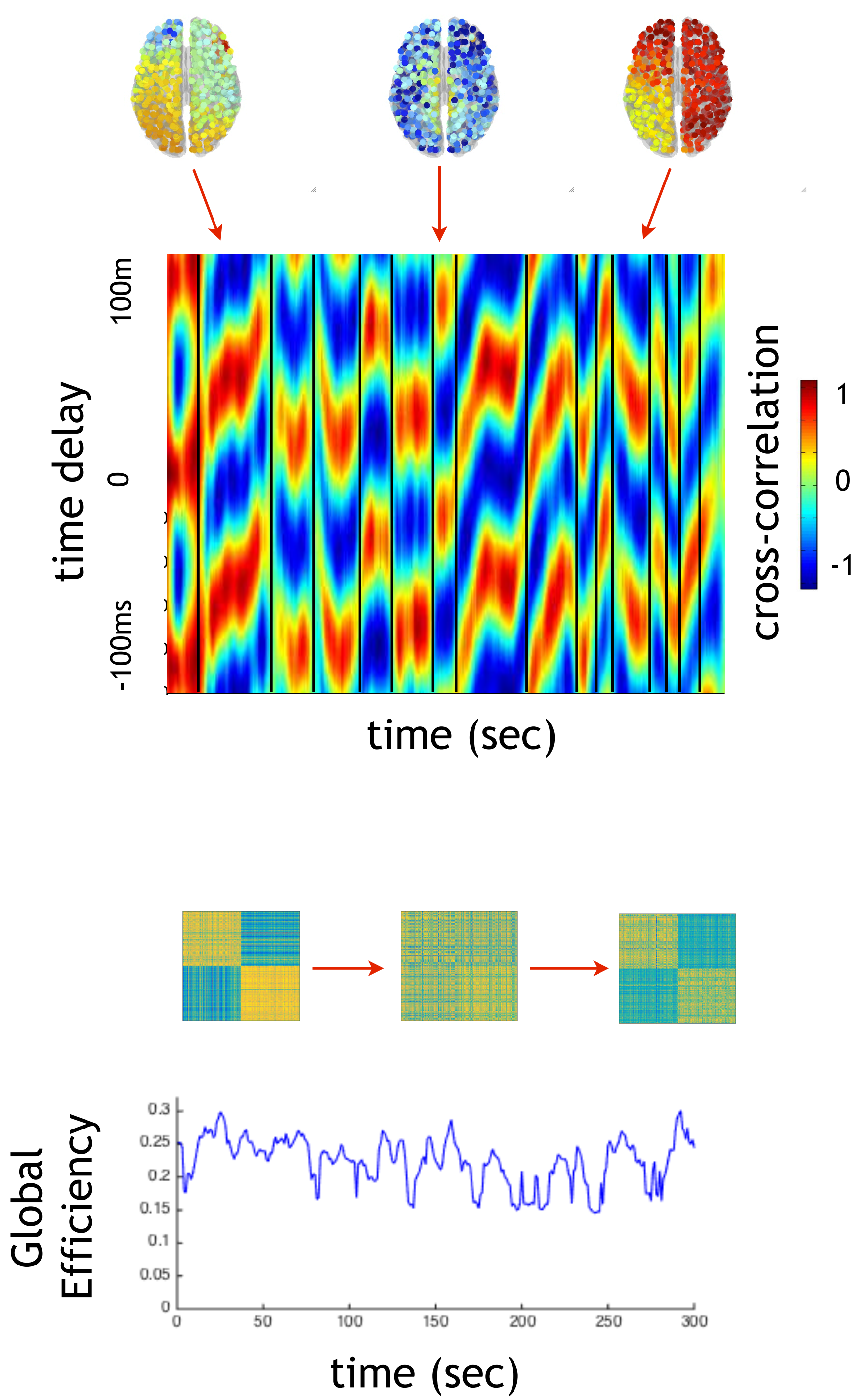



Transitions are associated with weak correlations which can be used to partition the data into metastable states

# II: Nodes and neural masses

Such dynamics provide a plausible generative model for dynamic functional connectivity

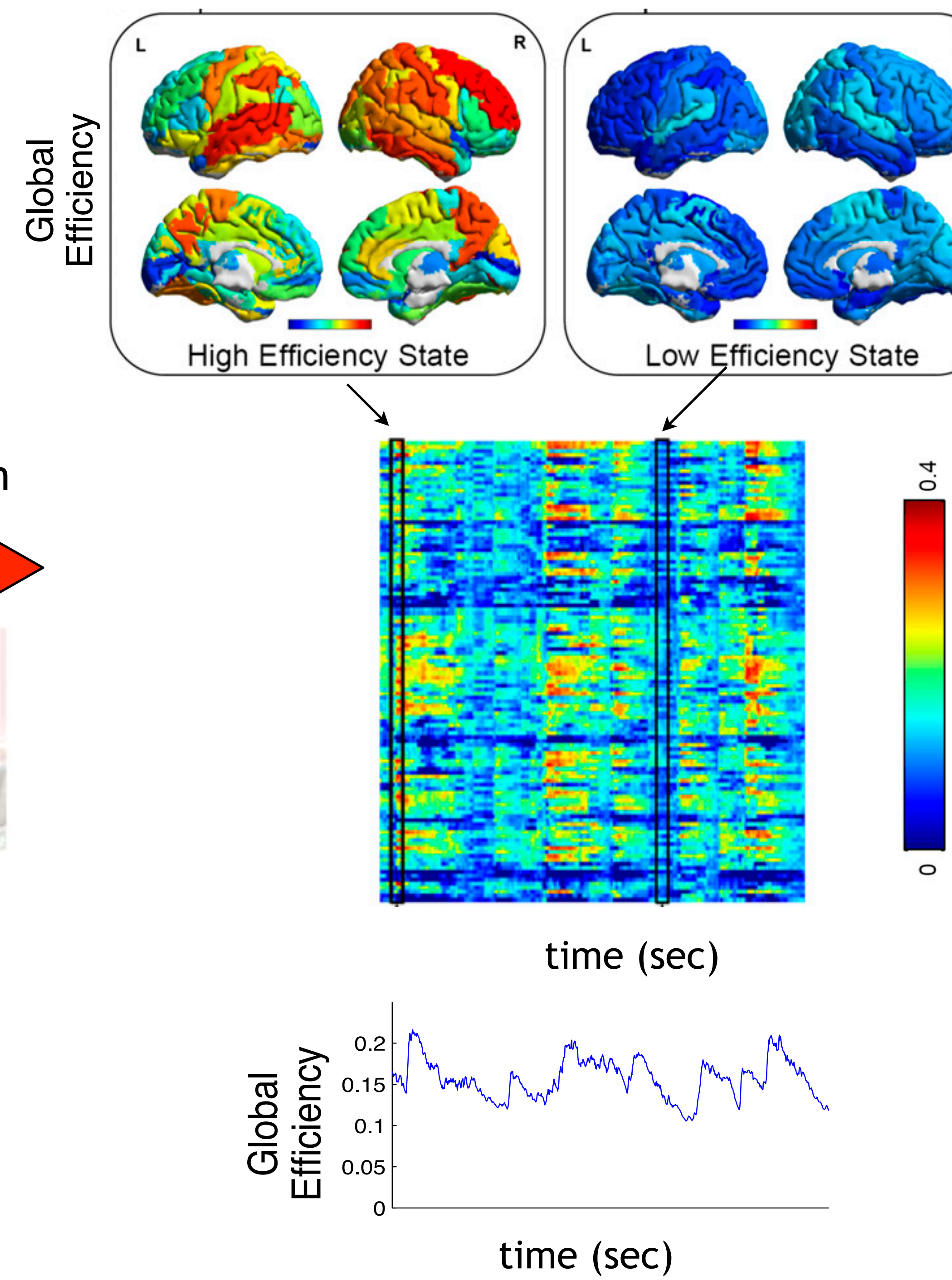
***model***




Observation

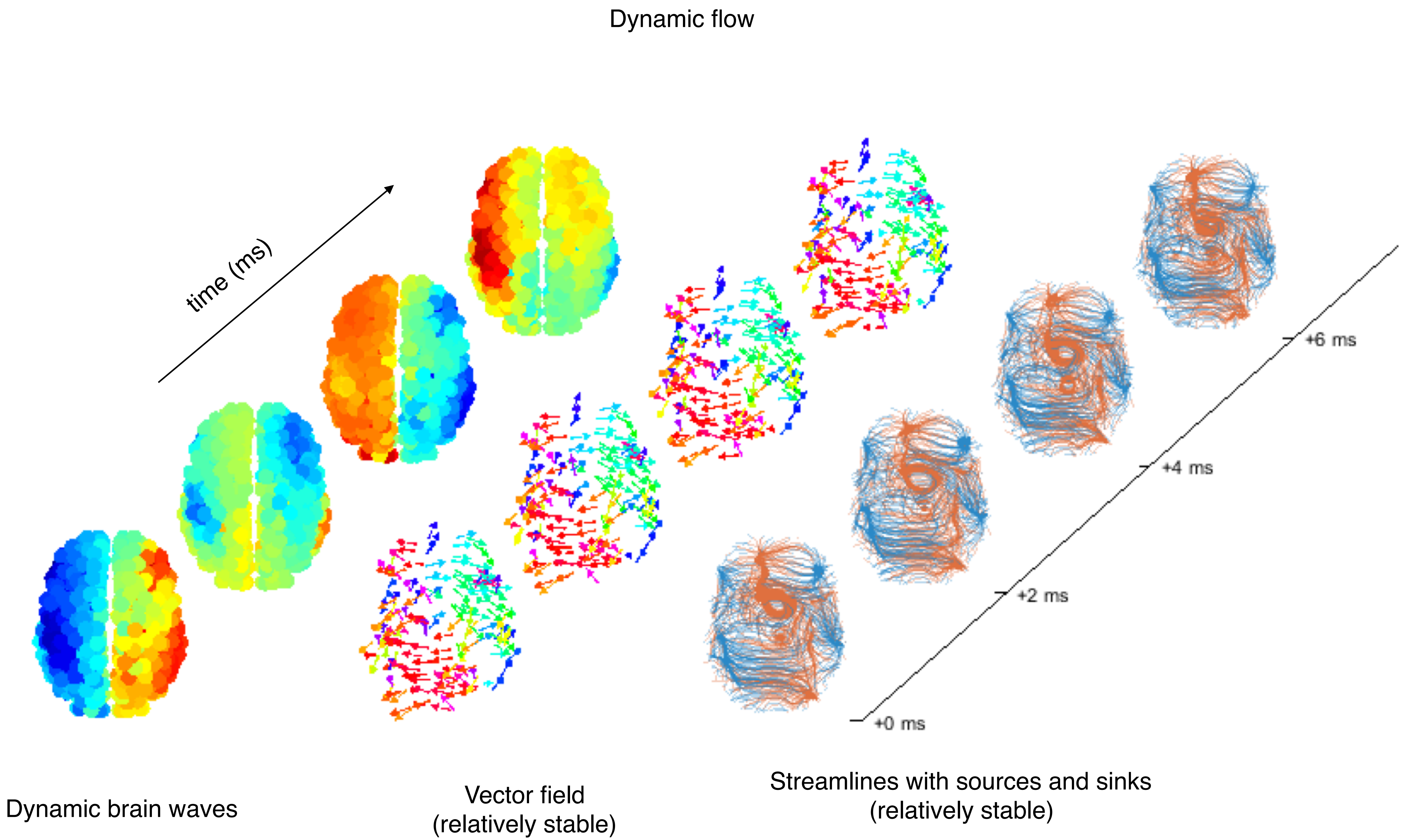
MRI

***HCP data***




Zalesky *et al*. (2013) *PNAS*

# II: Nodes and neural masses



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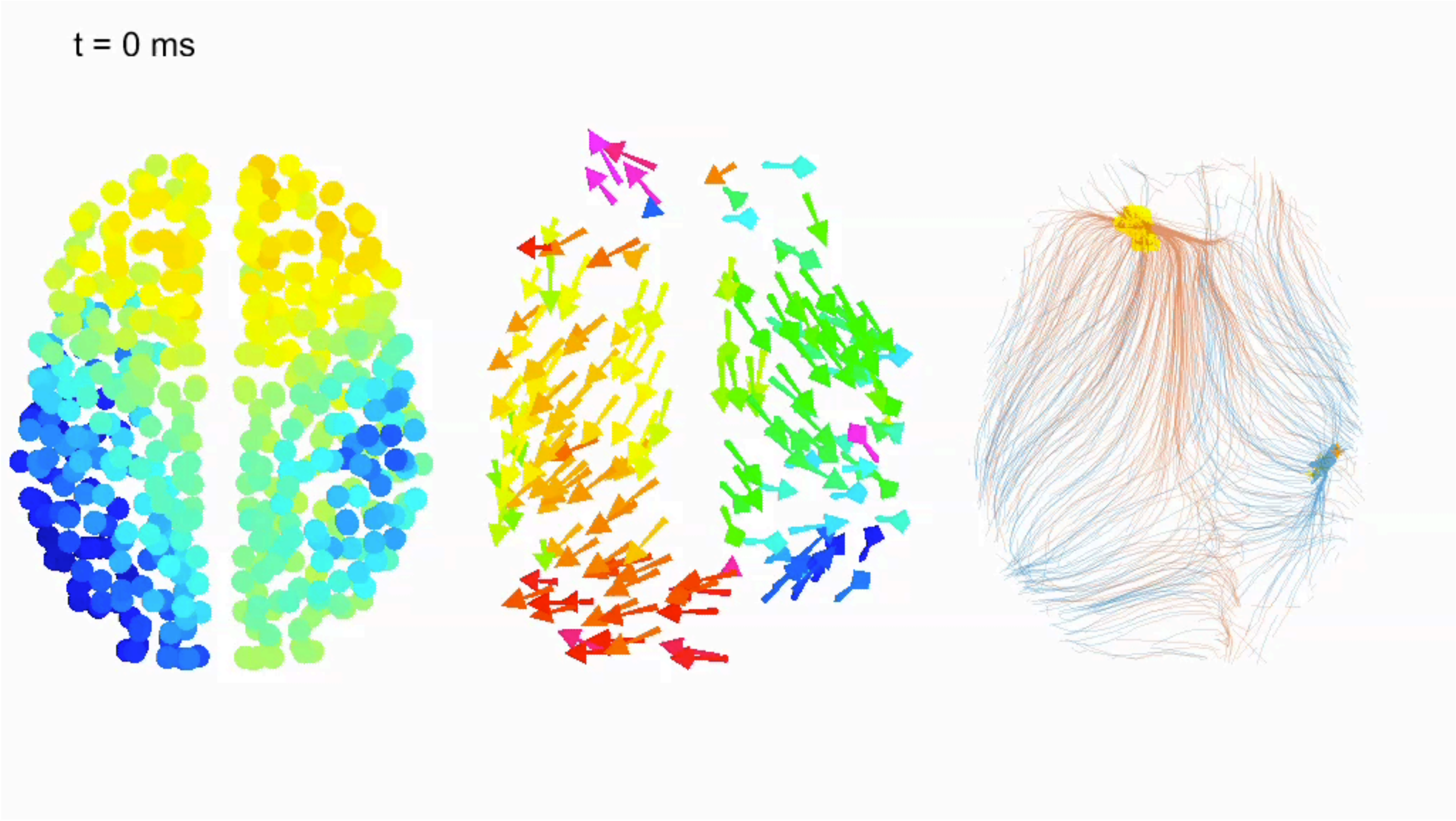
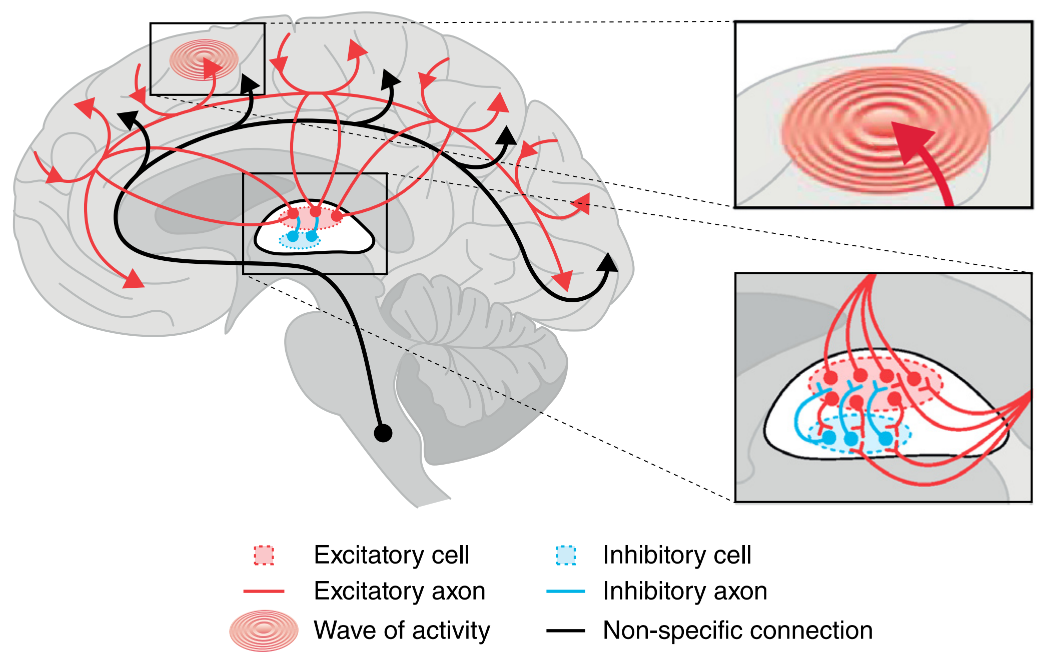


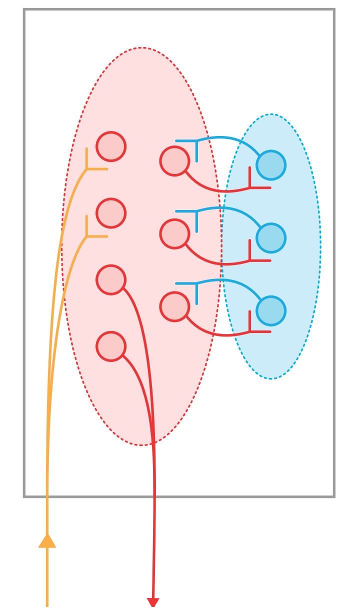
# III: Neural fields + modes

$$\frac{1}{\gamma_e^2}\left(\frac{\partial^2}{\partial t^2} + 2\gamma_e^2 \frac{\partial}{\partial t} + \gamma_e^2 - v_e^2\nabla^2\right)\phi_e\,(\mathbf{x},t) = Q_e(\mathbf{x},t).$$

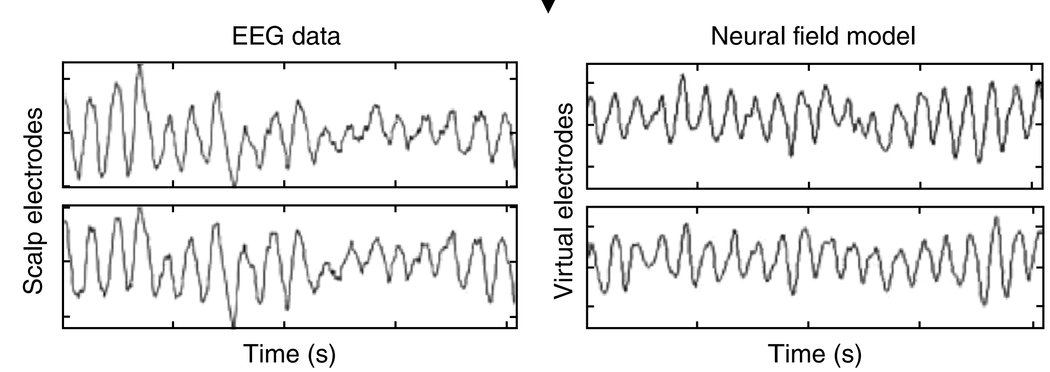
In neural field models, population activity spreads continuously across the cortex via a wave equation

Subcortical loops create resonant frequencies

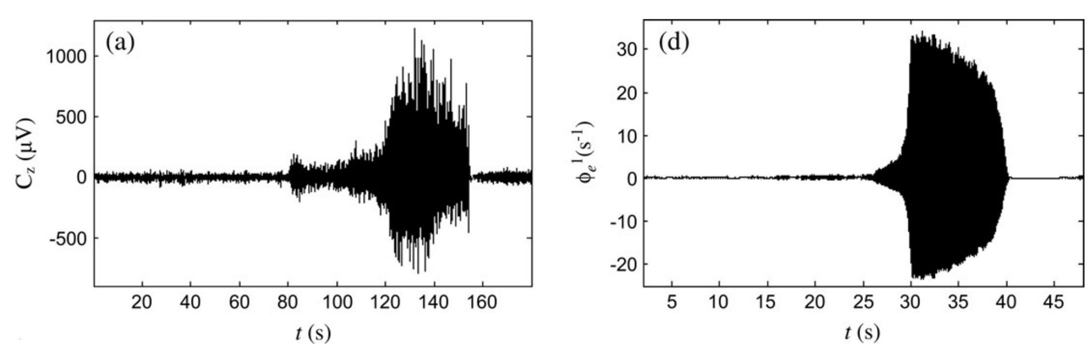


Robinson *et al* (2001, 2002) *PRE*




Numerical and analytic approaches then allow prediction of brain activity



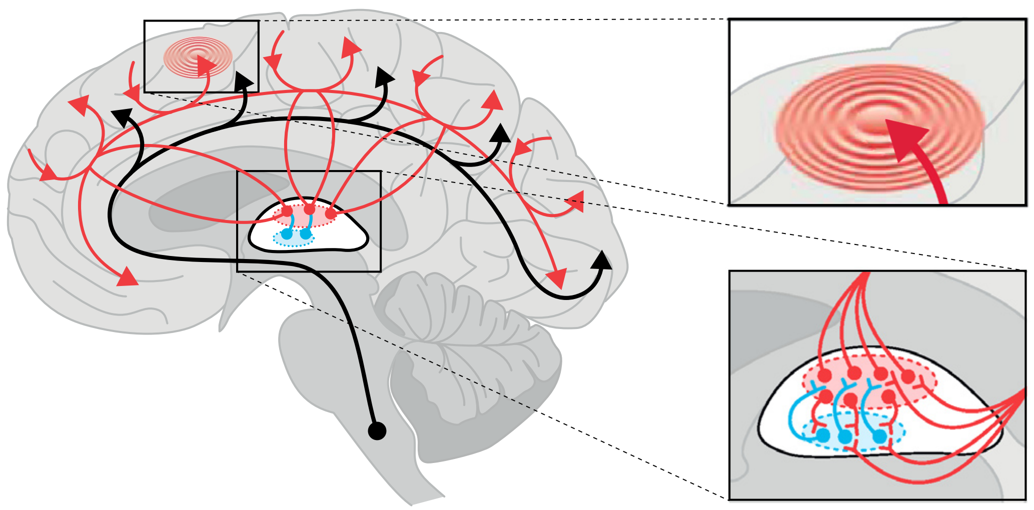

Seizures correspond to nonlinear (Hopf) bifurcations

Breakspear *et al* (2006) *Cerebral Cortex*

# III: Neural fields + modes

Neural fields can also be decomposed into (eigen-)modes of spatiotemporal activity, each with their own spectral fingerprint

$$\frac{1}{\gamma_e^2}\left(\frac{\partial^2}{\partial t^2} + 2\gamma_e^2\frac{\partial}{\partial t} + \gamma_e^2 - \nu_e^2\nabla^2\right)\phi_e\,(\mathbf{x},t) = Q_e(\mathbf{x},t).$$



$$\begin{aligned}\nabla^2 y_\eta(\mathbf{r}) &= -k_\eta^2 y_\eta(\mathbf{r}),\\ D'(\omega_\eta) &= -k_\eta^2 r_{ee}^2.\end{aligned}$$

Robinson *et al.* (2015) *NeuroImage*

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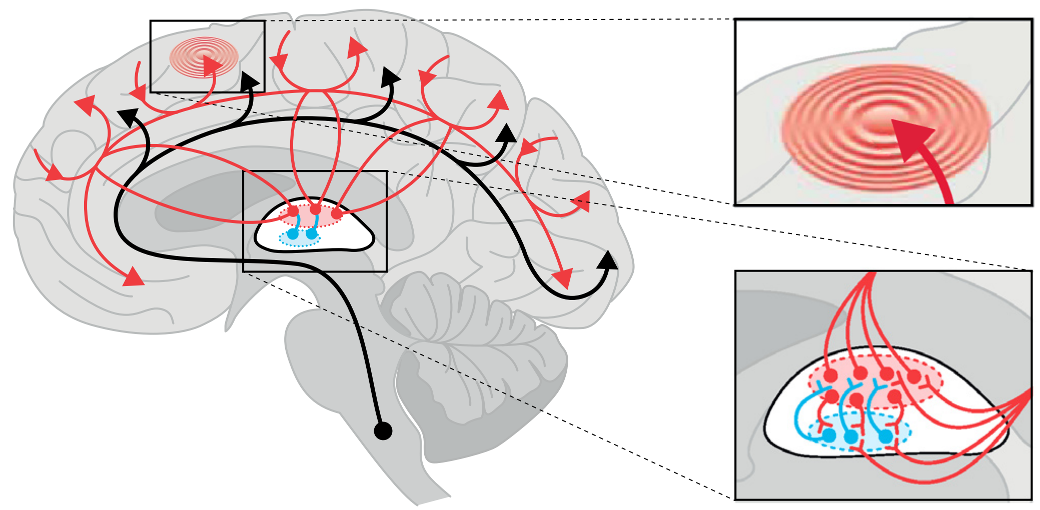

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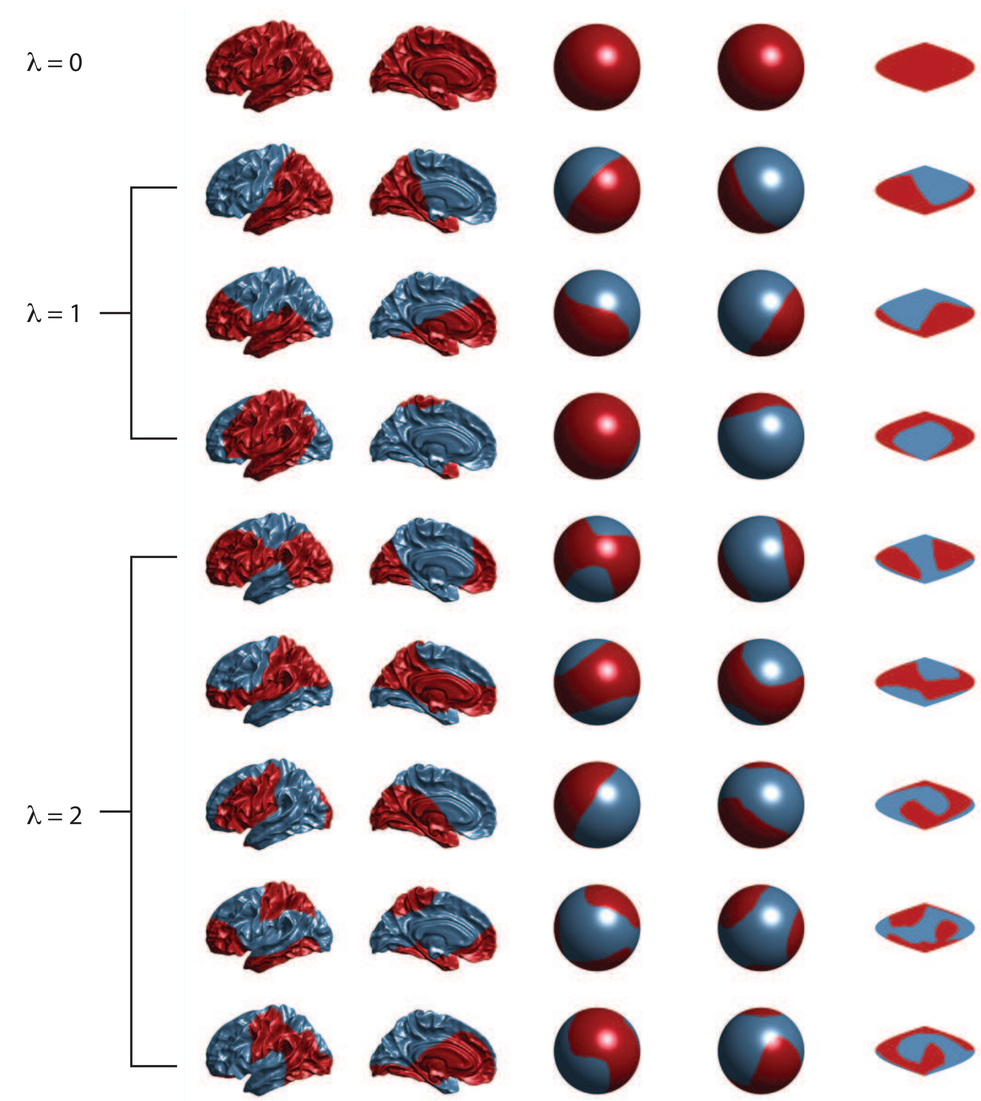
where,

$$\nabla^2 f = \sum_{i,j}\frac{1}{|g|^{1/2}}\frac{\partial}{\partial x^i}\left(|g|^{1/2}g^{ij}\frac{\partial f}{\partial x^j}\right),$$

is the Laplace-Beltrami operator




Robinson *et al.* (2015) *NeuroImage*

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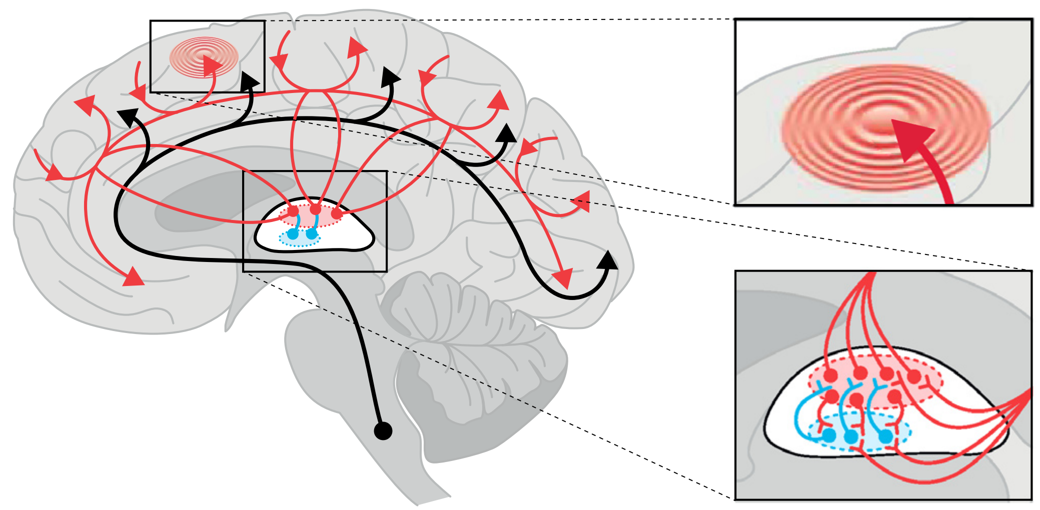
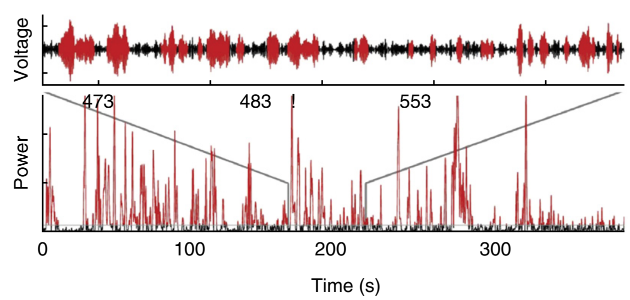


$$\phi_n = \phi_n^{(0)} + \phi_n^{(a)}(t) + \chi\phi_n^{(m)}(t)\phi_e(t - t_0/2),$$




Freyer, Ritter, Robinson, Breakspear (2009, 2011) *J. Neuroscience*

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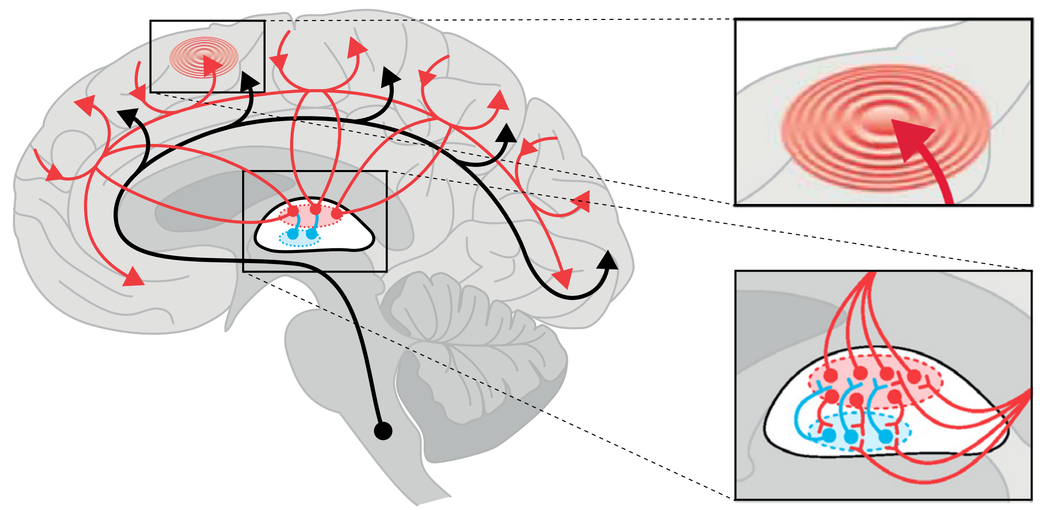

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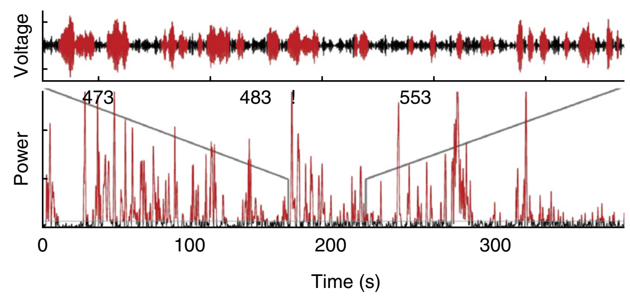


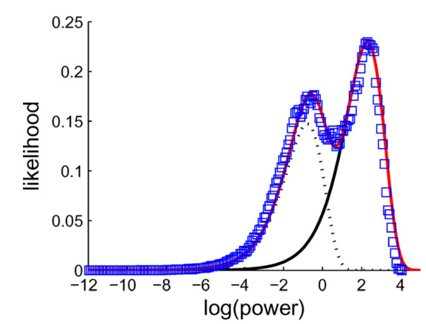


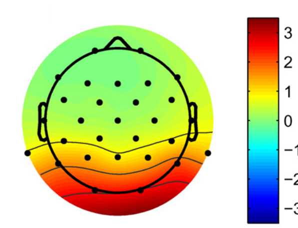


Freyer, Ritter, Robinson, Breakspear (2009, 2011) *J. Neuroscience*

# III: Neural fields + modes

Neural fields can also be decomposed into (eigen-)modes of spatiotemporal activity, each with their own spectral fingerprint

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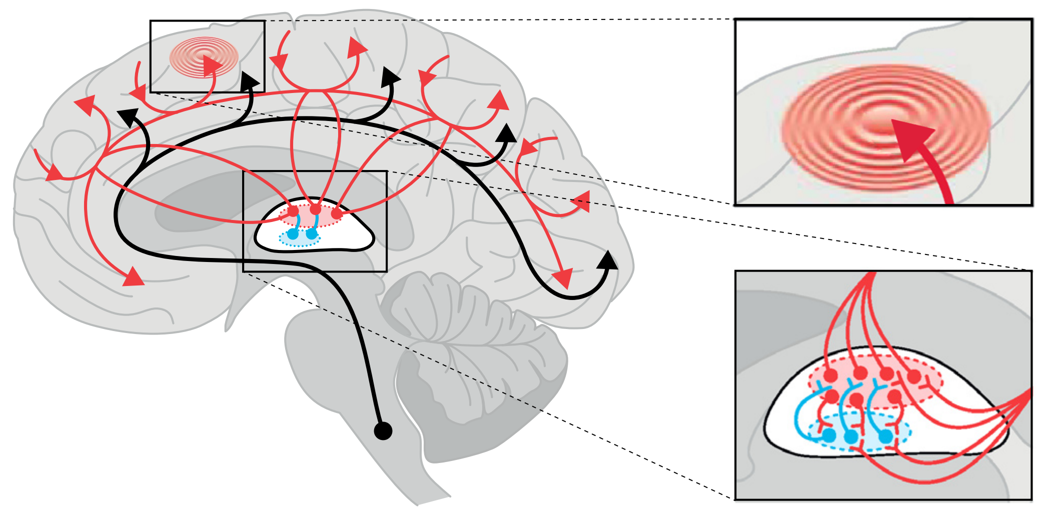

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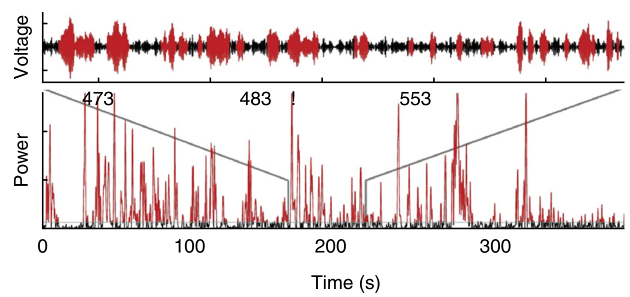


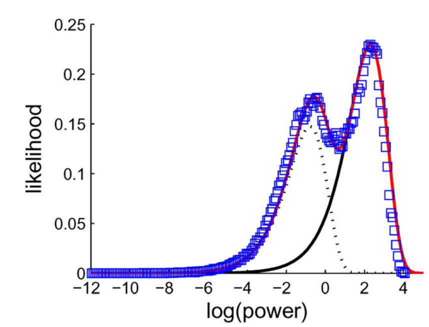


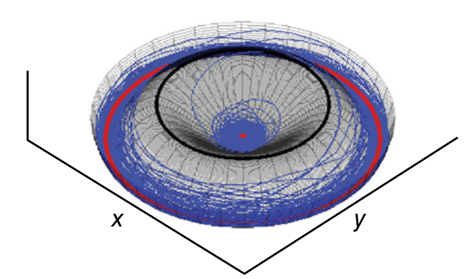


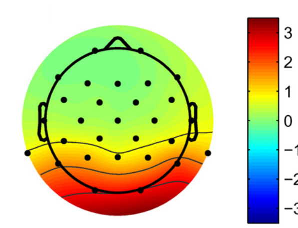


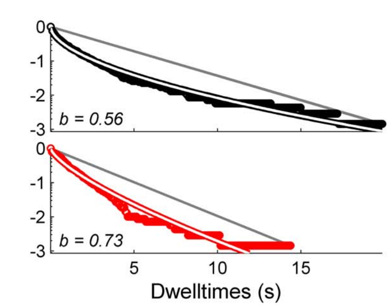


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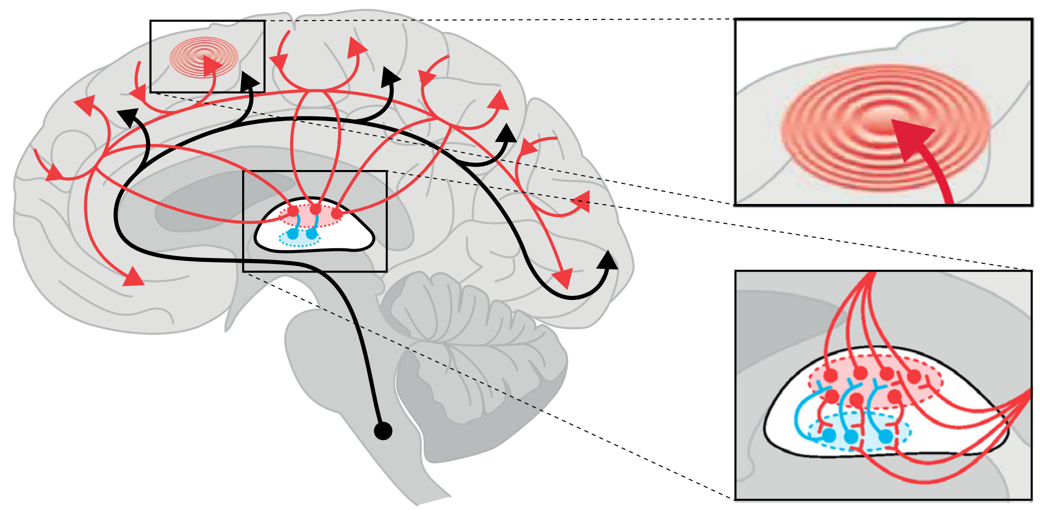

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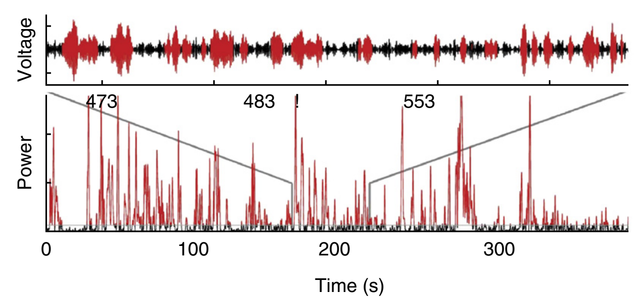


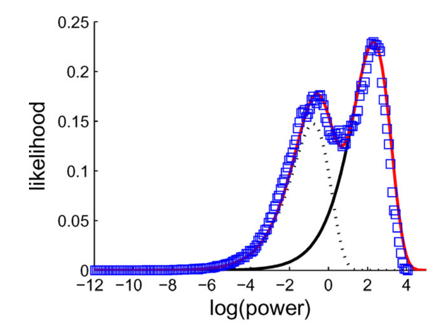


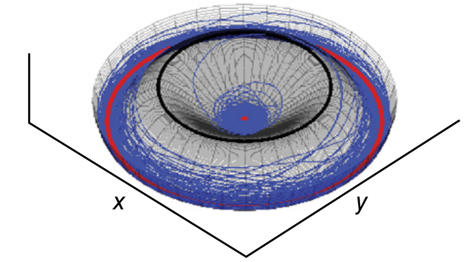


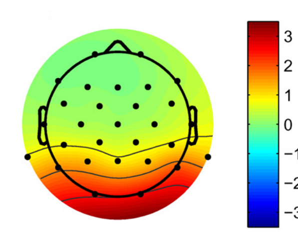

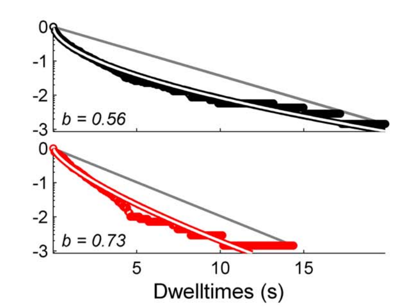


Freyer, Ritter, Robinson, Breakspear (2009, 2011) *J. Neuroscience*

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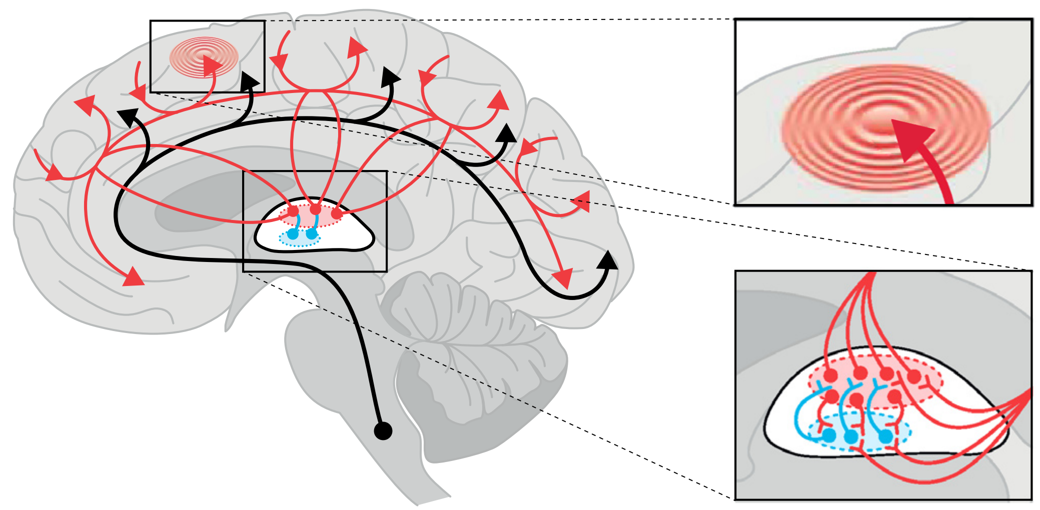

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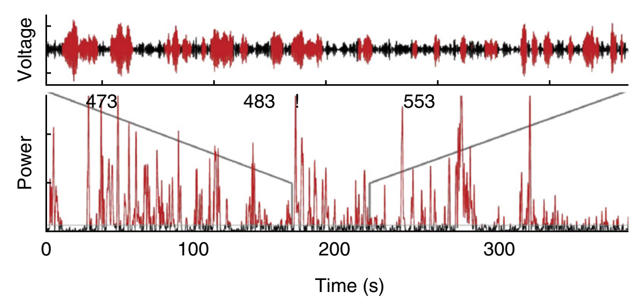
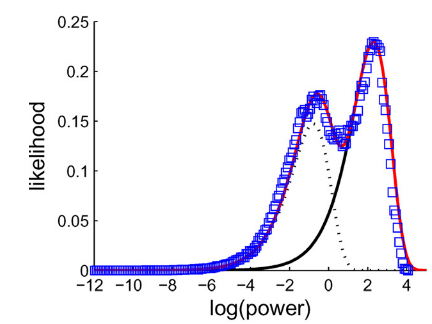
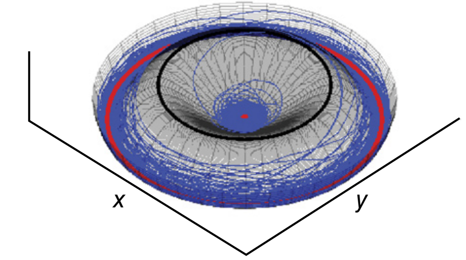
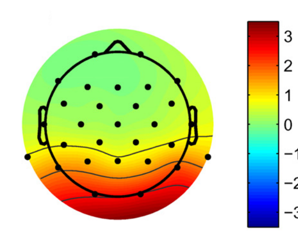
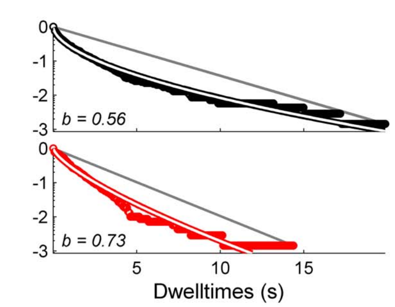


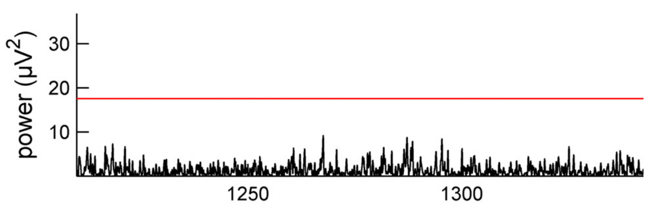



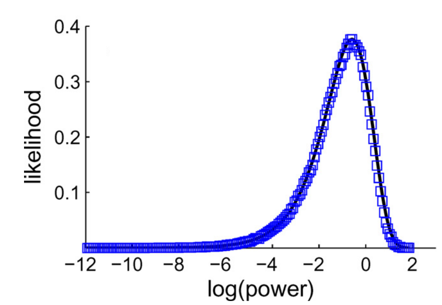






Phase-randomization




Freyer, Ritter, Robinson, Breakspear (2009, 2011) *J. Neuroscience*

# III: Neural fields + modes

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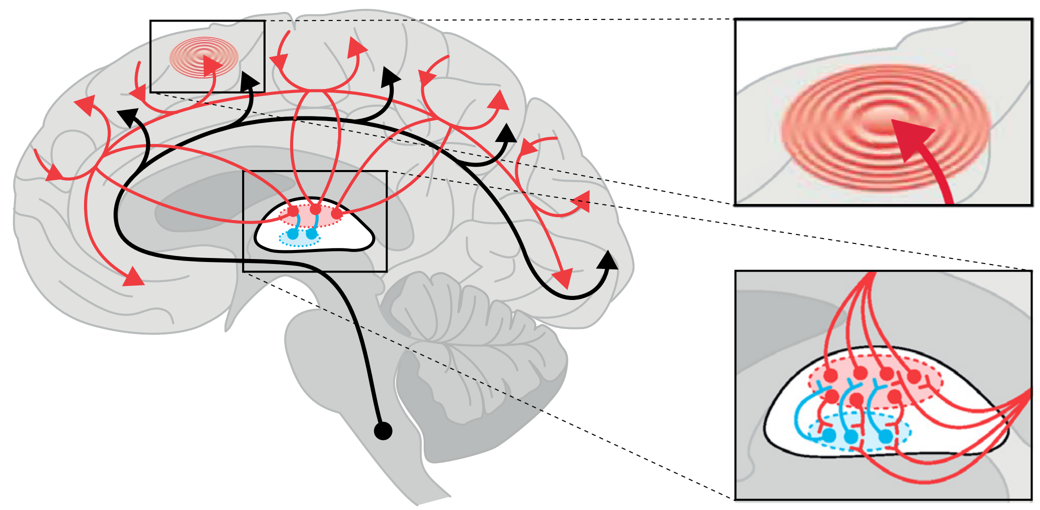

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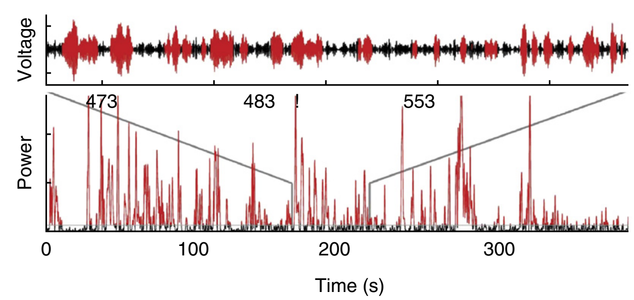


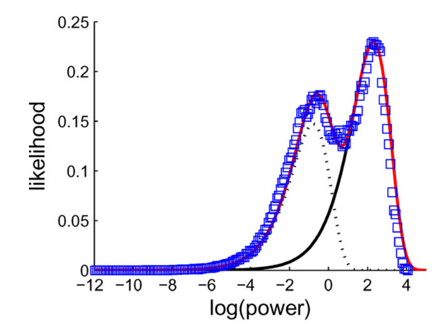


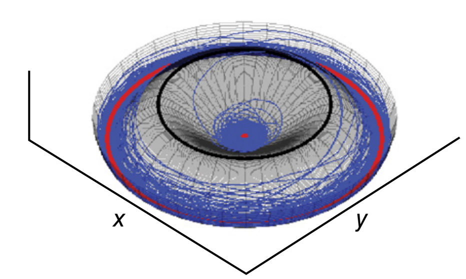


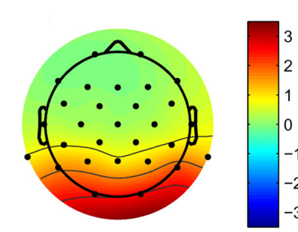


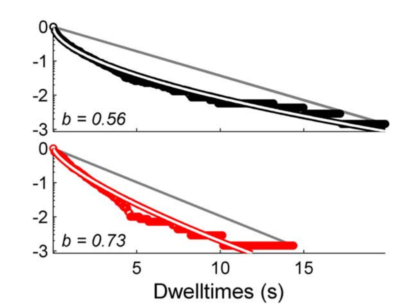


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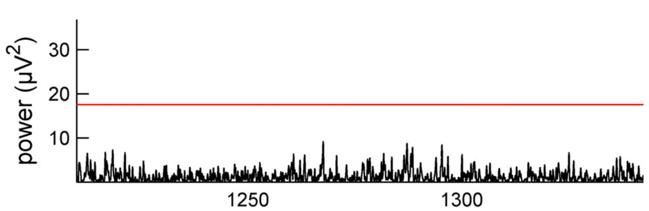
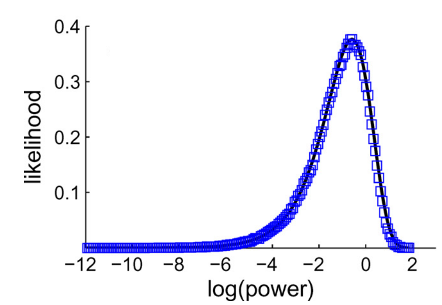
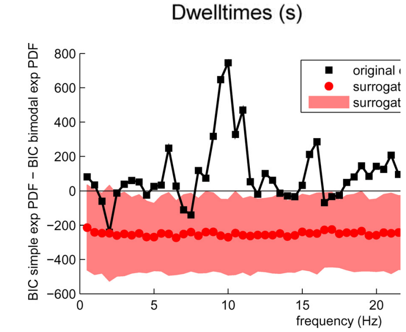


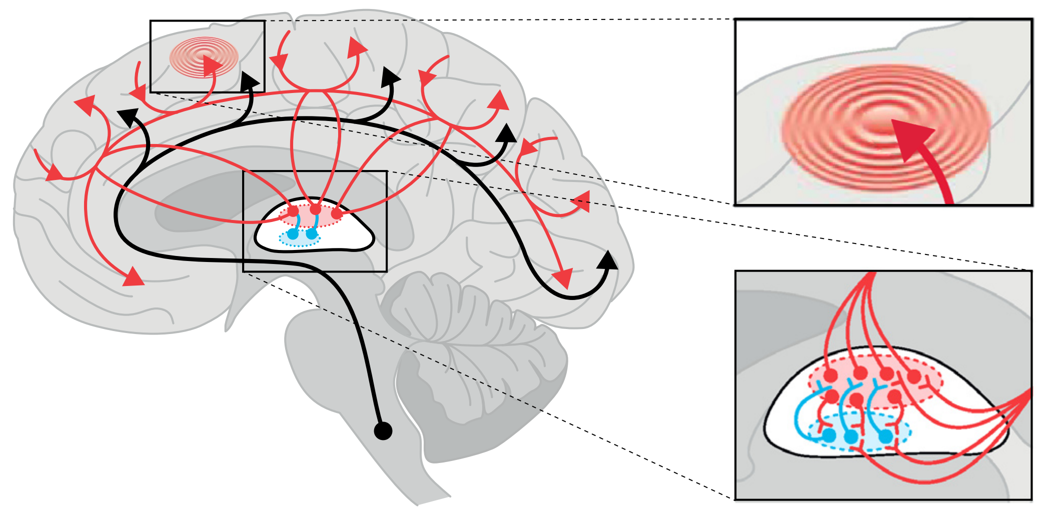




Freyer, Ritter, Robinson, Breakspear (2009, 2011) *J. Neuroscience*

# III: Neural fields + modes

Neural fields can also be decomposed into (eigen-)modes of spatiotemporal activity, each with their own spectral fingerprint

$$\frac{1}{\gamma_e^2}\left(\frac{\partial^2}{\partial t^2} + 2\gamma_e^2\frac{\partial}{\partial t} + \gamma_e^2 - \nu_e^2\nabla^2\right)\phi_e(\mathbf{x},t) = Q_e(\mathbf{x},t).$$



$$Y(\boldsymbol{x},t) = \sum_j a_j m_j(\boldsymbol{x})\, f(t) + \sigma\eta(\boldsymbol{x},t),$$

*modes* *noise*

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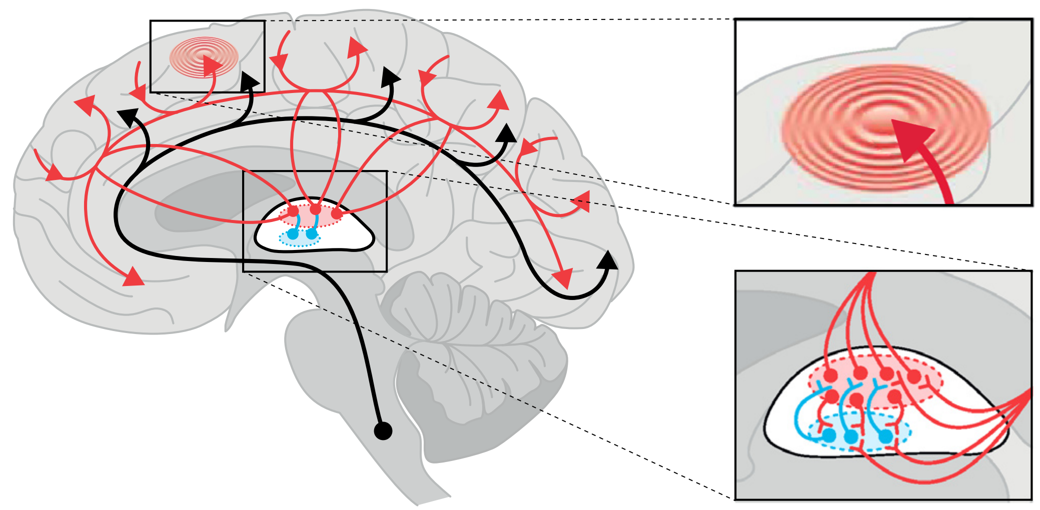
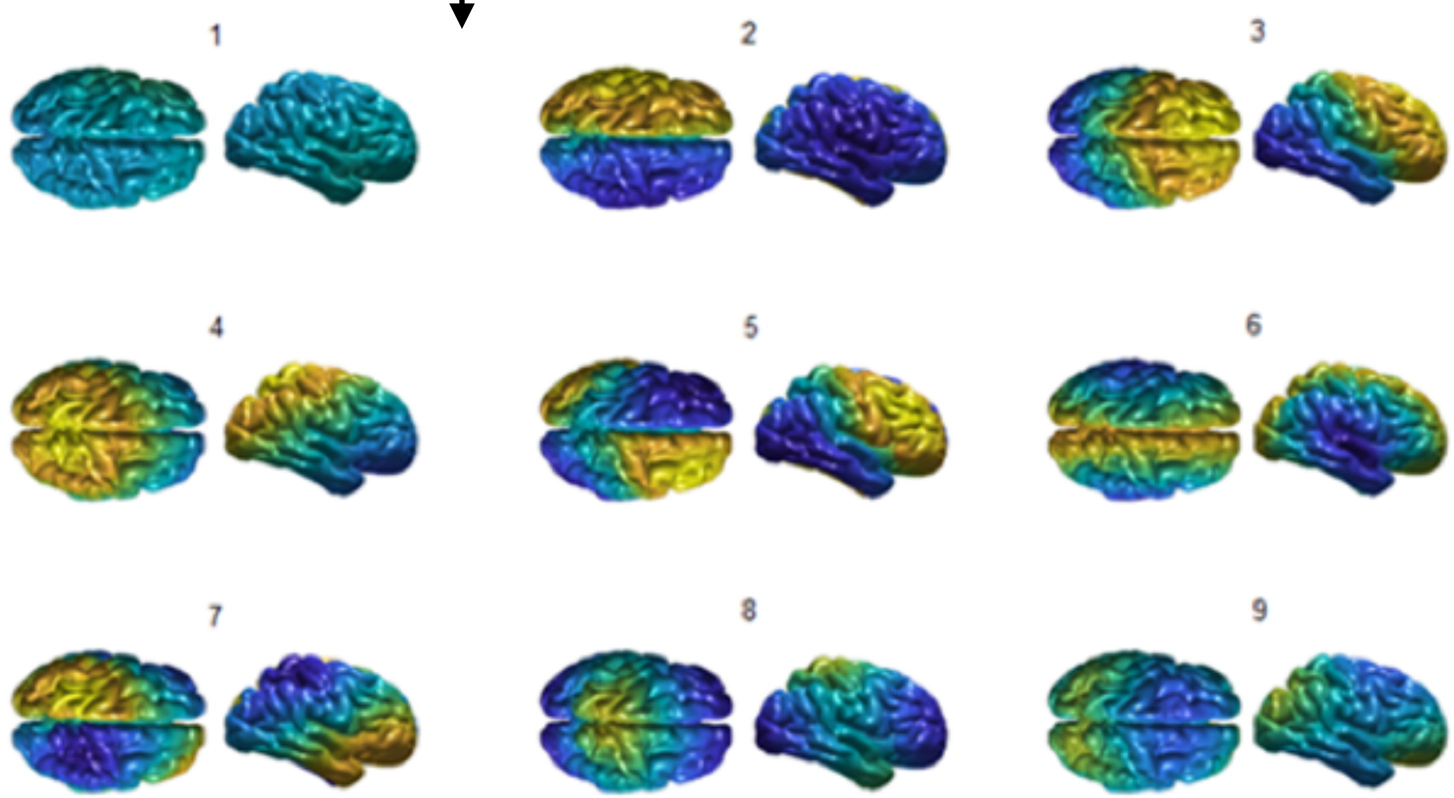


$$Y(\boldsymbol{x},t) = \sum_j \underbrace{a_j m_j(\boldsymbol{x})}_{\text{modes}} f(t) + \underbrace{\sigma\eta(\boldsymbol{x},t)}_{\text{noise}},$$



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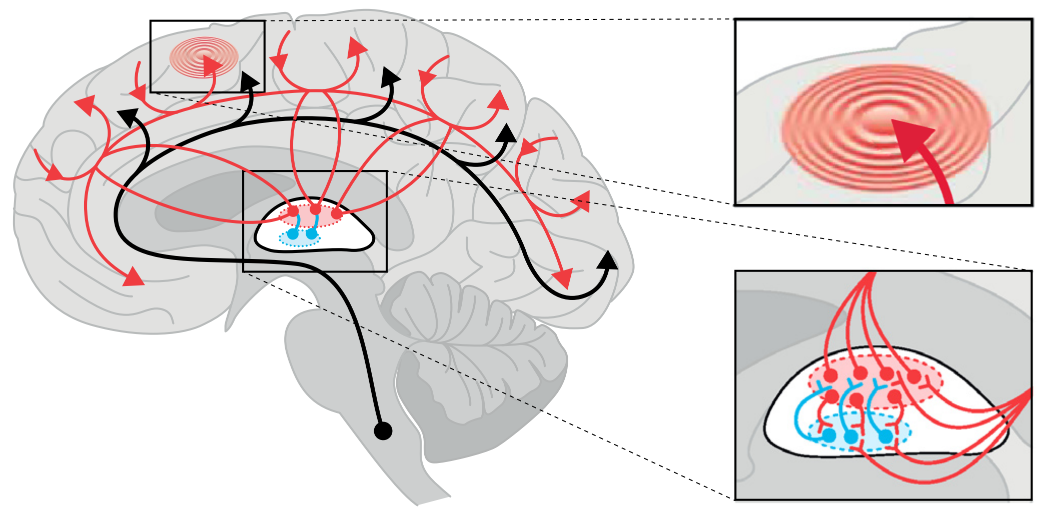
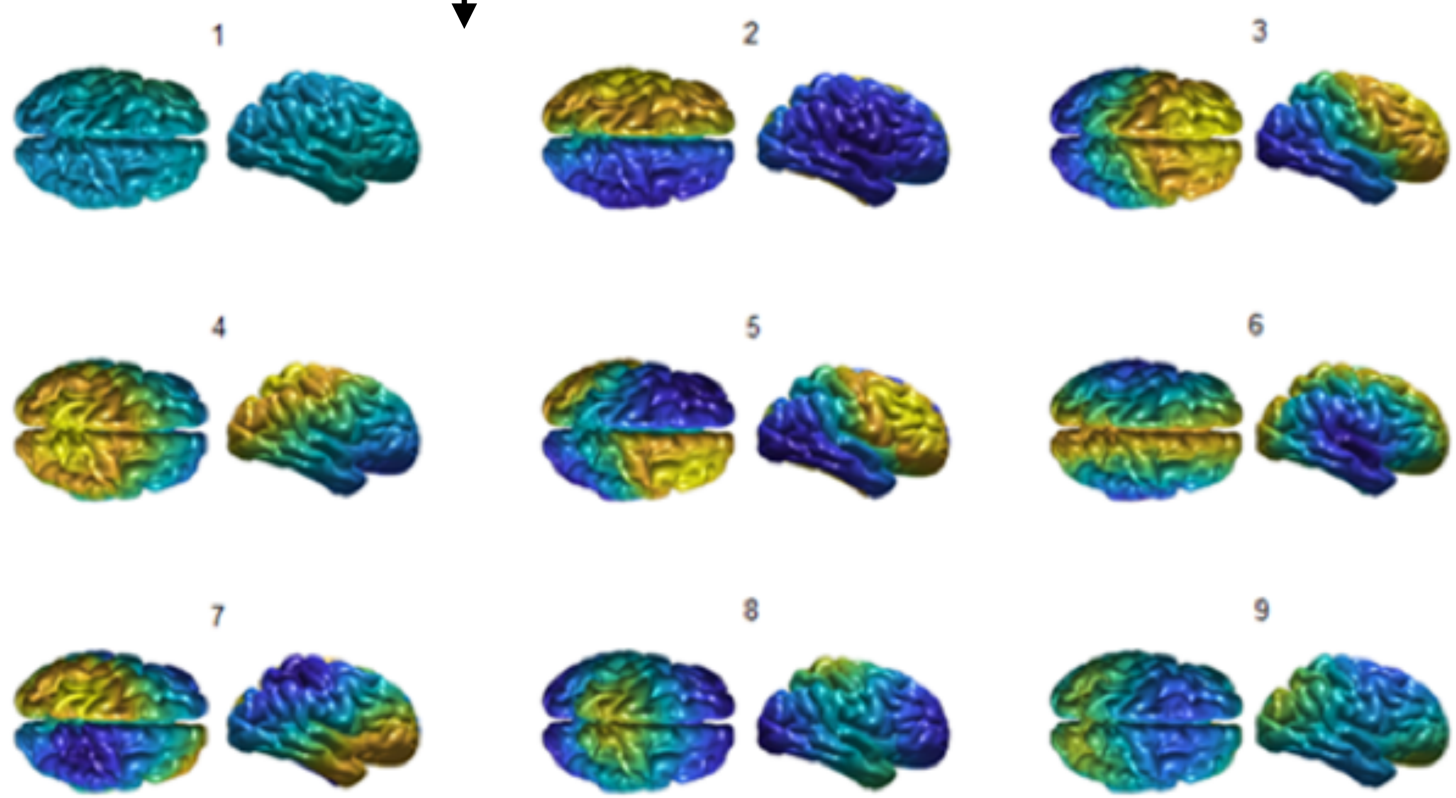


$$Y(\boldsymbol{x},t) = \sum_j a_j m_j(\boldsymbol{x})\, f(t) + \sigma\eta(\boldsymbol{x},t),$$

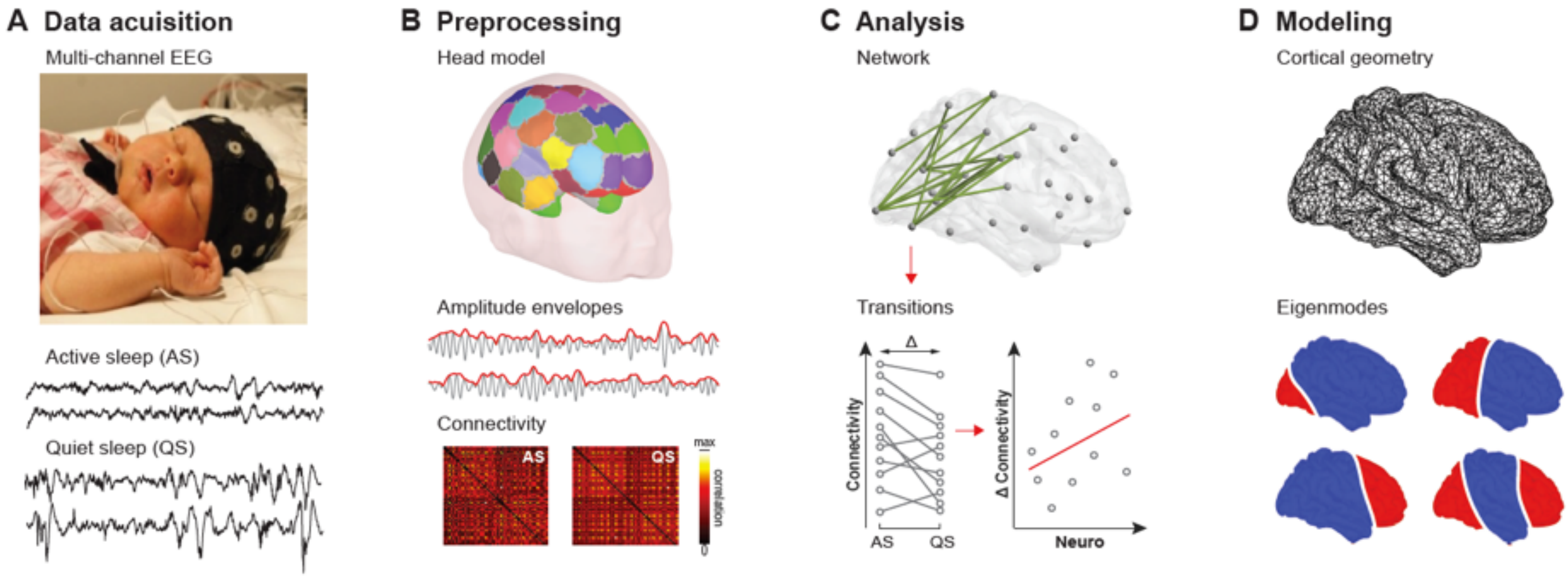
*modes* *noise*

*Low frequency*




*High frequency*

# III: Neural fields + modes




Scalp EEG data from extremely preterm (EP; *n*=42) and full-term (FT; *n*=52) neonates at term equivalent age

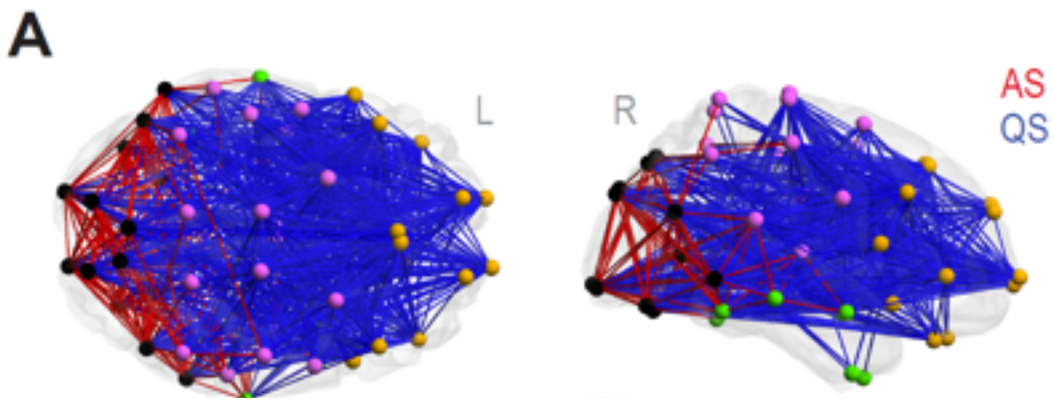
Source-reconstructed band limited (orthogonalized) functional connectivity

Contrasts of active sleep (AS) versus quiet sleep (QS) across groups

Neural field modelling

Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes




*Main effect of sleep (AS to QS):*

Tokariev, Roberts *et al.* (2019) *Nature Comms*

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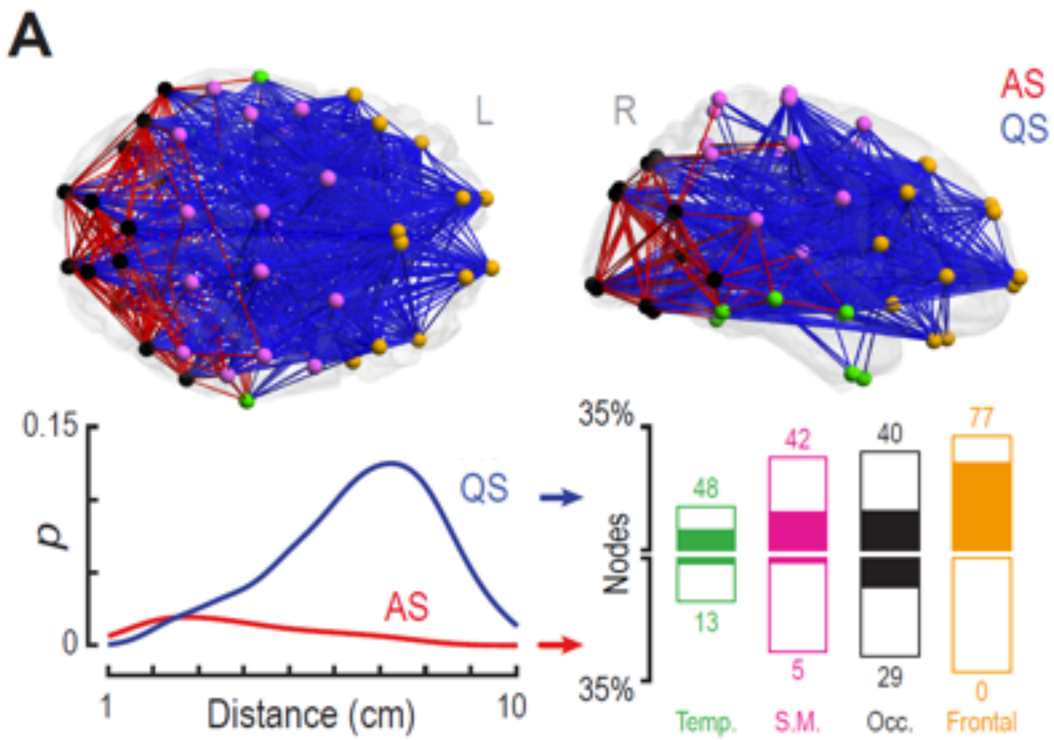


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Transition heralds a reorganization toward greater, longer range and more anterior functional connectivity

Tokariev, Roberts *et al.* (2019) *Nature Comms*

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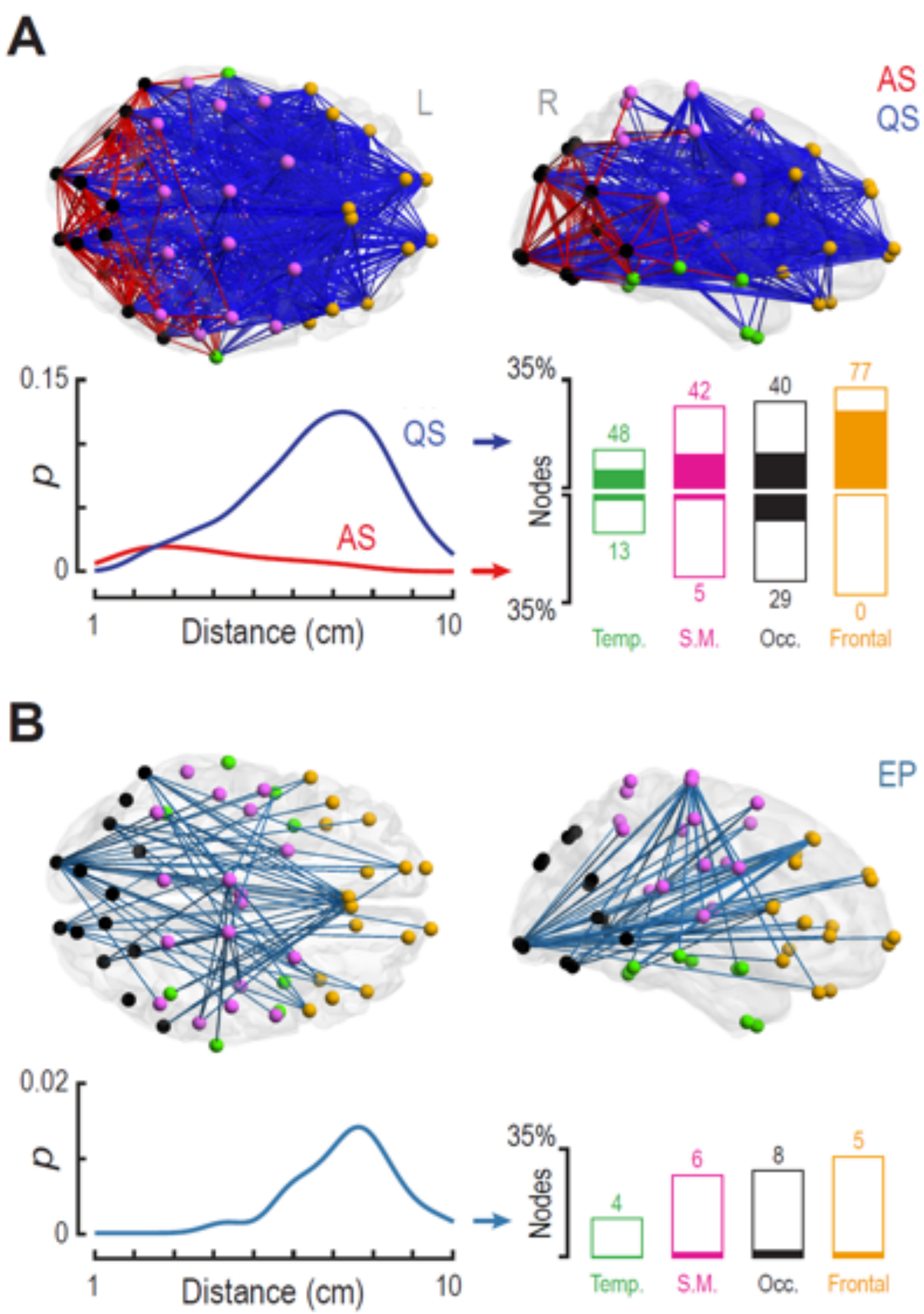



*Main effect of sleep (AS to QS):*

Transition heralds a reorganization toward greater, longer range and more anterior functional connectivity

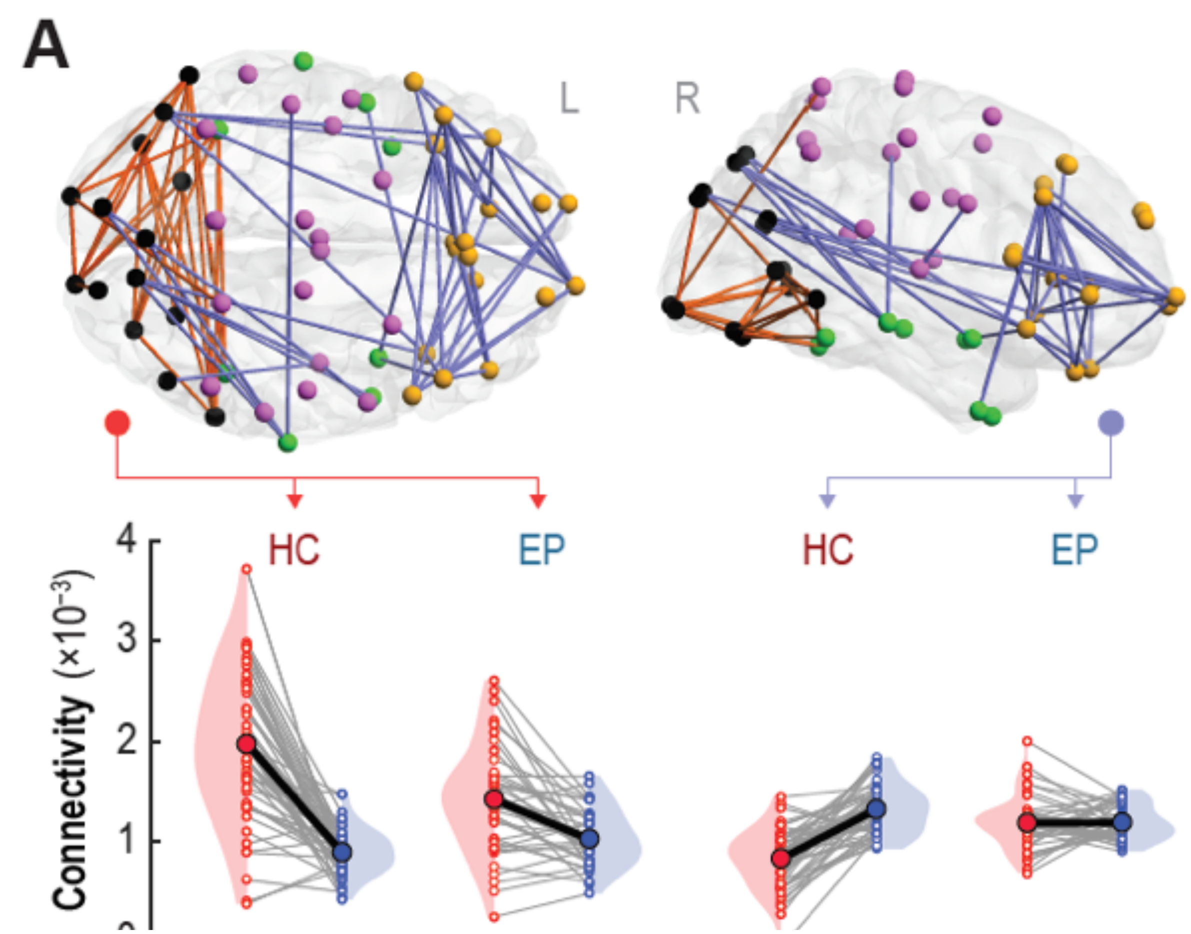
*Main effect of group:*

Across sleep states, preterm (EP) neonates possess a network of stronger long-range functional connectivity

Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes

*Sleep-group (interaction) effect:*
Transition (AS to QS) in HC is attenuated in EP in a largely A-P network




Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes

*Sleep-group (interaction) effect*:
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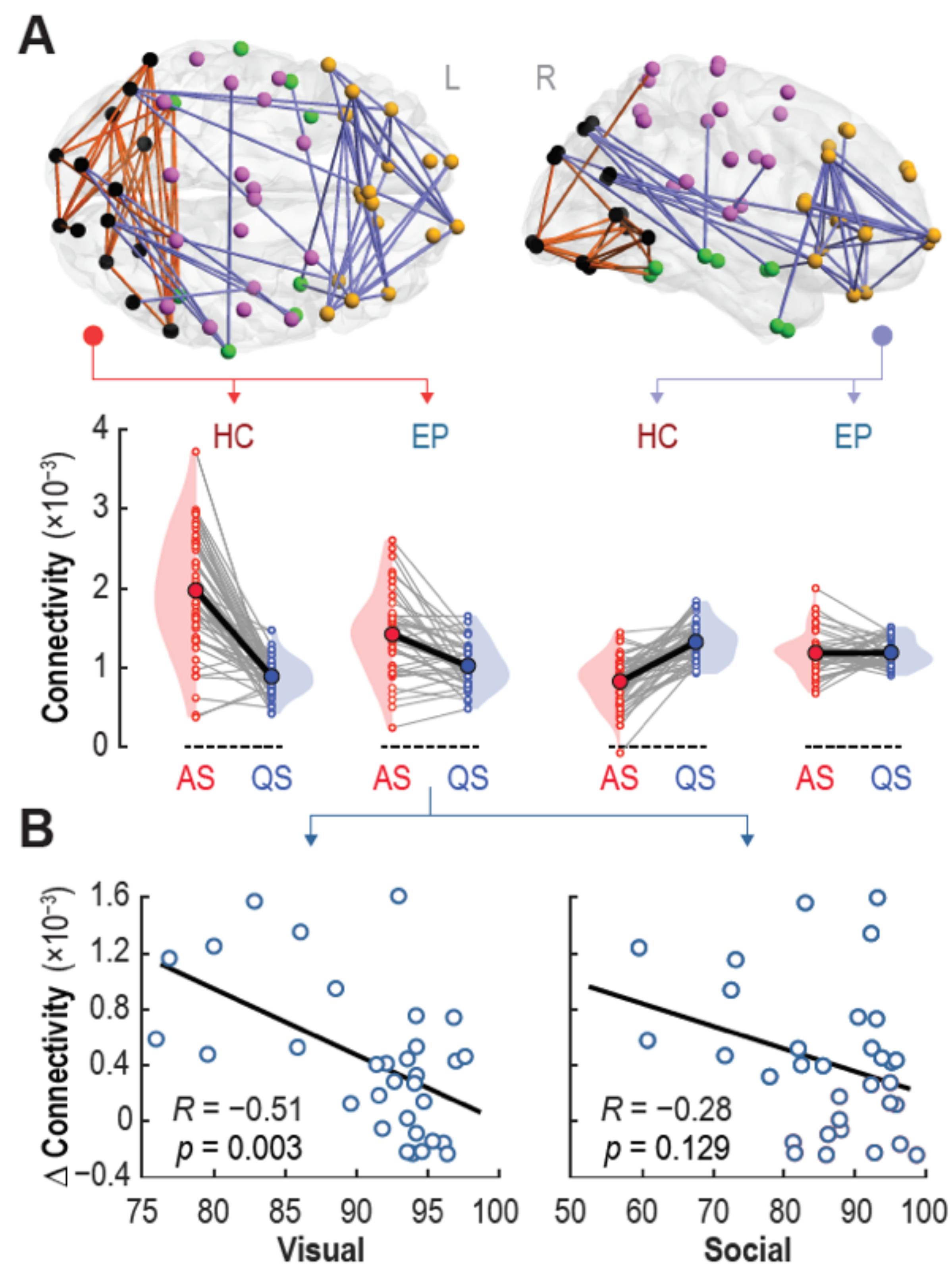
… which pre-empts visual performance at two years of life




Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes

$$Y(\boldsymbol{x}, t) = \sum_j a_j m_j(\boldsymbol{x})\, f(t) + \sigma\eta(\boldsymbol{x}, t),$$

Tokariev, Roberts *et al.* (2019) *Nature Comms*

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$$Y(\boldsymbol{x}, t) = \sum_j a_j m_j(\boldsymbol{x})\, f(t) + \sigma\eta(\boldsymbol{x}, t),$$

$$f(t) = \underbrace{\cos(\nu t)}_{\text{carrier frequency (alpha)}} . \underbrace{\cos(\omega t)}_{\text{low frequency fluctuations}},$$

Tokariev, Roberts *et al.* (2019) *Nature Comms*

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*carrier frequency (alpha)*

*low frequency fluctuations*

solve eigenmode solution on neonatal cortex

$$\Delta_{\mathcal{G}}\psi_j(v_i) = \lambda_j \psi_j(v_i), \quad \forall v_i \in \mathcal{V}$$

$$\Delta_{\mathcal{G}} = \frac{1}{2}\left((\mathbf{D}-\mathbf{A})^{\mathrm{T}}(\mathbf{D}-\mathbf{A})\right),$$

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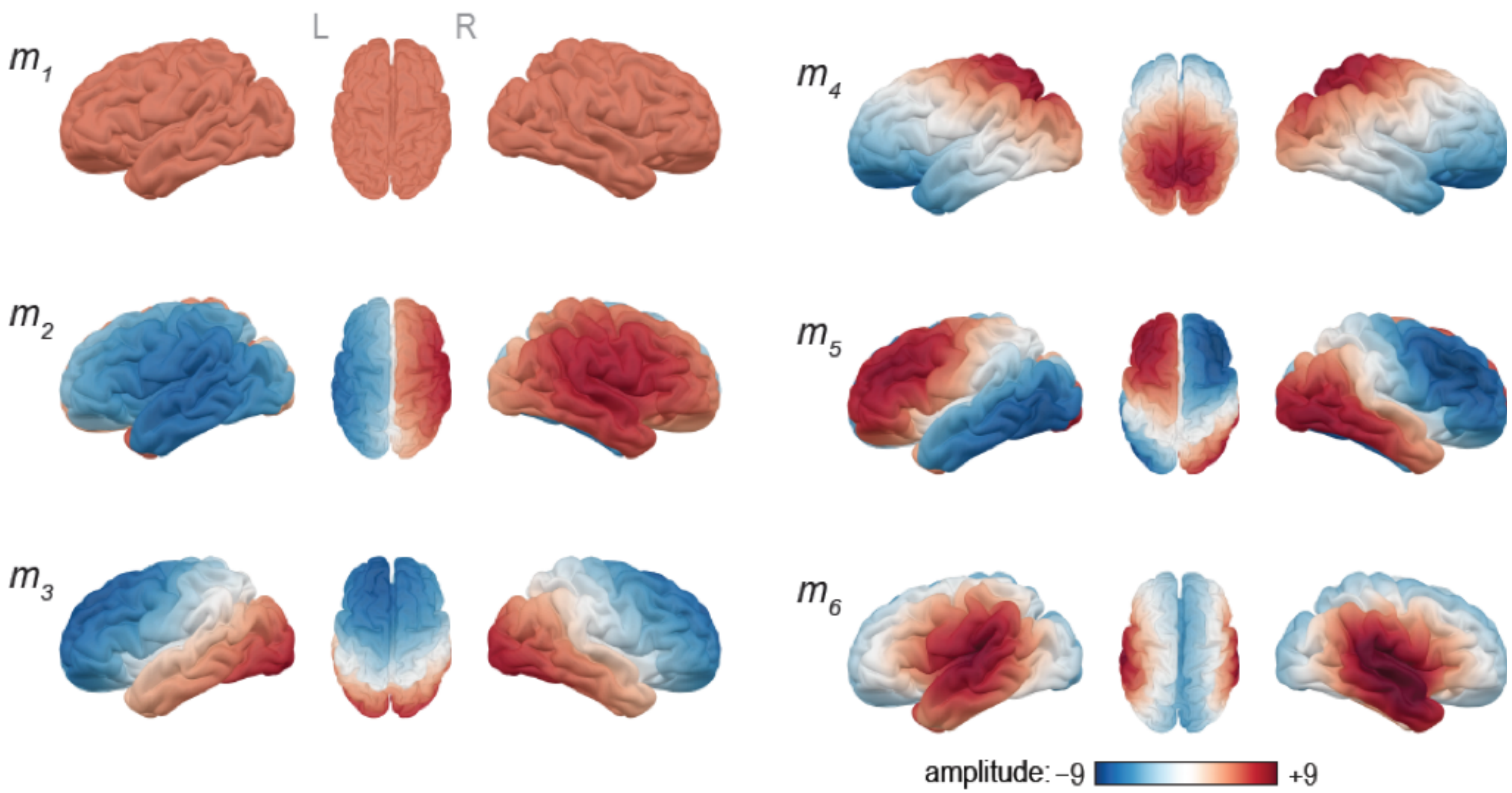


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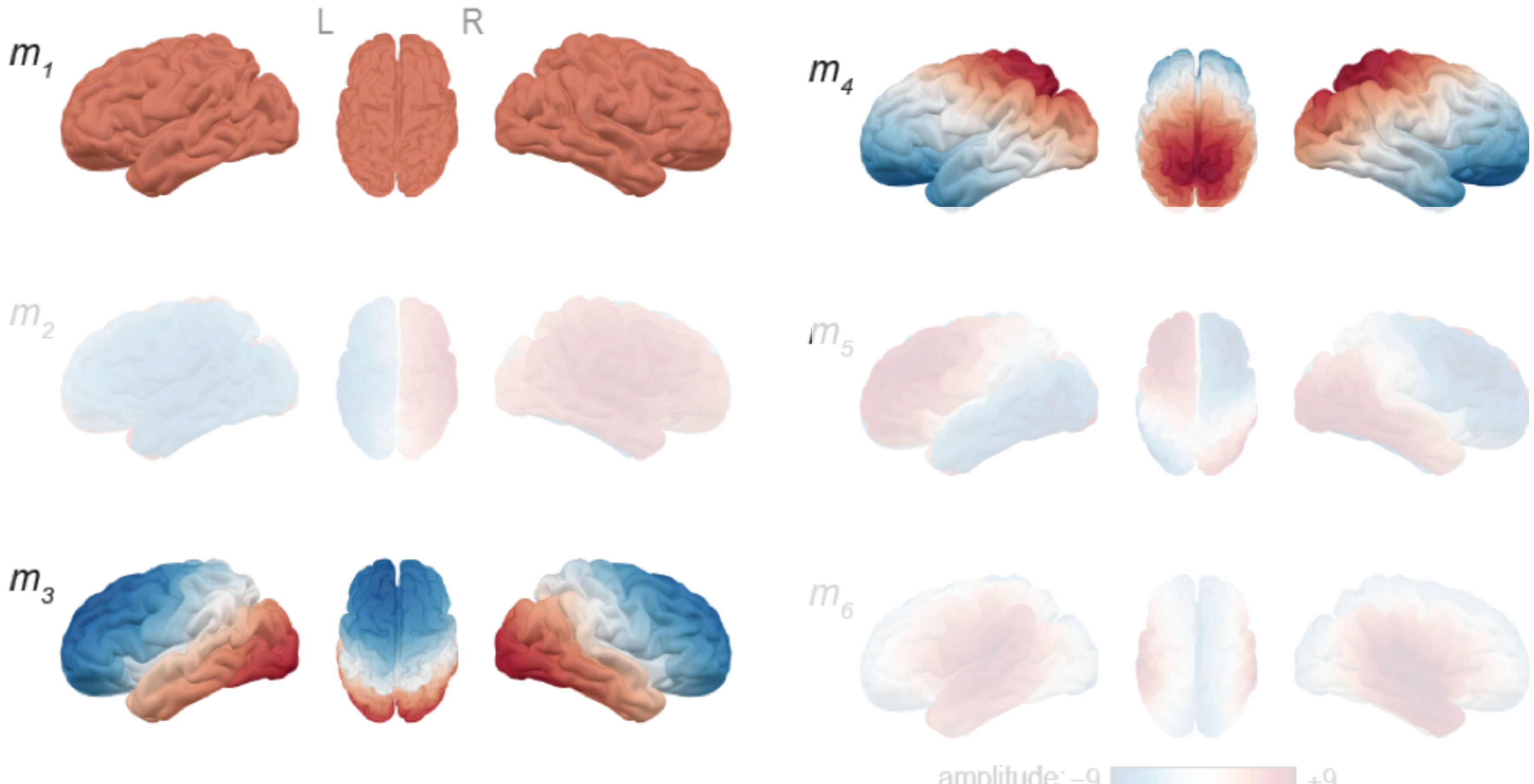


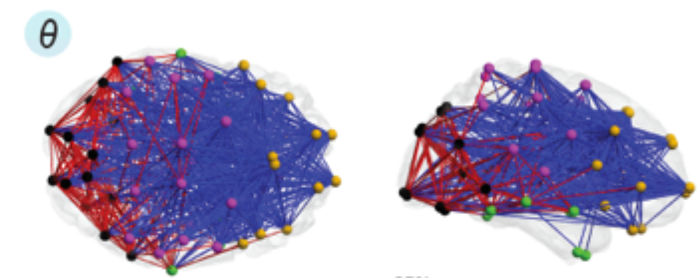


Choose first (global) third and fourth (A-P) modes and solve for each neonate

Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes

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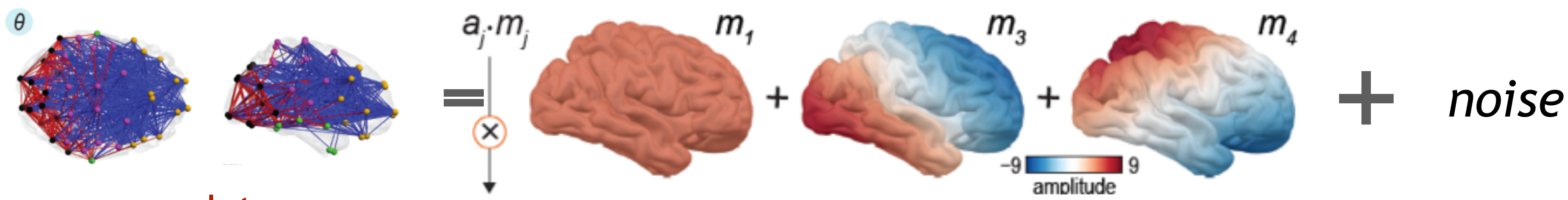


data

HC

EP

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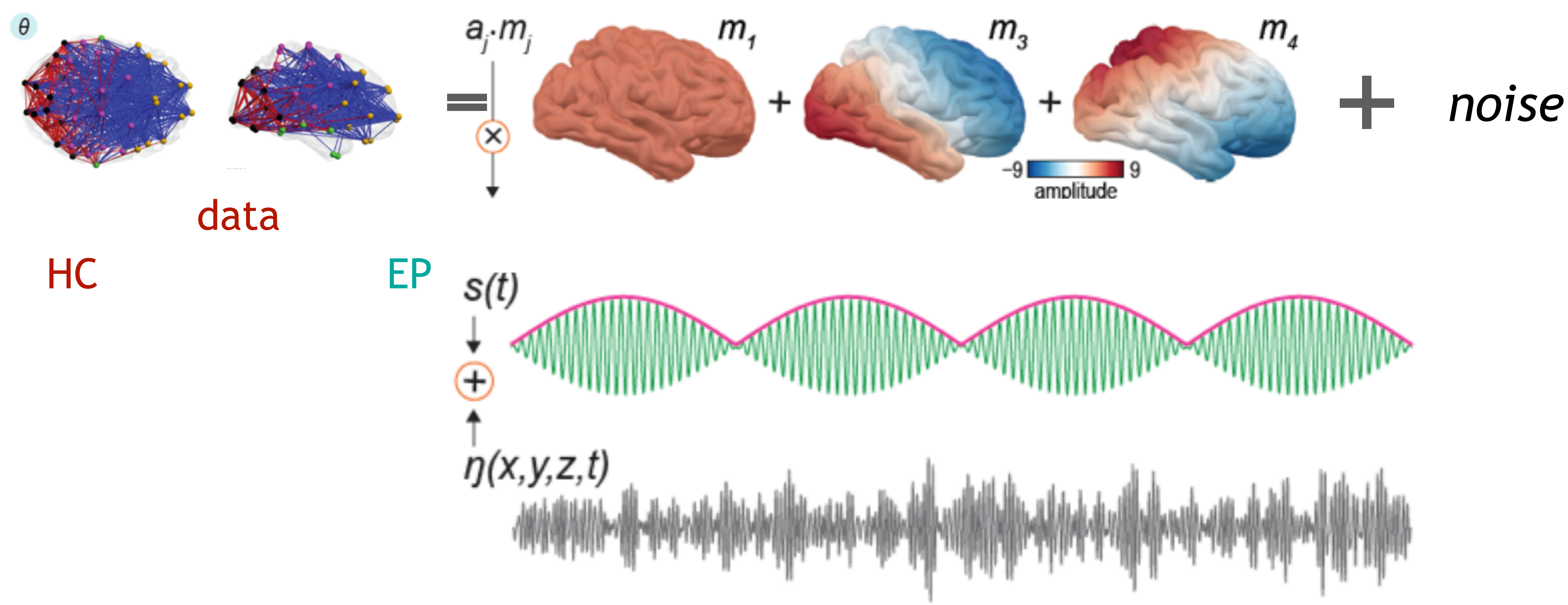


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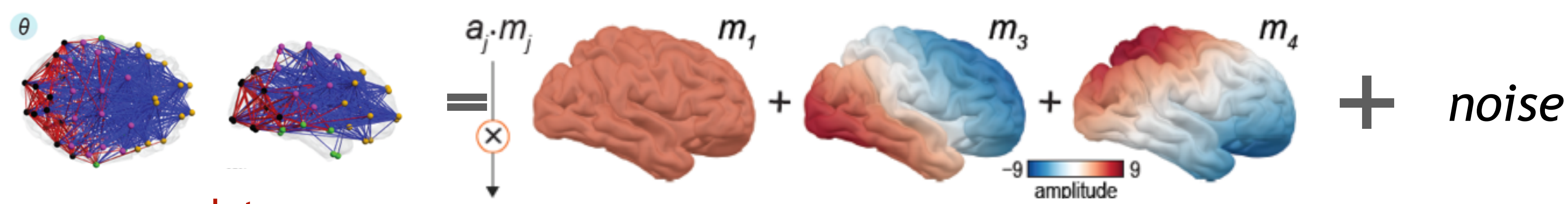
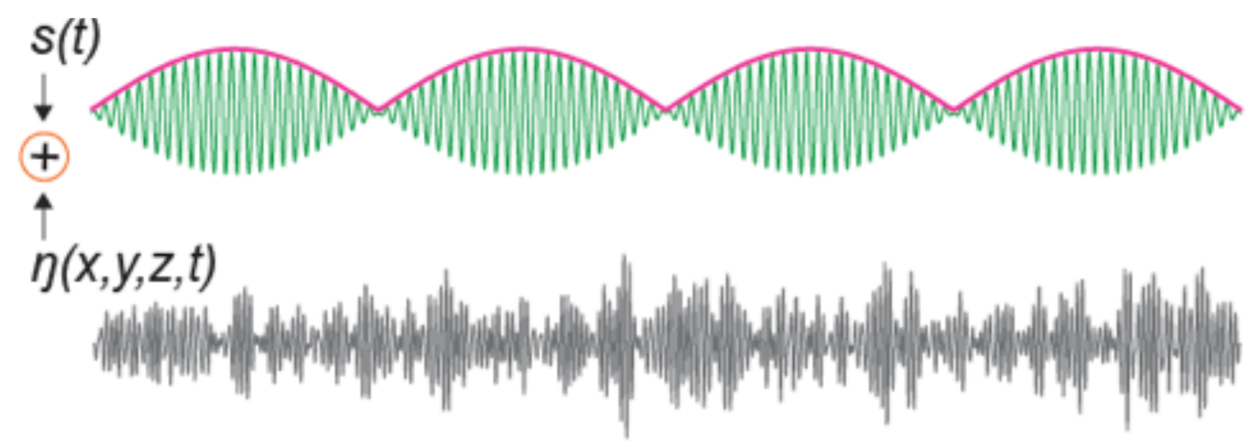
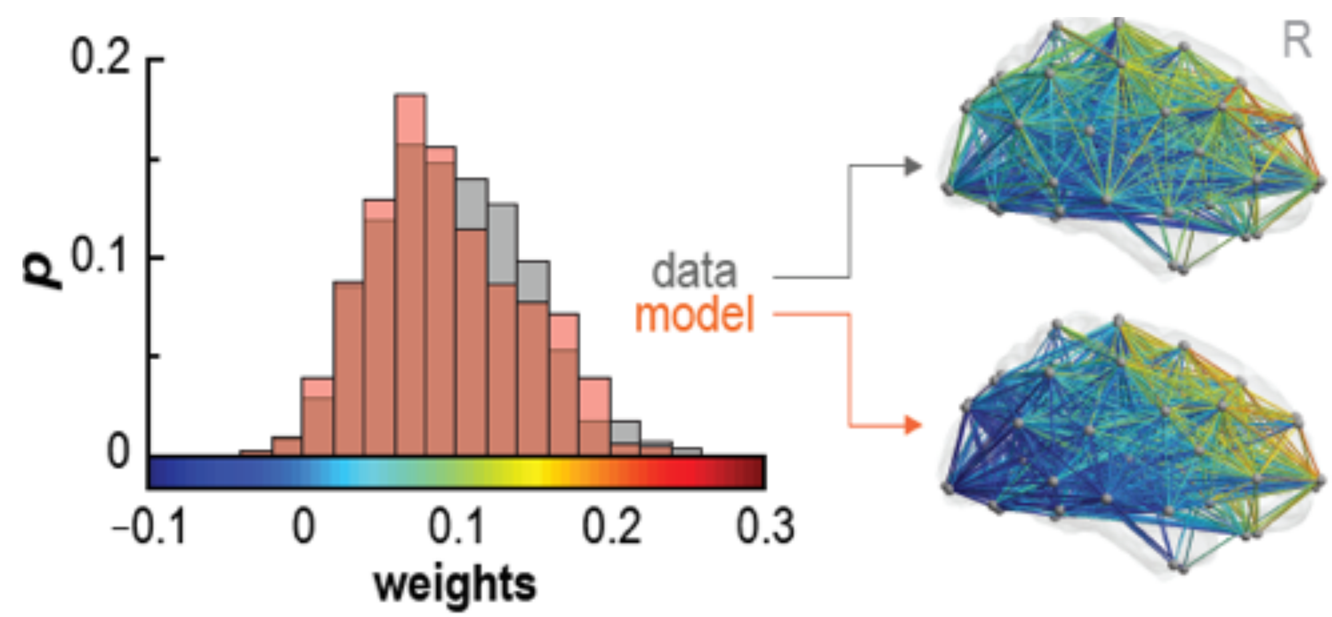



data

HC

EP

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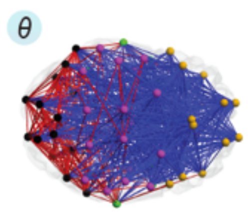
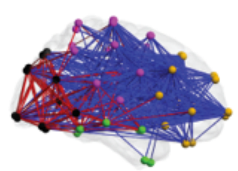
... and solve for each neonate



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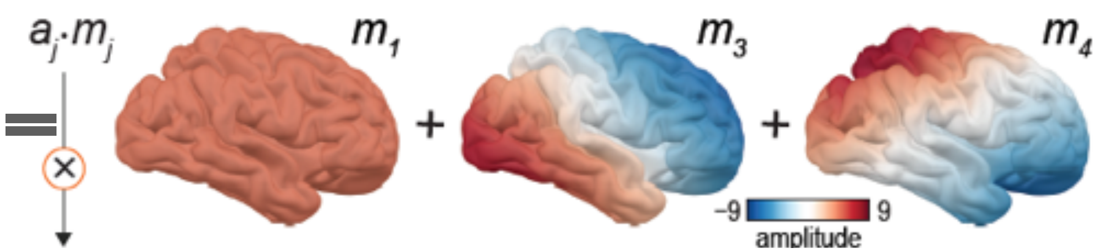


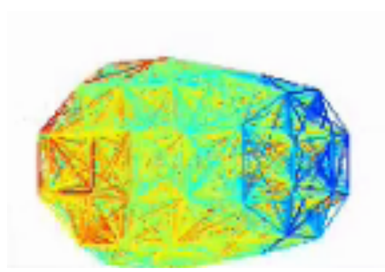

+ *noise*

data

HC

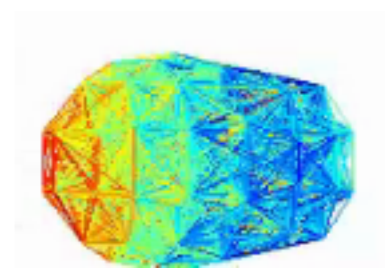
EP

data



=

model



+ *noise*

... and solve for each neonate

Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes

$$Y(\boldsymbol{x},t) = \sum_j a_j m_j(\boldsymbol{x})\, f(t) + \sigma\eta(\boldsymbol{x},t),$$

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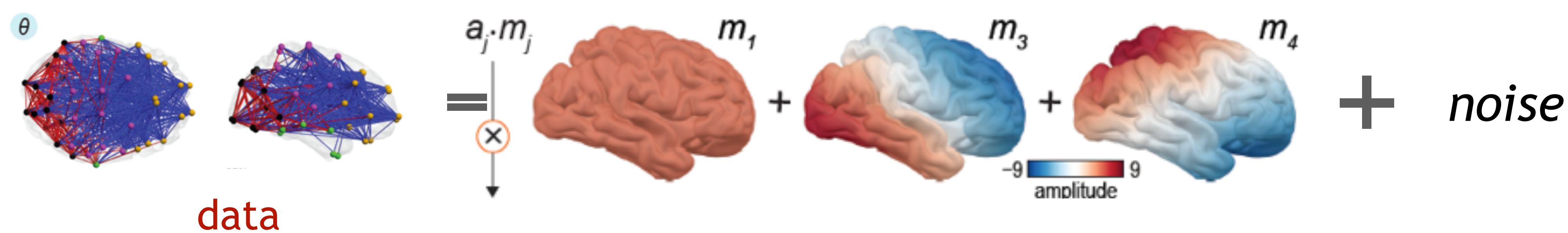


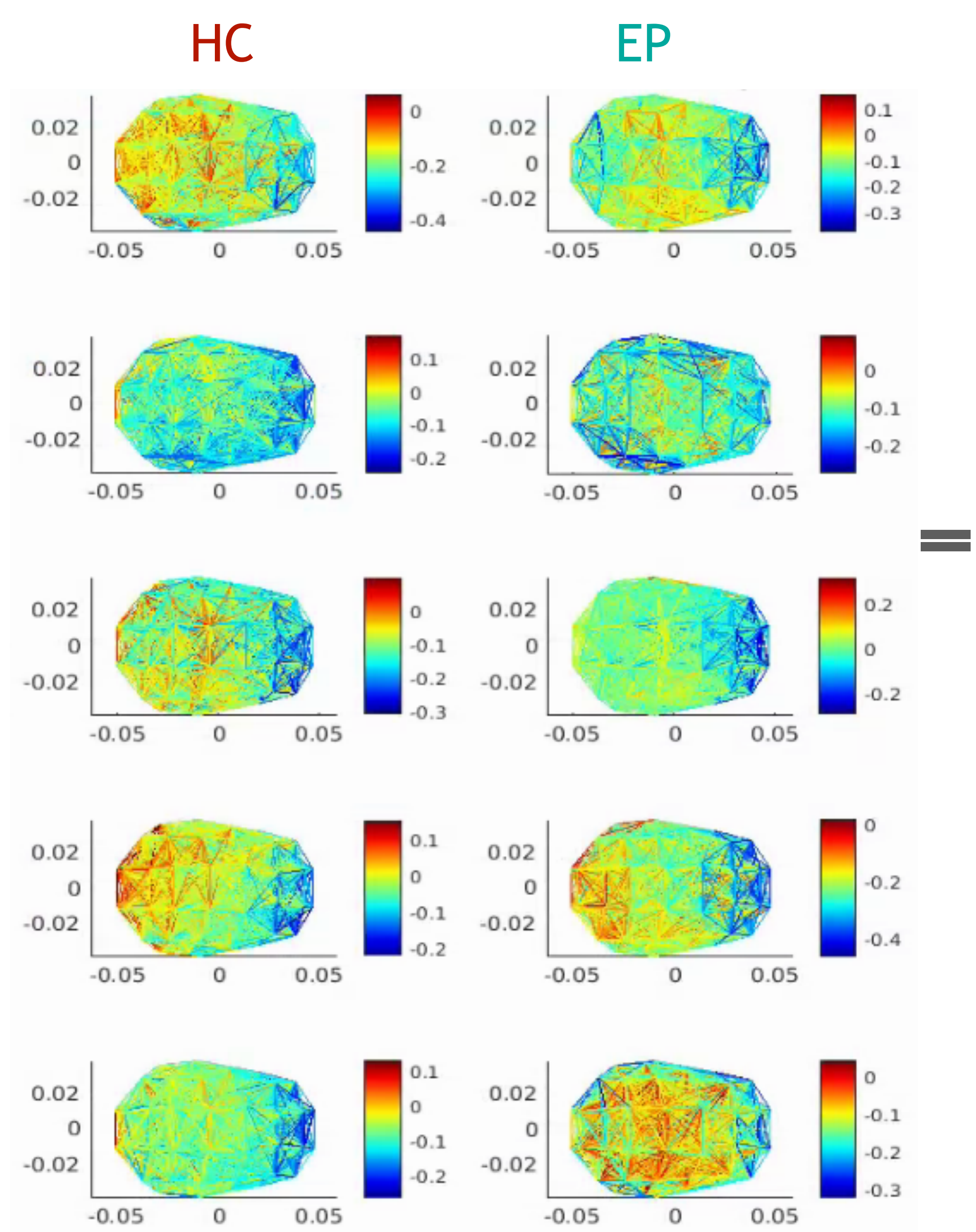


Tokariev, Roberts *et al.* (2019) *Nature Comms*

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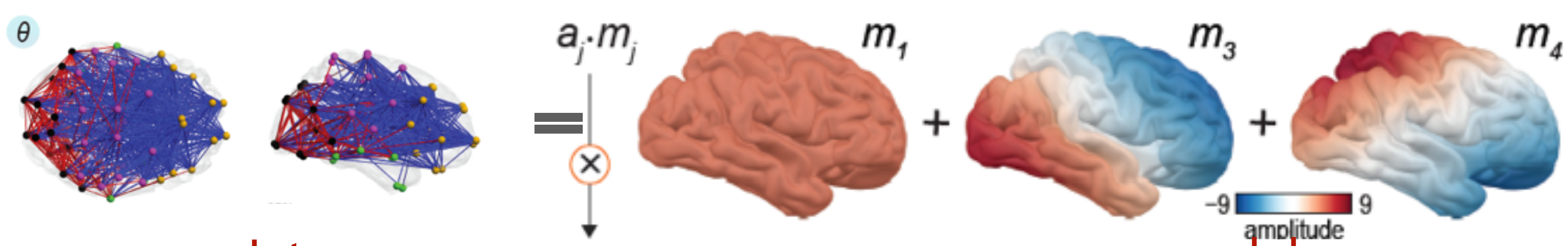
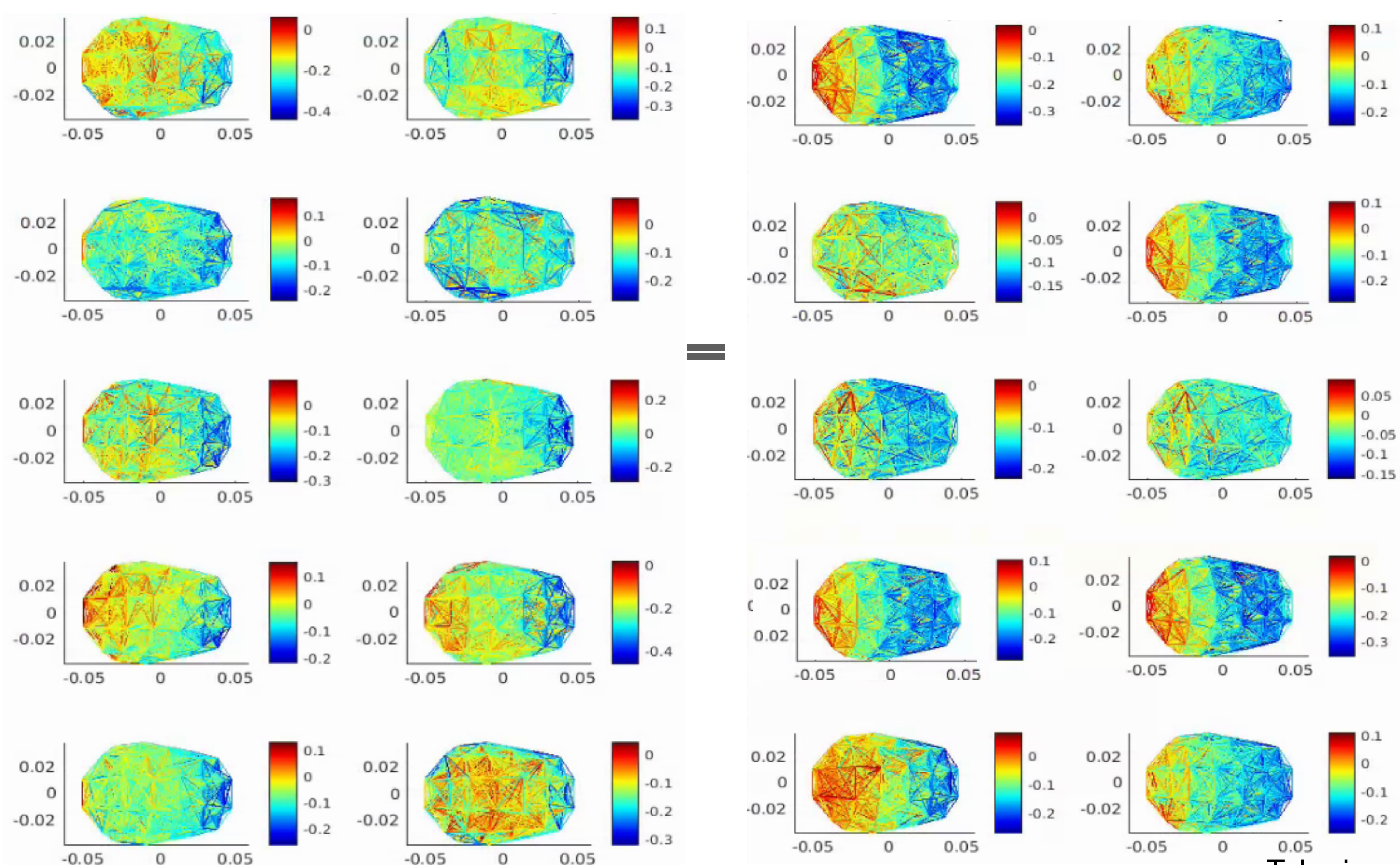



+ *noise*

data

model

HC EP HC EP



= 

+ *noise*

Tokariev, Roberts *et al.* (2019) *Nature Comms*

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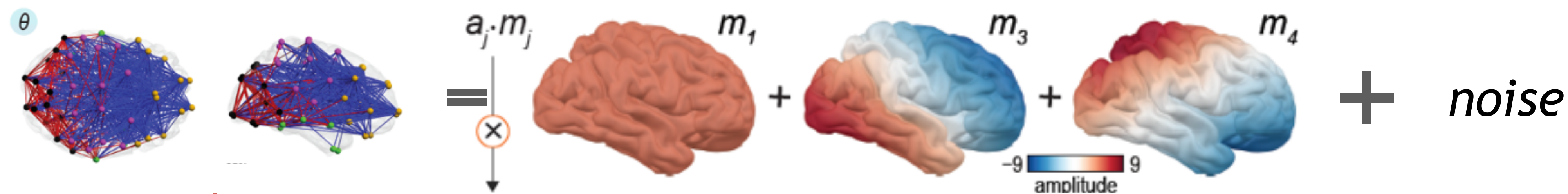
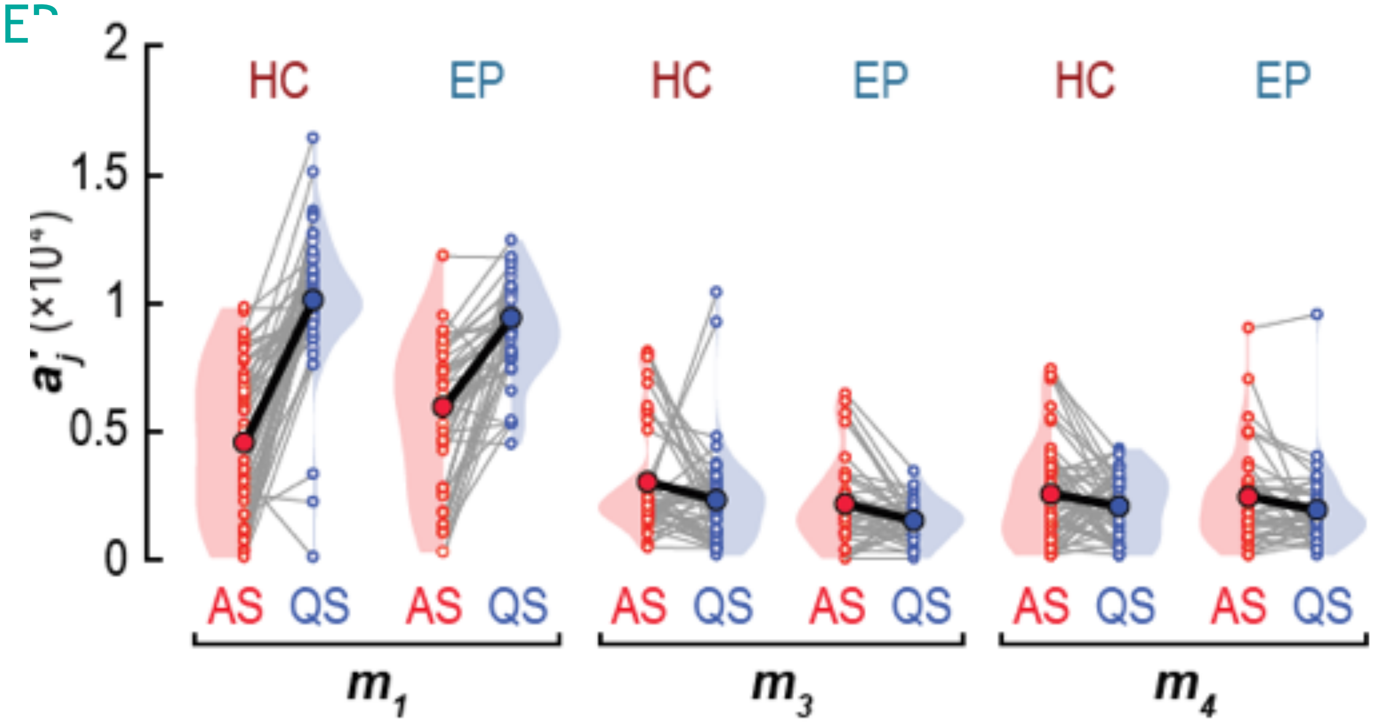



data

HC

EP




Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes

$$Y(\boldsymbol{x}, t) = \sum_j a_j m_j(\boldsymbol{x}) f(t) + \sigma\eta(\boldsymbol{x}, t),$$

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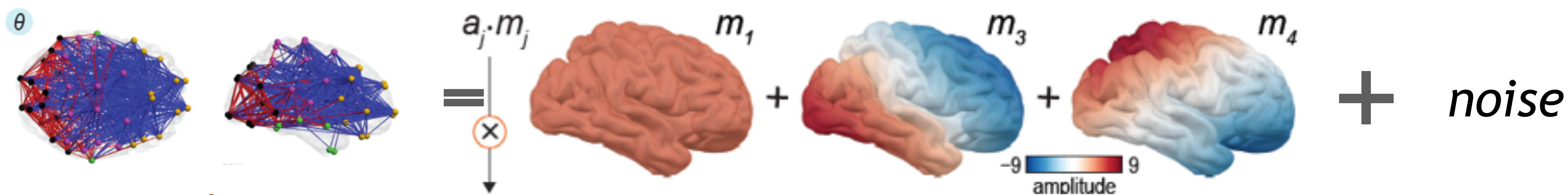
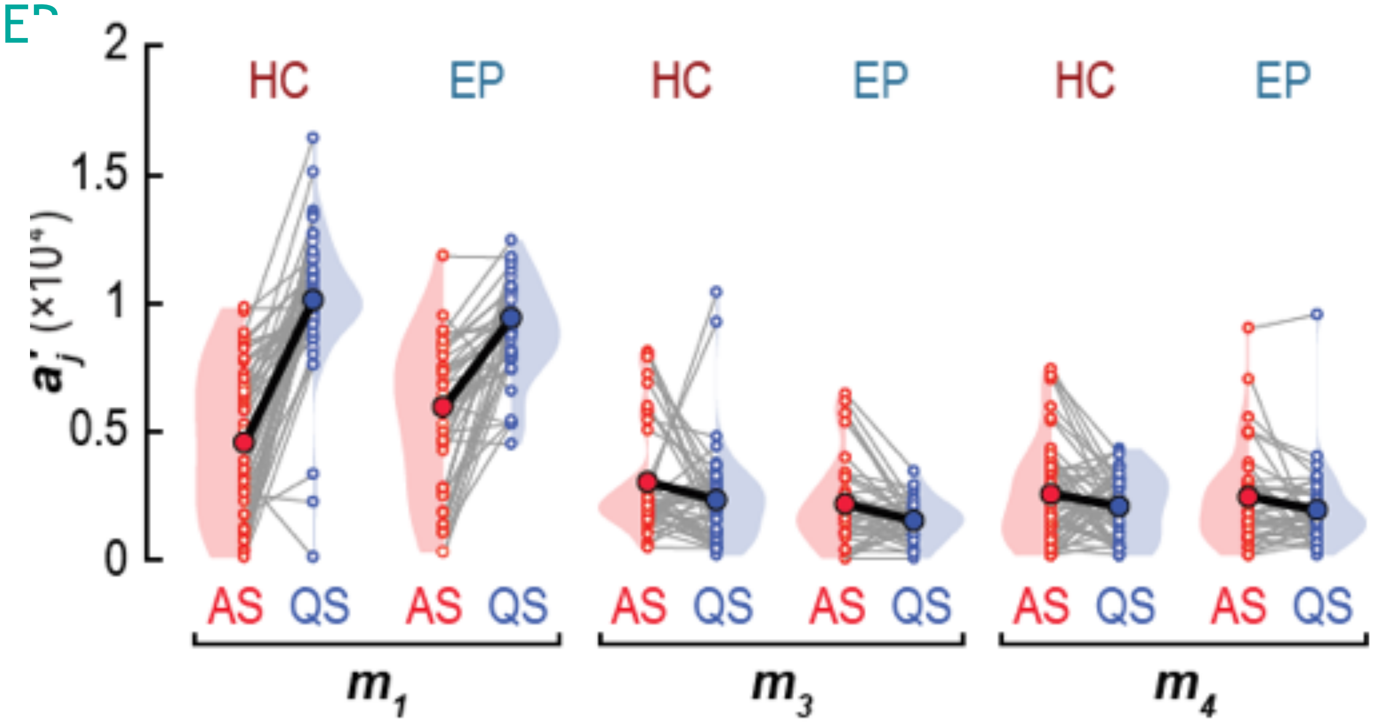



data

HC

E

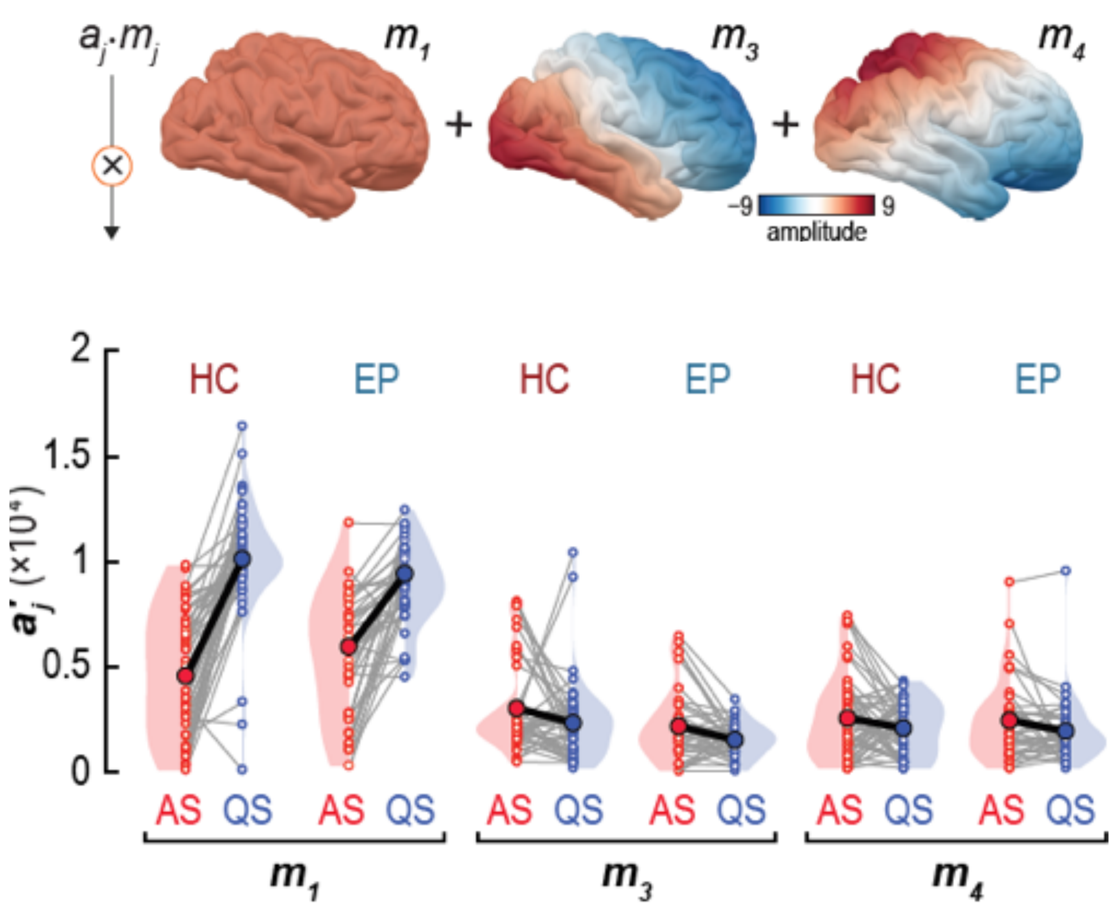



$F_{1,92} = 7.76$, $p = 0.006$

**Significant group by sleep effect**

Tokariev, Roberts *et al.* (2019) *Nature Comms*

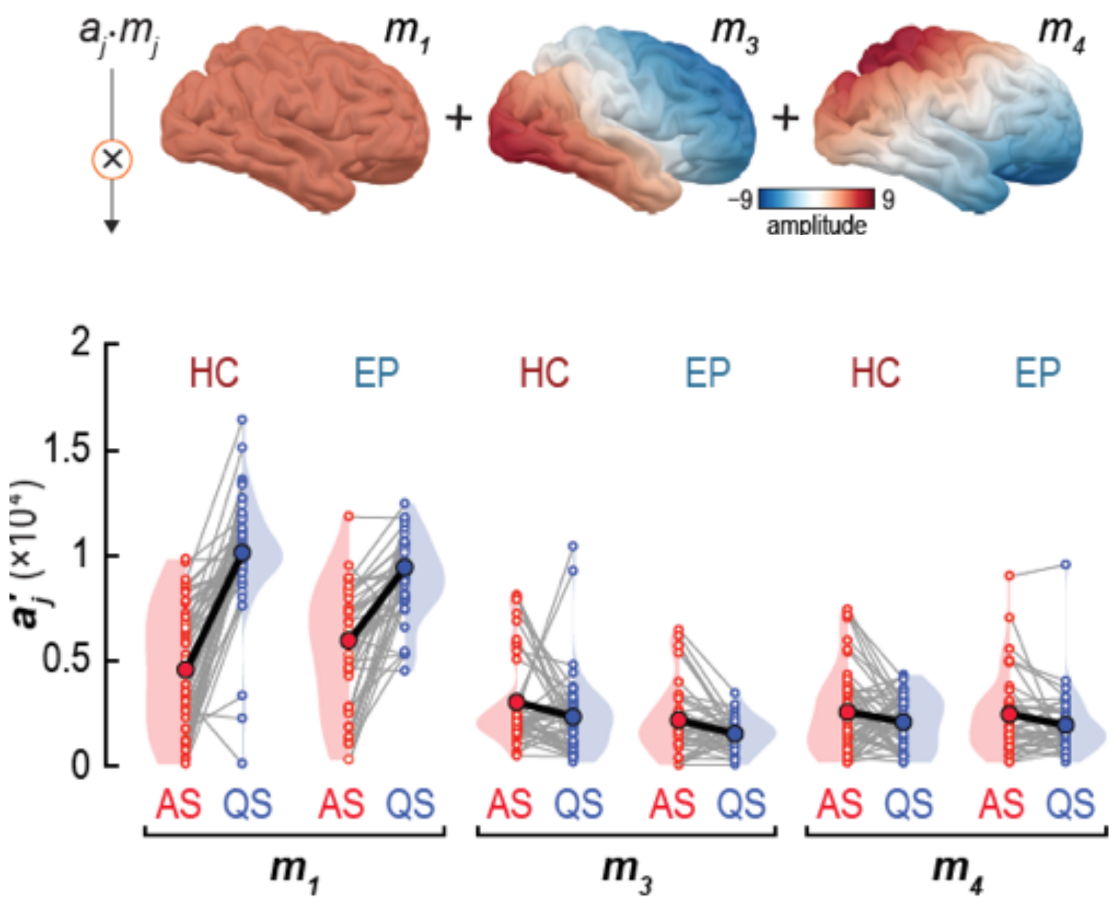
# III: Neural fields + modes




*Sleep-group (interaction) in brain modes*

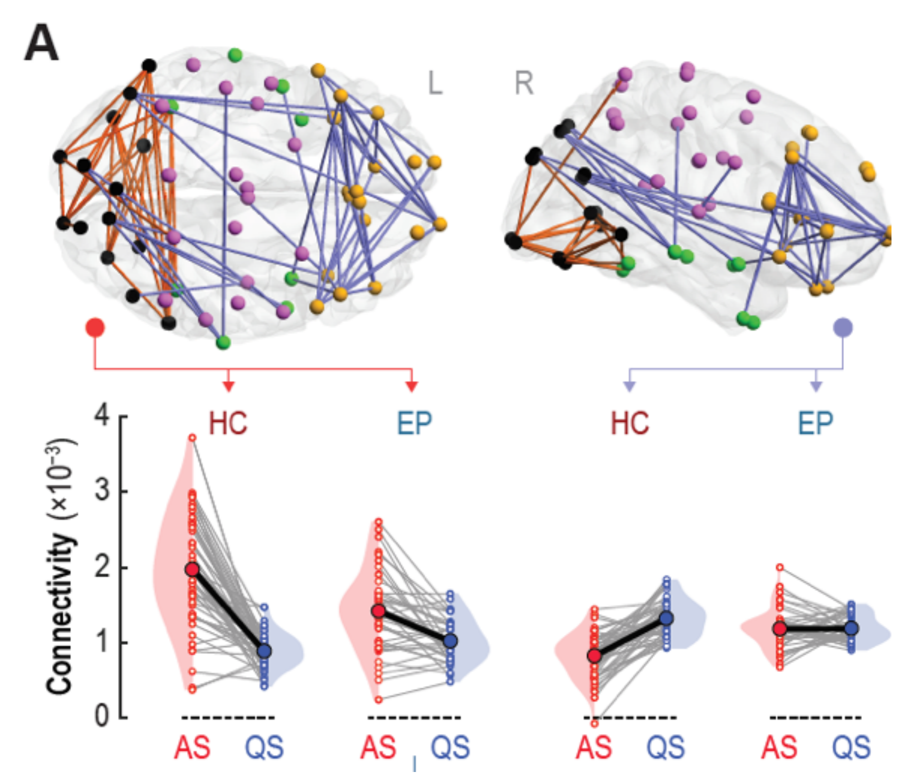
Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes




*Sleep-group (interaction) in brain modes*

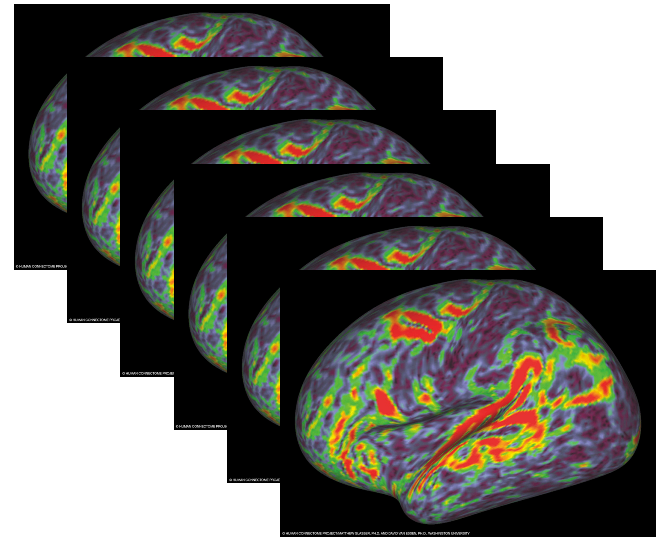
*Sleep-group (interaction) in brain networks*




Tokariev, Roberts *et al.* (2019) *Nature Comms*

# III: Neural fields + modes

CONNECTOME
COORDINATION FACILITY



Ye Tian, Daniel Margulies, Andrew Zalesky



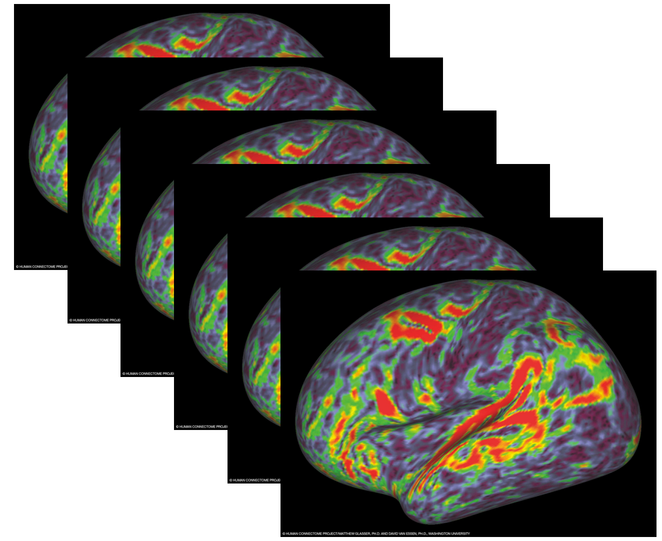
1. 1000+ rs and 700 task fMRI

Tian *et al.* (2020) *Nature Neuroscience*

# III: Neural fields + modes

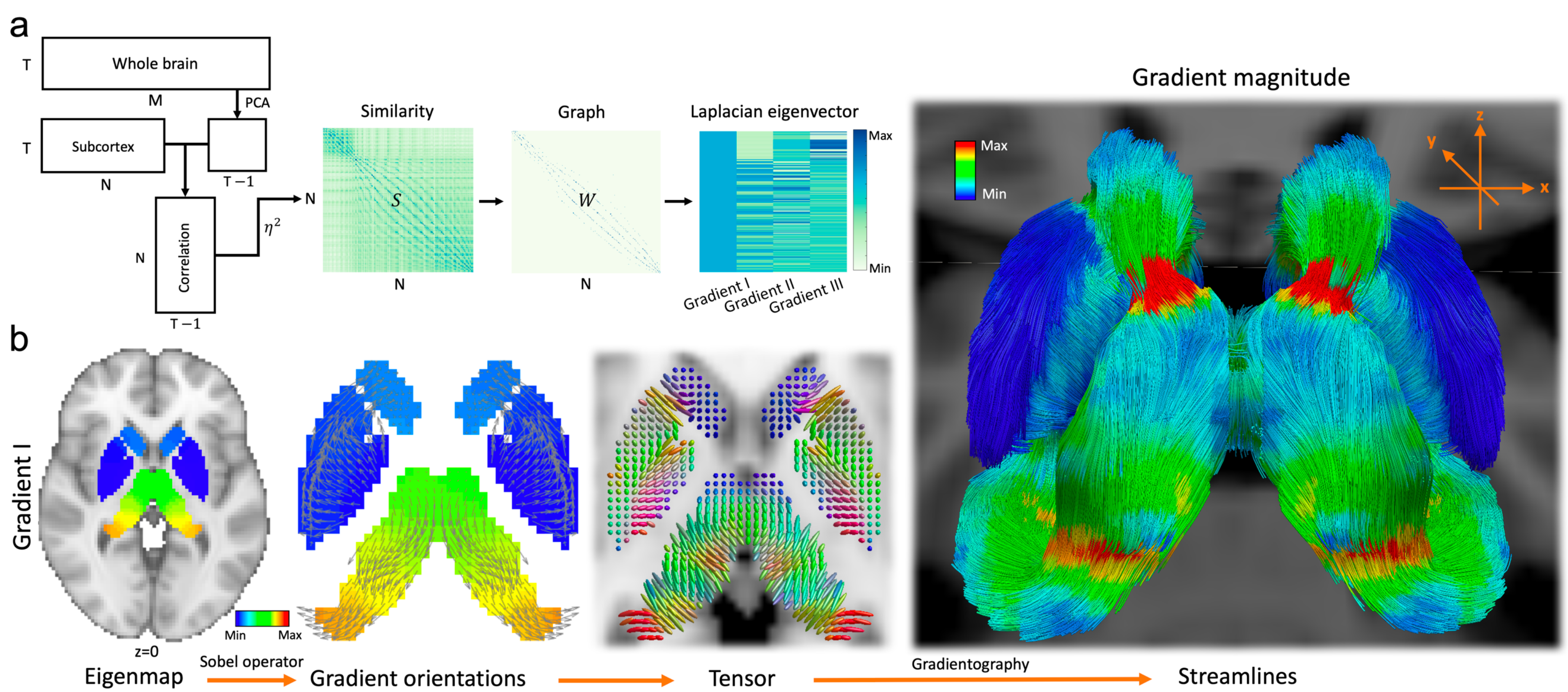
CONNECTOME
COORDINATION FACILITY

1. 1000+ rs and 700 task fMRI



Ye Tian, Daniel Margulies, Andrew Zalesky

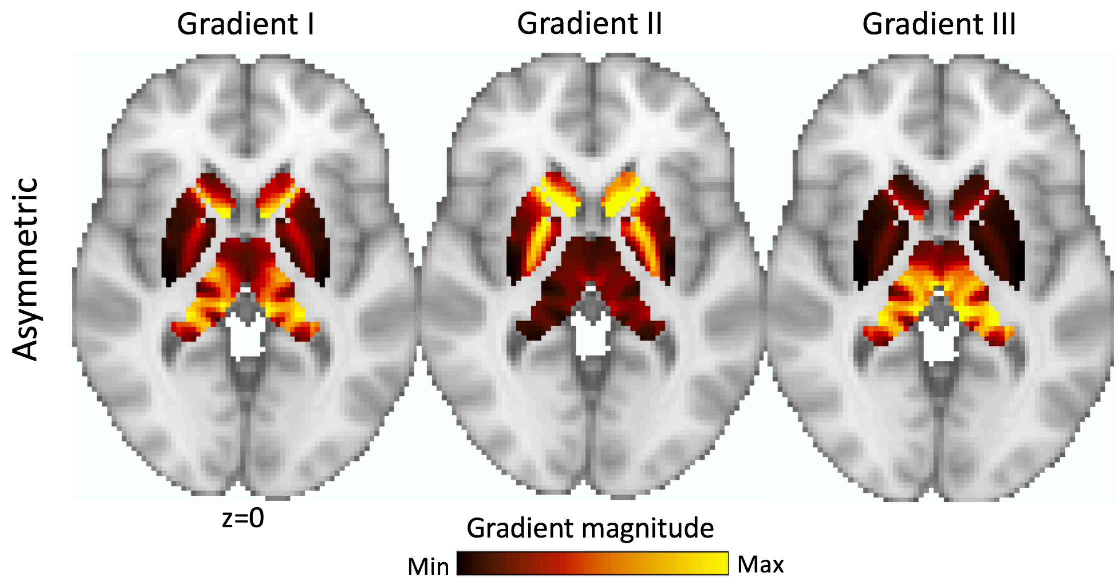
2. Eigenmodes of functional connectivity gradients




Tian *et al.* (2020) *Nature Neuroscience*

# III: Neural fields + modes

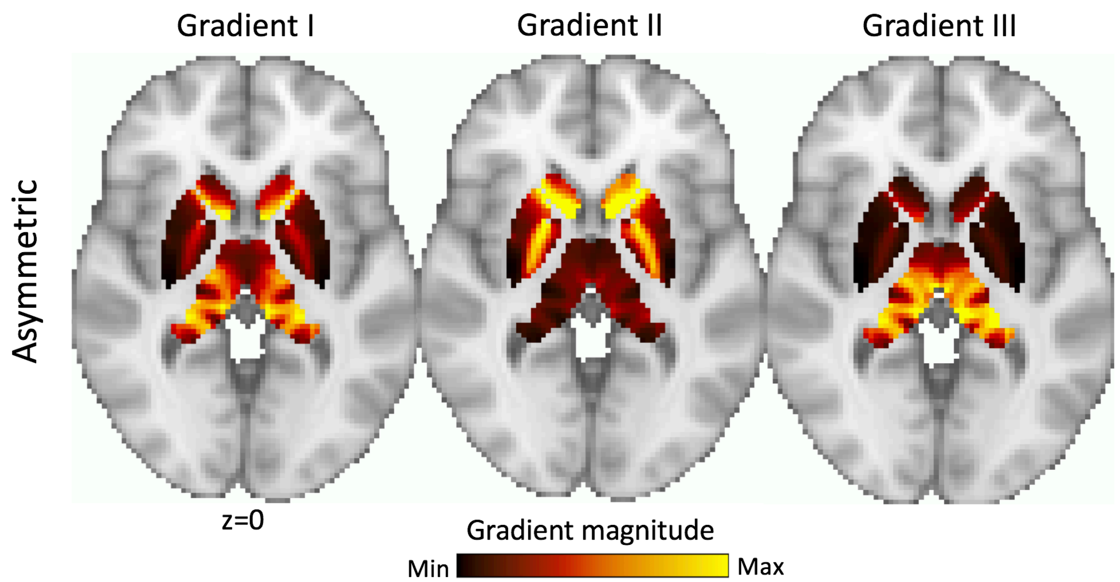
3. Subcortical gradients modes



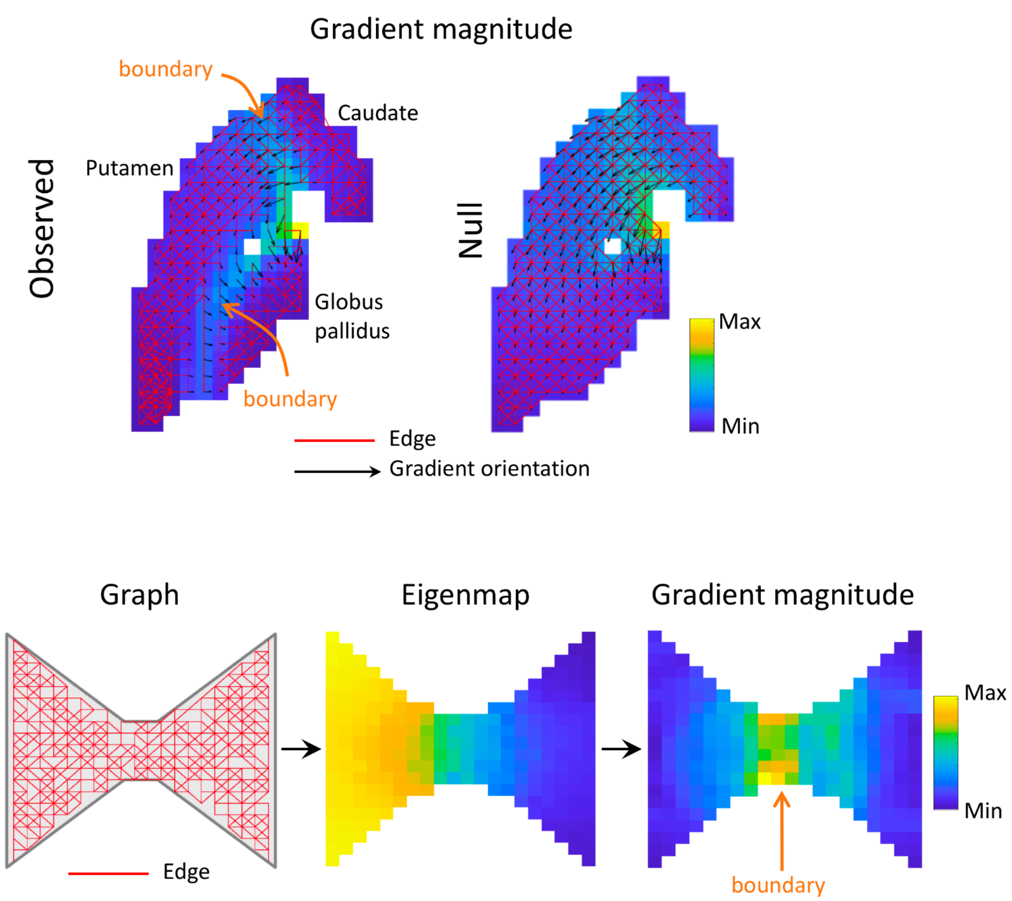

Tian *et al.* (2020) *Nature Neuroscience*

# III: Neural fields + modes

## 3. Subcortical gradients modes

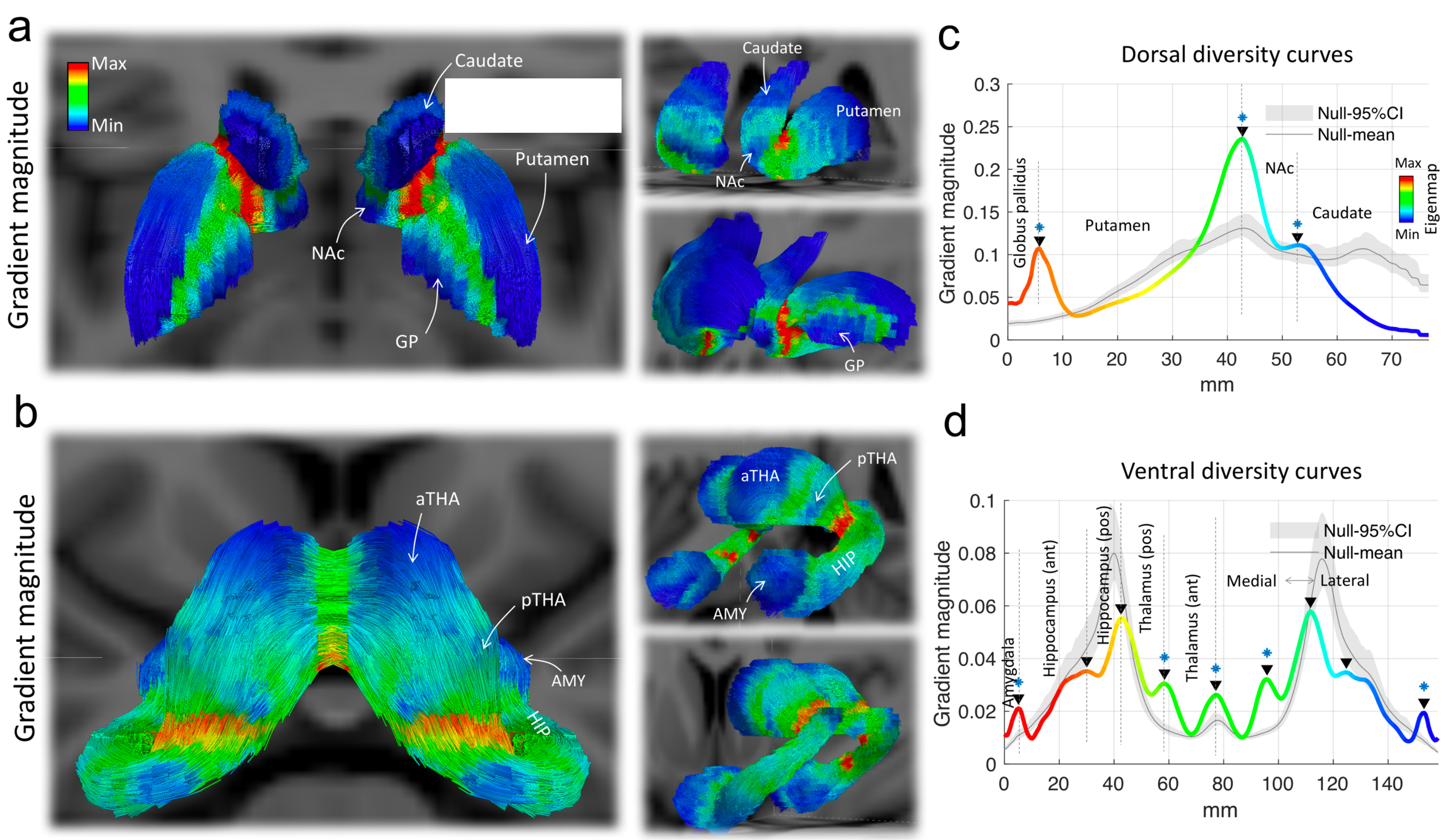



## 4. Test empirical gradients against geometrically constrained nulls




Tian *et al.* (2020) *Nature Neuroscience*

# III: Neural fields + modes




3. Gradient break-points

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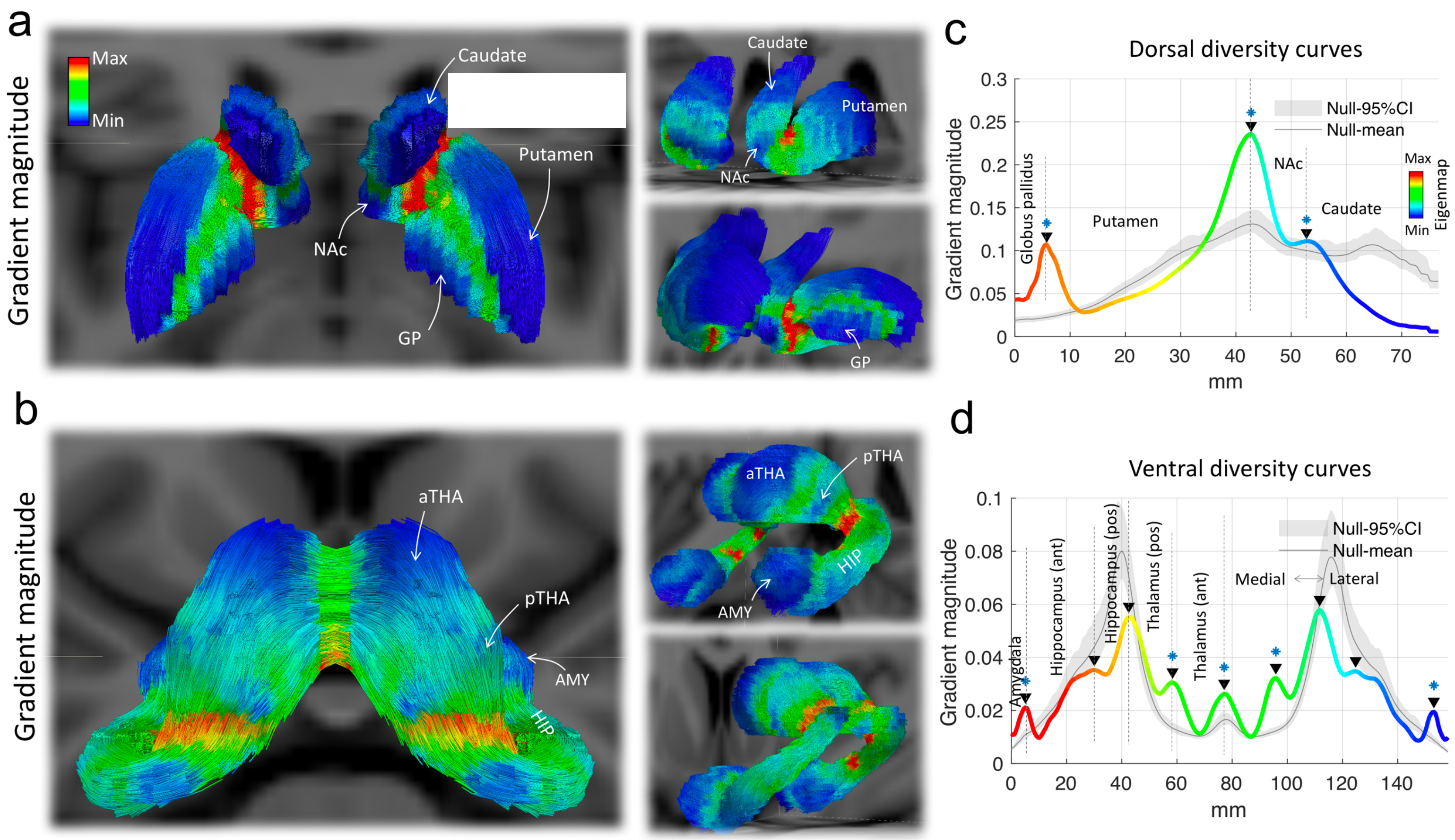
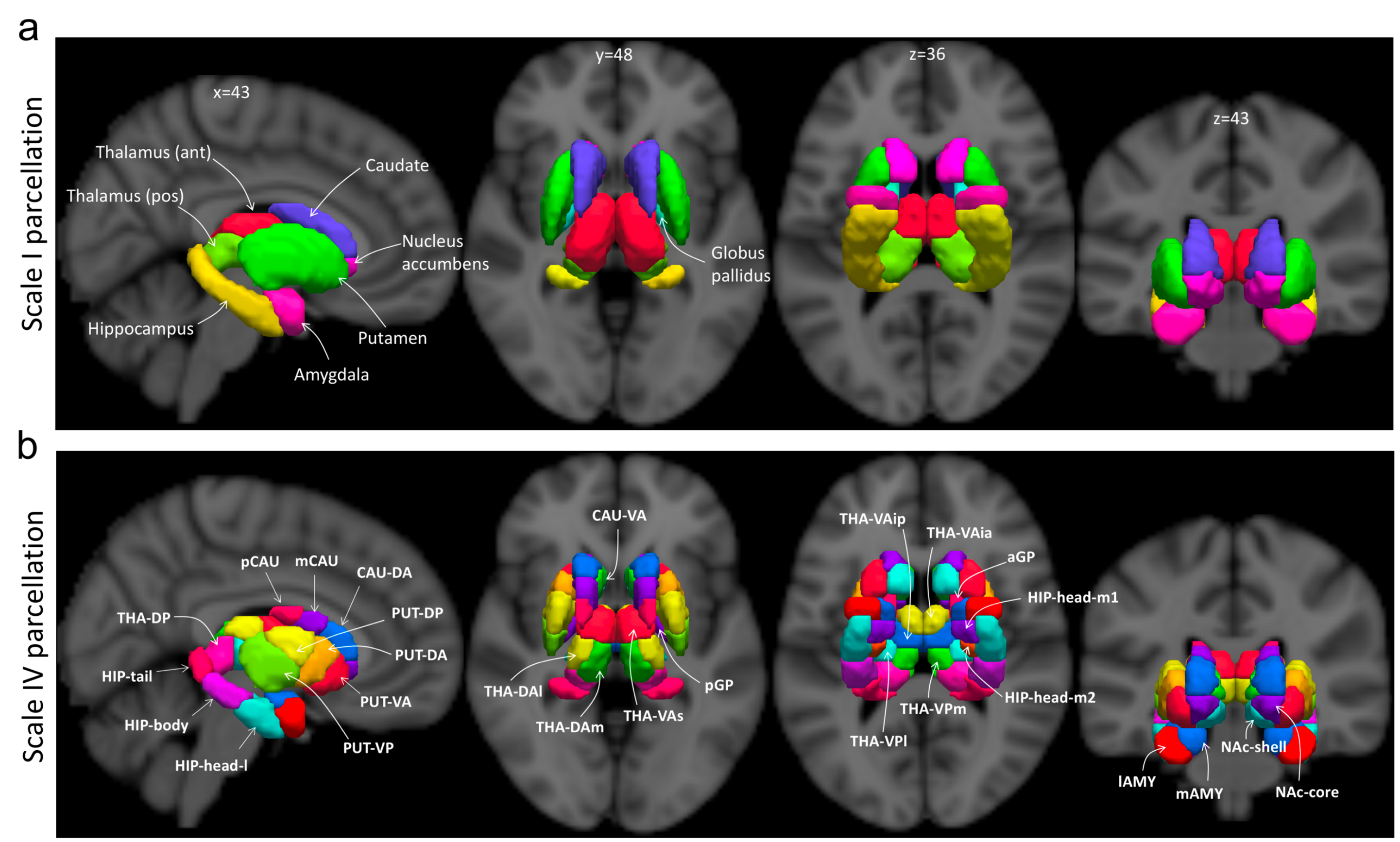
# III: Neural fields + modes




3. Gradient break-points

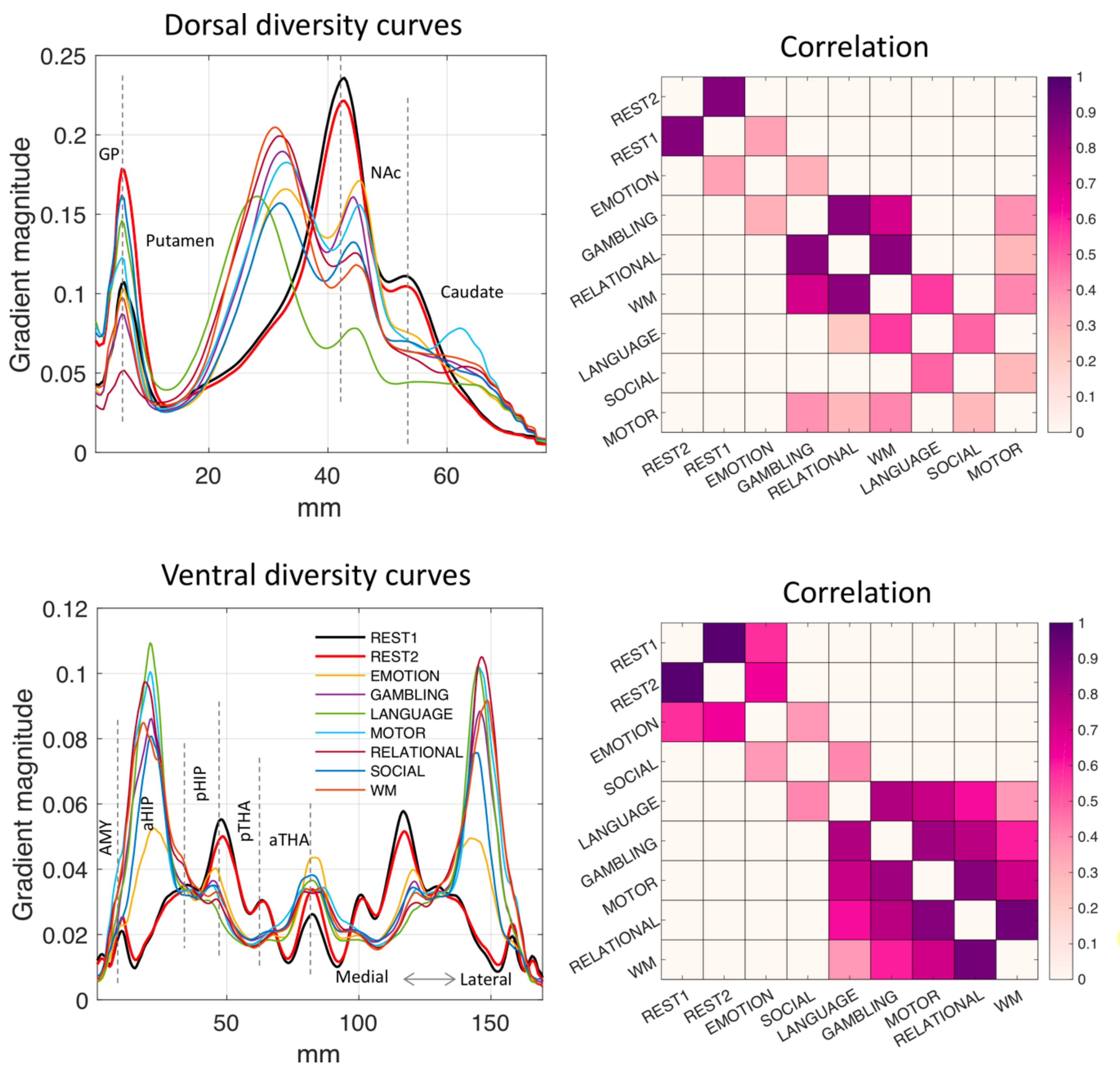
4. … yields hierarchical parcellation




Tian *et al.* (2020) *Nature Neuroscience*

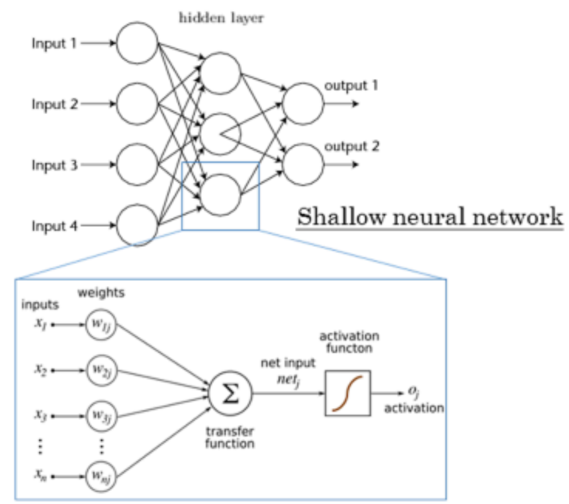
# III: Neural fields + modes

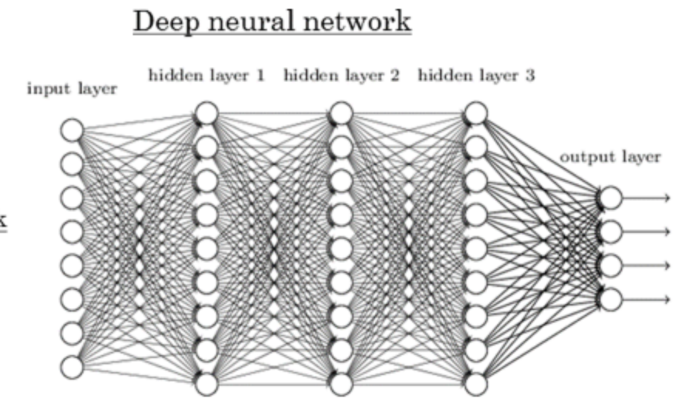
## 5. Task effects




Tian *et al.* (2020) *Nature Neuroscience*

# IV: Linking brain states and mental states



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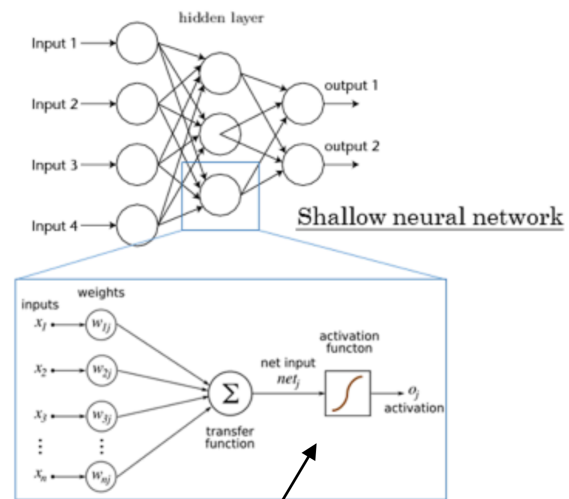


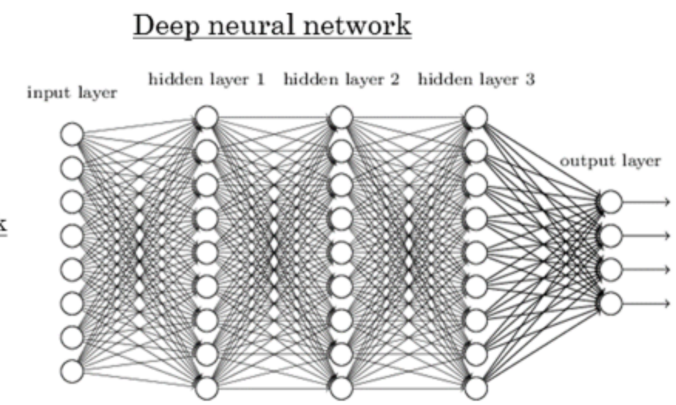


Gain control lies at the heart of conventional neural networks and deep ("brain-like") architectures

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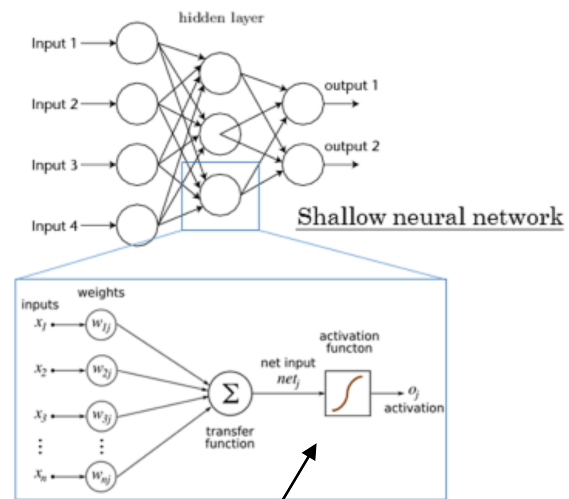
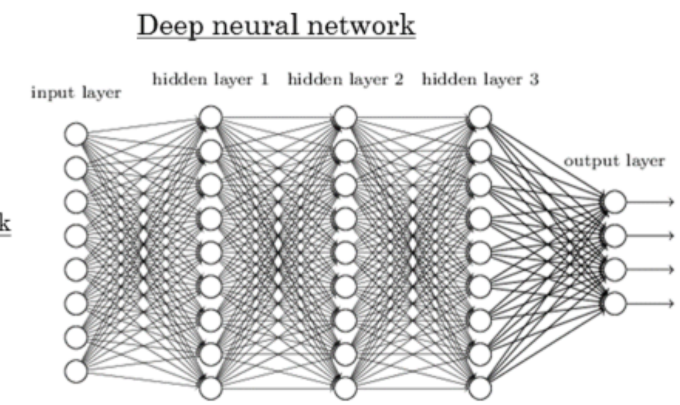
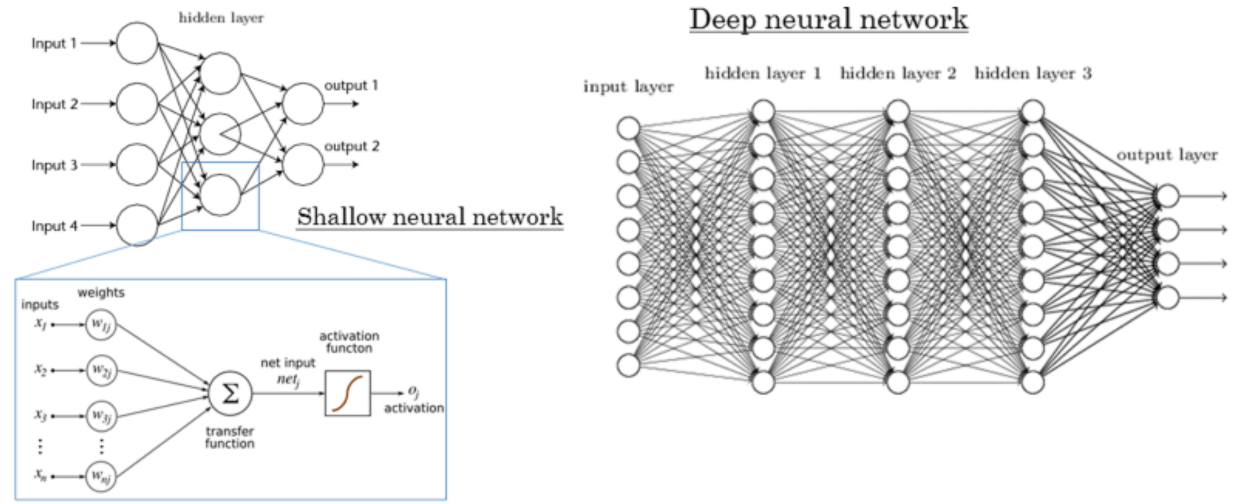


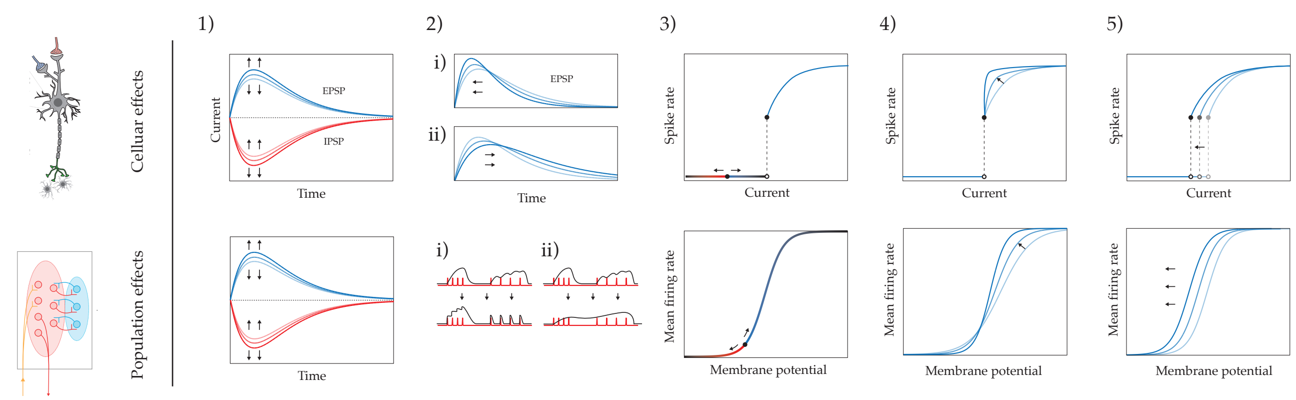




Gain control lies at the heart of conventional neural networks and deep ("brain-like") architectures

Weights are adjusted when learning but the system is otherwise essential static

# IV: Linking brain states and mental states




Contrasts with the dynamic, multiscale, adaptive brain

# Acknowledgements

Anton Tokariev, Sampsa Vanhatalo, Luca Cocchi, James Roberts, Mac Shine, Eli Muller, Ye Tian, Andrew Zalesky, Daniel Margulies


I respectively acknowledge the Awabakal people, the traditional custodians of the land on which we live and work in Newcastle