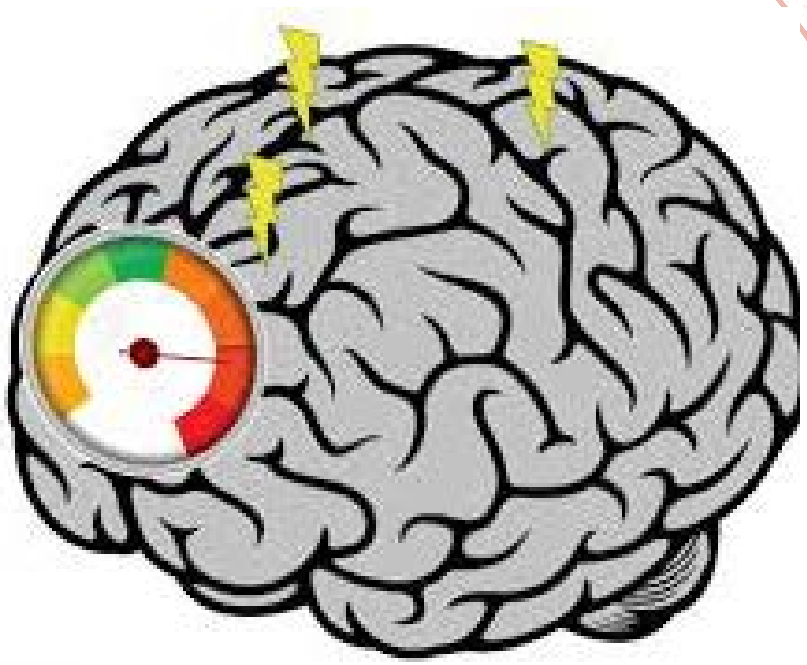

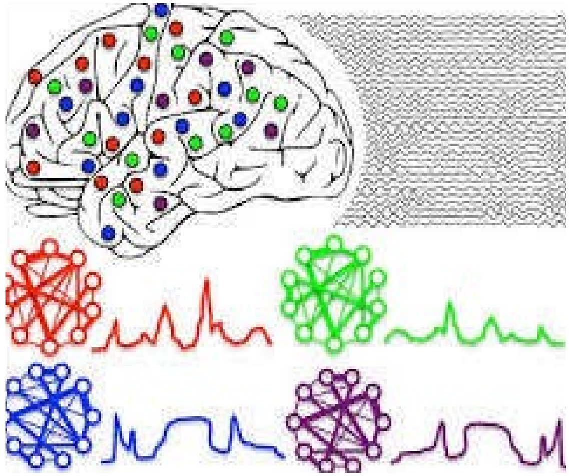

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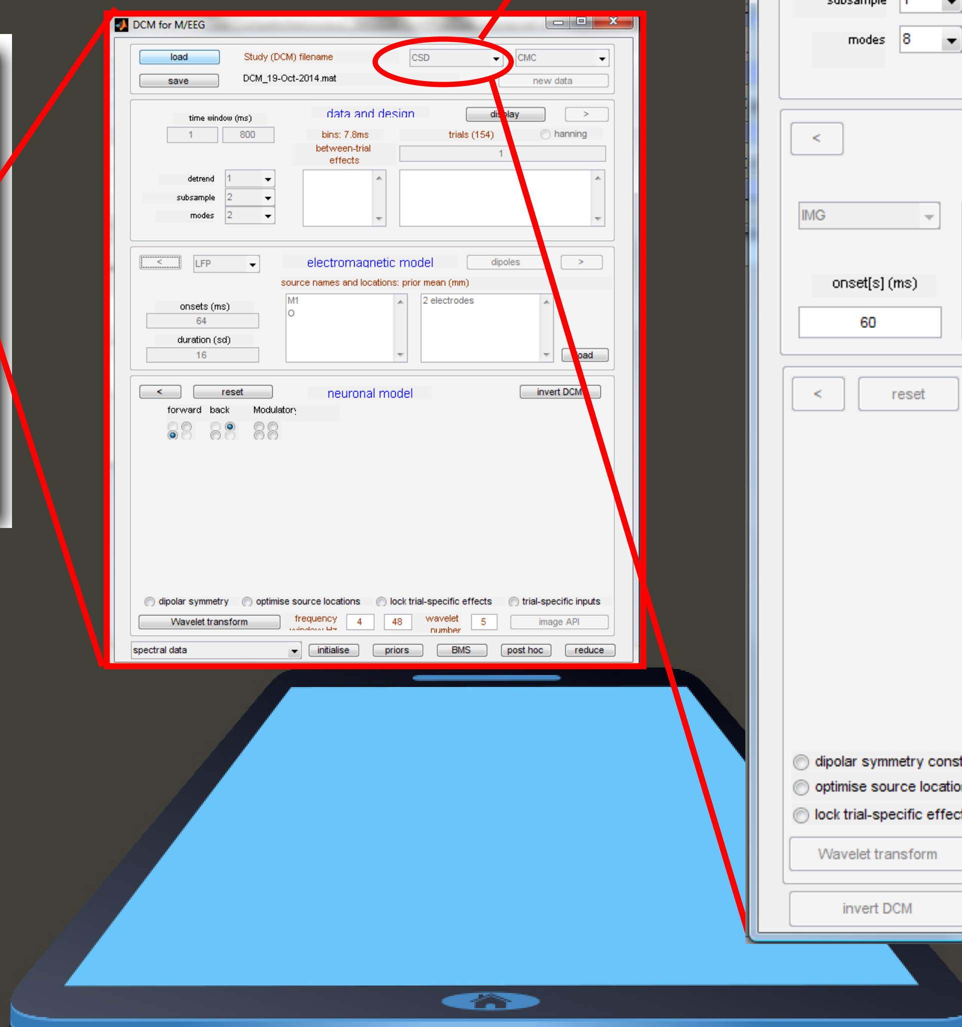
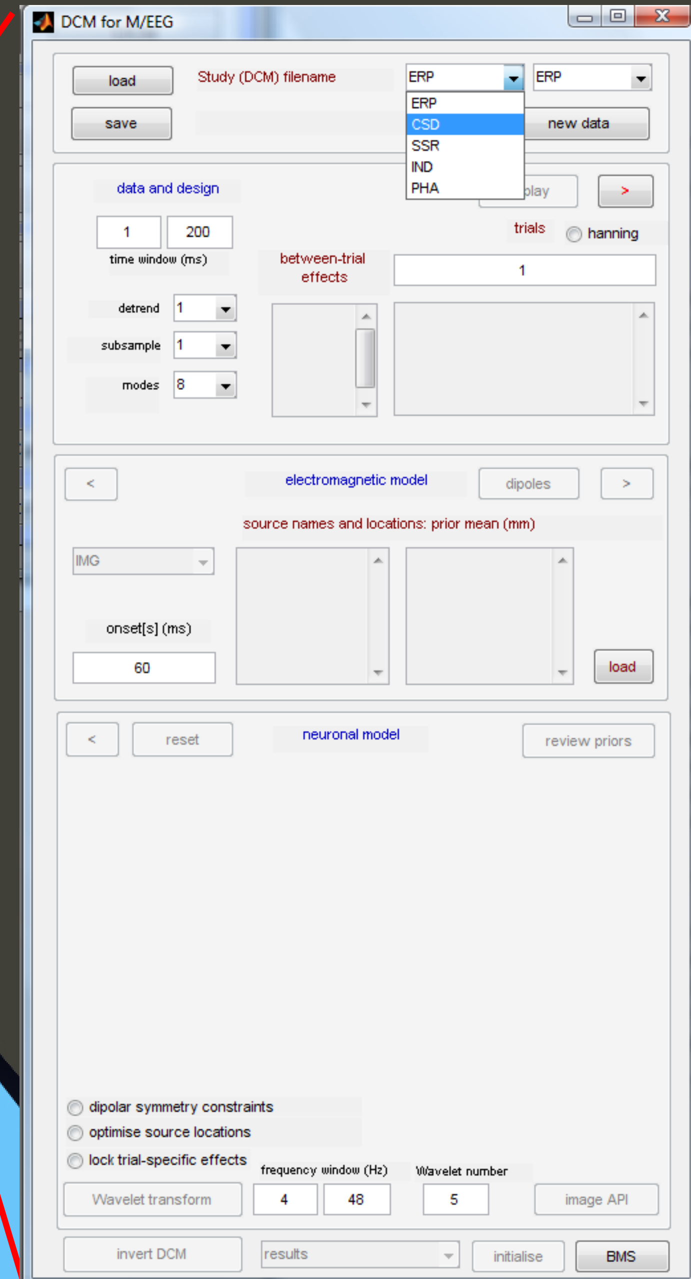
Dynamic Causal Modelling for Steady State Responses

- ✓ Similar statistical features
- ✓ Summarize activity in a compact way
- ✓ Quantitative description in terms of a **characteristic frequency**
- ✓ Cannot describe nonlinear frequency coupling (DCM for IR)
- ✓ Changes oscillatory power and coherence may not yield information directly (DCM for SSR)

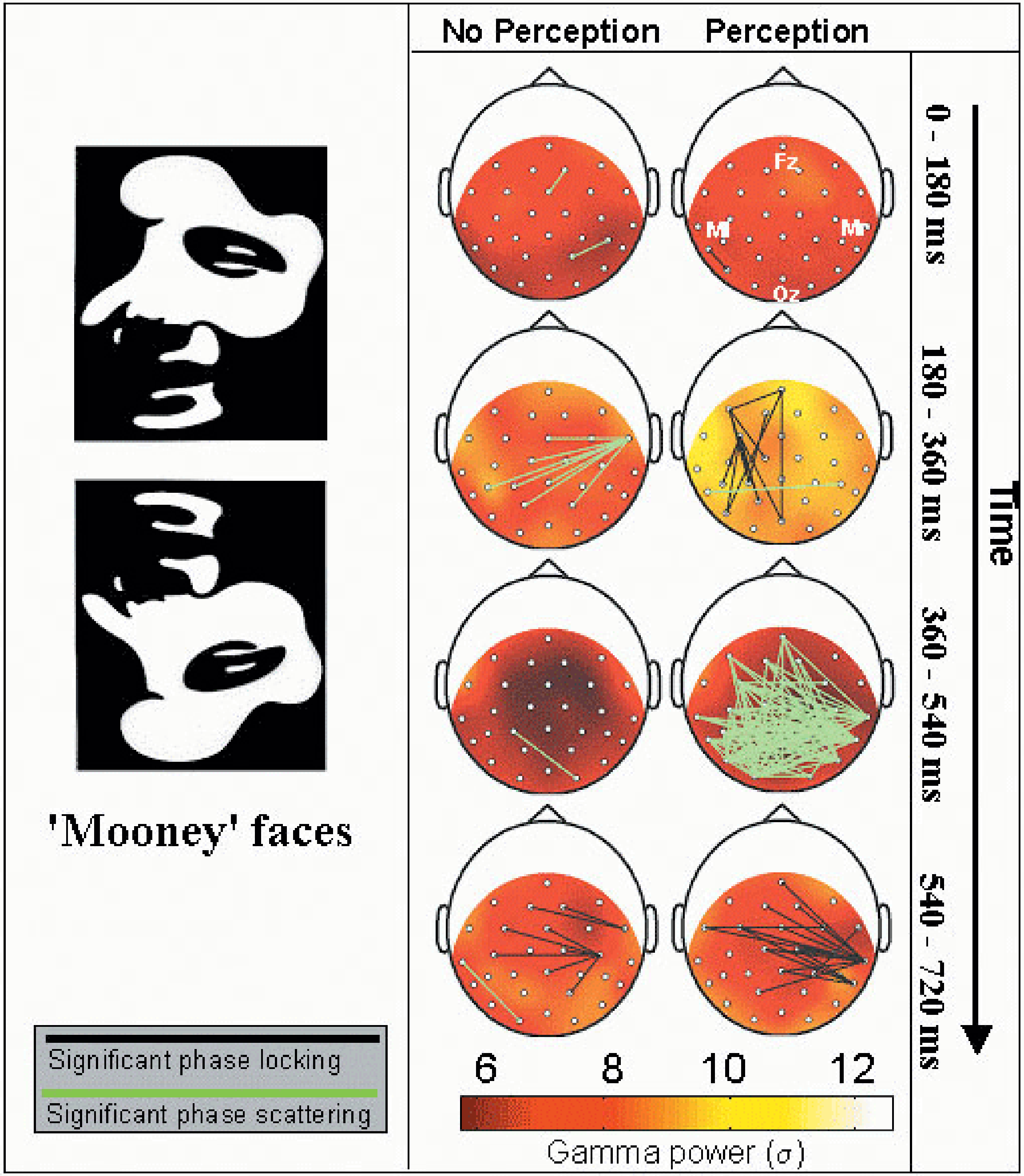
In SPM


SPM12b (6225): Menu
Convert
Time-frequ...
Images...
Preproces...
Average
Other...
3D Source Reconstr.
DCM
Specify 1st-level
Review
Specify 2nd-level
Estimate
Results
SPM for EEG/MEG
Displa...
Check Reg
Render...
EEG
Toolbox:
PPIs
ImCalc
DICOM Import
Help
Utils...
Batch
Quit


DCM for M/EEG
load
Study (DCM) filename
CSD
CMC
save
DCM_19-Oct-2014.mat
new data
time window (ms)
1
800
data and design
display
bins: 7.8ms
trials (154)
hanning
between-trial effects
detrend
subsample
modes
electromagnetic model
LFP
dipoles
source names and locations: prior mean (mm)
onsets (ms)
64
duration (sd)
16
M1
2 electrodes
reset
neuronal model
invert DCM
forward
back
Modulatory
dipolar symmetry
optimise source locations
lock trial-specific effects
trial-specific inputs
Wavelet transform
frequency window Hz
4
48
wavelet number
5
image API
spectral data
initialise
priors
BMS
post hoc
reduce


DCM for M/EEG
load
Study (DCM) filename
ERP
ERP
CSD
SSR
IND
PHA
save
new data
data and design
1
200
time window (ms)
trials
hanning
between-trial effects
1
detrend
subsample
modes
8
electromagnetic model
dipoles
source names and locations: prior mean (mm)
IMG
onset[s] (ms)
60
load
reset
neuronal model
review priors
dipolar symmetry constraints
optimise source locations
lock trial-specific effects
frequency window (Hz)
Wavelet number
Wavelet transform
4
48
5
image API
invert DCM
results
initialise
BMS

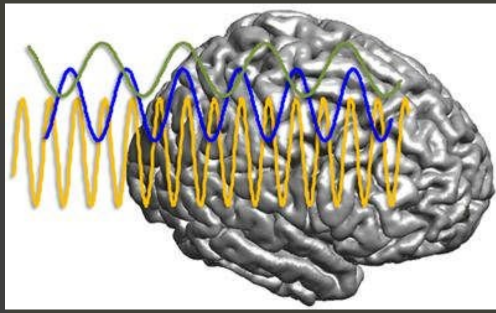
- ✓ Perception, attention, memory, executive control
- ✓ Highly parallel processing by the brain
- ✓ Information transfer
- ✓ Synchronized neuronal discharges
- ✓ Select relevant information

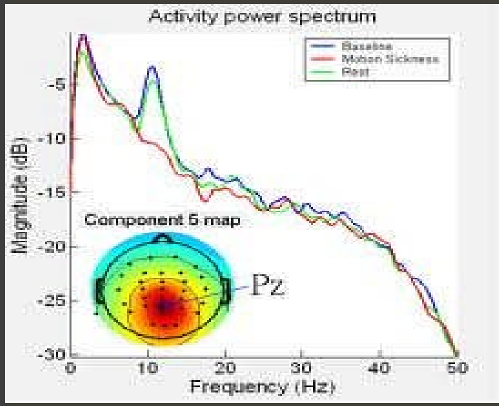


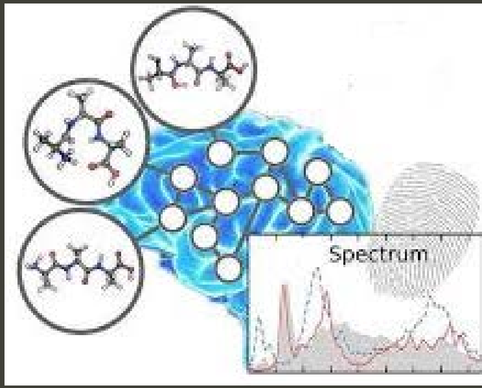
No Perception
Perception
Fz
Ml
Mr
Oz
0 - 180 ms
180 - 360 ms
360 - 540 ms
540 - 720 ms
Time
'Mooney' faces
Significant phase locking
Significant phase scattering
6
8
10
12
Gamma power (σ)

Oscillations

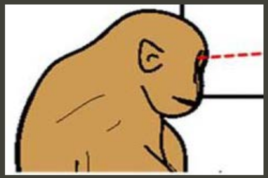
- ✓ Working memory *(Siegel et al. 2009,...)*
- ✓ Visual attention *(Feldman and Friston, 2010,...)*
- ✓ Size, contrast *(e.g. Pinotsis et al., 2014, Pinotsis et al., 2016,...)*
- ✓ Binding Input to cortical representations *(Schoffelen et al., 2005,...)*
- ✓ Information propagation *(e.g. Bastos et al. 2012,Tallon-Baudry et al., 1996...)*
- ✓ Psychiatric diseases, Autism... *(e.g. Uhlhaas and Singer, 2012, Dickinson et al., 2015,...)*

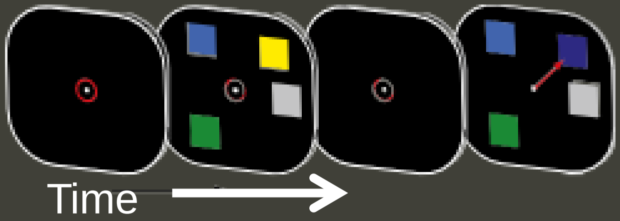




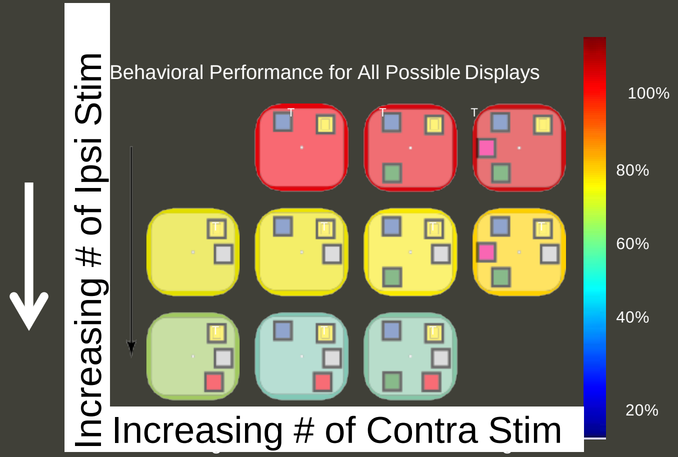


Working Memory Task (Miller Lab, MIT)





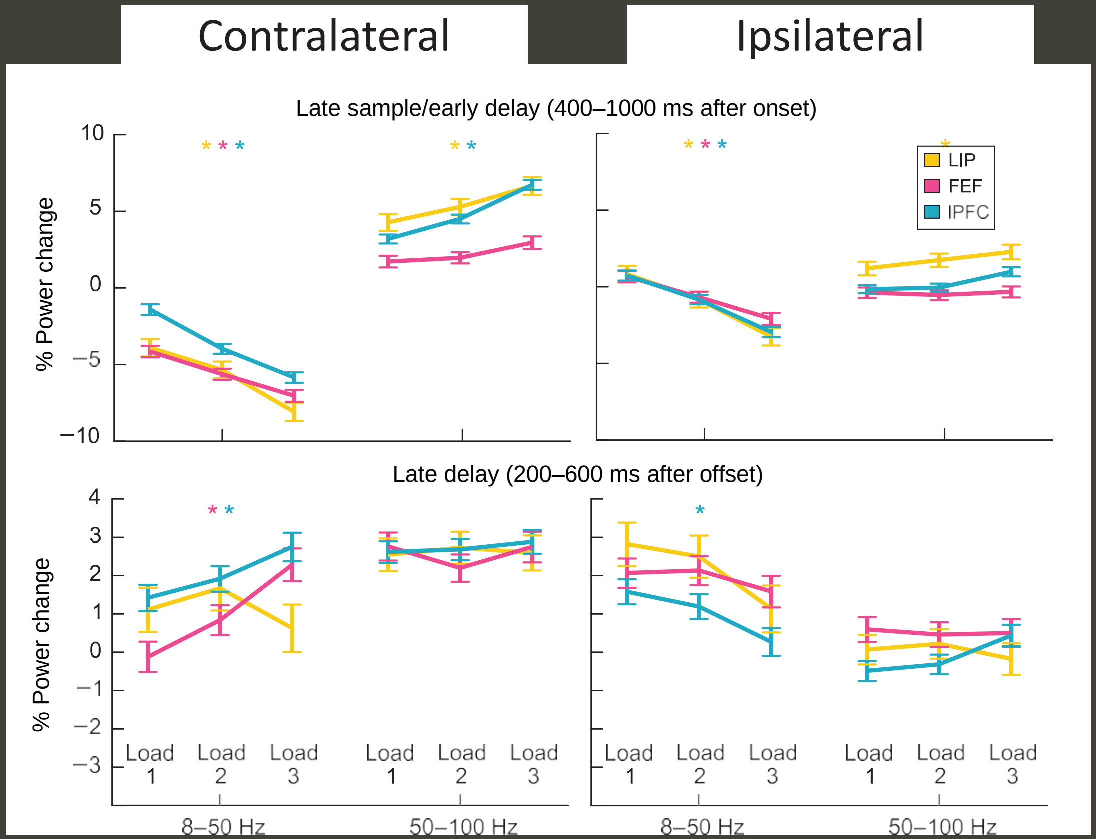
WM performance



When more than 2 items were presented in the same hemifield, the animal's behavioral performance decreased dramatically

Buschman et al., PNAS, 2011

Changes in oscillatory power may <u>not</u> yield information directly



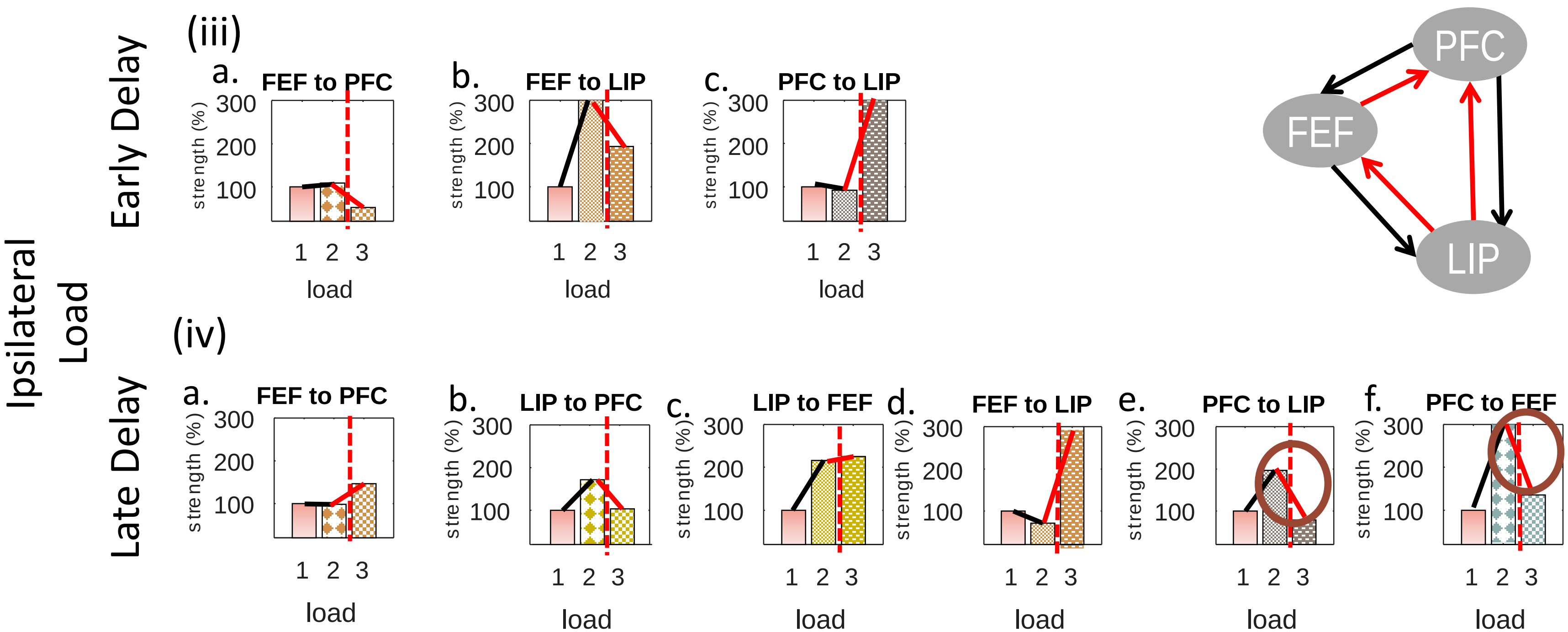
Load effects are weak (1-2% change)

Load effects are similar below and above WM Capacity Limit

→ *Power is **not** informative about the reduction in performance and the **mechanisms/network effects** resulting in the WM Capacity Limit*

Kornblith et al., Cerebral Cortex, 2015

Inferred model connectivity may explain behaviour



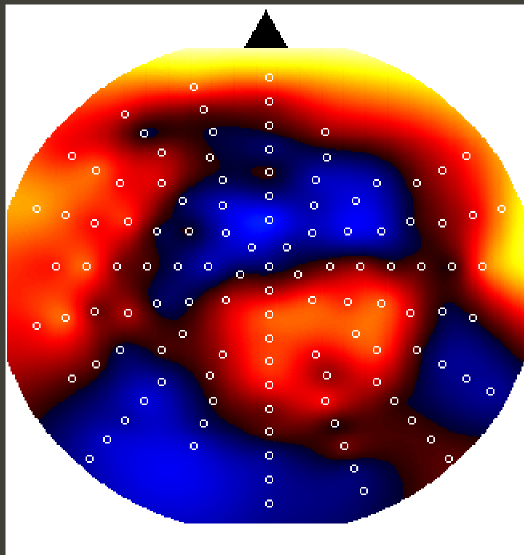
Above capacity – Ipsilateral only where performance is impaired

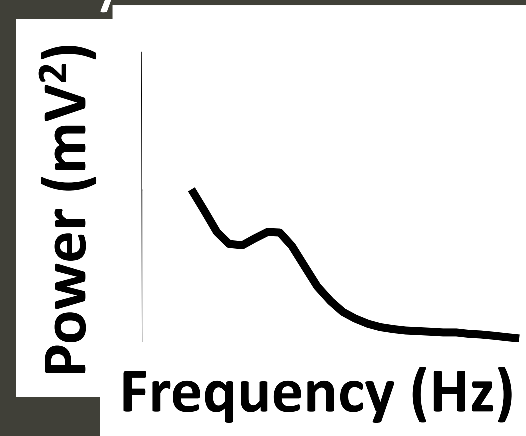
- *FB from PFC broke down– Could explain reduced performance that load effects on power did not explain.*
- *Predictive Coding model → No predictions from areas that contain memories*
- *No memories → The animal cannot perform the task*

Pinotsis et al., Cerebral Cortex, 2018

Steps

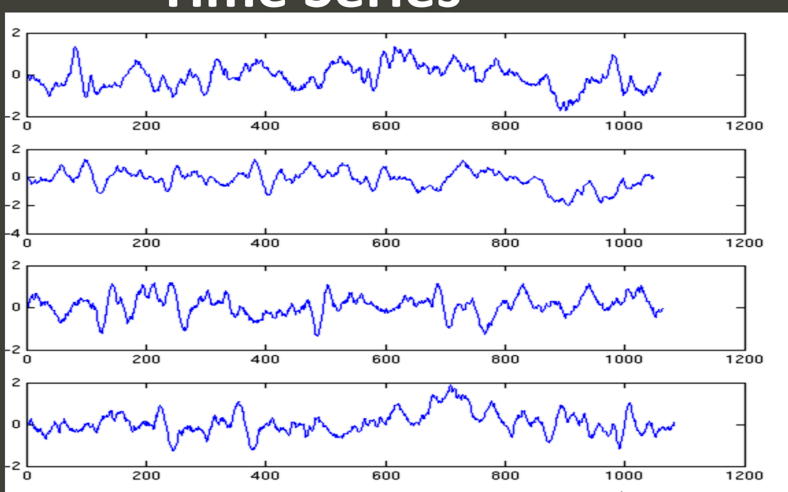
Cross Spectral Density

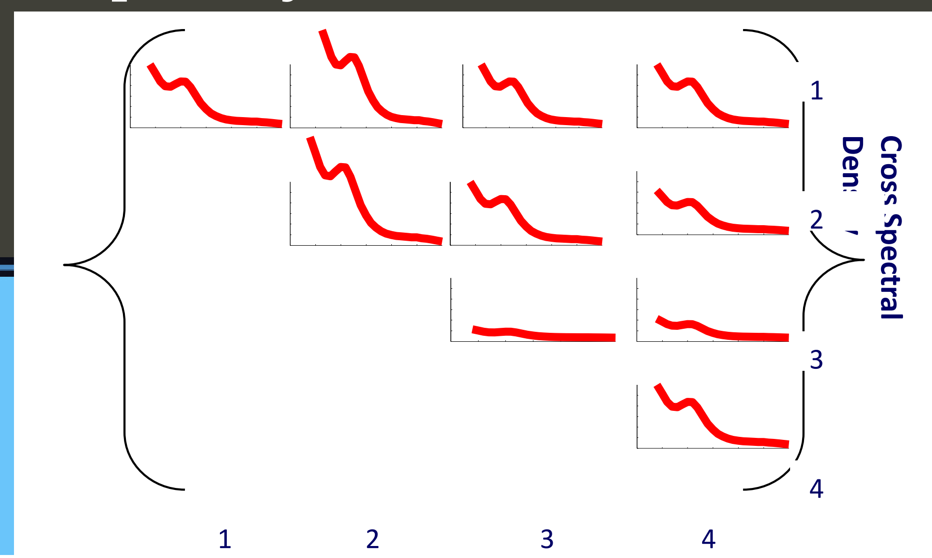




✓ Summarizes brain response in terms of power at each frequency

EEG - MEG – LFP Time Series



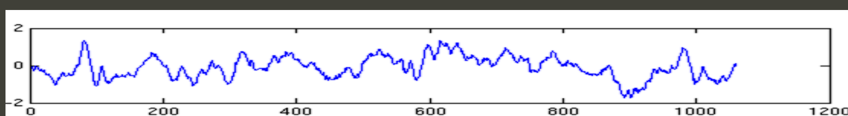


A few LFP channels or EEG/MEG spatial modes

From Time Series to Cross Spectral Densities

Vector Auto-regression *p*-order model:

Linear prediction formulas that attempt to predict an output *y[n]* of a system based on the previous outputs



$$y_n = \alpha_1 y_{n-1} + \alpha_2 y_{n-2} \ldots + \alpha_p y_{n-p} + e_n$$

$$\{\alpha_{1 \ldots p} \in A(p) : \{c \times c\}$$

Resulting in *a* matrices for *c* Channels

$$H_{ij}(\omega) = \frac{1}{\alpha_1^{ij} e^{iw} + \alpha_2^{ij} e^{iw2} + \ldots\ldots + \alpha_p^{ij} e^{iwp}}$$

$$g(\omega)_{ij} = f(A(p))$$

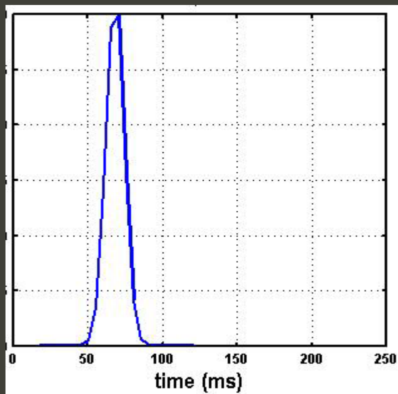
Cross Spectral Density for channels *i,j* at frequencies

$\omega = 2\pi f$

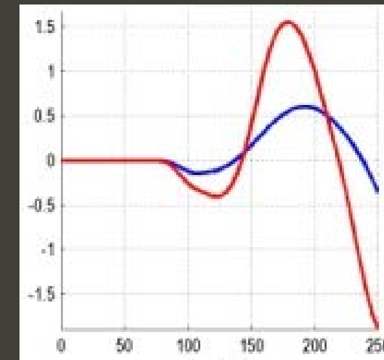
$$\begin{Bmatrix} g(\omega)_{11} & g(\omega)_{12} & \ldots \\ g(\omega)_{12} & \ldots & \\ & & \end{Bmatrix}$$

$$g(\omega)_{ij} = H_{ij}(\omega) \; \prod_{ij} H(\omega)_{ij}^{*}$$

A Brain Area as an Input - Output System



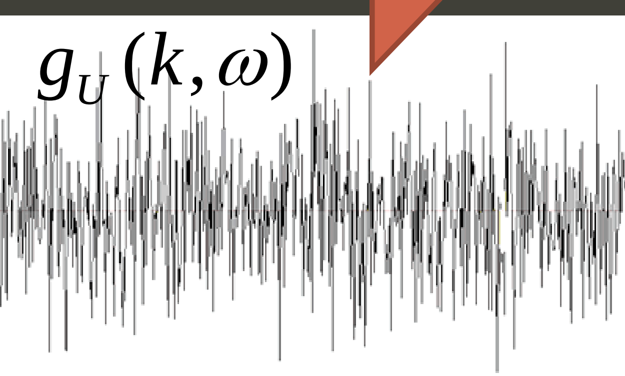
ERP

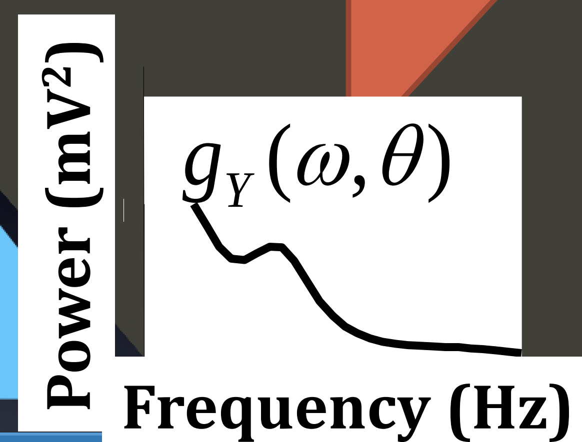


Driving input or neuronal innovations

(Model) Brain region

Predicted responses ERP or cross spectra

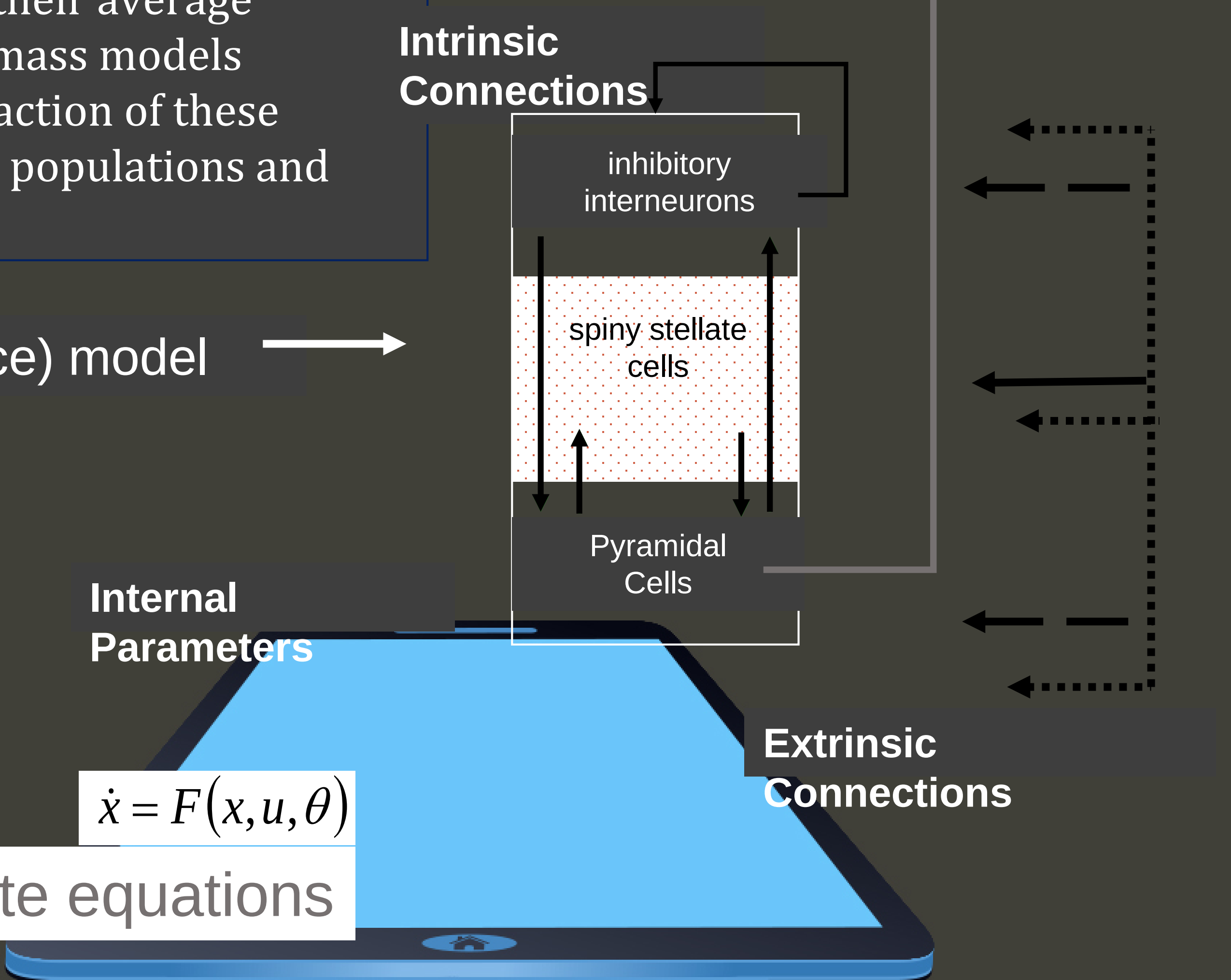




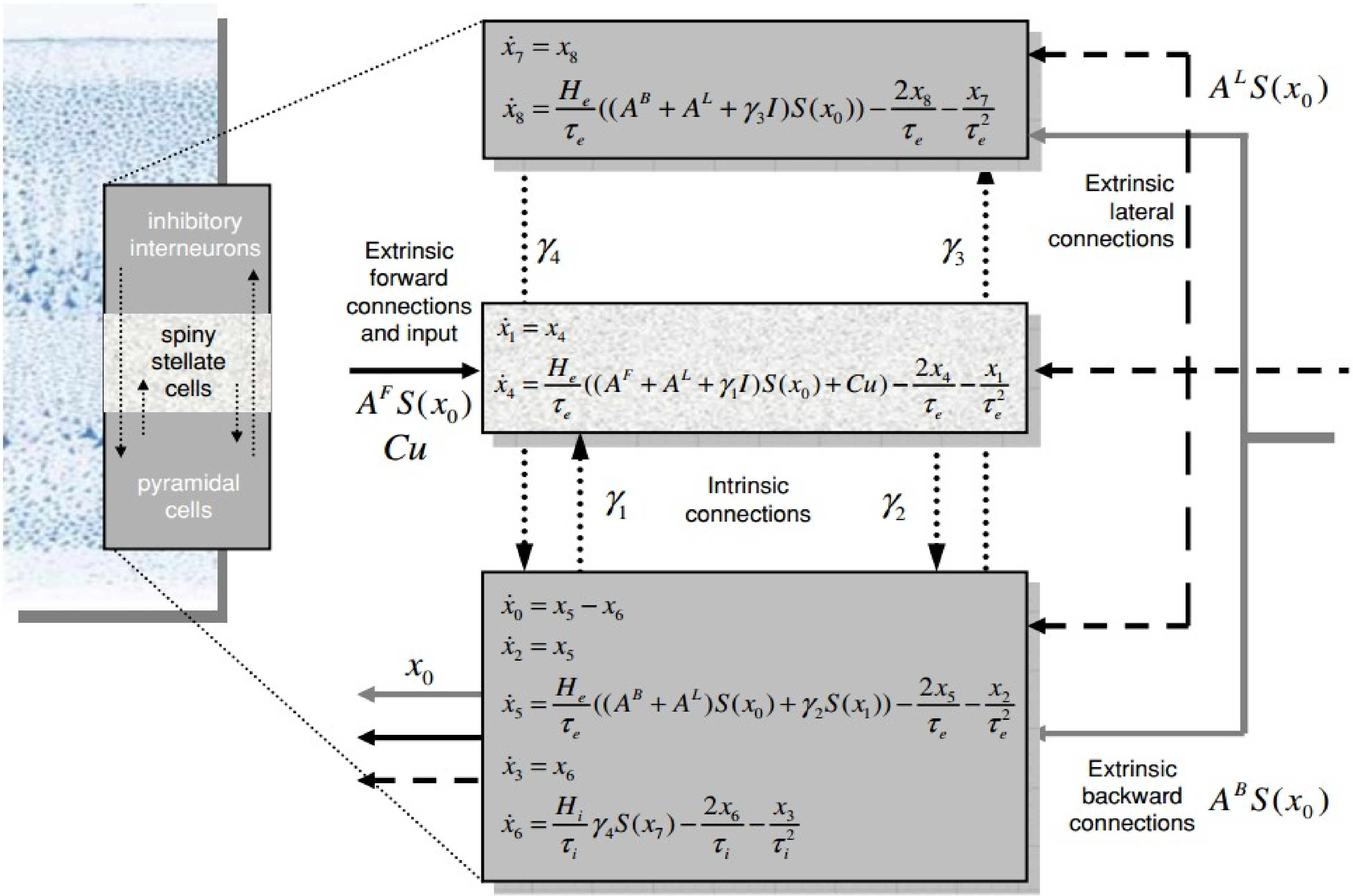
Same Neural Mass Models as ERP

Tens of thousands of neurons approximated by their average response. Neural mass models describe the interaction of these averages between populations and sources

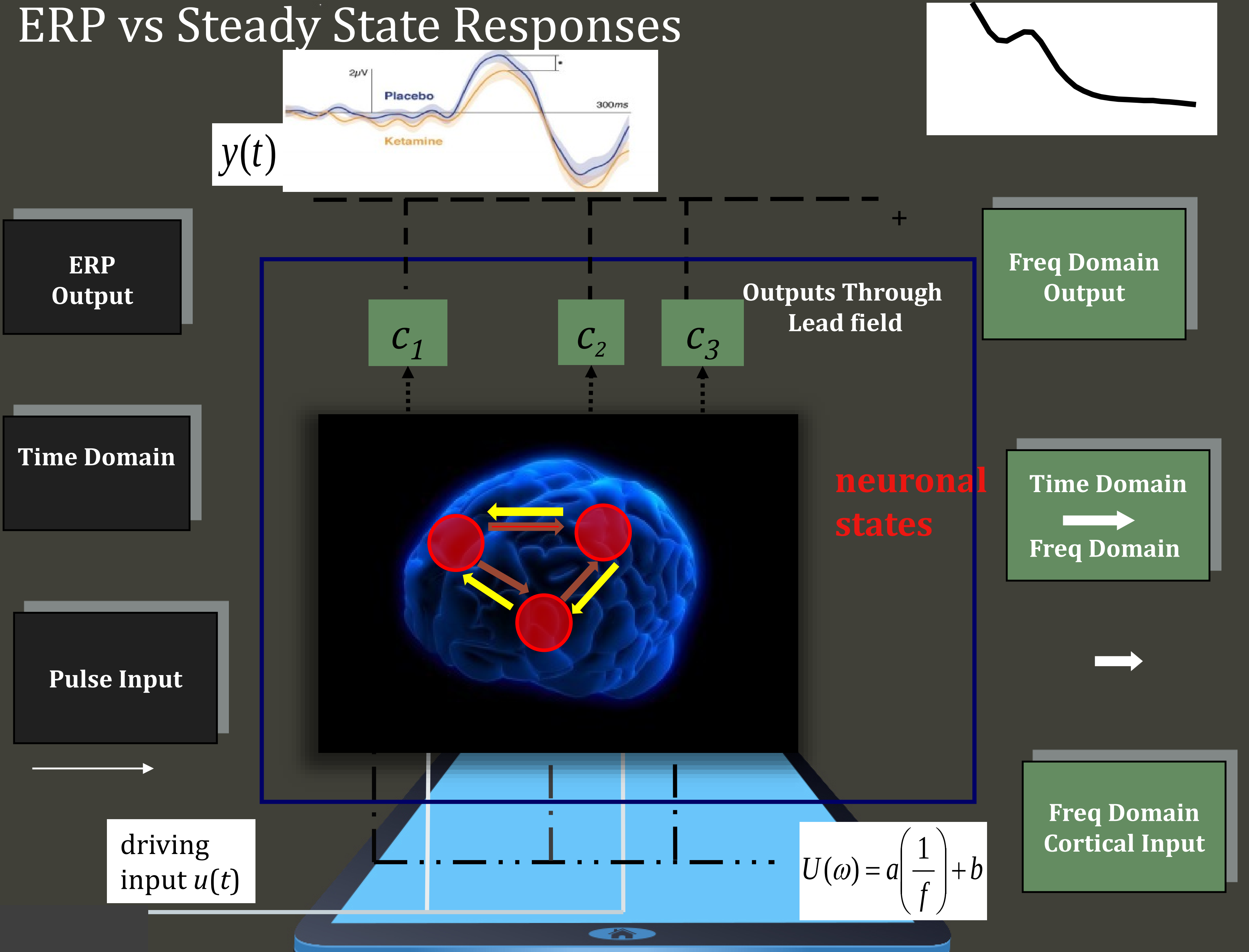
neuronal (source) model



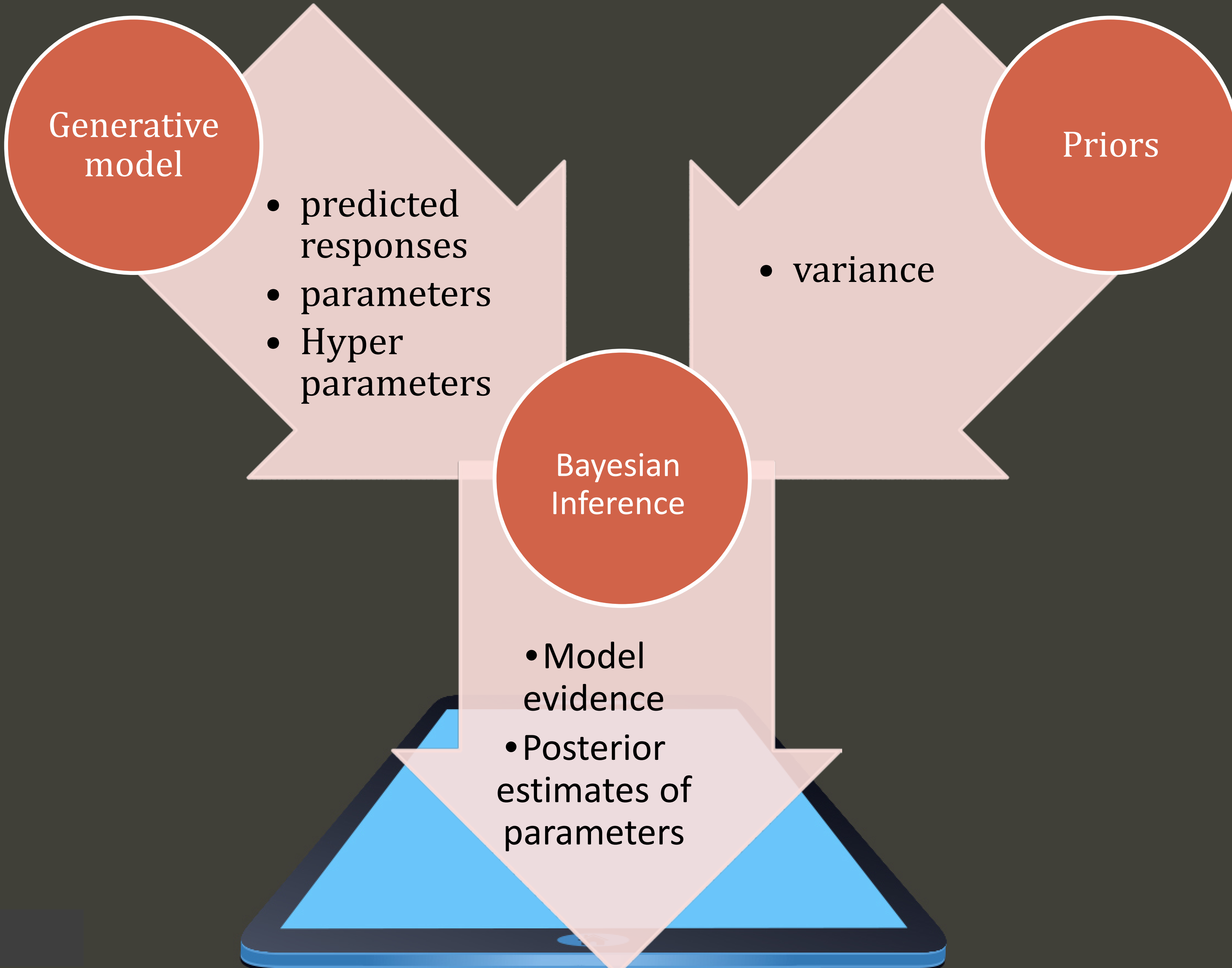
From DCM for ERPs talk in this course (Ryszard Auksztulewicz)



ERP vs Steady State Responses



Roadmap


Generative model
predicted responses
parameters
Hyper parameters
Priors
variance
Bayesian Inference
Model evidence
Posterior estimates of parameters

Bayesian Model Inversion

$$\mathbf{g}_Y(\omega) = g_Y(\omega,\theta) + g_N(\omega,\theta) + \varepsilon(\omega)$$

$$g_N(\omega,\theta) = \alpha_N + \frac{\beta_N}{\omega}$$

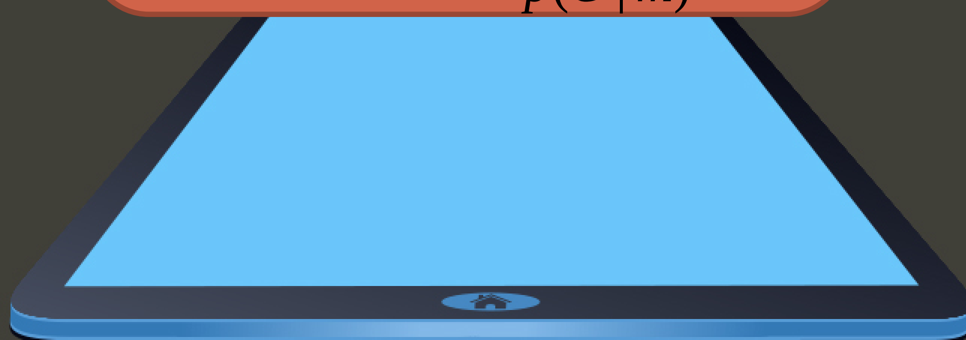
$$\mathrm{Re}(\varepsilon) \sim \mathcal{N}(0,\Sigma(\omega,\lambda)) \qquad \mathrm{Im}(\varepsilon) \sim \mathcal{N}(0,\Sigma(\omega,\lambda))$$

$$p(\theta,m) = N(\mu_\theta,\Sigma_\theta)$$

$$p(G\,|\,\theta,m) = N(\mathbf{g}_Y(\omega),\Sigma(\omega,\lambda))$$

$$p(G\,|\,m) = \int p(G\,|\,\theta,m)\,p(\theta)\,d\theta$$

$$p(\theta\,|\,G,m) = \frac{p(G\,|\,\theta,m)\,p(\theta,m)}{p(G\,|\,m)}$$



Bayesian Model Inversion

Measured data

Specify generative forward model (with prior distributions of parameters)

Variational Laplace Algorithm

Maximize a free energy bound to model evidence :

$$F = \log p(y|m) - D(q(\theta) \| p(\theta|y,m))$$

$$= \langle \log p(y|\theta,m) \rangle_q - D(q(\theta) \| p(\theta|m))$$

Iterative procedure:

1. Compute model response using current set of parameters and hyperparameters
2. Compare model response with data
3. Improve parameters and hyperparameters

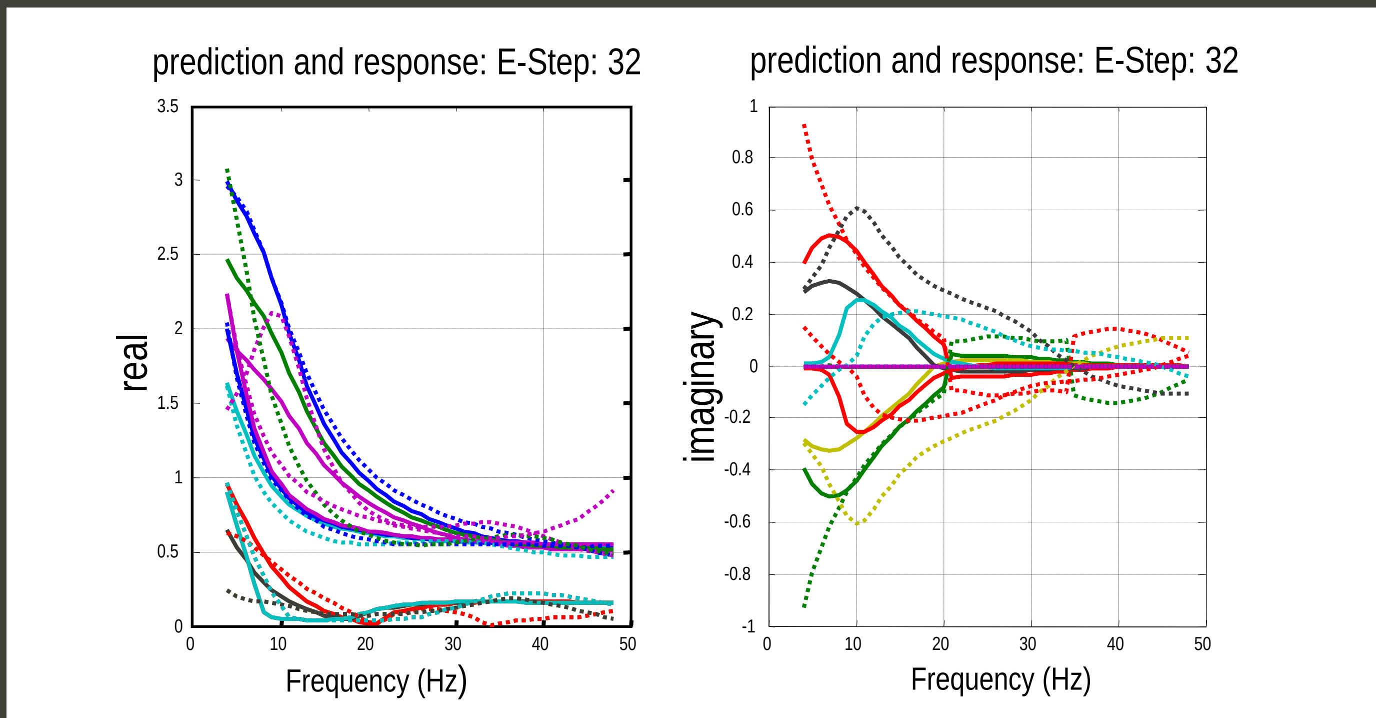
Model comparison via Bayes factor:

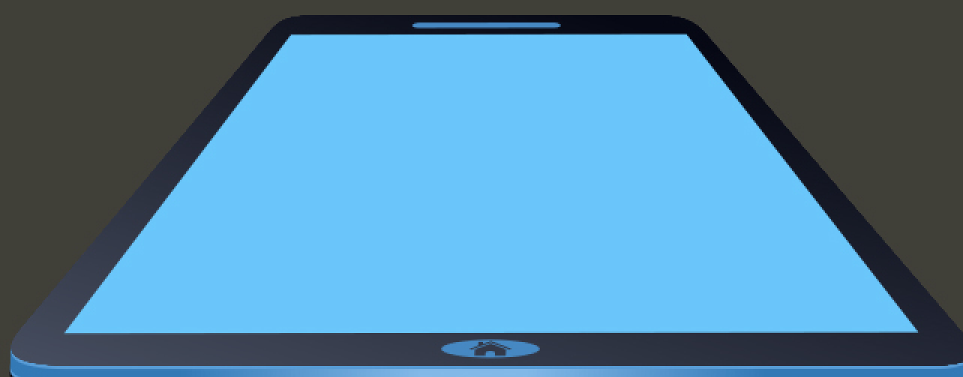
$$BF = \frac{p(y \mid m_1)}{p(y \mid m_2)}$$

$$q(\theta) \approx p(\theta|y,m)$$

Maximum accuracy over complexity constraints

Data fits have **two** parts: real and imaginary





Example 1: Pharmacological Manipulation of Glutamate and GABA

Question:

- ✓ Are our estimates of excitation and inhibition truthful?

$$H_e, H_i$$

AIM:

NOT to explain mechanisms of isoflurane BUT

to exploit isoflurane to <u>induce</u> known changes in synaptic transmission and THEN

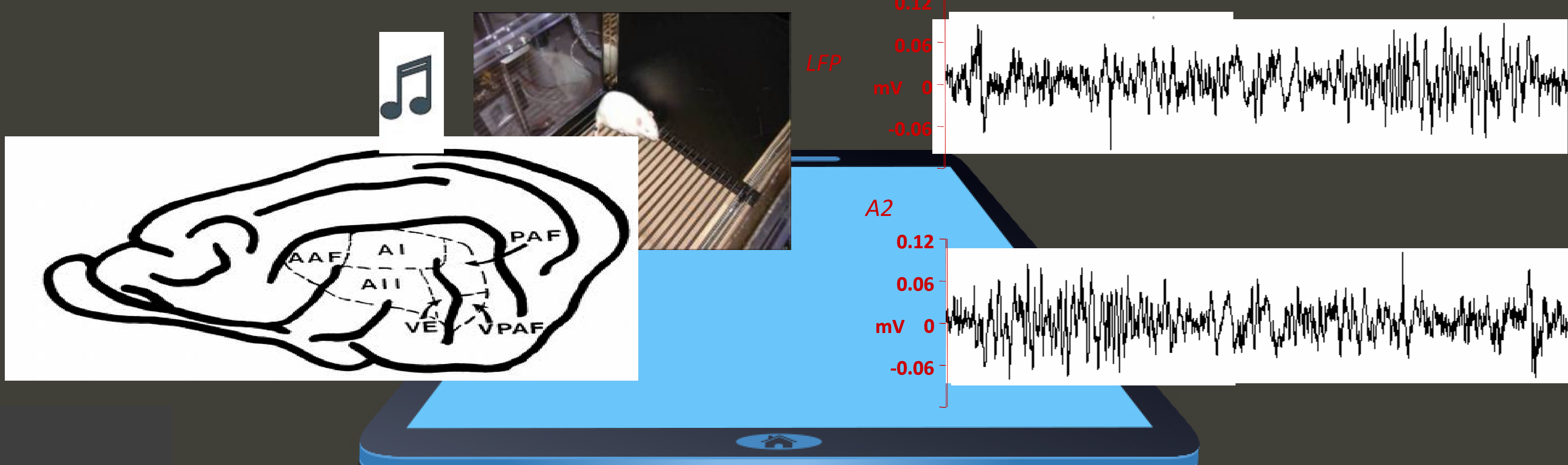
- ✓ use LFP recordings and DCM for SSR to <u>infer</u> synaptic changes

Moran et al., *PLoSONE, 2011*

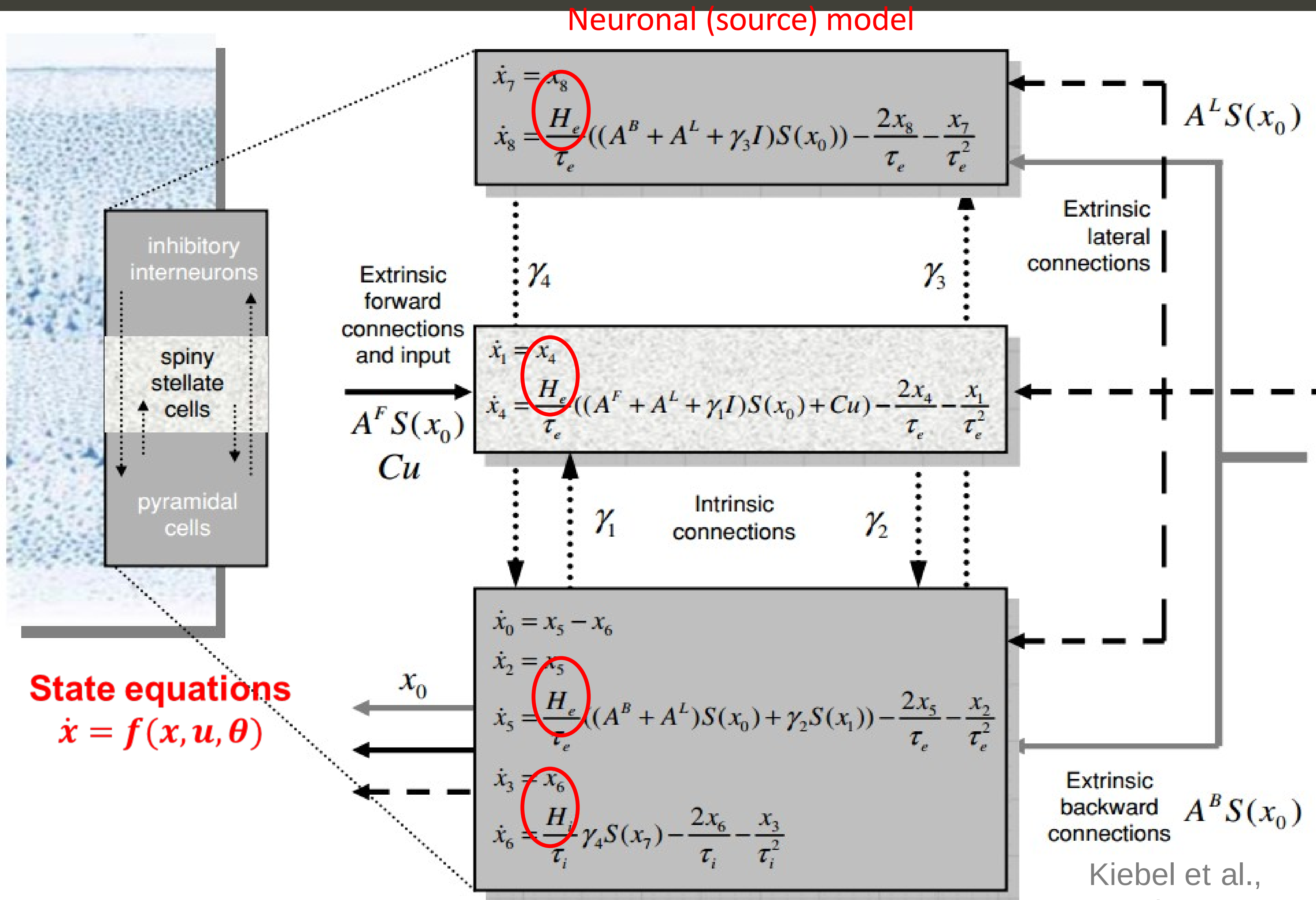
Pharmacological Manipulation of Glutamate and GABA

- ✓ Use animal LFP recordings from primary auditory cortex (A1) & posterior auditory field (PAF)
- ✓ Manipulate neurotransmitter processing via anaesthetic agent Isoflurane
- ✓ 4 levels of anaesthesia: each successively decreasing glutamate and increasing GABA (Larsen *et al* Brain Research 1994; Lingamaneni *et al* Anesthesiology 2001; Caraiscos *et al* J Neurosci 2004 ; de Sousa *et al* Anesthesiology 2000
- ✓ White noise stimulus & Silence

1.4 % Isoflurane	**1.8 % Isoflurane**	**2.4 % Isoflurane**	**2.8 % Isoflurane**



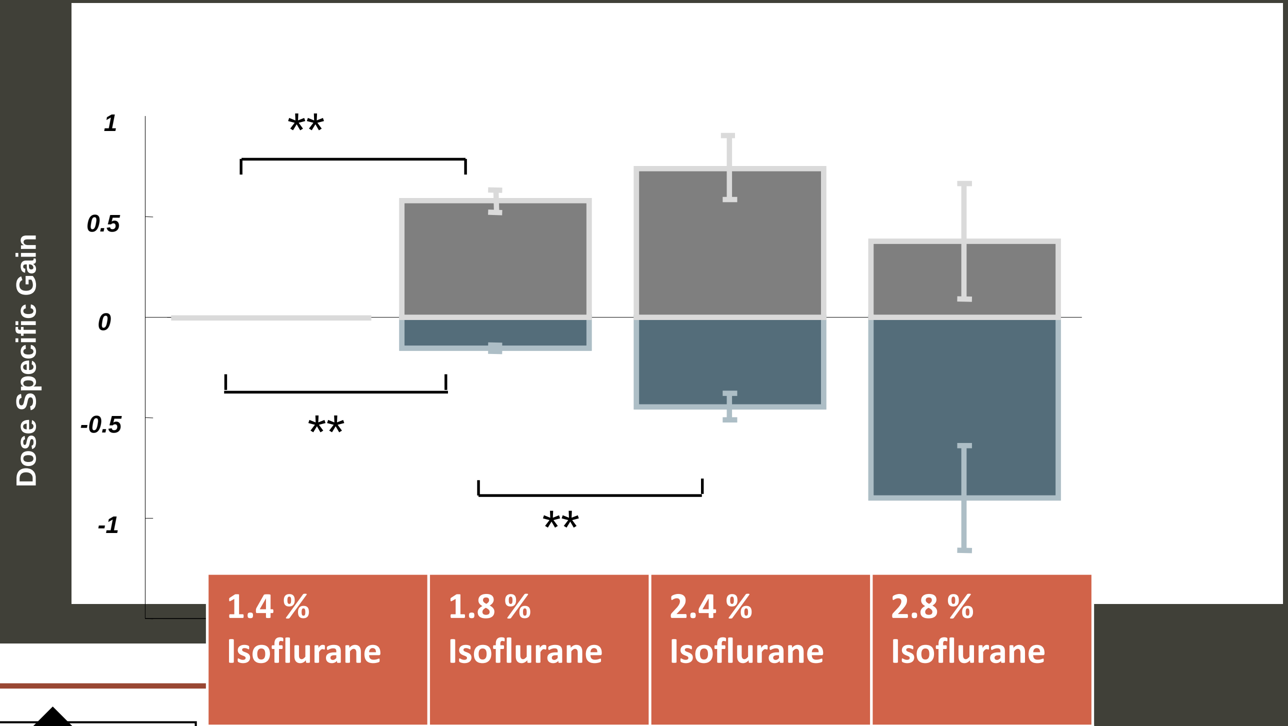
From DCM for ERPs talk in this course

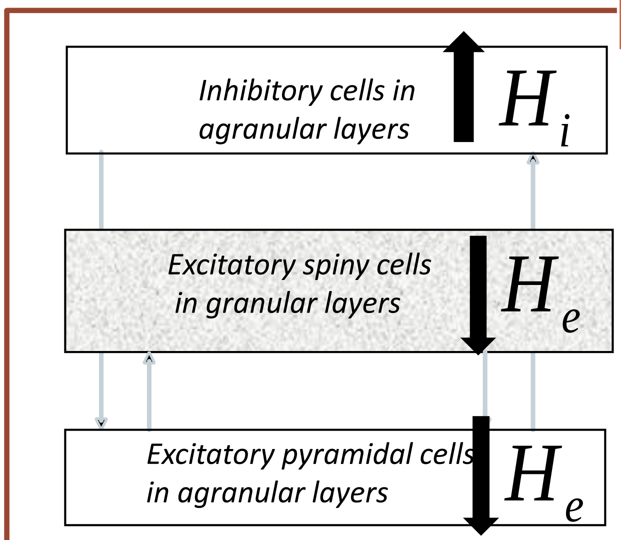


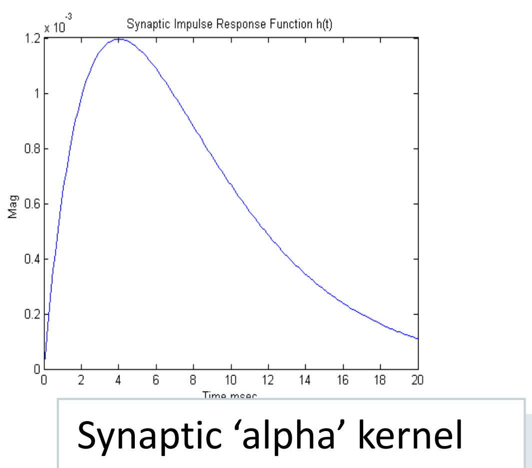
Kiebel et al., Neuroimage, 2008

Pharmacological Manipulation of Glutamate and GABA

Decreased Glutamate Release
Increased gabaergic transmission







Moran et al., *PLoSONE, 2011*

DCM for SSR recovers known drug-induced changes

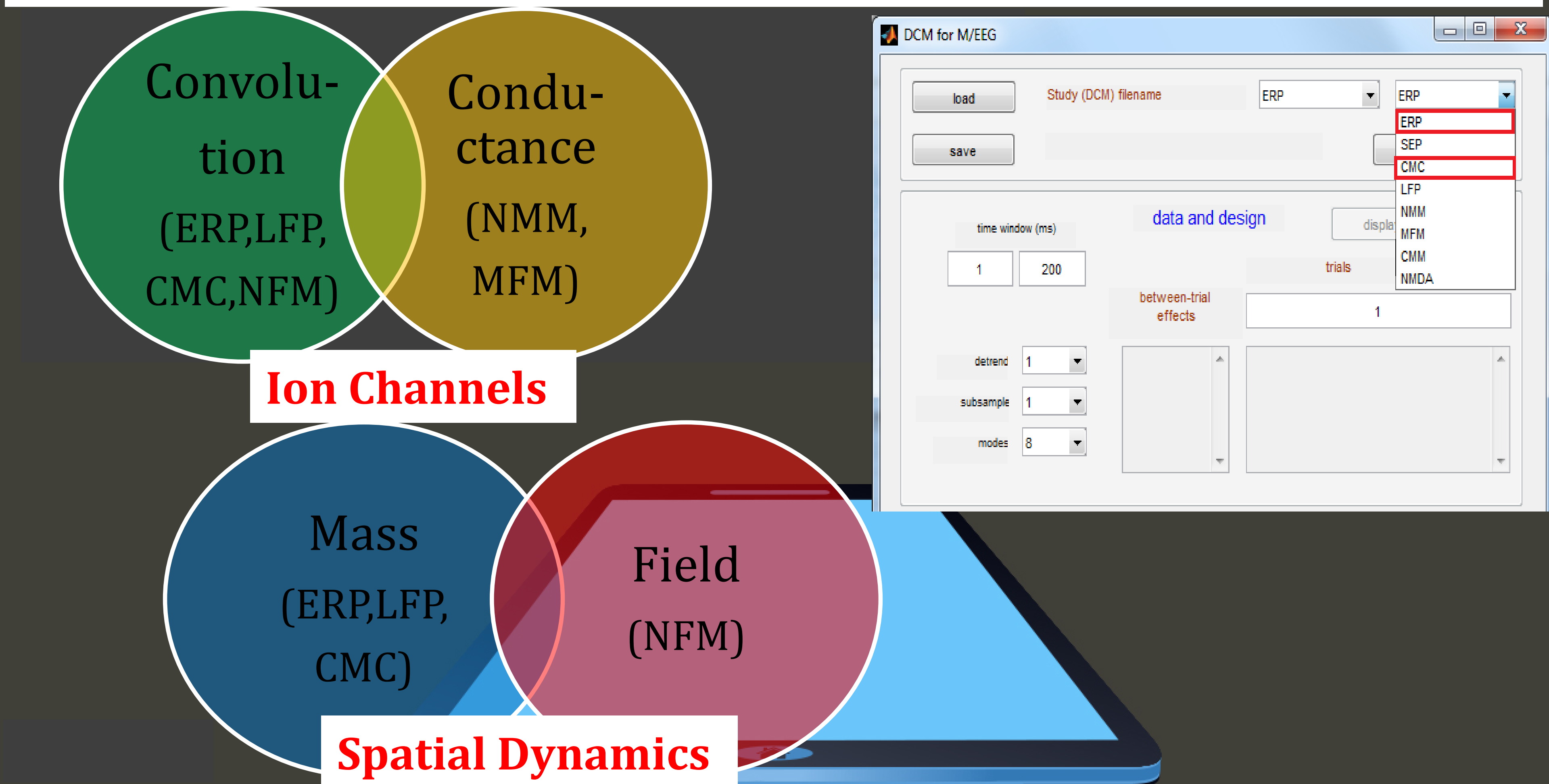
frontiers in
COMPUTATIONAL NEUROSCIENCE

REVIEW ARTICLE
published: 28 May 2013
doi: 10.3389/fncom.2013.00057

Neural masses and fields in dynamic causal modeling

Rosalyn Moran[1,2,3*†], **Dimitris A. Pinotsis**[1†] **and Karl Friston**[1]

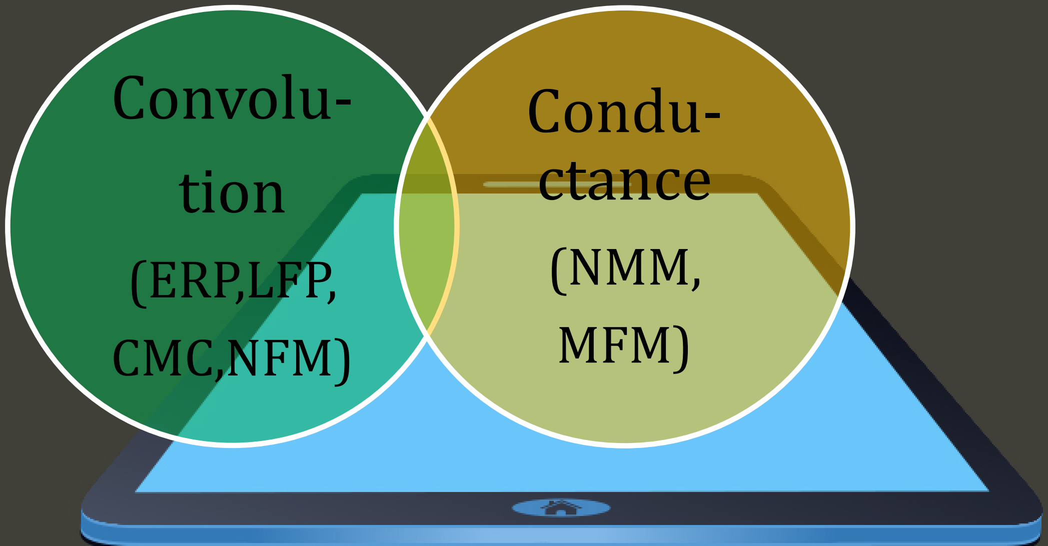
[1] Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, London, UK
[2] Virginia Tech Carilion Research Institute, Virginia Tech, Roanoke, VA, USA
[3] Bradley Department of Electrical and Computer Engineering, Virginia Tech, Blacksburg, VA, USA



Taxonomy – I

With or Without Ion Channels ?

- Characterize nonlinear synaptic transmission or linear convolution effects.
- Explain the relation between channel-specific conductances and observed cortical responses.



Conductance-based Mass Model

- ✓ More realistic parameterization of synaptic currents
- ✓ Same architecture
- ✓ A capacitor stores electric charges
- ✓ Neuronal population as a capacitor
- ✓ g=1/R
- ✓ V=IR (Ohms law) or
  V =I/g or
  gV=I

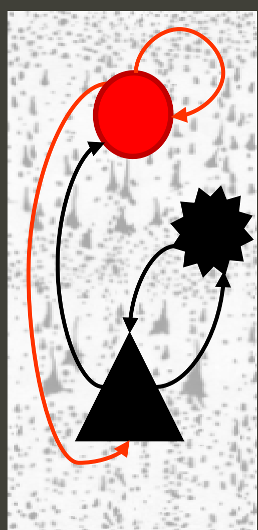
$$q(t) = CV(t)$$

$$I(t) = C\dot{V}(t)$$

Inhibitory interneuron

Spiny stellate cells

Pyramidal cells



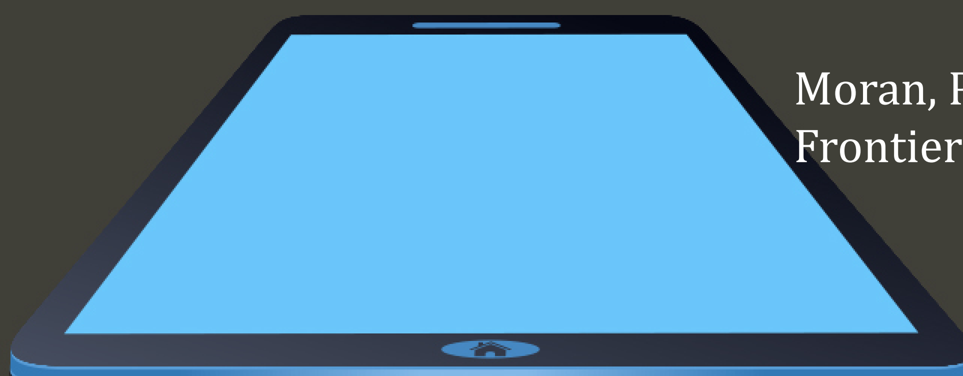
Current

Conductance

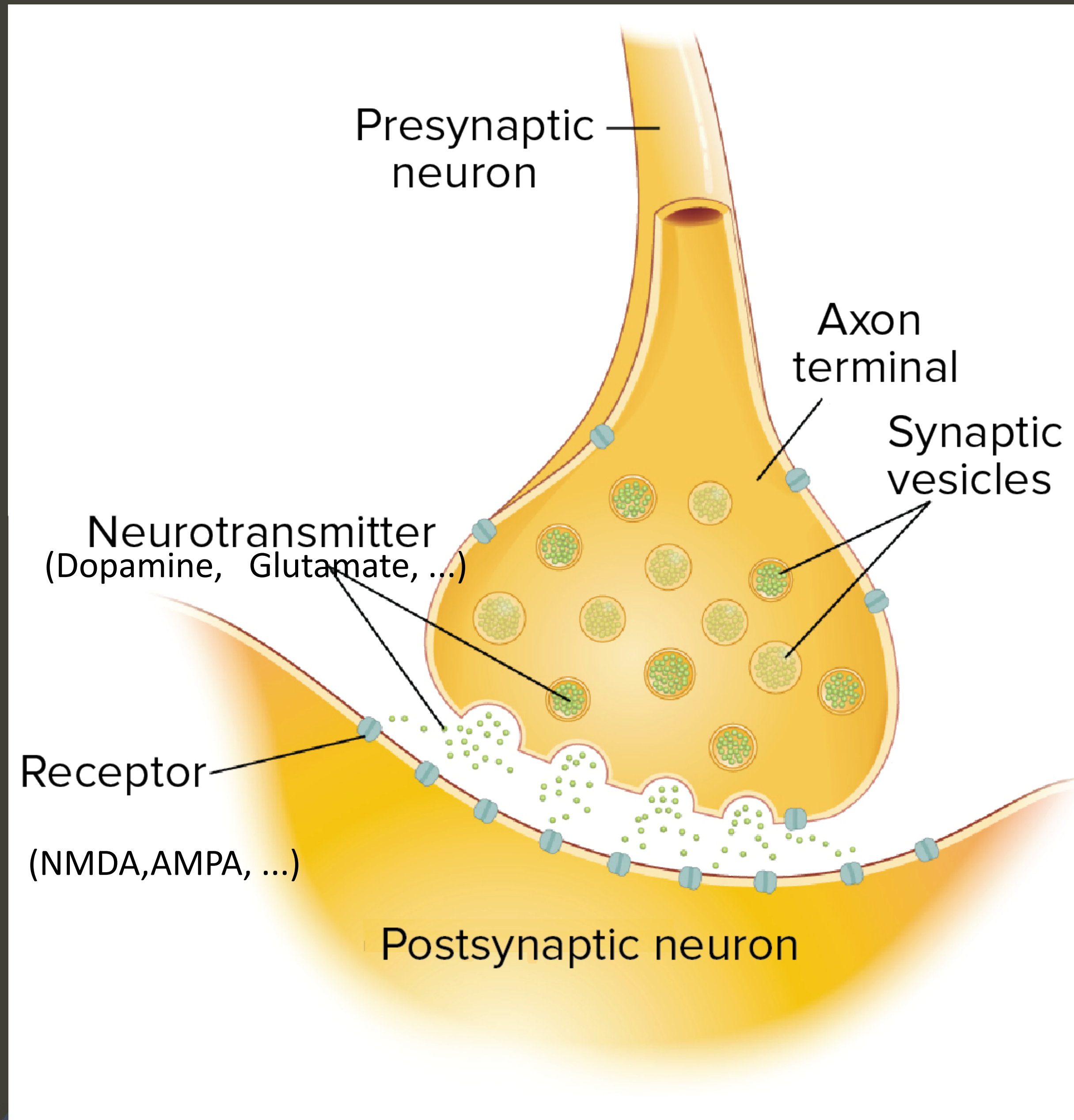
Reversal Pot – Potential Diff

$$C\dot{V} = g(V_{rev} - V) + \Gamma$$

noise



Moran, Pinotsis, Friston, Frontiers Comp Neuro, 2013


Presynaptic
neuron
Axon
terminal
Synaptic
vesicles
Neurotransmitter
(Dopamine, Glutamate, ...)
Receptor
(NMDA,AMPA, ...)
Postsynaptic neuron

Connectivity

$$\dot{g}(t) = \kappa[\gamma\sigma(V(t)) - g(t)]$$

Conductance

Time Constant

Afferent Firing

No. open channels

- ✓ Response of each population is determined by a set of synaptic time constants corresponding to opening and closing of channels and receptors
- ✓ Predicted dynamics are defined over these timescales <u>and</u> non-linear interaction between membrane potential and conductance

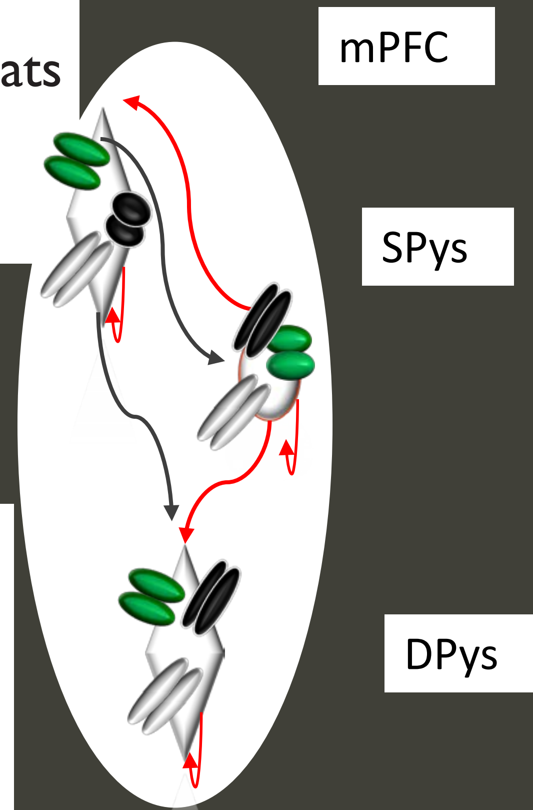
Pinotsis et al., Frontiers Comp Neuro, 2013

Neuropsychopharmacology (2015) 40, 268–277

www.neuropsychopharmacology.org

Losing Control Under Ketamine: Suppressed Cortico-Hippocampal Drive Following Acute Ketamine in Rats

Rosalyn J Moran*[1,2,6], Matthew W Jones[3,6], Anthony J Blockeel[3], Rick A Adams[2], Klaas E Stephan[2,4,5] and Karl J Friston[2]



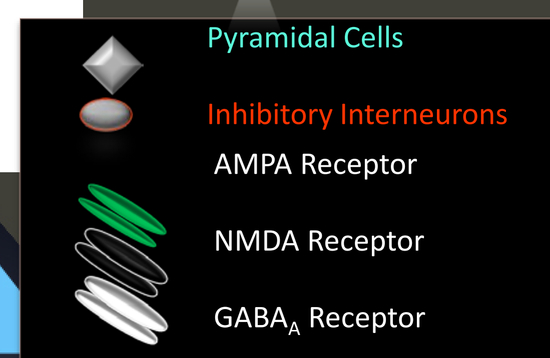
Neural state equations

$$C\dot{V} = g_{Na}(V_{Na} - V) + g_{Ca} f_{MG}(V_{Ca} - V) + g_{Cl}(V_{Cl} - V) + \Gamma$$

$$\dot{g}_{Na} = \kappa_{AMPA}(\gamma_{ec}\sigma - g_{Na})$$ Sodium

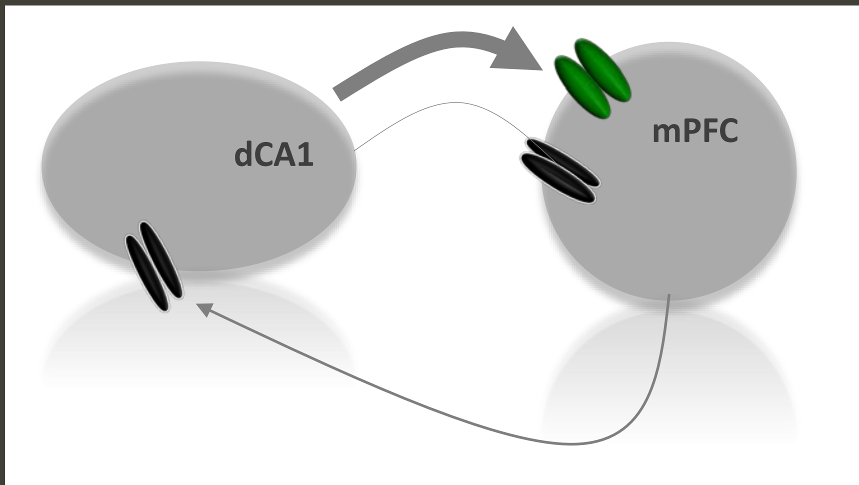
$$\dot{g}_{Cl} = \kappa_{GABA}(\gamma_{ii}\sigma - g_{Cl})$$ Clorine

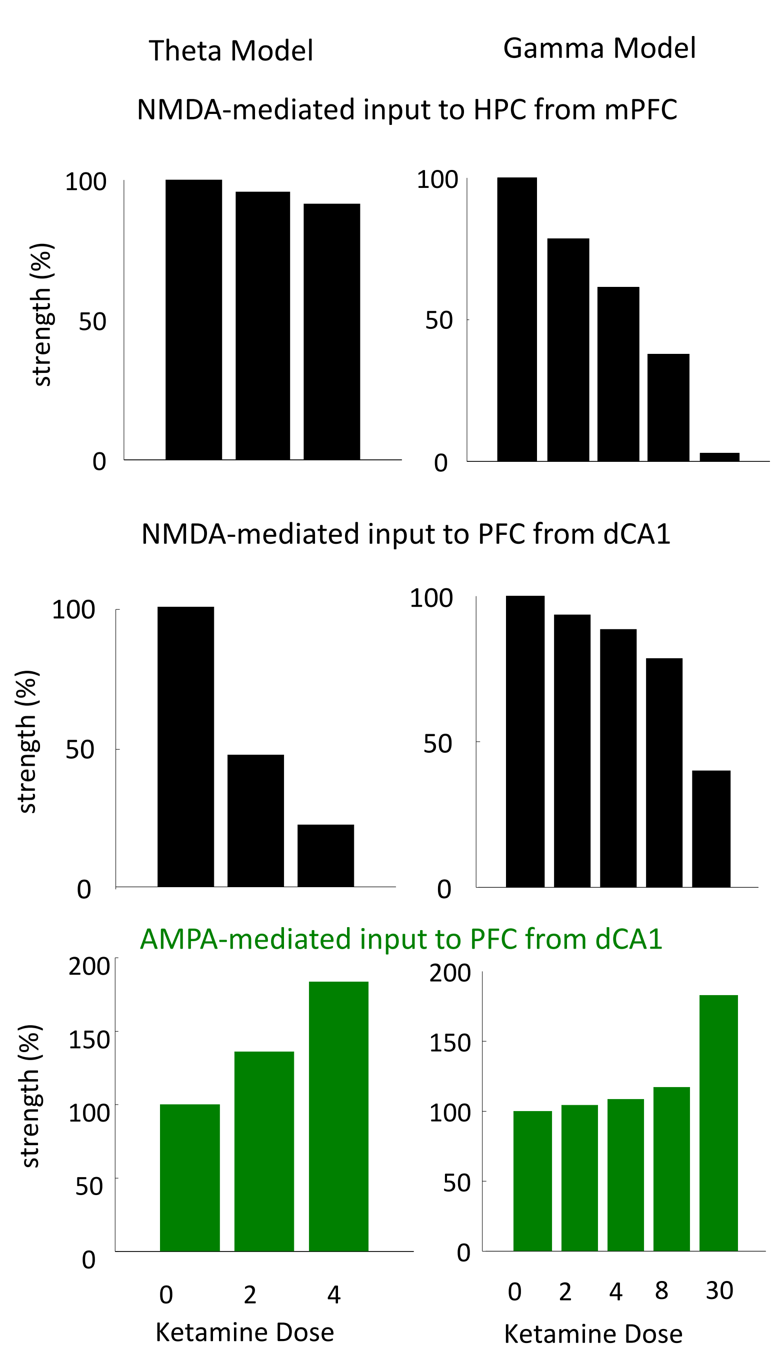
$$\dot{g}_{Ca} = \kappa_{NMDA}(\gamma_{ec}\sigma - g_{Ca})$$ Calcium



Theta reduction in the hippocampus and Gamma enhancement in hippocampus and neocortex.

Connectivity changes under Ketamine





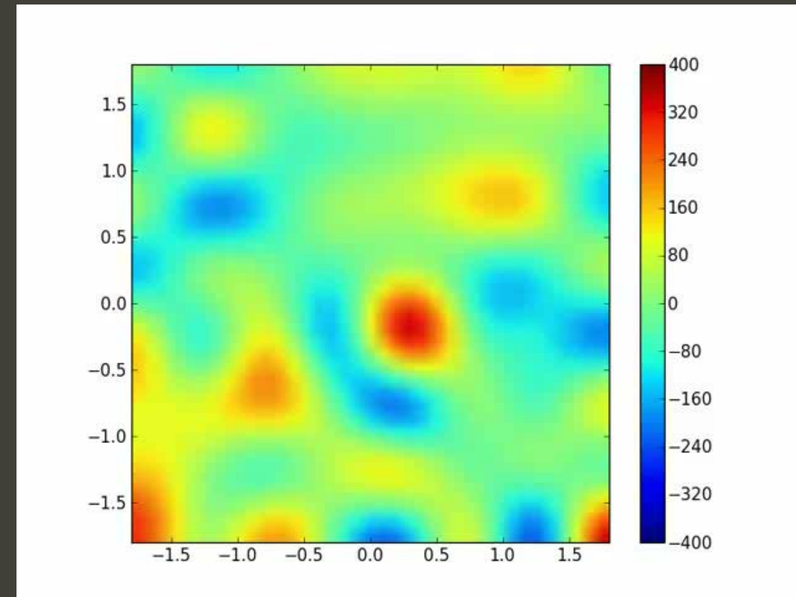
- ✓ Parametric effects of ketamine were consistent across theta and gamma ranges
- ✓ NMDAR-mediated responses decreased parametrically with dose from HPC to mPFC and from mPFC to HPC
- ✓ AMPAR-mediated forward connection from CA1 to mPFC increased with dose

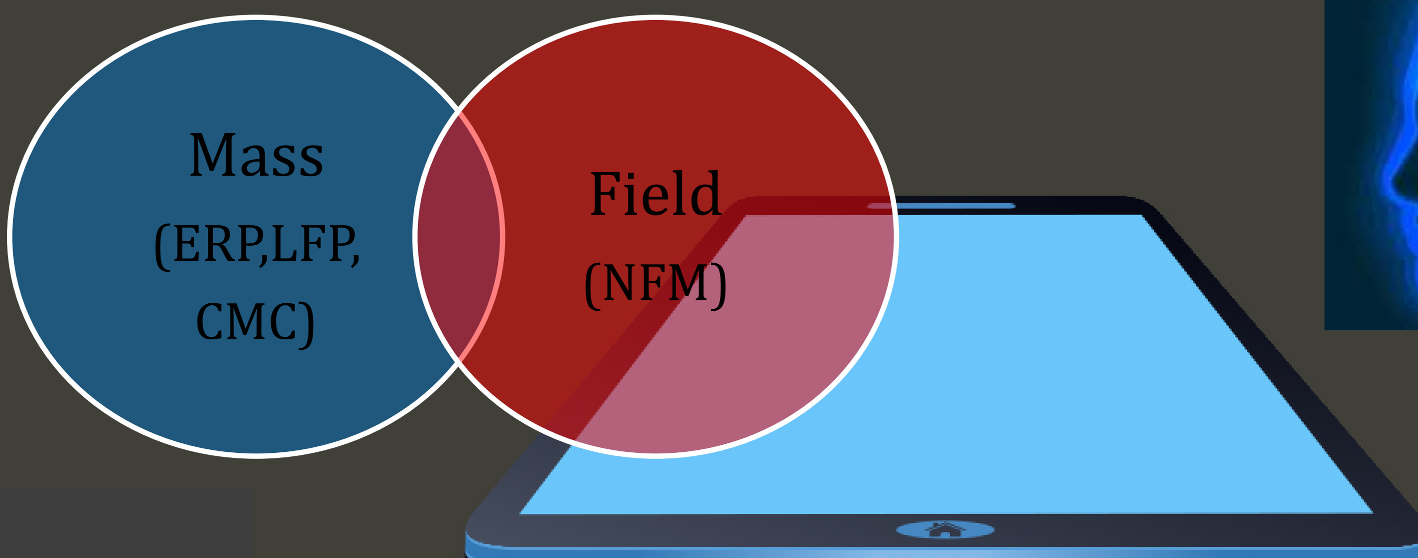
Moran et al., Neuropsychophrmacology, 2015

Taxonomy – II

With or Without Spatial Dynamics ?

- ✓ Characterize point or spatially extended neuronal processes
- ✓ Explain the relation between temporal or spatiotemporal properties of cortical sources and observed brain dynamics





Neural Field Models

Wave equations describing propagation of afferent input between points on the cortex and equations for voltages

LFP signal

Inhibitory cells in supragranular layers

$$\ddot{v}_2 + 2\kappa_i \dot{v}_2 + \kappa_i^2 v_2 = \kappa_i m_i \mu_2$$

$$\ddot{\mu}_2 + 2sc_{23}\dot{\mu}_2 - s^2(\mu_{2xx} - c_{23}^2 \mu_2) = \alpha_{23}(s^2 c_{23}\sigma(v_3) + s\dot{\sigma}(v_3))$$

a_{32}, c_{32}

a_{23}, c_{23}

$U(t)$

Excitatory spiny cells in granular layers

$$\ddot{v}_1 + 2\kappa_e \dot{v}_1 + \kappa_e^2 v_1 = \kappa_e m_e(\mu_1 + U)$$

$$\ddot{\mu}_1 + 2sc_{13}\dot{\mu}_1 - s^2(\mu_{1xx} - c_{13}^2 \mu_1) = \alpha_{13}(s^2 c_{13}\sigma(v_3) + s\dot{\sigma}(v_3))$$

a_{13}, c_{13}

a_{31}, c_{31}

s conduction velocity

Excitatory pyramidal cells in supra- and infragranular layers

$$\ddot{v}_3 + 2\kappa_e \dot{v}_3 + \kappa_e^2 v_3 = \kappa_e m_e \mu_3$$

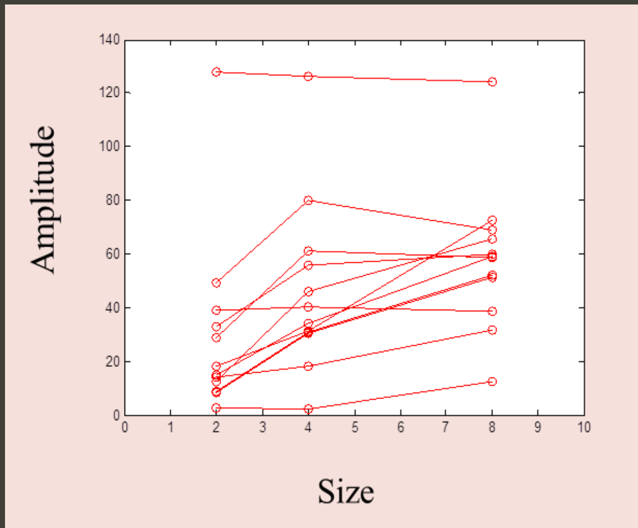
$$\ddot{\mu}_3 + 2sc_{31}\dot{\mu}_3 - s^2(\mu_{3xx} - c_{31}^2 \mu_3) = \alpha_{31}\left(s^2 c_{31}(\sigma(v_1) - \sigma(v_2)) + s\left(\dot{\sigma}(v_1) - \dot{\sigma}(v_2)\right)\right)$$

$$\dot{V} = -BV + D \otimes F \circ V + U$$

Pinotsis et al., Neuroimage, 2012

Example 3 : Hierarchical models and PEB with neural fields, cf. also Peter Zeidman' s talk next

Size induced intersubject variability of amplitude of visually induced gamma oscillations



$$\ln p(g(\omega),\theta^{(1)},\theta^{(2)}) = \sum_i \ln p(g(\omega)_i \mid \theta^{(1)}) + \ln p(\theta^{(1)} \mid \theta^{(2)}) + \ln p(\theta^{(2)})$$

$$p\left(g(\omega)_i \mid \theta^{(1)}\right) = \mathcal{N}(\Gamma_i(\theta^{(1)}),\Sigma_i(\theta^{(1)}))$$

$$p\left(\theta^{(1)} \mid \theta^{(2)}\right) = \mathcal{N}(\Gamma(\theta^{(2)}),\Sigma(\theta^{(2)}))$$

$$p\left(\theta^{(2)}\right) = \mathcal{N}(\eta,\Sigma)$$

$$\theta^{(1)} = (X \otimes I)\theta^{(2)} + \varepsilon^{(2)}$$

$$\theta^{(2)} = \eta + \varepsilon^{(3)}$$

- ✓ Gamma oscillations important for visual perception and affected by stimulus properties
- ✓ Gamma amplitude increases with size, cf. surround suppression , figure background segmentation, contour integration…(Super et al, 2010, Hess…)
- ✓ Either linear increase or saturation with size
- ✓ What determines an individual's spectral response?

$$g_{lm}(\omega) = \hat{g}_{lm}(\omega) + g_n(\omega) + \varepsilon^{(1)}$$

$$\hat{g}_{lm}(\omega) = \sum_k T_l(k,\omega) g_u(k,\omega) T_m(k,\omega)^{\dagger}$$

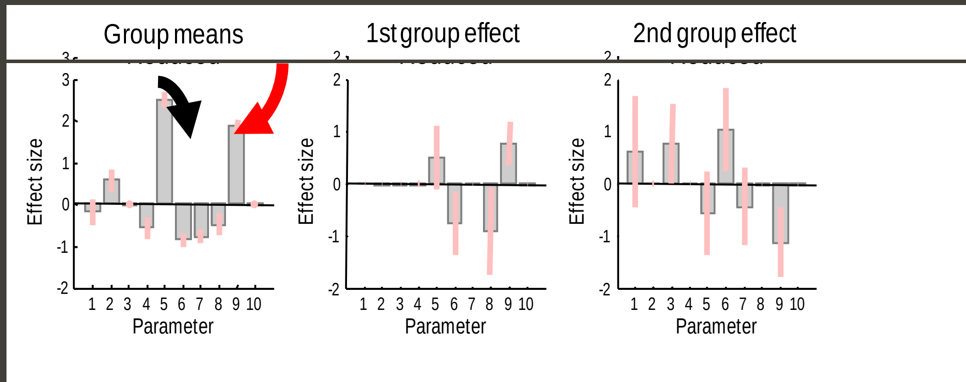
$$T_q(k,\omega) = L_q(k,\varphi) Q \cdot T(k,\omega,\theta^{(1)})$$

$$g_n(\omega) = \alpha_n + \beta_n / \omega$$

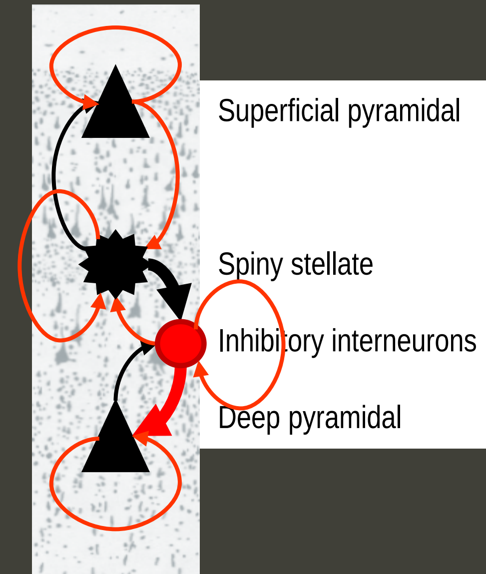
$$g_u(\omega) = \alpha_u + \beta_u / \omega$$

$$\mathrm{Re}(\varepsilon^{(1)}) \sim \mathcal{N}(0,\Sigma(\omega,\lambda)) \quad \mathrm{Im}(\varepsilon^{(1)}) \sim \mathcal{N}(0,\Sigma(\omega,\lambda))$$

Individual differences in oscillatory power reveal commonalities and differences across subjects



Posterior estimates for 2nd level parameters

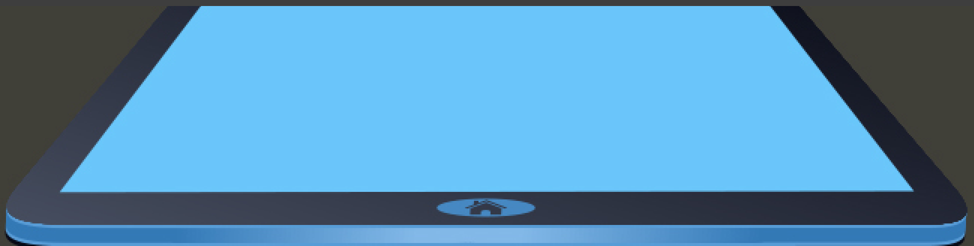


- ✓ Microscopic stimates of cortical function and structure obtained non- invasively
- ✓ Amplitude differences over subject best explained by individual differences in the intrinsic connectivity to and from inhibitory interneurons
- ✓ This reflects differences in the excitation to inhibition balance
- ✓ In accord with PC where size effects are mediated by differences in cortical excitability
- ✓ …and PING networks:
  local inhibition drives gamma oscillations

Pinotsis et al.,
Human Brain Mapping, 2016

Summary

- ✓ DCM is a generic framework for asking mechanistic questions based on neuroimaging data (e.g. drug-induced changes in the balance of synaptic transmission)
- ✓ Neural mass models parameterise intrinsic and extrinsic ensemble connections and synaptic measures (time constants, effective connectivity, neuromodulation…)
- ✓ DCM for SSR provides a compact characterisation of multi- channel LFP or M/EEG data in the frequency domain
- ✓ Bayesian inversion provides parameter estimates and allows model comparison for competing hypothesised architectures
- ✓ DCM for SSR uses power spectra to make inferences about hidden neuronal states and parameter. It has been validated using simulations, pharmacological interventions and developmental manipulations



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