Dynamic Causal Models of Neurophysiology

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Organization for Human Brain Mapping
Educational Course on Computational Neuroscience and Modeling of Neurodynamics
June 14th 2015, Honolulu, Hawaii

Outline

The DCM Approach

Models of Neural Population Activity

Quantifying the Goodness of Models and Model Parameters

How it works in practice

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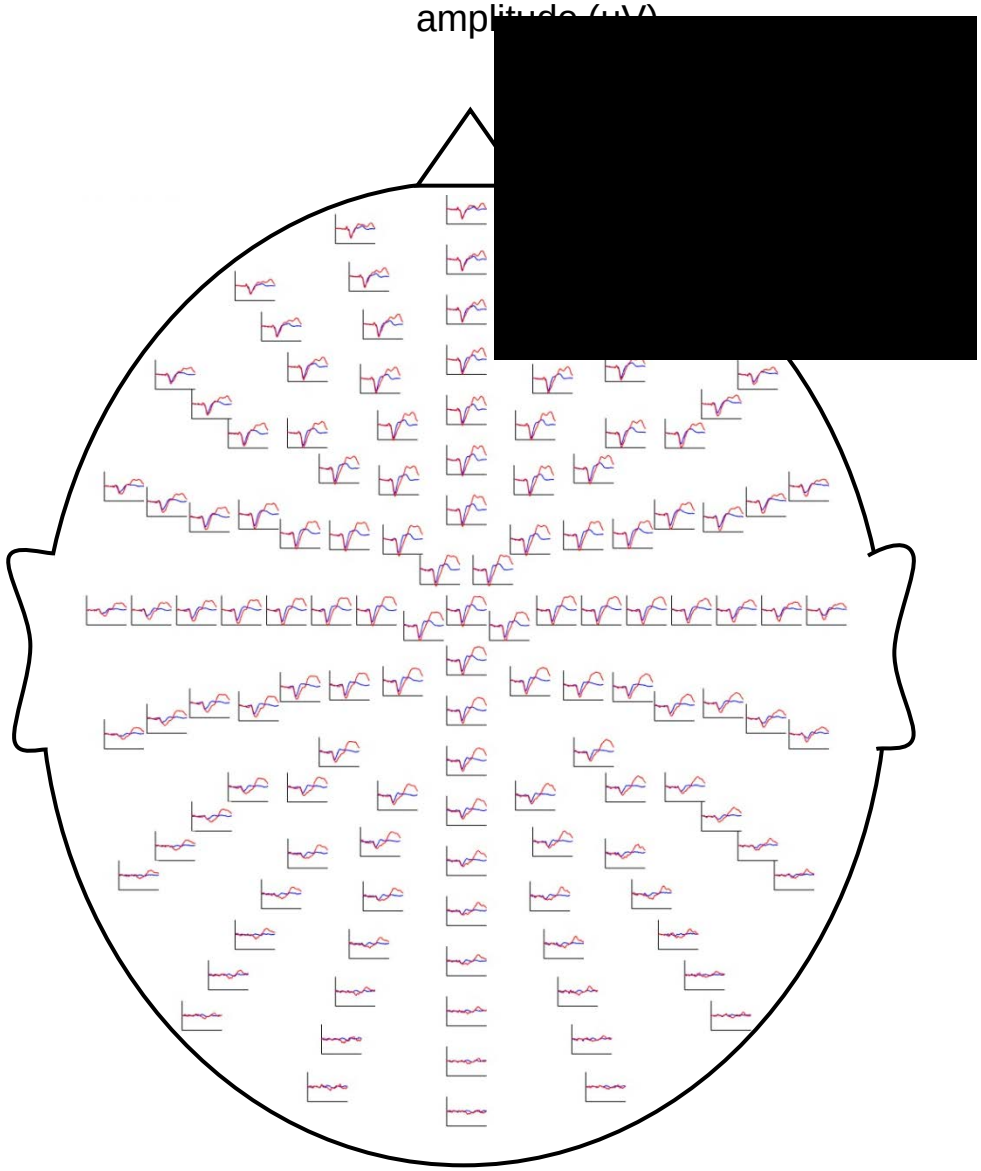
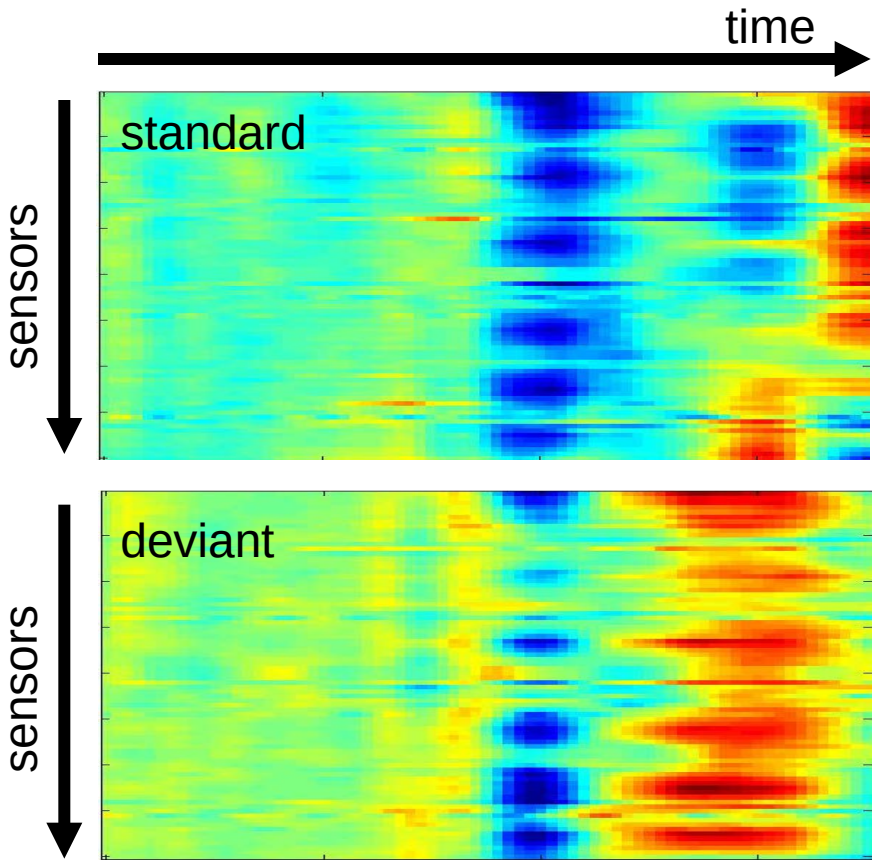
Quantifying the Goodness of Models and Model Parameters

How it works in practice

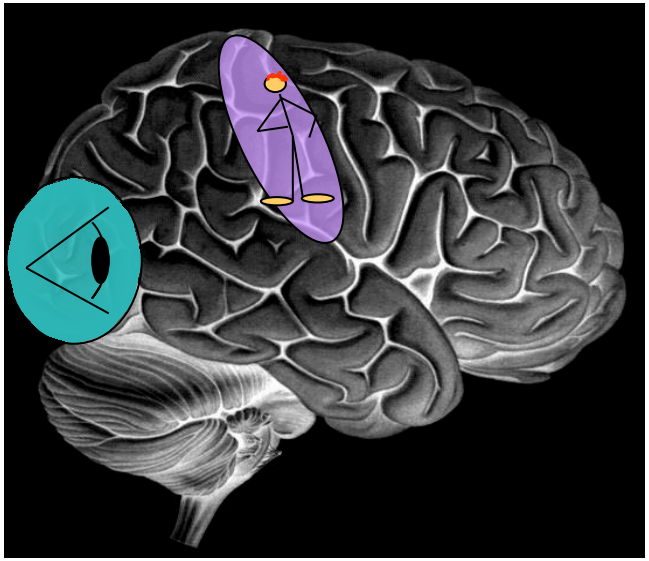
What does a sensor say about a synapse?



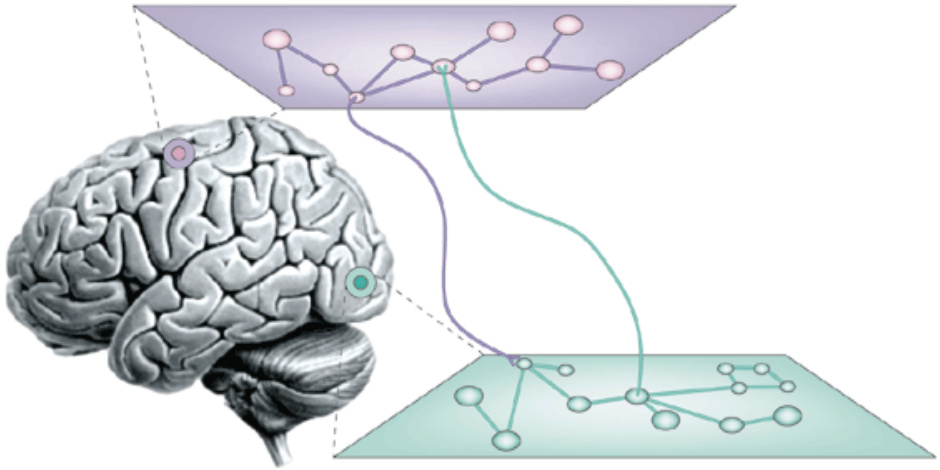


Principles of organisation: some fundamentals

Functional Specialisation

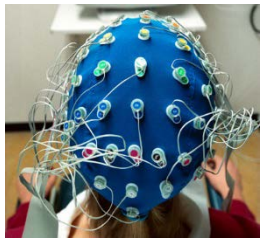


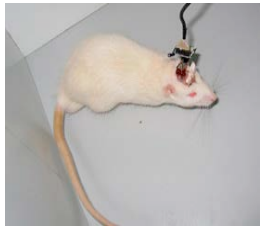
Functional Integration

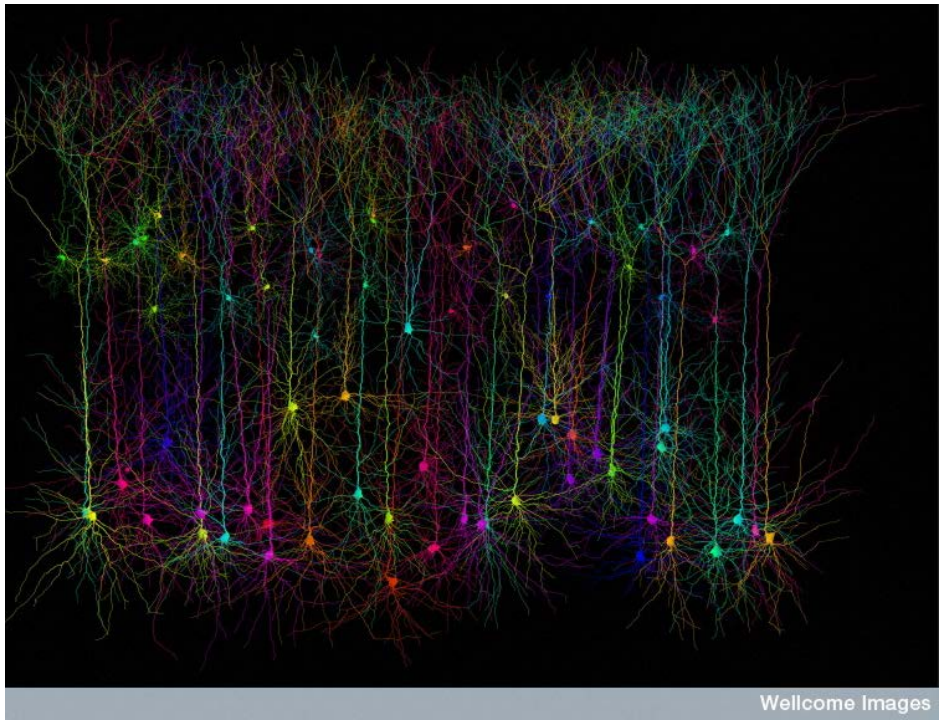


Principles of measurement

Synchronized Activity







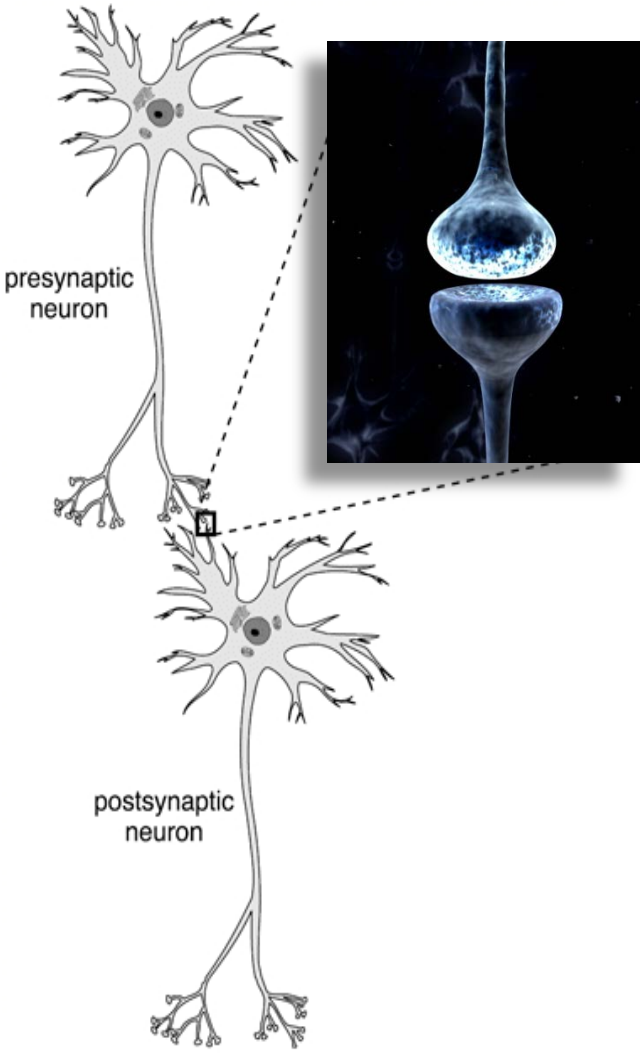
Fluctuating Electrical currents at the synapse (E/IPSPs) and fast fluctuations at cell bodies (APs)

Slower currents at synapses are spatially coherent in pyramidal cell dendrites

About 50000 simultaneous pyramidal cells give rise to measureable M/EEG signal (10nAm)

But cells around the pyramidal neurons contribute to the fluctuations

Origin of Current Source/Sinks

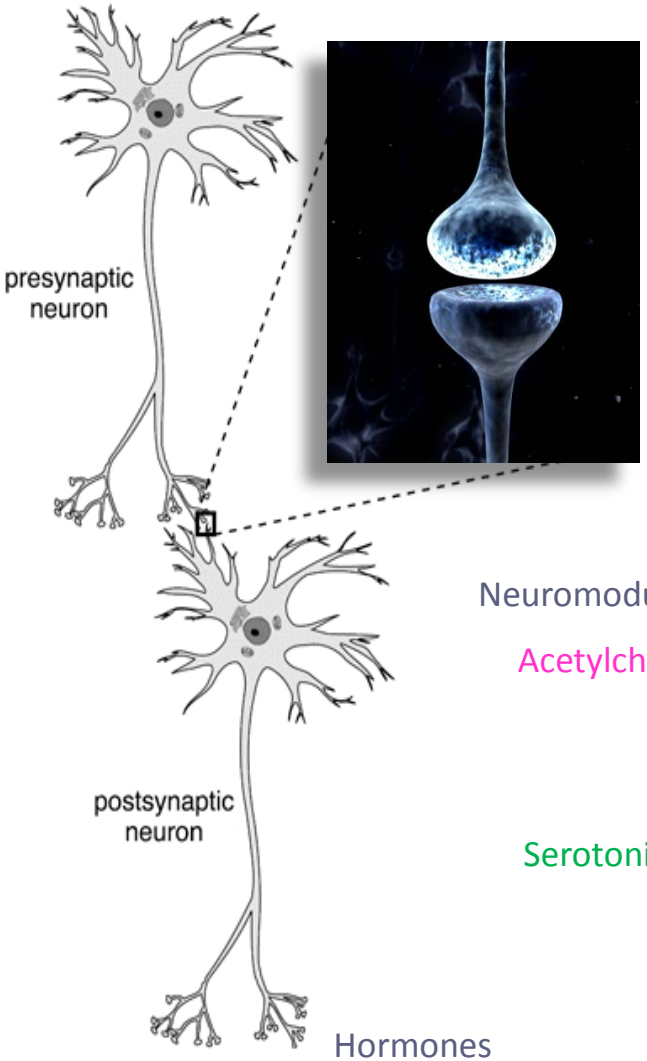


Glutamate
(excitatory) : Na+
Active Synaptic Sink, distributed sources

Neurotransmitters

γ-aminobutryic acid
(inhibitory) : Cl-
Active Synaptic Source, distributed Sinks

Origin of Current Source/Sinks



Glutamate
(excitatory) : Na+
Active Synaptic Sink, distributed sources

Neurotransmitters

γ-aminobutryic acid
(inhibitory) : Cl-
Active Synaptic Source, distributed Sinks

Neuromodulators

Acetylcholine

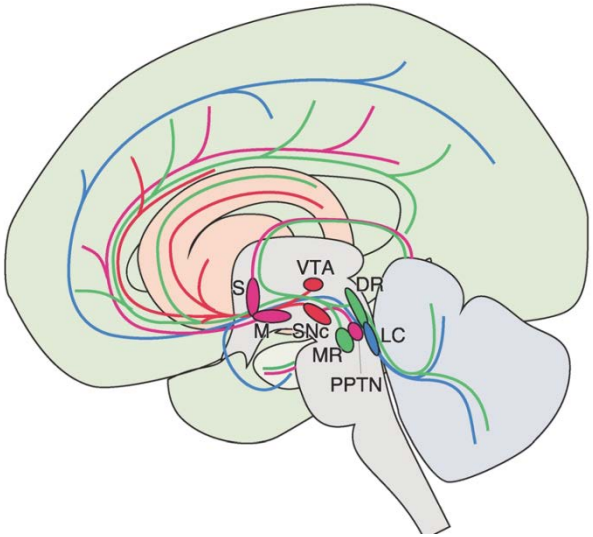
Dopamine

Noradrenaline

Serotonin

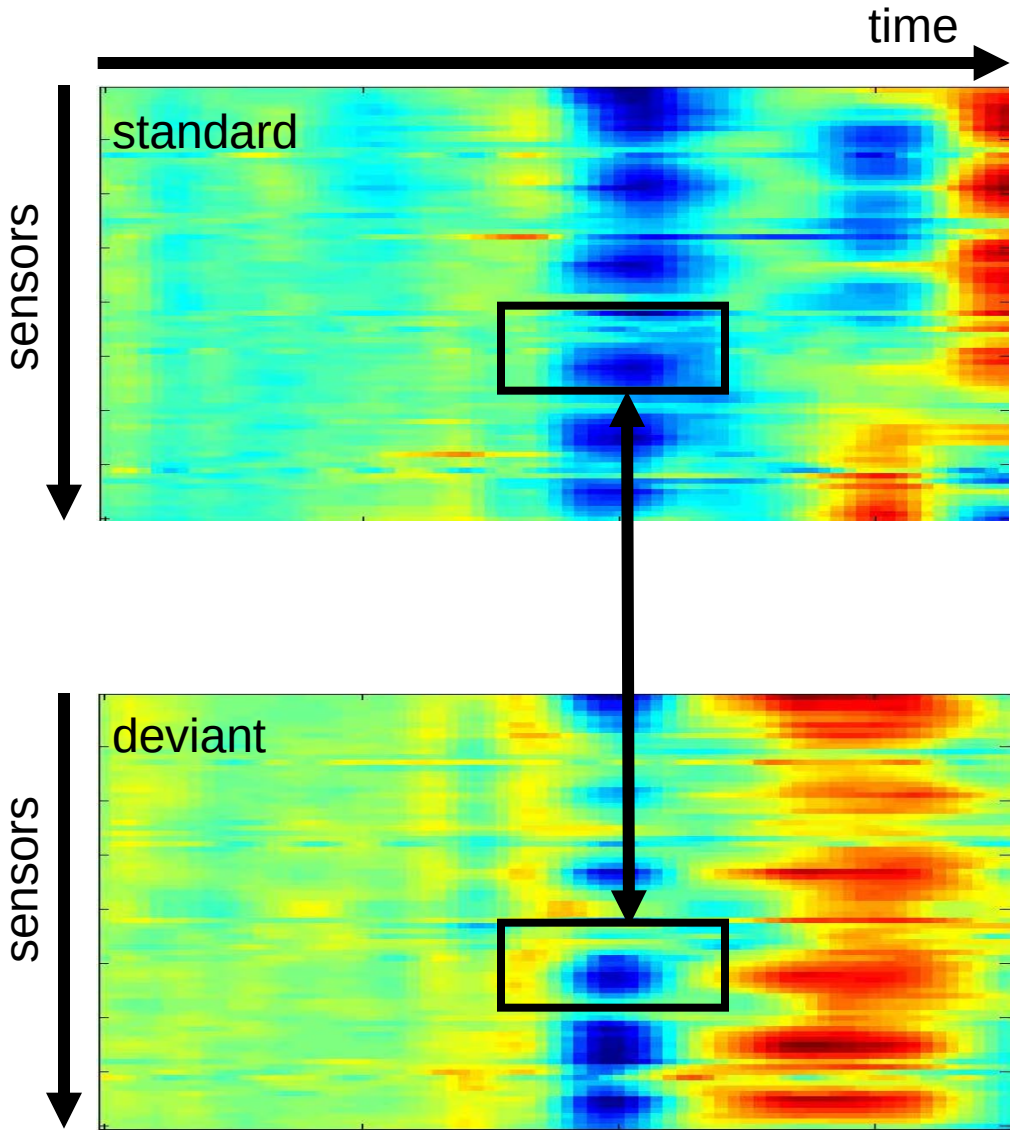
Hormones

Neuropeptides



Doya, 2002

Dynamic Causal Modelling- Motivation



Conventional Approach: Study latencies, peaks, i.e. data features

DCM Approach: How did these features arise from **connected** brain sources?

What connectivity exactly?

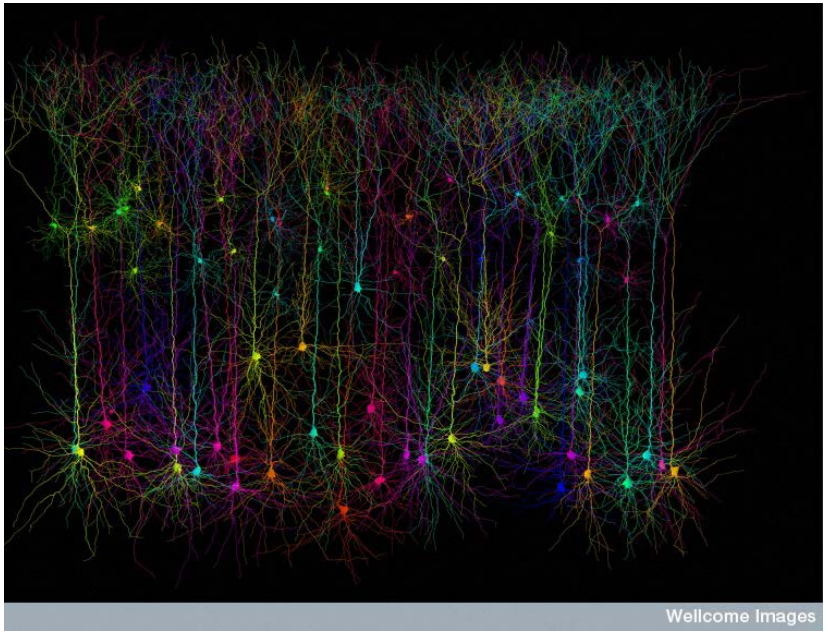
What connectivity exactly?

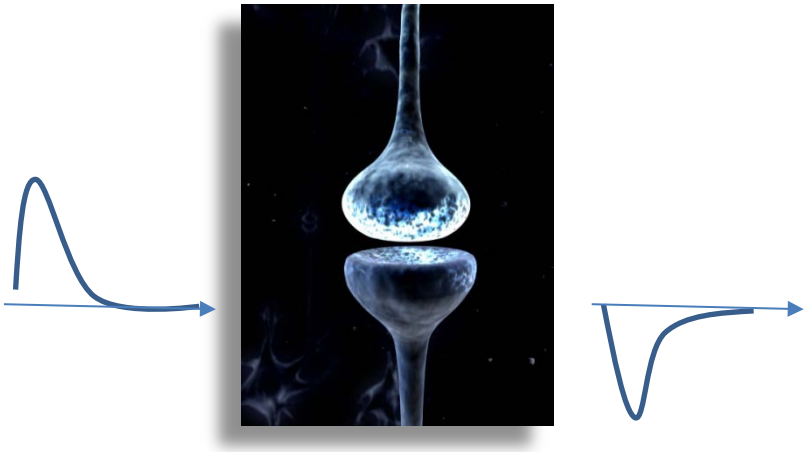
Synchronized Activity

In connected cell assemblies

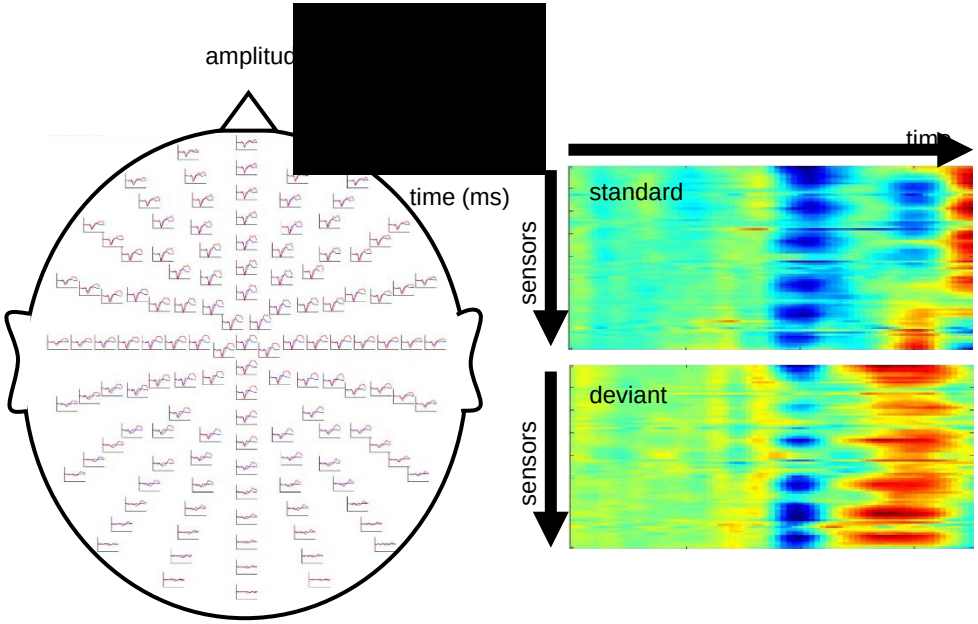
Result in dynamic Sinks and Sources

In the afferent population





What does a sensor say about a synapse?



Model the underlying dynamics:

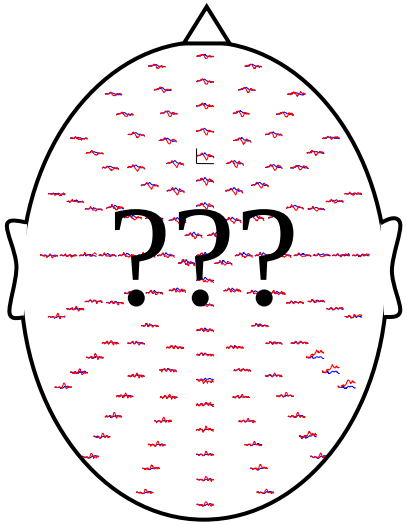
Synchronized Activity

In connected cell assemblies

Result in dynamic Sinks and Sources

In the afferent population

Dynamic Causal Modelling- Overview



Build a generative model for spatiotemporal data and fit to evoked responses.

Principles of functional segregation & functional integration

Dynamics of cell ensembles

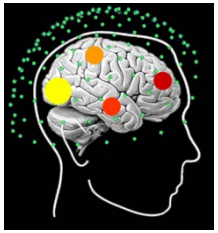
Then invert

Assume that both ERs are generated by temporal dynamics of a network of a few sources

Describe temporal dynamics by differential equations

$$\dot{x} = f(x, u, \theta)$$

Each source projects to the sensors, following physical laws

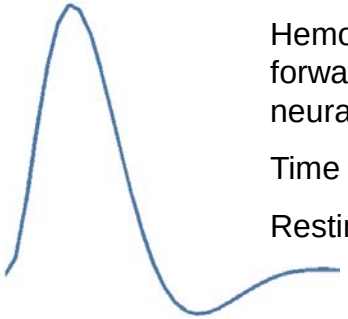


Solve for the model parameters using Bayesian model inversion

$$p(\theta \mid y, m)$$

$$p(y \mid m)$$

Dynamic Causal Modelling: Generic Framework



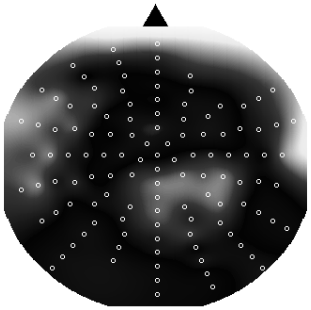
Hemodynamic
forward model:
neural activity BOLD

Time Domain Data

Resting State Data

Electromagnetic
forward model:
neural activity EEG
MEG
LFP

Time Domain ERP Data
Phase Coupling Data
Cross Frequency Coupling



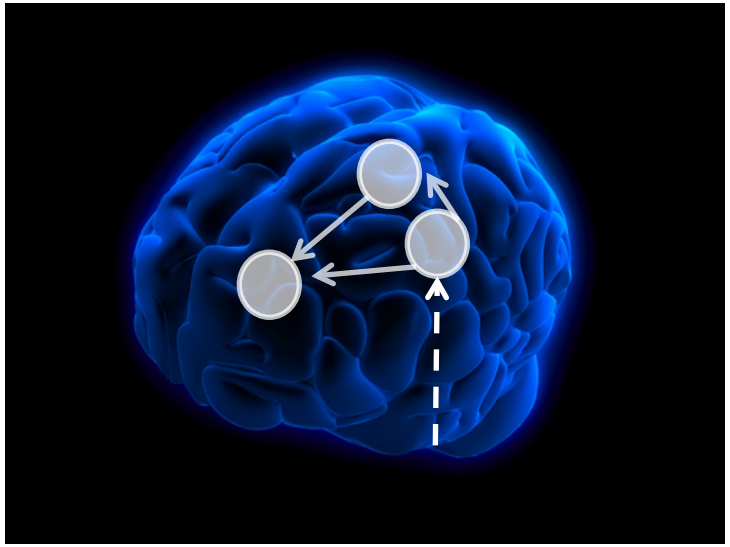
$$\frac{dx}{dt} = F(x,u,\theta)$$

Neural state equation:

fMRI

simple neuronal model

(slow time scale)



EEG/MEG

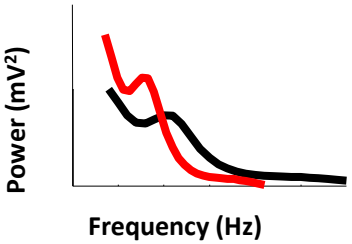
detailed neuronal model

(synaptic time scales)

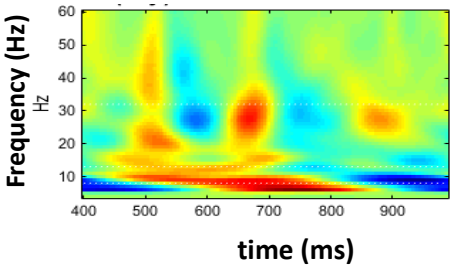
DCM: Neurophysiological Data Features

DCM for Event Related Potentials (ERPs)

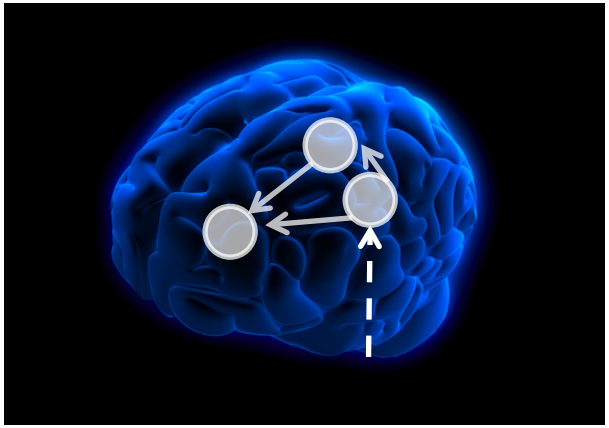
DCM for Cross Spectral Densities (CSDs)



DCM for Time Frequency Modulations (TFMs)



$$\frac{dx}{dt} = F(x, u, \theta)$$



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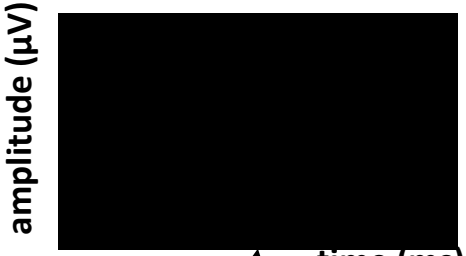
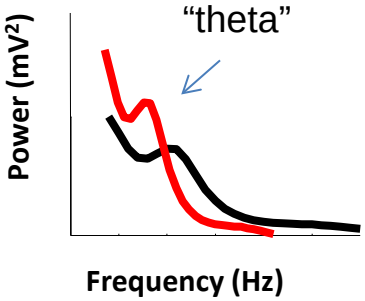
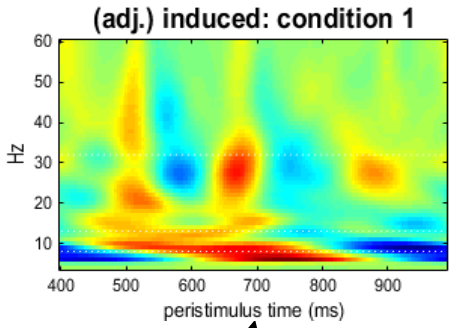
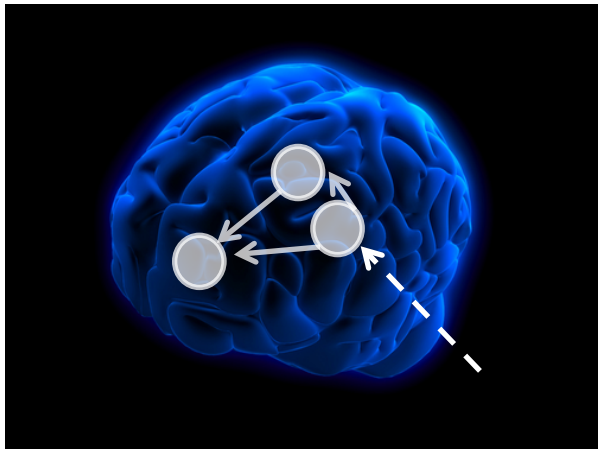






$$\frac{dx}{dt} = F(x, u, \theta)$$

Neural State Equation Can Generate Different Dynamics



Identical Form of Equations *F*:

DCM for ERP: Input *u* is a brief temporal pulse

DCM for CSD: No exogenous input, endogenous noise assumed to drive dynamics

DCM for TFMs: Both plus time modulated parameters: θ(t)

How are neural dynamics modeled in DCM?

frontiers in
COMPUTATIONAL NEUROSCIENCE

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Neural masses and fields in dynamic causal modeling

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[†] *These authors have contributed equally to this work.*

Dynamic causal modeling (DCM) provides a framework for the analysis of effective connectivity among neuronal subpopulations that subtend invasive (electrocorticograms and local field potentials) and non-invasive (electroencephalography and magnetoencephalography) electrophysiological responses. This paper reviews the suite of neuronal population models including neural masses, fields and conductance-based models that are used in DCM. These models are expressed in terms of sets of differential equations that allow one to model the synaptic underpinnings of connectivity. We describe early developments using neural mass models, where convolution-based dynamics are used to generate responses in laminar-specific populations of excitatory and inhibitory cells. We show that these models, though resting on only two simple transforms, can recapitulate the characteristics of both evoked and spectral responses observed empirically. Using an identical neuronal architecture, we show that a set of conductance based models—that consider the dynamics of specific ion-channels—present a richer space of responses; owing to non-linear interactions between conductances and membrane potentials. We propose that conductance-based models may be more appropriate when spectra present with multiple resonances. Finally, we outline a third class of models, where each neuronal subpopulation is treated as a
in other words, as a manifold on the cortical surface. By explicitly accounting for
propagation of cortical activity through partial differential equations (PDEs),
the topology of connectivity—through local lateral interactions among
may be inferred, even in the absence of spatially resolved data. We also
models allow for a detailed analysis of structure–function relationships
ur review highlights the relationship among these models and how the
sked of empirical data suggests an appropriate model class.

ds: dynamic causal modeling, electroencephalography, magnetoencephalography (MEG), local field
ential (LFP), neural mass models

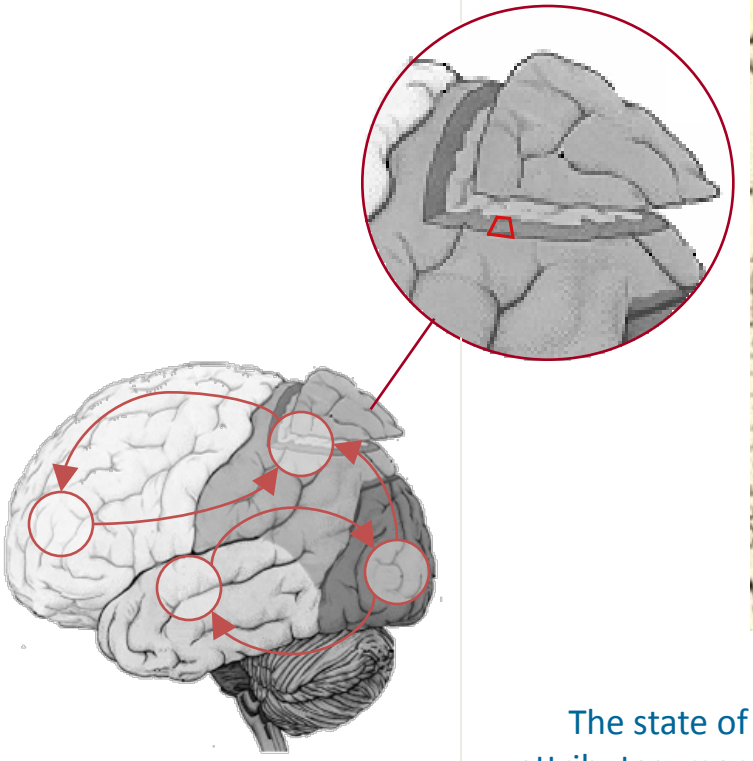
A suite of neuronal population models including neural masses, fields and conductance-based models…expressed in terms of sets of differential equations

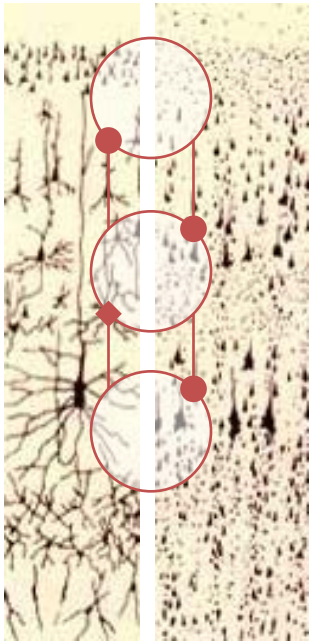
Macro- and meso-scale

macro-scale

meso-scale

micro-scale



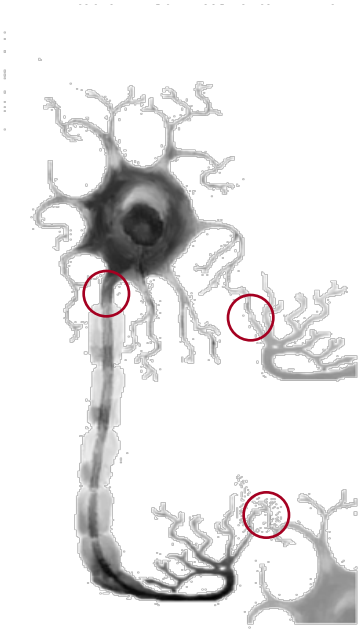


external granular
Layer: *inhibitory interneurons*

external pyramidal
Layer*: pyramidal cells*

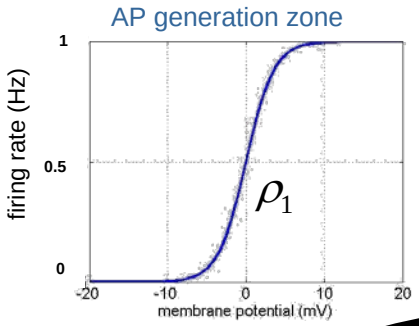
internal granular
layer*: spiny stellate cells*

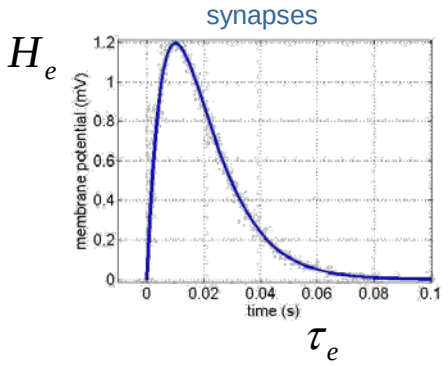
internal pyramidal
layer*: pyramidal cells*



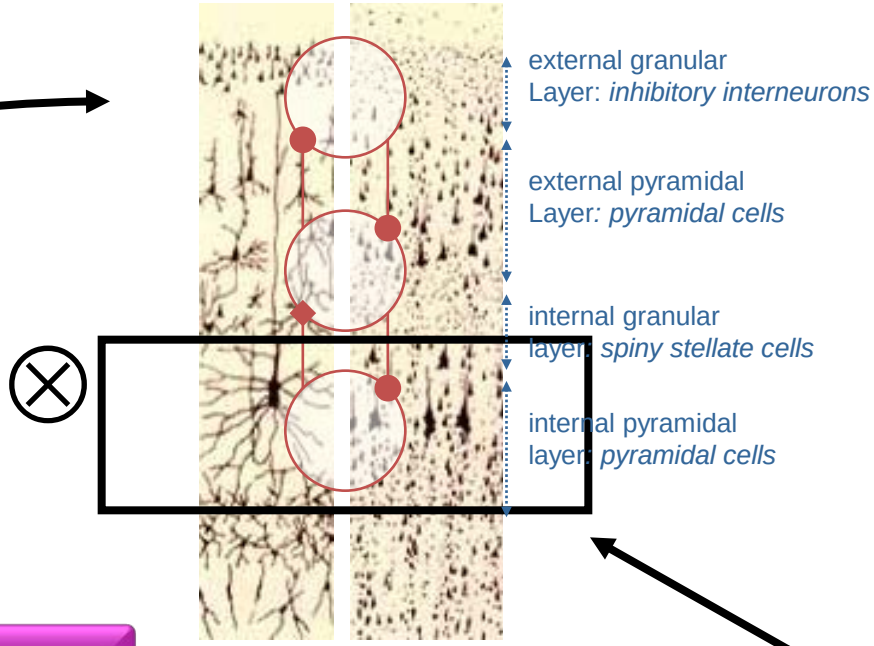
The state of a neuron comprises a number of attributes, membrane potentials, conductances etc. Modelling these states can become intractable. Mean field approximations summarise the states in terms of their ensemble density. **Neural mass models consider only point densities** and describe the interaction of the means in the ensemble

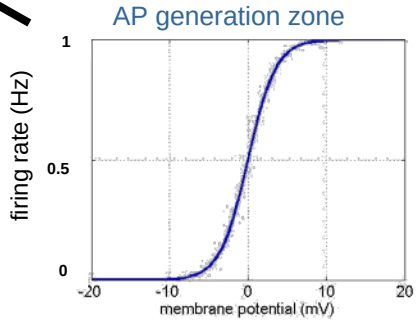
Meso-scale dynamics



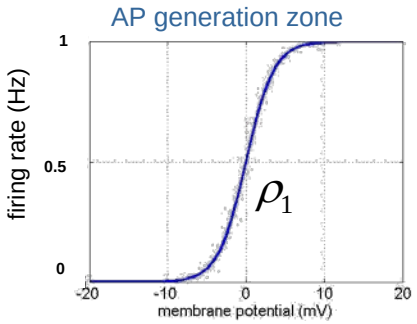


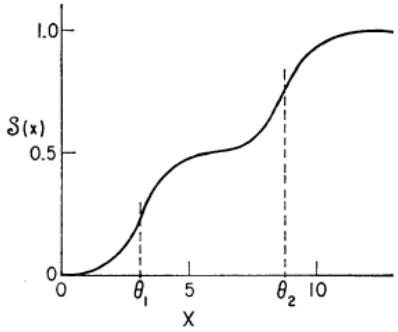
H_e **x Connectivity parameter**



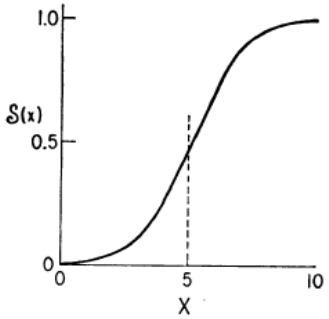


Meso-scale dynamics: the Sigmoid





Bimodal



Unimodal: ρ_1 the precision/gain

Wilson & Cowan, 1972

From first principles, the sigmoidal firing rate curve arrives by assuming an average potential excitation at each cell and a distribution of individual neuronal threshold potentials

Or

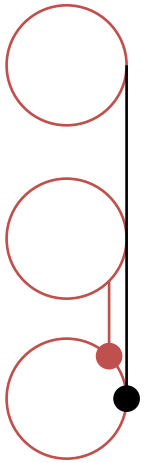
A distribution of number of synapses per cell and the same threshold

then integrate over excitation levels or above-threshold cells for:

Meso-scale dynamics: & connectivity

Post-synaptic effects on pyramidal cells

$$h(t) = \begin{cases} \frac{H_{e/i}}{\tau_{e/i}} t \exp(-t/\tau_{e/i}) & t \geq 0 \\ 0 & t < 0 \end{cases} \otimes S(v, \rho)$$



external granular
Layer: *inhibitory interneurons*

internal granular
layer*: spiny stellate cells*

internal pyramidal
layer*: pyramidal cells*

Meso-scale dynamics: & connectivity

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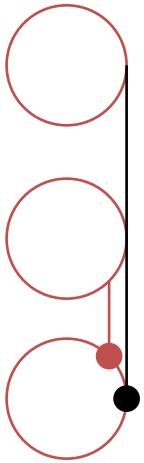

external granular
Layer: *inhibitory interneurons*

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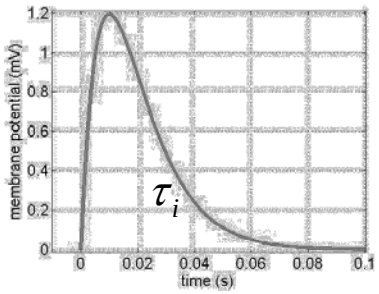
layer*: spiny stellate cells*

internal pyramidal
layer*: pyramidal cells*

γ_1

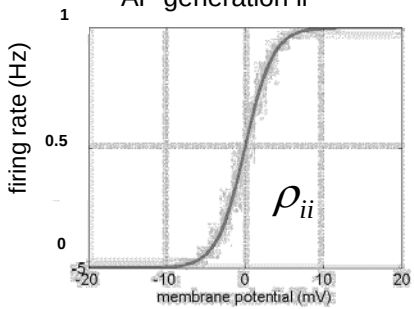
Synapses activated by GABA
from inhibitory interneurons

H_i



$\otimes$

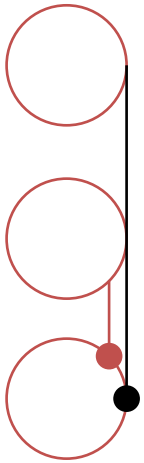
AP generation ii



Meso-scale dynamics: & connectivity

Post-synaptic effects on pyramidal cells

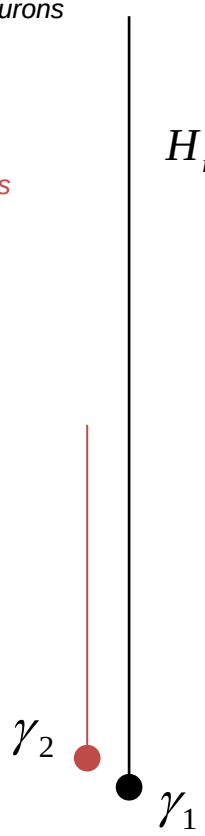
$$v(t) = (h \otimes S)(t) \qquad h(t) = \begin{cases} \dfrac{H_{e/i}}{\tau_{e/i}} t \exp(-t/\tau_{e/i}) & t \geq 0 \\ 0 & t < 0 \end{cases} \otimes S(v, \rho)$$



external granular Layer: *inhibitory interneurons*

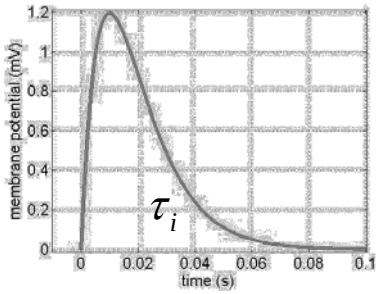
internal granular layer*: spiny stellate cells*

internal pyramidal layer*: pyramidal cells*



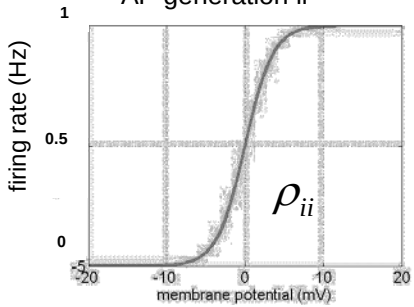
Synapses activated by GABA from inhibitory interneurons

H_i



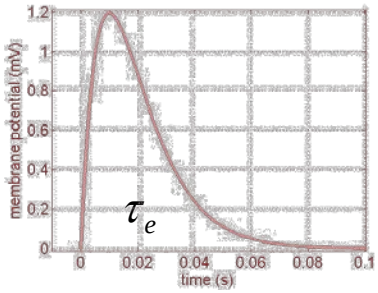
$\otimes$

AP generation ii



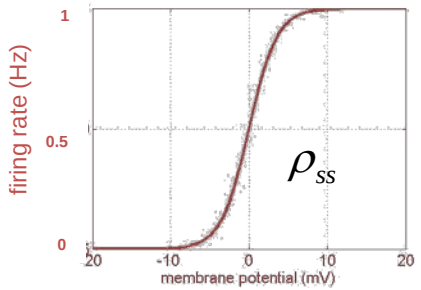
Synapses activated by glutamate from spiny stellate cells

H_e



$\otimes$

AP generation ss



Meso-scale dynamics: & connectivity

Post-synaptic effects on pyramidal cells

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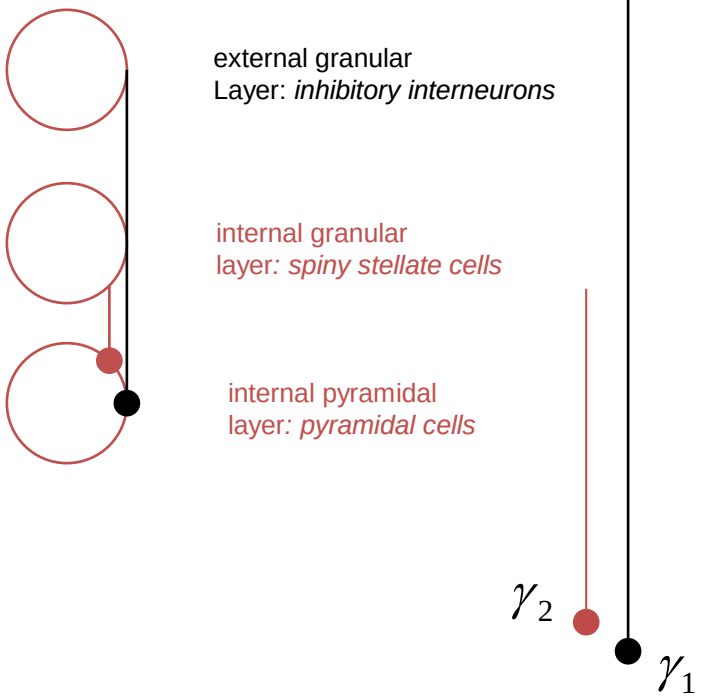
$$\ddot{v}(t) = \frac{H_{e/i}}{\tau_{e/i}} S - \frac{2\dot{v}(t)}{\tau_{e/i}} - \frac{v(t)}{\tau_{e/i}^{2}}$$



$$\dot{v}_{Pi} = i_{Pi}$$
$$\dot{i}_{Pi} = \kappa_i H_i \gamma_1 S(v_{ii}) - 2\kappa_i i_{Pi} - \kappa_i^2 v_{Pi}$$

Changes in PSP : inhibitory

$$\dot{v}_{Pe} = i_{Pe}$$
$$\dot{i}_{Pe} = \kappa_e H_e \gamma_2 S(v_{ss}) - 2\kappa_e i_{Pe} - \kappa_e^2 v_{Pe}$$

Changes in PSP : excitatory

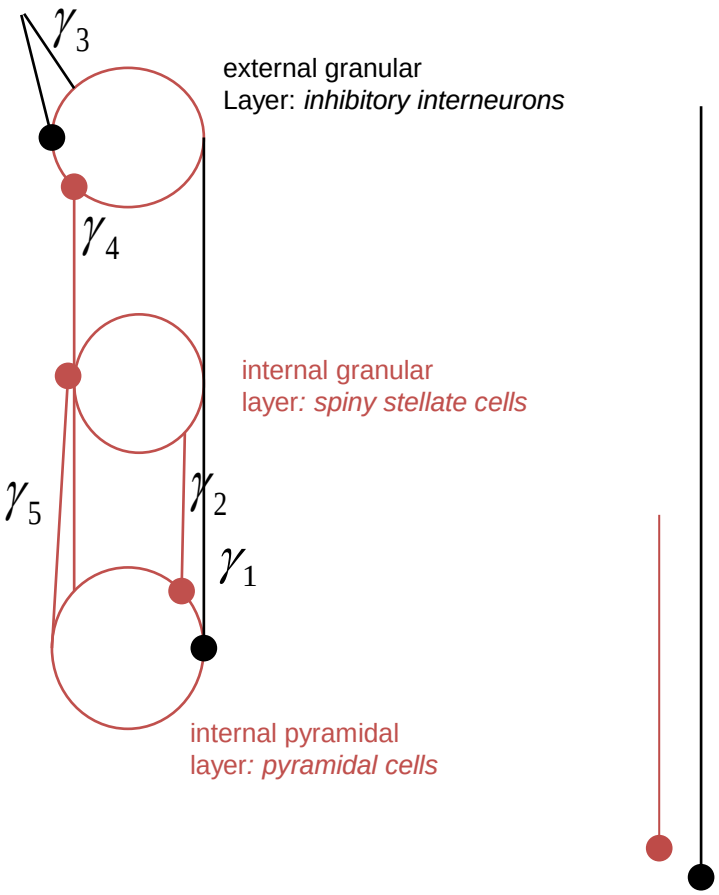
$$\dot{v}_{Pyr} = i_{Pe} - i_{Pi}$$

Net change in PSP

$$\theta \subseteq \rho_{ii}, \rho_{ss}, \tau_e, \tau_i, H_e, H_i, \gamma_1, \gamma_2$$

Model Parameters so far

Meso-scale dynamics: the convolution model



$$\dot{v}_{Ii} = i_{Ii}$$
$$\dot{i}_{Ii} = \kappa_i H_i \gamma_3 S(v_{II}) - 2\kappa_i i_{Ii} - \kappa_i^2 v_{Ii}$$
$$\dot{v}_{Ie} = i_{Ie}$$
$$\dot{i}_{Ie} = \kappa_e H_e \gamma_4 S(v_{Pyr}) - 2\kappa_e i_{Ie} - \kappa_e^2 v_{Ie}$$
$$\dot{v}_{II} = i_{Ie} - i_{Ii}$$

Net change in Interneuronal PSP

Net change in Spiny Stellate PSP

$$\dot{v}_{SS} = i_{SS}$$
$$\dot{i}_{SS} = \kappa_e H_e \gamma_5 (S(v_{Pyr}) + u) - 2\kappa_e i_{SS} - \kappa_e^2 v_{SS}$$

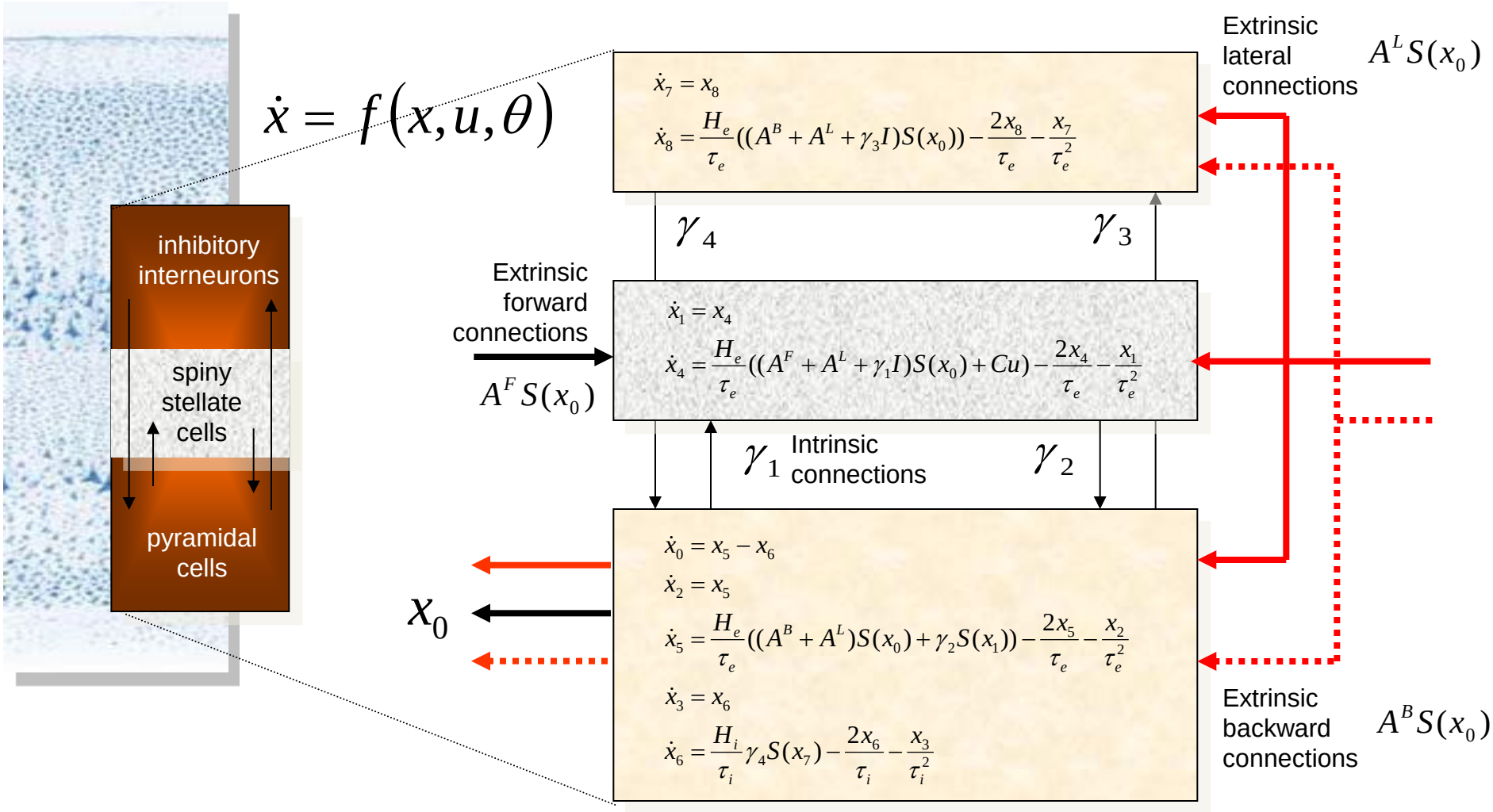
Net change in Pyramidal PSP

$$\dot{v}_{Pi} = i_{Pi}$$
$$\dot{i}_{Pi} = \kappa_i H_i \gamma_1 S(v_{ii}) - 2\kappa_i i_{Pi} - \kappa_i^2 v_{Pi}$$
$$\dot{v}_{Pe} = i_{Pe}$$
$$\dot{i}_{Pe} = \kappa_e H_e \gamma_2 S(v_{ss}) - 2\kappa_e i_{Pe} - \kappa_e^2 v_{Pe}$$
$$\dot{v}_{Pyr} = i_{Pe} - i_{Pi}$$

$$\theta \subseteq \rho, \tau_e, \tau_i, H_e, H_i, \gamma_1, \gamma_2, \gamma_3, \gamma_4, \gamma_5$$

Model Parameters for one source with intrinsic connections

Extrinsic Brain Connectivity



$$\theta \subseteq \rho, \tau_e, \tau_i, H_e, H_i, \gamma_1, \gamma_2, \gamma_3, \gamma_4, \gamma_5, A^F, A^B, A^L$$

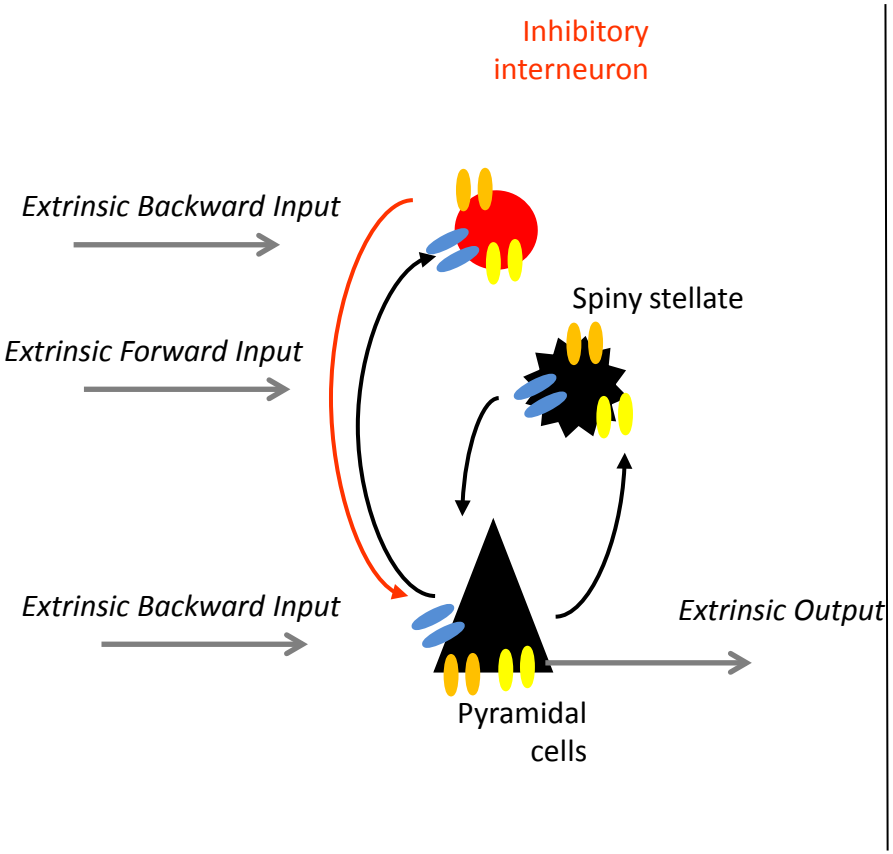
Model Parameters source with intrinsic and extrinsic connections

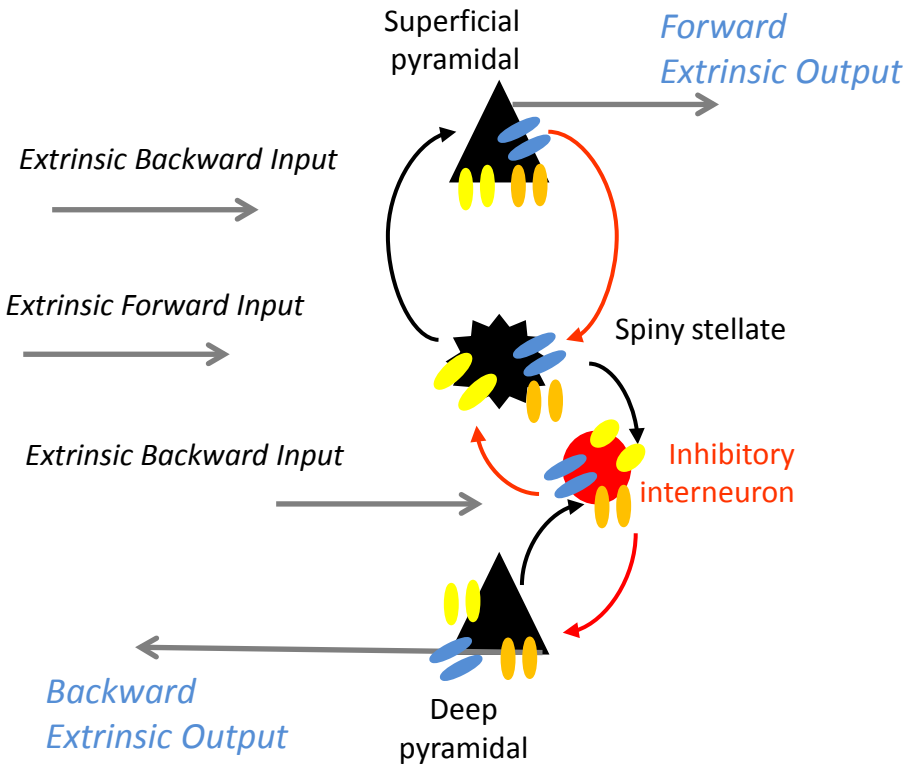
Conductance-Based Neural Mass Models in DCM

Neuron
Perspective

Canonical Microcircuits for Predictive Coding

Andre M. Bastos,[1,2,6] W. Martin Usrey,[1,3,4] Rick A. Adams,[5] George R. Mangun,[2,3,5] Pascal Fries,[6,7] and Karl J. Friston[8,*]





GABA Receptors

AMPA Receptors

NMDA Receptors

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

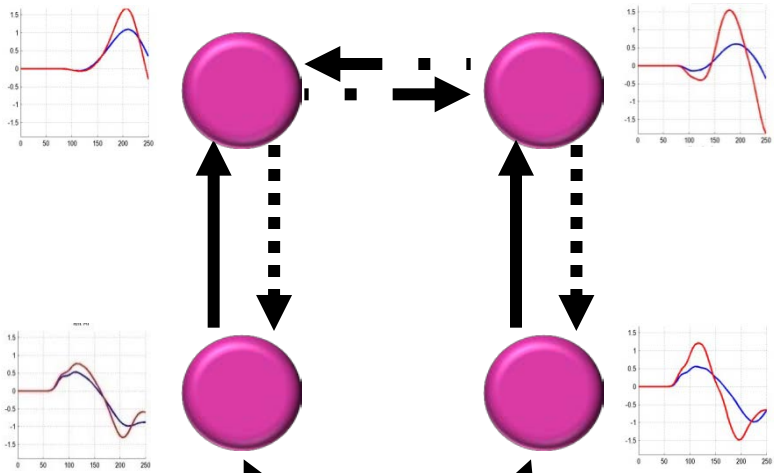
$$\dot{g} = \kappa(\gamma_{aff}\sigma(\mu_{aff} - V_{threshold}, \Sigma_{aff}) - g) + \Gamma$$

Moran et al. 2011, Neuroimage

4-subpopulation Canonical Microcircuit

The Full Generative Model

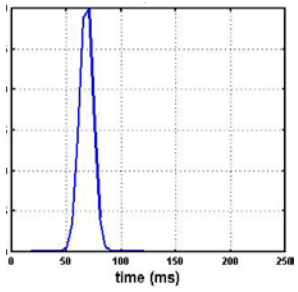
Source dynamics *f*

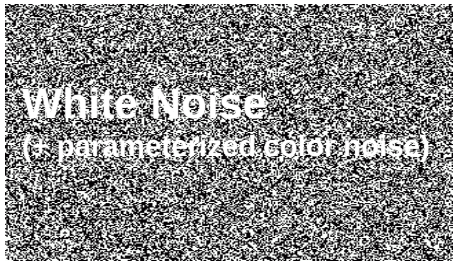


$$\dot{x} = f(x,u,\theta)$$

states *x*

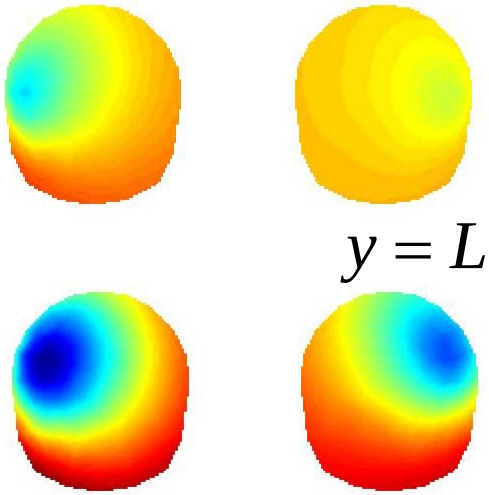
parameters *θ*



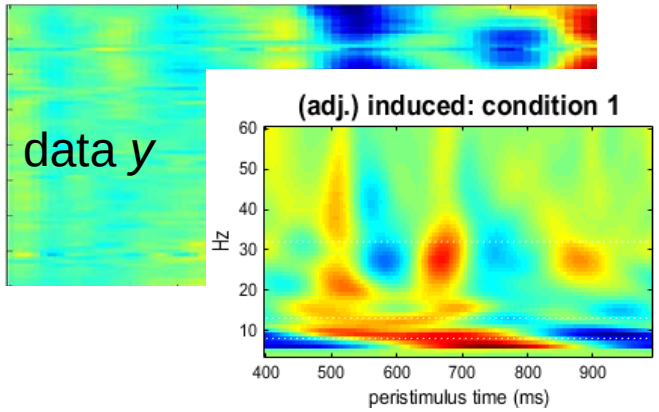


Input *u*

Spatial forward model *g*



$$y = L(x,\theta)$$



Outline

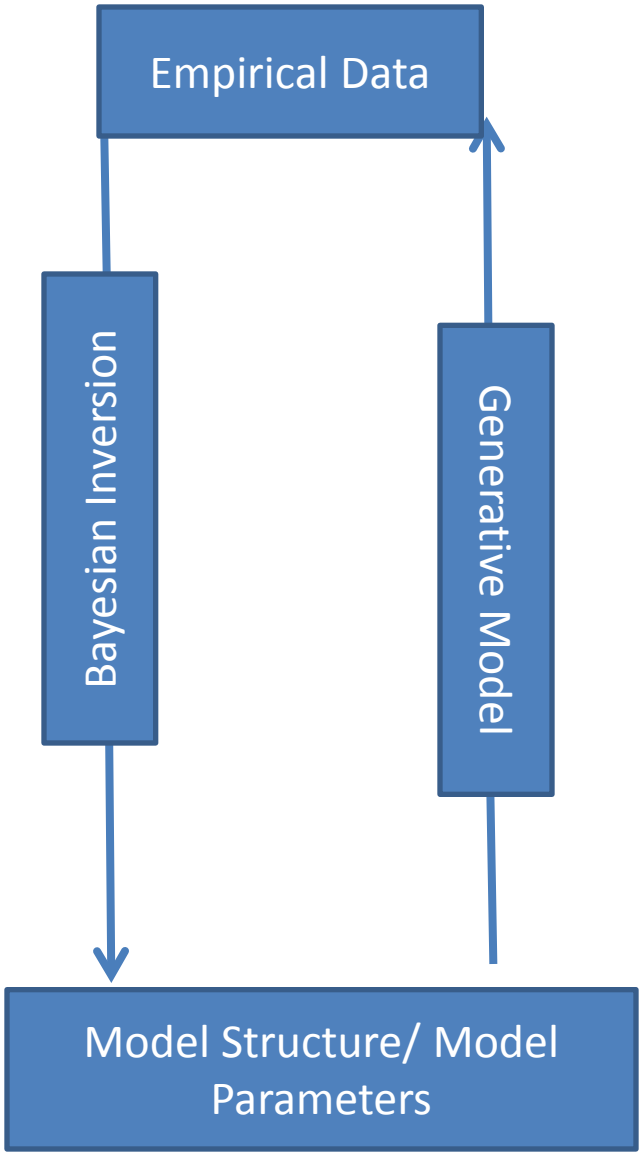
The DCM Approach

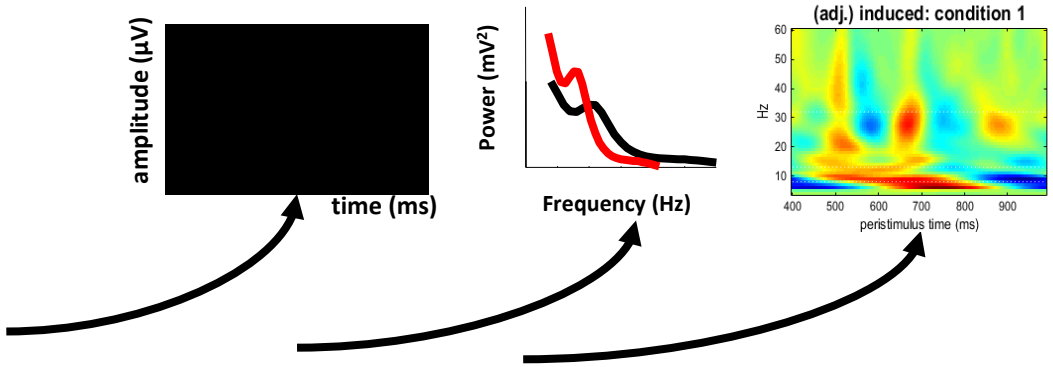
Models of Neural Population Activity

Quantifying the Goodness of Models and Model Parameters

How it works in practice

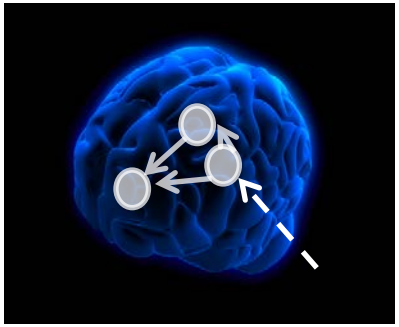
Dynamic Causal Modelling: Inversion Framework



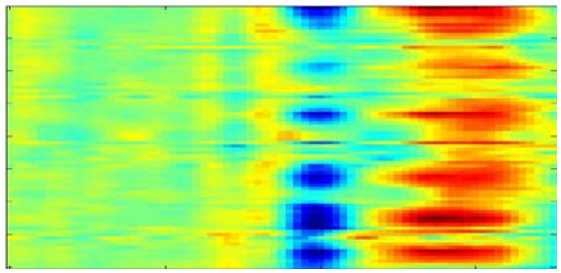


$$\frac{dx}{dt} = F(x,u,\theta)$$

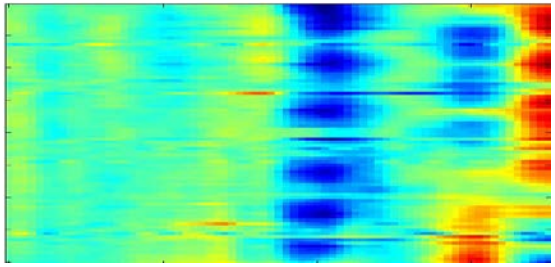
Neural State Equation Can Generate Different Dynamics

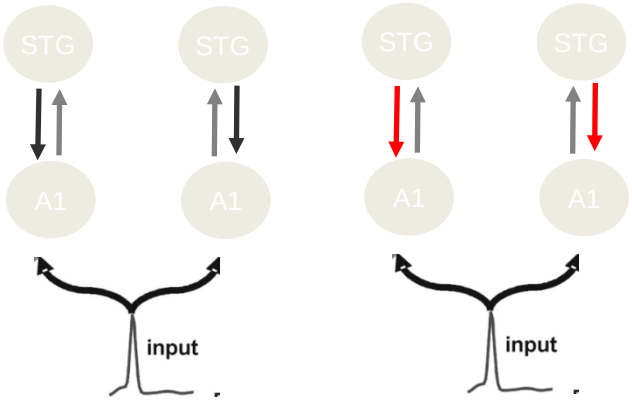


Model Selection & Hypothesis Testing



data *y*





Model *1* → $p(y \mid m_1)$, $p(\theta \mid y, m_1)$

Model *2* → $p(y \mid m_2)$, $p(\theta \mid y, m_2)$

⋮

Model *n* → $p(y \mid m_n)$, $p(\theta \mid y, m_n)$

Model selection: $p(y \mid m_i)$

Bayesian Statistics

new data

prior knowledge

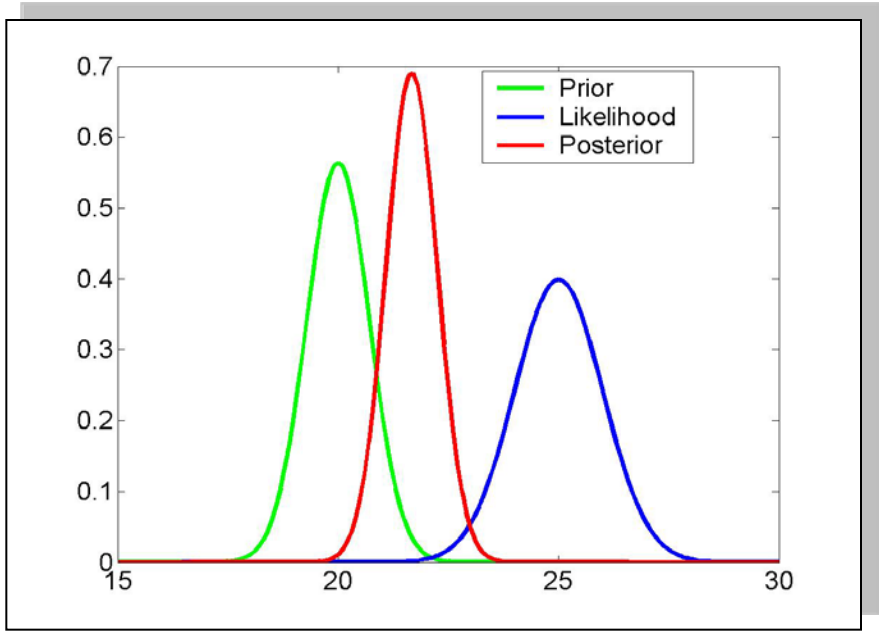
$$p(y \mid \theta) \qquad p(\theta)$$

$$p(\theta \mid y) \propto p(y \mid \theta)\, p(\theta)$$

posterior $\propto$ likelihood • prior

Bayes theorem allows one to formally incorporate prior knowledge into computing statistical probabilities.

In DCM for Neurphysiology priors include time constants, Extrinsic connectivity strengths, PSP, delays etc.



The “posterior” probability of the parameters given the data is an optimal combination of prior knowledge and new data, weighted by their relative precision.

Bayesian Inversion

Neural Parameters:
Dynamic Model

$$\theta = H_e, H_i, \kappa_e, \kappa_i, \kappa_a, \gamma_1, \gamma_2, \gamma_3, \gamma_4, \gamma_{5,} g, A_F, A_B, A_L$$

Observer function:
Forward Spatial Model

$$y = L(\vartheta) x_0$$

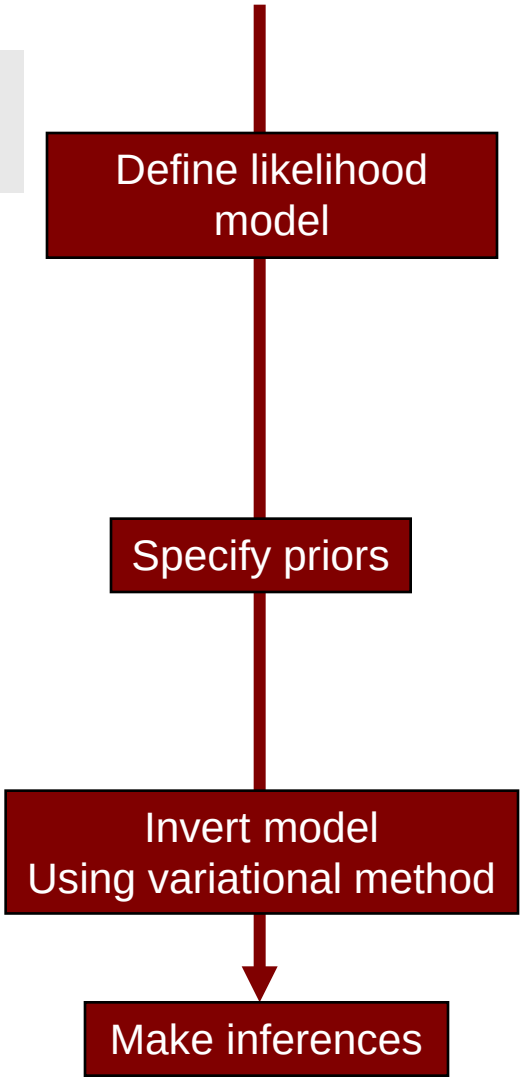
$$p(\theta, m) = N(\mu_\theta, \Sigma_\theta)$$

Inference on models

$$p(y \mid m) = \int p(y \mid \theta, m)\, p(\theta) d\theta$$

Inference on parameters

$$p(\theta \mid y, m) = \frac{p(y \mid \theta, m)\, p(\theta, m)}{p(y \mid m)}$$



VB in a nutshell (mean-field approximation)

Free-energy approximation to model evidence

$$\ln p(y|m) = F + KL\left[q(\theta,\lambda), p(\theta,\lambda|y)\right]$$

$$F = \left\langle \ln p(y,\theta,\lambda)\right\rangle_q - KL\left[q(\theta,\lambda), p(\theta,\lambda|m)\right]$$

Mean Field Partition

$$p(\theta,\lambda|y) \approx q(\theta,\lambda) = q(\theta)q(\lambda)$$

Maximise variational energies via gradient ascent

$$q(\theta) \propto \exp(I_\theta) = \exp\left[\left\langle \ln p(y,\theta,\lambda)\right\rangle_{q(\lambda)}\right]$$

$$q(\lambda) \propto \exp(I_\lambda) = \exp\left[\left\langle \ln p(y,\theta,\lambda)\right\rangle_{q(\theta)}\right]$$

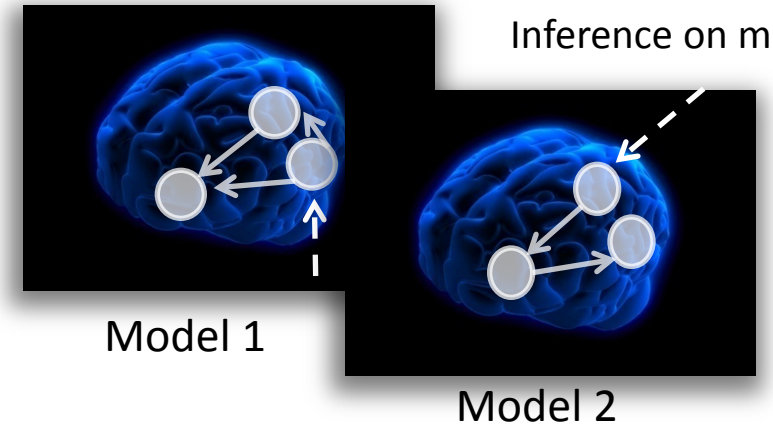
Using Laplace assumption: local covariance is a function of the mean

Dynamic Causal Modelling: Framework

Bayesian Inversion

Bayes' rules: $p(\theta \mid y, m) = \frac{p(y \mid \theta, m)\, p(\theta \mid m)}{p(y \mid m)}$

Free Energy: $F \underset{\max}{=} \ln p(y|m) - KL(q(\theta) \| p(\theta|y, m))$



Inference on models

Model 1

Model 2

Model comparison via Bayes factor:

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

Kass & Raftery 1995, *J. Am. Stat. Assoc.*

B_{12}	$p(m_1\|y)$	Evidence
1 to 3	50-75%	weak
3 to 20	75-95%	positive
20 to 150	95-99%	strong
≥ 150	≥ 99%	Very strong

Dynamic Causal Modelling: Framework

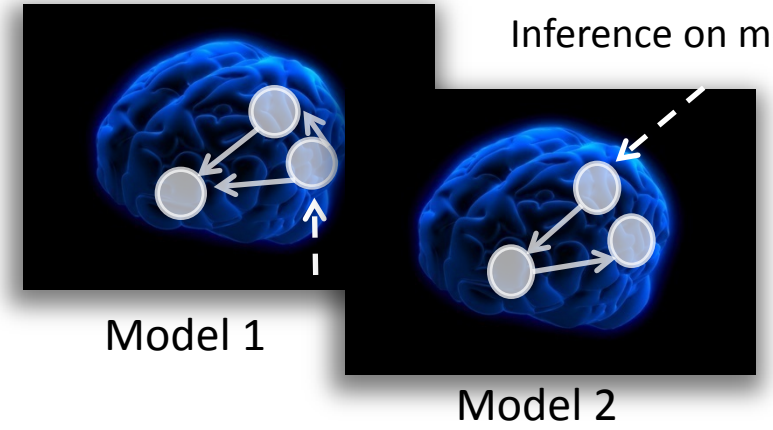
Bayesian Inversion

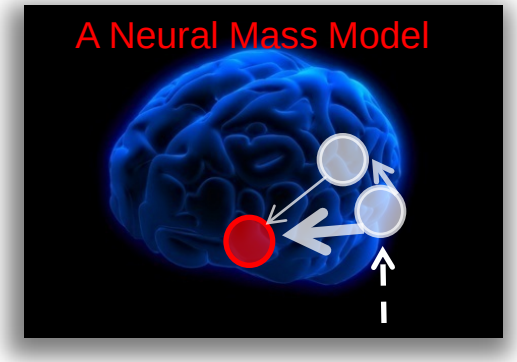
Bayes' rules: $p(\theta \mid y, m) = \dfrac{p(y \mid \theta, m)\, p(\theta \mid m)}{p(y \mid m)}$

Free Energy: $F \underset{\max}{=} \ln p(y|m) - KL(q(\theta) \,|\, p(\theta|y, m))$

Inference on parameters

Inference on models



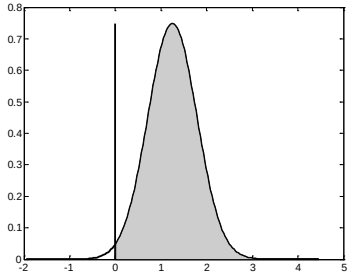


Model 1

Model comparison via Bayes factor:

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

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



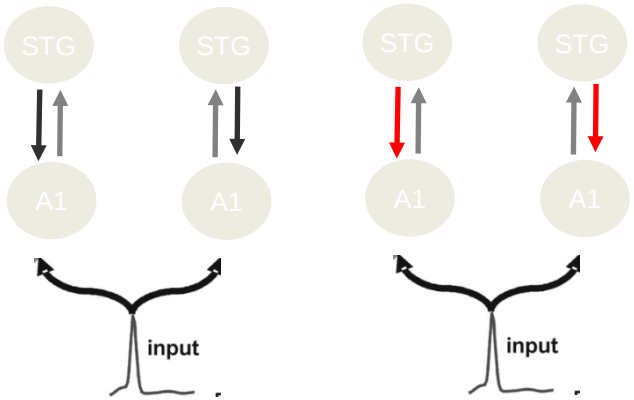
$p(conn > 0 \mid y) = 99.1\%$

Bayesian Model Comparison

The model goodness: Negative Free Energy

$$F = \log p(y \mid m) - KL\left[q(\theta), p(\theta \mid y, m)\right]$$

Accuracy - Complexity



$$KL\left[q(\theta), p(\theta \mid m)\right]$$
$$= \frac{1}{2}\ln\left|C_\theta\right| - \frac{1}{2}\ln\left|C_{\theta|y}\right| + \frac{1}{2}\left(\mu_{\theta|y} - \mu_\theta\right)^T C_\theta^{-1}\left(\mu_{\theta|y} - \mu_\theta\right)$$

The complexity term of *F* is higher

- the more independent the prior parameters (↑ effective DFs)
- the more dependent the posterior parameters
- the more the posterior mean deviates from the prior mean

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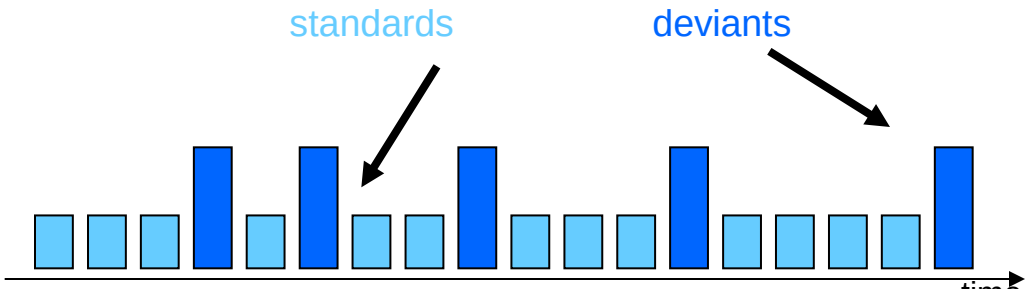
Mismatch negativity (MMN) – DCM Motivation

Paradigm



pseudo-random auditory sequence

80% standard tones – 500 Hz

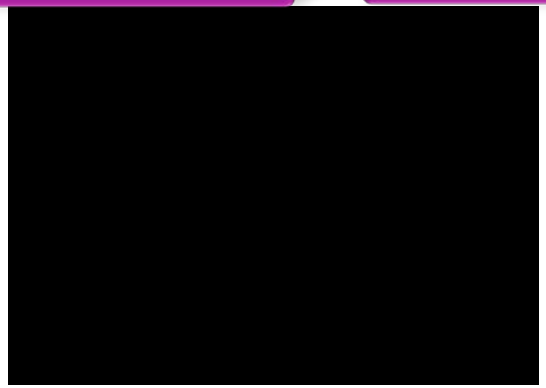
20% deviant tones – 550 Hz

Raw Data (128 channel EEG)

Preprocessing

Epoched

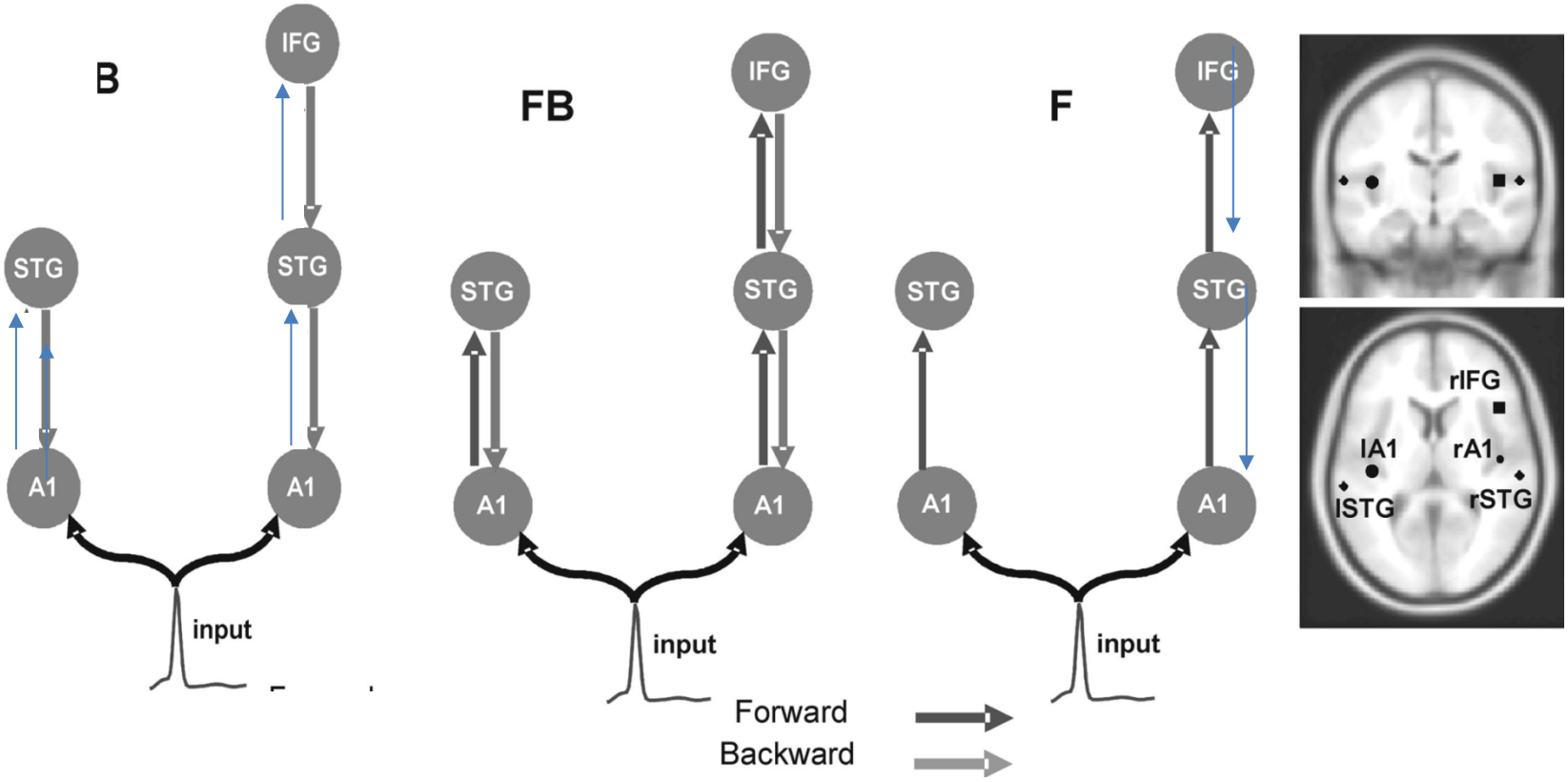
Source Priors



Garrido et al., (2007), *NeuroImage*

Model for mismatch negativity

Models for Deviant vs Standard Response Generation



Garrido et al., (2007), *NeuroImage*

GUI:

The FB Model

Which Data,

Which Model?

What time?

What Conditions

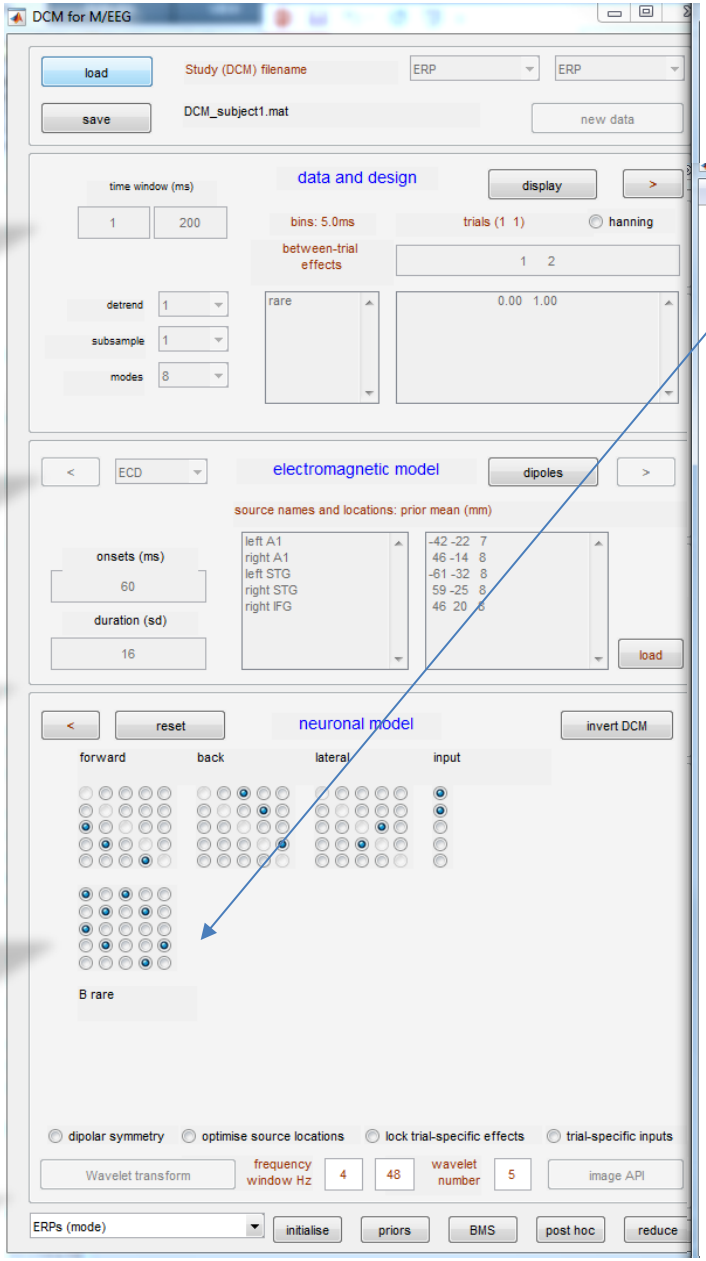
Design Matrix?

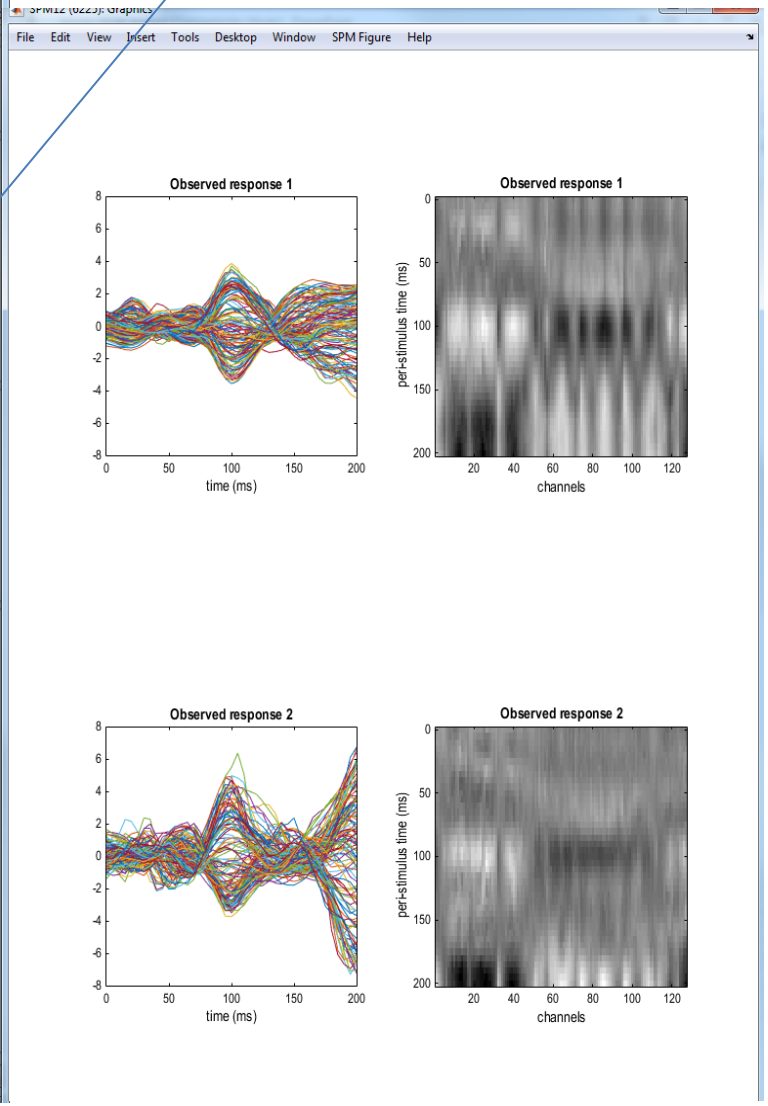
Sources?

Connectivity?

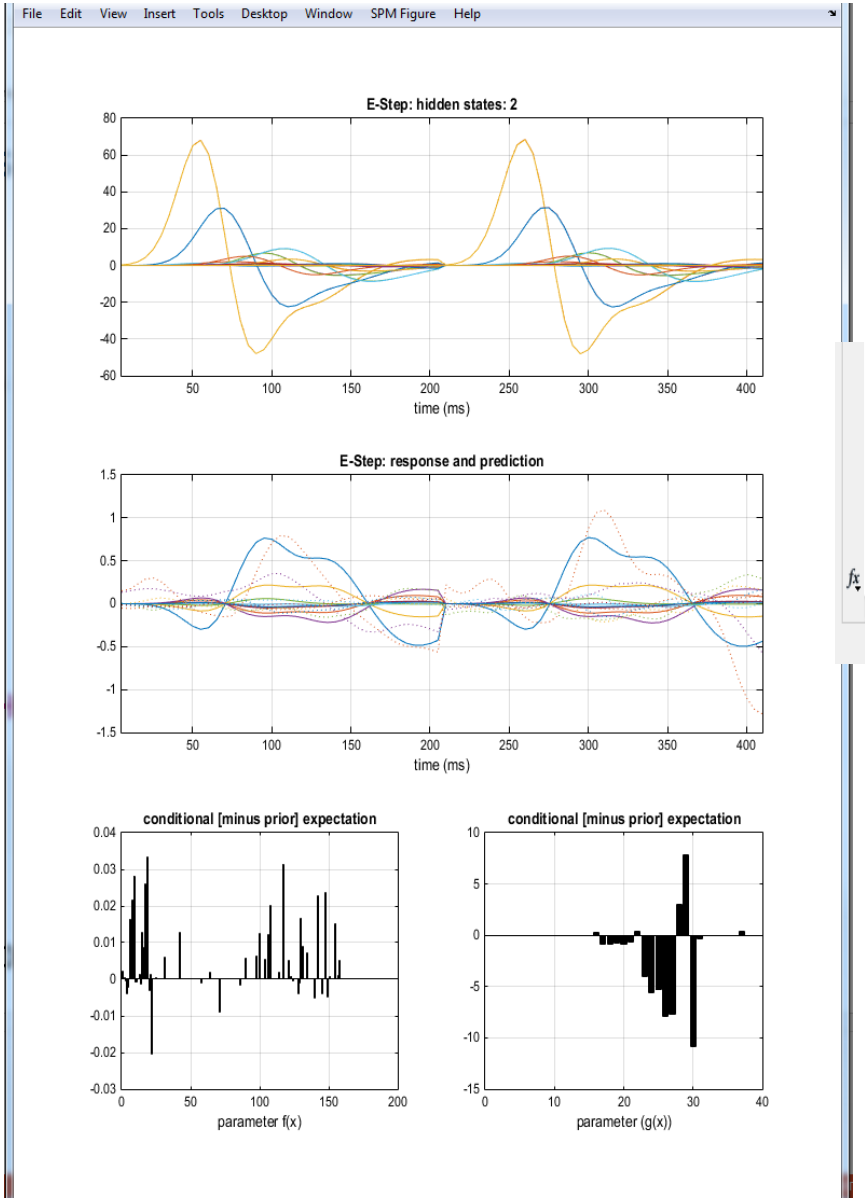
Condition Specific Effects?

Hit Invert!



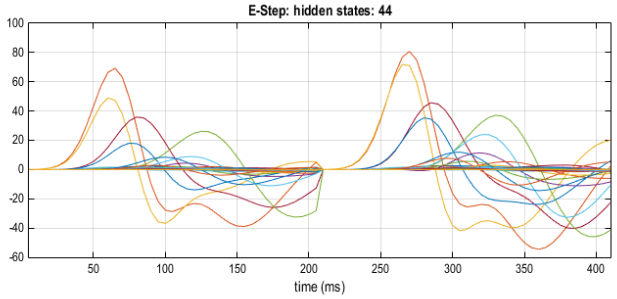


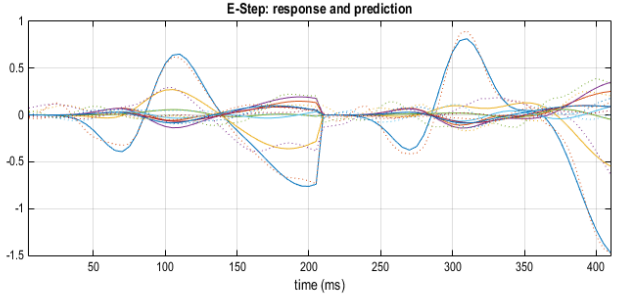
The F is Rising!

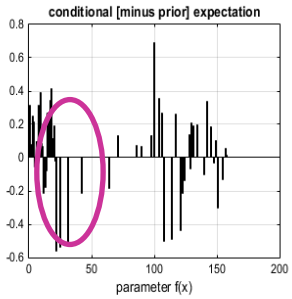


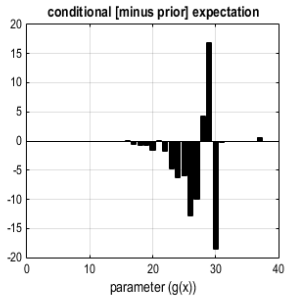

```
determining source compartment (1)
projecting electrodes on skin surface
combining electrode transfer and system matrix
Foward model complete - thank you
determining source compartment (1)
projecting electrodes on skin surface
combining electrode transfer and system matrix
EM(+) : 1  (8,8)    F: 0.000e+00 dF predicted: 7.587e+01  actual: 1.536e+02 (20.23 sec)
EM(+) : 2  (8,3)    F: 1.536e+02 dF predicted: 4.192e+01 >>
```

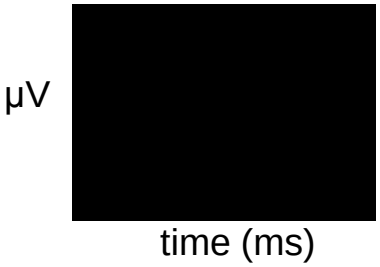
Trial Specific Effects

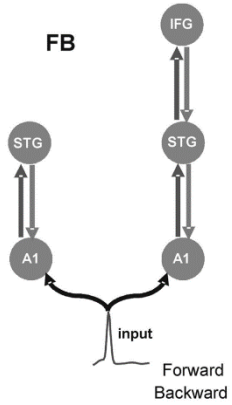


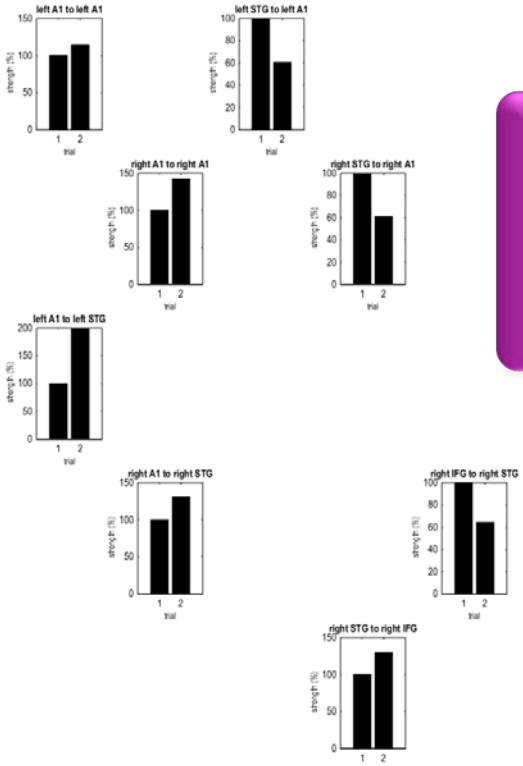








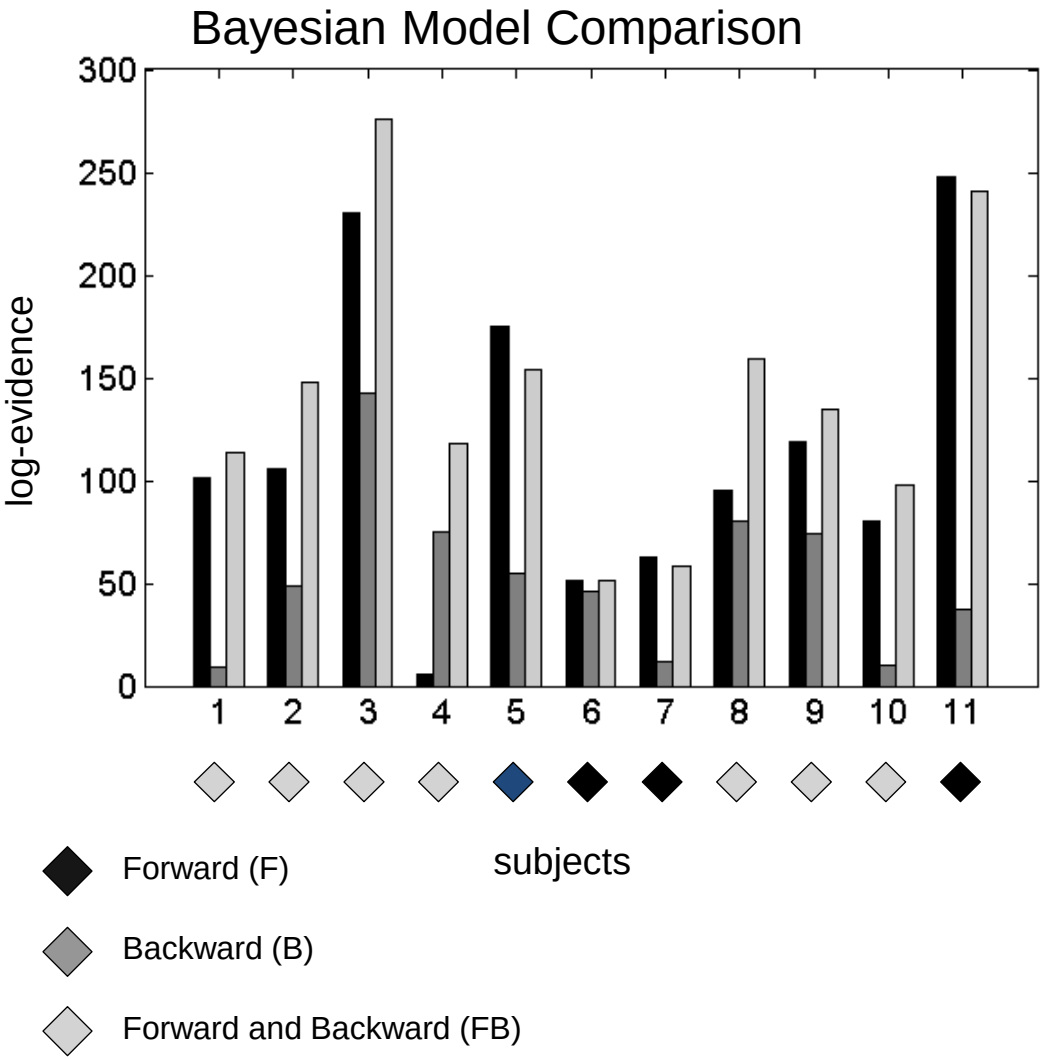


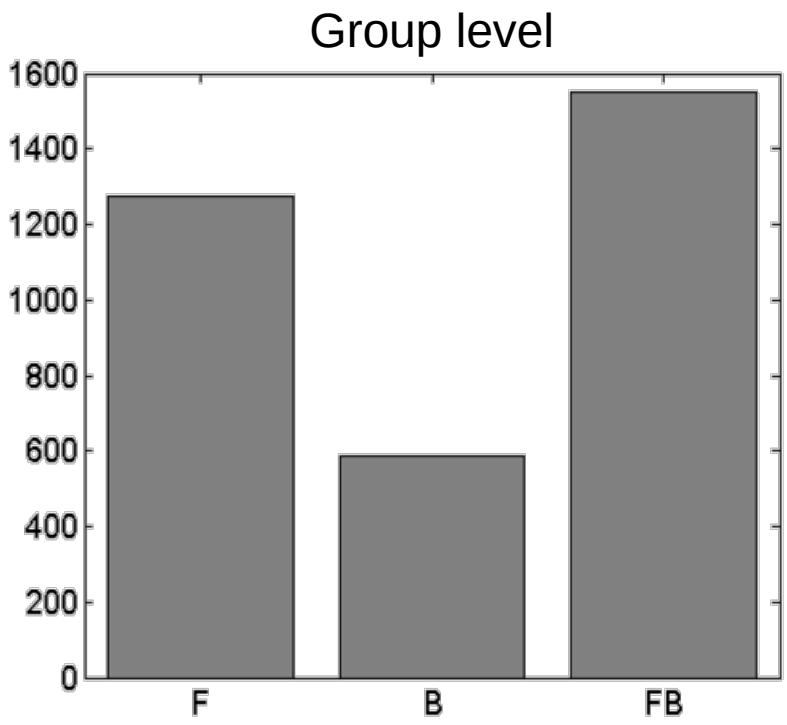


Rare Events
Decreased
Backward
Connectivity

Rare Events Increased
Forward Connectivity

Group model comparison



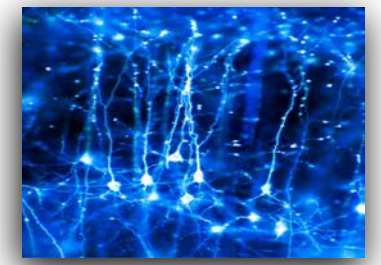


Garrido et al., (2007), *NeuroImage*

Summary

1. DCM enables testing hypotheses about how brain sources communicate.
2. DCM is based on a neurobiologically plausible generative model of evoked responses.
3. Differences between conditions are modelled as modulation of connectivity.
4. Inference using Bayesian model selection, Bayesian parameter testing, or mix Bayes and classical stats!

Thank You



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