Dynamic Causal Modeling for EEG

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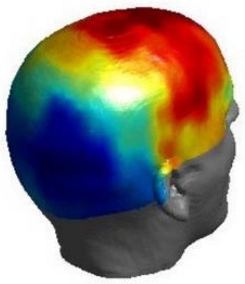
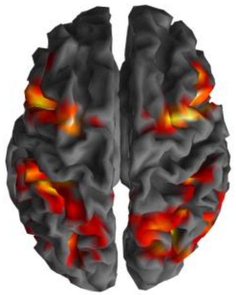
Computational Psychiatry Course 2018

EEG, MEG



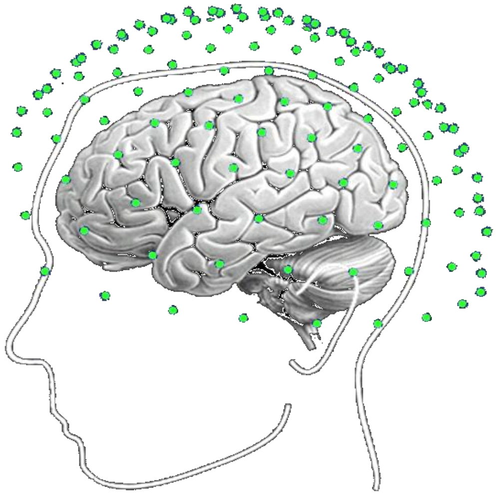
fMRI



Forward model:

Predicting measured activity

$$y = g(x, \theta) + \varepsilon$$

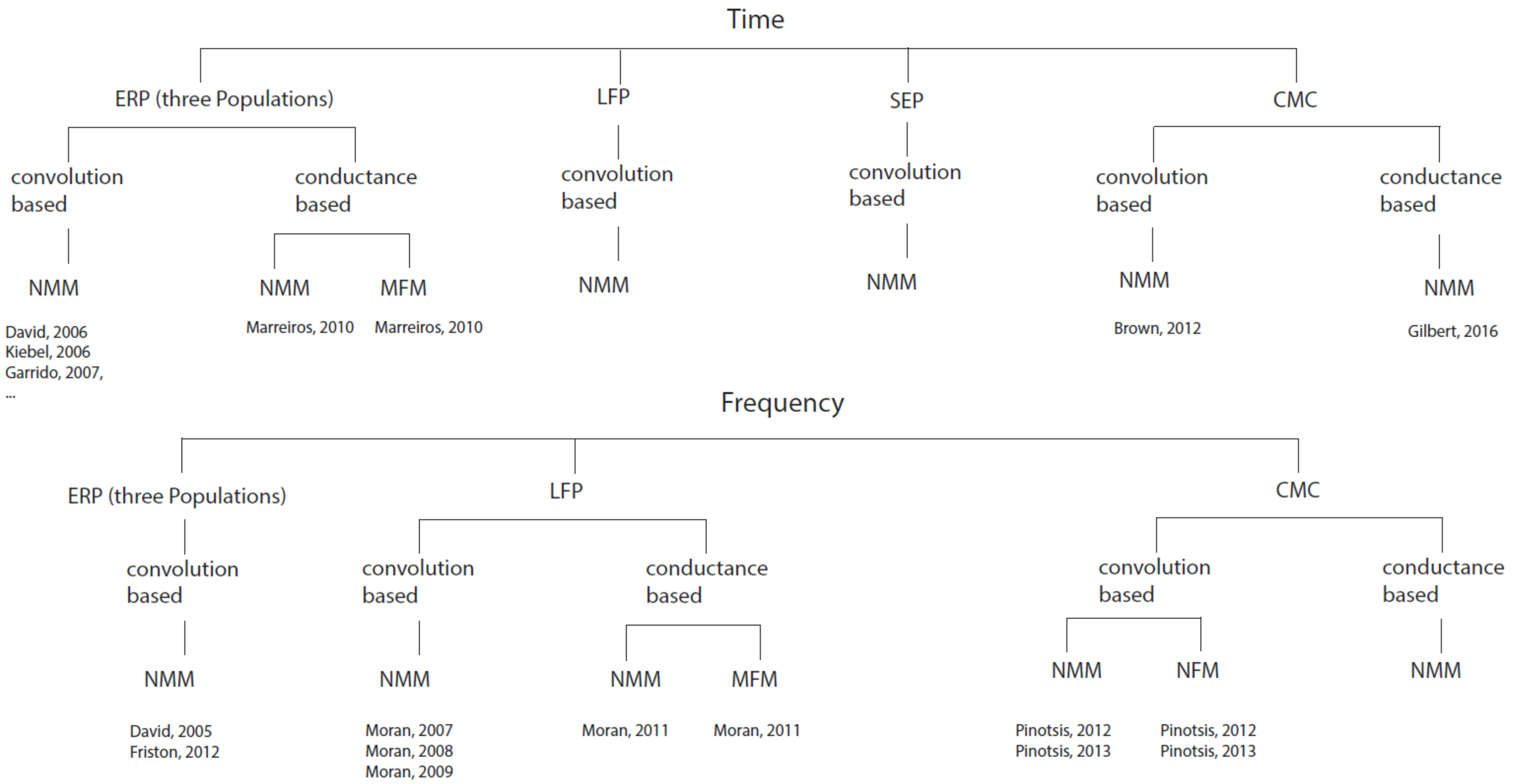


Model inversion:

Estimating neuronal mechanisms

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

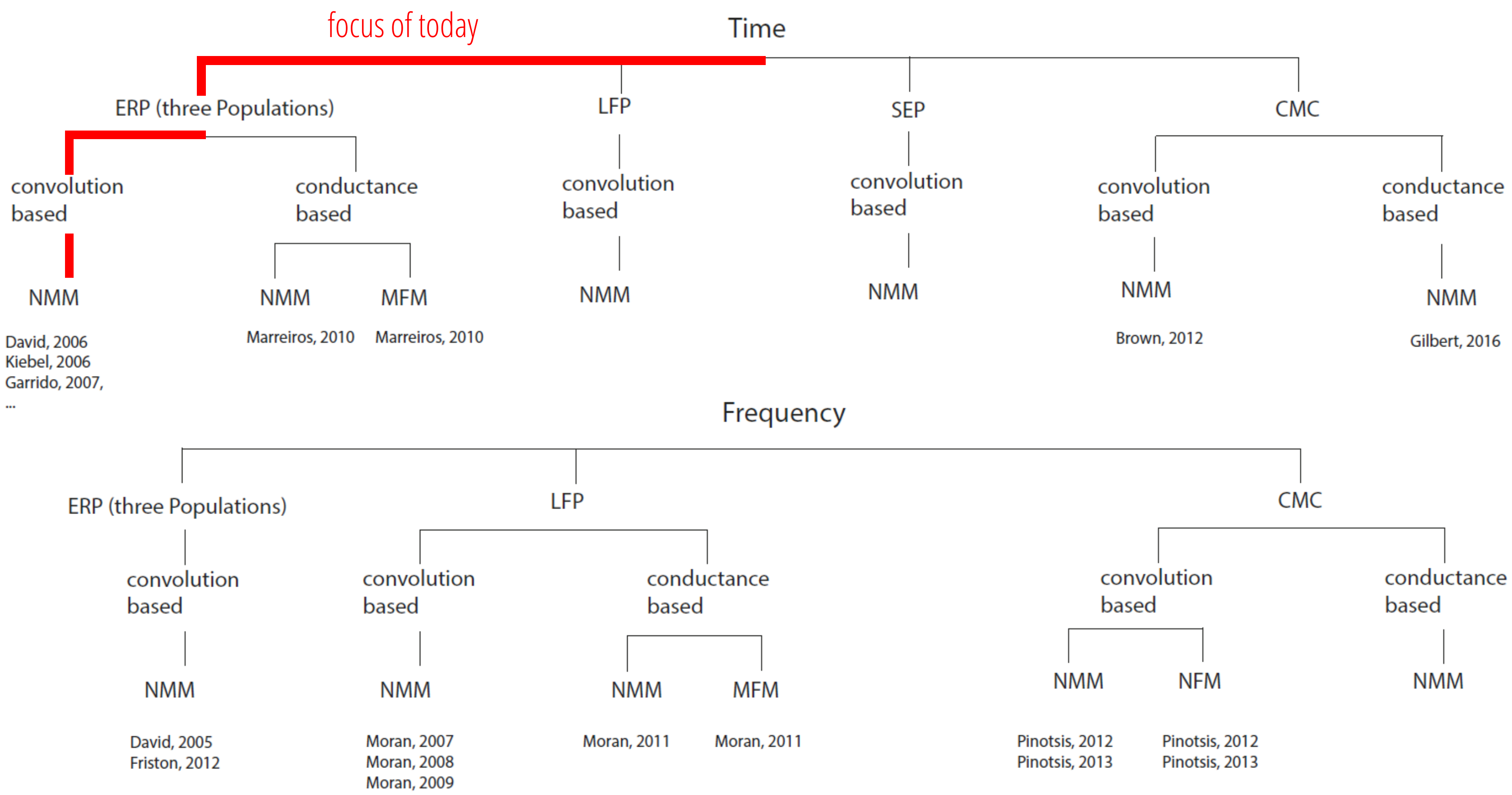
Friston et al., 2003, *NeuroImage*; David et al., 2006, *NeuroImage*



Glossary:

- ERP (Evoked Response Potential)
- LFP (Local Field Potential)
- SEP (Somatosensory Evoked Potential)
- CMC (Canonical Microcircuit)

- NMM (Neural Mass Model)
- MFM (Mean Field Model)
- NFM (Neural Field Model)



Glossary:

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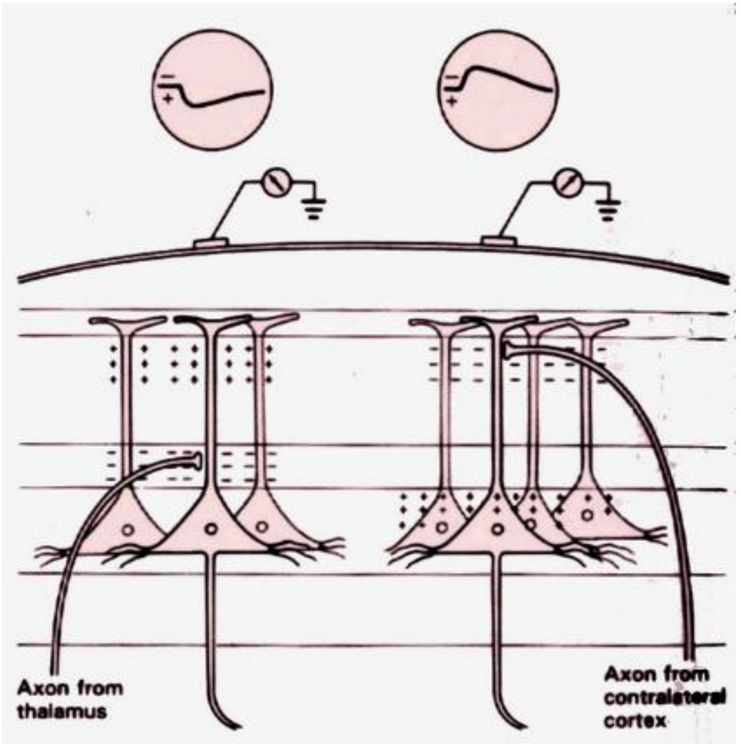
- NFM (Neural Field Model)

I. Macroscale

Scalp maps, dipoles and connected networks

EEG

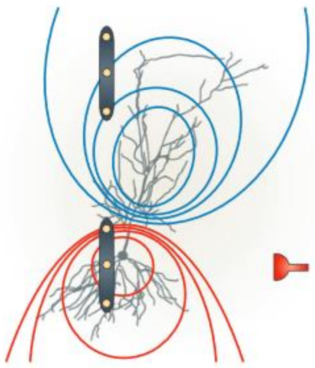
- Temporary accumulation of positive and negative charge during the generation of action potentials
- Resulting Electrical Potential (Energy) is a **scalar** quantity. It depends on the **medium**, and the location wrt the '**source**', thus leading to Potential Energy differences on the scalp.

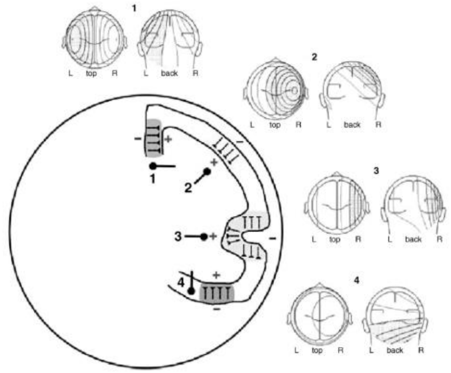


Buzsaki et al., 20012, Nature Reviews, Neuroscience

Forward Model

- Local Field Potentials (LFP)
  - Measure the activity much closer to the source.
  - ‘Simpler’ forward model, because we have a much more direct measure of source activity.
- Sensor-Level Data
  - Electrical Potential ‘travels’ from source to the scalp.
  - This mapping is usually referred to as **Leadfield matrix**





Aguiar et al, 2000, Symposium on Applied Computing

Ebersole, Handbook of Clinical Neurophysiology, 2004

Forward Model
> ECD

- Sensor-Level Data
  - Given some neural activity modeled as a **dipole** at some **location** in the cortex and some **momentum** (vector) , the **leadfield** matrix computes the projection of this activity onto the scalp.

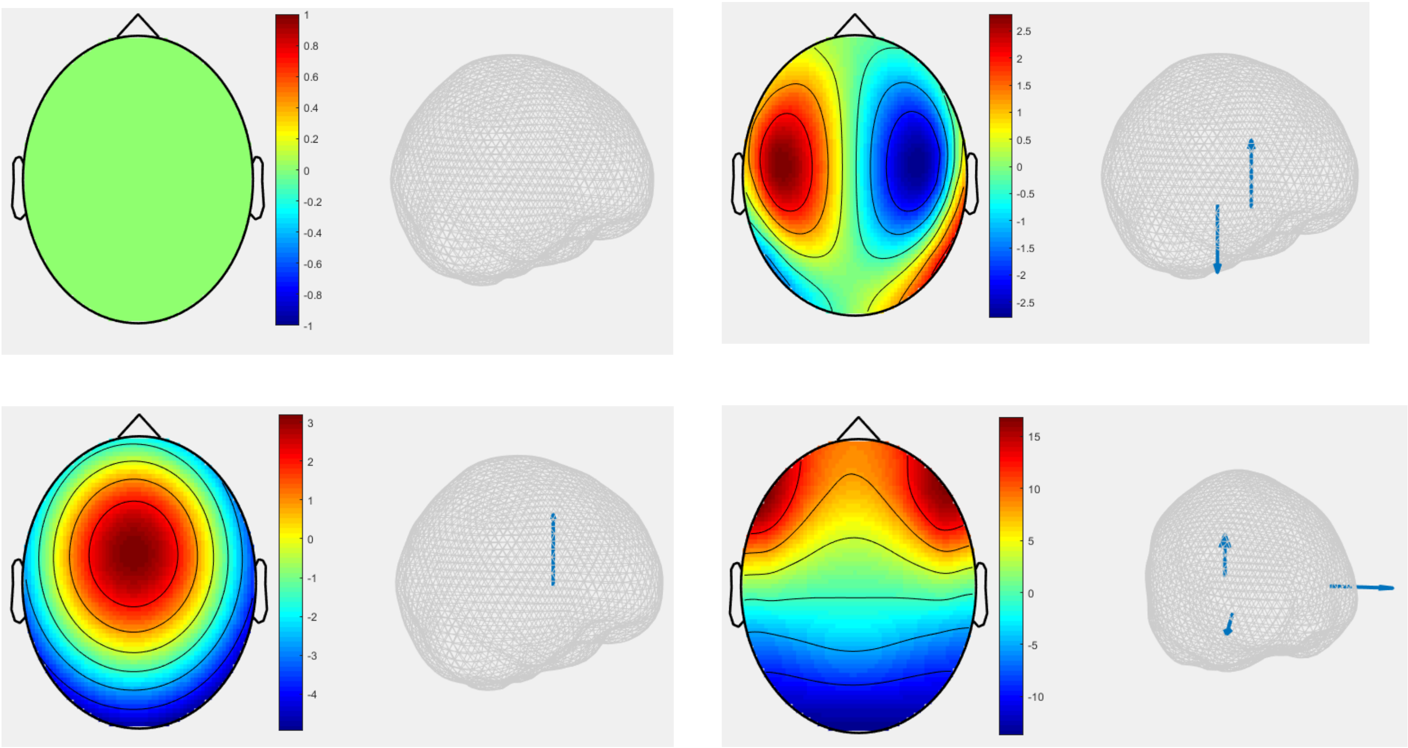


Figure | Different possible dipole configurations that lead to different scalp potentials.

Almost
Dynamic Causal Model

- We want to model the full sensor x time space
- Electrode Activity , Scalp Activity and Source Activity
- In DCM, the dipole moments are **constant** quantities, but act as **gain factor** on the **neural dynamics**!

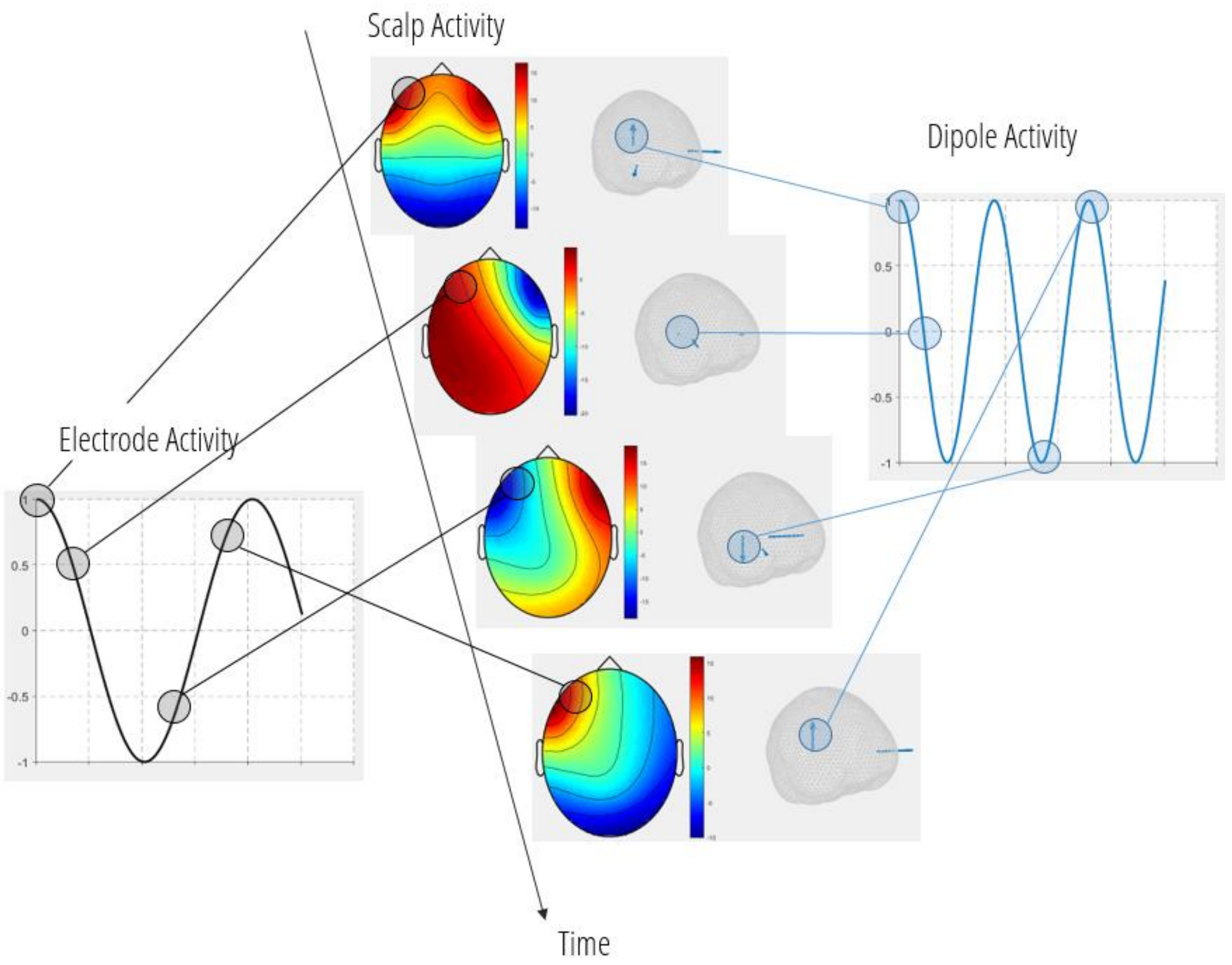


Figure | Changes in the scalp and electrode potential, as the dipole moments change over time.

Connected Network

Sources / Regions

Connections

- Forward
- Backward
- Lateral

Modulatory effects

Driving Input

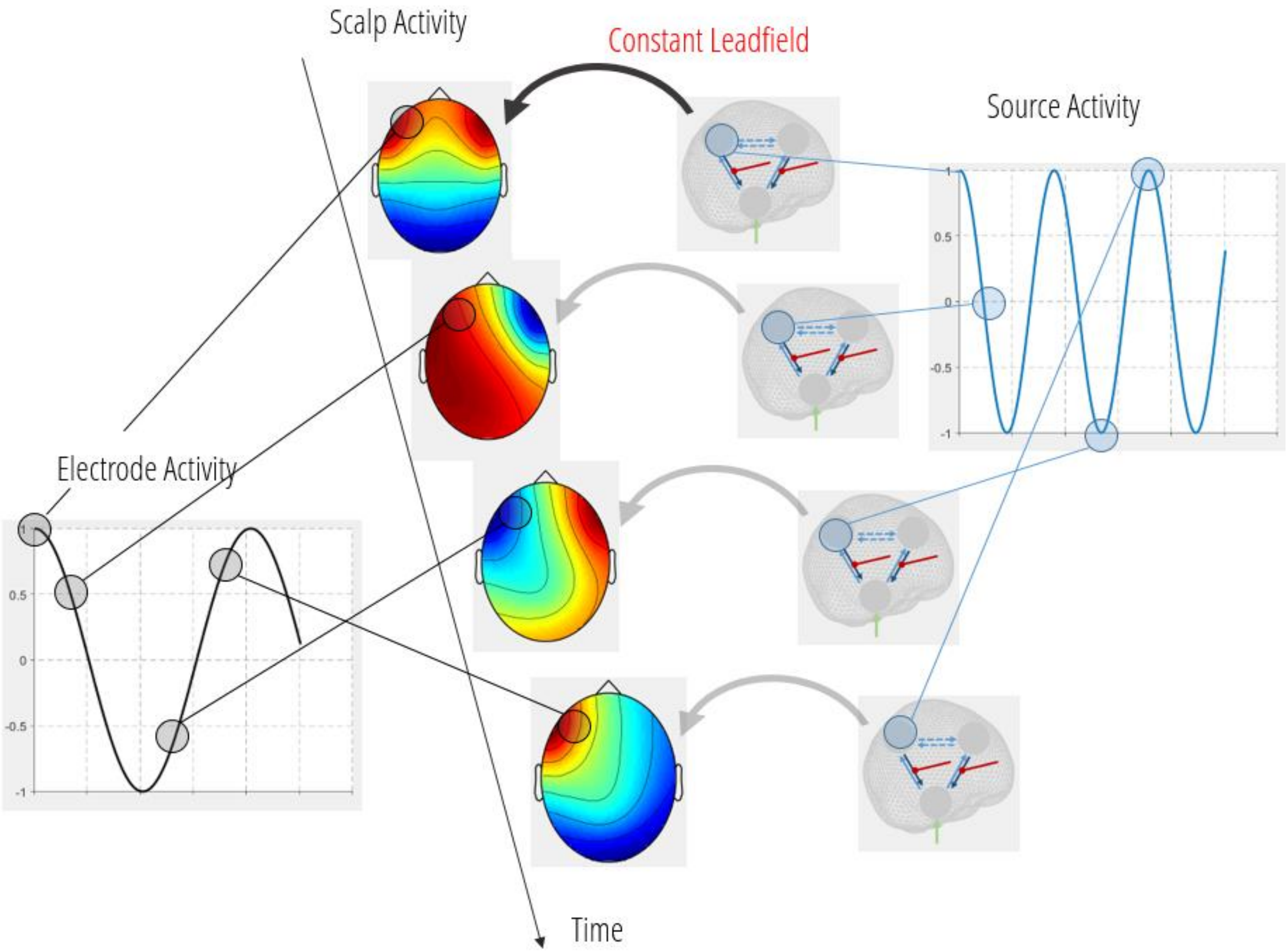


Figure | Changes in the scalp and electrode potential, as the underlying source activity changes over time. The moments of the leadfield act as constant gain factors.

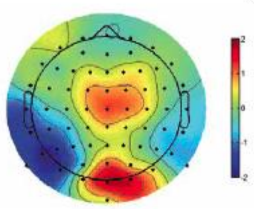
Hypothesis Testing

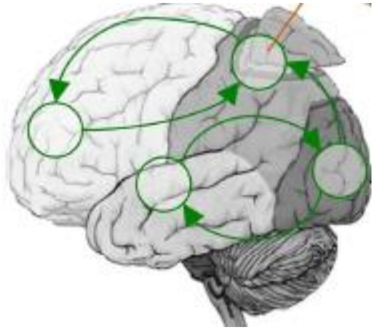
- Macroscale view (similar to DCM for fMRI)
- Framework to test multiple hypotheses as Bayesian Model Selection (BMS -> Stefan Frässle) questions:

Data **(Hidden) Neuronal Model**

Inverse Problem: Inference

$$p(\theta, \Sigma | y)$$





Forward model: Prediction

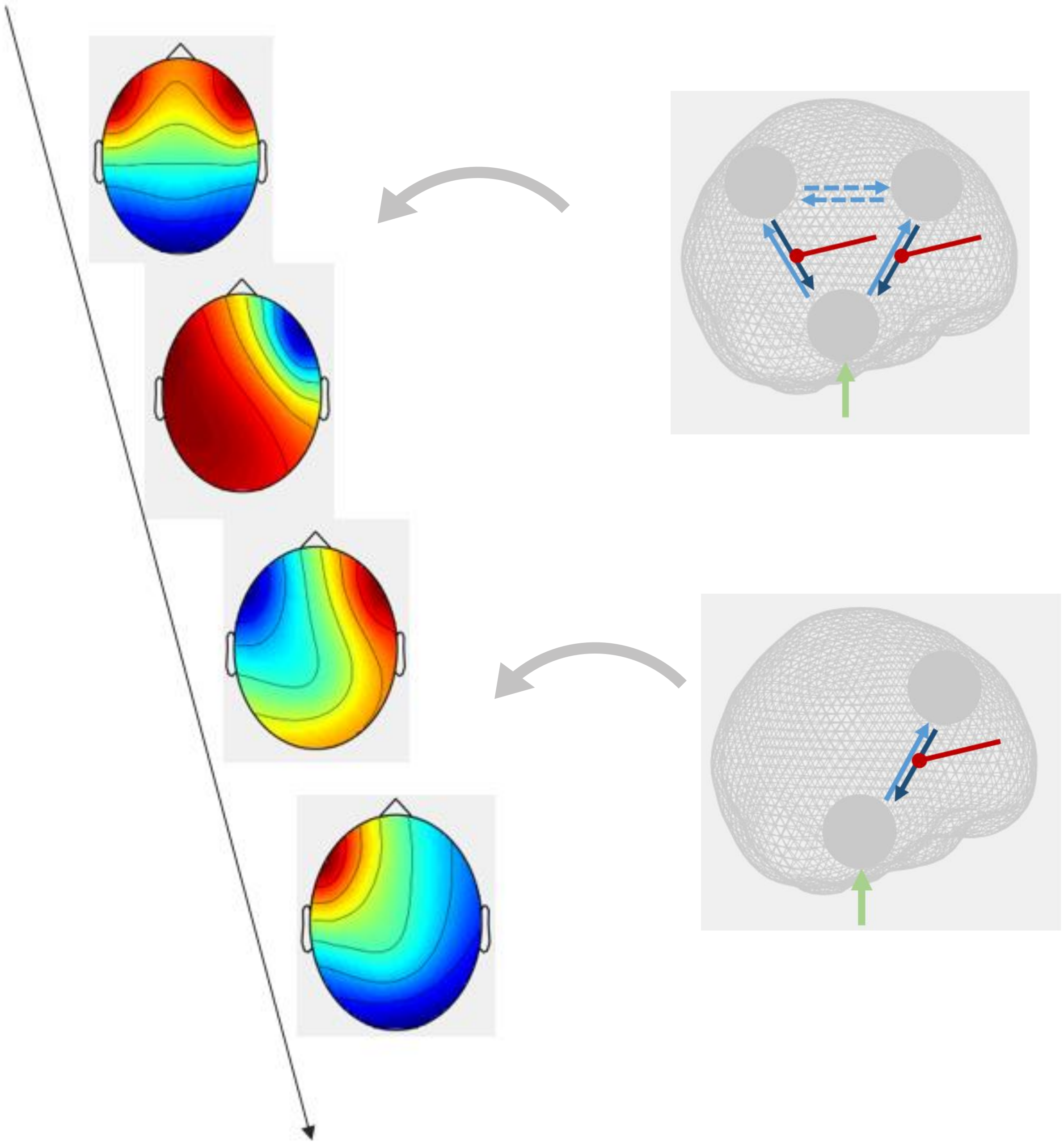
$$y = g(x, \theta) + \varepsilon$$

Dynamic Equations

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

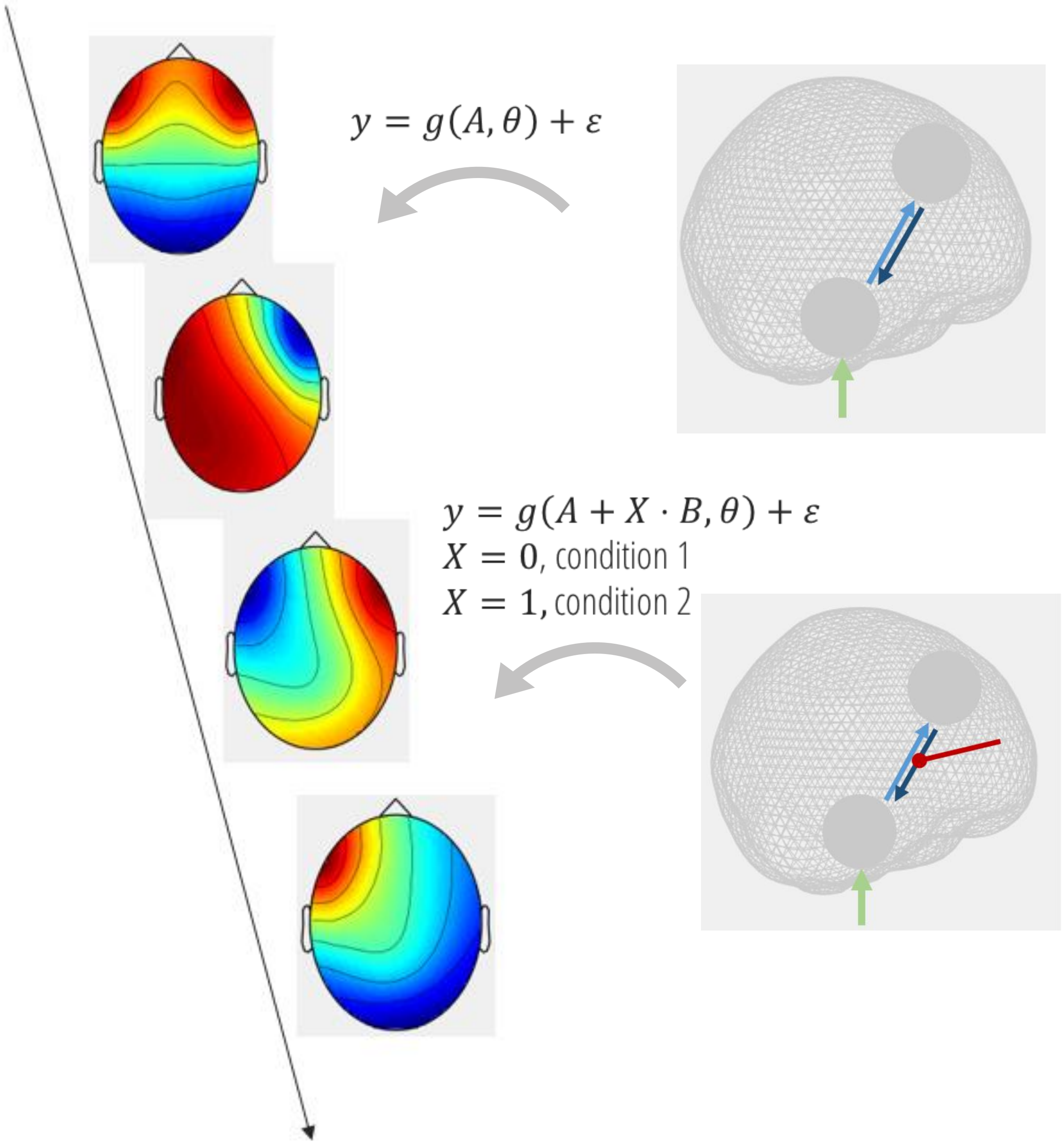
Hypothesis Testing

- Macroscale view (similar to DCM for fMRI)
- Framework to test multiple hypotheses as Bayesian Model Selection (BMS -> Stefan Frässle) questions:
  - Does a model including regions A, B and C explain the data better than a model including only A and B.
    Only possible for scalp data (not LFP or fMRI)!



Hypothesis Testing

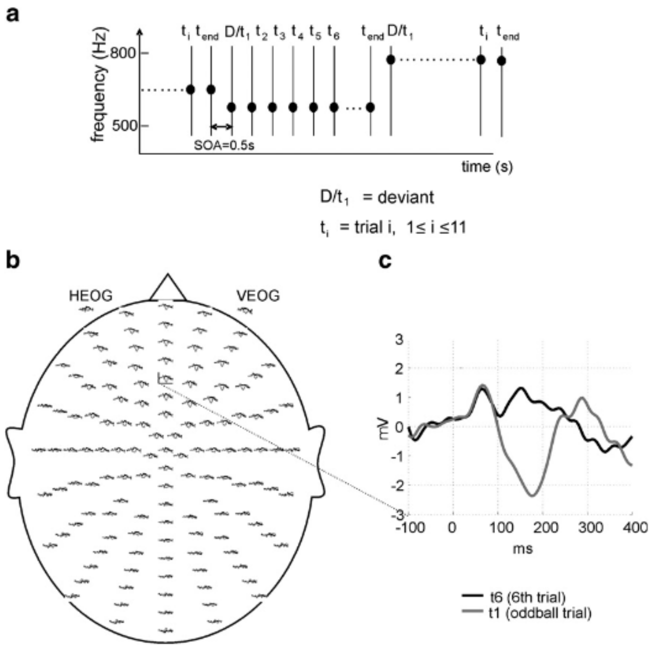
- Macroscale view (similar to DCM for fMRI)
- Framework to test multiple hypotheses as Bayesian Model Selection (BMS -> Stefan Frässle) questions:
    - Does a model including regions A, B and C explain the data better than a model including only A and B.
    - Can we explain a difference in activation between conditions as a condition specific modulation of one of the connections?

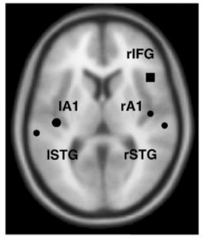


STUDY: IDENTIFYING MECHANISMS

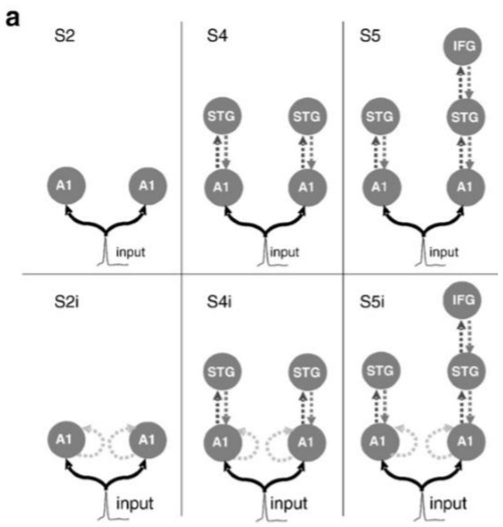
Competing Hypotheses with regard to mechanisms expressed through different modulation structure.

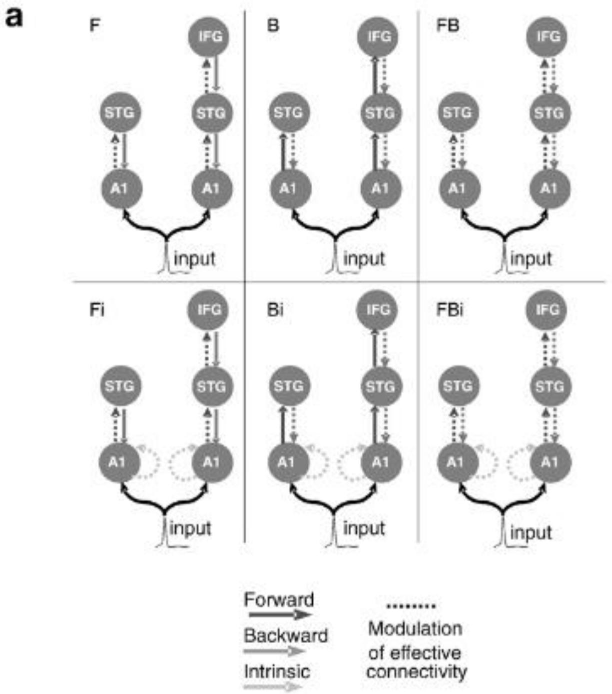
Experimental Design

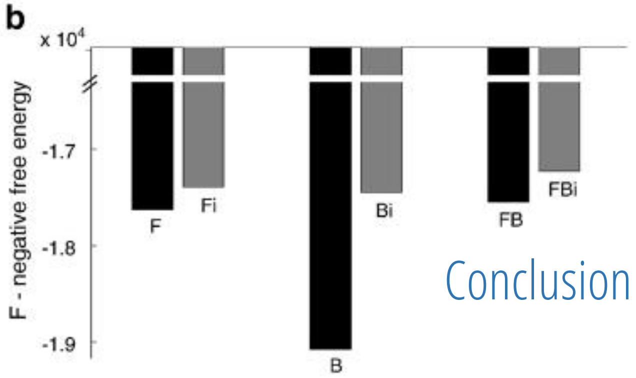




Effect of manipulation







Conclusion

Garrido et. al, 2008, NeuroImage

II. Mesoscale

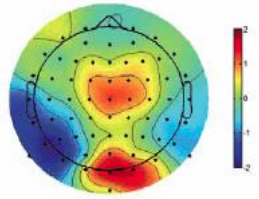
Layered Structure of the cortical column

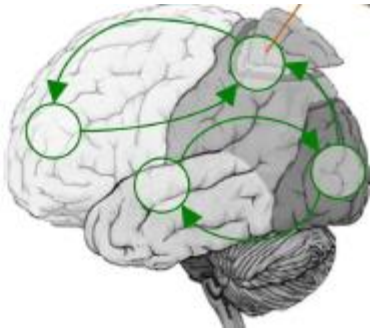
Data

(Hidden) Neuronal Model

Inverse Problem: Inference

$$p(\theta, \Sigma | y)$$





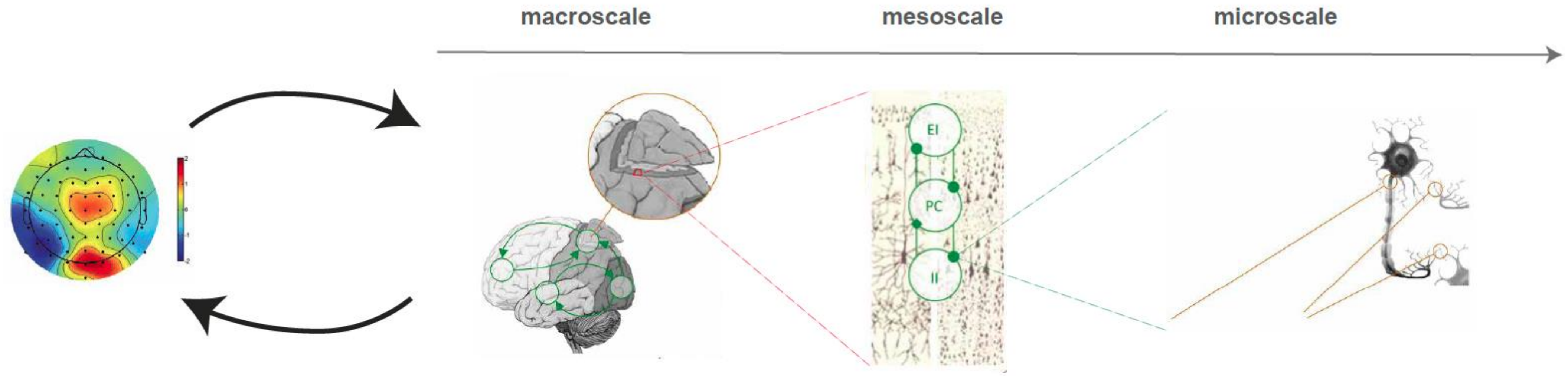
Forward model: Prediction

$$y = g(x, \theta) + \varepsilon$$

Dynamic Equations

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

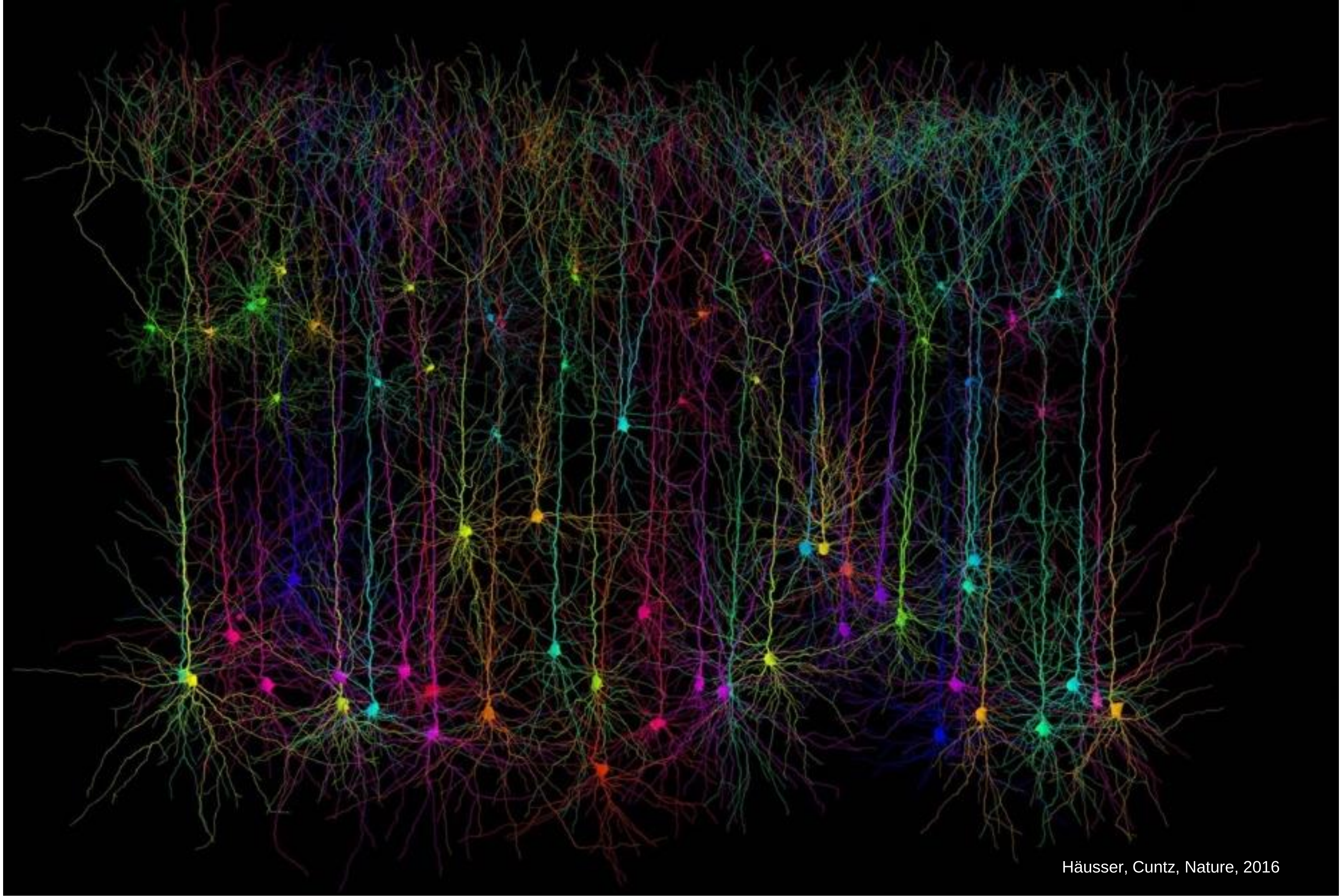
Data **(Hidden) Neuronal Model**



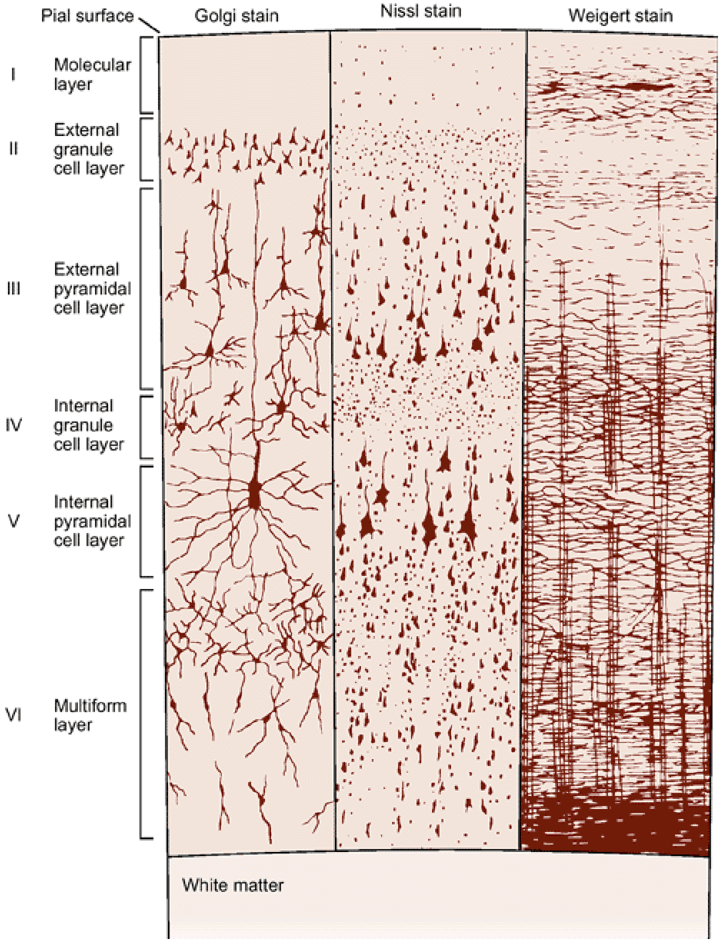
Recurrent network of cortical sources

Layered Structure of the cortical column

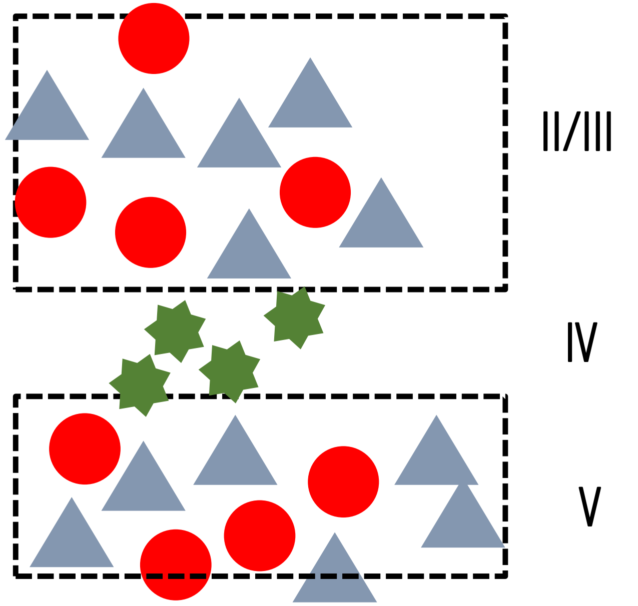
$$\frac{dx}{dt} = f(x, u, \theta)$$



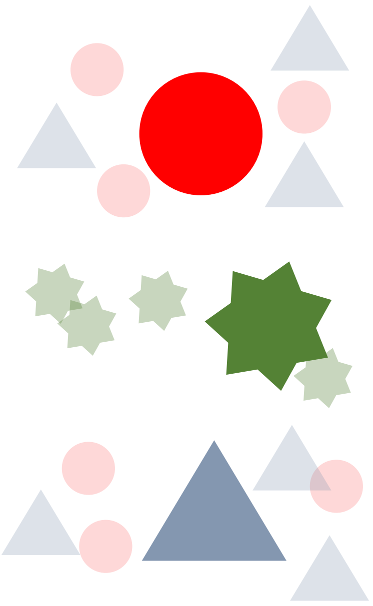
Häusser, Cuntz, Nature, 2016



Kandel et al. 2000 (from Heimer 1994)

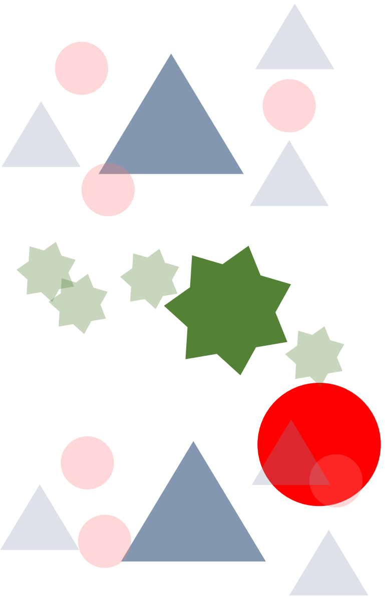


ERP



Superficial and deep pyramidal and inhibitory cells are combined in a single population

CMC

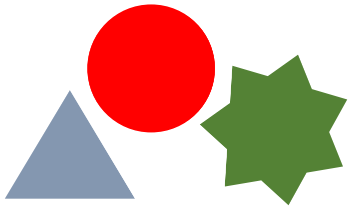


Superficial and deep pyramidal cell populations are modeled individually

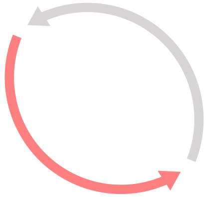
Mesoscale

Three types of Cell Populations:

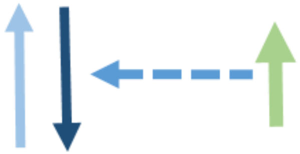
Pyramidal, Inhibitory, Stellate



Inhibitory / Excitatory effects on different populations



Extrinsic Connectivity / Driving Input

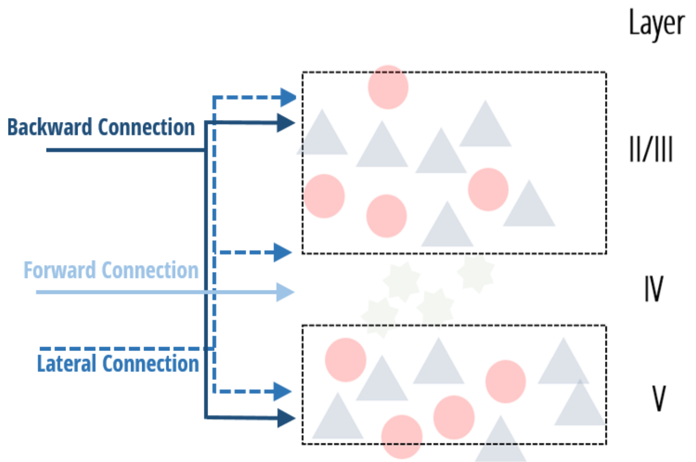


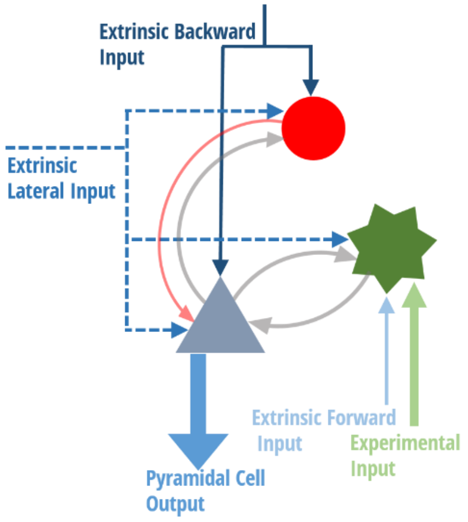
Mesoscale

- Name of a between source connection refers to the layer, which a connection targets
  Felleman & van Essen 1991
- Output from the Pyramidal cell population
- Pyramidal Cell contribute most to the EEG signal
- Driving input into stellate cell layer IV

Considerations:

- Importance of distinguishing layer III and V pyramidal cells to model task (e.g. Predictive coding)
- Modeling of particular data features, i.e. Oscillations of particular frequencies.

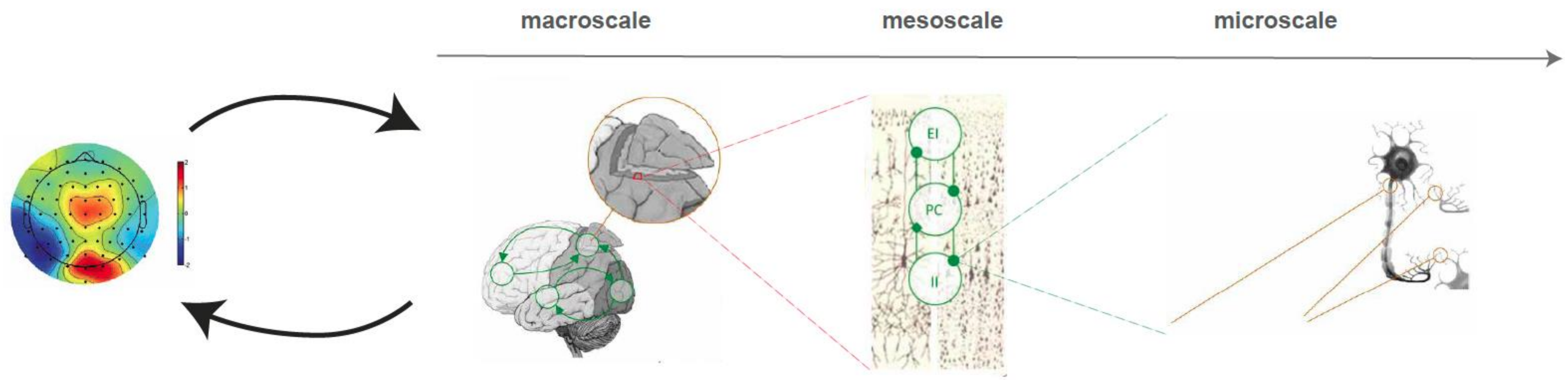




III. Microscale

Mechanisms governing the generation of average post-synaptic potentials

Data **(Hidden) Neuronal Model**



Recurrent network of cortical sources

Layered Structure of the cortical column

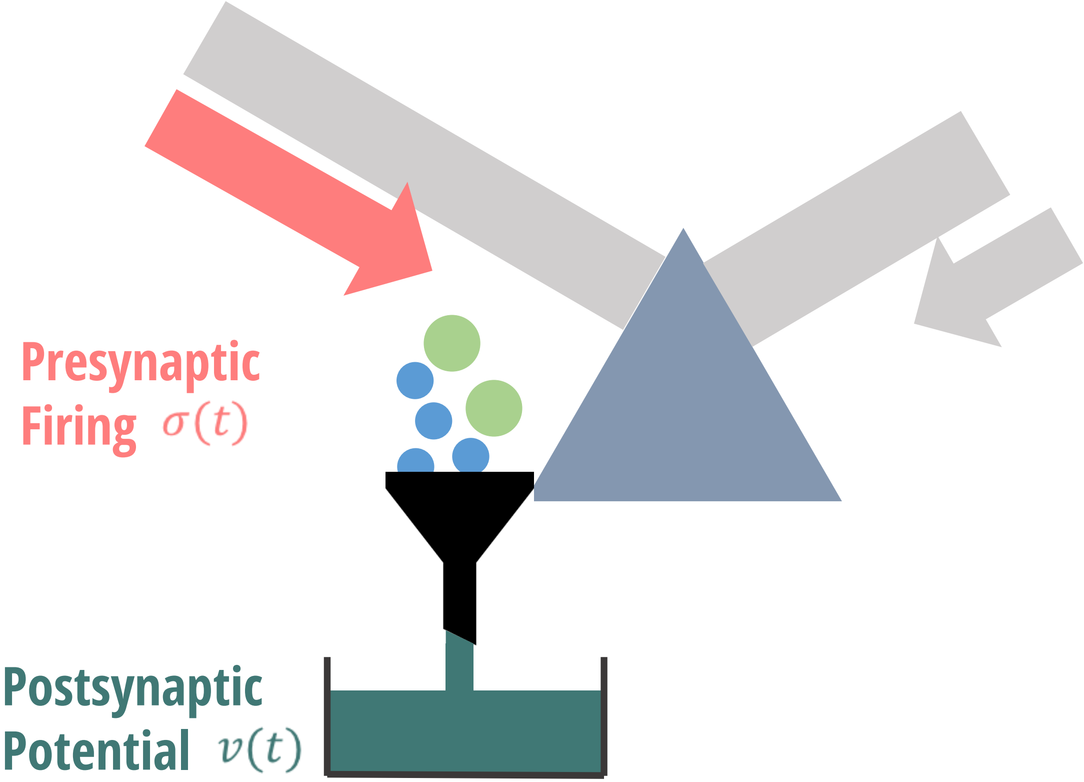
Mechanisms governing generation of average post-synaptic potentials:

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

Microscale
> convolution based DCM

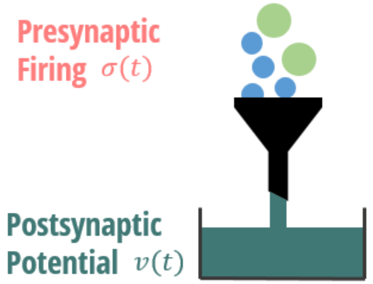
- Jansen and Rit (1995)
- A convolution kernel transforms the presynaptic firing rate into postsynaptic potential
- Kernel parametrized by two parameters

$$v(t) = \int_{-\infty}^{t} h(t-\tau, H, \kappa)\sigma(\tau)d\tau$$



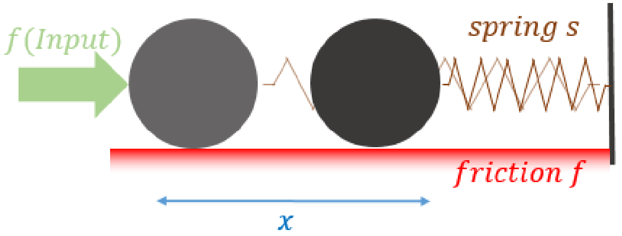
Voltage over time shows similarities with Harmonic Oscillator.

(This is a consequence of the convolution operation)



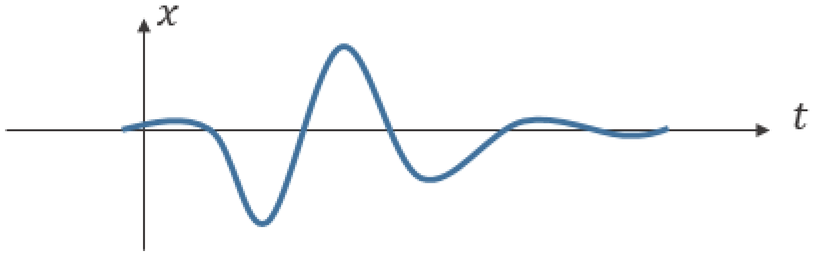
$$\ddot{v} = f(Input) - \frac{2}{\tau}\dot{v} - \frac{1}{\tau^2}v$$

Equation describing the post synaptic potential in the convolution based DCM.



$$\ddot{x} = f(Input) - f\dot{x} - sx$$

Equation describing the behavior of a mass attached to a spring (H.O.)



Microscale > convolution based DCM

- Jansen and Rit (1995)
- A convolution kernel transforms the presynaptic firing rate into postsynaptic potential
- Kernel parametrized by two parameters
- For mathematical convenience, the second order differential equations are transformed into first order differential equations.

Current state of the population.

How much firing arrives (and from where).

$$\frac{dx}{dt} = f(x, A, H, C, \sigma, \theta_{kernel})$$

What the cell population is connected to.

The size of the kernel.

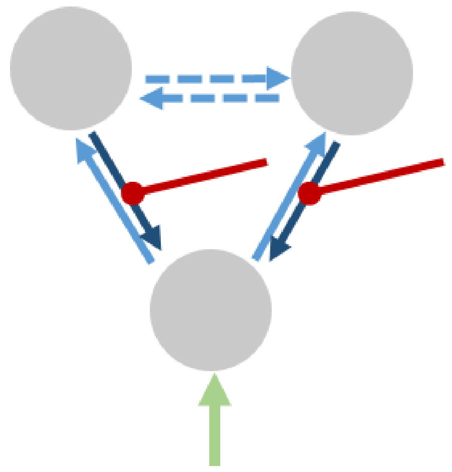
$$\ddot{v} = f(Input) - \frac{2}{\tau}\dot{v} - \frac{1}{\tau^2}v$$

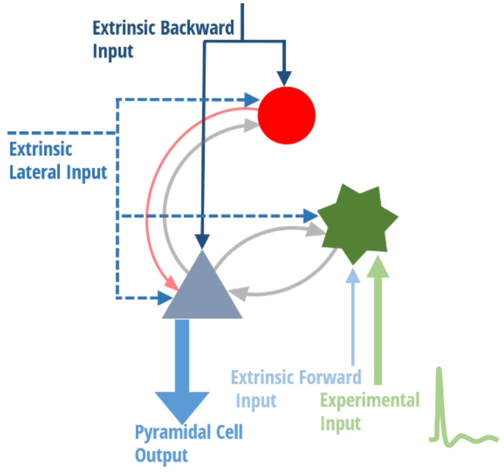
$$k_e A_{back} + k_e A_{lateral} + k_e G$$

$$k_e A_{Forward} + k_e A_{lateral} + k_e G + C$$

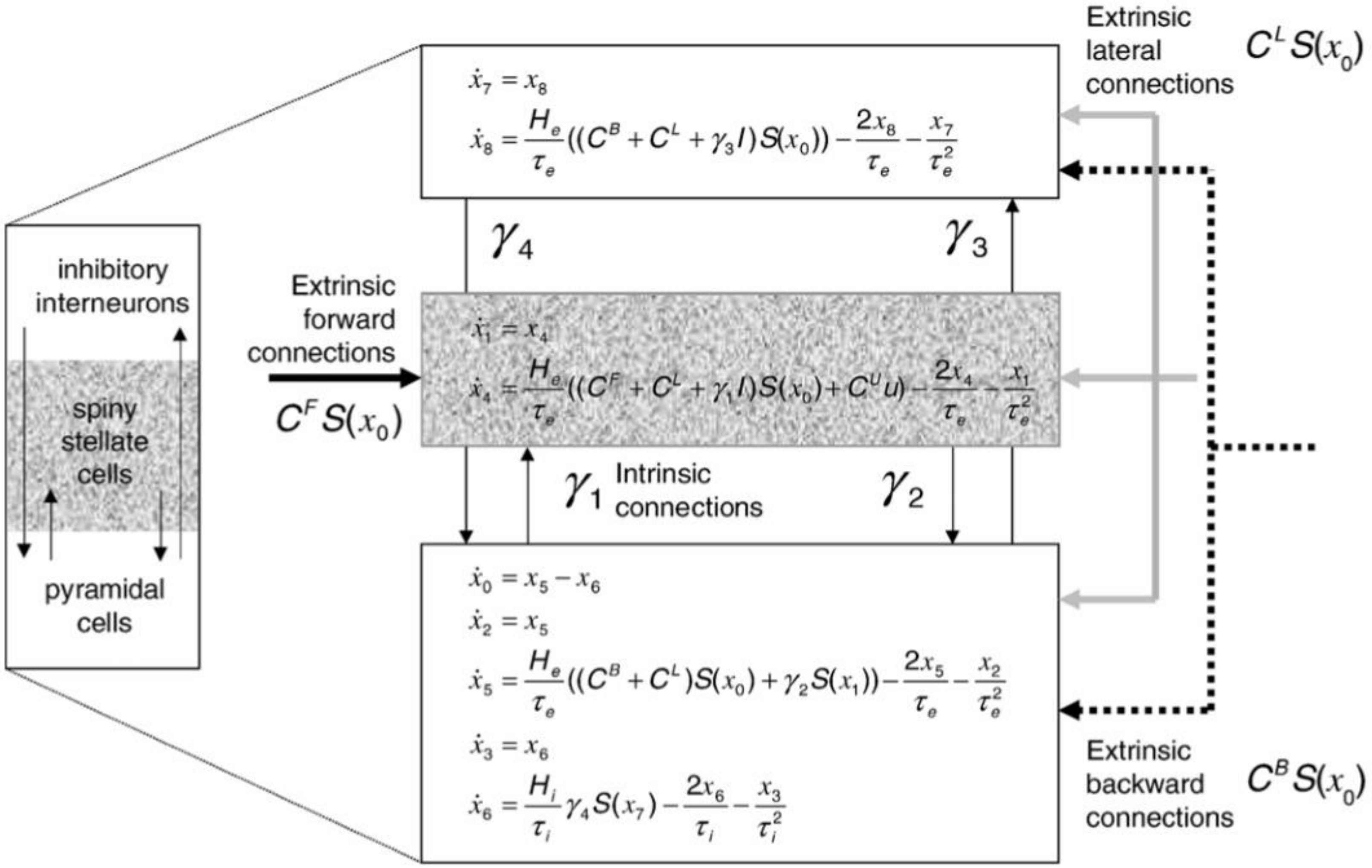
$$k_e A_{back} + k_e A_{lateral} + k_e G$$

$$k_i G$$





G : Coupling strength from to .

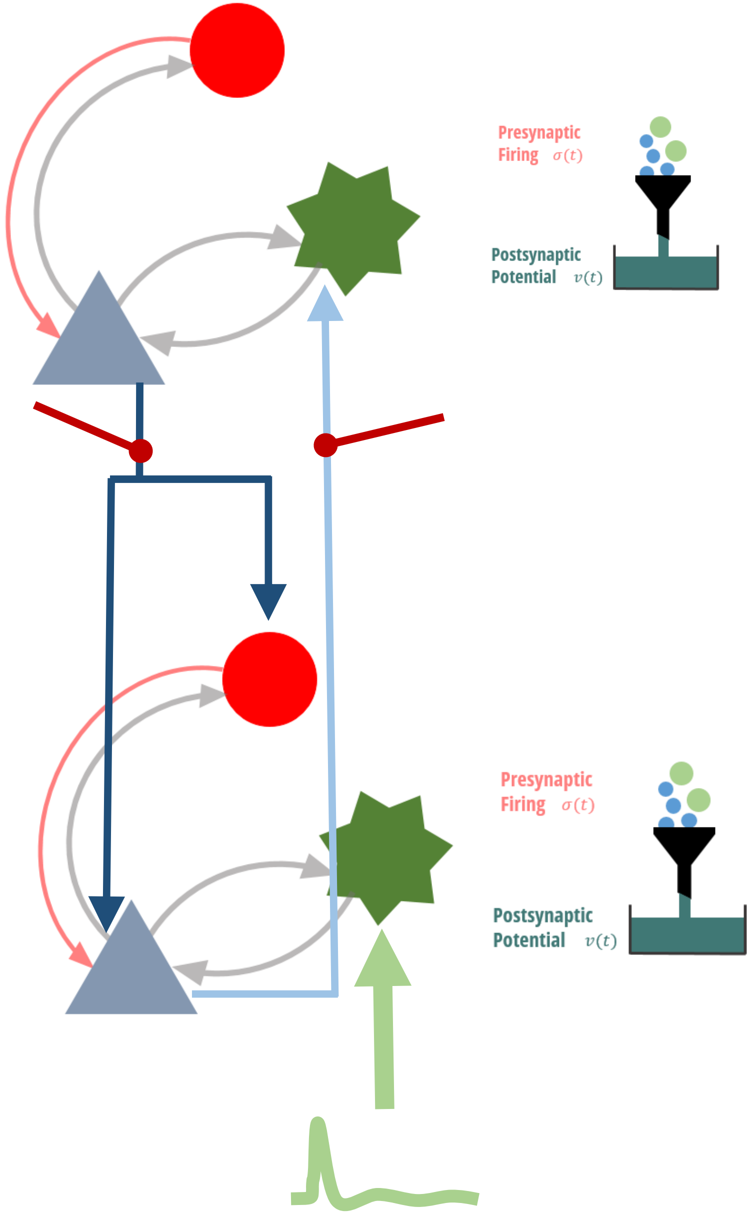


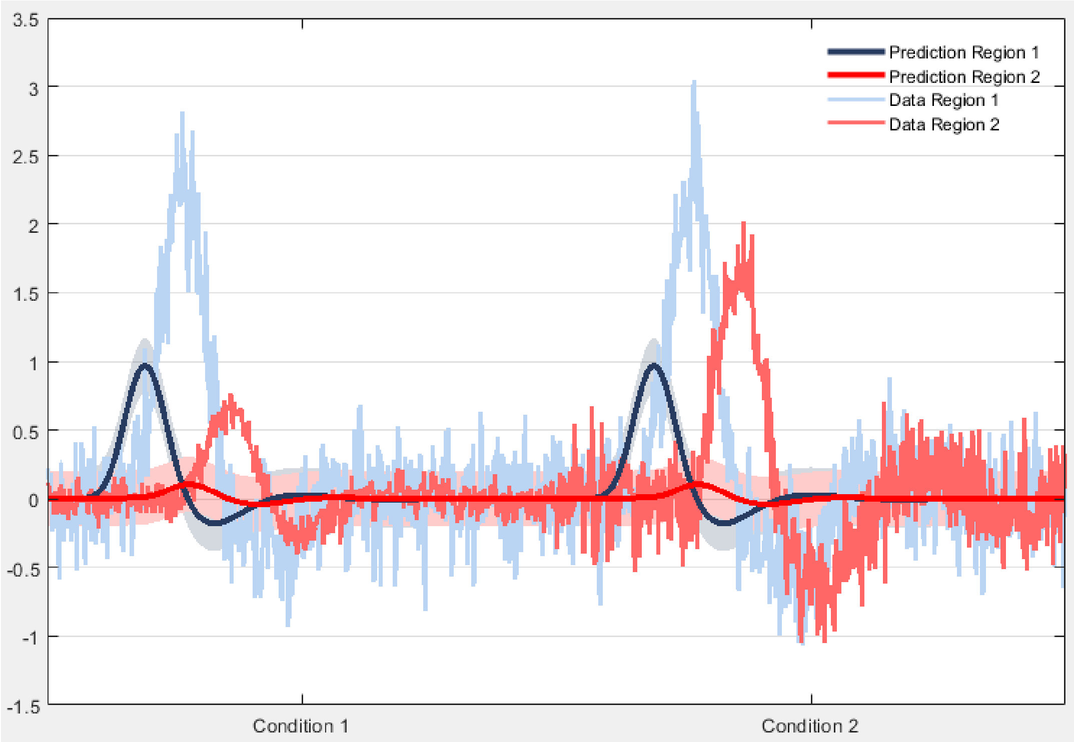
Single source model

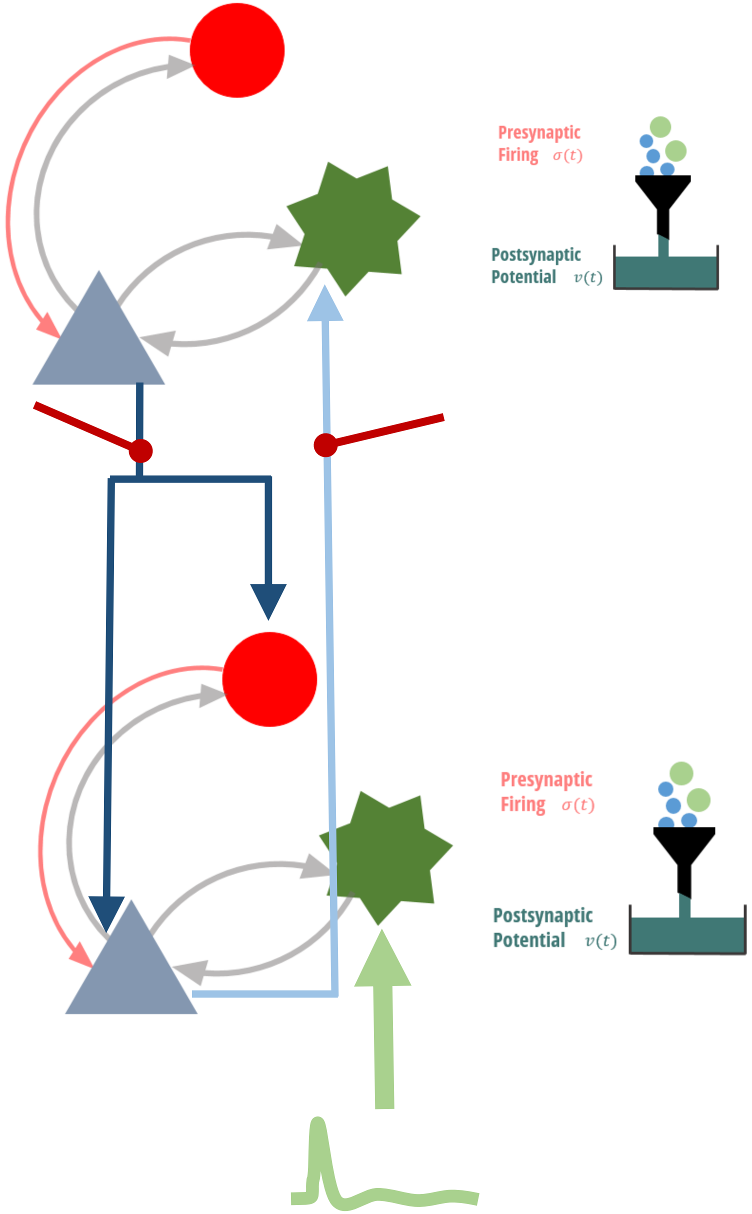
David et al, Neuroimage, 2006

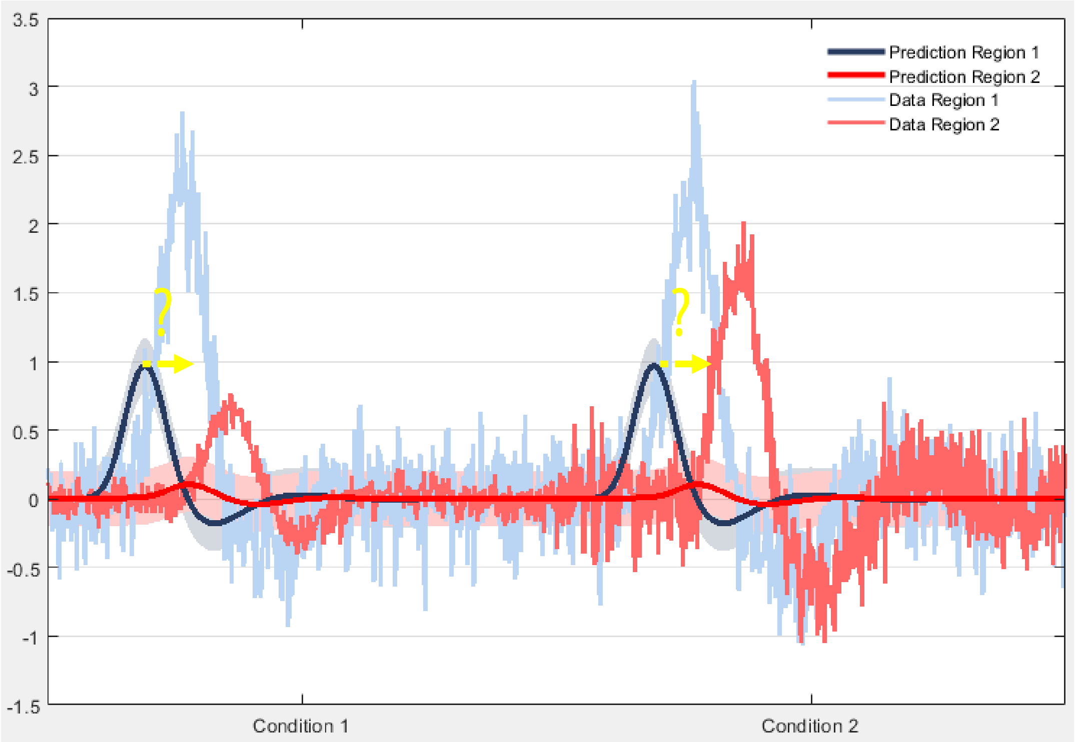
IV. Inferring on parameters

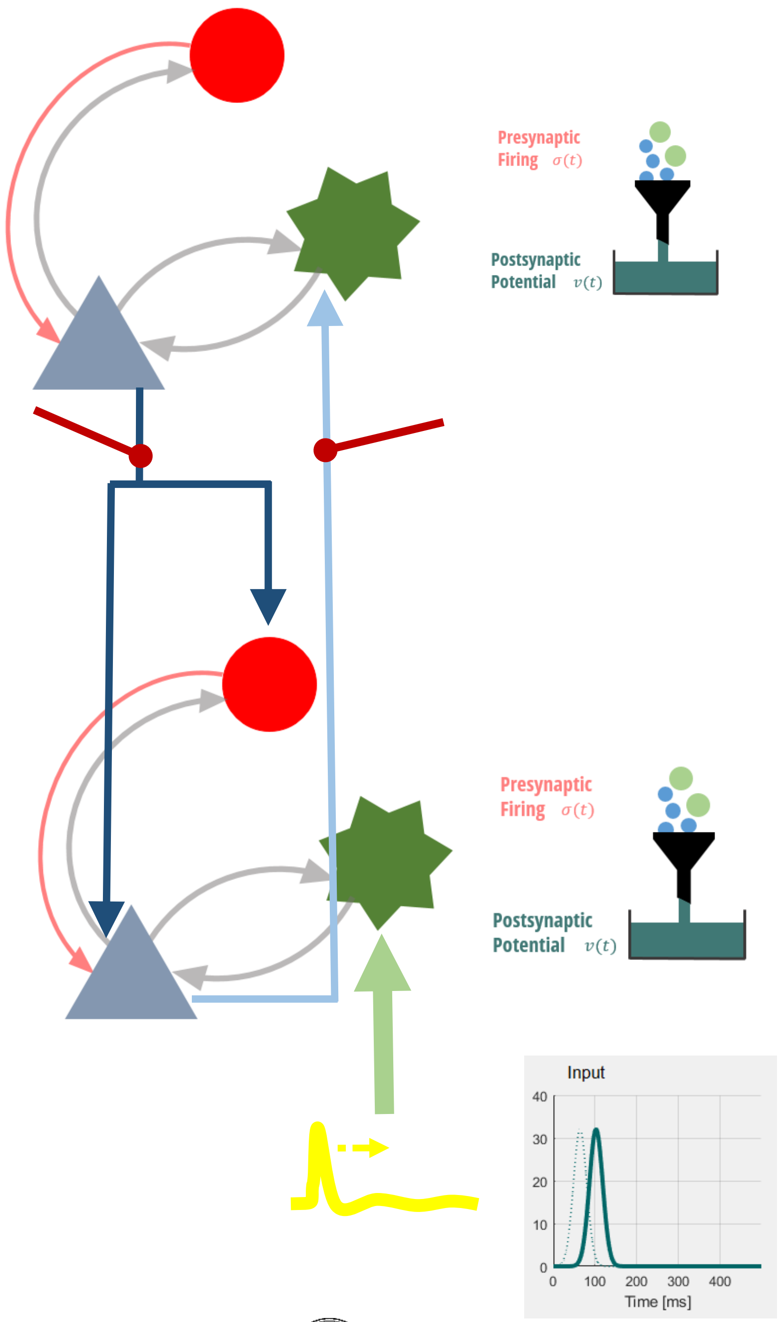
Getting a feeling for how different parameters affect different aspects generated data

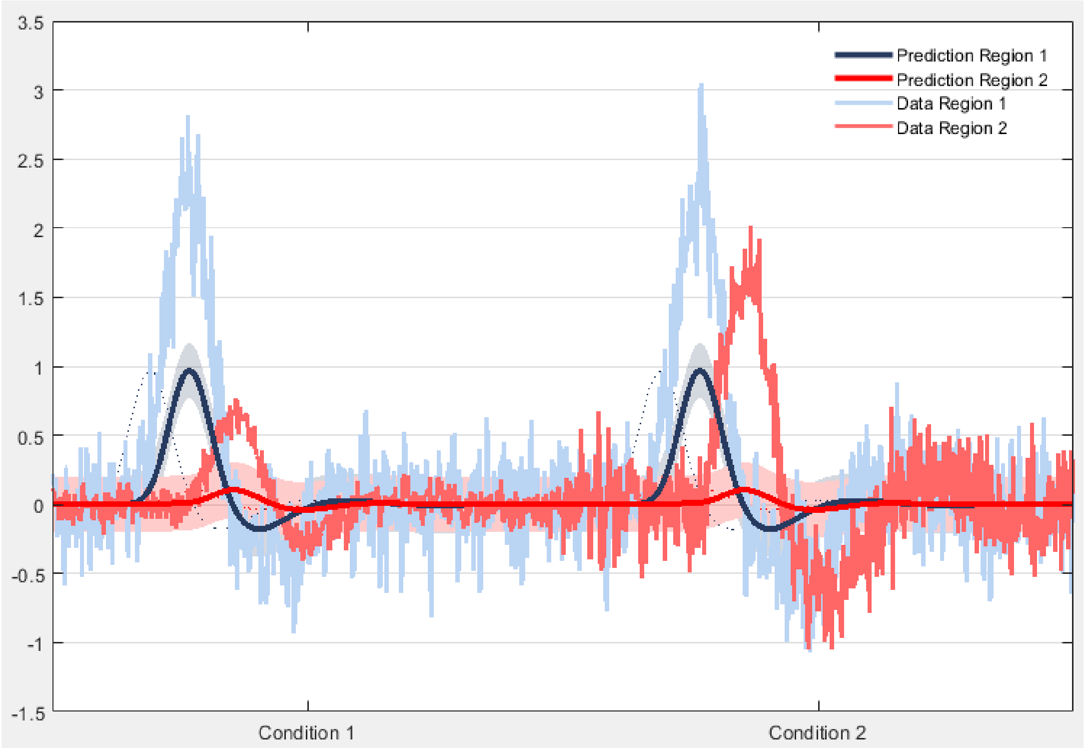

Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$


Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Condition 1
Condition 2


Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$


Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
?
?
Condition 1
Condition 2

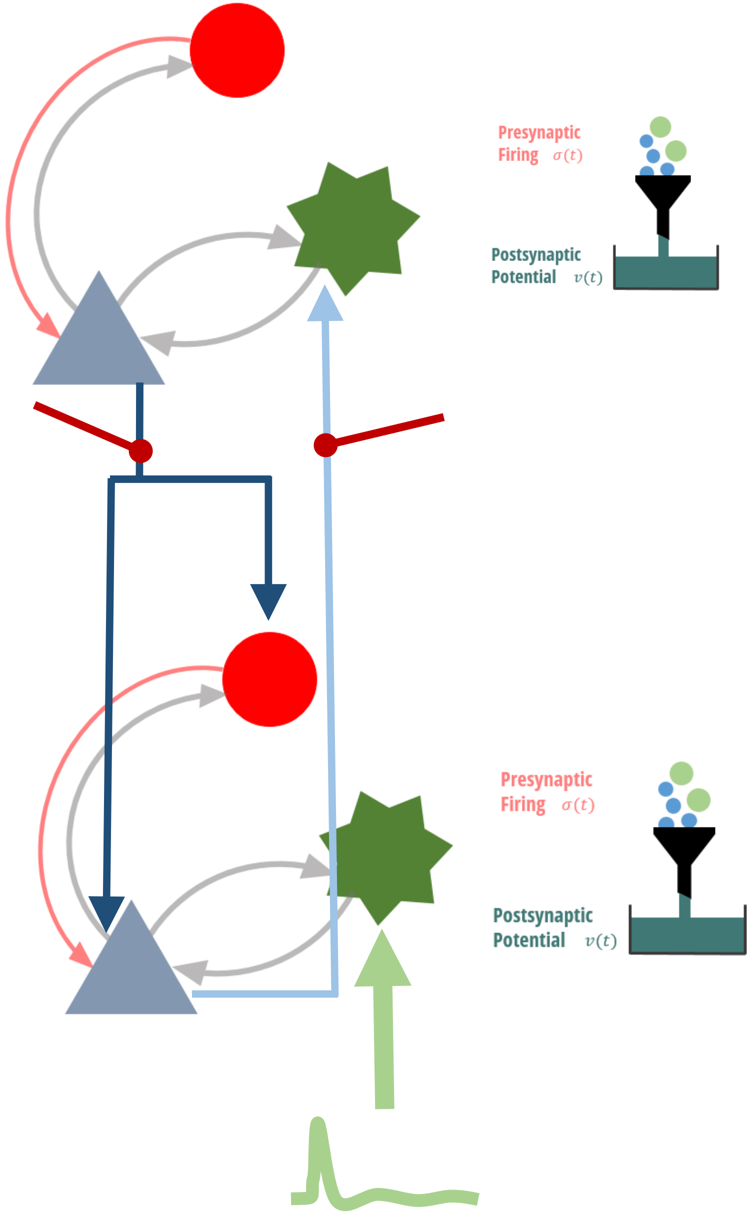




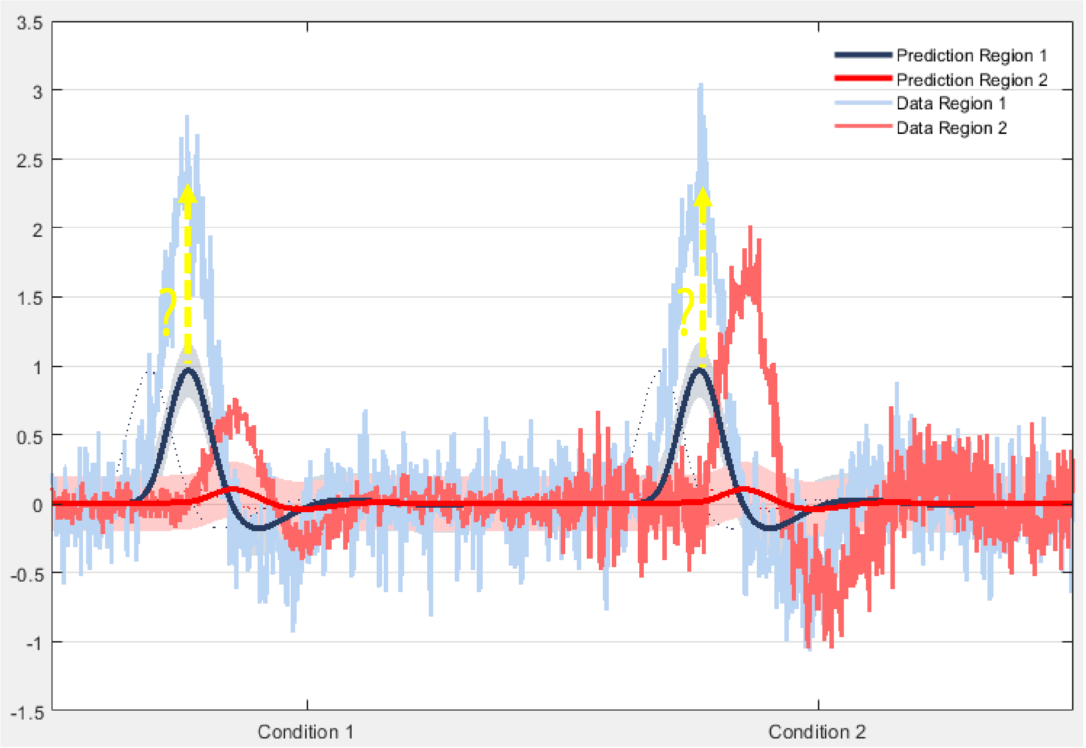
Translational Neuromodeling Unit

University of Zurich[UZH]

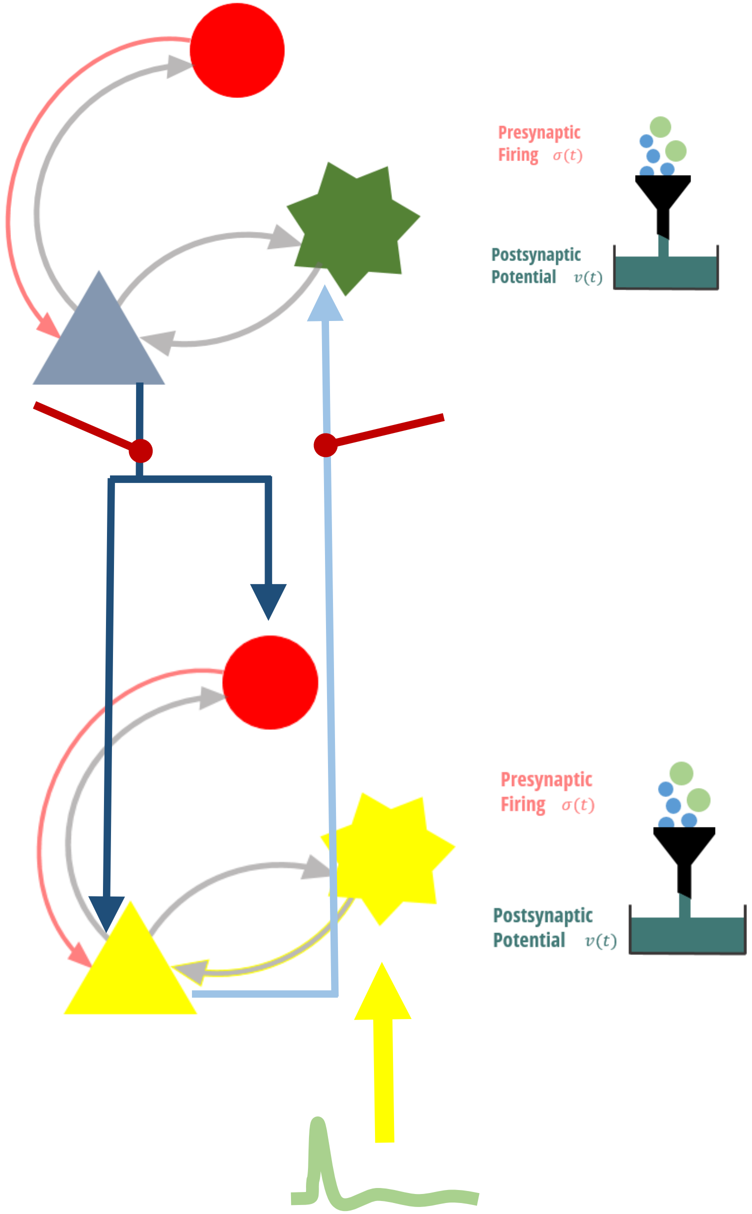
ETH Eidgenössische Technische Hochschule Zürich Swiss Federal Institute of Technology Zurich

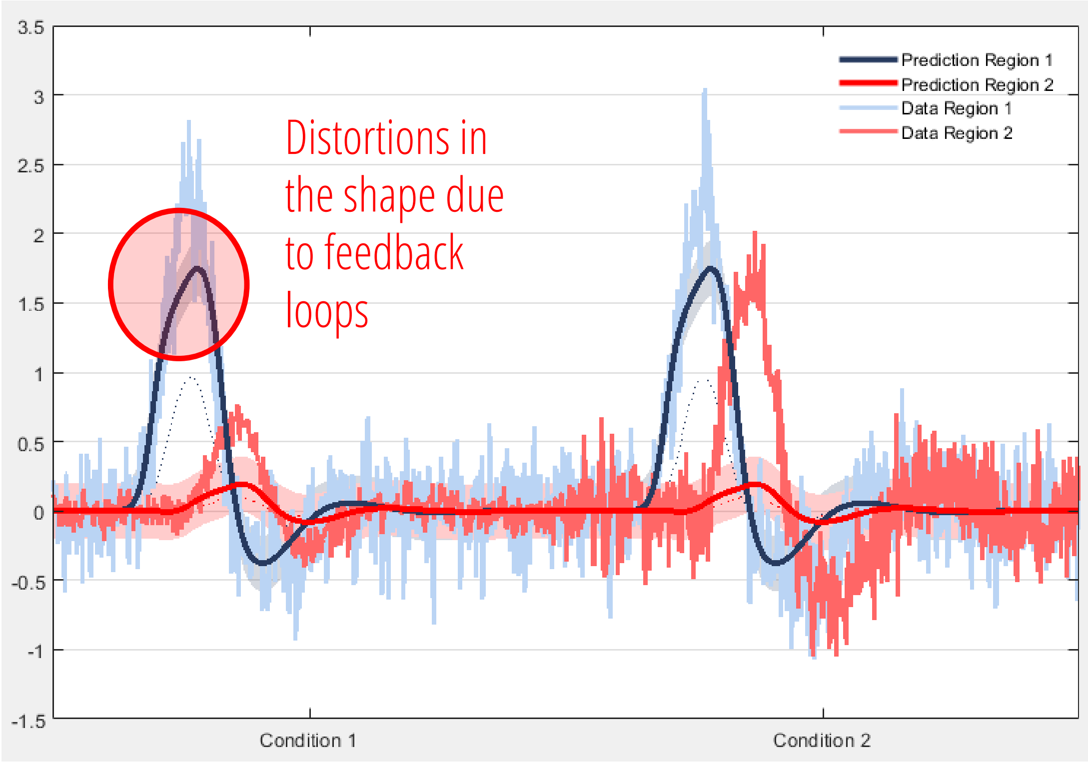


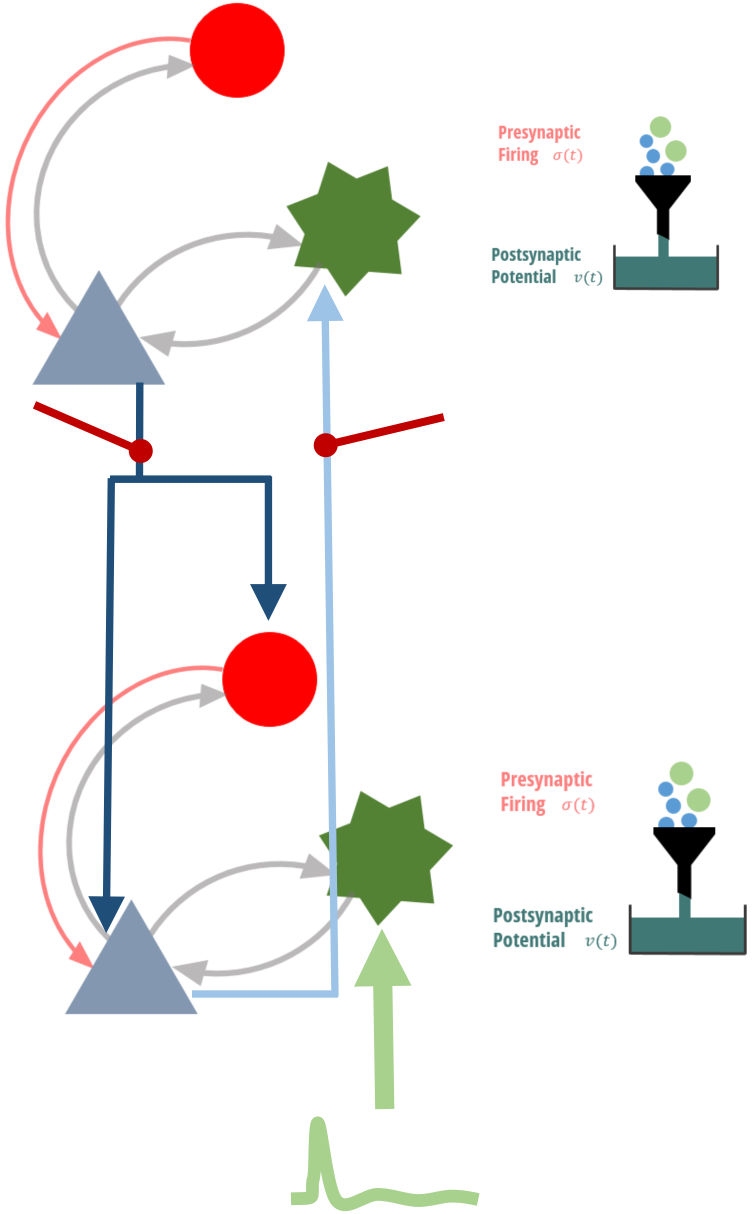
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$

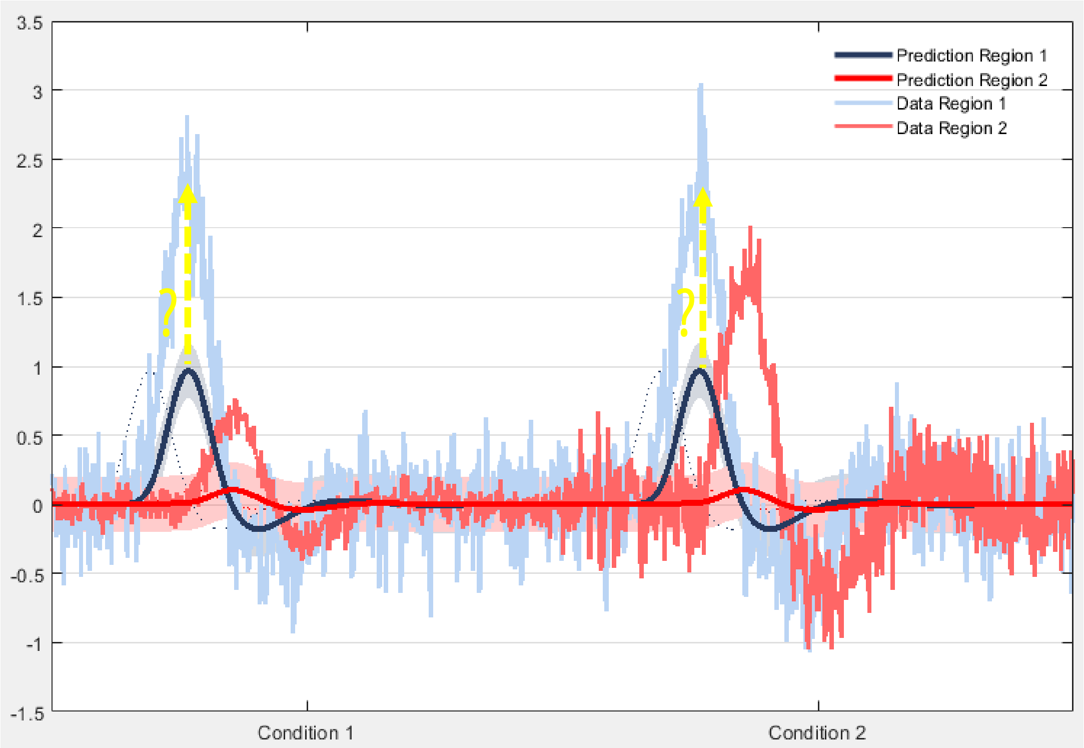


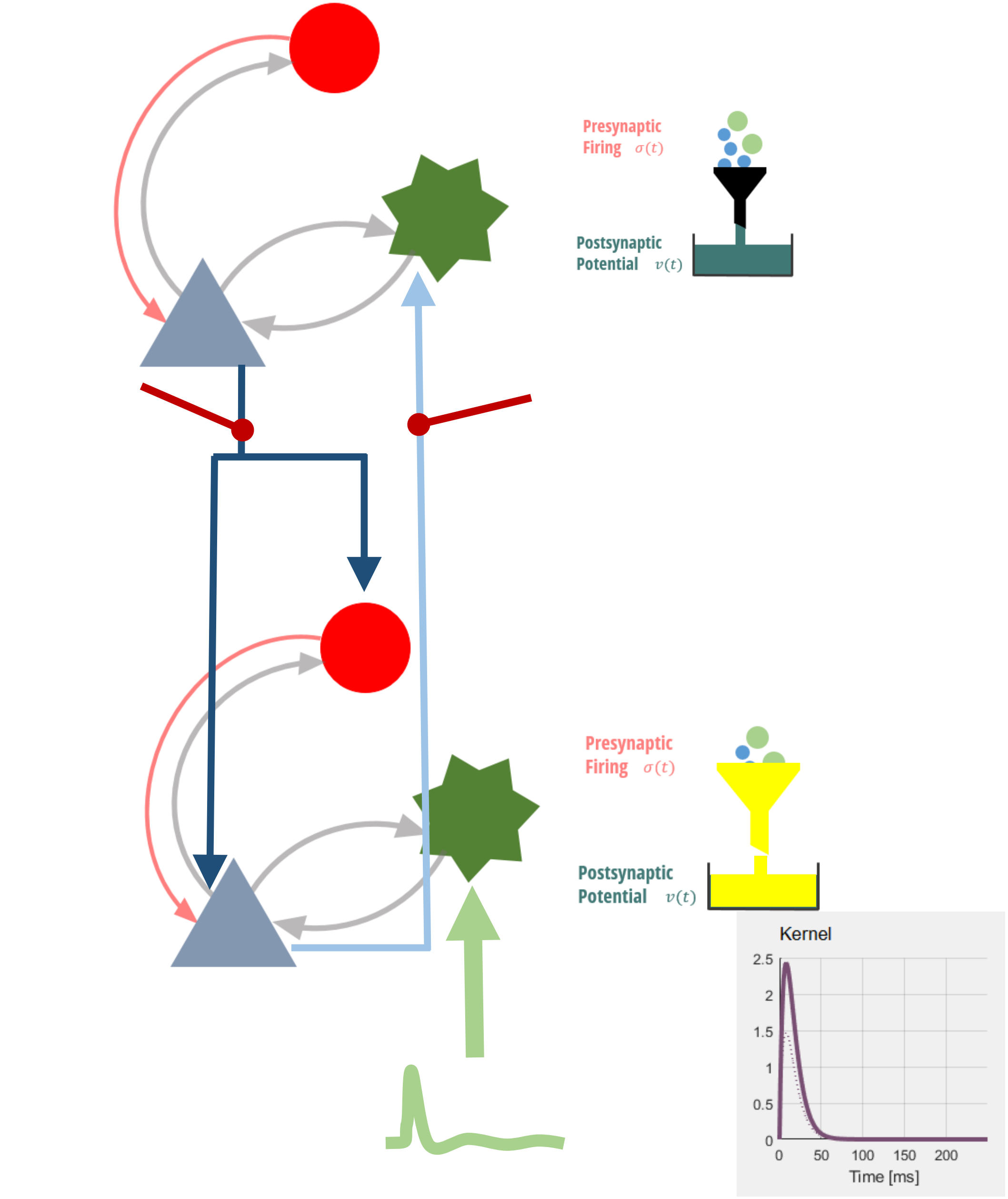
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
?
?
Condition 1
Condition 2

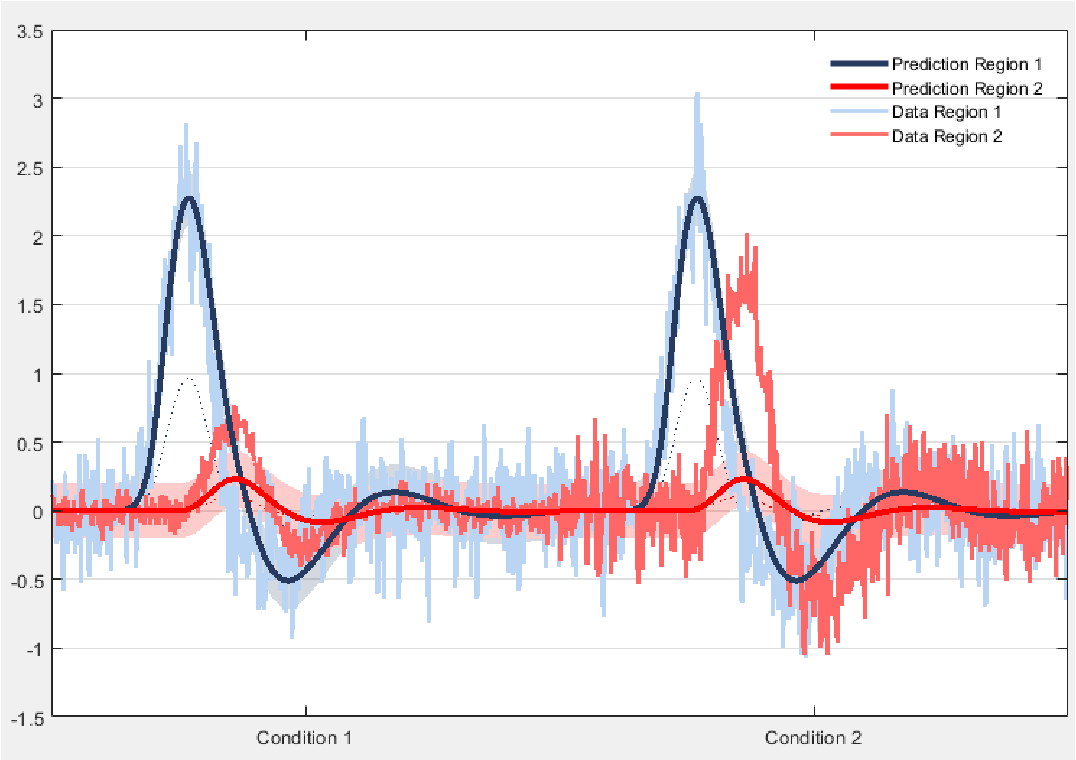

Presynaptic
Firing σ(t)
Postsynaptic
Potential v(t)
Presynaptic
Firing σ(t)
Postsynaptic
Potential v(t)

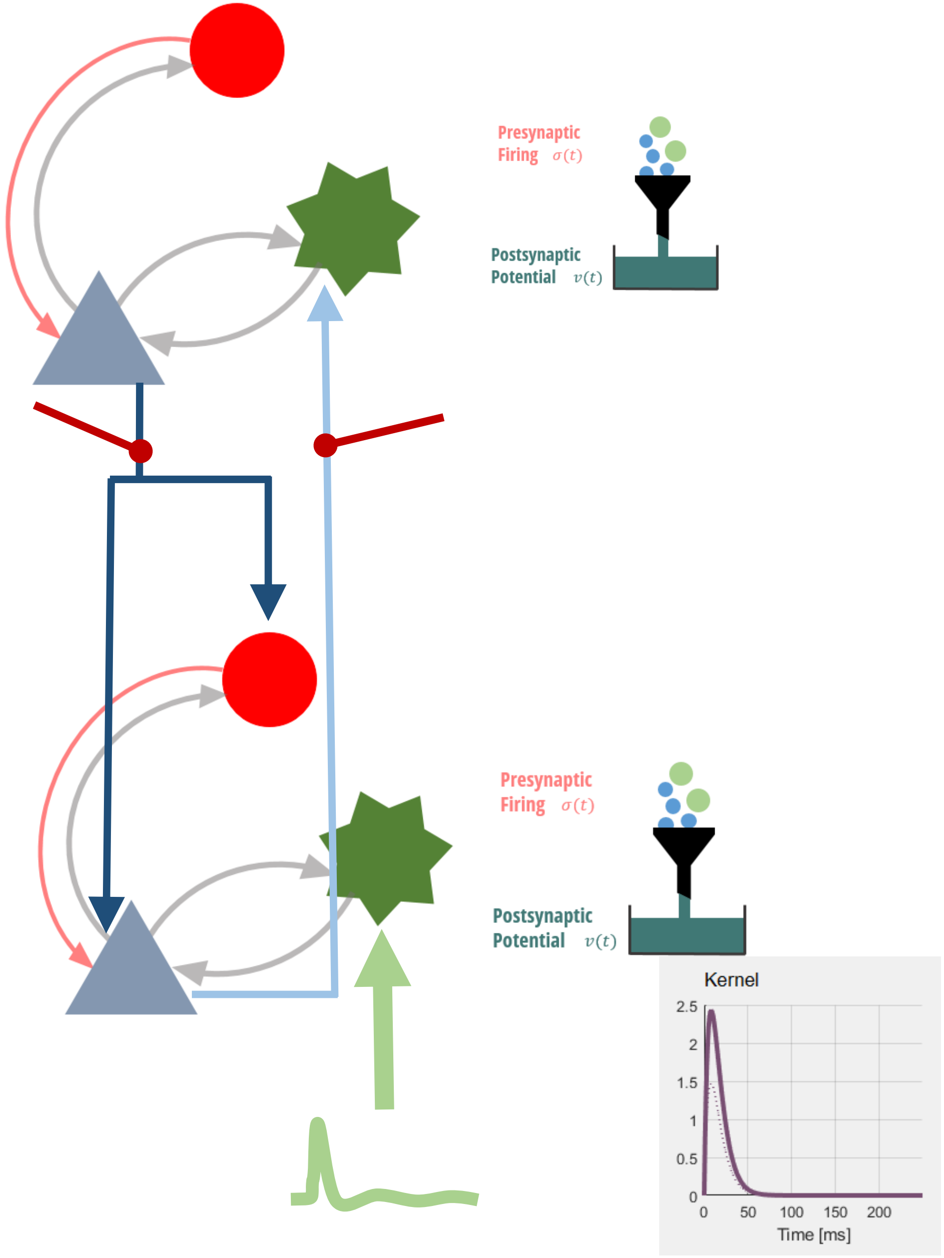

Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
Distortions in the shape due to feedback loops
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Condition 1
Condition 2

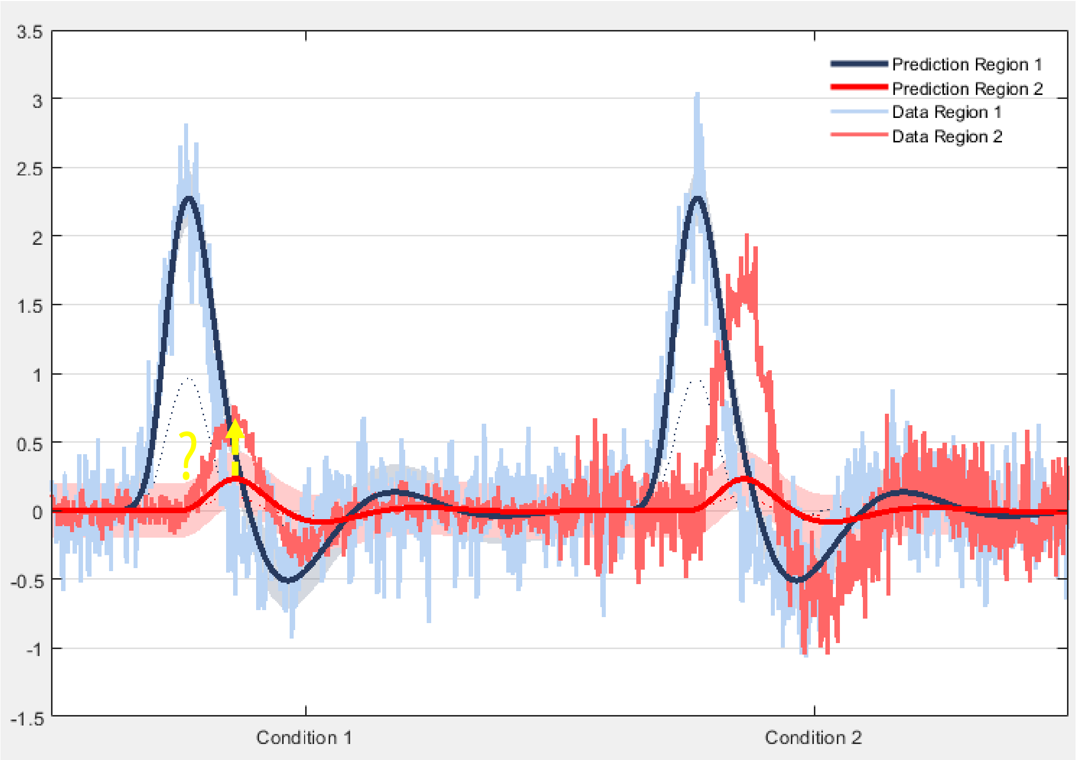

Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$

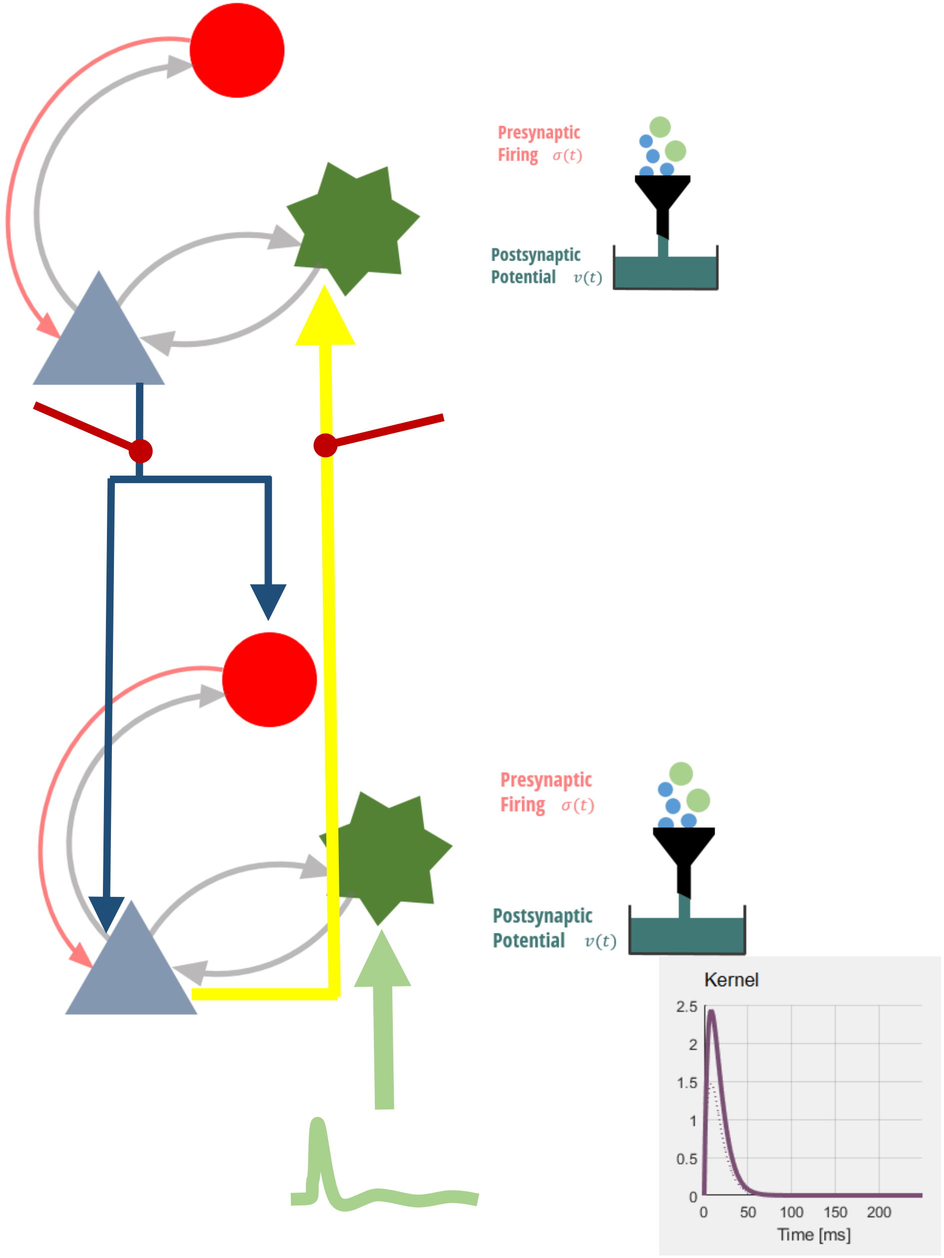

Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Condition 1
Condition 2

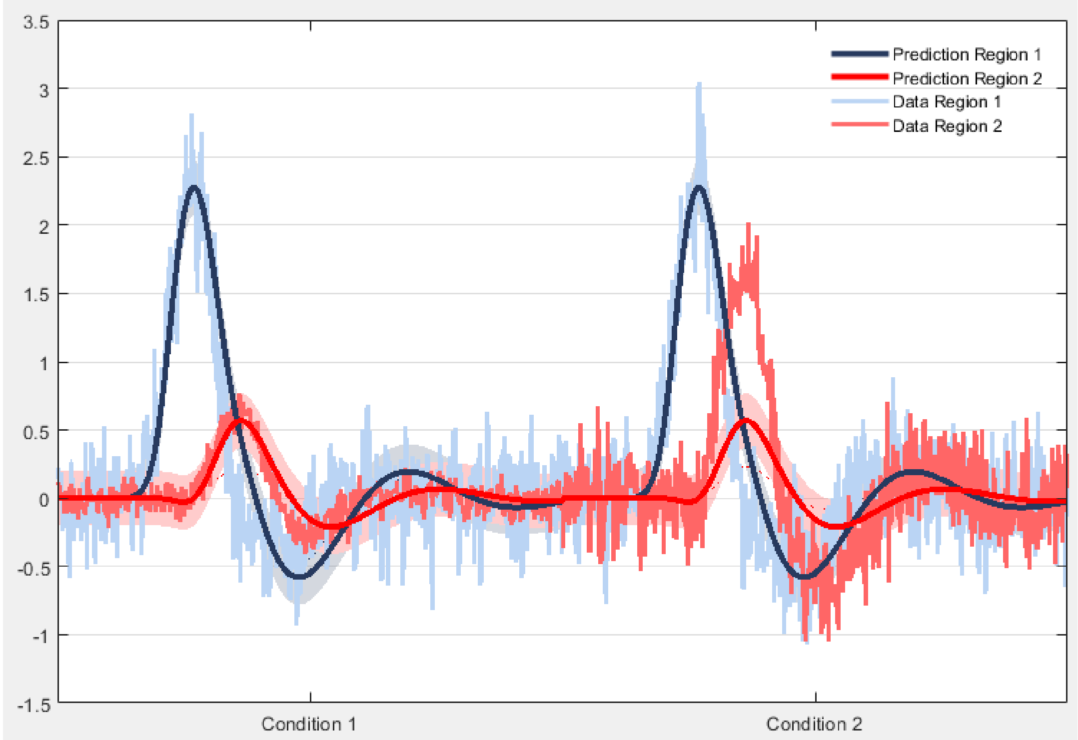

Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Kernel
2.5
2
1.5
1
0.5
0
0
50
100
150
200
Time [ms]


3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
Condition 1
Condition 2


Presynaptic Firing $\sigma(t)$
Postsynaptic Potential $v(t)$
Presynaptic Firing $\sigma(t)$
Postsynaptic Potential $v(t)$
Kernel
2.5
2
1.5
1
0.5
0
0 50 100 150 200
Time [ms]


3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
?
Condition 1
Condition 2

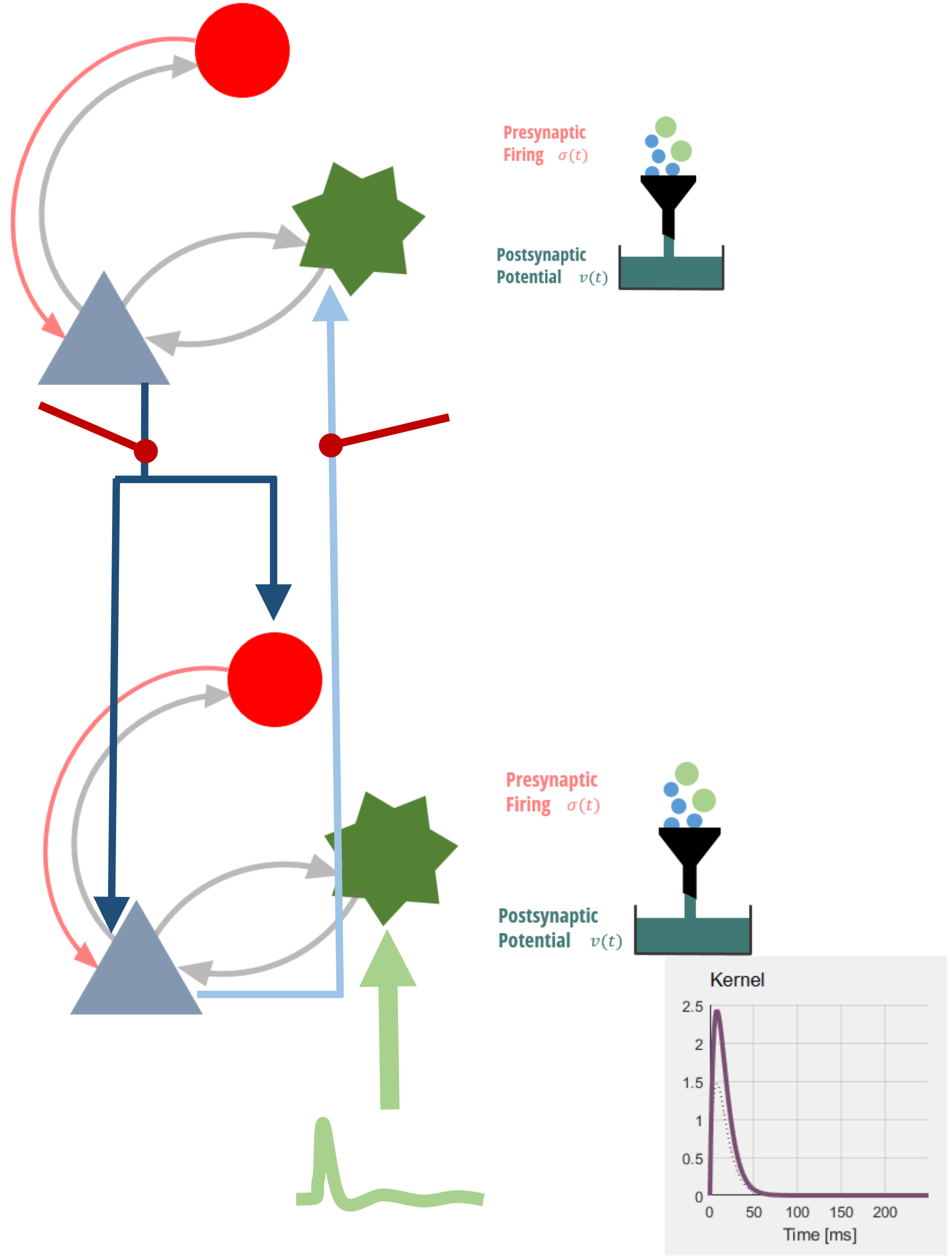


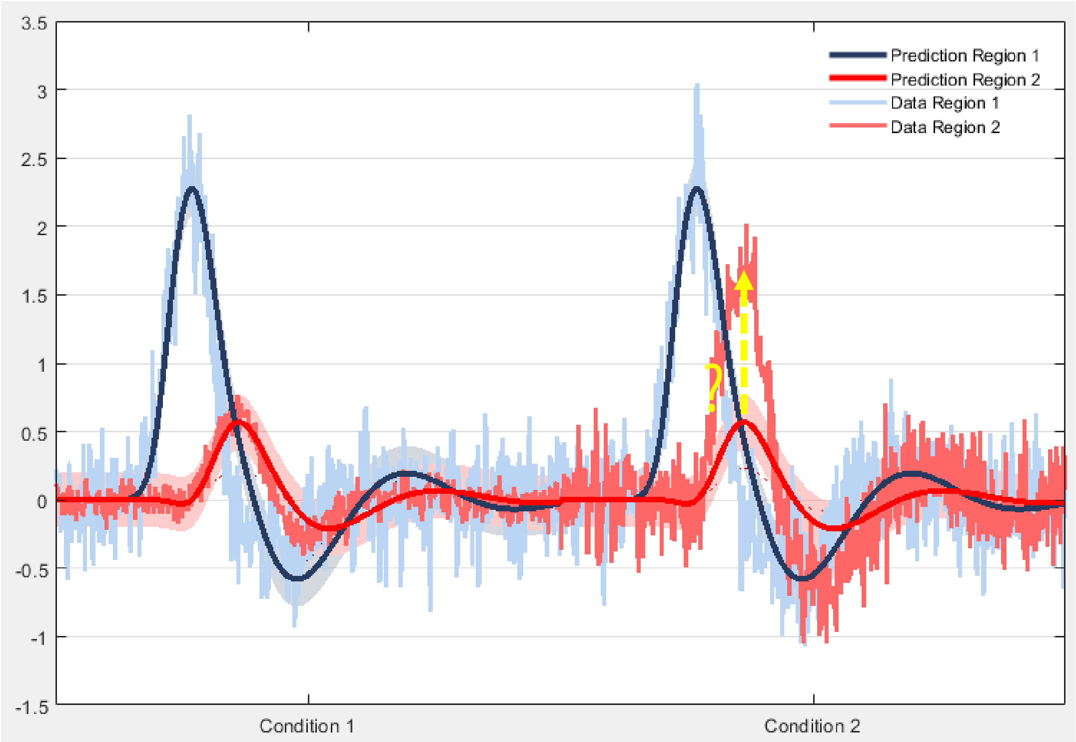


Translational Neuromodeling Unit

University of Zurich[UZH]

ETH Eidgenössische Technische Hochschule Zürich Swiss Federal Institute of Technology Zurich





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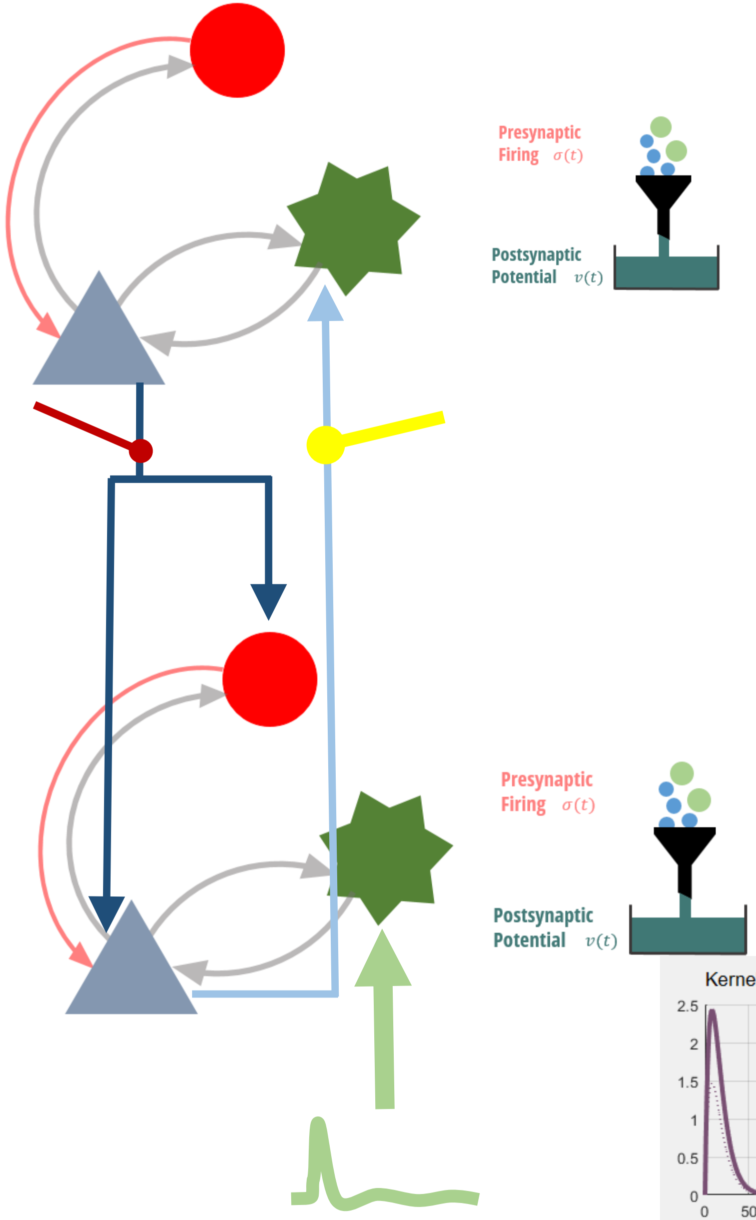

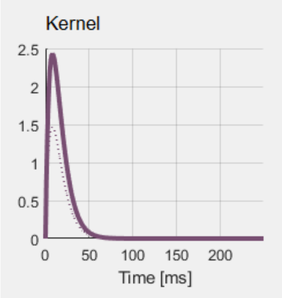

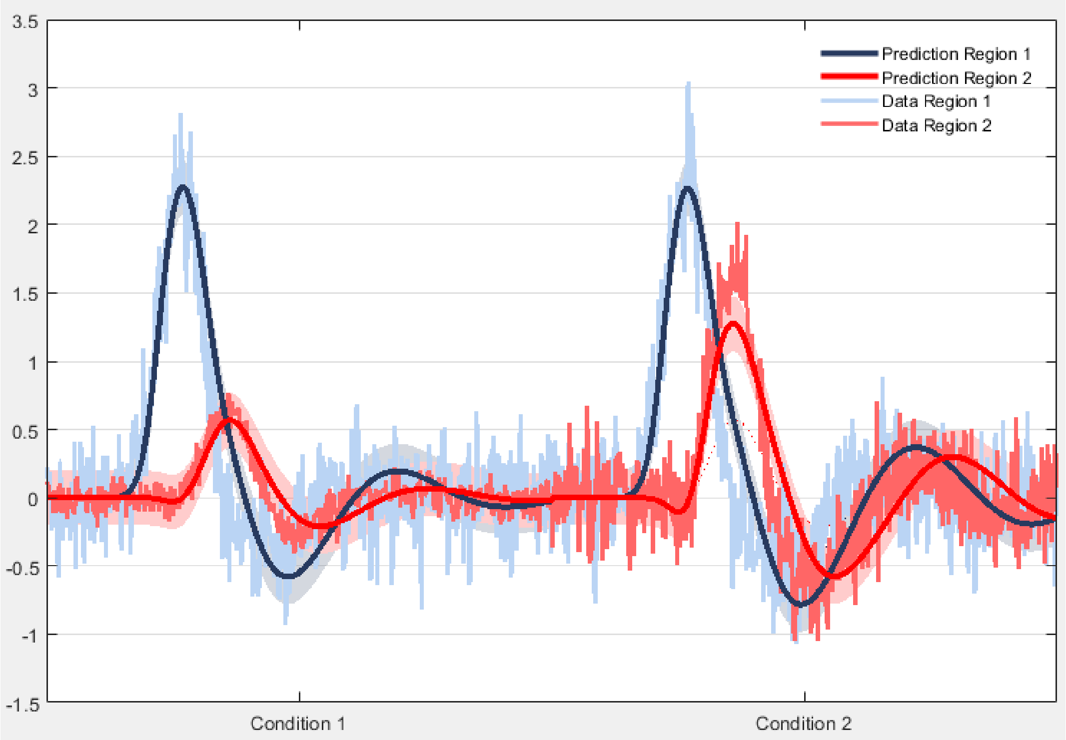

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Inferring on parameters

- Multiple manipulations might lead to similar changes in data features
- One objective measure, which of the competing hypotheses is the best, is Bayesian model selection
- Inference will only be as good as your model and inversion machinery
- Always check results for pitfalls

Inferring on parameters

- Multiple manipulations might lead to similar changes in data features
- One objective measure, which of the competing hypotheses is the best, is Bayesian model selection
- Inference will only be as good as your model and inversion machinery
- Always check results for pitfalls:
    - 'Blindly' trusting inversion results
    - 'Overinterpretation' of single parameter estimates
    - Priors

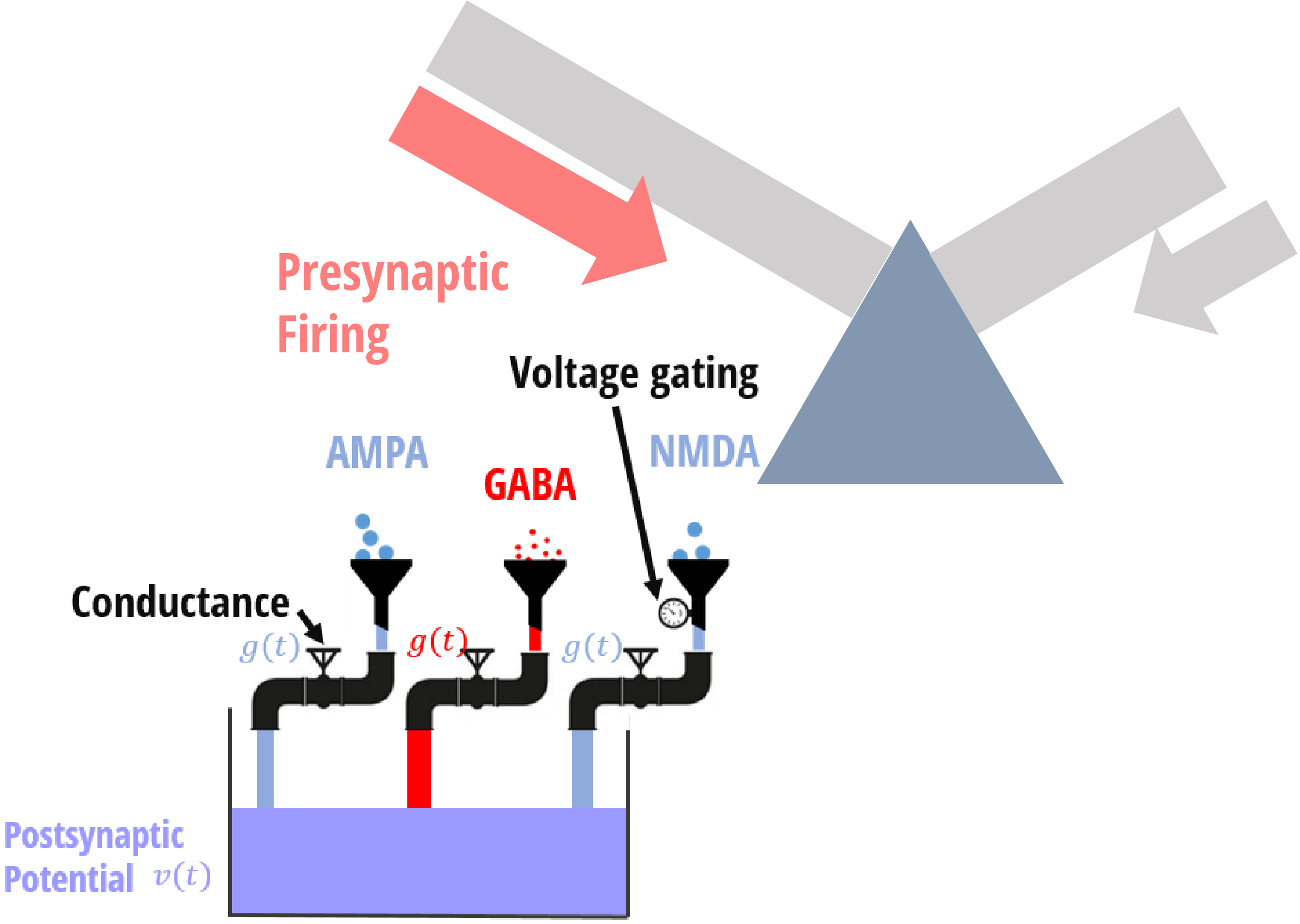
V. Conductance Based DCM

A very brief outlook on modeling synaptic mechanisms much more explicitly

Conductance based DCM

Morris- Lecar (1998)

Hodgkin and Huxley:
Current discharging the capacitor = Current passing through the resistor



S1

Extrinsic Cortical Input (u)

$$C\dot{V}^{(2)} = g_L(V_L - V^{(2)}) + g^{(2)}_{AMPA}(V_E - V^{(2)}) + g^{(2)}_{NMDA} f_{Mg}(V^{(2)})(V_E - V^{(2)}) + \Gamma_V$$
$$\dot{g}^{(2)}_{AMPA} = \kappa_{AMPA}(\gamma_{2,3}\sigma(\mu_V^{(3)} - V_R, \Sigma^{(3)}) - g^{(2)}_{AMPA}) + \Gamma_{AMPA}$$
$$\dot{g}^{(2)}_{NMDA} = \kappa_{NMDA}(\gamma_{2,3}\sigma(\mu_V^{(3)} - V_R, \Sigma^{(3)}) - g^{(2)}_{NMDA}) + \Gamma_{NMDA}$$

$\gamma_{3,2}$ $\gamma_{1,2}$ $\gamma_{2,3}$

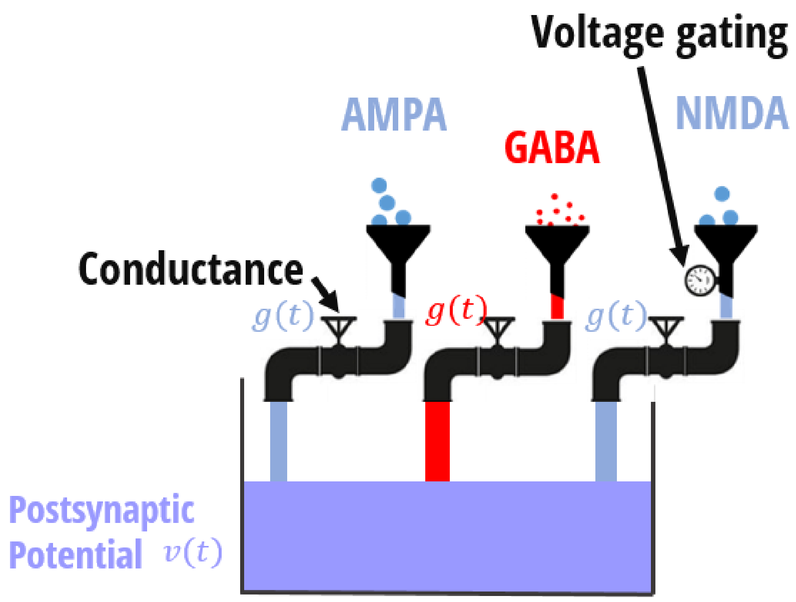
$$C\dot{V}^{(1)} = g_L(V_L - V^{(1)}) + g^{(1)}_{AMPA}(V_E - V^{(1)}) + g^{(1)}_{GABAa}(V_I - V^{(1)}) + u + \Gamma_V$$
$$\dot{g}^{(1)}_{AMPA} = \kappa_{AMPA}(\gamma_{1,3}\sigma(\mu_V^{(3)} - V_R, \Sigma^{(3)}) - g^{(1)}_{AMPA}) + \Gamma_{AMPA}$$
$$\dot{g}^{(1)}_{GABAa} = \kappa_{GABAa}(\gamma_{1,2}\sigma(\mu_V^{(2)} - V_R, \Sigma^{(2)}) - g^{(1)}_{GABAa}) + \Gamma_{GABAa}$$

$\gamma_{1,3}$ $\gamma_{3,1}$

$\gamma_{3,3}$

$$C\dot{V}^{(3)} = g_L(V_L - V^{(3)}) + g^{(3)}_{AMPA}(V_E - V^{(3)}) + g^{(3)}_{NMDA} f_{Mg}(V^{(3)})(V_E - V^{(3)}) + g^{(3)}_{GABAa}(V_I - V^{(3)}) + \Gamma_V$$
$$\dot{g}^{(3)}_{AMPA} = \kappa_{AMPA}([\gamma_{3,1}\sigma(\mu_V^{(1)} - V_R, \Sigma^{(1)}) + \gamma_{3,3}\sigma(\mu_V^{(3)} - V_R, \Sigma^{(3)})] - g^{(3)}_{AMPA}) + \Gamma_{AMPA}$$
$$\dot{g}^{(3)}_{NMDA} = \kappa_{NMDA}([\gamma_{3,1}\sigma(\mu_V^{(1)} - V_R, \Sigma^{(1)}) + \gamma_{3,3}\sigma(\mu_V^{(3)} - V_R, \Sigma^{(3)})] - g^{(3)}_{NMDA}) + \Gamma_{NMDA}$$
$$\dot{g}^{(3)}_{GABAa} = \kappa_{GABAa}(\gamma_{3,2}\sigma(\mu_V^{(2)} - V_R, \Sigma^{(2)}) - g^{(3)}_{GABAa}) + \Gamma_{GABAa}$$

Moran et al, Current Biology, 2011



Current state of the population.

How much firing arrives (and from where).

NMDA Voltage Gate

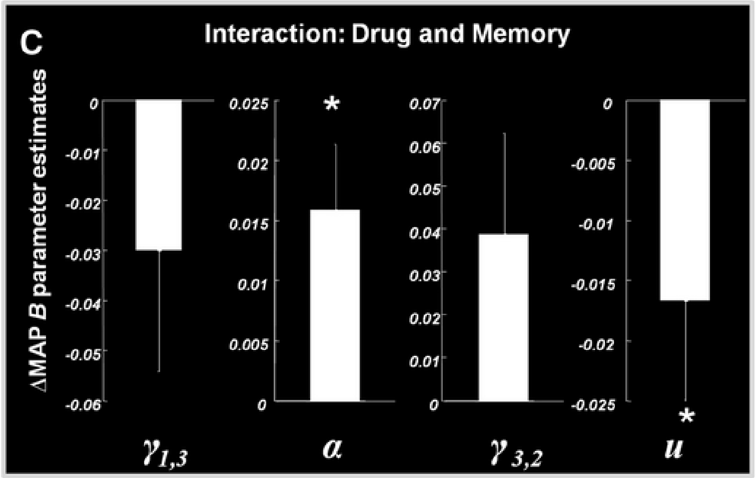
$$\frac{dx}{dt} = f(x, A, H, C, \sigma, g(t), \Pi)$$

What the cell population is connected to.

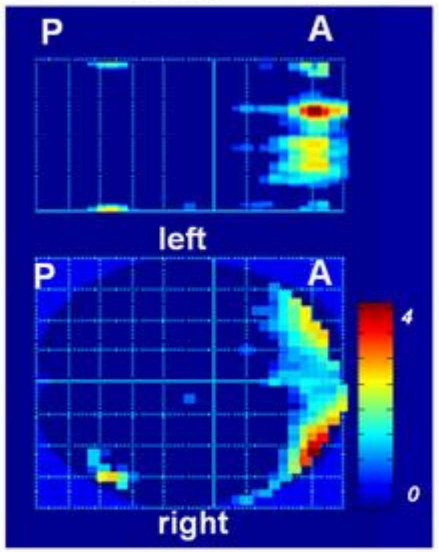
Resistance of the channels.

Study 1: Inferring on synaptic parameters

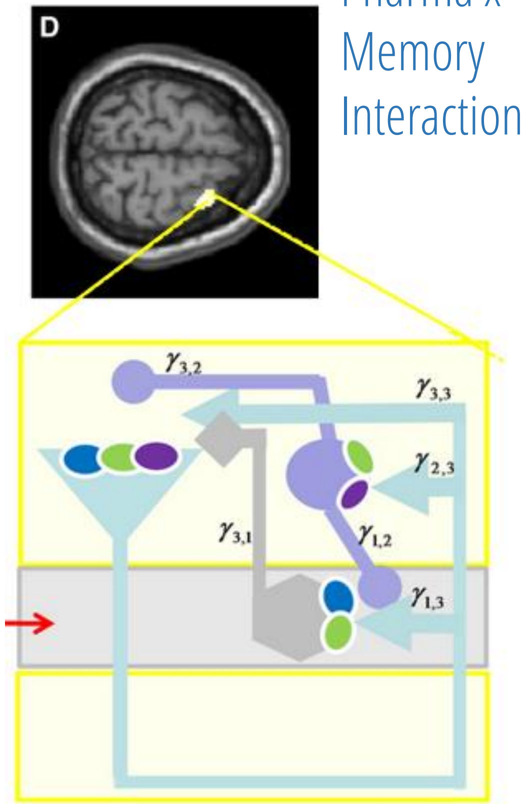
Hypotheses about parameter changes under pharma



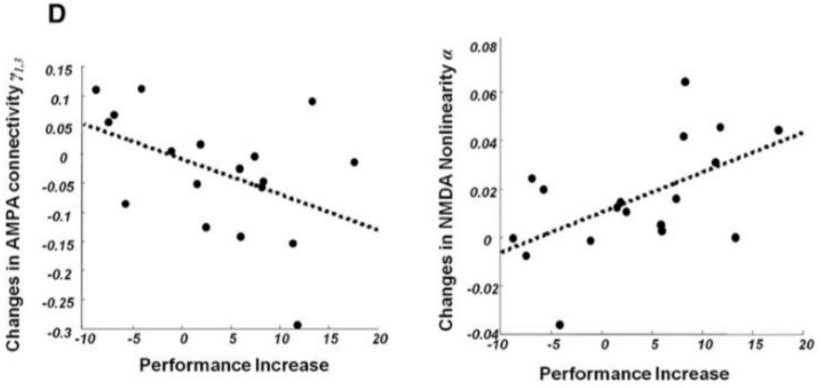
Working Memory activation



Pharma x Memory Interaction



Inferred parameters predict behavior



Moran et al, Current Biology, 2011

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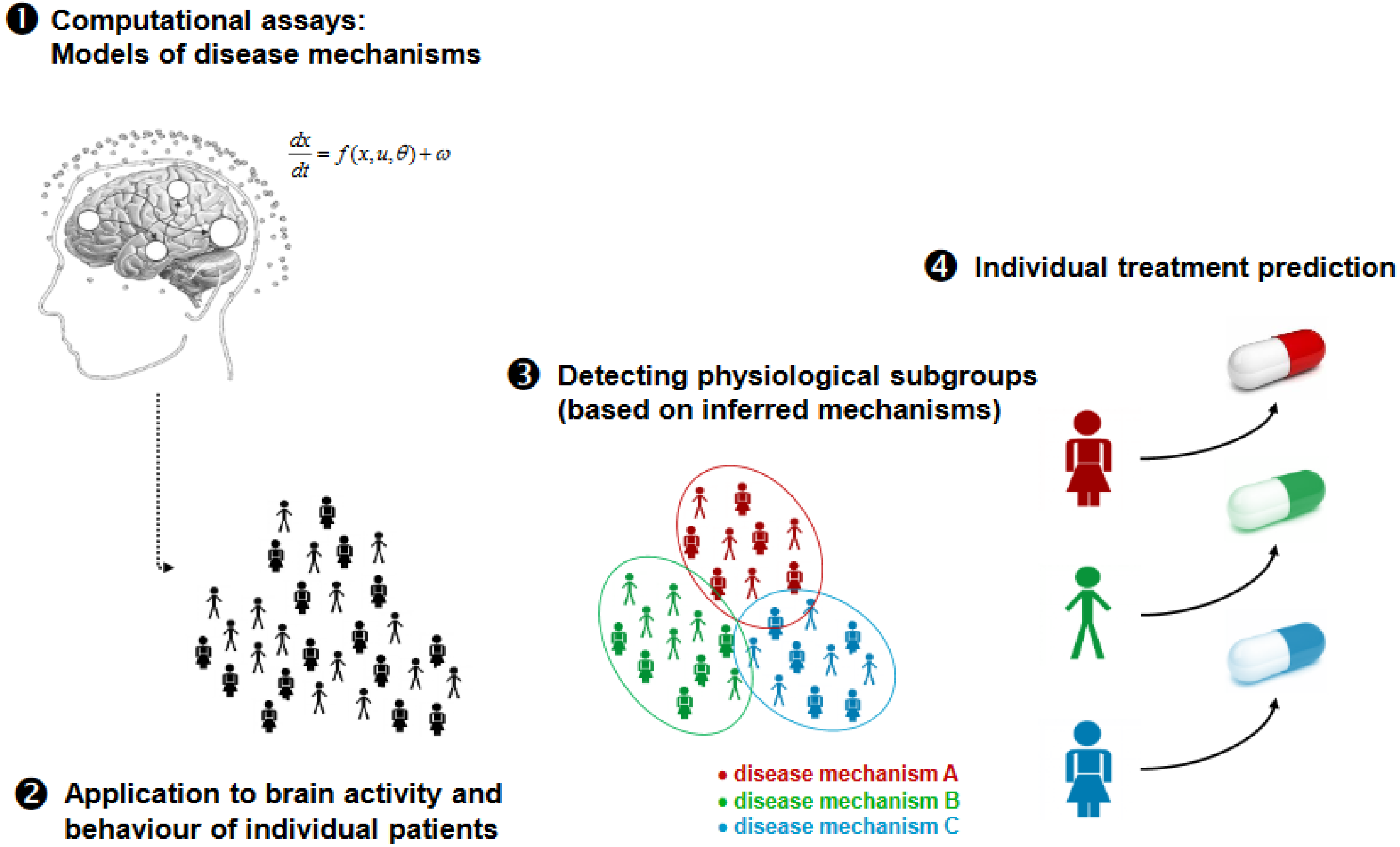
VI. Importance for computational psychiatry

Testable hypotheses from ‘cheap’, ‘fast’, ‘simple’ and non-invasive measurements



Stephan et al. 2015, *Neuron*

One can only infer on mechanisms,
that have actually been modeled.

Data

(Hidden) Neuronal Model

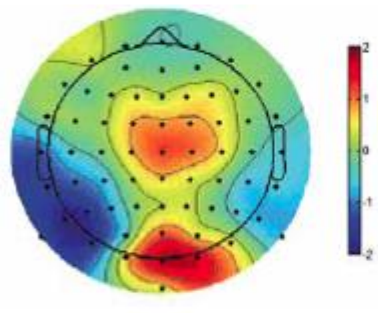
Inverse Problem: Inference

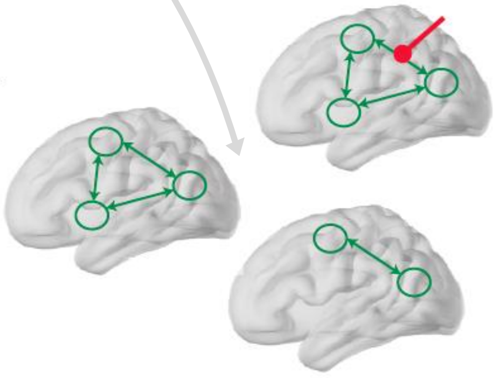
$$p(\theta, \Sigma | y)$$

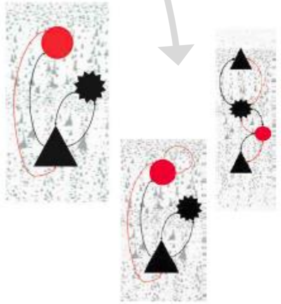
macroscale

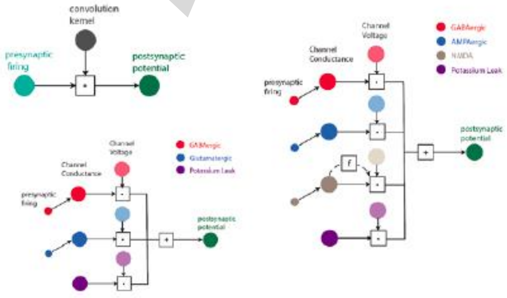
mesoscale

microscale









Forward model: Likelihood

$$y = g(x, \theta) + \varepsilon$$

Data Features

Network of cortical sources and modulation of connection strength

Structure of the cortical column

Mechanisms governing generation of average post-synaptic potentials

MANY THANKS TO STEFAN FRÄSSLE ,
JAKOB HEINZLE AND KLAAS ENNO STEPHAN
FOR SOME OF THE SLIDES!