camh
Centre for Addiction and Mental Health

Krembil Centre for Neuroinformatics

Using big data, artificial intelligence and brain modelling to fundamentally change our understanding of mental illness.

SUMMER SCHOOL 2021

Day 6

Bayesian Models of Learning and Integration of Neuroimaging

CAMH Land Acknowledgement

CAMH is situated on lands that have been occupied by First Nations for millennia; lands rich in civilizations with knowledge of medicine, architecture, technology, and extensive trade routes throughout the Americas. In 1860, the site of CAMH appeared in the Colonial Records Office of British Crown as the council grounds of the Mississaugas of the New Credit, as they were known at the time.

Today, Toronto is covered by the Toronto Purchase, treaty No. 13 of 1805 with the Mississaugas of the Credit.

Toronto is now home to a vast diversity of First Nations, Inuit, and Métis who enrich this city.

CAMH is committed to reconciliation. We will honour the land through programs and places that reflect and respect its heritage. We will embrace the healing traditions of the Ancestors, and weave them into our caring practices. We will create new relationships and partnerships with First Nations, Inuit, and Métis and share the land and protect it for future generations.

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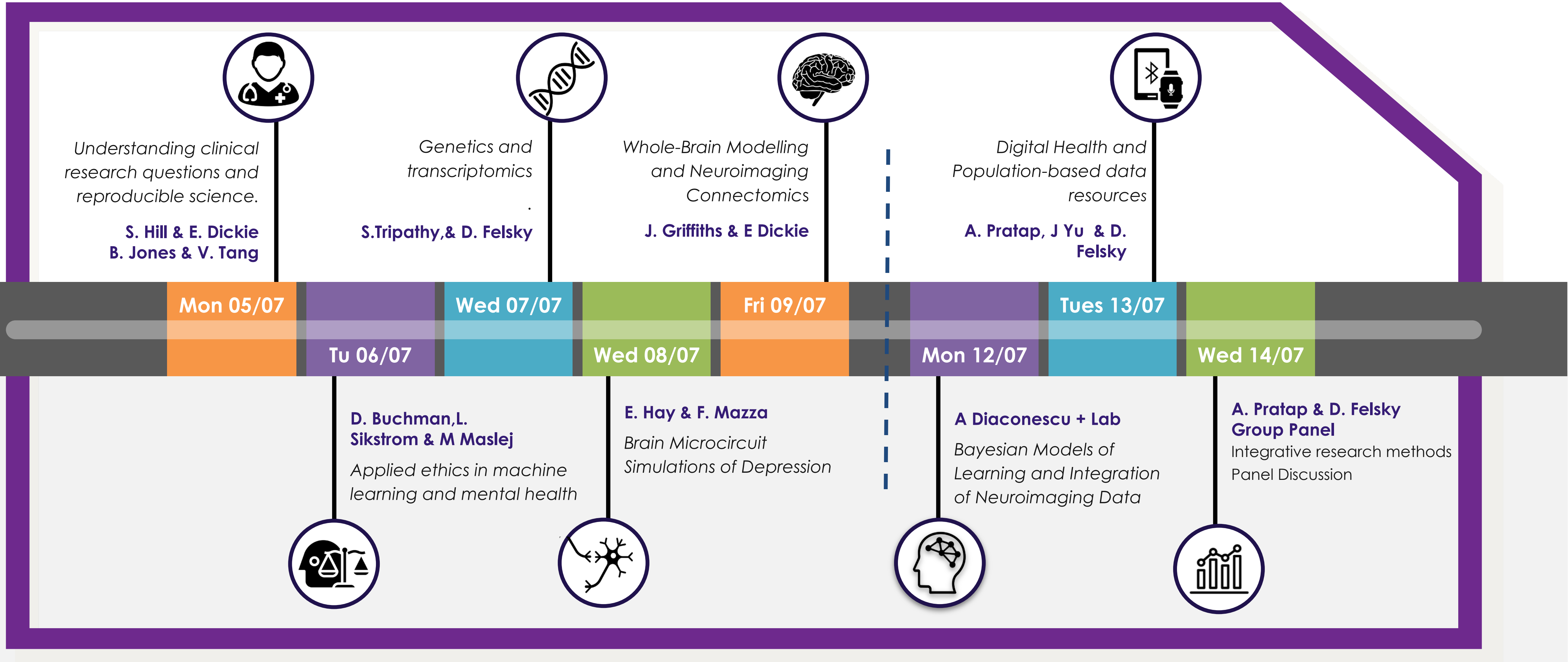
camh Shkaabe Makwa



Understanding clinical research questions and reproducible science.
S. Hill & E. Dickie
B. Jones & V. Tang
Mon 05/07
Tu 06/07
D. Buchman,L. Sikstrom & M Maslej
Applied ethics in machine learning and mental health
Genetics and transcriptomics
S.Tripathy,& D. Felsky
Wed 07/07
Wed 08/07
E. Hay & F. Mazza
Brain Microcircuit Simulations of Depression
Whole-Brain Modelling and Neuroimaging Connectomics
J. Griffiths & E Dickie
Fri 09/07
Mon 12/07
A Diaconescu + Lab
Bayesian Models of Learning and Integration of Neuroimaging Data
Digital Health and Population-based data resources
A. Pratap, J Yu & D. Felsky
Tues 13/07
Wed 14/07
A. Pratap & D. Felsky
Group Panel
Integrative research methods
Panel Discussion

Today's Agenda

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Day 6: Bayesian Models of Learning and Integration of Neuroimaging

9:00 am - 10:30 am	*Modelling Cognition using Bayesian Inference* Andreea Diaconescu
10:45 am - 12:15 pm	*Modelling Abnormal Beliefs* Daniel Hauke
1:00 pm - 2:30 pm	*Integration of Neuroimaging: Dynamic Causal Modelling for fMRI and EEG Data* Andreea Diaconescu, Colleen Charlton
2:45 pm - 4:15 pm	*Dynamic Causal Modelling for fMRI: Extensions and Simulations* Peter Bedford, Povilas Karvelis

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Visit GitHub Page: Day 6

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Day 6: Bayesian Models of Learning and Integration of Neuroimaging Data (July 12, 2021)

Instructors: Dr. Andreea Diaconescu

TA's: Colleen Charlton, Daniel Hauke, Peter Bedford, Povilas Karvelis

Compute Environment: MATLAB.

- All students in the interactive stream should have been emailed a link to a temporary MATLAB license that can be used for this course. Contact KCNI.School@camh.ca with any questions.
- Additional setup instructions are available in the day6 folder

Time (EST)	Session	
9:00-10:30	Lecture 1: Modelling Cognition using Bayesian Inference	Watch on Crowdcast
10:45-12:15	Tutorial 1: Modelling Abnormal Beliefs (Delusions)	Watch on Crowdcast
12:15pm-1:00pm	Lunch Break	Join us in gather.town
1:00-2:30pm	Lecture 2: Integration of Neuroimaging and Electrophysiological Data	Watch on Crowdcast
2:45-4:15pm	Tutorial 2: Modelling Neuroimaging Data	Watch on Crowdcast
4:30-5:00pm	Daily Social Chat? / Q & A	Join us in gather.town

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MATLAB code accompanying Day 6 of the KCNI school

This code runs on MATLAB R2020a, the license provided with this course. Please, contact the teacher or the TAs if you do not have access to this license.

Getting Started

1. Please, clone this repository recursively. Otherwise, you will not have all the necessary toolboxes to run the code. You can do so using the following command:

```
git clone --recursive https://github.com/krembilneuroinformatics/kcni-school-lessons.git
```

2. Open Matlab and navigate to the kcni-school-lessons/day6 folder.
3. Set your environment by running `'kcni_setup_paths'`

Tutorial 1: Modeling Abnormal Beliefs

1. Set your environment using `'kcni_setup_paths'`
2. Part 1: First steps with the HGF: Run `'HGF_tutorial_generate_task'` section by section (you can do so by clicking in the corresponding section of the script and clicking the 'Run and Advance' Button at the top of the Matlab window next to the green triangle labelled 'Run').
3. Part 2: Simulating prototypical patients: Run `'HGF_tutorial_generate_learners'` section by section

Tutorial 2: Dynamic Causal Modeling for fMRI

1. Set your environment using `'kcni_setup_paths'`
2. The master script is `'DCMCompareDemo'`. We will run it section by section to understand the different steps involved in the analysis.

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Who are your instructors?

Andreea O. Diaconescu
KCNI, CAMH
Computational Psychiatry
GitHub: AndreeaDiaconescu;
Twitter: @cognemo_andreea

Daniel Hauke
University of Basel, KCNI, CAMH
Computational Psychiatry
GitHub: Murdugan

Who are your instructors?

Colleen Charlton
KCNI, CAMH
Neuroscience, cognitive science
GitHub: colleenc11

Peter Bedford
KCNI, CAMH
Neuroscience, cognitive science
GitHub: peterjbedford

Povilas Karvelis
KCNI, CAMH
Computational psychiatry
GitHub: frank-pk, Twitter: @KarvelisPovilas

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Many thanks to our colleagues and collaborators *

Cognitive Network Modelling Team

- G. Allohverdi
- P. Bedford
- C. Charlton
- A. Coulter
- D. Hauke
- P. Karvelis
- P. Laessing
- C. Yu
- Z. Wang
- D. Wurgaft

CAMH

- G. Foussias
- A. Graff
- M. Kiang
- J. Lepock
- J. Kennedy
- N. Neufeld
- R. Mizrahi
- A. Ruocco
- A. Voineskos
- J. Zaheer
- C. Zai

University Health Network, MR Physics

- L. Kasper
- K. Uludag

Zurich

- D. Cole
- J. Heinzle
- S. Iglesias
- L. Kasper
- K. E. Stephan
- P. Tobler
- L. Weber

Basel

- C. Andreou
- S. Borgwardt
- D. Hauke
- F. Mueller
- A. Schmidt
- M. Wobmann

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Novartis Foundation

* listed alphabetically

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Today's Agenda

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Bayesian Models of Learning and Integration of Neuroimaging

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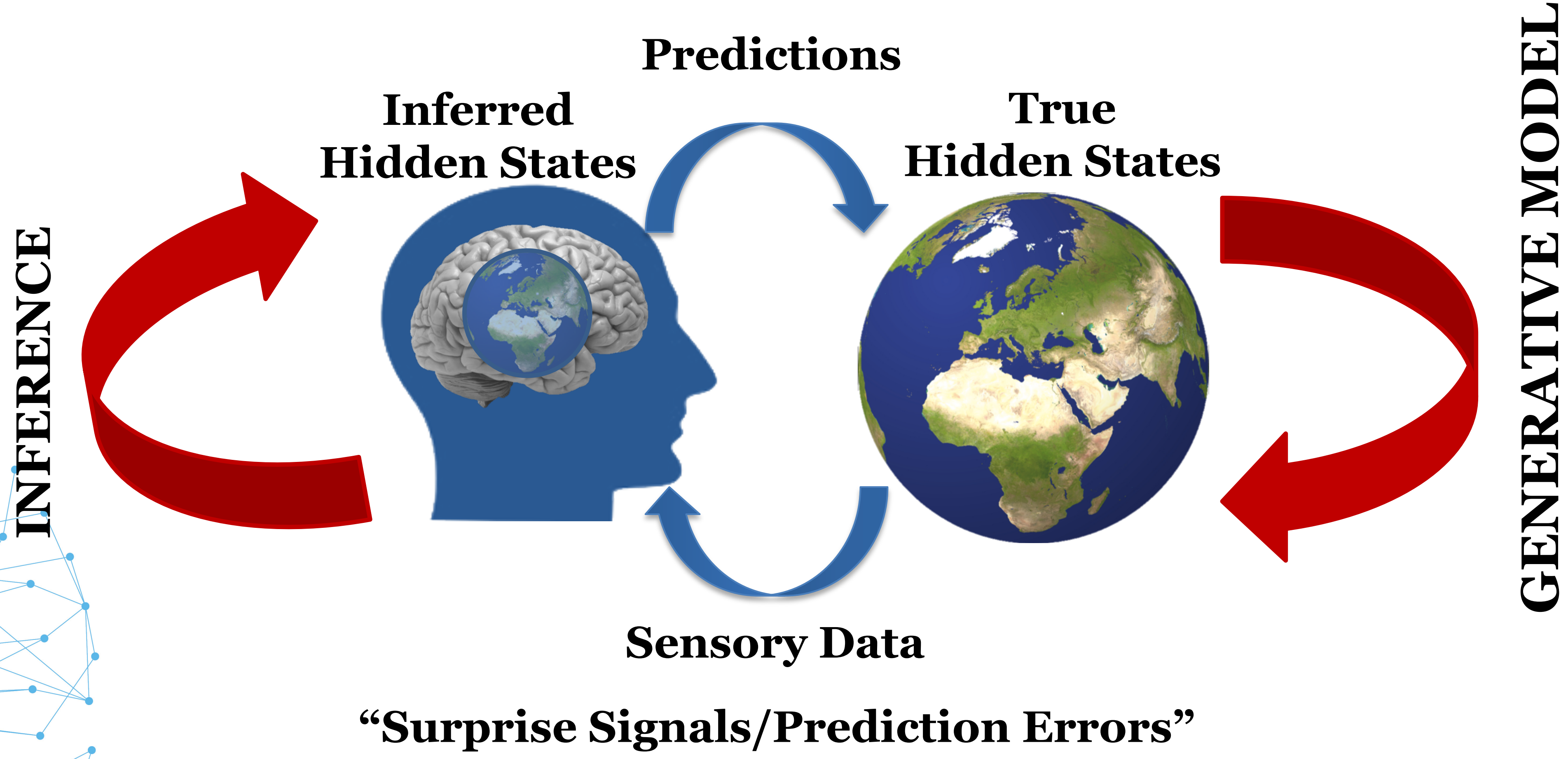
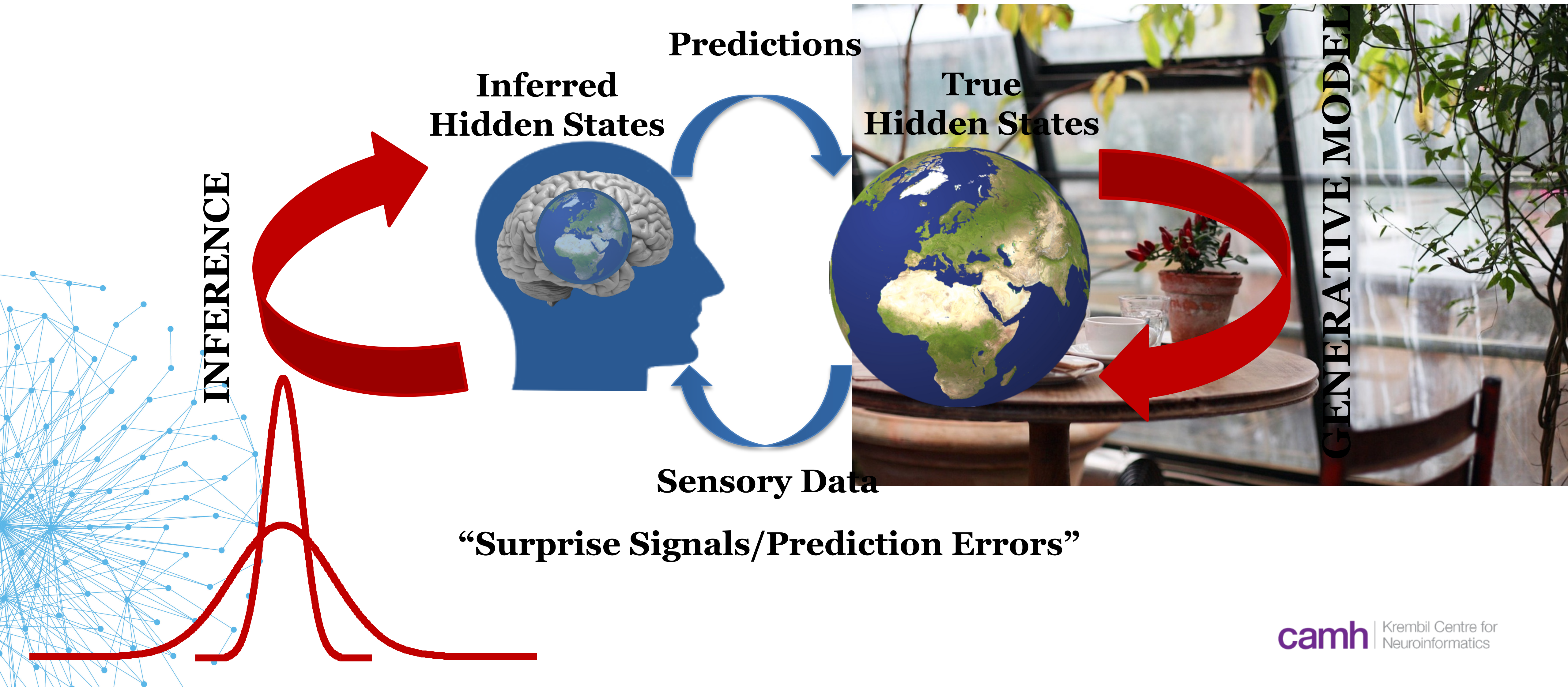
Cognition as Bayesian Inference

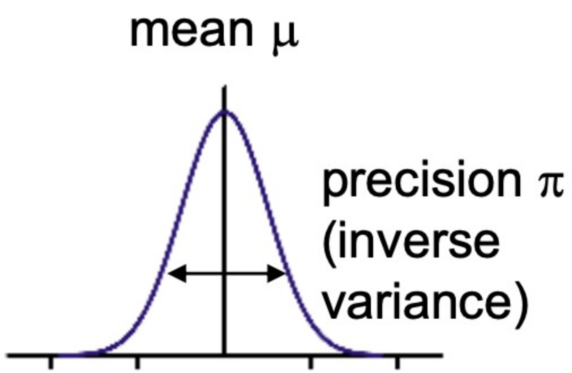


Cognition as Bayesian Inference



"Surprise Signals/Prediction Errors"

Definitions



- Beliefs are represented as probability distributions
- For example: Gaussian (Normal) distributions
  - The probability of x is normally distributed with mean μ and variance σ^2

$$p(x) = \mathcal{N}(x; \mu, \sigma^2)$$

  - Same thing, just expressed as precisions:

$$p(x) = \mathcal{N}(x; \mu, \pi)$$

$\mu = \text{mean}$

$\pi = \frac{1}{\sigma^2} = \text{precision}$

Stephan, 2020

States, parameters, inputs

- States: quantities that evolve in time
  - states $x_i^{(k)}$ at the i^{th} level and timepoint k
- Parameters: the structural determinants of the states
  - parameters ϑ (subject-specific)
- Inputs: Perturbations at each timepoint
  - inputs or perturbations $u^{(k)}$ at timepoint k

- variable evolving over time, for N trials

$$x^{(k)} = \begin{bmatrix} x_1^{(k)} \\ \vdots \\ \vdots \\ x_N^{(k)} \end{bmatrix}$$

- state equations (difference equation):

$$x^{(k)} = f(x^{(k-1)}, \theta_f, u^{(k-1)})$$

Stephan, 2020

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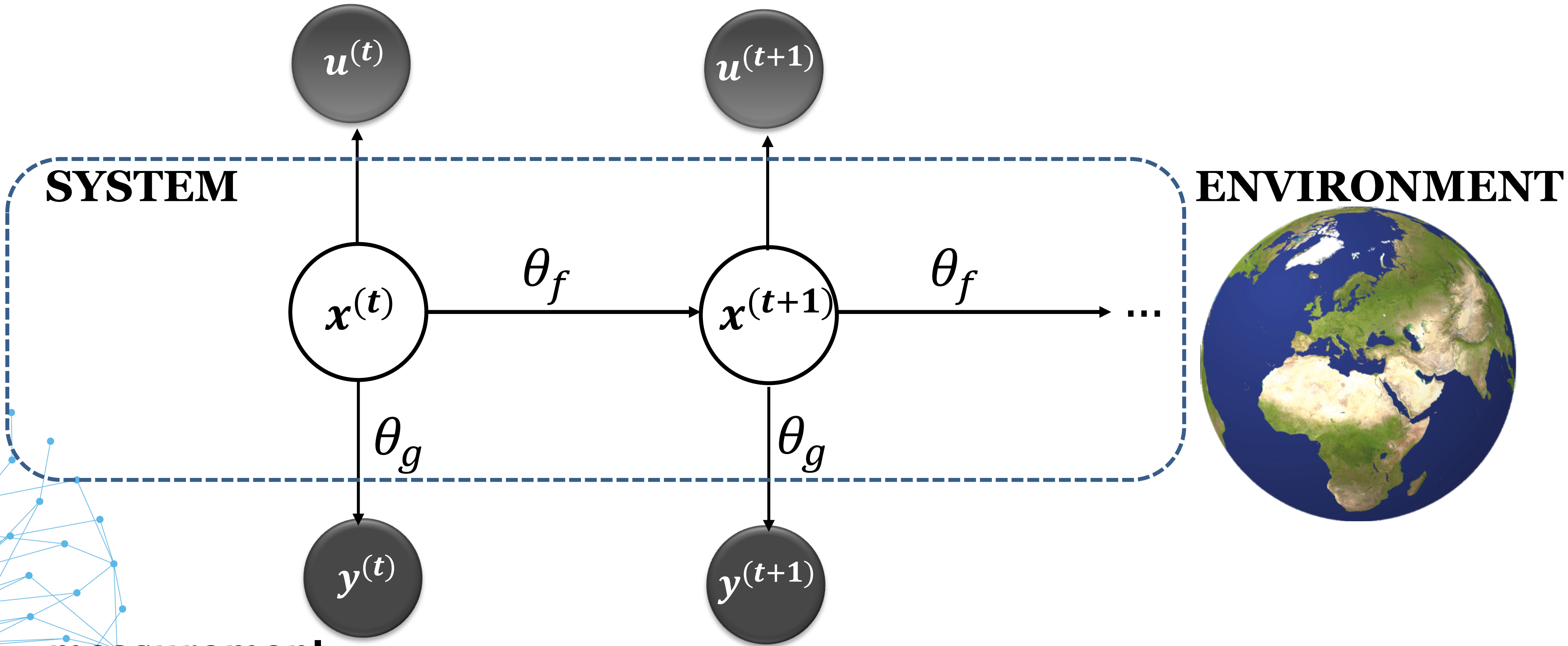
State-space representations: Markov Process



measurement (response) equation:

$$y^{(t)} = g\left(x^{(t)}, \theta_g\right) + \varepsilon^{(t)}$$

Stephan, 2020

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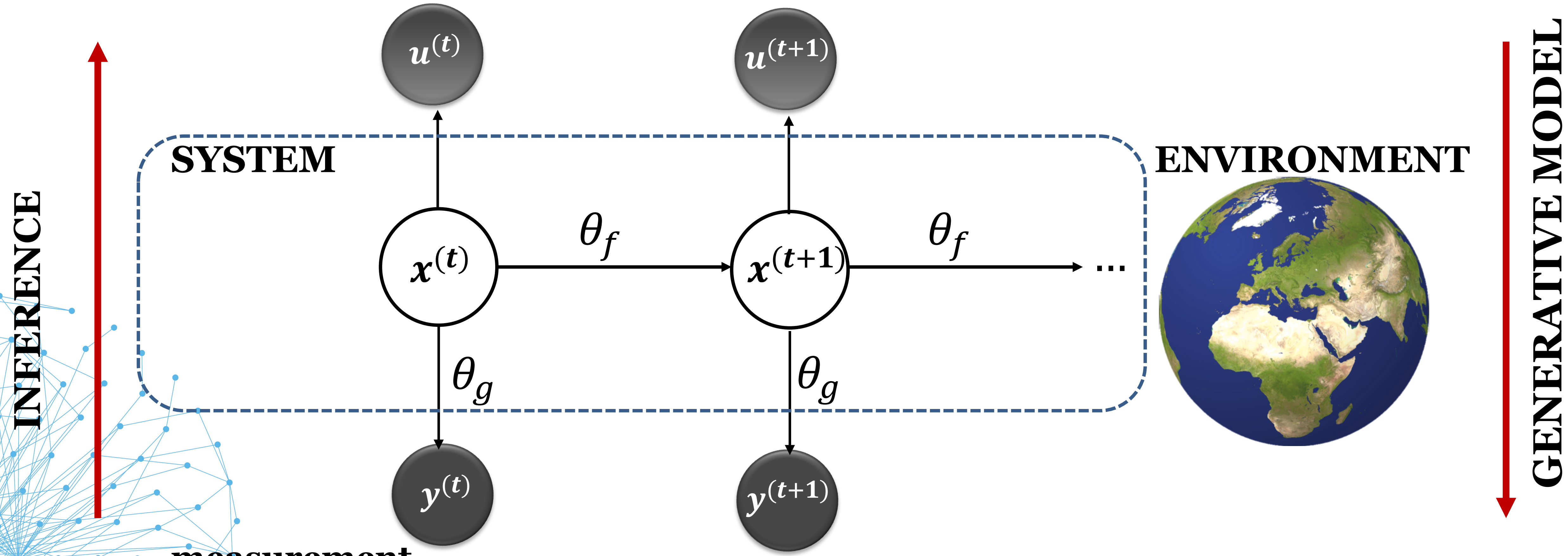
State-space representations: Markov Process



measurement (response) equation:

$$y^{(t)} = g\left(x^{(t)}, \theta_g\right) + \varepsilon^{(t)}$$

Stephan, 2020

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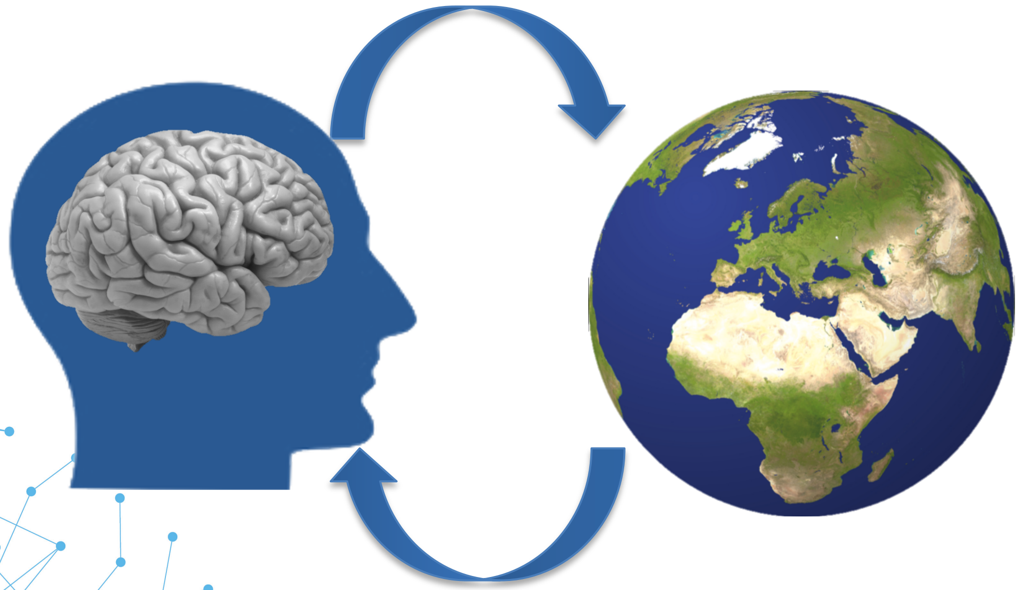
Bayesian Inference



The Bayesian Brain

Reverend Thomas Bayes
1702-1761

- The brain is an inference machine
- Conceptualise beliefs as probability distributions
- Updates via Bayes' rule:

$$\underbrace{p(\Theta|y,m)}_{\text{Predictions}} = \frac{\overbrace{p(\Theta|m)}^{\text{Prior Belief}}\overbrace{p(y|\Theta,m)}^{\text{Sensory Data}}}{\underbrace{p(y,m)}_{\text{Evidence}}}$$

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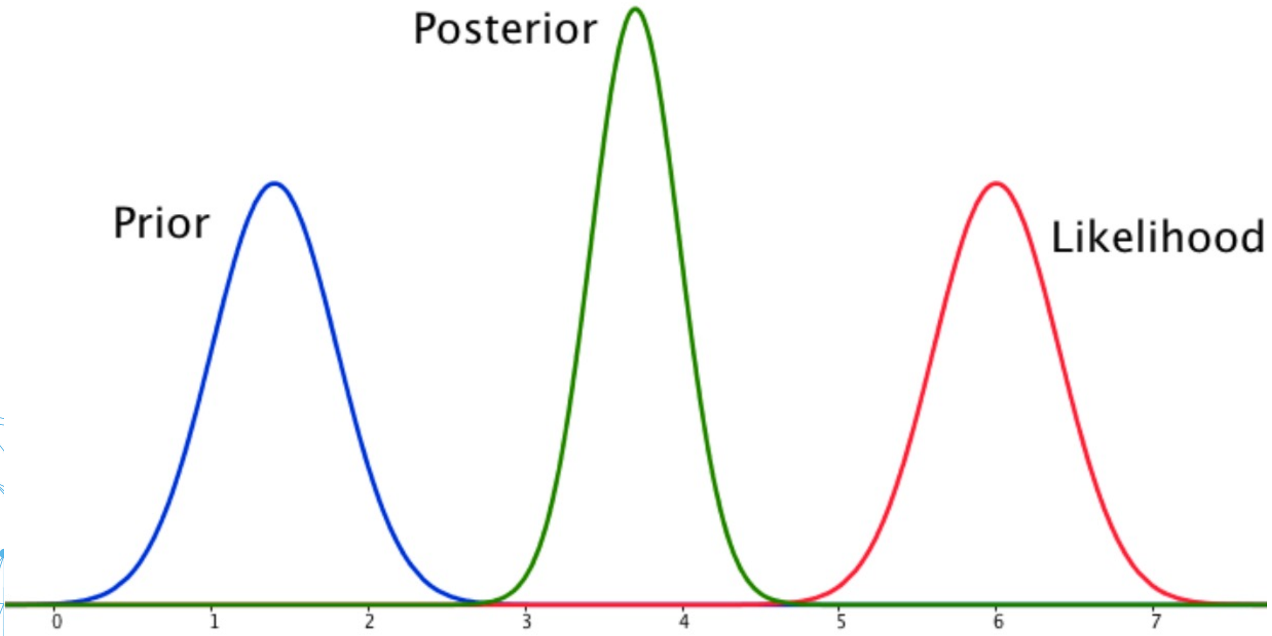
Bayesian Inference



Θ: parameters
y: data

The Bayesian Brain

Reverend Thomas Bayes
1702-1761

$$\underset{\text{Posterior}}{p(\Theta|y,m)} = \frac{\overset{\text{Prior} \times \text{Likelihood}}{p(\Theta|m)p(y|\Theta,m)}}{\underset{\text{Model evidence}}{p(y,m)}}$$

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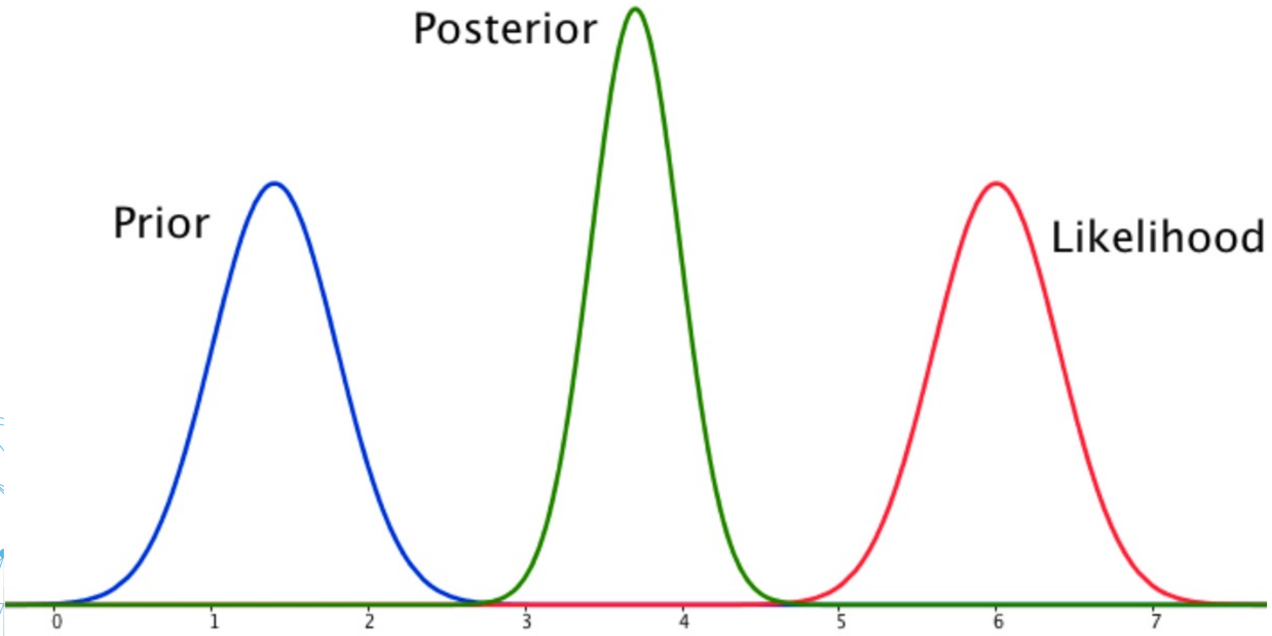
Bayesian Inference



Θ: parameters
y: data

The Bayesian Brain

Reverend Thomas Bayes
1702-1761

Prior × Likelihood = Generative Model

Posterior

$$p(\Theta|y,m) = \frac{p(\Theta|m)p(y|\Theta,m)}{\int p(\Theta|m)p(y|\Theta,m)d\Theta}$$

Model evidence

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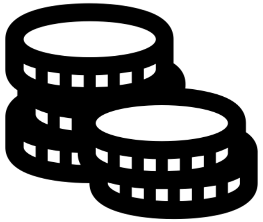
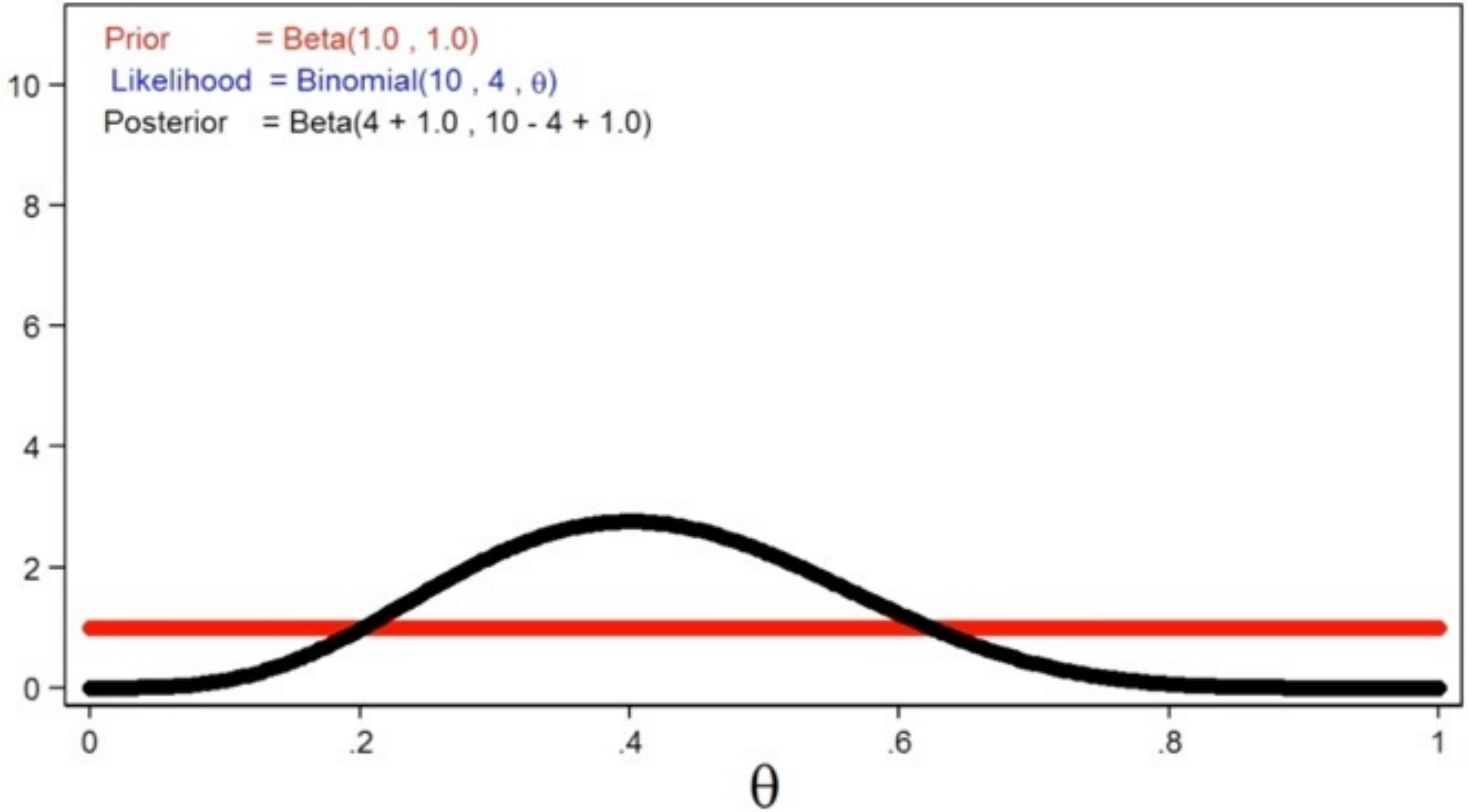
Bayes Rule: Binary Outcome

Coin toss:

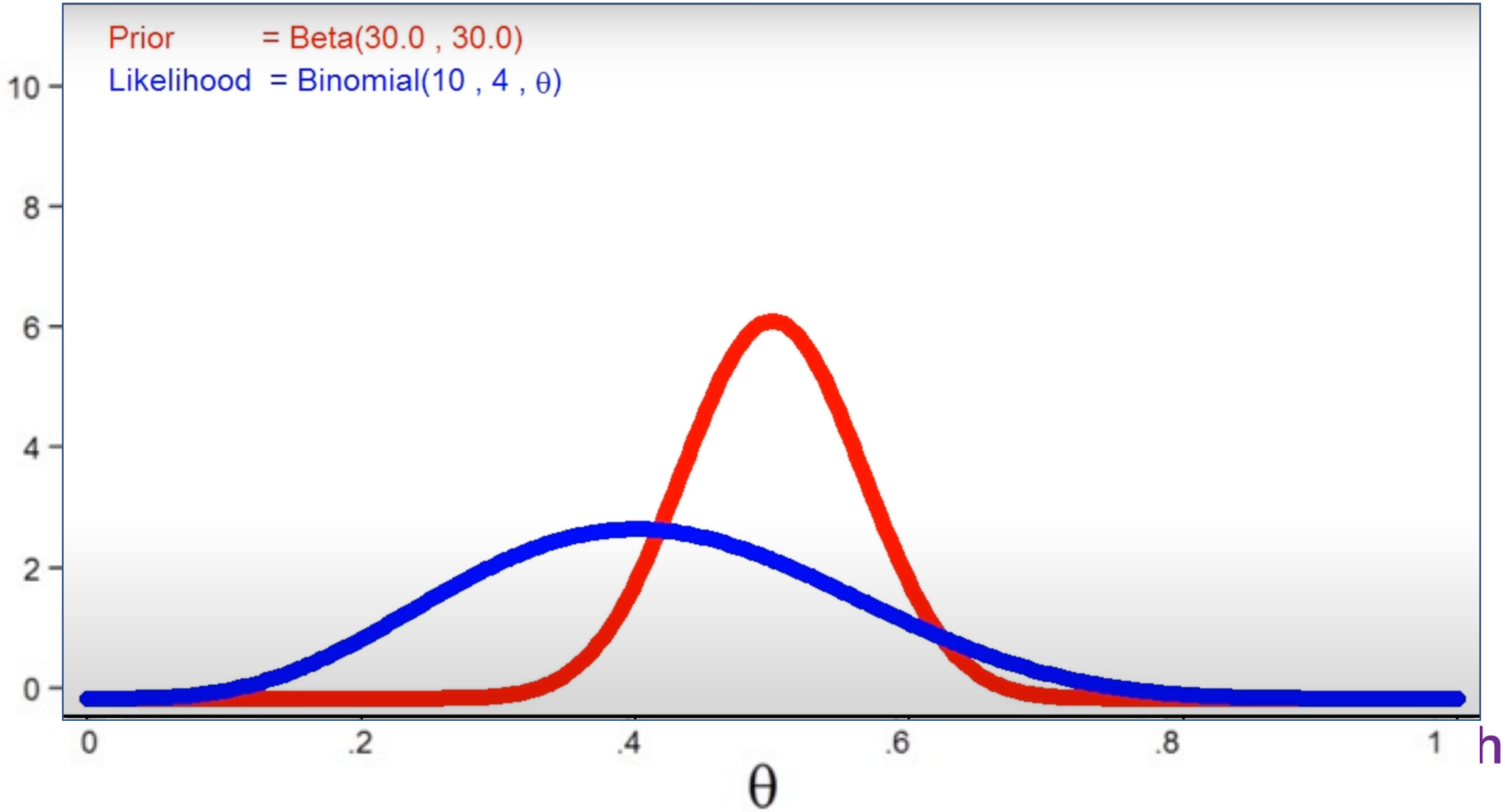


$$p(\Theta|y,m) = \frac{p(\Theta|m)p(y|\Theta,m)}{p(y,m)}$$



Bayes Rule: Binary Outcome

$$p(\Theta|y,m) = \frac{p(\Theta|m)p(y|\Theta,m)}{p(y,m)}$$



Bayes Rule: Binary Outcome

$$p(\Theta|y,m) = \frac{p(\Theta|m)p(y|\Theta,m)}{p(y,m)}$$

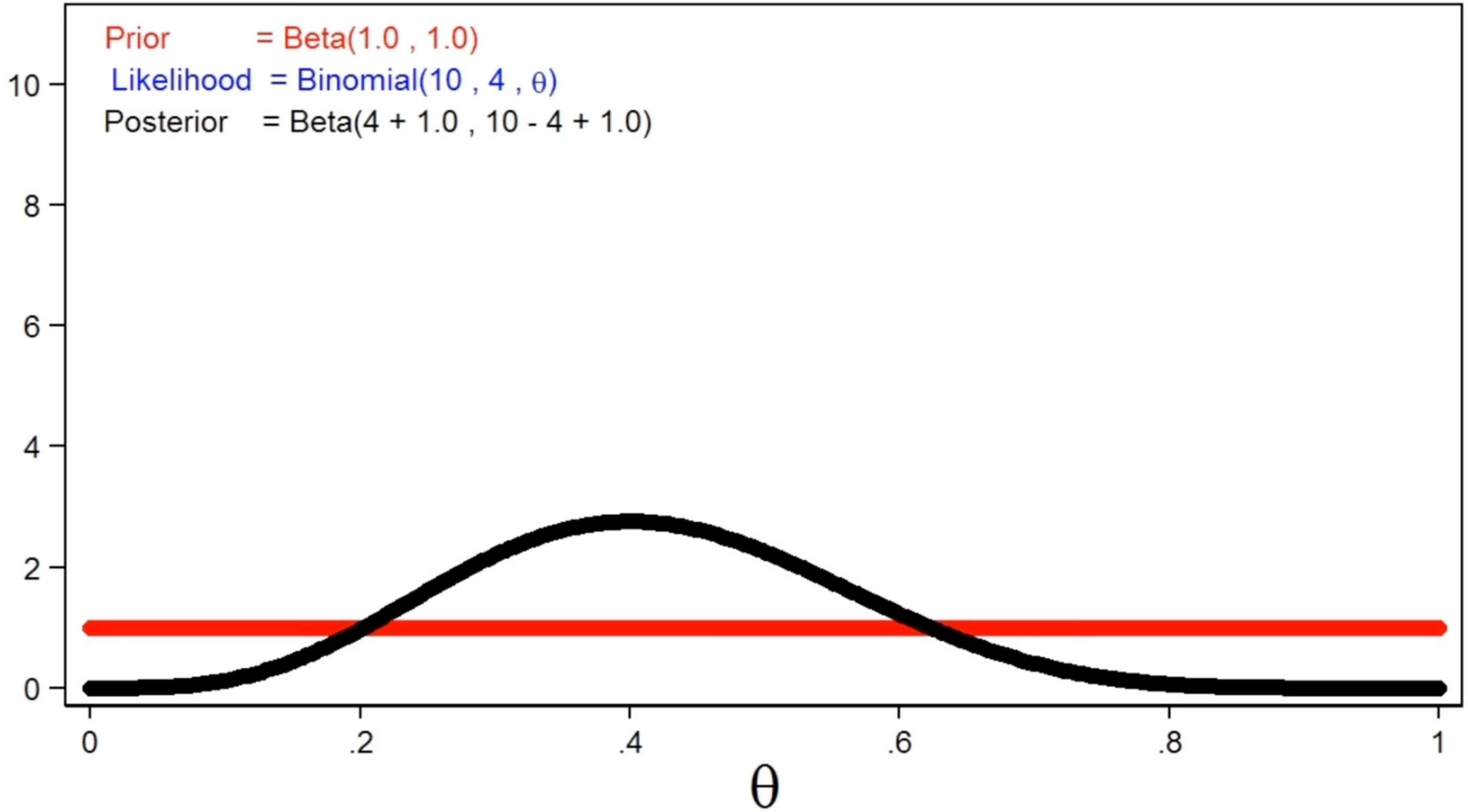
$$Posterior = Prior \times Likelihood$$

$$p(\theta|y) = P(\theta) \times P(y|\theta)$$

$$= \mathrm{Beta}(\alpha,\beta) \times \mathrm{Binomial}\,(\alpha,\beta,\theta)$$

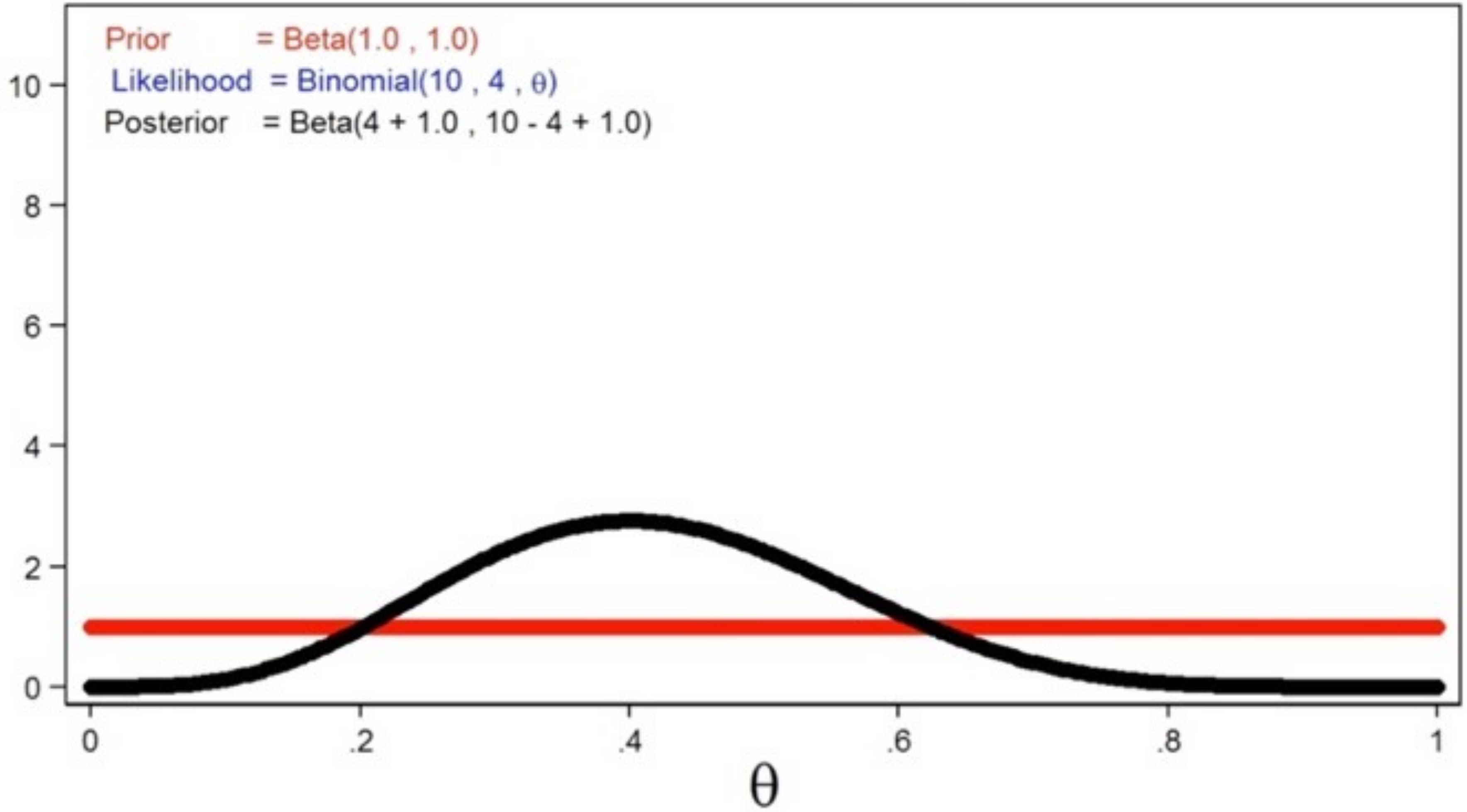
Bayes Rule: Binary Outcome

$$p(\Theta|y,m) = \frac{p(\Theta|m)p(y|\Theta,m)}{p(y,m)}$$



Frequentist versus Bayesian Approaches

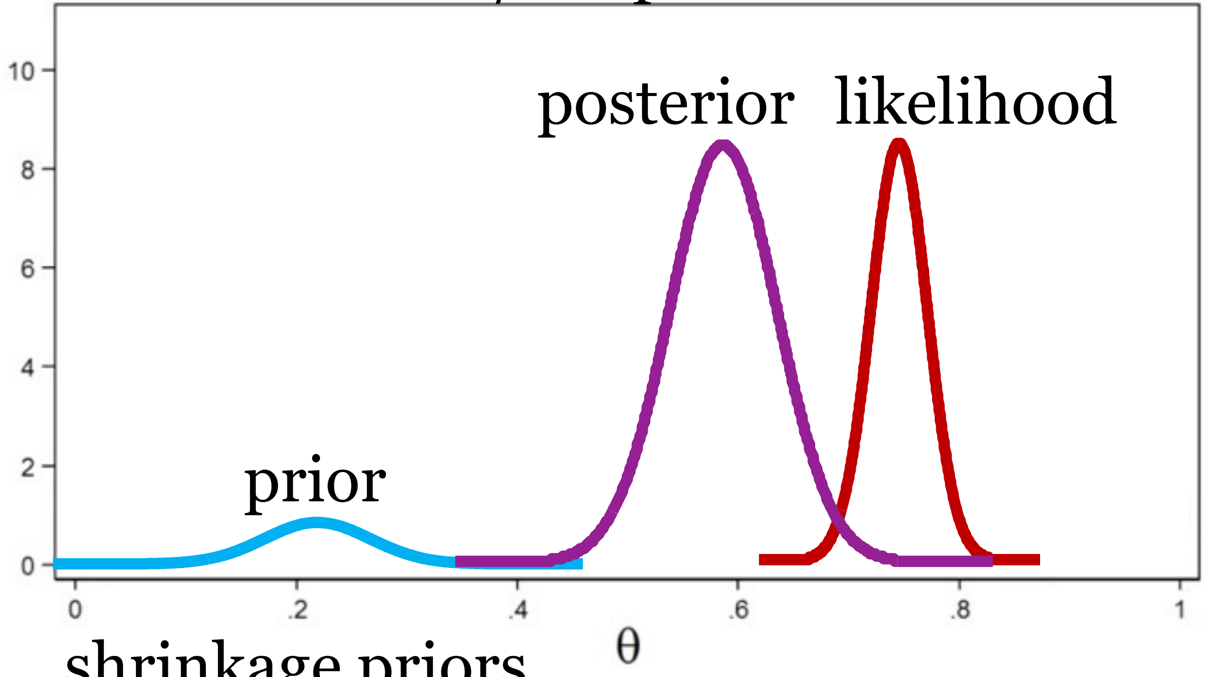
$$p(\Theta|y,m) = \frac{p(\Theta|m)p(y|\Theta,m)}{p(y,m)}$$



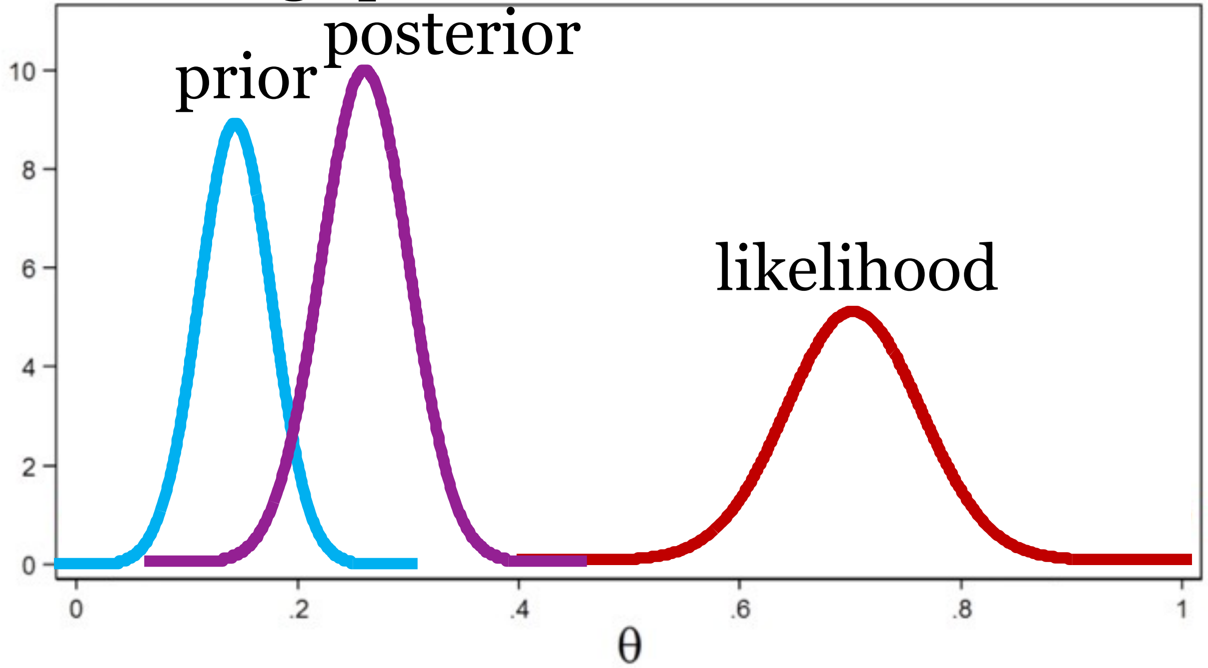
Categories of Priors

- Objective priors
  - noninformative/flat priors
- Subjective priors
  - subjective but not arbitrary
  - hypothesis-driven
  - can be the result of previous empirical studies
- Shrinkage priors
  - emphasize regularization and sparsity
- Empirical priors
  - learn parameters of prior distributions from the data ("empirical Bayes")

noninformative/flat priors

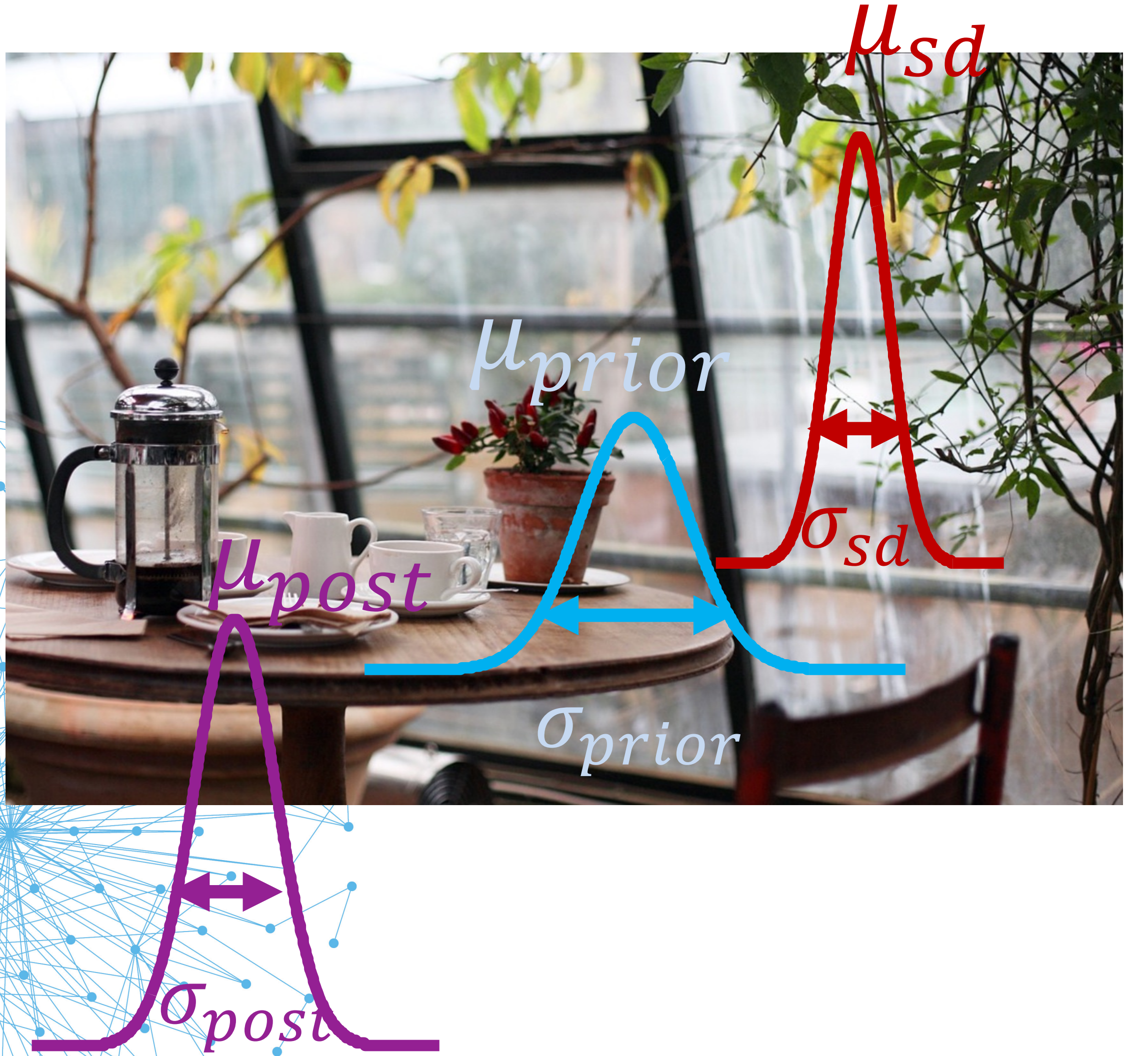


shrinkage priors



Simple Example: Temperature Estimation

INFERENCE



DECISION

Simple Example: Temperature Estimation

What is the temperature outside?

$$\boxed{y = \theta + \varepsilon}$$

Likelihood & Prior:

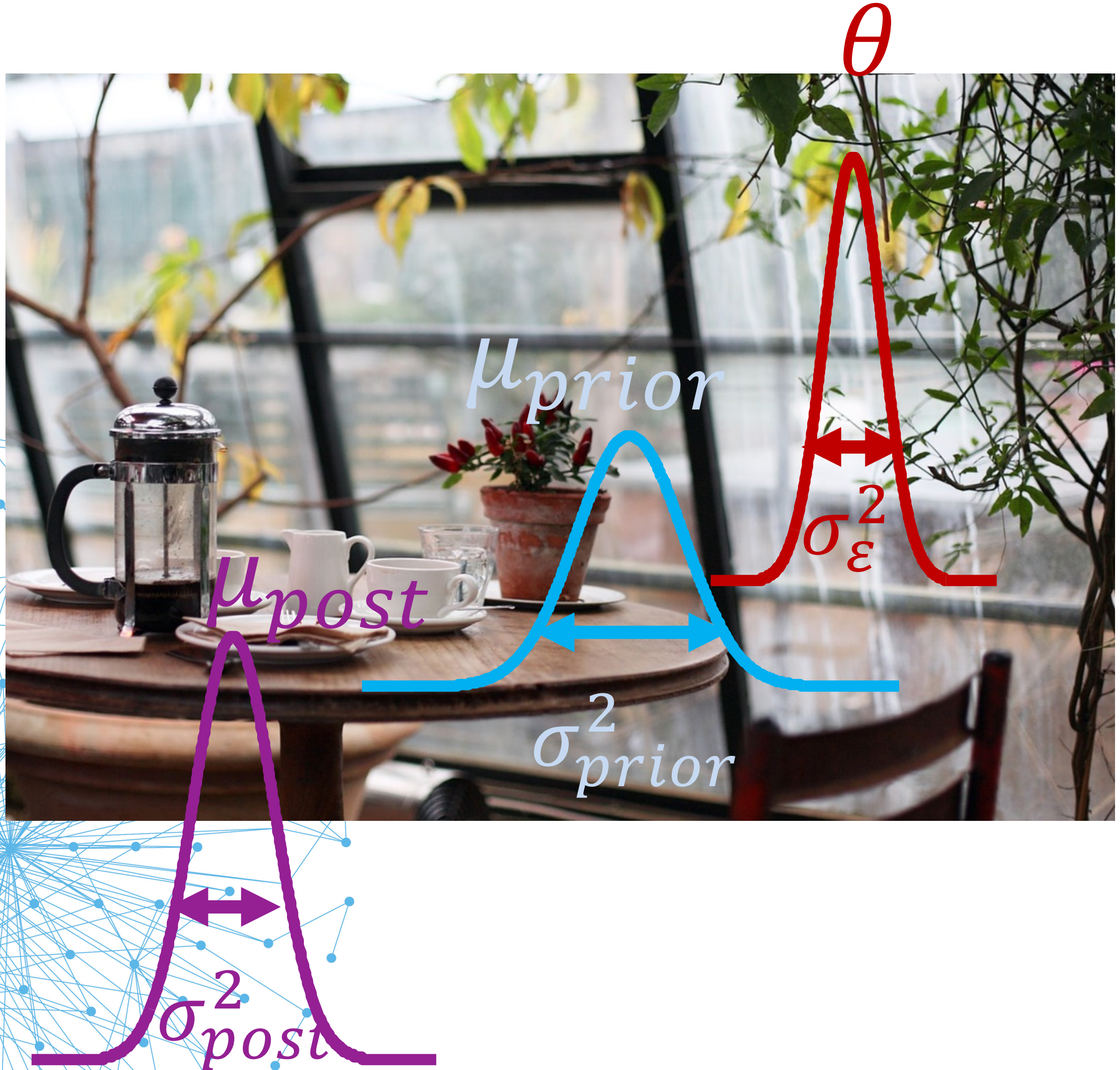
$$\boxed{p(y|\theta) \sim \mathcal{N}(\theta, \sigma_\varepsilon^2)}$$

$$\boxed{p(\theta) \sim \mathcal{N}(\mu_{prior}, \sigma_{prior}^2)}$$

Posterior:

$$\boxed{p(\theta|y) \sim \mathcal{N}(\mu_{post}, \sigma_{post}^2)}$$

Simple Example: Temperature Estimation



What is the temperature outside?

$$\boxed{y = \theta + \varepsilon}$$

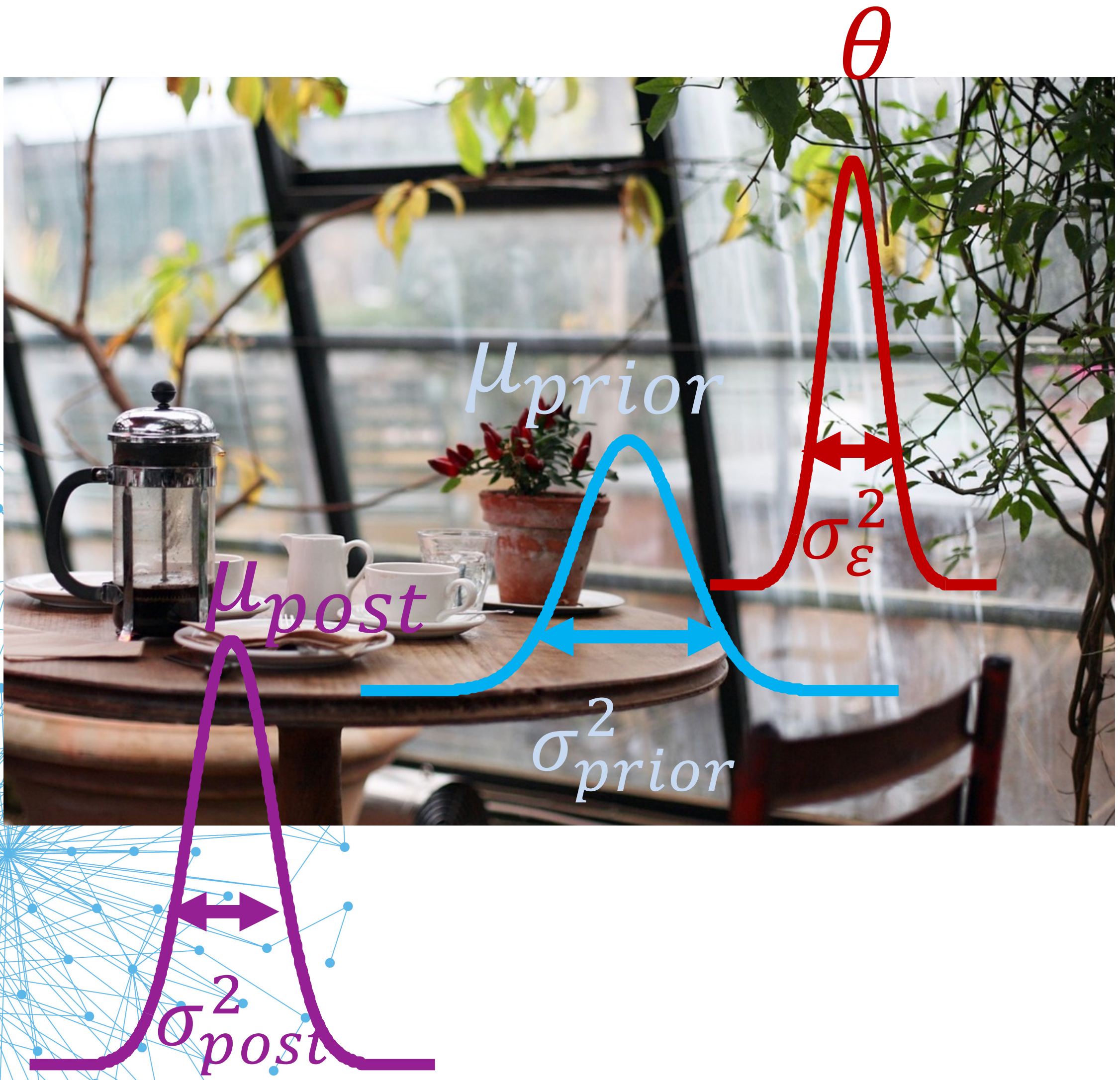
Posterior:

$$\boxed{p(\theta|y) \sim \mathcal{N}(\mu_{post}, \sigma_{post}^2)}$$

$$\frac{1}{\sigma_{post}^2} = \frac{1}{\sigma_\varepsilon^2} + \frac{1}{\sigma_{prior}^2}$$

$$\mu_{post} = \sigma_{post}^2\left(\frac{1}{\sigma_\varepsilon^2}y + \frac{1}{\sigma_\varepsilon^2}\mu_{prior}\right)$$

Simple Example: Temperature Estimation



What is the temperature outside?

$$\boxed{y = \theta + \varepsilon}$$

Posterior:

$$\boxed{p(\theta|y) \sim \mathcal{N}(\mu_{post}, \sigma_{post}^2)}$$

$$\pi_{post} = \pi_\varepsilon + \pi_{prior}$$

$$\mu_{post} = \frac{\pi_\varepsilon}{\pi_{post}} y + \frac{\pi_{prior}}{\pi_{post}} \mu_{prior}$$

Precision Ratio Weighting

Bayes versus Bayes

Bayes' Rule

$$p(\mathrm{A}|B) = \frac{p(B|A)p(A)}{p(B)}$$

Statistical rule describing the relationship between conditional probability distributions

Model fitting/Parameter estimation:

posterior **prior** **likelihood**

$$p(\Theta|data, m) = \frac{p(\Theta|m)p(data|\Theta, m)}{p(data|m)}$$

model evidence

Model Comparison:

Model of a computation performed by the brain:

posterior

$$P(\text{world}|\text{sensory input})$$

prior **likelihood**

$$= \frac{P(\text{world})P(\text{sensory data }|\text{world})}{P(\text{sensory input})}$$

model evidence

Bayes as a model of behaviour

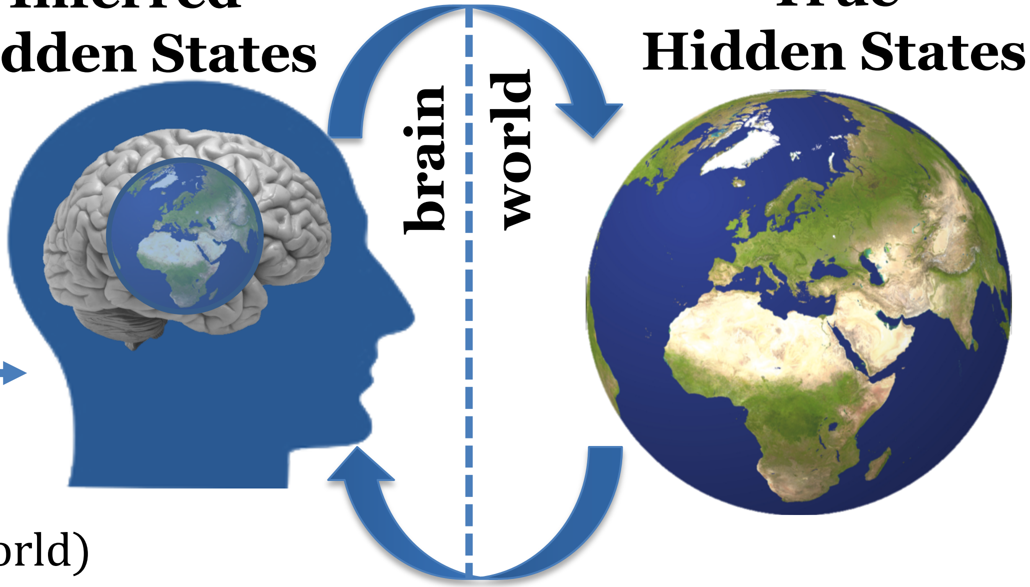
Perception as Bayesian Inference

posterior
$P(\text{state}|\text{sensory input})$

Predictions

Inferred Hidden States

True Hidden States



Inference

Generative Model

internal model of the world

prior
$P(\text{state of the world})$

Sensory Data

sensation
$P(\text{sensory data}\ |\text{state of the world})$

$$P(\text{state}|\text{sensory input}) = \frac{P(\text{state of the world})P(\text{sensory data}\ |\text{state of the world})}{P(\text{sensory input})}$$

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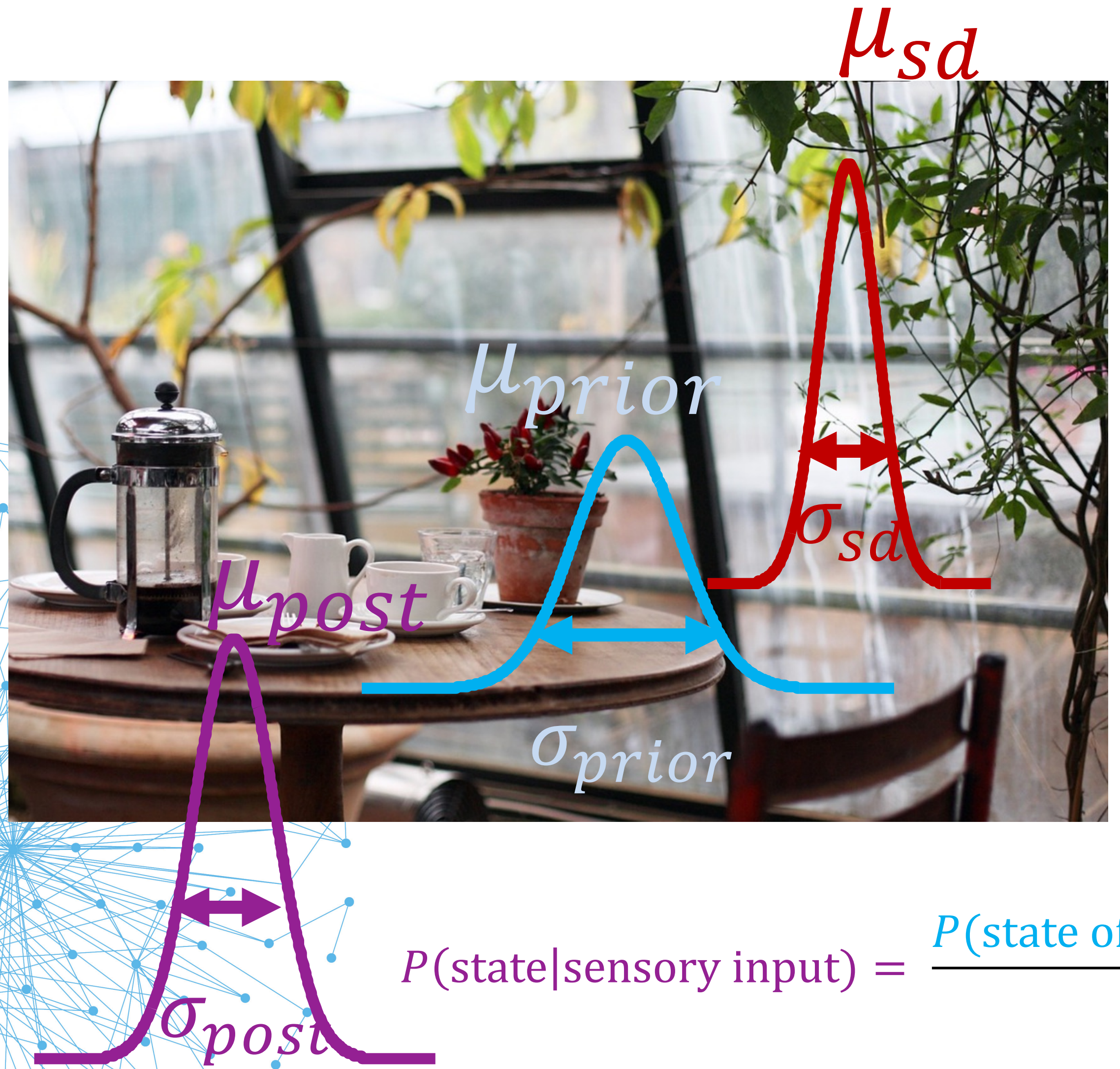
Optimal Integration: Uncertainty Considered



What is your prediction about the temperature outside?

$$\boxed{p(y|\theta) \sim \mathcal{N}(\mu_{sd}, \sigma_{sd})}$$

$$\boxed{p(\theta) \sim \mathcal{N}(\mu_{prior}, \sigma_{prior})}$$

$$\boxed{p(\theta|y) \sim \mathcal{N}(\mu_{post}, \sigma_{post})}$$

$$\pi_{post} = \pi_{\varepsilon} + \pi_{prior} \qquad \sigma = \pi^{-1}$$

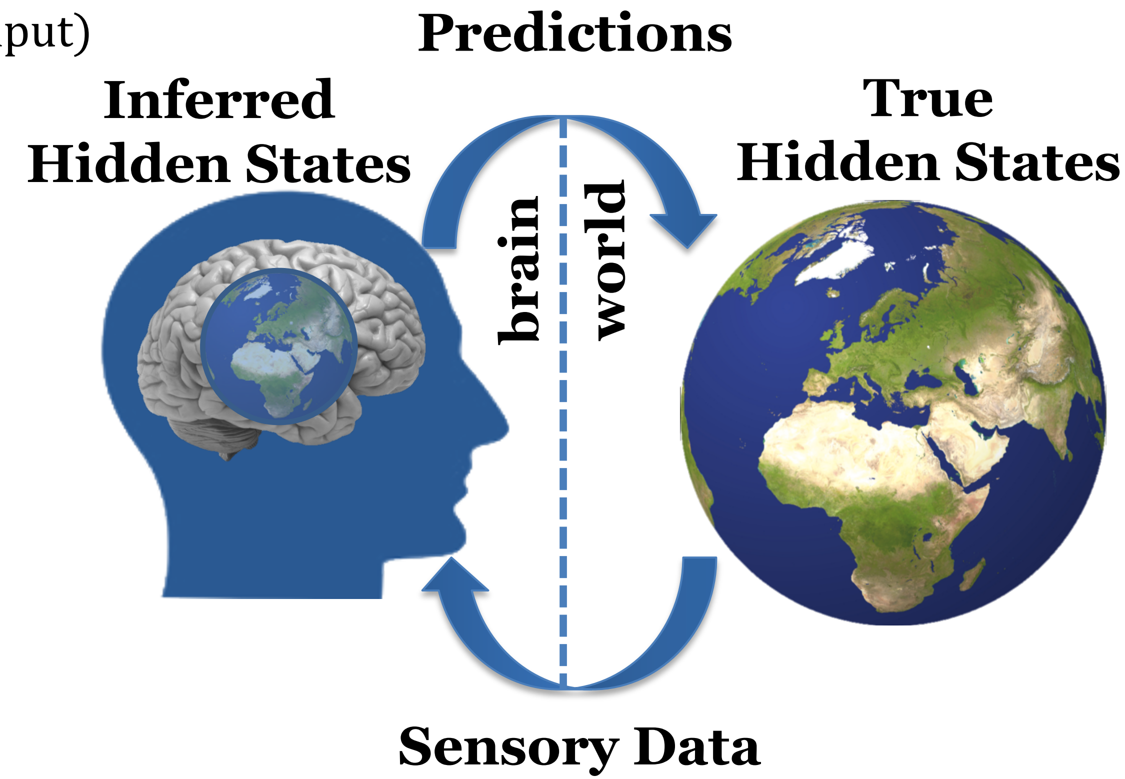
$$\mu_{post} = \frac{\pi_{\varepsilon}}{\pi_{post}} \mu_{sd} + \frac{\pi_{prior}}{\pi_{post}} \mu_{prior}$$

$$P(\text{state}|\text{sensory input}) = \frac{P(\text{state of the world})P(\text{sensory data }|\text{state of the world})}{P(\text{sensory input})}$$

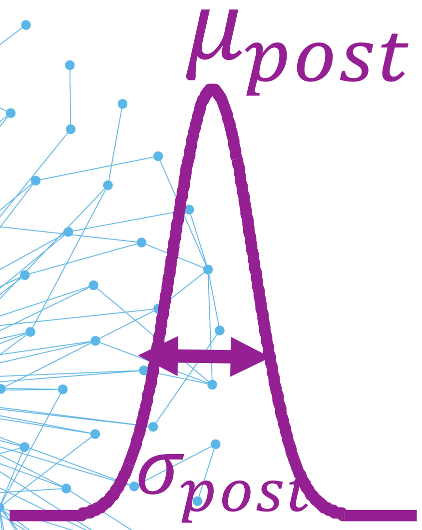
Optimal Bayesian Learning

posterior

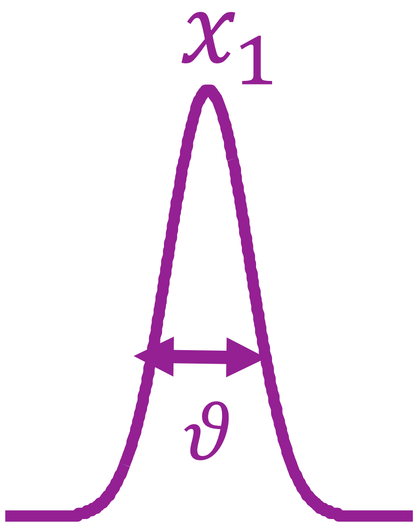
$P(\text{state}|\text{sensory input})$



Inference

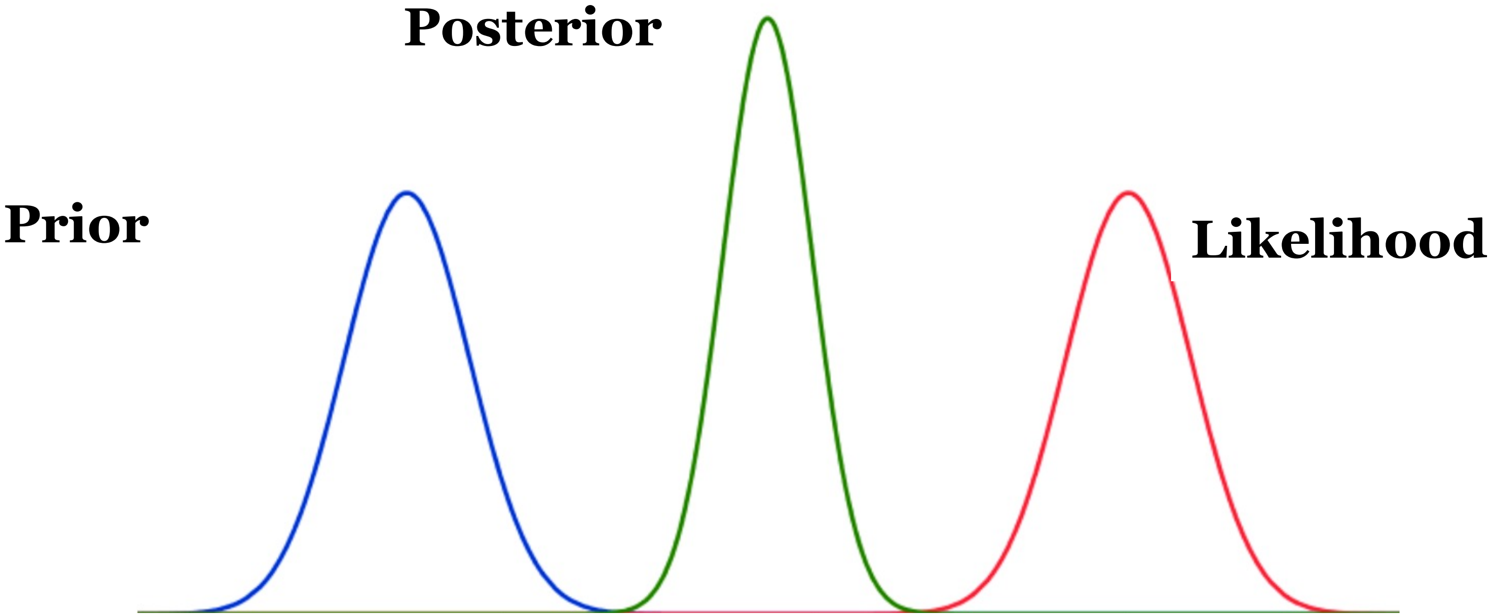


Generative Model



$$P(\text{state}|\text{sensory input}) = \frac{P(\text{state of the world})P(\text{sensory data }|\text{state of the world})}{P(\text{sensory input})}$$

Short Quiz



Synonyms/ Keywords:

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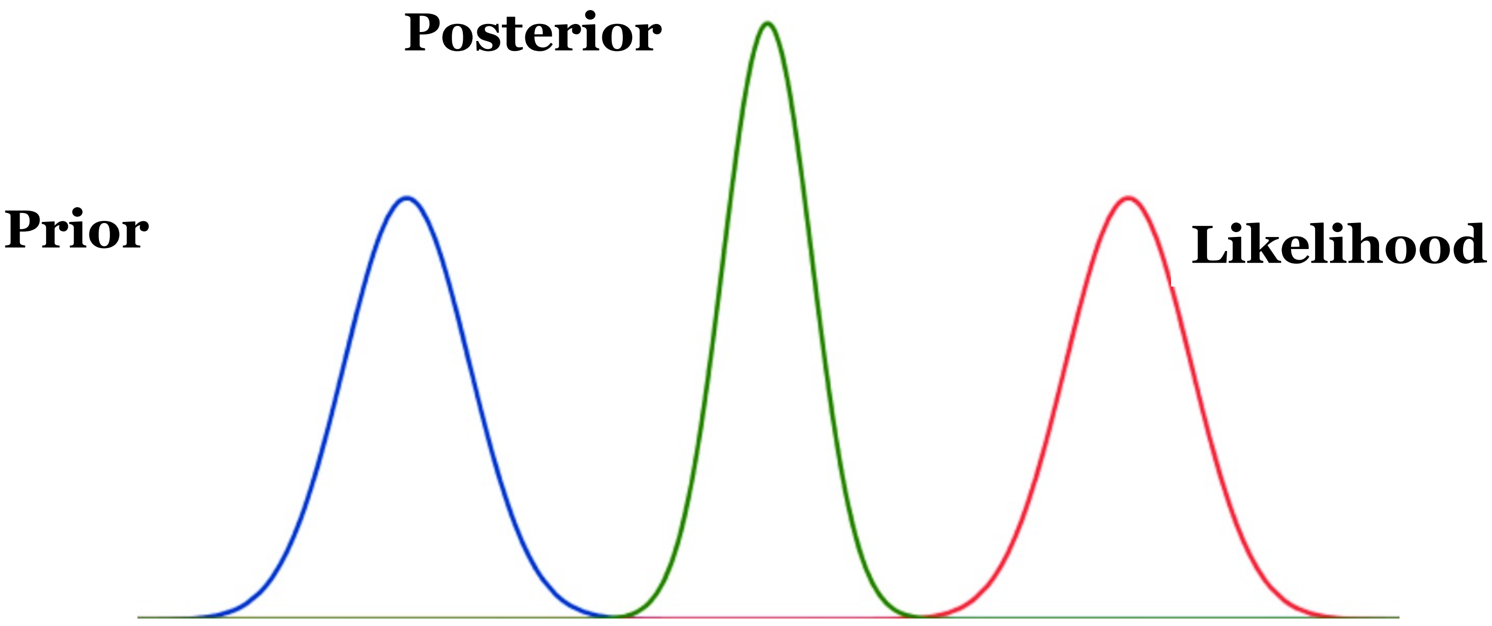
Short Quiz



Synonyms/ Keywords:
expectation
knowledge
bias

Synonyms/ Keywords:
belief update
training
learning

Synonyms/ Keywords:
data
sensory input
experience

Modelling Abnormal Beliefs

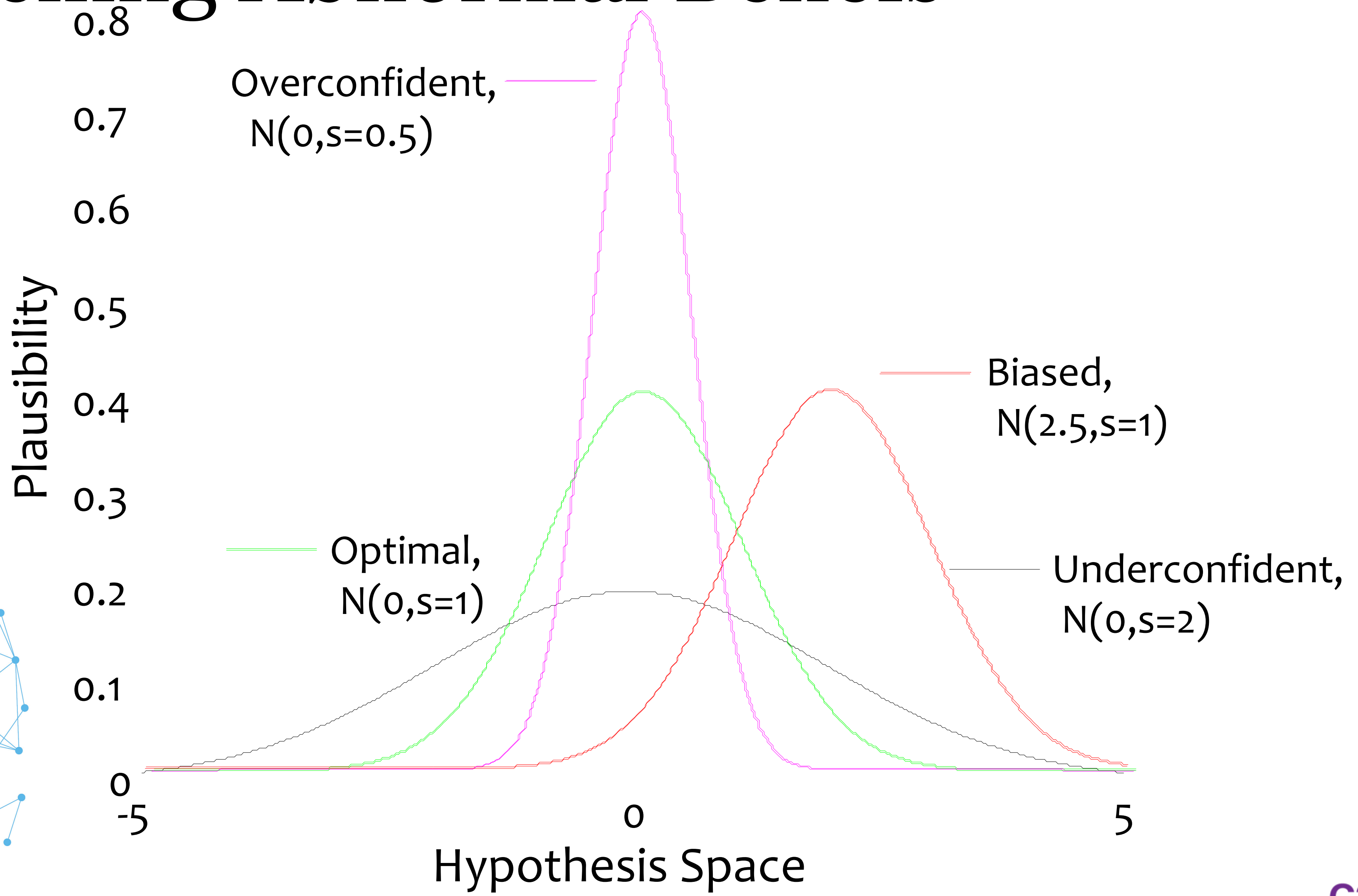
Wrong Priors

- Uncertainty too low → beliefs too rigid (underfitting)
- Uncertainty too high → high sensitivity to noise (overfitting)
- Displaced center of mass → biased interpretations
- Overestimated volatility → prior knowledge is partly neglected
- Underestimated volatility → failure to track changes in the world

Likelihood Function

- Precision too high/low → evidence is weighted too much/little

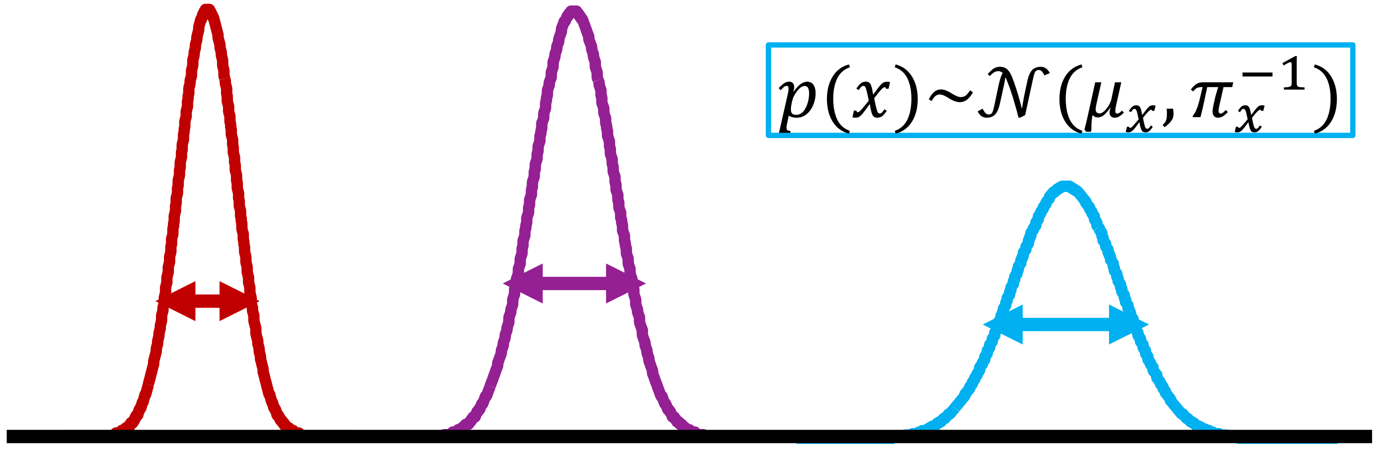
Modelling Abnormal Beliefs



How are these beliefs formed?

$$\boxed{p(u|x) \sim \mathcal{N}(\mu_{u|x}, \pi_{\varepsilon}^{-1})}$$

$$\boxed{p(x) \sim \mathcal{N}(\mu_{x}, \pi_{x}^{-1})}$$



$$\boxed{p(x|u) = \frac{p(u|x)p(x)}{\int p(u|x')p(x')dx'} \sim \mathcal{N}(\mu_{x|u}, \pi_{x|u}^{-1})}$$

Updates to the Sufficient Statistics

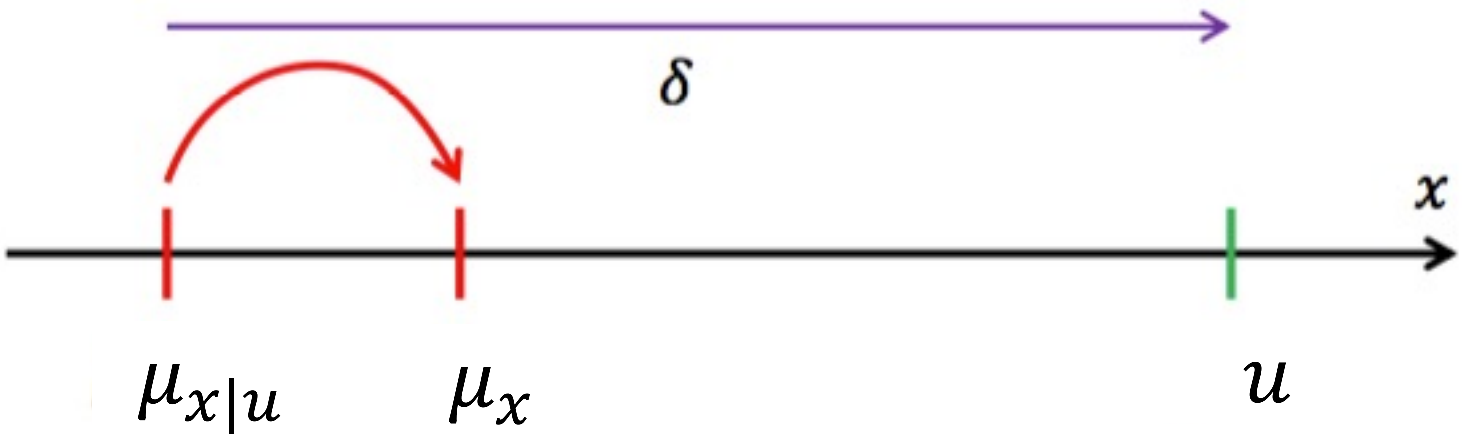
$$\pi_{x|u} = \pi_x + \pi_\varepsilon$$

Prediction Error

$$\mu_{x|u} = \mu_x + \frac{\pi_\varepsilon}{\pi_{x|u}}(u - \mu_x)$$

Belief Update

Weight (Learning Rate) $= \dfrac{\textit{how much we're learning here}}{\textit{how much we already know}}$



Mathys, 2019

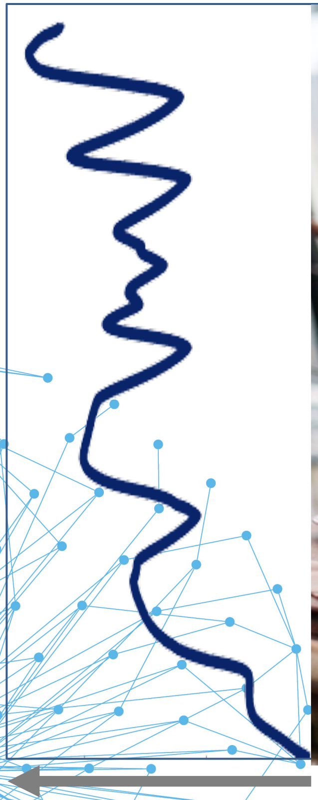
What about dynamics?

Temperature

We relax the assumption that the underlying hidden state x is stationary

- we replace it with a **Gaussian random walk**
- this gives us the **Kalman filter**:

What about dynamics?



Temperature

Kalman filter:

$$p\left(u^{(k)} \middle| x^{(k)}\right) \sim \mathcal{N}\left(u^{(k)} \middle| x^{(k)}, \varepsilon\right)$$

$$p\left(x^{(k)} \middle| x^{(k-1)}, \vartheta\right) \sim \mathcal{N}\left(x^{(k)} \middle| x^{(k-1)}, \vartheta\right)$$

ϑ = seasons

What about dynamics?

Prior:

$$\boxed{p(x^{(k-1)}) \sim \mathcal{N}(x^{(k-1)}; \mu_x^{(k-1)}, \frac{1}{\pi_x^{(k-1)}})}$$

Posterior:

$$\pi_x^{(k)} = \frac{1}{\sigma_x^{(k-1)} + \vartheta} + \frac{1}{\varepsilon} = \hat{\pi}_x^{(k-1)} + \hat{\pi}_u$$

Prediction Error

$$\mu_x^{(k)} = \mu_x^{(k-1)} + \frac{\hat{\pi}_u}{\pi_x^{(k)}} (u^{(k)} - \mu_x^{(k-1)})$$

Belief Update

Weight (Learning Rate) $= \frac{\textit{how much we're learning here}}{\textit{how much we already know}}$

ϑ = seasons

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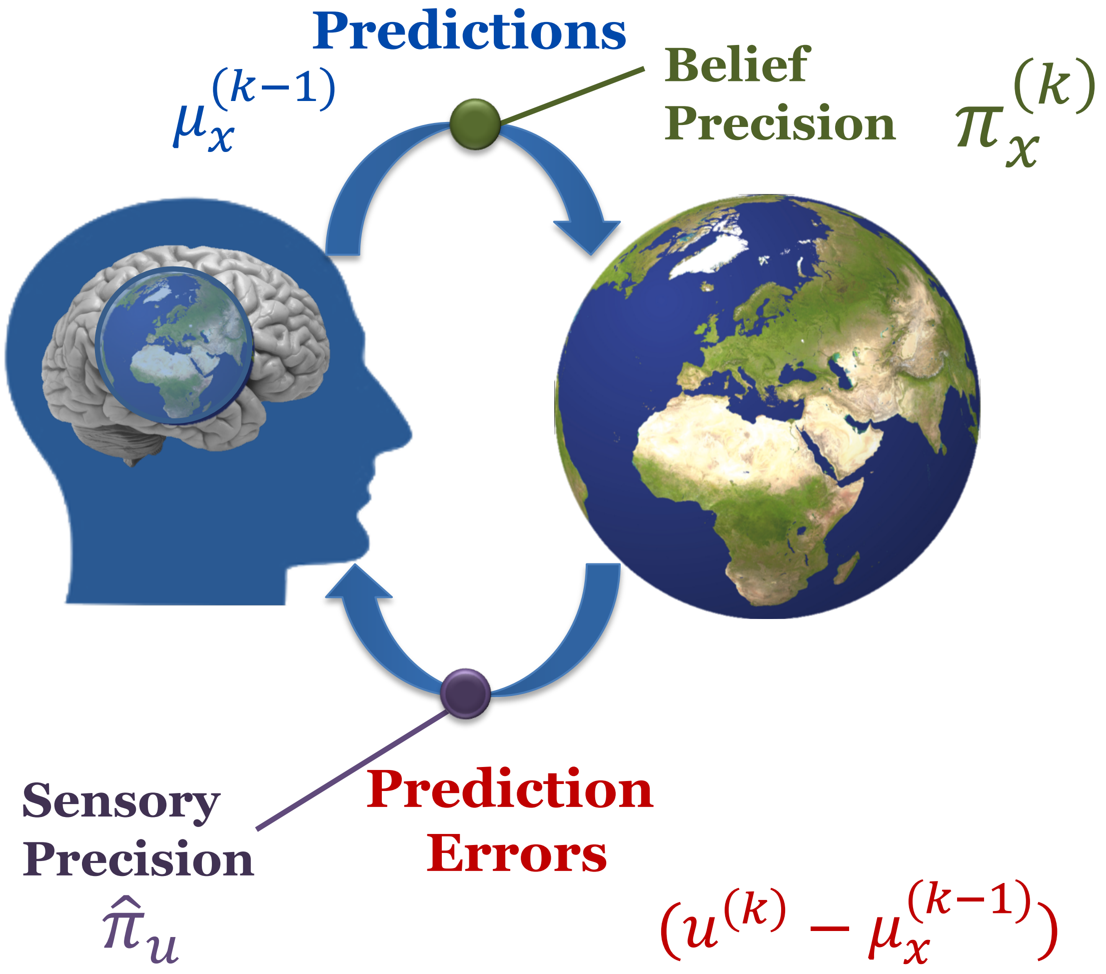
Kalman Filter

$$\mu_x^{(k)} = \mu_x^{(k-1)} + \frac{\hat{\pi}_u}{\pi_x^{(k)}}\left(u^{(k)} - \mu_x^{(k-1)}\right)$$



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What about dynamics?

Climate Change

Temperature

The hierarchical Gaussian filter (HGF): a computationally tractable model for individual learning under uncertainty (Mathys et al., 2011; 2014)

Level 3: Phasic volatility

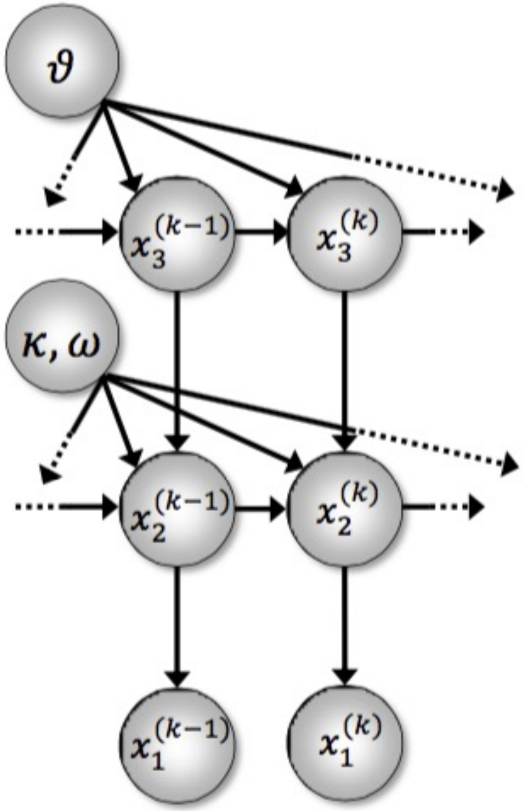
$$p\left(x_3^{(k)}\right) \sim \mathcal{N}\left(x_3^{(k-1)}, \vartheta\right)$$

Level 2: Tendency towards category 1

$$p\left(x_2^{(k)}\right) \sim \mathcal{N}\left(x_2^{(k-1)}, e^{\left(\kappa x_3^{(k-1)} + \omega\right)}\right)$$

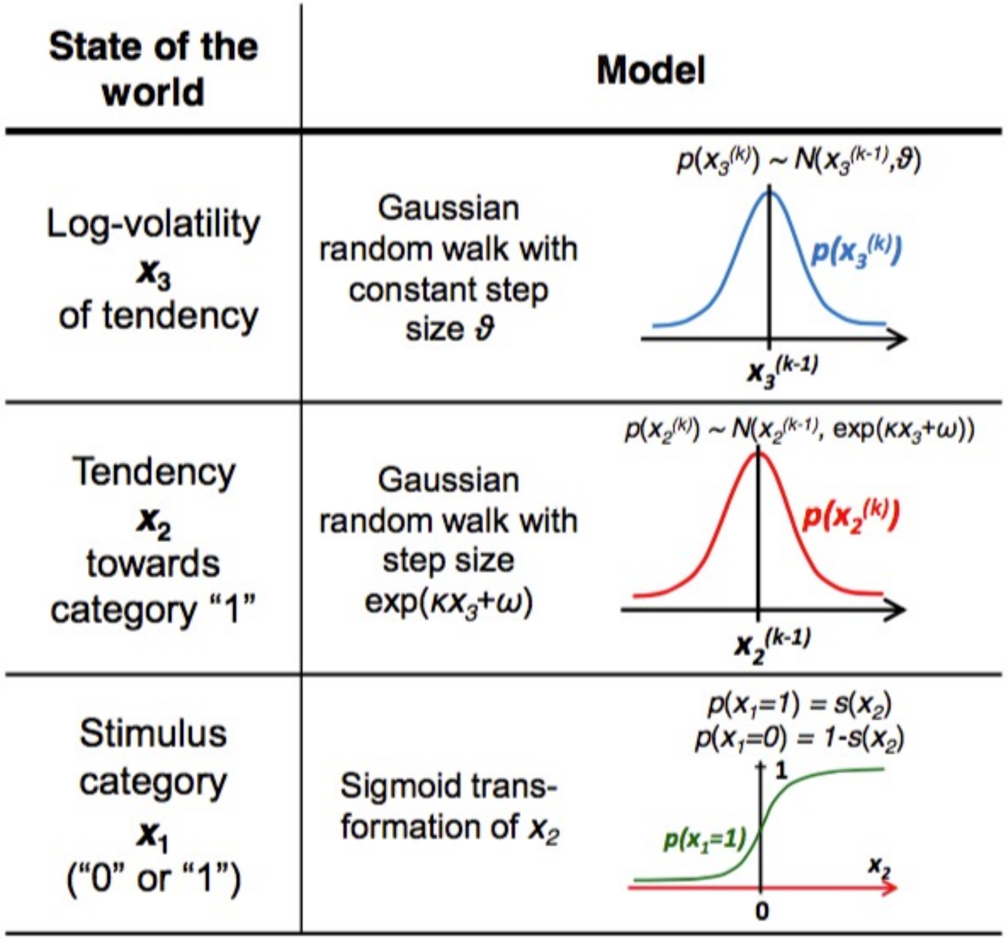
Level 1: Stimulus category

$$p(x_1 = 1) = \frac{1}{1 + e^{-x_2}}$$

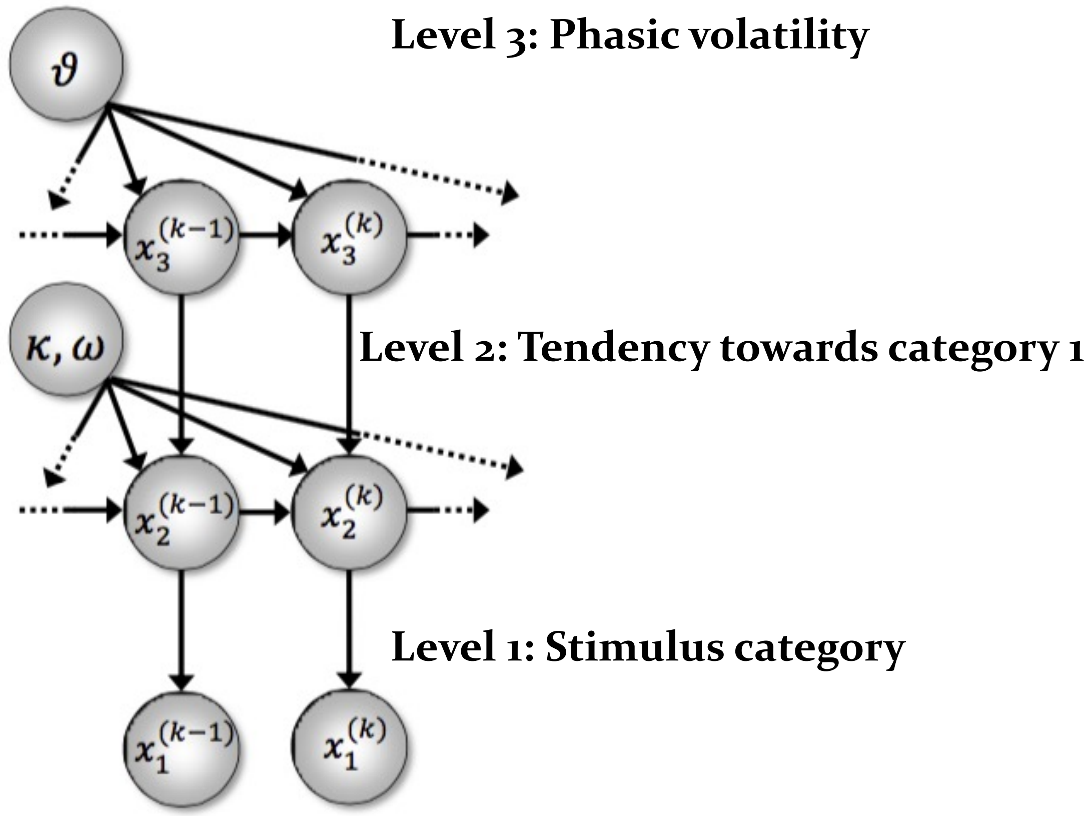


Mathys et al., *Front Hum Neurosci*, 2011

The hierarchical Gaussian filter (HGF): a computationally tractable model for individual learning under uncertainty

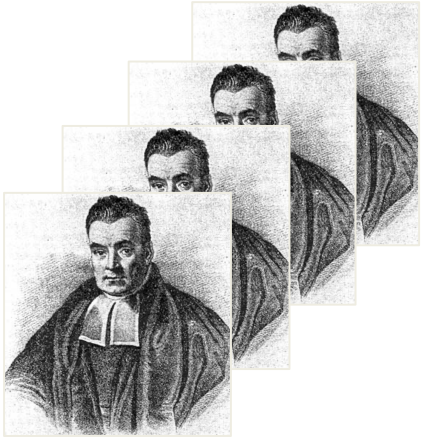


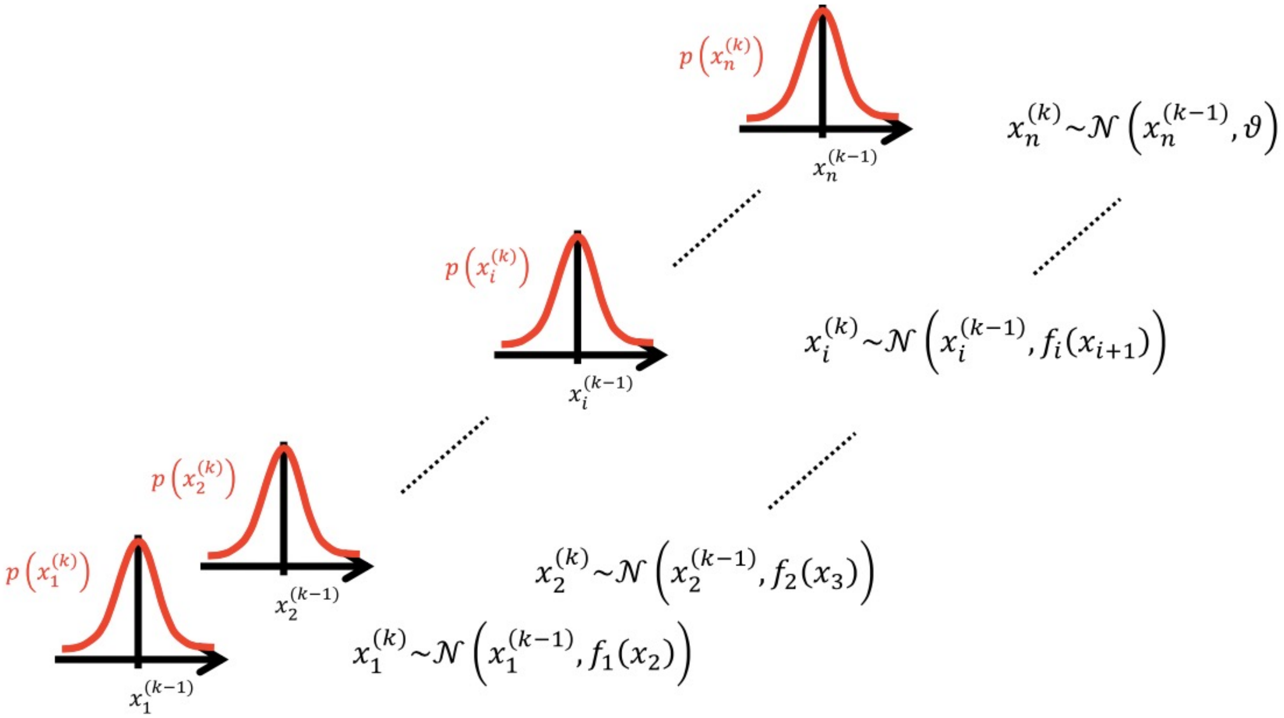
State of the world	Model	
Log-volatility x_3 of tendency	Gaussian random walk with constant step size ϑ	$p(x_3^{(k)}) \sim N(x_3^{(k-1)}, \vartheta)$; $p(x_3^{(k)})$; $x_3^{(k-1)}$
Tendency x_2 towards category "1"	Gaussian random walk with step size $\exp(\kappa x_3 + \omega)$	$p(x_2^{(k)}) \sim N(x_2^{(k-1)}, \exp(\kappa x_3 + \omega))$; $p(x_2^{(k)})$; $x_2^{(k-1)}$
Stimulus category x_1 ("0" or "1")	Sigmoid trans-formation of x_2	$p(x_1{=}1) = s(x_2)$; $p(x_1{=}0) = 1 - s(x_2)$; 1; $p(x_1{=}1)$; x_2; 0



Mathys et al., *Front Hum Neurosci*, 2011

Hierarchical Gaussian Filtering

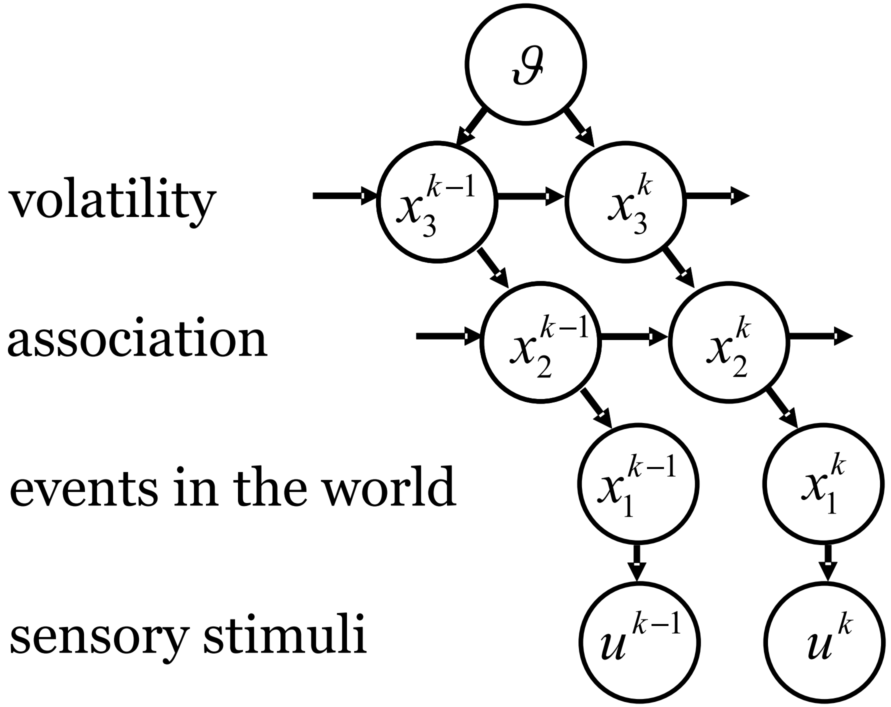


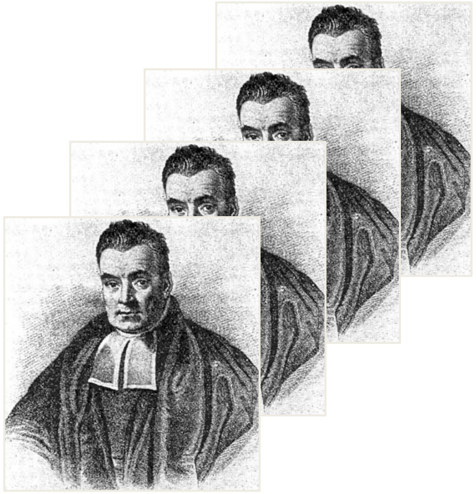


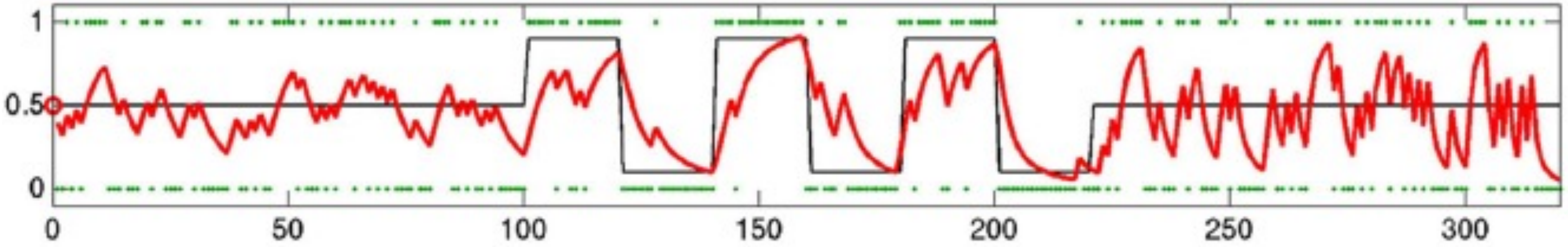
With only 1 level, the HGF is a Kalman filter.

Mathys et al., *Front. Hum. Neurosci.*, 2011

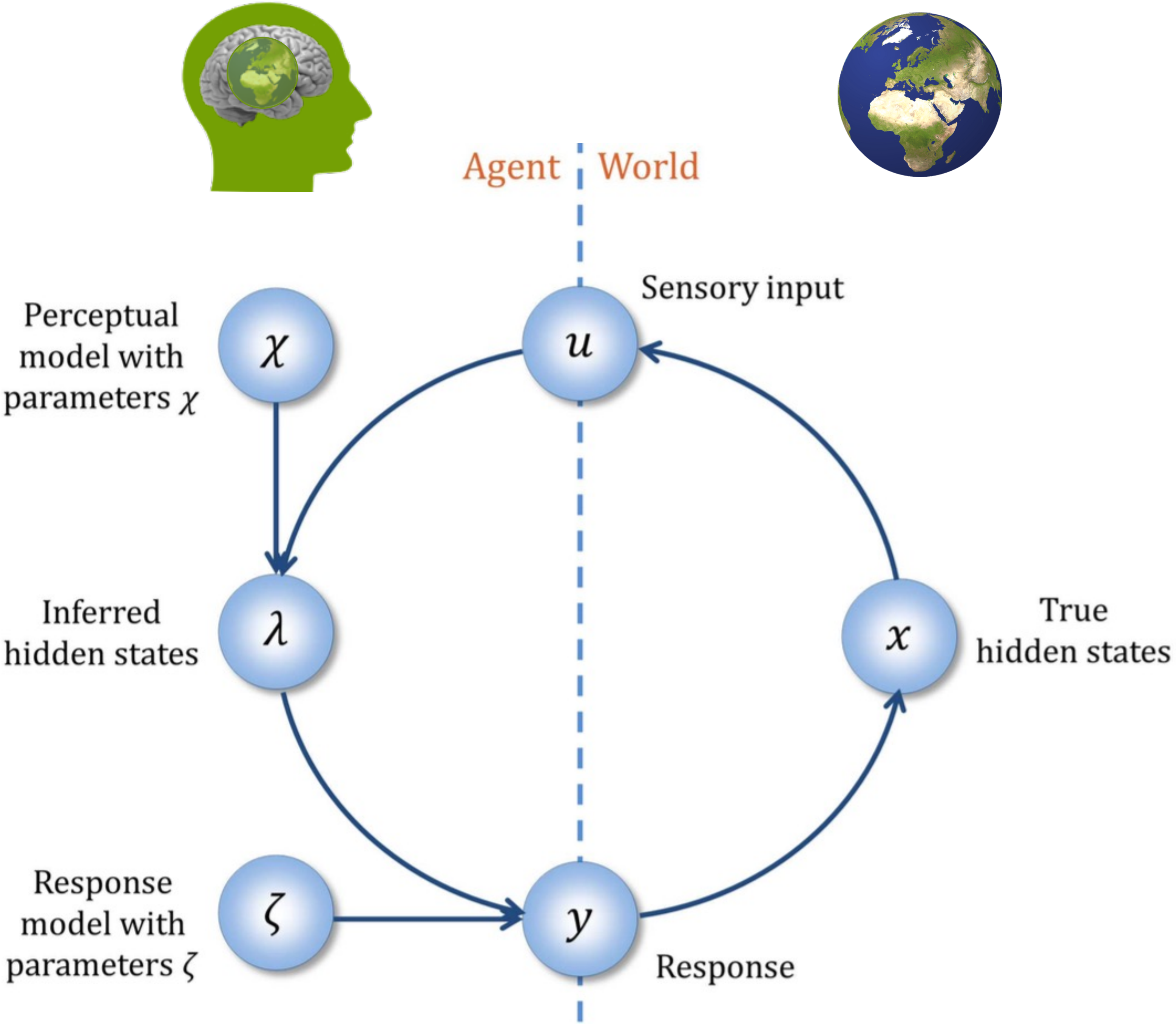
Hierarchical Gaussian Filtering







Mathys et al., *Front Hum Neurosci*, 2011
Mathys et al., *Front Hum Neurosci*, 2014



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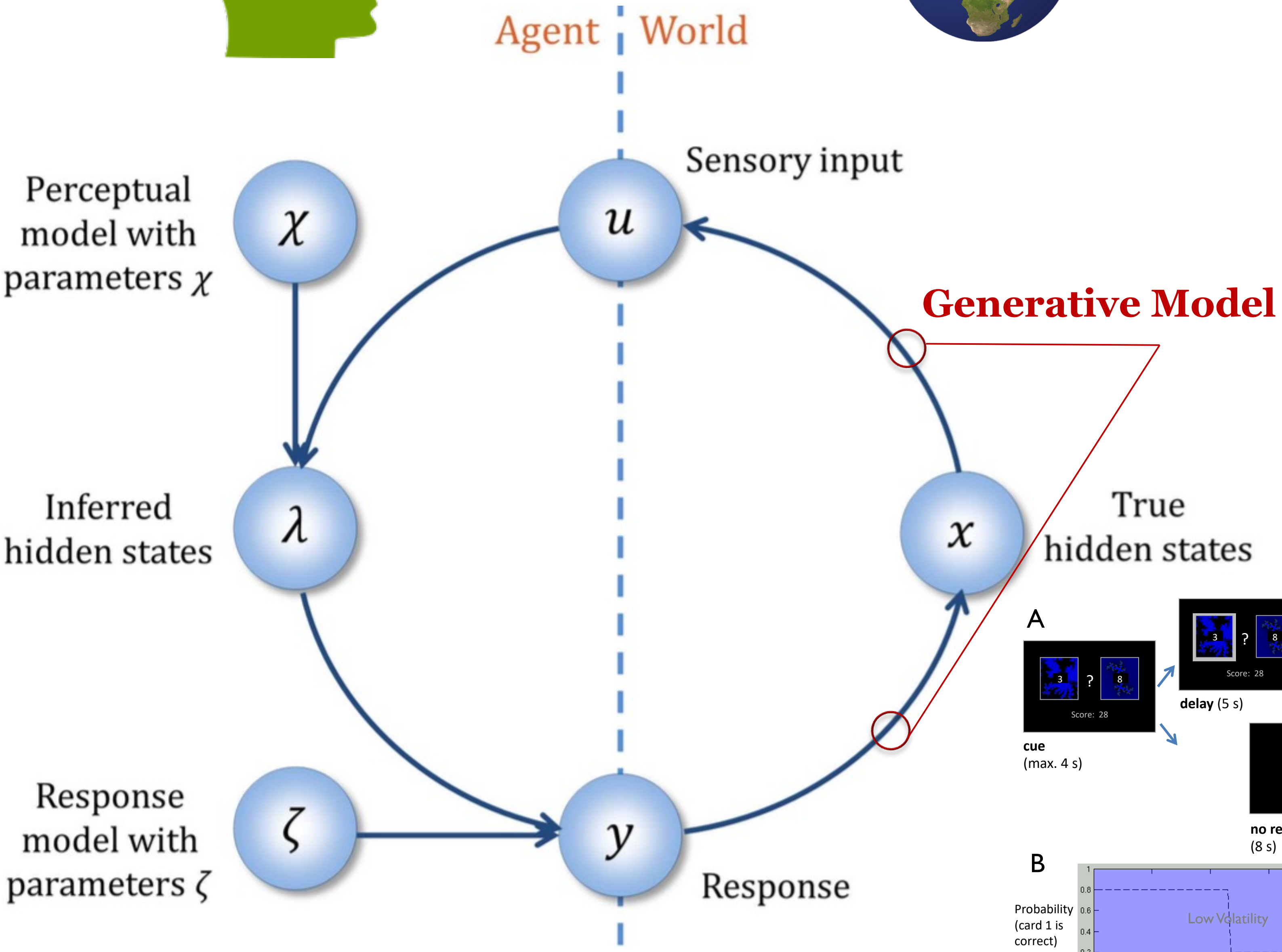
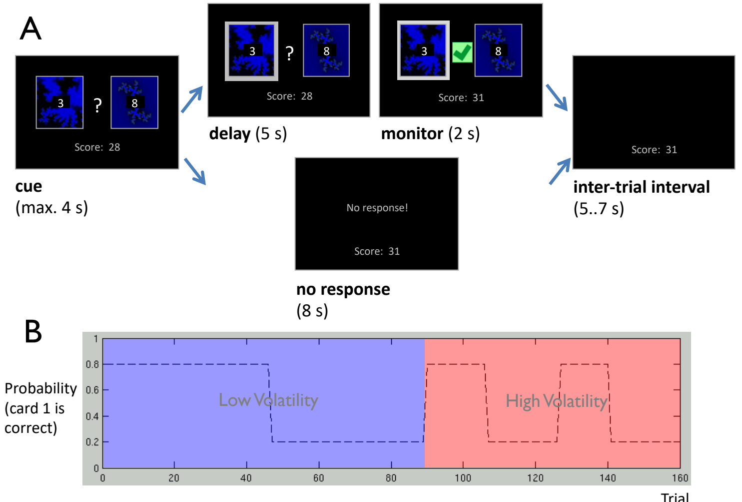
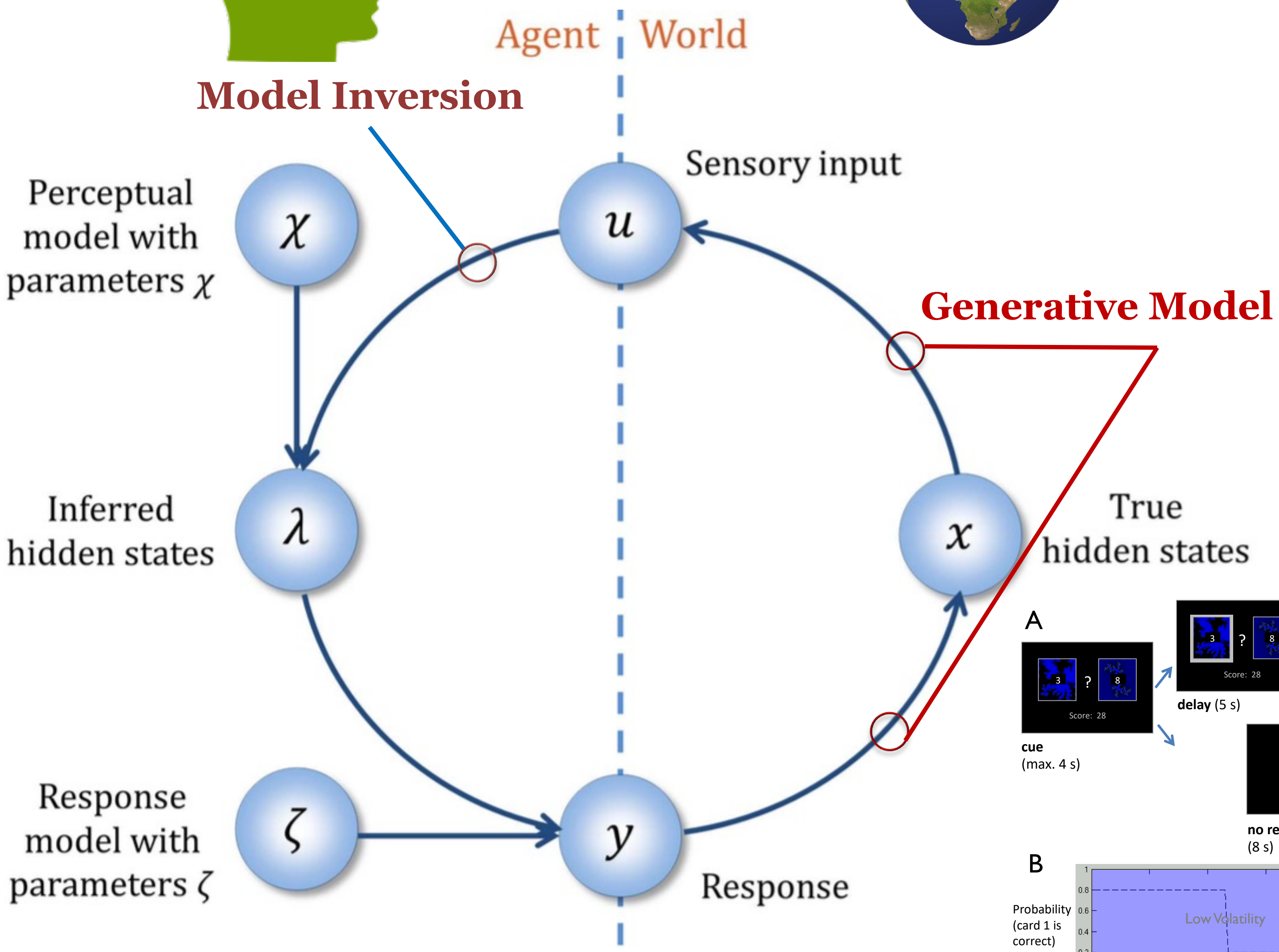
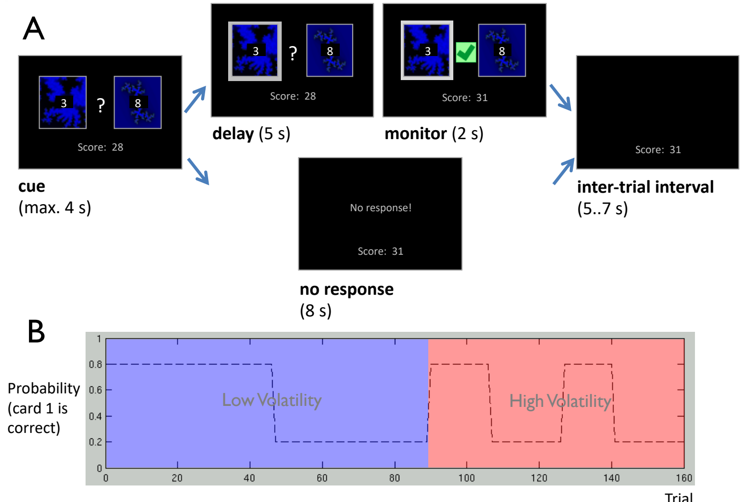

Agent
World
Perceptual model with parameters χ
χ
u
Sensory input
Generative Model
Inferred hidden states
λ
x
True hidden states
Response model with parameters ζ
ζ
y
Response

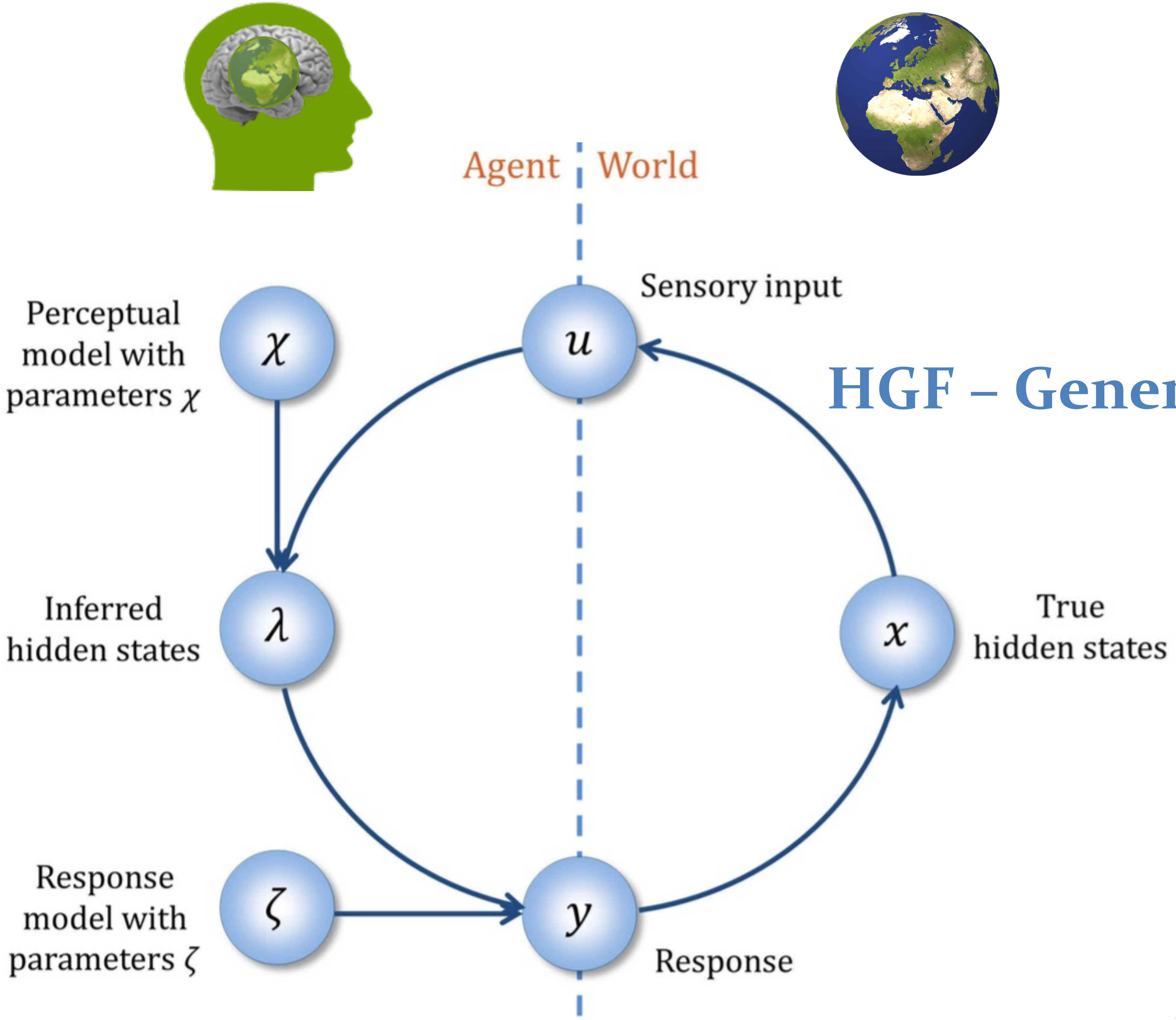

A
Score: 28
cue
(max. 4 s)
delay (5 s)
monitor (2 s)
Score: 31
inter-trial interval
(5..7 s)
No response!
no response
(8 s)
B
Probability
(card 1 is
correct)
Low Volatility
High Volatility
Trial


Agent
World
Model Inversion
Generative Model
Perceptual model with parameters χ
χ
u
Sensory input
Inferred hidden states
λ
x
True hidden states
Response model with parameters ζ
ζ
y
Response


A
Score: 28
cue (max. 4 s)
delay (5 s)
Score: 31
monitor (2 s)
inter-trial interval (5..7 s)
No response!
no response (8 s)
B
Probability (card 1 is correct)
Low Volatility
High Volatility
Trial

HGF

HGF – Generative Model



HGF: Variational Inversion and Update Equations

Agent | World

HGF: Model of Beliefs

Level 3: Belief about volatility

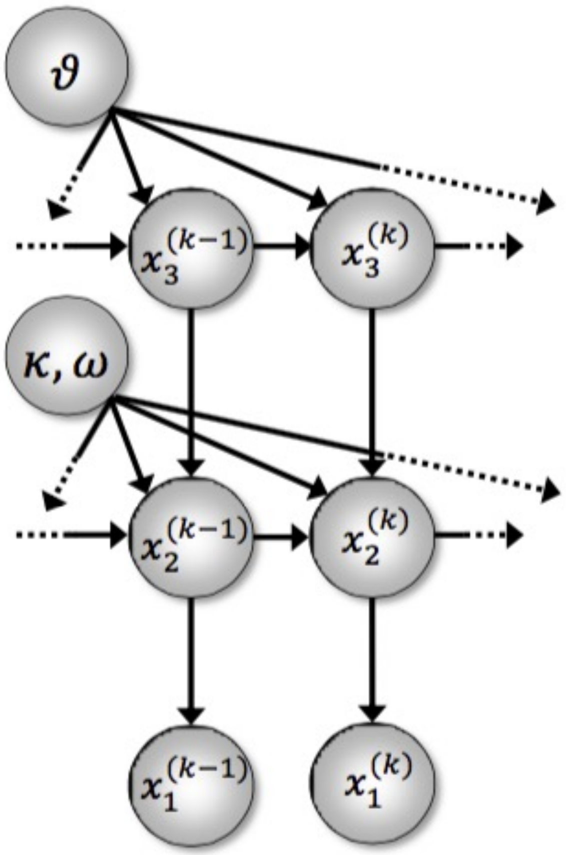
$\mathcal{N}(\mu_3^{(k)}, \sigma_3^{(k)})$

Level 2: Belief about tendency

$\mathcal{N}(\mu_2^{(k)}, \sigma_2^{(k)})$

Level 1: Prediction of categories

$Bern(\mu_1^{(k)})$



HGF: Model of Inputs

Level 3: Phasic Volatility

$p\left(x_3^{(k)}\right) \sim \mathcal{N}(x_3^{(k-1)}, \vartheta)$

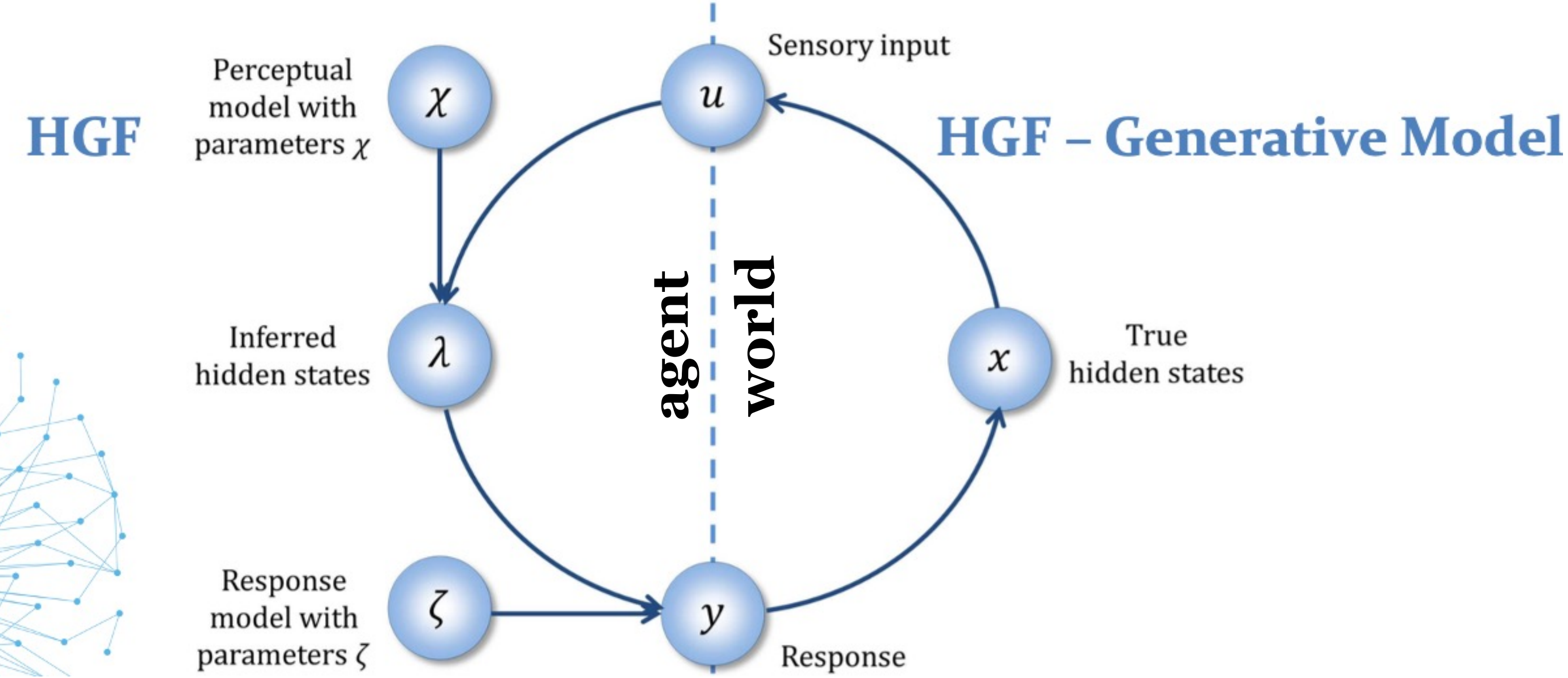
Level 2: Tendency towards category 1

$p\left(x_2^{(k)}\right) \sim \mathcal{N}(x_2^{(k-1)}, e^{(\kappa x_3^{(k-1)} + \omega)})$

Level 1: Observations: category 1

$$p\left(x_1^{(k)} = 1\right) = \frac{1}{1 + e^{-x_2}}$$

Variational Inversion and Update Equations



Inversion of HGF-GM: mean field approximation and fitting quadratic approximations to the resulting variational energies (Mathys et al., 2011)

This leads to **simple one-step update equations** (HGF)

Mathys et al., *Front. Hum. Neurosci.*, 2011; 2014

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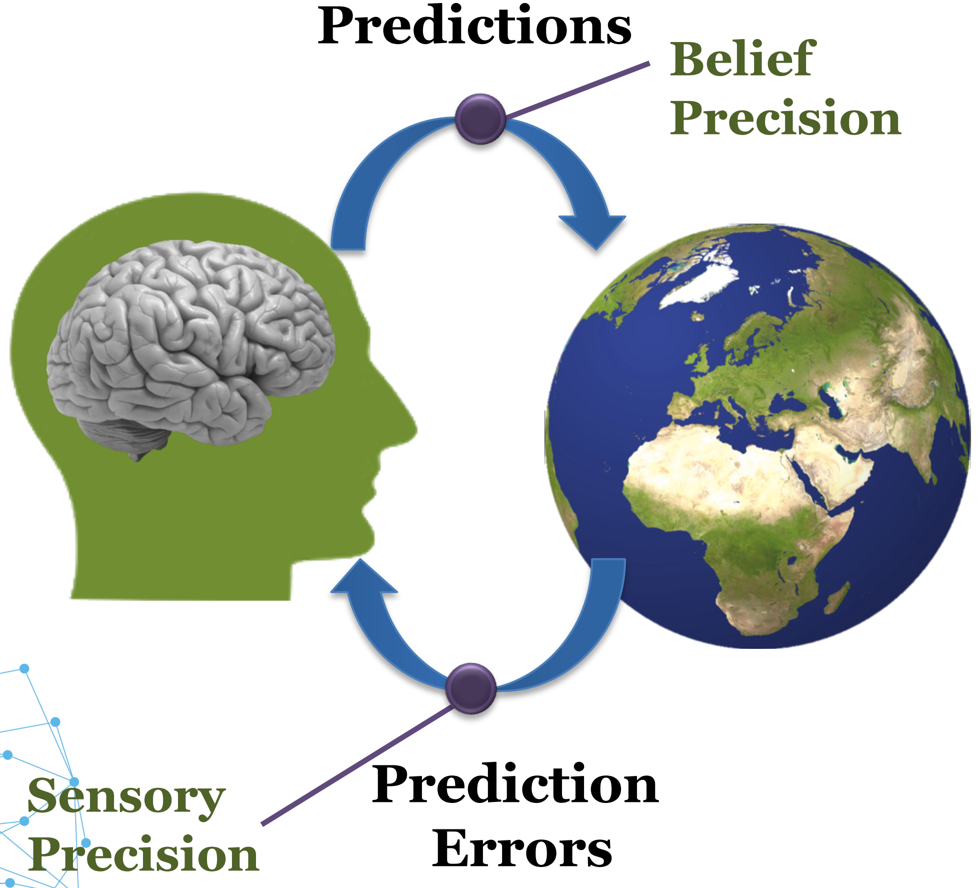
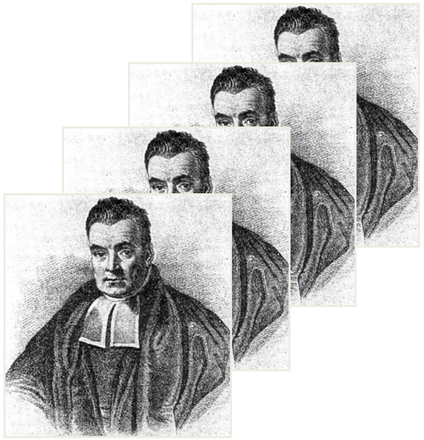
HGF: Update Equations



Mathys et al., *Frontiers Human Neurosci* 2011
Mathys et al., *Frontiers Human Neurosci* 2014

Hierarchy



- Updates as precision-weighted prediction errors

Sensory Precision

$$\Delta\mu_i^{(k)} \propto \frac{\hat{\pi}_{i-1}^{(k)}}{\pi_i^{(k)}} \delta_{i-1}^{(k)}$$

PE

Belief Update

Belief Precision

Updates at the First Level

Prior:

$$\boxed{p(x_2^{(k-1)}) \sim \mathcal{N}\left(x_2^{(k-1)}; \mu_2^{(k-1)}, \frac{\hat{\pi}_1^{(k)}}{\pi_2^{(k)}}\right)}$$

Posterior:

$$\frac{\hat{\pi}_1^{(k)}}{\pi_2^{(k)}} = \frac{\hat{\pi}_1^{(k)}}{\frac{1}{\sigma_2^{(k-1)} + \exp(k_2\mu_3^{(k-1)} + \omega_2)} + \hat{\pi}_1^{(k)}}$$

Outcome Precision

Informational Uncertainty

Environmental uncertainty (instead of the constant ϑ in the Kalman filter)

$$\mu_2^{(k)} = \mu_2^{(k-1)} + \frac{\hat{\pi}_1^{(k)}}{\pi_2^{(k)}}\left(u^{(k)} - \mu_1^{(k-1)}\right)$$

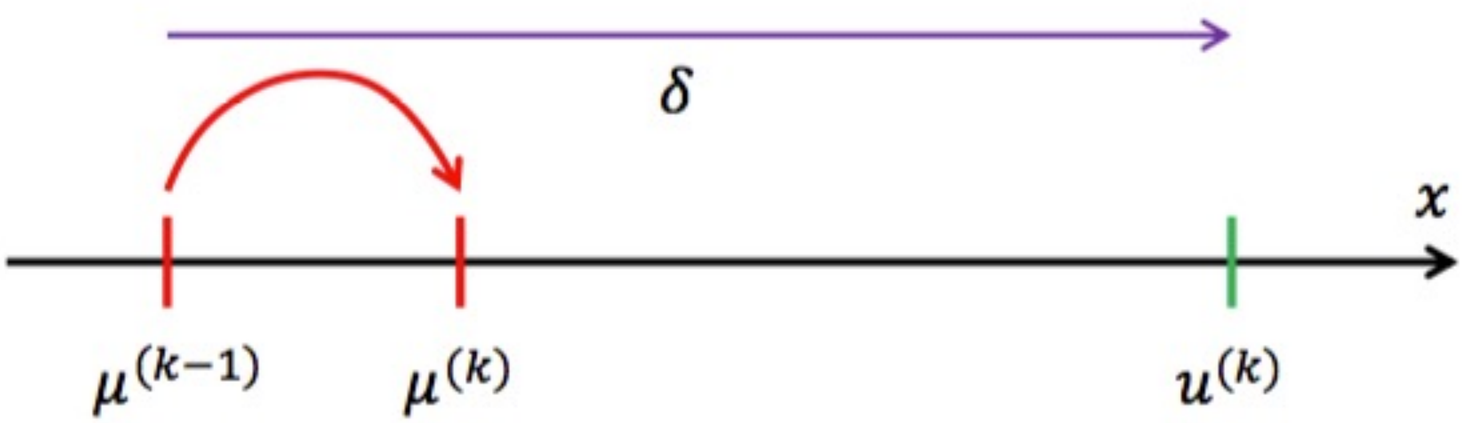
Unpacking the Learning Rate

Rescorla-Wagner Learning:

Learning Rate/Weight

Belief Update

$$\Delta\mu_i^{(k)} \propto \alpha\delta_{i-1}^{(k)}$$

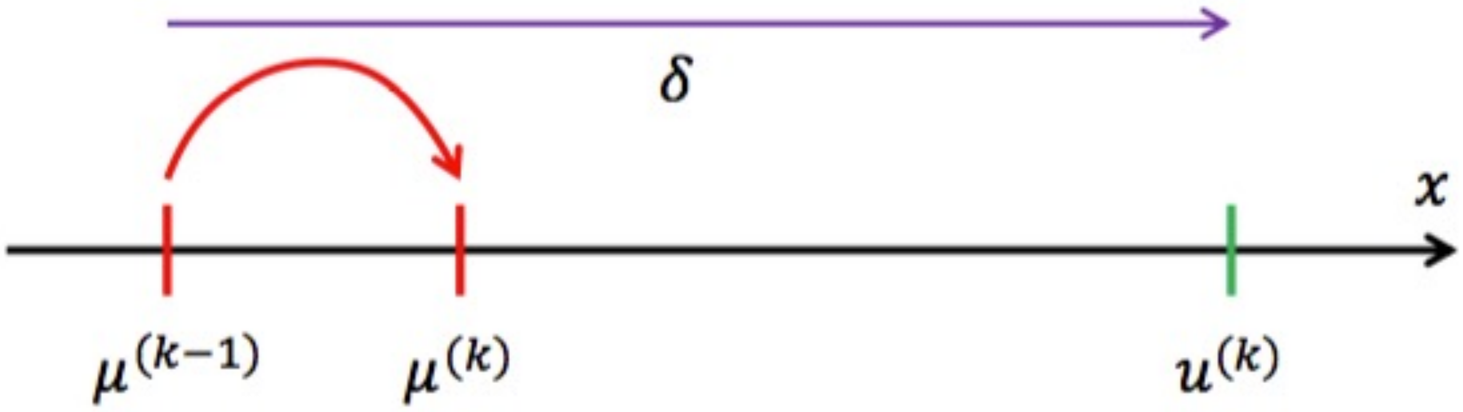


Unpacking the Learning Rate

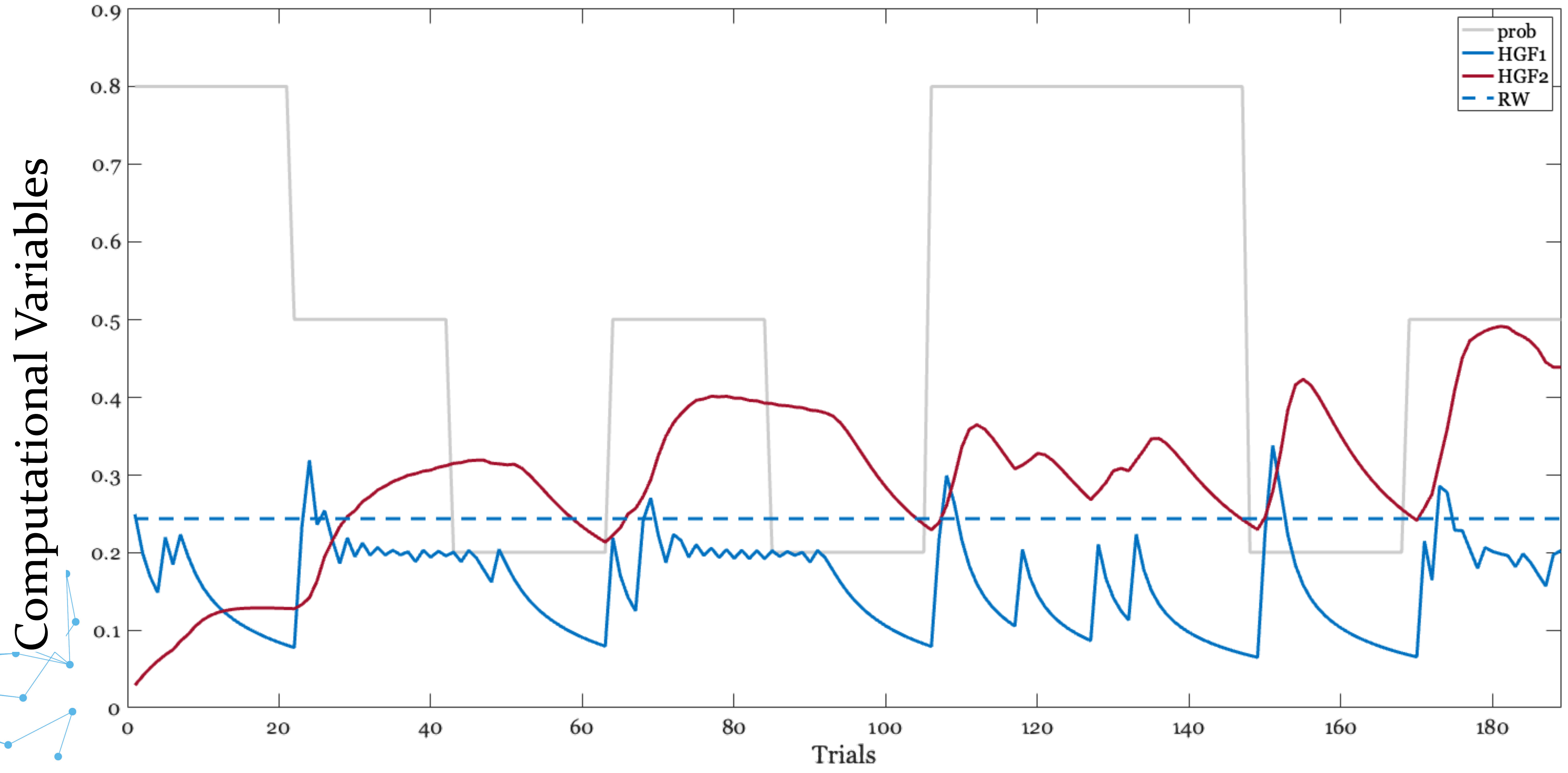
Hierarchical Gaussian Filter :

Belief Update $\rightarrow$ $$\Delta\mu_i^{(k)} \propto \frac{\hat{\pi}_{i-1}^{(k)}}{\pi_i^{(k)}} \delta_{i-1}^{(k)}$$ **Weight**

$$= \frac{\textit{how much we're learning here}}{\textit{how much we already know}}$$

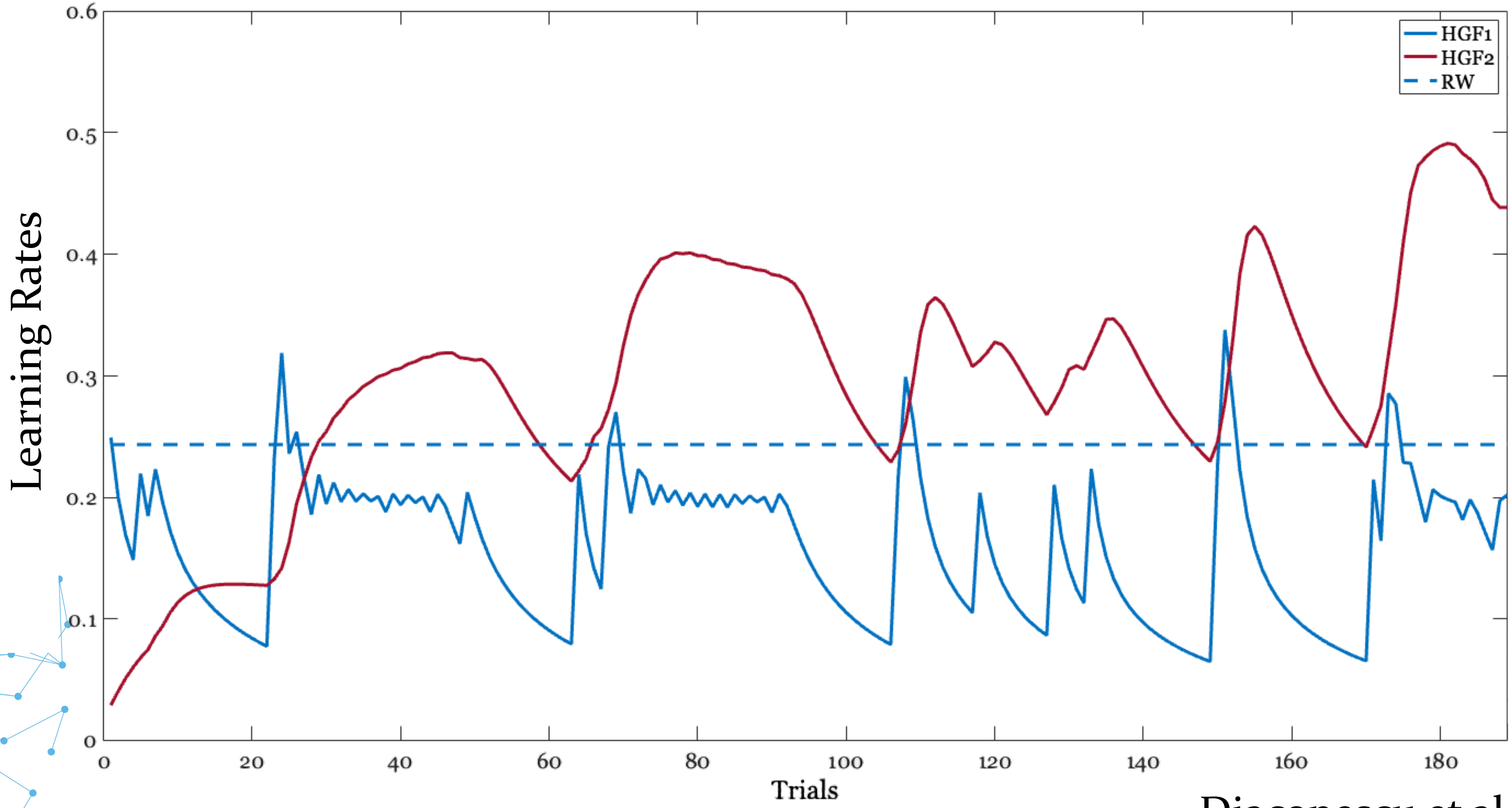


HGF: Dynamic Learning Rates



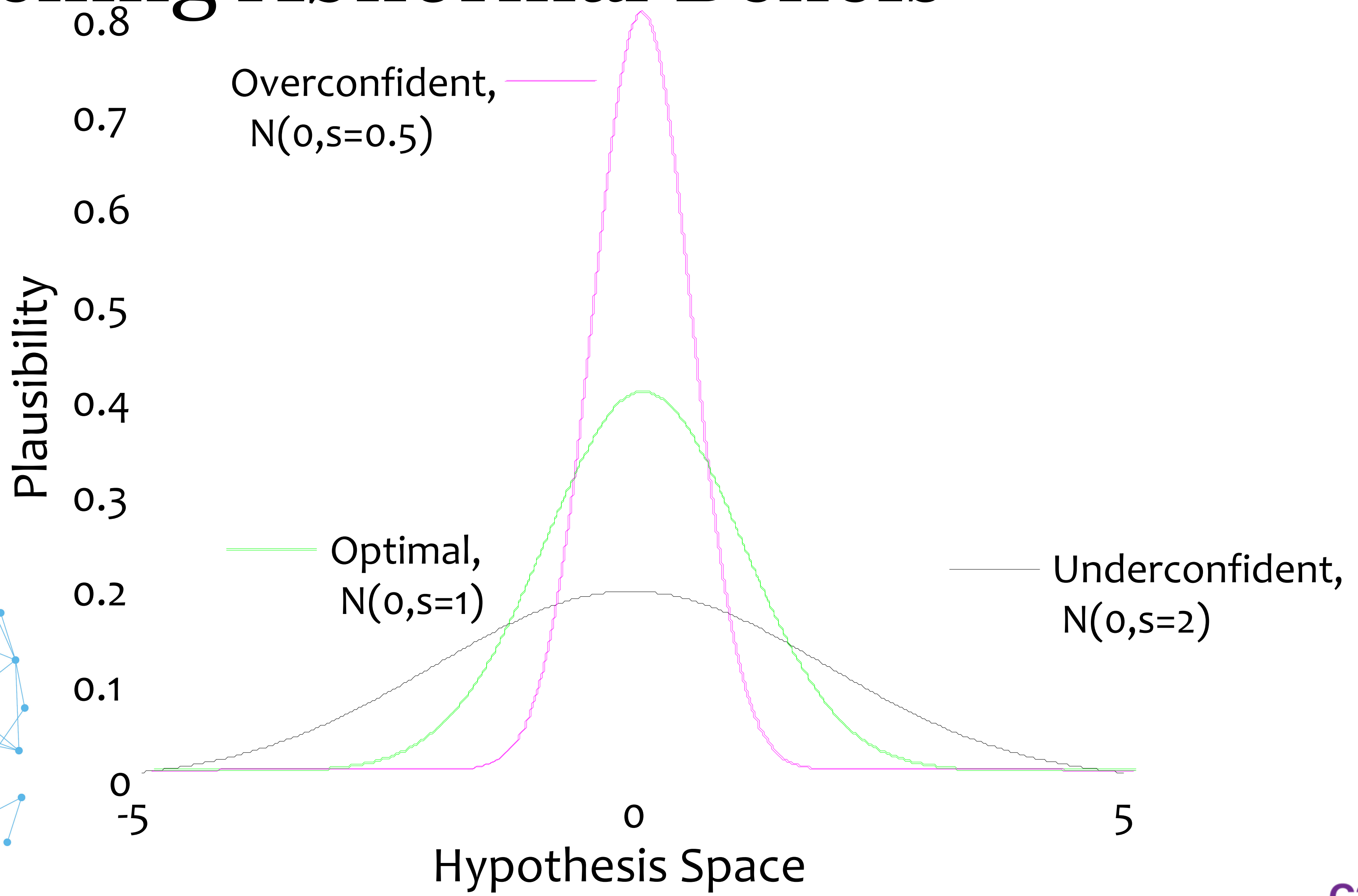
Diaconescu et al., 2014

HGF: Dynamic Learning Rates



Diaconescu et al., 2014

Modelling Abnormal Beliefs



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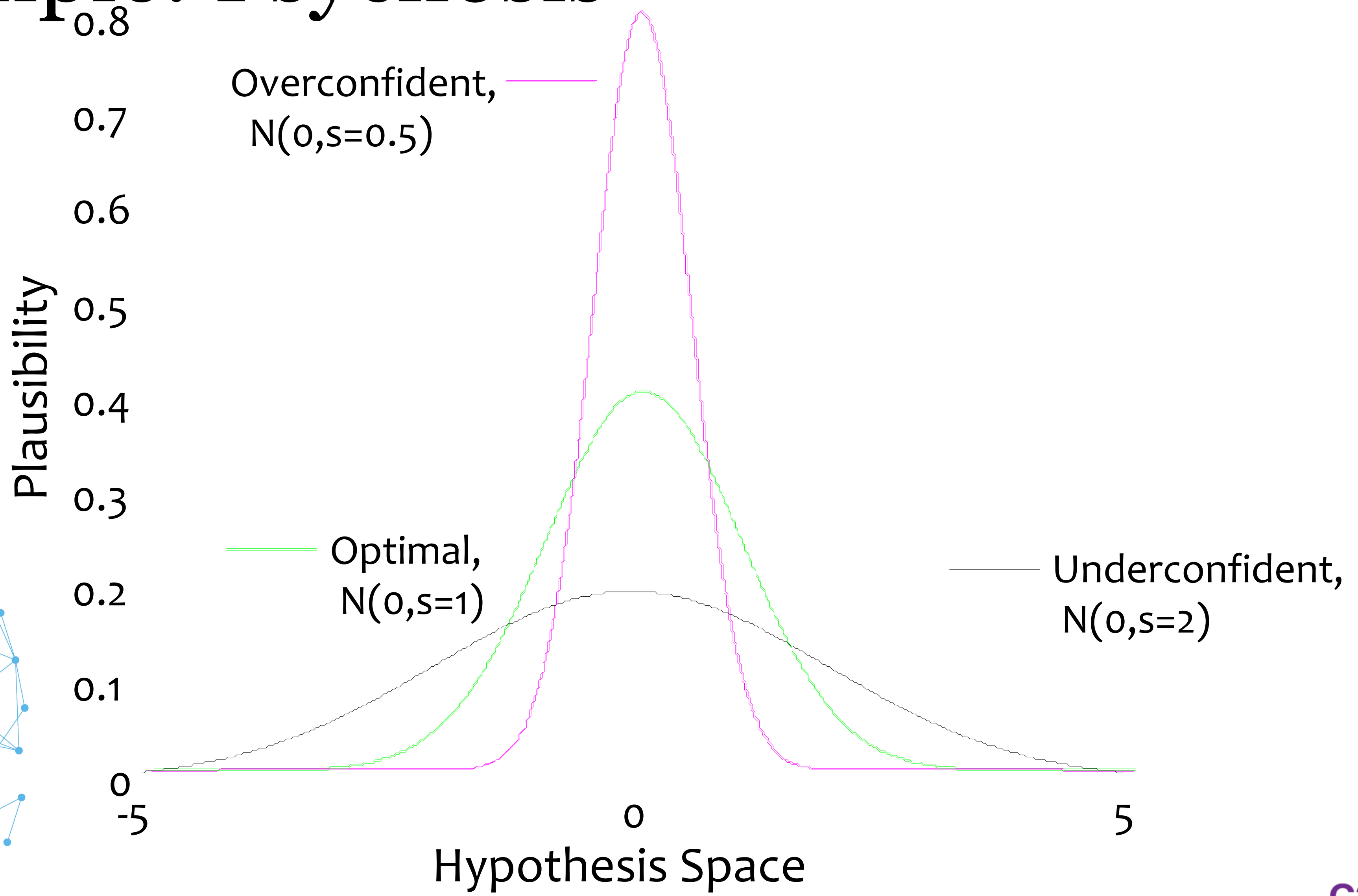
Example: Psychosis



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Thank You!

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Today's Agenda

Day 6:
Bayesian Models of Learning and Integration of Neuroimaging

9:00 am - 10:30 am	*Modelling Cognition using Bayesian Inference* Andreea Diaconescu
10:45 am - 12:15 pm	*Modelling Abnormal Beliefs* Daniel Hauke
1:00 pm - 2:30 pm	*Integration of Neuroimaging: Dynamic Causal Modelling for fMRI and EEG Data* Andreea Diaconescu, Colleen Charlton
2:45 pm - 4:15 pm	*Dynamic Causal Modelling for fMRI: Extensions and Simulations* Peter Bedford, Povilas Karvelis

Today's Agenda

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“My senses are sharpened.”

“Sights and sounds possess a keenness that I have never experienced before.”

Kapur, 2003

“I had to make sense - any sense - out of all these uncanny coincidences.

I did it by radically changing my conception of reality.”

Chadwick, 2009

"My senses are sharpened."

"Sights and sounds possess a keenness that I have never experienced before."

"I had to make sense - any sense - out of all these uncanny coincidences.

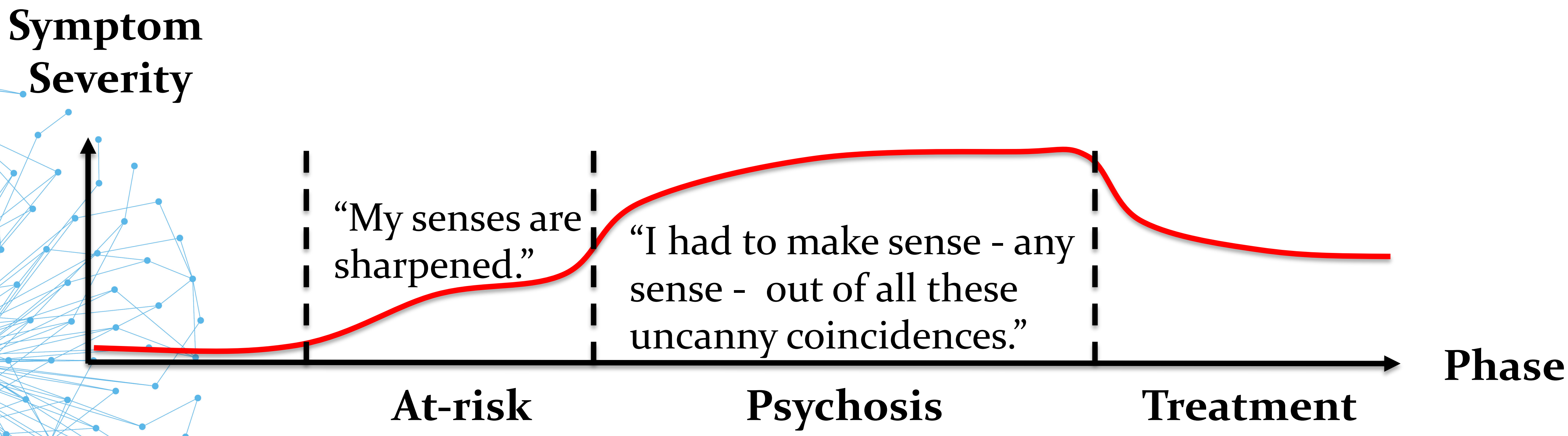
I did it by radically changing my conception of reality."

"My senses are sharpened."

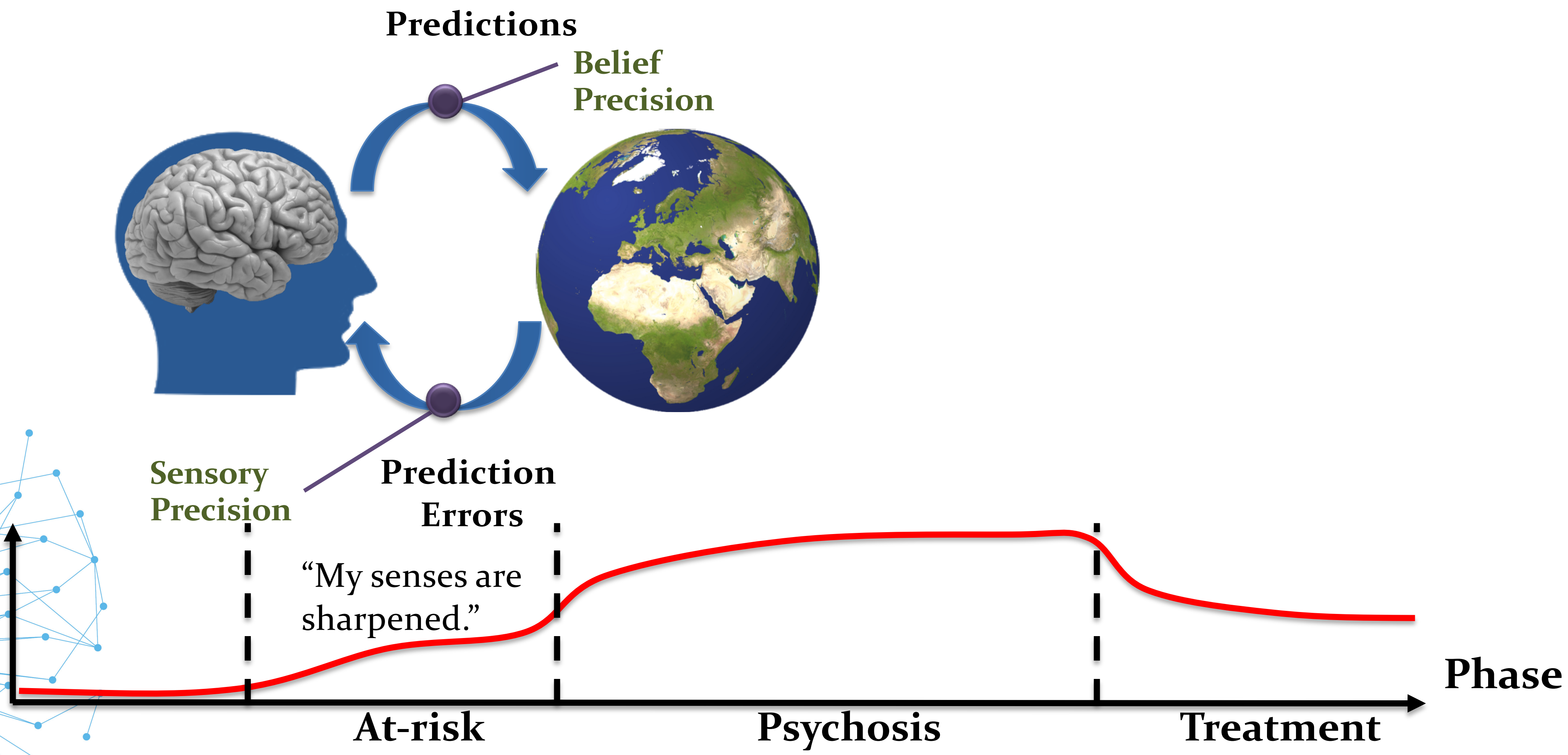
"I had to make sense - any sense - out of all these uncanny coincidences."

Psychosis

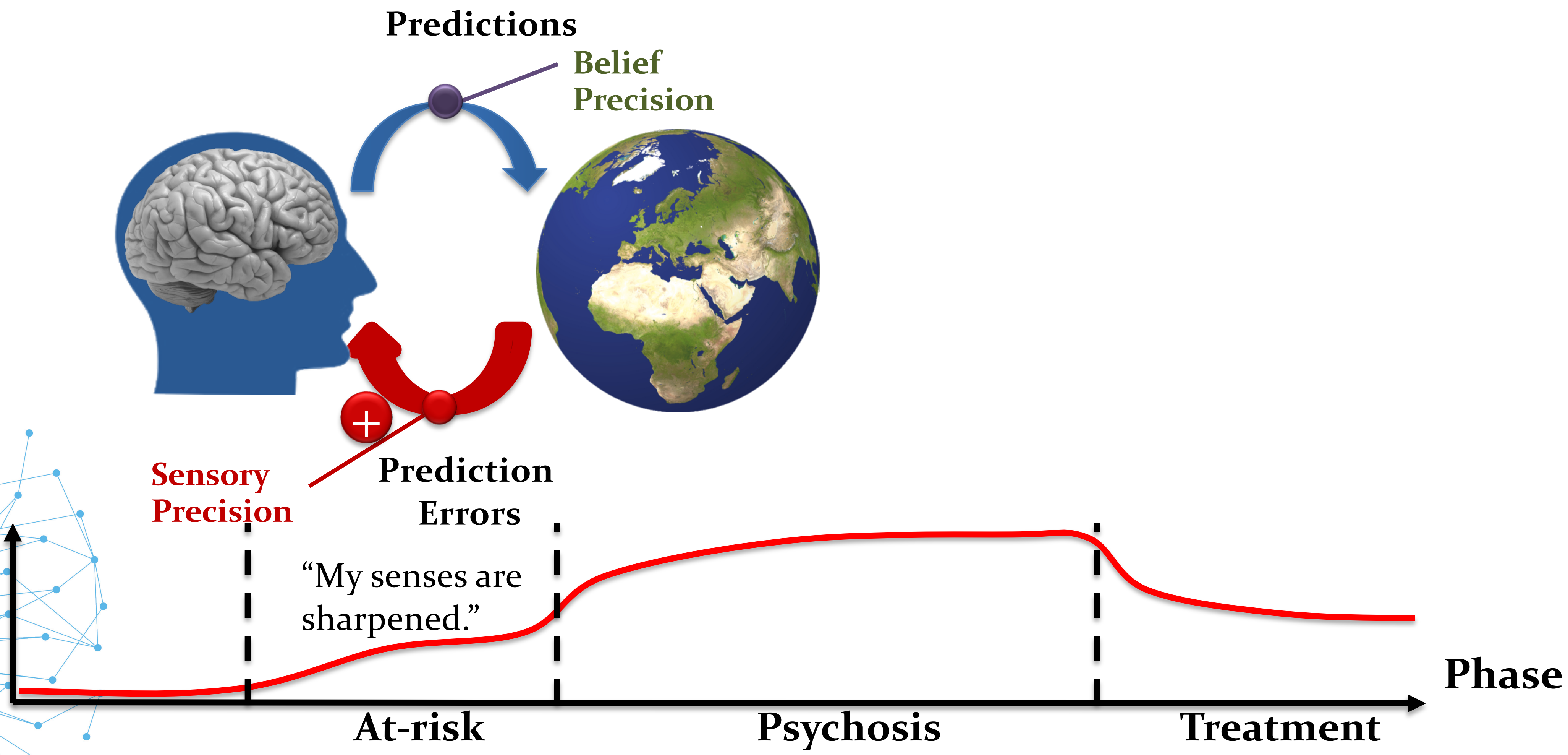
- Modelling early-psychosis



Hypothesis: Models of Psychosis Across Stages



Hypothesis: At-Risk Phase



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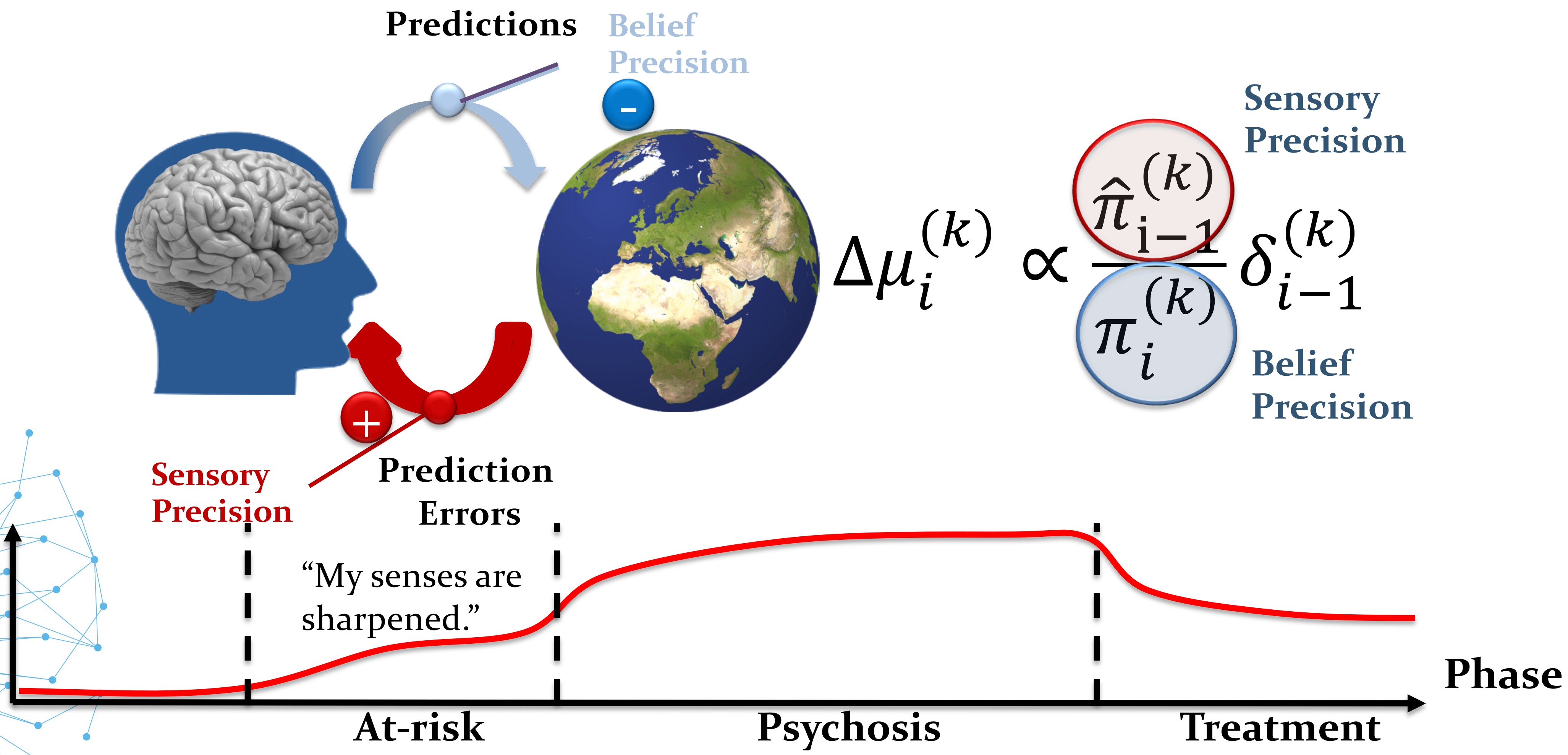
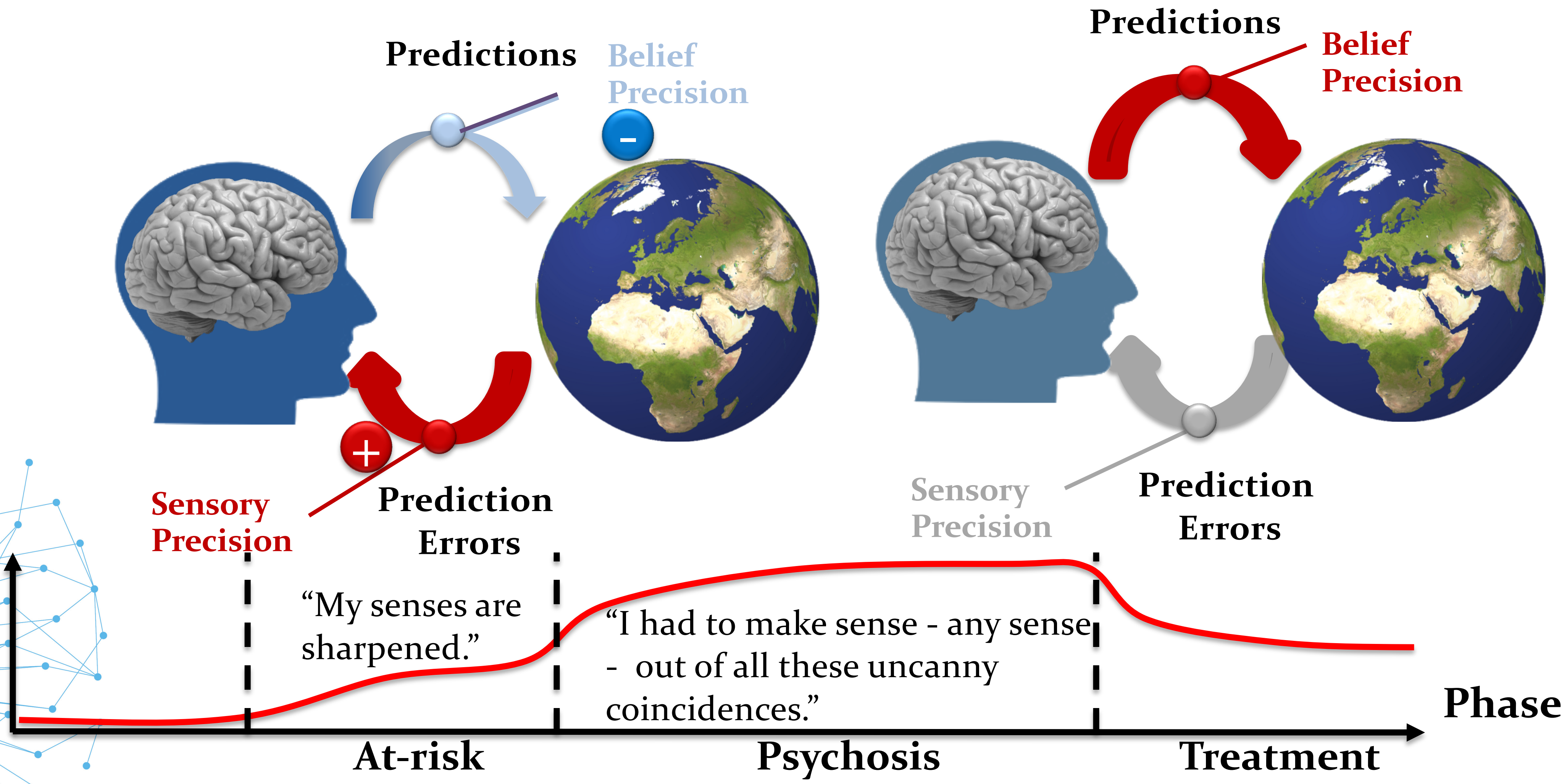
Hypothesis: At-Risk Phase



Hypothesis: Delusional Conviction



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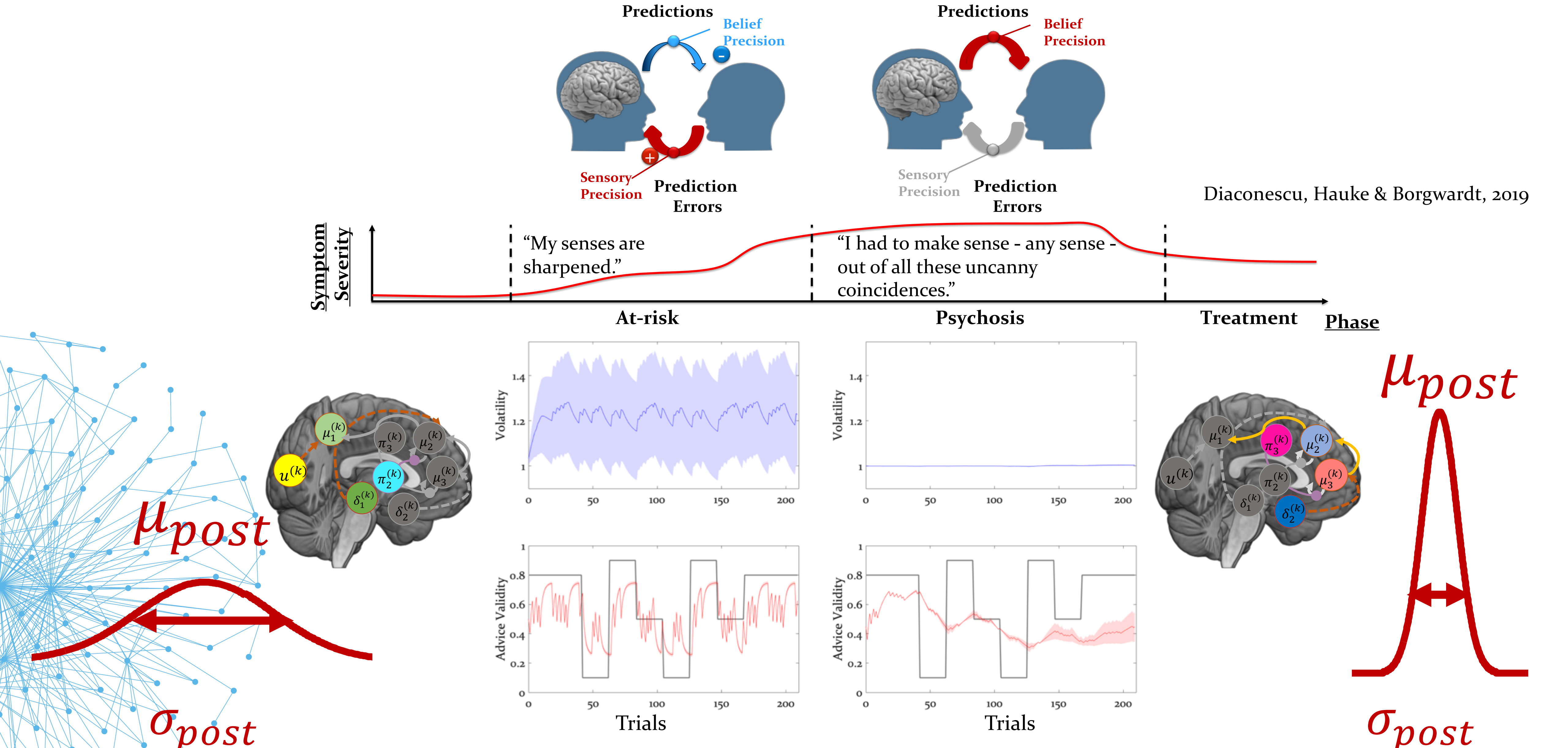
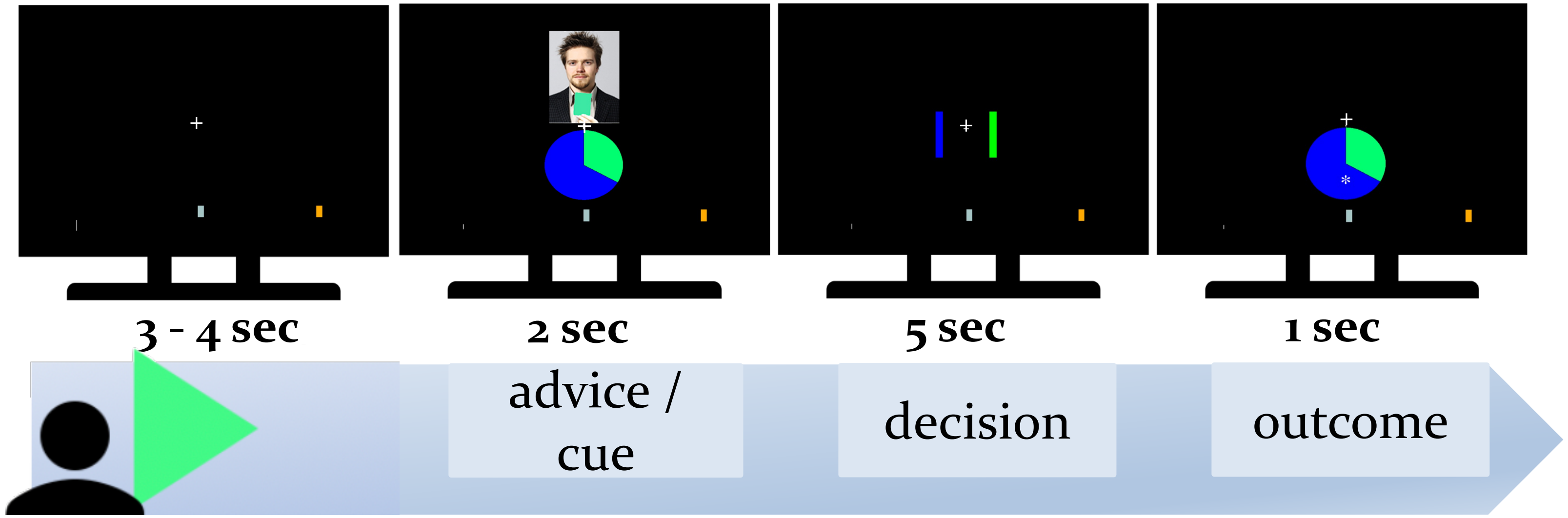
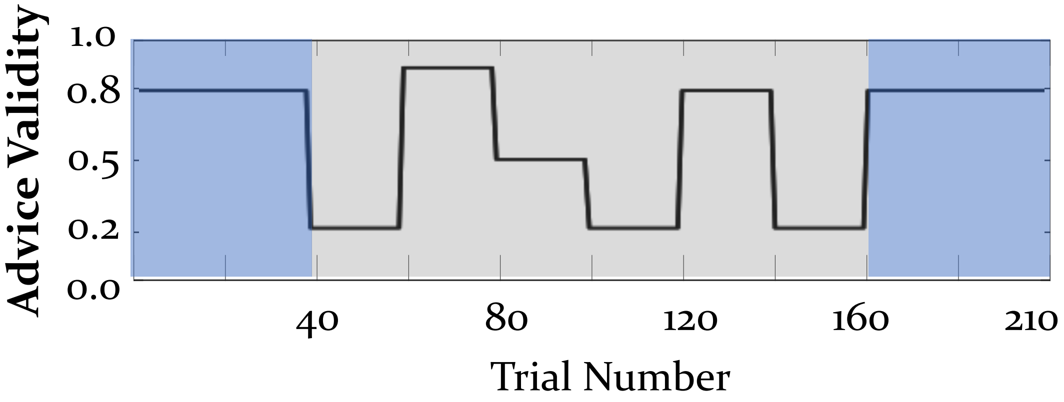
Early Psychosis and Persecutory Delusions



Diaconescu, Hauke & Borgwardt, 2019

Empirical Validation: Healthy Population





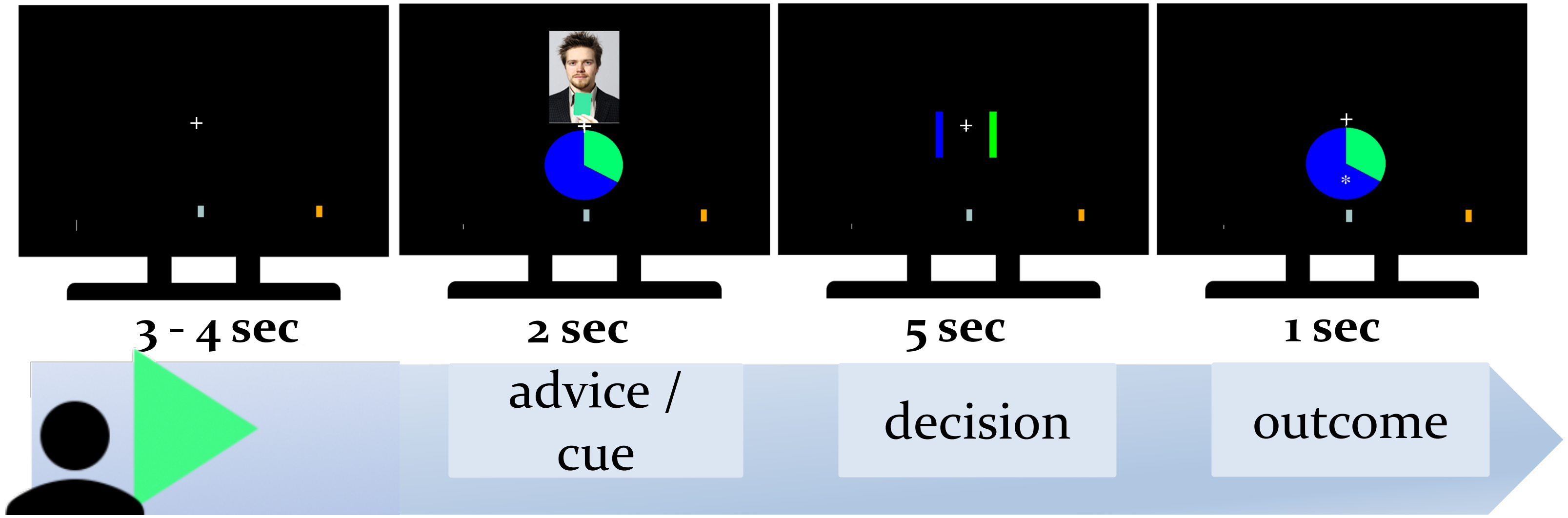
Key features of the task:

- recommendations of adviser were veridical (pre-recorded videos)
- **volatility of advice** (stable vs. volatile)

Diaconescu et al., 2014, *PLoS Computational Biology*

Diaconescu et al., 2017, *SCAN*

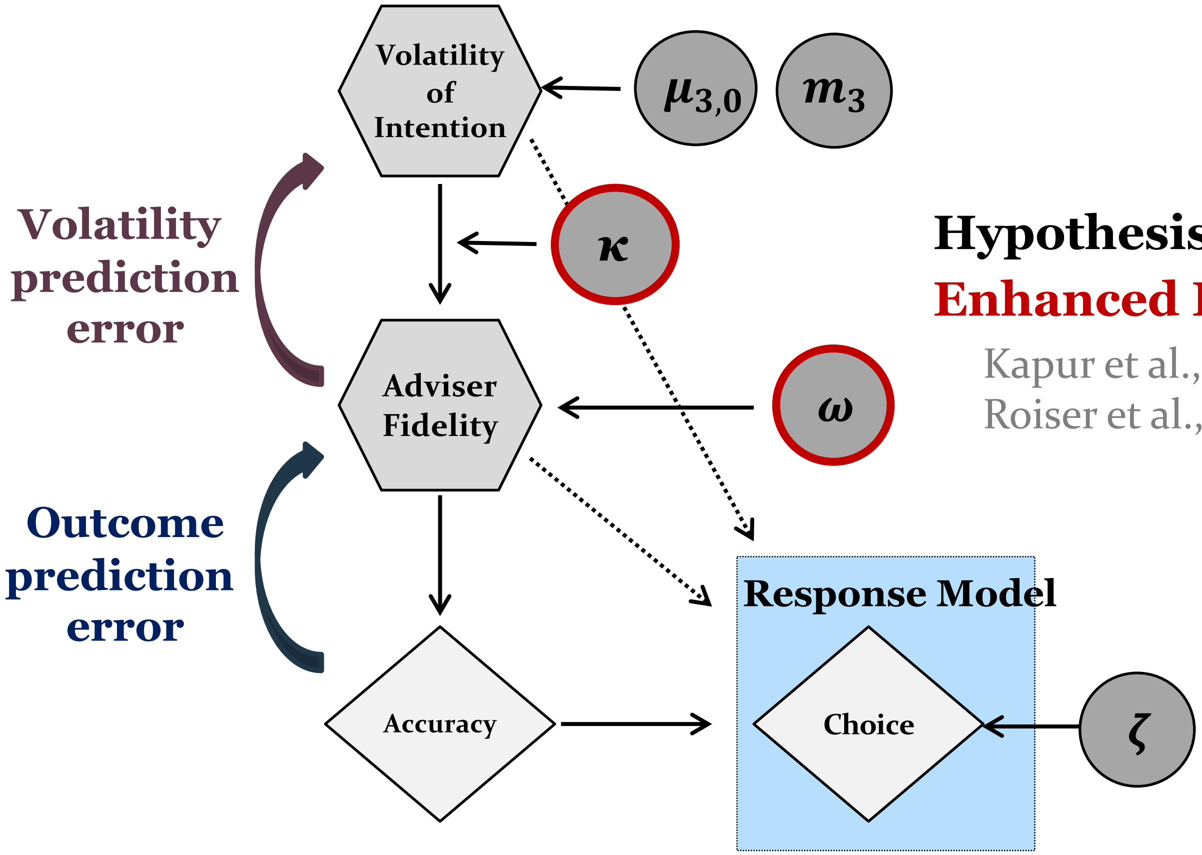
Clinical Applications



- 15 unmedicated (≤ 7 days of antipsychotic medication) first-episode psychosis patients (**FEP**)
- 16 individuals at clinical high-risk for psychosis (**CHR**)
- 16 healthy controls (**HC**) that were matched to **CHR** for age, gender, handedness, and cannabis consumption

How do we model persecutory beliefs?

Computational Model of Learning



Hypothesis I:
Enhanced Learning Rate/Aberrant Salience

Kapur et al., 2003
Roiser et al., 2009

Mathys et al., *Front Hum Neurosci*, 2014
Diaconescu et al., *PLoS Computational Biology* 2014

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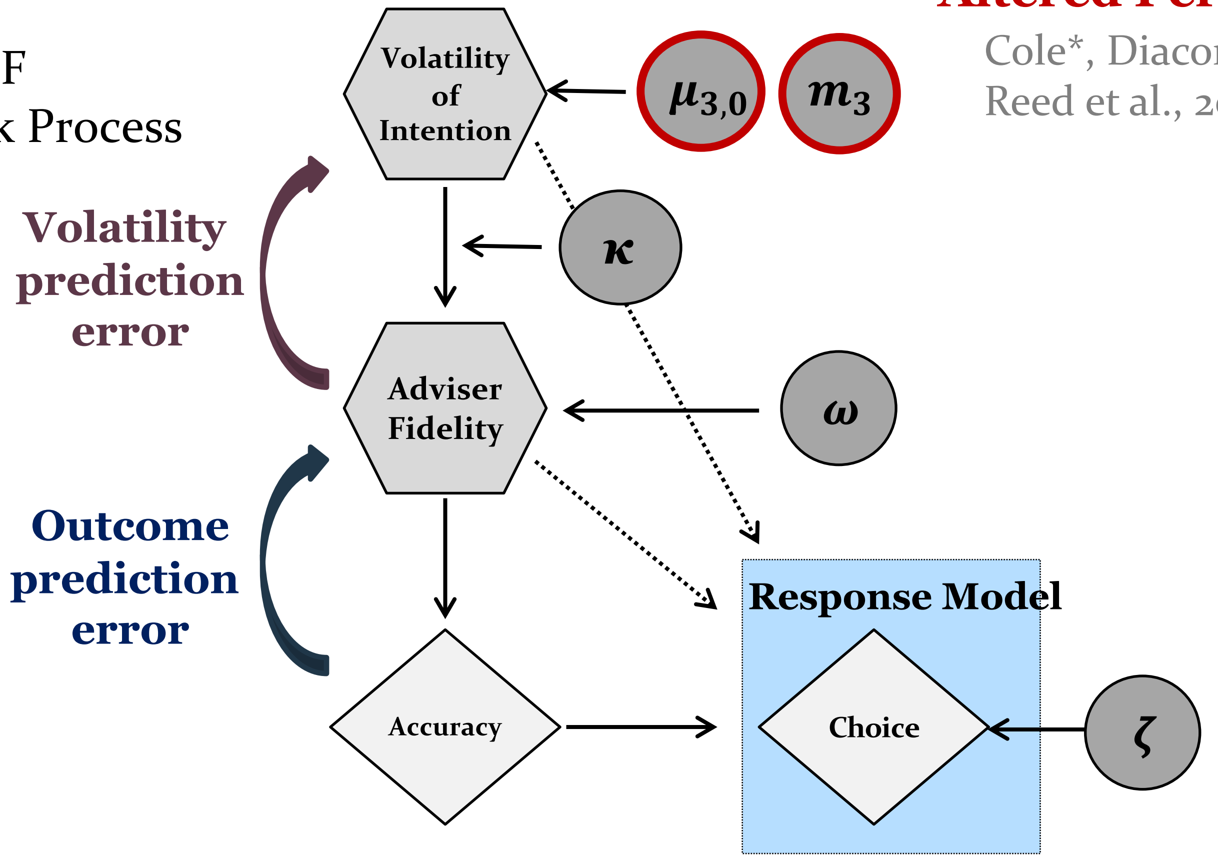
How do we model persecutory beliefs?

Computational Model of Learning

Mean Reverting HGF
Ornstein-Uhlenbeck Process



Hypothesis II:

Altered Perception of Volatility

Cole*, Diaconescu* et al., 2014
Reed et al., 2020

Mathys et al., *Front Hum Neurosci*, 2014
Diaconescu et al., *PLoS Computational Biology* 2014

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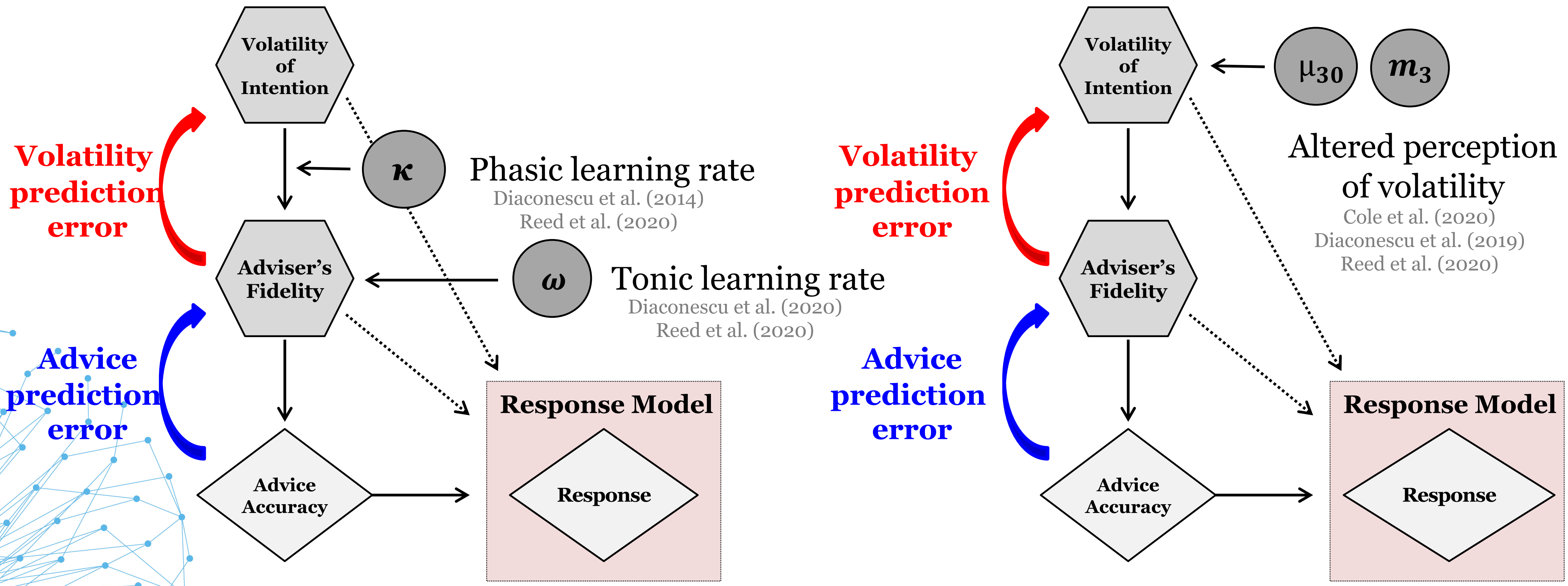
Models of Persecutory Delusions

Hypothesis I: HGF | **Hypothesis II: Mean-reverting HGF**



Mathys et al., *Front Hum Neurosci*, 2014
Diaconescu et al., *PLoS Computational Biology* 2014

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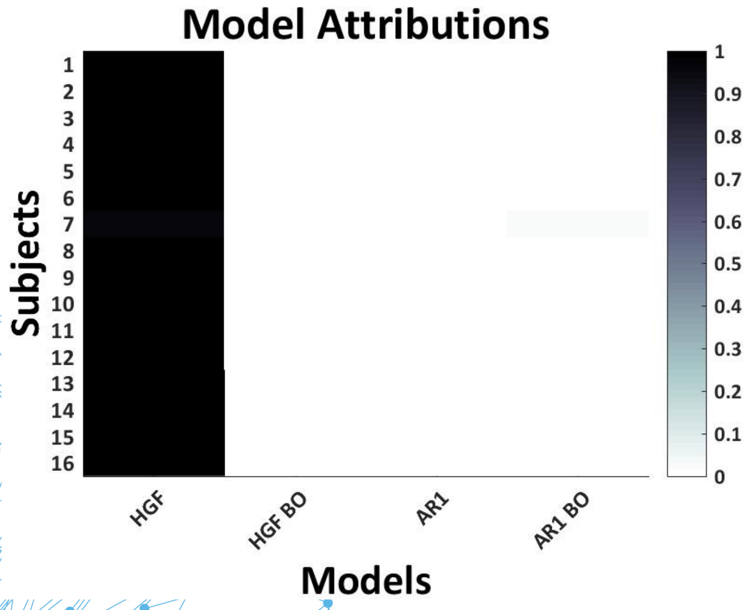
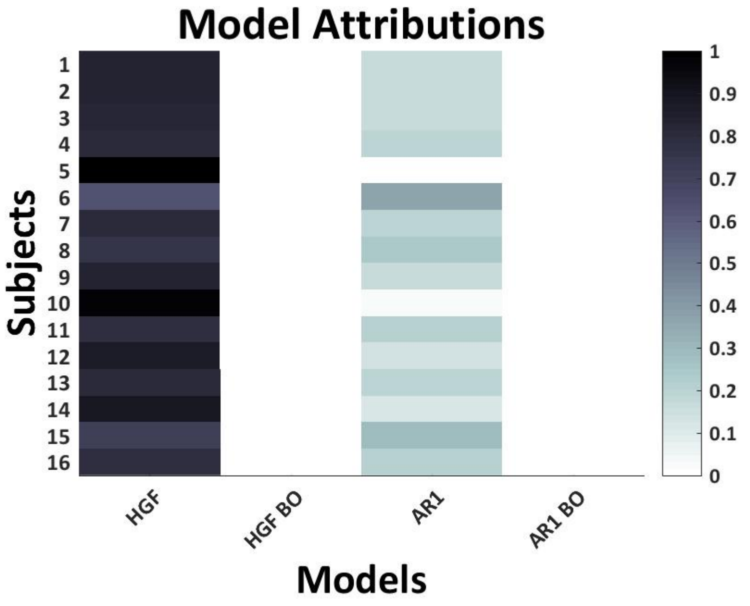
Model Attributions

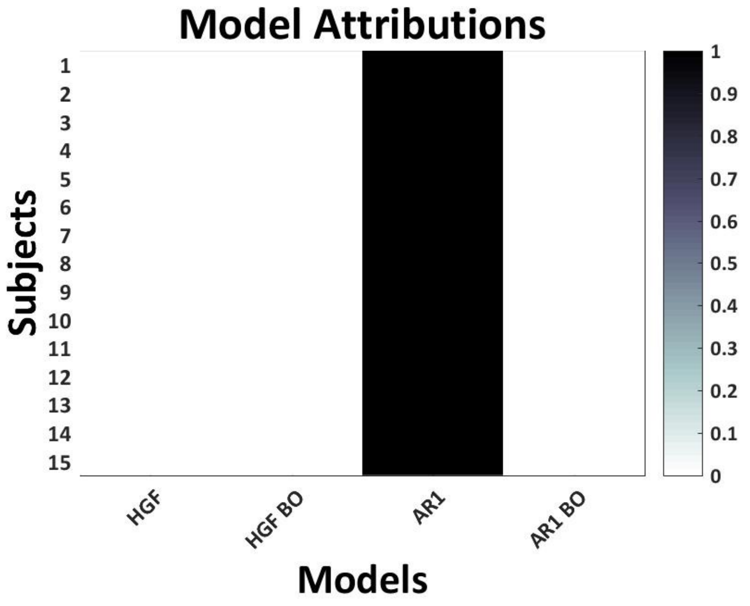
HC



CHR



FEP



Interpretation
Evidence for altered perception of environmental volatility in FEP.

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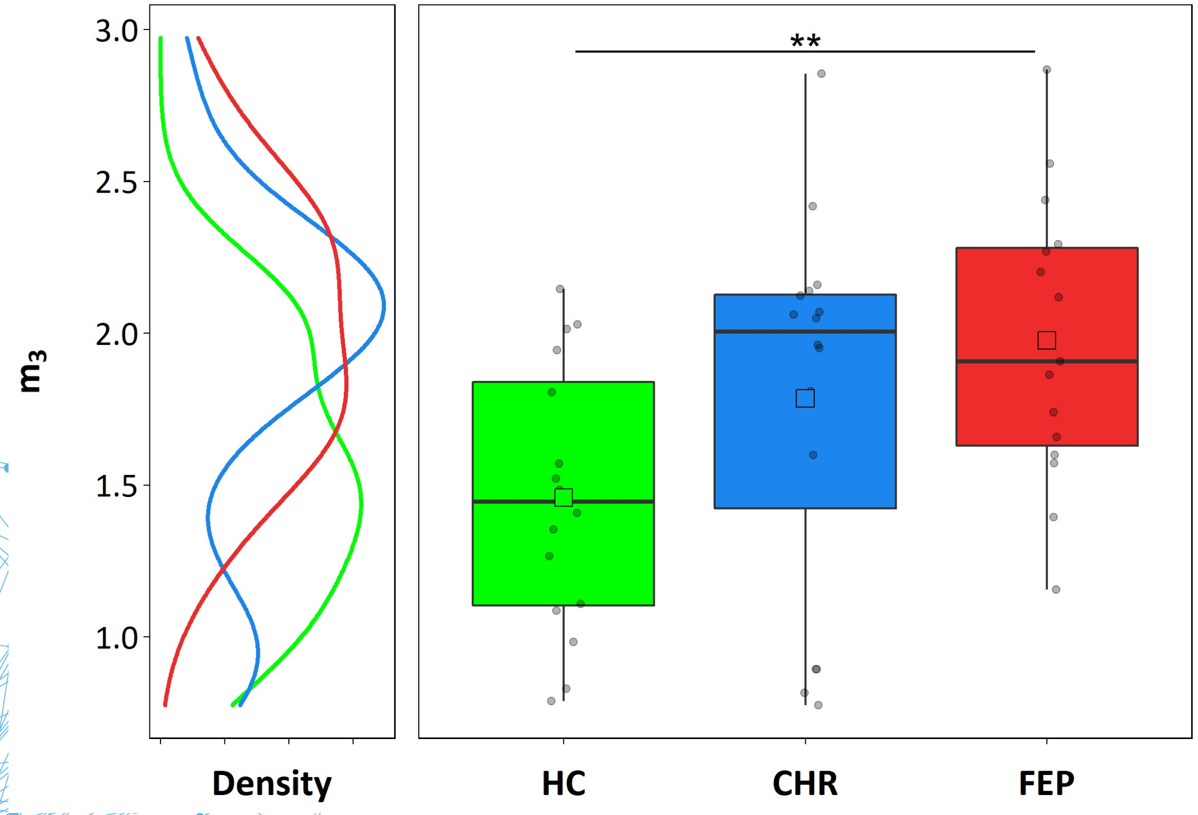
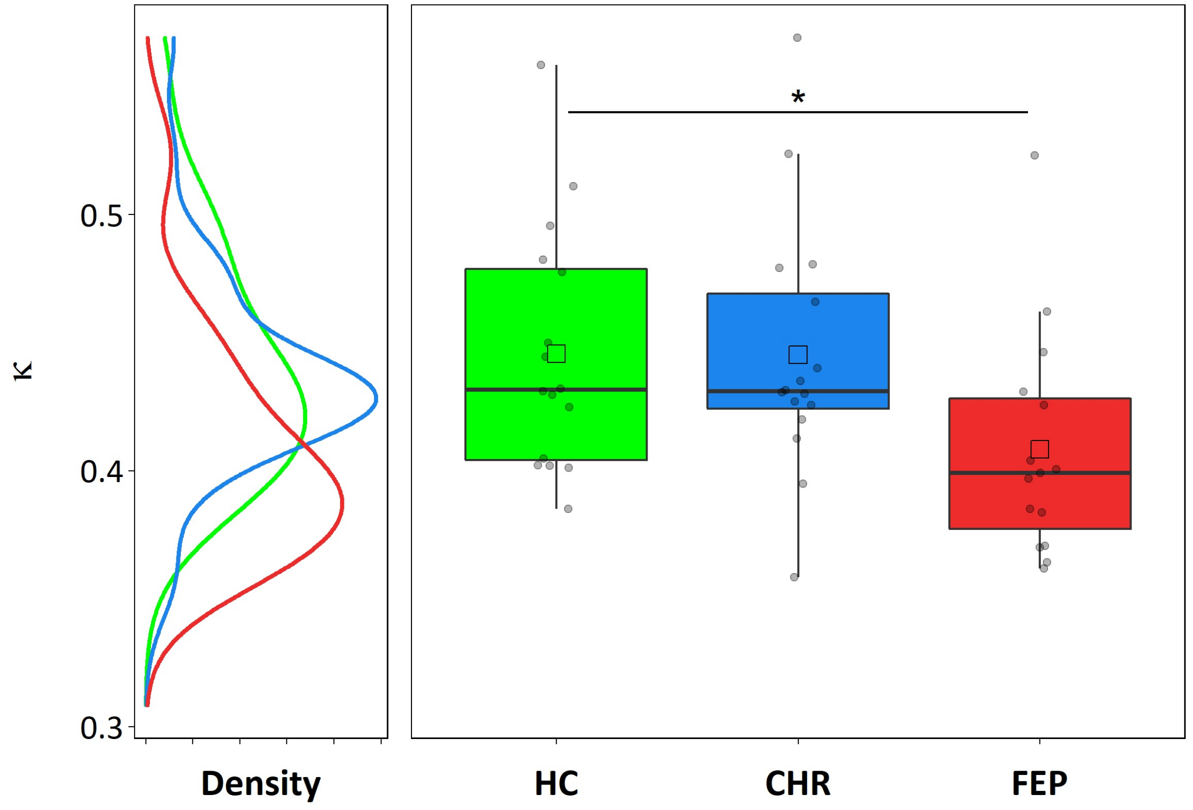
Enhanced Perception of Volatility & Decoupling





"Intentions were perceived as **increasingly volatile** over time in FEP compared to HC"

"FEP displayed **reduced coupling strength** between hierarchical levels compared to HC"

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Clinical Relevance: Parameters & Symptom Severity

m_3

- correlated positively with PANSS **positive symptoms** (r = 0.32, p = 0.026, p_{bf} = 0.158)

κ

- correlated negatively with PANSS **negative symptoms** (r = -0.39, p = 0.008, p_{bf} = 0.048)

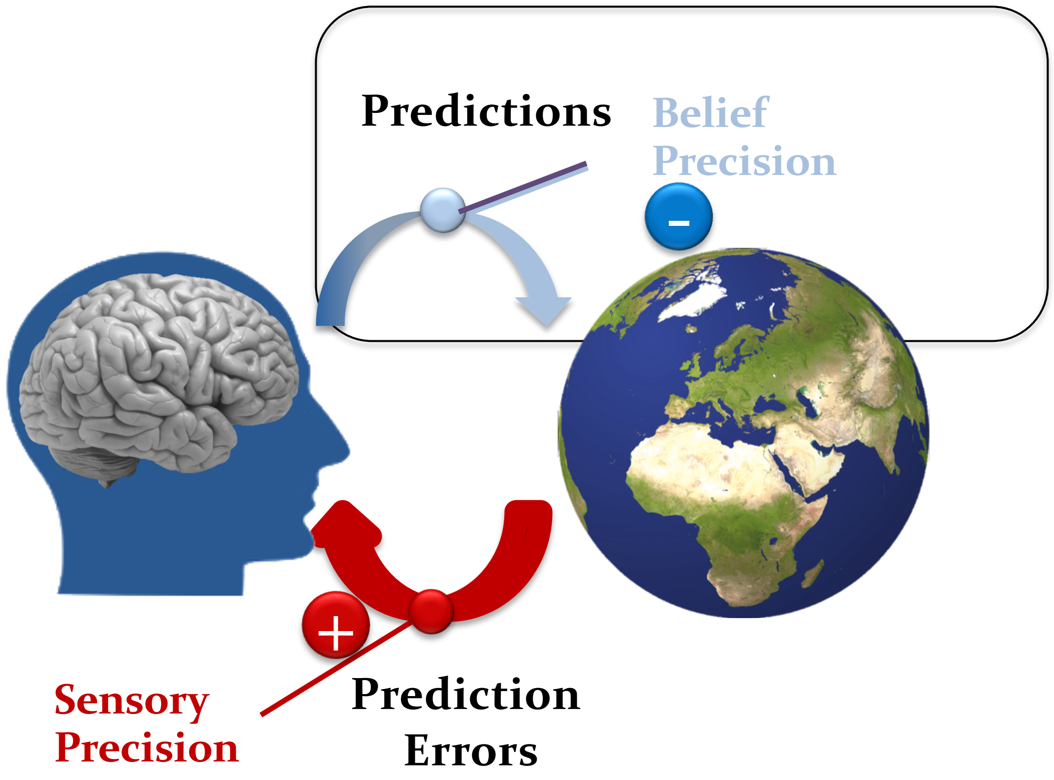
Example

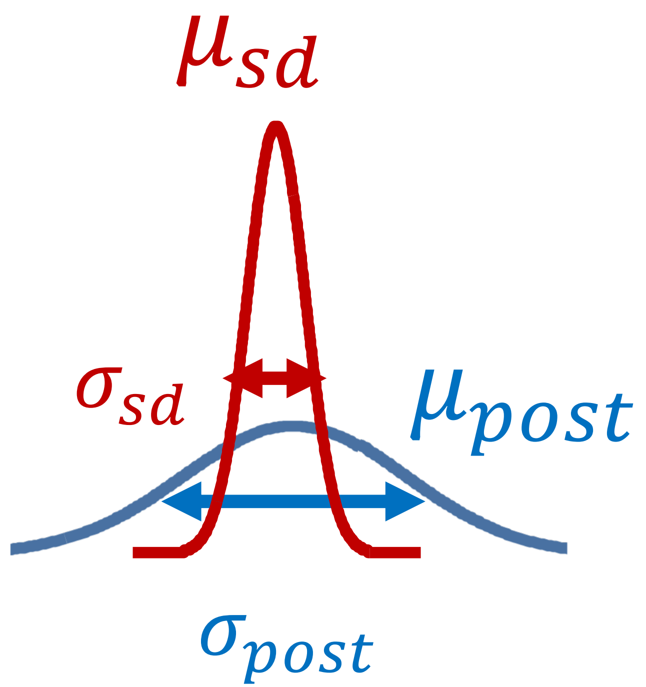
P3. Hallucinatory behavior
Verbal report or behavior indicating perceptions which are not generated by external stimuli. These may occur in the auditory visual, olfactory, or somatic realms. Basis for rating: Verbal report and physical manifestations during the course of interview as well as reports of behavior by primary care workers or family.

Example

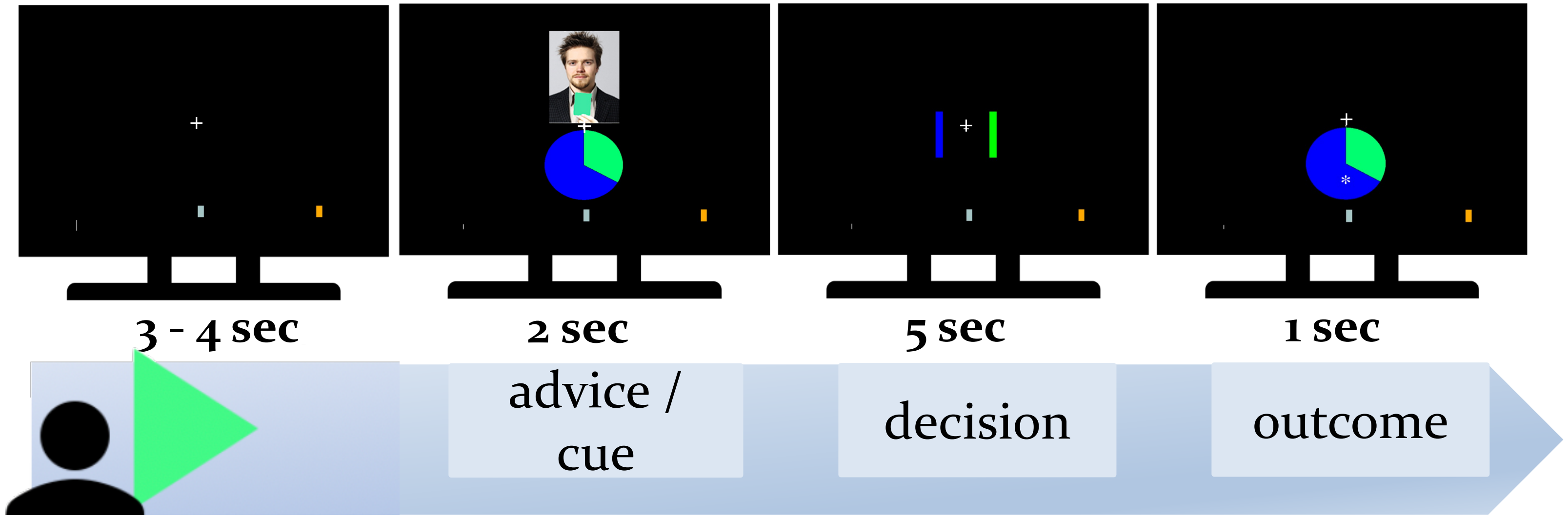
N1. Blunted affect
Diminished emotional responsiveness as characterized by a reduction in facial expression, modulation of feelings, and communicative gestures. Basis for rating: observation of physical manifestations of affective tone and emotional responsiveness during the course of interview.

Results: Early Psychosis and Belief Uncertainty





Applications: Delusional Conviction



	Low PD group		High PD group	
	M (SD)	*range*	*M (SD)*	*range*
Dispositional				
age	27.8 *(9.5)*	18-67	27.3 *(8.36)*	18-49
education	9.5 *(3.3)*	7-20	9.1 *(2.24)*	6-20
N	41 (15 male)		34 (14 male)	
Situational				
age	29.3 *(9.7)*	18-54	28.5 *(10.92)*	18-56
education	9.4 *(4.0)*	2-20	8.6 *(2.91)*	6-15
N	39 (16 male)		34 (15 male)	

Note: N=148, variables do not differ significantly between groups and between conditions

Katharina Wellstein

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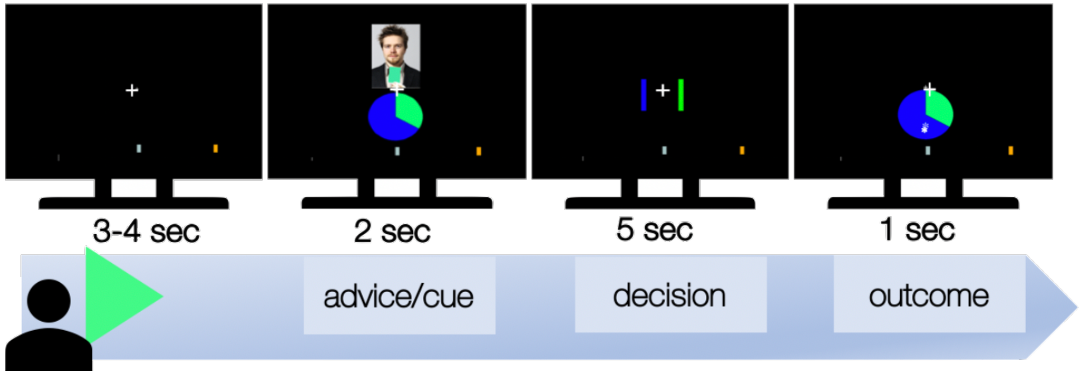
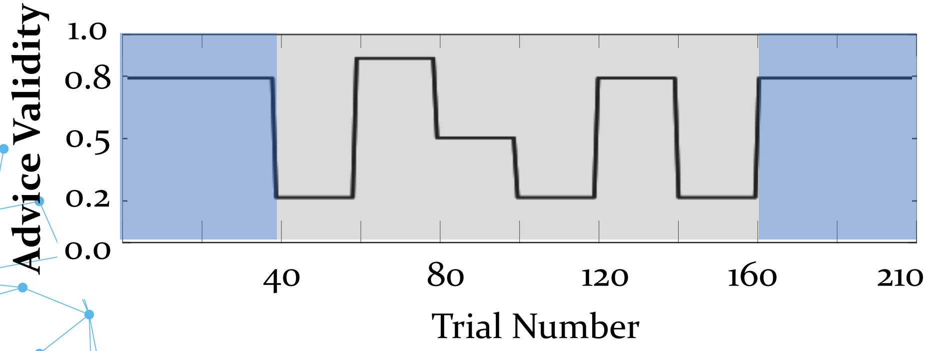
What about delusional conviction?

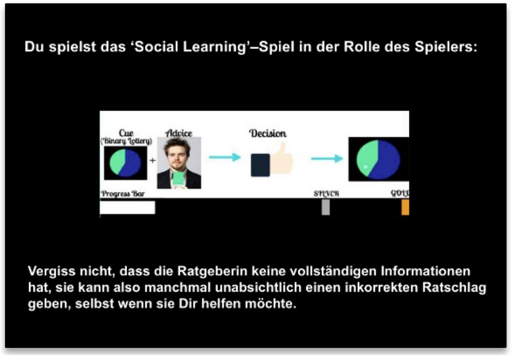




Experimental Frames:

Frame A: Dispositional Focus

Frame B: Situational Focus



Wellstein*, Diaconescu* et al., 2019, *Schizophrenia Research*.

Diaconescu*, Wellstein* et al., 2020, *Journal of Abnormal Psychology, Special Issue: Predictive Coding and Psychopathology*.

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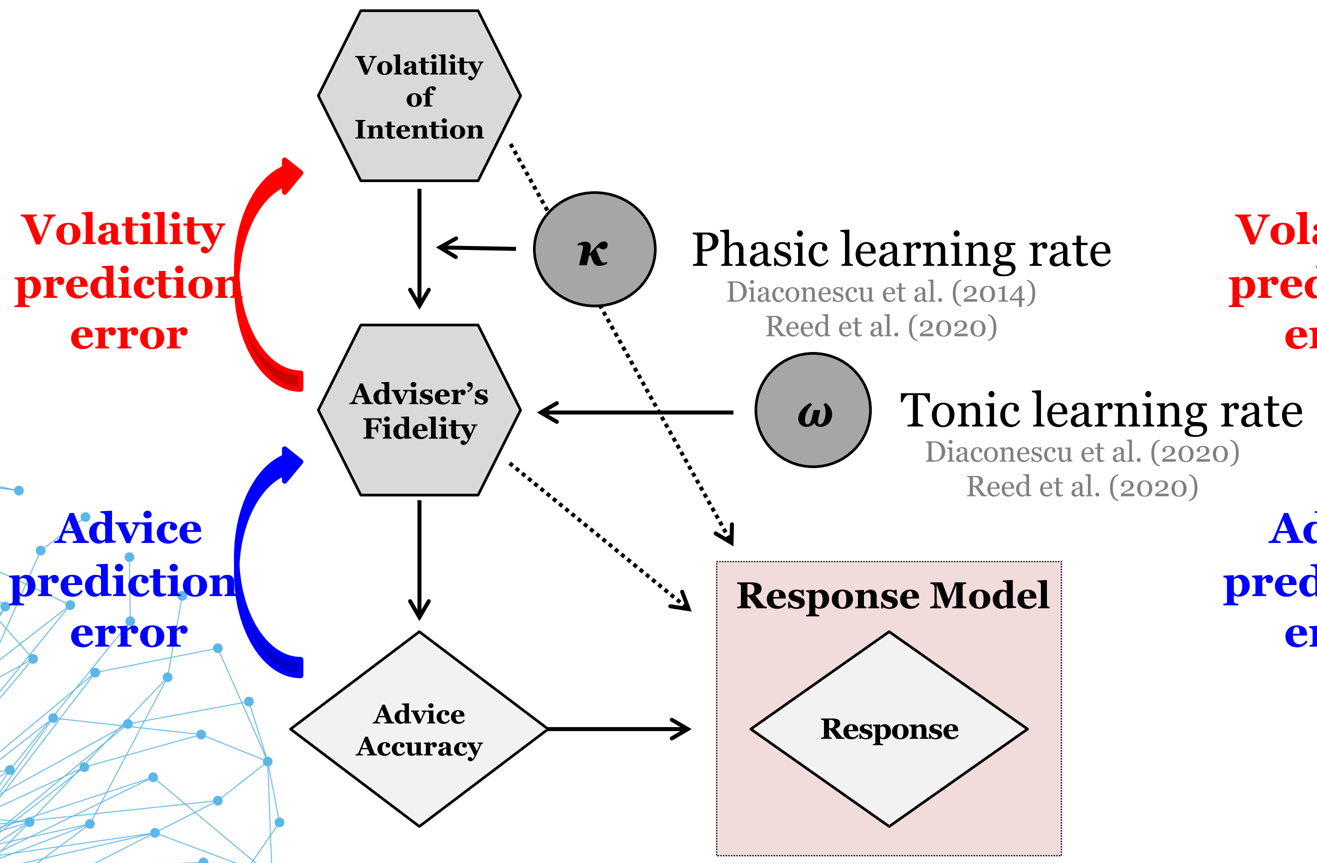
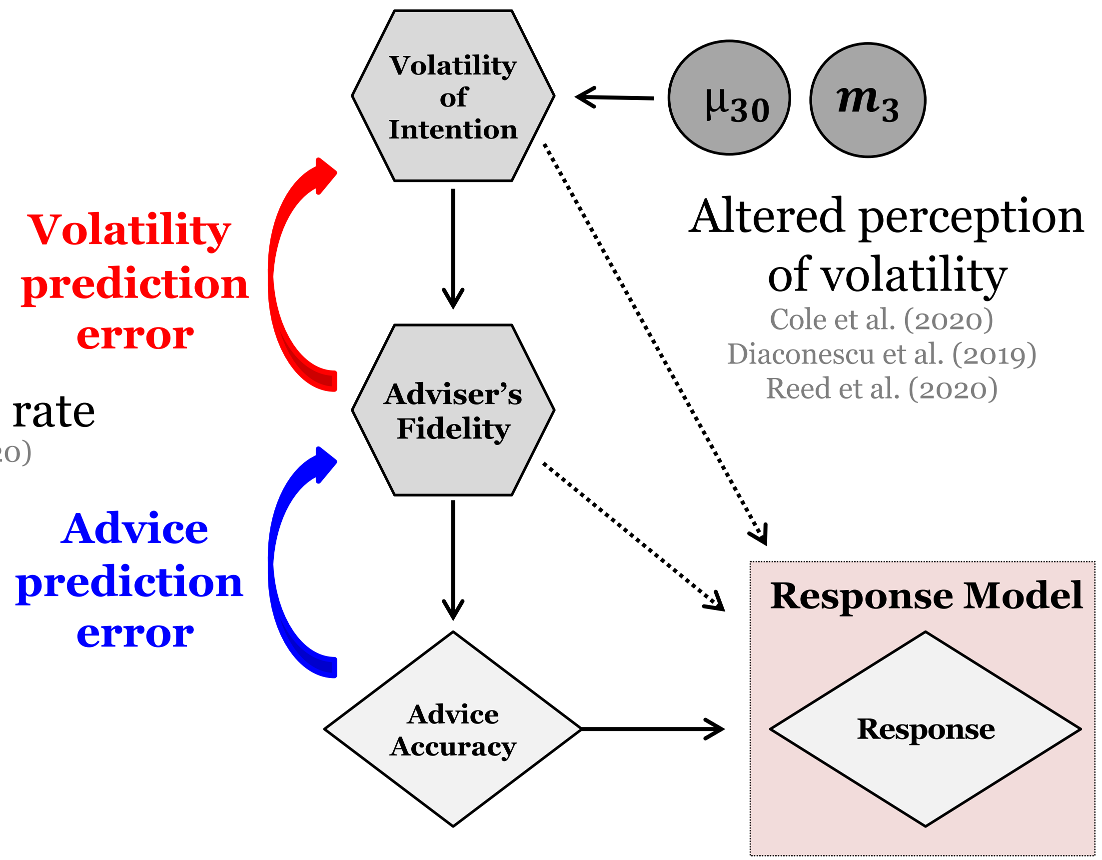
Models of Persecutory Delusions

Hypothesis I: HGF



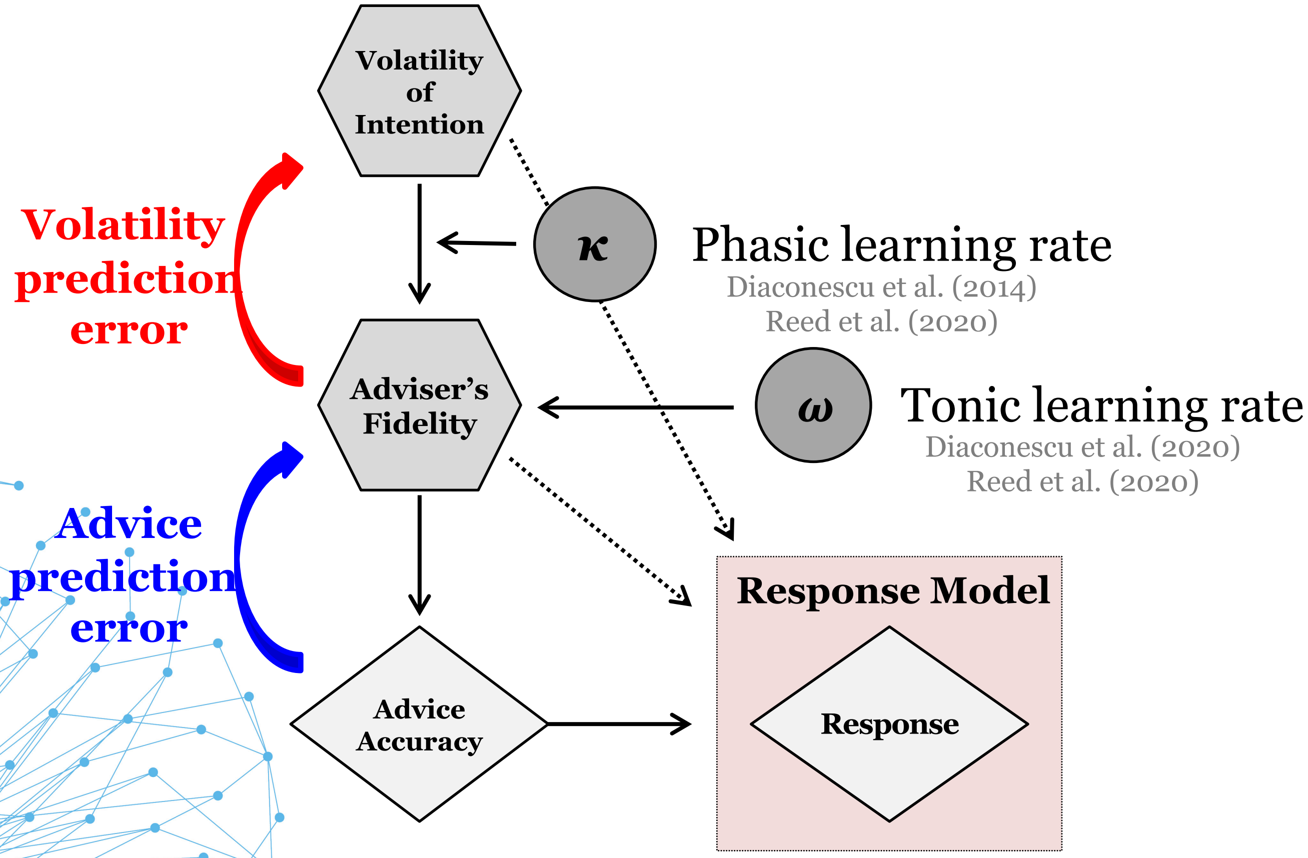
Hypothesis II: Mean-reverting HGF



Mathys et al., *Front Hum Neurosci*, 2014
Diaconescu et al., *PLoS Computational Biology* 2014

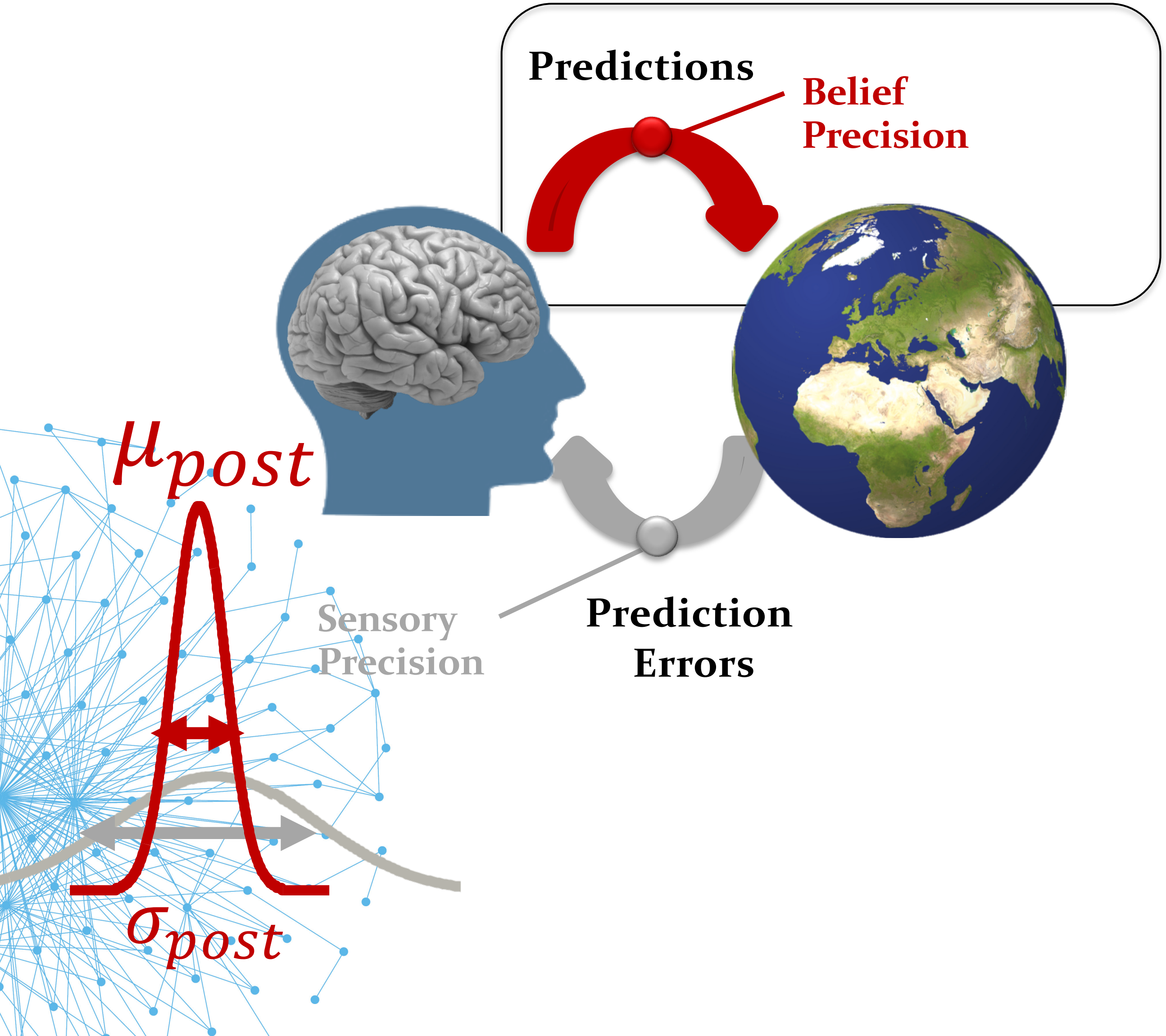
Models of Persecutory Delusions

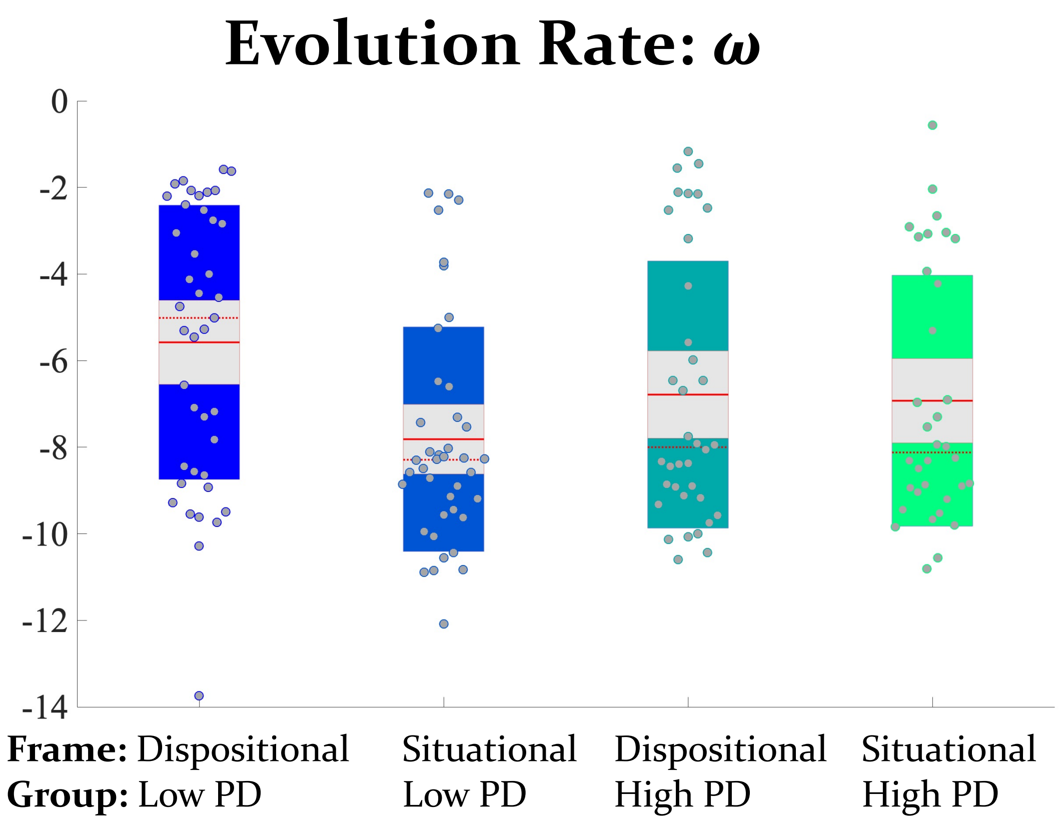
Hypothesis I: HGF



Mathys et al., *Front Hum Neurosci*, 2014
Diaconescu et al., *PLoS Computational Biology* 2014

Results: Paranoid Ideation and Precision





Conclusions

Generative model of beliefs

Level 3: Belief about volatility

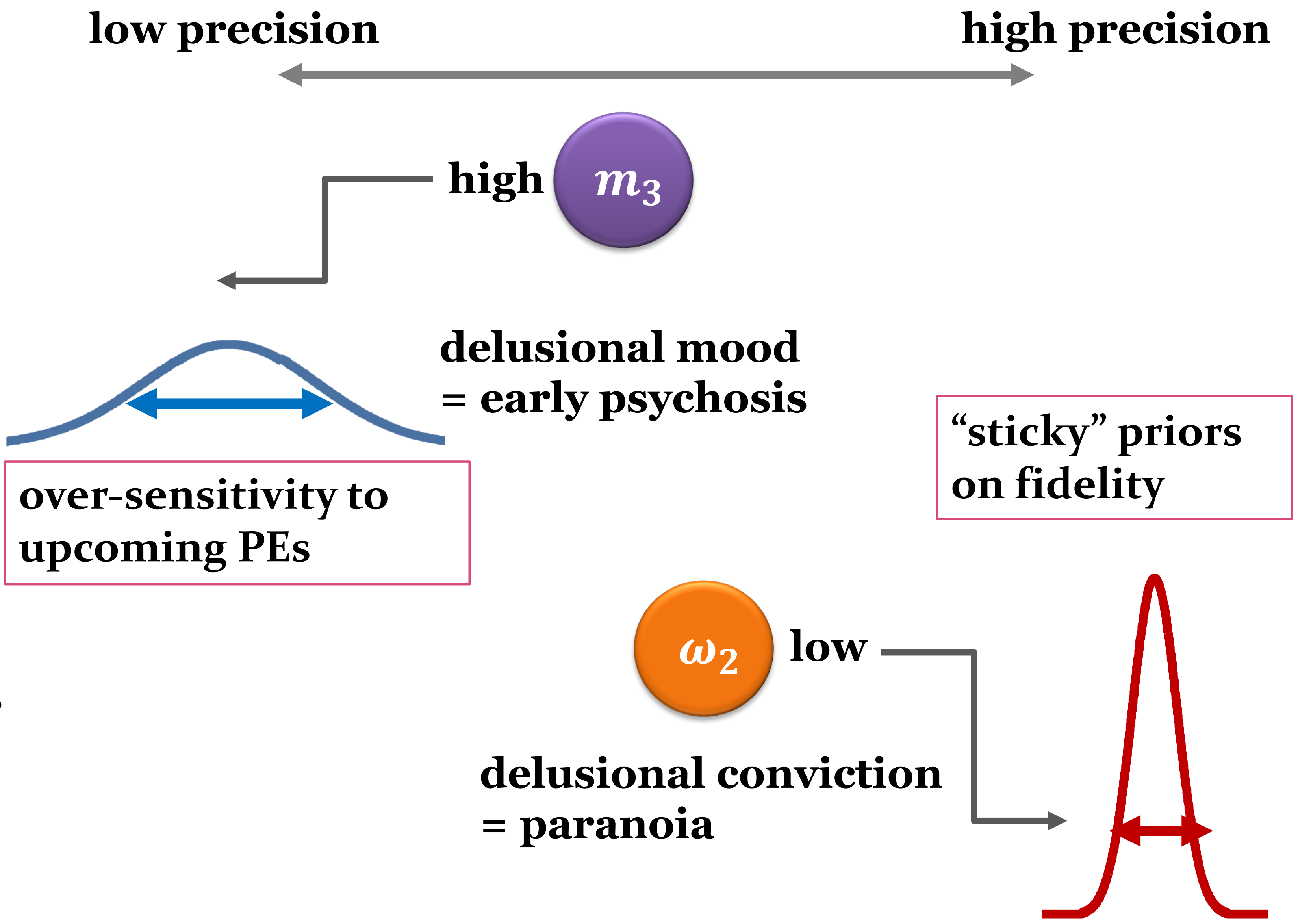
$$\mathcal{N}(\mu_3^{(k)}, \sigma_3^{(k)})$$

Level 2: Belief about fidelity

$$\mathcal{N}(\mu_2^{(k)}, \sigma_2^{(k)})$$

Level 1: Prediction of categories

$$Bern(\mu_1^{(k)})$$



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Today’s Agenda

Day 6:
Bayesian Models of Learning and Integration of Neuroimaging

9:00 am - 10:30 am	*Modelling Cognition using Bayesian Inference* Andreea Diaconescu
10:45 am - 12:15 pm	*Modelling Abnormal Beliefs* Daniel Hauke
1:00 pm - 2:30 pm	*Integration of Neuroimaging: Dynamic Causal Modelling for fMRI and EEG Data* Andreea Diaconescu, Colleen Charlton
2:45 pm - 4:15 pm	*Dynamic Causal Modelling for fMRI: Extensions and Simulations* Peter Bedford, Povilas Karvelis

Today's Agenda

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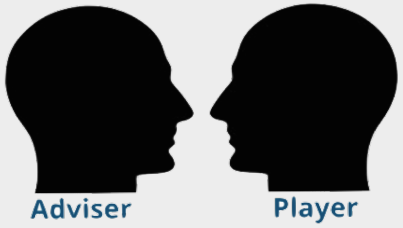
Three Levels of Inference

- *Computational Level*: predictions, prediction errors
- *Algorithmic Level*: reinforcement learning, hierarchical Bayesian inference, predictive coding
- *Implementational Level*: Brain activity, neuromodulation

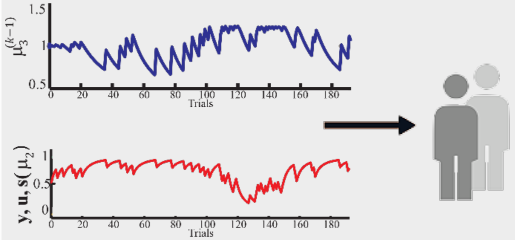
David Marr, 1982

- **3 ingredients**:

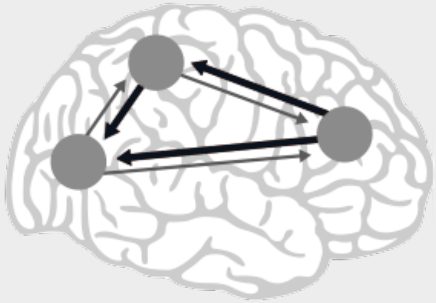
1. Experimental paradigm:



2. Computational model of learning:



3. Model-based fMRI analysis:



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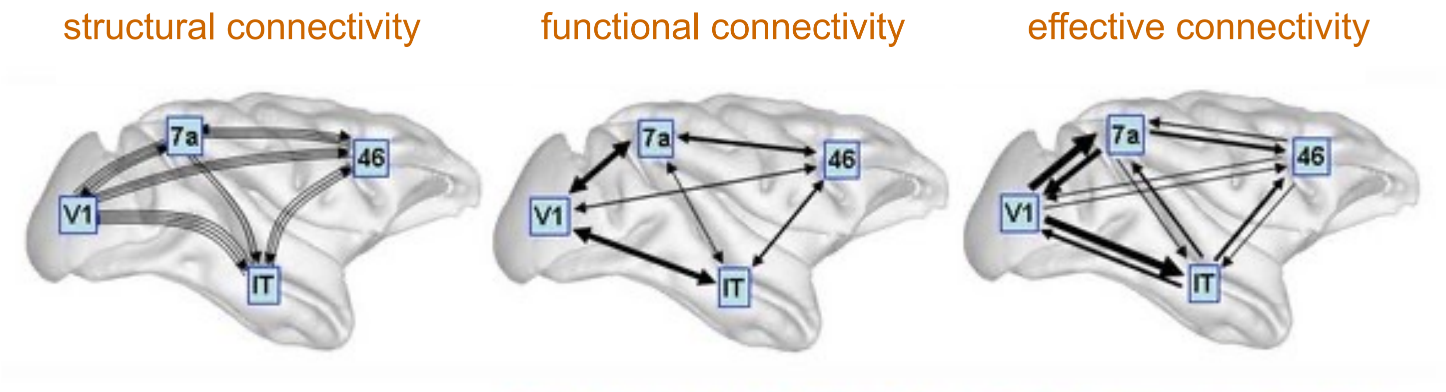
Introduction

structural, *functional* and *effective* connectivity



O. Sporns 2007, *Scholarpedia*

- ***structural* connectivity**
  = presence of axonal connections

- ***functional* connectivity**
  = statistical dependencies between regional time series

- ***effective* connectivity**
  = causal (directed) influences between neuronal populations

connections are recruited in a *context-dependent* fashion

Dynamic Causal Modelling (DCM)

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NeuroImage

NeuroImage 19 (2003) 1273–1302

www.elsevier.com/locate/ynimg

Dynamic causal modelling

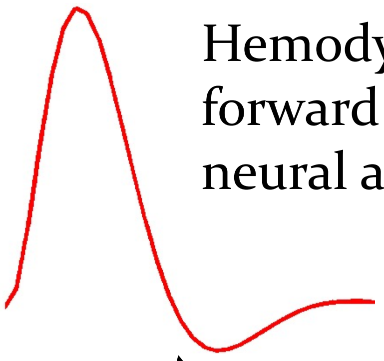
K.J. Friston,* L. Harrison, and W. Penny

The Wellcome Department of Imaging Neuroscience, Institute of Neurology, Queen Square, London WC1N 3BG, UK

Received 18 October 2002; revised 7 March 2003; accepted 2 April 2003

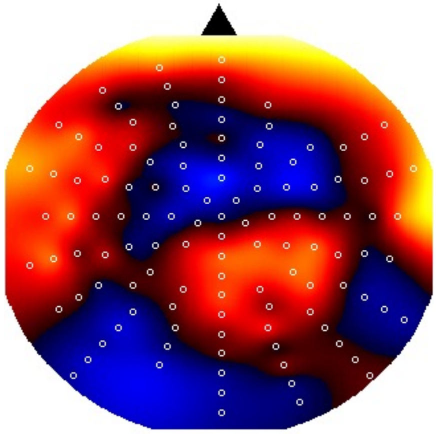
- DCM framework was introduced in 2003 for fMRI by Karl Friston, Lee Harrison and Will Penny (NeuroImage 19:1273-1302)
- Application: <u>FMRI data</u>

Dynamic Causal Modeling (DCM)



Hemodynamic
forward model:
neural activity→BOLD

Electromagnetic
forward model:
neural activity→EEG
MEG
LFP

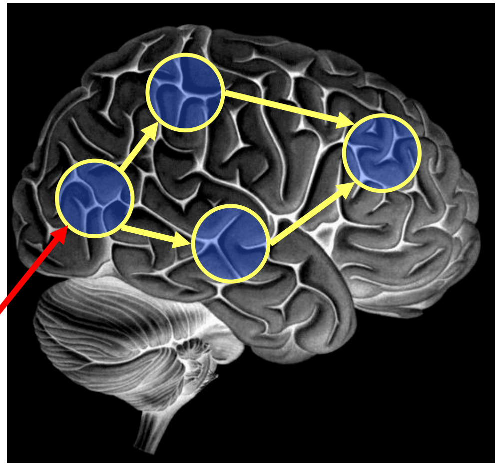


Neural state equation:

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

fMRI

simple neuronal model
complicated forward model



inputs

EEG/MEG

complicated neuronal model
simple forward model

Stephan & Friston 2007, *Handbook of Brain Connectivity*

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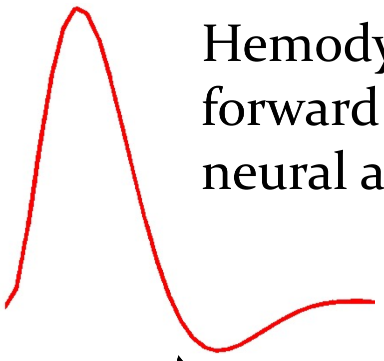
Dynamic Causal Modeling (DCM)



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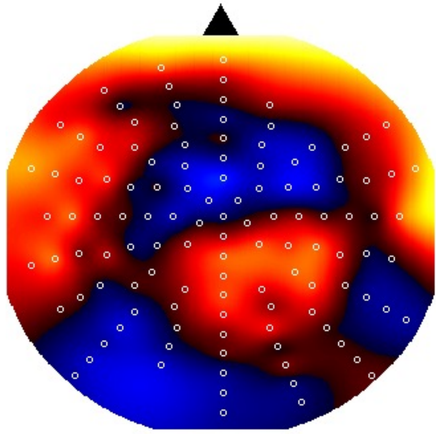

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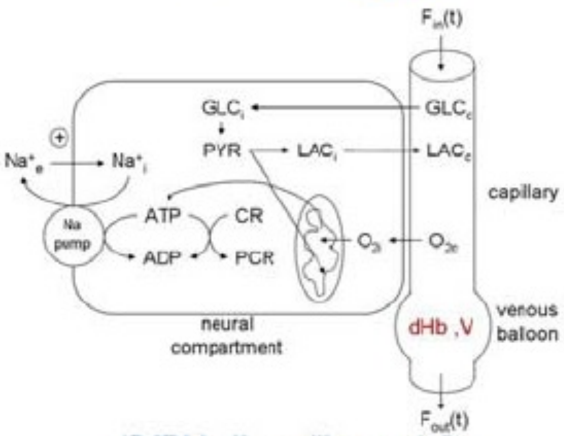
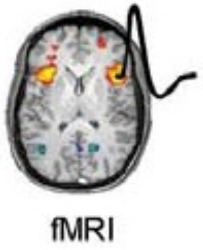
fMRI

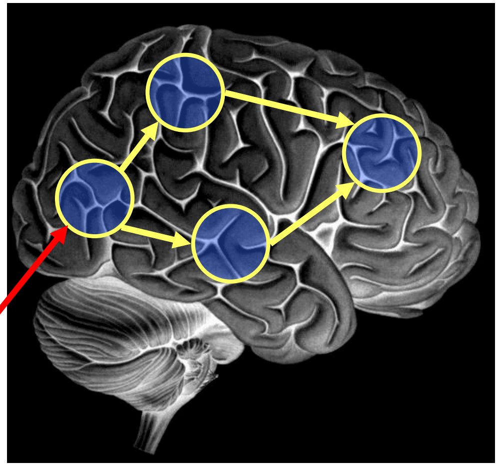
EEG/MEG



(fMRI balloon-like model)
metabolic and hemodynamic cascade

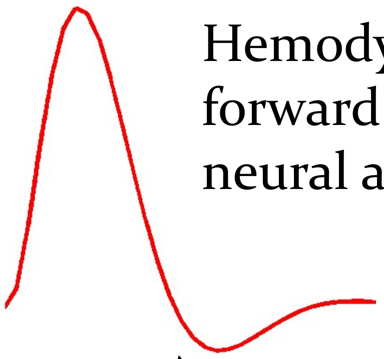


inputs



complicated neuronal model
simple forward model

Dynamic Causal Modeling (DCM)



Hemodynamic
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neural activity→BOLD

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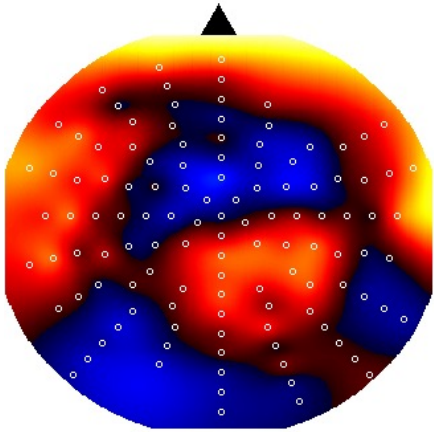

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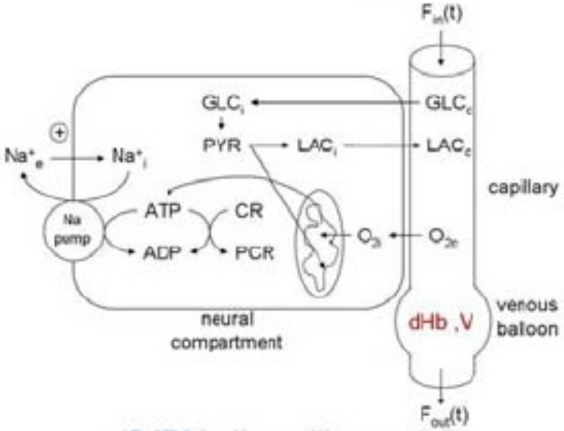
fMRI

EEG/MEG



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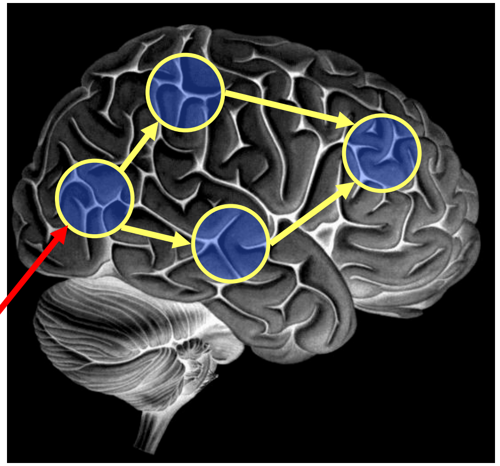
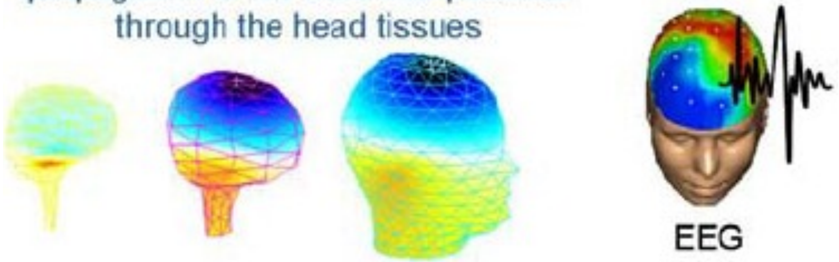


(EEG gain model)
propagation of the electrical potential
through the head tissues



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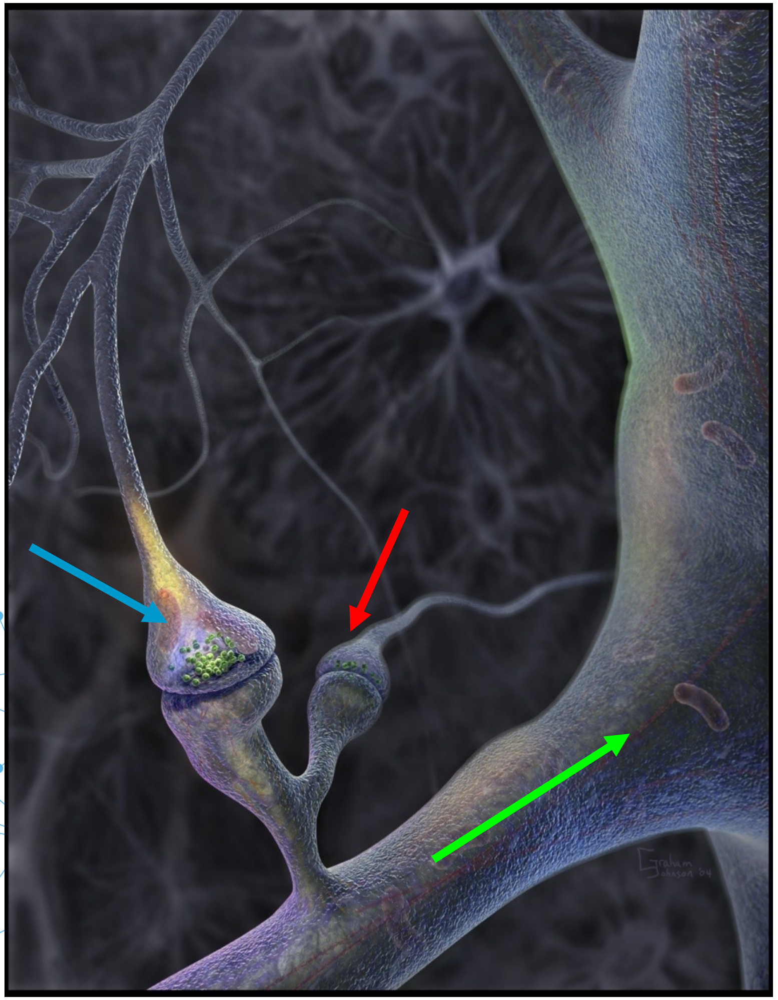
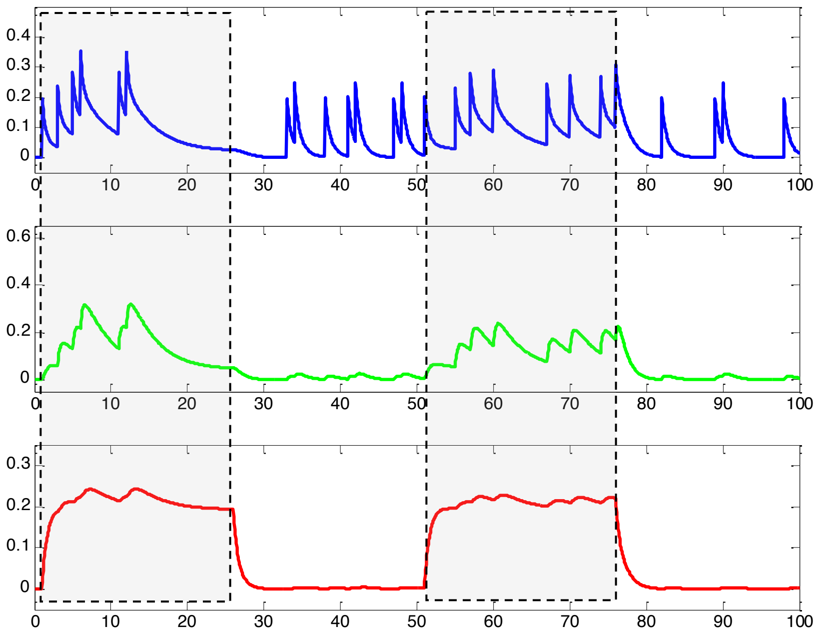
Connections are recruited in a context-dependent fashion





Synaptic strengths are context-sensitive:
They depend on spatio-temporal patterns of network activity.

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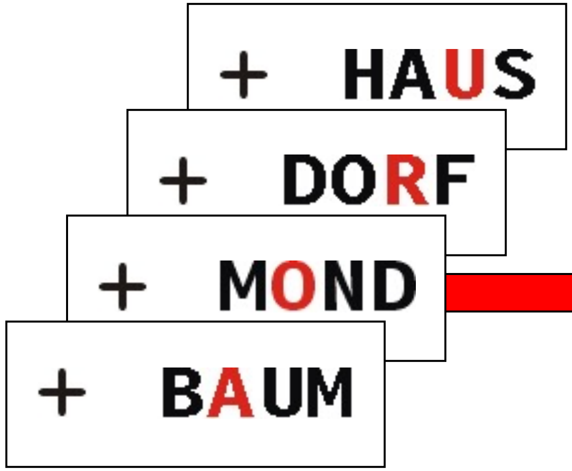
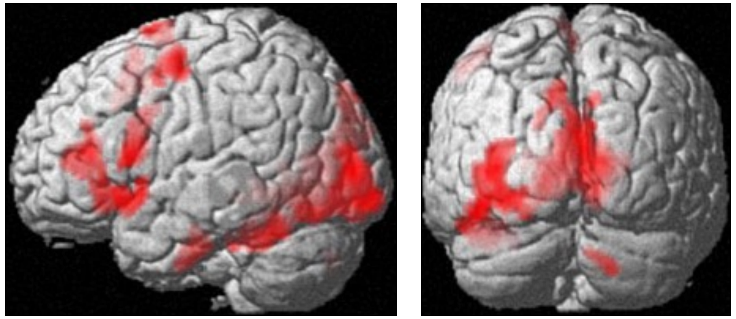
Dynamic Causal Modeling for fMRI: Example

Task-driven lateralisation

Does the word contain the letter A or not?



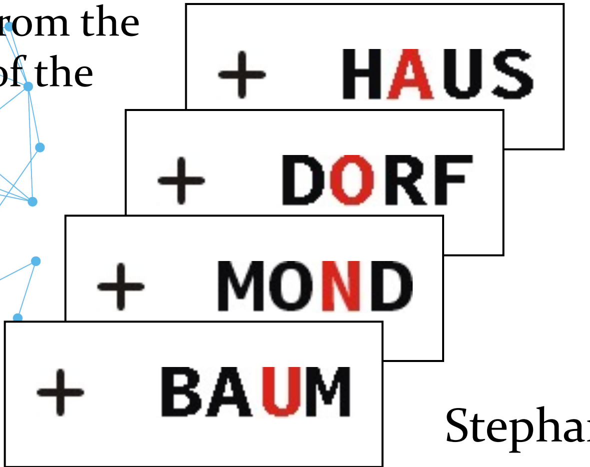


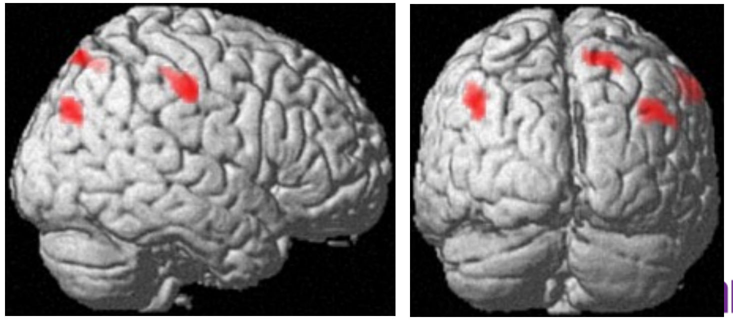
letter decisions > spatial decisions

time

group analysis (random effects), n=16, p<0.05 corrected analysis with SPM2

Is the red letter left or right from the midline of the word?





spatial decisions > letter decisions

Stephan et al. 2003, *Science*

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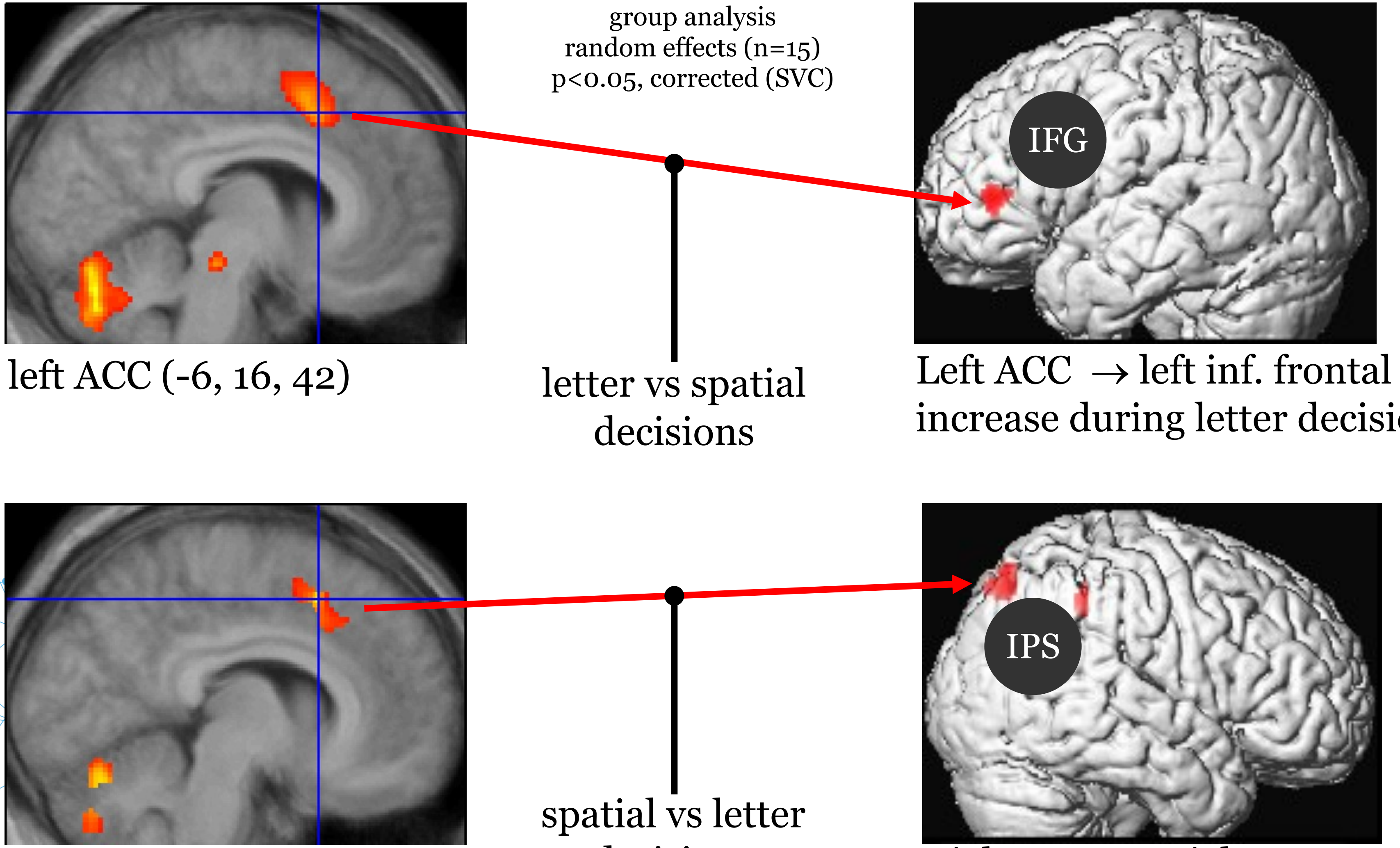
Bilateral ACC activation in both tasks – but asymmetric connectivity



left ACC (-6, 16, 42)

letter vs spatial decisions

Left ACC $\rightarrow$ left inf. frontal gyrus (IFG): increase during letter decisions.

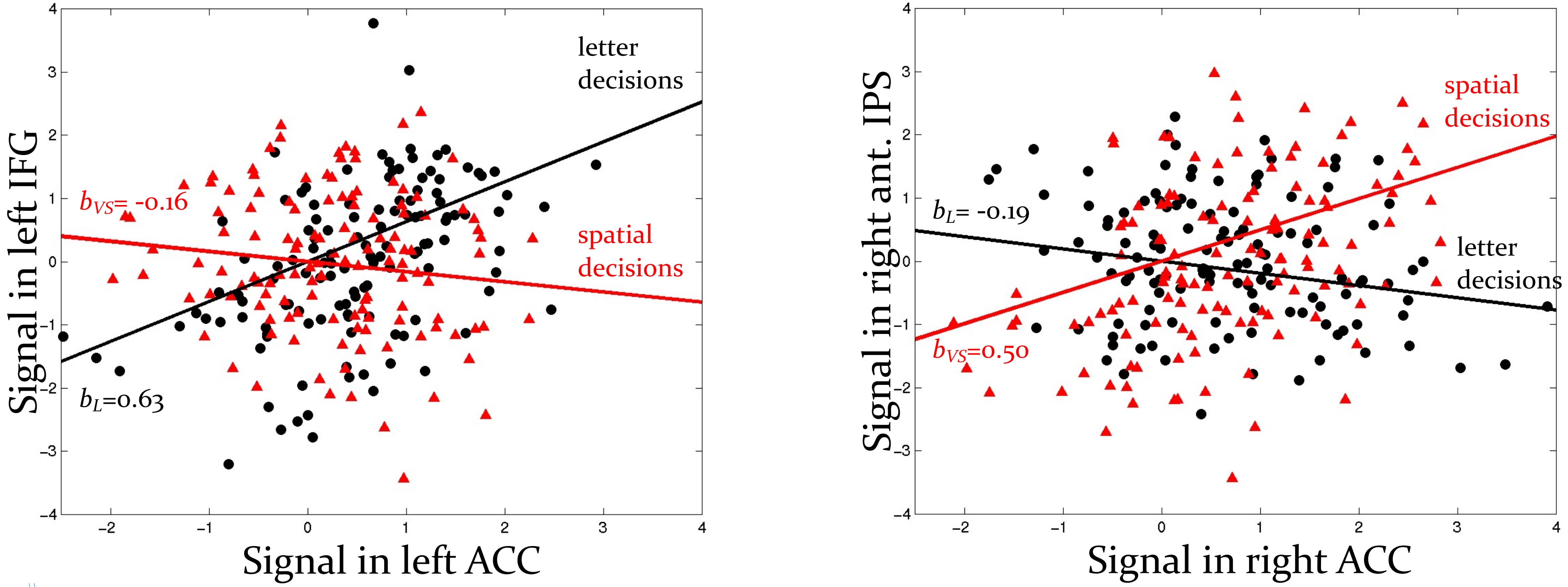
right ACC (8, 16, 48)

spatial vs letter decisions

Right ACC $\rightarrow$ right IPS: increase during spatial decisions.

Stephan et al. 2003, *Science*

Dynamic Causal Modeling for fMRI: Example

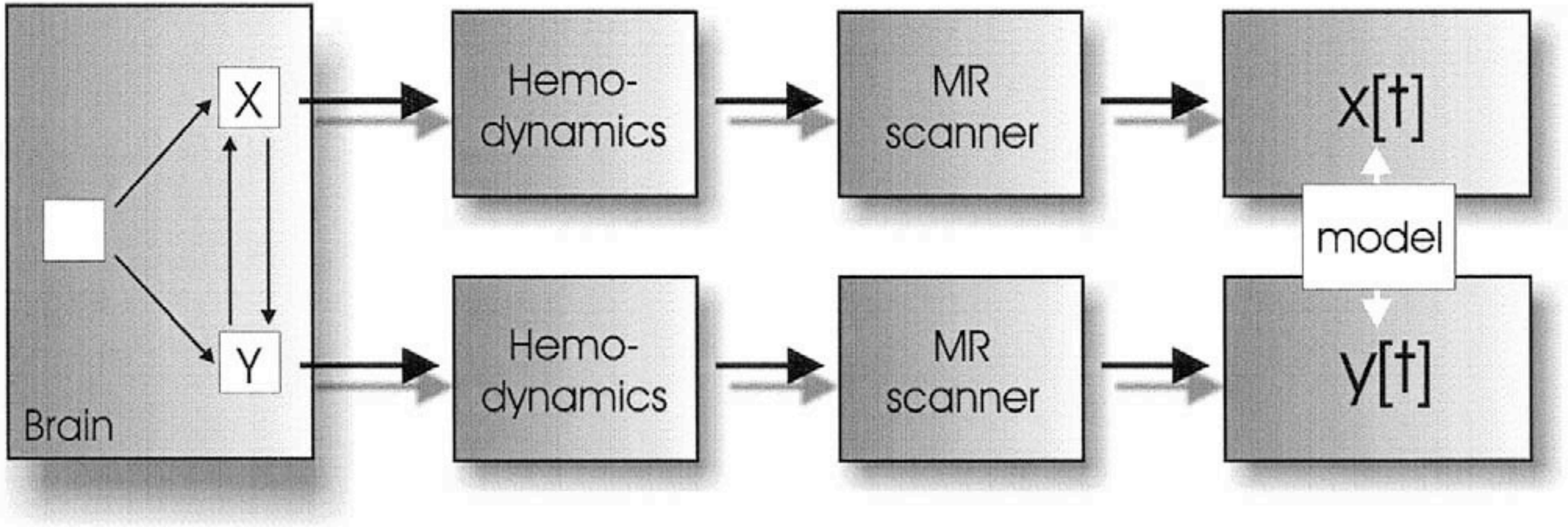


Left ACC signal plotted against left IFG

Right ACC signal plotted against right IPS

Stephan et al. 2003, *Science*

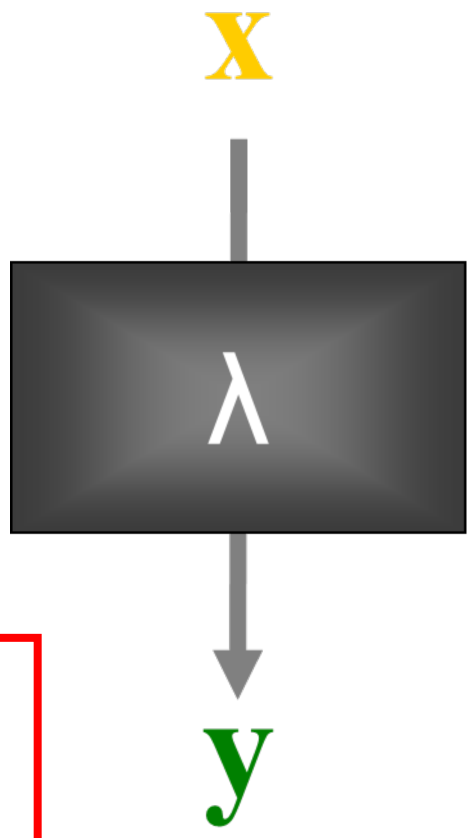
The problem of hemodynamic convolution



Goebel et al. 2003, *Magn. Res. Med.*

Neuronal vs. BOLD level

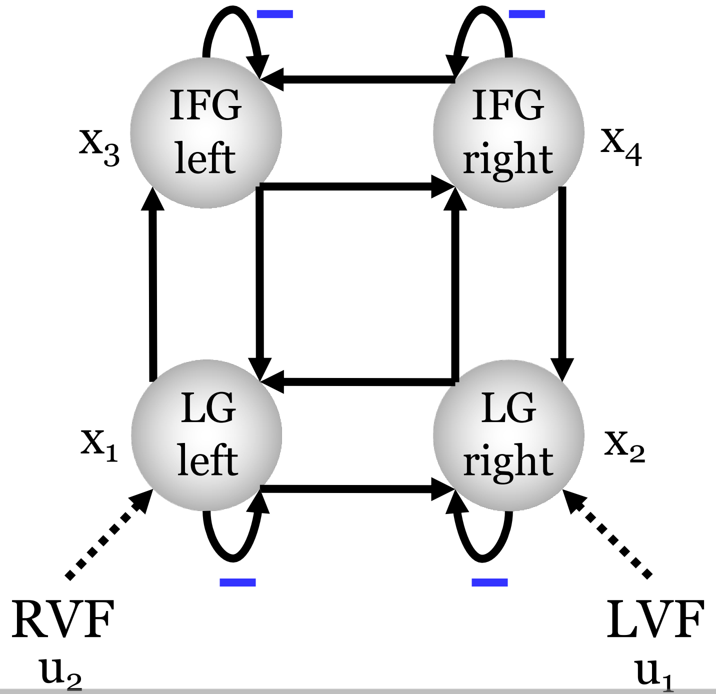
- Cognitive network model: directly at the neural level
- The modelled neuronal dynamics (x) are transformed into area-specific BOLD signals (y) by a hemodynamic model (λ).



The aim of DCM is to estimate parameters at the neuronal level such that the modelled and measured BOLD signals are maximally* similar.

Dynamic Causal Modeling for fMRI: Example

Example:
a linear system of dynamics in visual cortex



LG = lingual gyrus
IFG = inferior frontal gyrus

Visual input in the
- left (LVF)
- right (RVF)

visual field.

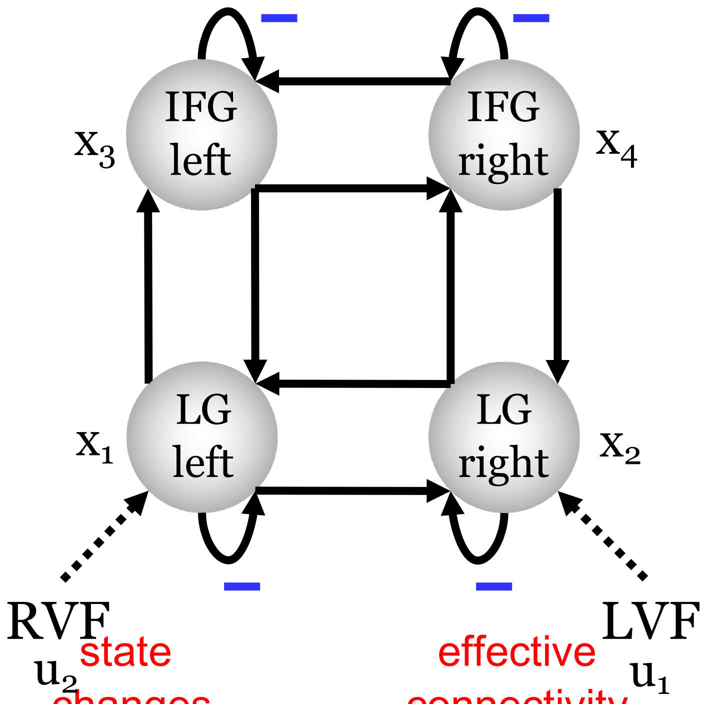
$$\dot{x}_1 = a_{11}x_1 + a_{12}x_2 + a_{13}x_3 + c_{12}u_2$$

$$\dot{x}_2 = a_{21}x_1 + a_{22}x_2 + a_{24}x_4 + c_{21}u_1$$

$$\dot{x}_3 = a_{31}x_1 + a_{33}x_3 + a_{34}x_4$$

$$\dot{x}_4 = a_{42}x_2 + a_{43}x_3 + a_{44}x_4$$

Example: a linear system of dynamics in visual cortex



LG = lingual gyrus
FG = fusiform gyrus

Visual input in the
- left (LVF)
- right (RVF)

visual field.

state changes; effective connectivity; system state; input parameters; external inputs

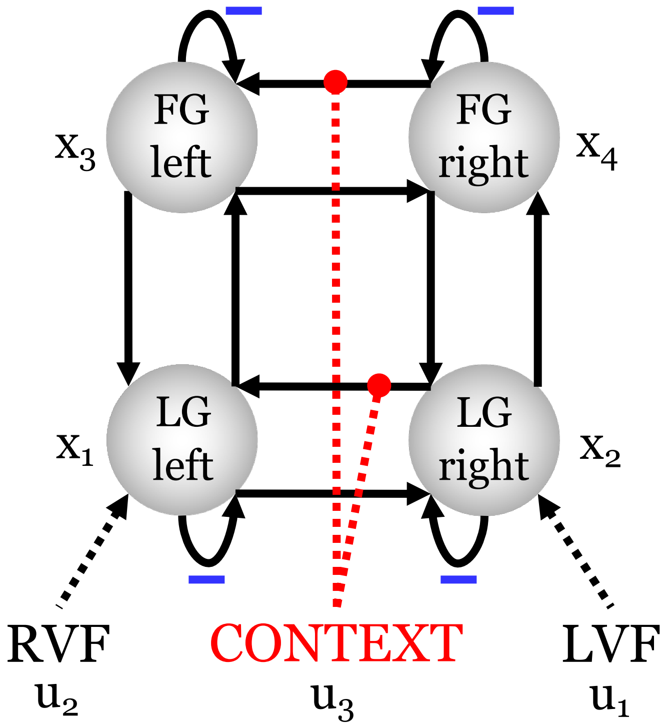
$$\boxed{\dot{x} = Ax + Cu}$$

$$\theta = \{A, C\}$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \\ \dot{x}_4 \end{bmatrix} = \begin{bmatrix} a_{11} & a_{12} & a_{13} & 0 \\ a_{21} & a_{22} & 0 & a_{24} \\ a_{31} & 0 & a_{33} & a_{34} \\ 0 & a_{42} & a_{43} & a_{44} \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{bmatrix} + \begin{bmatrix} 0 & c_{12} \\ c_{21} & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

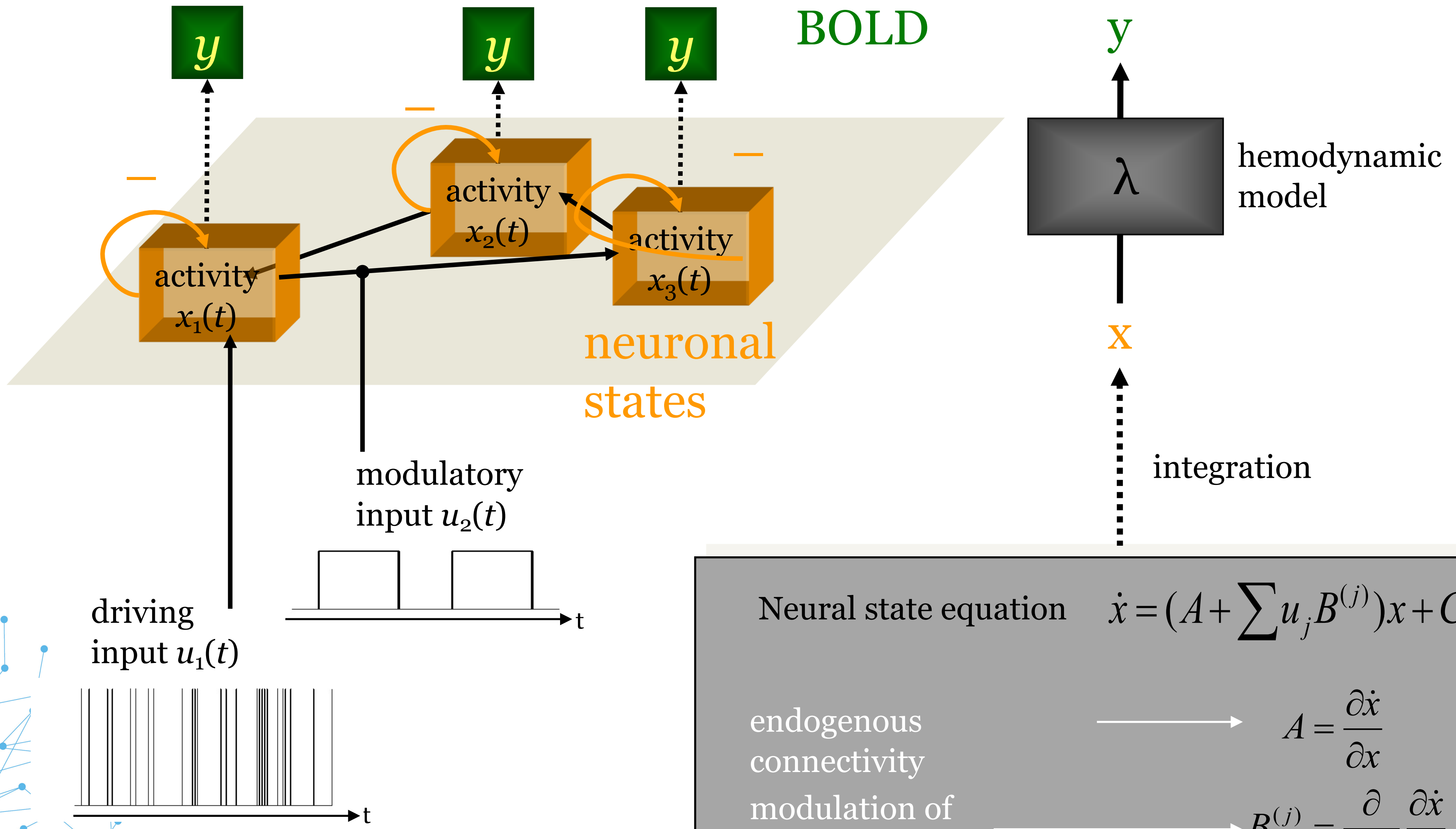
bil Centre for
binformatics

Extension: bilinear dynamic system



$$\dot{x} = (A + \sum_{j=1}^{m} u_j B^{(j)})x + Cu$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \\ \dot{x}_4 \end{bmatrix} = \left\{ \begin{bmatrix} a_{11} & a_{12} & a_{13} & 0 \\ a_{21} & a_{22} & 0 & a_{24} \\ a_{31} & 0 & a_{33} & a_{34} \\ 0 & a_{42} & a_{43} & a_{44} \end{bmatrix} + u_3 \begin{bmatrix} 0 & b_{12}^{(3)} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & b_{34}^{(3)} \\ 0 & 0 & 0 & 0 \end{bmatrix} \right\} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{bmatrix} + \begin{bmatrix} 0 & c_{12} & 0 \\ c_{21} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} u_1 \\ u_2 \\ u_3 \end{bmatrix}$$



Neural state equation $\dot{x} = (A + \sum u_j B^{(j)})x + Cu$

endogenous connectivity → $A = \frac{\partial \dot{x}}{\partial x}$

modulation of connectivity → $B^{(j)} = \frac{\partial}{\partial u_j} \frac{\partial \dot{x}}{\partial x}$

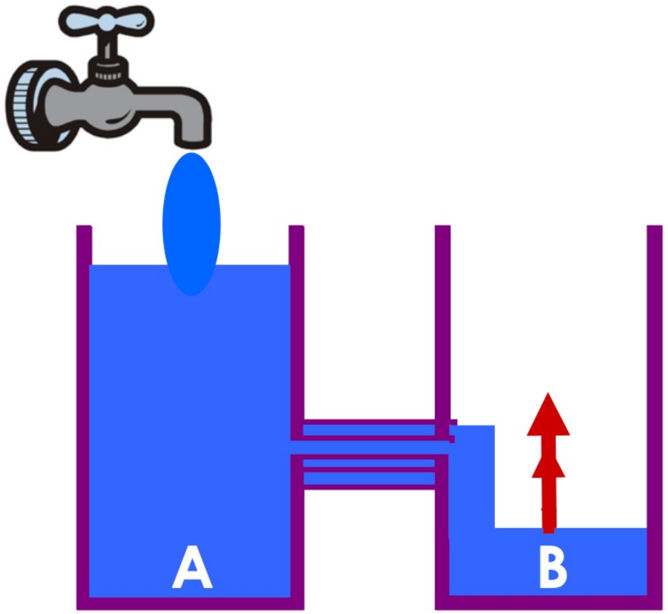
direct inputs → $C = \frac{\partial \dot{x}}{\partial u}$

Stephan & Friston (2007),
Handbook of Brain Connectivity

DCM parameters = rate constants

Integration of a first-order linear differential equation gives an exponential function:

$$\frac{dx}{dt} = ax \longrightarrow x(t) = x_0 \exp(at)$$

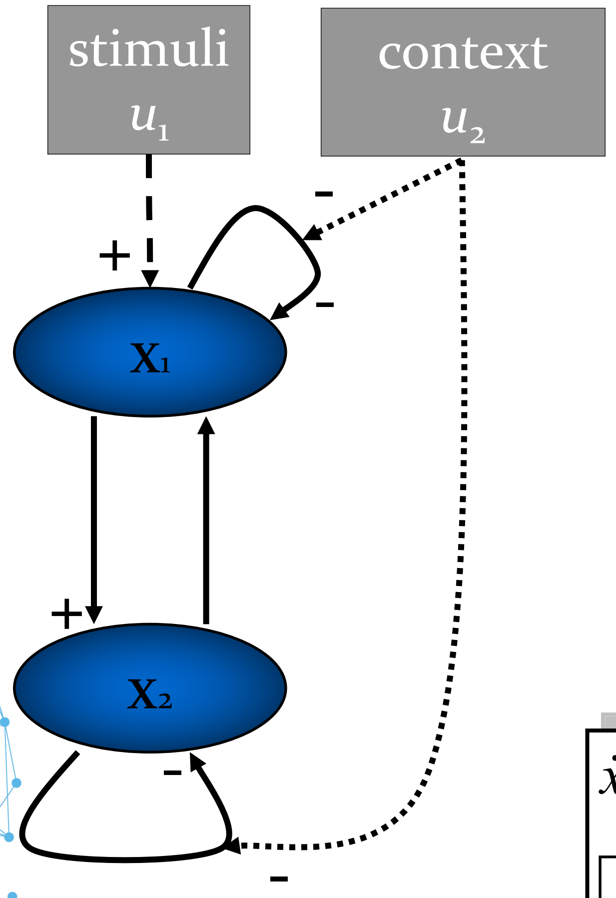


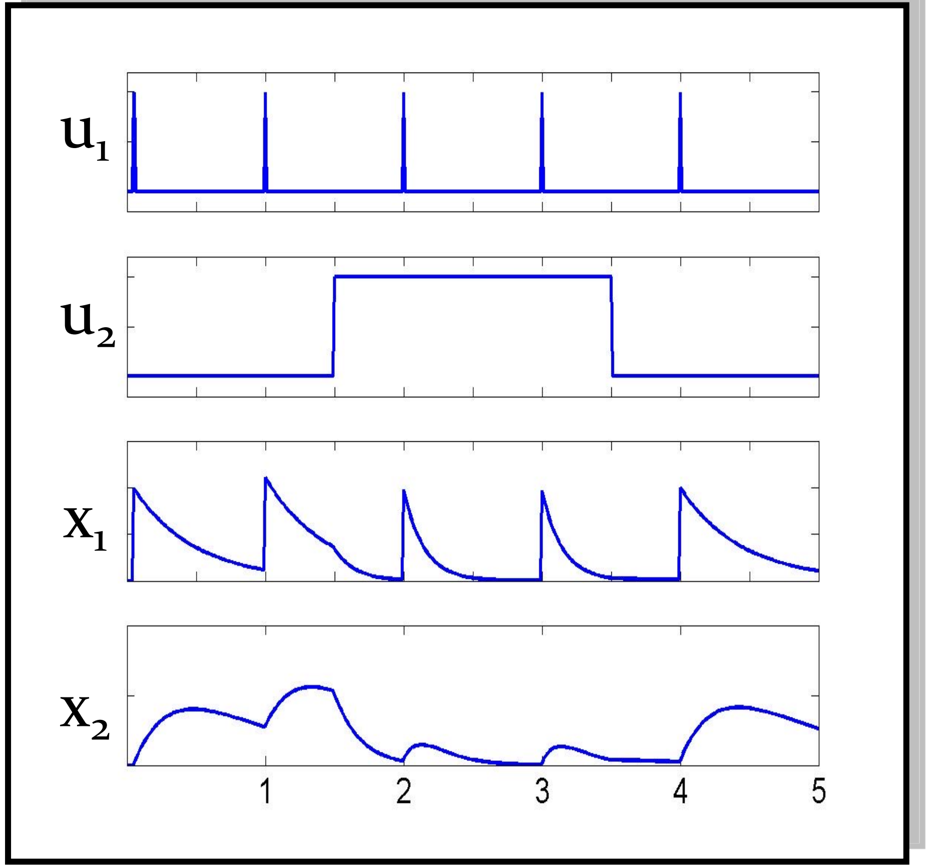
The coupling parameter a determines the half life of $x(t)$

$$x(\tau) = 0.5x_0$$
$$= x_0 \exp(a\tau)$$
$$\rightarrow a = \ln 2 / \tau$$

If A→B is 0.10 s^{-1} this means that, per unit time, the increase in activity in B corresponds to 10% of the activity in A

Example: context-dependent decay





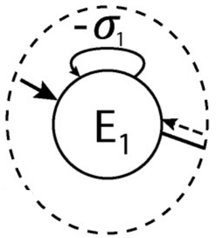
$$\dot{x} = Ax + u_2 B^{(2)} x + C u_1$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{bmatrix} = \begin{bmatrix} \sigma & a_{12} \\ a_{21} & \sigma \end{bmatrix} x + u_2 \begin{bmatrix} b^2_{11} & 0 \\ 0 & b^2_{22} \end{bmatrix} x + \begin{bmatrix} c_1 & 0 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

Penny, Stephan, Mechelli, Friston
NeuroImage (2004)

DCM for fMRI Extensions

Single State-DCM



$$\frac{dX_E(t)}{d(t)} = -\sigma \cdot X_E\,(t) + c\ \cdot u(t)$$

Friston et al. 2003

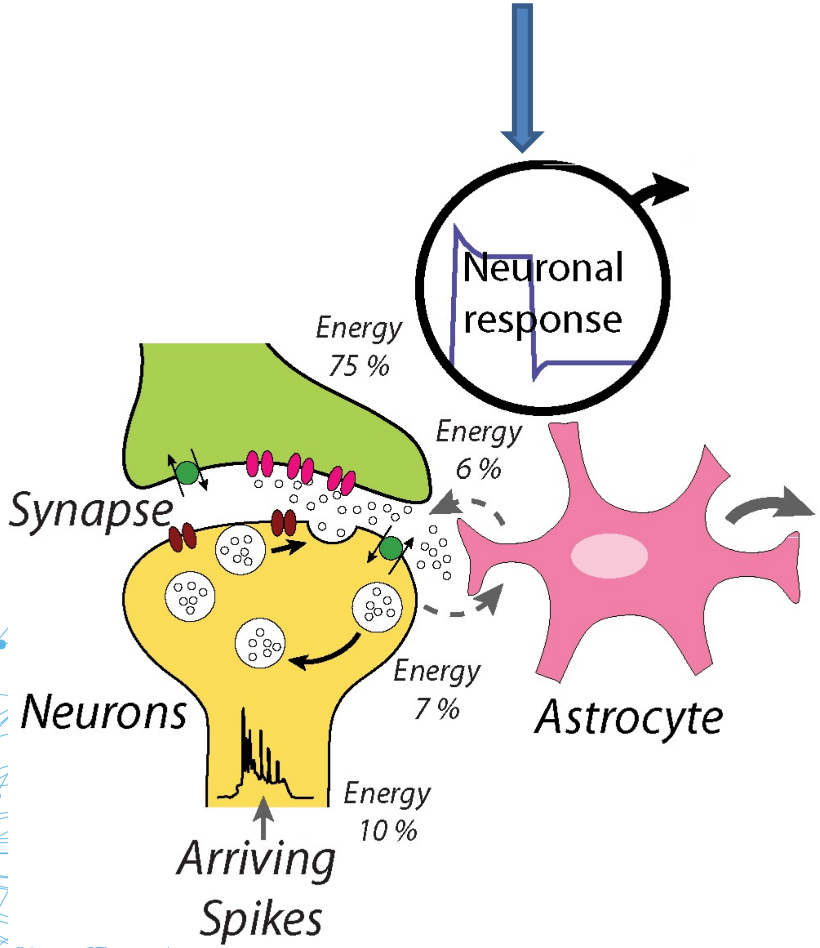
Thanks to Uludağ, 2021

How about the hemodynamic forward model?

From neuronal to hemodynamic response

Havlicek et al. 2015

1. Neural model

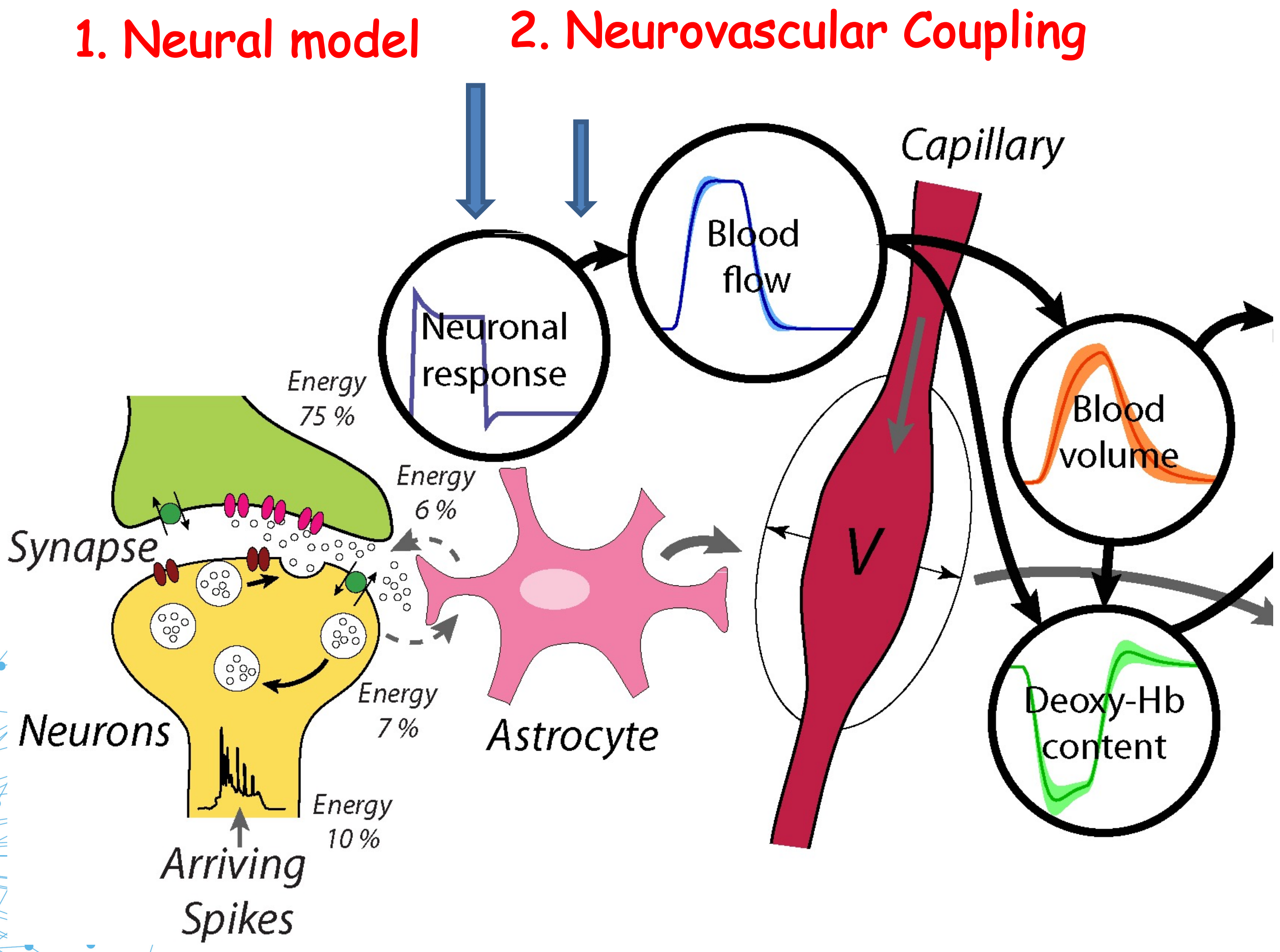


Uludağ, 2021

How about the hemodynamic forward model?

From neuronal to hemodynamic response

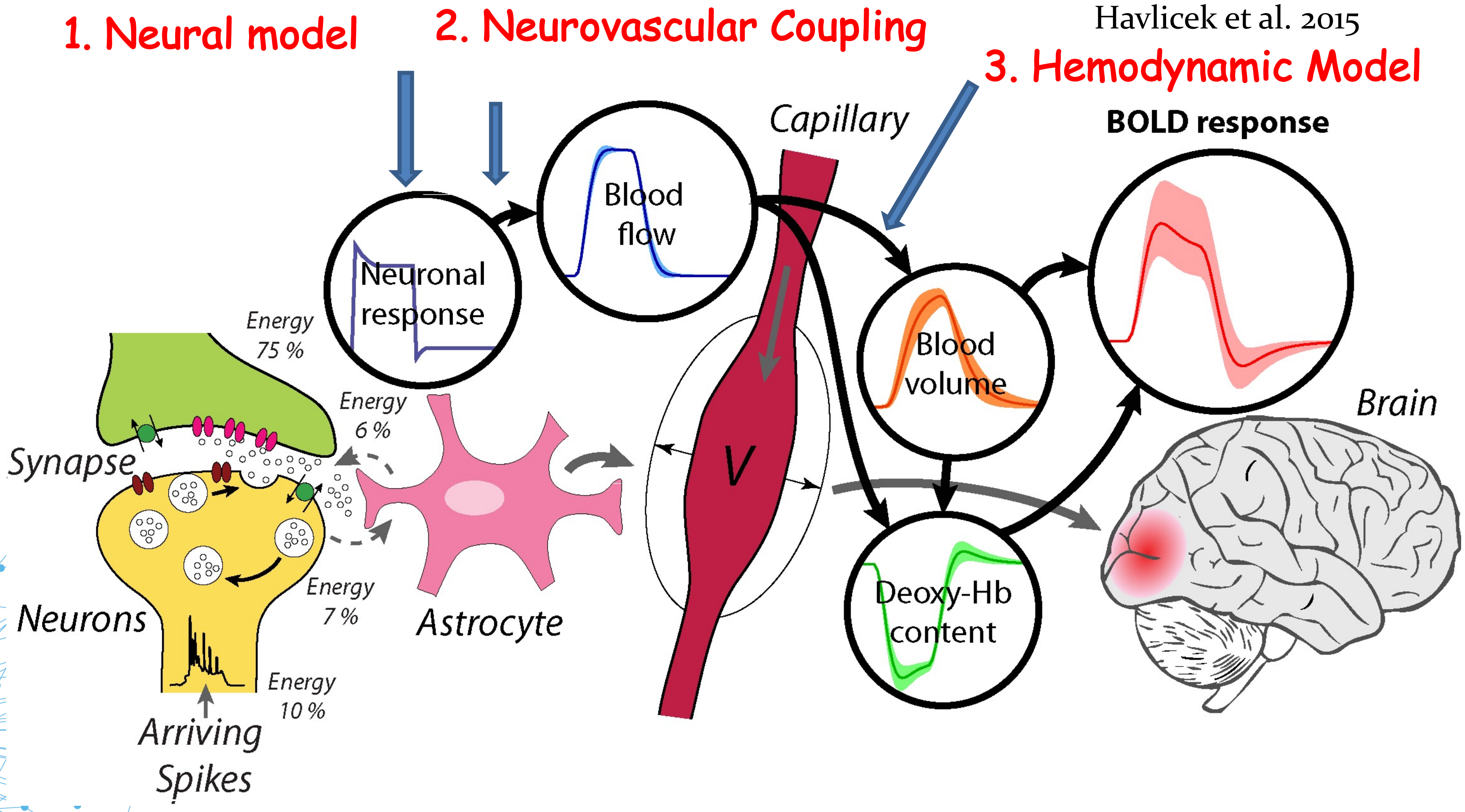
Havlicek et al. 2015



Uludağ, 2021

How about the hemodynamic forward model?

From neuronal to hemodynamic response



Uludağ, 2021

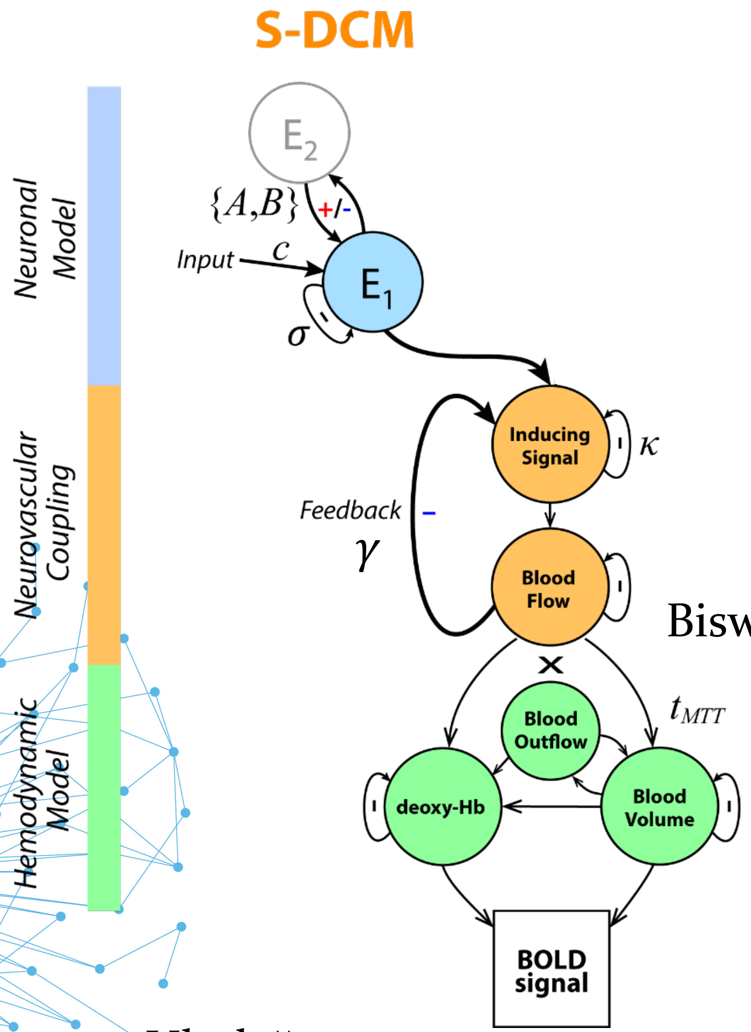
Dynamic Causal Modeling for fMRI

Friston et al. 2003

1.

2.

3.



Biswal et al., 1995

Zappe et al. 2008
Attwell et al. 2010

Uludağ, 2021

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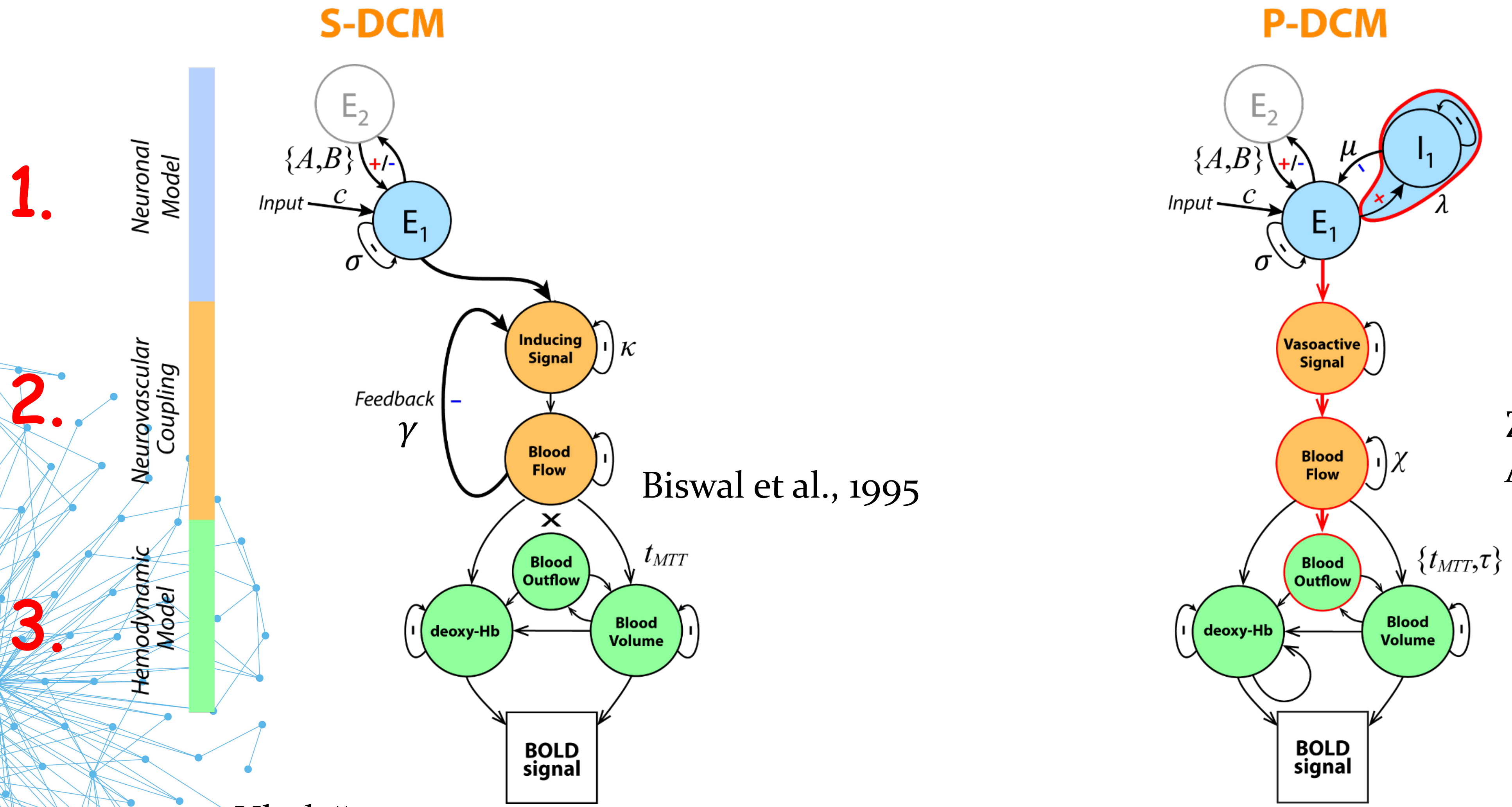
Dynamic Causal Modeling for fMRI

Friston et al. 2003

Havlicek et al. 2015



Zappe et al. 2008
Attwell et al. 2010

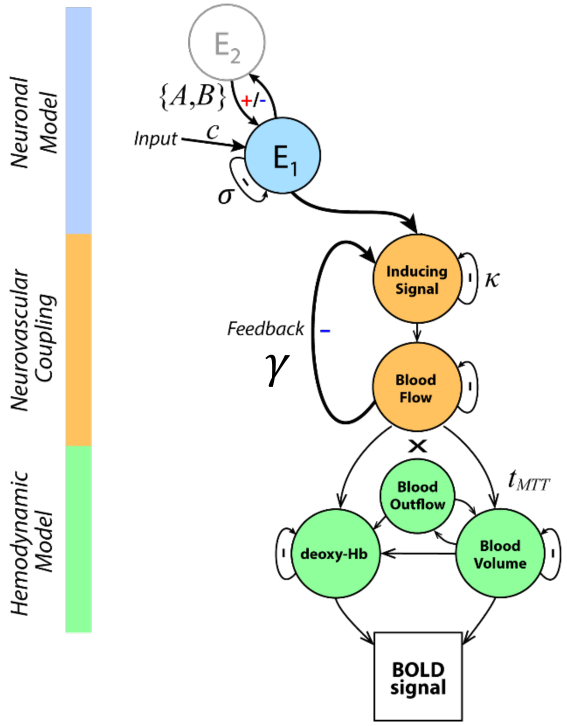
Uludağ, 2021

Dynamic Causal Modeling for fMRI

Main Differences: Neurovascular Coupling

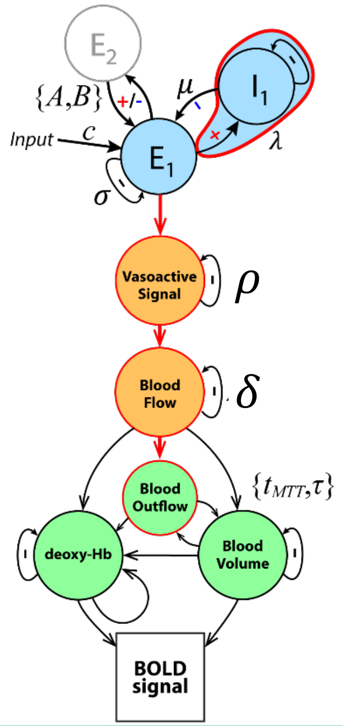
Friston et al. 2003

S-DCM



Havlicek et al. 2015

P-DCM



Neurovascular coupling	$\frac{ds(t)}{dt} = x_E(t) - \kappa s(t) - \gamma(f(t) - 1)$	$\frac{ds(t)}{dt} = x_E(t) - \rho s(t)$
& Blood flow	$\frac{df(t)}{dt} = s(t)$	$\frac{df(t)}{dt} = s(t) - \delta(f(t) - 1).$

Feedback based: damped oscillator **strictly feed-forward**

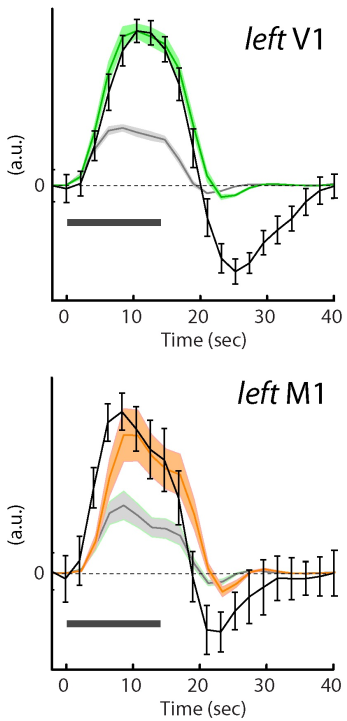
Uludağ, 2021

Dynamic Causal Modeling for fMRI

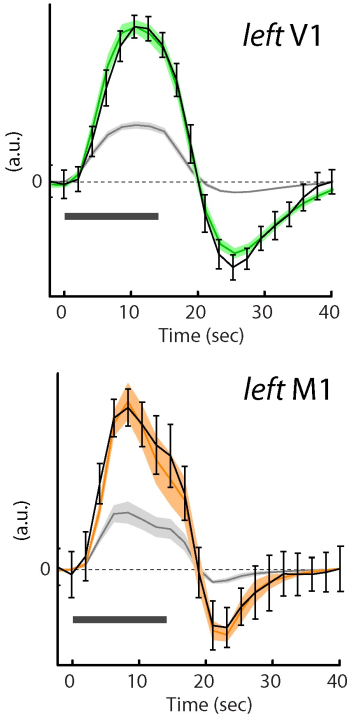
Results: Better Data-Fitting!

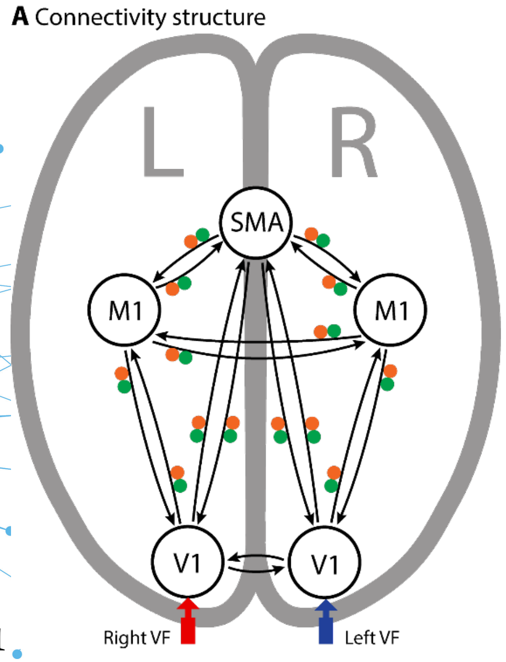
Havlicek et al. 2015

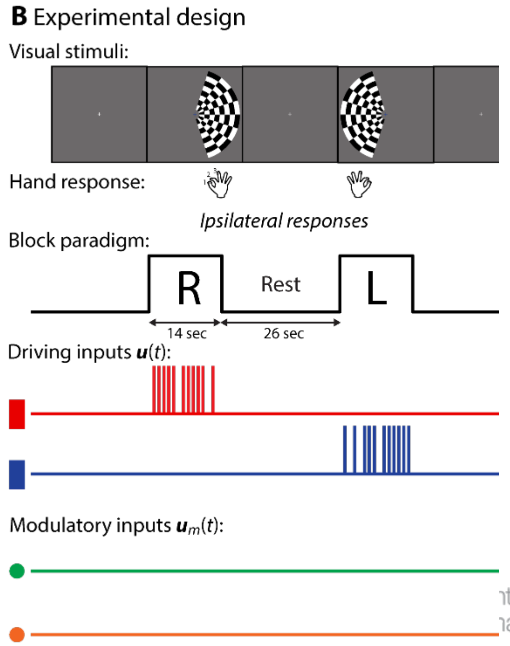
Standard-DCM:



P-DCM:



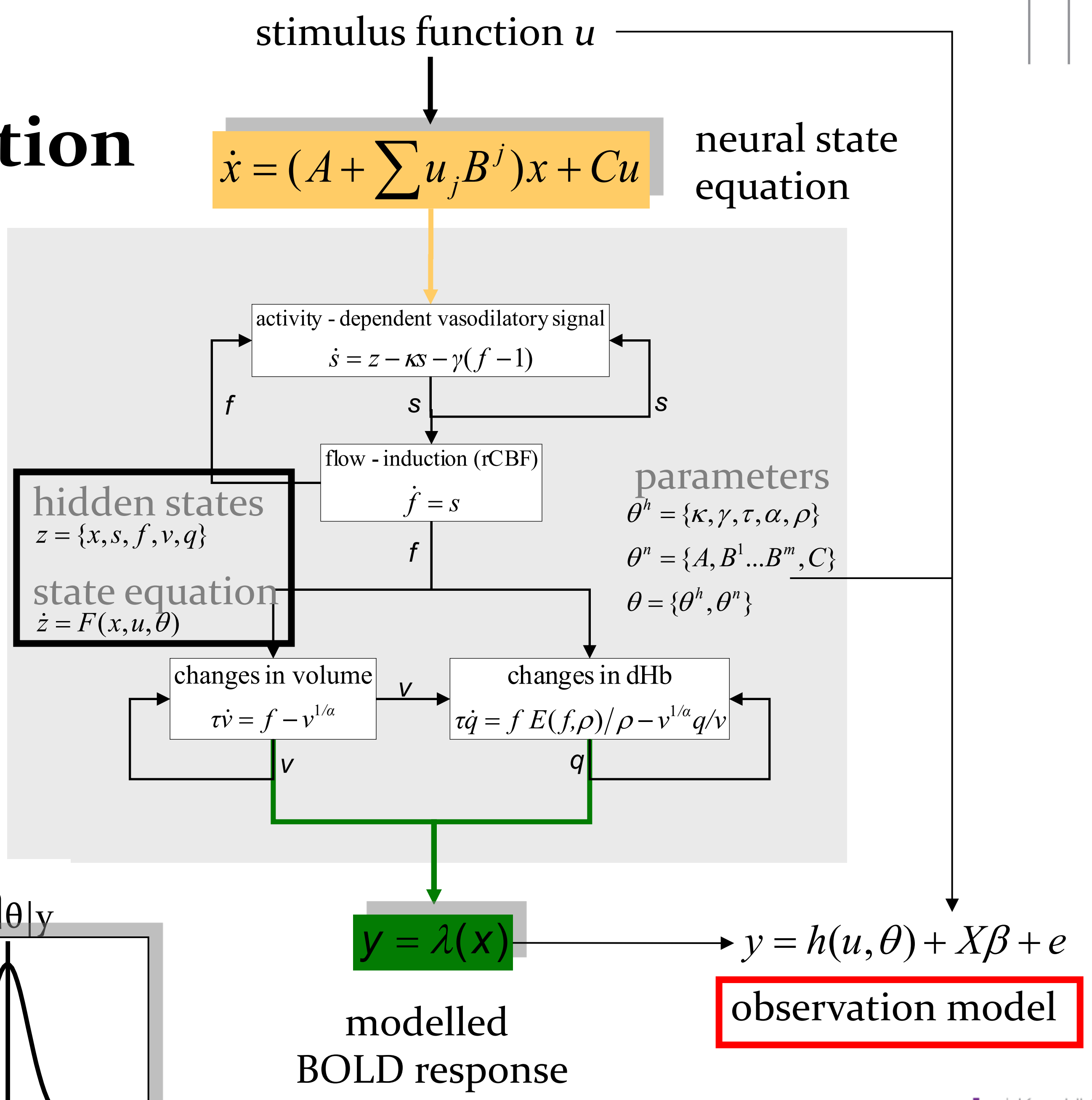


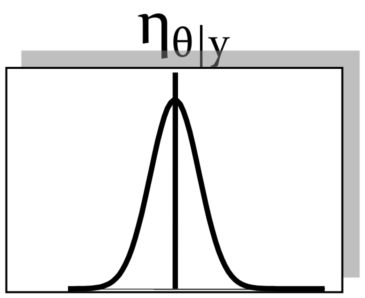


Uludağ, 2021

Overview: parameter estimation

- Combining the neural and hemodynamic states gives the complete forward model.
- An observation model includes measurement error e and confounds X (e.g. drift).
- Bayesian inversion: parameter estimation by means of variational EM under Laplace approximation
- Result: Gaussian a posteriori parameter distributions, characterised by mean $\eta_{\theta|y}$ and covariance $C_{\theta|y}$.





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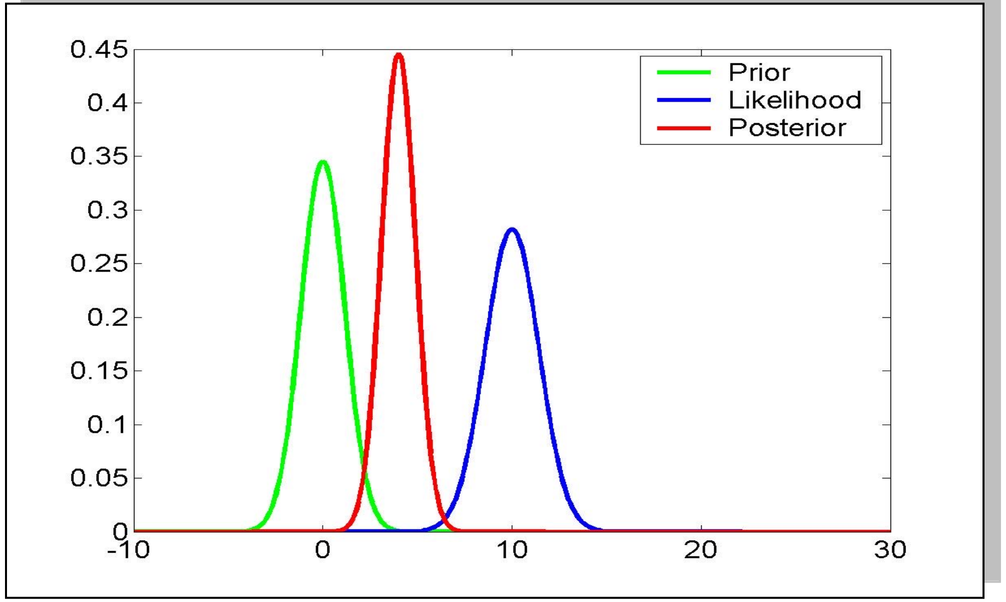
DCM uses a Bayesian approach

new data $\boxed{p(y\,|\,\theta)}$ **prior knowledge** $\boxed{p(\theta)}$

$$\boxed{p(\theta\,|\,y) \propto p(y\,|\,\theta)\,p(\theta)}$$

posterior $\propto$ **likelihood** $\cdot$ **prior**



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

In DCM:
empirical, principled & shrinkage priors.

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 statistics

Parameters governing

- Hemodynamics in a single region
- Neuronal interactions

Constraints (priors) on

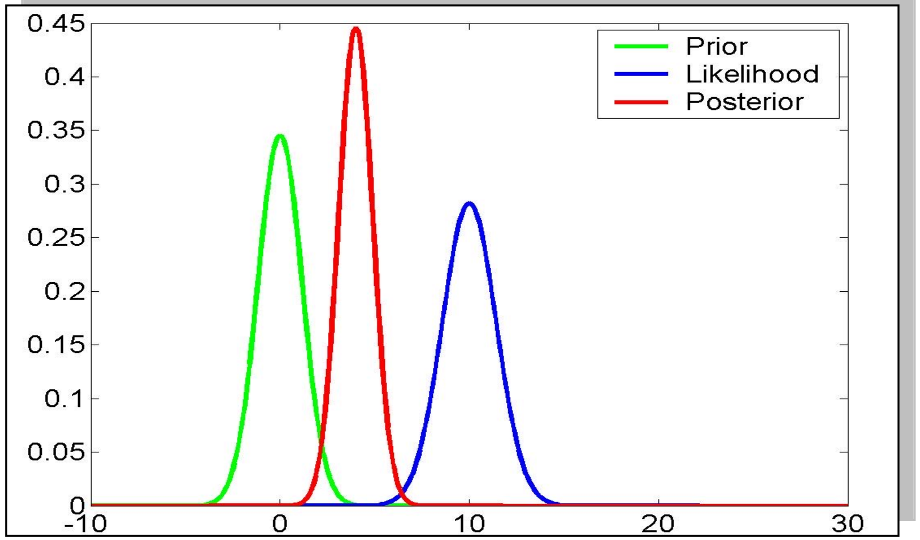
- Hemodynamic parameters
  - empirical
- Self connections are negative
  - principled
- Other connections
  - shrinkage

new data $\quad$ prior knowledge

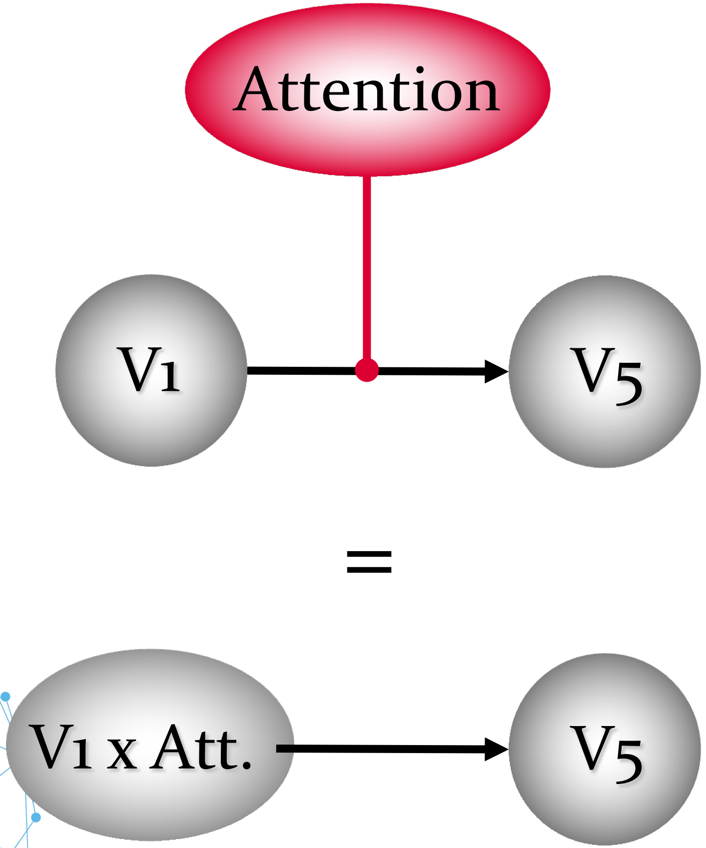
$$\boxed{p(y\,|\,\theta)} \qquad \boxed{p(\theta)}$$

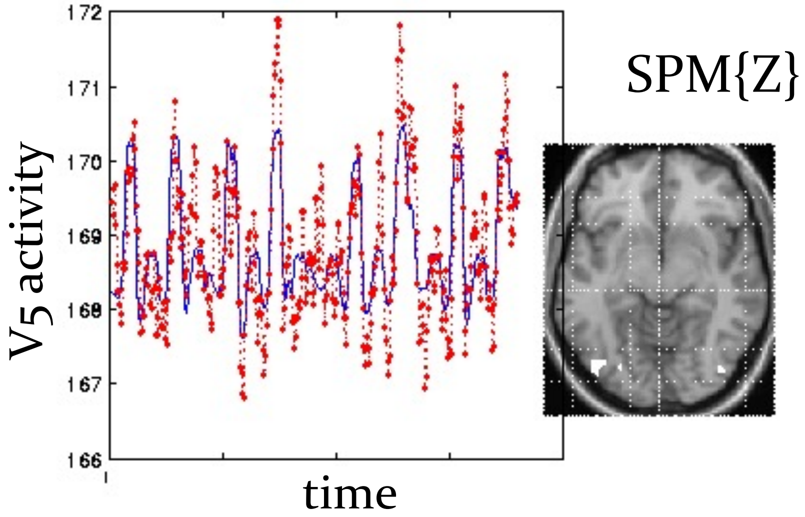
$$\boxed{p(\theta\,|\,y) \propto p(y\,|\,\theta)\,p(\theta)}$$

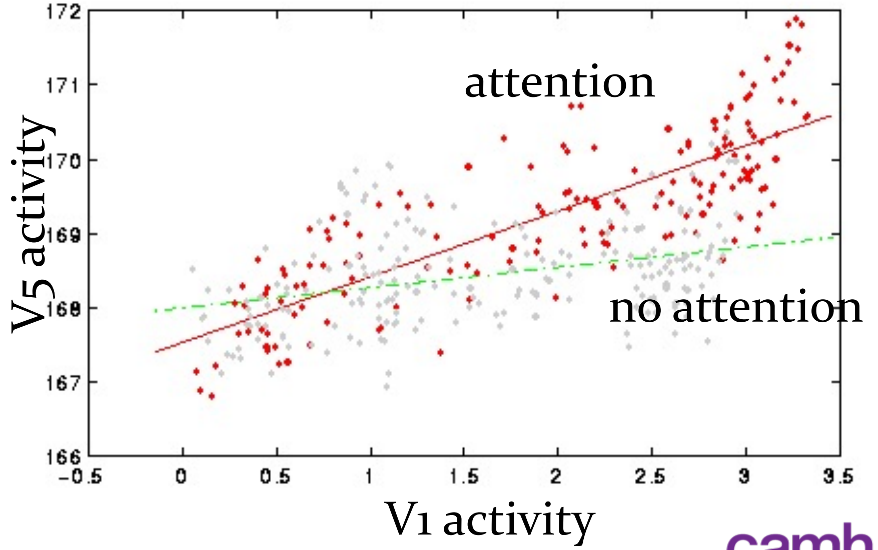
posterior $\propto$ likelihood · prior



Quiz: Can DCM Explain Your Data?







Friston et al. 1997, *NeuroImage*
Büchel & Friston 1997, *Cereb. Cortex*

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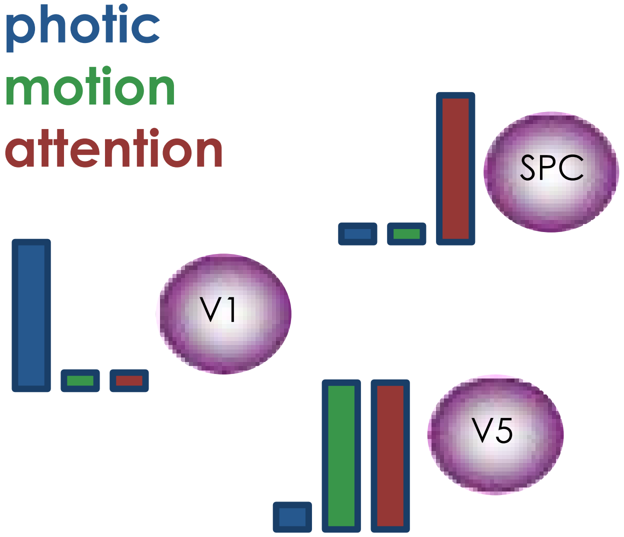
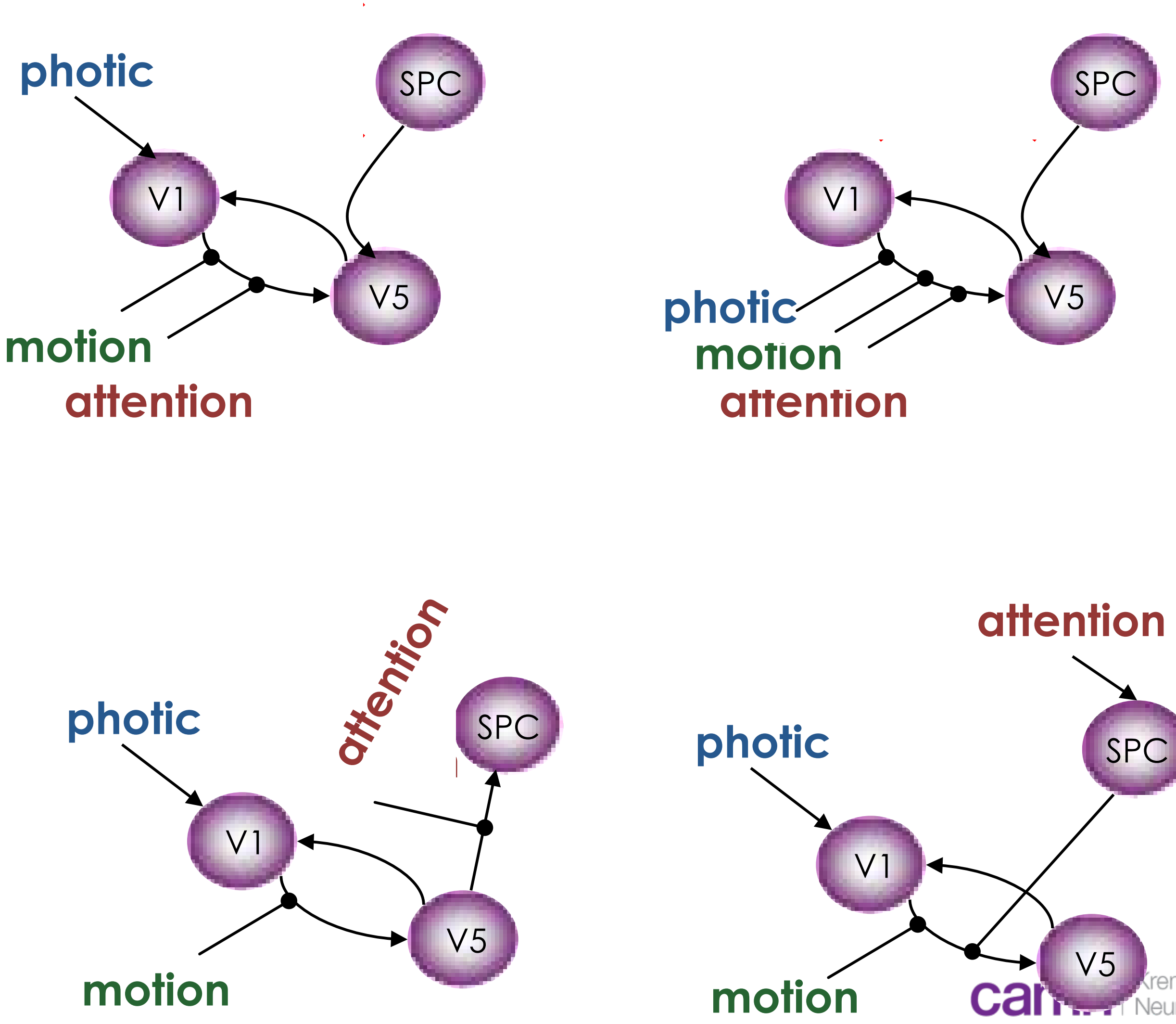
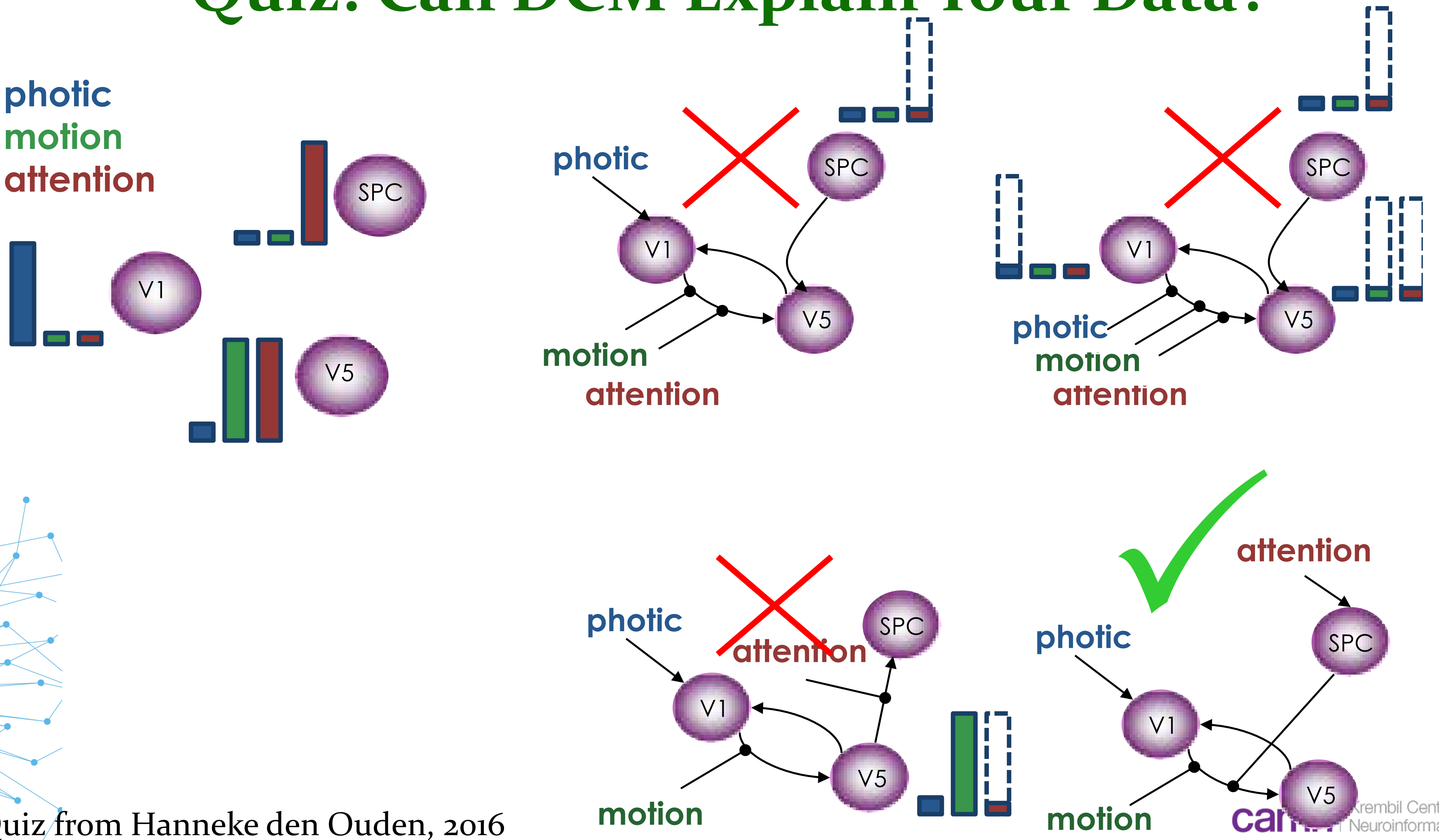
Quiz: Can DCM Explain Your Data?





Quiz from Hanneke den Ouden, 2016

Quiz: Can DCM Explain Your Data?

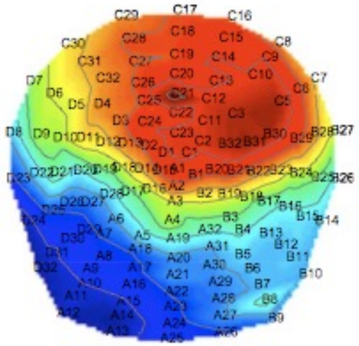


Quiz from Hanneke den Ouden, 2016

DCM Across Data Modalities

Hemodynamic
observation model:
temporal convolution

Electromagnetic
observation model:
spatial convolution

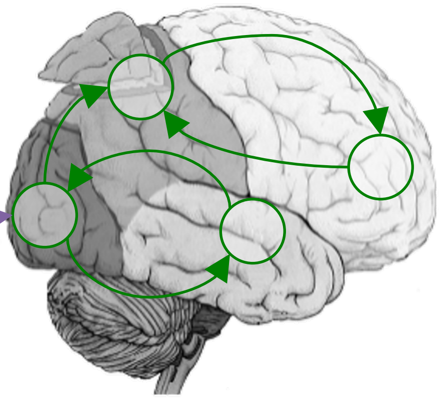


neural states dynamics

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

fMRI

EEG/MEG



- simple neuronal model
- slow time scale

- complicated neuronal model
- fast time scale

inputs

Thanks to J. Daunizeau

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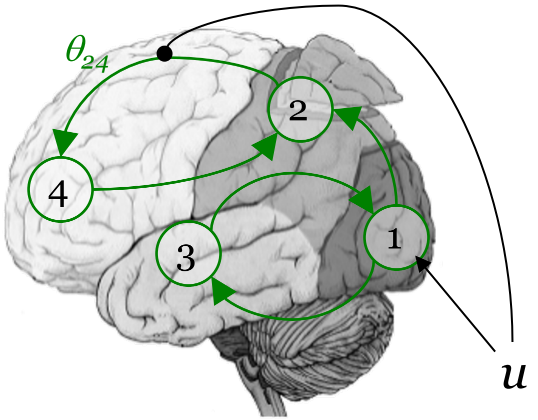
DCM Across Data Modalities

- DCM: model structure

$$\begin{cases} y = g(x,\varphi) + \varepsilon \\ \dot{x} = f(x,u,\theta) \end{cases}$$

likelihood

$$\Rightarrow p(y|\theta,\varphi,m)$$



- DCM: Bayesian inference

priors on parameters

parameter estimate: $$\hat{\theta} = \int \theta p(y|\theta,\varphi,m)\, p(\theta|m)\, p(\varphi|m)\, d\theta d\varphi$$

model evidence: $$p(y|m) = \int p(y|\theta,\varphi,m)\, p(\theta|m)\, p(\varphi|m)\, d\varphi d\theta$$

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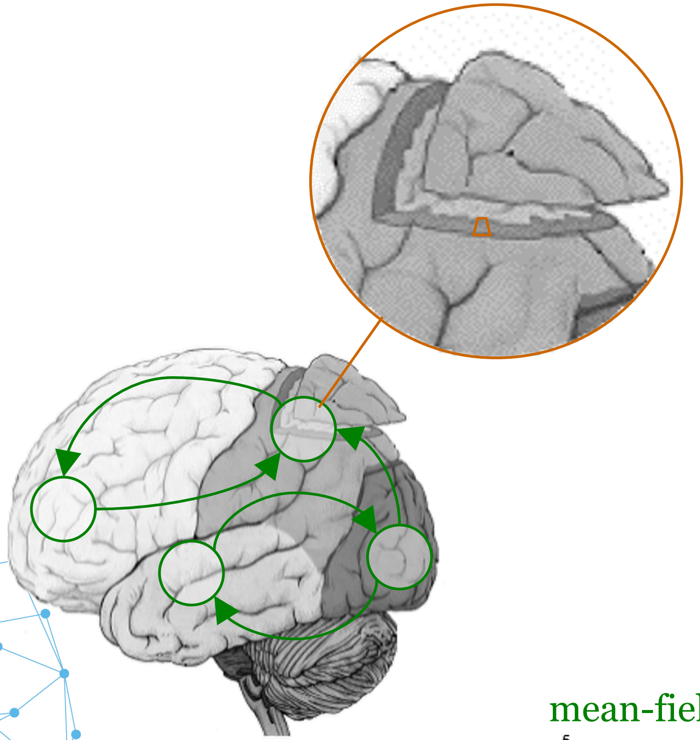
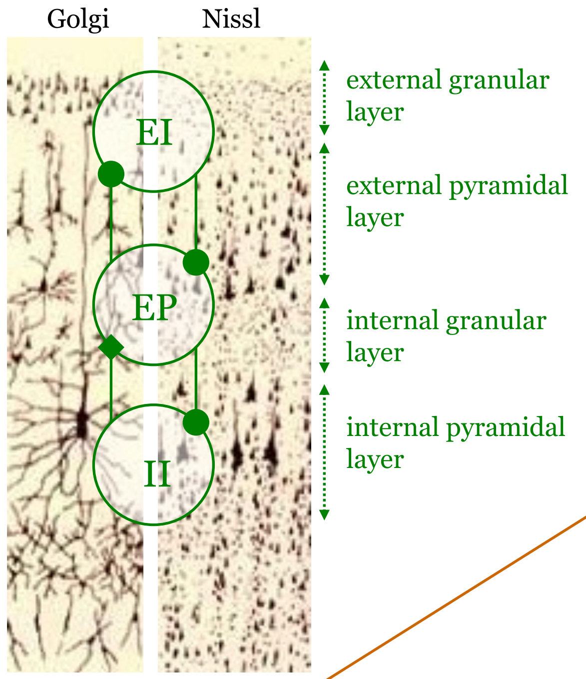
Neural ensembles dynamics

multi-scale perspective

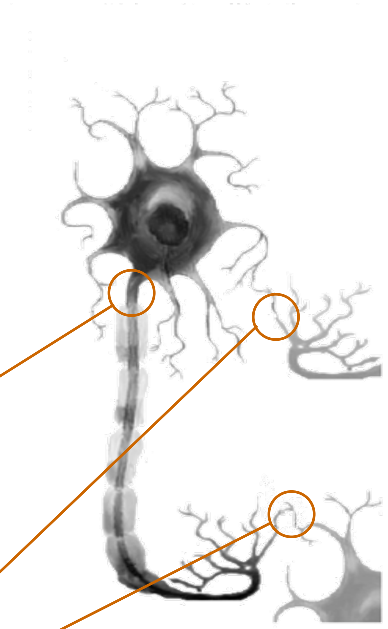
macro-scale



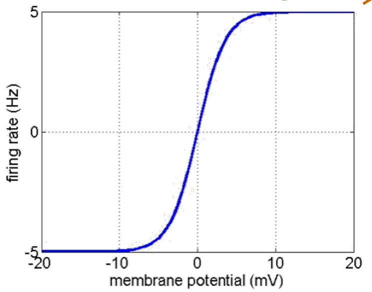
meso-scale



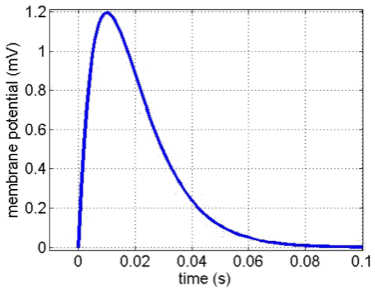
micro-scale



mean-field firing rate



synaptic dynamics



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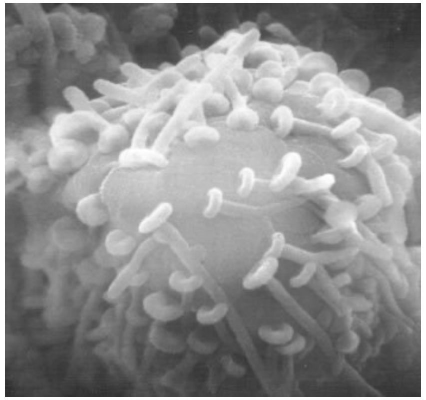
Neural ensembles dynamics

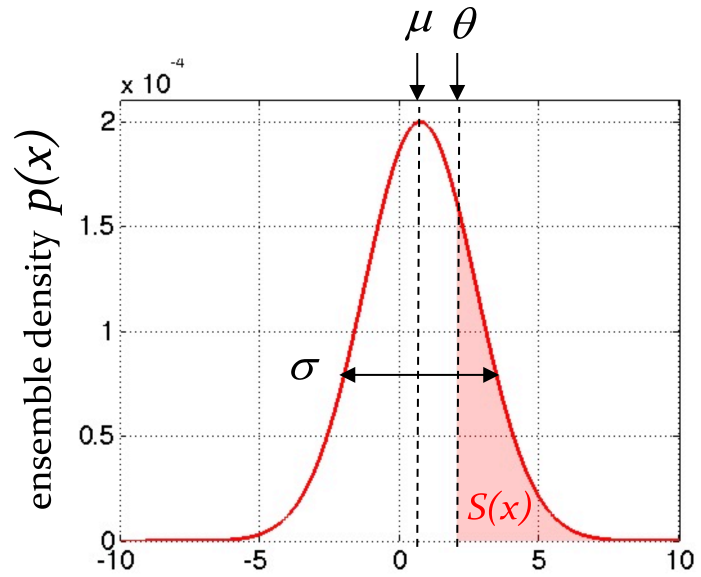
from micro- to meso-scale



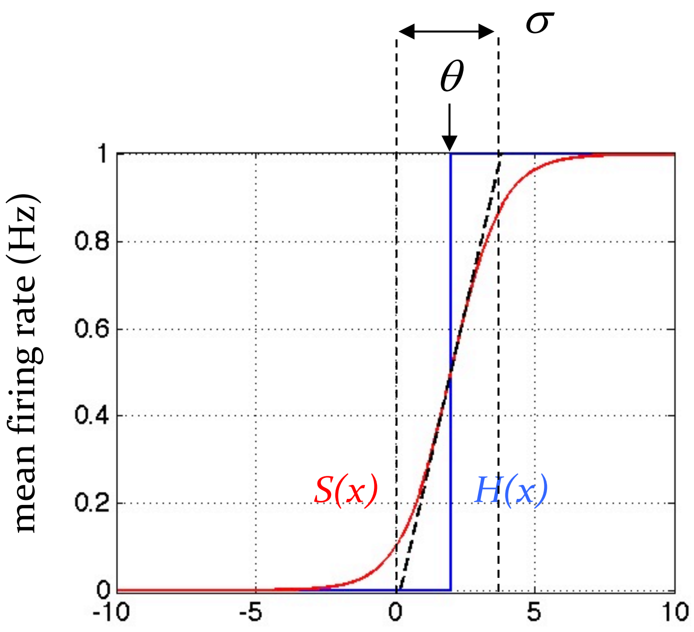
$x_j(t)$: post-synaptic potential of j^{th} neuron within its ensemble

$$\frac{1}{N-1}\sum_{j'\neq j} H\left(x_{j'}(t)-\theta\right) \xrightarrow{N\to\infty} \int H\left(x(t)-\theta\right)p\left(x(t)\right)dx$$

$\approx S(\mu)$ mean-field firing rate



membrane depolarization (mV)



mean membrane depolarization (mV)

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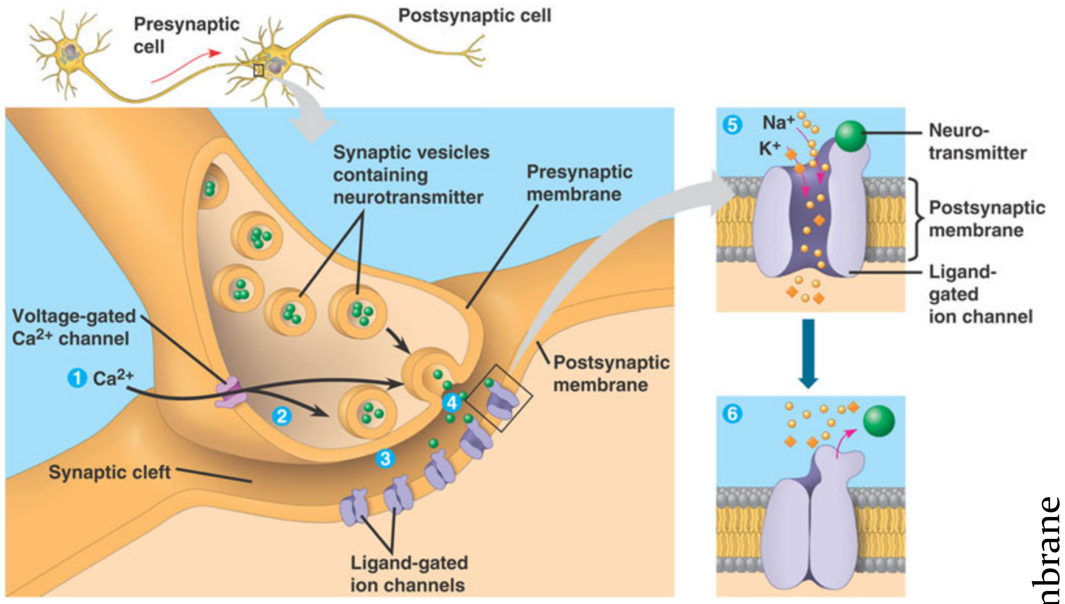
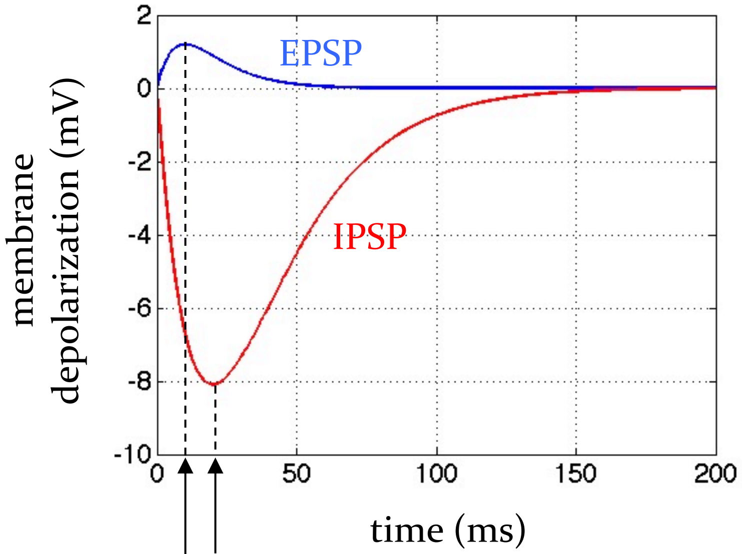
Neural ensembles dynamics

synaptic kinematics



post-synaptic potential



$$K_i^{-1}$$

$$K_e^{-1}$$

$$\begin{cases} \dot{\mu}_1 = \mu_2 \\ \dot{\mu}_2 = \kappa_{i/e}^2 S(\bullet) - 2\kappa_{i/e}\,\mu_2 - \kappa_{i/e}^2\,\mu_1 \end{cases}$$

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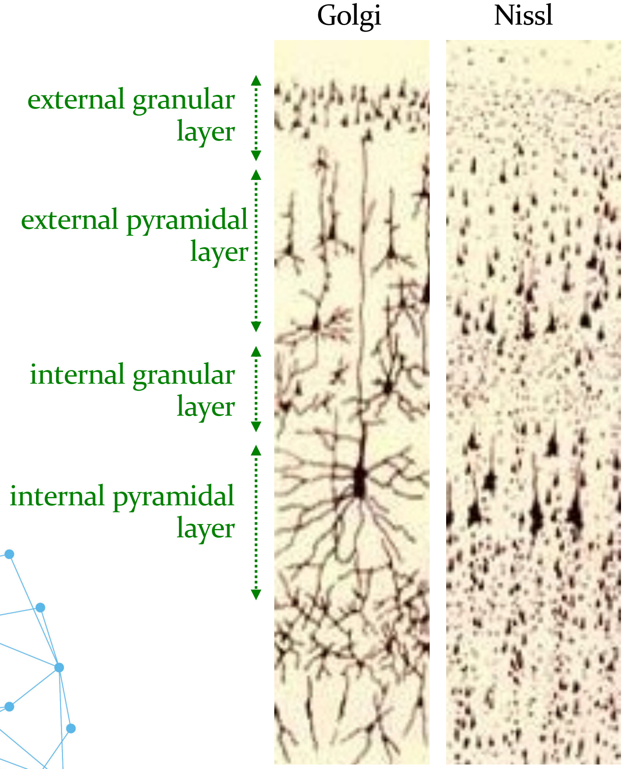
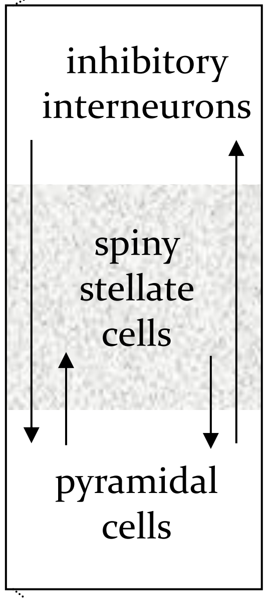
Neural ensembles dynamics

intrinsic connections within the cortical column





$$\dot{\mu}_7 = \mu_8$$
$$\dot{\mu}_8 = \gamma_3 \kappa_e^2 S(\mu_0) - 2\kappa_e \mu_8 - \kappa_e^2 \mu_7$$

γ_4 γ_3

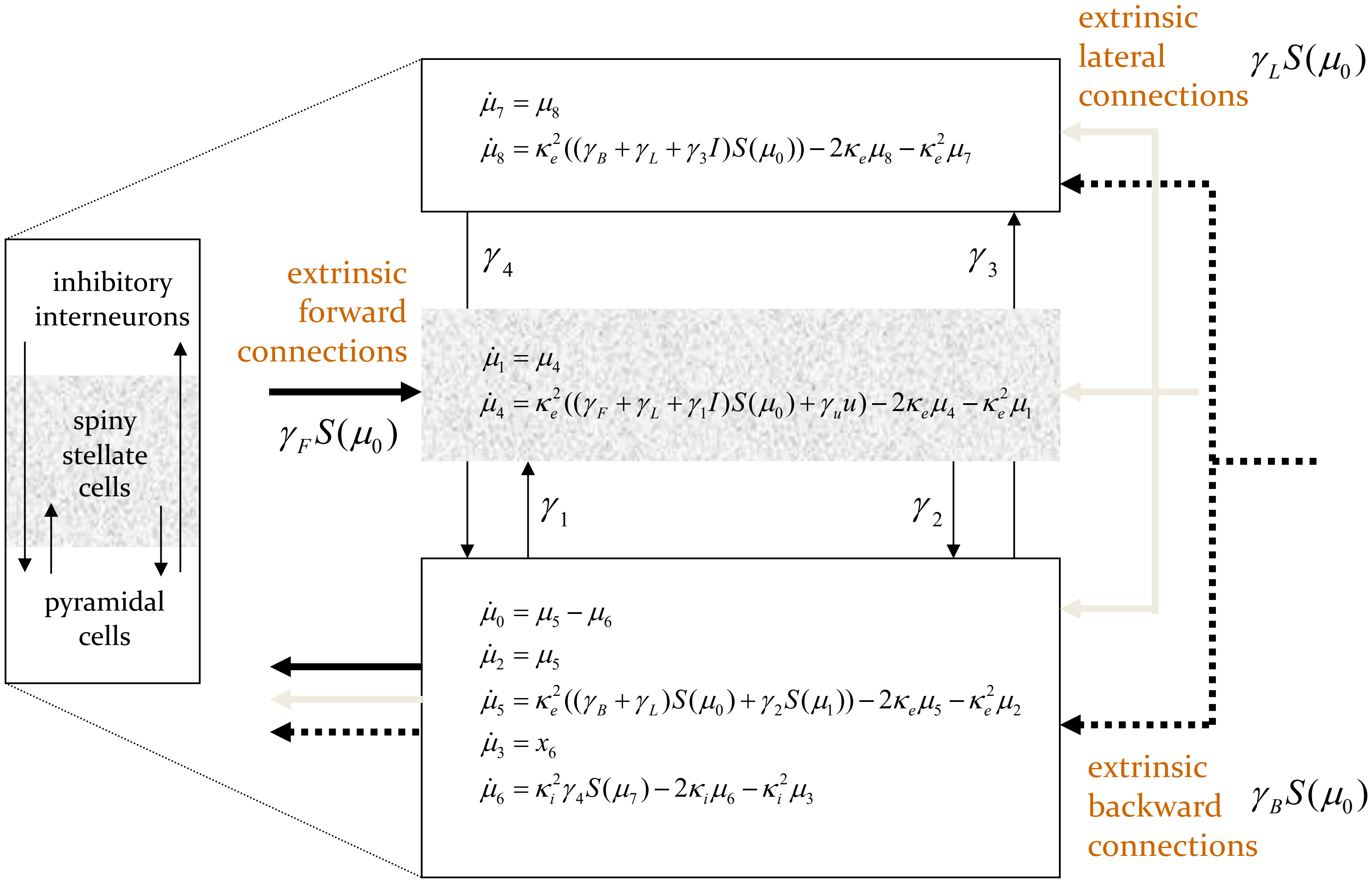
$$\dot{\mu}_1 = \mu_4$$
$$\dot{\mu}_4 = \gamma_1 \kappa_e^2 S(\mu_0) - 2\kappa_e \mu_4 - \kappa_e^2 \mu_1$$

γ_1 intrinsic connections γ_2

$$\dot{\mu}_0 = \mu_5 - \mu_6$$
$$\dot{\mu}_2 = \mu_5$$
$$\dot{\mu}_5 = \gamma_2 \kappa_e^2 S(\mu_1) - 2\kappa_e \mu_5 - \kappa_e^2 \mu_2$$
$$\dot{\mu}_3 = x_6$$
$$\dot{\mu}_6 = \gamma_4 \kappa_i^2 S(\mu_7) - 2\kappa_i \mu_6 - \kappa_i^2 \mu_3$$

Neural ensembles dynamics

extrinsic connections between brain regions



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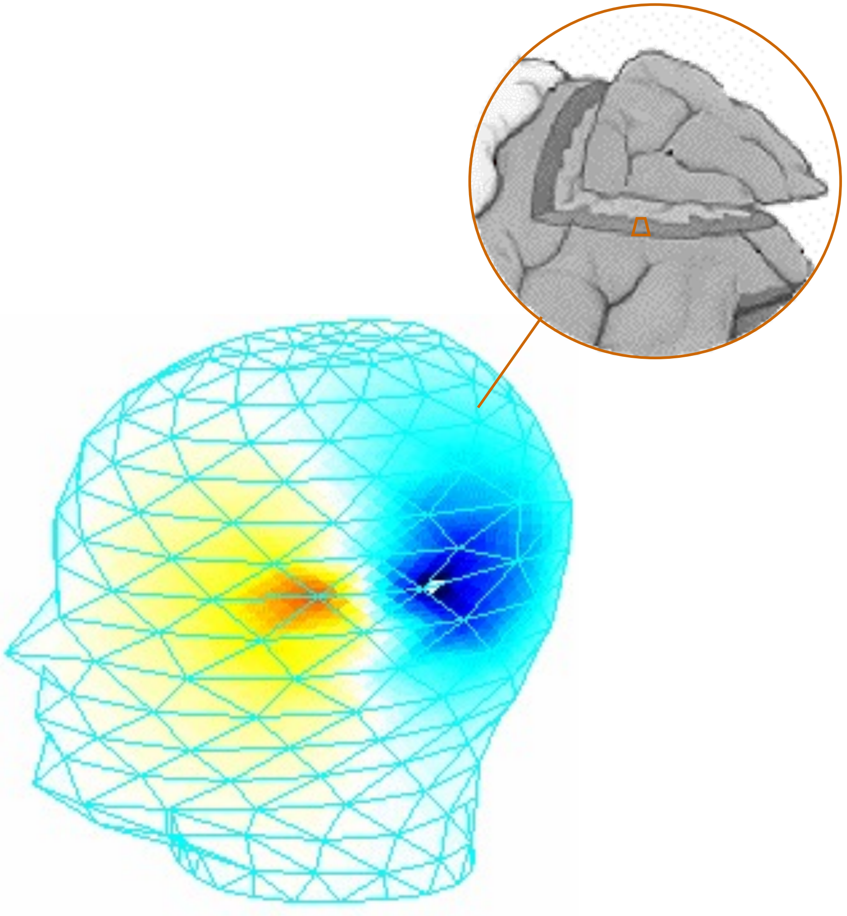
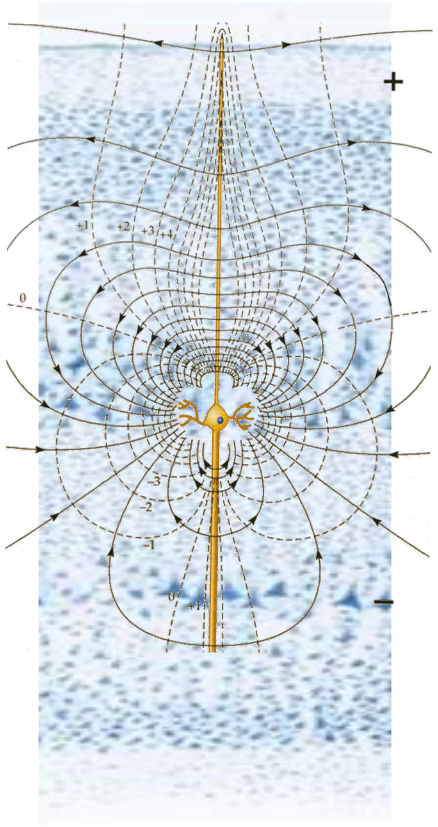
Observation mappings

the electromagnetic forward model

$$\mathbf{y}(t)=\sum_i \mathbf{L}^{(i)}\mathbf{w}_0^{(i)}\sum_j \beta_j \mu^{(ij)}(t)+\varepsilon(t) \qquad \varepsilon(t)\sim N\left(0,Q_y\right)$$





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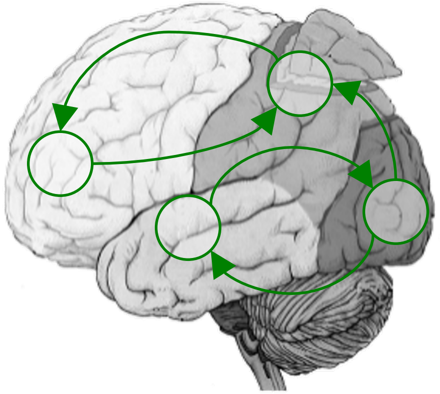
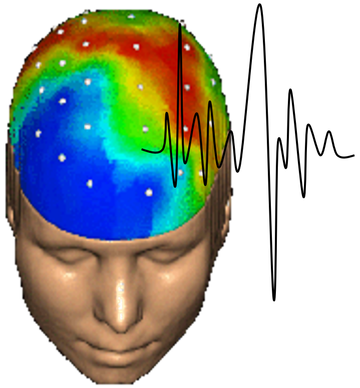
Bayesian inference
forward and inverse problems

forward problem

$$p\left(y \middle| \vartheta, m\right)$$

likelihood





posterior distribution

$$p\left(\vartheta \middle| y, m\right)$$

inverse problem

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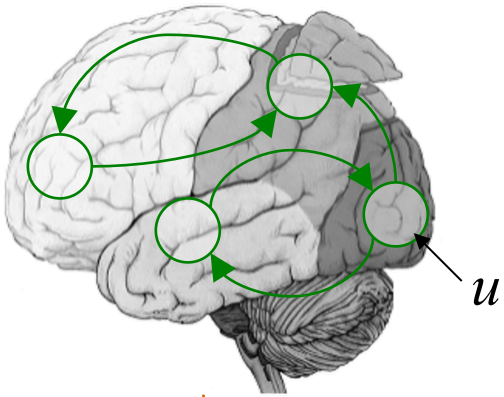
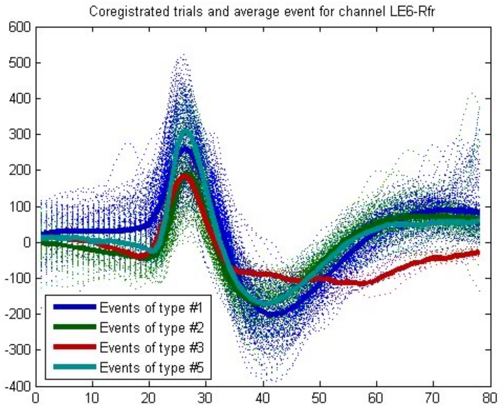
Bayesian inference
likelihood and priors



generative model m

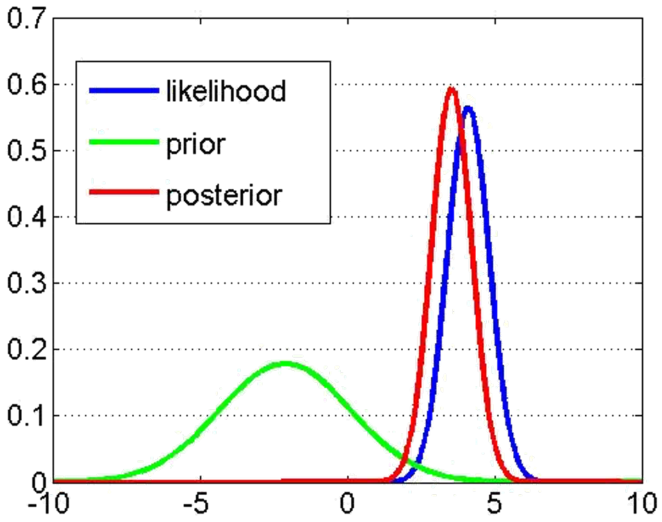
y



likelihood $p(y|\vartheta, m)$

prior $p(\vartheta|m)$

posterior $$p(\vartheta|y,m) = \frac{p(y|\vartheta,m)\,p(\vartheta|m)}{p(y|m)}$$



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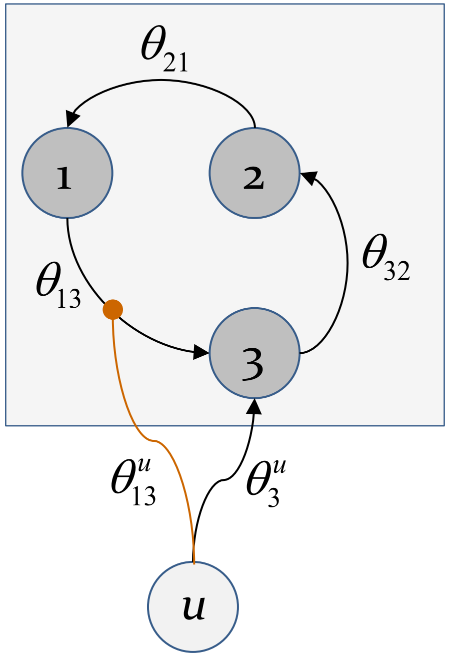
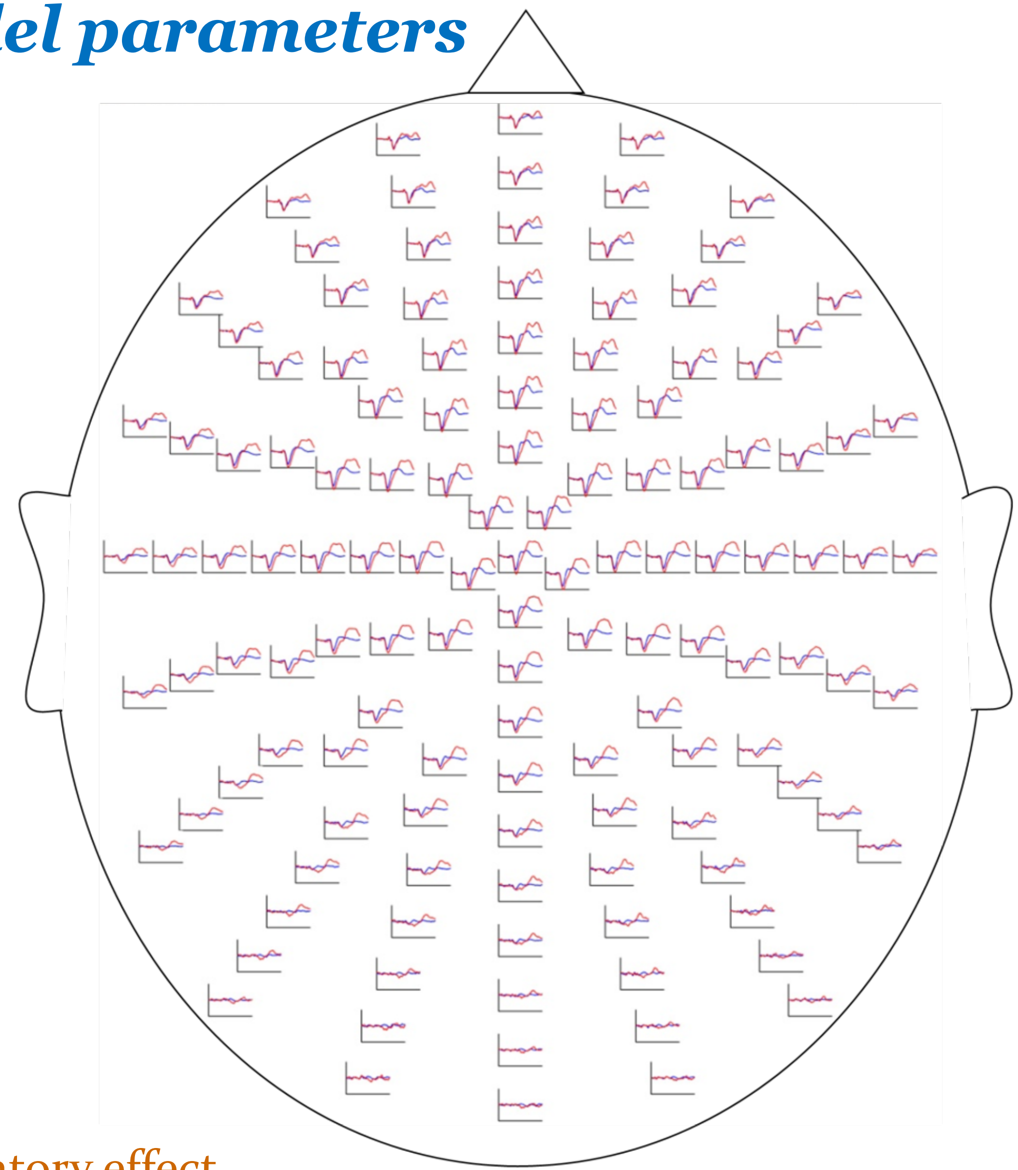
Bayesian inference

DCM: key model parameters





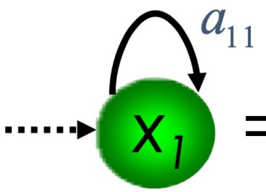
$(\theta_{21}, \theta_{32}, \theta_{13})$ state-state coupling

θ_{3}^{u} input-state coupling

θ_{13}^{u} input-dependent modulatory effect

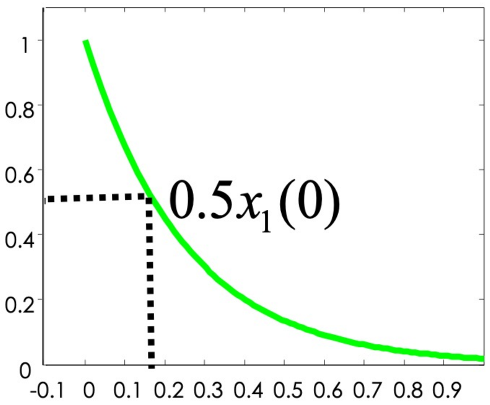
What are the DCM parameters?

DCM parameters = rate constants

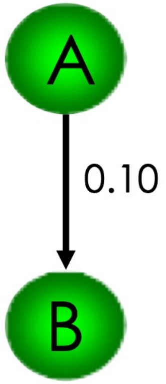


$$= \frac{dx}{dt} = a_{11}x_1 \qquad \longrightarrow \qquad x_1(t) = x_1(0)\exp(a_{11}t)$$

Decay function



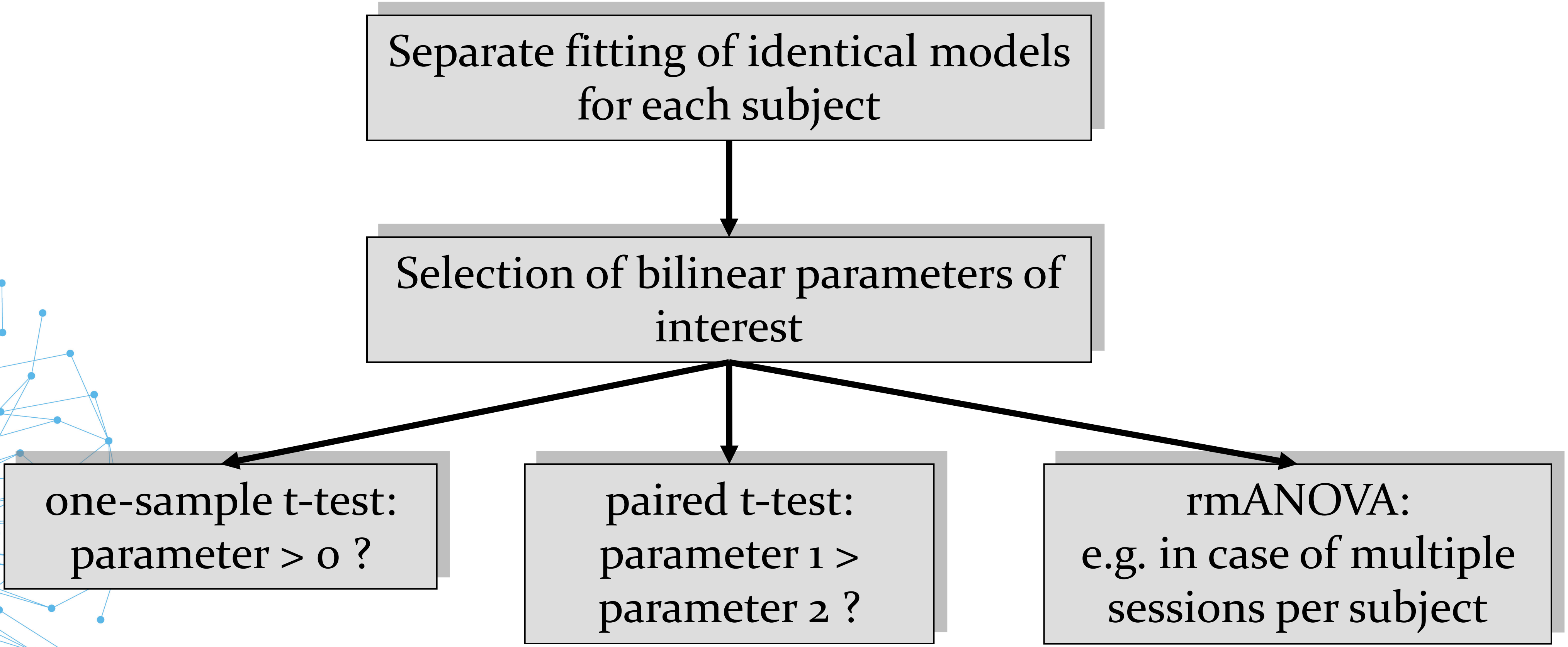
$\tau = \ln 2 / s$



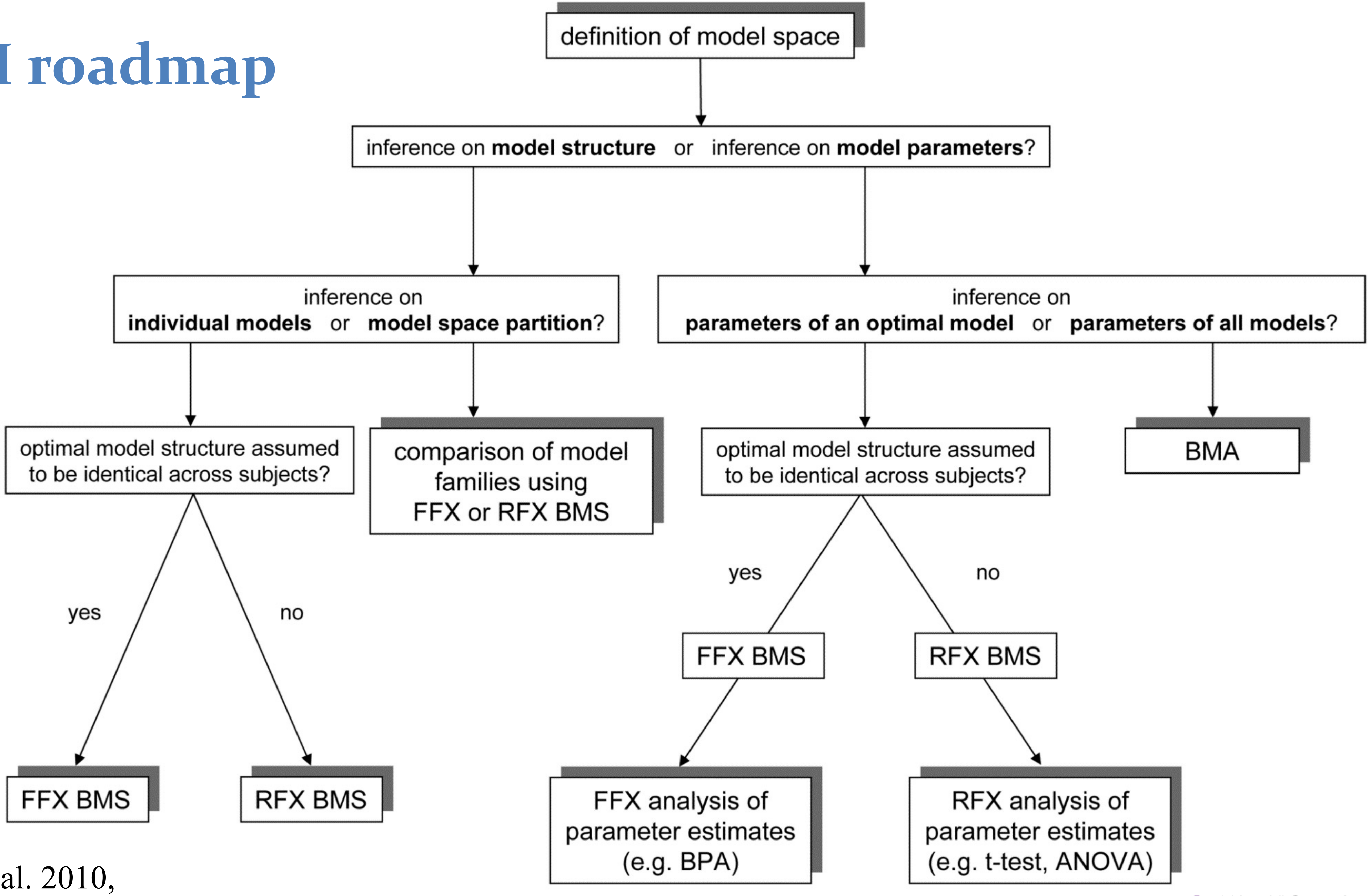
If A>B is 0.1 s^{-1}, this means that per unit time, the increase in activity in B corresponds to 10% of the current activity in A

Inference about DCM parameters: group analysis (classical)

- In analogy to other “random effects” analyses, 2nd level/group analyses can be applied to DCM parameters:



DCM roadmap



Stephan et al. 2010, *NeuroImage*

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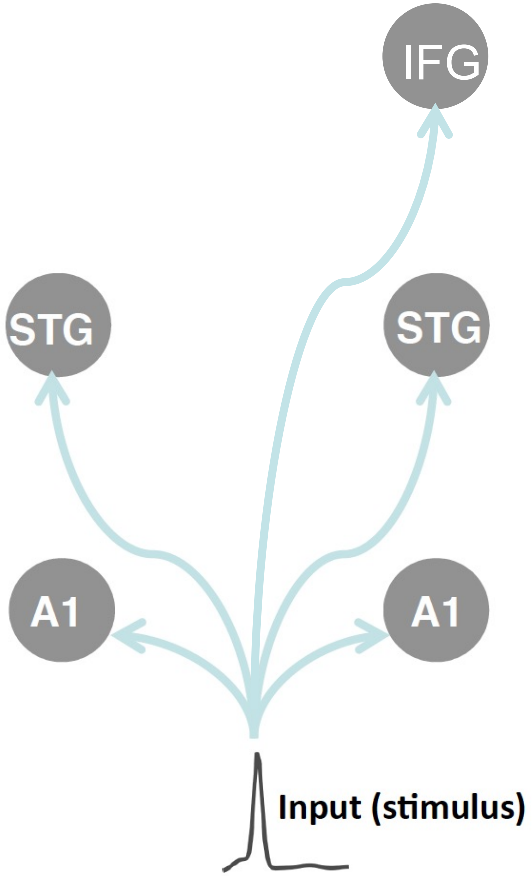
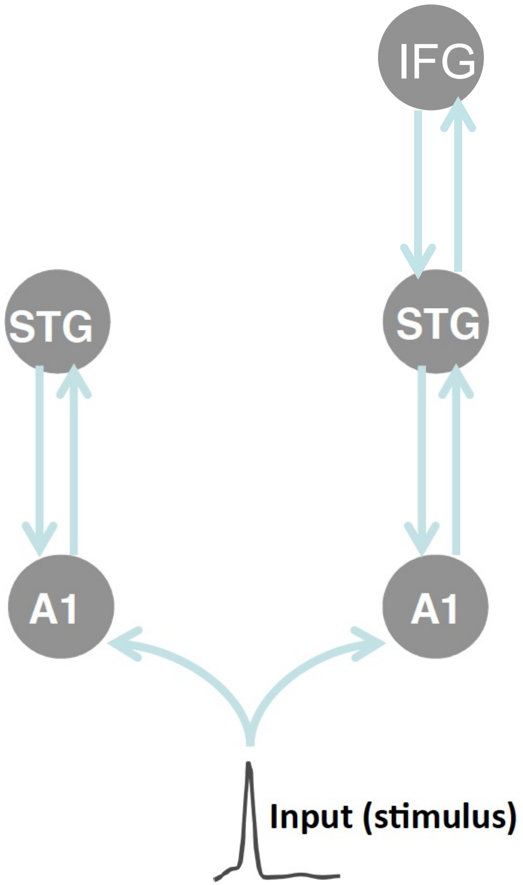
Value of DCM

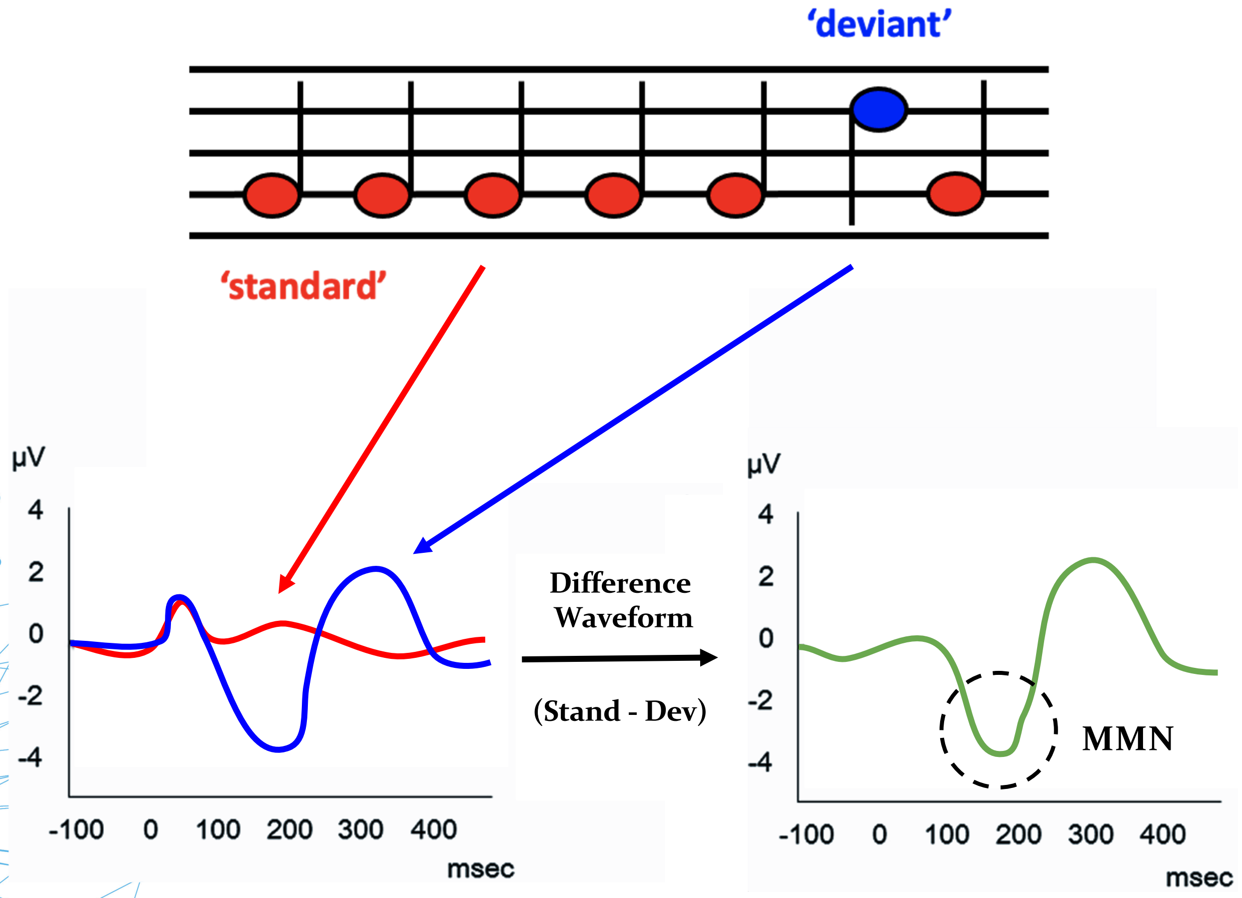
Conventional analysis:
Which regions are involved in task?



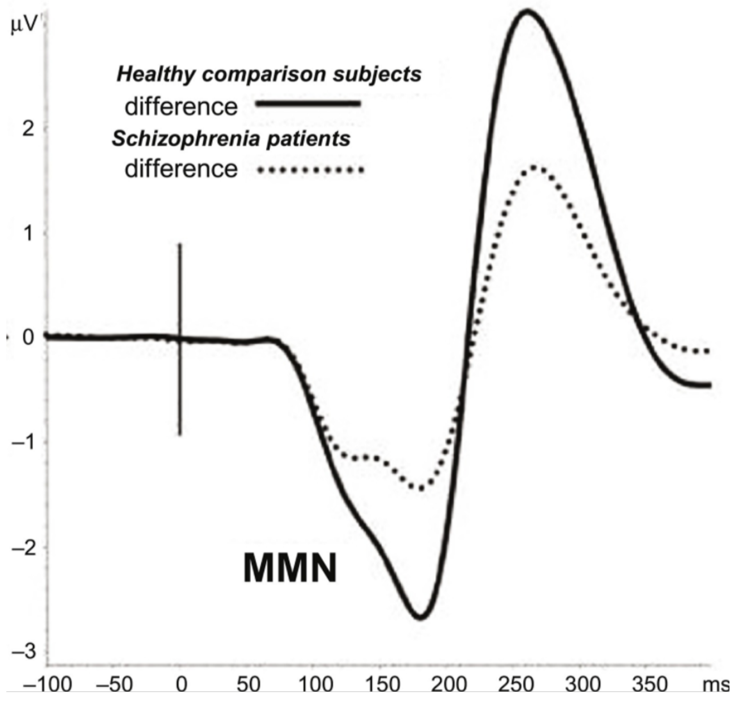
DCM analysis:
How do regions communicate?



Mismatch Negativity (MMN)

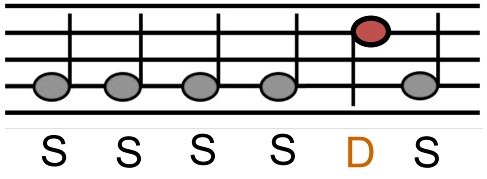


Schizophrenia vs. Controls

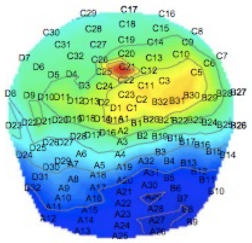


Modelling Auditory MMN Effect

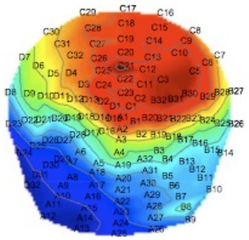
sequence of auditory stimuli



standard condition (S)

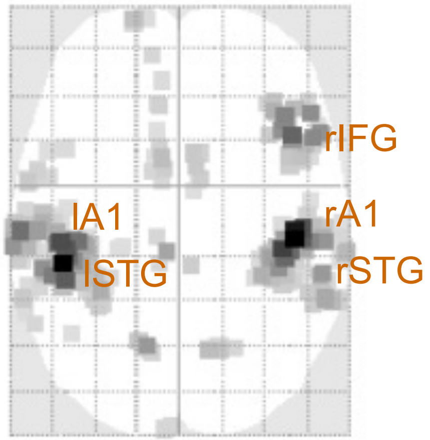


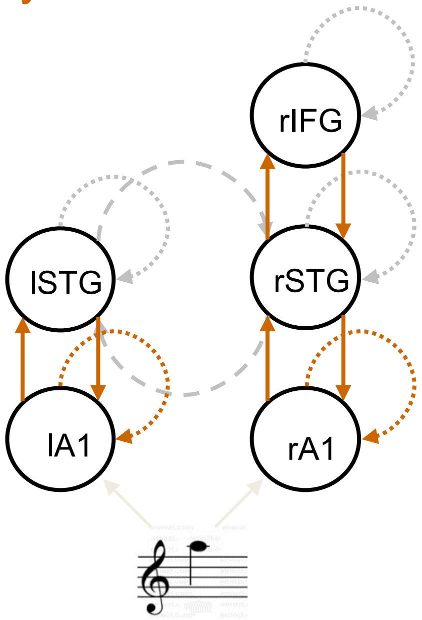
deviant condition (D)



t ~ 200 ms

S-D: **reorganisation**
of the connectivity structure





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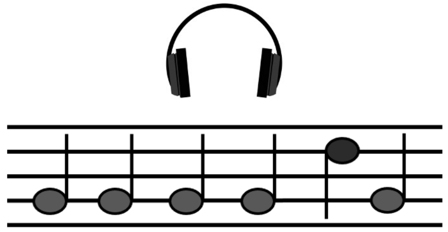
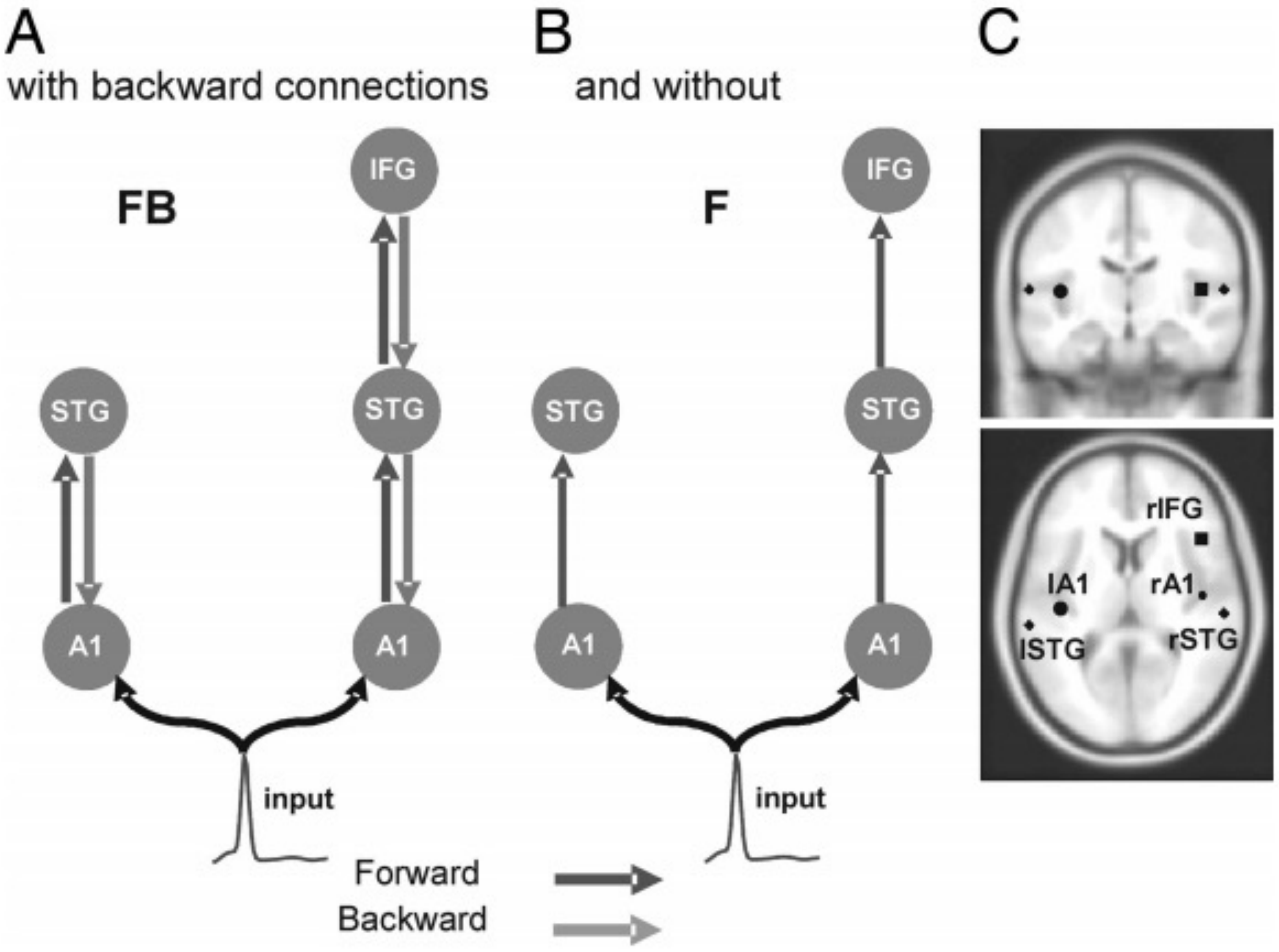
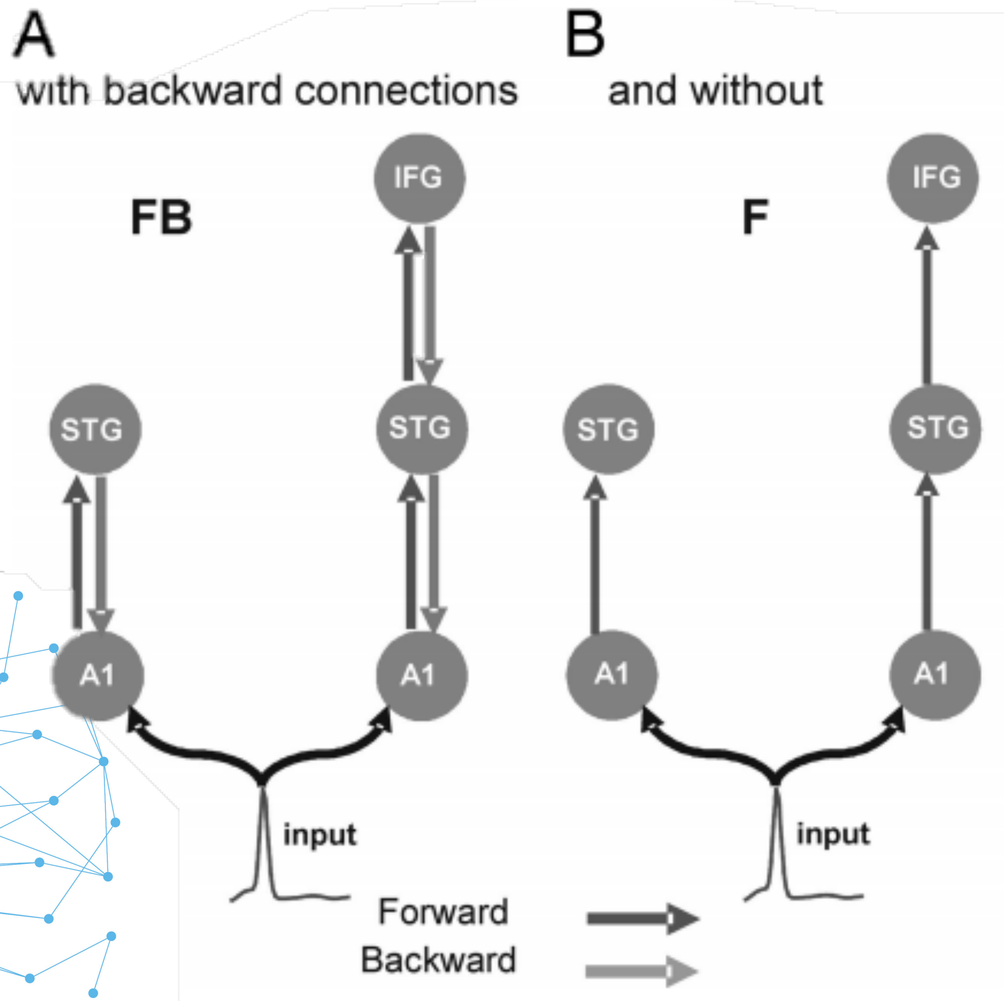
Example #1: Role of feedback connections

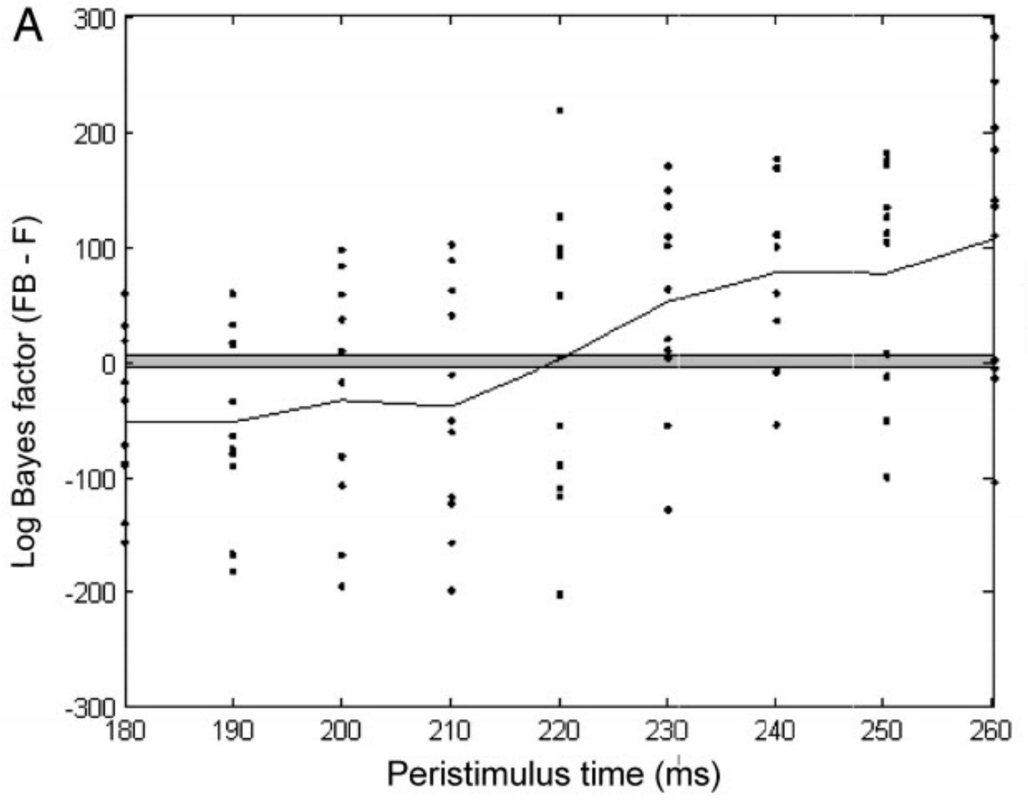




Garrido et al., 2007

Example #1: Role of feedback connections





Garrido et al., 2007

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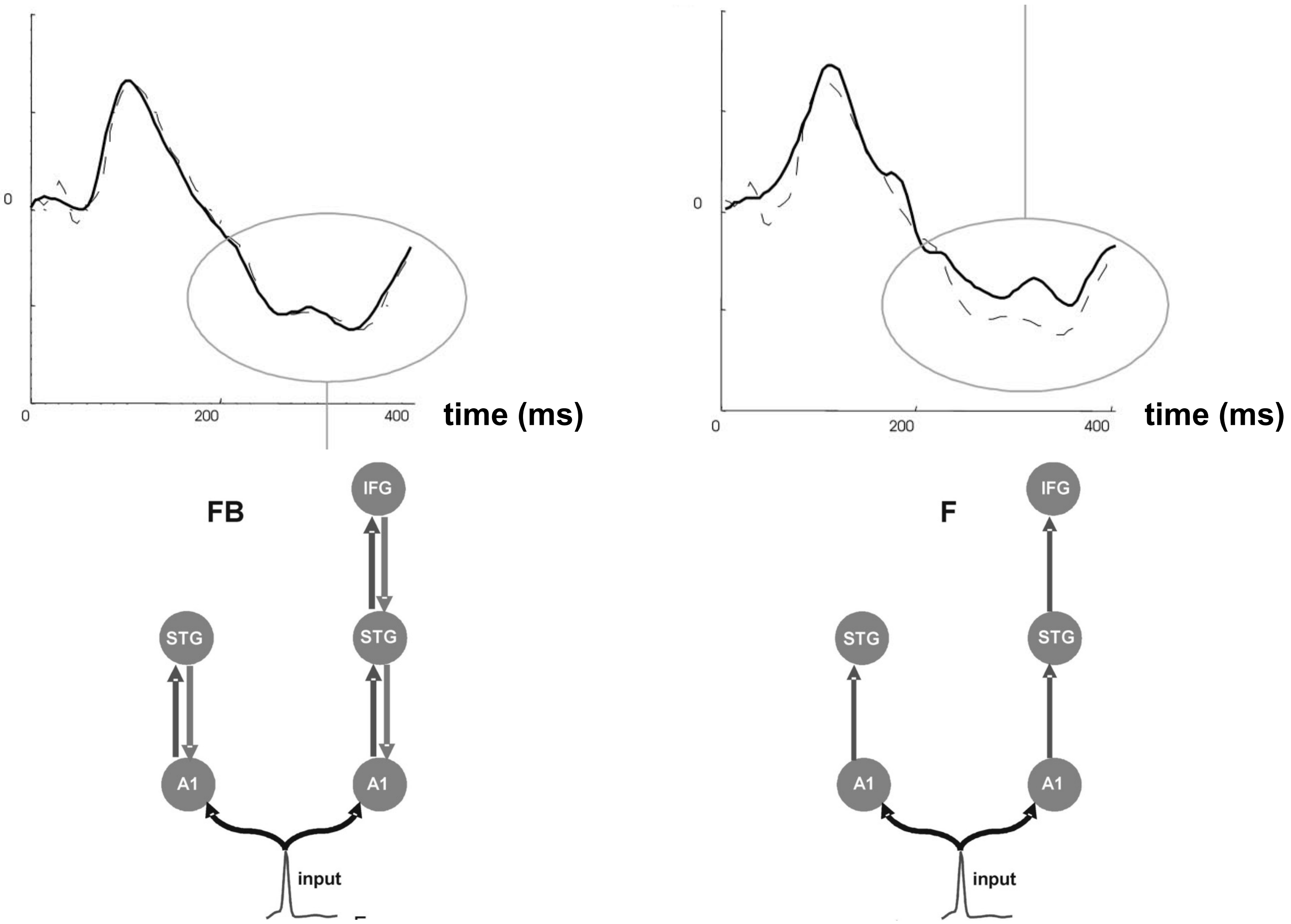
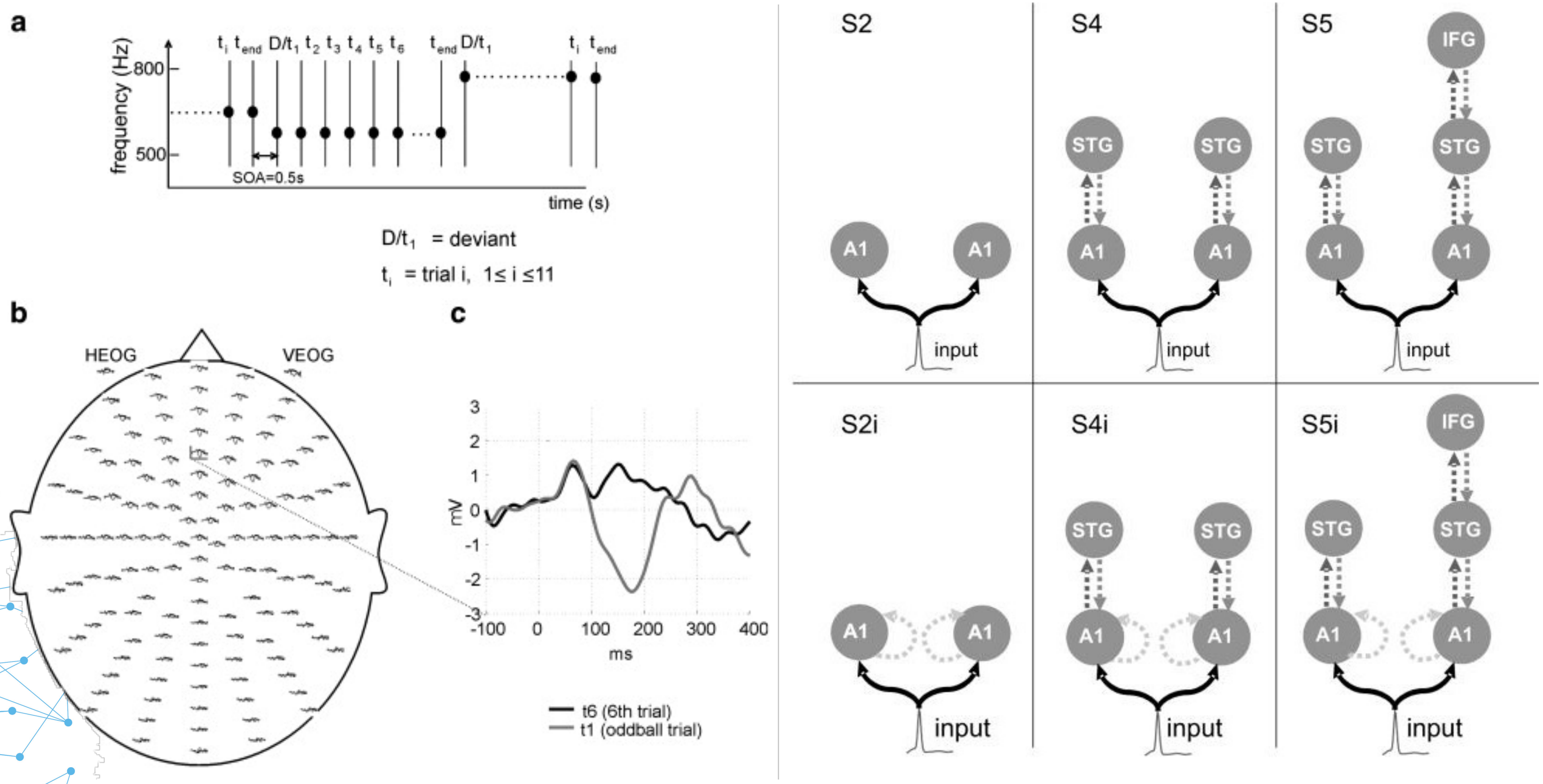
Example #1: Role of feedback connections



Garrido et al., 2007

Example #2: Networks and the MMN



Garrido et al., 2008

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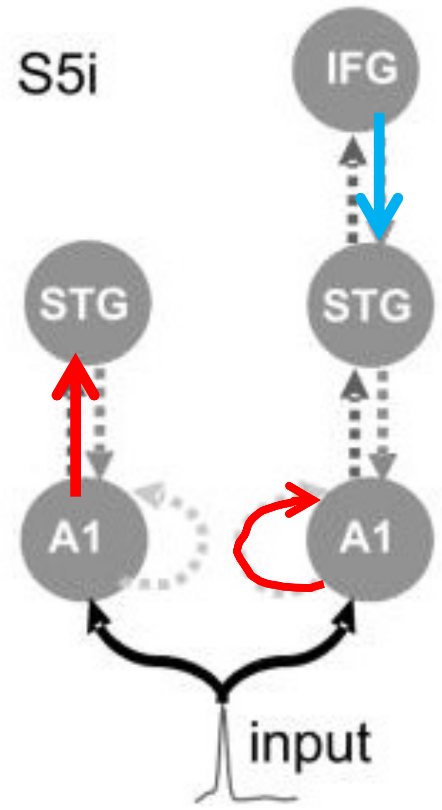
Example #2: Networks and the MMN



Deviants vs. Standards

- Significant coupling decrease ($p<0.003$) in backward connection linking **rIFG** to **rSTG**
- Trend increase ($p<0.1$) for:
  - Intrinsic connection within **rA1**
  - Forward connection linking **lA1** to **lSTG**

Garrido et al., 2008

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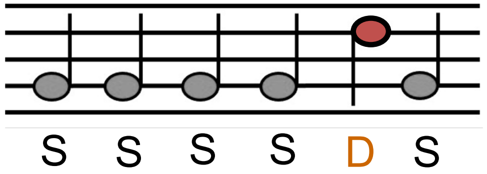
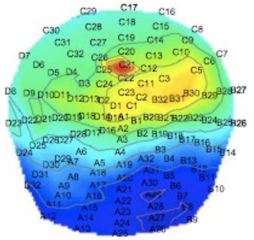
Modelling Auditory MMN Effect

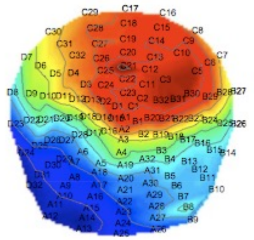
sequence of auditory stimuli



standard condition (S)

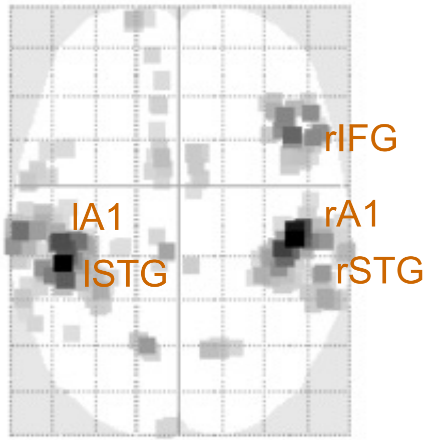


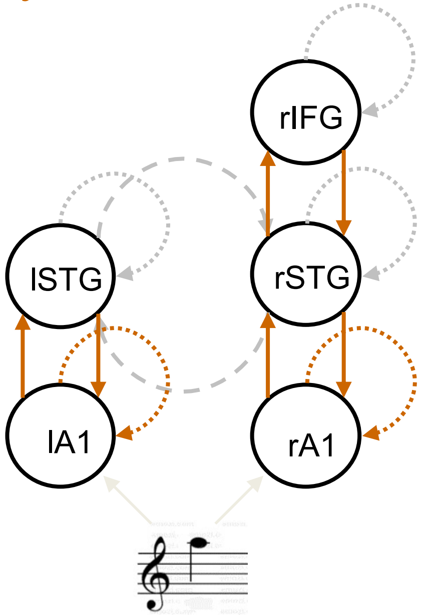
deviant condition (D)



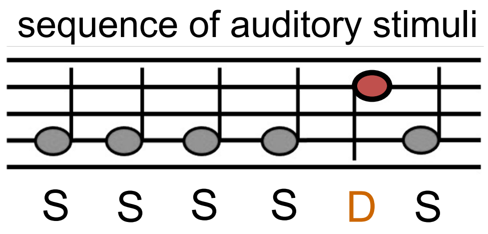
t ~ 200 ms

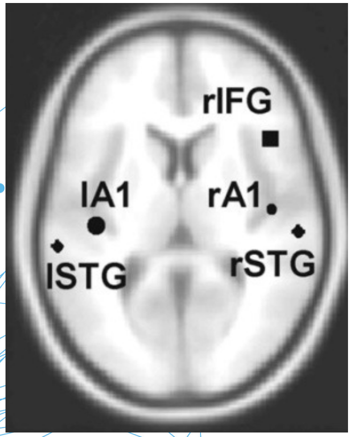
S-D: **reorganisation**
of the connectivity structure



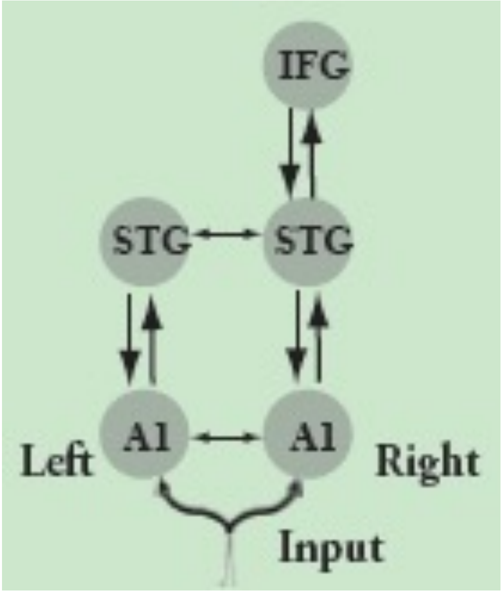


Modelling Auditory MMN Effect

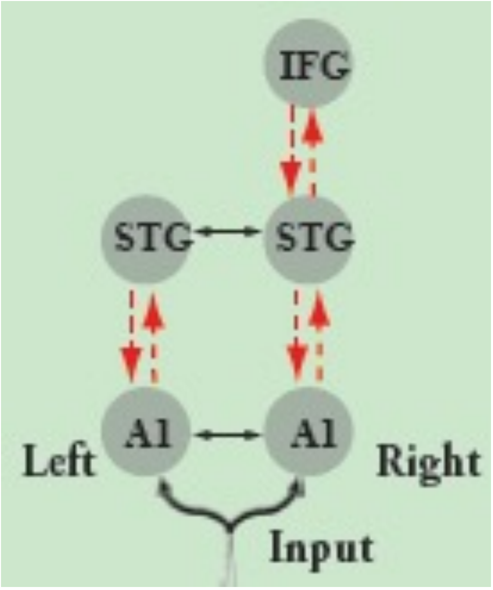




Baseline Connectivity: **A** Matrix

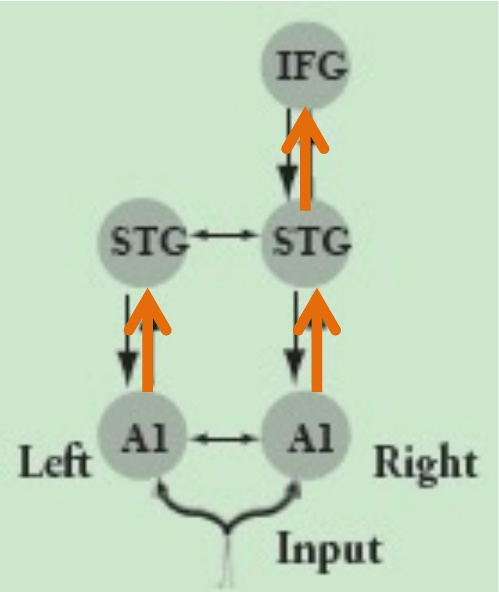


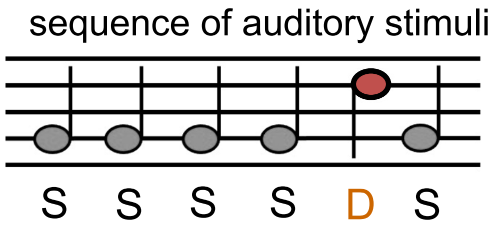
Cognitive Effect: **B** Matrix

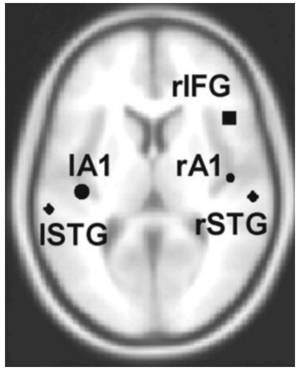


Modelling Auditory MMN Effect

Baseline Connectivity: A Matrix



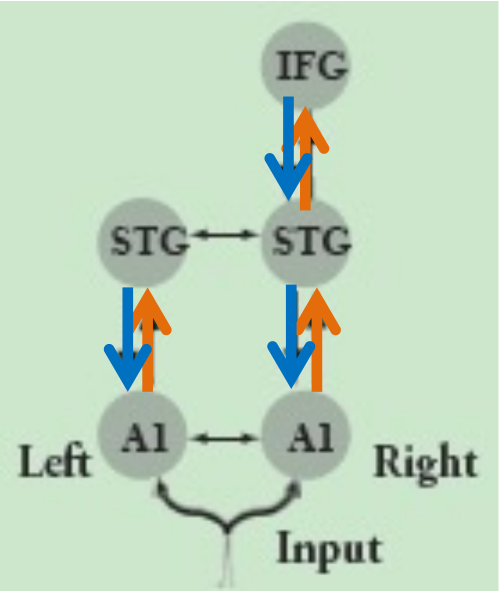


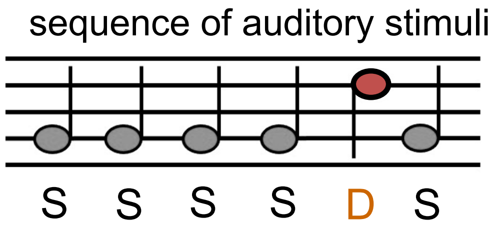


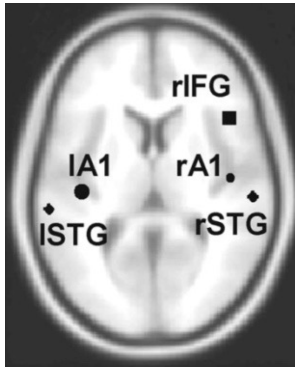
	left A1	right A1	left STG	right STG	right IFG
left A1					
right A1					
left STG	FC=1				
right STG		FC= 1			
right IFG				FC=1	

Modelling Auditory MMN Effect

Baseline Connectivity: A Matrix



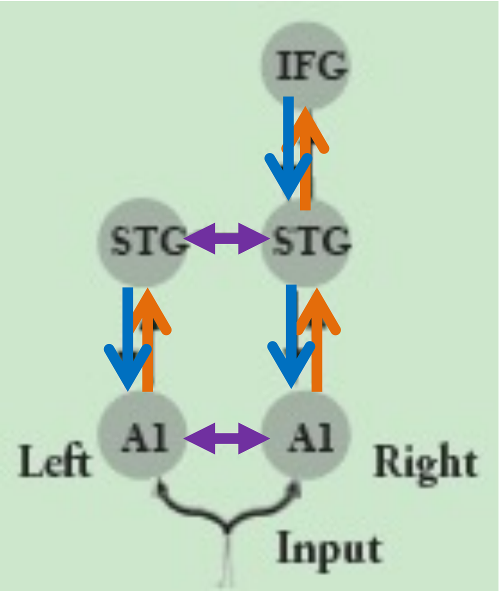


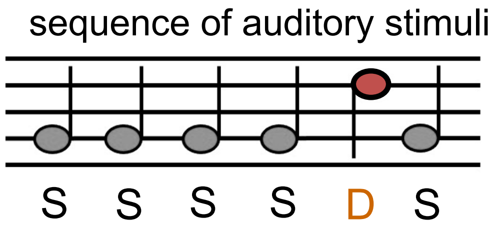


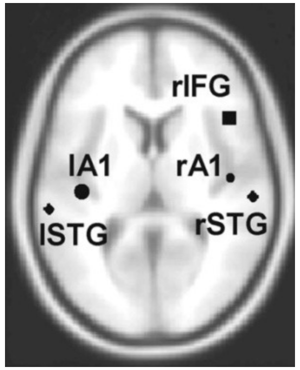
	left A1	right A1	left STG	right STG	right IFG
left A1			BC= 1		
right A1				BC=1	
left STG	FC				
right STG		FC			BC=1
right IFG				FC	

Modelling Auditory MMN Effect

Baseline Connectivity: A Matrix



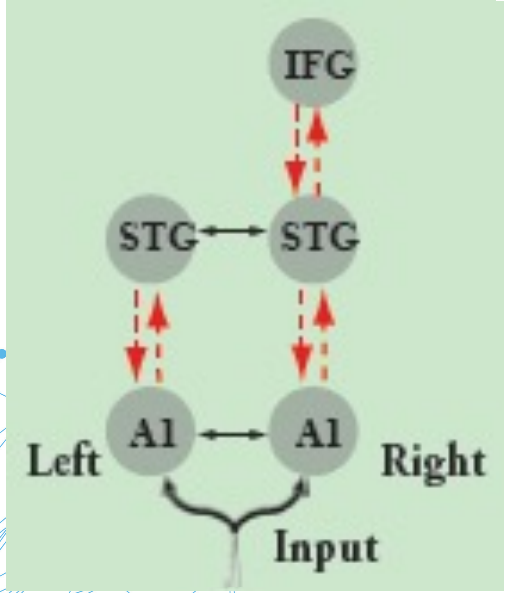


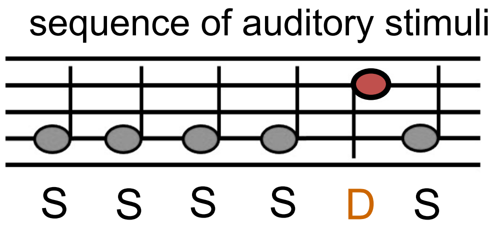


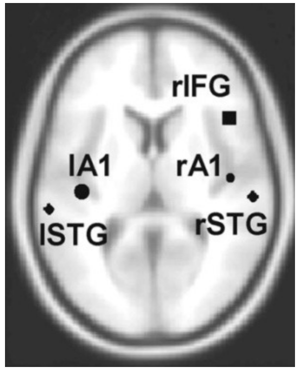
	left A1	right A1	left STG	right STG	right IFG
left A1		LC	BC		
right A1	LC			BC	
left STG	FC			LC	
right STG		FC	LC		BC
right IFG				FC	

Modelling Auditory MMN Effect

Cognitive Effect: **B** Matrix







	left A1	right A1	left STG	right STG	right IFG
left A1		**LC**	**BC**		
right A1	**LC**			**BC**	
left STG	**FC**			**LC**	
right STG		**FC**	**LC**		**BC**
right IFG				**FC**	

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MATLAB

```
options.dcm.sources.name ...
        = {'left A1', 'right A1', 'left STG',
           'right STG', 'right IFG'};
options.dcm.sources.mni=[[-42; -22; 7] [46; -14; 8] [-61; -32; 8]
           [59; -25; 8] [46; 20; 8]];
```

Baseline Connectivity: **A** Matrix

```
% Forward connections
dcmModel.A{1,1} = ...
    [0 0 0 0 0
    0 0 0 0 0
    1 0 0 0 0
    0 1 0 0 0
    0 0 0 1 0];
```

```
% Lateral connections
dcmModel.A{1,3} = ...
    [0 1 0 0 0
    1 0 0 0 0
    0 0 0 1 0
    0 0 1 0 0
    0 0 0 0 0];
```

```
% Backward connections
dcmModel.A{1,2} = ...
    [0 0 1 0 0
    0 0 0 1 0
    0 0 0 0 0
    0 0 0 0 1
    0 0 0 0 0];
```

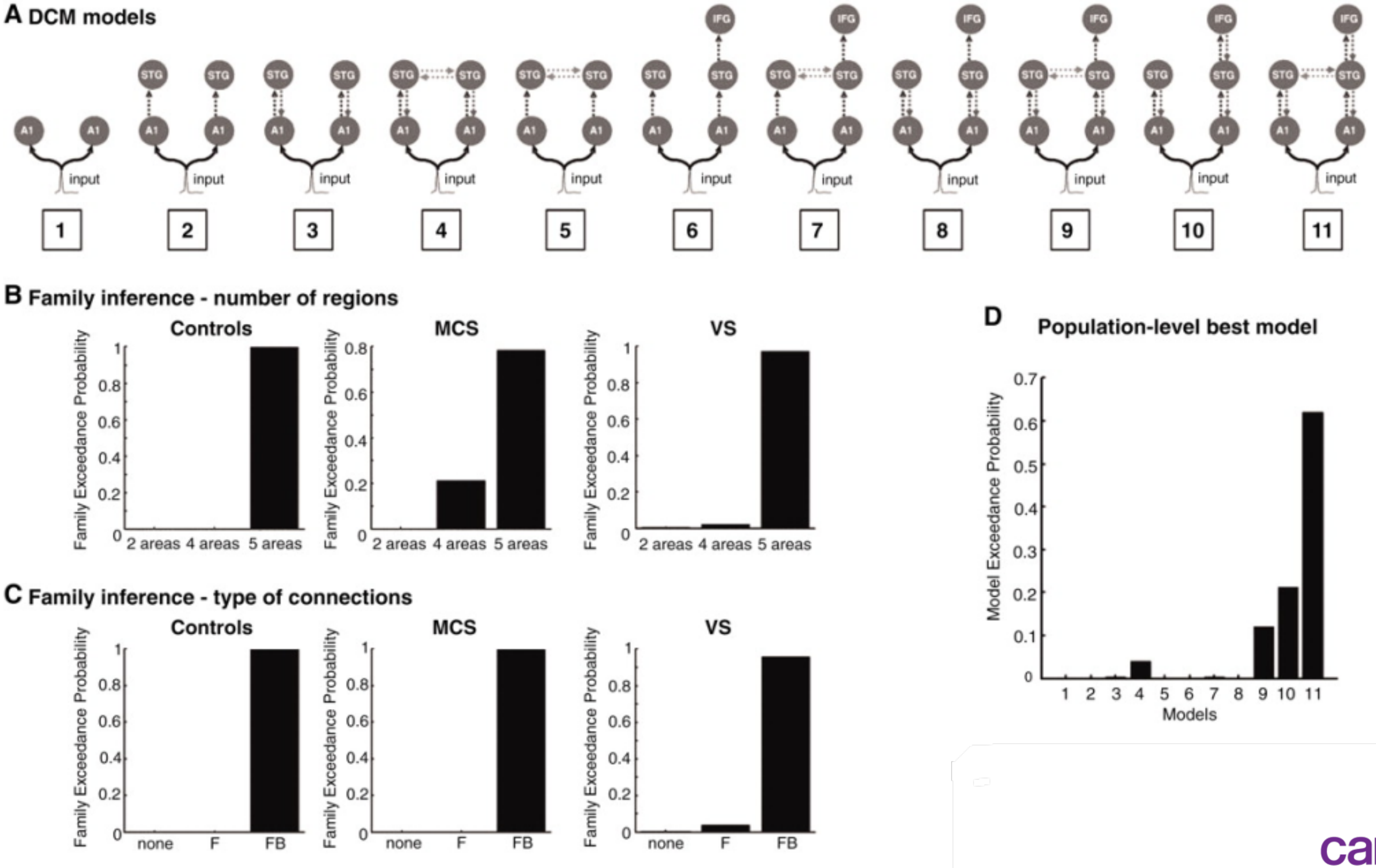
Cognitive Effect: **B** Matrix

```
% PE modulation
dcmModel.B{1,1} = ...
    [0 0 1 0 0
    0 0 0 1 0
    1 0 0 0 0
    0 1 0 0 1
    0 0 0 1 0];
```

Model Input: **C** Matrix

```
% Input
dcmModel.C = [1; 1; 0; 0; 0];
```

Example #3: Group Differences



Boly et al., 2011

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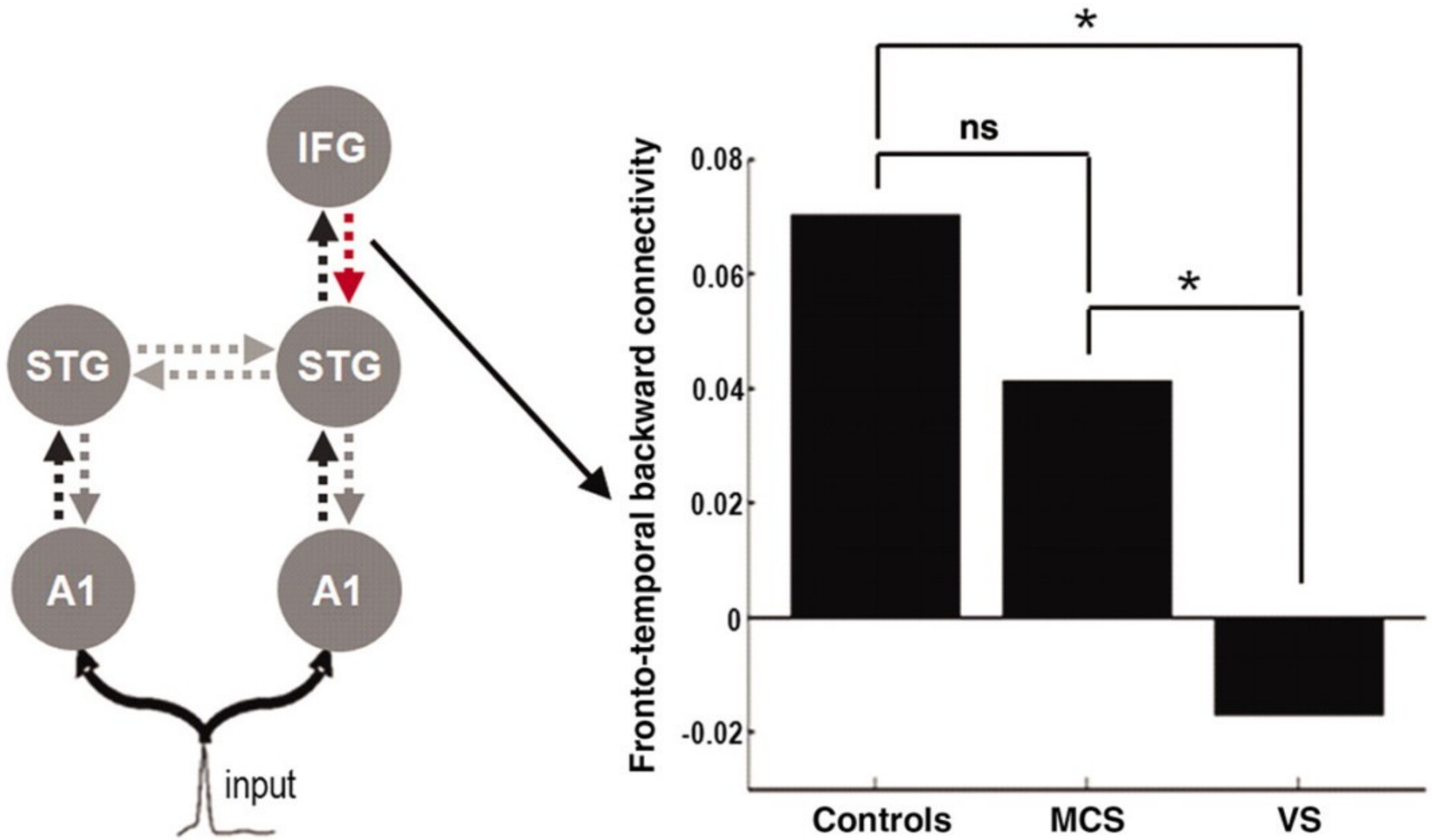
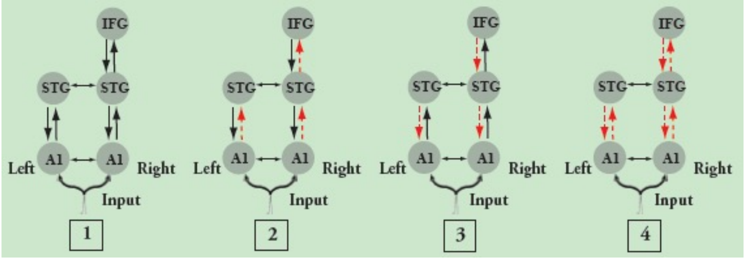
Example #3: Group Differences



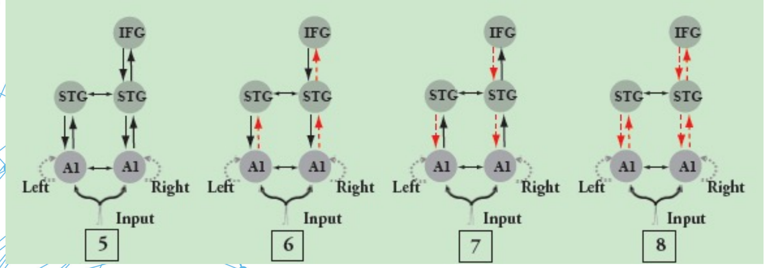
Boly et al., 2011

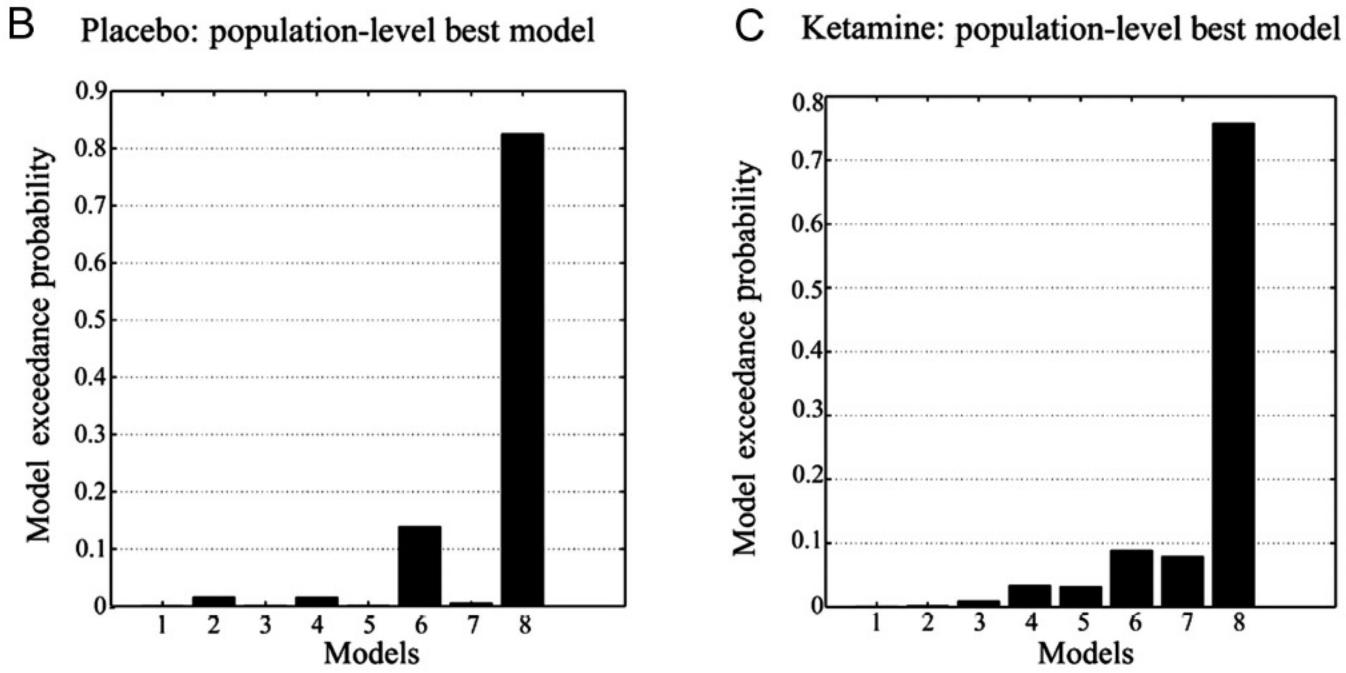
Example #4: Pharmacological Intervention

Inter-regional Synaptic Coupling



Adaptation and Inter-regional Synaptic Coupling





Schmidt, Diaconescu et al., 2013

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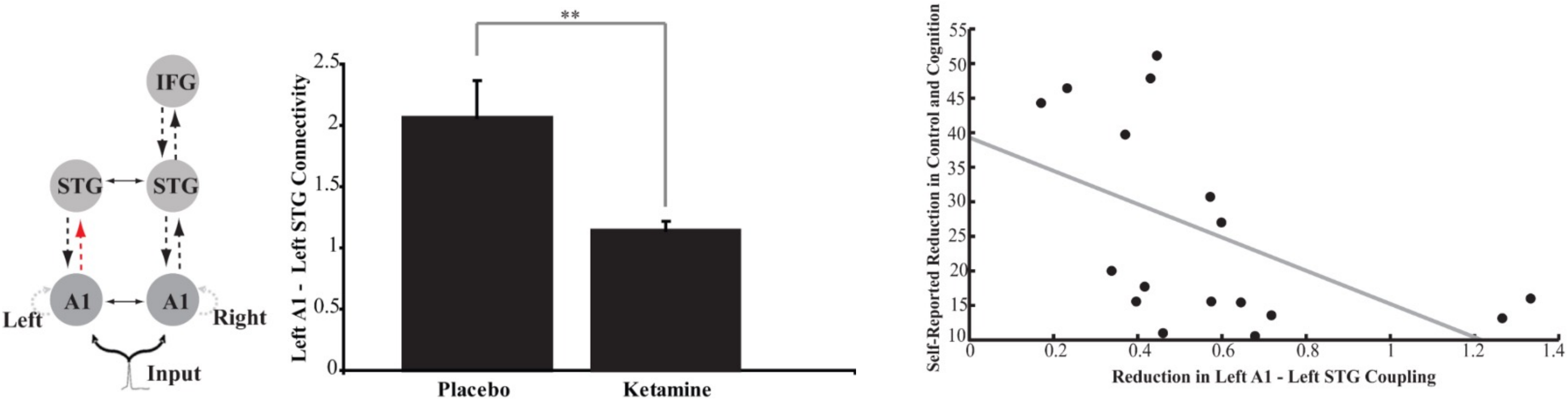
Example #4: Pharmacological Intervention



Schmidt, Diaconescu et al., 2013

Homework Assignment:

EEG Analysis:

----

1. Download the open source data file 'subject1.bdf' at \`https://www.fil.ion.ucl.ac.uk/spm/data/eeg_mmn/\`and place in a new folder */day6/eeg/data/

2. Set your environment using "kcni_setup_paths"

3. Main script is "mmn_master_script"

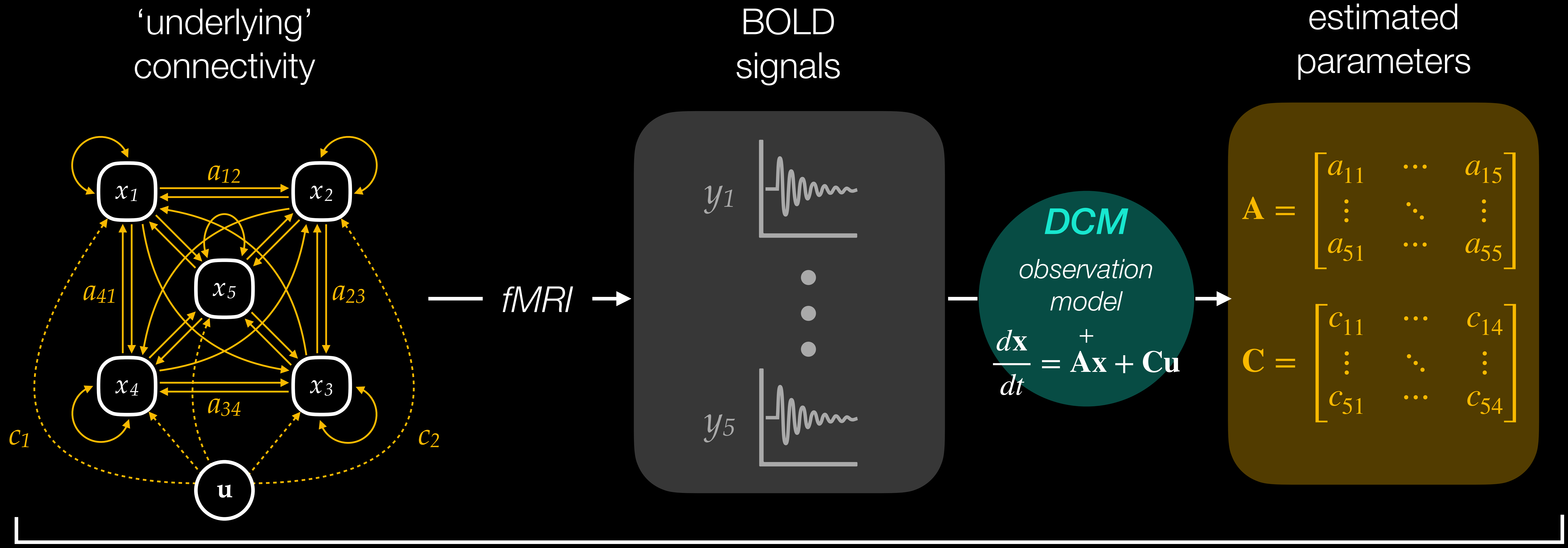
4. Use the EEG tutorial code to compare the top 30% of \`prediction error (PE) signals\` generating pseudo-conditions and ERPs of the top 30% and bottom 30% of PE.

-> Can you model these effects with DCM, and if yes, do you obtain the same connectivity parameter estimates?

Regression dynamic causal modelling for fMRI

Peter Bedford, July 2021

Linear DCM



single subject, 5 ROIs, 4 experimental inputs

DCM: Dynamic causal modelling. ROI: region of interest.
Dynamic causal modelling, Friston et al., 2003

Linear DCM: state equation

connectivity between regions

extrinsic ‘driving’ influences

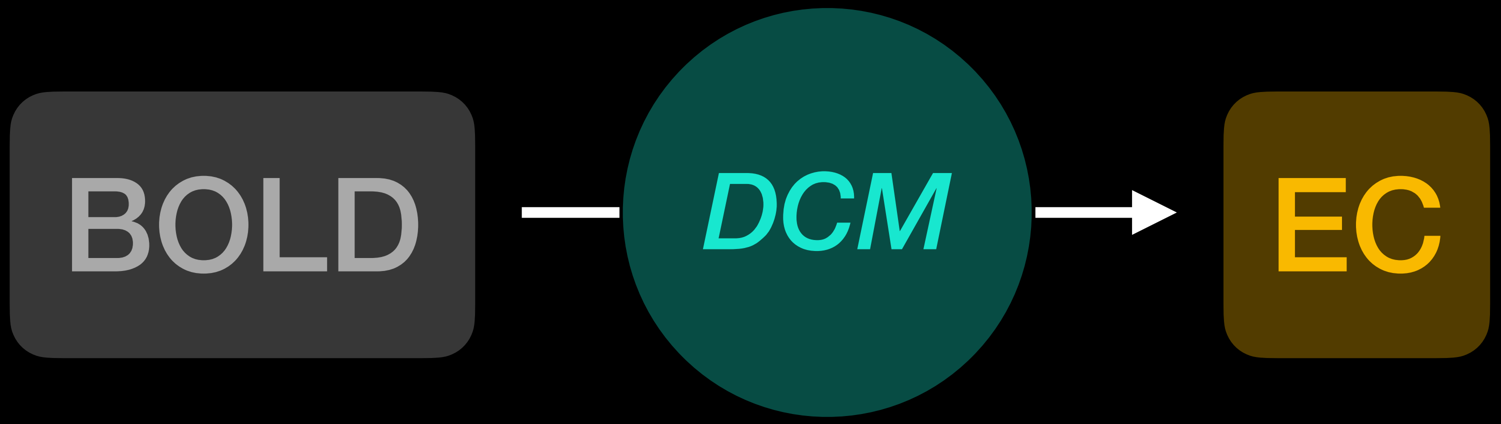
$$\frac{d\mathbf{x}}{dt} = \mathbf{A}\mathbf{x} + \mathbf{C}\mathbf{u}$$

Changes in hidden neuronal state

hidden neuronal state

experimental input

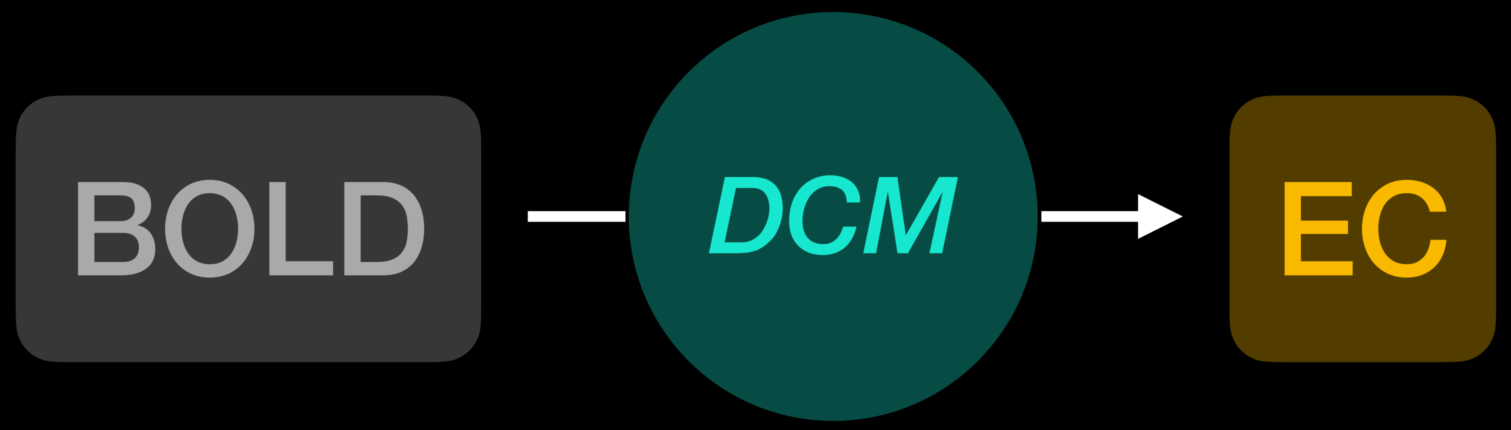
DCM vs rDCM



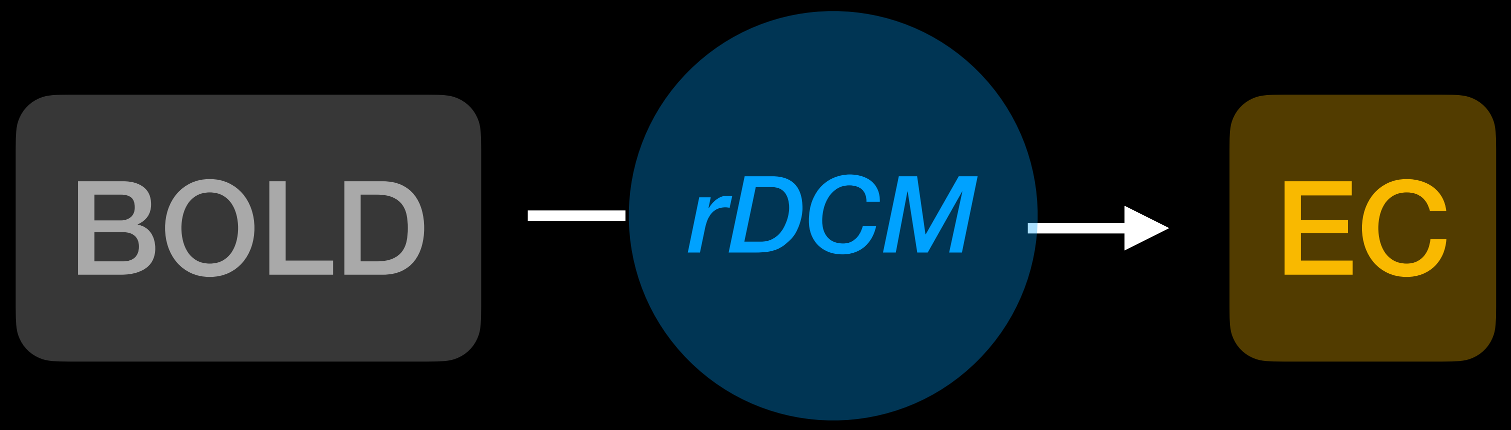
~10 regions or less
<100 connection strength parameters
hypothesis-based analysis only

EC: Estimated connectivity parameters

DCM vs rDCM



~10 regions or less
<100 connection strength parameters
hypothesis-based analysis only



~100 regions or more
>10000 connection strength parameters
enables exploratory analysis

Regression dynamic causal modeling for fMRI, Frässle et al., 2017

DCM vs rDCM

BOLD — *DCM* → EC

1. transform BOLD to frequency domain
2. linearize hemodynamic model
3. assume partial independence of connectivity parameters
4. use a Gamma prior for noise precision

BOLD — *rDCM* → EC

Regression dynamic causal modeling for fMRI, Frässle et al., 2017

DCM to rDCM, step 1: Transforming neural model into frequency domain

State equation:

$$\frac{d\mathbf{x}}{dt} = \mathbf{A}\mathbf{x} + \mathbf{C}\mathbf{u}$$

apply Fourier Transform:

$$\frac{\widehat{d\mathbf{x}}}{dt} = \mathbf{A}\hat{\mathbf{x}} + \mathbf{C}\hat{\mathbf{u}}$$

for FTs:

$$\frac{\widehat{d\mathbf{x}}}{dt} = i\omega\hat{\mathbf{x}} \quad \Rightarrow i\omega\hat{\mathbf{x}} = \mathbf{A}\hat{\mathbf{x}} + \mathbf{C}\hat{\mathbf{u}}$$

Regression dynamic causal modeling for fMRI, Frässle et al., 2017

DCM to rDCM, step 2: Linearizing hemodynamic model

Fixed hemodynamic response function (HRF): $\mathbf{h}$

Convolve $\mathbf{h}$ and $i\omega\mathbf{x}$:

$$i\omega\left(\widehat{\mathbf{h}\otimes\mathbf{x}}\right) = \mathbf{A}\left(\widehat{\mathbf{h}\otimes\mathbf{x}}\right) + \mathbf{C}\hat{\mathbf{h}}\,\hat{\mathbf{u}}$$

Let $\widehat{\mathbf{h}\otimes\mathbf{x}} = \widehat{\mathbf{y}_B}$

$$i\omega\widehat{\mathbf{y}_B} = \mathbf{A}\widehat{\mathbf{y}_B} + \mathbf{C}\hat{\mathbf{h}}\,\hat{\mathbf{u}}$$

$\widehat{\mathbf{y}_B} \equiv$ noise-free prediction of the data

Regression dynamic causal modeling for fMRI, Frässle et al., 2017

Discretize into *N* frequency/time points:
$\mathbf{m} = [0,1,\ldots,N-1]$

$$i\omega \rightarrow i\mathbf{m}\Delta\omega = 2\pi i \frac{\mathbf{m}}{NT}$$

Use linear approximation to exponential:

$$\approx \frac{1}{T}\left(e^{2\pi i \frac{\mathbf{m}}{N}} - 1\right)$$

Continuous:

$$i\omega \widehat{\mathbf{y}_B} = \mathbf{A}\widehat{\mathbf{y}_B} + \mathbf{C}\hat{\mathbf{h}}\,\hat{\mathbf{u}}$$

Discrete:

$$\left(e^{2\pi i \frac{\mathbf{m}}{N}-1}\right)\frac{\widehat{\mathbf{y}_B}}{T} = \mathbf{A}\widehat{\mathbf{y}_B} + \mathbf{C}\hat{\mathbf{h}}\,\hat{\mathbf{u}}$$

Regression dynamic causal modeling for fMRI, Frässle et al., 2017

DCM to rDCM, step 3: Assume partial independence between connectivity parameters

fMRI signal, with noise:

$$\mathbf{y}_i = \mathbf{y}_{B,i} + \epsilon_i, \qquad \epsilon_i \sim \mathcal{N}\left(0, \sigma_i^2 \mathbf{I}_{N\times N}\right)$$

state equation becomes:

$$\left(e^{2\pi i \frac{\mathbf{m}}{N}-1}\right)\frac{\hat{\mathbf{y}}}{T} = \mathbf{A}\hat{\mathbf{y}} + \mathbf{C}\hat{\mathbf{h}}\,\hat{\mathbf{u}} + \nu$$

with noise vector:

$$\nu = \left(e^{2\pi i \frac{\mathbf{m}}{N}} - 1\frac{\hat{\epsilon}}{T}\right) - \mathbf{A}\,\hat{\epsilon}$$

assume partial independence; noise precision parameter τ_i

$$\nu \sim \mathcal{N}\left(\nu; 0, \tau^{-1}\mathbf{I}_{N\times N}\right)$$

Regression dynamic causal modeling for fMRI, Frässle et al., 2017

rDCM state equation

HRF * experimental inputs

HRF * measured signals

design matrix $\mathbf{X} = \left[\underbrace{\hat{\mathbf{y}}_1, \ldots, \hat{\mathbf{y}}_R}, \underbrace{\hat{\mathbf{h}}\hat{\mathbf{u}}_1, \ldots, \hat{\mathbf{h}}\hat{\mathbf{u}}_K}\right]$

Dependent variable: $\mathbf{Y}_i \equiv \left(e^{2\pi i \frac{\mathbf{m}}{N}} - 1\right) \frac{\widehat{\mathbf{y}_i}}{T}$

$$\mathbf{Y} = \mathbf{X}\theta + \nu$$

noise: $\nu \sim \mathcal{N}\left(\nu; 0, \tau^{-1}\mathbf{I}_{N \times N}\right)$

parameter vector $\theta_r = \left[\underbrace{a_{r,1}, \ldots, a_{r,R}}, \underbrace{c_{r,1}, \ldots, c_{r,K}}\right]$

endogenous connectivity matrix column A_r

driving inputs matrix column C_r

$R \equiv$ number of regions. $K \equiv$ number of experimental inputs.

2 methods of implementing *sparsity* in network:

2 methods of imposing *sparsity* on connectivity matrix:

"Structural Prior" Method (ECst)

Fix connection strength parameter at zero for region pairs with no anatomical connection

$$\mathbf{A} = \begin{matrix} 1 & 0 & 1 & 1 & 0 \\ 0 & 1 & 0 & 0 & 1 \\ 1 & 0 & 1 & 1 & 1 \\ 1 & 0 & 1 & 1 & 0 \\ 0 & 1 & 1 & 0 & 1 \end{matrix} \xrightarrow{\text{rDCM inversion}} \hat{\mathbf{A}} = \begin{matrix} a_{11} & 0 & a_{13} & a_{14} & 0 \\ 0 & a_{22} & 0 & 0 & a_{25} \\ a_{31} & 0 & a_{33} & a_{34} & a_{35} \\ a_{41} & 0 & a_{43} & a_{44} & 0 \\ 0 & a_{52} & a_{53} & 0 & a_{55} \end{matrix}$$

priors — final estimates

rDCM sparsity

2 methods of imposing *sparsity* on connectivity matrix:

"Structural Prior" Method (ECst)

Fix connection strength parameter at zero for region pairs with no anatomical connection

$$\mathbf{A} = \begin{matrix} 1 & 0 & 1 & 1 & 0 \\ 0 & 1 & 0 & 0 & 1 \\ 1 & 0 & 1 & 1 & 1 \\ 1 & 0 & 1 & 1 & 0 \\ 0 & 1 & 1 & 0 & 1 \end{matrix} \xrightarrow{\text{rDCM inversion}} \hat{\mathbf{A}} = \begin{matrix} a_{11} & 0 & a_{13} & a_{14} & 0 \\ 0 & a_{22} & 0 & 0 & a_{25} \\ a_{31} & 0 & a_{33} & a_{34} & a_{35} \\ a_{41} & 0 & a_{43} & a_{44} & 0 \\ 0 & a_{52} & a_{53} & 0 & a_{55} \end{matrix}$$

priors — final estimates

"Sparsity Optimization" Method (ECsp)

'Find' probability that each connection is present, then prune improbable connections

$$\mathbf{A} = \begin{matrix} 1 & 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 & 1 \end{matrix} \xrightarrow{\text{rDCM inversion}} \mathbf{A} = \begin{matrix} a_{11} & a_{12} & a_{13} & a_{14} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} & a_{25} \\ a_{31} & a_{32} & a_{33} & a_{34} & a_{35} \\ a_{41} & a_{42} & a_{43} & a_{44} & a_{45} \\ a_{51} & a_{52} & a_{53} & a_{54} & a_{55} \end{matrix}$$

priors — final estimates

Whole-brain effective connectivity from resting-state fMRI discriminates between LSD and placebo conditions

LSD (Lysergic acid diethylamide) → MDD treatment

Could individual brain connectivity predict efficacy of LSD as antidepressant?

← Is brain connectivity predictive of subjective effects of LSD?

← Is brain connectivity predictive of LSD condition vs placebo?

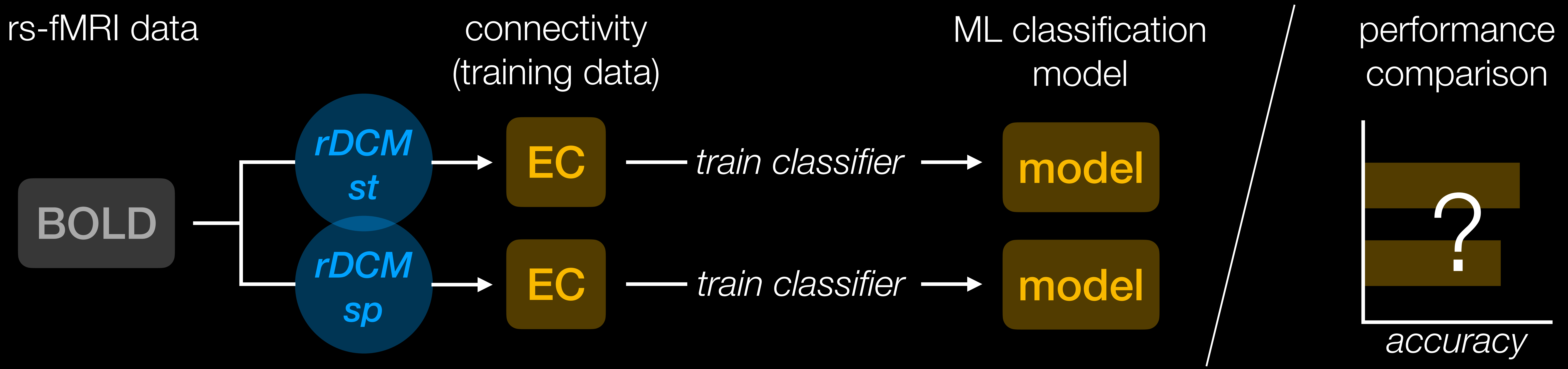
Experiment:

- 45 participants
- pharmacological double-blinded crossover (LSD vs placebo; 4 weeks interval)
- Whole-brain (132 ROIs) BOLD data from resting state fMRI

Experimental data provided by Felix Müller, Department of Psychiatry, University of Basel, Basel

Example: Effective connectivity of LSD vs Placebo during resting state

Question:
Is effective connectivity predictive of LSD vs placebo conditions?



rDCM: Regression dynamic causal modelling. ML: machine learning.
Regression dynamic causal modeling for resting-state fMRI, Frässle et al., 2021

rDCM for resting-state fMRI: state equation

~~HRF * experimental inputs~~

HRF * measured signals

design matrix $\mathbf{X} = \left[\hat{\mathbf{y}}_1, \ldots, \hat{\mathbf{y}}_R, \cancel{\hat{\mathbf{h}}\hat{\mathbf{u}}_1, \ldots, \hat{\mathbf{h}}\hat{\mathbf{u}}_K}\right]$

Dependent variable: $\mathbf{Y}_i \equiv \left(e^{2\pi i \frac{\mathbf{m}}{N}} - 1\right)\frac{\widehat{\mathbf{y}_i}}{T}$

$$\mathbf{Y} = \mathbf{X}\theta + \nu$$

noise: $\nu \sim \mathcal{N}\left(\nu; 0, \tau^{-1}\mathbf{I}_{N\times N}\right)$

parameter vector $\theta_r = \left[a_{r,1}, \ldots, a_{r,R}, \cancel{c_{r,1}, \ldots, c_{r,K}}\right]$

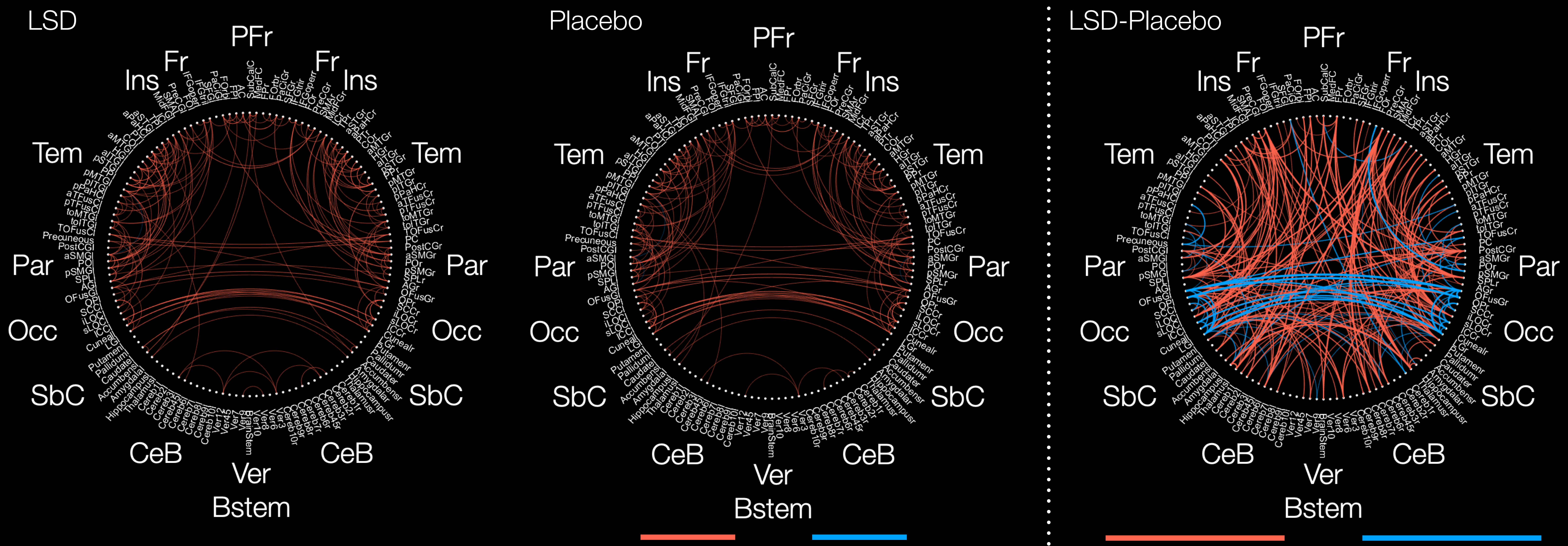
endogenous connectivity matrix column A_r

~~driving inputs matrix column C_r~~

$R \equiv$ number of regions. $K \equiv$ number of experimental inputs.

Results: Effective Connectivity (structural prior method)

5006 connections compared | 677 statistically-significantly different connections (13.5%)



$$\bar{a}_{ij} \equiv \frac{1}{2}\left(a_{ij} + a_{ji}\right)$$

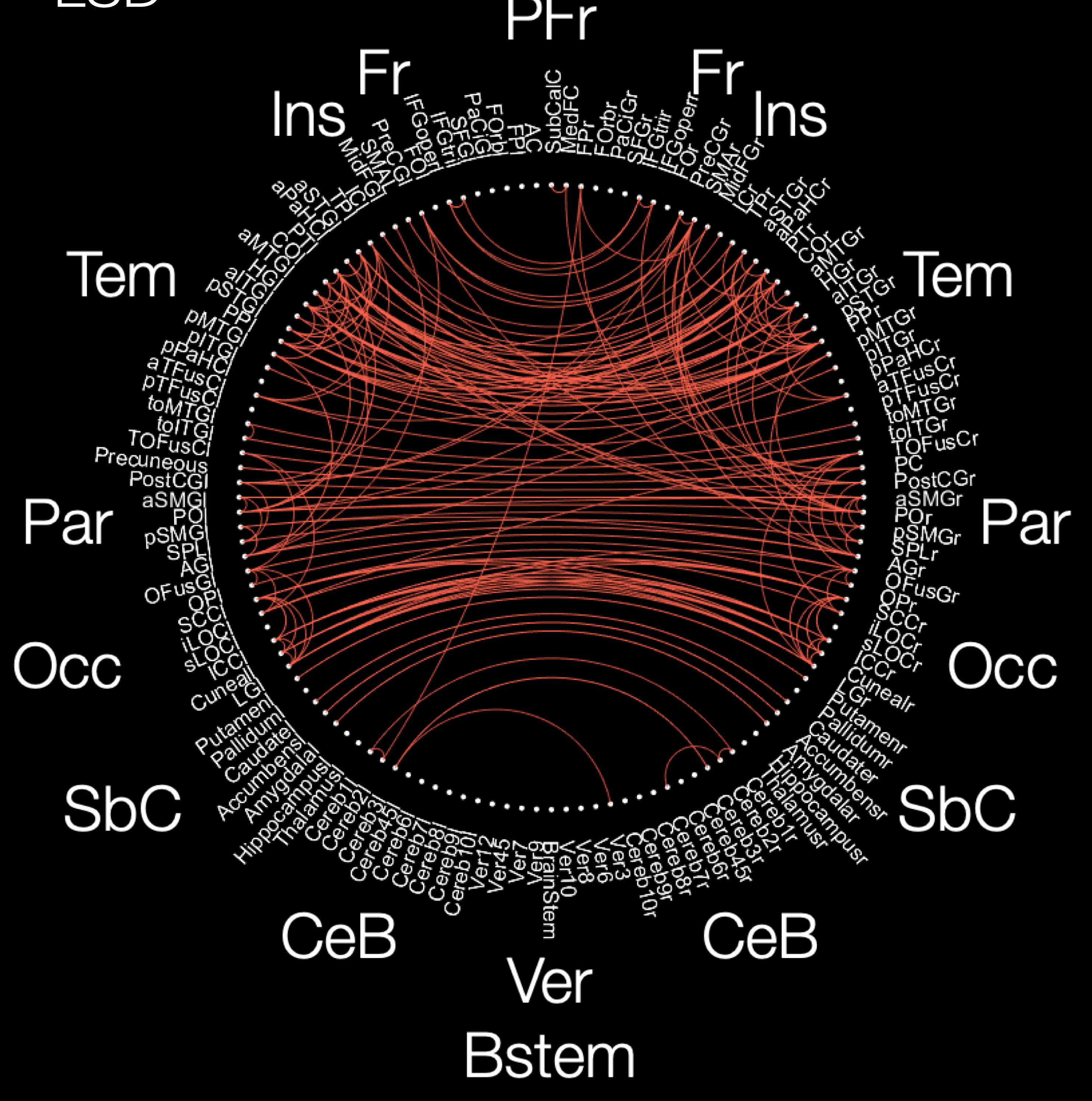
$\bar{a}_{ij} > 0$ $\quad$ $\bar{a}_{ij} < 0$

$\bar{a}_{ij}^{\mathrm{LSD}} > \bar{a}_{ij}^{\mathrm{PLA}}$ $\quad$ $\bar{a}_{ij}^{\mathrm{LSD}} < \bar{a}_{ij}^{\mathrm{PLA}}$

Results: Effective Connectivity (sparsity optimization method)

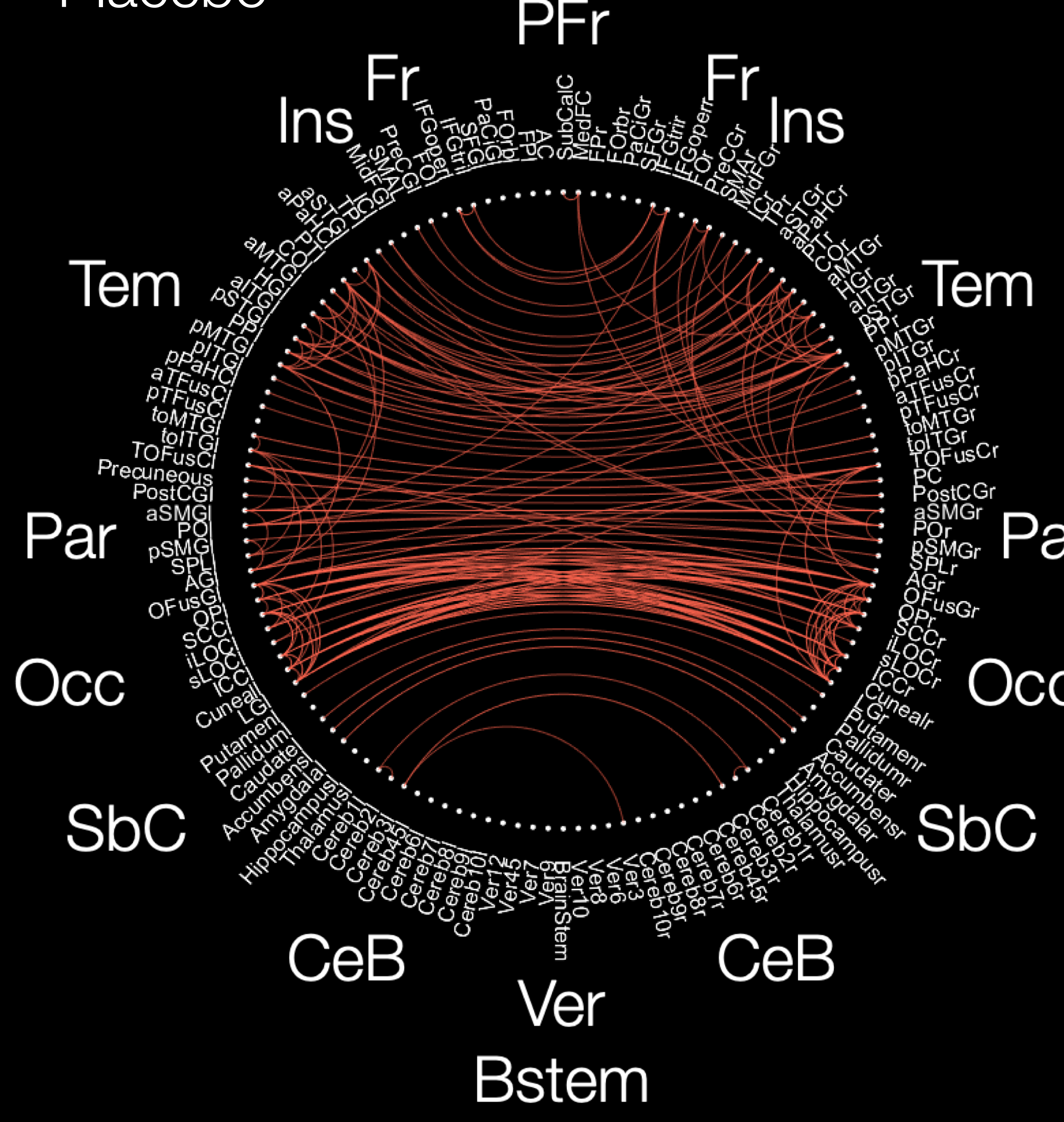
17424 connections compared | 2845 statistically-significantly different connections (16.3%)

LSD



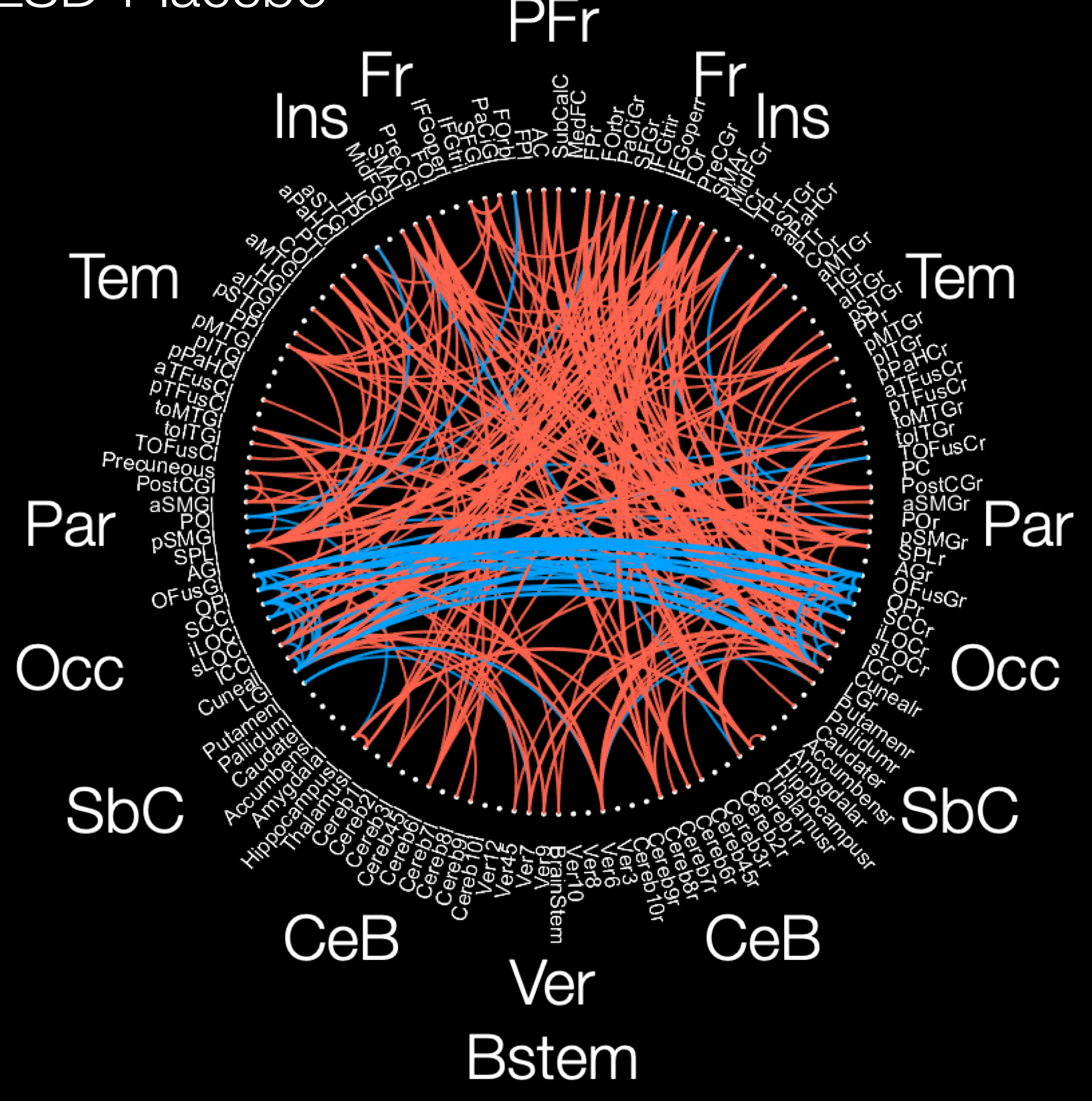
$$\bar{a}_{ij} \equiv \frac{1}{2}\left(a_{ij} + a_{ji}\right)$$

Placebo



$\bar{a}_{ij} > 0$ $\bar{a}_{ij} < 0$

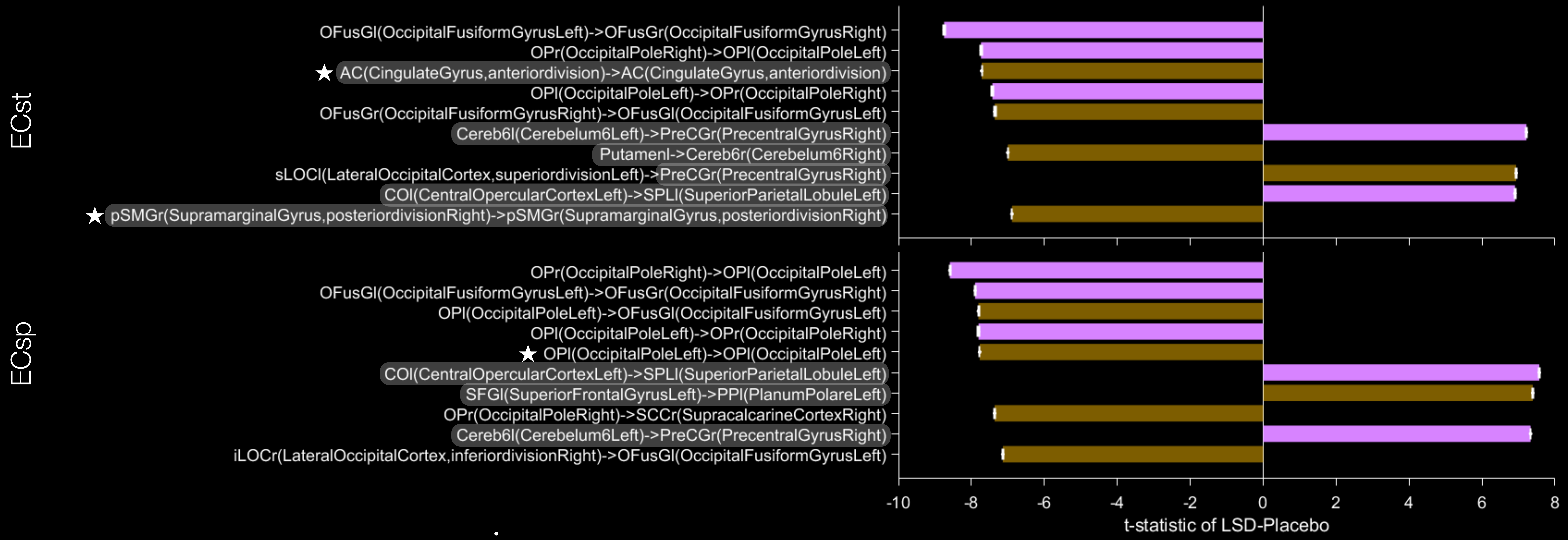
LSD-Placebo



$\bar{a}_{ij}^{\mathrm{LSD}} > \bar{a}_{ij}^{\mathrm{PLA}}$ $\bar{a}_{ij}^{\mathrm{LSD}} < \bar{a}_{ij}^{\mathrm{PLA}}$

Results: Changes in Effective Connectivity

Top 10 'Most-Different' (by t-statistic) Connections (all)



Connections in top 10 for both

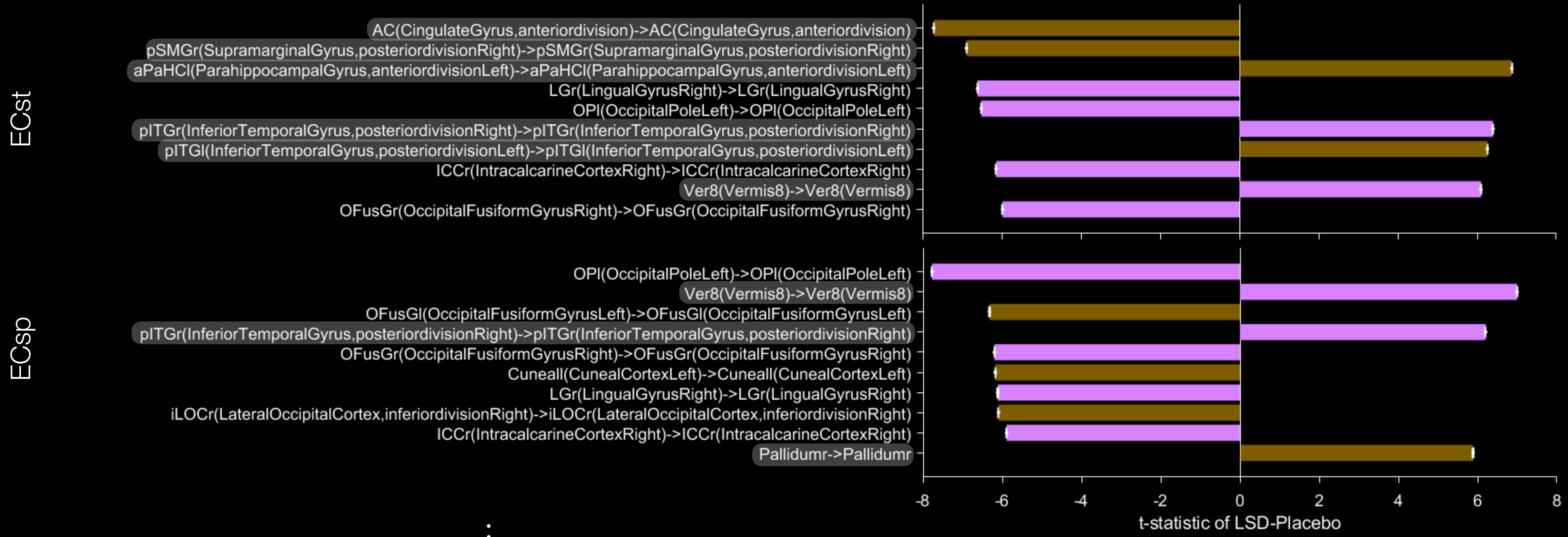
Connections not in visual areas

positive connections $\bar{a}_{ij}^{\mathrm{LSD}} < \bar{a}_{ij}^{\mathrm{PLA}}$ ⟵ | ⟶ $\bar{a}_{ij}^{\mathrm{LSD}} > \bar{a}_{ij}^{\mathrm{PLA}}$

★ negative connections $\left|\bar{a}_{ij}^{\mathrm{LSD}}\right| > \left|\bar{a}_{ij}^{\mathrm{PLA}}\right|$ ⟵ | ⟶ $\left|\bar{a}_{ij}^{\mathrm{LSD}}\right| < \left|\bar{a}_{ij}^{\mathrm{PLA}}\right|$

Results: Changes in Effective Connectivity

Top 10 ‘Most-Different’ (by t-statistic) Connections (self only)



Connections in top 10 for both

Connections not in visual areas

positive connections $\bar{a}_{ij}^{LSD} < \bar{a}_{ij}^{PLA}$ ⟷ $\bar{a}_{ij}^{LSD} > \bar{a}_{ij}^{PLA}$

negative connections $\left|\bar{a}_{ij}^{LSD}\right| > \left|\bar{a}_{ij}^{PLA}\right|$ ⟷ $\left|\bar{a}_{ij}^{LSD}\right| < \left|\bar{a}_{ij}^{PLA}\right|$

Random Forest with 10-fold cross-validation

	N_{regions}	N_{conns}	N_{feats}	N_{trees}
FC	132	17424	8646	8646
ECst	132	17424	4874	4874
ECsp	132	17424	17424	17424

	ACC	SEN	SPE	PPV	NPV	AUC	p
FC	0.89	0.92	0.88	0.90	0.93	0.95	2E-04
ECst	0.93	0.96	0.92	0.93	0.96	0.96	2E-04
ECsp	0.91	0.94	0.90	0.91	0.95	0.95	2E-04

FC (True \ predicted)	LSD	PLA
LSD	41	4
PLA	6	39

ECst (True \ predicted)	LSD	PLA
LSD	43	2
PLA	4	41

ECsp (True \ predicted)	LSD	PLA
LSD	42	3
PLA	5	40

	BAC
FC	0.90
ECst	0.94
ECsp	0.92

References

Frässle, S, Harrison, SJ, Heinzle, J, et al. Regression dynamic causal modeling for resting-state fMRI. *Hum Brain Mapp*. 2021; 42:2159– 2180. https://doi.org/10.1002/hbm.25357

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Müller, F, Lenz, C, Dolder, P, Lang, U, Schmidt, A, Liechti, M, Borgwardt, S. Increased thalamic resting-state connectivity as a core driver of LSD-induced hallucinations. *Acta Psychiatrica Scandinavica*. 2017; 136(6):648-657. https://doi.org/10.1111/acps.12818

Tutorial:
Dynamic causal modeling for fMRI

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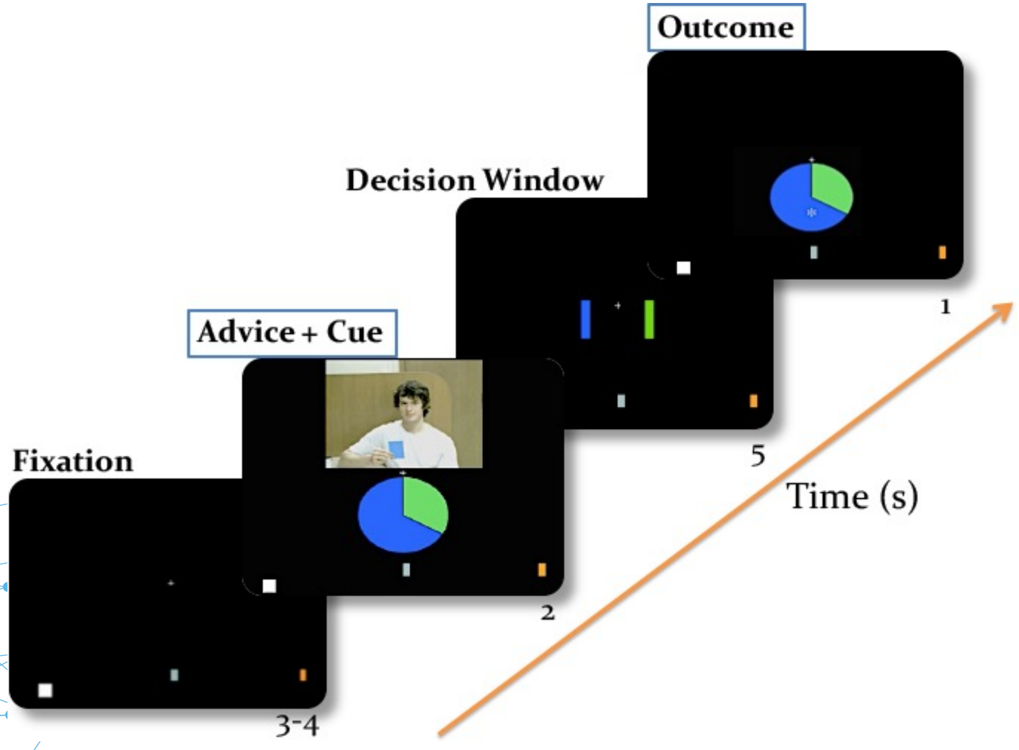
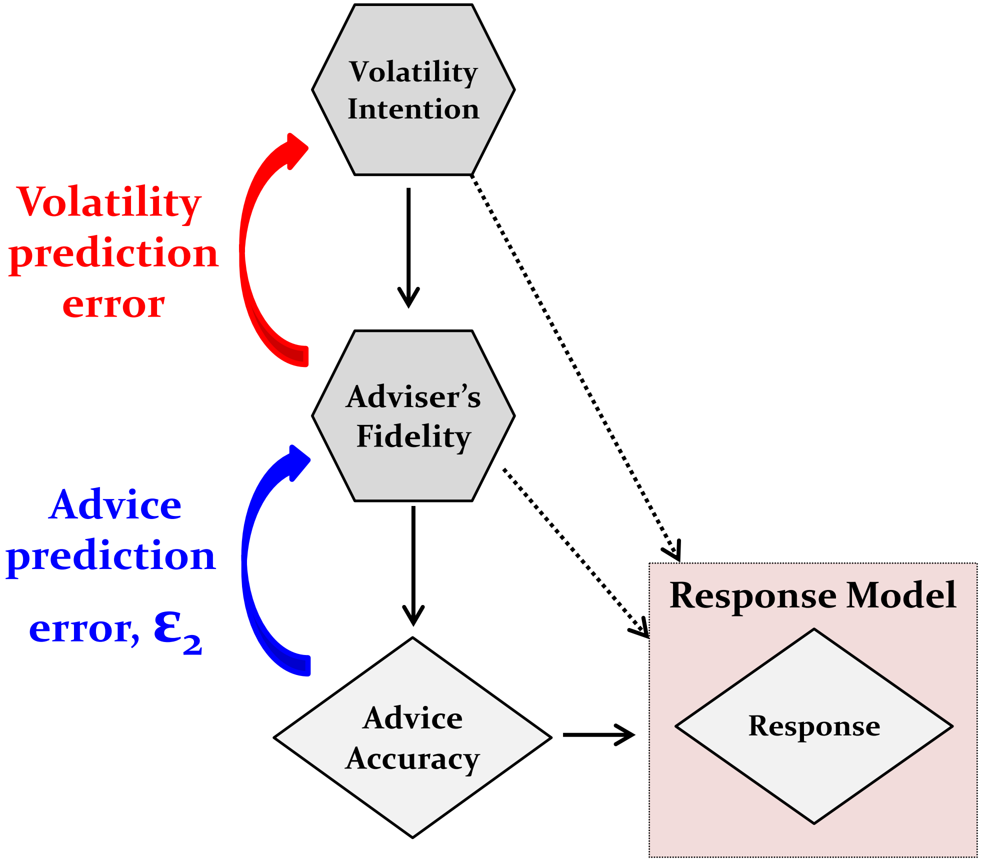
camh | Krembil Centre for Neuroinformatics

Experimental Paradigm

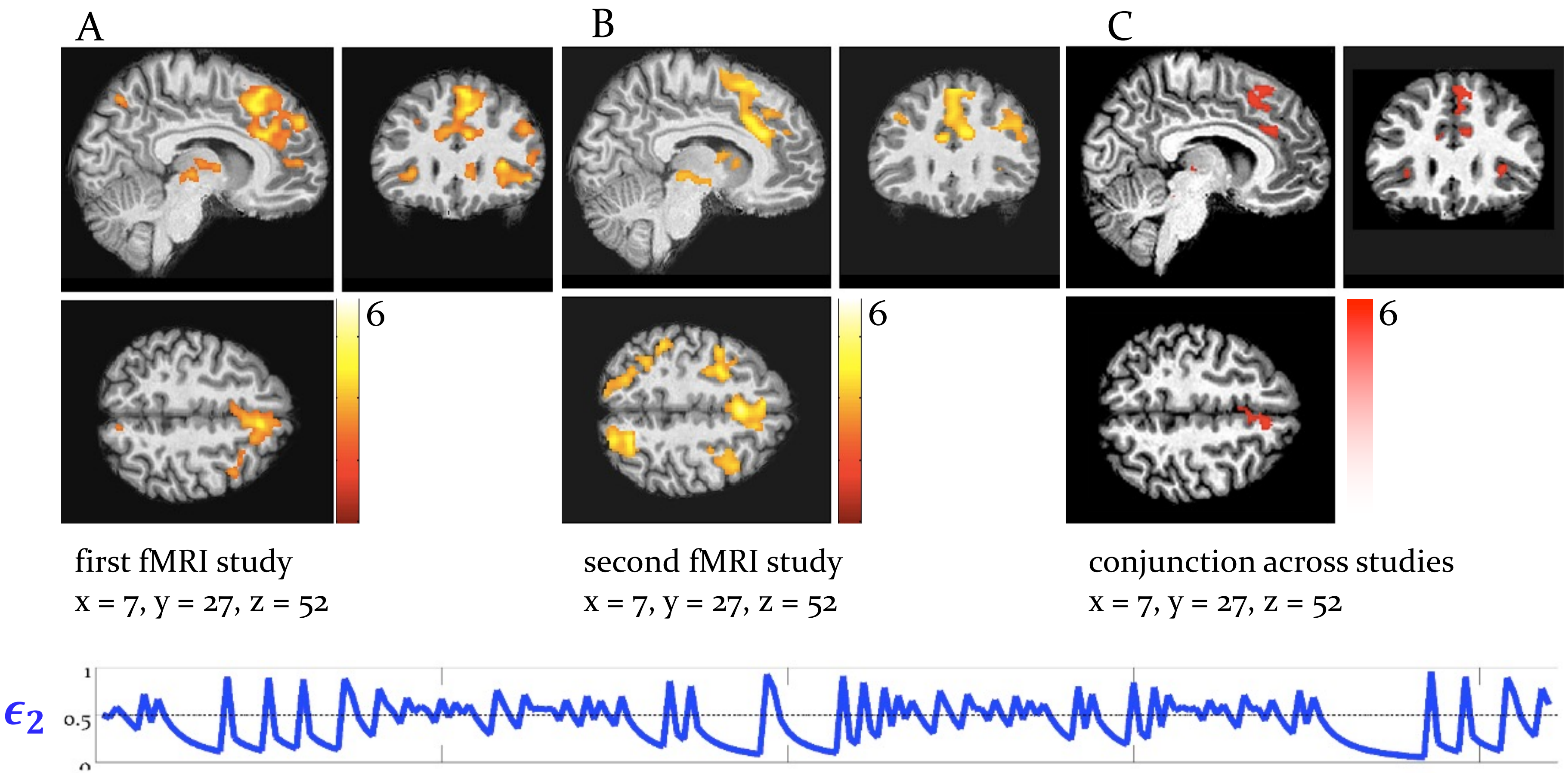
- Inferring on the intentions of others





Diaconescu et al., *PLoS CB* 2014

Advice Prediction Error



Diaconescu et al., *2017, Soc Cogn Affect Neurosci*

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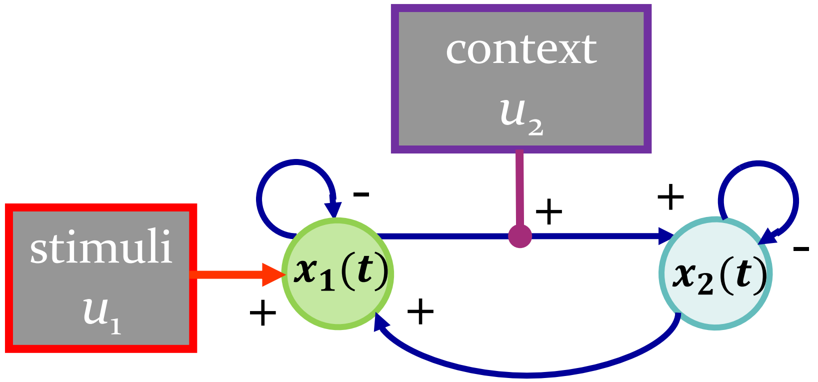
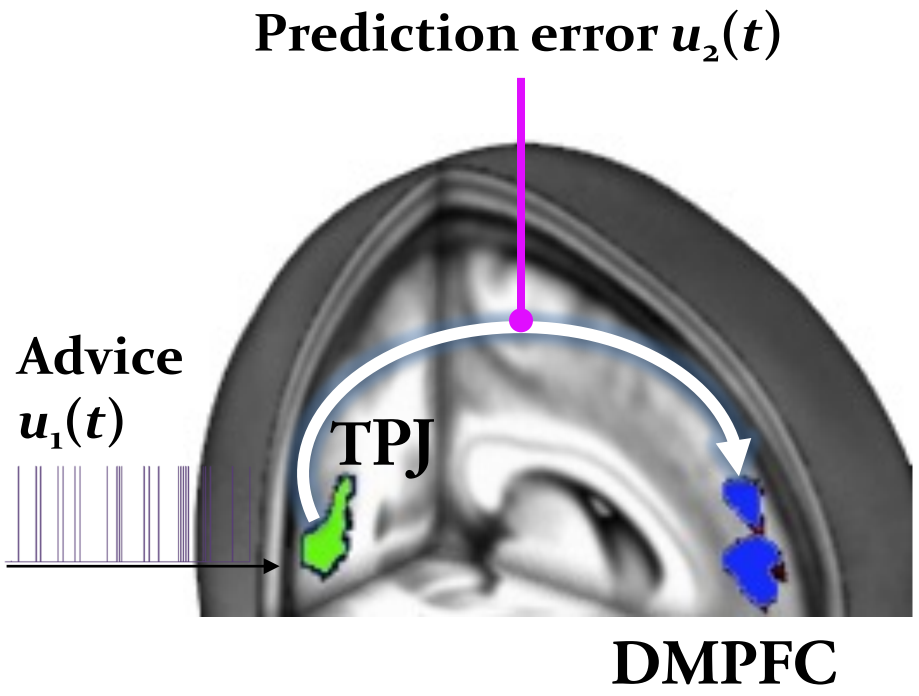
Dynamic Causal Modelling for fMRI



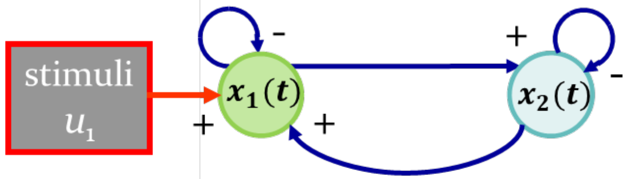


$$\dot{x} = Ax + u_2 B^{(2)} x + C u_1$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{bmatrix} = \begin{bmatrix} \sigma & 0 \\ a_{12} & \sigma \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ b_{12}^{(2)} & 0 \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + \begin{bmatrix} c_{11} & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

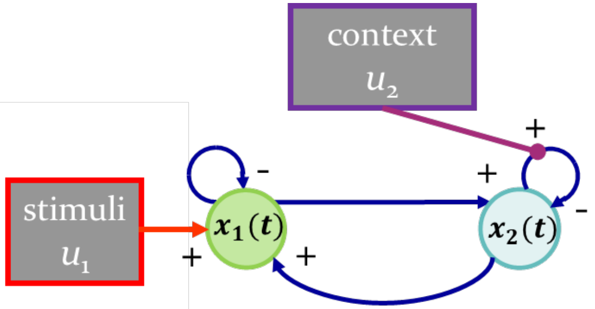
Model Space

1.
No modulation



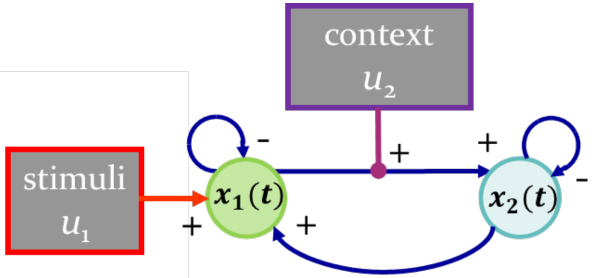
$$\begin{bmatrix}\dot{x}_1\\ \dot{x}_2\end{bmatrix} = \begin{bmatrix}\sigma & 0\\ a_{12} & \sigma\end{bmatrix}\cdot\begin{bmatrix}x_1\\ x_2\end{bmatrix} + u_2\begin{bmatrix}0 & 0\\ 0 & 0\end{bmatrix}\cdot\begin{bmatrix}x_1\\ x_2\end{bmatrix} + \begin{bmatrix}c_{11} & 0\\ 0 & 0\end{bmatrix}\cdot\begin{bmatrix}u_1\\ u_2\end{bmatrix}$$

2.
Modulation of self-inhibition



$$\begin{bmatrix}\dot{x}_1\\ \dot{x}_2\end{bmatrix} = \begin{bmatrix}\sigma & 0\\ a_{12} & \sigma\end{bmatrix}\cdot\begin{bmatrix}x_1\\ x_2\end{bmatrix} + u_2\begin{bmatrix}0 & 0\\ 0 & b_{22}\end{bmatrix}\cdot\begin{bmatrix}x_1\\ x_2\end{bmatrix} + \begin{bmatrix}c_{11} & 0\\ 0 & 0\end{bmatrix}\cdot\begin{bmatrix}u_1\\ u_2\end{bmatrix}$$

3.
Modulation of forward connection



$$\begin{bmatrix}\dot{x}_1\\ \dot{x}_2\end{bmatrix} = \begin{bmatrix}\sigma & 0\\ a_{12} & \sigma\end{bmatrix}\cdot\begin{bmatrix}x_1\\ x_2\end{bmatrix} + u_2\begin{bmatrix}0 & 0\\ b_{12} & 0\end{bmatrix}\cdot\begin{bmatrix}x_1\\ x_2\end{bmatrix} + \begin{bmatrix}c_{11} & 0\\ 0 & 0\end{bmatrix}\cdot\begin{bmatrix}u_1\\ u_2\end{bmatrix}$$

Types of model validity

1) Face Validity:
   - Model Specification
   - Simulation
   - Inversion
   - Diagnostics

In this tutorial

2) Construct Validity:
   - VOI Extraction
   - Model Specification
   - Inversion
   - Diagnostics
   - Model Selection

3) Predictive Validity