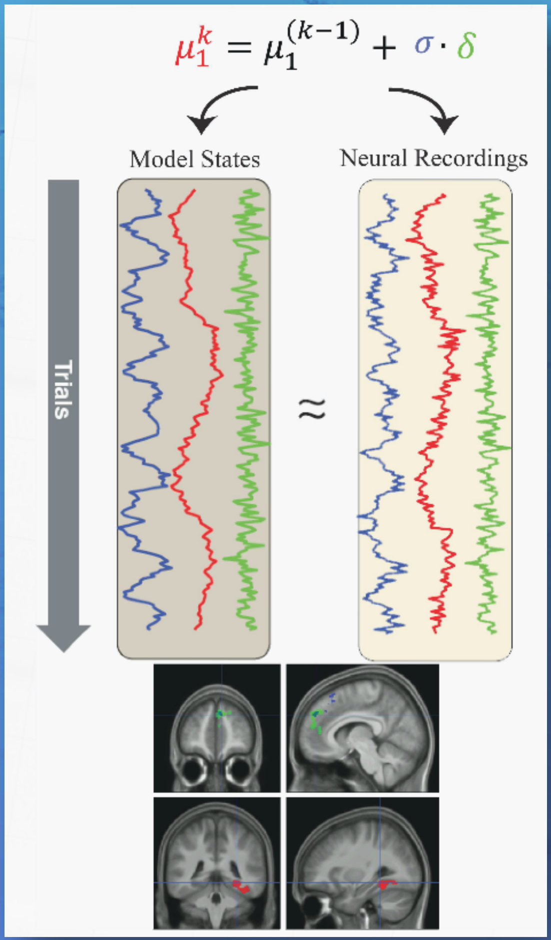
ETH zürich | University of Zurich[UZH] | Translational Neuromodeling Unit

Computational Neuroimaging

Andreea Diaconescu

Methods & Models 2018



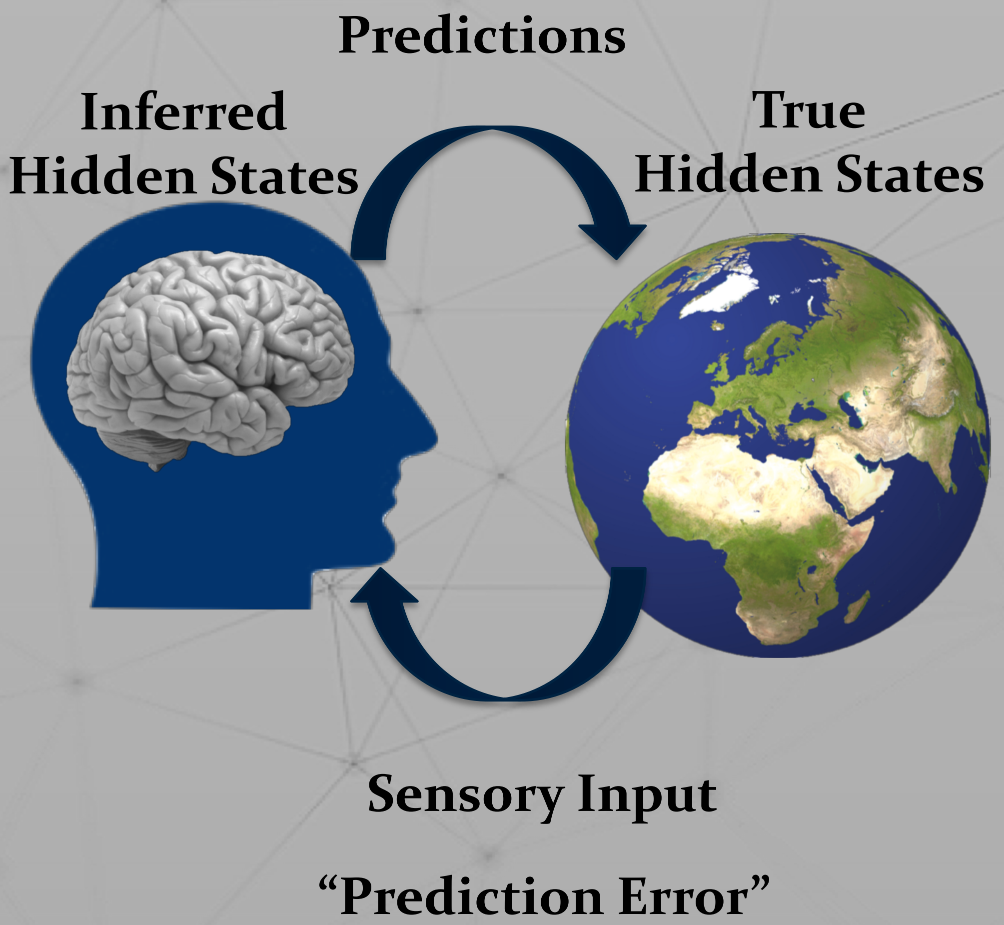
What is it all about?

Translational Neuromodeling Unit

- Why do we use functional magnetic resonance imaging?
  - To measure brain activity
- When does the brain become active?
  - When it learns
    i.e., when its predictions have to be adjusted
- Where do these predictions come from?
  - A model

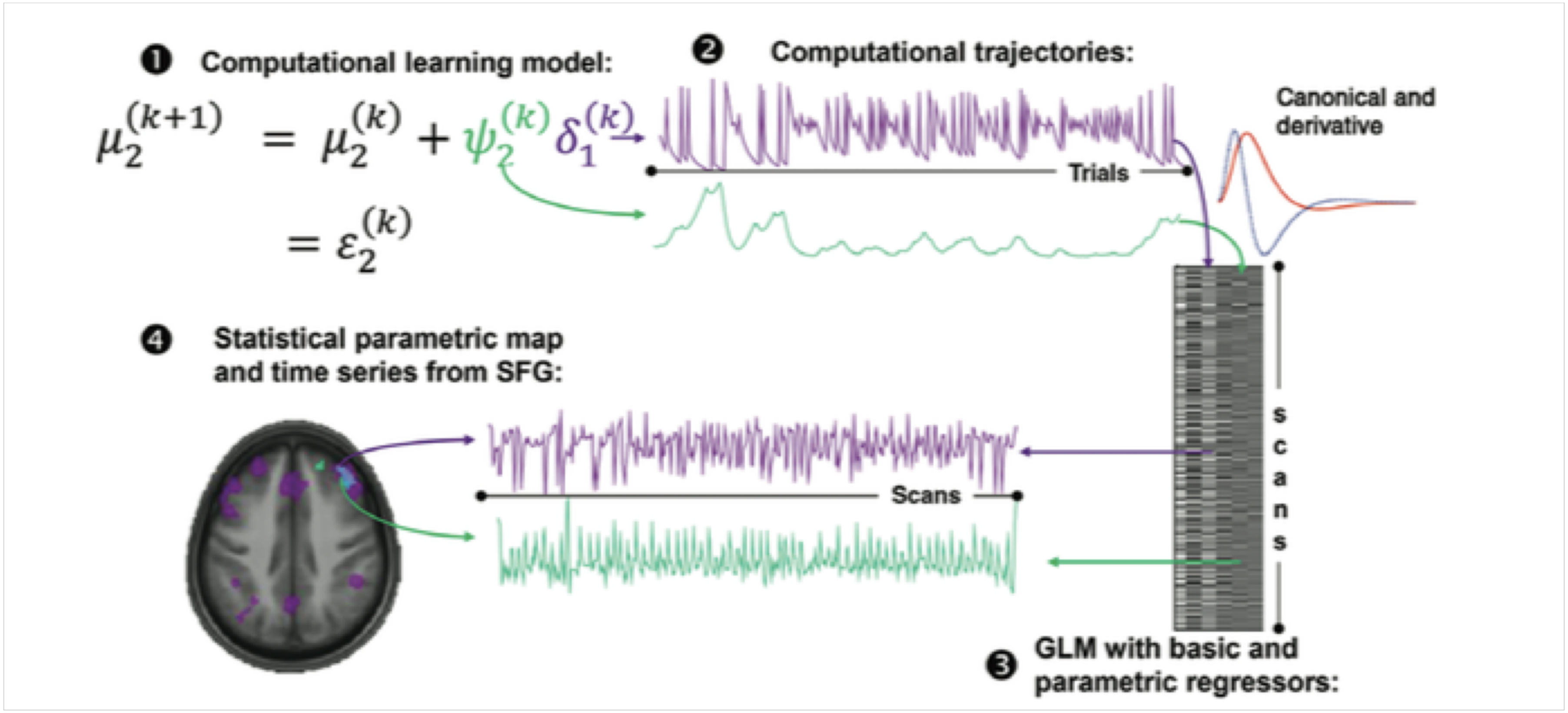
How to build a model

Translational Neuromodeling Unit



Computational Neuroimaging

Translational Neuromodeling Unit



Iglesias et al., 2016

Advantages of computational neuroimaging

Translational Neuromodeling Unit

- Computational neuroimaging permits us to:
  - **Infer** the computational mechanisms underlying brain function
  - **Localize** such mechanisms
  - **Compare** different models

Explanatory Gap

Translational Neuromodeling Unit

Biological

- Molecular
- Neurochemical

Cognitive

- Computational
- “cognitive/
- computational phenotyping”

Phenomenological

- Performance Accuracy
- Reaction Time
- Choices, preferences

Computational Models

Three Levels of Inference

Translational Neuromodeling Unit

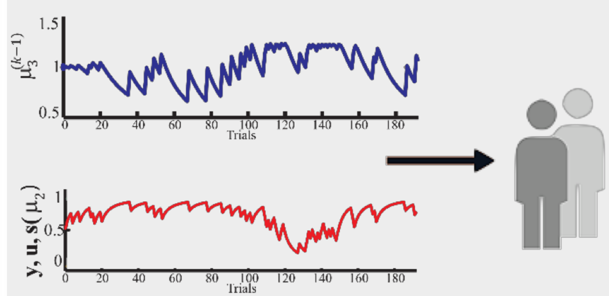
- *Computational Level*: predictions, prediction errors
- *Algorithmic Level*: reinforcement learning, hierarchical Bayesian inference, predictive coding
- *Implementational Level*: Brain activity, neuromodulation

David Marr, 1982

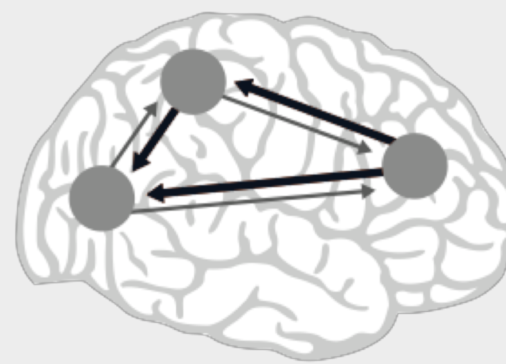
- **3 ingredients**:

1. Experimental paradigm:

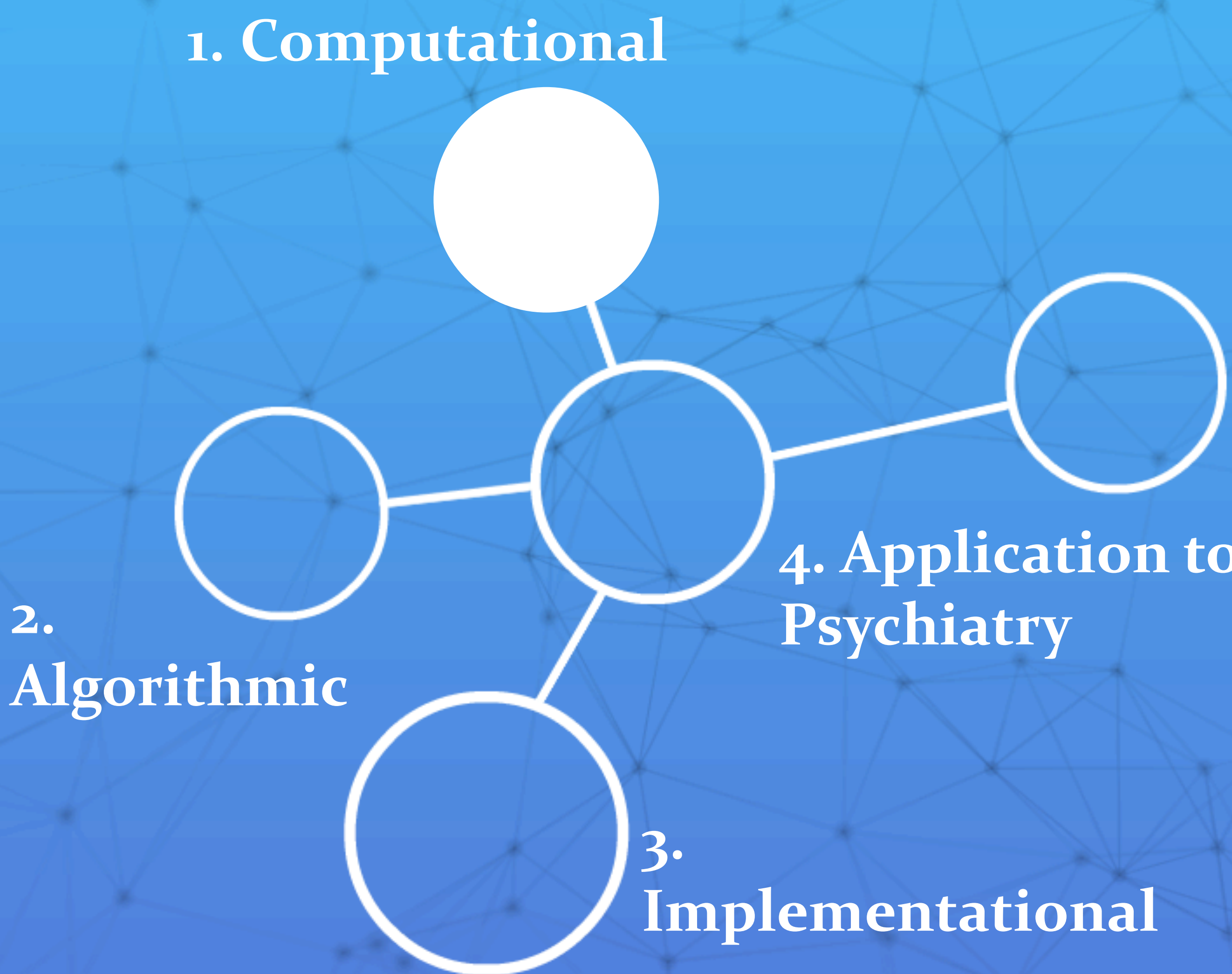
2. Computational model of learning:



3. Model-based fMRI analysis:



Outline


1. Computational
2. Algorithmic
3. Implementational
4. Application to Psychiatry

Example of a simple model

Translational Neuromodeling Unit

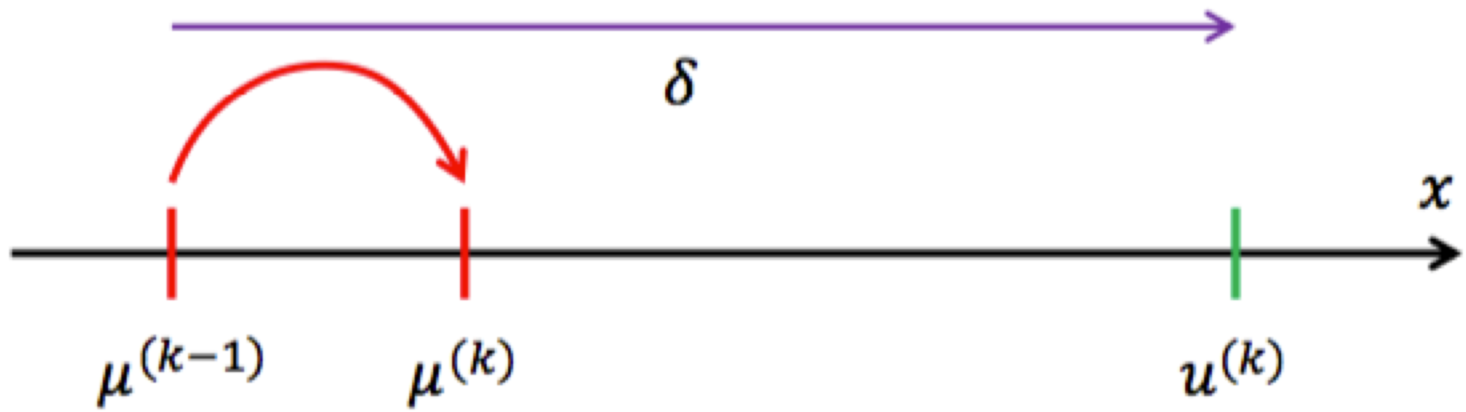
Rescorla-Wagner Learning:

Prediction Error

$$\mu^{(k)} = \mu^{(k-1)} + \alpha\left(u^{(k)} - \mu^{(k-1)}\right)$$

Inferred States

New Input



Example of a simple model

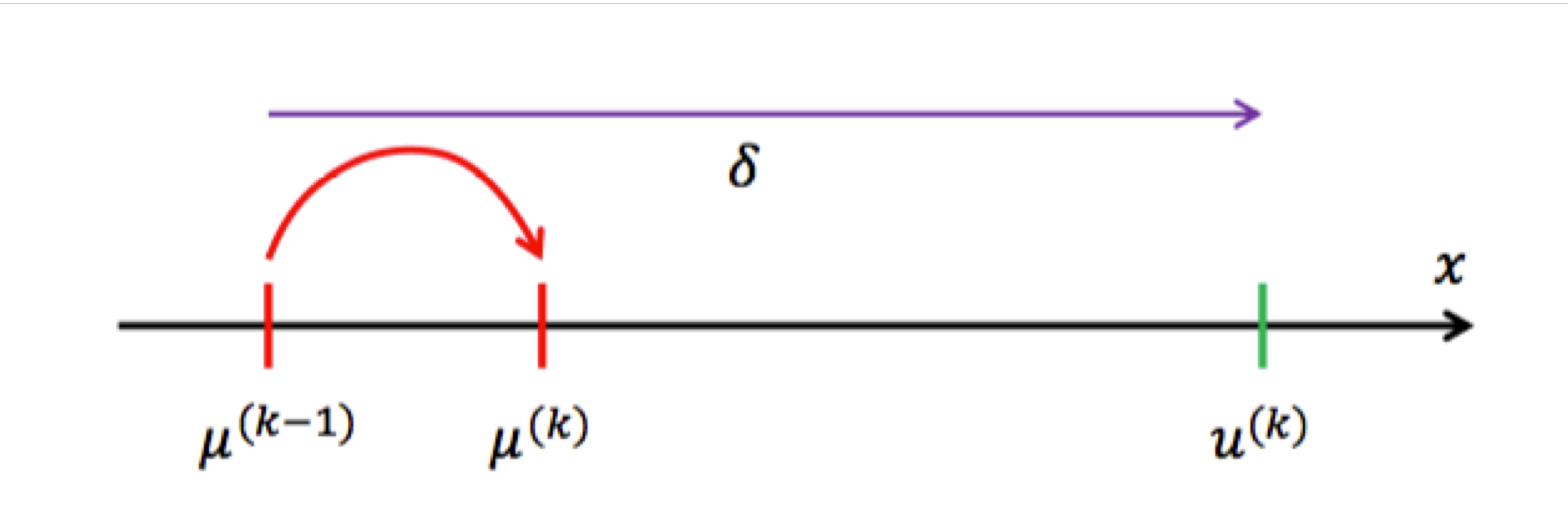
Translational Neuromodeling Unit

Rescorla-Wagner Learning:

Learning Rate

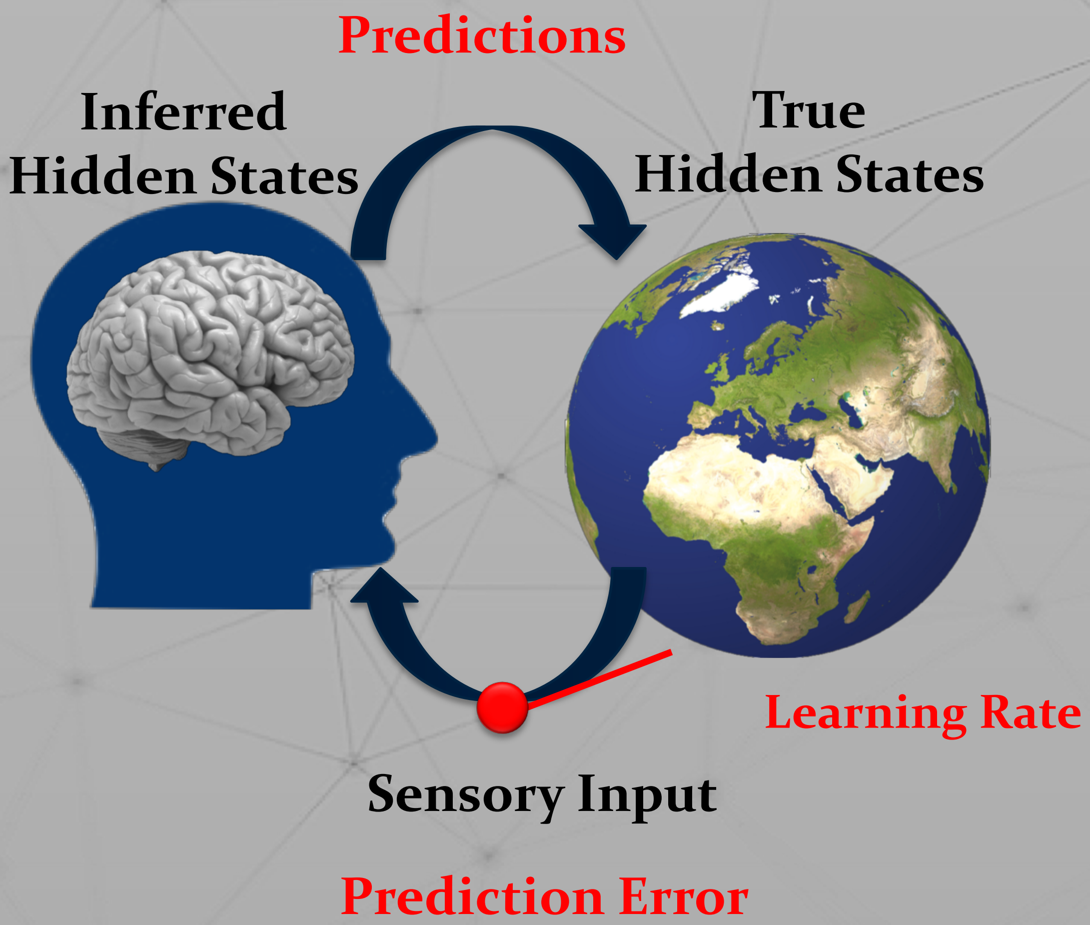
Belief Update

$$\Delta\mu^{(k)} \propto \alpha\delta$$



Computational Variables

Translational Neuromodeling Unit



Example of a simple model

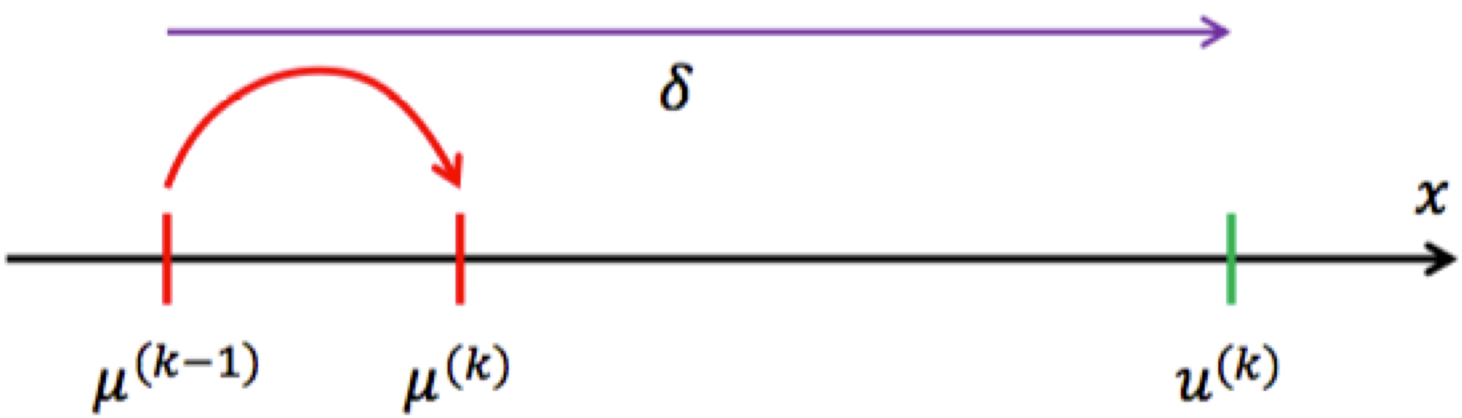
Translational Neuromodeling Unit

Rescorla-Wagner Learning:

Learning Rate

Belief Update

$$\Delta\mu^{(k)} \propto \alpha\delta$$



Example of a hierarchical model

Translational Neuromodeling Unit

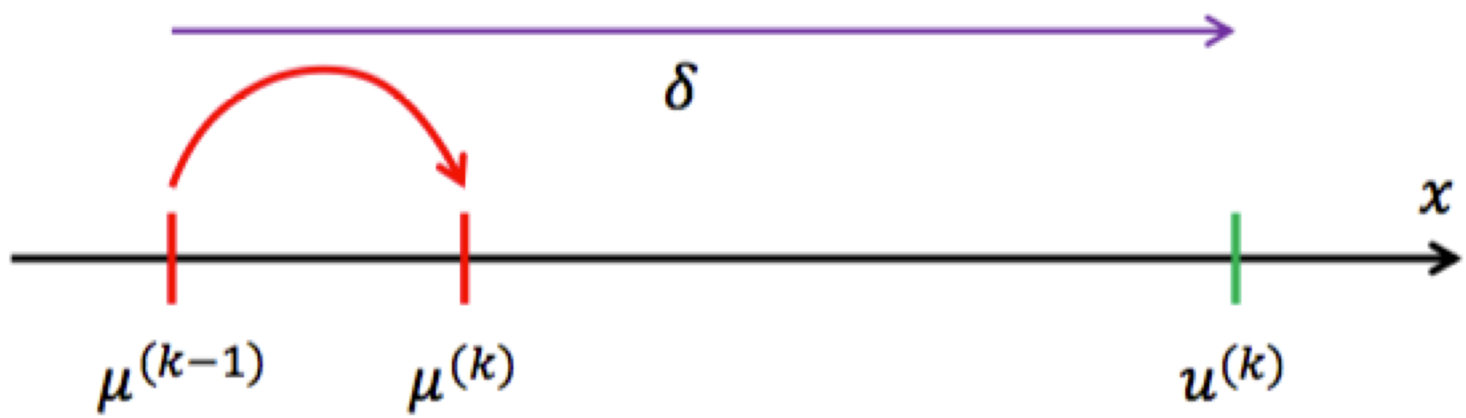
Hierarchical Gaussian Filter :

Weight

Belief Update

$$\Delta\mu^{(k)} \propto \frac{\hat{\pi}_{i-1}{}^{(k)}}{\pi_{i}{}^{(k)}}\delta$$

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

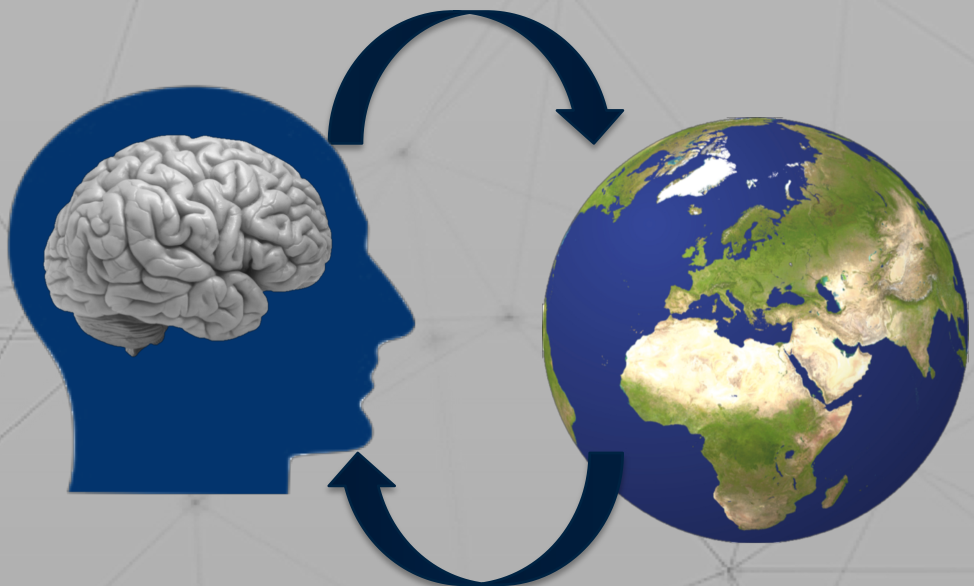


Bayesian Models

Translational Neuromodeling Unit

The Bayesian Brain

Predictions



Prediction Errors

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

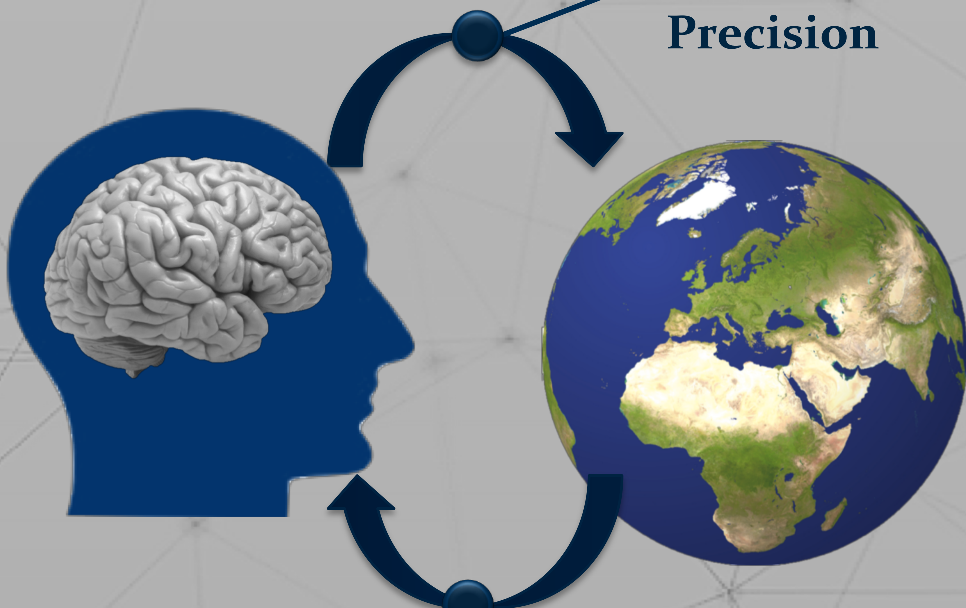
$$\underbrace{p(\Theta|y,m)}_{\text{Posterior Belief}} = \frac{\overbrace{p(\Theta|m)}^{\text{Prior Belief}}\overbrace{p(y|\Theta,m)}^{\text{Sensory Data}}}{\underbrace{\int p(\Theta|m)p(y|\Theta,m)d\Theta}_{\text{Evidence}}}$$

Hierarchical Gaussian Filter

Translational Neuromodeling Unit

Predictions

Belief Precision



Sensory Precision

Prediction Errors

Hierarchy

- Updates as precision-weighted prediction errors

Sensory Precision

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

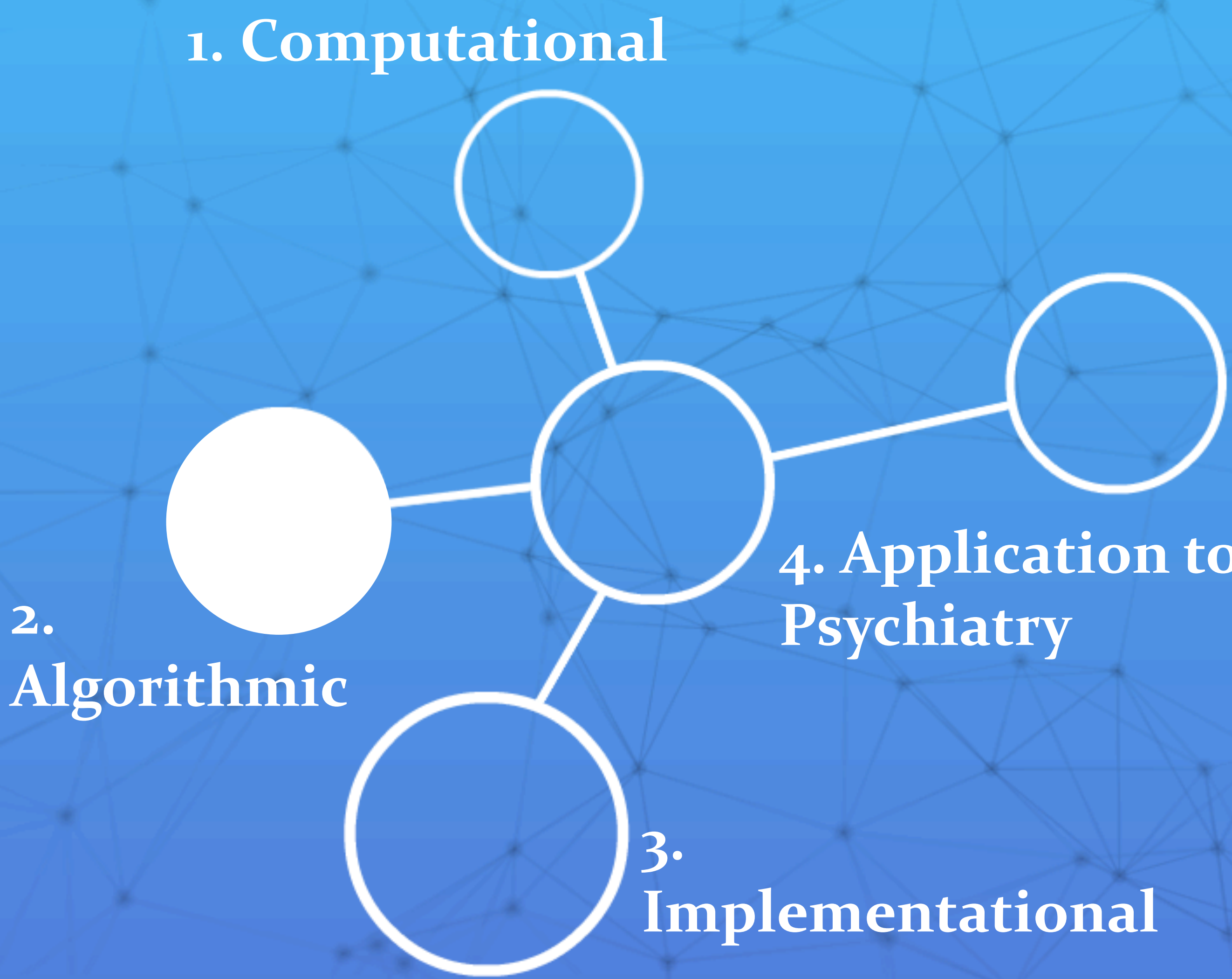
PE

Belief Update

Belief Precision

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

Outline


1. Computational
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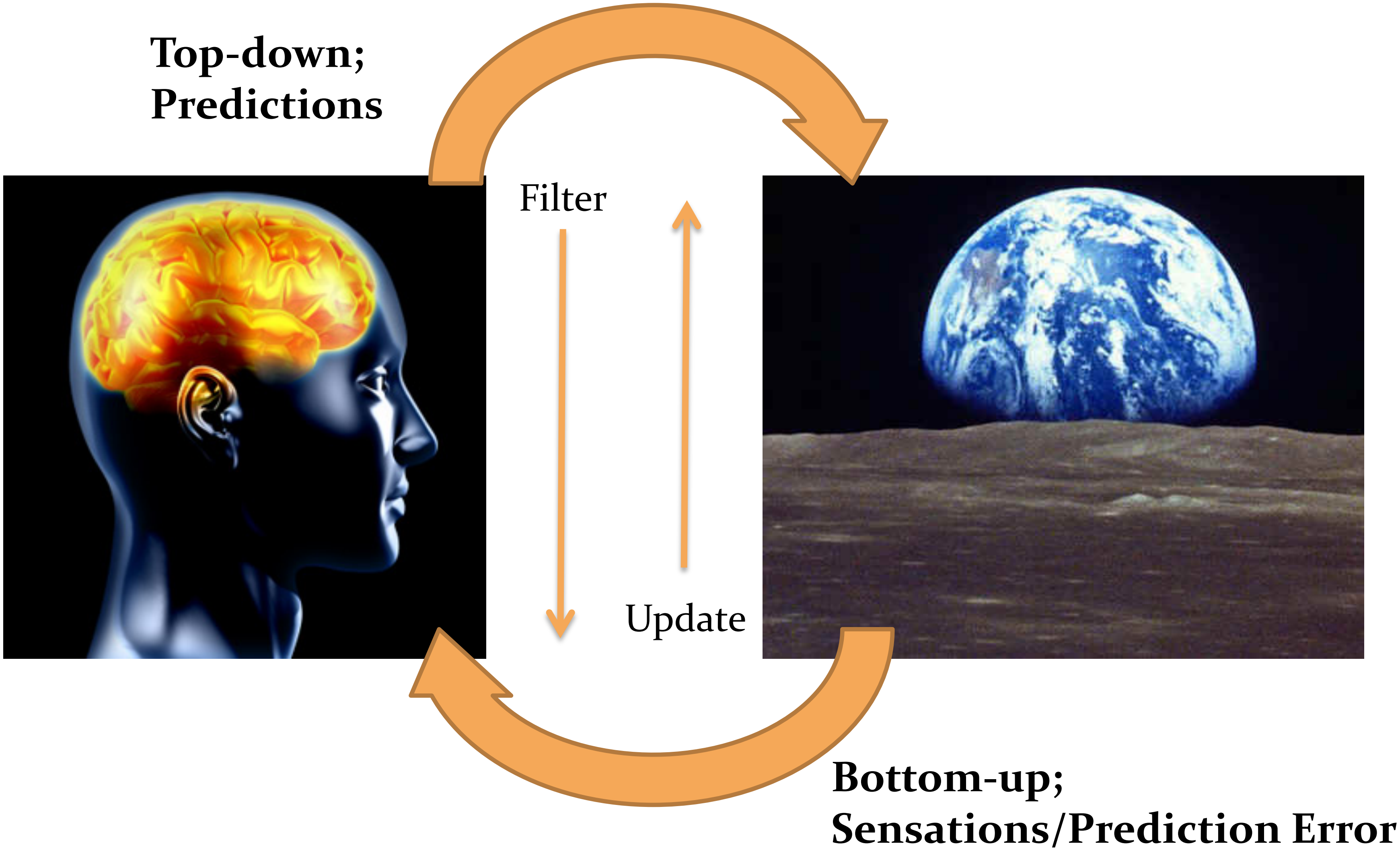
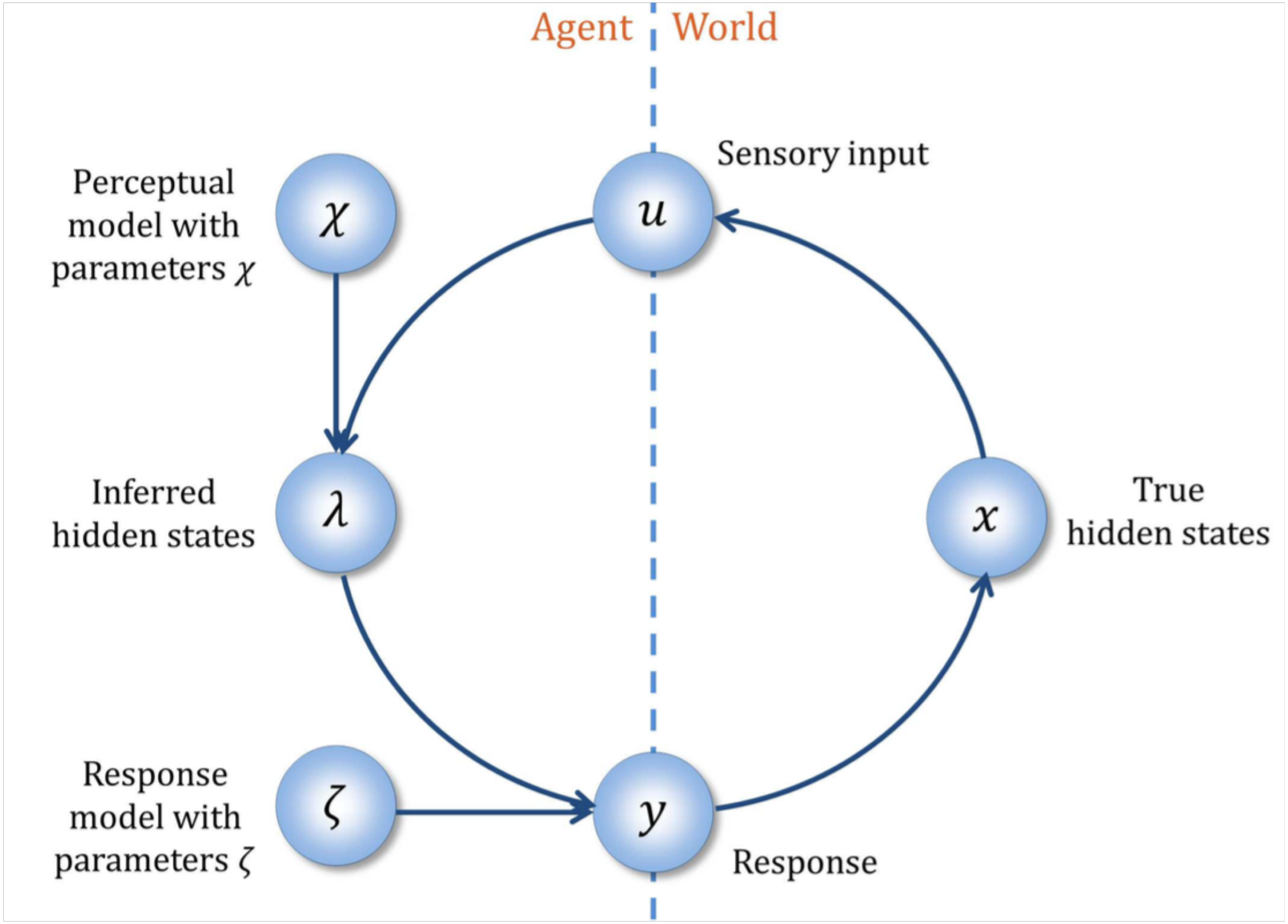
Perception (learning) via hierarchical interactions



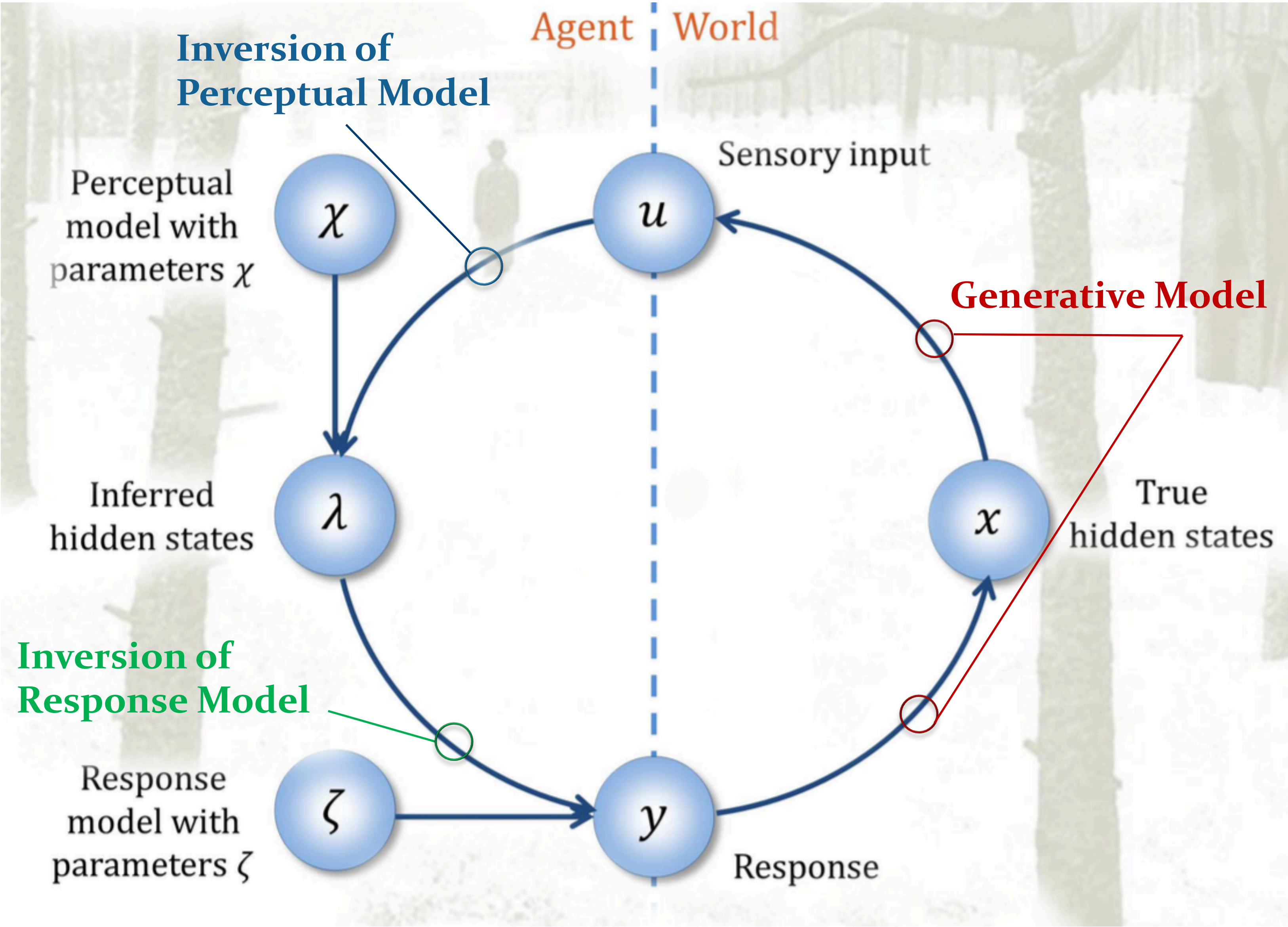
From perception to action

Translational Neuromodeling Unit

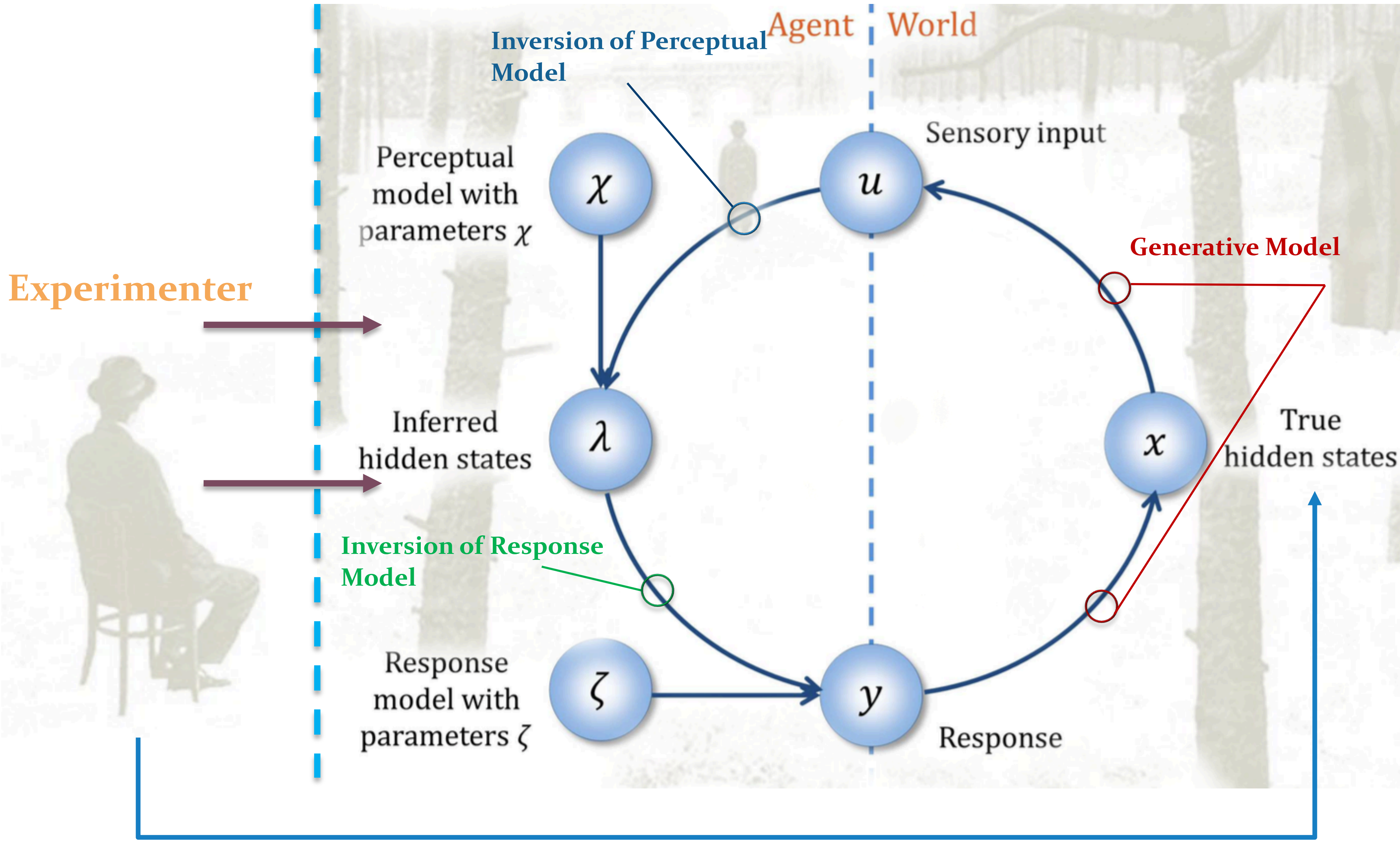


From perception to action

Translational Neuromodeling Unit



From perception to action to observation



Observing the observer

- The observer obtains input from the world via the sensory systems
- He/she has prior beliefs about the state of the world and how it is changing.
- Based on these prior beliefs and the sensory inputs, he/she makes **predictions.**

Daunizeau et al., PONE, 2011

Observing the observer

- The observer obtains input from the world via the sensory systems
- He/she has prior beliefs about the state of the world and how it is changing.
- Based on these prior beliefs and the sensory inputs, he/she makes **predictions.**

- As the experimenter, we want to infer on what the observer is thinking …
- But all we can observe is his/her behaviour.
- We invert the observer’s beliefs from his/her behaviour: computational model

Daunizeau et al., PONE, 2011

Generative Model

Translational Neuromodeling Unit

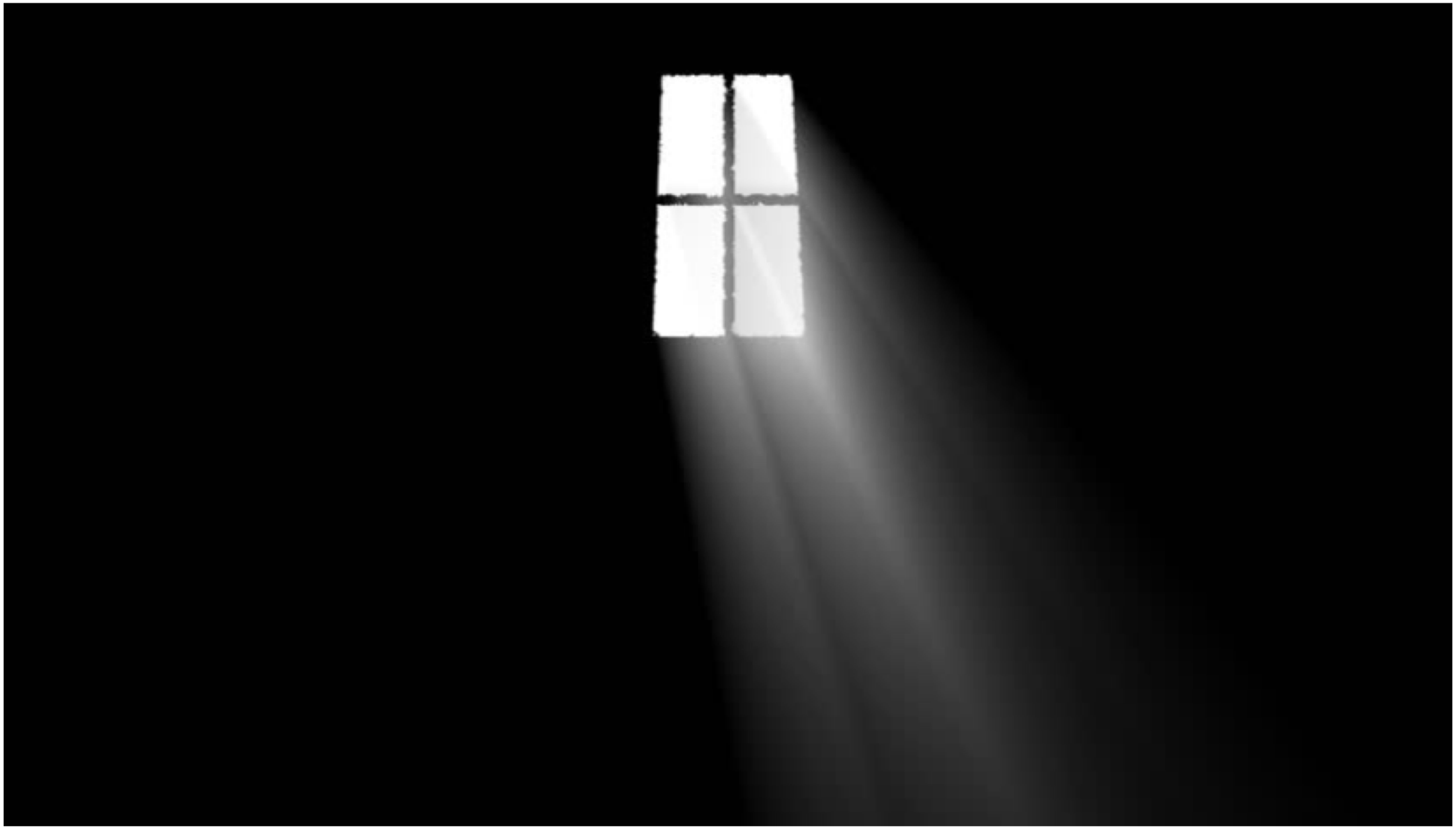
- The joint distribution for observations and perceptual model parameters takes the form:

$$p\left(y,\chi,\lambda^{(0)},\zeta\middle|u\right)=p\left(\chi,\lambda^{(0)},\zeta\right)\prod_{k=1}^{K}p\left(y^{(k)}|\lambda^{(k)}\left(\chi,\lambda^{(0)},u\right),\zeta\right)$$

$$\begin{aligned}
u &\stackrel{\text{def}}{=} \left\{u^{(1)},\dots,u^{(K)}\right\}\\
y &\stackrel{\text{def}}{=} \left\{y^{(1)},\dots,y^{(K)}\right\}\\
\lambda^{(k)} &\stackrel{\text{def}}{=} \left\{\mu_1^{(1)},\pi_1^{(k)},\dots,\mu_1^{(K)},\pi_1^{(K)}\right\}
\end{aligned}$$

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

Dark Room Experiment



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

Translational Neuromodeling Unit

Level 3: Phasic volatility

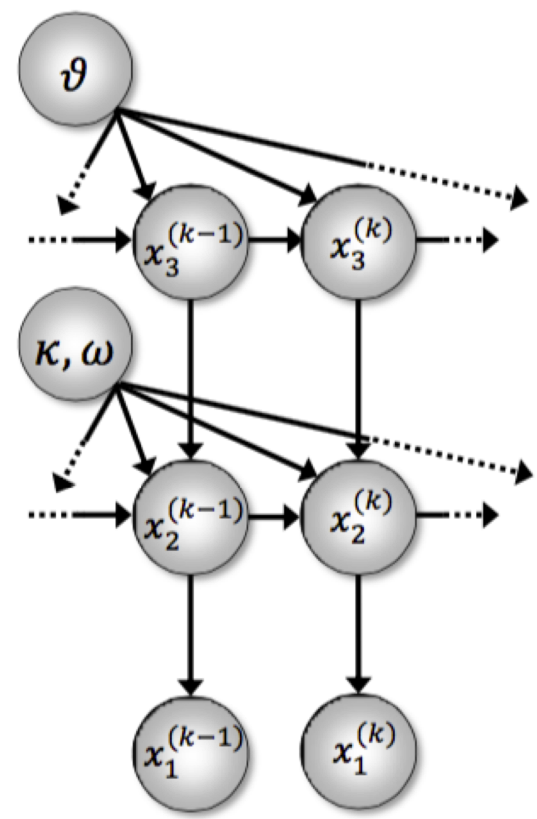
$$p\left(x_3^{(k)}\right) \sim \mathcal{N}(x_3^{(k-1)}, \vartheta)$$

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: 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

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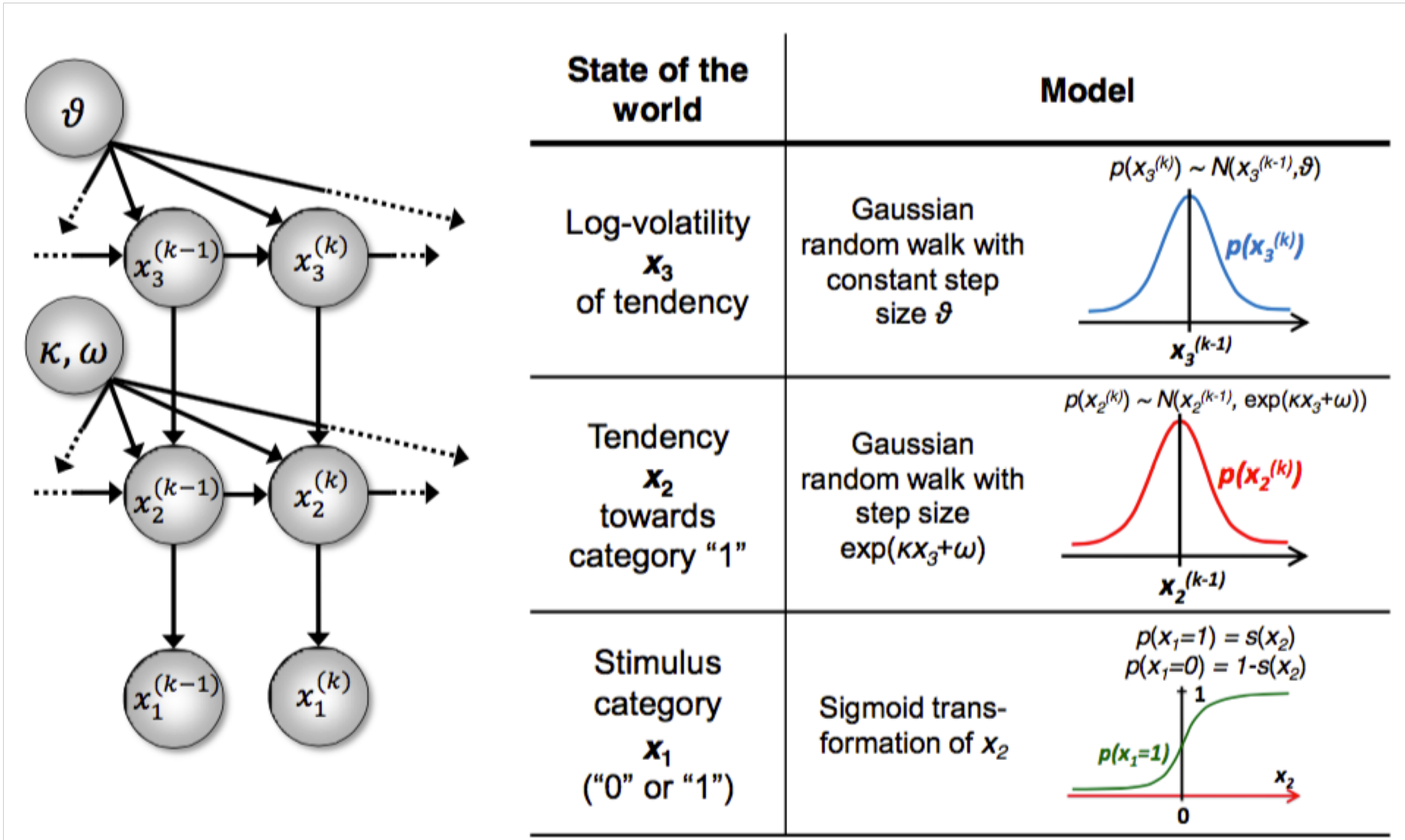
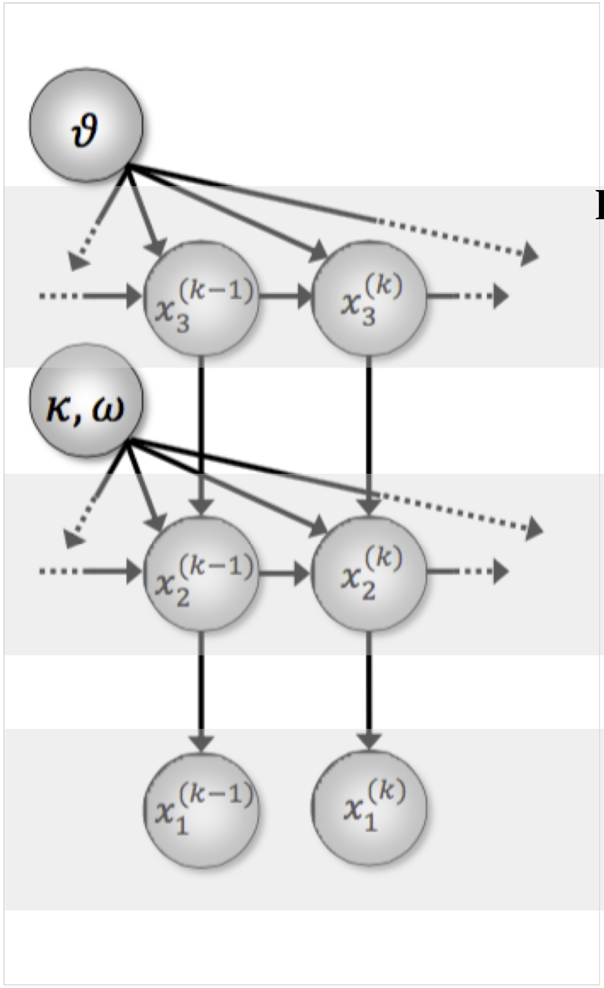


Mathys et al., *Front Hum Neurosci*, 2011

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

Translational Neuromodeling Unit



Beliefs (probability distributions over states and inputs)

Level 3: Belief about volatility

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

Level 2: Belief about tendency

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

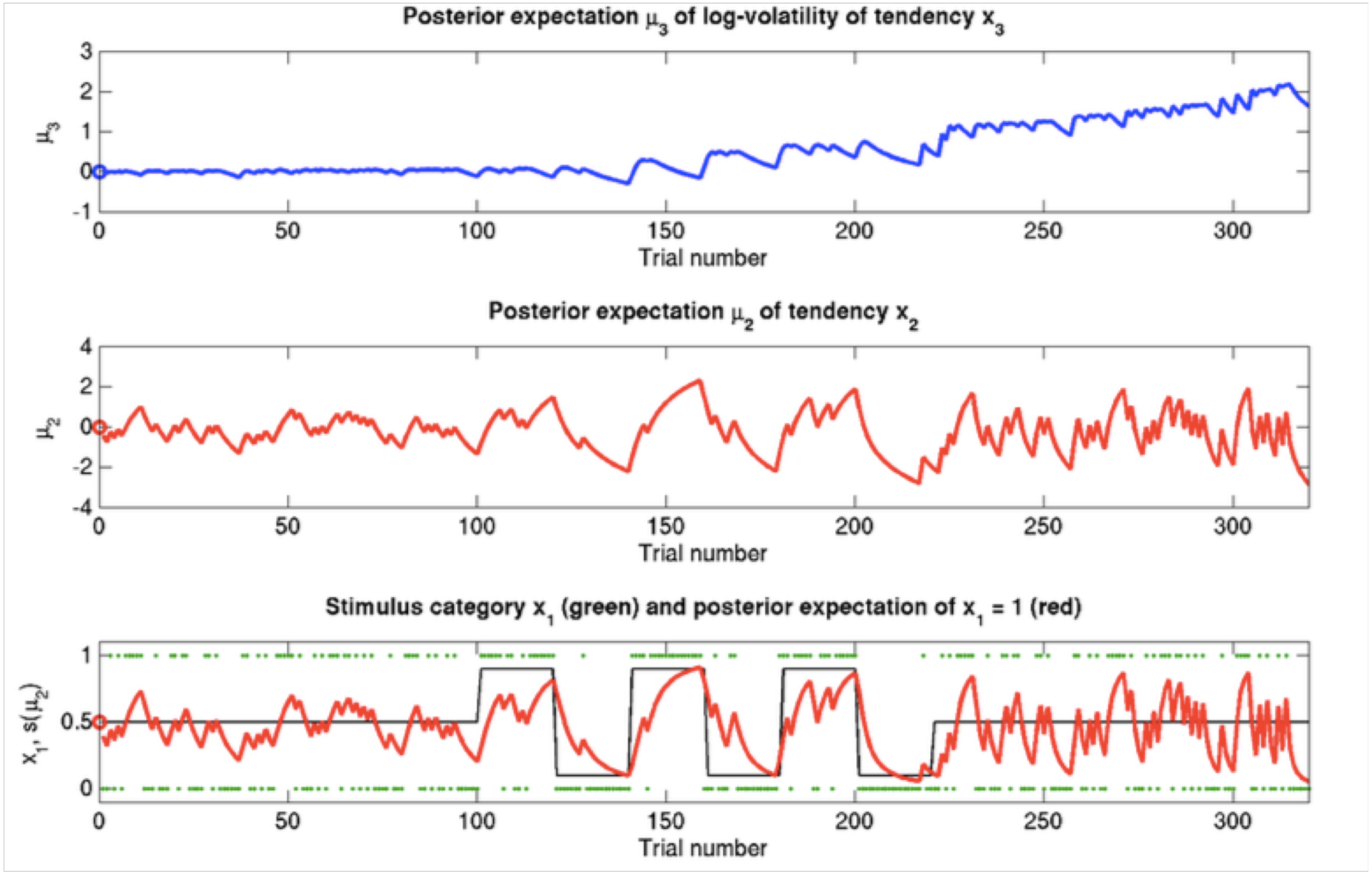
Level 1: Prediction of inputs

$$Bern(\hat{\mu}_1^{(k)})$$

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

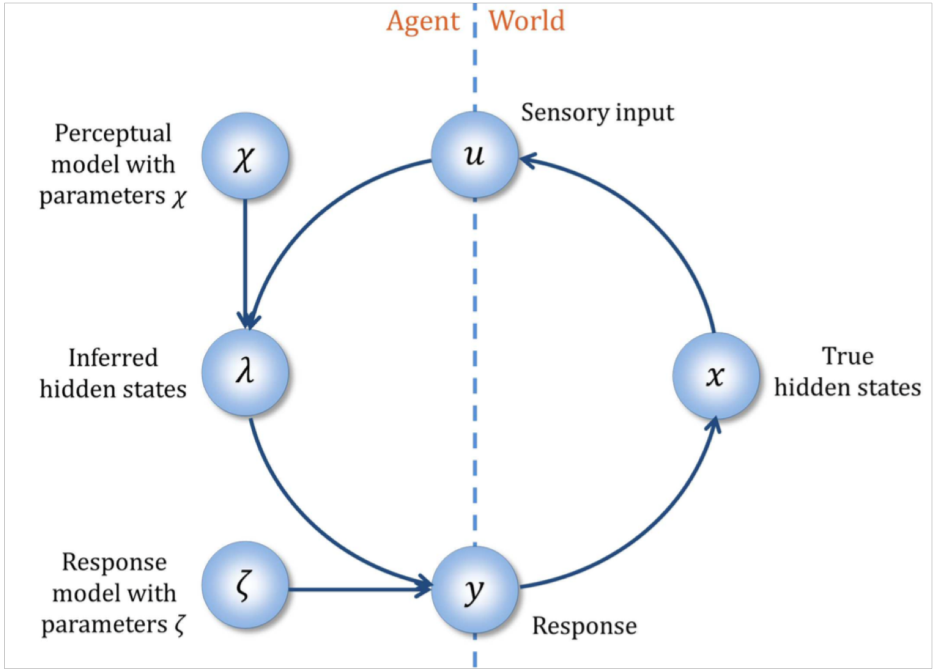
Hierarchical Learning

Simulations: $\vartheta = 0.5,\ \omega = -2.2,\ \kappa = 1.4$



From perception to action

Translational Neuromodeling Unit



- In behavioural tasks, we observe actions a
- How do we use them to infer on beliefs λ?
- Answer: we invert (estimate) a **response model**

Example of a simple response model

Translational Neuromodeling Unit

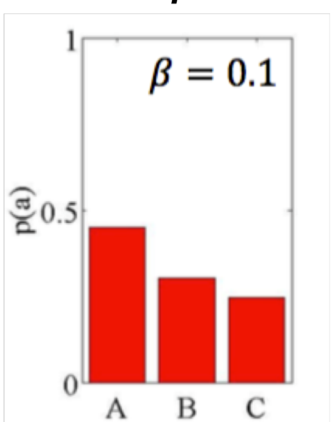
- Options A, B and C have values: $v_A = 8, v_B = 4, v_C = 2$

- We translate these values into action probabilities via a *Softmax* function:

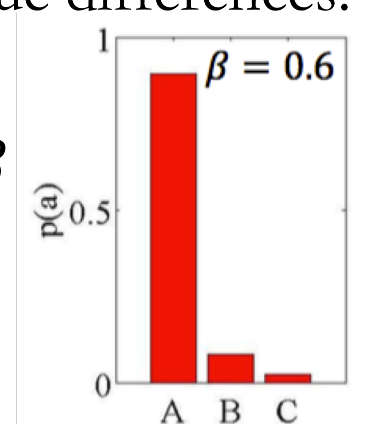
$$p(a = A) = \frac{e^{\beta v_A}}{e^{\beta v_A} + e^{\beta v_B} + e^{\beta v_C}}$$

- Parameter β determines sensitivity to value differences:

low β



high β



All the necessary ingredients

Translational Neuromodeling Unit

- Perceptual model (updates based on prediction errors)
- Value function (inferred state to action value)
- Response model (action value to response probability)

Generative Model

Translational Neuromodeling Unit

- The joint distribution for observations and perceptual model parameters takes the form:

$$p\left(y,\chi,\lambda^{(0)},\zeta \middle| u\right) = p\left(\chi,\lambda^{(0)},\zeta\right) \prod_{k=1}^{K} p\left(y^{(k)} | \lambda^{(k)}\left(\chi,\lambda^{(0)},u\right),\zeta\right)$$

$$u \stackrel{\text{def}}{=} \left\{u^{(1)},\dots,u^{(K)}\right\}$$

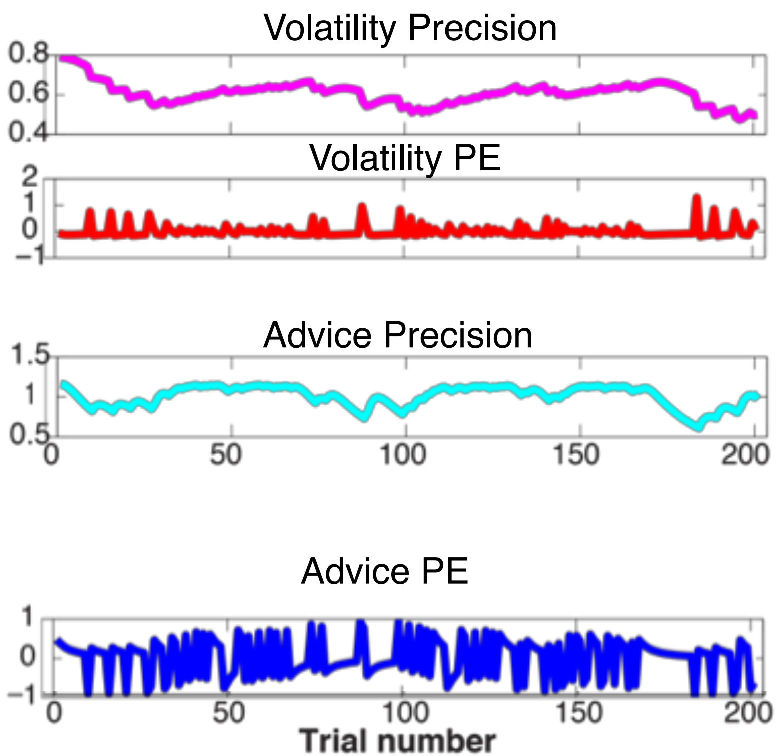
$$y \stackrel{\text{def}}{=} \left\{y^{(1)},\dots,y^{(K)}\right\}$$

$$\lambda^{(k)} \stackrel{\text{def}}{=} \left\{\mu_1^{(1)},\pi_1^{(k)},\dots,\mu_1^{(K)},\pi_1^{(K)}\right\}$$

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

Computational hierarchy

Translational Neuromodeling Unit



Low-Level Precision, PEs

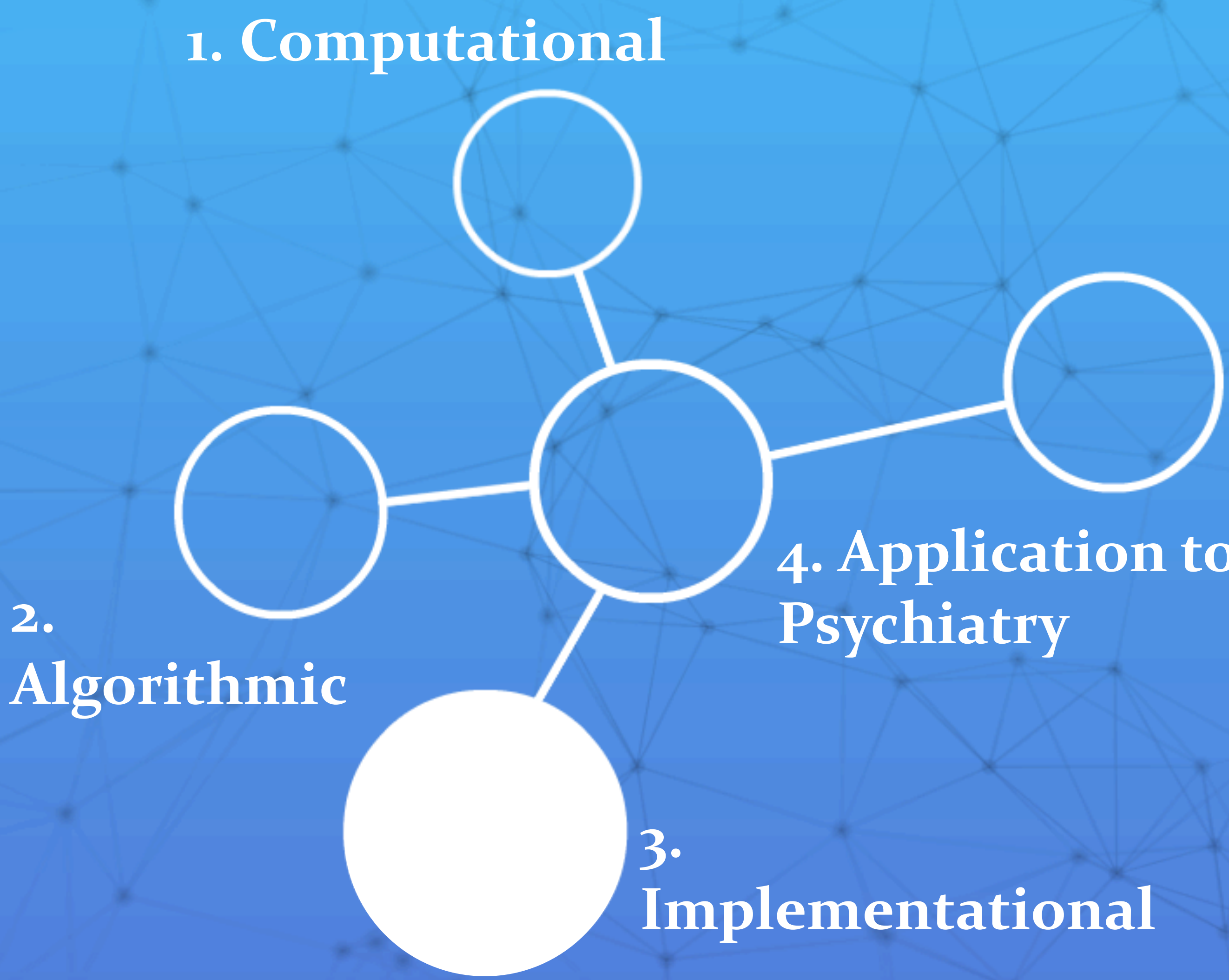
$$\pi_3^{(k)} = \hat{\pi}_3^{(k)} + \frac{1}{2}\left(\gamma_2^{(k)}\right)^2 + \left(\gamma_2^{(k)}\right)^2 \boldsymbol{\delta}_2^{(k)} - \frac{1}{2}\gamma_2^{(k)}\boldsymbol{\delta}_2^{(k)}$$

$$\boldsymbol{\delta}_2^{(k)} = \frac{\hat{\pi}_2^{(k)}}{\boldsymbol{\pi}_2^{(k)}} + (\boldsymbol{\pi}_2^{(k)})^2\hat{\pi}_2^{(k)}\left(\Delta\mu_2^{(k)}\right)^2 - 1;\ \Delta\mu_2^{(k)} = \frac{1}{\boldsymbol{\pi}_2^{(k)}}\boldsymbol{\delta}_1^{(k)}$$

$$\boldsymbol{\pi}_2^{(k)} = \hat{\pi}_2^{(k)} + \hat{\mu}_1^{(k)}\left(1 - \hat{\mu}_1^{(k)}\right)$$

$$\boldsymbol{\delta}_1^{(k)} = u^{(k)} - \hat{\mu}_1^{(k)};\ \hat{\mu}_1^{(k)} = s\left(\mu_2^{(k-1)}\right)$$

Outline


1. Computational
2. Algorithmic
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Computational fMRI: The advantage

Translational Neuromodeling Unit

The question event-related/block designs answer:

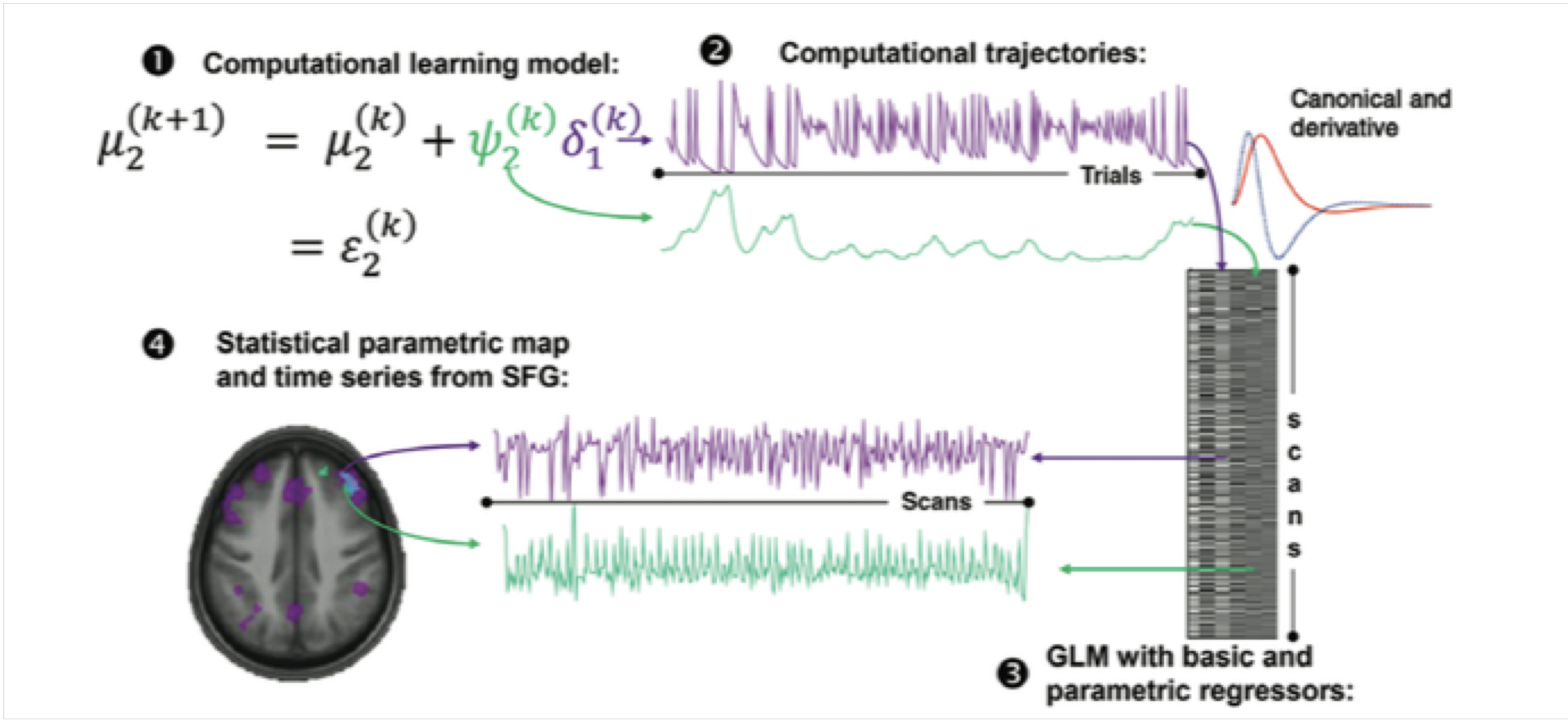
- Where in the brain do particular experimental conditions elicit BOLD responses?

The question model-based fMRI answers:

- How (i.e., by activation of which areas) does the brain implement a particular cognitive process?

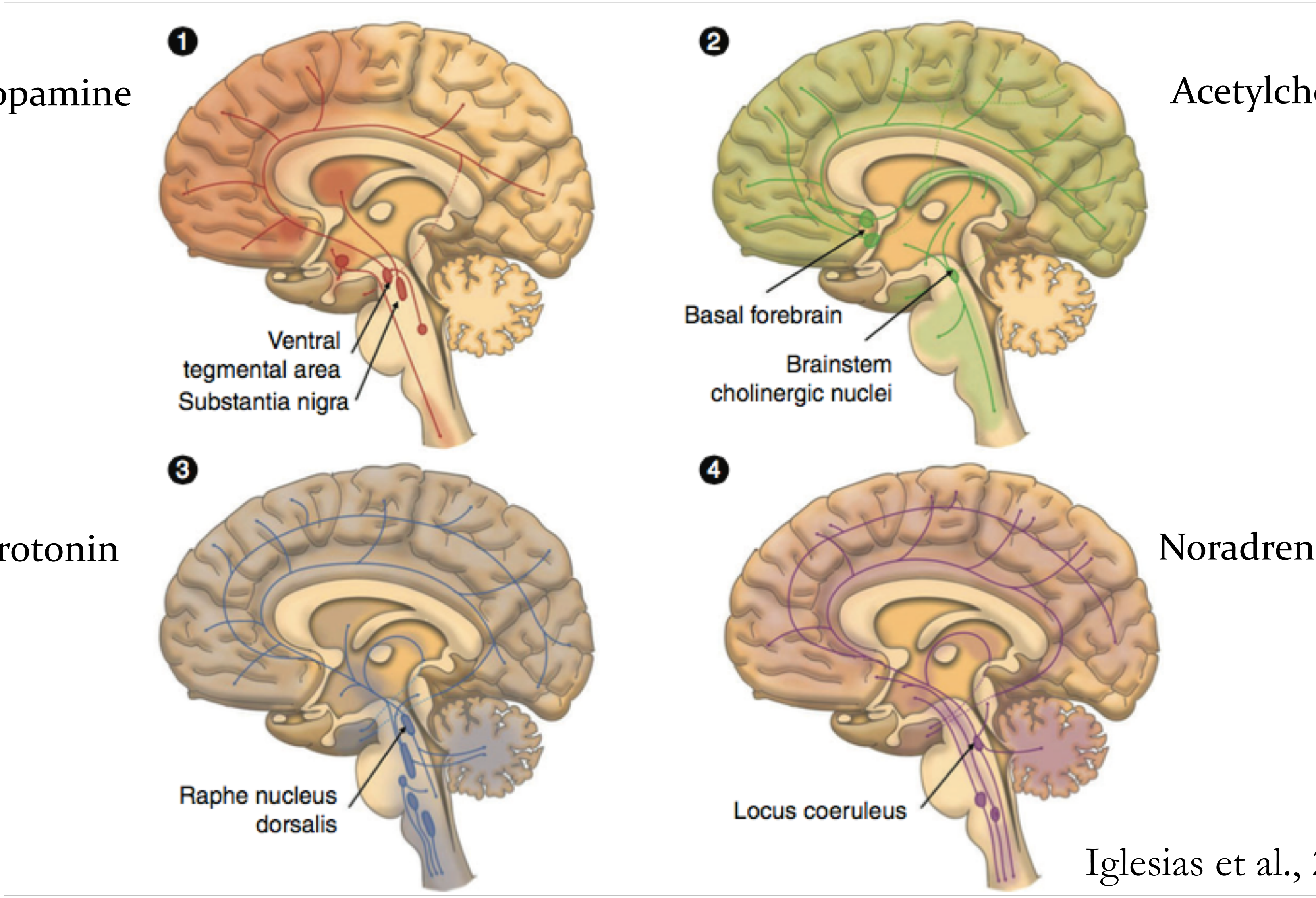
It is able to do so because its regressors correspond to particular cognitive processes instead of experimental conditions.

Computational fMRI analyses of neuromodulation



Iglesias et al., 2016

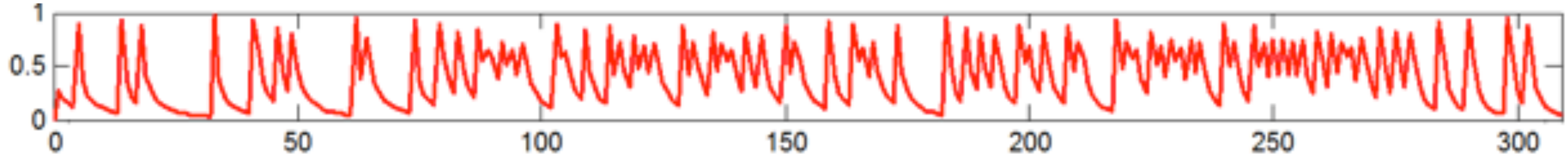
Computational fMRI analyses of neuromodulation



Iglesias et al., 2016

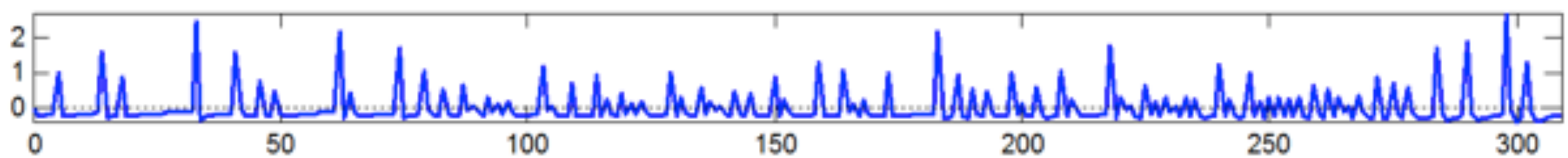
Application of the HGF: Two types of PEs

1. Outcome PE



ϵ_2

2. Cue-Outcome Contingency PE

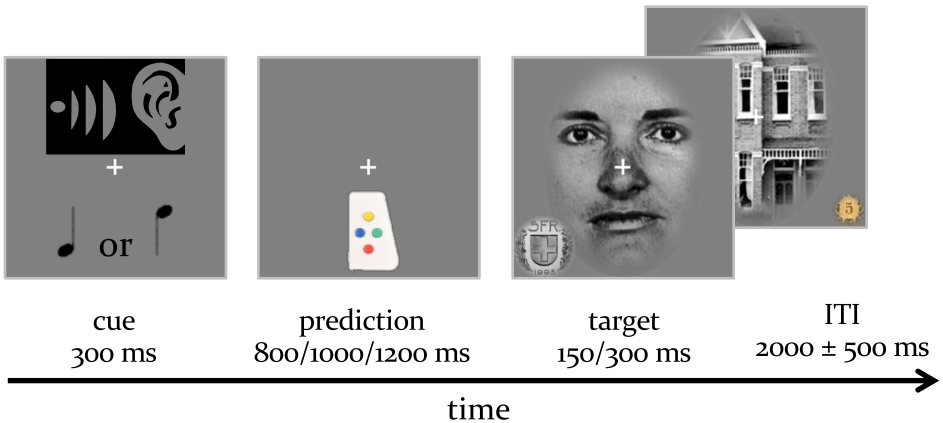


ϵ_3

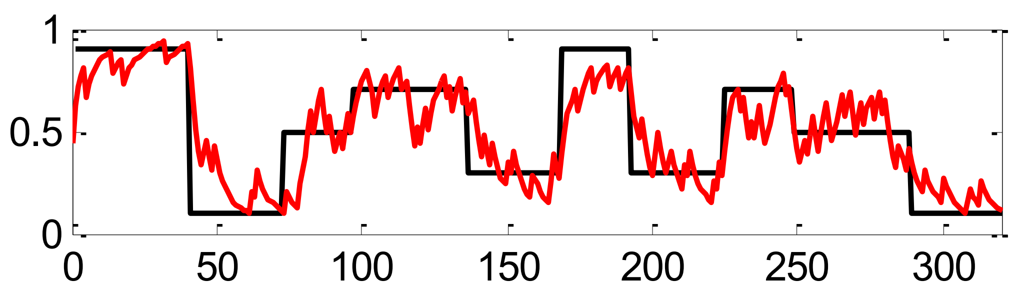
Iglesias et al., *Neuron*, 2013

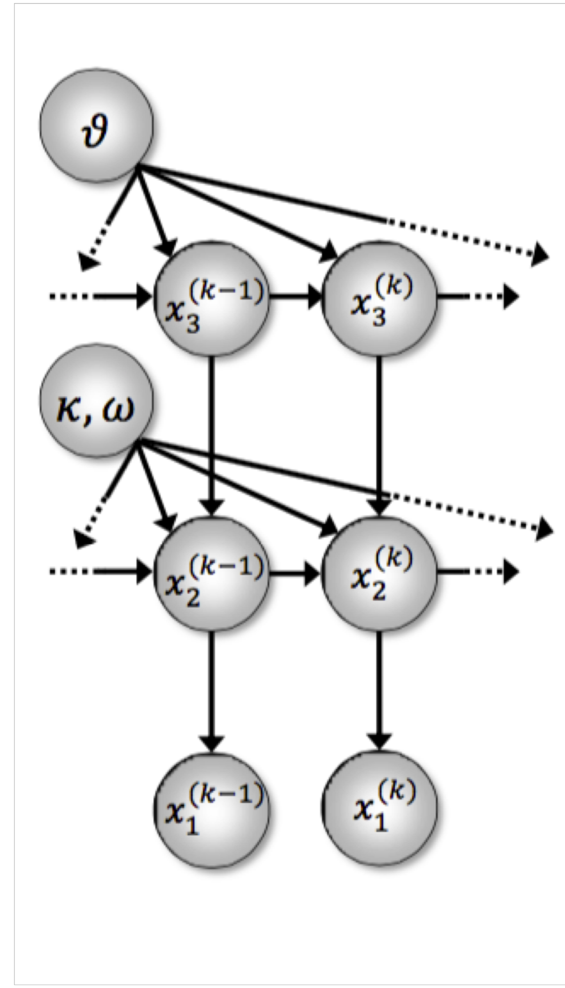
Application of the HGF: Sensory Learning

Translational Neuromodeling Unit



Changes in cue strength (black), and posterior expectation of visual category (red)



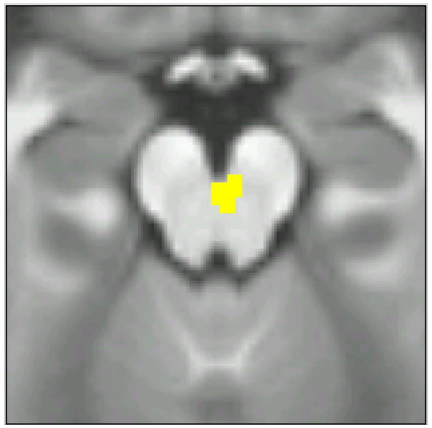


Iglesias et al., *Neuron*, 2013

Application of the HGF: Representation of precision-weighted PEs

Translational Neuromodeling Unit

1. Outcome PE

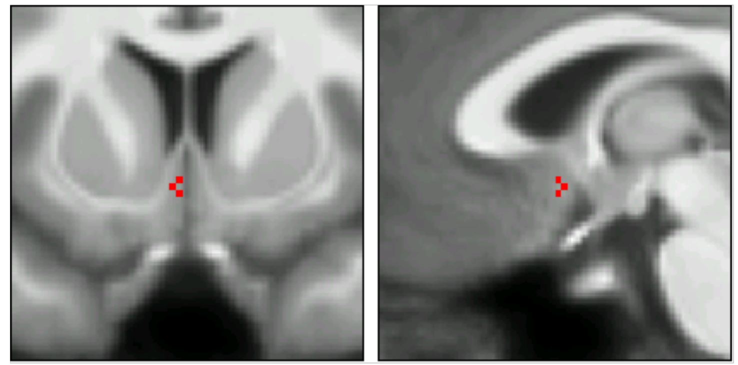


z = -18

- right VTA

Dopamine

2. Probability PE

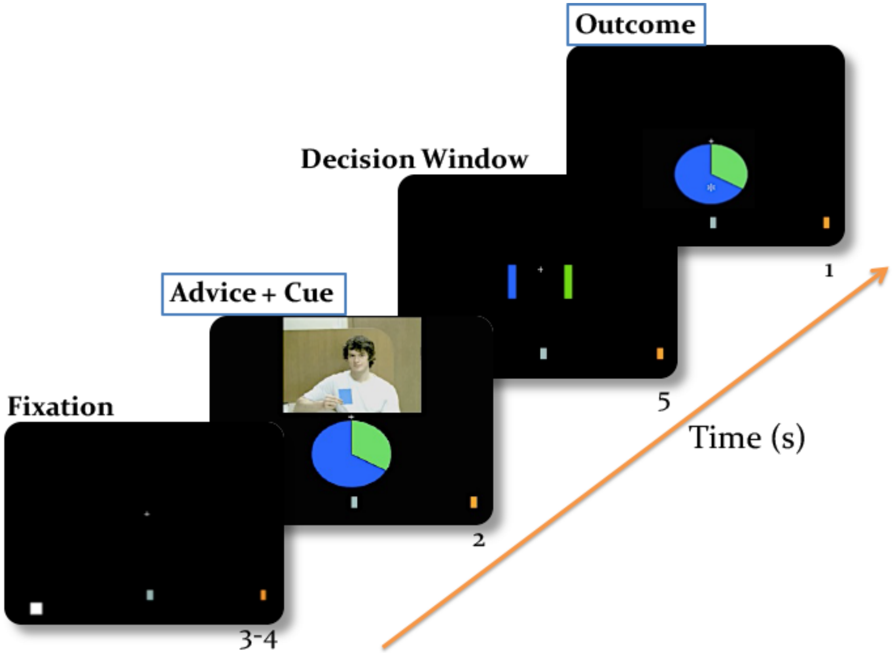


- left basal forebrain

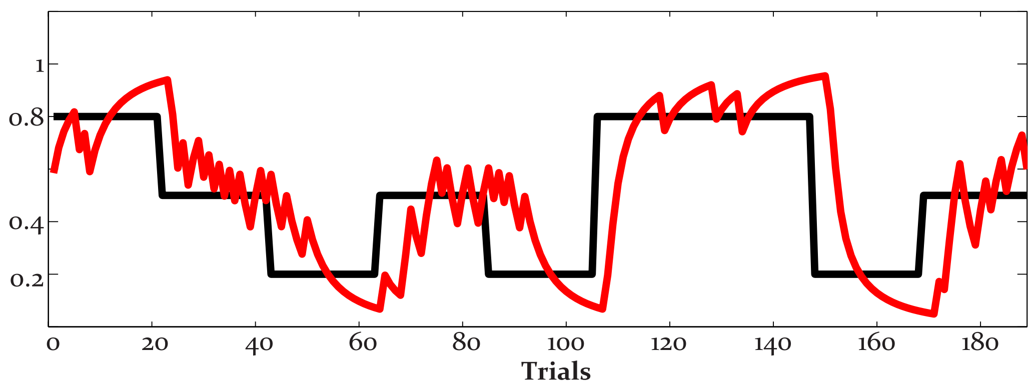
Acetycholine

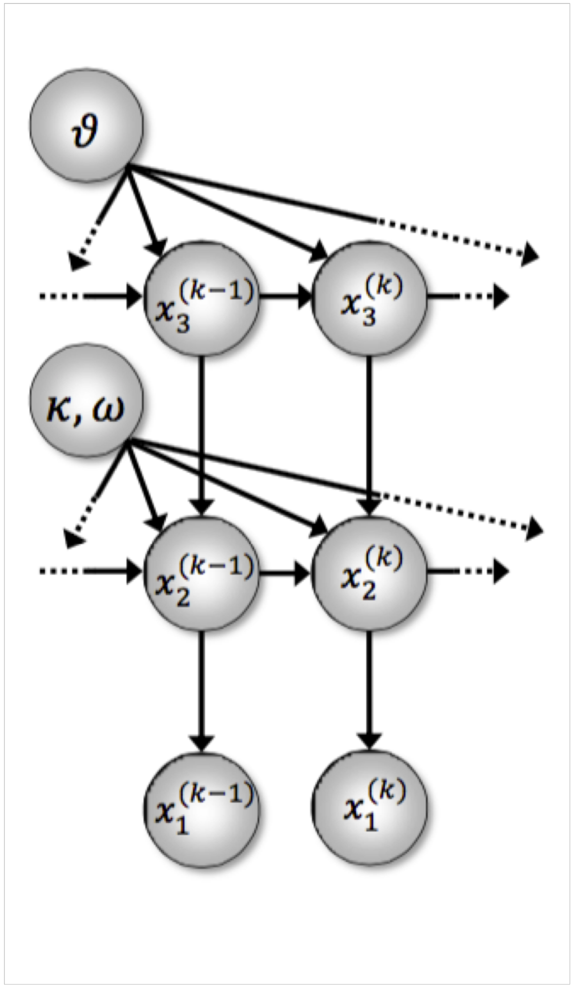
Iglesias et al., *Neuron*, 2013

Application of the HGF: Social Learning



Changes in advice accuracy (black), and posterior expectation of adviser fidelity (red)

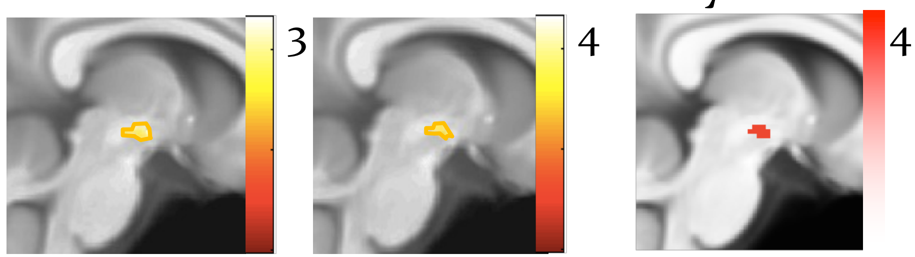




Diaconescu et al., *SCAN*, 2017

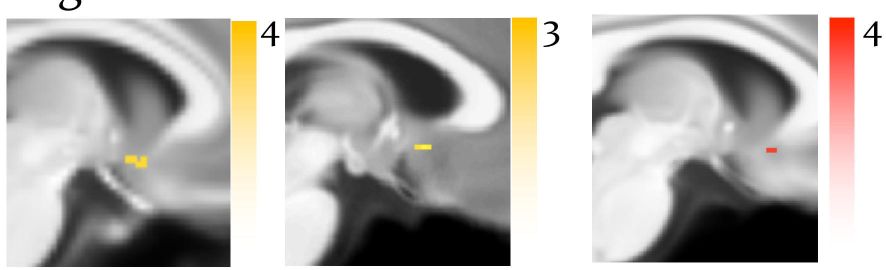
Representation of precision-weighted PEs in the social domain

Dopamine System:
low-level PEs about adviser fidelity



first fMRI study | **second fMRI study** | **conjunction**

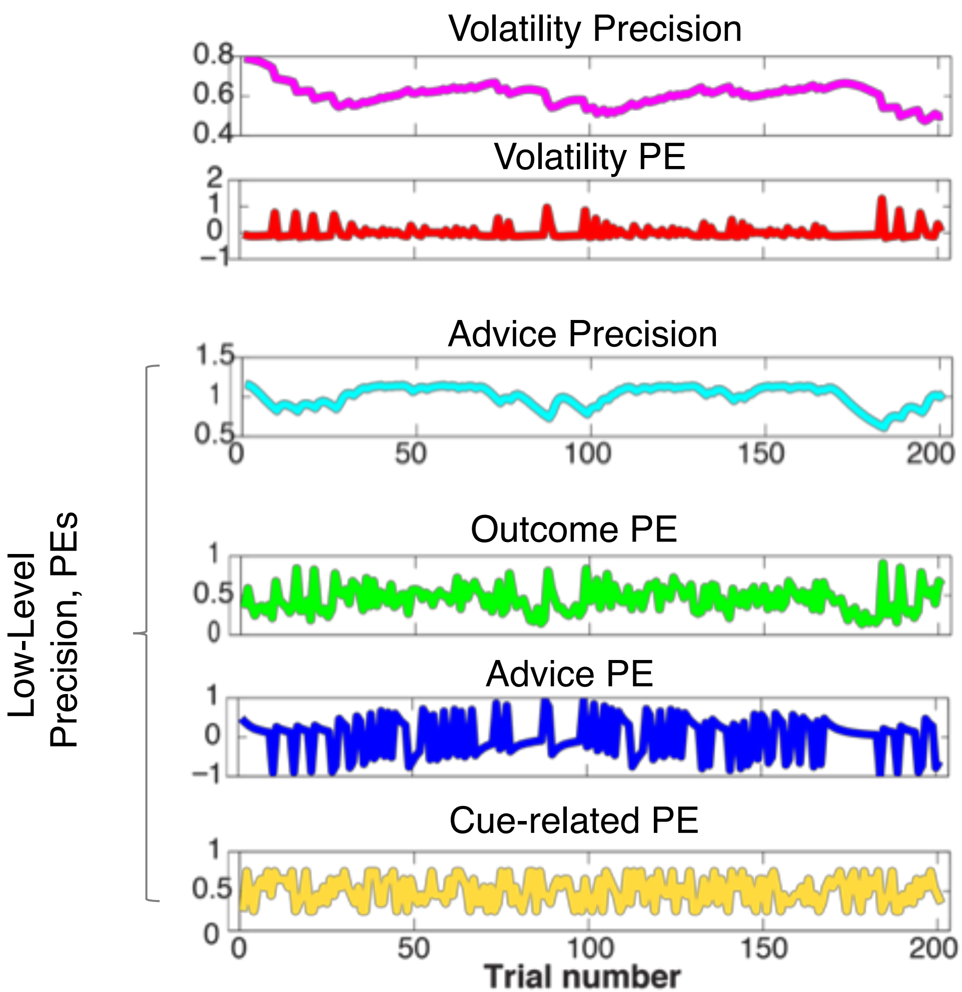
Cholinergic System:
high-level PEs about intentions



first fMRI study | **second fMRI study** | **conjunction**

Diaconescu et al., *SCAN*, 2017

Computational hierarchy & its neural signature



$$\pi_3^{(k)} = \hat{\pi}_3^{(k)} + \frac{1}{2}\left(\gamma_2^{(k)}\right)^2 + \left(\gamma_2^{(k)}\right)^2 \delta_2^{(k)} - \frac{1}{2}\gamma_2^{(k)}\delta_2^{(k)}$$

$$\delta_2^{(k)} = \frac{\hat{\pi}_2^{(k)}}{\pi_2^{(k)}} + (\pi_2^{(k)})^2 \hat{\pi}_2^{(k)}\left(\Delta\mu_2^{(k)}\right)^2 - 1;\ \Delta\mu_2^{(k)} = \frac{1}{\pi_2^{(k)}}\delta_1^{(k)}$$

$$\pi_2^{(k)} = \hat{\pi}_2^{(k)} + \hat{\mu}_1^{(k)}\left(1 - \hat{\mu}_1^{(k)}\right)$$

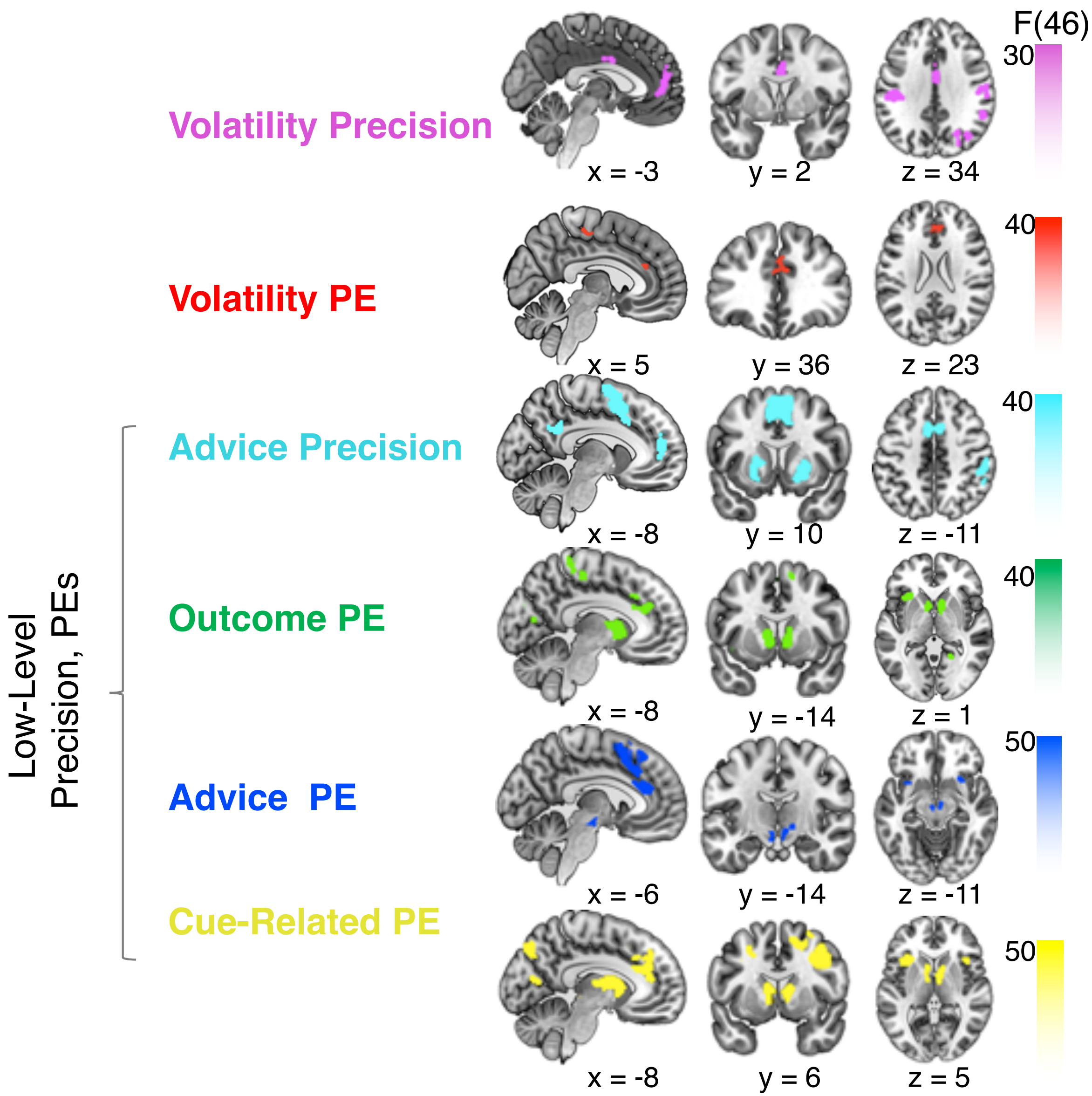
$$\delta_b^{(k)} = u^{(k)} - \mu_b^{(k)};\ \mu_b^{(k)} = \zeta\,\hat{\mu}_1^{(k)} + (1-\zeta)\tilde{c}^{(k)}$$

$$\delta_1^{(k)} = u^{(k)} - \hat{\mu}_1^{(k)};\ \hat{\mu}_1^{(k)} = s\left(\mu_2^{(k-1)}\right)$$

$$\delta_{\tilde{c}}^{(k)} = u^{(k)} - c^{(k)};\ c^{(k)} = p(c)$$

Computational hierarchy & its neural signature

Translational Neuromodeling Unit



Outline

1. Computational
2. Algorithmic
3. Implementational
4. Application to Psychiatry

"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."

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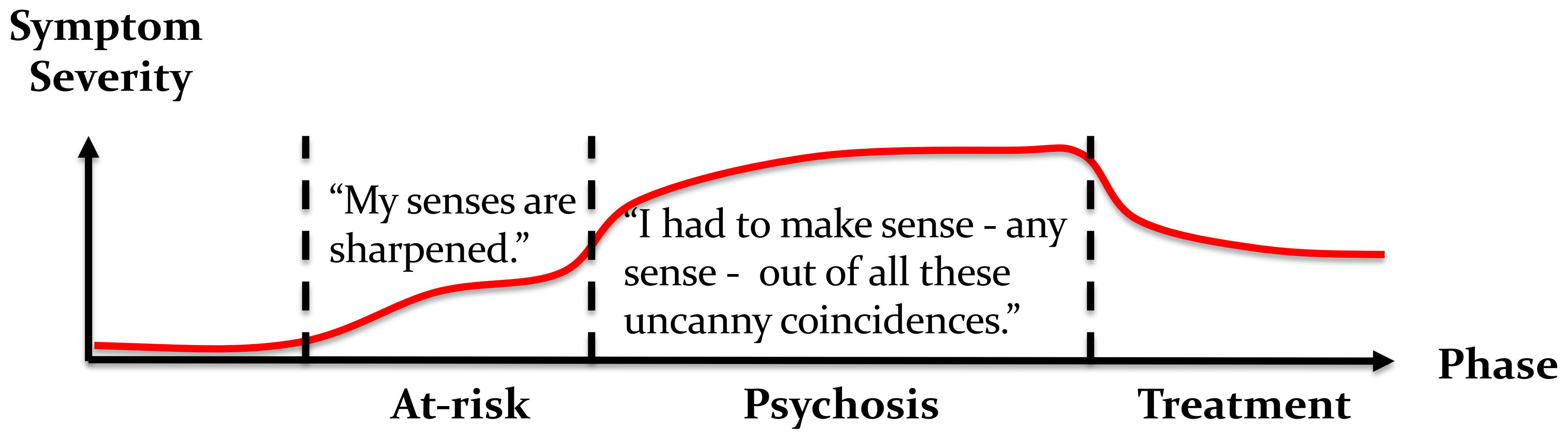
I did it by radically changing my conception of reality."

"My senses are sharpened."

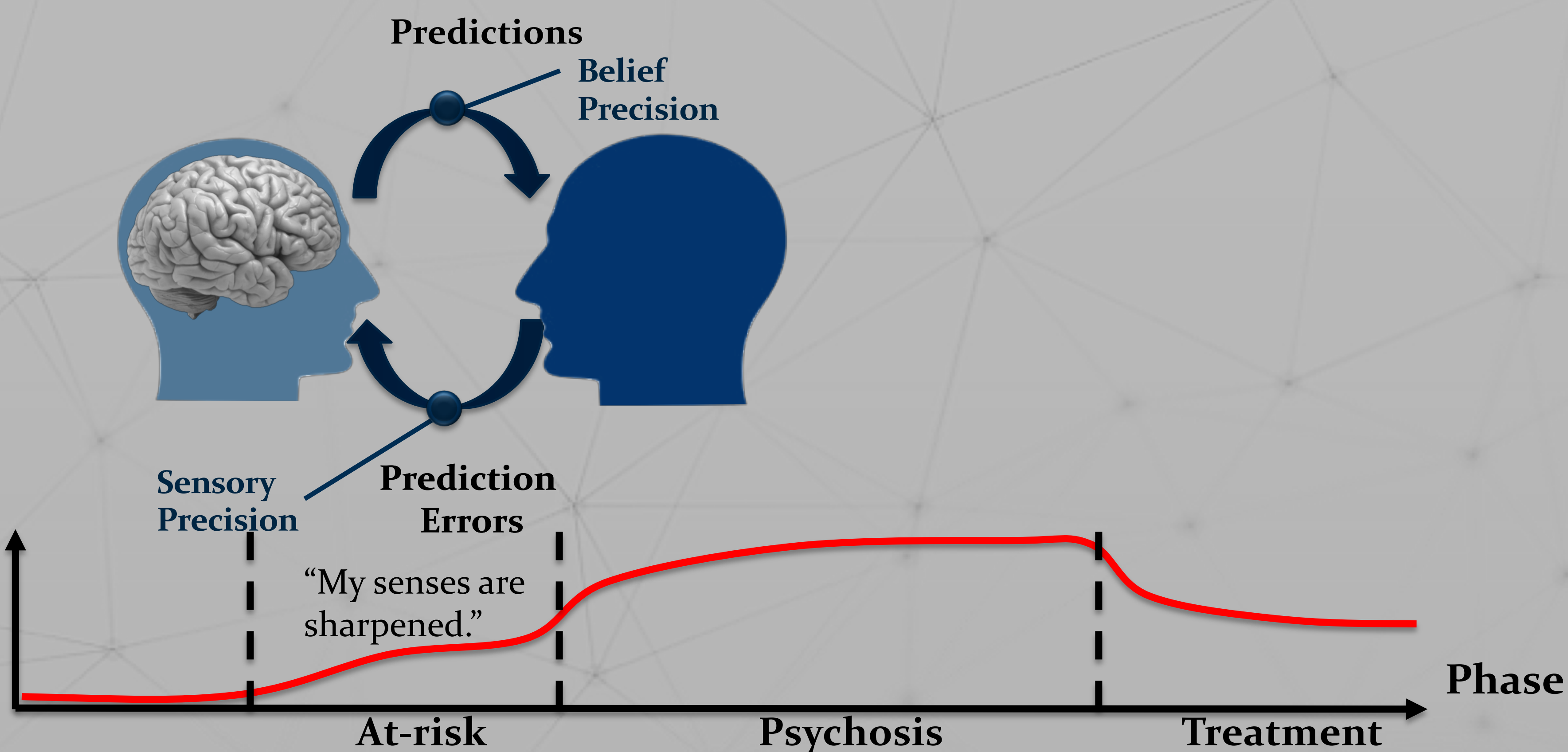
"I had to make sense - any sense - out of all these uncanny coincidences."

The Burden of Schizophrenia

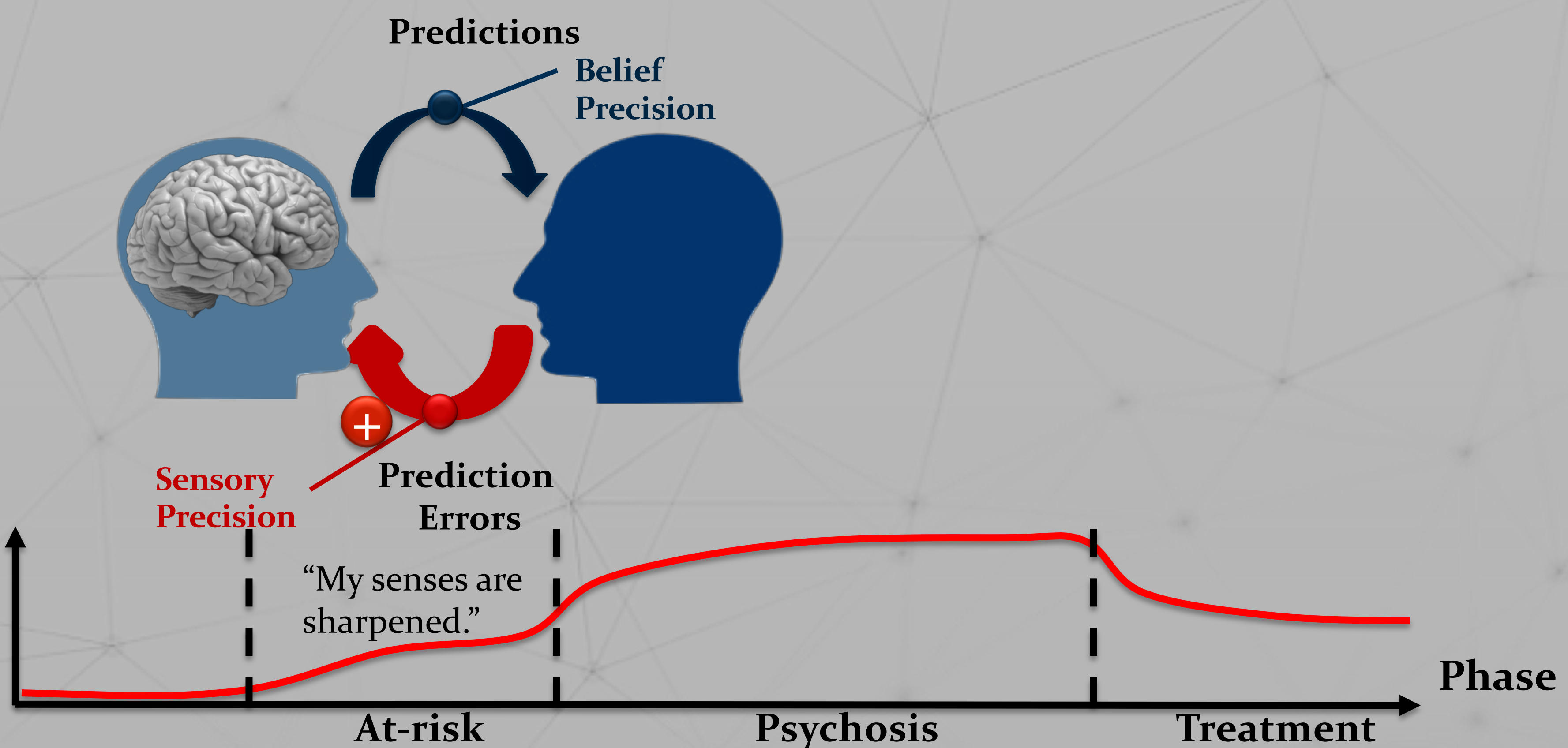
- Life-long disease



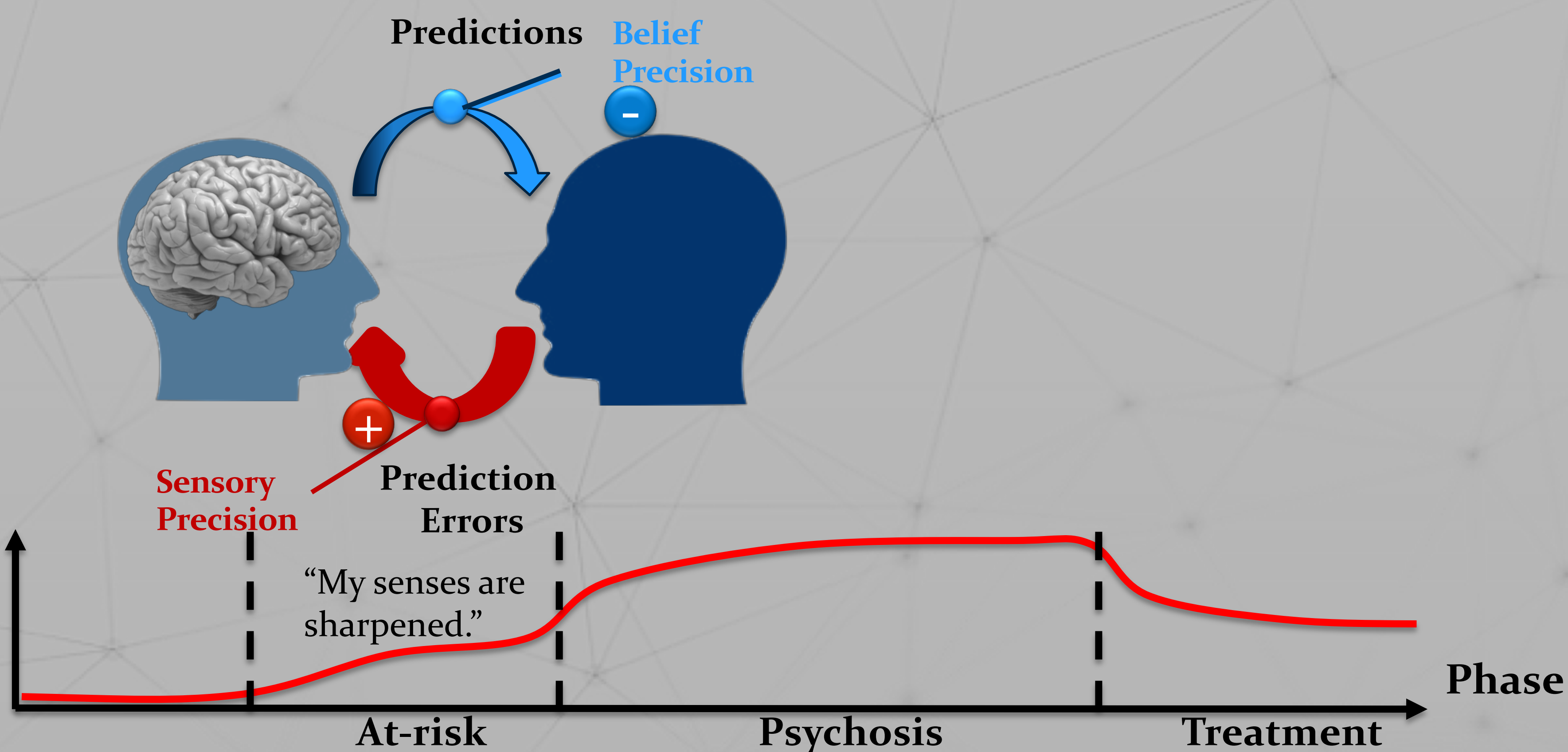
Models of Psychosis



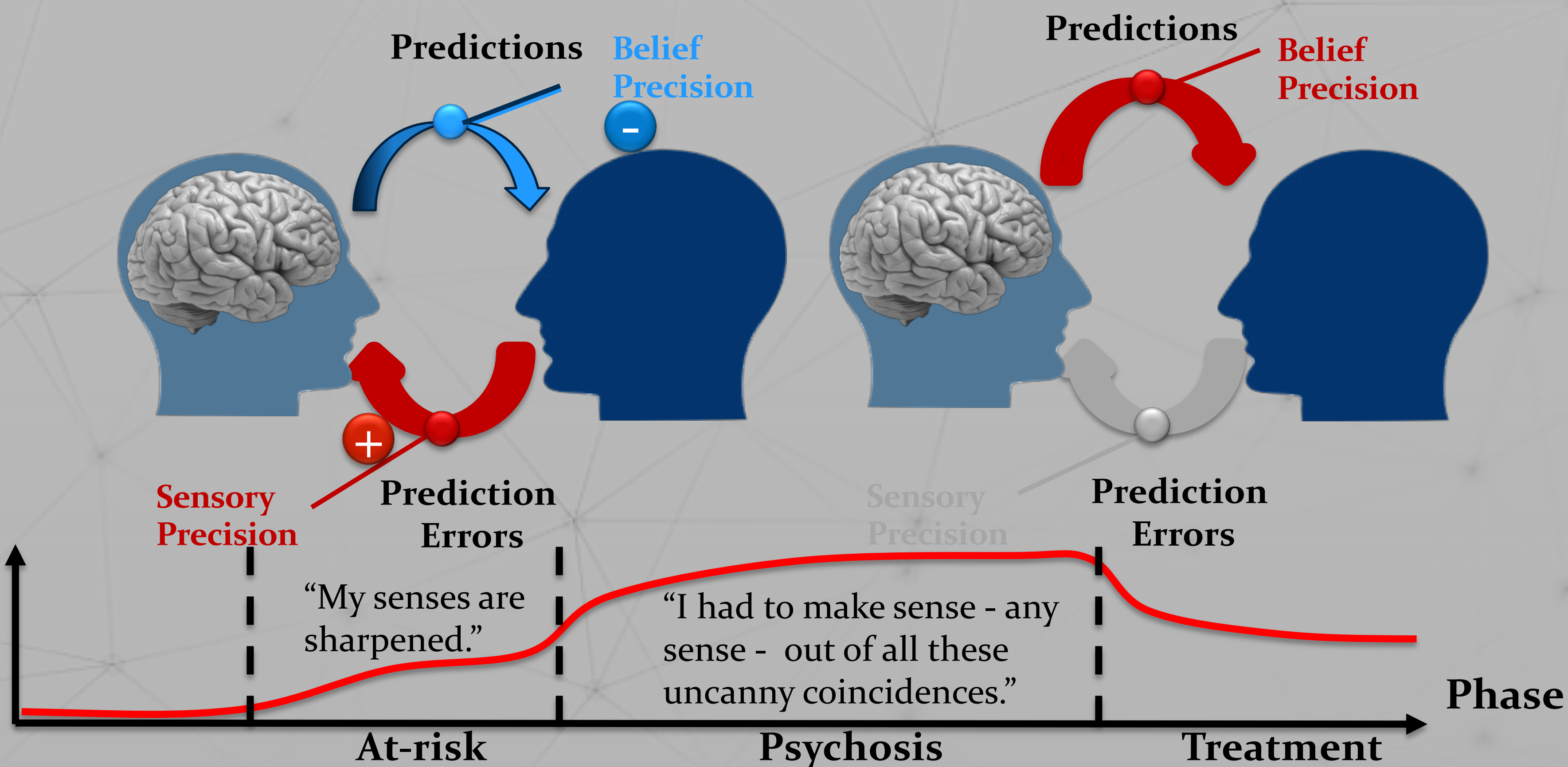
Models of Psychosis



Models of Psychosis: At-Risk Phase

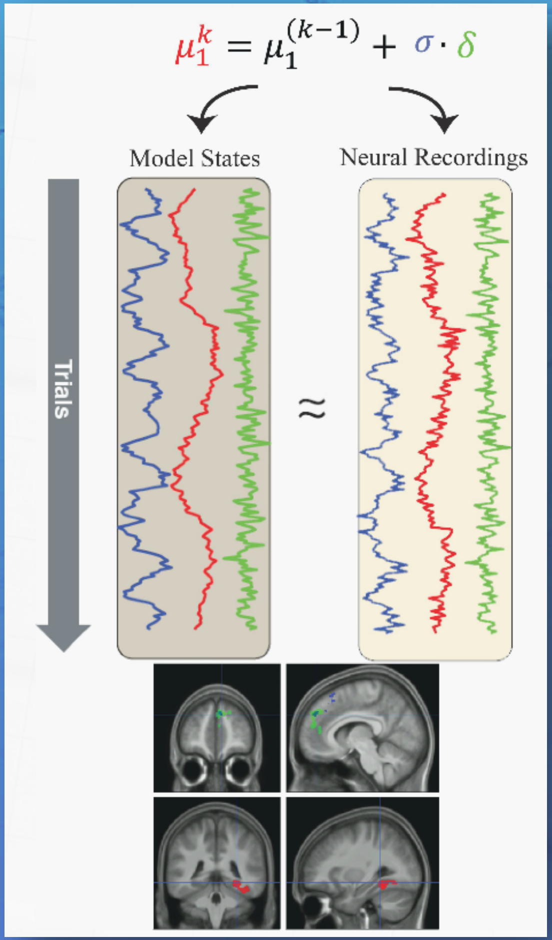


Models of Psychosis: Delusions



Tutorial

HGFtutorial_generate_task.m



References

Translational Neuromodeling Unit

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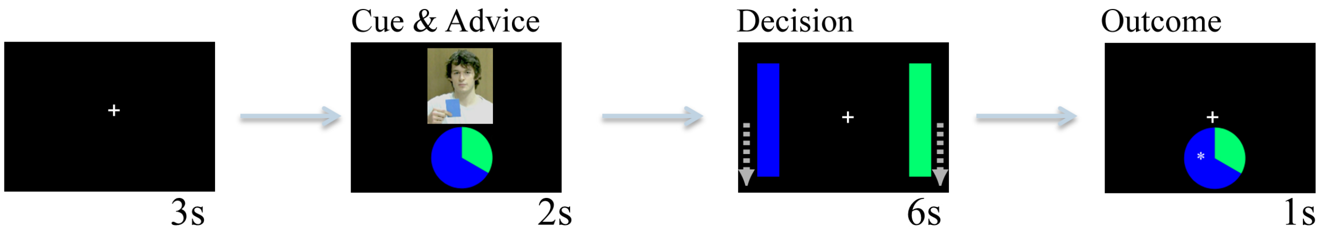
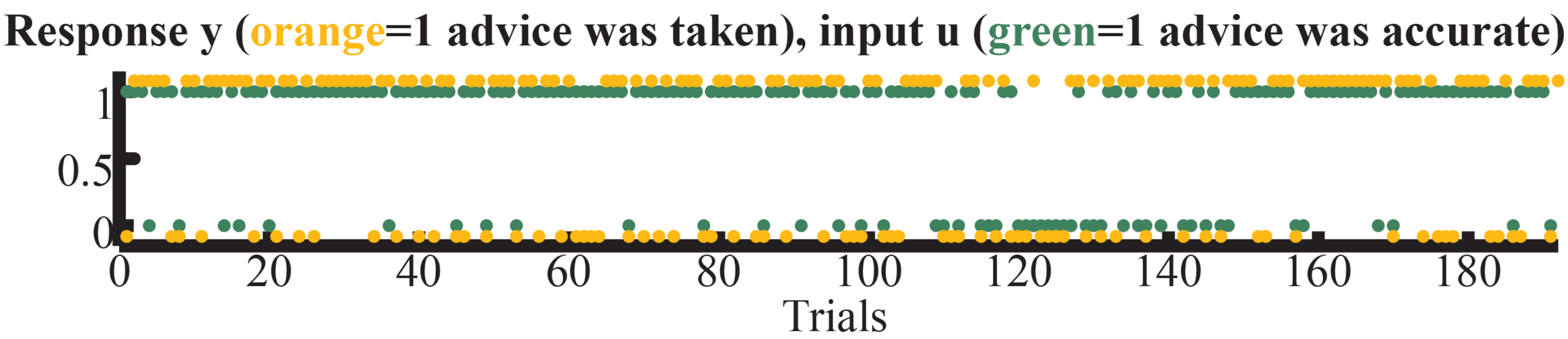
How do we construct regressors that correspond to cognitive processes and use them in SPM?

1. Pass individual subject trial history into SPM:





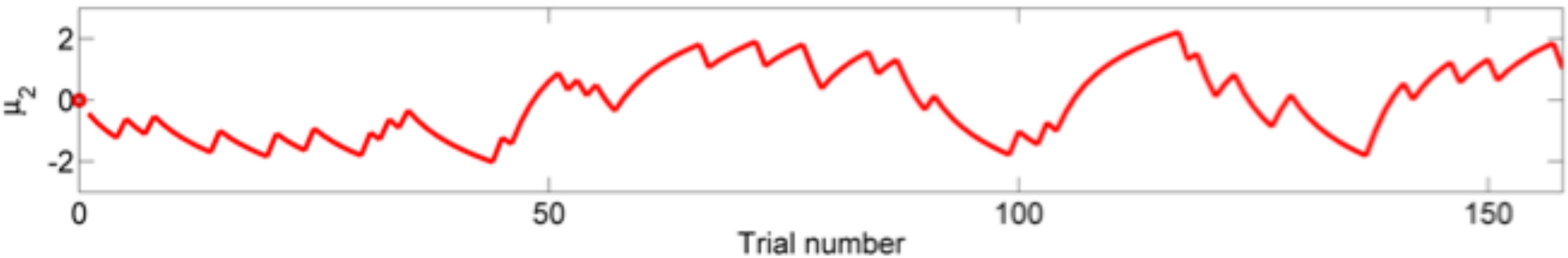
How do we construct regressors that correspond to cognitive processes and use them in SPM?

2. Estimated subject-by-subject model parameters:
   - Model Inversion:

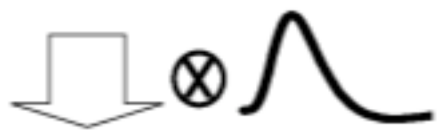
```
runnning model/param combination 4 of 546
Irregular trials: none
Ignored trials: none
Irregular trials: none

Optimizing...

Calculating the negative free energy...

Results:
     mu2_0: 1.0665
     sa2_0: 1.4966
     mu3_0: 1
     sa3_0: 1
        ka: 0
        om: -10
        th: 1.0000e-18
         p: [1.0665 1.4966 1 1 0 -10 1.0000e-18]
    ptrans: [1.0665 0.4032 1 0 -22.3327 -10 -34.5388]

       ze1: 0.8816
       ze2: 48.0000
         p: [0.8816 48.0000]
    ptrans: [2.0073 3.8712]

Negative free energy F: -82.9603
```

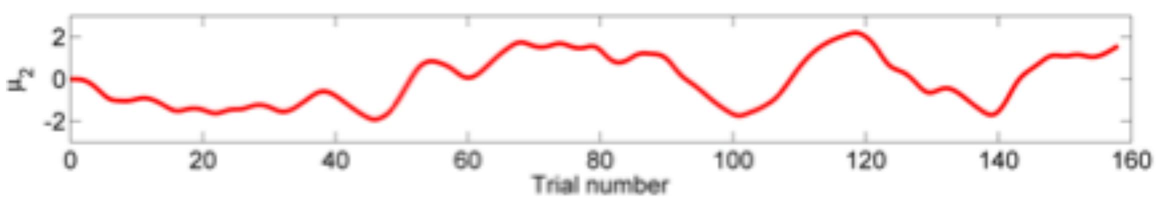
How do we construct regressors that correspond to cognitive processes and use them in SPM?

3. Generate model-based time-series:



3. Convolve them with HRF:

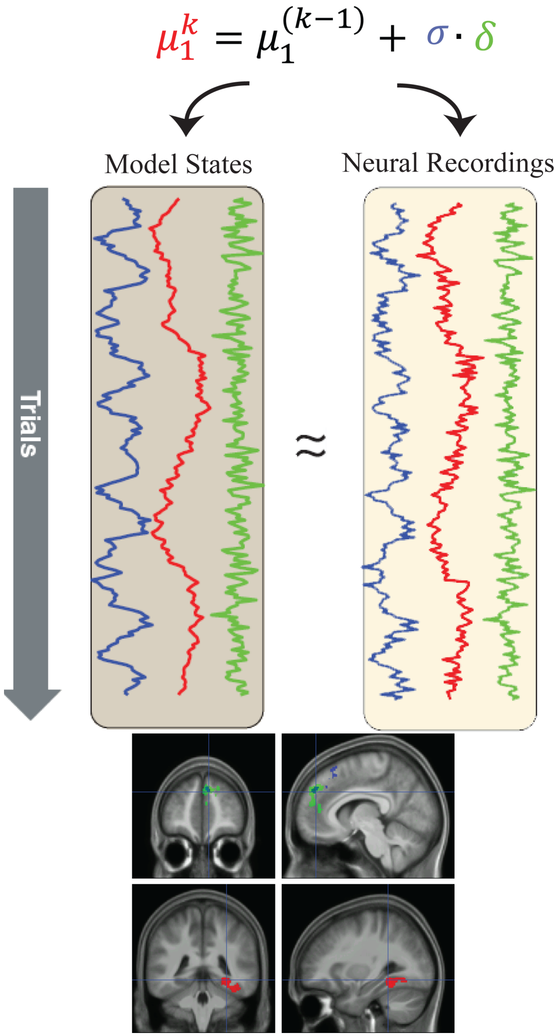




Adapted from O'Doherty et al., 2007

How do we construct regressors that correspond to cognitive processes and use them in SPM?

5. Construct your GLM:



Adapted from Behrens et al., 2010

Estimate: single subject

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6. First-level analysis:
   - Load your regressors:

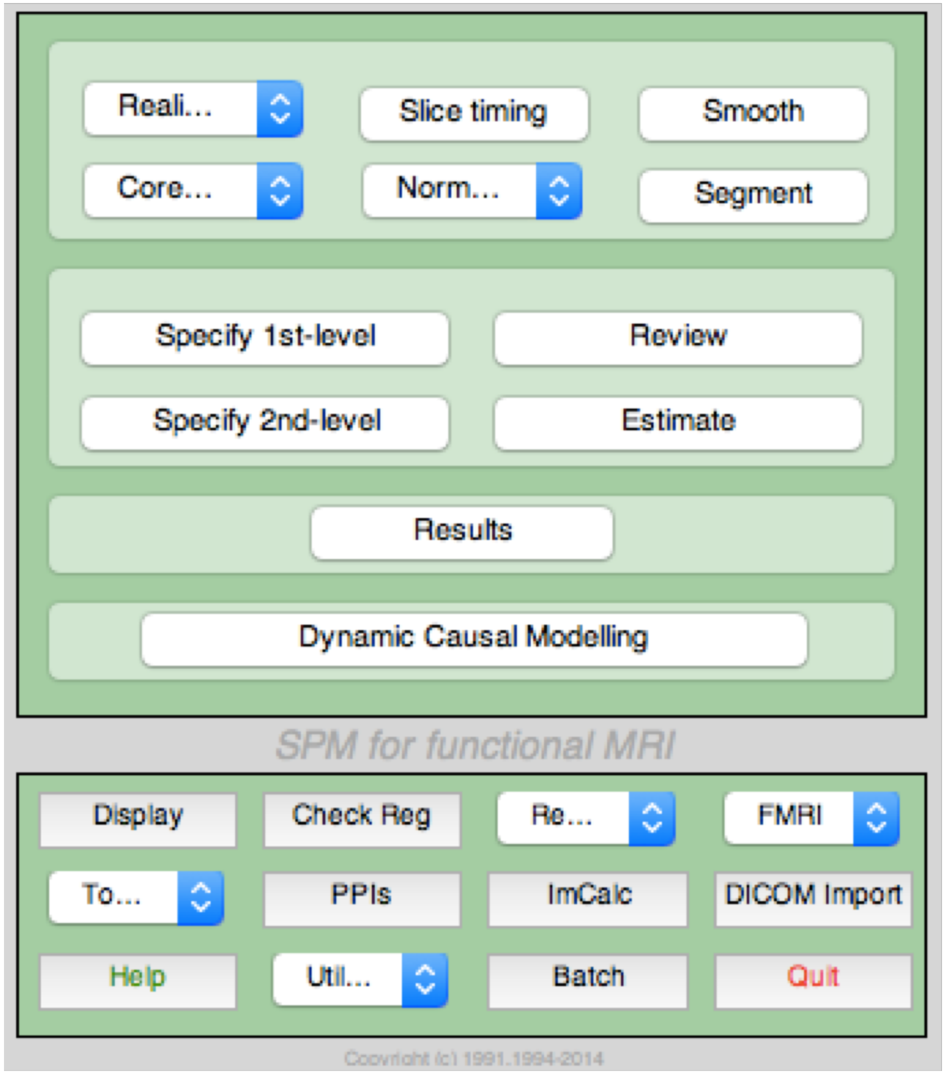
```
reg1 =

    [1x189 double]
    [1x189 double]
    [1x189 double]
```

mu1hat	<1x189 double>
positive_PE	<1x189 double>

Estimate: single subject

6. First-level analysis:
   - Open SPM: Specify first level analysis



Estimate: single subject

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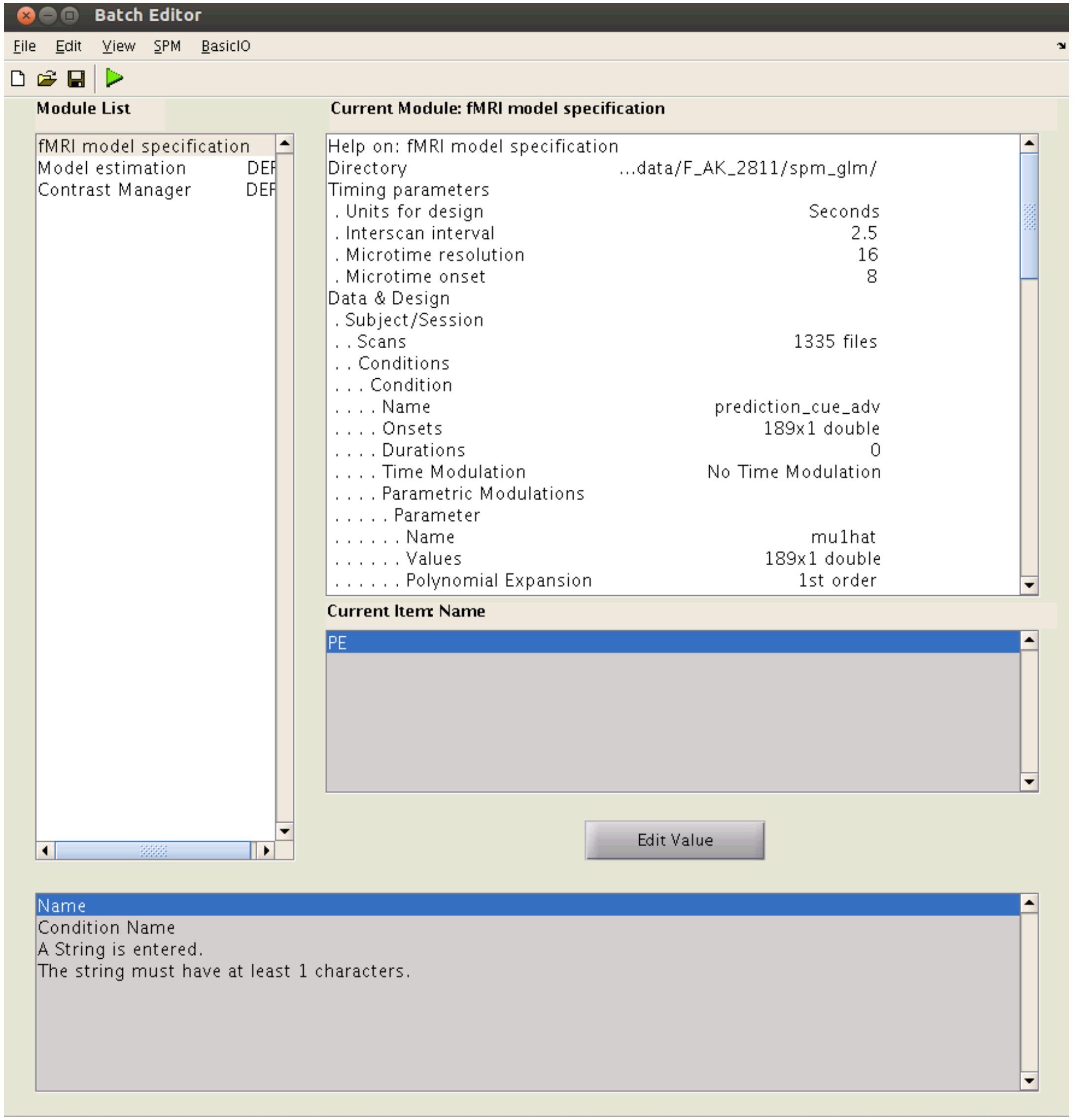
6. First-level analysis:
   - Load Design matrix into Batch editor



Estimate: single subject

6. First-level analysis:
   - Examine results:
     - PE