Computational neuroimaging (model-based fMRI)

Birte Toussaint

Translational Neuromodeling Unit

Universität Zürich[UZH]

ETH Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Methods & Models for fMRI Analysis
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With thanks to Andreea Diaconescu for lecture structure and images, and Klaas Enno Stephan for slides

Why computational neuroimaging?

- Why neuroimaging/ fMRI?
  → Measure brain activity

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- So far: “conventional” analyses
  → What can we learn from these?

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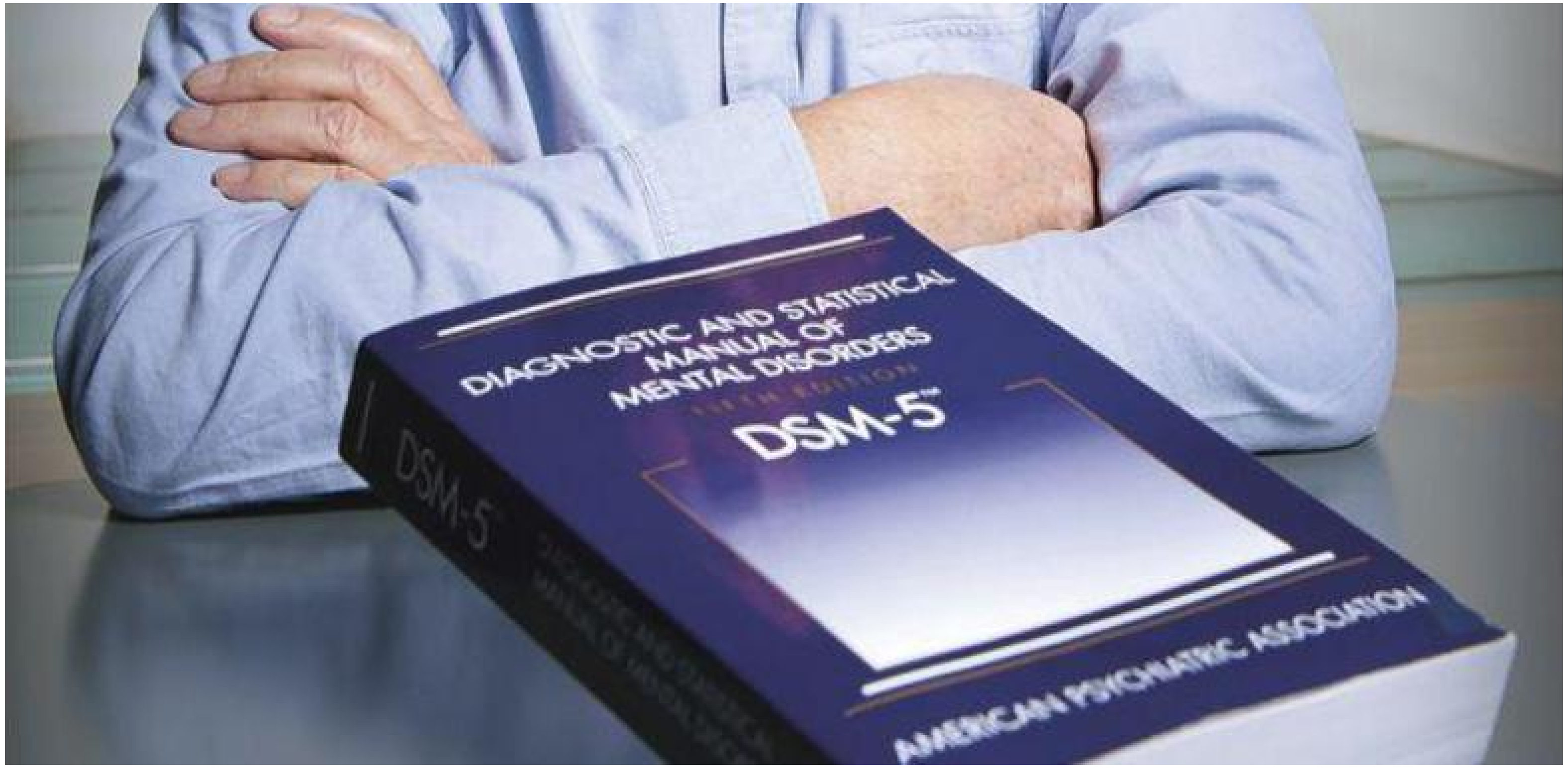
- We want to know more!

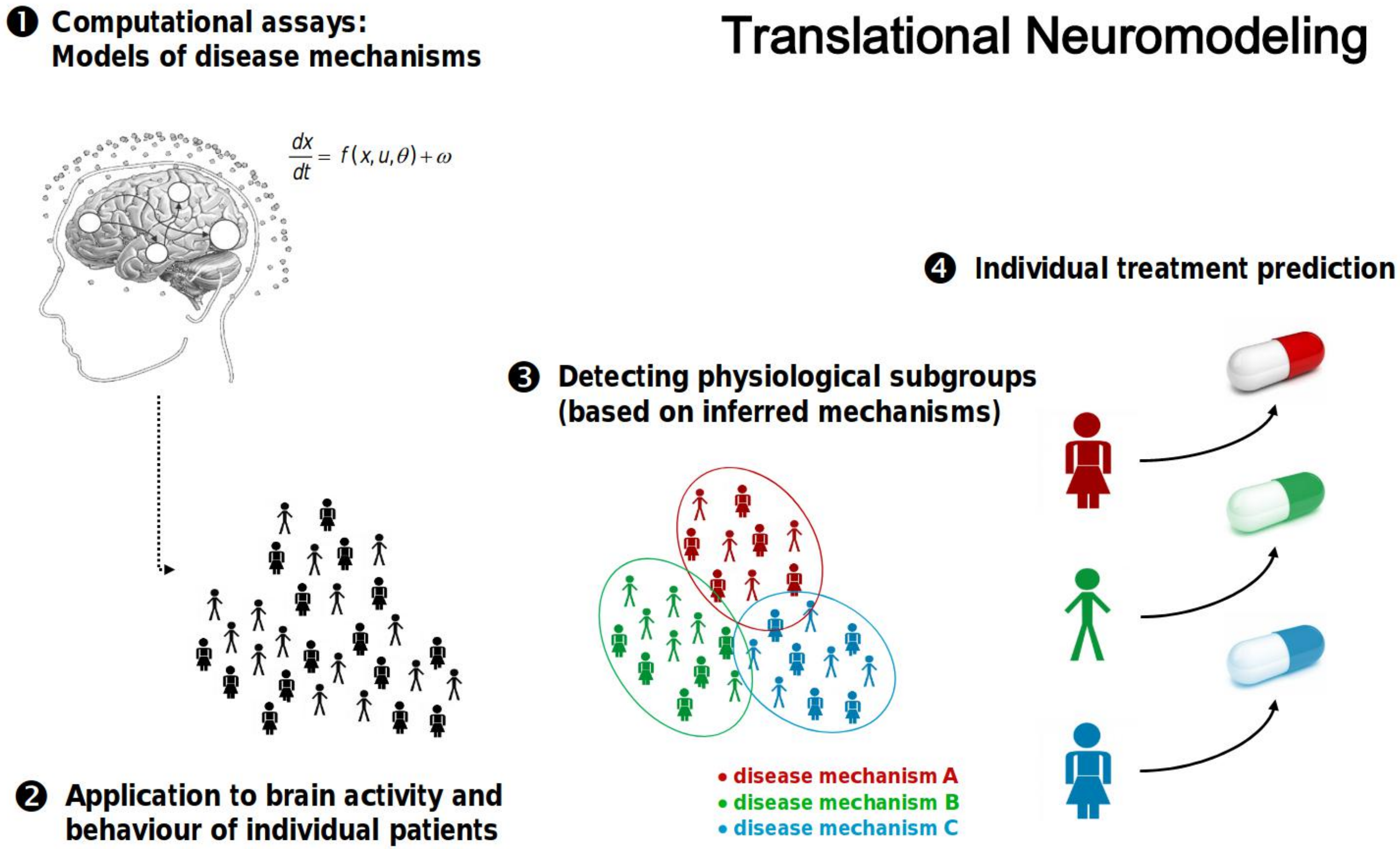
Why computational neuroimaging?

- Why neuroimaging/ fMRI?
  - → Measure brain activity
- So far: “conventional” analyses
  - → What can we learn from these?
- We want to know more!
  - → effective connectivity
  - → neural mechanisms
  - → “computational assays”

Lecture 2 recap:
Diagnostic classification in psychiatry

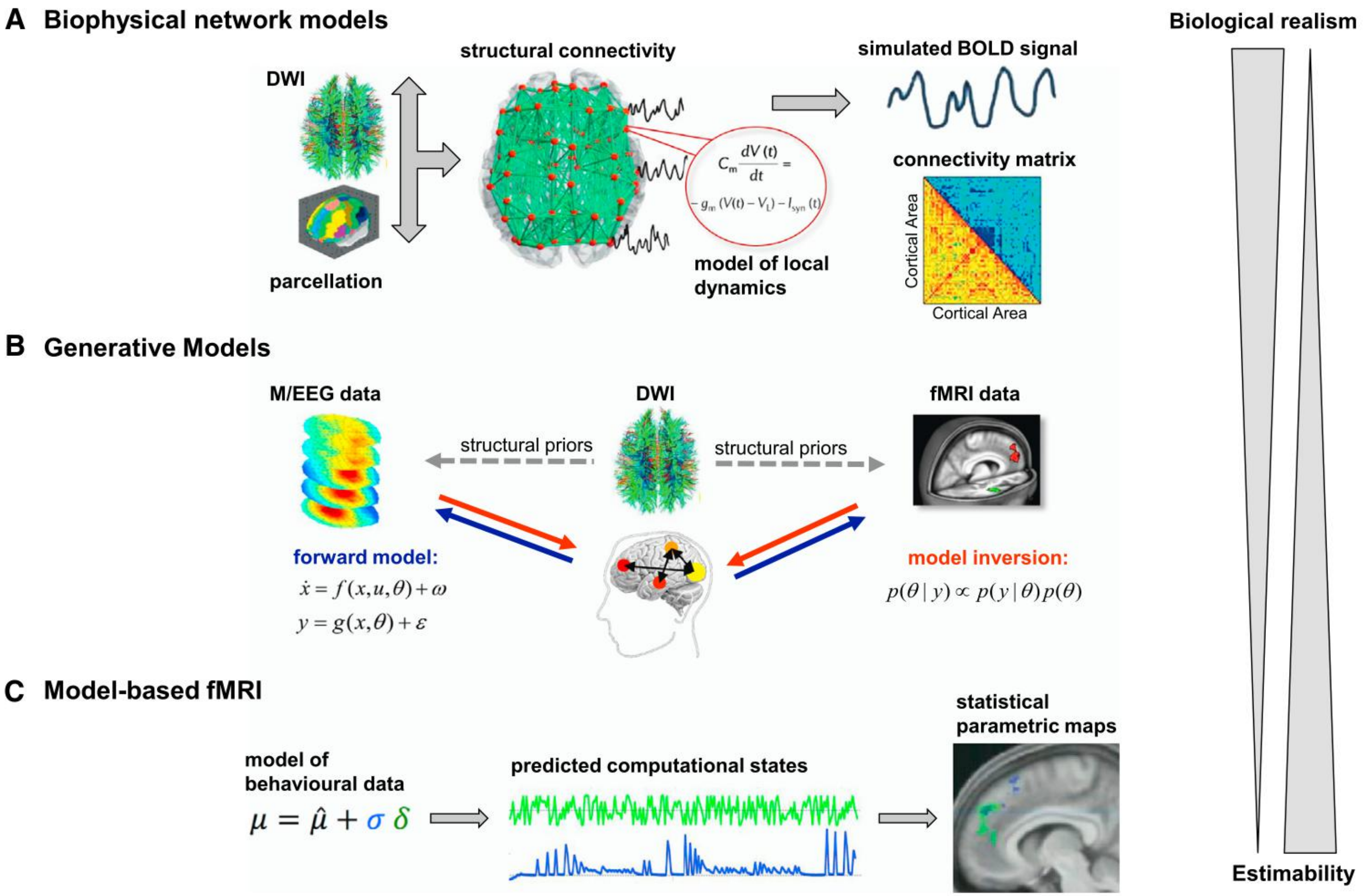


Lecture 2 recap:
Computational psychiatry



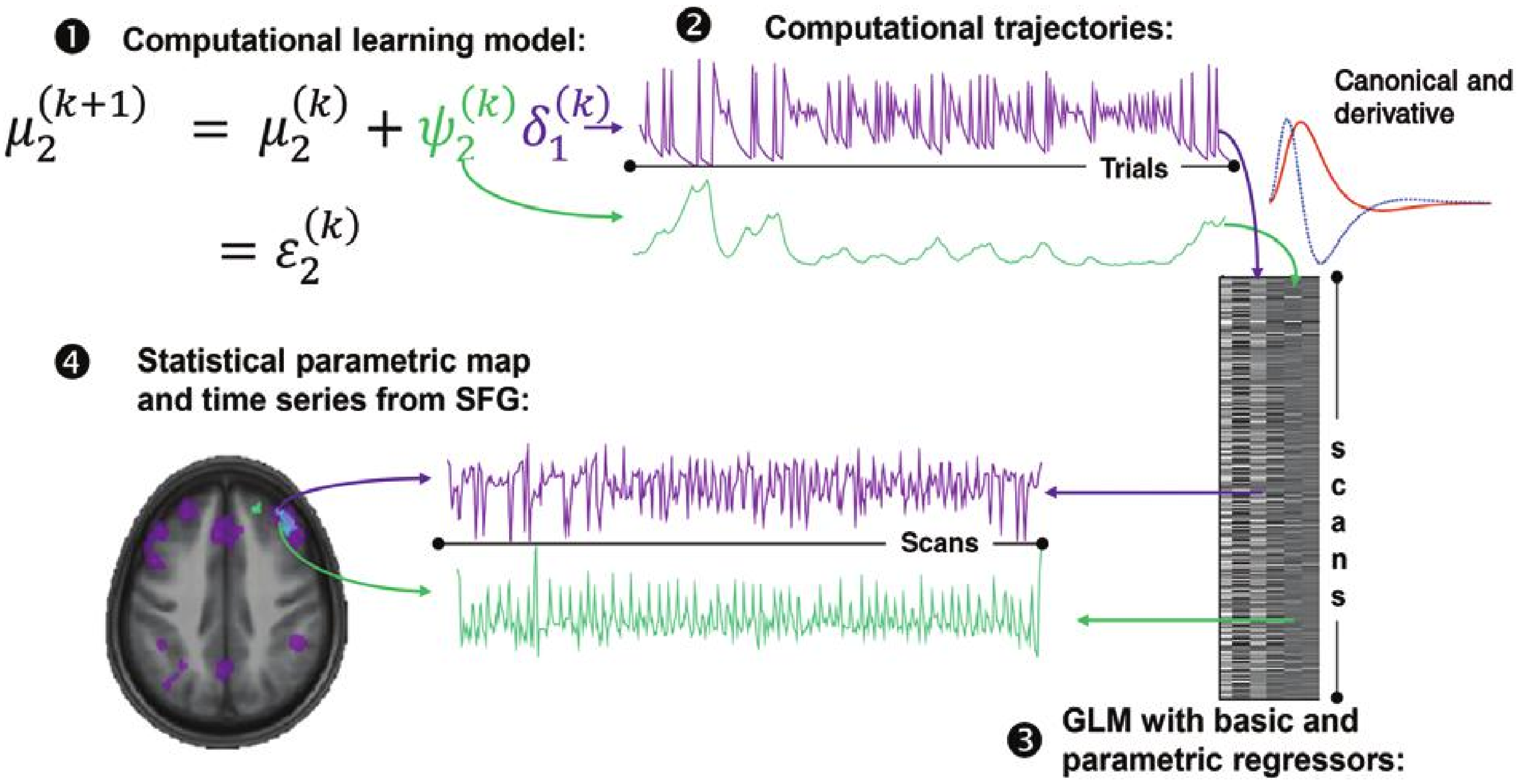
Stephan et al., 2015, *Neuron*

Computational neuroimaging examples



Stephan et al., 2015, *Neuron*

Model-based fMRI



Iglesias et al., 2017, *WIREs Cogn Sci*

Advantages of computational neuroimaging

Computational neuroimaging allows us to:

- **Infer** computational mechanisms underlying brain function
- **Localise** these mechanisms
- **Compare** different models

The “explanatory gap”

Biological

- Molecular
- Neurochemical

Cognitive

- Computational
- “Cognitive/ computational phenotyping”

Phenomenological

- Performance accuracy
- Reaction time
- Choices, preferences

The "explanatory gap"

Biological	Cognitive	Phenomenological
		
• Molecular • Neurochemical	• Computational • "Cognitive/ computational phenotyping"	• Performance accuracy • Reaction time • Choices, preferences

Computational models

Three levels of analysis

David Marr

- **Computational level**
  - What does the system do (and why)?
- **Algorithmic level**
  - How does the system do what it does? What representations does it use?
- **Implementational level**
  - How is the system physically realised?

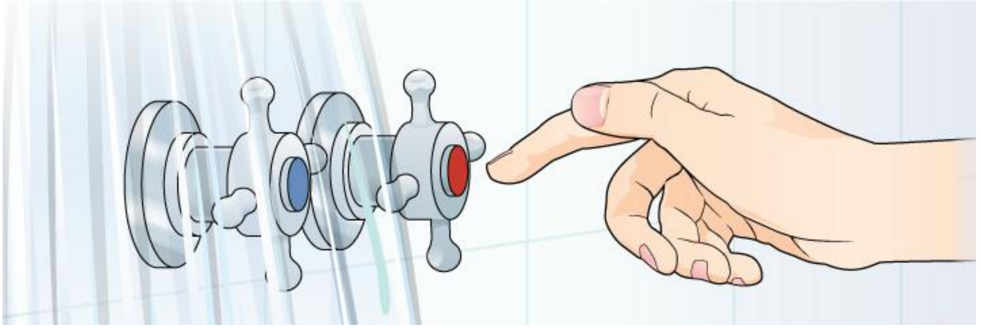
Using model-based fMRI to analyse brain function

- **Example: How does the human brain perceive temperature?**

1. Computational level

2. Algorithmic level

3. Implementational level



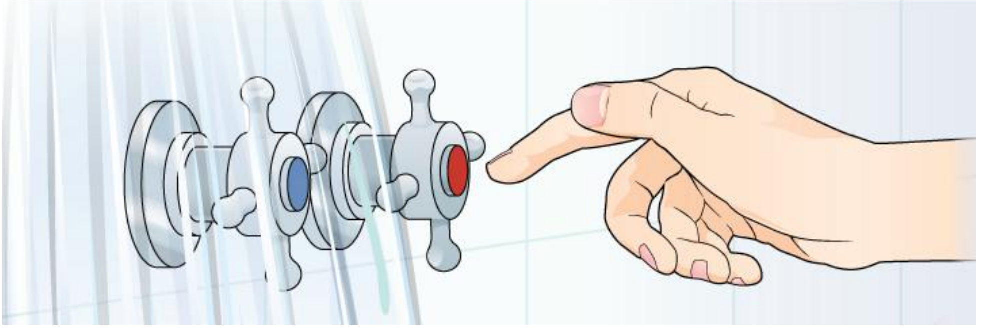
Using model-based fMRI to analyse brain function

- **Example: How does the human brain perceive temperature?**

  1. Computational level

  2. Algorithmic level

  3. Implementational level

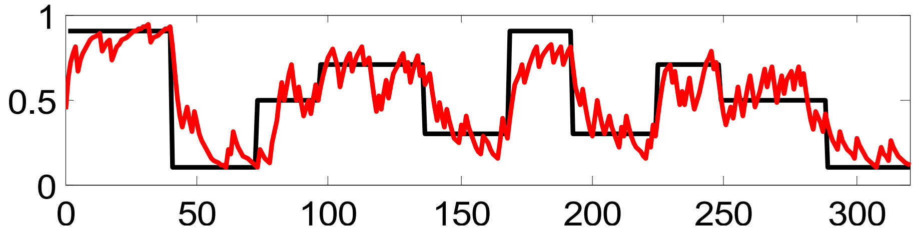


- **But first: why use model-based fMRI to answer this question?**

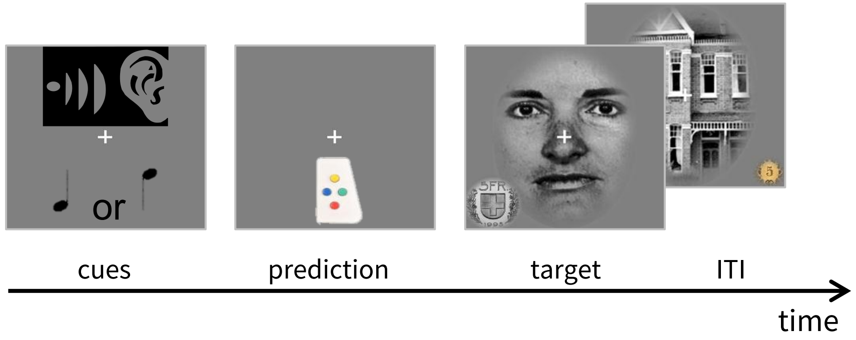
Using model-based fMRI to analyse brain function

- **3 ingredients:**

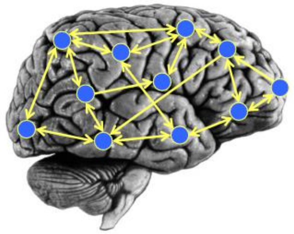
  1. Computational model



  2. Experimental paradigm



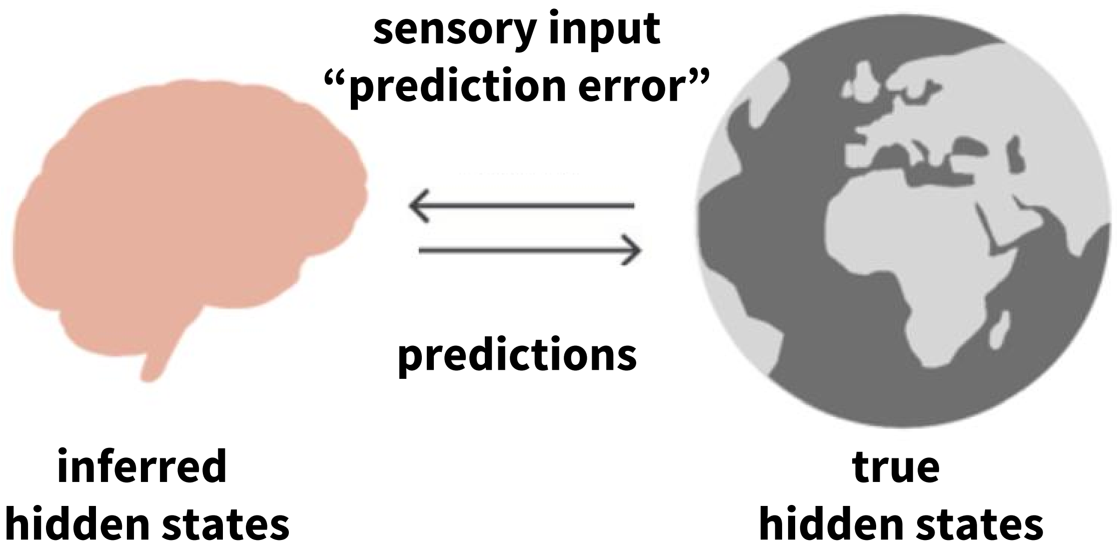
  3. Model-based fMRI analysis



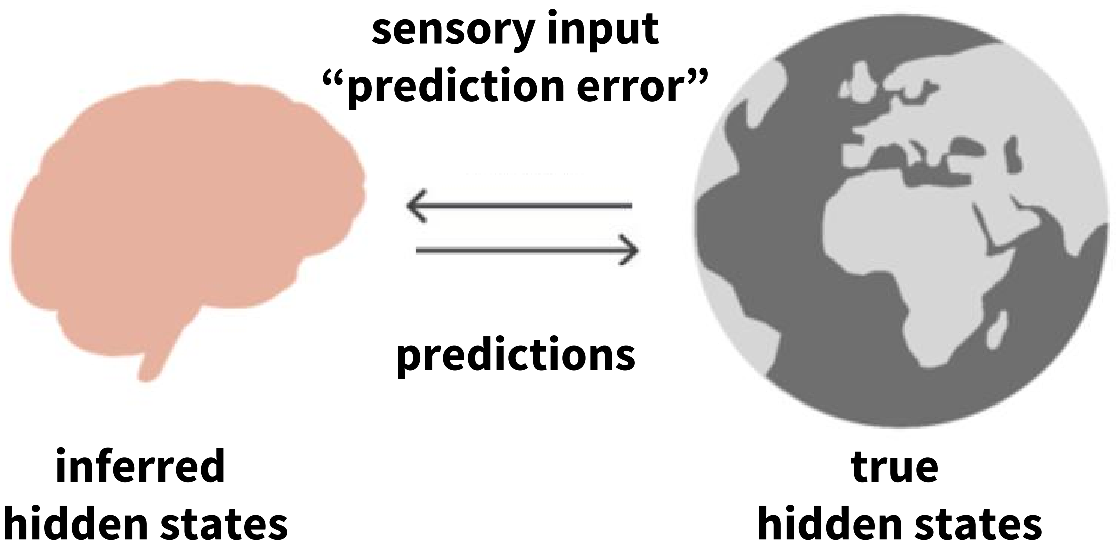
1. Computational level

- What does the brain do (and why)?

Bayesian Brain hypothesis

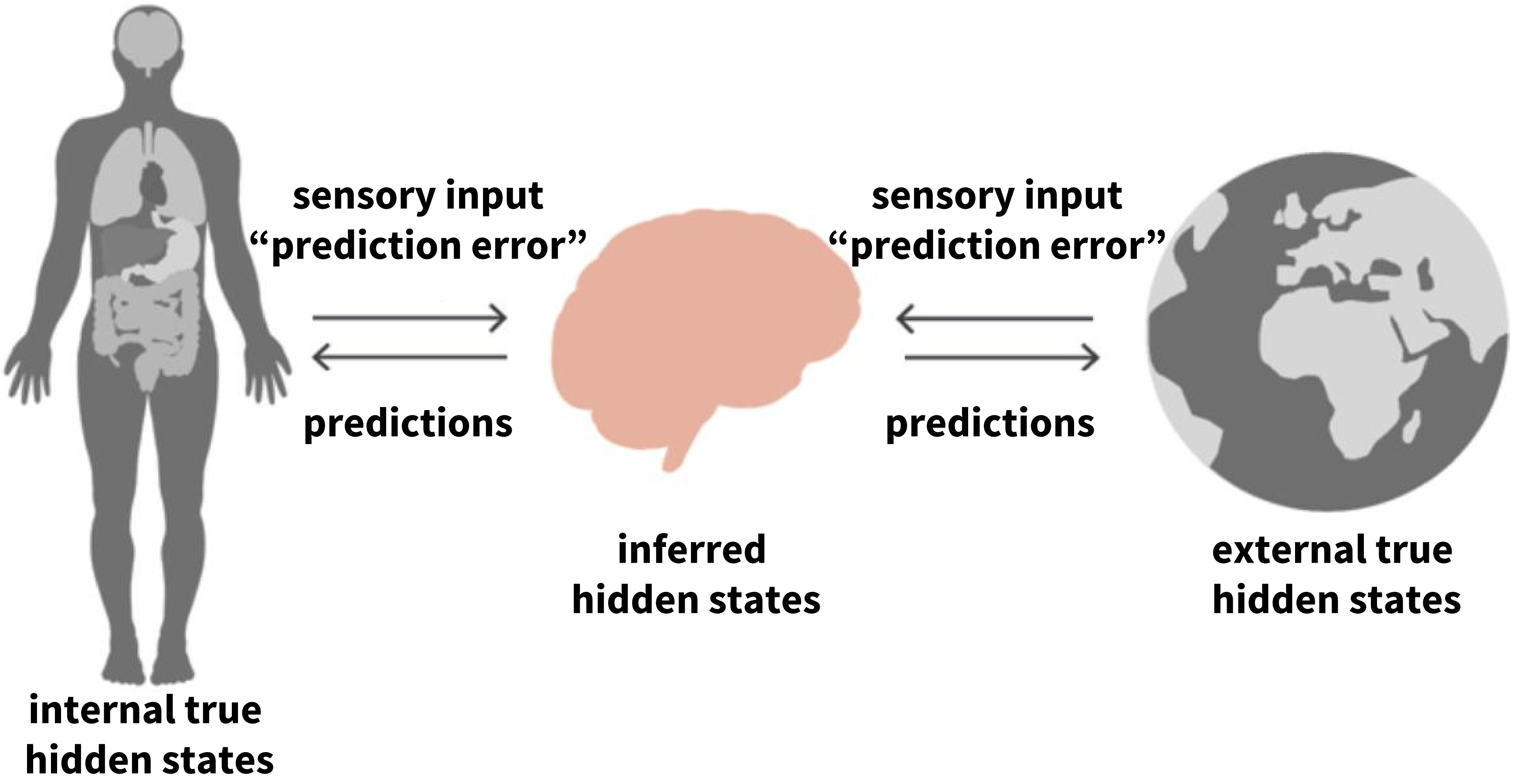


Bayesian Brain hypothesis



- The brain maintains a model of its environment

Bayesian Brain hypothesis

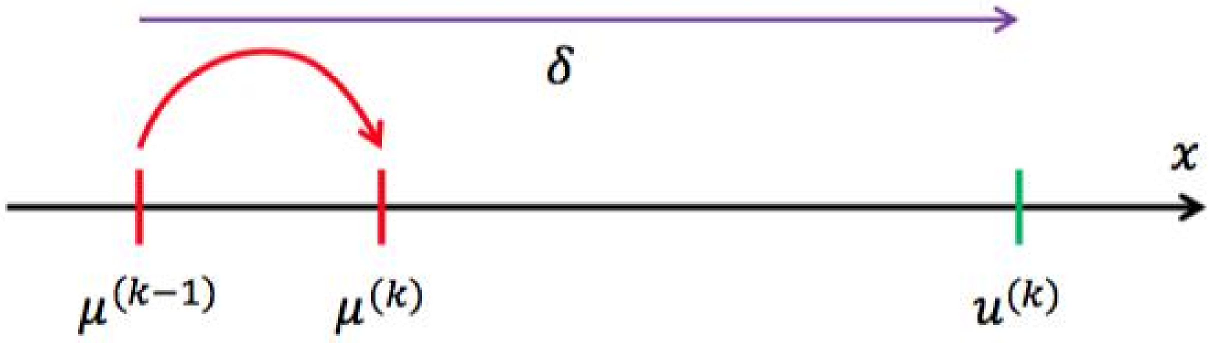


Example of a simple learning model

- Rescorla-Wagner

$$\mu^{(k)} = \mu^{(k-1)} + \alpha\overbrace{\boxed{\left(u^{(k)} - \mu^{(k-1)}\right)}}^{\text{prediction error}}$$

inferred states new input



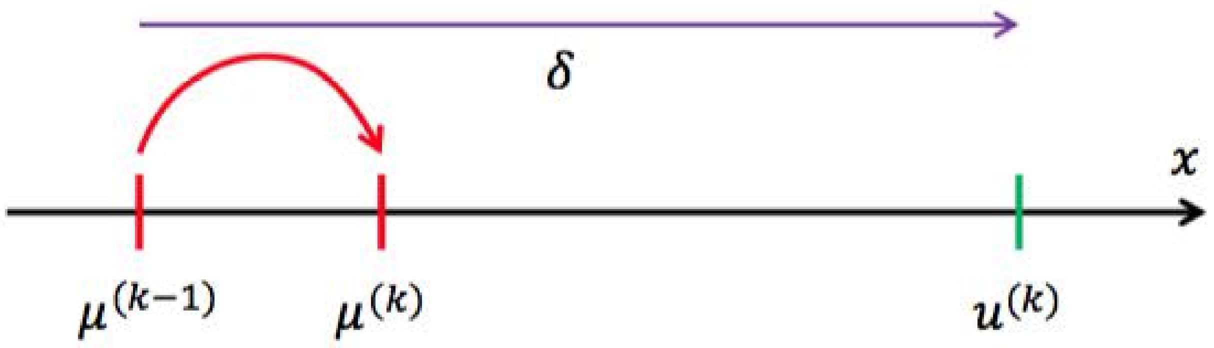
Example of a simple learning model

- Rescorla-Wagner
  - updates via fixed learning rate

learning rate

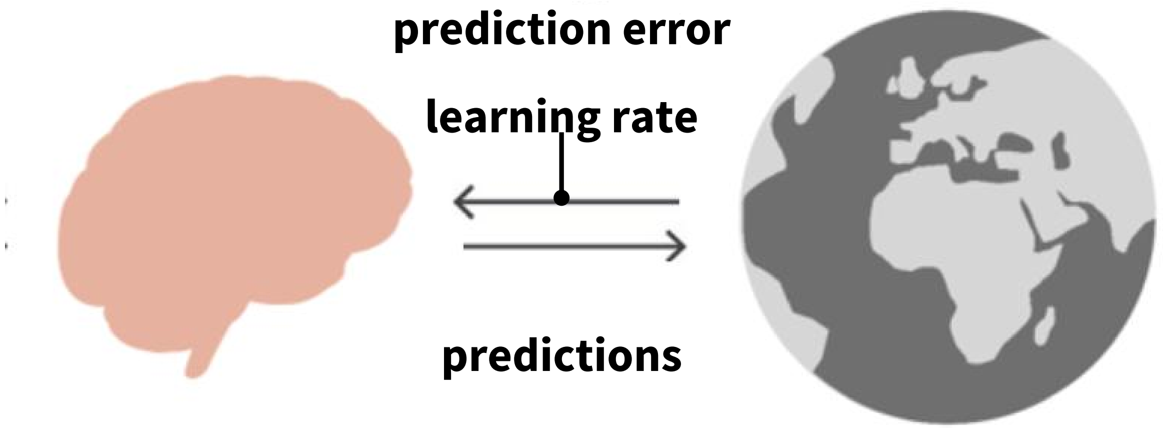
$$\Delta\mu^{(k)} \propto \boldsymbol{\alpha}\delta$$

belief update



Computational variables

- Rescorla-Wagner



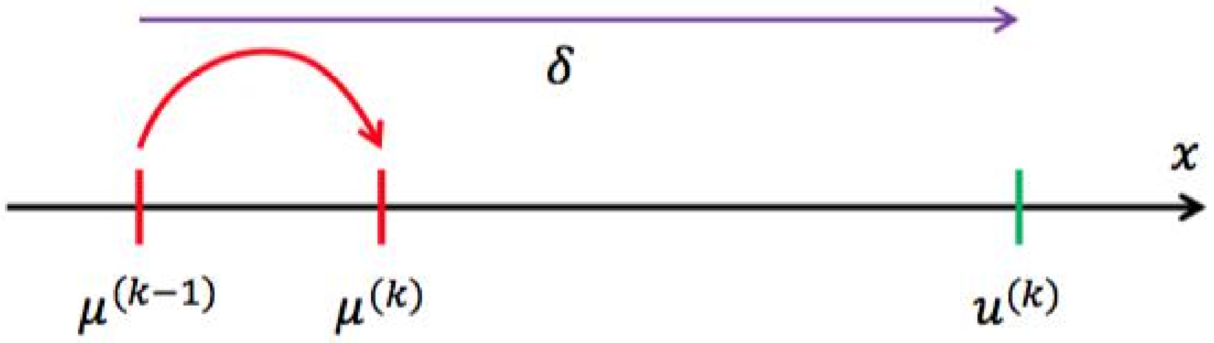
Example of a hierarchical learning model

- Hierarchical Gaussian Filter
  - beliefs: probability distributions

precision weight

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

belief update



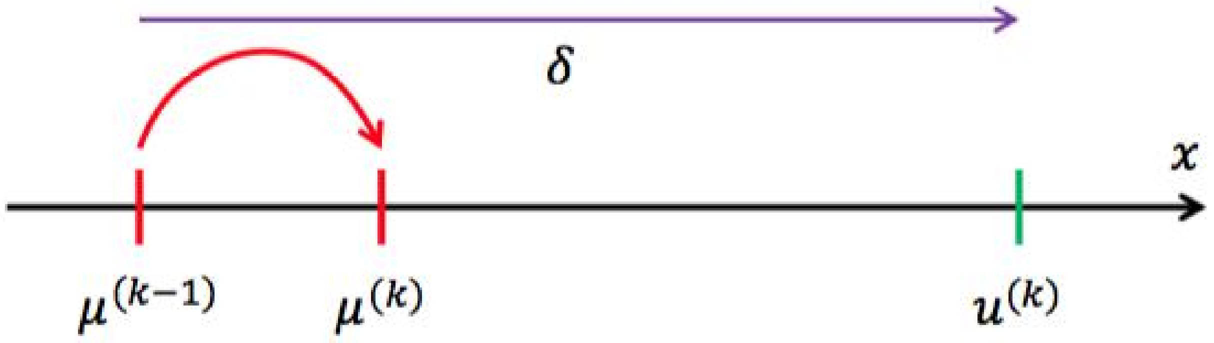
Example of a hierarchical learning model

- Hierarchical Gaussian Filter
  - updates via Bayes' Rule

precision weight

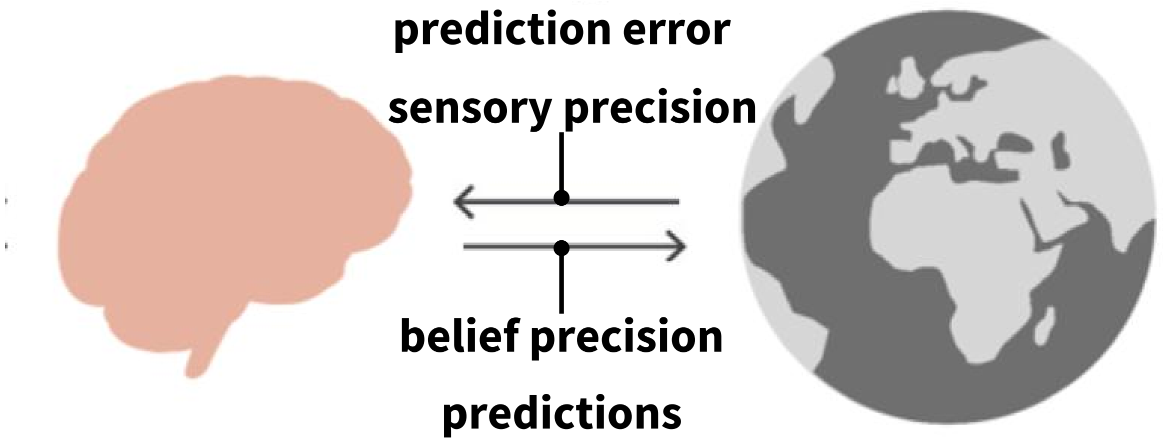
$$\Delta\mu^{(k)} \propto \frac{\hat{\pi}_{i-1}^{(k)}}{\pi_i^{(k)}}\delta$$

belief update $= \dfrac{\text{how much we're learning here}}{\text{how much we already know}}$



Computational variables

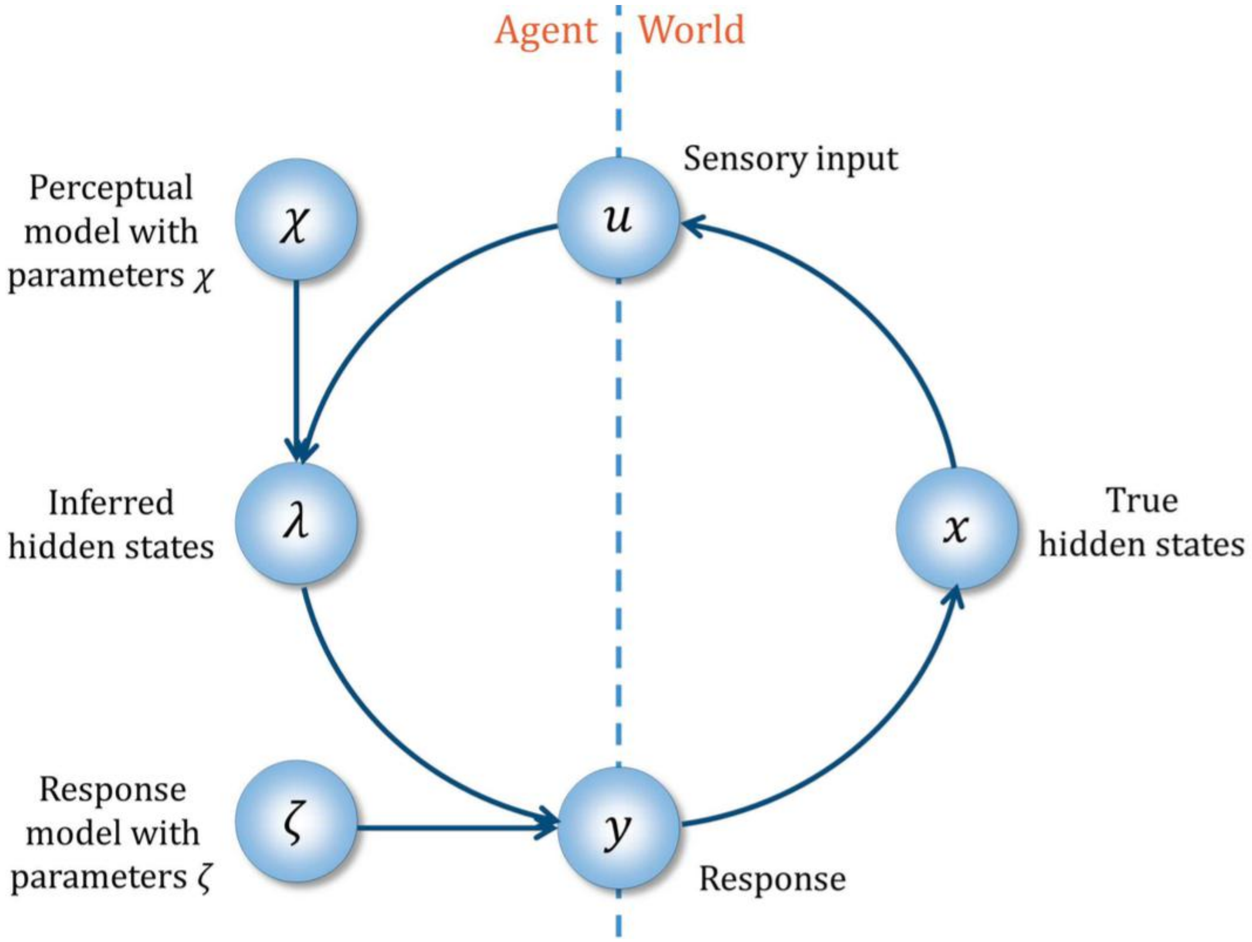
- Hierarchical Gaussian Filter



2. Algorithmic level

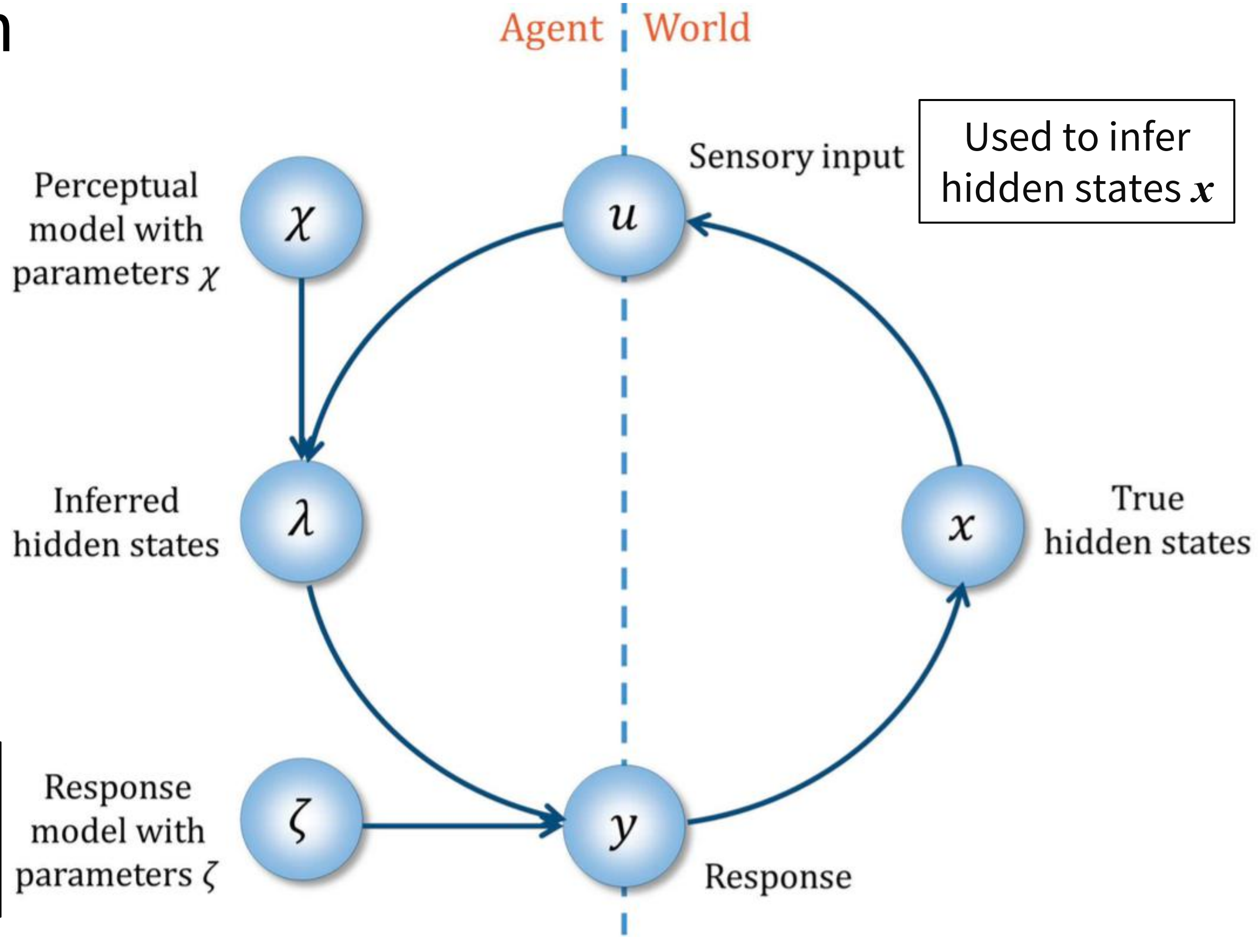
- How does the brain update its model?

A modelling framework



A modelling framework

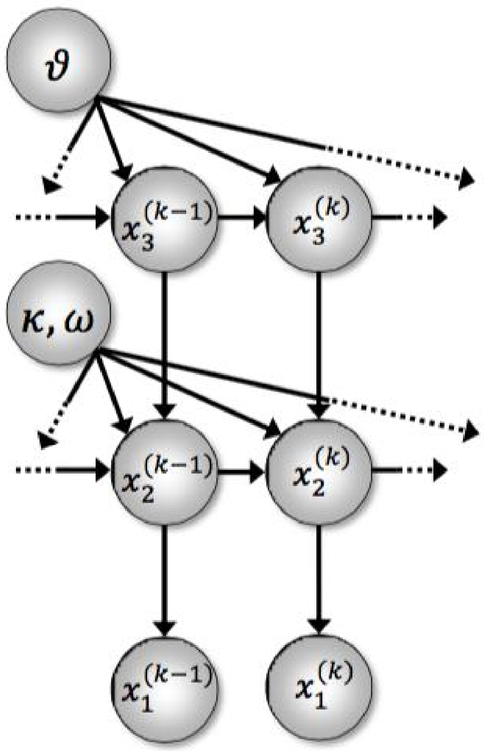
- Agent = brain

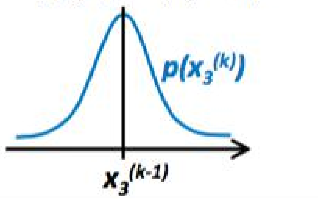
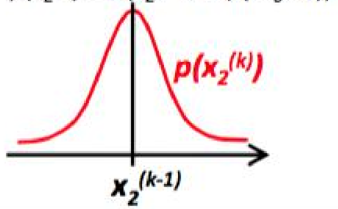
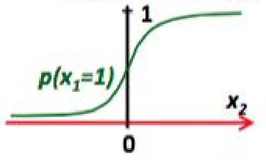


Used to infer hidden states $\boldsymbol{x}$

How the brain makes decisions based on its perceptual inference

Perceptual model:
The Hierarchical Gaussian Filter



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

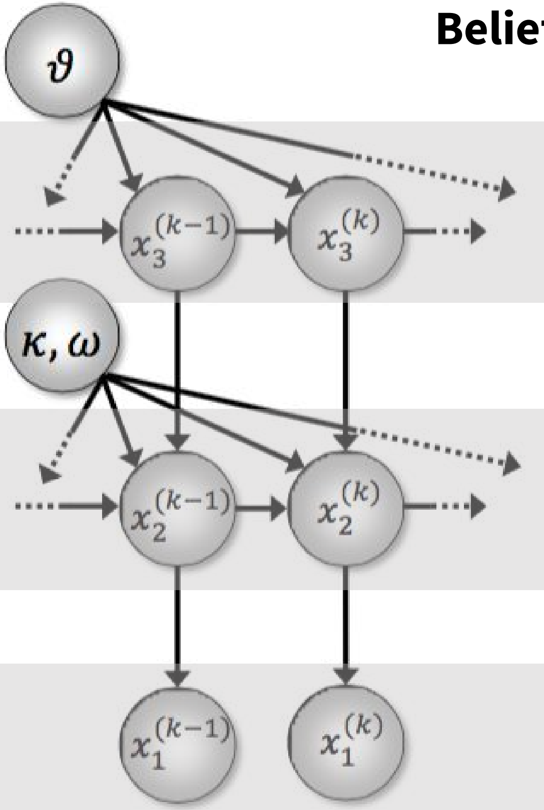
Mathys et al., *Front Hum Neurosci*, 2011

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

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

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

Perceptual model:
The Hierarchical Gaussian Filter



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

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

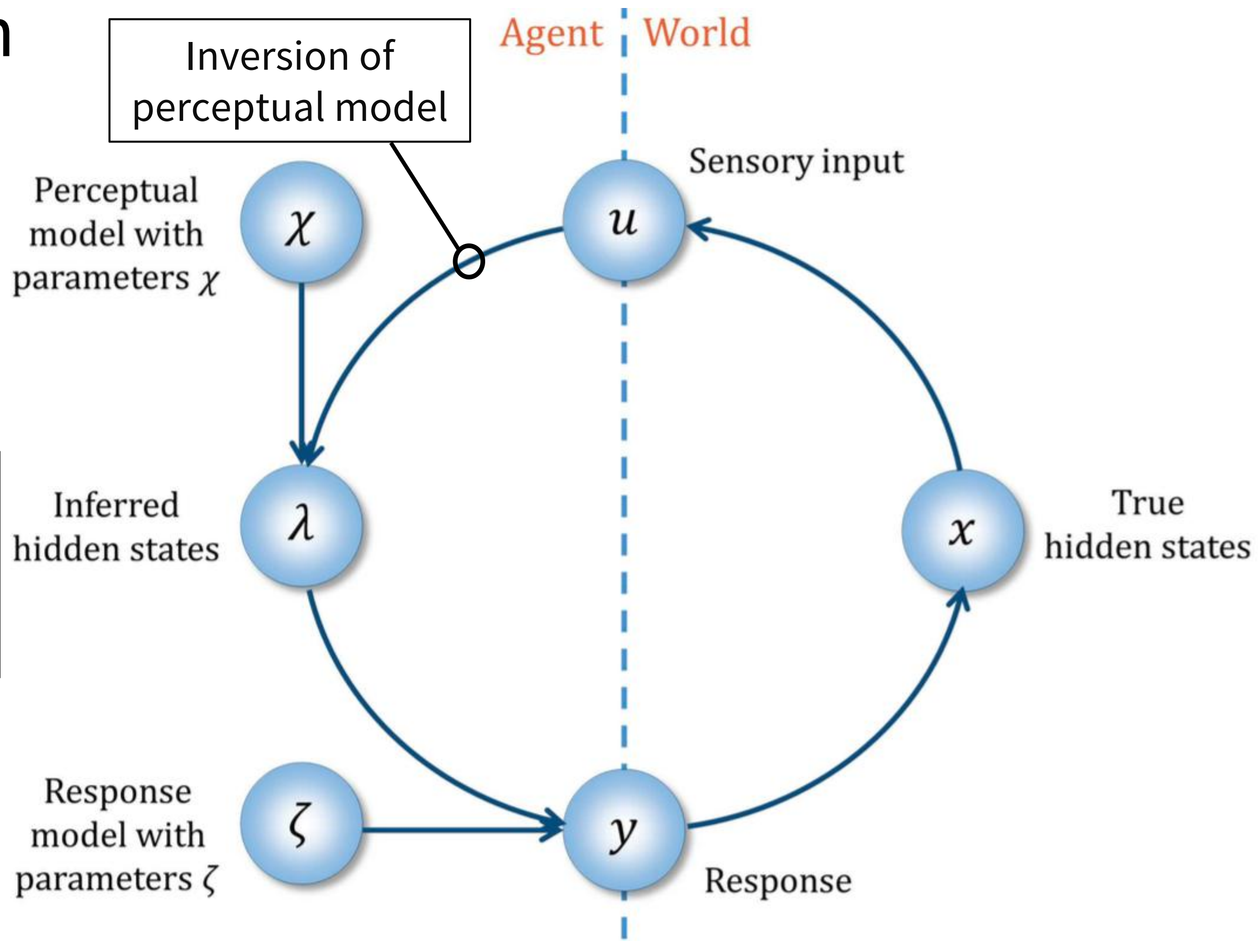
A modelling framework

- Agent = brain

Time-independent parameters $\chi = \{\kappa, \omega, \theta\}$

Beliefs encoded by probability distributions: $\lambda = \{\mu, \sigma\}$

Inversion of perceptual model



HGF belief updates

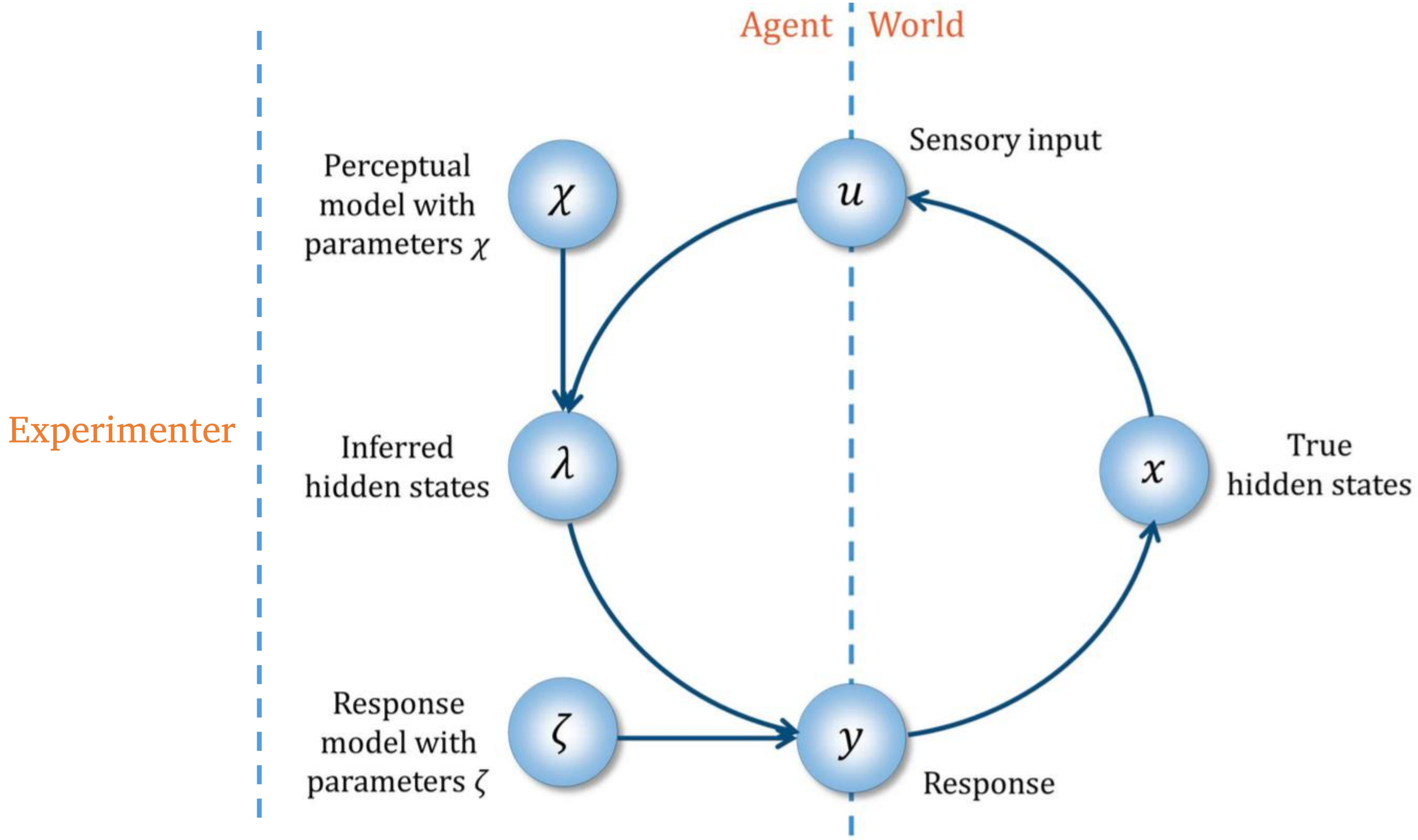
Update equations for expectations

Level 3	$\Delta\mu_3 = \sigma_3 \cdot \frac{\kappa}{2} \cdot w_2 \cdot \delta_2$	with	$\Delta\mu_3 = \mu_3^{(k)} - \mu_3^{(k-1)}$ $\sigma_3 = \sigma_3^{(k)}$ $w_2 = \frac{e^{\kappa\mu_3^{(k-1)}+\omega}}{\sigma_2^{(k-1)} + e^{\kappa\mu_3^{(k-1)}+\omega}}$ $\delta_2 = \frac{\sigma_2^{(k)} + \left(\mu_2^{(k)} - \mu_2^{(k-1)}\right)^2}{\sigma_2^{(k-1)} + e^{\kappa\mu_3^{(k-1)}+\omega}} - 1$
Level 2	$\Delta\mu_2 = \sigma_2 \cdot \delta_1$	with	$\Delta\mu_2 = \mu_2^{(k)} - \mu_2^{(k-1)}$ $\sigma_2 = \sigma_2^{(k)}$ $\delta_1 = \mu_1^{(k)} - s\left(\mu_2^{(k-1)}\right)$

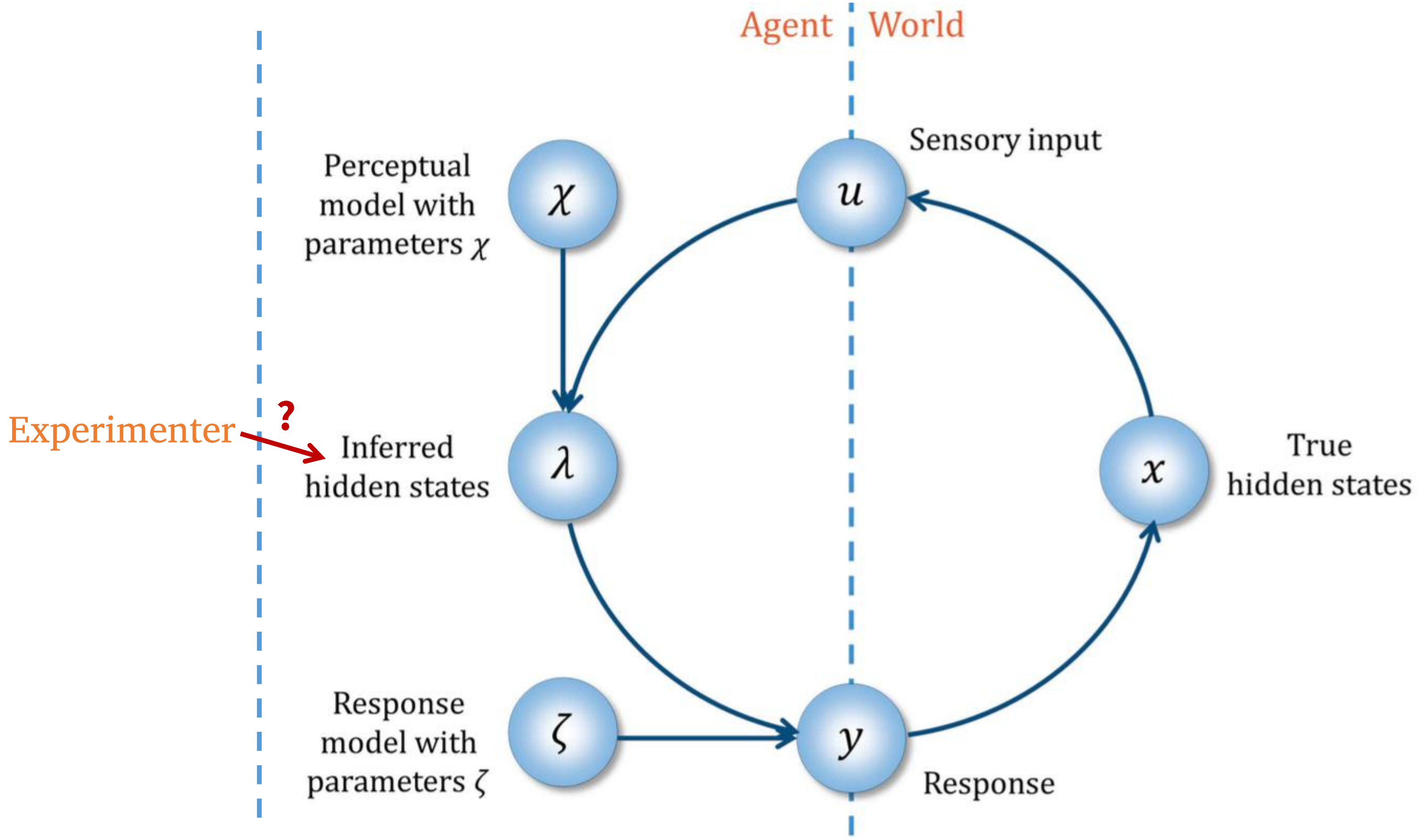
Expectation update
(Unweighted) learning rate
Weighting factor
Prediction error

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

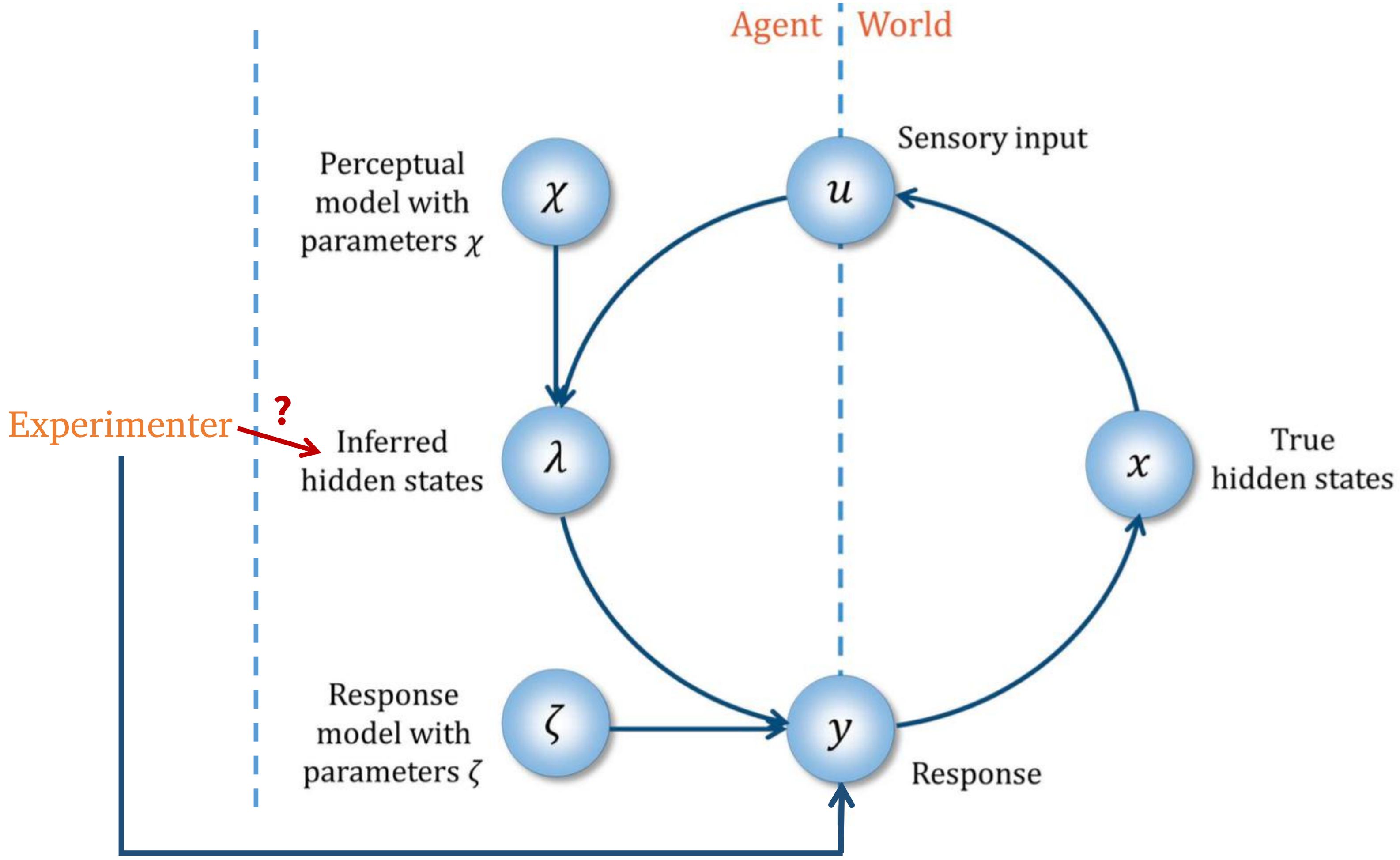
Observing the observer



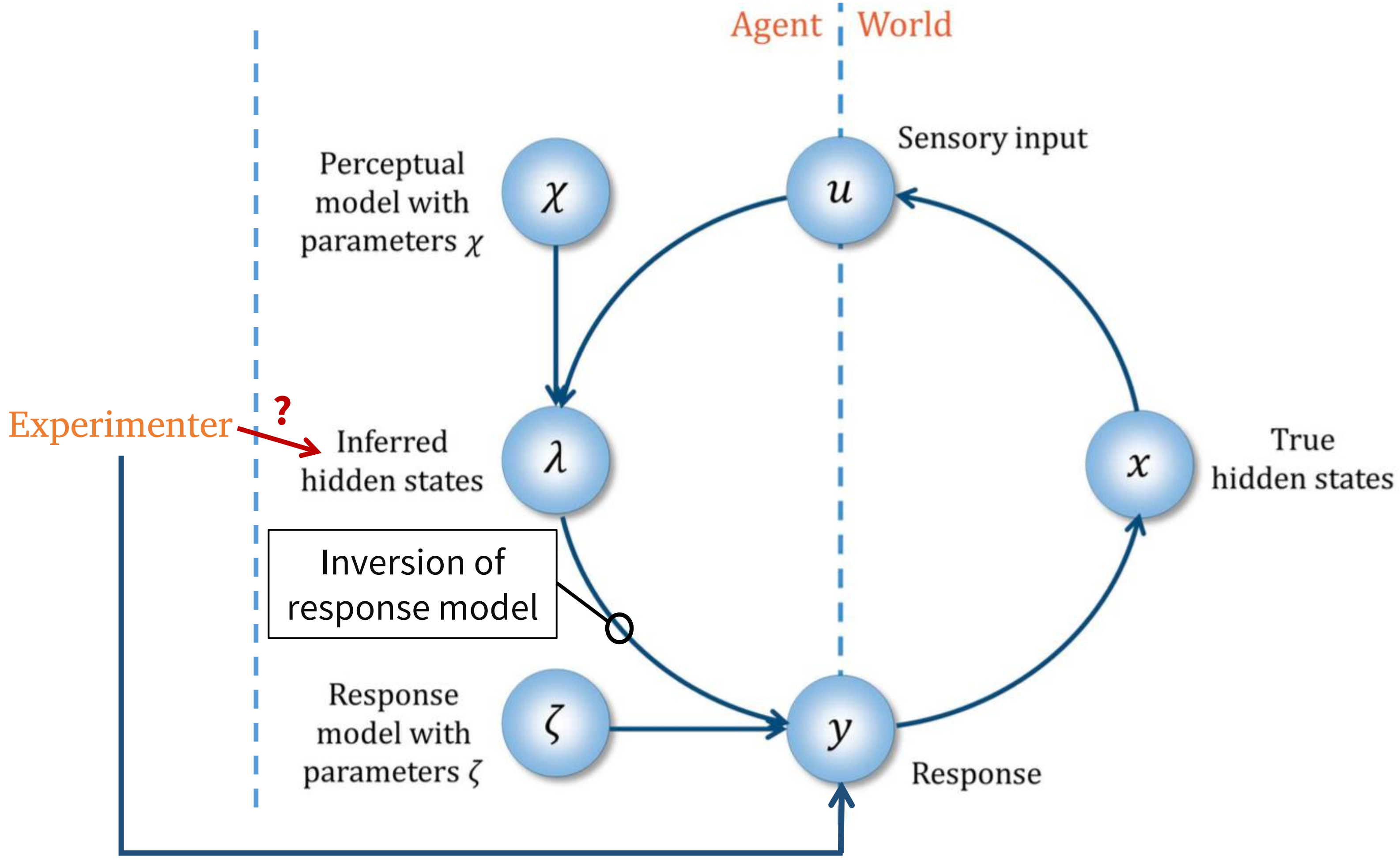
Observing the observer



Observing the observer



Observing the observer

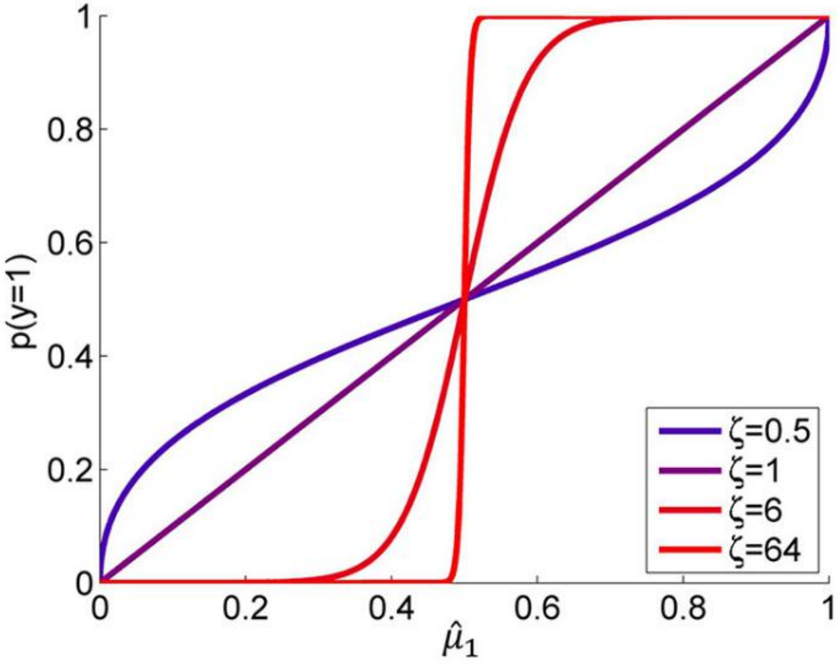


Example of a response model

- Translate beliefs into responses with a unit-square sigmoid:
  - Parameter ζ represents inverse response noise

Probability of
response "1"

(i.e., of predicting
a warm stimulus)



Prediction that next stimulus is "1"

Adapted from Mathys et al., *Front Hum Neurosci*, 2014

Estimating subject-specific parameters

- Joint distribution for observations and perceptual model parameters:

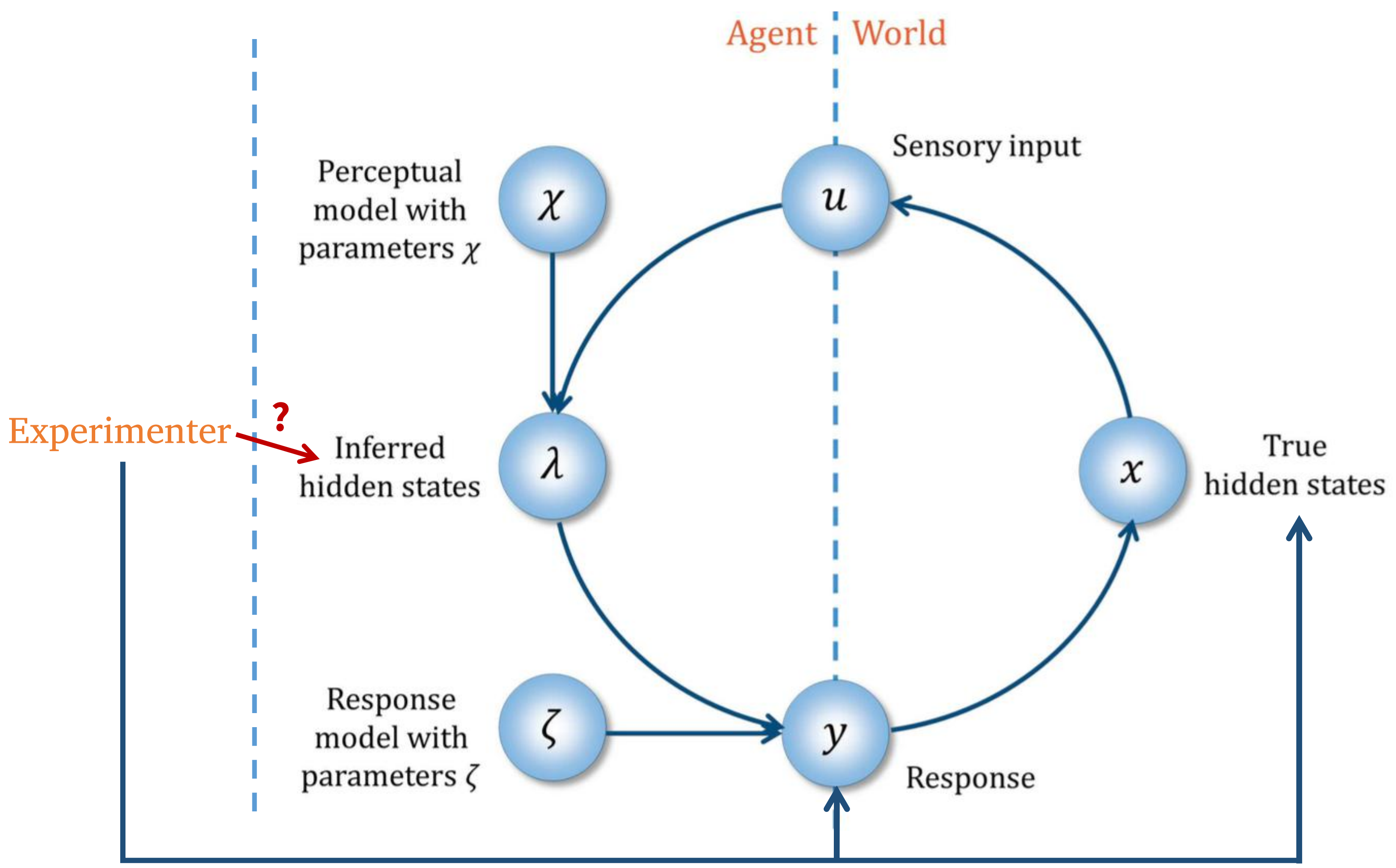
$$p(y,\chi,\lambda^{(0)},\zeta|u) = p(\chi,\lambda^{(0)},\zeta)\prod_{k=1}^{K} p(y^{(k)}|\lambda^{(k)}(\chi,\lambda^{(0)},u),\zeta)$$

where:

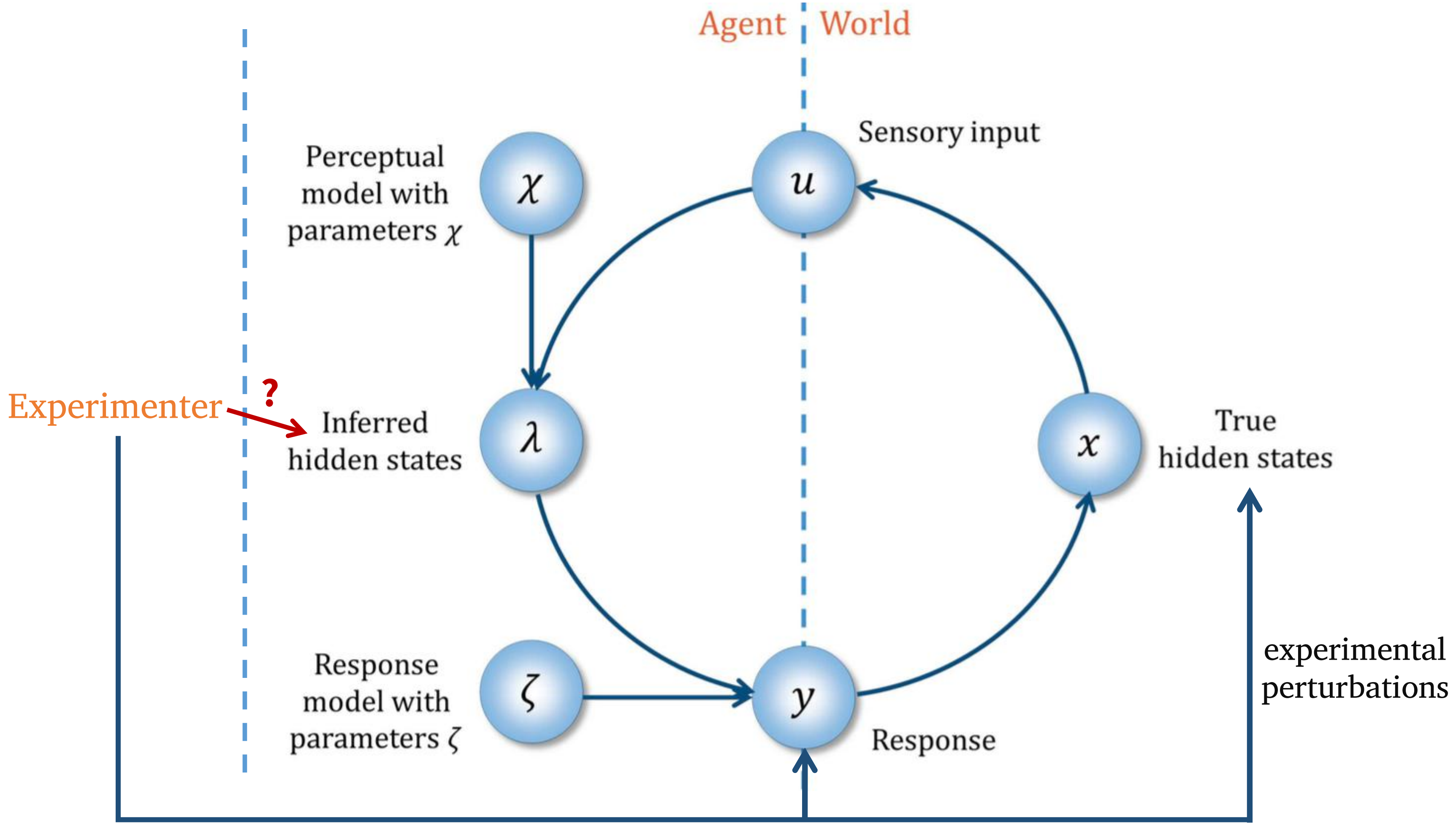
$$u \stackrel{\text{def}}{=} \{u^{(1)},\dots,u^{(K)}\}$$
$$y \stackrel{\text{def}}{=} \{y^{(1)},\dots,y^{(K)}\}$$
$$\lambda^{(k)} \stackrel{\text{def}}{=} \{\mu_1^{(1)},\pi_1^{(k)},\dots,\mu_1^{(K)},\pi_1^{(K)}\}$$

- Find maximum-a-posteriori estimate for parameters χ, $\lambda^{(0)}$, ζ

Observing the observer

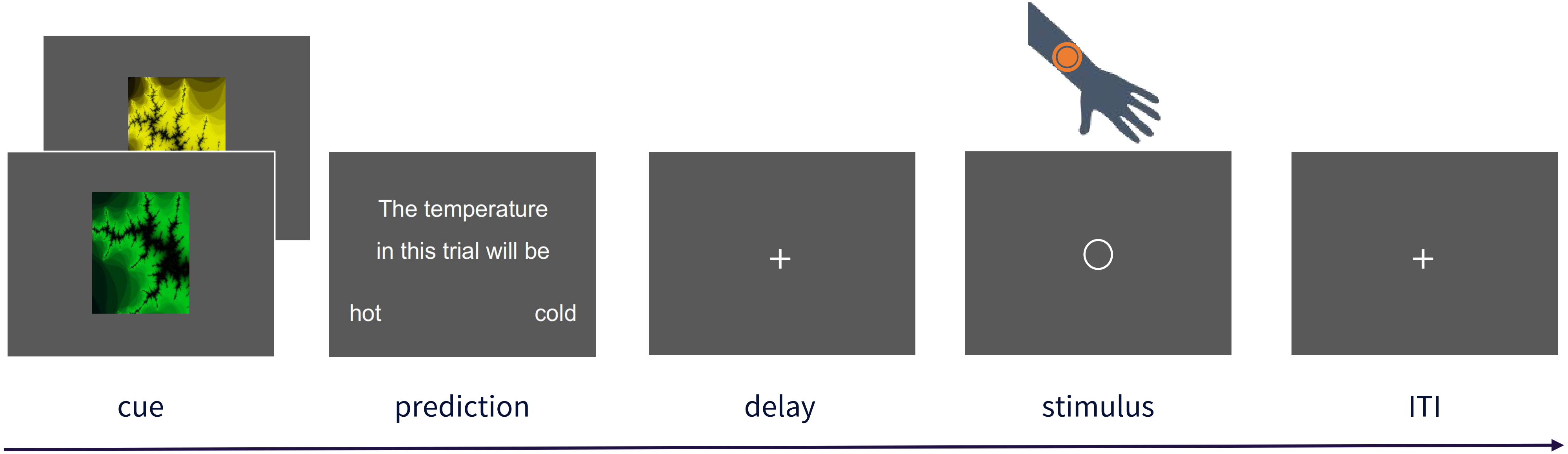


Observing the observer



Experimental paradigm

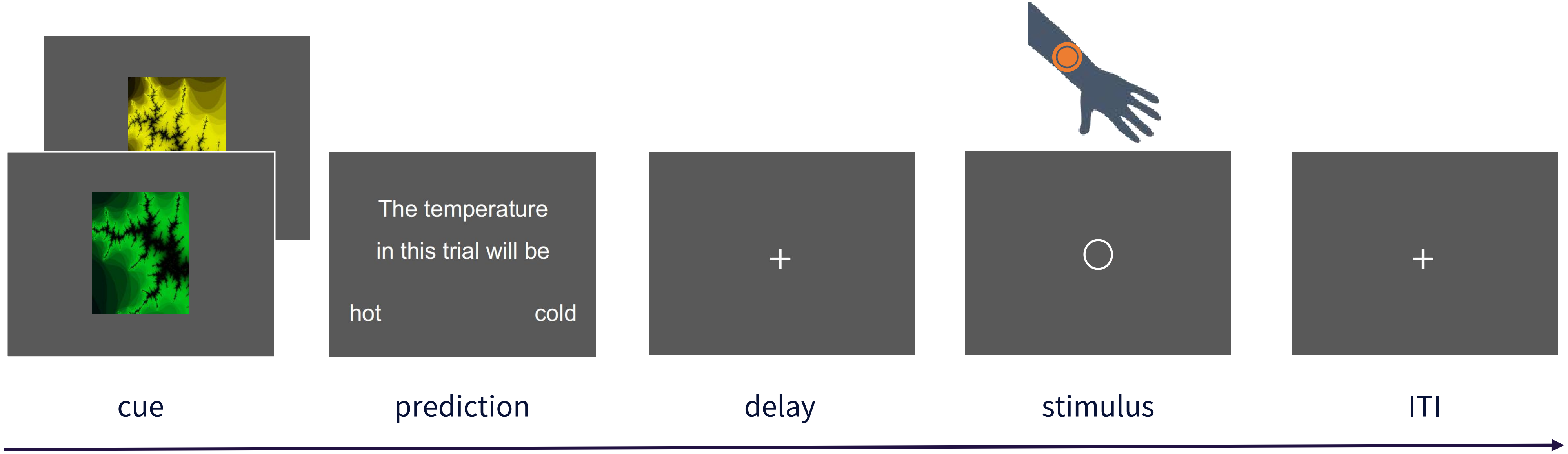
- Learning in an uncertain environment:



- $P(stimulus = hot \mid cue = green)$ **+** $P(stimulus = hot \mid cue = yellow) = 100\ \%$

Experimental paradigm

- Learning in an uncertain environment:



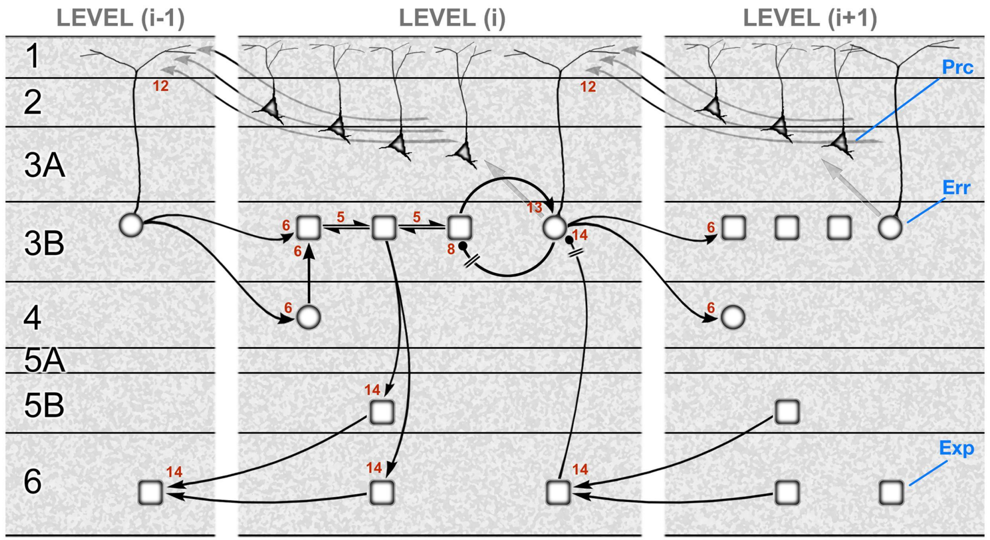
- $P(stimulus = hot \mid cue = green)$ **+** $P(stimulus = hot \mid cue = yellow) = 100\ \%$
- probabilities change: stable and volatile phases

3. Implementational level

- How is the brain's model of temperature physically realised?
  - What does the computational hierarchy look like?
    - whole-brain fMRI
    - identify which brain regions are involved
    - estimate effective connectivity
  - Which neurons/ circuits are involved?
    - laminar (= high resolution) fMRI
    - computational variables represented by separate neuronal populations?

    → i.e. in distinct cortical layers

→ model-based fMRI analysis

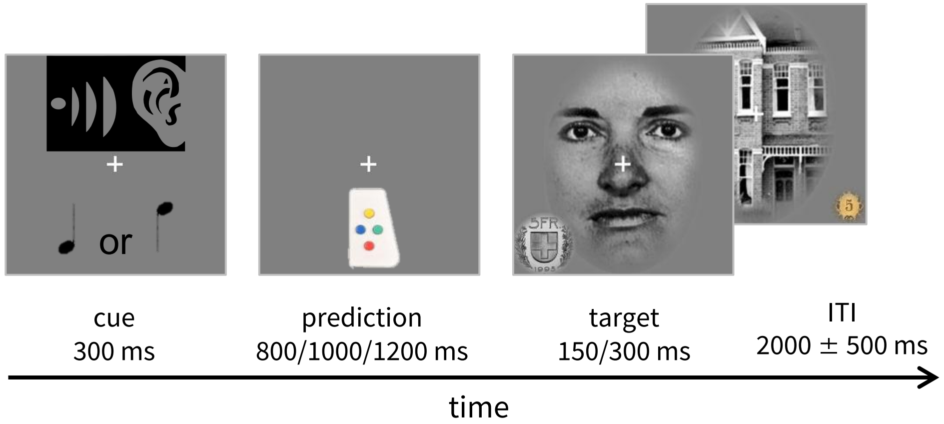


Shipp, *Front Psychol.*, 2016

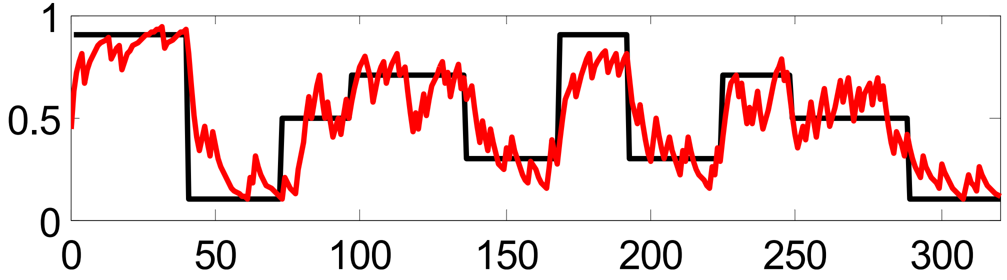
Steps for model-based fMRI

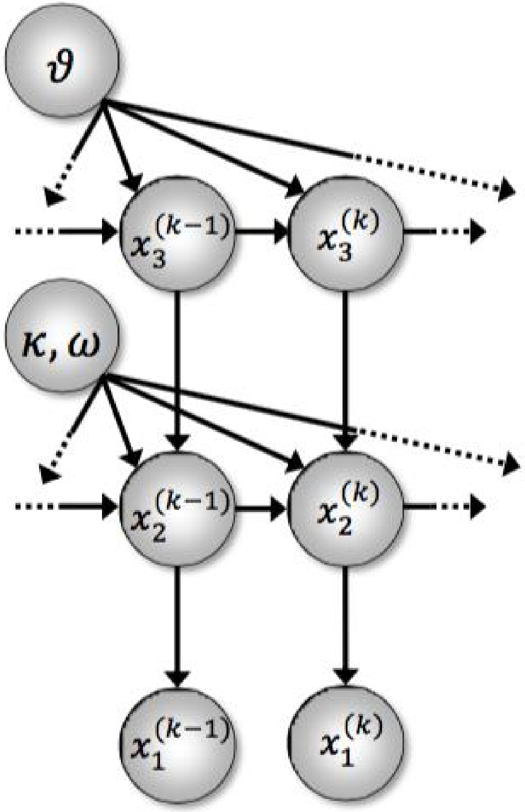
1. Choose a model
2. Find best-fitting parameters of model to behavioral data
3. Generate model-based time series
4. Convolve time series with HRF
5. Regress against fMRI data

Applications of model-based fMRI



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



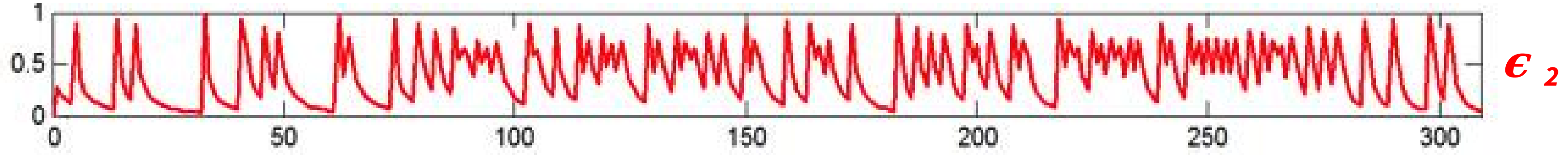


Iglesias et al., *Neuron*, 2013

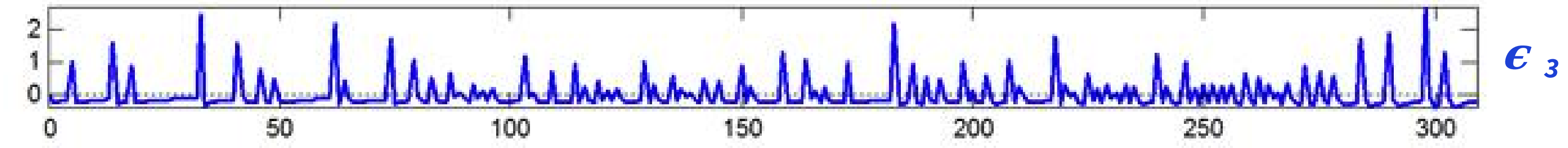
Applications of model-based fMRI

- 2 types of PE:

1. Outcome PE



2. Stimulus probability PE



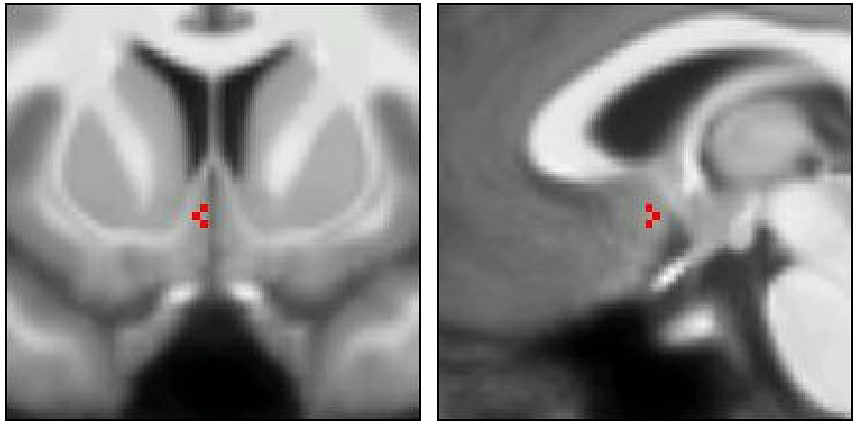
Iglesias et al., *Neuron*, 2013

Applications of model-based fMRI

1. Outcome PE

- right VTA
- dopamine

2. Stimulus probability PE



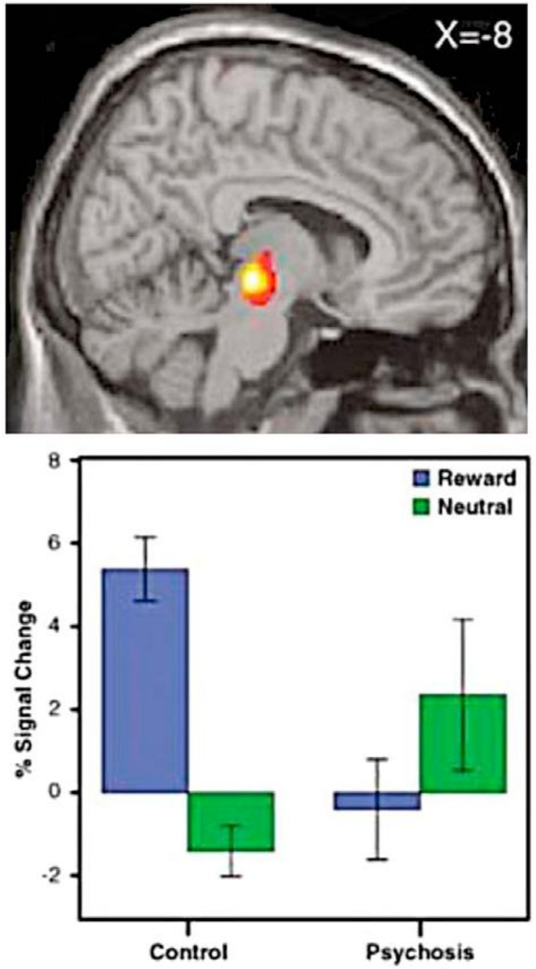
- left basal forebrain
- acetylcholine

Iglesias et al., *Neuron*, 2013

- **Key message:** abstract model-based quantities correlate with strong neuronal activation

Applications of model-based fMRI in psychiatry

- Theory of schizophrenia:
  - dysregulated activity of DA neurons
    - PE signals ill-timed and/or abnormal precision
    - “aberrant salience” of random/ irrelevant events
  - prediction:
    - diminished difference in PE response to relevant and neutral stimuli in patients
  - model-based fMRI studies:
    - PE responses in midbrain, ventral striatum differ between patients and controls
    - patients: less activity on rewarding/ aversive trials, more activity in response to neutral/ irrelevant cues



Murray et al., *Mol. Psychiatry*, 2008

A word about design efficiency

- **Event-related fMRI:** optimise efficiency by event spacing and sequencing
- **Model-based fMRI:** regressors and design matrix not fully specified before data collection
- To **estimate design efficiency:**
  - Simulate behavioural data, conduct behavioral pilot study
  - Obtain simulated/ pilot time course from the model
  - Optimise design efficiency

Model-based fMRI in a nutshell

- **Goal:** uncover hidden variables or processes
- **Use computational models** to generate regressors of interest
  - not just stimulus inputs and behavioural responses
- **Address questions** about specific cognitive processes
  - Which brain regions are activated in a particular cognitive task?

Further reading

- Stephan KE, Iglesias S, Heinzle J, Diaconescu AO (2015) Translational Perspectives for Computational Neuroimaging. Neuron 87: 716-732.

- Iglesias, S., Mathys, C., Brodersen, K.H., Kasper, L., Piccirelli, M., den Ouden, H.E.M., and Stephan, K.E. (2013). Hierarchical Prediction Errors in Midbrain and Basal Forebrain during Sensory Learning. Neuron *80*, 519–530.

- Diaconescu, A.O., Mathys, C., Weber, L.A.E., Kasper, L., Mauer, J., and Stephan, K.E. (2017). Hierarchical prediction errors in midbrain and septum during social learning. Soc. Cogn. Affect. Neurosci. *12*, 618–634.

- Iglesias, S., Tomiello, S., Schneebeli, M., and Stephan, K.E. (2016). Models of neuromodulation for computational psychiatry. Wiley Interdiscip. Rev. Cogn. Sci.

- Mathys, C., Daunizeau, J., Friston, K.J., and Stephan, K.E. (2011). A Bayesian foundation for individual learning under uncertainty. Front. Hum. Neurosci. *5*.

- Mathys, C.D., Lomakina, E.I., Daunizeau, J., Iglesias, S., Brodersen, K.H., Friston, K.J., and Stephan, K.E. (2014). Uncertainty in perception and the Hierarchical Gaussian Filter. Front. Hum. Neurosci. *8*.

Thank you.