Introduction to Computational (Generative) Modeling

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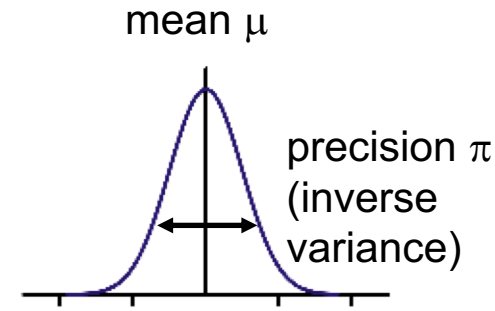
A brief note on mathematical notations



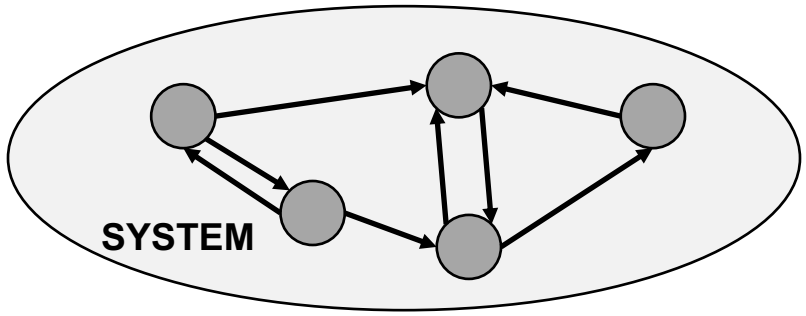
- For example: Gaussian (Normal) distributions
  - for scalars: $p(x) = N(x; \mu, \sigma^2)$ — μ = mean; σ^2 = variance
  - for vectors: $p(\mathbf{x}) = N(\mathbf{x}; \boldsymbol{\mu}, \boldsymbol{\Sigma})$ — Σ = covariance matrix = $E[(\mathbf{x}-\boldsymbol{\mu})(\mathbf{x}-\boldsymbol{\mu})^T]$

- same thing, just expressed wrt. precision
  - for scalars: $p(x) = N(x; \mu, \lambda^{-1})$ — μ = mean; $\lambda = 1/\sigma^2$ = precision
  - for vectors: $p(\mathbf{x}) = N(\mathbf{x}; \boldsymbol{\mu}, \Lambda^{-1})$ — Λ = precision matrix

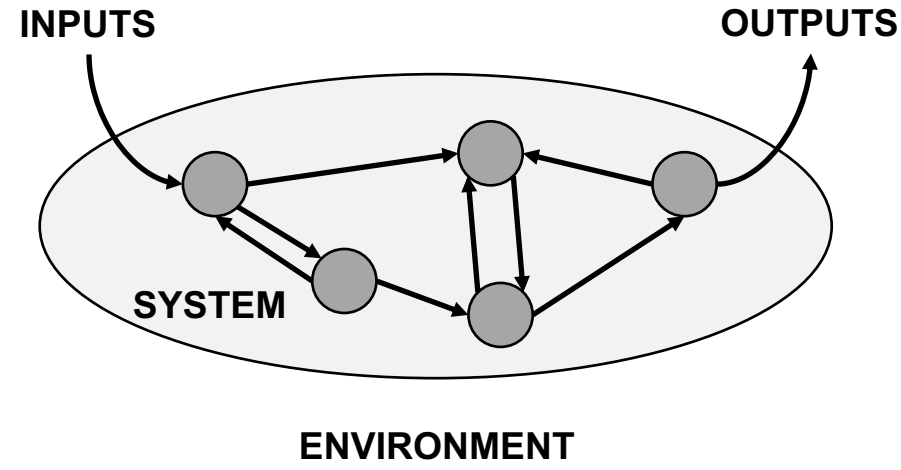
Systems

- system = a set of entities that interact to form a unified whole
- biological systems are open systems: they interact with their environment (exchange of energy, matter, information)

isolated system



open system

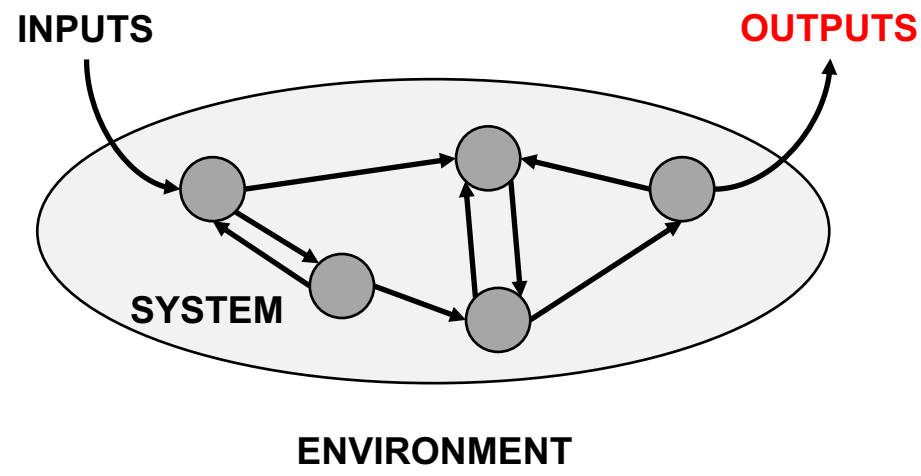


System models

- mathematically formal description of a system's behavior
  (at an algorithmic or biophysical level that cannot be observed directly)

- central concept: hidden (latent) system states cause noisy measurements

- system models describe (at least) three things:
  - how system states evolve in time
  - how states determine system outputs
  - how outputs are corrupted by noise



NB: Outputs can be
- actions (from the system's perspective)
- data (from an outside observer's view)

States, parameters, inputs

- mandatory system components:
  - what are the relevant variables whose dynamics are of interest? → **states** $\mathbf{x}(t)$
  - what are structural determinants of their interactions? → **parameters** θ
  - what perturbations need to be considered? → **inputs** $\mathbf{u}(t)$

- system states:

state vector

$$\mathbf{x}(t) = \begin{bmatrix} x_1(t) \\ \mathrm{M} \\ x_N(t) \end{bmatrix}$$

neurophysiological or algorithmic variables

state (or evolution) equations, e.g.:

$$\frac{d\mathbf{x}}{dt} = f\left(\mathbf{x}(t), \boldsymbol{\theta}_f, \mathbf{u}(t)\right)$$ as differential equation

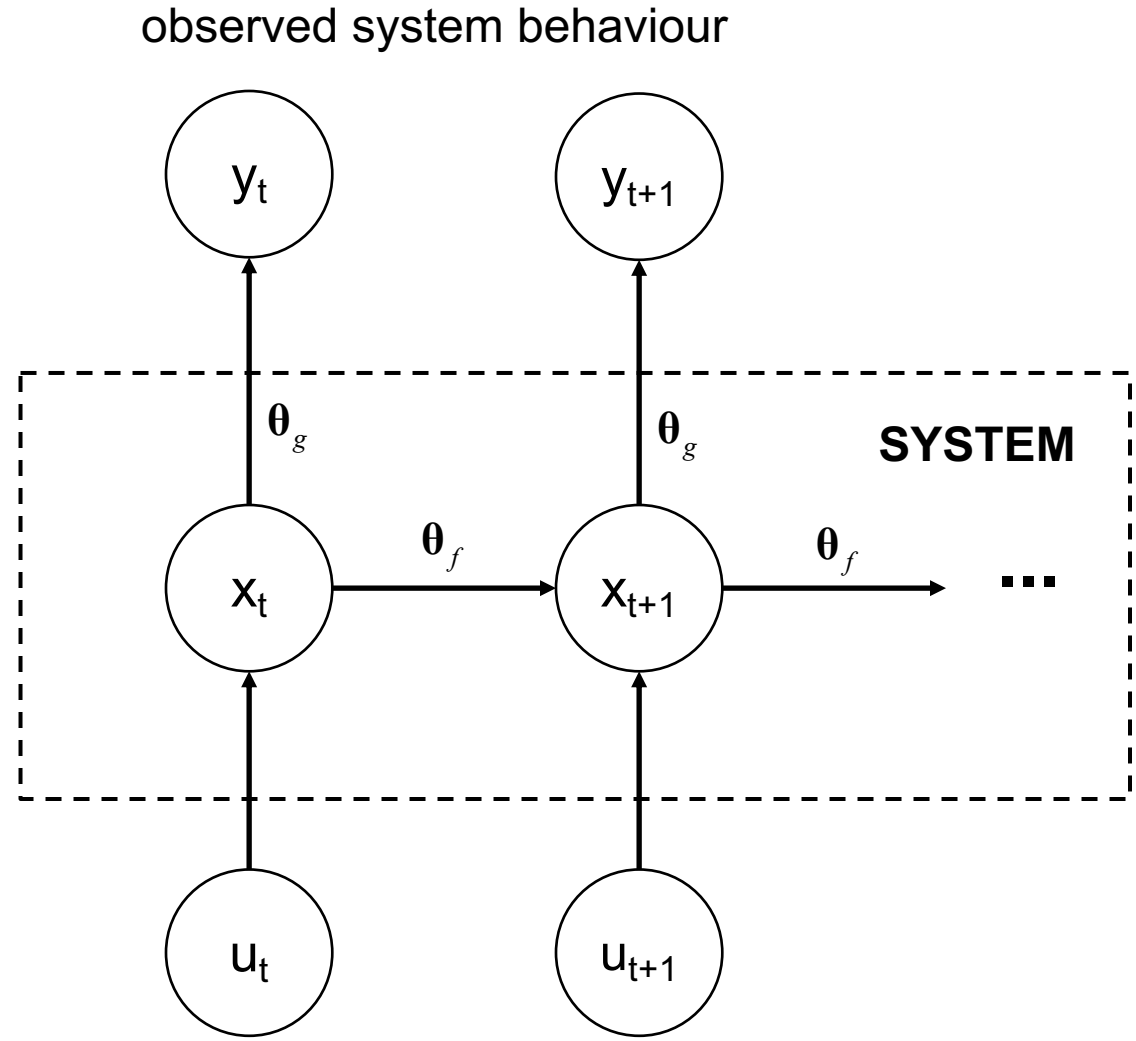
$$\mathbf{x}\left(t+1\right) = f\left(\mathbf{x}(t), \boldsymbol{\theta}_f, \mathbf{u}(t)\right)$$ as difference equation

For a discussion of system theory in the context of neuroimaging, see Stephan 2004, *J. Anat.*

State space representation

measurement
(or observation, response)
equation:

$$\mathbf{y}(t) = g\left(\mathbf{x}(t), \boldsymbol{\theta}_g\right) + \boldsymbol{\varepsilon}(t)$$



On this slide, time is indexed by subscripts.

Deterministic vs. stochastic state space models

- **deterministic models**
  - no state noise: $\frac{d\mathbf{x}}{dt} = f\left(\mathbf{x}(t), \boldsymbol{\theta}_f, \mathbf{u}(t)\right)$ ODEs

  → states $\mathbf{x}(t)$ fully determined by initial state $x(0)$, parameters $\boldsymbol{\theta}$ and inputs $\mathbf{u}(t)$

  → if inputs are known, inference on parameters sufficient to reconstruct state trajectories

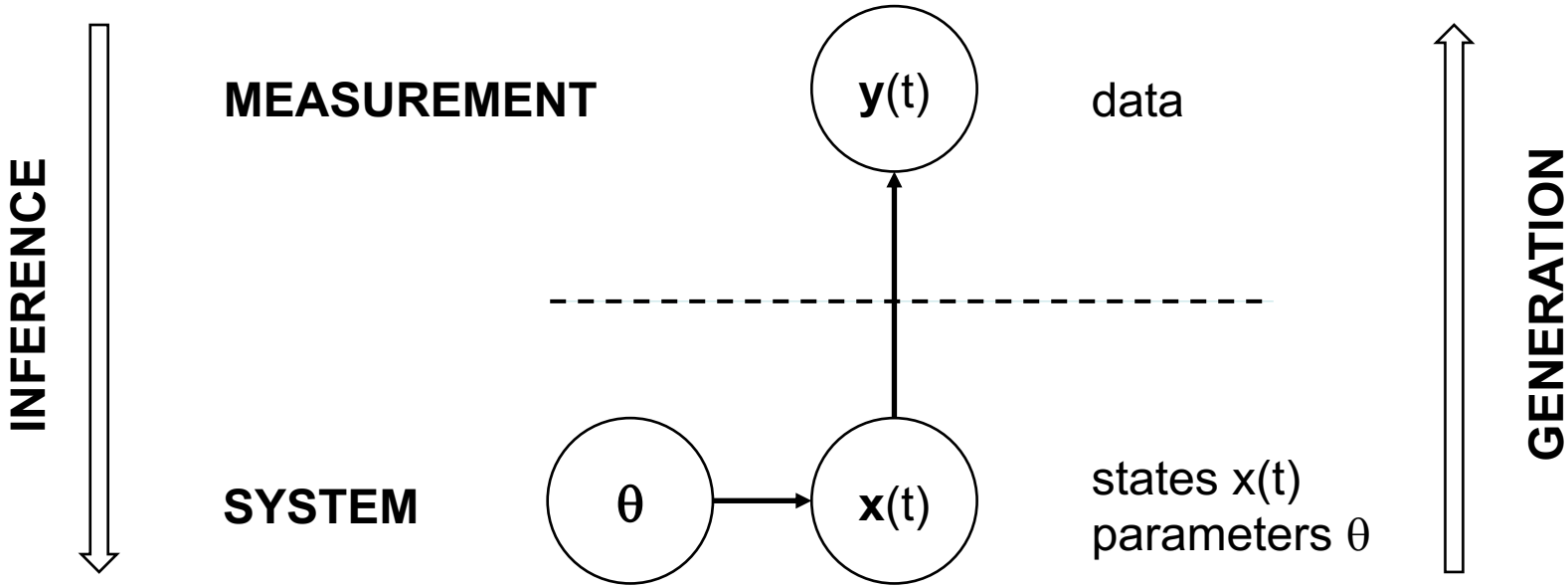
- **stochastic models**
  - state noise: $\frac{d\mathbf{x}}{dt} = f\left(\mathbf{x}(t), \boldsymbol{\theta}_f, \mathbf{u}(t)\right) + \omega(t)$ SDEs

  → states $\mathbf{x}(t)$ not fully determined by initial state, parameters and inputs

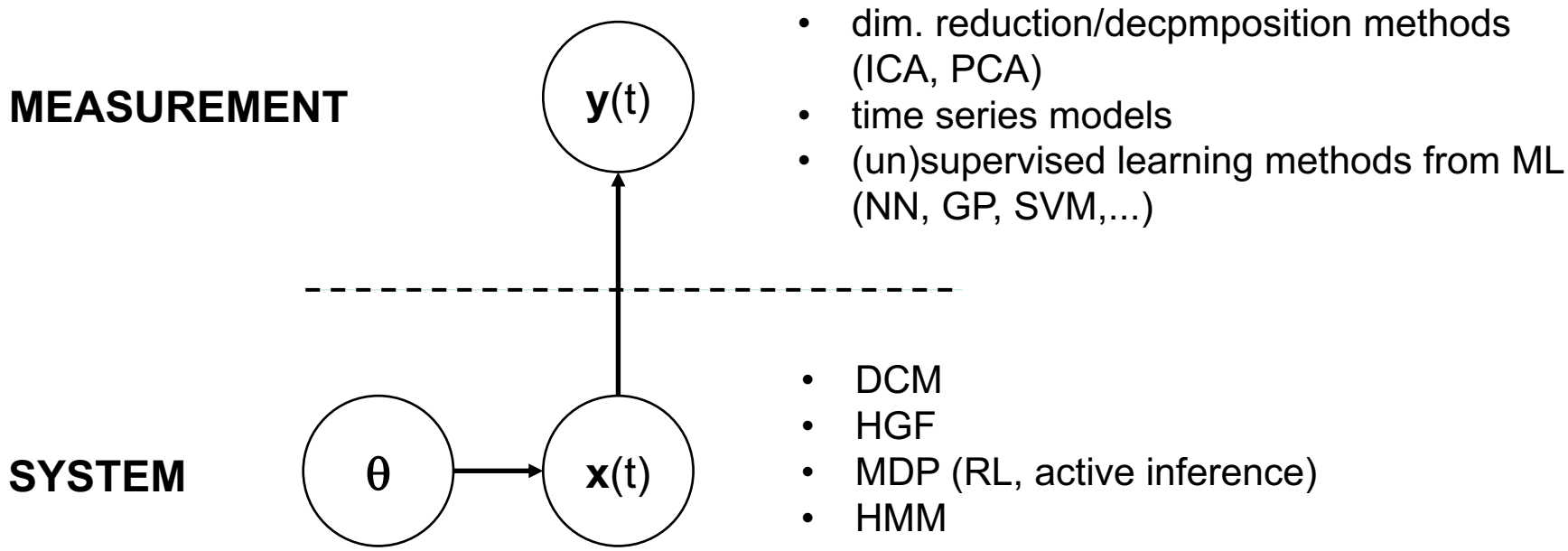
  → much tougher inference problem!

Models with/without latent states

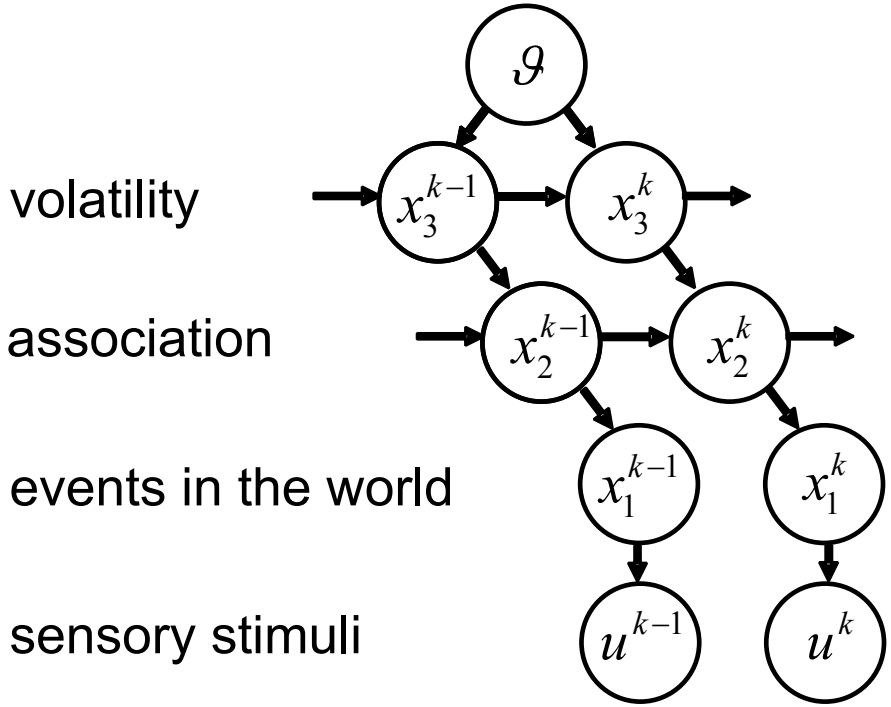
- many ways to categorise modeling approaches
- one possibility: distinguish presence vs. absence of latent states

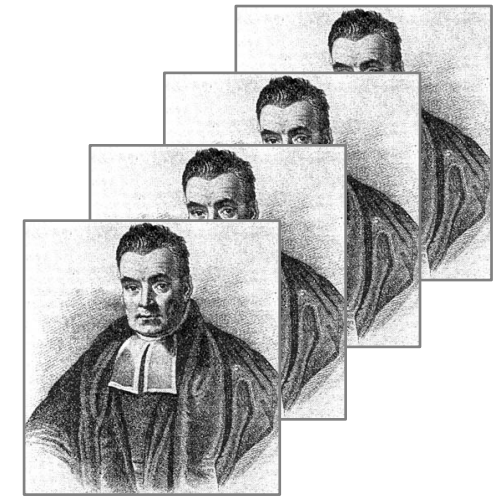


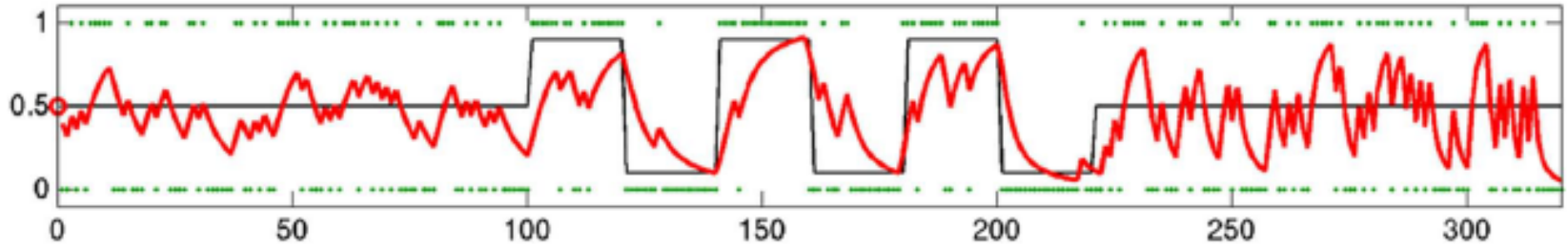
Examples of approaches with/without latent states



Examples of models discussed later in the course: HGF...

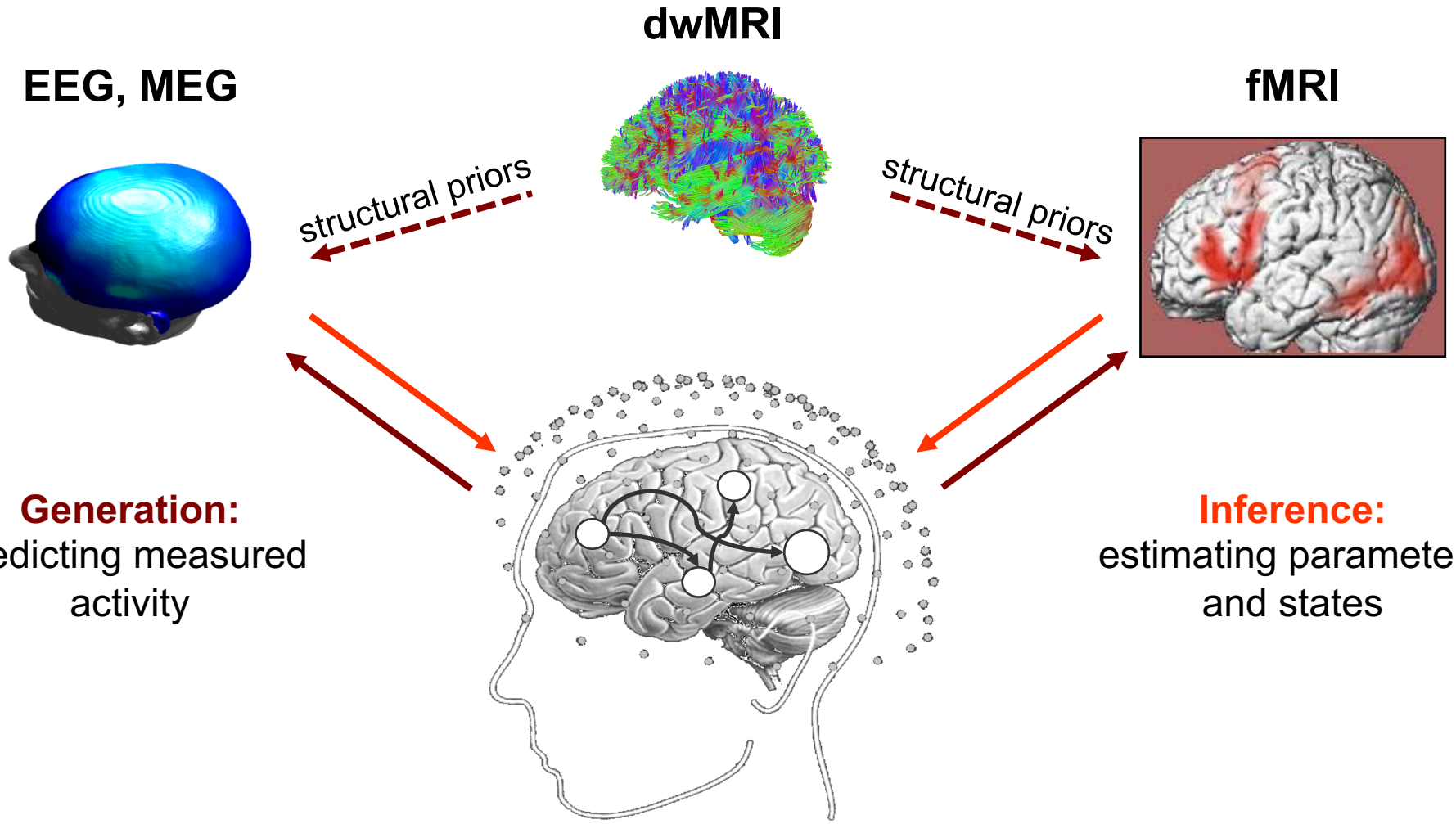






Mathys et al. 2011, 2014, *Front. Hum. Neurosci.*

... and DCMs of fMRI and EEG/MEG data



Maximum likelihood estimation (MLE)

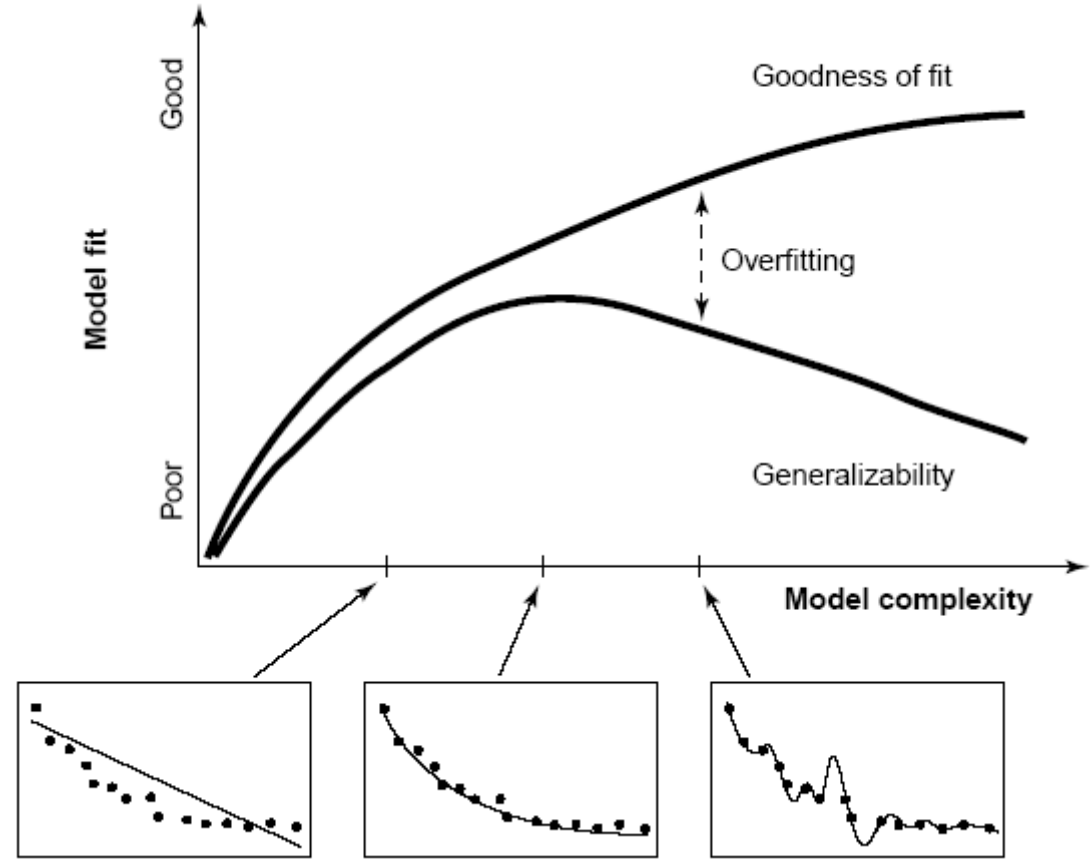
- Given a system model and measured data, we would like to estimate the values of the model parameters.
- Once we have specified our assumptions about the nature of the observation noise (e.g. IID Gaussian), we can compute the **likelihood $\mathbf{p(y|\theta)}$**, i.e.: Given a particular value of θ, how likely are the observed data y under the chosen model?
- We could then search for the parameter value that maximises the (log) likelihood. This is the parameter value for which the model fits the data best.
- This is known as **maximum likelihood estimation (MLE)**:

$$\hat{\boldsymbol{\theta}}_{ML} = \arg\max_{\theta} \ln p\left(\mathbf{y} \mid \boldsymbol{\theta}\right)$$

- (Yu will present the details of MLE tomorrow.)

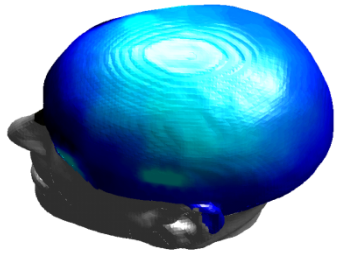
Overfitting

- MLE has various limitations. For example, for complex models and limited data, **overfitting** is a severe problem (see Yu's talk).
- For more robust inference, we turn to Bayesian methods
  → need to define a prior distribution of parameters
- Together, likelihood and prior define a **generative model**.



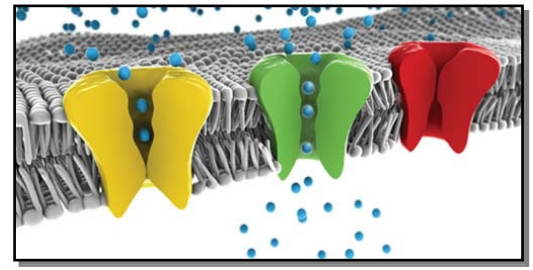
Pitt & Myung (2002) *TICS*

Generative models



$$p(\mathbf{y} \mid \boldsymbol{\theta}, m)\, p(\boldsymbol{\theta} \mid m)$$

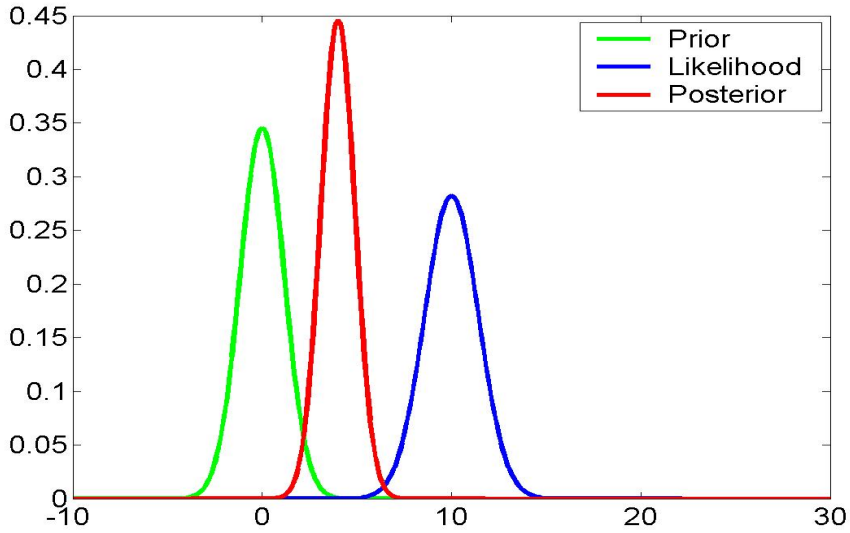
$$p(\boldsymbol{\theta} \mid \mathbf{y}, m)$$

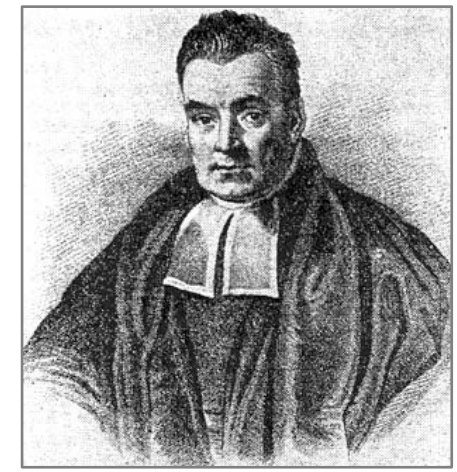


y = data, θ = parameters, m = model

1. a probabilistic forward mapping from parameters to data, defined by likelihood and prior (joint probability)
2. enforce mechanistic thinking: how could the data have been caused?
3. generate synthetic data (observations) by sampling from the prior – can model explain certain phenomena at all?
4. model inversion = inference about parameters → posterior p(θ|y,m)
5. natural basis for model comparison → model evidence p(y|m)

Bayes' rule





The Reverend Thomas Bayes
(1702-1761)

Likelihood × prior: generative model

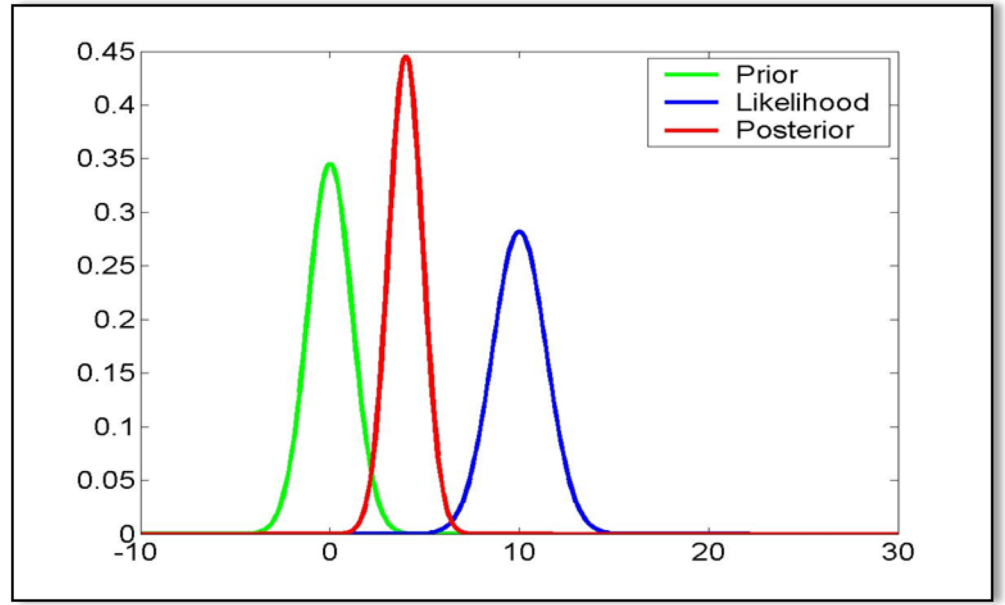
$$p(\boldsymbol{\theta} \mid \mathbf{y}) = \frac{p(\mathbf{y} \mid \boldsymbol{\theta})\, p(\boldsymbol{\theta})}{p(\mathbf{y})}$$

Model evidence: normalisation term and index for model goodness

"... the theorem expresses how a ... degree of belief should rationally change to account for availability of related evidence."

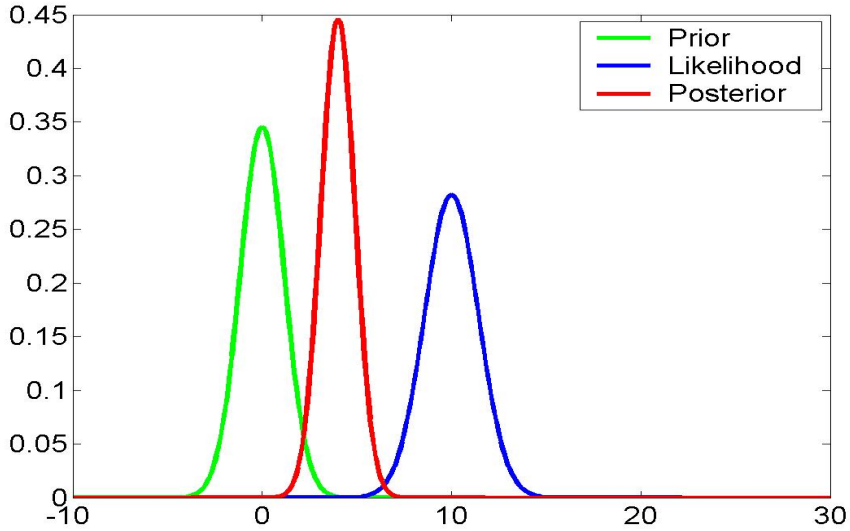
Wikipedia

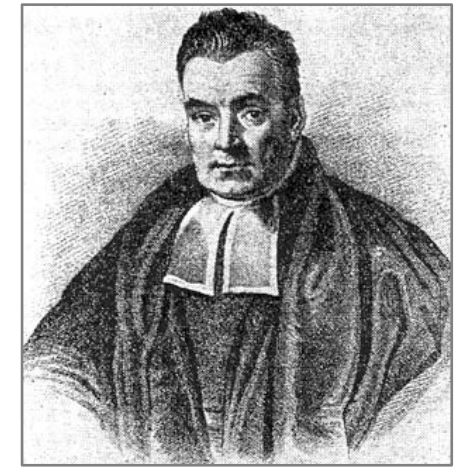
Bayesian inference: an animation



Code courtesy by Guillaume Flandin

Bayes' rule



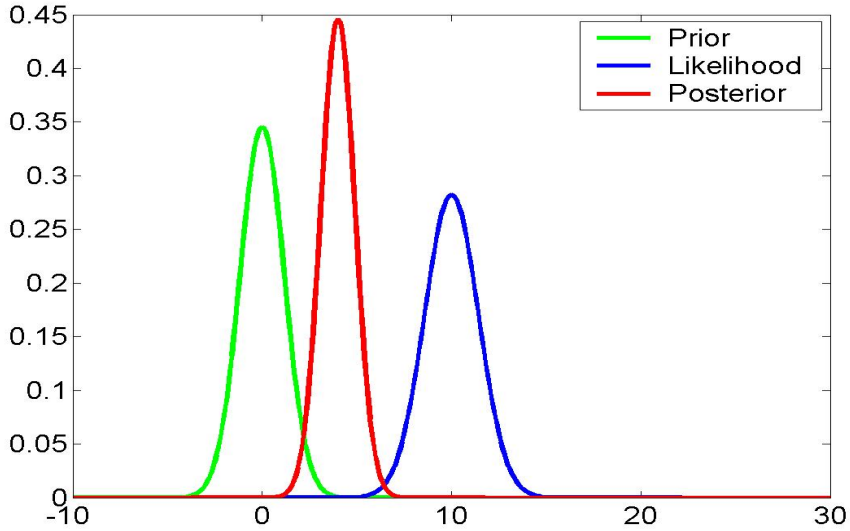


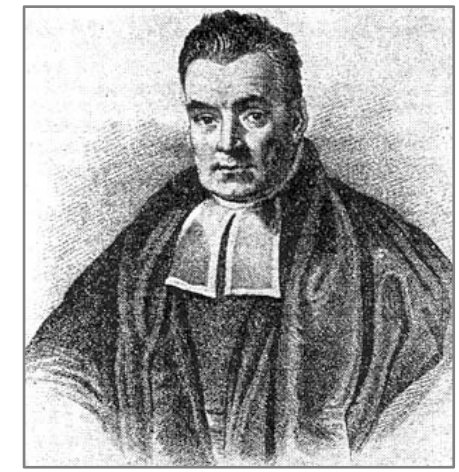
The Reverend Thomas Bayes
(1702-1761)

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

No change – just making the choice of a particular model explicit.

Bayes' rule





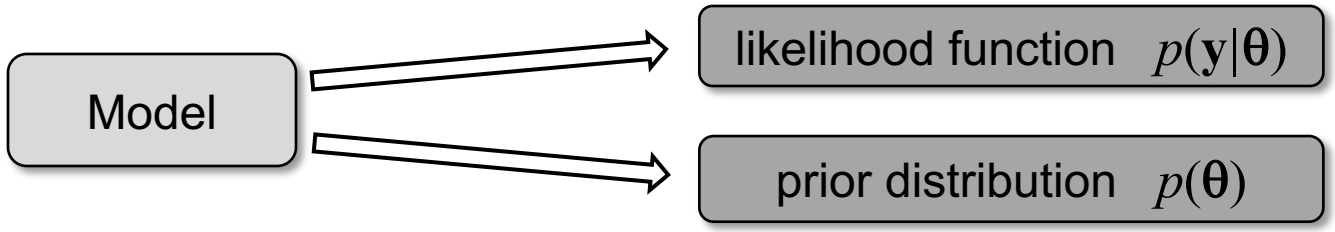
The Reverend Thomas Bayes
(1702-1761)

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

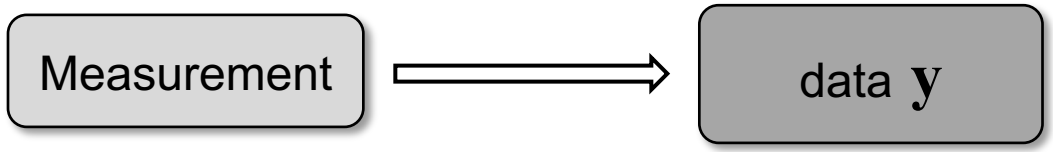
Evidence:
probability that data were generated by model m, averaging over all possible parameter values (as weighted by the prior).

Principles of generative modeling

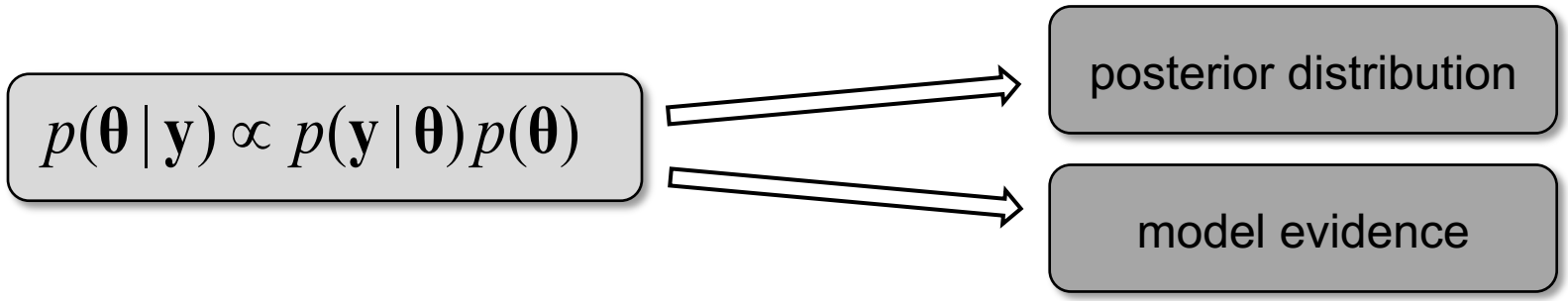
⇨ Specifying a **generative model**



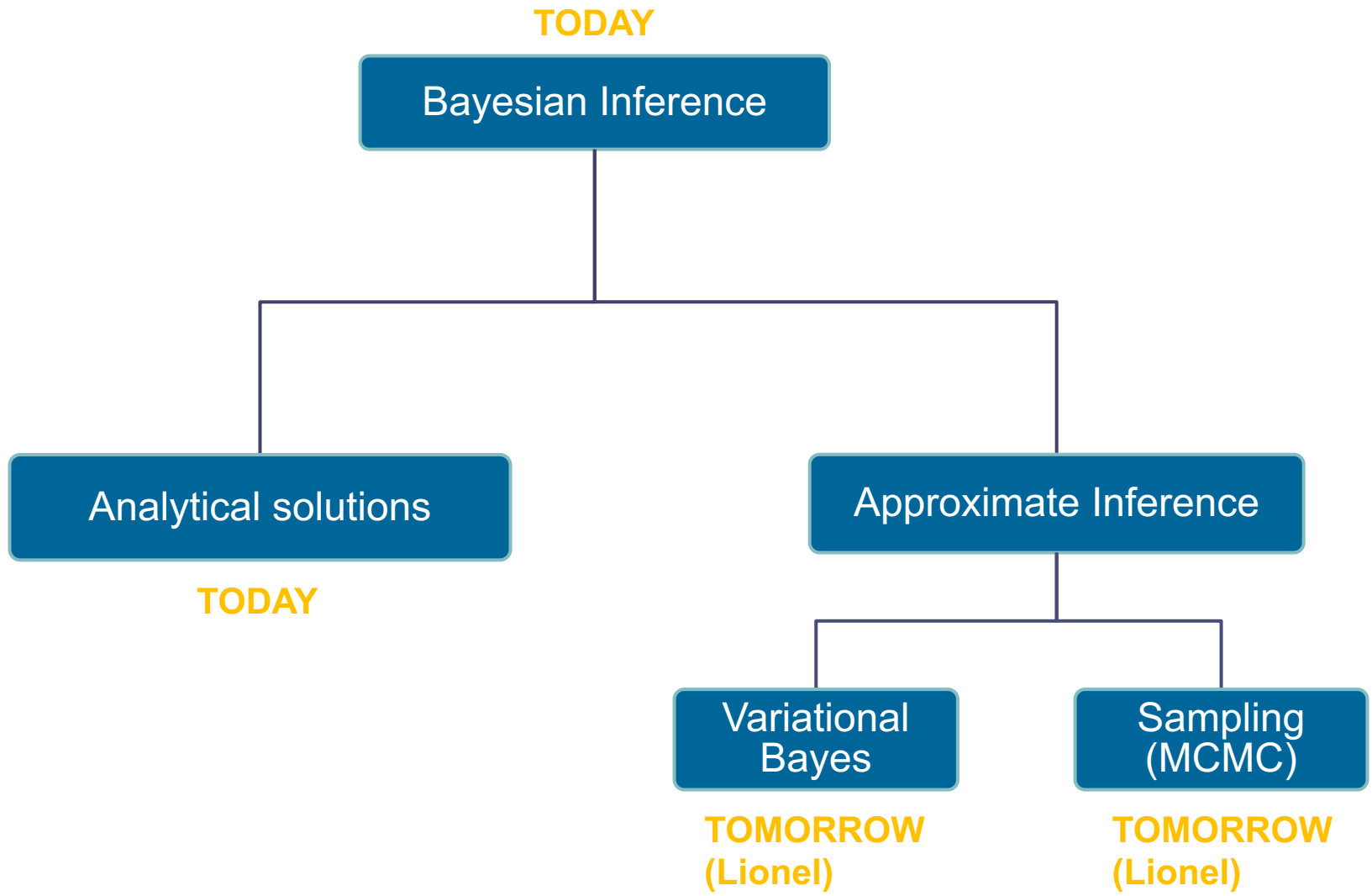
⇨ Observation of **data**



⇨ **Model inversion**



Methods for Bayesian inference



How is the posterior computed = how is a generative model inverted?

- **compute the posterior analytically**
  - requires conjugate priors
- **variational Bayes (VB)**
  - often hard work to derive, but fast to compute
  - uses approximations (approx. posterior, mean field)
  - problems: local minima, potentially inaccurate approximations
- **sampling methods (e.g. Markov Chain Monte Carlo, MCMC)**
  - theoretically guaranteed to be accurate (for infinite computation time)
  - problems: may require very long run time in practice, only heuristics to decide about convergence in practice

Conjugate priors

- for a given likelihood function, the choice of prior determines the algebraic form of the posterior
- for some probability distributions a prior can be found such that the posterior has the same algebraic form as the prior
- such a prior is called “conjugate” to the likelihood
- examples:
  - Normal $\propto$ Normal × Normal
  - Beta $\propto$ Binomial × Beta
  - Dirichlet $\propto$ Multinomial × Dirichlet

$$p(\boldsymbol{\theta} \mid \mathbf{y}) \propto p(\mathbf{y} \mid \boldsymbol{\theta}) p(\boldsymbol{\theta})$$

same form

A simple example: univariate Gaussian belief update

Likelihood & prior

$$p(y \mid \theta) = N(\theta, \lambda_e^{-1})$$

$$p(\theta) = N(\mu_{prior}, \lambda_{prior}^{-1})$$

Posterior $p(\theta \mid y) = N(\mu_{post}, \lambda_{post}^{-1})$

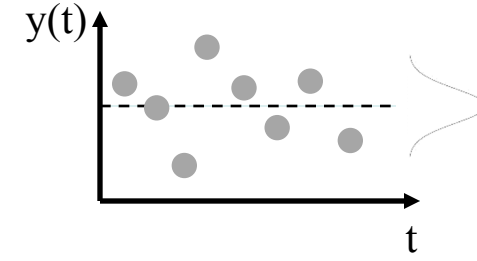
(for a single observation y)

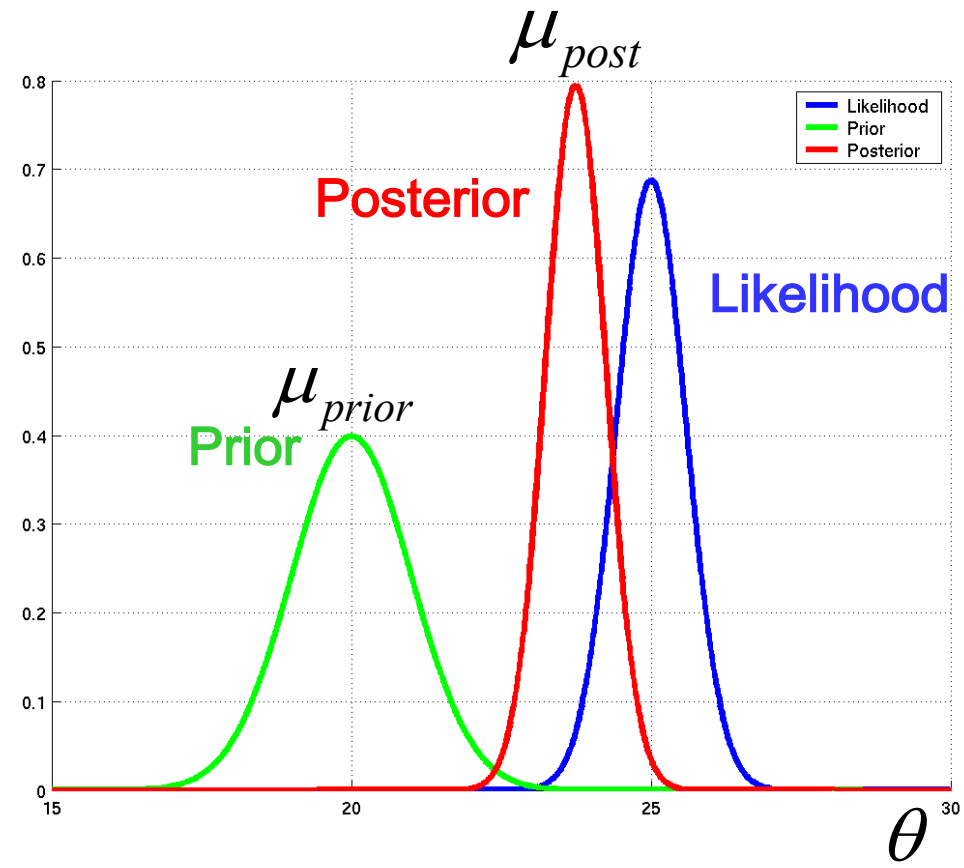
$$\lambda_{post} = \lambda_e + \lambda_{prior}$$

$$\mu_{post} = \frac{\lambda_e}{\lambda_{post}} y + \frac{\lambda_{prior}}{\lambda_{post}} \mu_{prior}$$

relative precision weighting:
posterior mean = precision-weighted combination of prior mean and data

$$\mathbf{y} = \theta + \boldsymbol{\varepsilon}$$





Slide courtesy by Will Penny

Model comparison and selection

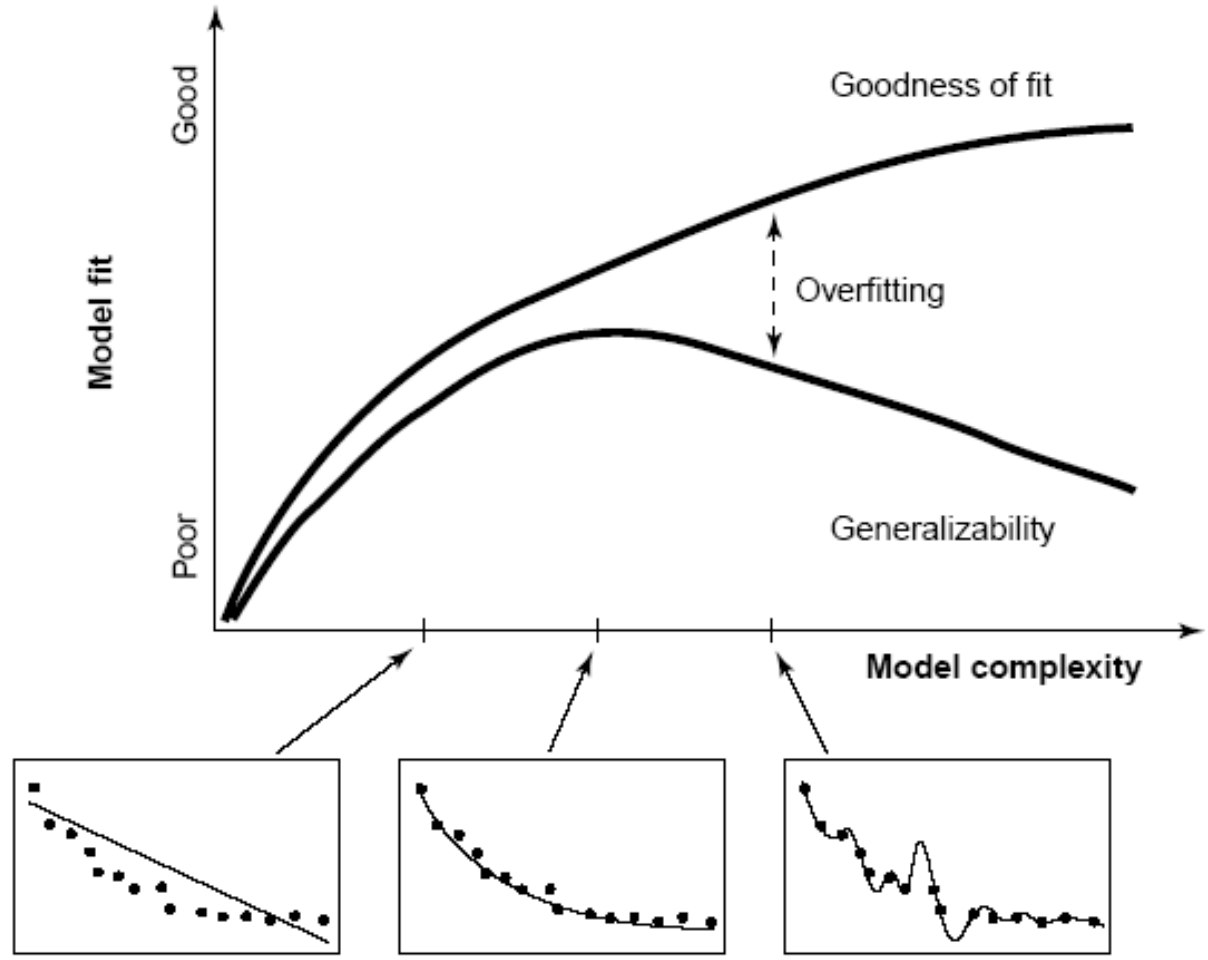
Given competing hypotheses on structure & functional mechanisms of a system, which model is the best?

⇩

Which model represents the best balance between model fit and model complexity?

⇩

For which model m does $p(y|m)$ become maximal?



Pitt & Miyung (2002) *TICS*

Bayesian model selection (BMS)

- First step of inference: define model space M

$$|M| \in [1, \infty[$$

- Inference on model structure m:

Posterior model probability

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

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

- For a uniform prior on m, model evidence sufficient for model selection

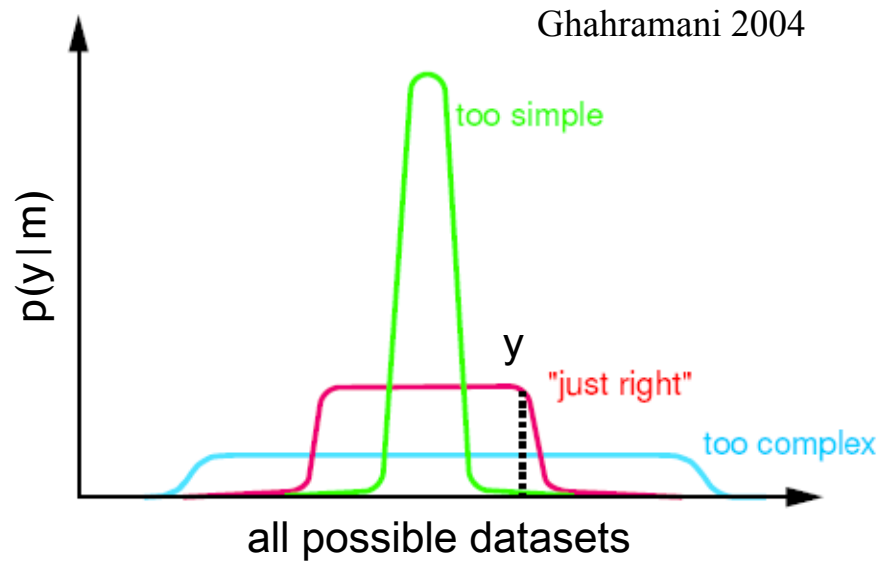
Model evidence:

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

Bayesian model selection (BMS)

Model evidence:

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



⟹ likelihood of the observed data being generated under model m, averaging over all parameter values (with weighting as specified by the prior)

⟹ accounts for both accuracy and complexity of the model

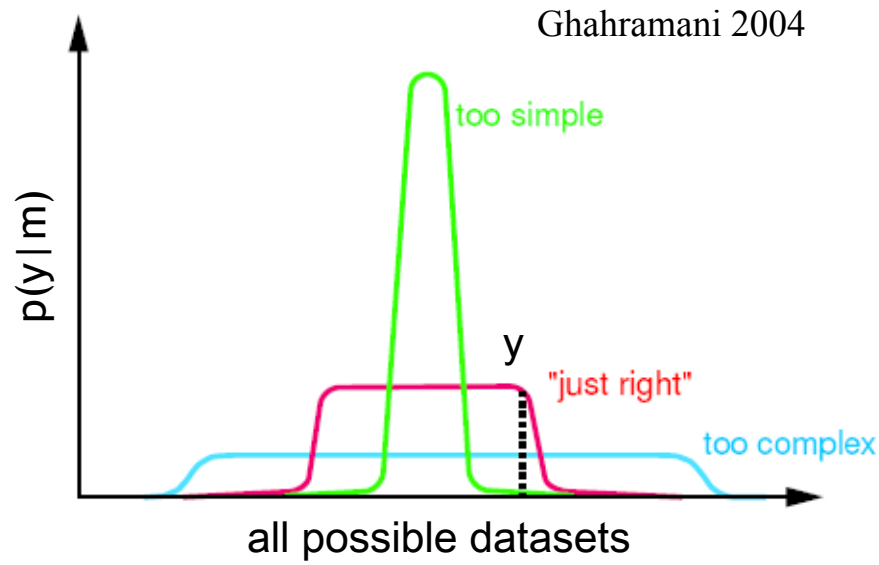
Various approximations:

- negative free energy (F)
- Akaike Information Criterion (AIC)
- Bayesian Information Criterion (BIC)

Bayesian model selection (BMS)

Model evidence:

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



⟹ "If I randomly sampled from my prior and plugged the resulting value into the likelihood function, how close would the predicted data be – on average – to my observed data?"

⟹ accounts for both accuracy and complexity of the model

Various approximations:

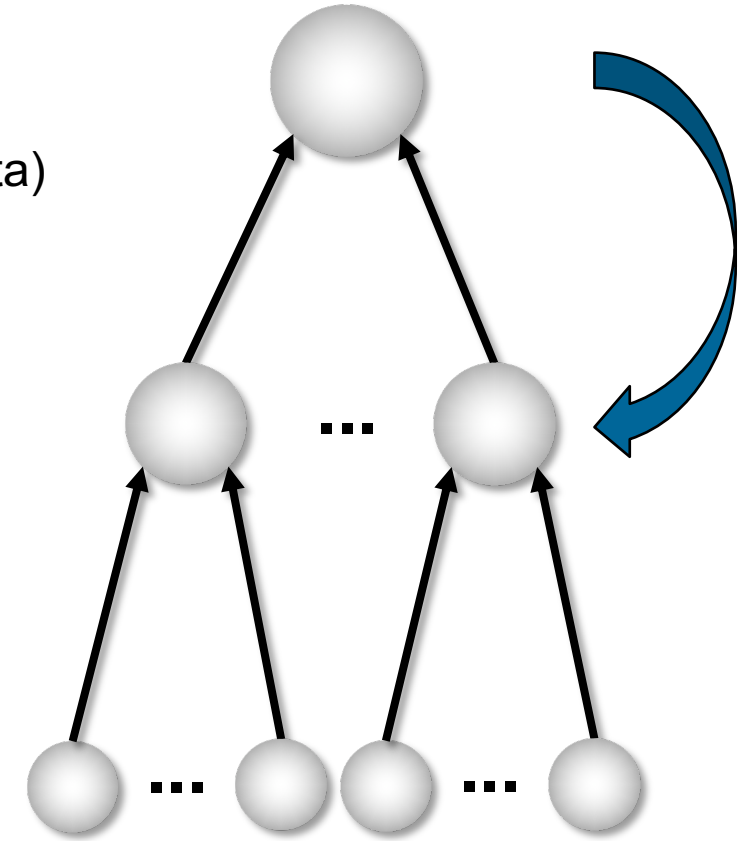
- negative free energy (F)
- Akaike Information Criterion (AIC)
- Bayesian Information Criterion (BIC)

Generative models as computational assays for addressing key clinical questions

SYMPTOMS
(behavioural or physiological data)

MECHANISMS
(computational, physiological)

CAUSES
(aetiology)



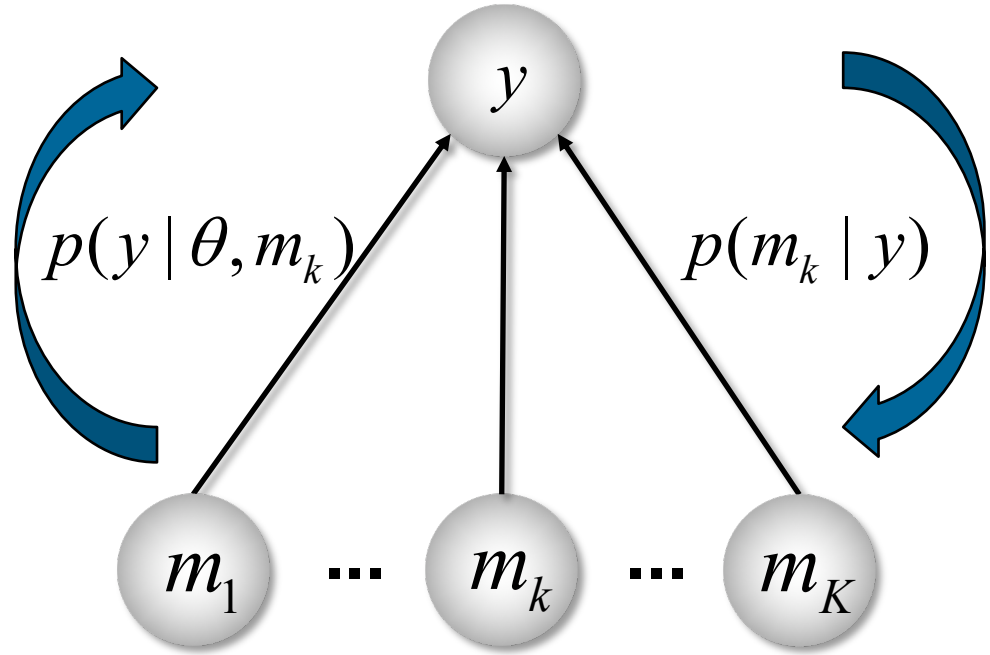
❶ **differential diagnosis** of alternative disease mechanisms

❷ **stratification / subgroup detection** into mechanistically distinct subgroups

❸ **prediction** of clinical trajectories and treatment response

❶ Differential diagnosis: model selection

SYMPTOM
(behaviour
or physiology)

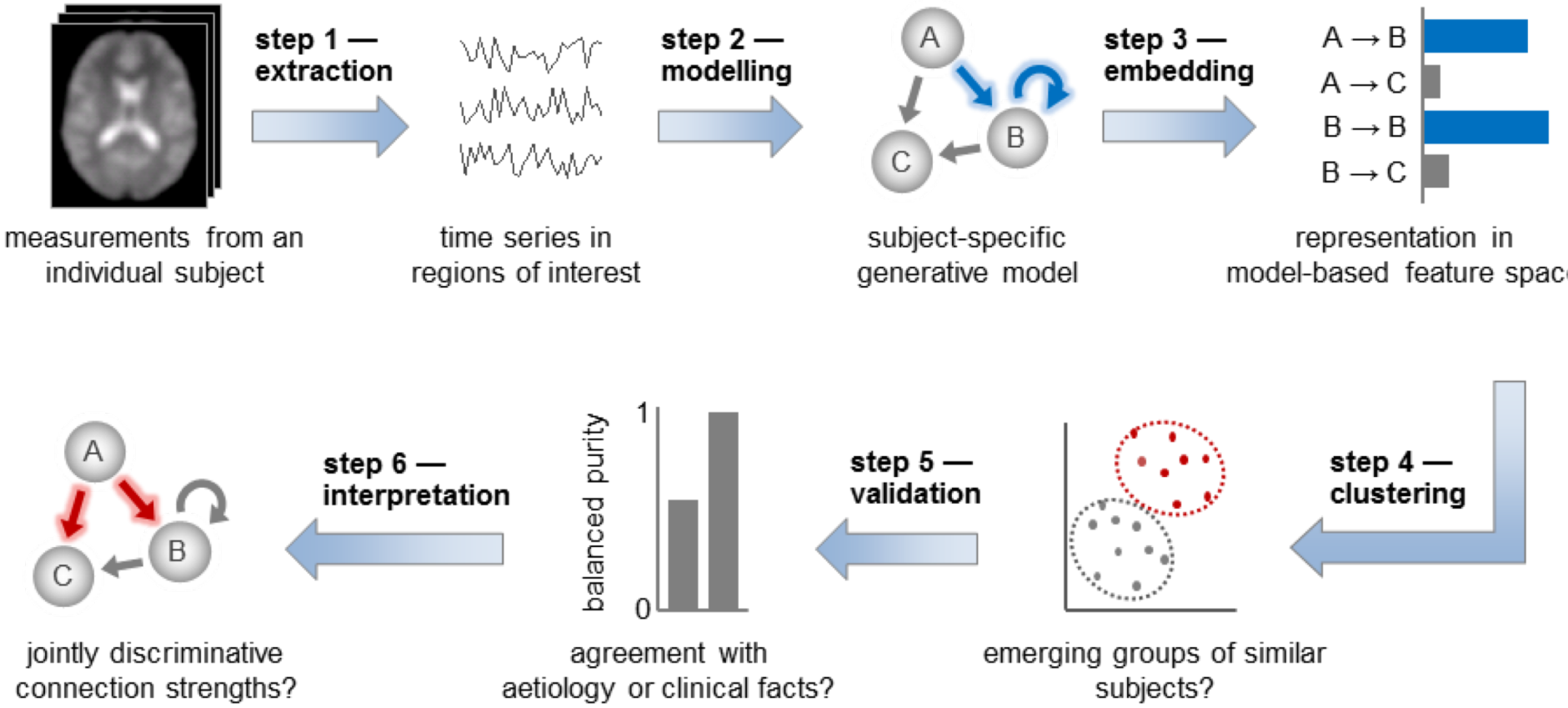


**HYPOTHETICAL
MECHANISM**

$$p(m_k \mid \mathrm{y}) = \frac{p(y \mid m_k)\,p(m_k)}{\sum_k p(y \mid m_k)\,p(m_k)}$$

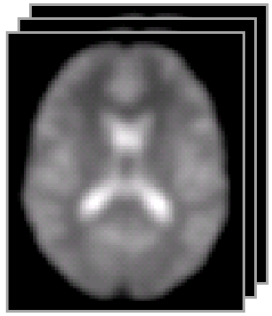
Stephan et al. 2017, *NeuroImage*

❷ Stratification / subgroup detection: Generative embedding (unsupervised)



Brodersen et al. 2014, *NeuroImage Clinical*

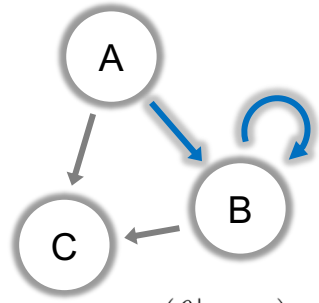
❸ Prediction: Generative embedding (supervised)



measurements from
an individual subject

**step 1 —
model inversion**

$\mathcal{X} \to \mathcal{M}_\Theta$



$p(\theta|x, m)$

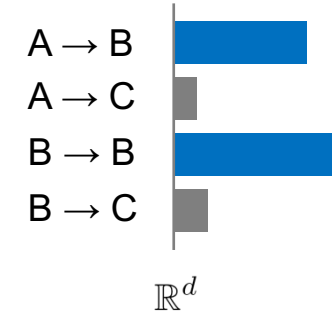
subject-specific
inverted generative model

**step 2 —
kernel construction**

$\mathcal{M}_\Theta \to \mathbb{R}^d$

$k : \mathbb{R}^d \times \mathbb{R}^d \to \mathbb{R}$

$k_\mathcal{M} : \mathcal{M}_\Theta \times \mathcal{M}_\Theta \to \mathbb{R}$

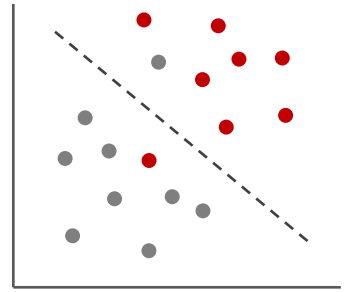


$\mathbb{R}^d$

subject representation in the
generative score space

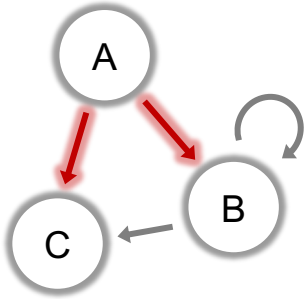
**step 3 —
support vector classification**

$$\hat{c} = \mathrm{sgn}\left(\sum_i^n \alpha_i^* k(x_i, x) + b^*\right)$$



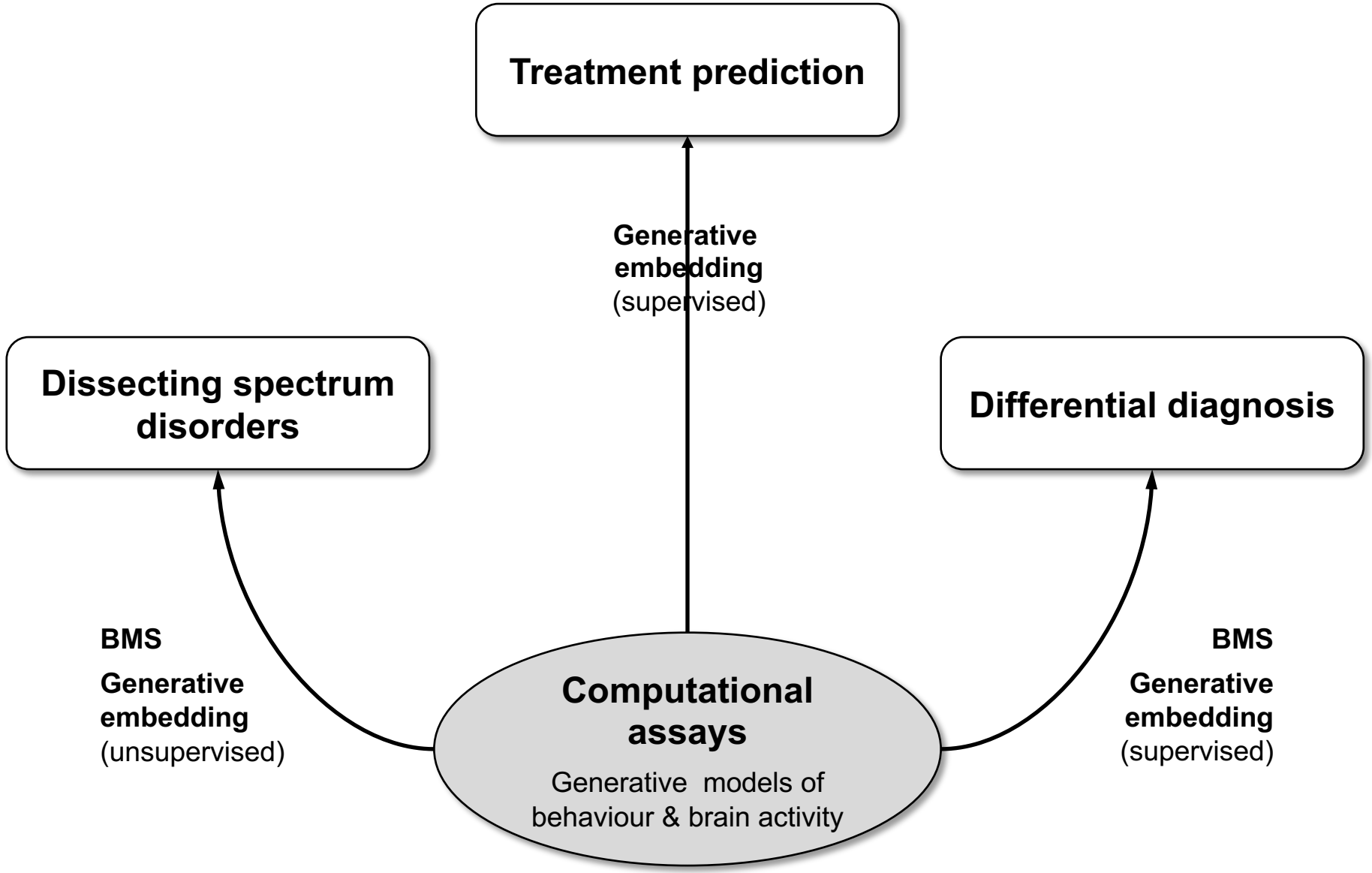
separating hyperplane fitted to
discriminate between groups

**step 4 —
interpretation**



jointly discriminative
model parameters

Brodersen et al. 2011, *PLoS Comput. Biol.*



adapted from:
Stephan & Mathys 2014, *Curr. Opin. Neurobiol.*

Further reading

Bayesian inference:

- Bishop CM (2006). Machine learning and pattern recognition. Springer, Heidelberg.

A simple introduction to General System Theory (in the context of neuroimaging):

- Stephan KE (2004) On the role of general system theory for functional neuroimaging. Journal of Anatomy 205: 443-470.

A generative modeling strategy for clinical applications:

- Stephan KE, Mathys C (2014) Computational Approaches to Psychiatry. Current Opinion in Neurobiology 25:85-92.
- Stephan KE, Schlagenhauf F, Huys QJM, Raman S, Aponte EA, Brodersen KH, Rigoux L, Moran RJ, Daunizeau J, Dolan RJ, Friston KJ, Heinz A (2017) Computational Neuroimaging Strategies for Single Patient Predictions. NeuroImage 145:180-199

Thank you