State Space Model (SSM) inversion: Inferring the system dynamics (model parameters)

Given a Set of Data & nonlinear deferential equations (DDEs):

$$\begin{cases} \dot{\boldsymbol{x}}(t) = \boldsymbol{f}(\boldsymbol{x}(t), \boldsymbol{u}(t), \boldsymbol{\theta}) + \boldsymbol{w}(t), & \boldsymbol{x}(0) = \boldsymbol{x}_{\boldsymbol{t}_0} \\ \boldsymbol{y}(t) = \boldsymbol{h}(\boldsymbol{x}(t)) + \boldsymbol{v}(t) & \end{cases}$$

$$\boldsymbol{w}(t) \sim \mathcal{N}(0, \sigma^2) \text{ and } \boldsymbol{v}(t) \sim \mathcal{N}(0, {\sigma'}^2)$$

***Aim**: identification unknown model parameters θ, from the observation in the best possible way.*

Bayesian inference: uses the language of probability to formalize ***model inversion***, as the quantification and propagation of uncertainty, defined via a probability, in the light of observations.

Bayes' theorem:

the process of passing from *prior* to *posterior* in the light of data by:

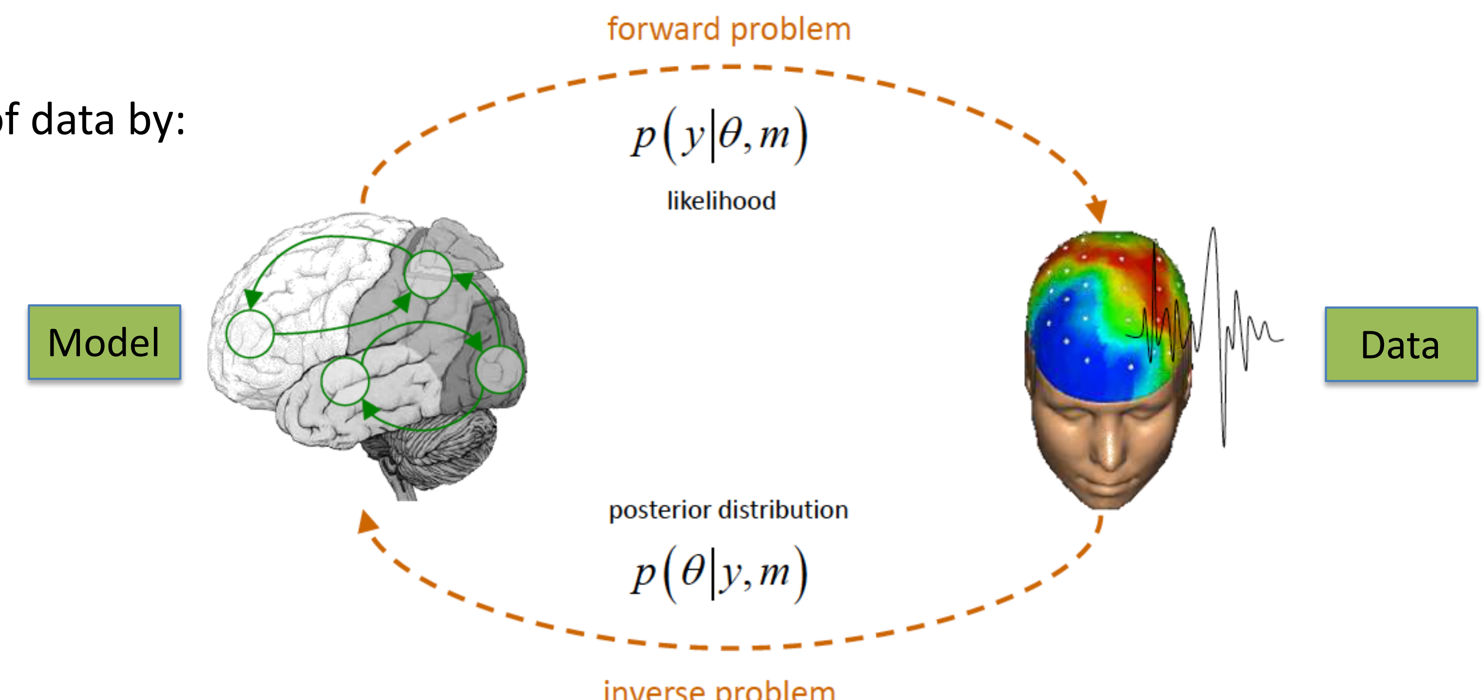
posterior

Likelihood

prior

$$p(\theta \mid y) = \frac{p(y \mid \theta)p(\theta)}{\int p(y \mid \theta)p(\theta)d\theta}$$

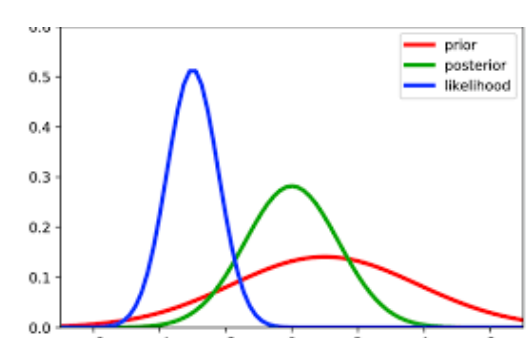
Marginal likelihood p(y)
(model evidence)



Prior: encodes what we knew about the model, before the application of the data.

Likelihood: is the probability of obtaining the set of observed data, with a given set of parameter values.

Posterior : is the conditional probability of of the model parameters (latent variables) given the data.



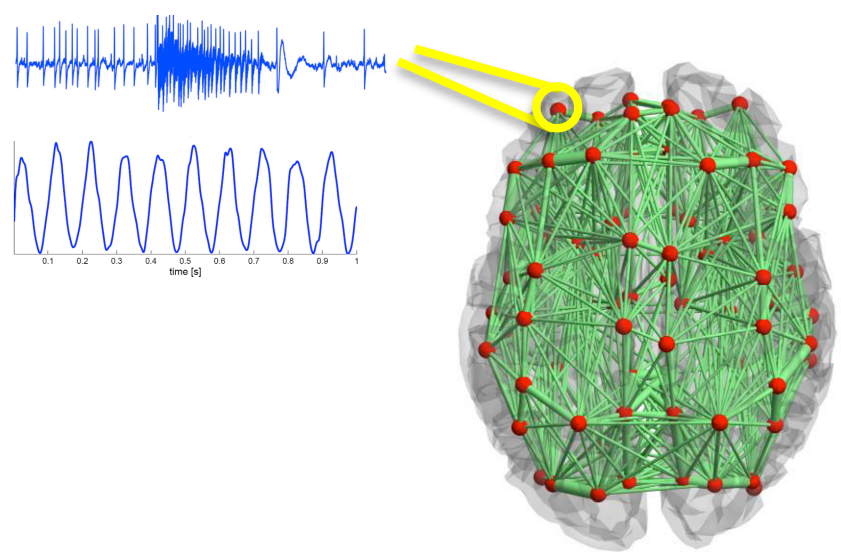
Bayesian inference

- Integrating patient-specific information through *prior*
- uncertainty (confidence) in the estimations through *posterior*
- out-of-smaple prediction for unseen data through *model evidence*
- The relation between parameters (*identifiability/degeneracy*)

Large-scale brain network modeling

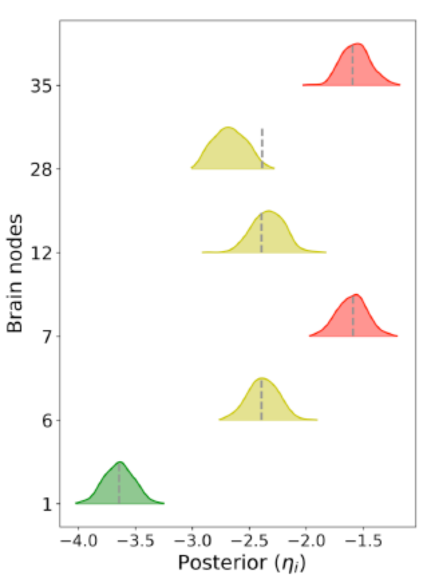
Neural Mass Models:

- Epileptor (epilepsy)
- Generic Hopf (coupled oscillators)
- Montbrio model (resting-state, …)
- Neural fields



Simulated/empirical Data:

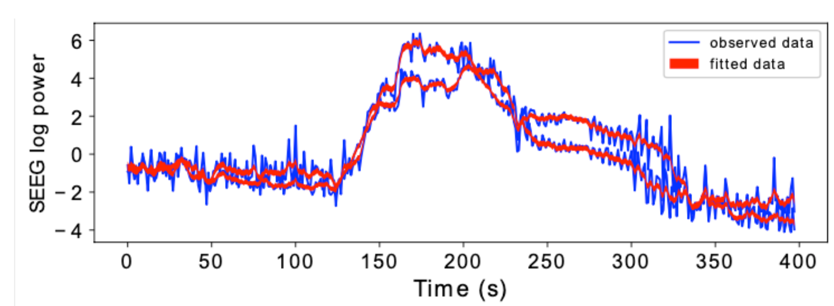
- SEEG (epilepsy)
- Source brain activity
- BOLD fMRI (resting-state)
- EEG/MEG/fMRI,…

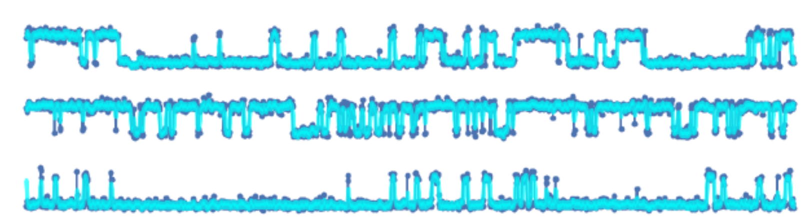


Brain region's parameter(s)?

homogeneity/heterogeneity (regional variance)
(normal/informative/hierarchical prior)

SC is fixed but G to scale the connectome?





The **likelihood** function is the central ingredient in both frequentist and Bayesian inference

$$p(y \mid \theta) = \int dz\; p(y, z \mid \theta)$$

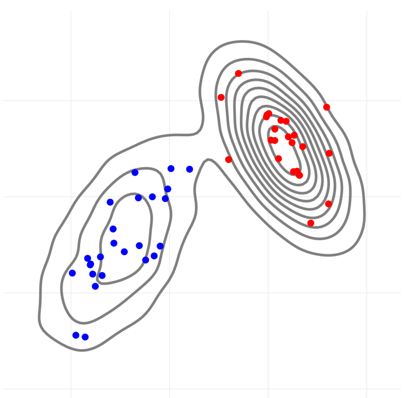
challenge: *likelihood is an integral over all possible trajectories in the latent space*

1) Likelihood based inference (non-parametric)

No objective function:
RMSE, correlation, …

PPLs such as Stan/PyMC3:

- Self-tuning Hamiltonian Monte Carlo (NUTS)
- Automatic Differentiation Variational Inference (ADVI)
- Maximum a Posteriori (MAP)



Stan

PyMC3

- probabilistic model in code
- Observed data

posterior

Diagnostics for convergence (\hat R)
for satisfying detailed balance condition (ergodicity)

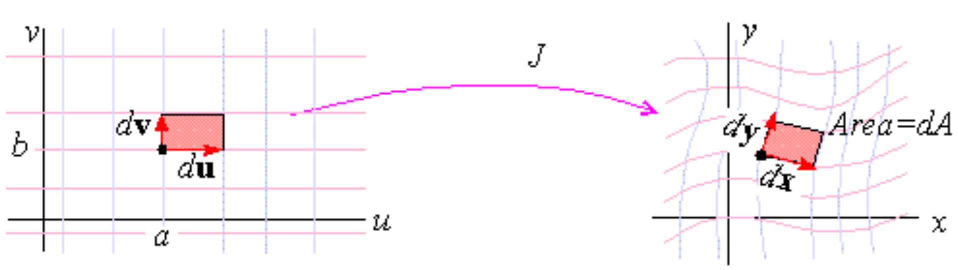
2) Approximate Likelihood inference (parametric)

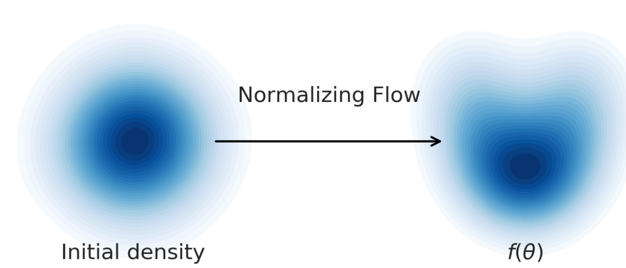
Data features

Simulated Based Inference (normalize flow)

Neural Net minimizes KL divergence

A new tool for constructing flexible probability distributions from simple base distributions using DNN





- prior distribution
- simulator (forward model)
- summary statistics

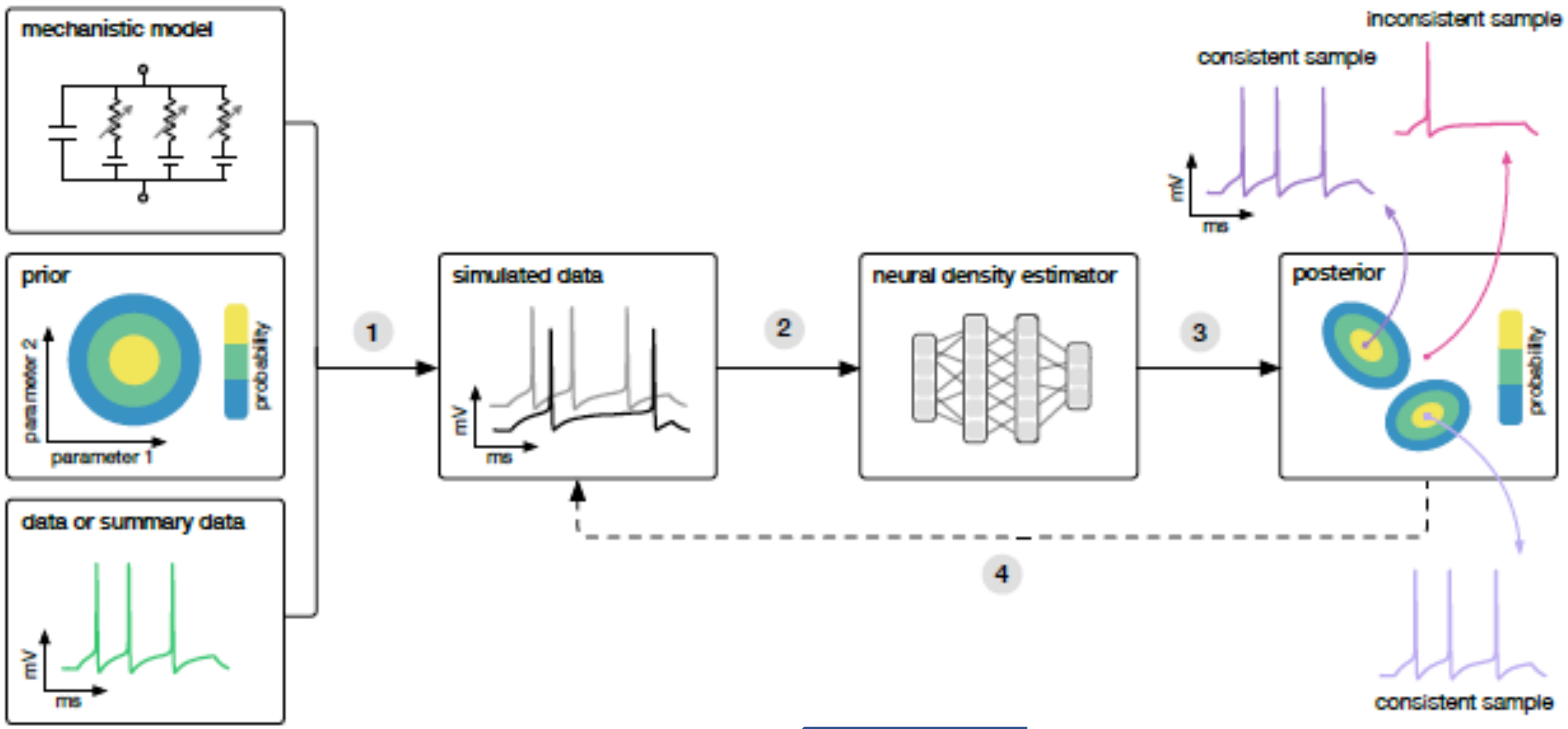
$$\mathbf{x} = f(\mathbf{z}) \rightarrow p(\mathbf{x}) = p(\mathbf{z}) \left|\det \frac{\partial f^{-1}}{\partial \mathbf{z}}\right|$$

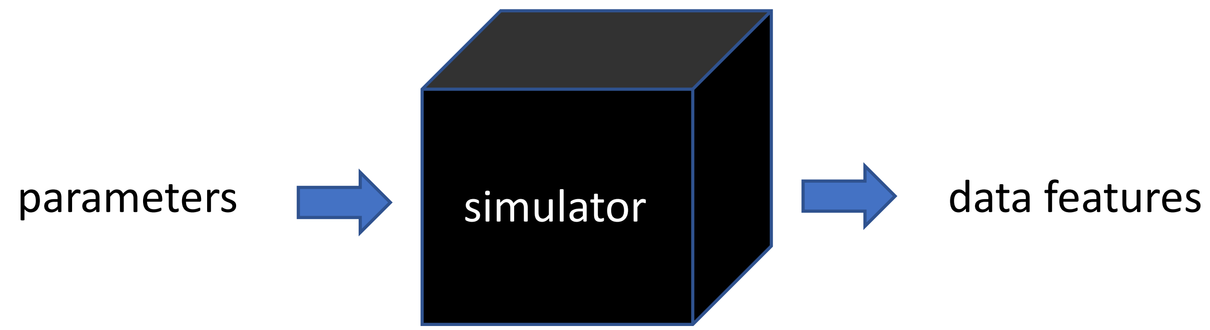
Deep Neural Network
multimodal high-dimensional distributions

posterior

Infer a parameterized (invertible) function that maps between observation space and latent variables to approximate posterior distribution.

Simulated Based Inference





Gonçalves et al, eLife (2020)

Amortized Bayesian inference (ABI) of Virtual Epileptic Patient (VEP)