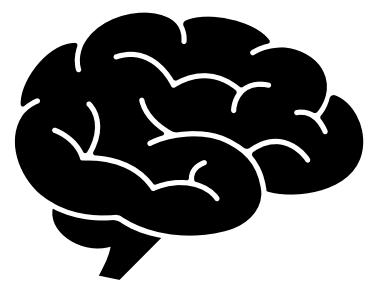


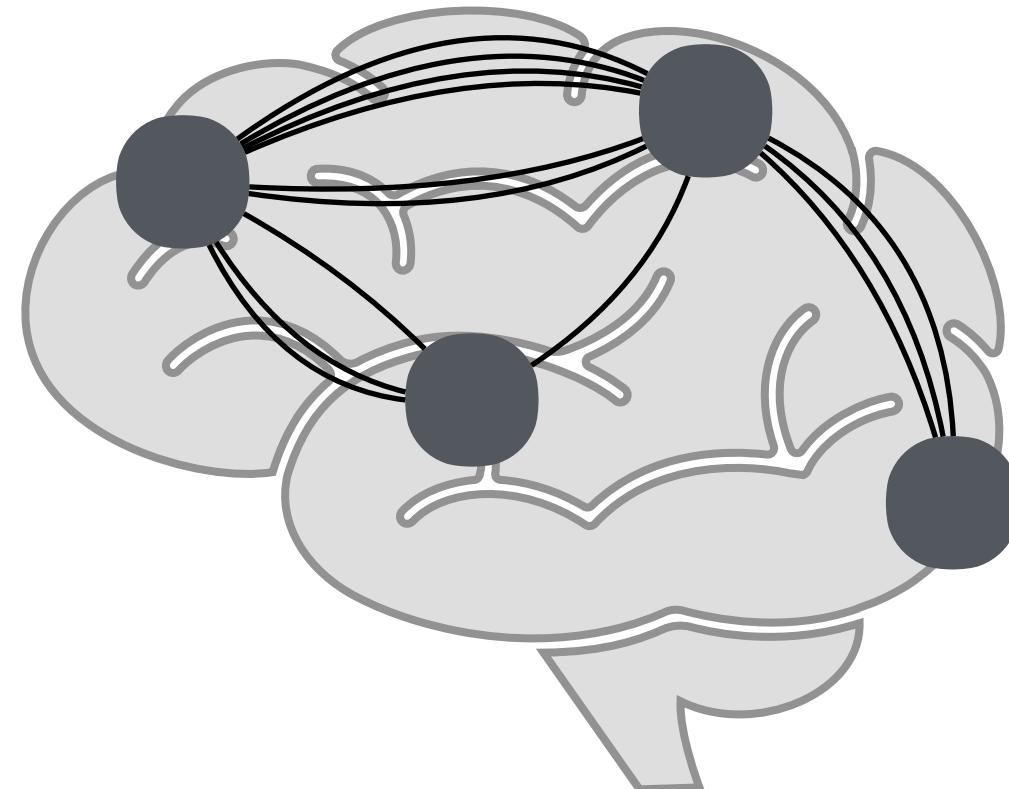
# Inférence Bayésienne de la modulation de la connectivité effective de réseaux de modèles de masse neurale à partir de données de neurostimulation

Sous la supervision jointe de Olivier David et Matthieu Gilson

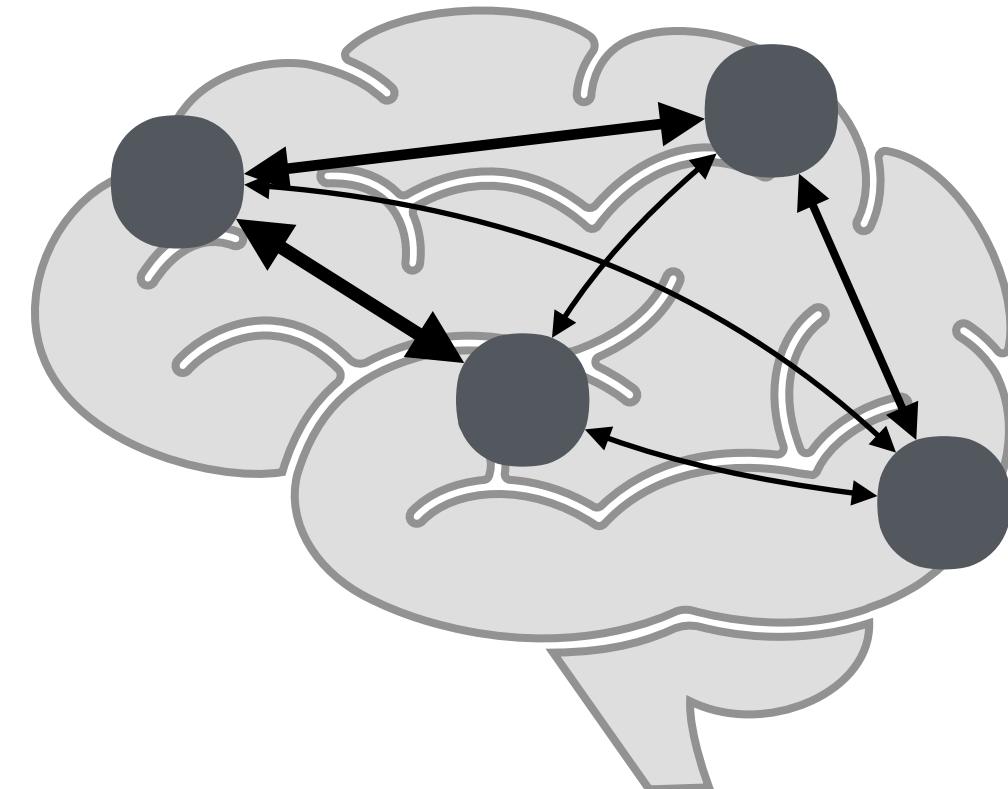
# Effective connectivity



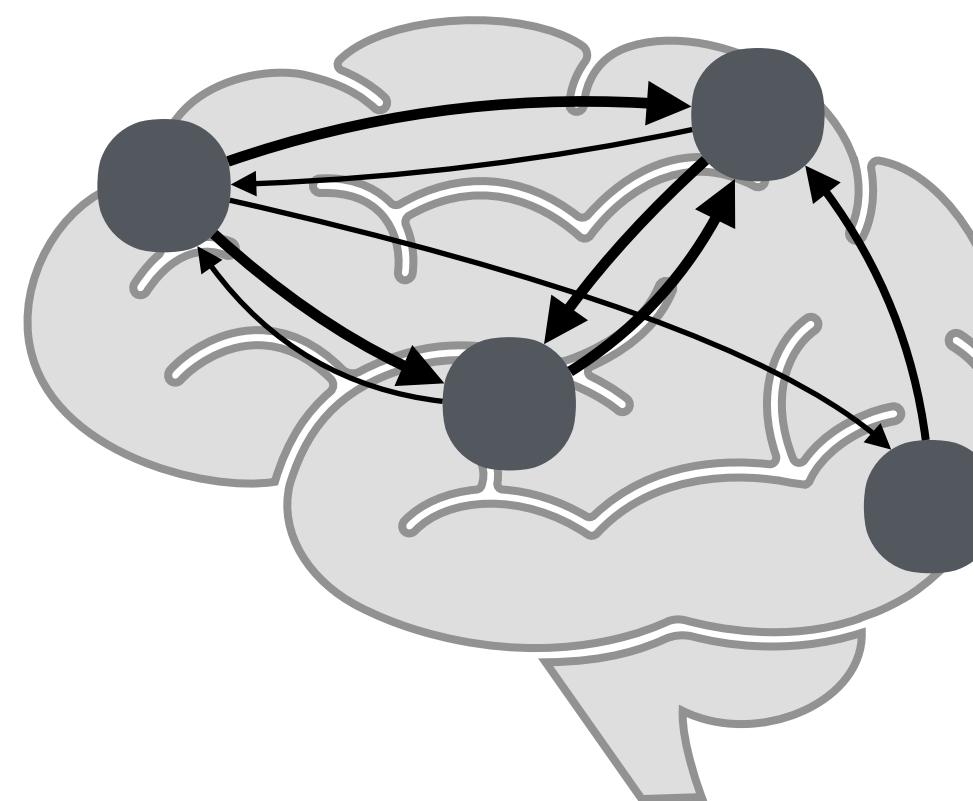
Structural connectivity (SC)



Functional connectivity (FC)



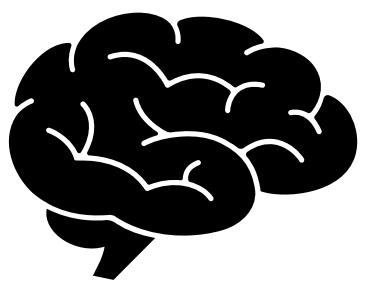
Effective connectivity (EC)



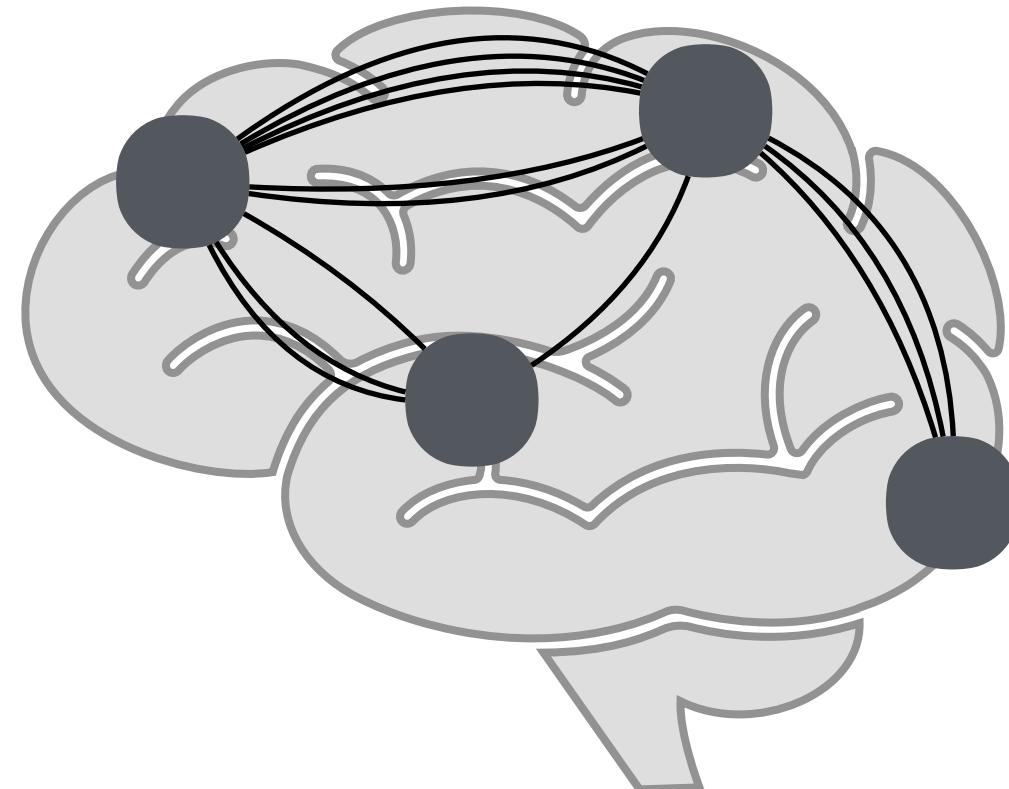
Adapted from O.Sporns 2007

- Anatomique
- Statique - non spécifique à tâche cognitive
- Non-directionnel (IRM-DTI)

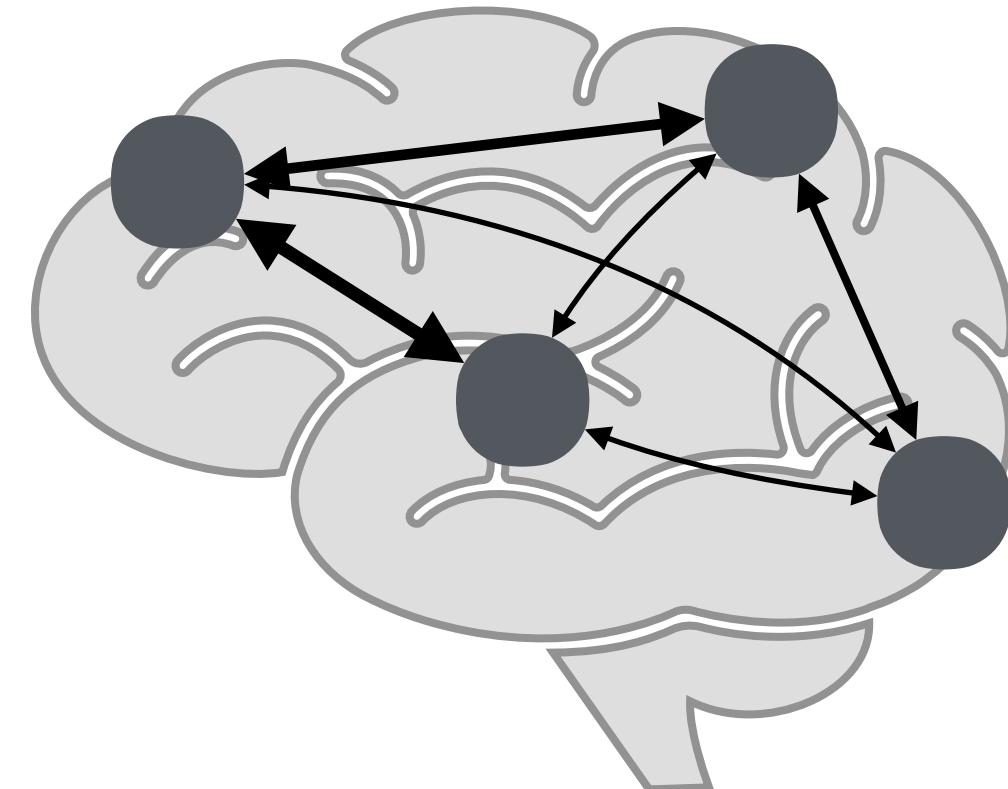
# Effective connectivity



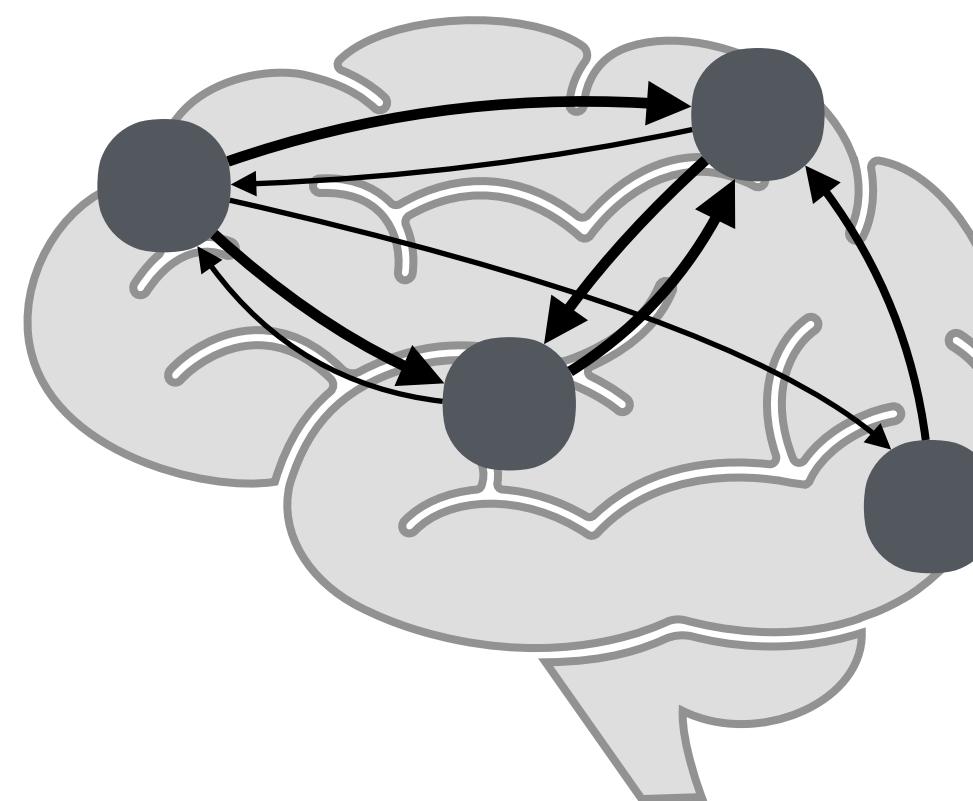
Structural connectivity (SC)



Functional connectivity (FC)



Effective connectivity (EC)

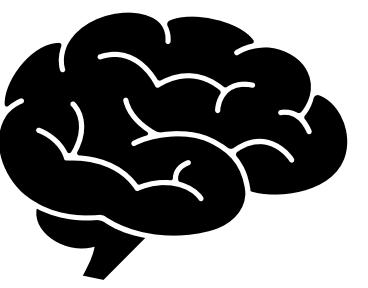


Adapted from O.Sporns 2007

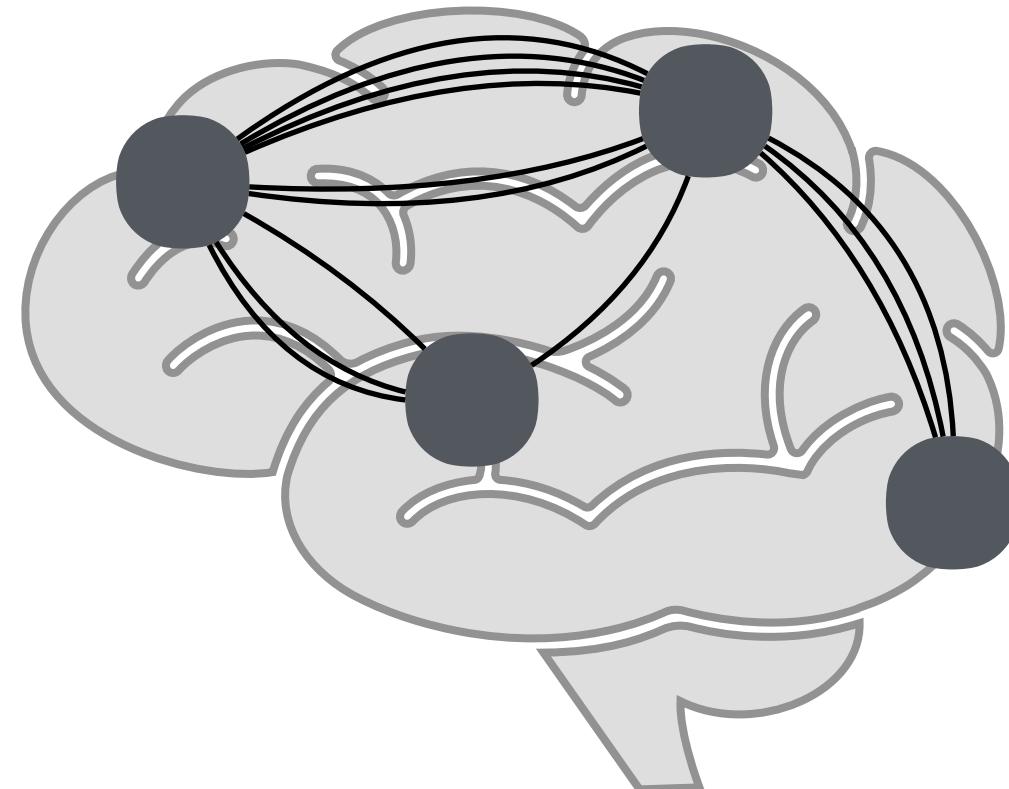
- Anatomique
- Statique - non spécifique à tâche cognitive
- Non-directionnel (IRM-DTI)

- Spécifique à tâche cognitive
- Non-Directionnel
- Proxy communication neuronale

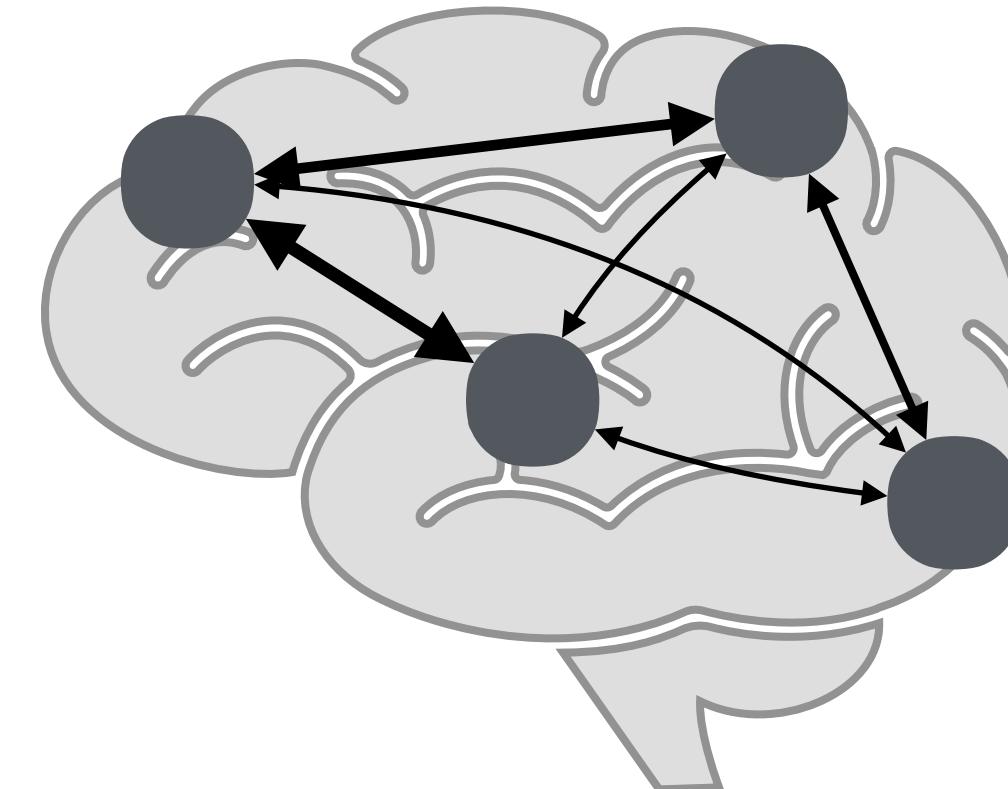
# Effective connectivity



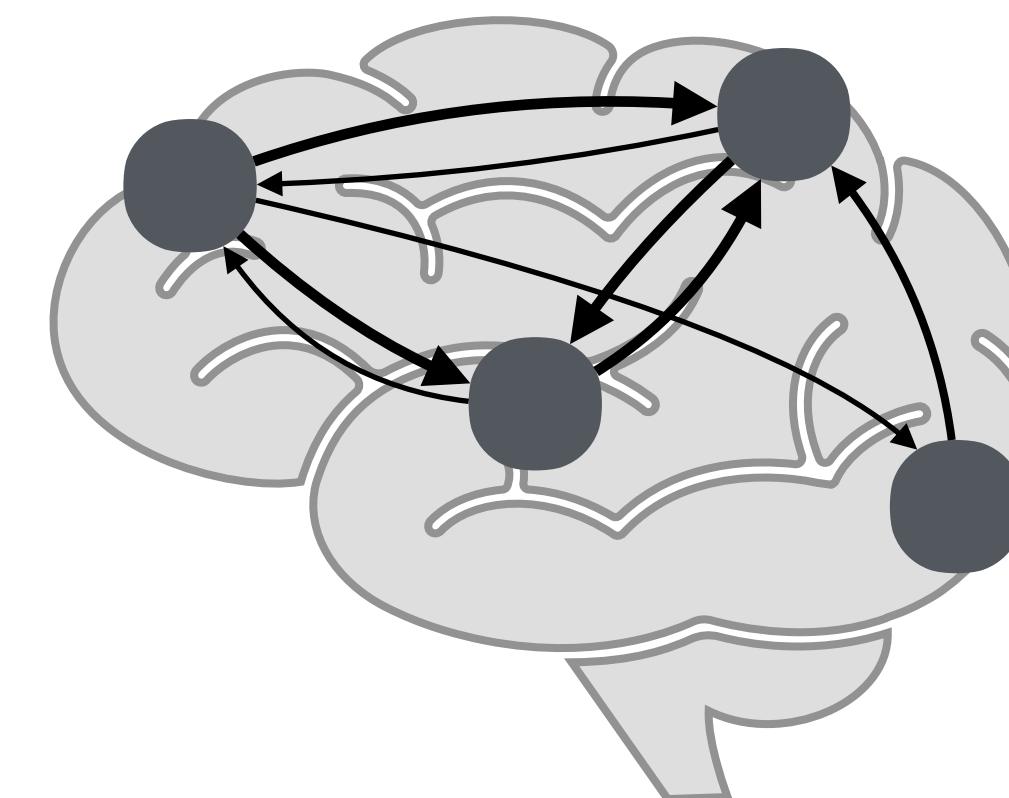
Structural connectivity (SC)



Functional connectivity (FC)



Effective connectivity (EC)



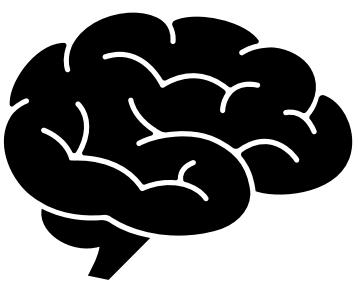
Adapted from O.Sporns 2007

- Anatomique
- Statique - non spécifique à tâche cognitive
- Non-directionnel (IRM-DTI)

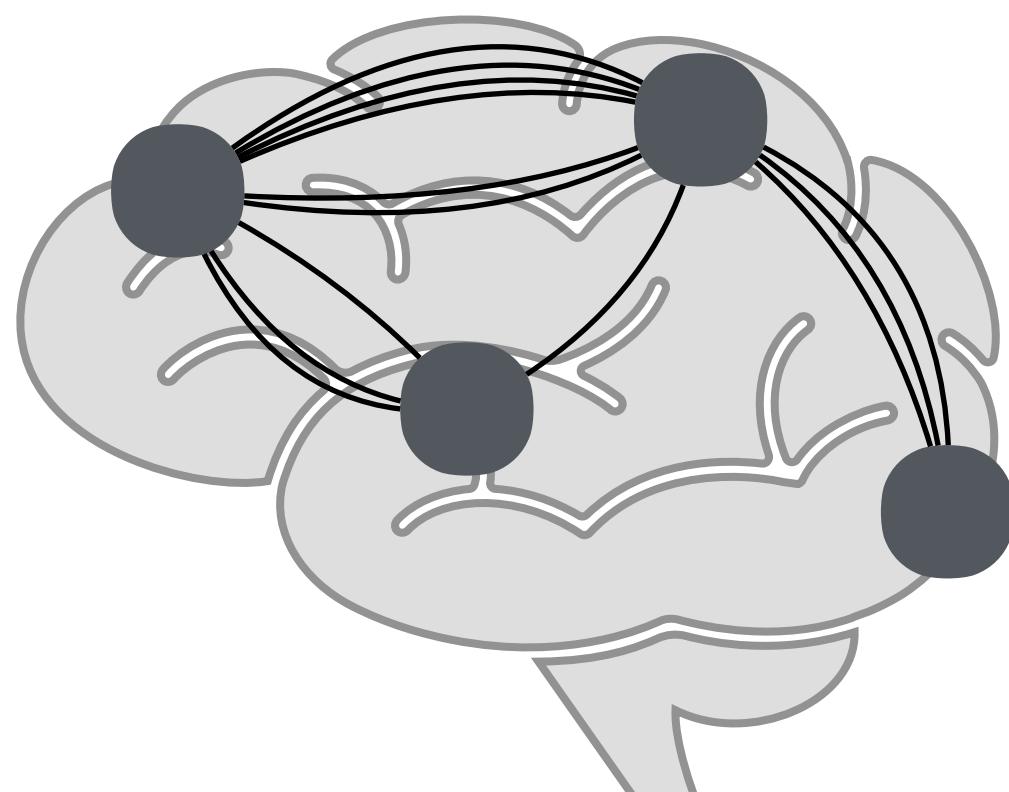
- Spécifique à tâche cognitive
- Non-Directionnel
- Proxy communication neuronale

- Spécifique à tâche cognitive
- Modulation de la connection anatomique
- Proxy communication neuronale

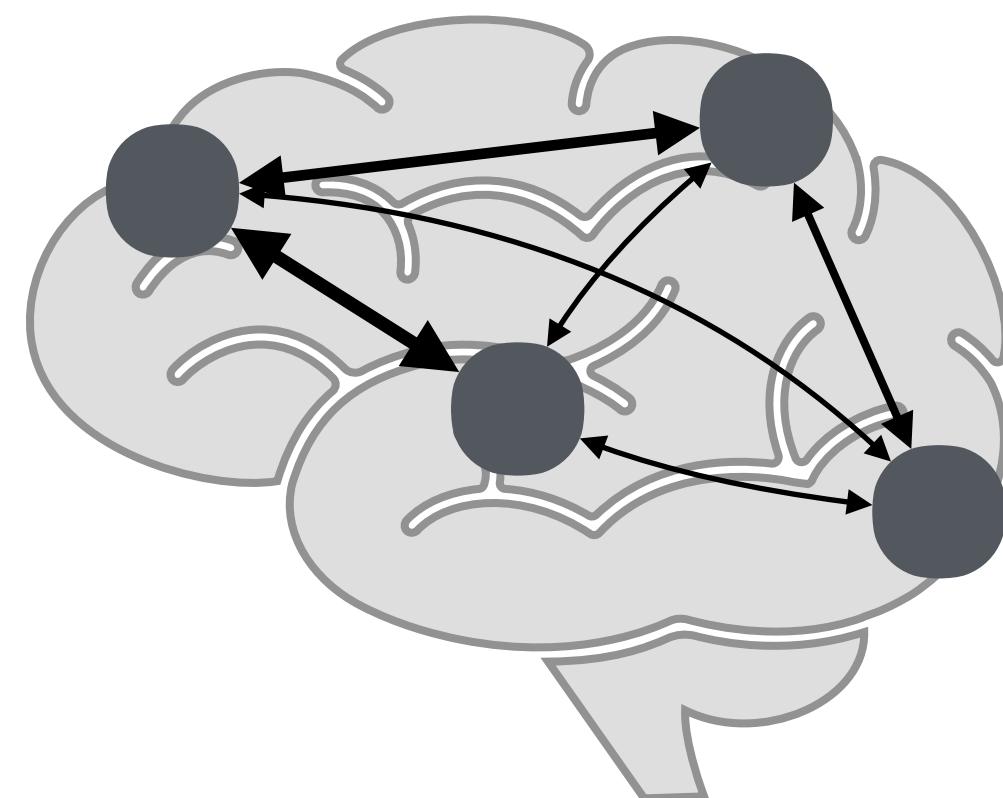
# Effective connectivity



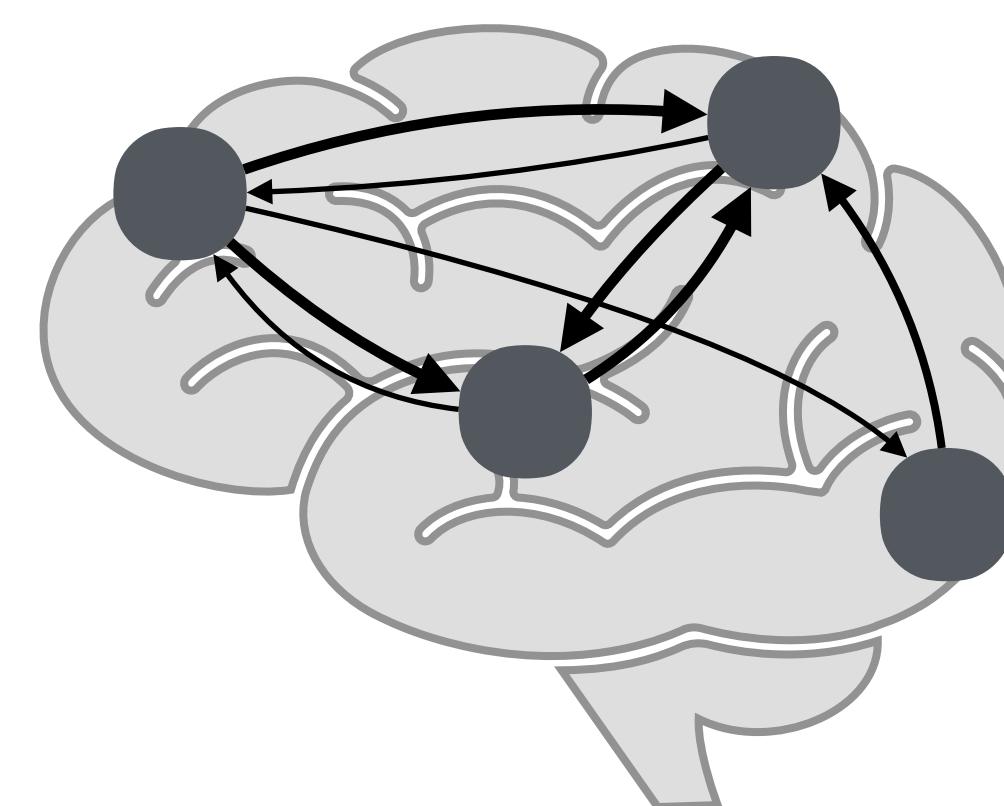
Structural connectivity (SC)



Functional connectivity (FC)



Effective connectivity (EC)

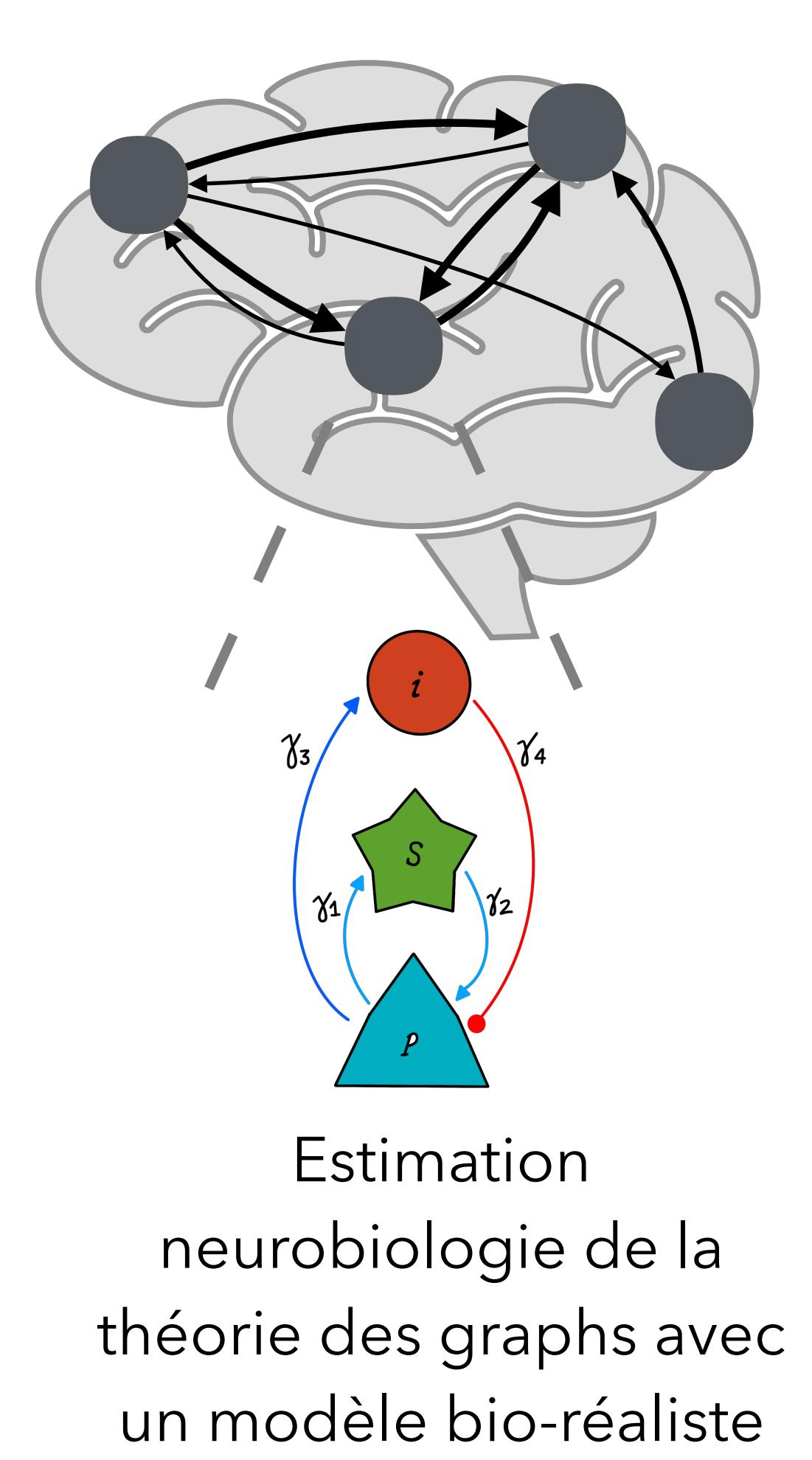


- Anatomique
- Statique - non spécifique à tâche cognitive
- Non-directionnel
- Non-directionnel (IRM-DTI)

Adapted from O.Sporns 2007

- Spécifique à tâche cognitive
- Non-Directionnel
- Proxy communication neuronale

- Spécifique à tâche cognitive
- Modulation de la connection anatomique
- Proxy communication neuronale



# Neural Mass Model



Dynamic Causal Modeling (DCM)  
ERPs David et al 2005 / 2006

Pyramidal

$$\dot{V}_{pe} = c_{pe}$$

$$\dot{c}_{pe} = \frac{H_e}{\tau_e}((A^B + A^L)S(v_p) + \gamma_2 S(v_s)) - \frac{2}{\tau_e}c_{pe} - \frac{1}{\tau_e^2}v_{pe}$$

$$\dot{V}_{pi} = c_{pi}$$

$$\dot{c}_{pi} = \frac{H_i}{\tau_i}(\gamma_4 S(v_i)) - \frac{2}{\tau_i}c_{pi} - \frac{1}{\tau_i^2}v_{pi}$$

$$\dot{V}_p = c_{pe} - c_{pi}$$

Inhibitory

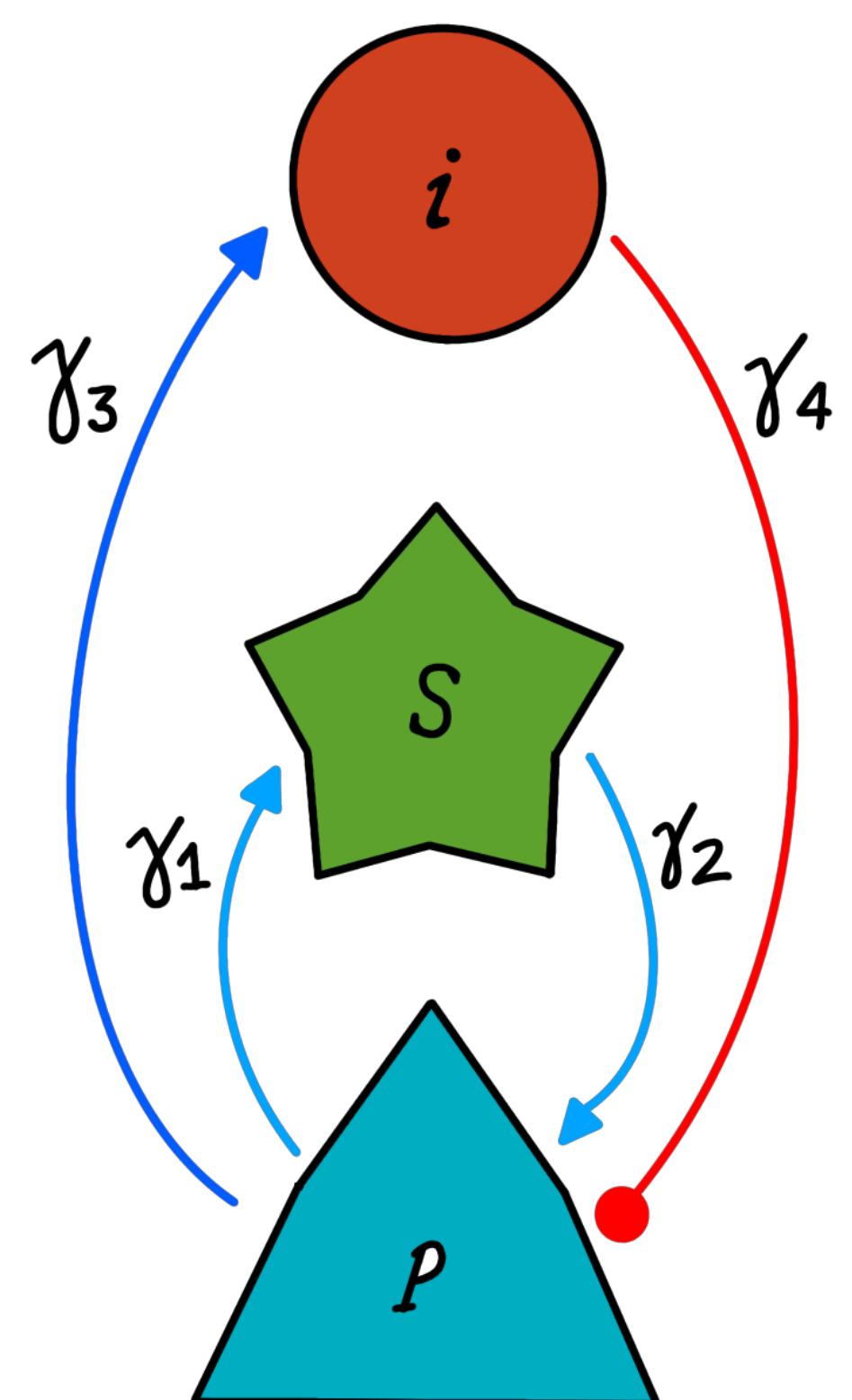
$$\dot{V}_i = c_i$$

$$\dot{c}_i = \frac{H_e}{\tau_e}(A^B + A^L + \gamma_3 S(v_p)) - \frac{2}{\tau_e}c_i - \frac{1}{\tau_e^2}v_i$$

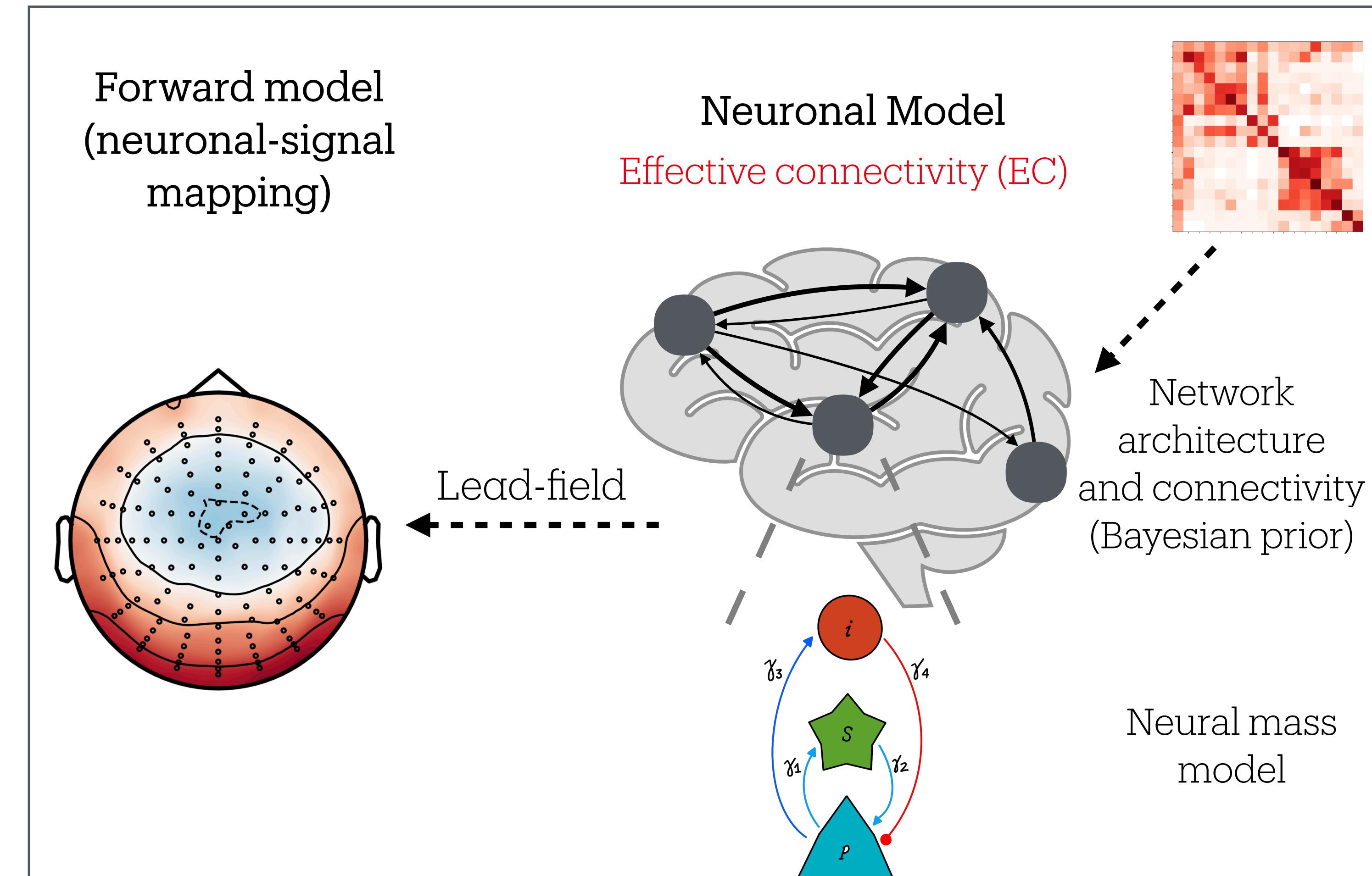
Stellate

$$\dot{V}_s = c_s$$

$$\dot{c}_s = \frac{H_e}{\tau_e}(S(u) + A^F + A^L + \gamma_1 S(v_p)) - \frac{2}{\tau_e}c_s - \frac{1}{\tau_e^2}v_s$$

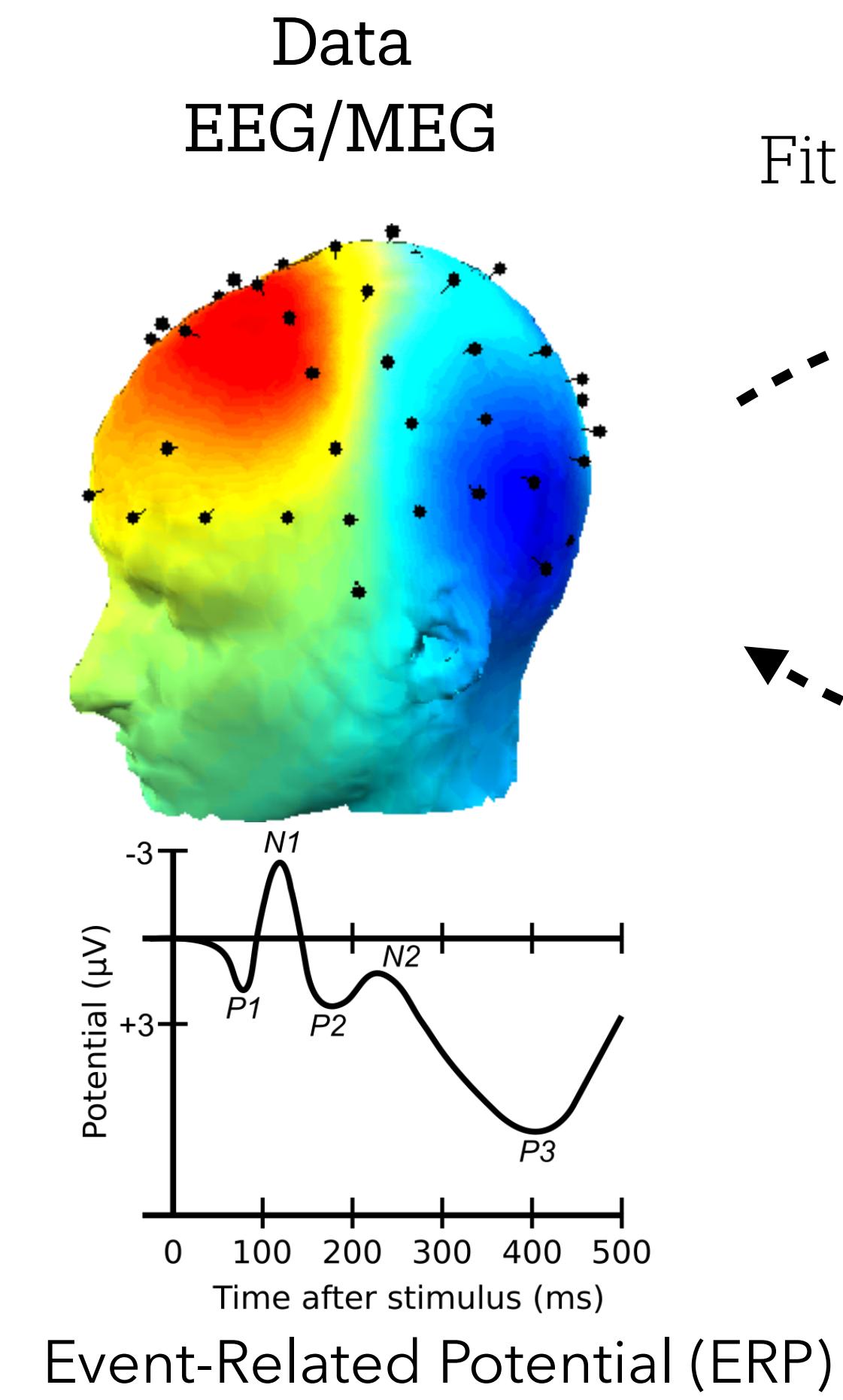


# Estimation with DCM



David et al., Neuroimage, 2005  
David et al., Neuroimage, 2006

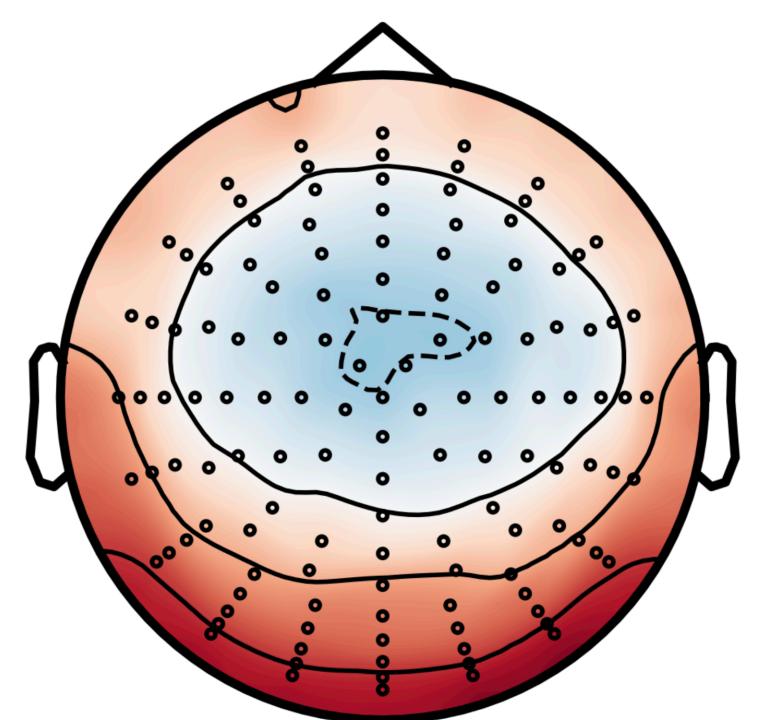
# Estimation with DCM



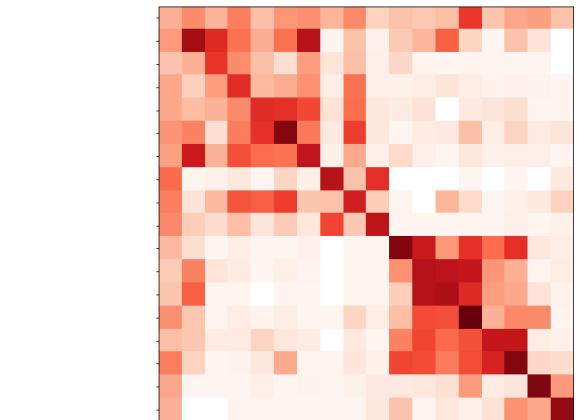
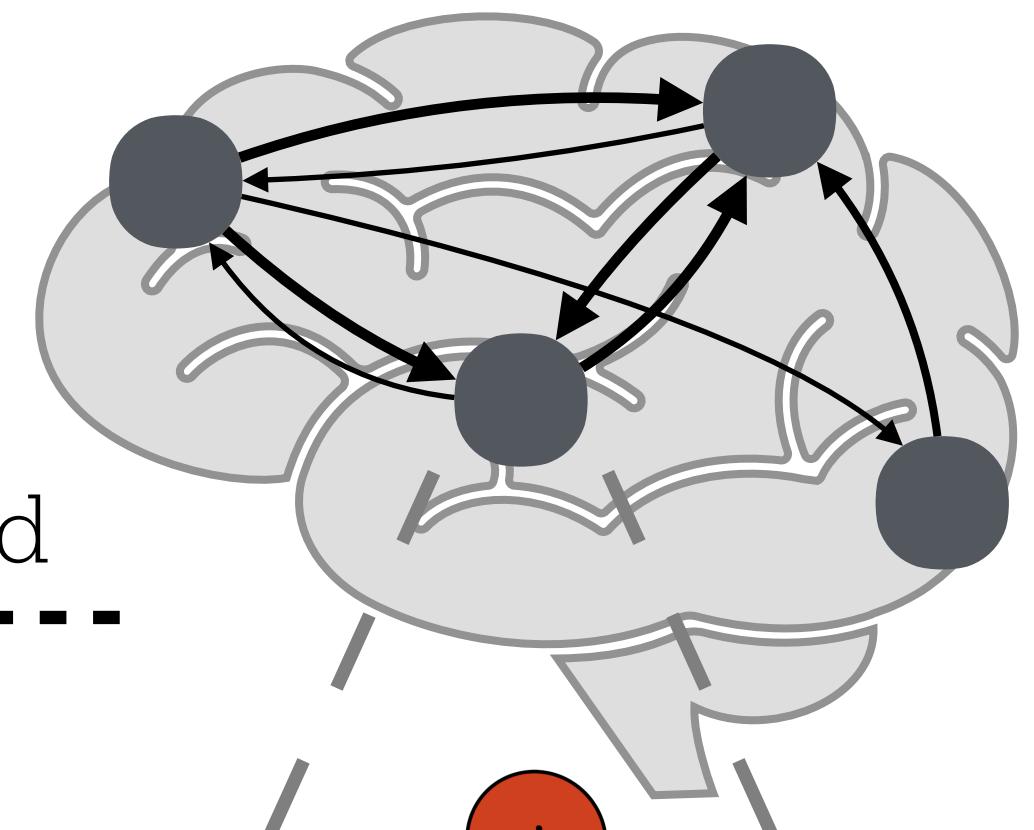
Fit / Bayesian Inference

Generative model

Forward model  
(neuronal-signal  
mapping)

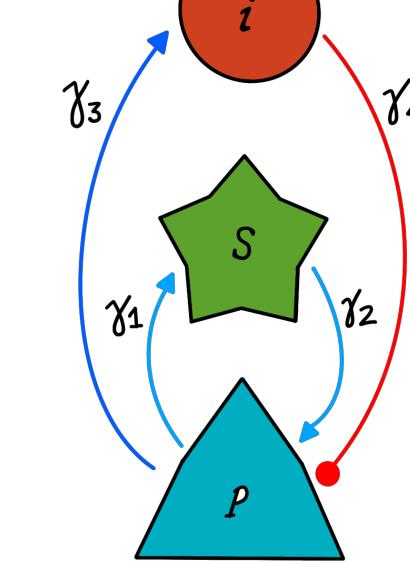


Neuronal Model  
Effective connectivity (EC)



Network  
architecture  
and connectivity  
(Bayesian prior)

Neural mass  
model



David et al., Neuroimage, 2005  
David et al., Neuroimage, 2006

# Estimation with DCM

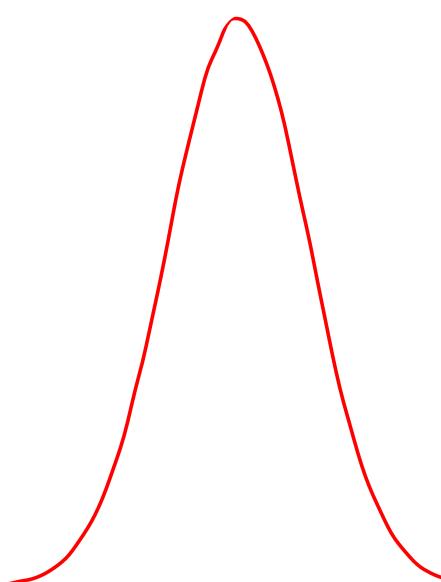


The current DCM approach has several limitations :

## Technical

- Bayesian algorithm (Variational inference) :

- Require precise prior knowledge
- Limited to small number of parameters
- Gaussian approximation



Gaussian curve example

# Estimation with DCM

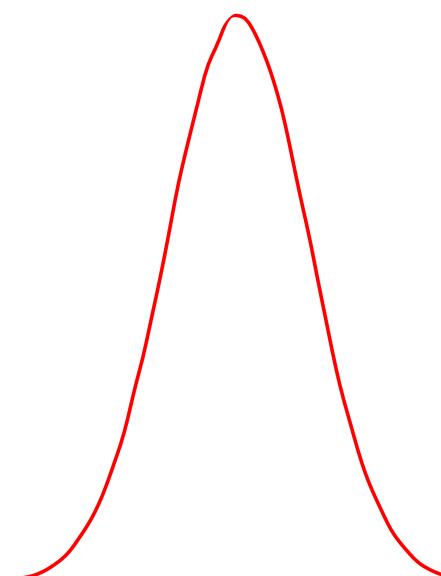


The current DCM approach has several limitations :

## Technical

- Bayesian algorithm (Variational inference) :

- Require precise prior knowledge
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Gaussian curve example

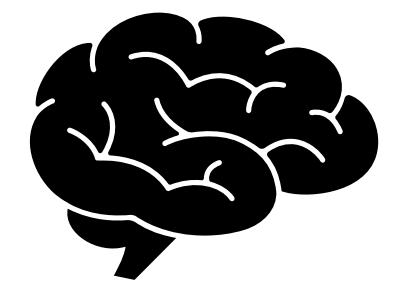
## Neuroscientific

- Prior definiton :

- Structural connectivity
- Compilation of results from previous article
- Qualitative / Imprecise

# Estimation with DCM

---



Suggested solution ?

Technical

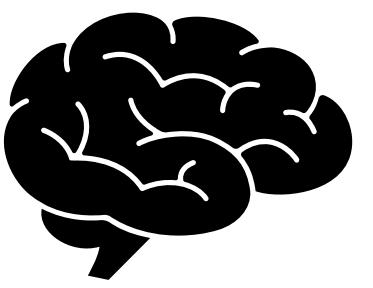
- State of the art bayesian approach :
  - The markov chain monte carlo method (MCMC)
  - Not yet applied for EC on DCM
  - Richness in posterior estimation

(Neal, 2011)

(Sengupta et al., 2016)

(Betancourt, 2018)

# Estimation with DCM



Suggested solution ?

Neuroscientific

- F-tract prior :

- Probabilistic tractography



Olivier DAVID, INS

(Stephan et al., 2009)  
(David et al., 2013)  
(Trebaul et al., 2018)

# Estimation with DCM



Suggested solution ?

Neuroscientific

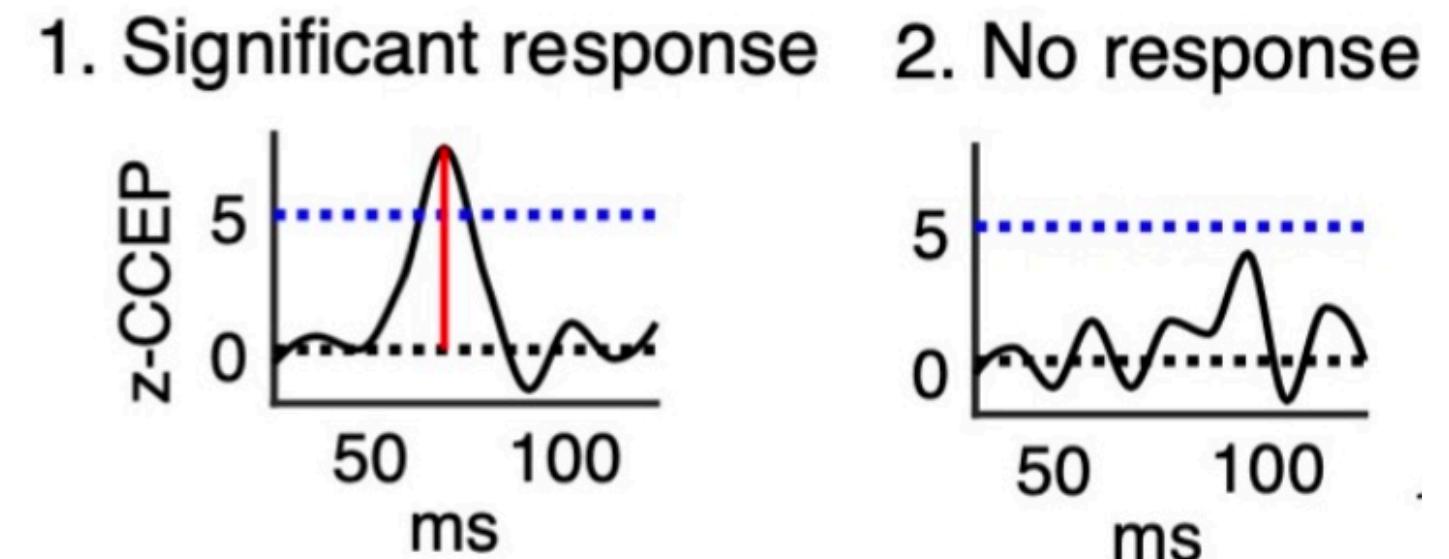
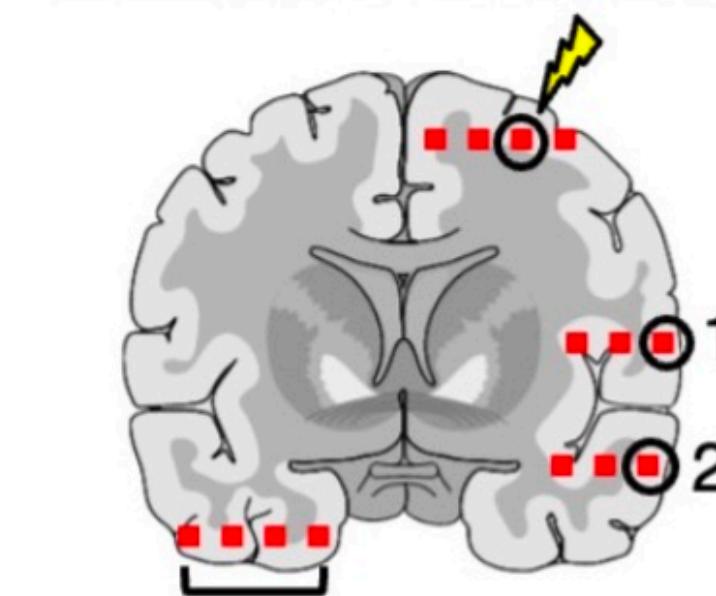
- F-tract prior :

- Probabilistic tractography
- Cortico-cortical evoked potential (CCEP)

(Stephan et al., 2009)  
(David et al., 2013)  
(Trebaul et al., 2018)

Example of F-tract protocole

Stimulation schematic



Seguin et al, 2022

- 1000 epileptic patients
- 20000 stimulation from intracranial electrodes
- high spatio-temporal resolution

# Estimation with DCM



Suggested solution ?

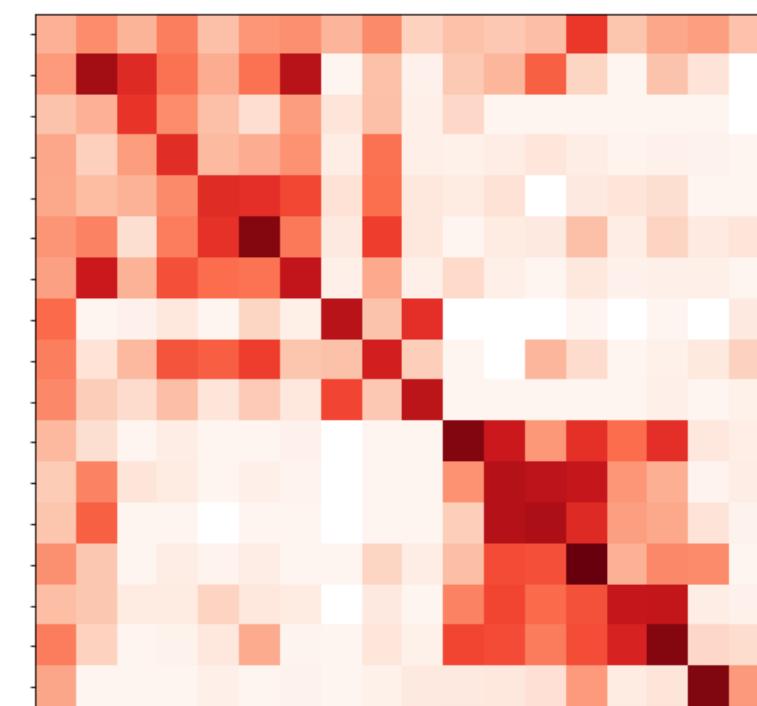
Neuroscientific

- F-tract prior :

- Probabilistic tractography
- Cortico-cortical evoked potential (CCEP)
- Empirical effective connectivity mapping

Probability of connection matrix

Brain region



High probability

Low probability

(Stephan et al., 2009)

(David et al., 2013)

(Trebaul et al., 2018)

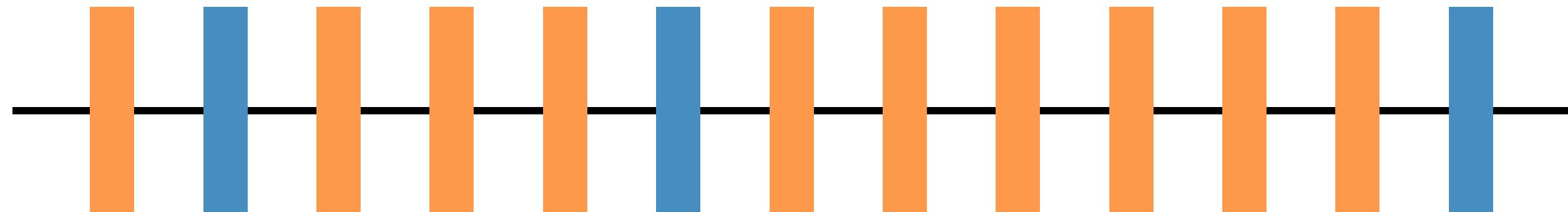
# Methods

# Methods



## EEG auditory oddball task

Exemple of a sequence of stimuli



### 2 Auditory stimuli :

- Standard events 1000Hz (80%)
- Rare events 2000Hz (20%)
- 600 trials (480 standard, 120 rare)



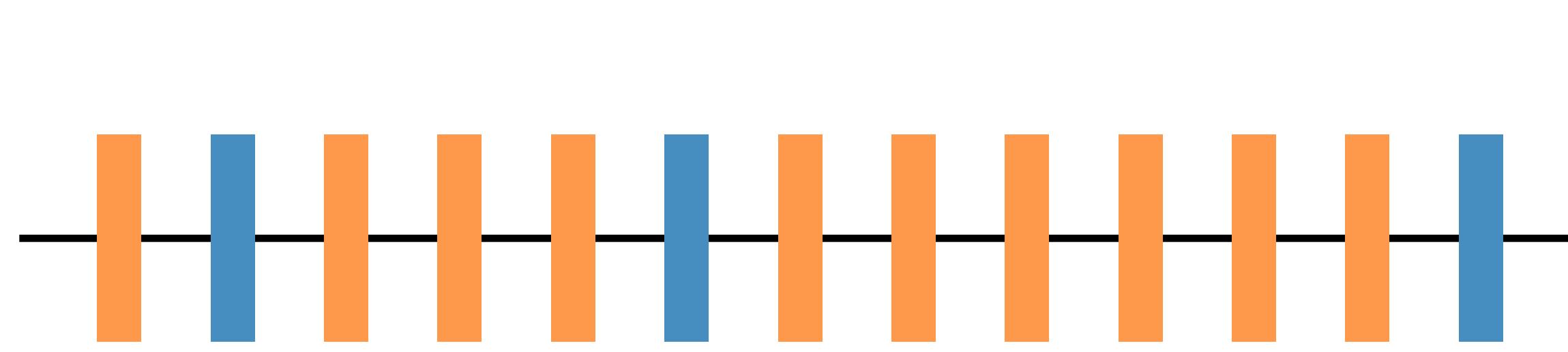
Garrido et al, 2007

# Methods

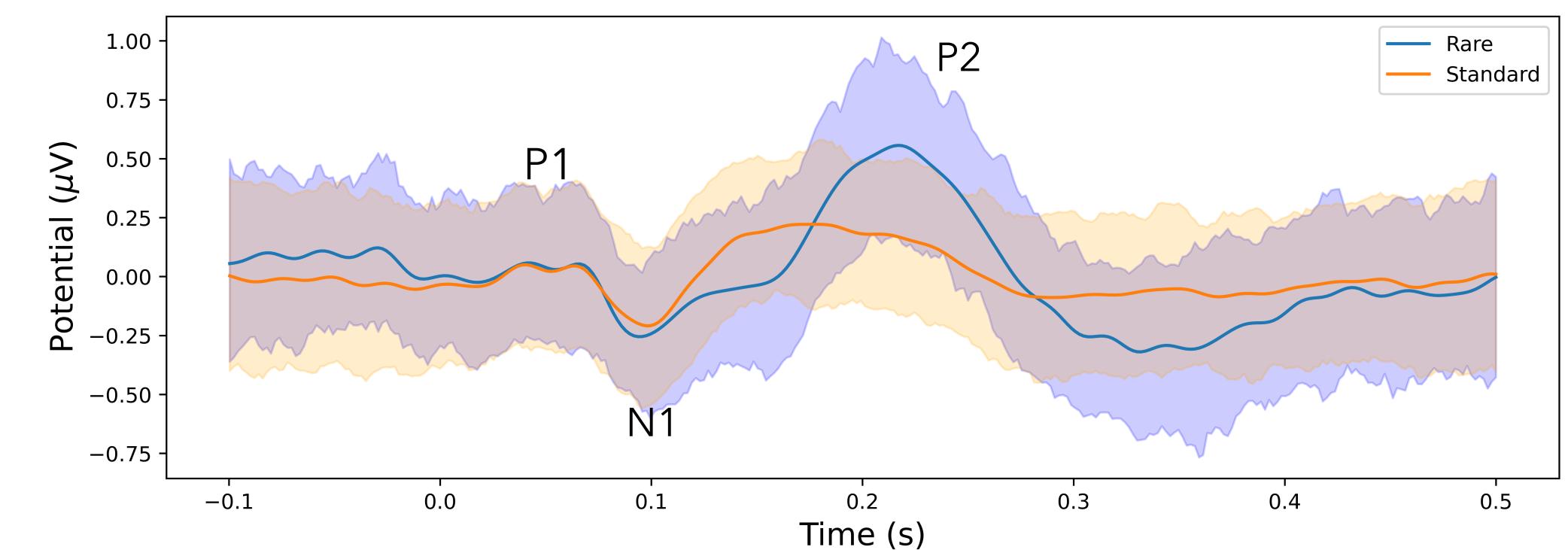


## EEG auditory oddball task

Exemple of a sequence of stimuli



Average response at the sensor A1



### 2 Auditory stimuli :

- Standard events 1000Hz (80%)
- Rare events 2000Hz (20%)
- 600 trials (480 standard, 120 rare)



### EEG data :

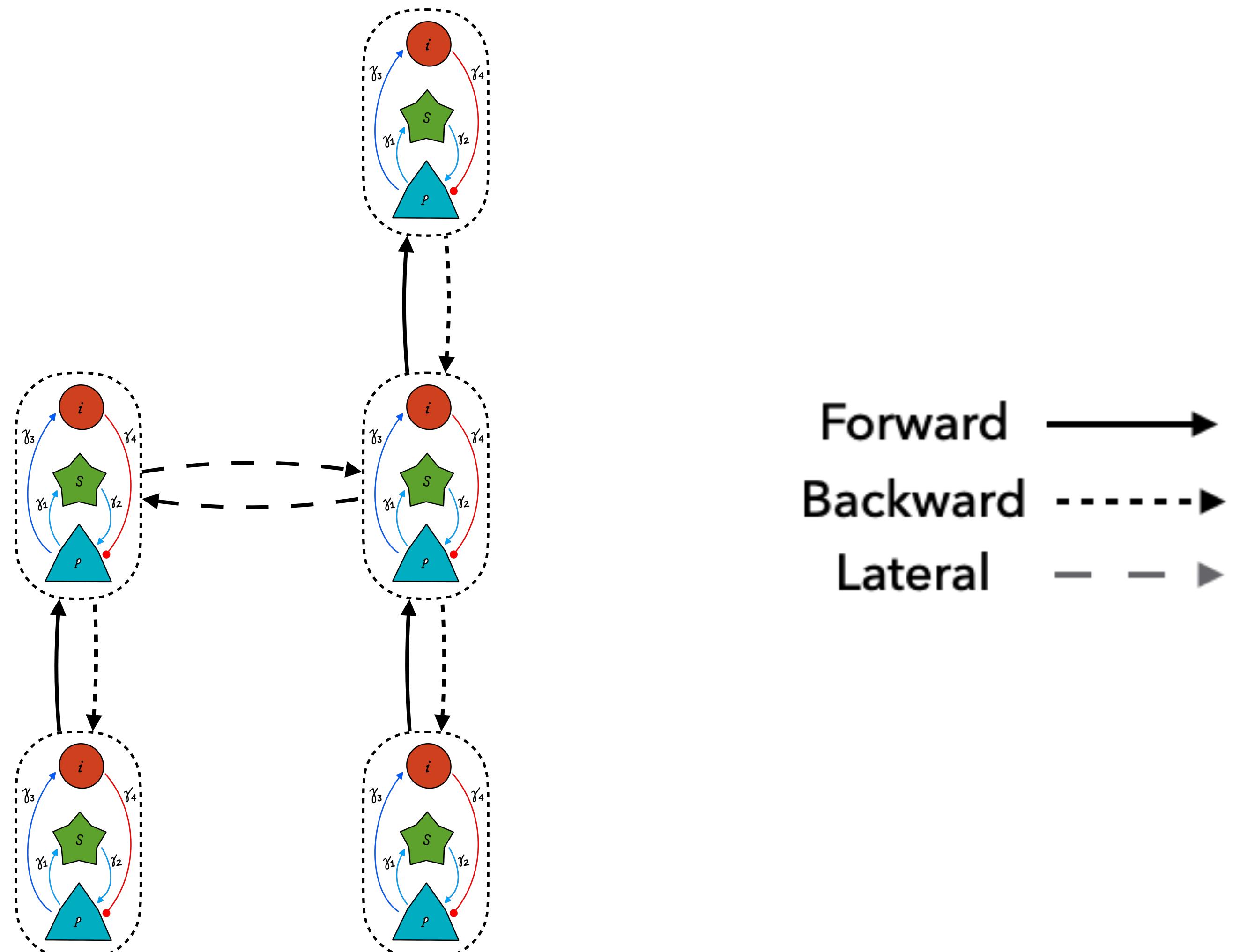
- Recorded 128 channels
- Single human subject recorded M.Garrido
- Tutorial SPM data

Garrido et al, 2007

# Methods



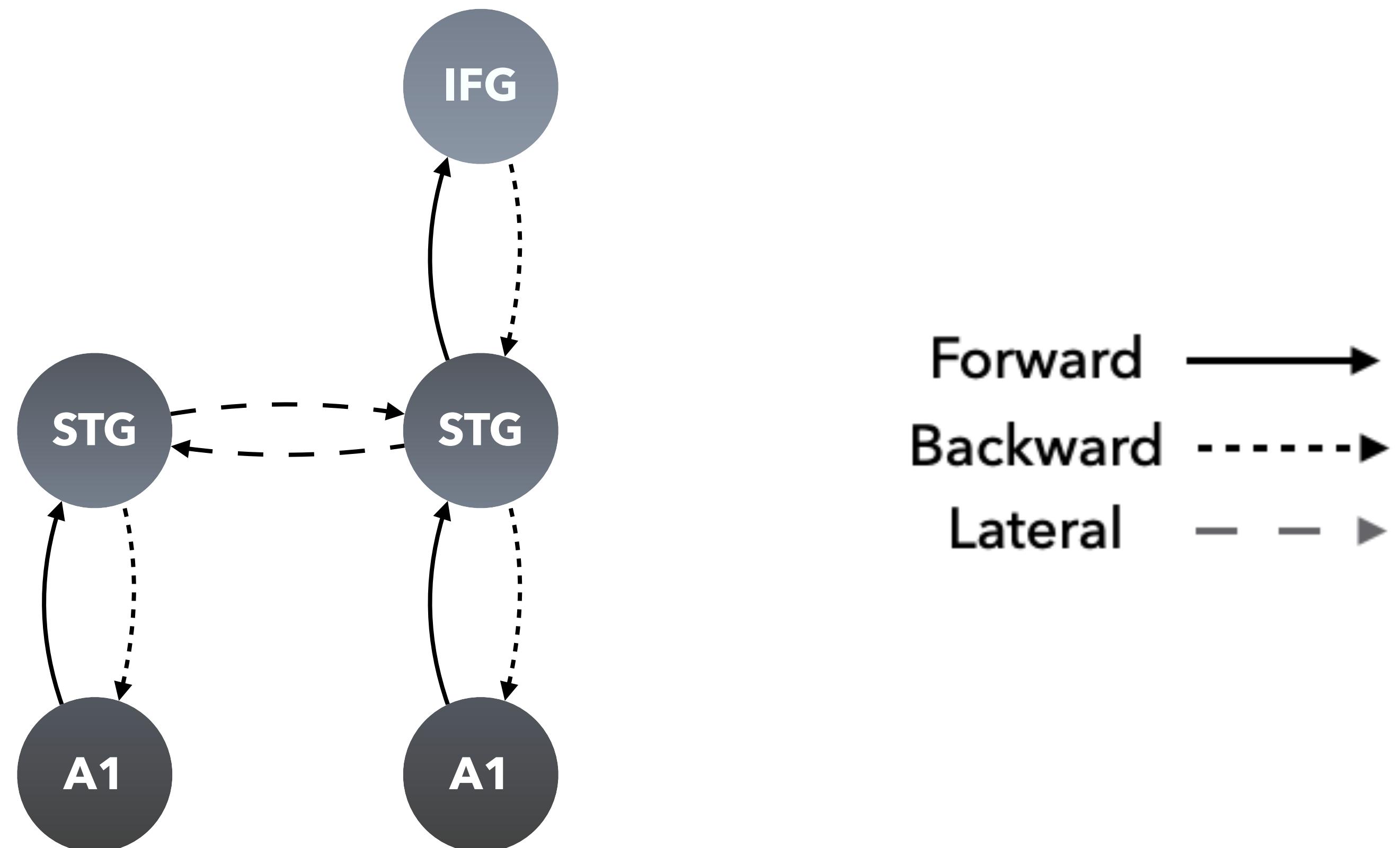
## Model specification



# Methods



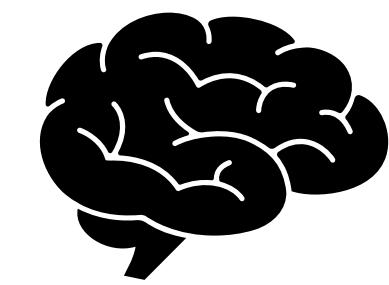
## Model specification



Garrido et al, 2007

A1: primary auditory cortex  
STG: superior temporal gyrus  
IFG: inferior frontal gyrus

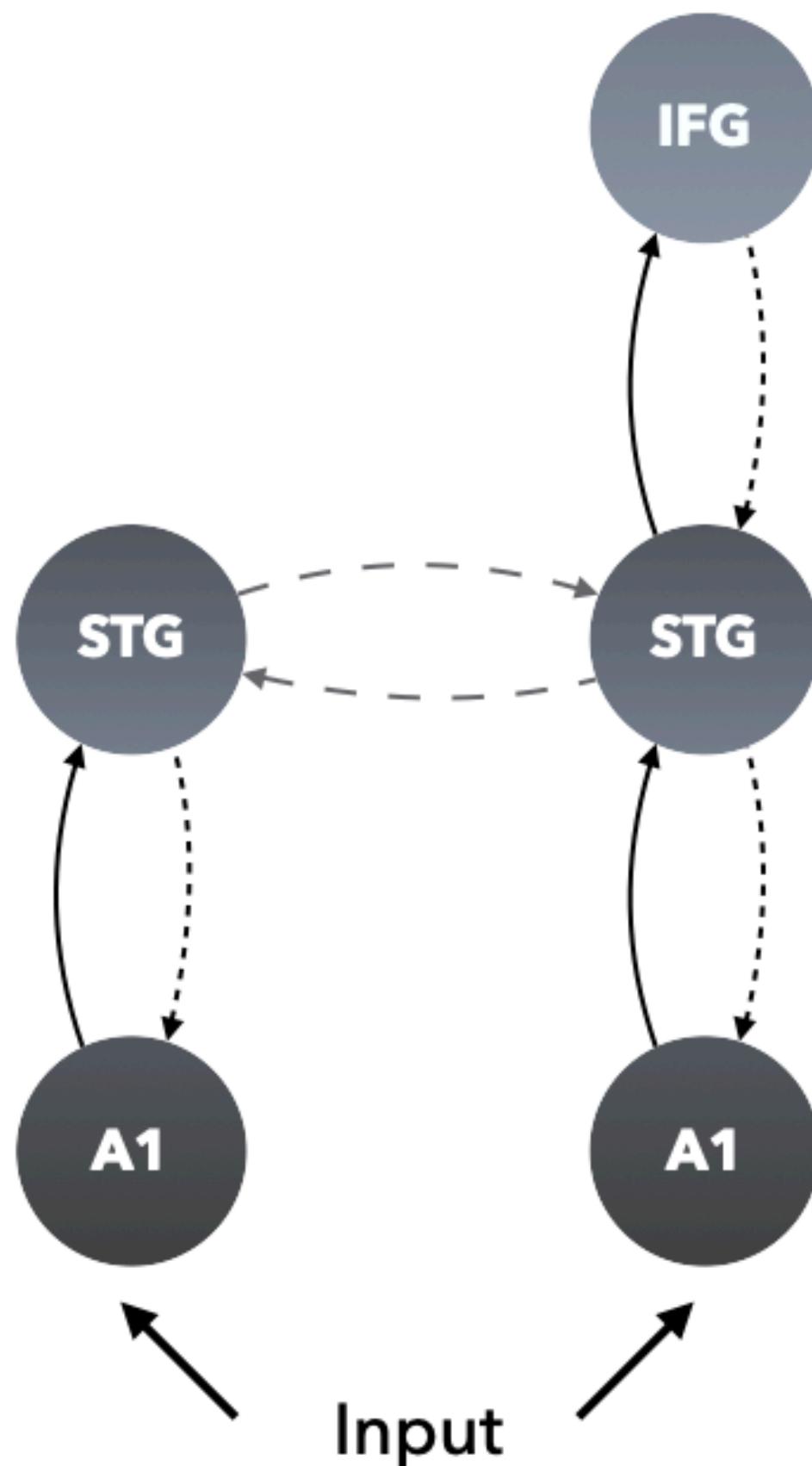
# Methods



## Model specification

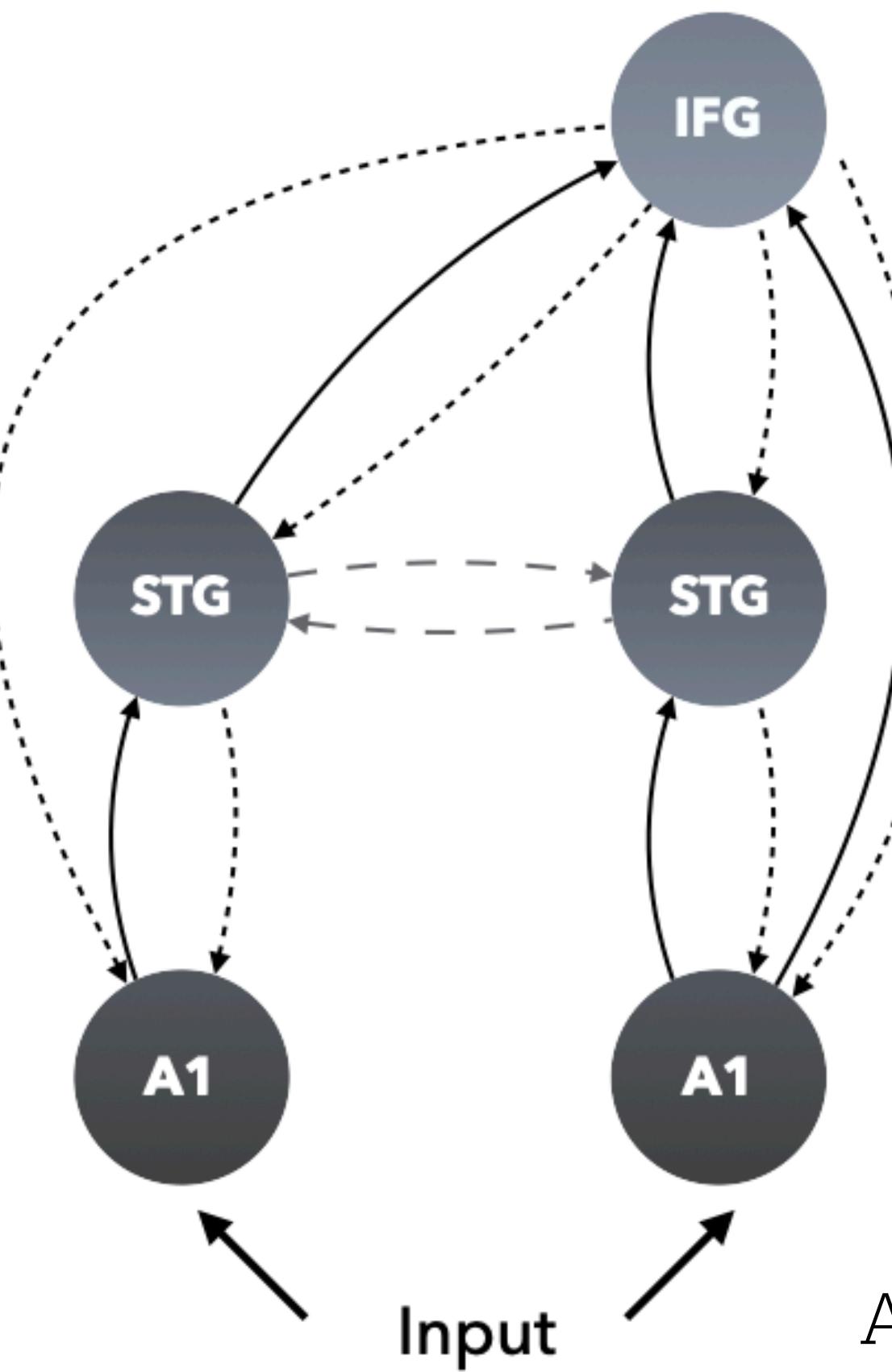
A

Garrido's architecture



B

F-tract architecture

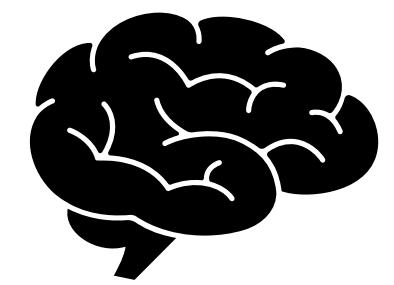


Forward →  
Backward →—→  
Lateral —→—→

Garrido et al, 2007

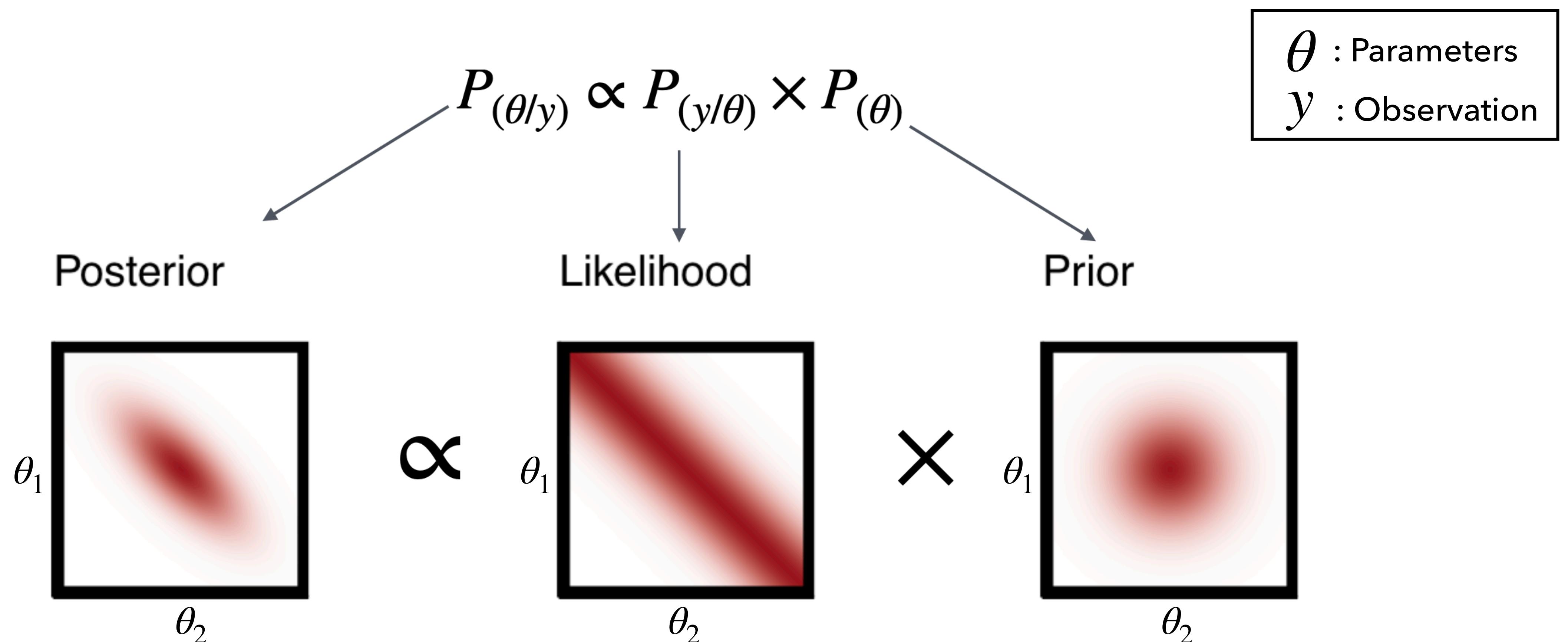
A1: primary auditory cortex  
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IFG: inferior frontal gyrus

# Methods



## Monte Carlo Markov Chain (MCMC)

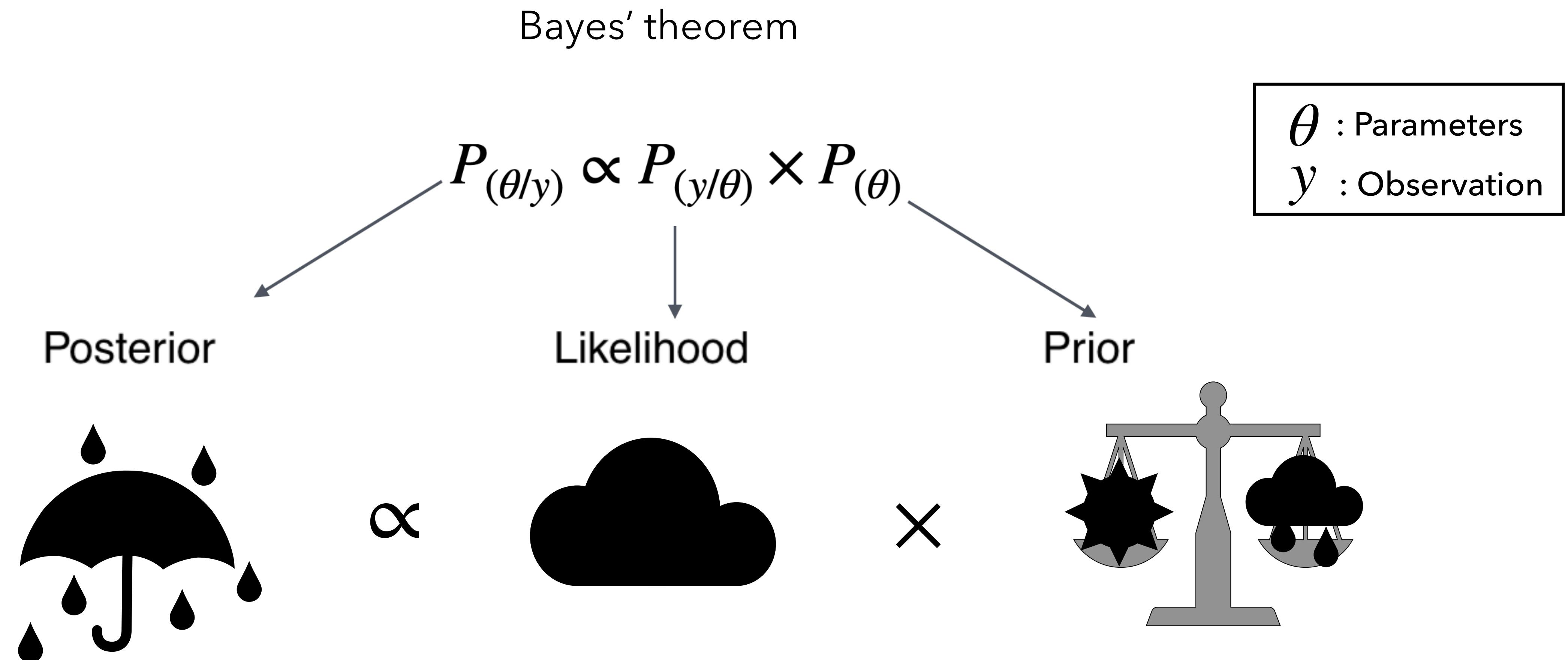
Bayes' theorem



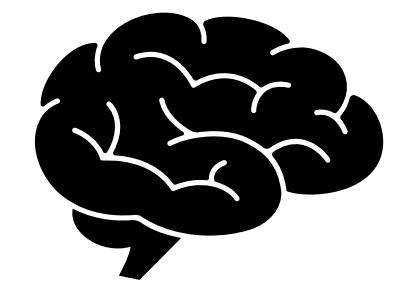
# Methods



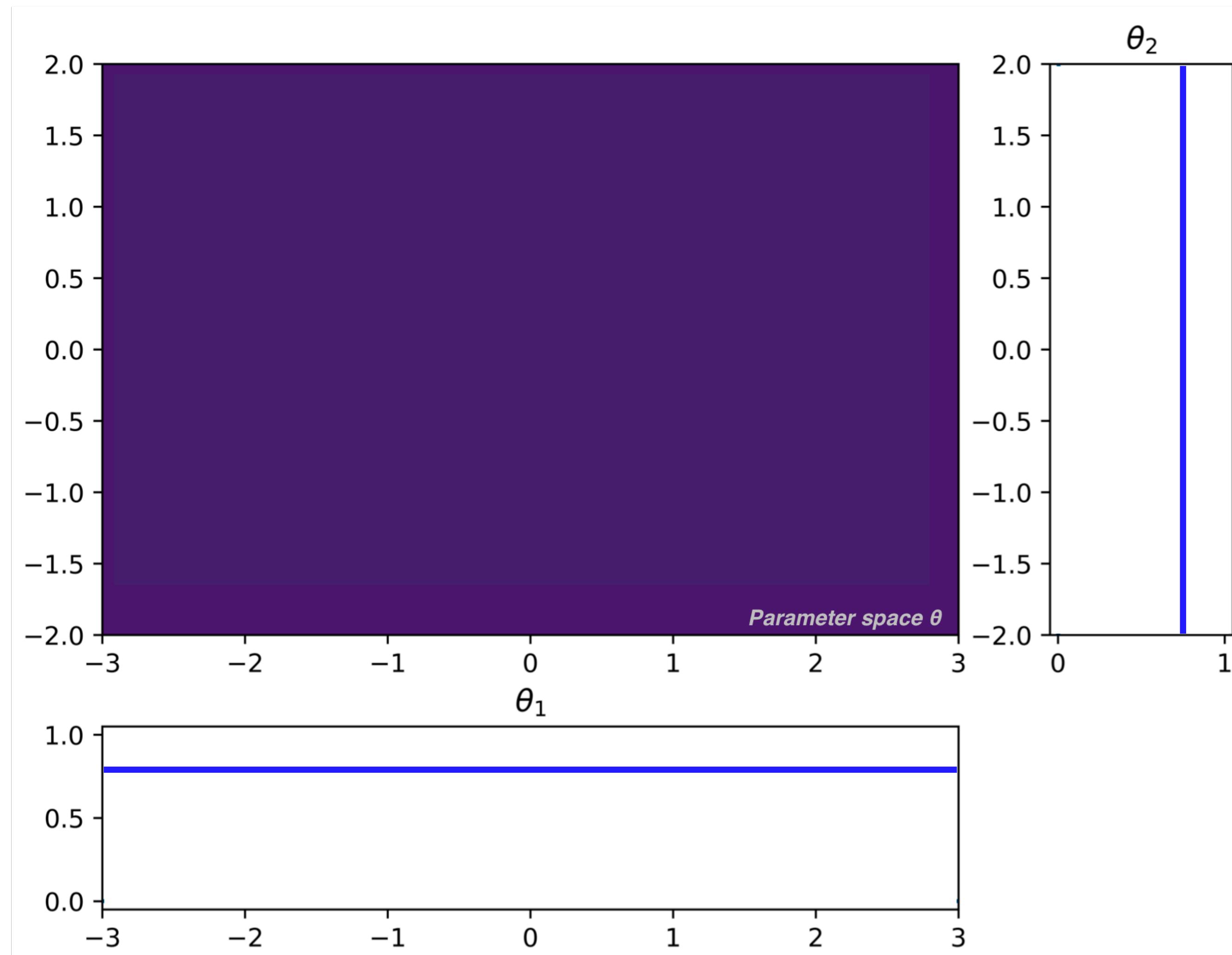
## Monte Carlo Markov Chain (MCMC)



# Methods



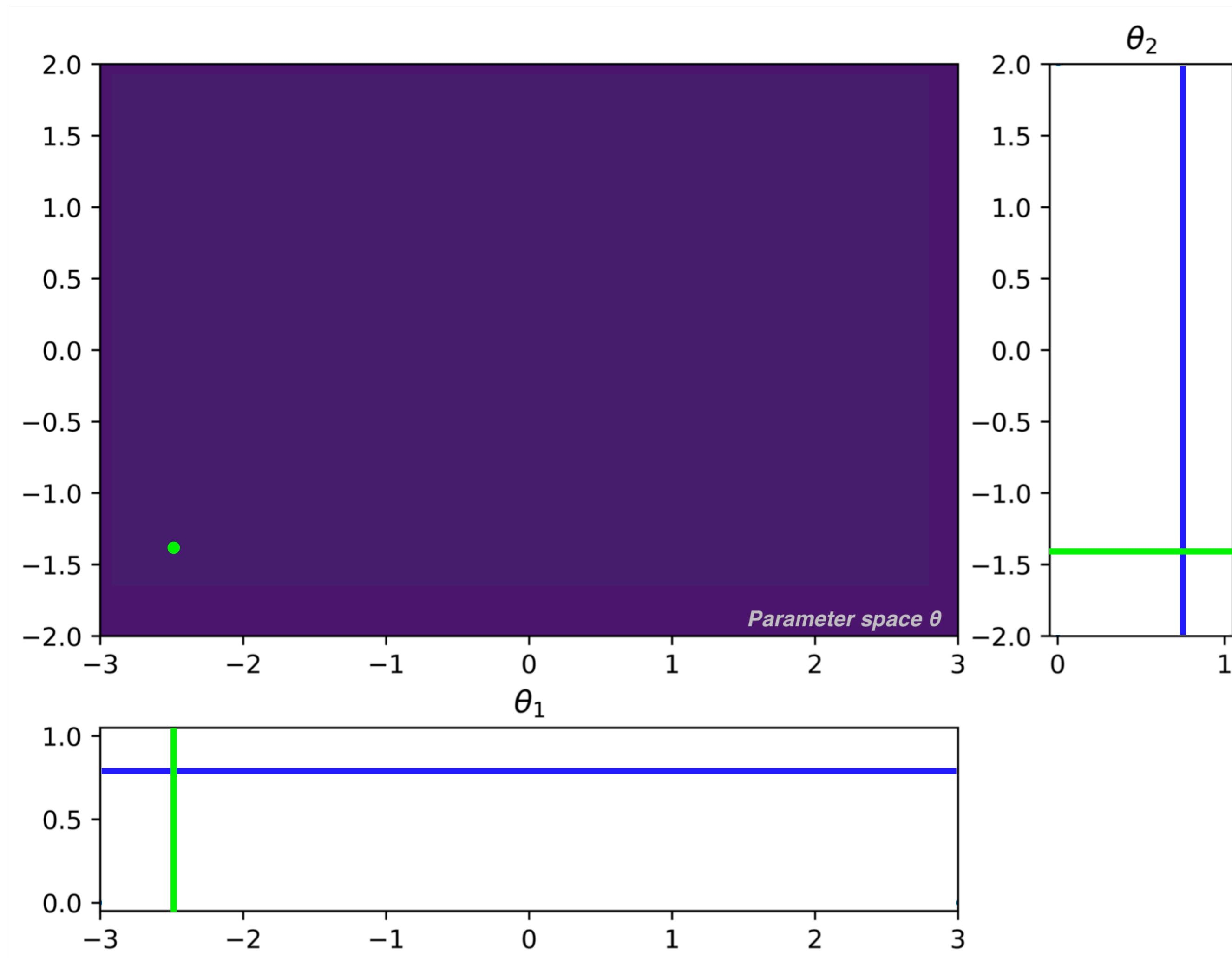
## Monte Carlo Markov Chain (MCMC)



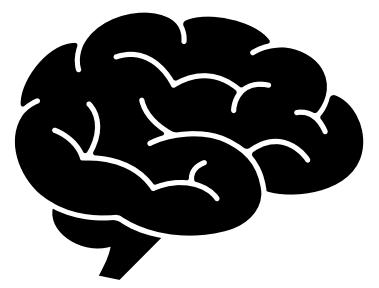
# Methods



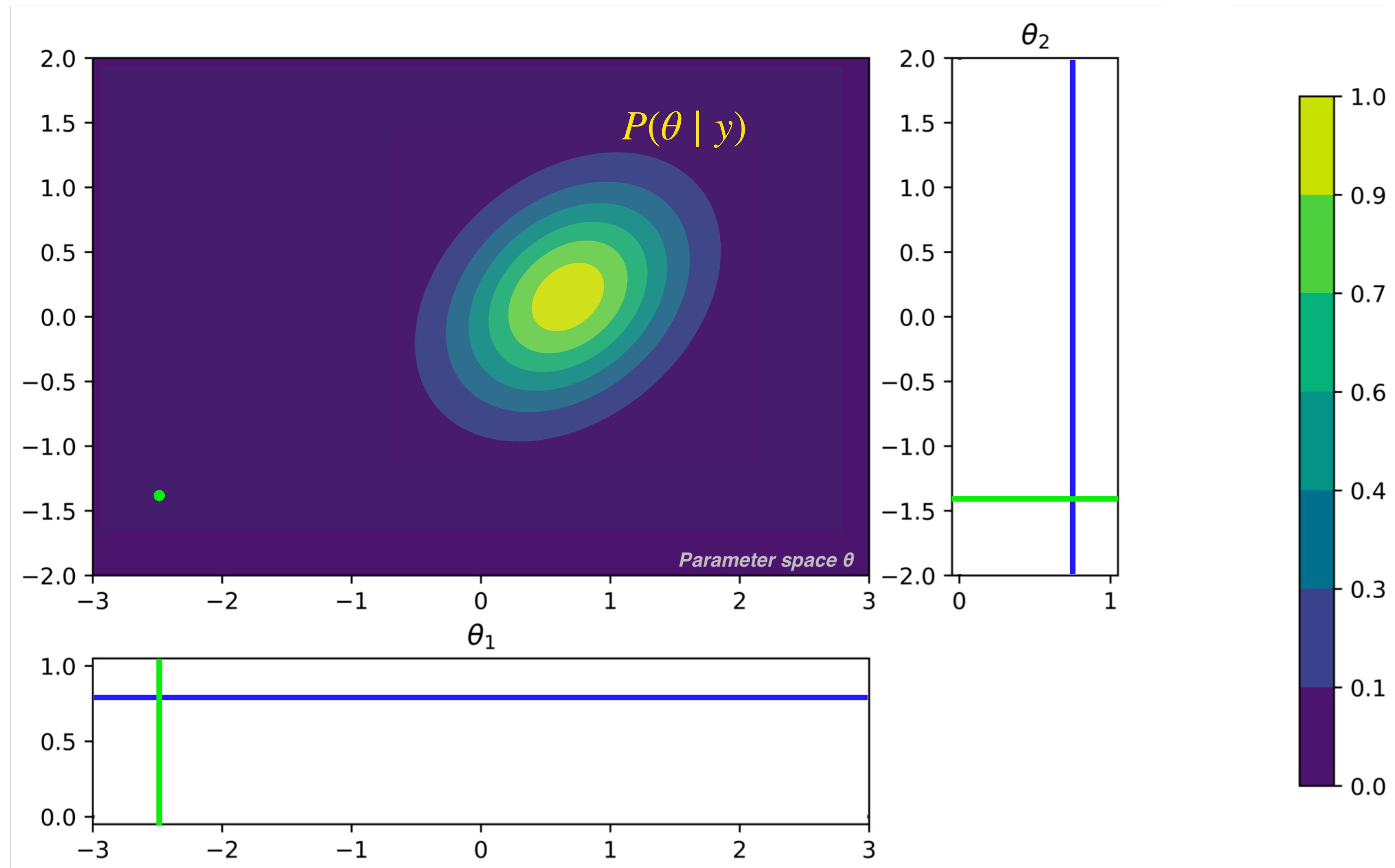
## Monte Carlo Markov Chain (MCMC)



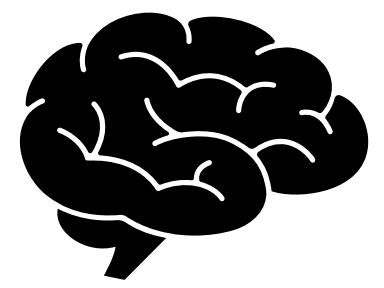
# Methods



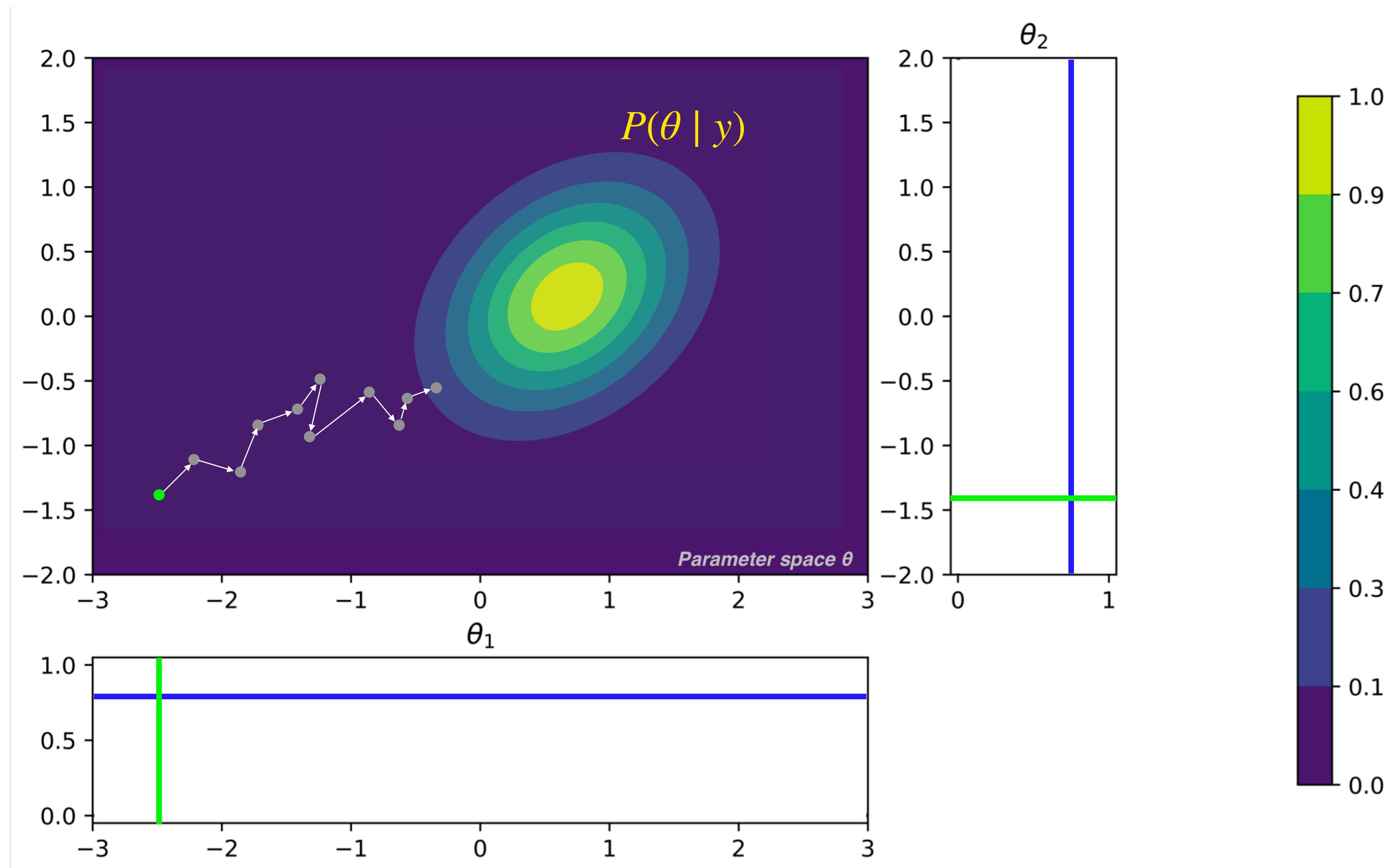
## Monte Carlo Markov Chain (MCMC)



# Methods



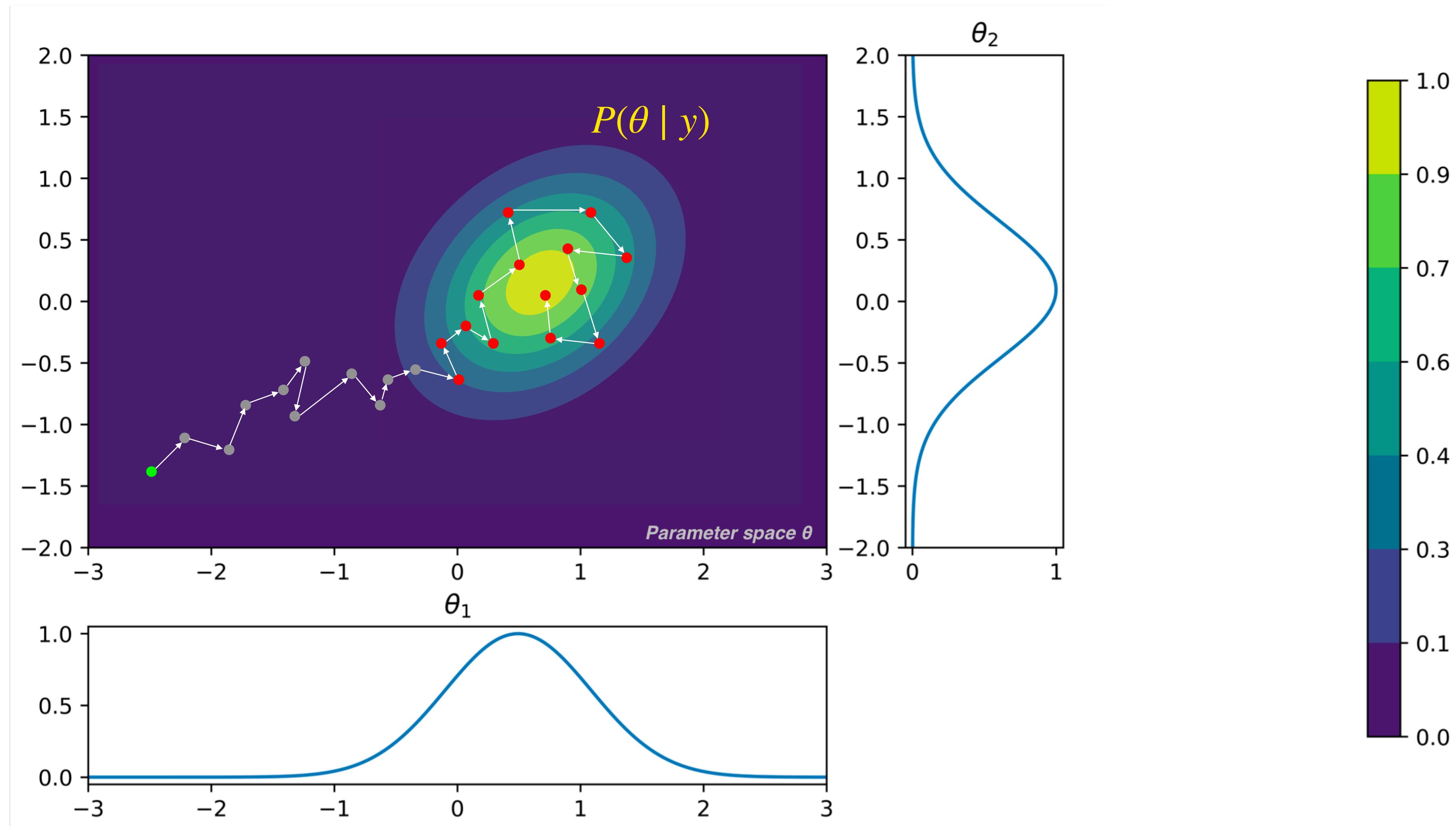
## Monte Carlo Markov Chain (MCMC)



# Methods



## Monte Carlo Markov Chain (MCMC)

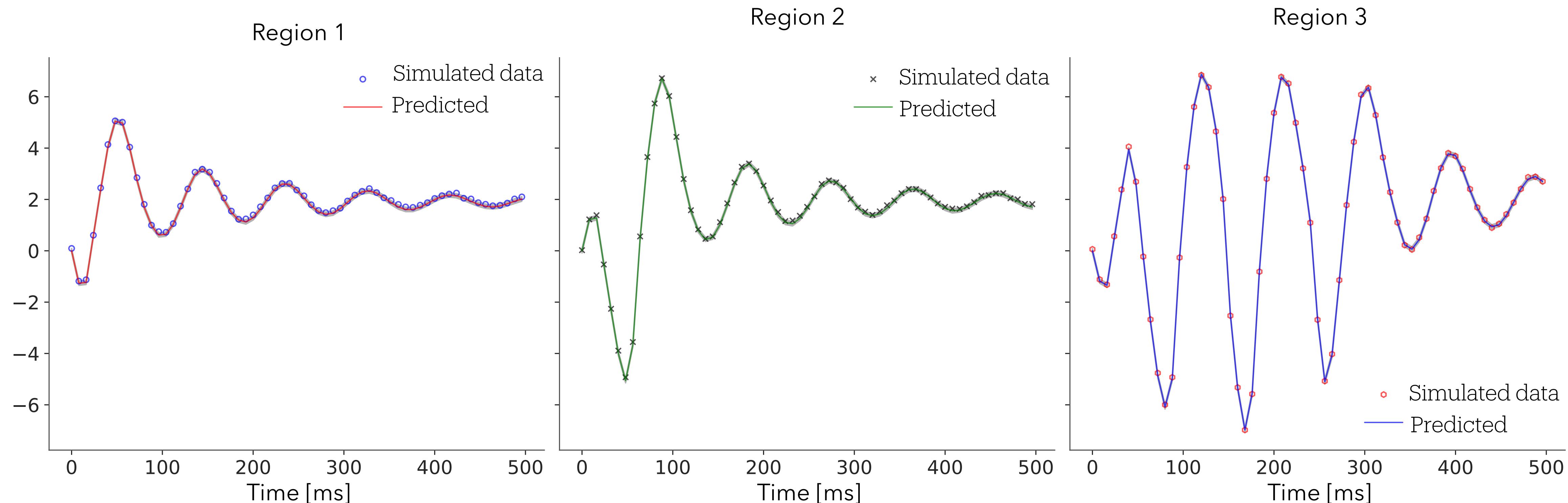


# Results

# Results



Does it work on simulated data ?



Event-related potential (ERPs)  
Neural mass model  
David et al., Neuroimage, 2005/2006

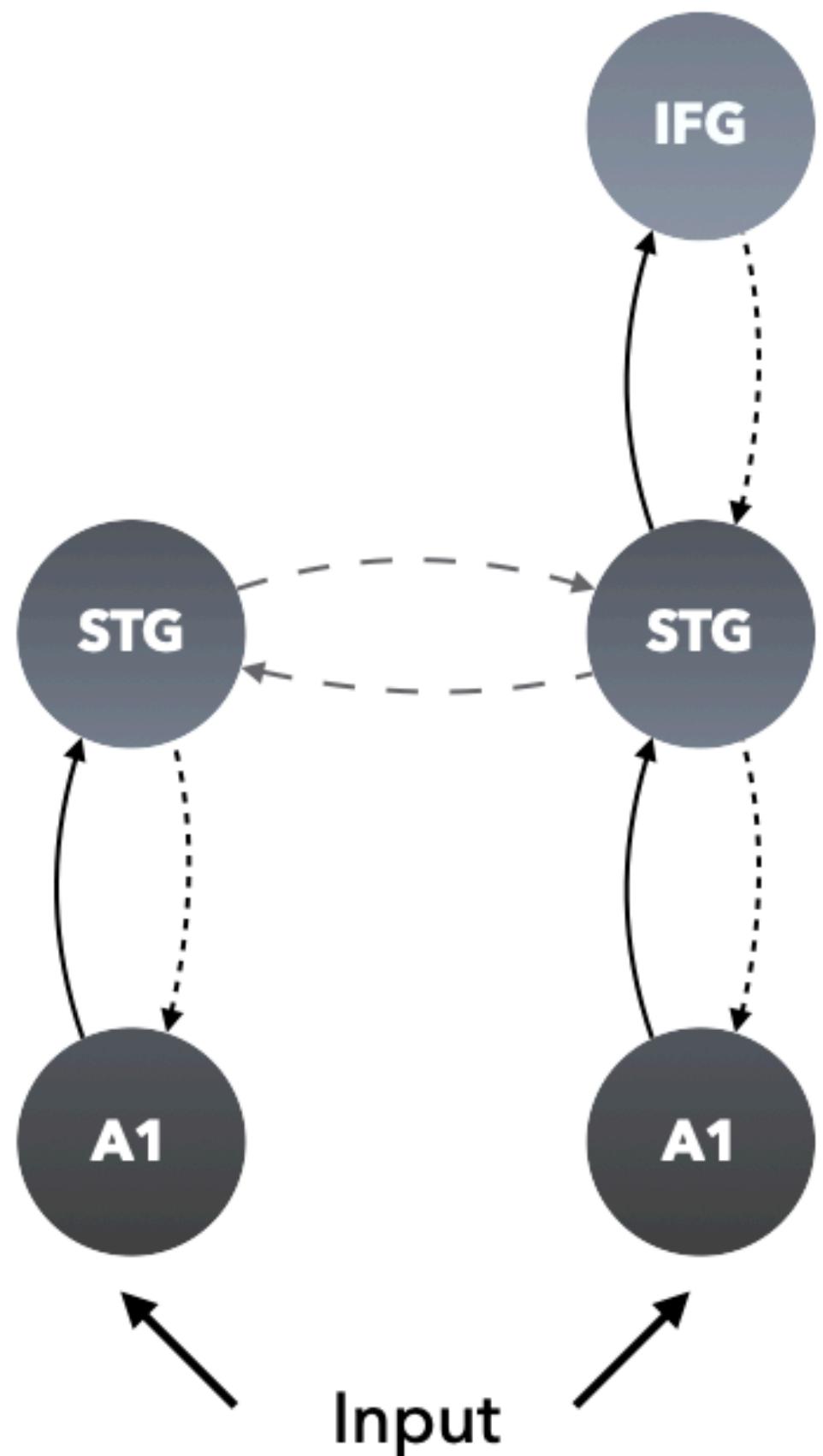
Estimation de la connectivité  
effective avec une méthode de  
**Markov chain Monte Carlo** (MCMC)

# Results



## Résultats stage M2

Garrido's architecture



A1: Cortex auditif primaire

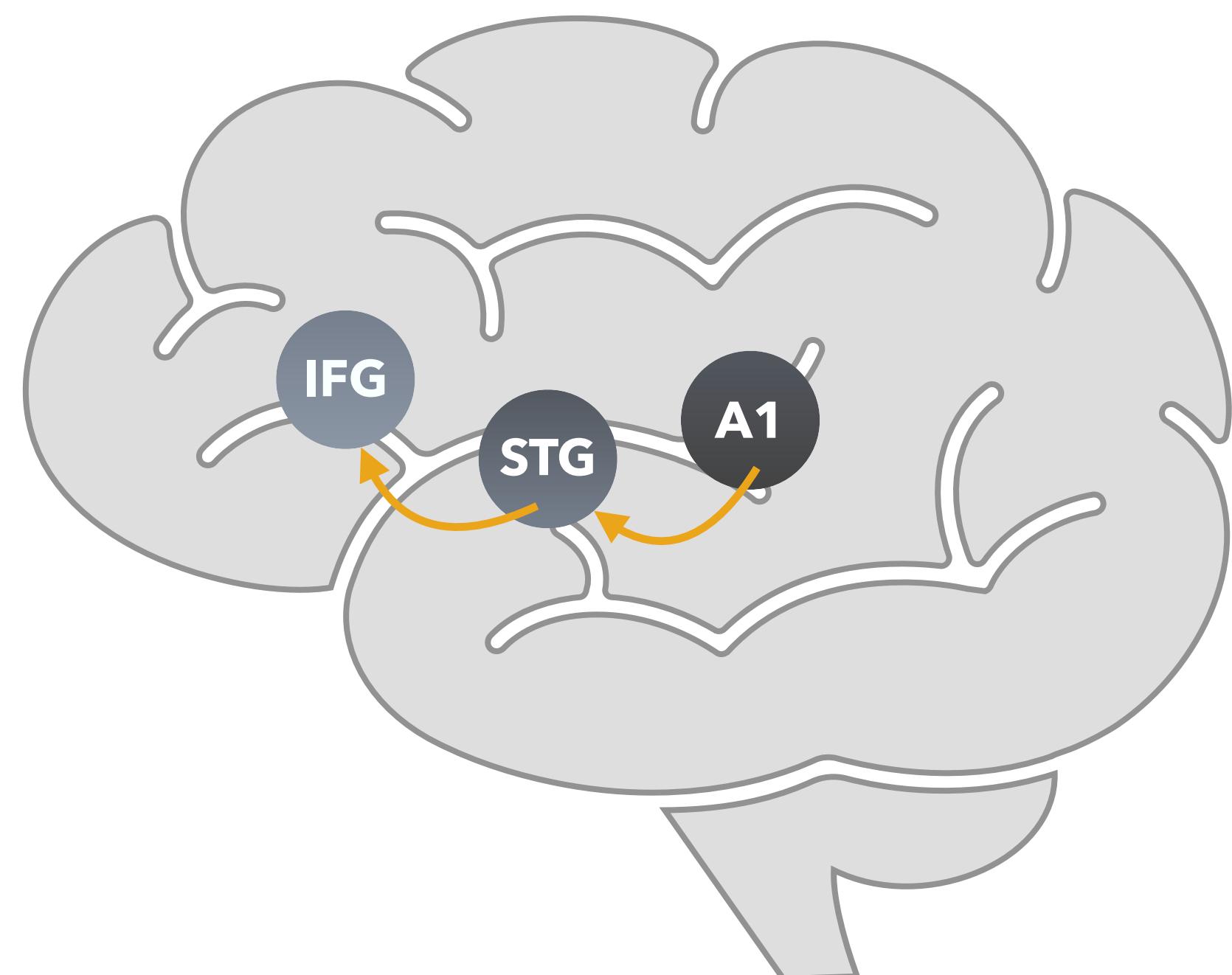
STG: gyrus temporal supérieur

IFG: gyrus frontal inférieur

EEG data :

- Un seul sujet humain enregistré par M.Garrido
- Tache de Oddball auditif

Forward →  
Backward ⤵→  
Lateral —→



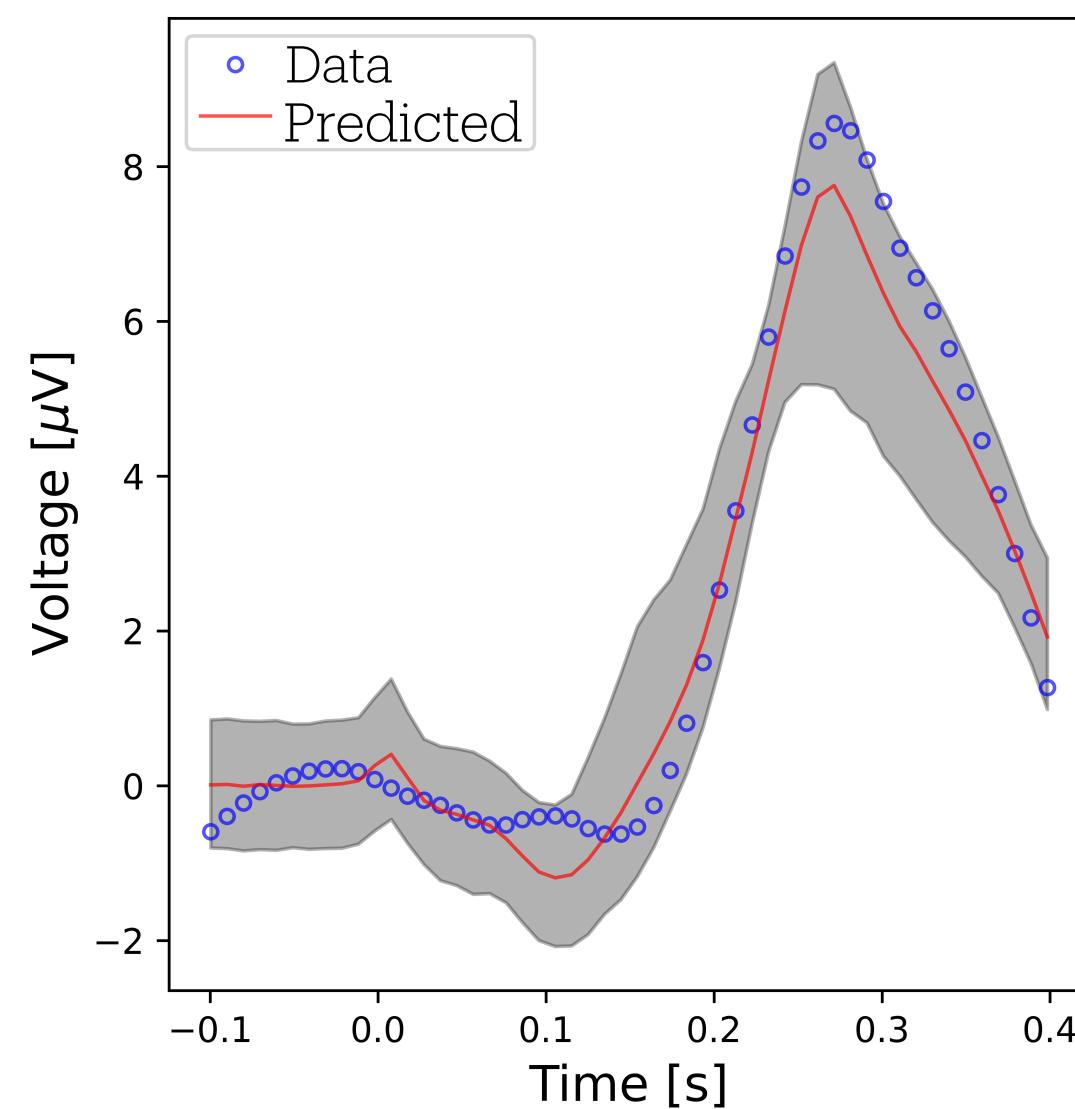
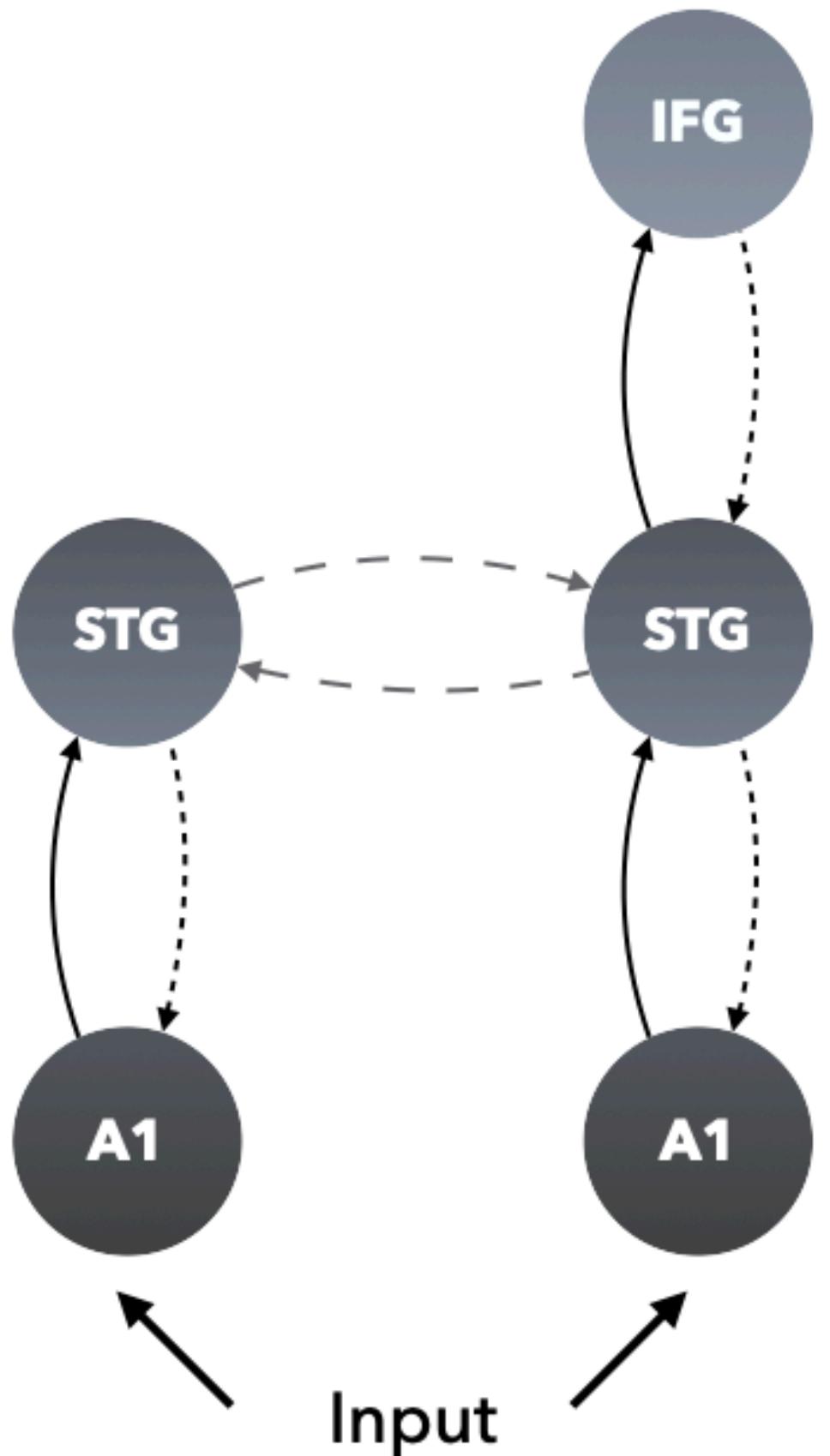
Garrido et al., Neuroimage, 2007

# Results



## Résultats stage M2

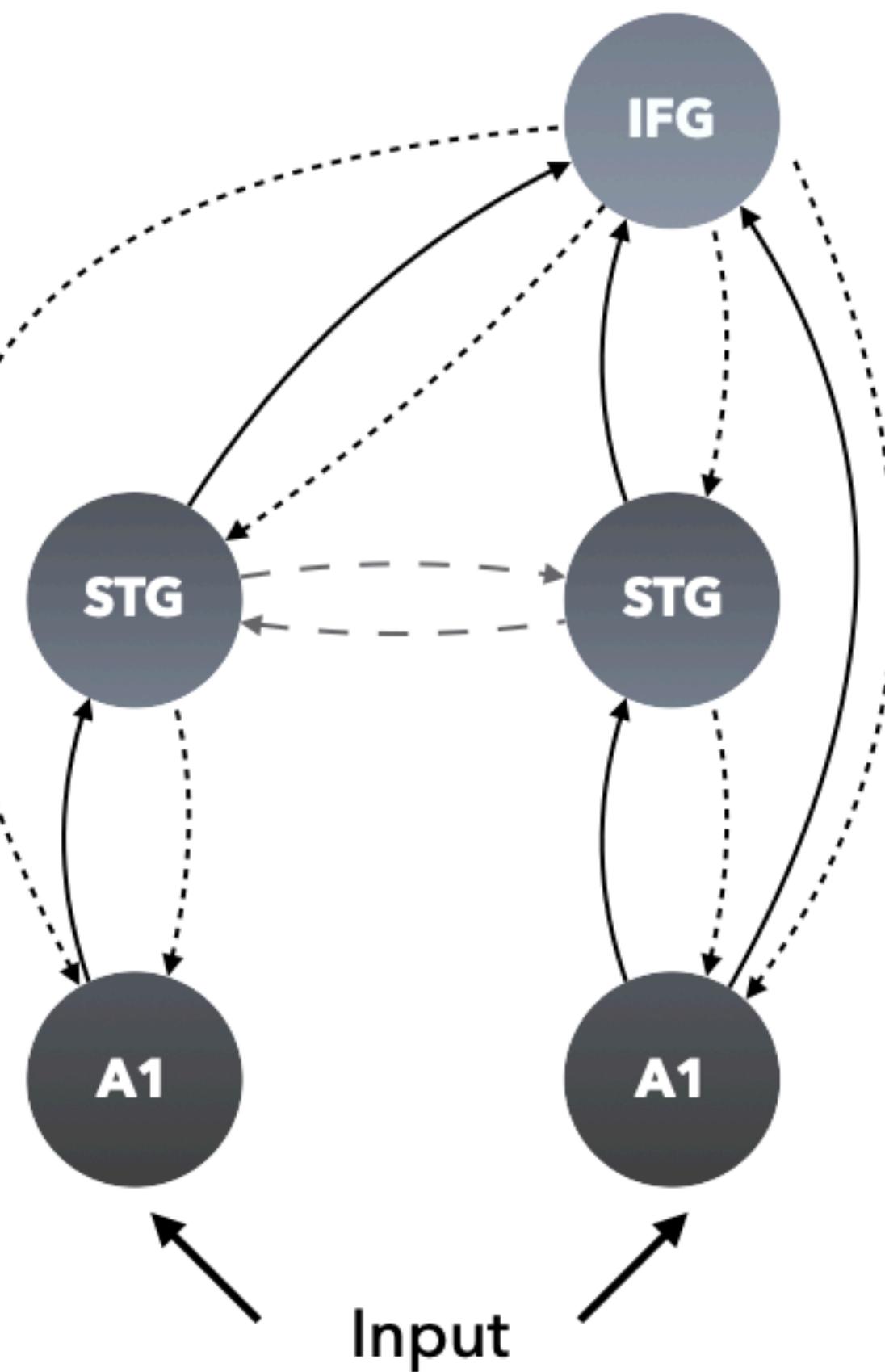
Garrido's architecture



Forward →  
Backward ⤵→  
Lateral —→

A1: Cortex auditif primaire  
STG: gyrus temporal supérieur  
IFG: gyrus frontal inférieur

F-tract architecture



Garrido et al., Neuroimage, 2007

# Projet de thèse

# Projet de thèse

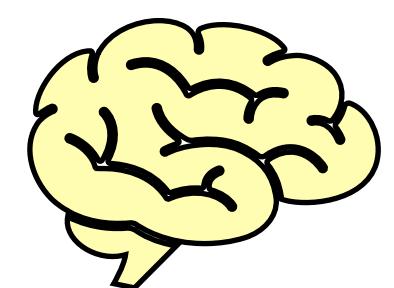
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Continuité des deux stages de Master

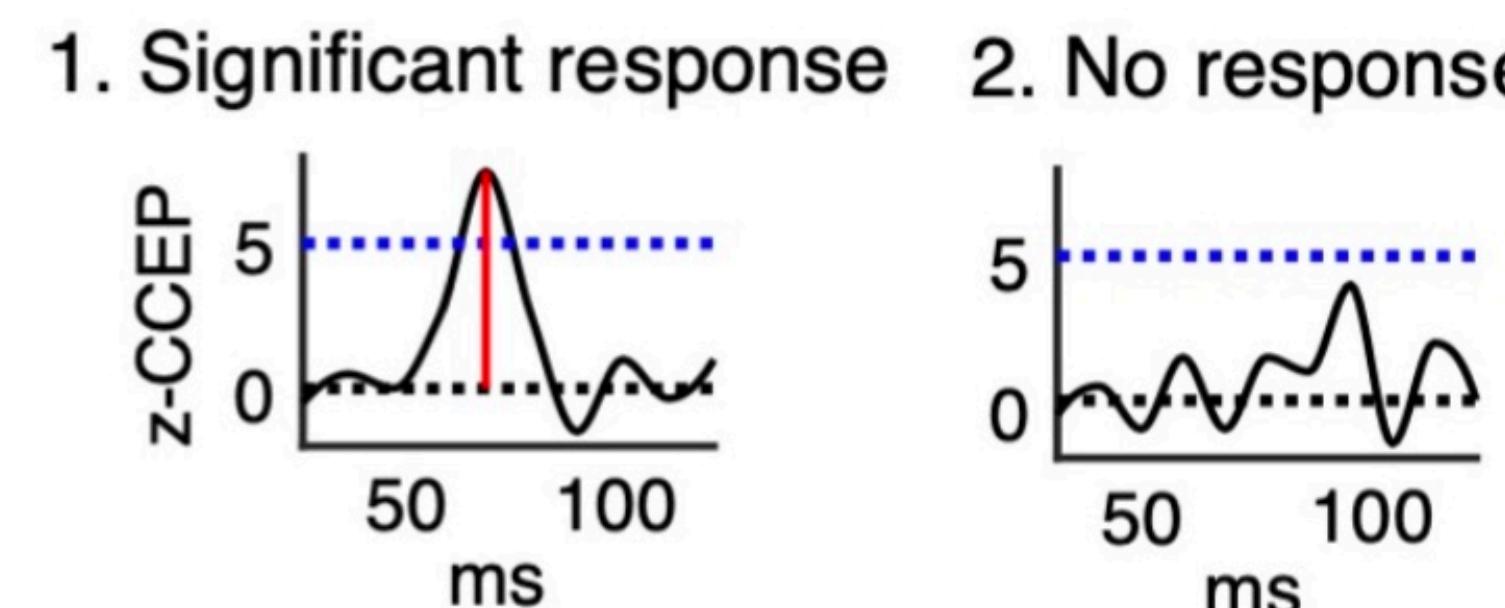
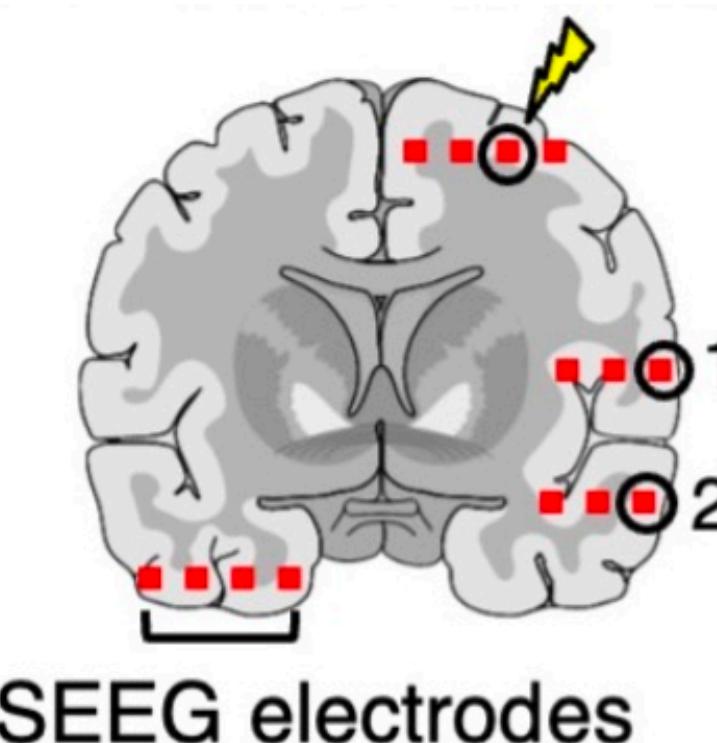
## 3 objectifs principaux

- Objectif 1: Optimisation d'un atlas de prior neuroanatomique et d'excitabilité pour cerveau humain complet à partir des données F-TRACT
- Objectif 2: Utilisation des priors F-TRACT pour estimer connectivité effective et excitabilité locale pour tâche cognitive en EEG/MEG
- Objectif 3: Analyse des effets neuromodulateurs locaux et en réseaux de la dopamine dans circuit cortico-striatal

# Projet de thèse

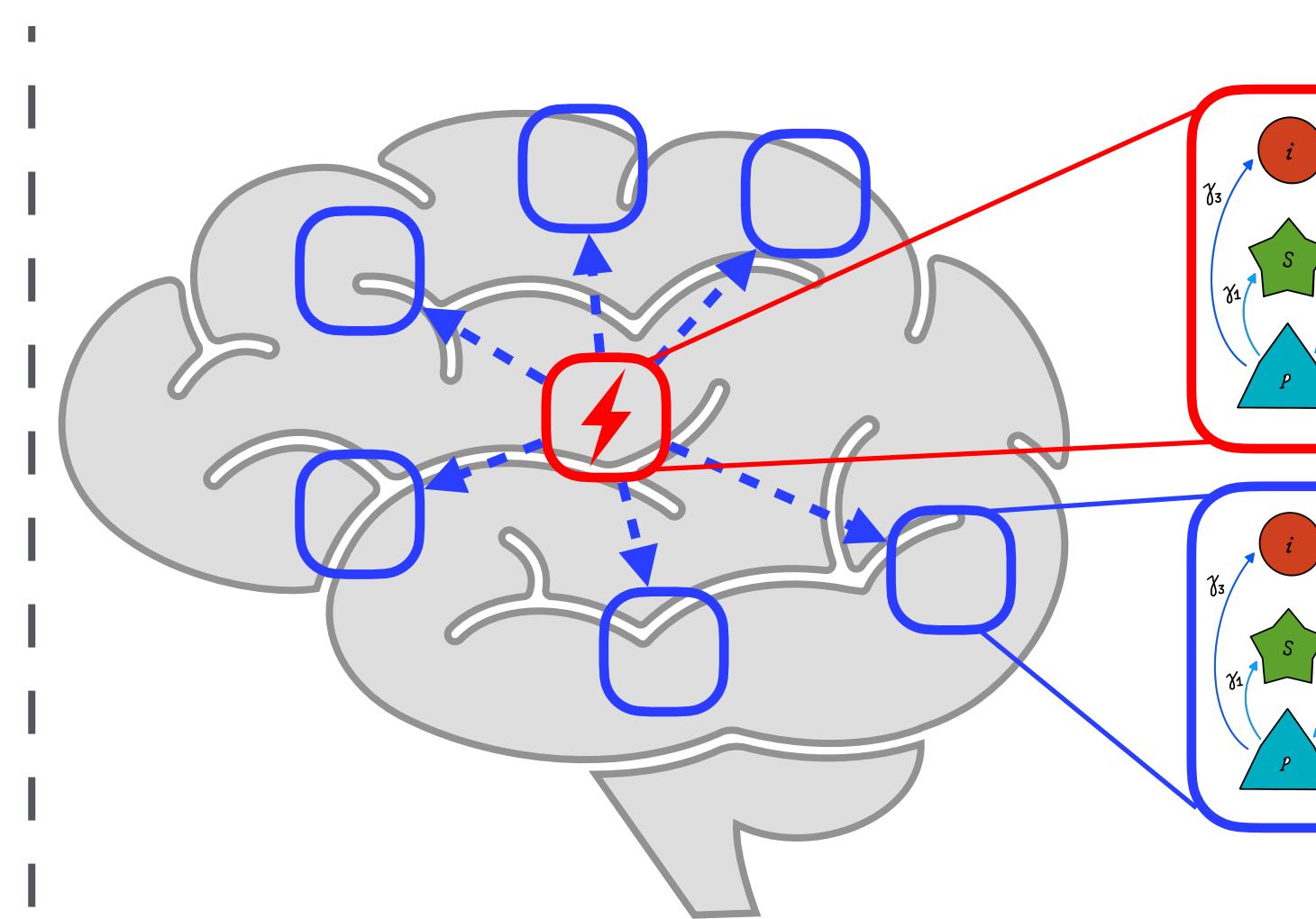


- Objectif 1: Optimisation d'un atlas de prior neuroanatomique et d'excitabilité pour cerveau humain complet à partir des données F-TRACT



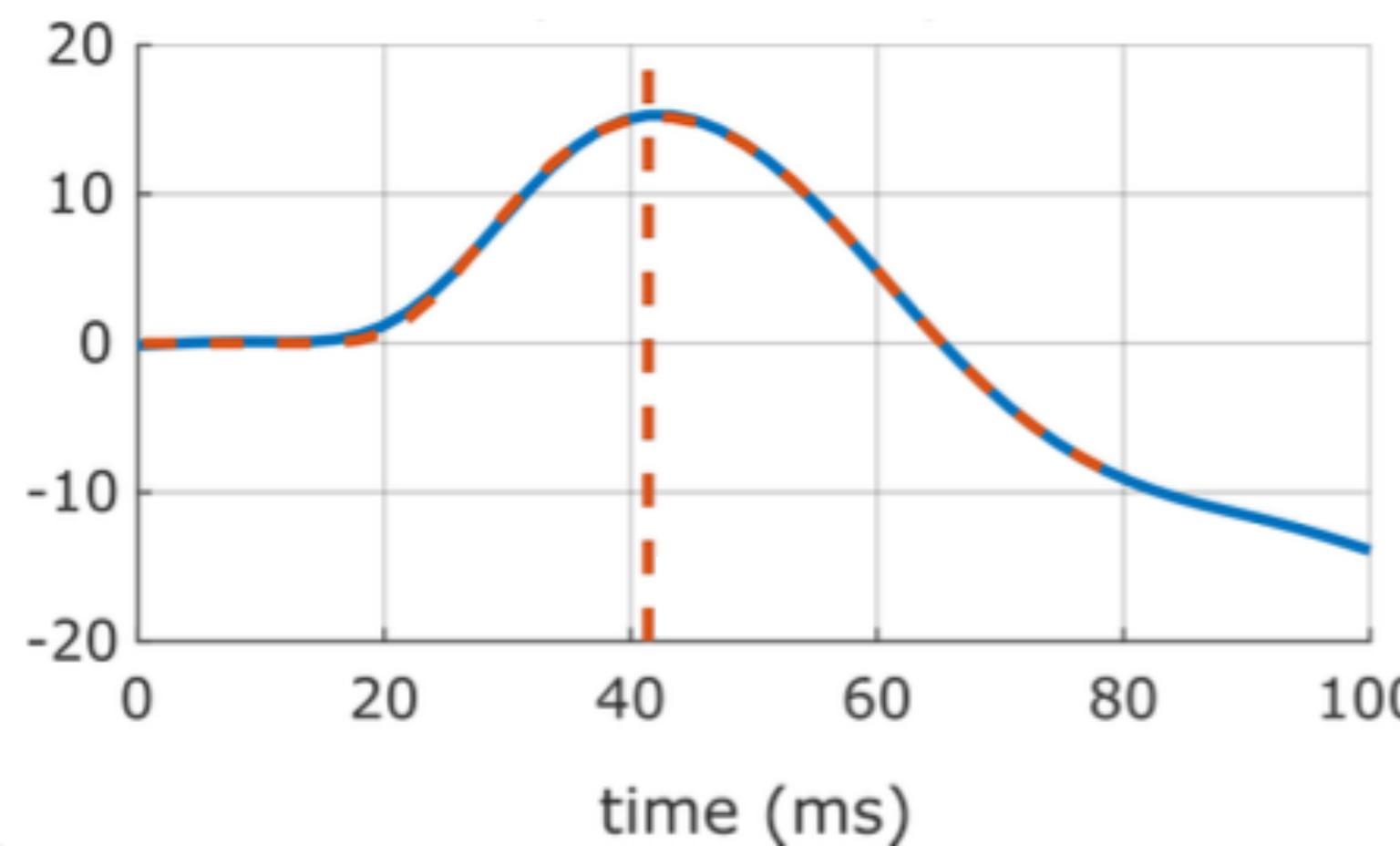
Seguin et al., *Neuron*, 2023

- Collaboration entre 25 centres spécialisés dans l'épilepsie dans le monde
- Sujets: Patients épileptiques > 1000



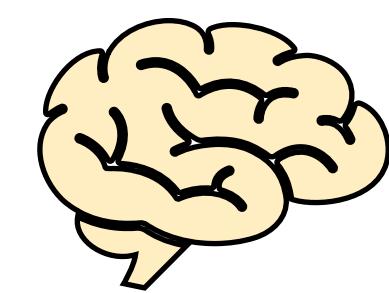
- Paramètres :
- connexion = poids, délai
  - locaux = excitabilité, constantes de temps (inhibitrice et excitatrice)

Paramétrisation d'un CCEP

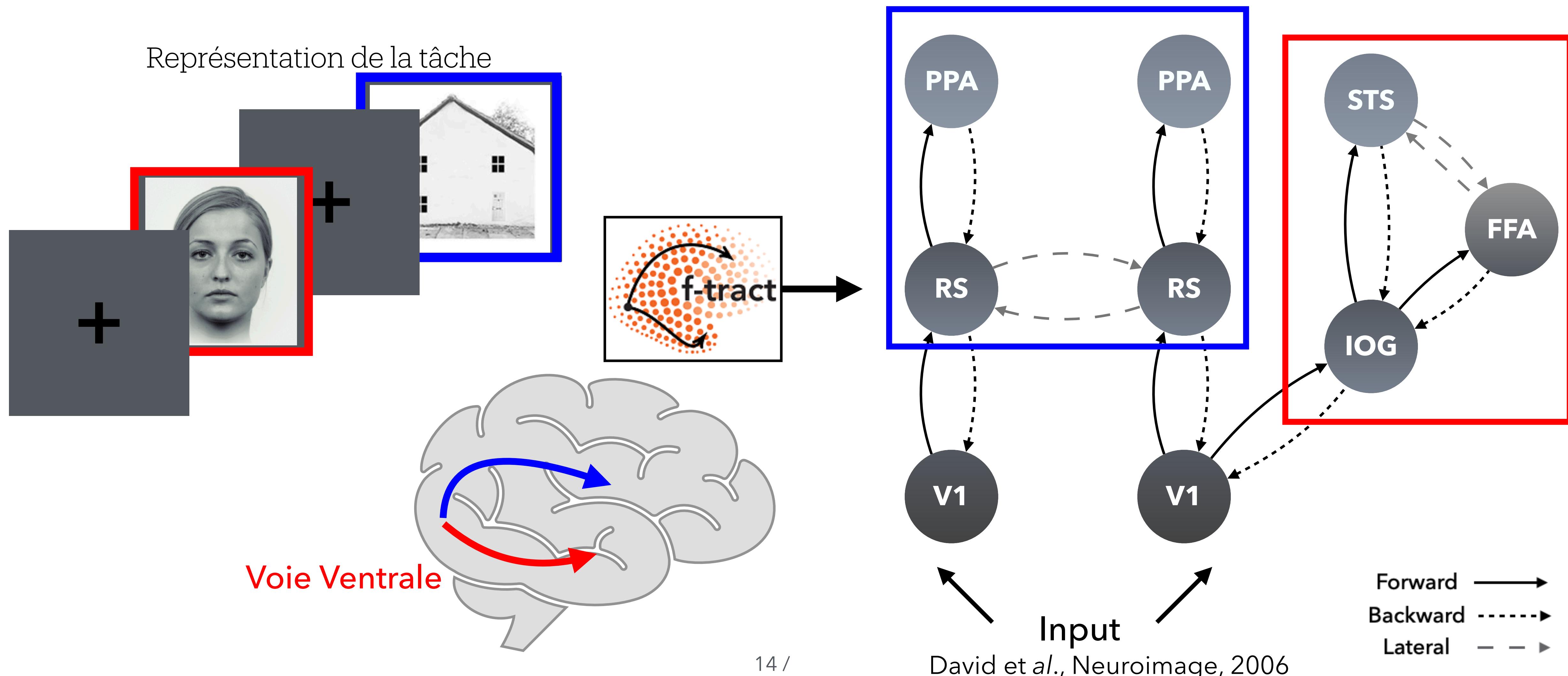


- Fit :
- Latence pic
  - Amplitude
  - Largeur

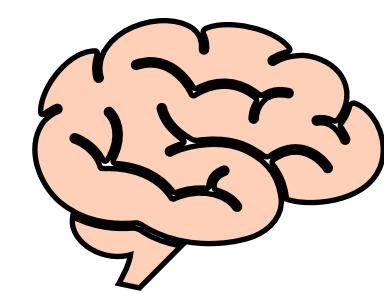
# Projet de thèse



- Objectif 2: Utilisation des priors F-TRACT pour estimer connectivité effective et excitabilité locale pour tâche cognitive en EEG/MEG



# Projet de thèse



- Objectif 3: Analyse des effets neuromodulateurs locaux ou en réseaux de la dopamine dans circuit cortico-striatal



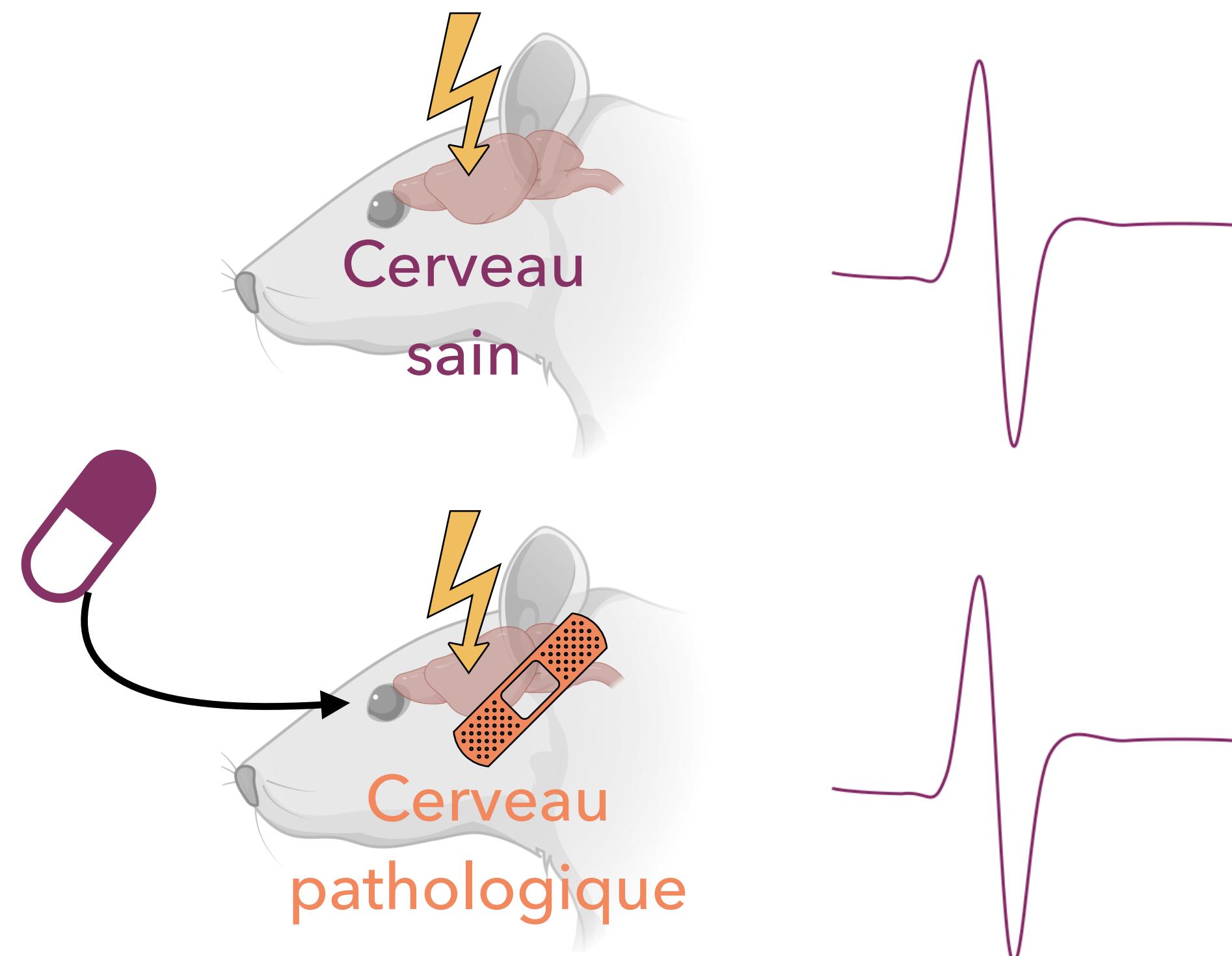
**SYNAPCELL**  
★

Collaboration avec la société  
SynapCell (Inovallée, Grenoble)

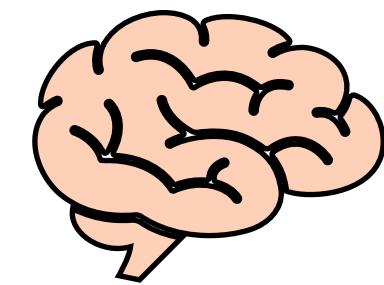
Etude pré clinique de composé  
pharmacologique

Enregistrement de potentiel évoqué induit par stimulation électrique direct,  
modèle de rat Parkinsonien (6-OHDA) et test levodopa (L-Dopa)

Données déjà acquises - Thèse CIFRE 2019-2022, Eloise Gronlier



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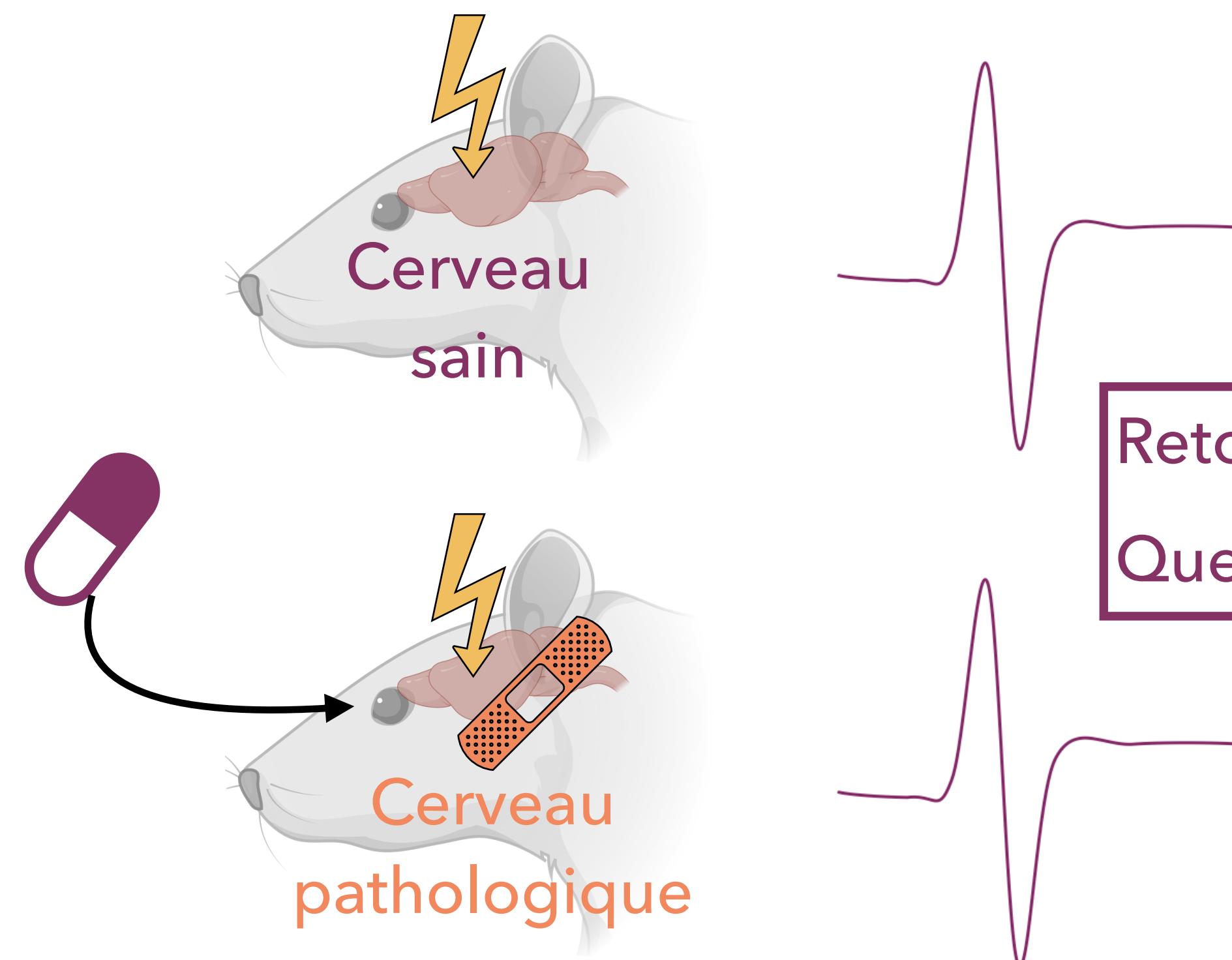
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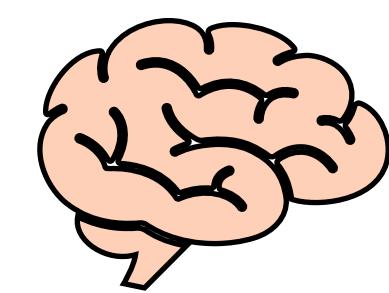
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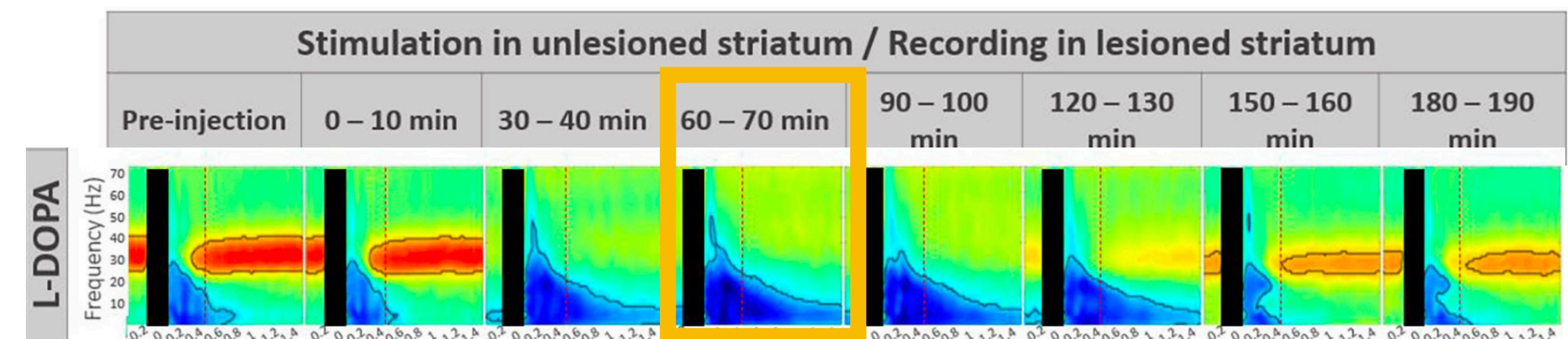
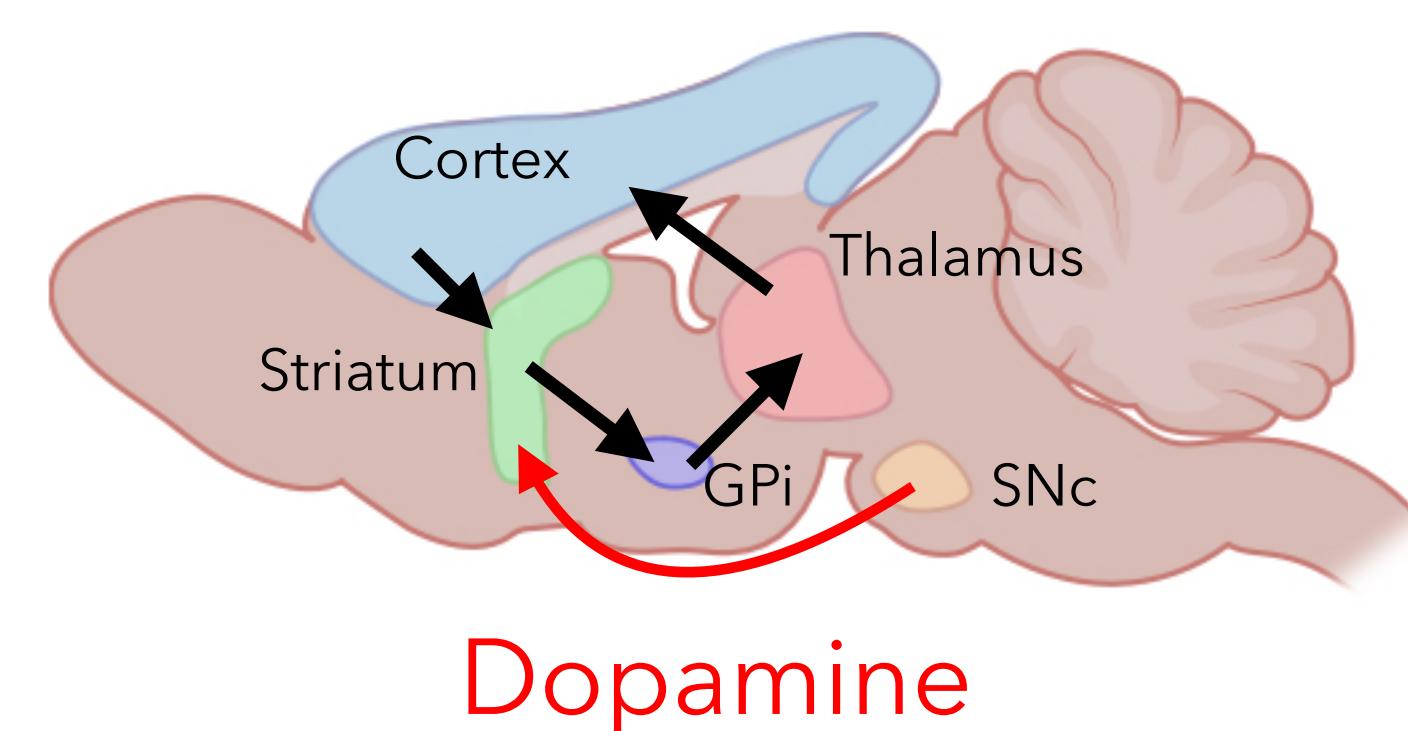
# Projet de thèse



- Objectif 3: Analyse des effets neuromodulateurs locaux ou en réseaux de la dopamine dans circuit cortico-striatal

**SYNAPCELL**  
★

Enregistrement de potentiel évoqué induit par stimulation électrique direct, modèle de rat Parkinsonien (6-OHDA) et test levodopa (L-Dopa)



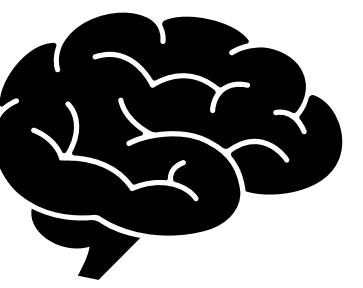
Gronlier et al., Neurobiology of Disease, 2022

Peut-on modéliser les mécanismes d'action de la dopamine au niveau de ce circuit ? Quel est son impact sur le réseau ?

# Inférence Bayésienne de la modulation de la connectivité effective de réseaux de modèles de masse neurale à partir de données de neurostimulation

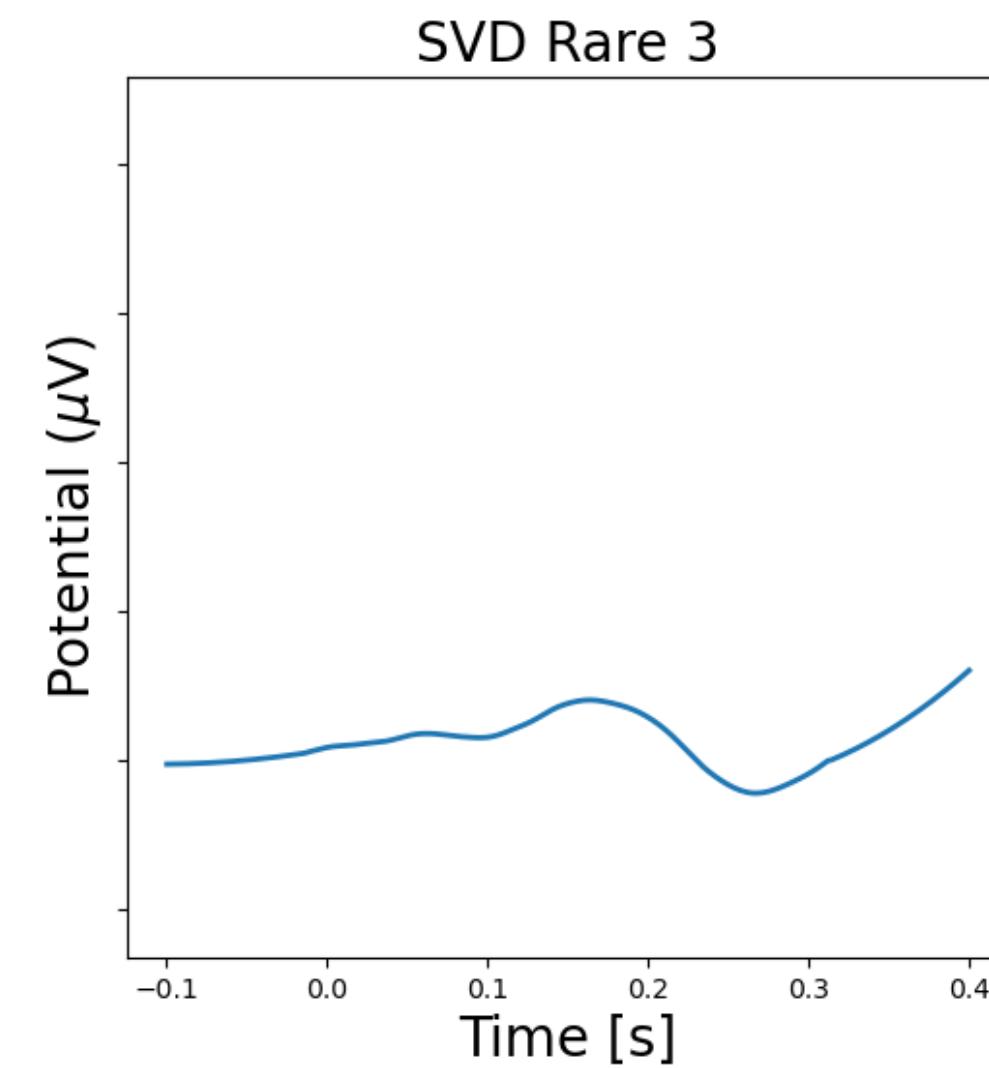
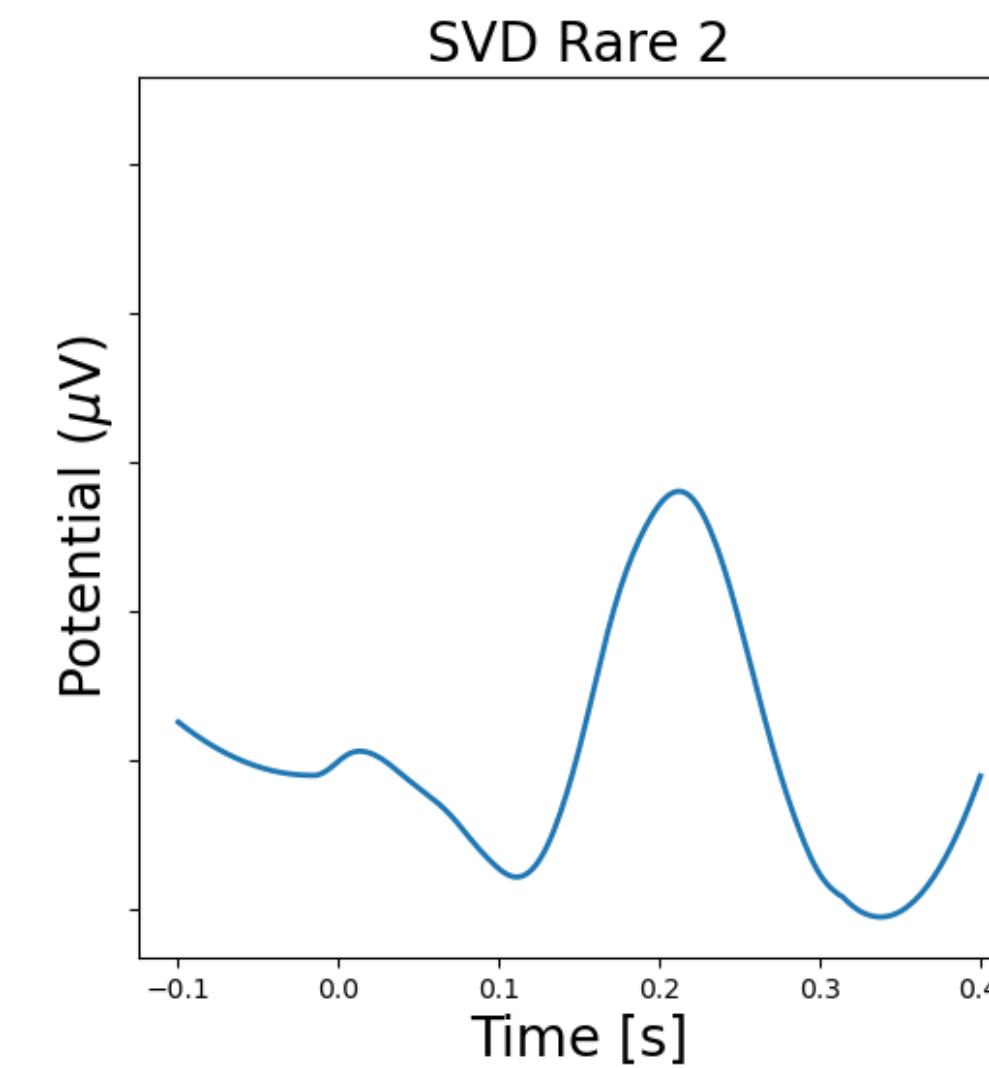
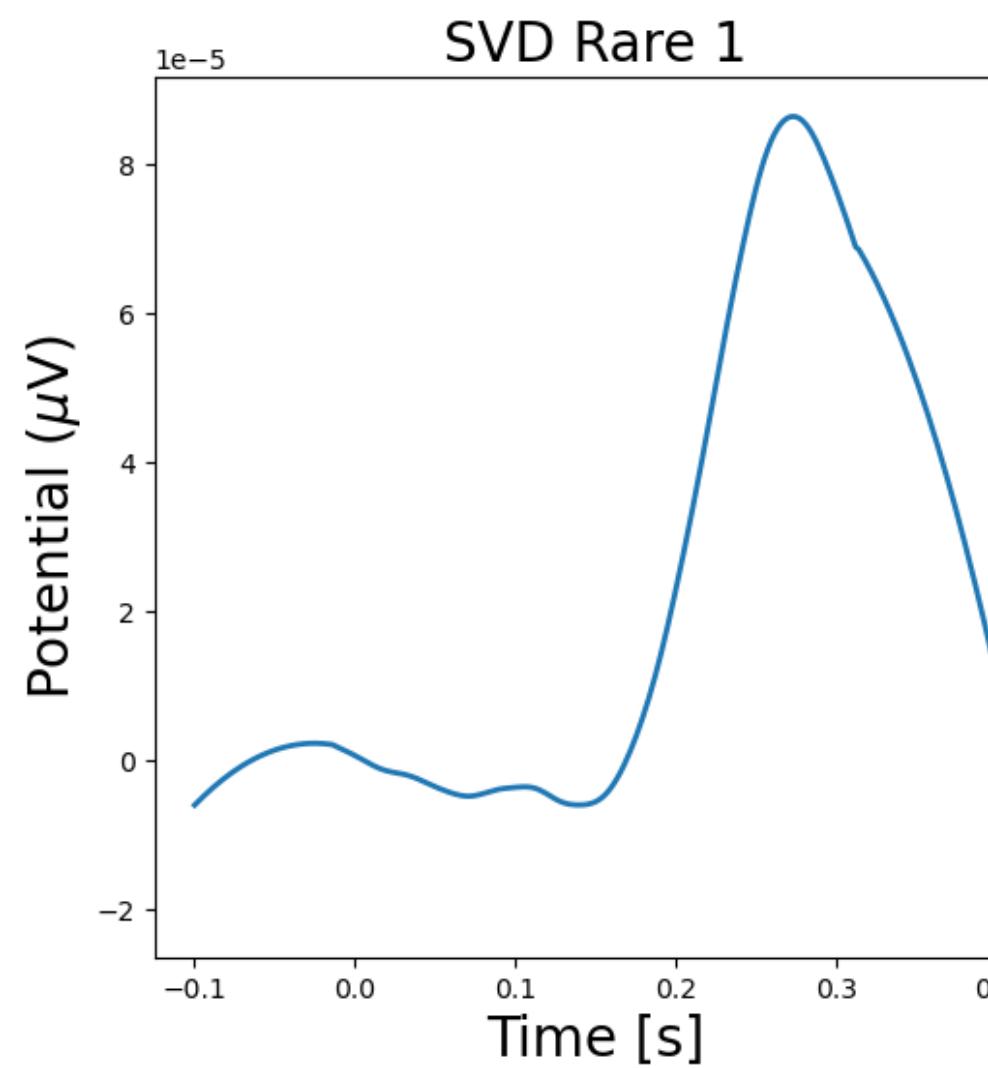
Sous la supervision jointe de Olivier David et Matthieu Gilson

# Methods

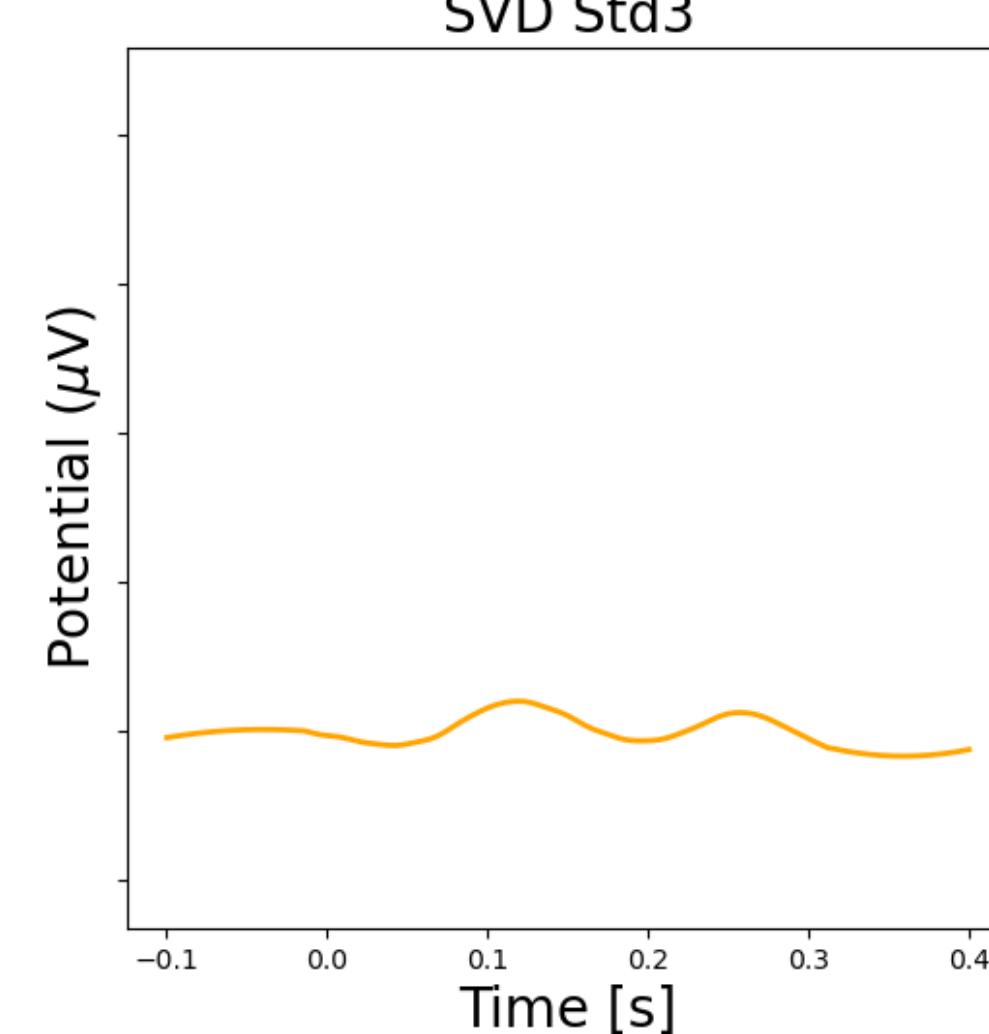
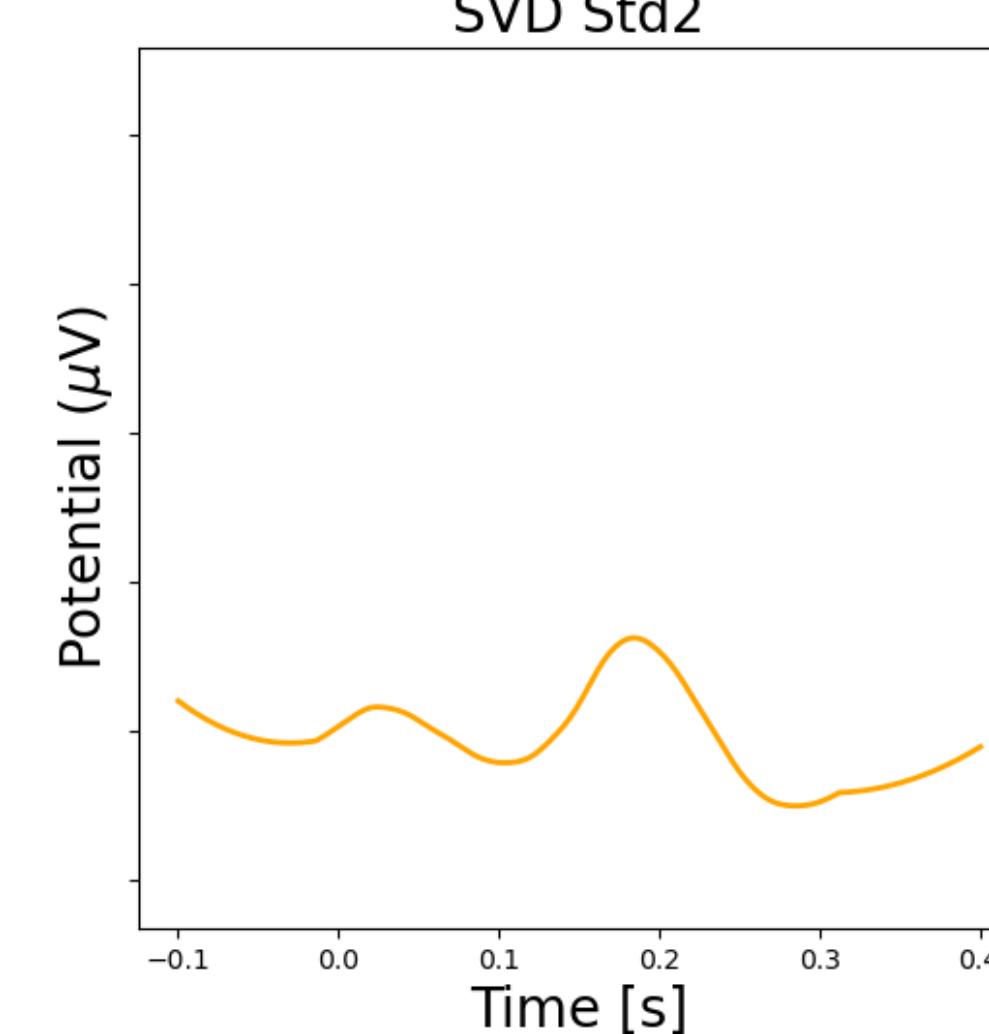
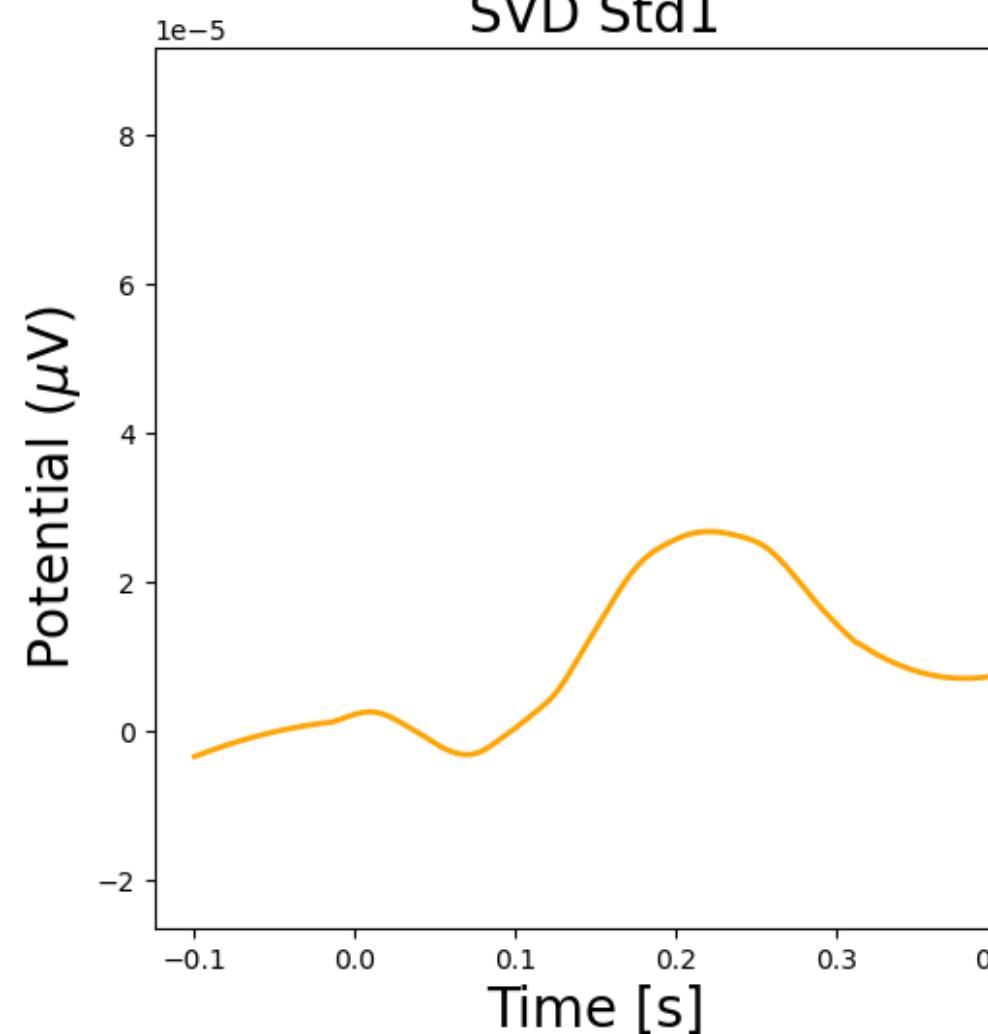


## Single Value Decomposition (SVD)

Rare



Standard



$SVD \cong PCA$

Reduction of 128  
sensors in 3 principal  
spatial modes

Explained variance  
90%

Garrido et al, 2007