

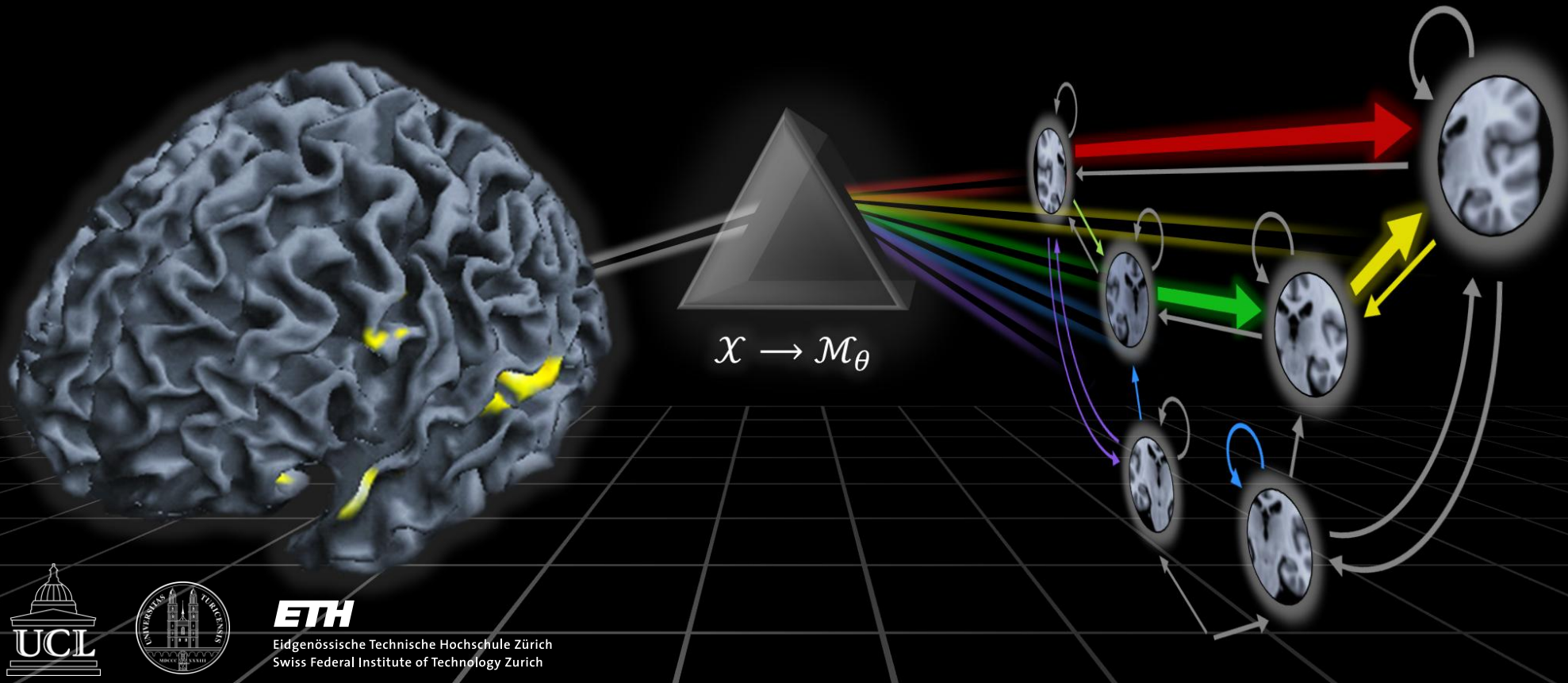
# Model-based clustering using generative embedding

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<sup>1</sup> Translational Neuromodeling Unit (TNU), ETH Zurich

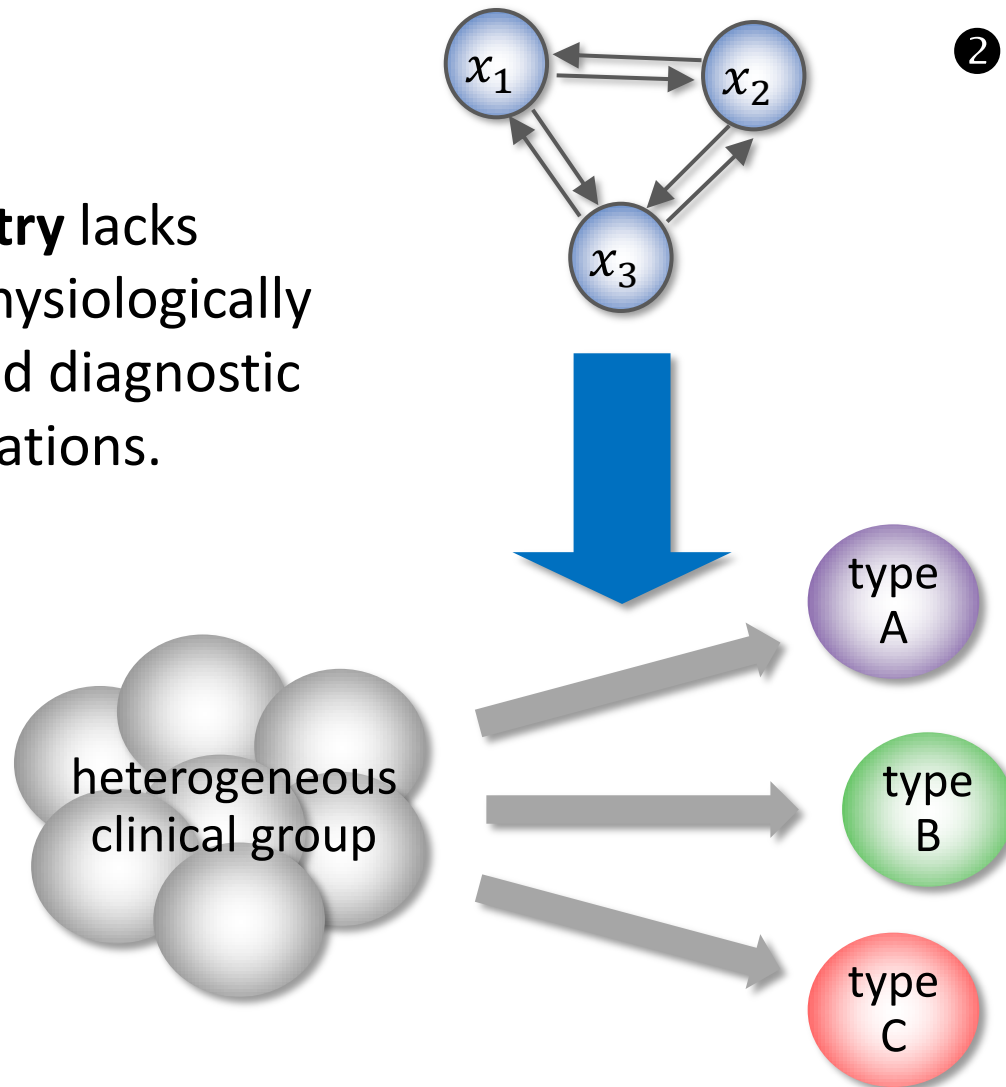
<sup>2</sup> Department of Psychiatry and Psychotherapy, Charité-Universitätsmedizin Berlin

<sup>3</sup> Wellcome Trust Centre for Neuroimaging, UCL



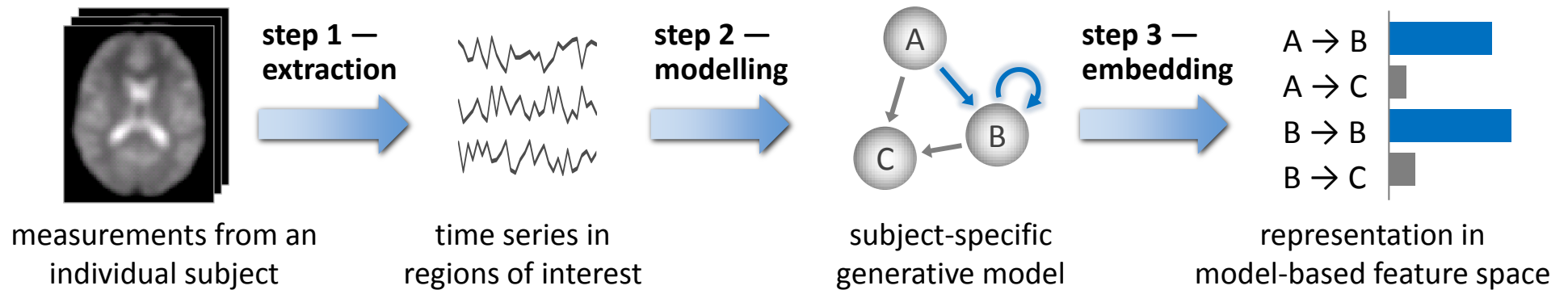
# Clinical vision: dissecting psychiatric spectrum diseases

❶ **Psychiatry** lacks pathophysiologically informed diagnostic classifications.



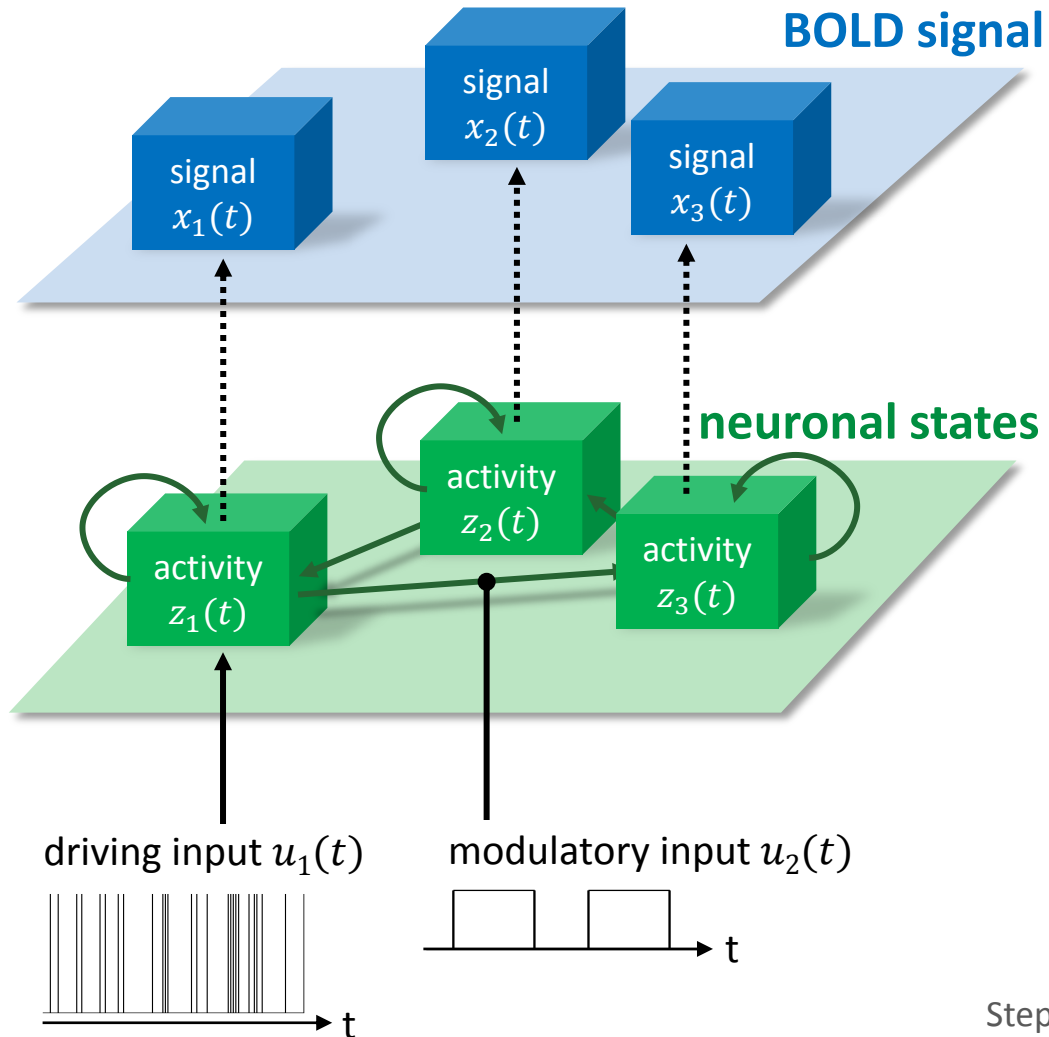
❷ **Generative embedding** may help dissect spectrum disorders into mechanistically defined subgroups.

# Generative embedding



Brodersen, Haiss, Ong, Jung, Tittgemeyer, Buhmann, Weber, Stephan (2011) *NeuroImage*  
Brodersen, Schofield, Leff, Ong, Lomakina, Buhmann, Stephan (2011) *PLoS Comput Biol*

# Choosing a generative model: DCM for fMRI



**haemodynamic forward model**

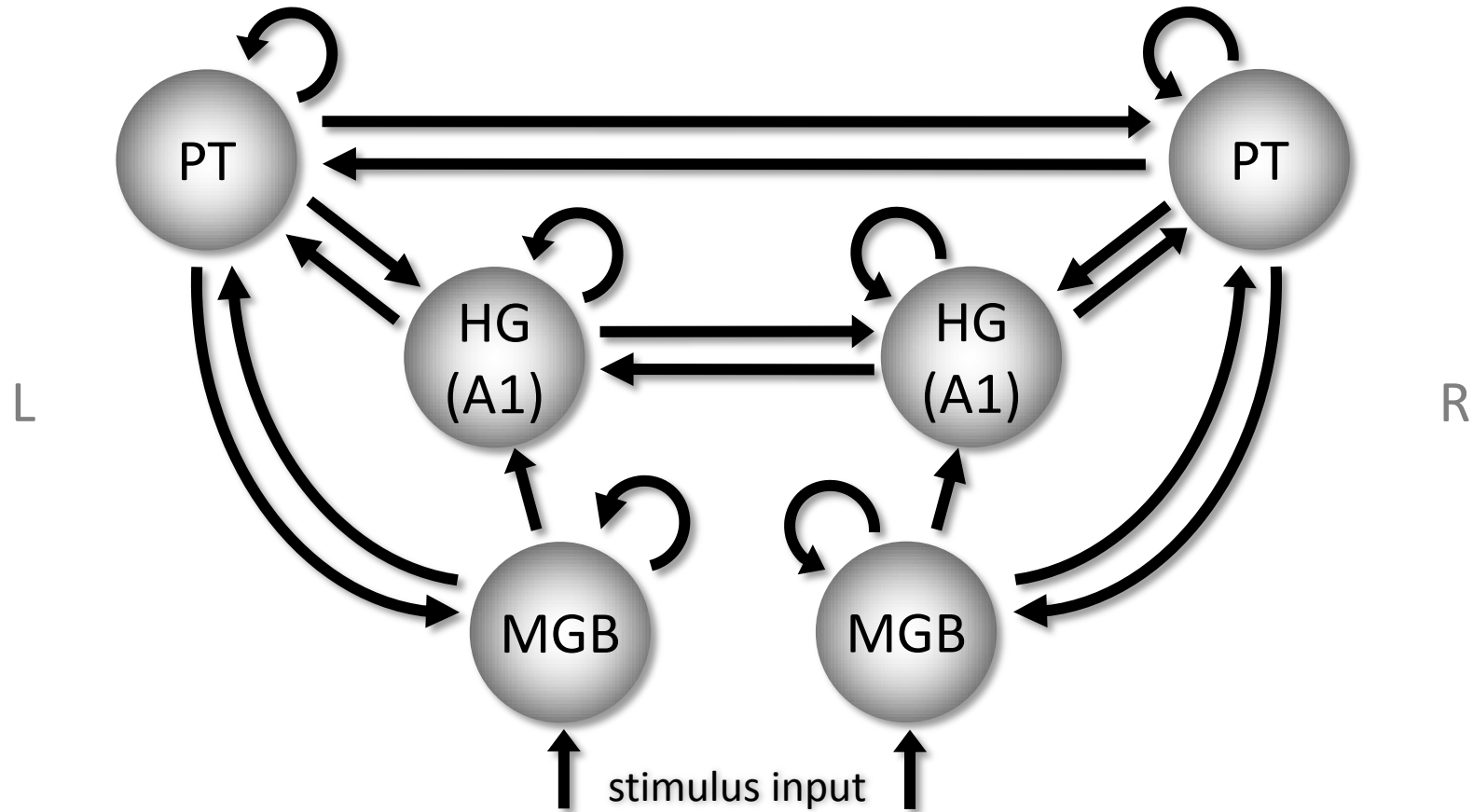
$$x = g(z, \theta_h)$$

**neural state equation**

$$\dot{z} = (A + \sum u_j B^{(j)})z + Cu$$

Friston, Harrison & Penny (2003) *NeuroImage*  
Stephan & Friston (2007) *Handbook of Brain Connectivity*

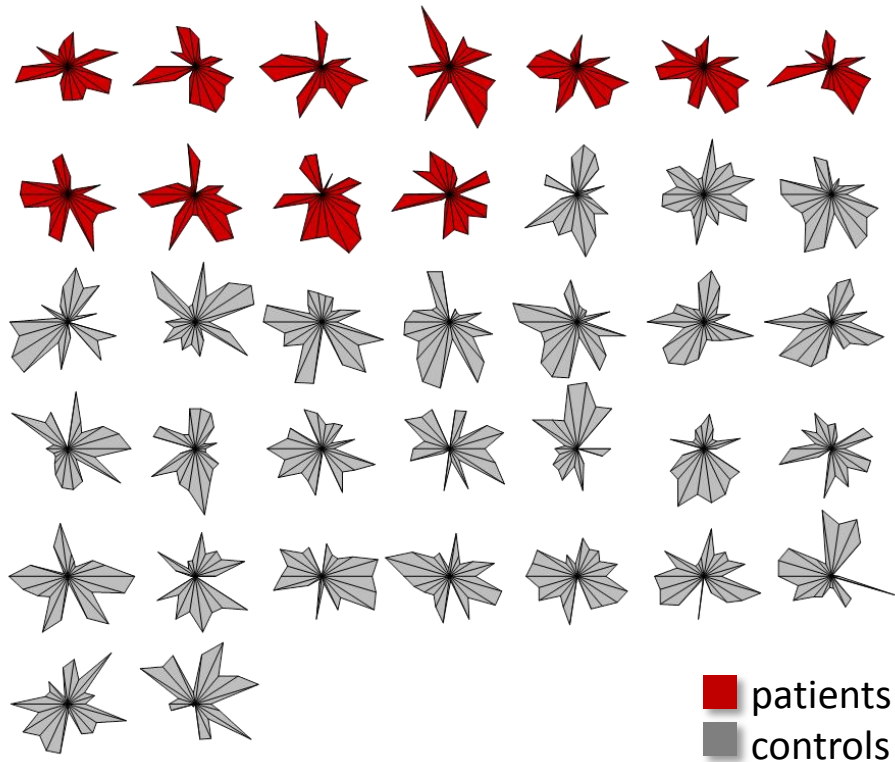
# Application to fMRI: detecting remote lesions in the brain



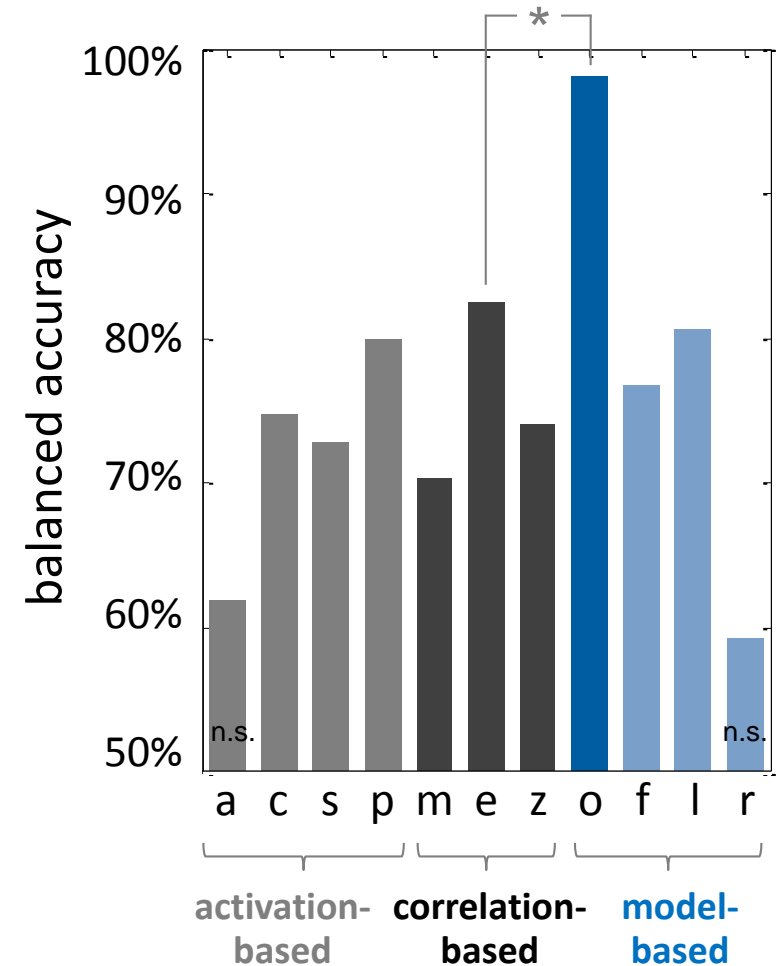
Brodersen, Schofield, Leff, Ong, Lomakina, Buhmann, Stephan (2011) *PLoS Comput Biol*  
Schofield, Penny, Stephan, Crinion, Thompson, Price, & Leff (2012) *Journal of Neuroscience*

# Application to fMRI: detecting remote lesions in the brain

## Connectional fingerprints

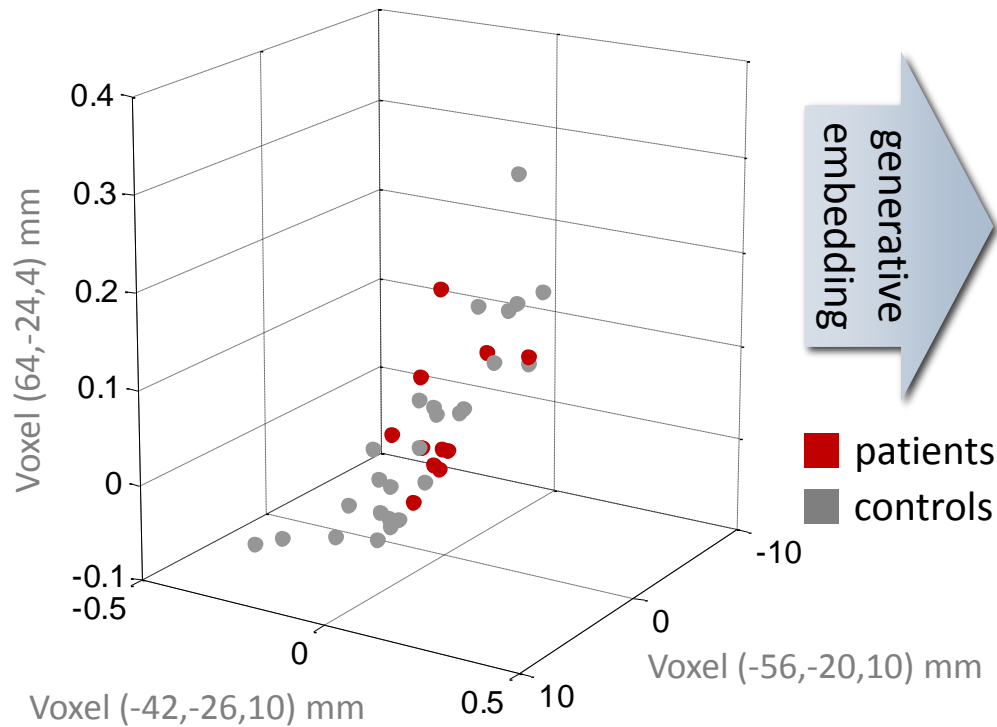


## Prediction accuracy

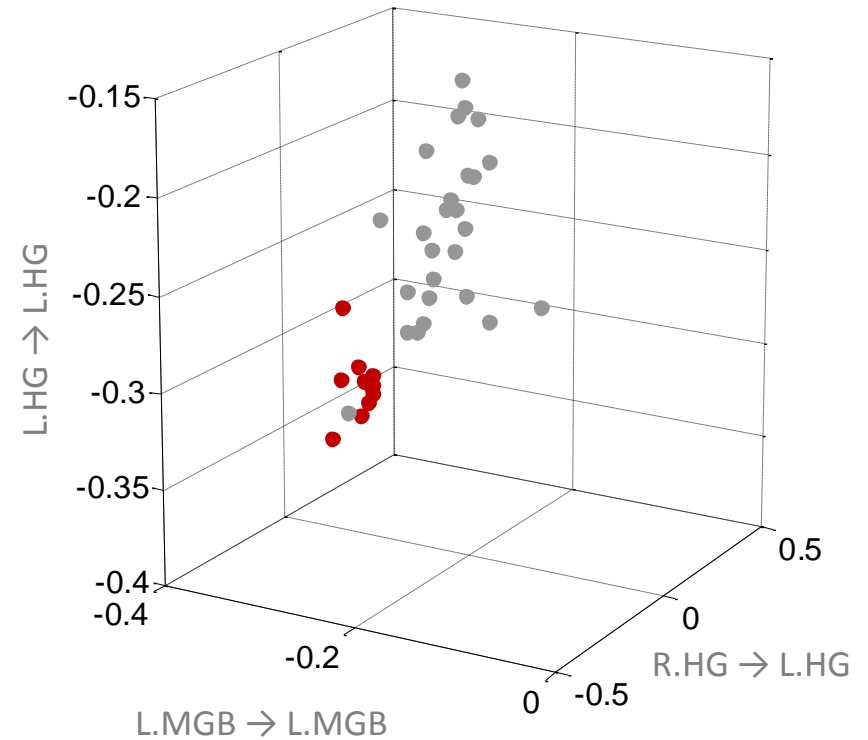


# Application to fMRI: detecting remote lesions in the brain

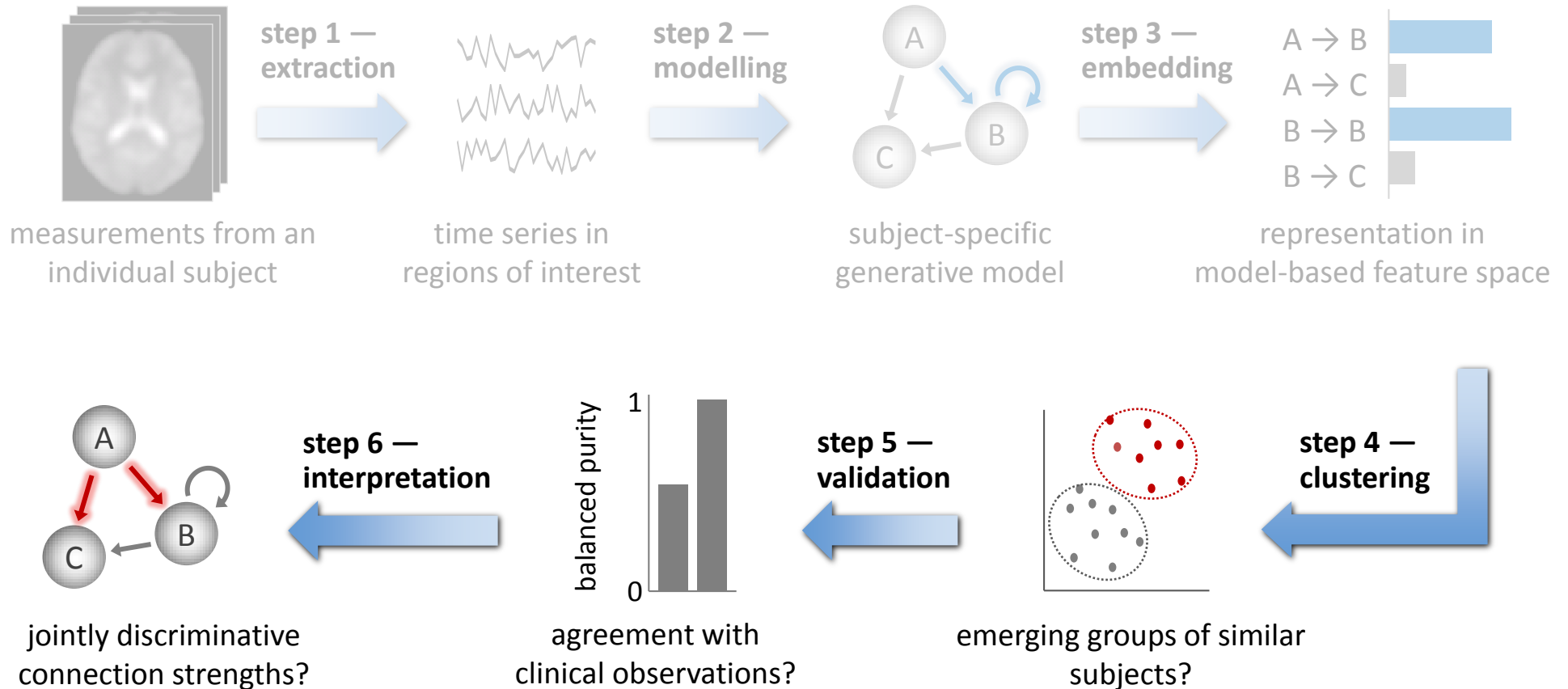
voxel-based activity space



model-based parameter space



# Generative embedding and **clustering**

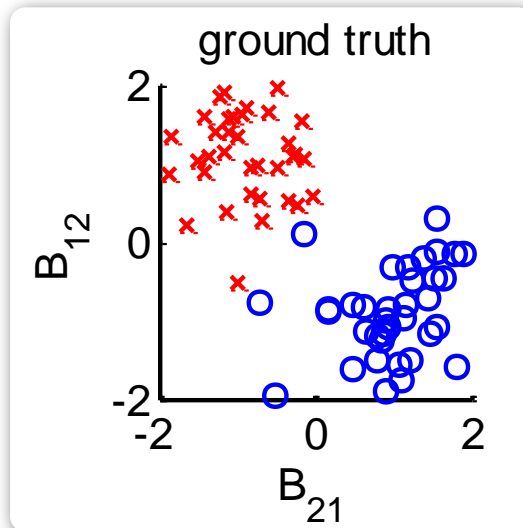


Brodersen et al. (in preparation)

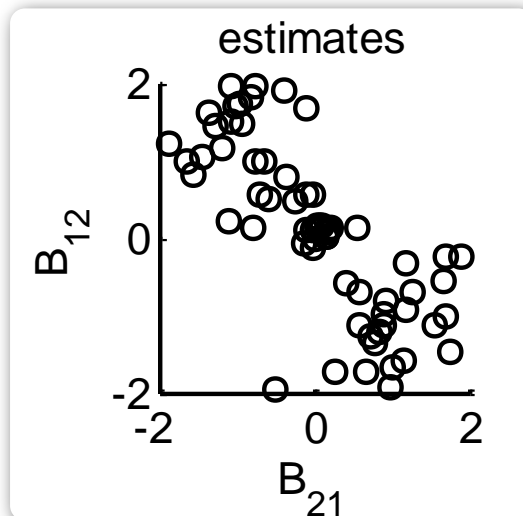


# Application to synthetic fMRI data

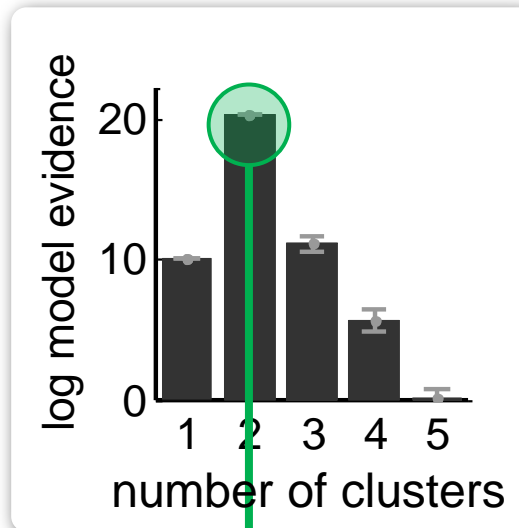
①  
definition of  
ground truth



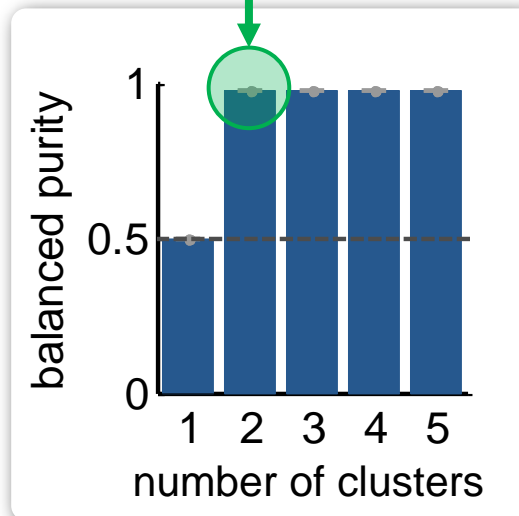
②  
data generation  
and generative  
embedding



③  
clustering using  
variational  
mixture models

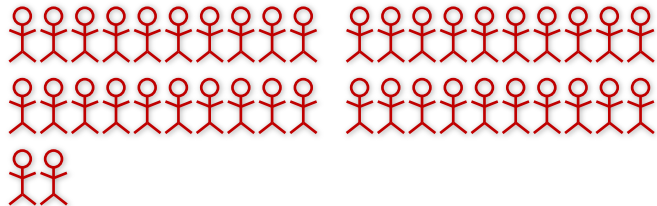


④  
validation

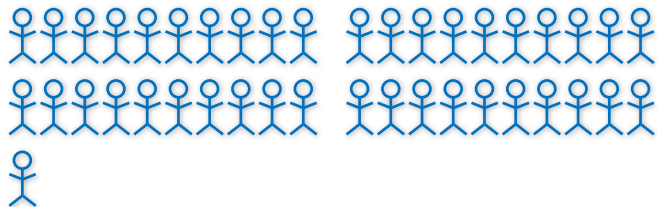


# Clinical application: dissecting schizophrenia

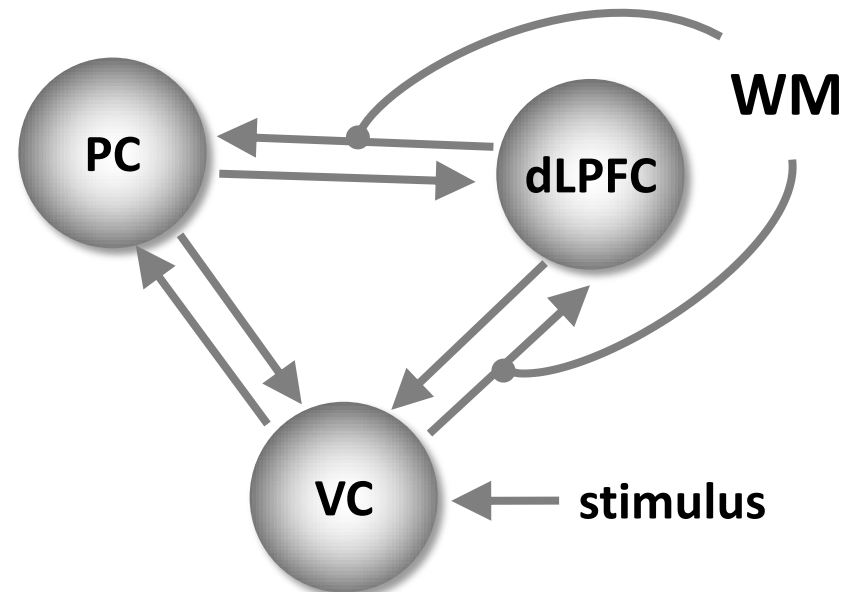
**42 patients diagnosed with schizophrenia**



**41 healthy controls**

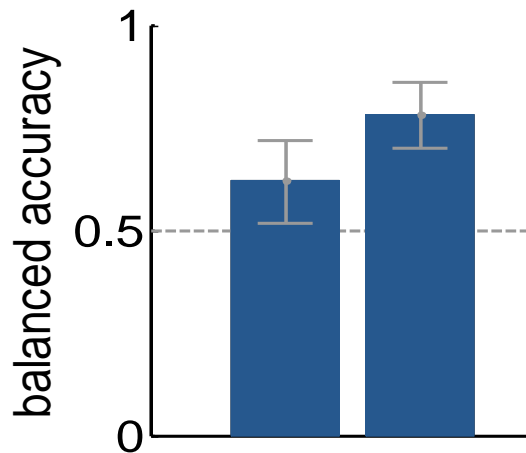


fMRI data acquired during working-memory task & modelled using a three-region DCM



# Classification vs. clustering

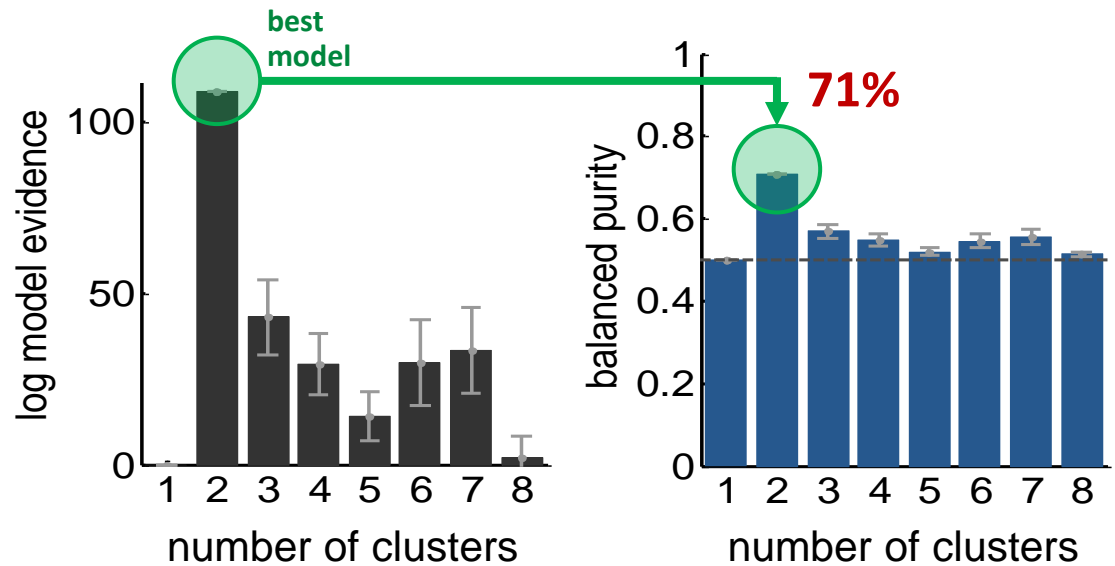
## Supervised setting: support vector classification



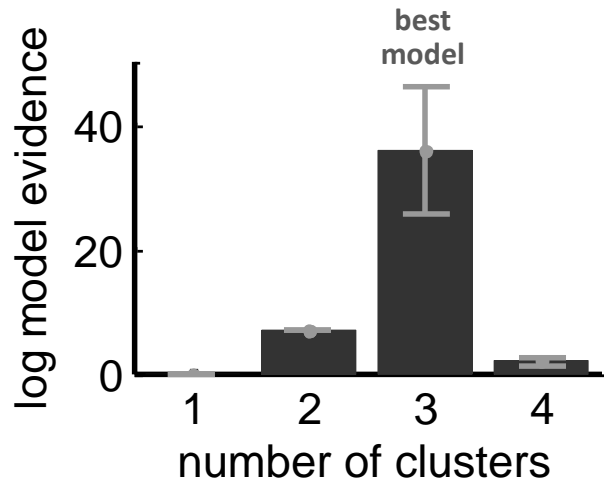
classification  
based on functional  
connectivity  
**61%**

classification using  
generative embedding  
**78%**

## New unsupervised setting: GMM clustering

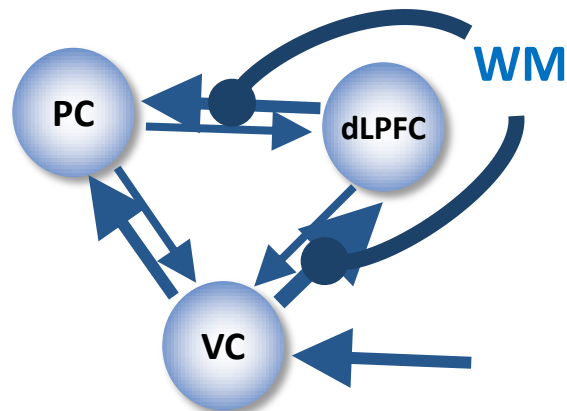


# Subclustering patients: clinical face validity



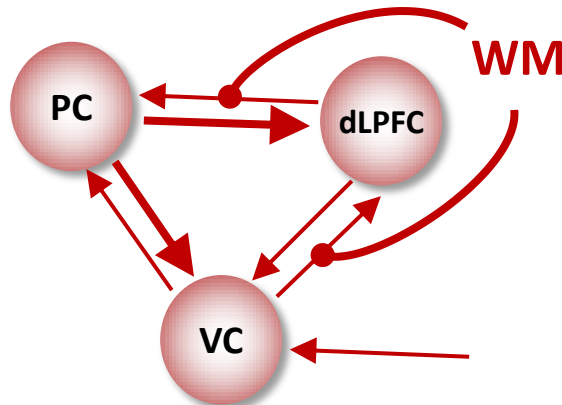
Further clustering of patients yields three distinct subgroups.

Patients in these groups differ ( $p < 0.05$ ) on the *positive and negative symptom scale (PANSS)*.



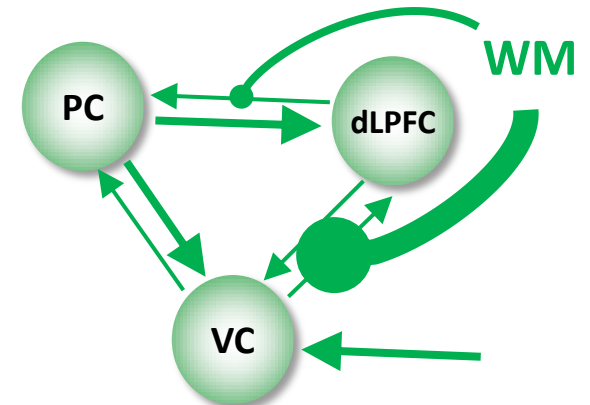
**cluster 1**

⇒ mean PANSS = 17.3



**cluster 2**

⇒ mean PANSS = 19.7



**cluster 3**

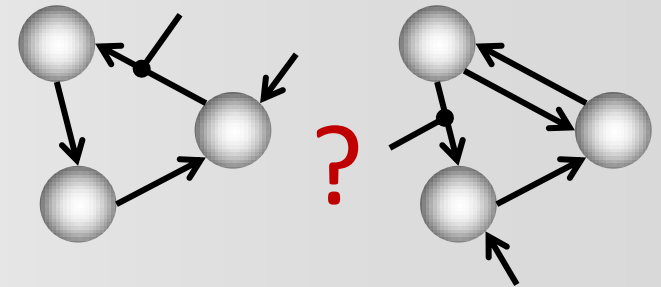
⇒ mean PANSS = 24.0

# Generative embedding and model selection

## Bayesian model selection

Which model is best w.r.t. the observed fMRI data?

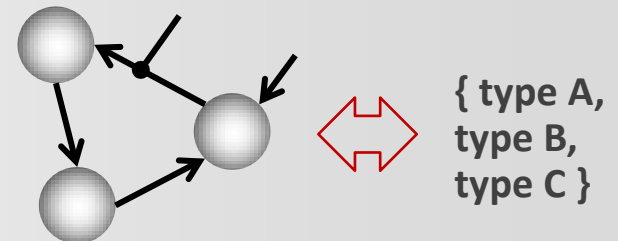
⇒ compute the model evidence  $p(y|m)$



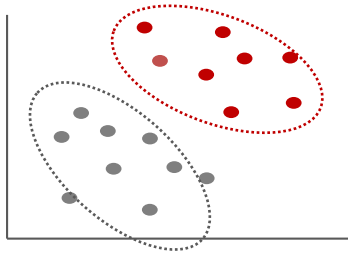
## Model selection using generative embedding

Which model is best w.r.t. an external criterion?

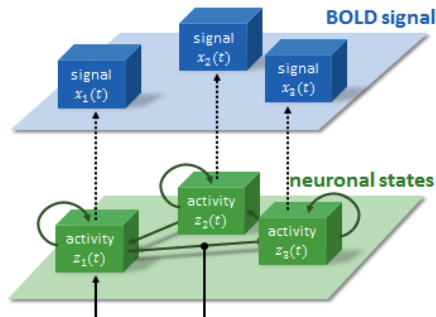
⇒ compute the classification or clustering accuracy



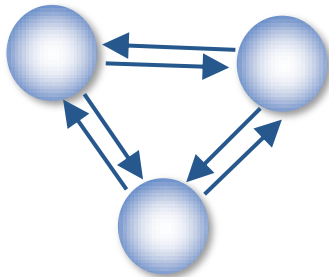
# Summary: generative embedding and clustering



- 1 Clustering using generative embedding may help decompose groups of patients with similar symptoms into **pathophysiologically distinct subtypes**.



- 2 Unlike previous approaches, our approach exploits discriminative information encoded in **'hidden' physiological quantities** (e.g., synaptic connection strengths).



- 3 Critically, generative embedding enables a **mechanistic interpretation** of the discovered structures.