

# Introduction to Computational Psychiatry

Klaas Enno Stephan



Translational Neuromodeling Unit



Universität  
Zürich<sup>UZH</sup>



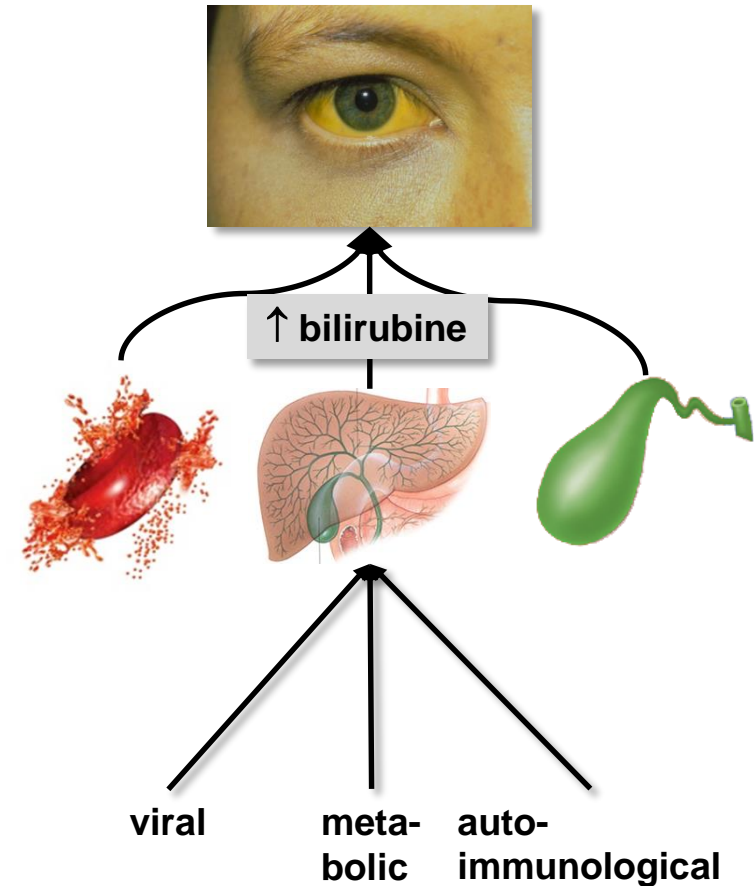
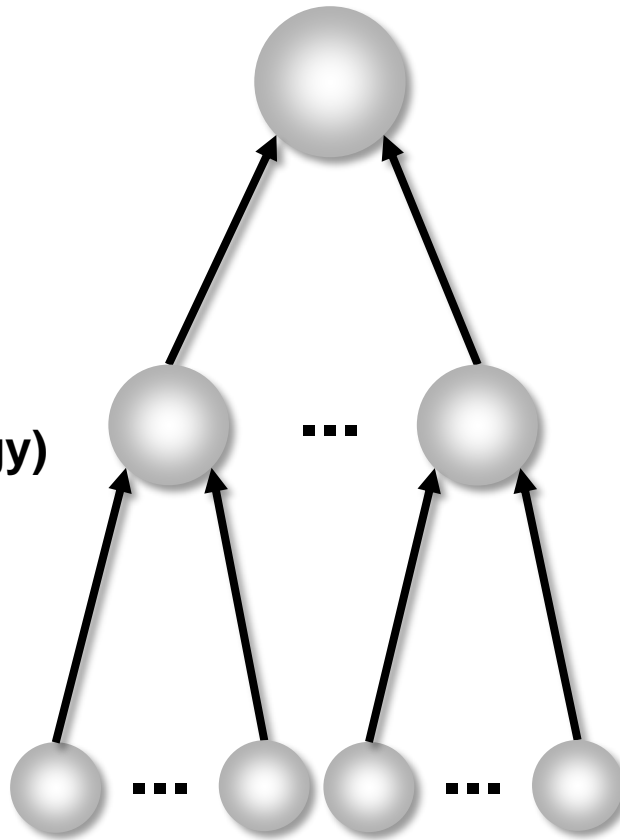
Eidgenössische Technische Hochschule Zürich  
Swiss Federal Institute of Technology Zurich

# From differential diagnosis to nosology

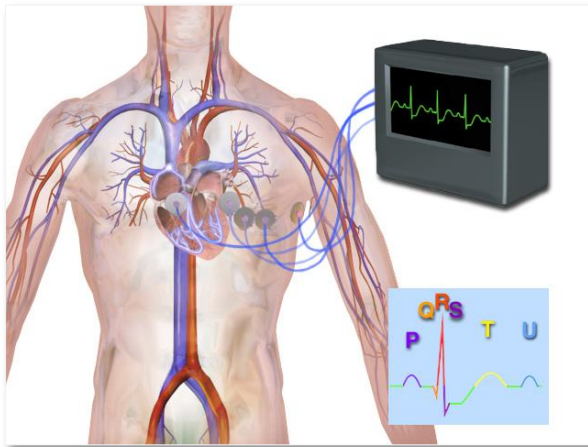
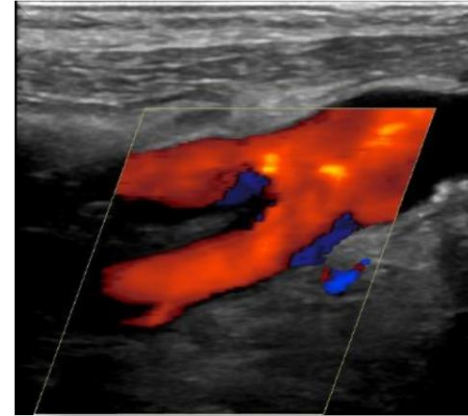
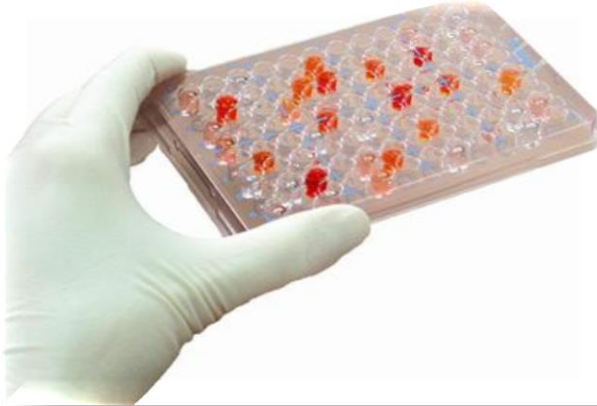
**SYMPTOM**

**MECHANISMS  
(pathophysiology)**

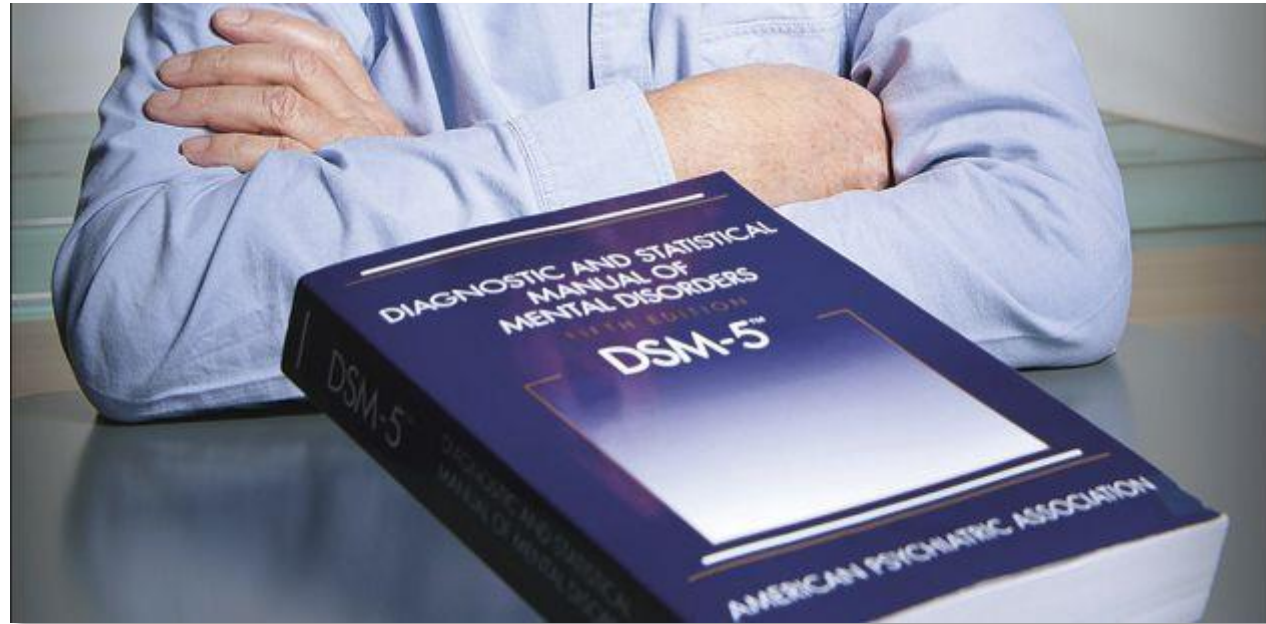
**CAUSES  
(aetiology)**



**>3,000 FDA-approved clinical tests in medicine**



# 1 diagnostic instrument in psychiatry



# Diagnostic and Statistical Manual of Mental Disorders (DSM)



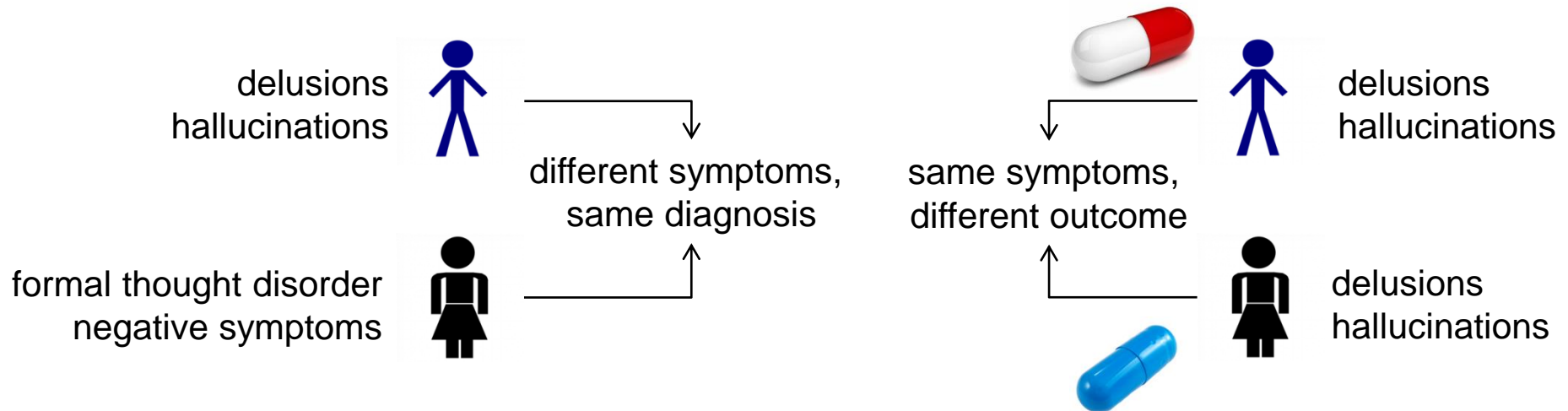
# DSM IV: Schizophrenia

- Delusions
- Hallucinations
- Formal thought disorder
- Grossly disorganized or catatonic behavior
- Negative symptoms: flat affect, anhedonia, avolition, alogia, asociality

≥ 2 symptoms  
over ≥ 1 month

+ social or occupational dysfunction

+ continuous signs of the disturbance persist for at least six months



# Psychiatric disorders = spectrum diseases



**polygenetic basis**  
**gene-environment interactions**  
**environmental variation**

**variability in clinical  
trajectory and treatment  
response**

**multiple disease mechanisms**



Molecular Psychiatry (2012) 17, 1174–1179

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## PERSPECTIVE

**Why** has it taken so long for biological psychiatry to develop clinical tests and what to do about it?

S Kapur<sup>1</sup>, AG Phillips<sup>2</sup> and TR Insel<sup>3</sup>



**We often take DSM too seriously  
(or forget about its original purpose).**

**Trying to develop clinical tests based on constructs which are  
inherently heterogenous is not a promising strategy.**



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## **PERSPECTIVE**

Why has it taken so long for biological psychiatry to develop clinical tests and what to do about it?

S Kapur<sup>1</sup>, AG Phillips<sup>2</sup> and TR Insel<sup>3</sup>

From reinforcement learning models to  
psychiatric and neurological disorders

Tiago V Maia<sup>1,2</sup> & Michael J Frank<sup>3,4</sup>

## Computational psychiatry

P. Read Montague<sup>1,2</sup>, Raymond J. Dolan<sup>2</sup>, Karl J. Friston<sup>2</sup> and Peter Dayan<sup>3</sup>

## Computational approaches to psychiatry

Klaas Enno Stephan<sup>1,2,3</sup> and Christoph Mathys<sup>3</sup>

## Computational psychiatry: the brain as a phantastic organ

*Karl J Friston, Klaas Enno Stephan, Read Montague, Raymond J Dolan*

## Computational Psychiatry

Xiao-Jing Wang<sup>1,2,3,\*</sup> and John H. Krystal<sup>3,4,5,6</sup>

## Translational Perspectives for Computational Neuroimaging

Klaas E. Stephan,<sup>1,2,3,\*</sup> Sandra Iglesias,<sup>1</sup> Jakob Heinzle,<sup>1</sup> and Andreea O. Diaconescu<sup>1</sup>

Computational Psychiatry: towards a mathematically  
informed understanding of mental illness

Rick A Adams,<sup>1,2</sup> Quentin J M Huys,<sup>3,4</sup> Jonathan P Roiser<sup>1</sup>

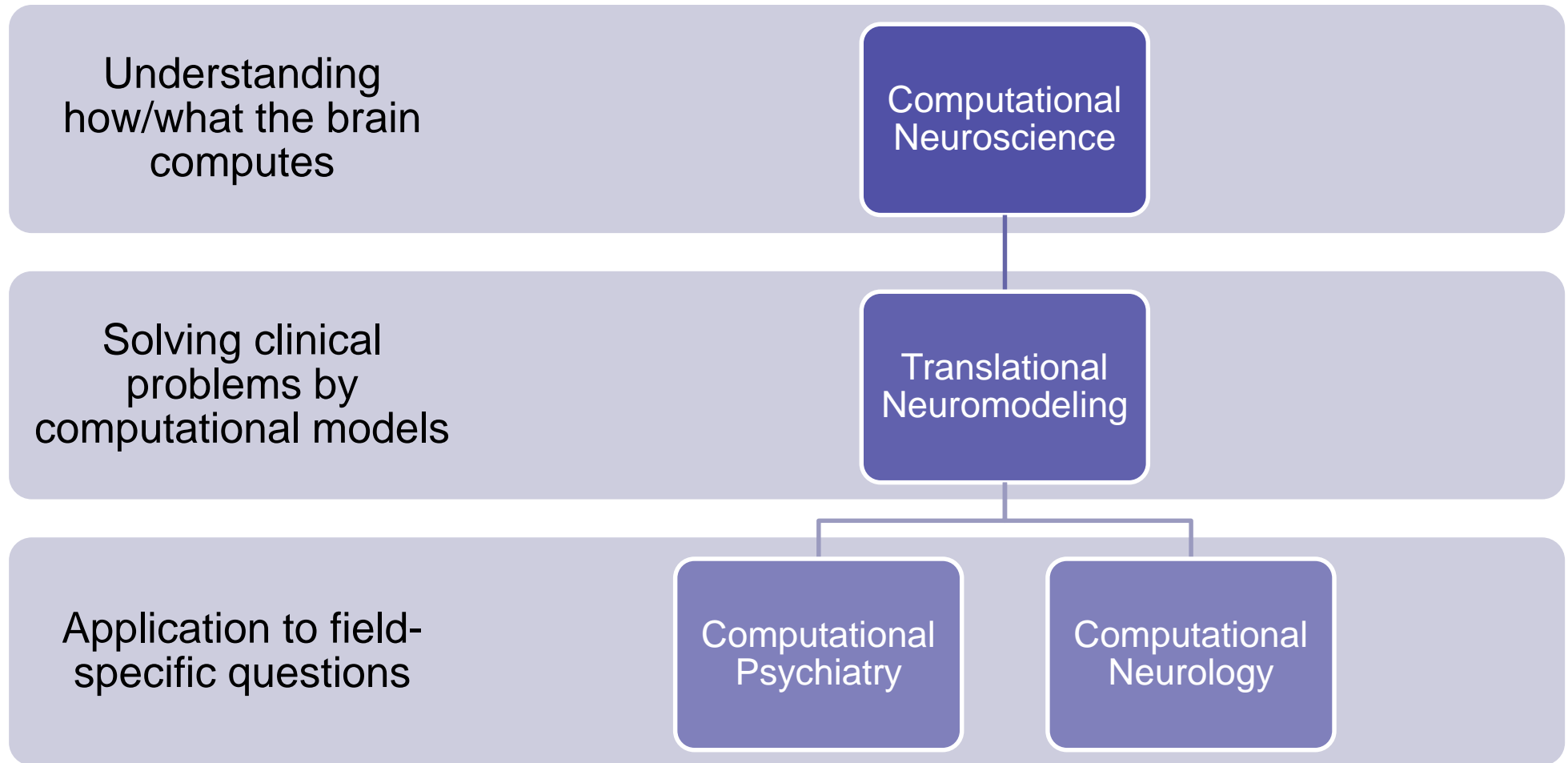
Computational psychiatry as a bridge from  
neuroscience to clinical applications

Quentin J M Huys<sup>1,2,5</sup>, Tiago V Maia<sup>3,5</sup> & Michael J Frank<sup>4</sup>

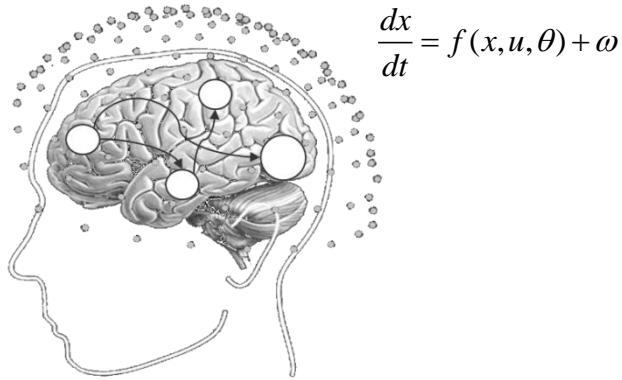
# What exactly do we mean by "computational"?

- in computer science:
  - “computation” = a well-defined process (algorithm) that transforms an input set into an output set in a finite number of steps
- in neuroscience: two common usages
  - *methodological approach*
    - investigations of neural or cognitive systems by algorithmic, as opposed to analytical, approaches  
→ “computational neuroscience”
  - *information processing* (Marr's “algorithmic level”)
    - as opposed to physiological implementation

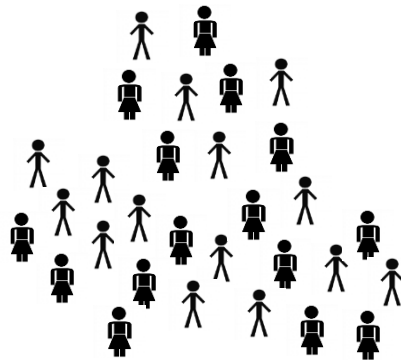
# A taxonomy of computational fields in neuroscience



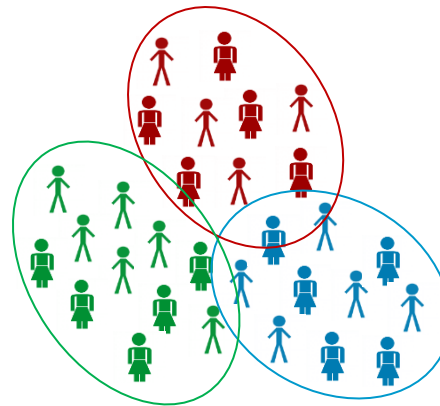
# 1 Computational assays: Models of disease mechanisms



# 2 Application to brain activity and behaviour of individual patients



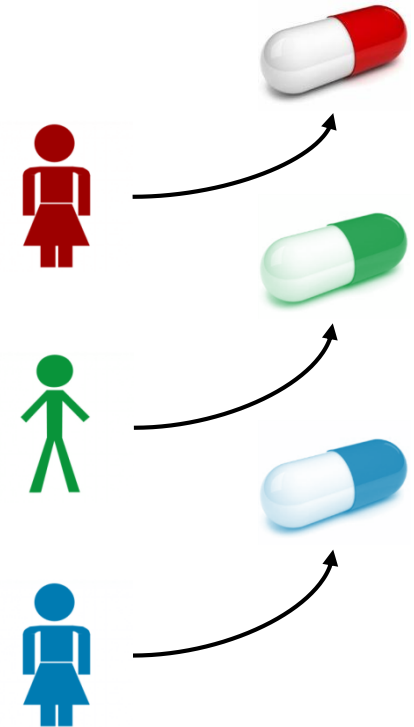
# 3 Detecting physiological subgroups (based on inferred mechanisms)



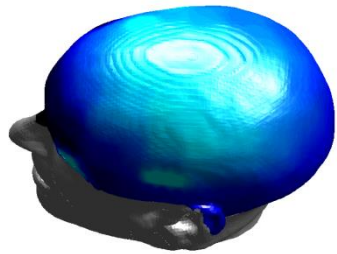
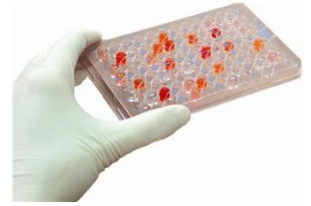
- disease mechanism A
- disease mechanism B
- disease mechanism C

# Translational Neuromodeling

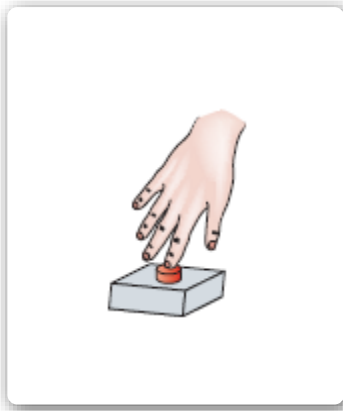
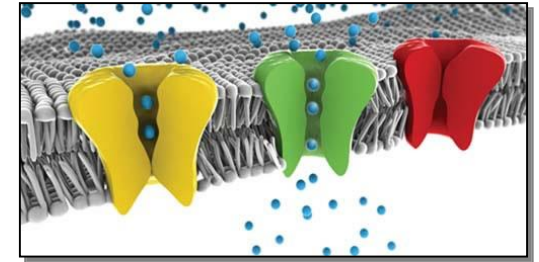
# 4 Individual treatment prediction



# Generative models as "computational assays"



$$\begin{aligned} & \xleftarrow{p(y | \theta, m) \cdot p(\theta | m)} \\ & \xrightarrow{p(\theta | y, m)} \end{aligned}$$



$$\begin{aligned} & \xleftarrow{p(y | \theta, m) \cdot p(\theta | m)} \\ & \xrightarrow{p(\theta | y, m)} \end{aligned}$$



# Computational assays: key clinical questions

## **SYMPTOMS**

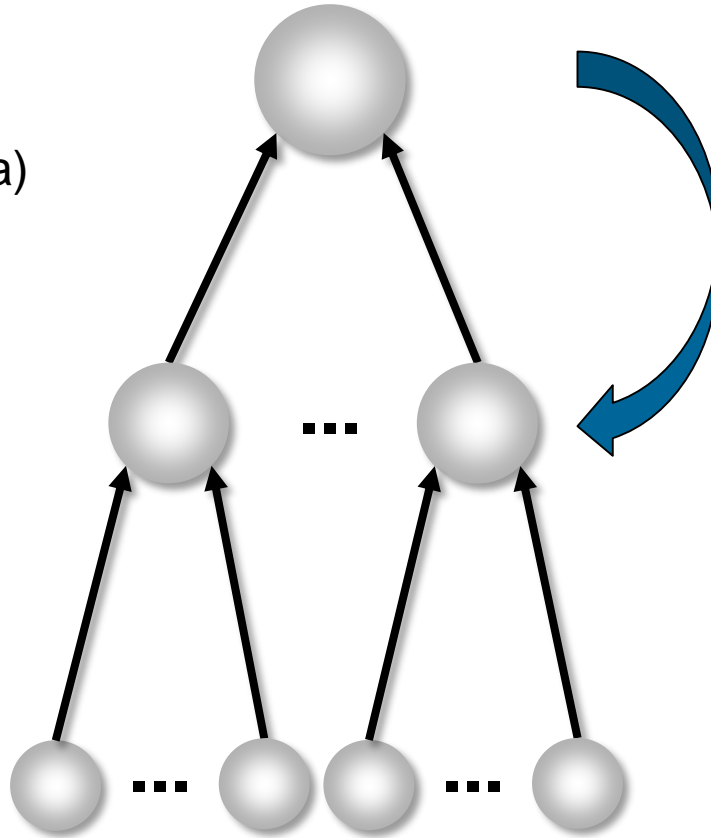
(behavioural or physiological data)

## **MECHANISMS**

(computational, physiological)

## **CAUSES**

(aetiology)



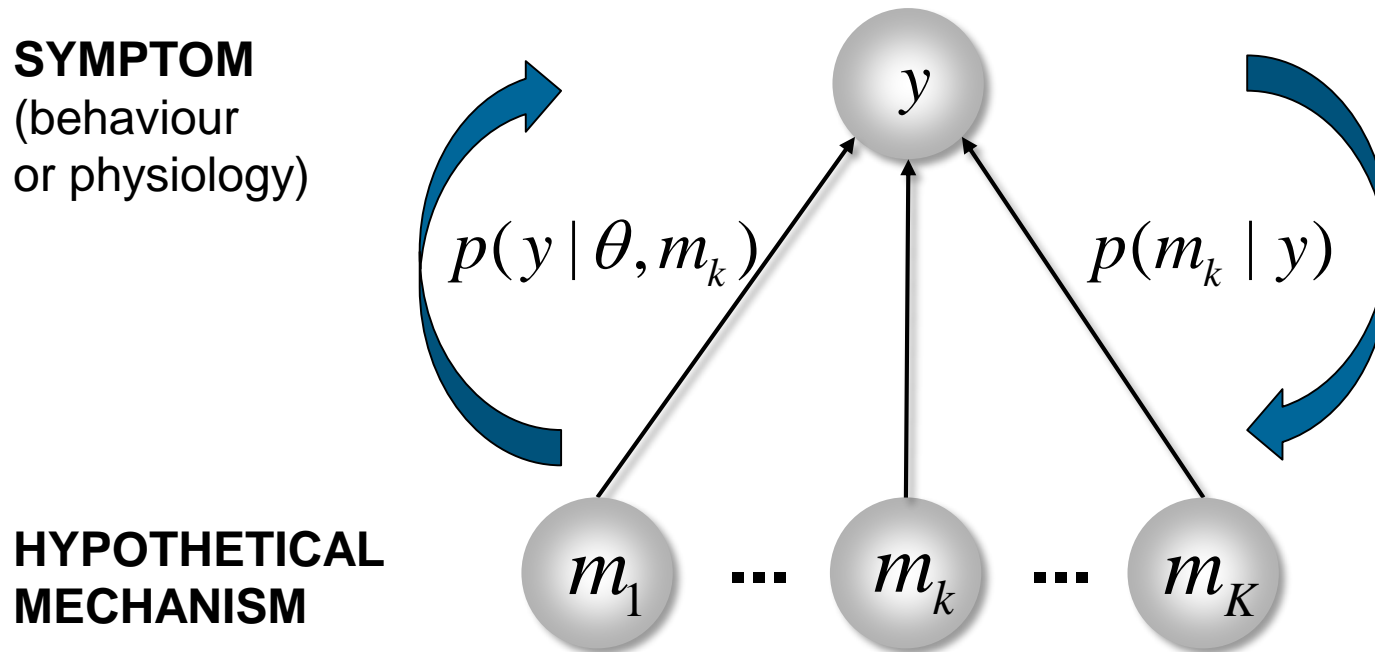
**differential diagnosis**  
of alternative disease  
mechanisms

**spectrum dissection**  
into mechanistically  
distinct subgroups

**prediction** of clinical  
trajectories and  
treatment response



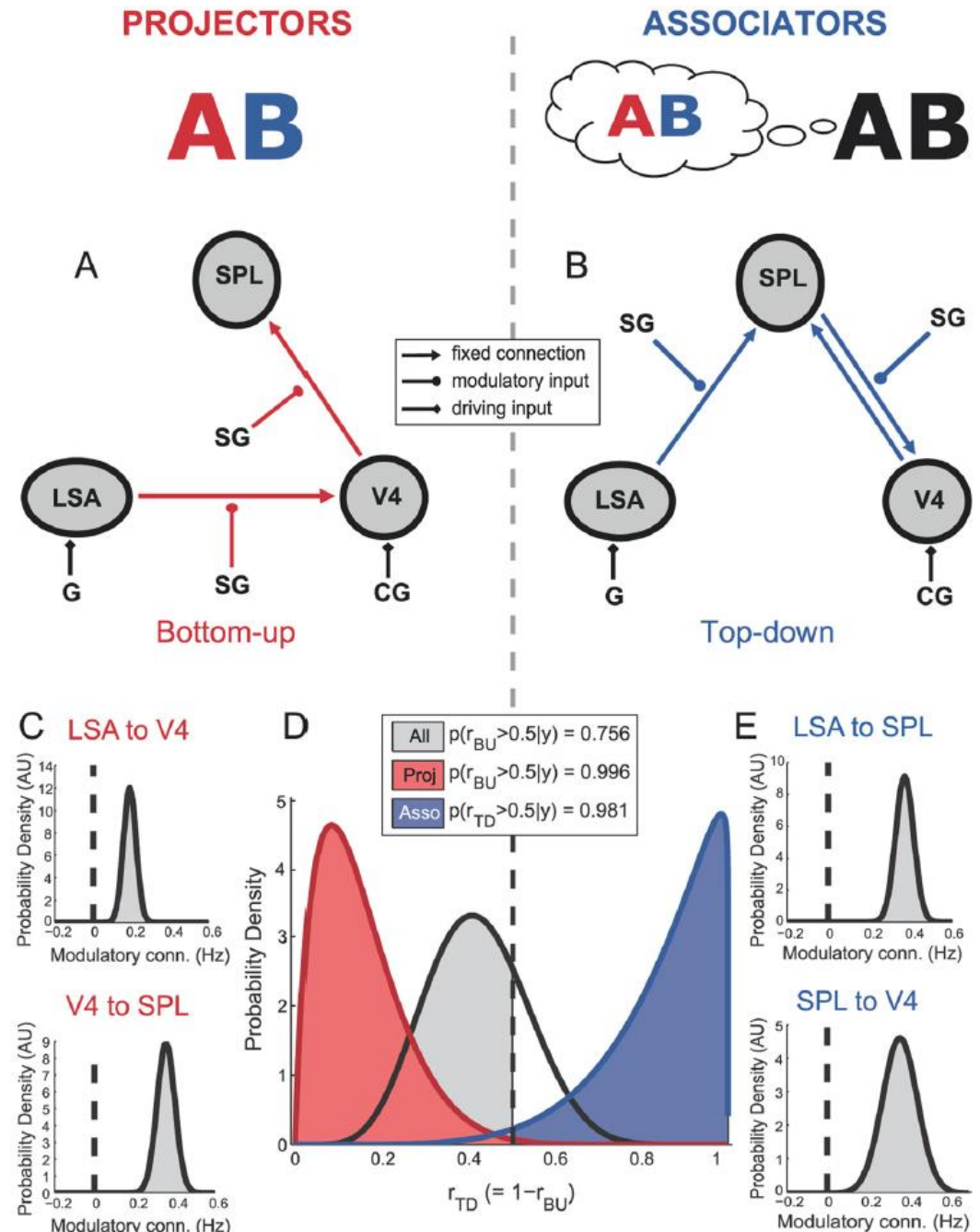
# Differential diagnosis by model selection



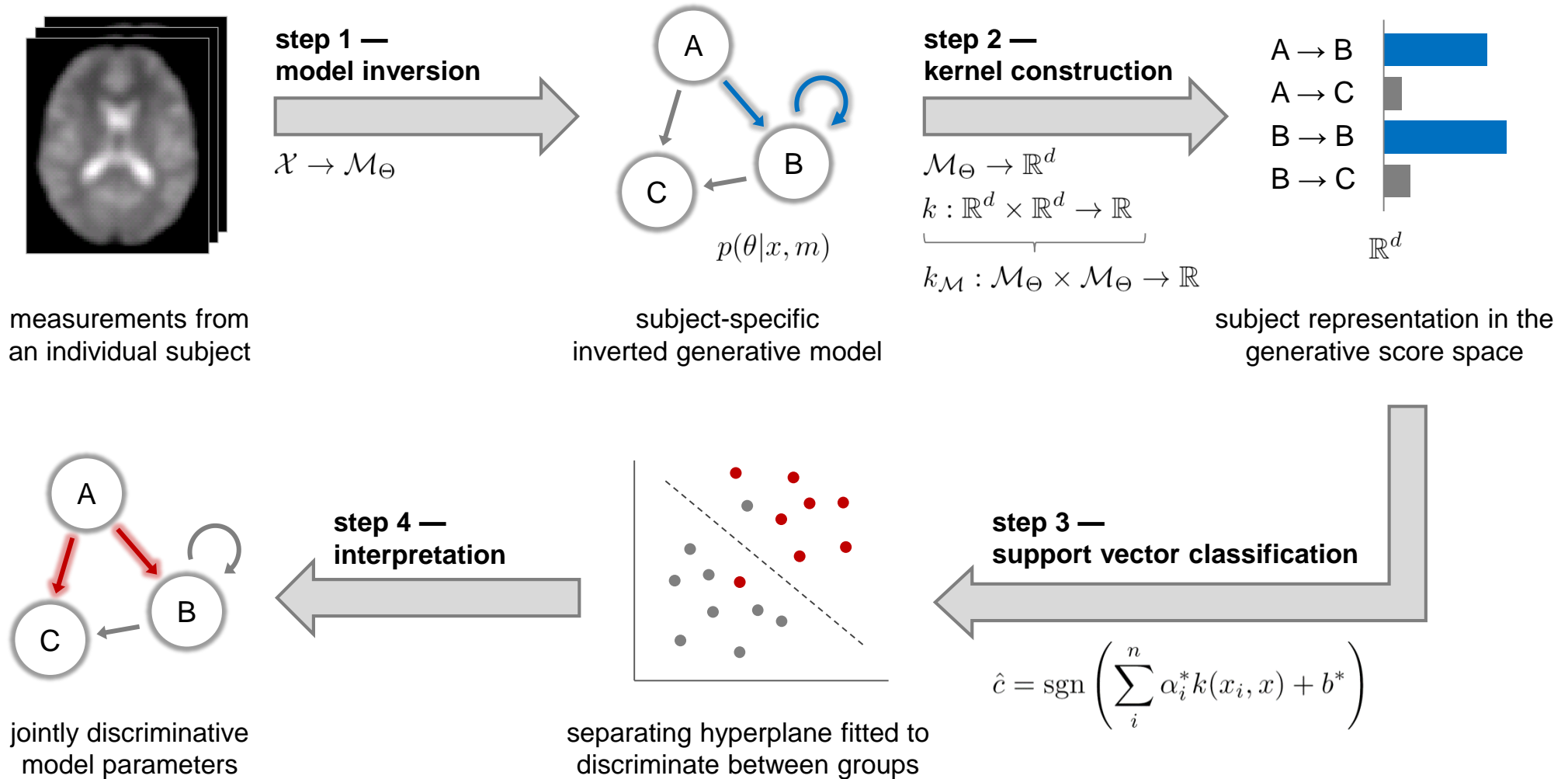
$$p(m_k | y) = \frac{p(y | m_k) p(m_k)}{\sum_k p(y | m_k) p(m_k)}$$

# Synaesthesia

- “projectors” experience color externally colocalized with a presented grapheme
- “associators” report an internally evoked association
- Bayesian model selection of competing DCMs separates projectors (bottom-up mechanisms) and associators (top-down)

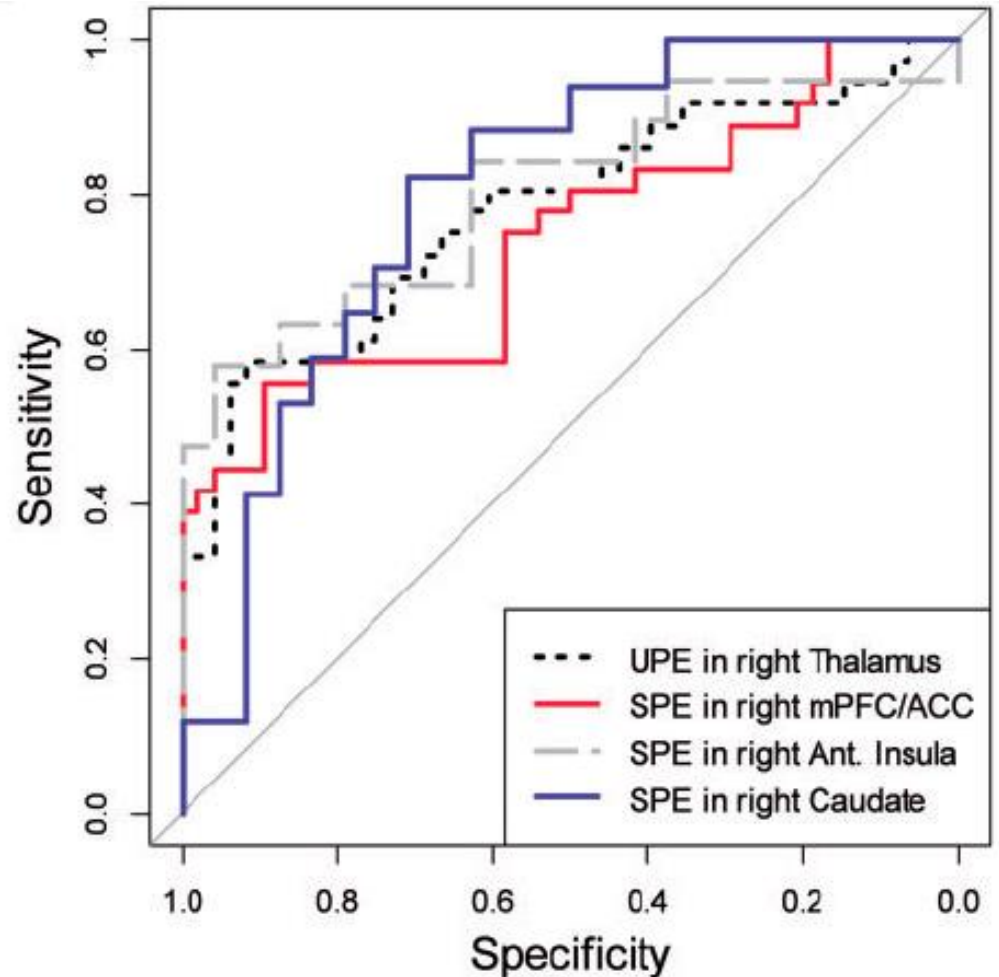


# Generative embedding (supervised)



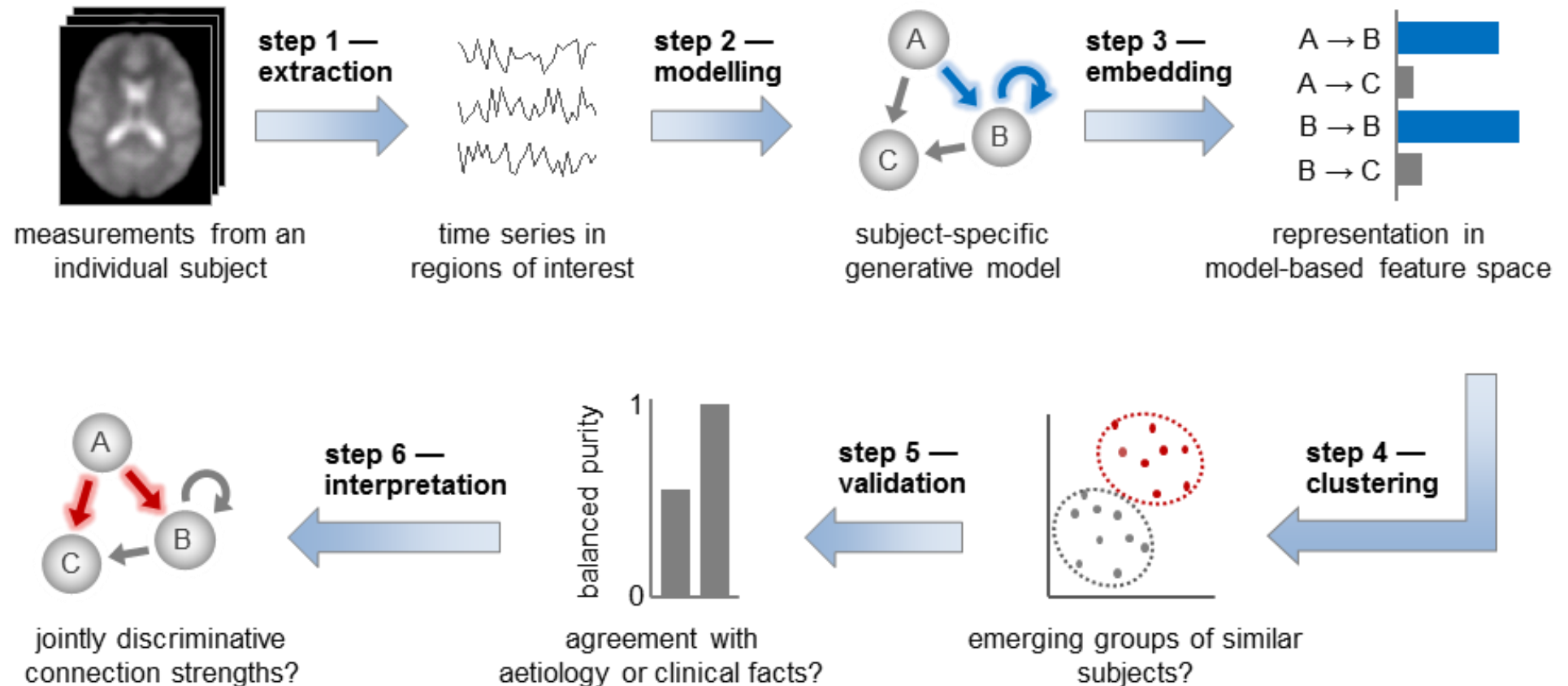
# Predicting future drug abuse

- fMRI of occasional stimulant users (stop-signal task), Bayesian hidden Markov model
- prediction error (PE) activity in several brain regions predicted drug abuse symptoms 3 years later
- model-based prediction outperformed predictions based on clinical variables and conventional fMRI analyses



UPE = unsigned PE  
SPE = signed PE

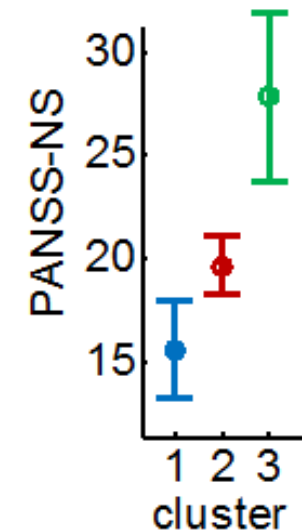
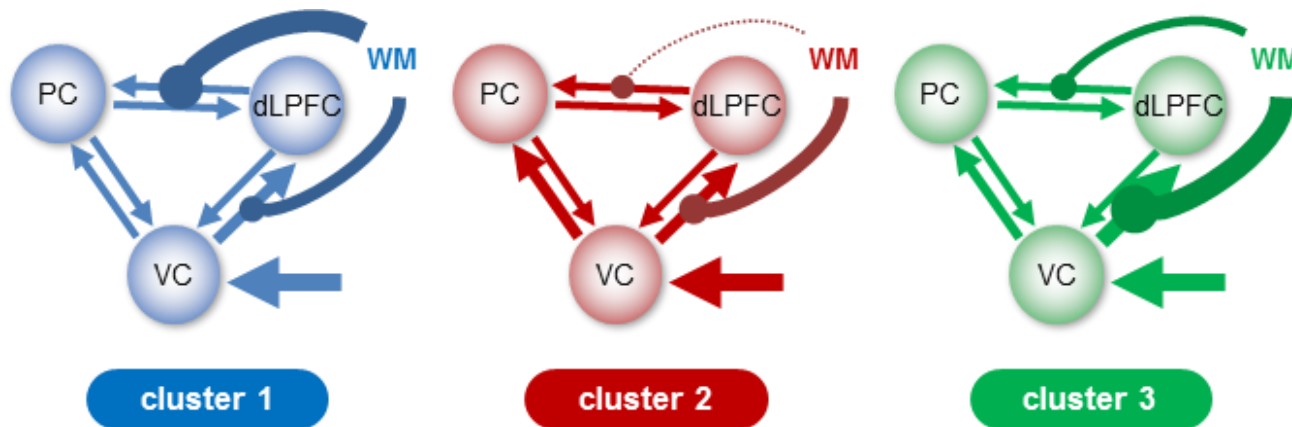
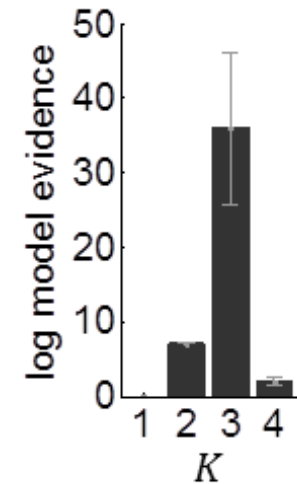
# Generative embedding (unsupervised)



# Detecting subgroups of patients in schizophrenia

Optimal  
cluster  
solution

- three distinct subgroups (total N=41)
- subgroups differ ( $p < 0.05$ ) wrt. negative symptoms on the *positive and negative symptom scale* (PANSS)



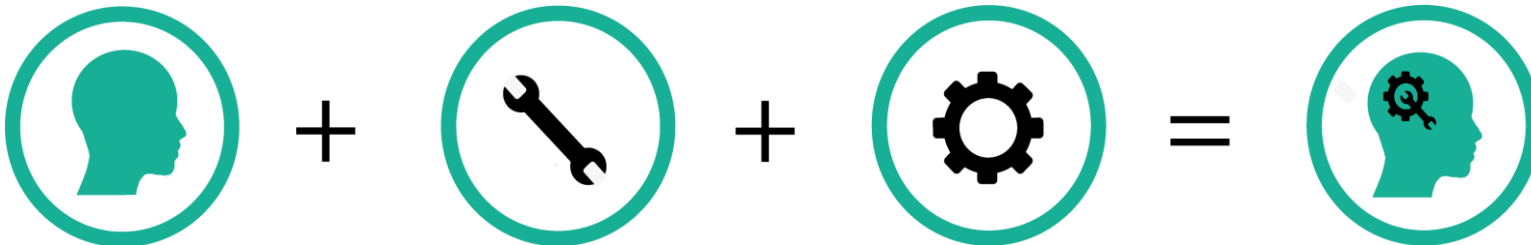
# Key challenges for CP/TN (and our local response)

1. **Highly interdisciplinary → mutual teaching**
2. **Methodology in its infancy → open source code and data sharing**
3. **Prospective validation studies → uniting computational & biomedical scientists in new types of organisations**

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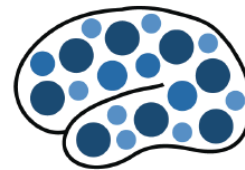
COMPUTATIONALPSYCHIATRYCOURSE





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TAPAS

[www.translationalneuromodeling.org/tapas](http://www.translationalneuromodeling.org/tapas)

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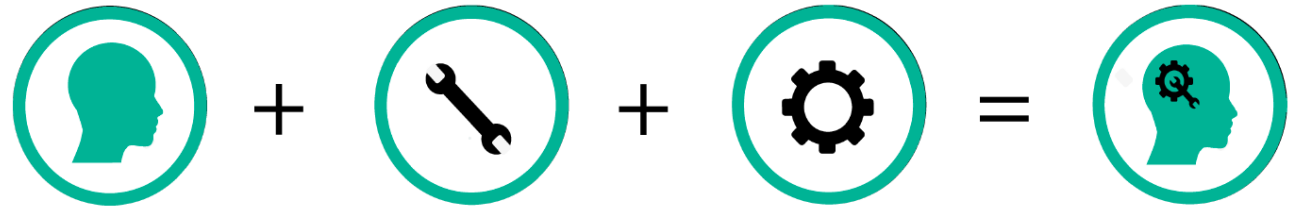


Translational Neuromodeling Unit

[www.tnu.ethz.ch](http://www.tnu.ethz.ch)  
twitter: @tnuzurich



# CPC 2016



## COMPUTATIONAL PSYCHIATRY COURSE

TNU, Zurich, 29.08. – 02.09.2016

- 2nd edition
- originated from our previous local courses on Computational Psychiatry
- key features
  - theoretical lectures & practical demonstrations coupled
  - open source software only
  - computation in a broad sense: models of physiology and behaviour
  - 26 international presenters from 16 different institutions



## Day 1

Introduction to  
Computational  
Psychiatry

Schizophrenia

Mood  
Disorders

Autism

Conceptual Basis of  
Computational  
Modeling

Variational  
Bayes



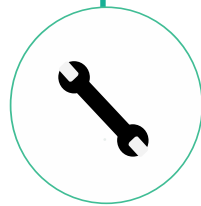
## Day 2

Bayesian Model  
Selection and  
Averaging

Markov Chain  
Monte Carlo

Markov  
Decision  
Processes

Machine  
Learning  
Techniques

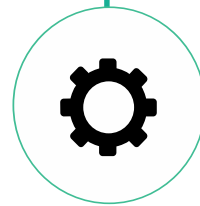


## Day 3

Bayesian Models  
of Perception

Predictive  
Coding

Active  
Inference



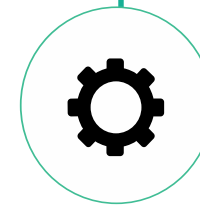
## Day 4

Hierarchical  
Bayesian  
Inference

DCM for fMRI

DCM for EEG

Reinforcement  
Learning



## Day 5

Compulsion,  
control, and  
habits

The search for the "Bayesian  
Priors" in the  
Brain, in Health and Mental  
Illness.

Computational  
neuromodulation in  
human decision-making

Biophysical models  
and NMDA  
channelopathies



# Further reading

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**Welcome & Thank You**