Computational Psychiatry Course Zurich 2015

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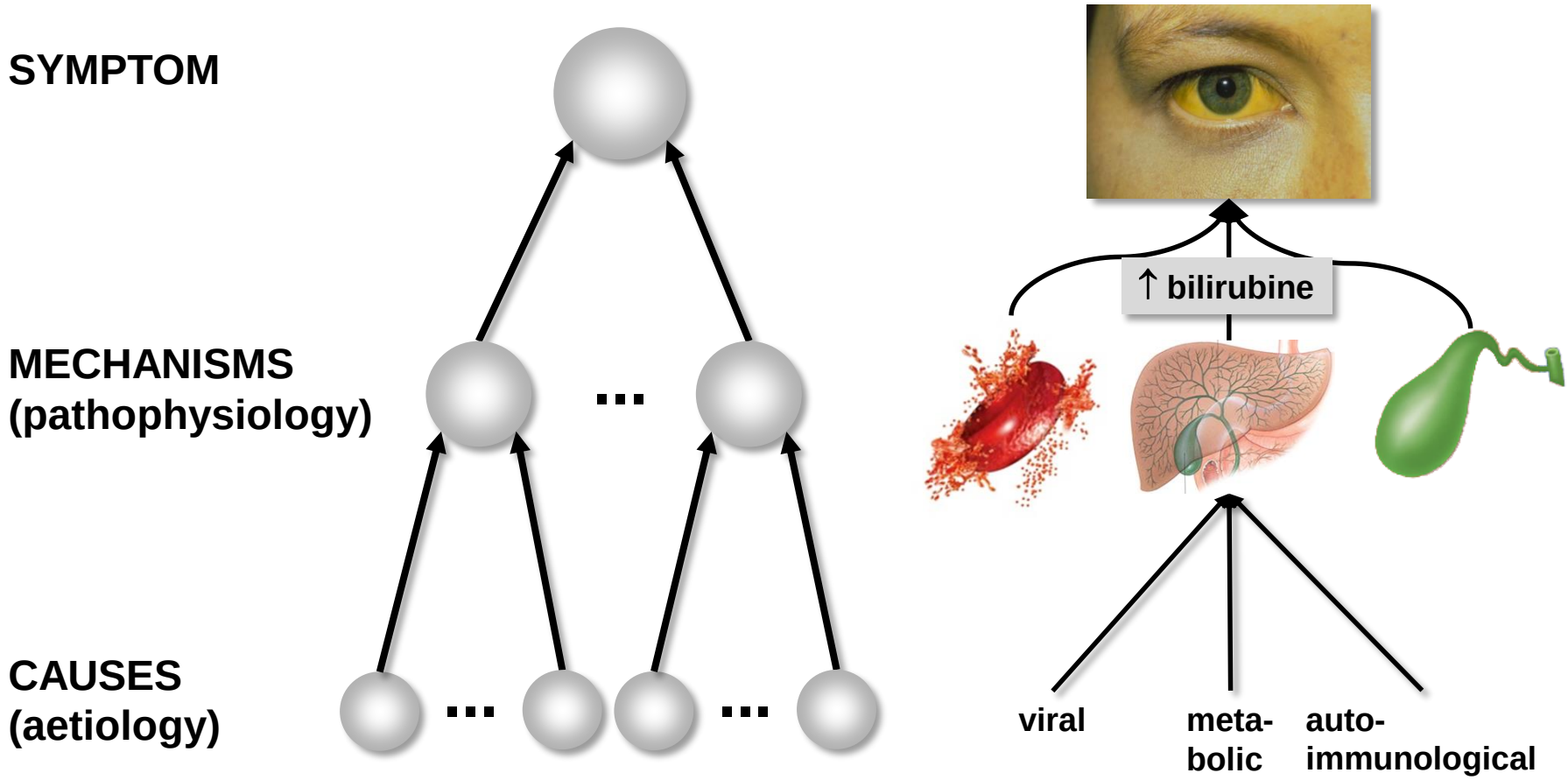
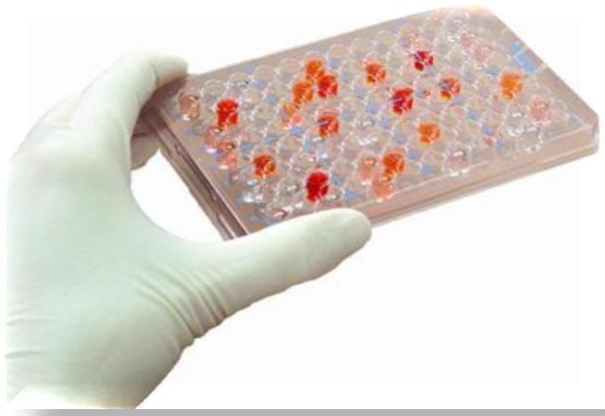
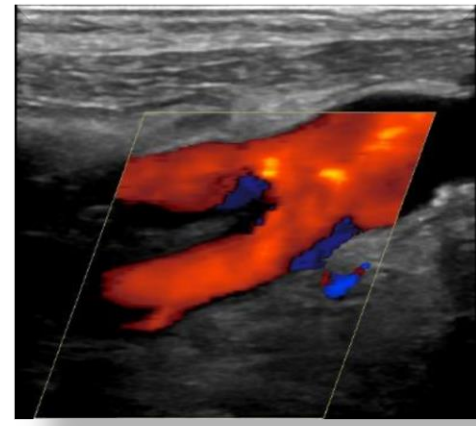
Swiss Federal Institute of Technology Zurich

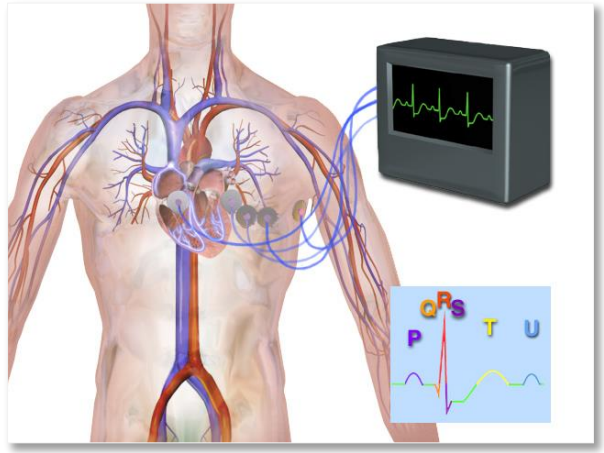
From differential diagnosis to nosology



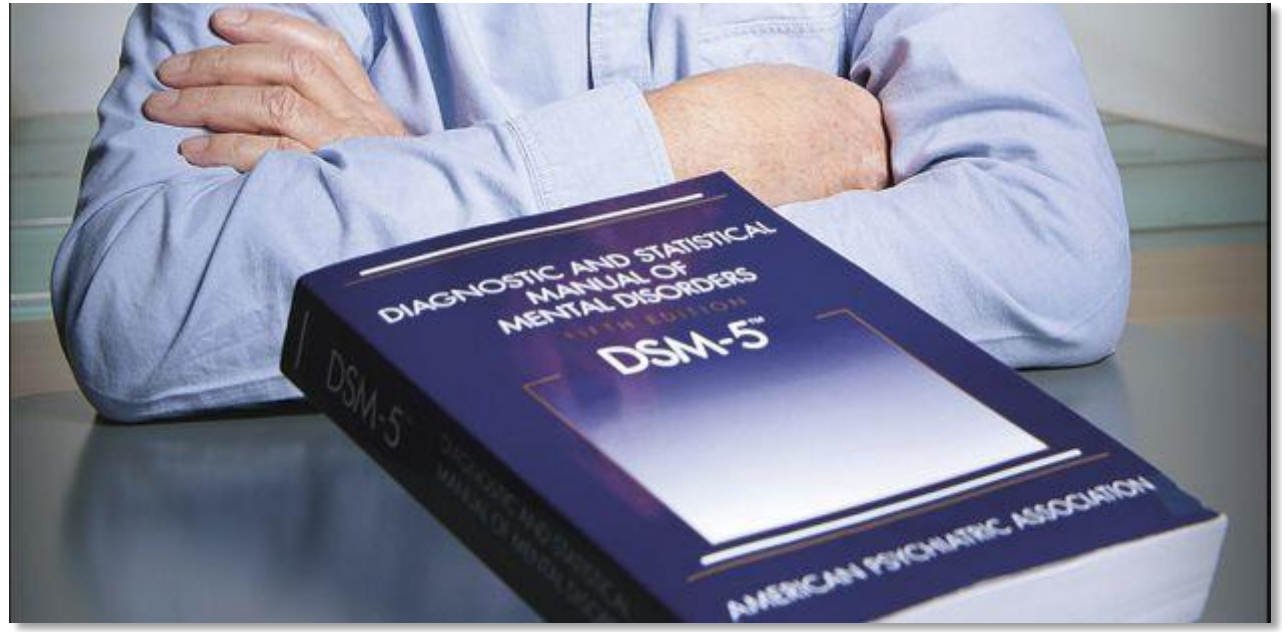
>3,000 FDA-approved clinical tests in medicine







1 diagnostic instrument in psychiatry



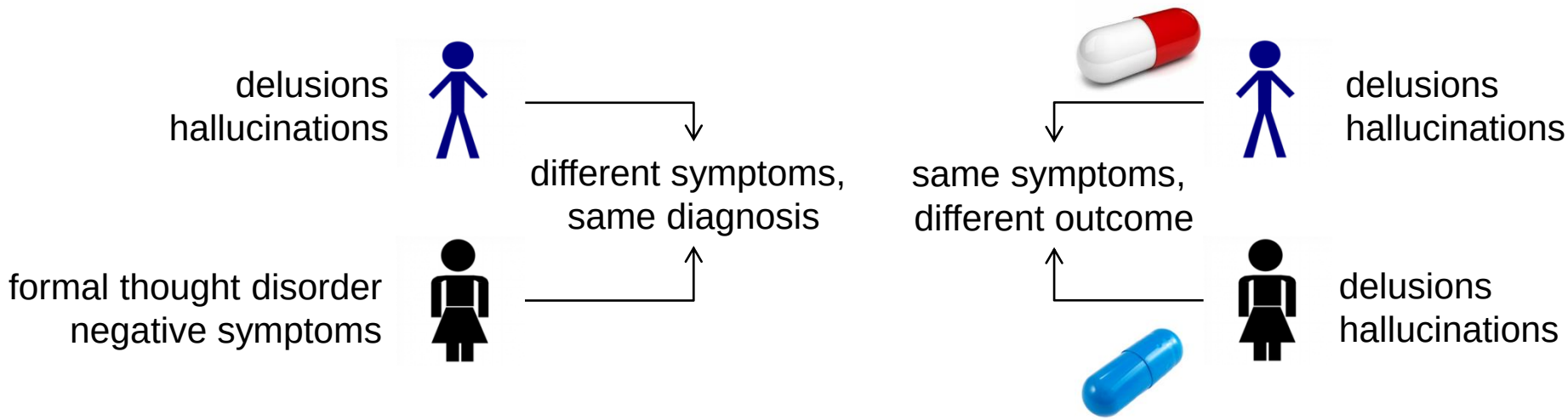
Diagnostic and Statistical Manual of Mental Disorders (DSM)

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 diseases = spectrum diseases

polygenetic basis

gene-environment interactions

individual beliefs

variability in clinical trajectory and treatment response

multiple disease mechanisms

Molecular Psychiatry (2012) 17, 1174 – 1179

www.nature.com/mp

PERSPECTIVE

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

S Kapur[1], AG Phillips[2] and TR Insel[3]

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.

Molecular Psychiatry (2012) 17, 1174 – 1179

www.nature.com/mp

PERSPECTIVE

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

S Kapur[1], AG Phillips[2] and TR Insel[3]

nature neuroscience

From reinforcement learning models to psychiatric and neurological disorders

Tiago V Maia[1,2] & Michael J Frank[3,4]

Neuron
Perspective

Great Expectations: Using Whole-Brain Computational Connectomics for Understanding Neuropsychiatric Disorders

Gustavo Deco[1,2,*] and Morten L. Kringelbach[3,4]

Opinion

Cell PRESS

Special Issue: Cognition in Neuropsychiatric Disorders

Computational psychiatry

P. Read Montague[1,2], Raymond J. Dolan[2], Karl J. Friston[2] and Peter Dayan[3]

[1] Virginia Tech Carilion Research Institute and Department of Physics, Virginia Tech, 2 Riverside Circle, Roanoke, VA 24016, USA
[2] Wellcome Trust Centre for Neuroimaging, University College London, 12 Queen Square, London, WC1N 3BG, UK
[3] Gatsby Computational Neuroscience Unit, Alexandra House, 17 Queen Square, London, WC1N 3AR, UK

Neuron
Perspective

Computational Psychiatry

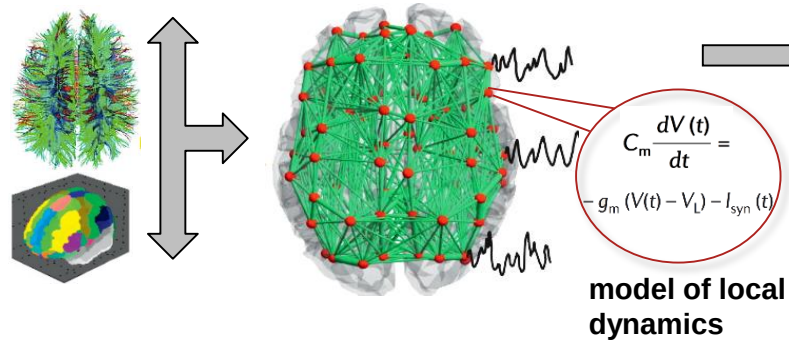
Xiao-Jing Wang[1,2,3,*] and John H. Krystal[3,4,5,6]

Neuron
Review

Translational Perspectives for Computational Neuroimaging

Klaas E. Stephan,[1,2,3,*] Sandra Iglesias,[1] Jakob Heinzle,[1] and Andreea O. Diaconescu[1]

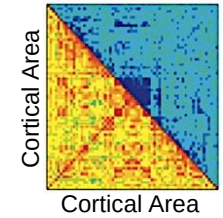
Biophysical network models



model of local dynamics

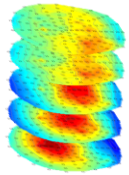
simulated BOLD signal

connectivity matrix



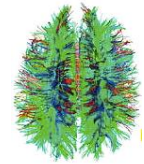
Generative models (DCM)

EEG data



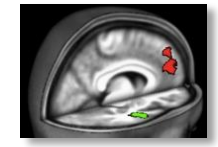
structural priors

DWI



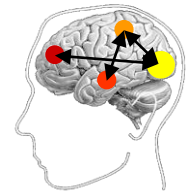
structural priors

fMRI data



forward model:

$$\dot{x} = f(x,u,\theta) + \omega$$
$$y = g(x,\theta) + \varepsilon$$

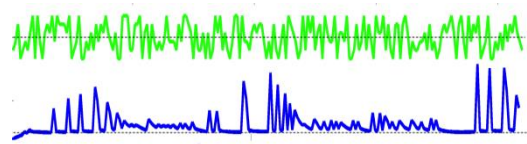


model inversion:

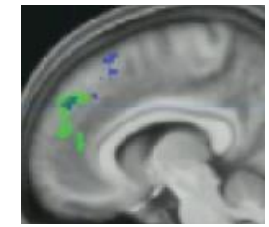
$$p(\theta \mid y) \propto p(y \mid \theta)\, p(\theta)$$

Computational models of neuromodulation

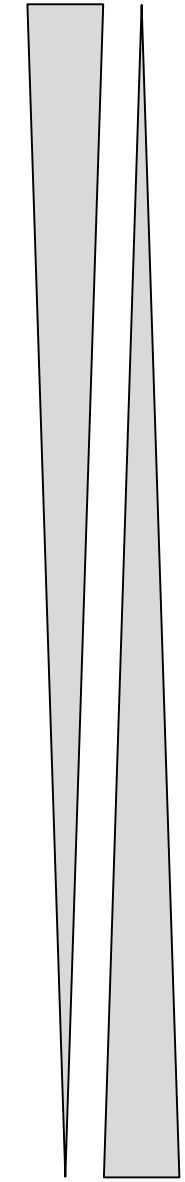
$$\mu = \hat{\mu} + \sigma\, \delta$$



computational states



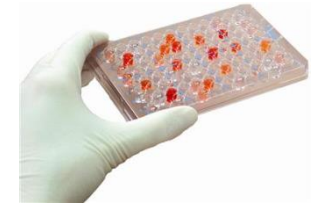
Biological realism

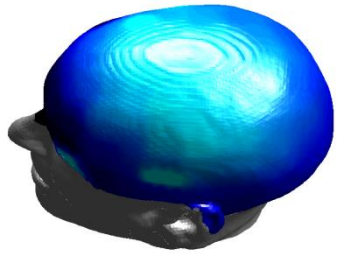


Estimability

Stephan et al. 2015, *Neuron*

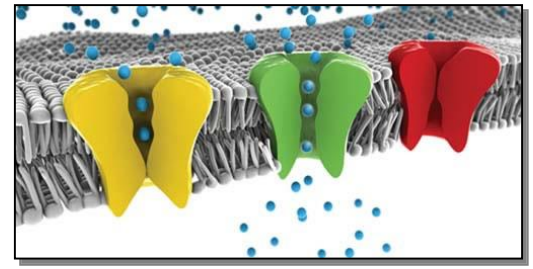
Generative models as "computational assays"

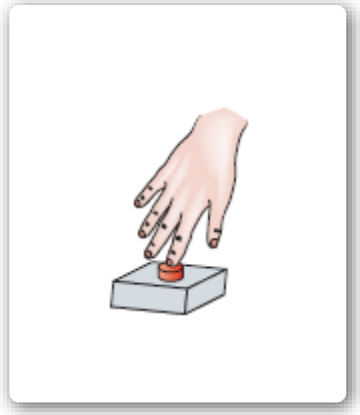




$$p(y \mid \theta, m) \cdot p(\theta \mid m)$$

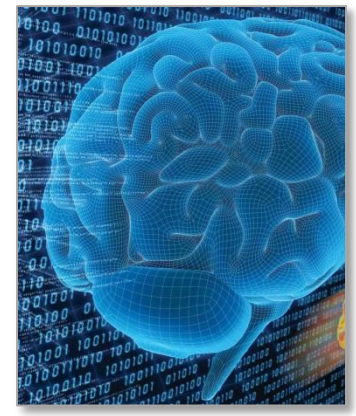
$$p(\theta \mid y, m)$$





$$p(y \mid \theta, m) \cdot p(\theta \mid m)$$

$$p(\theta \mid y, m)$$

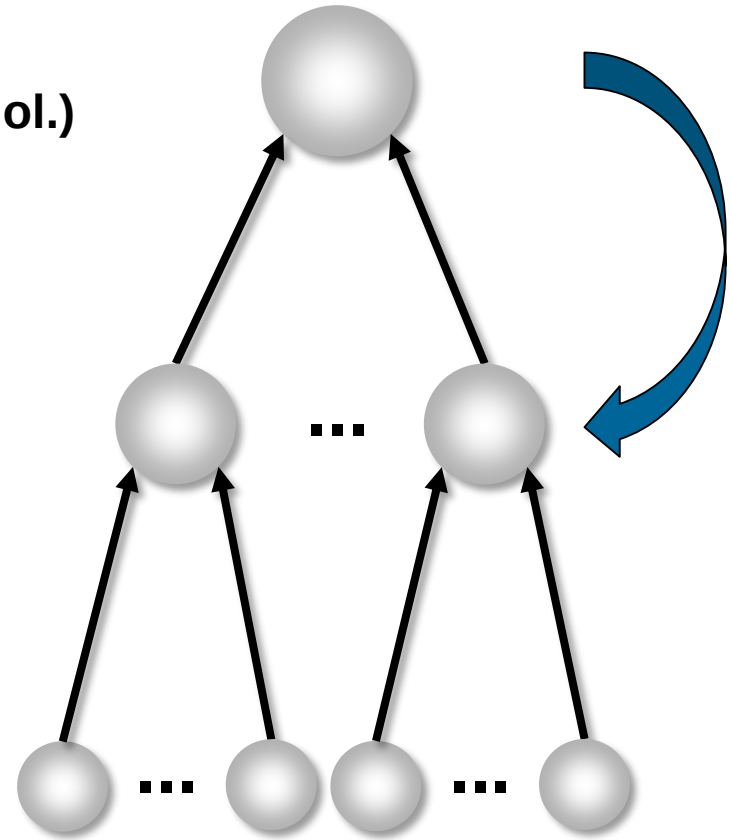


Generative models of disease symptoms

SYMPTOM
(behav. or physiol.)

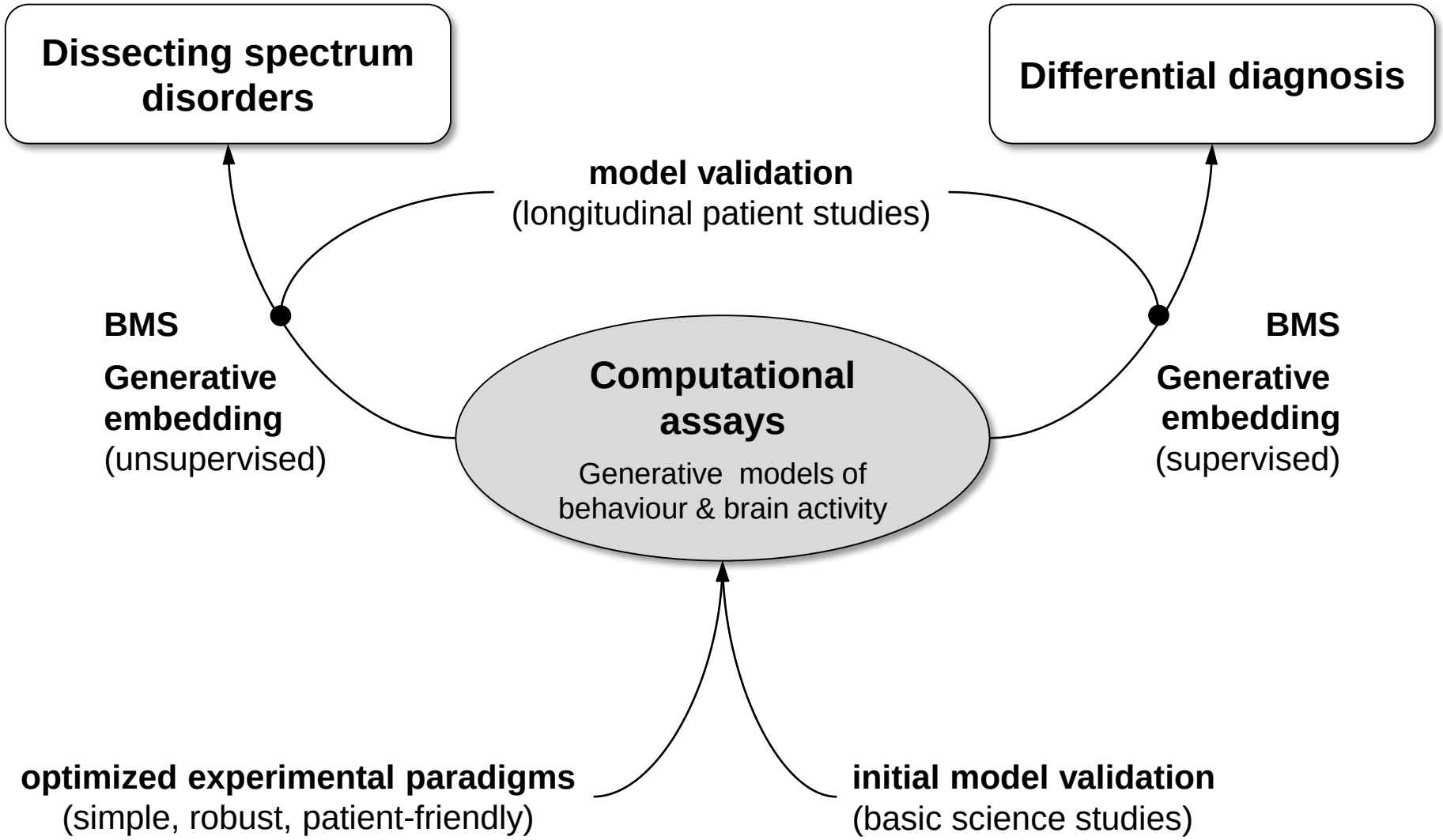
MECHANISMS
(computation, physiology)

CAUSES
(aetiology)



differential diagnosis
via model selection

spectrum dissection
into mechanistically distict subgroups



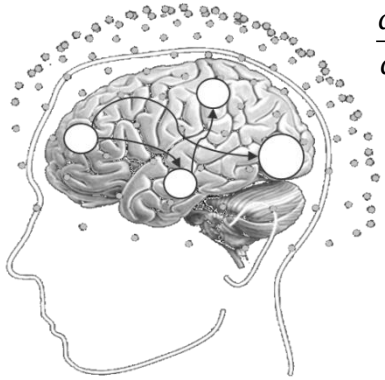
Stephan & Mathys 2014, *Curr. Opin. Neurobiol.*

**“All models are wrong,
but some are useful.”**

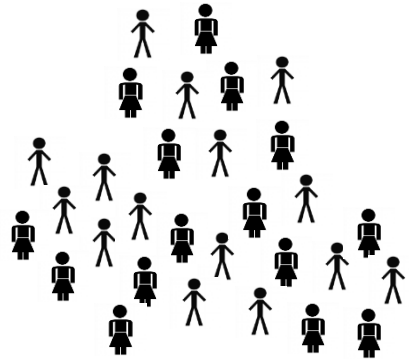
George E.P. Box (1919-2013)

Translational Neuromodeling

❶ Computational assays: Models of disease mechanisms

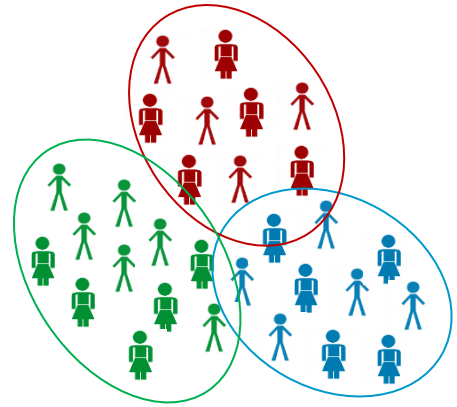


$$\frac{dx}{dt} = f(x,u,\theta) + \omega$$



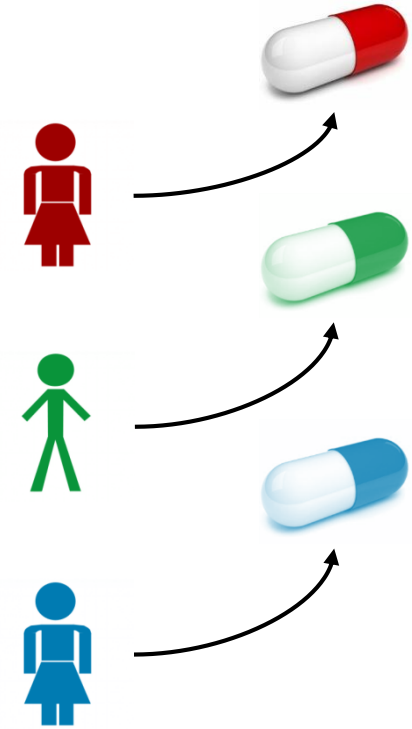
❷ Application to brain activity and behaviour of individual patients

❸ Detecting physiological subgroups (based on inferred mechanisms)



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

❹ Individual treatment prediction



Stephan et al. 2015, *Neuron*

Three major challenges

1. **Highly interdisciplinary: mutual teaching!**
2. **Evolving methodology: open source and benchmarking!**
3. **Validation against clinical problems: new types of organisations!**

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Translational Neuromodeling Unit

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

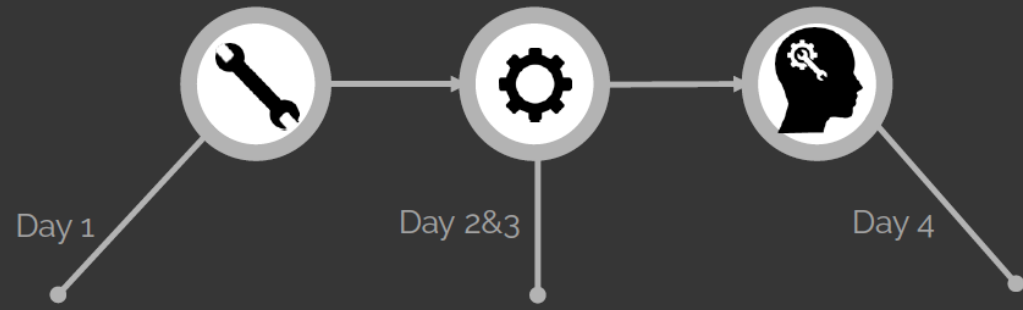
Development of mathematical models & software

Multimodal measurements

Research clinic for patient studies

Longitudinal studies for model validation & translation

COURSESTRUCTURE



Basics:
selecting between models & inferring parameters

- Variational Bayes
- MCMC
- Bayesian Model Selection
- Bayesian Model Averaging

Models:
behavior & physiology

- Hierarchical Gaussian Filter
- Markov Models
- Drift Diffusion Model
- Free Energy
- Predictive Coding
- Reinforcement Learning
- DCM for Behavior
- DCM for EEG
- DCM for fMRI

Applications:
models in psychiatry and neuroeconomics

Contents

- **Basic computational techniques**
  - approximate inference: VB, MCMC
  - model comparison
- **Generative models of behaviour**
  - hierarchical Bayesian models
  - drift diffusion models
  - predictive coding & active inference
  - Markov decision processes
  - reinforcement learning
- **Generative models of physiology**
  - DCM for fMRI
  - DCM for EEG
  - behavioural DCMs

This course

- arose from our previous local CP courses

- key features
  - theoretical lectures & practical demonstrations coupled
  - open source software only
  - computation in a broad sense: models of physiology and behaviour
  - broad scope – many external presenters

- an experiment

Welcome & Thank You