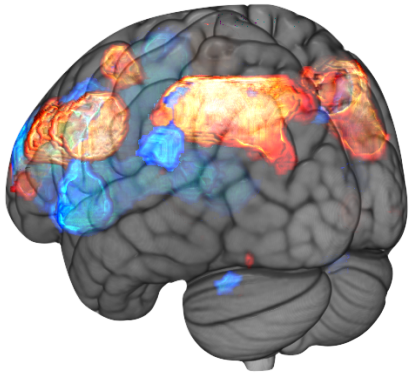
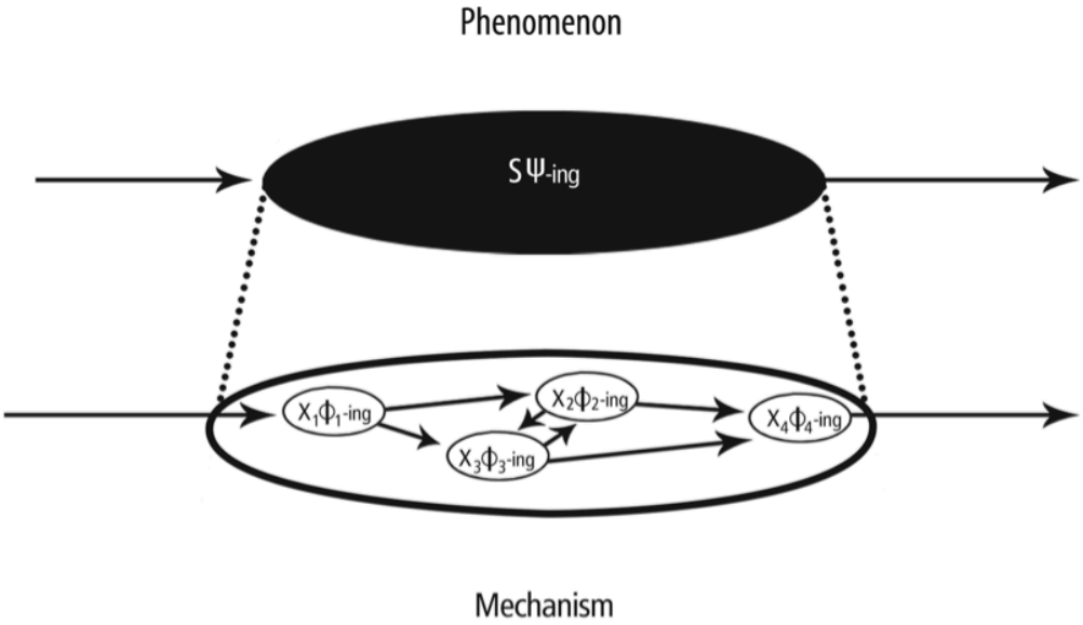
Towards a neurobiologically-derived cognitive taxonomy



Romy Lorenz

Sir Henry Wellcome Postdoctoral Fellow
University of Cambridge, Stanford University & Max Planck Institute for Human Cognitive and Brain Sciences

How does neural tissue give rise to the mind?

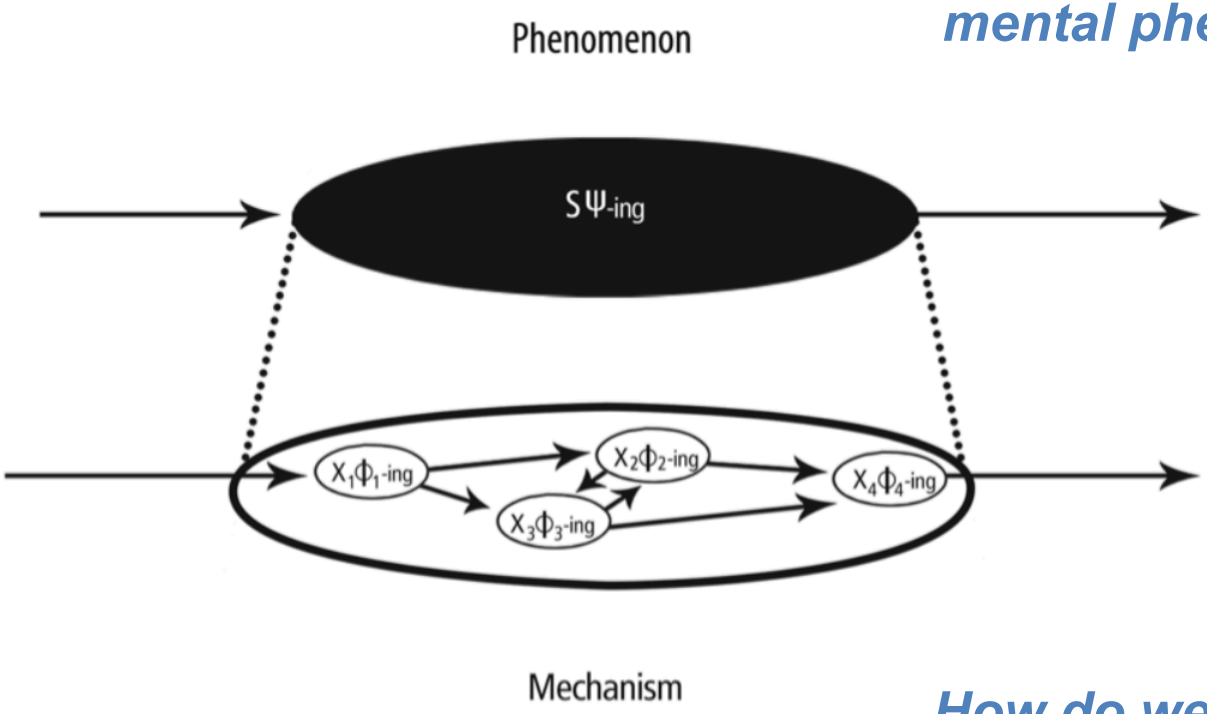


- A mechanisms underlies a **mental phenomenon** (i.e., system S is engaged in behavior Y)
- Behavior of the system S as a whole can be broken down into organized **causal interactions** among the activities of the **parts.**

Craver & Tabery 2017

How does neural tissue give rise to the mind?

How do we define mental phenomena?

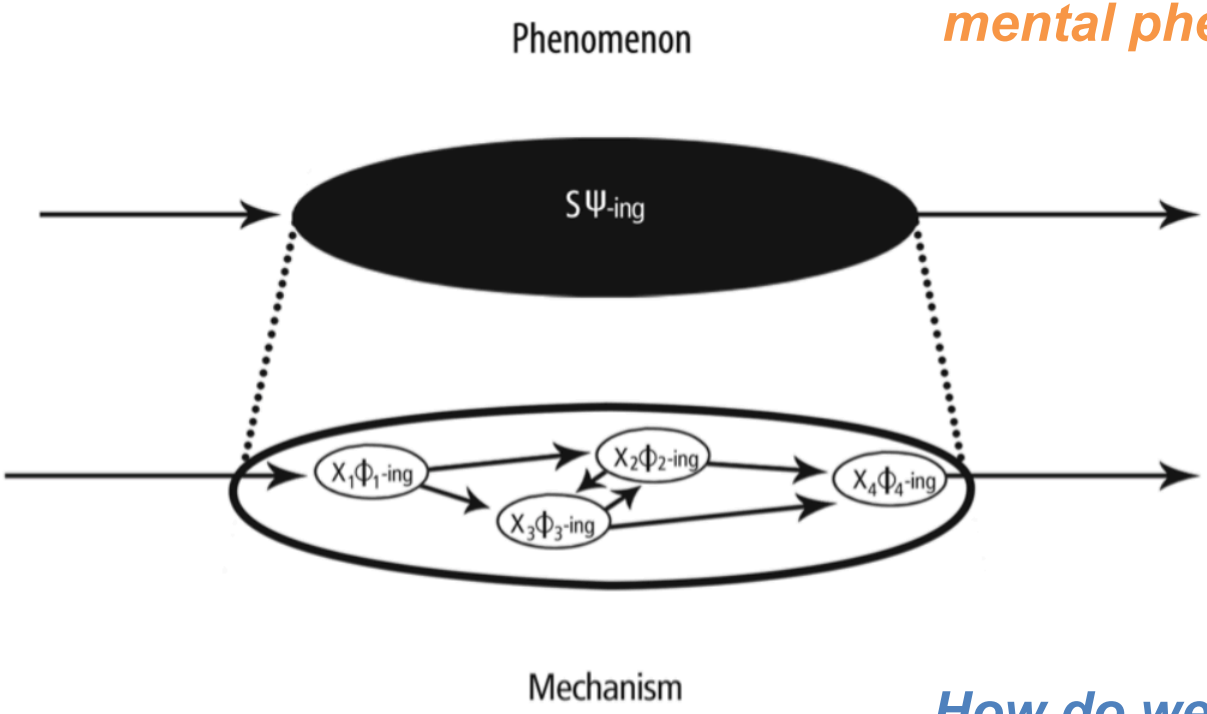


How do we draw causal inference?

How do we define the components (neurons, regions, networks)?

How does neural tissue give rise to the mind?

How do we define mental phenomena?



How do we draw causal inference?

How do we define the components (neurons, regions, networks)?

Overview

1. Motivation
2. Neuroadaptive Bayesian optimization
   - 2.1 Human brain mapping
   - 2.2 Non-invasive brain stimulation
   - 2.3 Biomarker discovery
3. Implications for study pre-registration
4. What next?

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Aims of cognitive neuroscience

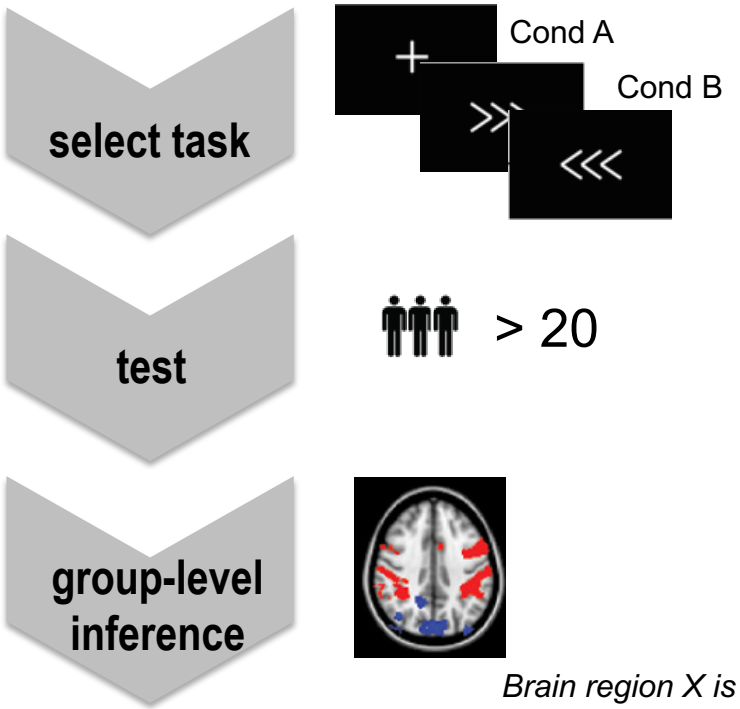
Research questions

What are the fundamental aspects of cognition?

What are the fundamental roles of distinct networks in the brain?

How can cognitive processes be modulated or enhanced?

Standard approach



broad ⟷ narrow

Aims of cognitive neuroscience

Lorenz et al. *TiCS* 2017

Human-brain mapping

- Over-specified inferences about functional-anatomical mappings
  - right IFG Hampshire & Sharp *TiCS* 2015
  - dACC *Wager et al. PNAS 2016*

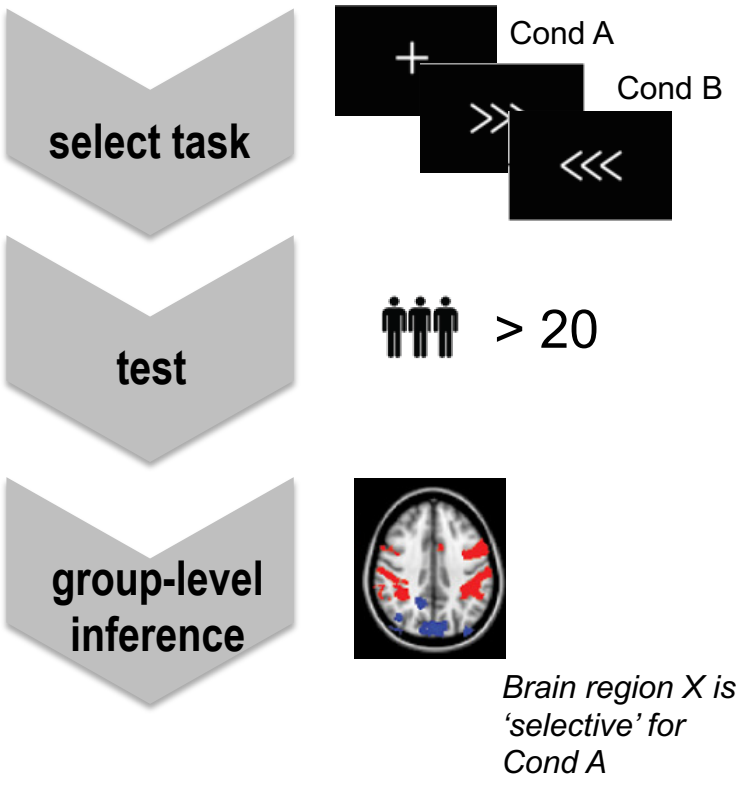
Biomarker discovery

- Which exact task conditions will be sensitive to certain patient group?
  Sprooten et al. *Human Brain Mapping* 2017

Non-invasive brain stimulation

- Many *free* parameters, confusion surrounding efficacy

Standard approach



broad ⟷ narrow

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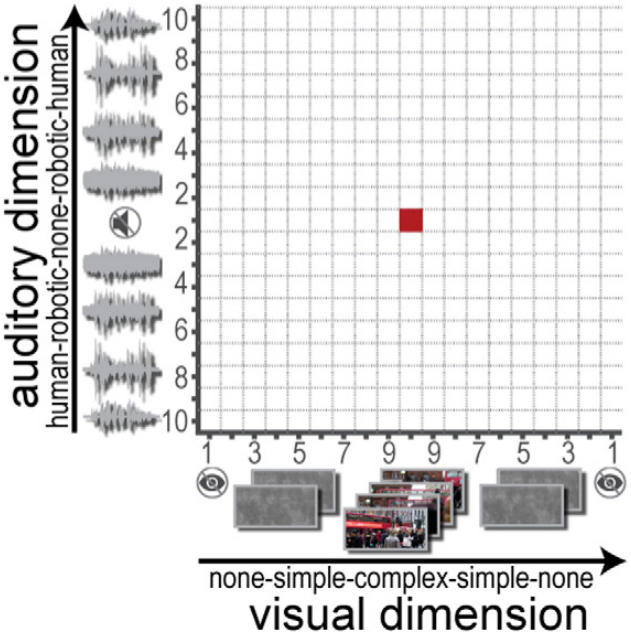
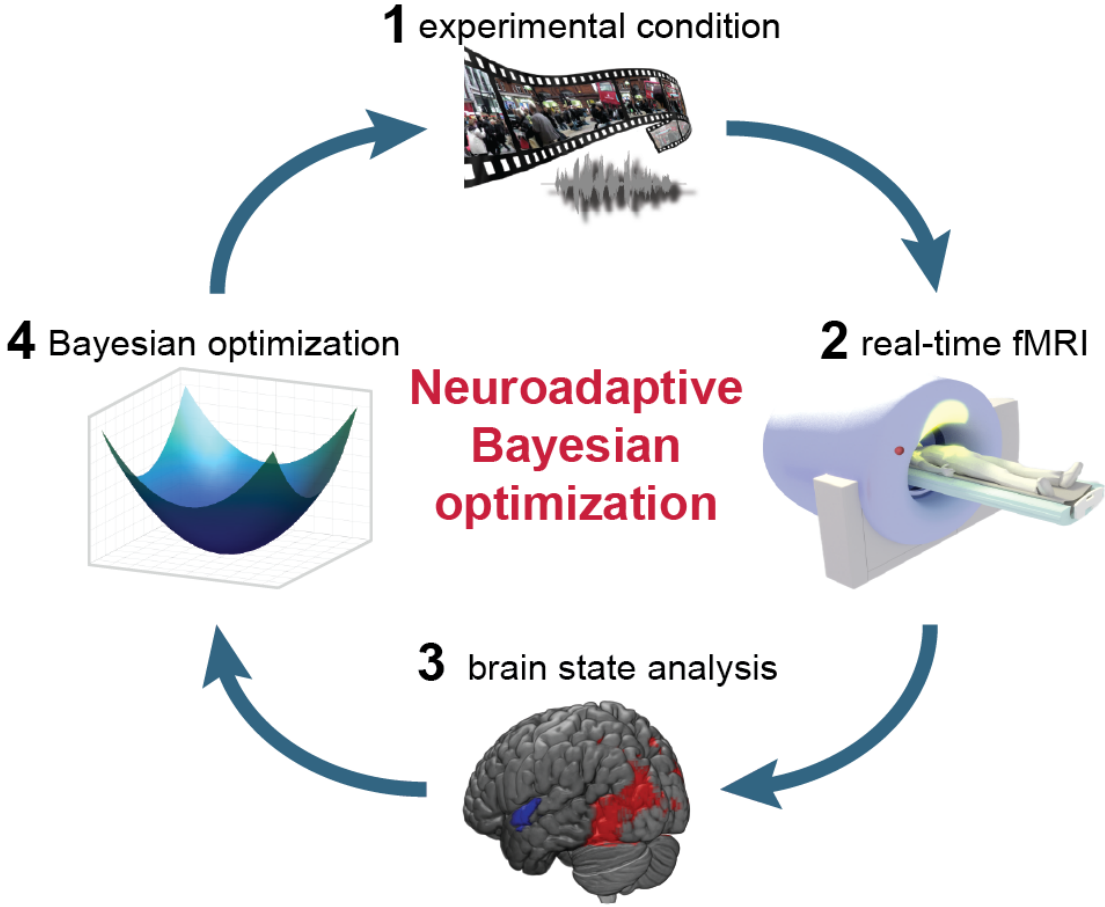
The framework



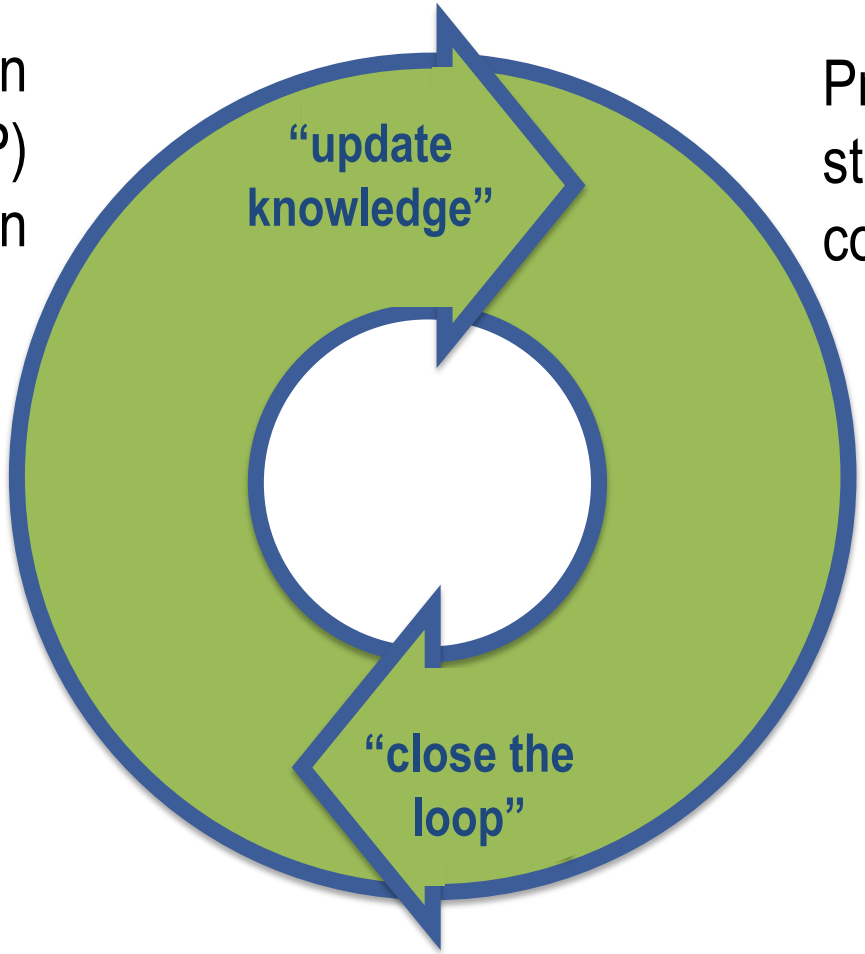
Start with **broad** experiment space and iteratively find optimal experimental condition



Lorenz et al. *NeuroImage* 2016

Bayesian optimization

Gaussian process (GP) regression

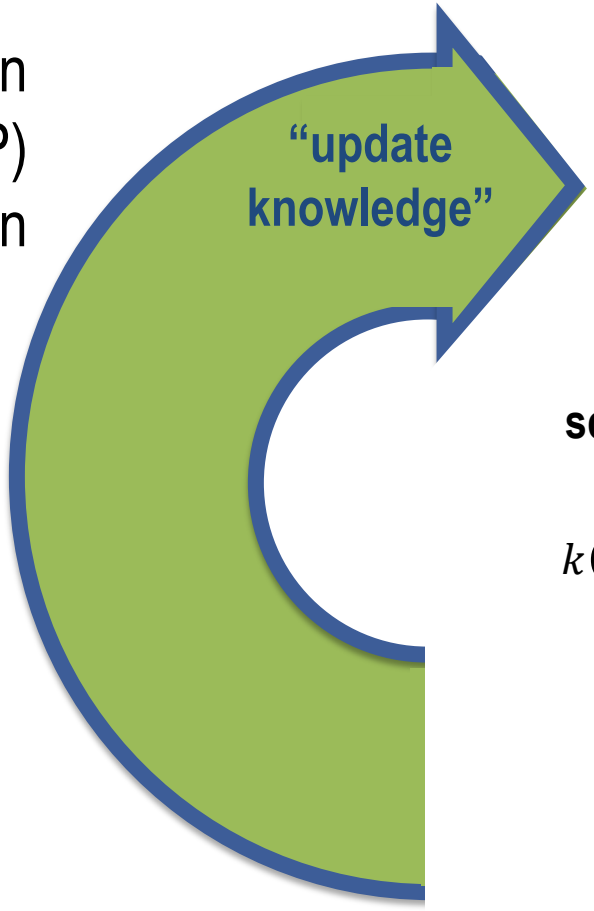


Propose new stimuli combination

Rasmussen & Williams 2006
Brochu et al. *arXiv* 2010

Bayesian optimization

Gaussian process (GP) regression



choice of covariance function

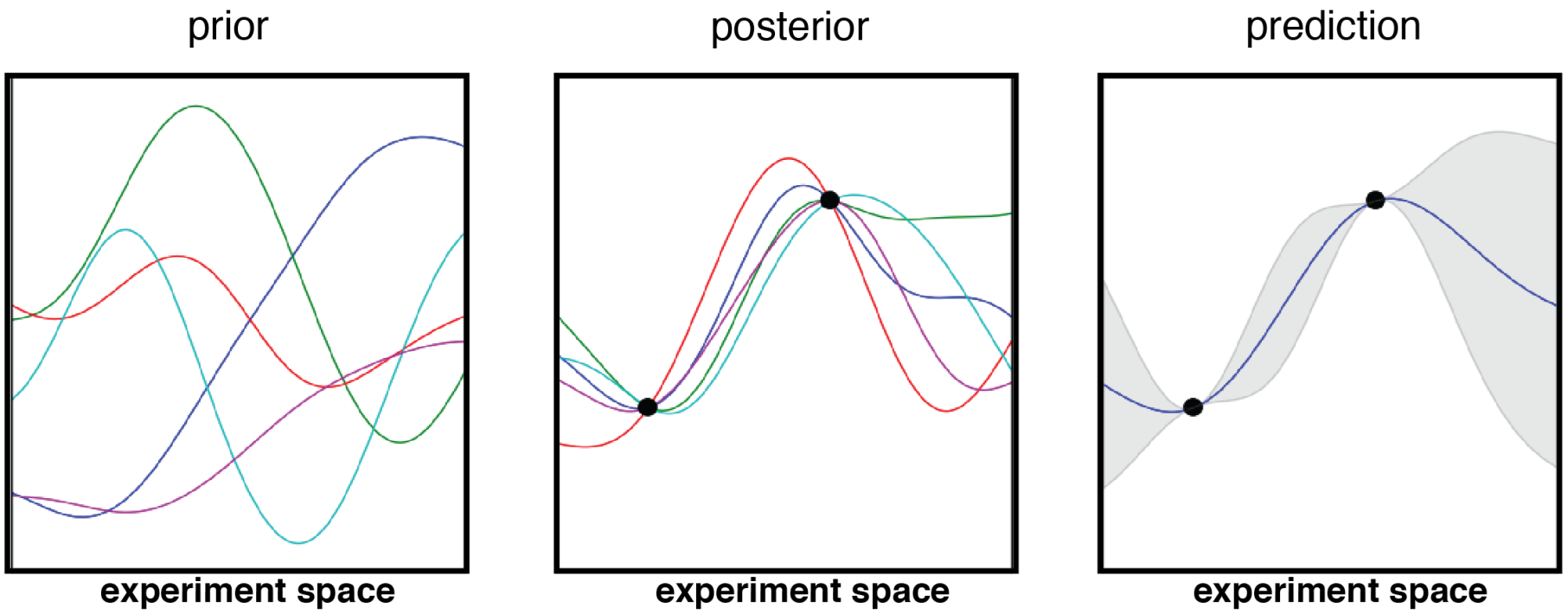
squared exponential kernel:

$$k(x,y) = \sigma^2 \exp\left\{-\frac{(x-y)^2}{2\,l^2}\right\}$$

$x, y \in \mathbb{R}^2$	audio-visual stimulus
$\sigma^2 \in \mathbb{R}$	variance of covariance kernel
$l \in \mathbb{R}$	length of covariance kernel

Rasmussen & Williams 2006
Brochu et al. *arXiv* 2010

GP regression (1D – example)



Bayesian optimization

Expected improvement acquisition function:

$$EI(x) = (m(x) - f_{max})\mathrm{q}(z) + var(x)p(z)$$

$m(x)$: predicted mean

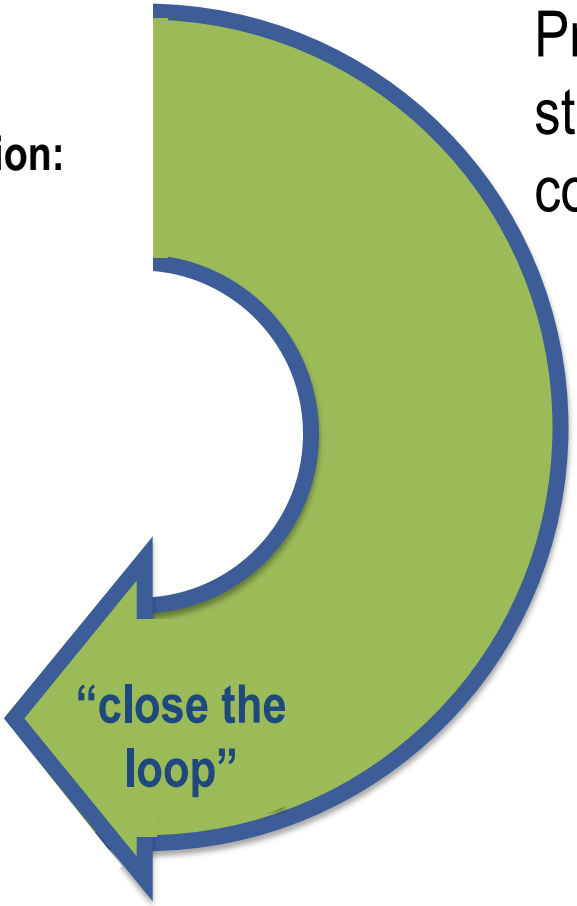
$var(x)$: predicted variance

f_{max}: maximum predicted value

$q()$: cumulative distribution function

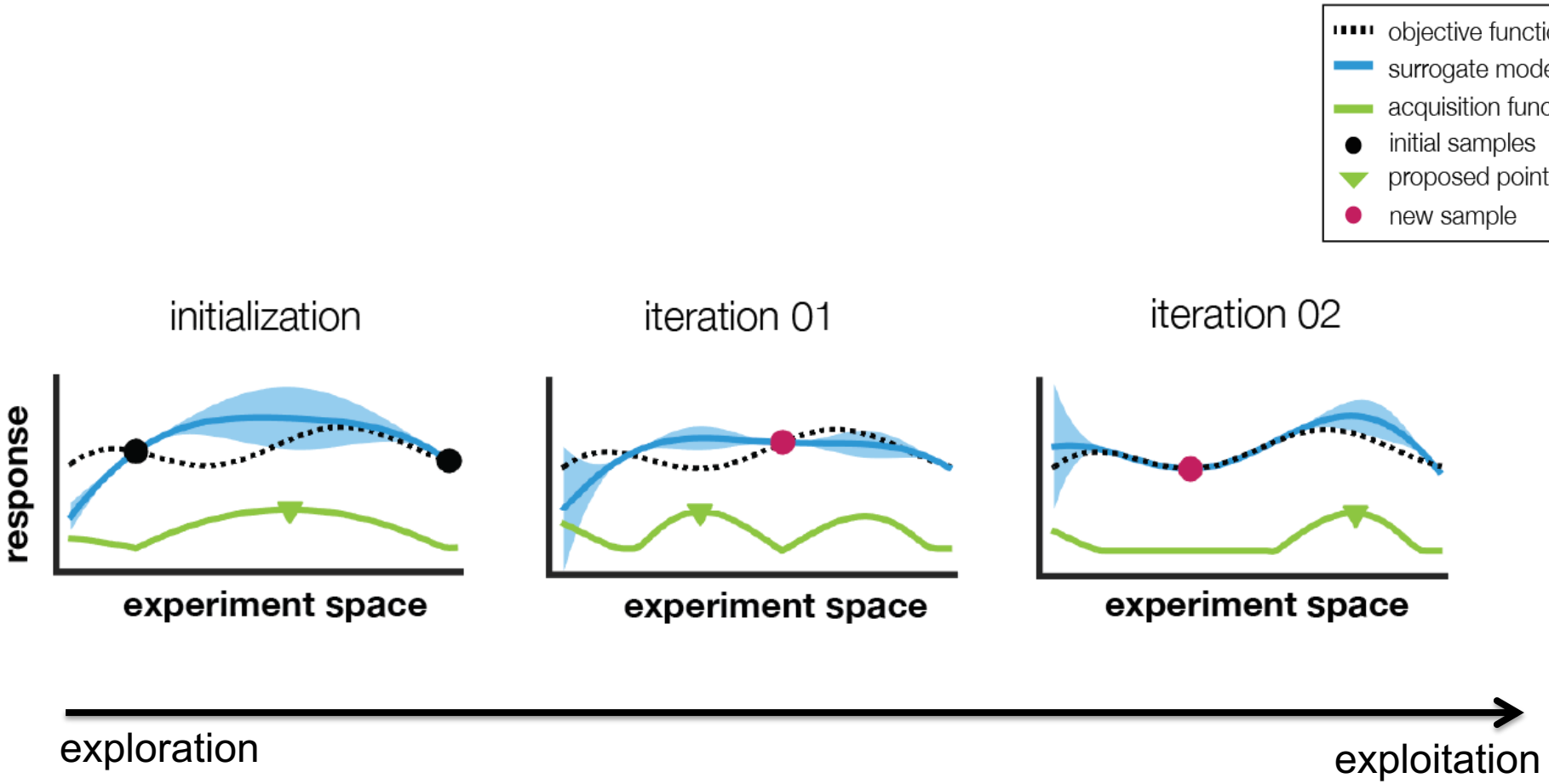
$p()$: probability density function

$$z = \frac{m(x) - f_{max}}{var(x)}$$



Rasmussen & Williams 2006
Brochu et al. *arXiv* 2010

Bayesian optimization (1D – example)



Lorenz et al. *TiCS* 2017

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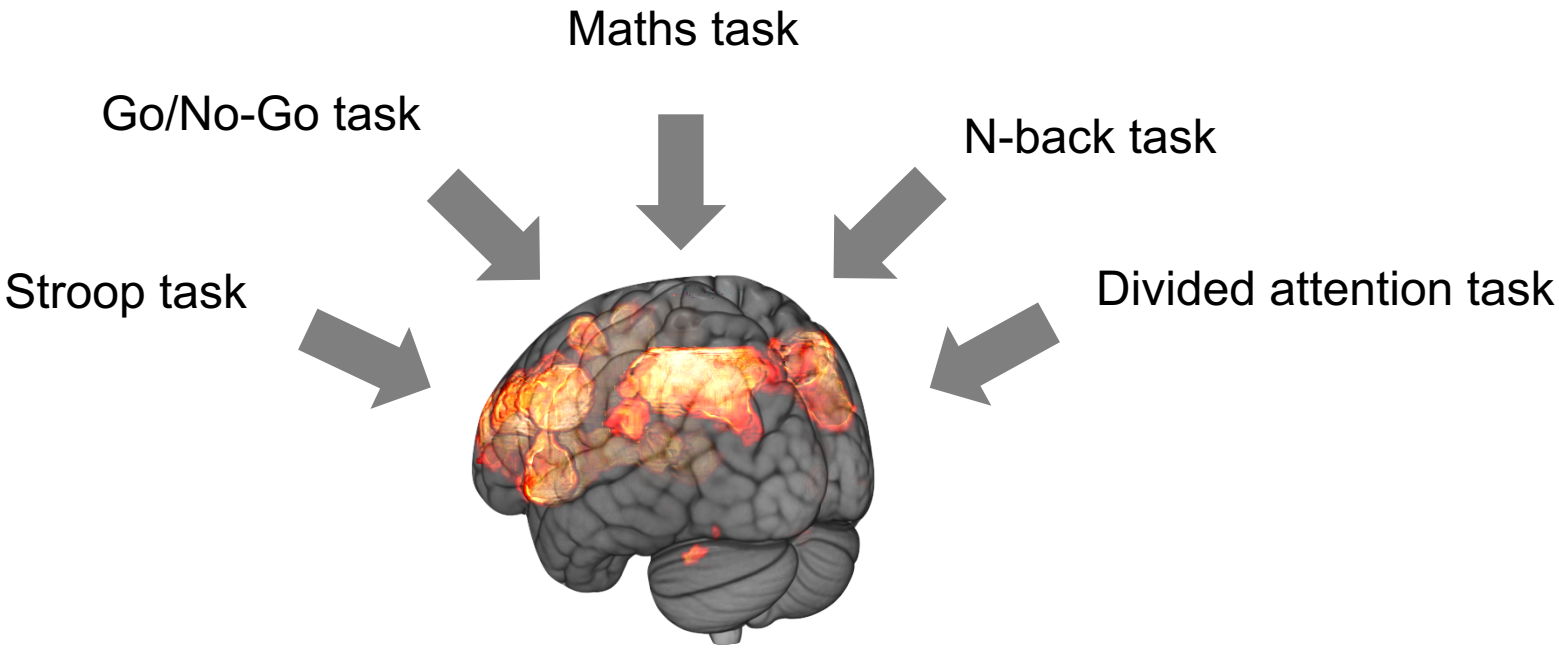
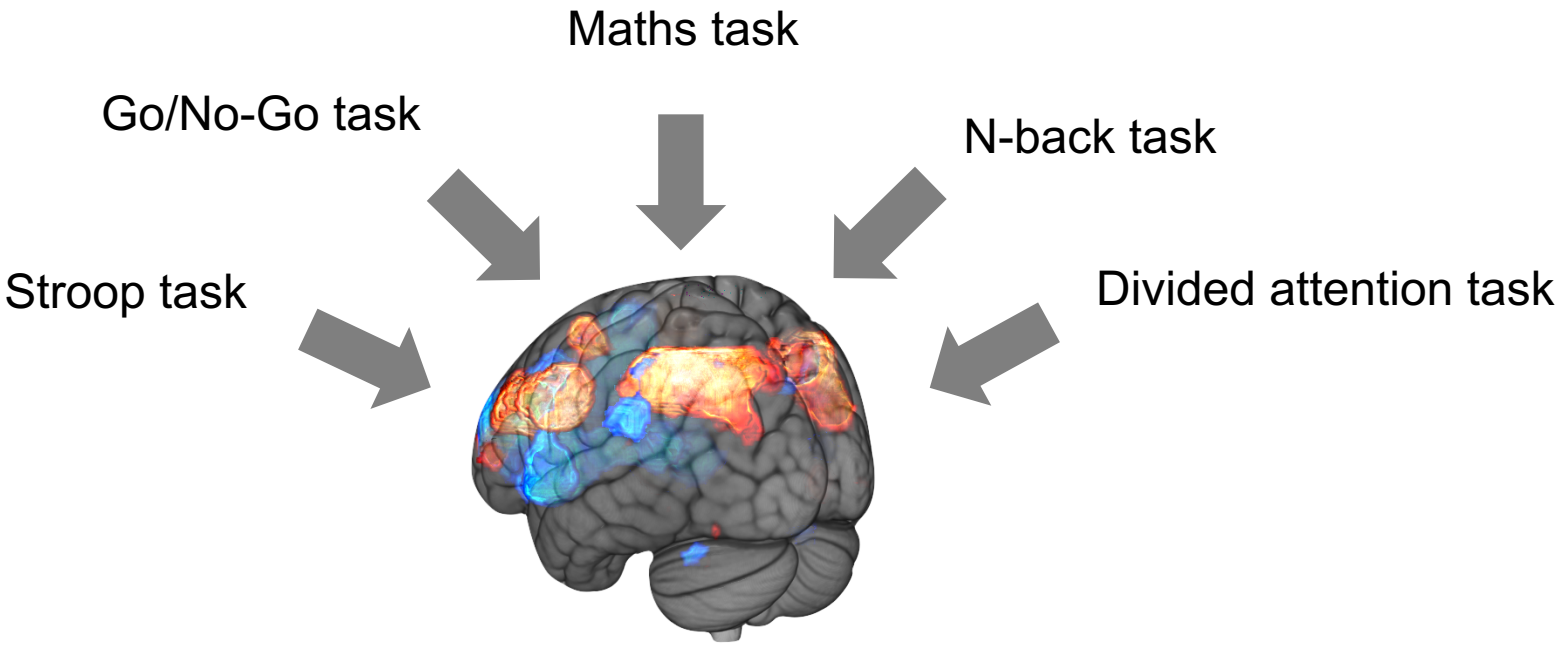
Many-to-many mapping problem



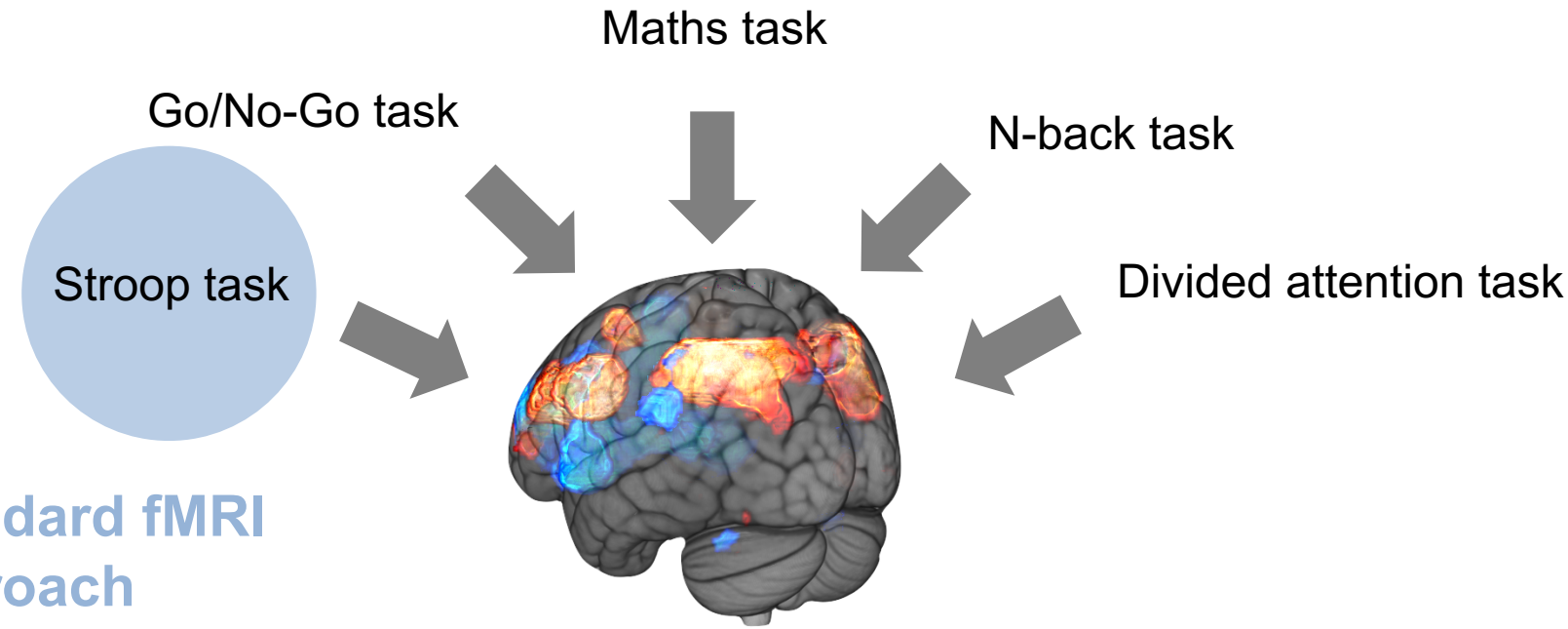
Duncan & Owen *TiNS* 2000
Fedorenko et al. *PNAS* 2013

Many-to-many mapping problem



Hampshire et al. *Neuron* 2012

Many-to-many mapping problem

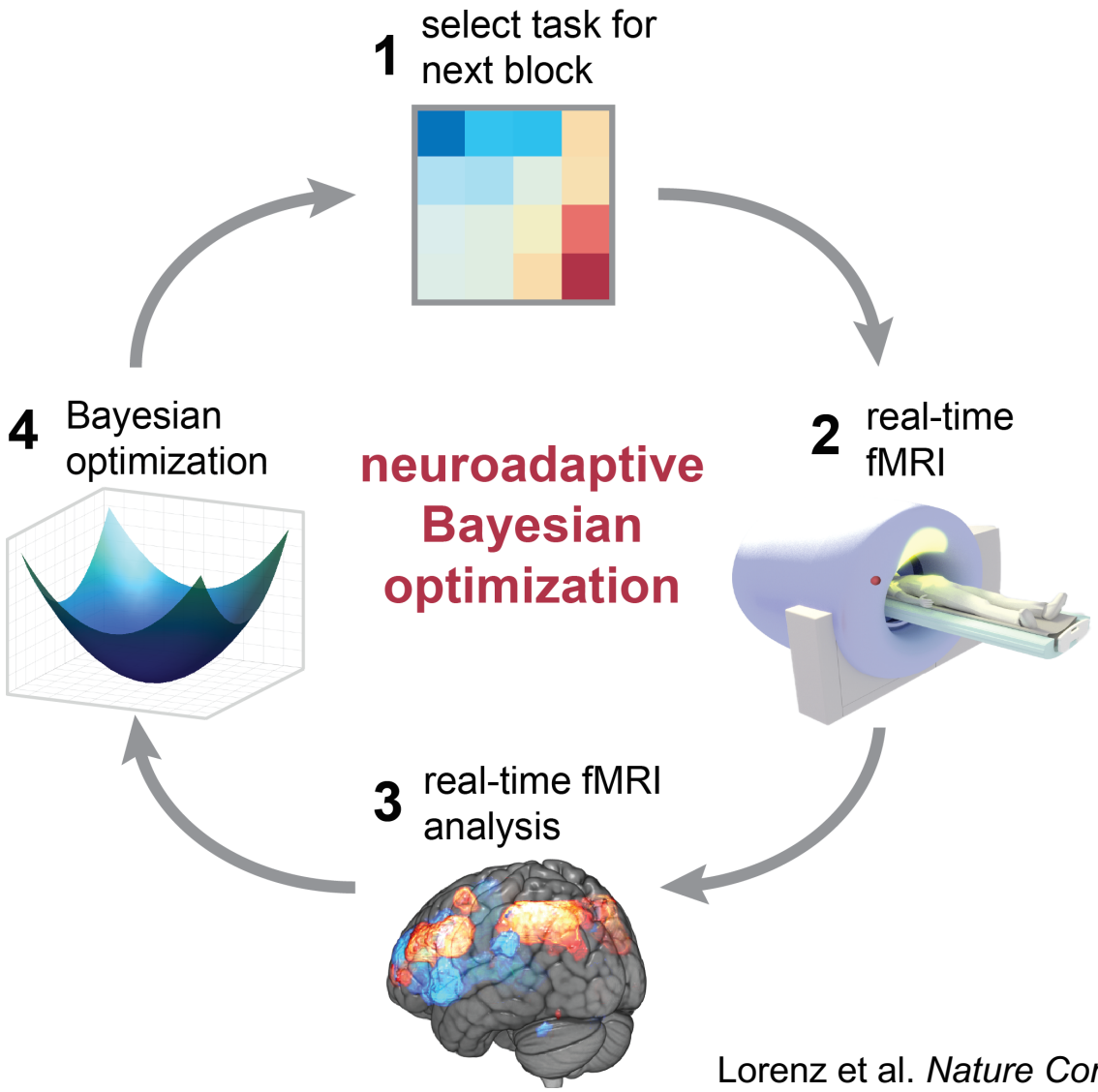


Standard fMRI approach

- **Limited generalizability**
- **Limited reproducibility**

Lorenz et al. *TiCS* 2017
Westfall et al. *Wellcome Open Research* 2017

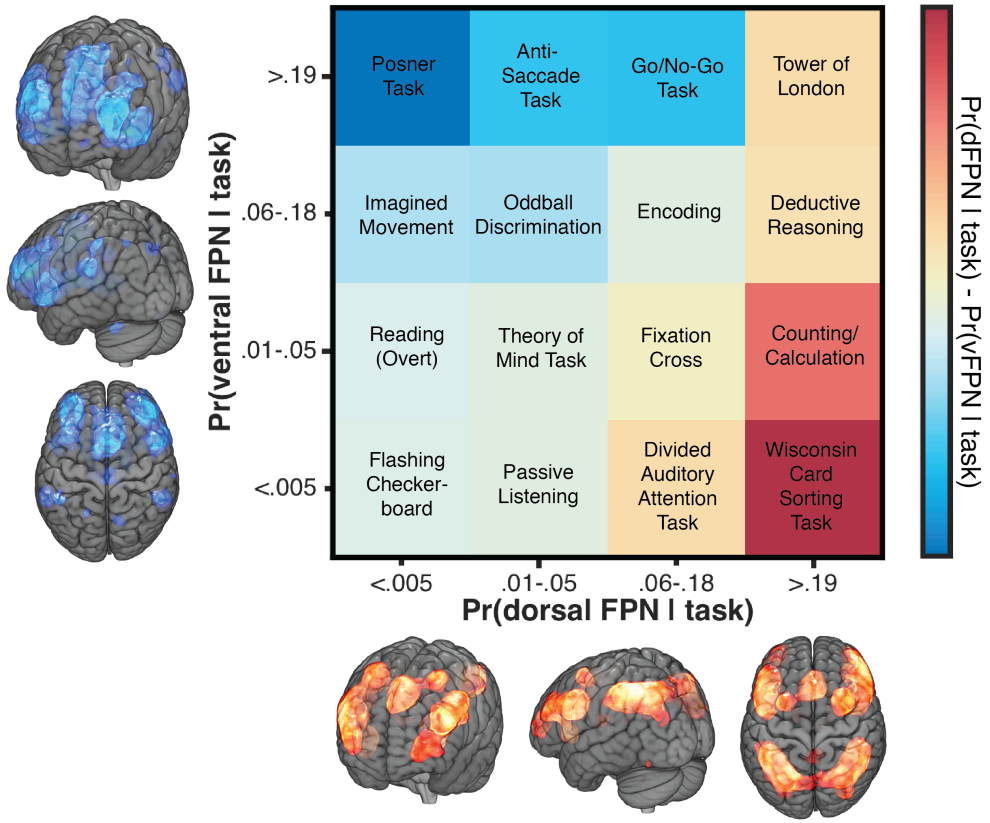
Searching across cognitive tasks



Lorenz et al. *Nature Communications* 2018

Task space based on meta-analysis

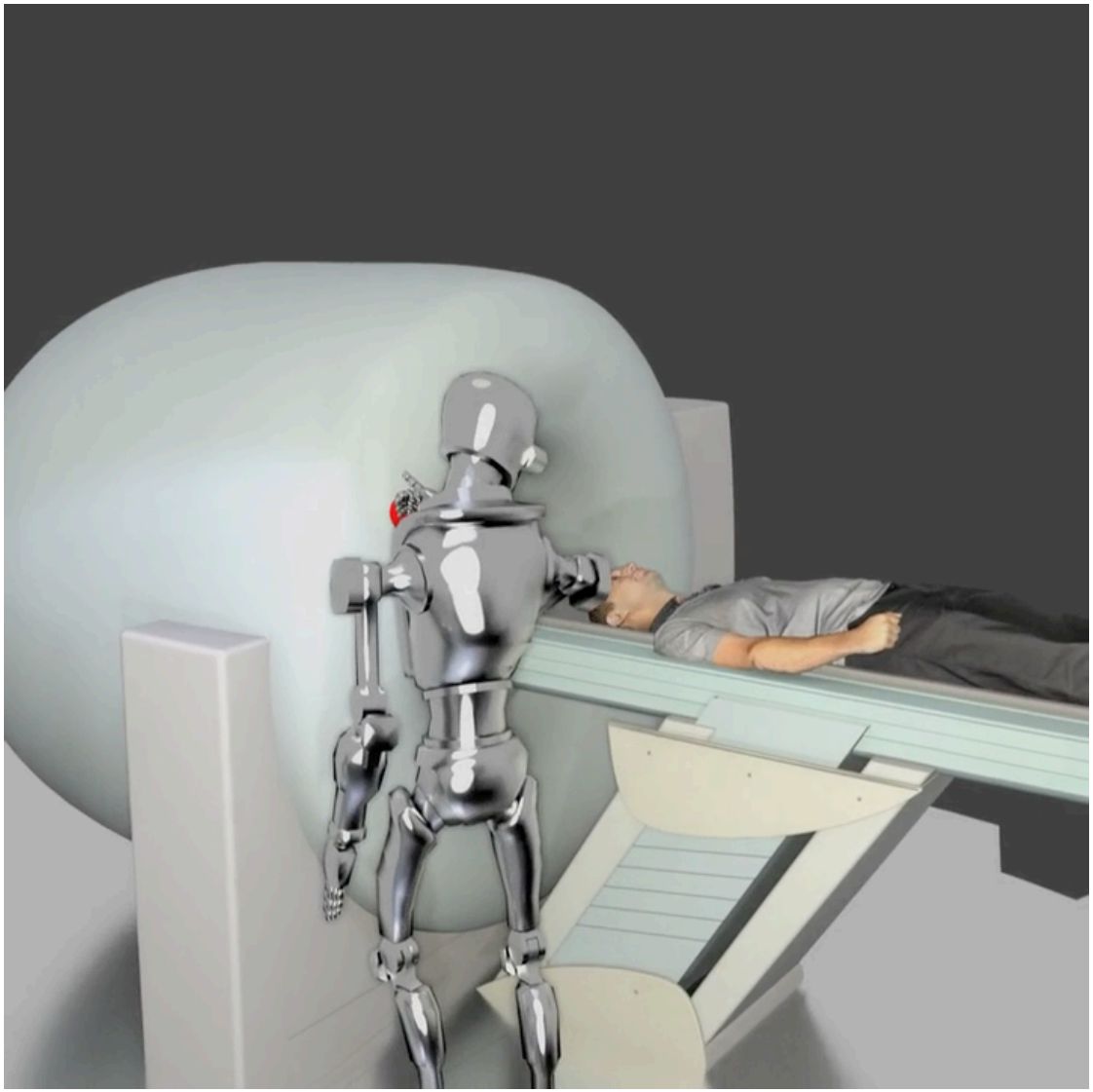
= 10



FPN = frontoparietal network

maps & space from
Yeo et al. *Cerebral Cortex* 2015

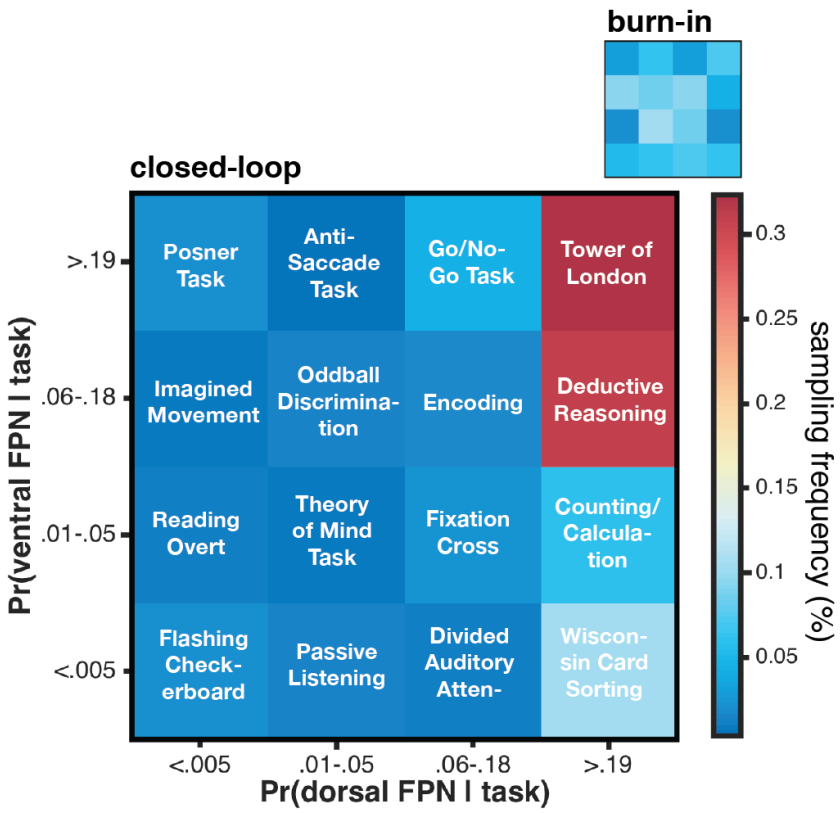
Searching across cognitive tasks

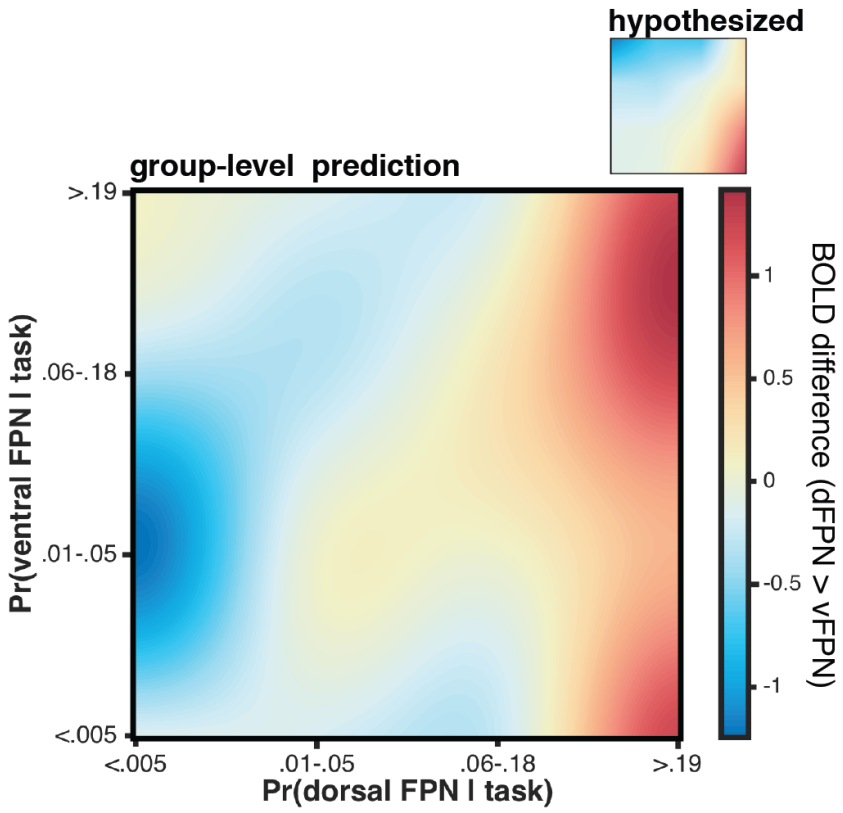


Find optimal tasks

Study 1 | Study 2 | Study 3

= 10

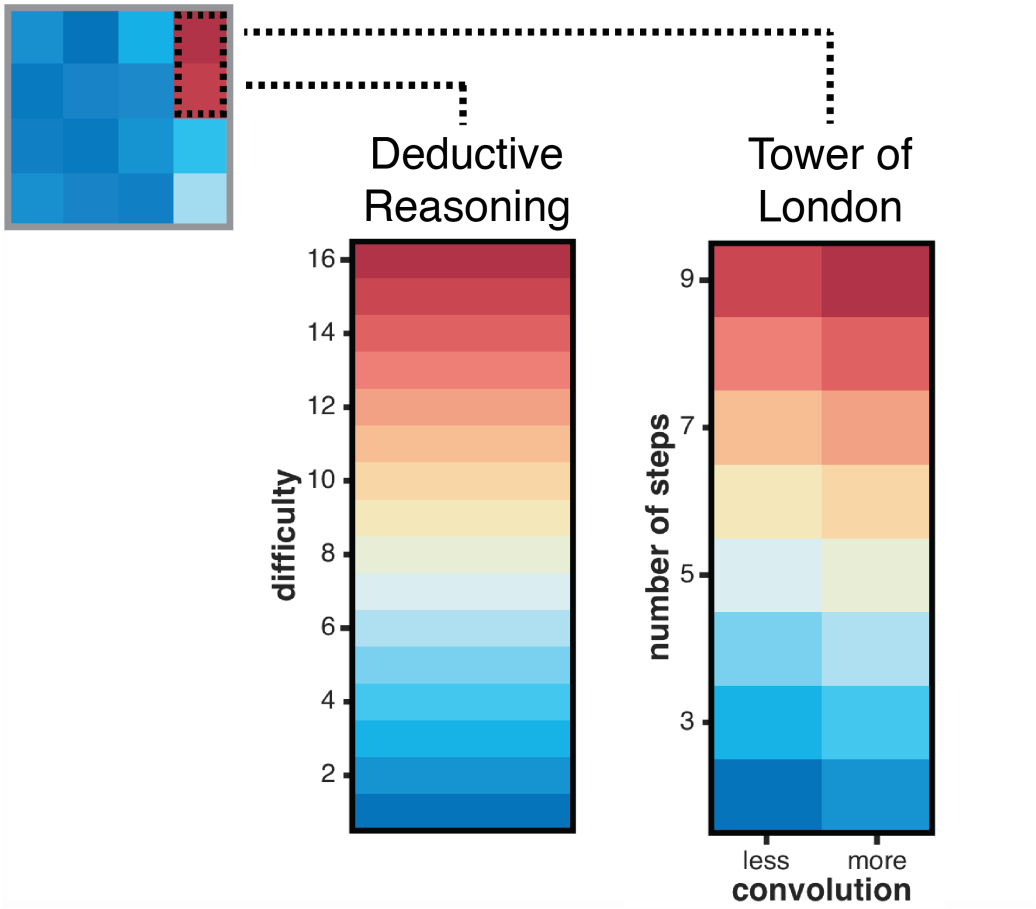




Tower of London & Deductive Reasoning tasks maximally dissociate FPNs

Zoom in task space and fine-tune tasks

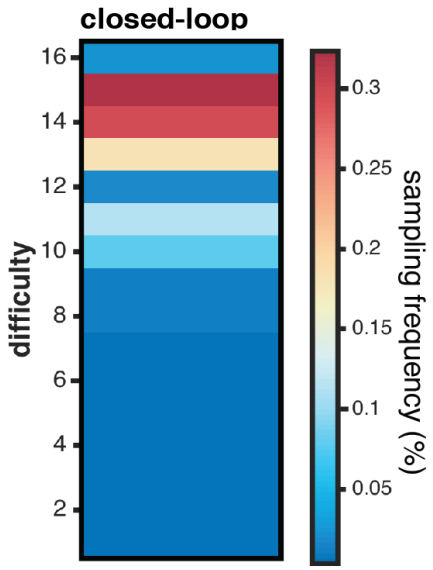
Study 1 | Study 2 | Study 3

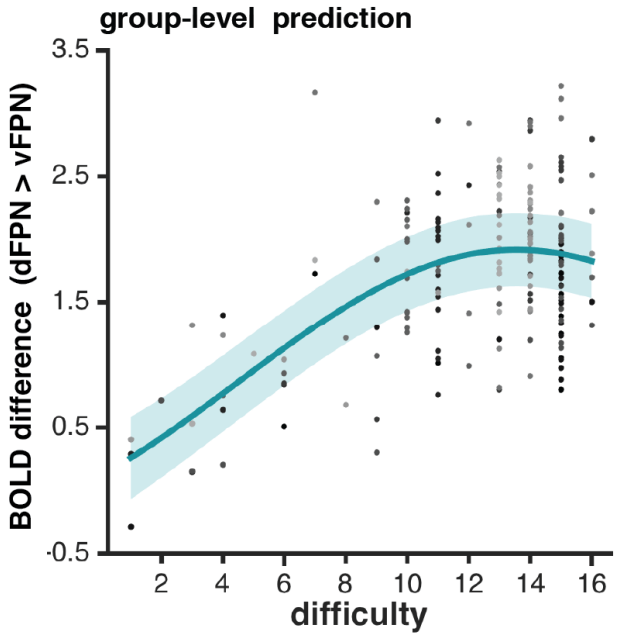


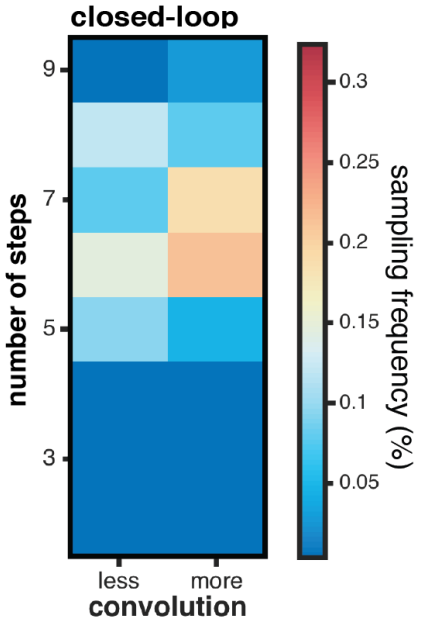
Find optimal task parameters

Study 1 | Study 2 | Study 3

= 10







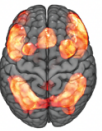
Deductive Reasoning

Tower of London

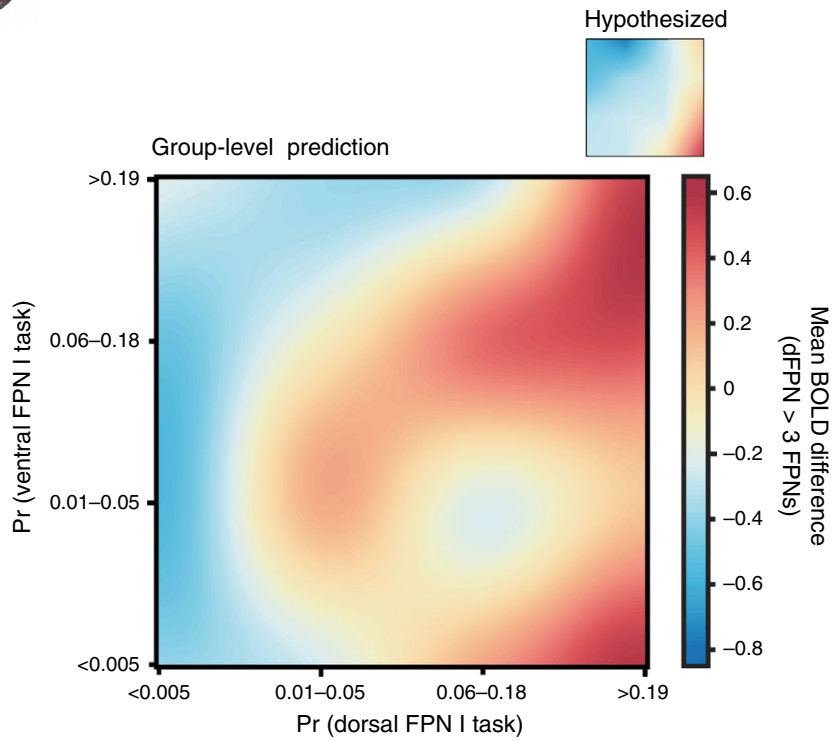
Find *unique* functional activation profile

Study 1 → Study 2 → **Study 3**

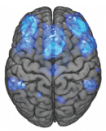
= 10



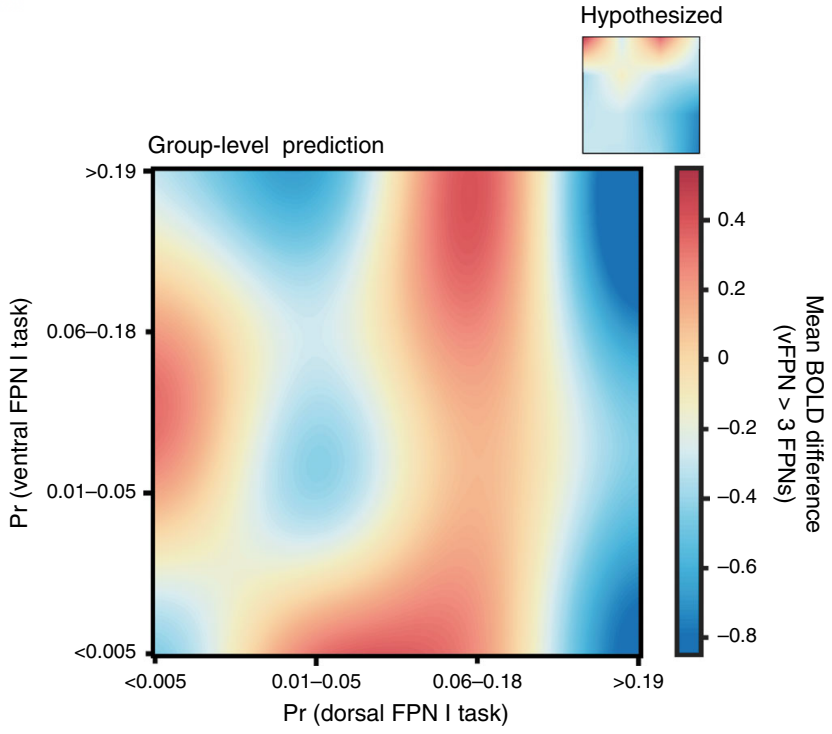
dorsal FPN > 3 other FPNs



Tower of London, Deductive Reasoning, Encoding & Wisconsin Card Sorting



ventral FPN > 3 other FPNs



Go/No-Go, Divided Auditory Attention, Imagined Movement, Passive Listening & Overt Reading

Results

- Results deviate from previous meta-analyses and hypothesized functional labels for these FPNs
- Cognitive tasks identified for each network do not share a prima facie intuitive underlying cognitive label/process
- High intra- and inter-subject reliability (subject-level results)
- Starting point for neurobiologically-derived cognitive taxonomy

Lorenz et al. *Nature Communications* 2018

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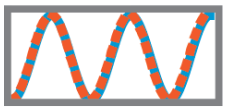
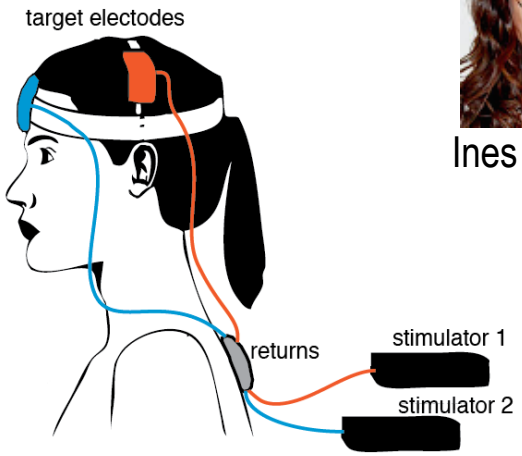
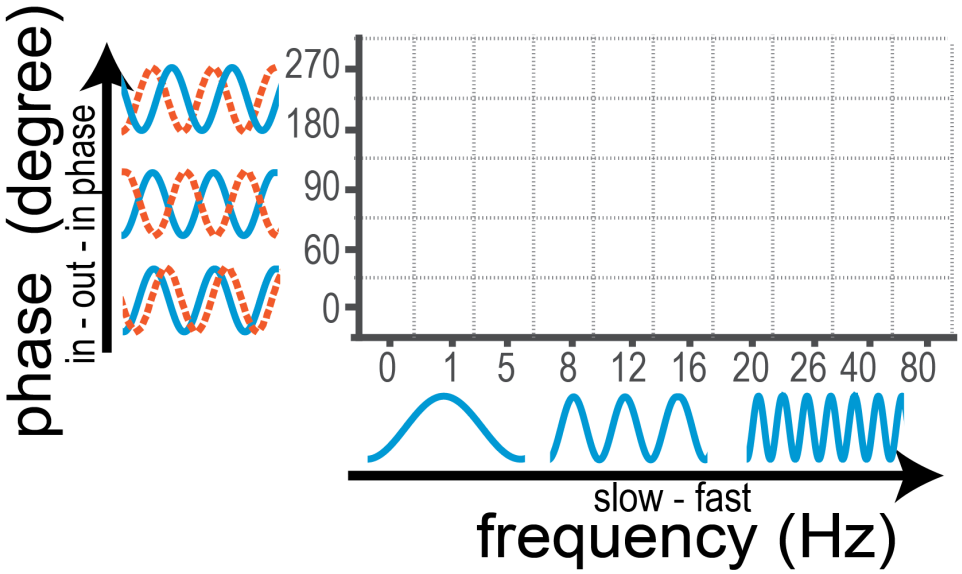
Transcranial alternating current stimulation (tACS)

- **Status Quo**
  - Ad hoc definition of frequency and phase
  - Cohort testing



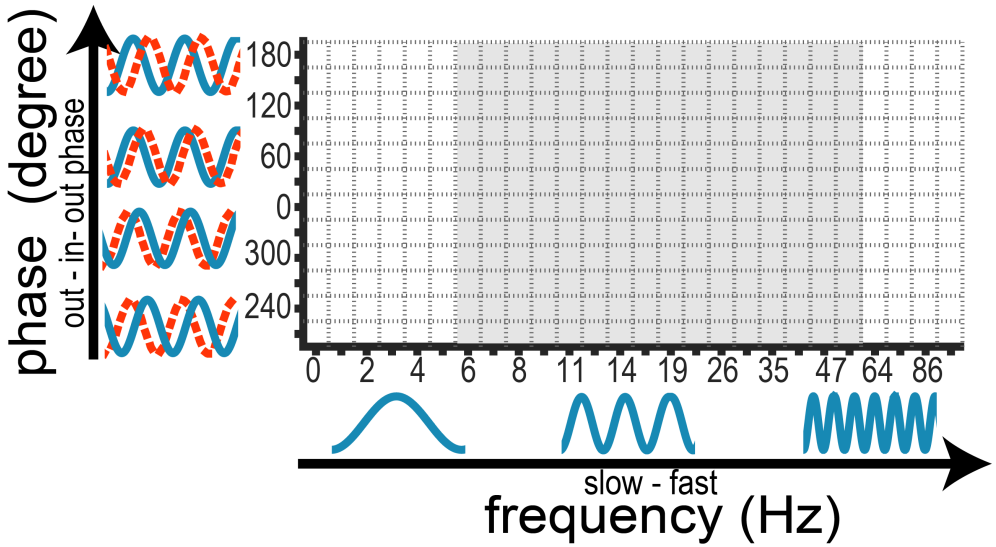


Ines Violante



- **Limitation**
  1. How to choose frequency and phase?
  2. Stimulation parameters may vary due to anatomy or pathology

Proof-of-principle



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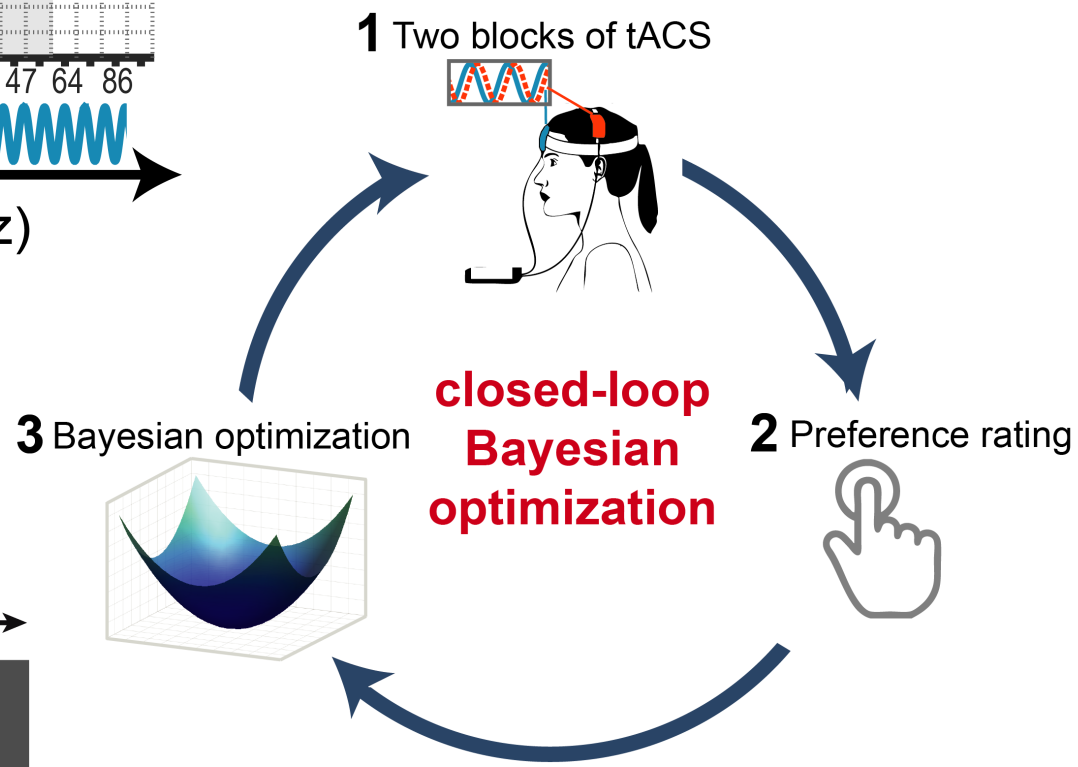
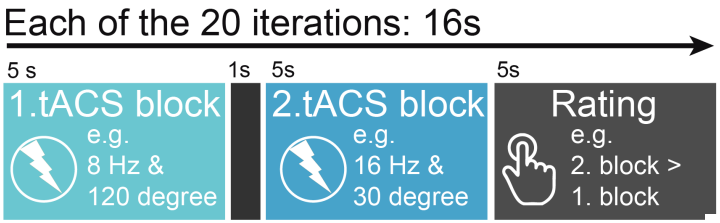
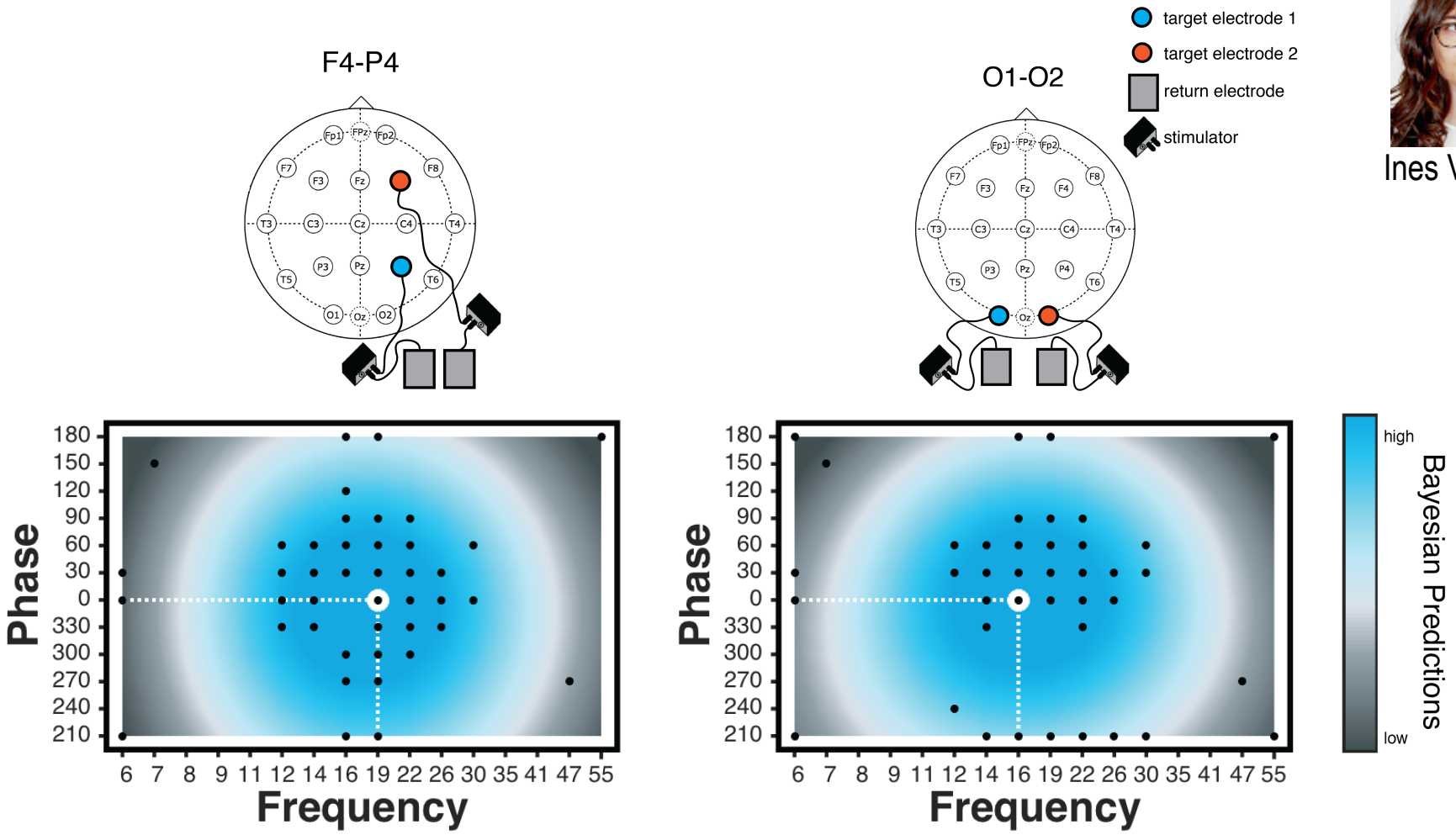




Lorenz et al. *Brain Stimulation* 2019

Proof-of-principle

Ines Violante



Lorenz et al. *Brain Stimulation* 2019

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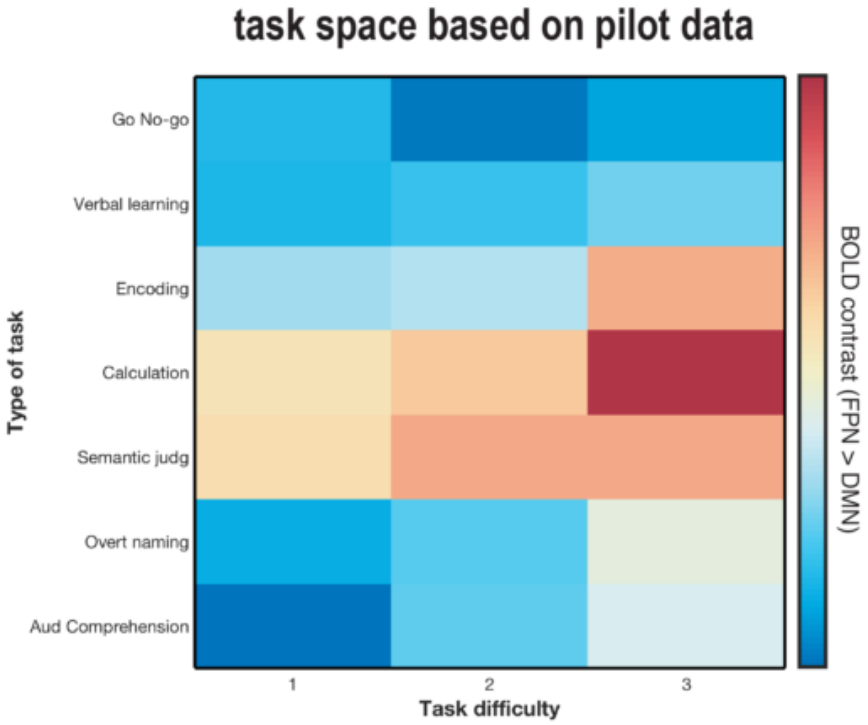
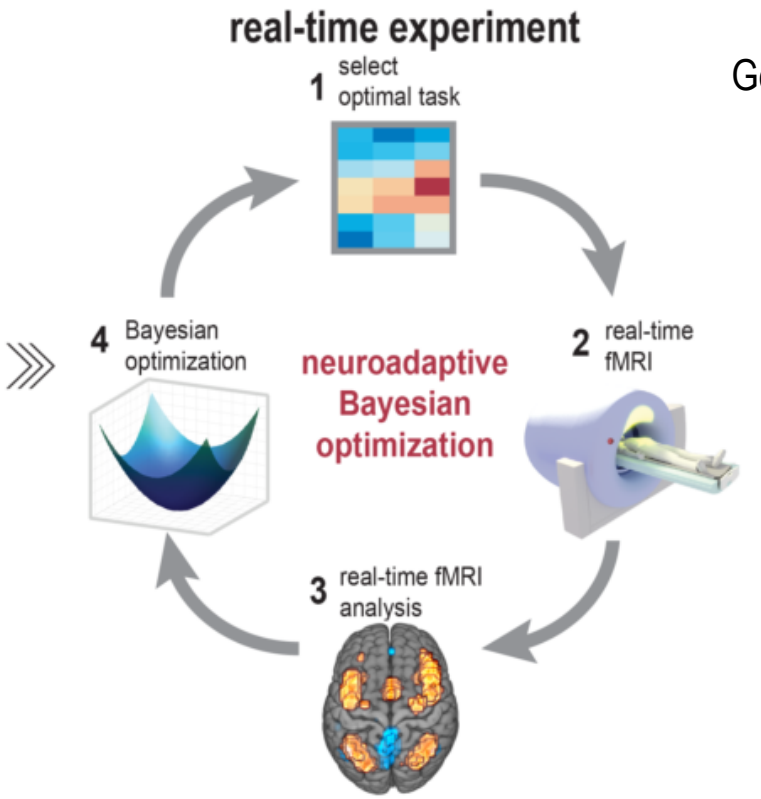
Biomarker discovery

14 stroke patients + 14 controls

Fatemeh Geranmayeh

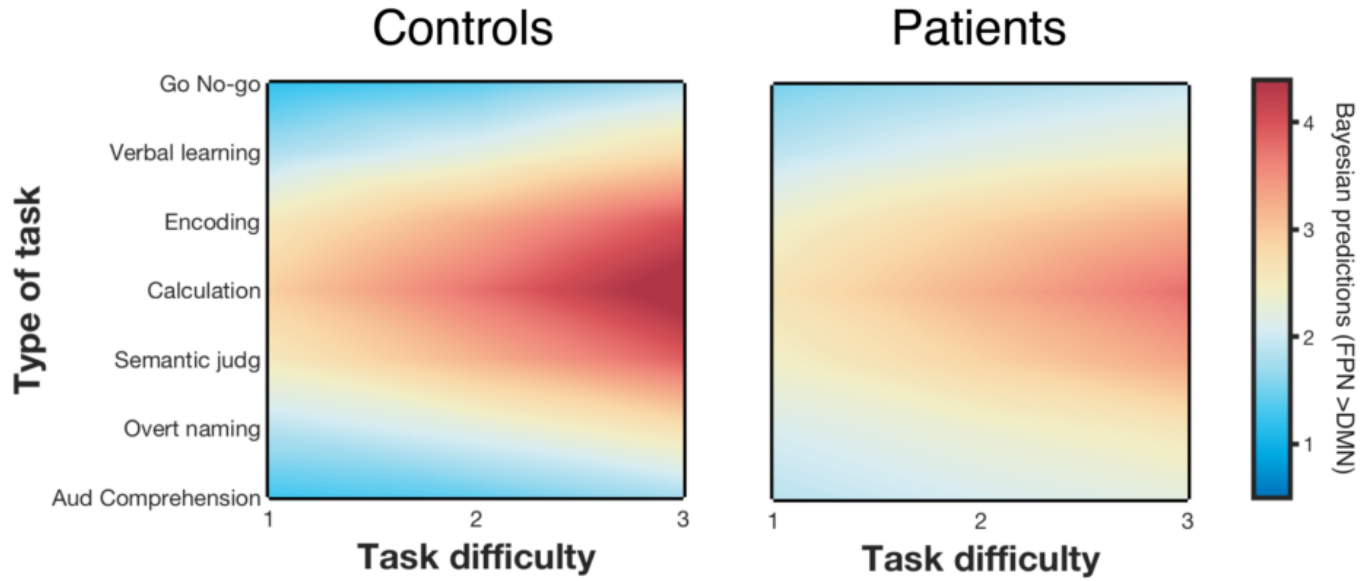




Lorenz et al. *in preparation*

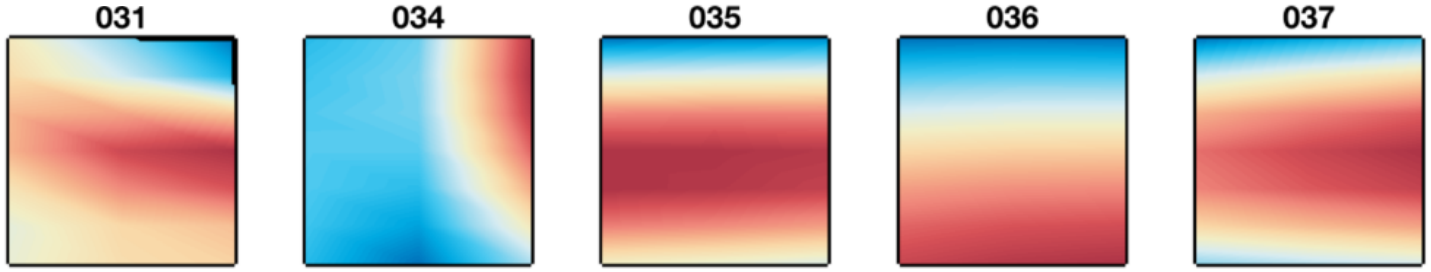
Biomarker discovery

Group results



Fatemeh Geranmayeh

Subject results



Lorenz et al. *in preparation*

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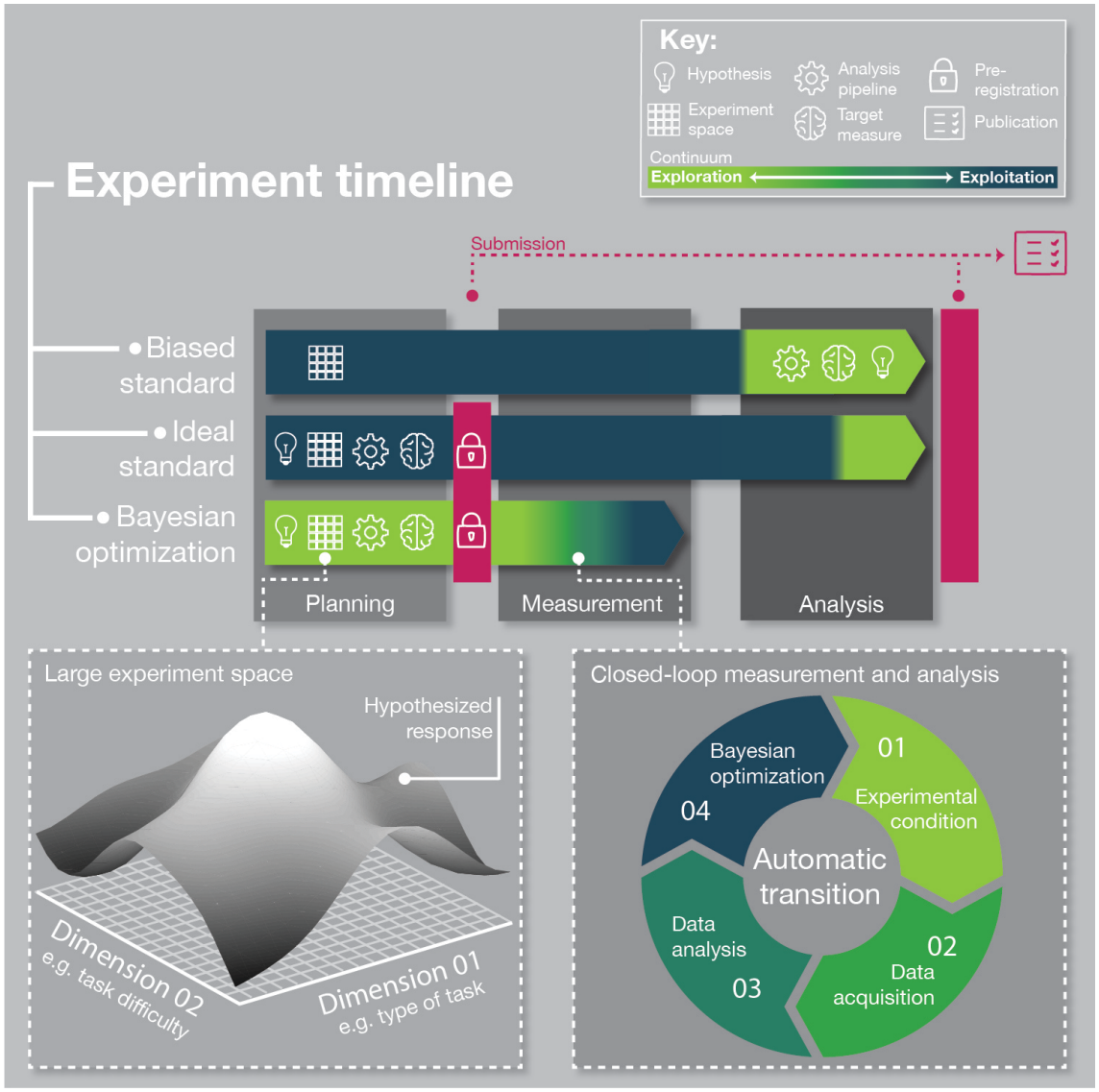
Implications for improving reproducibility



- More **flexible hypothesis** possible (exploration)
- Improved **specificity** & **generalizability** of research findings
- Can be combined with **pre-registration**

Lorenz et al. *TiCS* 2017

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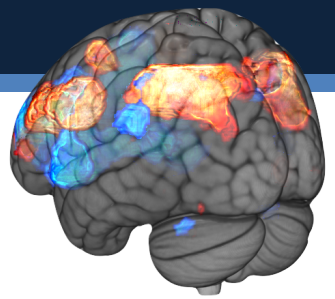
From ‘big data’ to mechanism?



FPN mapping → **FPN mechanism**

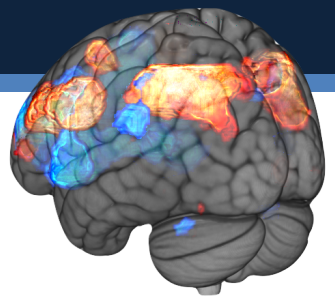
coarse mapping → fine mapping

Large-scale automated meta-analysis

Neuro-adaptive Bayesian optimization

Computational Modeling & Behaviour

From ‘big data’ to mechanism?



FPN mapping → **FPN mechanism**

coarse mapping → fine mapping

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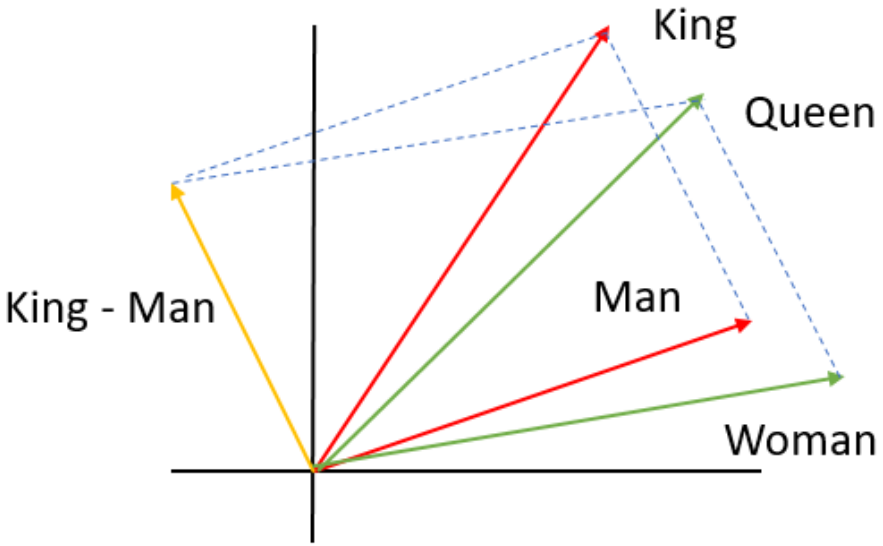
Neuro-adaptive Bayesian optimization

Computational Modeling & Behaviour

Text-mining and automated meta-analyses

- *BrainMap* based on manual entries
- *Neurosynth* based on word frequency in abstracts
- Take advantage of developments in deep learning to learn **word embeddings** (e.g. *word2vec, doc2vec*)



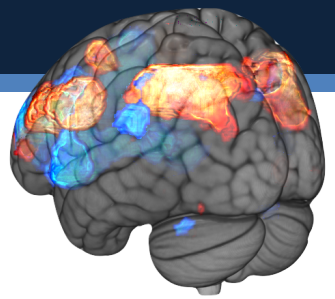
Words mapped into high-D vector space

Word embeddings have nice properties: you can make **analogies**!

Man: Woman as *King: Queen*
*Father: Doctor as Mother: **Nurse***

Capture & correct for current biases in the field?

From ‘big data’ to mechanism?



FPN mapping → **FPN mechanism**

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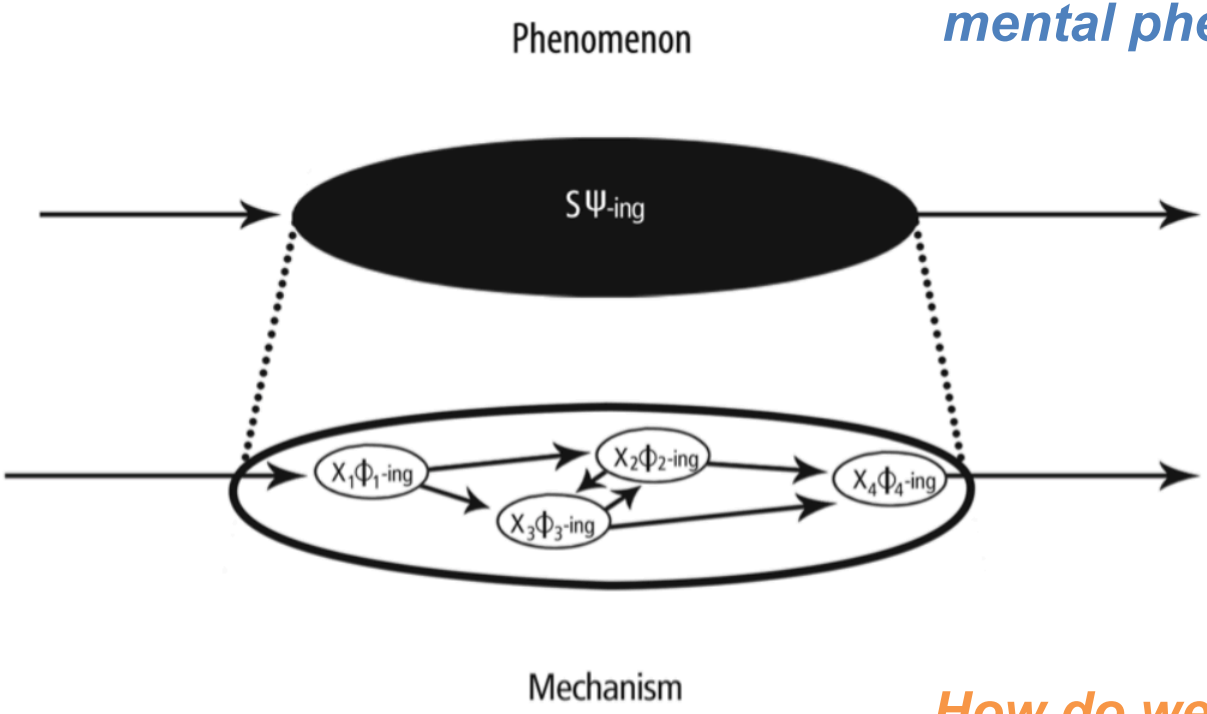
Neuro-adaptive Bayesian optimization

Computational Modeling & Behaviour

How does neural tissue give rise to the mind?

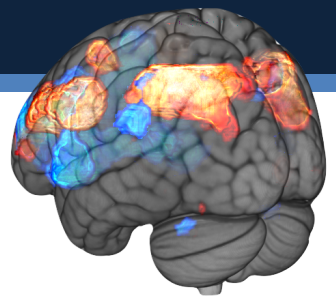
How do we define mental phenomena?



How do we draw causal inference?

How do we define the components (neurons, regions, networks)?

From ‘big data’ to mechanism?



FPN mapping → **FPN mechanism**

coarse mapping → fine mapping

Large-scale automated meta-analysis

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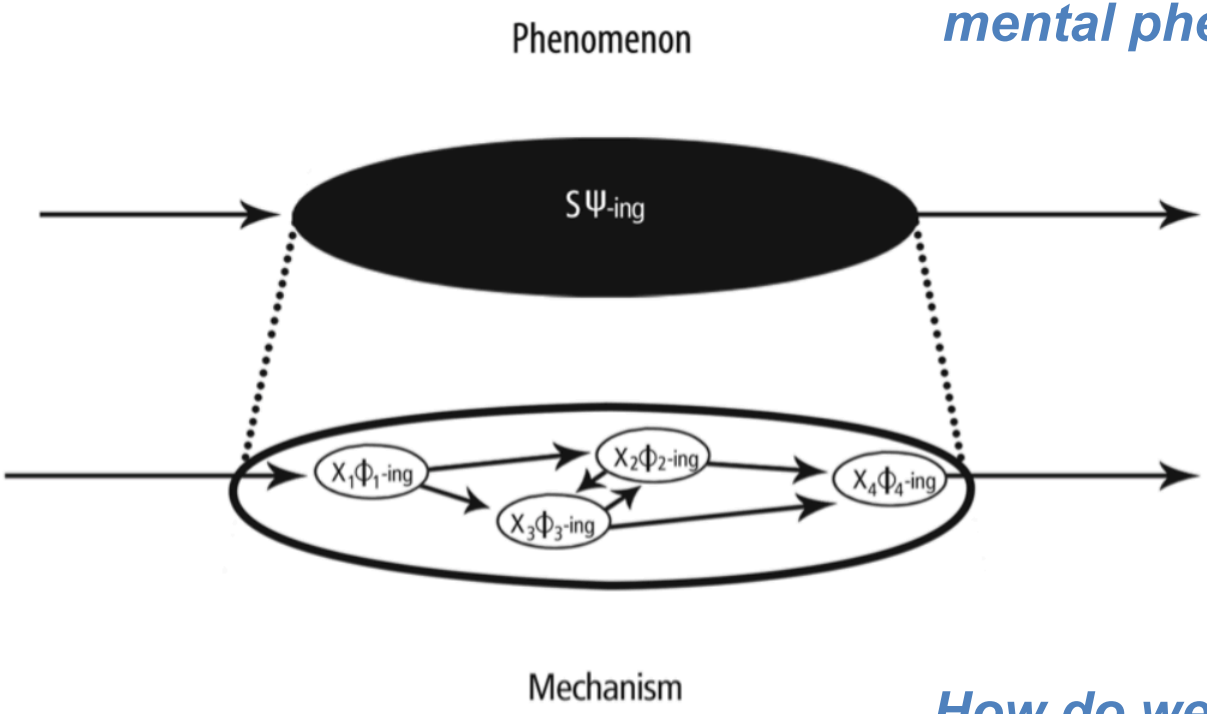
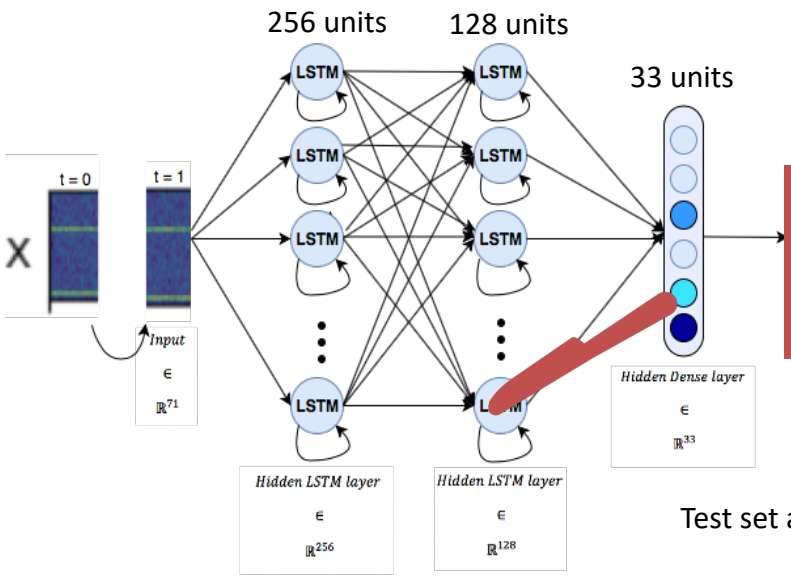


How do we draw causal inference?

How do we define the components (neurons, regions, networks)?

Deep neural networks for learning cognitive tasks

1. Train neural net to learn 6 tasks



Inspired by Yang et al. *Nat Neurosci* 2019

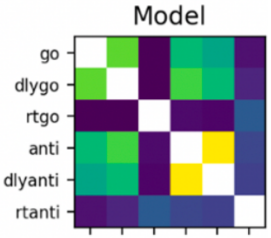
Digitally lesion units or ensembles of units and study for which tasks performance drops

Test set accuracy: **93.28%**

Pedro Costa

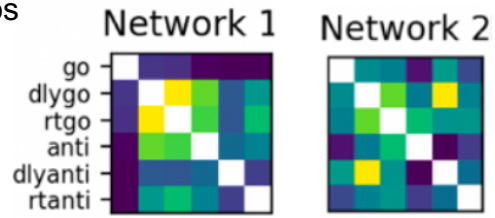
2. Which tasks are similar?

Correlations of hidden unit's variance



3. What about brain?

Correlation of meta-analytic derived brain maps



Representational Similarity Analysis

Costa, Popescu, Leech & Lorenz *CNS Conference* 2019

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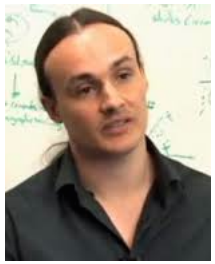
Ricardo P. Monti

Rob



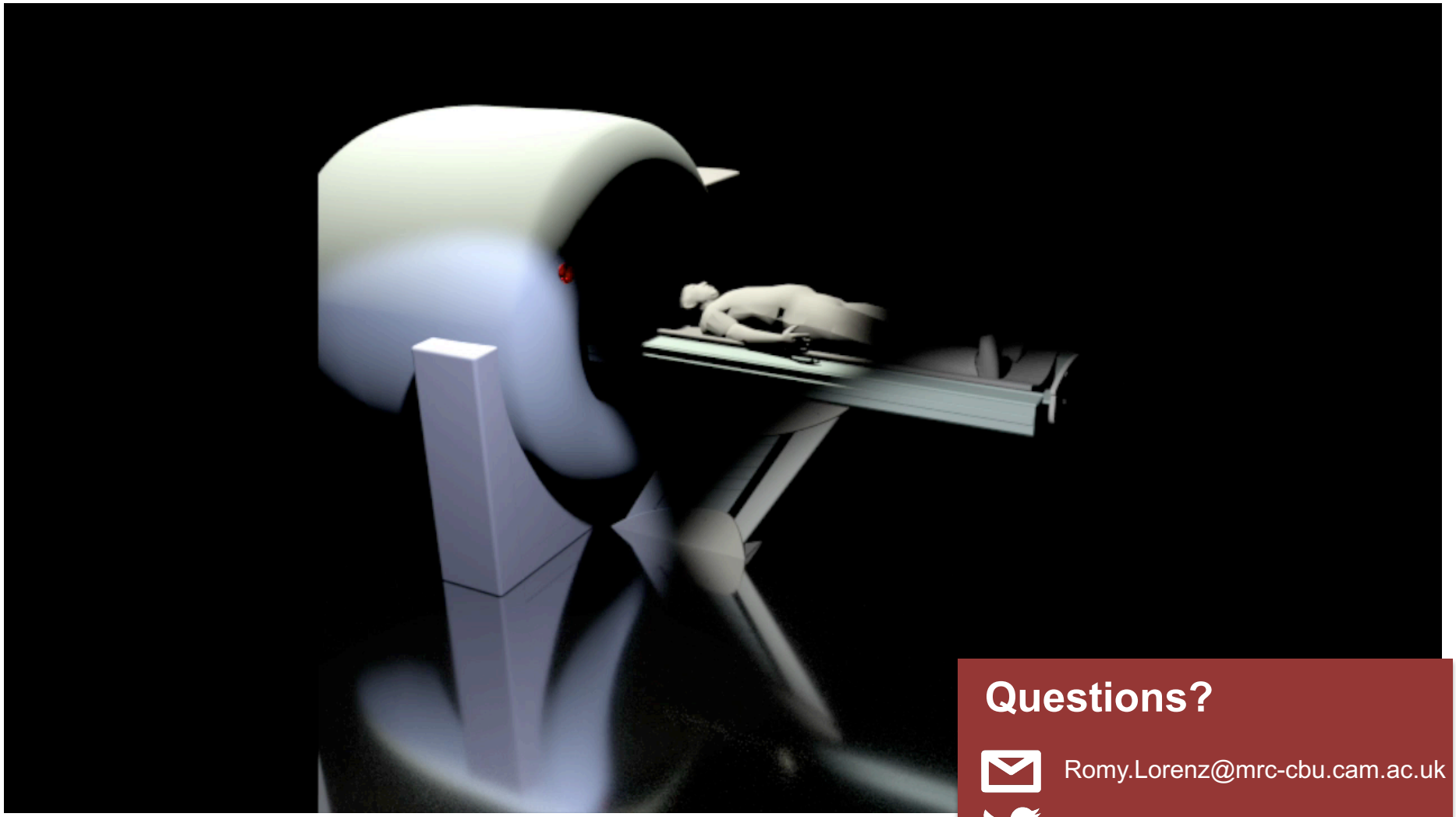
Adam

Ines

Fatemeh

Ricardo

Questions



Questions?

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