Experimental design

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With thanks to:
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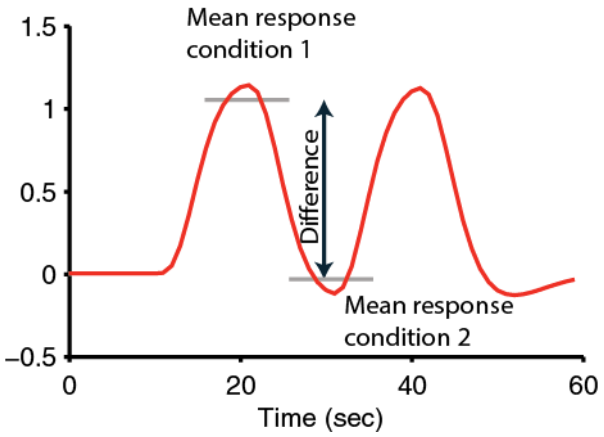
Christian Ruff
Rik Henson

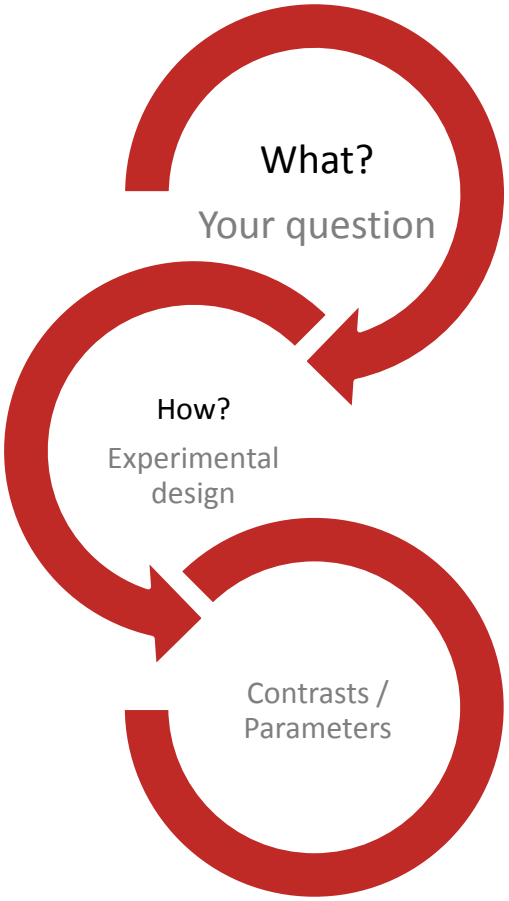
Goal

The BOLD signal does NOT provide you with an absolute measure of neural activity

Therefore, you need to compare activity across conditions (use contrasts).



The sensitivity of your design depends on maximizing the relative change between conditions



Experimental designs

Subtraction

Conjunction

Factorial

Parametric

Psycho-physiological Interaction (PPI)

Indexing neural representations

Simple subtraction

Aim: Isolation of a cognitive process

- Compare the neural signal for a task that activates the cognitive process of interest and a second task that controls for all but the process of interest

F.C. Donders, 1868

>> The critical assumption of „pure insertion“

Assume that adding components does not affect other processes

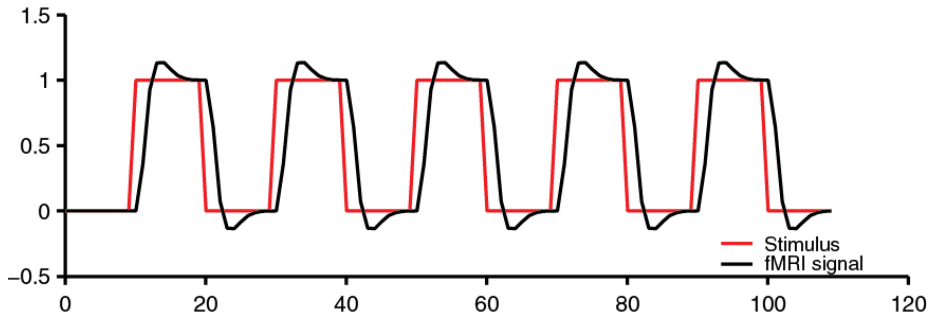
> A good control task is critical!

- Question: Which region is specialized for assigning names to faces?

Simple subtraction

Aim: Isolation of a cognitive process

- Compare the neural signal for a task that activates the cognitive process of interest and a second task that controls for all but the process of interest



Simple subtraction

Aim: Isolation of a cognitive process

- Compare the neural signal for a task that activates the cognitive process of interest and a second task that controls for all but the process of interest

Not a great contrast

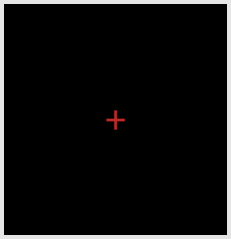
- Rest may not be truly rest
- Will give wide-spread activation. Hard to draw conclusions about specific cognitive processes
- Null events or long SOAs (stimulus onset asynchrony) essential for estimation, which may result in an inefficient design.
- But can be useful to find regions generally involved in the task

Choosing your baseline

Problem: Difficulty of finding baseline tasks that activates all but the process of interest

Different stimuli and task

vs.



'Meryl Streep'

'I am so hungry…'

→ Several components differ!

Related stimuli

vs.

Famous?

Mum?

→ P implicit in control task?
→ Difficulty matched?

Same stimulus, different tasks

vs.

Name the person!

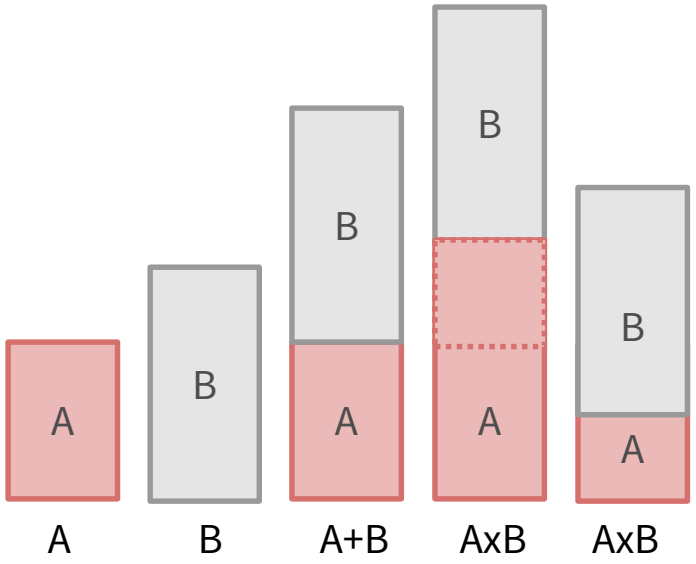
Name the gender!

→ Specific naming-related activity

Subtraction

Problems:

- Difficulty of finding baseline tasks that activate all but the process of interest
- Subtraction depends on the assumption of “pure insertion”
  - an extra cognitive component can be inserted without affecting the pre-existing components



Friston et al., (1996)

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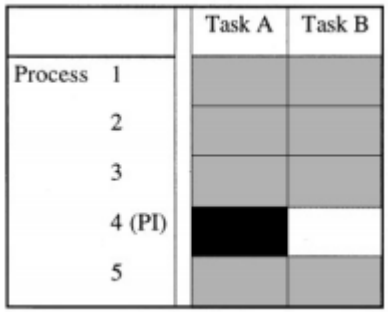
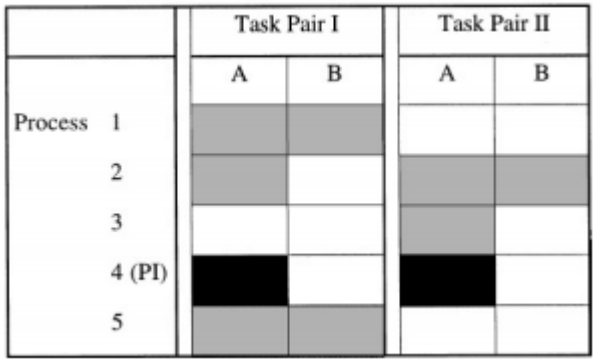
Conjunction

Minimization of "the baseline problem" by isolating the same cognitive process by two or more separate contrasts

Subtraction



Conjunction analysis



only the component of interest is common to all task pairs

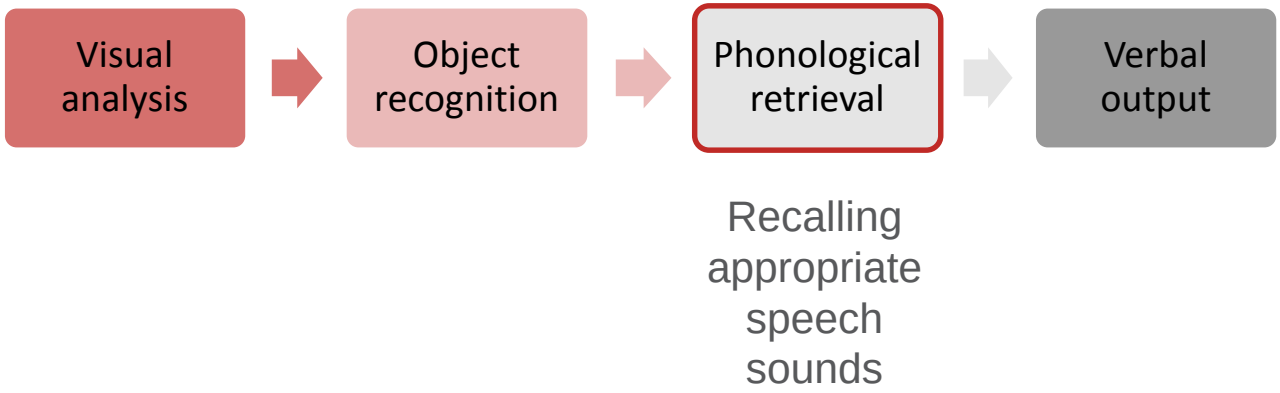
Conjunctions can be conducted across different contexts: tasks, stimuli, senses (vision, audition), …

Note: The contrasts entering a conjunction have to be independent

Conjunction analysis

Which neural structures support phonological retrieval, independent of item?

What is this object?



Conjunction analysis

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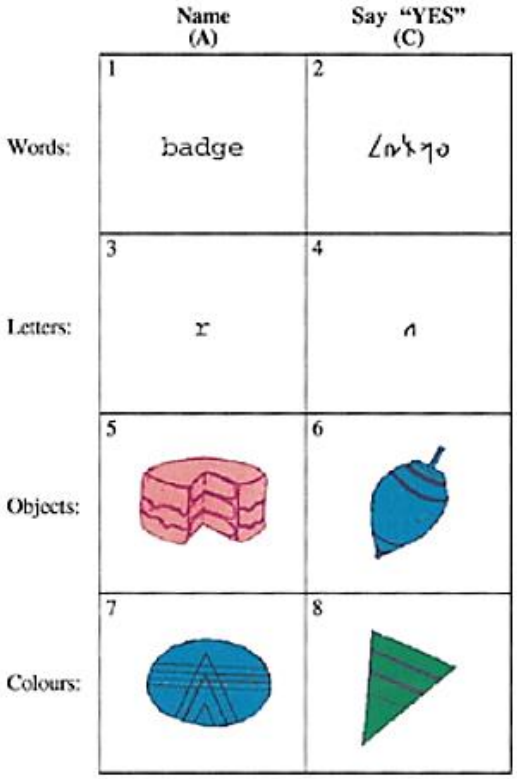
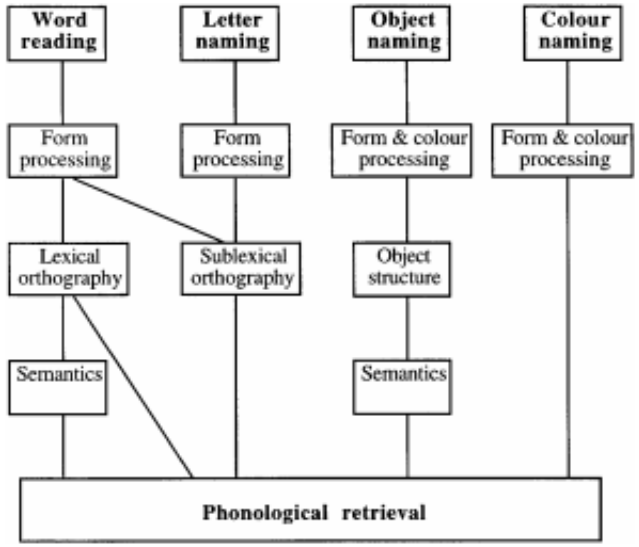




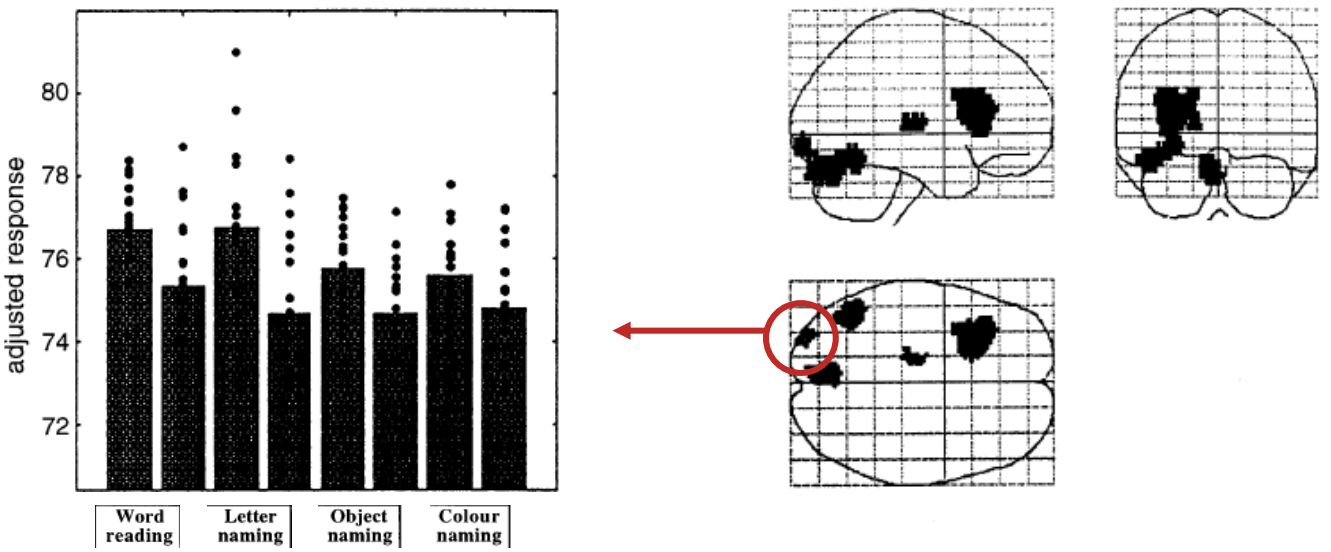
Phonological retrieval is the only cognitive component common to all task pair differences

Price & Friston (1996)

Conjunction analysis

Isolates the process of Phonological retrieval, no interaction with visual processing etc

Overlap of 4 subtractions



Areas are identified in which task-pair effects are jointly significant and are not significantly different

Price & Friston (1996)

Experimental designs

Subtraction

Conjunction

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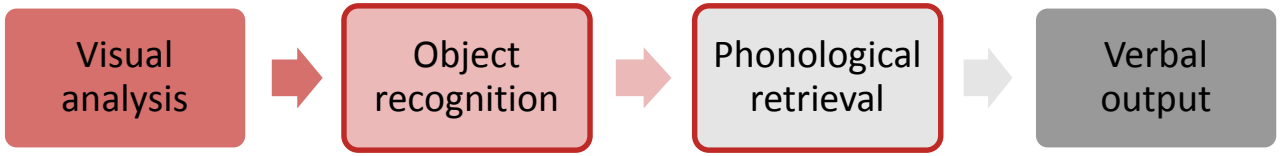
Psycho-physiological Interaction (PPI)

Indexing neural representations

Factorial design

Is the inferiotemporal cortex sensitive to both object recognition and phonological retrieval of object names?



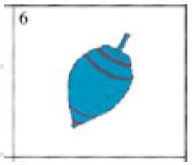
Factorial design

Is the inferiotemporal cortex sensitive to both object recognition and phonological retrieval of object names?

A — Say ‘yes’ when you see an abstract image

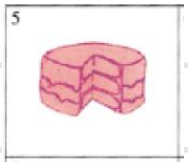
Visual analysis → Verbal output

B — Say ‘yes’ when you see an object



Visual analysis → Object recognition → Verbal output

C — Name the object



Visual analysis → Object recognition → Phonological retrieval → Verbal output

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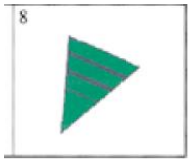
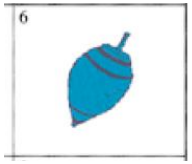
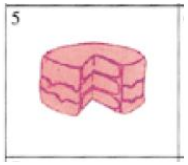


B — Say 'yes' when you see an object

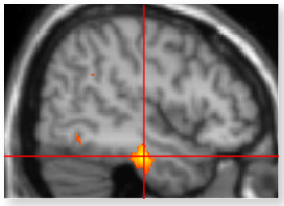


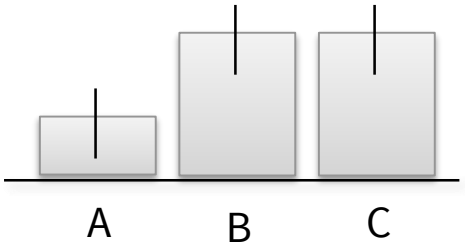
C — Name the object



Friston et al., (1997)

Results in inferotemporal cortex:





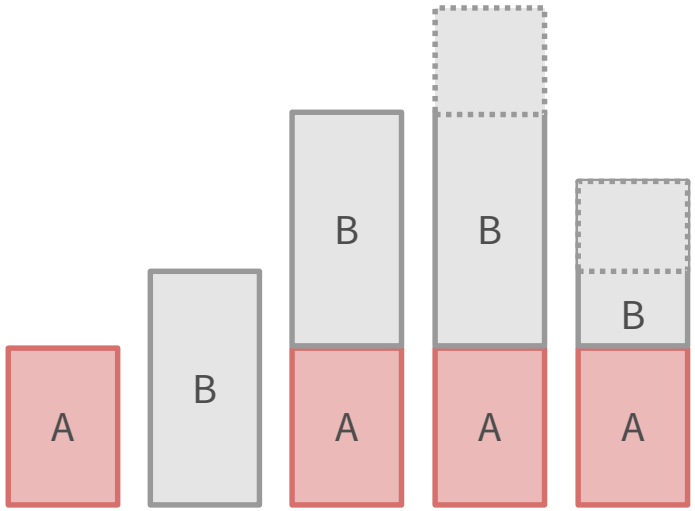
B > A Object recognition

C = B IT not involved in phonological retrieval?!

Problem:
We assumed that IT response to object recognition is context independent

Interactions

Is the task the sum of its component processes, or does A modulate B?



Object recognition

Phonological retrieval

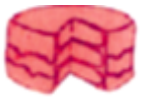
Vary A and B independently!

Main effects

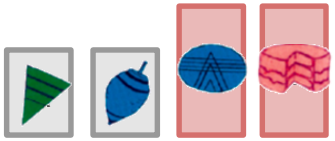
Factorial design

Is the task the sum of its component processes, or does A modulate B?

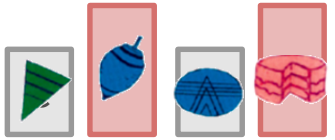
Price et al., (1996);
Friston et al., (1997)

	No phonological retrieval	Phonological retrieval
No object recognition	A 	C 
Object recognition	B 	D 

Main effect, phonological retrieval: (C + D)>(A + B)



Main effect, object recognition: (B + D)>(A + C)



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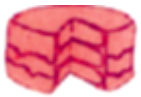
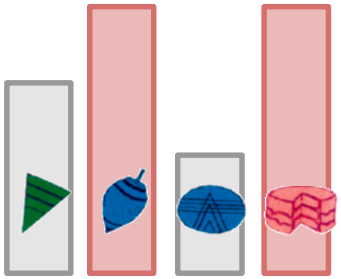
Object recognition	B 	D 

Inferotemporal (IT) responses do discriminate between situations where phonological retrieval is present or not. In the absence of object recognition, there is a *deactivation* in IT cortex, in the presence of phonological retrieval.

Interaction:

(D - C) > (B - A)



Experimental designs

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Parametric designs

Does activity vary systematically with a continuously varying parameter?

Varying the stimulus-parameter of interest on a continuum, in multiple (n>2) steps...

... and relating BOLD to this parameter

Possible tests for such relations :

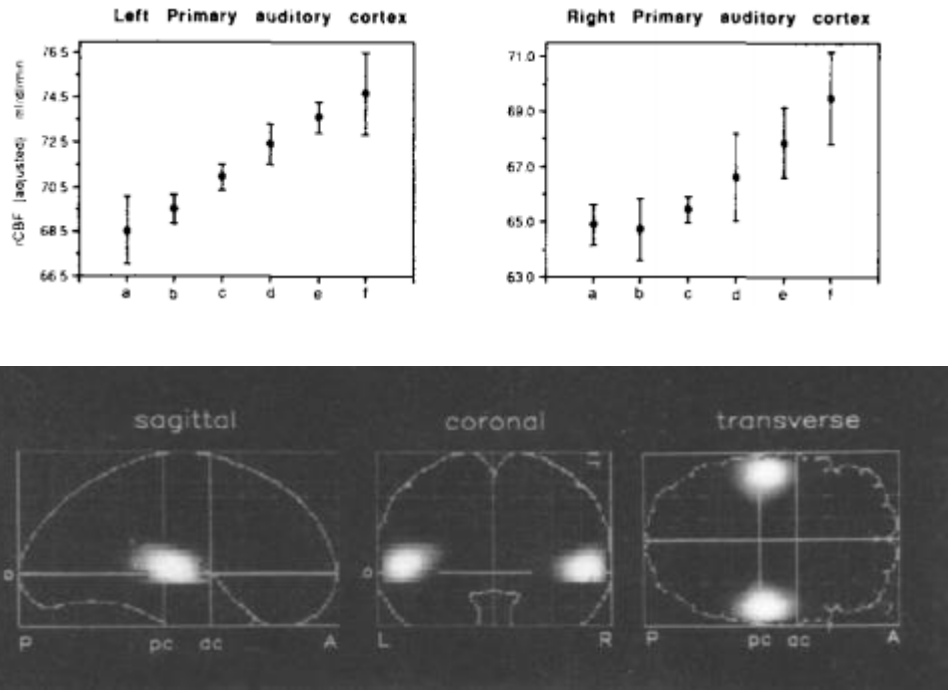
- Linear
- Nonlinear: Quadratic/cubic/etc.
- „Data-driven“ (e.g., neurometric functions, computational modelling)

Avoids pure insertion but does assume no qualitative change in processing

Parametric designs

PET

- Auditory words presented at different rates (rest, 5 rates between 10wpm and 90 wpm)
- Activity in primary auditory cortex is linearly related to word frequency

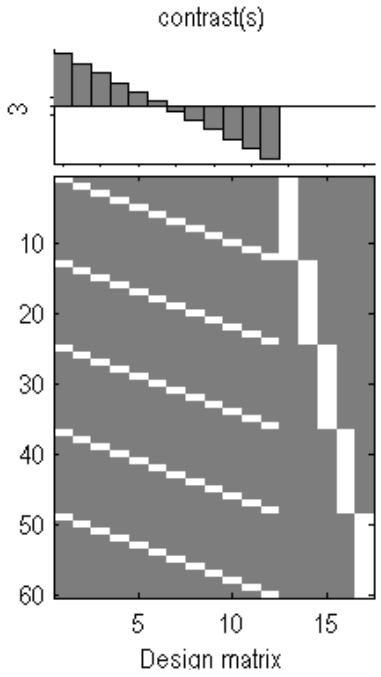


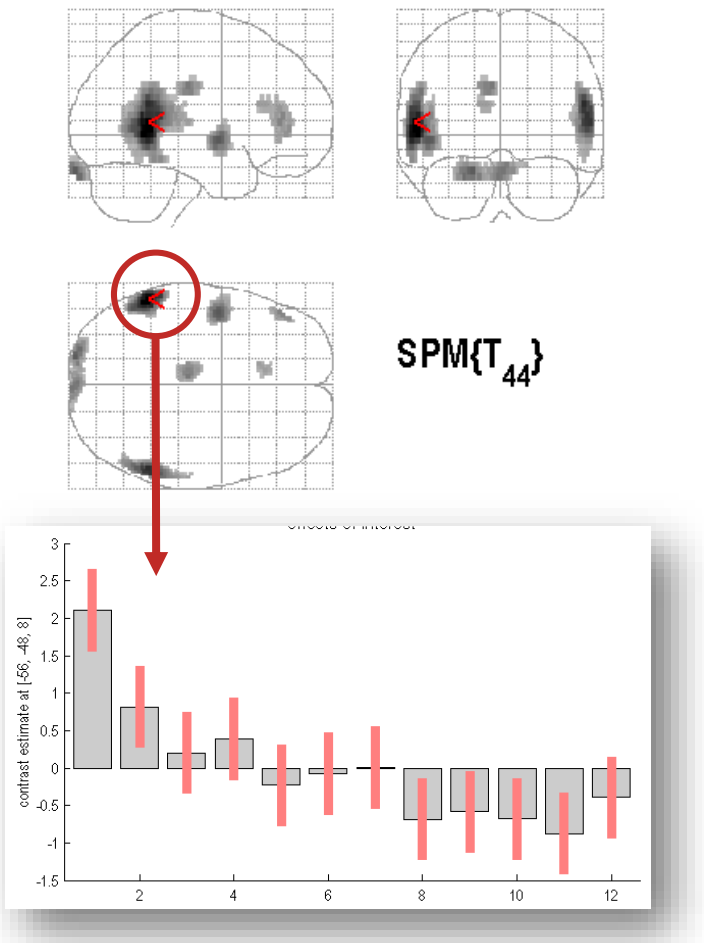
Price et al. 1992

A linear parametric contrast

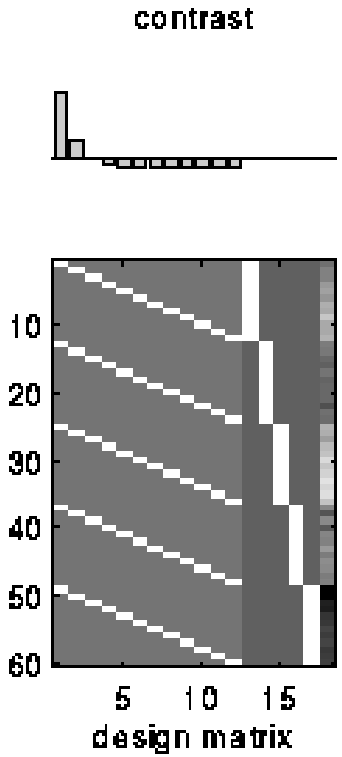
Is there an adaptation effect if people listen to words multiple times?

Linear effect of time





Non-linear effect of time



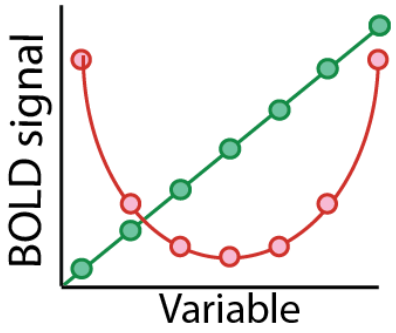
A non-linear parametric design matrix

Polynomial expansion:

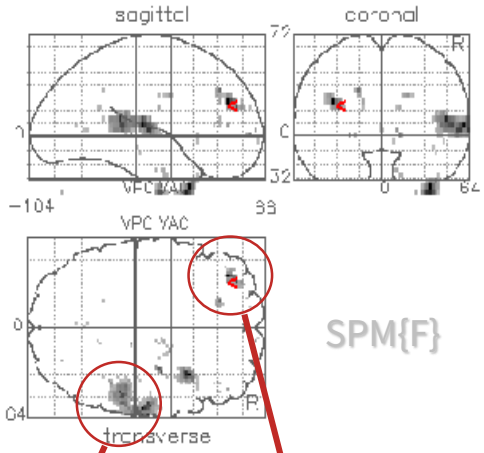
$f(x) = b_1 x + b_2 x^2 + \ldots$

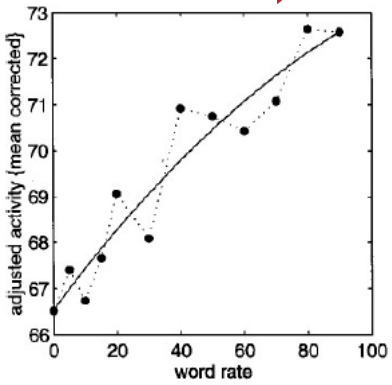
…up to $(N-1)^{th}$ order for N levels

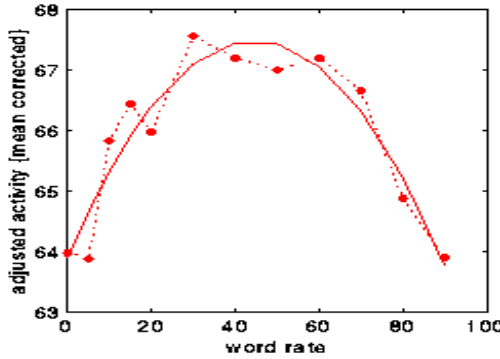
SPM offers polynomial expansion as option during creation of parametric modulation regressors.



F-contrast [1 0] on linear param
F-contrast [0 1] on quadratic param

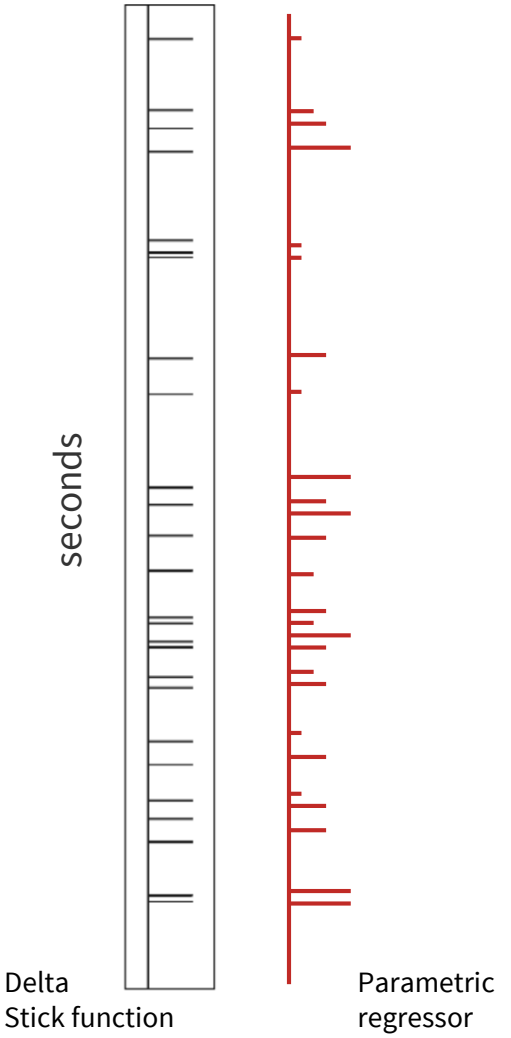


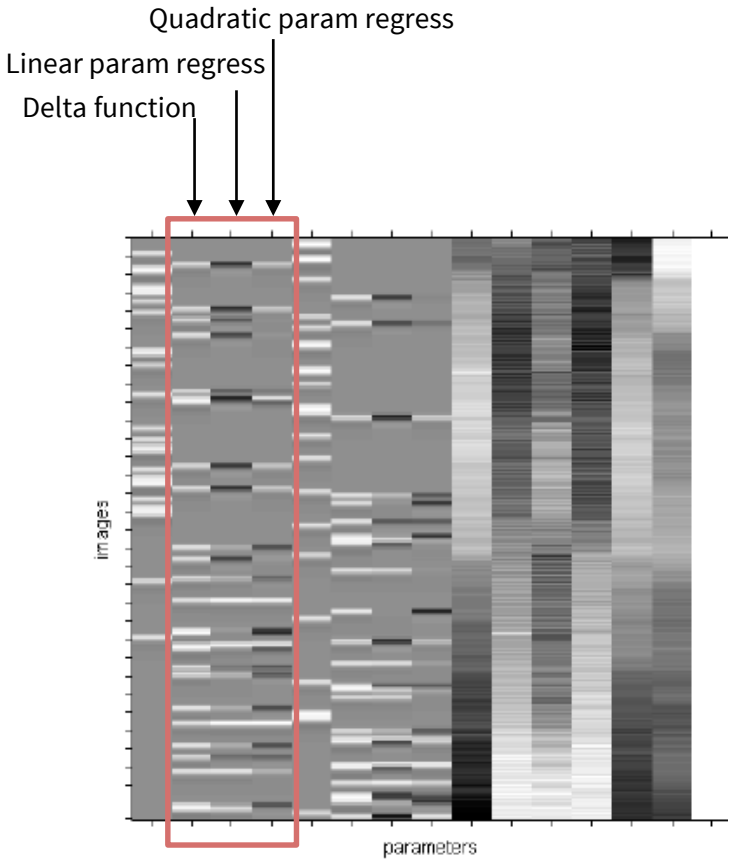




Büchel et al., (1996)

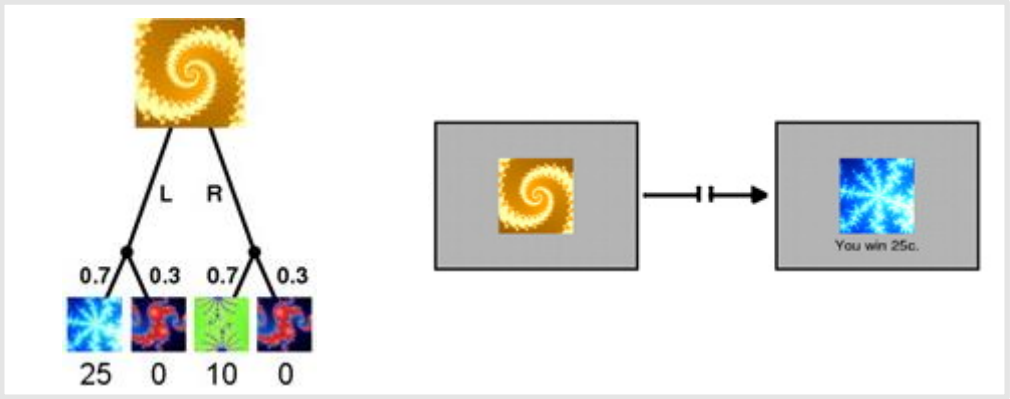
Parametric modulation



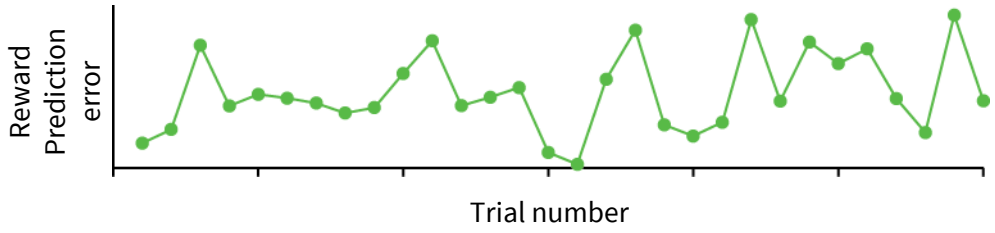


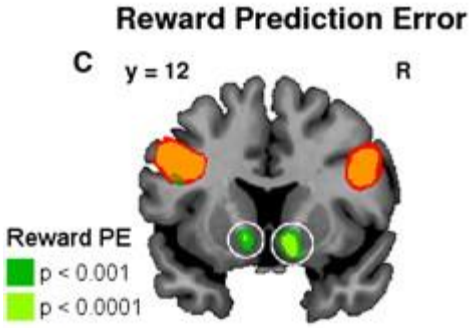
Parametric design: Model-based regressors

- Signals derived from a computational model are correlated against BOLD, to determine brain regions showing a response profile consistent with the model, e.g. Rescorla-Wagner prediction error



Time-series of a model-derived reward prediction error





Gläscher & O'Doherty (2010)

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Psycho-physiological Interaction (PPI)

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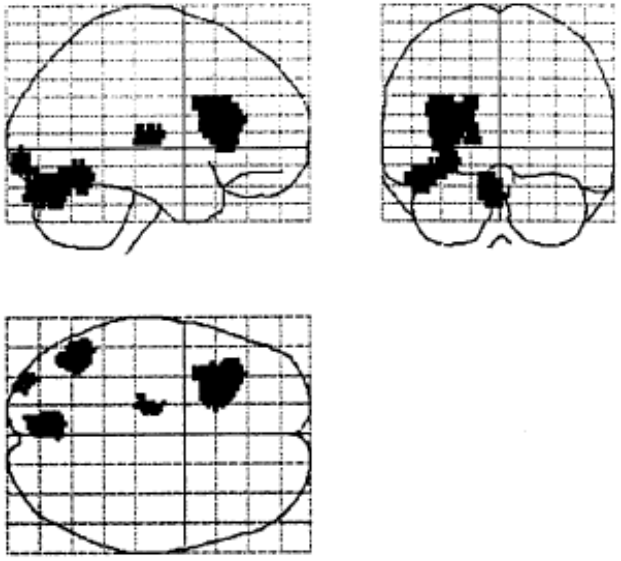
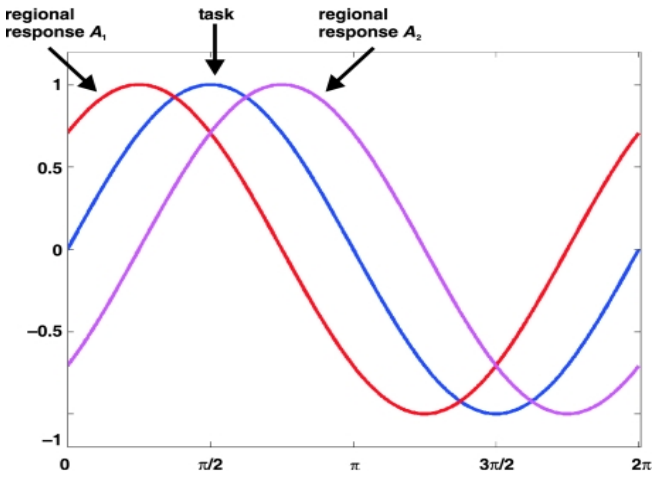
Psycho-physiological Interaction (PPI)

Functional connectivity measure

Can activity in a part of the brain be predicted by an interaction between task and activity in another part of the brain?

If two areas are jointly correlated to a task component (‘co-activated’) this does not mean that they are functionally connected to each other

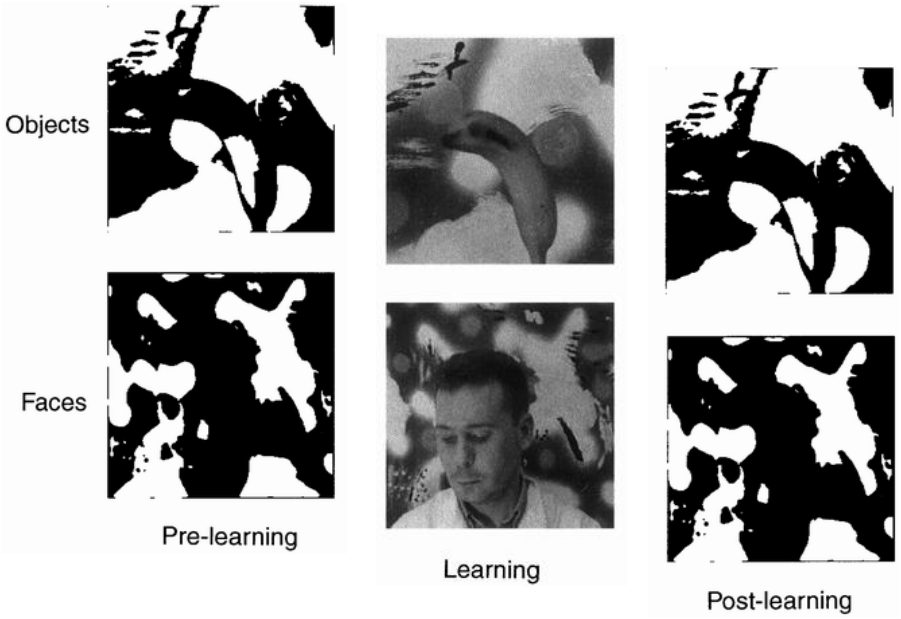




Stephan, 2004

Psycho-physiological Interaction (PPI)

Factorial design

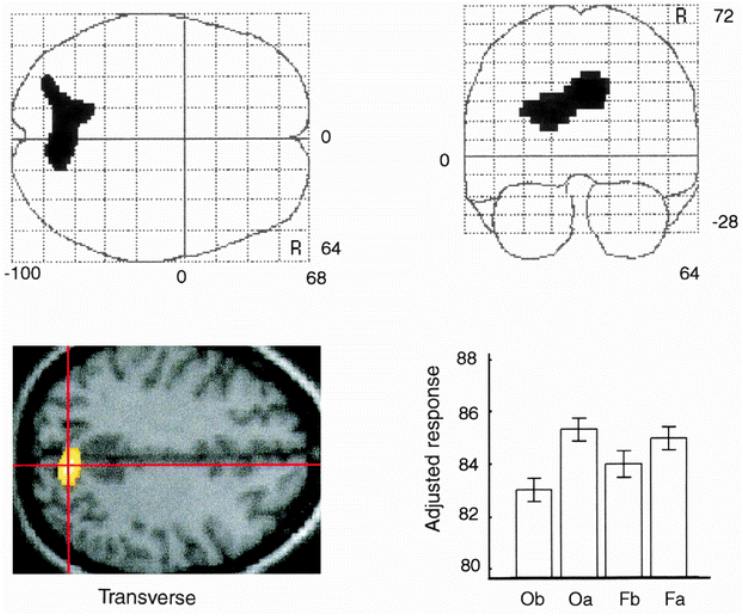


Stimuli	Learning: before	Learning: after
Objects	Objects before (Ob)	Objects after (Oa)
Faces	Faces before (Fb)	Faces after (Fa)

Dolan et al., 1997

Psycho-physiological Interaction (PPI)

Main effect of learning



Learning

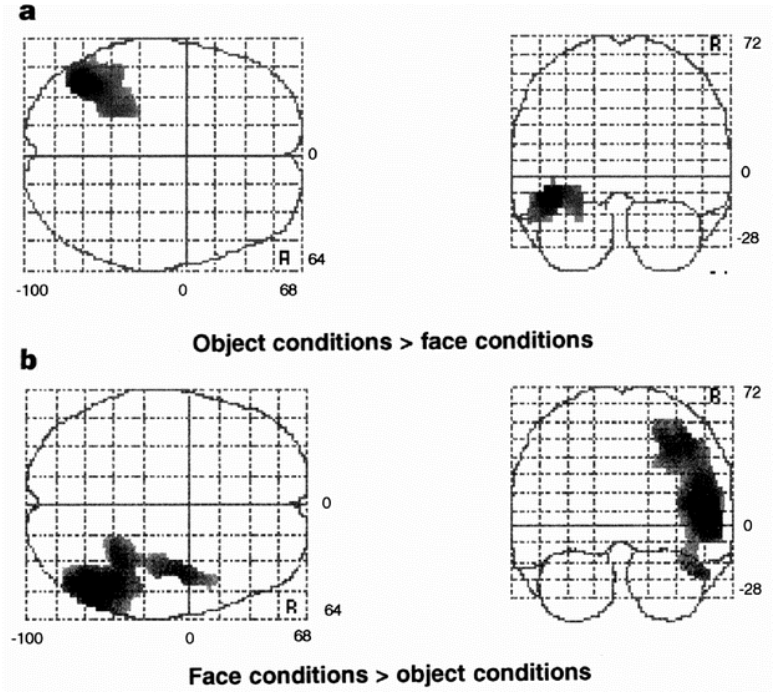
Stimuli

Objects before (Ob)	Objects after (Oa)
Faces before (Fb)	Faces after (Fa)

Dolan et al., 1997

Psycho-physiological Interaction (PPI)

Main effect of stimulus



Learning

Stimuli

Objects before (Ob)	Objects after (Oa)
Faces before (Fb)	Faces after (Fa)

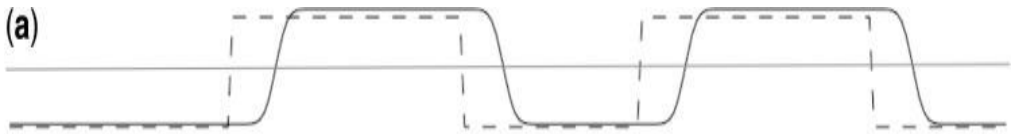
Does learning involve functional connectivity between parietal cortex and stimuli specific areas?

Dolan et al., 1997

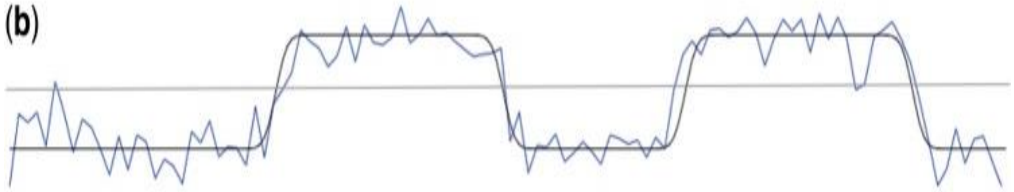
Psycho-physiological Interaction (PPI)

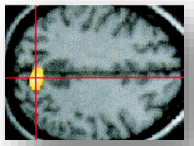
Does learning involve functional connectivity between parietal cortex and stimuli specific areas?

Main effect of task (Faces - objects)



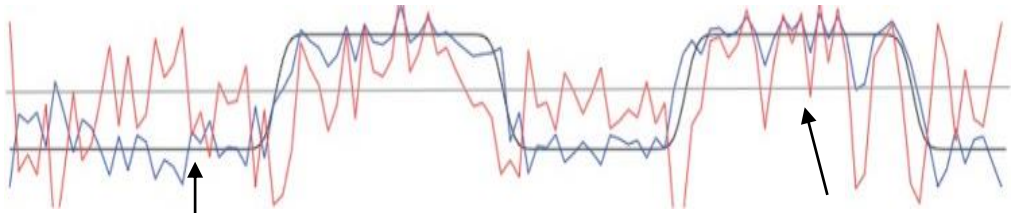
Activity in parietal cortex





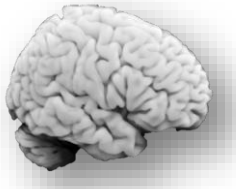
Seed region

PPI regressor = HRF convolved task x seed ROI regressors



Anti-correlated during rest

correlated during task



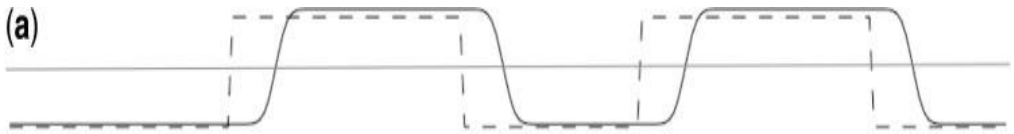
Whole brain

O'Reilly (2012)

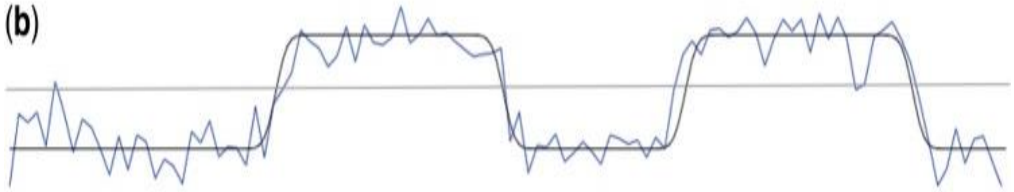
Psycho-physiological Interaction (PPI)

Does learning involve functional connectivity between parietal cortex and stimuli specific areas?

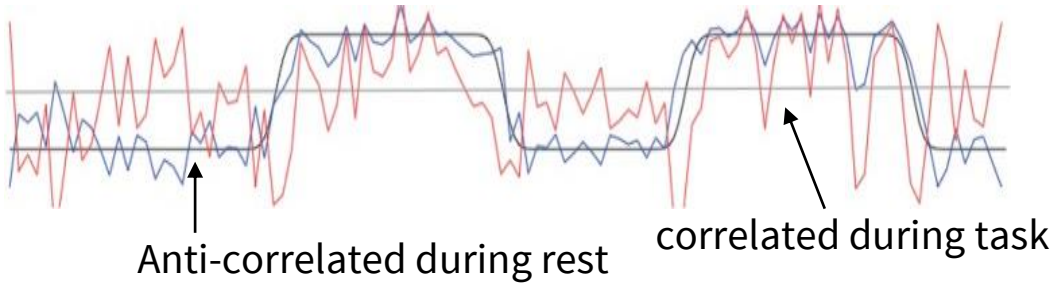
Main effect of task (Faces - Objects)

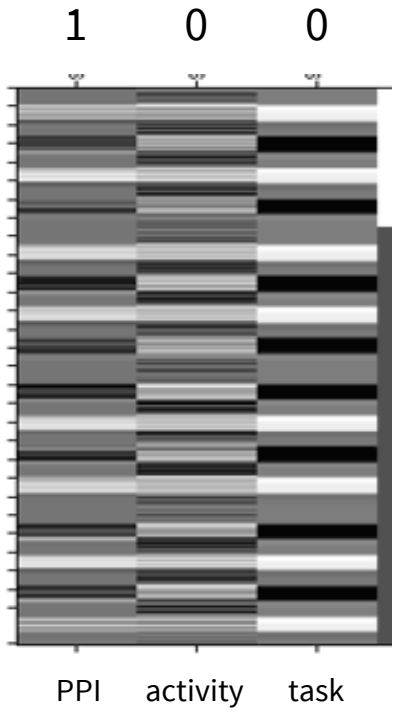


Activity in parietal cortex



PPI regressor = HRF convolved task x seed ROI regressors



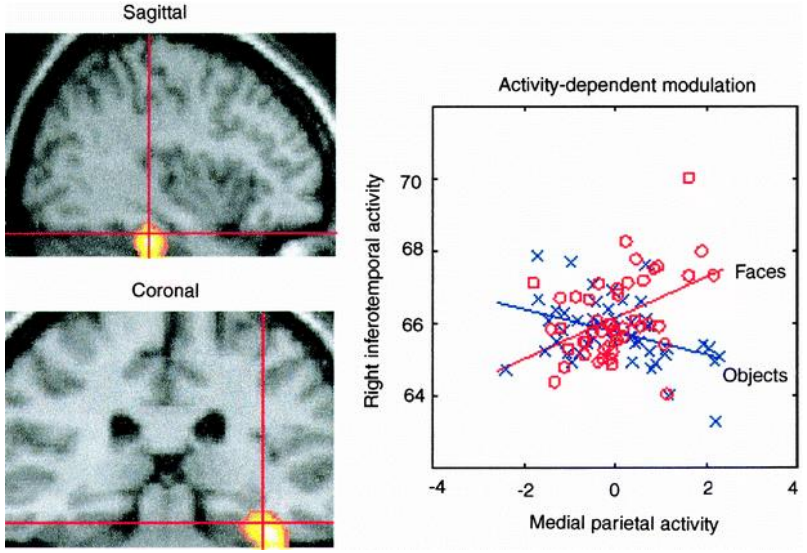


The interaction term should account for variance over and above what is accounted for by the main effect of task and physiological correlation

O'Reilly (2012)

Psycho-physiological Interaction (PPI)

ITC can differentiate between faces and objects only if parietal activity is high

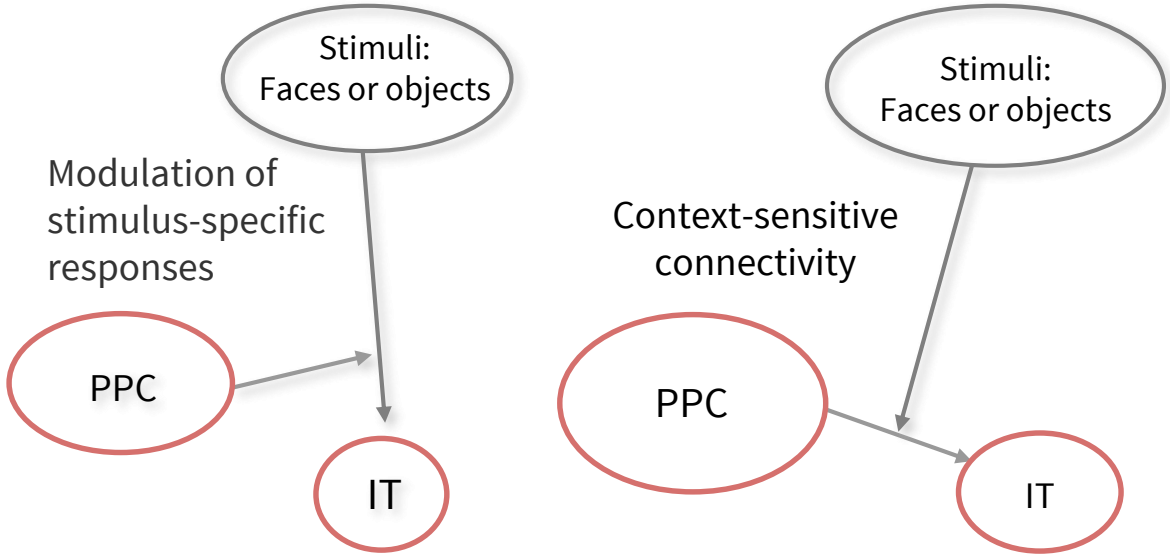


The right fusiform region responds to faces (relative to objects) when, and only when, parietal activity is high

Dolan et al., 1997

Psycho-physiological interactions (PPI)

A standard PPI analysis does not make inferences about the **direction** of information flow (causality)



Experimental designs

Subtraction

Conjunction

Factorial

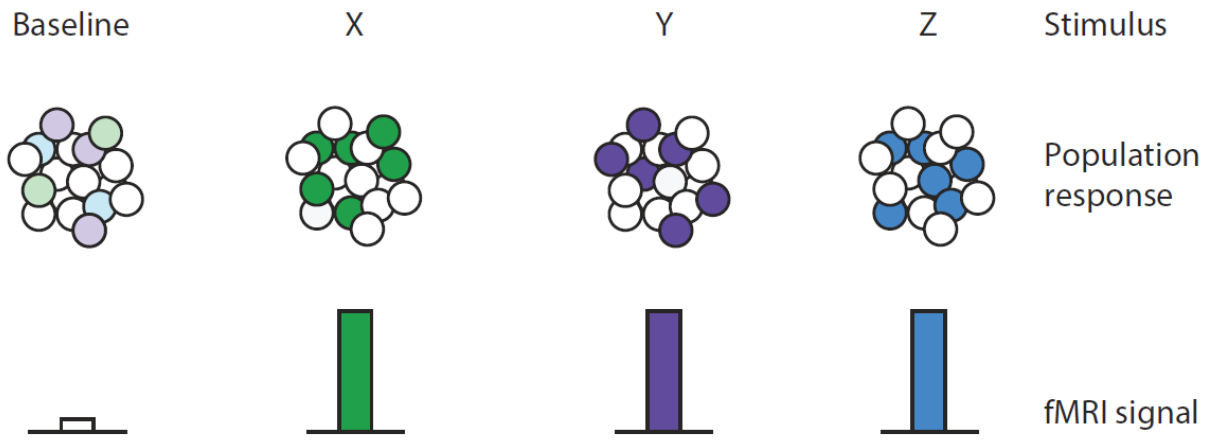
Parametric

Psycho-physiological Interaction (PPI)

Indexing neural representations

Representational neuroimaging

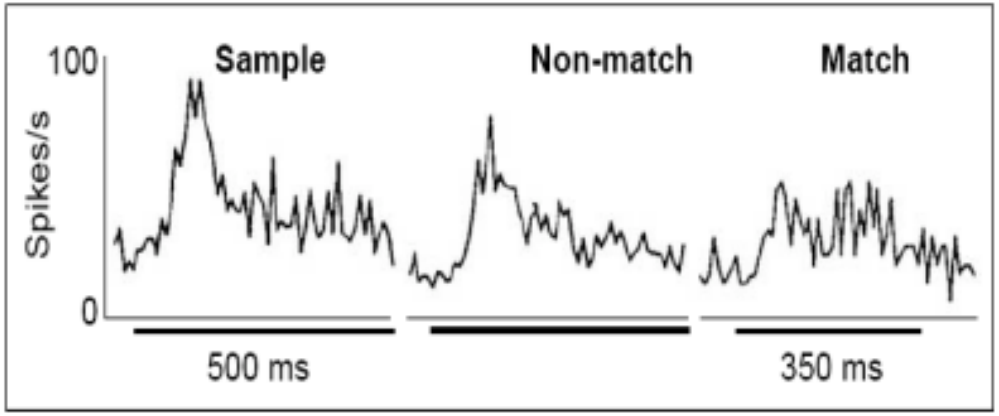
Approaches described so far investigate the *involvement* of regions in a specific mental activity rather than the *representational content* of regions or voxels



Barron, Garvert, Behrens 2016

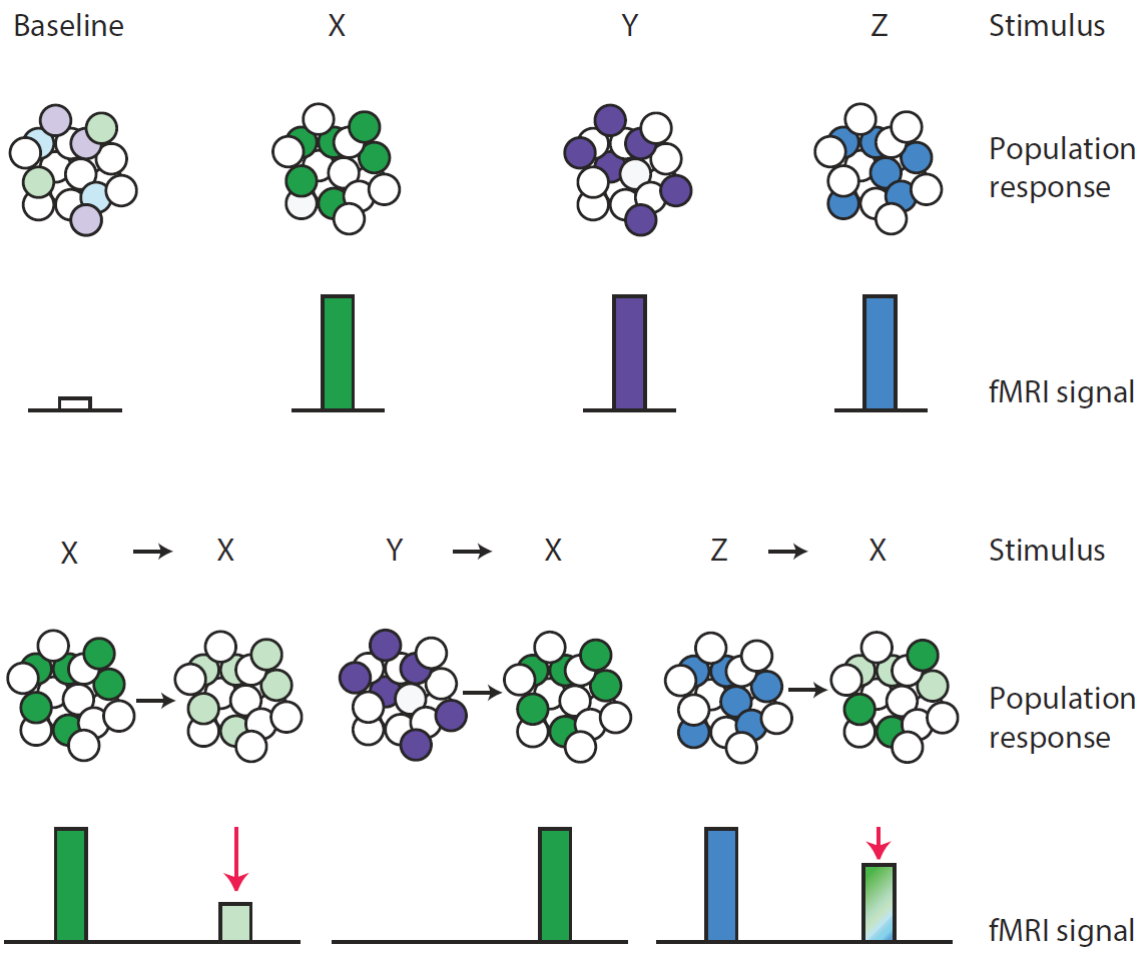
Repetition suppression

Neurons in inferotemporal cortex display a diminished response if a stimulus is repeated



Li et al. (1993),
Grill-Spector (2006)

Conventional fMRI vs fMRI adaptation

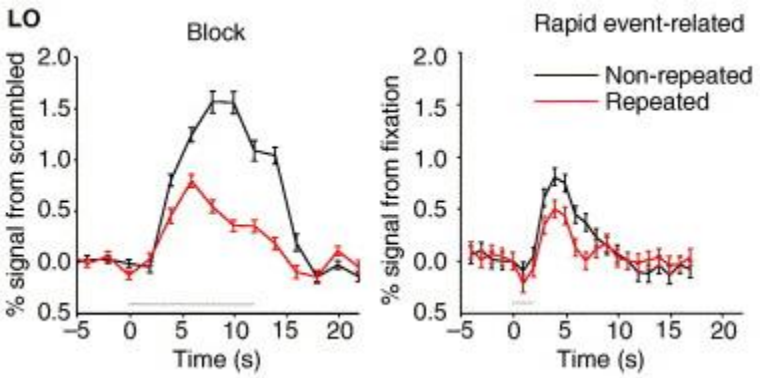


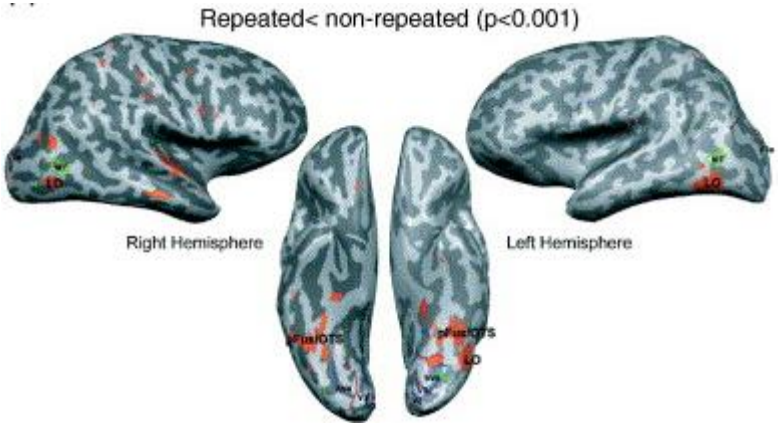
Repetition suppression as an index of representational similarity

Barron, Garvert, Behrens 2016

fMRI adaptation

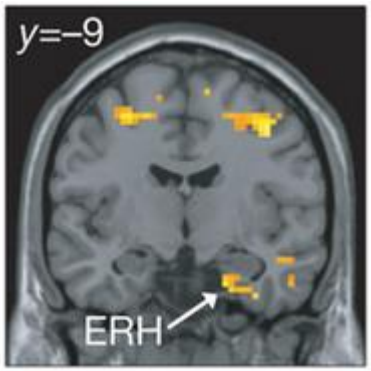
Object-repetition effects measured with fMRI

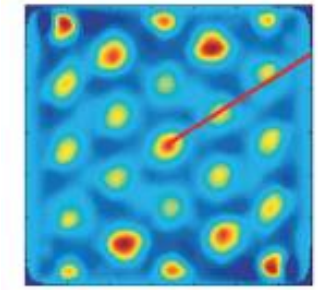


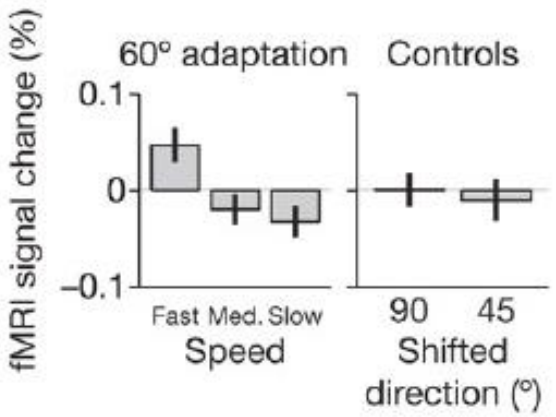


Grill-Spector et al. (2006)

fMRI adaptation as a tool for measuring complex computations in the human brain





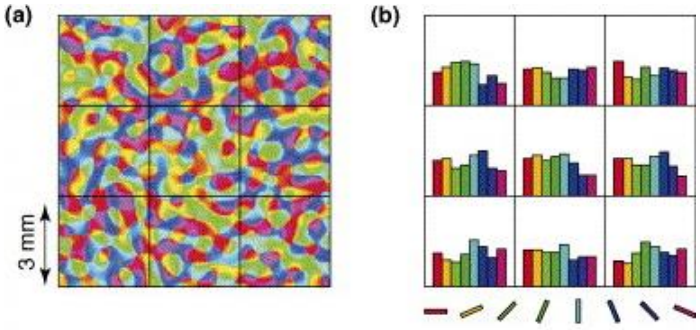


Doeller et al. (2010)

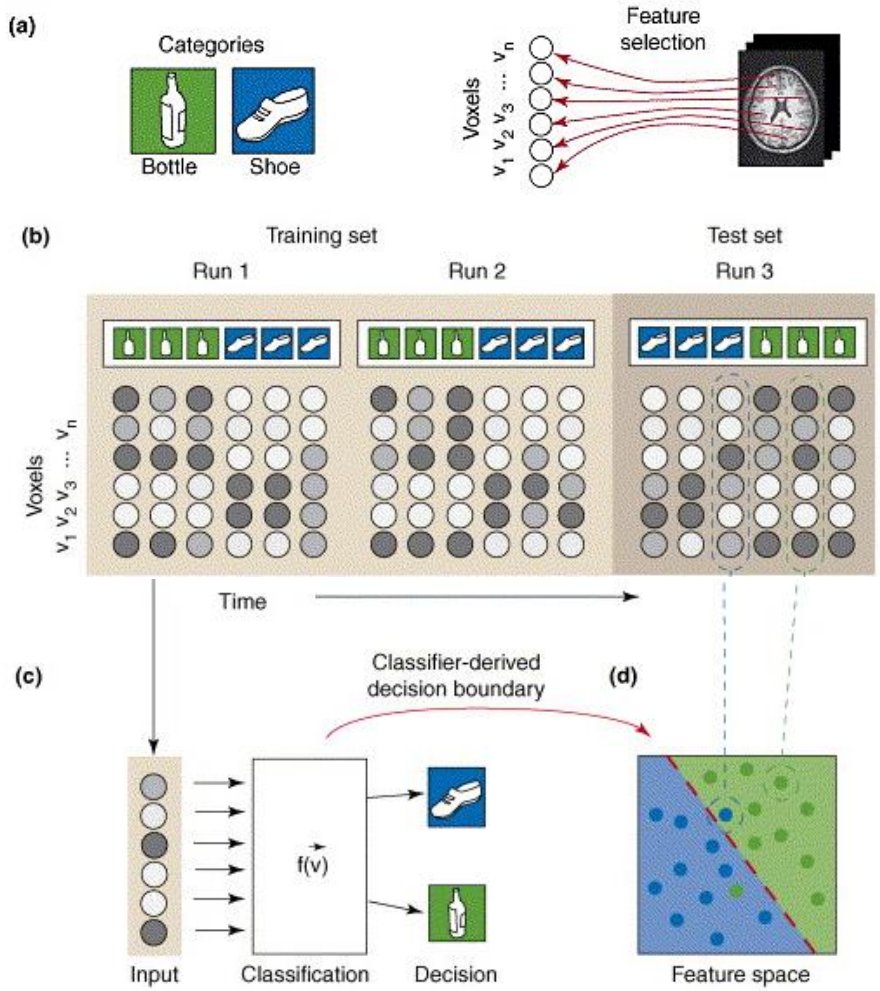
Multivariate vs. univariate methods

Multivariate methods investigate the *representational content* of regions

- Information is represented in a distributed fashion
- fine-grained spatial structure across voxels



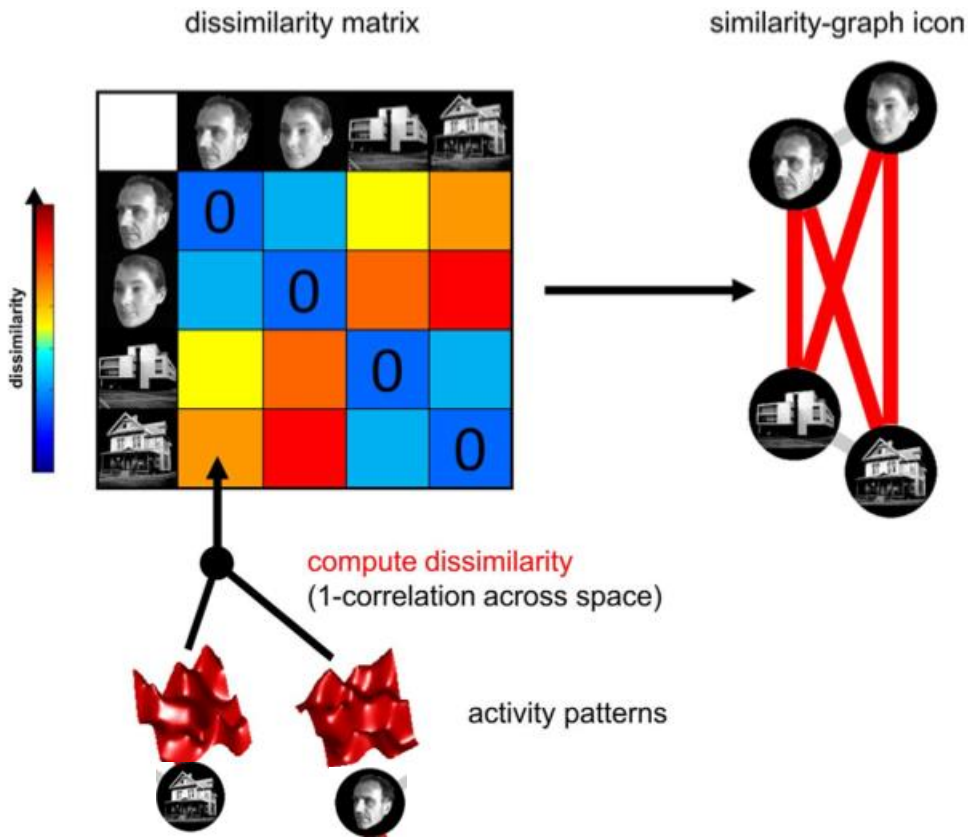
Multi-variate pattern analysis



Norman et al. 2006

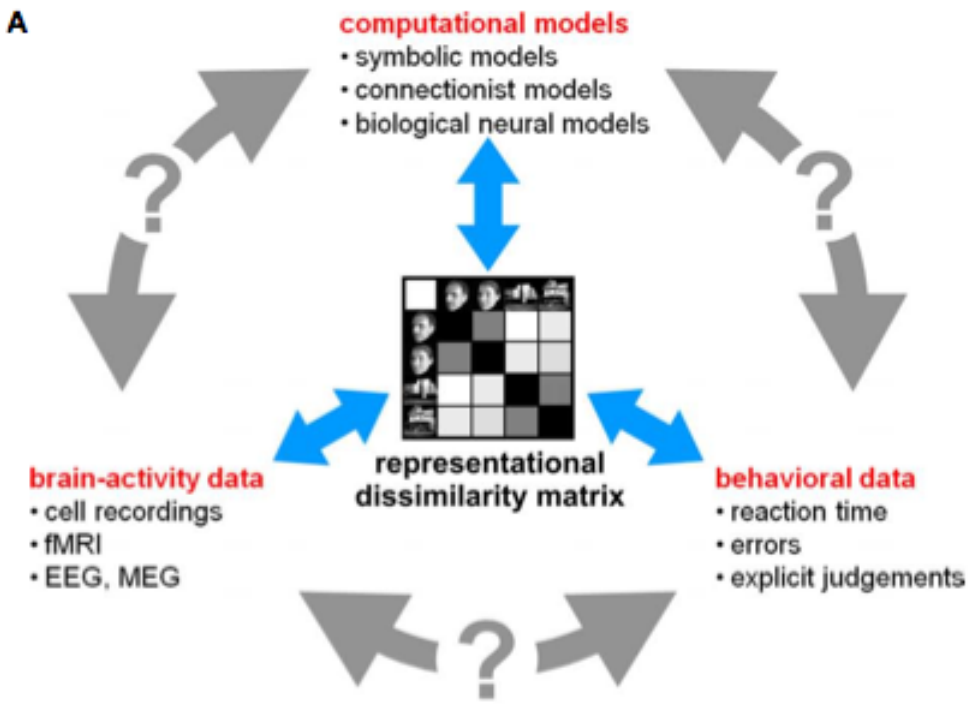
Representational similarity analysis

Comparing representations across experimental conditions



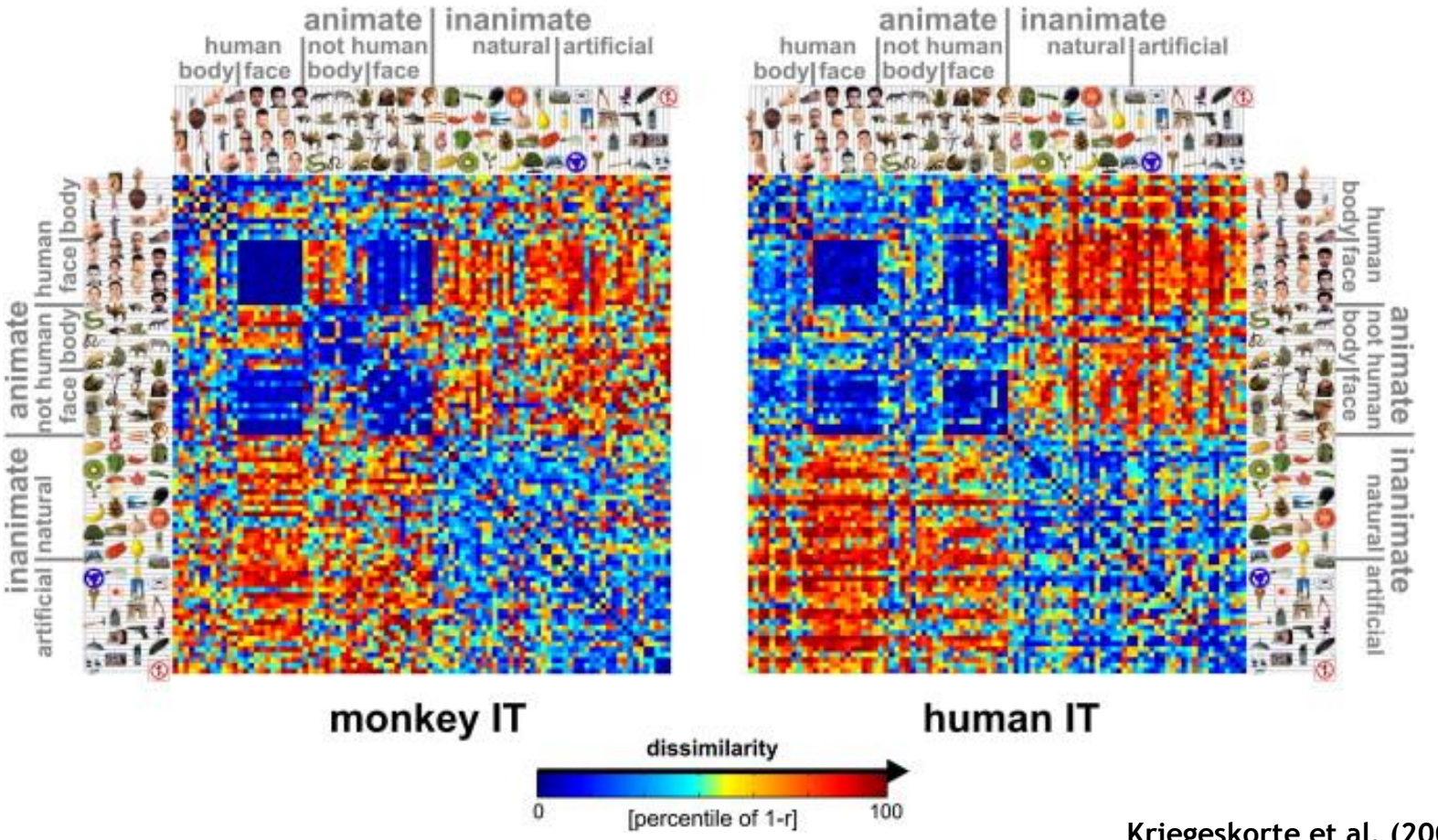
Kriegeskorte **et al. (2008)**

Connecting research branches



Kriegeskorte et al. (2008)

Matching object representations in inferior temporal cortex of man and monkey



Kriegeskorte et al. (2008)

Questions?