Lab session 7:

Midterm review of lab material

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Session no.	Date (all Wednesday)	Topic/activity	Topic of quiz that day	Topic of lab write-up (assignment) due that day
1	13-Jan	Lab overview		
2	20-Jan	Brain anatomy		
3	27-Jan	Data preprocessing	Brain anatomy (no. 1)	
4	3-Feb	Set up GLM model	Functional brain anatomy (no. 2)	
5	10-Feb	Single-subject SPM contrasts	Data preprocessing and GLM model (no. 3)	Brain anatomy (no. 1)
6	17-Feb	Within-subject MVPA		Single-subject SPM contrasts (no. 2)
7	24-Feb	SIBR tour and review for mid-term exam		Within-subject MVPA (no. 3)
No lab	2-Mar	No lab (mid-term exam)		
No lab	9-Mar	No lab (spring break)		
8	16-Mar	Group-level SPM contrasts		
9	23-Mar	Between-subjects MVPA		Group-level SPM contrasts (no. 4)
10	30-Mar	Voxel-wise modeling		Between-subjects MVPA (no. 5)
11	6-Apr	Functional connectivity analysis (*no assignment*)		
12	13-Apr	Review for final exam		Voxel-wise modeling (no. 6)
No lab	20-Apr	No lab		
No lab	27-Apr	No lab (final exam)		

Upon successful completion of this lab course, you should be able to…

- Process raw fMRI data in preparation for statistical data analysis;
- Visualize brain activation to discover which brain regions are active, or inactive, in a given cognitive or behavioral task;
- Conduct "mind-reading" to infer what a person is thinking about based on distributed brain activation patterns;
- ***LATER:*** *Predict the brain activation pattern associated with thinking about a specific concept; and*
- State and elaborate on how the above data analysis methods complement each other

General sequence of data preprocessing and analysis

For each individual subject: → **1 Data preprocessing** → **2** Set up (specify conditions) and run GLM model → **3** Generate condition contrasts (e.g. Tools – Buildings)

Across **all subjects in a group:** → **4** Generate condition contrasts (e.g. Tools – Buildings)

If there are multiple groups of subjects ***(in our case, no)*****:** → **5** Condition contrasts between two groups (e.g. Depressed – Control)

NOTE: Data analysis of each individual subject is not limited to GLM condition contrasts (e.g. one can do MVPA)

Sample midterm question about **data preprocessing**

(*NOTE: all sample questions are somewhat easier than exam questions*)

- List four preprocessing steps (in the typical order in which they are done), and explain *what* each does, and *why* each is done
  - ANSWER: next slide

Data preprocessing sequence

1. Motion correction
    - Ensures that brain activity of voxel *i* corresponds to the same volume of brain tissue throughout whole experiment

2. Slice-time correction
    - Brain slices are not collected simultaneously each image acquisition; need to correct for this

3. Spatial normalization
    - Morphs each subject's brain to a common/template brain

4. Smoothing
    - Reduces amount of noise per voxel by averaging over nearby voxels

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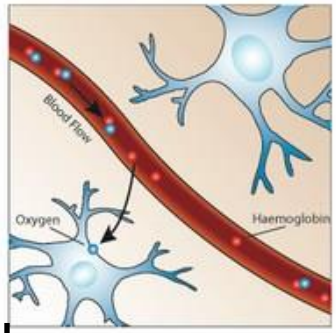
Sample midterm question about **setting up GLM analysis**

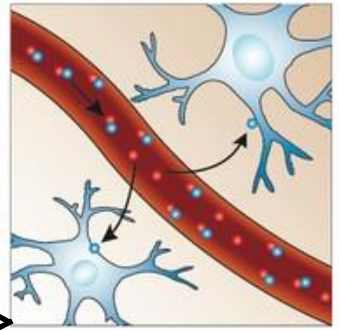
- What does "HRF" stand for in GLM analysis? *What* is it used for measuring, and *how* is it used?
  - ANSWER: HRF = Hemodynamic response function, which is a rise-and-fall waveform that reflects changes in blood flow. It is drawn-out and delayed relative to the brief period of neural activity that precedes it. The HRF is used to measure the brain activation level associated with a condition in GLM (general linear model) analysis. The "beta" value is the brain activation level that is estimated, one beta per condition. GLM analysis is performed on each voxel separately (after smoothing is performed on the raw data). The HRF is used in measuring beta values by fitting the HRF to the observed MRI signal. Both the degree of fit, and the magnitude (height, or amplitude) of the fitted waveform, determine the beta value of a condition. The same HRF shape is assumed for all brain regions, participants, and conditions.

The *H*emodynamic *R*esponse *F*unction of the BOLD MRI signal

- MRI signal in the brain increases by a few % points after there are increases in neural activity



Resting


Activated

D: ***4-5s rise***

E: ***5s long plateau (Evidence of neural activity shows up as the rise and plateau)***

G: ***Return to baseline (or undershoot)***

C: ***2s delay***

Time

A: ***Pre-activation baseline of MRI signal***

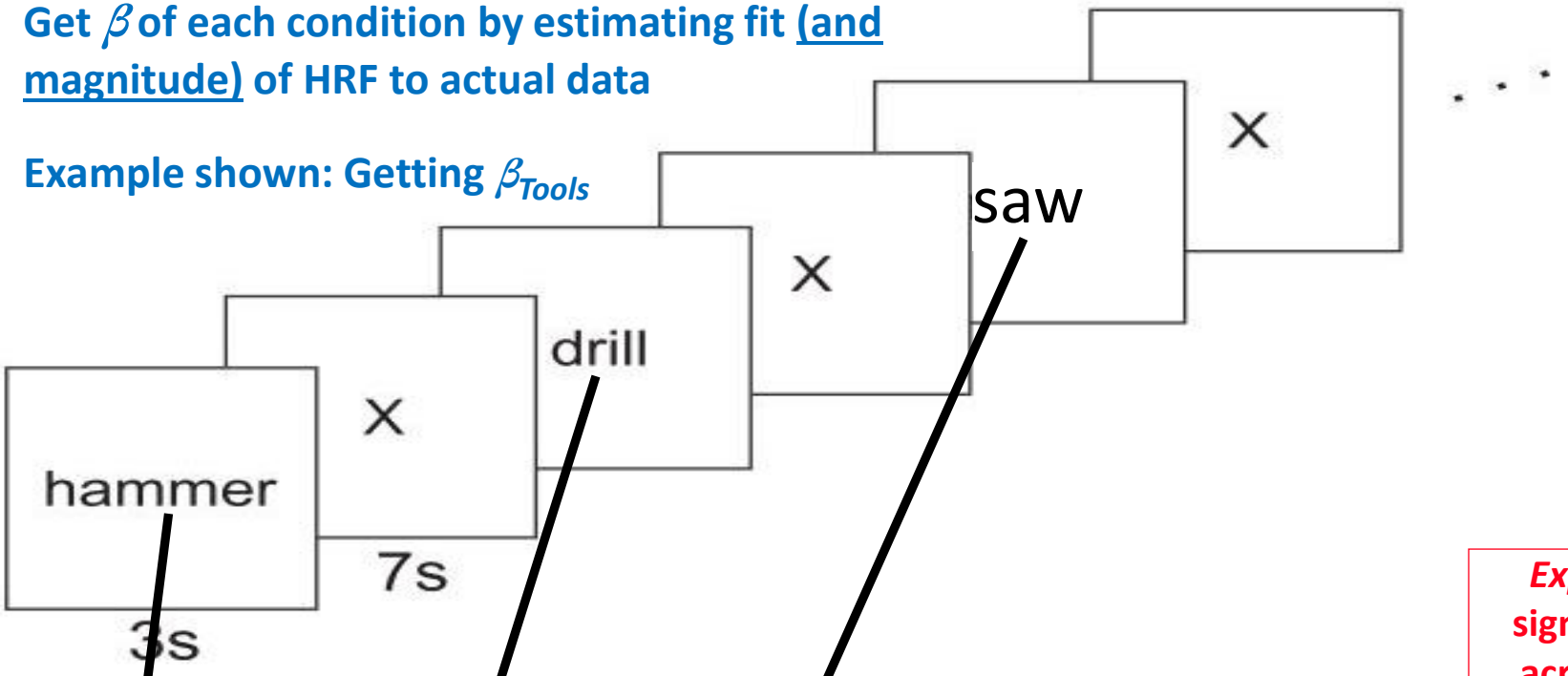
B: ***Neural activity onset*** **(lasts for, say, *3s*)**

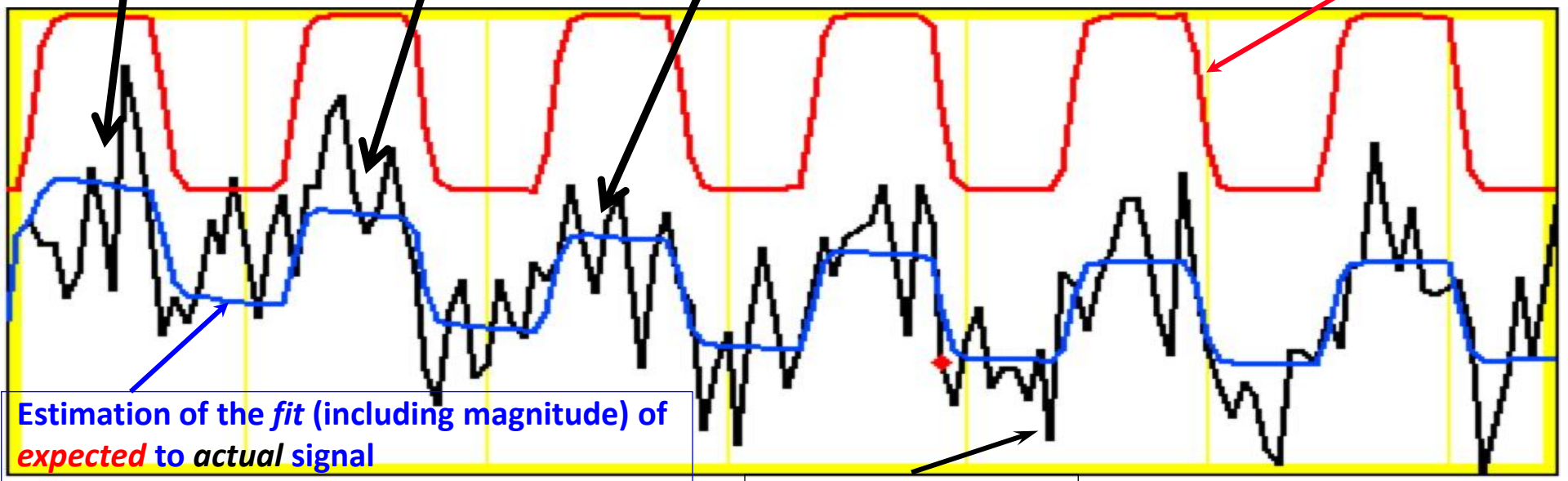
F: ***4-6s fall***

Image adapted from AFNI web site

Get β of each condition by estimating fit (and magnitude) of HRF to actual data

Example shown: Getting β_{Tools}





Expected MRI signal (the HRF) across all trials

Estimation of the *fit* (including magnitude) of *expected* to *actual* signal

(Determines the value of β_{Tools} at each voxel)

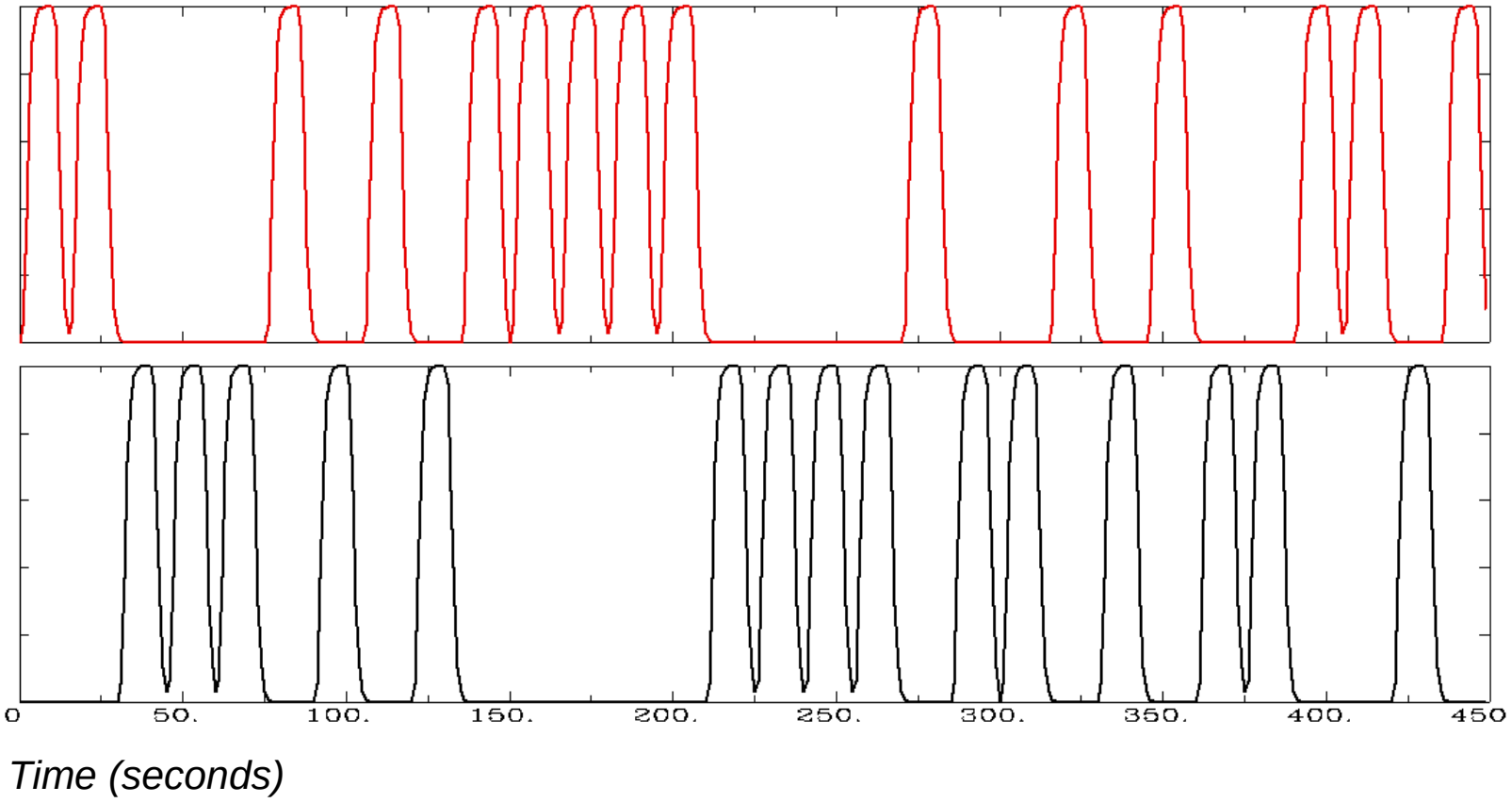
Actual MRI signal across all trials

Waveform image from AFNI web site

Estimate how HRF at each trial of a condition fits (and its magnitude) the actual MRI signal

Tools

Build -ings



(*Expected signal at each trial of the Tools and Buildings conditions shown above*)

What is “brain activation level” in fMRI?

- Voxel-wise GLM regression model: $y = \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \ldots + \beta_n x_n + \varepsilon$

  y: MRI signal (time series) at a voxel – **different** across voxels

  x: independent variables/conditions (regressors) – **same** across voxels

  β: regression coefficients (HRF fits/magnitudes) – **different** across voxels

  ε: residuals (data unaccounted for by model) – **different** across voxels

We estimate β for each condition (e.g. β_{Tools} and $\beta_{Buildings}$)

… and we also estimate the β for Baseline/”Resting”

General sequence of data preprocessing and analysis

For each individual subject: → **1** Data preprocessing → **2** Set up (specify conditions) and run GLM model → **3** **Generate condition contrasts (e.g. Tools – Buildings)** →

Across **all subjects in a group:** → **4** Generate condition contrasts (e.g. Tools – Buildings)

If there are multiple groups of subjects ***(in our case, no)*****:** → **5** Condition contrasts between two groups (e.g. Depressed – Control)

Sample midterm questions about **GLM/SPM condition contrasts**

- Why is a condition contrasted to baseline/resting in GLM analysis? What activation is being "subtracted"?
  - ANSWER: A condition (say, the "Tools" condition) is contrasted against baseline because a researcher is interested in discovering the brain activation that is uniquely associated with that condition. Baseline activity is "subtracted" away, leaving brain areas that activate more (or less) to that condition versus baseline. This is done because practically *all* parts of the brain are active to some extent no matter what a person is doing. To determine the brain areas *uniquely* active (or suppressed) during a condition, baseline brain activity must be subtracted out.

- Why else might a condition be included in a contrast in GLM analysis (besides baseline/resting)?
  - ANSWER: Sometimes two different conditions activate the *same* brain regions when each one is separately contrasted against baseline. For example, construction tools and eating utensils might *each* activate motor regions when each is separately compared to baseline. To determine whether one of these two tool conditions activates motor regions *more* than the other, they would be contrasted against each other. Generally, contrasting a particular condition against similar conditions makes the result increasingly specific (unique) to that condition, e.g. *Tools* vs. other objects = activation specific to Tools, minus activation associated with objects in general.

Programming statistical β contrasts to compare…

- Activation of one condition vs. Baseline ("Resting")
- Activation between two different conditions
  - Baseline cancels out (see below)

Contrast	Baseline multiplier	Tools multiplier	Buildings multiplier	Statistical result (*t-stat and p-value*) in <u>each</u> voxel
$\beta_{Tools} - \beta_{Baseline}$	-1	1	0	***Tools activation that is > "Resting"***
$\beta_{Buildings} - \beta_{Baseline}$	-1	0	1	***Buildings activation that is > "Resting"***
$\beta_{Tools} - \beta_{Buildings}$ *i.e. (Tools - Baseline) - (Buildings - Baseline)*	0	1	-1	***(Tools > "Resting") that is > (Buildings > "Resting")***
$\beta_{Buildings} - \beta_{Tools}$ *i.e. (Buildings - Baseline) - (Tools - Baseline)*	0	-1	1	***(Buildings > "Resting") that is > (Tools > "Resting")***

From our lab:
Multiplier vectors for β contrasts
Each category vs. average of others

Category no.	Contrast name	Baseline	1	2	3	4	5	6	7	8	9	10	11	12	Constant
1	Animals_vs_others	[0	11	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	0]
2	Bodyparts_vs_others	[0	-1	11	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	0]
3	Buildings_vs_others	[0	-1	-1	11	-1	-1	-1	-1	-1	-1	-1	-1	-1	0]
4	Buildingparts_vs_others	[0	-1	-1	-1	11	-1	-1	-1	-1	-1	-1	-1	-1	0]
5	Clothing_vs_others	[0	-1	-1	-1	-1	11	-1	-1	-1	-1	-1	-1	-1	0]
6	Furniture_vs_others	[0	-1	-1	-1	-1	-1	11	-1	-1	-1	-1	-1	-1	0]
7	Insects_vs_others	[0	-1	-1	-1	-1	-1	-1	11	-1	-1	-1	-1	-1	0]
8	Kitchen_vs_others	[0	-1	-1	-1	-1	-1	-1	-1	11	-1	-1	-1	-1	0]
9	Manmade_vs_others	[0	-1	-1	-1	-1	-1	-1	-1	-1	11	-1	-1	-1	0]
10	Tools_vs_others	[0	-1	-1	-1	-1	-1	-1	-1	-1	-1	11	-1	-1	0]
11	Vegetables_vs_others	[0	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	11	-1	0]
12	Vehicles_vs_others	[0	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	11	0]

… we can also do MVPA (instead of or in addition to GLM analysis)

For each individual subject: → **1** Data preprocessing → **2** Set up (specify conditions) and run GLM model → **3** Generate condition contrasts (e.g. Tools – Buildings)

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If there are multiple groups of subjects ***(in our case, no)*****:** → **5** Condition contrasts between two groups (e.g. Depressed – Control)

NOTE: Data analysis of each individual subject is not limited to GLM condition contrasts (e.g. one can do MVPA)

Sample midterm questions about **MVPA**

- Describe major differences between what GLM analysis and MVPA do
  - ANSWER: GLM analysis considers each single voxel *in isolation.* GLM analysis is used primarily to show where activation is higher (or lower) for a condition (i.e. a set of stimuli or events), relative to baseline or another condition.
  - ... on the other hand, MVPA considers *interactions* of voxels, and compares multi-voxel *patterns* of activation among different individual stimuli. That is, MVPA asks whether individual stimuli can be distinguished from each other from their activation patterns. If so, it is likely that those voxel patterns store information about the stimuli (for example, information about the different features that jointly define an object concept). MVPA uses the data to a fuller extent, and is thus more sensitive, than GLM analysis.

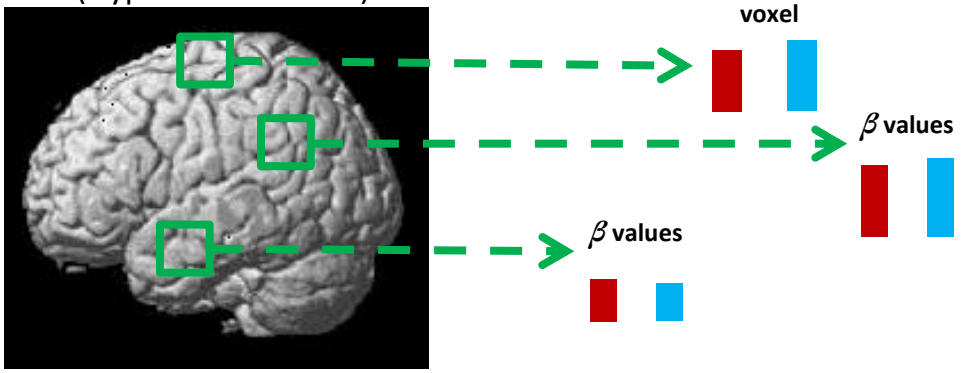
- If GLM analysis reveals no differences in activation between conditions, does this imply that MVPA would be unable to detect activation differences? Why?
  - ANSWER: No, this is not implied. MVPA can detect differences in multi-voxel activation patterns among different stimuli *even* when each separate voxel's activation levels across all the different stimuli are only slightly different from each other. See next slide for visual demonstration of this.

Are there differences in activation between object concepts? GLM and MVPA approach this question differently

Tools vs. **other** object categories

GLM contrast in each voxel

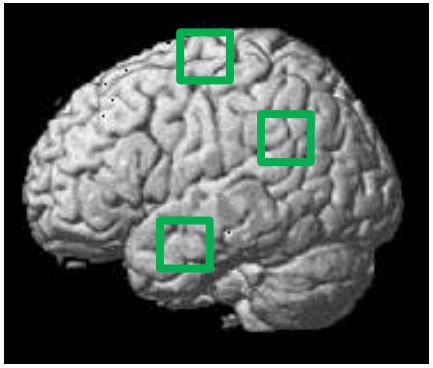
(Hypothetical result)



- GLM considers each single voxel *in isolation*
- Within a voxel, GLM compares conditions' activation *levels* (β)
- On the left: It appears **Tools** does not activate the brain differently, compared to **other** categories, in each voxel (see the three voxels)

MVPA using pattern of 3 voxels

Get response signal from each selected voxel (not to scale) for each object concept…



Object concept	Voxel activation pattern (3 voxels)
hammer:	
saw:	
church:	
butterfly:	
.	.
.	.
.	.

- MVPA considers *interactions* of voxels, and compares *patterns*; it uses the data to a fuller extent, and is thus more sensitive, than GLM
- On the left: Although GLM (above) shows no significant difference in activation *levels* in any single voxel for **Tools** vs. **others**, the voxel activation *patterns* between **Tools** and **other** concepts *are* different (i.e. are reliably distinguishable)

Pseudo-mathematical definition of MVPA

A classifier is a mapping function *f* of the form:

f: *voxel activation pattern* $\rightarrow \boldsymbol{Y}_i$, $i = 1,\ldots,m$

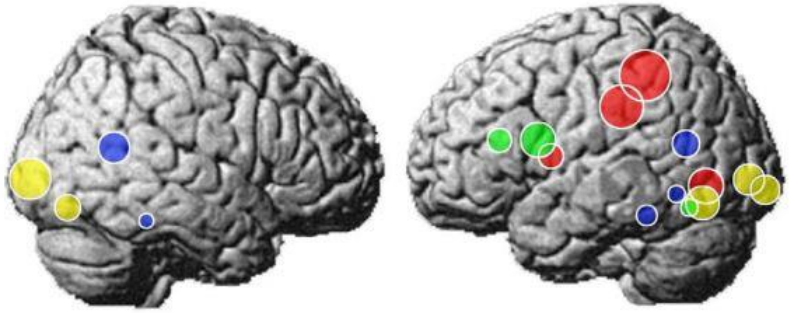
- Where $\boldsymbol{Y}_i$ are the $m = 60$ object concepts (*leg, chair, car,...*)
- And where the *voxel activation pattern* is the response signals of the n selected voxels (i.e. selected features)

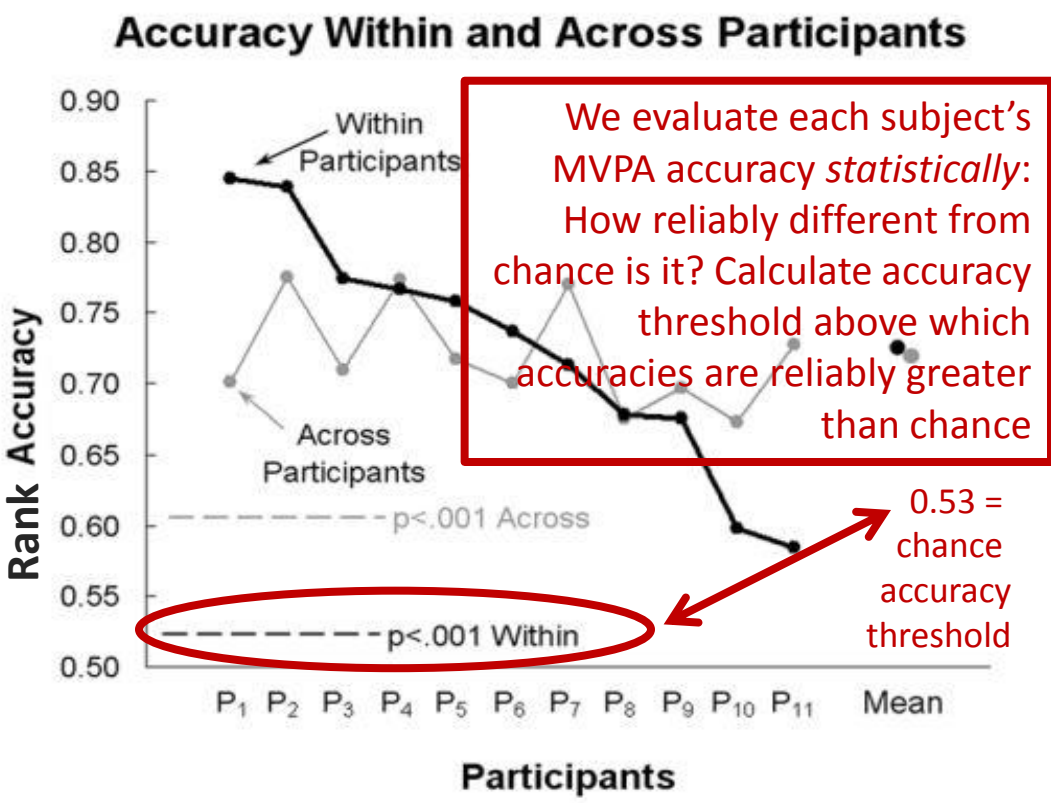
Interpreting MVPA results

- Only when we successfully classify using voxels from (*i*) *specific* and (*ii*) *functionally interpretable* brain areas…

- … can we suggest that those activation patterns are the neural codes by which object concept meaning is *represented* (i.e. stored, processed) in the brain

We can classify individual object concepts using a relatively small number of functionally interpretable voxels (Just et al., 2010)





Category	Exemplar 1	Exemplar 2	Exemplar 3	Exemplar 4	Exemplar 5
body parts	leg	arm	eye	foot	hand
furniture	chair	table	bed	desk	dresser
vehicles	car	airplane	train	truck	bicycle
animals	horse	dog	bear	cow	cat
kitchen utensils	glass	knife	bottle	cup	spoon
tools	chisel	hammer	screwdriver	pliers	saw
buildings	apartment	barn	house	church	igloo
building parts	window	door	chimney	closet	arch
clothing	coat	dress	shirt	skirt	pants
insects	fly	ant	bee	butterfly	beetle
vegetables	lettuce	tomato	carrot	corn	celery
man-made objects	refrigerator	key	telephone	watch	bell

Lastly…

- See Blackboard for:
  - Keys to select quizzes and assignments

- See past slides for refreshers on:
  - Orientation terminology (e.g. *posterior*, etc.)
  - Planes (i.e. *coronal*, *axial*, *sagittal*)
  - Brain anatomy (including general brain function)

References

Just, M. A., Cherkassky, V. L., Aryal, S., & Mitchell, T. M. (2010). A neurosemantic theory of concrete noun representation based on the underlying brain codes. PLoS One, 5(1), e8622. doi:10.1371/journal.pone.0008622