PPI Analyses

If two brain regions are working together (e.g., cooperatively) during a task…

then the activity of one region should predict activity in the other,

and the regions are said to be ***functionally connected***

Functional connections between regions may be stronger in certain experimental conditions

In a ***Psychophysiological Interaction (PPI)*** analysis, we consider

the *physiological* activity of some (seed) region

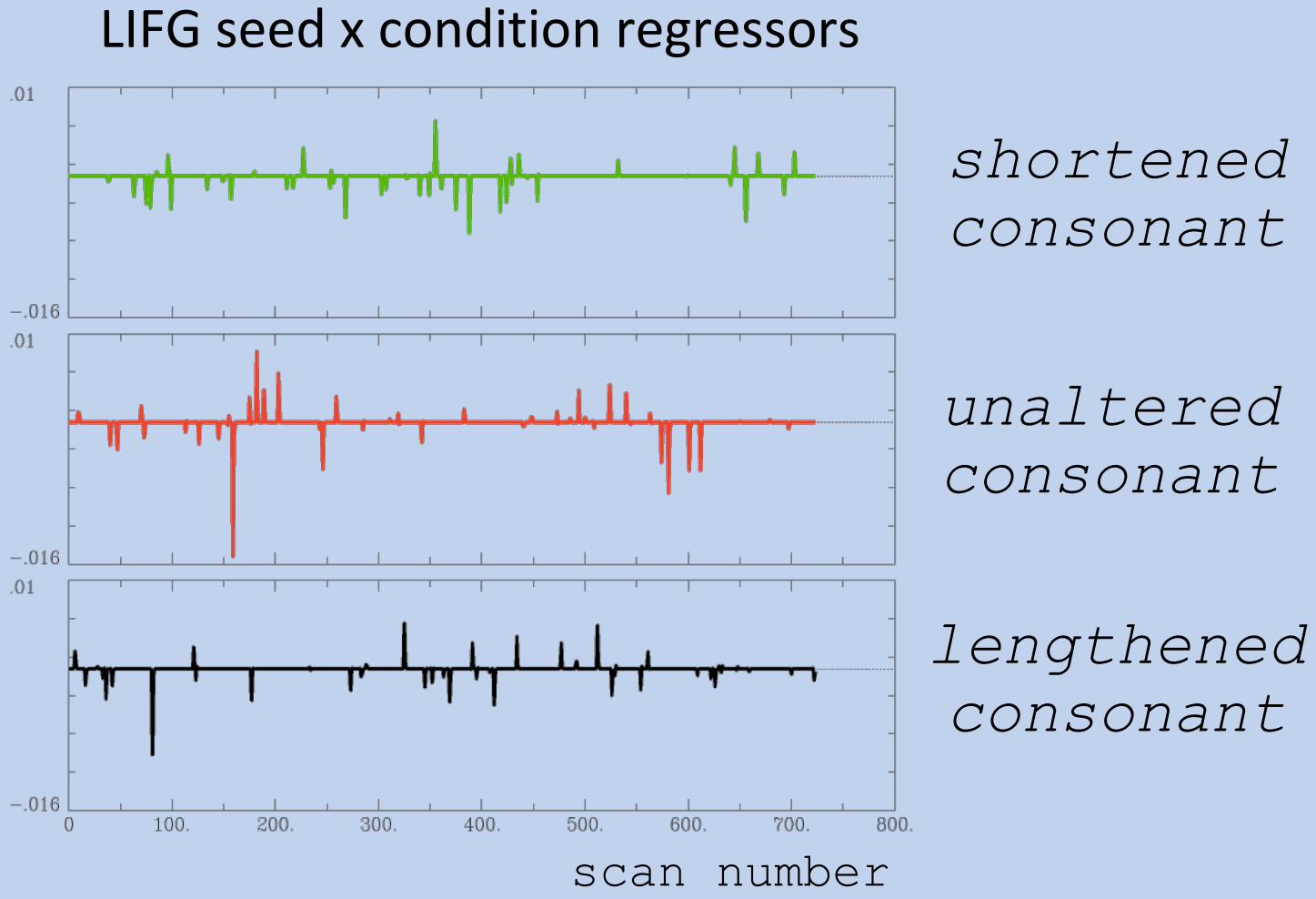
in each of the *psychological* conditions of interest

and how each set of activity predicts activation elsewhere in the brain

In a PPI analysis, we use *seed x condition* regressors, which reflect the activity of the seed region during each condition

Consider a study where

- we use LIFG as a seed
- and are interested in how connectivity with seed changes based on a factor of *Acoustic Modification*



Trying to predict activation

Regressors:

Activity of seed

Predicted activation in each condition

Activity of seed in each condition

Participant motion

```
3dDeconvolve \
    -input ${subj}/renamed/briks/proc_py/${subj}.proc_py/pb03_${subj}_r*_scale+tlrc.HEAD
    \
    -censor timing/censor/${subj}_censor.1D \
    -polort 5 \
    -num_stimts 13 \
    \
    -stim_file 1 gppi/LIFG_p05_TokenType/seed/${subj}_LIFG_p05_rall_detrend_ts.1D \
    -stim_label 1 LIFGseed \
    \
    -stim_file 2 timing/gppi/GAM_files/shortened.xmat.1D \
    -stim_label 2 Shortened \
    -stim_file 3 timing/gppi/GAM_files/unaltered.xmat.1D \
    -stim_label 3 Unaltered \
    -stim_file 4 timing/gppi/GAM_files/lengthened.xmat.1D \
    -stim_label 4 Lengthened \
    \
    -stim_file 5 gppi/LIFG_p05_TokenType/seed/${subj}_Inter_Neur_LIFG_shortened.1D \
    -stim_label 5 shortenedXseed \
    -stim_file 6 gppi/LIFG_p05_TokenType/seed/${subj}_Inter_Neur_LIFG_unaltered.1D \
    -stim_label 6 unalteredXseed \
    -stim_file 7 gppi/LIFG_p05_TokenType/seed/${subj}_Inter_Neur_LIFG_lengthened.1D \
    -stim_label 7 lengthenedXseed \
    \
    -stim_file 8 ${subj}/renamed/briks/proc_py/${subj}.proc_py/dfile_rall.1D'[0]' \
    -stim_label 8 roll     \
    -stim_file 9 ${subj}/renamed/briks/proc_py/${subj}.proc_py/dfile_rall.1D'[1]' \
    -stim_label 9 pitch \
    -stim_file 10 ${subj}/renamed/briks/proc_py/${subj}.proc_py/dfile_rall.1D'[2]' \
    -stim_label 10 yaw   \
    -stim_file 11 ${subj}/renamed/briks/proc_py/${subj}.proc_py/dfile_rall.1D'[3]' \
    -stim_label 11 z-axis    \
    -stim_file 12 ${subj}/renamed/briks/proc_py/${subj}.proc_py/dfile_rall.1D'[4]' \
    -stim_label 12 x-axis    \
    -stim_file 13 ${subj}/renamed/briks/proc_py/${subj}.proc_py/dfile_rall.1D'[5]' \
    -stim_label 13 y-axis    \
    \
    -fout -rout -tout -bout \
    -bucket ./gppi/LIFG_p05_TokenType/decon/${subj}_LIFG_p05_TokenType_gppi_decon
```

Seed selection

If your seed region is sensitive to Factor A, and connectivity with another region is modulated by Factor B, then there is an interaction between Factors A and B

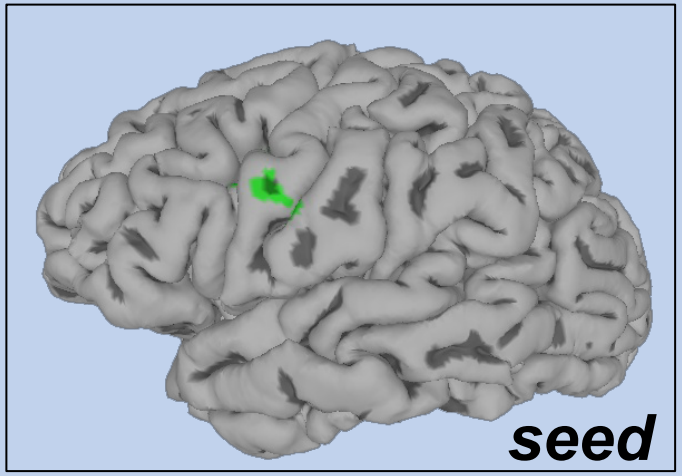
This is testing for an interaction in the pattern of functional connections between regions (rather than in some individual cluster, as in univariate analysis)

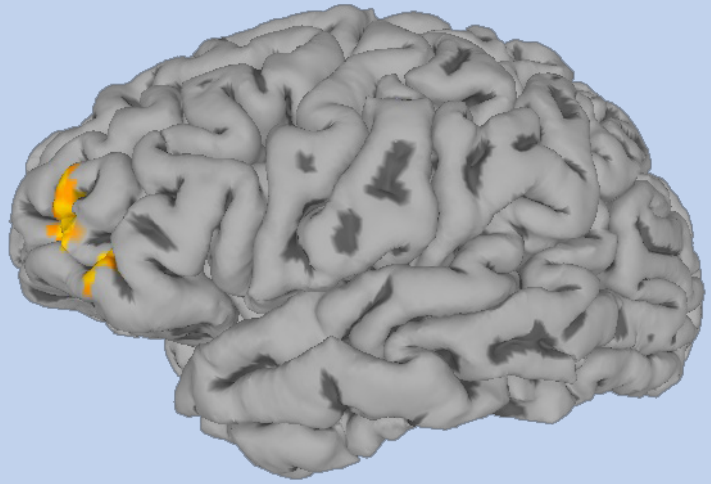
Example:

Seed region sensitive to *Lexical Competition*

Connectivity with seed changes depending *Acoustic Modification*

Connectivity with LIFG





Connectivity between LIFG and LMFG depends on Acoustic Modification

Example:

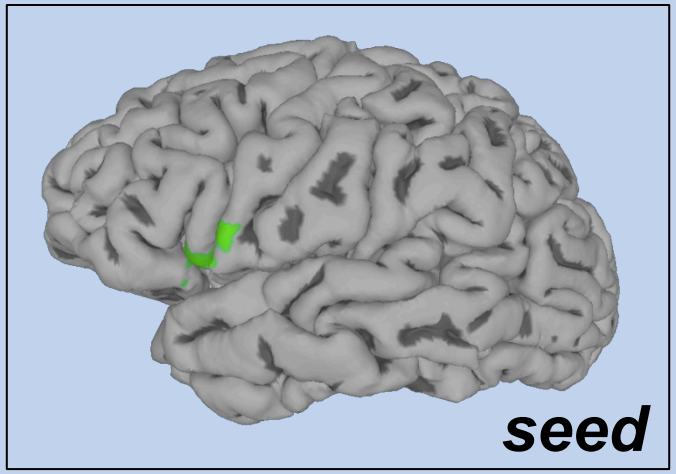
Univariate analysis found a frontal region that was sensitive to whether speech sounds came from the same sound category or different sound categories

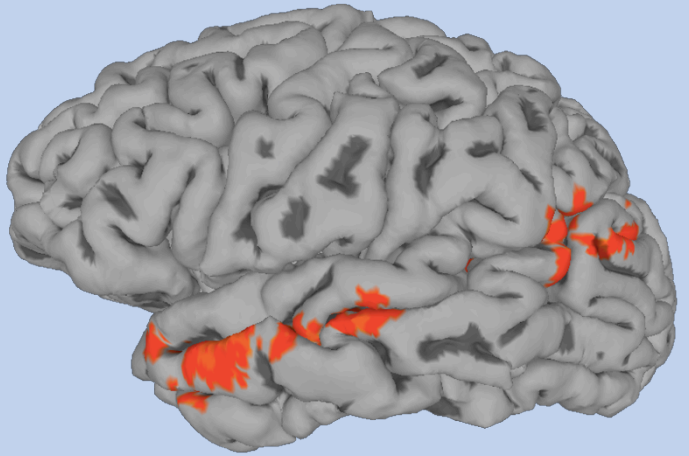
We asked how connectivity with this seed changed over time (from first scan to second)

Consistent with theoretical view that sensitivity to phonetic category structure emerges first in frontal regions, later in temporal

PPI analysis does not tell you about directionality!

Connectivity with LIFG





Connectivity increases from Scan 1 to Scan 2

Multi-Voxel Pattern Analyses (MVPA)

MVPA considers the *pattern* of brain activity across several voxels

Step 1: Estimate the pattern of brain activity for every single trial

Step 2: Train a machine to look at brain activity from a particular trial and categorize the trial as belonging to one class or another (based on, e.g., stimulus properties / behavioral response)

Step 3: Test classification of novel trials

Which voxels are informative for distinguishing between particular classes?

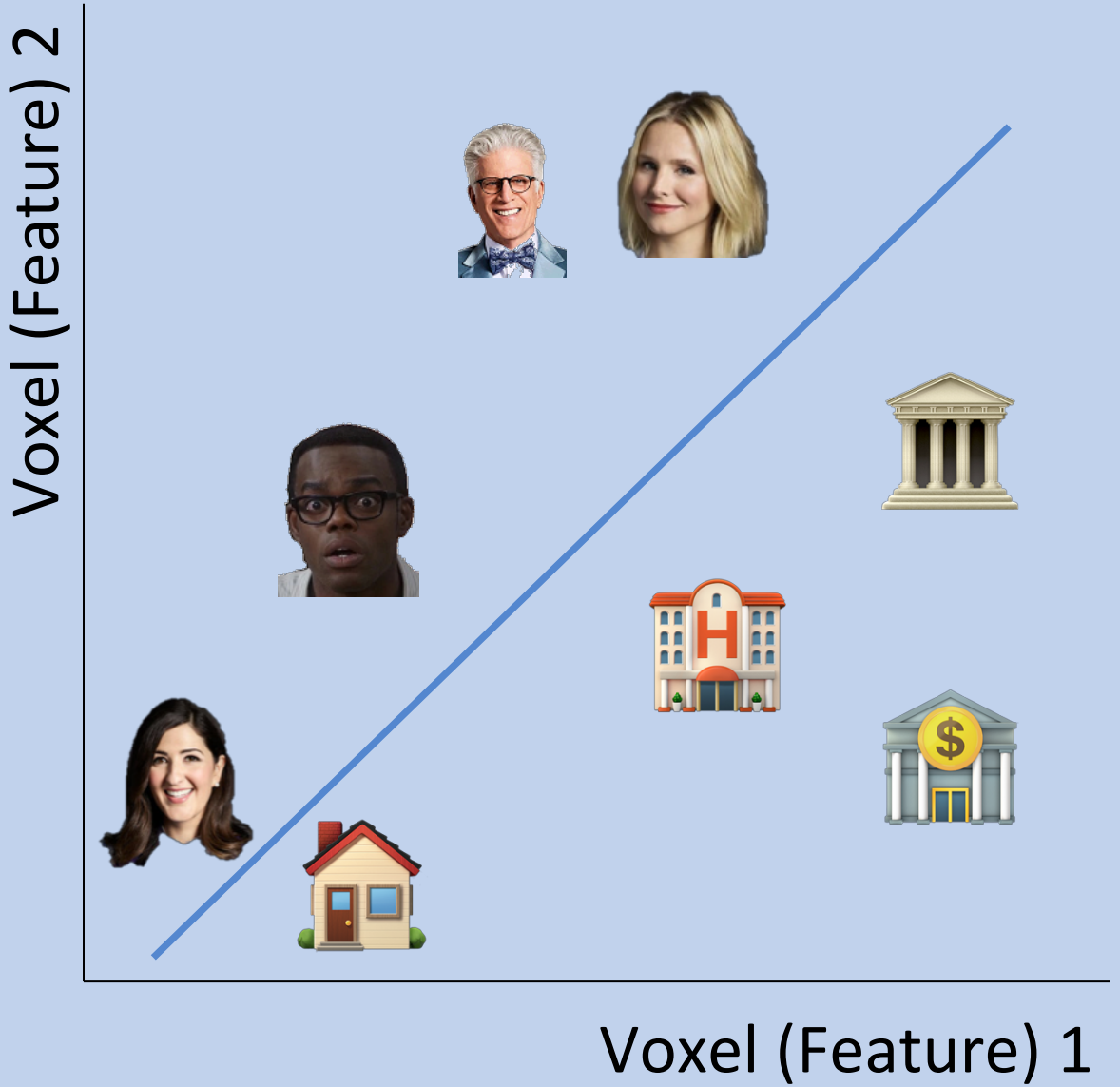
Estimating brain activity

- Rather than estimating a ß for each *condition* (as in a typical deconvolution), we estimate a ß for every *trial*
- *Slow event-related* or *block* design is optimal, since it is difficult to estimate trial-by-trial ßs when trials are close together
  - ➢ Downside: Fewer trials ➔ Less power for univariate analysis
- *Fast event-related* is possible, but ß estimates may not be as accurate – strategy is to do a separate regression for every trial (Mumford et al., 2012; 2014)

Beta map for a single trial

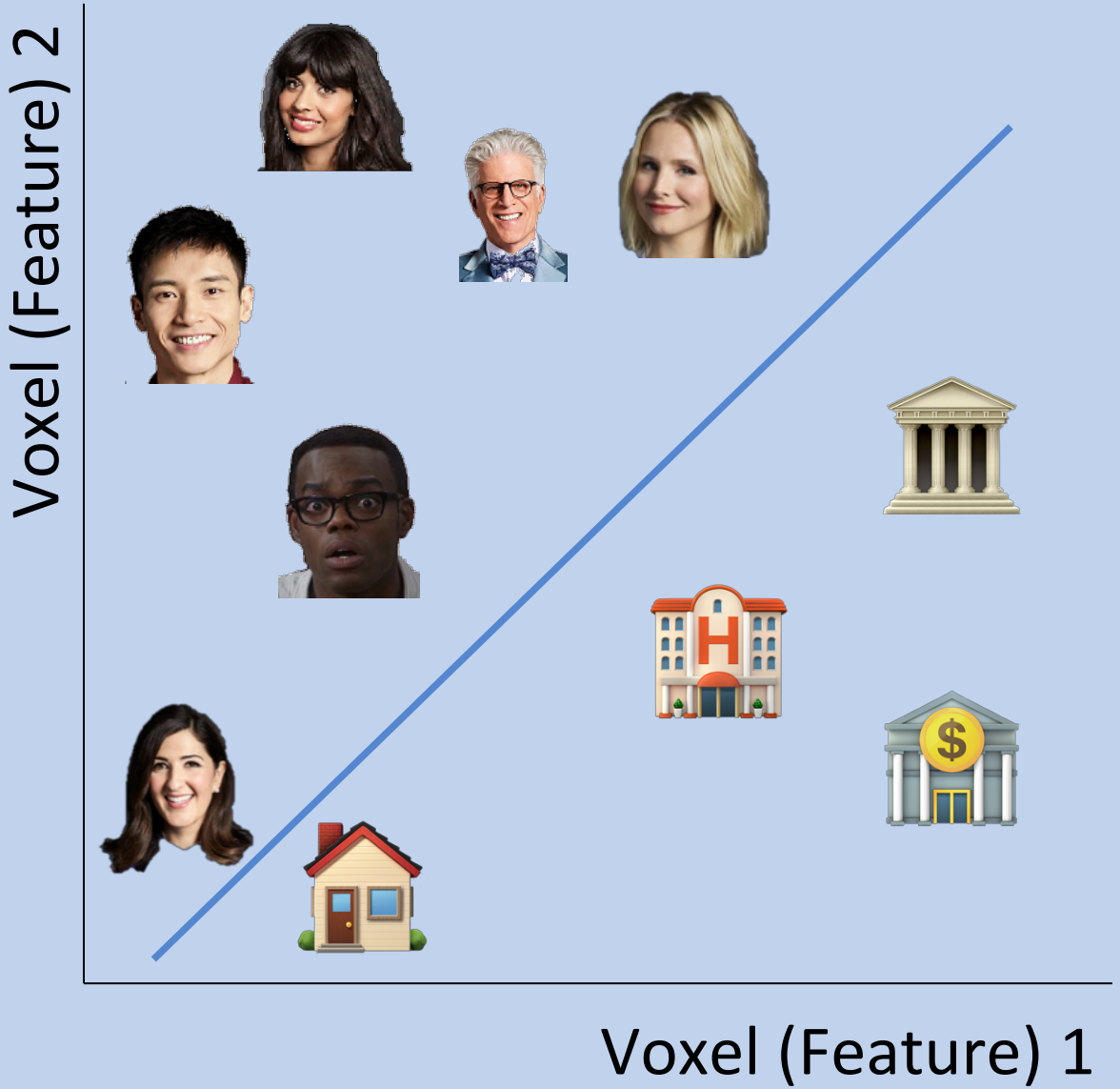
The logic of classification

- Suppose we are trying to classify houses and people
- Each trial corresponds to a point in plot (or a *vector* in multidimensional space)
- During training, machine finds optimal line (or hyperplane, in MDS) to maximize distance between classes
- *Vectors* near boundary *support machine*'s ability to classify (so called *support vector machines*)



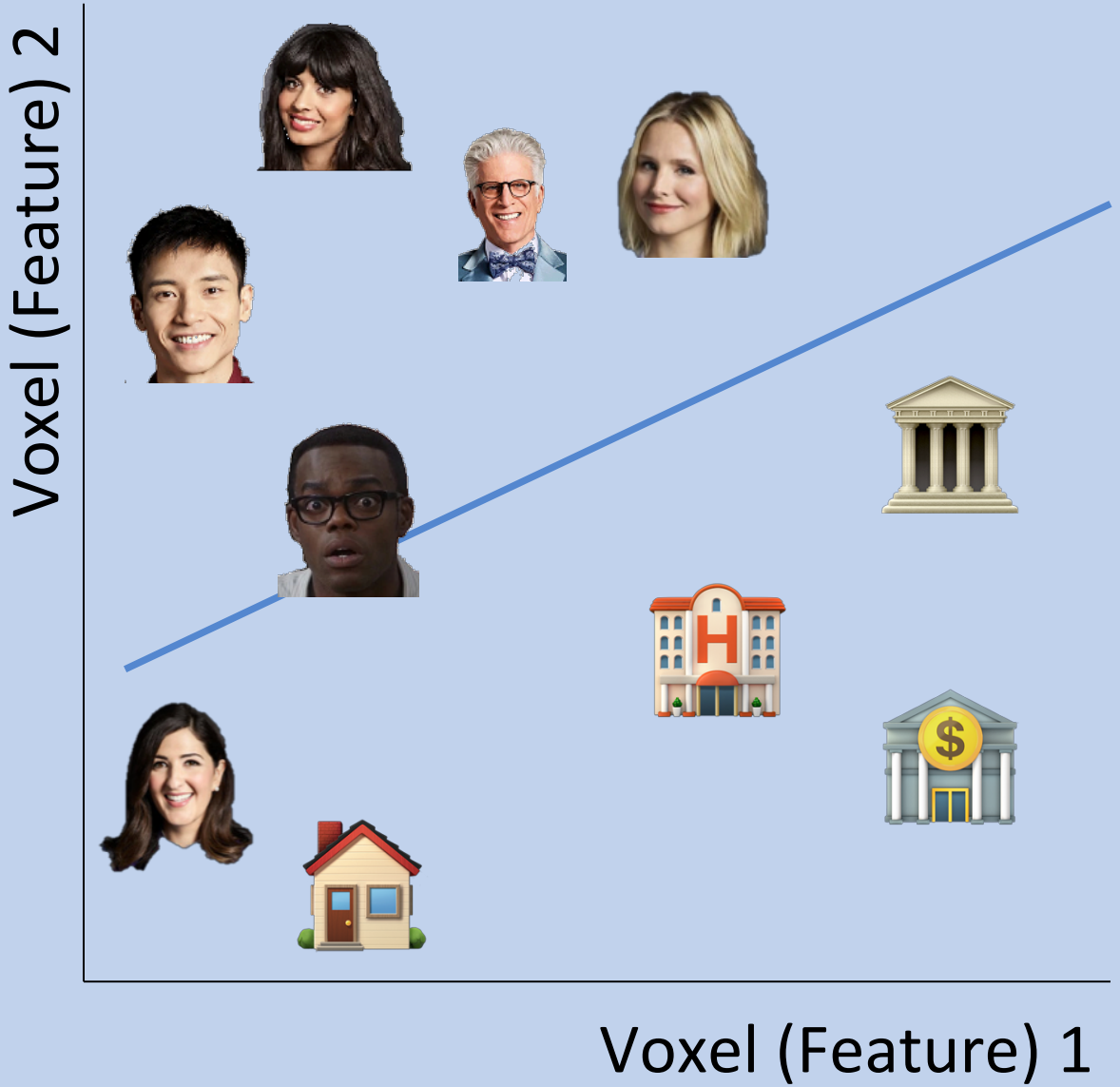
The logic of classification

- If training trials include those near the boundary, we will have good generalization to novel stimuli



The logic of classification

- If training trials include those near the boundary, we will have good generalization to novel stimuli
- But if training trials don't include the vectors that support the solution, we may have poor generalization to test stimuli
- For this reason, important to *cross-validate* classification solution: Rotate which stimuli are used for training and which for testing

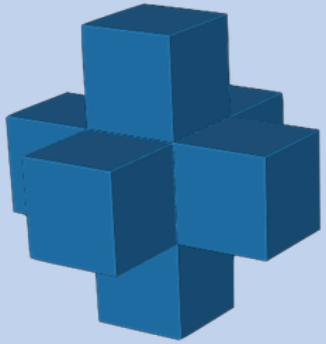


In examples so far, we have only been looking at two voxels, but real data will consider many more

Curse of dimensionality: If there are a lot of voxels, we've got a lot of features to learn. *Requires a lot of data and computing power*

How might we reduce the number of dimensions?

1) Limit the number of voxels (by choosing some **region of interest**)
2) Choose a classification algorithm that limits dimensions
   a) **Searchlight** – Train and test only within a roving cube; assumes informative voxels are near each other
   b) **Recursive Feature Elimination (RFE)** – Initially train on all voxels (features), then eliminate the ones that aren't as informative



How do we know if we have good classification?

- If we use a searchlight, calculate chance based on how many options there are (e.g., 2 classes ➔ chance = 50%)
- Using RFE artificially inflates chance (because throwing least uninformative voxels)
  - ➢ Estimate chance by running permutations, where labels are assigned randomly

Additional Reading

De Martino, F., Valente, G., Staeren, N., Ashburner, J., Goebel, R., & Formisano, E. (2008). Combining multivariate voxel selection and support vector machines for mapping and classification of fMRI spatial patterns. *Neuroimage*, *43*(1), 44-58.

Goebel, R. (2014). Multi-Voxel Pattern Analysis (MVPA). Retrieved from http://www.brainvoyager.com/bvqx/doc/UsersGuide/MVPA/MultiVoxelPatternAnalysisMVPA.html

Mumford, J. A., Turner, B. O., Ashby, F. G., & Poldrack, R. A. (2012). Deconvolving BOLD activation in event-related designs for multivoxel pattern classification analyses. *Neuroimage*, *59*(3), 2636-2643.

Mumford, J. A., Davis, T., & Poldrack, R. A. (2014). The impact of study design on pattern estimation for single-trial multivariate pattern analysis. *Neuroimage*, *103*, 130-138.

O'Reilly, J. X., Woolrich, M. W., Behrens, T. E., Smith, S. M., & Johansen-Berg, H. (2012). Tools of the trade: Psychophysiological interactions and functional connectivity. *Social Cognitive and Affective Neuroscience*, *7*(5), 604-609.