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HST.583 Functional Magnetic Resonance Imaging: Data Acquisition and Analysis
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Laboratory 1: Introduction to fMRI Data Analysis

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Instructions

Get fMRI data from internet

1. First log on to the iMac using your Athena login and password.
2. Click on Safari in the dock at the bottom of the screen (looks like a compass); this is Mac OS X's internet browser.
3. Type in www.neurolens.org into the address field.
4. Click on "Tutorials" from top links.
5. Right click on "Data and PDF document (29 megs)" under Tutorial 1, and choose "Download linked files as ..."
6. Click on "Desktop" under "Places" on left pane; then click the "Save" button to save *Tutorial1.zip* onto your Mac desktop.
7. Click on *Tutorial1.zip* which will decompress into the *Tutorial1* folder.

Run Neurolens fMRI Analysis Software

1. Click on Spotlight which is the little magnifying glass in the top right corner of your screen, a blue text field bar will open.
2. Type in "Neurolens"
3. Click on the Neurolens icon which should be the "Top Hit". This will open Neurolens; you will see it in the dock.
4. Right-click on the Neurolens icon in the dock, and choose "Keep in Dock". This will keep the icon in the dock even after it quits.

Open tutorial document

1. We will be using a *modified* document for this tutorial, NOT the one that came with *Tutorial1.zip*!
2. Click the *Tutorial* folder. A new finder window will open up
3. Click on "MacData" under "Places" in left-hand plane.
4. Click on afs.course => other => HST.583
5. Double-click on "Tutorial1New.pdf"; this will open up the tutorial in a new window
6. Keep this window on your desktop; you can refer to it to complete the lab 1 exercises.

Load and analyze real fMRI data

1. Start following the instructions listed on page 5 of the tutorial, under *Exercise 1: Loading the DICOM files*. As a short-cut, you can just drag the *DICOM* sub-folder in the *Tutorial1* folder onto the Neurolens icon in the dock. This will load the data.
2. Continue through to exercise 4.

3. Answer the lab questions on subsequent page.
4. BONUS (if you have time): complete exercises 5 and 6.

Laboratory 1: Questions

Use Neurolens, the tutorial document, and your textbook to help answer all questions! Feel free to answer using graphical explanations (i.e. a sketch!)

1. Take a look at the $-\log(p)$ map you generated in exercise 4. Voxels whose time course match the model with statistical significance are non-zero (i.e. either yellow or blue, not green). There are two such regions located side-by-side near the posterior section (i.e. towards the rear) of the brain; this area is known as the visual cortex.

a. Do these regions appear to be in the right places based on how the visual fields map to the visual cortex? Explain.

Yes, these regions do appear to be in the right places. The contrast we use to generate this statistical map was $[1 -1]$, which yields positive t -statistic values corresponding to regions with a stronger response to the left-hemifield stimulus than to the right-hemifield stimulus, and negative t -statistic values corresponding to regions with stronger responses to the right-hemifield stimulus than the left. As a result, the *right* occipital lobe is the main region showing positives values, and the *left* region shows negative values. This is consistent with the *contralateral* retinotopic mapping of the visual system, i.e., the left hemifield is mapped onto the right side and the right hemifield is mapped on to the left one.

b. One of these regions is yellow (i.e. positive), and one is blue (i.e. negative). Why is this the case? Does the negative patch indicate a region of deactivation as opposed to activation?

The negative values in the left occipital area don't necessarily indicate deactivation, and most likely indicate activation. These values are negative because of the contrast we specify. These negative values indicate that those voxels in the left occipital area show weaker (less positive) response to the left-hemifield stimulus than to the right-hemifield one. In other words, the left occipital area may be activated by both types of stimuli (which can be shown by using the contrasts $[1 0]$ and $[0 1]$), it was just that the activation was stronger under the right-hemifield stimuli. In fact, if one examines the time series of the voxels in the left occipital area, one should be able to see that for most of the voxels, there is positive activation during the stimuli on both sides, but the response amplitude was apparently greater under the right stimuli than under the left ones. However, there are indeed some voxels in the left occipital area, especially

those located more rostrally and ventrally, which do appear to be deactivated by stimuli in the contralateral hemifield. This is true for both hemispheres.

c. There are also blue and yellow patches in other areas of the brain. Command-click on some of these voxels to see the corresponding time-course and model fit in the original data window. Do you think we have located new functional areas outside the visual cortex that respond to visual stimulation?

← Most of the other blue or yellow voxels are false positives and unlikely representative of additional functional areas (although it can't be completely ruled out). Most of them are located in or along the ventricles or along (but outside of) the ventral and lateral surfaces of the brain. These regions are known to be subject to susceptibility artifacts resulting from inhomogeneities where the brain tissue meets nasal or oral cavities, eye sockets, etc, or to motion problems that aren't entirely corrected (e.g. if the subject shifts a little to the left, then on the far right there's no brain where there used to be), or to other physiological sources of noise. The combination of the increased noise and the spatial smoothing probably made it look like there were areas of activation where there in fact weren't any.

← A couple of you suggested that a few blue areas corresponded to optic nerve and therefore were true activations; I accepted this. However, take a look at the time course; it suggests that the same stimulus produces _opposite effects_; i.e. our stimulus paradigm in both designs had two ON periods, and in this region, each of the ON periods produced opposite effects. Hard for me to believe this is physiological... Because of our [1 -1] contrast, it received a significant t-score. .

2. Why was spatial smoothing done when analyzing the fMRI data? Could we *not* smooth the data before model fitting? What would be benefits and drawbacks of this more direct approach?

← From Huettel, page 277:

← "All fMRI data have spatial correlation due to both functional similarity of adjacent brain regions and to blurring introduced by the vascular system. By using a filter that matches the expected spatial correlation of the data, one can increase SNR considerably with minimal loss of spatial resolution."

← Of course in reality, we don't know the spatial extent of the correlation, so we don't know the ideal filter size. As a result, we could indeed increase SNR by smoothing, but we could also lose some spatial resolution (drawback).

← Additionally, spatial smoothing will lower false-positive rate and random “salt and pepper” activations that are noise in reality. See figure on pg 277.

← We could of course not smooth the data to ensure the highest spatial resolution, but of course, we’ll take a hit in SNR; if we don’t have enough detection power, we could miss activation completely.

3. In this exercise, we performed model-fitting in one operation, implementing the two design regressors as well as the polynomial drift terms. Some researchers remove polynomial drift terms to first create a drift-corrected data set. They then perform their model-fitting using the design regressors on this drift-corrected set. Is this a better/ worse/ equivalent approach? Explain.

← This was a fun one, and you guys provided some great answers! Basically, I took most of your answers, if they were reasonably well thought out.

Having said that, I (and the two fMRI stats guys I checked with :-)) am a firm believer that if there is any chance that your design terms and drift terms have ANY degree of co-linearity (i.e. they are not completely orthogonal), you should include all terms in your model and perform multiple regression in a single step. You will get the highest t-scores this way. Essentially, if you fit in two steps, and there is there is real activation that can be modeled by the drift (i.e. drift and design are not orthogonal), you will remove this signal. This signal is essentially lost, and will not get fit by your real design matrix, whose betas contribute to the t-score. Now yes, even if you model in a single step, you will fit some of your design-related signal to drift terms - however, because you are ALSO fitting with the true design matrix (which should fit the activation-related signal better), you’ll get higher β_{design} and a smaller β_{drift} leading to a higher t-statistic. Another way of looking it at, is that your overall residual error will be smaller when all regressors are fit at once, since the fit is more “accurate”. This would improve the sensitivity in the activation maps, since the residual error goes into the denominator of the t-statistic fraction.

← Many of you suggested that a two-step approach will decrease your DOF, and therefore increase your t-score. This is true, but for most fMRI experiments with number of measurements in the 100’s, I think this is a very small effect; think about $\sqrt{200}$ versus $\sqrt{197}$. You’ll see that the better fit by performing multiple regression in one step has an overwhelming effect, most of time.

← Now, what if the design and drift terms are perfectly orthogonal?! Well, the two approaches are identical, save for the DOF!! The residuals and beta values should be exactly the same, and the more DOF will benefit the two-step approach, albeit very slightly.

← In sum, for most scenarios where there is significant independence between drift and true activation signal, either way works well, and results are similar. Use an extreme case as an example; consider a 60 s OFF period followed by a 60s ON period and a linear drift term. These terms are quite co-linear; if you model in two steps, you'll really miss activation.... Try it!

←

4. Run the Linear Modeling Action once more. After entering the design matrix, and specifying the contrasts, click on the "Outputs" tab. Unclick $-\log(p)$ and choose "Standard error for effect" check boxes. Change the "Threshold" level to zero. Click "Run". The standard error for effect window should pop-up.

a. Choose the standard error window; move from the inferior to superior (lower to higher) slices of the brain using the mouse pointer or the scroll-wheel. Notice that the orbits (eyes) are considerably brighter (i.e. positive) than most of the brain tissue. Why would this be the case?

b. Qualitatively, what is the standard error map telling you? For optimal detection, what would we like to see in this map? Explain.

← The standard error map is related to the variance of the residual time series, after linear fitting. T-score is computed by dividing the effect size by the standard error of effect map. So you want these values to be as small as possible, i.e. low variance in the residual signal, indicating either low noise or tight fit. For optimal detection, we'd like this map to be essentially near zero in our regions of interest.

← Now the orbits have essentially a high variance in the residual signal. For one, people move their eyes during an fMRI experiment! Second, the orbit is fluid filled, and thus is not as rigid as tissue. The fluid is more prone to slosh around (even slightly), from thermal motion, physiological motion, and even scanner vibration. This will also increase variance of the signal.

5. List three ways to increase activation detection sensitivity in fMRI and elaborate on why the methods would work. Answers can be from an experimental design, acquisition, or data analysis point-of-view.

← So many ways!!!

← Here's a list of a few:

- 1) More trials**
- 2) Longer blocks**
- 3) Higher field strengths**
- 4) Multichannel imaging coils**
- 5) Restrict head motion**

- 6) Monitor respiratory and cardiac signal to use as regressors**
- 7) Gate to cardiac signal**
- 8) Smooth data**
- 9) Temporally filter data to remove autocorrelation**
- 10) Design experiments s.t. design vectors are orthogonal to drift vectors**
- 11) Use FIR analysis if HRF is not well known**
- 12) Use model-free analysis if there is no prior info about expected signals**
- 13) Create tasks that better isolates cognitive area of interest**
- 14) Choose better TE to optimize BOLD contrast**