HST.583 Functional Magnetic Resonance Imaging: Data Acquisition and Analysis
Fall 2006

Final Exam
HST.583
December 18, 2006

Instructions:
There are 130 points on this exam, unevenly distributed through 7 problems.
Please immediately confirm that you have all 10 pages. This is a two-hour exam.

Read the whole exam first. **Write legibly**. Describe what you are thinking. Even if the final answer is wrong, you will be given credit for your reasoning and approach to the problem. Be efficient, assess what you can answer right away; divide your time so that you can cover all the problems, allocating less time to the easiest parts. Don't spend too much time on a single question. **Try not to leave questions blank; we cannot give partial credit without something written down.**
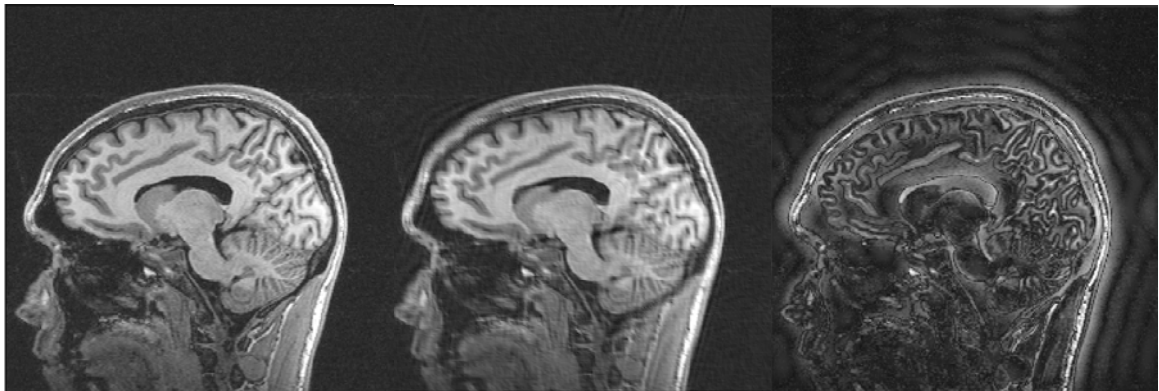
Question 1.
a)

Image courtesy of D.S. Bolar.

In the above set, the left figure represents the original image. The middle figure displays the image after discarding (**high, low**) frequency k-space information. The right figure displays the image after discarding (**high, low**) frequency k-space information. Please circle the correct bolded term. (**2 pts**)

b) From a k-space perspective (i.e. sampling in the frequency domain), how would you increase spatial resolution? The field-of-view (FOV)? (**4 pts**)

Question 2.
a) Describe experimentally how spatial SNR (SNR0) and temporal SNR (tSNR) can be estimated (you did this in lab 5). (**4 pts**)

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b) Which parameter, SNR0 or tSNR, is more relevant for functional imaging? Why? (Hint: think about fMRI statistics and relevant metrics of significance)   (*4 pts*)

c) Describe two ways to increase SNR0. Describe two ways to increase tSNR. (*4 pts*)

Question 2.

The deoxyhemoglobin dilution model predicts the following relationship between the BOLD MRI signal and CBF (figure a), and has been supported experimentally:
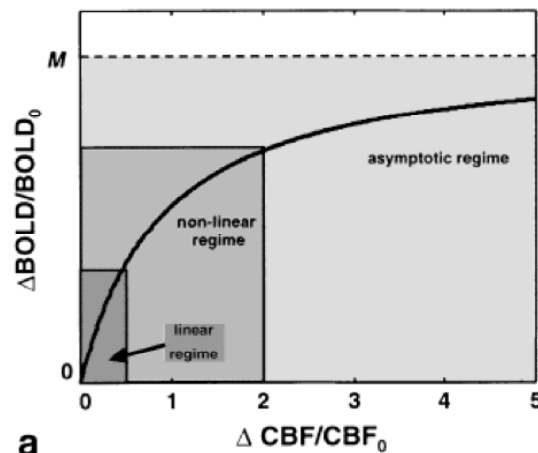
From Hoge, R., et al. "Investigation of BOLD signal dependence on cerebral blood flow and oxygen consumption: the deoxyhemoglobin dilution model." *Magnetic Resonance in Medicine* 42 no. 5 (1999): 849-63.
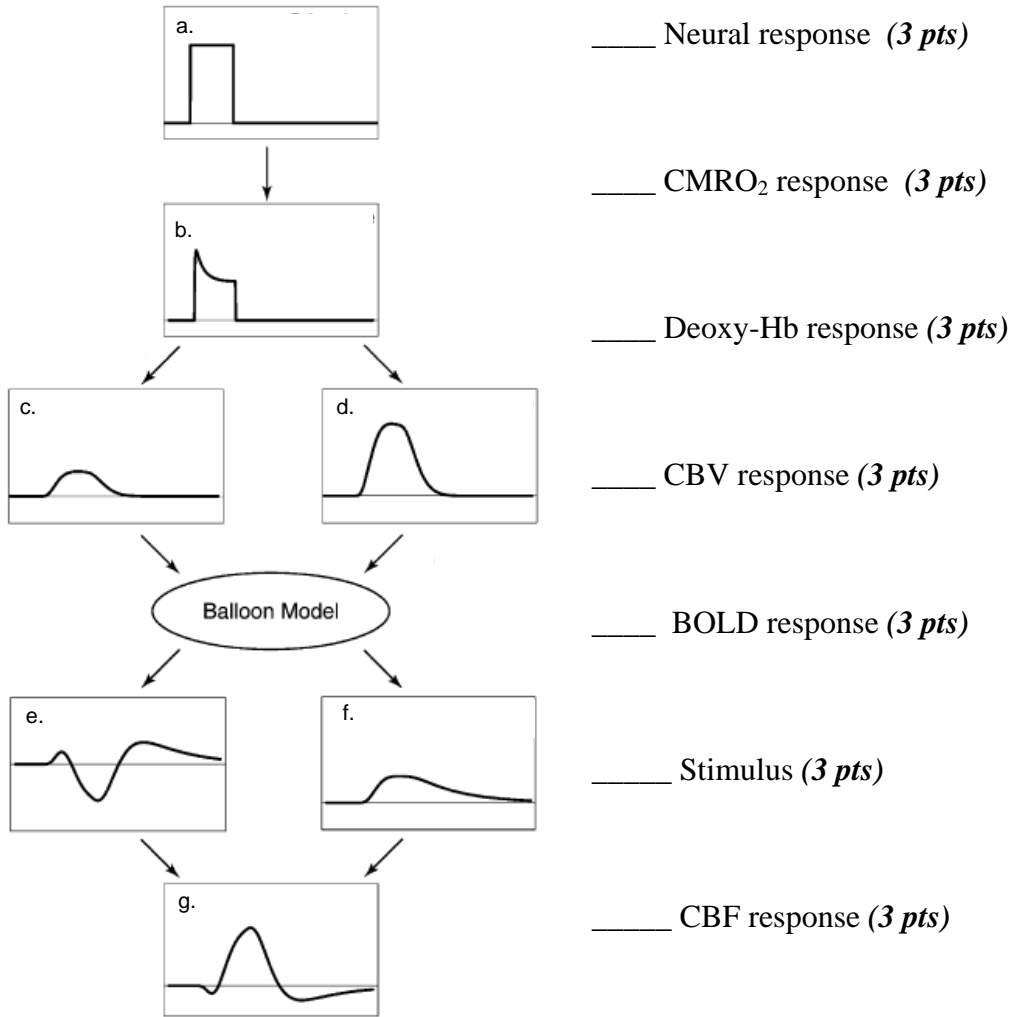
Courtesy of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc. Used with permission.

a) As relative flow increases, the relative change in BOLD response approaches an asymptotic limit. Describe from a physiological standpoint why this may happen. (*4 pts*)

b) The plot depicted is known is one of many so-called "iso-contours", in the sense that a specific physiologic parameter remains approximately constant on this line.   To which parameter are Hoge et. Al referring? (*3 pts*)

Question 3

The figure below describes one of the proposed models linking the applied stimulus to the measured output response.

a) Match the following responses to the corresponding boxes, by writing the appropriate letter in each blank. Additionally, provide a brief justification for your choice in the space provided. The explanation should consider features of the waveform.

_____ Neural response *(3 pts)*

_____ CMRO$_2$ response *(3 pts)*

_____ Deoxy-Hb response *(3 pts)*

_____ CBV response *(3 pts)*

_____ BOLD response *(3 pts)*

_____ Stimulus *(3 pts)*

_____ CBF response *(3 pts)*

From Buxton, R. B., et al. "Modeling the hemodynamic response to brain activation." *NeuroImage* 23 supplement 1 (2004): S220-S233.

Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission

b) Name some candidate signaling molecules that couple event b) to events c) and d), and briefly describe the mechanism of action. *(4 pts)*

c) Traditional fMRI is based on the fact that an increase in neural activity leads to an increase in the BOLD signal. Describe a way to increase the BOLD signal that does not require an increase in neural activity. Why does this method work? *(4 pts)*

Question 4.
What are the trade-offs between using a FIR model and a gamma model? *(4 pts)*

Question 5.
Consider the following experimental design in which there are 10 time points (Ntp=10) collected with a TR=2s. During this collection, two types of stimuli are presented to the subject (Nc=2). The data will be analyzed using an FIR model with a time window of 6 seconds (TW=6s); the analysis will also include covariates for a mean offset and linear trend.

a. How many rows and columns will the design matrix have? *(2 pts)*

b. Write out the design matrix given that stimulus type 1 is presented at t = 0, 2, 10, 14 sec, and stimulus type 2 is presented at t = 6, 12, 18 sec. *(4 pts)*

Question 6.
a) List two (2) specific goals of using Common Coordinate Systems to analyze and/or interpret fMRI data. *(4 pts)*

b) Briefly describe two examples of Common Coordinate Systems commonly in use today. *(4 pts)*

c) Given any specific Common Coordinate System, what are inherent limitations in the use of that coordinate system for analyzing, interpreting and sharing neuroimaging data. *(4 pts)*

Question 7. *(56 points total)*

Cortex

Striatum

Substania Nigra

Thalamus
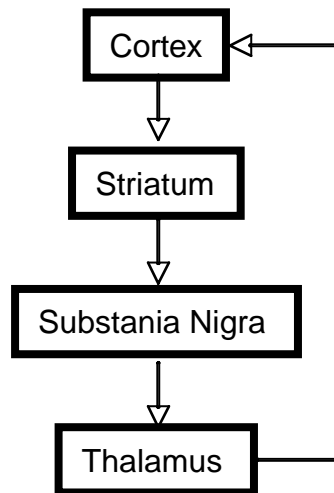
Because of your stellar performance in HST.583, you have just been awarded a prestigious post-doctoral fellowship award to work the research lab of a Nobel Laureate professor at MIT and have been given the task of implementing the lab's first fMRI study. The lab uses animal models to study central nervous system control of movement. A simplified schematic of the neural network model that has been developed in the laboratory over the past 20 years to explain how the brain controls movement is shown in the adjacent Figure. (Note: the Substantia Nigra, pars reticulata is located in the midbrain- middle part of the brainstem).

The lab director is hugely enthusiastic about launching this new imaging initiative, and despite her lack of imaging experience, on your first day in the lab she outlines the following proposal for the work you will do in her lab. She wants you to conduct a pilot experiment to test her hypothesis that in the human brain each of the four regions in the neural network shown in the Figure will show increased fMRI signals during both imagined and real motor movements.

She has a very limited budget (she is used to doing behavioral experiments) and so tells you that the pilot will be limited to scanning two (2) subjects and that this should be sufficient to generate preliminary data for a grant as well as a good manuscript. Each subject will be scanned during rest, during complex bilateral finger movements and during mental imagery of the same complex bilateral finger movements. With the help of a collaborating cognitive scientist she has determined that 10 minute long scans during which the subject performs an event related experimental paradigm would be optimal. She proposes to repeat this paradigm 6 times (collect 6 identical scans) during the session.

She tells you that you will be using the new Trio TIM 3T scanning system at the Martinos Center. You know that the Martinos Center has both a head coil and an occipital surface coil available. However, she asks you to collect data using only the surface coil centered over the back of the subject's head.

For the functional scans she suggests using a T2-weighted EPI sequence, with TE=10ms, TR=1000ms and flip angle 90 degrees and a TR of 1 second.   She wants to collect 30 coronal slices each 8 mm thick so she can have whole brain coverage.

For the anatomical scan she wants you to use a proton density image that has a high signal-to-noise ratio and can be acquired very fast (50 seconds) with high spatial resolution.

She is all excited about a new image analysis software package that allows the user to enter all the experimental variables in the beginning, upload the scan data then press a button and it returns (after a night of unspecified processing) statistical maps of the results.

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Drawing upon the wisdom and knowledge you gained in HST.583, you take a deep breath and prepare yourself to critically evaluate the decisions she has made.

a) What is your opinion about using a cohort size of 2 subjects to test a hypothesis in an fMRI study?   What is your recommendation for the number of subjects to study and why? *(4 pts)*

For 4 BONUS points:
b) What is your recommendation for how to best estimate an appropriate sample size?

c) What is your opinion about using an event related design for the initial study? Defend or refute this choice and make your own recommendation giving your rationale. Include in your recommendation a VERY specific description of your proposed paradigm(s).   Be sure to cover what the subject is instructed to do, how instructed, the timing, etc. Include a schematic drawing. You will use this design to answer more questions below, so read ahead to be sure you are including all necessary information. *(14 pts)*

d) Do you agree with her choice of acquisition parameters for the anatomical image? For the functional images (TE, TR, flip angle, slice thickness, number)? Why or Why not? If not, what would you change and why? Are there additional acquisition sequences you recommend? If so, specify the rationale for adding the scan and the acquisition parameters.

For the anatomical image: *(3 pts)*

For the functional images:
    1) The imaging sequence: T2-weighted EPI *(3 pts)*

    2) Sequence parameters: TE *(3 pts)*

    3) Sequence parameter: TR/flip angle *(3 pts)*

    4) Sequence parameters: slices (thickness, number) *(3 pts)*

    5) Additional sequence? *(3 pts)*

e) Do you agree with her decision to use the surface coil? Why or Why not? *(4 pts)*

f) Finally, drawing another deep breath, you ask if she knows exactly what is done to the data by the fMRI analysis program. After ascertaining that she has no appreciation of the complexities of fMRI signal processing, you endeavor to describe exactly how you propose to analyze this data set.

Your written response can be a list of words or phrases, one per step followed by a phrase that justifies the step. Include all pre-processing steps, statistical modeling methods and parameters. For the statistical model, refer back to your experimental paradigm to specify each condition. Include your contrasts and what specific hypothesis each will be used to test. *(14 pts)*

FILL IN BLANK FOR EXTRA CREDIT!

Top ten signs you've been scanning too much...
(Courtesy of Jody Culham, http://psychology.uwo.ca/fmri4newbies/ScanningTooMuch.html)

10. While pouring syrup on your Eggo waffles, you note that you missed a few voxels.
9. Your knowledge of brain anatomy exceeds your knowledge of geography. As in, "The transverse occipital sulcus intersects the intraparietal sulcus near the level of the parieto-occipital fissure" and "The Sahara is in Afghanistan, I think."
8. You have developed a rapid ritual for checking your body for metal that resembles the macarena.
7. When you see drawings of brains in the popular media, you instantly decide whether or not they are anatomically correct.
6. Friends wonder how you can run a four million dollar scanner and still fail to program a VCR.
5. You suffer frequent left/right confusion and find yourself saying things like, "Make a left turn at the lights... No, I meant a *radiological* left!"
4. At parties, you scope out people's subject-worthiness: "It was great talking to you. Say, what are you doing Friday night?... Do you have any metal in your body?..."
3. Not only can you recognize the brains of your frequently-scanned co-workers, but also their teeth from the bite bar impressions.
2. When reminded of a special occasion, you remember it fondly because the scanner was free all day long and you collected lots of good data.

1. _____

_____

THANKS FOR YOUR PARTICIPATION AND HAVE A GREAT HOLIDAY!!
- Randy & Div