

Introduction to Functional MRI

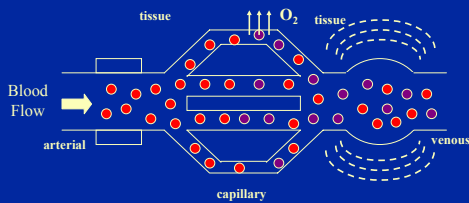
Douglas C. Noll
 Department of Biomedical Engineering
 Functional MRI Laboratory
 University of Michigan



Outline

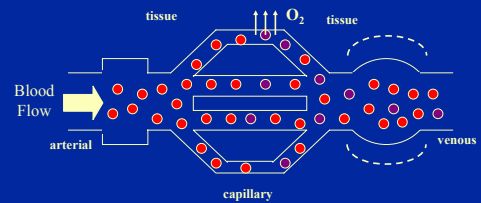
- Brief overview of physiology and physics of BOLD fMRI
- Background for Experimental Task Design in fMRI
- Basics Approaches to Experimental Task Design in fMRI

Hemodynamics: Basal State



	O2 & Glu Metabolism	Blood Flow	Blood Volume	Blood O2
Baseline	—	—	—	—

Hemodynamics: Active State



	O2 & Glu Metabolism	Blood Flow	Blood Volume	Blood O2
Active	↑	↑↑↑	↑	↑↑

Principles of Functional MRI

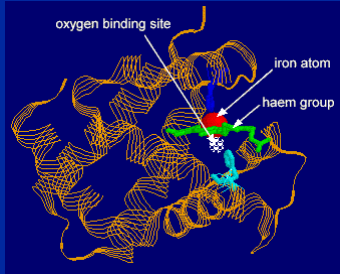
- MRI can image all of these changes:
 - Metabolism — MR Spectroscopy
 - Blood Flow — Arterial Spin Tagging
 - Blood Volume — Several approaches
 - Blood Oxygenation — BOLD Functional MRI
- The most commonly used of these is BOLD fMRI
 - Easy to use
 - High sensitivity (relative to other techniques)
 - Contrast agents/multinuclear coils not needed

Magnetic Susceptibility

- Susceptibility \sus'cep'ti-bil'i-ty, n.
 The state or quality of being susceptible; the capability of receiving impressions of being affected (Webster's)
- Magnetic Susceptibility
 - The property of a material of being magnetized by an externally applied magnetic field
 - Induced magnetization is proportional to applied field:

$$\Delta B = \chi_m B_0$$

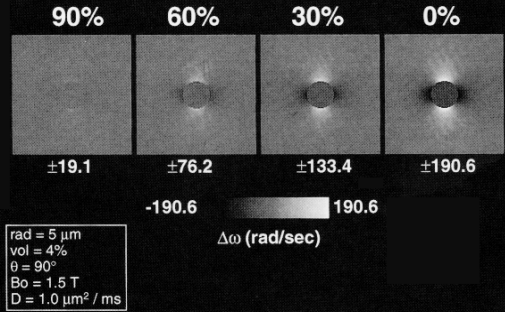
Hemoglobin



- Magnetic properties of hemoglobin:
 - Oxygenated hemoglobin is diamagnetic
 - Deoxy-hemoglobin is paramagnetic
- The presence of deoxy-hemoglobin distorts the local magnetic field
 - After contrast development interval, this leads to reduction of signal strength

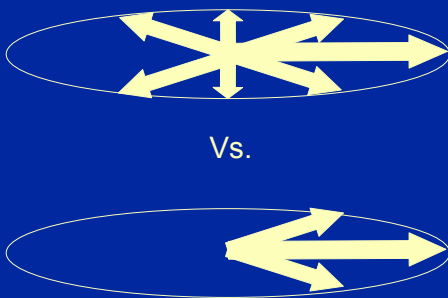
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ΔO_2 saturation



Bandettini and Wong. Int. J. Imaging Systems and Technology, 6,133 (1995)

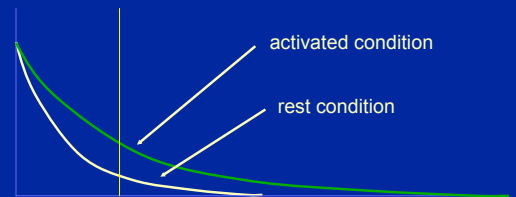
Increased Dephasing



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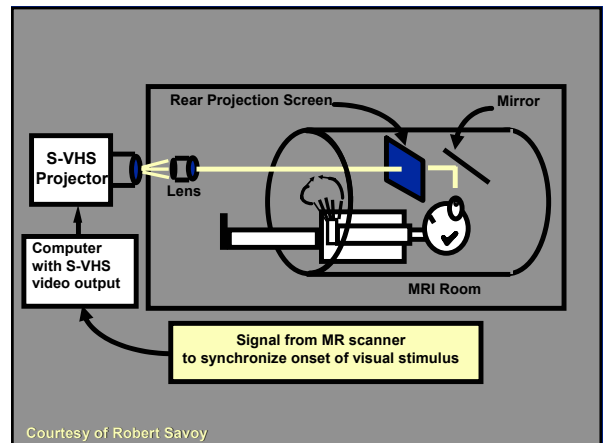
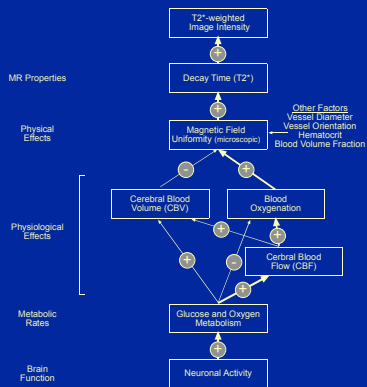
Signal Changes with Deoxy-Hb

The decay rate is proportional to the amount of deoxygenated hemoglobin.



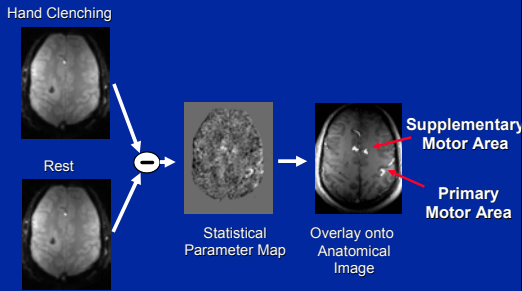
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The BOLD Effect



Courtesy of Robert Savoy

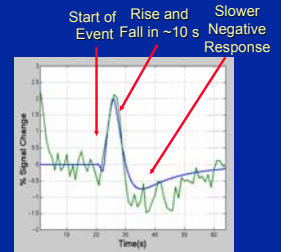
Typical Functional MRI Study



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Time Course Response in Functional MRI

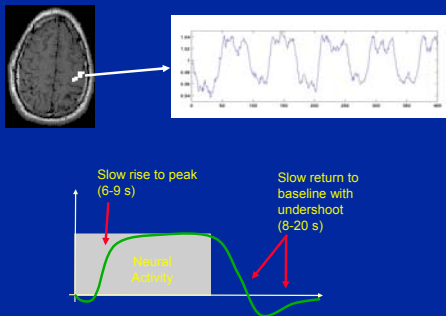
- Brief neuronal events can elicit a (positive) blood flow and oxygenation response.
- Responses to events as brief as 50 ms have been recorded.



Functional MRI response to a visual stimulus of duration 2s

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Response to Long Periods of Stimulation



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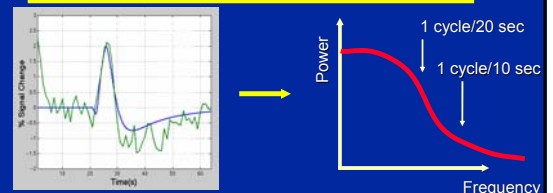
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Background for Task Design

- The BOLD fMRI signal is relative
 - Image intensity is not just a reflection of blood oxygenation, but lots of other stuff
 - Can't tell much by looking at a single image
- Functional MRI involved comparison of conditions
 - Comparison between active conditions
 - Comparison to a baseline condition

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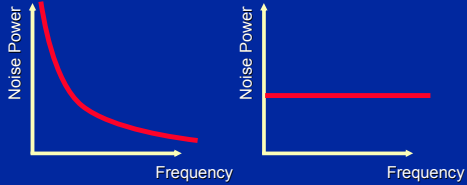
Background for Task Design



- The BOLD response is quite slow – only the low frequencies can be imaged

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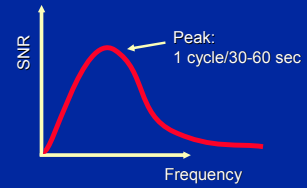
Noise in fMRI



- Two main sources of noise in fMRI
 - $1/f$ noise (drifts and trends in signals)
 - Thermal additive noise (white or flat spectrum)

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Signal-to-Noise Ratio

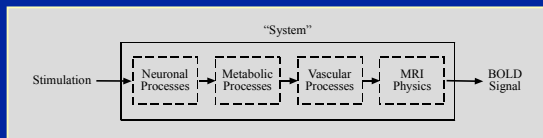


- Considering the two effects of noise and signals, there is a sweet spot where the best fMRI can be done
 - Full cycle every 30 to 60 seconds
 - Epochs of duration 15 to 30 seconds

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Linear Systems

- Systems theory characterizes input/output relationships
- When examining the BOLD response we often look at a system composed of several subsystems



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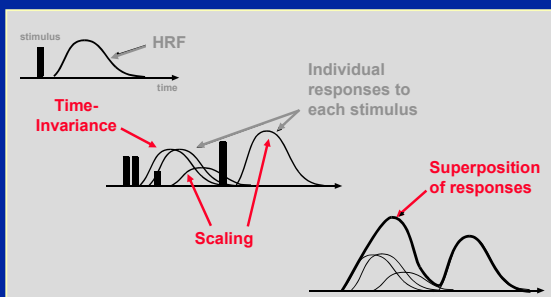
Linearity

A “linear system” satisfies the following:

- Scaling
 - Increasing stimulation by some ratio will increase the output by the same ratio
- Superposition (additivity)
 - Combining (adding) any two stimuli will lead to an output that is the sum of the two responses
- Time invariance
 - A response is the same irrespective of when it comes or what precedes or follows it

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Superposition and Predicted Responses



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Why Is Linearity Good?

- Extensive theory of linear systems
- Allows definition of an impulse response function
 - Commonly known as the hemodynamic response function (HRF)
- Predicted responses are easily determined
 - Can also allow “deconvolution” of response to get estimates of the system input

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Cognitive Subtraction

- Idea: If two tasks differ by a cognitive process of interest, then differences in observed neural activity can be attributed to that process.
- Related Idea: Pure Insertion. The two tasks differ by the “insertion” of the process of interest
- Not always true, but commonly assumed in many fMRI studies.

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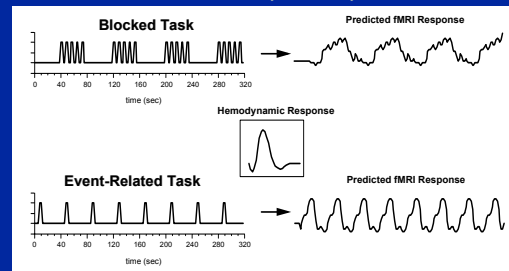
Two Main Classes of fMRI Design

- Blocked designs
 - Like tasks are clustered together in blocks of length 15-120 seconds
 - Tasks are close together to allow the appearance of continuous activation during the block
- Event related designs
 - Responses to individual neural events are imaged
 - Responses are allowed to overlap
 - Individual events (single behavioral trials) are culled out in the analysis

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Task Design and Predicted Responses

Two task designs and predicted fMRI responses based on linear system analysis



Detre

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Two condition Blocked Designs

- Also “subtractive” designs
- Design issues:
 - Two conditions differ by process of interest
 - Conditions should be as homogeneous as possible to minimize variation within block
 - Conditions should be densely populated by tasks to maximize actual performance time
 - Trials within condition should be roughly equally spaced with SOA's of less than 3-5 second
 - Optimal block length: 15-30 seconds

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Two condition Blocked Designs

- Challenges:
 - Might need instruction blocks
 - Task start-up time (e.g. N-back task requires N trials to fully load memory)
 - Habituation and other behavioral effects (all tasks are the same)
 - Violations of pure insertion (e.g. difficult blocks may lead to changes in attention)
 - Rigid format – not suitable for all studies
- Advantages:
 - Simple analysis
 - Excellent statistical power

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Multiple Condition Blocked Designs

- Typical:
 - Uses a fixed order within a run (ABCABC...)
 - Counter-balanced across runs (BCABCA...)
 - Randomized blocks are also ok but should be validated if a small number of blocks are used
 - Block should be long enough to reach signal plateau

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Parametric Blocked Designs

- Uses blocks with a parametric task manipulation
 - E.g. graded visual stimuli, graded memory conditions (e.g. N-back)
 - Often easier to interpret and justify than the cognitive subtraction hypothesis – look for those areas that vary exactly as the parametric manipulation
 - Analysis might use an ANOVA to find main effect of manipulation and then do a post-hoc analysis looking for increases that match manipulation

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Event-Related fMRI

- Responses to brief events are usually weaker than responses to blocks of events, but these data sets have more information
- Event related fMRI studies must consider the long duration of the BOLD hemodynamic response (delay = 2-3 sec, overall duration 8-12 sec)
- Should responses to events overlap?
 - This points to the two major experimental design philosophies in event-related fMRI

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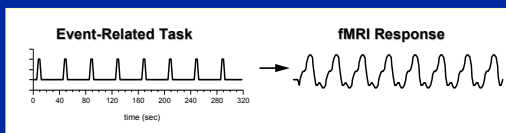
Event Related Designs

- Several different variants
 - Simple task, non-overlapping, stretched out
 - Multiphasic task, stretched out
 - Randomized ITI
 - Fixed ITI, randomized conditions
 - Mixed block/event-related designs

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Event-Related fMRI - Extended Trials

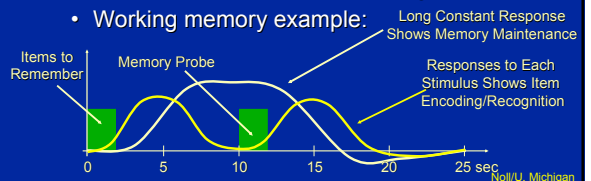
- Behavioral trials have a long gaps between them (long ITI)
 - Typically 10-20 sec ITI is used
- Example:



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Event-Related fMRI - Extended Trials

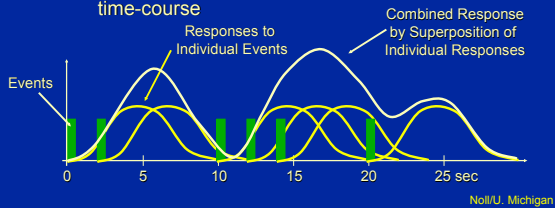
- Behavioral trials are extended in duration to allow responses to the individual events to be seen
 - Often 10-15 sec is added at the end to get to its baseline state
 - Subtasks have unique temporal signature
- Working memory example:



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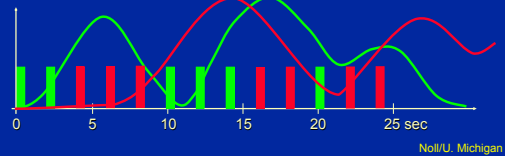
Event-Related fMRI - Randomized ITI

- Behavior trials are presented rapidly, but with random timing
 - Overlapping responses are superimposed to yield a unique time-course
 - Randomization causes the variation in the time-course



Event-Related fMRI – Randomized Trials

- Behavior trials are presented rapidly, but with random ordering
 - Overlapping responses are superimposed to yield a unique time-course
 - E.g. **A****B****B****B****A****A****B****B****A****B****B**...
 - Trial types **A** and **B** will have a unique temporal signature



Event-Related Designs

- Advantages
 - Avoids habituation/behavioral issues
 - Very flexible
 - Allows self-paced tasks
 - Can assign subevents when they really occur (e.g. a behavioral response)
 - Can separately analyze correct/incorrect responses
 - Can still do parametric manipulations

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Event-Related Designs

- Disadvantages
 - Sensitive to accuracy of shape of the BOLD response (often called hemodynamic response function or HRF)
 - Reduced sensitivity relative to blocked designs (the most sensitive ER designs have trials clustered into mini-blocks – that is long runs of particular trial types)
 - Difficult to include instruction blocks

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Mixed ER/Blocked Designs

- Looks like a blocked design, but individual trials are analyzed within blocks
 - Often done so that behavioral errors can be analyzed

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Control/Baseline Conditions

- Raichle hypothesis (*Nature Reviews: Neuroscience* 2:685-692, 2001):
 - There are a set of “activities” associated with resting with eyes open (e.g. passive viewing of a blank screen)
 - During goal-directed behavior these resting state activities are suppressed
 - May often see deactivations related to suppression of resting state activity
- Selection of control conditions must be carefully considered

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