Time Series Analysis in AFNI

Outline: 6+ Hours of Edification

- Philosophy
- Sample FMRI data
- Theory underlying FMRI analyses: the HRF
- "Simple" or "Fixed Model" regression analysis
  - ★ Theory and Hands-on examples
- "Deconvolution" or "Variable Model" analysis
  - ★ Theory and Hands-on examples
- Advanced Topics

Data Analysis Philosophy

- <u>Signal</u> = Measurable response to stimulus
- <u>Noise</u> = Components of measurement that interfere with detection of signal
- Statistical detection theory:
  - ★ Understand relationship between stimulus & signal
  - ★ Characterize noise statistically
  - ★ Can then devise methods to distinguish noise-only measurements from signal+noise measurements, and assess their reliability
  - ★ Methods and usefulness depend strongly on the assumptions
    - ✧ Some methods are "robust" against erroneous assumptions, and some are not

<u>FMRI Philosopy: Signals and Noise</u>

- FMRI Stimulus→Signal connection and noise statistics are both poorly characterized
- Result: there is no "**best**" way to analyze FMRI time series data: there are only "**reasonable**" analysis methods
- To deal with data, must make some assumptions about the signal and noise
- Assumptions will be wrong, but must do *something*
- Different kinds of experiments require different kinds of analyses
  - ★ Since signal models and questions you ask about the signal will vary
  - ★ It is important to understand what is going on, so you can select and evaluate "reasonable" analyses

Meta-method for creating analysis methods

- Write down a mathematical model connecting stimulus (or "activation") to signal

- Write down a statistical model for the noise

- Combine them to produce an equation for measurements given signal+noise

  ★ Equation will have unknown parameters, which are to be estimated from the data

  ★ N.B.: signal may have zero strength

- Use statistical detection theory to produce an algorithm for processing the measurements to assess signal presence and characteristics

  ★ e.g., least squares fit of model parameters to data

Time Series Analysis on Voxel Data

- Most common forms of FMRI analysis involve fitting an activation+BOLD model to each voxel's time series **separately** (AKA "univariate" analysis)

  ★ Some pre-processing steps may do inter-voxel computations

    ✧ e.g., spatial smoothing to reduce noise

- Result of model fits is a set of parameters at each voxel, estimated from that voxel's data

  ★ e.g., activation amplitude, delay, shape

  ★ "SPM" = statistical parametric map

- Further analysis steps operate on individual SPMs

  ★ e.g., combining/contrasting data among subjects

Some Sample FMRI Data Time Series

- First: Block-trial FMRI data

  ★ "Activation" occurs over a sustained period of time (say, 10 s or longer), usually from more than one stimulation event, in rapid succession

  ★ BOLD (hemodynamic) response accumulates from multiple close activations and is large

  ★ BOLD response is often visible in time series

- Next 4 slides: same brain voxel in 9 imaging runs

  ★ black curve (noisy) = data

  ★ red curve (above data) = ideal model response

  ★ blue curve (within data) = model fitted to data

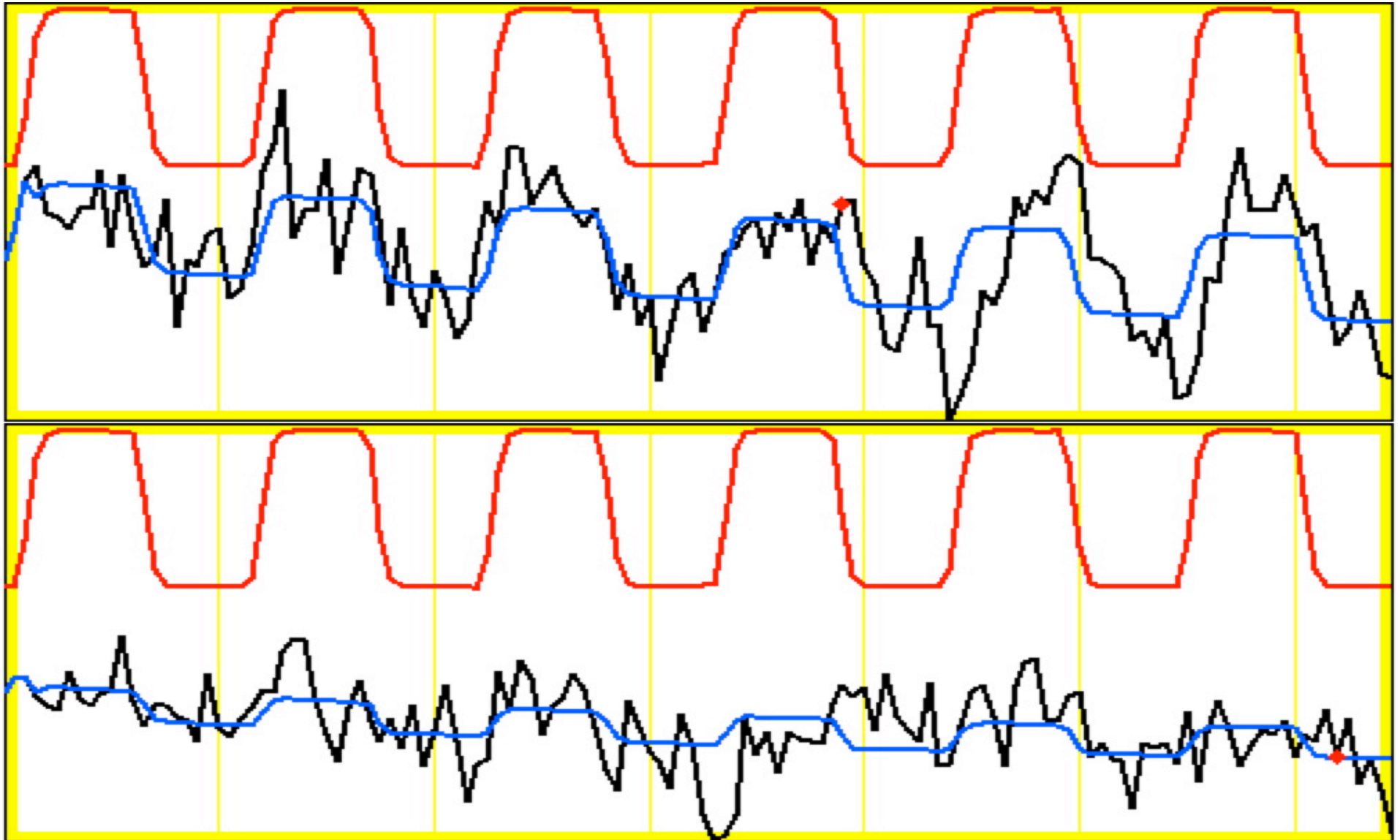 ★ somatosensory task (finger being rubbed)

Same Voxel: Runs 1 and 2 (of 9)
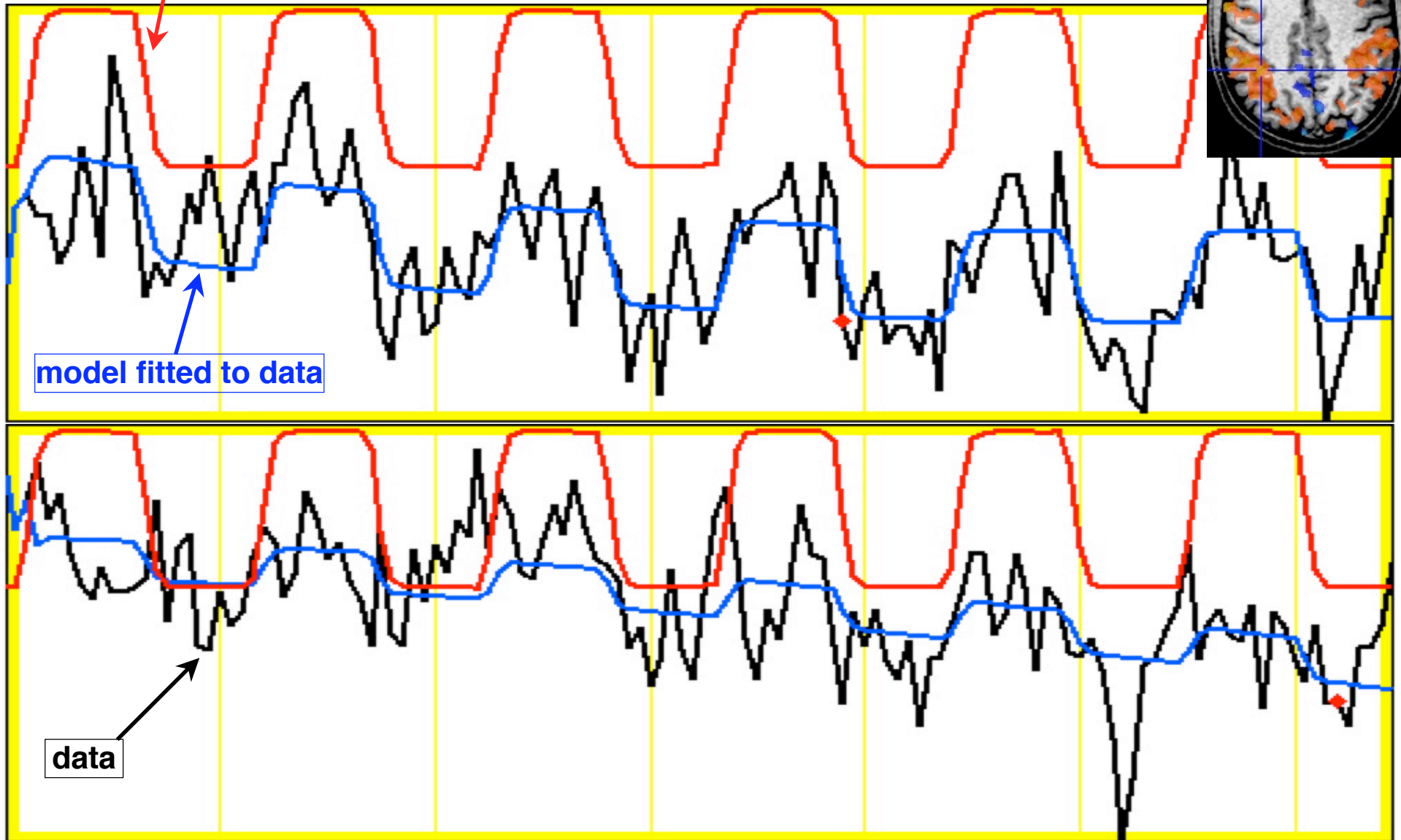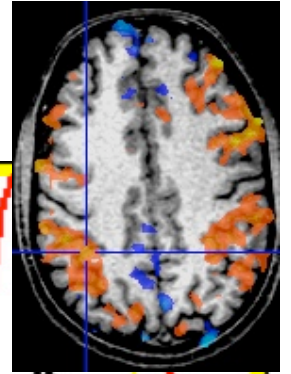
model

model fitted to data

data

Block-trials: 27 s "on" / 27 s "off"; TR=2.5 s; 130 time points/run

Same Voxel: Runs 3 and 4

Block-trials: 27 s "on" / 27 s "off"; TR=2.5 s; 130 time points/run

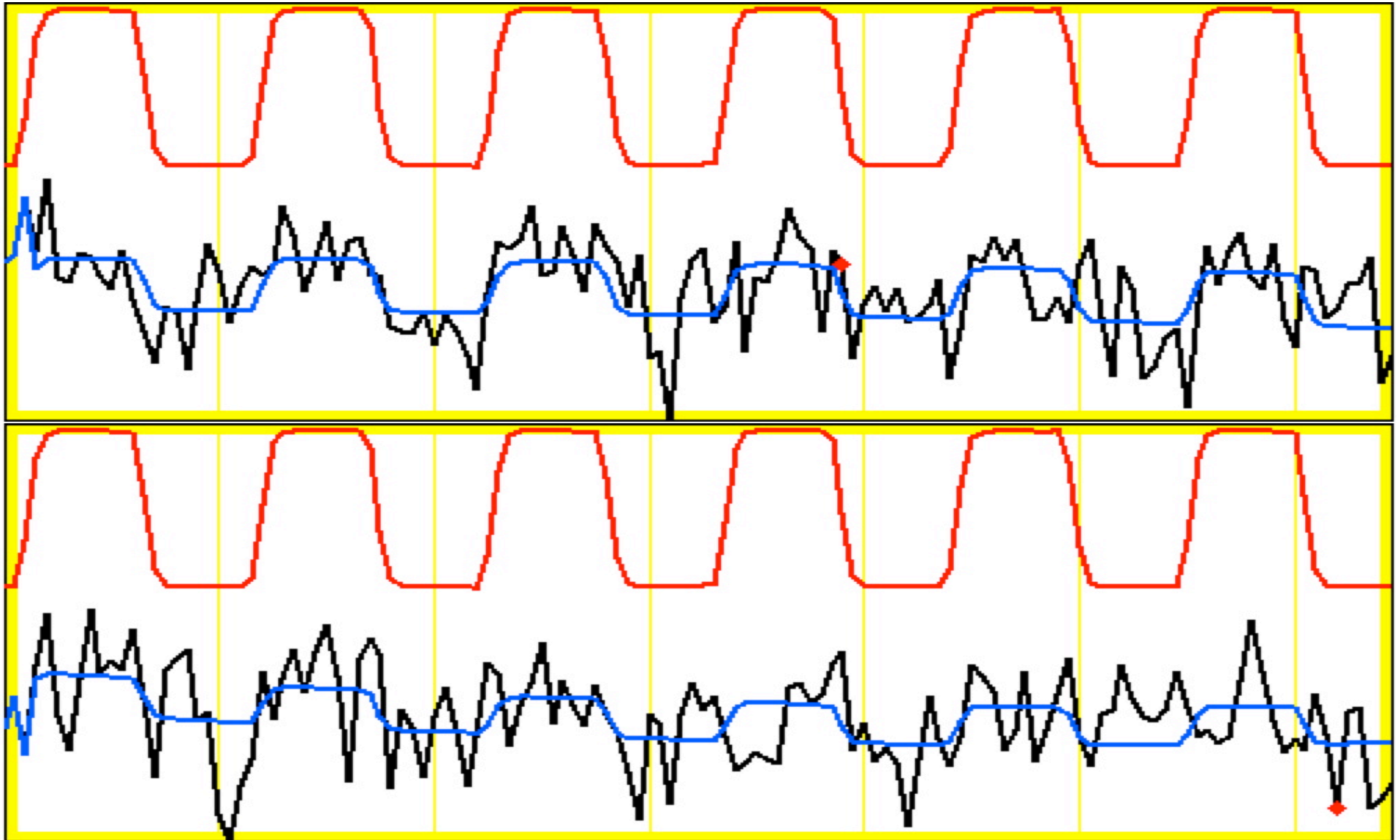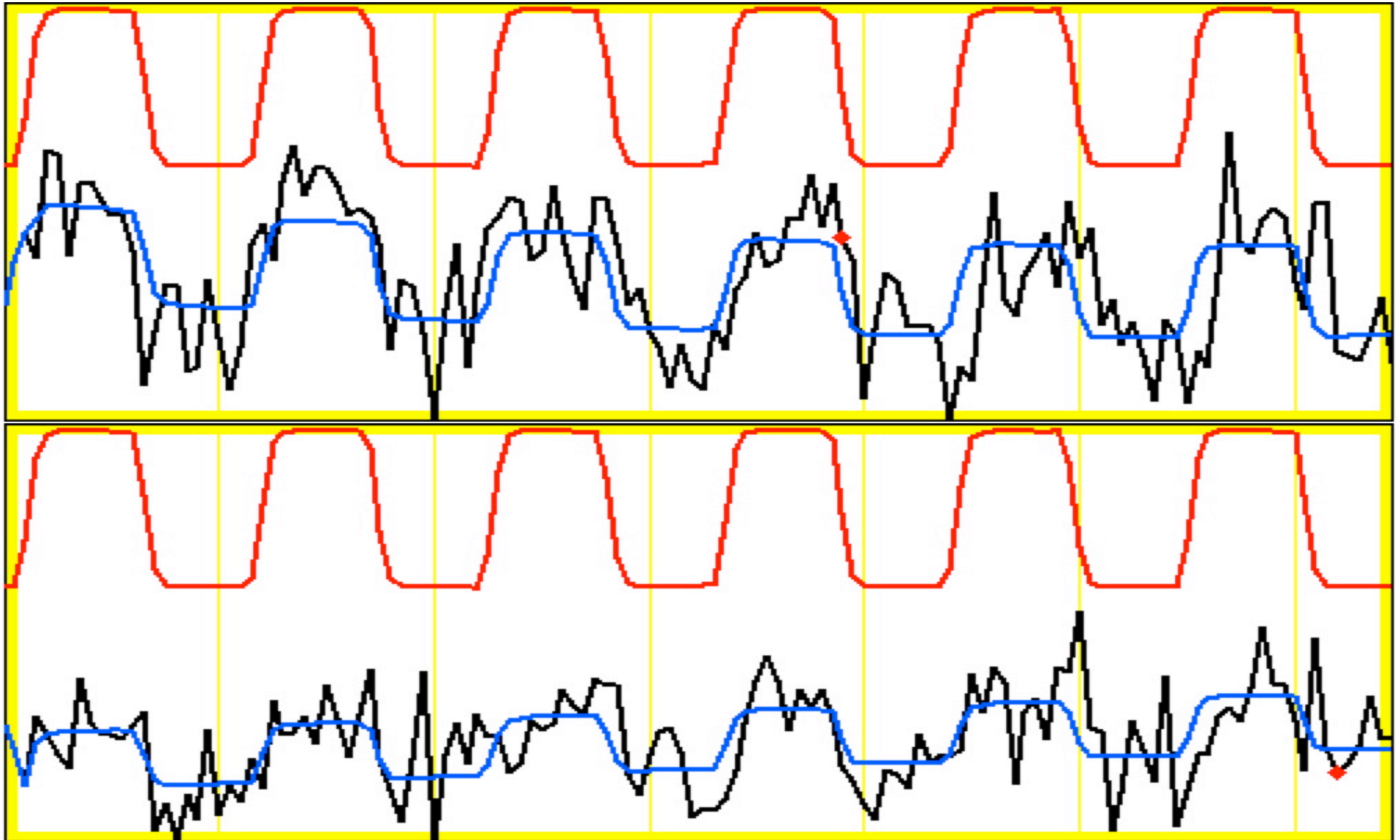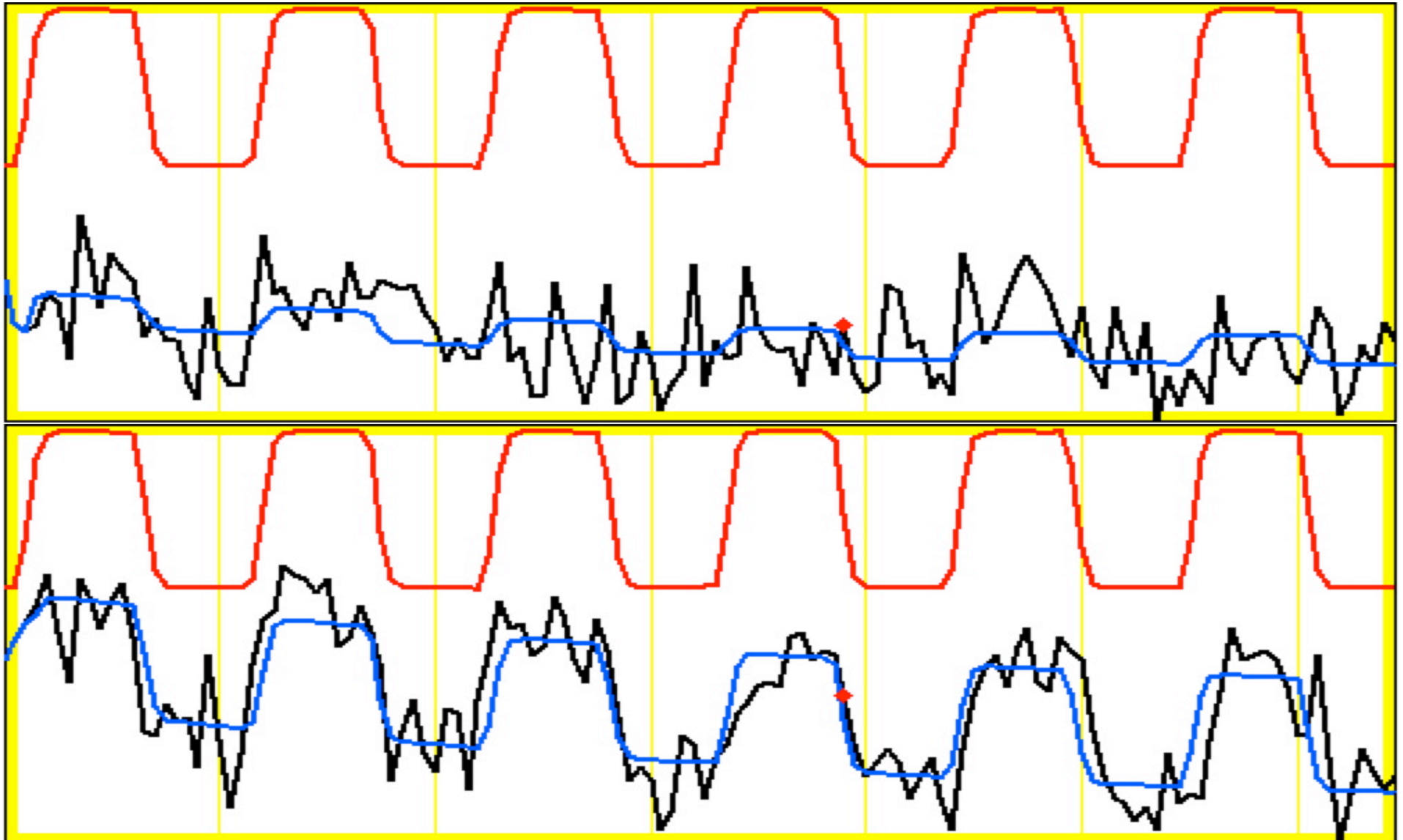## Same Voxel: Runs 5 and 6

Block-trials: 27 s "on" / 27 s "off"; TR=2.5 s; 130 time points/run

Same Voxel: Runs 7 and 8

Block-trials: 27 s "on" / 27 s "off"; TR=2.5 s; 130 time points/run

Same Voxel: Run 9 and Average of all 9

⇒ Activation amplitude and shape are variable! Why???

More Sample FMRI Data Time Series

- Second: Event-related FMRI

  - ★ "Activation" occurs in single relatively brief intervals

  - ★ "Events" can be randomly or regularly spaced in time

    - ✧ If events are randomly spaced in time, signal model itself looks noise-like

  - ★ BOLD response to stimulus tends to be weaker since fewer nearby-in-time "activations" have overlapping hemodynamic responses

- Next slide: Visual stimulation experiment

"Active" voxel shown in next slide
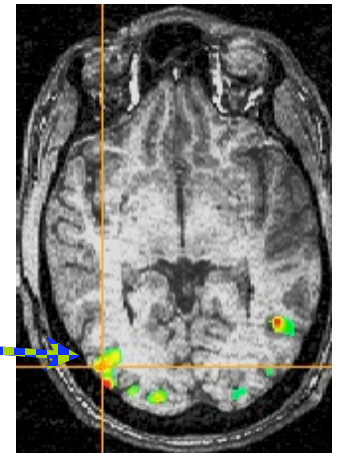
Two Voxel Time Series from Same Run
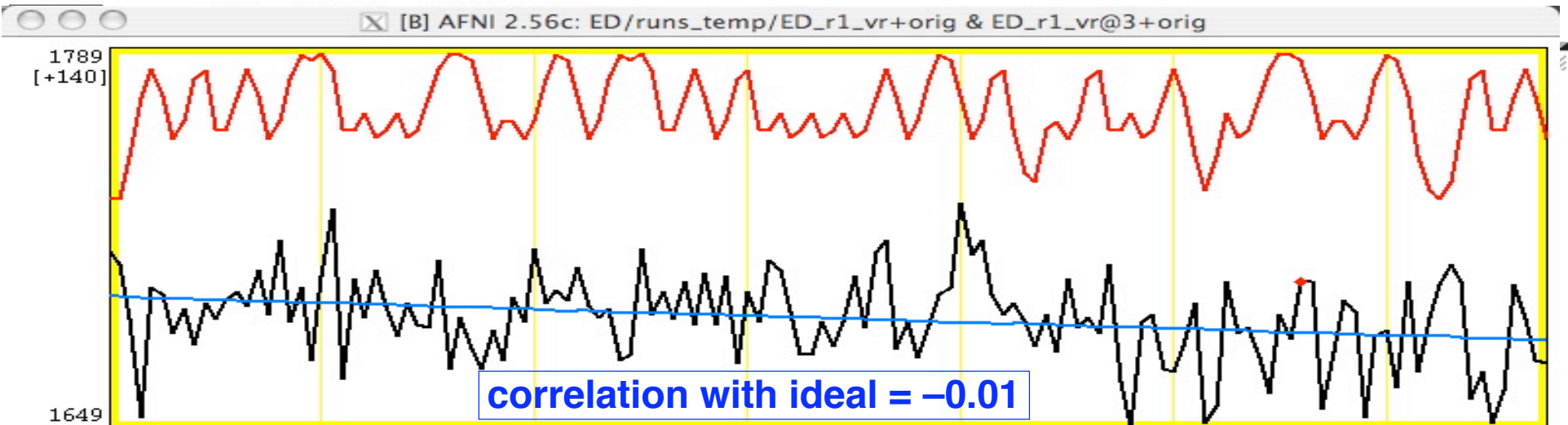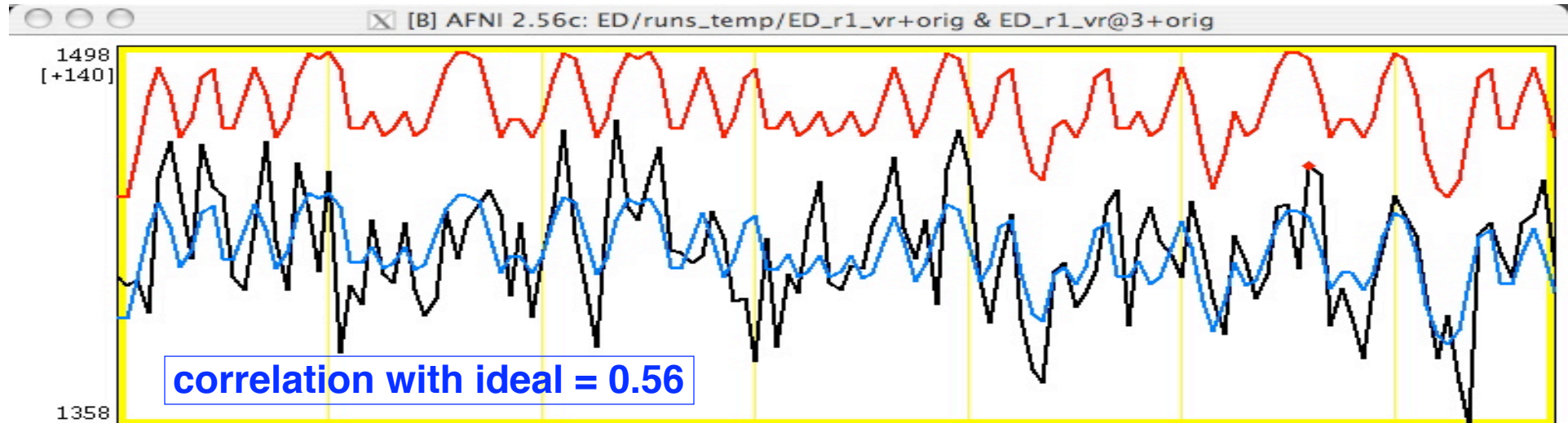
correlation with ideal = 0.56

correlation with ideal = –0.01

Lesson: ER-FMRI activation is not obvious via casual inspection

Hemodynamic Response Function (HRF)

- HRF is the idealization of measurable FMRI signal change responding to a single activation cycle (up and down) from a stimulus in a voxel
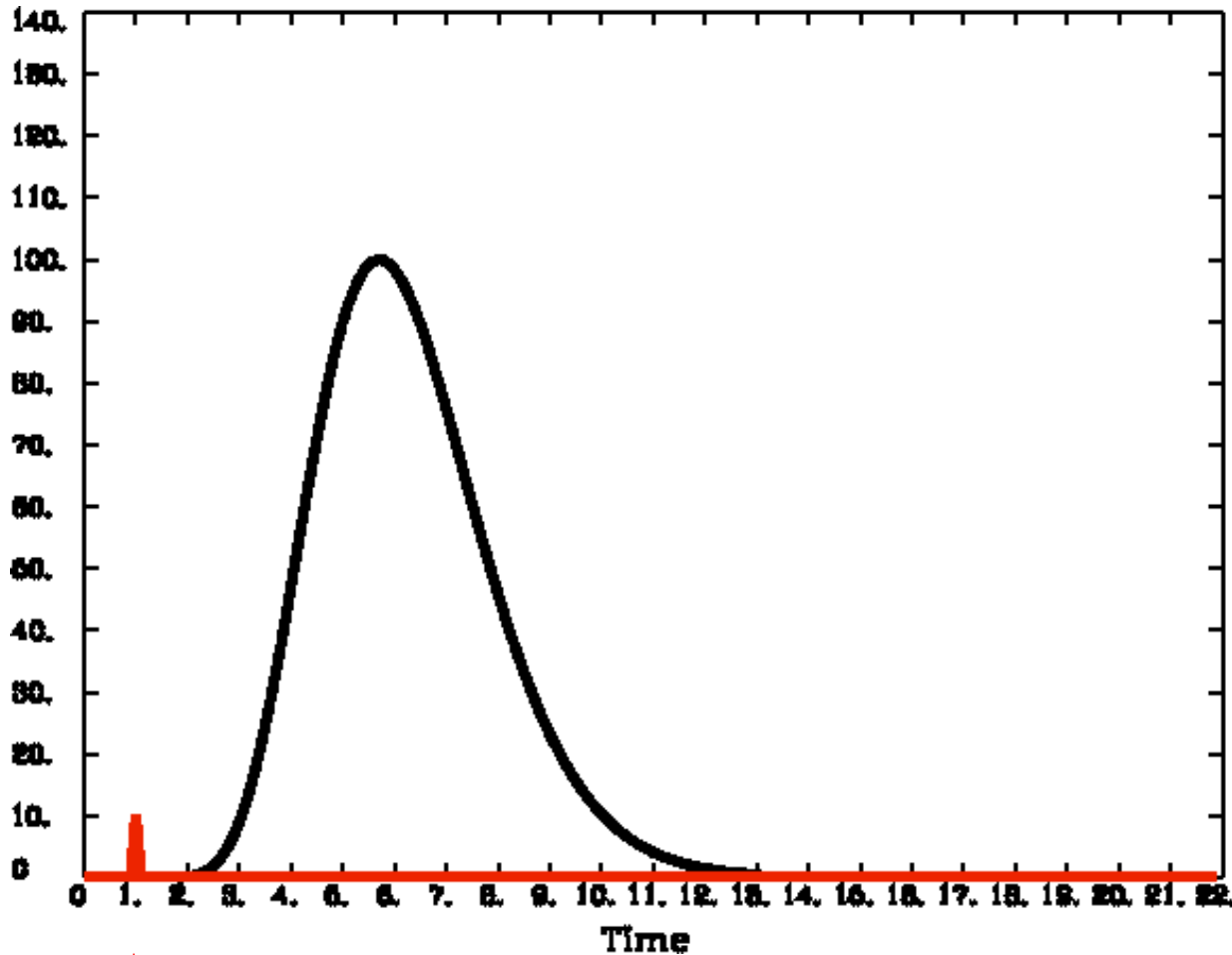
Response to brief activation (< 1 s):
- delay of 1-2 s
- rise time of 4-5 s
- fall time of 4-6 s
- model equation:

$$h(t) \propto t^b e^{-t/c}$$

- $h(t)$ is signal change t seconds *after* activation

1 Brief Activation

Linearity of HRF

- Multiple activation cycles in a voxel, closer in time than duration of HRF:

  ★ Assume that overlapping responses add
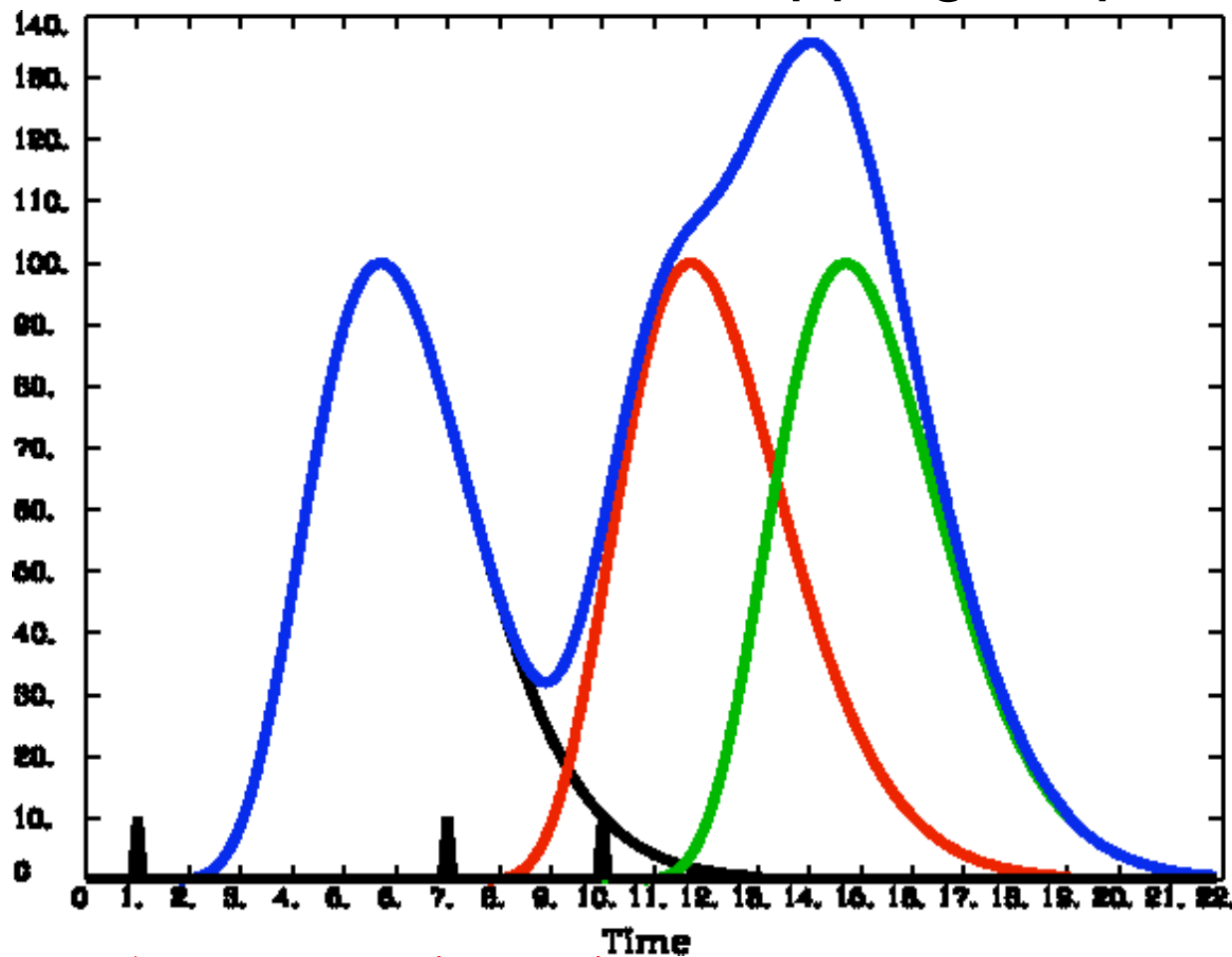
- Linearity is a pretty good assumption
- But not apparently perfect — about 90% correct
- Nevertheless, is widely taken to be true and is the basis for the "general linear model" (GLM) in FMRI

3 Brief Activations

Linearity and Extended Activation

- Extended activation, as in a block-trial experiment:
  - ★ HRF accumulates over its duration (≈ 10 s)
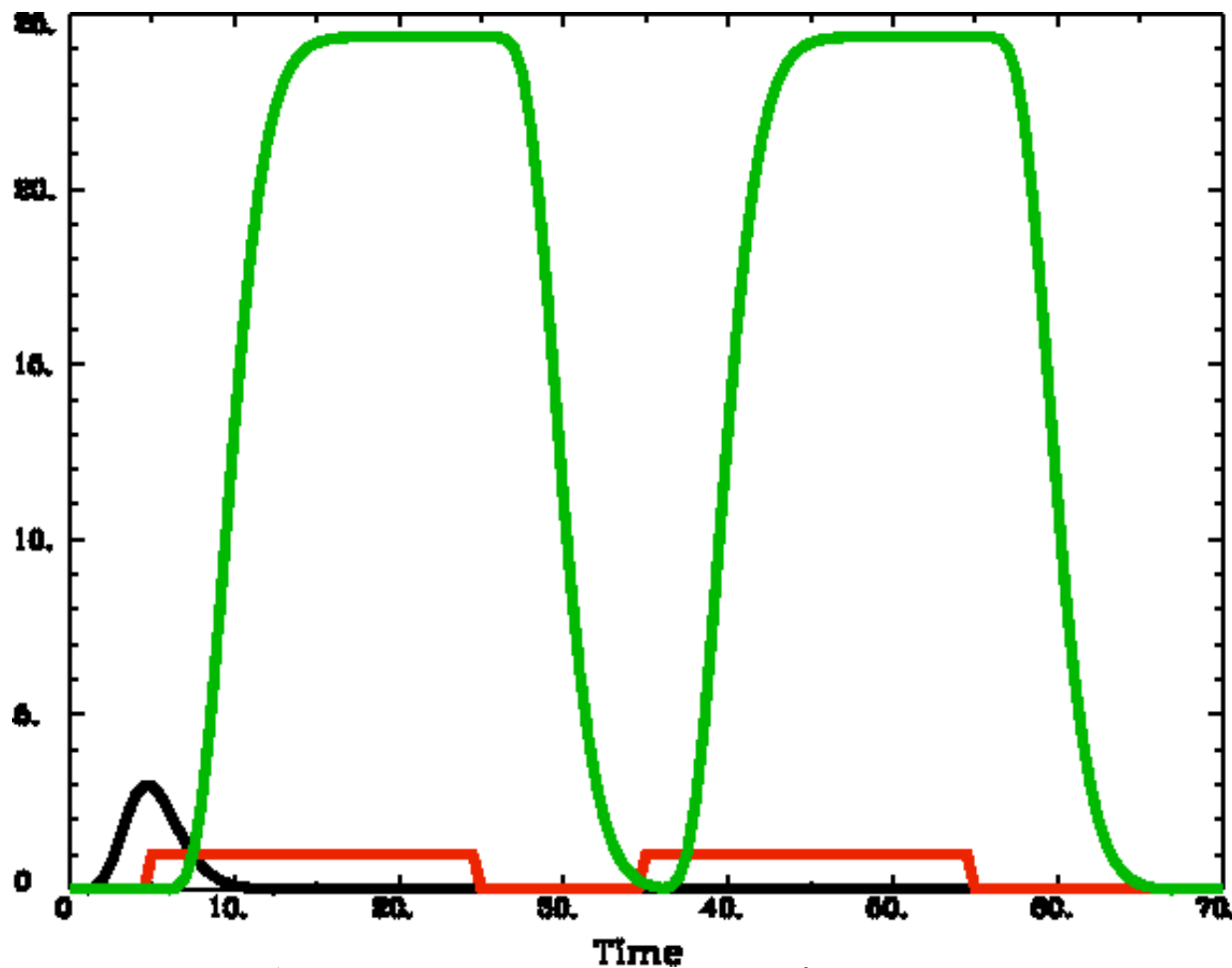
- **Black** curve = response to a single brief stimulus
- **Red** curve = activation intervals
- **Green** curve = summed up HRFs from activations
- Block-trials have larger BOLD signal changes than event-related experiments

2 Extended Activations

Convolution Signal Model

- FMRI signal we look for in each voxel is taken to be sum of the individual trial HRFs

  - ★ Stimulus timing is assumed known (or measured)

  - ★ Resulting time series (**blue** curves) are called the **convolution** of the HRF with the stimulus timing

- Must also allow for baseline and baseline drifting

  - ★ Convolution models only the FMRI signal **changes**

22 s

120 s
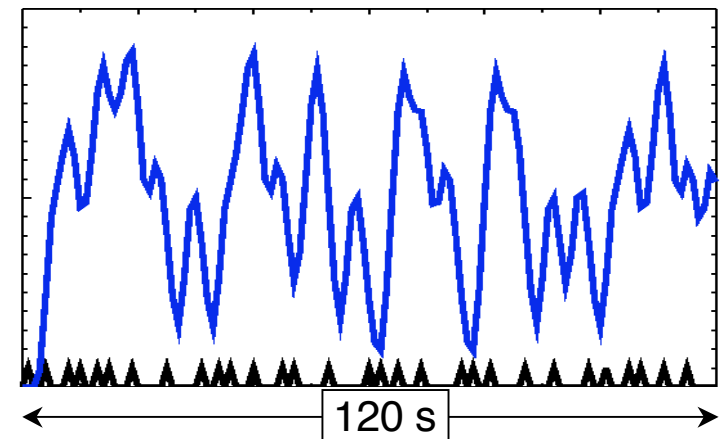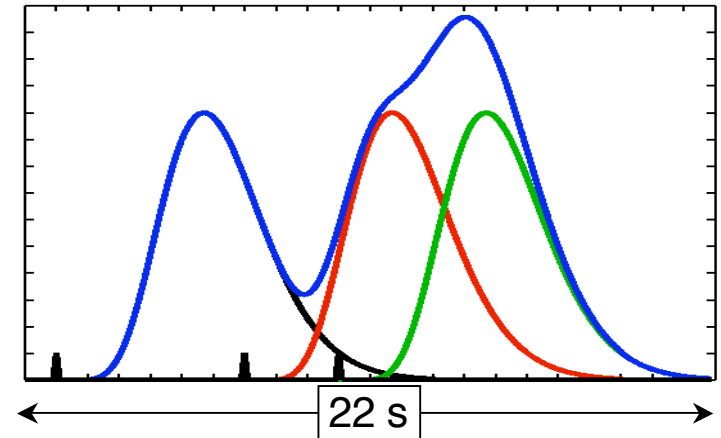
- Real data starts at and returns to a nonzero, slowly drifting baseline

Simple Regression Models

- Assume a fixed shape $h(t)$ for the HRF
  - ★ e.g., $h(t) = t^{8.6} \exp(-t/0.547)$ [MS Cohen, 1997]
  - ★ Convolved with stimulus timing (e.g., AFNI program **waver**), get ideal response function $r(t)$
- Assume a form for the baseline
  - ★ e.g., $a + b \cdot t$ for a constant plus a linear trend
- In each voxel, fit data $Z(t)$ to a curve of the form
  $$Z(t) \approx a + b \cdot t + \beta \cdot r(t)$$
  - a, b, β are unknown parameters to be calculated in each voxel
  - a, b are "nuisance" parameters
  - β is amplitude of $r(t)$ in data = "how much" BOLD

Simple Regression: Example

Constant baseline: a

Quadratic baseline: $a+b\cdot t+c\cdot t^2$
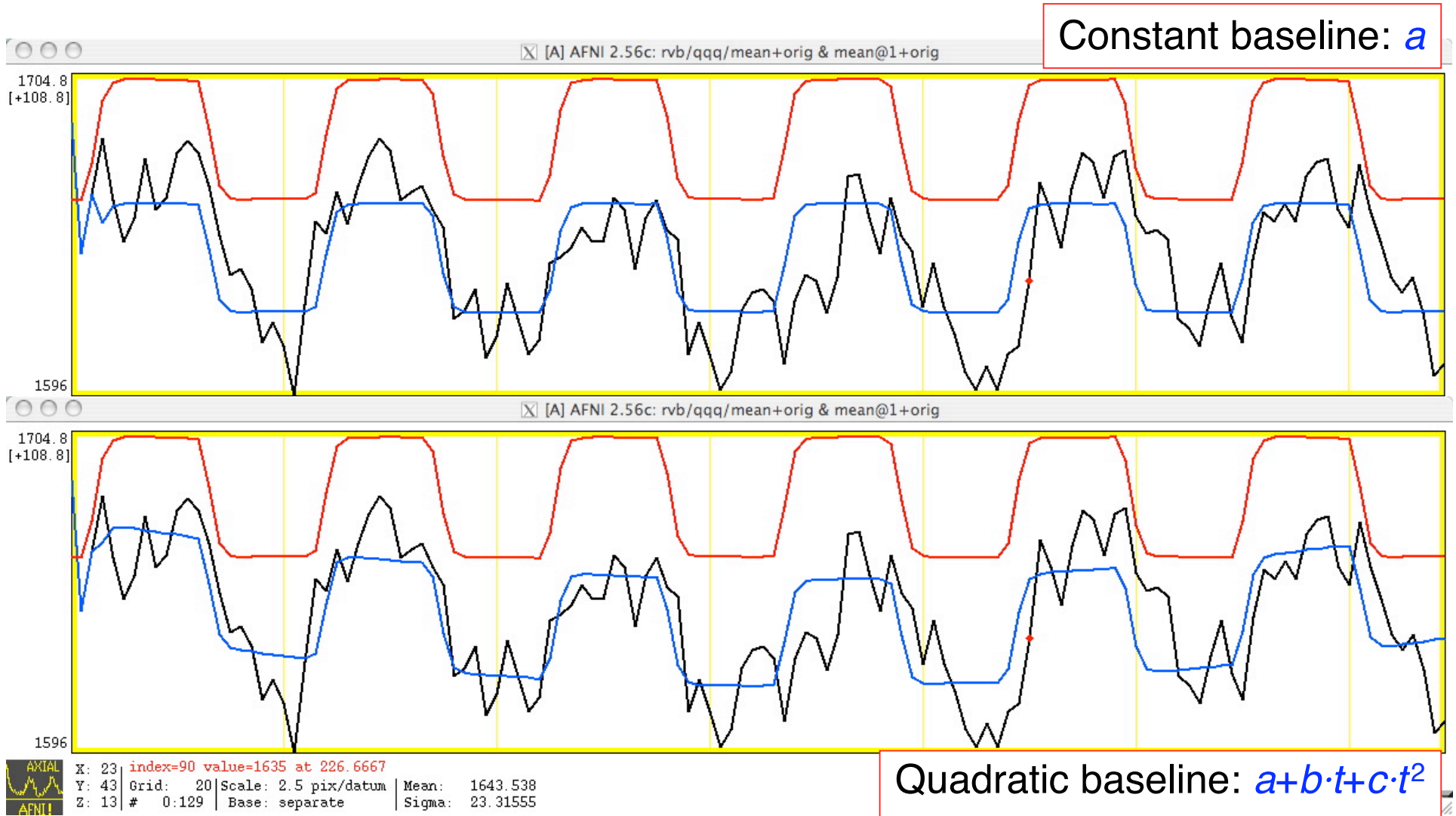
• Necessary baseline model complexity depends on duration of **continuous** imaging — e.g., 1 parameter per 100 seconds

Multiple Stimuli = Multiple Regressors

- Usually have more than one class of stimulus or activation in an experiment

  ★ e.g., want to see size of "face activation" vis-à-vis "house activation"; or, "what" vs. "where" activity

- Need to model each separate class of stimulus with a separate response function $r_1(t)$, $r_2(t)$, $r_3(t)$, ….

  ★ Each $r_j(t)$ is based on the stimulus timing for activity in class number j

  ★ Calculate a β_j amplitude = amount of $r_j(t)$ in voxel data time series $Z(t)$

  ★ Contrast βs to see which voxels have differential activation levels under different stimulus conditions

    ✧ e.g., statistical test on the question $\beta_1 - \beta_2 = 0$?

Multiple Regressors: Cartoon
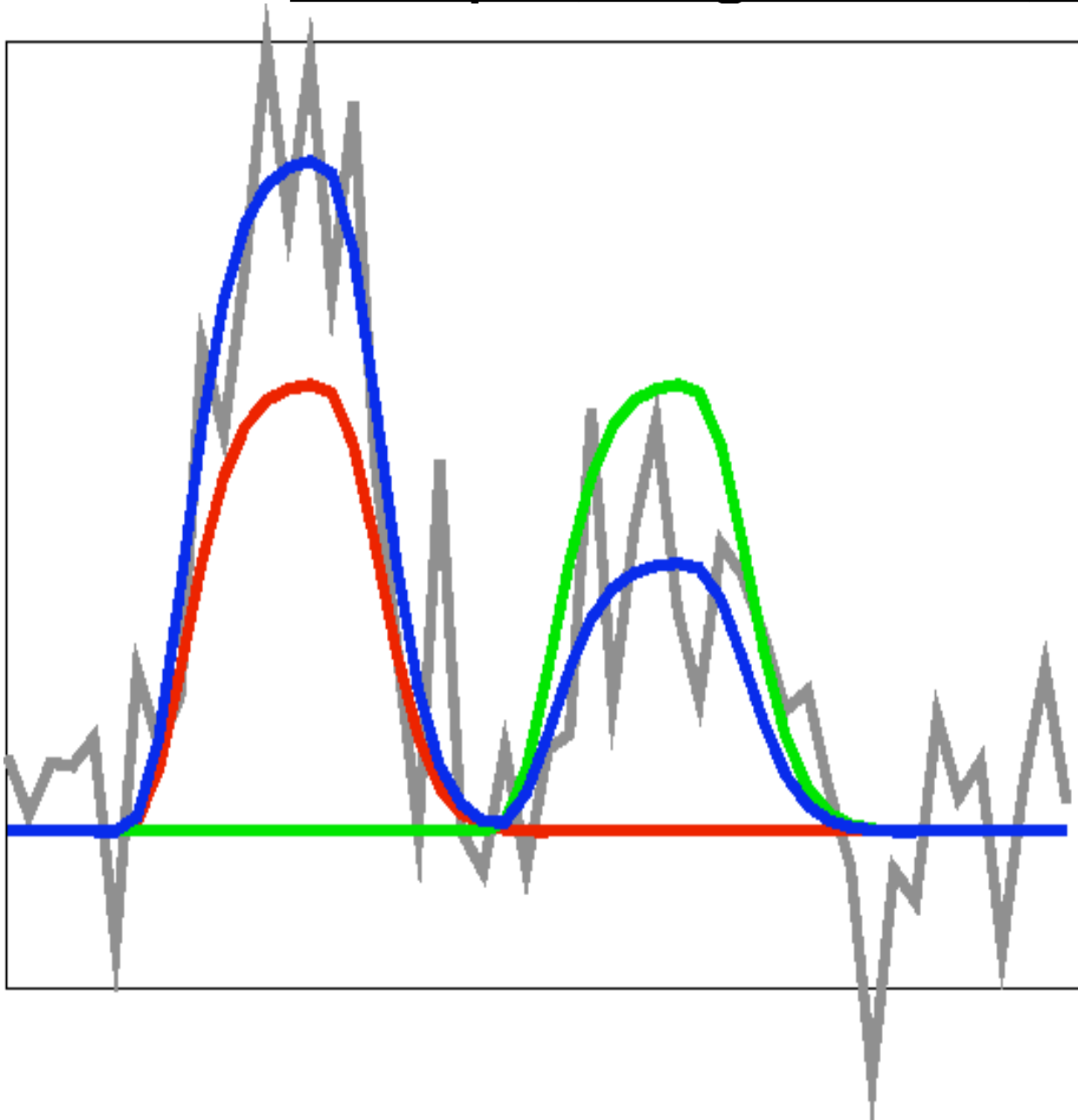
- **Red** curve = signal model for class #1
- **Green** curve = signal model for #2
- **Blue** curve = $\beta_1 \cdot$ **#1** $+ \beta_2 \cdot$ **#2** where β_1 and β_2 vary from 0.1 to 1.7 in the animation
- Goal of regression is to find β_1 and β_2 that make the blue curve best fit the data time series
- **Gray** curve = **1.5**$\cdot$**#1**+**0.6**$\cdot$**#2**+noise = simulated data

Multiple Regressors: Collinearity!☹!
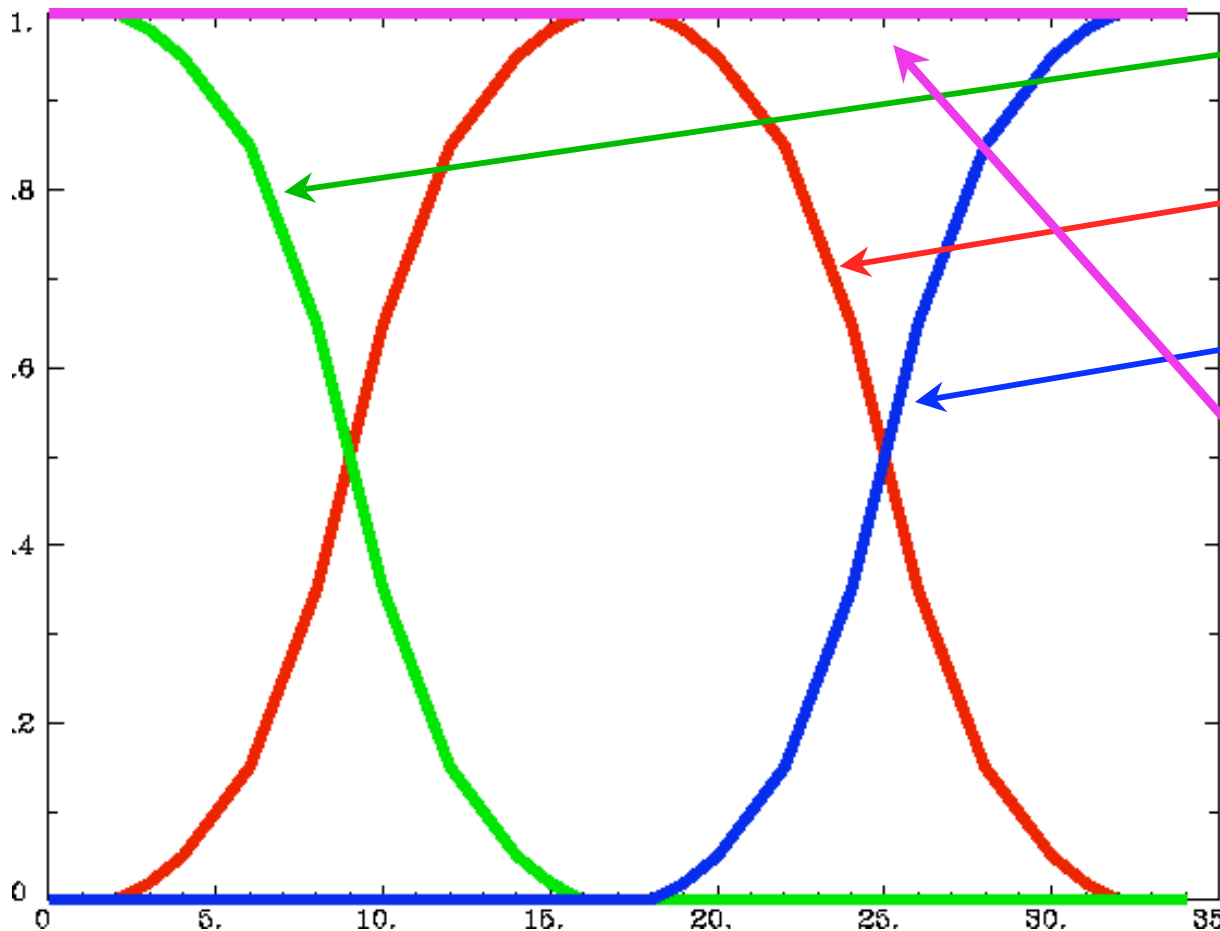
- **Green** curve = signal model for #1
- **Red** curve = signal model for class #2
- **Blue** curve = signal model for #3
- **Purple** curve = **#1** + **#2** + **#3** which is exactly = 1
- We cannot — *in principle or in practice* — distinguish sum of 3 signal models from constant baseline!☹!

No analysis can distinguish the cases

$Z(t)$=10+ 5·**#1**   and

$Z(t)$= 0+15·**#1**+10·**#2**+10·**#3**

and an infinity of other possibilities

Collinear designs are **bad bad bad**!

Multiple Regressors: Near Collinearity

Red & **Green** stimuli average 2 s apart
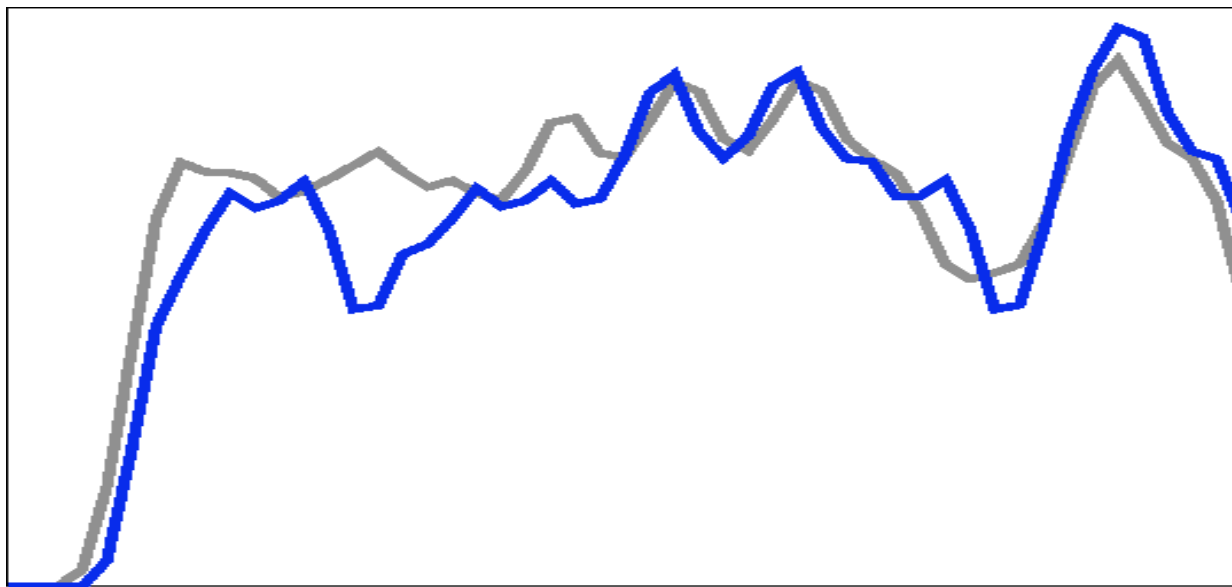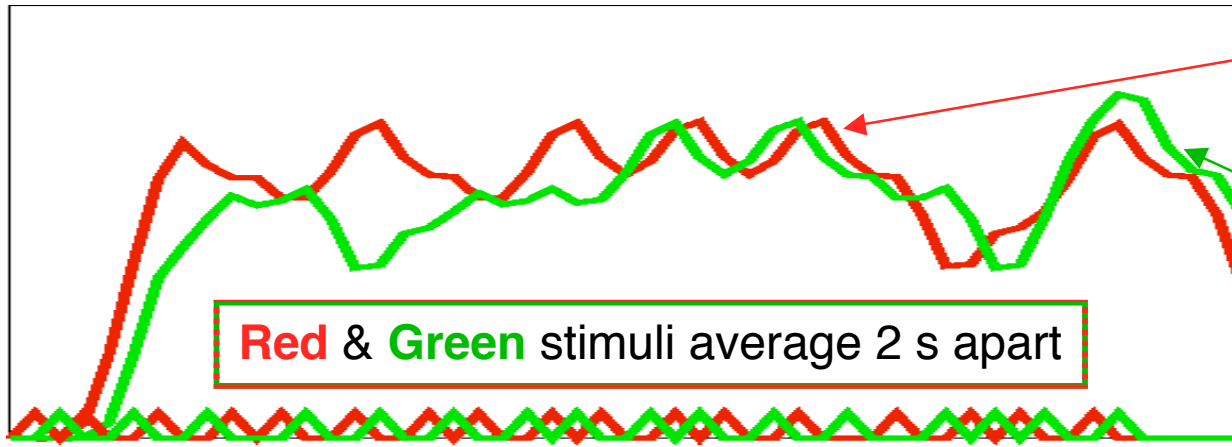
- **Red** curve = signal model for class #1
- **Green** curve = signal model for #2
- **Blue** curve = $\beta_1 \cdot$ **#1** $+ (1-\beta_1) \cdot$ **#2** where β_1 varies randomly from 0.0 to 1.0 in animation
- **Gray** curve = **0.66**$\cdot$**#1** + **0.33**$\cdot$**#2** = simulated data *with no noise*
- Lots of different combinations of **#1** and **#2** are decent fits to gray curve

Stimuli are too close in time to distinguish response **#1** from **#2**, considering noise

Equations: Notation

- Will generally follow notation of Doug Ward's manual for the AFNI program **3dDeconvolve**
- Time: continuous in reality, but in steps in the data
  - ★ Functions of continuous time are written like $f(t)$
  - ★ Functions of discrete time expressed like $f(n \cdot TR)$ where $n=0,1,2,\ldots$ and TR=time step $= t_n$
  - ★ Usually use subscript notion f_n as shorthand
  - ★ Collection of numbers assembled in a column is a **vector** and is printed in boldface:

$$
\left\{ \begin{array}{c} \text{vector of} \\ \text{length } N \end{array} \right\} = \begin{bmatrix} f_0 \\ f_1 \\ f_2 \\ M \\ f_{N-1} \end{bmatrix} = \mathbf{f} \qquad \begin{bmatrix} A_{00} & A_{01} & L & A_{0,N-1} \\ A_{10} & A_{11} & L & A_{1,N-1} \\ M & M & O & M \\ A_{M-1,0} & A_{M-1,1} & L & A_{M-1,N-1} \end{bmatrix} = \mathbf{A} = \left\{ M \times N \text{ matrix} \right\}
$$

Equations: Single Response Function

- In each voxel, fit data Z_n to a curve of the form
  $$Z_n \approx a + b \cdot t_n + \beta \cdot r_n \quad \text{for } n=0,1,\ldots,N\text{-}1 \; (N=\# \text{ time pts})$$
  - a, b, β are unknown parameters to be calculated in each voxel
  - a, b are "nuisance" baseline parameters
  - β is amplitude of $r(t)$ in data = "how much" BOLD
  - Baseline model might be more complicated for long (> 200 s) continuous imaging runs:
    - $T < 300$ s: $a+b\cdot t+c\cdot t^2$
    - Longer: $a+b\cdot t+c\cdot t^2 + \lceil T/200 \rceil$ low frequency components
    - Might also include as extra baseline components the estimated subject head movement time series, in order to remove residual contamination from such artifacts

Equations: Multiple Response Functions

- In each voxel, fit data Z_n to a curve of the form

$$Z_n \approx [\text{baseline}]_n + \beta_1 \cdot r_n^{(1)} + \beta_2 \cdot r_n^{(2)} + \beta_3 \cdot r_n^{(3)} + \text{L}$$

  - β_j is amplitude in data of $r_n^{(j)} = r_j(t_n)$; i.e., "how much" of jth response function in in the data time series

  - In simple regression, each $r_j(t)$ is derived directly from stimulus timing **and** user-chosen HRF model

    - In terms of stimulus times: $r_n^{(j)} = \sum_{k=1}^{K_j} h(t_n - \tau_k^{(j)})$

    - If stimulus occurs on the imaging TR time-grid, stimulus can be represented as a 0-1 time series:

$$\begin{bmatrix} s_0^{(j)} & s_1^{(j)} & s_2^{(j)} & s_3^{(j)} & \text{L} \end{bmatrix}$$ where $s_k^{(j)} = 1$ if stimulus #j is on at time $t = k \cdot \text{TR}$, and $s_k^{(j)} = 0$ if #j is off at that time:

$$r_n^{(j)} = h_0 s_n^{(j)} + h_1 s_{n-1}^{(j)} + h_2 s_{n-2}^{(j)} + h_3 s_{n-3}^{(j)} + \text{L} = \sum_{q=0}^{p} h_q s_{n-q}^{(j)}$$

Equations: Matrix-Vector Form

- Express **known** data vector as a sum of **known** columns with **unknown** coefficents:

$$\begin{bmatrix} z_0 \\ z_1 \\ z_2 \\ M \\ z_{N-1} \end{bmatrix} \approx \begin{bmatrix} 1 \\ 1 \\ 1 \\ M \\ 1 \end{bmatrix} \cdot a + \begin{bmatrix} 0 \\ 1 \\ 2 \\ M \\ 1 \end{bmatrix} \cdot b + \begin{bmatrix} r_0^{(1)} \\ r_1^{(1)} \\ r_2^{(1)} \\ M \\ r_{N-1}^{(1)} \end{bmatrix} \cdot \beta_1 + \begin{bmatrix} r_0^{(2)} \\ r_1^{(2)} \\ r_2^{(2)} \\ M \\ r_{N-1}^{(2)} \end{bmatrix} \cdot \beta_2 + L$$

or

$$\begin{bmatrix} z_0 \\ z_1 \\ z_2 \\ M \\ z_{N-1} \end{bmatrix} \approx \begin{bmatrix} 1 & 0 & r_0^{(1)} & r_0^{(1)} & L \\ 1 & 1 & r_1^{(1)} & r_1^{(1)} & L \\ 1 & 2 & r_2^{(1)} & r_2^{(1)} & L \\ M & M & M & M & O \\ 1 & N-1 & r_{N-1}^{(1)} & r_{N-1}^{(2)} & L \end{bmatrix} \begin{bmatrix} a \\ b \\ \beta_1 \\ \beta_2 \\ M \end{bmatrix}$$

or

'≈' means "least squares"

$$\mathbf{z} \approx \mathbf{R} \, \beta$$

vector of data   matrix of columns   vector of coeff
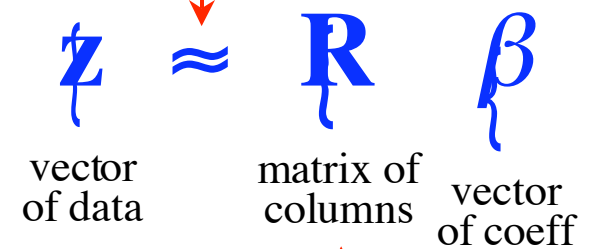
the "design" matrix

$\mathbf{z}$ depends on the voxel; $\mathbf{R}$ doesn't

Visualizing the **R** Matrix

- Can graph columns, as shown below
  - But might have 20-50 columns
- Can plot columns on a grayscale, as shown at right
  - Easier to show many columns
  - In this plot, darker bars means larger numbers

response to stim B column #4

response to stim A: column #3

linear trend: column #2

constant baseline: column #1
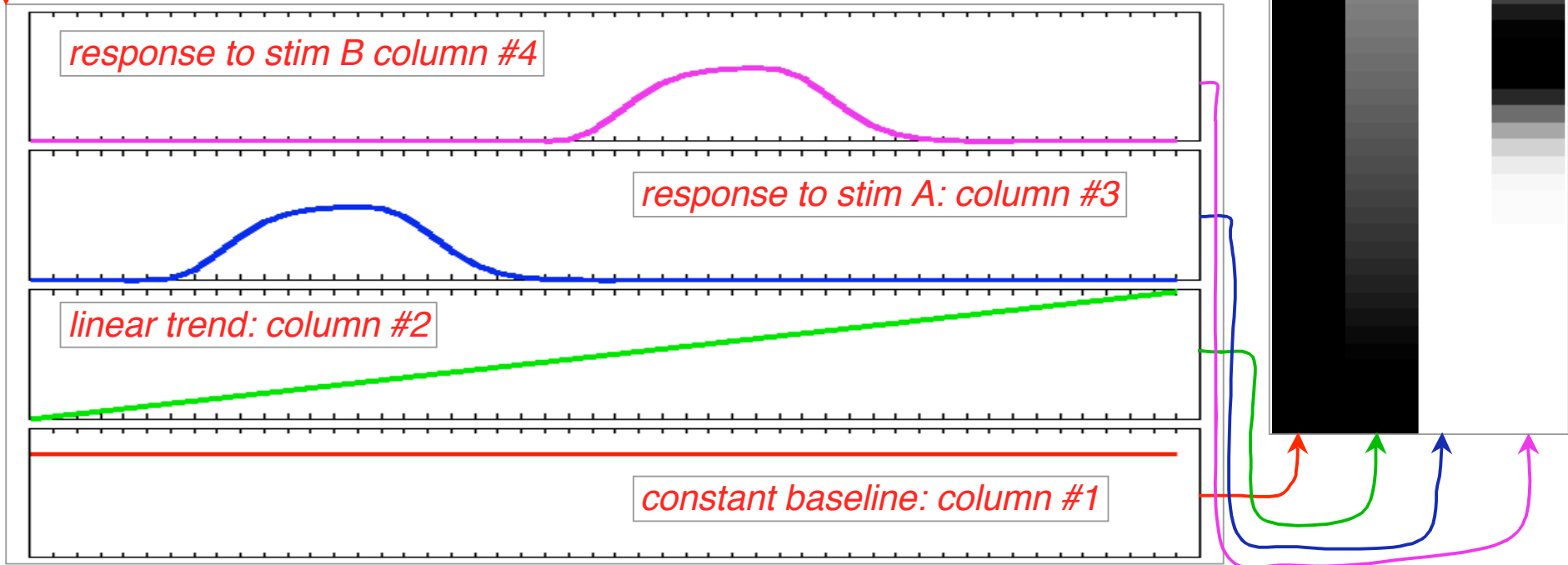
Solving $\mathbf{z} \approx \mathbf{R}\beta$ for β

- Number of equations = number of time points
  - ★ 100s per run, but perhaps 1000s per subject
- Number of unknowns usually in range 5–50
- Least squares solution: $\hat{\beta} = \left[\mathbf{R}^T\mathbf{R}\right]^{-1}\mathbf{R}^T\mathbf{z}$
  - ★ $\hat{\beta}$ denotes an *estimate* of the true (unknown) β
  - ★ From $\hat{\beta}$, calculate $\hat{\mathbf{z}} = \mathbf{R}\hat{\beta}$ as the *fitted model*
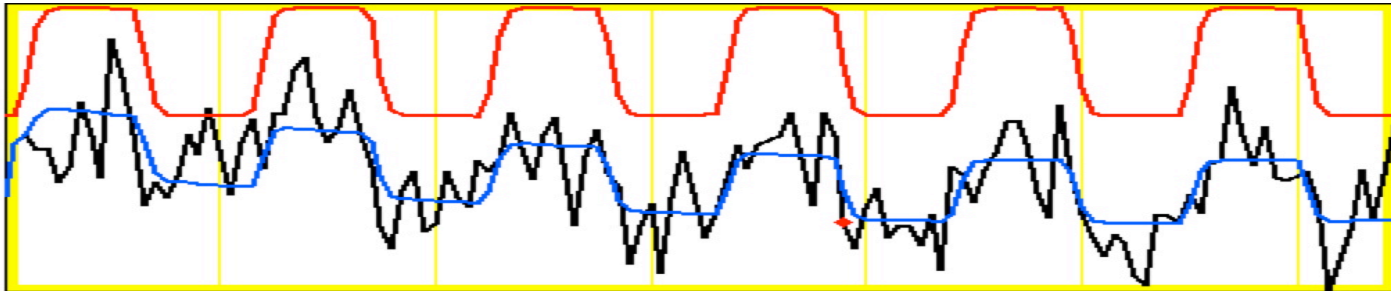
  - ✧ $\mathbf{z} - \hat{\mathbf{z}}$ is the ***residual time series*** = noise (we hope)
- Collinearity: when matrix $\mathbf{R}^T\mathbf{R}$ can't be inverted
  - ★ Near collinearity: when inverse exists but is huge

Simple Regression: Recapitulation

- Choose HRF model $h(t)$ [AKA *fixed-model regression*]
- Build model responses $r_n(t)$ to each stimulus class
  - ★ Using $h(t)$ and the stimulus timing
- Choose baseline model time series
  - ★ Constant + linear + quadratic + movement?
- Assemble model and baseline time series into the columns of the **R** matrix
- For each voxel time series **z**, solve $\mathbf{z} \approx \mathbf{R}\boldsymbol{\beta}$ for $\hat{\boldsymbol{\beta}}$
- **Individual subject maps**: Test the coefficients in $\hat{\boldsymbol{\beta}}$ that you care about for statistical significance
- **Group maps**: Transform the coefficients in $\hat{\boldsymbol{\beta}}$ that you care about to Talairach space, and perform statistics on these $\hat{\boldsymbol{\beta}}$ values

Sample Data Analysis: Simple Regression

- Enough theory (for now: more to come later!)

- To look at the data: type **cd AFNI_data1/afni** ; then **afni**

- **Switch Underlay** to dataset **epi_r1**
  - ★ Then Sagittal **Image** and **Graph**
  - ★ **FIM→Pick Ideal** ; then click **afni/ideal_r1.1D** ; then **Set**
  - ★ Right-click in image, **Jump to (ijk)**, then **29 11 13**, then **Set**
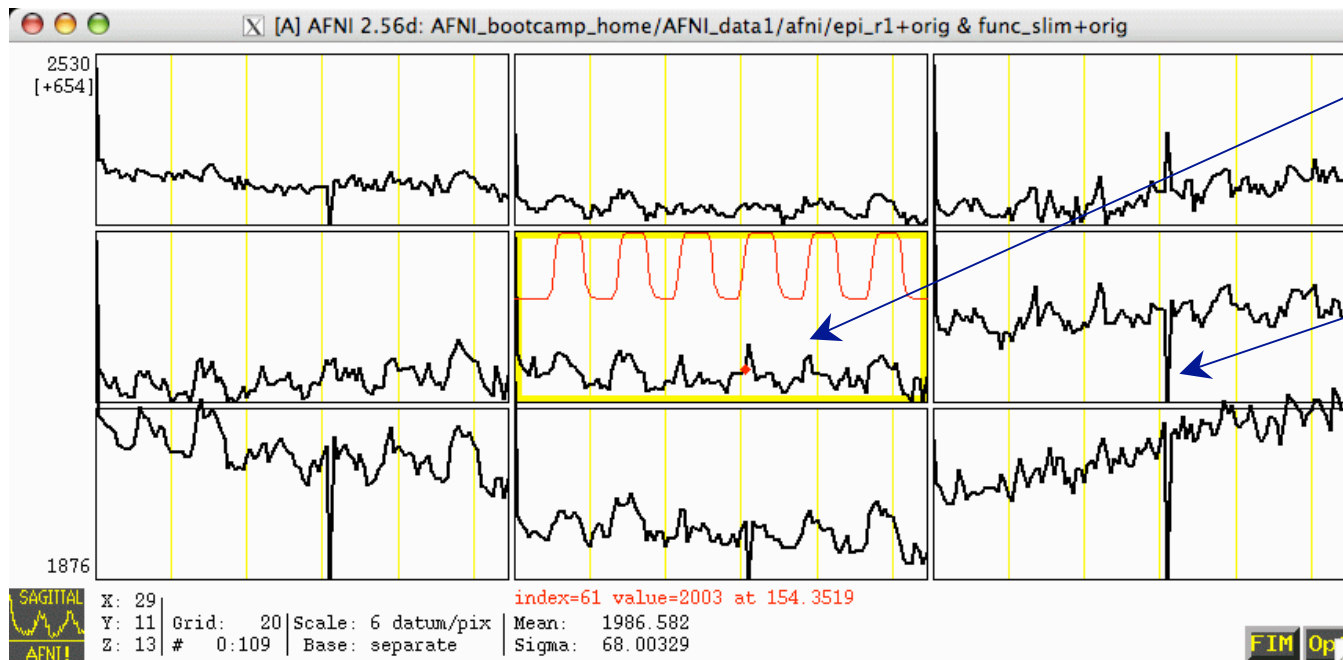
- Data clearly has activity in sync with reference
- Data also has a big spike, which is annoying
  - Subject head movement!

Preparing Data for Analysis

- Six preparatory steps are possible

  ★ Image registration (realignment): program **3dvolreg**

  ★ Image smoothing: program **3dmerge**

  ★ Image masking: program **3dClipLevel** or **3dAutomask**

  ★ Conversion to percentile: programs **3dTstat** and **3dcalc**

  ★ Censoring out time points that are bad: program **3dToutcount** or **3dTqual**

  ★ Catenating multiple imaging runs into 1 big dataset: program **3dTcat**

- Not all steps are necessary or desirable in any given case

- In this first example, will only do registration, since the data obviously needs this correction

Data Analysis Script

- In file **epi_r1_decon**:

```
waver -GAM                                    \
      -input epi_r1_stim.1D                   \
      -TR 2.5                                 \
      > epi_r1_ideal.1D


3dvolreg -base 2                              \
         -prefix epi_r1_reg                   \
         -1Dfile epi_r1_mot.1D                \
         -verb                                \
         epi_r1+orig



3dDeconvolve                                  \
   -input epi_r1_reg+orig                     \
   -nfirst      2                             \
   -num_stimts 1                              \
   -stim_file  1 epi_r1_ideal.1D              \
   -stim_label 1 AllStim                      \
   -tout                                      \
   -bucket epi_r1_func                        \
   -fitts  epi_r1_fitts
```

- **waver** creates model time series from input stimulus timing in file **epi_r1_stim.1D**
- Plot a 1D file to screen with
    1dplot epi_r1_ideal.1D

3dvolreg (3D image registration) will be covered in a later presentation

- **3dDeconvolve** = regression code
- Name of input dataset
- Index of first sub-brick to process
- Number of input model time series
- Name of first input model time series file
- Name for results in AFNI menus
- Indicates to output *t*-statistic for β weights
- Name of output "bucket" dataset (statistics)
- Name of output model fit dataset

Contents of .1D files

epi_r1_stim.1D   epi_r1_ideal.1D

0	0
0	0
0	0
0	0
0	0
0	0
0	0
0	0
0	0
1	0
1	24.4876
1	122.869
1	156.166
1	160.258
1	160.547
1	160.547
1	160.547
1	160.547
0	136.059
0	37.6781
0	4.38121
0	0.288748
0	0
0	0
...	...

- 1 line per time point
- TR=2.5 s
- 0=stim OFF
- 1=stim ON
- Note that "ideal" is delayed from stimulus
- Graphs at right created with **1dplot**
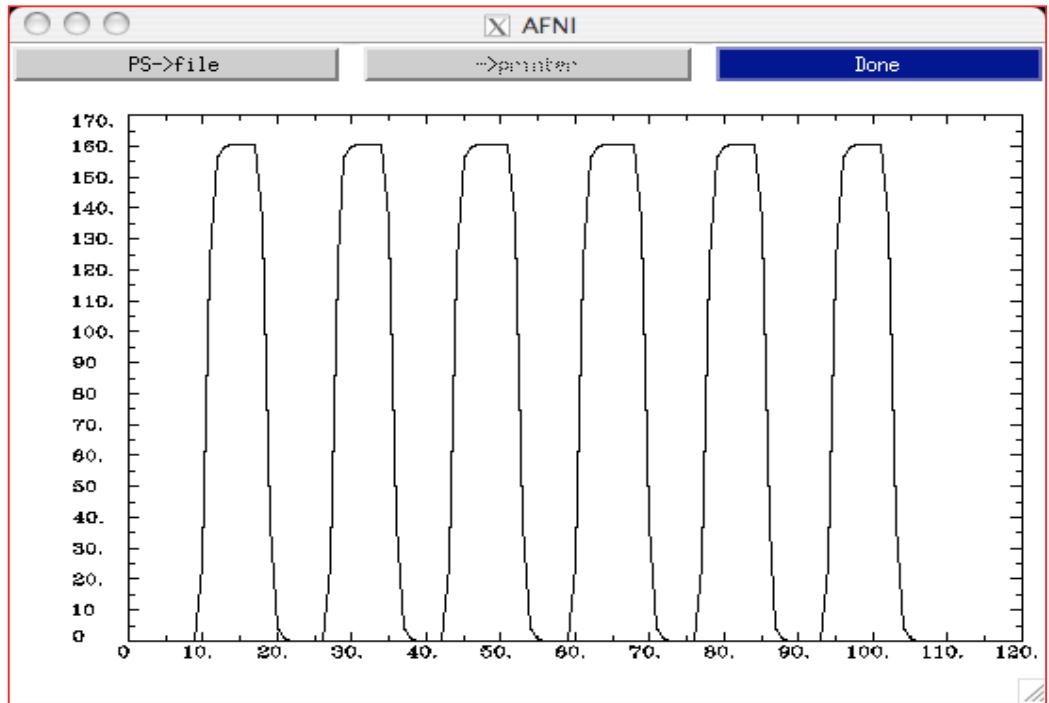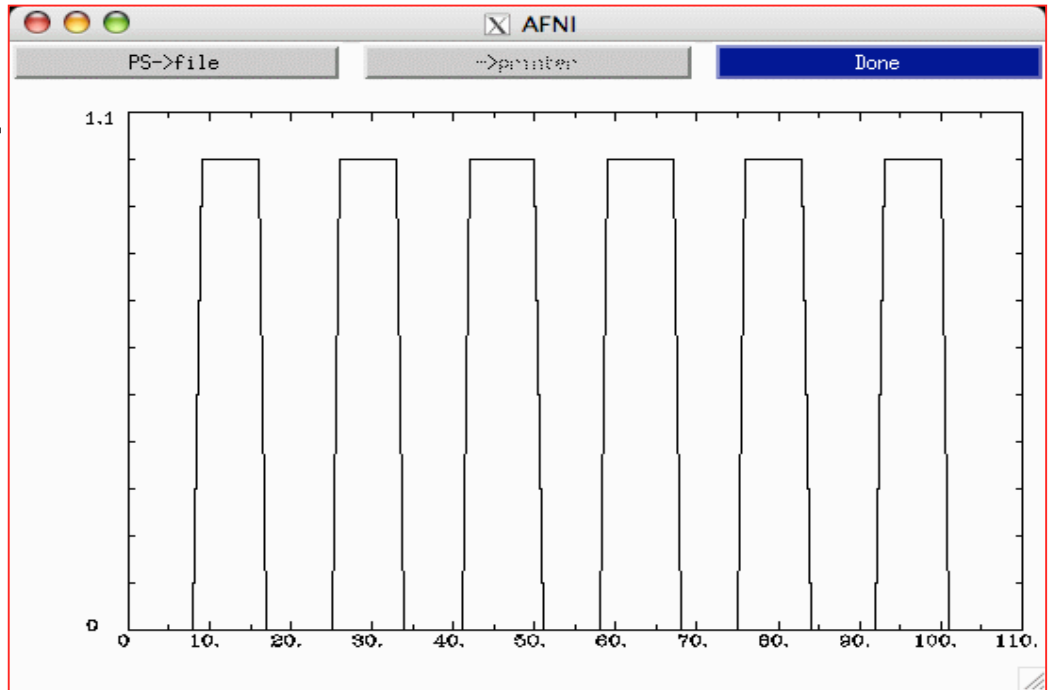
To Run Script and View Results

- type **source epi_r1_decon** ; then wait for programs to run
- type **afni** to view what we've got
  - ★ **Switch Underlay** to epi_r1_reg (output from **3dvolreg**)
  - ★ **Switch Overlay** to epi_r1_func (output from **3dDeconvolve**)
  - ★ **Sagittal Image** and **Graph** viewers
  - ★ **FIM→Ignore→2** to have graph viewer not plot 1st 2 time pts
  - ★ **FIM→Pick Ideal** ; pick **epi_r1_ideal.1D** (output from **waver**)
- Define Overlay to set up functional coloring
  - • **Olay→Allstim[0] Coef** (sets coloring to be from model fit β)
  - • **Thr→Allstim[0] t-s** (sets threshold to be model fit t-statistic)
  - • **See Overlay** (otherwise won't see the function!)
  - • Play with threshold slider to get a meaningful activation map (e.g., t=4 is a decent threshold)

More Viewing the Results

- Graph viewer: **Opt→Tran 1D→Dataset #N** to plot the model fit dataset output by **3dDeconvolve**

  - Will open the control panel for the **Dataset #N** plugin

  - Click first **Input** on ; then choose **Dataset epi_r1_fitts+orig**

  - Also choose **Color dk-blue** to get a pleasing plot

  - Then click on **Set+Close** (to close the plugin panel)

  - Should now see fitted time series in the graph viewer instead of data time series

  - Graph viewer: click **Opt→Double Plot→Overlay** on to make the fitted time series appear as an overlay curve

  - This tool lets you visualize the quality of the data fit

- Can also now overlay function on MP-RAGE anatomical by using **Switch Underlay** to **anat+orig** dataset

  - Probably won't want to graph the **anat+orig** dataset!

Stimulus Correlated Movement?

- **3dvolreg** saved the motion parameters estimates into file **epi_r1_mot.1D**
- For fun: **1dplot epi_r1_mot.1D**
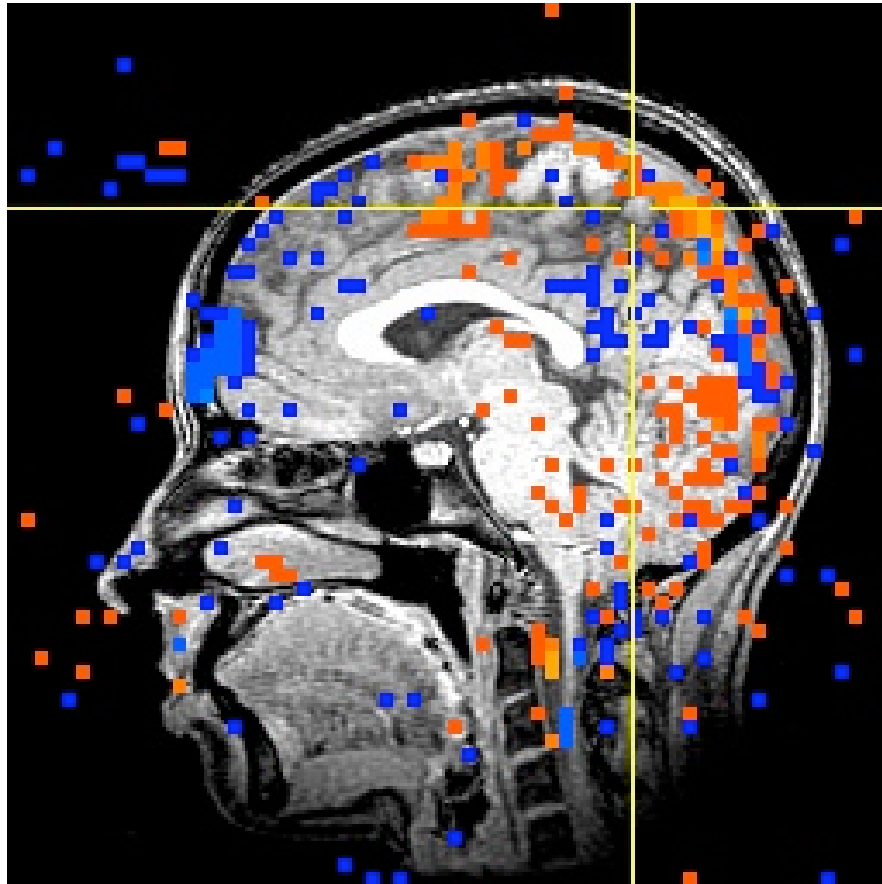
- Extensive "activation" (i.e., correlation of data time series with model time series) along the top of the brain is an indicator of stimulus correlated motion artifact
- Can remain even after registration, due to errors in registration, magnetic field inhomogeneities, etc.
- Can be partially removed by using the estimated movement history (from **3dvolreg**) as additional baseline model functions

Removing Residual Motion Artifacts

- Last part of script **epi_r1_decon**:

```
3dDeconvolve                              \
    -input epi_r1_reg+orig                \
    -nfirst       2                       \
    -num_stimts 7                         \
    -stim_file  1 epi_r1_ideal.1D         \
    -stim_label 1 AllStim                 \
    -stim_file  2 epi_r1_mot.1D'[0]'    \
    -stim_base  2                         \
    -stim_file  3 epi_r1_mot.1D'[1]'    \
    -stim_base  3                         \
    -stim_file  4 epi_r1_mot.1D'[2]'    \
    -stim_base  4                         \
    -stim_file  5 epi_r1_mot.1D'[3]'    \
    -stim_base  5                         \
    -stim_file  6 epi_r1_mot.1D'[4]'    \
    -stim_base  6                         \
    -stim_file  7 epi_r1_mot.1D'[5]'    \
    -stim_base  7                         \
    -tout                                 \
    -bucket epi_r1_func_mot               \
    -fitts  epi_r1_fitts_mot
```

These new lines add 6 regressors to the model and assign them to the baseline (**-stim_base** option)

Output files: take a moment to look at results

Some Results: Before and After
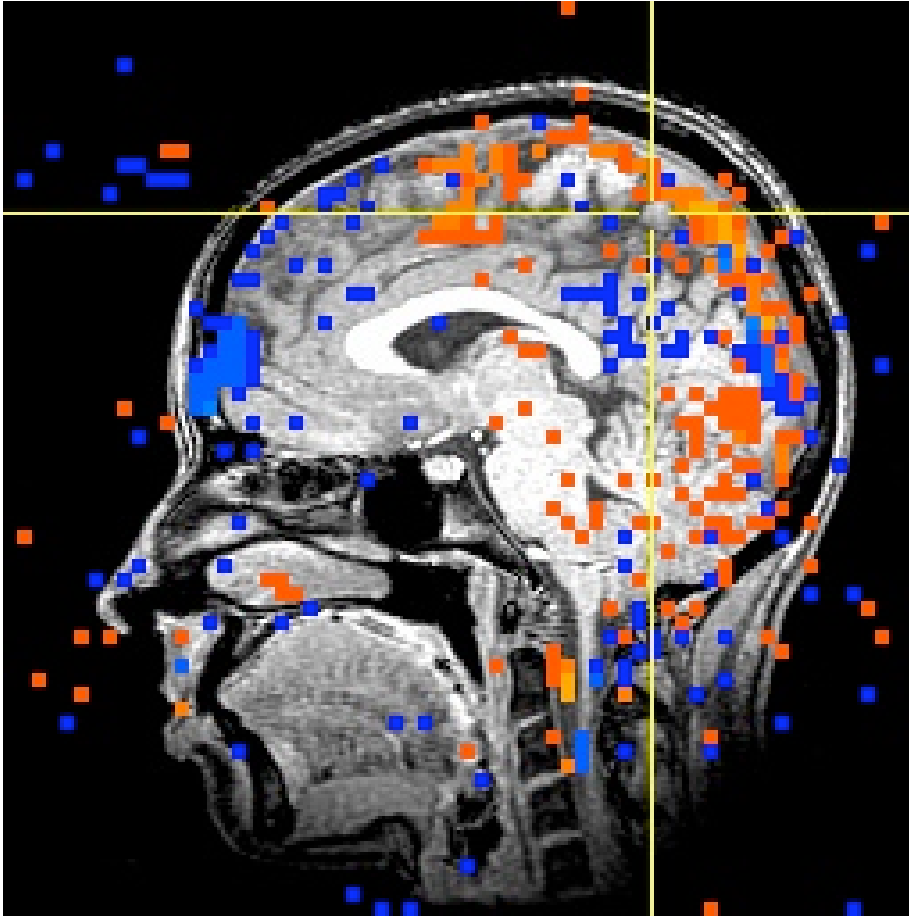
No: movement parameters
are not in baseline model
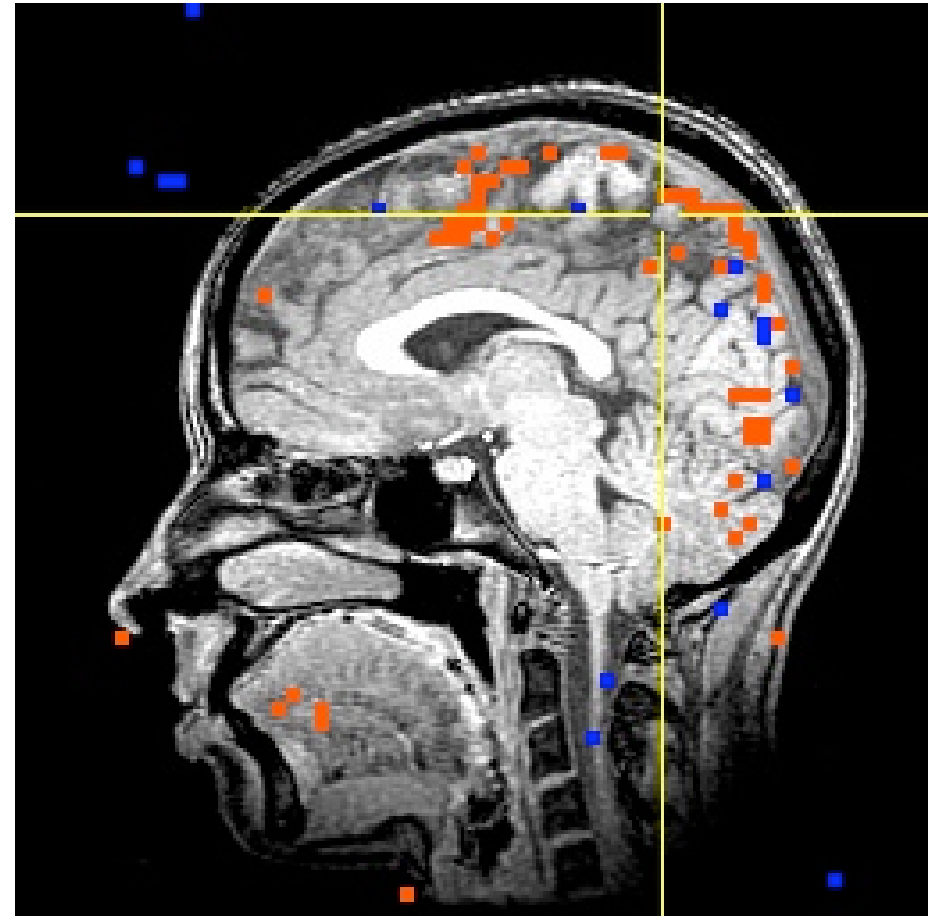
Yes: movement parameters
are in baseline model

t-statistic threshold set to a p-value of 10^{-4} in both images

Multiple Stimulus Classes

- The experiment analyzed here in fact is more complicated

  ★ There are 4 related visual stimulus types

  ★ One goal is to find areas that are differentially activated between these different types of stimuli

  ★ We have 4 imaging runs, 108 useful time points each (skipping first 2 in each run) that we will analyze together

    ◇ Already registered and put together into dataset **rall_vr+orig**

  ★ Stimulus timing files are in subdirectory **stim_files/**

  ★ Script file **waver_ht2** will create HRF models for regression:
  ```
  cd stim_files
  waver -dt 2.5 -GAM -input scan1to4a.1D > scan1to4a_hrf.1D
  waver -dt 2.5 -GAM -input scan1to4t.1D > scan1to4t_hrf.1D
  waver -dt 2.5 -GAM -input scan1to4h.1D > scan1to4h_hrf.1D
  waver -dt 2.5 -GAM -input scan1to4l.1D > scan1to4l_hrf.1D
  cd ..
  ```

  ★ type **source waver_ht2** to run this script

    ◇ Might also use **1dplot** to check if things are reasonable

Regression with Multiple Model Files

- Script file **decon_ht2** does the job:

```
3dDeconvolve -xout -input rall_vr+orig                               \
    -num_stimts 4                                                    \
    -stim_file 1 stim_files/scan1to4a_hrf.1D  -stim_label 1 Actions  \
    -stim_file 2 stim_files/scan1to4t_hrf.1D  -stim_label 2 Tool     \
    -stim_file 3 stim_files/scan1to4h_hrf.1D  -stim_label 3 HighC    \
    -stim_file 4 stim_files/scan1to4l_hrf.1D  -stim_label 4 LowC     \
    -concat contrasts/runs.1D                                        \
    -glt 1 contrasts/contr_AvsT.txt    -glt_label 1 AvsT             \
    -glt 1 contrasts/contr_HvsL.txt    -glt_label 2 HvsL             \
    -glt 1 contrasts/contr_ATvsHL.txt -glt_label 3 ATvsHL            \
    -full_first -fout -tout                                          \
    -bucket func_ht2
```

- Run this script by typing **source decon_ht2** (takes a few minutes)

> •Stim #1 = visual presentation of active movements
> •Stim #2 = visual presentation of simple (tool-like) movements
> •Stims #3 and #4 = high and low contrast gratings

Regressors for This Script

Actions	HighC	LowC	Tools

via **1dgrayplot**
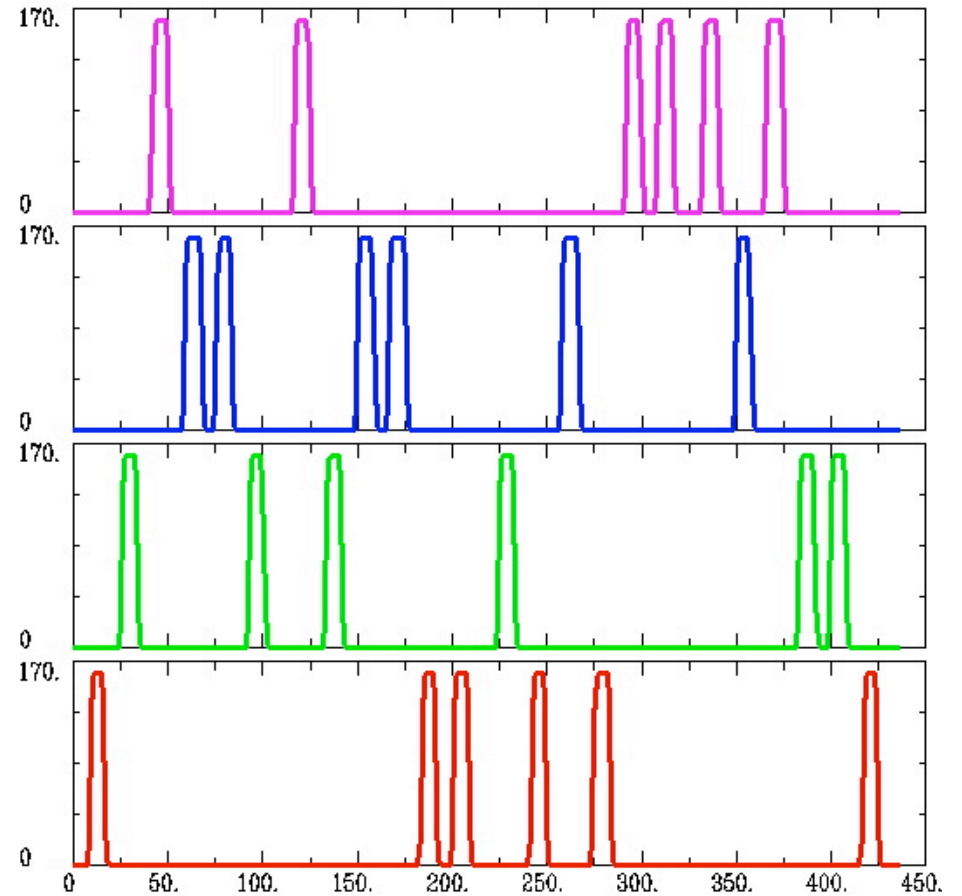
via **1dplot**

New Features of 3dDeconvolve - 1

`-concat contrasts/runs.1D` = file that indicates where new imaging runs start

0
108
216
324
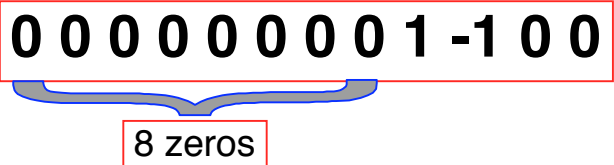
`-full_first` = put **full model** statistic first in output file, rather than last

`-fout -tout` = output both *F*- and *t*-statistics

- The full model statistic is an *F*-statistic that shows how well the sum of all 4 input model time series fits the voxel time series data

- The individual models also will get individual *F*- and *t*-statistics indicating the significance of their individual contributions to the time series fit

New Features of 3dDeconvolve - 2

```
-glt 1 contrasts/contr_AvsT.txt    -glt_label 1 AvsT
-glt 1 contrasts/contr_HvsL.txt    -glt_label 2 HvsL
-glt 1 contrasts/contr_ATvsHL.txt -glt_label 3 ATvsHL
```

- **GLT**s are General Linear Tests

- **3dDeconvolve** provides tests for each regressor separately, but if you want to test combinations or contrasts of the β weights in each voxel, you need the **-glt** option

- File **contrasts/contr_AvsT.txt** = 0 0 0 0 0 0 0 0 1 -1 0 0
(one line with 12 numbers)

  8 zeros

- Goal is to test a linear combination of the β weights

  ★ In this data, we have 12 β weights: 8 baseline parameters (2 per imaging run), which are first in the β vector, and 4 regressor magnitudes, which are from **-stim_file** options

  ★ This particular test contrasts the Actions and Tool βs

    • tests if $\beta_{Actions} - \beta_{Tool} \neq 0$

New Features of 3dDeconvolve - 3

- File **contrasts/contr_HvsL.txt** = $\boxed{0\ 0\ 0\ 0\ 0\ 0\ 0\ 0\ 0\ 1\ \text{-}1}$
  - Goal is to test if $\beta_{\text{HighC}} - \beta_{\text{LowC}} \neq 0$

- File **contrasts/contr_ATvsHL.txt** = $\boxed{0\ 0\ 0\ 0\ 0\ 0\ 0\ 0\ 1\ 1\ \text{-}1\ \text{-}1}$
  - Goal is to test if $(\beta_{\text{Actions}} + \beta_{\text{Tool}}) - (\beta_{\text{HighC}} + \beta_{\text{LowC}}) \neq 0$
  - Regions where this statistic is significant will have had different amounts of BOLD signal change in the activity viewing tasks versus the grating viewing tasks
    - This is a way to factor out primary visual cortext

- **-glt_label 3 ATvsHL** option is used to attach a meaningful label to the resulting statistics sub-bricks

Results of **decon_ht2** Script

- Menu showing labels from **3dDeconvolve** run

- Images showing results from third contrast: **ATvsHL**

- Play with this yourself to get a feel for it

Statistics from 3dDeconvolve

- An *F*-statistic measures significance of how much a model component reduced the variance of the time series data

- Full *F* measures how much the signal regressors reduced the variance over just the baseline regressors (**sub-brick #0 below**)

- Individual partial-model *F*s measures how much each individual signal regressor reduced data variance over the full model with that regressor excluded (**sub-bricks #19, #22, #25, and #28 below**)

- The **Coef** sub-bricks are the β weights (e.g., **#17, #20, #23, #26**)

- A *t*-statistic sub-brick measure impact of one coefficient

```
# 0 Full F-stat    #13 Run  #4 t^0 Coe #26 LowC[0] Coef
# 1 Run  #1 t^0 Coe #14 Run  #4 t^0 t-s #27 LowC[0] t-st
# 2 Run  #1 t^0 t-s #15 Run  #4 t^1 Coe #28 LowC F-stat
# 3 Run  #1 t^1 Coe #16 Run  #4 t^1 t-s #29 AvsT LC[0] coe
# 4 Run  #1 t^1 t-s #17 Actions[0] Coe #30 AvsT LC[0] t-s
# 5 Run  #2 t^0 Coe #18 Actions[0] t-s #31 AvsT F-stat
# 6 Run  #2 t^0 t-s #19 Actions F-stat #32 HvsL LC[0] coe
# 7 Run  #2 t^1 Coe #20 Tool[0] Coef   #33 HvsL LC[0] t-s
# 8 Run  #2 t^1 t-s #21 Tool[0] t-st   #34 HvsL F-stat
# 9 Run  #3 t^0 Coe #22 Tool F-stat    #35 ATvsHL LC[0] c
#10 Run  #3 t^0 t-s #23 HighC[0] Coef  #36 ATvsHL LC[0] t
#11 Run  #3 t^1 Coe #24 HighC[0] t-st  #37 ATvsHL F-stat
#12 Run  #3 t^1 t-s #25 HighC F-stat
```

Alternative Way to Run waver

- Instead of giving stimulus timing on the TR-grid as a set of 0s and 1s

- Can give the actual stimulus times (in seconds) using the **-tstim** option

  ★ **waver -dt 1.0 -GAM -tstim 3 12 17 | 1dplot -stdin**
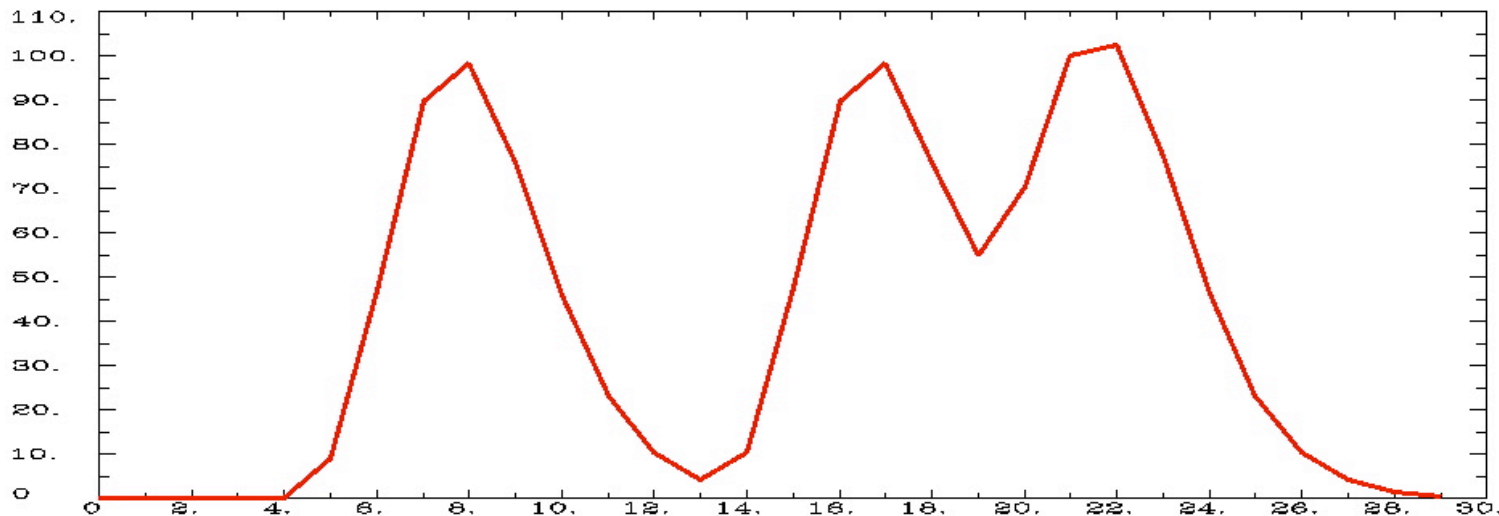
- If times are in a file, can use **-tstim `cat filename`** to place them on the command line after **-tstim** option

  ★ This is most useful for event-related experiments

Note backward single quotes

Deconvolution Signal Models

- Simple or Fixed-shape regression
  - ★ We fixed the shape of the HRF
  - ★ Used waver to generate the signal model from the stimulus timing
  - ★ Found the amplitude of the signal model in each voxel
- Deconvolution or Variable-shape regression
  - ★ We allow the shape of the HRF to vary in each voxel, for each stimulus class
  - ★ Appropriate when you don't want to over-constrain the solution by assuming an HRF shape
  - ★ However, need to have enough time points during the HRF in order to resolve its shape

Deconvolution: Pros and Cons

☺ Letting HRF shape varies allows for subject and regional variability in hemodynamics

☺ Can test HRF estimate for different shapes; e.g., are later time points more "active" than earlier?

☹ Need to estimate more parameters for each stimulus class than a fixed-shape model (e.g., 4-15 vs. 1)

☹ Which means you need more data to get the same statistical power (assuming that the fixed-shape model you would assume was in fact "correct")

☹ Freedom to get any shape in HRF results can give weird shapes that are difficult to interpret

Expressing HRF via Regression Unknowns

- The tool for expressing an unknown function as a finite set of numbers that can be fit via linear regression is an **expansion in basis functions**

$$h(t) = \beta_0 \psi_0(t) + \beta_1 \psi_1(t) + \beta_2 \psi_2(t) + \mathsf{L} = \sum_{q=0}^{q=p} \beta_q \psi_q(t)$$

  - ★ The basis functions $\psi_q(t)$ are known, as is the expansion order **p**

  - ★ The unknowns to be found (in each voxel) comprises the set of weights β_q for each $\psi_q(t)$

- Since **β** weights appear only by multiplying known values, and HRF only appears by in final signal model by linear convolution, resulting signal model is still solvable by linear regression

Basis Function: "Sticks"

- The set of basis functions you use determines the range of possible HRFs that you can compute
- "Stick" (or Dirac delta) functions are very flexible
  - ★ But they come with a strict limitation
- $\delta(t)$ is 1 at $t=0$ and is 0 at all other values of t
- $\psi_q(t) = \delta(t-q \cdot \mathrm{TR})$ for $q=0,1,2,\ldots,p$
  - $\Rightarrow h(0) = \beta_0$
  - $\Rightarrow h(\mathrm{TR}) = \beta_1$
  - $\Rightarrow h(2 \cdot \mathrm{TR}) = \beta_2$
  - $\Rightarrow h(3 \cdot \mathrm{TR}) = \beta_3$
  - $\Rightarrow$ et cetera
  - $\Rightarrow h(t) = 0$ for any t not on the TR grid
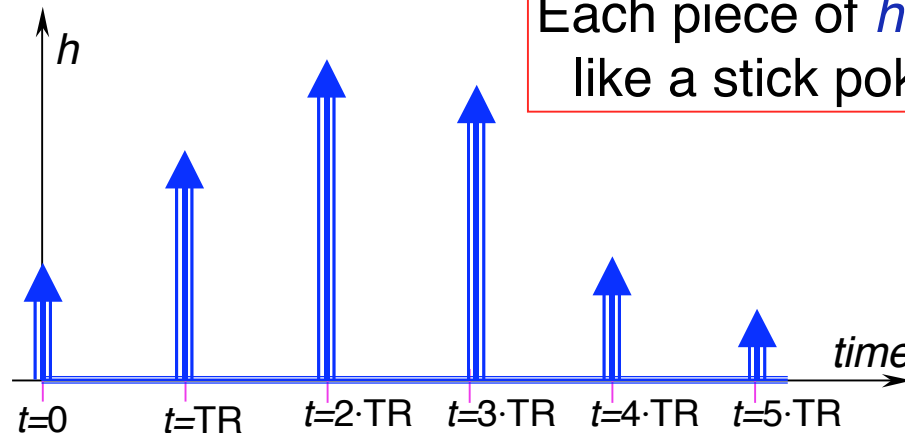
Each piece of $h(t)$ looks like a stick poking up

h

$t=0$ $t=\mathrm{TR}$ $t=2 \cdot \mathrm{TR}$ $t=3 \cdot \mathrm{TR}$ $t=4 \cdot \mathrm{TR}$ $t=5 \cdot \mathrm{TR}$

time

Sticks: Good Points

- Can represent arbitrary shapes of the HRF, up and down, with ease

- Meaning of each β_q is completely obvious

  ★ Value of HRF at time lag $q{\cdot}$TR after activation

- **3dDeconvolve** is set up to deal with stick functions for representing HRF, so using them is very easy

  - What is called p here is given by command line option `-stim_maxlag` in the program

  - When choosing p, rule is to estimate longest duration of neural activation after stimulus onset, then add 10-12 seconds to allow for slowness of hemodynamic response

Sticks and TR-locked Stimuli

- $h(t) = 0$ for any t not on the TR grid
- This limitation means that, using stick functions as our basis set, we can only model stimuli that are "locked" to the TR grid
  - ★ That is, stimuli/activations don't occur at fully general times, but only occur at integer multiples of TR
- For example, suppose an activation is at $t=1.7 \cdot TR$
  - ★ We need to model the response at later times, such as $2 \cdot TR$, $3 \cdot TR$, etc., so need to model $h(t)$ at times such as $t=0.3 \cdot TR$, $1.3 \cdot TR$, etc., after the stimulus
  - But the stick function model doesn't allow for such intermediate times
    - *or*, can allow Δt for sticks to be a fraction of TR for data
    - e.g., $\Delta t = TR/2$, which implies twice as many β_q parameters to cover the same time interval (time interval needed is set by hemodynamics)
    - then would allow stimuli that occur at TR-grid or halfway in-between

Deconvolution and Collinearity

☹ Regular stimulus timing can lead to collinearity!

Equations at each time point: Cannot tell β_0 from β_4, or β_1 from β_5

β_0 β_1 β_2 β_3 β_0 β_1 β_2 β_3 β_0 β_1 β_2 β_3
$+\beta_4$ $+\beta_5$ $+\beta_4$ $+\beta_5$ $+\beta_4$ $+\beta_5$

β_0 β_1 β_2 β_3

β_0 β_1 β_2 β_3 β_4 β_5

HRF from stim #1

β_0 β_1 β_2 β_3 β_4 β_5

β_0 β_1 β_2 β_3 β_4 β_5

time

stim #1
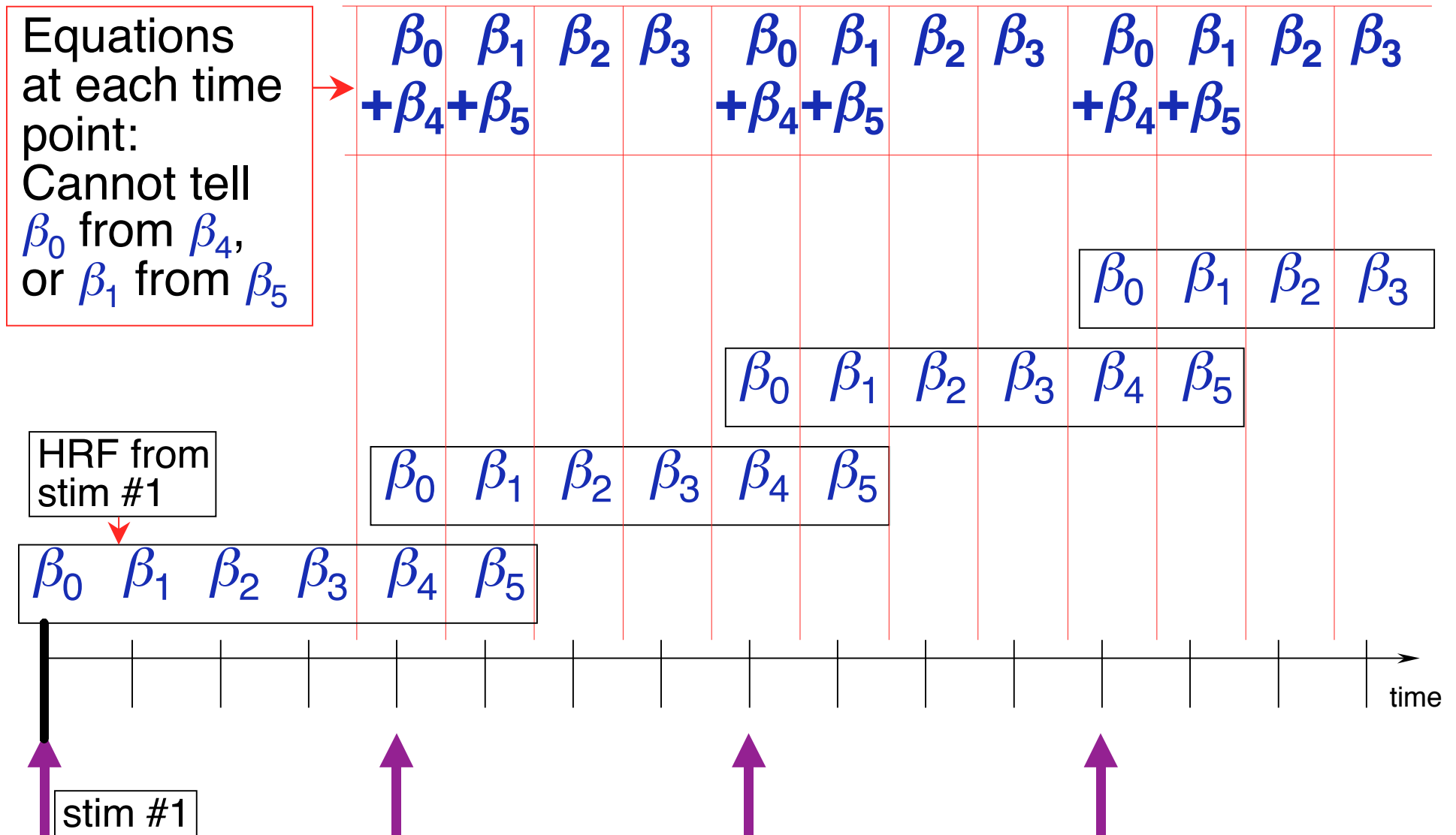
3dDeconvolve with Stick Functions

- Instead of inputting a signal model time series (e.g., created with **waver** and stimulus timing), you input the stimulus timing directly

  ★ Format: a text file with 0s and 1s, 0 at TR-grid times with no stimulus, 1 at time with stimulus

- Must specify the maximum lag (in units of TR) that we expect HRF to last after each stimulus

  ★ This requires you to make a judgment about the activation — brief or long?

- **3dDeconvolve** returns estimated values for each β_q for each stimulus class

  ★ Usually then use a GLT to test the HRF (or pieces of it) for significance

New Features of 3dDeconvolve - 4

- **`-stim_maxlag k p`** = option to set the maximum lag to **p** for stimulus timing file #**k** for **k=0,1,2,…**

  - ★ Stimulus timing file input using command line option **`-stim_file k filename`** as before
  - ★ Can also use **`-stim_minlag k m`** option to set the minimum lag if you want a value **m** different from **0**
  - ★ In which case there are **p-m+1** parameters in this HRF

- **`-stim_nptr k r`** = option to specify that there are **r** stimulus subintervals per TR, rather than just 1

  - ★ This feature can be used to get a finer grained HRF, at the cost of adding more parameters that need to be estimated
  - • Need to make sure that the input stimulus timing file (from **`-stim_file`**) has **r** entries per TR
  - • TR for **`-stim_file`** and for output HRF is data $TR \div r$

Script for Deconvolution - The Data

- **cd AFNI_data2**
  - ★ data is in **ED/** subdirectory (10 runs of 136 images, TR=2 s)
  - ★ script in file **@analyze_ht05**
    - ✧ stimuli timing and GLT contrast files in **misc_files/**
  - ★ start script *now* by typing **source @analyze_ht05**
    - ✧ will discuss details of script while it runs
- This is an event-related study from Mike Beauchamp (LBC/NIMH)
  - ★ Four classes of stimuli (short videos)
    - ✧ Tools moving (e.g., a hammer pounding) - **TM**
    - ✧ People moving (e.g., jumping jacks) - **HM**
    - ✧ Points outlining tools moving (no objects, just points) - **TP**
    - ✧ Points outlining people moving - **HP**
  - ★ Goal is to find if there is an area that distinguishes natural motions (HM and HP) from simpler rigid motions (TM and TP)

Script for Deconvolution - Outline

- Registration of each imaging run (there are 10): **3dvolreg**
- Smooth each volume in space (136 sub-bricks per run): **3dmerge**
- Create a brain mask: **3dAutomask** and **3dcalc**
- Rescale each voxel time series in each imaging run so that its average through time is 100: **3dTstat** and **3dcalc**
  - ★ If baseline is 100, then a β_q of 5 (say) indicates a 5% signal change in that voxel at time laq #q after stimulus
- Catenate all imaging runs together into one big dataset (1360 time points): **3dTcat**
- Compute HRFs and statistics: **3dDeconvolve**
  - ★ Each HRF will have 15 output points (lags from 0 to 14) with a TR of 1.0 s, since the input data has a TR of 2.0 s and we will be using the **-stim_nptr k r** option with **r=2**
- Average together central points 4..9 of each separate HRF to get peak % change in each voxel: **3dTstat**

Script for Deconvolution - 1

```
#!/bin/tcsh

if ( $#argv > 0 ) then
    set subjects = ( $argv )
else
    set subjects = ED
endif
```

This script is designed to run analyses on a lot of subjects at once. We will only analyze the ED data here. The other subjects will be included in the Group Analysis presentation.

```
#===============================================================
# Above command will run script for all our subjects - ED, EE, EF - one after
# the other if, when we execute the script, we type: ./@analyze_ht05 ED EE EF.
# If we type ./@analyze_ht05 or tcsh @analyze_ht05, it'll run the script only
# for subject ED.  The user will then have to go back and edit the script so
# that 'set subjects' = EE and then EF, and then run the script for each subj.
#===============================================================

foreach subj ($subjects)
```

Loop over subjects

```
    cd $subj
```

First step is to change to the directory that has this subject's data

Script for Deconvolution - 2

```
#==============================================================
# volume register and time shift our datasets, and remove the first
# two time points
#==============================================================

foreach run ( `count -digits 1 1 10` )
    3dvolreg -verbose                          \
        -base {$subj}_r{$run}+orig'[2]'  \
        -tshift 0                             \
        -prefix  {$subj}_r{$run}_vr         \
        {$subj}_r{$run}+orig'[2..137]'

# will store run data in runs_orig directory

#==============================================================
# smooth data with 3dmerge.
#==============================================================

    3dmerge -1blur_rms 4                       \
            -doall                            \
            -prefix {$subj}_r{$run}_vr_bl  \
            {$subj}_r{$run}_vr+orig
end
```

Loop over imaging runs 1..10

Image registration of each run to its #2 sub-brick

Lightly blur each dataset to reduce noise and increase functional overlap between runs and subjects

End of loop over imaging runs

Script for Deconvolution - 3

```
#=========================================================
# create masks for each run using 3dAutomask
#=========================================================

foreach run ( `count -digits 1 1 10` )
    3dAutomask -prefix mask_r{$run} {$subj}_r{$run}_vr_bl+orig
end

#=========================================================
# create a mask enveloping masks of the individual runs
#=========================================================

3dcalc -a mask_r1+orig -b mask_r2+orig -c mask_r3+orig    \
       -d mask_r4+orig -e mask_r5+orig -f mask_r6+orig    \
       -g mask_r7+orig -h mask_r8+orig -i mask_r9+orig    \
       -j mask_r10+orig                                   \
       -expr 'step(a+b+c+d+e+f+g+h+i+j)'                  \
       -prefix full_mask
```

Loop over imaging runs 1..10

This mask dataset will be 1 inside the largest contiguous high intensity EPI region, and 0 outside that region — this makes a brain mask

Script for Deconvolution - 4

```
#=================================================================
# re-scale each run's baseline to 100.
# If baseline is 100, and result of 3dcalc on one voxel is 106, then
# we can say that at that voxel shows a 6% increase is signal activity
# relative to baseline.
# Use full_mask to remove non-brain
#=================================================================
```

Mean of the run[th] dataset, through time: run=1..10

```
foreach run ( `count -digits 1 1 10` )
    3dTstat -prefix mean_r{$run} {$subj}_r{$run}_vr_bl+orig

    3dcalc -a {$subj}_r{$run}_vr_bl+orig  \
           -b mean_r{$run}+orig           \
           -c full_mask+orig              \
           -expr "(a/b * 100) * c"        \
           -prefix scaled_r{$run}

    /bin/rm mean_r{$run}+orig*
end
```

- Divide each voxel value ('a') by its temporal mean ('b') and scale by 100
- Result will have temporal mean of 100
- Voxels not in the mask will be set to 0 (by 'c')

Script for Deconvolution - 5

```
#=================================================================
# Now we can concatenate our 10 normalized runs with 3dTcat.
#=================================================================

 3dTcat -prefix {$subj}_all_runs            \
      scaled_r1+orig scaled_r2+orig        \
      scaled_r3+orig scaled_r4+orig        \
      scaled_r5+orig scaled_r6+orig        \
      scaled_r7+orig scaled_r8+orig        \
      scaled_r9+orig scaled_r10+orig
```

"Gluing" the runs together, since **3dDeconvolve** only operates on one input dataset at a time

```
#=================================================================
# move unneeded run data into separate directories
#=================================================================


mkdir runs_orig runs_temp

mv {$subj}_r*_vr* scaled* runs_temp
mv {$subj}_r* runs_orig
```

Gets this stuff out of the way so that we don't see it when we run AFNI later

Script for Deconvolution - 6

```
#================================================================
# run deconvolution analysis
#================================================================

3dDeconvolve -input {$subj}_all_runs+orig -num_stimts 4              \
   -stim_file 1 ../misc_files/all_stims.1D'[0]' -stim_label 1 ToolMov \
          -stim_minlag 1 0 -stim_maxlag 1 14 -stim_nptr 1 2          \
   -stim_file 2 ../misc_files/all_stims.1D'[1]' -stim_label 2 HumanMov\
          -stim_minlag 2 0 -stim_maxlag 2 14 -stim_nptr 2 2          \
   -stim_file 3 ../misc_files/all_stims.1D'[2]' -stim_label 3 ToolPnt \
          -stim_minlag 3 0 -stim_maxlag 3 14 -stim_nptr 3 2          \
   -stim_file 4 ../misc_files/all_stims.1D'[3]' -stim_label 4 HumanPnt\
          -stim_minlag 4 0 -stim_maxlag 4 14 -stim_nptr 4 2          \
   -glt 4 ../misc_files/contrast1.1D  -glt_label 1 FullF             \
   -glt 1 ../misc_files/contrast2.1D  -glt_label 2 HvsT              \
   -glt 1 ../misc_files/contrast3.1D  -glt_label 3 MvsP              \
   -glt 1 ../misc_files/contrast4.1D  -glt_label 4 HMvsHP            \
   -glt 1 ../misc_files/contrast5.1D  -glt_label 5 TMvsTP            \
   -glt 1 ../misc_files/contrast6.1D  -glt_label 6 HPvsTP            \
   -glt 1 ../misc_files/contrast7.1D  -glt_label 7 HMvsTM            \
   -iresp 1 TMirf -iresp 2 HMirf -iresp 3 TPirf -iresp 4 HPirf       \
   -full_first -fout -tout -nobout -polort 2                         \
   -concat ../misc_files/runs.1D                                     \
   -progress 1000                                                    \
   -bucket {$subj}_func
```

Script for Deconvolution - 6a

```
3dDeconvolve -input {$subj}_all_runs+orig -num_stimts 4                    \
   -stim_file 1 ../misc_files/all_stims.1D'[0]' -stim_label 1 ToolMov \
          -stim_minlag 1 0 -stim_maxlag 1 14 -stim_nptr 1 2              \
   -stim_file 2 ../misc_files/all_stims.1D'[1]' -stim_label 2 HumanMov\
          -stim_minlag 2 0 -stim_maxlag 2 14 -stim_nptr 2 2              \
   -stim_file 3 ../misc_files/all_stims.1D'[2]' -stim_label 3 ToolPnt \
          -stim_minlag 3 0 -stim_maxlag 3 14 -stim_nptr 3 2              \
   -stim_file 4 ../misc_files/all_stims.1D'[3]' -stim_label 4 HumanPnt\
          -stim_minlag 4 0 -stim_maxlag 4 14 -stim_nptr 4 2              \
```

- Input dataset is the catenated thing created earlier
- There are 4 time series models
- All stimuli time series are in one file with 4 columns:
  ../misc_files/all_stims.1D
  - The selectors like '**[2]**' pick out a particular column
  - Each stimulus and HRF will be sampled at TR/2 = 1.0 s, due to the use of **-stim_nptr k 2** for each **k**
  - Lag from 0 to 14 is about right for hemodynamic response to a brief stimulus

Script for Deconvolution - 6b

```
-glt 4 ../misc_files/contrast1.1D   -glt_label 1 FullF        \
-glt 1 ../misc_files/contrast2.1D   -glt_label 2 HvsT         \
-glt 1 ../misc_files/contrast3.1D   -glt_label 3 MvsP         \
-glt 1 ../misc_files/contrast4.1D   -glt_label 4 HMvsHP       \
-glt 1 ../misc_files/contrast5.1D   -glt_label 5 TMvsTP       \
-glt 1 ../misc_files/contrast6.1D   -glt_label 6 HPvsTP       \
-glt 1 ../misc_files/contrast7.1D   -glt_label 7 HMvsTM       \
```

- Run many GLTs to contrast various pairs and quads of cases
  - Each case has 15 points in its HRF, so each GLT needs 60 inputs indicating how to combine all these β weights
  - Plus 3 zero inputs per imaging run (30 more inputs) to skip over the β weights for the baseline parameters
- One example: HvsT (**contrast2.1D**) - all one line in the file!

```
 0   0   0   0   0   0   0   0   0   0   0   0   0   0   0 \      skip 30 baseline
 0   0   0   0   0   0   0   0   0   0   0   0   0   0   0 \      parameters
-0  -0  -0  -1  -1  -1  -1  -1  -1  -1  -0  -0  -0  -0  -0 \      −TM: 3..9 seconds
 0   0   0   1   1   1   1   1   1   1   0   0   0   0   0 \      +HM: 3..9 seconds
-0  -0  -0  -1  -1  -1  -1  -1  -1  -1  -0  -0  -0  -0  -0 \      −TP: 3..9 seconds
 0   0   0   1   1   1   1   1   1   1   0   0   0   0   0        +HP: 3..9 seconds
```

Script for Deconvolution - 6c

```
-iresp 1 TMirf -iresp 2 HMirf -iresp 3 TPirf -iresp 4 HPirf          \
-full_first -fout -tout -nobout -polort 2                            \
-concat ../misc_files/runs.1D                                        \
-progress 1000                                                       \
-bucket {$subj}_func
```

• Output HRF (**-iresp**) 3D+time dataset for each stimulus class
  • Each of these datasets will have TR=1.0 s and have 15 time points (lags 0..14)
  • Can plot them atop each other using **Dataset#N** plugin
• **-nobout** = don't output statistics of baseline parameters
• **-polort 2** = use a quadratic polynomial (3 parameters) for the baseline in each run
• **-concat** … = use this file to indicate when each run starts
• **-progress 1000** = display some results every 1000th voxel
• **-bucket** … = save statistics into dataset with this prefix

Script for Deconvolution - 7

```
#==============================================================
# make slim dataset.  Too many sub-bricks in our bucket dataset.
# Use 3dbucket to slim it down and include sub-bricks of interest only.
#==============================================================

3dbucket -prefix {$subj}_func_slim -fbuc {$subj}_func+orig'[125..151]'

#==============================================================
# Remember IRF datasets created by 3dDeconvolve?
# There are 15 time lags in each voxel.  Remove lags 0-3 and 10-15 b/c not
# interesting.  Then find mean percent signal change for lags 4-9 in each
# voxel with '3dTstat'.
# Then transform to Talairach coordinates with 'adwarp'.
#==============================================================

  foreach cond (TM HM TP HP)
    3dTstat -prefix {$subj}_{$cond}_irf_mean  {$cond}irf+orig'[4..9]'

    adwarp  -apar {$subj}spgr+tlrc  -dpar {$subj}_{$cond}_irf_mean+orig
  end

cd ..
end
```

End of loop over subjects; go back to upper directory whence we started

```
#==============================================================
# End of script!
# Take the {$subj}_{$cond}_irf_mean+tlrc datasets and input into 3dANOVA2.
#==============================================================
```

Results: Humans vs. Tools
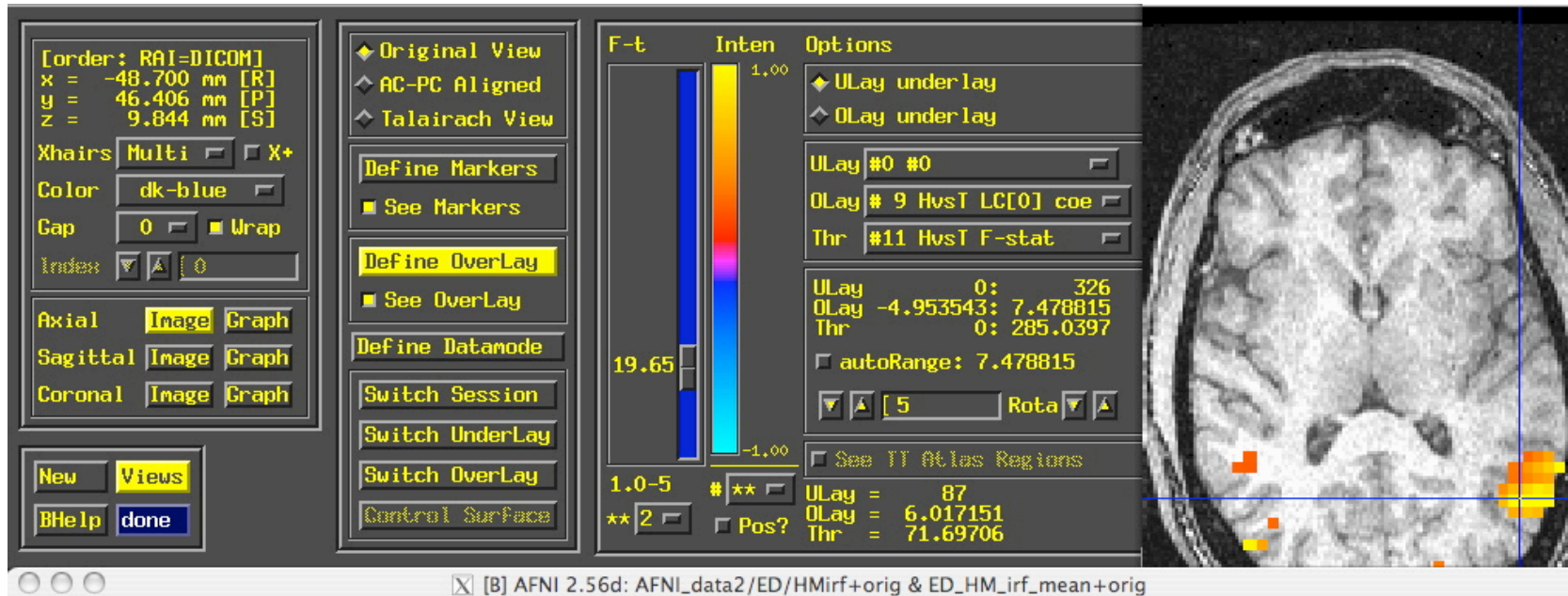
- Color overlay is HvsT contrast

- **Blue** curves are Human HRFs

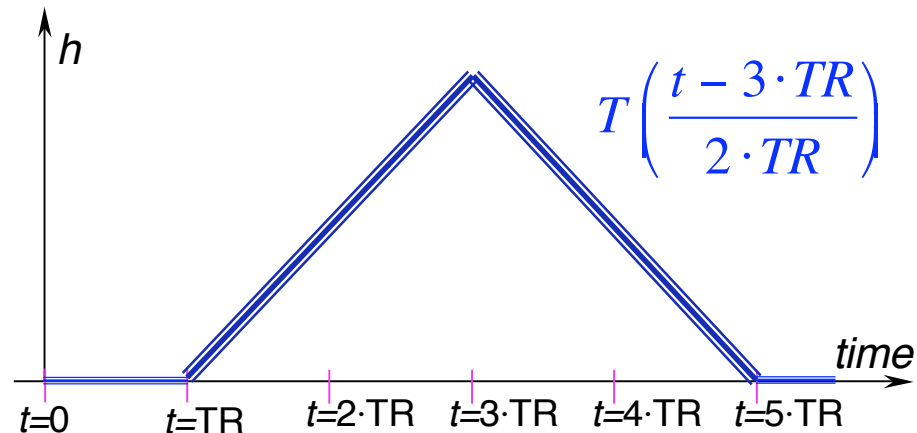- **Red** & **Green** curves are Tool HRFs
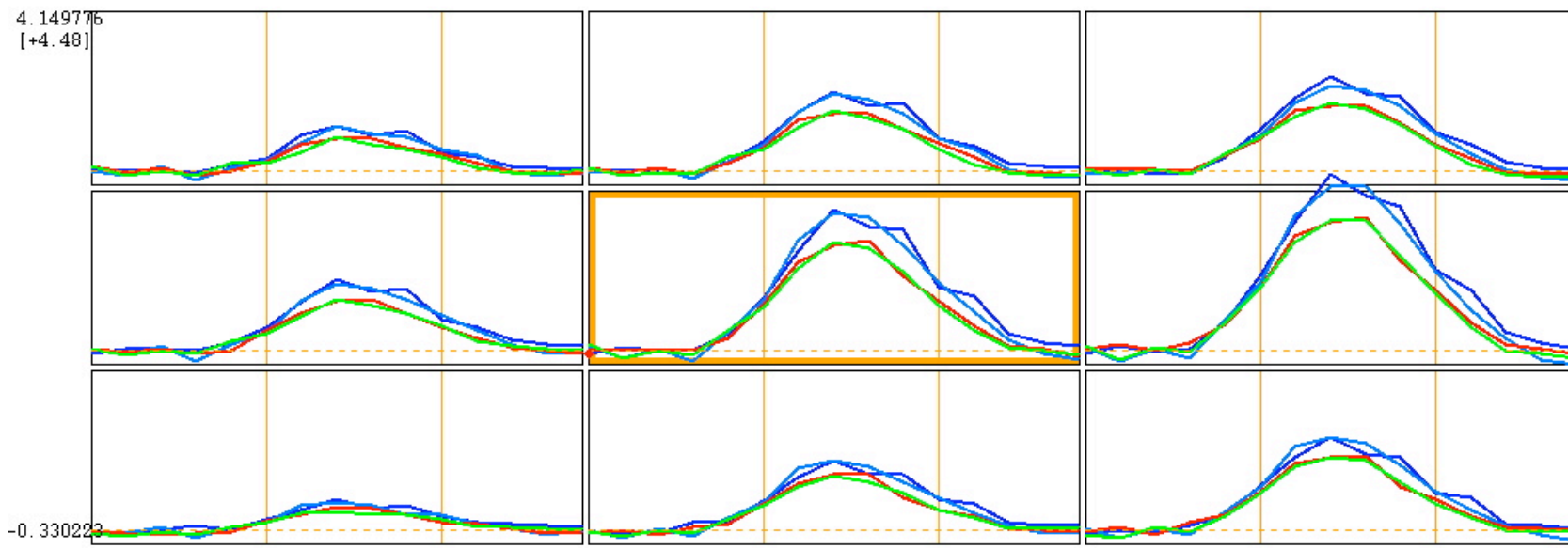
Other Fun 3dDeconvolve Options

- **-mask** = used to turn off processing for some voxels
  - ★ speed up the program by not processing non-brain voxels
- **-input1D** = used to process a single time series, rather than a dataset full of time series
  - ★ test out a stimulus timing sequence
  - ★ **-nodata** option can be used to check for collinearity
- **-censor** = used to turn off processing for some time points
  - ★ for time points that are "bad" (e.g., too much movement)
- **-sresp** = output standard deviation of HRF estimates
  - ★ can plot error bars around HRF in AFNI graph viewer
- **-errts** = output residuals (i.e., difference between fitted model and data)
  - ★ for statistical analysis of time series noise
- **-jobs** = run with multiple CPUS
  - ★ extra speed, if you have a dual- or quad-processor system!

3dDeconvolve with Free Timing

- The fixed-TR stick function approach doesn't fit with arbitrary timing of stimuli

  ★ When subject actions/reactions are self-initiated, timing of activations cannot be controlled

- If you want to do deconvolution, then must adopt a different basis function expansion approach

  ★ One that has a finite number of parameters but also allows for calculation of $h(t)$ at any arbitrary point in time

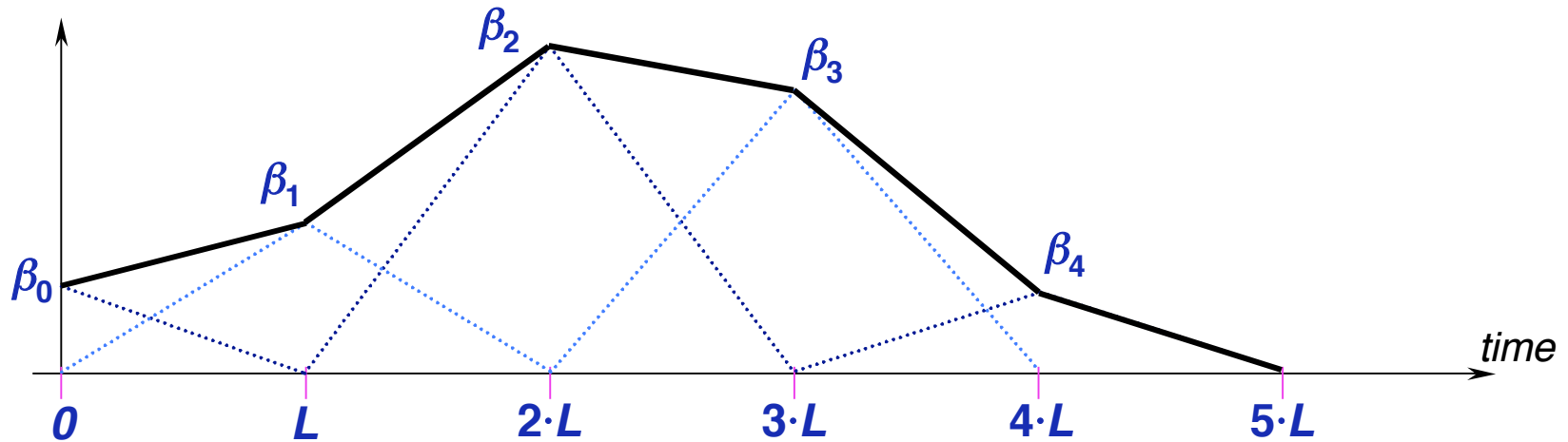- Simplest set of such functions are closely related to stick functions: **tent functions**

$$T(x) = \begin{cases} 1 - |x| & \text{for } -1 < x < 1 \\ 0 & \text{for } |x| > 1 \end{cases}$$

$$T\left(\frac{t - 3 \cdot TR}{2 \cdot TR}\right)$$

time

$t{=}0$ $t{=}TR$ $t{=}2{\cdot}TR$ $t{=}3{\cdot}TR$ $t{=}4{\cdot}TR$ $t{=}5{\cdot}TR$

Tent Functions = Linear Interpolation

- Expansion in a set of spaced-apart tent functions is the same as linear interpolation

$$\beta_0 \cdot T\left(\frac{t}{L}\right) + \beta_1 \cdot T\left(\frac{t-L}{L}\right) + \beta_2 \cdot T\left(\frac{t-2\cdot L}{L}\right) + \beta_3 \cdot T\left(\frac{t-3\cdot L}{L}\right) + L$$
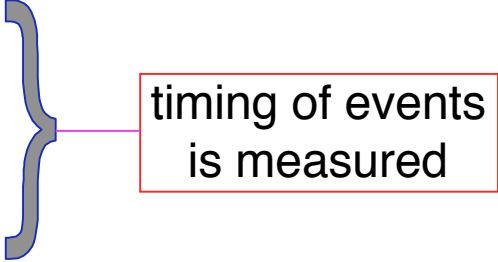

- Tent function parameters are also easily interpreted as function values

- Must decide on relationship of tent function spacing *L* and time grid TR

At This Point …

- **3dDeconvolve** is not set up to use tent functions directly

- In the past, we have now explained in grotesque detail how to set up a combination of **waver**, **3dcalc**, and **3dDeconvolve** to "trick" the system into doing deconvolution with tent functions (or other basis sets)

- However, you are saved from this excruciation

- At this moment, we have an interactive Matlab script that will set up the details for you

- In the near future, we will put tent functions directly into **3dDeconvolve**, allowing the direct use of non-TR locked stimulus timing

  ★ Date of this promise: 13 July 2004

Advanced Topics in Regression

- Can have activations with multiple phases that are not always in the same time relationship to each other
  - ★ e.g., solving a visually presented puzzle:
    - ◇ subject sees puzzle
    - ◇ subject cogitates a while
    - ◇ subject responds with solution

    timing of events is measured

- With fixed-shape regression, this isn't too hard, since we can treat each phase as a separate stimulus class and lay down a separate fixed-shape HRF for each type of stimulus time
  - ★ But fixed-shape regression is probably not reasonable for this problem, since (at least) the "cogitation" phase isn't fixed among the trials
- Deconvolution assumes that the HRF (although unknown) is the same among all trials in the same class

One Solution: Multiple HRFs

- By treating each phase of the activation that is temporally uncoupled from the other phases as a separate stimulus class, then can compute a separate HRF for each

  - ★ Using basis function deconvolution, since timing will be arbitrary

- This will only work if the fluctuations in timing are great enough so that the different HRFs don't always overlap in the same way

  - ★ Otherwise, it becomes impossible to tell the tail end of HRF #1 from the start of HRF #2, if they are always locked together in the same temporal relationship

Noise Issues

- "Noise" in FMRI is caused by several factors, not completely characterized

  ★ MR thermal noise (well understood)

  ★ Cardiac and respiratory cycles (partly understood)

    ✧ In principle, could measure these sources of noise separately and then try to regress them out

  ★ Scanner fluctuations (e.g., thermal drift)

  ★ Small subject head movements

  ★ Very low frequency fluctuations (periods longer than 100 s)

- Data analysis should try to remove what can be removed and allow for the statistical effects of what can't be removed

  ★ "Serial correlation" in the noise time series affects the t- and F-statistics calculated by **3dDeconvolve**

  ★ At present, nothing is done to correct for this effect

Nonlinear Regression

- Linear models aren't everything
  - ★ For example, could try to fit HRF of the form $h(t) = a \cdot t^b \cdot e^{-t/c}$
  - ★ Unknowns b and c appear nonlinearly in this formula
- Program **3dNLfim** can do nonlinear regression (including nonlinear deconvolution)
  - ★ User must provide a C function that computes the model time series, given a set of parameters (e.g., a, b, c)
  - ★ Program then drives this C function repeatedly, searching for the set of parameters that best fit each voxel
  - ★ Has been used to fit pharmacological wash-in/wash-out models (difference of two exponentials) to FMRI data acquired during pharmacological challenges
    - ✧ e.g., injection of nicotine, cocaine, etc.