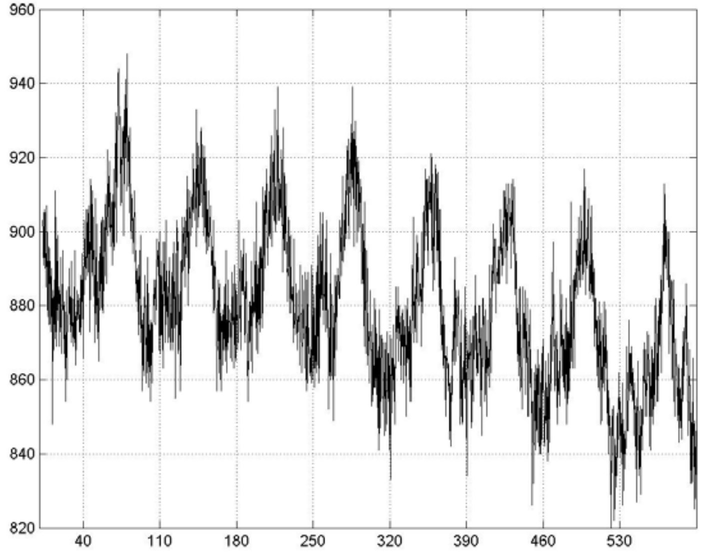
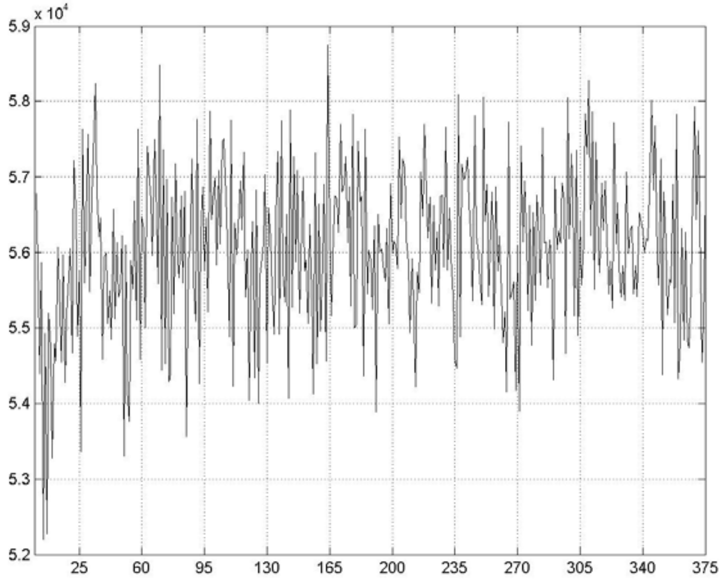
Statistical Analysis of BOLD Data

- Goal is to find task related brain activation
- EPI SNR ~ 100 = 1.0/0.01
- BOLD signal ~ 1%
- Therefore need averaging to increase SNR to find significant task vs control changes.
- No "correct" approach especially considering the variety of fMRI experiment in both paradigm and acquisition parameters.
- Model based Examples:
  - t-Test, Correlation, GLM
- Non-parametric Examples:
  - Fuzzy Clustering, Kolmogorov-Smirnov (ordered cdf difference)
- Data Driven - PCA, ICA

Example fMRI Time Series from Blocked Design

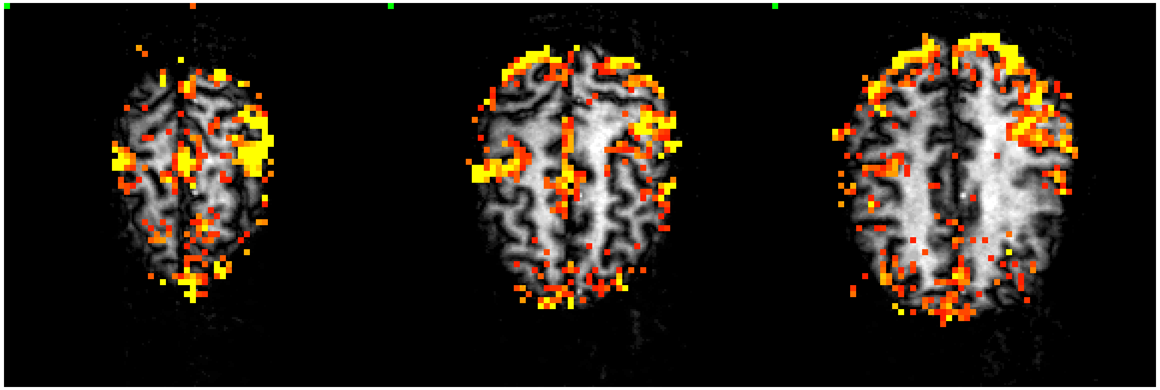




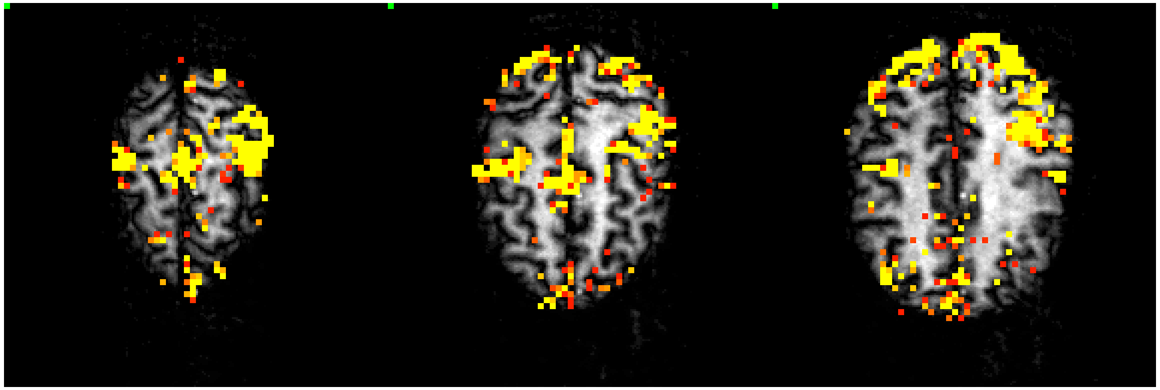
Statistical Parametric Maps (SPM)

- Need to normalize difference by variability (i.e. SNR).
- Measure of statistical quality not just percent change.
- On a voxel-by-voxel basis calculate a statistic
- Threshold in terms of the probability of a Type I error on the assumed sampling distribution to form the SPM.
- Typically overlaid onto an anatomic image.

Percent Change Map (1-3%)



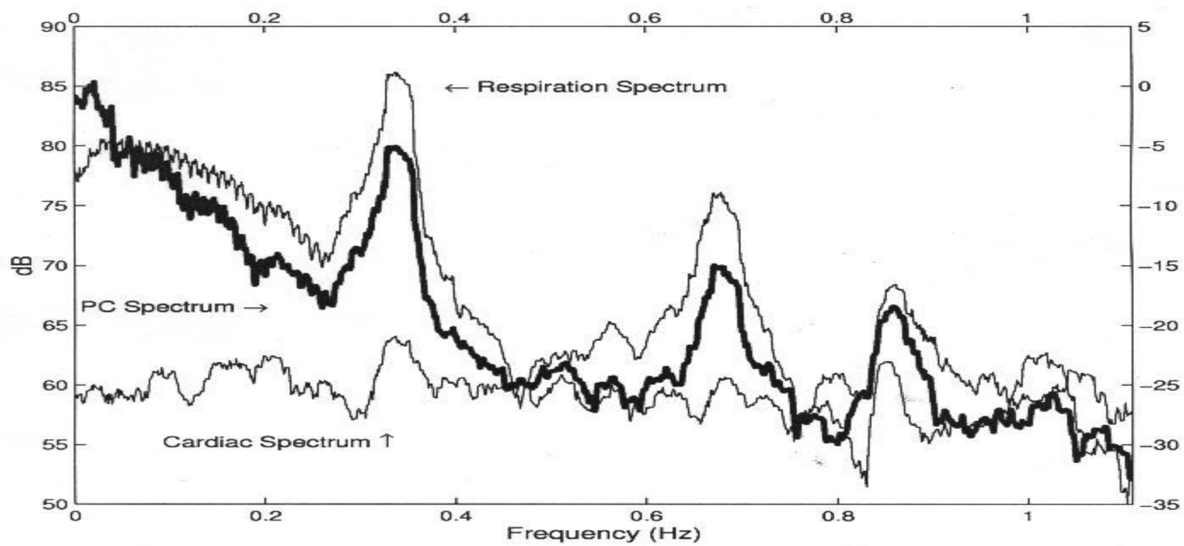
Student's t Map (p > 0.01)



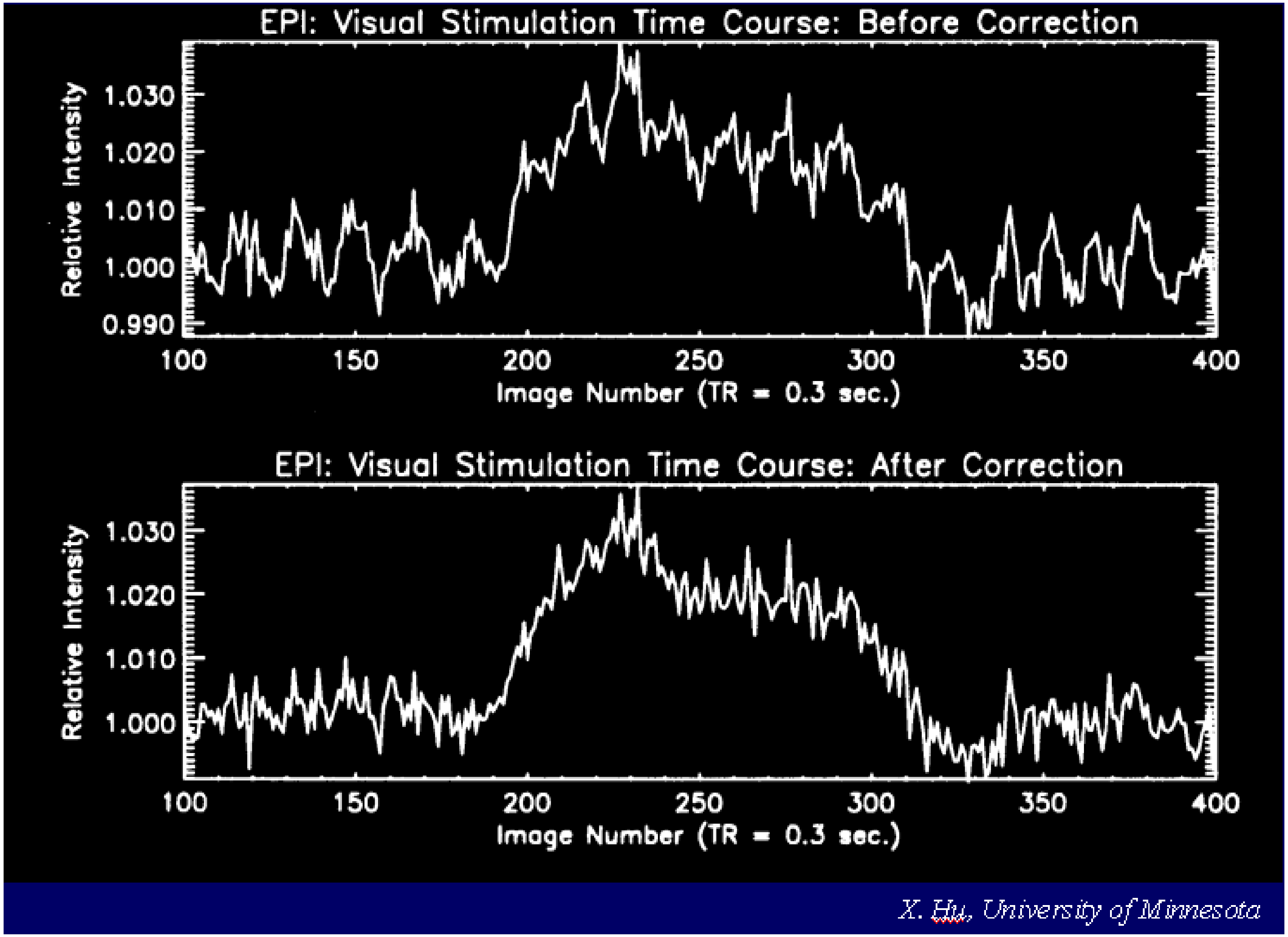
fMRI Noise

- Assumed to be both normally distributed and temporally independent.
- Due to physiologic processes the noise has both spatial and temporal structure.
  - Cardiac, Respiration and vasomotor.
- Select Stimulus frequency away from physiologic noise harmonics and aliased components.
- Physiologic retrospective correction.

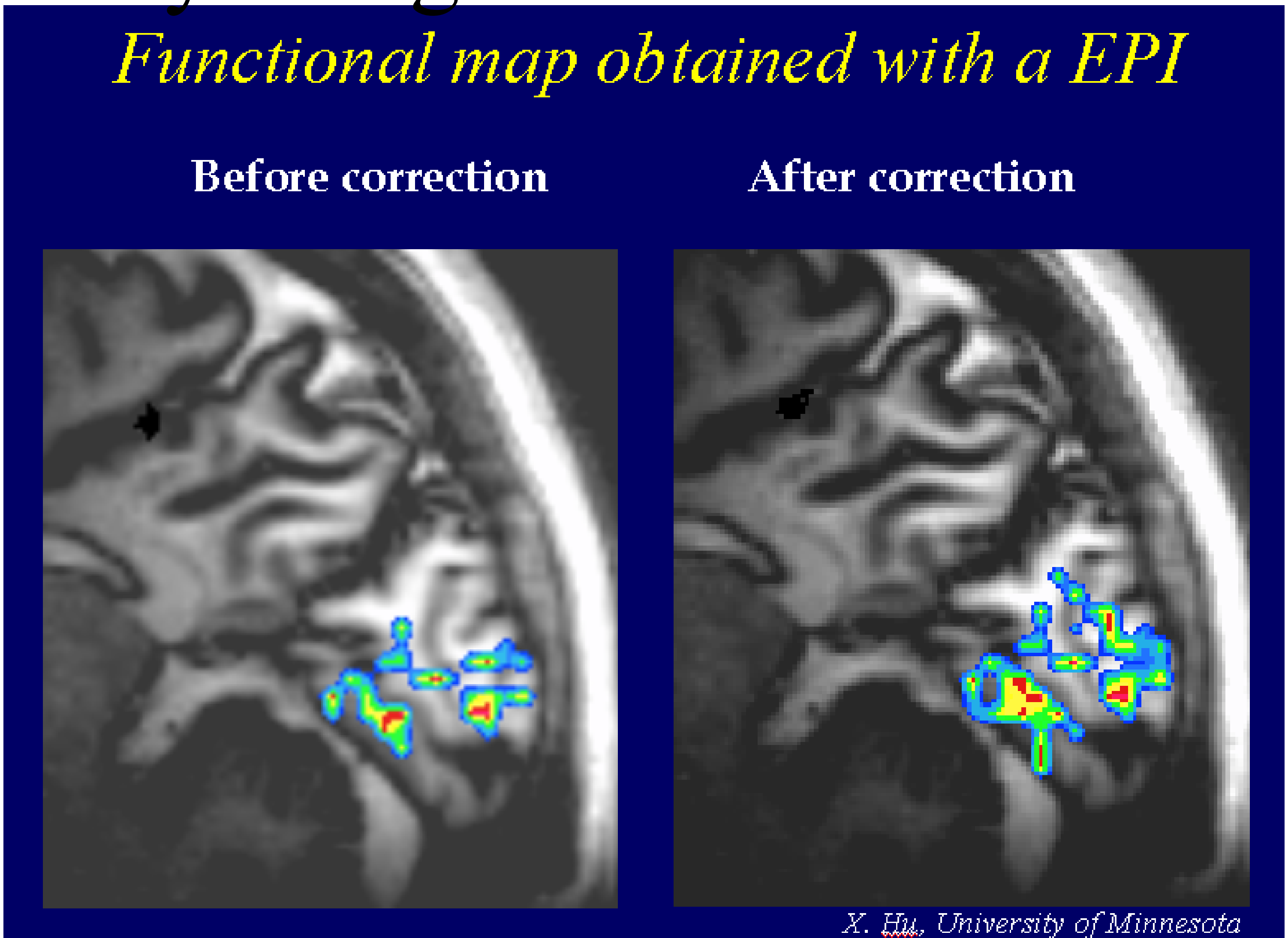
Average fMRI power spectrum



Physiological artifact correction

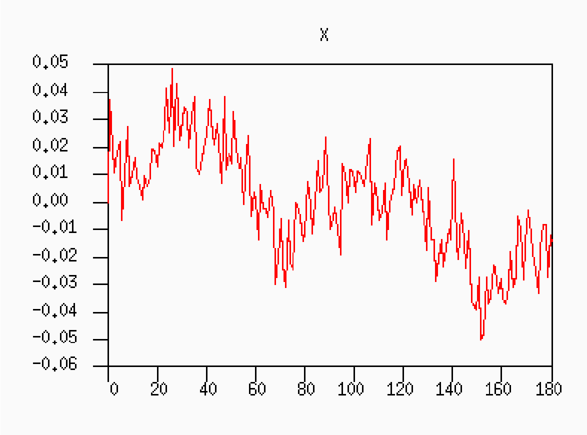


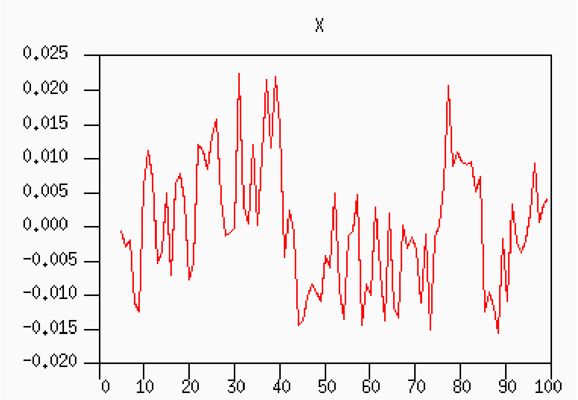
Physiological artifact correction



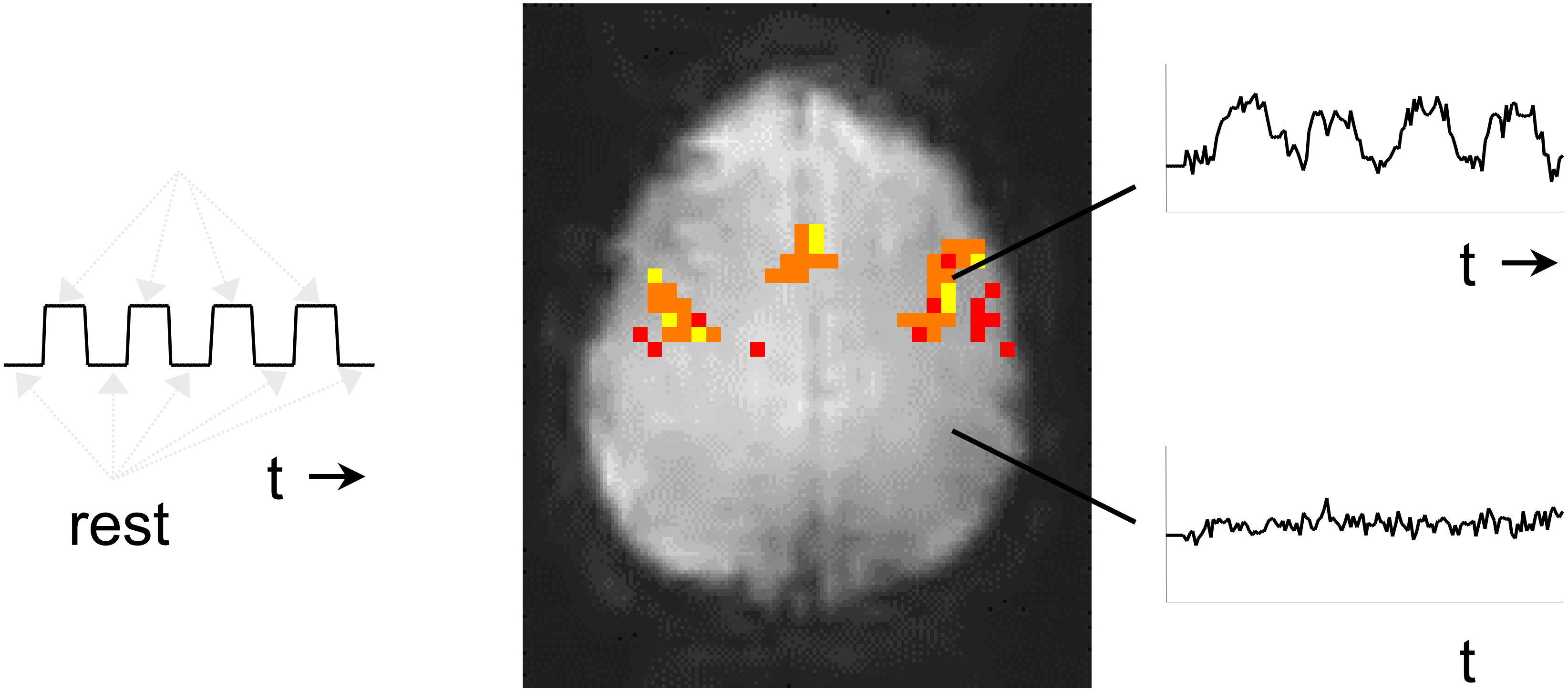
Subject Motion

- Detection
  - Center of mass
  - Cine
- Prevention
  - Bite bar, head restraint
- Rigid body correction
- Baseline drift





A typical fMRI experiment



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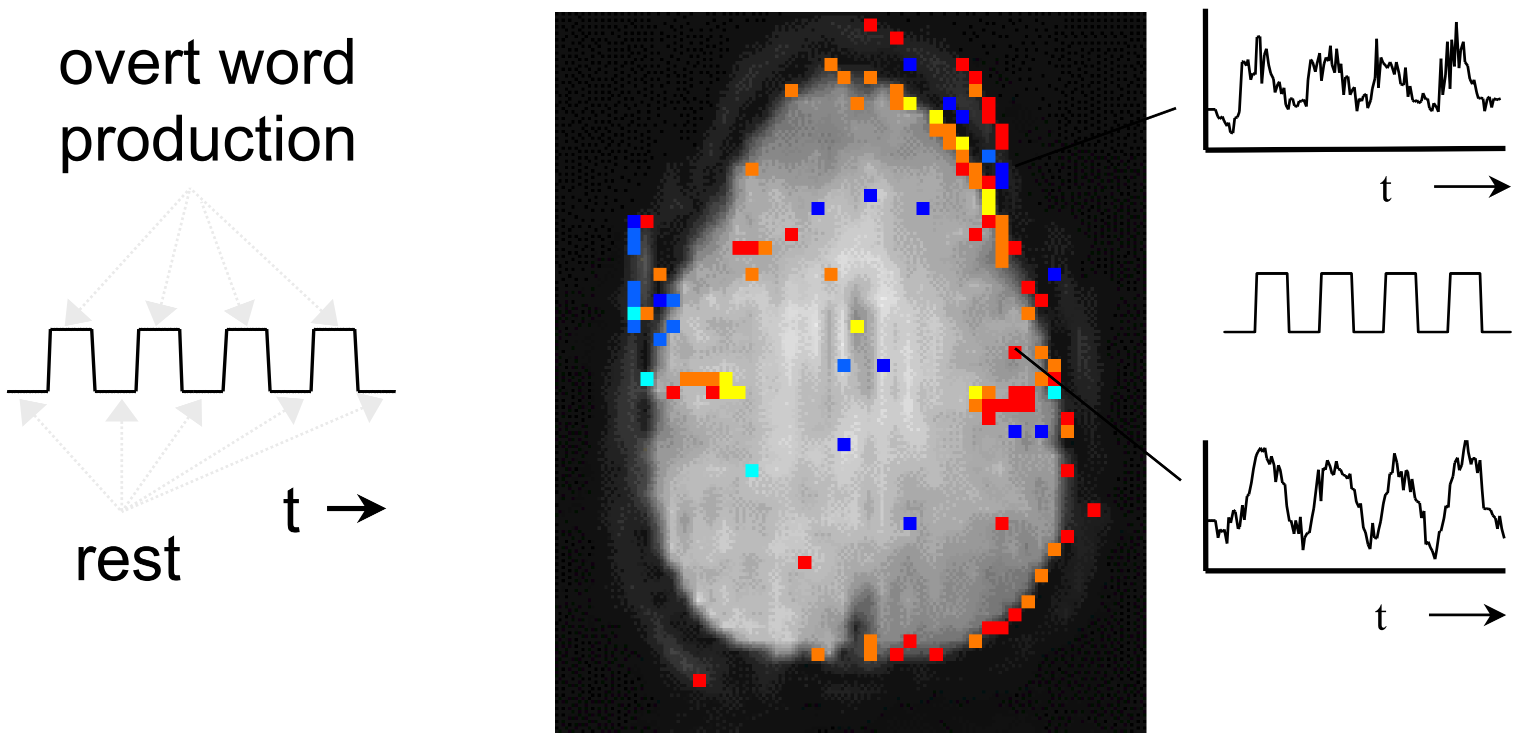
National Institutes of Health

Corruption of data due to motion



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Student's T test

- T-test is conventional statistic to find significance of a difference of means of two populations.
- The two populations are formed by grouping time course values from task and control periods.
- Integral of t-distribution tail past t-value yields the p-value

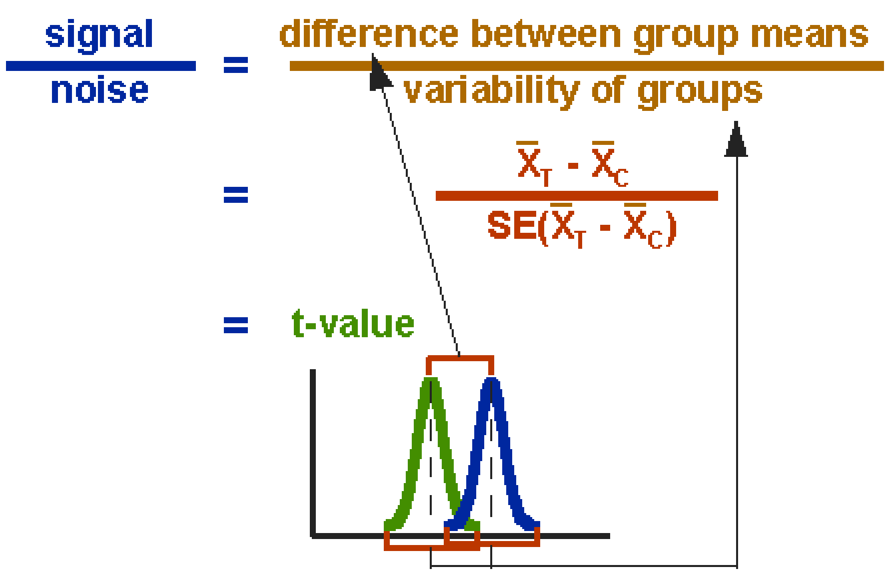

Figure 3. Formula for the t-test.

$$t = \frac{\bar{X}_T - \bar{X}_C}{\sqrt{\frac{var_T}{n_T} + \frac{var_C}{n_C}}}$$

Figure 5. Formula for the t-test.

http://trochim.human.cornell.edu/kb/stat_t.htm

Multiple comparisons

- Conventional significance means p-values <0.05 (or 0.01).
- 5% of a 64x64matrix = 0.05*4096 = 208 expected false positives due to noise alone.
- Bonferroni correction - divide by number of comparisons to get a threshold p-value to maintain an 0.05 effective image slice p-value. 0.05/4096 = .00001
- Too conservative: doesn't take into account a prior knowledge of spatial extent. (i.e. isolated activation pixels less likely than clusters)
- Xiong - correction based on spatial smoothness of data; too restrictive.

Correlation

- t-Test implicit "box-car" reference function.
- Hemodynamic response is delayed and broadened:
  - 2 sec onset delay
  - 6 sec ramp to peak
- Correlation allows arbitrary reference, trapezoid used to partially account for rise and fall of hemodynamic response.
- Correlation is a measure of the projection of time-course vector onto reference vector. Correlation r-value is cosine of the angle between these vectors.
- Cross-correlation peak method allows for differing activation onsets

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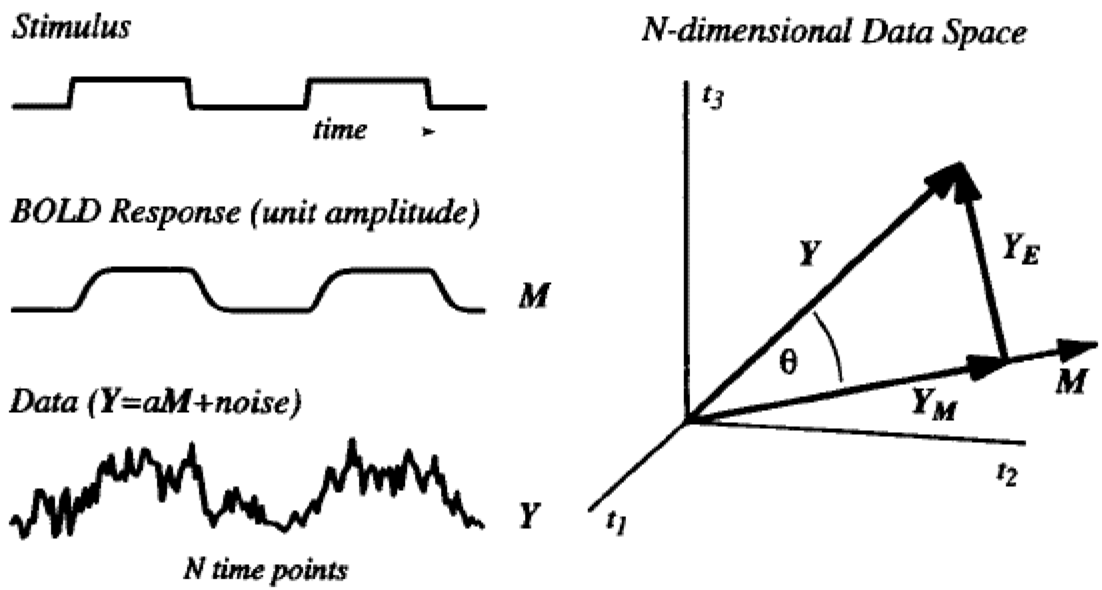

Vectors in data space:

M = *model vector for unit amplitude response*
Y = *data vector*

Y_M = *projection onto model* $= \left(\frac{Y \cdot M}{M}\right)\left(\frac{M}{M}\right)$

Y_E = *error vector* $= Y - Y_M$

Parameter estimates:

a = *response amplitude* $= \frac{Y_M}{M}$

σ^2 = *noise variance* $= \frac{Y_E^2}{N-1}$

Statistics:

r = *correlation coefficient* $= \cos\theta = \frac{Y_M}{Y}$

t = *t-statistic* $= \left(\sqrt{N-1}\right)\cot\theta = \left(\sqrt{N-1}\right)\frac{Y_M}{Y_E}$

General Linear Model (GLM)

- Generalization of correlation but with multiple reference functions (i.e. model).
- Linear combination of a set of model functions plus noise where the Reference functions can themselves be non-linear.
- Hemodynamic functions (empirical models).
- Linear drift
- Range of onset delay
  - set of incrementally delayed model functions
  - model derivative per Taylor expansion approx..
- Fourier analysis is extreme case with model energy spread among harmonics but delay is capture by phase of fundamental frequency.

General Linear Model

$$Y = \mathbf{M}a + e$$

Y = data vector

$\mathbf{M}$ = matrix of model functions

a = amplitude vector

e = noise vector

2 model functions

N time points

$$\begin{pmatrix} Y(t_1) \\ Y(t_2) \\ \cdots \\ Y(t_N) \end{pmatrix} = \begin{pmatrix} M_1(t_1) & M_2(t_1) \\ M_1(t_2) & M_2(t_2) \\ \cdots & \cdots \\ M_1(t_N) & M_2(t_N) \end{pmatrix} \begin{pmatrix} a_1 \\ a_2 \end{pmatrix} + \begin{pmatrix} e_1(t_1) \\ e_2(t_2) \\ \cdots \\ e_N(t_N) \end{pmatrix}$$

Amplitudes

Data **Design Matrix** **Noise**

$$F_{2,\nu} = \frac{Y_M^2/2}{Y_E^2/\nu}$$

$$a = (\mathbf{M}^T\mathbf{M})^{-1}\mathbf{M}^T Y$$

$$C = (\mathbf{M}^T\mathbf{M})^{-1} = \text{covariance matrix}$$