Functional MRI

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History of fMRI

-1990: Ogawa observes BOLD effect with T2*. Blood vessels became more visible as blood oxygen decreased.

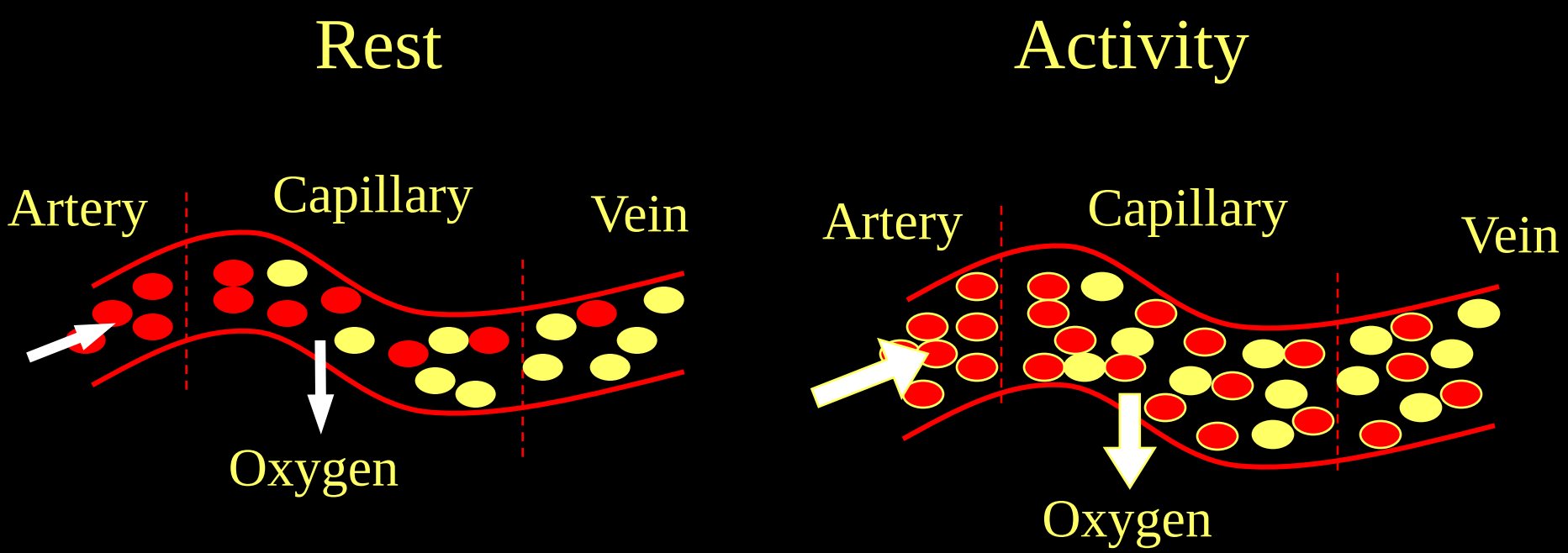
-1991: Belliveau observes first functional images using a contrast agent.

-1992: Ogawa et al. and Kwong et al. publish first functional images using BOLD signal.

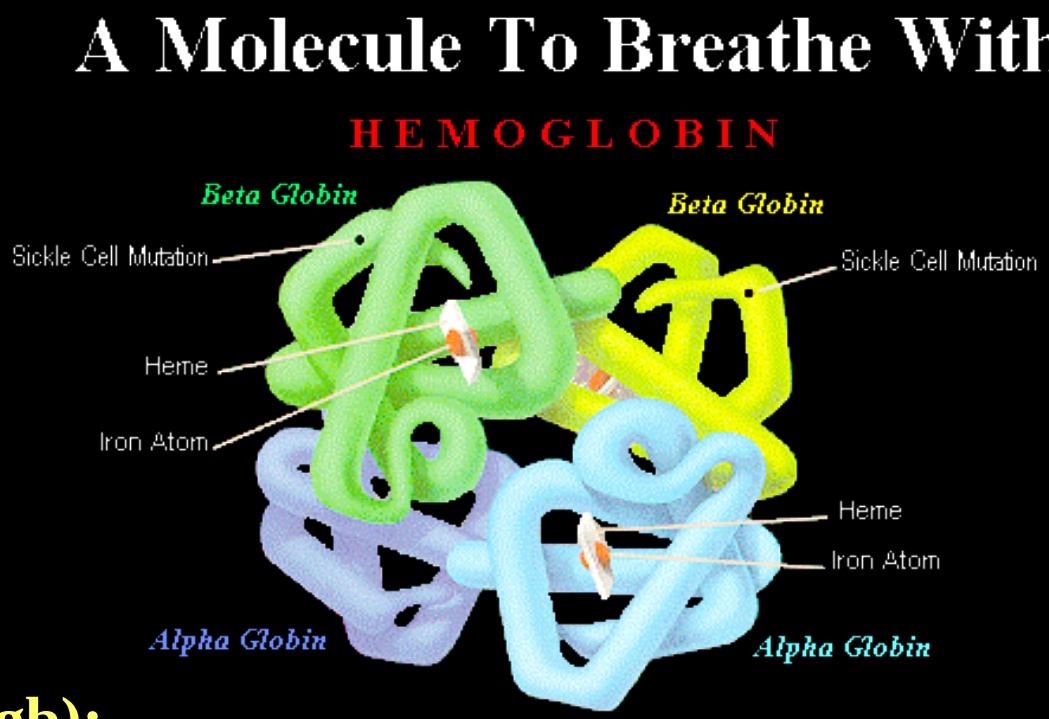
The Blood Oxygen Level Dependant (BOLD) Signal

- Magnetic properties differ between oxygenated and deoxygenated blood
- Magnetic properties affect the MR signal
- Hence, the MR signal is dependant on the blood oxygen level!

Hemodynamics of the brain



Hemoglobin

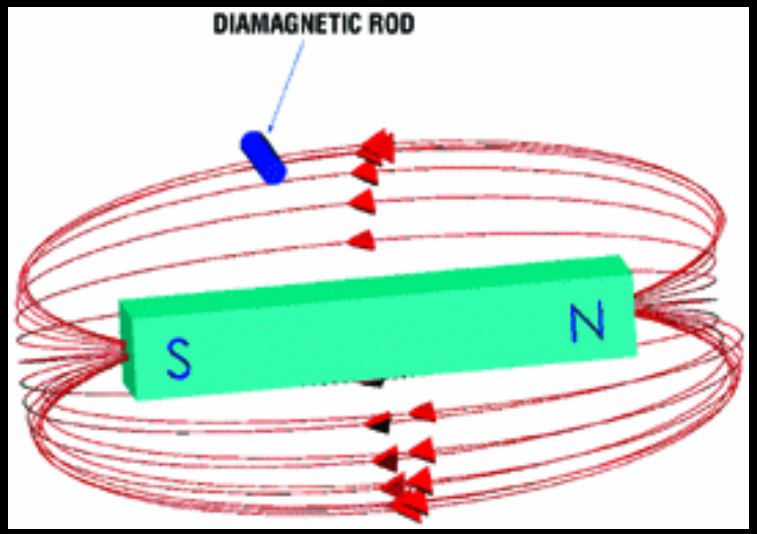


Hemoglogin (Hgb):

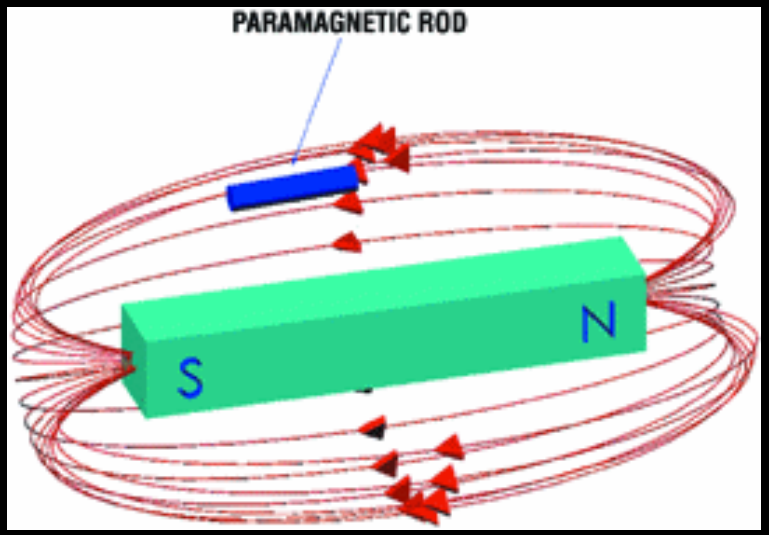
- each globin chain contains a heme group
- each heme group can attach an oxygen atom (O_2)
- oxy-Hgb (four O_2) is diamagnetic
- deoxy-Hgb is paramagnetic

Source: http://wsrv.clas.virginia.edu/~rjh9u/hemoglob.html, Jorge Jovicich

Dia- and paramagnetic materials

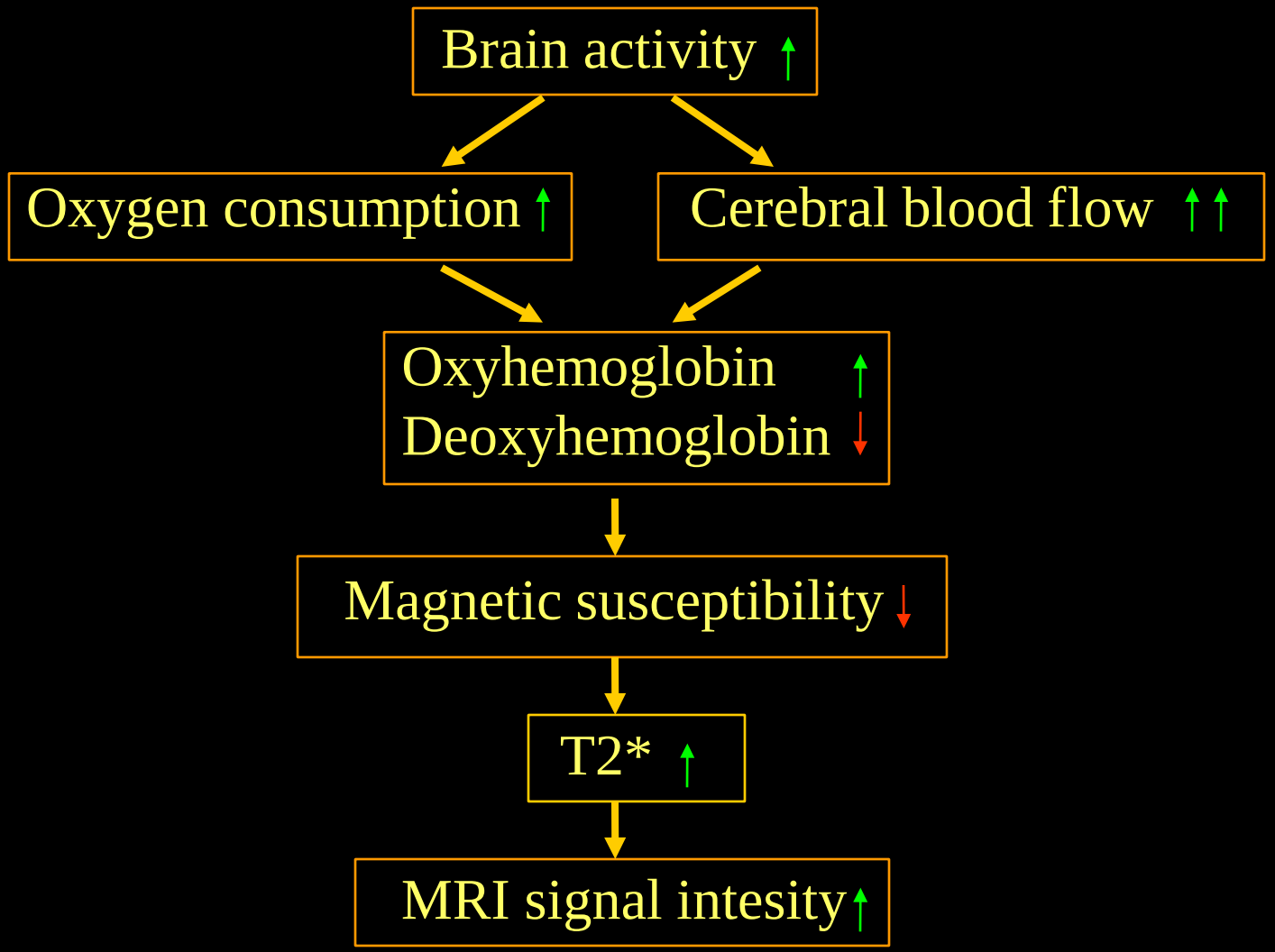


Oxyhemoglobin

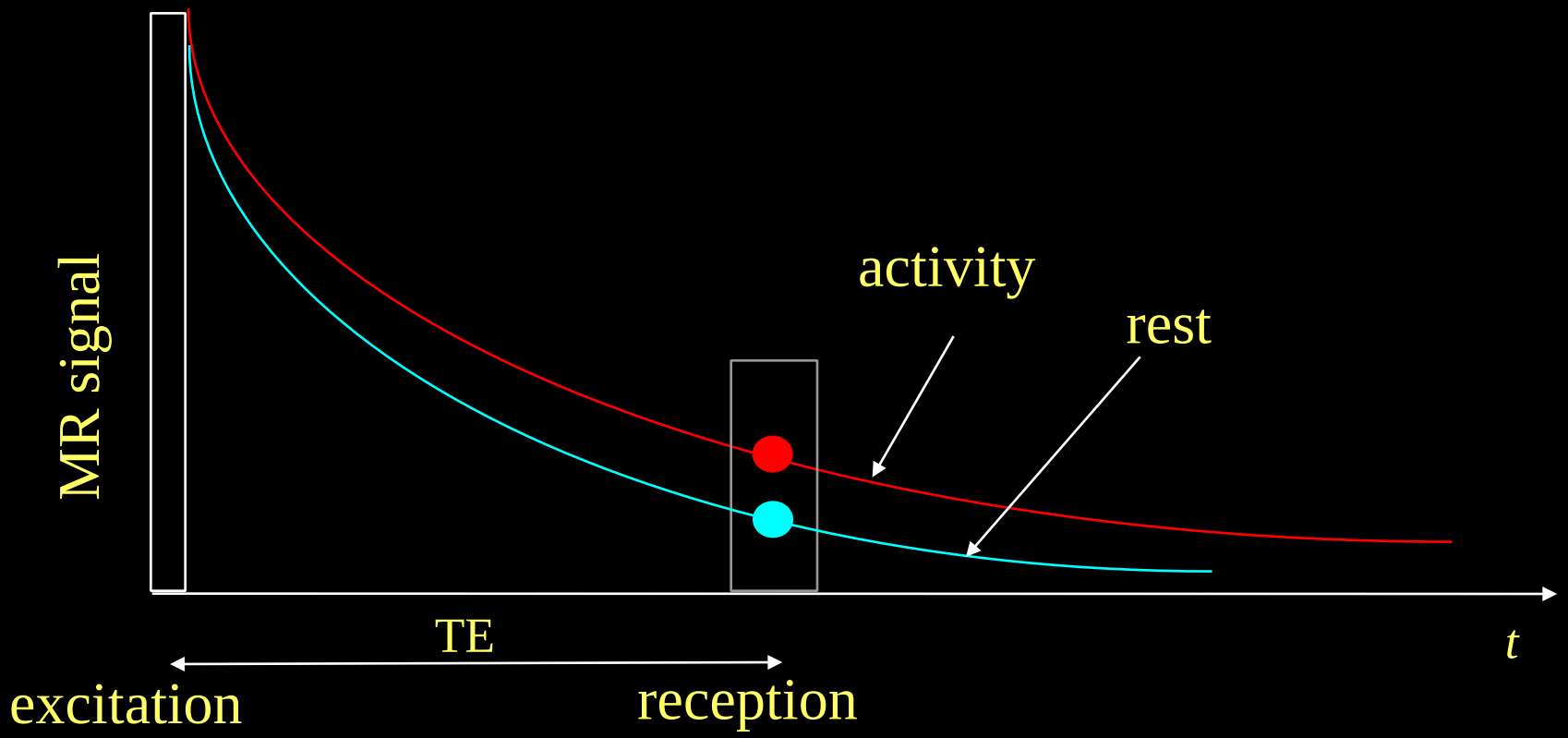


Deoxyhemoglobin

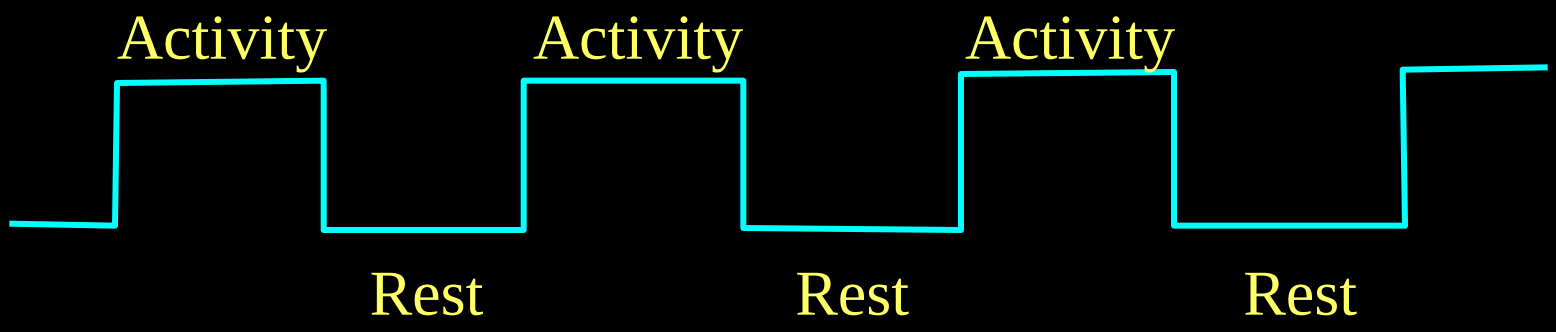
Mechanism of BOLD fMRI



T2* Effect in fMRI



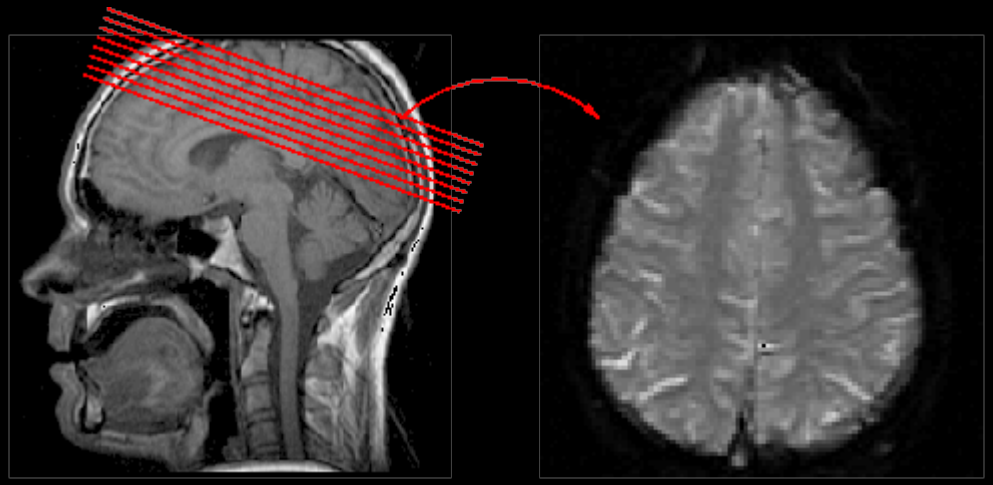
A typical fMRI experiment



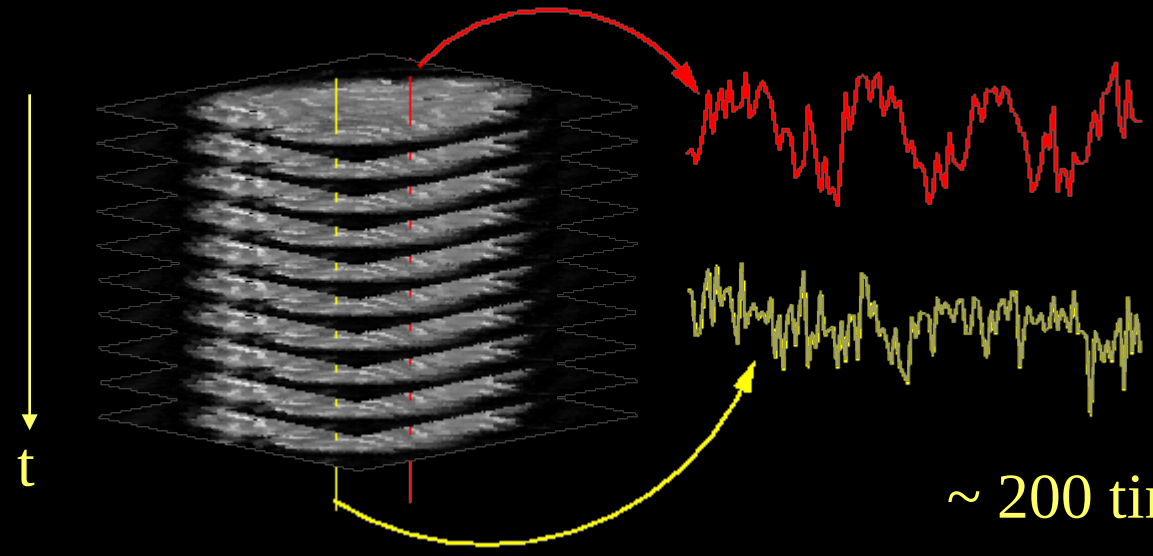
The activity time series is called ***paradigm***

Example of activities:

- Sensory
- Motor
- Higher cognitive functions, e. g. language, math, …



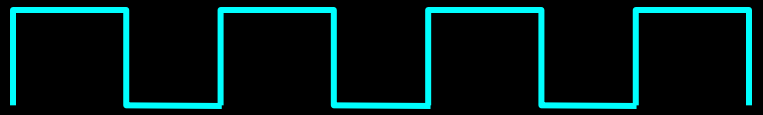
128 x 128



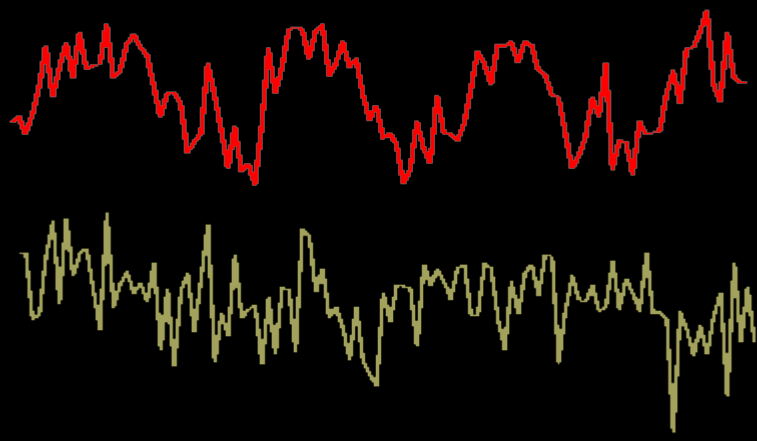
~ 200 time frames

Locate time-series that are similar to the paradigm

Paradigm y(t) =



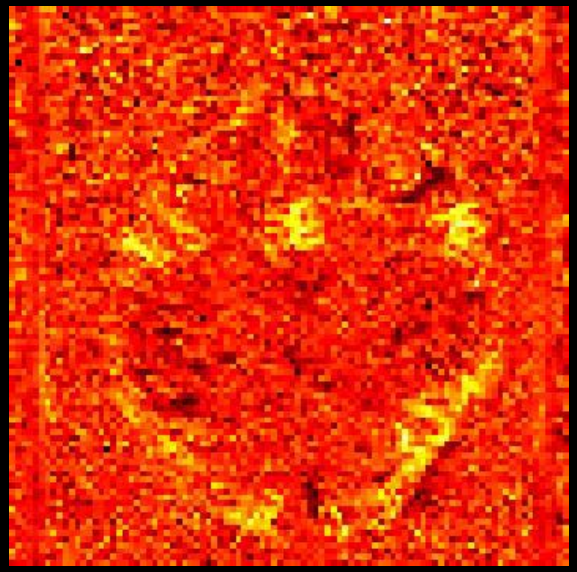
x(t) =



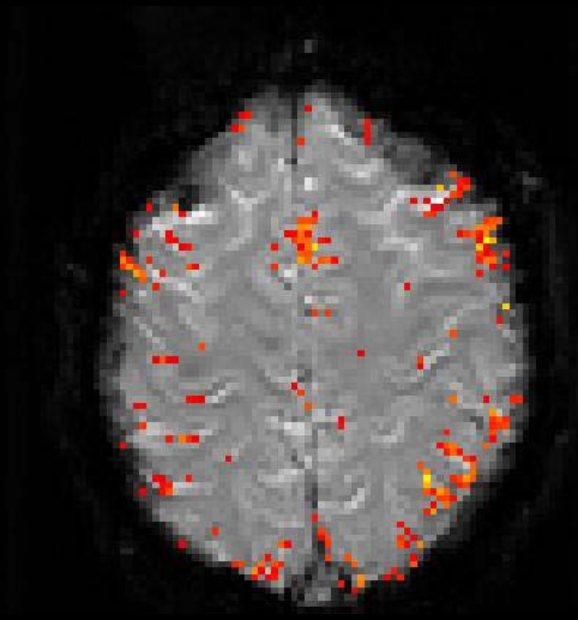
High correlation

Low correlation

Correlation map

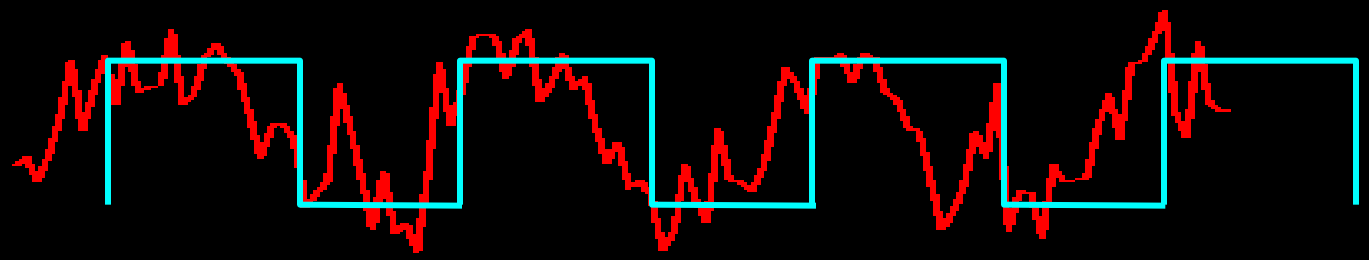


Threshold



Problem 1

?

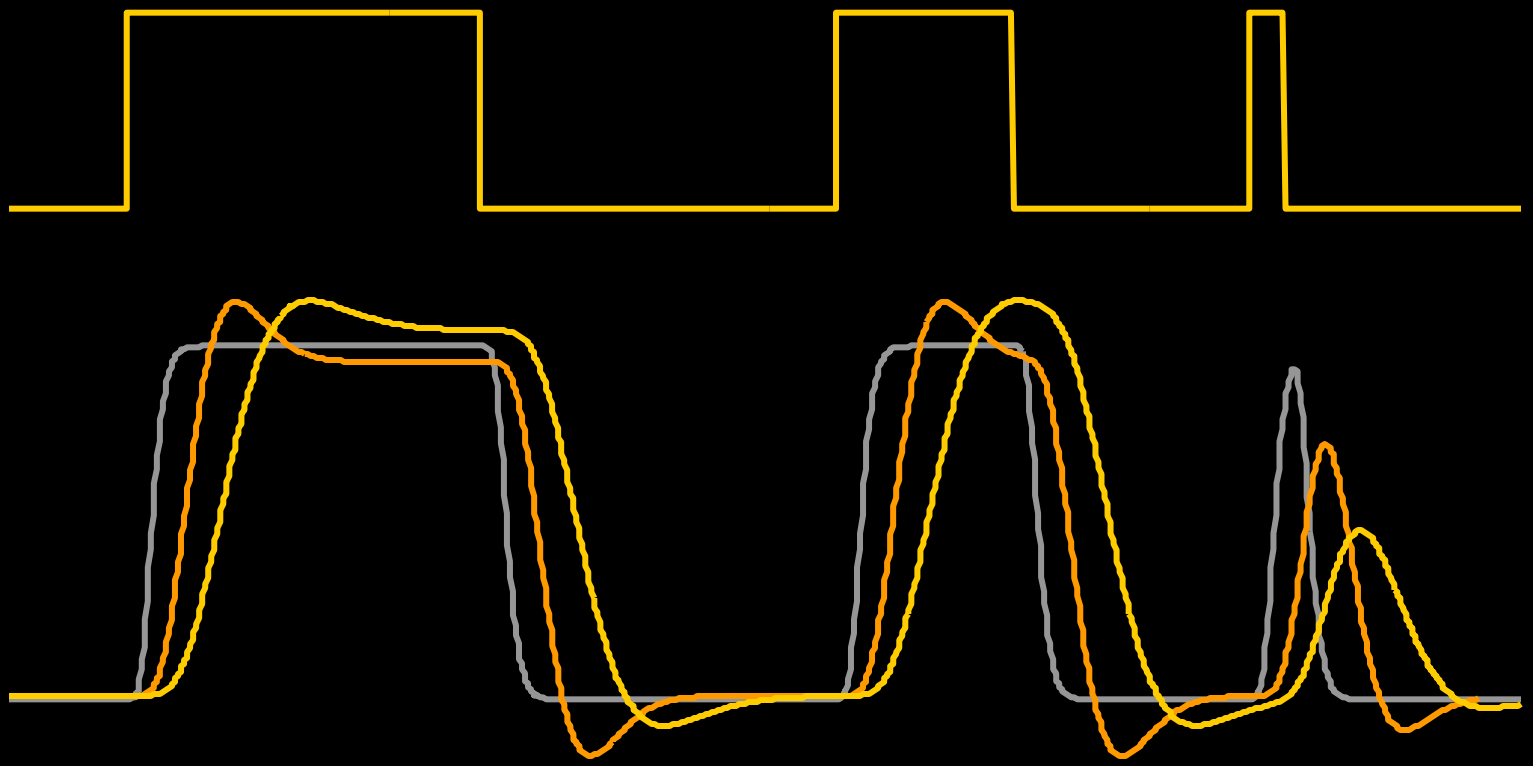


- Unknown delay between the paradigm and the measured signal.
- Unknown shape of the BOLD response

The BOLD response

- Different non-linear models of the response
  - Buxton's "Balloon" model
  - Difference of Gamma functions
- Convolve the activity pattern (paradigm) with the impulse response

The BOLD response



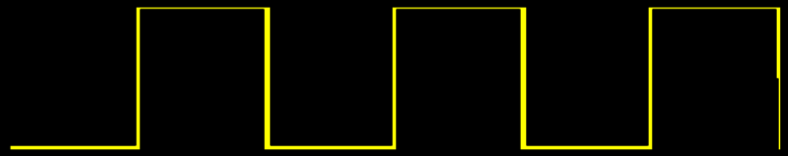
Solution

- Use a set of temporal basis functions that can be linearly combined to model the response
- This can be obtained by
  - Linearizing a non-linear response model using e.g. principal component analysis (PCA)
  - Using harmonic basis functions (sine and cosine functions)

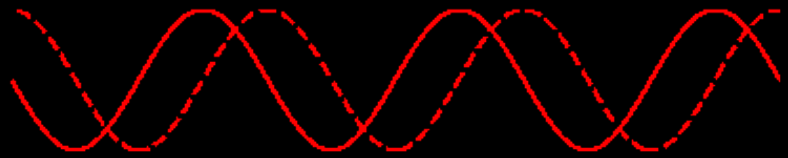
Example

Expand the paradigm into a sum of sinusoidal functions

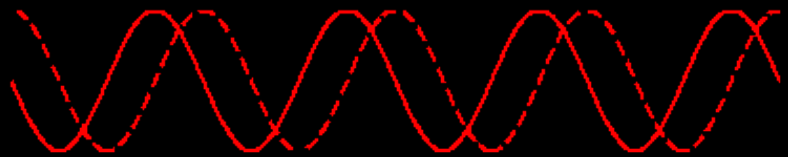
Paradigm



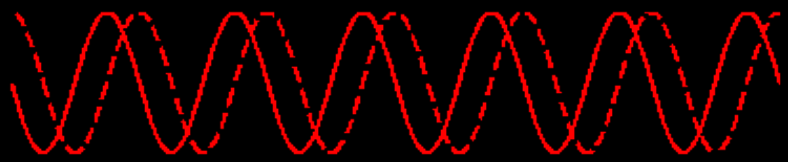
$y_1(t)$ and $y_2(t)$



$y_3(t)$ and $y_4(t)$

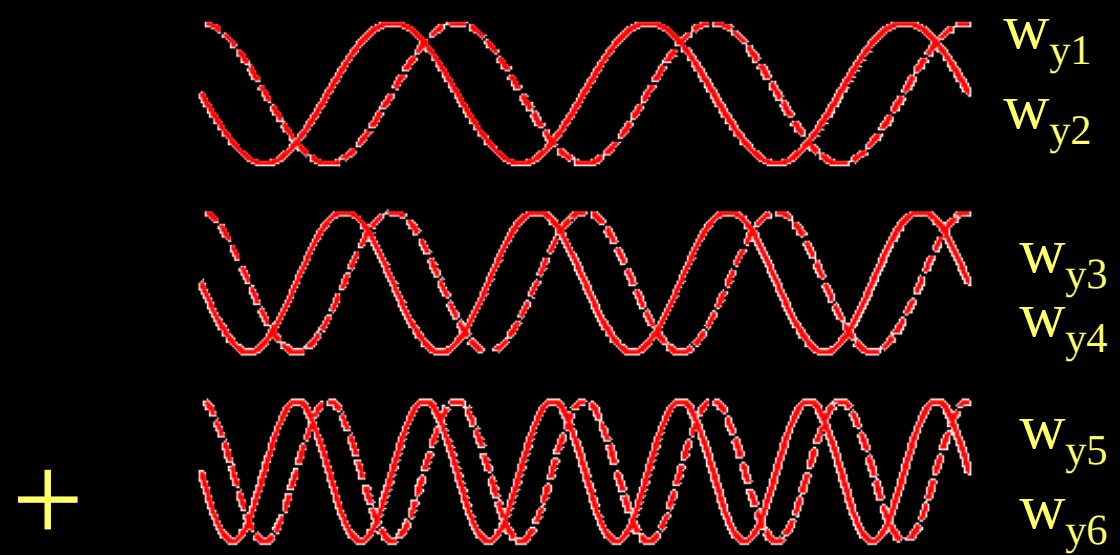


$y_5(t)$ and $y_6(t)$



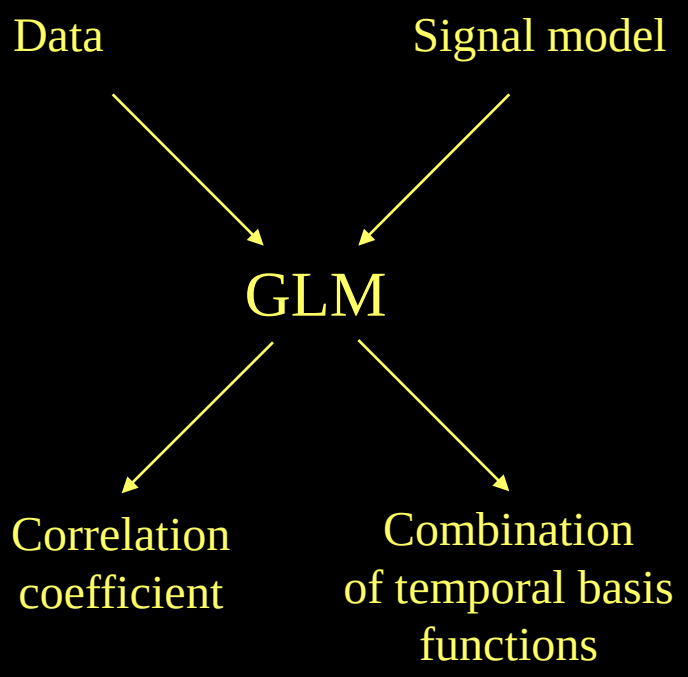
Adaptive response-modeling

$$y(t) = w_{y1}y_1(t) + w_{y2}y_2(t) + \ldots + w_{y6}y_6(t)$$

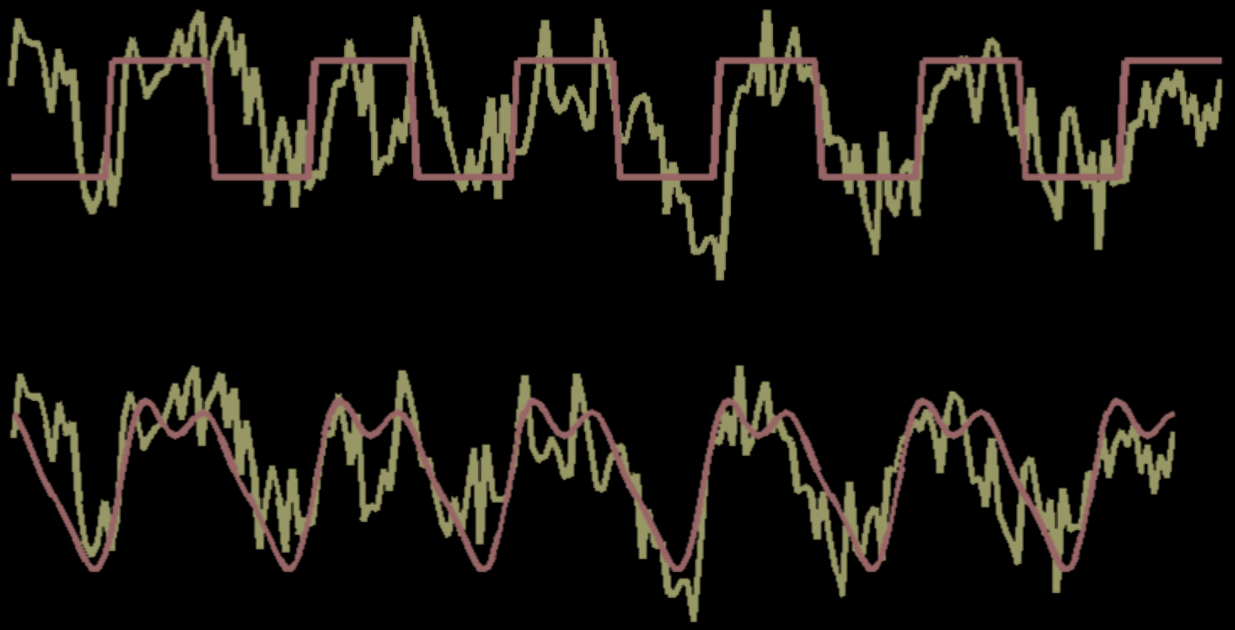


General Linear Model (GLM)

- Find the linear combination of temporal basis function (model signals) that gives maximum correlation with the data
- Linear regression!

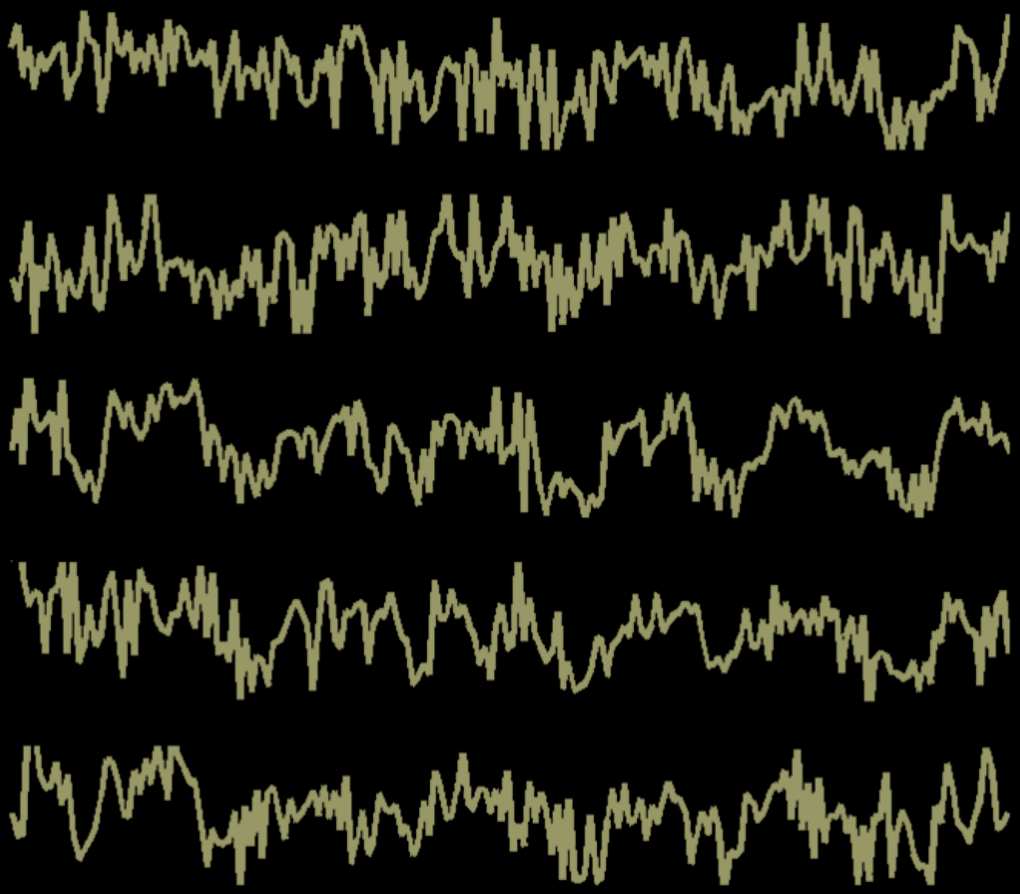


Adaptive response-modeling



Problem 2

Low signal-to-noise ratio in the time series



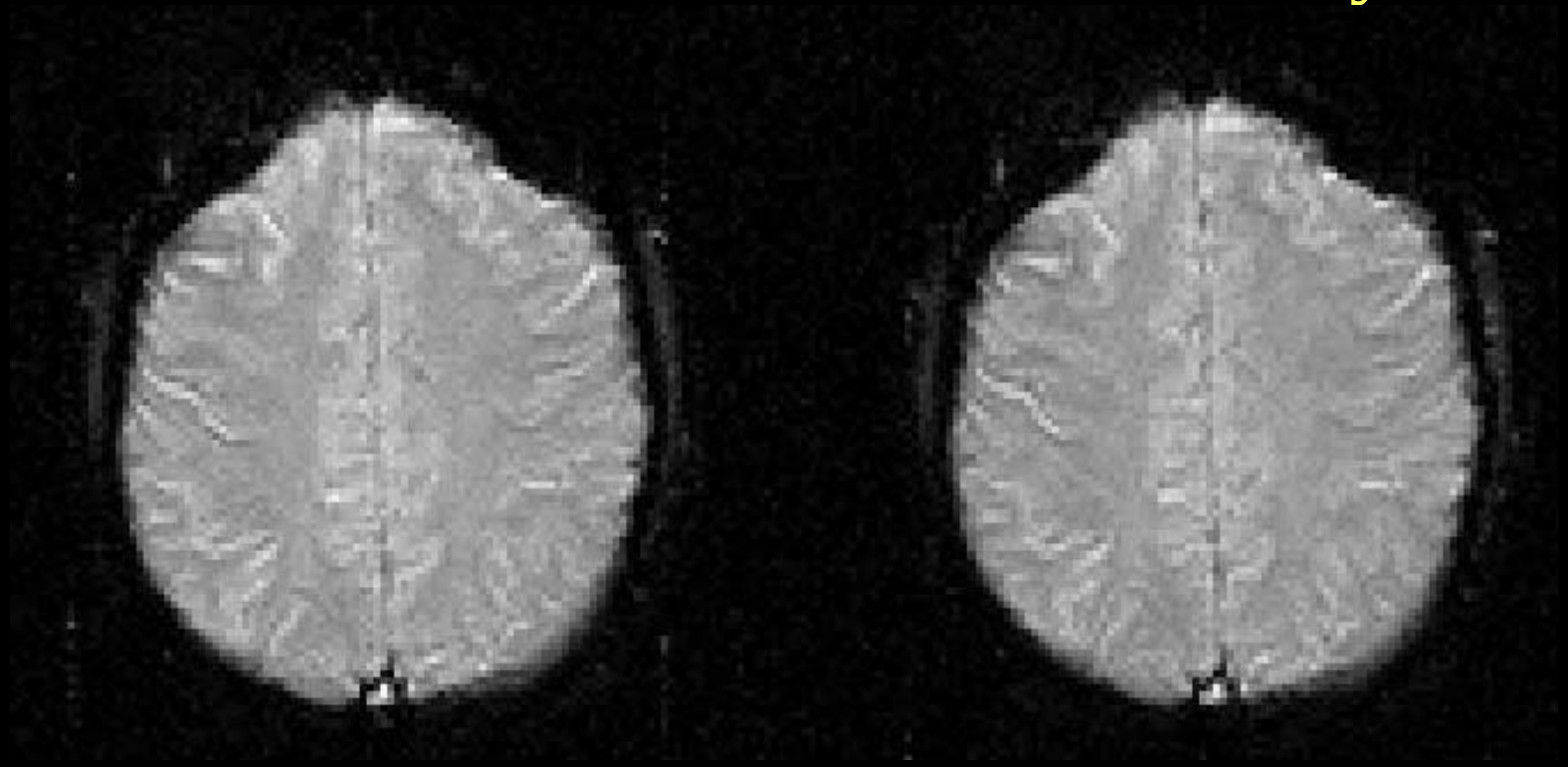
Low SNR

- Very high noise levels
  - Motion
  - Thermal noise
  - Magnetic field variations
- Low signal strength
  - Bold effect is weak
- SNR: 5 – 10 %

The BOLD Signal

Rest

Activity

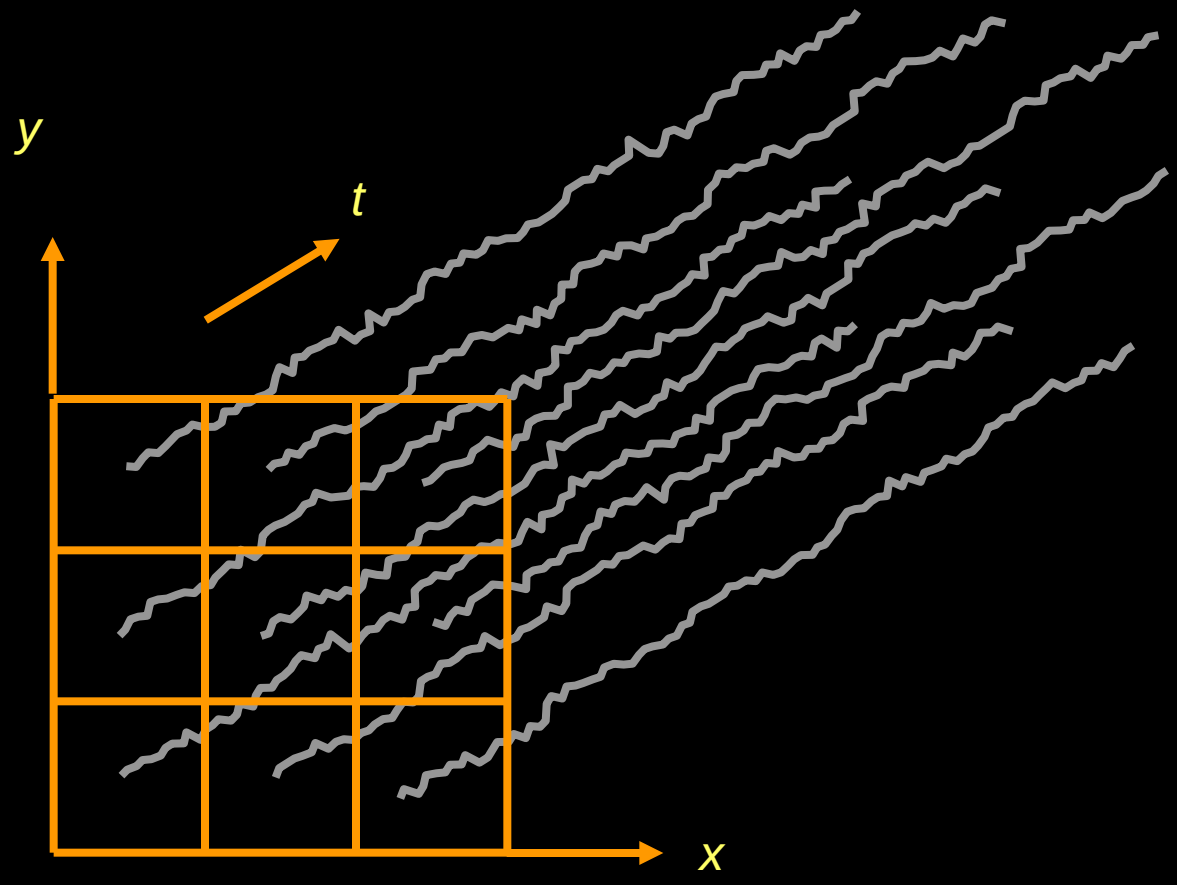


Solution

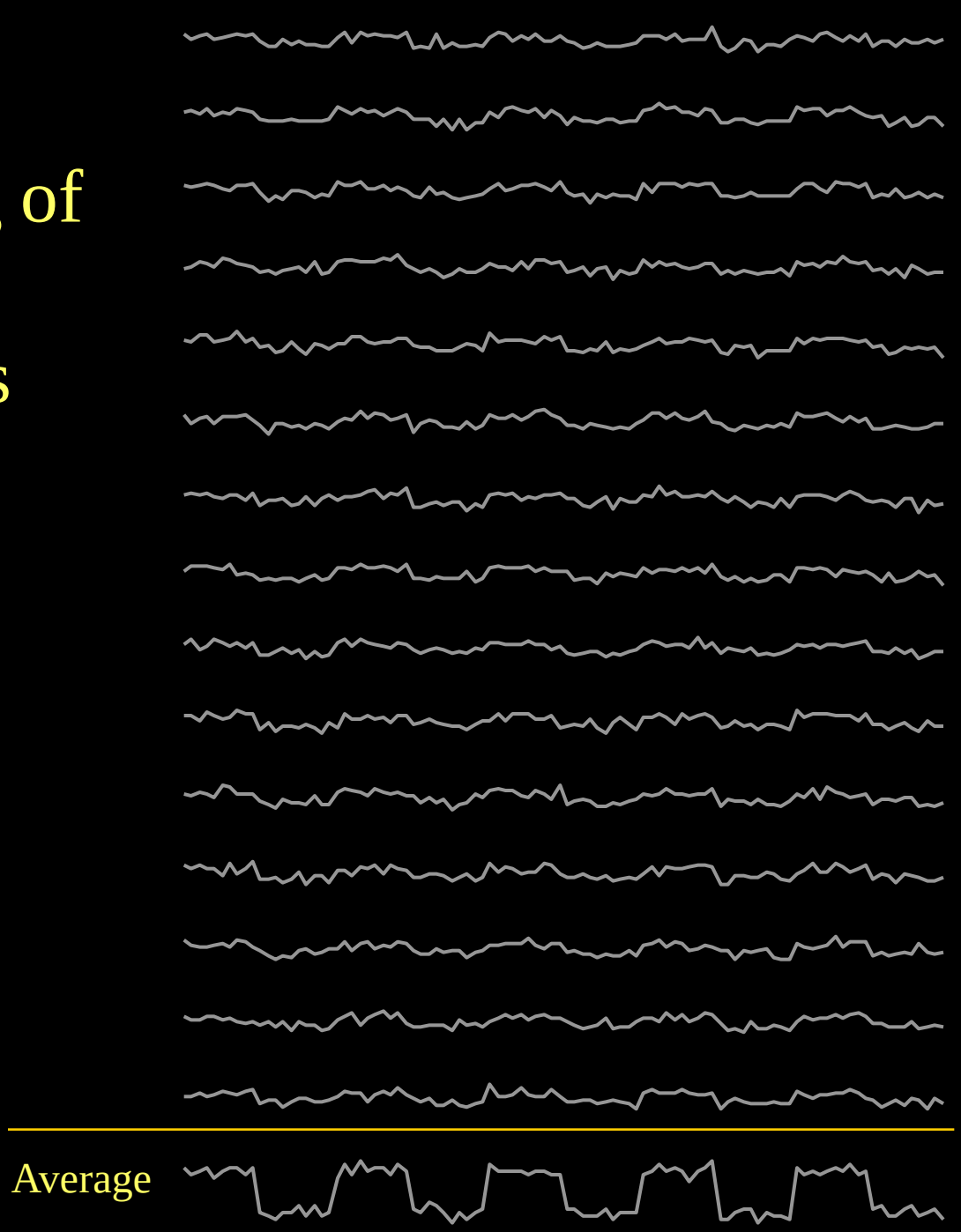
Spatial low-pass filtering

Local averaging of the time sequences

Local averaging of the time sequences



Local averaging of the time sequences



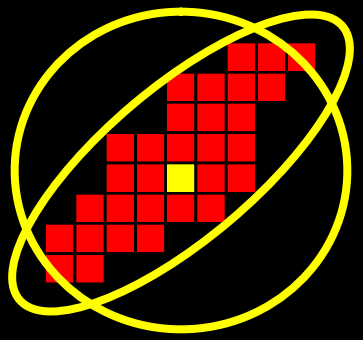
Problem 3

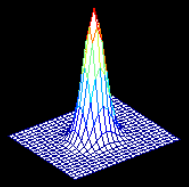
LP-filtering reduces the spatial resolution!

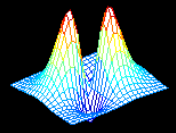
Solution:

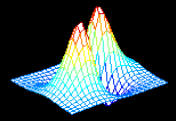
Adaptive spatial filtering

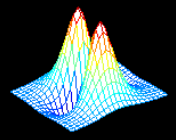
Steerable filters

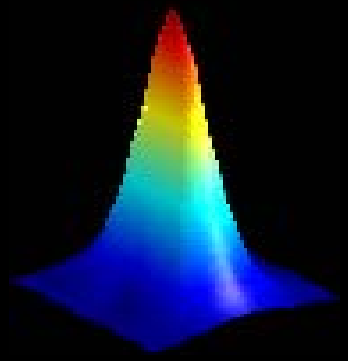


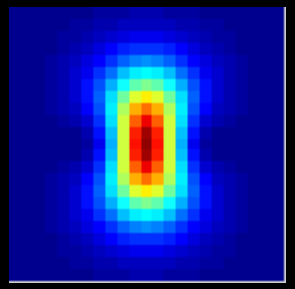












Optimization problem

- The parameters in the temporal model
- The parameters in the spatial filter

- How can these be optimized simultaneously?

Canonical correlation analysis

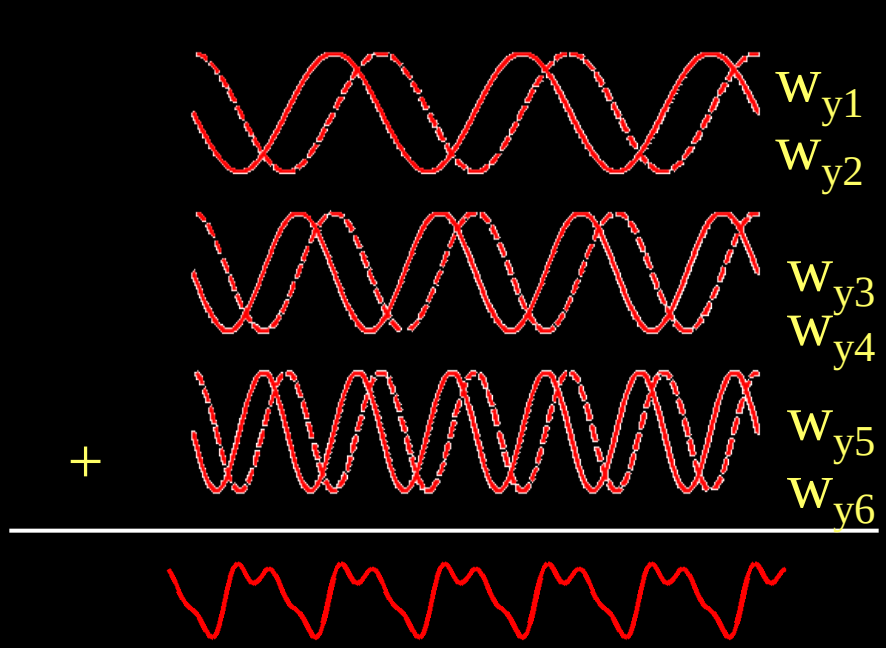
- Multi-dimensional generalization of ordinary correlation analysis.

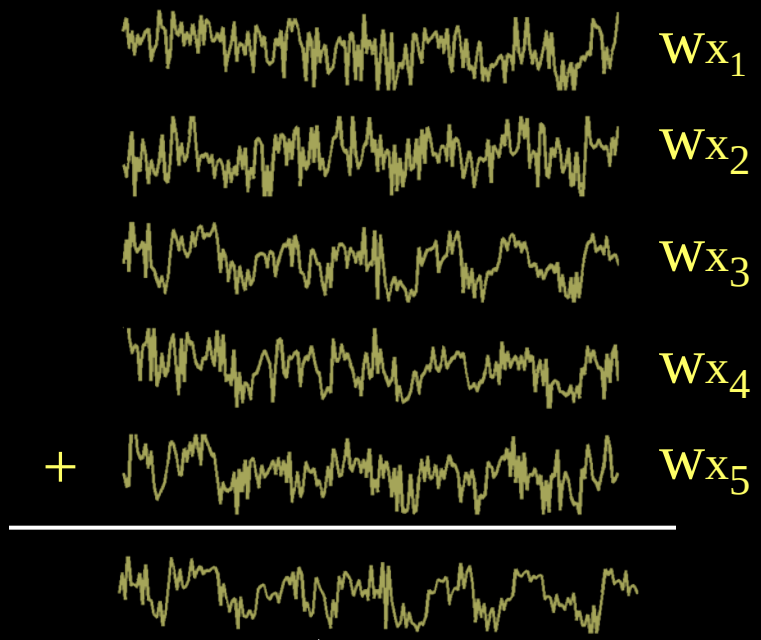
$$x(t) = w_{x1}x_1(t) + w_{x2}x_2(t) + \ldots + w_{xm}x_m(t)$$

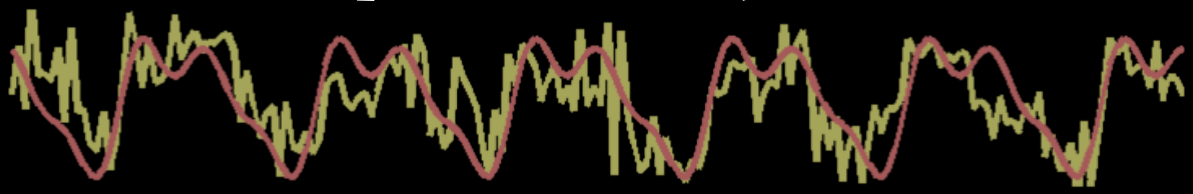
$$y(t) = w_{y1}y_1(t) + w_{y2}y_2(t) + \ldots + w_{yn}y_n(t)$$

- Find coefficients that maximizes the correlation between x(t) and y(t).

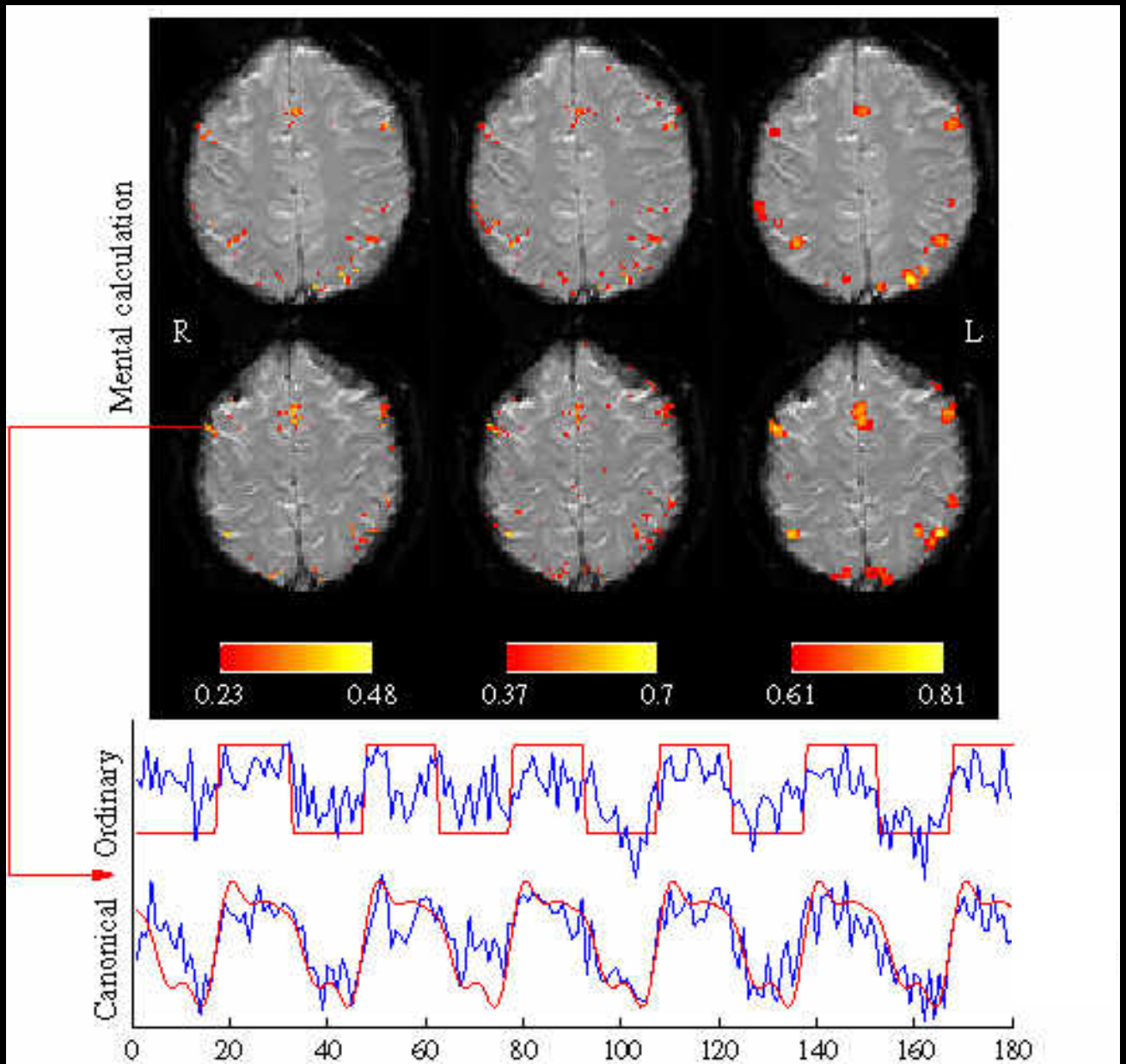
Canonical correlation analysis in fMRI







Results



Korrelation:

0.38

0.80

Sensitivity / selectivity

- Many degrees of freedom → high sensitivity
- High sensitivity leads to low selectivity
- Risk of finding false signals in the noise

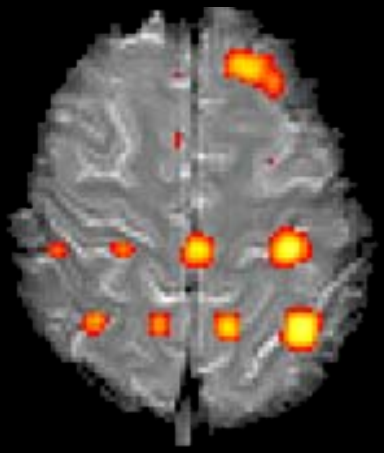
- Need to constrain the solution space in order to limit the false positive rate!

Results on simulated data

Simulated activation

Ordinary correlation

Gaussian LP-filtering



Canonical correlation

Exploratory fMRI

- If there is no good model for the temporal signal
  - Ex: disturbances, uncontrollable activity
- Try to find ”interesting signals”

”Blind Source Separation”

- Suppose the measured signals is a linear mixture of a number of independent sources

$$\mathbf{x}(t) = \mathbf{A}\mathbf{s}(t)$$

- Goal: To reconstruct the unknown sources

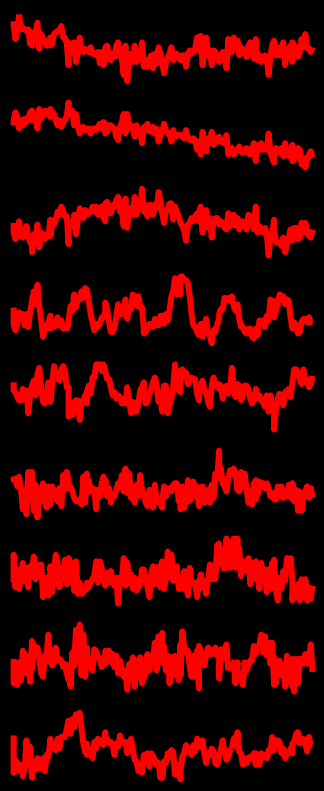
$$\mathbf{s}(t) \sim \mathbf{y}(t) = \mathbf{W}\mathbf{x}(t)$$

”Blind Source Separation”

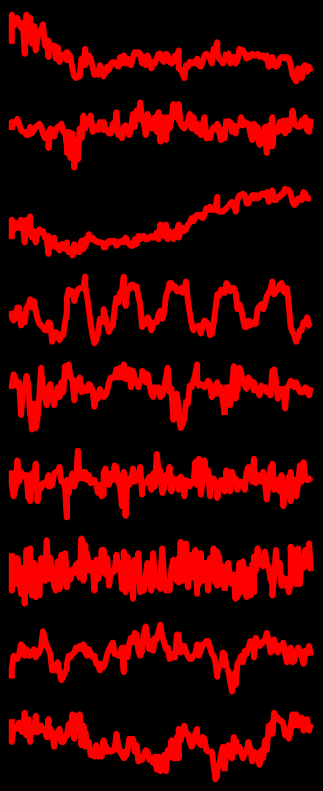
- PCA - ”Principal Component Analysis”
  - Gives uncorrelated signals, but usually not the sources
- ICA - ”Independent Component Analysis”
  - Often gives signals similar to the sources but slow and non-deterministic
- CCA - ”Canonical Correlation Analysis”
  - Maximizes the autocorrelation
  - Deterministic and fast

Results

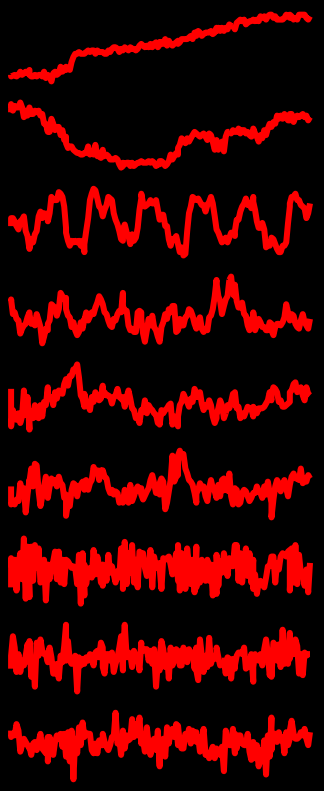
PCA



ICA



CCA



Statistical inference

- The correlation coefficient don’t say much about the degree of activation.
- Few samples → high risk for false positives
- For fixed spatial filtering and under certain assumptions a parameterized statistical model can be assumed
- Enables thresholding on a certain p-value

Non-parametric statistics

- Adaptive spatial filtering makes the statistics differ in each voxel
- Then, parametric statistics can not be used!
- Therefore we have to use non-parametric statistics
- Simulate the H_0-hypothesis (no correlation) by randomly permuting the samples.
- Care must be taken to preserve the auto-correlation structure in the signal.

Visualization