Design Optimization

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fMRI designs: overview

- **Introduction:** fMRI noise
- **fMRI design types:** blocked designs
  event-related designs
  mixed design
  adaptation designs
- **Efficiency:** mathematical description
  efficiency in practice
- **Statistical designs:** nb factors / nb of sessions
  within / between variance

Introduction

fMRI noise

- It exists different sources of noise which can interfere with the experiment (determines the SNR):

⇒ Thermal (intrinsic) noise

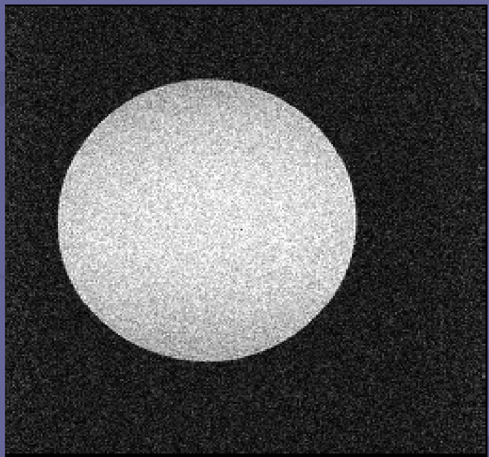
⇒ System noise: static field inhomogeneities (scanner drift = Δ resonance frequency H^+), nonlinearities and instabilities on the gradient fields, off-resonance or loading effects in the radiofrequency transmitter and receiver coils

⇒ Physiological noise: cardiac / respiratory activity (aliasing pblm) / motion

fMRI noise

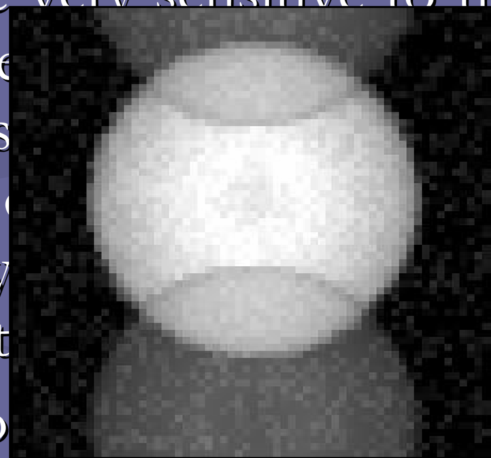
- **Thermal noise** is produced due to the thermal motion of electrons inside the subject's body and in the large electronic circuits of the MRI scanner.

This type of intrinsic scanner noise is uncorrelated to the task and the hemodynamic signal, and therefore can be described as “white” noise. This type of noise increases with increased resolution, i.e. for smaller voxel size.



fMRI noise

- **N/2 Ghost:** EPI scans suffer from ghosting artefacts in the phase encoding direction. During acquisition, k-space data are sampled by an alternating positive/negative read gradient. This results in a single ghost shifted by half a FOV.
- **Susceptibility artefacts:** The EPI images are very sensitive to the changes of the magnetic susceptibility, i.e. the … ns of different properties (brain/air) like regions … es or the temporal pole may disappear. Artefacts … by the presence of magnetic material in proximity … g. implants, braces, or even someone moving in t…



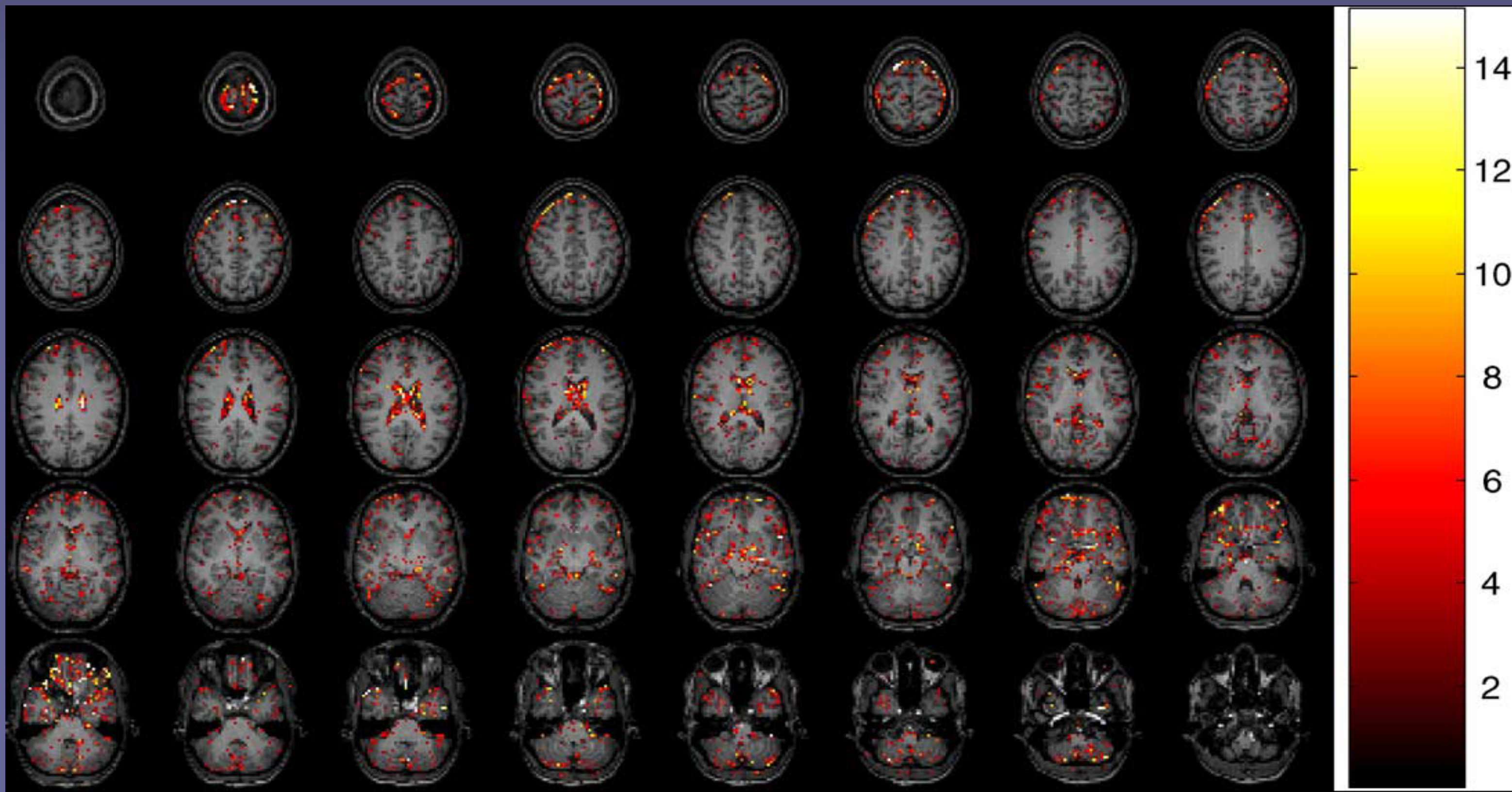
- **Scanner drift:** Drift is created most pro… all instability of scanner gradients. It can create slow changes in voxel intensity over time (2 sessions = 2 mean intensities).

fMRI noise

- **Cardiac and respiratory artefacts:** The pulsation of the blood and changes connected to breathing can change blood flow and oxygenation.

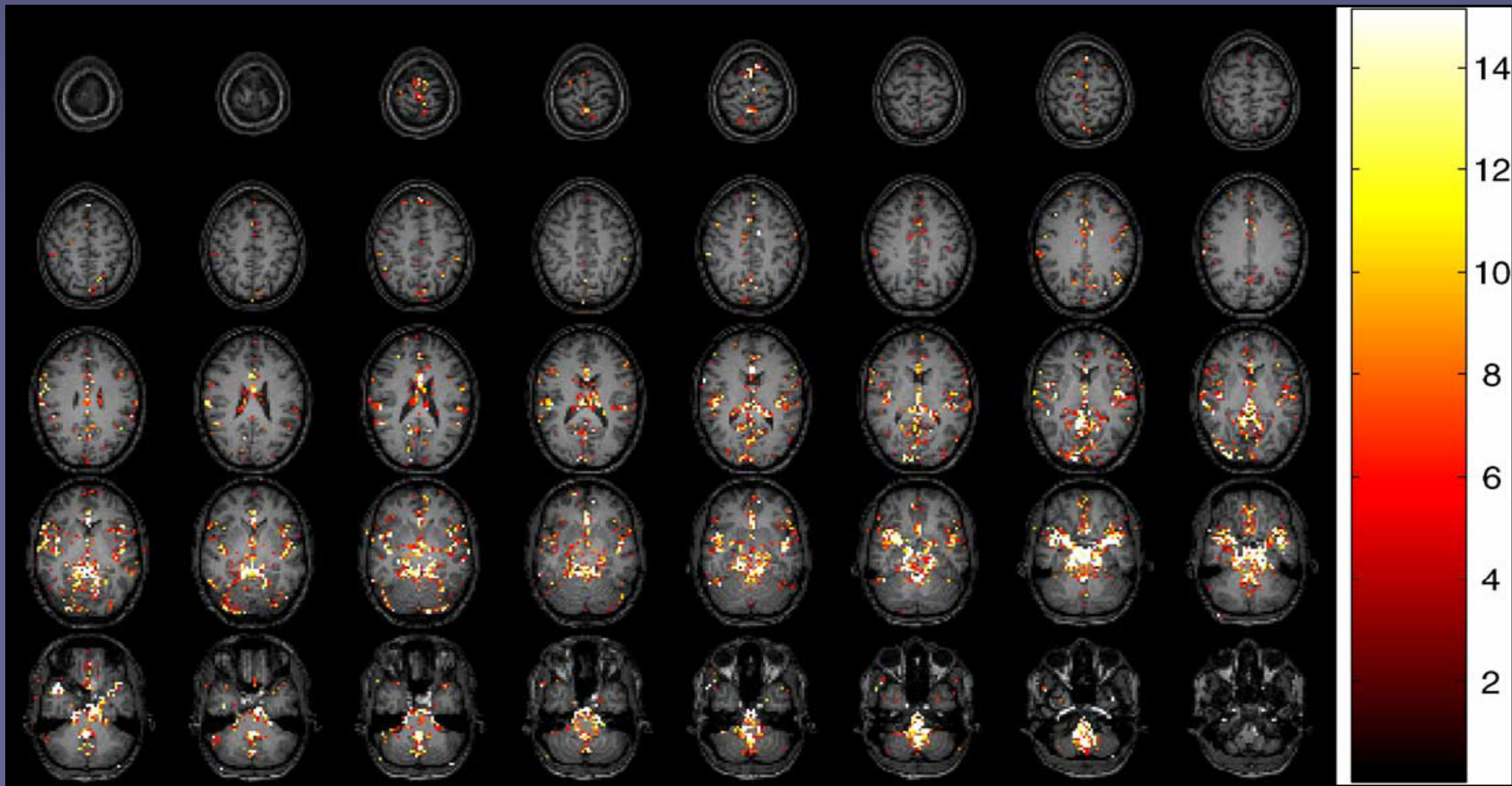
- These factors create high frequency signal artefacts, for example, the cardiac cycle is too fast (500 ms) to be sampled with a relatively average TR (2000 ms). However, when this is the case, the variability become attributed to a lower frequency (**aliasing**), creating an even larger problem.

fMRI noise



Respiratory-induced noise is dominant near the edges of the brain as well as near in the larger veins and in the ventricles (Lund et al., 2006)

fMRI noise

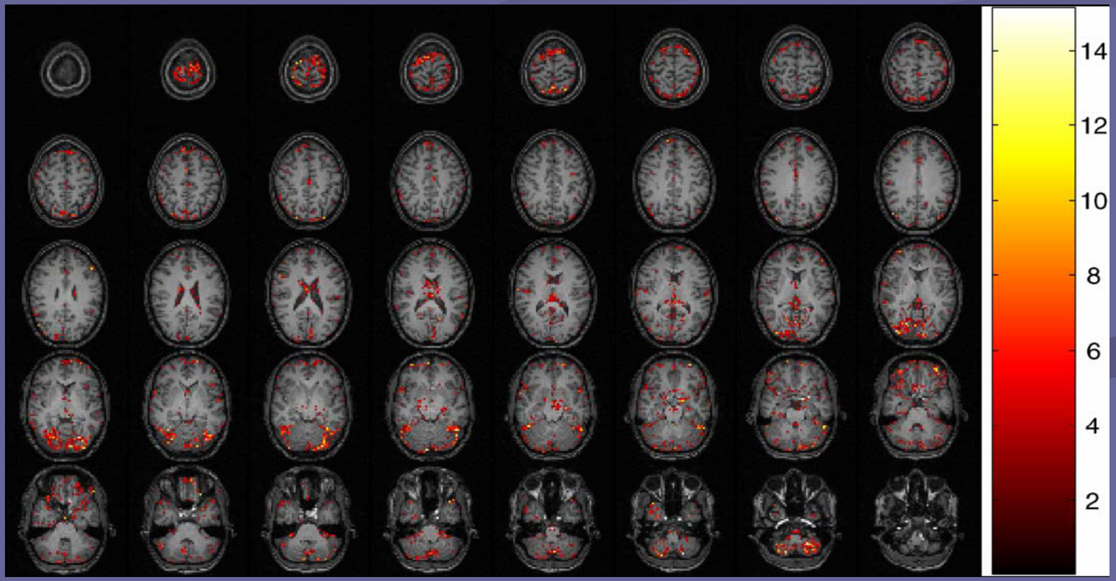


Cardiac-induced noise is dominant near larger vessels, e.g. medial cerebral artery and Circle of Willis (Lund et al., 2006)

fMRI noise

- Subject motion is a common source of series artefacts. Even relatively small motion (of the range much smaller than a voxel size e.g 1.6-3.2 mm) can create serious artefacts due to the partial volume effects. Typically motion of about half a voxel in size will render the data useless (that's why there is a motion correction step in the analysis).

Lund et al. 2006



fMRI noise

- Common solution: filtering

⇒ Avoid low and high frequency confounds

- Goal of the design: optimization (efficiency)

⇒ Have a sufficiently high frequency (avoid noise)

⇒ Increase the number of observations (statistical design)

⇒ Increase the variability (NRJ = Σ signal^2 = f(var)), i.e. decrease the overlap between same BOLD responses & increase the differential overlap (event-related design)

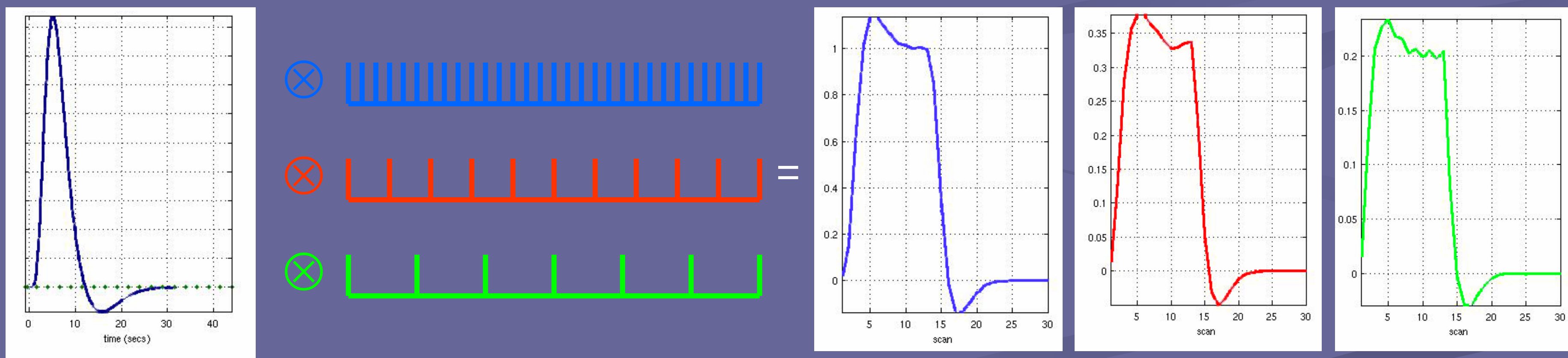
Take Home message 1

- Avoid any ferromagnetic object in the scanner (susceptibility artefacts can be caused by a bra !!)
- Scan as long as possible to avoid scanner/session effect
- Avoid low frequency in a design
- Minimize biological artefacts (monitoring of cardiac and respiratory rhythms when possible and motion correction both as pre-processing and as regressors for the residuals)

fMRI design types

Blocked designs

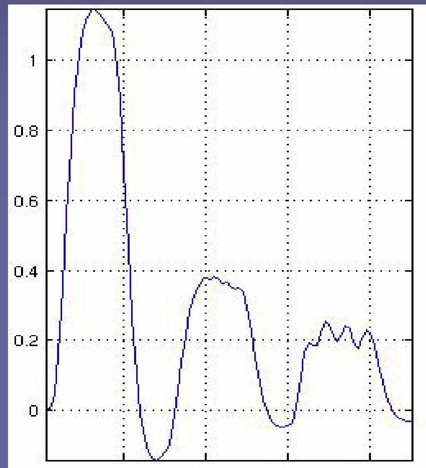
- Powerful in terms of detection, i.e. to determine which voxels are activated.
- Poor estimation power, i.e. a weak ability to determine the time course of the response ⇒ <u>summation of hemodynamic responses</u>.



Ex: 1 stimulus every 1 sec / 3 sec / 5 sec
TR: 2.5 sec Highpass filter: 128Hz

Blocked designs

- The advantage of short ISI is that the response is greater than for long ISI because responses to different stimuli summate thus increasing the response amplitude



1Hz 0.3Hz 0.2Hz

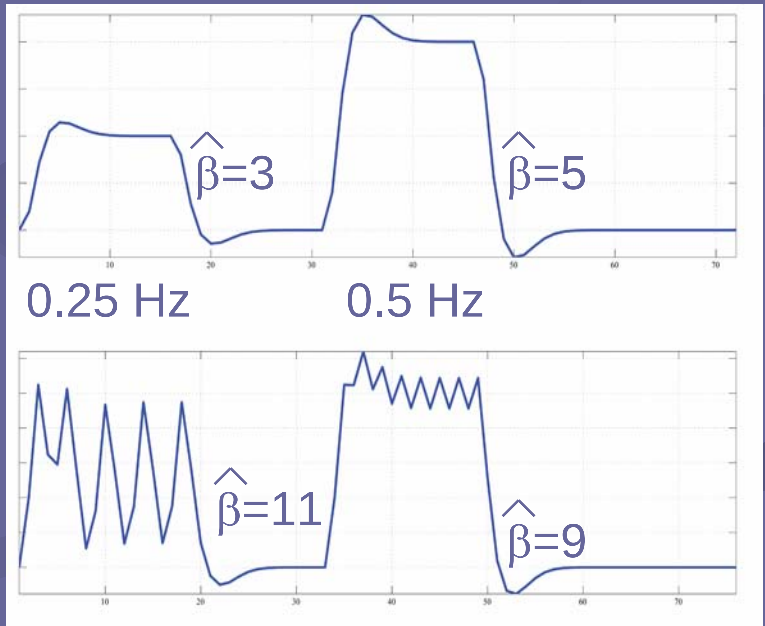
- The disadvantage of short ISI is that it exists an hemodynamic refractoriness period, a neuronal refractoriness period, i.e. late neuronal components may be interrupted by early components of next stimulus. There is also a cost for task related performances (particularly for patients), trade off rate/performance.

Blocked designs

- **Modelling blocks vs. events:** It is extremely important to distinguish between the experimental design (blocked or event related) and the neural model (epoch or event).

Block design and block model = the parameters reflect the fit for the whole blocks; i.e. activation for stimuli presented at higher rate elicited more activations than those presented at lower rate.

Block design but Event model = the parameters reflect the fit for the each event; i.e. activation for stimuli presented at lower rate elicited more activations than those presented at higher rate (we have twice as many stimuli at 0.5 than 0.25Hz but the mean activity isn't the double, the response per stimuli must be less)

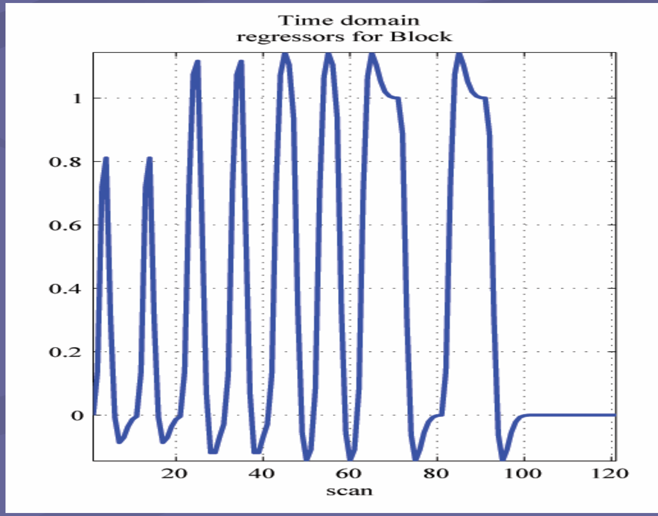


Blocked designs

Optimization:

- Signal strength varies with the length of blocks.

- With short blocks (less than 10s), the signal does not return to baseline during null-blocks decreasing the strength of the signal.
- With long block lengths, a large response is evoked during the task blocks and the response returns to baseline during null-blocks.



5 / 10 / 15 / 30 sec

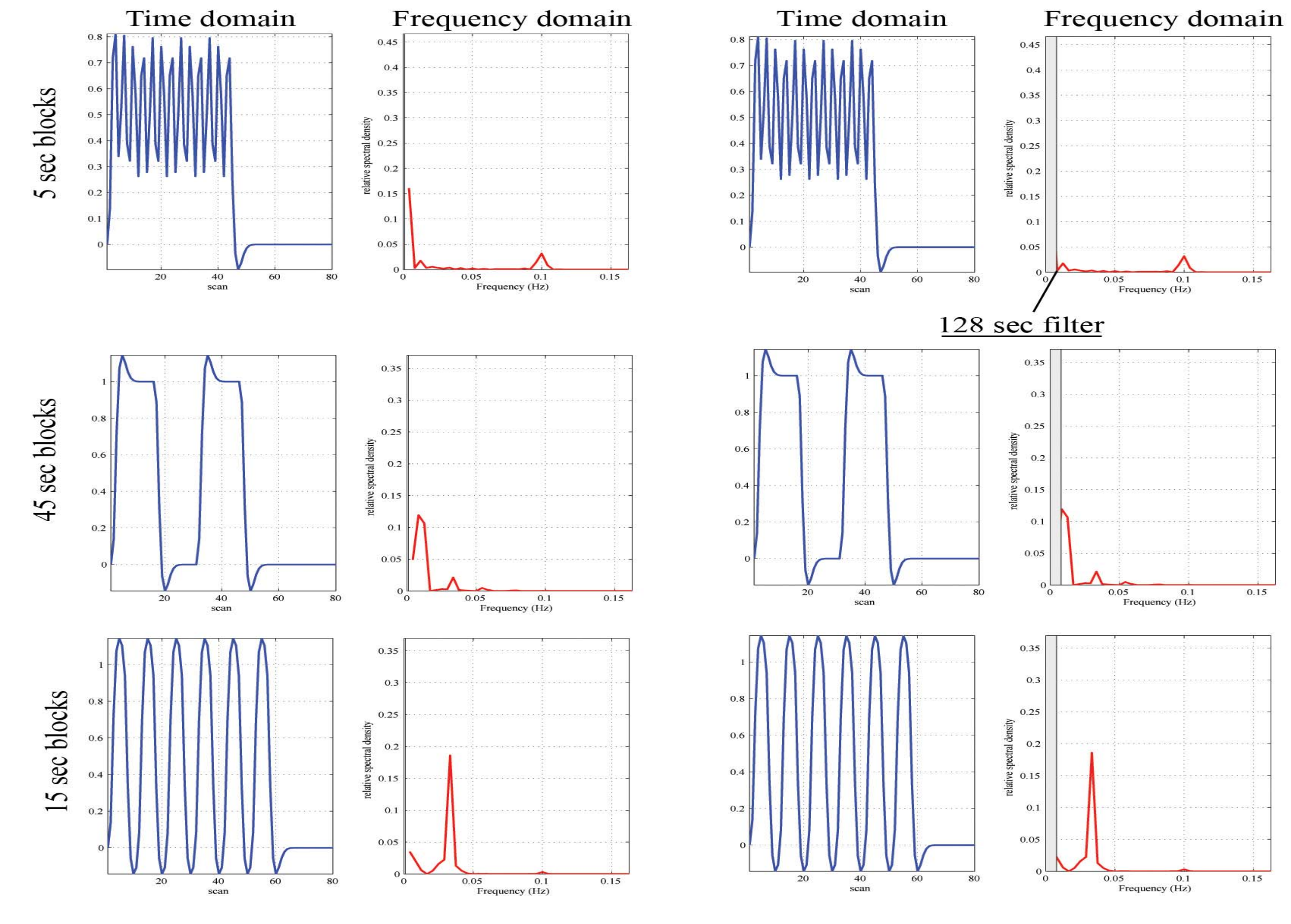
Blocked designs

Optimization:

- So far we want short ISI and long blocks
- However, the detection power increases with high frequency alternation because i) it depends on the number of events/blocks and ii) the noise in the BOLD time course which occurs mainly at low frequencies.

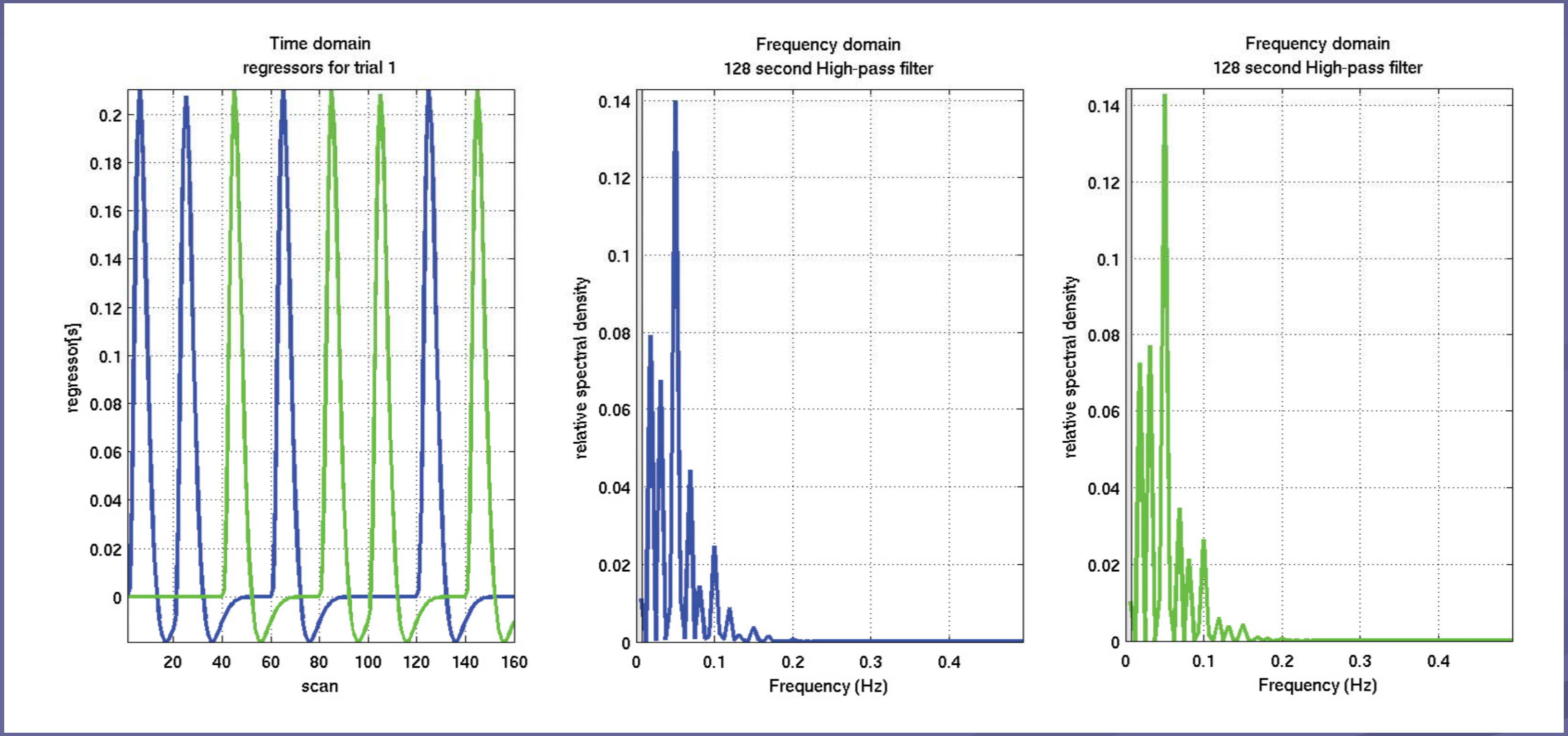
> **Blocks with durations longer than the hemodynamic response reach a compromise between signal strength and noise (optimal 16s)**

Blocked designs



Event-related designs

- Example of a **Periodic designs**



Alternates two conditions A A B A B B A B every 20 sec

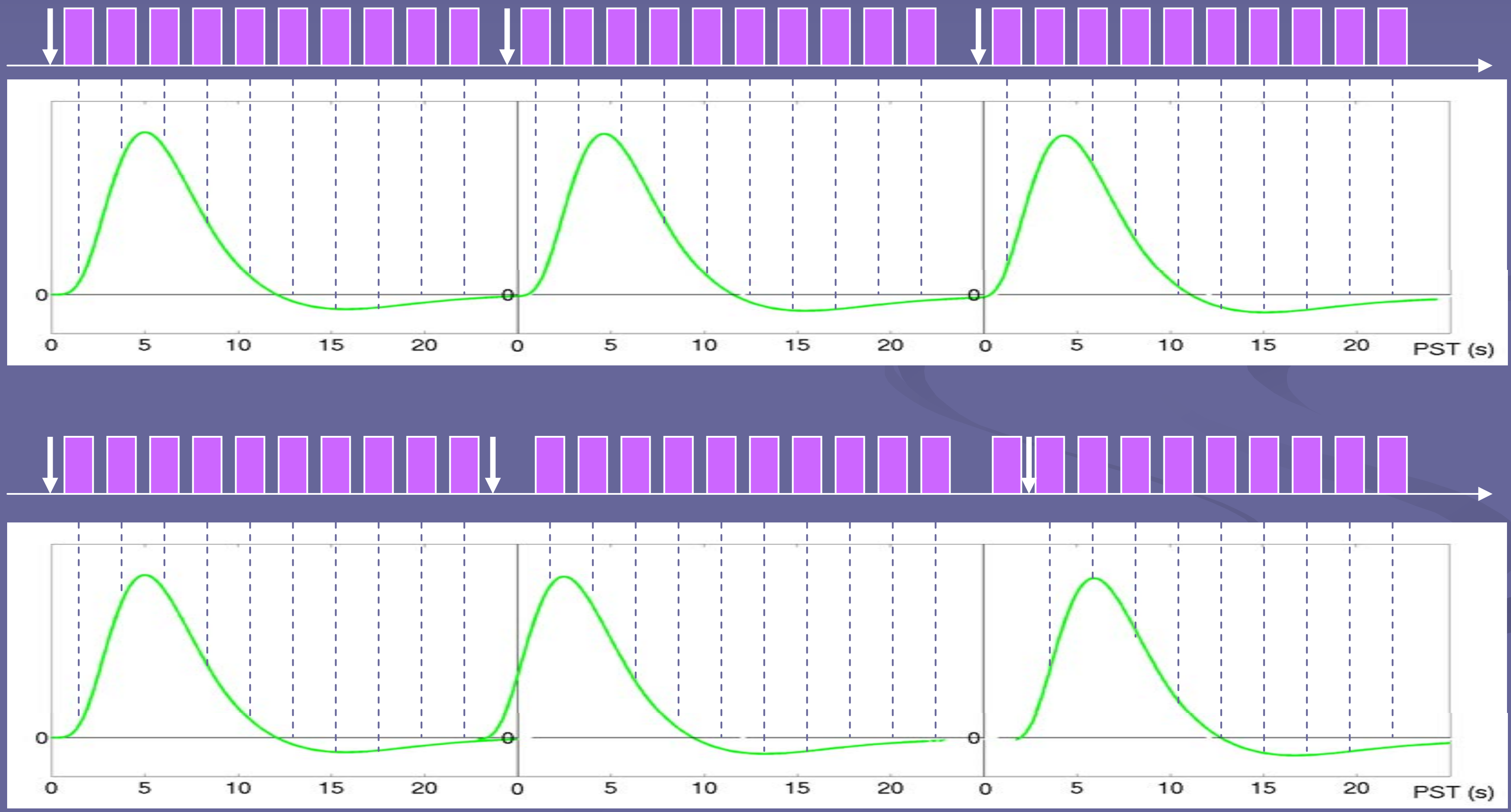
Event-related designs

- Estimation power of event-related design is often good as they allow to inquire the hemodynamic shape for each condition and compare parameters such as the amplitude or the timing between conditions.

- By contrast, the detection power is relatively weak in comparison with blocked design. This is explained by the simple fact that experimental power depends on the number of events that are averaged.

Event-related designs

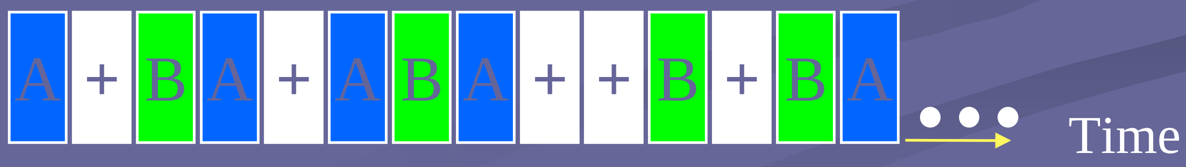
- Optimization: Jittering



Rapid Event-related designs

- Stimuli are closely spaced in time, i.e. there is an overlap of the hemodynamic responses.
- Raw signal uninterpretable but trials can be in a total random sequence such as it is highly resistant to habituation, set, and expectation.

- By introducing ‘null events’ one creates differential ISI, i.e. differential overlaps between hemodynamic responses which allows a full characterization of this response.



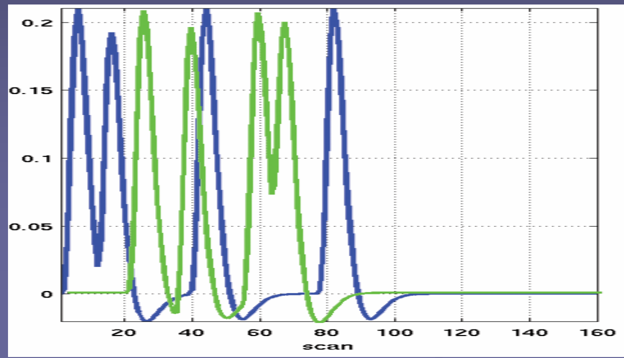
Rapid Event-related designs

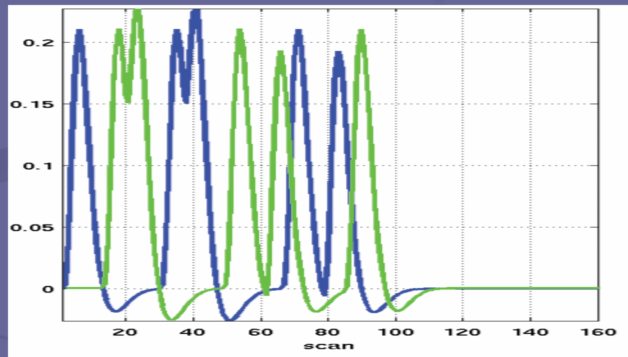
Optimization

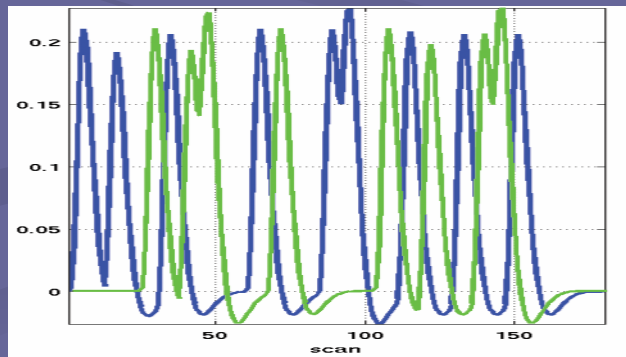
- **Jittered designs** rely on the likelihood of a given ISI following each stimulus (stationary stochastic designs)

- **Randomized designs** rely on the likelihood of a stimulus being presented at each time point

- **Semirandon designs**, rely on the systematic probability variation of stimuli over time (dynamic stochastic designs)







Mixed designs

- Stimuli are displayed in discrete blocks

⇒ investigate sustained processes and brain responses (state-related processes). This is different from semirandom designs where, whatever the stimulation rate, we assume that the process is always the same (looking for transient activity for each stimulus).

- Within each block multiple types of events

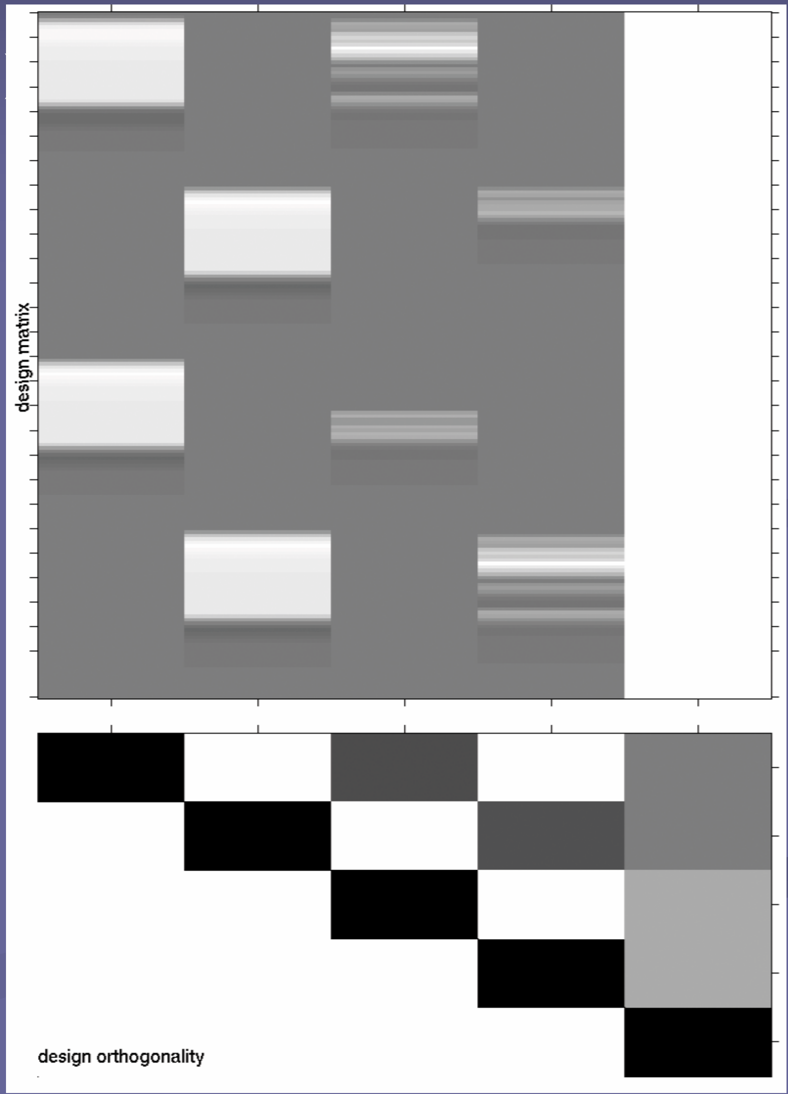
⇒ because different types of stimuli, transient responses are likely to occurs.

- Mixed designs can investigate interaction between processes working at different time-scales.

Mixed designs

- **Example: Chawla et al. 1999.**
- Epochs of attention to motion or color (same stimulus display, i.e. moving green colored dots). During each block, red moving dots appeared and the subjects had to detect target stimuli (7% faster red dots or brighter).

- Optimization
- Randomized, some long SOAs to 'de-correlate' epoch and event-related.



http://www.fil.ion.ucl.ac.uk/spm/course/slides05/ppt/event.ppt)

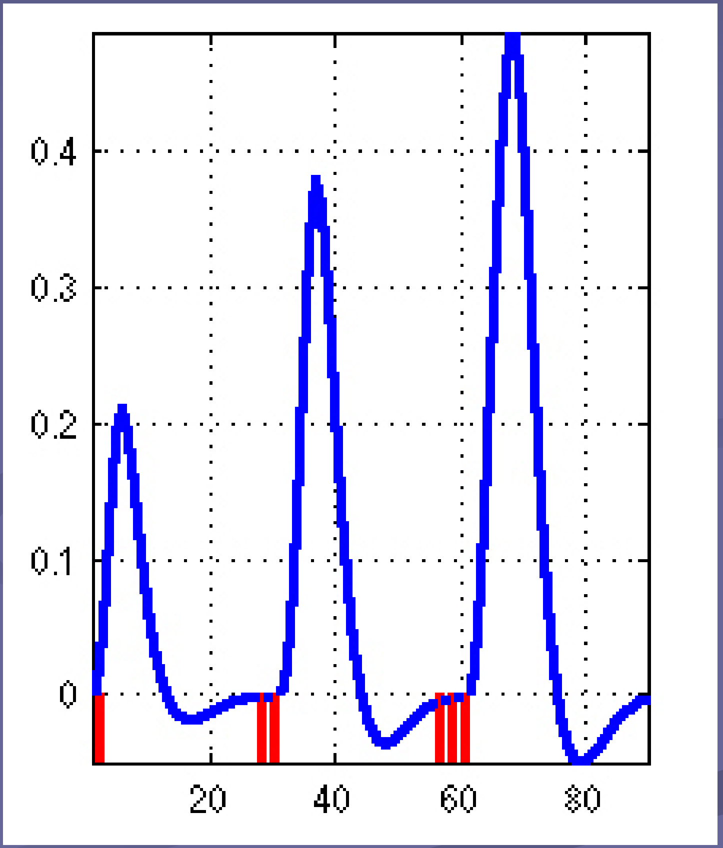
Adaptation designs

- fMRI adaptation designs (afMRI) use the refractory period to enquire functional differences within a given voxel.

- The predicted hemodynamic response relies often on a linear prediction. This means that for an impulse (a short-duration stimulus), the hemodynamic system responds in the same manner. The parameters of the hemodynamic response are then directly interpreted as reflecting both the intensity and the duration of the neural response given the scaling (the magnitude of the system output is proportional to the system input) and superposition (the total response to a set of inputs is the sum of individual inputs) properties of linear systems .

Adaptation designs

- The hemodynamic response is linear for ISI > 6s and nearly linear down to ISI ~ 3s. If the ISI is short, the response to a subsequent stimuli is weaker than for a longer ISI (*Boynton and al., 1996, J Neurosci 16, 4207-4221; Dale & Buckner, 1997, Hum Br Map 5, 329-340*). This phenomenon is known as the hemodynamic refractory period.



1st:0.21 2nd:0.17 3rd:0.12

Adaptation designs

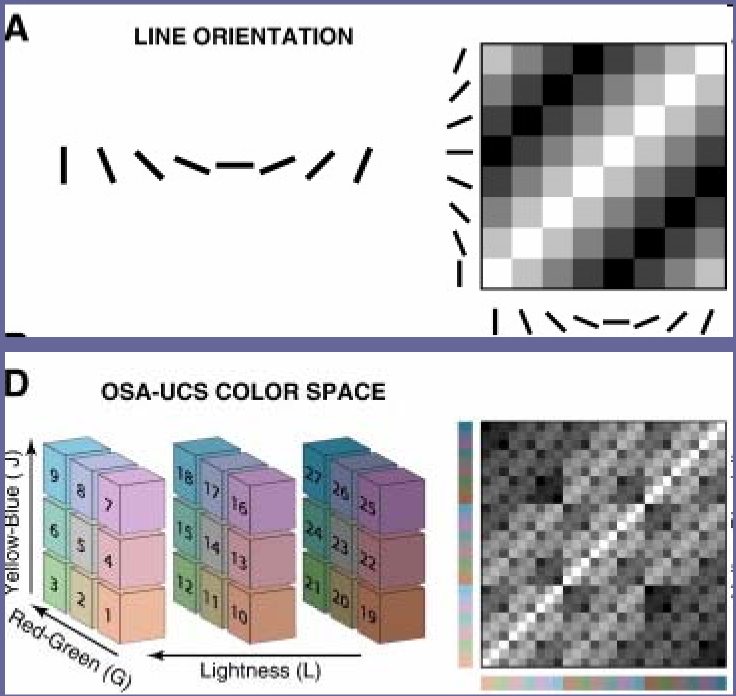
Extension of adaptation: carry over

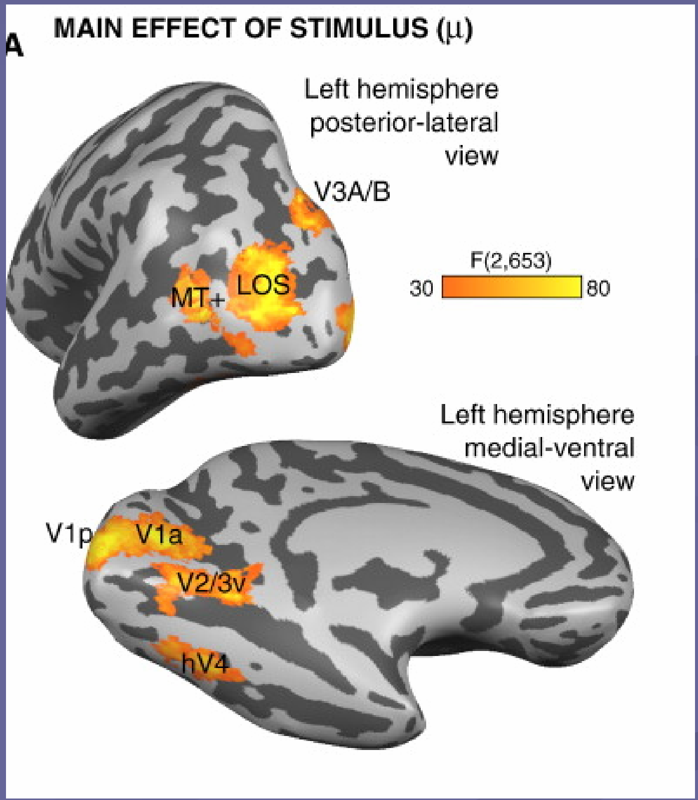
-Continuous carry-over can be used to estimate simultaneously the mean difference in neural activity between stimuli (for the purpose of distributed pattern analysis) as well as the effect of one stimulus upon another (carry-over effects ~ adaptation).

- Direct and carry-over effects are orthogonal when the order of presentation of stimuli is serially first-order balanced, i.e. each stimulus is preceded equally often by every other stimulus (including self-adjacencies).

Adaptation designs

Extension of adaptation: carry over

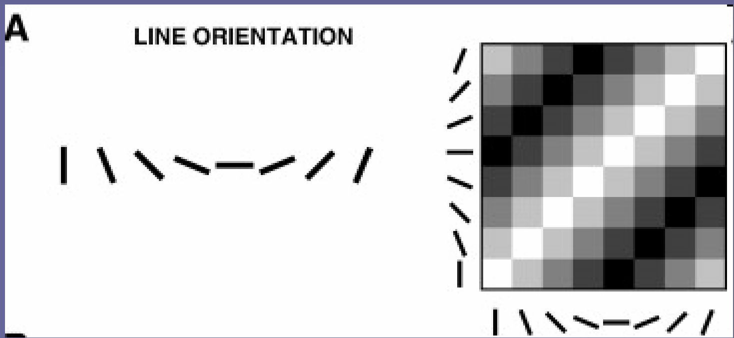


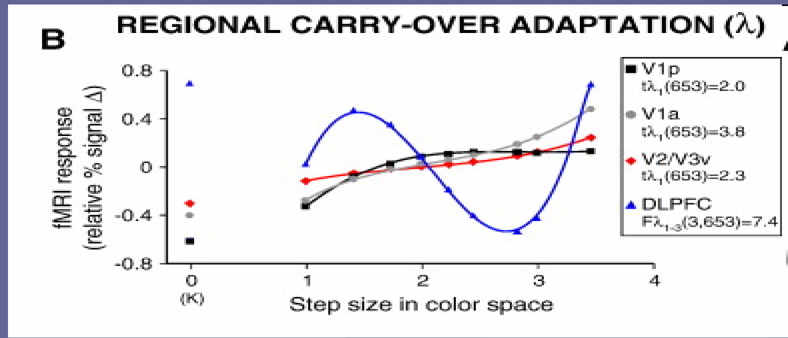


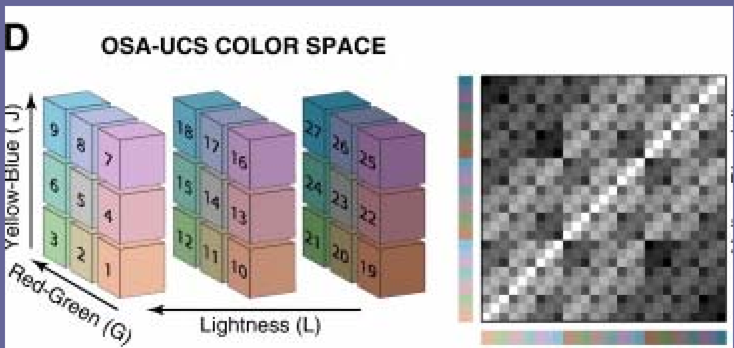
http://www.cfn.upenn.edu/aguirre/wiki/public:continuous_carry-over_for_bold_fmri

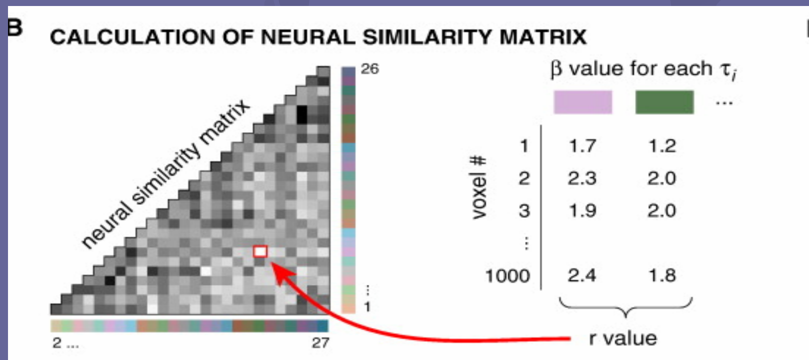
Adaptation designs

Extension of adaptation: carry over









http://www.cfn.upenn.edu/aguirre/wiki/public:continuous_carry-over_for_bold_fmri

Take Home message 2

- Choose your design according to your topic:

- Detection (block designs), Estimation (event-related designs), Estimation of event during different 'states'(mixed designs), How works a region (afMRI)
- Think frequency, decorrelation and sequence order

http://www.cfn.upenn.edu/aguirre/wiki/public:continuous_carry-over_for_bold_fmri

Design Efficiency

fMRI designs & efficiency

⇒ Optimize the covariance matrix = increase the variability

- ✓ $Y = X\beta + e$ (data=model*reg coef + error)
- ✓ $\hat{\beta} = (X^T X)^{-1} X^T Y$ (we search β)

- ✓ $\gamma = C\hat{\beta}$ (contrast = combination of $\hat{\beta}$)
- ✓ $t = \gamma \,/\, (std * sqrt(C\,(X^T X)^{-1}\,C^T))$ (usual t-test effect / error)

'noise' variance and design variance

- ✓ $Eff = 1 \,/\, trace\,(C\,(X^T X)^{-1}\,C^T)$ (you want the error to be small)

fMRI designs & efficiency

$\Rightarrow$ Optimize the covariance matrix ??

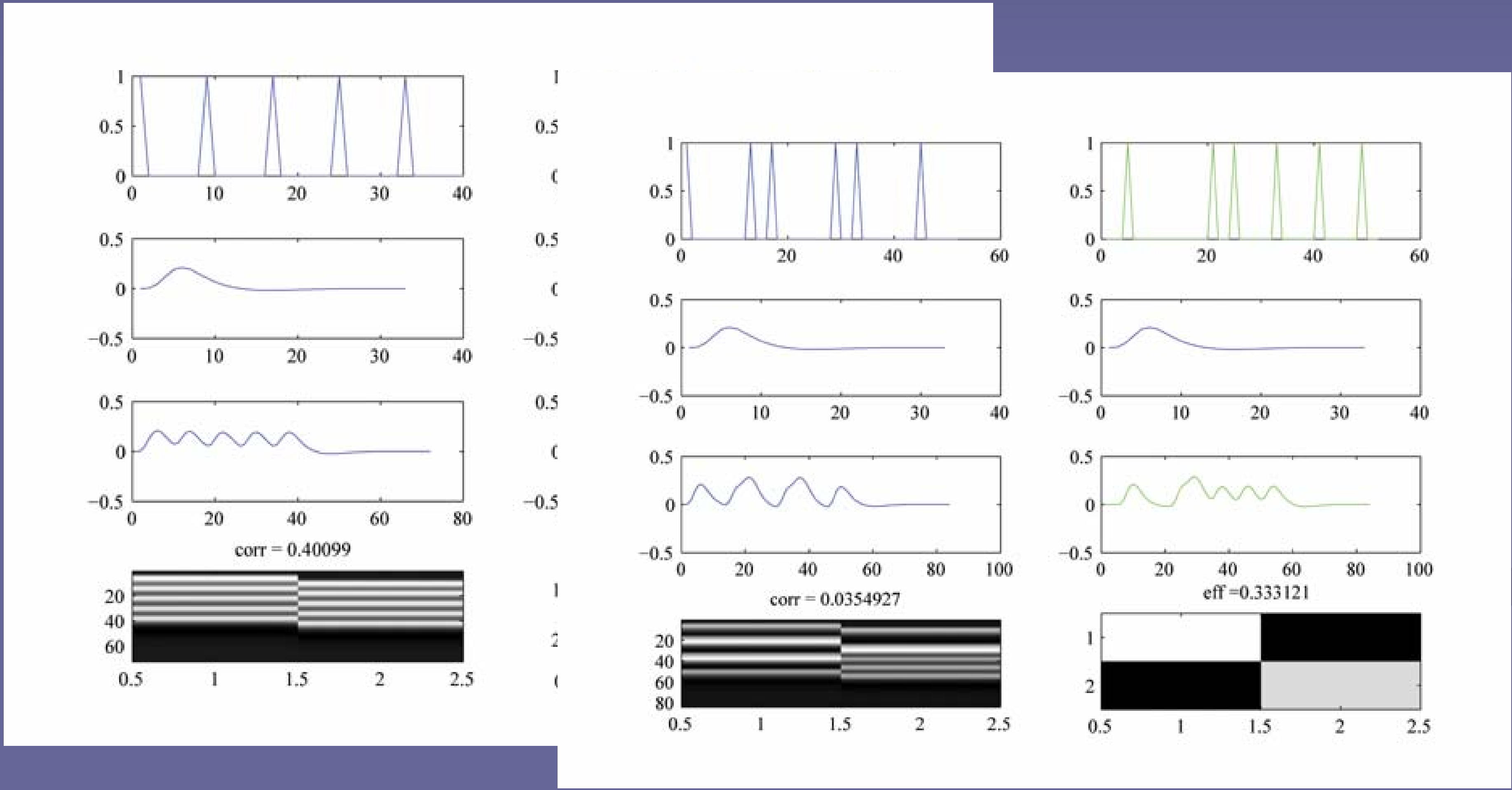
- *Eff* = 1 / trace $(C\,(X^TX)^{-1}\,C^T)$

$\Rightarrow$ (X^TX) is the information matrix which reflects the orthogonality (correlation) of the regressors
$\Rightarrow$ Cov(ij) = E [(Xi-µi) (Xj- µ j)] and Cov(ij) is the covariance matrix
$\Rightarrow$ corr(ij) = cov(ij) / sqrt (var(i) var(j)) ; if one decorrelates i and j by construction, this means cov(ij) decreases

- If conditions are highly correlated (e.g. when i present, j absent, r = -1), the trace of $(X^TX)^{-1}$ increases and Eff decreases; conversely decorrelating ij will increase Eff

fMRI designs & efficiency

- Decorrelating i and j



fMRI designs & efficiency

- A convenient way to construct designs and decorrelate condition is to introduce null-events

⇒ Think about the conditions + null events; create a probability of occurrence (you can think in term of transition matrices - A&B p=1; A, B, null (1/3) p<1)

⇒ + ISI ≠ TA or TR (interleaved acquisition)

⇒ + no low frequency

	A	B
A	0.5	0.5
B	0.5	0.5

→

	A	B
A	0.33	0.33
B	0.33	0.33

Useful Tools (FREE !!)

- http://surfer.nmr.mgh.harvard.edu/optseq/
- http://www.columbia.edu/cu/psychology/tor/software.htm
- http://jasonkao.myweb.uga.edu/research.htm

Statistical designs

Nb of factors

- 1 factor (activation vs. rest) – easy to interpret
- 2 factors & 2 levels (A1 A2 B1 B2) = increase the generality of the experiment

Effect	*Contrast*
Simple	A / B1 [1 1 –2 0] & A / B2 [1 1 0 –2]
	B / A1 [-2 0 1 1] & B / A2 [0 –2 1 1]
Main	A [1 1 -1 -1] B [-1 -1 1 1]
Interaction	A x B [1 -1 -1 1]

⇒ 2 steps procedure (hierarchical mixed model): for each subjects estimates the parameters (~ weighted mean) and then across subjects. A well designed study increases the efficiency at the 1st level (i.e. for each subject)

Nb of sessions

- During an fMRI experiment, several sessions are performed = increases intra-subject variability (scanner changes; motion; subject state)

$t = C\beta / sqrt(C\,(X^{T}X)^{-1}\,C^{T})$ *then for C (1-1)*

$t = (Mean\ A - Mean\ B) / sqrt(S^2(1/T_A + 1/T_B)) \sim (T_A + T_B - 2)\ df$

with T the values for A and B along the time series

S^2 *the common variance* $((T_A-1)S^2_A + (T_B-1)S^2_B)/(T_A+T_B-2)$

- This is for 1 session .. one additional session decreases the statistical power : t ~ $(T_A + T_B - 4)$ df
- **Better to scan as long as possible ! (e.g. it's better to get 400 volumes in 1 session than 2x200 volumes)**

Within or between subjects

Fixed and random effects analyses:

Fixed $\Rightarrow$ $yi = X\beta i + ei$ *with i the subjects*

$yi = C\beta / (1/sqrt(nS_{C\beta^\wedge})$ *[sum of within subject variance]*

Random $\Rightarrow$ $yi = C\beta / (1/S^2_{(between+ within)})$

$yi = X\beta i + Zy + ei$

[Z code the different subjects = between]

- **Better to have lot of subjects (of each experimental group) than lot of sessions per subjects !**

Take Home message 3

- Decorrelatate as much as possible the conditions
- Avoid low frequency in the design to oppose conditions
- Factorial designs are quite powerful
- More subjects is better than more scans
- Long sessions are better than short ones (at least sessions that keep your subject awake or alive)

End

References

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websites

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- Pernet C. – general design considerations

  http://www.sbirc.ed.ac.uk/cyril/cp_fmri.html

- *Convolution*:

  http://mathworld.wolfram.com/Convolution.html

- *Covariance matrix:*

  http://en.wikipedia.org/wiki/Covariance_matrix