Event-related fMRI: Modelling of hemodynamic timeseries

Christian Ruff
Laboratory for Social and Neural Systems Research
University of Zurich

With thanks to the FIL methods group and Rik Henson
Realignment → Smoothing → General linear model → Statistical parametric map (SPM)

- Image time-series
- Kernel
- Design matrix
- Statistical inference

- Normalisation
- Template
- Parameter estimates

Gaussian field theory

p < 0.05
1. Block/epoch vs. event-related fMRI
2. (Dis)Advantages of efMRI
3. GLM: Convolution
4. BOLD impulse response
5. Temporal Basis Functions
6. Timing Issues
7. Design Optimisation – “Efficiency”
Block/epoch designs examine responses to series of similar stimuli

Event-related designs account for response to each single stimulus

P = Pleasant
U = Unpleasant

~4s
Advantages of event-related fMRI

1. Randomised trial order
efMRI: Randomised trial order

Blocked designs may trigger expectations and cognitive sets

Intermixed designs can minimise this by stimulus randomisation
Advantages of event-related fMRI

1. Randomised trials order
2. Post-hoc subjective classification of trials
efMRI: Post-hoc classification of trials

Advantages of event-related fMRI

1. Randomised trials order
2. Post-hoc subjective classification of trials
3. Some events can only be indicated by participant
efMRI: Online event definition
Advantages of event-related fMRI

1. Randomised trials order
2. Post-hoc subjective classification of trials
3. Some events can only be indicated by participant
4. Some events cannot be blocked due to stimulus context
efMRI: Stimulus context

Oddball

...
Advantages of event-related fMRI

1. Randomised trials order
2. Post-hoc subjective classification of trials
3. Some events can only be indicated by participant
4. Some events cannot be blocked due to stimulus context
5. More accurate model even for epoch/block designs?
“Event” model may capture state-item interactions (with longer SOAs)

“Epoch” model assumes constant neural processes throughout block

P = Pleasant
U = Unpleasant
Modeling block designs: Epochs vs events

Designs can be blocked or intermixed, BUT models for blocked designs can be epoch- or event-related.

Epochs are periods of sustained stimulation (e.g., box-car functions)
Events are impulses (delta-functions)

Near-identical regressors can be created by 1) sustained epochs, 2) rapid series of events (SOAs<~3s)

In SPM12, all conditions are specified in terms of their 1) onsets and 2) durations
... epochs: variable or constant duration
... events: zero duration
Modeling block designs: Epochs vs events

- Blocks of trials can be modeled as boxcars or runs of events
- BUT: interpretation of the parameter estimates may differ
- Consider an experiment presenting words at different rates in different blocks:
  - An “epoch” model will estimate parameter that increases with rate, because the parameter reflects response per block
  - An “event” model may estimate parameter that decreases with rate, because the parameter reflects response per word
Disadvantages of intermixed designs

1. Less efficient for detecting effects than blocked designs (see later…)

2. Some psychological processes have to/may be better blocked (e.g., if difficult to switch between states, or to reduce surprise effects)
Overview

1. Block/epoch vs. event-related fMRI
2. (Dis)Advantages of efMRI
3. GLM: Convolution
4. BOLD impulse response
5. Temporal Basis Functions
6. Timing Issues
7. Design Optimisation – “Efficiency”
BOLD impulse response

- Function of blood oxygenation, flow, volume
- Peak (max. oxygenation) 4-6s poststimulus; baseline after 20-30s
- Initial undershoot can be observed
- Similar across V1, A1, S1…
- … but possible differences across:
  - other regions
  - individuals
• Early event-related fMRI studies used a long Stimulus Onset Asynchrony (SOA) to allow BOLD response to return to baseline

• However, overlap between successive responses at short SOAs can be accommodated if the BOLD response is explicitly modeled, particularly if responses are assumed to superpose linearly

• Short SOAs are more sensitive; see later
GLM for a single voxel:

\[ y(t) = u(t) \otimes h(\tau) + \epsilon(t) \]

\( u(t) \) = neural causes (stimulus train)

\[ u(t) = \sum \delta(t - nT) \]

\( h(\tau) \) = hemodynamic (BOLD) response

\[ h(\tau) = \sum \beta_i f_i(\tau) \]

\( f_i(\tau) \) = temporal basis functions

\[ y(t) = \sum \sum \beta_i f_i(t - nT) + \epsilon(t) \]

\[ y = X \beta + \epsilon \]
General Linear Model in SPM

Stimulus every 20s

Gamma functions $f_i(\tau)$ of peristimulus time $\tau$ (Orthogonalised)

Sampled every TR = 1.7s

Design matrix, $X$

$[x(t) \otimes f_1(\tau) \mid x(t) \otimes f_2(\tau) \mid ...]$

SPM$\{F\}$
Overview

1. Block/epoch vs. event-related fMRI
2. (Dis)Advantages of efMRI
3. GLM: Convolution
4. BOLD impulse response
5. Temporal Basis Functions
6. Timing Issues
7. Design Optimisation – “Efficiency”
Temporal basis functions
Temporal basis functions

• **Fourier Set**
  - Windowed sines & cosines
  - Any shape (up to frequency limit)
  - Inference via F-test

• **Finite Impulse Response**
  - Mini “timebins” (selective averaging)
  - Any shape (up to bin-width)
  - Inference via F-test
Temporal basis functions

- **Fourier Set / FIR**
  - Any shape (up to frequency limit / bin width)
  - Inference via F-test

- **Gamma Functions**
  - Bounded, asymmetrical (like BOLD)
  - Set of different lags
  - Inference via F-test

- **“Informed” Basis Set**
  - Best guess of canonical BOLD response
  - Variability captured by Taylor expansion
  - “Magnitude” inferences via t-test…?
Informed basis set

- Canonical HRF (2 gamma functions)
Informed basis set

- Canonical HRF (2 gamma functions)
  - Canonical
  - Temporal

  plus Multivariate Taylor expansion in:
  - time (Temporal Derivative)
Informed basis set

- Canonical HRF (2 gamma functions)
  - Multivariate Taylor expansion in:
    - time (Temporal Derivative)
Informed basis set

- Canonical HRF (2 gamma functions)
- Multivariate Taylor expansion in:
  - time (Temporal Derivative)
  - width (Dispersion Derivative)
Informed basis set

- Canonical HRF (2 gamma functions)
- plus Multivariate Taylor expansion in:
  - time (Temporal Derivative)
  - width (Dispersion Derivative)
Informed basis set

- Canonical HRF (2 gamma functions) plus Multivariate Taylor expansion in:
  - time (Temporal Derivative)
  - width (Dispersion Derivative)

- "Magnitude" inferences via t-test on canonical parameters (providing canonical is a reasonable fit)

- "Latency" inferences via tests on ratio of derivative : canonical parameters
Which temporal basis set?

In this example (rapid motor response to faces, *Henson et al, 2001*)...

... canonical + temporal + dispersion derivatives appear sufficient to capture most activity

... may not be true for more complex trials (e.g. stimulus-prolonged delay (>~2 s)-response)

... but then such trials better modelled with separate neural components (i.e., activity no longer delta function) + constrained HRF
Overview

1. Block/epoch vs. event-related fMRI
2. (Dis)Advantages of efMRI
3. GLM: Convolution
4. BOLD impulse response
5. Temporal Basis Functions
6. **Timing Issues**
7. Design Optimisation – “Efficiency”
Timing issues: Sampling

- TR for 80 slice EPI at 2 mm spacing is ~ 4s
Timing issues: Sampling

- TR for 80 slice EPI at 2 mm spacing is ~ 4s
- Sampling at [0, 4, 8, 12…] post-stimulus may miss peak signal
Timing issues: Sampling

- TR for 80 slice EPI at 2 mm spacing is ~ 4s
- Sampling at [0,4,8,12…] post-stimulus may miss peak signal

- Higher effective sampling by:
  1. Asynchrony; e.g., SOA=1.5TR
  2. Random Jitter; e.g., SOA=(2±0.5)TR
- Better response characterisation
Timing issues: Slice Timing

T1 = 0 s
T16 = 2 s

T = 16, TR = 2 s
T0 = 16
T0 = 9

X2  X3
"Slice-timing Problem":

- Slices acquired at different times, yet model is the same for all slices
- Different results (using canonical HRF) for different reference slices
- (Slightly less problematic if middle slice is selected as reference, and with short TRs)

Solutions:

1. Temporal interpolation of data … but less good for longer TRs

2. More general basis set (e.g., with temporal derivatives) … but inferences via F-test
Overview

1. Block/epoch vs. event-related fMRI
2. (Dis)Advantages of efMRI
3. GLM: Convolution
4. BOLD impulse response
5. Temporal Basis Functions
6. Timing Issues
7. Design Optimisation – “Efficiency”
Design efficiency

- HRF can be viewed as a filter (Josephs & Henson, 1999)
- We want to maximise the signal passed by this filter
- Dominant frequency of canonical HRF is ~0.04 Hz

→ The most efficient design is a sinusoidal modulation of neural activity with period ~24s (e.g., boxcar with 12s on/ 12s off)
Sinusoidal modulation, $f = 1/33$

Stimulus ("Neural") $\times$ HRF $\rightarrow$ Predicted Data

A very "efficient" design!
Blocked, epoch = 20 sec

Stimulus ("Neural")

HRF

Predicted Data

Blocked-epoch (with small SOA) quite “efficient”
Blocked (80s), SOAmin=4s, highpass filter = 1/120s

Stimulus ("Neural")  $\times$  HRF  $\times$  Predicted Data

"Effective HRF" (after highpass filtering) (Josephs & Henson, 1999)

Very ineffective: Don’t have long (>60s) blocks!
Randomised design spreads power over frequencies

Stimulus ("Neural") \times HRF = Predicted Data

Randomised, SOAmin=4s, highpass filter = 1/120s
Design efficiency

- T-statistic for a given contrast: $T = \frac{c^T b}{\text{var}(c^T b)}$

- For maximum $T$, we want maximum precision and hence minimum standard error of contrast estimates ($\text{var}(c^T b)$)

- $\text{Var}(c^T b) = \sqrt{\sigma^2 c^T (X^T X)^{-1} c}$ (i.i.d)

- If we assume that noise variance ($\sigma^2$) is unaffected by changes in $X$, then our precision for given parameters is proportional to the design efficiency: $e(c, X) = \{ c^T (X^T X)^{-1} c \}^{-1}$

- We can influence $e$ (a priori) by the spacing and sequencing of epochs/events in our design matrix

- $e$ is specific for a given contrast!
Design efficiency: Trial spacing

- Design parametrised by:
  - $SOA_{\text{min}}$: Minimum SOA
  - $p(t)$: Probability of event at each $SOA_{\text{min}}$

- Deterministic
  $p(t) = 1$ iff $t = nSOA_{\text{min}}$

- Stationary stochastic
  $p(t) = \text{constant}$

- Dynamic stochastic
  $p(t)$ varies (e.g., blocked)

Blocked designs most efficient! (with small $SOA_{\text{min}}$)
• However, block designs are often not advisable due to interpretative difficulties (see before)

• Event trains may then be constructed by modulating the event probabilities in a dynamic stochastic fashion

• This can result in intermediate levels of efficiency

3 sessions with 128 scans
Faces, scrambled faces
SOA always 2.97 s
Cycle length 24 s
Design efficiency: Trial sequencing

- Design parametrised by:
  
  \( SO_{min} \quad \text{Minimum SOA} \)
  
  \( p_i(h) \quad \text{Probability of event-type } i \text{ given history } h \text{ of last } m \text{ events} \)

- With \( n \) event-types \( p_i(h) \) is a \( n \times n \) Transition Matrix

- Example: Randomised AB

\[
\begin{array}{cc}
A & B \\
A & 0.5 & 0.5 \\
B & 0.5 & 0.5 \\
\end{array}
\]

\( \Rightarrow \) ABBBABAABABAAAA...
Design efficiency: Trial sequencing

• Example: Null events

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.33</td>
<td>0.33</td>
</tr>
<tr>
<td>B</td>
<td>0.33</td>
<td>0.33</td>
</tr>
</tbody>
</table>

=> AB-BAA--B---ABB...

• Efficient for differential and main effects at short SOA

• Equivalent to stochastic SOA (Null Event like third unmodelled event-type)
Design efficiency: Trial sequencing

• Example: Alternating AB

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

=> ABABABABABABABAB...

• Example: Permuted AB

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>AB</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>BA</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>BB</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

=> ABAABABABABABBA...
Design efficiency: Conclusions

- Optimal design for one contrast may not be optimal for another
- Blocked designs generally most efficient (with short SOAs, given optimal block length is not exceeded)
- However, psychological efficiency often dictates intermixed designs, and often also sets limits on SOAs
- With randomised designs, optimal SOA for differential effect (A-B) is minimal SOA (>2 seconds, and assuming no saturation), whereas optimal SOA for main effect (A+B) is 16-20s
- Inclusion of null events improves efficiency for main effect at short SOAs (at cost of efficiency for differential effects)
- If order constrained, intermediate SOAs (5-20s) can be optimal
- If SOA constrained, pseudorandomised designs can be optimal (but may introduce context-sensitivity)