



# Retrieving the HRF at rest:

An application to brain tumor fMRI scans

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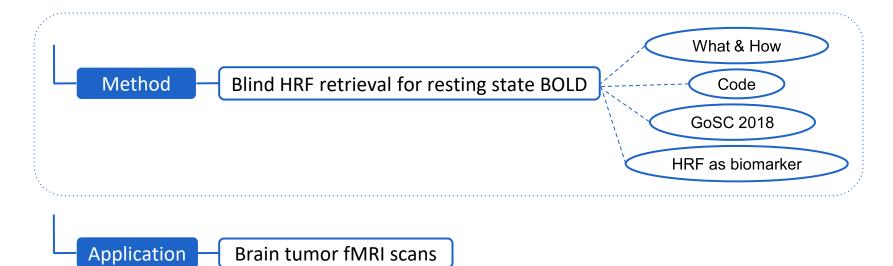








## Structure:



Data set > Hannelore Aerts

## fMRI - BOLD signal - General Linear Model (GLM)

Linear Time Invariant model

$$y(t) = s(t) \otimes h(t) + c + \varepsilon(t)$$

The processed BOLD signal at time t, y(t), is modeled as the convolution of:

- neural state s(t) and
- a hemodynamic response function *h(t)*,

where  $\otimes$  denotes convolution,  $\varepsilon(t)$  is the unexplained error and c indicates the baseline magnitude

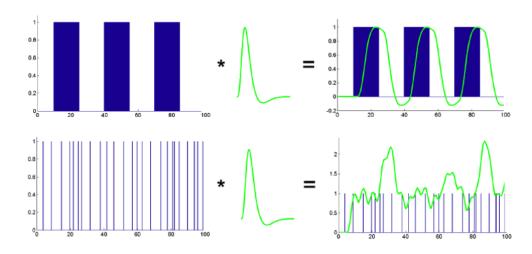


Figure: Cartoon of the BOLD signal resulting from blocked and event-related stimuli, without noise.

## fMRI - BOLD signal - General Linear Model (GLM)

Linear Time Invariant model

$$y(t) = s(t) \otimes h(t) + c + \varepsilon(t)$$

**AIM**: solve the equation for h(t)

#### Task fMRI

s(t) could be substituted with a hypothetical model of the neural activation for s(t), i.e. stimulus function

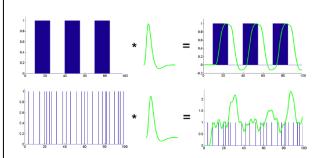


Figure: Cartoon of the BOLD signal resulting from blocked and event-related stimuli, without noise.



## Resting-state fMRI

no explicit stimulus and timing for HRF onset

#### **Point Process**

Discrete BOLD events govern the brain dynamic at rest (e.g. Tagliazucchi et al. 2012)

- Reflected by relatively large amplitude BOLD signal peaks
- Identified when the stand. BOLD signal <u>crosses a given</u> <u>threshold</u> (1 SD)
- Corresponding to point process neural events

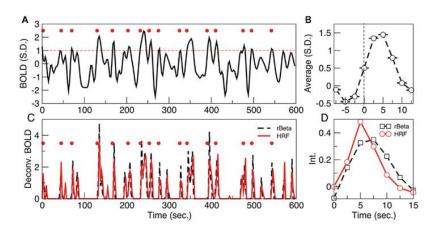


Figure: From Tagliazucchi et al. (2012) BOLD point process:  $S_b(t)$ 

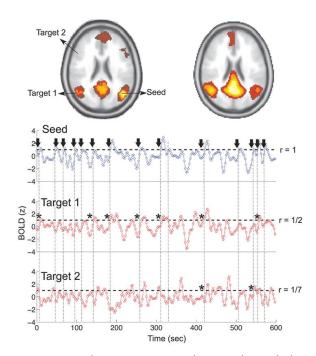


Figure: Simultaneous BOLD peaks reproduce whole series FC pattern.

## Extract the HRF from those pseudo-events: from neuronal pseudo-events to BOLD peaks

Assumption: Peak of the BOLD signal <u>lags (L)</u> behind the peak of the spontaneous point process event ( $L = \kappa \cdot TR/N$  seconds; 0 < L < PST).

In order to **obtain the time lag**  $\emph{k}$ , search all integer values in the interval  $[0, PST \cdot N/TR]$ , where PST is the peristimulus time, choosing the one for which the noise squared error is the smallest,  $\min_{\forall 0 < L < PST} |y(t) - s_b(t-L) \otimes h(t)|^2$ , indicating the spontaneous event onset.

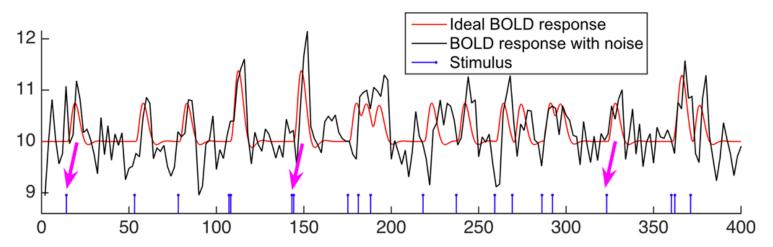


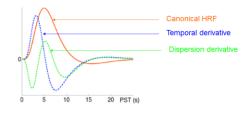
Figure: Time lag from stimulus to BOLD peak.

#### HRF basis vectors

We assume that the <u>hemodynamic responses</u> for all resting state spontaneous point process events and at all locations in the brain are fully <u>contained in an d-dimensional linear subspace H of  $R^d$ .</u>

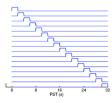
Then, any hemodynamic response *h* can be represented uniquely as the linear combination of the corresponding basis vectors, such as:

- (a) **Canonical** HRF with its (b) delay/dispersion derivatives (canon2dd)



- (a) two gamma functions
- (b) allow variations about the canonical form

- (smoothed) Finite Impulse Response (sFIR): makes minimal assumptions about the shape of the response



## Three HRF parameters

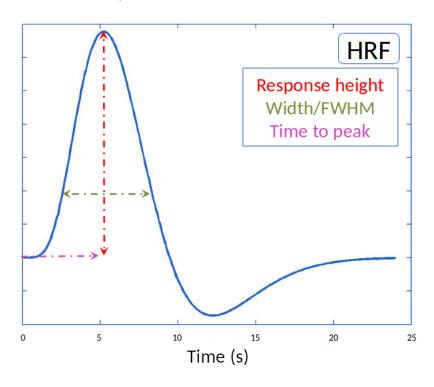
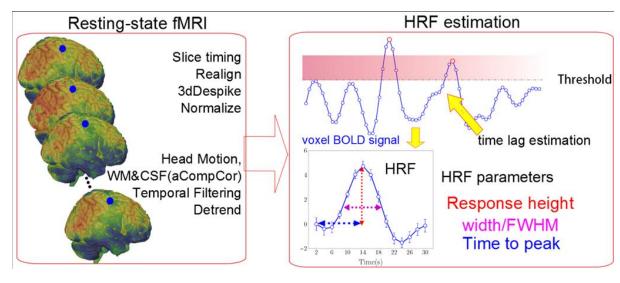


Figure: Schematic display of a typical HRF with its three characteristic parameters as potential measures of response magnitude, latency, and response duration.

## Flow chart: quick recap



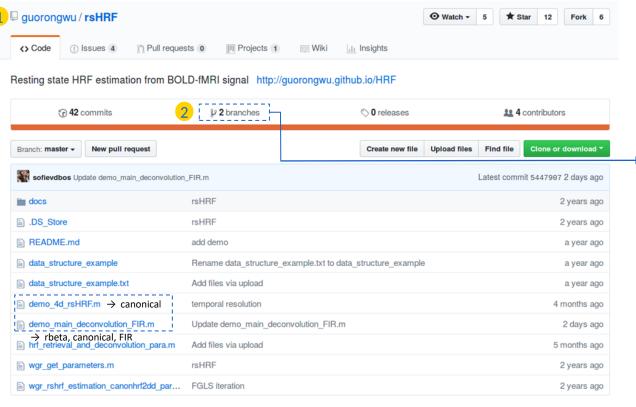


- rsfMRI = non-invasive
- single voxel level

Figure: Flowchart of the blind HRF retrieval method in rfMRI.

## Method: Blind HRF retrieval for resting state BOLD

#### Code - GoSC 2018





13,000+ STUDENTS, 108 COUNTRIES
13 YEARS, 608 OPEN SOURCE ORGANIZATIONS

33,000,000+

Google Summer of Code is a global program focused on bringing more student developers into open source software development. Students work with an open source organization on a 3 month programming project during their break from school.

#### 2 branches:

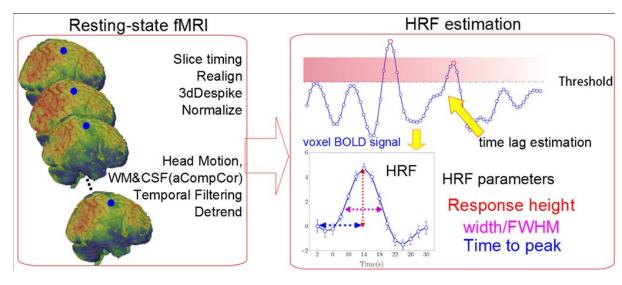
- master (MATLAB)
- python (GSoC 2018) -=> BIDSapp

#### **Madhur Tandon**

Building a portable open pipeline (Python) to detect the hemodynamic response function at rest

Q&A: Daniele Marinazzo, Asier Erramuzpe Aliaga, Nigel Colenbier, Sofie Van Den Bossche

### Flow chart: quick recap





- rsfMRI = non-invasive
- single voxel level

Figure: Flowchart of the blind HRF retrieval method in rfMRI.

#### Once the rsHRF is retrieved it can be used to:

- deconvolve BOLD data in order to eliminate confounders on temporal precedence
- map it onto the brain surface and look at its variability

## HRFs vary across <u>brain regions</u> and <u>individuals</u>

intra-subject spatial variability:e.g. variations in the vasculature

inter-subject variability: psychophysiological factors→ HRF as a pathophysiological indicator

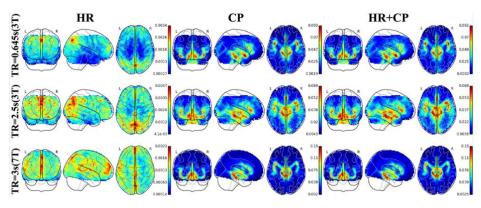
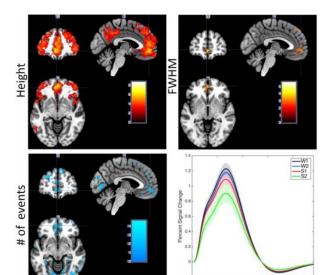


Figure: Quasi-periodic and non-periodic cardiac fluctuation regressors.

## HRF modulated by several psycho-physiological factors

## Loss of consciousness (Wu et al., 2015)



W1: Awake

W2: Recovery of consciousness

S1: Mild sedationS2: Deep sedation

To identify regions which showed significant activation differences among four clinical states, a linear T contrast was computed, searching for a linear relationship between HRF and the level of consciousness of the subjects across the four conditions.

Contrast (W1 W2 S1 S2) [1.5 0.5 -1.5 -0.5]

Statistical differences in all the three HRF parameters, as well as in the number of spontaneous events, mainly in frontal areas

## HRF modulated by several psycho-physiological factors

#### e.g. ASD, post-traumatic stress disorder

Aberrant hemodynamic responses in autism: Implications for resting state fMRI functional connectivity studies



Wenjing Yan<sup>a</sup>, D. Rangaprakash<sup>a,b</sup>, Gopikrishna Deshpande<sup>a,c,d,e,\*</sup>

## Hemodynamic variability in soldiers with trauma: Implications for functional MRI connectivity studies

D. Rangaprakash<sup>a,b</sup>, Michael N. Dretsch<sup>c,d</sup>, Wenjing Yan<sup>a</sup>, Jeffrey S. Katz<sup>a,e,f</sup>, Thomas S. Denney Jr.<sup>a,e,f</sup>, Gopikrishna Deshpande<sup>a,e,f,\*</sup>

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#### Neurovascular uncoupling



Cancer cells display remarkable phenotypic variability, including ability to induce **angiogenesis**, seed metastases, and survive therapy.

"...the abnormal neovasculature in glioblastomas (GBM's) <u>may not be</u> <u>able to dilate normally</u> in response to increased neuronal activity." (Hou et al., 2006)

- 1. Loss of ability to autoregulate
- Neurovaculature already maximally dilated due to the presence of ischemia

### Data and ideas

- 11 glioma patients
- > arise from brain tissue
  - Extract rsHRF (FIR) for tumor regions and contralateral control regions
  - Look at HRF maps: Differences? Peritumoral regions?
  - MVPA
  - ..

# All your ideas are welcome!

