

# Spatial Expansion of HRF Estimation Model

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## Non-Spatial (Individual) Model

### I. Canonical + Derivative Model

- $V$ : number of voxels.
- $T$ : number of timepoints (the length of timecourse data).
- $S$ : number of experimental designs (stimuli).
- $k_\beta$ : number of  $\beta$ s fitted for each stimulus.
- For the DD (canonical + derivative) model,  $k_\beta = 2$ .
- $Y_i$ : timecourse data for the  $i$ th voxel, where  $i = 1, \dots, V$ .
- $X_0$ : convoluted design matrix,  $T \times Sk_\beta$  matrix.

$$X_0 = (n_1 \circ H_c \ n_1 \circ H_{c'} \ \dots \ n_S \circ H_{c'})$$

where  $n_i$  is the onset function for the  $i$ th stimulus,  $H_c$  is a vector of the canonical HRF function, and  $X_{c'}$  is a vector of its derivative. By convoluting each stimulus function with the canonical HRF and its derivative, we obtain the design matrix  $X_0$  for ordinary linear regression.

Then, we assume a normal distribution for the error term in linear regression.

$$Y_i = X_0\beta_i + \epsilon_i \quad \text{for } i = 1, \dots, V, \quad \epsilon_i \sim N(0, I)$$

where  $\beta_i = (\beta_{1,i}, \dots, \beta_{Sk_\beta,i})'$

For the non-spatial model, we can individually fit  $\beta_i$  using the linear regression model.

$$\hat{\beta}_i = (X'_0 X_0)^{-1} X'_0 Y_i$$

### II. B-Spline Model

- $V$ : number of voxels.
- $T$ : number of timepoints (the length of timecourse data).
- $S$ : number of experimental designs (stimuli).
- $k_\beta$ : number of  $\beta$ s fitted for each stimulus.
- For the B-Spline model,  $k_\beta = 5$ , i.e. number of B-spline basis is 5.
- $Y_i$ : timecourse data for the  $i$ th voxel, where  $i = 1, \dots, V$ .

We define design matrix  $W$  where each column is each B-spline basis. Thus, it's  $T \times k_\beta$  matrix. Then,  $X_0$  is a convoluted design matrix,  $T \times Sk_\beta$  matrix.

$$X_0 = (n_1 \circ W \ n_2 \circ W \ \cdots \ n_S \circ W)$$

Then, we assume a normal distribution for the error term in linear regression.

$$Y_i = X_0\beta_i + \epsilon_i \quad \text{for } i = 1, \dots, V, \quad \epsilon_i \sim N(0, I)$$

where  $\beta_i = (\beta_{1,i}, \dots, \beta_{Sk_\beta,i})'$

For the non-spatial model, we can individually fit  $\beta_i$  using the linear regression model.

$$\hat{\beta}_i = (X_0' X_0)^{-1} X_0' Y_i$$

### III. Smooth FIR Model

- $V$ : number of voxels.
- $T$ : number of timepoints (the length of timecourse data).
- $S$ : number of experimental designs (stimuli).
- $k_\beta$ : number of  $\beta$ s fitted for each stimulus.
- For the Smooth FIR model,  $k_\beta = 8$ .
  - order of FIR filter is set to be 8.
- $Y_i$ : timecourse data for the  $i$ th voxel, where  $i = 1, \dots, V$ .

Assume that  $x(t)$  is a  $T$ -dimensional vector of stimulus inputs, which is equal to 1 at time  $t$  if a stimulus is present at that time point and 0 otherwise. Now we can define the design matrix corresponding to the FIR filter of order  $d$  as:

$$X_0 = \begin{pmatrix} x(d) & \cdots & x(1) \\ x(d+1) & \cdots & x(2) \\ \vdots & & \vdots \\ x(T) & \cdots & x(T-d+1) \end{pmatrix}$$

$$\hat{\beta}_{sFIR,i} = (X_0^T X_0 + \sigma^2 \Sigma^{-1})^{-1} X_0^T Y_i$$

where the elements of  $\Sigma$  are given by

$$\Sigma_{ij} = v \exp(-\frac{h}{2}(i-j)^2),$$

$$h = \frac{1}{\sqrt{7/TR}}, \text{ and } \frac{\sigma^2}{v} = 1.$$

This is equivalent to the solution of the least-square problem with a penalty function, i.e.,  $\beta_{sFIR}$  is the solution to the problem:

$$\max [(y - X\beta)^T (y - X\beta) + \sigma^2 \Sigma_{ij} \beta_i \beta_j]$$

where  $\Sigma_{ij}$  are the components of the matrix  $\Sigma^{-1}$ .

### IV. Canonical + Derivative AR(p) Model

## Spatial Model: Thin Plate Spline Regression

Using generalized additive model (GAM) thin plate spline regression, our objective is to model  $\beta$  as a spatial model, using 3D coordinates as regressors.

- $k_\gamma$ : number of  $\gamma$ s fitted for thin plate spline regression of each  $\beta$ .

Each  $\beta$  is modeled as follows:

$$(\beta_{k,1}, \beta_{k,2}, \dots, \beta_{k,V})' = B_k \gamma_k, \quad k = 1, \dots, Sk_\beta$$

where  $B_k$  is a  $V \times k_\gamma$  model matrix for thin plate spline regression for the  $k$ th  $\beta$ , and  $\gamma_k$  is a  $k_\gamma \times 1$  coefficient vector.

Let  $Y = (Y_1' \ Y_2' \ \dots \ Y_V')'$ , which is a  $VT \times 1$  vector.

Then,

$$Y = X P B \Gamma + \epsilon, \quad \epsilon \sim N(0, I)$$

where

- $Y = (Y_1' \ Y_2' \ \dots \ Y_V')'$ :  $VT \times 1$  vector
- $X = \begin{pmatrix} X_0 & 0 & \dots & 0 \\ 0 & X_0 & \dots & 0 \\ \vdots & \ddots & & 0 \\ 0 & 0 & \dots & X_0 \end{pmatrix}$ :  $VT \times VS k_\beta$  matrix
- $P$  = Permutation matrix:  $VS k_\beta \times VS k_\beta$  matrix
- $P \begin{pmatrix} \beta_{1,1} \\ \beta_{1,2} \\ \vdots \\ \beta_{Sk_\beta, V-1} \\ \beta_{Sk_\beta, V} \end{pmatrix} = \begin{pmatrix} \beta_{1,1} \\ \beta_{2,1} \\ \vdots \\ \beta_{Sk_\beta-1, V} \\ \beta_{Sk_\beta, V} \end{pmatrix}$
- $B = \begin{pmatrix} B_1 & 0 & \dots & 0 \\ 0 & B_2 & \dots & 0 \\ \vdots & \ddots & & 0 \\ 0 & 0 & \dots & B_{Sk_\beta} \end{pmatrix}$ :  $VS k_\beta \times Sk_\beta k_\gamma$  matrix
- $\Gamma = (\gamma_1', \dots, \gamma_{Sk_\beta}')'$ :  $Sk_\beta k_\gamma \times 1$  vector.

Then we can fit  $\Gamma$  using linear regression model.

$$\hat{\Gamma} = ((X P B)' (X P B))^{-1} (X P B)' Y$$

Fitted spatial  $\beta$  will be expressed as below:

$$\hat{\beta}_S = \begin{pmatrix} \hat{\beta}_1 \\ \hat{\beta}_2 \\ \vdots \\ \hat{\beta}_V \end{pmatrix} = P B \hat{\Gamma}$$

# Application Results

## Data Description

### Valid Voxels

### Timecourse Data

## I. Canonical + Derivative Model

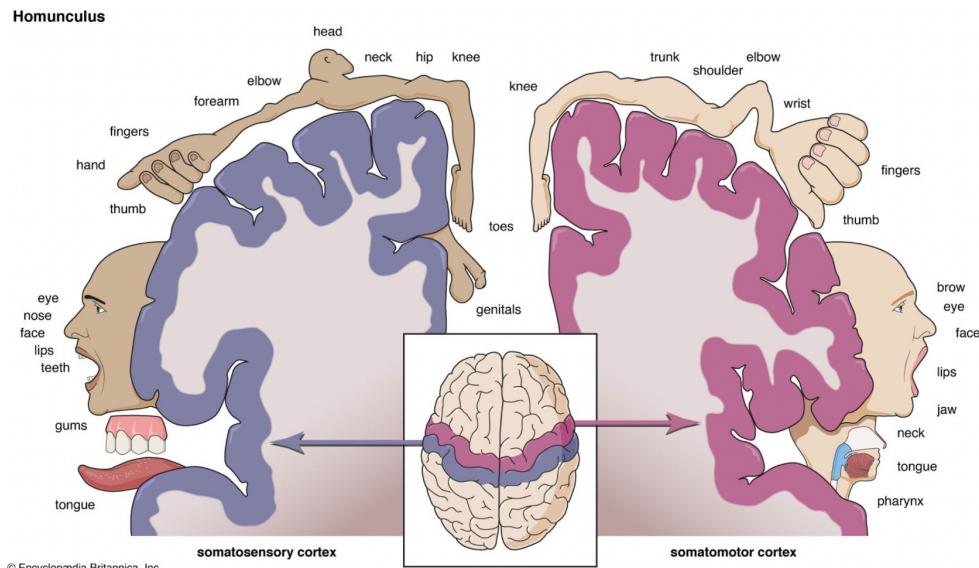
For the application of spatial modeling for HRF estimation, we utilized data from the HCM primary motor cortex of 30 subjects.

- $V = 8888$
- $T = 284$
- $S = 6$ 
  - Cue
  - Tongue
  - Left Foot
  - Right Foot
  - Left Hand
  - Right Hand
- $k_\beta = 2$  for the DD (canonical + derivative) model
- $k_\gamma = 20$

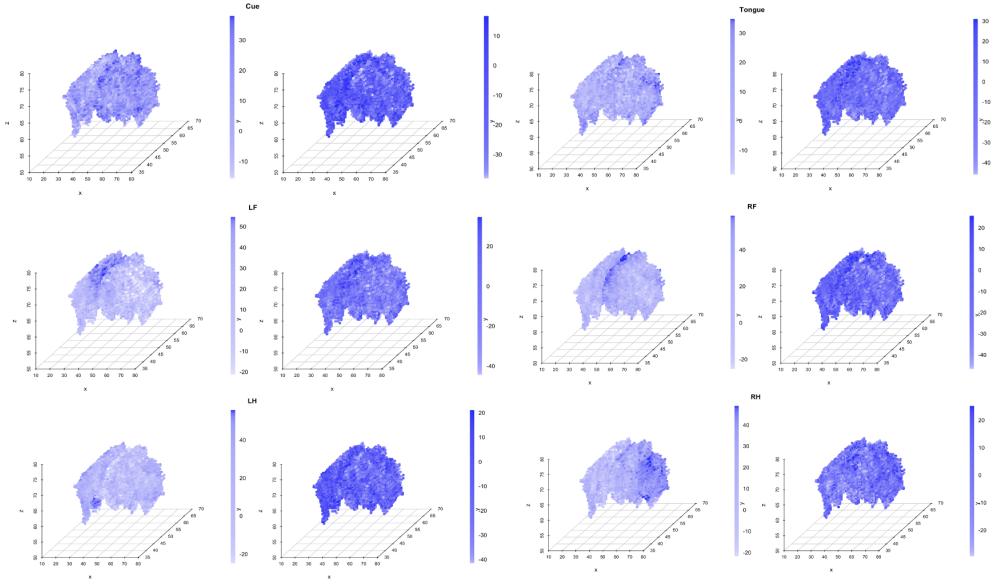
## Fitted Beta

We generated plots of the fitted beta for the 6 experimental designs for each voxel, where darker shades of blue represent larger values.

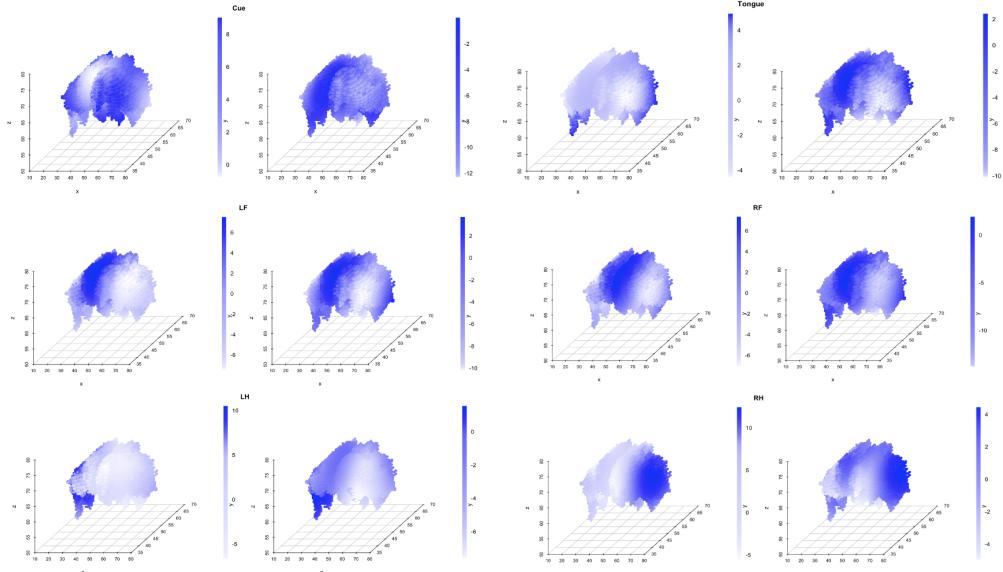
## Expected Motor Homunculus Structure



## Non-spatial (Individual) Model



## Spatial Model

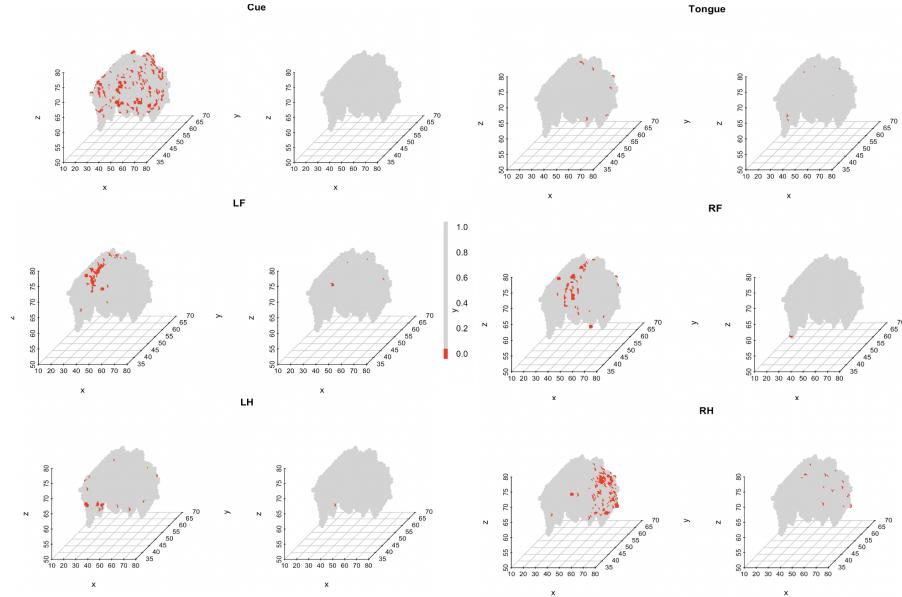


It is clear that the fitted beta for each stimulus design corresponds more closely to the motor homunculus structure for the spatial model compared to the non-spatial model.

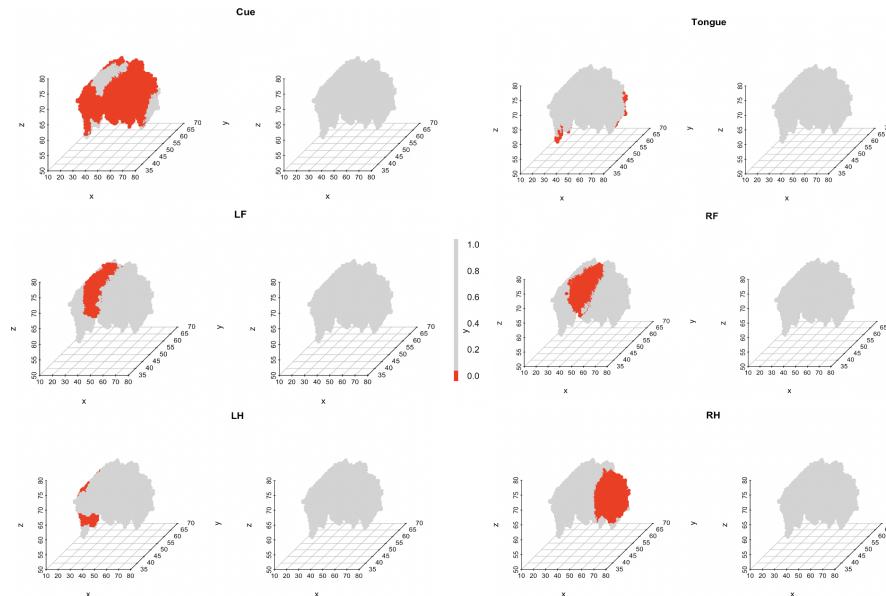
## Inference in Beta

We generated plots of p-values for one-sample t-tests of fitted  $\beta$ s among 10 patients using both the non-spatial model and the spatial model. Red points highlight voxels with p-values less than 0.05.

### Non-Spatial Model



### Spatial Model



We can observe that significant betas (p-values less than 0.05) correspond more clearly to the motor homunculus structure for the spatial model than the non-spatial model.

## Fitted Parameters

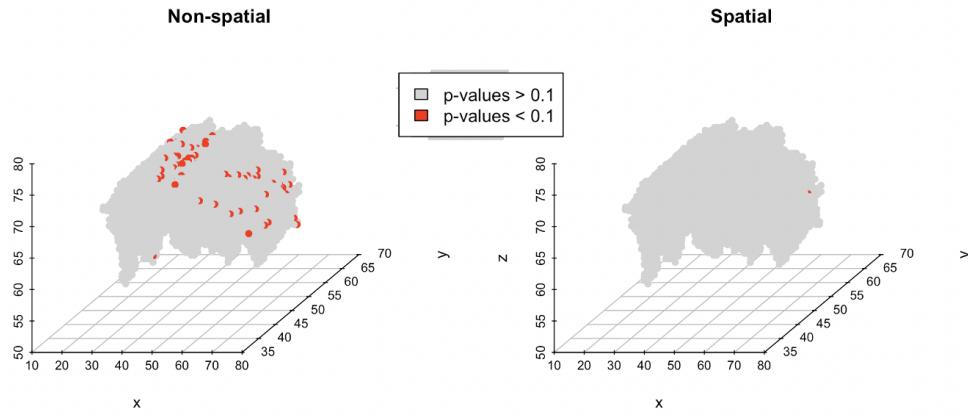
### Non-Spatial Betas

### Spatial Model

### Mis-modeling with Error Terms

We calculated mis-modeling p-values using Gaussian random field theory, using error terms from fitted and observed timecourse data [Loh, Ji Meng, et al. 2008].

Smaller p-values indicate larger mis-modeling.



With a threshold of 0.1, it is clear that the spatial model shows less mis-modeling compared to the non-spatial model.

## **II. Smooth FIR Model**

**Fitted Parameters**

**Fitted Betas**

**Inference on Beta**

**Inference on Fitted Parameters**

**Mis-modeling**

## **III. Spline Model**

**Fitted Parameters**

**Fitted Betas**

**Inference on Beta**

## **IV. Canonical + Derivative AR(p) Model**

**Fitted Betas**

**Inference on Fitted Betas**

**Fitted Parameters**

**Inference on Fitted Parameters**

**Fitted  $\phi$**

**Spatial Dependency in  $\phi$ ?**

## Inference on Each Experiment

### Model Specification:

- Full Model:  $Y = X_1\beta_1 + X_2\beta_2 + \cdots + X_6\beta_6 + \epsilon$ 
  - where  $\beta_i = (\beta_{i1}, \dots, \beta_{ik_\beta})^T$ ,  $i = 1, \dots, 6$
- Reduced Model for  $i$ th Experiment:  $Y = X_1\beta_1 + X_2\beta_2 + \cdots + X_{i-1}\beta_{i-1} + X_{i+1}\beta_{i+1} + \cdots + X_6\beta_6 + \epsilon$ 
  - This model assumes  $\beta_i = 0$