Detecting Subtle Shape Differences in Hemodynamic Responses

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Introduction: Hemodynamic Response (HDR)

✧ Nature of HDR remains elusive

- Changes in cerebral flow and fluctuations of oxyhemoglobin and deoxyhemoglobin are captured by BOLD during FMRI scanning
- BOLD signal: an indicator but indirect measure of neuronal activities
- Complex relationship between BOLD and neural activation
  - Same neuronal activity may evoke different HDR shapes across trials, regions, conditions, subjects, or groups

✧ Estimation of HDRs: 3 approaches

- Fixed-shape method (**FSM**): presuming a fixed-shape HDR
  - One basis: gamma variate, canonical curve
- Estimated-shape method (**ESM**)
  - A few bases: tents, cubic splines, FIR, inverse logit, …
- Adjusted-shape method (**ASM**)
  - 2 or 3 bases: canonical curve, time derivative, dispersion derivative

✧ Research aims

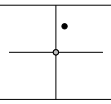
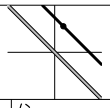
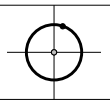
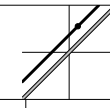
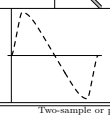
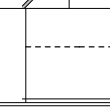
- Which HDR estimation method among the three is preferable?
- How to perform group analysis with multiple effect estimates per condition from **ESM**?

Schematic Comparisons of Testing Methods for ESM

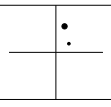
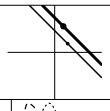
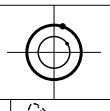
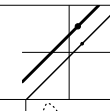
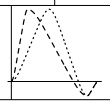
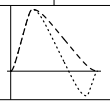
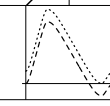
✧ Candidate testing methods

- Multivariate (**MVT**)
- Approximation through the interaction effect by univariate testing (**XUV**)
- Area under the curve (**AUC**)
- Euclidean distance (**L2D**)
- Approximate testing through the interaction effect by multivariate testing (**XMV**)

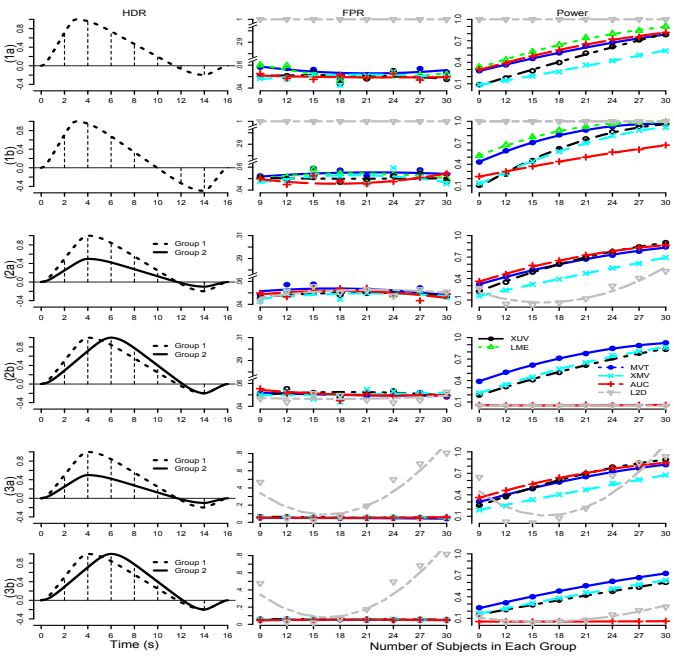
One-sample

Method	MVT/LME	AUC	L2D	EXC (XUV and XMV)
H_0	$\alpha_1 = ... = \alpha_m = 0$	$\alpha_1 + ... + \alpha_m = 0$	$(\alpha_1^2 + ... + \alpha_m^2)^{1/2} = 0$	$\alpha_1 = ... = \alpha_m$
Dimensions in $\mathbb{R}^m$	0	$m-1$	$m-1$	1
DFs for F-statistic	$m, n-m-q+1$	$1, n-q$	$1, n-q$	$m-1, (m-1)(n-q)$
Geometric representation of H_0 and H_1 ($m=2$)				
Geometric representation of HDR when detection failure occurs due to improper H_0 formulation	no		no	

Two-sample or paired

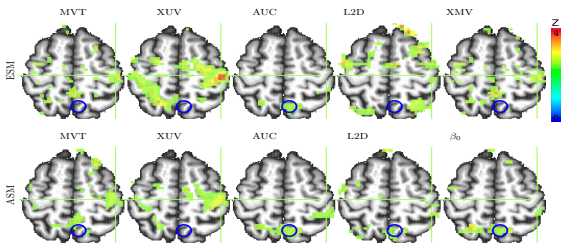
Method	MVT	AUC	L2D	EXC (XUV and XMV)
H_0	$\alpha_{11} = \alpha_{21}, ..., \alpha_{1m} = \alpha_{2m}$	$\sum_{j=1}^m \alpha_{1j} = \sum_{j=1}^m \alpha_{2j}$	$(\sum_{j=1}^m \alpha_{1j}^2)^{1/2} = (\sum_{j=1}^m \alpha_{2j}^2)^{1/2}$	$\alpha_{11} - \alpha_{21} = ... = \alpha_{1m} - \alpha_{2m}$
Dimensions in $\mathbb{R}^m$	0	$m-1$	$m-1$	1
DFs for F-statistic	$m, n-m-q+1$	$1, n-q$	$1, n-q$	$m-1, (m-1)(n-q)$
Geometric representation of H_0 and H_1				
Geometric representation of HDR when detection failure occurs due to improper H_0 formulation	no			

Comparisons of Testing Methods with Simulations



Comparisons of Testing Methods via Real Data

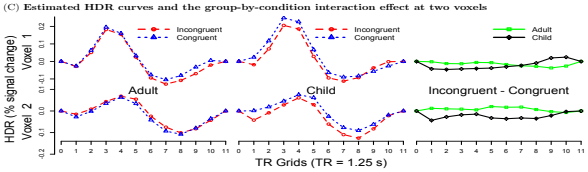
(A) **Significance maps**



(B) **Significance level at two voxels**

Voxel		ESM: p-value					ASM: p-value				
No.	coordinates	MVT	XUV	AUC	L2D	XMV	MVT	XUV	AUC	L2D	β_0
1	41 -22 54	0.020	0.0002	0.67	0.18	0.013	0.015	0.0025	0.34	0.14	0.42
2	6 -64 46	0.0017	0.119	0.009	0.482	0.0012	0.037	0.22	0.0040	0.092	0.010

(C) **Estimated HDR curves and the group-by-condition interaction effect at two voxels**



Conclusions

- **FSM** or **ASM** may fail to detect shape subtleties
- **ESM** more accurately characterizes BOLD responses
- Better to take individual effect estimates of **ESM** for group analysis
  - Use **LME** for one group with no other explanatory variables
  - Combine **XUV**, **XMV**, **MVT**, and **AUC**

Acknowledgements

The research was supported by the NIMH & NINDS Intramural Research Programs of the NIH.