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# A Paradigm Free Regularization Approach to Recover Brain Activations: Validation on Task fMRI

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## Introduction

Resting-state functional MRI (rs-fMRI) provides insight into brain function in the absence of stimuli and allows to map brain activity for subjects whose condition does not allow to perform tasks. This has emphasized the need to recover neural activations from fMRI signals in the absence of an experimental paradigm. To avoid the need for prior information on the timing of the activations, techniques to deconvolve brain activity from the blood-oxygen-level-dependent (BOLD) response have been proposed [1, 2, 3, 4]. In particular, by supposing the brain activates in constant blocks, Farouj et al. [4] developed an approach which involves both spatial and temporal regularization (Total Activation, TA). However, it splits the optimization problem into two decoupled spatial and temporal regularization which doubles the number of parameters to set and requires the solver to alternate between the constraints. Starting from the idea that large image variations should be preserved as they occur during brain activation, whereas small variations should be smoothed to remove noise, we previously proposed an alternative paradigm-free algorithm based on partial differential equations (PDEs) named PFFMRI (Paradigm-Free fMRI) [5, 6]. In this work, we validate PFFMRI on task-fMRI data from 51 subjects using the experimental paradigm as ground truth and compare its performance to TA. We also show that PFFMRI recovers activity that agrees with the general linear model (GLM) without knowledge of the experimental paradigm.

## Methods

PFFMRI recovers brain activations and smooths small variations by solving the following optimization problem:

$$I = \arg \min_I \|I_0 - H \star I\|_2^2 + \lambda \|\nabla I\|_2^2 \quad (1)$$

where  $\|I_0 - H \star I\|_2^2$  is the data fitting term,  $\|\nabla I\|_2^2$  is the regularization term,  $\lambda$  is the regularization parameter,  $I_0$  and  $I$  are the original and regularized image, and  $H$  the hemodynamic response function [7]. Note that the regularization applies on the 4-D image, acting simultaneously in the 3-D space and time and attempts to preserve large image variations occurring in time or space. To solve the problem in Eq. 1 we derived a regularization process based on gradient descent computed with PDEs as explained in previous works [5, 6]. To evaluate the performance of PFFMRI, we quantified its ability to recover brain activation during a motor task. It should be noted that, while PFFMRI was designed to be used in the absence of an experimental paradigm, testing it on task-fMRI data provides us with a ground truth to quantitatively assess performance. We used the preprocessed data [8] of 51 subjects provided by the Human Connectome Project (HCP) [9] that were additionally detrended and normalized. We focused on the motor tasks where subjects were asked to move fingers of their left or right hand. To highlight the ability of PFFMRI to recover brain activations without knowledge of the experimental paradigm, we qualitatively compared brain regions recovered using PFFMRI to those recovered using the GLM implemented in FSL. We also compared the performance of PFFMRI with the deconvolution implemented in TA [4]. Spherical 3mm-radius ROIs in the motor cortex were defined for each finger starting from the coordinates centers proposed by Roux et al. [10] and concatenated to obtain a single ROI for each task. The task ground truth time-courses were constructed as piece-wise constant signals with ones when the subjects were performing the movements and zeros elsewhere. We computed the whole-brain voxel-wise Pearson correlation maps between the time-course of the task and the recovered signals obtained using PFFMRI and TA. For each subject we computed the mean and standard deviation of the correlation inside the ROIs.

## Results

Figure 1 illustrates, for one subject, the correlation maps computed with PFFMRI and the values of the regression coefficients obtained using the GLM. Regions with a high PFFMRI correlation overlap with regions with large GLM regression coefficients. Figure 2 illustrates the mean correlations values estimated for each ROI using PFFMRI and TA. Figure 2 also illustrates the convergence to a stable solution with respect to the number of iterations: the mean correlations values estimated for each ROI across the data sample increase while increasing the number of iterations, until it converges after 25 iterations. Figure 3 illustrates for one subject the recovered signals using PFFMRI and TA averaged in the gray-matter masked ROIs, overlapped to the averaged fMRI data and the experimental paradigm.

## Discussion

When comparing the regions recovered using the GLM and PFFMRI, we noted overall very good agreement between the methods. It should be emphasized that, while the GLM requires knowledge of the task, PFFMRI does not. These results highlight that PFFMRI can be used to recover brain activity in absence of an experimental paradigm, such as rs-fMRI. When comparing correlation maps obtained for PFFMRI and TA, correlation values obtained with PFFMRI were significantly higher than those obtained with TA suggesting an improved recovery of brain activity.

## Conclusion

In this paper we validated our approach to recover brain activity from fMRI signals without prior knowledge. Our findings shows that PFFMRI enabled us to solve a unique problem, coupling the space and time dimension and to recover brain activation overlapping the ones obtained with the GLM. Our results also shows higher correlations of the recovered time-courses with the ground truth compared to TA. This opens a new channel for the analyses of rs-fMRI and the recovery of paradigm-free neural activity.

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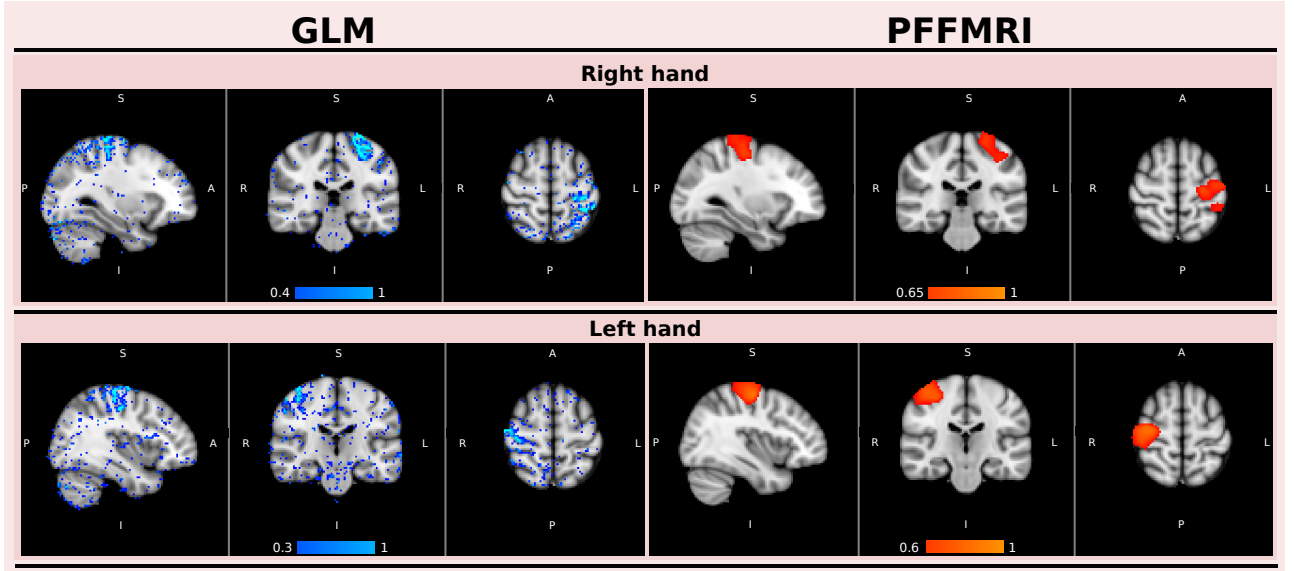
Data were provided [in part] by the Human Connectome Project, WU-Minn Consortium (Principal Investigators: David Van Essen and Kamil Ugurbil; 1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University.

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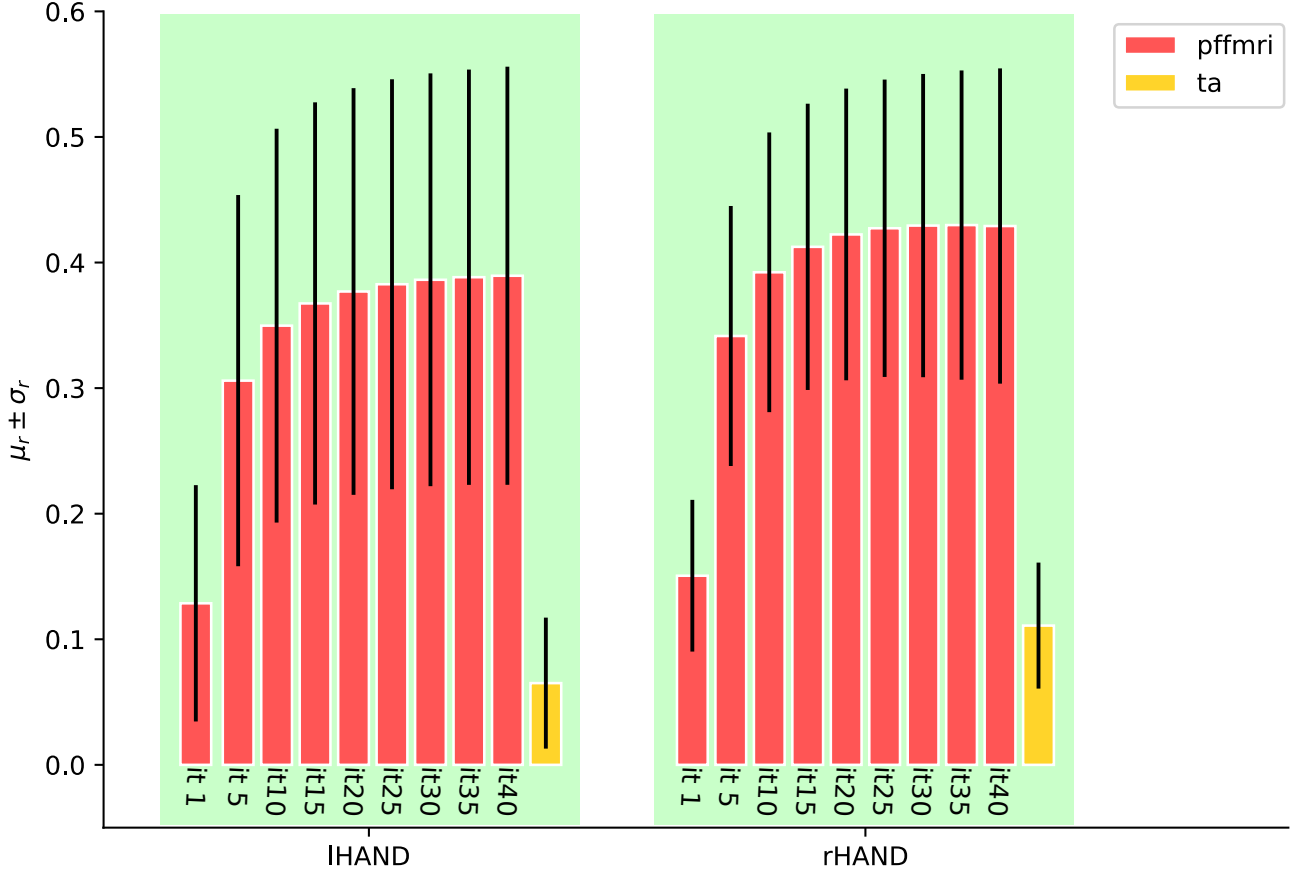
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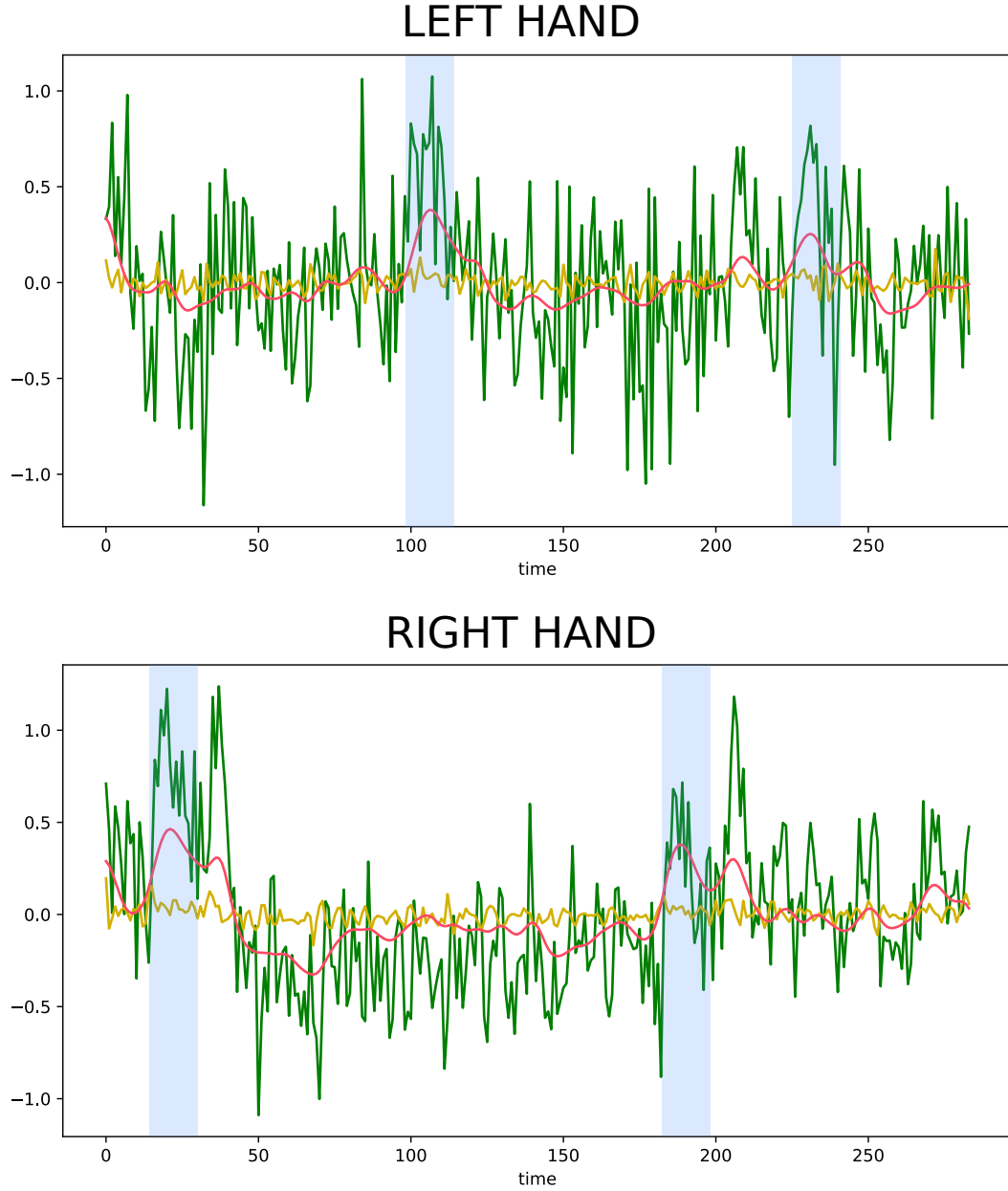
## Figures



**Figure 1:** On the left column, in blue-lightblue, the  $\beta$ -regressors map obtained using the GLM implemented in the FSL superimposed to the MNI brain. On the right column, in red-yellow, the whole brain voxel-wise Pearson correlation maps between the recovered time courses using the PFFMRI (35 iterations and  $\lambda = 0.9999$ ) and the task, superimposed to the MNI brain. The values  $r$  of the correlations are indicated by the color-bars. The top row corresponds to the right hand and the bottom to the left hand. A: anterior; P: posterior; S:superior; I: inferior; R: right; L: left.



**Figure 2:** Barplots of the mean ( $\mu_r$ )  $\pm$  standard deviations ( $\sigma_r$ ) of the correlation values computed between the recovered time-courses with the ground truth computed among the sample data (51 subjects) inside two ROIs related to the tasks of the left and right hand. For each task, the bars in red represents the results using the Paradigm-Free fMRI (PFFMRI) for the iteration (it)1 to 40 and  $\lambda = 0.9999$ . The yellow bars represents the results obtained using the Total Activation (TA) toolbox. (IHAND: left hand; rHAND: right hand).



**Figure 3:** Reconstructed signals obtained with the Paradigm-Free fMRI (PFFMRI, red) after 30 iterations and  $\lambda = 0.9999$  and the Total Activation (TA, yellow) toolbox, superimposed on the acquired motor-task fMRI signals (green). The plot on the top is related to the region of interest (ROI) involved in the movement of the left hand, the plot at the bottom is associated to the right hand movement. All the signals were averaged among the voxels belonging to the gray-matter masked ROIs. The blue areas represent the occurrence and the duration of the motor tasks.