# DETECTING SPONTANEOUS BRAIN ACTIVITY IN FUNCTIONAL MAGNETIC RESONANCE IMAGING USING FINITE RATE OF INNOVATION

Zafer Doğan<sup>1,2</sup>, Thierry Blu<sup>3</sup>, and Dimitri Van De Ville<sup>1,2</sup>

<sup>1</sup>Medical Image Processing Lab (MIPLAB), Institute of Bioengineering, EPFL, CH-1015 Lausanne, Switzerland <sup>2</sup>Department of Radiology and Medical Informatics, University of Geneva, CH-1211 Geneva, Switzerland <sup>3</sup>Department of Electronic Engineering, Chinese University of Hong Kong, Shatin N.T. Hong Kong

### ABSTRACT

Several methods have been developed for the sampling and reconstruction of specific classes of signals known as signals with finite rate of innovation (FRI). It is possible to recover the innovations of the signals from very low-rate samples by using adequate exponential reproduction sampling kernels. Recently, the FRI theory has been extended to arbitrary sampling kernels that reproduce approximate exponentials.

In this paper, we develop the method for the detection of spontaneous brain activity in functional magnetic resonance imaging (fMRI) data. We model the fMRI timecourse for every voxel as a convolution between the innovation signal– a stream of Diracs– and the hemodynamic response function (HRF). Relaxing the exact exponential reproduction constraint given by Strang-Fix condition, we design an adequate FRI sampling kernel using the canonical HRF model that allows us to retrieve the innovation instants in continuous domain. We illustrate the feasibility of our method by detecting spontaneous brain activity on the simulated and degraded fMRI data using an iterative denoising scheme.

*Index Terms*— Finite rate of innovation, functional magnetic resonance imaging, hemodynamic response function, Strang-Fix conditions

## 1. INTRODUCTION

Conventional analysis of functional magnetic resonance imaging (fMRI) data is based on event-related designs. Typically, prior knowledge about the experimental paradigm is used to construct temporal regressors, which are then fitted to the time course of every voxel using the general linear model (GLM) approaches. Then, the analysis is followed by a statistical hypothesis testing for a given contrast weights to relate the experimental paradigm to the measured blood oxygenated-level-dependent (BOLD) signal [1]. The BOLD signal of every voxel in fMRI data can be represented as a convolution of an activity signal with the hemodynamic response function (HRF).

An exact temporal model of the activity signal cannot be modelled in cases when the activity occurs spontaneously, for example, hallucinations in schizophrenia, or interictal discharges in epilepsy, or in cognitive paradigm experiments. Moreover, detecting spontaneous brain activity may provide characteristic patterns of the brain activity referred as resting-state networks [2]. Such spontaneous activity cannot be deduced by standard GLM approaches. Therefore, there is an increasing need for alternative methodologies that enable analysis of fMRI data without predefined responses. fMRI deconvolution methods have been proposed to uncover the underlying activity signal at the fMRI timescale. Within convolution framework, the linear system assumption is retained while regularisation terms are generally used to promote sparsity in the activity signal [3]. In [4], a wavelet basis is tailored to mimic the properties of the hemodynamic response. Recently [5], an fMRI data analysis method called total activation has been proposed to explore the underlying activity signal based on sparse spatio-temporal priors and characterisation of the HRF.

In this paper, we propose a novel method to detect spontaneous brain activity in fMRI data using a recent sampling and reconstruction framework called finite rate of innovation. We consider the fMRI signal in a typical continuous to discrete sampling setup as in Fig. 1 where the spontaneous activity signal is modelled as an FRI signal –a stream of Diracs with time instants and amplitude are defined as the innovation parameters of the signal. Unlike deconvolution frameworks, we showed that it is possible to recover the unknown activity instants in continuous domain with a temporal resolution less than the can repeat time (TR) of the fMRI data.

The paper is organized as follows. We start with an overview of the FRI sampling theory in particular for the exponential reproducing kernels in Sec. 2. Then, we show how to extend the same framework for the canonical HRF in Sec. 3. Simulation results are shown in Sec. 4 and we finally conclude in Sec. 5.

This work was supported in part by the Swiss National Science Foundation (under the grants 2053530-132808 and PP00P2-123438) and in part by the Center for Biomedical Imaging (CIBM) of Geneva-Lausanne Universities and Hospitals, and the EPFL.

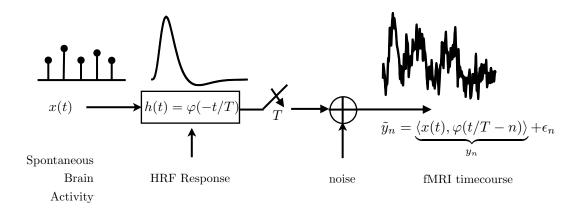


Fig. 1: fMRI signal model: The original continuous-time activity signal x(t) is filtered with the HRF before being uniformly sampled with a sampling period T. Then, the samples are assumed to be degraded by additive white noise such that fMRI time course samples are given by  $\tilde{y}_n = \langle x(t), \varphi(t/T - n) \rangle + \epsilon_n$  where the sampling kernel  $\varphi(t)$  is the scaled and time-reversed version of the HRF

### 2. FRI SAMPLING THEORY

The sampling theory plays a central role in modern signal processing providing the link between continuous and discretedomains. The question is to find the best way to reconstruct x(t) from the discrete samples of the observed signal  $\tilde{y}_n$ . The classical answer to the sampling problem is provided by the famous Shannon sampling theorem with extensions to classes of nonbandlimited signals that belong to shift-invariant subspaces [6]. Recently, it has been shown that it is possible to develop sampling schemes for classes of signals that are neither band limited nor belong to a fixed subspace [7]. These signals are completely characterised by a finite number of free parameters per unit time and are called signals with finite rate of innovation (FRI), e.g, streams of Diracs, piecewise polynomial and piecewise sinusoidal signals [8]. In a recent work [9], the sampling kernels that are used in the FRI framework have been extended to any arbitrary kernels which requires an implicit design to fullfill the exponential reproduction constrain of Strang-Fix condition approximately. This had impact in specific applications of FRI signals such as calcium imaging [10].

Considering Fig. 1, assume that the stimulus function x(t) is a stream of K Diracs

$$x(t) = \sum_{k=0}^{K-1} x_k \delta(t - t_k),$$
(1)

where  $x_k \in \mathbb{C}$  are the amplitudes and  $t_k \in \mathbb{R}$  are the time instants. We restrict time instants to an interval  $t_k \in [0, \tau]$ . Moreover, let us also assume for the moment that we have an exponential reproducing kernel  $\varphi$  satisfying:

$$\sum_{n \in \mathbb{Z}} c_{m,n} \varphi(t-n) = e^{\alpha_m t}, \qquad (2)$$

for proper coefficients  $c_{m,n}$  with  $m = 0, \ldots, P$  and  $\alpha_m = \alpha_0 + m\lambda \in \mathbb{C}$ . Now, based on the acquisition model in Fig.

1, the noiseless samples satisfy

$$y_n = \langle x(t), \varphi(t/T - n) \rangle = \sum_{k=0}^{K-1} x_k \varphi(\frac{t_k}{T} - n), \quad (3)$$

where n = 0, ..., N - 1. Once we have N samples of  $y_n$  with the kernel  $\varphi$ , the FRI theory states that the underlying stream of Diracs can be retrieved as follows. First, we linearly combine the samples  $y_n$  using the coefficients of (2) to obtain a new sequence:

$$s_m = \sum_{n=0}^{N-1} c_{m,n} y_n.$$
 (4)

Then, using (3) in (4), we have:

$$s_m = \left\langle x(t), \sum_{n=0}^{N-1} c_{m,n} \varphi(\frac{t}{T} - n) \right\rangle$$
(5)  
$$= \left\langle \sum_{k=0}^{K-1} x_k \delta(t - t_k), e^{\alpha_m \frac{t_k}{T}} \right\rangle$$
  
$$= \sum_{k=0}^{K-1} x_k e^{\alpha_m \frac{t_k}{T}} = \sum_{k=0}^{K-1} a_k u_k^m,$$

where  $a_k = x_k e^{\alpha_0 \frac{t_k}{T}}$  and  $u_k = e^{\lambda \frac{t_k}{T}}$ . Then, the pairs of unknowns  $\{a_k, u_k\}_{k=0}^{K-1}$  can be retrieved from the moments  $s_m$  using the well-known Prony's method in spectral estimation [7]. Next, we define a filter h with z-transform

$$H(z) = \sum_{m=0}^{K} h_m z^{-m} = \prod_{k=0}^{K-1} (1 - u_k z^{-1}), \qquad (6)$$

where the roots corresponds to the values  $u_k$  by construction. Then, it follows that  $h_m$  annihilates the sequence  $s_m$  as:

$$h_m * s_m = \sum_{i=0}^{K} h_i s_{m-i} = 0.$$
 (7)

By construction, the zeros of the filter h uniquely defines the values  $u_k$  provided that the instants  $t_k$ 's are distinct. Finally, the weighs  $x_k$  are determined by solving first K equations of (5) with the estimated  $u_k$ 's.

### 3. APPROXIMATE RECOVERY OF ACTIVITY SIGNALS IN FMRI

We now go back to the problem of reconstructing the activity signal x(t) using a sampling kernel given by the canonical HRF as in statistical parametric mapping (SPM) software [11] from the non-ideal measurements  $\tilde{y}_n$  that cannot reproduce exact exponentials. The first step is to relax the condition in (2), such that we want to find coefficients  $c_n$ :

$$\sum_{n \in \mathbb{Z}} c_n \varphi(t-n) \approx e^{\alpha t},\tag{8}$$

where  $c_n = c_0 e^{\alpha n}$ . For sufficiently fast decaying kernels, the choice  $c_0 = (\hat{\varphi}(\alpha))^{-1}$  yields an accurate bound for the approximation error [9]. To select the parameters  $\alpha_m$ , we turn back to elements  $c_{m,n} = c_{m,0}e^{\alpha_m n}$  represented as:

$$\mathbf{C} = \underbrace{\begin{bmatrix} c_{0,0} & 0 & \cdots & 0 \\ 0 & c_{1,0} & \vdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & c_{P,0} \end{bmatrix}}_{\mathbf{D}} \underbrace{\begin{bmatrix} 1 & e^{\alpha_0} & \cdots & e^{\alpha_0(N-1)} \\ 1 & e^{\alpha_1} & \cdots & e^{\alpha_1(N-1)} \\ \vdots & \vdots & \ddots & \vdots \\ 1 & e^{\alpha_P} & \cdots & e^{\alpha_P(N-1)} \end{bmatrix}}_{\mathbf{V}},$$

where **D** is a diagonal, and **V** is a Vandermonde matrix. Hence, for **C** to be better conditioned, we want the absolute values of the diagonal elements of **D** to be nearly the same and the elements in **V** to lie on the unit circle [12]. While choosing  $\alpha_m$  to be purely imaginary makes the Vandermonde matrix **V** better conditioned, the coefficients are now related to the Fourier transform of the sampling kernel,  $c_{m,0} = \hat{\varphi}(j\omega_m)^{-1}$ . Since the HRF signal a low-pass blurring kernel, the condition on the diagonal entries of **D** is satisfied when all the exponentials are close to zero. This fact leads to a trade-off in the choice of  $\omega_m$  and we choose to use the frequency range only up to the full width at half maximum (FWHM) of the spectrum of the HRF that is given in Fig. 2. We define the exponentials as

$$\alpha_m = j\omega_m = j\frac{\pi}{L}(2m - P) \quad m = 0, \dots, P, \qquad (9)$$

and then optimize the values P and L, accordingly. Here, the ratio of  $\frac{\pi}{L}$  defines the spacing of the chosen frequencies in the spectrum.

Another issue that real data represents is that the measurements are degraded in the presence of noise. Here, we followed the iterative Cadzow denoising method to overcome this situation [13].

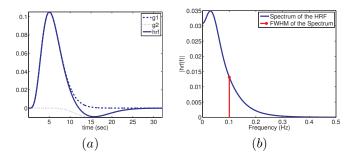


Fig. 2: HRF and its spectrum: (a) two gamma representation of HRF where g1 is a gamma function modelling the peak and g2 is a gamma function modelling the undershoot (b) Spectrum of the canonical HRF, where FWHM defines the maximum value for the chosen frequency  $\alpha_m$ 

#### 4. RESULTS

We used the SPM package with the default parameters to generate a canonical HRF signal sampled at TR = 0.5s as given in Fig. 2 (a). We know that approximate reproduction of exponentials are stable if we choose  $c_{m,n} = c_{m,0}e^{j\omega_m}$  with  $c_{m,0} = \hat{\varphi}(j\omega_m)^{-1}$ . Hence, we only need to know Fourier transform of the HRF at  $j\omega_m, m = 0, \ldots, P$ . We start noting that P can be chosen arbitrarily while the Prony's method requires 2K values of  $s_m$  in (7). This means that the parameters of a stream of K Diracs can be retrieved when  $P \ge 2K - 1$ . Once we choose a specific value for P, we are only left with the problem of choosing the value L. We have already seen in Sec. 3 that the conditioning of the matrix C depends of the selection of the frequencies on the unit circle. Therefore, we choose the value L considering FWHM of the spectrum of the HRF function as given in Fig. 2 (b).

For the simulation, we generated the activity signal x(t) as K randomly spaced Diracs with unit amplitudes and we focus on the retrieval of the location. Using the fMRI signal model in Fig. 1, we obtain the samples followed by an additive noise. Hence, the samples are  $y_n = \langle x(t), \varphi(t/T - n) \rangle + \epsilon_n$  where  $\epsilon_n$  is independently distributed gaussian noise with zero mean and variance  $\sigma^2$ . The variance is chosen according to the target signal-to-noise ratio defined as SNR (dB) =10 log  $\frac{\mathbf{y}}{N\sigma^2}$ . Next using (4), we first compute the moments  $s_m$  that is followed by the Cadzow denoising framework. Then, we obtain the innovation parameters  $\{t_k, x_k\}_{k=0}^{K-1}$  by solving the annihilation system in (7) and the system of equations in (4), respectively.

In Fig. 3 (a) to (c), we show the detection of 1 to 3 Diracs in an fMRI data respectively. The signals are degraded by AWGN at 5dB to simulate a realistic case and the analysis is done for a window size of 40 s. The result revealed that we can retrieve the spontaneous activity signal in continuous domain with a localisation error less than the scan repeat time of the fMRI data.

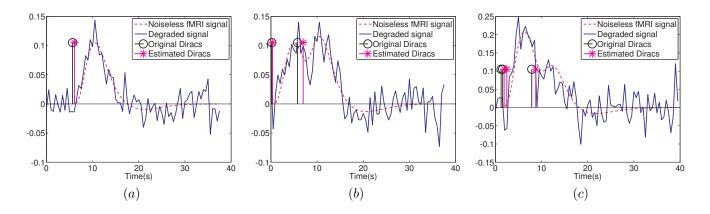


Fig. 3: Detection of brain activity events in the considered fMRI window at SNR 5dB; (a) detection of K = 1 Dirac, (b) detection of K = 2 Diracs (c) detection of K = 3 Diracs; the number and position of the moments are chosen as P = 8K and L = 8(P + 1)

#### 5. CONCLUSIONS

We have proposed a new framework for the analysis of FMRI data using a continuous domain theory. Modelling the spontaneous activity signal as an FRI signal, i.e., a stream of Diracs, we considered the fMRI time course as a filtered version of the activity signal with the HRF. Using the canonical HRF model, we showed how to design an appropriate kernel that allows approximate reproduction of exponentials which is essential in FRI framework. Using the Cadzow denoising scheme, the proposed algorithm retrieved the spontaneous activity signal from simulated fMRI data in continuous domain with better temporal resolution than the scan repeat time of the data sequence at low SNR. These preliminary results show the feasibility of FRI for activity detection in fMRI and future work will look into its application to experimental data. Moreover, in our future research we will focus on the variability of the HRF over brain regions and over individuals.

#### 6. REFERENCES

- K. Worsley and K. Friston, "Analysis of fMRI time-series revisited - again," *NeuroImage*, vol. 2, pp. 173–181, 1995.
- [2] B. B. Biswal, "Resting state fmri: A personal history," *NeuroImage*, vol. 62, no. 2, pp. 938 944, 2012.
- [3] C. Caballero Gaudes, N. Petridou, S. T. Francis, I. L. Dryden, and P. A. Gowland, "Paradigm free mapping with sparse regression automatically detects single-trial functional magnetic resonance imaging blood oxygenation level dependent responses," *Human Brain Mapping*, vol. 34, no. 3, pp. 501–518, 2013.
- [4] I. Khalidov, J. Fadili, F. Lazeyras, D. V. D. Ville, and M. Unser, "Activelets: Wavelets for sparse representation of hemodynamic responses," *Signal Processing*, vol. 91, no. 12, pp. 2810 – 2821, 2011.
- [5] F. I. Karahanolu, C. Caballero-Gaudes, F. Lazeyras, and D. V. D. Ville, "Total activation: fmri deconvolution through spatio-temporal regularization," *NeuroImage*, vol. 73, no. 0, pp. 121 – 134, 2013.
- [6] M. Unser and T. Blu, "Cardinal exponential splines: Part itheory and filtering algorithms," *IEEE Trans. Signal Process*, vol. 53, pp. 1425–1438, 2005.

- [7] M. Vetterli, P. Marziliano, and T. Blu, "Sampling signals with finite rate of innovation," *IEEE Transactions on Signal Processing*, vol. 50, no. 6, pp. 1417–1428, 2002, IEEE Signal Processing Society's 2006.
- [8] P. Dragotti, M. Vetterli, and T. Blu, "Sampling moments and reconstructing signals of finite rate of innovation: Shannon meets strang ndash;fix," *Signal Processing, IEEE Transactions on*, vol. 55, no. 5, pp. 1741 –1757, may 2007.
- [9] J. Urigen, T. Blu, and P. Dragotti, "Fri sampling with arbitrary kernels," *Signal Processing, IEEE Transactions on*, vol. 61, no. 21, pp. 5310–5323, 2013.
- [10] J. Onativia, S. R. Schultz, and P. L. Dragotti, "A finite rate of innovation algorithm for fast and accurate spike detection from two-photon calcium imaging," *Journal of Neural Engineering*, vol. 10, no. 4, pp. 046017, 2013.
- [11] K. Friston, J. Ashburner, S. Kiebel, T. Nichols, and W. Penny, Eds., Statistical Parametric Mapping: The Analysis of Functional Brain Images, Academic Press, 2007.
- [12] F. A. Berman, Lihu, "On perfect conditioning of vandermonde matrices on the unit circle.," *ELA. The Electronic Journal of Linear Algebra [electronic only]*, vol. 16, pp. 157–161, 2007.
- [13] T. Blu, P.-L. Dragotti, M. Vetterli, P. Marziliano, and L. Coulot, "Sparse sampling of signal innovations," *IEEE Signal Process*ing Magazine, vol. 25, no. 2, pp. 31–40, 2008.
- [14] P. L. Dragotti, J. Oativia, A. Urigen, and T. Blu, "Approximate strang-fix: sampling infinite streams of diracs with any kernel," 2013.