Model the single-venule fMRI signal at the millisecond scale

Yi He[1,2], Kun Zhang[3], and Xin Yu[1,2]

[1]*Research Group of Translational Neuroimaging and Neural Control, High-Field Magnetic Resonance, Max Planck Institute for Biological Cybernetics, Tuebingen, Baden-Wuerttemberg, Germany,* [2]*Graduate School of Neural Information Processing, University of Tuebingen, Tuebingen, Baden-Wuerttemberg, Germany,* [3]*Department of Empirical Inference, Max Planck Institute of Intelligent System, Tuebingen, Germany*

Target Audience Scientists who are interested in modeling fMRI signal and developing novel methods for vascular hemodynamic mapping.

Purpose We sampled the fMRI signal in two temporal dimension of a 2D gradient-echo MR slice. The first is through multi-echo train to sample the decay function G(t) from 3ms to 34.5ms (10 echoes) with 3.5ms interval. The second dimension is to sample the MGE slice every TR at 100ms, containing the fMRI signal corresponding to the block-design function. Traditionally, the T2* value can be estimated from G(t) decay function for each time point and linear regression analysis can be performed to acquire a T2* functional map. Here, we developed an algorithm to directly estimate both G(t) and f(t) (hemodynamic function) simultaneously. This method allows us to estimate the hemodynamic response function from individual venules penetrating the deep layer cortex with millisecond scale accuracy.

Methods All images were acquired with a 14.1 T/26cm horizontal bore magnet (Magnex), interfaced to an AVANCE III console (Bruker) and equipped with a 12 cm gradient set, capable of providing 100 G/cm with a rise time of 150 us (Resonance Research). A transreceiver surface coil with 6mm diameter was used to acquire fMRI images. A Muti-Echo-Line-Scanning fMRI (MELS-fMRI) was developed to map the BOLD signal (Abstract ID: 5873). The fMRI signal was collected in the line-scanning format as previously reported [1, 2, 3]. We applied MGE sequence into the line-scanning fMRI method and acquire fMRI signal with additional decay function G(t). The spatial resolution of the 2D raw image is at 100x100μm so that we can identify fMRI signal from individual venules penetrating the deep layer cortex [4]. MRI signal intensity X(t) from 0 ms to 130 ms was shown in Fig 2.C. We use the model

$$\mathrm{X(t)} = G(t) \times f(t) + E(t),$$

Where G(t) has the form $\mathrm{G(t)} = ce^{\frac{-t}{\tau}}$. The objective function to minimize is

$$\mathrm{J[G,f]} = \frac{1}{2}\sum_{t=1}^{T}\big(X(t) - G(t)f(t)\big)^2 + \frac{\lambda}{2}\|f\|_H^2$$

Note that c is not identifiable, in that we can always exchange a factor between G(t) and f(t) without changing the squared loss. However, because of the regularization term, the scale of f(t) becomes smaller and smaller in the process of minimizing the above function. To avoid this phenomenon, we fix c = 1 (we already divide the raw data by 10000).

We use the kernel method [3] to represent the hemodynamic function f(t). Substituting $\mathrm{f(t)} = \sum_{i=1}^{n}\alpha_i k(t,t_i)$ and using $< \mathrm{k(.,t_i)}, \mathrm{k(.,t_j)} >_H = \mathrm{k(t_i,t_j)}$, we obtain

$$\begin{aligned} J[G,f] &= \frac{1}{2}|\mathbf{X} - \mathbf{G}\odot \mathrm{f}|^2 + \frac{\lambda}{2}\alpha^{\intercal}K\alpha \qquad (1)\\ &= \frac{1}{2}|\mathbf{X} - \mathrm{diag}(\mathbf{G})K\alpha|^2 + \frac{\lambda}{2}\alpha^{\intercal}K\alpha \\ &= \frac{1}{2}\alpha^{\intercal}(K\mathrm{diag}^2(\mathbf{G})K + \lambda K)\alpha - \mathbf{X}^{\intercal}\mathrm{diag}(\mathbf{G})K\alpha + \frac{1}{2}\mathbf{X}^{\intercal}\mathbf{X}. \qquad (2)\end{aligned}$$

We used the alternate optimization procedure for α and τ. Minimizing the above function w.r.t. α. We obtain

$$\begin{aligned}\alpha &= (\mathrm{diag}^2(\mathbf{G})K + \lambda I)^{-1}\mathrm{diag}(\mathbf{G})\mathbf{X} \\ &= (K + \lambda\cdot\mathrm{diag}^{-2}(\mathbf{G}))^{-1}\mathrm{diag}^{-1}(\mathbf{G})\mathbf{X}.\end{aligned}$$

We used the gradient descent method to update τ by minimizing (1). The gradient is

$$\frac{\partial J[G,f]}{\partial \tau} = -\sum_{t=1}^{T}\Big(X(t) - G(t)f(t)\Big)\cdot f(t)\cdot G(t)\cdot\frac{\mathrm{mod}(t,100)}{\tau^2}.$$

We iteratively repeated the above two procedures to update τ and α, respectively, until convergence. In the literature[5], it has been reported that τ is usually time-varying. If we did not specify how it changed over time, we could still use the above gradient-based method to learn all values for τ. Suppose τ changes smoothly over time. Inspired by kernel-ridge regression, we can parametrize the vector by

$$\vec{\tau} = K_\tau(K_\tau + \lambda_\tau I)^{-1}\boldsymbol{\beta},$$

Where λ_τ is a regularization parameter and β is the parameter vector to estimate.

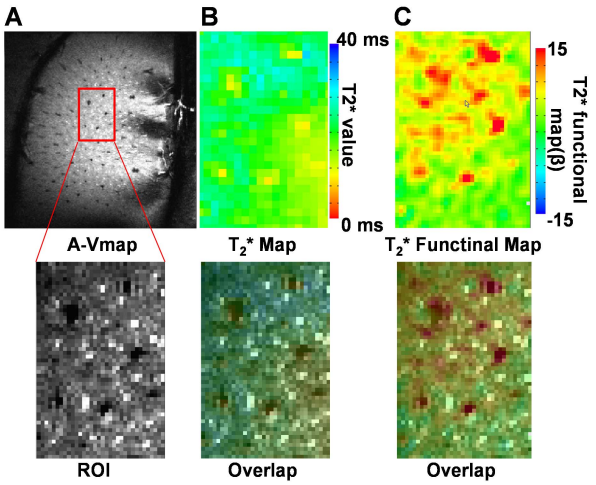

Fig 1. A. Single vessel map shows the individual penetrating venules as dark dots. B. The T2* map overlaps on the single vessel map. C. The T2* functional map overlaps on the single vessel map.

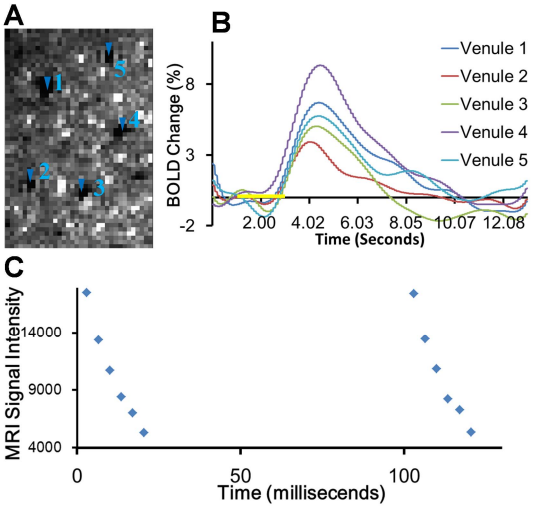

Fig 2. A. Localization of five venules based on the signal intensity (dark dots highlighted by blue arrowheads). B. The hemodynamic response function of the 5 venules with 2s stimulation on (yellow line). C. MRI signal intensity X(t) from 0 ms to 130 ms.

Results Fig 1.A shows the single-vessel map to present venules as dark spots and arterioles as bright spots. The estimated mean T2* map overlapped with the venule voxels (Fig 1B), showing lowest T2* value from venule voxels. The T_2* functional map can be estimated by linear regression analysis on the T_2* map time datasets, showing the most active voxels overlapping with individual venules. Through the model method, the HRF of 5 venules were derived from f(t), showing a clearly different onset time from the five venules.

Conclusion This method makes it possible to distinguish the vascular signal propagation at the scale of milliseconds.

Reference 1 Yu *et al*. Nature Method, 11:55–58, (2014). 2. Yu *et al.* ISMRM, 4360, (2014). 3 Silva & Koretsky, PNAS, 99:15182-7 (2002). 4. Yu et al. NI, 59:1451-60, (2012). 5. B. Scholkopf *et al.* Learning with kernels, 2002.