INCORPORATION OF GRAY MATTER $T_1$ AND $T_2^*$ IMPROVES BRAIN ACTIVATION STATISTICS IN fMRI

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**Purpose:** The proton spin density ($M_0$) as well as the MR relaxivities, transverse ($T_2^*$), and longitudinal relaxation times, provide the basic contrast mechanisms in functional MRI (fMRI). Although the MR magnetization physically depends on tissue and imaging parameters in a nonlinear fashion, a linear model is what is conventionally used in fMRI activation studies. Furthermore, the standard practice has been to discard the first scans to avoid magnetic saturation effects even though they have important information on the MR relaxivities. It is also well-known that activation occurs in gray matter (GM) while performing a task. We present a statistical fMRI model for Differential $T_2^*$ Contrast Incorporating $T_1$ and $T_2^*$ of GM, so-called DeTeCT-ING, that uses complex-valued time courses to estimate $T_1$ and $T_2^*$ for each voxel, then to incorporate GM MR relaxivities into statistical model in order to better detect brain activation, all from a single pulse sequence by utilizing the first scans. We show the performance of the DeTeCT-ING Model on an fMRI data set and compare it with the conventionally used magnitude-only (MO) and newer complex-valued (CA) fMRI models.

**Methods:** The temporally varying magnitude of the MR signal, $M_t$, can be represented by incorporating the effect of the task execution as follows: $M_t = [M_{t-1} \exp(-TR/T_1) \cos(\phi) + M_0(1 - \exp(-TR/T_1))] \sin(\phi) \exp(-TE/T_2^* + \delta z_t) + \chi_t \beta_t$ where $\phi$ is the flip angle (FA), TR and TE are the repetition and echo times, $\delta$ is the differential task signal change, the coefficient for the reference function $z_t, \chi_t$ is the $i^{th}$ row of the design matrix $X$, and $\beta_t$ is the linear drift coefficient. The complex-valued observations with phase $\theta_t$ at time $t$ can therefore be described as $y_t = M_t(\cos(\theta_t) + i \sin(\theta_t)) + (\eta_{R_t} + i \eta_{I_t})$, where $(\eta_{R_t}, \eta_{I_t}) \sim N(0, \sigma^2 I_2)$. Working in the complex domain with the data having normally distributed noise allows for the use of nonlinear Least Squares estimation (NLSE).

To construct a generalized likelihood ratio (GLR) test of the hypothesis, $H_0: T_1 = T_1(GM), T_2^* = T_2^*(GM), \delta = 0$ (no activation) vs. $H_1: T_1 = T_1(GM), T_2^* = T_2^*(GM), \delta \neq 0$ (activation), the likelihood function is maximized by the numerical minimization of $\sum_{i=1}^{n} [(y_{R_i} - M_t \cos(\theta_i))^2 - (y_{I_i} - M_t \sin(\theta_i))^2]$ under the null (tildes) and alternative (hats) hypothesis. The GLR statistics, $-2 log \lambda = 2nlog(\sigma^2/\delta^2)$, has an asymptotic $X^2_2$ distribution in large samples and two-sided testing can then be done by $Z = sign(\delta)\sqrt{-2log\lambda}$. An fMRI experiment with a bilateral finger-tapping task was performed on a 3T MRI scanner. The paradigm followed a block design with an initial 20s rest followed by 16 epochs of 15s on and 15s off. An echo planar pulse sequence (FA=90°, BW=125 kHz, matrix=96x96, FOV=24cm, slice thickness=2.5mm, TR=1s, repetitions=510) was used. TE was designed as: 40.4ms at first 10 TR, equispaced in [40.4,52.9] for the next 5 TR; this was repeated once again, fixed to 40.4ms at last 490 TR. Activation is thresholded with Bonferroni correction.

**Results:** The parameter maps estimated from the first 20 TR images by using NLSE are shown in Figs. 1(a)-(c). Figs. 2(a)-(c) show activation images using the GLR from CA, MO and DeTeCT-ING Models.

**Discussion:** $M_0$, $T_1$, and $T_2^*$ values are highly indicative of GM bordered in Figs. 1(a)-(c). Fig. 2 shows a high correspondence between decay coefficients deemed to be GM and bordered active areas that should be in GM. It is obvious that CA and DeTeCT-ING Models demonstrated superior power of detection over MO model in left motor cortex and supplementary motor area in which the activation occurs. Fig. 3(c) shows that DeTeCT-ING Model produces no false positives outside brain unlike CA model. A higher power of detection can be seen in the bordered left motor cortex in Fig. 2(c) compared to the corresponding areas in Figs. 2(a) and (b).

**Conclusion:** This works strongly indicates that modeling MR magnetization by the signal equation and incorporating MR relaxivities into the activation along with utilizing the first scans of complex-valued fMRI data provides higher power to detect the active voxels.

**References:**


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**Fig. 1:** Estimated tissue parameter maps. a) $M_0$, b) $T_1$ (in ms.), c) $T_2^*$ (in ms.).

**Fig. 2:** Activation images thresholded at 5% FEW rate. a) CA, b) MO, c) DeTeCT-ING.
Incorporating Simultaneously Estimated $T_1$ and $T_2^*$ of Gray Matter Improves Brain Activation Statistics in fMRI

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INTRODUCTION

The proton spin density ($M_0$) and the MR relaxivities, longitudinal ($T_1$) and transverse ($T_2^*$) relaxations, provide the basic contrast mechanisms in fMRI. Although the MR magnetization physically depends on tissue and imaging parameters in a nonlinear fashion, a linear model is what is conventionally used in fMRI activation studies. Furthermore, the standard practice has been to discard the first scans to avoid magnetic saturation effects even though they have important information on the MR relaxivities. It is also well-known that the voxels in gray matter (GM) contain neurons that are to be active while performing a task. We present a statistical fMRI model for Differential $T_2^*$ Contrast Incorporating $T_1$ and $T_2^*$ of GM, so-called DeTeCT-ING, that uses complex-valued time courses to estimate $T_1$ and $T_2^*$ for each voxel, then to incorporate GM MR relaxivities into statistical model in order to better detect brain activation, all from a single pulse sequence by utilizing the first scans.

METHODS

The temporally varying magnitude of the MR signal, $M_t$, can be represented by incorporating the effect of the task execution as follows:

$$M_t = M_0 \left[ \frac{TE}{T} \cos(\phi) + M_1 \left[ 1 - \exp \left( \frac{-TE}{T_1} \right) \right] \sin(\phi) \exp \left( -\frac{TE}{T_2^* + \delta \gamma} \right) + \gamma_t \beta_t \right].$$

$\delta$: differential signal change  
$\beta_t$: coefficient for a time trend, $t$  
$\gamma_t$: reference function  
$TE_t$: temporally varying echo time

The complex-valued observations at time $t$ can then be described as:

$$y_t = M_t \left( \cos \theta + i \sin \theta \right) + (\eta_0 + i \eta_1),$$

where $N(0, \Sigma)$.

To construct a generalized likelihood ratio (GLR) test of the hypothesis,

$$H_0 : T_1 = T_1^*(\text{GM}), \quad T_2^* = T_2^*(\text{GM}), \quad \delta = 0 \quad \text{vs.} \quad H_1 : T_1 = T_1^*(\text{GM}), \quad T_2^* = T_2^*(\text{GM}), \quad \delta \neq 0 \quad \text{(Inactive)}$$

$$H_0 : T_1 = T_1^*(\text{GM}), \quad T_2^* = T_2^*(\text{GM}), \quad \delta \neq 0 \quad \text{(Active)}$$

the likelihood function is maximized by the numerical minimization of

$$\sigma_t^2 \left( M_0, T_1, T_2^*, \delta, \beta_t, \phi, \theta, \eta_0, \eta_1, TE_t, \gamma_t \right) = \frac{1}{2n} \sum_{t=1}^{n} \left[ \left( y_t - M_t \cos \theta \right) + (y_t - M_t \sin \theta) \right] \text{under } H_0 (\cdot) \text{ and } H_1 (\cdot).$$

The GLR statistics, $-2 \log \lambda = 2n \log \left( \frac{\sigma_t^2}{\sigma_t^2} \right)$ has an asymptotic $\chi^2$ distribution in large samples and two-sided testing can then be done by

$$Z = \text{sign}(\delta) \sqrt{2n \log \left( \frac{\sigma_t^2}{\sigma_t^2} \right)}.$$ 

RESULTS AND DISCUSSION

We show the performance of the DeTeCT-ING Model by comparing with the conventionally used magnitude-only (MO) and newer complex-valued (CA) fMRI models on a bilateral finger tapping fMRI data with

- a block design as given in Fig.1(b),
- an EPI pulse sequence ($\phi=90^\circ$, BW=125 kHz, FOV=24 cm, matrix=96x96, TR=1s, slice thick.=2.5mm, 510 TRs).
- temporarily varying TE as designed in Fig.1(a).

- $M_0$, $T_1$, and $T_2^*$ values are highly indicative of GM bordered in Figs. 3(a)-(c).
- Fig. 4 shows a high correspondence between decay coefficients deemed to be GM and bordered active areas that should be in GM.
- CA and DeTeCT-ING Models demonstrated superior power of detection over MO model in left motor cortex and supplementary motor area in which the activation occurs.
- DeTeCT-ING Model produces no false positives outside brain unlike CA model.
- A higher power of detection can be seen in the bordered left motor cortex in Fig. 4(c) compared to the corresponding areas in Figs. 4(a) and (b).

CONCLUSION

This work strongly indicates that modeling MR magnetization by the signal equation and incorporating MR relaxivities into the activation along with utilizing the first scans of complex-valued fMRI data provides higher power to detect the active voxels.

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METHODS

The temporally varying magnitude of the MR signal, $M_t$, can be represented by incorporating the effect of the task execution as follows:

$$M_t = M_0 \exp \left( \frac{T_R}{T_1} \cos(\phi) + M_0 \left( 1 - \exp \left( - \frac{T_R}{T_2^*} \right) \right) \sin(\phi) \exp \left( - \frac{TE}{T_2^*} \delta \zeta \right) + \chi_t \beta \right).$$

- $\delta$: differential signal change
- $\beta$: coefficient for a time trend, $t$
- $\zeta$: reference function
- $TE$: temporarily varying echo time
- $T_R$: temporarily varying echo time

The complex-valued observations at time $t$ can then be described as:

$$y_t = \begin{bmatrix} \cos \theta + i \sin \theta \end{bmatrix} \cdot (\eta_k + i \eta_i) \cdot \begin{bmatrix} \eta_k \cdot \eta_i \end{bmatrix} \sim N(0, \Sigma).$$

To construct a generalized likelihood ratio (GLR) test of the hypothesis,

$$H_0: T_1 = T_1^* \text{(GM)}, \quad T_2^* = T_2^{**} \text{(GM)}, \quad \delta = 0 \quad \text{vs.} \quad H_1: T_1 = T_1^* \text{(GM)}, \quad T_2^* = T_2^{**} \text{(GM)}, \quad \delta \neq 0$$

the likelihood function is maximized by the numerical minimization of

$$\sigma^2 = \frac{1}{2} \sum_{t=2}^{T} \left( y_t - M_0 \cos \theta \right)^2 + \left( y_t - M_0 \sin \theta \right)^2,$$

under $H_0$ (-) and $H_1$ (^).

The GLR statistics, $-2 \log \lambda = 2n \log \left( \frac{\sigma^2}{\sigma_0^2} \right)$, has an asymptotic $\chi^2$ distribution in large samples and two-sided testing can then be done by $Z = \text{sign}(\delta) \sqrt{2n \log(\sigma^2 / \sigma_0^2)}$.

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We show the performance of the DeTeCT-ING Model by comparing with the conventionally used magnitude-only (MO)¹ and newer complex-valued (CA)² fMRI models on a bilateral finger tapping fMRI data with

- a block design as given in Fig. 1(b),
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