STATISTICAL MODELS FOR THE COUPLING OF ASL AND BOLD MAGNETIC RESONANCE MODALITIES TO STUDY BRAIN FUNCTION AND DISEASE

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Abstract

ASL fMRI data provides a quantitative measure of blood perfusion, that can be correlated to neuronal activation. In contrast to BOLD measure, it is a direct and closer to neuronal activity measure. However, ASL data has a lower SNR and resolution. We aim at using both signals advantages to improve the estimation of the response functions.

Motivation

Functional MRI is not routinely used in clinic

WHY?
- Standard BOLD fMRI does not provide quantitative measurement.
- Need for accurate estimates of physiological parameters, in particular in normal ageing and pathologies such as Alzheimer's disease or stroke, that involve an altered vascular response.

	BOLD Blood Oxygen Level Dependent [1]	**ASL** Arterial Spin Labelling [2]
Image	CONTRAST Imaging	QUANTITATIVE Imaging
Measurement	Percent signal change: CBF + CBV + $CMRO_2$ (cerebral blood flow and volume, oxygen consumption)	✓ Quantitative measurement: absolute CBF (cerebral blood flow *ml blood/100ml tissue/min*)
SNR	✓ ~5% signal variation	~1% signal variation
Temporal resolution	✓ TR = 1s, 1 data point/TR	TR = 3s, 1 data point/2TR
Spatial resolution	✓ 2x2x2 mm^2 or 1.5x1.5x1.5 mm^3 in multi-band EPI sequences	~3x3 mm2 (in-plane resolution) x 6mm (slice direction)
Localisation	Veins and venuls	✓ Closer to neural activity
	✓ More suited for event-related designs	✓ Less intersubject variability

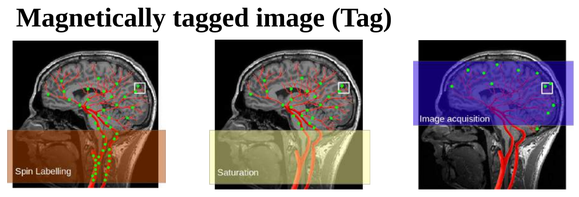
We could take advantage of the combination of ASL and BOLD in the study of brain function and disease

Arterial Spin Labelling

Arterial Spin Labelling fMRI data provides a quantitative measurement of blood perfusion in the brain.

Control image

Magnetically tagged image (Tag)



$$Control - Tag = \Delta M \propto CBF$$

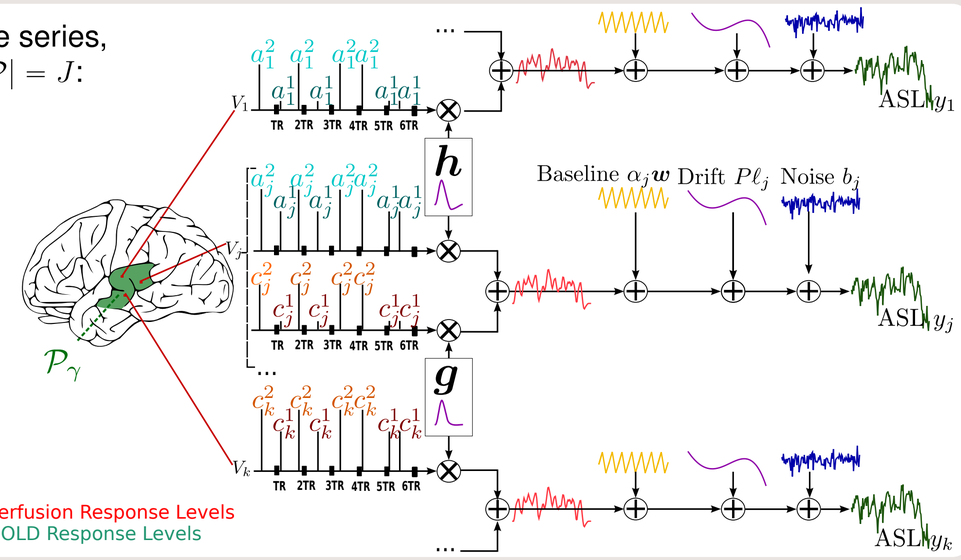
Model

ASL Joint detection estimation (JDE) framework [3]: a parcel-based approach

In a given parcel $\mathcal{P}$, the generative model for ASL time series, with M experimental conditions, reads $\forall\, j \in \mathcal{P}$, with $|\mathcal{P}| = J$:

$$\boldsymbol{y}_j = \sum_{m=1}^{M} \underbrace{c_j^m \boldsymbol{W} \boldsymbol{X}^m \boldsymbol{g}}_{\text{perfusion component}} + \underbrace{a_j^m \boldsymbol{X}^m \boldsymbol{h}}_{\text{BOLD component}} + \alpha_j \boldsymbol{w} + \boldsymbol{P}\boldsymbol{\ell}_j + \boldsymbol{b}_j$$

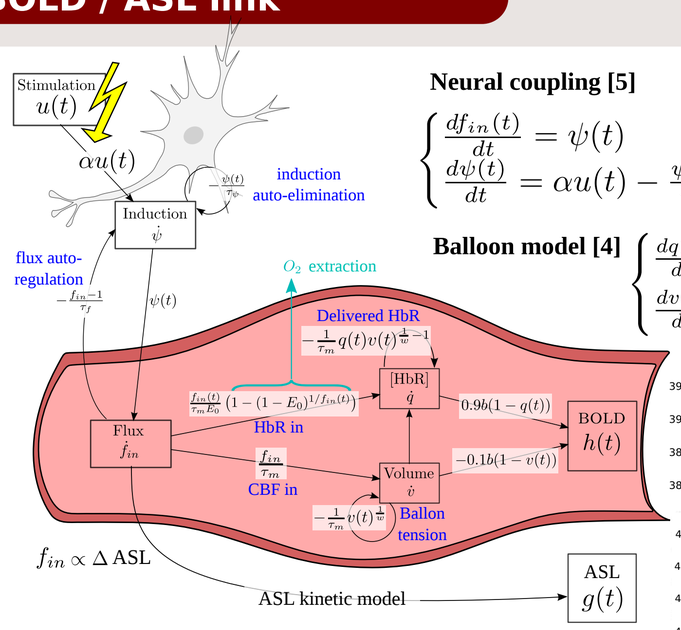
- Perfusion component: c_j^m = PRLs, $\boldsymbol{g}$ = PRF, $\boldsymbol{X}^m$ = stim
- BOLD component: a_j^m = BRLs, $\boldsymbol{h}$ = BRF, $\boldsymbol{X}^m$ = stim
- Perfusion baseline: "offset"
- Control/tag vector $\boldsymbol{w} = [\frac{1}{2}, -\frac{1}{2}, \frac{1}{2}, -\frac{1}{2} ...]$, $\boldsymbol{W} = diag(\boldsymbol{w})$
- Drift term
- Noise term: white Gaussian noise



(*) PRLs: Perfusion Response Levels
BRLs: BOLD Response Levels

BOLD / ASL link

Physiological link between BOLD and ASL signals



Neural coupling [5]

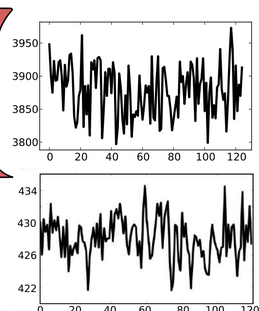
$$\begin{cases} \frac{df_{in}(t)}{dt} = \psi(t) \\ \frac{d\psi(t)}{dt} = \alpha u(t) - \frac{\psi(t)}{\tau_\psi} - \frac{f_{in}(t)-1}{\tau_f} \end{cases}$$

Balloon model [4]

$$\begin{cases} \frac{dq(t)}{dt} = \frac{1}{\tau_m}\left(f_{in}(t)\frac{1-(1-E_0)^{1/f_{in}(t)}}{E_0} - q(t)v(t)^{\frac{1}{w}-1}\right) \\ \frac{dv(t)}{dt} = \frac{1}{\tau_m}\left(f_{in}(t) - v(t)^{\frac{1}{w}}\right) \end{cases}$$

The system of ordinary differential equations is linearized, as Khalidov et al. did in [6], to obtain a physiologically-inspired linear operator that links the BOLD or Hemodynamic Response Function (BRF or HRF) to the Perfusion Response Function (PRF).

$$\boldsymbol{\Omega}$$



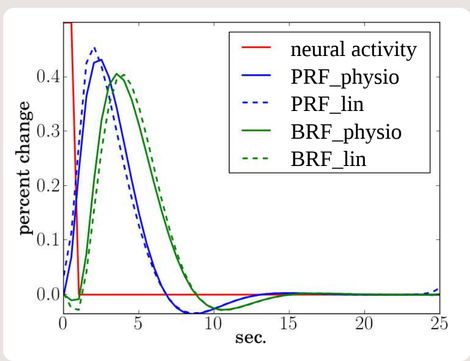
$$h(t) = V_0[k_1(1-q(t)) + k_2(1-\frac{q(t)}{v(t)}) + k_3(1-v(t))]$$
$$\approx 0.9b(1-q(t) - 0.1b(1-v(t)))$$

$$g(t) = f_{in}(t) - 1$$

$$\boxed{\mathbf{g} = \boldsymbol{\Omega}\mathbf{h}}$$

condition number
$cond(\boldsymbol{\Omega}) = 1.745$

Behaviour of the linear operator $\boldsymbol{\Omega}$, considering response functions generated with the physiological model:



$$\boldsymbol{h}_{lin} = \boldsymbol{\Omega}^{-1}\boldsymbol{g}_{physio}$$
$$\boldsymbol{g}_{lin} = \boldsymbol{\Omega}\boldsymbol{h}_{physio}$$

Model estimation and first results

Physiologically informed Bayesian analysis of ASL fMRI data

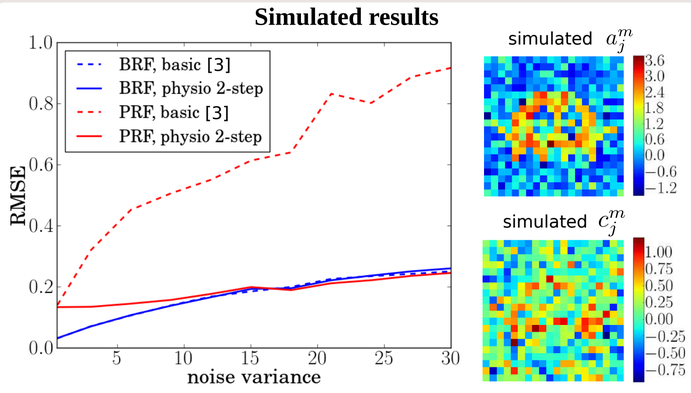
Step $\mathcal{M}_1$:
Hemodynamics estimation, by filtering out the perfusion component (ie $\boldsymbol{C} = \boldsymbol{0}, \boldsymbol{g} = 0$). The ASL signal and the residuals $\boldsymbol{r}$ read: $\forall\, j = 1:J$,

$$\boldsymbol{y}_j = \sum_{m=1}^{M} a_j^m \boldsymbol{X}^m \boldsymbol{h} + \boldsymbol{P}\boldsymbol{\ell}_j + \alpha_j \boldsymbol{w} + \boldsymbol{b}_j^{\mathcal{M}_1}$$
$$\boldsymbol{r}_j = \boldsymbol{y}_j - \sum_{m=1}^{M} \widehat{a}_j^{m,\mathcal{M}_1} \boldsymbol{X}^m \widehat{\boldsymbol{h}}^{\mathcal{M}_1} - \boldsymbol{P}\widehat{\boldsymbol{\ell}}_j^{\mathcal{M}_1}$$

Step $\mathcal{M}_2$:
From $\boldsymbol{r}$, the perfusion component is extracted by using the HRF estimate exhibited in step 1 ($\boldsymbol{g} = \boldsymbol{\Omega}\widehat{\boldsymbol{h}}^{\mathcal{M}_1}$, $\boldsymbol{A} = \boldsymbol{0}$). $\forall\, j = 1:J$,

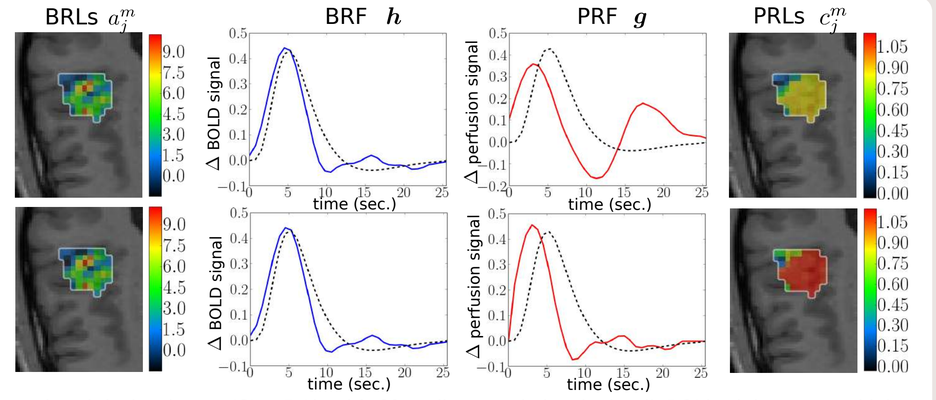
$$\boldsymbol{r}_j = \sum_{m=1}^{M} c_j^{m,\mathcal{M}_2} \boldsymbol{W}\boldsymbol{X}^m \boldsymbol{\Omega}\widehat{\boldsymbol{h}}^{\mathcal{M}_1} + \alpha_j \boldsymbol{w} + \boldsymbol{b}_j^{\mathcal{M}_2}$$

Simulated results



RMSE for the BRF and PRF computed by using the two JDE versions, wrt noise variance ranging from 0.5 to 30. The PRF estimation has been improved, wrt the ground truth, for very low SNR situations.

Real data



Paradigm fast event-related design (mean ISI = 5.1), with 60 auditory and visual stimuli. ROI in right temporal lobe. The effect of the physiologically-inspired regularization yields a more plausible PRF shape for the 2-steps approach. Results on PRL maps seem to highlight a better sensitivity of the proposed approach.

Conclusion

ASL fMRI data analysis has been performed by considering a physiological link between the CBF and BOLD components embedded in the ASL signal, which allows to retrieve more physiologically plausible PRF and HRF shapes.

Perspectives

- Deeper analysis of the validity of the link between PRF/HRF.
- Quantification of ASL fMRI data.
- Larger validation (ie whole brain analysis), and BOLD/ASL comparison on the same experimental paradigm and the same individuals.

References

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