A Probabilistic Approach to Model-Free Arterial Spin Labeling Perfusion Quantification

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Introduction: Arterial Spin Labelling (ASL) offers measurements of cerebral perfusion that can be made non-invasively using MRI. Multi inversion time ASL data is commonly analysed by the fitting of the time series data to a kinetic curve model. However, the estimates produced from this method are highly dependent upon the model chosen, which is a particular concern in pathological tissue where the assumptions made become invalid. An alternative 'model-free' approach, used in Dynamic Susceptibility Contract (DSC) MRI, has been previously applied to ASL [1]. This method assumes that the signal is the result of a convolution between an arterial input function *AIF*, representing the temporal shape of the incoming contrast, and a residue function *r* that describes the fraction of contrast that remains after a time *t*:

$$y_j(t) = f_j g(AIF \otimes r)(t) = f_j \int_0^t AIF(t-\tau) r(\tau) d\tau ,$$

where the magnitude f_j is a measure of the perfusion in voxel *j*. The advantage of this approach is that it makes fewer assumptions than a model-based method, since the residue function is extracted from the data using AIF also derived from the patient. In this work we present an improved approach to model-free analysis for ASL data, based on a probabilistic approach to the deconvolution problem. This allows us to retain the freedom of the model-free method, whilst incorporating appropriate prior information such as the smoothness of *r*. Additionally, we use information about the blood transit time to improve the selection of AIF in a similar manner to [2].

Methods: A number of methods exist to perform deconvolution, the main one in use for DSC MRI is Singular Value Decomposition (SVD) [3]. To regularise the solution in the face of ill-conditioning, the smallest singular values, those smaller than 10% of the largest value, are typically discarded [3]. This regularization, however, tends to introduce oscillations in the shape of the residue function, making it inaccurate. A Bayesian approach to deconvolution has more recently been proposed [4], however this relied on parameterised residue function shape. We propose an alternative solution to the deconvolution problem based on deconvolution of the haemodynamic response function in fMRI [5]. Like previous approaches, in our probabilistic method, we adopt the matrix form of the convolution equation:

$$\mathbf{y}_j = f_j \mathbf{X}\mathbf{r} + \mathbf{e}_j ,$$

where the matrix **X** represents the AIF such that **Xr** represents the discrete from of the convolution of the AIF with the residue function. In the equation we also include the corruption of the data by additive white noise **e**. No functional form is assumed for the residue function; instead it is subjected to a Gaussian prior for the norm of its second derivative. This incorporates the assumption that the residue function is temporally smooth, as encoded by a temporal correlation matrix with an adaptive amount of smoothing, which itself is estimated from the data. In this formulation the residue functions were determined across defined regions, as opposed to SVD where this is performed on a voxelwise basis. Our approach assumes that the residue function is homogeneous across each defined region, although the perfusion can vary from voxel to voxel. This approach increases the robustness of the residue function estimation in the face of poor signal-to-noise ratio. For this study cubic regions were defined with a length of 5 voxels per side, as illustrated in Fig. 1 (right). The generative and noise models are combined with the prior information on the different unknown parameters of the model via Bayes' theorem. The parameters of interest are then estimated from the joint posterior distribution using Gibbs sampling.

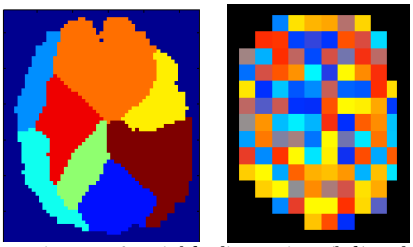

Figure 1: Arterial feeding regions (left) and regions used for residue function evaluation (right) in middle slice.

The model free approach to perfusion analysis requires an AIF to be identified for each voxel. In this work we extracted the arterial signal directly from ASL images collected without flow suppression. An alternative approach would be to collect images with and without flow suppression and get arterial information from the difference [1]. Signal from arteries within the image were identified: voxels with intensities in the top 0.5% of the mean image. These were then clustered into interconnected groups and those with fewer than 5 members discarded. The remaining groups were considered to represent arterial segments for the determination of feeding regions (below). The AIF to be used in voxels within each feeding region was determined as the mean shape within the group.

Ideally the AIF used in a particular voxel should come from a vessel that feeds the tissue contained in that voxel. A number of approaches have been used to determine from where each voxel should source its AIF. In this analysis we use a method that incorporates both Euclidean distance and arrival time information in a similar manner to [2]. We use the time-to-half-integral as a robust relative measure of arrival time. This arrival time information is then used to create a local 'speed of flow' map. This can then be used to gauge the time taken for the blood to travel from each arterial group to each voxel using a shortest path analysis [7]. Thus the brain can be divided up into feeding regions associated with each arterial segment, shown in Fig. 1 (left).

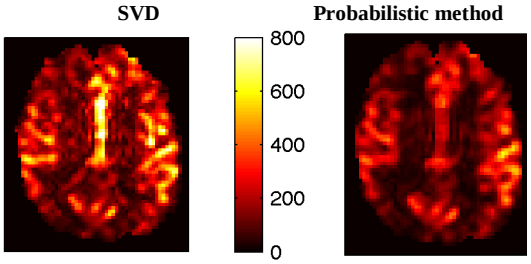

Figure 2: Maps of perfusion, f, for middle slice.

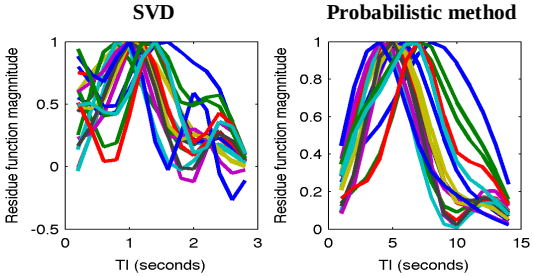

Figure 3: Residue functions in a selection of regions in middle slice.

Results: The method was applied to ASL data acquired using the GRASE sequence [8] at 1.5 T with 14 inversion times (200 to 2800 ms with 200 ms interval). The perfusion maps resulting from both SVD and the Bayesian method are shown in Fig. 2, with the residue function in selected regions in Fig. 3 (for the SVD results this is the average over the estimated residue functions in that region).

Discussion: The primary advantage of our probabilistic approach to mode-free ASL is that the residue function can be estimated without the need to define the residue function shape *a priori*. At the same time temporal smoothness can be enforced, thus avoiding the artefacts common in an SVD approach, as seen in Fig. 3. Thus it is feasible to extract the residue functions from the data even in the face of pathological changes to the shape.

The main area of discrepancy between the methods arises in the perfusion estimates, as seen in Fig. 2. This arises because the regions used here for the residue function estimation are not chosen to reflect the underlying structure of the brain and contain a relatively large number of voxels. Thus a future implementation of this method will use smaller and more locally defined regions for residue function estimation. The Bayesian Framework will also permit more sophisticated spatially regularised voxelwise residue functions in the future. The final algorithm will provide a method for the model-free analysis of ASL data, which is genuinely robust to pathological changes in brain tissue, enhancing the clinical applicability of ASL.

References

1. Petersen, E.T., *et al.*, Magn. Reson. Med., 2006. **55**(2): p. 219-232.
2. Christensen, S., *et al.* in *ISMRM*, 2007. Berlin.
3. Østergaard, L., *et al.*, Magn. Reson. Med., 1996. **36**(5): p. 715-725.
4. Mouridsen, K., *et al.*, NeuroImage, 2006. **33**(2): p. 570-579.
5. Makni, S., *et al.*, IEEE Trans. Sig. Proc., 2005. **53**(9): p. 3488-3052.
6. Tzourio-Mazoyer, N., *et al.*, NeuroImage, 2002. **15**: p. 273-289.
7. Tsitsiklis, J.N., IEEE Trans. Automatic Control, 1995. **40**: p. 1528-1538.
8. Günther, M., *et al.*, Magn. Reson. Med., 2005. **54**(2): p. 491-498.