A General Framework for the Analysis of Vessel Encoded Arterial Spin Labelling

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Introduction: Vessel Encoded Arterial Spin Labelling (VE-ASL) [1,2] is a non-invasive MR method for vascular territory imaging. Unlike other selective ASL techniques [3-5] that seek to label individual or groups of vessels over a number of acquisitions, VE-ASL spatially modulates the ASL label so that over multiple cycles the signal from each one is uniquely encoded. Thus, data acquisition is more efficient since some signal will be received from every vessel during each cycle. Appropriate analysis permits the different contributions to be resolved and vascular territories visualised. Two main approaches for analysis have emerged: the inversion of the encoding matrix that describes the labelling process [2,6] or voxelwise clustering of the data across the cycles [6]. The former exploits known information about the encoding setup, but requires sufficient encoding cycles if complete information about the territories is to extracted. Clustering, however, classifies each voxel to a single source artery making it more robust, but is poor in areas that receive mixed supply from multiple arteries, such as in watershed regions. In this work we derive a general probabilistic framework for VE-ASL analysis that combines and extends the advantages of both approaches.

Methods: The VE-ASL signal in a voxel can be described in matrix form as $\mathbf{s}=\mathbf{Ef}$, with $\mathbf{s}$ the vector of signals over multiple encoding cycles, $\mathbf{f}$ a vector of flow as supplied by each of the labelled arteries plus the static tissue contribution, and $\mathbf{E}$ the encoding matrix describing the contribution of each artery during each acquisition cycle. This vector equation can be inverted to provide flow territory estimates from every artery in every voxel. The entries in $\mathbf{E}$ depend on the geometry of the spatial modulations employed and the relative location of the arteries being labelled. Previously a sinusoidal modulation has been assumed to estimate the true encoding matrix [6]. We derived a general formula for an entry in $\mathbf{E}$ based upon the geometry and a theoretical description of the VE-ASL encoding profile obtained from simulation using the Bloch equations. The encoding matrix, however, can be ill conditioned (depending upon the number of cycles) leading to inaccurate territory separation. Clustering of voxels that have similar signal over the encoding cycles is an alternative, but makes the assumption that each voxel is fed by only a single artery, making flow estimates inaccurate in mixed supply areas. Within our framework classification is employed in place of clustering permiting the encoding matrix to be retained. Classification provides the option to employ an assumption of two (or more) arteries supplying any voxel, with the classification being performed over every combination of labelled arteries. The important advantage of introducing classification alongside the encoding matrix is that when there are insufficient encoding cycles to form a well-conditioned encoding matrix overall, the subsets of the encoding matrix implicitly defined by each class are well conditioned. To reach an optimal solution it was necessary to solve for vessel locations and the classification together. To do this we took a probabilistic approach, assuming white additive noise to form the likelihood and applying Bayes theorem. Uninformative priors were specified for the vessel flow and Automatic Relevancy Determination (ARD) priors [7] for the proportions of each class and the vessel locations. The ARD priors provided data driven reduction of complexity, such that unnecessary classes were removed and in the case of poor data quality the vessel location resort to pre-specified values derived from the acquisition.

To test the method, simulated data were generated for a VE-ASL experiment with 6 cycles (tag, control, 2 anterior-posterior and 2 left-right encodings as used in [2]), the flow territories are shown in the top row of Figure 1 for four vessels with locations placing them at the corners of a square. This was subjected to the following analyses: **MI**, matrix inversion using assumed vessel locations; **GMM**, Gaussian mixture model clustering (similar to [6]); **GF1** and **GF2**, using the general framework presented here with 1 or 2 vessels in each class respectively. The same analyses were applied to VE-ASL data acquired with the same 6 cycles from a healthy subject. Finally the probabilistic method was also applied to a further dataset for labelling of vessels above the Circle of Willis (CoW) with 24 cycles (6 tag, 6 control, 4 anterior-posterior, 2 left-right).

Results: Figure 1 shows the results from the simulated data. Separation of territories was poor for MI analysis since too few encoding cycles were employed to make the matrix well conditioned. GMM clustering did not suffer the same difficulties, but was unable to resolve all the separate territories due to substantial areas of overlap between the lower three. GF1 more closely represented the true territories, but was unable to correctly estimate mixing in areas where the territories overlapped. GF1 is essentially a form of probabilistic clustering, since it assumes each voxel is sourced from only a single artery. However, GF2 allows for two arteries to supply each voxel and thus its results more closely matched the true territories, only being limited in the few regions where three territories mixed. Similar comparative results emerged from analysis of the real data, Figure 2: MI was unable to fully separate the individual territories, though plausible colour coded territory images were produced when colouring based on the major contribution in each voxel. GMM clustering gave much clearer separation of flow within individual territories, but was thrown by mixing in the posterior territories. GF2 could resolve individual territories and indicated that there was some mixing between the left and right vertebral territories in this subject. Figure 3 shows the analysis from labelling above the CoW where GF2 estimated anatomically plausible territories, with good separation observed in individual images (not shown) and evidence of territory overlap in watershed areas.

Discussion: The extent of territory overlap in the simulated data is extreme compared to that expected in the brain, hence the particularly poor performance of the clustering method. However, experience with real data suggests that mixed supply areas are an issue in practice as seen here in Figure 2. While we acknowledge that the most advanced clustering methods have not been applied here, simple clustering is ultimately limited by the one artery per voxel assumption. In contrast, our framework generalises clustering to a multi-source classification that is better suited to this problem. For most VE-ASL data acquired thus far, direct inversion of the encoding matrix is ill-conditioned, in practice this could be avoided in future by routinely acquiring more encoding cycles. The analysis proposed here would still offer benefits, as it would produce more accurate perfusion estimates in the face of low SNR by virtue of considering parts of the full encoding matrix in turn.

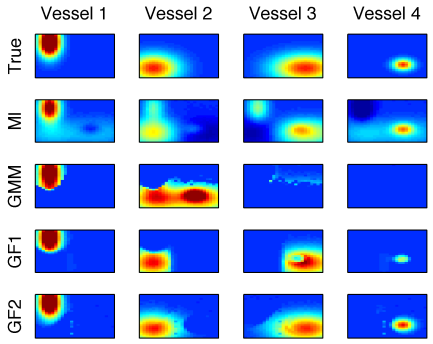

Figure 1: Simulated data results for the various analyses, showing individual perfusion supplied by each vessel within same square region.

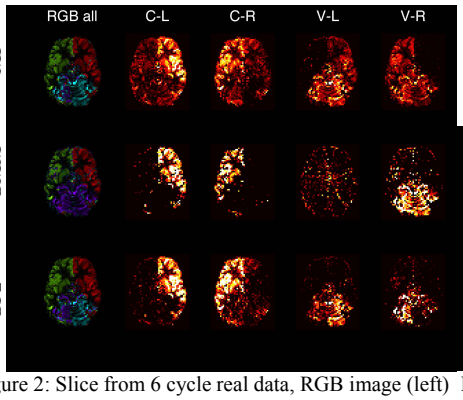

Figure 2: Slice from 6 cycle real data, RGB image (left) based on vessel with largest contribution to voxel, individual artery contribution to each voxel (right).

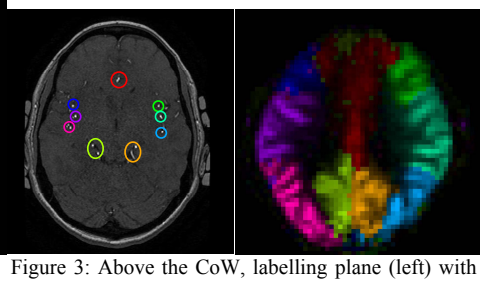

Figure 3: Above the CoW, labelling plane (left) with vessels marked, perfusion territories (right) colours indicate artery with largest contribution to each voxel.

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