Non-Parametric Quantification of Cerebral Haemodynamics from Dynamic Susceptibility Contrast MRI

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Introduction: DSC-MRI analysis is based on Tracer Kinetic Theory and typically involves the deconvolution of the observed signal with an arterial input function, which is an ill-posed inverse problem. The current standard Singular Value Decomposition (SVD) method [1] and its time insensitive variant oSVD [2], typically underestimate perfusion and introduce non-physiological oscillations into the resulting residue function. An alternative vascular model (VM) [3] based method permits only a restricted family of shapes for the residue function that may not be appropriate in pathologies like stroke. The goal therefore of this work was to develop a deconvolution algorithm that produces accurate perfusion values whilst estimating the residue function over a wide range of practical physiological and pathological conditions. Here we propose a novel deconvolution method that can estimate cerebral perfusion along with a physiologically plausible residue function without requiring it to belong to a specific class of functional shapes.

Figure 1: Compensating for delay in AIF and estimating the shape of residue function with control points. The convolution result is scaled with estimated CBF to generate CTC.

Material and Methods: In the proposed method, the residue function was estimated from a number of control points (Fig. 1) that form the basis of a smooth piecewise cubic spline interpolation. Each control point had two degrees of freedom, being allowed to vary in both amplitude and time. The control point parameters were estimated along with flow and bolus delay using a Bayesian non-linear model fitting algorithm [4]. Each consecutive control point was related to its precursor by a ratio factor that was determined by the optimization algorithm and priors were provided to encourage a smooth monotonically decreasing function. Non-informative priors were provided for flow and bolus delay. The method was initialised with an exponential residue function and flow and bolus delay values from oSVD (maximum of the oSVD solution).

Simulations were performed with a Cerebral Blood Volume (CBV) of 4ml/100g, Cerebral Blood Flow (CBF) in the range 10-70 ml/100g/min, delay of 0 and ±5 sec, and three residue functions: exponential, linear & box. Concentration time curves (CTC) were generated as in [1] to which Gaussian noise was added to achieve an SNR of 20. For each combination of CBF, residue function and delay a total of 100 CTC were generated. Non-linear regression coefficients were calculated for the comparison of models from the simulated data. Data from one clinical patient with an underlying atherosclerotic disease was included for empirical validation. Acquisition was performed on Siemens Trio at 3 T, GRE-DSC:TR/TE=1.5sec/30msec, 128x128x78 matrix, 1.7x1.7x5mm^3 voxels. The simulation and clinical results were compared with oSVD [2] and the vascular model [3].

Results: Figure 2 shows that the shapes of the estimated residue function from the method proposed were in good agreement with the simulated shape with no oscillations, while the oSVD solution was highly oscillatory. Figure 3 shows absolute vs. estimated flow for an exponential residue function, lower flow values being estimated accurately by all the three methods. Higher flow values were underestimated substantially by oSVD (R^2_{exp}= 0.65), VM showed less bias (R^2_{exp}= 0.86), with the proposed method showing best correlation across all flow values (R^2_{exp}= 0.98) (R^2_{exp}: regression coefficient for estimated vs. absolute simulated flows with exponential residue function). The method was delay insensitive for
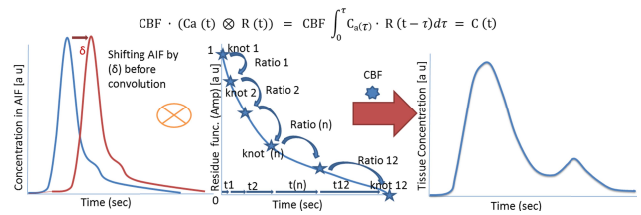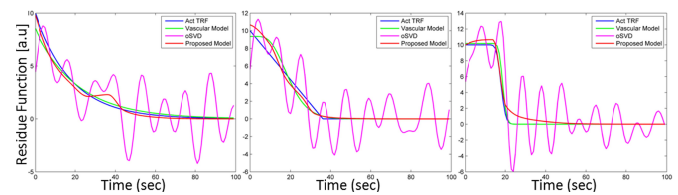

Figure 2: Simulated Exponential, Linear and Box residue function shapes (left to right) and estimated shape using oSVD, VM and Proposed method.
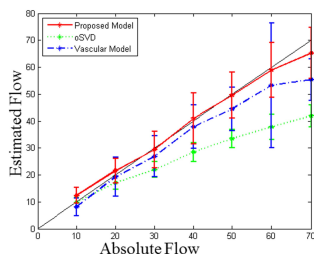
bolus arrival (Fig. 4). Clinical data analysis (Fig. 5) revealed similar results showing non-physiological oscillations in the residue function and lower estimation of flow by SVD (Fig. 5a) compared to the other methods (Fig. 5b-c). The proposed method and VM solutions were smooth with comparable flow estimates (Fig. 5d).

Discussion: Estimation of residue function shape is critical if one is to estimate flow heterogeneity and bolus dispersion [5]. Our approach was to estimate the tissue response function at a subset of points and then use cubic spline interpolation to generate the complete smooth function. Thus the approach is less sensitive to number of CTC sample points (TR) than other methods. For *in vivo* analysis the actual residue function shape is not known *a priori* and, particularly in pathology, may not be drawn from the set of functions currently assumed for typical residue functions, hence analysis with a non-parametric approach is desirable. Our method offers an effective non-parametric residue function shape estimation avoiding the strict model-based assumptions of the VM method. However, the constraints impose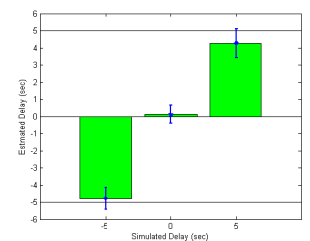d by the control point formulation ensure that physiologically realistic smooth functions are estimated unlike the oscillations seen in the SVD based method.

Figure 3: Simulated Abs. Flow vs. Est. Flow using oSVD, VM and Proposed model for exponential residue function.

Figure 4: Simulated bolus arrival delay (0 & ±5sec) vs. estimated delay.

Reference: [1] L. Ostergaard et al, *Magnetic Resonance in Medicine*, vol. 36, no. 5, pp. 715-25, Nov. 1996. [2] O. Wu et al, *Magnetic Resonance in Medicine*, vol. 50, no. 1, pp. 164-74, Jul. 2003. [3] K. Mouridsen et al, *NeuroImage*, vol. 33, no. 2, pp. 570-9, Nov. 2006. [4] M. a Chappell et al, *IEEE Transactions on Signal Processing*, vol. 57, no. 1, pp. 223-236, Jan. 2009. [5] L. Ostergaard et al, *Journal of Cerebral Blood Fow and Metabolism*, vol. 19, no. 6, pp. 690-9, Jun. 1999.
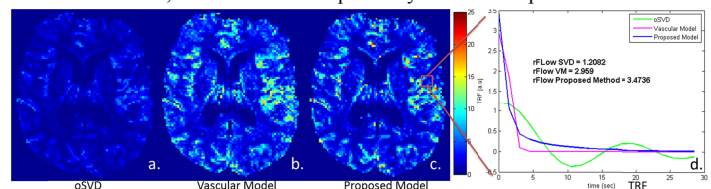
Figure 5: Axial slice of brain showing flow maps with three methods and corresponding residue functions from one voxel.