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Clustering-based deconvolution of brain CT perfusion data

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Abstract: Computed Tomography Perfusion (CTP) imaging relies on robust deconvolution methods to estimate kinetic parameters, from separation of the arterial input function and residue (i.e. tissue retention) function. While techniques based on singular value decomposition (SVD) provide computational efficiency, their lack of physiological constraints on the residue function can reduce accuracy of perfusion parameter estimation. We propose a clustering-based deconvolution framework, representing voxel-level time density curves (TDCs) as linear combinations of physiologically informed basis functions. Features extracted from TDCs guide optimal basis selection via clustering, which mitigates the high noise inherent in individual voxels, while non-negative linear least-squares and grid-search are used to estimate physiological parameters of interest. Results demonstrate improved stability and alignment with physiological expectations.

Keywords: CT Perfusion; Kinetic Analysis; Clustering; Stroke

1 Introduction

Computed Tomography Perfusion (CTP) imaging is a widely used functional imaging technique to evaluate blood circulation in the brain. A critical aspect of CTP analysis is the estimation of quantitative parameters maps of blood flow (CBF), blood volume (CBV), and mean transit time (MTT), which involves solving an ill-posed deconvolution problem to separate the arterial input function $C_a(t)$ (tracer delivery) and residue function $R(t)$ (tracer retention in tissue). One commonly used approach to this end is the Singular Value Decomposition method. SVD-based techniques, such as block-circulant SVD and Tikhonov regularization, have significantly improved the robustness of deconvolution in perfusion imaging. However, SVD

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approaches do not incorporate physiological assumptions on tracer kinetics, which can limit the accuracy and physiological relevance of the derived residue functions. To address these limitations, kinetic models have been developed that explicitly describe the transport and exchange of contrast agents between intravascular and extravascular spaces. Such models refine kinetic quantification by integrating assumptions on tracer kinetics, summarised in terms of tissue diffusion properties. To mitigate the high noise of voxel-level CTP data (Figure 1C), our approach incorporates a clustering step that aggregates voxels with similar patterns.

2 Methods

The tissue concentration curve $C_T(t)$ (in homogeneous tissue) is typically modelled as the convolution of the arterial input function (AIF) $C_a(t)$ with the tissue residue function $R(t)$, scaled by blood flow F, as

$$C_T(t) = \int_0^t R_F(t-s)C_a(s)ds. \tag{1}$$

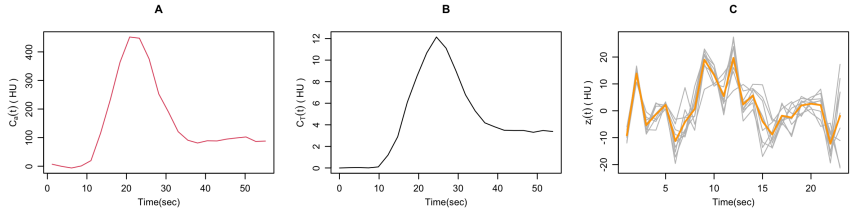

FIGURE 1. **(A)** Arterial input function $C_a(t)$. **(B)** Average time diffusion curve (TDC) across multiple slices of the brain. **(C)** Voxel-level TDCs ($Z_i(t)$, in grey), and mean TDC of nine neighbouring voxels (in orange).

2.1 Kinetic Models

As described by Chung *et al* (2023), residue function of the Adiabatic Approximation to Tissue Homogeneity (AATH) model is expressed as

$$R_F(t) = \begin{cases} 0, & 0 \le t < T_0 \\ F, & T_0 \le t < T_0 + T_c \\ EF\, e^{-\frac{EF}{V_e}(t-T_c)}, & t \ge T_0 + T_c \end{cases} \tag{2}$$

where T_0 is the delay time between the AIF and TDC, $T_c = \frac{V_i}{F}$ is the capillary transit time, and E (with $0 \le E \le 1$) represents the fraction of tracer that is extracted into the extravascular space during a single capillary transit. From these, rate constants $k_1 = EF$ and $k_2 = \frac{EF}{V_e}$ determine the exchange between intra-vascular and extra-vascular spaces. When T_c

is close to 0, the capillary transit time may be approximated by a delta function, and the residue function $R_F(t)$ reduces to that of Kety (1951). Furthermore, in the special case of irreversible leakage (i.e., $k_2 = 0$), the residue function simplifies to a constant value of EF for $t \geq T_c$.
The plug flow model (Chung *et al*, 2023) assumes that blood moves as a uniform plug through the vasculature, that all elements of the contrast agent travel at the same velocity without dispersion. While this plug flow model offers an intuitive interpretation of perfusion parameters, it may thus oversimplify complex perfusion dynamics.

2.2 Clustering-Based Deconvolution

CTP voxel-level data are highly noisy, as shown in Figure 1(c). Direct kinetic modelling on such data may introduce bias. To address this, inspired by O'Sullivan (2006), we represent the voxel-level time density curve $z_i(t)$ of heterogeneous tissue at a given location i as a linear combination of K basis elements $\mu_k(t) = \int_0^t R_k(t-s)C_a(s)ds$, $k = 1, \ldots, K$, using as many cluster residue functions $R_k(t)$, such that

$$z_i(t) = \sum_{k=1}^{K} \alpha_{ik}\mu_k(t) + \epsilon(t). \tag{3}$$

To obtain the cluster residue functions $R_k(t)$, we first extract features from the time density curve for each voxel (Figure 2). Silhouette scores and total within-cluster sum of squares are used to optimise K. A clustering-based approach (e.g., k-means) is employed to obtain the basis elements. The form of residue functions R_k used in this paper is derived from two models: the AATH irreversible model and the plug flow model. The parameters associated with R_k are obtained via nonlinear optimization, and optimal coefficients α_{ik} via non-negatively constrained linear least-squares.

3 Results

A set of feature maps from a case study on stroke data collected at Cork University Hospital is presented in Figure 2. Output delay and blood flow maps effectively delineate the injured regions with clear contrast, as shown in Figure 3, along with parameters μ_k and their distributions in the brain.

4 Discussion

Clustering-based deconvolution of voxel-level CTP data helps mitigate their noisy nature, by aggregating spatially and kinetically coherent voxels into clusters prior to kinetic analysis, to improve final kinetic mapping. Future work will focus on incorporating more elaborate kinetic models and refining clustering to better retain more complex perfusion dynamics.

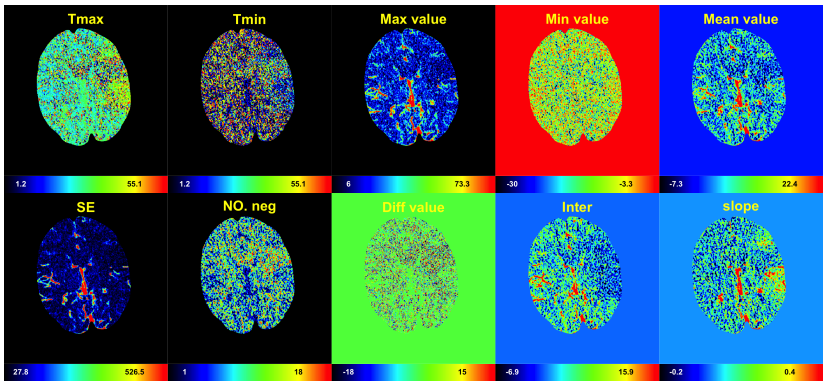

FIGURE 2. An example of extracted feature maps.

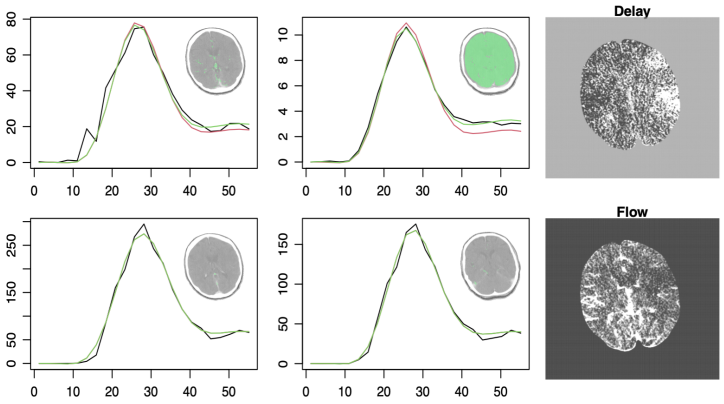

FIGURE 3. $K = 4$ mean cluster TDCs and kinetic maps for delay and flow.

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