Analysis of Dynamic Perfusion MRI Data by Neural Networks

Axel Wismüller[1], Oliver Lange[1],
Dominik R. Dersch[2], Klaus Hahn[1],
and Gerda L. Leinsinger[1]

[1]Institut für Radiologische Diagnostik,
Ludwig-Maximilians-Universität München,
Klinikum Innenstadt, Ziemssenstr. 1, 80336 München, Germany
e-mail: Axel.Wismueller@physik.uni-muenchen.de
[2]Hypovereinsbank AG, München, Germany

Abstract.

We present a neural network clustering approach to the analysis of dynamic cerebral contrast-enhanced perfusion magnetic resonance imaging (MRI) time-series. In contrast to conventional extraction of a few voxel-based perfusion parameters alone, neural network clustering does neither discard information contained in the complete signal dynamics time-series nor is its interpretation biased by the indicator-dilution theory of non-diffusible tracers, which may not be applicable under pathological conditions of a disrupted blood-brain barrier. We performed exploratory data analysis in patients with cerebrovascular disease. Minimal free energy vector quantization provided a self-organized segmentation of voxels w.r.t. fine-grained differences of signal amplitude and dynamics, thus identifying different vessel sizes, side asymmetries and local deficits of brain perfusion. We conclude that neural network clustering can provide a useful extension to the computation of conventional perfusion parameter maps. Thus, it can contribute to the analysis of cerebral circulation by non-invasive neuroimaging.

1.   Introduction

Cerebrovascular diseases are among the leading causes of illness and death in the industrial countries. The analysis of cerebral circulation, therefore, is an issue of enormous clinical importance.

Dynamic susceptibility contrast material-enhanced gradient echo MRI provides a non-invasive method for cerebrovascular perfusion analysis. It enables high spatial and temporal resolution and avoids the disadvantage of patient exposure to ionizing radiation. After intravenous bolus administration of a non-diffusible paramagnetic substance such as gadolinium, brain perfusion can be studied by observing, as a function of time, the contrast agent-induced changes of proton magnetic properties. In theory, perfusion parameters such as regional

cerebral blood flow (rCBF), regional cerebral blood volume (rCBV), and mean transit time (MTT) can be calculated from the resulting tissue concentration-time curves. For this purpose, the indicator dilution theory for nondiffusible intravascular tracers is used. Besides other constraints, its applicability implies strict intravascular presence of the indicator substance which requires an intact blood-brain barrier. This prerequisite is fulfilled in examinations of healthy subjects. In patients suffering from tumors or stroke, however, the presence of an intact blood-brain barrier is questionable. Therefore, the applicability of model-based theoretical concepts of flow quantification is limited in clinical practice.

In this paper, we present an approach to the analysis of perfusion MRI data that does not imply speculative presumptive knowledge on contrast agent dilution models, but strictly focusses on the observed complete MRI signal time-series. Neural network clustering enables a self-organized data-driven segmentation of dynamic contrast-enhanced perfusion MRI time-series w.r.t. fine-grained differences of signal amplitude and dynamics, such as side asymmetry and local deficits of brain perfusion in patients with stroke, thus providing a useful extension to the computation of conventional perfusion parameter maps. As a result, we obtain both a set of prototypical time-series and a corresponding set of pixel clusters. The inspection of these clustering results provides a practical tool for the neuroradiologist to quickly scan the data set for regional differences or abnormalities of brain perfusion.

2.   Methods

2.1.   Clustering Algorithm

Let n denote the number of subsequent scans in a dynamic perfusion MRI study. Let K denote the number of pixels in each scan. The dynamics of each pixel $\nu \in \{1, \dots, K\}$, i. e. the sequence of signal values $x^{\nu}(\tau)$ over all scan acquisition time frames τ can be interpreted as a vector $\mathbf{x}^{\nu} \in \mathbb{R}^{n}$ in the n-dimensional feature space of possible signal time-series at each pixel (Pixel Time Course, PTC). Clustering identifies N groups j of pixels with similar PTCs denoted by the index $j \in \{1, \dots, N\}$. These groups or clusters are represented by prototypical time-series called Codebook Vectors (CVs) $\mathbf{w}_{j}$ located at the center of the corresponding clusters. VQ procedures determine these cluster centers by an iterative adaptive update according to

$$\mathbf{w}_{j}(t+1) = \mathbf{w}_{j}(t) + \epsilon(t)\, a_{j}\left(\mathbf{x}(t), W(t), \kappa\right)\left(\mathbf{x}(t) - \mathbf{w}_{j}(t)\right), \qquad (1)$$

where $\epsilon(t)$ denotes a learning parameter, a_{j} a so-called cooperativity function which, in general, depends on the codebook $W(t)$, a cooperativity parameter κ, and a, in general, randomly chosen feature vector $\mathbf{x} \in \{\mathbf{x}^{\nu}|\nu \in \{1, \dots, K\}\}$. In the context of perfusion MRI data analysis, one should clearly note the difference between the time τ of the time-series representing a specific component of the feature vector $\mathbf{x}^{\nu}$ and the time t which denotes the iteration step of the

VQ procedure. In the fuzzy clustering scheme proposed by Rose, Gurewitz, and Fox [4], the cooperativity function a_j reads

$$a_j(\mathbf{x}(t), W(t), \kappa \equiv \rho(t)) = \frac{\exp(-E_j(\mathbf{x}(t))/2\rho^2)}{\mathcal{Z}}. \qquad (2)$$

Here, the 'energy' $E_j(\mathbf{x}(t)) = \|\mathbf{x}(t) - \mathbf{w}_j(t)\|^2$ measures the distance between the codebook vector $\mathbf{w}_j$ and the data vector $\mathbf{x}$. $\mathcal{Z}$ denotes a partition function given by $\mathcal{Z} = \sum_j \exp(-E_j(\mathbf{x})/2\rho^2)$ and ρ is the cooperativity parameter of the model. This so-called 'fuzzy range' ρ defines a length scale in data space and is annealed to repeatedly smaller values in the VQ procedure. Noting the analogy to statistical mechanics, ρ can be interpreted as the temperature T in a multiparticle system by $T = 2\rho^2$ [4]. The learning rule (1) with a_j given by (2) describes a stochastic gradient descent on the error function

$$F_\rho(W) = -\frac{1}{2\rho^2} \int P(\mathbf{x}) \ln \mathcal{Z} d^n x, \qquad (3)$$

which is a free energy in a mean-field approximation [1]. Here, $P(\mathbf{x})$ denotes the probability density of feature vectors $\mathbf{x}$. For the minimal free energy VQ procedure, the codebook vectors mark local centers of this multidimensional probability distribution. Thus, for the application to perfusion MRI signal analysis, the codebook vector $\mathbf{w}_j$ is the weighted average perfusion MRI signal of all the PTCs $\mathbf{x}$ belonging to group j with respect to a fuzzy tesselation of the feature space.

For mathematical details as well as a thorough discussion of application issues with regard to medical image analysis using neural networks, we refer to [8]. Functional MRI data analysis employing minimal free energy clustering has been presented previously [5], [6], clustering approaches using other algorithms can be found e.g. in [2], [3].

2.2. Imaging Protocol

Dynamic susceptibility contrast-enhanced perfusion weighted MRI was performed on a 1.5 T system (Magnetom Vision, Siemens, Erlangen, Germany) using a 2D gradient echo echoplanar imaging (EPI) sequence employing 10 transversal slices with a matrix size of 128×128 pixels, pixel size $1.88 \times 1.88 \, \text{mm}$, and a slice thickness of $3.0 \, \text{mm}$ (TR = $0.8 \, \text{ms}$, TE = $0.54 \, \text{ms}$, FA = $90°$). The dynamic study consisted of 38 scans with an interval of $1.5 \, \text{s}$. The perfusion sequence and an antecubital vein bolus injection (injection flow $3 \, \text{ml/s}$) of gadopentetate dimeglumine ($0.15 \, \text{mmol/kg}$ body weight, Magnevist™, Schering, Berlin, Germany) were started simultaneously.

3. Results

Clustering results for a 38 scan dynamic contrast-enhanced MRI perfusion study in a patient with a subacute stroke affecting the right basal ganglia are presented in figs. 1 and 2.
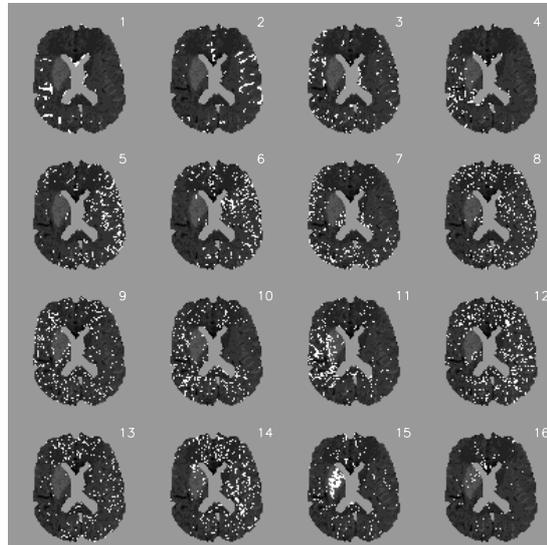
Figure 1: Cluster assignment maps for minimal free energy vector quantization of a dynamic perfusion MRI study in a patient with stroke in the right basal ganglia.
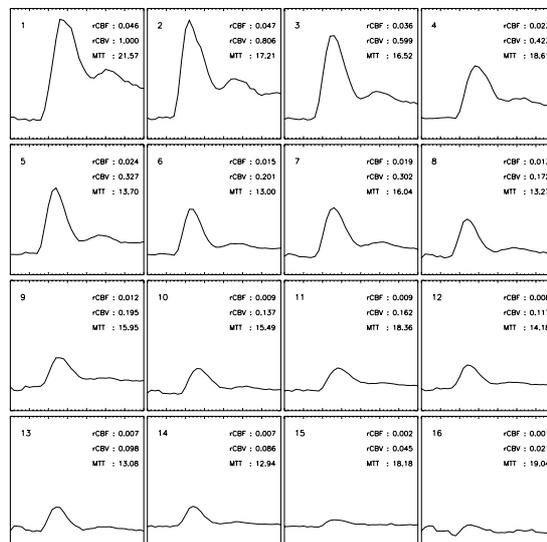
Figure 2: Cluster-specific concentration-time curves of the same perfusion study as in fig. 1. Cluster numbers correspond to fig. 1. Cluster-specific MTT values are indicated as multiples of the scan interval (1.5 s), rCBV values are normalized w.r.t. the maximal value (cluster #1).

Fig. 1 shows the 'cluster assignment maps' overlaid onto an EPI scan of the perfusion sequence, fig. 2 the CVs belonging to the pixel clusters of fig. 1.

The region of the cerebrovascular insult in the right basal ganglia is clearly depicted by cluster #15. Note the small corresponding CV amplitude. Cluster #11 contains peripheral and adjacent regions. Clusters #1, #2 represent larger vessels located in the sulci. Note the large amplitudes and apparent recirculation peaks in the corresponding CVs in fig. 2.

Clusters #2, #5, #6, and #14 may be attributed to large, intermediate and small parenchymal vessels of the non-affected left side, represented by subsequently increasing cluster-specific MTT, decreasing rCBF, rCBV, and smaller recirculation peaks. The procedure is even able to depict subtle differences of contrast agent first-pass times: Note the ability to distinguish between left and right side perfusion as indicated by minimal time-to-peak differences of clusters #1 and #2. Pixels representing regions supplied by a common arterial input tend to be collected into separate clusters: For example, clusters #5 and #6 contain many pixels that can be attributed to the supply region of the left middle cerebral artery, whereas clusters #4 and #11 include regions supplied by the right middle cerebral artery.

4. Discussion

Our study shows that neural network clustering can provide a self-organized segmentation of perfusion MRI data identifying groups of pixels sharing common properties of signal dynamics. In contrast to the conventional extraction of perfusion parameters alone, neural network clustering (i) does not discard information contained in the signal dynamics of MRI time-series, (ii) its interpretation is not biased by the indicator-dilution theory of non-diffusible tracers, the applicability of which is questionable under pathological conditions of a disrupted blood-brain barrier. Specific aspects of our clustering approach to this specific application with regard to data preprocessing or normalization will be published in [7].

In our study, minimal free energy VQ was able to unveil regional differences of brain perfusion characterized by subtle differences of signal amplitude and dynamics. It could provide a rough segmentation with regard to vessel size, detect side asymmetries of contrast-agent first pass, and identify regions of perfusion deficit in patients with stroke.

Although we conjecture from our results that neural network clustering can provide a useful extension of conventional data processing in dynamic susceptibility perfusion MRI studies, large controlled clinical trials are needed to establish the validity of the method and to finally evaluate its contribution to clinical decision making in cerebrovascular disease. Nevertheless, we hope that neural network vector quantization can serve as a useful strategy for exploratory data analysis of cerebral circulation with applications ranging from biomedical basic research to clinical assessment of patient data.

References

[1] D.R. Dersch. *Eigenschaften neuronaler Vektorquantisierer und ihre Anwendung in der Sprachverarbeitung*. Verlag Harri Deutsch, Reihe Physik, Bd. 54, Thun, Frankfurt am Main, 1996. ISBN 3-8171-1492-3.

[2] H. Fischer and J. Hennig. Neural-network based analysis of MR time series. *Magn. Reson. Med.*, 41(1):124–131, 1999.

[3] C. Goutte, P. Toft, E. Rostrup, F.A. Nielsen, and L.K. Hansen. On clustering fMRI time series. *Neuroimage*, 9:298–310, 1999.

[4] K. Rose, E. Gurewitz, and G.C. Fox. Vector quantization by deterministic annealing. *IEEE Transactions on Information Theory*, 38(4):1249–1257, 1992.

[5] A. Wismüller, D.R. Dersch, B. Lipinski, K. Hahn, and D. Auer. Hierarchical clustering of fMRI time-series by deterministic annealing. *Neuroimage*, 7(4):593, 1998.

[6] A. Wismüller, D.R. Dersch, B. Lipinski, K. Hahn, and D. Auer. A neural network approach to functional MRI pattern analysis − clustering of time-series by hierarchical vector quantization. In L. Niklasson, M. Bodèn, and T. Ziemke, editors, *ICANN'98 — Proceedings of the 8th International Conference on Artificial Neural Networks, Skövde, Sweden. Perspectives in Neural Computing*, volume 2, pages 123–128, London, Berlin, New York, 1998. Springer-Verlag.

[7] A. Wismüller, D.R. Dersch, F. Vietze, G. Leinsinger, K. Hahn, and D. Auer. Cluster analysis of biomedical image time-series. *International Journal of Computer Vision*, 2001. Submitted.

[8] A. Wismüller, F. Vietze, and D.R. Dersch. Segmentation with neural networks. In Isaac Bankman, Raj Rangayyan, Alan Evans, Roger Woods, Elliot Fishman, and Henry Huang, editors, *Handbook of Medical Imaging*, Johns Hopkins University, Baltimore, 2000. Academic Press. ISBN 0120777908.