An Adaptive Extended Colour Scale for Comparison of Pseudo Colouring Techniques for DCE-MRI Data

Thorsten Twellmann[1], Oliver Lichte[1], Axel Saalbach[1], Axel Wismüller[2] and Tim W. Nattkemper[4]

[1]Applied Neuroinformatics Group, Bielefeld University, 33501 Bielefeld
[2]Department of Radiology, University of Munich, 80336 Munich
Email: ttwellma@techfak.uni-bielefeld.de

Abstract. Pseudo colouring techniques are frequently used for analysing multivariate image data such as dynamic contrast enhanced mr images. Dedicated features of the high dimensional signal are mapped to pseudo colour codes and are superimposed on the image data. Nevertheless, the examination and comparison of different mapping functions is difficult, because the variability of the multivariate signal and pseudo colour scale have to be adequately and simultaneously presented. In this paper, we propose a setup for examination of different pseudo colour scales based on self organising maps. Thereby, the data distribution of the high dimensional signal is represented by a structured set of signal prototypes. Application of the pseudo colouring techniques to these prototypes leads to an extended colour scale which simultaneously gives a comprehensive display of the signal space together with the colour codes.

1 Introduction

Multivariate imaging techniques have become an important source of information to aid diagnosis in many medical fields. One example is the dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) technique which has been successfully applied e.g. for diagnosis of breast cancer. Nevertheless, analysis of this kind of data is a challenging task for the human observer due to the multivariate nature of the data: For each case a temporal sequence of n_t three dimensional images is recorded associating each voxel at position $\mathbf{p}$ with a vector $\mathbf{x_p} = (x_{\mathbf{p}1}, .., x_{\mathbf{p}n_t})$. After recording of a *pre-contrast image*, a *contrast agent* (CA) is injected in the bloodstream and a sequence of *post-contrast* images is recorded. The vector $\mathbf{x_p}$ describes the temporal course of CA concentration in local tissue. Even though these temporal patterns allow to infer information about the state of the local tissue [1] (e.g. malignant, benign or normal), this information is distributed on the n_t images and tools are required for it's integration and evaluation.

A common approach to aid analysis of multivariate image data is to augment the visualisation with *pseudo colouring techniques* (PCT). Thereby, suitable features are extracted from the underlying high dimensional signal and mapped to

a colour value which is superimposed on the image data at the corresponding spatial coordinate. The value of these augmented images strongly depends on the adequacy of the features as descriptors for the phenomenon under observation.

Different techniques have been proposed for extracting features from DCE-MRI signals which are suitable for characterising different states of tissue. These techniques can be divided in two groups. The first groups consists of *model-based* techniques such as *pharmacokinetic models* [2] or the *three-time-point method* (3TP) [3]. Fitting these models to the measured signal allows to infer the physiological parameterisation of the local tissue which in turn can be displayed as pseudo colours [4]. *Model-free* techniques utilising *artificial neural networks* (ANN) provide a promising alternative which does not depend on an explicit description of a signal model. The information e.g. about signals of different tissue classes is extracted from labelled training data which is frequently obtained during a standard evaluation procedure such as visual inspection or laboratory tests. Thus, these techniques can be applied even if the underlying process is not clear or if the signal pattern is very complex.

In recent years, the number of manuscripts in which new or modifications of existing PCTs are proposed has rapidly grown. Typically, new techniques are discussed and compared by means of a small number of images showing exemplarily visualisations e.g. of lesions. The disadvantage of these example images is that they display the colour coding of the multivariate signal, but only provide limited information about the underlying multivariate signals itself. As a consequence, it is difficult for the observer to examine the relation between the multivariate signal and the assigned colour code.

In this paper, we propose a method for qualitative evaluation of PCTs. The method simultaneously displays a representative set of examples $\mathbf{w} \in \mathcal{S}$ describing the data distribution in the multivariate signal space $\mathcal{S}$ and the corresponding colour codes $\mathbf{c}(\mathbf{w}) \in \mathcal{C}$ associated with the examples by an arbitrary PCT. To this end, the data distribution in the signal space is mapped to a two dimensional manifold using a *self organising map* (SOM) [5] adapted with training data of the investigated signal domain. Afterwards, the SOM is colourised using PCTs and is presented to the user. We believe that this *adaptive extended colour scale* (AECS) provides valuable information for comparing different techniques, educating unexperienced users in the interpretation of augmented images or for examination of different parameterisations of PCTs.

In the remainder of this manuscript, we will describe the AECS and exemplarily demonstrate it's application in a study of two methods for DCE-MRI analysis. In chapter 2, we briefly introduce an ANN based PCT which was recently developed in our group. Additionally, the *three-time-points* method is described as the reference PCT to compare with. In chapter 3, the AECS is described and applied for visualisation of the two PCTs of chapter 2. The corresponding results are discussed in the last chapter.

2 Pseudo colouring of DCE-MRI data

Inspection of DCE-MRI image data is a challenging task for a human observer, because the information for discriminating different types of tissue is distributed on the entire sequence of 3D images. Consequently, efficient techniques for dimension reduction are required which, at best, display the desired information in a single image. Pseudo colouring techniques map certain characteristics of the high dimensional signal to different combination colours leading to a visualisation of the DCE-MRI data as a single colourised image which guides the observers attention to locations of suspicious tissue.

2.1 Model-based approach: The Three-Time-Points method

The *three-time-points* method (3TP) is a patented technique for the evaluation of DCI-MRI data in breast and prostate cancer diagnosis. 3TP is based on a model of the CA kinetic signals which is mainly described by the strength of the signal uptake after administration of the CA and the presence of a CA wash-out after an early concentration peak. These parameters are derived from a dynamic sequence consisting of $n_t = 3$ images (one pre-contrast, one early and one late post-contrast image). Each signal pattern $\mathbf{x_p}$ is displayed with a pseudo colour code $\mathbf{c}_{3TP}(\mathbf{x}_p) = (i_\mathbf{p}, h_\mathbf{p})$. The signal uptake $x_{\mathbf{p}2} - x_{\mathbf{p}1}$ is mapped to the colour intensity $i_\mathbf{p}$. The colour hue $h_\mathbf{p}$ is defined by the presence of a significant signal wash-out or uptake between the two post-contrast images:

$$h_\mathbf{p} = \begin{cases} \text{red}, & : \text{ if } x_{\mathbf{p}3} < x_{\mathbf{p}2} \ \wedge \ |x_{\mathbf{p}2} - x_{\mathbf{p}3}| > \sigma x_{\mathbf{p}2} \\ \text{blue}, & : \text{ if } x_{\mathbf{p}3} > x_{\mathbf{p}2} \ \wedge \ |x_{\mathbf{p}2} - x_{\mathbf{p}3}| > \sigma x_{\mathbf{p}2} \\ \text{green}, & : \text{ else} \end{cases} \tag{1}$$

The parameter σ controls the tolerance during the equality test between $x_{\mathbf{p}3}$ and $x_{\mathbf{p}2}$ and is chosen during a calibration step. Experiments have shown that the colour intensity and hue correlates with the tissue parameters *microvascular permeability* and *extracellular volume fraction*.

2.2 ANN based model-free approach

Model-based techniques such as 3TP or pharmacokinetic models assume a certain model of the CA kinetic and thus require a priori knowledge about the underlying physiological process. In contrast to this, model-free techniques based on ANNs infer information from the measured data and ancillary source such as manual lesion segmentations or laboratory tests. Therefore, ANNs can be deployed for deriving implicit models e.g. of different type of tissue from the data itself.

We are currently evaluating a system for DCE-MRI evaluation which is based on a supervised hierarchical ANN (a detailed description of the architecture has been submitted to an international journal). The ANN follows a divide-and-conquer strategy for the classification of the DCE-MRI pattern. Thereby, the

signal space is divided in a set of subregions $\mathcal{V}_i$ by vector quantisation algorithm. Subsequently, a single layer neural network with softmax activation is assigned to each subregions $\mathcal{V}_i$ for classification of examples $\mathbf{x_p} \in \mathcal{V}_i$ as malignant, normal or benign. The class label of the training data is derived from manual lesion segmentations. Each lesion is attributed as a whole to be malignant or benign according the outcome of a histopathological examination. Thus, the adapted ANN provides a mapping

$$M : \mathcal{S} \to \mathcal{C} : \quad \mathbf{x_p} \mapsto [0;1]^3 \tag{2}$$

which maps each example $\mathbf{x_p}$ to a three dimensional vector $\mathbf{c}(\mathbf{x})$ with components $c_j,\ j = 1, \ldots, 3$ describing the confidence that the evaluated pattern belongs to the class of malignant, normal or benign tissue, respectively. This output vector $\mathbf{c}(\mathbf{x})$ is interpreted as a RGB colour and is superimposed on the DCE-MRI image data. A comparable approach to model-free evaluation of DCE-MRI data was proposed by Lucht et al. [6].

3 Adaptive extended colour scales

Basis of the extended colour scale is a structured set of prototypes $\mathbf{w}_i \in \mathcal{S}, i = 1, \ldots, N$ which represents the major part of the variability of the multivariate data. This set of prototypes is calculated by adapting a SOM with a suitable set of training data Γ.

The SOM is an unsupervised neural network consisting of a lattice of neurons. Each neuron of this lattice has an associated prototype $\mathbf{w}_i \in \mathcal{S}$ which is adapted during the training of the SOM. Thereby, examples $\mathbf{x} \in \Gamma$ are presented to the SOM in random order. For each presented example at time step t, the best matching prototypes $\mathbf{w}^*(\mathbf{x})$ and the prototypes located in the neighbourhood of $\mathbf{w}^*(\mathbf{x})$ are moved towards the presented example according

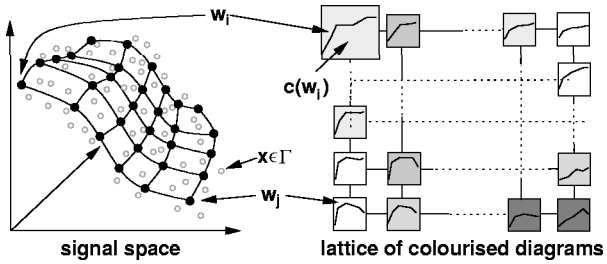
$$\mathbf{w}_i(t+1) = \mathbf{w}_i(t) + \alpha(t) h_{\mathbf{w}^*(\mathbf{x}),i}(t)(\mathbf{x} - \mathbf{w}_i(t)) \tag{3}$$

with a time dependent learning rate $\alpha(t)$ and neighbourhood function $h_{\mathbf{w}^*(\mathbf{x}),i}(t)$. Following the concept of neighbourhood learning, data points which are close in the signal space are likely to be mapped to nearby nodes on the SOM lattice, i.e. the topology of the signal space is preserved.

After adaptation of the SOM, the lattice structure of prototypes $\mathbf{w}_i$ is displayed as a lattice of diagrams (see Fig.1). Each diagram shows a plot of the corresponding $\mathbf{w}_i$ which itself can be interpreted as prototype of a subset $\{\mathbf{x}_i\} \subset \Gamma$. Additionally, the background of the each diagram is colourised with the colour obtained from the evaluation of $\mathbf{w}_i$ with the investigated PCT, leading to the extended colour scale.

For the domain of DCE-MRI signals, a SOM consisting of a two-dimensional 15×15 lattice of neurons is adapted with a set of training data Γ containing an equal number of malignant, benign and normal signals taken from the DCE-MRI sequences of 14 cases (approx. 5000 pattern total). Afterwards, the adapted SOM is colourised by both methods introduced in chapter 2. Due to the limited space, we provide the colour images of both extended colour scales online [7].

Fig. 1. The SOM lattice, unfolded in $\mathcal{S}$ after adaptation, is displayed as a lattice of diagrams colourised by one of the investigated PCT. Each diagram shows a plot of a prototype $\mathbf{w}_i$ and the associated pseudo colour code $\mathbf{c}(\mathbf{w}_i)$.



4 Discussion

The prototypes of the trained SOM represent the major part of variability of DCE-MRI signals. Benign signals showing a continuously increasing CA concentration and malignant signals showing a fast uptake followed by a wash-out of CA concentration are both represented as dense clusters on the SOM. Prototypes representing normal signals are located in the upper right part of the SOM. A comparison of the SOM coloured by the ANN and 3TP indicates a significant conformance between display of benign (blue) and malignant (red) signals. In contrast to 3TP, the region of signals indicated as malignant by the ANN is vaster and passes into the region of benign signals indicated by colour codes changing from red to purple to blue. Here, the different meaning of the green colour becomes evident. 3TP displays suspicious signals with a fast uptake followed by an indistinct wash-out as bright green, while the same colour code is used by the ANN for signals which are classifier as normal with high confidence.

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