# Unsupervised tissue segmentation from dynamic contrast-enhanced magnetic resonance imaging

Gabriele Chiusano [a,*], Alessandra Staglianò [a], Curzio Basso [b], Alessandro Verri [a]

[a] Dipartimento di Informatica, Bioingegneria, Robotica e Ingegneria dei Sistemi, Università degli Studi di Genova, Via Dodecaneso 35, 16146 Genova, Italy
[b] CAMELOT Srl, Via Greto di Cornigliano 6R, 16152 Genova, Italy

## ARTICLE INFO

## ABSTRACT

Objective: Design, implement, and validate an unsupervised method for tissue segmentation from dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI).
Methods: For each DCE-MRI acquisition, after a spatial registration phase, the time-varying intensity of each voxel is represented as a sparse linear combination of adaptive basis signals. Both the basis signals and the sparse coefficients are learned by minimizing a functional consisting of a data fidelity term and a sparsity inducing penalty. Tissue segmentation is then obtained by applying a standard clustering algorithm to the computed representation.
Results: Quantitative estimates on two real data sets are presented. In the first case, the overlap with expert annotation measured with the DICE metric is nearly 90% and thus 5% more accurate than state-of-the-art techniques. In the second case, assessment of the correlation between quantitative scores, obtained by the proposed method against imagery manually annotated by two experts, achieved a Pearson coefficient of 0.83 and 0.87, and a Spearman coefficient of 0.83 and 0.71, respectively.
Conclusions: The sparse representation of DCE MRI signals obtained by means of adaptive dictionary learning techniques appears to be well-suited for unsupervised tissue segmentation and applicable to different clinical contexts with little effort.

© 2014 Elsevier B.V. All rights reserved.

## 1. Introduction

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a powerful imaging modality which, by allowing for the investigation of biological processes along the temporal axis, provides information about perfusion, capillary permeability, and tissue vascularity [1]. Typically, DCE-MRI is obtained by acquiring a series of T1-weighted sequences *before*, *during*, and *after* the injection of a contrast agent, such as gadoterate meglumine (Gd-DOTA). The contrast agent uptake is higher where the vascularization is stronger, resulting in signal enhancement and brighter image intensities after the injection. Clinically relevant, quantitative information can be extracted by a voxel-wise analysis of the time-varying intensity signal, also known as *enhancement curve*, which shows a stereotyped behavior across voxels of the same tissue.

From the computational viewpoint the analysis of DCE-MRI poses several problems arising from the large amount of noise affecting the signal, patient movements during acquisition, and the need of discriminating between different tissues. Recently, several computational methods based on DCE-MRI have been proposed for quantitative assessment of several diseases like prostate cancer [2], breast cancer [3,4], cardiac and cerebral ischemia [5], renal dysfunction [6], and rheumatoid arthritis [7,8].

This paper presents a data driven method for unsupervised tissue segmentation from DCE-MRI acquisition. Aside from the manual selection of a region of interest (ROI) the method is automatic. Given a DCE-MRI acquisition, after a preliminary stage in which signal distortions due to patient movement are attenuated by means of a motion compensation technique, a sparse representation is obtained from a dictionary of basis signals learned from the data. Since the basis signals resemble the prototypical behavior of the enhancement curves corresponding to different tissues, tissue segmentation is effectively achieved by applying standard clustering techniques on the obtained representation. By computing a different dictionary of basis signals for each dataset, our method exploits in full the adaptivity of dictionary learning.
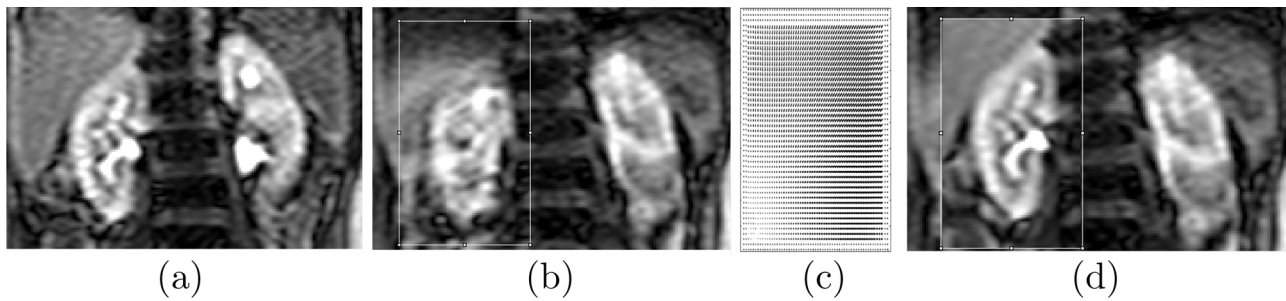
**Fig. 1.** An example of motion compensation. (a) Image at time $t_1$. (b) Image at time $t_2$, in which a wide movement of right kidney in the ROI is highlighted. (c) The computed displacement field in the ROI, displayed at a larger scale. (d) The image at time $t_2$ after motion compensation.

The rest of this paper is organized as follows: in Section 2 the literature on DCE-MRI analysis is overviewed. Section 3 describes the proposed technique, while Section 4 presents the experimental results obtained on synthetic and real data. Finally, we draw our conclusions in Section 5.

## 2. Related work

In the literature, DCE-MRI analysis is tackled by means of two different parametric approaches: the first approach relies on a pharmacokinetic model of the contrast agent dynamics tuned to the specific process (or disease) under study [2,4,5]. Consequently, the estimated parameters have a direct physiological interpretation. The second approach parametrizes the shape of the enhancement curves with no direct link to the problem physiology [3,7–9]. Segmentation is achieved after fitting a geometric model on the acquired enhancement curves.

In other methods, feature vectors extracted from the raw data [10], or the raw data directly [6], are used as a basis for discriminating among different tissues, by means of supervised and unsupervised classification methods respectively. In all these cases, the proposed algorithms are fine-tuned to the specific medical context and often require a fair amount of work in the construction of the feature models.

Over the last decades, the signal processing community has shown a growing interest on adaptive sparse coding, starting from the seminal work of Olshausen and Fields [11]. Instead of using over-complete, fixed dictionaries, like Wavelets [12], an adaptive dictionary and the corresponding sparse-codes are learnt from data within an optimization framework (see [13–19] for example). Very good results have been reported in denoising [13], compression [13], scene categorization, object recognition (see [20,15] for more examples) and image super-resolution. Other works cast the dictionary learning problem as a factor-analysis problem, with the factor loading corresponding to the number of the dictionary elements used: in this case the number of atoms is automatically obtained. Other works use non-parametric Bayesian methods [21,22] and the Indian buffet process [23,24].

The use of temporal-curves instead of image patches has been proposed by [25] on electromyographic data and, independently, by us in a preliminary conference version of this paper, [26], on DCE-MRI data. In [25] the proposed method computes dictionary and sparse codes of 1-D dimensional signals acquired over time, in order to learn interpretable spatio-temporal primitives from motion capture data and to differentiate between spatio-temporal primitives by using the obtained atoms. The problem is formulated as a tensor factorization problem with tensor group norm constraints over the atoms as well as smoothness constraints.

## 3. The proposed method

In this section we describe the three stages of the proposed method: motion compensation, learning the representation, and tissue segmentation.

### 3.1. Motion compensation

During the past three decades several registration techniques have been developed and widely applied to medical imaging. Motion correction of DCE-MRI time series is a particular case of image registration, in which tissue motion and deformation are the result of breathing and sudden, sussultatory movements combined with perfusion of the contrast agent: strong deformation and large displacements are especially prominent in dynamic cardiac imaging [27,28], breast imaging [29], and abdominal imaging [30]. In all these cases, a registration procedure is mandatory and may pose difficult computational problems.

In this work, even if the acquisition process lasts from 6 to 20 min, deformation and displacement are usually quite small. Spatial registration is necessary to compensate for the slight motion artifacts produced by the presence of soft tissues in the kidney, whilst is almost never needed in the wrist. Consequently, in this work, we adopt a simple motion compensation method based on standard optical flow computation: in particular, we employ a 2-dimensional optical flow method available in the Insight Toolkit Library (ITK). Given the simplicity of the given registration tasks, the adopted procedure produces results adequate for our purpose. As shown in Fig. 1, motion compensation is only performed within a ROI outlined by hand.

### 3.2. Learning the representation

The idea behind sparse and adaptive dictionary learning is to represent a certain family of signals, in our case enhancement curves, as linear combination of a few elements selected from a dictionary of basic signals, called *atoms*. As already mentioned, both the atoms and the coefficients of the linear combinations are learned from the input data.

Let us now briefly review dictionary learning in the special case of time-varying signals like DCE-MRI data. We denote an enhancement curve sampled at times $t = 1, \ldots, p$ by means of a $p$-dimensional vector $x = (x^1, \ldots, x^p)^\top$. Without loss of generality we also assume that, for all $t$, $x^t$ measures the difference between the samples at time $t$ and 1. This is equivalent to set $x^1 = 0$ for every $x$.