

# Application of Locally Linear Embedding to diffusion-weighted MRI data: Potential new contrast patterns in multiple sclerosis

P. Mannfolk<sup>1</sup>, M. Nilsson<sup>1</sup>, J. Lätt<sup>1</sup>, E-M. Larsson<sup>2</sup>, F. Ståhlberg<sup>1,2</sup>, R. Wirestam<sup>1</sup>, and S. Brockstedt<sup>1</sup>

<sup>1</sup>Medical Radiation Physics, Lund University, Lund, Sweden, <sup>2</sup>Department of Diagnostic Radiology, Lund University, Lund, Sweden

## Introduction

From sets of diffusion-weighted (DW) MRI signal data, several contrast parameters can be established, such as the apparent diffusion coefficient (ADC), the fractional anisotropy (FA) of the diffusion tensor, the apparent kurtosis coefficient (AKC) [1] and, using the q-space methodology [2], the full width at half maximum (FWHM) of the dynamic displacement distribution. In many cases these parameters reveal a marked difference between healthy and pathological tissue [3]. The parameters are generally calculated from several samples of the diffusion related signal attenuation curve using a robust theoretical framework and they have an established physical interpretation. In order to pursue the question whether more information may be hidden in such data sets, in this study we have used, a non-linear dimensionality reduction technique, Locally Linear Embedding (LLE) [4], together with Independent Component Analysis (ICA) [5] to find underlying degrees of freedom characterizing different tissue types according to their signal-versus- $b$  curves.

## Theory

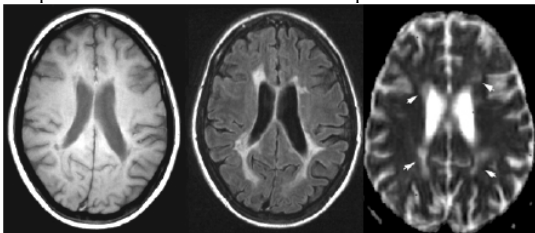
The purpose of the LLE algorithm is to compute a low dimensional embedding of high dimensional data, with nearby points in the high dimensional input data remaining nearby in the resulting low dimensional embedding. In other words, the resulting embedding reflects local geometric properties of a point and its nearest neighbours. The input data is assumed to consist of  $N$   $D$ -dimensional real valued vectors  $\vec{X}_i$  sampled from a smooth underlying manifold, which for diffusion means  $N$  voxels sampled with  $D$   $b$ -values. Under the assumption that the manifold is sufficiently well sampled, we can expect that a data point and its nearest neighbours describe a locally linear patch in the non-linear manifold. Global properties of the manifold can then be described by a geometrical description of all the patches via linear coefficients that reconstruct each point from its neighbours. The original formulation of LLE creates the above described characterization by first identifying the  $K$  nearest neighbours for all data points, as measured by Euclidean distance. The coefficients obtained in the first step of the LLE algorithm are then used to compute a low-dimensional representation  $\vec{Y}_i$  of the original data with dimensionality  $d$ . The final step of LLE can be performed by solving a sparse  $N \times N$  eigenvalue problem, which results in  $d$  eigenvectors. However, the eigenvectors are only orthogonal and not statistically independent. In order to achieve statistically independent components, i.e. separate sources, an additional ICA can be performed on the components retained from LLE.

## Method

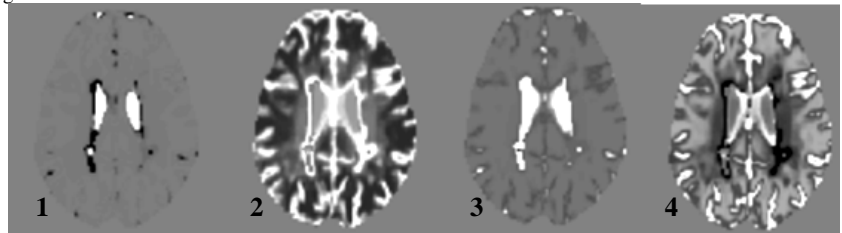
DW images were acquired from one patient suffering from multiple sclerosis (MS) using a 3.0 T Siemens Allegra Magnetom head scanner. A SE-EPI pulse sequence was modified to allow diffusion encoding in six directions with 30  $b$ -values, with a maximum  $b$ -value of 6600 s/mm<sup>2</sup>. Other scanning parameters were TE/TR = 135/4000 ms,  $\delta/\Delta = 20/88$  ms, 10 slices with thickness 5 mm, FOV = 215×215 mm<sup>2</sup>, matrix size = 100×128. In a pre-processing step before the LLE analysis, the signal vectors were divided by the signal value for  $b=0$  to avoid T2 effects, ensuring that the embeddings found by LLE only correspond to the diffusion related signal attenuation. Hence, the input to LLE consisted of the normalized signal vectors for each voxel, i.e.  $N$  voxels with dimensionality 30 ( $D=30$ ). The resulting eigenvectors were finally processed with ICA as described above.

## Results

Conventional T1-weighted, ADC and FLAIR images are displayed in Fig. 1. In Fig. 2, the results of LLE-ICA processing are displayed. Note that the various components of LLE characterize the two posterior lesions as being different.



**Fig 1.** T1-weighted, FLAIR and ADC images from the MS patient. Four lesions, one in each corner of the ventricles, are indicated by white arrows in the ADC image.



**Fig 2.** LLE-ICA results. Four components obtained with LLE input parameters  $K/d = 5/4$ . Each component demonstrates an independent source of the signal versus  $b$ -curve.

## Discussion

For conventional models used in the post processing of DW data, a risk exists that the signal vectors originating from two different types of tissue are mapped onto the same scalar even though they display differences in the signal-versus- $b$  curve. For example, this has been demonstrated for AKC [6]. The complete signal-versus- $b$  curve contains extensive information about the self-diffusion process in the tissue and this information is not necessarily best extracted by parameters such as ADC or the fractional anisotropy (FA) of the diffusion tensor. By applying LLE to DW data, additional information might be obtained that does not correspond to presently available models. Our results demonstrate that even when existing models do show a difference between tissue types (ADC in Fig. 1), another mapping of the data might better visualize the pathology, in this case the MS lesions. It might also be the case that LLE is able to separate different stages of lesion progression, an observation which however requires further investigation. For example, component 3 in the LLE-ICA analysis displayed in Fig. 2 indicates that the MS plaque in the posterior right corner of the ventricles is highly similar to CSF. This might be explained by increased water content in degenerated tissue, which is supported by clinical findings in the T1-weighted image. Furthermore, component 4 in Fig. 2 might indicate that the borders of the MS plaques share similar properties in terms of the signal-versus- $b$  curve. Such enhanced contrast features may be of value, for example, in tissue segmentation procedures as a complement to conventional contrast parameters. This might be explained by increased water content in degenerated tissue, which is supported by clinical findings in the T1-weighted image.

## References

- [1] Lu H. et al. [2006] NMR Biomed. 19(2):236-247
- [2] Cohen Y., Assaf Y. [2002] NMR Biomed. 15(7-8):516-542
- [3] Assaf Y. et al. [2002] Magn. Reson. Med. 47:115-126

- [4] Roweis S.T., Saul L.K. [2000] Science. 290:2323-2326
- [5] Comon P. [1994] Signal Processing. 36:287-314.
- [6] Lätt J. et al. [2007] Magn. Reson. Imaging. doi:10.1016/j.mri.2007.04.001