

Chapter 17

Manifold Learning for Medical Image Registration, Segmentation, and Classification

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ABSTRACT

The term manifold learning encompasses a class of machine learning techniques that convert data from a high to lower dimensional representation while respecting the intrinsic geometry of the data. The intuition underlying the use of manifold learning in the context of image analysis is that, while each image may be viewed as a single point in a very high-dimensional space, a set of such points for a population of images may be well represented by a sub-manifold of the space that is likely to be non-linear and of a significantly lower dimension. Recently, manifold learning techniques have begun to be applied to the field of medical image analysis. This chapter will review the most popular manifold learning techniques such as Multi-Dimensional Scaling (MDS), Isomap, Local linear embedding, and Laplacian eigenmaps. It will also demonstrate how these techniques can be used for image registration, segmentation, and biomarker discovery from medical images.

INTRODUCTION

The use of machine learning in the analysis of medical images plays an increasingly important role in many real-world, clinical applications ranging from the acquisition of images of moving

organs such as the heart, liver and lungs to the computer-aided detection, diagnosis and therapy. For example, machine learning techniques such as clustering can be used to identify classes in the image data and classifiers may be used to differentiate clinical groups across images or tissue

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types within an image. These techniques may be applied to images at different levels: At the lowest level or voxel level one may be interested in classifying the voxel as part of a tissue class such as white matter or grey matter. At a more intermediate level, classification may be applied to some representation or features extracted from the images. For example, one may be interested in classifying the shape of the hippocampus as belonging to a healthy control or to a subject with dementia. At the highest level, clustering may be applied in order to classify entire images.

One of the key challenges in applying machine learning techniques to medical images is the fact that medical images are often represented as data points in a very high-dimensional space, yet they only occupy a small part of this space. Another key challenge that is often faced is commonly referred to as the *small sample size* problem: While the data lives in a very high-dimensional space we often only have a comparatively small number of images from which to learn. In this context manifold learning techniques offer a powerful approach to find a representation of images or image-derived features that facilitates the application of machine learning techniques such as clustering or regression.

The basic idea of manifold learning is closely related to that of dimensionality reduction techniques such as Principal Component Analysis (PCA). The key assumption in applying manifold learning techniques is that dimensionality of the original data can be reduced with a negligible loss of information. For example, a 3D brain image with $256 \times 256 \times 128$ voxels may be viewed as a point in a more than 8 million dimensional vector space. However, brain images from different subjects have a large degree of similarity in their appearance. Thus, most regions of this high-dimensional space correspond to images that have no similarity to brain images. Instead the assumption is that the images are data points on a low dimensional manifold, which is embedded in the high-dimensional space. The goal of

manifold learning algorithms is to uncover or *learn* this low dimensional manifold directly from the data (Cayton 2005).

The assumption of a manifold structure for medical images has some important consequences, in particular for the measurement of distances between images: Since the images lie on or near to a non-linear manifold, the Euclidean distance between images in the original high-dimensional space is usually not meaningful. So, instead of using the Euclidean distance between images, one may compute a ‘geodesic’ distance within a learned manifold as a distance metric, a distance which will depend upon the context, for example whether the manifold learning technique is being used for clinical classification or feature extraction, etc. In many practical applications operating directly on the images can be too costly and thus not practical. However, after uncovering the manifold structure in the data, the manifold can be “flattened” into a lower dimensional space in which the Euclidean distance provides a suitable approximation of the geodesic distance.

MANIFOLD LEARNING TECHNIQUES

This section describes some of the most important manifold learning techniques. It follows the comprehensive overviews given in (van der Maaten, 2009) and (Pless, et al., 2009). A set of images $\{\mathbf{x}_1, \dots, \mathbf{x}_N\}$ is described by N images $\mathbf{x}_i \in \mathbb{R}^D$, each being defined as a vector of intensities, where D is the number of voxels per image or region of interest. Assuming that $\{\mathbf{x}_1, \dots, \mathbf{x}_N\}$ lie on or near a d dimensional manifold \mathcal{M} embedded in \mathbb{R}^D and $d \ll D$, it is possible to learn a new, low dimensional representation $\{\mathbf{y}_1, \dots, \mathbf{y}_N\}$ with $\mathbf{y}_i \in \mathbb{R}^d$ of the input images.

In many of the techniques described, a matrix is typically used to represent the relations between pairs of data items, which, for the purpose of this chapter, can be assumed to be either the original

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