ON COMPARISON OF MANIFOLD LEARNING TECHNIQUES FOR DENDRITIC SPINE CLASSIFICATION

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ABSTRACT

Dendritic spines are one of the key functional components of neurons. Their morphological changes are correlated with neuronal activity. Neuroscientists study spine shape variations to understand their relation with neuronal activity. Currently this analysis performed manually, the availability of reliable automated tools would assist neuroscientists and accelerate this research. Previously, morphological features based spine analysis has been performed and reported in the literature. In this paper, we explore the idea of using and comparing manifold learning techniques for classifying spine shapes. We start with automatically segmented data and construct our feature vector by stacking and concatenating the columns of images. Further, we apply unsupervised manifold learning algorithms and compare their performance in the context of dendritic spine classification. We achieved 85.95% accuracy on a dataset of 242 automatically segmented mushroom and stubby spines. We also observed that ISOMAP implicitly computes prominent features suitable for classification purposes.

***Index Terms*—** Dendritic Spines, Classification, Manifold Learning, ISOMAP, Microscopic Imaging, Neuroimaging

1. INTRODUCTION

Ramon y Cajal discovered dendritic spines in the 19th century and suggested that spine morphology changes with variations in neuronal activity[1]. This hypothesis has been supported by many studies [2]. Consequently, dendritic spine analysis has become very important for neurobiological research and can potentially enable the neuroscientists to decode the underlying relationship between neuron activity variations and spine morphology changes [1]. In the literature, dendritic spines have been classified into four types: mushroom, stubby, filopodia and thin [3]. Examples of these four classes are presented in Figure 1. Quantitative spine analysis is an important research topic in contemporary neurobiological research and currently such analysis is performed manually due to the lack of reliable automated tools. This makes the research process slow and subjective. The availability of reliable automated resources would expedite the research in this area.

Fig. 1. Spine Classes: Mushroom, Stubby, Thin, Filopodia (Left to Right)

Manifold learning is an important methodology with applications in a wide range of areas including data compression, pattern recognition, and machine learning [4]. Manifold learning can be seen as a dimensionality reduction problem, with the goal of producing a compressed representation of high-dimensional data. It can also be viewed as an algorithm to compute degrees of freedom that would be sufficient to reproduce most of the variability in data [4]. Mathematically, we can formulate the dimensionality reduction or manifold learning problem as follows: given an N-dimensional random variable $\mathbf{x} = (x_1, x_2, ..., x_N)^T$, compute its low dimensional representation, $\mathbf{y} = (y_1, y_2, ..., y_D)^T$ such that $D \leq N$, keeping maximum information from original high-dimensional data according to some criterion [5]. Different algorithms apply different criterion to reduce dimensionality, e.g., principal component analysis (PCA) uses maximum variance as criteria.

The reason behind their success is the inherent redundancy in most natural images and the fact that natural images having high-dimensional data mostly lie near a low-dimensional manifold [4]. To the best of our knowledge, the application of these techniques to spine analysis have not been reported in the literature.In this study, we use several manifold learning techniques for spine classification and compare their performance. Classification results achieved with various settings are comparable to those of a human expert. This analysis is based on two-photon laser scanning

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microscopy (2PLSM) images.

The main contributions of this paper are comparison of unsupervised manifold learning techniques and visual analysis of ISOMAP [6] based extracted features. Analysis of ISOMAP features lead to the conclusion that ISOMAP has the capability to implicitly compute the distinguishing features appropriate for classification.

Rest of this paper is organized as follows: Section 2 contains a brief literature review. The data set used in this study and methodology is described in section 3. Results are presented and discussed in Section 4. Section 5 contains the conclusion and future research directions.

2. LITERATURE REVIEW

Automated segmentation process of dendritic spines has been studied extensively in the literature, but only a few studies address the spine shape classification. Rodriguez et al. [7] computed morphological features and performed classification using a decision tree. They considered 3D confocal laser scanning microscopy (CLSM) images. Son et al. [8] and Shi et al. [9] also used morphological features and proposed a decision tree based classification system for CLSM images.

Koh et al. [10] proposed a morphological feature based technique applying a rule based classifier for 2PLSM images. A recent study on spine analysis considered morphological features to classify 2PLSM spine images and compared the performance of state-of-the-art classifiers [11].

Most of these studies compute morphological features and perform classification using rule based algorithms, also there are only a few studies that consider 2PLSM images. To the best of authors' knowledge, manifold learning based spine analysis is not reported in the literature. In this research, we aim to fill these gaps and apply and compare different manifold learning approaches to the spine classification problem.

3. METHODOLOGY

Mice post natal 7 to 10 days old animals are imaged using 2PLSM.[1] We acquired 15 stacks of 3D images and projected them to 2D using maximum intensity projection (MIP) to use for this study. 15 dendrite branches have been used to extract a data set of 242 spines for this research, 182 spines are mushroom and 60 are stubby.

Before applying manifold learning algorithms, we applied the disjunctive normal shape models (DNSM) [12] based algorithm to segment spines. This algorithm exploits DNSM based shape and appearance priors to segment spines with good accuracy [13]. This algorithm takes a region-of-interest (ROI) as input. We selected the ROI in a way that the spine head center is positioned almost in the center of the ROI. Further, we scaled the ROI to 150x150 pixels. Finally, each ROI was aligned in a way that spine necks are in vertical position. A few images from this dataset are given in Figure2. After preparing the dataset, we applied the DNSM based segmentation algorithm to segment the spine images. Segmentation results are not perfect but good enough for shape analysis. It is important to note that classification techniques used in this paper are sensitive with respect to segmentation, different segmentation approach could lead to different classification results.

[1] All animal experiments are carried out in accordance with European Union regulations on animal care and use, and with the approval of the Portuguese Veterinary Authority (DGV).

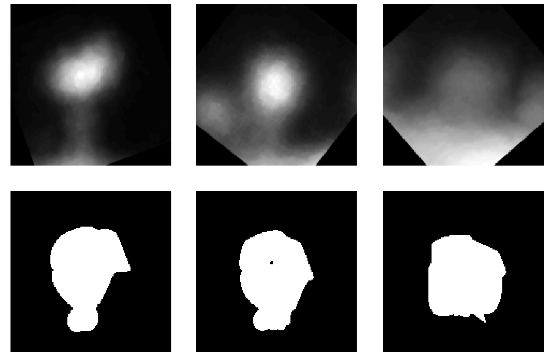

Fig. 2. A few images from dataset, without segmentation (above) and segmented images (below). First 2 spines are labeled as Mushroom and 3rd spine as Stubby.

3.1. Manifold Learning

In this paper we consider several manifold learning techniques and compared their performance.

PCA is a widely used classical technique that provides a transformed lower dimensional representation attempting to preserve maximum variance, but it is not very effective in various application due to its global linearity property [14]. Multidimensional scaling (MDS) provides a lower dimensional representation attempting to preserve the distance between points, but it suffers from similar problems as PCA [15]. Locally linear embedding (LLE) is a nonlinear dimensionality reduction approach that finds the low-dimensional representation striving to keep embedding of high-dimensional data [16].

ISOMAP is another non-linear dimensionality reduction approach that possesses the best features of PCA and MDS [6]. It can be viewed as an extension of MDS by replacing the Euclidean distance metric with geodesic distance. The Laplacian eigenmaps method constructs a graph by applying the K-nearest neighbors (KNN) and computes its weights in such a way that the norm of the gradient is minimized in the least squares sense [17]. Local Tangent Space Alignment (LTSA) also constructs the graph using KNN and for dimensionality reduction it applies an approximation to local tangent spaces for each neighborhood [18].

Firstly, the segmented spine images were used to construct 22,500 dimensional feature vectors by concatenating the stacked columns of each spine image. These feature vectors were further used to construct the feature matrix. Finally, manifold learning algorithms were applied on this feature matrix to produce lower dimensional feature matrices.

3.2. Classification

In order to compare the performance of these manifold learning techniques, we selected three different classifiers, support vector machines (SVM), KNN, and random forests (RF), to test their performance. The linear kernel is used for SVM, K=8 is used for KNN, and 10 decision trees are used for RF classifier. The idea behind applying different classification techniques is to test the performance of these manifold learning approaches irrespective of the classification technique applied.

4. RESULTS

We compared the performance of six manifold learning techniques using three different classifiers. Classification results and visual analysis of ISOMAP based features are discussed in this section.

4.1. Classification Results

We selected only two features for manifold learning, the reason behind selecting two features will become clear later in this section when we discuss ISOMAP based features. We applied three different classifiers to compare the performance of these techniques to make sure that performance is the result of feature transformation not because of the classifier.

Classification results using SVM, KNN, and RF are presented in Table 1. It is evident from achieved results that performance of these manifold learning approaches is dependent upon classifier. It makes sense because just like manifold learning techniques, classifiers also use different decision criteria. For SVM classifier, Laplacian eigenmaps method performs best. However, for KNN classifier ISOMAP gives best classification results and for RF classifier, the complete feature set gives best accuracy.

Table 1. Classification Results with SVM, RF, and KNN classifiers

Features	SVM	KNN	RF
Complete Features	84.71%	**84.71%**	**85.12%**
ISOMAP	85.54%	**84.71%**	81.41%
PCA	82.64%	83.88%	78.51%
LLE	85.54%	83.47%	83.06%
Laplacian	**85.95%**	83.47%	80.17%
LTSA	77.27%	82.23%	80.58%
MDS	84.30%	80.99%	79.75%

These observations imply that one should visually analyze the produced feature space before making a decision about the classification approach. Another conclusion that can be drawn from these results is that none of these manifold learning techniques perform best for all scenarios. The best performance is achieved with Laplacian eigenmaps based features with SVM classifier. It even performs better than complete

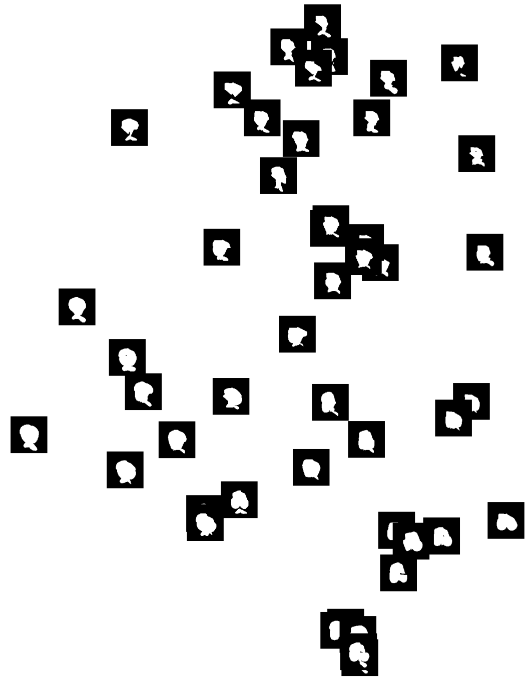

Fig. 3. ISOMAP 2D features: Spine head diameter varies along x-axis and neck length changes along y-axis.

features set that supports the argument that manifold learning can potentially result in two advantages: dimensionality reduction and classification performance improvement. However, it is important finding that the decision of whether to use manifold approach or use complete feature set is associated with the choice of the classifier.

4.2. ISOMAP Feature Space Analysis

Samples from two-dimensional ISOMAP feature space is illustrated in Figure 3. Visual analysis of feature space results in interesting observation, the head diameter of spines varies along the horizontal axis and the neck length along the vertical axis. This validates the claim by Ghani et al. [11] that head diameter and neck length are the most important features for the classification of mushroom and stubby spines. This leads to an important finding that ISOMAP implicitly computes degrees of freedom of a dataset, in this case it is 2. A similar analysis has been previously performed on faces and digits dataset [6].

4.3. Classification using Morphological Features

In order to compare the classification results using manifold learning with a standard morphological feature based technique, we implemented the algorithm described in [11] and computed the classification results, given in the Table 2. It is concluded that most manifold learning based approaches perform better than the morphological feature based technique.

Table 2. Classification results using morphological features based approach

Classifier	Accuracy
SVM	78.51%
KNN	80.17%
RF	81.41%

5. CONCLUSION

Six state-of-the-art unsupervised manifold learning techniques have been compared in this study for dendritic spine classification. It is found that the Laplacian eigenmaps method results in the best performance. It is also concluded that most manifold learning techniques result in better performance as compared to the baseline morphological feature based technique. It is also observed that ISOMAP computes degrees of freedom in a dataset and it is found that for the dendritic spines dataset used in this research, we have two degrees of freedom. Another interesting observation is, manifold learned features perform better than complete features with some of the classifiers applied, hence the decision of applying manifold learning techniques must be made taking into account the choice of the classifier to be used as well. Future work could involve larger dataset to precisely characterize manifolds.

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