Medical Image Analysis 18 (2014) 914–926

Contents lists available at ScienceDirect

Medical Image Analysis

journal homepage: www.elsevier.com/locate/media

Multi-modal registration for correlative microscopy using image analogies

Tian Cao [a,*], Christopher Zach [c], Shannon Modla [d], Debbie Powell [d], Kirk Czymmek [d,e], Marc Niethammer [a,b]

[a] Department of Computer Science, University of North Carolina at Chapel Hill, United States
[b] Biomedical Research Imaging Center, University of North Carolina at Chapel Hill, United States
[c] Microsoft Research, Cambridge, United Kingdom
[d] Delaware Biotechnology Institute, University of Delaware, United States
[e] Carl Zeiss Microscopy, United States

ARTICLE INFO

Article history:
Received 30 April 2013
Received in revised form 22 November 2013
Accepted 5 December 2013
Available online 18 December 2013

Keywords:
Multi-modal registration
Correlative microscopy
Image analogies
Sparse representation models

ABSTRACT

Correlative microscopy is a methodology combining the functionality of light microscopy with the high resolution of electron microscopy and other microscopy technologies for the same biological specimen. In this paper, we propose an image registration method for correlative microscopy, which is challenging due to the distinct appearance of biological structures when imaged with different modalities. Our method is based on image analogies and allows to transform images of a given modality into the appearance-space of another modality. Hence, the registration between two different types of microscopy images can be transformed to a mono-modality image registration. We use a sparse representation model to obtain image analogies. The method makes use of corresponding image training patches of two different imaging modalities to learn a dictionary capturing appearance relations. We test our approach on backscattered electron (BSE) scanning electron microscopy (SEM)/confocal and transmission electron microscopy (TEM)/confocal images. We perform rigid, affine, and deformable registration via B-splines and show improvements over direct registration using both mutual information and sum of squared differences similarity measures to account for differences in image appearance.

1. Introduction

Correlative microscopy integrates different microscopy technologies including conventional light-, confocal- and electron transmission microscopy (Caplan et al., 2011) for the improved examination of biological specimens. For example, fluorescent markers can be used to highlight regions of interest combined with an electron-microscopy image to provide high-resolution structural information of the regions. To allow such joint analysis requires the registration of multi-modal microscopy images. This is a challenging problem due to (large) appearance differences between the image modalities. Fig. 1 shows an example of correlative microscopy for a confocal/TEM image pair.

Image registration estimates spatial transformations between images (to align them) and is an essential part of many image analysis approaches. The registration of correlative microscopic images is very challenging: images should carry distinct information to combine, for example, knowledge about protein locations (using fluorescence microscopy) and high-resolution structural data (using electron microscopy). However, this precludes the use of simple alignment measures such as the sum of squared intensity differences because intensity patterns do not correspond well or a multi-channel image has to be registered to a gray-valued image.

A solution for registration for correlative microscopy is to perform landmark-based alignment, which can be greatly simplified by adding fiducial markers (Fronczek et al., 2011). Fiducial markers cannot easily be added to some specimen, hence an alternative image-based method is needed. This can be accomplished in some cases by appropriate image filtering. This filtering is designed to only preserve information which is indicative of the desired transformation, to suppress spurious image information, or to use knowledge about the image formation process to convert an image from one modality to another. For example, multichannel microscopy images of cells can be registered by registering their cell segmentations (Yang et al., 2008). However, such image-based approaches are highly application-specific and difficult to devise for the non-expert.

In this paper we therefore propose a method inspired by early work on texture synthesis in computer graphics using image analogies (Hertzmann et al., 2001). Here, the objective is to transform the appearance of one image to the appearance of another image

* Corresponding author. Tel.: +1 919 699 9542.
E-mail address: tiancao@cs.unc.edu (T. Cao).

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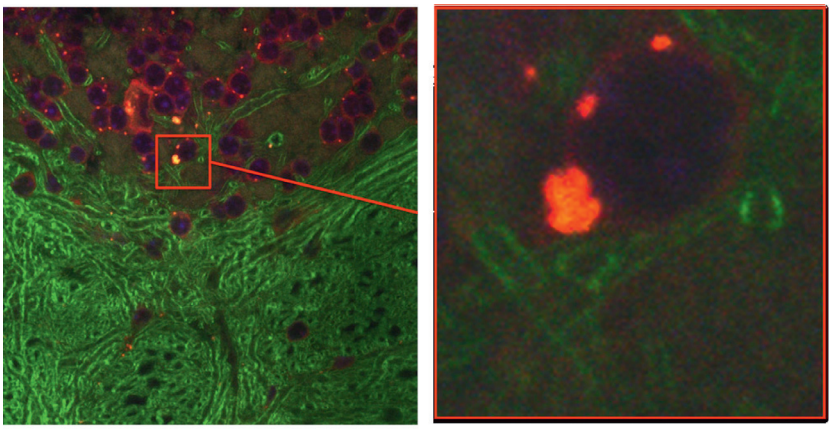
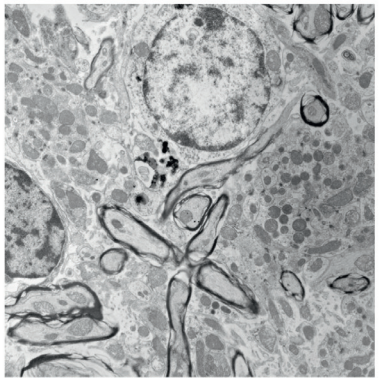
http://dx.doi.org/10.1016/j.media.2013.12.005



(a) Confocal Microscopic Image (b) Resampling of Region in (a)



(c) TEM Image

Fig. 1. Example of correlative microscopy. (a) Is a stained confocal brain slice, where the red box shows an example of a neuron cell and (b) is a resampled image of the boxed region in (a). The goal is to align (b) to (c). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

(for example transforming an expressionistic into an impressionistic painting). The transformation rule is learned based on example image pairs. For image registration this amounts to providing a set of (manually) aligned images of the two modalities to be registered from which an appearance transformation rule can be learned. A multi-modal registration problem can then be converted into a mono-modal one. The learned transformation rule is still highly application-specific, however it only requires manual alignment of sets of training images which can easily be accomplished by a domain specialist who does not need to be an expert in image registration.

Arguably, transforming image appearance is not necessary if using an image similarity measure which is invariant to the observed appearance differences. In medical imaging, mutual information (MI) (Wells et al., 1996) is the similarity measure of choice for multi-modal image registration. We show for two correlative microscopy example problems that MI registration is indeed beneficial, but that registration results can be improved by combining MI with an image analogies approach. To obtain a method with better generalizability than standard image analogies (Hertzmann et al., 2001) we devise an image-analogies method using ideas from sparse coding (Bruckstein et al., 2009), where corresponding image-patches are represented by a learned basis (a dictionary). Dictionary elements capture correspondences between image patches from different modalities and therefore allow to transform one modality to another modality.

This paper is organized as follows: First, we briefly introduce some related work in Section 2. Section 3 describes the image analogies method with sparse coding and our numerical solution approach. Image registration results are shown and discussed in Section 4. The paper concludes with a summary of results and an outlook on future work in Section 5.

2. Related work

2.1. Multi-modal image registration for correlative microscopy

Since correlative microscopy combines different microscopy modalities, resolution differences between images are common. This poses challenges with respect to finding corresponding regions in the images. If the images are structurally similar (for example when aligning EM images of different resolutions (Kaynig et al., 2007), standard feature point detectors can be used.

There are two groups of methods for more general multi-modal image registration (Wachinger and Navab, 2010). The first set of approaches applies advanced similarity measures, such as mutual information (Wells et al., 1996). The second group of techniques includes methods that transform a multi-modal to a mono-modal registration (Wein et al., 2008). For example, Wachinger introduced entropy images and Laplacian images which are general structural representations (Wachinger and Navab, 2010). The motivation of our proposed method is similar to Wachinger's approach, i.e. transform the modality of one image to another, but we use image analogies to achieve this goal thereby allowing for the reconstruction of a microscopy image in the appearance space of another.