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A marker-free automatic alignment method based on scale-invariant features

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ABSTRACT

In electron tomography, alignment accuracy is critical for high-resolution reconstruction. However, the automatic alignment of a tilt series without fiducial markers remains a challenge. Here, we propose a new alignment method based on Scale-Invariant Feature Transform (SIFT) for marker-free alignment. The method covers the detection and localization of interest points (features), feature matching, feature tracking and optimization of projection parameters. The proposed method implements a highly reliable matching strategy and tracking model to detect a huge number of feature tracks. Furthermore, an incremental bundle adjustment method is devised to tolerate noise data and ensure the accurate estimation of projection parameters. Our method was evaluated with a number of experimental data, and the results exhibit an improved alignment accuracy comparable with current fiducial marker alignment and subsequent higher resolution of tomography.

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1. Introduction

Electron tomography (ET) is a promising technology that allows the three-dimensional imaging of cellular ultrastructure. The structure is reconstructed from a tilt series of micrographs taken at different orientations. However, transformation and deformation of the sample are inevitable when the sample is tilted along a fixed axis. To obtain high-quality reconstructed results, accurate alignment is critical before reconstruction.

There are two types of alignment methods, fiducial marker-based alignment and marker-free alignment. Fiducial marker-based alignment is currently the most accurate alignment method. Unfortunately, fiducial markers are not always accessible, because sometimes it is impossible to have gold beads embedded in a sample and sometimes it is difficult to find enough gold beads at the region of interest. Moreover, the use of colloidal gold may interfere with the sample and introduce undesirable artifacts. Additionally, the selection of markers is usually manual and very time-consuming. In contrast, marker-free alignment does not require fiducial markers. It can be subdivided into two categories of methods, correlation methods and feature-based methods. Correlation methods, such as cross-correlation (Guckenberger, 1982) and common lines (Liu et al., 1995), have been widely used in coarse alignments to solve large translation or in-plane rotation problems. However, these methods neglect motion in real space and result in accumulated correlation errors. To compensate for these shortcomings, Winkler and Taylor (2006) proposed a solution combining cross-correlation with a reconstruction reprojection method, but this method consumes excessive computational resources. Compared with correlation methods, feature-based methods provide a model that is closer to the real conditions and is not computationally intensive. Feature-based methods utilize image features as virtual markers and align images by minimizing the reprojection error of virtual markers. The principle of feature-based alignment is same as that of marker alignment. Usually, features can be determined by informative surroundings, such as a Harris Corner (Brandt et al., 2001; Brandt and Ziese, 2006), Canny edge, or contour line (Phan et al., 2009), and appointed landmarks (Sorzano et al., 2009). Castaño-Díez et al. (2007, 2010) used image patches instead of corner points in the proceeding cryo-ET series. These features are iteratively tracked from the corresponding area of adjacent images according to the normalized cross-correlation. However, such a tracking method is not always robust, especially in the case of low Signal-to-Noise Ratio (SNR) where there are insufficient distinguishable gray levels. These methods mainly

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introduce two types of errors that are highly influential with respect to geometry parameter determination, feature localization error and false matching.

Although feature-based methods are more accurate than correlation methods, three key issues remain to be resolved. The first is how to accurately detect and locate interest points (features). As mentioned above, virtual markers are extracted with a computer vision technique, which inevitably introduces localization errors. The second is how to partition a huge amount of features into tracks. Typically, an alignment operation involves hundreds of images. For every image, thousands of features could be extracted. Tracking hundreds of thousands of features is very time-consuming. In addition, marker mismatching and matching collisions must be resolved during tracking. The third issue is how to optimize projection parameters after tracking. It is very difficult to solve this problem because there are a large number of tracks and the length of each track is relatively short compared to the size of the image stack. Because not all of the tracks are consistent, a robust method for parameter optimization must be used.

To overcome these problems, we propose a new marker-free method based on Scale-Invariant Feature Transform (SIFT) to solve marker-free alignment. SIFT is a well-known technique used in computer vision that can locate points in scale-space and utilize redundant feature information. Compared to other previous methods, our method has several advantages. First, we utilize SIFT to detect and recognize a huge number of significant virtual markers that are invariant to the changes of scale, orientation, noise etc. After the "significant" or "interesting" points are detected, we focus only on the important parts of the tilt series, which potentially ignores background areas. Second, in addition to the detection of localization, the distinctive information of features is characterized, which makes feature matching and tracking more robust. Furthermore, our method contains an effective tracking model to make feature tracking more efficient and resistant to dubious matching. Third, in contrast to previous methods using a simplified version of the affine model (for example, the research in Brandt et al., 2001; Brandt and Ziese, 2006), our method uses a more parameterized model, which benefits from our high-quality tracking and can make further analysis of tilt series possible, resulting in more accurate alignment. Experimental datasets were tested and proved that our alignment method can optimize the parameters with subpixel accuracy of the reprojection residual.

The remainder of the paper is organized as follows. In Section 2, we introduce the framework of our method. First, we introduce the usage of SIFT in electron micrographs and demonstrate our effective matching strategy and tracking model. Then, an incremental bundle adjustment procedure designed especially for our approach is proposed. In Section 3, we present our experimental results and analysis. Section 4 is focused on discussion and conclusion.

2. Method

Our method consists of four steps. The first step is to extract the precise location and descriptions of features from projection images. We utilize SIFT to obtain subpixel feature localizations and descriptor vectors with redundant information, which ensures that the extracted features are invariant to scale, rotation and illumination changes. The second step is to match corresponding features. Because of the large number of feature points, we propose a location-based search method to ensure accuracy and accelerate the matching speed. The third step is to track matching pairs consistently across the tilt series. Based on the transitivity of matched peers, here we first develop a matching strategy to reduce the matching cost and then propose a novel tracking model to reduce tracking complexity. The final step is to optimize the projection parameters with the configured tracks and, if necessary, to geometrically transform the images. We first present the parameter optimization model of our method, and then propose an incremental bundle adjustment method to solve the optimization problem. Our approach obtains results with improved accuracy which is comparable with that got by fiducial marker alignment.

2.1. Feature extraction with SIFT

One feature is composed of two parts, the location and distinctive information (descriptor). In previous feature-based methods, only the gray values in the neighborhood are considered for cross-correlation, and the abundant information that the neighborhood renders is neglected. Thus, such processes are apt to mismatch and do not generate high-quality tracks. Our method utilizes the SIFT detector (Lowe, 2004) to extract features. SIFT can localize the most stable points in images and form the neighborhood information into a 128-dimensional descriptor that contains gradient and magnification information in a redundant manner. In fact, SIFT has been widely used in low SNR image analysis, for example, Alzheimer's disease detection in medicine (Toews et al., 2010) and image stitching in ET (Kaynig et al., 2010). These reports showed a high accuracy of localization and discrimination of detail of SIFT. Mikolajczyk and Schmid (2005) compared the SIFT descriptor with other invariant feature descriptors and drew the conclusion that SIFT performed the best under the changes of scale, rotation and illumination.

SIFT consists of the following four major stages: (1) Scale-space extrema detection. (2) Keypoint localization. (3) Orientation assignment. (4) Keypoint descriptor.

Scale-space extrema detection is to identify the locations which appear repeatedly for the same object in different views and scales. To detect locations that are invariant to the scale change of images, we search for stable features across all possible scales using a continuous scale function known as scale space. The scale space is a collection of the image function convolved with various Gaussian kernels, which is defined as the function $L(x, y, \sigma)$:

$$L(x, y, \sigma) = \frac{1}{2\pi\sigma^2} e^{-(x^2+y^2)/2\sigma^2} * I(x, y) \tag{1}$$

where $I(x, y)$ is the input image, $*$ is the convolution operation in x and y. σ is the Gaussian scale and various values of σ will produce different scale in the scale space. To efficiently detect stable key locations in scale space, Lowe (1999) adopted scale-space extrema in the difference-of-Gaussian (DoG) function, defined as $D(x, y, \sigma)$, which can be computed from the difference of two nearby scales separated by a constant multiplicative factor k:

$$\begin{aligned} D(x, y, \sigma) &= (G(x, y, k\sigma) - G(x, y, \sigma)) * I(x, y) \\ &= L(x, y, k\sigma) - L(x, y, \sigma) \end{aligned} \tag{2}$$

The DoGs of various Gaussians compose the DoG space. DoG is an approximation of the scale-normalized Laplacian-of-Gaussian, which is required for true scale invariance (Lindeberg, 1994). An extremum point (maxima or minima of the DoG images which is detected by comparing a central pixel to its 26 neighbors in 3×3 regions at the current and adjacent scales) of scale-space can produce the most stable features for one image (Mikolajczyk, 2002).

Keypoint localization is to fit a candidate with its adjacent data according to the location, scale, and ratio of the principal curvatures. Candidate points that have low contrast or are poorly localized along the edges (points with peak value in the DoG but sensitive to noise) will be rejected in this stage. This process provides a substantial improvement in the stability of features.

Orientation assignment is to assign one or several orientations to each keypoint based on gradient directions. Orientations are

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