The Role of Open-Source Software in the Study of Embryogenesis

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Abstract. This paper focuses on the important role of open-source software in the development of a fully-automatic and accurate registration system for images of Quadrature Tomographic Microscopy. The system is correspondence-based, using the framework provided by open-source RGRL (Rensselear Generalized Registration Library). The library implements several well-known techniques and the ability to mix-and-match techniques for components of the framework allows testing of ideas and development of the robust system in a timely fashion.

1 Introduction

Infertility now affects 10% of the population at reproductive age. *In Vitro* Fertilization (IVF) is one of the methods for assisted reproduction. To increase the success rate, doctors transfer multiple embryos back into the mother during one cycle. This brings the rate of live deliveries to 30-40%, of which about 63% are singletons, 32% are twins, and 5% are triplets or more.

One reason for the low success rate and high multiple-birth of IVF is the uncertainty of the quality of an embryo. The development of "fusion microscope" enables the study of distinguishing features of viable embryos [6]. This instrument combines 5 imaging modalities for subsurface imaging, including Quadrature Tomographic Microscopy (QTM) and Differential Interference Contrast (DIC) microscopy. Registration is crucial for such a system for the purpose of information fusion.

The focus of this paper is on the software aspect of intra-modality registration of QTM images. The algorithmic aspect of the work is presented in [7]. QTM is based on a modified Mach-Zener Interferometer. The laser source is split into signal and reference beams. The signal beam goes through the sample (embryo) and the reference beam travels the same distance as the signal beam, but is undisturbed. Both are combined later by an unpolarized beamsplitter and their interference is imaged simultaneously by 4 CCD cameras, each having its own coordinate system. An embryo is imaged three times by different hardware configurations. Example images are shown in Fig. 1.

Placing all images in the same coordinate system defines 2 registration problems: (1) alignment of images taken simultaneously by the 4 CCD with the same hardware configuration, and (2) alignment of images taken at different times to compensate for movement of the embryo. Challenges include substantial changes
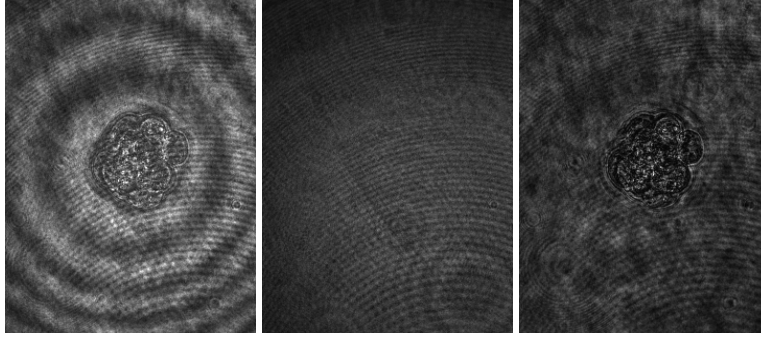
Fig. 1. QTM images of a live embryo taken with different hardware configurations. Accurate registration is required to eliminate the movement of the embryo between imaging. Left: mixture of reference and signal. Middle: reference alone, which does not contain the image of the embryo. Right: signal alone.
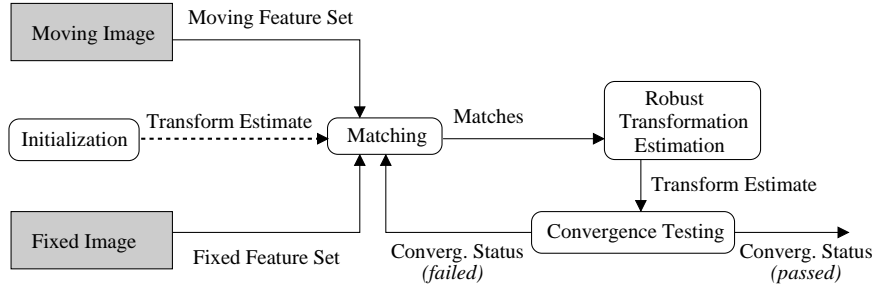
Fig. 2. Architecture of the inner loop of general correspondence-based registration. Each computational component, enclosed in the box, takes one or more representation objects as input, and produces one representation object as output, indicated by the arrow.

in appearance and estimation of an affine transformation with reflection between images taken by different cameras. We design a system that handles both problems, and the development relies heavily on open-source libraries for feature extraction and image registration.

2 Correspondence-Based Image Registration

2.1 The Framework of RGRL

RGRL [4] (Rensselear Generalized Registration Library) is a library for correspondence-based registration. This library is part of VXL, which is an open-source package designed for computer vision applications [5]. The RGRL has been the foundation for development of several medical applications, including DB-ICP retinal

image registration [2] and registration of serial lung CT images [3]. The framework has an inner flow loop implementing a basic but flexible correspondence framework (see Fig. 2). It consists of following major components:

Feature: Pre-computed or constructed dynamically, features are the basic primitives of correspondence-based registration. Different feature types define different alignment error distance measures.

Initialization: This component generates one or more initial transformation estimates, which are tested sequentially.

Matching: The matching process generates correspondences from the two image feature sets. The details depend on the feature type as well as on the type of matching, such as nearest-neighbor or most-similar appearance.

Robust transform estimation: This process estimates the spatial relationship that maps the moving image onto the fixed image using the matches. The estimation is robust to handle outliers and mis-matches.

Convergence testing: The registration process terminates when the estimation has converged to a stable solution or is determined to be oscillating.

The role of each component is isolated by being designed as an abstract base class, with a wide-variety of techniques being implemented as derived classes. The outer loops controlled by a "registration engine" allow for multiple initial estimates, multiple feature types, and multiple resolutions for generalization.

2.2 Registration of QTM Images

We handle the two registration problems separately, but with the same framework provided by RGRL. For alignment of the 4 CCD camera spaces, we perform registration on a man-made pattern which contains lines crossing at random angles. For elimination of the embryo movement, we register two synthesized images: one from the registered signal-only images and one from the rest. The synthesized images are similar in appearance. The two registration problems differ substantially in terms of image features that are meaningful for registration. This difference leads to different choices of feature-types, initializers, and matchers. With a proper choice of derived classes for the registration components, we achieved full automation, high accuracy, and robustness.

For alignment of the camera spaces, features extracted from the images are the cross-overs and the center points of the lines. Feature extraction relies on VXL libraries. For each image, a set of landmark (cross-over) pairs is generated and each pair is associated with an invariant descriptor of angles between lines. The *initializer*, which implements invariant indexing, generates a list of hypothesized correspondence pairs, rank-ordered based on the similarity of the invariant features. Each hypothesis provides an initial transformation, which is refined using an ICP (Iterative Closest Point) *matcher* on center points of the lines. The *feature type* for the center points is a point location associated with a tangent direction. The robust *transformation estimator* minimizes the sum of point-to-line distances using an M-estimator.

The purpose of image alignment of different configuration is to eliminate embryo movement between imaging. Therefore, we want features that concentrate in the embryo. Edge points are not good candidates, since they are mostly on the fringes in the background. We extract harris-corners as the keypoints for registration and the *feature type* is a point location associated with a small local region. The *initializer* also runs invariant indexing, but the invariant feature is a 128-component histogram of normalized gradients (Lowe's SIFT descriptor[1] [1]). The *matcher* is a variant of ICP that matches keypoint based on intensity structure (a block matcher). Only keypoints from the moving image are retained for refinement of the transformation. The block matcher creates a temporary correspondence (and feature) by taking the small region centered on a feature in the moving image and finding the best corresponding region in the fixed image based on an intensity match. The center locations of the corresponding regions provide a point-to-point distance measure for the robust *transformation estimator*.

3   Discussion and Conclusion

We tested the system on a set of 20 live embryos. The alignment accuracy is 0.09 pixel (639-675 nanometers), and there is no failure thus far. For elimination of embryo movement, we also tested ideas of initialization with RANSAC and matching using ICP matcher by choosing different derived classes. Both methods are not as robust as our final selections. The use of open-source software allow us to focus on the high-level design of the algorithms, test out ideas in a timely fashion, and achieve full automation for accurate registration of QTM images.

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[1] We re-implemented the algorithm for extraction of SIFT descriptor, and this part of code is not open-source.