I'mCell: A touch pad tool for annotating cell images

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***Abstract* - Time-lapse microscopy imaging of live cells has been used by numerous biomedical studies to analyze cell function and behavior. Algorithms for automatically interpreting these data require manual annotations for training and evaluation. This paper describes an easy-to-use, portable tool called *I'mCell* that enables researchers to use a touch pad to annotate object regions in images efficiently. A user study was conducted that involved three domain experts in cell imaging who annotated 100 phase-contrast images of live muscle cells with the proposed touch pad tool and two pointer-based annotation tools. The study showed that the proposed tool provided a convenient and accurate means for manual annotation. The paper concludes with suggestions how the proposed tool could be used to crowdsource annotations of thousands of cell boundaries.**

Keywords: Segmentation, microscopy imaging, gold-standard annotations, user study, cell image analysis.

I. INTRODUCTION

Analyses of medical and biological images often involve measurements of object properties such as size, orientation, movement direction and speed, or morphological class [1, 2, 3]. Automated methods that provide such measurements are validated by comparisons to gold standard annotations that are typically established in a time-consuming manual process. Manual annotations are also needed to train image analysis algorithms that use machine learning techniques. Popular annotation tools require human-computer interaction with a mouse pointer. *ImageJ* [4], for example, is an open-source, pointer-based tool that is widely used by cell biologists in the tedious process to annotate time-resolved data produced by automated microscopes at high throughput. "*iPad*" [5] is a pointer-based tool for the Mac-based OsiriX environment that can be used by radiologists, for example, to annotate lung tumors. With the proliferation of tablet computers, the question has recently arisen whether image annotations can be produced similarly accurately with touch-based as with pointer-based human-computer interaction. Drawing an object contour directly with a finger might be easier than using the mouse. Not much work has been reported in the literature that attempts to answer the question of efficacy of touch-based annotation. Li and Liu [6] recently developed an iPad annotation tool and reported promising preliminary results for touch-based segmentation of microscopy images. The contribution described in this paper is also an iPad-based annotation tool; the focus, however, is on testing the efficacy of the tool in a formal user study, which involved three expert participants who each segmented 100 phase-contrast images of bovine vascular smooth muscle cells.

II. METHODS

A. Image Annotation Tool *I'mCell*

I'mCell enables users to annotate the contour of objects in images on a touch pad by filling in object regions with their fingers or a stylus. It was implemented as an iPad application using the Matlab Mobil iPad App. As a user makes drawings on the touch screen, *I'mCell* displays them in a color of choice in juxtaposition over the object in the image with the transparency value of 0.3. An example of an annotation juxtaposed in red over the cell image is shown in Fig. 1.

Figure 1: Portion of a screenshot during the use of I'mCell. The red region indicates an annotation performed by a user. When saved, the annotation is stored as a binary mask.

I'mCell has brush and eraser tools with a functionality similar to that of physical tools, i.e., colored pencil and rubber eraser, that children use with coloring books. The user can choose the size of the brush. A small brush makes it possible to fill in small or thin objects; a large brush enables efficient annotations of large objects. When the user draws an annotation, the application stores the trajectory that the user's finger or stylus makes while touching from the trajectory start point to its end point as a Bezier path. There are two options: The *brush* option saves the path with the color that the user chose; the *eraser* option saves the path with the original image pattern.

I'mCell uses the built-in interfaces of the iPad, including the commands *Zoom-in/Zoom-out* and *ScrollView* to view the image and adjust the size of the view. The user can manage the zoom function by tapping a *Zoom-on/Zoom-off* button. *Zoom-off* enables the drawing function. The clear function removes all paths.

I'mCell can load multiple images, so that the user can efficiently annotate a whole folder of images instead of having to load a single image at a time. Being able to load multiple images is a feature that participants of a previous study [7] requested, when they experienced that this feature is missing in Amira. With *I'mCell,* the user can move between images by tapping the buttons "Prev" or "Next." With this feature, the user can see his or her previous annotations and consider them when annotating the current image. *I'mCell* also provides the "Fill" function that copies the annotation of the previous image and juxtaposes it into the current image. This feature is particularly useful when the objects in subsequent images are not changing much, such as cells in time-lapse microscopy image sequences. The user can select the fill command first and then adjust the marked region of the object a little to achieve the annotation he or she wants.

B. Methodology of Annotation Collection

A user study was designed to investigate whether the proposed touchpad tool *I'mCell* works at least as good as, or better, than tools existing for desktop computers. Three domain experts in cell imaging were asked to label the contours of 100 phase-contrast images of bovine vascular smooth muscle cells, which were isolated from two types of rabbit aorta: New Zealand White rabbit aorta and Watanabe Heritable Hyperlipidemic (WHHL) rabbit aorta (Brown Family Research). The images were collected with a magnification factor of 10 using a Zeiss Axiovert S100 microscope (Carl Zeiss), a motorized stage (Ludl, Hawthorne, NY), a cooled CCD camera (Princeton Instruments, Trenton, NJ), and Metamorph software (Universal Imaging).

The experts annotated each image with three different tools: *Amira*, *ImageJ*, and *I'mCell*.The first tool, *Amira* [8], was newly introduced to the participating domain experts. It had resulted in the smallest inter-annotator variations in a previous study [7]. The second tool, *ImageJ* [4], was anticipated to yield accurate results since the experts were familiar with it. Annotator A1 had used *ImageJ* for 2 years for annotation work in his research, annotator A2 for 5 years, and annotator A3 for 4 years. The third tool evaluated was *I'mCell*, the new touchpad tool. After attending a training session on *Amira* and *I'mCell*, the annotators were given the images in a particular order and were asked to annotate them on their own time. When segmenting the same cell three times in a row, an annotator may get used to the task and perform better with the third tool used. Annotators were provided different orders of tools to use when creating the annotations to prevent such a bias.

C. Methodology of Annotation Evaluation

The following measures of accuracy and precision were used to compare the image regions X and Y segmented by two annotators, respectively: The accuracy $A= |X\cap Y|/|X|$ is the number of pixels in overlapping regions X and Y, as fraction of the number of pixels in X, where X is deemed to be the gold standard and Y the attempt to match it. The precision $P=|X\cap Y|/|X\cup Y|$ is the number of pixels in overlapping regions X and Y, as a fraction of the number of pixels annotated in both regions. Since the accuracy measure is not symmetric, A was computed for the pairs XY=A1A2, A2A1, A1A3, A3A1, A2A3 and A3A2. Precision P was computed for pairs XY= A1A2, A1A3, and A2A3. The evaluation tool SAGE [6] was used to evaluate the accuracy and precision scores for each pair of annotations and compute averages over the 100 images that each participant annotated.

III. Results

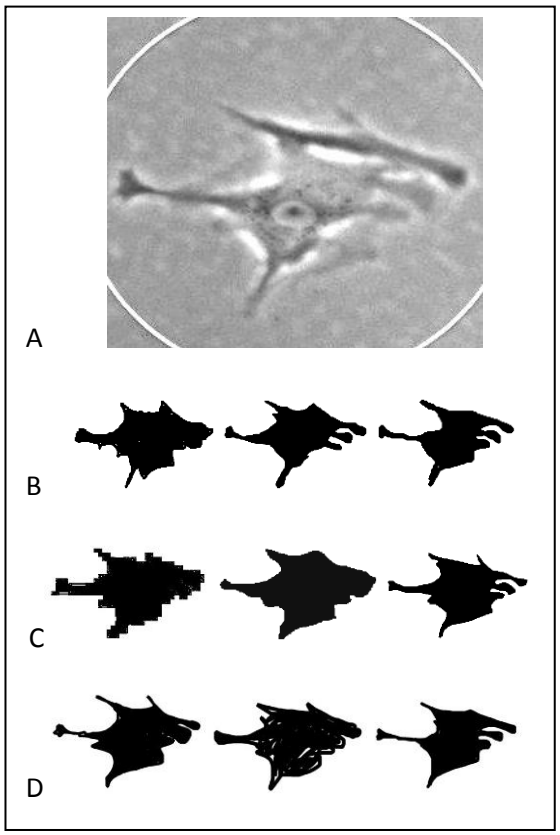
Examples of annotations collected by the three experts with the three tools are shown in Fig. 1. Additional examples can be found in the thesis by Kim [9]. The results of the annotation evaluation are summarized in Tables 1 and 2. The average accuracy scores A for annotations with *Amira* were 0.81, *ImageJ* 0.64 and *I'mCell* 0.66. The respective standard deviations were 0.07, 0.35, and 0.08. Drawings by annotator A1 yielded the highest agreement, 0.84, drawings by annotator A2, the lowest, 0.54. The difference between these scores, 0.3, is significantly larger than the difference 0.16 between scores for best and worst performing annotation tool. Visual inspection revealed that annotator A2 indeed produced "rougher" annotations than the other annotators (Fig. 2, middle column). The average precision scores P for annotations with *Amira* were 0.67, *ImageJ* 0.32 and *I'mCell* 0.48 with respective standard deviations of 0.03, 0.22, and 0.06.

TABLE 1: ACCURACY RESULTS FOR 100 CELL IMAGES

Annot. Method	Average Accuracy A of Annotations					
	A1A2	***A2A1***	***A1A3***	***A3A1***	***A2A3***	***A3A2***
Amira	0.80	0.85	0.70	0.87	0.74	0.87
ImageJ	0.20	0.97	0.64	0.84	0.96	0.23
I'mCell	0.56	0.72	0.66	0.78	0.66	0.60

TABLE 2: PRECISION RESULTS FOR 100 CELL IMAGES

Annot. Method	Average Precision P of Annotations		
	A1A2	***A1A3***	***A2A3***
Amira	0.70	0.64	0.68
ImageJ	0.18	0.57	0.20
I'mCell	0.45	0.56	0.44



Example Results: Phase-contrast image of a cell (A). Cell region annotations provided by three domain experts with *Amira* (B), *ImageJ* (C), and *I'mCell* (D).

IV. DISCUSSION OF RESULTS

The results of the annotator study show that the proposed touchpad tool *I'mCell* yielded segmentations that were more accurate and precise than those obtained with the popular open source tool *ImageJ*. Annotating with the commercial tool *Amira* produced the most accurate and precise results. Since the inter-annotator differences were significantly larger than the differences produced by different annotation tools, these results suggest that *I'mCell* may be recommended as an annotation tool, especially if annotators prefer a mobile touch pad and cannot afford the costs of a commercial system.

V. FUTURE WORK: CROWDSOURCING

Crowdsourcing is a relatively new way of gathering annotations from a numerous unknown people connected by the Internet, so that the process of establishing gold standard segmentations becomes faster and cheaper [10, 11]. Given the popularity of tablet computers, *I'mCell* might be a convenient, mobile tool for online workers to participate in the crowdsourcing of cell image annotations. Future work proposed for *I'mCell* will test whether crowdsourcing can yield cell image annotations that are deemed to be sufficiently accurate and precise by domain experts. Given the impact of tools on inter-annotator variations shown in this paper, crowd-sourcing might be able to provide annotations that are as good as what experts can produce. Large groups of citizen scientists or paid individuals from the general public may then participate in advancing the understanding of fundamental biological processes and thus contribute to treatment and prevention of disease.

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