Automating Lifecycle-Phase Identification in Microscopy Images of Zebrafish Embryos

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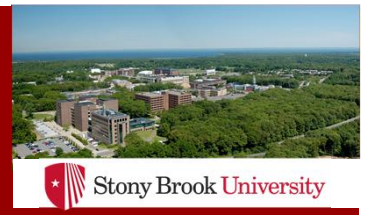


Introduction

Biologists rely heavily on microscopy imagery to view and analyze cellular data. In order to analyze the imagery they need to manually look through numerous time frames and within each time frame examine all the depth slices. This is a tedious and time-consuming task for biologists. Here we tackle the problem imposed by the zebrafish embryos, where during cell-division the organization of microtubule fibers change. The microtubule fibers form a bridge as a series of dots prior to abscission and finally condense to a single dot (remnant) when the abscission is complete. See stages 4 and 5 in figure 1. Our goal is to use machine learning and computer vision to automate the process of localizing the bridges and remnants that occur during cell-division.

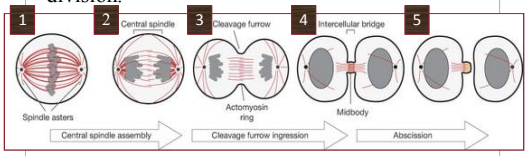


*Figure 1: Cell-Division Process**

**** Courtesy of Shai Edar, Natalie Elia, Ben Gurion University***

Objectives

Given consecutive times frames, each consisting of 30 depth slices, we would like to identify and localize the bridges and remnants. The images are 0.324 microns per pixel, with Z step-size of 900 microns and 2 minutes interval between consecutive frames. The input is 3 channels: DIC, 488 for bridges, and 561 for remnants.

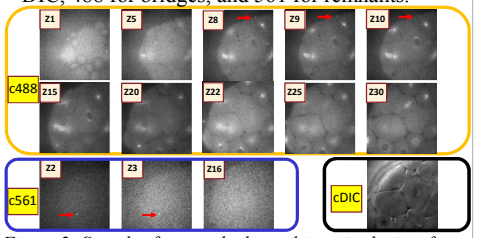


Figure 2: Samples from each channel in a single time frame

Source: ***The Elia Lab for Cellular Imagery, Ben Gurion University***

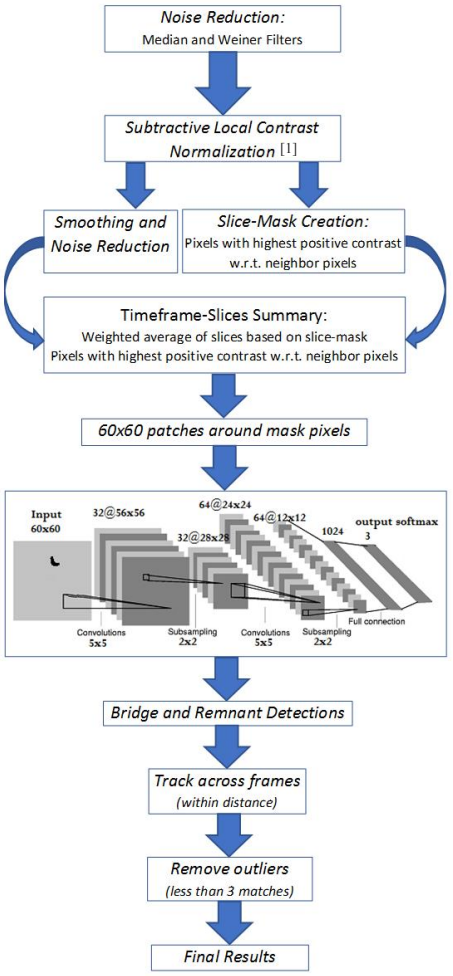


Figure 3: Operation Diagram

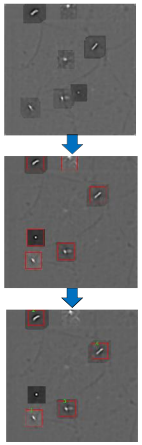
Challenges

- ***The dataset is very small***; about 70 time frames with an average of 0.6 bridge per frame. Annotated data is scarce since it takes biology experts about a week to annotate a 2 hours capture.
- ***Extremely noisy images***.
- ***Bridges are only visible in a couple of slices*** in the frame and not visible in the rest.
- ***The bridge appearance is sometimes very similar to cell nuclie*** and sometimes is very fade especially near the beginning and end of its lifetime.

Methods

We operate in 3 main steps:

1. ***Preprocessing:*** denoising and compressing the slices of each timeframe into a single image identifying areas of interest.
2. ***CNN detection*** on 60x60 patches around areas of interest using a shallow convolutional network inspired by AlexNet [2]
3. ***Tracking*** bridges and removing outliers



The whole operation details can be viewed in figure 3.

Method Advantages:

- The preprocessing step does not take a lot of time while allowing to maximize on the information retrieved and speedups the localization process.
- Shallow CNN allows faster operation and training while utilizing a very small dataset
- Identifying areas of interest allows us to process only those by the CNN.

Results

Fig. 4 shows a sample of our results. First 3 rows shows bridges and the last row shows remnants in channels 488 and 561 respectively.

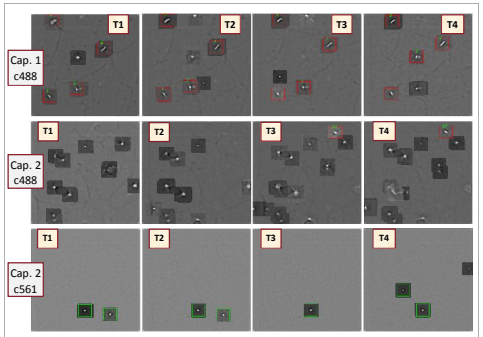


Figure 4: Sample Results

- Average Running Time: 21 sec per timeframe
- Remnant Detection Accuracy: 100%
- Bridges: vary in difficulty to detect (fig. 5)

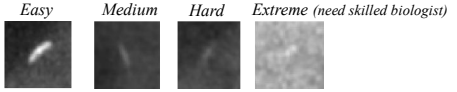


Figure 5: Instances of Bridges with varying difficulty

F-score with different levels of bridge difficulty:

	≤ Medium	≤ Hard	≤ Extreme (all)
F-score	0.82	0.75	0.68

Running on every slice in a sliding window manner:

- Average run time:120 sec/slice (≈ 60 min) per timeframe.
- Inspect whole slice + very high noise level

→ too many false positives.

Conclusions

Our proposed method is effective in localizing patterns in the lifecycle of zebrafish embryos (bridges and remnants) in microscopy imagery given a handful of training data. It provides balance between speed and accuracy. Speedup is partially achieved by capturing the essence of the slices, allowing us to combine them and work only on the areas of interest in each timeframe.

References

[1] K. Jarrett, K. Kavukcuoglu, M. Ranzato, and Y. LeCun, "What is the best multi-stage architecture for object recognition!?" in CCV'09.
[2] A. Krizhevsky, I. Sutskever, and G. Hinton. ImageNet classification with deep convolutional neural networks. In NIPS, 2012.