EE 368/CS 232 Project Proposal

Automatic Cell Detection of Liver Tissue Section Image

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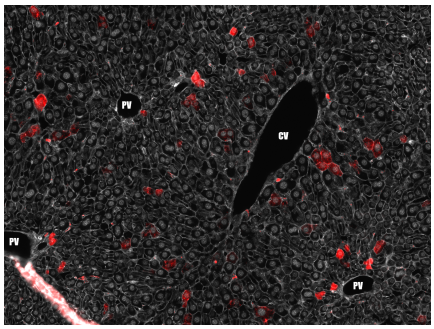
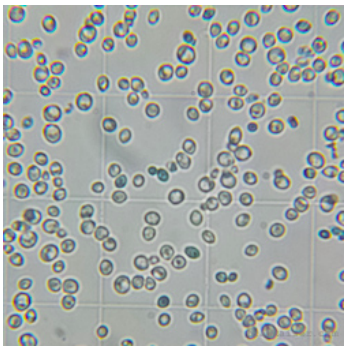
1 Introduction

The Nusse Lab of the Stanford Institute of Stem Cell Biology & Regenerative Medicine studies the regenerative properties of the liver. The goal of this project is to help graduate students in the Nusse Lab automate the tasks of cell counting and characterization of liver tissue section images, leveraging image processing and machine learning techniques.

Currently, the cell counting tasks of tissue section images are done by hand, in a manual and laborious manner, because general purpose image processing software such as Image J does not adequately address the specific need for these types of images and there are no commercially available products solving this problem [Gri15]. While previous projects have dealt with cell counting or characterization of cell culture images, this project tackles the more difficult problems presented by tissue section images due to their non-homogeneous nature and the high levels of details present in these images [MMB94]. For example, tissue section images typically contains an order of magnitude more resolution and features than cell culture images, as shown in Figure 1.



(a) Sample tissue cross-section



(b) Sample cell culture

Figure 1: Tissue cross section vs. cell culture

There are numerous benefits associated with potentially automating these tasks, based on a survey of existing literature [WGvH+16, MMB94]. Automating these tasks using image processing and machine learning may result in significant time savings as well as reduce measurement variability due to operator-dependent and parameter-sensitive conditions. Additionally, automation has the potential of quantifying numerous cell morphology characteristics that are difficult or expensive to do so manually [Gri15].

2 Goals and Proposed Tasks

This project aims to achieve at least two of the following goals.

1. Accurately detect cell counts irrespective to their stain at a precision of greater than 90%.
2. Correctly classify features, such as portal vein, central vein, and bile duct, at a precision of greater than 90%.

3. Accurately detect cell type and clones based on fluorescent markers at a precision rate of greater than 90%.

4. Accurately quantify morphological features, including cell size and cell relative position, at a precision of greater than 90%.

5. Correct segmentation of clustered nuclei at a precision rate of greater than 90%.

To help achieve these goals, the project tasks will fall roughly into the following two buckets.

Image processing [WGvH+16, Ca09, LWVL03]

1. Preprocess the images, such as binarization using locally adaptive thresholding to compensate for non-uniform lighting or cross-referencing multi-channel images to sharpen features.

2. Remove immaterial regions using morphological operations, including but not limited to low-pass filtering for removing small artifacts, closing and opening for smoothing cell boundaries

3. Segment images by detecting edges using gradient-based edge operators, including Prewitt, Sobel, and Roberts, as well as other methods including Laplacian of Gaussian and Canny edge detector

Feature classifications [WGvH+16, LWVL03]

1. Classification of fluorescent marker cells using dimension reduction methods such linear discriminant analysis or principle component analysis, potentially combined with histogram thresholding.

2. Use unsupervised learning algorithms such k-means clustering to identify image features, including cells, nuclei, and veins.

3. Train feature-based models and use human-labeled datasets to correctly classify features, including cell types, clones associations, and vein types.

3 Dataset and Collaboration

The image set is provided by PhD student Dani Zhao of the Nusse Lab as part of her work studying a special population of hepatocytes that are hepatocyte stem cells in the uninjured adult mouse liver. There are currently 24 images, each with three color channels that is about 1.5 to 2 MB per image. More images could be obtained upon request. A sample liver tissue image with labeled features is shown in figure 2.

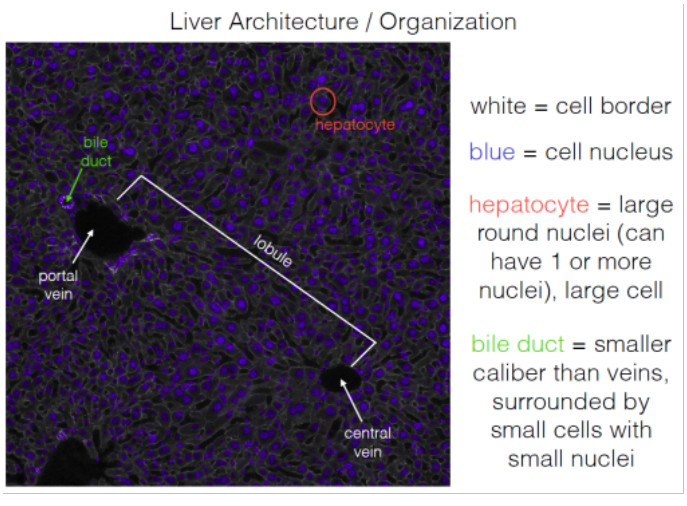


Figure 2: Sample Liver Tissue Cross Section

4 Tools

- MATLAB - image processing toolbox
- ImageJ as benchmark;
- Android device ***not*** used

5 Note

The same dataset and common infrastructure may be shared with the final project of CS 221: Artificial Intelligence Principles and Techniques, which will focus mainly on the analysis of the performance of classification algorithms. The CS 221 instructor has expressed approval of the potential project sharing, and guidelines on the CS 221 final project can be found at the following site: <http://web.stanford.edu/class/cs221/project.html>

References

[Ca09] J. Cheng and J. C. Rajapakse ^{ast}. Segmentation of clustered nuclei with shape markers and marking function. *IEEE Transactions on Biomedical Engineering*, 56(3):741–748, March 2009.

[Gri15] IV Grishagin. Automatic cell counting with imagej. *Analytical Biochemistry*, 2015.

[LWVL03] Constantinos G. Loukas, George D. Wilson, Borivoj Vojnovic, and Alf Linney. An image analysis-based approach for automated counting of cancer cell nuclei in tissue sections. *Cytometry Part A*, 55A(1):30–42, 2003.

[MMB94] Fumio Maruhashi, Sei Murakami, and Kenji Baba. Automated monitoring of cell concentration and viability using an image analysis system. *Cytotechnology*, 15(1):281–289, 1994.

[WGvH$^+$16] P. Wuttisarnwattana, M. Gargesha, W. van't Hof, K. R. Cooke, and D. L. Wilson. Automatic stem cell detection in microscopic whole mouse cryo-imaging. *IEEE Transactions on Medical Imaging*, 35(3):819–829, March 2016.