BME 547 Project Proposal: Protein Microarray Image Processing Server

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# Background:

Protein Microarrays are an emerging field for point-of-care diagnostics in medicine. These microarrays are able to quantify picomolar amounts of protein within complex biological fluids (blood, urine, sputum). As a research tool, scientists can use microarray data to track the interactions and activities of proteins, and to determine their function, and determining function on a large scale1. As a clinical tool, medical staff can use microarray data to track patient biomarker levels to make critical diagnostic and therapeutic decisions. However, there is a need for engineering solutions to fully translate protein microarray technology to the clinic.

The Chilkoti lab at Duke University has been developing a protein microarray system known as the D4. The D4 is operated with printed reagent spots on a proprietary polymer brush surface on a glass slide. Once run, a fluorescent microscope camera takes a picture of the slide. Fluorescent spots within the image are manually segmented. The pixel values within the spots (feature brightness), pixel values around the spots (background brightness), and the specific location of the spots are measured and recorded. The brightness of the spots correlate to the concentration of protein within a tested sample. The test is being developed for use in developing countries like the Congo for diagnosing Ebola, China for Liver Cancer, and Tanzania for breast cancer. However, there are limitations to the technology that can be addressed through this biomedical software final project.

 

*Figure 1:* Two Representative images of the D4. Each column of spots (5 replicates for 4 biomarkers) corresponds to a different protein biomarker for liver cancer. LEFT: high protein concentrations run on the D4. RIGHT: low protein concentrations run on the D4.

# The problem:

While the D4 architecture is well poised for point-of-care use, with long shelf life, takes 30 minutes to run, and is self-contained, the last step—the detection and analysis of the image—**is not user friendly and not automated**. Manually segmenting spots and analyzing the brightness of the spots is cumbersome, requires subjective user intervention, and adds turn-around time. Additionally, if the D4 if deployed to developing countries, the collected images will need to be stored and backed up in a central location, with location, time, and patient identifiers tagged with the images. This is essential for the development of microarray technology as a telemedicine solution. Fortunately, there are computing tools available through software that can be employed to address these issues.

# The Solution:

We propose the creation of client software with a graphical user interface that will allow a user to upload the D4 fluorescent images (much like the ones shown in fig. 1, which are .tiff images), add simulated patient information or de-identification codes, tag the location/date/time of the upload, add sample information (blood, sputum, urine), multiplex information of the geometric placement of spots (how many replicates, how many biomarker spots), add operator information, and batch number of the D4 chips (for quality control). This client software can be run on a prototype portable detector device that Jason Liu has developed in the lab!

The client software will issue a RESTful API request to a cloud service, an image storage and processing server will save any uploaded image with its associated patient and test information. The server will also perform image processing on the image, automating the previous manual procedure for analysis. This will include a Hough circle transform on the image data to segment the spot locations, identification and quantification spot and background brightness, and some test for the image to ensure the collected image is high quality and in-focus [this can be through some histogram or signal to noise calculation] (otherwise, the operator should be informed to run the test again and collect a better image, to ensure tests are run properly). Multiple users can upload and retrieve their images and the associated processed image data. The user actions will be tracked as the project spec requires (user actions/metrics, store uploaded images and timestamps, and store processed image data).

# Conclusions:

This project has serious implications in the future of telemedicine with microarray data—if executed exactly as shown here, I fully believe the code and methodologies developed in this project could be published and used by researchers/doctors. I would definitely be using it with my device.

Sources:

1. <https://en.wikipedia.org/wiki/Protein_microarray>