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Predicting Red Blood Cell Deformability from Microscopy Images Using Deep Learning

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Introduction

Red blood cell (RBC) deformability characterizes the cell's ability to squeeze through the microvasculature. Transfusion RBC deformability varies based on donor characteristics [1,2] and the storage time [3]. More deformable blood increases skin blood flow [4], haemoglobin levels [5], and is hypothesized to endure for longer periods in the body after transfusion compared to less deformable cells. The identification and use of long-lasting transfusion blood would reduce the frequency of needed transfusions for chronic transfusion patients, reducing their risk of iron overload or other transfusion-related morbidities. We have developed a convolutional neural network (CNN) approach to determine blood cell deformability, compared against microfluidic cell sorting, that is accessible to anyone with an adequate optical microscope.

Hypothesis

We hypothesize that a convolutional neural network model can classify different RBC deformability levels using optical microscope images compared to microfluidic sorting.

Objectives

- Determine if deformability can be determined using CNNs compared to microfluidic sorting among:
  - a single donor and
  - multiple donors.

Microfluidic Ratchet Device Design

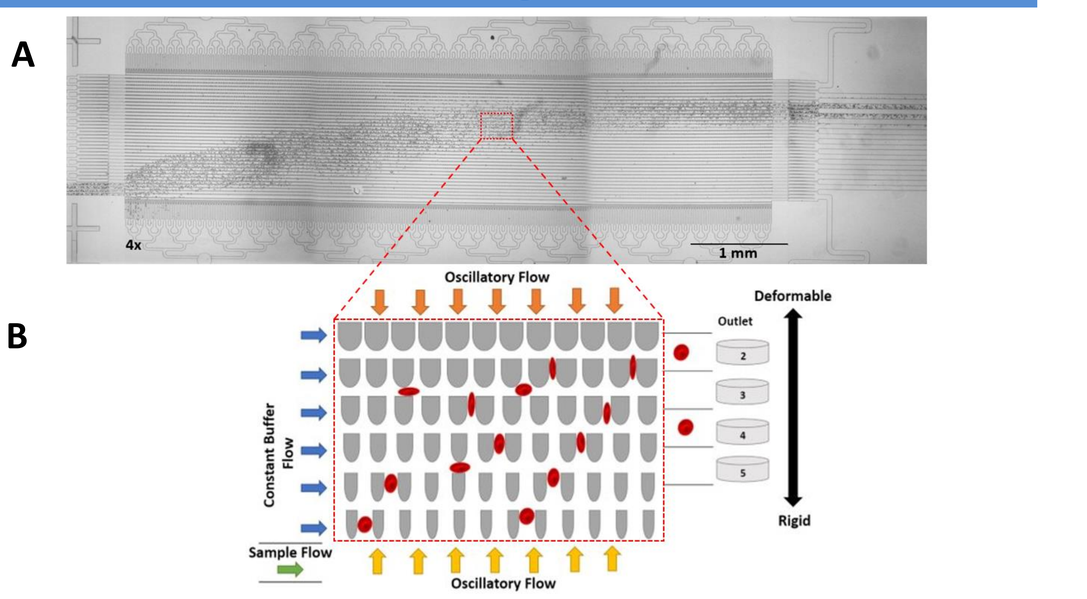

Figure 1: Microfluidic Ratchet Device Design. **A**: An RBC sample is run through a microfluidic deformability sorting device. **B**: The cells are squeezed through progressively narrower tapered constrictions. Once the cells reach their constriction limit, they are sorted to a distinct deformability outlet. RBC deformability determined by the device is the "ground truth" for the machine learning model.

Microfluidic Sorting Results

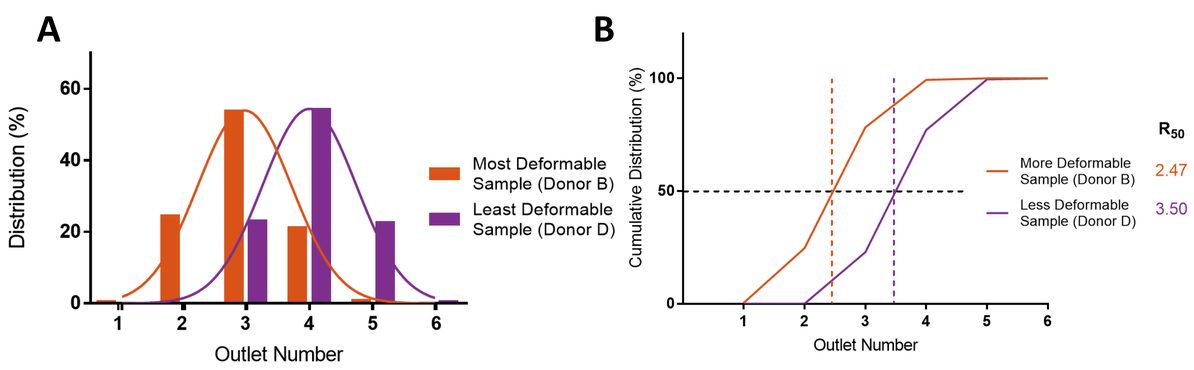

Figure 2: Sample microfluidic sorting results from donors with deformable and more rigid blood profiles. **A**: Normal distribution of sorted cells; outlets 2 to 5 are used for image classification. **B**: Cumulative distribution plot of sorted cells; the 50% crossover frequency is defined as the donor's rigidity score.

Deep Learning Data Pipeline

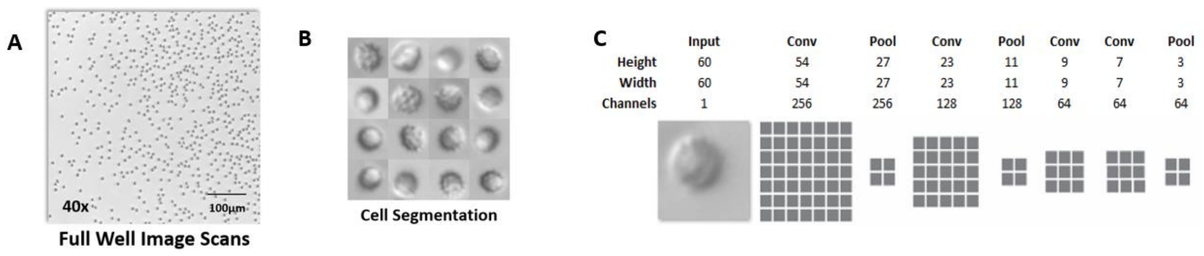

Figure 3: Deep Learning Data Pipeline. **A**: 40x brightfield full well image scans conducted on Nikon optical microscope. **B**: Cells are segmented into 60x60 pixel images and augmented by random multiples of 90-degree rotations to create balanced classes. **C**: Schematic of convolutional neural network, similar to AlexNet [6].

Individual Donor Deformability Prediction

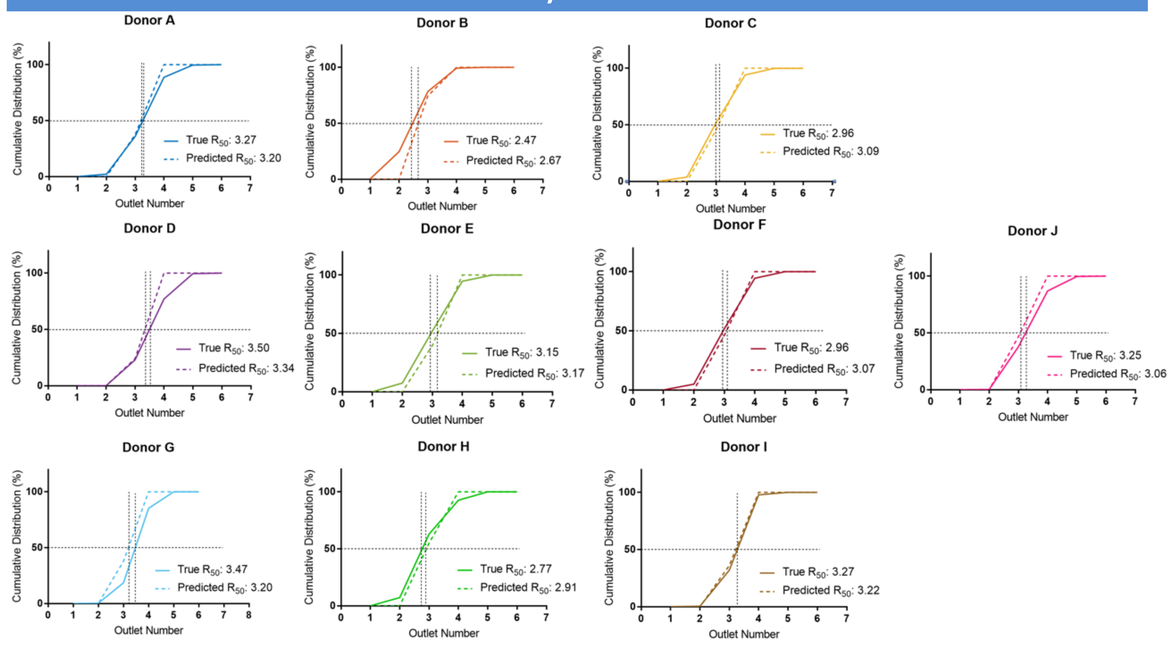

Figure 4: RBC deformability profile prediction for 10 donors compared to microfluidic sorting. R50 rigidity scores are similar for both methods. Deep learning testing accuracies ranged from 68% (Donor F) to 98% (Donor D) with an aggregate average (±SD) of 84±11%.

Combined Donor Deformability Prediction

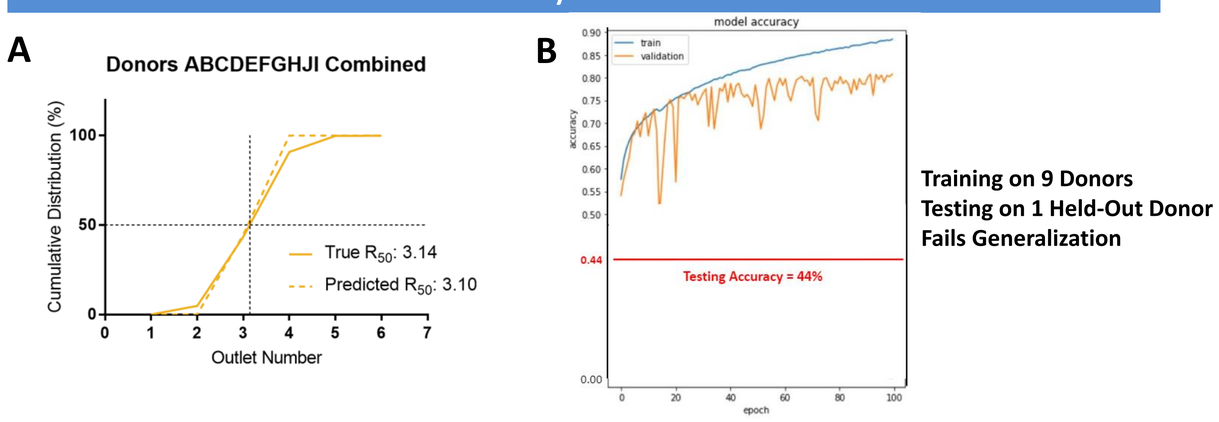

Figure 5: Combined Donor Deformability Prediction. **A**: Training on 10 donors and testing on held-out subset of these 10 donors yields comparable results to single donor deformability predictions. **B**: Training on 9 donors and testing on 1 held-out donor. Method fails with 44% accuracy. The model is not able to generalize deformability to an unseen donor dataset.

Differentiating Between Donors

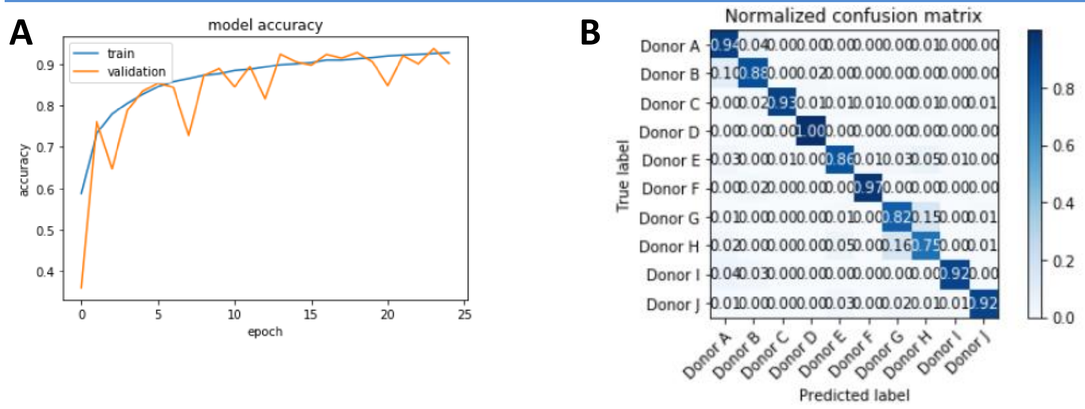

Figure 6: Differentiating between all 10 donors (all images from deformability outlet 3). **A**: Model converges readily in 25 epochs, achieving 93% training accuracy and 90% validation and testing accuracy. **B**: Normalized confusion matrix displaying true positive donor predictions along the diagonal. The model more readily identifies differences between donors than differences in deformability, providing a reason for failure in deformability generalization (**Figure 5B**).

Conclusions and Future Directions

In summary, we developed a deep learning model that accurately determines a RBC's deformability compared with microfluidic deformability sorting. The model works well on individual donors and with many donors combined but fails to generalize deformability prediction when provided data from a new donor. This generalization failure is likely caused by there being greater inter-donor RBC image variation than inter-donor RBC deformability commonality. Future work aims to predict RBC storage time from microscopy images due to storage-related morphological changes.

References

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