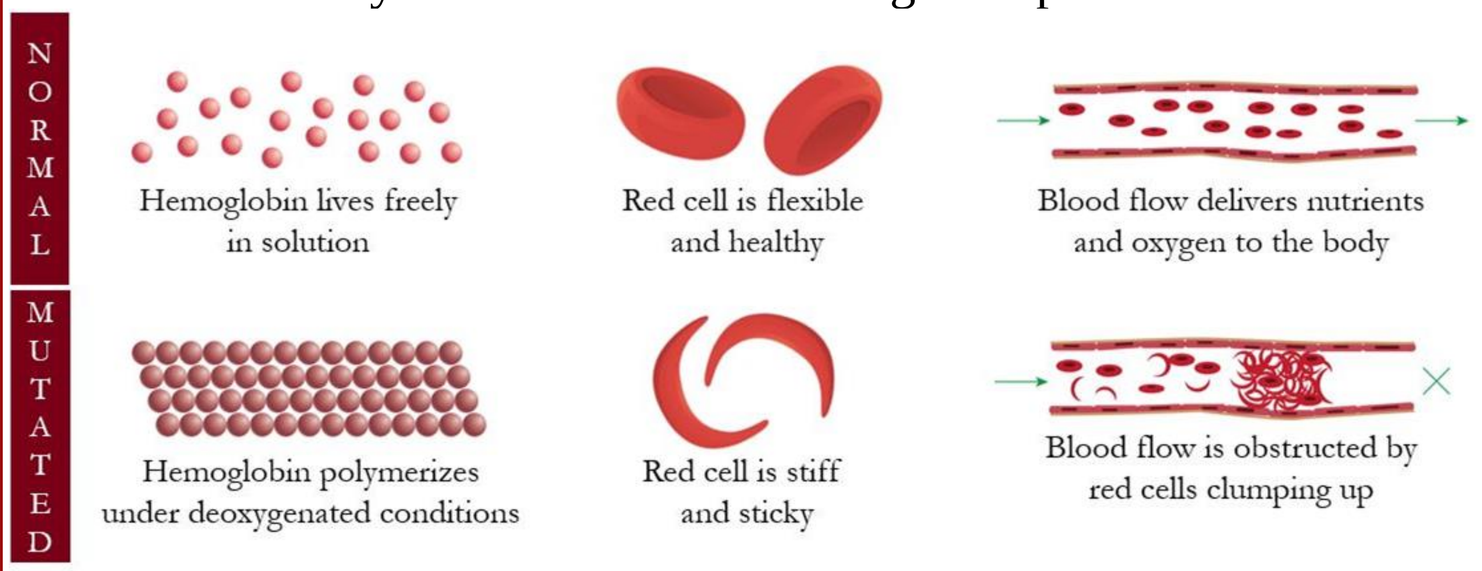
# Development of a Novel Microfluidic Assay Design for Evaluating Mechanical Properties of Single Red Blood Cells

Joseph Hanson | José M. Valdez | David K. Wood, Department of Biomedical Engineering

## Sickle Cell Disease

Sickle Cell Disease (SCD) is an inherited blood disorder characterized by a mutation in the hemoglobin protein.




SCD treatments today are very limited, and the effects of blood flow obstruction are not well defined. In order to create new, more effective treatments, better methods for determining patient severity and predicting patient response must be developed.

The aim of this work is to design a platform for determining the membrane mechanics of single red blood cells (RBC's). The single cell data obtained by this device will be used to model whole blood populations, and provide insight into case severity and treatment efficacy.

## Microfluidic Device

The design was drafted in AutoCAD, and consists of two entry ports, three exist ports, and a channel obstructed by beams.

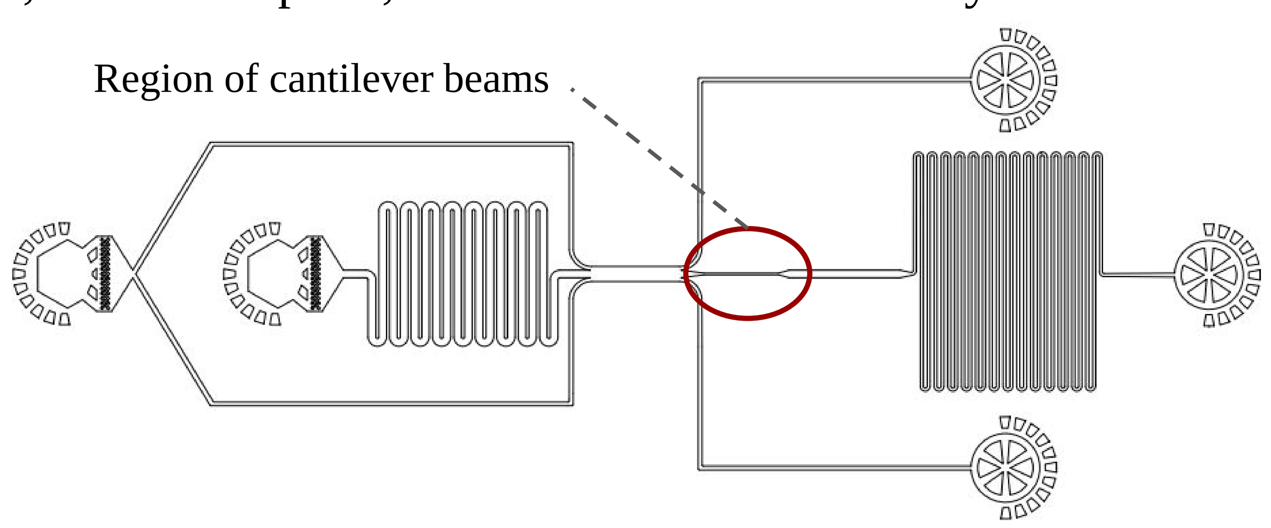



Figure 1: Device AutoCAD design. The entry ports support the focusing fluid and blood entry. Due to the laminar nature of flow in the device, the cells are focused to the middle cantilever beam region (see Figure 4).

The device's features were printed onto a wafer using photolithography. A reverse of the wafer is created by soft lithography using polydimethylsiloxane (PDMS), and then epoxy is used to copy the PDMS design.

The final device consists of a dual layer epoxy mold. In order to assemble the mold, a device was developed to align the features under a microscope.

## Alignment Device Design

The dual layer mold necessitated the development of an alignment device with the ability to:

- Mount to a microscope stage and not obstruct the lens.
- Enable minuscule adjustments to position one of the molds.
- Hold one of the molds in place.

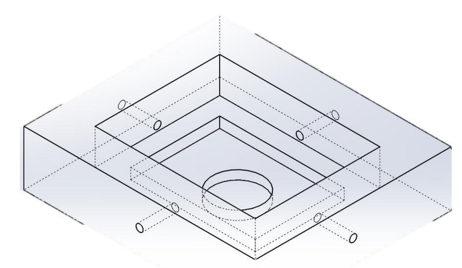


Figure 2 : Solidworks design of device.

Figure 3 : Image of final 3D printed device

The final device was designed in Solidworks and 3D printed using PLA plastic filament . The device consists of two concentric rectangles, where a single mold fits snugly in the bottom. Thinly threaded screws fill the four holes around the edge and are used to make fine horizontal adjustments to the top mold. A hole in the bottom of the device allows the features to be viewed through a microscope while being aligned.

## Cantilever Beam

Unlike previous devices of this nature, which have focused on finding deformation by measuring the surface area and velocity of RBCs, this approach uses cantilever beams, which will make direct contact with the RBC membranes.

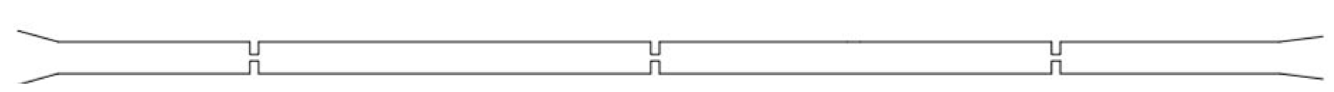
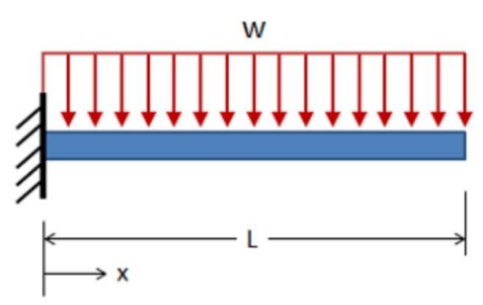


Figure 4: Segment in the center of the microfluidic device identified in Figure 1.

The image above isolates the region of the device where cantilever beams are found. Measuring the deformation of these beams can be extrapolated to determine the cell's mechanical properties.




$$\delta_{max} = \frac{FL^4}{8EI}$$

Figure 5: The expected deflection ($\delta$) of a cantilever beam can be expressed as a function of the beam's length (L), the beam's moment of inertia (I), the force applied by the cell (F), and the Young's Modulus in PDMS (E=870 kPA)

Using the model depicted above, the force applied to the beam by a RBC can be determined, and subsequently the force exerted on the RBC. Measurements of the cell's deformation under the strain can then be used to calculate its stiffness.

## Conclusions

- Created device to determine red bed blood cell membrane properties.
- Cantilever beam design provides a new approach for measuring cell deformation.
- Fabricated alignment device that can be used to create dual layer molds.

## Future Directions

- Unlike the data depicted in Figure 6, which indirectly measures deformation using transit times, this work will instead measure membrane deformation directly through the use of cantilever beam deflection.
- Further tests will be conducted in order to evaluate the mechanical properties of red blood cells.

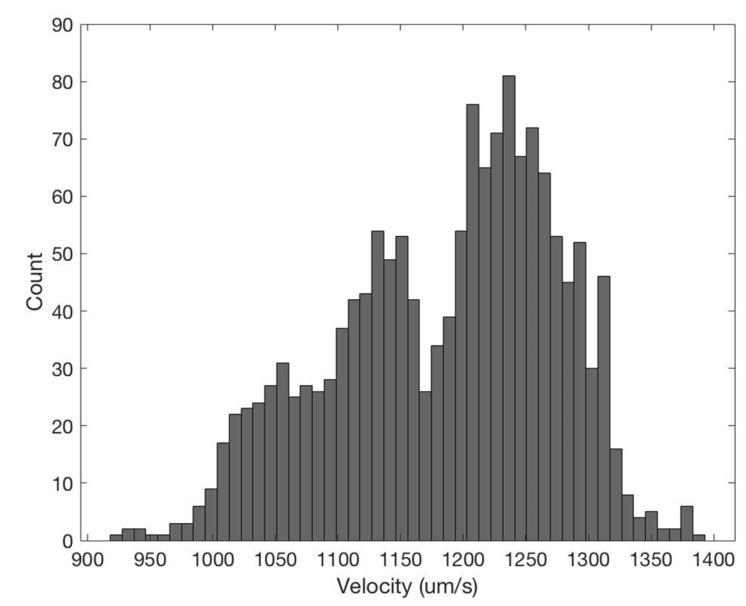



Figure 6: Velocity distribution data from red blood cell transit time measurements with stiff and normal cells.

- The device will be replicated and used to collect additional data to be used in whole blood rheological analysis of SCD.
- These measurements will be used to determine the efficacy of treatments, identify case severity, and provide insight into the behavior of whole blood populations.

## Acknowledgements

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