Hematology on a Compact Disc via Interplay of Rotational and Capillarity-Driven Interactions

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Rahul Agarwal

Under the guidance of

Prof. Suman Chakraborty

DEPARTMENT OF MECHANICAL ENGINEERING
INDIAN INSTITUTE OF TECHNOLOGY KHARAGPUR

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ABSTRACT

Microfluidics is an adolescent technology. The concept of fluid manipulation at small scales has existed for quite a long time. There has been a tremendous growth in scientific output describing the behaviour of fluid in micro-environments. This ranges from simple pressure driven flow through a circular microchannel, flow under carefully controlled externally applied electric, magnetic or acoustic fields, deflection of fluid with the pressure of photons, flow driven by surface energy of the substrate to actuation and manipulation of fluid in a rotating environment. The science of such fluid manipulation is rather well developed. However, the engineering required to translate such science from academia to commercial products is still in its nascent to adolescent stage. The key challenges are often not the equipment, but the control, accuracy, cost, complexity and precision. These have inhibited the translation of microfluidics technology from academia to biomedical products, as quite obviously, accuracy and precision are two of the most important criteria for adoption of any technology in biomedical devices, particularly diagnostic devices. It is important to point out here that it is not the case that diagnostic devices do not incorporate the technology, but these devices are often prohibitively expensive thereby disallowing the advantages of fully automated miniaturized diagnostic devices to reach the masses.

This thesis is an attempt at addressing these challenges. The approach adopted for this purpose is the one in which instead of focussing on fluid manipulation methods, mechanical properties of the fluid, blood in this thesis, are exploited to explore avenues of estimating or measuring blood composition. One of the major advantages of such an approach is a direct reduction in the cost of target device as now, the chemical reagents are not required. Apart from the actual manufacturing cost of the reagent, the added costs of storage and transportation are also eliminated. A direct way of utilizing the mechanical properties of blood is to study its motion in externally imposed dynamical conditions. The choice of framework in this study is rotational microfluidics due to its advantages such as actuation, motion, separation, etc with a simple act of spinning the platform.

Centrifugal force and Coriolis force are two of the forces of interest that arise due to the spin. Coriolis force is often overlooked in the interest of simplicity and its low magnitude in comparison to the primary centrifugal force. In this study, various situations are explored in which Coriolis effect might be useful even at low to moderate rotational speeds. Then, capillary force is brought into play as well. The superposition of centrifugal force, Coriolis force and capillary force with blood rheology provides useful insight into the influence of one or more of these over hemodynamics and lead to formulation of guidelines for more efficient exploitation of these external forcing parameters for better designing of the Point-of-Care (POC) devices. Certain sweet spots in terms of operating conditions are also identified to enable the use of these principles for development of rapid test devices.

Subsequently, methods are provided to develop centrifugal microfluidic devices to measure blood composition. The components of blood targeted in this study are hematocrit, viscosity, Erythrocyte Sedimentation Rate (ESR), RBC count, WBC count, Platelet count and concentration of hemoglobin. Simple operational and measurement methods are provided. Hematocrit, ESR and viscosity are estimated by measuring the flow rate of blood in a microchannel and measuring a defined length with a regular 15 cm ruler. Cell counts and hemoglobin are estimated with the aid of a routine laboratory microscope and computer algorithms for image processing. The data estimated from all of the devices is benchmarked with the data from an Automated Hematology Analyser (AHA).

The use of POC (Point of Care) devices in practice almost always involves utilizing the capillary blood. As the examiner has correctly described, the blood from a finger prick is directly dispensed onto the device. In the lab setup however, it is not feasible to arrange for the availability of freshly drawn blood samples from finger pricks. Additionally, the volume of such a blood sample is typically 100-200 μL. Now, in order to benchmark the device against an Automated Hematology Analyzer (AHA) or a biochemistry analyzer, an additional volume of blood is necessary, typically larger than 1 mL. This would lead to inconsistencies as the performance of the POC device with capillary blood (the blood drawn from a finger prick) would be benchmarked against the measured blood composition of a veinous sample. Hence, in order to avoid any such compatibility issues, in the laboratory framework, a veinous blood sample is typically used, which needs to be stored in an EDTA coated tube to prevent coagulation and for transportation, from the hospital to the laboratory.

The results and methods presented in this thesis open up exciting avenues of POC device development in a chemical free regime. The presented measurement and fabrication methods are simple and potentially executable by untrained personnel. These devices could be deployed at kiosk-based settings which are essentially similar to the health camps frequently organised by social service organizations. Not only this, a significant cost reduction could eventually contribute to improved health of the society at large by encouraging mass adoption of such devices.

Keywords: Rotational microfluidics, centrifugal microfluidics, blood rheology, complete blood count, hematocrit, Coriolis force, centrifugal force, hybrid disc.