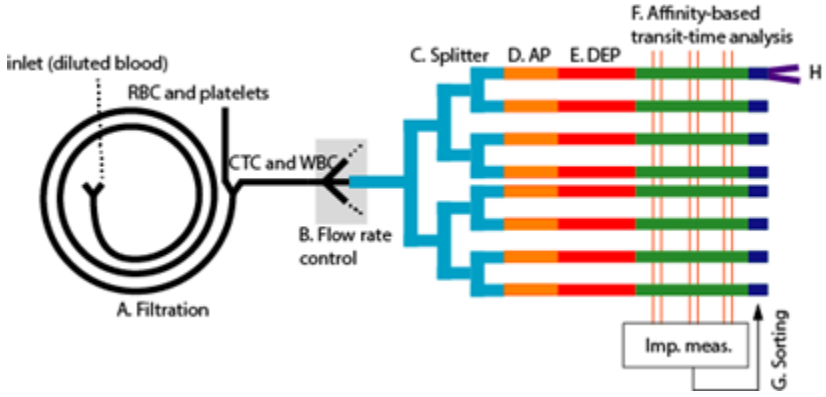
Docket #: S17-169

Microfluidics device for high-throughput liquid biopsy and other cellular analyses

Engineers in Prof. Amin Arababian's laboratory have developed a microfluidics system for ultra high-throughput, low-cost, label-free cell detection in liquid biopsies, fetal cell analysis and other applications. Currently, the electronics hardware required for highly multiplex detection on 100s of parallelized microfluidics channels would overwhelm the space available on the chip and be difficult to interpret due to interference. This new system overcomes these problems through an electronics sharing scheme and novel signal processing software that effectively labels each microfluidics channels with an “ID number”. The system can then decode the location of a target cell with a minimal number of electronic channels. The technology enables label-free specific detection through “interaction zones” – functionalized segments that hamper flow through a channel depending a cell's unique set of surface biomarkers. This approach eliminates the conjugation step required for traditional cell sorting methods, thereby reducing both the time and reagent costs. This “Lab-on-a-Chip” flow cytometry technology could enable ultra-high-throughput cell analysis with multiplex detection at a single-cell level. It has point-of-care end-user applications in liquid biopsies, fetal cell detection or whole blood cell counting.



Schematic of Lab-on-Chip (LOC) system architecture: *First, a diluted blood sample is injected into the LOC, where smaller red blood cells (RBCs) and platelets are separated from the larger white blood cells (WBCs) and circulating tumor cells (CTCs). Then multiple 1:2 fluidic splitters separate the single flow into massively parallelized channels. Each fluidic channel has multiple interaction zones for multiplexed surface marker detection. These zones are separated by electrodes which identify cells of interest through impedance measurements and transit-time analysis. After detection, targeted cells can be sorted and collected for down-stream analysis (e.g. FACS and DNA sequencing).*

Stage of Research

We are in the process of testing our concept using polystyrene beads and known cell lines. Coupling with optical microscope image monitoring, we are in the status of characterizing the "error rate" of the proposed system. The instrumentation (the impedance analyzer) is built with discrete IC and customized on-FPGA processing. Presumably the electronics can be further miniaturized using integrated circuit (CMOS) technology.

Applications

- **Microfluidics** - lab-on-a-chip electronics detection scheme for ultra-high-throughput cell analysis with multiplexed surface marker detection at single-cell level, end-user applications could include:
  - liquid biopsy to detect circulating tumor cells (CTCs), circulating tumor DNA (ctDNA) or exosomes for cancer diagnostics and treatment monitoring
  - whole blood cell counting

    - point-of-care diagnostics using cell based assays
    - fetal cell detection in maternal blood sample

Advantages

- **Multiplexed for ultra-high-throughput:**
    - massively parallelized analysis through >100 channels without scaling the number of detection electronics
    - multiplexed surface marker detection with functionalized microfluidics channels and simple transit time analysis
- **Fast sorting time** - label-free detection eliminates conjugation step
- **Reduced cost** - potential to be much less expensive than conventional flow cytometer with lower reagent costs from label-free detection
- **High sensitivity and specificity:**
    - can detect rare cells such as CTCs and fetal cells
    - surface marker interactions provide higher specificity than traditional size-based sorting

Patents

- Published Application: 20190039060
- Published Application: 20190039060
- Issued: 11,266,984 (USA)

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