Microfluidic Time-Division Multiple Access Resistive Pulse Sensor for Particle Analysis

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Abstract

This research applies the principle of time-division multiple access (TDMA) to resistive pulse sensing to realize a scalable, multichannel system for microparticle analysis. Particles are pumped through an eight-channel microfluidic device designed for enhanced throughput. Multiplexing hardware combines signals from each of the eight channels into a single electrical output for low-cost data acquisition. A de-multiplexing software algorithm recovers the eight signals for particle analysis on each channel. When tested with polystyrene beads, the system can detect single particles for counting and sizing applications. The success of this TDMA-based approach demonstrates the potential for a resistive pulse sensing system with an arbitrary number of microfluidic channels and a single output to a data acquisition device. Such an accomplishment is integral to the development of portable, affordable devices for cell counting.

Introduction

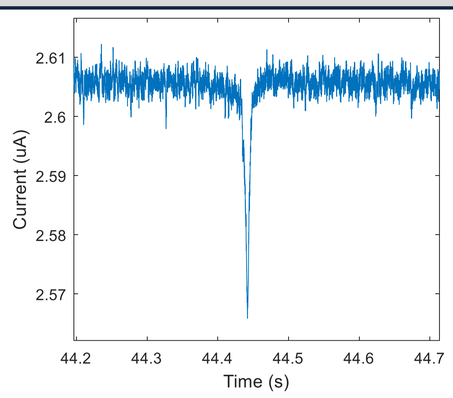


***Figure 1**: Current-Time Trace with Visible Dip Indicating Particle Passage through Orifice*

- Resistive pulse sensing is a method of cell detection and counting based on measuring a change in resistance as a cell passes through an orifice.
- Lab-on-a-chip (LOC) technology emulates laboratory-based tests – generally performed with bulky, expensive equipment – on compact devices.
- Realizing portable, high-throughput, low-cost resistive pulse sensing will require a single-output device, capable of interfacing with inexpensive data acquisition hardware.

Theory of Operation

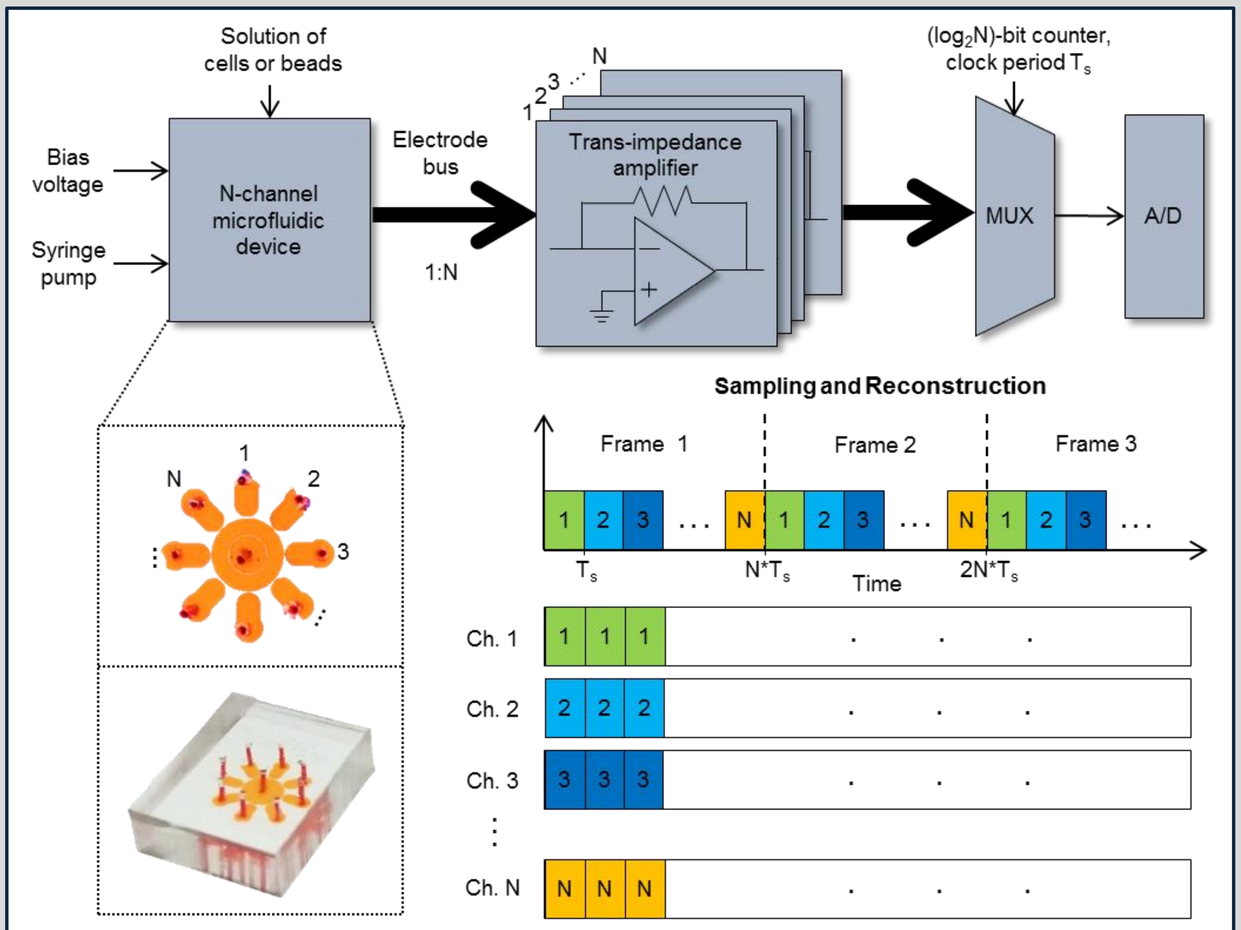


***Figure 2**: System Setup Depicting Multiplexing/Demultiplexing Operating Principle*

Eight-Channel Implementation: Hardware Design

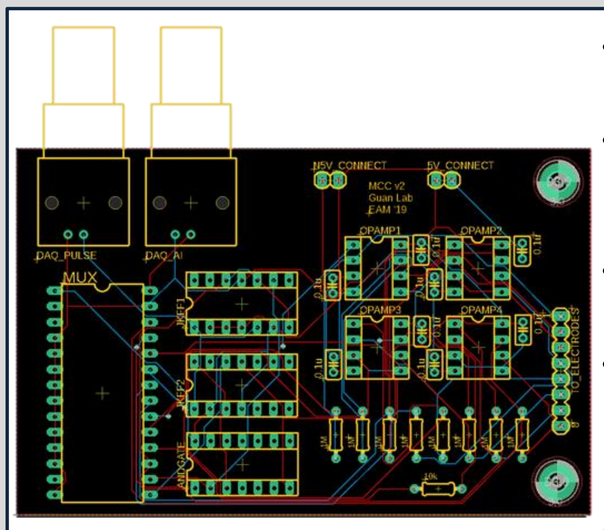


***Figure 3**: PCB Layout*

- Sensing electrodes from microfluidic channels land at a pin header.
- Transimpedance amplifiers (built with TL072 op amps) provide current-to-voltage conversion.
- The eight op-amp outputs are input to an analog multiplexer (ADG406).
- A three-bit counter (built with two 74LS73 JK flip-flops and one DM7408 AND gate) cycles the multiplexer from S1 through S8.
- The multiplexer output is input to a DAQ device (USB-6363) for sampling.

Particle Detection on Eight Channels

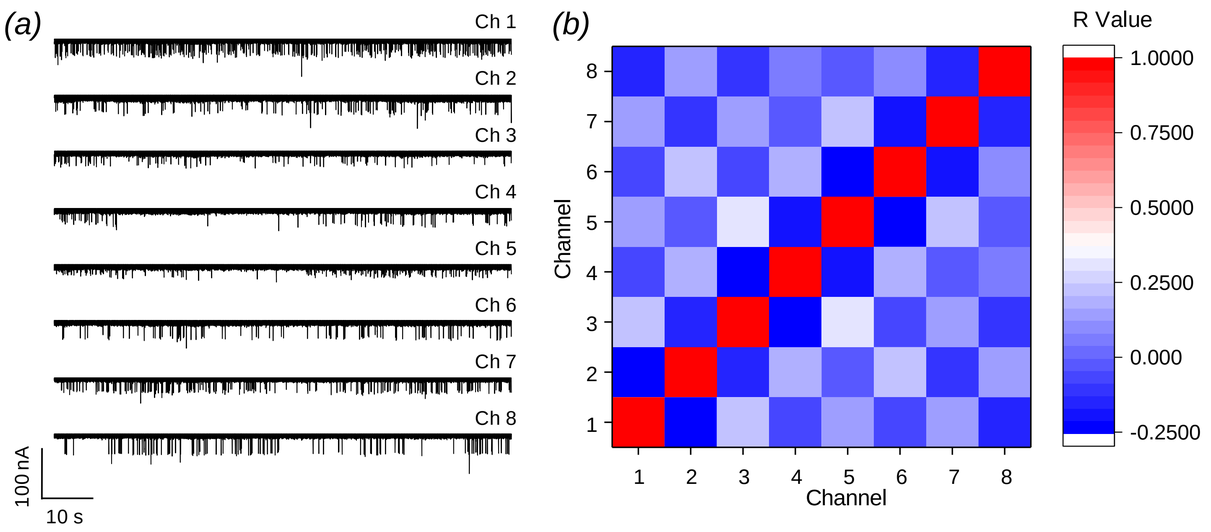
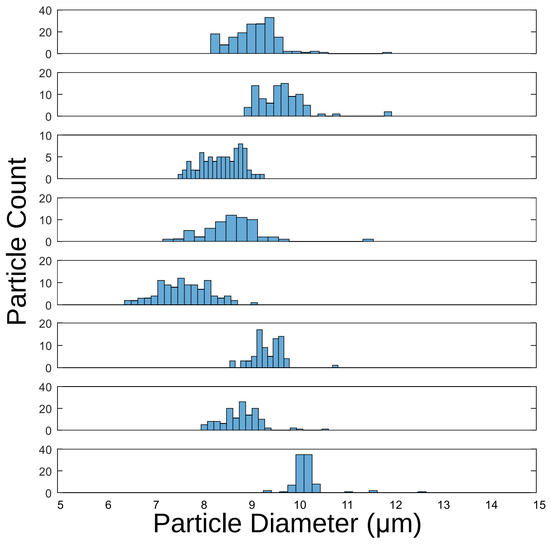


***Figure 4**: (a) Current-time traces for eight-channel device testing with 10 μm beads. (b) Heatmap depicting cross-correlation between channel pairs.*

- When an eight-channel microfluidic device was driven with a solution of 10 μm particles, the system successfully detected particles using all eight channels with high throughput.
- Crosstalk between non-identical channel pairs is minimal ($R < 0.33$).

Particle Sizing on Eight Channels



- Particle diameter *d* was extrapolated from the change in resistance of a channel during particle transit using the formula:

$$\frac{\Delta R}{R_{nominal}} = \frac{D}{L}\left[\frac{\arcsin\left(\frac{d}{D}\right)}{\sqrt{\left(1-\left(\frac{d}{D}\right)^2\right)}} - \frac{d}{D}\right],$$

where *D* is the channel diameter.

- The Gaussian distributions, centered at or near 10 μm, imply that each channel is functional for particle sizing applications.

***Figure 5**: Histogram of Particle Diameters*

Conclusion

- An eight-channel microfluidic resistive pulse sensor was developed and validated for particle detection and sizing on eight channels with minimal crosstalk.

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