

REAL-TIME PROCESSING OF CODE-MULTIPLEXED COULTER SIGNALS BASED ON A TWO-STAGE DEEP LEARNING STRUCTURE

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ABSTRACT

Coulter counters electrically detect and size suspended particles from intermittent changes in impedance between electrodes. By combining the impedance-based sensing with microfabrication, Coulter counters can be distributed across a lab-on-a-chip platform for code-multiplexed monitoring of microfluidic manipulations. In this paper, we augment a code-multiplexed Coulter sensor network with a deep learning-based decoding algorithm for multiplexed detection of cancer cells sorted into different microfluidic channels.

KEYWORDS: Coulter counter, Machine learning, Convolutional neural network, Impedance sensing

INTRODUCTION

Coulter counters employ an impedance-based detection mechanism to detect and characterize particles suspended in an electrolyte. Through microfabrication techniques, this robust technology can readily be integrated into a Lab-on-a-Chip (LoC) system, which enables integrated platforms for quantitative sample analysis. To integrate multiple Coulter sensors into an LoC platform for spatiotemporal monitoring of suspended particles, we have introduced a code-multiplexed Coulter sensor network, called Microfluidic CODES [1]. In the Microfluidic CODES, the geometries of distributed Coulter sensors are engineered to produce sensor-specific signature waveforms when a particle is detected. By placing these uniquely-designed sensors to particular regions of interest on a microfluidic platform, they are used to provide information on the spatiotemporal states of suspended particles for various applications. Because the signals from each Coulter sensor in the Microfluidic CODES are summed together to produce a single electrical output, this output should be processed to recover information from individual sensors on the device.

THEORY

In this paper, to interpret code-multiplexed Coulter signals, we developed an algorithm based on deep learning. Specifically, our algorithm was based on a two-stage convolutional neural network (ConvNet) (Figure 1a). Given an input signal, the first stage in our algorithm, the region proposal network (RPN), searched for bounding boxes (i.e., time intervals) that contained signature waveforms. The height and length of each bounding box were used to estimate the size and speed of each detected particle, respectively. These identified signature waveforms were then extracted and fed into the second stage, the sensor classification network (SCN). The SCN was trained to predict the probability with which a given sensor signal belongs to each and every coded Coulter sensor on the device. In this way, we determined the sensor identity for each detected particle along with the particle size and speed. Both RPN and SCN shared the same structure, each containing 4 convolutional layers and 217056 trainable parameters (Figure 1b).

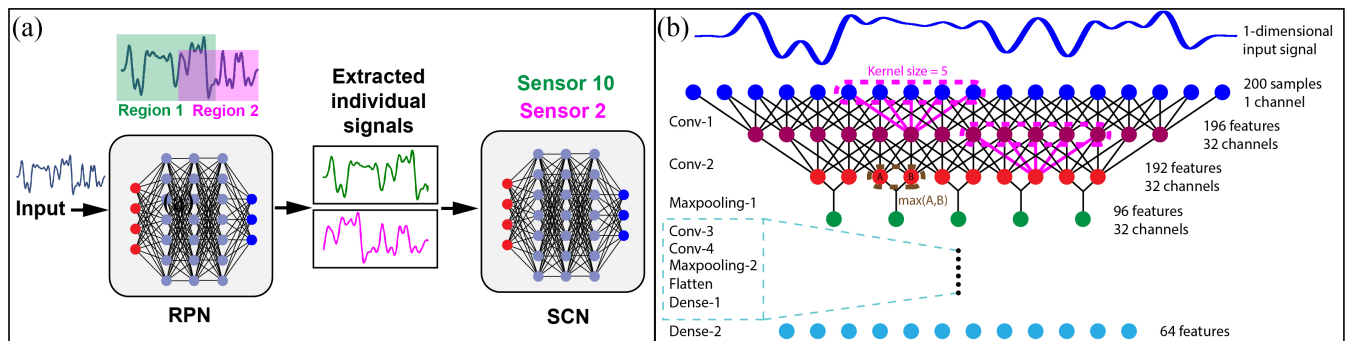


Figure 1: (a) A conceptual illustration of the workflow of the deep learning algorithm. (b) A schematic showing the ConvNet structure.

EXPERIMENTAL

To test the algorithm, we fabricated a Microfluidic CODES device and recorded experimental signals by driving a suspension of human cancer cells through our device. The microfluidic device consisted of two layers. The top layer was a polydimethylsiloxane (PDMS) microfluidic layer fabricated using soft lithography, and the bottom layer was a glass substrate with Cr/Au electrodes micropatterned using a lift-off process. The electrodes formed a network of 10 sensors, each encoded by a distinct electrode pattern (Figure 2a). The electrode pattern for each sensor was aligned with a distinct microfluidic channel and dictated the signature Coulter signal generated.

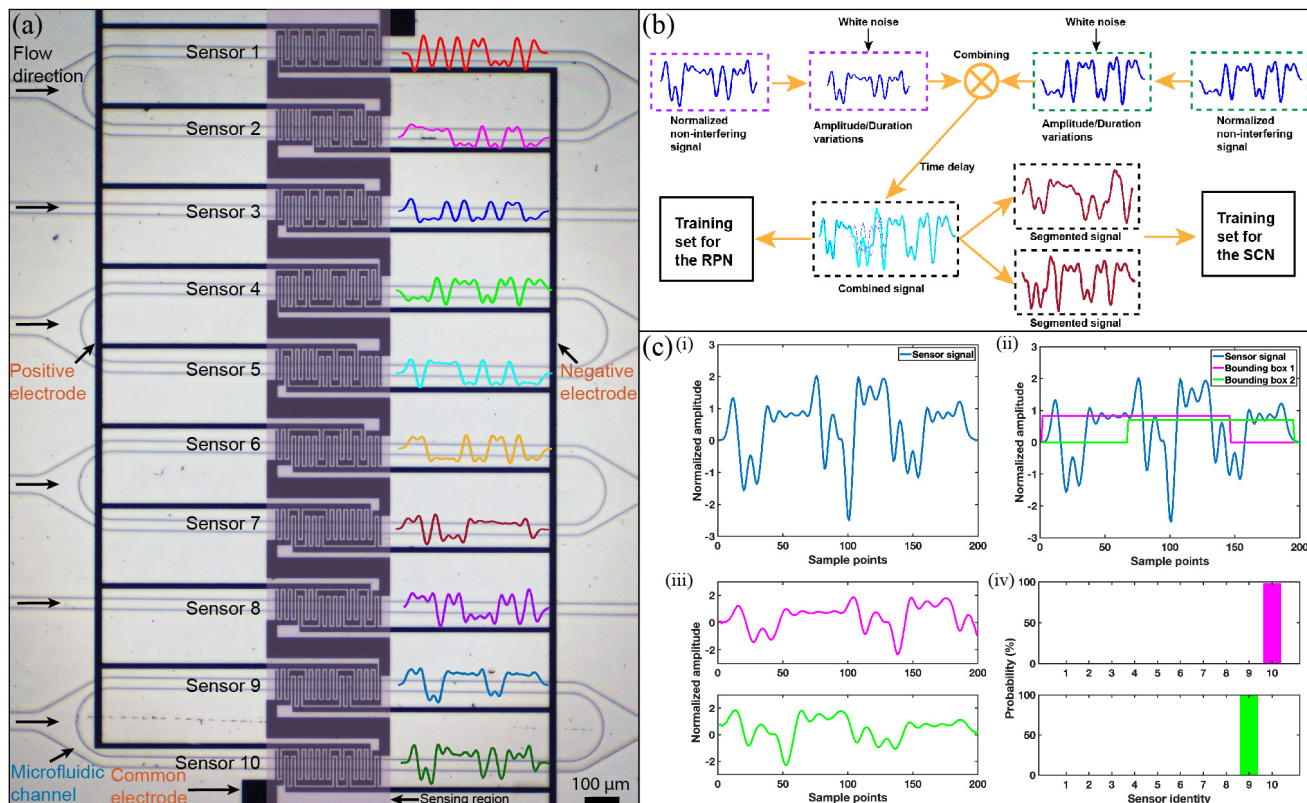


Figure 2: (a) An image of the fabricated microfluidic device with micromachined surface electrodes on a glass substrate and PDMS microfluidic channels. (b) Diagram showing the construction of the training data. (c) Process of querying a sensor signal: (i) The input signal. (ii)(iii) The RPN identifies two signature waveforms. (iv) Sensor identity prediction of SCN for each identified signature waveform.

RESULTS AND DISCUSSION

To create a sufficiently large training dataset, we augmented each non-interfering sensor signal by digitally varying its bounding parameters, namely the amplitude and duration. Then we randomly combined those augmented signals to simulate interfering sensor signals for the ConvNet training (Figure 2b). Trained ConvNets were then used to interpret recorded experimental data (Figure 2c). We processed over 1000 experimental signals to acquire the size and speed distributions of particles of interest. We achieved an $\sim 90\%$ decoding accuracy and a 780-particles/sec processing speed, which could potentially enable real-time processing of data from code-multiplexed Coulter sensor networks.

REFERENCES

- [1] Liu, R., et al., "Microfluidic CODES: a scalable multiplexed electronic sensor for orthogonal detection of particles in microfluidic channels," *Lab on a Chip*, 2016, **16**, 1350.

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