CONVOLUTIONAL NEURAL NETWORK BASED PROCESSING OF CODE-MULTIPLEXED COULTER SIGNALS

Ningquan Wang, Ruxiu Liu, and A. Fatih Sarioglu
Georgia Institute of Technology, Atlanta, USA

ABSTRACT

Coulter counters are used to count and size small particles suspended in an electrolyte by measuring the number and the amplitude of intermittent changes in electrical current as particles flow through a small aperture between two electrodes. We have recently introduced a technique, Microfluidic CODES, which transforms the Coulter counter into a code-multiplexed sensor network for distributed sensing of particles dispersed over a lab-on-a-chip device. Microfluidic CODES relies on micromachined electrode patterns to produce distinguishable signal waveforms that provide information on both the location and the physical properties of target particles. In this paper, we introduce a machine learning-based decoding algorithm for interpreting signals from a Microfluidic CODES device. Our approach utilizes a convolutional neural network, which reduces the constraints on the design of coded electrodes and also increases the data processing speed.

KEYWORDS: Lab on a chip, Microfluidic CODES, Machine Learning, Coulter sensor

INTRODUCTION

Coulter sensing is based on the transient impedance modulation as a particle traverses an electrolyte-filled constriction between two electrodes. In its conventional form, the output waveform of a Coulter detector is analyzed to find the number and amplitude of pulses to count and size particles, respectively. We have recently developed the Microfluidic CODES technology, which employs micropatterned electrode networks for code-multiplexed distributed Coulter sensing within a microfluidic device [1]. In the Microfluidic CODES, the spatial information from suspended particles is compressed into a one-dimensional electrical waveform, which needs to be computationally analyzed for recovering the information. In this paper, we introduce an algorithm based on deep learning, specifically convolutional neural networks (ConvNets) [2], to process code-multiplexed Coulter sensor signals.

THEORY

The ConvNet is commonly used in image recognition problems due to its effectiveness in representing local salience in an image. Two features of the Microfluidic CODES sensor output make the ConvNet well suited to perform the signal processing: First, signals generated by the same sensor in Microfluidic CODES share a similar pattern, and second, the scale of the sensor signal is related to the physical property of the particle detected.

We designed a ConvNet with 4 convolutional layers, each of which is followed by a max-pooling layer and rectified linear unit (ReLU) nonlinearities (Figure 1). Following the convolutional layers are two fully-connected layers and an output layer. The output layer has 13 nodes, in which the first 10 nodes represent 10 classes (i.e., 10 different coded Coulter sensors on the microfluidic device) and the last 3 nodes represent the bounding parameters, namely, the start time, amplitude, and duration of the sensor waveform. Given a signal, the ConvNet predicts the identity of the specific sensor and the corresponding bounding parameters. Bounding parameters are then used to estimate the flow speed (i.e., signal duration) and the size of the particle (i.e., signal amplitude). When the input signal consists of interfering sensor signals due to coincident particles, the ConvNet first detects the strongest sensor signal. Once this signal is subtracted from the original input, the residual signal is fed into the same ConvNet in a recursive loop.

EXPERIMENTAL

We tested our ConvNet on a microfluidic device with 10 code-multiplexed Coulter sensors. The device consisted of two layers. The top layer was a microfluidic layer fabricated using soft lithography. 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 2). The spatial electrode pattern for each sensor determined the distinct Coulter signal each sensor produced.

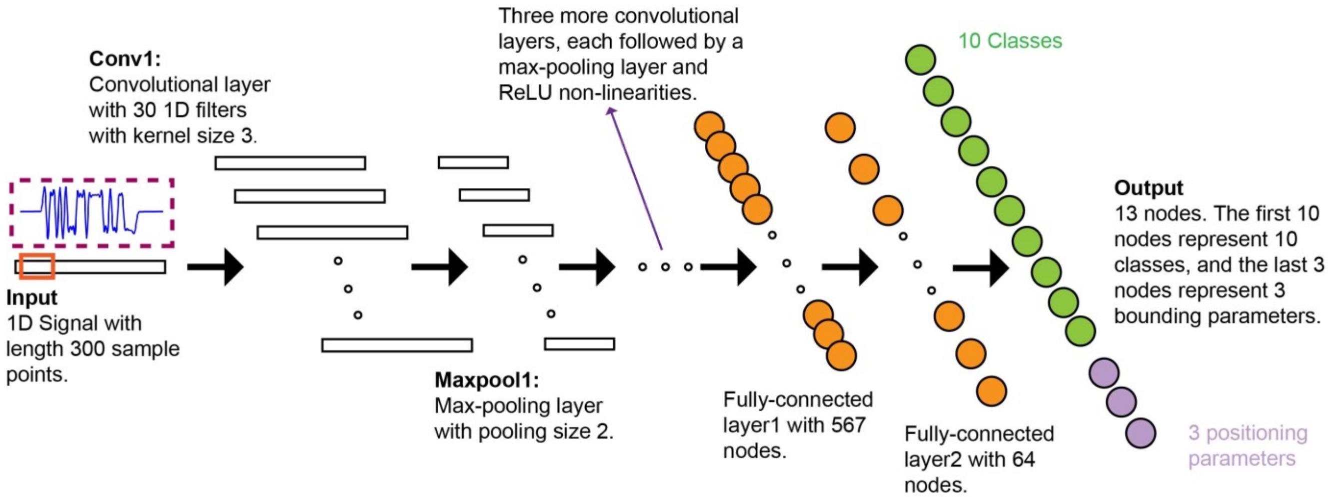

Figure 1. The structure of the ConvNet.

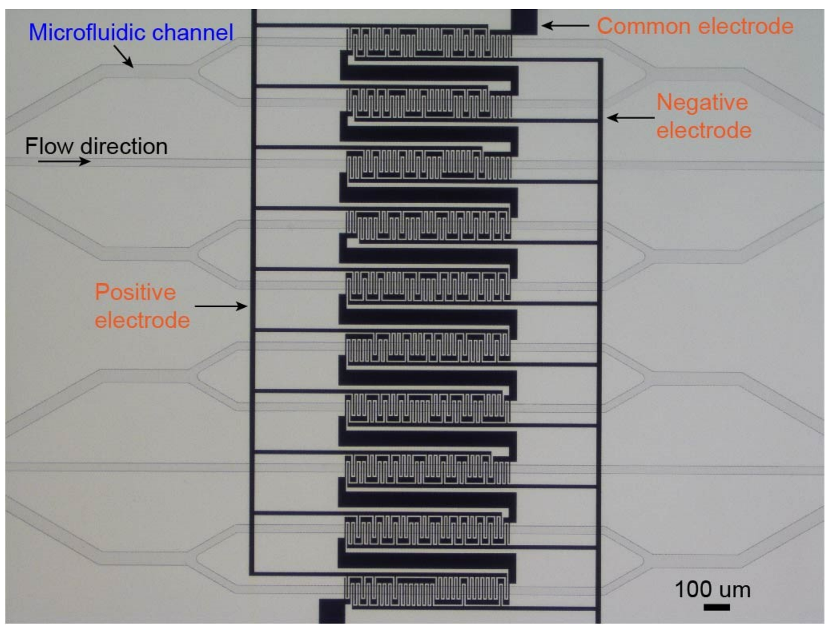

Figure 2. Image of the fabricated microfluidic device with micromachined coplanar electrodes on a glass substrate aligned with PDMS microfluidic channels. The device has 10 Coulter sensors, each of which generates a distinct sensor signal when a particle is detected.

For our testing, we processed human cancer cells suspended in phosphate buffer saline on the microfluidic device. The RMS amplitude of the sensor network signal was recorded using a lock-in amplifier. To generate a large training dataset, we augmented each non-interfering signal by creating additional ones with different bounding parameters (Figure 3a). Then we randomly combined those augmented signals to simulate interfering sensor signals for the ConvNet training. For each training case, only the identity of the strongest signal was provided to the ConvNet.

RESULTS AND DISCUSSION

Figure 3b and 3c show ConvNet predictions for a non-interfering sensor signal and a signal that includes the interference of two sensors, respectively. Based on our results, we have achieved >100 times improvement on the processing speed compared to the correlation-based analysis employed earlier to process the sensor network data [3]. This will potentially enable real-time processing of data from code-multiplexed Coulter sensor networks.

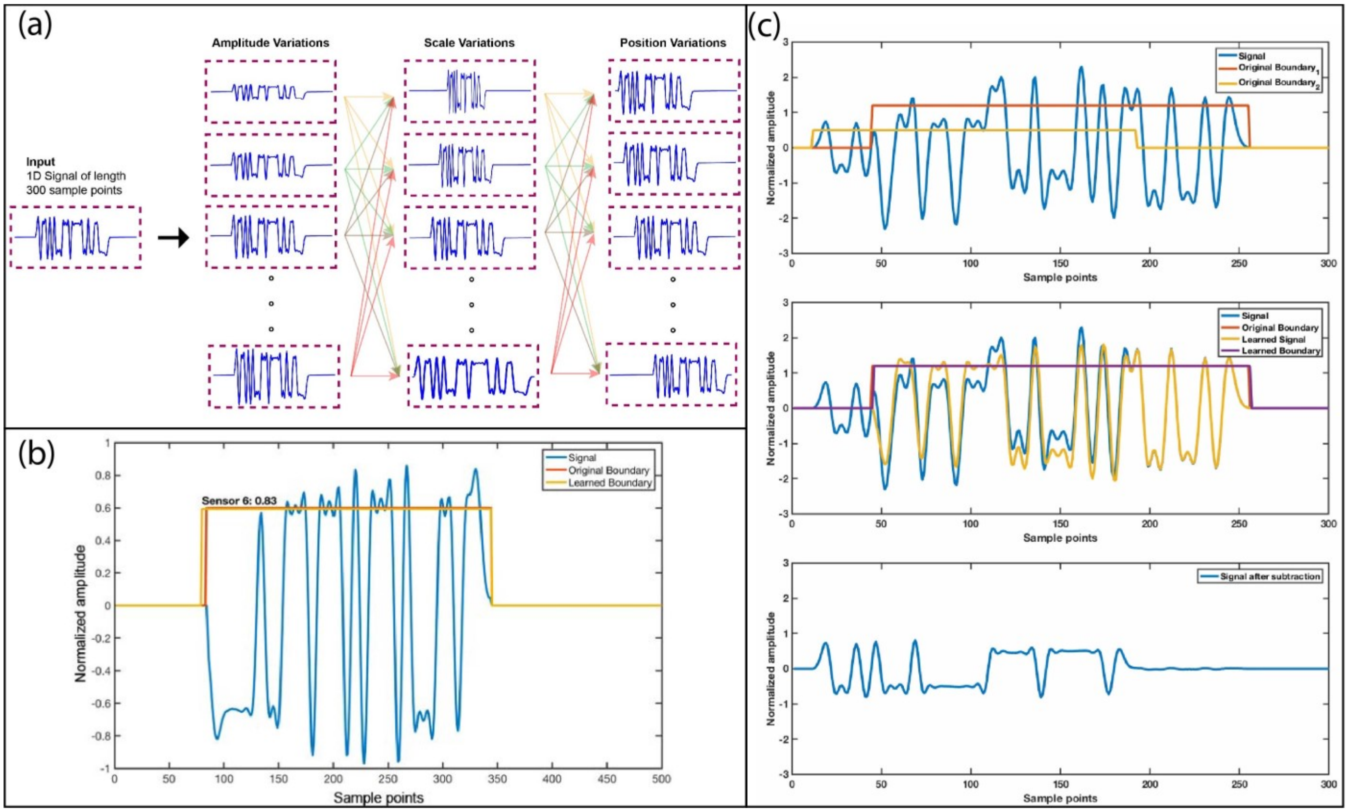

Figure 3. (a) Each non-interfering sensor signal was augmented by varying the amplitude, scale (duration), and position (starting point). After augmentation, single signals were randomly combined to generate interfering sensor signals as the training data. (b) Given a non-interfering signal, the ConvNet outputs the probability with which the input belongs to each sensor in the network. The identity of the sensor with highest probability was determined as the classification result (sensor 6 with a probability of 83% in this specific example). The ConvNet also output the bounding parameters, which were used to build a bounding box for the signal. (c) Given an interference signal, the strongest sensor signal was first detected and reconstructed based on the sensor identity and the bounding parameters and was then subtracted from the original signal.

CONCLUSION

We introduce a new signal processing algorithm for Microfluidic CODES based on deep learning of sensor signal features by ConvNets. This machine learning-based signal processing approach significantly simplifies the physical design constraints of Microfluidic CODES networks and at the same time, increases the signal processing speed, making real-time decoding of sensor data possible.

ACKNOWLEDGEMENTS

This work was supported by National Science Foundation Award No. ECCS 1610995, ECCS 1752170, and the Beckman Young Investigator Award to A.F.S.

REFERENCES

[1] R. Liu, N. Wang, F. Kamili, and A. F. Sarioglu, "Microfluidic CODES: A Scalable Multiplexed Electronic Sensor For Orthogonal Detection of Particles in Microfluidic Channels," *Lab Chip*, 16, 1350-1357, 2016.

[2] Alex. Krizhevsky, et al., "ImageNet Classification with Deep Convolutional Neural Networks." *Communications of the ACM*, 60, 84–90, 2017.

[3] N. Wang, R. Liu, and A. F. Sarioglu, "Microfluidic Platform with Multiplexed Electronic Detection for Spatial Tracking of Particles", *J Vis Exp*, 121, e55311, 2017.

CONTACT
* A. F. Sarioglu; phone: +1-404-894-5032; sarioglu@gatech.edu