PARTICLE SIZE DETERMINATION VIA SUPERVISED MACHINE LEARNING IN MICROFLUIDIC IMPEDANCE SPECTROSCOPY

Douwe S. de Bruijn[1*], Henricus R.A. ten Eikelder[1], Vasileios A. Papadimitriou[2], Wouter Olthuis[1], Albert van den Berg[1]

[1]BIOS Lab-on-a-Chip group, MESA+ Institute, Max Planck – University of Twente Center for Complex Fluid Dynamics, University of Twente, The Netherlands and
[2]Chemical Engineering TU Delft, The Netherlands

ABSTRACT

Impedance flow cytometers based on coplanar electrodes often have a significant signal dependency on the particle position. In this work we show that supervised machine learning can be employed to accurately predict the particle size of monodisperse polystyrene beads in an inhomogeneous electric field. This approach offers accurate results for the presented irregular signal shape (due to sensor geometry, particle position, and electrode alignment) without the need for signal template fitting and a compensation function.

KEYWORDS: Supervised Machine Learning, Neural Network, Particle Size, Electrical Impedance Spectroscopy, Microfluidics

INTRODUCTION

Impedance flow cytometry offers label-free and non-invasive detection of cells and particles at high throughput. Popular systems with coplanar electrodes are easy to fabricate, but they often have a significant signal dependency on the particle position, due to the inhomogeneous electric field (see Fig. 1a and b) [1]. Currently, the measured particle diameter is corrected by e.g. fitting the impedance measurement to a pre-defined template function and subsequently to a correction function [2], which creates labelled data for other machine learning applications [3].

We present the use of a feedforward neural network (NN) to train on the irregular signal shapes in our system, which does not require a signal template and correction function, to accurately predict the particle size of monodisperse polystyrene beads in an inhomogeneous electric field.

THEORY

As a bead passes through the microfluidic channel both the impedance magnitude and the shape of the signal (Fig. 1c) depend strongly on the height of the bead with respect to the coplanar electrodes, due to the inhomogeneous electric field. In earlier work we have shown a correlation between particle height and the measured electrical opacity [4], which requires the impedance measurement at two frequencies. We assume the NN can also exploit this correlation to correct the measured particle size depending on its position, hence the impedance response at two frequencies will be fed to the network.

Our NN without hidden layers acts as linear regression (Fig. 1d). Hidden layers have been also investigated as an architecture (deep learning), but without any improvement, therefore we stick to this simplest and fast NN.

EXPERIMENTAL

A microfluidic device with two coplanar microelectrodes (Fig. 1a) was used. The device consists of a PDMS chip on glass and has been described before [4]. The impedance was recorded at 0.5 and 12 MHz simultaneously using a lock-in amplifier (HF2LI, Zurich Instruments). Monodisperse polystyrene beads of 5, 6 and 7 µm (Polysciences and Sigma Aldrich, std dev respectively <0.1 µm, <0.2 µm and <0.2 µm) were used to train and test the NN. The NN was trained on three sets of data of <u>only</u> 5, 6 or 7 µm beads (85% training and 15% validation) and was tested using data of a mixture of these 5, 6 and 7 µm beads captured in a separate experiment. The input-output neural network (Fig. 1d) with linear activation function was implemented in Python 3.7 using TensorFlow 2.5.0.

RESULTS AND DISCUSSION

Fig. 1e displays the calculated diameter D of a mixture of 5, 6 and 7 µm beads based on merely the impedance peak height at 0.5 MHz and 12 MHz. Clearly no differentiation between the three monodisperse beads can be made at the individual frequencies. The improvement using the NN is shown in Fig. 1f. Three distinct peaks can be differentiated and a Gaussian distribution is fitted (mean ± std dev; 5.06±0.16 µm, 5.91±0.17 µm and 6.98±0.21 µm). Furthermore, the NN is able to interpolate and extrapolate bead sizes (based on training with only two particle diameters)(results not shown), therefore the chip can be characterized with only two sets of trainings beads.

We have not seen clear improvements of the NN with deep learning, this might be due to the limited size of the training data (883 of 5 µm, 485 of 6 µm and 302 of 7 µm). A larger dataset likely improves the result even more.

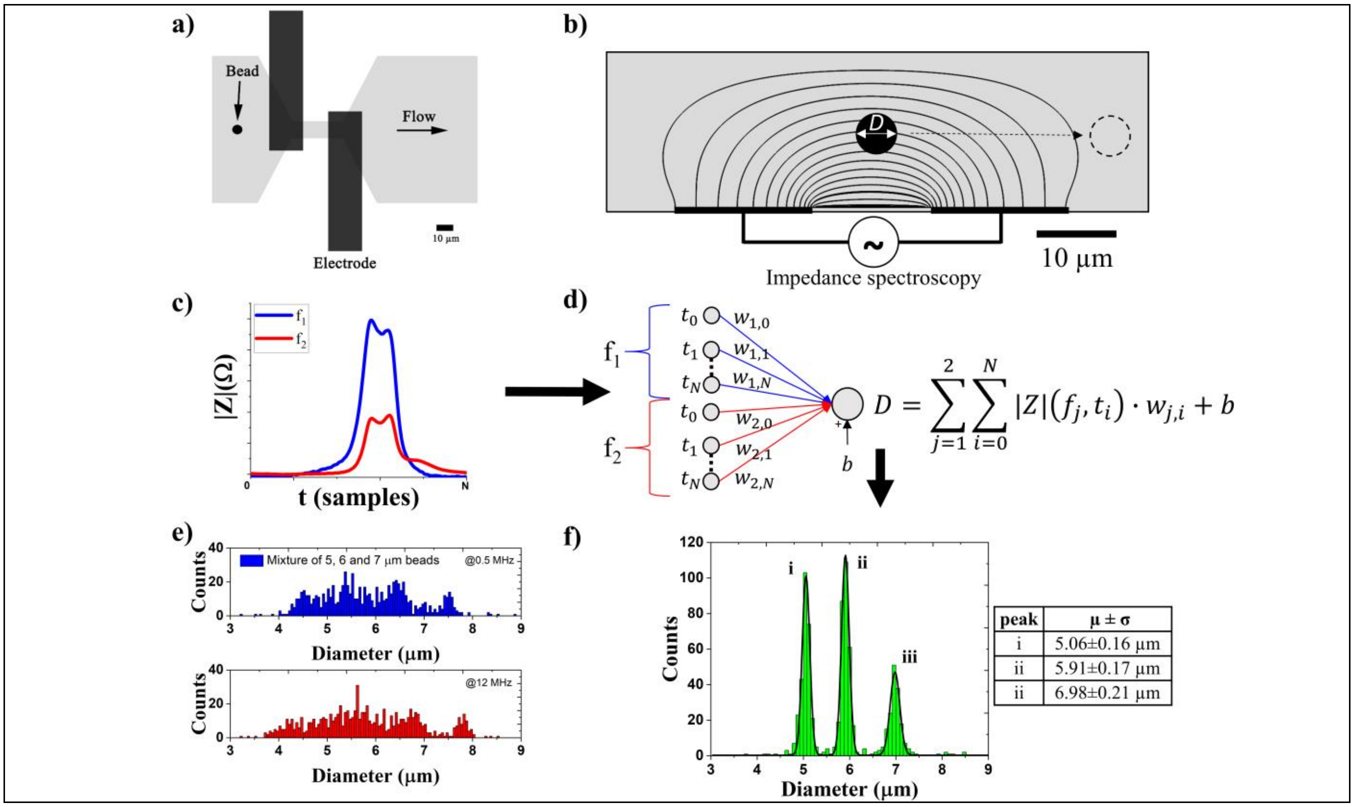

Figure 1: a) Schematic of the microfluidic chip with coplanar electrodes. b) Side view of chip illustrating the inhomogeneous electric field. c) Typical impedance response of a passing bead over time. d) Illustration of the neural network to compute the bead diameter D. The input consists of the impedance signal |Z| at two frequencies (0.5 and 12 MHz) and is evaluated using weights $w_{j,i}$ and a bias b. e) Histograms of bead diameter of a mixture of 5,6 and 7 µm beads calculated using only the impedance peak height at 0.5 MHz and 12 MHz. f) Histogram of bead diameter determined by the NN.

CONCLUSION

We successfully show accurate particle size determination in an inhomogeneous electric field enabled by supervised machine learning. Irregular signal shapes are easily processed by the NN, thus no template fitting and correction function are required.

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CONTACT

* D.S. de Bruijn; d.s.debruijn@utwente.nl