Automated Monitoring for Optical Coherence Tomography-based Biosensing Using Deep Learning

Heejong Kim[1], Chun-Nam Yu[2], William Kennedy[2], Michael Eggleston[2], Shreyas Shah[2]

[1] *Department of Computer Science and Engineering, New York University, NY, USA*
[2]*Nokia Bell Labs, 600 Mountain Ave, New Providence, NJ 07974, USA*
shreyas.shah@nokia-bell-labs.com

Abstract: Microparticle biosensors embedded in 3D tissue-mimics were spatiotemporally monitored in a completely automated pipeline using deep learning. Localization and estimation of microparticle response from OCT imaging was achieved using 3D convolutional neural networks. The automated pipeline was demonstrated using glucose-responsive microparticles as a proof-of-concept.
Keywords: Optical coherence tomography, convolutional neural networks, biosensors, microparticles

1. Introduction

Biosensing approaches to achieve continuous and real-time *in vivo* monitoring of biochemical markers are highly desirable for improving medical care. Although continuous glucose monitoring is well-established and commercially available, detecting and monitoring other types of biomarkers in an *in vivo* setting has remained elusive. This is partly due to challenges in developing strategies which can couple the complex binding activity of a target biomarker with a sensing modality to detect and monitor the binding within the tissue or blood over time.

In our recent previous work, we developed a novel methodology for biosensing using optical coherence tomography (OCT) to achieve dynamic monitoring of biochemical-responsive microparticle biosensors embedded in tissue-mimics [1]. We demonstrated 3D spatial tracking of the microparticles biosensors distributed throughout a hydrogel-based tissue-mimic as well as temporal monitoring of the physical and spectral changes of the microparticles in response to dynamically fluctuating biochemical concentrations. While this novel biosensing strategy is a major advance, the current tracking method requires significant user input to manually identify and optimize microparticle monitoring in three-dimensional time series data. The lack of automation in this process is a key barrier in ultimately realizing continuous and real-time biochemical monitoring.

Herein, we present a deep learning-based approach for the spatiotemporal detection and estimation of microparticle biosensor response within a dynamically-changing biochemical microenvironment (Fig. 1). This is part of a pipeline to completely automate the OCT-based monitoring of biochemicals in an *in vivo* setting.

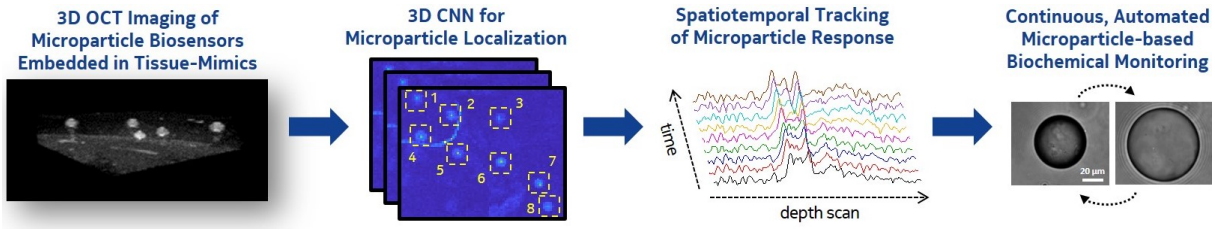

Fig. 1: Microparticle Detection and Size Estimation Pipeline

2. Methods

Our automatic pipeline is divided into two stages: microparticle detection and size estimation (Fig. 1). We turn each 3D OCT scan into sub-volumes of 10×150×81 voxels(100μm×100μm×530μm) and used the sub-volumes as inputs for training a 3D convolutional neural network. The 3D CNN is trained to classify if an input volume contains a microparticle or not. Here we assume that there is at most one microparticle in each volume. If a volume is classified to contain a particle, the intensities are summed up across the z-axis, and the point of the maximum intensity in the x-y plane is used as the location of the particle. In the second stage, we estimate the size of each microparticle by finding two peaks in the depth scan corresponding to the top and bottom of the particle.

2.1. Convolutional Neural Network for Microparticle Detection

There have been previous studies on using deep learning techniques to track microparticles [2], but they were applied to high-resolution microscopy images with 2D CNN and tracking microparticles in 3D OCT scans with 3D CNN has never been proposed. The architecture of our 3D CNN follows the typical design of CNNs used in computer vision. We use convolutional layers with small filters of size 3×3×3 voxels, followed by rectified linear units (ReLU), and maxpooling layers of stride 2 to reduce the input dimensions. We repeat this construct for 5

978-1-7281-5891-4/20/$31.00 ©2020 IEEE

times before 2 linear layers that reduce the output dimension to 2 with softmax activation for classification. The training and test data comes from four different sets of glucose-flow experiments with 7-9 particles each across different timepoints, captured as 3D OCT scans of volumes 1mm×1mm×4mm. We also take OCT images on a set of microparticles with added background scatter but without glucose flow as training data, to improve the robustness of the 3D CNN towards noise. We manually locate the microparticles, and generate positive training examples by placing random bounding boxes around the particles. An equal number of negative training examples are generated by sampling bounding boxes from the background. The CNNs are trained using stochastic gradient descent. We also tried 2D CNN to detect particles in the x-y plane, but they are not as accurate as 3D CNN.

2.2. Microparticle Size Estimation

The microparticle biosensors are designed to undergo physical swelling and deswelling synchronized to variations in the biochemical concentration. After acquiring the location of the microparticles using 3D CNNs, the peaks representing the top and bottom of a given microparticle were first identified from the depth scan. Thereafter, Lorentzian curve fitting was employed to calculate the peak-to-peak distance, which in turn corresponds to the size of the microparticle.

3. Results and Discussions

We first perform an independent evaluation of the 3D CNN classification accuracy on presence/absence of microparticle. We use three glucose flow experiments (set 1,2,3) as test sets. We use two of the datasets not being tested, together with another fixed glucose flow experiment (set 0) and some microparticle images with high scatter as training data, to evaluate how well the 3D CNN transfer to microparticles in an unseen experiment. We can see from Fig. 2(a) that the 3D CNN has accuracies between 88% to 98% in classifying 3D regions.

We then perform an end-to-end evaluation of the pipeline. The 1mm×1mm area is divided into a 10×10 grid for the 3D CNN to classify. To handle microparticles lying at the boundaries of grid cells, we also make the 3D CNN classify a 9×9 grid shifted by half the size of a grid cell in the x and y dimensions, and take the union on the set of microparticles identified with the original set. We then filter out false positives by eliminating any microparticle that changes its size by more than 50% in one time step. Fig. 2(b) shows the microparticles identified by our 3D CNN and their size estimates over time in one of the glucose flow experiments (Fig. 2(c)). Six out of eight microparticles are identified and tracked over time, and their size evolution is consistent with the concentration of glucose. Two of the particles are excluded by the algorithm due to unstable and noisy depth scans. We prefer having false negatives compared to false positives because we only need to reliably track the size of a reasonable number of microparticles to monitor biochemical concentration.

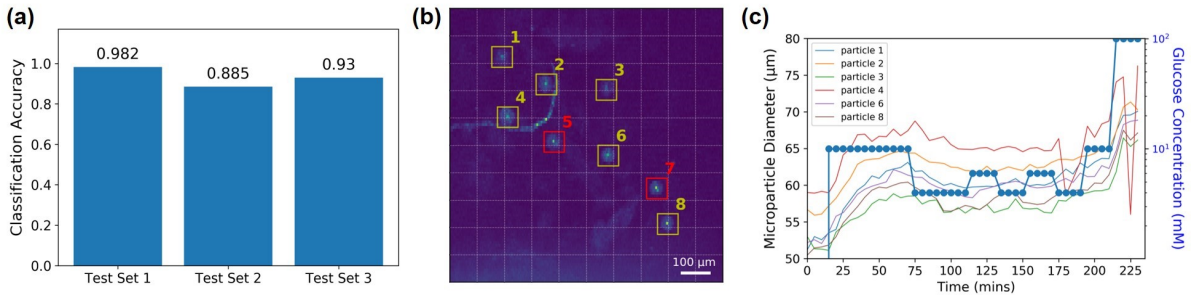

Fig. 2: (a) Microparticle classification accuracies (presence/absence) (b) Microparticles identified (in yellow) and missed (in red) (c) Changes in microparticle sizes with glucose concentration

Overall we have demonstrated an automatic pipeline for tracking the location and size of biochemical-sensitive microparticles in OCT using 3D CNN, and evaluated the system on a glucose concentration monitoring experiment as a proof-of-concept. This 3D CNN approach is highly flexible and can be adapted through training with appropriate data to different types of microparticles designed to monitor diverse biochemical targets. It is also fast and can be made to run in real-time on embedded systems with AI chip accelerations for different medical devices. This combination of OCT and deep learning technologies can lead to many interesting applications of automatic continuous *in vivo* monitoring of biochemicals.

References

1. S. Shah, M. Zheng, M.S. Eggleston, *Remote Monitoring of Microparticle Biosensors Using Optical Coherence Tomography*, IEEE Photonics Conference (2020).
2. J. M. Newby et. al, *Convolutional neural networks automate detection for tracking of submicron-scale particles in 2D and 3D* PNAS vol. 115 no. 36 (2018).