Invited Paper

LAB-ON-A-CHIP SYSTEMS FOR BACTERIAL BIOFILM DETECTION AND ANALYSIS

Reza Ghodssi, Mariana T. Meyer, Young W. Kim, and Sowmya Subramanian

Institute for Systems Research, Department of Electrical and Computer Engineering
The Fischell Department of Bioengineering
University of Maryland, College Park, MD, USA

Bacterial biofilms cause severe clinical infections and contamination of environmental facilities. To investigate fundamental mechanisms of biofilm formation, non-invasive characterization of biofilm is desirable. In addition, sensing of biofilm at early stages of growth is critical in managing biofilm-associated adverse effects, such as chronic infectious diseases. A micro-scale device has significant advantages for biofilm investigations, including low volume requirements, high throughput experiments, sensitive detection, and real-time monitoring. In this paper, we summarize microfluidic Lab-on-a-Chip (LoC) biofilm characterization platforms, as well as a micro-scale sensor for early detection of biofilms using a surface acoustic wave (SAW).

LoC devices have been developed with the aim of aiding efficient studies of bacterial biofilms. The inherent properties of microfluidic systems, including compatibility with non-invasive sensing mechanisms, simple parallel operation, and provision of a tightly controllable microenvironment, are leveraged to provide platforms enabling comprehensive study of bacterial biofilms under a variety of conditions. A microfluidic device featuring biofilm detection via an optical method was developed to allow for real time monitoring of biofilm growth [1]. Furthermore, novel geometries in valved microfluidics were created to provide more rigorous control of biofilm studies (Fig. 1) [2]. This device enables division of one biofilm into multiple sections and permits evaluation of multiple properties while concurrently comparing experimental conditions to the control on the same biofilm. Since biofilm growth is stochastic, its spatiotemporal measurement provides valuable information about the complex structure of a biofilm, and can thereby significantly aid in understanding the properties of the biofilm. This is crucial in developing effective drugs and in investigating the fundamental mechanisms of biofilms. As we integrated a micro-channel with an arrayed photodiode, the microfluidic platform was able to detect the spatiotemporal biofilm changes without the use of any external bulk instrument, such as a confocal microscope (Fig. 2) [3].

While in vitro biofilm models provide a means for scientific characterization of biofilm growth and response in a controlled environment, there exists a clinical need for in situ biofilm detection at the early growth stage for effective biofilm treatments. To this end, a SAW-based biosensor has been developed. The resonant frequency of the sensor was monitored continuously during bacterial biofilm growth as shown in Fig. 3 [4]. Reliable operation of the sensor was verified through three consecutive biofilm growth experiments, the results of which closely corresponded to each other (Fig. 3b).

Microsystems present significant advantages for biofilm analysis as well as detection. Based on the Lab-on-a-Chip and real time sensing platforms presented above, we envision the application of microsystems toward both in vitro biofilm studies for drug development and in vivo biofilm sensing for effective biofilm infection management.

References

[1] M. T. Meyer, V. Roy, W. E. Bentley, and R. Ghodssi, "Development and validation of a microfluidic reactor for biofilm monitoring via optical methods," *Journal of Micromechanics and Microengineering*, vol. 21, May 2011.

[2] M. T. Meyer, Y. W. Kim, H. Ben-Yoav, M. Gnerlich, and R. Ghodssi, "ALD-assisted passivation technology for biofilm studies in microfluidics," in *Proceedinsg of the 2013 International Conference on Microtechnologies in Medicine and Biology (MMB)*, Marina del Rey, CA, USA, 2013, pp. 10-11.

[3] Y. W. Kim, M. Mosteller, M. T. Meyer, H. Ben-Yoav, W. E. Bentley, and R. Ghodssi, "Microfluidic biofilm observation, analysis, and treatment (Micro-BOAT) platform," in *Hilton Head Workshop 2012: A Solid-State Sensors, Actuators and Microsystems Workshop*, Hilton Head, SC, 2012, pp. 233-236.

[4] Y.W. Kim, S.E. Sardari, M.T. Meyer, H.C. Wu Y.W. Kim, S. E. Sardari, M. T. Meyer, A. A. Iliadis, H. C. Wu, W. E. Bentley, and R. Ghodssi, "An ALD aluminum oxide passivated surface acoustic wave sensor for early biofilm detection," *Sensors and Actuators B: Chemical*, vol. 163, pp. 136-145, March 2012.

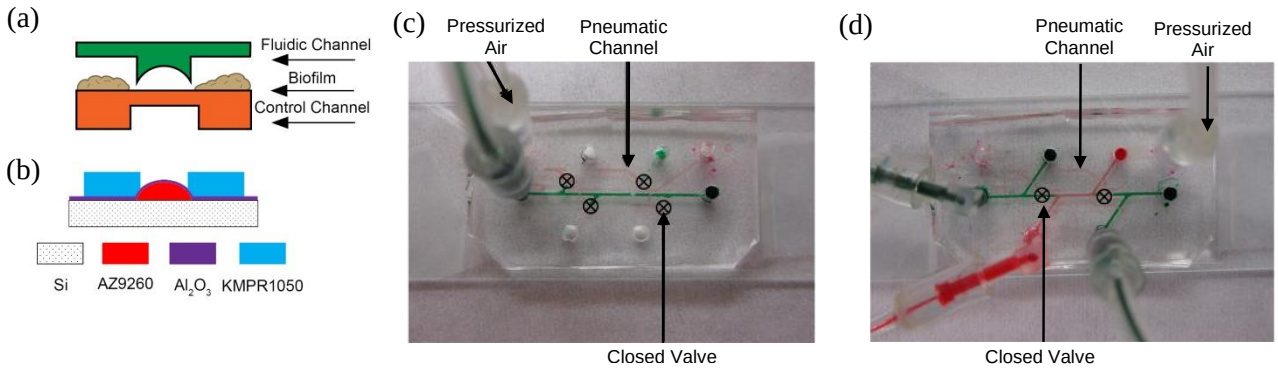

Fig. 1: (a) Cross-sectional diagram of valved microfluidic platform for biofilm sectioning. Both channels are molded in PDMS; the shallow section of the fluidic channel is closed by applying pressure to the control channel and deflecting the membrane, (b) Schematic of multi-depth photoresist mold for fluidic channel featuring ALD-deposited Al_2O_3 passivating AZ 9260, (c-d) Operation of microfluidic biofilm-sectioning device with channel locations indicated by colored water. Closed valves are indicated by X's in circles, (c) Creation of central channel for biofilm formation, (d) Use of valves to trisect center channel for performing experiments on biofilm sections [2].

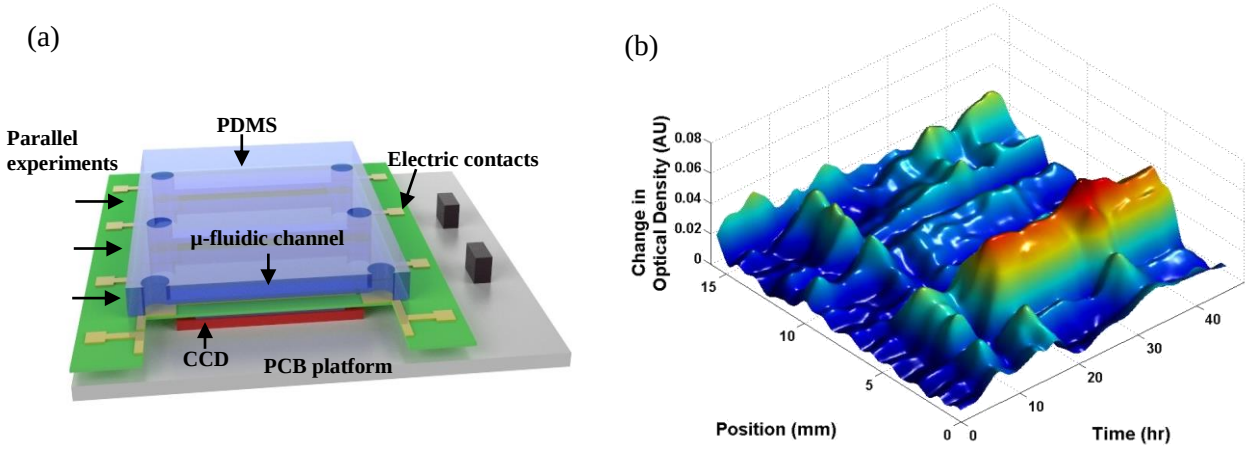

Fig. 2: (a) A schematic of the microfluidic platform with CCD components for spatiotemporal optical density measurements, (b) Surface reconstruction of biofilm morphology changes in the channel over time. Waterfall images are reconstructed using MATLAB based on the OD from the CCDs. The result illustrates the capability to investigate localized biofilm morphology differences [3].

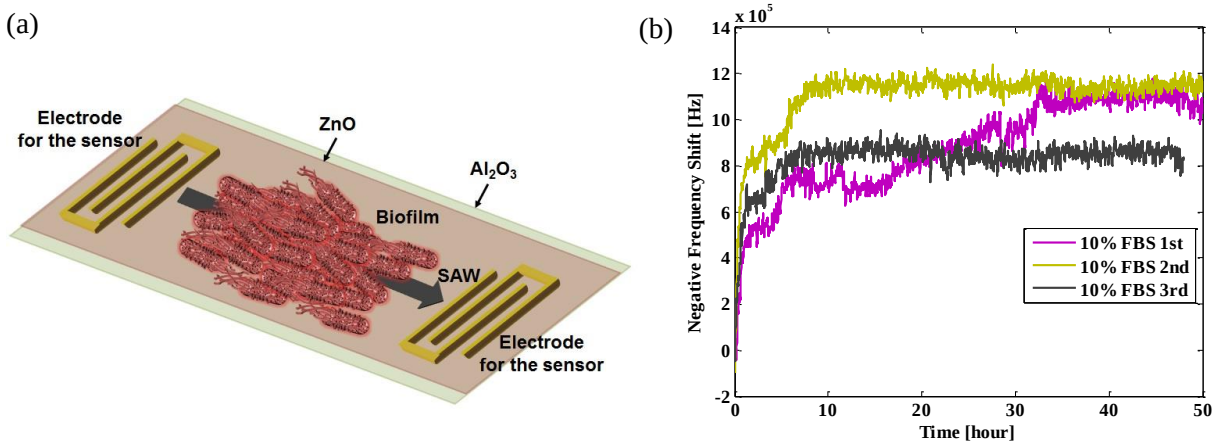

Fig. 3: (a) A schematic of the SAW sensor, (b) Resonant frequency shift results in three consecutive *E. coli* biofilm growth experiments in an animal serum (10% Fetal Bovine Serum) [4].

Contact: *R. Ghodssi, tel: +1-301-405-8158; ghodssi@umd.edu