UCLA Samueli Electrical & Computer Engineering

Ph.D. Defense

Label-Free Optical Mapping for Large-Area Biomechanical Dynamics of Multicellular Systems

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Engineering Bldg. IV – Faraday Room #67-124

Abstract Mechanical forces play pivotal roles in the processes for cells to sense, adapt and respond to external stimuli in their surrounding microenvironment. Current technologies for mapping large-area dynamic biomechanical properties face limitations, primarily due to their small field of view. On the other hand, for a multicellular system to function properly, dynamic equilibrium and coordinated interplays between biomechanical, biochemical, and bioelectrical properties are crucial. Disruptions in any of these properties can cause an imbalance, negatively impacting downstream processes, and leading to fatal failure of the whole system. Therefore, the capability to perform real-time monitoring of these dynamic changes can provide groundbreaking insights into the bidirectional interactions in biological systems.

In this dissertation, a novel platform for mapping large-area biomechanical dynamics is proposed, designed, and established. The platform utilizes a massive number of optical diffractive elements embedded periodically in an elastic membrane to track the traction force generated by the cells seeded on top. Observation field of view up to 10.6 mm by 10.6 mm is achieved, which is more than 2 orders of magnitude improvement compared to traditional TFM. Meanwhile, high spatiotemporal resolution is maintained, allowing us to measure transient activities at cellular level.

To demonstrate the capabilities of our platform for visualizing the large-area biomechanical dynamics in real-time, monolayer tissue composed of millions of neonatal rat ventricular myocytes (NRVMs) are seeded on our devices. For the first time, global trends and local heterogeneities of mechanical waves created by cardiac beatings are recorded concurrently with unprecedented details. Conduction patterns, activation time, activation durations, conduction velocities and dominant frequencies are analyzed temporally and spatially. Moreover, the label-free feature of our platform introduces minimized interruption to the physiological activities of cells, thereby extending the observation time of experiments. Recordings of biomechanical dynamics from the same culture up to 7 days are reported. This is a dramatic enhancement compared to conventional optical mapping using fluorescent dyes, which often has hours-long observation windows.

Lastly, we integrated the platform with a fluorescent imaging system to conduct simultaneous mappings of the calcium ion concentration and biomechanical dynamics resulting from the cardiac beating. It is the first demonstration of detailed mechanical wave propagation and the corresponding calcium ion transient. Our innovative approach holds promise for studying the complex interplay between biomechanical, biochemical, and bioelectrical properties in biological systems.

Biography Yen-Ju Lin received her B.S and M.S. degrees in Electrical Engineering from National Taiwan University. She is currently a PhD candidate in the Electrical and Computer Engineering Department (ECE), University of California, Los Angeles (UCLA). Her research interests include optical biosensors and Bio–Micro-Electro-Mechanical System (Bio-MEMS).

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