Multimodal Stimulation and Measurement Platform for Micro-Engineering Heart Tissues (µEHTs)

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The development of advanced cardiac models is essential for accurate disease modeling, drug testing, and therapeutic development. Engineering heart tissues (EHTs) are a cutting-edge field that merges principles from biomedical engineering, tissue engineering, and regenerative medicine to create functional heart tissue for medical applications. This field has gained significant attention due to its potential to address various heart diseases [1], which are leading causes of mortality worldwide [2]. The micro-scale versions of EHTs (µEHTs) offer promising avenues for high-throughput applications and integration towards more natural *in-vivo* condition in a dish [3]. By closely emulating the in vivo environment, these advanced µEHT systems provide more reliable and translatable insights into cardiac physiology, pathology, and therapeutics.

In this study, we integrate several physiologically relevant modes of functions into the same multimodal stimulation and measurements platform. In the platform we utilize and combine the modified microfluidic structure for µEHTs [3] with electrical stimulation, perfusion, and a control of physiologically relevant oxygen [4] (BioGenium Microsystems, Finland). Additionally, we utilize the 2D oxygen mapping and video-based beating and contraction force analysis. The microfluidic µEHT structure facilitates controlled perfusion, delivering nutrients, oxygen, and metabolic waste removal, while integrated electrical stimulation promotes cardiomyocyte maturation and synchronization and functional alignment. Hypoxic conditions were induced to simulate ischemic heart disease, enabling the study of tissue responses and recovery. Real-time monitoring of cardiac function was achieved through phase contract and fluorescent microscopy and 2D oxygen mapping underneath the µEHT constructs, providing precise measurements of contractile force, electrophysiological properties, activity, and metabolic responses.

Combining physiologically relevant application of perfusion, electrical stimulation, and hypoxia significantly enhances the physiological relevance of the µEHT used for the studies. This integrated multimodal stimulation and measurement platform offers novel tool for drug screening, disease modeling, and the development of personalized therapeutic strategies, thereby advancing cardiovascular research and regenerative medicine.

References

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