Collaborative Research: CPS: Medium: AI-Boosted Precision Medicine through Continual in situ Monitoring of Microtissue Behaviors on Organs-on-Chips

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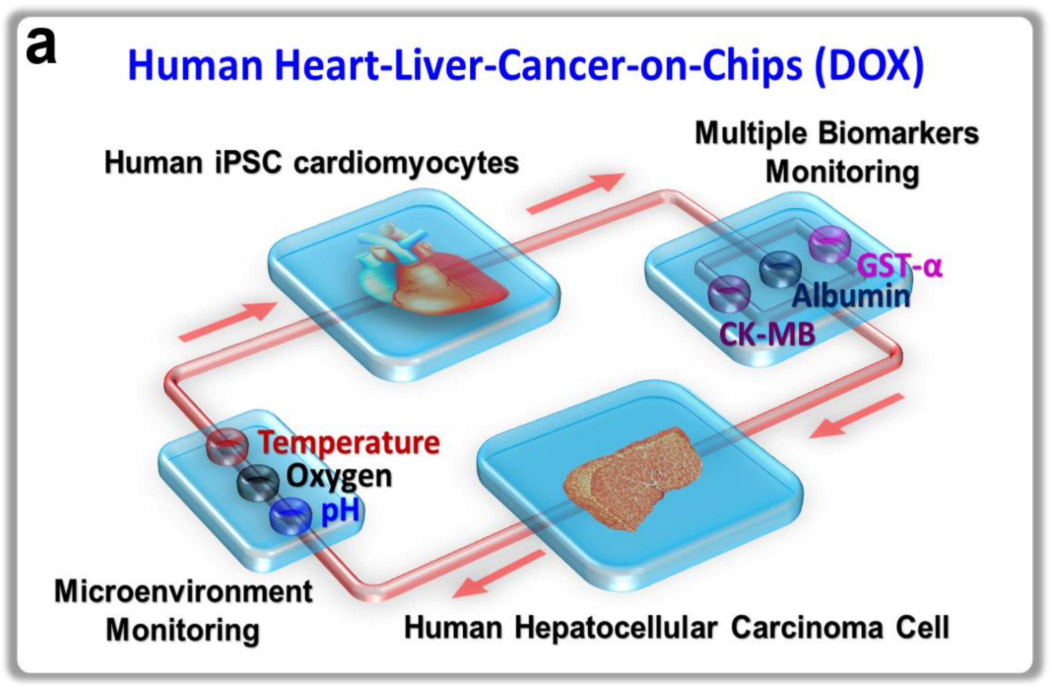
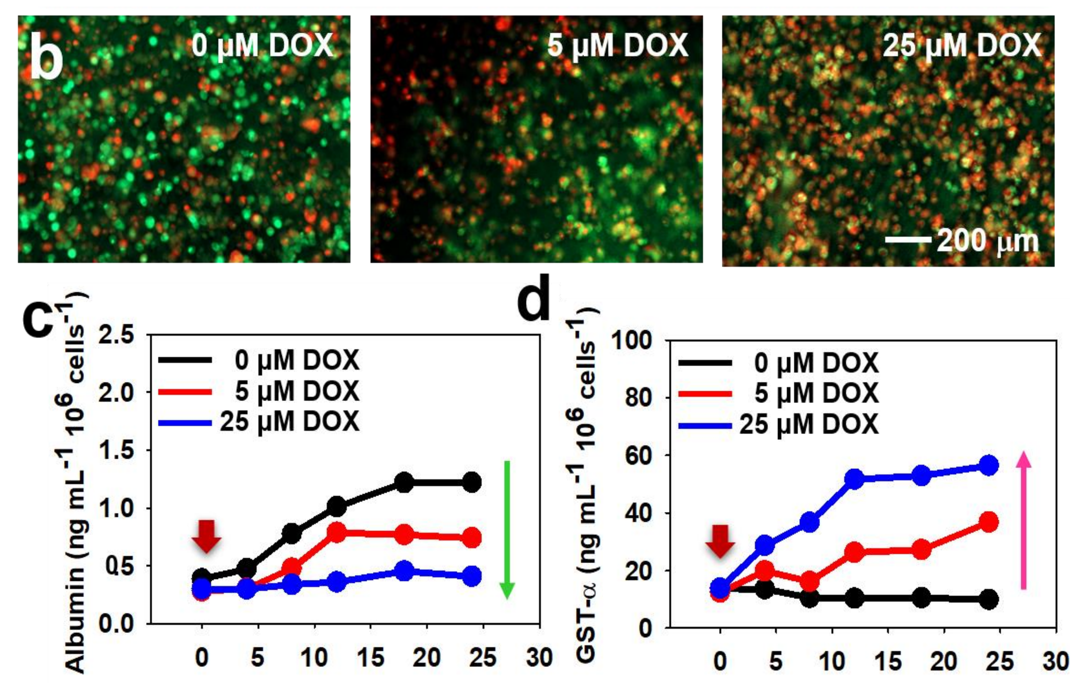
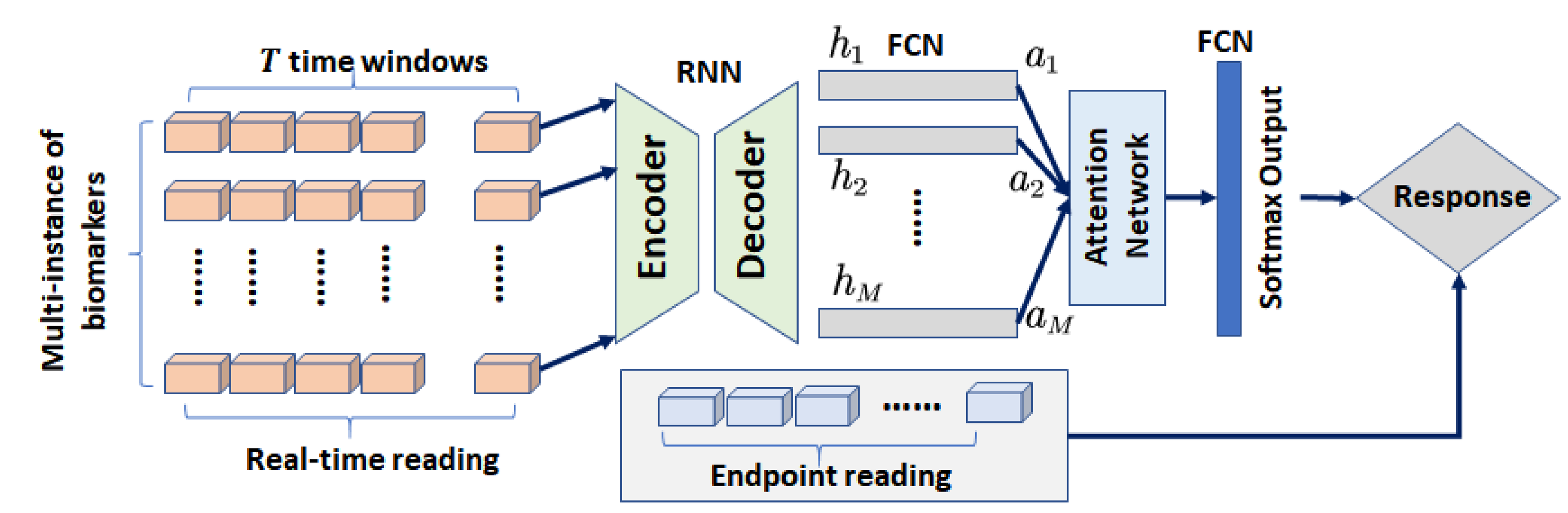


Platform



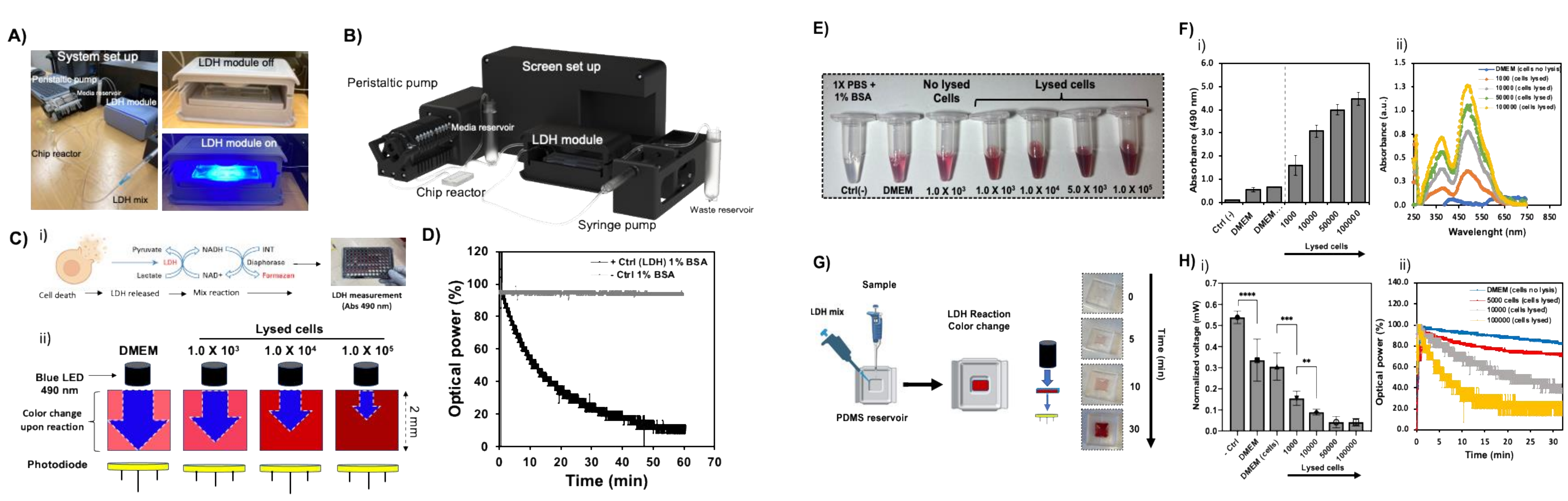
Data Analysis



Predictive Modeling

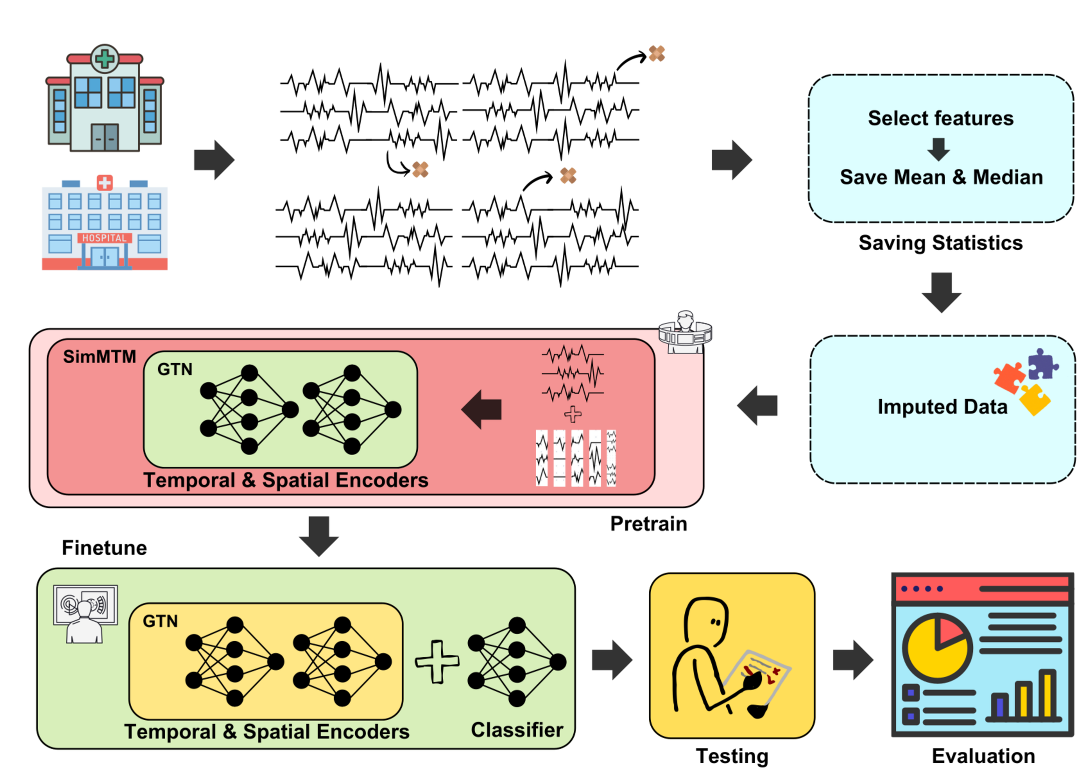
- The ability to predict patient responses to anti-cancer therapeutic agents remains a Holy Grail.
- Getting the right choice of therapy early can mean superior anti-tumor outcomes and increased survival, while the wrong choice means tumor relapse, development of resistance, side effects without the desired benefit, and increased cost of treatment.
- There is a need to develop an engineered cyber-physical system that combines advanced biological models with state-of-the-art AI methods for predictive, automated screening of anti-cancer drugs and optimizations of their dosing.

- The successful development of the proposed framework and multi-organ-on-a-chip platform can be naturally extended to other cancer treatment, drug combination, and dose optimization in anticancer regimen as a rapid and safe testing-bed.
- Second, the built multi-organ-on-a-chip platform will serve as a standard prototype and template for many other 3D-bioprinted or microfabricated human-based tissue models integratable with multi-dimensional biophysicochemical parameter monitoring.
- Third, the dynamic real-time biophysicochemical parameter readings would raise challenges for multi-modal temporal data modeling, a key issue in the Big Data era.



Data Collection

Lactate Dehydrogenase (LDH) sensing module. A-B) General overview of the module and its components. C-i) Schematic representation of LDH assay for cytotoxicity evaluation. C-ii) Schematic of light absorption in cell culture medium through LDH reaction, as higher LDH is present in the media, a lower light absorption is detected by the photodiode. D) Optical power graph vs Time of negative and positive controls. E) Different initial cells seeding for LDH evaluation, in these experiments, cells were lysed after 24 h, blank (only DMEM) and negative controls were also quantified. F-i-ii) LDH quantification of different controls and conditions (absorbance 490 nm and UV-VIS spectrum using a standard well plate reader). G) Schematic representation of light detection, for LDH reaction and the system module characterization, we employed a PDMS reservoir (8 x 8 x 2 mm). H-i) Normalized voltage or Optical power graph vs Time of LDH at different initial cell seeding, (after 24 h of seeding in 96 well plates, cells were lysed, and media was recovered to measure LDH in our system). H-ii) Continuous LDH reaction and online monitoring during the first 30 min of reaction.



Small Dataset Mitigation

- The PIs will develop a generalized, self-dose-optimizing "multi-sensor-integrated multi-organ-on-a-chip" platform, which can be used to accurately predict both efficacy and safety of anti-cancer regimens in this project.
- The first innovation is the adoption of three-dimensional bioprinting for generating the vascularized ductal carcinoma model and vascularized cardiac tissue model, leading to the construction of a truly biomimetic human myocardium for evaluating drug toxicity.
- Additionally, the real-time yet non-invasive monitoring of key biophysicochemical parameters will generate large-scale multi-dimensional data to enable accurate data-driven predictive modeling.
- Moreover, the platform will enable self-dose-optimization on the chips through a novel joint Bayes modeling implemented by two deep learning models capable of addressing multiple-instance learning, and dependency in sequences of multi-dimensional data, respectively.

Broader Impacts

The project has additional social impacts, including minimizing the exponentially growing ethical issues surrounding the use of animals in the past years through increased adoption of the engineered human cancer and heart tissue model systems.

The project will provide opportunities to promote STEM education for K-12 students and research skills for undergrad and graduate students. The research outcomes will be delivered through workshops and tutorials in leading conferences and journals and be further promoted through collaboration with research institutes from the pharmaceutics industry in the Greater Boston area.

Cancers are among the leading causes of death around the world with an estimated annual mortality of close to 10 million, within which a total of 1,688,780 new cases and 600,9200 deaths are expected to occur in the US alone. The proposed AI-Boosted Precision Medicine will enable improved anti-tumor outcomes and increased survival to benefit patients worldwide.

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