Automated Force Measurement System for 3D Printed Muscle Tissues

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Despite a huge medical need for treatments of degenerative muscle diseases in our aging societies, there are today no approved pharmaceutical therapies. Key for successful drug development are biologically relevant predictive tissue models. Recent progresses in bio-printing allow today to bio-engineer functional human 3D skeletal muscle tissue models in a 24-well plate [1]. However, there is no solution on the market for combined electrical stimulation and force readout for efficiently allowing to use such muscle tissue models in drug screening and analyze the effects of compounds on muscle maturation, calcium signaling and contractibility. The developed approach uses flexible posts which are displaced when the muscle tissues contracts. Each of the 24 wells of a well-plate can be located below the measurement optics while being stimulated by the integrated electronic pulse stimulation generator and kept at stable environmental conditions with the help of a stage top incubator. By integration of these key features the system allows the automatic screening of novel compounds to eventually address musculoskeletal diseases.

The growing worldwide demand for high throughput solutions for quantitative evaluation of the effects of novel compounds onto skeletal muscle tissues is not addressed by the current market offer. Especially there is no automated solution on the market for combined electrical stimulation and force readout that allows the efficient use of 3D printed muscle tissue models in drug screening.

Based on this market need, Life Imaging Services (LIS), Novartis, Weidmann Medical Technology, ZHAW and CSEM started a collaboration to develop a system capable of measuring the forces created by 3D printed muscle tissues. To be able to readout forces created by the muscle tissues, a specialized insert with two posts is placed in the wells of a well-plate. The muscle tissue is printed around the posts and differentiated over a period of approximately 10 days.

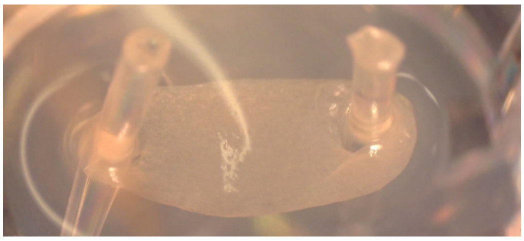

Figure 1: Picture of the muscle tissues printed around two posts.

Once the muscle tissue is fully developed it can be stimulated by the systems integrated electrical stimulation generator. By contracting the muscle bends the flexible post of the insert. The movement of the post is related to the force the muscle tissue applies on the post.

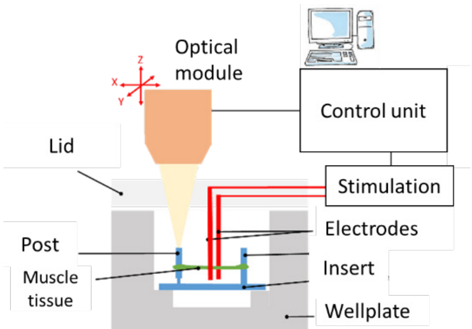

Figure 2: Schematic representation of automated force measurement system based on well-plate inserts that translates the muscles force into post displacement.

An image processing algorithm performs the GPU based image calculations in real-time for framerates up to 70 fps, to give the operator an instant feedback about the muscle's performance. The system is able to detect movements of the post as small as 1 µm.

The integrated stage top incubator (STI) developed by LIS enables the control of temperature, moisture and CO_2 concentration, in order to keep the muscle tissue viable during longer experimental procedures. Additionally, the entire system setup is temperature controlled due to the presence of an outer casing thus avoiding fogging of the STIs transparent lid which would render the optical displacement measurement unusable.

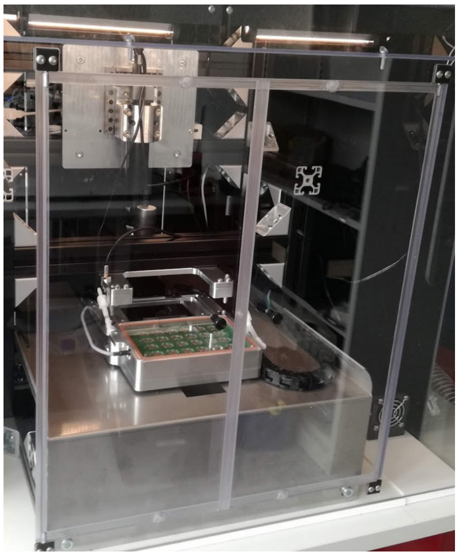

Figure 3: Automated force measurement system for 3D printed muscle tissues developed by the partners of the ongoing InnoSuisse project.

The integrated electronic pulse stimulator has been developed within the frame of the ongoing InnoSuisse project as commercially available pulse generators are bulky and do not offer the required flexibility to drive each of the well-plates 24 channels with an independent pulse profile.

The integration of the electronic pulse stimulation generator, stage top incubator, XY-positioning system, a temperature-controlled measurement chamber, measurement optics and processing algorithms into a complete and automated measurement system render the systematic screening of novel compounds possible.

[1] S. Laternser, H. Keller, O. Leupin, *et al.*, A Novel Microplate 3D Bioprinting Platform for the Engineering of Muscle and Tendon Tissues. SLAS Technol Transl Life Sci Innov. 2018;23(6):599-613. doi:10.1177/2472630318776594.