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Automated 3D Microphysiometry Facilitates High-Content and Highly Reproducible Oxygen Measurements within 3D Cell Culture Models

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Abstract:

Microphysiometry is a powerful technique to study metabolic parameters and detect changes to external stimuli. However, applying this technique for automated label-free and real-time measurements within cell-laden three-dimensional (3D) cell culture constructs remains a challenge. Herein, we present an entirely automated microphysiometry setup that combines needle-type microsensors with motorized sample and sensor positioning systems inside a standard tissue-culture incubator. The setup records dissolved oxygen as a metabolic parameter along the z-direction within cell-laden 3D constructs in a minimally invasive manner. The microphysiometry setup was applied to characterize the spatial oxygen distribution within thick cell-laden 3D constructs, study the time-dependent changes on the oxygen tension within 3D breast cancer models following a chemotherapeutic treatment, and identify kinetics and recovery effects after drug exposure over 5 weeks. Our data suggest that the microphysiometry setup enables highly reproducible measurements without human intervention, due to the high degree of automation and positional accuracy. The results demonstrate the applicability of the setup to provide valuable long-term insights into oxygenation within 3D models using minimally invasive, label-free, and entirely automated analysis methods.

Keywords: 3D cell culture, hydrogels, oxygenation, label-free, gelatin methacryloyl (GelMA), biosensor, metabolic monitoring