

PROCEEDINGS

# An Ultrathin Microwell Platform for Mechanosensitive Cell Culture

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## ABSTRACT

Biophysical cues of the native extracellular matrix (ECM), which is inherently soft and dynamic, play a critical role in regulating cell behavior, including morphology, cytoskeletal organization, and fate decisions. In contrast to conventional rigid substrates such as glass and plastic, hydrogel substrates and molecularly thin protein nanosheets self-assembled at liquid-liquid interfaces have emerged as promising systems for mimicking physiologically relevant environments, where cells can sense and actively respond to the soft environment [1-3]. Although these systems have demonstrated the mechanosensing capability of various types of cells, they are difficult to control, mechanically fragile, and experimentally complex, limiting their accessibility and reproducibility.

Here, we present an ultrathin microwell platform fabricated via sacrificial droplet printing, termed the Ultrathin Mechanosensitive microwell, that enables liquid-like mechanosensing of cells. By precisely controlling droplet volume, films with thicknesses of 10 – 50  $\mu\text{m}$  are formed at the bottom of the microwells, allowing cells inside the microwells to effectively sense the mechanics of the underlying environment. When supported on liquid, the ultrathin films enable a transition toward fluid-like mechanical perception, providing a controllable and simplified alternative to conventional liquid interfaces. In addition, the incorporation of a spherical microwell geometry enables passive confinement of cells, preventing losing cells prior to adhesion. This dual functionality not only stabilizes cell positioning but also facilitates reliable interrogation of mechanosensitive behaviors in a highly compliant environment.

Proof-of-concept experiments using bone marrow-derived mesenchymal stem cells (BMSCs) reveal distinct substrate-dependent responses: cells remain rounded or form aggregates on films supported by liquid, while they spread on films adhered to rigid supports, indicating a clear transition in mechanosensing behavior. These observations demonstrate that the platform effectively captures differences in cellular responses to underlying mechanical environments. Overall, this approach provides a simple, robust, and versatile platform for studying cell-material interactions in soft and fluid-like conditions, offering a practical alternative to existing hydrogel and liquid-interface systems for mechanobiology research.

## KEYWORDS

Mechanotransduction; cell-material interaction; microfabrication

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**Conflicts of Interest:** A Singapore provisional patent was filed by Y.T. and C.H..



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