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TANDEM: biomicrofluidic systems with transverse and normal diffusional environments for multidirectional signaling

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ABSTRACT

Biomicrofluidic systems that can recapitulate complex biological processes with precisely controlled 3D geometries are a significant advancement from traditional 2D cultures. To this point, these systems have largely been limited to either laterally adjacent channels in a single plane or vertically stacked single-channel arrangements. As a result, lateral (or transverse) and vertical (or normal) diffusion have been isolated to their respective designs only, thus limiting potential access to nutrients and 3D communication that typifies *in vivo* microenvironments. Here we report a novel device architecture called "TANDEM", an acronym for "**T**ransverse **A**nd **N**ormal **D**iffusional **E**nvironments for **M**ultidirectional Signaling", which enables multiplanar arrangements of aligned channels where normal and transverse diffusion occur *in tandem* to facilitate multidirectional communication. We developed a computational transport model in COMSOL and tested diffusion and culture viability in one specific TANDEM configuration, and found that TANDEM systems demonstrated enhanced diffusion in comparison to single-plane counterparts. This resulted in improved viability of hydrogel-embedded cells, which typically suffer from a lack of sufficient nutrient access during long-term culture. Finally, we showed that TANDEM designs can be expanded to more complex alternative configurations depending on the needs of the end-user. Based on these findings, TANDEM designs can utilize multidirectional enhanced diffusion to improve long-term viability and ultimately facilitate more robust and more biomimetic microfluidic systems with increasingly more complex geometric layouts.

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