ORIGAMI-ENABLED MICROFLUIDICS

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ABSTRACT

Conventional polymer microfluidics manipulate flows for cell culture and analysis of biological specimens at low cost, but they do not accurately replicate the 3D microstructure and complex transport of living tissues. We present a new paradigm for rapidly creating microfluidics that embody the 3D microstructure and complex transport of natural tissues. In this origami-based approach, polyimide tape patterned to define flow pathways and crease locations is co-folded with nanoporous membranes in an interlocked architecture. The folding produces a multi-material, 3D microfluidic architecture with pressure-driven flow in continuous channels mimicking vasculature and diffusion across nanoporous membranes mimicking perfusion from the bloodstream into adjacent tissues. The simulated perfusion is experimentally characterized using a chemical marker. The results are consistent with Fick's Law, indicating that the origami-enabled, multi-material architecture replicates biomimetic flow and diffusive transport.

INTRODUCTION

Creating biomimetic, chip-based tissue models with 3D microstructure remains a challenge. Traditional microfluidic architectures excel at creating in-plane complexity [1-3], but increasing 3D complexity requires a corresponding increase in the number of fabrication steps. In addition, the traditional materials of polymer microfluidics can accurately mimic flow through blood vessels, but they do not accurately replicate more complex in vivo transport. For example, fluids perfuse from capillary beds into neighboring tissues, and nutrients in the liver diffuse from the bloodstream to the hepatocytes to prevent shear stress from pressure-driven flow. The present work demonstrates the design and simple, straightforward manufacture of self-aligned, origami-enabled, multi-material microfluidic devices that enable both flow and diffusive transport in a scalable 3D platform.

EXPERIMENTAL

Figure 1 shows schematic diagrams of the basic origami-folded architecture. One inlet and outlet serve one set of unstructured microchannels; a second inlet and outlet serve a second set of microchannels that are interleaved between the first. Adjacent microchannels are separated by the folded nanoporous membrane. Figure 2 illustrates the fabrication process, in which a strip of laser-cut polyimide tape is cross-folded with a strip of nanoporous membrane. The final structure (Figure 3) includes a set of two "source" microchannels above and below a third "target" microchannel. Figure 4 shows an alternate device in which the out-of-plane microstructure is complemented by in-plane microstructure, in this case a hexagonal flow architecture that reflects the hexagonal symmetry of a liver lobule.

To characterize the device's flow/diffusion performance, the channels are first filled with water. A syringe pump drives a solution of 1000:1 water:acetic acid through the source channels and water through the target channel at various flow rates. The flow exiting the target channel is captured, and its pH is recorded vs. flow rate.

Figure 1: (a) Schematic diagram of the architecture of the flow/diffusion microfluidic device, showing the interlocked folding of polyimide channels and nanoporous membrane perpendicular to each other. Gray indicates the polyimide tape in which the functional chambers (large circles) and the inlet and outlet ports (four smaller circles) are defined; red indicates the portions of the polyimide tape in which the functional chambers are connected to the inlet and outlet ports; and yellow indicates the nanoporous membrane. (b) Schematic diagram of the resulting flow architecture, gray and yellow indicating polyimide channels and nanoporous membranes, respectively. Red indicates the interior of the source channels (analogous to blood vessels), and blue indicates the interior of the target channels (analogous to adjacent tissues). Source channels are connected to a common inlet and outlet, while target channels have their own inlet and outlet. The source and target channels are connected to each other via diffusion across the nanoporous membrane that separates them.

Figure 2: (a) Diagram of the interlocked cross-folding process; photograph of channels and creases laser-cut in polyimide tape.

Figure 3: (a) Photograph of a 2 cm square, origami-folded microfluidic flow/diffusion device with attached tube connectors. The polyimide layers are 240 μm thick; each functional chamber comprises three polyimide layers as shown in Figure 1b, for a total chamber thickness of 720 μm . The nanoporous membranes are 10 μm thick polycarbonate Whatman Nuclepore Track-Etched Membranes with a pore size of 0.2 μm . (b) Photograph of the device under test.

Figure 4: (a) Photograph and (b) layout of polyimide tape patterned such that, upon co-folding with a nanoporous membrane, it mimics the in-plane hexagonal and out-of-plane layered architecture of a liver lobule, with miniature blood vessels interspersed with sheets of hepatocytes. (c) Photograph of the completed hexagonal microfluidic device (20 mm in its widest dimension).

RESULTS

Flow through a laminar, pressure-driven network reflects the network's flow resistances, and flow distribution is largely independent of flow rate. In contrast, diffusive transport should increase concentration in the target channel in inverse proportion to the flow rate. The increase in concentration of H_3O^+ in the target channel (neglecting the effects of buffering) is plotted vs. the inverse flow rate in Figure 5, showing an increasing trend that is consistent with Fick's Law. The results indicate that the simple origami-folded devices are functionally free of pressure-driven leakage between the interacting fluid networks while also exhibiting the intended diffusive behavior.

Figure 5: Change in concentration of H_3O^+ as deduced from pH values measured in the flow exiting the target channel and plotted vs. the inverse flow rate. Effects of buffering are neglected. The change in concentration increases as flow rate decreases, consistent with the predictions of Fick's Law in which flux is determined by the difference in concentration, the geometry, and the diffusivity. With the reduced residence time of higher flow rates, the same flux produces a smaller change in concentration, in contrast to the expected behavior for pressure-driven flow.

The devices created in this way exceed the capabilities of conventional microfluidics. Their fabrication is simple and straightforward, and their creased origami structure automatically ensures correct interlayer alignment. This technique offers an accessible pathway to 3D microstructured, engineered tissues that manifest the complex flow/diffusion functionality of native tissues.

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