Supplementary Information for:

Multiscale 3D microfluidic platform for intraorganoid delivery

Author List: Maria Jose Quezada[1,2,3†], Jamin Lee[1,4,5,6 †], Zengyao Lv[7†], Khizar Nandoliya[8†], Ingrid Cheung[1,9†], Qiong Wang[6,†], Woo-Yeol Maeng[6], Naijia Liu[6], Amir Vahabikashi[10], Kyoung-Ho Ha[6], Yong-Woo Kang[6], Dae-Hyeon Song[11], Yuming Huang[6], Clara Asseily[2], Rakan Walid da Cruz[2], Shreyaa Khanna[1], Jintao Liu[12,13], John D. Finan[14], Lara Leoni[15], Daniele Procissi[15], Yonggang Huang[6,7,16], Gyu-Chul Yi[4,5], Juyeol Bae[12,13*], John A. Rogers[2,6,16*] & Colin K. Franz[1,6,9,17*]

Affiliations:

[1]Regenerative Neurorehabilitation Laboratory, Shirley Ryan Ability Lab, Chicago, IL 60611, USA.

[2]Department of Biomedical Engineering, Northwestern University, Evanston, IL 60208, USA.

[3]Department of Physical Therapy and Human Movement Sciences, Northwestern University, Chicago, IL 60611, USA.

[4]Interdisciplinary Program in Neuroscience, College of Science, Seoul National University, Seoul, 08826, South Korea.

[5]Center for Novel Epitaxial Quantum Architectures, Department of Physics and Astronomy, Seoul National University, Seoul, 08826, South Korea.

[6]Querrey Simpson Institute for Bioelectronics, Northwestern University, Evanston, IL, 60208, USA.

[7]Department of Civil and Environmental Engineering, Northwestern University, Evanston, IL 60208, USA.

[8]Department of Neurological Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, USA.

[9]Department of Physical Medicine and Rehabilitation, Northwestern University.

[10]Bioengineering Department and Institute for Mechanobiology, Northeastern University, Boston, MA, 02115, USA.

[11]Department of Materials Science and Engineering, Korea Advanced Institute of Science and Technology, Daejeon, 34141, South Korea.

[12]Department of Mechanical Engineering, Chonnam National University, 77 Yongbong-ro, Buk-gu, Gwangju 61186, Republic of Korea.

[13]Advanced Medical Device Research Center for Cardiovascular Disease, Chonnam National University, 77 Yongbong-ro, Buk-gu, Gwangju 61186, Republic of Korea

[14]Department of Mechanical and Industrial Engineering, University of Illinois Chicago, Chicago, IL 60607, USA.

[15]Department of Radiology, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, USA.

[16]Department of Materials Science and Engineering and Department of Mechanical Engineering, Northwestern University, Evanston, IL 60208, USA.

[17]The Ken and Ruth Davee Department of Neurology, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, USA.

[†] These authors contributed equally

* Corresponding Authors

Correspondence to Juyeol Bae, John A. Rogers and Colin K. Franz

Supplementary Fig. 1 | Fabrication processes for the multiscale 3D microfluidic platform. 3

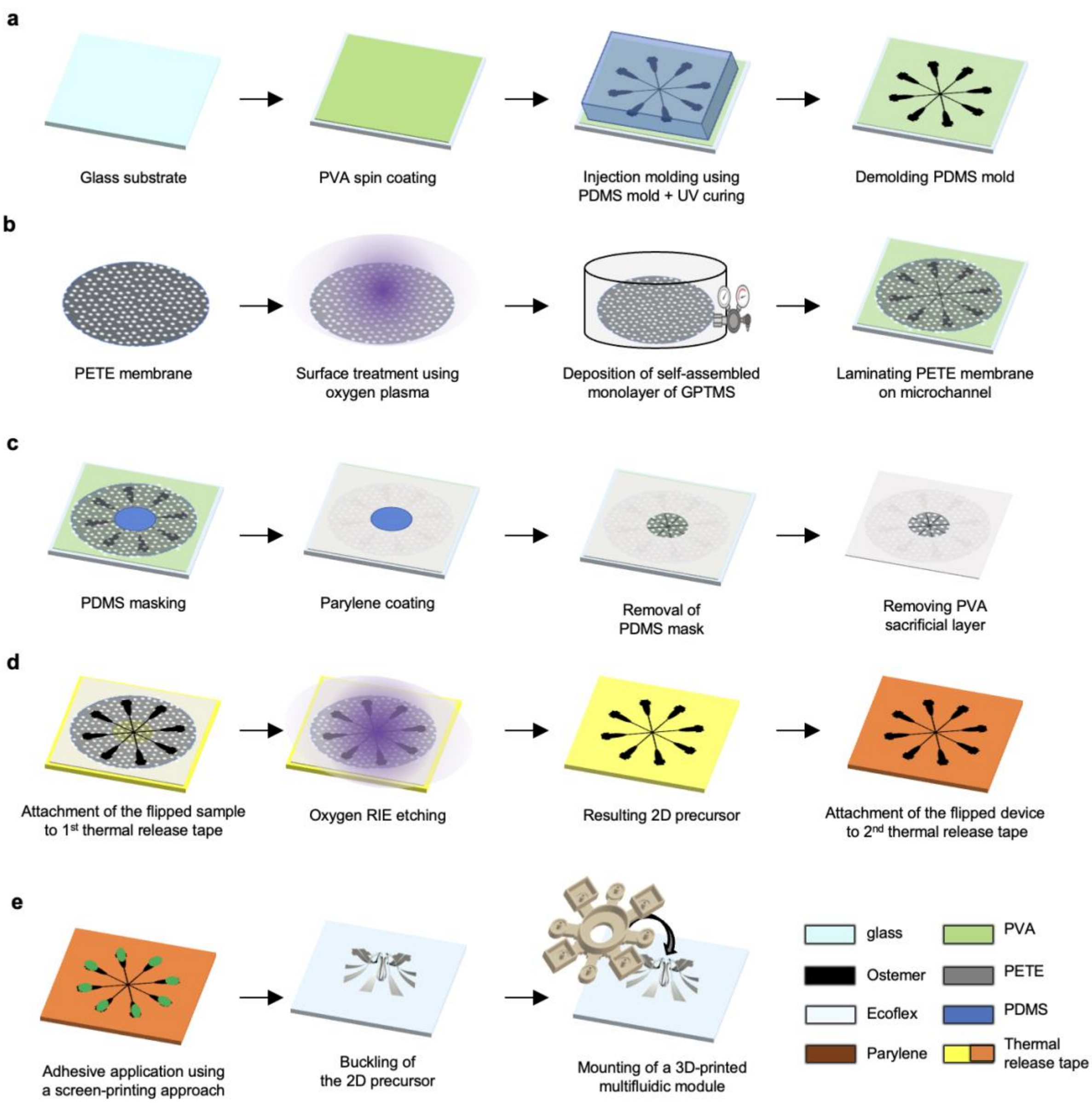
Supplementary Fig. 2 | Dimensional characteristics of the planar precursor................................ 4

Supplementary Fig. 3 | Mechanical characteristics of the material used for buckling the precursor into 3D microchannel.. 5

Supplementary Fig. 4 | A microfluidic device for multiplexed delivery of solutes at targeted localized region.. 5

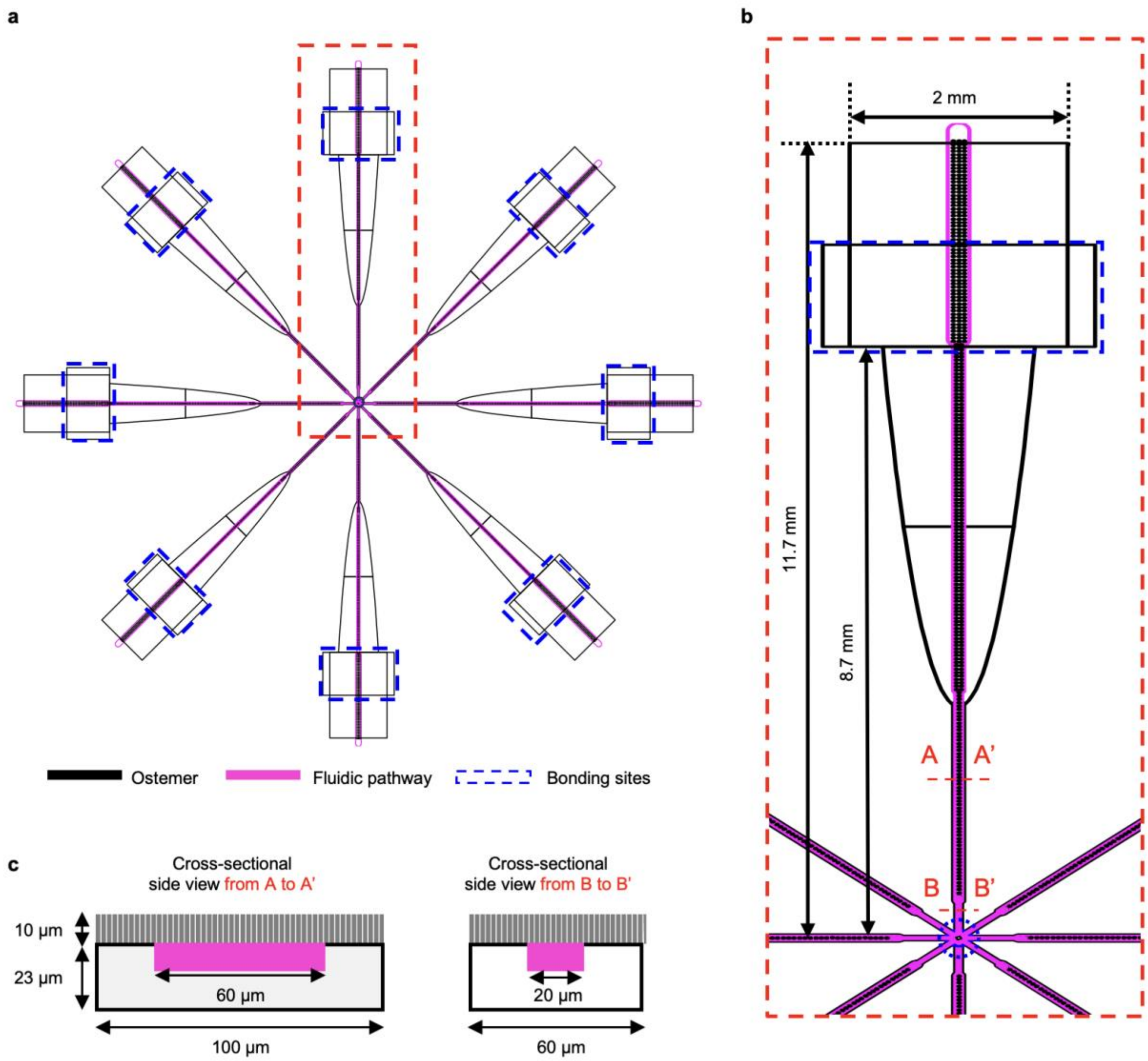
Supplementary Fig. 5 | Top view of experimental setup for characterizing the mechanism of solute transport through the porous interface into the agarose phantom. 6

Supplementary Table 1 | List of antibodies and molecular probes. 6



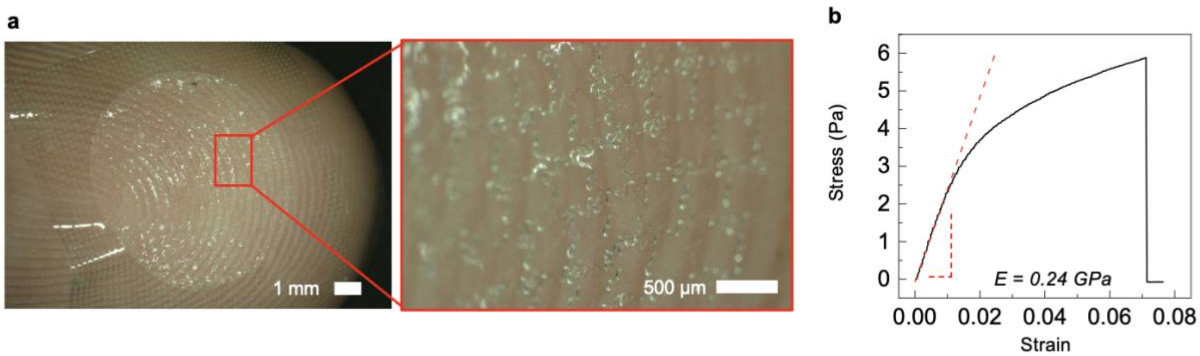
Supplementary Fig. 1 | Fabrication processes for the multiscale 3D microfluidic platform.

a, Soft-lithography step for preparing microchannel layer. **b,** Lamination step for bonding the PETE membrane onto the prepared microchannel layer. **c,** Deposition step for selectively coating parylene on the surface of the PETE membrane. **d,** Etching step for defining the PETE sheet into the same 2D layout as the microchannel layer. **e,** Packaging step including buckling the 2D precursor and mounting the 3D-printed millifluidic modules onto the periphery of the buckled 3D microchannel.



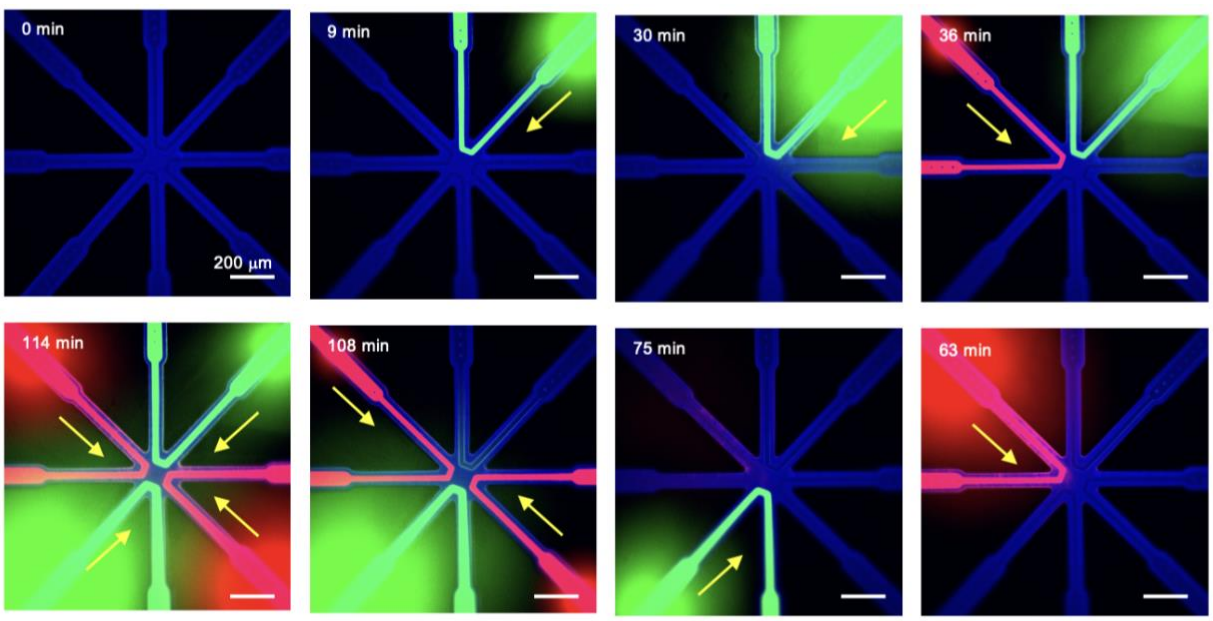
Supplementary Fig. 2 | Dimensional characteristics of the planar precursor.

a, 2D layout showing the design of the planar precursor. **b,** Enlarged view of a single wing in the 2D layout. **c,** Cross-sectional side views of the planar precursor along lines A–A' and B–B' in the enlarged view of the wing.



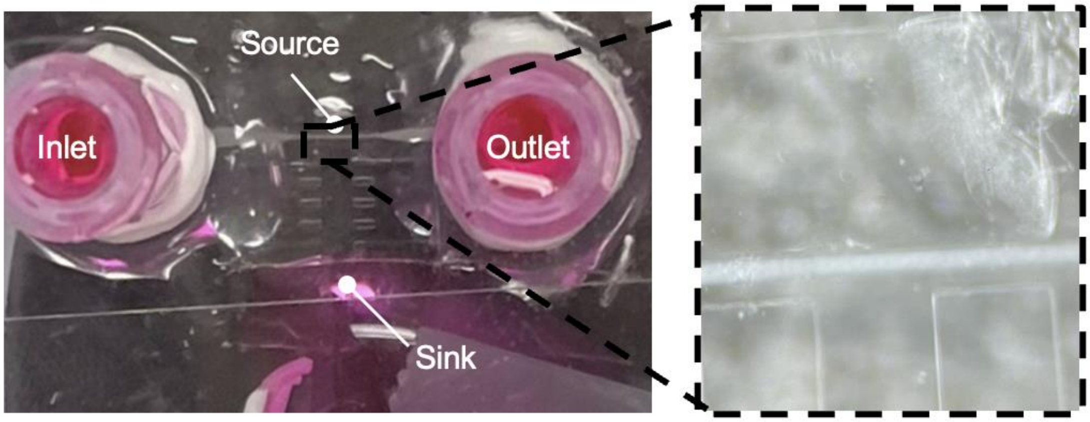
Supplementary Fig. 3 | Mechanical characteristics of the material used for buckling the precursor into 3D microchannel.

a, Photographs showing an Ostemer microchannel layer placed on a fingerprint. The magnified view reveals that the layer conforms to the fingerprint ridges because the polymer is flexible (Young's modulus of 10.29×10^6 N/m²). **b** Stress–strain curve obtained from tensile testing of the PETE membrane used to seal the microchannel layer.



Supplementary Fig. 4 | A microfluidic device for multiplexed delivery of solutes at targeted

Time-lapse widefield fluorescence microscopy showing multiplexed spatiotemporal delivery of 50 μM SRB and 100 μM fluorescein isothiocyanate (FITC) into 2-mm-thick 1% agarose. Arrows indicate the flow direction of the solutions from the upstream wing.



Supplementary Fig. 5 | Top view of experimental setup for characterizing the mechanism of solute transport through the porous interface into the agarose phantom.

Antibody	**Species**	**Dilution**	**Catalogue number, Company**
Olig2	rabbit	1:100	AB9610, Millipore Sigma
Pax6	mouse	1:200	ab245110, abcam
Islet1	goat	1:2000	AF1837, Bio-Techne
NF Vio R667	human	1:1000	130-131-154, Miltenyi Biotec
NeuN Vio R667	human	1:1000	130-131-153, Miltenyi Biotec
Goat anti Mouse Alexa Fluor™ 555	mouse	1:1000	A-21424, Thermo Fisher Scientific
Donkey anti Rabbit Alexa Fluor™ 647	rabbit	1:1000	A-31573, Thermo Fisher Scientific
Donkey anti Rabbit Alexa Fluor™ 555	rabbit	1:1000	A-31572, Thermo Fisher Scientific
Donkey anti Goat Alexa Fluor™ 555	goat	1:1000	A-21432, Thermo Fisher Scientific
DAPI		1:50	D1306, Invitrogen
DRAQ5		1:100	ab108410, Abcam
Cholera Toxin Subunit B (Recombinant), Alexa Fluor™ 555 Conjugate		1:100	C22843, Invitrogen

Supplementary Table 1 **| List of antibodies and molecular probes.**