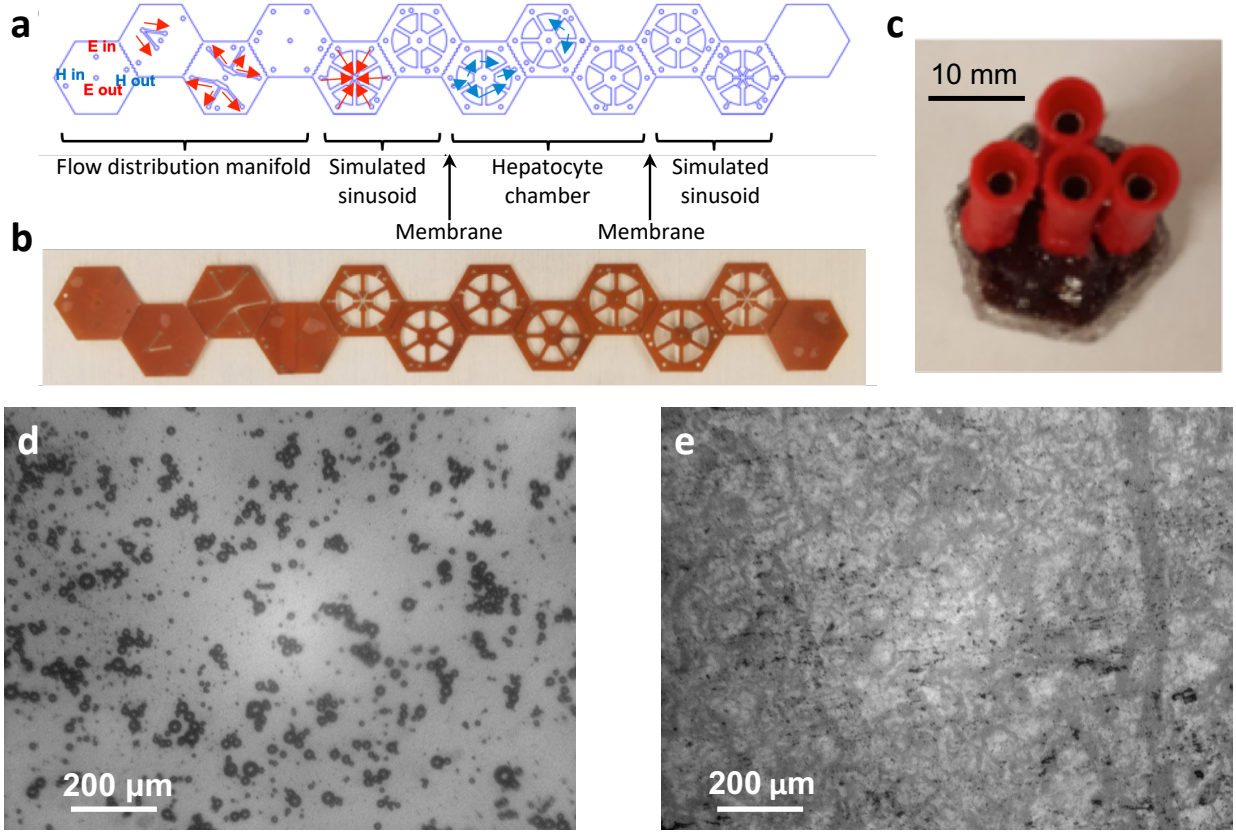


**Figure S1.** (a) Schematic diagram and (b) patterned polyimide tape corresponding to a hexagonal implementation of the oLOC architecture; (c) photograph of a hexagonal oLOC chip; (d, e) optical microscope images of fluid that has exited the hexagonal oLOC from the hepatocyte channel (d) and the simulated sinusoids (e) when approximately 16 micron diameter microspheres suspended in ethanol are flowed through the hepatocyte channel and ethanol is flowed through the simulated sinusoids. No microspheres are observed in the flow exiting the simulated sinusoids, which supports the conclusion that direct leakage of objects at a cellular size scale does not occur between the hepatocyte and simulated sinusoid flow channels.

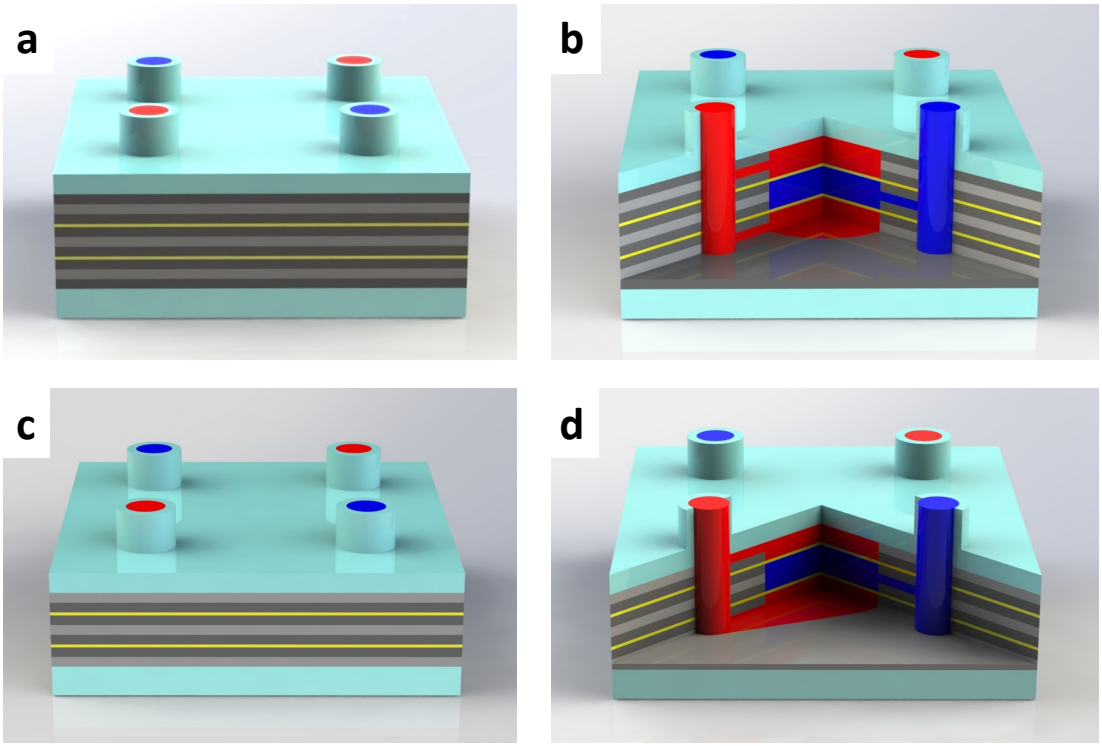


**Figure S2.** (a) Schematic and (b) cross-sectional cutaway diagrams of the completed Generation 1 oLOC; (c) schematic and (d) cross-sectional cutaway diagrams of the completed Generation 2 oLOC.

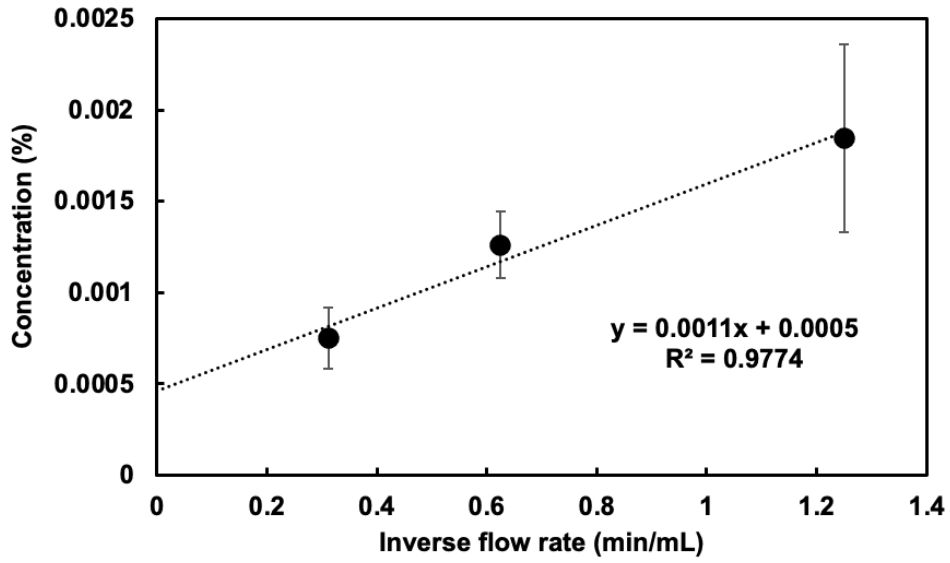


**Figure S3.** Plot of concentration of trypan blue in the flow exiting the middle flow path as a function of inverse flow rate when a 0.1% solution of trypan blue in deionized water is flowed through the top and bottom flow paths and deionized water is flowed through the middle flow path with a higher pressure applied across the top and bottom flow paths than across the middle flow path. The magnitude of the constant contribution to concentration increase matches the concentration change predicted from Darcy's law for pressure-driven flow through porous media, indicating that it reflects expected flow through the nanoporous membrane rather than leakage.

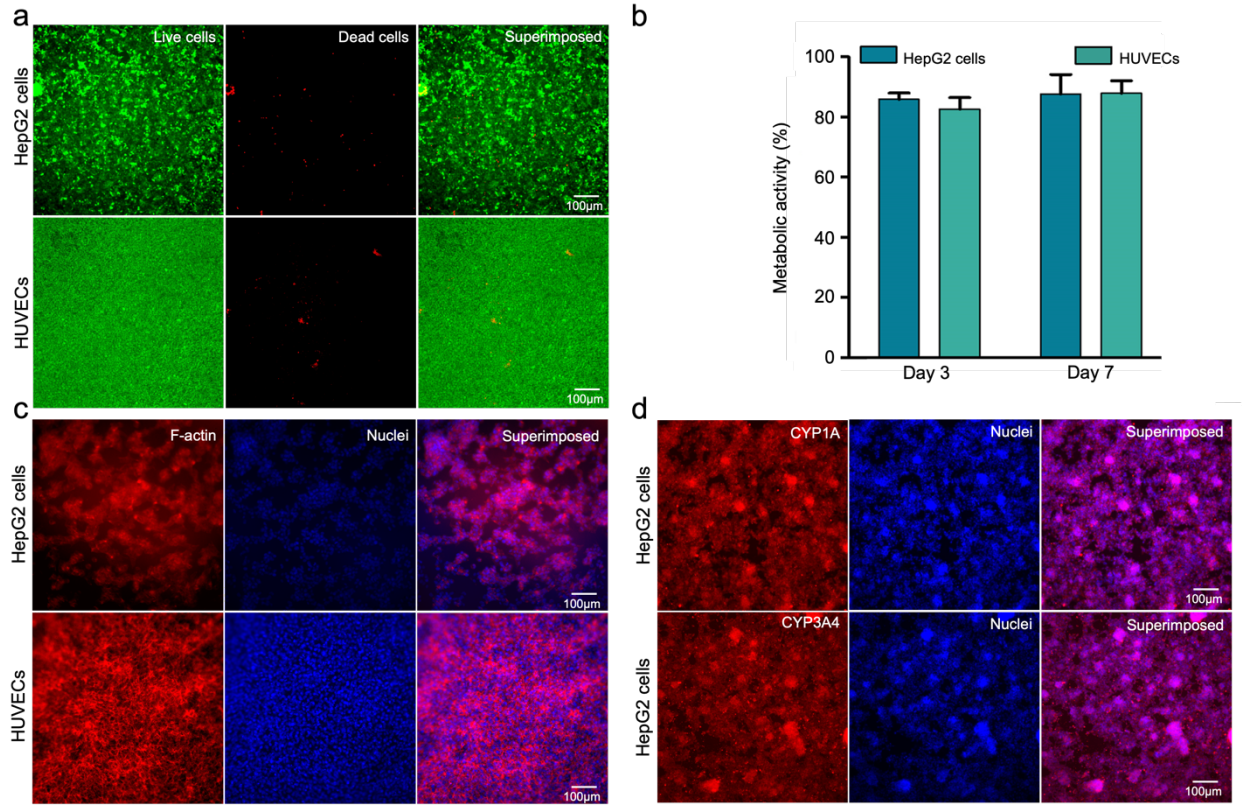


**Figure S4.** (a) Viability of HepG2 cells and HUVECs assessed using Calcein AM (green) and EthD-1 (red) on day 7 of culture; (b) quantified metabolic activity of HepG2 cells and HUVECs at different periods of culture; (c) F-actin and nuclei staining of HepG2 cells and HUVECs at day 7 of culture; (d) immunostaining of HepG2 cells with CYP1A and CYP3A at day 7 of culture.

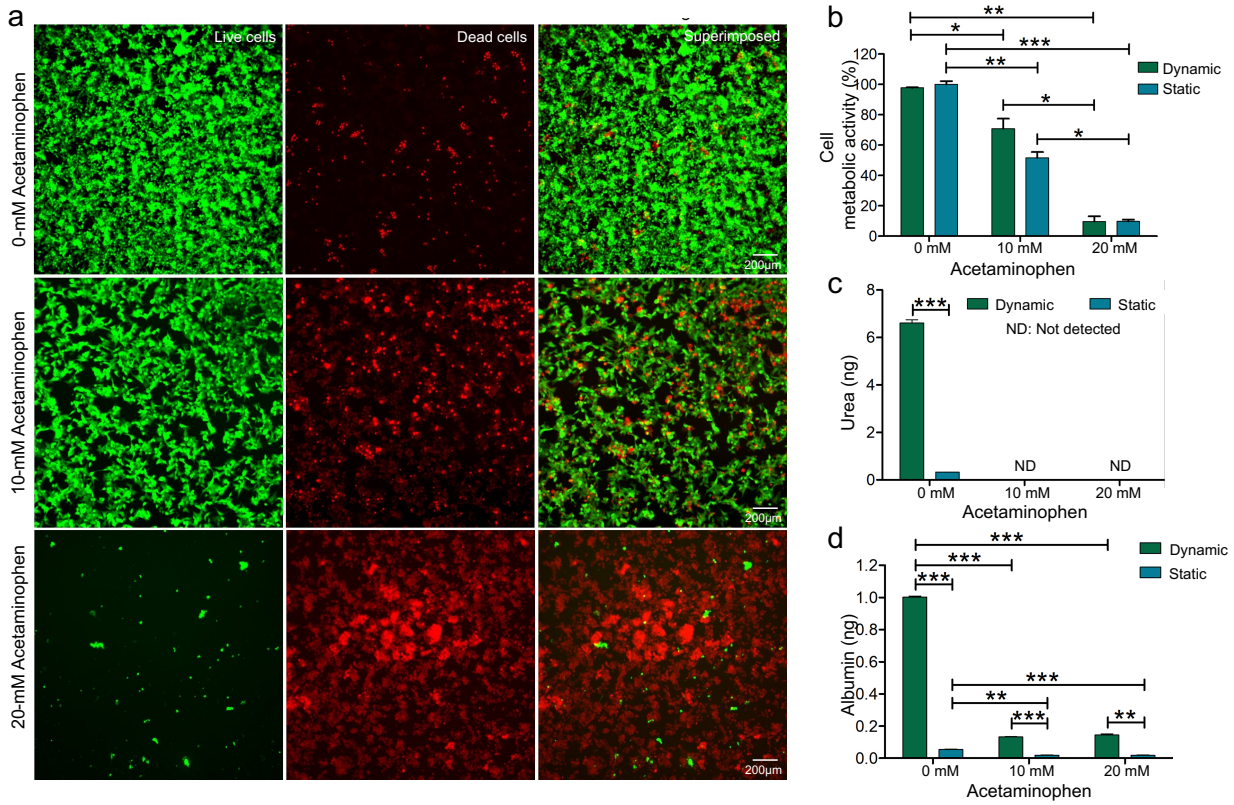


**Figure S5.** (a) Cytotoxicity of acetaminophen on HepG2 cells shown via cell viability assay using Calcein AM (green) and EthD-1 (red) staining after 48 h of acetaminophen treatment; (b) quantified metabolic activity of HepG2 cells at different concentrations of acetaminophen; (c) quantified 48-h urea production by HepG2 cells at different concentrations of acetaminophen; and (d) quantified 48-h albumin production by HepG2 cells at different concentrations of acetaminophen. Asterisk represents significant difference between the dynamic culture group and the static culture group using two-way ANOVA ($p \leq 0.05$).

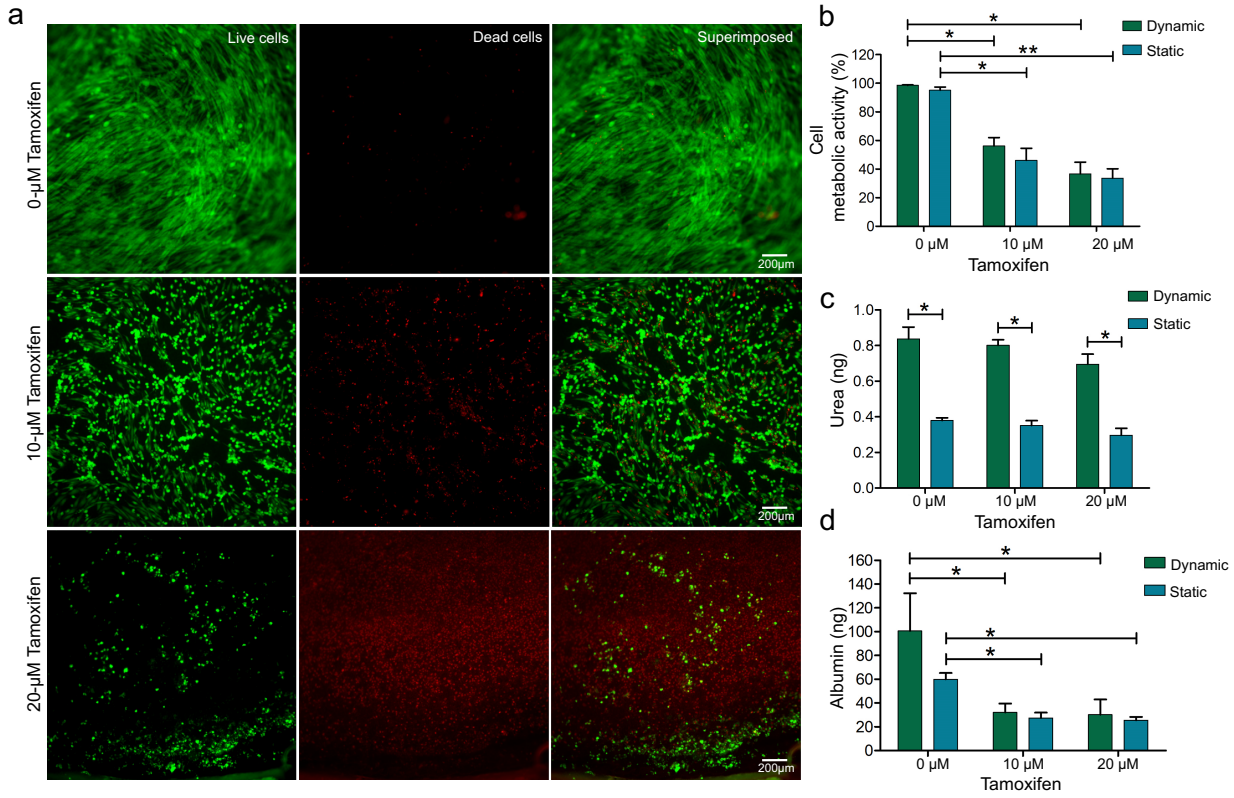


**Figure S6.** (a) Cytotoxicity of tamoxifen on primary hepatocytes shown via cell viability assay using Calcein AM (green) and EthD-1 (red) staining after 48 h of tamoxifen treatment; (b) quantified cell metabolic activity of hepatocytes at different concentrations of tamoxifen; (c) quantified 48-h urea production by hepatocytes at different concentrations of tamoxifen; and (d) quantified 48-h albumin production by hepatocytes at different concentrations of tamoxifen. Asterisk represents significant difference between the dynamic culture group and the static culture group using two-way ANOVA ($p \leq 0.05$).

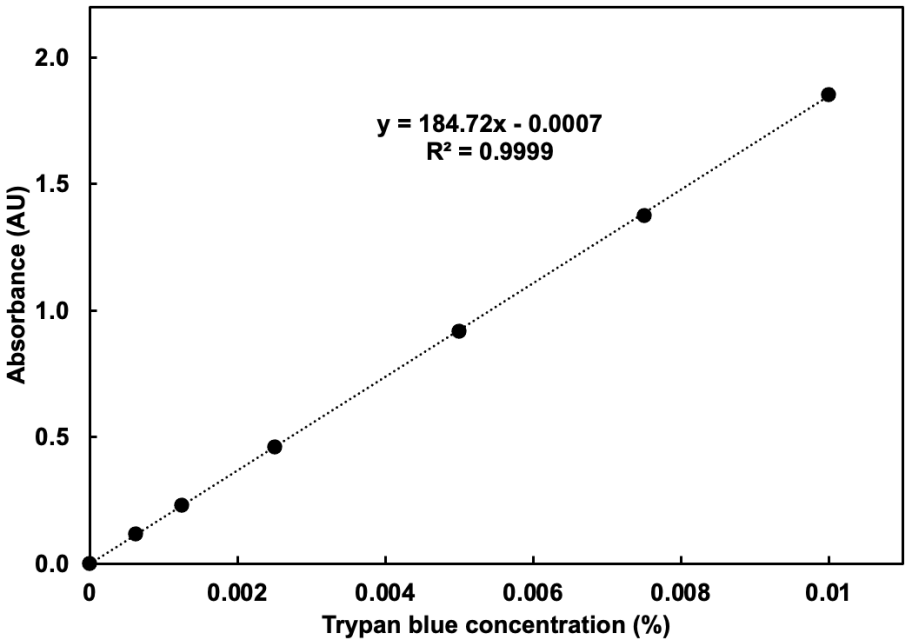


**Figure S7.** Plot of calibration line showing measured absorbance vs. known trypan blue concentration.