Electronic Supplementary Material (ESI) for Lab on a Chip.

A Photonic Biosensor-Integrated Tissue Chip Platform for Real-Time Sensing of Lung Epithelial Inflammatory Markers

John S. Cognetti, Maya T. Moen, Matthew G. Brewer, Michael R. Bryan,

Joshua D. Tice, James L. McGrath, and Benjamin L. Miller

Supplementary Information

Figure S1. Single Channel Device. a) An exploded view of the device layers. A glass coverslip, silicone chip holder, two sealing layers, adhesive channel layer, and PDMS cap with inlet/outlet. b) Top view of the device with the photonic ring resonator sensors centered within the sealing layer and channel. c) Photo of the device on a temperature-controlled aluminum stage, addressed from the right by an 8-channel fiber array. d) Top view of the device under flow.

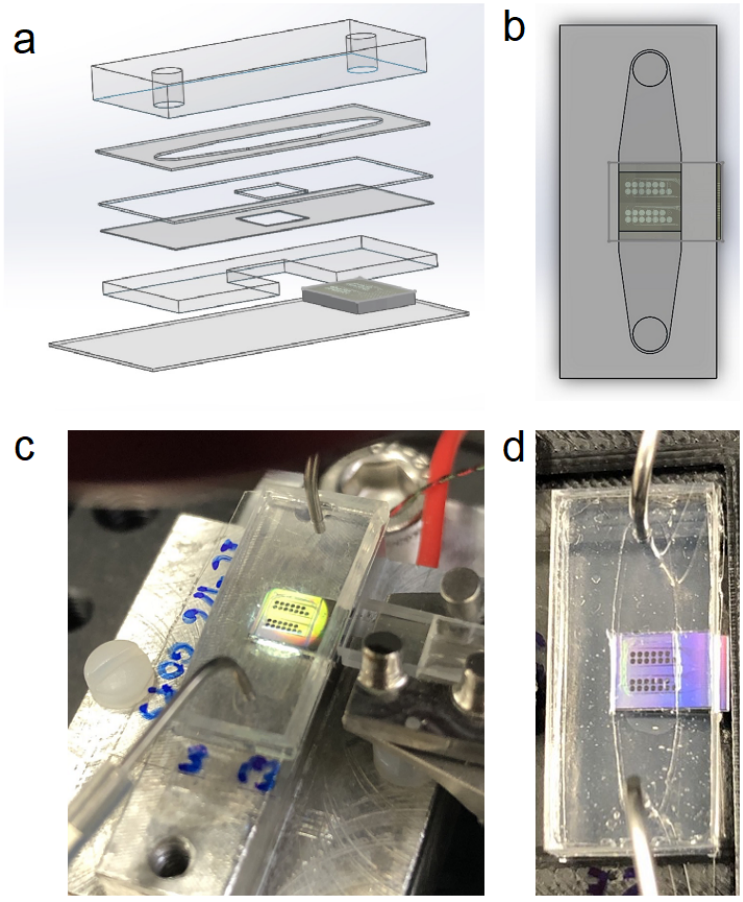

Figure S2. Data Analysis. a) Raw spectra for all 7 channels within Keysight's viewer application. Each channel (distinguished by color) contains peaks for 2 rings, which are repeated approximately ever 2 nm, yielding 6 peaks in each 6-nm scan. b) Custom python analysis script user interface, which allows the user to select peaks at each timepoint and assign them to either the control or capture ring. Inset is an early timepoint (blue) and late timepoint (green), showing how the peaks move over time. Here the left/bottom peak is from the capture ring (IL-6 in the shown data) and in the spectrum from the later timepoint shows the left peak has shifted more than the right peak. c) A normalized plot of each peak's location over time, showing a greater shift for the capture ring. d) Subtracted shift, showing the relative wavelength shift of the capture ring vs. the control ring. This data shows a calibration of IL-6. The x-axis represents time but roughly corresponds to concentration, with the final shift of about 48 pm occurring at the highest concentration of IL-6 (1 µg/mL).

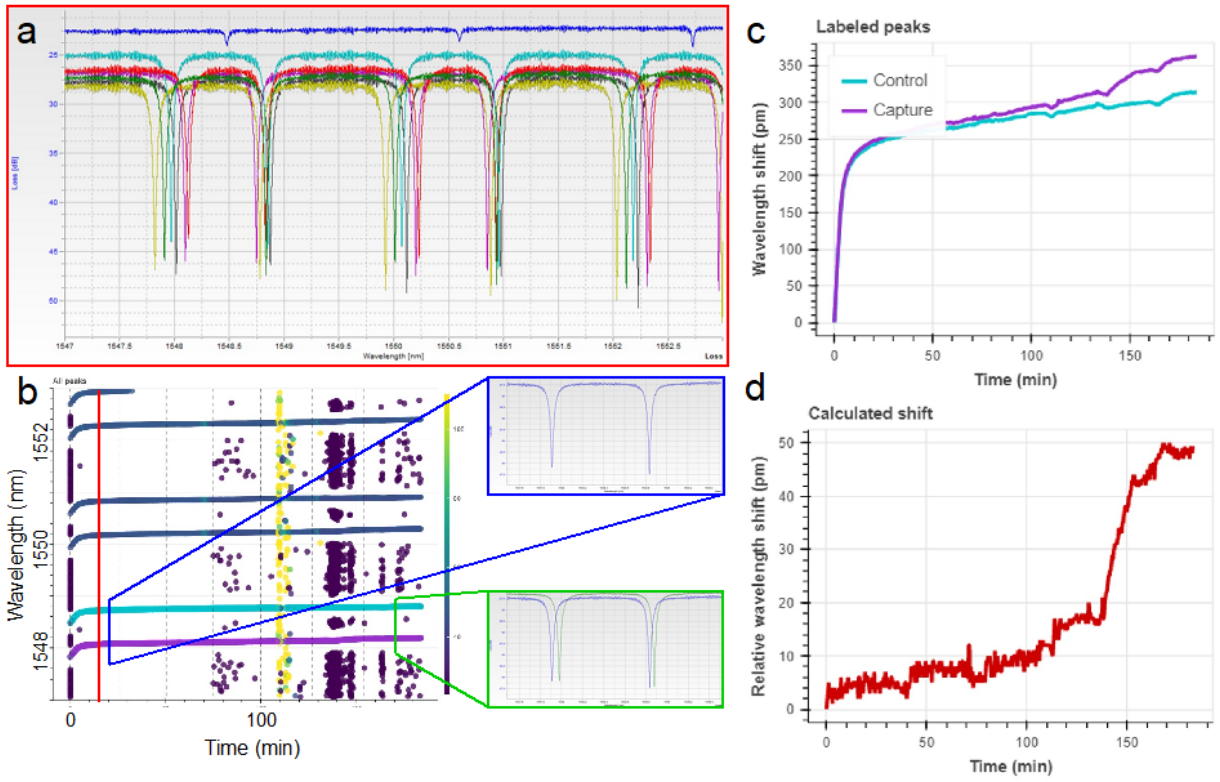

Figure S3. Nonspecific Binding and Diffusion Through Bottom Channel. a) Ring functionalization scheme. Each control antibody is matched to the antibody isotype of the corresponding capture antibody. "High" and "Low" for the mouse antibodies refers to the concentration used to match that of IL-1β vs IL-8, since their stock concentrations were different. b) Nonspecific binding for two IL-1β channels (both represent control-subtracted relative shifts) over about 3 hours, and c) relative shifts after adding analyte. d) a significant relative blueshift is seen for IL-6, meaning the isotype control antibody used is not an ideal match. e) Significant redshifts seen for IL-6 once analyte is added. f) Nonspecific and g) analyte-specific shifts for IL-8.

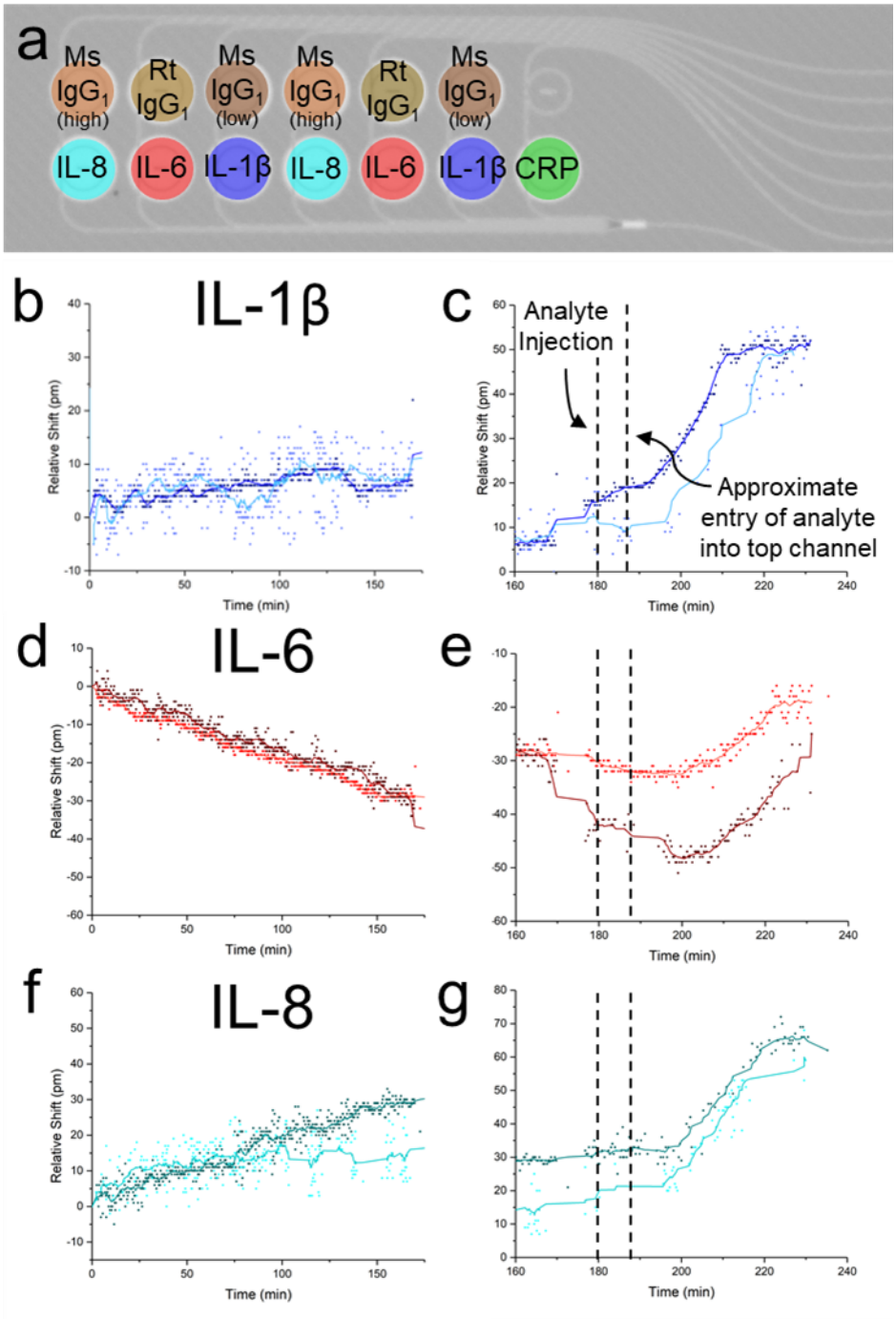

Figure S4. COMSOL Fluid Flow Model. a) Side view, b) end view, c) top view and d) oblique view of the device geometry used for COMSOL simulations. Top and bottom channels sandwich the four membranes, which have a trapezoidal trench above them, sealed with silicone and adhesive on top. The photonic chip is below the bottom channel and a sealing layer. e) Fluid flow simulation with a constant volumetric flow rate of 30 µL/min in the top channel, with the bottom channel sealed (streamlines are proportional in length to velocity). The membranes effectively isolate the bottom channel from flow, resulting in largely diffusion-mediated transport.

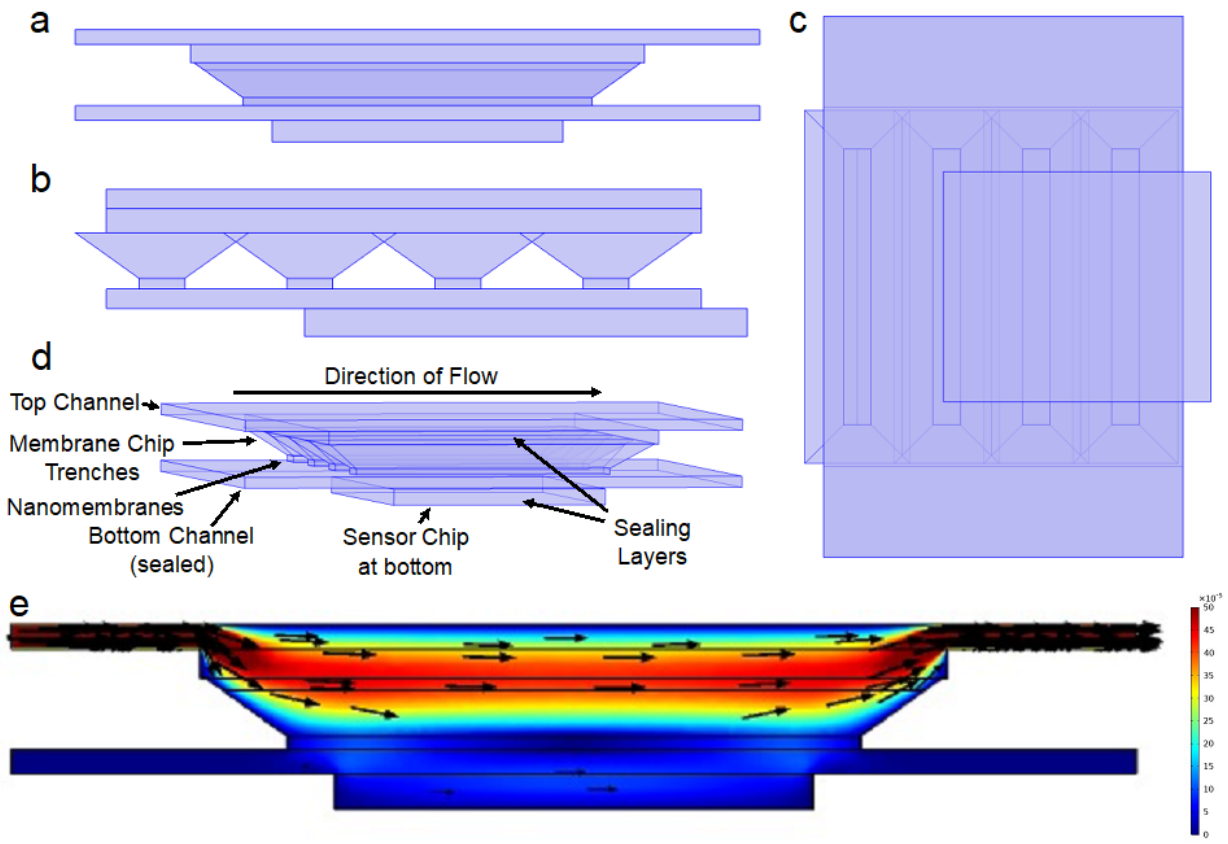

Figure S5. COMSOL Concentration Profile. Side view concentration profile at a) 10 s, b) 60 s, and c) 300 s. The left image is a side view of the device with flow in the top channel going left to right. The square on the right is a top view of the sensor surface, with rectangles corresponding with the three membranes that are situated over the chip. d) Surface average of the concentration at the level of the membrane (teal line) and sensor chip (blue) over time.

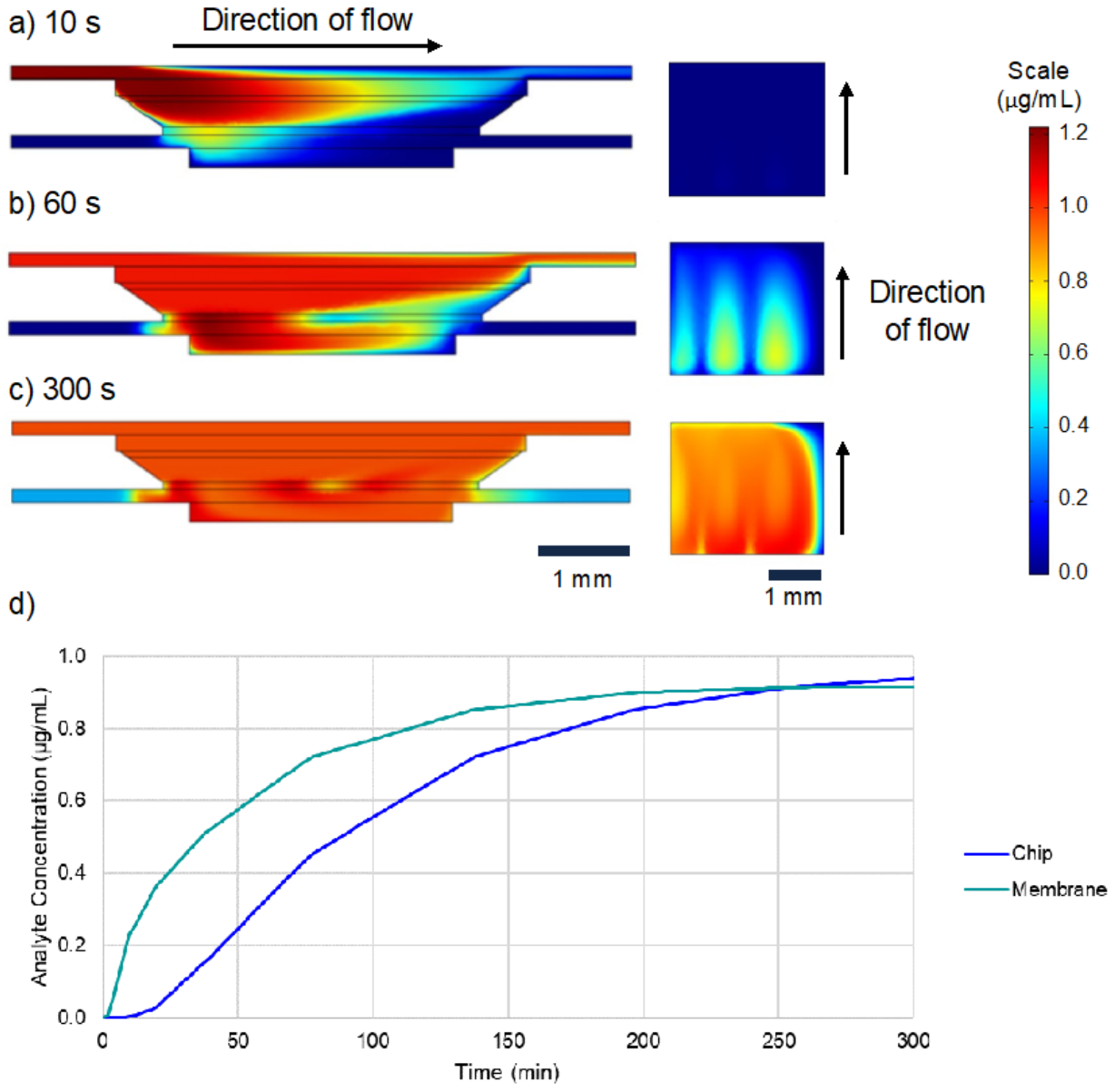

Figure S6. Concentration Profile Time Course. A gif file showing the concentration of IL-6 in the device as a function of time, up to 500 s. Here a constant source of analyte (1 µg/mL) is flowed in the top channel at 30 µL/min and the bottom channel is static to allow for diffusion to the level of the sensor surface. The scale bar is in COMSOL default units, with 5E-5 corresponding to 1 µg/mL.

[GIF file uploaded separately]

Figure S7. Partial Cell Layer LPS Stimulation Experiment. a) Diagram of the nanomembrane chip with cells removed from the two right-most membranes. b) Photonic chip functionalization schematic with alternating IL-6- and IL-1β-functionalized channels. The furthest-right edge of the source of cellular secretion approximately lines up with Channel 7. c) Subtracted traces for channels 2, 4, and 6 (IL-1B) and d) 3, 5, and 7 (IL-6) over time. e) Maximum relative shift for each channel moving left to right across the photonic chip. f) A COMSOL simulation showing the cross section of the channel showing the diffusion of IL-6 in the bottom channel after 5 minutes. g) A side view of the same simulation, showing that while analyte secreted into the top channel, which has a flow rate of 30 uL/min, is immediately swept out via the top outlet, the sealed bottom channel allows the analyte to diffuse to the level of the sensor. h) Quantification of IL-6 concentration across the width of the photonic chip at different time points. i) Concentration of IL-6 on the surface of the photonic chip, with the analyte flowing bottom-to-top in the top channel (though there is no flow directly above the chip). Panels a, b, e, f, and h are aligned vertically to show the relation between the membranes, sensors, and cytokine concentrations across the device cross-section.

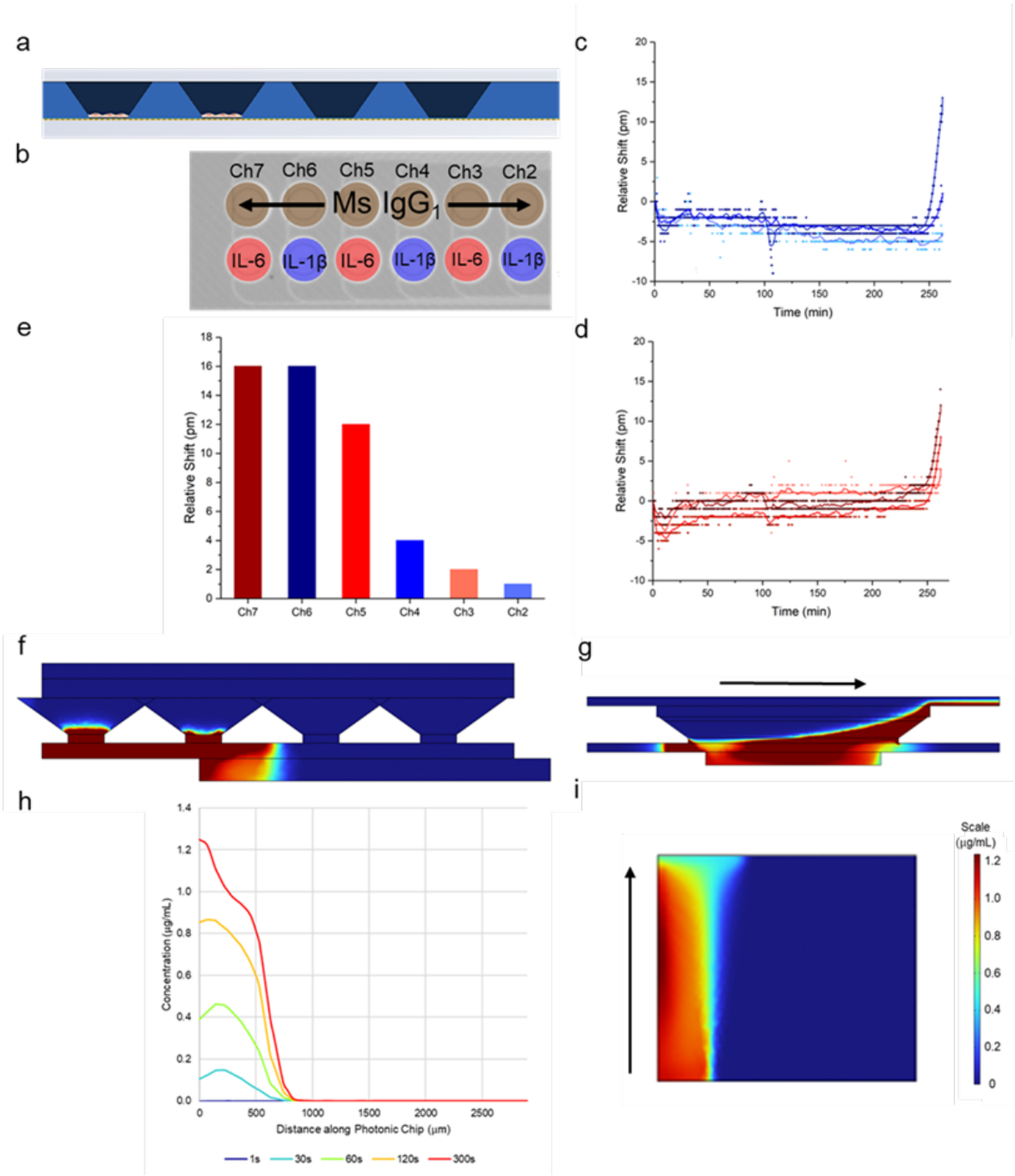

Figure S8. Partial Cell Layer Concentration Profile Time Course. A gif file showing the diffusion of IL-6 in a 2-channel microfluidic device with sources of cellular secretion (1 μg/mL) at the two left-most membranes.

[GIF file uploaded separately]

Figure S9. Antibody Stability in Incubator. a) Concentration curves for CRP in single-channel microfluidic devices, incubated at 37°C for 0, 4, and 6 days. b) Maximum shift (at 10 µg/mL) for each timepoint shows negligible effect of incubation on antibody affinity.