


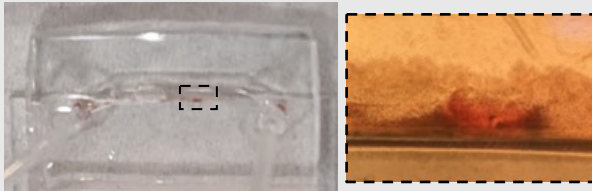

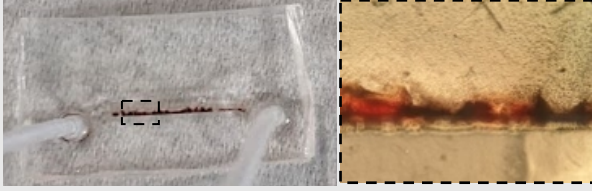
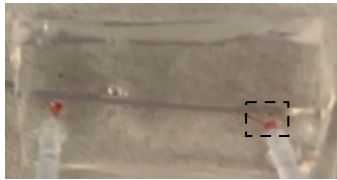
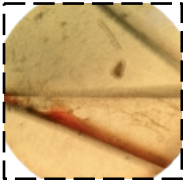
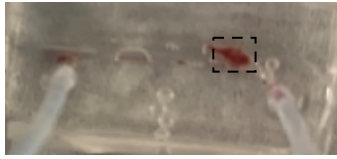
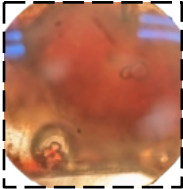
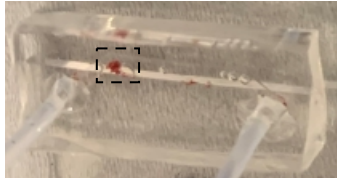

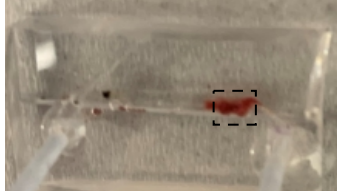
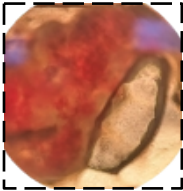

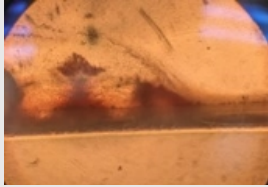

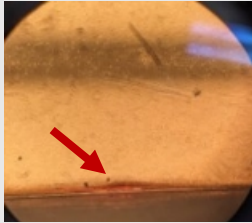


The following tables represent the complete data for the coagulation characterization experiments comparing the effect of actuation status and channel height on the coagulation of blood flow through the microchannel. In Phase 1 of the experiments, the focus is on qualitative visualization of coagulation remaining in the channel after the experiment. There, the results are presented in the form of images and qualitative characterization. In general, “minor coagulation” indicates that only small streaks of coagulated blood remained attached to the channel walls after the experiment. “Moderate coagulation” indicates that larger masses of coagulated blood remained which may partially block the channel area, but the flow of fresh blood was able to continue around it. “Total blockage” indicates that major coagulation blocked the entire cross-sectional area of the channel and the flow of blood was stalled. In Phase 2, quantitative results were obtained by measurement of inlet pressure with a high-range manometer. Therefore, results are presented as the time of perfusion of blood before a measurable pressure increase occurred, then the time at which the channel was totally blocked by coagulation, if either event occurred. “A” actuation status indicates continuous acoustic actuation. “C” indicates control (no actuation applied).

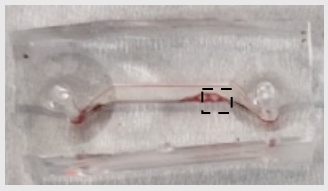
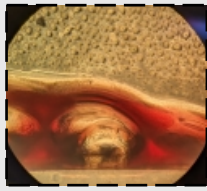
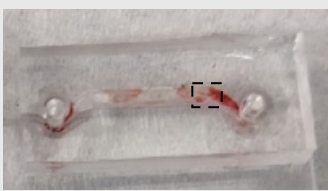
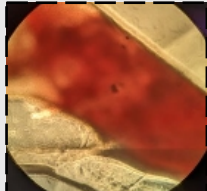
Phase 1: Visual Analysis (No pressure monitoring)

| | Sample # | Height (µm) | Actuation Status | Qualitative Result | Image (if available) |
|---------------|----------|-------------|------------------|-------------------------------|--|
| Experiment #1 | 1 | 600 | A | Minor coagulation |  |
| | 2 | 600 | C | Total blockage by coagulation |  |
| Experiment #2 | 1 | 600 | A | Minor coagulation | - |
| | 2 | 600 | C | Minor coagulation | - |
| Experiment #3 | 1 | 600 | A | No coagulation |  |
| | 2 | 600 | C | Minor coagulation |  |
| | 3 | 250 | A | No coagulation |  |
| | 4 | 250 | C | Moderate coagulation |  |

Phase 1: Visual Analysis (No pressure monitoring), Continued

| | Sample # | Height (µm) | Actuation Status | Qualitative Result | Image (if available) |
|----------------------|----------|-------------|------------------|------------------------------------|--|
| Experiment #4 | 1 | 600 | A | Minor coagulation |   |
| | 2 | 600 | C | Moderate coagulation (no blockage) |   |
| | 3 | 250 | A | Moderate coagulation |   |
| | 4 | 250 | C | Total blockage by coagulation |   |
| Experiment #5 | 1 | 600 | A | Moderate coagulation |  |
| | 2 | 600 | C | Moderate coagulation |  |
| | 3 | 250 | A | Minor coagulation |  |
| | 4 | 250 | C | Minor coagulation |  |

Phase 2: Pressure Monitoring by Manometer

| | Sample # | Height (µm) | Actuation Status | Time of first pressure increase (min) | Time of total blockage (min) | Image (if available) |
|----------------|----------|-------------|------------------|---------------------------------------|------------------------------|---|
| Experiment #6 | 1 | 600 | A | No pressure increase | No blockage |   |
| | 2 | 250 | C | 43 | 49 |   |
| Experiment #7 | 1 | 250 | A | No pressure increase | No blockage | - |
| | 2 | 250 | C | No pressure increase | No blockage | - |
| Experiment #8 | 1 | 600 | A | No pressure increase | No blockage | - |
| | 2 | 600 | C | 32 | 37 | - |
| | 3 | 250 | A | No pressure increase | No blockage | - |
| | 4 | 250 | C | 1 | 5 | - |
| Experiment #9 | 1 | 600 | A | No pressure increase | No blockage | - |
| | 2 | 250 | A | No pressure increase | No blockage | - |
| Experiment #10 | 3 | 250 | A | No pressure increase | No blockage | - |
| | 4 | 250 | C | No pressure increase | No blockage | - |

Phase 2: Pressure Monitoring by Manometer, Continued

| | Sample # | Height (µm) | Actuation Status | Time of first pressure increase (min) | Time of total blockage (min) | Image (if available) |
|-----------------------|-----------------|--------------------|-------------------------|--|-------------------------------------|-----------------------------|
| Experiment #11 | 1 | 250 | A | 27 | 32 | - |
| | 2 | 250 | C | 14 | 31 | - |
| Experiment #12 | 1 | 600 | A | 12 | No blockage | - |
| | 2 | 250 | A | 4 | 17 | - |

Supplementary 2: The following are calculations made to estimate the CO₂ release performance of the gas exchange device based on the measured values related to oxygenation. We start with the established model for membrane gas exchange for a microchannel [1,2] which can predict the output partial pressure of gas in the blood flow based on inlet conditions and channel geometry. The relevant equations are as follows (note that the equation is symmetric with regard to gas exchange into or out of the microchannel):

$$P_{g,out} = P_{g,in} + \frac{Q}{S_A} \left(\frac{P_{g,gas} - P_{g,in}}{R_{g,tot}} \right) \quad (1)$$

where $P_{g,out}$ is the partial pressure of a gas, g (O₂ or CO₂) in the blood at the outlet of the channel, $P_{g,gas}$ is the partial pressure of g in the gas supply channel, $P_{g,in}$ is the partial pressure of g in the blood at the channel inlet, S_A is the surface area for gas exchange, Q is the flow rate of blood, $S_{B,g}$ is the solubility of g in blood, and $R_{g,tot}$ is the total resistance to gas exchange calculated by:

$$R_{g,tot} = \frac{e_m}{P_{m,g}} + \frac{1}{S_{B,g} D_{B,g}} \quad (2)$$

where e_m is the thickness of the gas exchange membrane, $P_{m,g}$ is the permeability of the membrane to g , H is the microchannel height, and $D_{B,g}$ is the diffusivity of g in blood. Relevant values are presented in the following table.

| Parameter | Value | Unit | Comment |
|--------------------------|---------|---|--|
| $P_{O_2,out}$ (control) | 48.8 | mmHg | Measured value for best performing configuration |
| $P_{O_2,out}$ (actuated) | 67 | mmHg | Measured value for best performing configuration |
| $P_{O_2,gas}$ | 760 | mmHg | Assuming supply of pure oxygen at atmospheric pressure |
| $P_{CO_2,gas}$ | 0 | mmHg | Assuming supply of pure oxygen at atmospheric pressure |
| $P_{O_2,in}$ | 40.3 | mmHg | Measured from venous draw before channel flow |
| $P_{CO_2,in}$ | 43 | mmHg | Representative, found in [3] |
| S_A | 0.198 | cm ² | Calculated according to geometry in Figure 3 (b) |
| Q | 0.05 | ml/min | For best performing configuration |
| S_{B,O_2} | 7.9e-4 | mlO ₂ mlB ⁻¹ mmHg ⁻¹ | [1] |
| S_{B,CO_2} | 5.05e-3 | mlCO ₂ mlB ⁻¹ mmHg ⁻¹ | [2] |
| e_m | 20 | μm | |
| P_{m,O_2} | 3.6e-7 | mlO ₂ cm ⁻¹ min ⁻¹ mmHg ⁻¹ | [1] |
| P_{m,CO_2} | 1.95e-6 | mlCO ₂ cm ⁻¹ min ⁻¹ mmHg ⁻¹ | [1] |
| H | 600 | μm | For best performing configuration |
| D_{B,O_2} | 1.4e-6 | cm ² s ⁻¹ | [1] |
| D_{B,CO_2} | 3.05e-6 | cm ² s ⁻¹ | [2] |

We first note that for the geometric parameters of the microchannels used in this study, the relative contribution to gas exchange resistance due to mass transfer through the membrane (left-hand term) is three to four orders of magnitude smaller than the contribution due to solution-diffusion of the gas through the blood volume (right-hand term), and is this therefore negligible in this calculation (5.56×10^3 vs 2.71×10^7 cm² min mmHg mlO₂⁻¹ for oxygen, for example). Then with only the right-hand term of the equation remaining, resistance to gas exchange will be linearly inversely proportional to the changing effective diffusivity of that gas in the blood volume. The key assumption we will make is that the relative change to the diffusivity value due to active mixing by membrane microstreaming is similar for both O₂ and CO₂, then the relative change to gas exchange resistance will also be similar.

Using that value for resistance to oxygen exchange, given the measured $P_{O_2,in}$ of 40.3 mmHg, the theoretical prediction for $P_{O_2,out}$ for channel flow with no acoustic actuation by Equation 1 is 48.2 mmHg. This is very close to the measured value of 48.8 mmHg, lending credibility to the equation and experiment. Then, calculating the effective $R_{O_2,tot}$ by the measured partial pressure for channel flow with and without actuation, the values are 2.53×10^7 and 7.76×10^6 cm² min mmHg mlO₂⁻¹, respectively, indicating the effective diffusivity was increased by a factor of 3.2.

Finally, we use Equations 1 and 2 again to predict the CO₂ release for the case of no actuation, then multiply the calculated effective diffusivity of CO₂ in blood by 3.2 and make the calculation again to estimate the actuated case. With a representative $P_{CO_2,in}$ of 43 mmHg, the equations predict ΔP_{CO_2} of 1.03 mmHg for the non-actuated and 3.18 mmHg for the actuated case.

At this point, we may also calculate the total rate of oxygen exchange scaled by gas transfer area, $\Delta V_{O_2}/\Delta t$, by the relationship in [1]:

$$\Delta V_{O_2}/\Delta t = S_A (P_{O_2,out} - P_{O_2,in}) \quad (3)$$

Where $S_{O_2,out}$ is the oxygen saturation of blood at the channel inlet, and $S_{O_2,in}$ is that at the inlet (93% and 68%, respectively for the best performing configuration). The calculated value is 40 ml/min/m².