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Electronic Supplementary Information

Lung Assist Device: Development of Microfluidic Oxygenators for Preterm Infants with Respiratory Failure

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Supplementary Figures

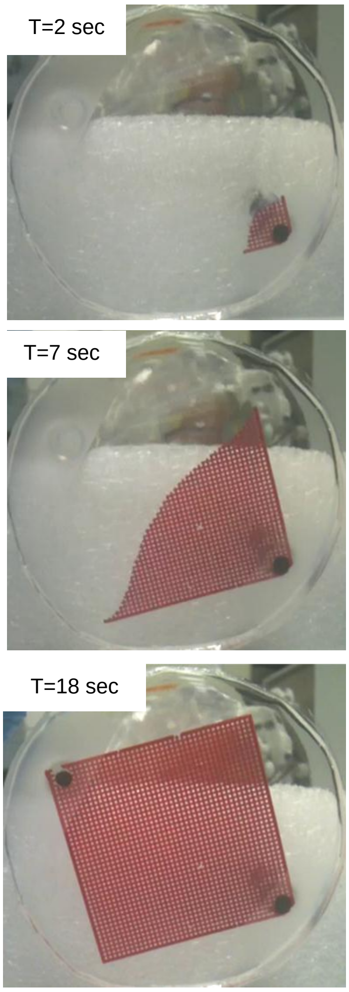

Figure S1. Smooth distribution of blood during the priming. Blood was infused at a flow rate of 1 mL/min from the inlet located at the bottom right corner, distributed along the vascular network across the membrane, and then exited from the outlet located at the up left corner.

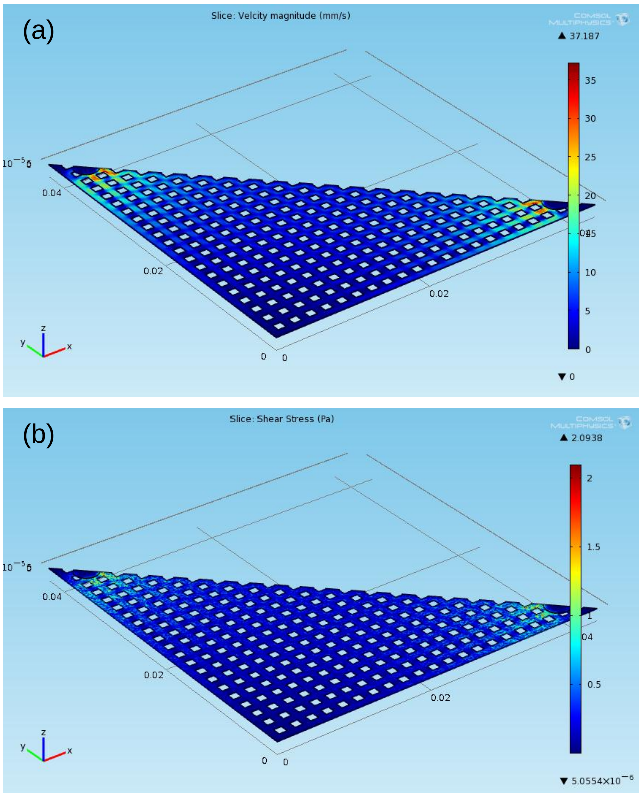

Figure S2. Numerical results of a 3D symmetry non-Newtonian model given by Equation 3. (a) the velocity distribution and (b) the shear stress distribution at blood flow of 1mL/min.

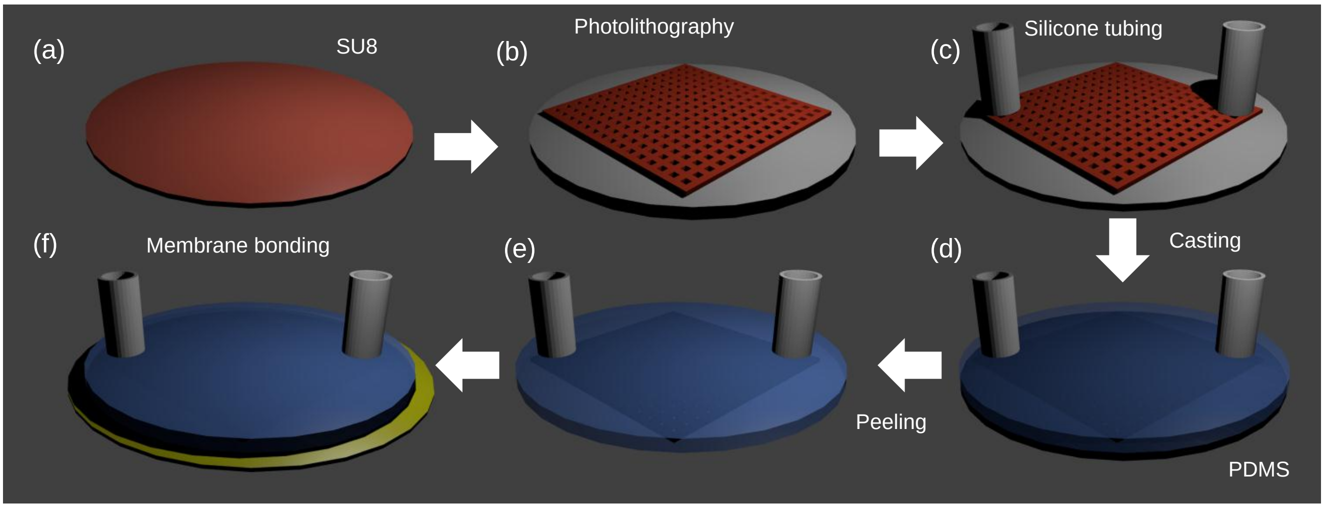

Figure S3. Process flow of microfluidic oxygenator

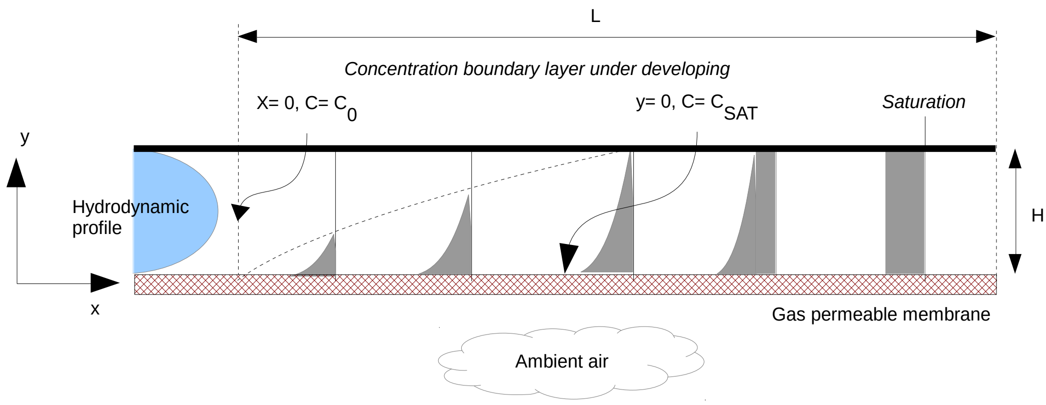

Figure S4. The oxygen gas transfer model for a straight microfluidic channel with a gas permeable membrane.

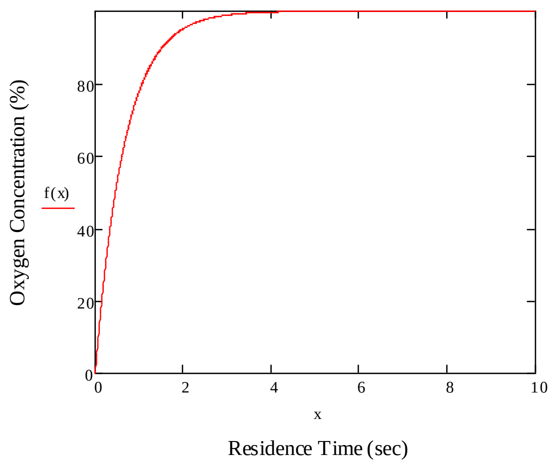

Figure S5 Theoretical estimation for the percentage of oxygenation versus the residence time through the microchannel given by Equation S6.

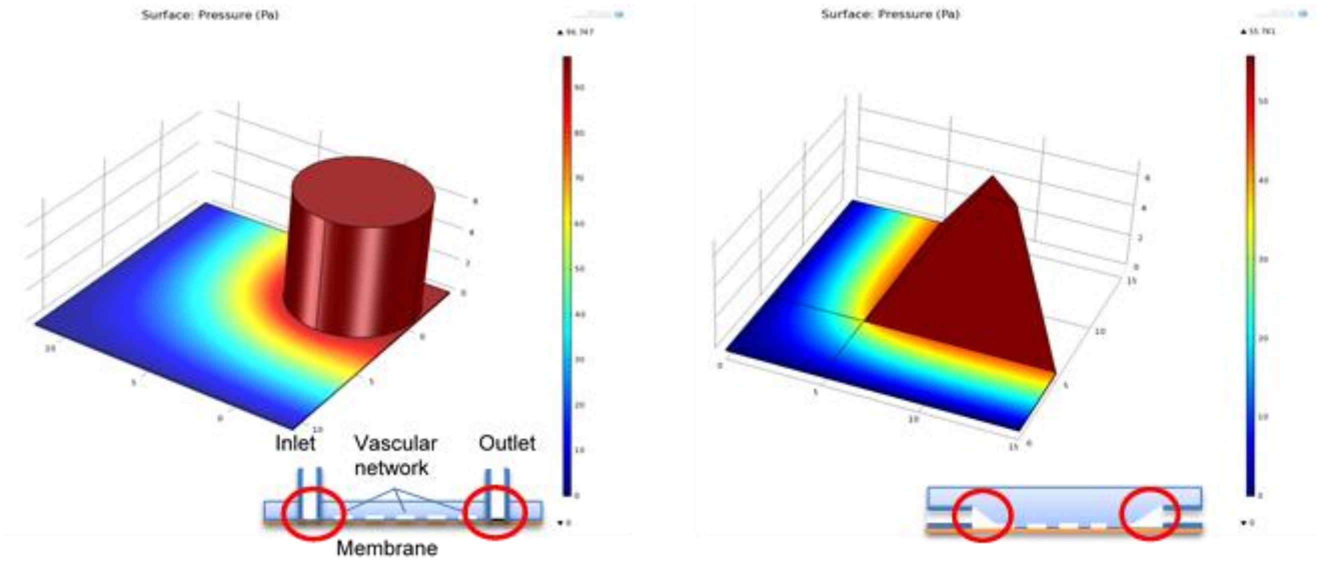

Figure S6. (a) Initial design of interconnection with vertical inlet and outlet and its local hydraulic resistance at the inlet region; (b) modified design of interconnection with horizontal inlet and outlet and its local hydraulic resistance at the inlet region

1. Gas exchange in blood

1.1 Equation for calculating the carbon dioxide content in blood

$$ctCO_2\ (B) = 9.286 \times 10^{-3} \times pCO_2 \times ctHb \times \left(1 + 10^{\boldsymbol{pH_{ery}} - pK_{ery}}\right) + ctCO_2\ (\boldsymbol{P}) \times \left(1 - \frac{ctHb}{21.0}\right)$$

$$pH_{ery} = 7.19 + 0.77 \times (pH - 7.40) + 0.035 \times (1 - sO_2)$$

$$pK_{ery} = 6.125 - \log\left(1 + 10^{\boldsymbol{pH_{ery}} - 7.84 - 0.06 \times sO_2}\right)$$

$$ctCO_2\ (P) = 0.23 \times pCO_2 + cHCO_3\ (\boldsymbol{P})$$

$$cHCO_3\ (P) = 0.23 \times pCO_2 \times 10^{pH - \boldsymbol{pK}\ (\boldsymbol{P})}$$

$$pK\ (P) = 6.125 - log(1 + 10^{pH - 8.7})$$

Total concentration of CO_2 in whole blood: $ctCO_2\ (B)$ [mmol CO_2/L blood]; partial pressure of CO_2: pCO_2 [kPa], total concentration of hemoglobin: *ctHb* [mmol Hb/L blood]; pH of erythrocyte (red blood cell): pH_{ery} [unitless]; pK of erythrocyte (red blood cell): pk_{ery} [unitless]; total concentration of CO_2 in plasma: $ctCO_2\ (P)$ [mmol CO_2/L blood]; concentration of bicarbonate in plasma: $cHCO_3\ (P)$ [mmol HCO_3-/L blood]; pK of plasma: *pK(P)* [unitless][1, 2].

1.2 Equation for calculating the oxygen content in blood

$$ctO_2\ (B) = 0.000031 \times pO_2 + 1.39 \times sO_2 \times ctHb_{(g)}$$

Total concentration of O_2 in whole blood: $ctO_2\ (B)$ [mL O_2/mL blood]; partial pressure of O_2: pO_2 [mmHg]; concentrational solubility coefficient for O_2 in plasma: 0.000031 [mL O_2 /mmHg/mL blood]; O_2 saturation: sO_2 [unitless]; total concentration of hemoglobin: $ctHb_{(g)}$ [g Hb/mL blood]; Huefner's constant (theoretical oxygen-carrying capacity of haemoglobin): 1.39 [mL O_2/g Hb][1-3].

2 Theoretical calculation for cardiovascular and pulmonary function as the basis for the development of the lung assist device

2.1 Cardiac output and estimation of extracorporeal bypass volume for the oxygenator device

The fraction of cardiac output volume that would flow through the oxygenator was calculated using heart rate and cardiac stroke volume. It was assumed that 10 % of cardiac output volume circulating extracorporeally would not lead to cardiovascular compromise[4]. The following assumption was made for heart rate: 150 min^{-1}, stroke volume: 2 mL · kg^{-1} (body weight)[5] and extracorporeal shunt from cardiac output: 10 %. Extracorporeal bypass volume = heart rate · stroke volume · percent extracorporeal shunt = 30 mL · kg^{-1} · min^{-1}.

2.2 Lung gas exchange

2.2.1 Ventilation volume

We estimated the gas exchange of the lung to compare it with the gas exchange achieved with the oxygenator. The ventilation volume of the lung was calculated multiplying resting tidal volume (TV) and breathing rate. The resting tidal volume which is the volume of air moved into or out of the lungs during quiet breathing was estimated to be 4 mL · kg^{-1} and the breathing rate was assumed to be 50 – 60 min^{-1}.[6] Thus, the ventilation expressed as volume per minute was estimated to be 200 – 240 mL · kg^{-1} · min^{-1}.

2.2.2 Gas exchange calculated from concentration differences in oxygen and carbon dioxide

Differences in the oxygen and carbon dioxide concentrations in inhaled and exhaled air was used to estimate the gas exchange of the lung. In the inspired air the concentration of oxygen is 21 % and carbon dioxide 0 %. In the expired air the oxygen concentration is about 17 % and carbon dioxide 4 %.[7] Using the estimated ventilation volume of the lung, the following gas exchange would be achieved:

Oxygen = ventilation volume (oxygen concentration inspiration air – oxygen concentration expiration air) = 200 to 240 mL · kg^{-1} · min^{-1} · (21 % - 17 %) = 8 to 9.6 mL · kg^{-1} · min^{-1}.

Carbon dioxide = ventilation volume (carbon dioxide concentration expiration air – carbon dioxide inspiration air) = 200 to 240 mL · kg^{-1} · min^{-1} · (4 %) = 8 to 9.6 mL · kg^{-1} · min^{-1}.

2.2.3 Oxygen transport capacity

Hemoglobin is the major carrier of oxygen in blood. We assumed a concentration of 0.16 g/mL of hemoglobin in blood[8] and binding capacity of 1.34 mL (oxygen) / g (hemoglobin)[9]. The estimated extracorporeal bypass volume was assumed to be 30 mL/kg/min. In 30 mL of blood with an oxygen saturation of 100 %, 6.4 mL of oxygen is transported (0.16 g/mL · 1.34 mL/g · 30 mL).

2.2.4 Estimated gas exchange

The lung assist device is supposed to be an arterial-venous bypass. Under respiratory failure the arterial blood is not full saturated with oxygen. It was assumed that the incoming blood into the lung assist device has 70 % oxygen saturation[10] and the output have 100 % oxygen saturation. Total transport capacity in 30 mL of blood is 6.4 mL of oxygen. The increase in the oxygen saturation in blood from 70 % to 100 % would lead to an uptake of oxygen by: 6.4 mL · kg^{-1} · min^{-1} · 30 % = 1.9 mL· kg^{-1} · min^{-1}. In conclusion, the lung assist device should facilitate gas transfer through its membranes by 1.9 mL· kg^{-1} · min^{-1}.

3. Mass Transport Model

The transport of gas molecules through the nonporous and porous PDMS membranes is described by solution-diffusion mechanism. The permeability, P, can be expressed as

$$P = \frac{J \cdot L}{A \cdot \Delta P} \tag{S1}$$

where J is the volume flow rate (mL/s), A is the membrane area exposed to gas stream (cm^2), ΔP is the pressure gradient (cmHg), L is the thickness of membrane (cm). From literature the permeability of O_2 and CO_2 is 600 Barrer and 3200 Barrer respectively for dense PDMS[11] and 1.6 Barrer and 7.5 Barrer respectively for dense PC[12]. For a 15 µm thick nonporous PDMS membrane under standard ambient temperature and pressure (SATP) condition, the mass flux of oxygen M_{PDMS_O2} is estimated as 1.028×10^{-5} g/(m^2 s). For the porous PDMS membrane, since the pores are closed and not interconnected, the effective membrane thickness can be estimated as 14.653 µm due to its porosity (2.3%), and its flux of oxygen $M_{porous\ PDMS\_O2}$ is calculated as 1.052×10^{-5} g/(m^2 s). The pores in PC membranes

used in this study are track etched through the 6 µm-thick membrane and have the pore size of 50nm and 100nm that are close to the mean free path of 72 nm under SATP. At this condition, the collisions between molecule and pore wall are dominant over molecule-molecule collisions, therefore the gas transport is via Knudsen flow. The volume flow rate J_{pore} in a single pore can be estimated as[13]

$$J_{pore} = \frac{\pi d^3}{12 P_m} \sqrt{\frac{8RT}{\pi M}} \frac{\Delta P}{L} \tag{S2}$$

where d is the pore diameter, Pm is the mean partial pressure of diffusion gas in pores, R is gas constant, T is temperature, and M is the molecular weight of gas. The mass flux through pores M_{pore} can then be expressed as

$$M_{pore} = J_{pore} \cdot \alpha \cdot \rho \tag{S3}$$

where α is the pore density which is 6x10^8 1/cm^2 and 4x10^8 1/cm^2 for membranes with 50 nm and 100 nm pore size respectively, and ρ is the density of gas. Consider that the gas transport in the etched through porous membrane happens via both the Knudsen diffusion in the pores and the conventional diffusion through the polycarbonate material, the total mass flux can be expressed as

$$M_{total} = M_{pore} \cdot \phi + M_{PC} \cdot (1-\phi) \tag{S4}$$

where Φ is the porosity which is 1.2% and 3.1% for membranes with 50 nm and 100 nm pore size respectively. Therefore, the total mass flux through the etched-through membrane is 4.111x10^{-5} g/(m^2 s) and 5.123x10^{-4} g/(m^2 s) for membranes with 50 nm and 100 nm pore size respectively.

After the gas transport through the membrane was characterized, a simple convective mass transfer model was developed to characterize the gas transfer properties in the microfluidic oxygenator. The geometry of a microchannel is shown in Figure 2. The ratio of the length of the developing region for the concentration boundary layer to the channel height is defined by the Peclet number which is a measure of the ratio of the convective to diffusive mass transport.

$$Pe = \frac{UH}{D_{O_2}} \tag{S5}$$

where U is the mean fluid velocity, D_{O2} is the oxygen diffusivity in the fluid, and H is the channel height. In our design, the Peclet number is around 1000 which suggests that the gas transfer occurs in the form of developing concentration boundary layer. This simplified model can be solved by using steady-state convective-diffusion equation and yield the following relation[14]:

$$\frac{C_{SAT} - C_M(x)}{C_{SAT} - C_0} = \exp\left(\frac{-T_{res}}{H} h_D\right) \tag{S6}$$

where C_{SAT} is the saturated concentration of oxygen in the fluid, C_0 is the initial oxygen concentration in the fluid before entering the microchannel, $C_M(x)$ is an average oxygen concentration at position x in the microchannel, T_{res} is the residence time of fluid through the microchannel, and h_D is the oxygen transfer coefficient in the fluid. After 5 sec of residence time, the fluid in the microchannel is oxygenated to nearly 100% (Figure S5).

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