Published in final edited form as:

ASAIO J. 2008 ; 54(4): 383–389. doi:10.1097/MAT.0b013e31817ed9c8.

Microchannel Technologies for Artificial Lungs: (2) Screen-filled Wide Rectangular Channels

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Abstract

Artificial lungs with blood-side channels on a 10 to 40 μm scale would be characterized, similar to the natural lungs, by tens of thousands to hundreds of millions parallel blood channels, short blood paths, low pressure drops, and low blood primes. A major challenge for developing such devices is the requirement that the multitude of channels must be uniform from channel to channel and along each channel. One possible strategy for developing microchannel artificial lungs is to fill broad rectangular channels with micro scale screens that can provide uniform support and stability. The present work explores the effectiveness of 40 μm screen-filled blood-side channels and, as a comparison, 82 μm screen-filled channels. Small concept-devices, consisting of a single 69 mm wide and 3 or 6 mm long channel, were tested using 30% hematocrit blood and oxygen or air on the gas side. The measured oxygen fluxes in the devices were in the range of 4 to 9×10^{-7} moles/(min-cm²), with the latter close to the theoretical membrane limit. The pressure drop was in the range of 1 to 6 mmHg. Extrapolating the data to a device designed to process 4 L/min suggests a required blood prime of only 35 mL.

Introduction

Artificial lungs have been used for over 50 years, mainly as part of a heart-lung machine in widespread heart-lung bypass procedures. Such support procedures are usually only an hour or two in length. These same heart-lung machines, however, also have modest use in procedures known as extracorporeal membrane oxygenation, or ECMO, for periods of days or weeks to support failing lungs and/or hearts. This latter procedure has been particularly successful as a therapy for congenital pathologies of newborns, with modest success in children and 40 to 50% success in adults. Because artificial lungs have the potential of playing key roles in the treatment of many pathologies of both acute and chronic lung failure, applications requiring usages of days, weeks, months or even years, many attempts at developing and using appropriate devices and strategies have been made. Few designs to-date, however, have proven to be effective enough to become accepted therapies. The challenge of developing devices that can be generally effective and safely used for long periods has proved daunting. Effective artificial lungs for long-term use should have no plasma leakage, low priming volume, fast gas exchange, low pressure drop for both blood and gas flows, small foreign contact surface, blood compatibility and easy set-up and maintenance.

The technology of the artificial lungs themselves has changed many times over the years. Most current artificial lungs, both commercial and experimental devices, are of the membrane type and consist of a bundle of microporous hollow fibers, with cross-flow blood external to the fibers and gas flowing within the fiber lumens.¹⁻⁵ Although the efficiency and blood compatibility of artificial lungs have drastically improved since the early years, no major changes of the technology have occurred in the last 20 years. Current devices are not adequate for many of the potential applications, such as in the treatment of acute respiratory distress syndrome, which has a high mortality, or as a bridge to transplant. The blood-side passages, in all designs to date, are 20 to 40 times the size of a red cell (on the order of 150 to 300 microns) and are unlike the natural lungs in which the blood-side passages are the same size, or smaller, than the red cells. Efficient gas transfer can only be achieved in these large blood-side passages by inducing transverse mixing that moves all of the red cells to and from the exchange surfaces, resulting, often, in long blood paths and large pressure drops. Developing microchannel blood-side passages, on the order of 10 to 40 microns, should result in efficient gas transfer, short blood-side passages, low-pressure drops, and small priming volumes. Indeed, Page *et al.*^{6,7} found that the oxygenation saturation of whole blood (hct = 30%), flowing in single circular microchannels embedded in a silicone rubber slab surrounded by air, raises from a venous saturation of 66% to an arterial saturation of 98% with a residence time of about 0.15 seconds in a 10 μm channel and about 0.75 seconds in a 25 μm channel.

Devices with small blood-side passages, however, would require anywhere from tens of thousands to hundreds of millions of parallel channels, and a major difficulty is the challenge of assuring a reasonably tight uniformity of these blood-side passages.

The present paper describes one experimental attempt at developing microchannels, namely one that consists of screen-supported blood-side wide rectangular channels that are 40 or 82 μm in height. The objective of this work is to explore the concept of developing easily fabricated devices using components that are commercially available and to examine how the effectiveness of these devices depend on such parameters as residence time, channel height and length and blood pressure. It was not our goal to develop a total device, and only basic unit prototypes were tested. Investigating the performance of such devices provides insight into potential advantages and disadvantages of devices with such small blood-side passages.

Materials and Methods

Figure 1 shows a schematic drawing of the basic unit test device. The blood enters a long venous manifold, flows transversely over the blood-gas exchange region and exits through the oxygenated manifold. The venous and oxygenated manifolds are 69 mm long, 5 mm wide and trapezoidal in depth, being 9 mm deep at one end and tapered to less than 0.5 mm deep at the other end (Figure 1B). The deep sections are at opposite ends of the device. The gas exchange region, where the blood flows transversely from the venous manifold to the oxygenated manifold, is either 3 or 6 mm long. The basic support is cut from a polycarbonate plate. A stainless steel wire screen (Dynamesh), either 40 μm (39-41 μm) or 82 μm (78-86 μm) thick, is placed on top of the polycarbonate plate with the screen pattern aligned at 45° to the plate axis. It provides support for the gas exchange membrane and induces transverse mixing of the flowing blood. The screen is securely attached to the polycarbonate plate with a self-leveling acetoxysilicone adhesive (A-564, Factor II, Inc.). The glue is applied over the entire polycarbonate surface with the exception of the gas-exchange area between the two manifolds. To further hold the membrane to the screen, however, glue is also applied to about 7 mm at each end of the gas-exchange area and in three intermediate strips (3 or 6 mm wide) across the exchange area. The gas exchange membrane is a 100 μm thick silicone rubber sheet (Specialty Silicone Products, Inc.) that is placed on top of the screen. In preliminary experiments, we discovered that uniformity of the glue thickness is critical for reproducibility and that variations

in glue thickness must be minimized. Variations in glue thickness could be as large as the dimension of the blood side passage. The entire device was placed under a metal block with a flat surface during curing of the adhesive to ensure uniformity. In order to minimize deformation of the silicone membrane due to pressure on the blood side, a relatively coarse 280 μm wire screen (McMaster Carr) was placed on the gas side of the membrane and sandwiched by a polycarbonate block with a corrugated surface. The ventilating gas, passing over this coarse wire screen, flowed in a direction transverse to the direction of the blood flow in the gas exchange region. The blood, driven by a Cole Parmer Masterflex peristaltic pump, entered one trough manifold at the deep end, crossed the exchange area, and exited the device at the deep end of the other trough manifold. The inlet blood pressure was measured at a side arm at the blood entrance and the outlet blood pressure was controlled by the position of the end of the exit tube. The gas pressure was controlled by the position of the end of the gas exit tube, which was submerged in water.

The basic test devices had a single gas exchange channel, as illustrated in Figure 1. The blood-side channel heights were set by the stainless steel screens, either 40 or 82 μm in thickness. Three of the basic test units were tested and are labeled 40-3-1, 82-3-1 and 82-6-1, in which the first number denotes the average thickness of the wire screen in μm , *i.e.*, the channel height, the second number is the length in mm of the blood-side gas exchange region, which is the nominal path-length the blood traversed from one trough manifold to the other, and the last number is the number of exchange areas in the device. A fourth test unit, with multiple blood channels, was also tested. It had a 40 μm screen and consisted of 19 exchange areas sandwiched between 10 sets of inlet and outlet trough manifolds. It is labeled 40-3.4-19. For each device, the data gathered on different days and different experimental conditions were distinguished by suffixes *xy* as in 40-3-1-*xy*. The specifications of each device are listed in Table 1. The total exchange area and liquid volume in the exchange area were calculated based on the specifications (wire diameter, mesh opening) of the wire screen provided by the supplier. A sample calculation is given in the Appendix I.

Before tests with blood, the devices were visually checked for blood-path uniformity with dyed-water tests. A desirable device is one in which the dye was observed to pass uniformly from the inlet manifold to the outlet manifold along the entire 69 mm length of the exchange area. The devices were subsequently washed with water, during which uniform dye gradients were observed as the dye was displaced with the water.

Slaughterhouse-collected bovine blood was used in all experiments. It was treated with anticoagulant heparin 15,000U/L and EDTA (0.75 g/l) and filtered with a milk hair filter. The blood was standardized to a hematocrit of between 28 and 31% with sodium bicarbonate buffer. The blood was conditioned, by recirculating it over ventilating gas of the appropriate pO_2 and pCO_2 , to a standard pH between 7.35 and 7.5 and oxygen saturation between 63 and 68%. During the recirculation, the blood was further passed through a 20 μm transfusion filter to remove any larger tissue debris that may have entered during collection at the slaughterhouse. After achieving the desired condition, the blood was pumped into the test device. The pH, CO_2 and O_2 contents of the blood entering and exiting the device were analyzed with a Ciba-Corning Model 860 blood-gas analyzer.

The base set of experiments involved the use of a 100 μm thick membrane, placing the device with the membrane side up, setting the inlet blood-side pressure to approximately 6 mmHg and ventilating with pure oxygen. In a typical experiment, the device was first primed with 0.15 M NaCl and care was taken to avoid trapping any gas bubbles in the device. Two lead crystal blocks, 471 g each, were placed onto the device to hold the silicone membrane in place and minimize bulging of the membrane. Switching the inlet liquid flow to the preconditioned blood started the experiment. Oxygen was fed into the gas passage. Typically, the gas exit

pressure was adjusted to 1-2 cm of water. Clamps were used on the large device (40-3.4-19) to prevent the silicone membrane from bulging. After each experiment, the device was cleaned by flowing saline and then water through all the channels. It was stored either filled with water or dried before the next experiment.

The objective of these studies is to determine the oxygen transfer rate in the gas exchange regions of the devices. The manifold troughs, however, were also covered by the membrane and conceivably a minor amount of oxygen transfer could take place over these locations. A special mock-trough device with one manifold (69 mm long, 4.5 mm wide, and 9 mm deep) was constructed and tested. A 100 μm membrane separated the blood in the manifold and an oxygen atmosphere.

Variations from the base set of experiments include tests with (1) an increased membrane thickness, (2) an elevated inlet blood pressure, (3) a reduced gas-side pO_2 and (4) the membrane side down.

Results

Figure 2 shows measured oxygen flux, in moles/(min·cm²), for three devices: 40-3-1, 82-3-1 and 82-6-1. Details of the experiments with the 40-3-1 device are shown in Table 2. Each data point represents an average of from 4 to 10 measurements. For clarity, the error bars are omitted on Figure 2, but standard deviations are included in Table 2. The flux decreases, as might be expected, with increased residence time. With longer residence times, more oxygen is transferred, the blood-side pO_2 rises, the pO_2 gradient and flux decrease. The higher blood-side pO_2 also reduces the hemoglobin buffering of oxygen. The figure shows consistency in flux from one 40 μm device, with a 3 mm blood path, and two 82 μm devices, one with a 3 mm blood path and the other with a 6 mm blood path. The 82-6-1 device has twice the membrane area of the other two devices and the similar fluxes imply approximately twice the rate of gas transfer. The measured blood pressure drop from inlet to outlet, shown in Table 2, was less than 6 mmHg in all experiments. Figure 3 shows the increase in % saturation of the blood as a function of residence time for the same three devices. The inlet saturation ranged from 63 to 68%. Again for clarity, the error bars are omitted and the standard deviations are included in Table 2. Due to the smaller blood volume, the residence time to achieve a given change in saturation was significantly shorter with a 40 μm blood channel than with the two 82 μm high blood channels.

Tests with the special mock-trough device at blood flow rates of 1.66 and 1.17 mL/min showed saturation changes of 1.2 and 2.0%, respectively, suggesting that the gas transfer to blood flowing in the troughs was minor, and no adjustments to test data were considered necessary.

The effect of the thickness of the silicone membrane on oxygen uptake was examined by testing device 82-3-1 under base conditions using the 100 μm thick membrane and then retesting the same device after adding a second 100 μm thick membrane on top of the first membrane to increase the total membrane thickness to 200 μm . The oxygen uptake was 0.64 ± 0.05 $\mu\text{moles/min}$ using a 100 μm membrane and 0.63 ± 0.07 $\mu\text{moles/min}$ with the double layer membrane, suggesting that little, if any, of the transport resistance is due to the membrane.

The inlet blood pressure in the base set of experiments was set at approximately 6 mmHg. Figure 4 shows that increasing the inlet blood pressure to 20 mmHg increased the oxygen flux 20 to 30 % in device 40-3-1.

The ventilating gas in the base set of experiments was 100% oxygen. The effect of gas-side pO_2 on oxygen uptake was investigated in tests with device 82-6-1. The tests were all conducted with a residence time of 1.3 seconds. Using air as the ventilating gas instead of oxygen reduced

the average flux from 4.20×10^{-7} to 1.68×10^{-7} moles/(min·cm²), a reduction by a factor of 2.5. Although the pO₂ with oxygen is almost five times that with air, the uptake rate would not be expected to be five times greater. The higher gas-side pO₂'s with pure oxygen increase the blood-side pO₂'s faster, pushing the hemoglobin saturation higher on the dissociation curve in the distal section on the blood path where transport rates would be reduced.

An unexpected observation when testing these devices is the inferior oxygen uptake rate observed when the devices were placed upside down, that is, with the gas side and membrane underneath the blood passage. (In the base set of experiments, the gas side and membrane were above the blood passage.) For example, with device 82-3-1, over the range of residence time from 0.4 to 1 s, the O₂ flux was reduced by 40-60% in the up-side-down configuration. In addition, the flux was sometimes observed to deteriorate with time in the gas side down configuration. The deterioration could be reversed, however, by turning the device upside down briefly, suggesting that blood components or debris may have settled and are trapped in pockets where the membrane bulges into open sections of the screen. Any collection of static material on the membrane would effectively increase transport resistance. With the membrane side up, the bottom of the blood passage is the smooth polycarbonate plate.

The results of a test of the multi-exchange area device, 40-3.4-19, are shown at the bottom of Table 2. The total O₂ uptake at comparable increases in saturation was about 11 times, not 19 times, that of a single channel device (compare in Table 2 40-3-1-e3 and 40-3.4-19). The flux for this multichannel device, thus, was 2.1×10^{-7} mol·min⁻¹·cm⁻² and is lower than that of the single channel devices (Figure 2). Although this test of the multichannel device had an outlet saturation of 95% and the flux is expected to decrease as the saturation increases, its performance does not show linear scale-up from the single channel devices. A photograph showing a 19 channel device during uptake is shown in Figure 5. Note the color change of the blood from the inlet troughs to the outlet troughs.

Discussion

The objective of this and associated work⁸ is to examine the advantages and disadvantages of easily fabricated devices with small blood-side passages and thereby provide guidance for developing compact, low pressure-loss artificial lungs. Such devices, however, require tens of thousands to hundreds of millions of nearly identical parallel channels. Making the channels uniform along their length and width and from channel to channel presents a major challenge. Any non-uniformity would result in preferential passage of blood through the wider channels, rendering the narrower ones less effective. The present work explores the potential of filling wide rectangular blood channels with micro screens to form interconnecting, narrow blood passages. The screens should help to provide channel height uniformity and stability. Another advantage is that the woven screens force the blood to flow with some degree of transverse mixing, reducing the blood-side resistance to oxygen transport and thereby reducing the necessary channel length and material exposure.

A disadvantage of screen-filled microchannels, however, is that they provide considerably more foreign surface exposure for the blood. Another disadvantage of using screen-filled channels is that the height of the channel will be limited by the availability and practicality of very small screens. Ten μm channels, for instance, are probably not feasible. Although 25 micron wire mesh screens are available, they are expensive, difficult to handle, wrinkle easily and less tolerant to small variations in screen thickness than the thicker screens. We found that wire mesh screens with a 40 micron thickness are easy to handle and readily available at reasonable cost.

The gas exchange efficiency of the devices tested is relatively high, as demonstrated by the data in Figures 2 and 3 and Table 2. Because of the high capacity of hemoglobin for oxygen and the non-linear shape of the oxyhemoglobin curve, the flux, averaged over the entire exchange region, is expected to vary depending on the saturation level of the blood. At low saturation levels, the flux is expected to be high and at high saturation levels, in the 90% level, the flux should be relatively low.

The volume of blood in the 82-3-1 channel is over twice that in the 40-3-1 channel and, although the uptake and fluxes of oxygen are very similar, Figure 2, the change in percent saturation, Figure 3, is, as expected, considerably better in the lower volume 40 μm channel. Smaller is better.

The transport of oxygen from the gas phase to the blood requires passage through the silicone rubber membrane and layers of blood in the transfer channel. The rate of transfer, thus, will depend on the resistance offered by the membrane and the blood. As a reference, two limiting cases may be considered: (1) the rate of transfer assuming infinite mixing on the blood side so the only resistance is that offered by the membrane, i.e., the membrane-limit case, and (2) the rate of transfer assuming no resistance from the membrane and no mixing on the blood side, i.e., the blood-phase-limit case. The former is a relatively simple linear diffusion case.

Assuming a 100 μm thick silicone rubber membrane (with a resistance of 8.0×10^7 ((mmHg/cm) cm^2)/(mmoles/min)^{*}), a gas phase $p\text{O}_2 = 700$ mmHg and a blood phase $p\text{O}_2 = 45$ mmHg, on average, the predicted rate of transport for the membrane-limit would be 8.2×10^{-7} moles/(min- cm^2). Calculating the blood-phase-limit is more complicated. Because blood hemoglobin reacts with oxygen and that reaction is expressed by the non-linear oxyhemoglobin relation, the blood phase transport is not simple diffusion. The common method for calculating convective blood-side transport in blood oxygenators is to assume that blood can be treated as a continuum⁹, which is reasonable in traditional oxygenators in which the blood-side passages are very large relative to red blood cells. It would not be reasonable in the case of devices with microchannels, however. One attempt at calculating theoretical oxygen transport in small vessels¹⁰ predicted oxygen transport in open circular vessels with diameters in the range of 20 to 40 μm . The present case is even more complicated, however, due to tortuous path the red cells would have to follow over the screens. A simple limiting case, on the other hand, that just assumes oxygen diffusion in plasma can be considered as a lower bound on blood phase transport. Assuming the diffusion resistance of oxygen in plasma to be 4.6×10^8 ((mmHg/cm) cm^2)/(mmoles/min)¹⁰, the predicted rate of transport for the plasma-limit with one-sided transfer in a 40 μm blood channel, again with a $\Delta p\text{O}_2$ of 700 - 45 mmHg, would be 3.6×10^{-7} moles/(min- cm^2). The corresponding value for the 82 μm channel would be 1.7×10^{-7} moles/(min- cm^2). With no blood-side mixing the plasma layer offers considerably more diffusion resistance to transport than does the membrane.

These estimates of the membrane-limit and plasma-limit suggest, for instance, that the plasma layer, with no blood-side mixing, offers over six times more resistance to oxygen transport in the 82 μm channel than does the membrane. It is not surprising, therefore, that within uncertainties the experiment with doubling the membrane thickness had little effect on the observed rate of oxygen transfer.

Figure 2 indicates experimental oxygen fluxes ranging from 3.8×10^{-7} to 8.9×10^{-7} moles/(min- cm^2), which are generally less than the membrane-limit but substantially greater than the plasma-limit. This suggests, as would be expected, that the screens induce blood side mixing and at the higher flow rates approach infinite mixing that would push the transport to the membrane-limit. The average flux of five tests of the 40-3-1 device, with inlet blood pressure

^{*}Source: Web site of supplier, Specialty Silicone Products

of about 6 mmHg, is 6.9×10^{-7} moles/(min·cm²). This value is about 86% of the membrane limit, but 260% greater than the plasma-limit.

Since the flux data from both the 40 and 82 μ m channels fall along the same line, the implication is that the mixing is similar in the two channels and strong enough to push the transport away from the no mixing plasma-limit. The extensive transverse mixing significantly reduces the oxygen partial pressure gradient in the blood, and the oxygen flux into the blood is no longer a strong function of the blood passage dimension.

Experiment 40-3-1-e3 in the present study shows a saturation increase from 68% to 94% and its flux of 5.8×10^{-7} moles/(min·cm²). This flux is over five times that observed by Page et al.⁶ in 25 μ m open circular channels imbedded in silicone rubber slabs. No blood-side mixing was present in their experiments and calculations (Appendix II); most of the transport resistance is on the blood side. Although oxygen was used in the gas phase of experiment 40-3-1-e3 and air was used in the gas phase of the 25 μ m circular channel by Page *et al.*⁶, the effectiveness of the transverse mixing enhancement induced by the screens in the larger 40 μ m channels is indicated by these flux observations.

The present test devices are relatively easy to fabricate, but uniformity of the exchange region is important and presents a major challenge. The results reported are for devices that are visually uniform, but quantification of uniformity is needed. Non-uniform sections along the width of the exchange region result in preferential and non-uniform paths for blood flow and non-uniform gas exchange. The effective exchange area becomes limited to the paths with high blood flow instead of the entire exchange area. The consequence is that the effective exchange area is reduced, and the true residence time is shortened. This problem is mitigated to some extent by the tortuous flow paths and mixing of the blood, due to the presence of the screens. Using higher blood-side pressure also may result in more uniform blood flow through the channels and optimize the conditions for oxygen uptake. Indeed, raising the blood-side pressure from the base case value of 6 mmHg at the entrance to 20 mmHg resulted in about a 20 to 30% increase in oxygen uptake (Figure 4). The oxygen uptake rate should not be affected by the blood side pressure unless there is a change in the channel geometry. The enhanced uptake may be a result of two factors: (1) An increase of the blood pressure could cause bulging of the elastic silicone rubber membrane outward, expanding the blood volume in the exchange region and increasing the blood flow residence time. (2) Any non-uniformity of the wire mesh and glue thickness would cause uneven channel height across the exchange volume, but high blood pressure and any outward deformation of the silicone membrane would tend to even out the non-uniformity, resulting in more uniform blood flow across the exchange region.

The importance and difficulty of producing uniform channels is further illustrated by the results of the experiments with a 19 multichannel device. Instead of the expected 19 times the uptake of the single channel devices, it had only 11 times the transfer (Table 2, compare 40-3-1-e3 and 40-3.4-19). An effective device would require uniformity not only within each exchange region, but across all of the multiple channels as well.

Another concern with such narrow blood exchange paths is the potential blockage by clots or particle agglomerates that would degrade device performance. None of the experiments showed any evidence of blood clots, largely a result of the anticoagulants used, and the devices could be thoroughly cleaned after each experiment and re-used without evidence of degradation. Sometimes, however, decline in performance was observed during an experiment. Disturbing the device, such as momentarily turning it up-side-down, returned the device to its initial transfer rates. Although the exact cause for the decline in performance is not known, one possibility is settling of RBC agglomerates or other debris in the narrow passages between

wires and restricting blood flow through them. The blockages were apparently dislodged by disturbing the device.

These experiments demonstrate that an efficient blood-gas exchange device with small blood passages can be fabricated using readily available components and a rather unsophisticated fabrication technique. Undoubtedly it can be improved with further development. The extensive mixing of blood in the exchange region reduced the blood side resistance to oxygen flow resulting in much higher gas exchange efficiency. Extrapolating from the data for device 40-3-1, a device with an exchange volume of 35 mL would be sufficient to oxygenate 4 L/min of blood from 68% to 94% saturation using pure O₂ gas. The blood channels of these devices were bounded on only one side by a membrane and gas channel; devices with gas channels on both sides can be expected to be considerably more efficient (see the estimates in reference 8). Further improvement of these devices can be attained by using other more uniform-structured material than wire mesh in the blood passage region and/or by improving the technique to secure the silicone membrane to the device so as to generate a higher degree of uniformity in the exchange regions. Additional improvement can also be attained by further reducing the height of the blood passages.

Acknowledgments

This research was supported by the National Institutes of Health Grant No. R01 HL 071928.

Appendix

Appendix I

Figure 1A. Blood volume and exchange area in screen-filled rectangular channels

The area of repeating unit of the wire screen = $(a+b)^2 \text{ mm}^2$

The area of the gas exchange area of a 3 mm path-length device = 138 mm^2

The number of repeating unit in the gas exchange area = $(138)/(a+b)^2$

For each repeating unit, gas exchange can take place in the open area and in the area where the wires are single strand (the grey patterned portion).

The total gas exchange area per repeating unit = (a^2+2ab)

Total exchange area per device with 3 mm exchange path-length = $(a^2+2ab)(138)/(a+b)^2$

Liquid Volume in Gas Exchange Area

Liquid volume per repeating unit = $a^2c + 2abc/2$, in which c is the average thickness of the screen

$$\text{Total liquid volume} = (a^2c + abc)(138)/(a+b)^2$$

Appendix II

Transport mechanisms in 25 μm open circular channels

Page *et al.*⁶ experimentally measured oxygen transport to human blood flowing in 25 μm circular channels that were imbedded in a silicone rubber sheet that was 125 μm thick. They adjusted the blood to a 30% hematocrit and show that oxygen uptake depends on residence time. Their Figure 9.5 shows that the saturation increased from 68% to about 94% with a residence time of about 0.55 seconds. Assuming the standard Hill equation for the oxyhemoglobin relation, with $p_{50} = 26.6$ mmHg and $n = 2.7$, the pO_2 's at 68% and 94% saturation are 35.2 and 73.7 mmHg, respectively. Assuming a blood flow rate of 11 $\mu\text{L/hr}$, one of the values used by the authors, the total oxygen uptake can be calculated from: $kQ\Delta p + 1.34C_{Hb}Q\Delta S$, in which k = oxygen solubility in plasma = 3.40×10^{-5} (mL O_2)/(mL_{blood} · mmHg), Q = blood flow rate = 1.83×10^{-4} mL/min, Δp = change in $pO_2 = 73.7 - 35.2 = 38.5$ mmHg, C_{Hb} = hemoglobin concentration = 10 g/dL = 0.1 g/mL, and ΔS = change in saturation = $0.94 - 0.68 = 0.26$. The oxygen uptake, thus, was 6.63×10^{-6} (mL O_2)/min = 2.96×10^{-10} moles/min. A blood flow rate of 1.83×10^{-4} mL/min = 3.05×10^{-6} mL/sec and a residence time of 0.55 seconds implies a channel length of 0.342 cm, and an oxygen flux = $(2.96 \times 10^{-10})/(\pi \cdot 0.0025 \cdot 0.342) = 1.10 \times 10^{-7}$ moles/(min·cm²). An estimate of the 'membrane-limit' for the experiment reported in Page *et al.*⁶ can be calculated using classical heat transfer solutions for a circular cylinder imbedded in the center of a flat slab¹¹. The rate of oxygen transport, assuming no resistance on the blood side and only resistance from the silicone rubber, would be $(2\pi L/(\ln(8z/\pi D)))P((pO_2)_2 - (pO_2)_1)$, in which L = the channel length = 0.342 cm, z = the half width of the silicone rubber slab = 62.5 μm , D = the channel diameter = 25 μm , P = oxygen permeability in silicone rubber used = 2.53×10^{-8} mmoles/(min·cm²·(mmHg/cm)),¹⁰ $(pO_2)_2$ = pO_2 at the outer surface of the silicone rubber = 150 mmHg, and $(pO_2)_1$ = average pO_2 in the blood = 54 mmHg. This estimate of the transport that would occur with no resistance on the blood side would be 2.82×10^{-9} moles/min with an average flux of 1.05×10^{-6} moles/(min·cm²). This latter value is almost ten times that observed, implying most of the resistance was, indeed, on the blood side.

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Figure 1.

(a) Schematic top view of device; (b) schematic side view of device; (c) photograph of components of device before assembly, c-1 = polycarbonate plate with corrugated surface, c-2 = 280 μm thick wire screen, c-3 = 100 μm silicone rubber membrane, c-4 = 40 or 82 μm thick wire screen, c-5 = polycarbonate plate with blood channels.

Figure 2.
The oxygen flux in moles/(min·cm²) as a function of residence time for devices 40-3-1 (▲), 82-3-1 (□), and 82-6-1 (■).

Figure 3.
Change in saturation as a function of residence time for devices 40-3-1 (▲), 82-3-1 (□), and 82-6-1 (■).

Figure 4.
The oxygen flux in moles/(min-cm²) as a function of residence time for device 40-3-1 with blood-side pressure at about 6 mm Hg (▲) and at about 20 mm Hg (◇).

Figure 5.
Photograph of a multichannel device during uptake experiment.

Table 1

Device Parameters

Device	Exchange path-length, mm	Wire mesh thickness, μm	# of exchange areas	Total exchange area, cm^2	Blood volume in exchange area, cm^3
82-3-1	3	82	1	1.16	0.007
82-6-1	6	82	1	2.38	0.015
40-3-1	3	40	1	1.27	0.004
40-3.4-19	3.4	40	19	37.48	0.117

Table 2
Performance and pressure profile of device 40-3-1

Device-experiment (time, min)	Residence time, s	Uptake, moles min ⁻¹ * 10 ⁷	Fractional Saturation		Pressure, mmHg	
			Inlet	Outlet	Inlet P [*]	Δ P ^{**}
40-3-1-c1 (71)	0.18	9.1±0.2	0.63±0.002	0.74±0.003	5.4	4.1
40-3-1-d1 (123)	0.18	12.2±1.3	0.64±0.02	0.82±0.02	20.1	0.7
40-3-1-d4 (64)	0.18	15.8±2	0.66±0.0	0.86±0.02	21.4	3.1
40-3-1-e1 (84)	0.18	12.7±0.6	0.64±0.01	0.81±0.01	23.8	3.6
40-3-1-e2 (113)	0.18	11.3±1	0.65±0.01	0.80±0.01	5.9	5.8
40-3-1-e3 (111)	0.52	7.4±0.3	0.68±0.0	0.94±0.01	5.9	5.8
40-3-1-e4 (85)	0.35	8.1±0.7	0.67±0.0	0.86±0.02	5.9	5.8
40-3-1-e4 (65)	0.26	10.2±0.7	0.68±0.01	0.87±0.01	19.0	2.6
40-3-1-e5 (65)	0.26	7.6±1.9	0.68±0.003	0.82±0.03	7.3	2.5
40-3-4-19 (118)	1.47	80±5	0.65±0.0	0.95±0.02	--	--

* P is pressure above atmospheric
** Δ P is the difference in inlet and outlet pressure