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Evaluation model of an extracorporeal gas exchange device made of silicone rubber

T. Rieper[1], B. Wehrstein[2], A. N. Maurer[2], C. Mueller[1], H. Reinecke[1]
[1]Laboratory for Process Technology, Department of Microsystems Engineering - IMTEK, University of Freiburg, Germany, tina.rieper@imtek.uni-freiburg.de
[2]Novalung GmbH, Heilbronn, Germany

Abstract

We present an evaluation model of an extracorporeal gas exchange device whose principle bases on diffusive gas exchange through a membrane. To generate a homogeneous liquid flow along the gas exchange membrane micro channels covered by silicone rubber membranes were realized. Therefore a fabrication chain which generates reliable and leakage-free bonds and enables the integration of inlet and outlet structures was developed. The gas exchange capability of the evaluation model depending on the membrane thickness and on the blood flow rate was tested with heparinized bovine blood. Thereby the applicability of the evaluation models for gas exchange tasks was proven. For a mean membrane thickness of 151 µm an oxygen enhancement of 21.6 ml_{O2}/l_{blood} and a carbon dioxide reduction from 90.6 mmHg to 49.4 mmHg were achieved with a blood flow rate of 2.4 ml/min.

1 Introduction

The functional principle of membrane oxygenators is based on diffusive gas exchange between a liquid and a gas compartment. Here, the blood flowing through the liquid compartment is rich of carbon dioxide and poor in oxygen. On the other side, ventilating gas with a high oxygen partial pressure streams through the gas compartment. A gas exchange membrane serves as separation between the compartments. Due to the concentration gradients carbon dioxide diffuses out of the blood and oxygen diffuses into it. Therefore the blood leaving the gas exchange device is enriched with oxygen while carbon dioxide is depleted. Such devices facilitate thus the support of insufficient lungs. In general, the gas exchange efficiency of state-of-the-art extracorporeal gas exchange devices is often limited by their non-uniform liquid flow along the gas/liquid interface [1]. Most of these devices consist of bundles or mats of hollow fibres, which can serve as both, gas or liquid compartment. The aim of this work is to overcome the limitation of the gas exchange due to inhomogeneous flow by a guided, homogeneous flow along the gas/liquid interface.

As a result of this materials are considered which allow new structuring possibilities and hence a new freedom of geometries. New structuring possibilities would facilitate novel setup concepts, which might be less sensitive to its positioning, paving the way to practical and feasible paracorporeal devices. Additionally less rigid materials would make such systems more ergonomic and thus more comfortable.

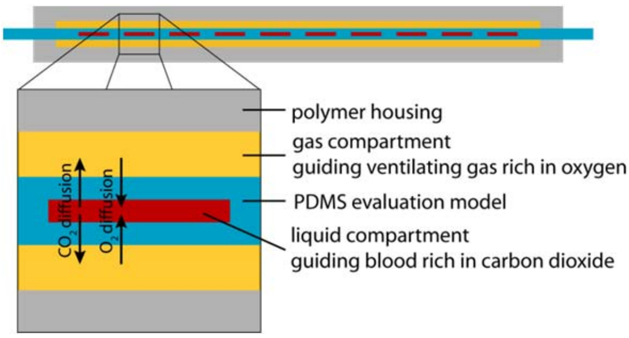

Image 1: Schematic of the cross section through the evaluation models mounted in the housing for the experimental setup.

2 Methods

The evaluation model presented in this work is made completely out of silicone rubber (PDMS). This is due to its high gas permittivity and the simple possibility of structuring PDMS by casting a tool. Moreover biocompatible forms of PDMS exist. PDMS is already established in medical engineering and medical science. The gas compartment is not realized within the evaluation model than rather formed by the housing (see Image 1). On the one hand the evaluation model is designed to proof the concept's applicability for the medical lung support and on the other hand to survey the dimensioning the evaluation model is based on. For this purpose the evaluation model does not necessarily have to meet the volume throughput required for a lung support application.

The evaluation model overcomes the above mentioned limitation of gas exchange efficiency by a homogeneous blood flow in parallel micro channels, covered by gas exchange membranes on both sides.

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The micro channels are dimensioned to combine low gas diffusion length and a low pressure drop within the blood. Thereby the concept of the evaluation model could be used for pumpless applications. Besides the buried PDMS channels guiding the blood, integrated in- and outlet structures were developed, which allow a simple connection with the macro environment (e.g. pump hoses).
To realize the buried channels two silicone sheets need to be bonded leakage-free. One of the sheets consists of a structured PDMS membrane that serves as the gas exchange membrane and contains the micro channel structures. The second sheet is a gas exchange membrane. In order to generate a leakage-free and strong bond between those two sheets and integrated inlet and outlet structures a new fabrication chain was developed.

2.1 Layout

The micro channels of the evaluation model were dimensioned using a numerical simulation of the gas exchange in blood that flows in channels with rectangular cross section [2]. The simulation showed that channel cross sections of 1 mm x 0.1 mm combine reasonable diffusion lengths and fluidic resistance. A channel length of 100 mm is required to achieve the necessary amount of gas exchange. In order to increase the volume throughput and to further decrease the pressure drop over the fluidic compartment the model provides 40 parallel channels.
Due to the complexity of the mold for the structured sheets the thickness of the gas exchange membrane of the sheets was fixed to 100 µm. The membrane thickness of the unstructured sheets its varied to analyse its influence on the gas exchange. The inlet and outlet structures are supposed to distribute the liquid as homogenously as possible to every of the 40 parallel channels while inducing a low pressure drop and low shear rates in the flow. Due to the fluidic resistance of the micro channels, which is high in comparison, this can be achieved by an adapted cone structure. The wide end of this cone is attached to the 40 parallel micro channels and the narrow one is connected to commercially available silicone tubes with a diameter of 2 mm. Therefore the evaluation model can be connected to pump hoses by usual barb tube connectors.

2.2 Fabrication

A process chain for the fabrication and leakage-free bonding of structured and unstructured PDMS sheets was developed (see Image 2). This process chain enables, to some extent, the monolithic integration of commercially available silicone tubes as connection to the macro environment. The PDMS sheets are manufactured by curing silicone rubber in a mold during processing in a hot embossing machine. One mold shows the negative fluidic structures of the micro channels and of the inlet and outlet regions. Silicone tubes forming the fluidic connection through the sheet from the outside to its structured side are inserted in the mold. The addition curing PDMS (Elastosil RT601, Wacker GmbH, Germany) is mixed and stirred manually as advised by the data sheet [3], and subsequently cooled to slow down the polymerization. Afterwards the PDMS is poured into the open mold and evacuated in a desiccator to remove entrapped air bubbles. The mold is closed and put in the hot embossing chamber. There the curing is accelerated by elevated temperature while a force is applied to achieve a homogeneous membrane thickness in a controlled environment. Excessive PDMS is displaced out of the mold.
The mold for the unstructured sheets consists of two grinded brass plates. A steel handling frame is placed between the two plates to define the aimed sheet thickness. Therefore a variety of sheet thicknesses can be made using different handling frames. The processing sequence is as described above except that this time PDMS is poured on one brass plate with handling frame. For ease of demolding the evacuated PDMS is covered with a polymer foil before the mold is closed. After the curing of the sheets, they can be demolded. The structured sheet is placed structured side up on top of a handling plate with cavities for the integrated silicone tubes. Any entrapped air has to be avoided between sheet and handling plate as distortions will prevent an accurate bonding. For the bonding a 5 µm thick layer of uncured PDMS is applied selectively on top of the elevated structures of the sheet by contact printing with a PDMS coated roller. The handling frame is used to place the unstructured sheet bubble-free on top of the structured sheet. The adhesion between cured and uncured PDMS supports this process. After removal of the handling frame, the bonding is carried out in an oven process with a maximum temperature of 130°C.

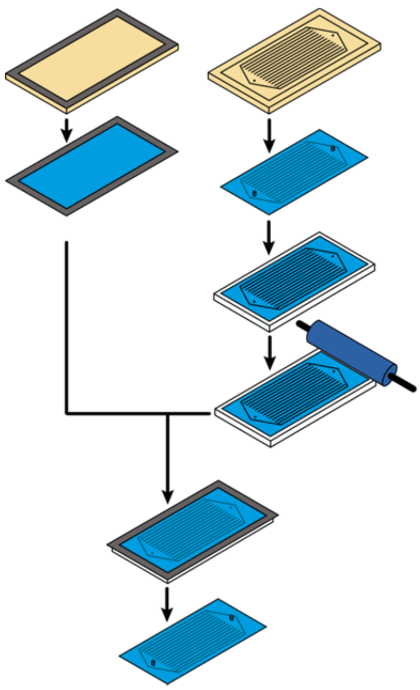

Image 2: Fabrication chain of the evaluation models.

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2.3 Gas exchange characterization

The gas exchange efficiency of the evaluation model is characterized with bovine blood as test liquid and oxygen as ventilating gas. The blood is heparinized and its parameters like oxygen partial pressure, carbon dioxide partial pressure, pH and temperature are adjusted according to ISO 7199. Afterwards the blood is pumped via a peristaltic pump through the evaluation model while oxygen streams through the gas compartment. The pump hoses are connected directly to the evaluation model via barb tube connectors. Samples of the blood are extracted at the inlet and outlet to measure the gas parameters with a blood gas analyzer (Radiometer ABL 715). The gas exchange is characterized for blood flow rates of 1.1, 2.4 and 4.8 ml/min. For the entire experimental setup see Image 3.

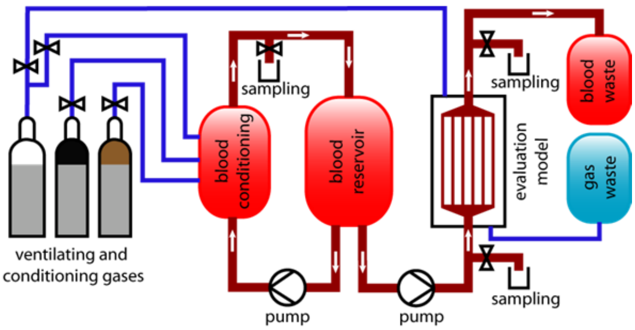

Image 3: Schematic of the experimental setup for the gas exchange characterization of the evaluation models.

The carbon dioxide depletion in this work is defined as the difference between the partial pressure measured in the in-flowing and out-flowing blood. The oxygen transfer can be calculated from the measured oxygen saturation and partial pressures.

2.4 Characterization of gas permeation

Besides the analysis of the influence of the membrane thickness within the evaluation model a further investigation on the dependency of the gas permeation through membranes on their thickness was done to come to a more general conclusion. Therefore the permeation of oxygen and carbon dioxide through PDMS membranes is measured. Here membranes with thicknesses of 50,100 and 200 µm, which are manufactured in the same way as described for the unstructured sheets, are analyzed. Two gas tight chambers are separated by such a PDMS membrane. After both chambers are evacuated, the partial pressure of either oxygen or carbon dioxide is raised in one chamber and the pressure increase in the second chamber is detected. Based on this effect and the documented pressure difference the volume flow of gas molecules through the membrane and consequently the permeability of the membrane can be calculated. The permeability is a material characteristic, which should be independent of its geometry such as the thickness. This applies for long diffusion lengths.

3 Results

Structured sheets were fabricated with a membrane thickness of 103.5 µm while unstructured sheets were fabricated with defined membrane thicknesses between 45 and 200 µm. The homogeneity of the membrane thickness is ±5 µm, independently of the absolute value. Variations in the thickness result from particles on the polymer foil leading to dents or from particles on the handling frame resulting in increased thickness values. No bonding interfaces are distinguishable in the cross sections of the evaluation models (see Image 4). The silicone tubes are integrated into the structured sheets fluidically tight. Leakage-free evaluation models were fabricated with the sheets (see Image 5).

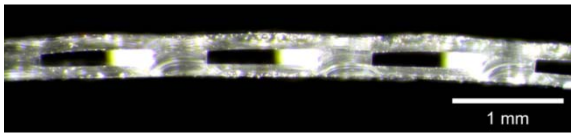

Image 4: Cross section through 4 of the 40 parallel micro channels of one evaluation model with a mean membrane thickness of approx. 100 µm.

The priming volume of the evaluation model is 1.4 ml with 1 ml resulting from the inlet and outlet. The filling of the micro channels with bovine blood shows a good homogeneity (see Image 5). The demanding wetting of the hydrophobic PDMS surface enhances the risk of trapped air bubbles and thus clogging of single channels.

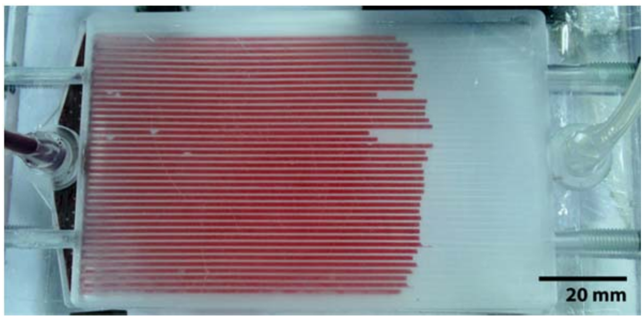

Image 5: Filling of the evaluation model with bovine blood. The evaluation model is mounted in the housing, which serves as gas compartment. The filling is homogeneous except for three channels which are partially blocked by entrapped air bubbles.

For a mean membrane thickness of 151 µm an oxygen enhancement of 21.6 ml_{O2}/l_{blood} and a carbon dioxide reduction from 90.6 mmHg to 49.4 mmHg were achieved with a blood flow rate of 2.4 ml/min. The gas exchange decreases with increasing flow rate since the contact time between liquid and gas is reduced (see Image 6).

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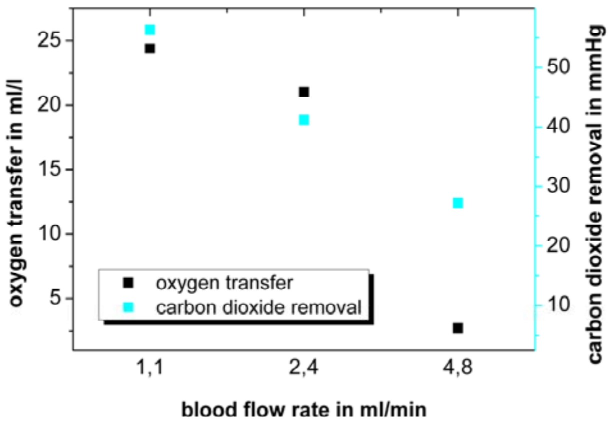

Image 6: Gas exchange of an evaluation model with a membrane thickness of 151 µm. Heparinized bovine blood served as a test liquid. The gas exchange was measured for a variation of blood flow rates.

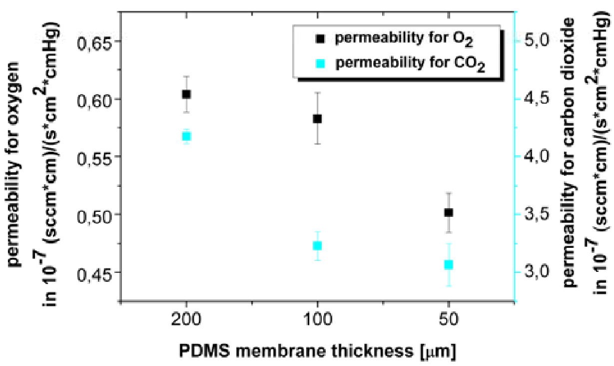

Image 7: Measured permeability for oxygen and carbon dioxide of PDMS membranes with thicknesses of 200, 100 and 50 µm.

The characterization of the gas permeation through membranes showed that the permeability of membranes decreases with lower membrane thicknesses (see Image 7). As a matter of fact there is a higher permeation of gas molecules through thinner membranes but the influence of the diffusion length and consequently the membrane thickness is limited by an increasing impact of ad- and desorption processes. Analysis of the gas exchange with the evaluation models confirmed no significant increase in the gas exchange while reducing the membrane thickness from 100 to 50 µm.

4 Conclusions

The developed fabrication chain allows for manufacturing of leakage-free fluidic structures in silicone rubber featuring buried micro channels and integrated connectors to the macro environment. This fabrication chain can be easily adapted for a manifold of applications.

The gas exchange characterization proved the applicability of the evaluation models for gas exchange tasks. Still, in order to be competitive with established extracorporeal gas exchange devices, the gas exchange capability has to be further increased. Since decreasing membrane thicknesses do not indicate a sufficient influence but rather lead to challenges in the handling and fabrication of the evaluation models and reduce its mechanical stability, other approaches for an increase of the gas exchange capability are required. This could be done for example by optimizing the channel dimensions. Thinner channels would reduce the diffusion length within the blood. On the other hand the fluidic resistance and pressure drop would be increased and furthermore the skimming effects and the shear stress within the blood flow would be amplified. More investigations on the influence of channel dimensions on the blood flow are essential. Another opportunity are longer channels, since the gas exchange area and consequently the contact time between gas and liquid flow would be increased.

The functionality of the evaluation model can be further increased by an optimization of the hemocompatibility and wetting characteristics of the used material. Investigations are ongoing. An in plane approaching flow would also increase the functionality of the evaluation model as the blood is less harmed. This optimizations are a prerequisite for the transfer of the here presented concept to in vivo applicable extracorporeal gas exchange devices.

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