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Title: Efficient gas–liquid contact using microfluidic membrane devices with staggered herringbone mixers

A microfluidic gas–liquid–contacting membrane device is presented. The device combines a membrane with a staggered herring bone static mixer, which enables increased mass transport and reduced pressure loss for application in miniaturized extracorporeal membrane oxygenation.

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Efficient gas–liquid contact using microfluidic membrane devices with staggered herringbone mixers†

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We describe a novel membrane based gas–liquid-contacting device with increased mass transport and reduced pressure loss by combining a membrane with a staggered herringbone static mixer. Herringbone structures are imposed on the microfluidic channel geometry *via* soft lithography, acting as mixers which introduce secondary flows at the membrane interface. Such flows include Dean vortices and Taylor flows generating effective mixing while improving mass transport and preventing concentration polarization in microfluidic channels. Furthermore, our static herringbone mixer membranes effectively reduce pressure losses leading to devices with enhanced transfer properties for microfluidic gas–liquid contact. We investigate the red blood cell distribution to tailor our devices towards miniaturised extracorporeal membrane oxygenation and improved comfort of patients with lung insufficiencies.

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1 Introduction

Membranes facilitate bubble-free gas–liquid contact by separating the gas side from the liquid stream using a material which is permeable to gases but impervious to liquids. The driving force behind the dissolution of gas in the liquid stream is the concentration gradient of the gas component across the membrane into the fluid. This effect leads to concentration polarisation, where the dissolved component is enriched at the membrane–liquid interface impeding efficient transfer and further dissolution of the component. Depending on the membrane application, this phenomenon leads to higher energy consumption, reduced flux and membrane fouling. Mixing of the liquid phase disturbs concentration polarisation and thus greatly promotes the dissolution of gas in the liquid at the membrane interface.

A large variety of concepts for micromixers based on specific channel layouts have been reported,^{1–4} spanning from T-junction⁵ and Y-junction⁶ to zigzag⁷ and split-and-recombine⁸ channel architectures. In contrast, static mixing is

based on the manipulation of the flow profile inside the channel and various surface structures have been reported including slanted ribs, grooves and staggered herringbone mixers (SHMs).⁹ Amongst these structures, SHMs mix fluids extremely effectively by the concurrent induction of two secondary flow vortices in the channels.^{10–12} These vortices create enhanced fluid motion at the interface between the liquid and the channel walls.¹³ Precise engineering of the geometrical parameters of both the channel architecture and the SHM maximises the contact of streamlines with the adjoining channel boundaries. Therefore, SHMs are an ideal solution for breaking the concentration polarisation layers in membrane applications. Some approaches to enhance membrane performance using Dean vortices or Taylor flows have been reported,¹⁴ and micropatterning has been used to increase the contact area and improve the separation performance in microfluidic membrane devices.^{15–22} However, SHM geometries have been neglected for membrane technology to date, as the underlying technology is not adaptable to large-scale manufacturing. In contrast, membrane technology is gaining importance in microfluidic setups with applications in point-of-care diagnostics and treatment, as well as in microfluidic portable devices such as blood sugar sensors and oxygenators. This area allows the combination of micro-fabrication with membrane technology, giving access to potentially highly efficient but small-sized membrane devices. Here, we develop a microfluidic gas–liquid-contacting chip using a flat-sheet membrane with staggered herringbone topography. The surface topography acts as a flow promoter which strongly improves gas transport across the membrane into

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the fluid stream and reduces pressure loss along the device. Furthermore, we showcase the applicability of our concept by oxygenating water as a model fluid and tracing red blood cells (RBCs) in the staggered herringbone membrane mixer device.

2 Results

We fabricate our gas–liquid contactors with polydimethylsiloxane (PDMS), which exhibits ideal properties of a membrane for gas–liquid contact as it is highly permeable to oxygen and can be micro-fabricated *via* facile soft lithography (Fig. 1a–c). The PDMS contactor chip features ten 21 mm long, 500 μm wide and 50 μm high channels connected with a single inlet and outlet for the gas and liquid sides. The manifold design on the gas side features rectangular channel boundaries (Fig. 2a), whereas the channel restrictions are rounded on the liquid side to avoid dead volume with reduced flow and increased pressure drop (Fig. 2b). The two PDMS slabs featuring the channel geometries for the gas and liquid sides are aligned and plasma-bonded while a 127 μm thick PDMS membrane (McMaster-Carr) is sandwiched. To gain access to the device, chip-to-world connections are introduced by punching holes into the respective channel inlets

Fig. 1 Principle for the fabrication of SHM contactors by soft lithography. (a) Silica wafers for gas and liquid channels are prepared by SU8 lithography. (b) A second SU8 layer creates the herringbone structures (insert). (c) Both channels are replica-molded with Sylgard 184 10 : 1 PDMS. (d) A 127 μm PDMS membrane plasma-bonded to liquid (red) and gas (blue) channels. (e) Cross-flow arrangement of the contactor device with punched connections.

Fig. 2 Top-view photographs of gas and liquid channels filled with dye. (a) Gas channel with blue dye. (b) Red-dyed liquid channel and a magnified microscopy image of herringbone indentations. (c) Reference straight channel without herringbones coloured red. (d) Assembly of herringbone liquid (red) and gas (blue) channels. The scale bars represent 10 mm and 500 μm in the magnified images.

and outlets through the liquid hemisphere of the chip (Fig. 1e and Fig. 2d). The herringbone pattern on the liquid side has a topology depth of 50 μm and a width of 125 μm .

The herringbone structures are combined in groups of six, 12×6 channel indentations in total.¹³ For comparison and benchmarking, we also prepare devices with completely

smooth channel surfaces, as shown in Fig. 2c. To characterise our microfluidic gas–liquid contactors, we perform measurements where oxygen is transferred from a compressed air gas stream through the membrane into a water stream in a cross-flow conformation. The total membrane transport area is designed to be 105 mm² for the SHM and the straight channel geometries. A deoxygenated (Systec vacuum degasser) water stream is supplied through 1/16" PEEK tubing connected to a water reservoir. The flow is provided by pressurising the reservoir with nitrogen.

The dissolved oxygen content in the water stream is determined at the liquid outlet of the contactor using a FireSting oxygen sensor from Pyro Science and recorded every second. Before each experiment, we remove all oxygen from the chip by flushing the gas channel side with nitrogen at 20 mL min^{−1}. Furthermore, to inhibit atmospheric oxygen from permeating through the PDMS device, we place our contactor in aqueous sodium sulfite solution (30 g L^{−1}) generating an efficient oxygen barrier. After flushing the device with nitrogen, we switch to compressed air (20 mL min^{−1}) and record the transferred oxygen from the gas channel into the water phase, as plotted in Fig. 3.

We calculate the Reynolds number using the equation $Re = \rho v d_h / \eta$ with v being the average liquid velocity, and ρ and η being the density and viscosity of water, respectively. For both channel architectures, the same hydraulic diameter $d_h = 4 \times A/P$ is used with A being the channel area (500 μm × 50 μm) and P being the channel perimeter (2 × 500 μm + 2 × 50 μm). Our Reynolds numbers vary between 1 and 10 to match the conditions in a blood oxygenation device. Across this Re interval, the oxygen flow range is significantly increased in the SHM device.

The results confirm that our SHM mixers improve the oxygen uptake in water. The transferred oxygen (Fig. 3) for the SHM exceeds that for the straight channel by 66%, 20% and 10% for Reynolds numbers of 10, 2.3 and 1. With decreasing Reynolds number, the difference between the SHM and the

straight channel decreases. The oxygen transport through the membrane is faster in the SHM compared with that in the straight channels, as shown by the steep increase in oxygen saturation in Fig. 3d. This reveals that the concentration boundary layer in the SHM is reduced and more oxygen can dissolve faster in the aqueous phase. In whole blood experiments, the percentage increase of oxygen transport will scale higher since blood has significantly larger tendencies for concentration polarisation compared with water.

This effect is highest at $Re = 10$ and lowest at $Re = 1$ although the residence time, represented by the ratio of the liquid channel volume to the liquid flow rate (V_{H_2O}/V_{H_2O}), is slightly higher for the SHM compared to that for the straight channels (≈ 1 s for $Re = 10$). We further validate these results by using a litmus pH indicator and CO₂ as the gas, as presented in Fig. 4a–d. The pH drop, indicated by a colour change from blue to red, results from purging pure CO₂ through the gas channel at 20 mL min^{−1} and aqueous litmus solution through the water channel at 0.15 mL min^{−1} ($Re = 1$). We present photographs of the entire contactor devices and magnifications of the most interesting regions at the liquid outlet for the SHM in Fig. 4a–b and the straight channel in Fig. 4c–d. We observe better uptake of CO₂ in the case of the SHM device, as indicated by the fact that the blue colour is completely absent at the liquid outlet of the SHM device while there is a residual blue colour at the outlet of the flat channel device, depicted by magnifications in Fig. 4b and c.

To further understand the impact of the herringbone topology on the flow characteristics inside the liquid channel, we investigate the pressure drop *via* computational fluid dynamic simulations in Comsol v4.4. Flow field visualisations are given in the ESI†. Interestingly, the pressure losses in the channels with SHMs are lower compared to those in the straight channels, plotted in Fig. 5. The simulations are performed with the previously described channel geometries, velocity inlet and pressure outlet boundary conditions, physical properties of water and up to 6.9 million for the straight

Fig. 3 Results of oxygen transfer from the gas channel through the PDMS membrane into the water channel. At $t = 0$, the gas flow is switched from nitrogen to compressed air. The resulting transferred oxygen in the water phase is sensed at the liquid outlet. Flow rates are varied to achieve Reynolds numbers of 10 (a), 2.3 (b) and 1 (c). Error bars represent the standard deviation for measurements performed in triplicate. Results for SHM liquid channel geometries are shown as dashed lines while those for straight channels are solid lines. The results of (a)–(c) are compared in (d) with $Re = 10$ in black, $Re = 2.3$ in grey and $Re = 1$ in light grey.

Fig. 4 Contact results at $Re = 1$ and (a)–(d) pH shift reactions after dissolving CO_2 in water/litmus solution, showing improved transport through SHMs in (a) which is magnified in (b) compared with the straight geometry in (d) which is magnified in (c). The litmus pH indicator changes its colour from blue to red due to the decreased pH by dissolving CO_2 through the membrane into water.

and 26.4 million mesh elements for the SHM device layout. We achieve mesh-independent results by solving with multiple meshes at pressure variances below 2.5% and Richardson extrapolation.^{23,24} To confirm the reduced pressure loss experimentally, we produce single channel devices with straight and SHM geometries and bond them to a glass substrate. The channel geometries are connected to sufficiently long straight tubes with a diameter of 1/16" aligned vertically to the channels in the device. We transform the height difference of the fluid level into the hydrostatic pressure drop. We observe a greatly reduced pressure drop in the SHM device as indicated by the computational fluid dynamic simulations. We believe that rotating fluid vortices induced by the herringbone topography cause the decreased effective friction for the liquid at the channel boundary. Whereas we have no-slip conditions in the flat channel geometry with a typical parabolic

flow profile, the rotating vortices in the SHM generate a positive slip length, which results in a straighter flow profile and a lower pressure drop. Part of the reduced pressure loss can be explained by the larger mean cross-sectional area of the SHM channel topology. This means that SHM structured channels induce higher mass transport efficiency with reduced pressure loss. From the simulated data, we determine pipe flow resistances. The coefficient for a straight tube and laminar flow is $64/Re$. The coefficient for our SHM at $65/Re$ is close to that for a straight tube, whereas the flat rectangular channels induce a 45% higher pressure drop coefficient at $93/Re$. The lowered pressure loss indicates reduced shear rates inside the liquid which can be crucial for handling biological fluids such as blood.

To illustrate the performance of our gas–liquid contacting devices, we study the red blood cell distribution across channels with SHM topology, as we envision their application as miniaturised blood oxygenators in the future. We dilute whole blood with phosphate buffer solution in a ratio of 1:100 and monitor the red blood cell distribution as a function of the position inside the channel width using a high-speed camera. The recorded high-speed movies are transformed into cell distribution data using an established Matlab code. We record the movies at the center of the chip across the entire channel width. For all Re , we observe a decreased RBC content at the channel boundaries, as shown in Fig. 6. The RBC distribution in the flat channels is nearly independent of the flow rate and the RBC count decreases to 0 towards the channel boundaries. The asymmetrical shift to the right can be explained by an outliner and blurry channel borders in the movies. For the channels with SHM topology, the RBC distribution is more uniform across the channel and the RBC count is non-zero at the channel boundaries. In our microfluidic gas–liquid membrane device, this represents improved transport and exchange of RBCs at the membrane

Fig. 5 (a) Setup of pressure loss experiments. (b) Pressure loss results from CFD simulations (lines) and experimental measurements for SHM (grey) and straight channel (black) in mbar. Error bars represent the standard deviation from measurements performed in triplicate.

Fig. 6 Distribution of red blood cells plotted over the channel width for Reynolds numbers 10 (a), 2.3 (b) and 1 (c). Cells are counted in a single channel with (full dots) and without SHM topology (empty dots). The dashed and solid lines represent a guide for the eye. High-speed movies are recorded at half of the channel length over the entire channel width and transformed into cell distribution data. The SHM channels show uniformly distributed RBCs over the entire channel width compared with the flat topology.

and hence better oxygenation of blood in a miniaturized blood oxygenator.

3 Conclusions

In summary, we have applied the static mixing principle using herringbone structures to a novel gas–liquid-contacting device. We obtain increased mass transport of oxygen through the membrane compared to that in a flat liquid channel. Furthermore, we find a decreased pressure loss in liquid channels with herringbone structures *versus* straight channel geometries. Despite the higher liquid channel surface area, the pressure loss decreases because of reduced friction at the channel boundaries. For fluids with RBC, we find improved transport at the channel boundaries. These results will foster the development of superior gas–liquid contactors and miniaturized portable oxygenation devices.

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