GAS-PERMEABLE POLYDIMETHYLSILOXANE-ON-SILICON MEMBRANES FOR EXTRACORPOREAL MEMBRANE OXYGENATION

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ABSTRACT

We have developed a simple, low-cost, and robust PDMS (polydimethylsiloxane)-on-silicon micromachined gas-exchange membrane that can form the basis of compact extracorporeal membrane oxygenation (ECMO) treatment for respiratory distress. We investigated two fabrication approaches, one of which involves a porous silicon support formed by traditional double-sided deep reactive ion etch (DRIE), while the other features a surface-micromachined "cavern" design with isotropically etched inter-connected buried cavities that serve as gas-flow channels. *In vitro* and *in vivo* testing has confirmed the functionality of both designs.

BACKGROUND

The COVID-19 pandemic highlighted the need for various respiratory-assistive devices such as mechanical ventilators and extracorporeal membrane oxygenation (ECMO) devices. Mechanical ventilators work by forcing air at high pressure into the patient's impaired lungs, but extended use can cause ventilator-induced lung injury (VILI). In contrast, ECMO bypasses the lungs altogether to transfer oxygen directly into the bloodstream, but its drawbacks include large size and operational complexity requiring high staff-to-patient ratios. Furthermore, the standard hollow-fiber membranes used in present-day ECMO devices require the use of anticoagulants (raising the risk of bleeding) and blood pumps (causing blood cell lysis) [1]. In recent years, various micro-machining approaches have been explored to address these issues [2, 3]. In particular, our group has demonstrated the use of a thin, gas-permeable PDMS layer on top of a porous silicon chip to facilitate efficient oxygen and CO_2 exchange between blood and air [4]. Such a microfluidics-based architecture (Fig. 1) aims to promote laminar blood flow and low pressure drop, potentially eliminating the need for anticoagulants and blood pumps.

DESIGN AND FABRICATION

In our earlier ECMO work, we bonded a 5µm-thick PDMS layer to a 1µm-thick polysilicon membrane that had 0.5µm pores and spacings [4]. Since this pore density was originally designed for liquid-to-*liquid* membrane filtration, we set out to develop an optimized membrane design for a liquid-*gas* interface. Using computational fluid dynamics (CFD) analysis, we determined that due to the high (lateral) diffusivity of gas molecules in PDMS, the silicon "membrane" could in fact have pores and spacings as large as 10µm and thicknesses of 50-100µm (10^5-10^6 times stiffer than before) without significantly affecting performance (Fig. 2).

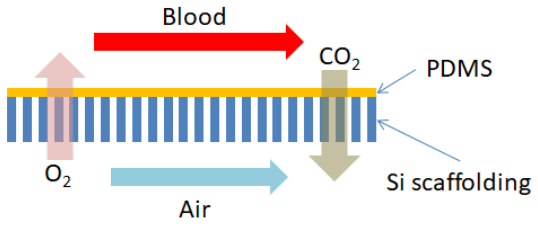

Figure 1: Basic concept of a micromachined ECMO chip with a PDMS membrane bonded to a silicon support chip. Oxygen diffuses from the air through the PDMS into the blood while CO_2 diffuses the other way, emulating the action of the lungs.

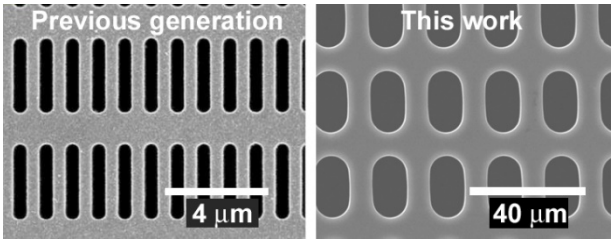

Figure 2: Two generations of our ECMO silicon scaffolding. Note order-of-magnitude difference in scale bars. The new design (right) can have greater pore spacing due to the high diffusivity of gas within the PDMS layer above the scaffolding. It also has a 50-100x thicker membrane for superior strength. These samples were imaged without PDMS to show the pores more clearly.

Consequently, we designed and fabricated a coarser silicon "scaffolding" with 10µm pores and spaces in a 50-100 µm-thick membrane on a 400-µm thick chip. We tried two different fabrication approaches for the silicon structure: Design A is a traditional double-sided process (Fig. 3a) in which we etched 10µm-wide pores in the top surface of the wafer and hollowed out the back side using DRIE, while Design B is a single-sided "cavern" design (Fig. 3b) where 50-100µm deep pores are etched into a monolithic wafer and lined with thermal oxide, the bottom of the pores are stripped of oxide, and an isotropic SF_6 etch is used to "carve out" an interconnected 2D array of gas-conducting cavities (Figs. 4a-e).

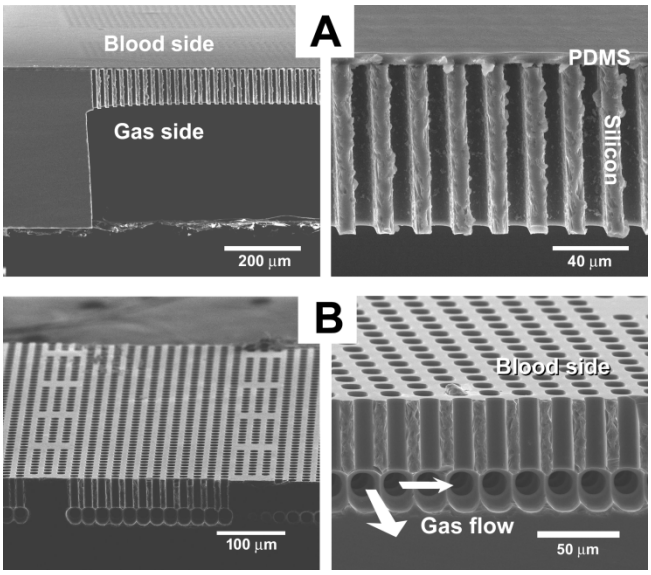

Figure 3: Scanning electron micrograph (SEM) cross-sections: (Design A) Double-side-DRIE chip with PDMS layer on top of silicon scaffolding. (Pores are faintly visible under the PDMS.) Right-hand figure shows close-up of PDMS layer; (Design B) Single-side-DRIE "cavern" chip (pre-PDMS) formed by isotropic SF_6 undercutting of oxide-lined holes. Right-hand figure shows close-up of connecting "caverns" that serve as 2D gas channels.

978-1-940470-04-7/HH2022/$25©2022TRF
DOI 10.31438/trf.hh2022.65

Solid-State Sensors, Actuators, and Microsystems Workshop
Hilton Head Island, South Carolina, June 5-9, 2022

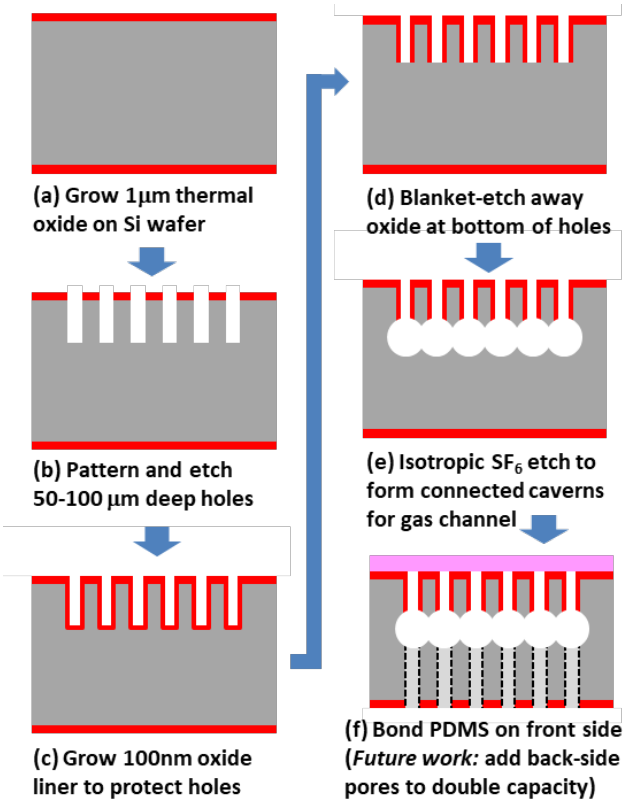

Figure 4: Process flow for the Design-B "cavern" ECMO chip.

An additional benefit of the "cavern" design, which was inspired by prior work on sub-surface isotropic reactive ion etching [5-7], is that access holes could be etched from *both* sides of the wafer into the central cavity, enabling double-sided functionality and a more efficient configuration for gas exchange (Fig. 4f).

DEVICE TESTING

ECMO chips from both designs were tested *in vitro* and *in vivo* for gas-exchange efficiency between air and liquid (Figs. 5-6). The Design-A "traditional" membranes had an *in vitro* gas-transfer flux of 0.013 mL/min and 0.024 mL/min at 2.5 and 10 psi respectively. The membranes were also tested in an extracorporeal pig model. They were able to be pressurized up to 25 psi of sweep gas without rupture or gas embolization, with a flux of 0.035 mL/min.

The Design-B "cavern" chip was tested *in vitro* and showed an oxygen flux of 0.010 mL/min at 2.5 psi of sweep gas pressure and 0.015 mL/min at 10 psi, somewhat lower than Design A due to the narrower internal gas channel. Overall, both designs performed robustly during assembly and testing in our laboratory setup, a promising step in the scale-up toward clinical-level devices [4, 8].

FUTURE APPLICATIONS

In addition to life-sustaining treatment for severe respiratory distress associated with COVID-19, our PDMS-on-silicon ECMO platform could potentially be used in portable lungs for chronic obstructive pulmonary disease (COPD) and patients awaiting lung transplant. It could also conceivably be used as an "artificial placenta" to treat extreme preterm babies (gestation age between 23-28 weeks), which is a category of patients that cannot get standard ECMO due to the risk of intracranial hemorrhage associated with anticoagulation [8].

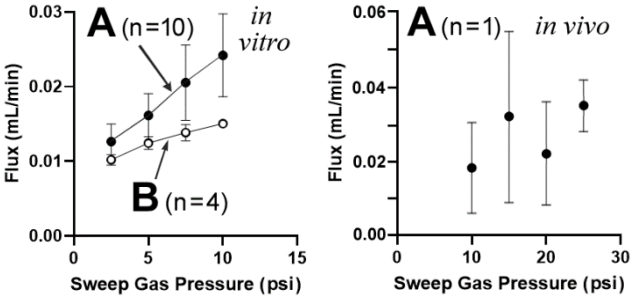

Figure 5: Measured gas flux through PDMS membrane from air to liquid for: Design-A chip in vitro *(left, solid dots) and* in vivo *(right); Design-B "cavern" chip* in vitro *(left, hollow circles). Chip size in both cases was 10×65mm (active membrane area 240mm^2).*

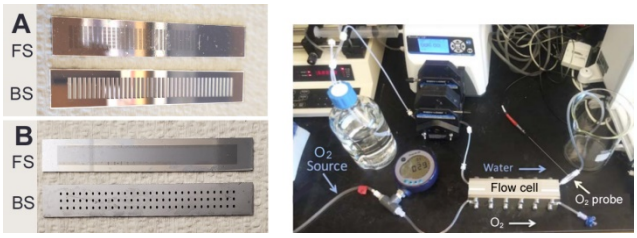

Figure 6: (Left) PDMS-coated ECMO chips from Designs A and B. FS=front side, BS=back side; (Right) Test bench showing a flow cell containing an ECMO chip, with water and oxygen flowing on either side, for measuring gas flux across the PDMS membrane.

This work was funded in part by NIH grant U01EB025136 and a Catalyzing Pediatric Innovation grant from the West Coast Consortium for Technology and Innovation in Pediatrics (CTIP). Wafer fabrication was performed at the Berkeley Marvell Nanolab, Stanford Nanofabrication Facility (SNF), Stanford Nano Shared Facilities (SNSF), and Rogue Valley Microdevices, Oregon, USA. The authors may be contacted through benjamin.chui@ucsf.edu.

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