

ICNMM2016-8052

Ultrathin Silicon Membranes
for Improving Extracorporeal
Blood Therapies

Tucker Burgin

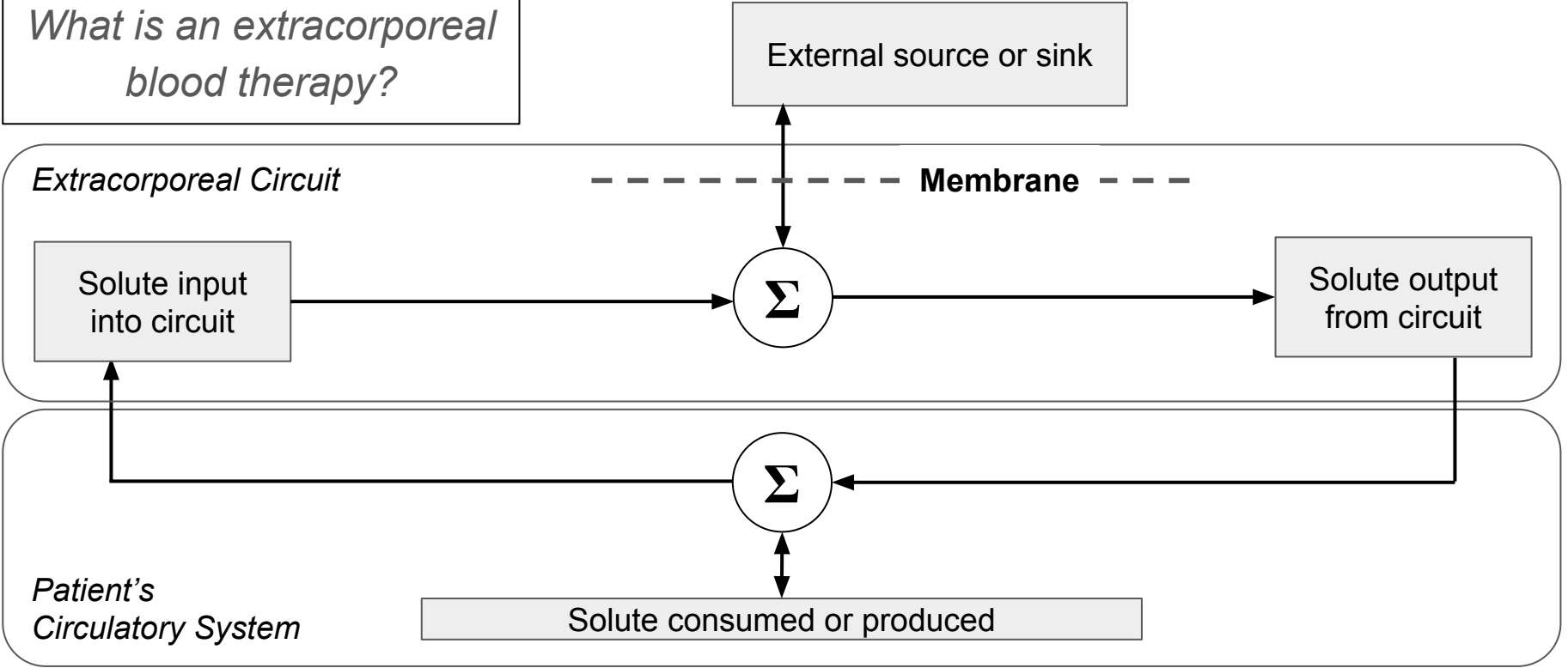
with

Dean Johnson, Henry Chung, Alfred Clark, Jr.,
and James McGrath



Extracorporeal Therapies

What is an extracorporeal blood therapy?



Hemodialysis

- Primarily used to treat chronic kidney failure
- Designed to clear a wide variety of “uremic toxins” from blood
 - Toxins and their carriers vary in molecular weight (size and diffusivity) across three orders of magnitude
 - Also variable: toxicity, rate of accumulation, etc.

ECMO

- Intensive care support for heart or lungs
- Works by adding oxygen to and/or removing carbon dioxide from blood
- Half of patients are neonatal; half of the remainder are pediatric

Hemodialysis

- Usually four-hour treatments delivered three times per week
- Terrible prognosis -- 3-5 years
- More frequent, low-dose treatment would help

Miniaturization would enable wearable device → continuous treatment is more effective

ECMO

- High incidence of complications, mostly hemorrhage
- Requires frequent blood transfusions -- increases death by 24% per 10 mL/kg/day ^[1]

Miniaturization would reduce volume or frequency of transfusions → treatment is safer

Traditional Membranes

Introduction

Hemodialysis

ECMO

Conclusion



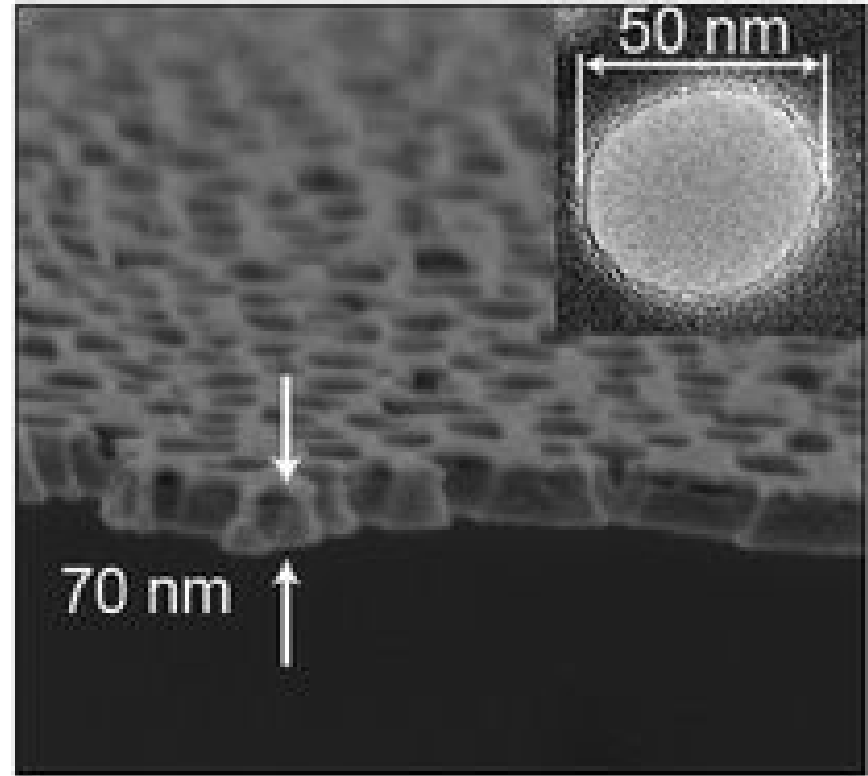
Fiber bundle membrane

- Separates blood from external fluid in flow-counterflow
- Huge membrane surface area (1 to 3 m²)
- Designed for maximal single-pass transport efficiency
- Polymeric membrane, e.g. cellulose or polysulfone: **many microns or millimeters thick**

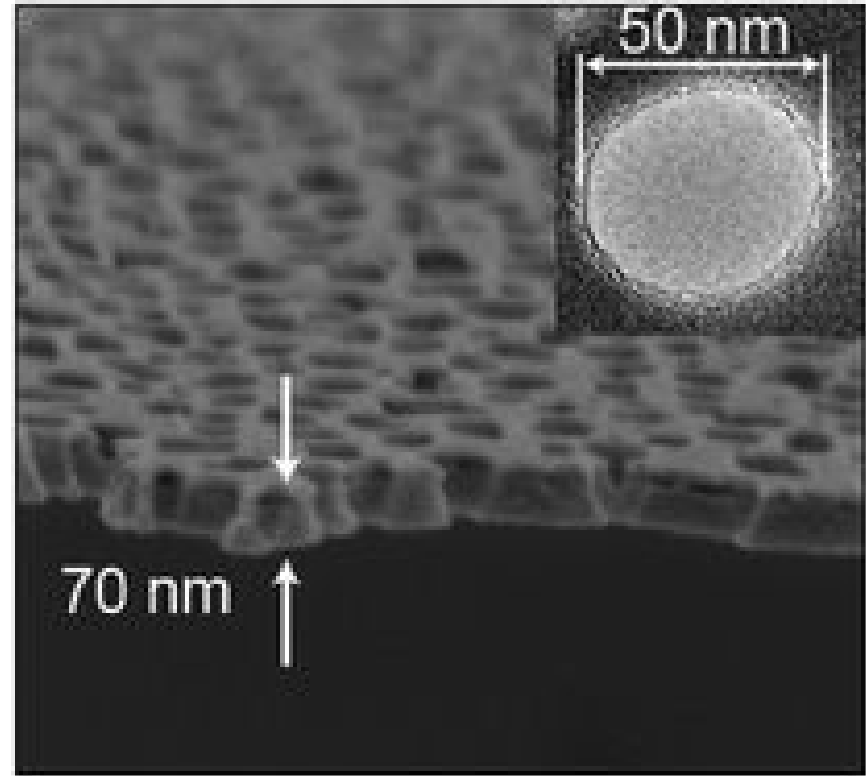


Silicon “nanomembranes”

- Original discovery of porous nanocrystalline silicon (pnc-Si) by Striemer et al. in 2007
- Progression to silicon nitride (SiN) reported by DesOrmeaux in 2014
 - More mechanically robust
 - Less chemically reactive



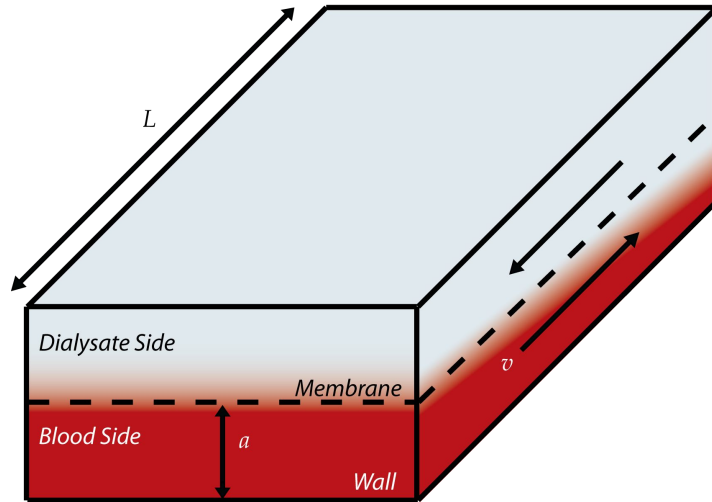
- Membrane thickness in tens of nanometers
 - Hundreds to thousands of times thinner than conventional polymer membranes
 - Reduces average diffusion time across membrane by 10^4 to 10^6 times
- Pore size of comparable scale
 - Tunable for application
 - Appropriate scale for size-based restriction of protein transport



Hypothesis: *The extraordinary thinness of silicon nanomembranes can be leveraged to enable miniaturized extracorporeal blood therapy devices and in doing so improve treatment safety and/or efficacy.*

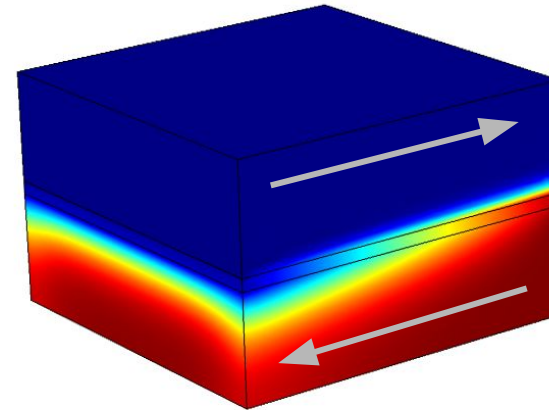
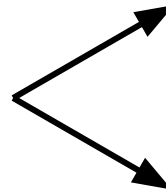
Approach: *Build and validate models that describe these therapies, and then apply them towards evaluating the size and efficacy of nanomembrane-based equivalents to traditional devices.*

General hemodialysis system



Analytical solutions to the Convection-Diffusion equation

$$\bar{c}(\bar{x}, \bar{t}) = \sum_{n=1}^{\infty} \frac{2 \sin(z_n) \cos(z_n \bar{x})}{z_n + \sin(z_n) \cos(z_n)} e^{-z_n^2 \bar{t}}$$



Computational modeling with COMSOL Multiphysics

Analytical

Pros	Cons
Fast enough for many calculations	Restricted to simple geometry
Accuracy depends only on model parameters	Requires simplifying assumptions

Simplifying Assumptions

Plug flow

velocity is constant everywhere

High Peclet number

diffusion only normal to membrane

No edge effects

thin-slit geometry only

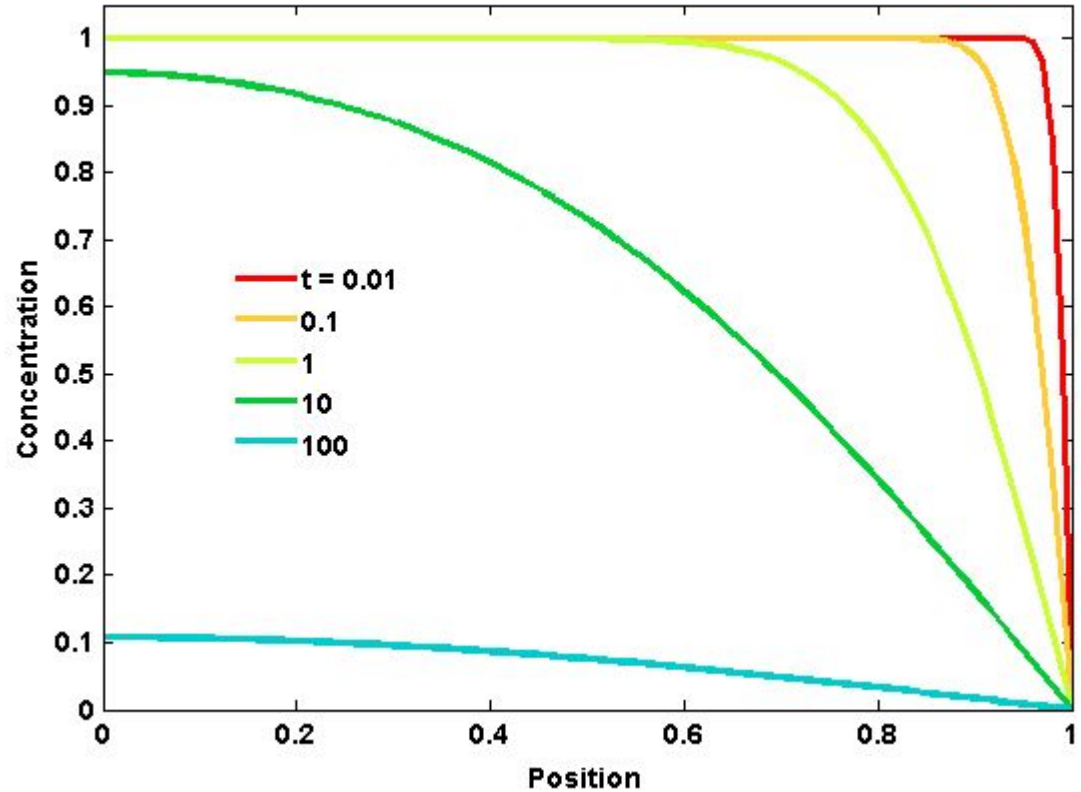
Dialysate is a sink

no transport back into blood

Assumptions allow us to approximate hemodialysis by solving a very simple differential equation:

$$\frac{\partial \bar{c}}{\partial \bar{t}} = \frac{\partial^2 \bar{c}}{\partial \bar{x}^2}$$

$$\bar{x} = \frac{x}{a}; \quad \bar{c} = \frac{c}{c_0}; \quad \bar{t} = \frac{tD_0}{a^2}$$



Computational

Pros

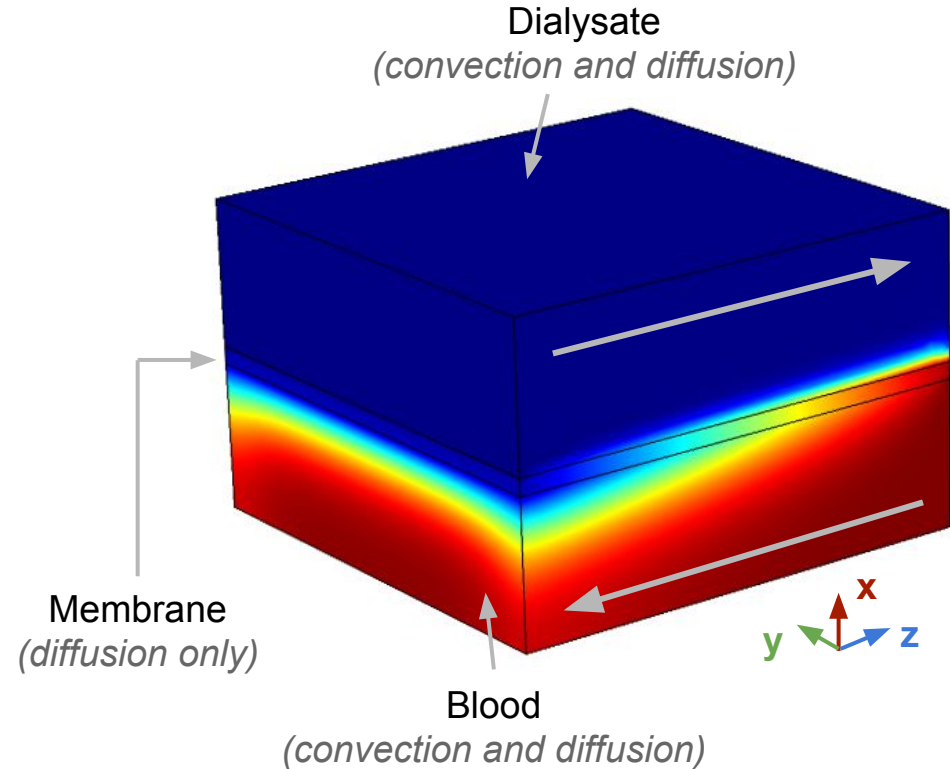
Applicable to much wider range of geometries

Requires no special assumptions

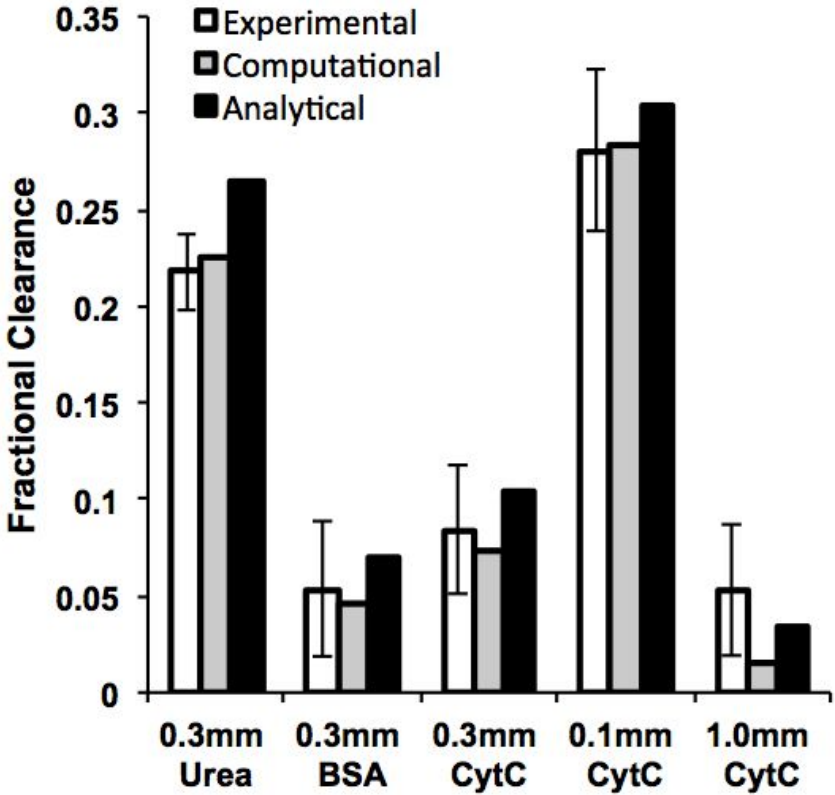
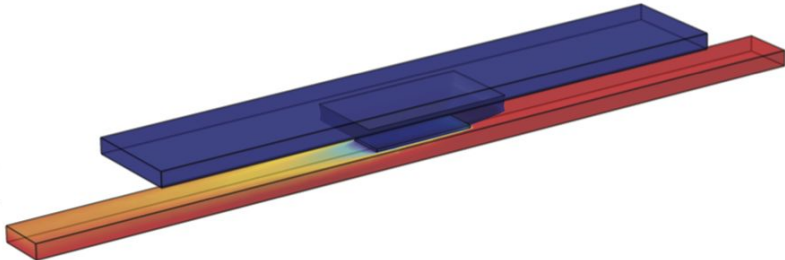
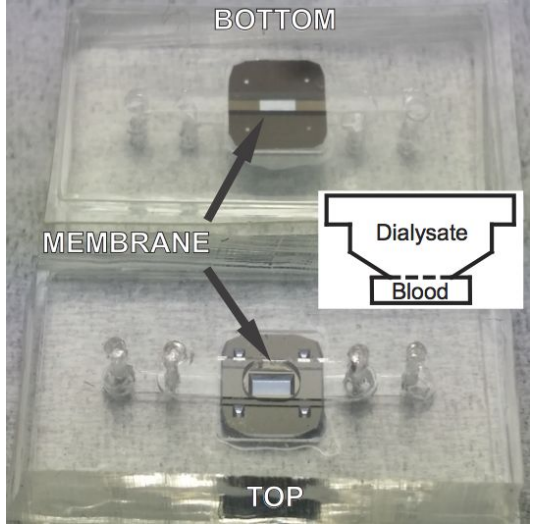
Cons

Potentially very slow solution time

Requires validation to ensure accuracy

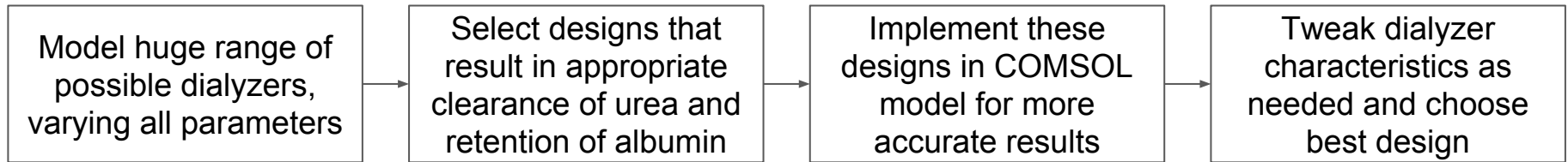


Experimental Validation



Now that we know the pros and cons of each model, we can put them to use cooperatively in designing a miniaturized hemodialyzer

Approach:



Taking advantage of fast solutions from the analytical model

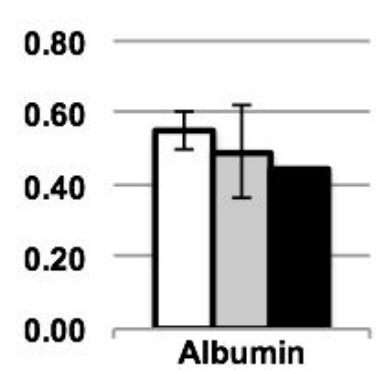
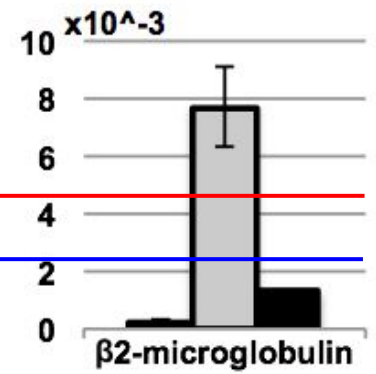
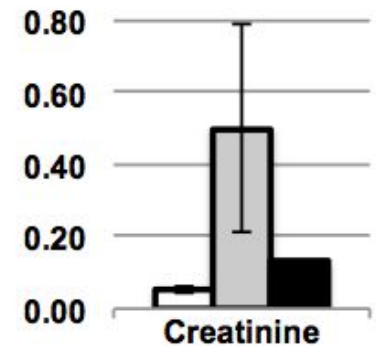
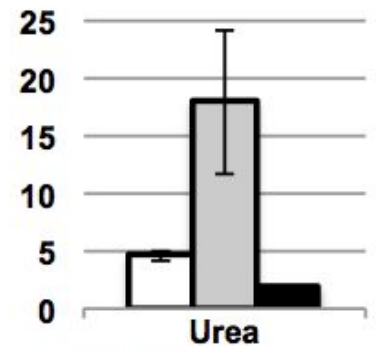
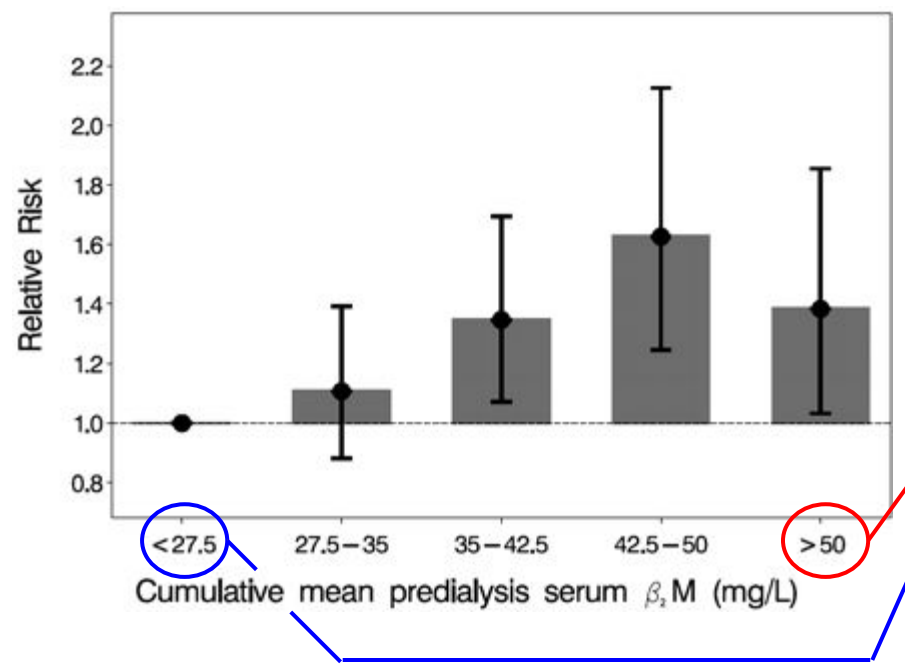
Representing entire range of sizes in uremic toxins

The computational COMSOL model is slower but accommodates real device geometry

Fine tuning and final design selection are best done manually

Results

All-Cause Mortality



Healthy Traditional Nanomembrane



ECMO is described by the same convection-diffusion equation as hemodialysis, but with the addition of a reactive term...

$$\frac{\partial c_O}{\partial t} = D_O \nabla^2 c_O + v \nabla c_O - \Gamma \quad (\text{Oxygen})$$

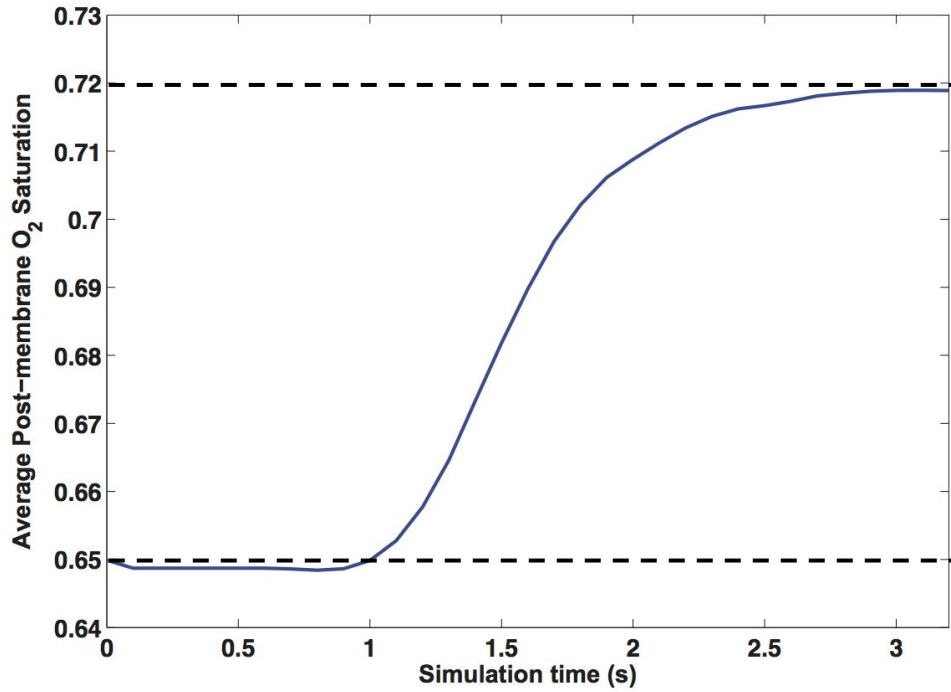
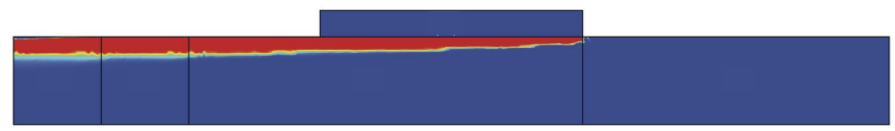
$$\frac{\partial c_{Hb}}{\partial t} = D_{Hb} \nabla^2 c_{Hb} + v \nabla c_{Hb} - \Gamma \quad (\text{Deoxyheme})$$

$$\frac{\partial c_{HbO}}{\partial t} = D_{Hb} \nabla^2 c_{HbO} + v \nabla c_{HbO} + \Gamma \quad (\text{Oxyheme})$$

All three equations must be solved simultaneously to account for the reaction!



ECMO Model



Final -----

↑

*Experimental values
(to the nearest hundredth)*

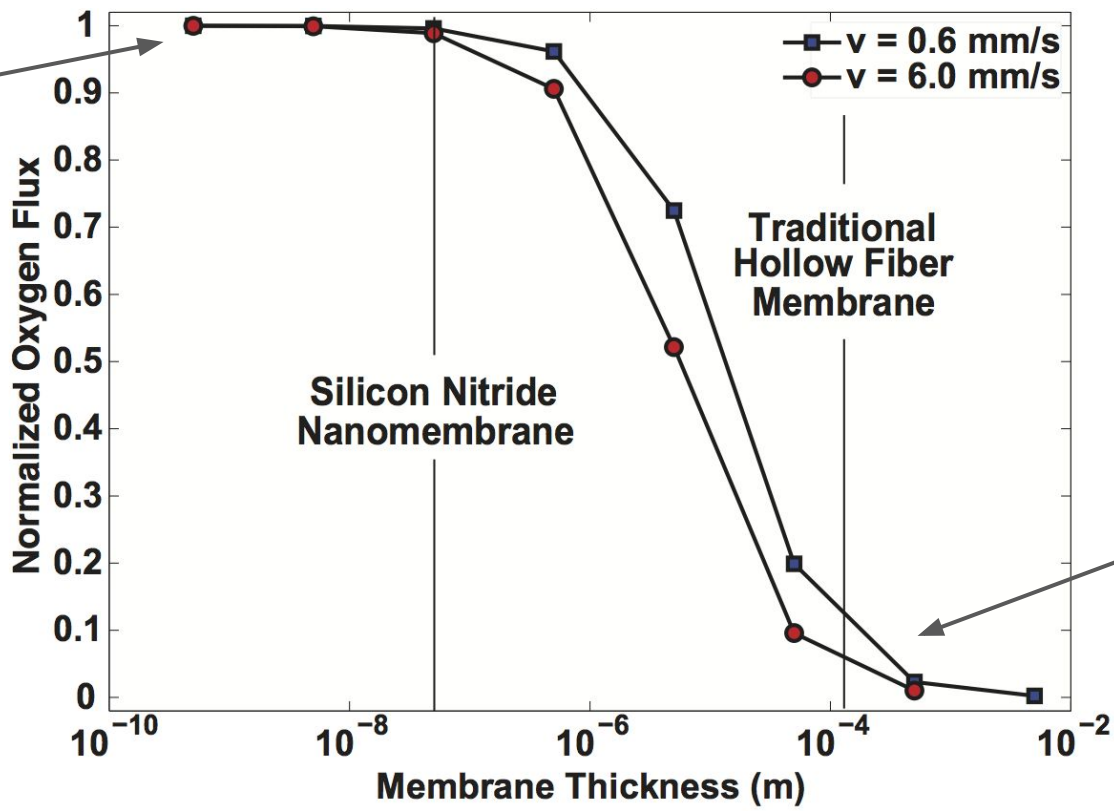
↓

Initial -----



ECMO Model

Limited by transport away from membrane



Traditional Hollow Fiber Membrane

Silicon Nitride Nanomembrane

Limited by diffusion within membrane



Comparative Analysis

Introduction

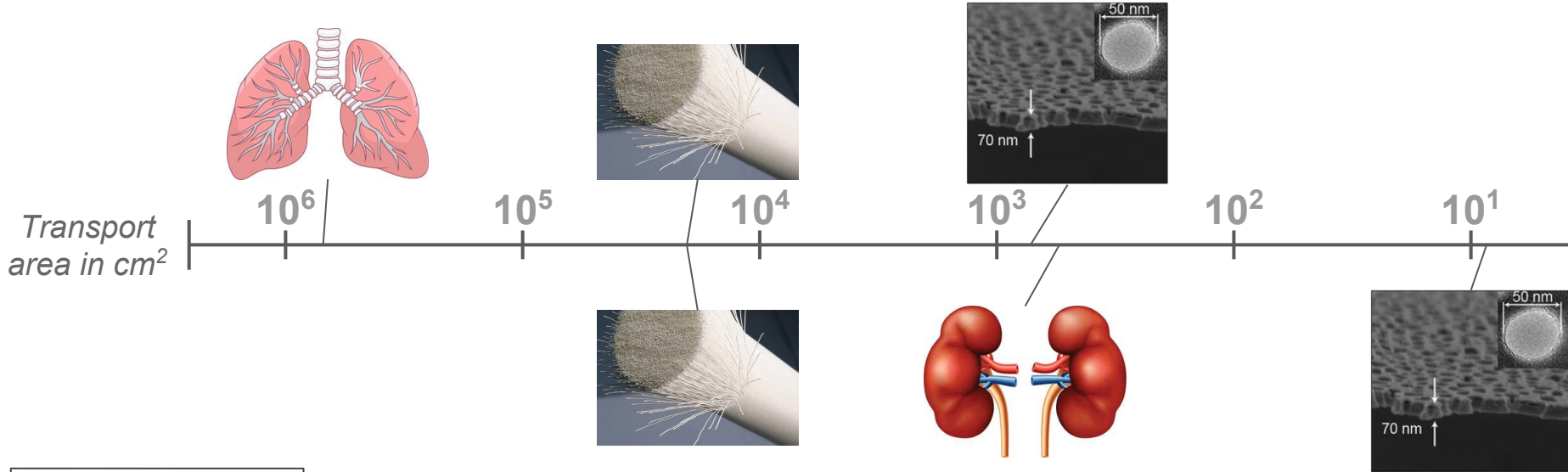
Hemodialysis

ECMO

Conclusion

ECMO

Marginal improvement

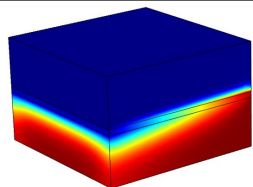


Hemodialysis

Regime change!

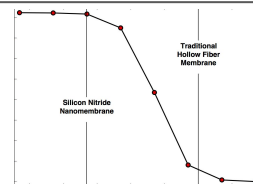
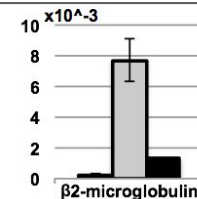


- Extracorporeal blood therapies are in need of miniaturization
 - Kept large by traditional hollow-fiber membranes
 - Ultrathin nanomembranes enable device size reduction



- Models allow us to predict and analyze membrane transport
 - Modeling approach tailored to application and physics
 - Models experimentally validated in the lab

- Hemodialysis can be miniaturized to an extraordinary degree
 - Allows for wearable, continuous-treatment device
 - Regime change from traditional alternatives



- ECMO can be miniaturized, but benefits are more limited
 - Marginal improvement over traditional membranes
 - Necessary membranes too large to produce with current tech