Joint Department of
BIOMEDICAL ENGINEERING
UNC CHAPEL HILL | NC STATE UNIVERSITY

The Role of Viscous Drag in Angiogenic Sprouting

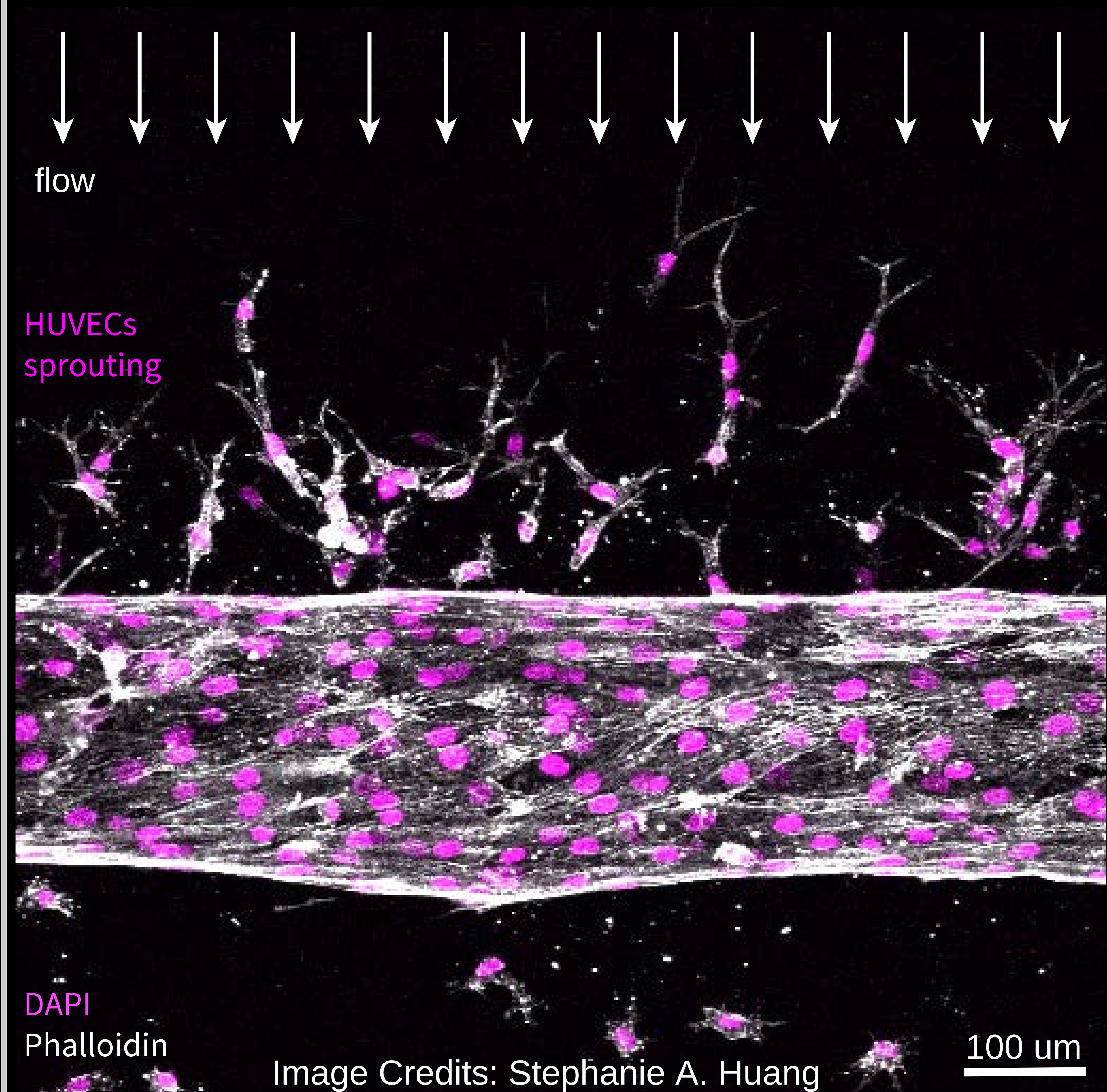
Abel J. Abraham, YunZen Wu, Elizabeth Doherty, Mitesh Rathod, William J. Polacheck

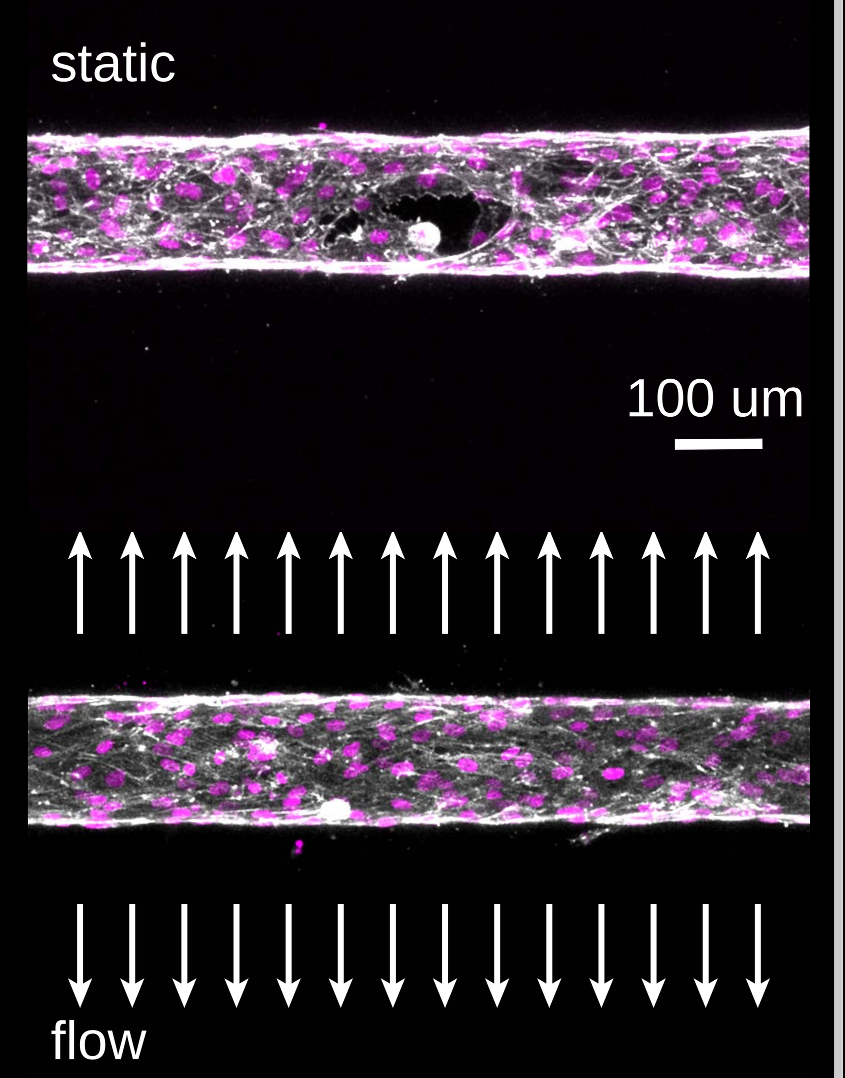
Joint Department of Biomedical Engineering, University of North Carolina, Chapel Hill, NC, USA

Motivation

Tumors are known to hijack angiognesis, and studies have shown they can locally increase pressure.[1]

In the lab we find that angiogenesis can be directed towards areas of higher pressure, ie 'upstream'





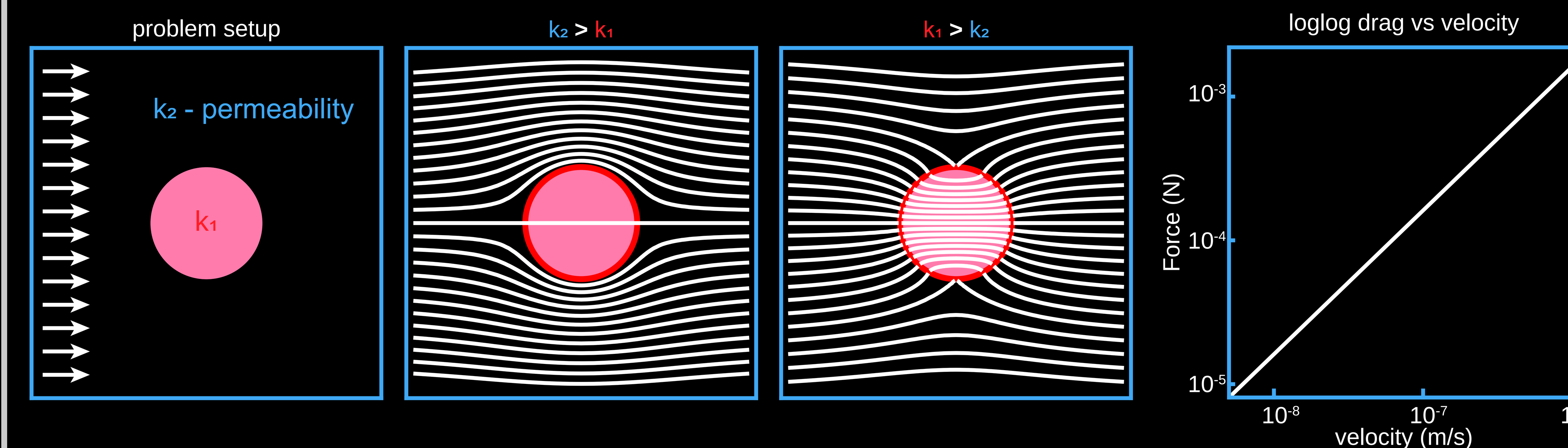
Main Question:

Does drag on the vessel lead to angiogenesis?

If so, how?

Analysis

Flow in porous media past a porous cylinder contains a closed form (but messy) formula for drag[2]



To use this formula for drag, we used $k_1 \sim 10^{-19}\ m^2$ and $k_2 \sim 10^{-13}\ m^2$ as detailed in our analysis below:

In reality k_1 is for a composite structure, a porous outer layer of cells filled with fluid

so we use a formula for the effective permeability of a porous media with fluid filled inclusions[3]

$$k_{eff} = \frac{k(a^2(1+2C) - 12k(C-1) - 4a(1+2C)\lambda\sqrt{k})}{a^2(1-C) + 6k(2+C) + 4a(C-1)\lambda\sqrt{k}}$$

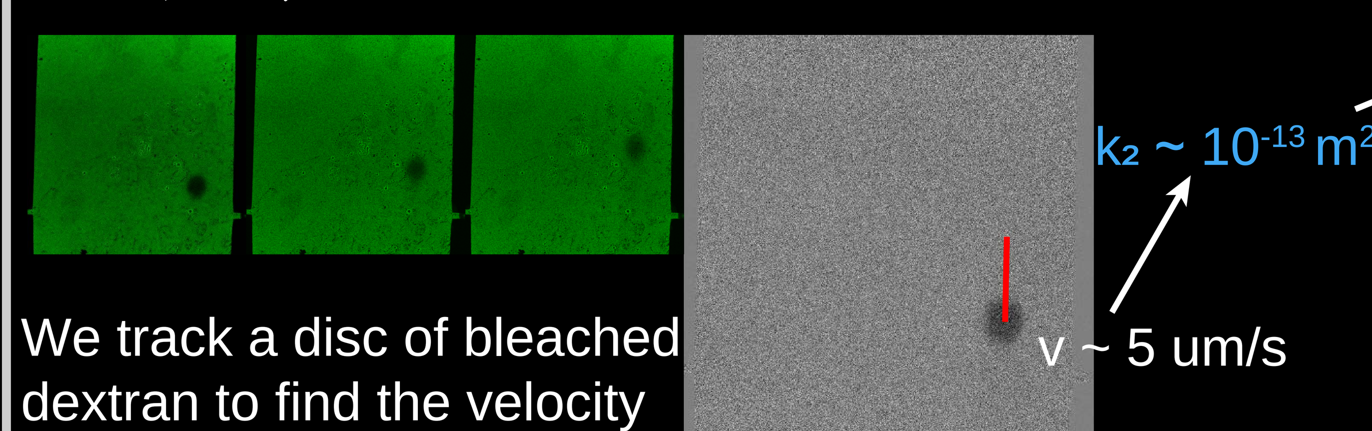
From the literature, the permeability of endothelial cells[4,5,6] is $k_{EC} \sim 10^{-21}\ m^2$ so $k_1 \sim 10^{-19}\ m^2$

To measure k_2 for collagen we can use Darcy's law from FRAP experiments

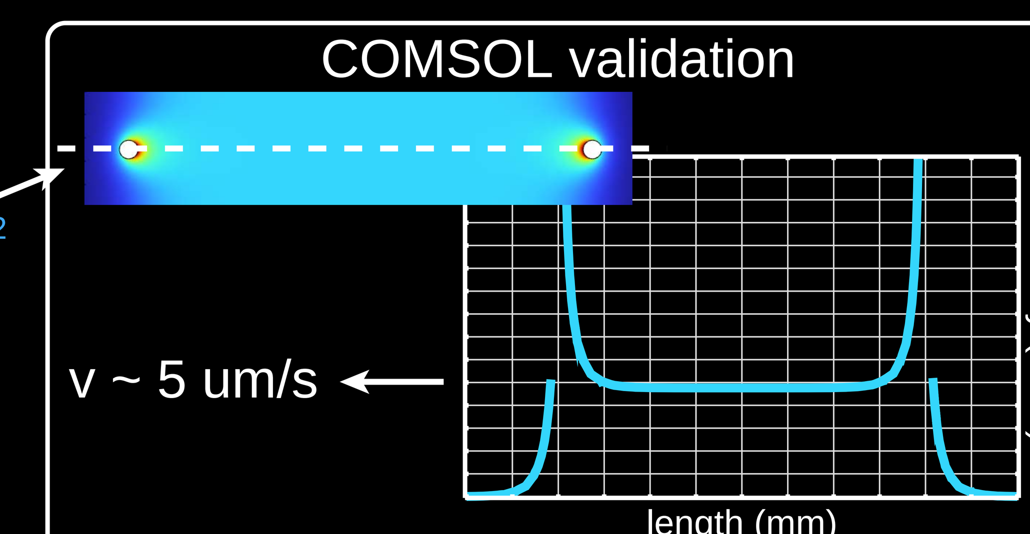
Darcy's law:

$$q = \frac{v}{\phi} = \frac{-k}{\mu L}\Delta P \longrightarrow k = \frac{-v\mu L}{\phi \Delta P}$$

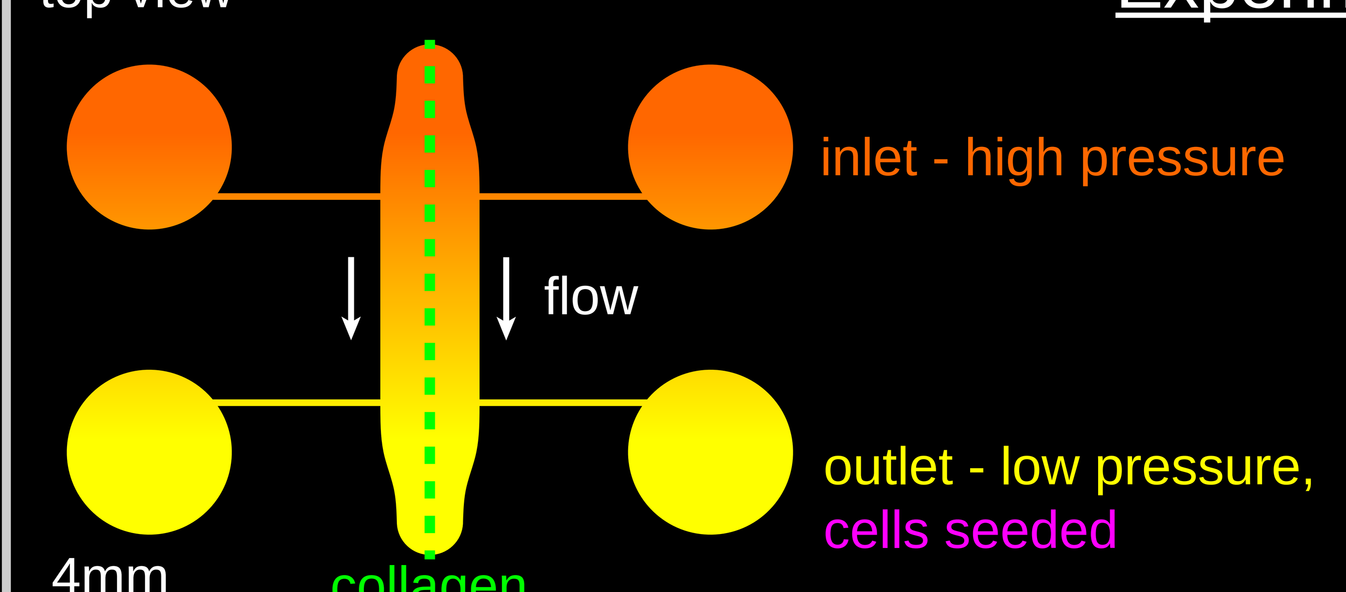
thus we can measure velocity for a prescribed pressure drop



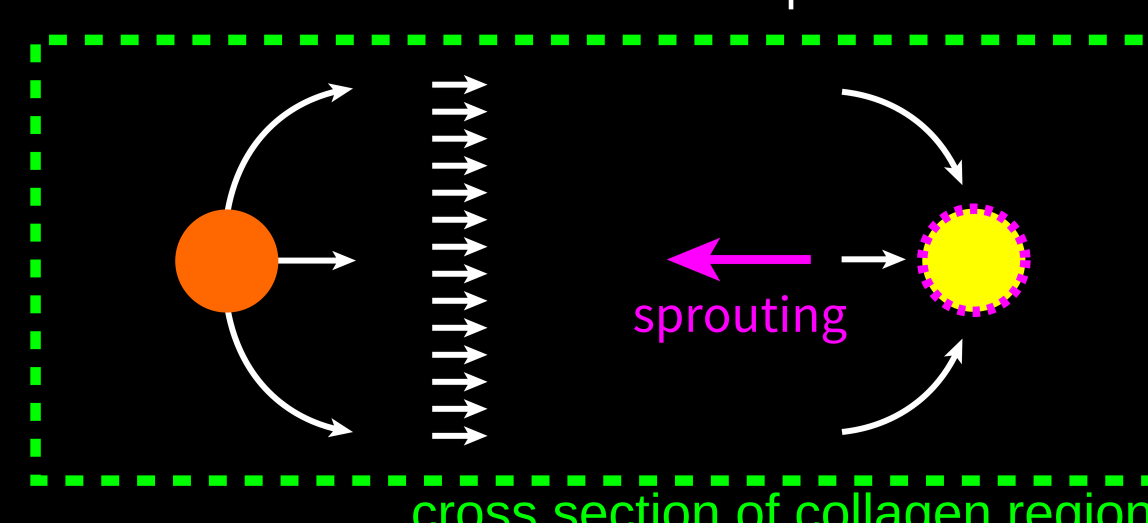
We track a disc of bleached dextran to find the velocity



Experiment

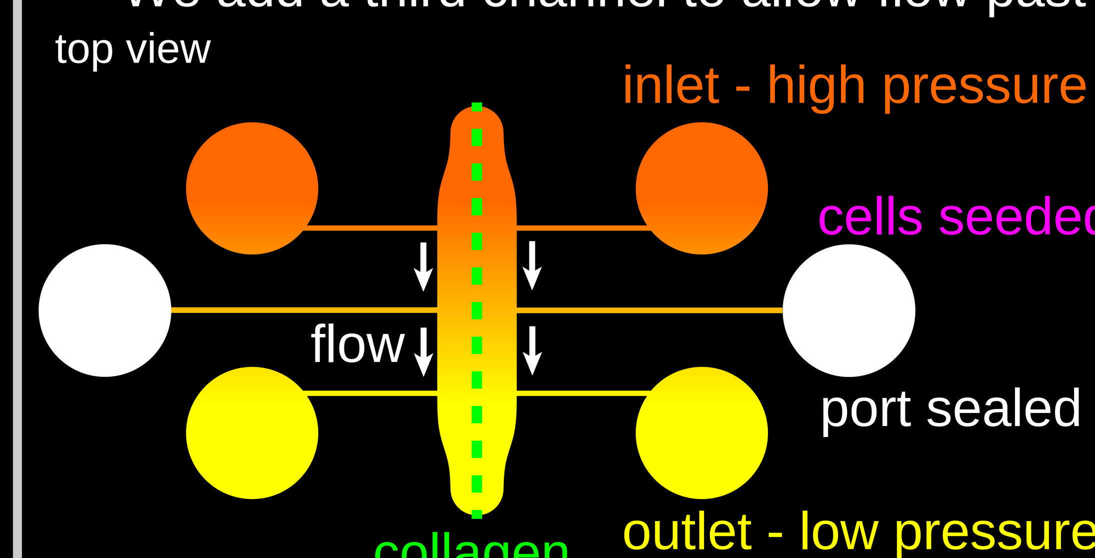


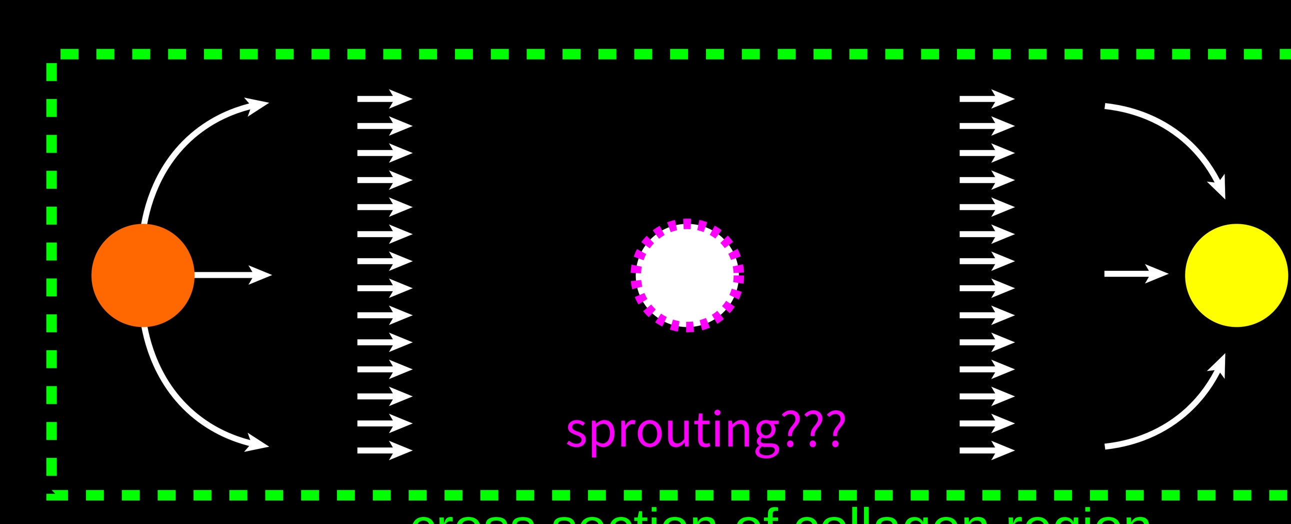
water columns are used to prescribe flow



Planned Experiments

We add a third channel to allow flow past our vessel, more like our analysis.





This provides a stronger test for drag induced angiogenesis and allows use of our formulas!

References

[1] Heldin, C. H., Rubin, K., Pietras, K., & Östman, A. (2004). High interstitial fluid pressure—an obstacle in cancer therapy. Nature Reviews Cancer
[2] Deo, S., & Ansari, I. A. (2019). Brinkman flow through a porous cylinder embedded in another unbounded porous medium. Journal of Porous Media
[3] Markov, M., Kazatchenko, E., Mousatov, A., & Pervago, E. (2010). Permeability of the fluid-filled inclusions in porous media. Transport in porous media
[4] Luckett, P. M., Fischbarg, J., Bhattacharya, J. A. H. A. R., & Silverstein, S. C. (1989). Hydraulic conductivity of endothelial cell monolayers cultured on human amnion. American Journal of Physiology-Heart and Circulatory Physiology
[5] Helton, E. S., Palladino, S., & Ubogu, E. E. (2017). A novel method for measuring hydraulic conductivity at the human blood-nerve barrier in vitro. Microvascular research
[6] Chang, Y. S., Munn, L. L., Hillsley, M. V., Dull, R. O., Yuan, J., Lakshminarayanan, S., ... & Tarbell, J. M. (2000). Effect of vascular endothelial growth factor on cultured endothelial cell monolayer transport properties. Microvascular research

POLACHECK LAB

Thanks to BME Dept. for support via the Lucas Scholar Fellowship and the Abrams Scholar program!