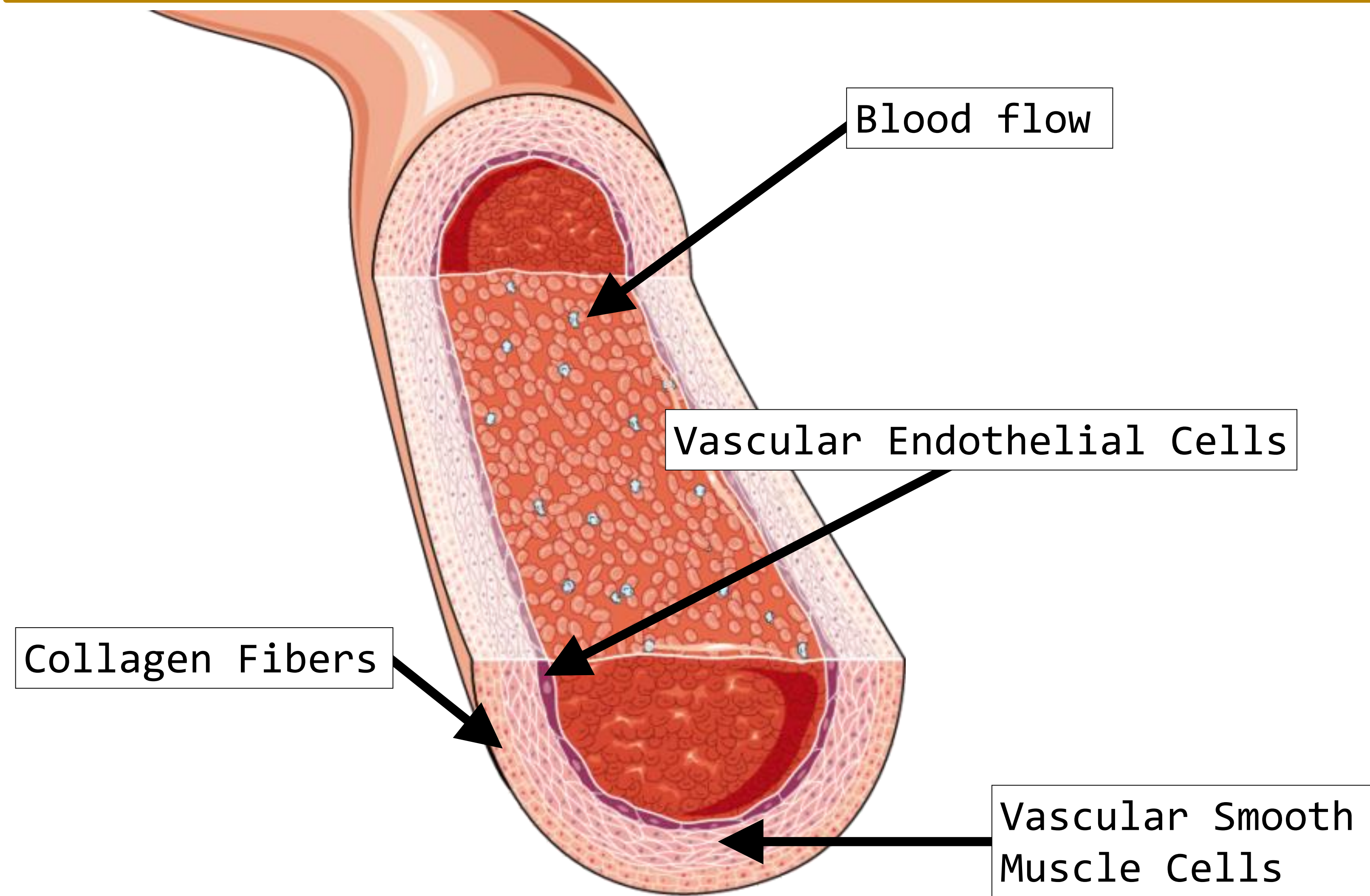


Denise Hsu¹, Alexandra Tchir¹, Joshua Hutcheson^{*1}, and Sharan Ramaswamy^{*1}.
¹ Department of Biomedical Engineering, Florida International University, Miami, FL, ^{*}Co-Advised Principal Investigators

Introduction

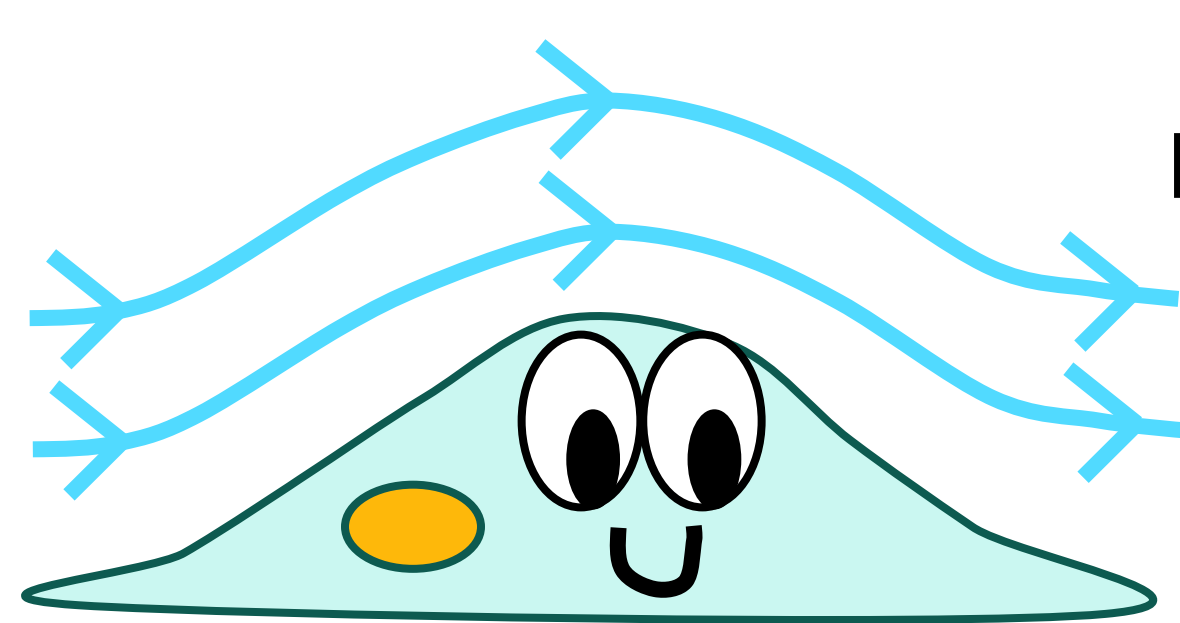


- The blood vessel consists of a layer of vascular endothelial cells (VasEC) and a sublayer of vascular smooth muscle cells (VasSMC).
- Vascular maintenance and remodeling involves autocrine signaling within the VasECs and VasSMCs, as well as paracrine signaling between the VasECs and VasSMCs.
- The human cardiovascular system is subjected to pulsatile flow and pressure from heart pulsation, and this pulsatile flow subjects blood vessels to oscillatory shear stresses.
- To study the effects of oscillatory shear stresses on vascular tissues, we will condition and examine the phenotype of VasECs under various oscillatory shear stresses.
- To examine the effects of paracrine signaling, we will assess the VasSMC phenotype after exposure to biochemical end-products from conditioned VasEC media.

Vascular Bifurcation

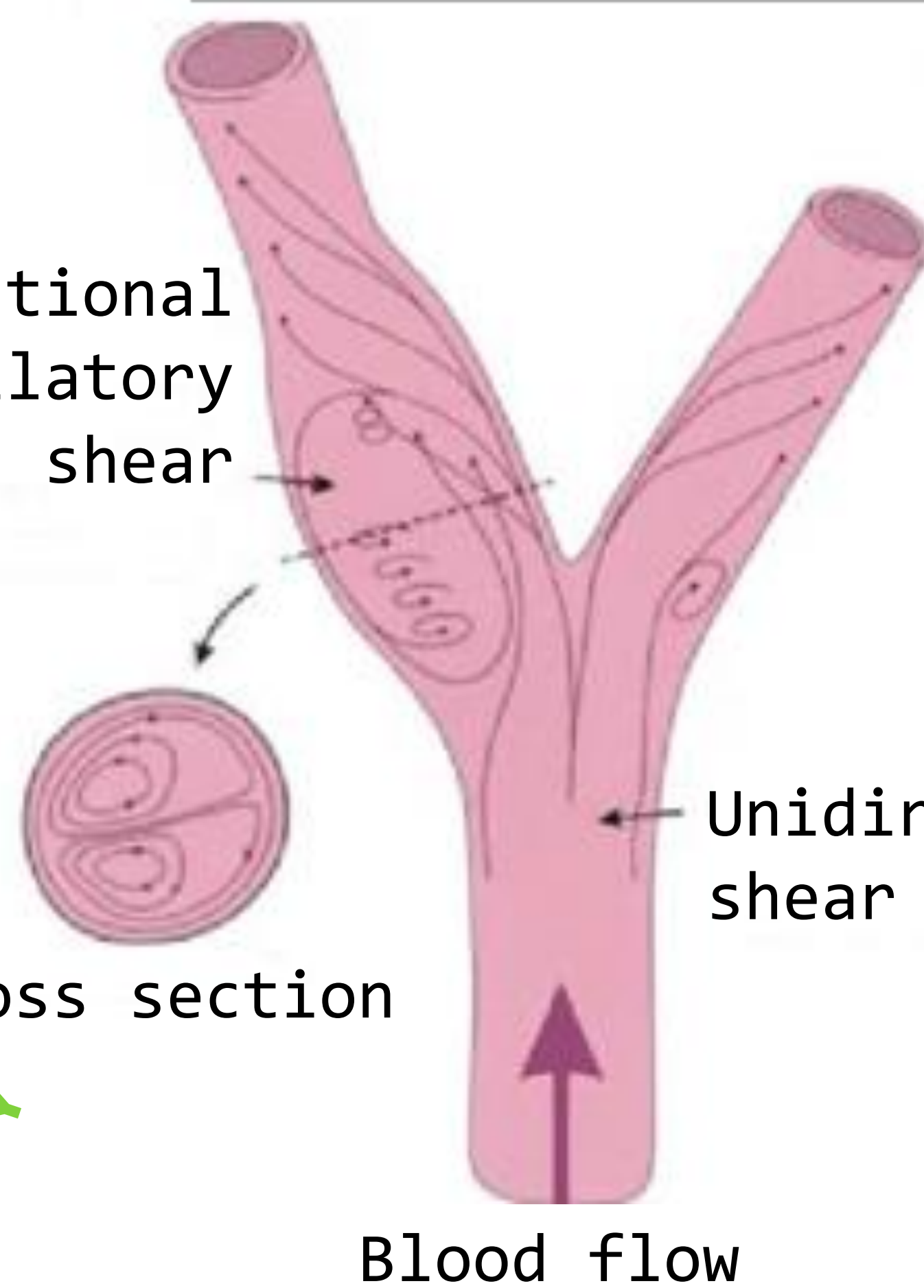
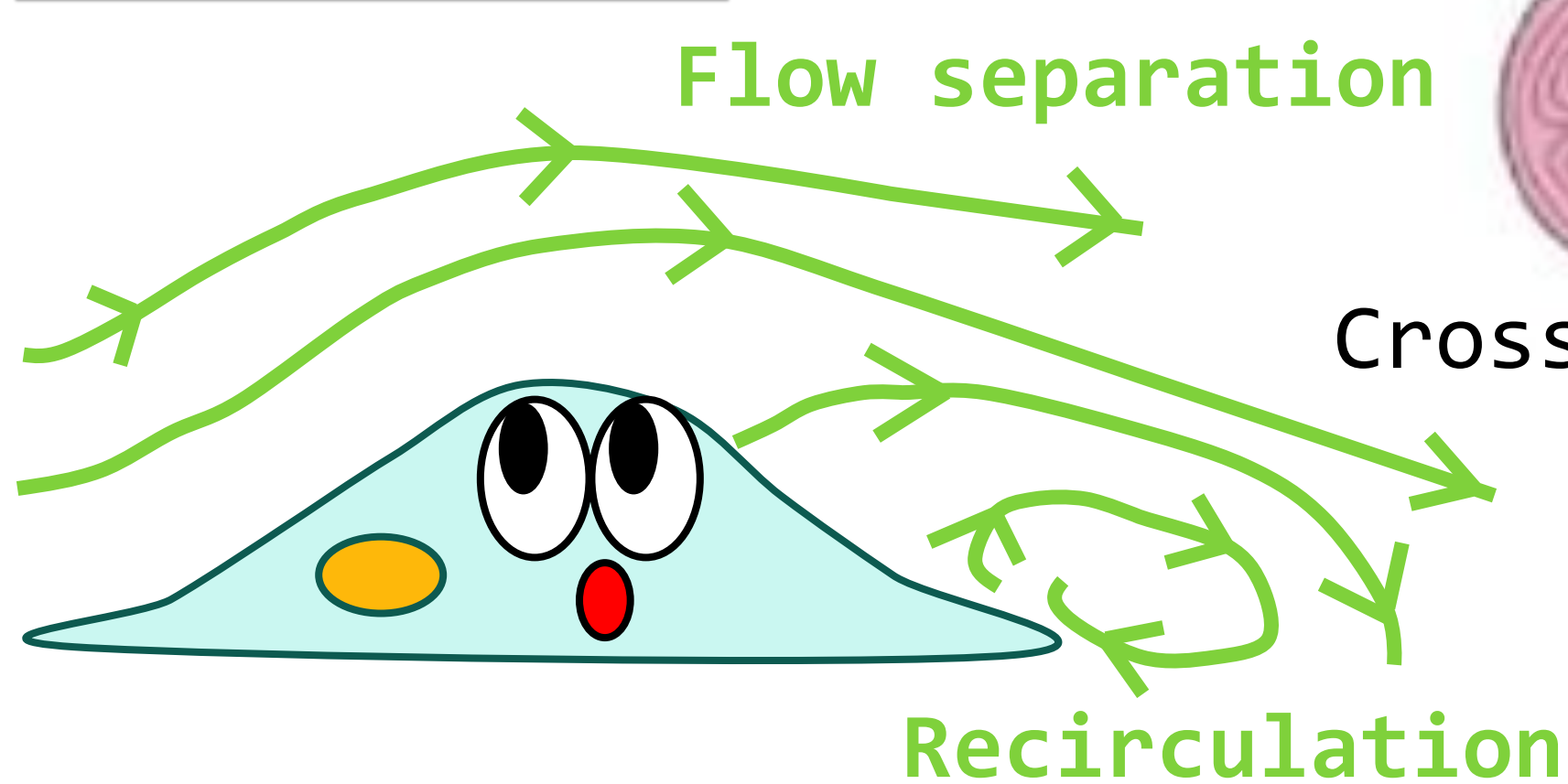
Undisturbed Laminar Flow

Smooth streamlines

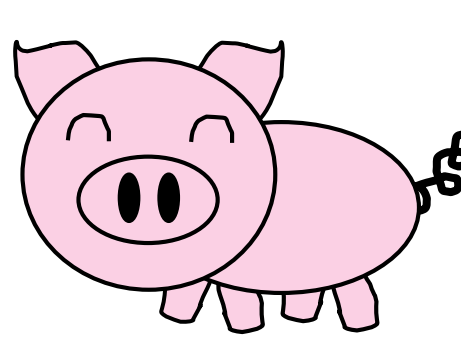

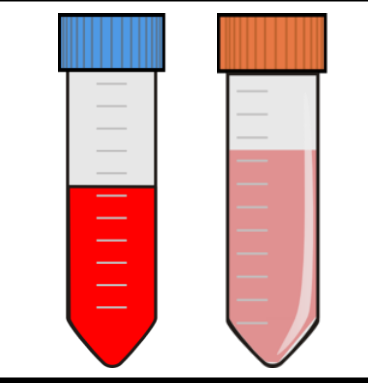
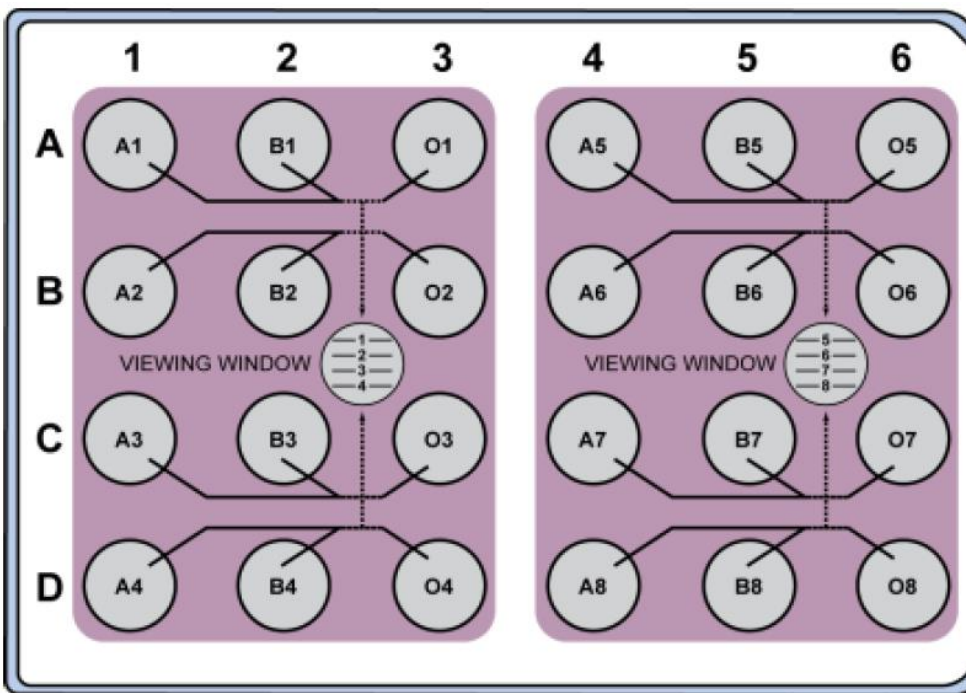




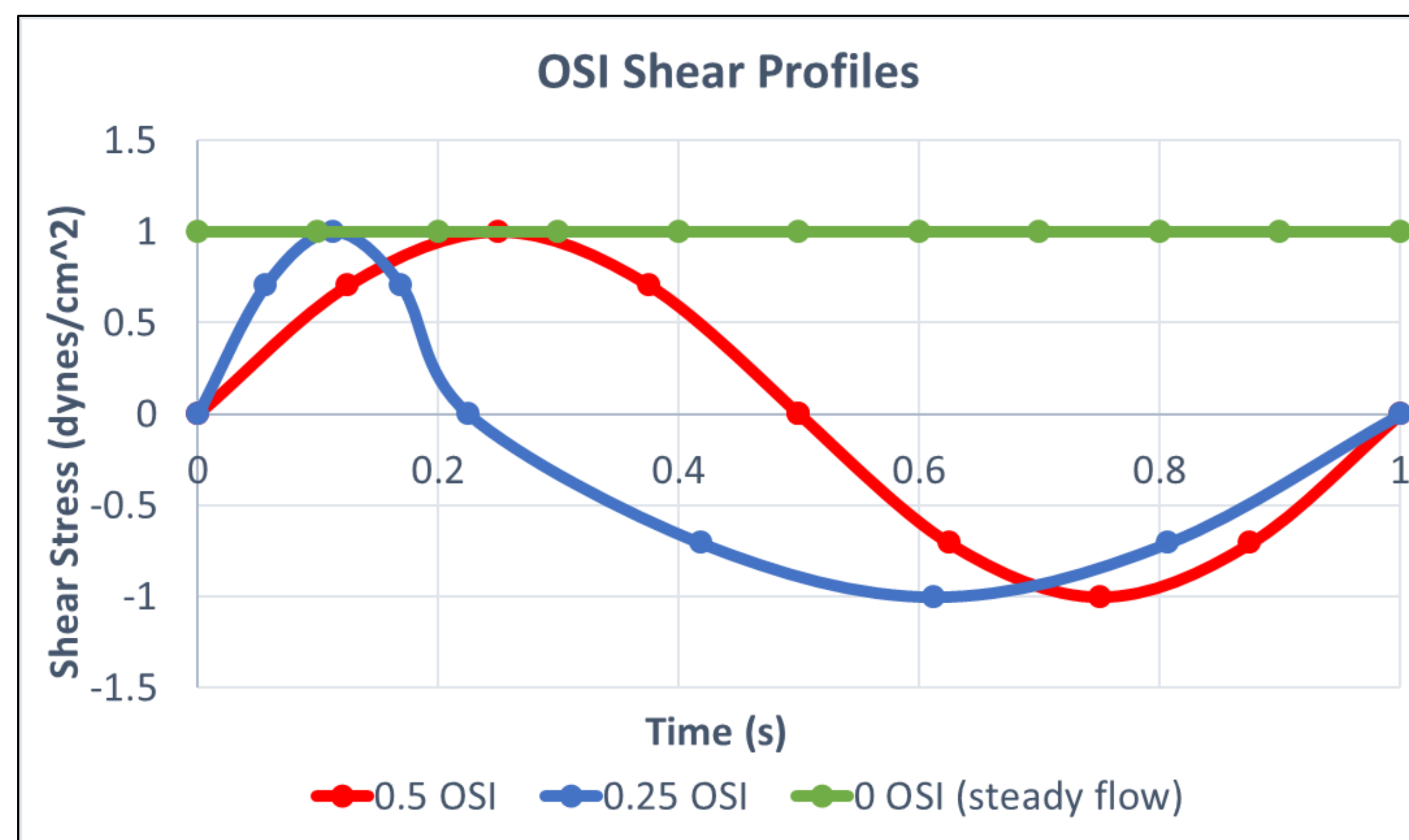
Bi-directional oscillatory shear

Disturbed Flow

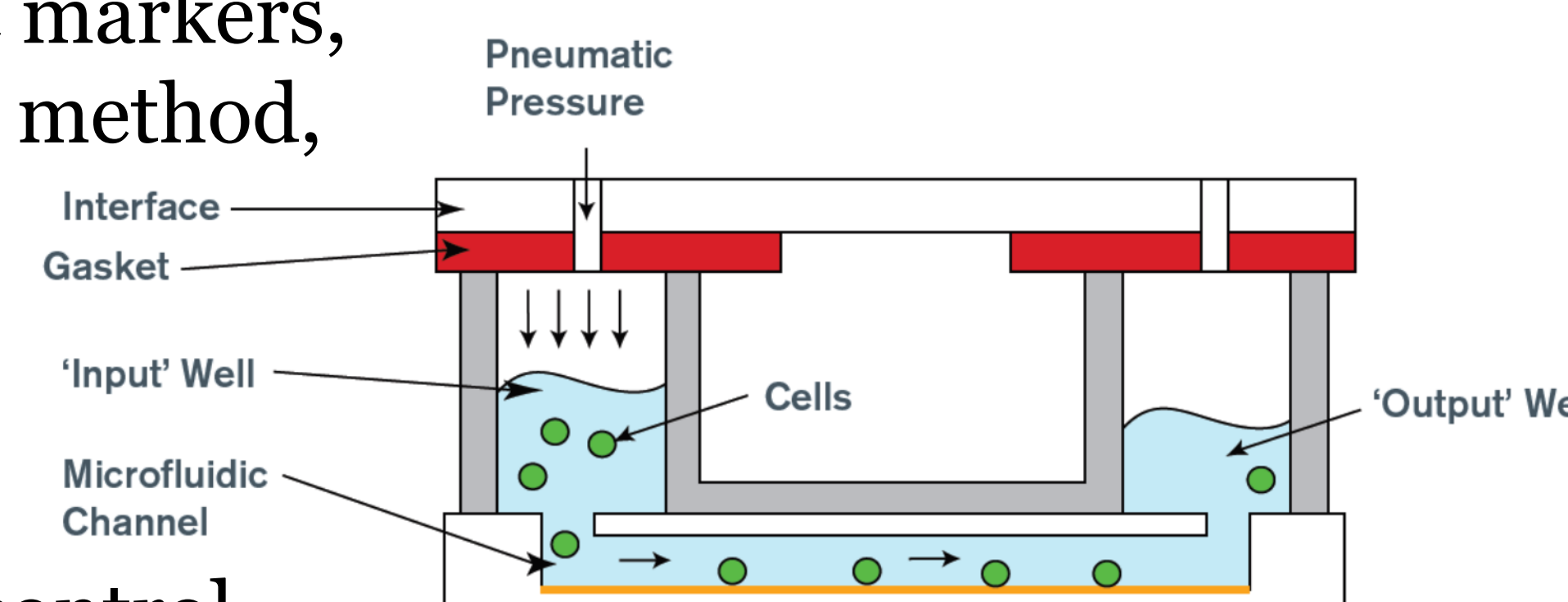


Methods

ITEM	DESCRIPTION
Porcine Vascular Cell Type  	Vascular Endothelial Cells (VasEC) Vascular Smooth Muscle Cells (VasSMC)
Conditioning Media 	100% Fresh media 50% Spent media from VasEC 50% Fresh media
Seeding Method Conditioning time: 48 hrs 	Bioflux 24-well Plate  6-cm Culture Dish 

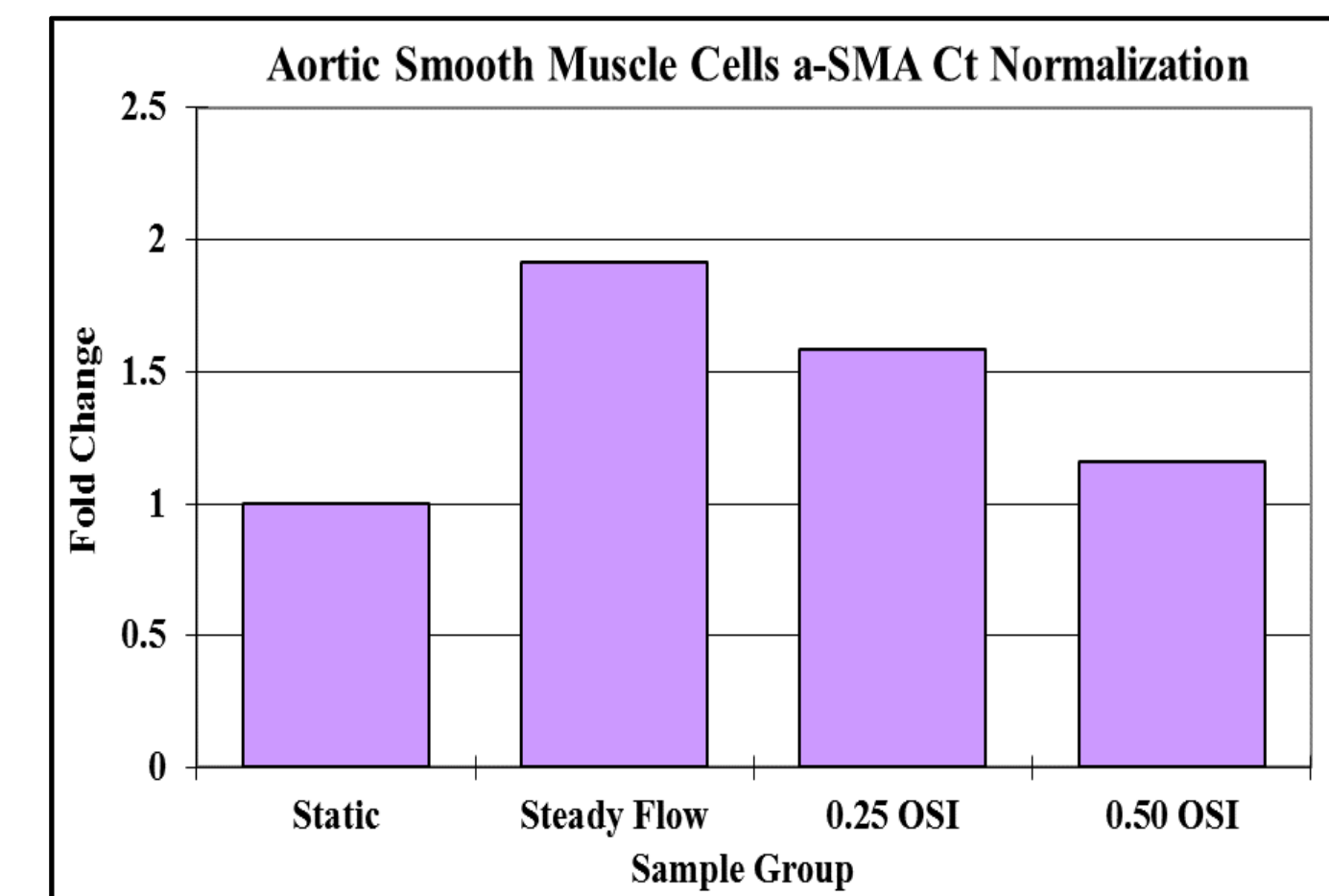
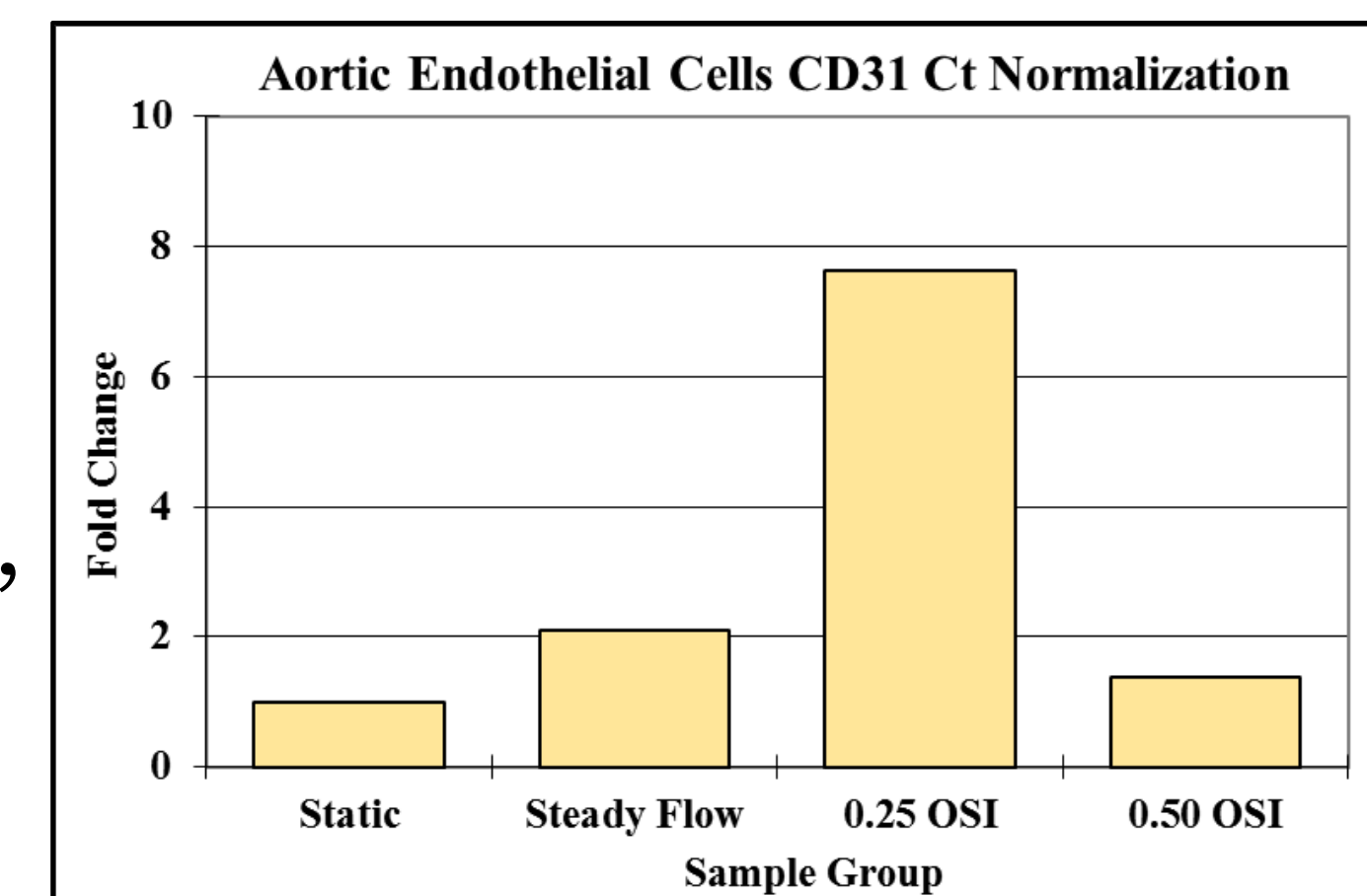


- Oscillatory shear index (OSI) is a parameter that quantifies the change in direction and magnitude of wall shear stresses.
- $0 \leq OSI \leq 0.5$
- $OSI = \frac{1}{2} \left(1 - \frac{\int_0^T \tau_\omega dt}{\int_0^T |\tau_\omega| dt} \right)$
- where τ_ω = wall shear stress, T = cycle duration, t = time
- Four OSI magnitudes are to be applied to endothelial cells:
 - No flow (static)
 - Steady flow (OSI = 0)
 - 0.25 OSI
 - 0.50 OSI
- Data analysis consists of RT-PCR gene expression assessment of key phenotypic markers, followed by Livak method, or $\Delta\Delta C_T$, to compute fold change using static (no flow) sample group as control.



Results

- CD31 is a single-chain transmembrane glycoprotein fairly specific for endothelial differentiation.
- Alpha-SMA, an actin isoform, is a differentiation marker of smooth muscle cells.
- A higher expression of alpha-SMA from VasSMC in non-static groups of conditioned media may indicate fluid motion promoting paracrine signaling for fibrotic development.
- Previous studies have shown the role of disturbed flow in VasEC physiology and pathogenesis of vascular diseases.
- We observed that through OSI-initiated paracrine signaling, the biochemical end-products released from VasECs under disturbed flow is also transmitted to the sublayer VasSMC, thereby potentially affecting their phenotype.



Pitfalls and Future Work

- Bioflux microfluidic channels are 2-dimensional models, and are not the most suitable representation for a 3-dimensional cardiovascular system.
- Only shear stresses are being examined, stretch and pressure changes are not considered.