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Computational Fluid Dynamics Study to Determine Shear Stress and Flow Patterns within the SMART (Sample Microenvironment from Resected Metastatic Tumors) Platform System

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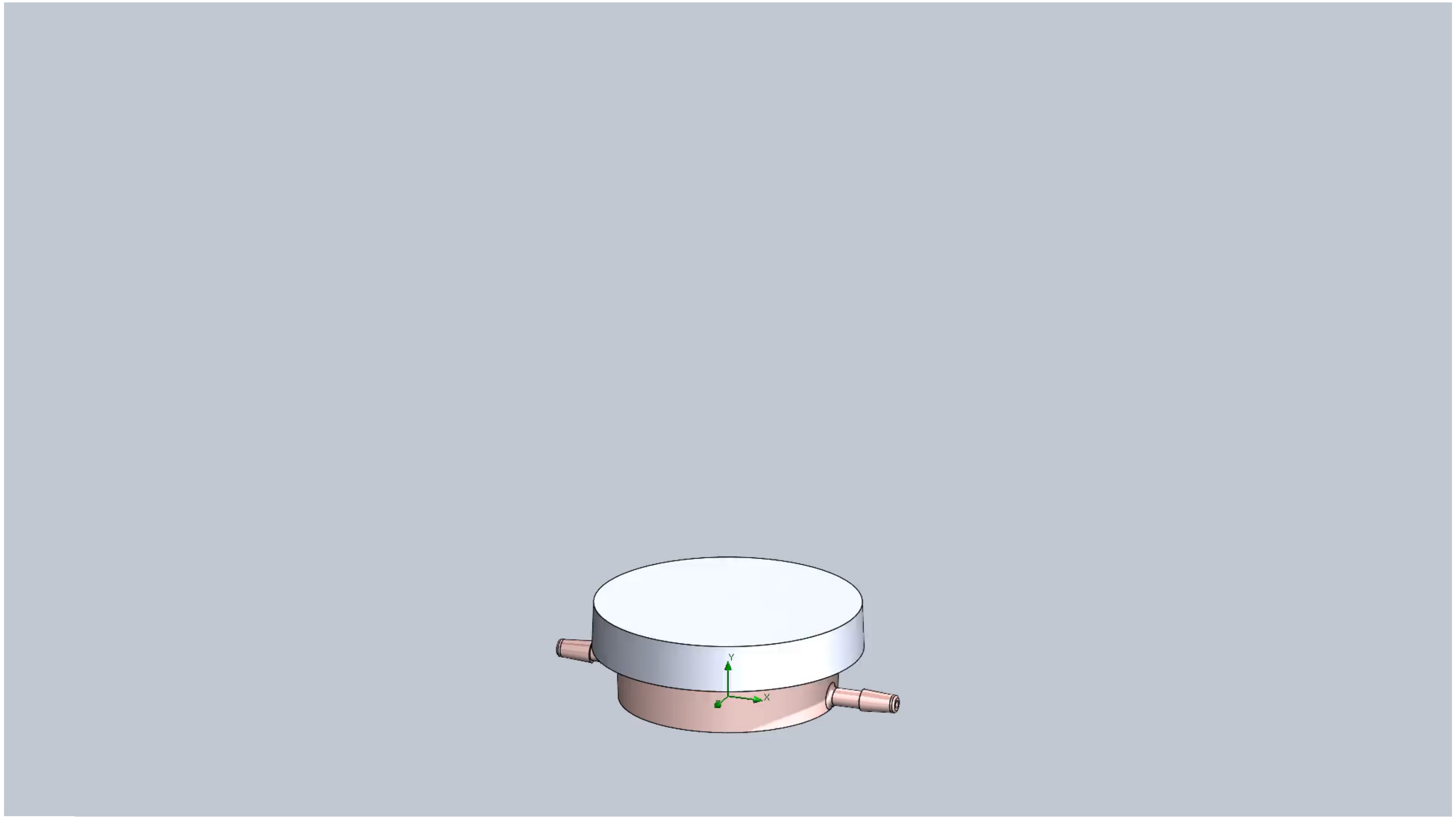
Agenda

- Introduction
- Initial Exploration of Geometry
- Fluid Properties
- Shear Stresses
- Model Validation
- Conclusion and Next Generation Design

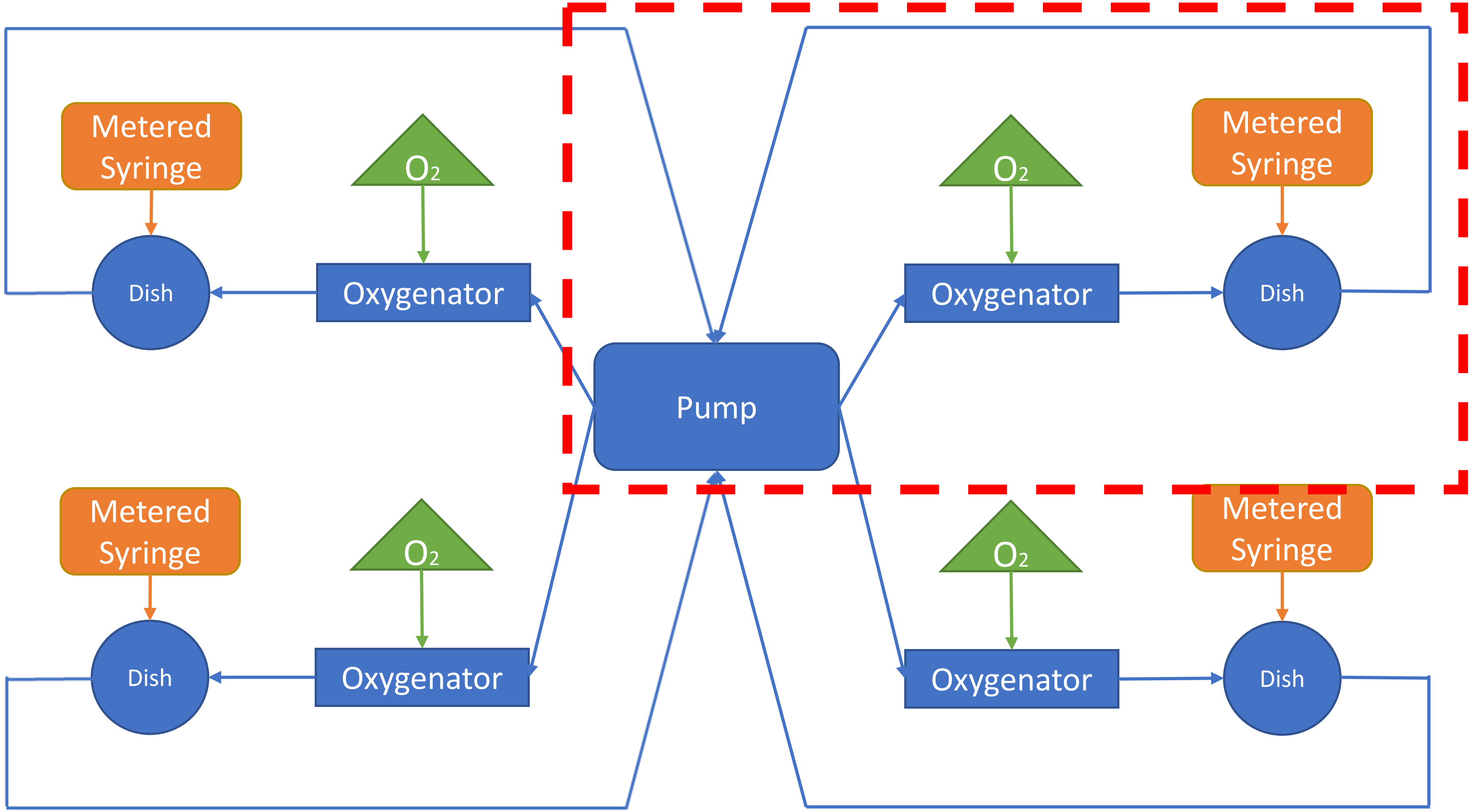
What is the SMART Platform?

- **S**ample **M**icroenvironment from **R**esected Metastatic **T**umors
- Purpose
  - Maintain resected tumors *ex vivo*
  - Allow examination of tumor microenvironment
  - Allow drug testing

Exploded View



System Diagram



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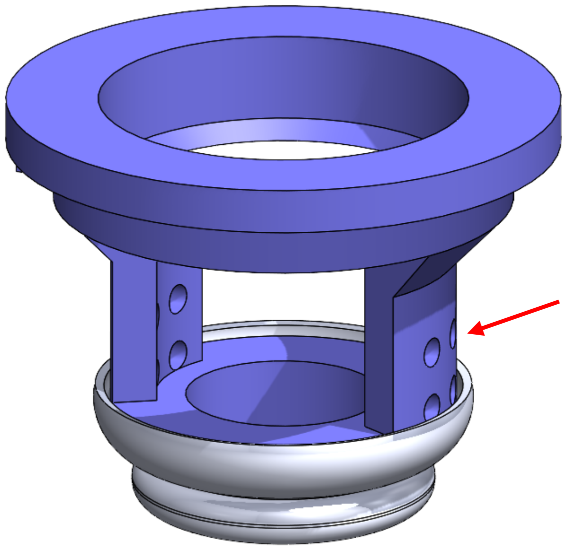
Study Goals

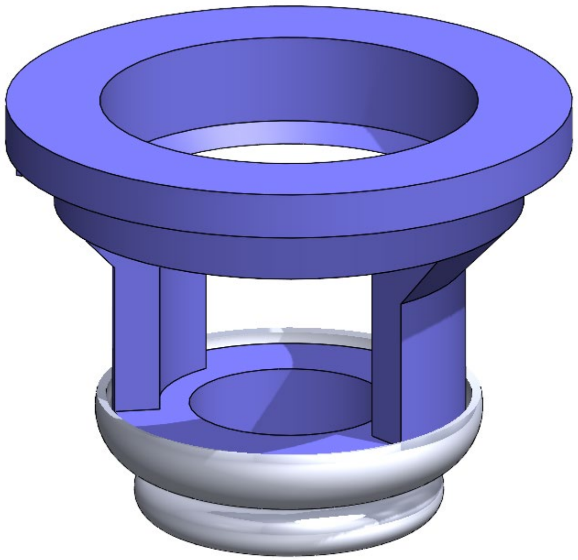
1. Examine flow patterns
   - Flow homogeneity
2. Examine shear stresses on tissue
   - Magnitude
   - Distribution

Initial Exploration

Initial Exploration

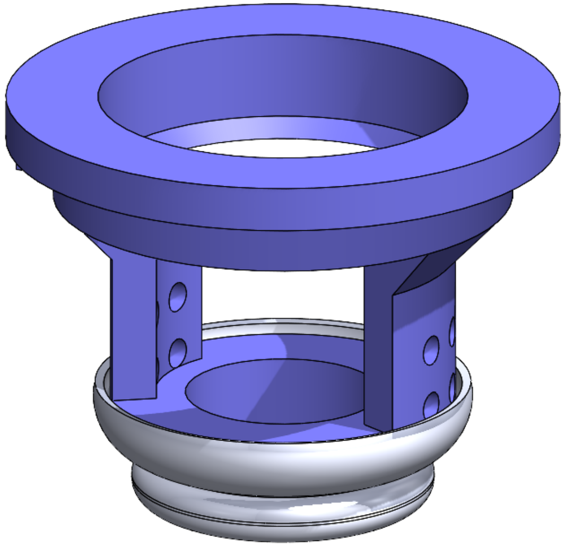
- Crossflow Holes have little effect on flow

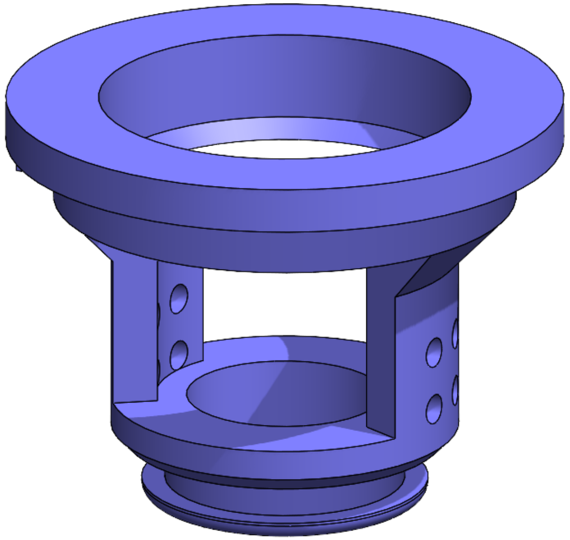




Initial Exploration

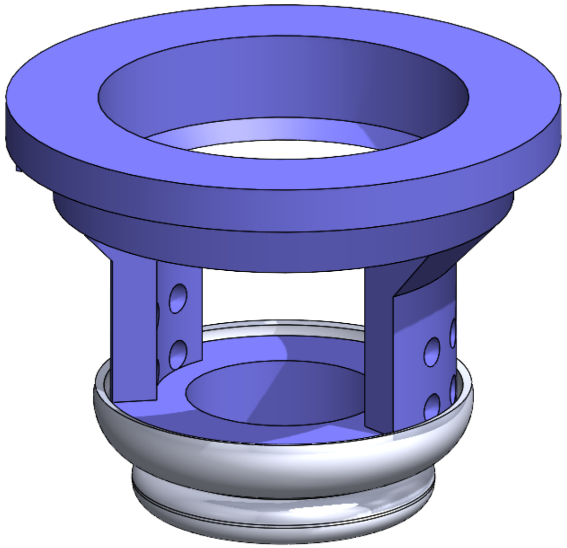
- Membrane presence dramatically changes flow patterns

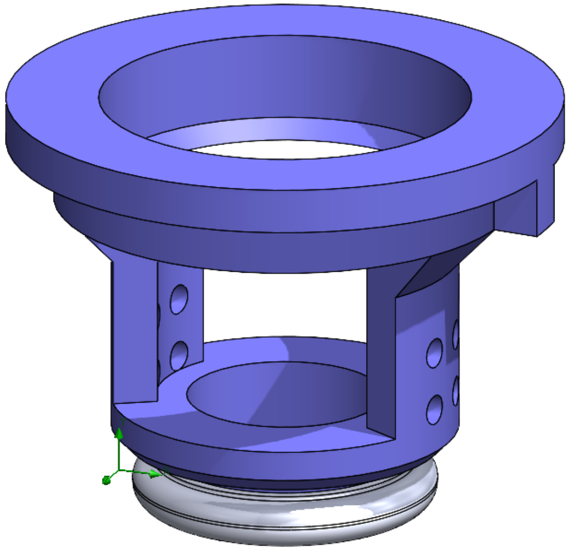




Initial Exploration

- Membrane flap length has no effect on membrane shear stress





Fluid Properties

Matching Simulation Conditions

<u>Initial Exploration Conditions</u>

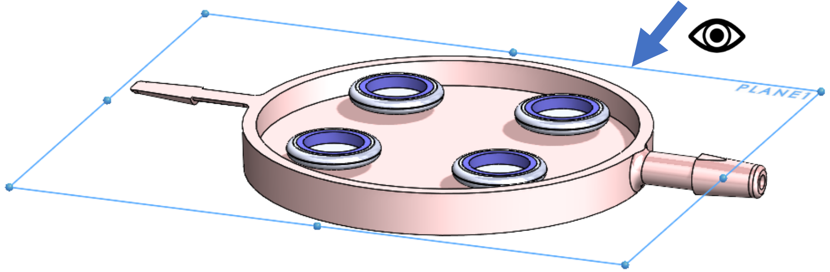
- Water
- 30 mL/min

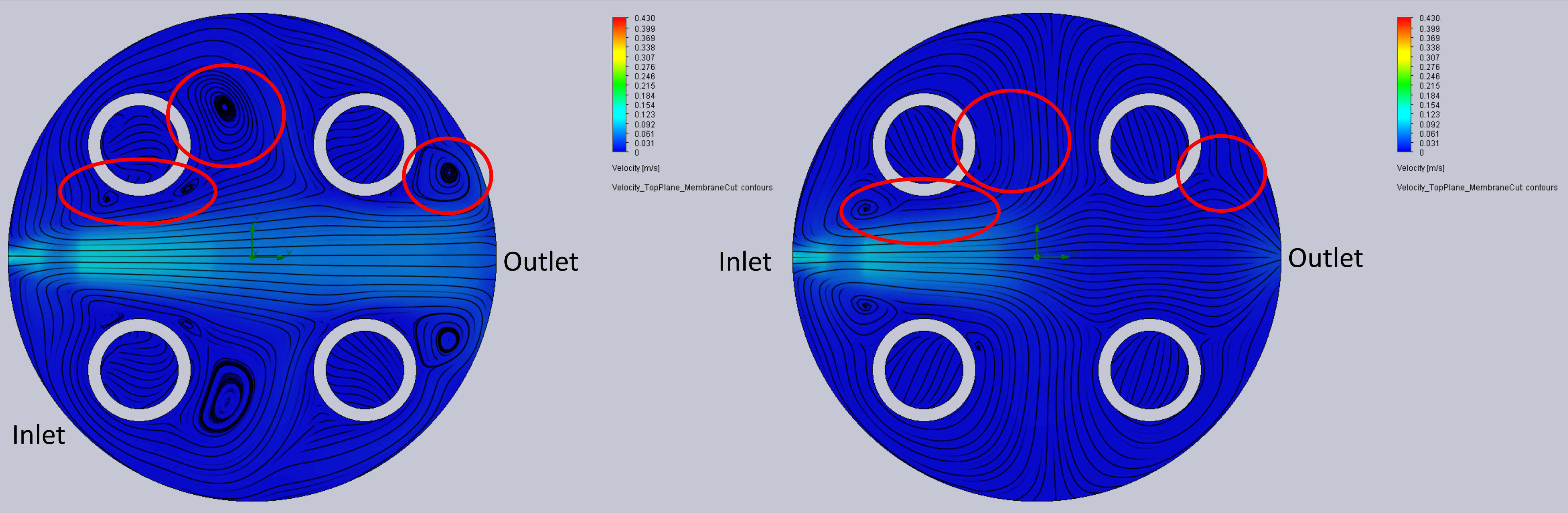
<u>Real-World Conditions</u>

- Custom perfusate
- 15.5 mL/min

Fluid Affects Flow Patterns

Top Cross Section through Membrane Sutures – Velocity



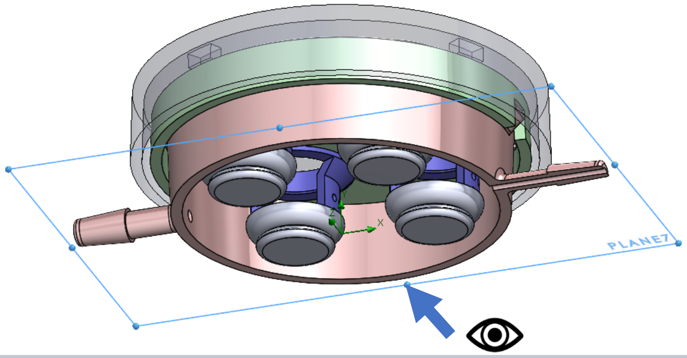


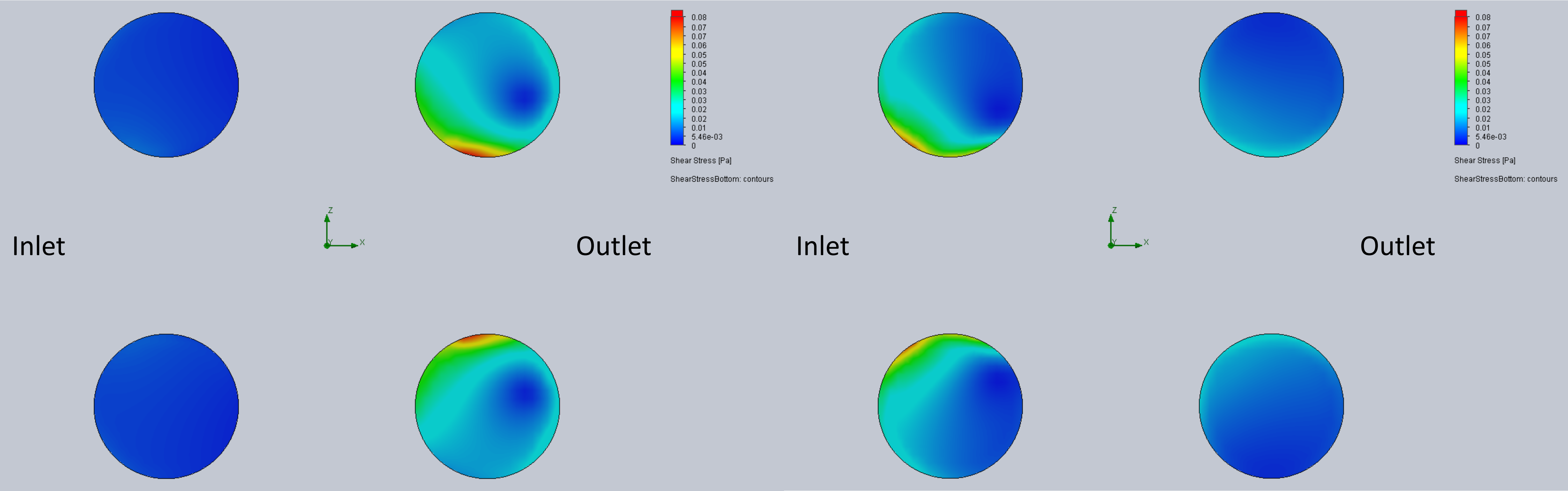
Water

Blood

Fluid Affects Shear Stress

Membrane Bottom Cross Section – Shear Stress



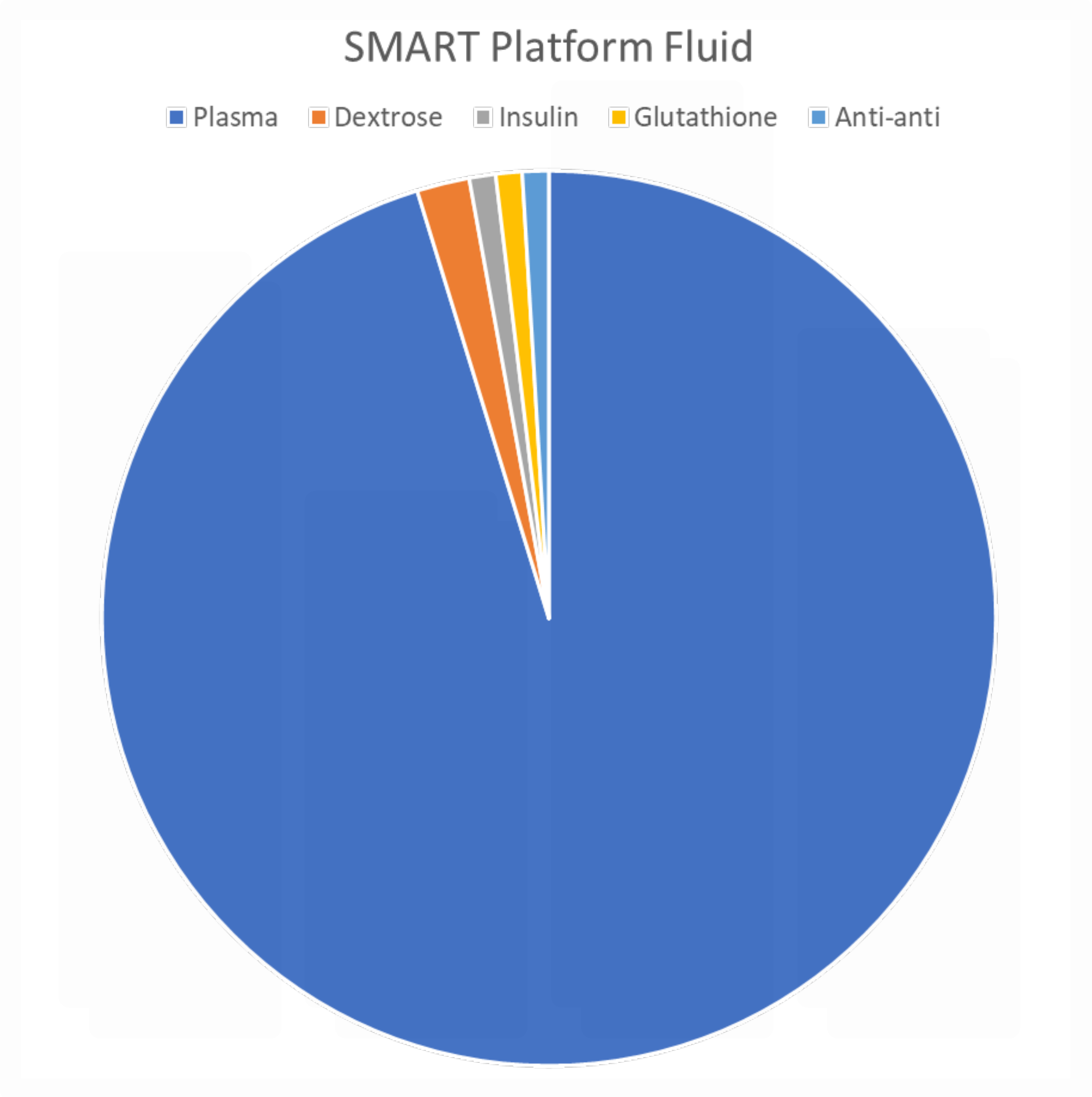


Water

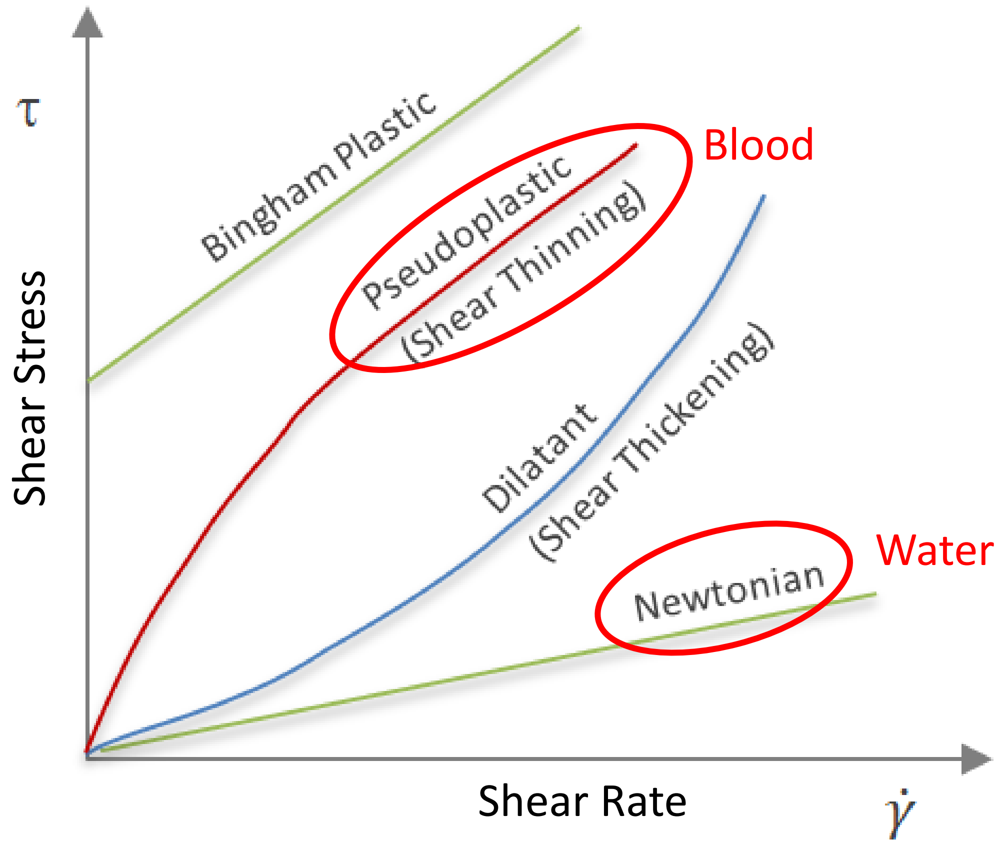
Blood

SMART Platform Fluid

- Plasma (13mL)
- Dextrose (260uL of 5%)
- Insulin (130uL of 100u/mL)
- Glutathione (130uL of 100mM)
- Anti-anti (130uL)



Modeling the Fluid



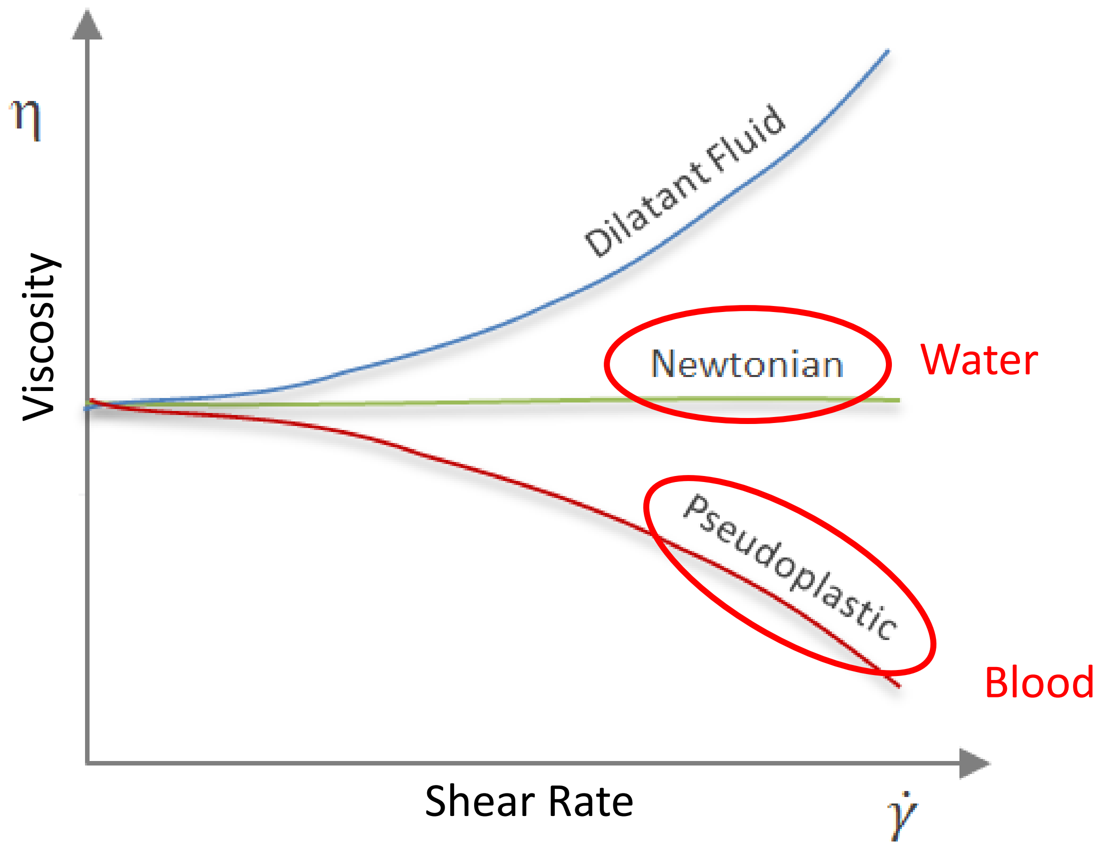


Image from polymerdatabase.com

Modeling Plasma

- Approximately 92% water
- Brust et al. (2013) found blood plasma is viscoelastic in elongational flows
- Varchanis et al. (2018) found that elastic nature of plasma dominates in flows with high shear and high extensional rates
  - Characteristic of microvasculature
- Behavior attributed to proteins
  - Poon (2020, BioRxiv preprint) notes that culture media with added proteins is also shear thinning

A Newtonian Plasma Model

Water

Name	Water
Comments	Properties of Water are taken on the Saturation line at T<0.9Tc
Density	(Table)
Dynamic viscosity	(Table)
Specific heat (Cp)	(Table)
Thermal conductivity	(Table)
Cavitation effect	☑
Radiation properties	☐

→

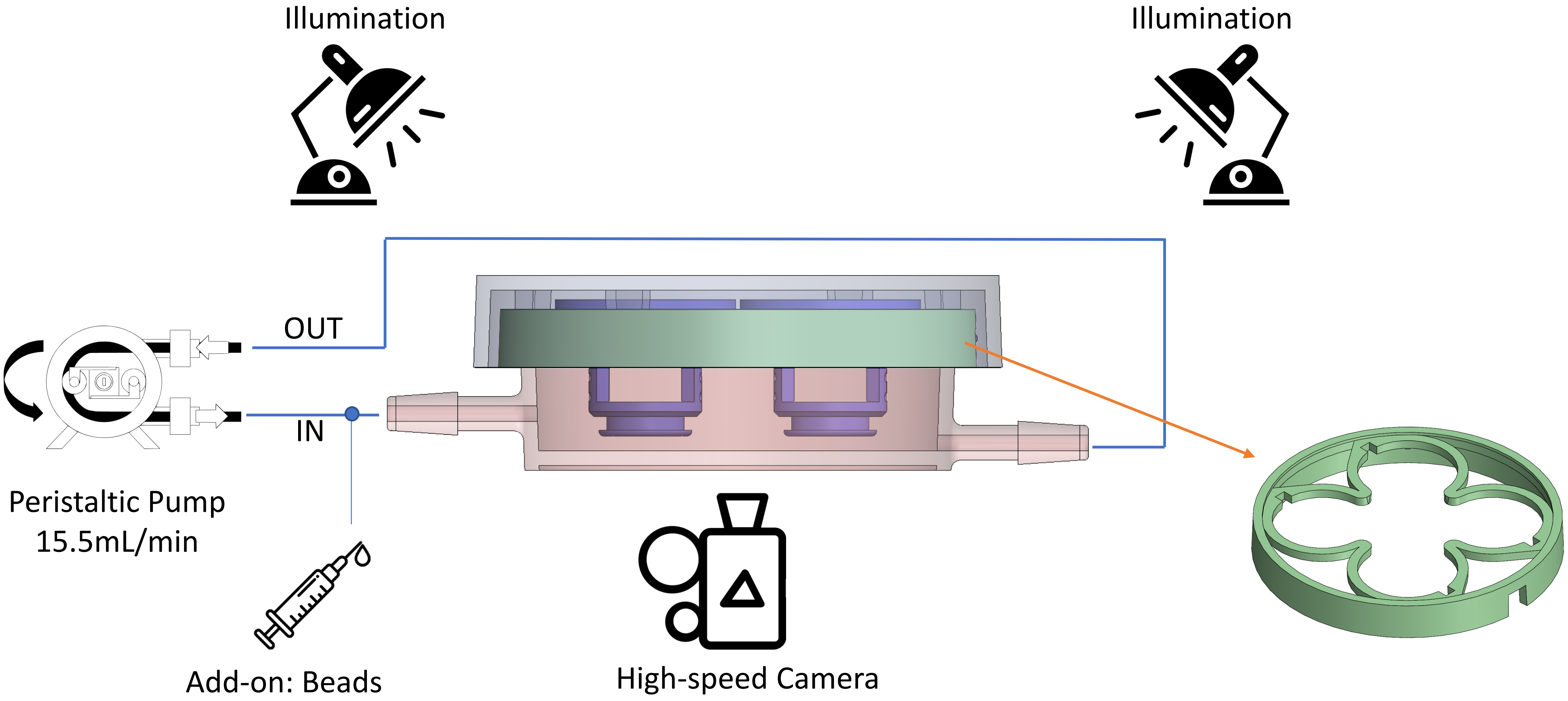
Newtonian Plasma

Name	Plasma (Newtonian)
Comments	
Density	1022.15 kg/m^3
Dynamic viscosity	0.00161 Pa*s
Specific heat (Cp)	3930 J/(kg*K)
Thermal conductivity	0.001365 W/(m*K)
Cavitation effect	☐
Radiation properties	☐

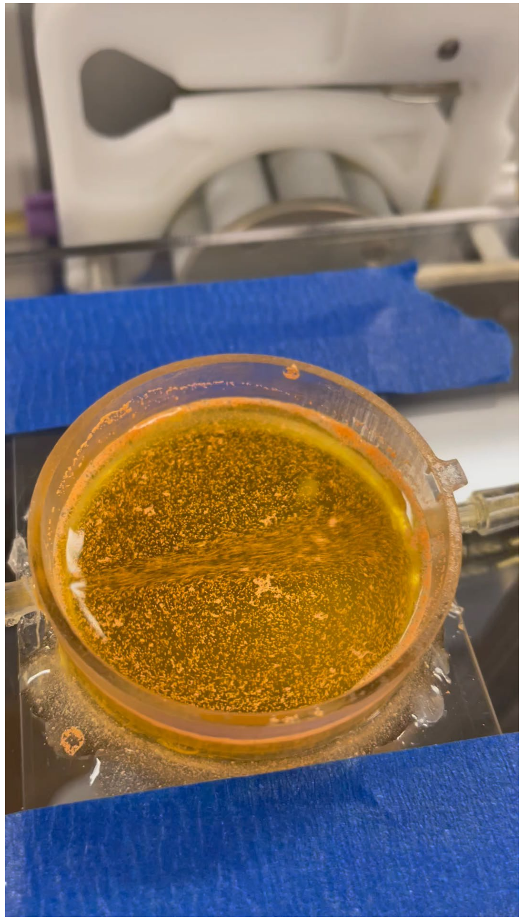
- Later measured density of perfusate to be 1.012 g/cm^3

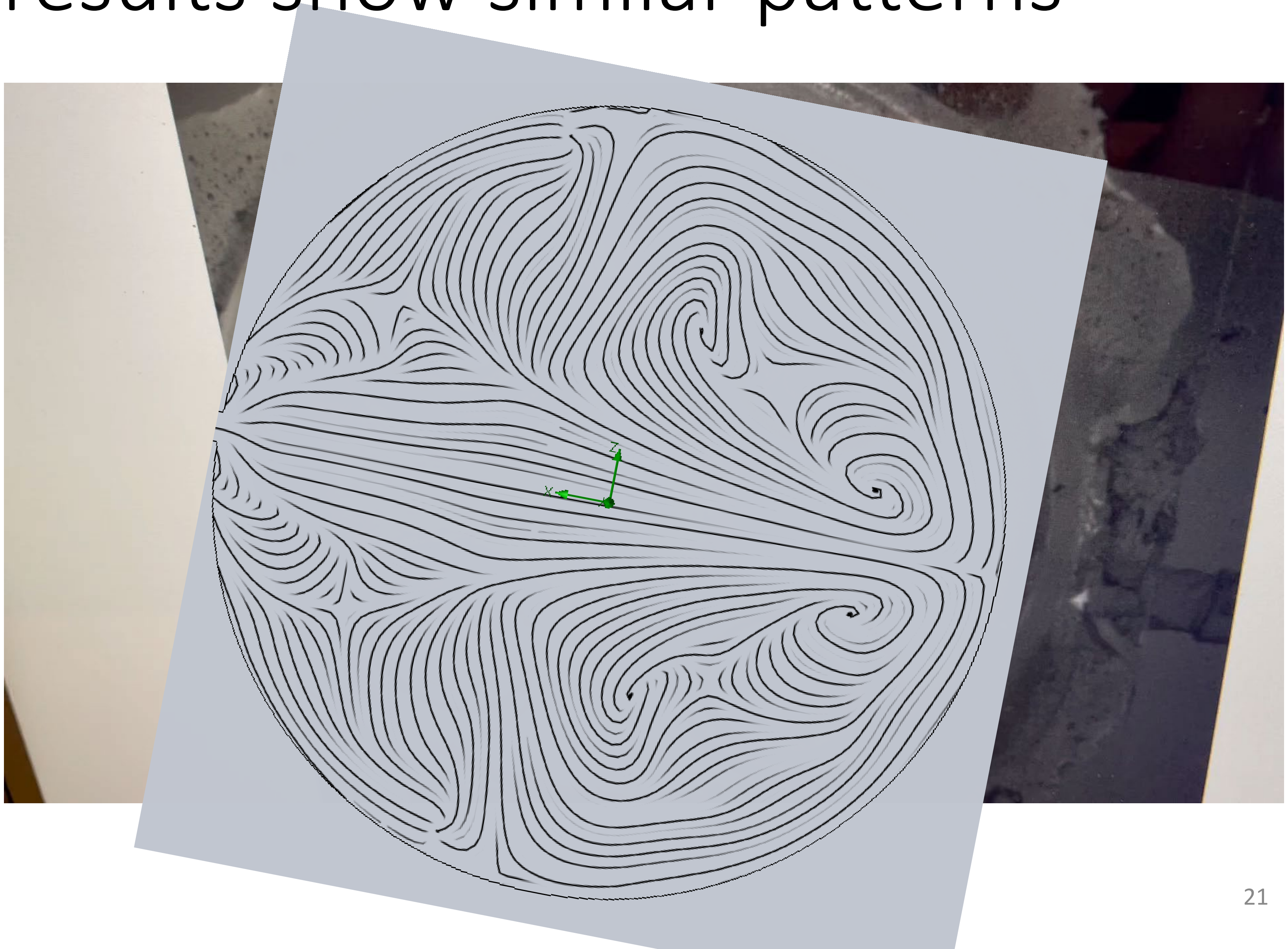
Experimental Validation of Flow

Flow Visualization Experimental Setup



Preliminary results show similar patterns





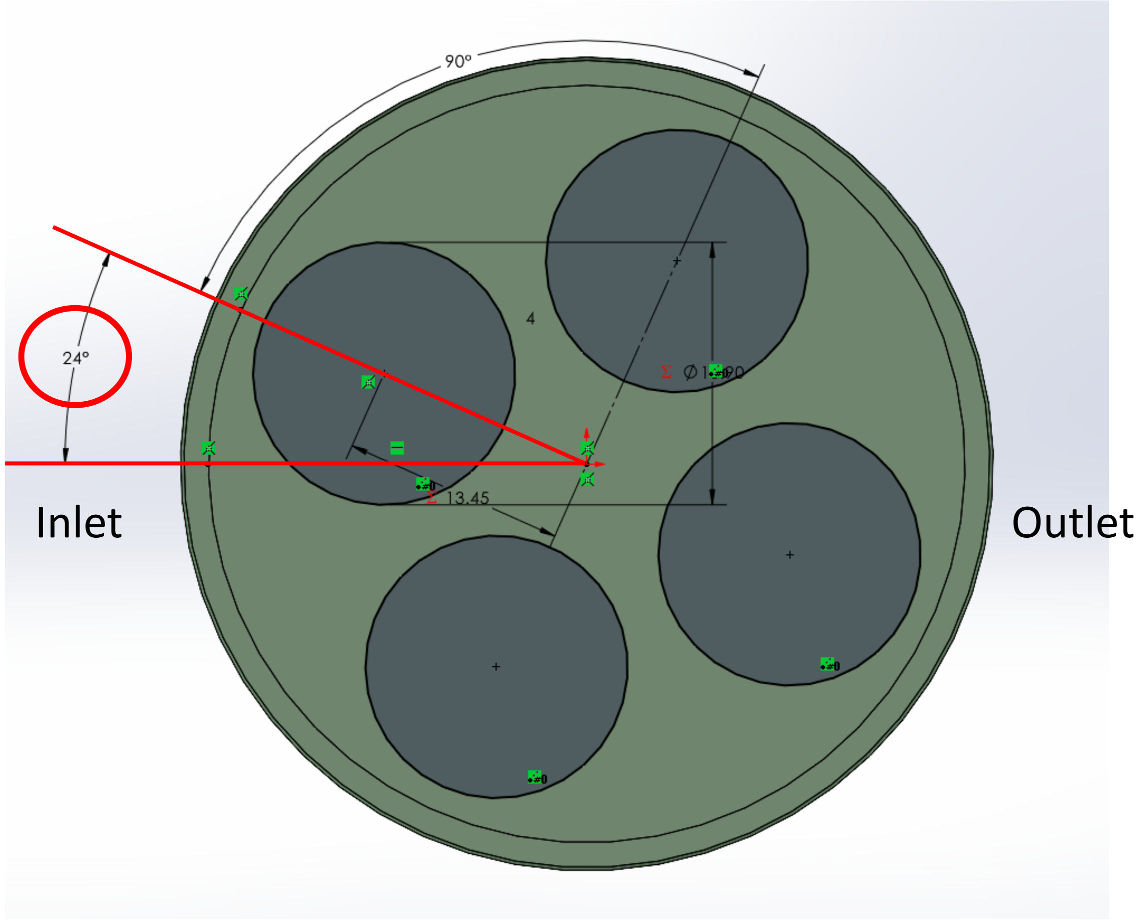
Shear Stress

Physiological shear stress is difficult to determine

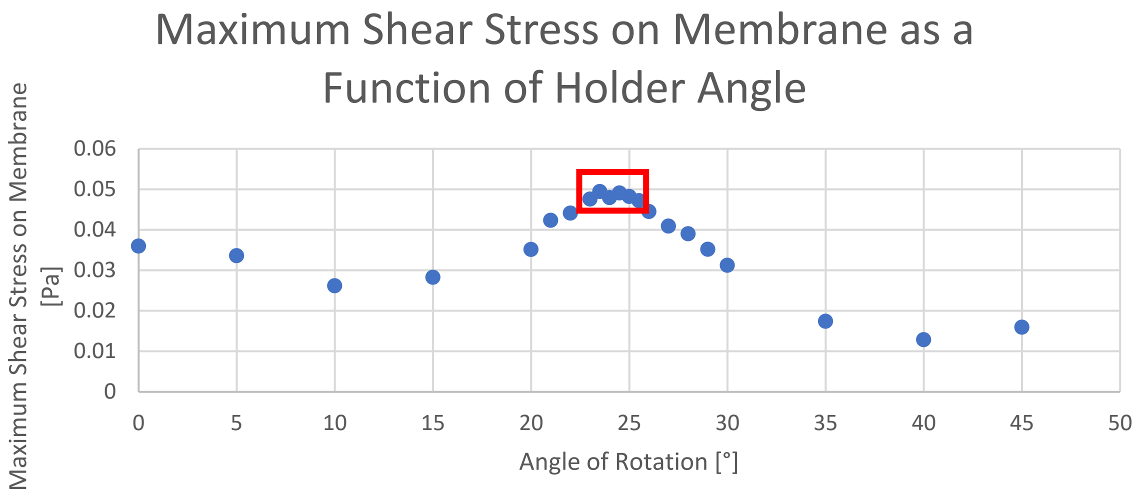
- Peritoneal cavity shear stresses have not been measured directly
- Hyler et al. (2018) estimate maximum physiological shear values do not exceed 0.5 Pa
  - Calculate shear stresses in their model to range from 0.013 Pa to 0.032 Pa
  - Note that shear stress at these levels effect healthy and cancerous tissue behavior
- Ip et al. (2016) claim physiological shear stress is below 0.01 Pa

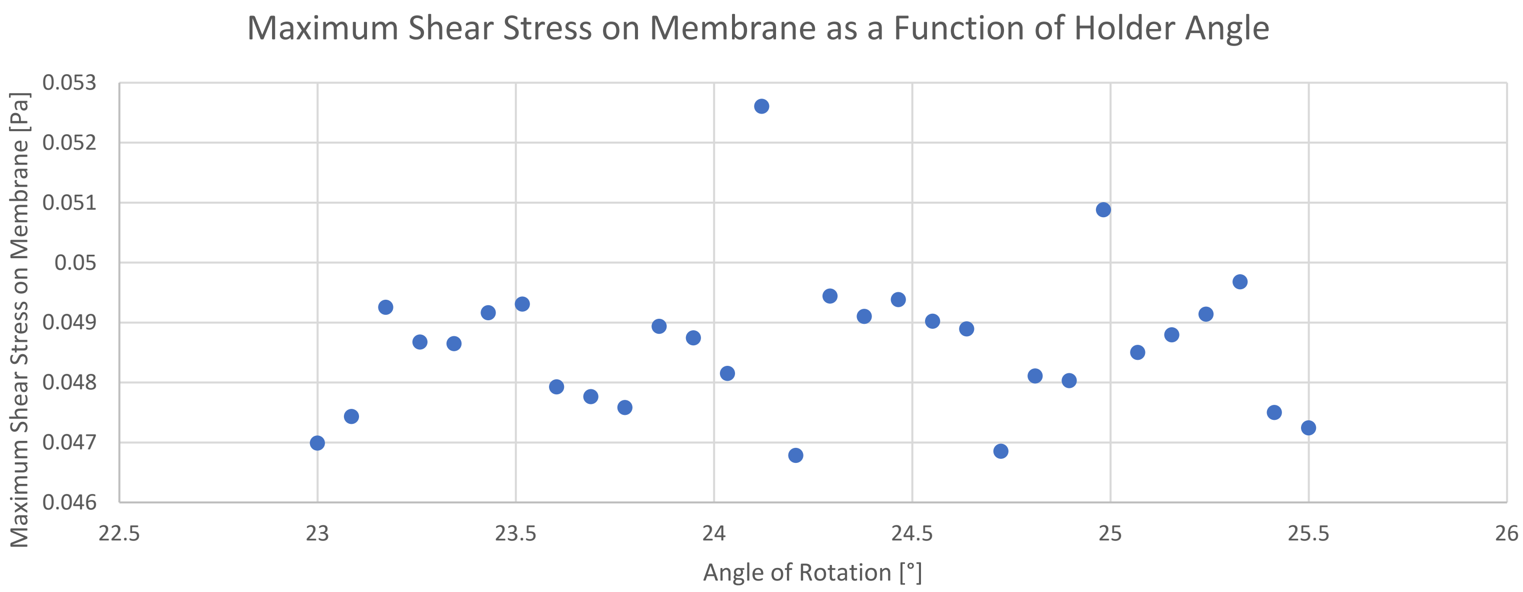
Maximum Shear Stress – A Parametric Study

- Find angle that provides maximum value of peak shear stress across bottom of membrane
- Iterative process
    - Values between 0° and 45°
    - Narrow window to steps of approximately 0.3°
- Tolerances
    - Manufacturing tolerance approximately 50-100μm
    - Notch for keeping lid in place allows approximately 0.3° of rotation to either side



Maximum Shear Stress – A Parametric Study





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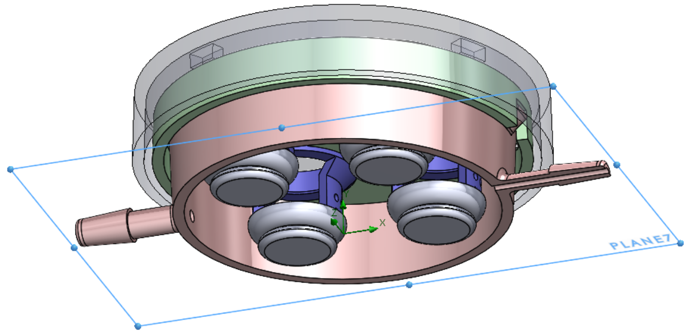
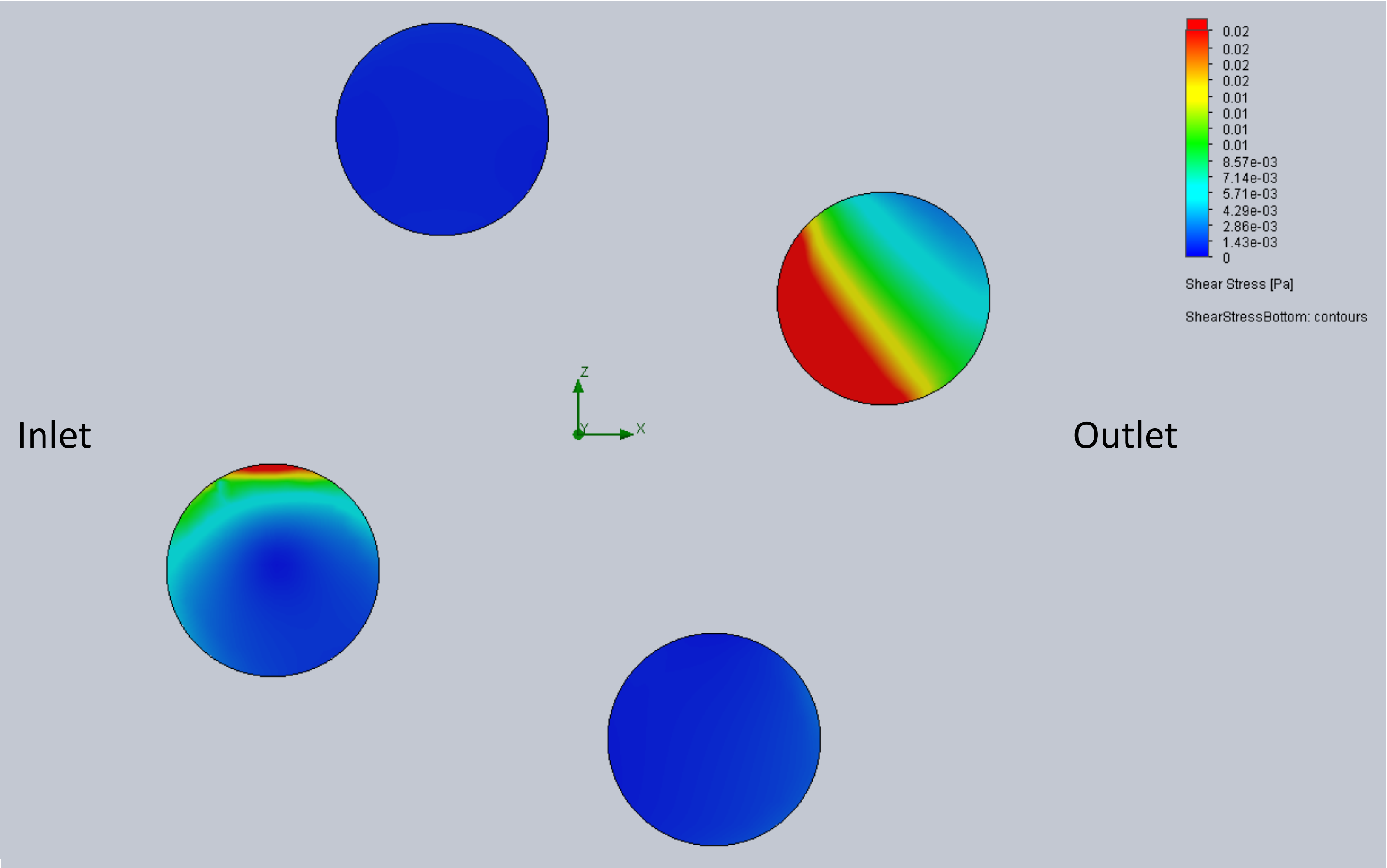
Calculated Shear Stress

Membrane Bottom Cross Section – Shear Stress

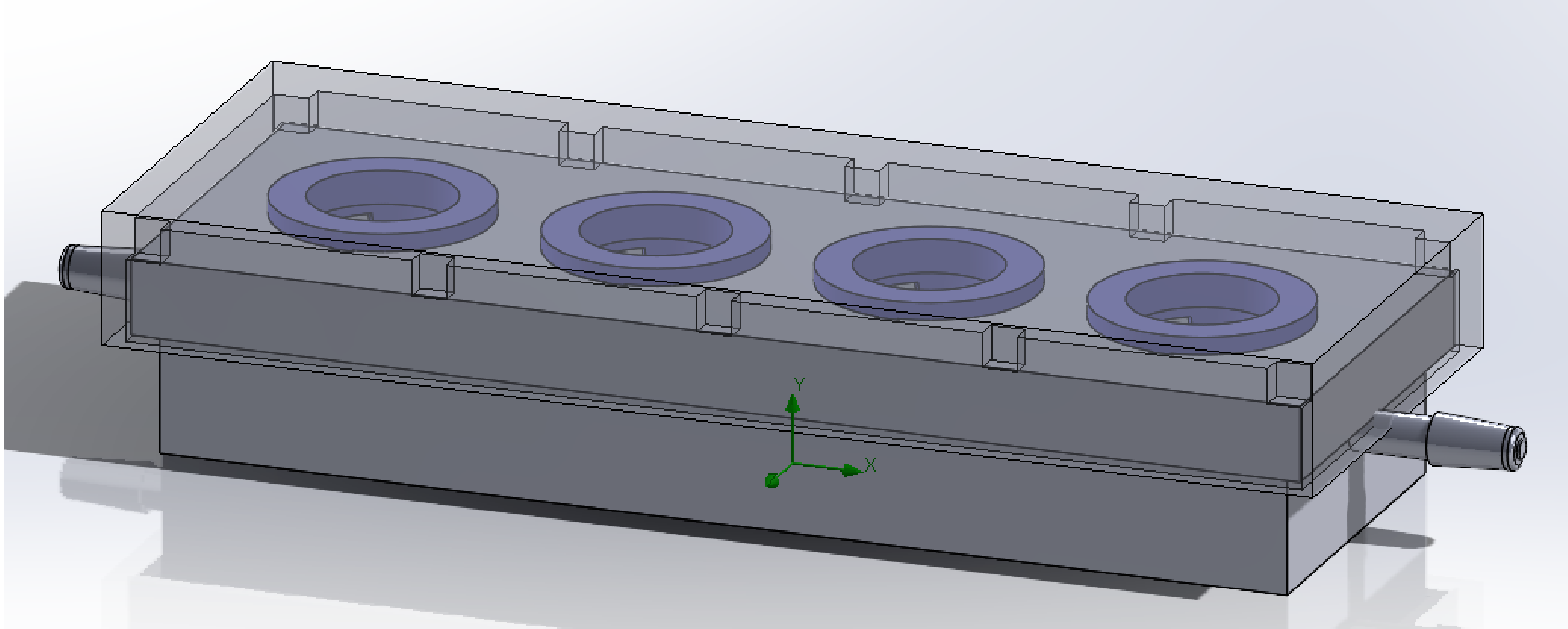




Conclusion and Next Generation

Next Generation SMART Platform

- Linear design for homogenous flow and shear stresses
- Preliminary modeling indicates shear stresses below 0.01 Pa



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Conclusions

- Constructed a Newtonian model of plasma as an approximation for SMART platform perfusate
- Computationally modeled flow patterns and shear stresses
  - Testing underway to validate computational models
  - Current design does not produce homogenous flow patterns
  - Current design does not produce homogenous shear stresses
    - Testing underway to determine if shear stresses are within a physiologically relevant range
- Proposed alternative design to meet homogenous flow and shear stress requirements

Acknowledgements

Thank you to all of our collaborators for their support and input, as well as their flexibility in collaborating in unprecedented times. Thank you also to Robert Lutz and the National Institute of Biomedical Imaging and Bioengineering for running the Biomedical Engineering Summer Internship Program.

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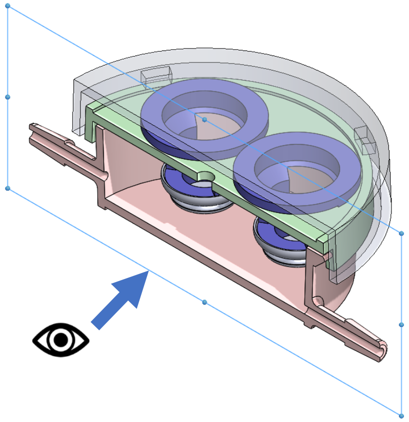
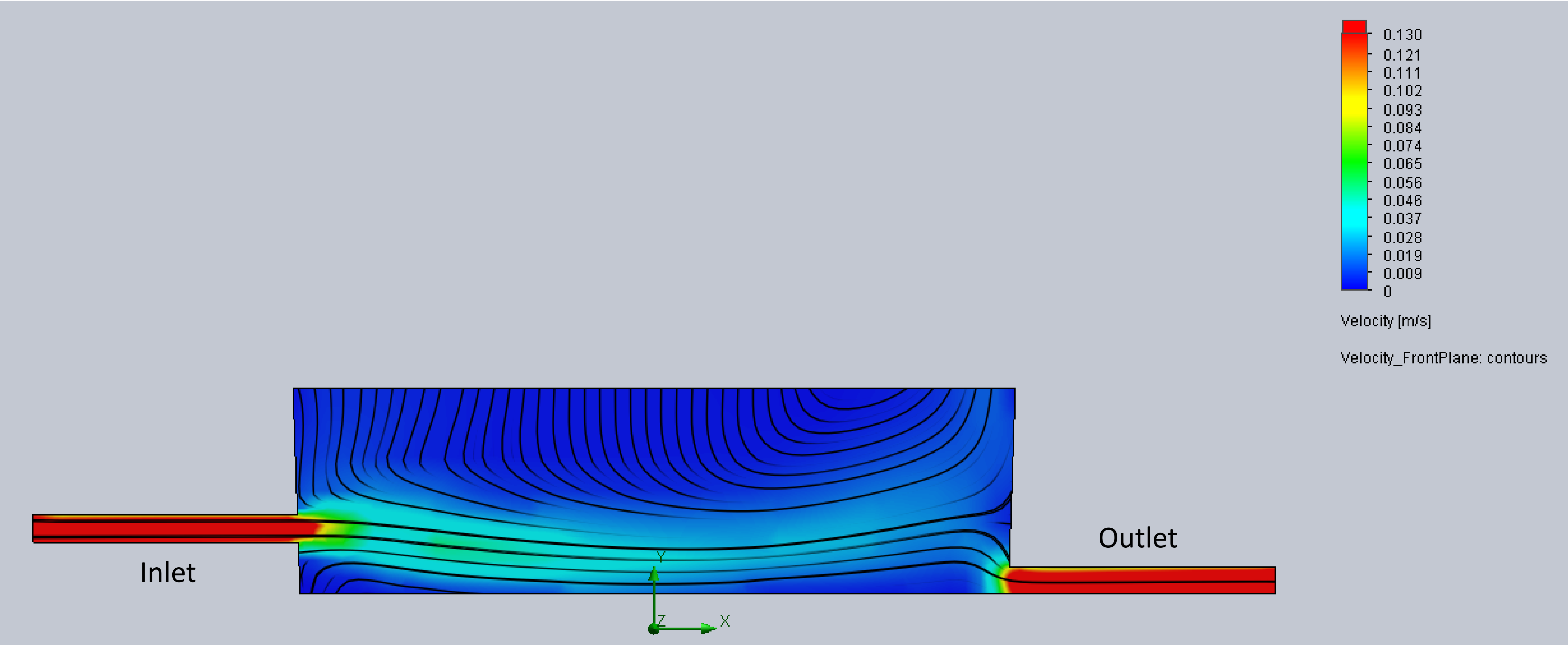
Effect of Fluid

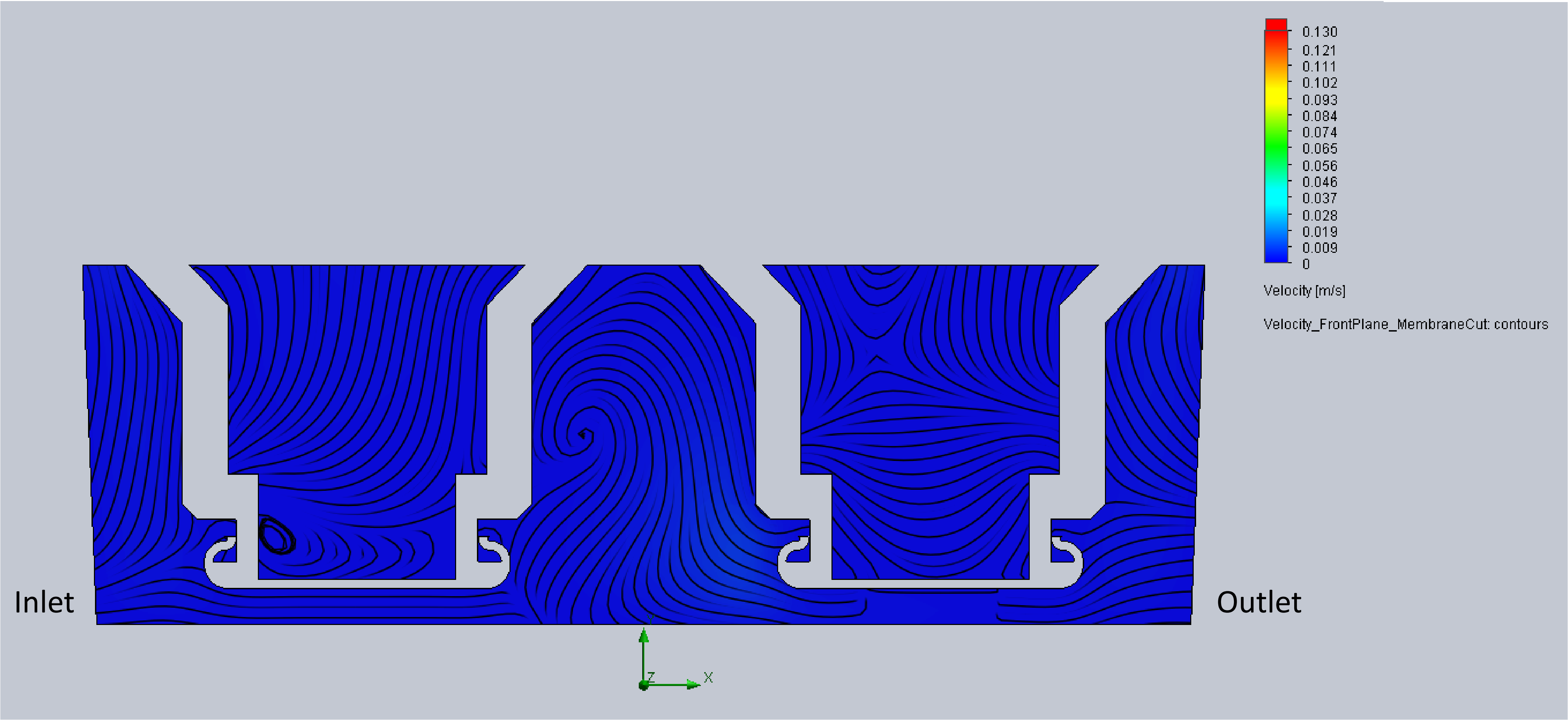
Lengthwise Cross Section through Center – Velocity

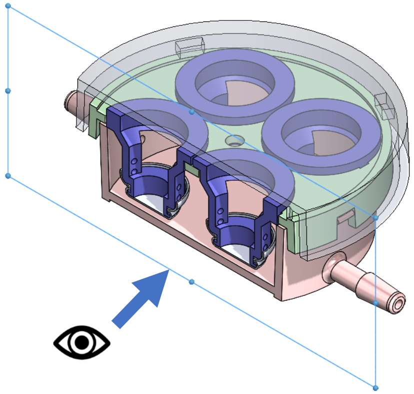




Effect of Fluid

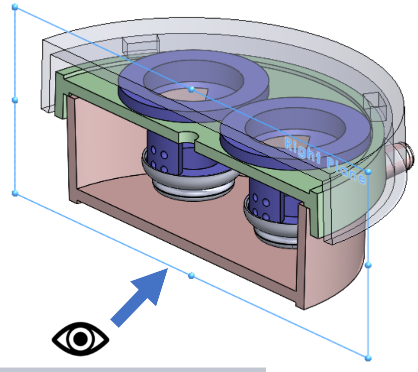
Lengthwise Cross Section through Holders – Velocity

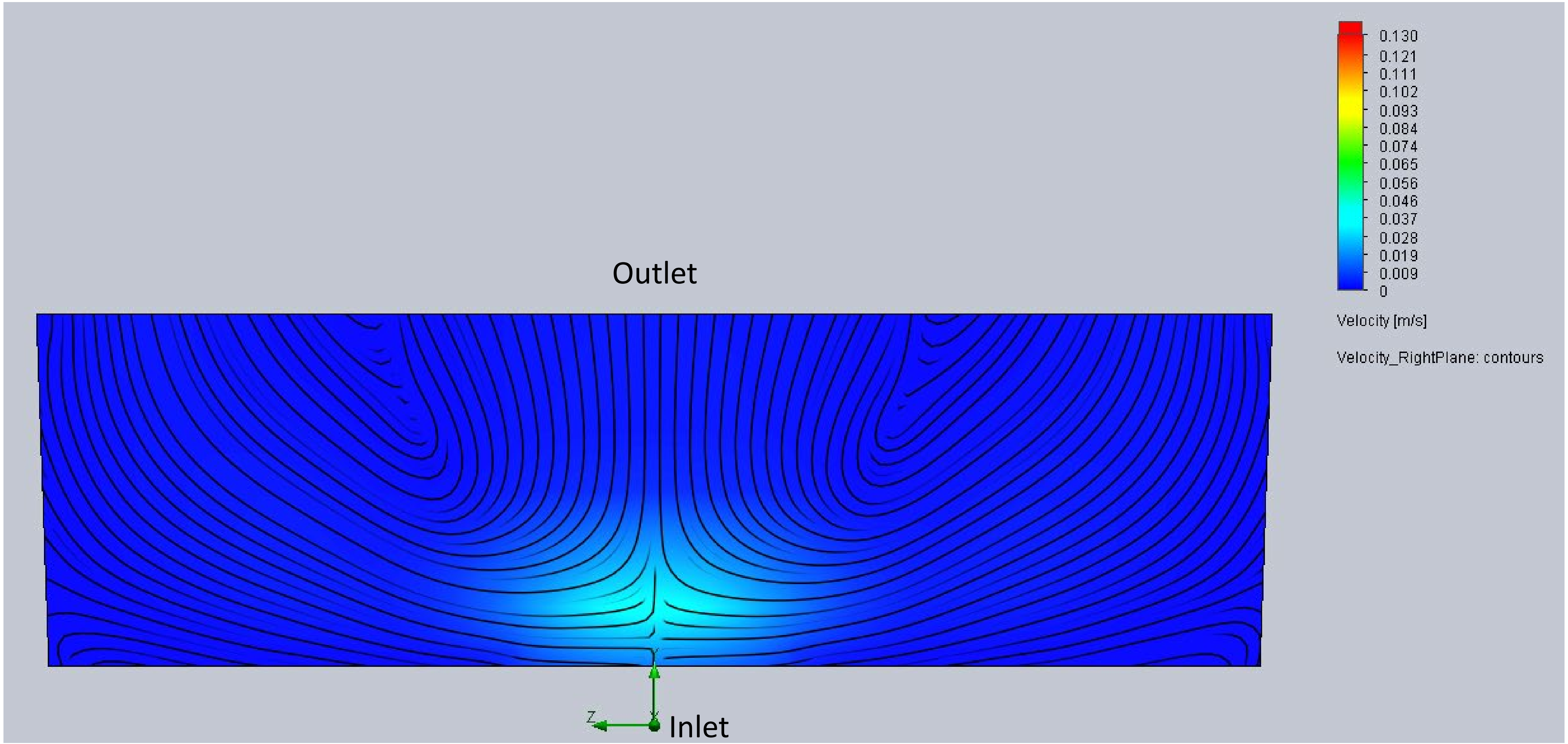




Effect of Fluid

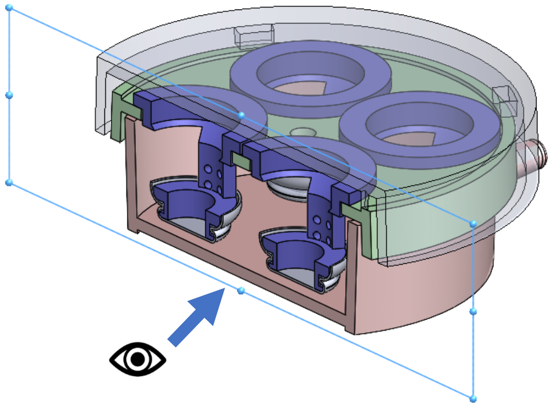
Widthwise Cross Section through Center – Velocity

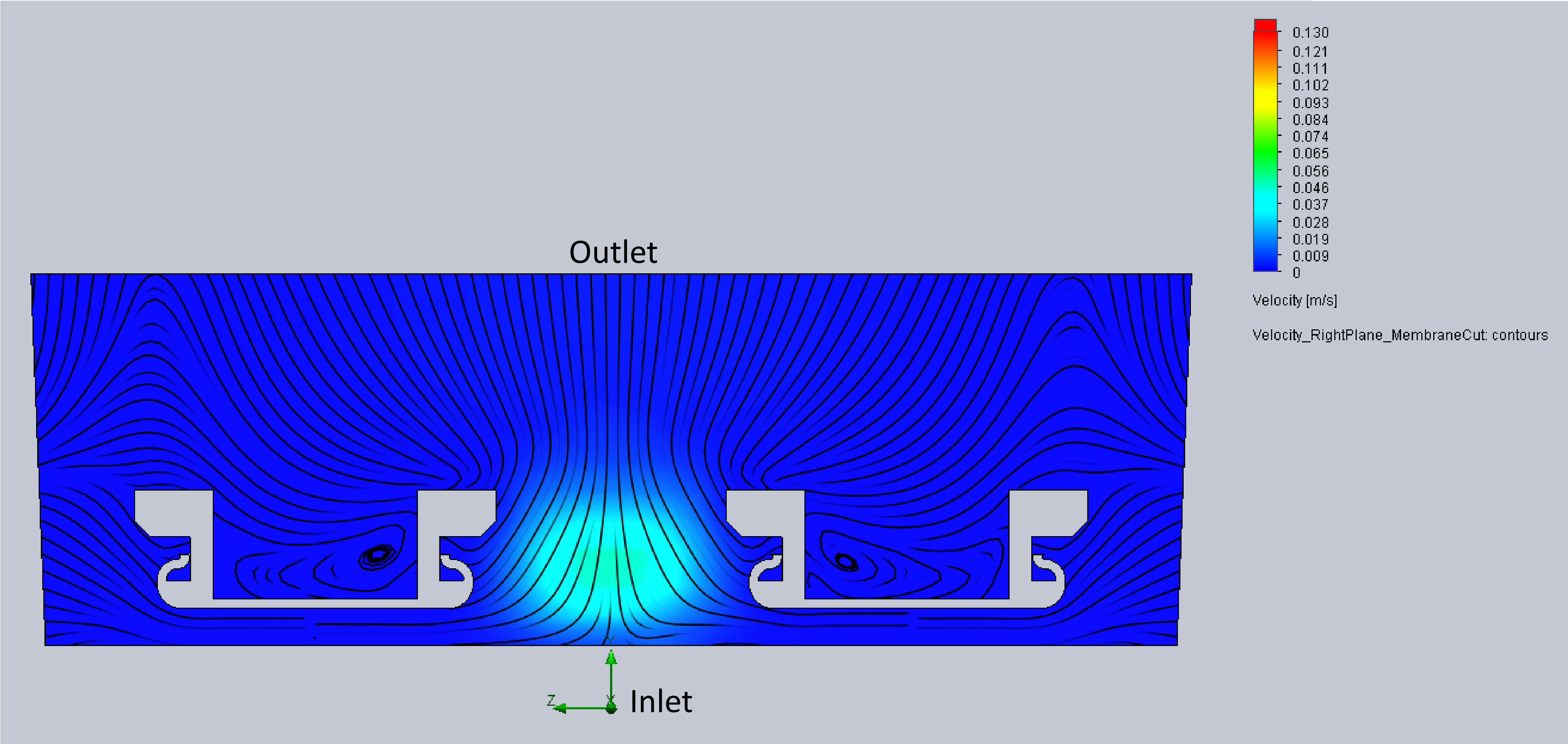




Effect of Fluid

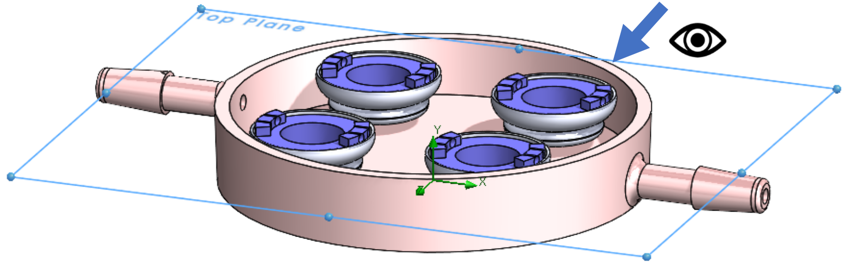
Widthwise Cross Section through Holders – Velocity

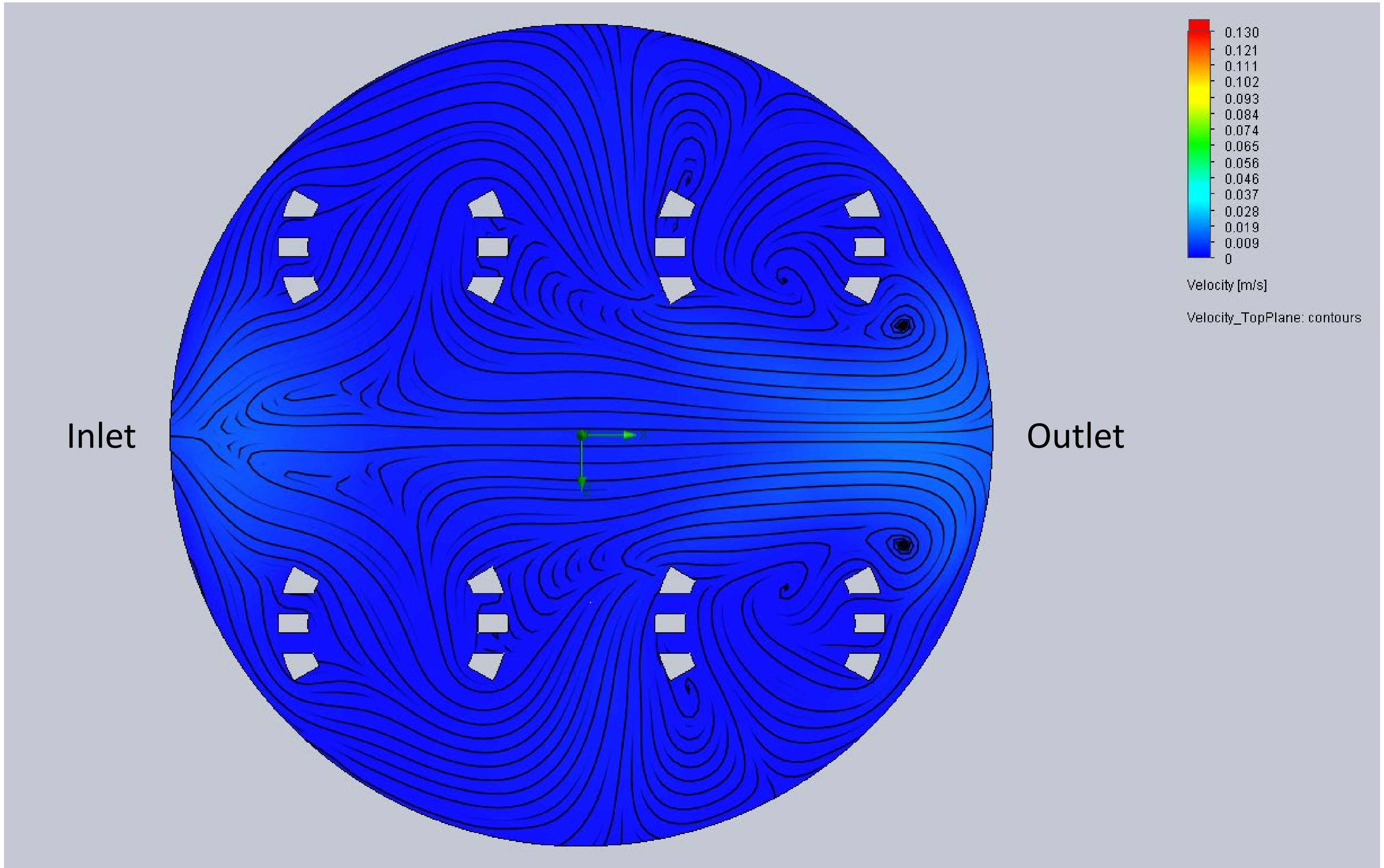




Effect of Fluid

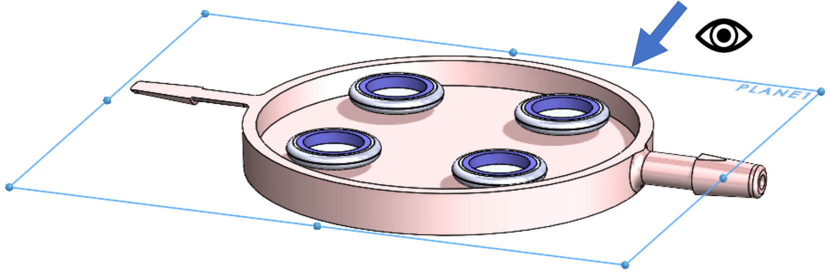
Top Cross Section through Holder Holes – Velocity



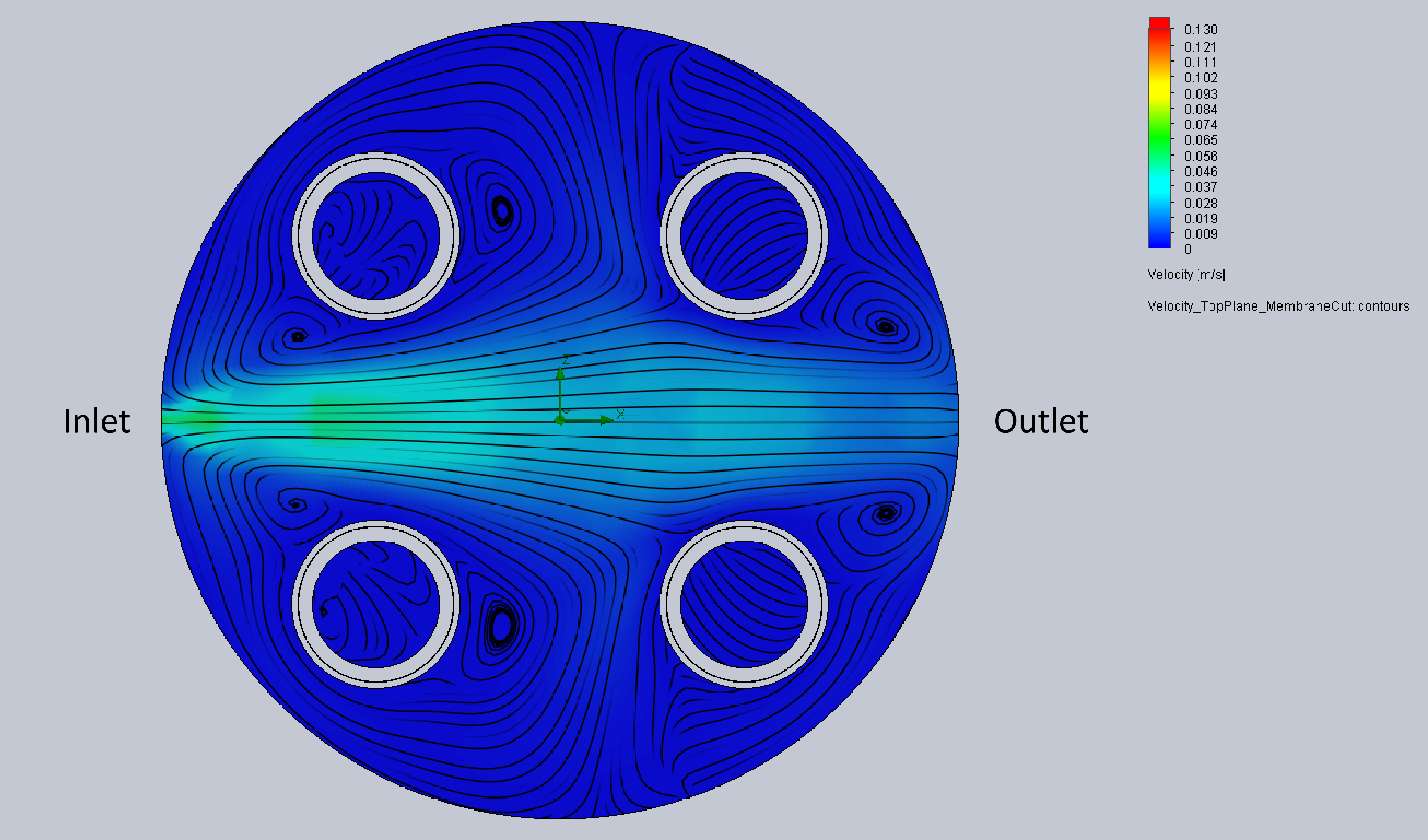


Effect of Fluid

Top Cross Section through Membrane Sutures – Velocity



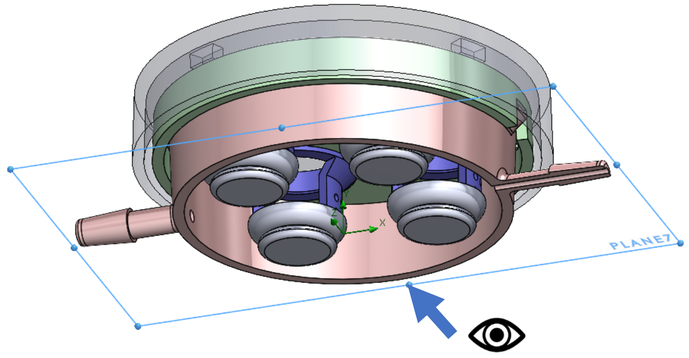
Inlet

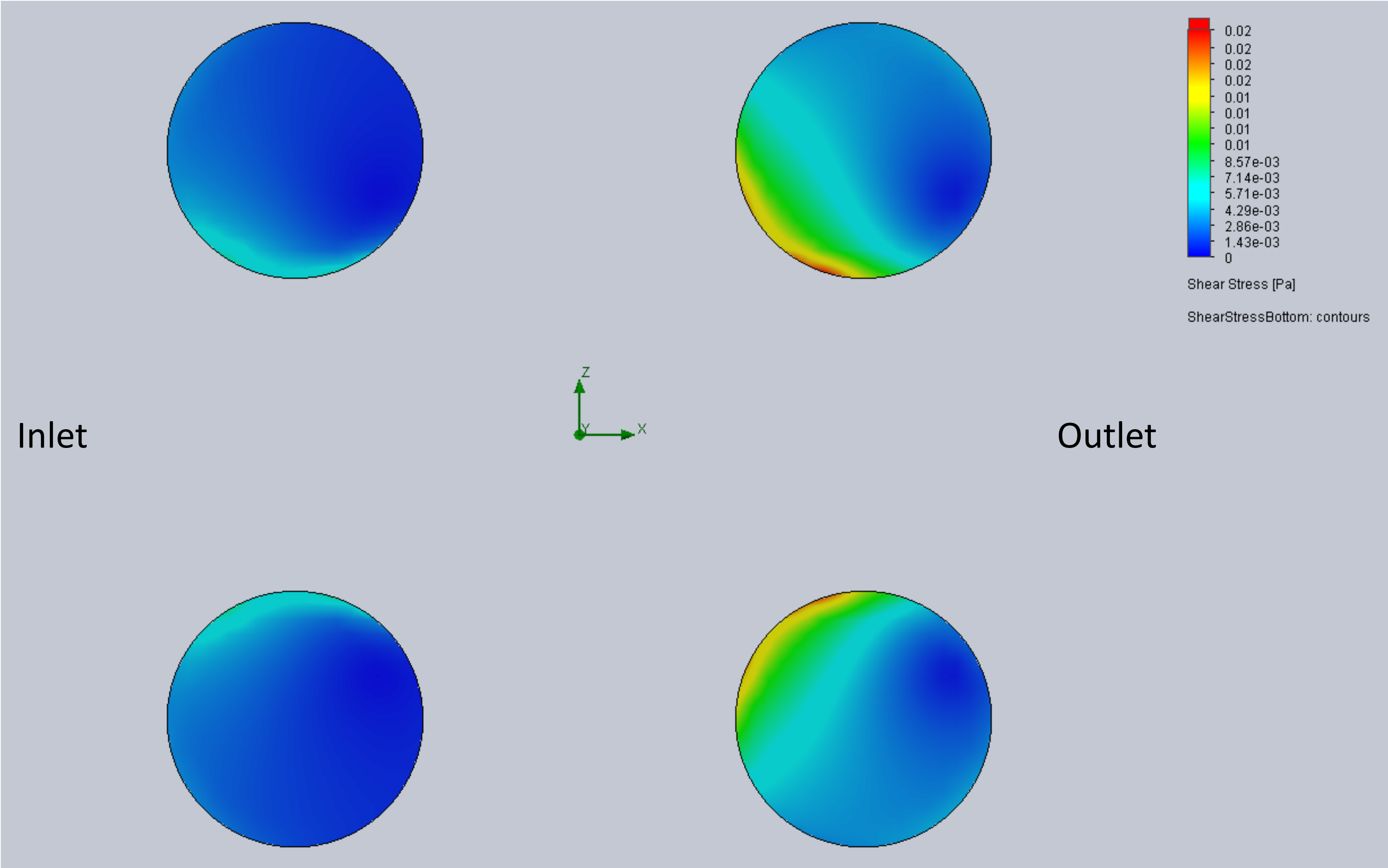


Outlet

Effect of Fluid

Membrane Bottom Cross Section – Shear Stress





Effect of Fluid

Membrane Top Cross Section – Shear Stress