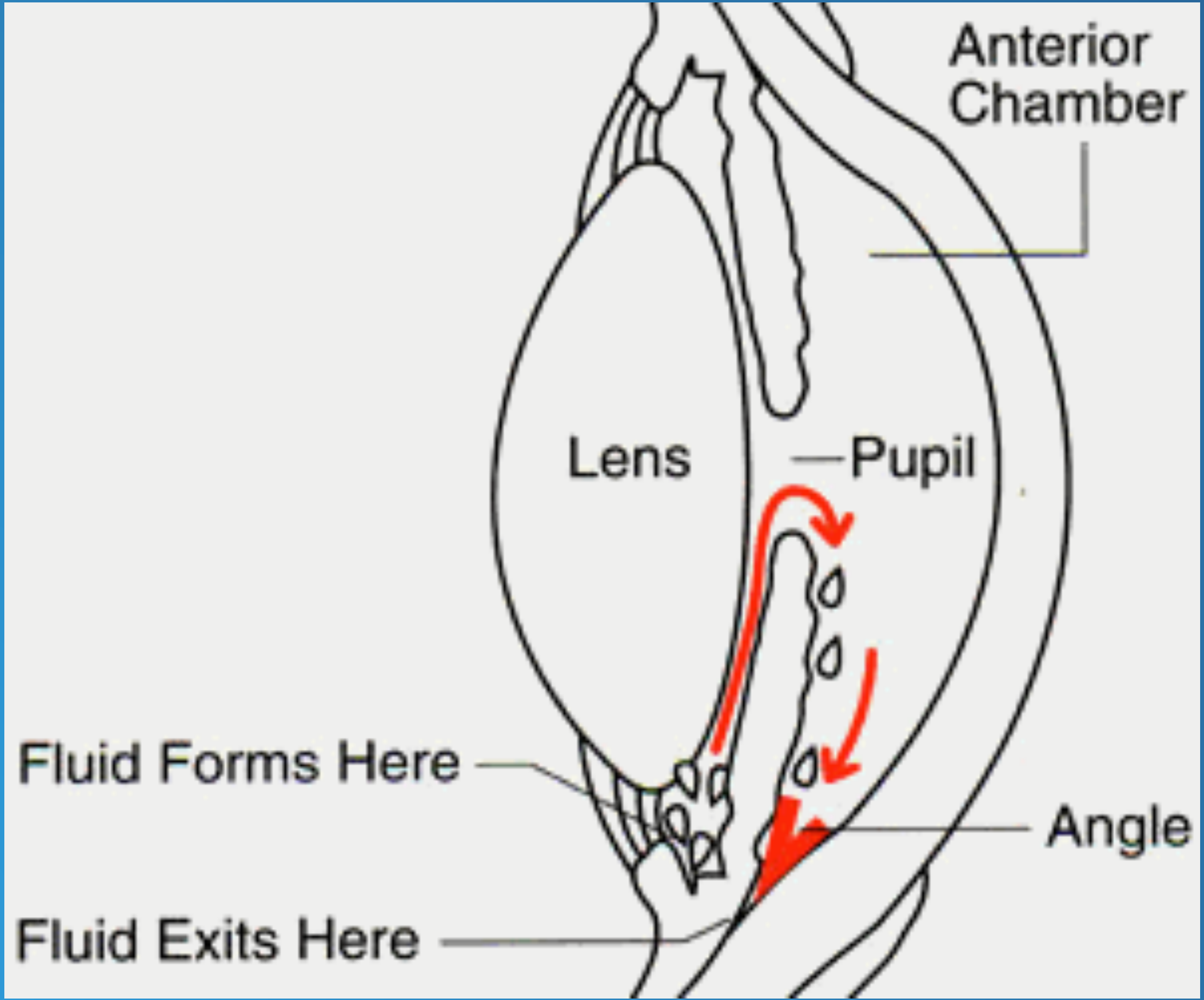
Introduction to Problem

- Glaucoma: 2nd leading cause of blindness in the world
- Risk factor for developing glaucoma:
    - high intraocular pressure (IOP) - regulated by aqueous humor flow in anterior chamber
- Strong correlation between those with diabetes and developing glaucoma

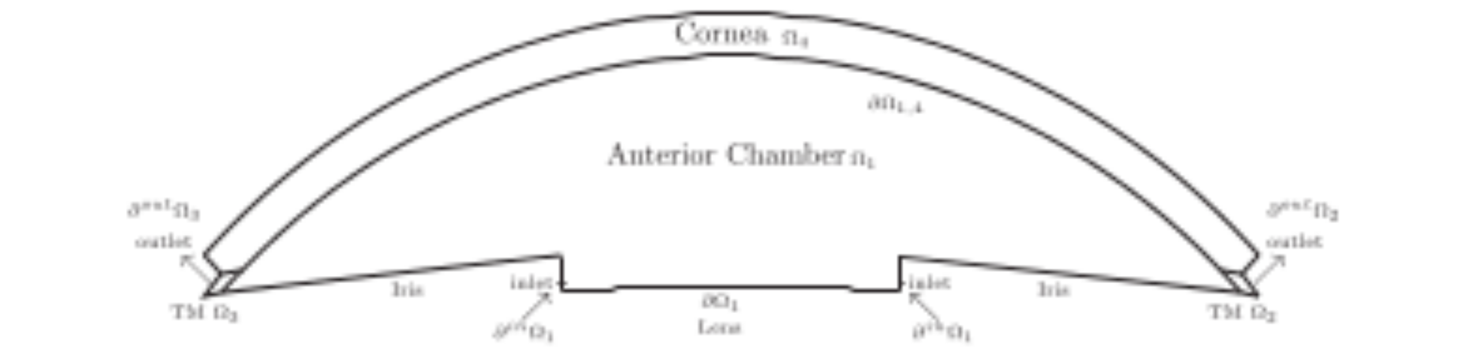

Anterior Chamber
Lens
Pupil
Fluid Forms Here
Angle
Fluid Exits Here

Open-angle Glaucoma

- Open-angle glaucoma is the more common form of glaucoma (90% of glaucoma patients)
- Results when resistance to outflow increases due to obstructions in the trabecular meshwork and Schlemm's canal
- Normal IOP is considered to be within the range of 1500 Pa to 2900 Pa (glaucoma.org)

Previous Models

- 2-D Model:
  - Developed by J.A. Ferreira et. al (2014)
  - Models pressure in relation to increased resistance in Trabecular Meshwork/Schlemm's Canal
  - Does not account for buoyancy-driven flow



J.A. Ferreira et. al.

- Equations:
  - System 1 applies to anterior chamber (Navier-Stokes)
  - System 2 applies to Trabecular Meshwork/Schlemm's canal (Darcy's Law)

$$\begin{cases} \rho \frac{\partial \mathbf{v}}{\partial t} - \nabla \cdot \mu(\nabla \mathbf{v} + (\nabla \mathbf{v})^T) + \rho(\mathbf{v}.\nabla)\mathbf{v} + \nabla p = 0 \quad \text{in } \Omega_1, t > 0, \\ \nabla.\mathbf{v} = 0 \quad \text{in } \Omega_1, t > 0. \end{cases} \tag{1}$$

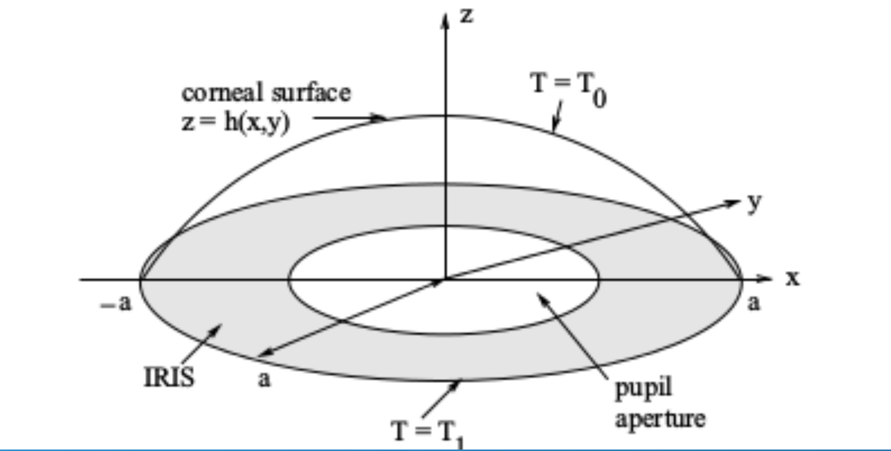
$$\begin{cases} \mathbf{v} = -\frac{K}{\mu} \nabla p \quad \text{in } \Omega_2, \Omega_3, t > 0, \\ \nabla.\mathbf{v} = 0 \quad \text{in } \Omega_2, \Omega_3, t > 0. \end{cases} \tag{2}$$

Results

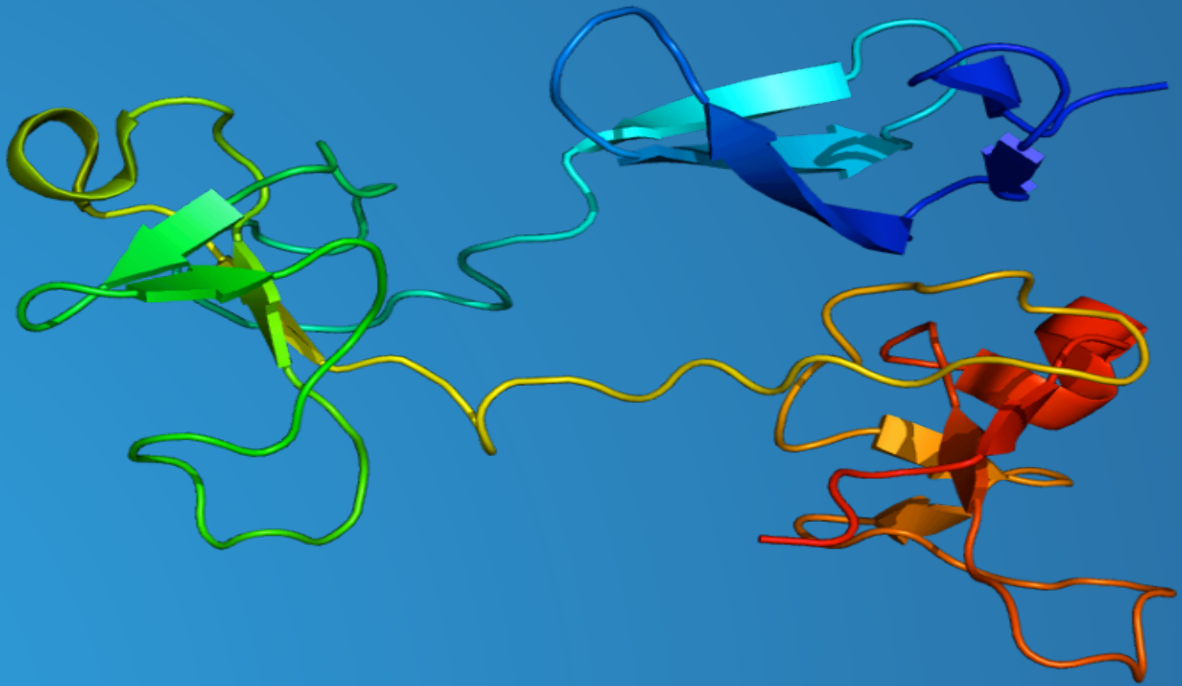
Porosity (ϵ)	Permeability (m^2) of TM	Pressure in anterior chamber (Pa)
0.4	7.59×10^{-14}	1271
0.3	2.35×10^{-14}	1429
0.25	1.19×10^{-14}	1655
0.225	8.09×10^{-15}	1867
0.2	5.33×10^{-15}	2211
0.175	3.36×10^{-15}	2805
0.15	1.99×10^{-15}	3905
0.125	1.09×10^{-15}	6154
0.1	5.27×10^{-16}	11437

Previous Models

- 3-D Model:
  - Developed by Fitt and Gonzalez (2006)
  - Buoyancy-driven flow
  - Excludes Trabecular Meshwork/Schlemm's Canal



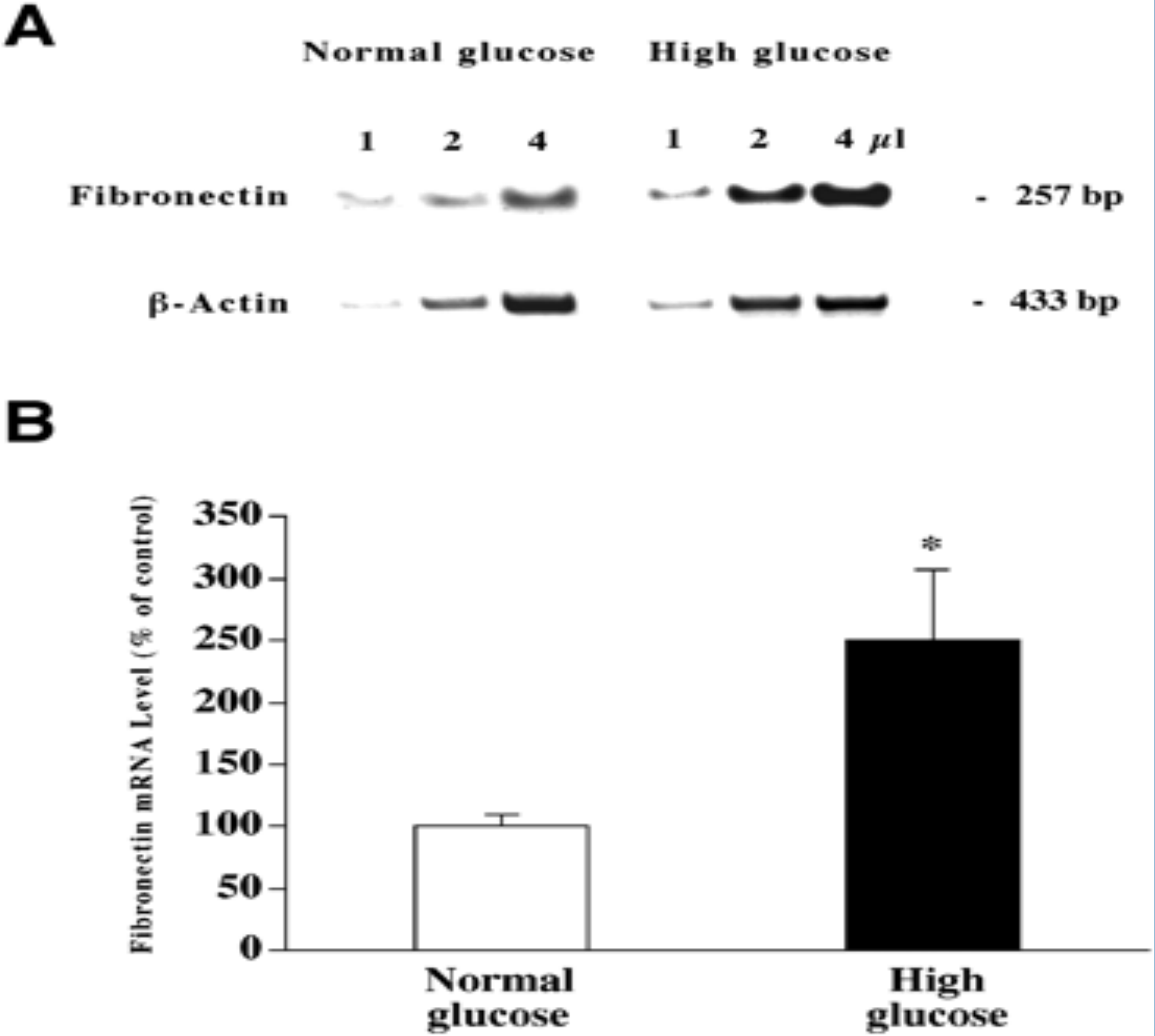
Fibronectin



http://en.wikipedia.org/wiki/Fibronectin

Fibronectin

- Serves as linker in Extracellular Matrices
  - ...like the one found in the Trabecular Meshwork
- Studies have found increased glucose concentration results in a higher rate of fibronectin production (Roy, Sayon and Tsuyoshi Sato, 2002)
- “These findings indicate that a high glucose level in aqueous humor of patients with diabetes may increase fibronectin synthesis and accumulation in trabecular meshwork and accelerate the depletion of trabecular meshwork cells…”


A
Normal glucose
High glucose
1
2
4
1
2
4 μl
Fibronectin
β-Actin
- 257 bp
- 433 bp
B
Fibronectin mRNA Level (% of control)
350
300
250
200
150
100
50
0
*
Normal glucose
High glucose

Objectives

- **Model IOP under different glucose concentrations in aqueous humor**
- Compare results of commercial and academic software
- Develop parallel code to solve equations in model

Method & Equations

- Flow of AH in anterior chamber simulated using modified Navier-Stokes equations:

$$\rho\bar{v} \cdot \nabla \bar{v} = -\nabla p + \mu \nabla^2 \bar{v} + \rho_0 \bar{g} \beta (T - T_{ref})$$

$$\nabla \cdot \bar{v} = 0$$

$$\rho C_p \bar{v} \cdot \nabla T = k \nabla^2 T$$

- Flow in Trabecular Meshwork/Schlemm's canal:

$$\alpha = \frac{\mu}{\Delta p} \Delta e \bar{v} - f(g_c)$$

Finite Element Method

- No guarantee for solution to 3D Navier-Stokes
- Solve using numerical methods
- Split geometry up into discrete set of cells
    - creates a mesh
- Galerkin method
    - converts PDEs to system of linear equations

Parameters

Parameter	Value
Initial Velocity	1.2 mm/s
Outlet Pressure	1200 Pa
Reference Temperature	22 C
Aqueous Humor Density	1000 kg/m3
Aqueous Humor Viscosity	0.001 kg/(ms)
Aqueous Humor Specific Heat	4182 J/(kgK) [water property]
Aqueous Humor Thermal Conductivity	0.6 W/ (mK)
Glucose Concentration	99.1001 mg/dL (healthy eye); 144.1456 mg/dL (type 2 diabetic eye)

Hardware and Software

- Hardware:
  - Star1
  - Darter
- Software:
  - Deal.II - FEM software library
  - Cubit - mesh generator
  - COMSOL Multiphysics Tool

COMSOL

- multi-physics simulation tool:
  - 2D
    - gives a basic understanding of fluid flow in eye
  - 2D - axis-symmetry
    - perform simulation in 2D but create 3D result based on that
  - 3D
    - slow, but most accurate simulation of fluid flow

Deal.II

- C++ FEM software library
- Step-35:
  - Standard Navier-Stokes flow
  - Modified to incorporate 2D mesh generated in Cubit
- 3D simulations:
  - Simulations are too slow
  - Modify to make parallel

Deal.II

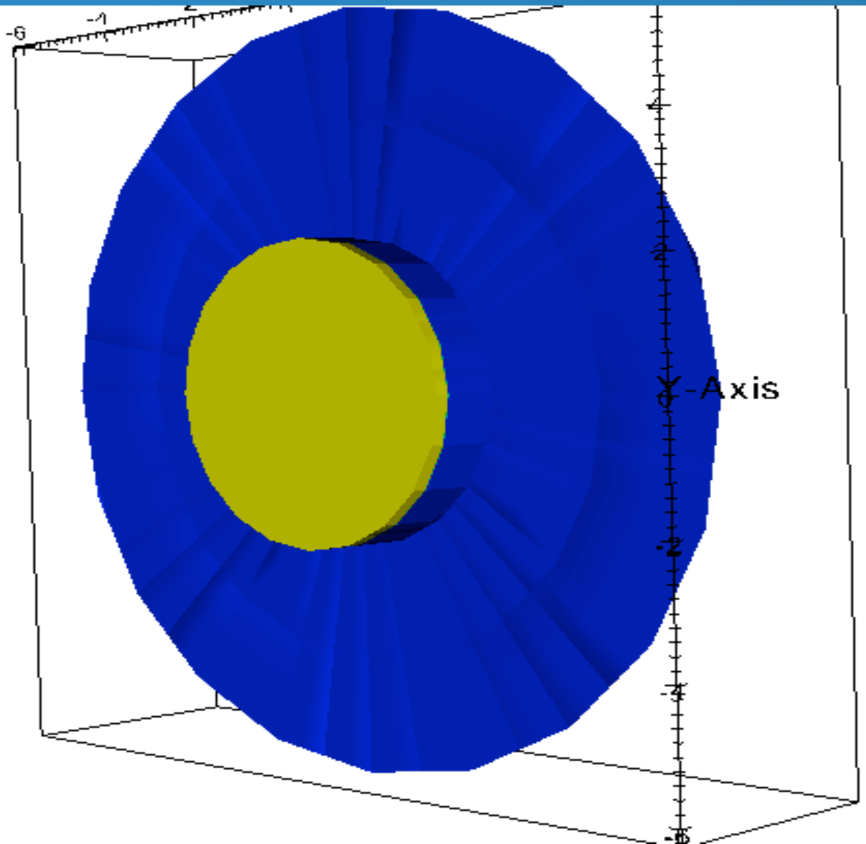
```
SparseMatrix<double> vel_Laplace_plus_Mass;
SparseMatrix<double> vel_it_matrix[dim];
SparseMatrix<double> vel_Mass;
SparseMatrix<double> vel_Laplace;
SparseMatrix<double> vel_Advection;
SparseMatrix<double> pres_Laplace;
SparseMatrix<double> pres_Mass;
SparseMatrix<double> pres_Diff[dim];
SparseMatrix<double> pres_iterative;
```

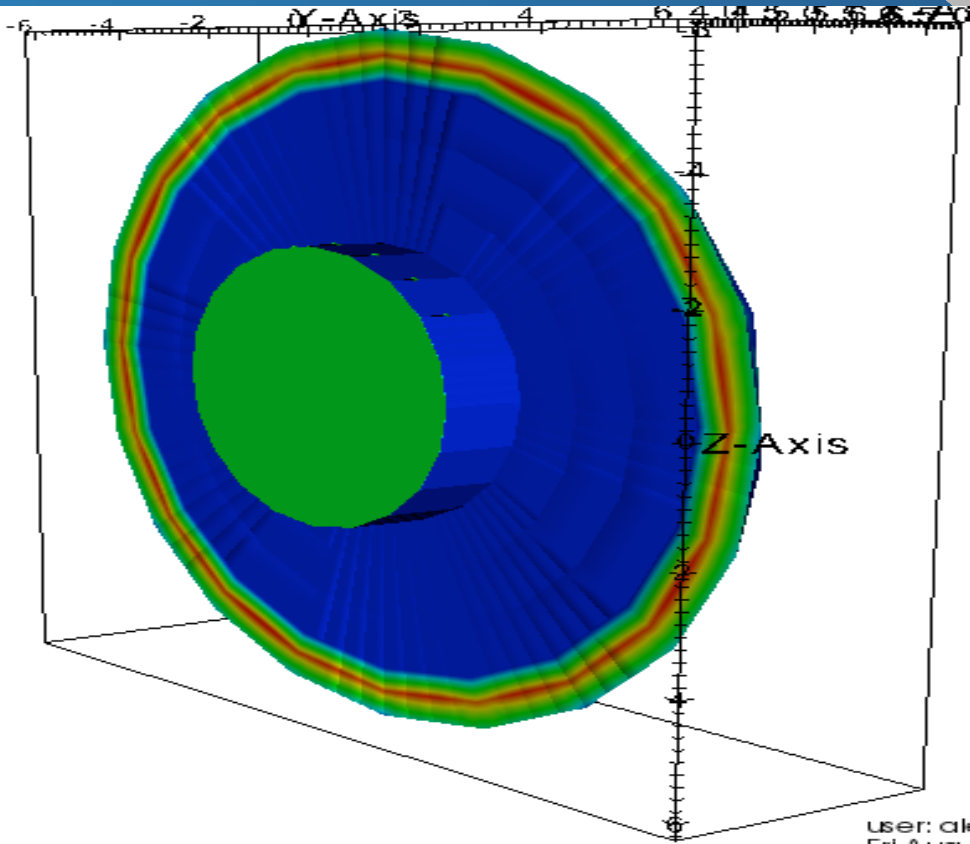
```
Vector<double> pres_n;
Vector<double> pres_n_minus_1;
Vector<double> phi_n;
Vector<double> phi_n_minus_1;
Vector<double> u_n[dim];
Vector<double> u_n_minus_1[dim];
Vector<double> u_star[dim];
Vector<double> force[dim];
Vector<double> v_tmp;
Vector<double> pres_tmp;
Vector<double> rot_u;
```

Deal.II

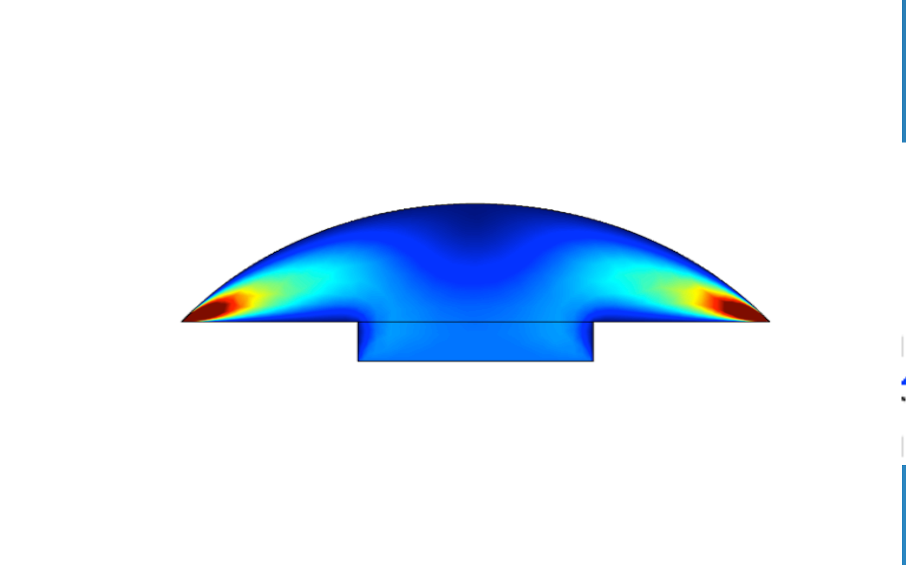
```
 for (typename Triangulation<dim>::active_cell_iterator cell = triangulation. begin_active(); cell != triangulation.end(); +
+cell)
      {
      for (unsigned int f=0; f<GeometryInfo<dim>::faces_per_cell; ++f)
                {
                  if (cell->face(f)->at_boundary())
                   {
                  double x=cell->face(f)->center()[0];
                  double y=cell->face(f)->center()[1];
                  //double z=cell->face(f)->center()[2];
                  if (x==4.0)
                              {
                                cell->face(f)->set_boundary_indicator (1);
                              }
                  else if (x==5.0 && ((y>=5.7 && y<=6.245) || (y<=-5.7 && y>=-6.245)))
                        {
                                cell->face(f)->set_boundary_indicator (2);
                               }
                   }
                }
      }
```

Mesh Refinement





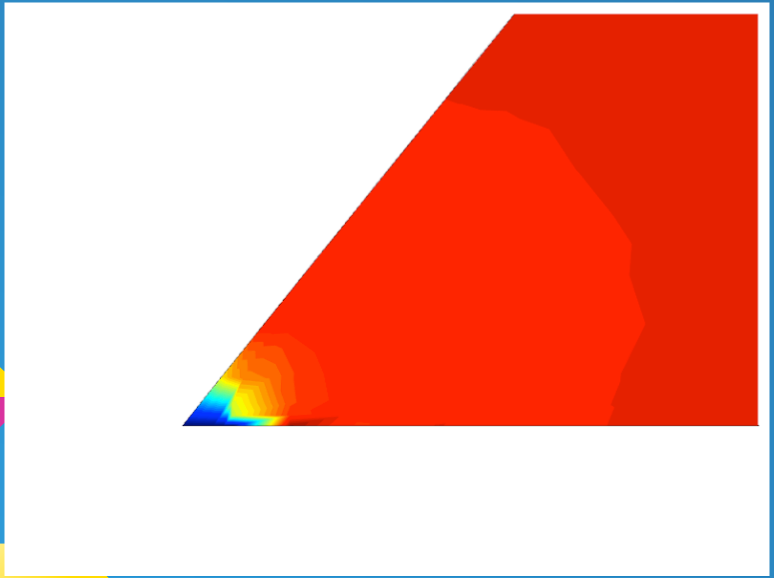
Velocity - 2D



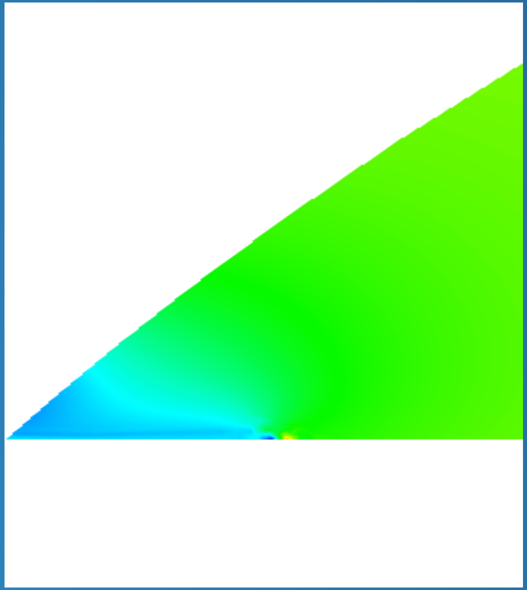
COMSOL Simulation

Deal.II Simulation

Pressure - 2D

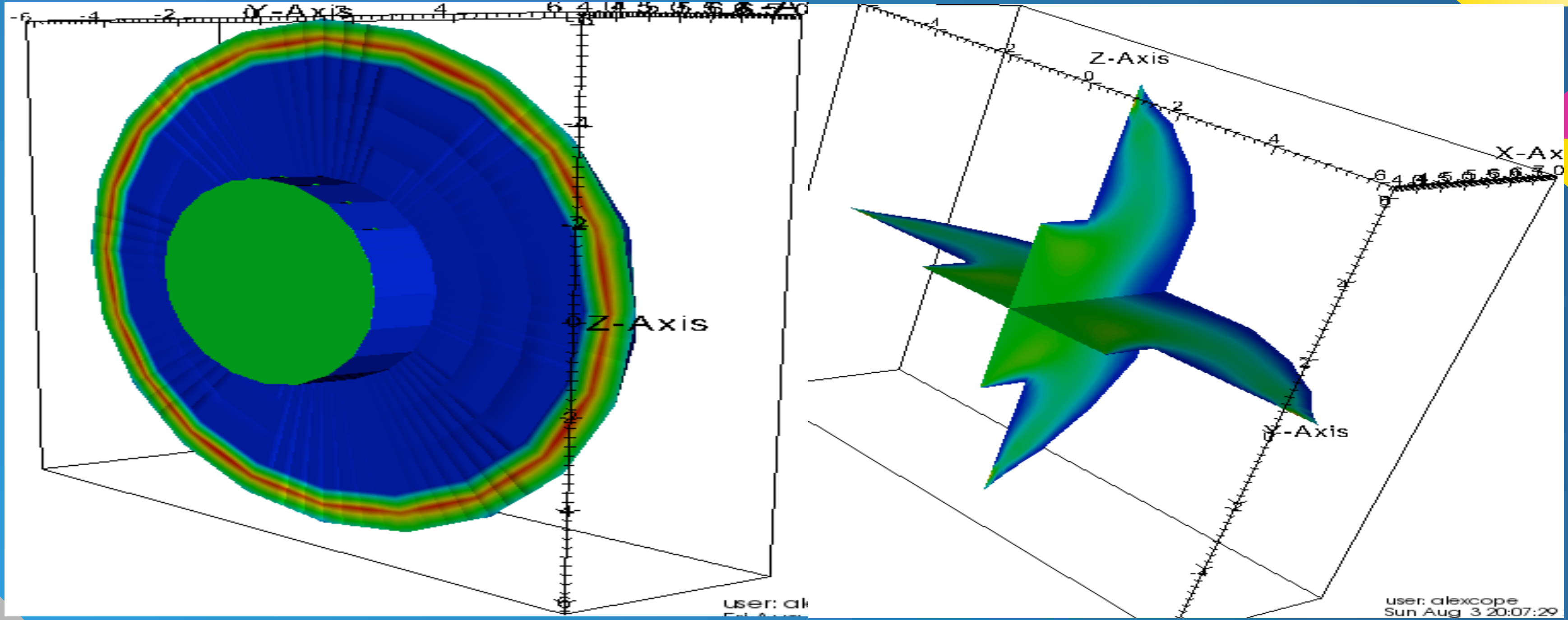


COMSOL Simulation

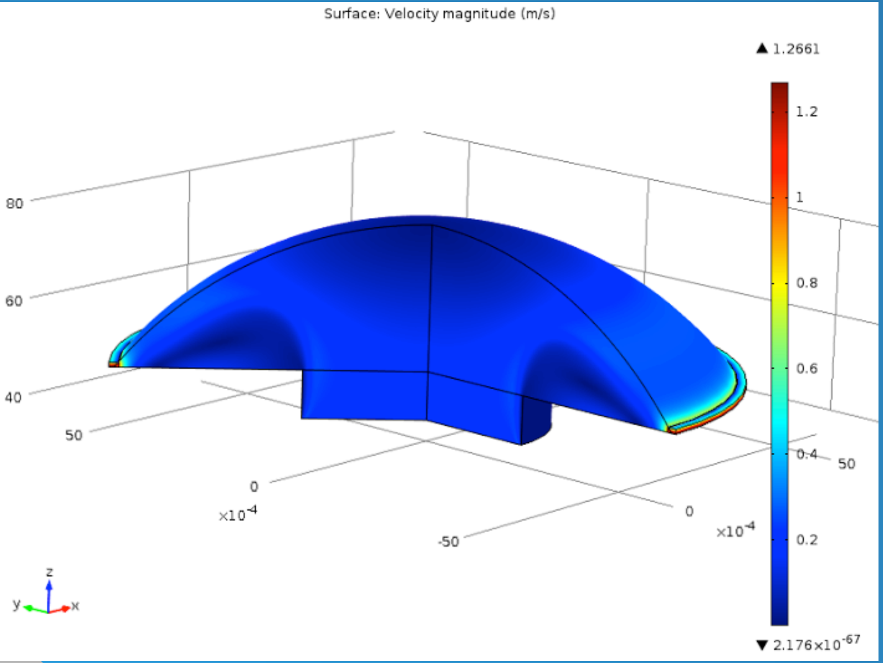


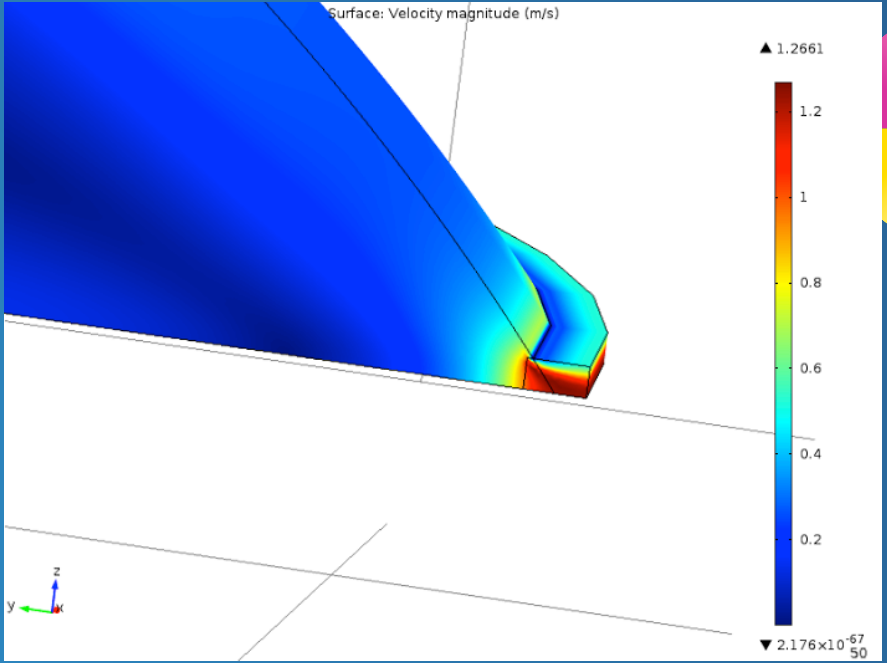
Deal.II Simulations

Velocity - 3D (Deal.II)

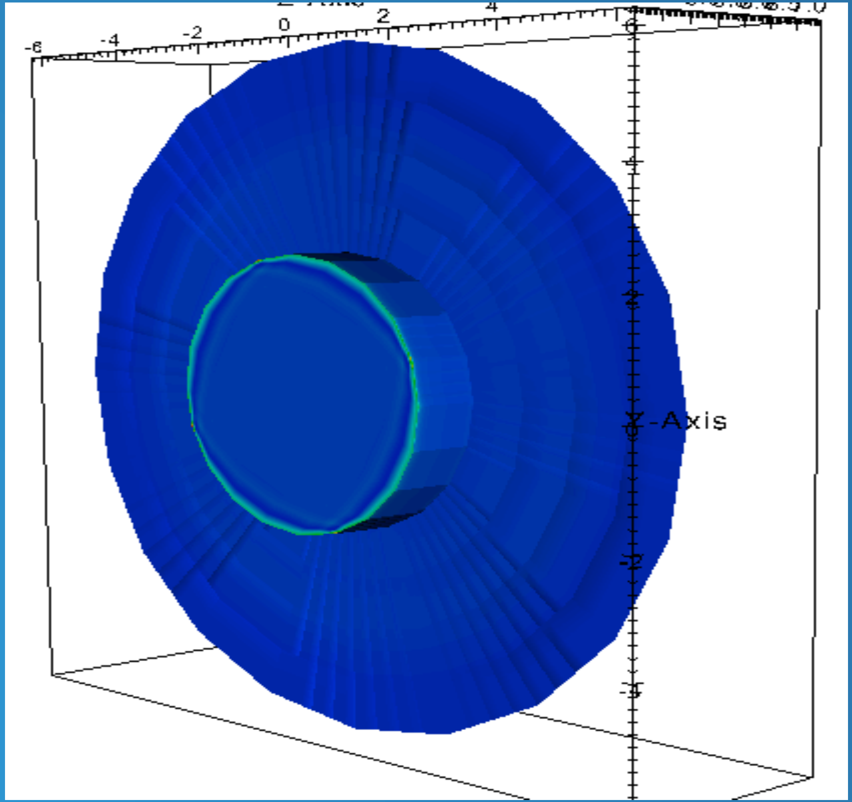


Velocity - 3D (COMSOL)

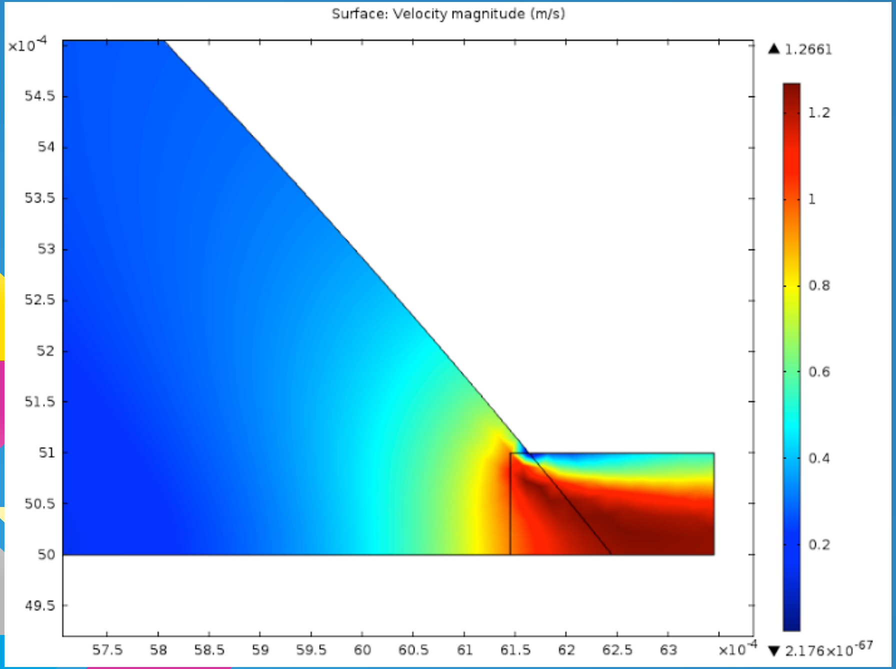


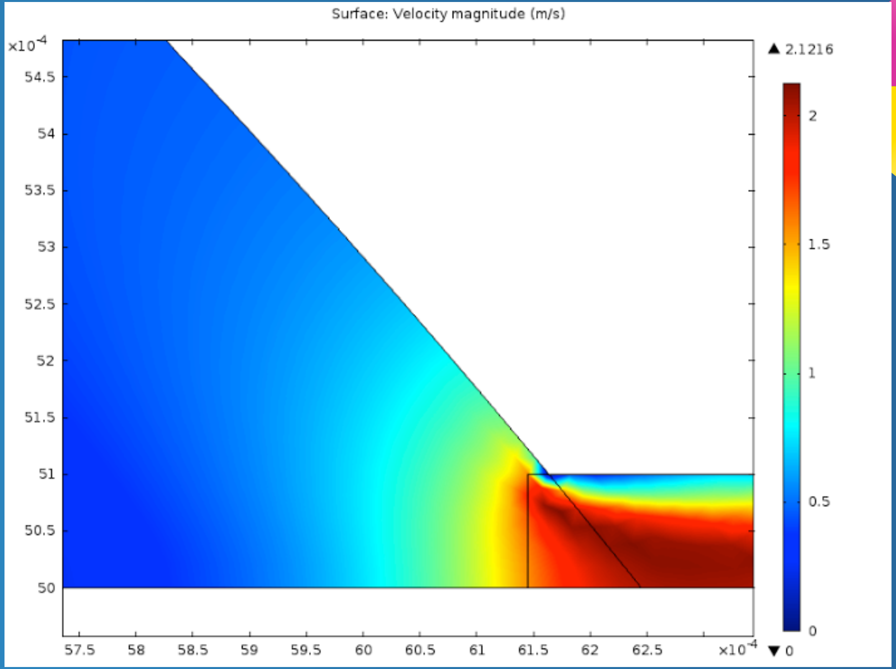


Pressure - 3D (Deal.II)

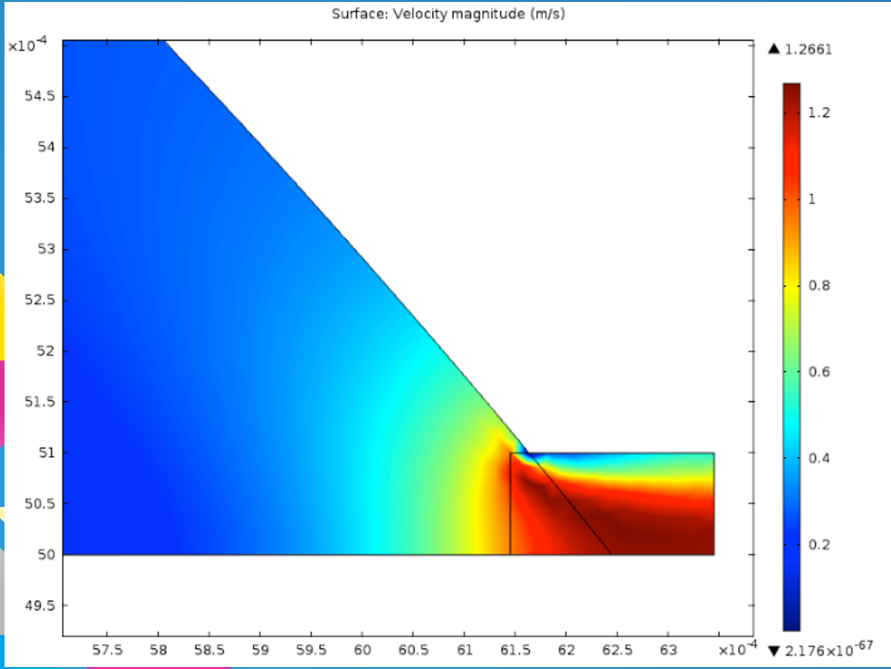


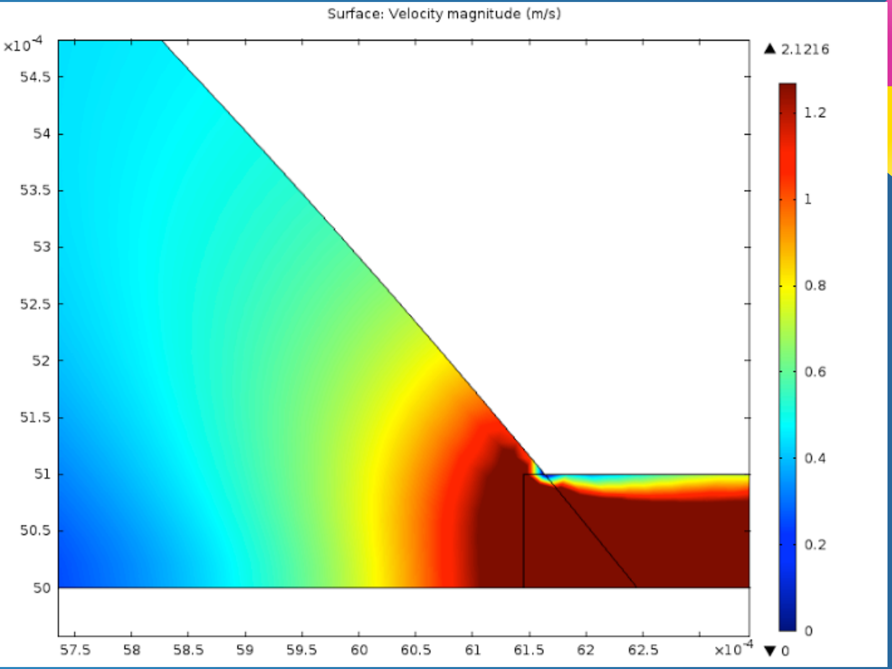
Relative Data (COMSOL)





Relative Data (COMSOL)





Parallel Code

- Code has been developed to solve 1D Laplace problem in parallel

$$\Delta u = 0$$

- Makes use of MPI and Trilinos packages
- Galerkin Method

Example

```
int tmp2=0;
  for (int i=0;i<NumMyElements;++i)
    {
      off=offset[MyGlobalElements[i]];
      double aij_tmp[off];
      int col_loc_tmp[off];
      for (int j=tmp2;j<off+tmp2;++j)
                {
                  aij_tmp[j-tmp2]=aij[j];
                  col_loc_tmp[j-tmp2]=col_loc[j];
                }
      A.InsertGlobalValues(MyGlobalElements[i],off,aij_tmp,col_loc_tmp);
      tmp2=off;
  }
```

Output for N=5 with 3 processors

Processor	Row Index	Col Index	Value
0	0	0	1
0	0	1	0
0	1	0	-1
0	1	1	2
0	1	2	-1
1	2	2	2
1	2	3	-1
1	2	1	-1
1	3	2	-1
1	3	3	2
1	3	4	-1
2	4	4	1
2	4	3	0

Solution time: 0.000562 (sec.)
total iterations: 4

	MyPID	GID	Value
Solved x: Epetra::Vector	MyPID	GID	Value
			0
0 0			
			0
1 25			
Solved x: Epetra::Vector	1	2	50
			1
3 75			
Solved x: Epetra::Vector	2	4	100

Problems

- Deal.II code documentation makes many assumptions about its users
  - assumes a strong background in mathematics, particularly numerical and finite element methods
  - users not familiar with these concepts may be better suited using a different piece of software
- COMSOL
  - modifying equations is not straightforward
- These issues drastically slowed down our progress

Conclusions and Future Goals

- Velocity patterns seem consistent
  - why not pressure?
- 3D simulations need continued refinement
  - Deal.II 3D simulations will need to be run in parallel
- Begin modifying equations for 2D simulations
- Begin expanding Laplace 1D code to work for 2D/3D.

Acknowledgments

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- Ben Ramsey and Jacob Pollack

References

1. Canning, C. R. (2002, 12). Fluid flow in the anterior chamber of a human eye. Mathematical
Medicine and Biology, 19(1), 31-60. doi: 10.1093/imammb19.1.31

2. Crowder, T.r., and V.j. Ervin. "Numerical Simulations of Fluid Pressure in the Human Eye." Applied Mathematics and Computation 219.24 (2013): 11119-1133. Print.

3. Ferreira, J.a., P. De Oliveira, P.m. Da Silva, and J.n. Murta. "Numerical Simulation of Aqueous Humor Flow: From Healthy to Pathologic Situations." Applied Mathematics and Computation 226 (2014): 777-92. Print.

4. Heys, J. J., Barocas, V. H., & Taravella, M. J. (2001, 12). Modeling Passive Mechanical Interaction Between Aqueous Humor and Iris. Journal of Biomechanical Engineering, 123(6), 540. doi: 10.1115/1.1411972

References

5. Fitt, A. D., and G. Gonzalez. "Fluid Mechanics of the Human Eye: Aqueous Humour Flow in The Anterior Chamber." Bulletin of Mathematical Biology 68.1 (2006): 53-71. Print.

6. Roy, Sayon and Tsuyoshi Sato. "Effect of High Glucose on Fibronectin Expressions and Cell Proliferation in Trabecular Meshwork Cells." Investigative Ophthalmology and Visual Science 43.1 (2002): 170-175. Print.

7. Villamarin, Adan, Sylvain Roy, Reda Hasballa, Orestis Vardoulis, Philippe Reymond, and Nikolaos Stergiopulos. "3D Simulation of the Aqueous Flow in the Human Eye." Medical Engineering & Physics 34.10 (2012): 1462-470. Print.