BIOMEDICAL
ENGINEERING

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Automatic Simulation-Driven Medical Device Optimization Design and Advanced Multiphase Modeling

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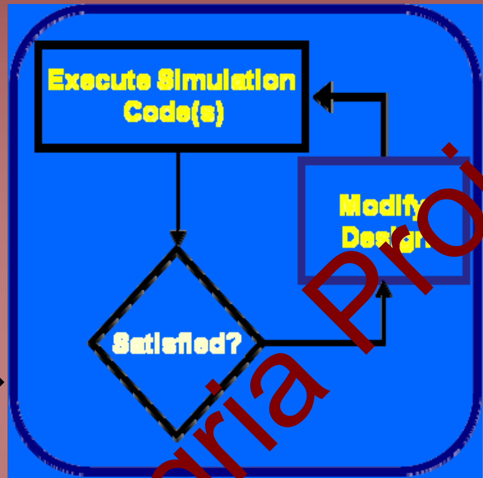
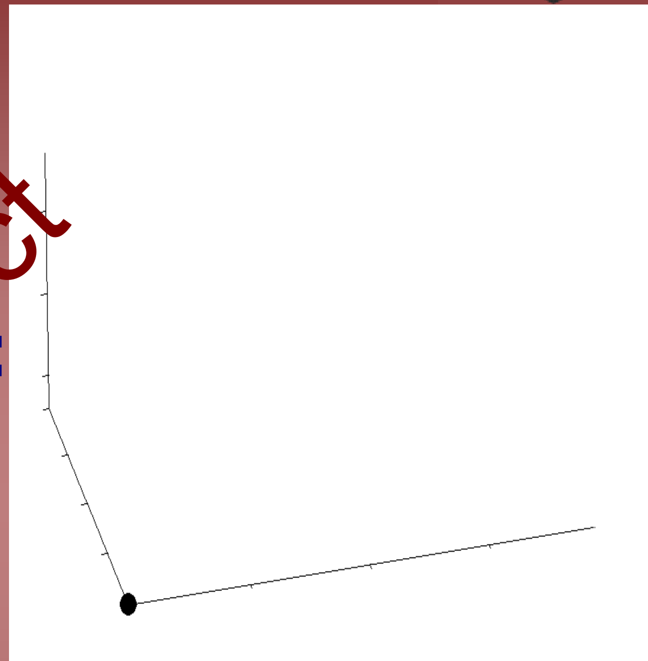
July 2, 2010

Outline

- Background
- Hypothesis
- Case Study 1: PVAD
- Case Study 2: Magnetic Cell Separator
- Case Study 3: Mixture Theory

Manual Design Evaluation Process

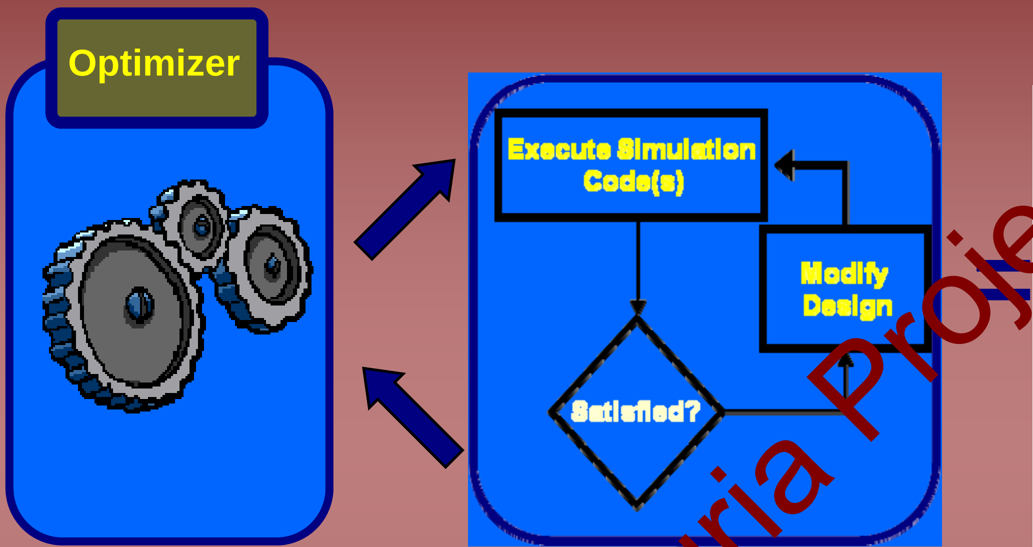


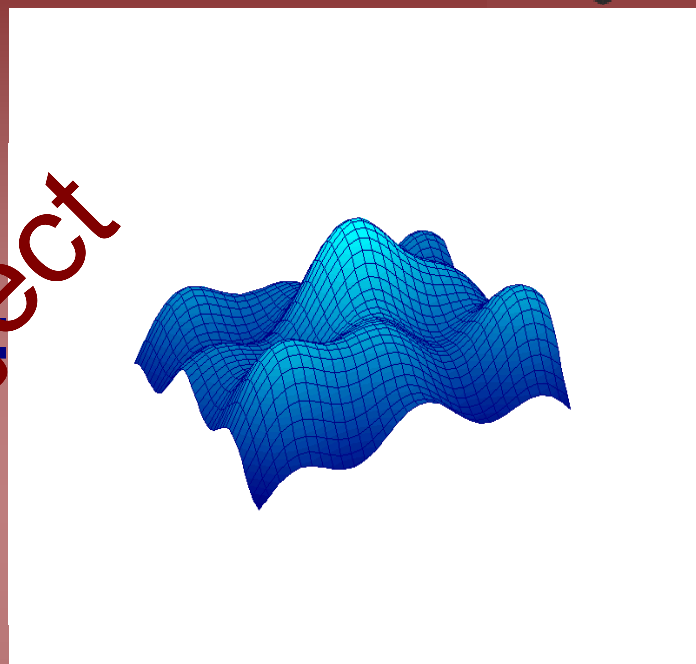


Manual Design Process
- Time consuming
- Error prone tasks
- Engineers spend more time preparing

Results
- Produces limited number of designs
- Produces questionable design quality

Automated Design Optimization





Optimizer as a Software Robot

- Automates and iterates design process
- Engineer defines simulation process
- Engineer defines goals and constraints

Results

- Increases evaluations
- Improves quality
- Engineers spend more time analyzing
- Saves valuable engineering time

Case Study 1:
PediaFlow Ventricular Assist Device

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Motivation

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PediaFlow

- Birth to 2 yrs (3 to 15 kg),
- A mixed-type turbodynamic pump
- Magnetically levitated rotor

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PediaFlow

Magnetically Levitated Miniature Mixed Flow Blood Pump

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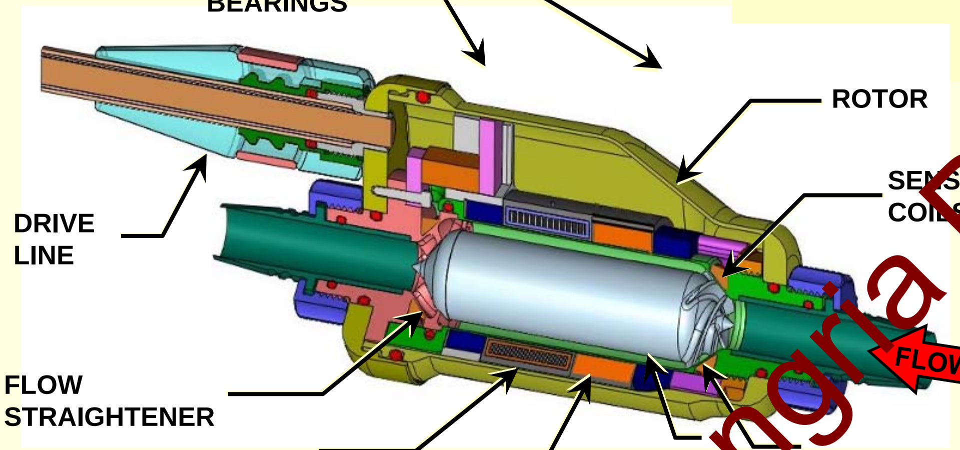

- **PF3: World's smallest maglev VAD**

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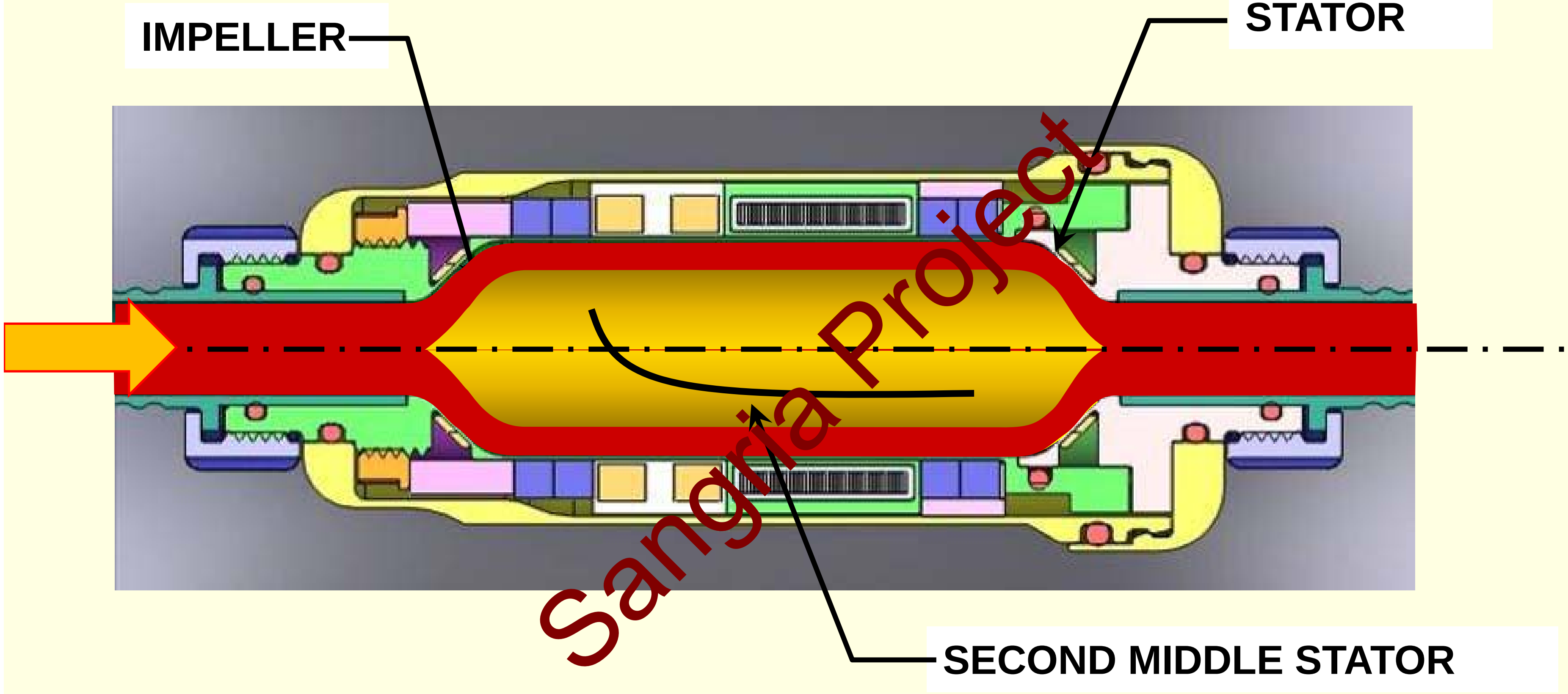
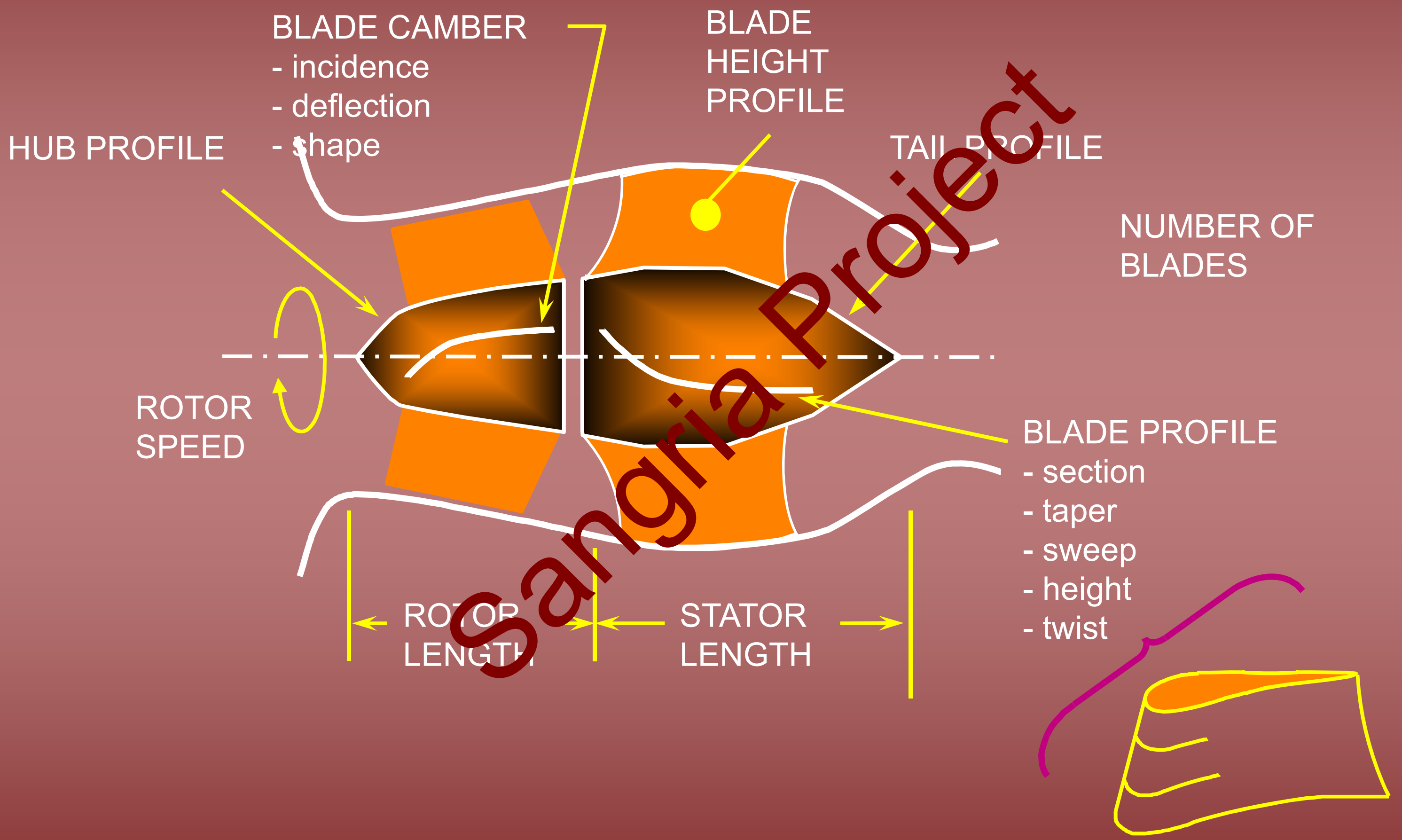
Blood Flow Path



Pump Design Parameters



"Optimization" by Trial and Error

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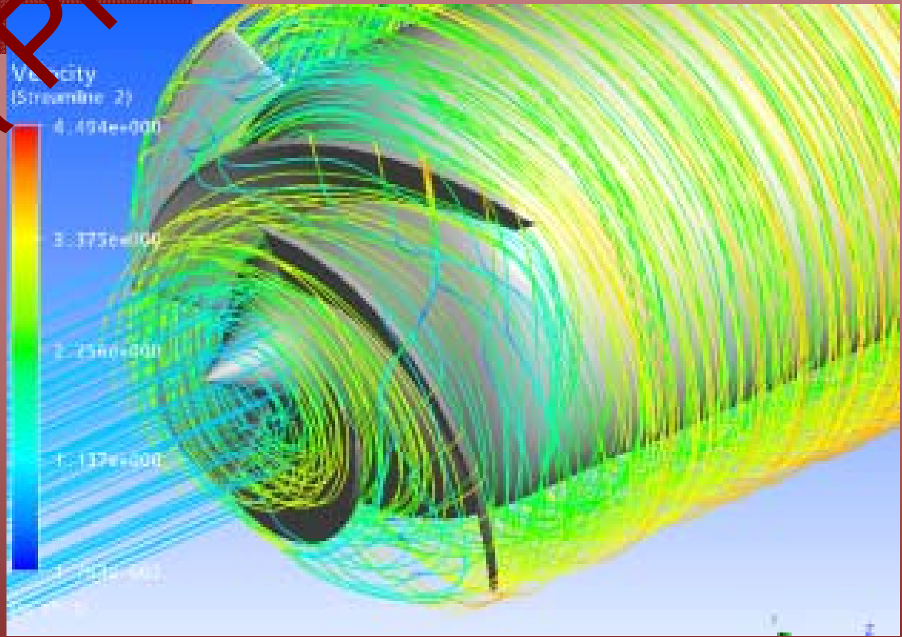
CFD Analysis

- ANSYS CFX 12.0
- Steady-state incompressible flow
- SST turbulent model
- Newtonian fluid

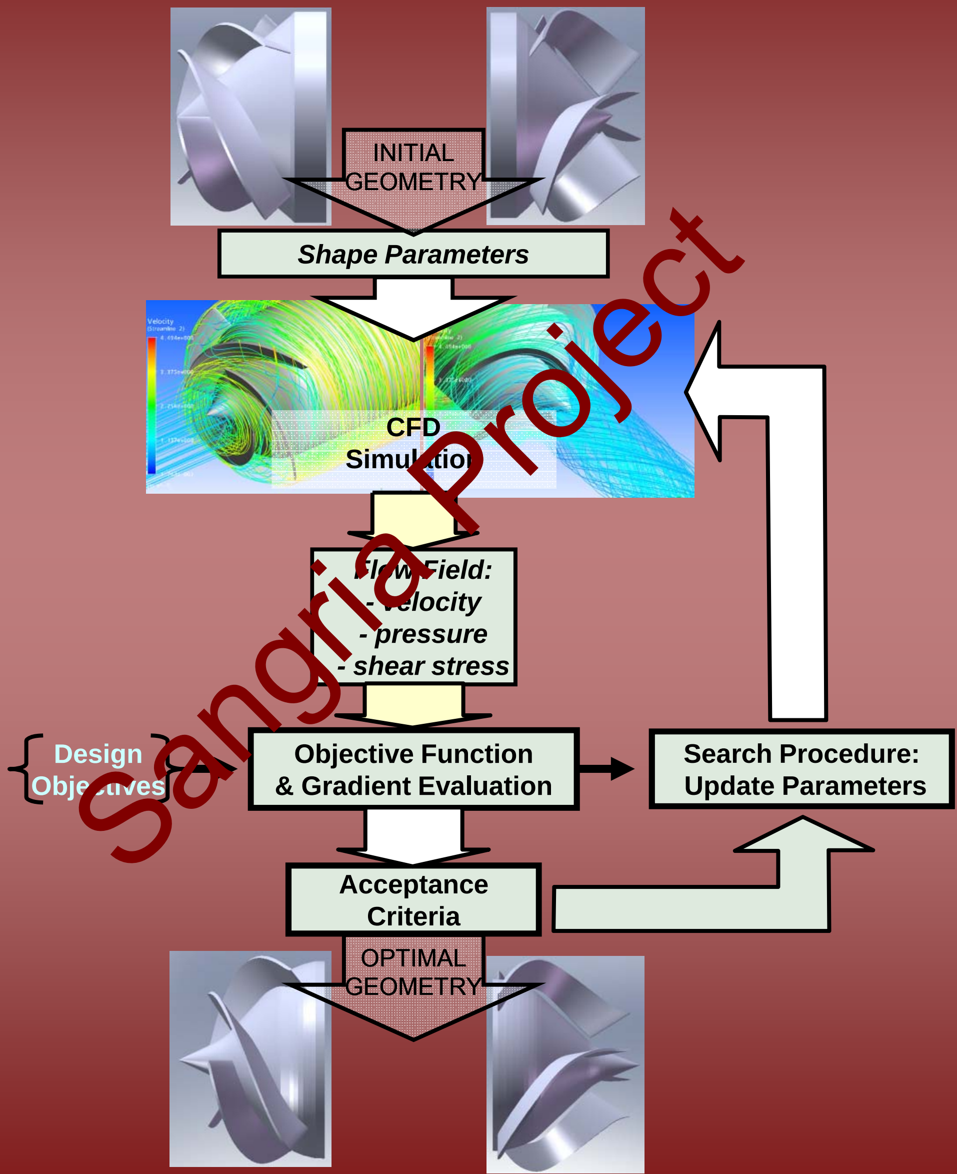


CFD Analysis

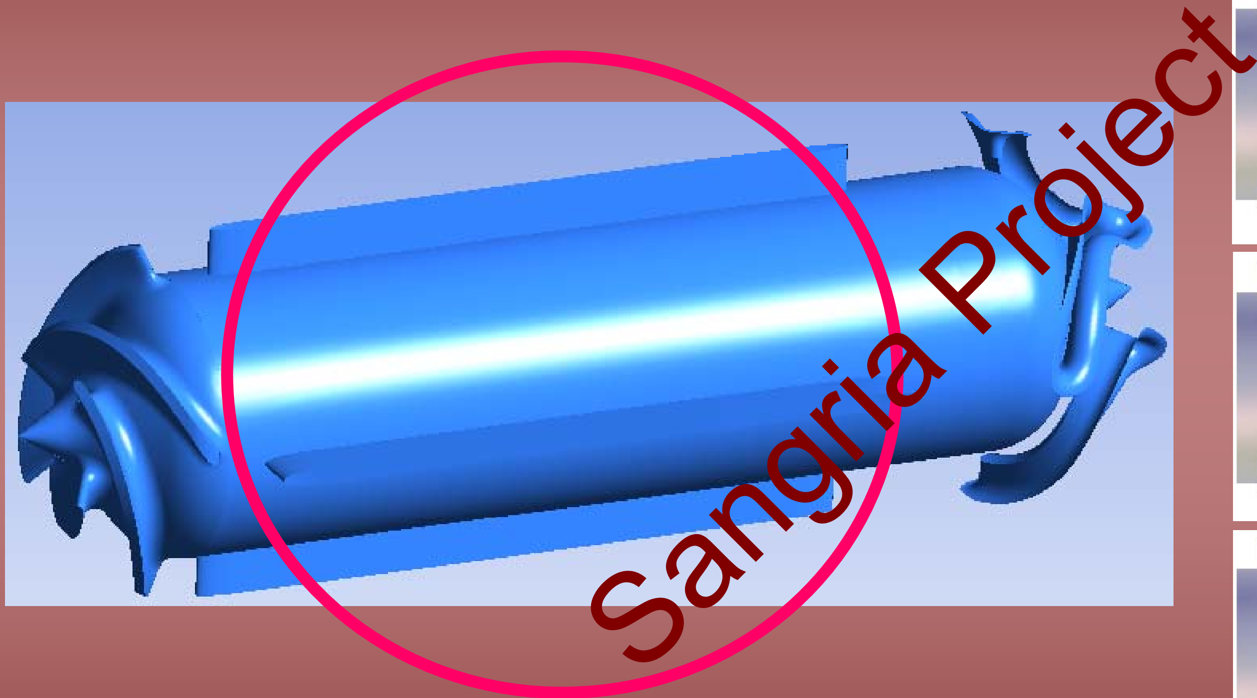
Rotating machine design using ANSYS Turbosystem

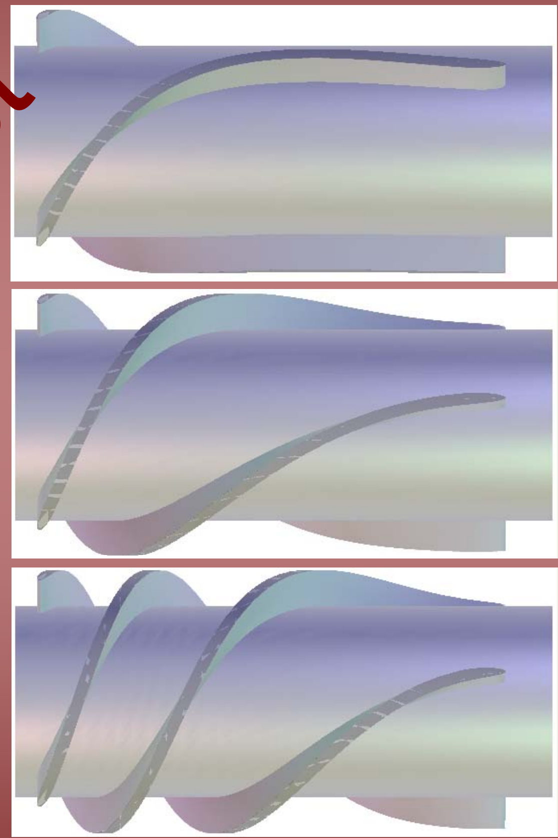
CFX-Pre: pre-processor
CFX-Solve: solver
CFX-Post: post-processor

Elements of (Shape) Optimization



Parametric Models of Turbomachinery Blades



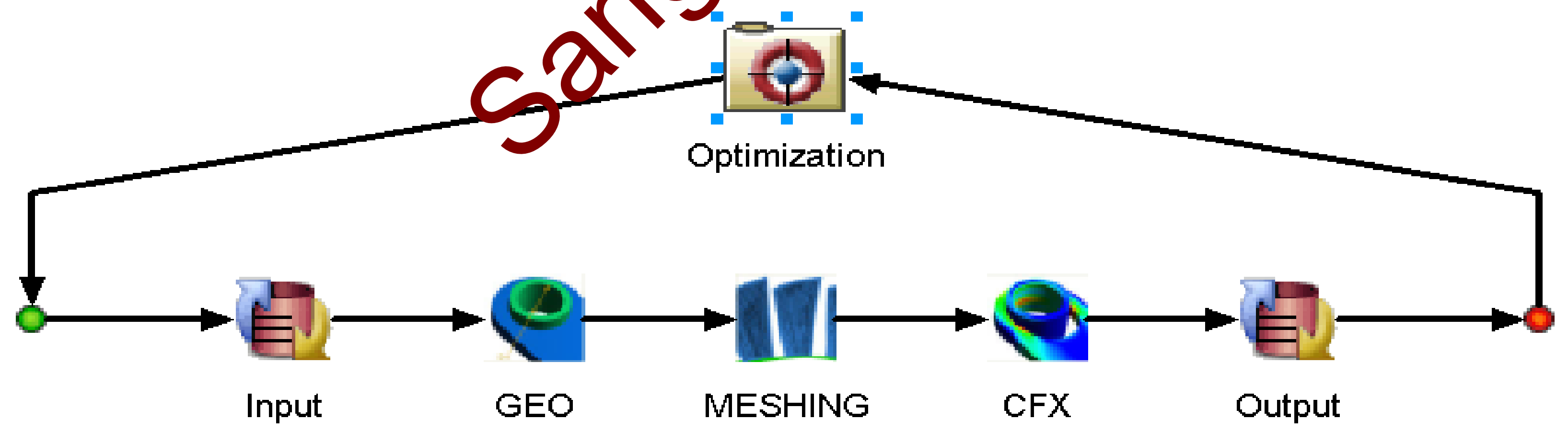


Middle Stator Blades

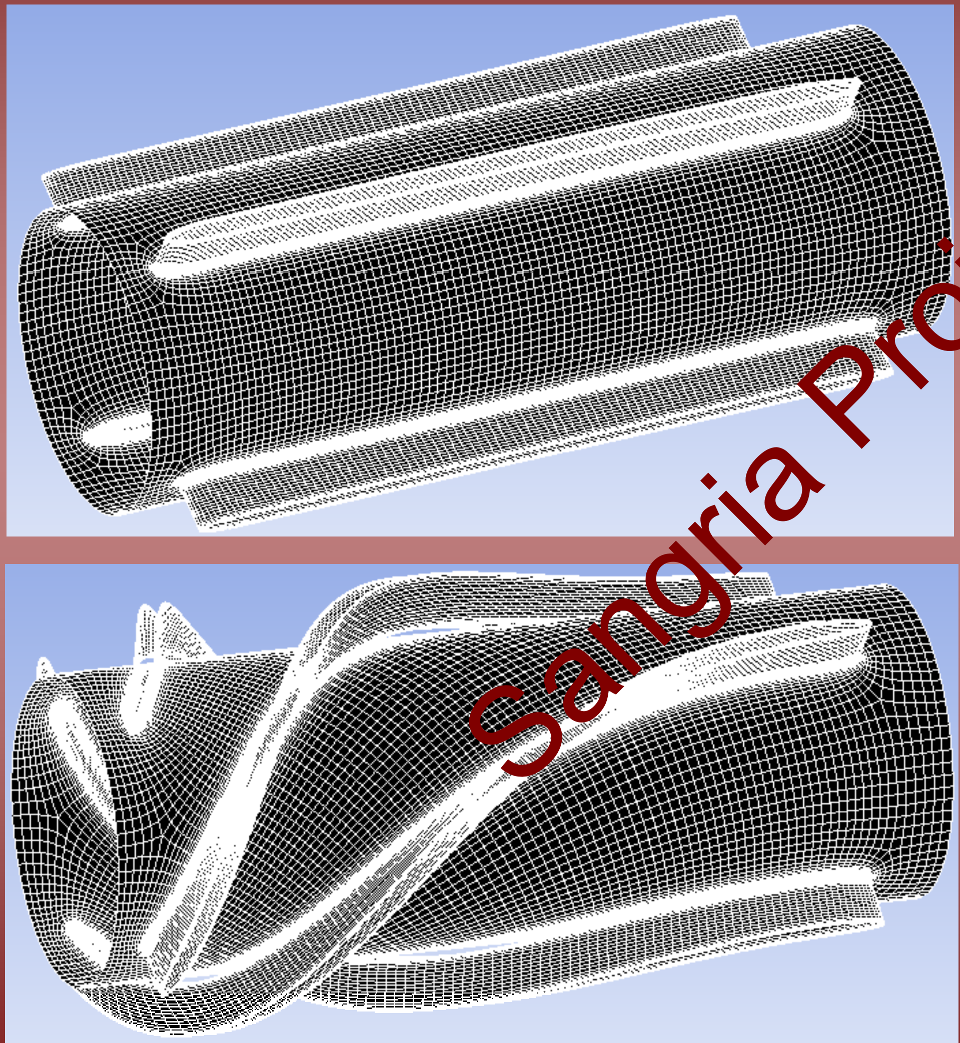
Automated Optimization

- **Optimizer**: Isight (SIMULIA)
- **Algorithm**: NLPQL
- **Objective**: Maximize Efficiency
- **Constraint**: Static Head >= 80 mmHg

- Optimization automatically changes design variables to find the "best" design satisfying specified criteria.



Results: Hexahedral Mesh



Control total number of mesh
Maintain good mesh quality

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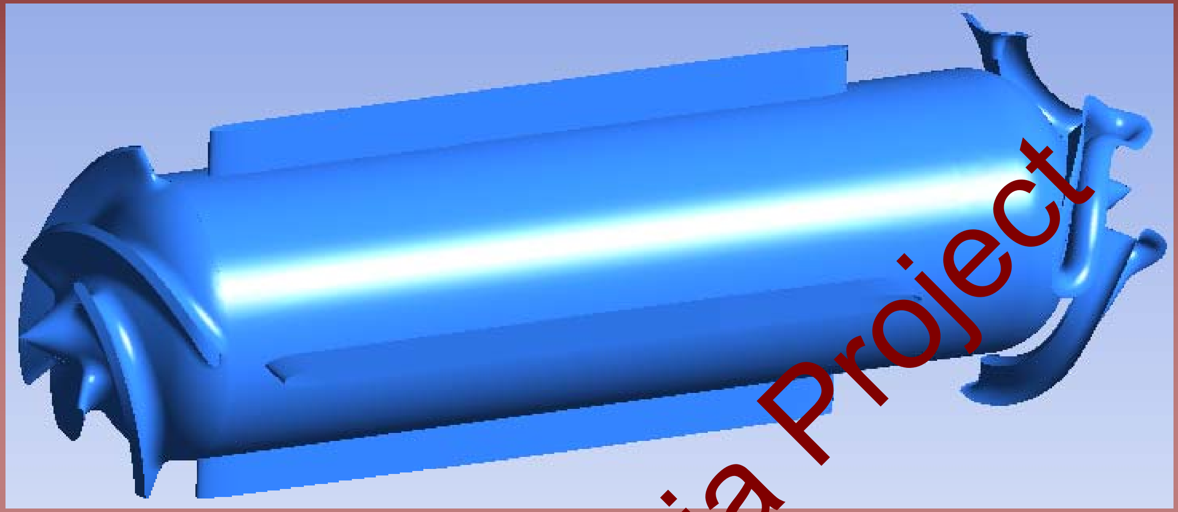
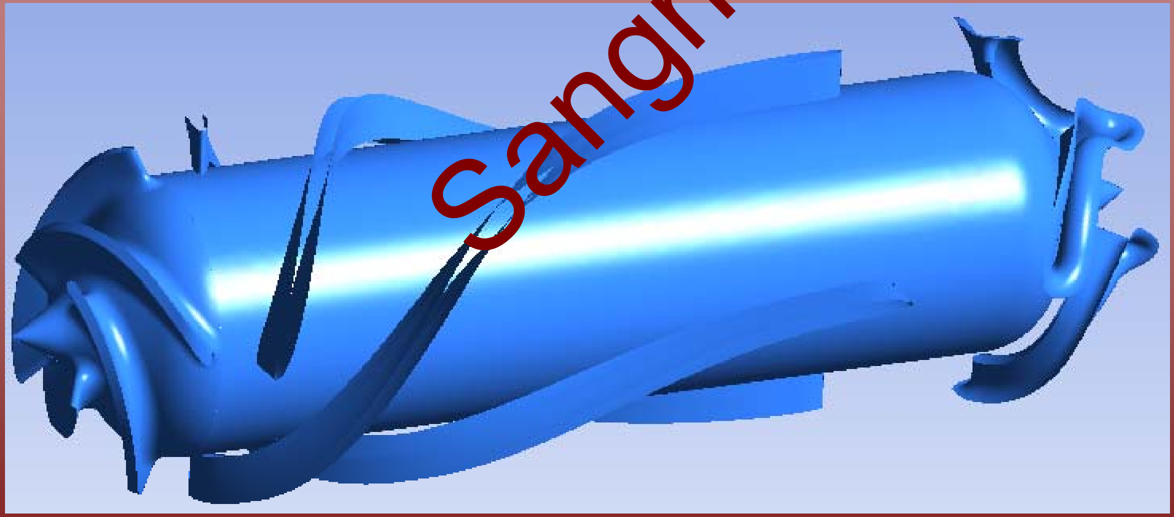
Results: Shape Optimization



Initial Blade



Optimal Blade

Results: Streamlines

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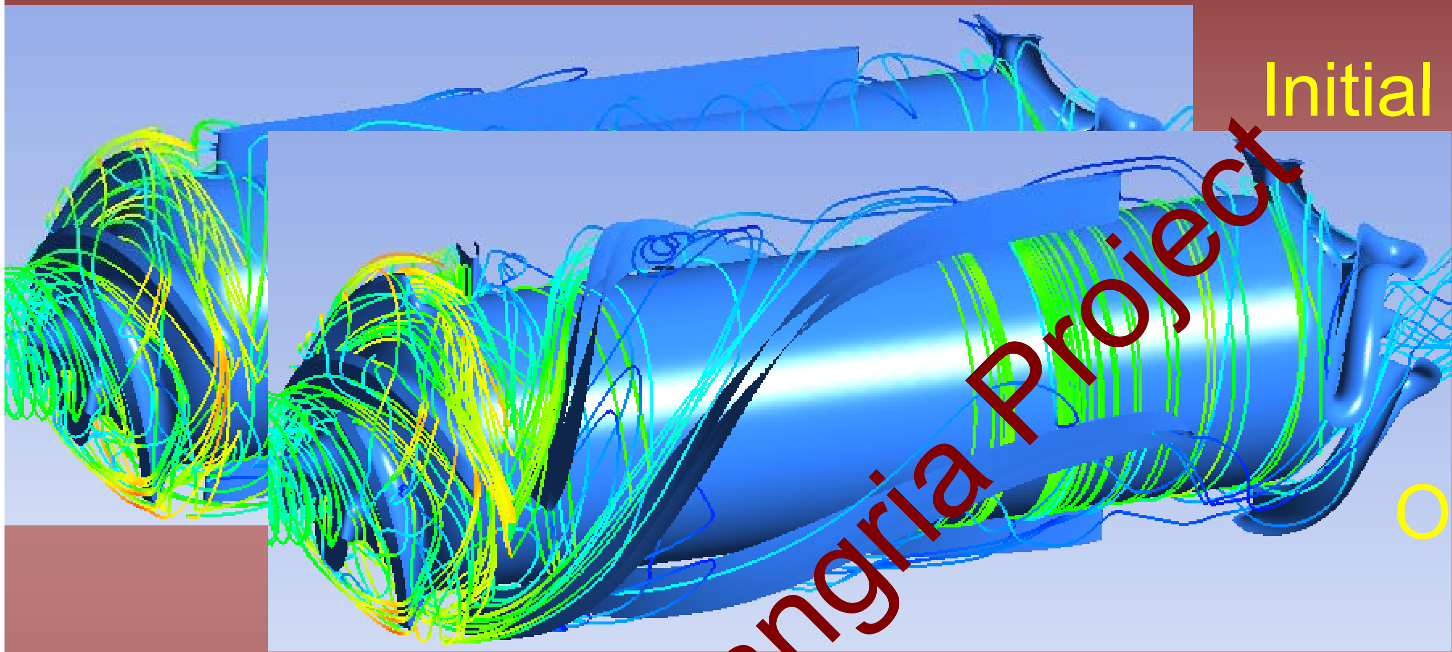

Initial Blade

Optimal Blade

	Initial Design	Optimal Design
Pressure Rise	108	**157**
Efficiency	12.9 %	**18.7 %**

45.3% increase in Pressure

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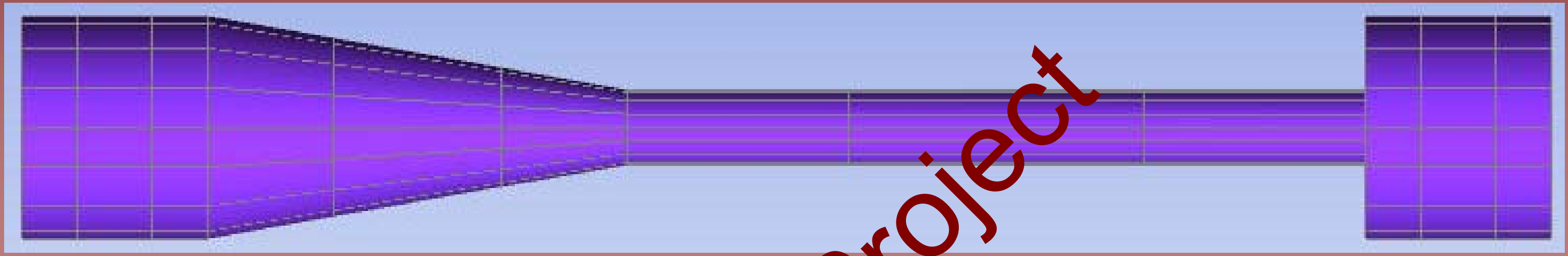
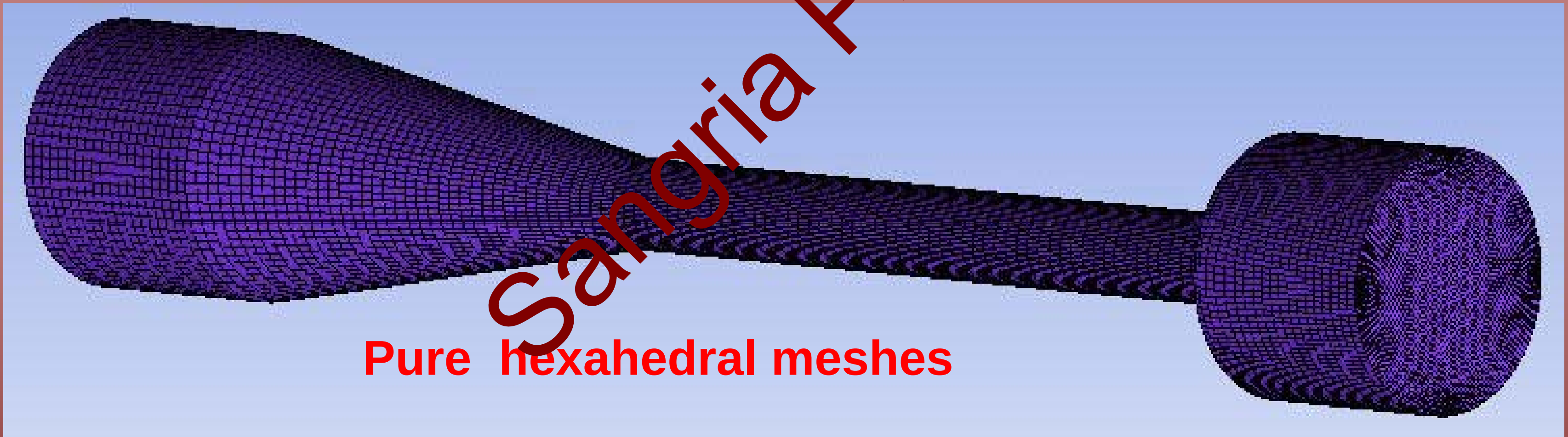
FDA Nozzle





Pure hexahedral meshes

Working with Sam

Time Table

	2nd Quarter, 2010	3rd Quarter, 2010	4th Quarter, 2010	1st Quarter, 2011	2nd Quarter, 2011	3rd Quarter, 2011	4th Quarter, 2011
Blood Damage (FDA Nozzle and PVAD)							
Gradient-Based Opt.							
Response Surface Opt.							
Multi-Point Opt.							
Multi-Objective Opt.							

Accomplishments

CARDIO-MD

Journal papers

- **Kim, J**., Antaki, J., *Simulation-Based Automatic Optimization of the PediaFlowTM VAD, in preparation*.
- JF Antaki1, MR Ricci, JE Verkaik, ST Snyder, TM Maul, **J Kim**, D Paden, BE Paden, HS Borovetz, *PediaFlow™ Maglev Ventricular Assist Device: A Prescriptive Design Approach*, Cardiovascular Engineering Technology 1(1), 2010

Conference abstracts and proceedings

- **Kim, J**., Antaki, J., *Simulation-Based Automatic Optimization of the PediaFlowTM VAD*. NIH-FDA-NSF Workshop 2010.
- **Kim, J**., Antaki, J., *Simulation-based Design and Optimization of the PediaFlow VAD*. NIH-FDA-NSF Workshop 2009.
- Shu, F., Verkaik, J., Snyder, S., Paden, D., **Kim, J**., Antaki, J., *Ventricular Assist Device for Toddlers with Hybrid Magnetic-Mechanical Bearings*. ASAIO Abstracts, 2009. **55**(2):p.147.
- **Kim, J**., Hund, S., Daly, A., Kameneva, M, Antaki, J., *Eulerian Method for Numerical Prediction of Hemolysis in PediaFlow VAD*. 5th IFAO Proceedings, 2009. **5**:p.59.
- **Kim, J.**, Antaki, J., *Computational Fluid Dynamic Shape Optimization of the PediaFlowTM VAD*. ASAIO Abstracts, 2009. **55**(2):p.155.

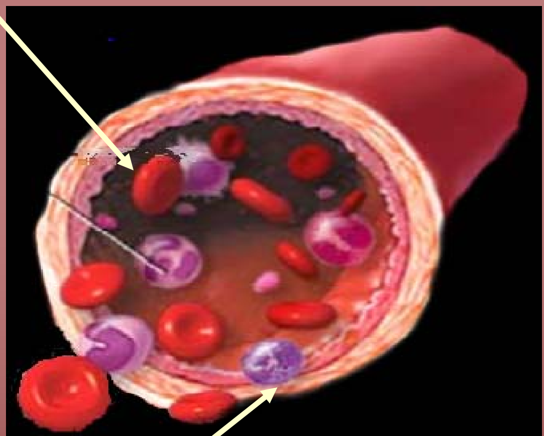
Pumpkin PVAD quarterly reports (April 2010, July 2010)

Case Study 2:
Magnetic Cell Separator

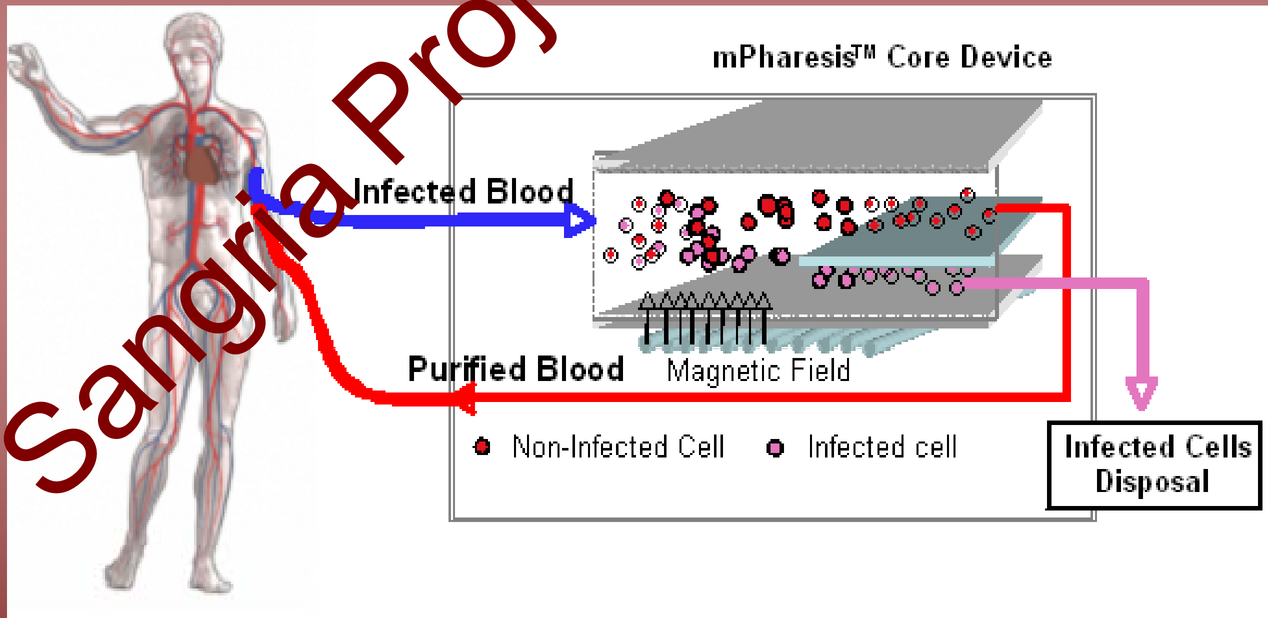
mPhoresis™ Magnetic Cell Separator

- A dialysis-like device that separate malaria infected RBCs from the blood using magnetic field.

Healthy Red Blood Cell

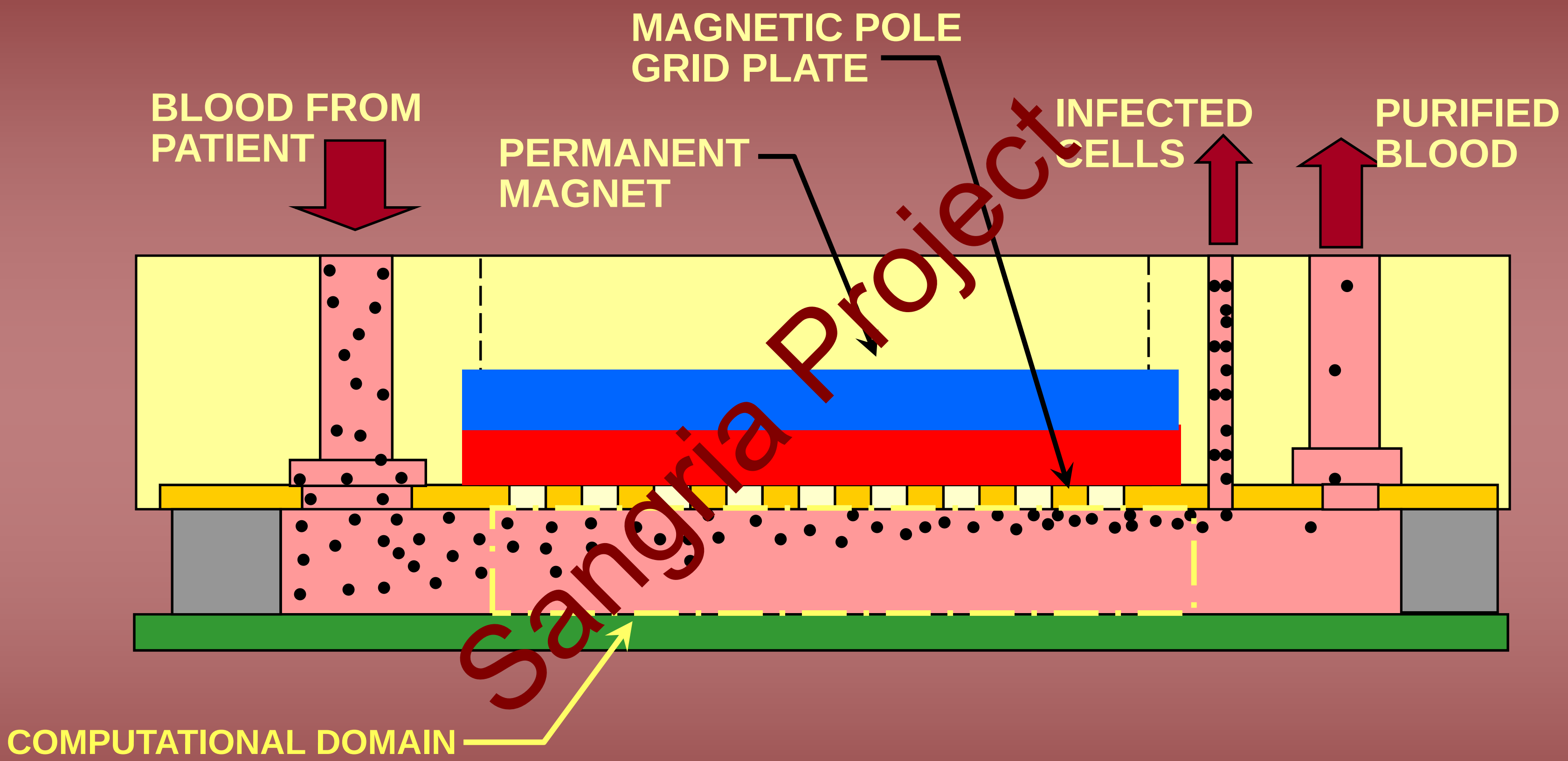


Infected Red Cell



- The malaria parasite converts hemoglobin into hemozoin.
- Hemozoin becomes paramagnetic.

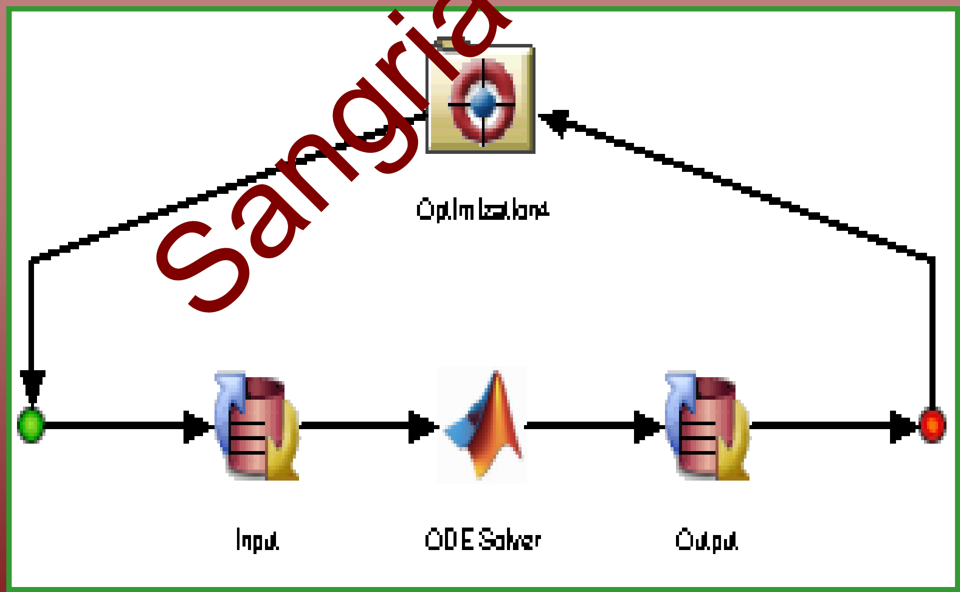
Methods:
Boundary Value Problem



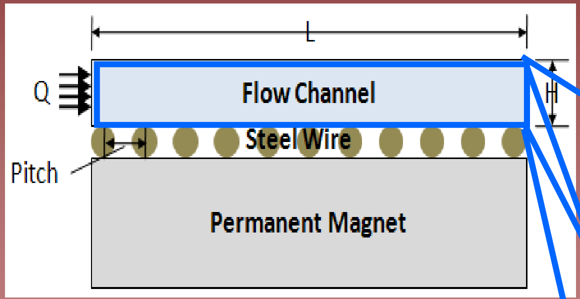
Infected cells are drawn towards the pole plate by the magnetic field, and are skimmed away.

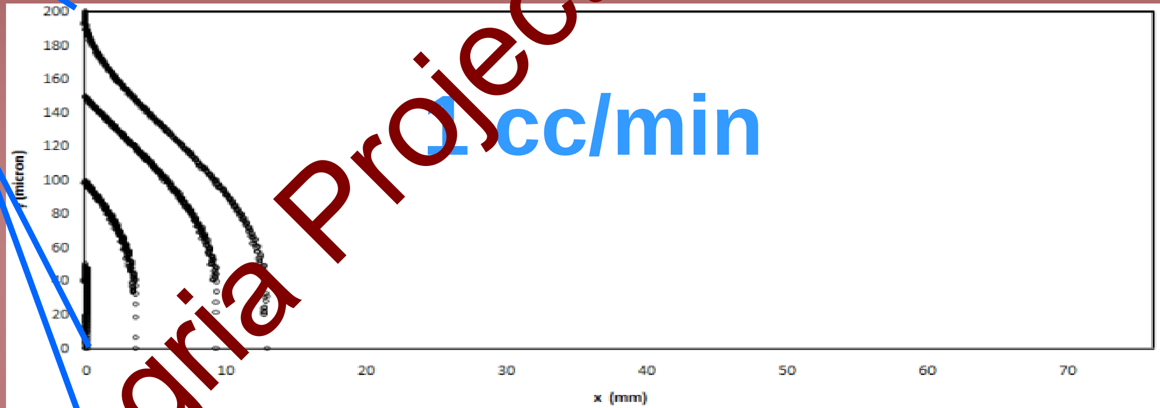
Methods: Automated Design

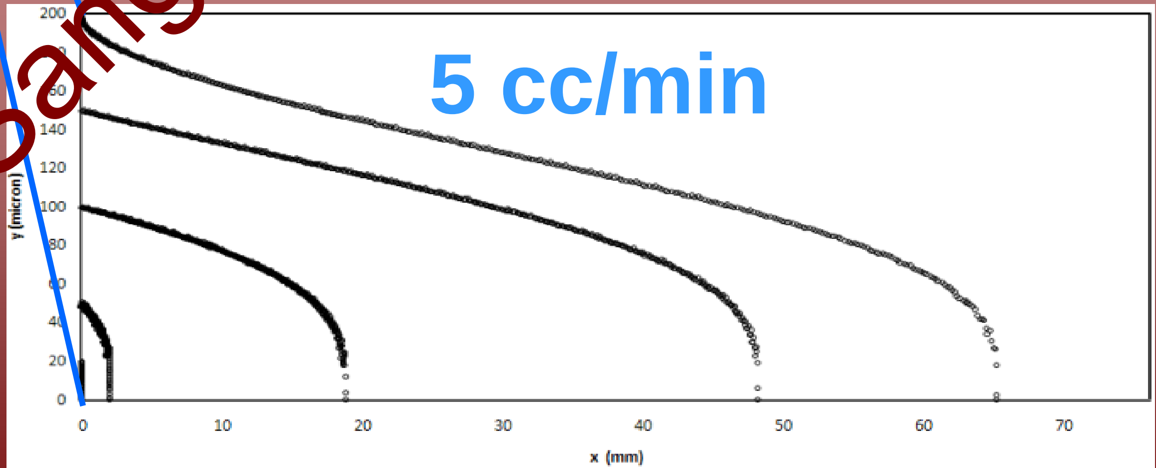
- **Design Variable**: Height, Flow Rate, Wire Pitch
- **Objective**: Minimize Length
- **Constraint**: 99% Beads Captured
- **Optimizer**: Isight (SIMULIA)
- **Algorithm**: NLPQL



Results: Bead Trajectories







Magnetic Particles (Spherotech, Inc.)

- Diameter of 0.3 micron
- Mass of 1.8378e-017 kg
- Susceptibility of 0.26

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Results: Automatic Optimization

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- NLPQL provided a local optimal point, depending on a starting point.
- Need different initial points to find a best optimal point.

Minimize Length	Side Bounds	Initial	Optimal	Initial	Optimal
flow rate, cc/min	1 to 10	5	1	10	9
height, micron	50 to 300	200	50	300	50
pitch, micron	100 to 400	200	100	400	100
length, mm		65.4	0.7	927.6	6.9
Iteration			29		19

Needed to capture 99% beads

Time Table

	2nd Quarter, 2010	3rd Quarter, 2010	4th Quarter, 2010	1st Quarter, 2011	2nd Quarter, 2011	3rd Quarter, 2011	4th Quarter, 2011
Magnetic Particle Dynamics							
Lagrangian-Eulerian							
Mixture Theory							
Design Optimization							

Acomplishments

Journal papers

- **Kim, J**., et al., *Magnetic particle Dynamics, in manuscript*.

Conference abstracts and proceedings

- **Kim, J**., Gandini, A., Antaki, J., *Numerical Study of Magnetic Field Separator to Remove Malaria-Infected Red Blood Cells from the Whole Blood*. NIH-FDA-NSF Workshop 2010.

Case Study 3:
Developing an Advanced Multiphase Model: Mixture Theory

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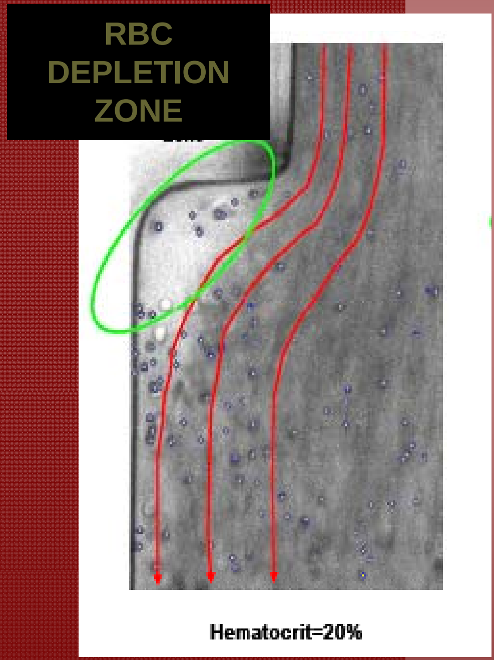
Blood Properties

- Plasma
  - occupies 55-60% of total blood volume
- RBCs
  - 40-45% of blood volume
  - 8-10 µm diameter
  - biconcave discoids
  - aggregation and deformability
  - RBC tumbling
- White blood cells and Platelets
  - only contain 5% by volume
  - important roles in immunity and hematostasis



Zhao et al.

Microscopic Characteristics in Blood Flow

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- Microhemorheology
  - Shear thinning, Fahraeus effect, Fahraeus-Lindqvist effect, Plasma skimming, Platelet margination, etc.
  - Device-related micro-hemorheological study is lacking.
- Single Phase Model
  - cannot predict the concentration profile of blood cells (phase separation)
  - is invalid at micro scale.
- There is no reliable hemorheological model that can predict hemodynamics for blood flow in blood contacting devices.

Multiphase Modeling: Mixture Theory

- the Theory of Interacting Continua
- based on the ideas of diffusion proposed by Fick
- a homogenization approach
  - each component is regarded as a single continuum and at each instant of time, every point in space is considered to be occupied by a particle belonging to each component of the mixture.
- The foundation of the theory is given in books by Truesdell (1984); Dobran (1991) and Rajagopal and Tao (1995).
- Johnson et al (1991) and Massoudi et al. (1999) have formulated a two-phase flow theory based on this mixture theory.

Benefits of the Mixture Theory

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- To predict the phase separation of plasma-RBC mixture
  - velocity field of RBCs and plasma
  - concentration field of RBCs and plasma
- Can be applied to physiological Hematocrit (40~50%)
- The results will be used as the input to numerical platelet deposition model or/and blood damage model.

A brief review of Mixture Theory

- $\mathbf{X}_1$ and $\mathbf{X}_2$ denote the positions of particles of S_1 and S_2

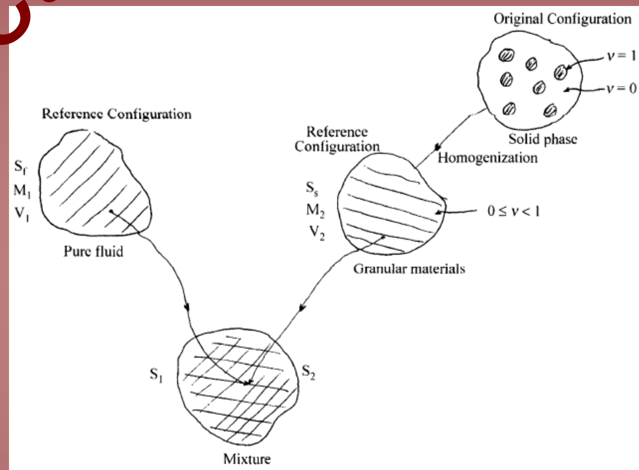
$$\mathbf{x}_1 = \chi_1(\mathbf{X}_1, t), \quad \text{and} \quad \mathbf{x}_2 = \chi_2(\mathbf{X}_2, t).$$

- The kinematical quantities associated with these motions are

$$\mathbf{v}_1 = \frac{d_1 \chi_1}{dt}; \quad \mathbf{v}_2 = \frac{d_2 \chi_2}{dt}, \qquad \mathbf{a}_1 = \frac{d_1 \mathbf{v}_1}{dt}$$

$$\mathbf{a}_2 = \frac{d_2 \mathbf{v}_2}{dt}, \qquad \mathbf{L}_1 = \frac{\partial \mathbf{v}_1}{\partial \mathbf{x}_1}, \quad \mathbf{L}_2 = \frac{\partial \mathbf{v}_2}{\partial \mathbf{x}_2},$$

$$\mathbf{D}_1 = \frac{1}{2}(\mathbf{L}_1 + \mathbf{L}_1^T), \quad \mathbf{D}_2 = \frac{1}{2}(\mathbf{L}_2 + \mathbf{L}_2^T), \qquad \mathbf{W}_1 = \frac{1}{2}(\mathbf{L}_1 - \mathbf{L}^T{}_1), \mathbf{W}_2 = \frac{1}{2}(\mathbf{L}_2 - \mathbf{L}^T{}_2)$$



Massoudi and Rao, 2001

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A brief review of Mixture Theory, cont’

- ρ_1 and ρ_2 are the bulk densities of the mixture components.

$$\rho_1 = \nu\,\rho_{10}\,, \quad \rho_2 = \phi\,\rho_{20},$$

  - ρ_{10} is the pure density of the component 1, ρ_2 is the pure density of component 2.
  - v is the volume fraction of the component 1, and φ is the volume fraction of component 2.
  - For a saturated mixture φ= 1 - v.

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A brief review of Mixture Theory, cont’

- The mixture density, ρ_m and the mean velocity $\mathbf{v}_m$ of the mixture are defined

$$\rho_m = \rho_1 + \rho_2, \qquad \rho_m \mathbf{v}_m = \rho_1 \mathbf{v}_1 + \rho_2 \mathbf{v}_2.$$

- The individual stress tensors

$$\mathbf{T}_1 = (1-\phi)\mathbf{T}_f \qquad \mathbf{T}_2 = \mathbf{T}_s$$

- A mixture stress tensor

$$\mathbf{T}_m = \mathbf{T}_1 + \mathbf{T}_2$$

  - The mixture stress tensor reduces to that of a pure fluid as $\varphi \to 0$ and to that of the solid phase as $v \to 0$

A brief review of Mixture Theory, cont’

Conservation of Mass

Conservation of Linear Momentum

Phase 1: Plasma

$$\frac{\partial \rho_1}{\partial t} + \mathrm{div}\,(\rho_1 \mathbf{v}_1) = 0$$

$$\rho_1 \frac{D_1 \mathbf{v}_1}{Dt} = \mathrm{div}\,\mathbf{T}_1 + \rho_1 \mathbf{b}_1 + \mathbf{f}_I$$

Phase 2: RBC

$$\frac{\partial \rho_2}{\partial t} + \mathrm{div}\,(\rho_2 \mathbf{v}_2) = 0$$

$$\rho_2 \frac{D_2 \mathbf{v}_2}{Dt} = \mathrm{div}\,\mathbf{T}_2 + \rho_2 \mathbf{b}_2 - \mathbf{f}_I$$

Constitutive Equations

- Stress Tensor for plasma: T_1
- Stress Tensor for RBC: T_2
- Interaction force: f_I

Constitutive Equations for Plasma

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- Plasma can be assumed to be a linearly viscous fluid.

$$\mathbf{T}_1 = [\,-p(1-\phi) + \lambda(1-\phi)\mathrm{tr}\,\mathbf{D}_1]\,\mathbf{I} + 2\mu(1-\phi)\mathbf{D}_1$$

- p is the fluid pressure, μ is the viscosity, $\mathbf{D}_1$ is the symmetric part of the velocity gradient, and λ is the second coefficient of viscosity.

$$\mathbf{D}_1 = \frac{1}{2}\left[\nabla \mathbf{v}_1 + (\nabla \mathbf{v}_1)^{\mathrm{T}}\right]$$

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Constitutive Equation for RBC Phase

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- The RBC phase is represented as an anisotropic non-linear density-gradient-type fluid.

$$\mathbf{T_2} = f(\phi, \nabla\phi, \mathbf{D_2}, \mathbf{D_2}^2)$$

$$\mathbf{T_2} = [\beta_o + \beta_1 \nabla\phi \bullet \nabla\phi + \beta_2 \mathrm{tr}\mathbf{D_2}]\mathbf{I} + \beta_3 \mathbf{D_2} + \beta_4 \nabla\phi \otimes \nabla\phi + \beta_5 \mathbf{D_2}^2$$

- $\rho_2 = \varphi\rho_{RBC}$, and the β's are material properties.

$$\mathbf{D_2} = \frac{1}{2}\left[\nabla\mathbf{v}_2 + (\nabla\mathbf{v}_2)^{\mathbf{T}}\right]$$

Constitutive Equation for RBC Phase, cont'

- β_0 is similar to pressure
- β_2 corresponds to the second coefficient of viscosity
- β_1 and β_4 are the material parameters connected with the distribution of the RBCs
- β_3 is the viscosity
- β_5 is similar to the *cross-viscosity* of a Reiner-Rivlin fluid.

Constitutive Equation for RBC Phase, cont'

- β_0 is similar to pressure
- β_2 corresponds to the second coefficient of viscosity
- β_1 and β_4 are the material parameters connected with the distribution of the RBCs
- β_3 is the viscosity
- β_5 is similar to the *cross-viscosity* of a Reiner-Rivlin fluid.

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Constitutive Equation for RBC Phase, cont'

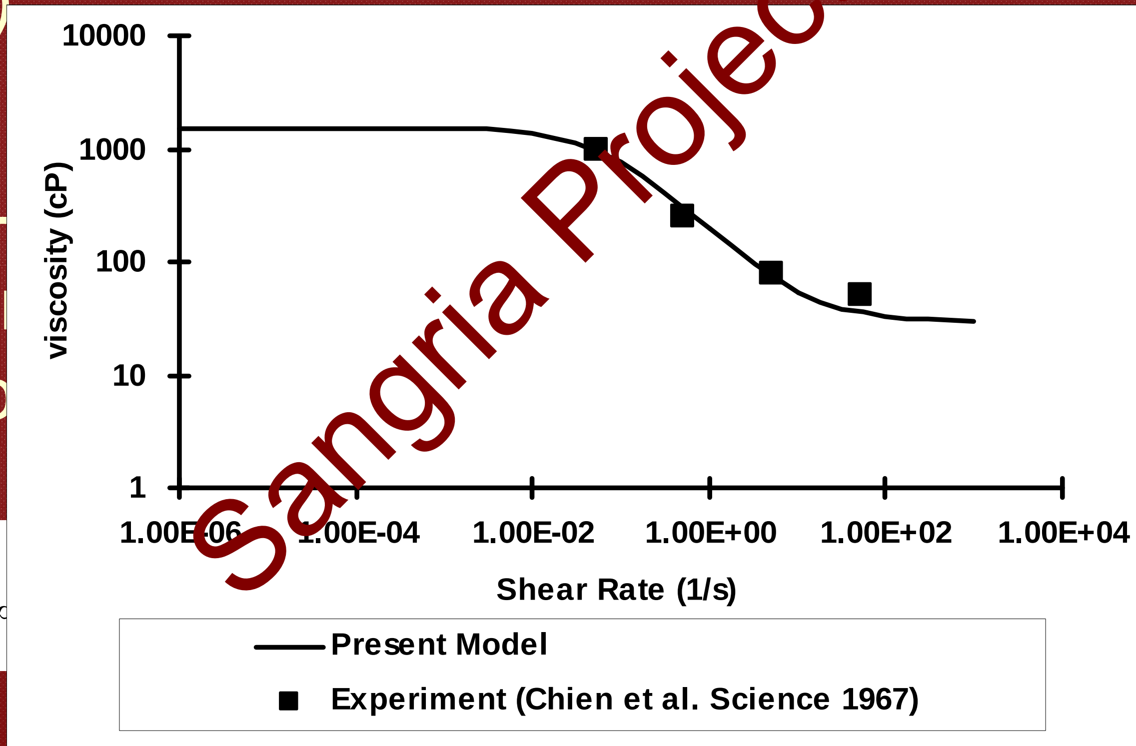
- The viscous effects (β_3) is assumed to be predominate over the effects of the gradient of RBC volume fraction, the second coefficient of viscosity and the normal stresses.
- $\beta_1, \beta_2, \beta_4,$ *and* β_5 are negligible.
- The stress tensor for the RBCs reduces to the structure.

$$\mathbf{T_2} = \beta_0 \mathbf{I} + \beta_3 \mathbf{D_2}$$

Constitutive Equation for RBC Phase, cont'

- β_0 and β_3 are given by Massoudi and Antaki, (2008)
- Shear- … by adopti… the RBC p… et al.

$$\beta_3(\phi) = (\mu_\infty \ldots \tfrac{2}{2})]^{1/2}$$



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Constitutive Equation for Interaction Forces

- The mechanical interaction force can be assumed to be of the form (Johnson 1990).

DIFFUSION

DRAG

$$\mathbf{F}_I = \mathbf{A}_1\,\mathbf{grad}\,\varphi + \mathbf{A}_2 F(\varphi)(\mathbf{v}_2 - \mathbf{v}_1)$$
$$+ \mathbf{A}_3\varphi(2\,\mathbf{tr}\,\mathbf{D}_1^2)^{-1/4}\mathbf{D}_1(\mathbf{v}_2 - \mathbf{v}_1)$$
$$+ \mathbf{A}_4\varphi(\mathbf{W}_2 - \mathbf{W}_1)(\mathbf{v}_2 - \mathbf{v}_1) + \mathbf{A}_5\,\mathbf{a}_{vm}$$

SHEAR LIFT

SPIN LIFT

VIRTUAL MASS

$$\mathbf{A}_2 = \frac{9}{2}\frac{\mu_f}{a^2} \qquad \mathbf{A}_3 = \frac{3(6.46)}{4\pi}\frac{\rho_f^{1/2}\mu_f^{1/2}}{a} \qquad \mathbf{A}_4 = \frac{3}{4}\rho_f \qquad \mathbf{A}_5 = \frac{2\pi}{3}a^3\varphi\frac{1+2\varphi}{1-\varphi}$$

Constitutive Equation for Interaction Forces, cont'

- No investigations as to what form A_1 may have
- The remaining coefficients have not been extensively studied for general two-component flows.
  - Need experiments for 1-D Mixture Theory
- The forms given above are ad-hoc applications of results that are strictly valid under more restricted conditions.

OpenFOAM

- FVM-based open source code
- C++
- Linux environment
- No black box
- Suitable for developing a new flow model

Time Table

	2nd Quarter, 2010	3rd Quarter, 2010	4th Quarter, 2010	1st Quarter, 2011	2nd Quarter, 2011	3rd Quarter, 2011	4th Quarter, 2011
1D Mixture Model (Five Sub-Studies)							
2D/3D Mixture Model (Expansion Channel, Exotic Channel)							
Design Optimization							

Accomplishments

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Journal papers

- Massoudi, M., **Kim, J.**, Hund, S., Antaki, J., *A Mixture Theory formulation for Blood Flow*, in manuscript

Conference abstracts and proceedings

- Massoudi, M., **Kim, J.**, Hund, S., Antaki, J., *A Mixture Theory formulation for Blood Flow*. The 47th Annual Technical Meeting of Society of Engineering Science, 2010.

Acknowledgements

- Dr. Antaki
- Dr. Massoudi
- Dr. Kameneva
- Dr. Gandini
- Lab mates

Thanks for your time!

Questions?