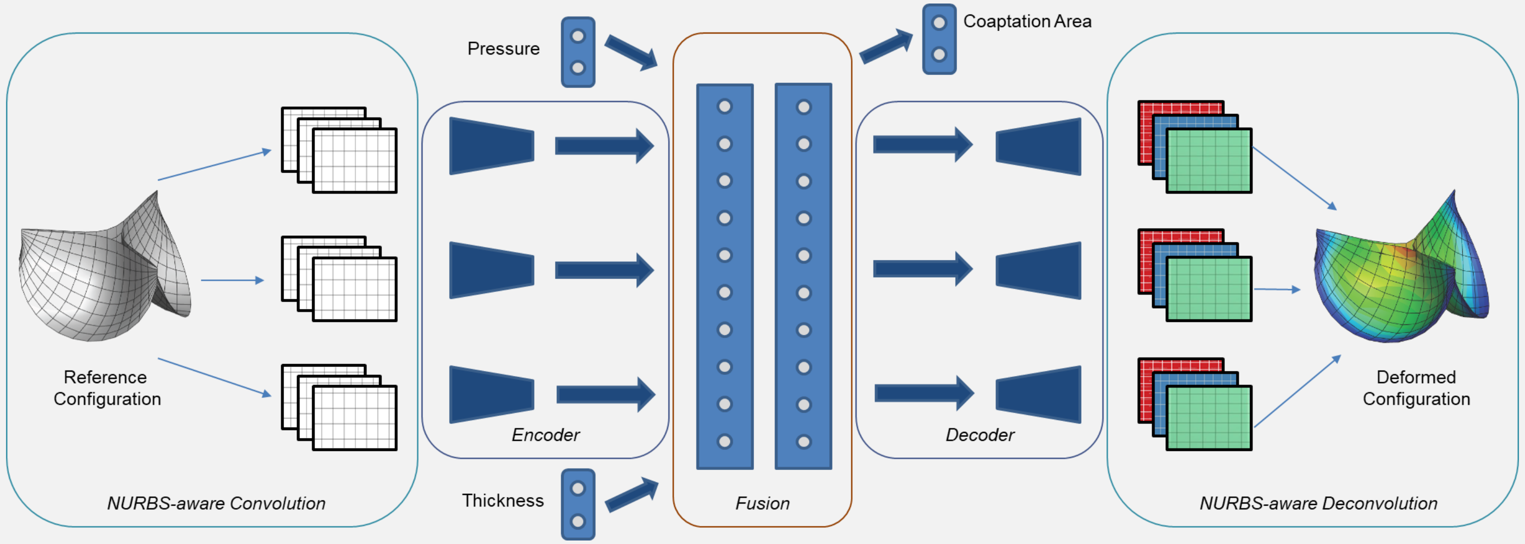
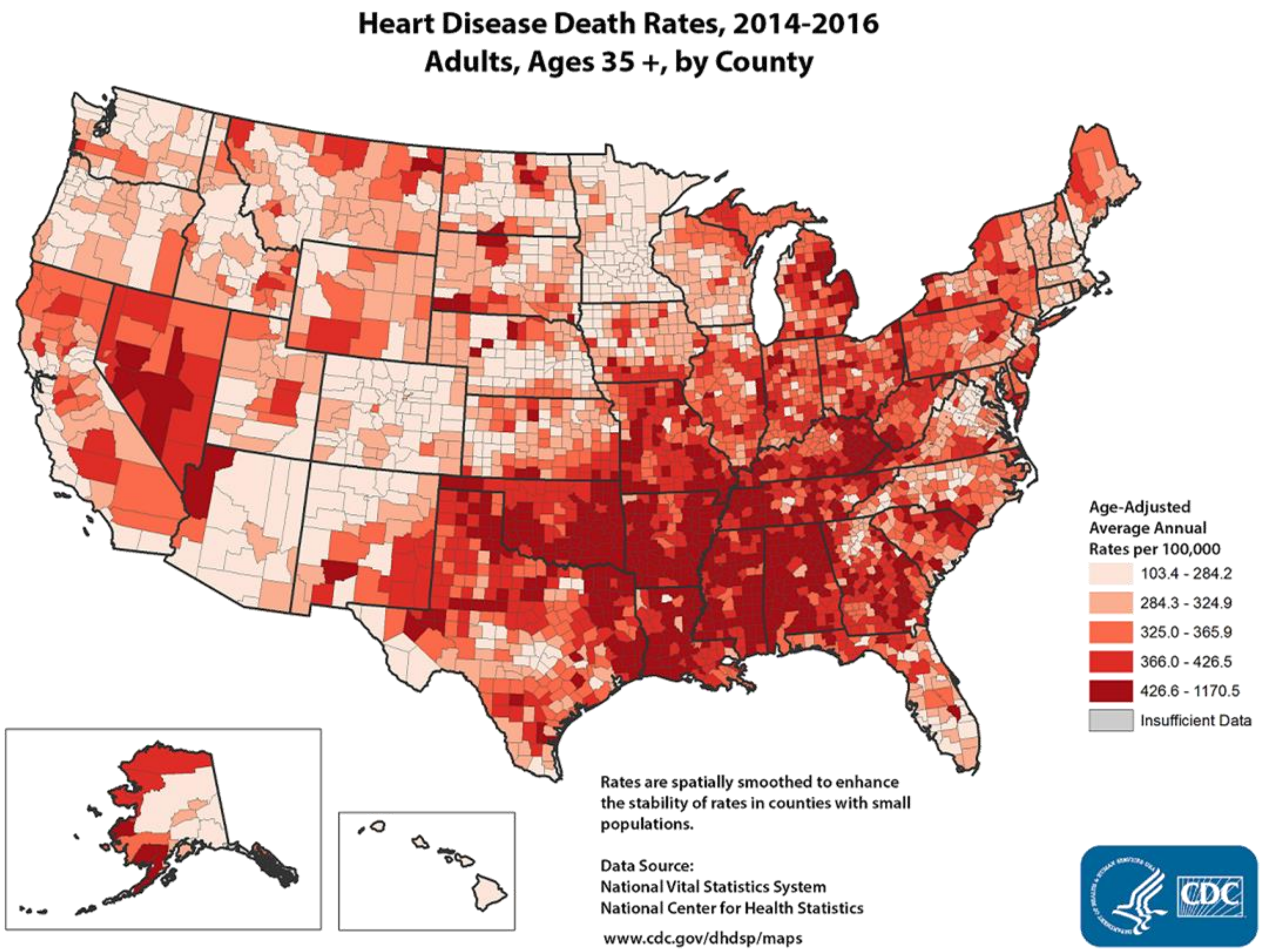


DEEP LEARNING FRAMEWORK FOR DIAGNOSTICS AND PATIENT-SPECIFIC DESIGN OF BIOPROSTHETIC HEART VALVES

ADITYA BALU
SAHITI NALLAGONDA
MING-CHEN HSU
SOUMIK SARKAR
ADARSH KRISHNAMURTHY

Heart Diseases

- Leading cause of death
  - In both the US and the world
  - 1 in every 4 deaths
  - A heart attack every 40s
- Loss of revenue
  - $200 billion each year



St. Jude Medical
More control. Less risk.
$6.336B

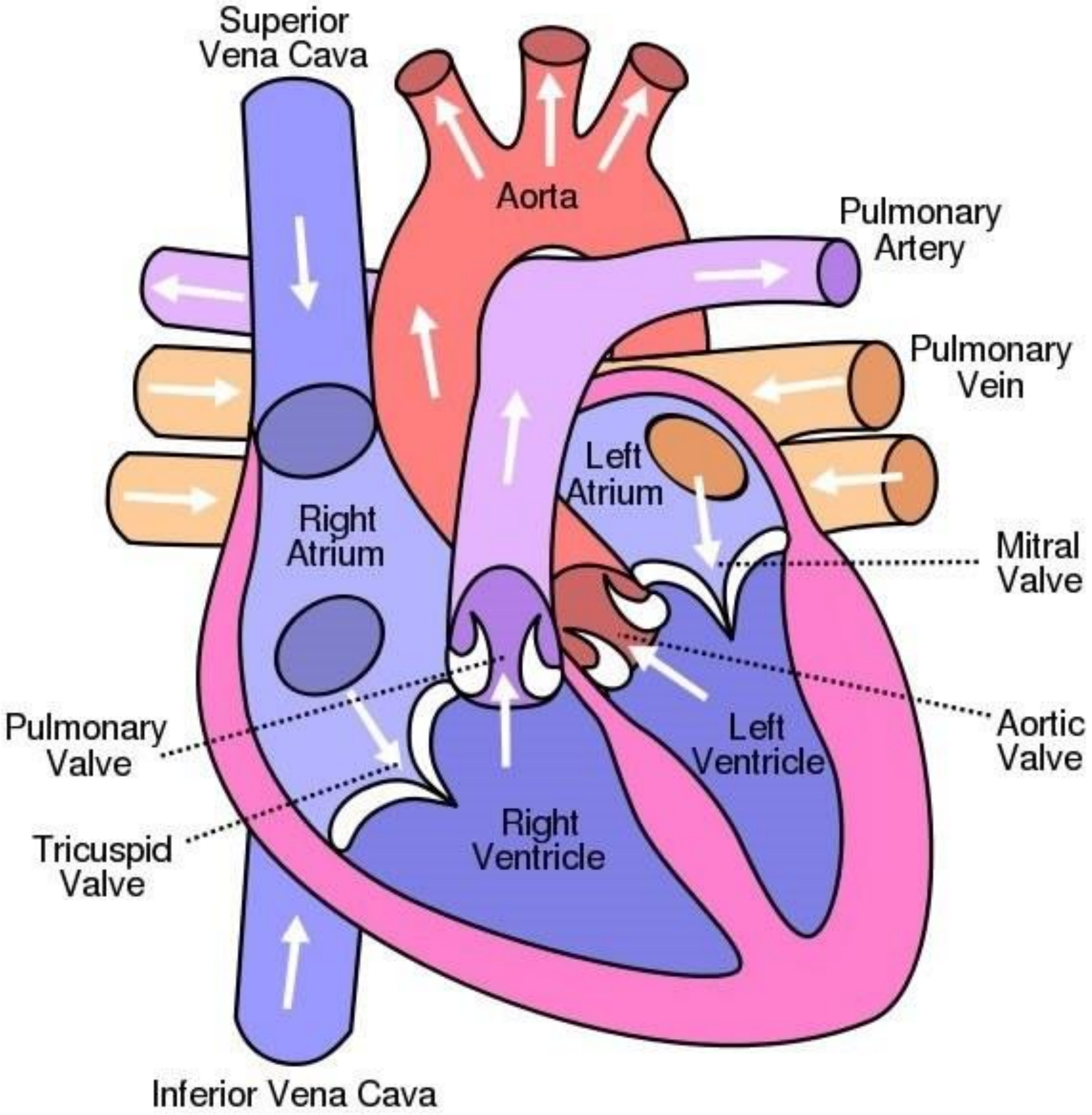
Medtronic
$11.588B

Boston Scientific
$6.116B

Edwards
$3.518B

Valvular Diseases

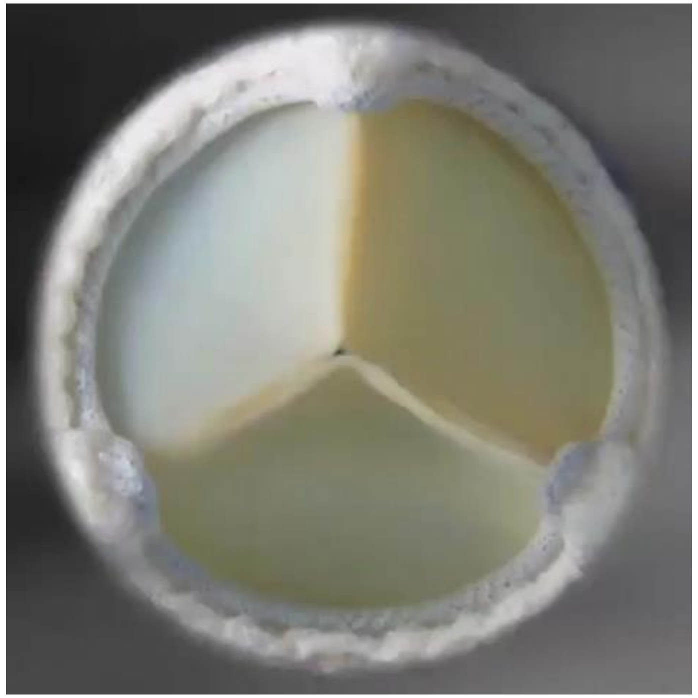
- Valvular Heart diseases
  - Affects more than 2.5% of US population
- Causes
  - Calcification (Narrowing at the opening)
  - Regurgitation (Leakage and reverse flow)
- Intervention
  - Surgical replacement
  - 90,000 prosthetic heart valves per year

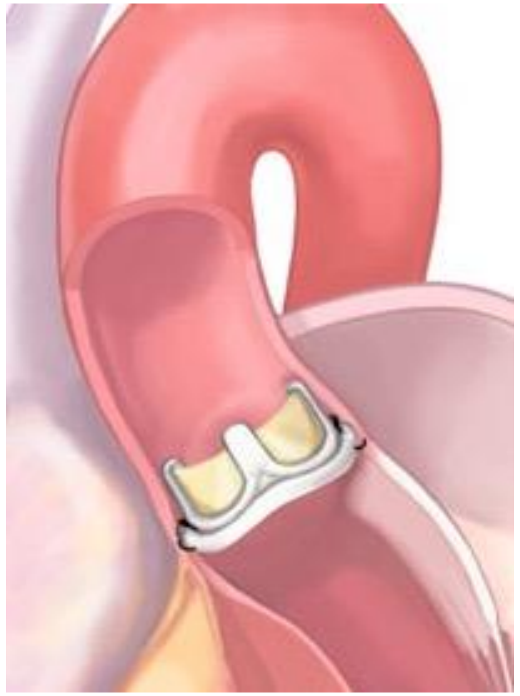


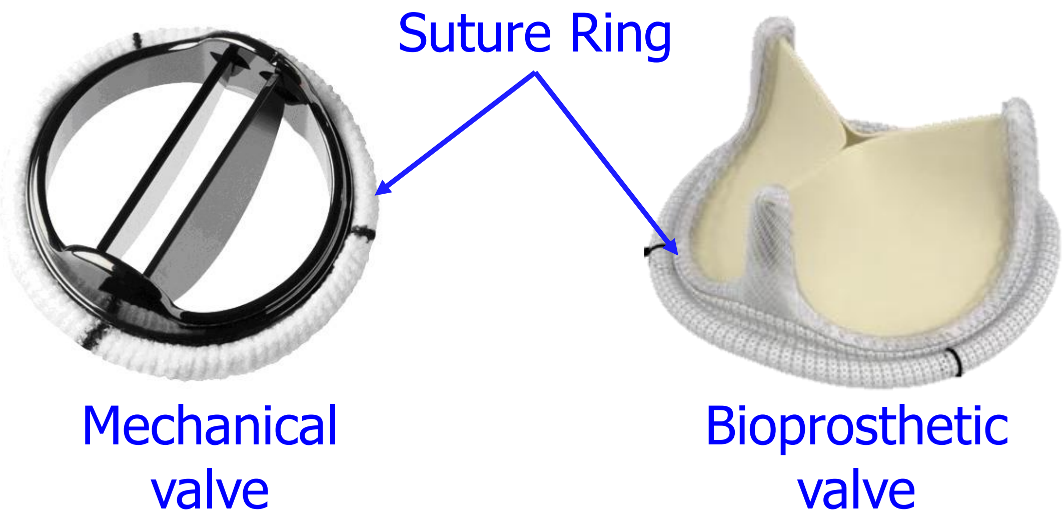
[1] https://www.webmd.com/heart-disease/guide/heart-valve-disease#1

Artificial Heart Valves

- Mechanical Valve
  - Advantages
    - Durable
  - Disadvantages
    - Causes damage to blood cells
    - Need blood thinner to prevent clots
    - Noisy (can cause sleepless nights)
- Bioprosthetic Valves
  - Use bovine or porcine pericardium
  - Advantages
    - Replicates the valve tissue
  - Disadvantages
    - Durability due to fatigue
    - Prone to calcification



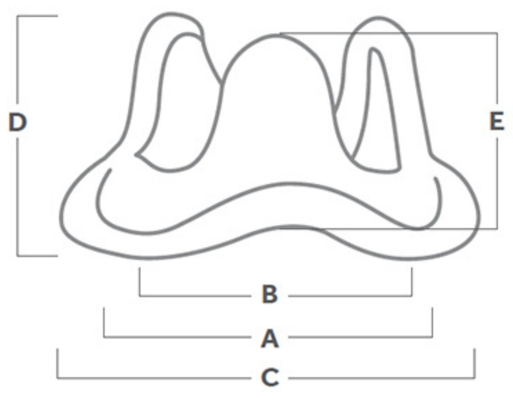




Patient-Specific Replacement Heart Valves

- Common sizes
- Disadvantages of wrong sizing
  - Poor valve function (regurgitation, low flow rate)
  - Durability
- BHV Replacements
  - 10 years

MOSAIC™ AORTIC VALVE, MODEL 305

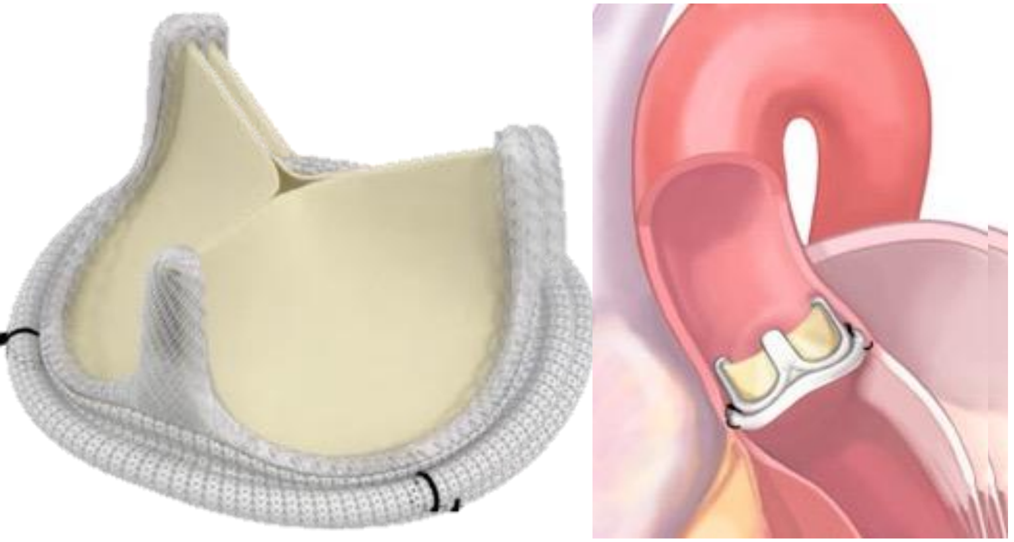


Order Number	Valve Size (Stent O.D.† (±0.5 mm)	Orifice Diameter (Stent O.D. (±0.5 mm)	Suture Ring Diameter (±1 mm)	Valve Height (±0.5 mm)	Aortic Protrusion (±0.5 mm)
	(A)	(B)	(C)	(D)	(E)
305C219	19	17.5	25.0	13.5	11.0
305C221	21	18.5	27.0	15.0	12.0
305C223	23	20.5	30.0	16.0	13.5
305C225	25	22.0	33.0	17.5	15.0
305C227	27	24.0	36.0	18.5	15.5
305C229	29	26.0	39.0	20.0	16.0

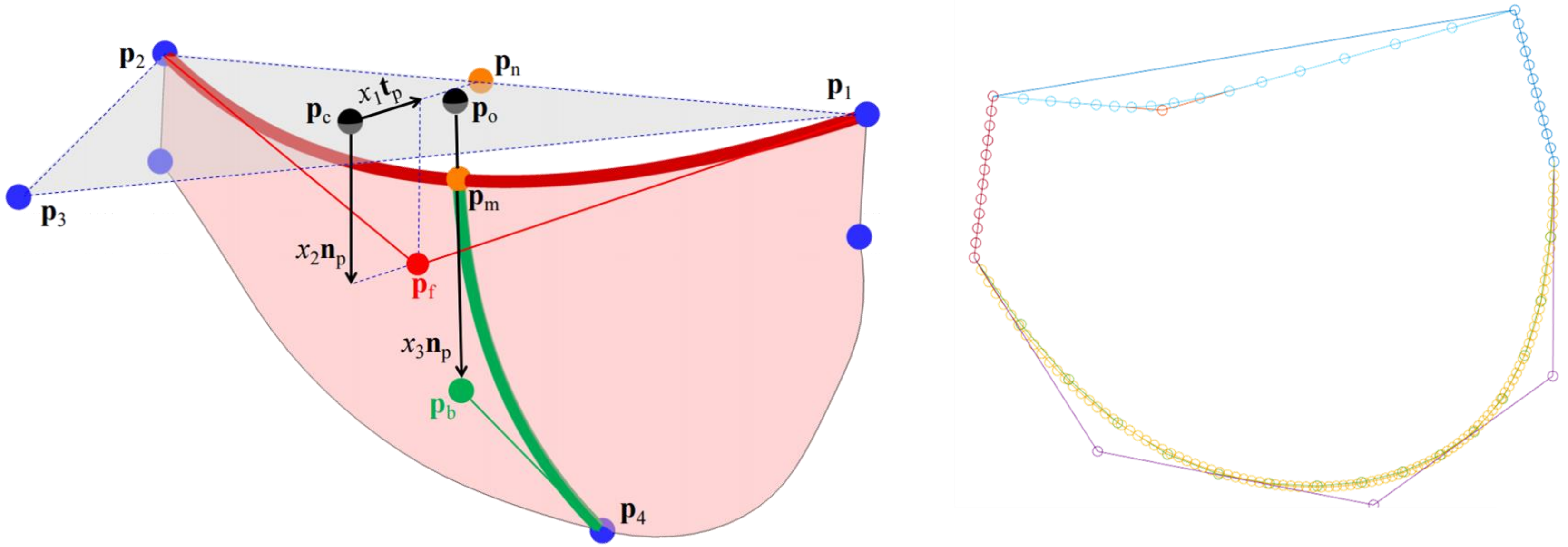
[2] https://www.medtronic.com/ca-en/healthcare-professionals/products/cardiovascular/heart-valves-surgical/mosaic-mosaic-ultra-bioprostheses.html
[3] https://www.heartvalvechoice.com/tissue-vs-mechanical-heart-valve/

Patient-Specific Design of Heart Valves

- Design heart valves for every patient using their medical results



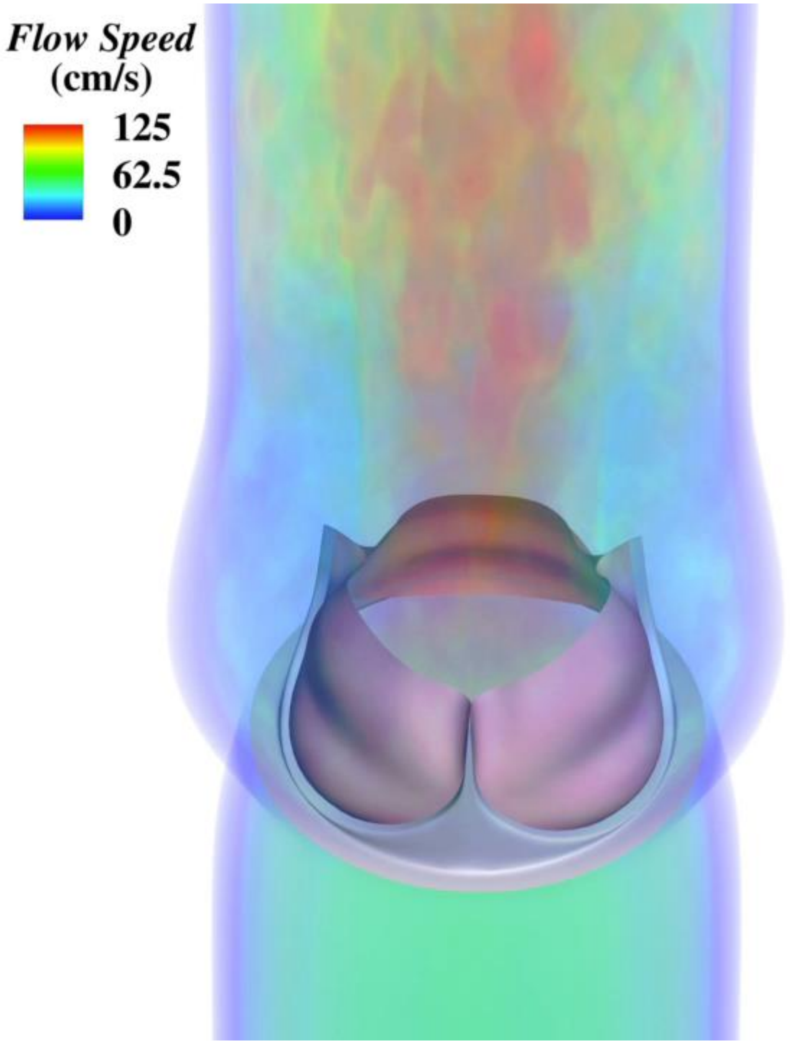
An aortic bioprosthetic heart valve with its placement on aorta



A view of one leaflet of the heart valve with its parametric curve boundary

Valve Function

- Coaptation Area
- Open area

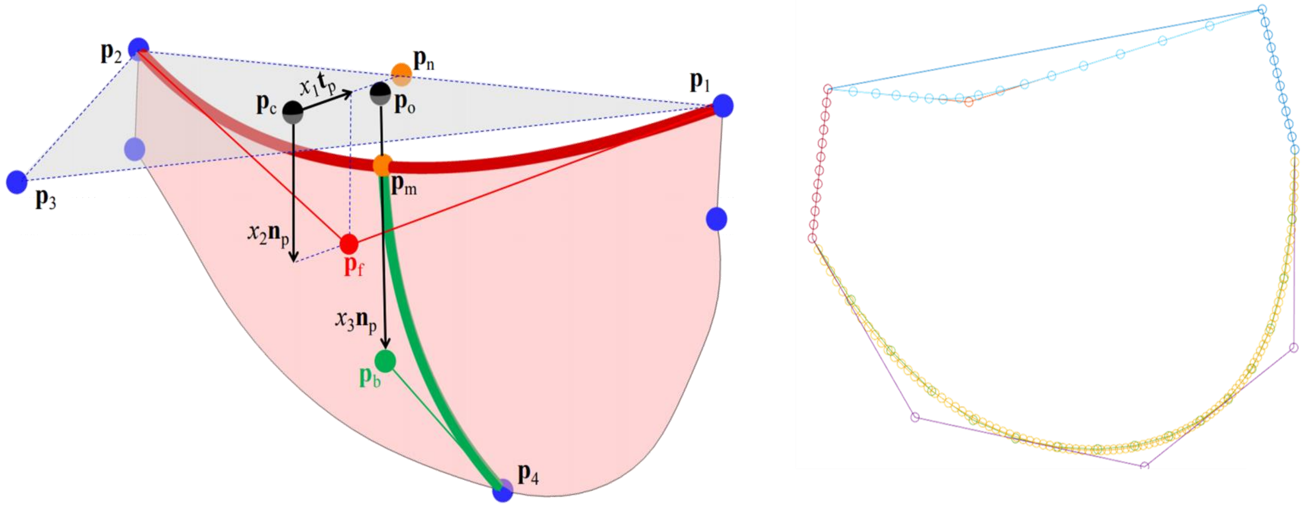


Open Area

Coaptation Area

Design of BHV

- Custom design requires evaluation of the valve function
- Simulation speeds up the process

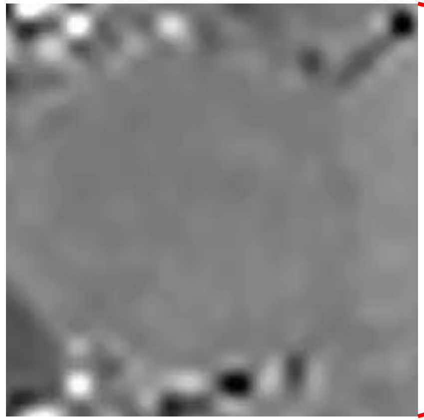


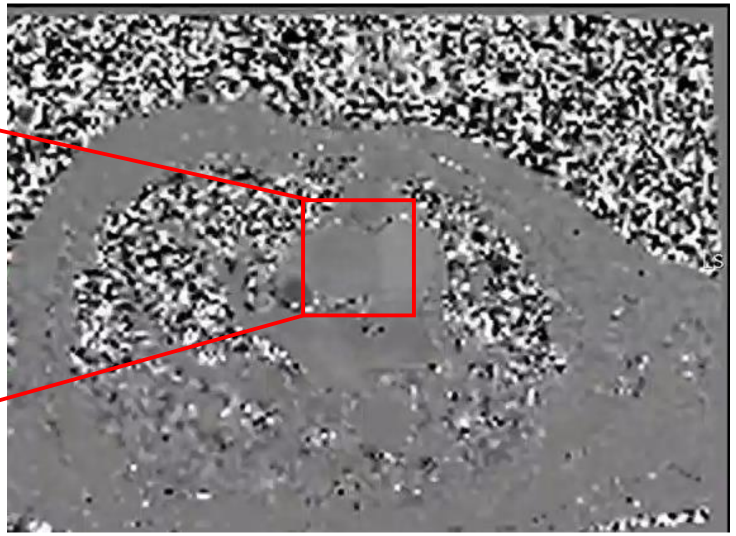
A view of one leaflet of the heart valve with its parametric curve boundary

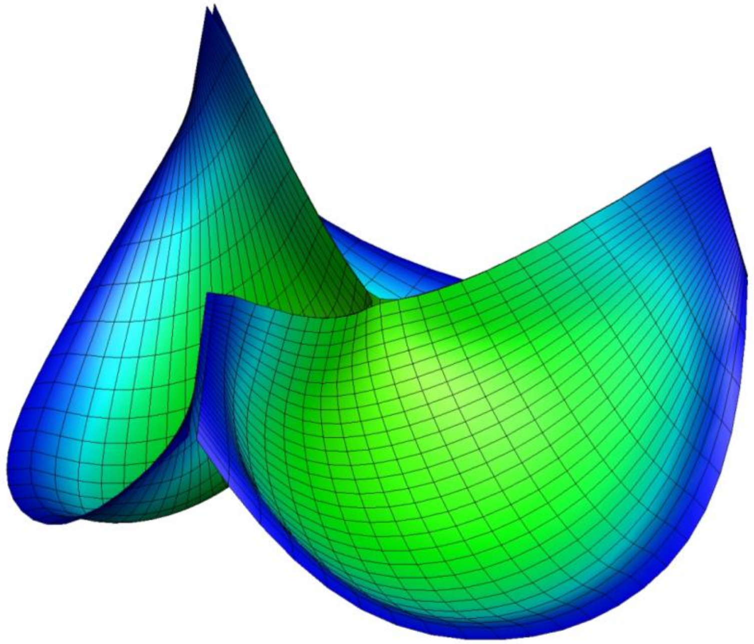
Simulations of BHVs

- Imaging analysis for surgical decision making is difficult
- Simulation of physics is necessary

Phase contrast MRI image data

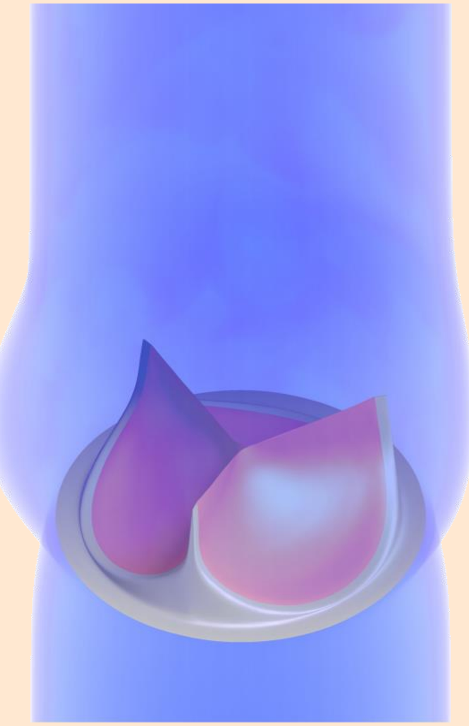




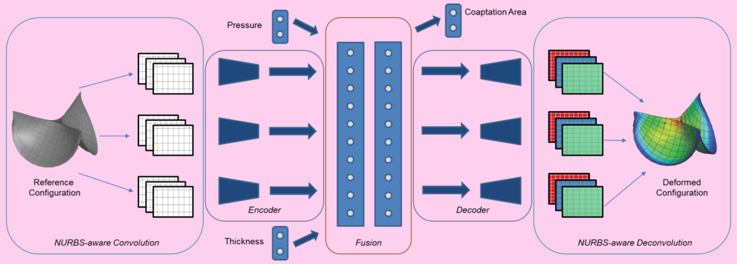


[4] M. C. Hsu et al., "Dynamic and fluid–structure interaction simulations of bioprosthetic heart valves using parametric design with T-splines and Fung-type material models," Computational Mechanics, 55 (2015) 1211-1225

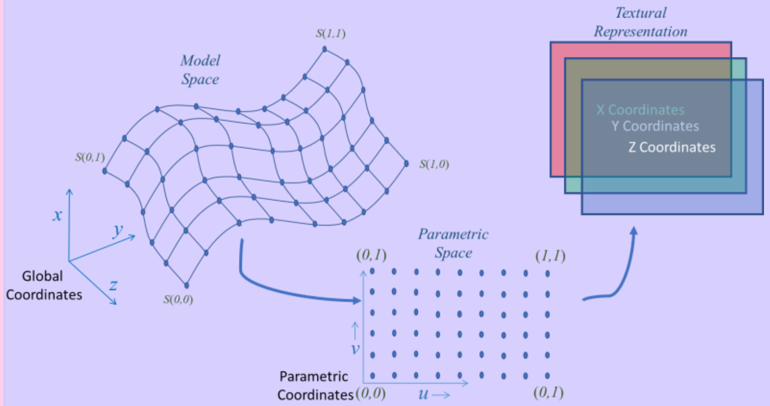
Outline



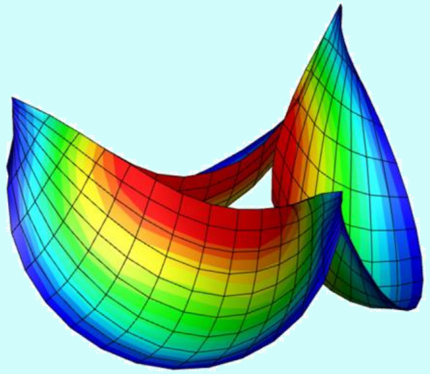
Computational Modeling of BHVs



ML Framework for Valve Mechanics



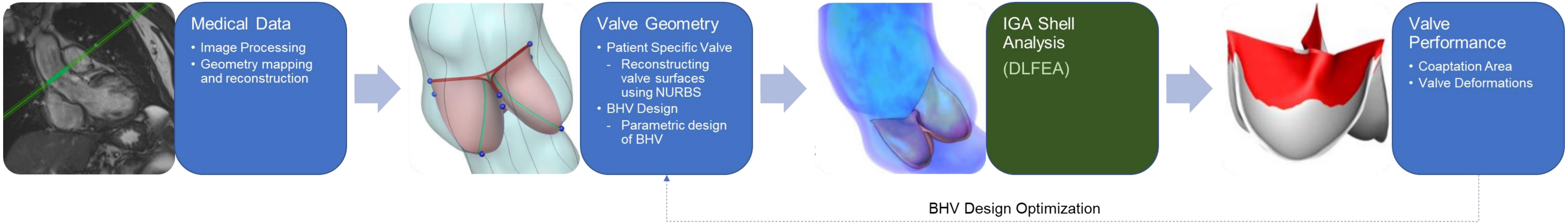
Data Representation and Data Generation



Results and Conclusions

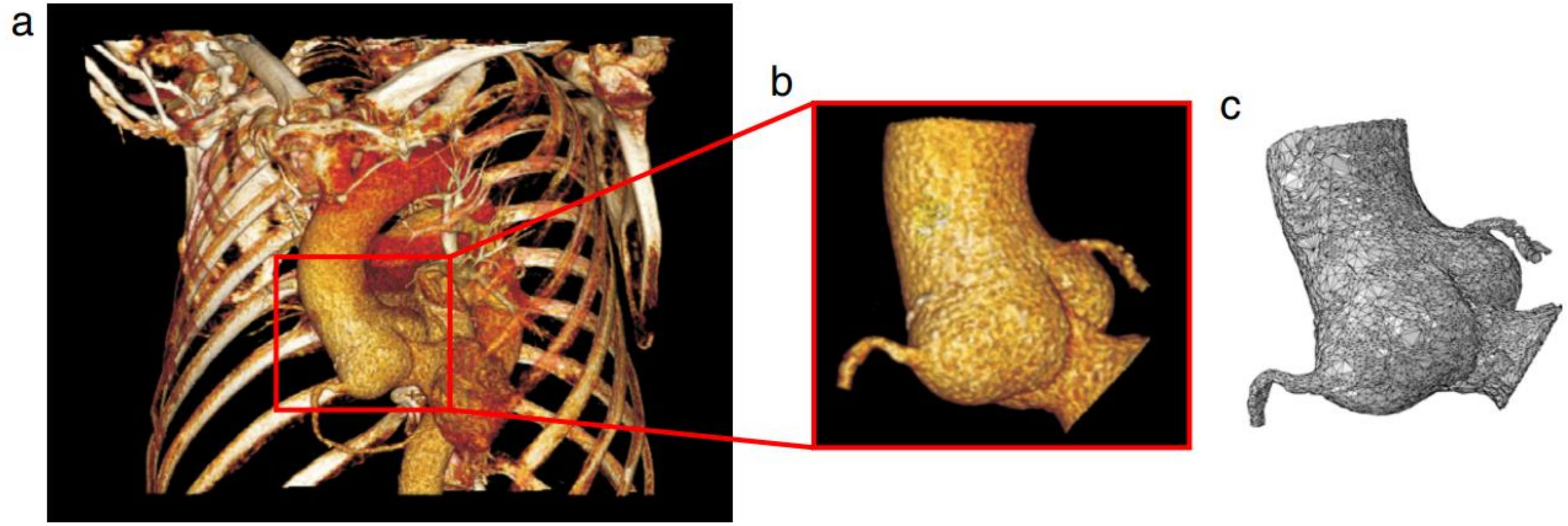
Computational Modeling Frameworks for BHVs

- Reconstruct the heart valve from medical images
  - Generate geometric representation of the heart valve (NURBS)
- Perform valve closure simulations
  - Use Isogeometric analysis



[5] S Morganti, F Auricchio, DJ Benson, FI Gambarin, S Hartmann, TJR Hughes, and A Reali. Patient-specific isogeometric structural analysis of aortic valve closure. Computer Methods in Applied Mechanics and Engineering, 284:508–520, 2015
[6] Fei Xu, Simone Morganti, Rana Zakerzadeh, David Kamensky, Ferdinando Auricchio, Alessandro Reali, Thomas JR Hughes, Michael S Sacks, and Ming-Chen Hsu. A framework for designing patient-specific bioprosthetic heart valves using immersogeometric fluid–structure interaction analysis. International journal for numerical methods in biomedical engineering, 34(4):e2938, 2018.

Reconstruction of Aortic Valve



Reconstruction of Aortic Root from CTA for a patient

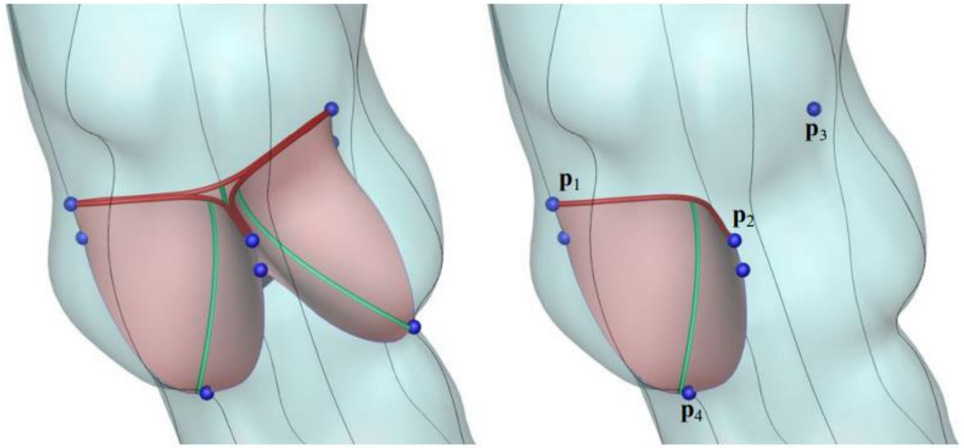


Figure 3: The key geometric features used to parametrically control the valve designs. The blue key points define the attachment of the valve to the root. The red and green curves are parametrically controlled for valve design.

[5] S Morganti, F Auricchio, DJ Benson, FI Gambarin, S Hartmann, TJR Hughes, and A Reali. Patient-specific isogeometric structural analysis of aortic valve closure. Computer Methods in Applied Mechanics and Engineering, 284:508–520, 2015
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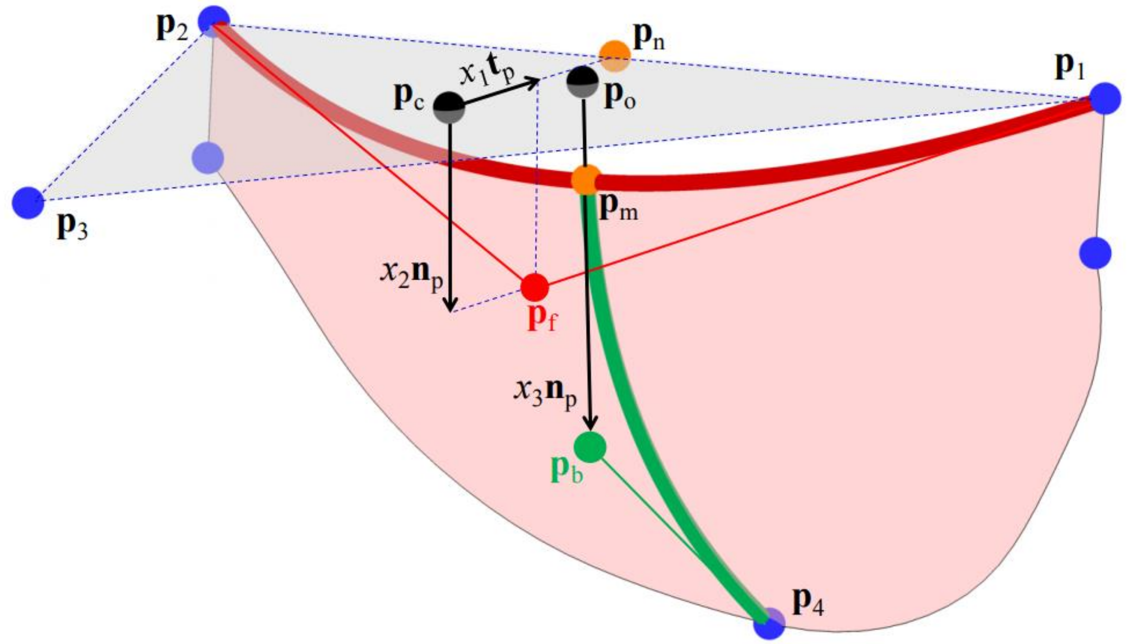
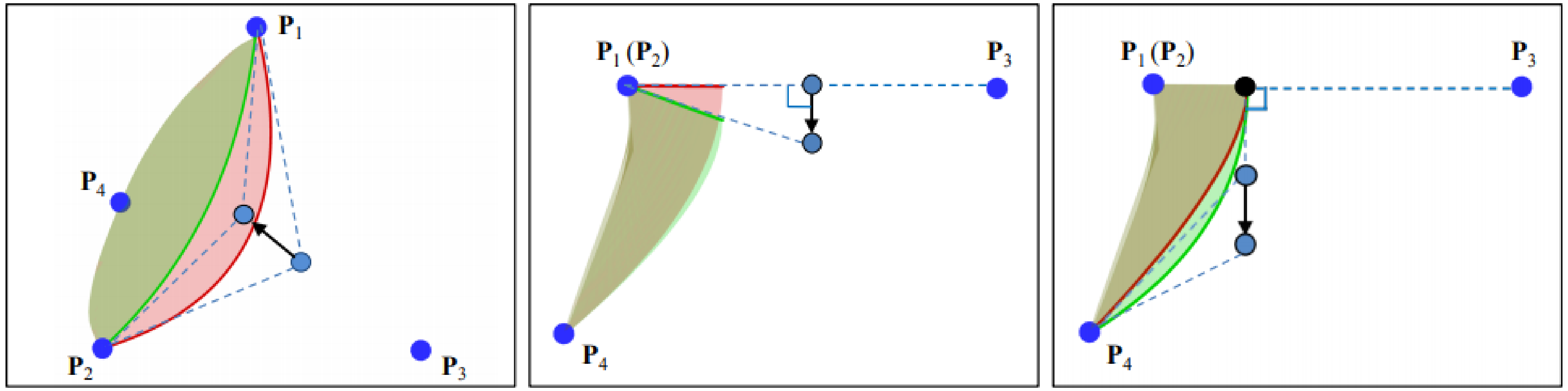
Valve Reconstruction and design

- Interface valve with the patient's aortic root
- Define parameters for the designing
- Vary them to get good performance



Parametric Design of Heart Valve Geometry

- Parameters of the heart valve affecting the geometry
  - Belly curvature (x_3)
  - Height of free edge (x_2)
  - Curvature of free edge (x_1)



(a) Increasing x_1 (b) Increasing x_2 (c) Increasing x_3

[5] S Morganti, F Auricchio, DJ Benson, FI Gambarin, S Hartmann, TJR Hughes, and A Reali. Patient-specific isogeometric structural analysis of aortic valve closure. Computer Methods in Applied Mechanics and Engineering, 284:508–520, 2015
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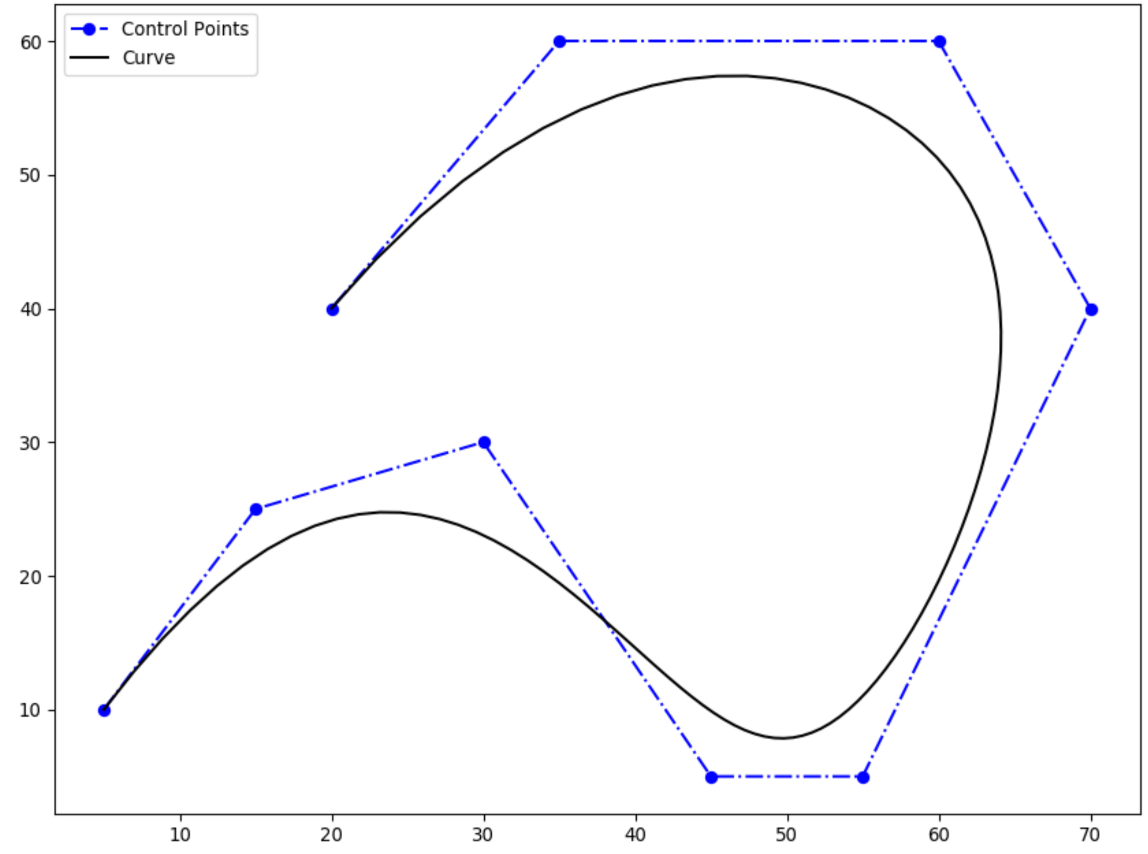
Non-Uniform Rational B-Spline Representation

- Approximate the geometry using:
  - Control Points
  - Basis Functions (Piecewise polynomial)
  - Knot vectors
  - Weights



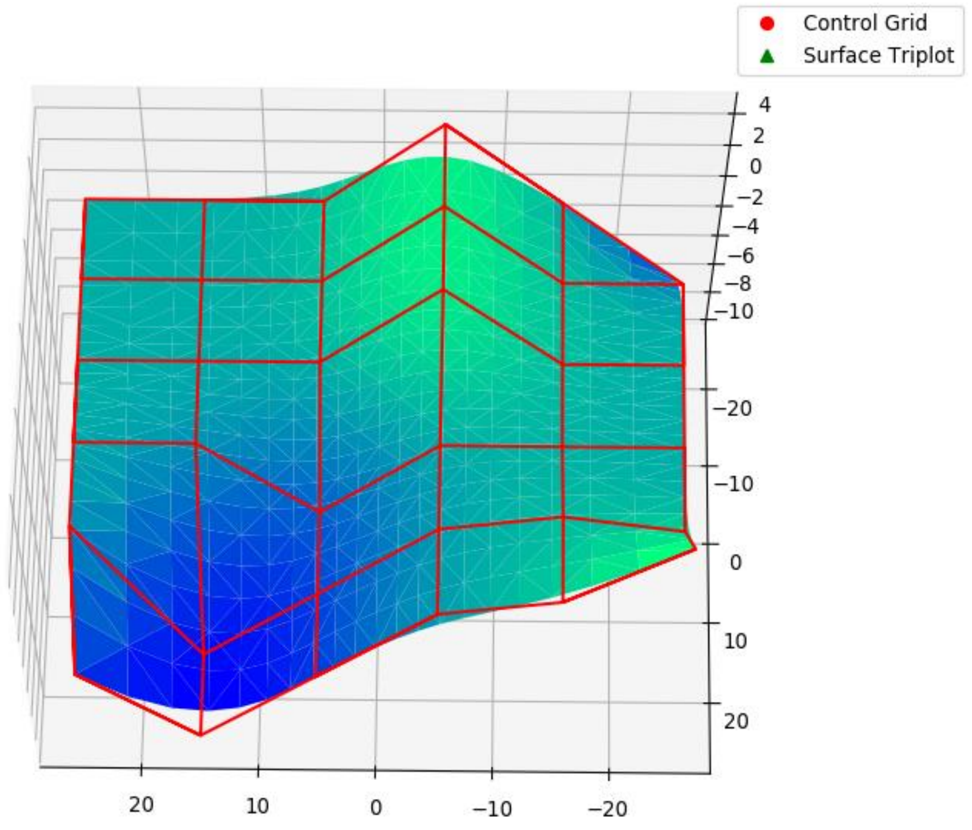
A sample NURBS curve representation

[7] http://web.me.iastate.edu/idealab/c-nurbs-python.html

Non-Uniform Rational B-Spline Representation

- Approximate the geometry using:
  - Control Points
  - Basis Functions
  - Knot vectors
  - Weights

- Tensor Product for surfaces



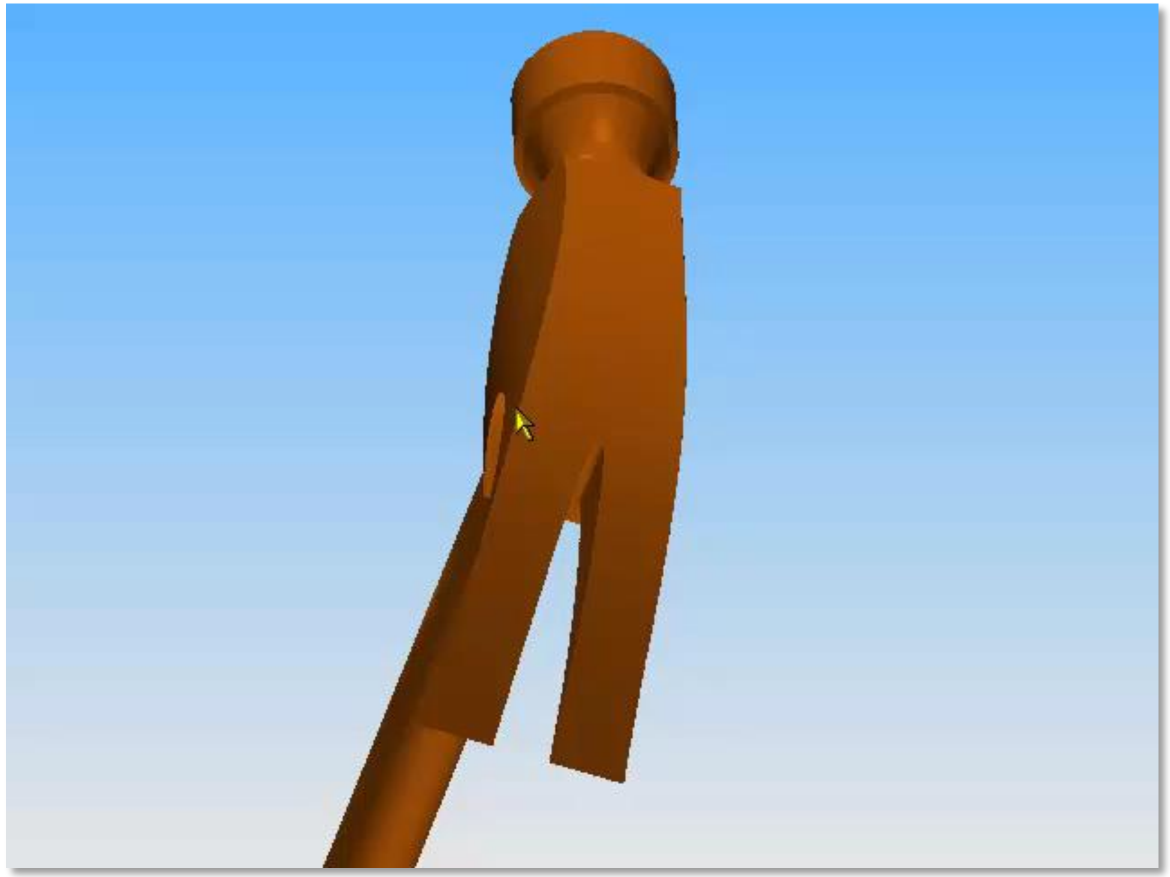
A sample NURBS surface representation

[7] http://web.me.iastate.edu/idealab/c-nurbs-python.html

Non-Uniform Rational B-Spline Representation

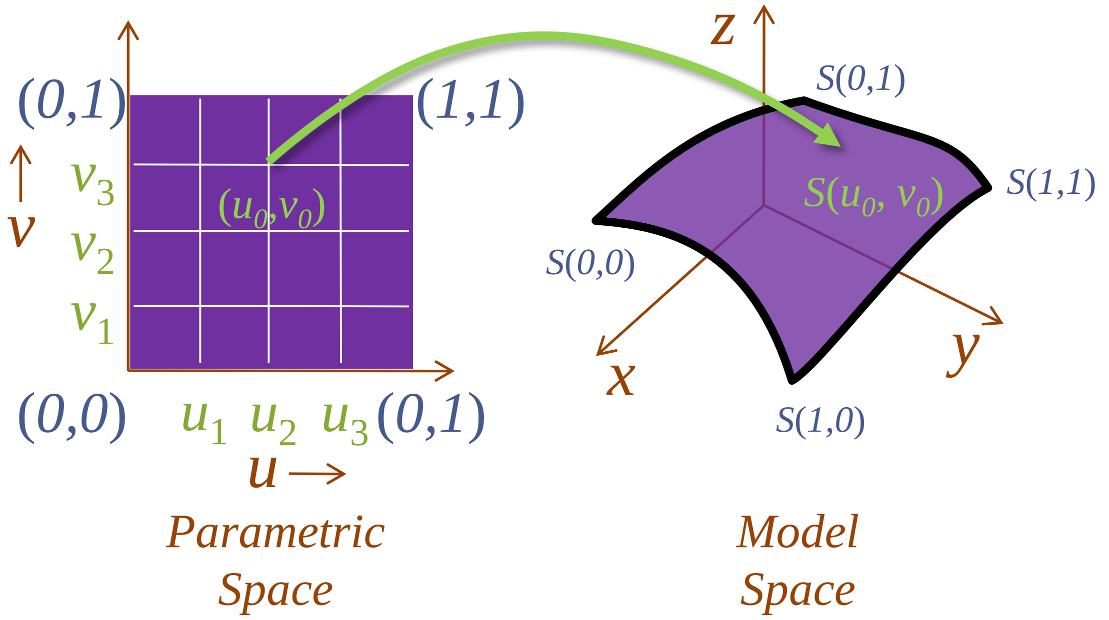
De facto surface representation

- Most general spline
- Piecewise-polynomial tensor product surfaces
- Can represent complex geometry such as heart valves



[7] https://github.com/orbingol/NURBS-Python
[8] Piegl, L., & Tiller, W. (2012). *The NURBS book*. Springer Science & Business Media.

NURBS Evaluation



Compact definition:
Defined completely by
- Control mesh
- u and v knot vectors

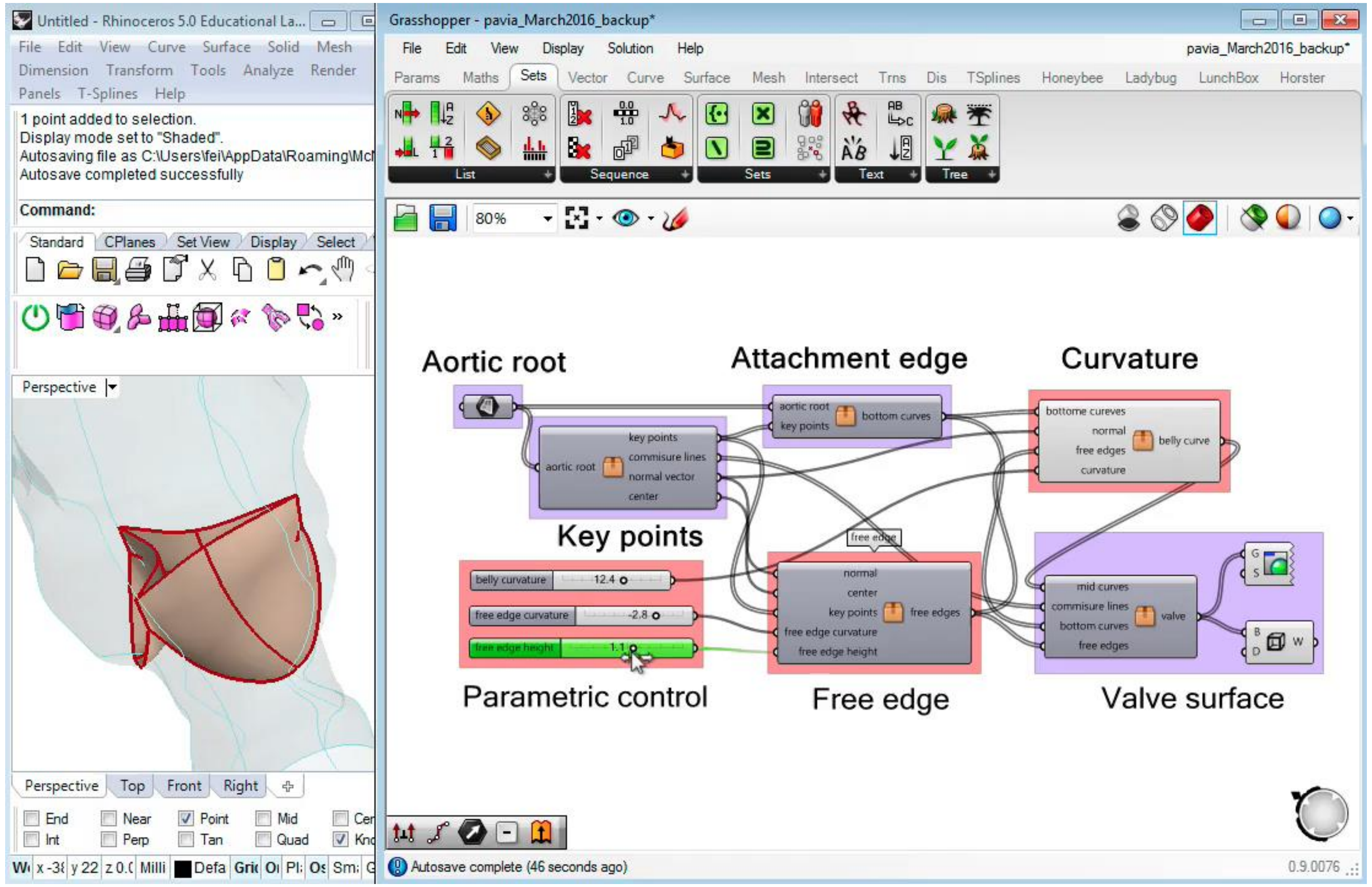
Basis Functions   Control Points   p = degree   Knots (u or v)

$$S(u,v)=\frac{\sum_{j=0}^{m}\sum_{i=0}^{n}N_i^p(u)N_j^q(v)w_{ij}P_{ij}}{\sum_{j=0}^{m}\sum_{i=0}^{n}N_i^p(u)N_j^q(v)w_{ij}}$$

$$N_i^p(u)=\frac{u-u_i}{u_{i+p}-u_i}N_i^{p-1}(u)+\frac{u_{i+p+1}-u}{u_{i+p+1}-u_{i+1}}N_{i+1}^{p-1}(u)$$

$$N_i^0(u)=\begin{cases}1 & if\ \ u_i\le u<u_{i+1}\\ 0 & otherwise\end{cases}$$

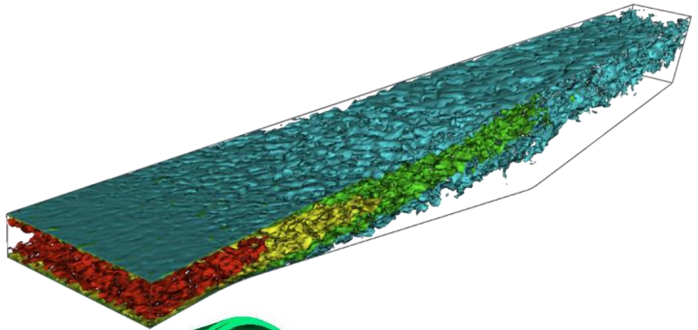
Patient Specific Design of Heart Valve Geometry

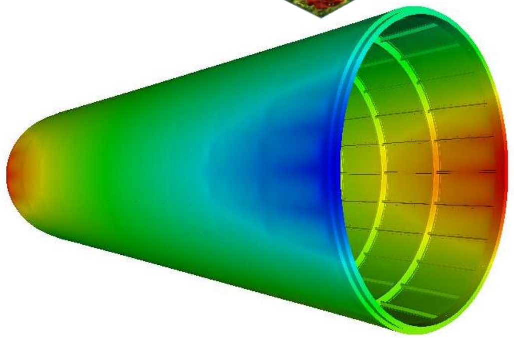


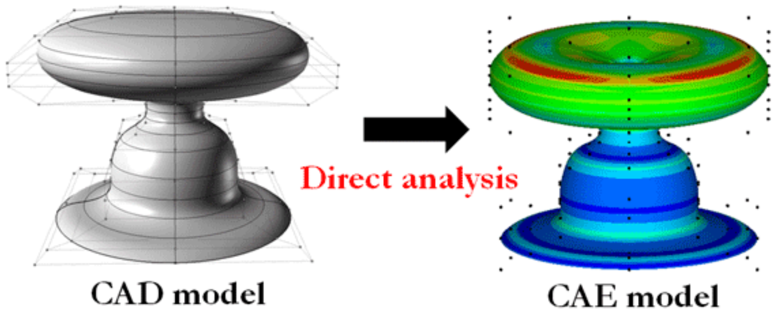
[9] https://web.me.iastate.edu/jmchsu/heart-valves.html

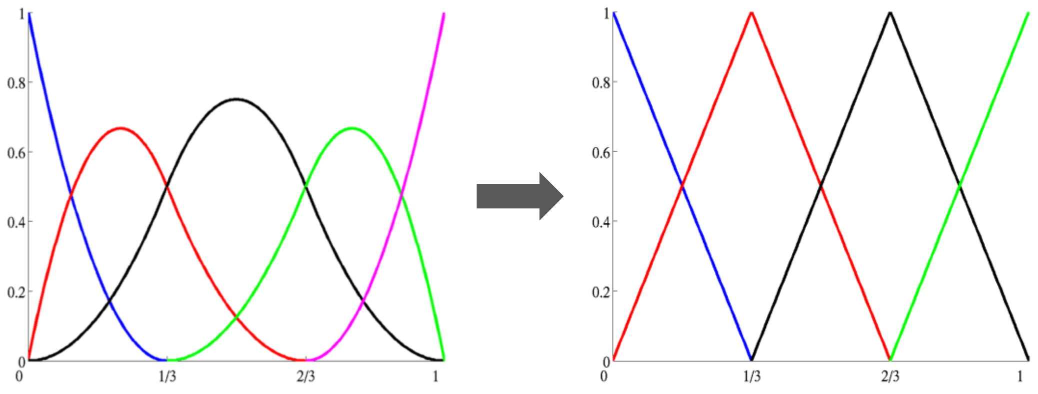
Isogeometric Analysis

- Based on technologies such as NURBS
- Same ("exact") functional description is used for **geometry** and **simulation**.
- Includes standard FEA as a special case, but offers other possibilities:
  - Precise and efficient geometric modeling
  - Superior approximation properties
  - Smooth and higher-order basis functions
  - **Integration of design and analysis**



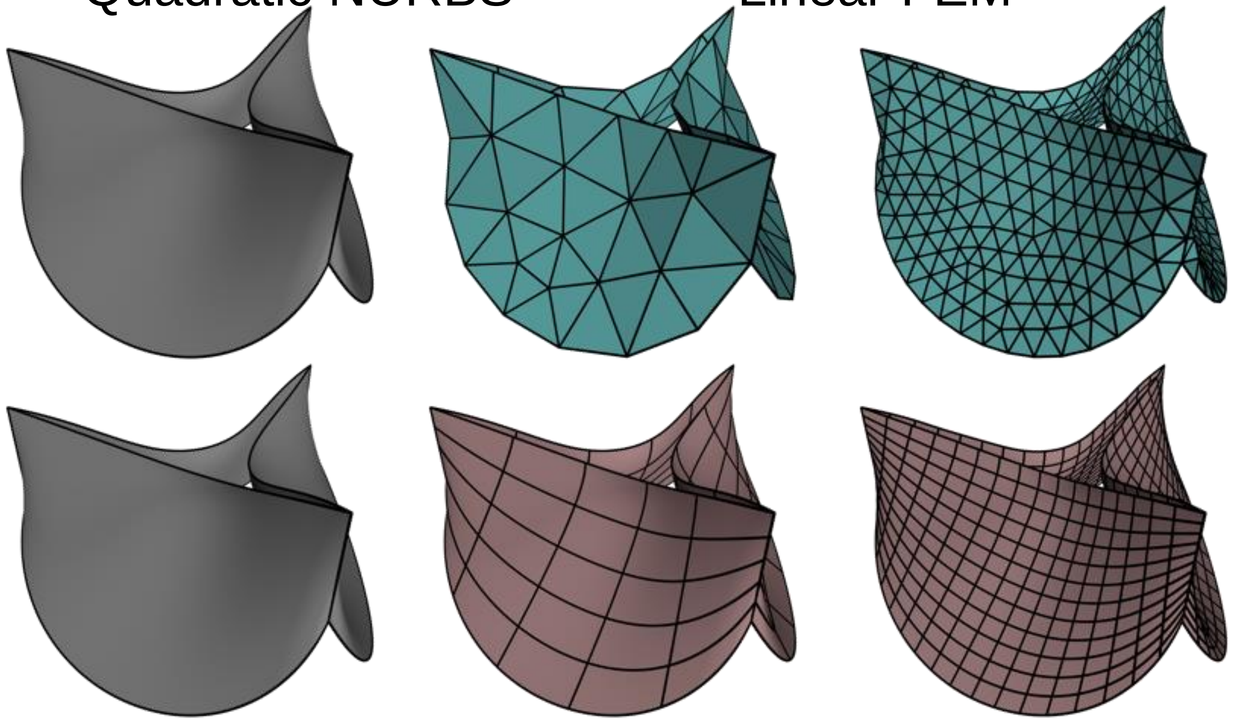






Quadratic NURBS

Linear FEM



FEM

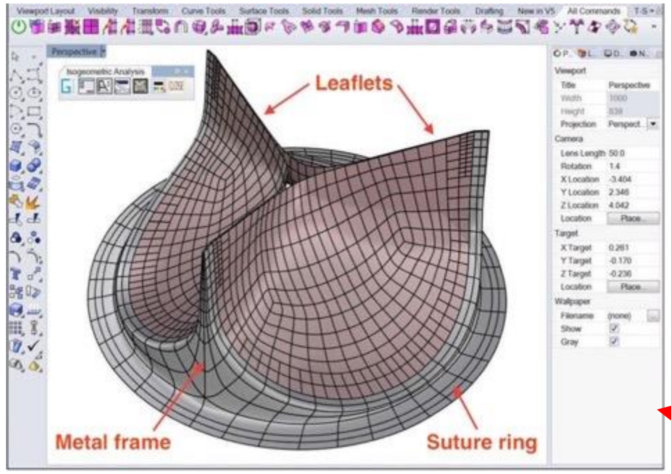
IGA

CAD Model

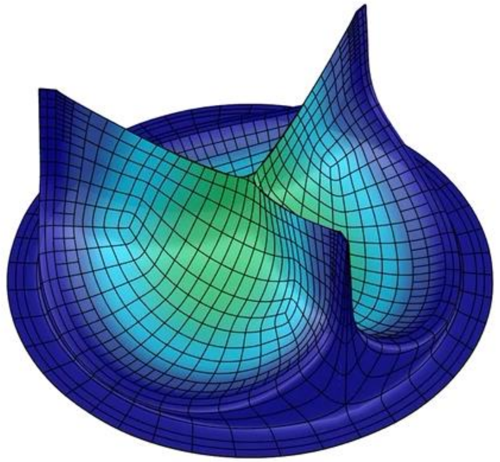
Coarse Mesh

Refined Mesh

CAD Model



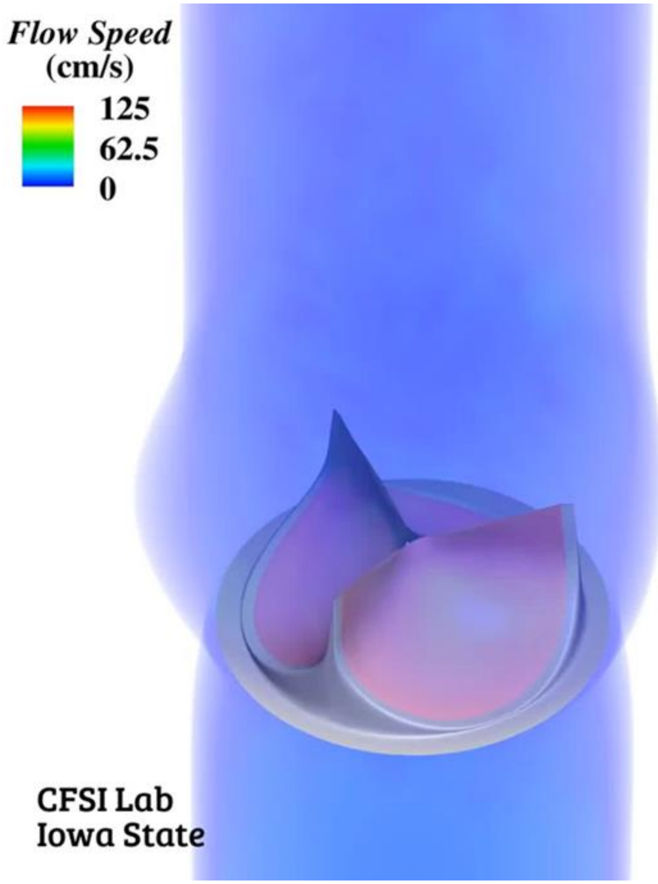
Isogeometric Analysis



Analysis Mesh

Challenges of Using IGA for BHV Design

- Patient-specific design of bioprosthetic heart valves (BHV) require extensive exploration of design parameter space
- Computational analysis is tedious and compute intensive
- Lot of historical simulation data
- Real-time decision support tool for analyzing valve function is difficult

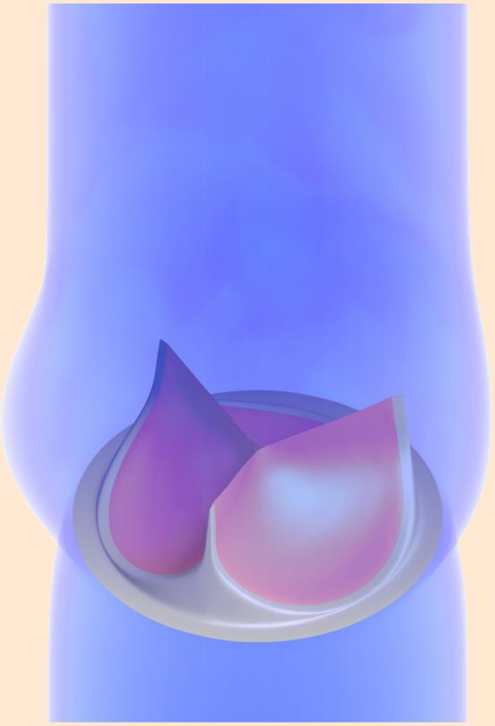


M.C. Hsu et.al., "Dynamic and fluid–structure interaction simulations of bioprosthetic heart valves using parametric design with T-splines and Fung-type material models," Computational Mechanics, 55 (2015) 1211-1225

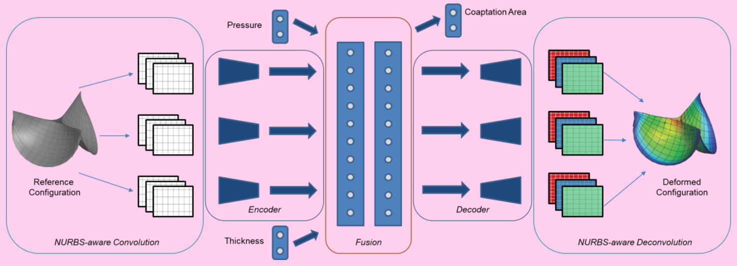
Deep Learning

- Lots of Uses in Medical Sciences
- Can learn complex phenomenon like the biomechanics
- Can provide real-time support

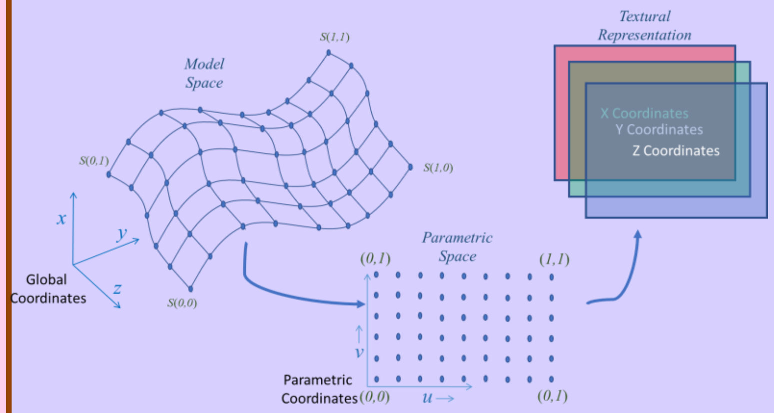
Outline



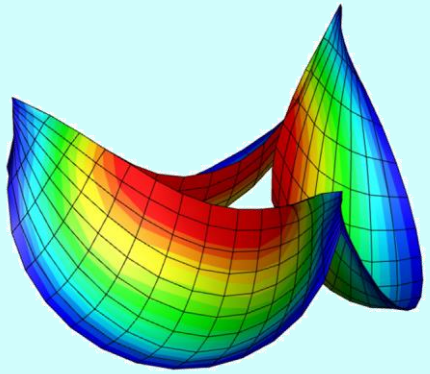
Computational Modeling of BHVs



ML Framework for Valve Mechanics



Data Generation



Results and Conclusions

ML Framework for Valve Biomechanics

Physical characteristics to learn:

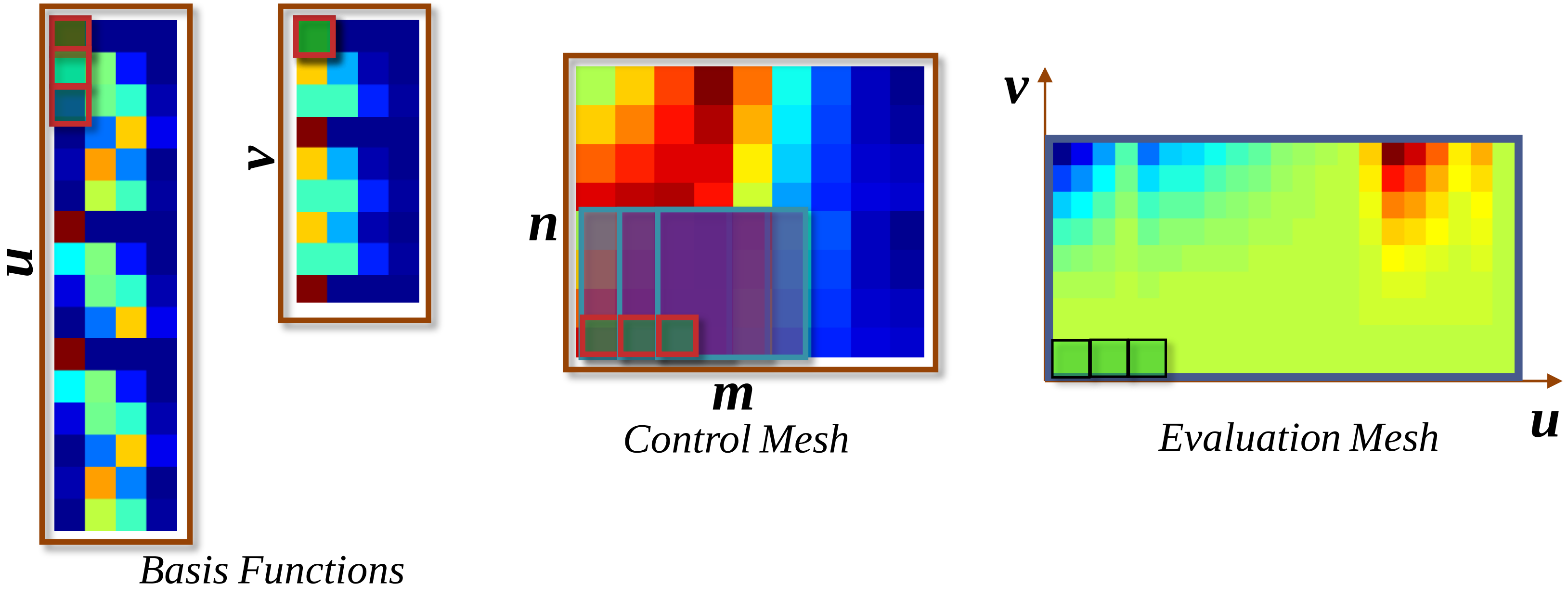
1. Learn from 3D input space and predict 3D output deformation
2. Learn the effect of loads and boundary conditions
3. Interaction among the different leaflets
4. Material behavior and dependence on the thickness of the leaflets

Embed phenomenon for learning:

1. Data Representation
2. Model Representation
3. Training Algorithms

Convolutional Neural Networks

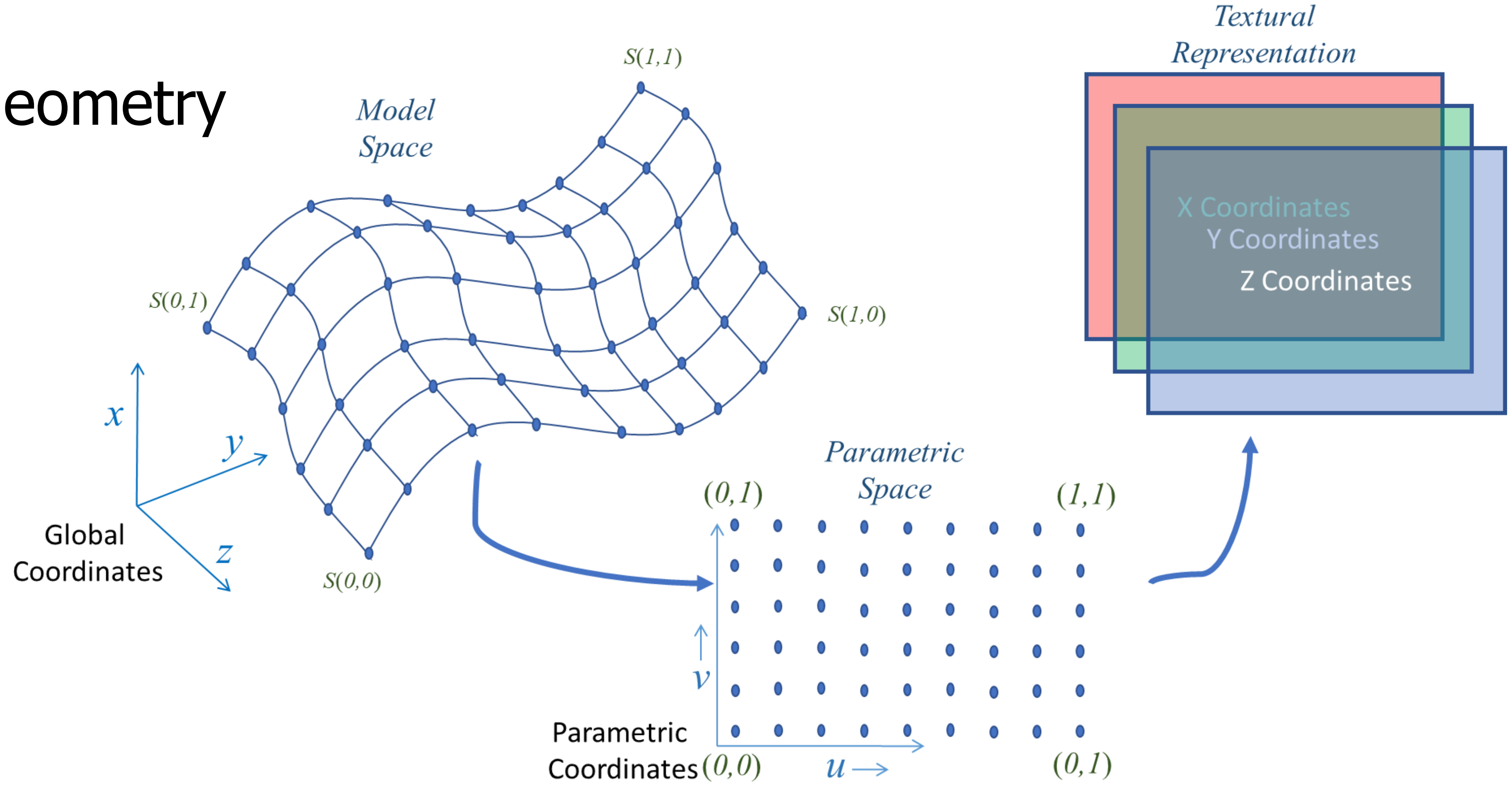
- Convolution Operator
- Neural Networks
- Convolutional Neural Networks
- NURBS as Convolution



[3] Krishnamurthy, Adarsh, Rahul Khardekar, Sara McMains, Kirk Haller, and Gershon Elber. "Performing efficient NURBS modeling operations on the GPU." *IEEE Transactions on Visualization and Computer Graphics* 15, no. 4 (2009): 530-543.

NURBS-aware Convolution

- Use textural representation of the NURBS control points as input to a regular CNN
  - Localization of geometry



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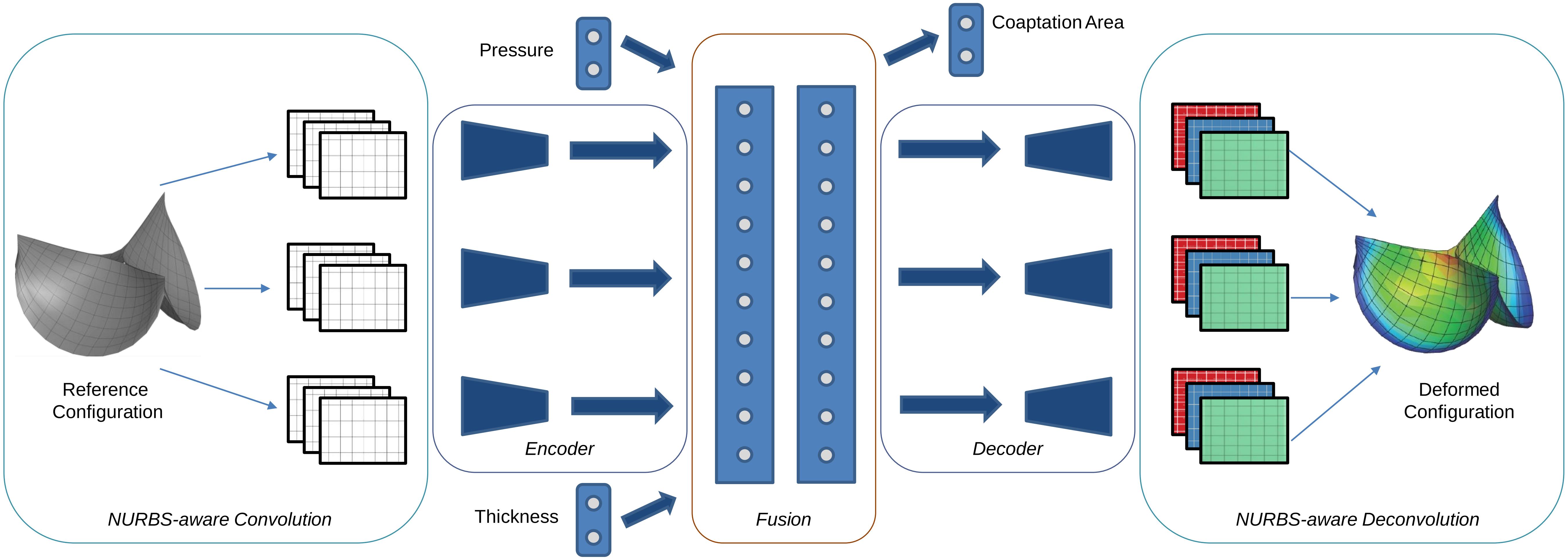
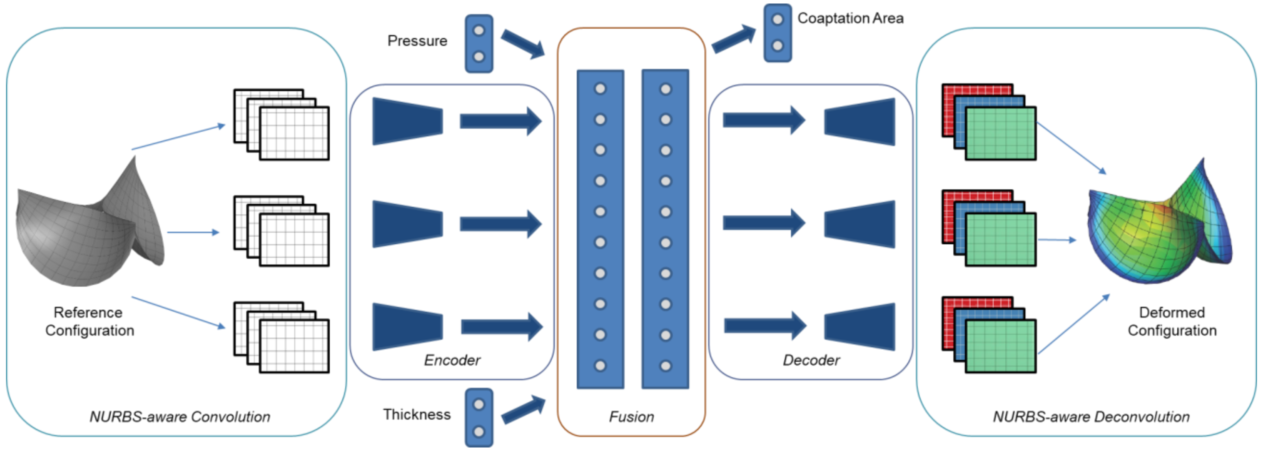
CNN Architecture



DLFEA Hyper-parameters

- Encoder and Decoder architecture
  - Number of convolution layers
  - Number of filters in each layer



- Repetition size for capturing the effect of pressure and thickness

- Number of neurons in FC layer (Data Fusion)
  - Need to be carefully selected for performance vs. underfitting

- Number of FC layers and size of deconvolution

ML Framework for Valve Biomechanics

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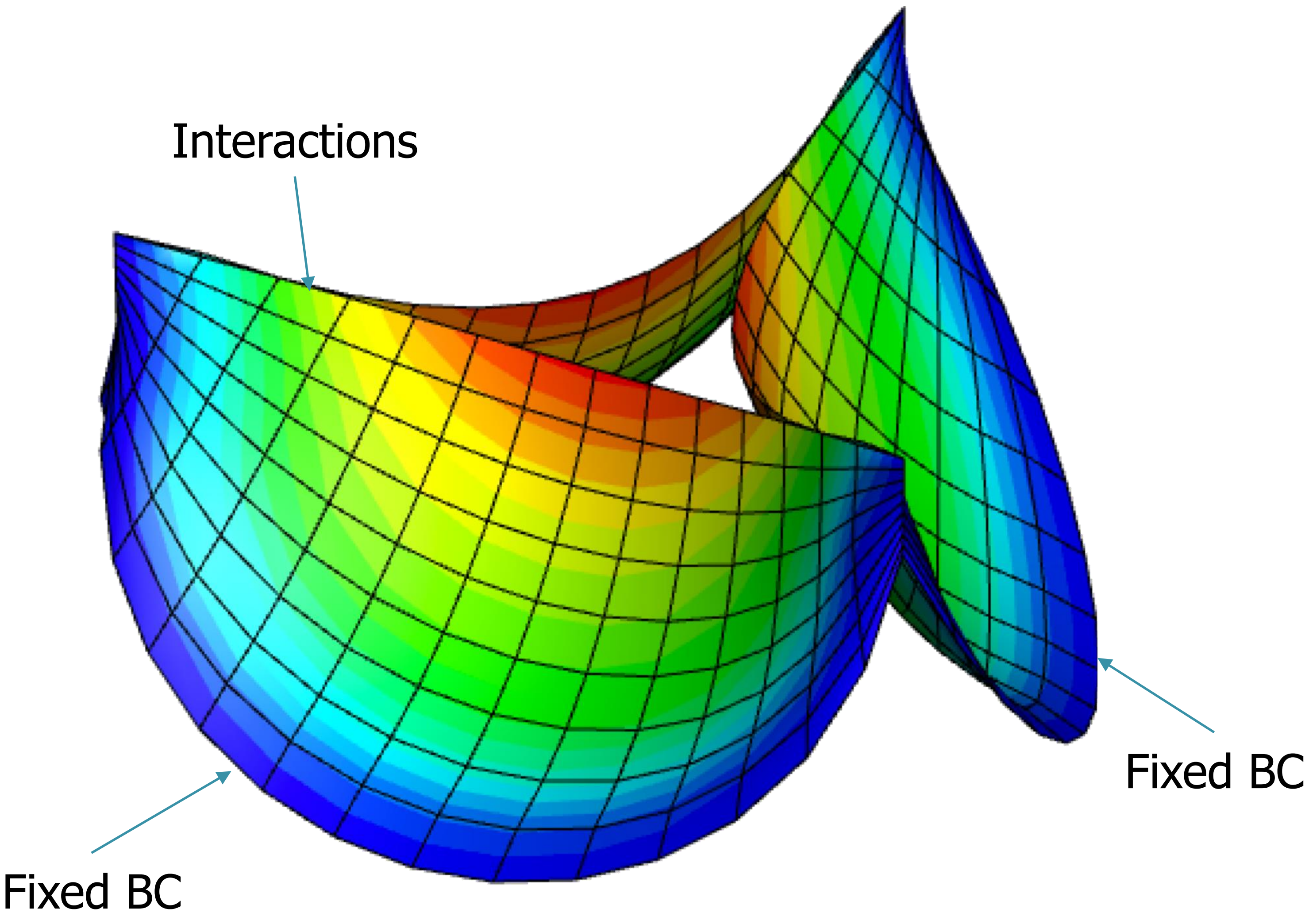
Training Algorithm

- Optimization algorithm: Adam
- Loss function:
  - Account for
    - fixed boundary conditions
    - Interaction

$$l_{bc} = 1 + abs(\frac{y_{true}}{max(y_{true})}) * l$$

$$l = \frac{1}{|\mathcal{D}|} * \sum_{k \in \mathcal{D}} ({y_{pred}}_k - {y_{true}}_k)^2$$



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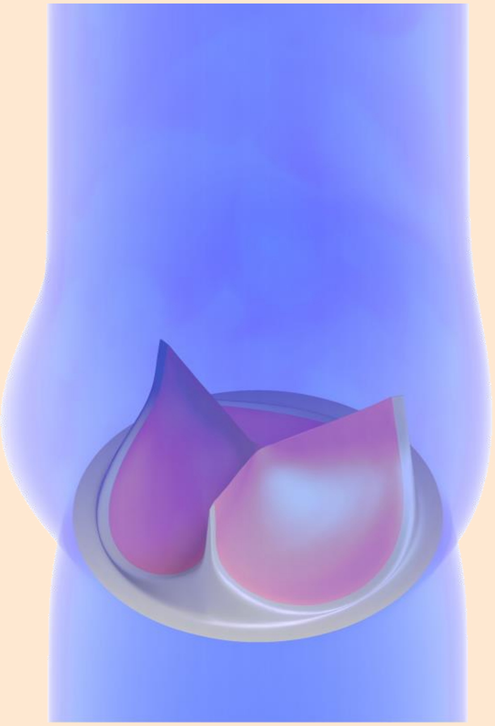
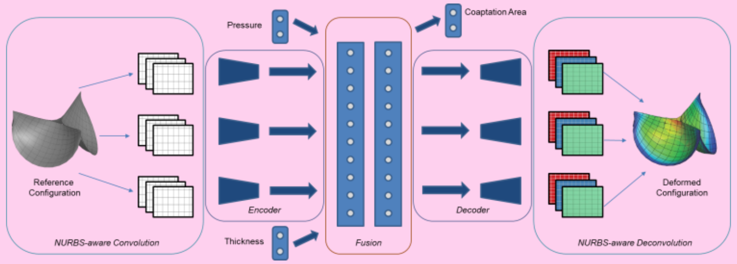
3. Training Algorithms

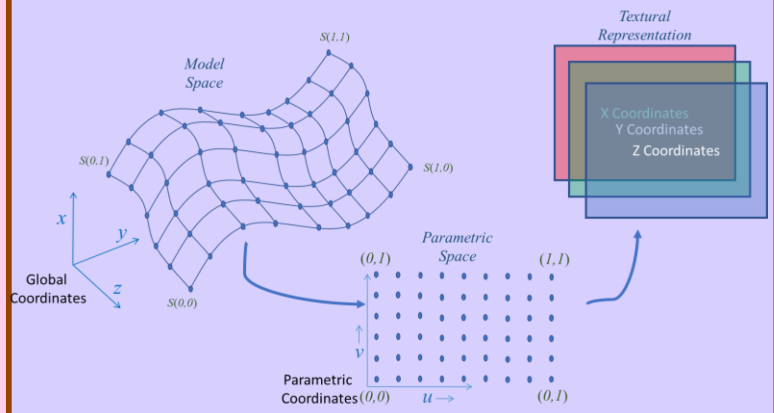
Outline



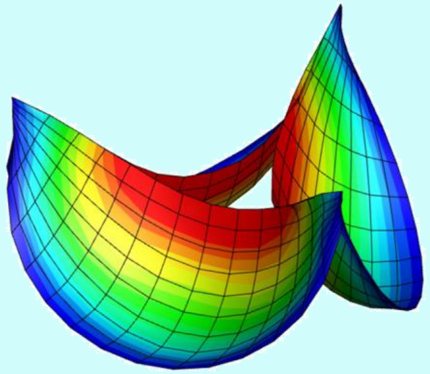
Computational Modeling of BHVs



ML Framework for Valve Mechanics



Data Generation



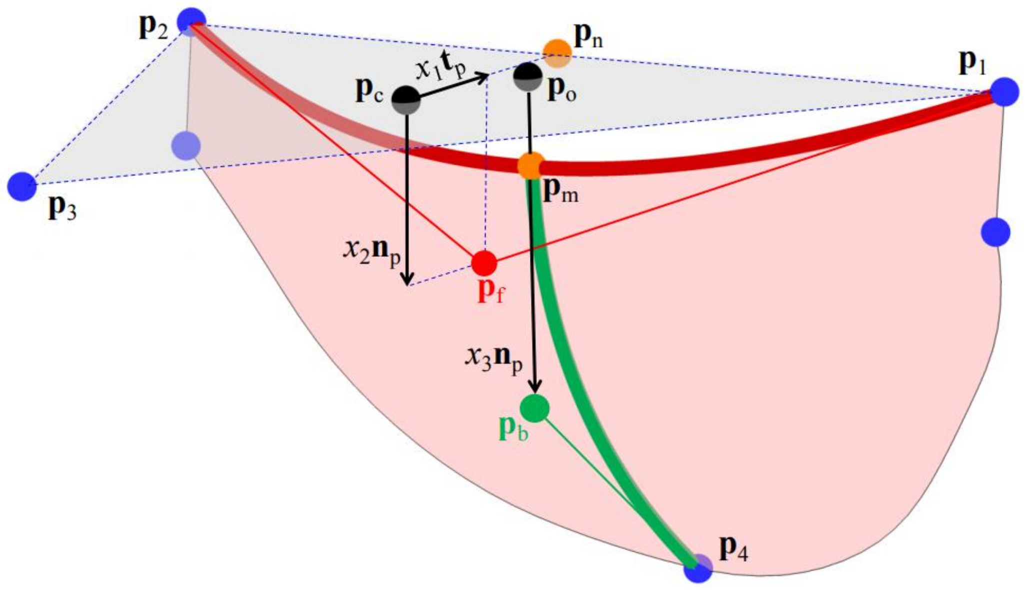
Results and Conclusions

Data Generation

- Geometry Parameters

Parameter	1	2	3	4	5
Curvature of free edge (cm)	0.05	0.25	0.45	-	-
Belly curvature (cm)	0.2	0.6	0.9	1.2	1.4
Height of free edge (cm)	- 0.1	0.1	0.3	0.5	-

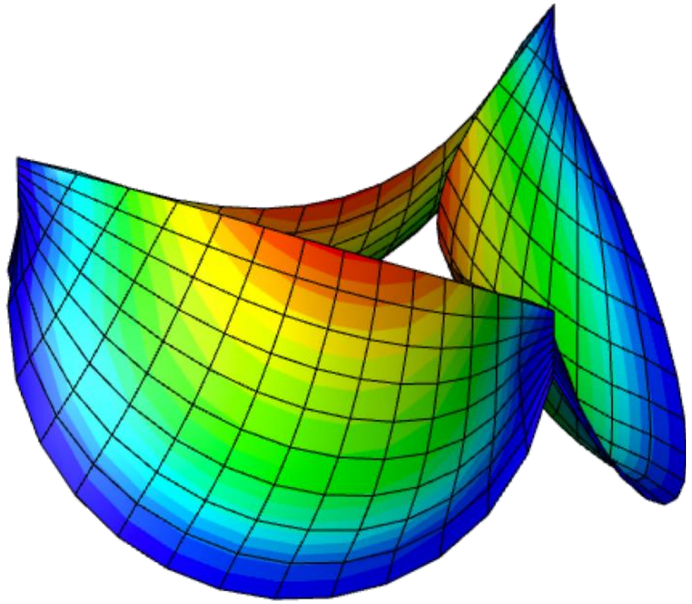
- Aortic Pressure
  - From 70 mm-Hg to 90 mm-Hg (21 values)
- Heart Valve Thickness
  - From 0.00386cm to 0.0772cm (20 values)
- 18,668 simulations



Isogeometric Analysis of Heart Valves

- Perform valve closure simulation

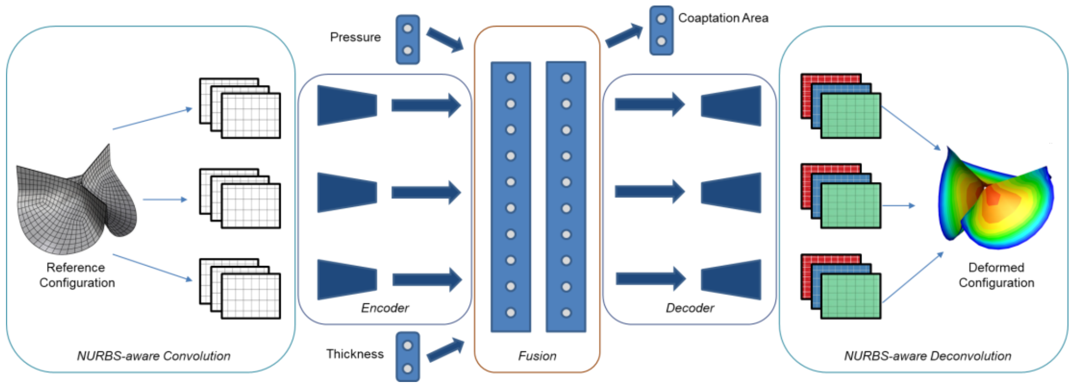
- Store key metrics from the analysis
  - Coaptation area
  - Deformed geometry



Deformations

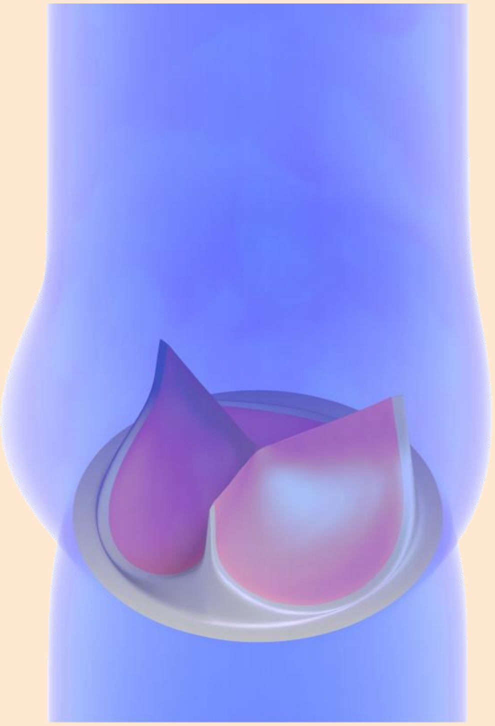
Coaptation Area

Training Process

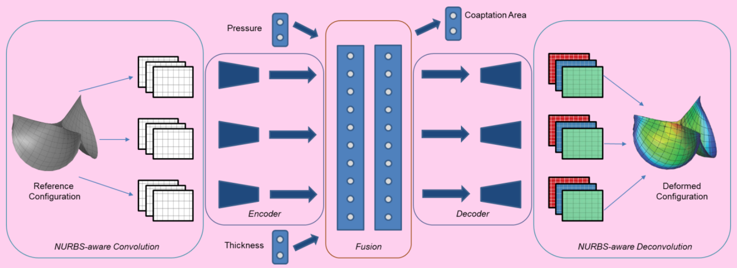


- End-to-end training
- Split the data for training, validation, and testing
  - 60% of data for training
  - 20% for validation
  - 20% for testing the generalization capability of the model
- Fine-tune the hyper-parameters for lowest validation loss

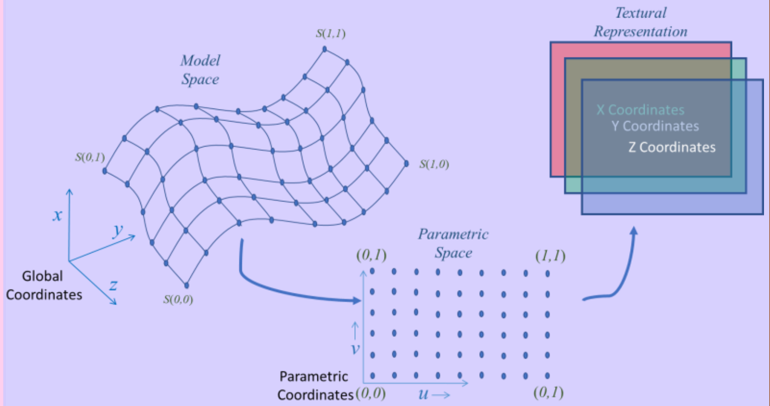
Outline



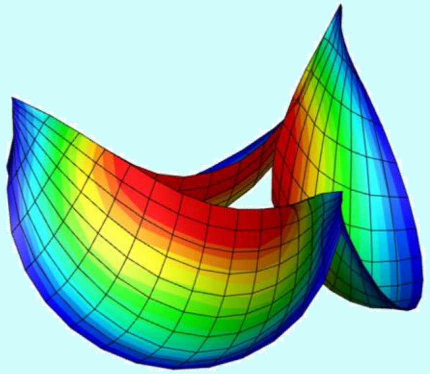
Computational Modeling of BHVs



ML Framework for Valve Mechanics



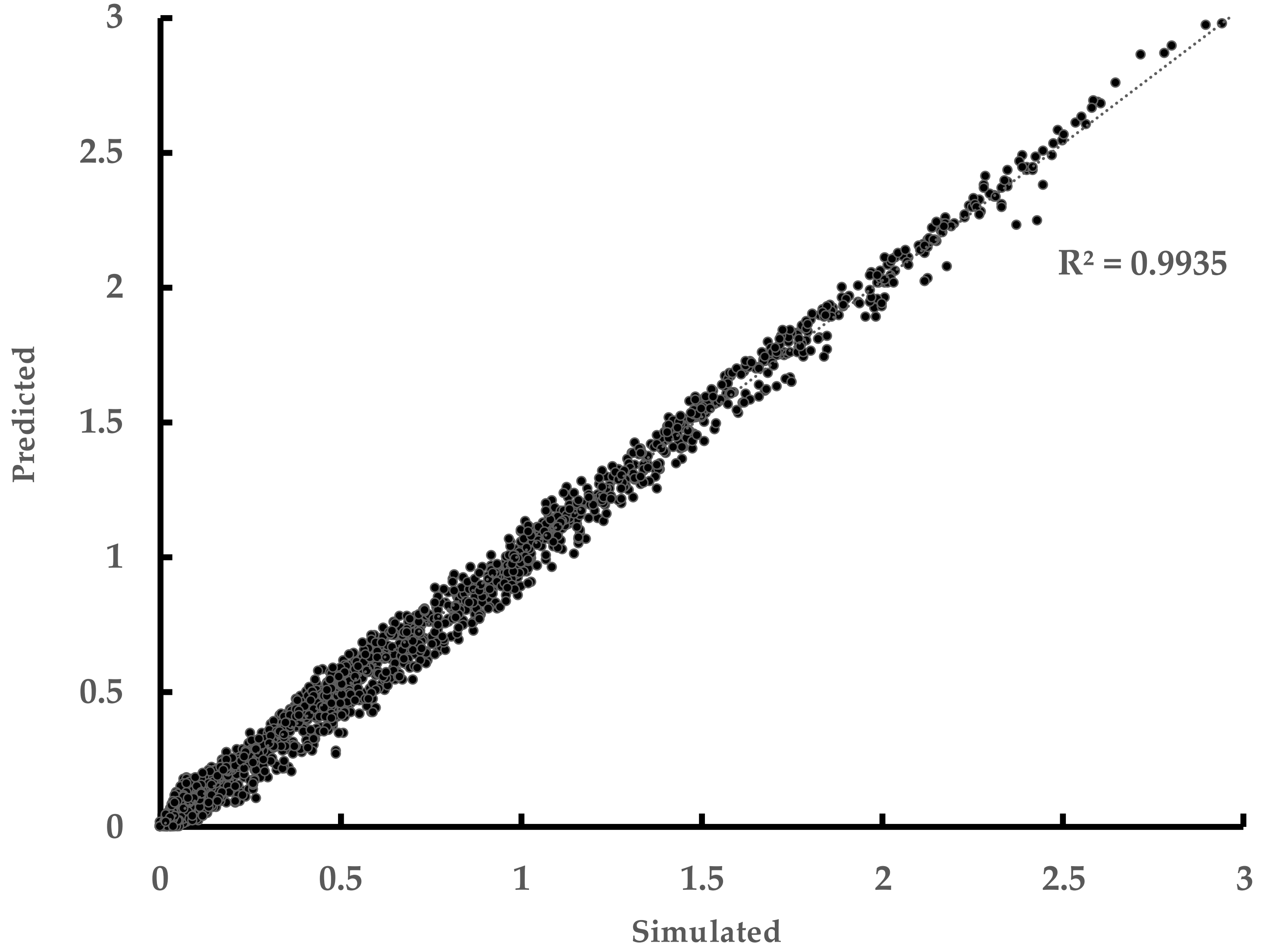
Data Generation



Results and Conclusions

Statistical Results

- Coaptation Area
  - RMSE: $0.056cm^2$
  - Median: $0.03cm^2$
  - Correlation Coefficient: 0.994



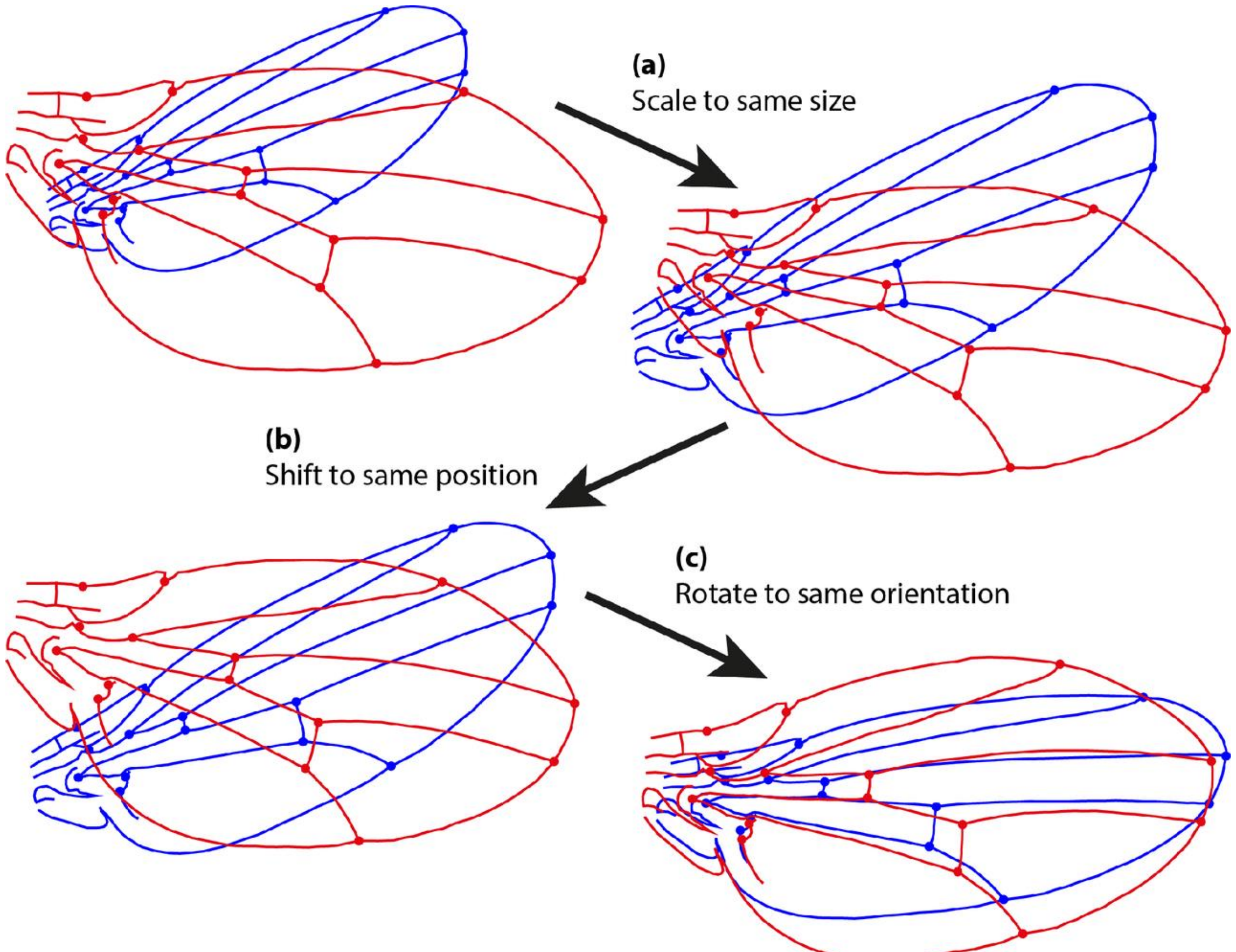
Statistical Results

- Procrustes Matching:
  - Accounts for shift and transformation in geometry
  - Provides a dissimilarity measure (cm)

$$D^2_{OPA}(X_1, X_2) = \|X_2 - \beta X_1 \Gamma - 1_k \gamma^{\mathrm{T}}\|^2,$$

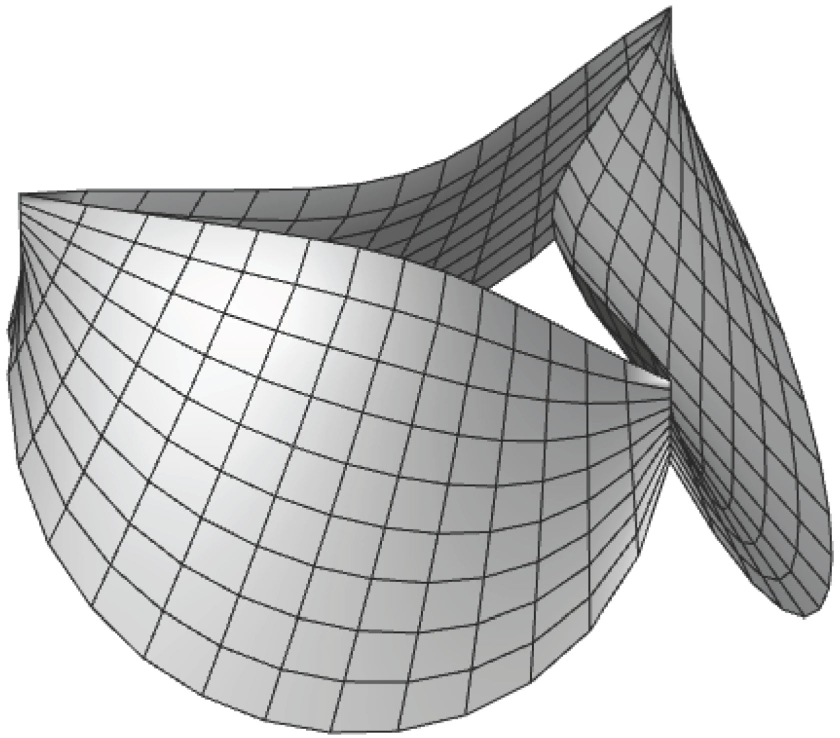
Γ is rotation matrix,
γ is translation matrix,
β is scale factor

- Results:
  - Median value of 0.0442cm
  - 10% of maximum deformation

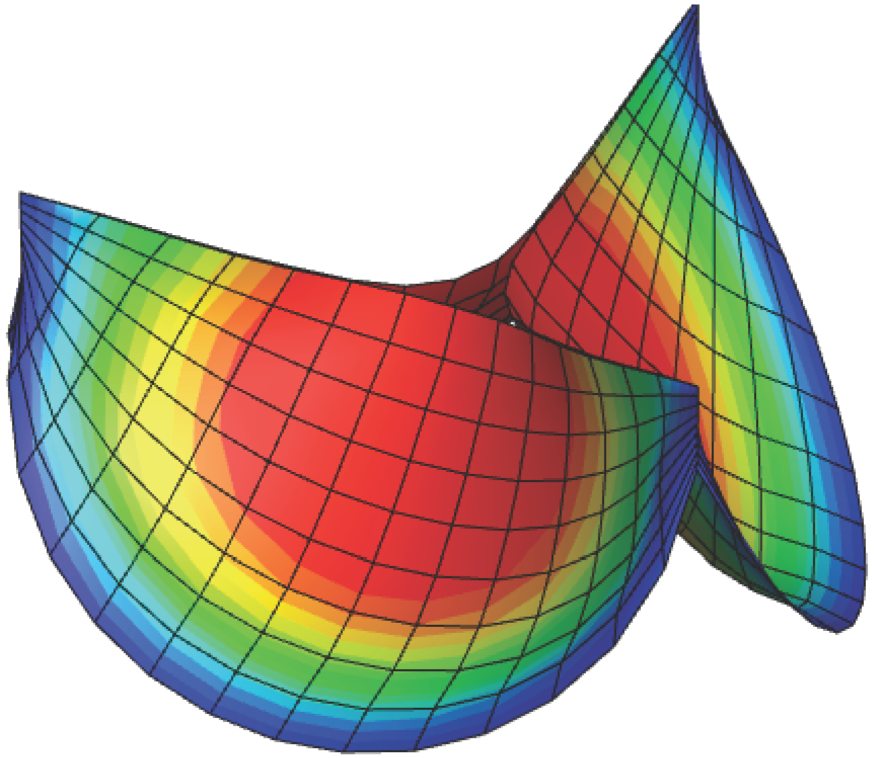


Anecdotal Results

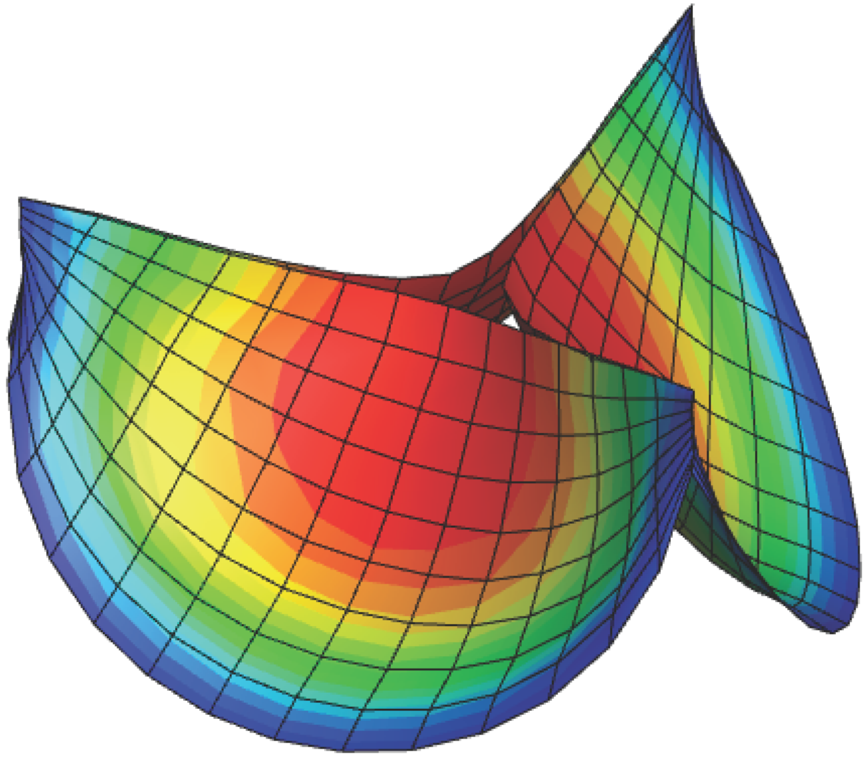
Reference Configuration



Structural Analysis Results

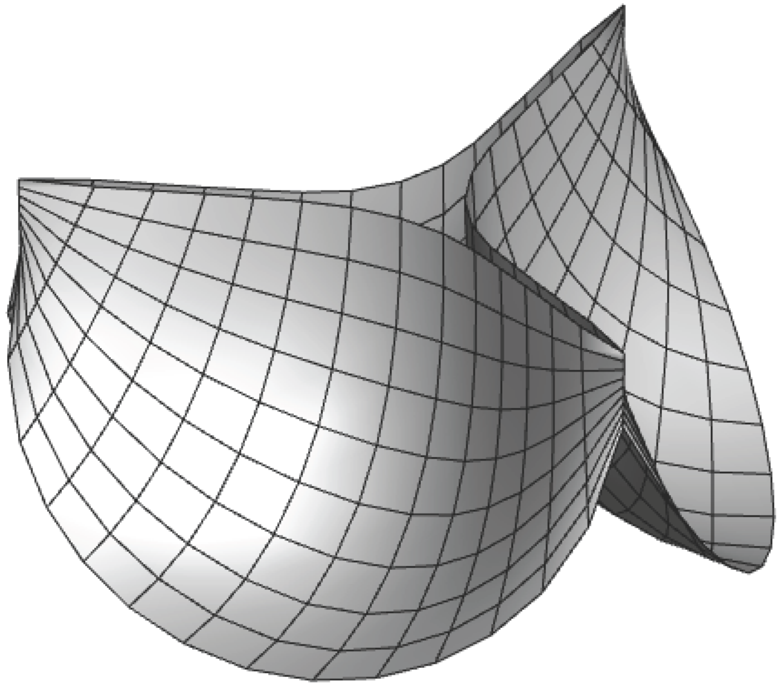
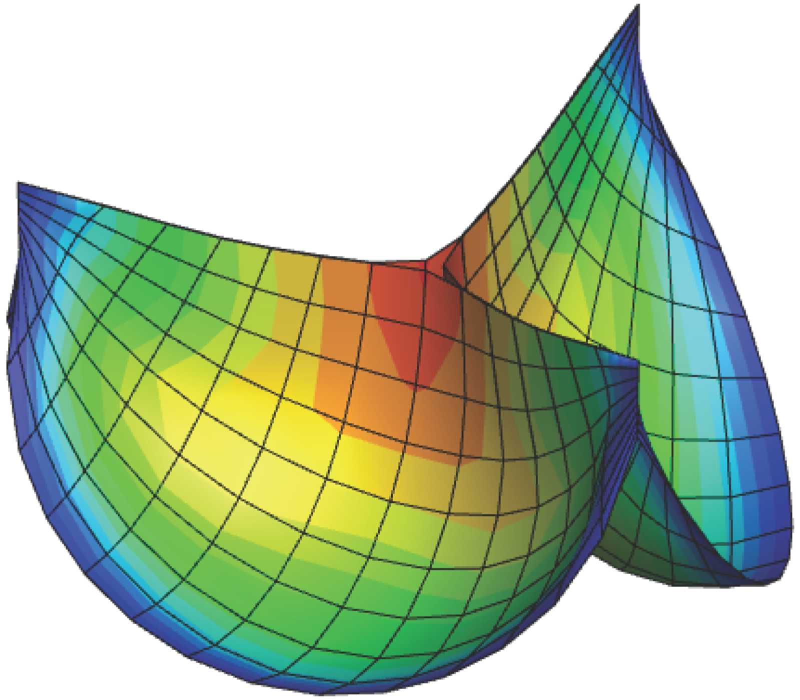
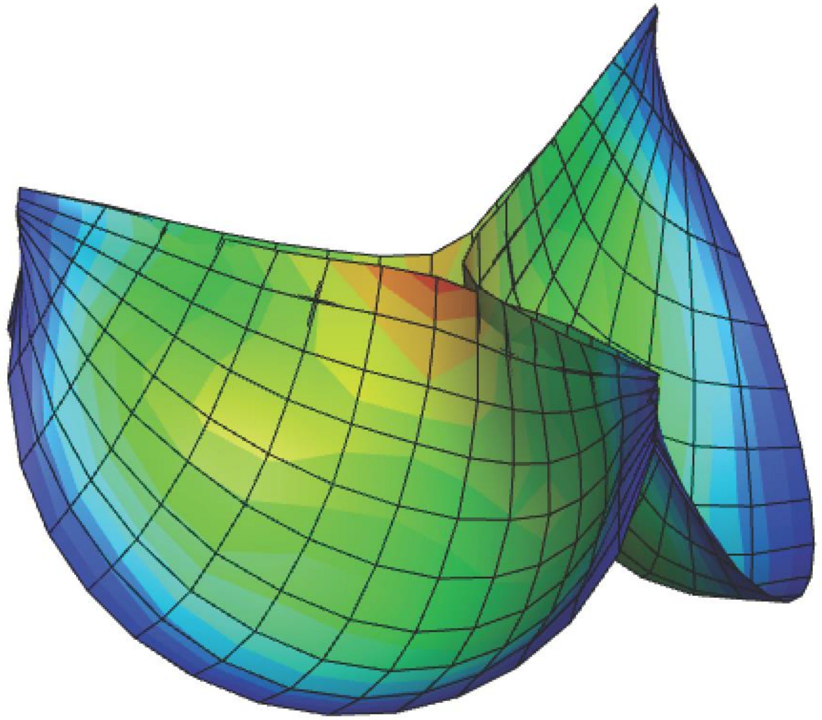


Predictions from DLFEA



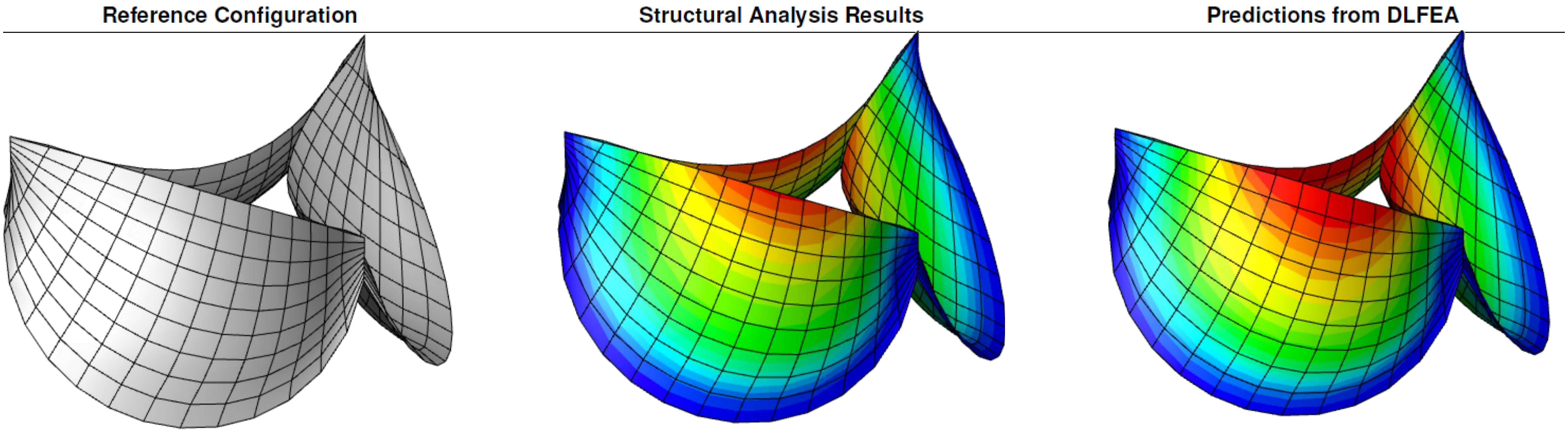
Pressure (mm-Hg)	Thickness (cm)	x_1 (cm)	x_2(cm)	x_3(cm)	Simulated CA (cm^2)	Predicted CA (cm^2)
89	0.0695	0.1	0.45	0.9	0.4505	0.3913

Anecdotal Results

Reference Configuration	Structural Analysis Results	Predictions from DLFEA
		

Pressure (mm-Hg)	Thickness (cm)	x_1 (cm)	x_2(cm)	x_3(cm)	Simulated CA (cm^2)	Predicted CA (cm^2)
75	0.0540	0.3	0.45	0.8	2.9276	2.9659

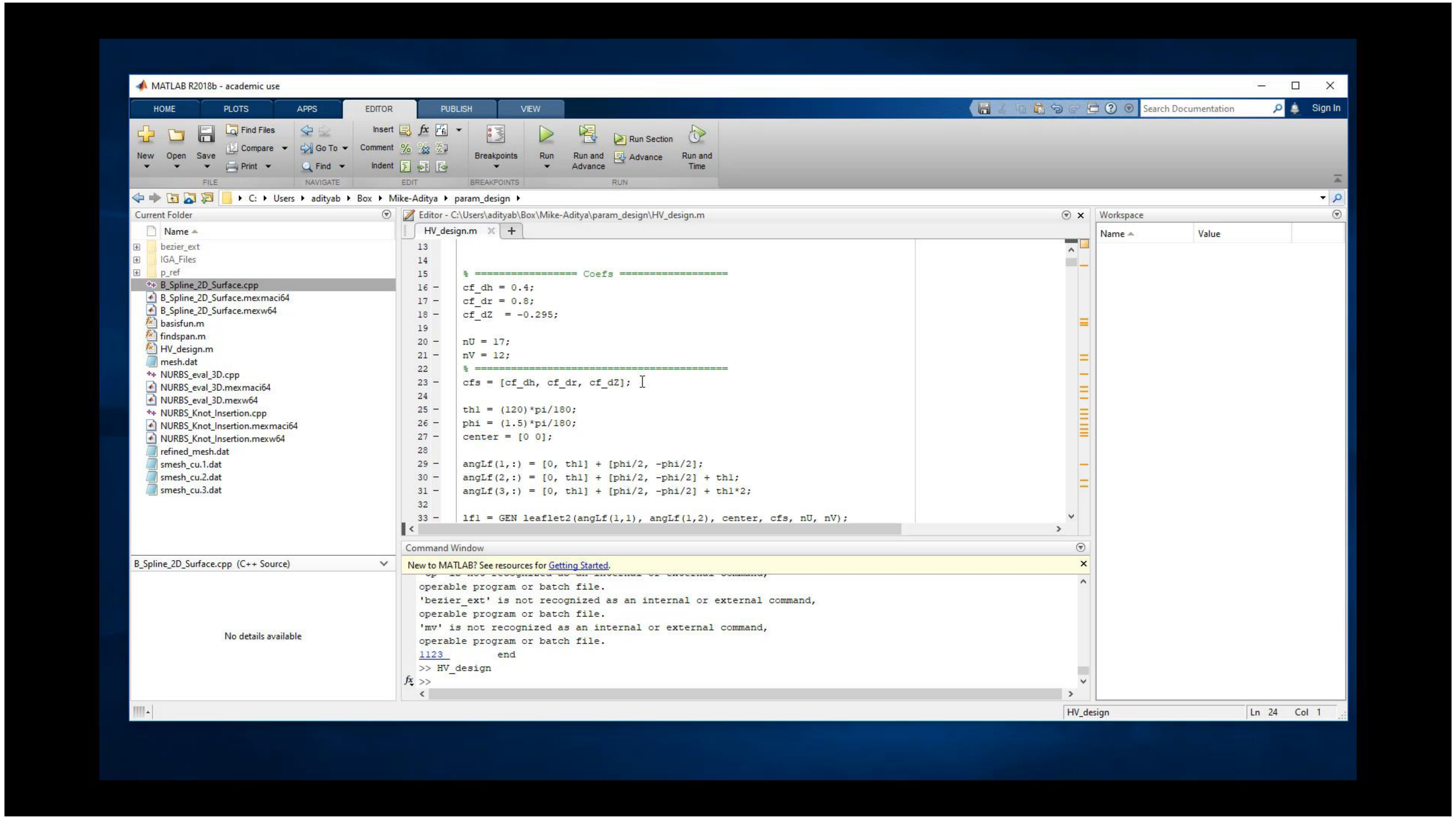
Anecdotal Results



Pressure (mm-Hg)	Thickness (cm)	x_1 (cm)	x_2(cm)	x_3(cm)	Simulated CA (cm^2)	Predicted CA (cm^2)
73	0.0579	0.1	0.45	0.6	0.0217	0.0207

Timings & Demo

- IGA:
  - 2 core, 32 threads each
  - ~5mins of runtime
- DLFEA:
  - Training: ~3-4 hours in P40s
  - Deployment: <5s in Titan Xp



Conclusions

- Fast simulation of heart valves using DLFEA
- DLFEA is able to learn the deformation biomechanics
  - Including complicated dependence on geometry and boundary conditions
- Results show DLFEA matches the fidelity of valve simulations
  - Can provide interactive decision support

Future Work

- Interactive design and optimization framework using DLFEA
    - Improve performance of design-through-analysis pipelines

- Add additional components to the ML framework to enable direct prediction of results from raw medical images
    - End-to-end learning

Acknowledgements

- Funding Sources
  - National Science Foundation
    - CMMI:1644441 – CM: Machine-Learning Driven Decision Support in Design for Manufacturability
    - OAC:1750865 – CAREER: GPU-Accelerated Framework for Integrated Modeling and Biomechanics Simulations of Cardiac Systems
  - nVIDIA
    - Titan Xp GPU for Academic Research

Thank You!

Questions?

Extra Slides