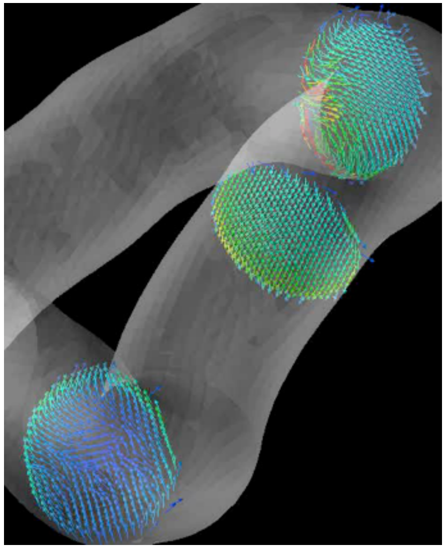
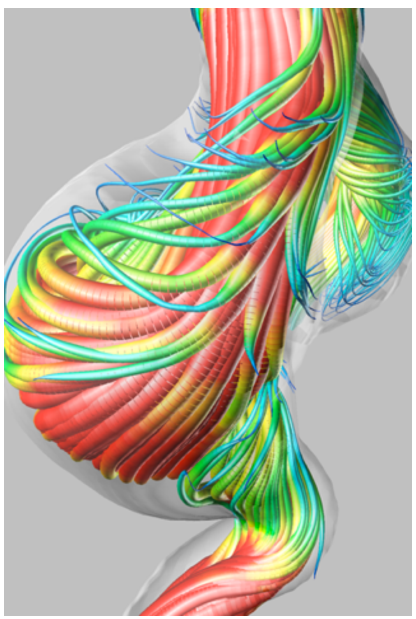
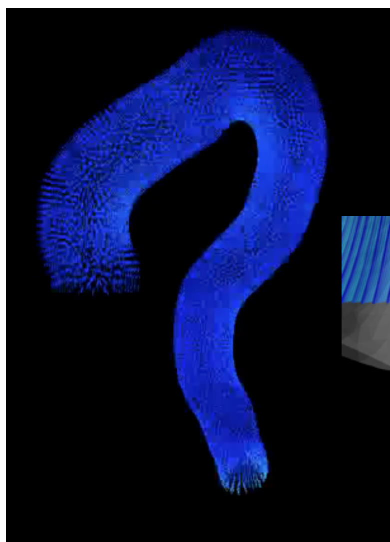
CREST
戦略的創造研究推進事業
Core Research for Evolutional Science and Technology



Computational approach elucidating the mechanisms of cardiovascular diseases





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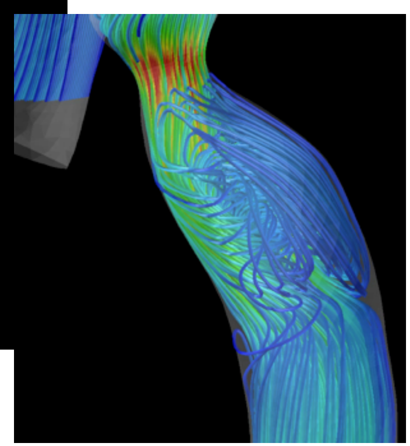
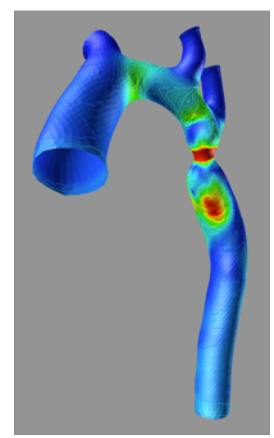
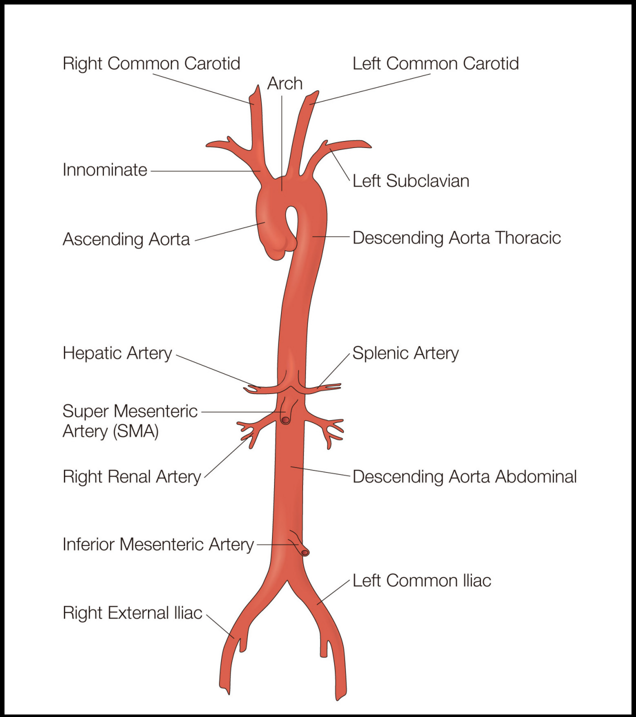


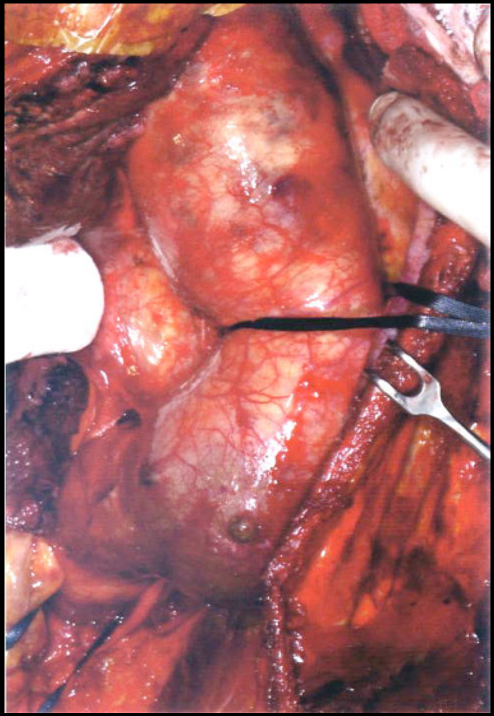


Contents

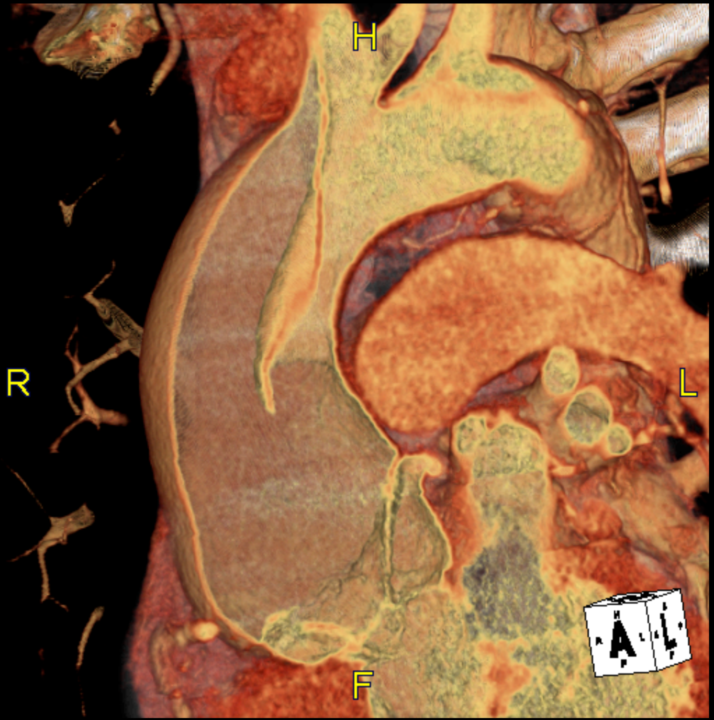
- Medical background for cardiovascular diseases
- Flow computations using patient-specific geometries
- Examining flow characteristics in the aorta using simplified geometries
- Machine learning to predict important quantities
- Conclusions and future works

Background





Aortic aneurysm



Aortic dissection

Aortic aneurysm is a life-threatening disease that slowly develops with advancing age of the patient . It presents risk of rupture. Many reports have described the risk factors, but the natural history of aneurysm development remains unclear. However, at least, stress from blood flow to the vessel wall is regarded as playing an important role in these diseases.

Backgrounds

For cardiovascular diseases, several treatment options might be used such as open surgery and stent graft treatment. Even if the initial treatment technically succeeds, some patients show recurrence and progression of disease many years after treatment.

- In this patient's case, kinking slowly started and suddenly accelerated. Such long-term morphological change seems to interact synergically with hemodynamics.
- However, not all the patients show this kind of adverse event. This means that the relation between aorta shapes and blood flow seems to have positive feedback.
- The prediction whether this phenomenon will occur or not, is extremely important from the view point of clinical medicine.

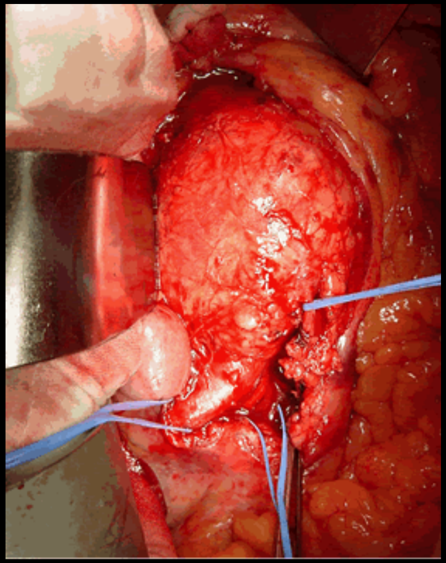
Factors influencing cardiovascular disease

Lifestyle

Inheritable characters

Morphology

Disease



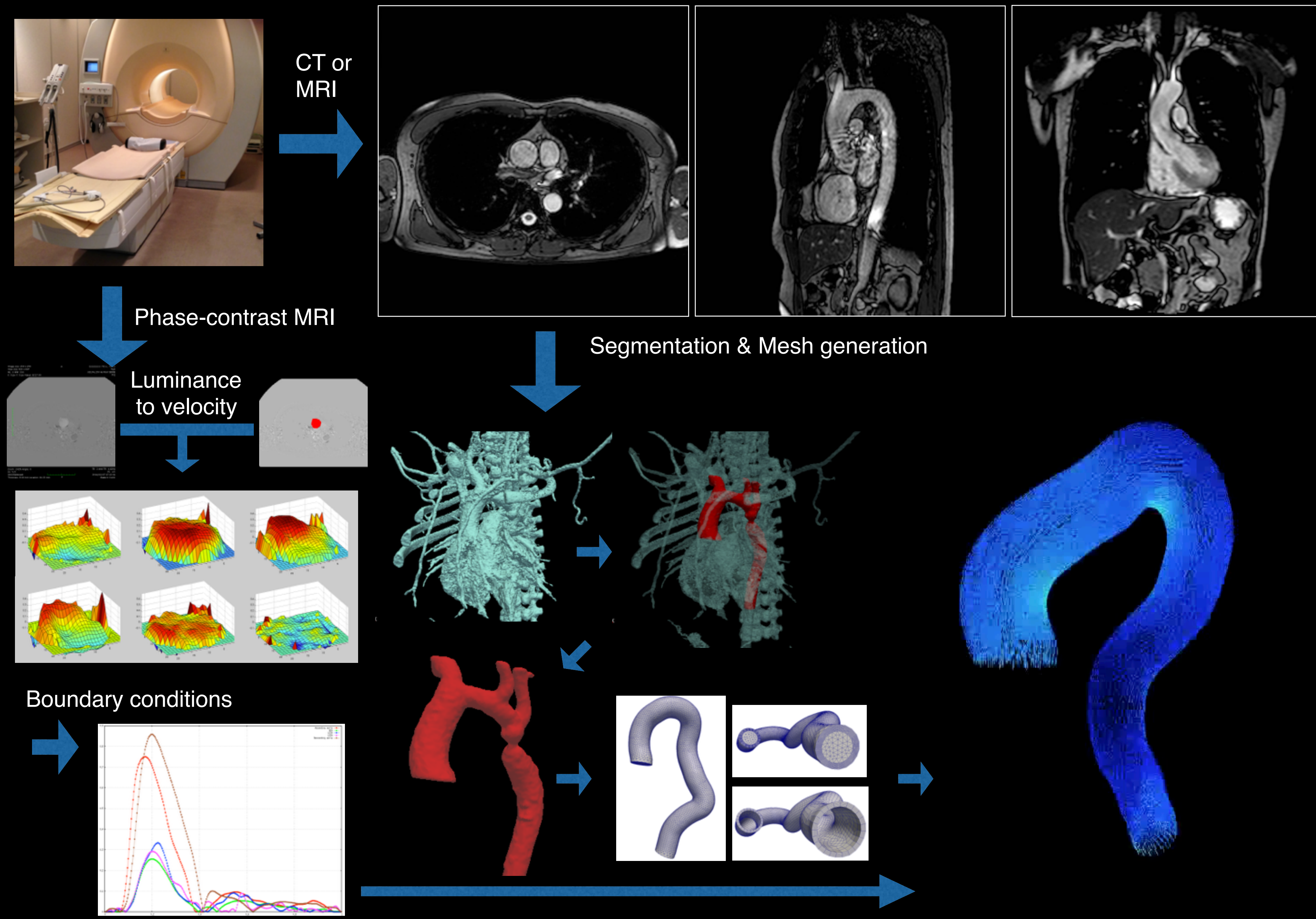
Morphology

Flow characteristics

Vessel wall stresses

Disease

Simulation using medical imaging data



Computational Method

T. Tezduyar and K. Takizawa

- Deforming-Spatial-Domain/Stabilized-Space–Time Method (DSD/SST)
- Variational Multiscale (VMS) method

[1] T.E. Tezduyar, "Stabilized finite element formulations for incompressible flow computations", Advances in Applied Mechanics, Vol. 28, pp. 1–44 (1992).

[2] K. Takizawa and T.E. Tezduyar, "Multiscale space–time fluid–structure interaction techniques", Computational Mechanics, Vol. 248, No. 3, pp. 247–267 (2011).

[3] T.E. Tezduyar, K. Takizawa, C. Moorman, S. Wright and J. Christopher, "Multiscale Sequentially-Coupled Arterial FSI Technique", Computational Mechanics, Vol. 46 17–29 (2010).

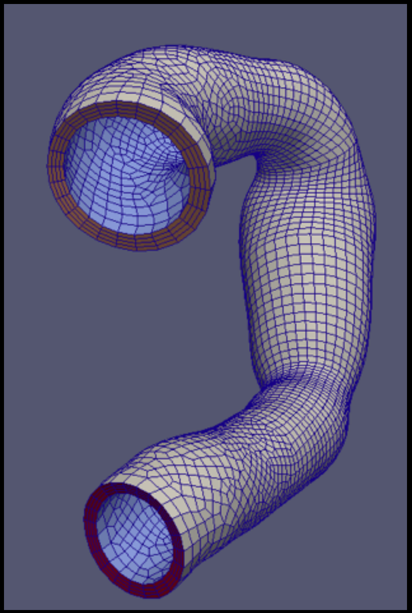
FSI (Fluid-structure Interaction) procedure

Sequentially-Coupled Arterial FSI (SCAFSI) Technique

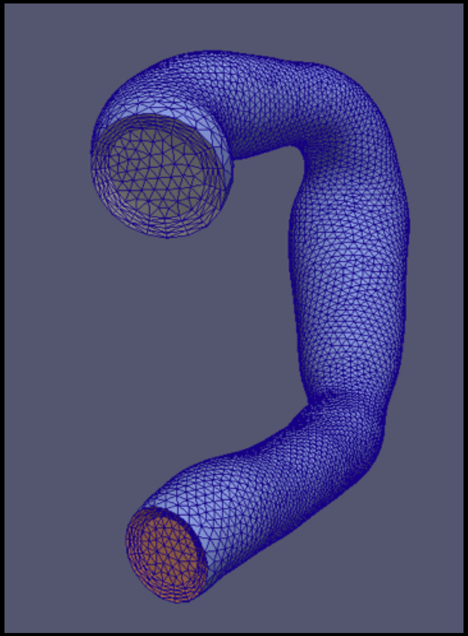
1. Compute the vessel wall motion for one heart period using the equation for structure. Measured pressure history data are given as an external force.

2. Compute the mesh motion for the fluid region by imposing the surface mesh displacement as a Dirichlet condition.

3. Compute the flow field on the prescribed moving mesh calculated in the previous step.



Hexahedral mesh for structure

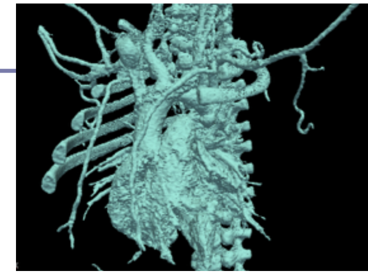


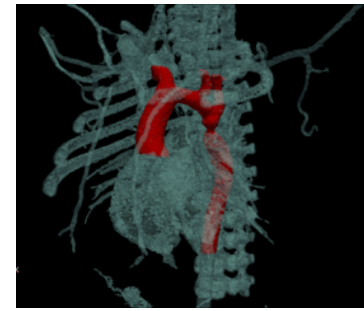
Tetrahedral mesh for fluid

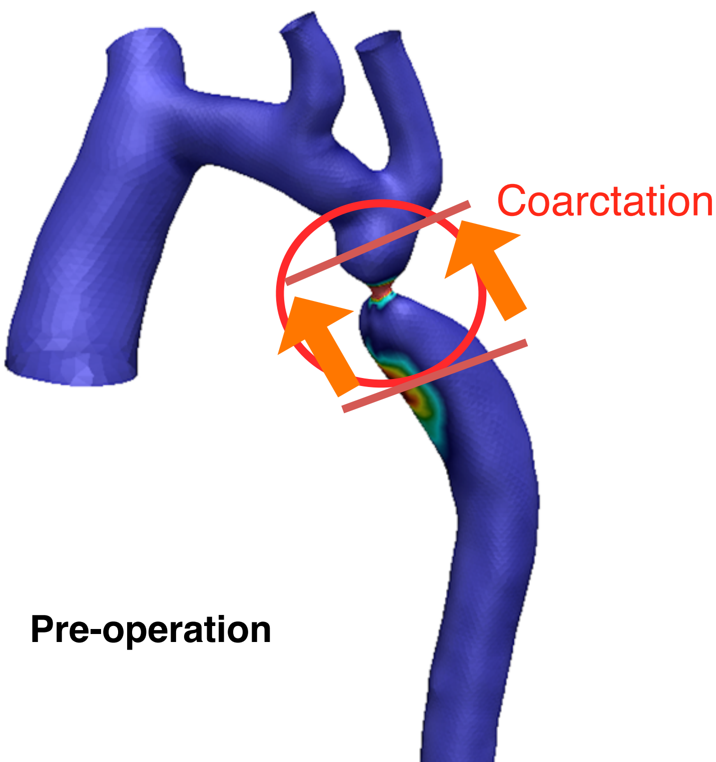
[3] T.E. Tezduyar, K. Takizawa, C. Moorman, S. Wright and J. Christopher, "Multiscale Sequentially-Coupled Arterial FSI Technique", *Computational Mechanics*, Vol. 46 17–29 (2010).

Example: coarctation case

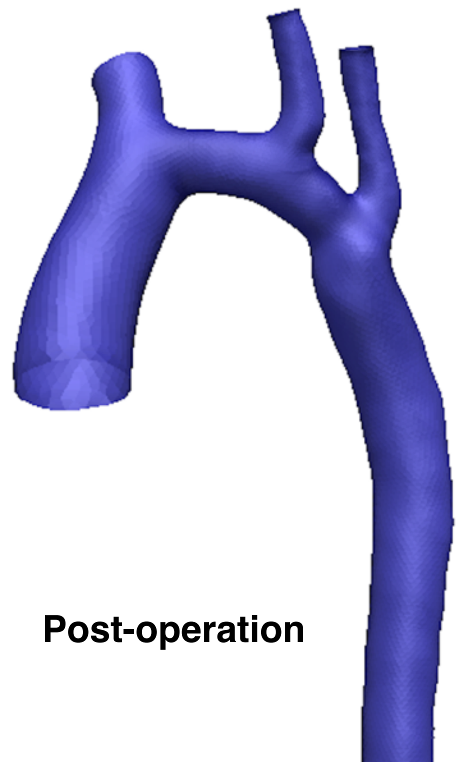
- Three-month-old baby, weight 4.9 kg
- Ascending aorta: 9 mm diameter
- Narrowest part: 1.8 mm diameter, max. velocity 3.2 m/s.
- Heart rate 110/min



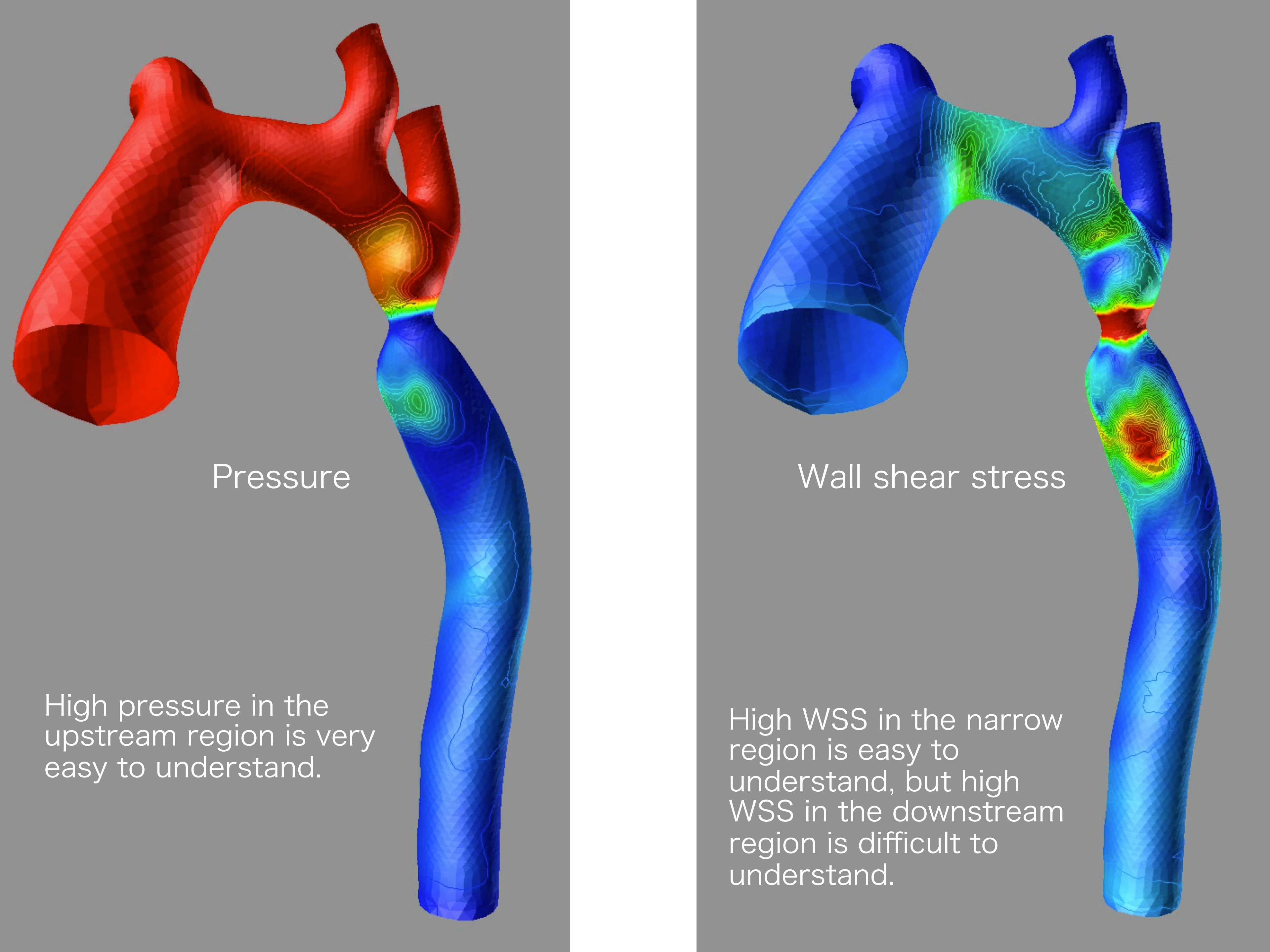




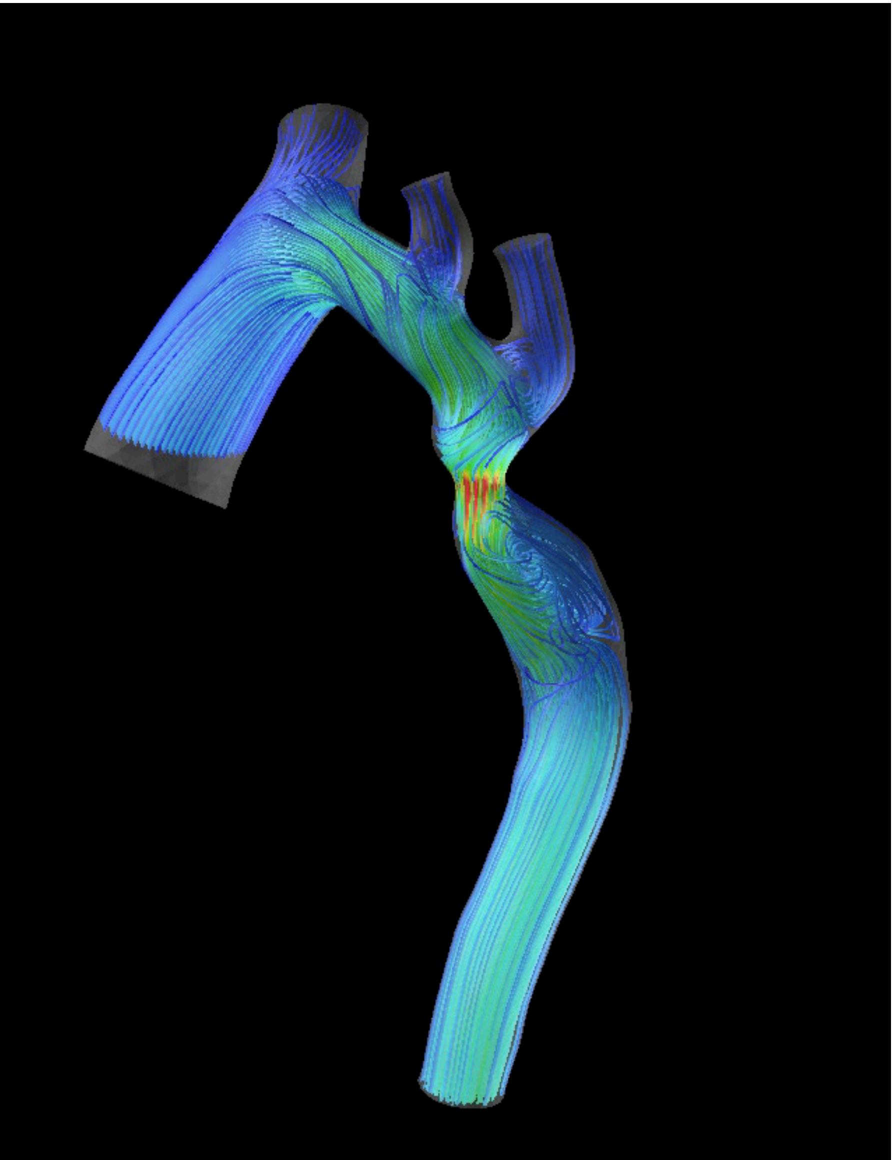
Pre-operation

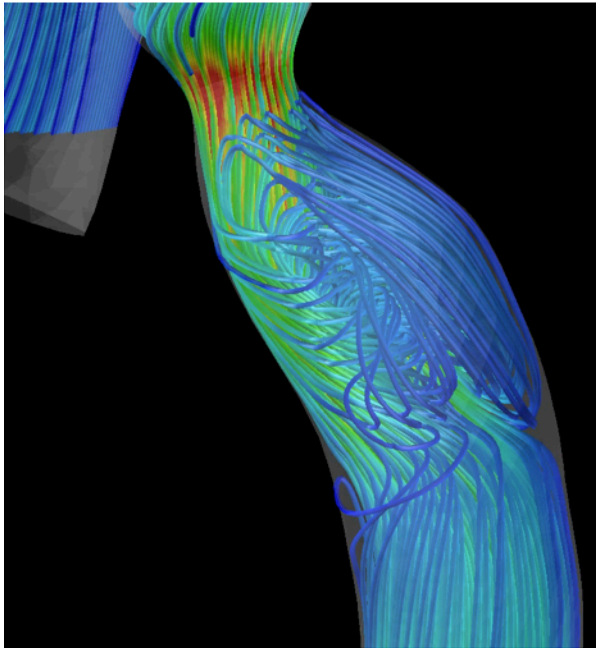


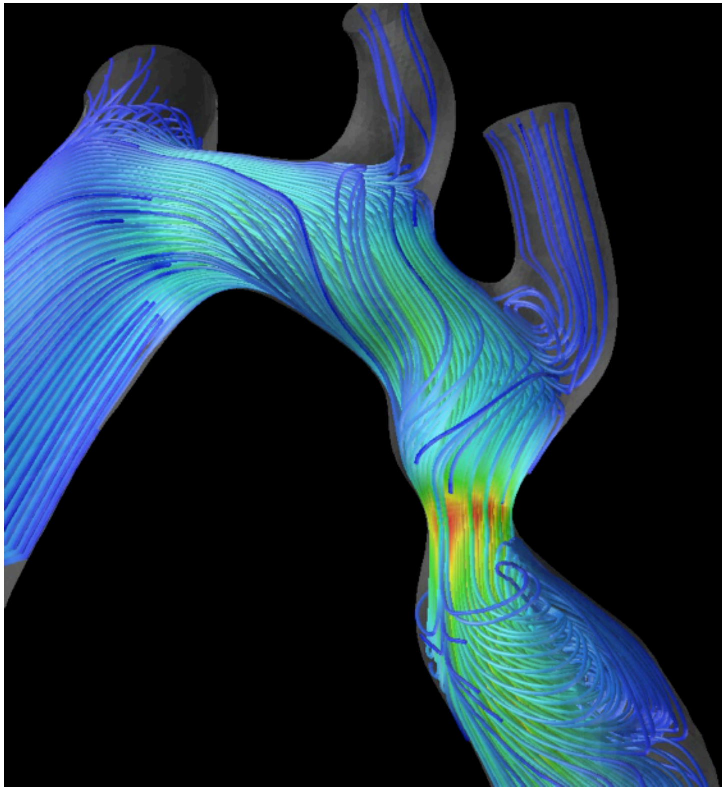
Post-operation

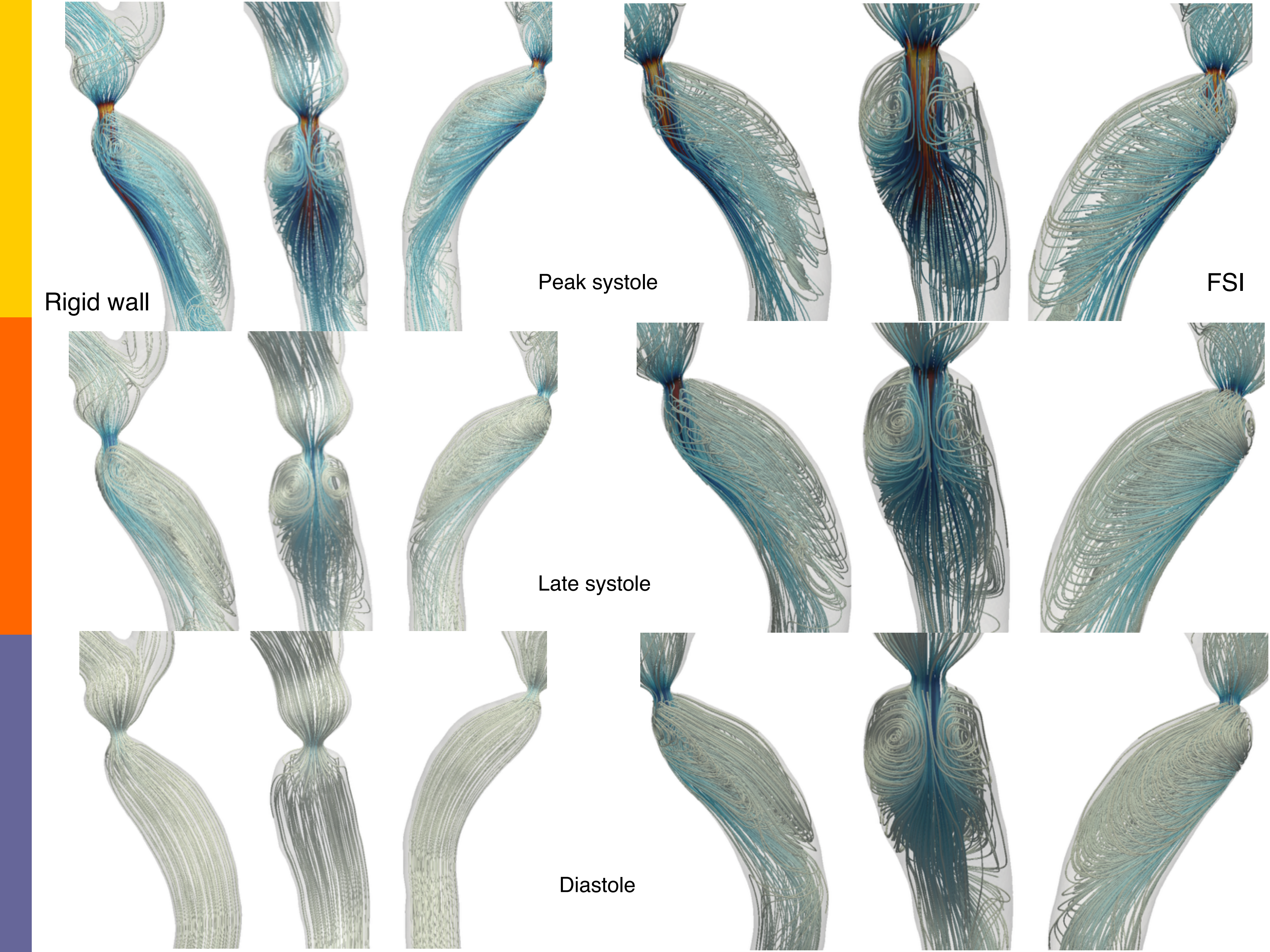

Pressure
High pressure in the upstream region is very easy to understand.
Wall shear stress
High WSS in the narrow region is easy to understand, but high WSS in the downstream region is difficult to understand.

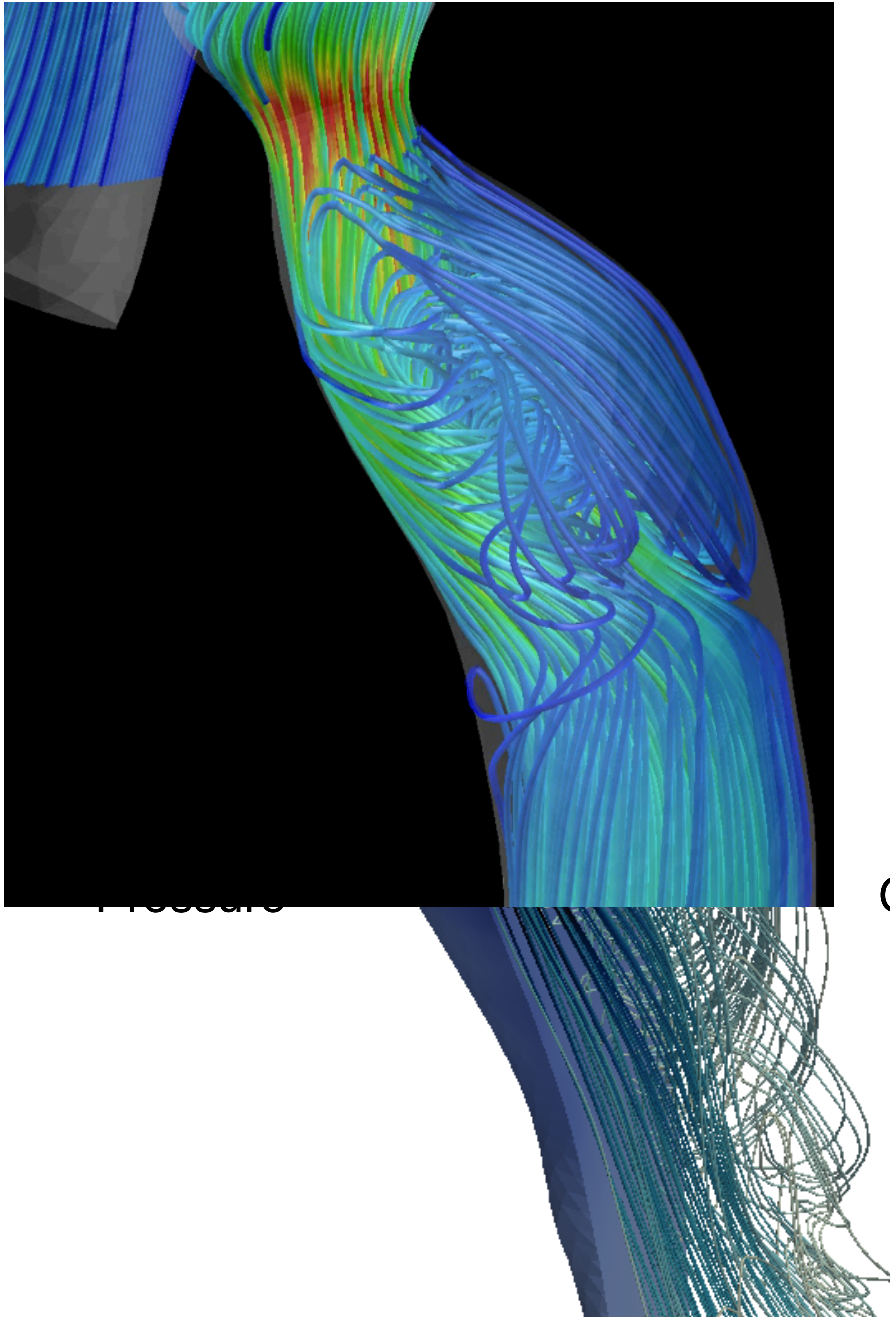
Streamlines

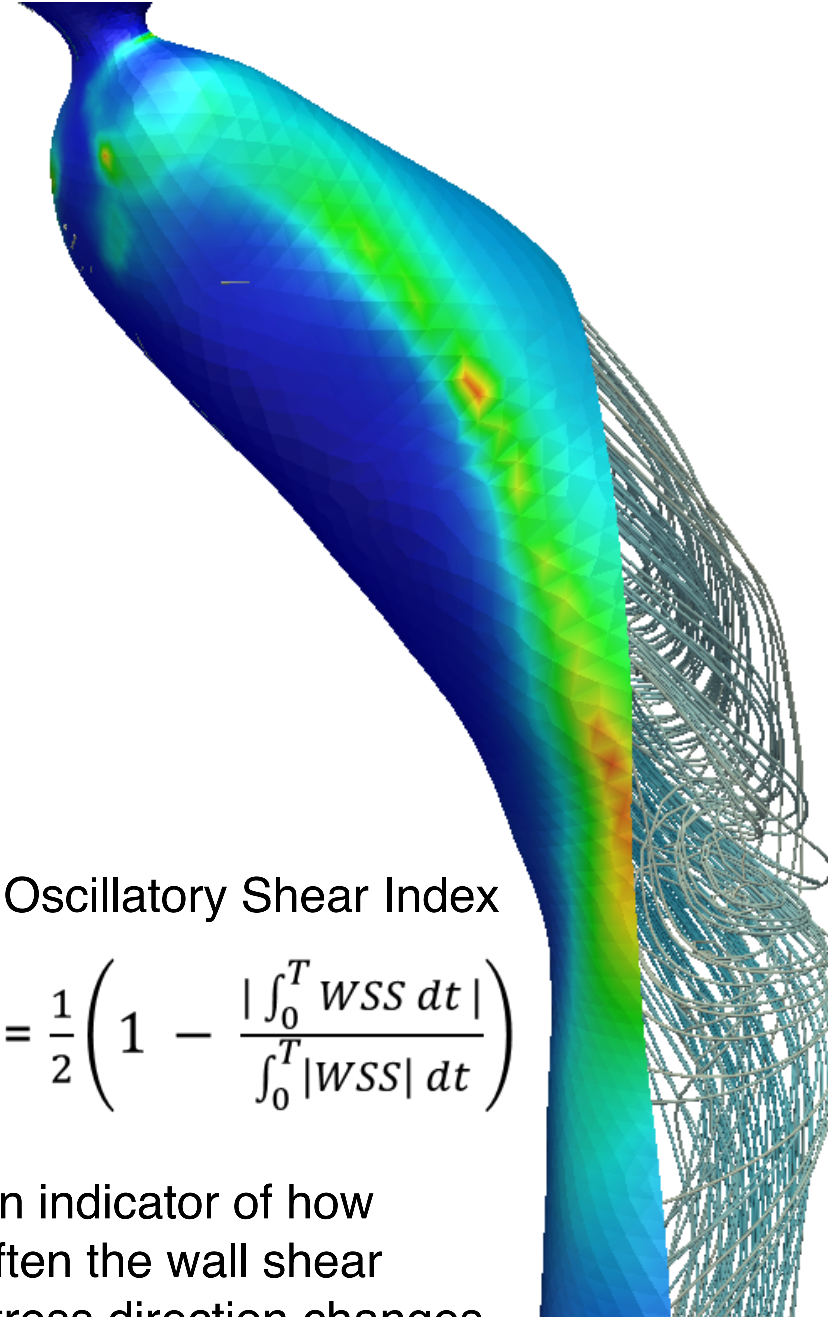







Rigid wall
Peak systole
FSI
Late systole
Diastole

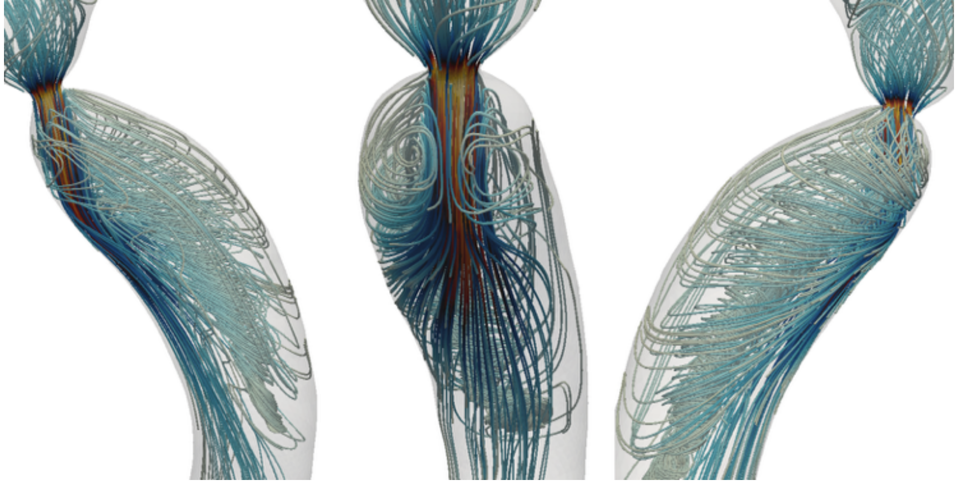


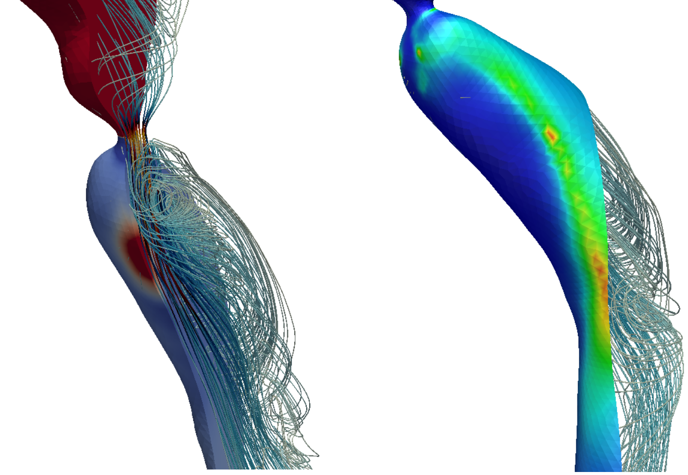


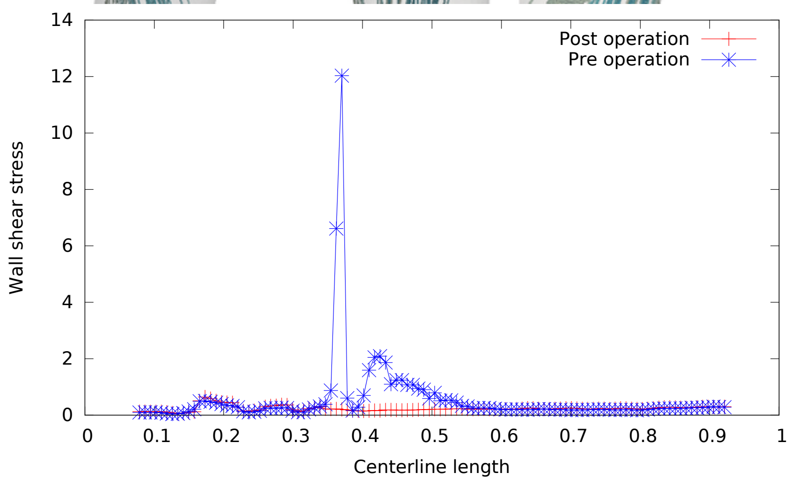
OSI: Oscillatory Shear Index

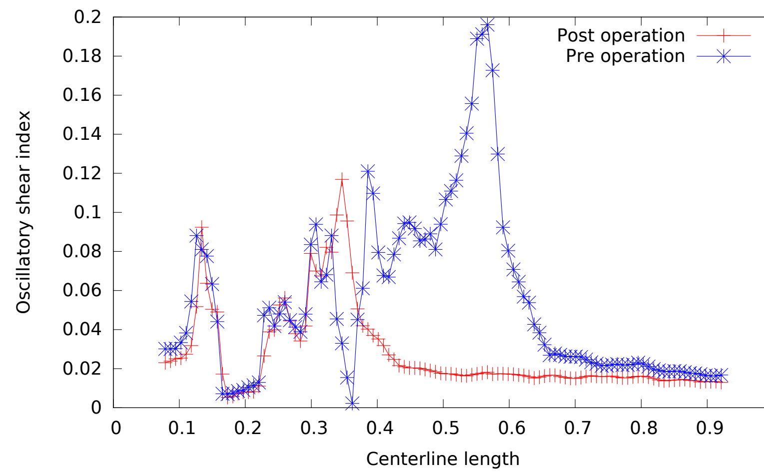
$$\mathrm{OSI} = \frac{1}{2}\left(1 - \frac{\left|\int_0^T WSS\,dt\right|}{\int_0^T |WSS|\,dt}\right)$$

An indicator of how often the wall shear stress direction changes



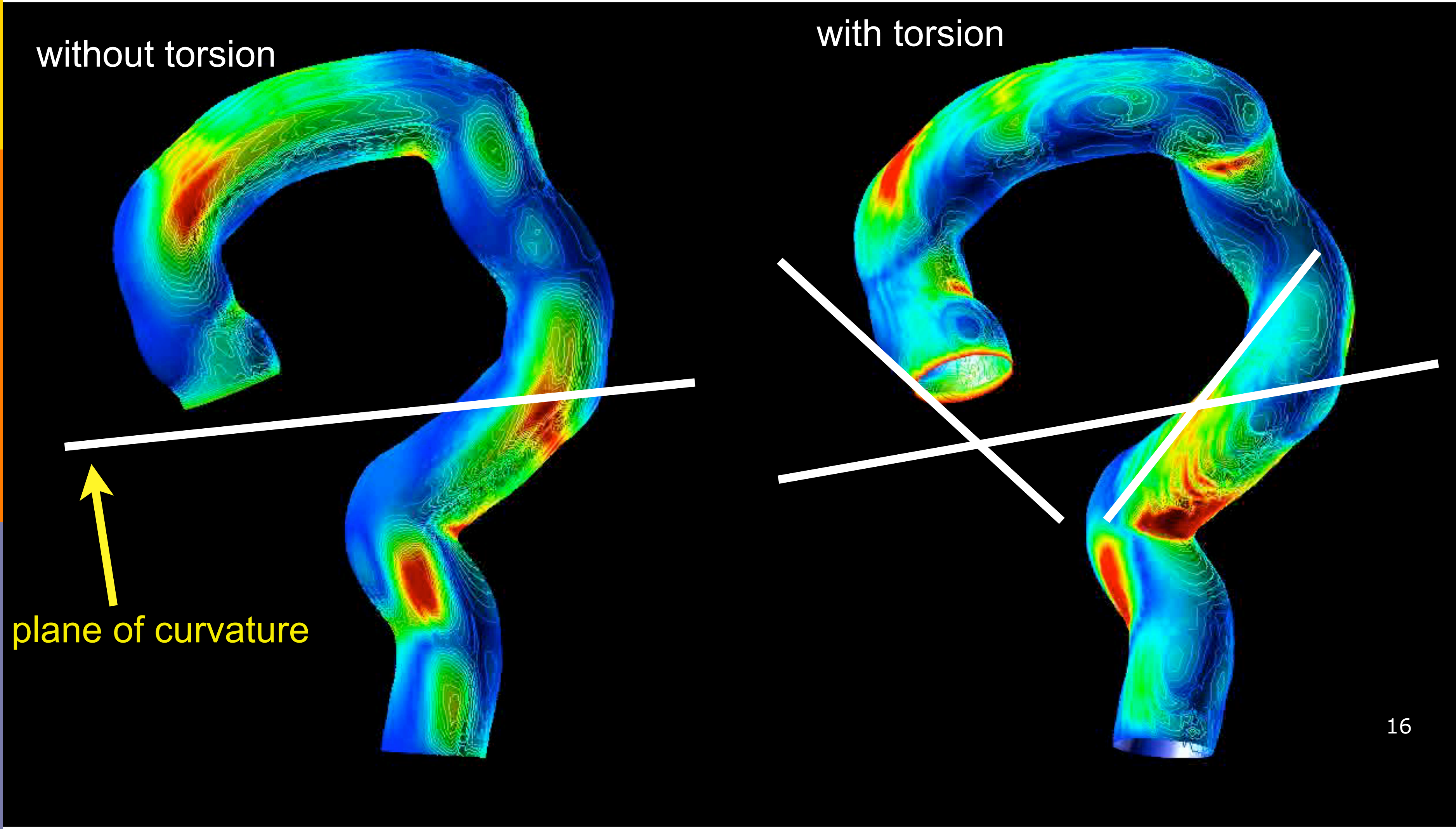






- Large WSS and OSI are observed just downstream of the coarctation, which is caused by an instability of the jet from the orifice.
- This phenomenon can be regarded as one reason for dilation sometimes observed in downstream of coarctation.
- These high wall shear stress and high OSI regions disappeared in the post-operation shape.

Geometrical and fluid dynamical characteristics of vessels and blood flows

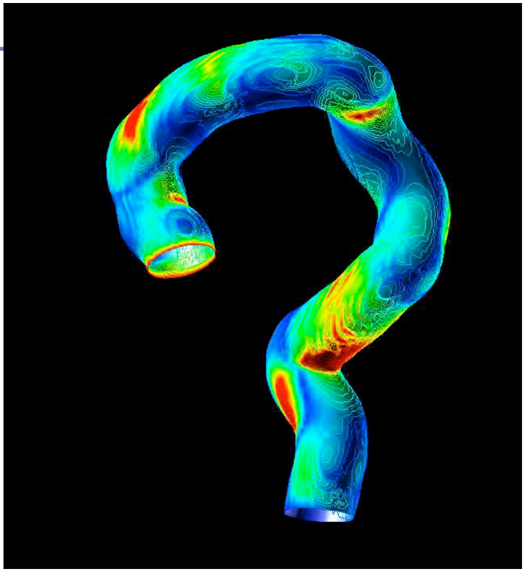


Geometrical representation of the aorta

Frenet–Serret formula

$$\frac{d}{ds}\begin{pmatrix} \boldsymbol{\tau} \\ \boldsymbol{n} \\ \boldsymbol{b} \end{pmatrix} = \begin{pmatrix} 0 & Cv & 0 \\ -Cv & 0 & To \\ 0 & -To & 0 \end{pmatrix}\begin{pmatrix} \boldsymbol{\tau} \\ \boldsymbol{n} \\ \boldsymbol{b} \end{pmatrix}$$

- **Radius**: Almost linearly decreasing for healthy aorta. Not considered here.
- **Curvature**: Human aorta goes upward from heart and then turns downward. Therefore, differences among individuals are small. Curvature effect is characterized by **Dean's number**.
- **Torsion**: Human aorta goes through several organs and borns. Therefore, torsion differences among individuals are large.



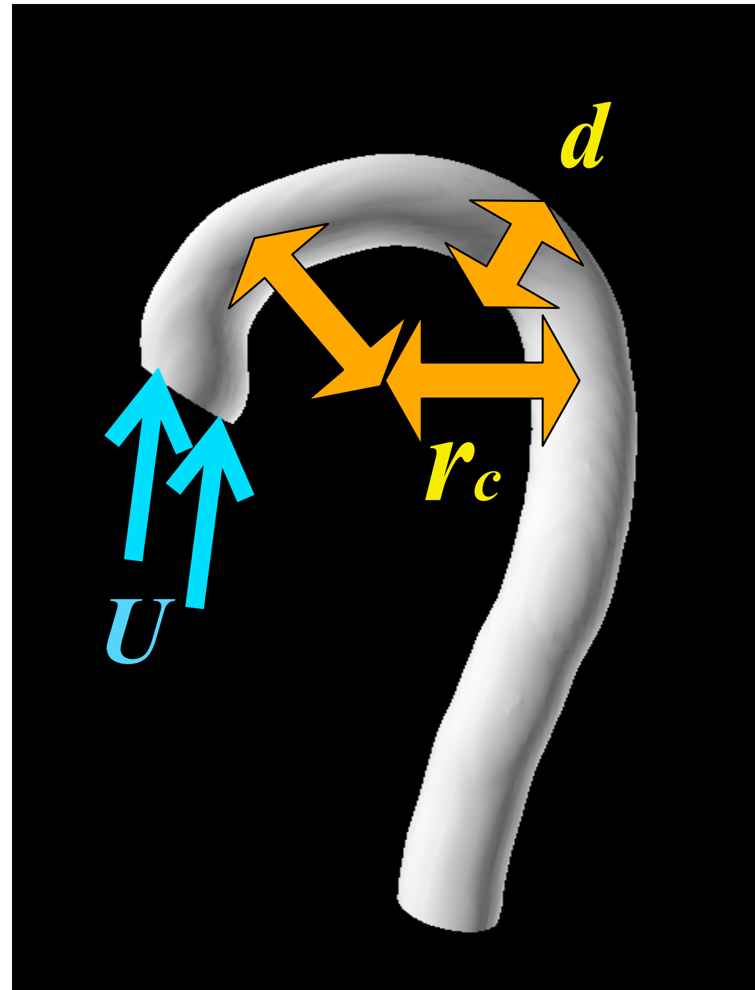
Non-dimensional parameters

- Reynolds number

$$Re = \frac{Ud}{\nu}$$

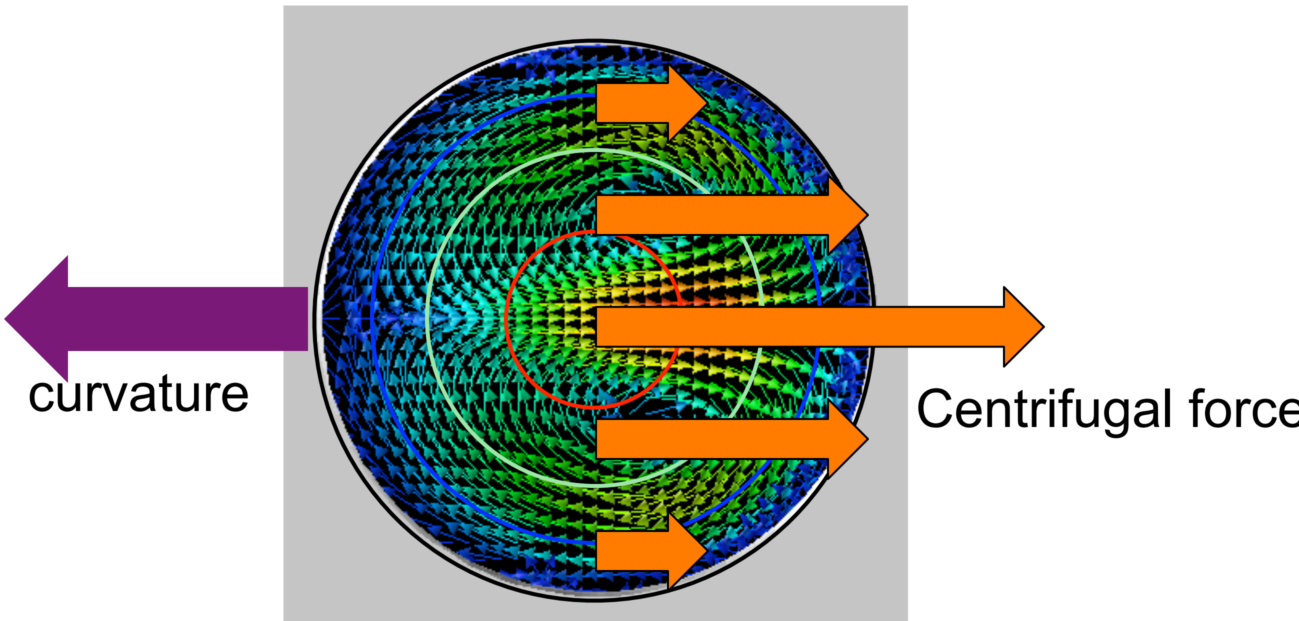
- Dean number

$$De = 4\sqrt{\frac{d}{r_c}}$$



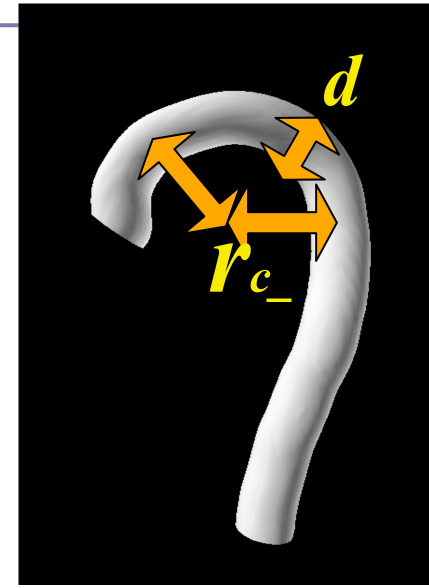
Dean's vortices

Characteristic secondary flows are observed in curved tubes.



Hagen-Poiseuille flow profile

Dean's twin vortices

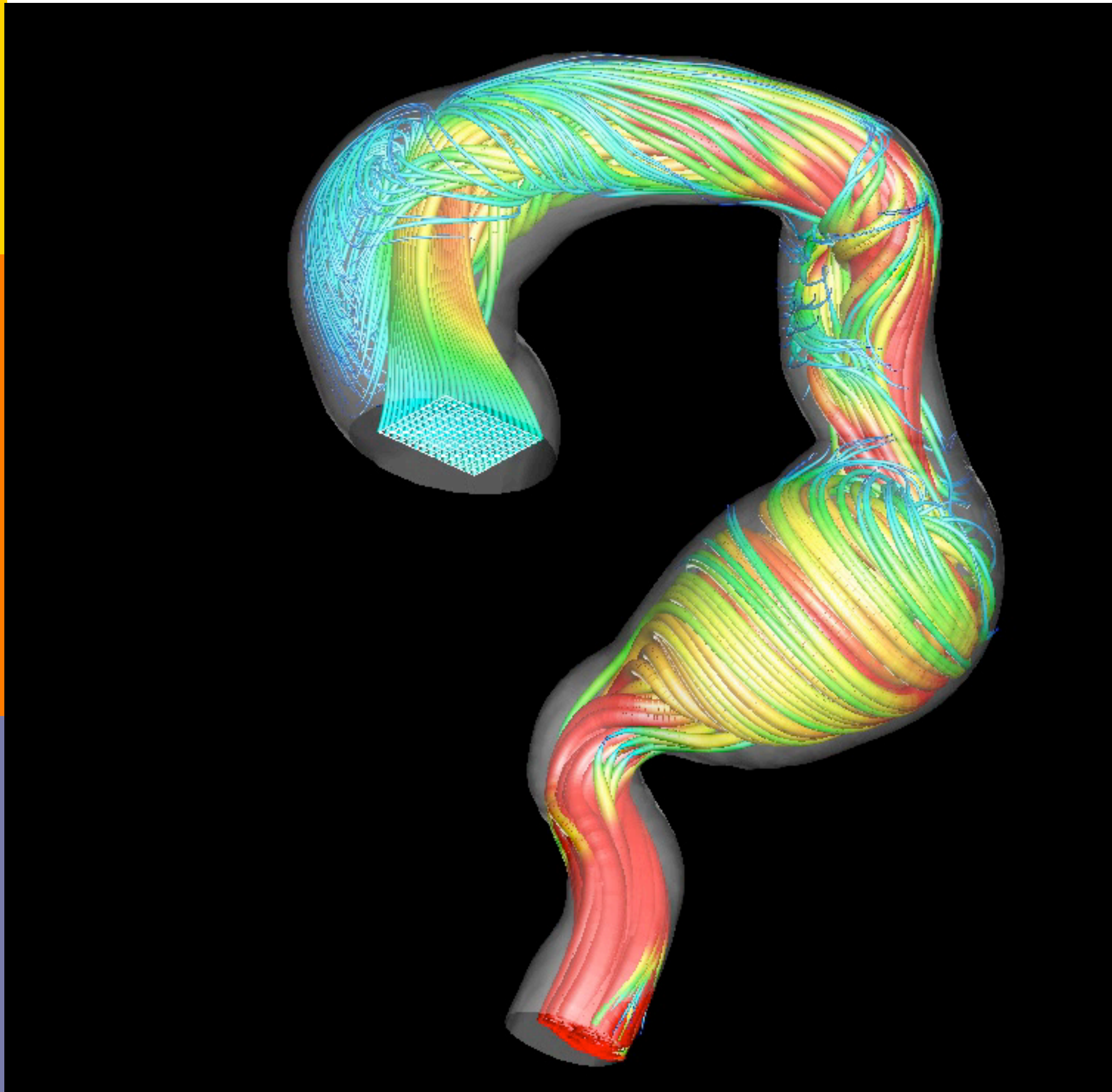


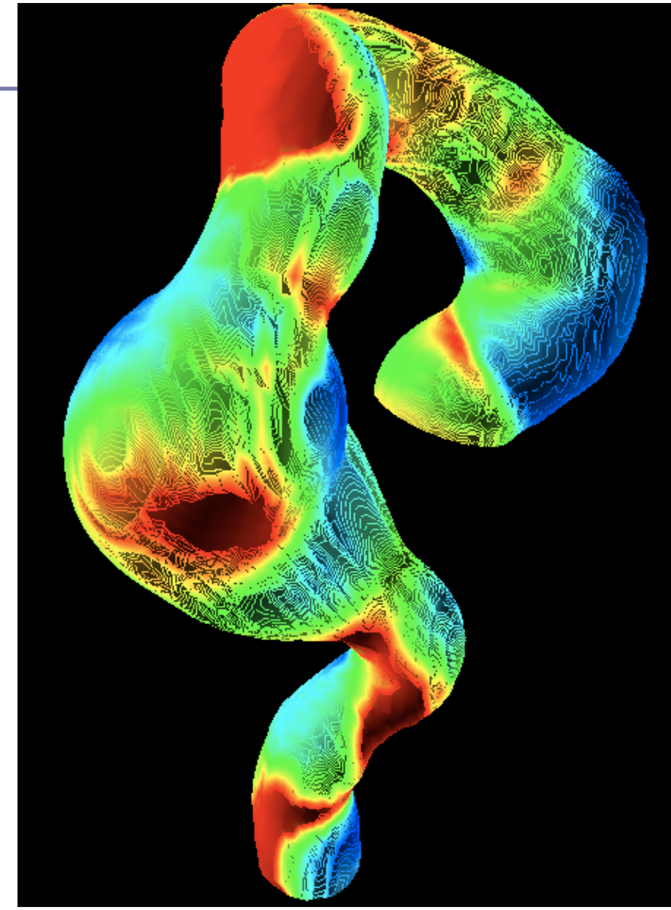
Dean number

$$De = 4\sqrt{\frac{d}{r_c}} \approx 5$$

(1) In the straight circular tube, Hagen-Poiseuille flow profile is achieved.
(2) If the tube has curvature, then the centrifugal force acts in the opposite direction of the curvature.
(3) The centrifugal force is proportional to the velocity in the axis direction.
(4) A set of opposite-sign vortices is generated as a secondary flow.

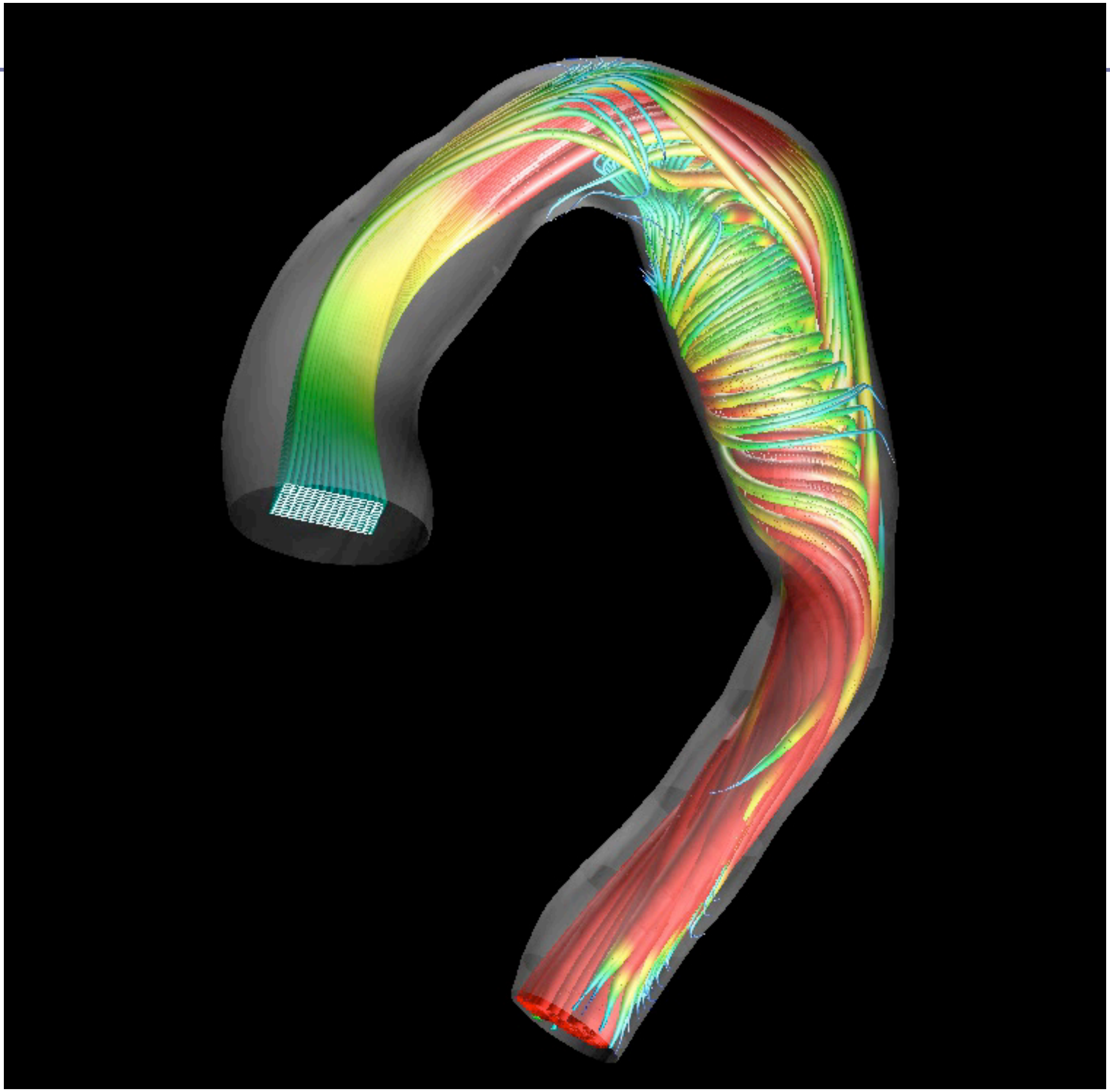
Blood flow visualized by instantaneous streamlines

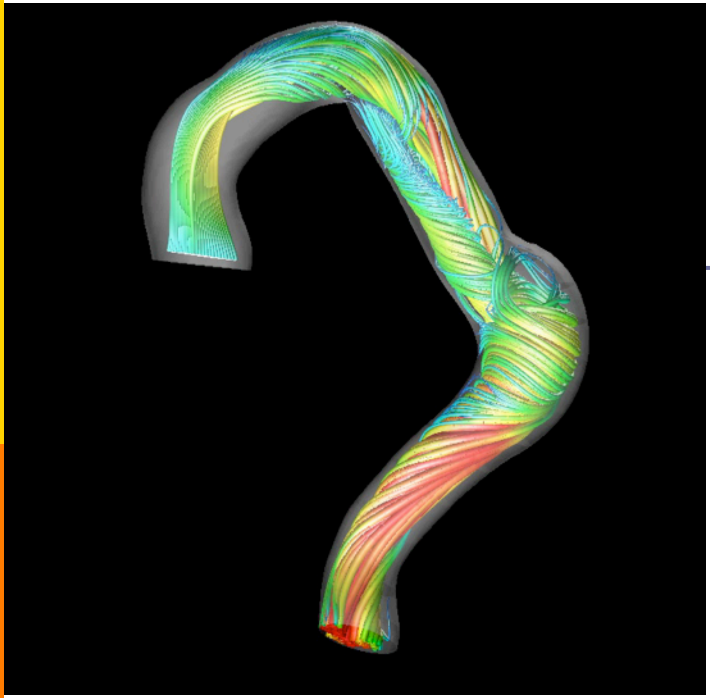




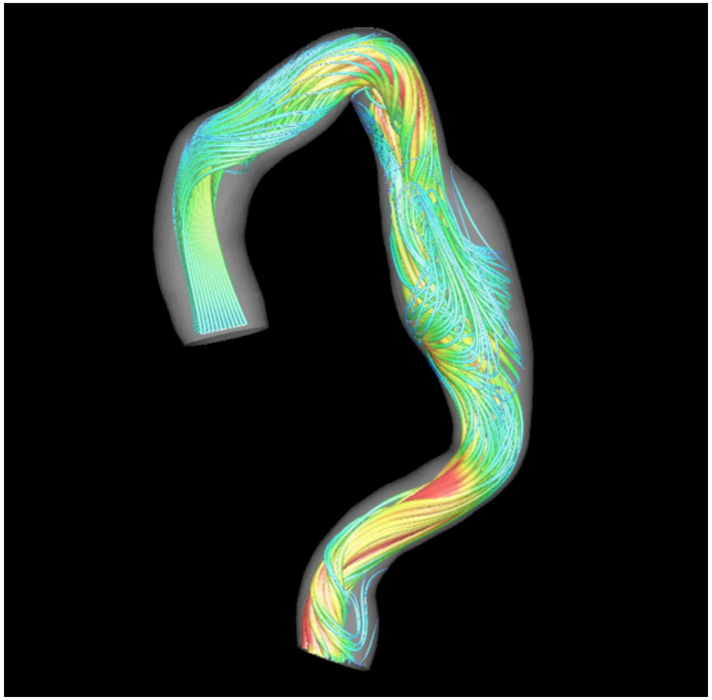
Distribution of time-averaged wall shear stress

Swirling flow visualized by instantaneous streamlines (A001)

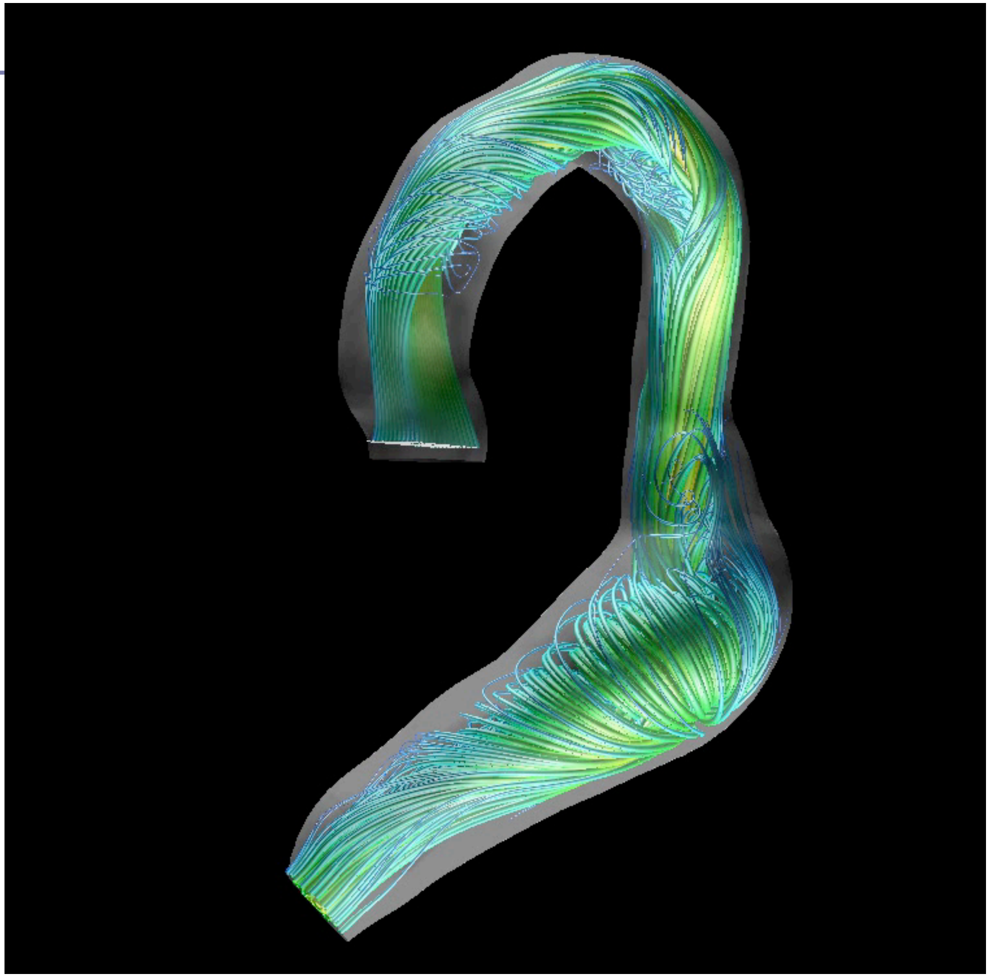




A006

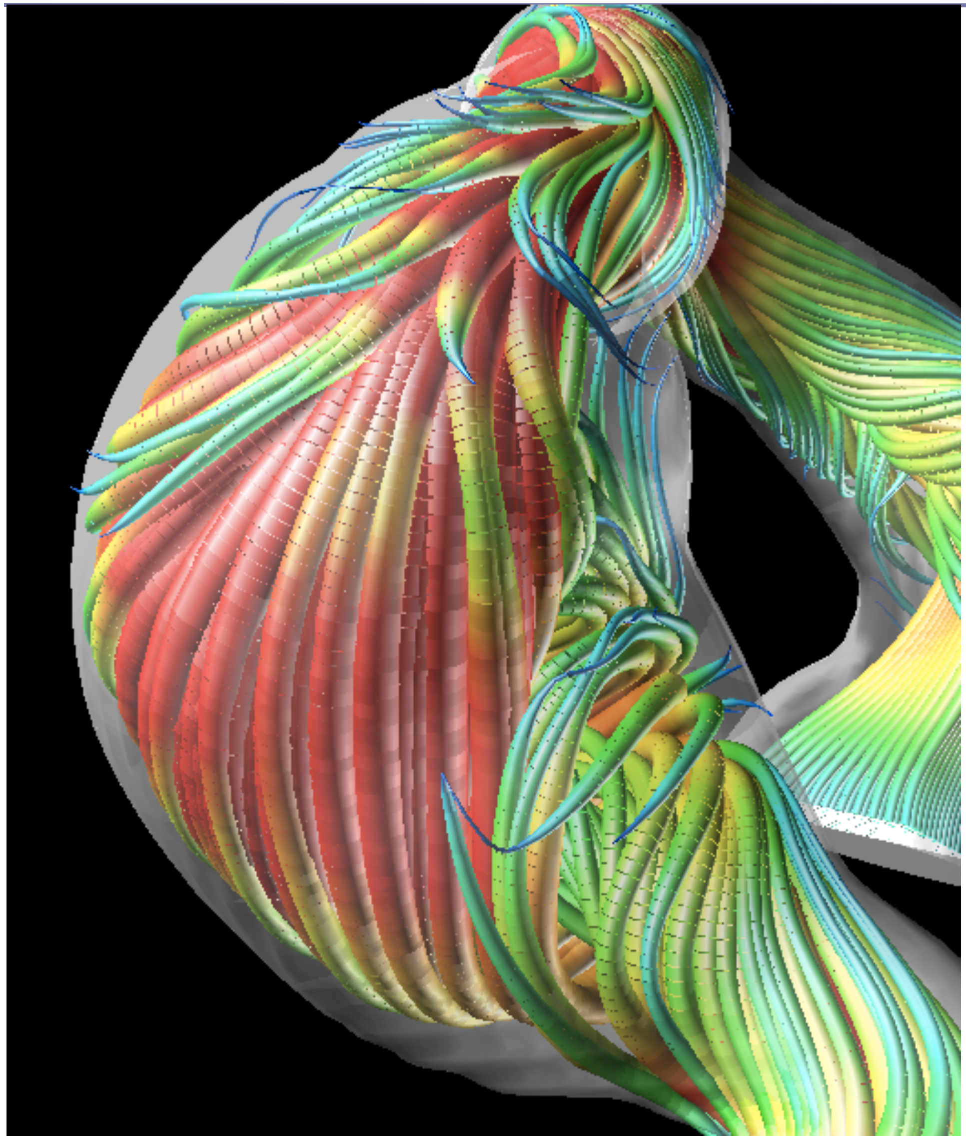


A004

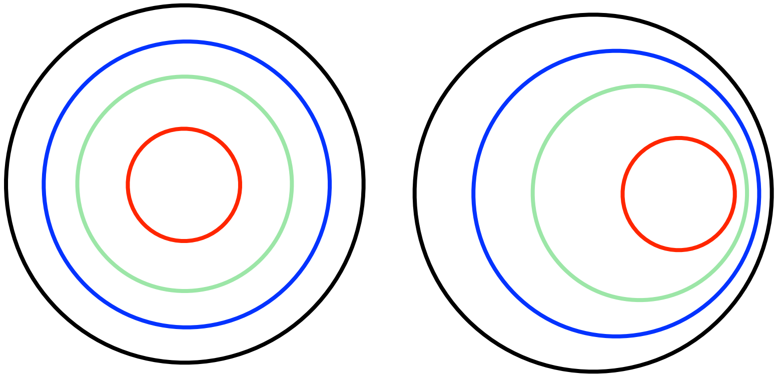


A010 with stagnation point

Naked flow

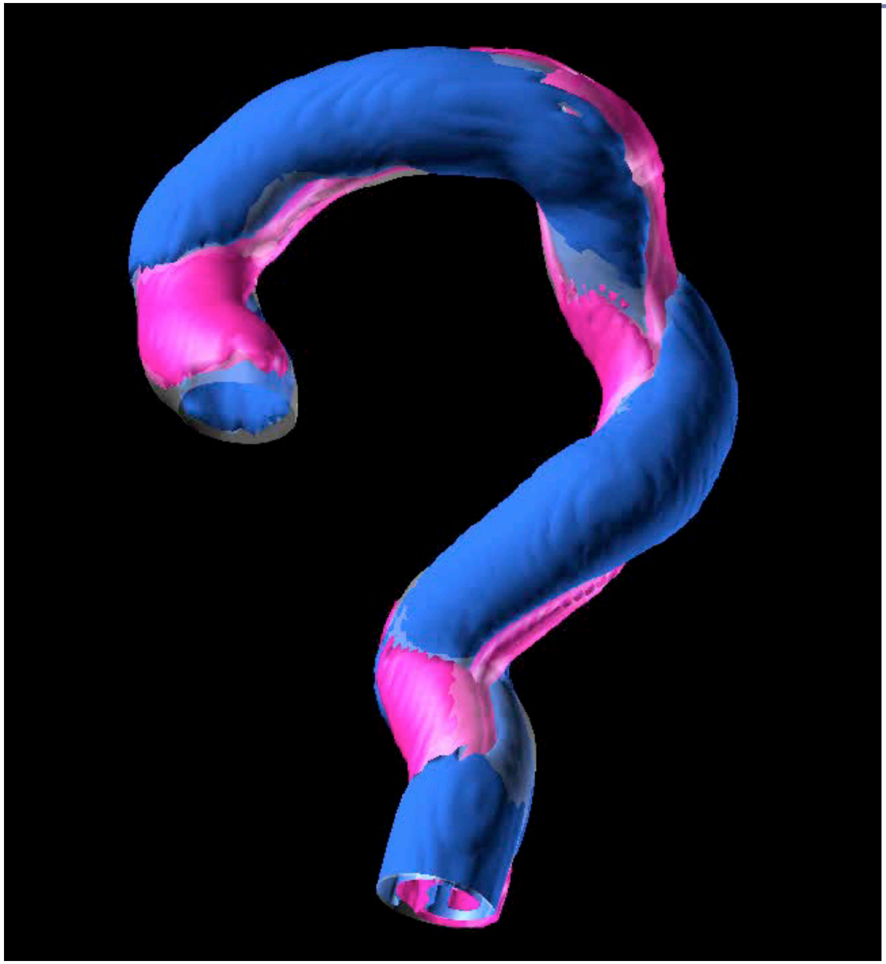


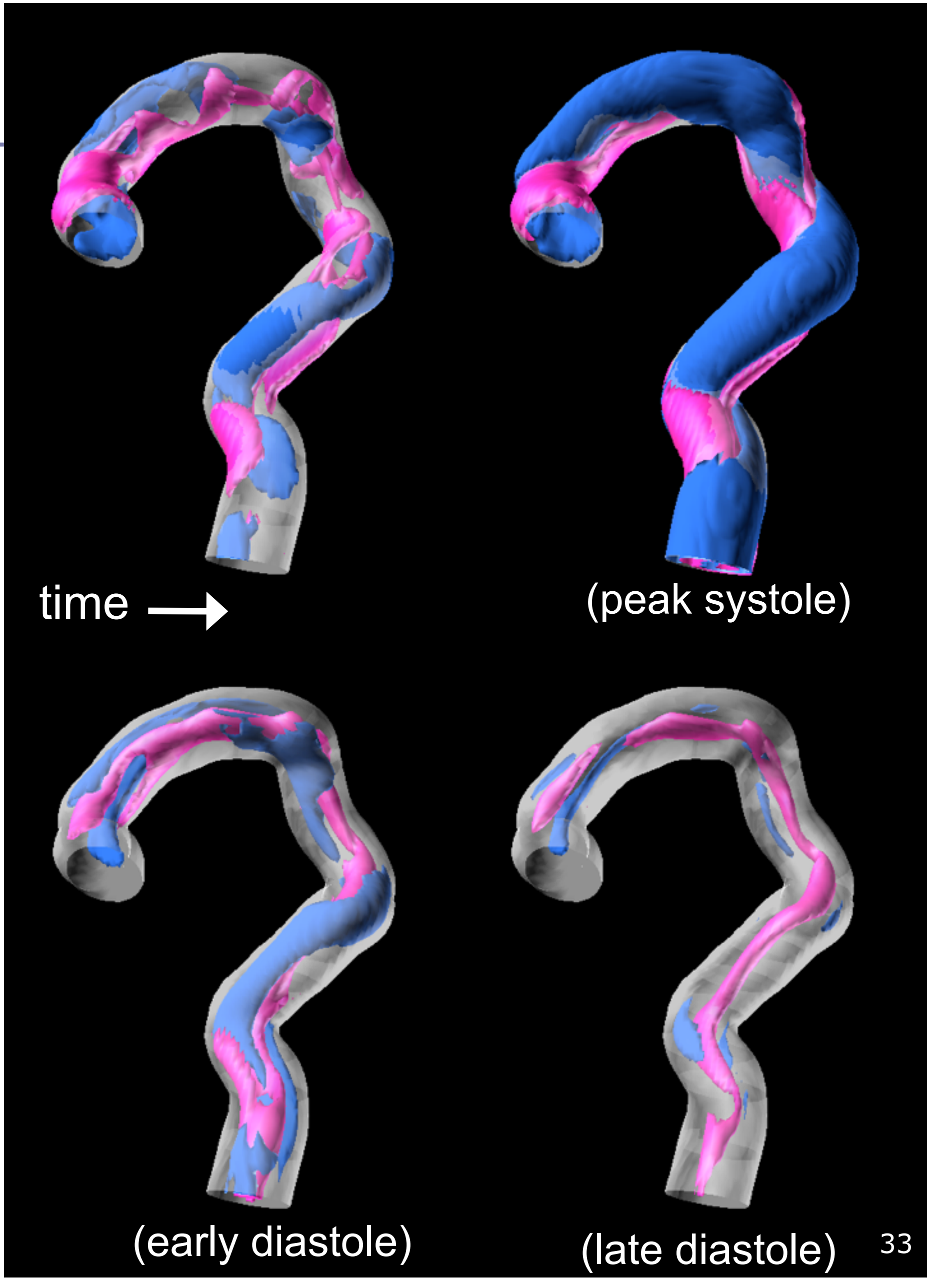
- If the vessel is straight, Poiseuille-like flow profile is achieved. The strong velocity is confined to the center region of the vessel.
- In the case with curvature and torsion, this strong velocity is conducted to the near-wall region, which causes strong wall shear stress.



Streamwise vorticity contours

red, clockwise
blue, counter-clockwise

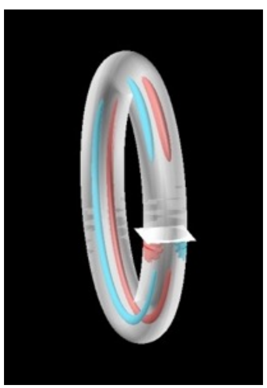




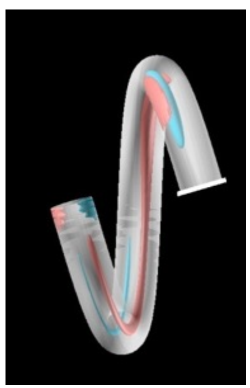
Simple spiral tubes

- The aorta has numerous shape factors, such as the radius, shape of cross-sections, and shape of centerlines.
- We are going to examine the fundamental flow characteristics using simplified spiral geometries.

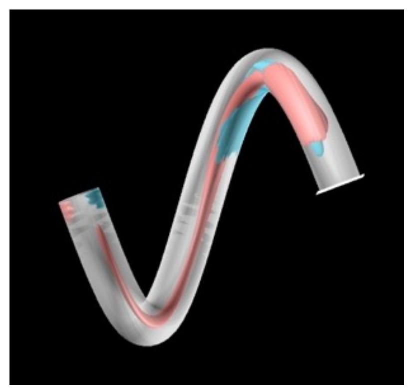
$$\begin{cases} x = a\cos u \\ y = a\sin u \\ z = hu \end{cases} \qquad \mathrm{Cv} = \frac{a}{a^2+h^2} \qquad \mathrm{To} = \frac{h}{a^2+h^2}$$



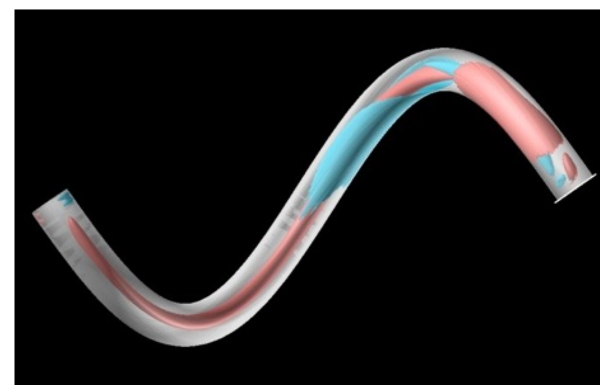
$\chi = 16.7$
$\tau = 0.0$



$\chi = 16.2$
$\tau = 2.7$



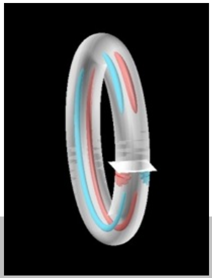
$\chi = 15.0$
$\tau = 5.0$

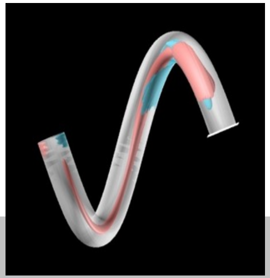


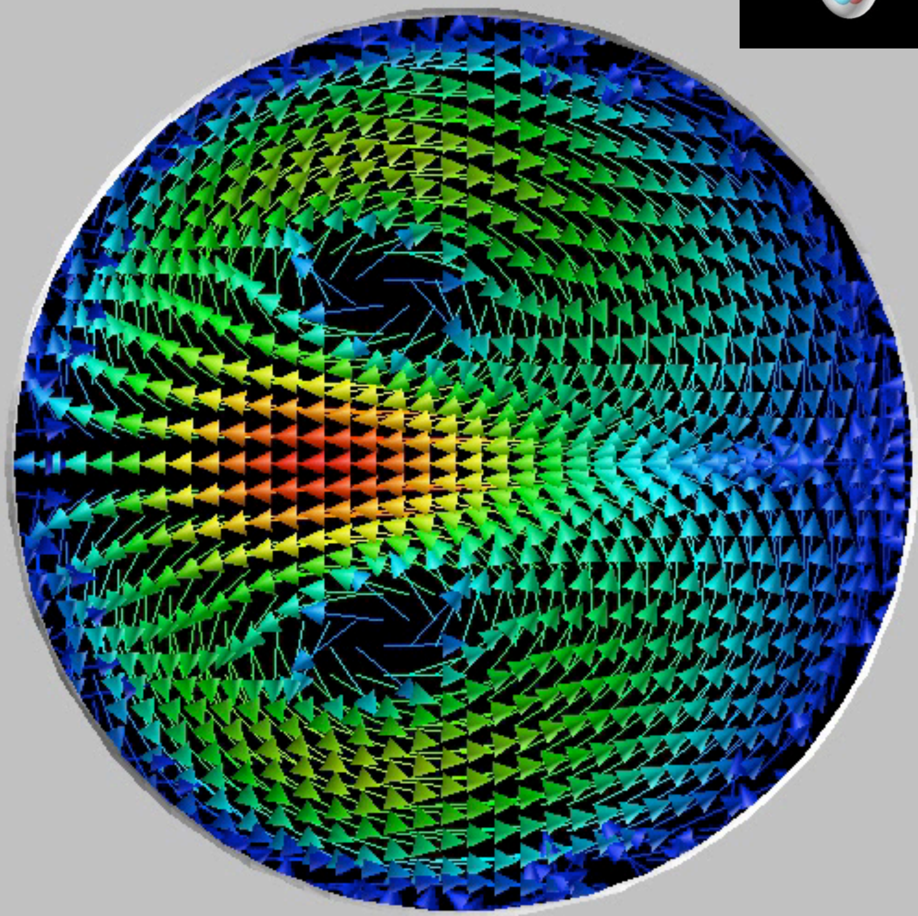
$\chi = 11.5$
$\tau = 7.7$

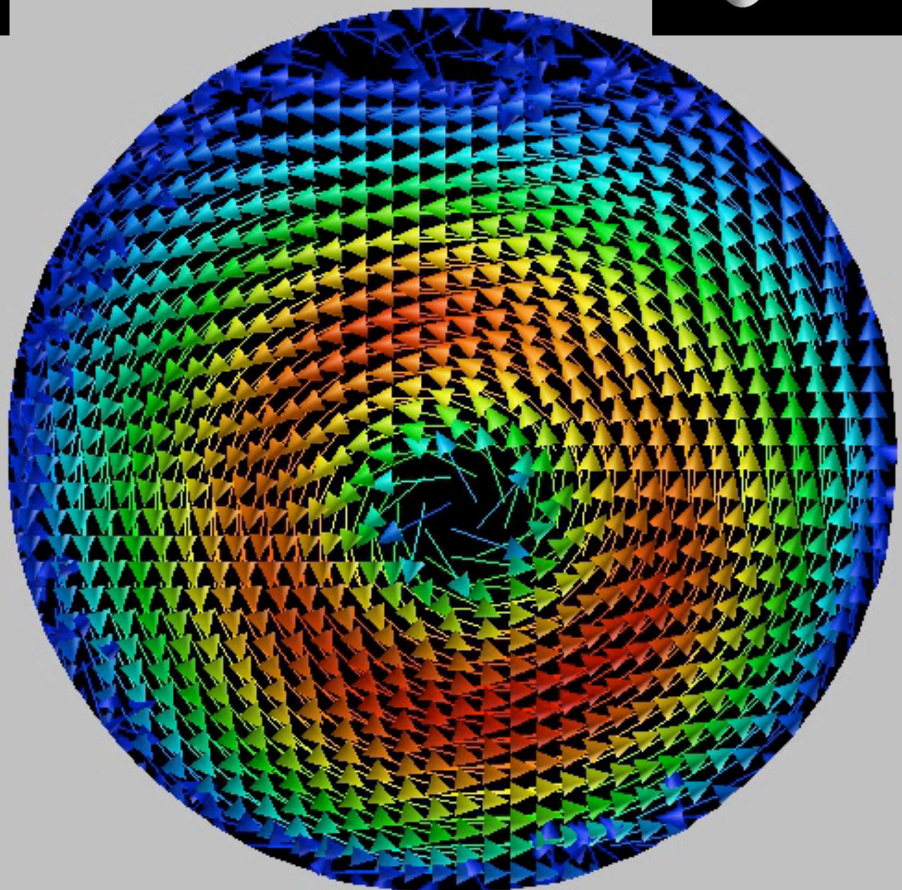
Consider these simple spiral tubes to investigate the dependence of the flows on several parameters. The pulsate velocity profile is given in the in-flow boundary.

Secondary flows







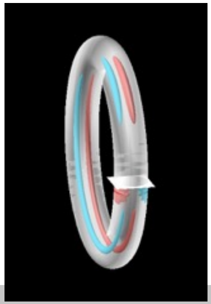


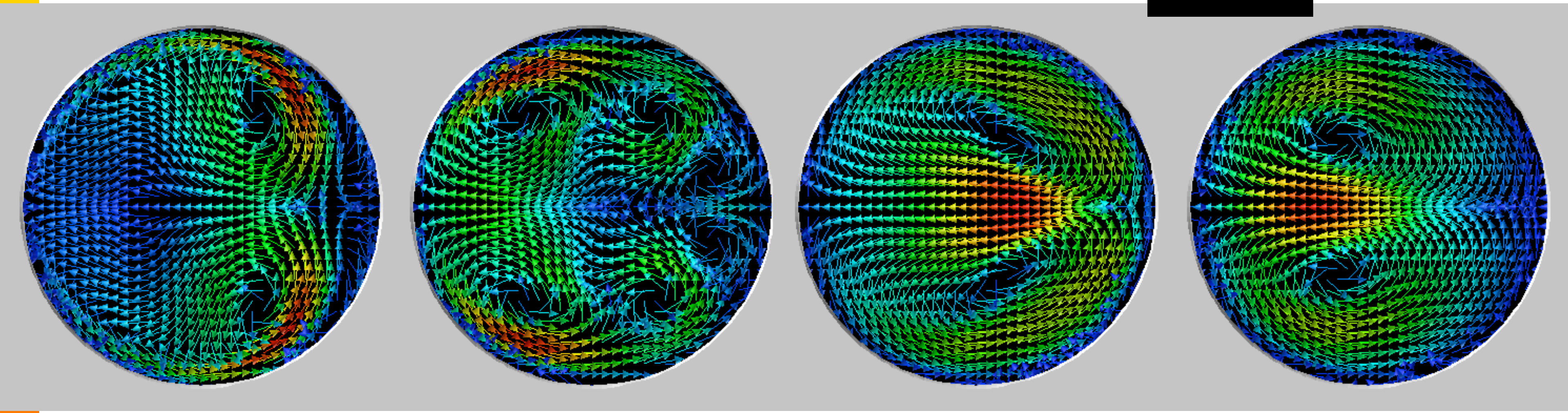
Torsion = 0.0

Torsion = 5.0

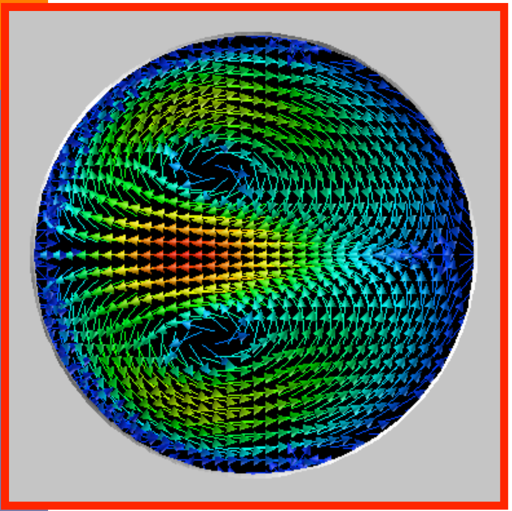
In the right hand side movie, merging and growing history of the one vortex can be seen.

Secondary flow in a simple spiral tube (zero torsion case)





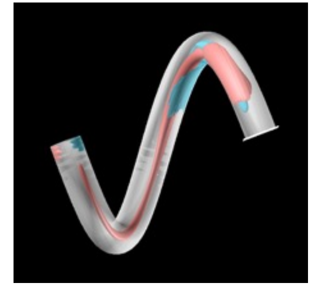
(peak systole) (late systole) (early diastole) (late diastole)

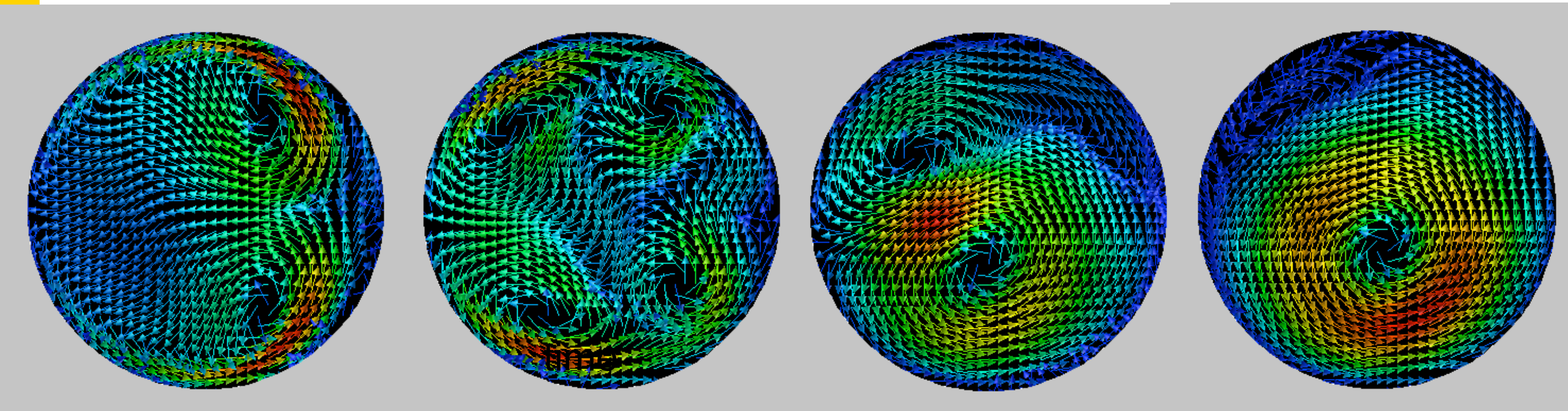


steady case

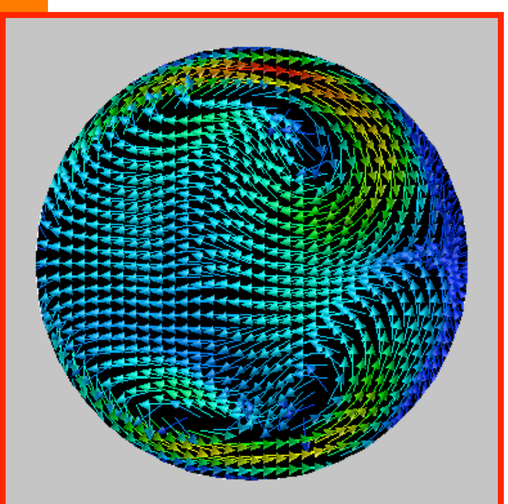
In the zero-torsion case, two Dean’s vortices are apparent throughout the whole cardiac cycle. Furthermore, these characteristics are the same for the steady case.

Secondary flow in a simple spiral tube (non-zero torsion case)





(peak systole) (late systole) (early diastole) (late diastole)

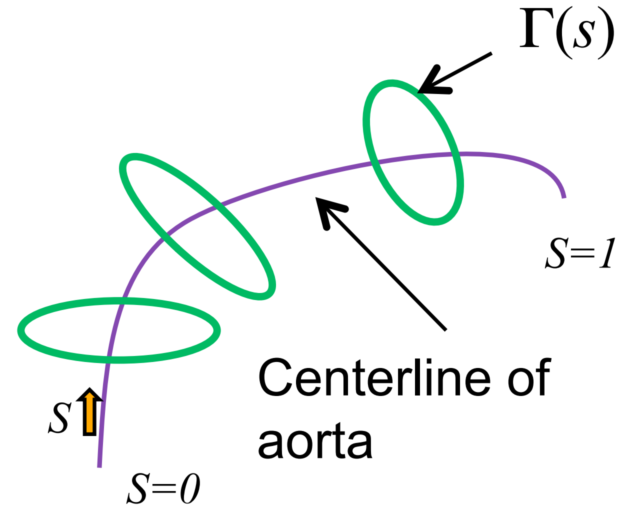


steady case

In the peak systole phase, symmetric Dean's vortices are generated just as in the zero-torsion case. However, in the diastole phase, they merge; one of them dominates the other. Actually, the lower right small vortex in the second figure persists and expands.

This phenomenon differs completely from that of the steady flow case for equivalent geometry. In the steady case, nearly symmetric Dean's vortices exist.

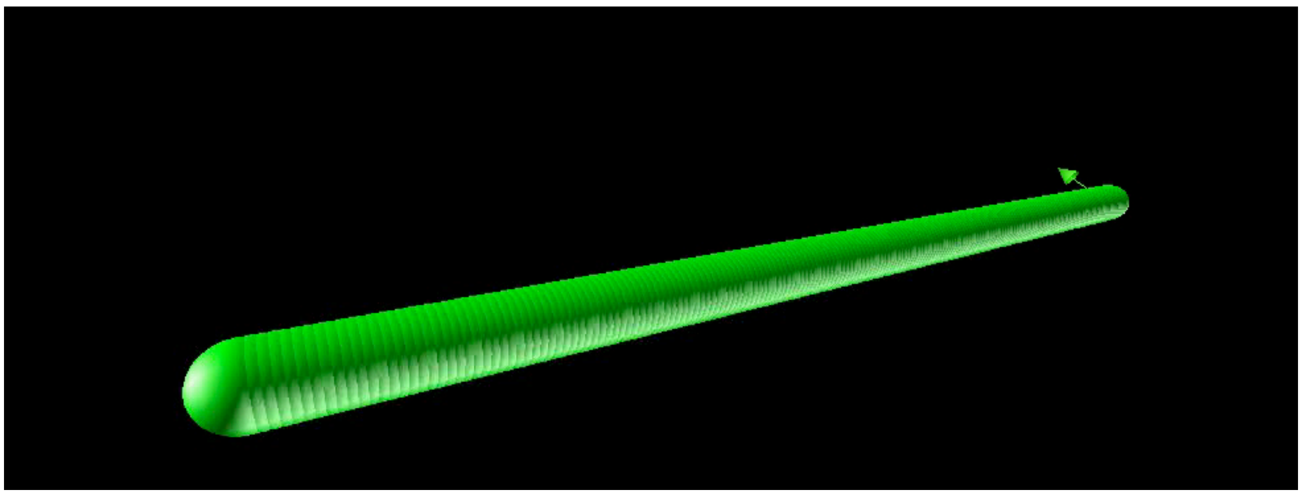
Torque on the aortic wall



To evaluate the swirling flow effect, we compute the torque as

$$T(s) = \int_{\Gamma(s)} (\boldsymbol{r} \times \boldsymbol{\sigma}) \cdot \boldsymbol{\tau} d\Gamma$$

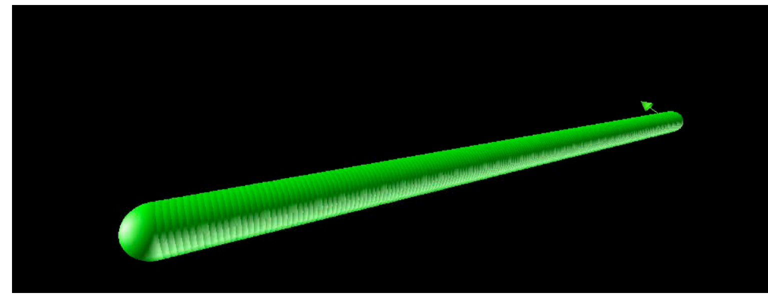
1D elastic rod (Kirchhoff rod)

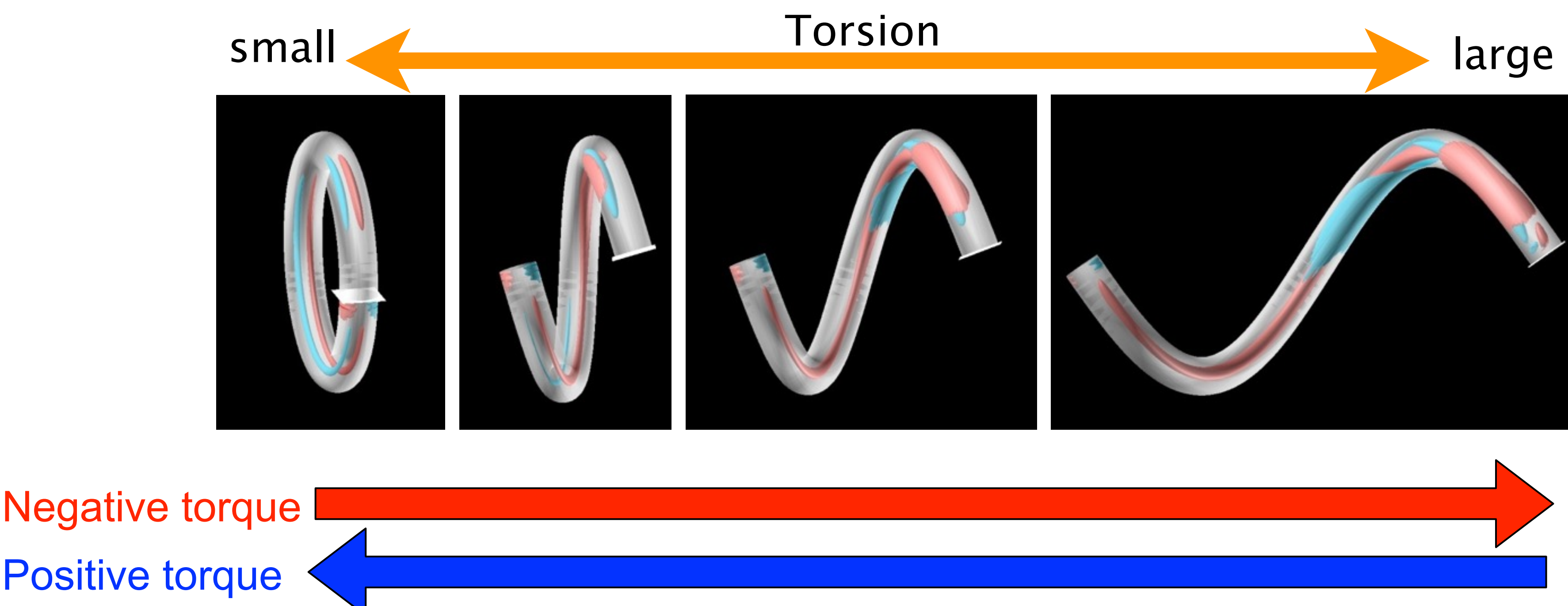


It is apparent that the rod forms a spiral if the positive torque is applied at the end.

Relation between torque and torsion

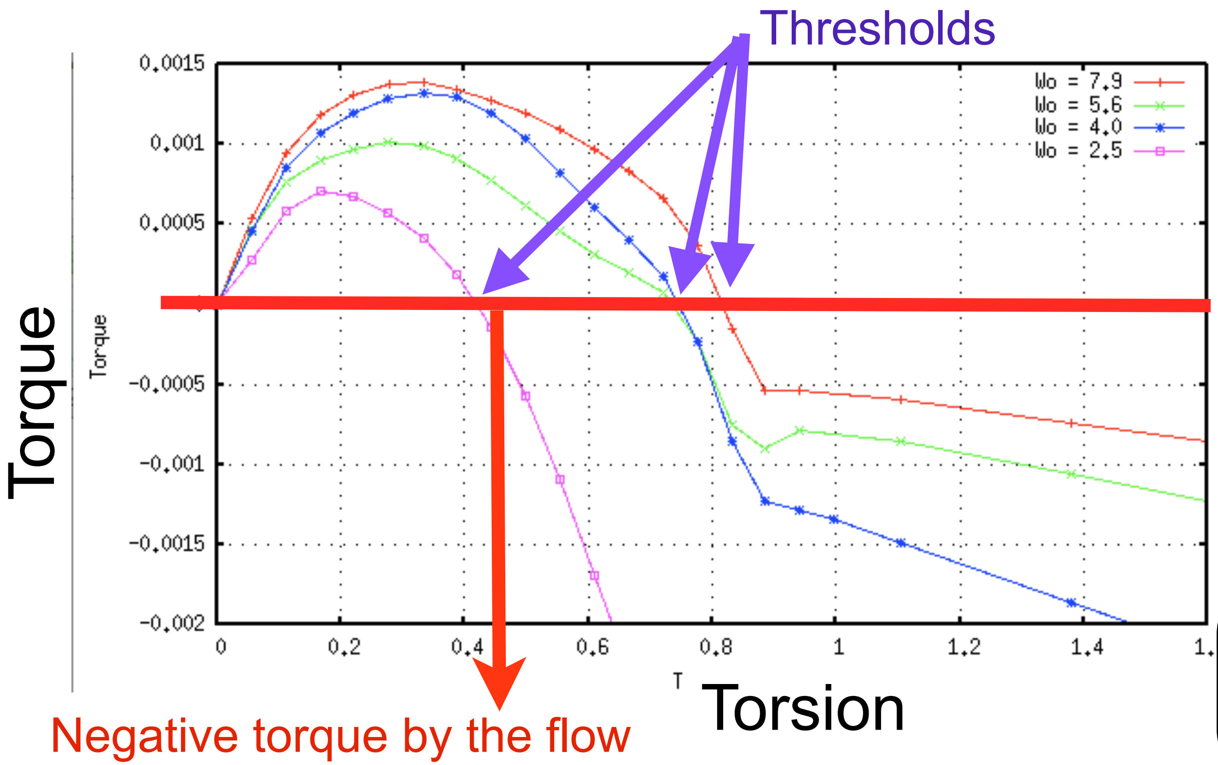
As for the relation between torque and torsion in a one-dimensional elastic rod, negative torque intensifies torsion, whereas the positive torque works to reduce torsion.





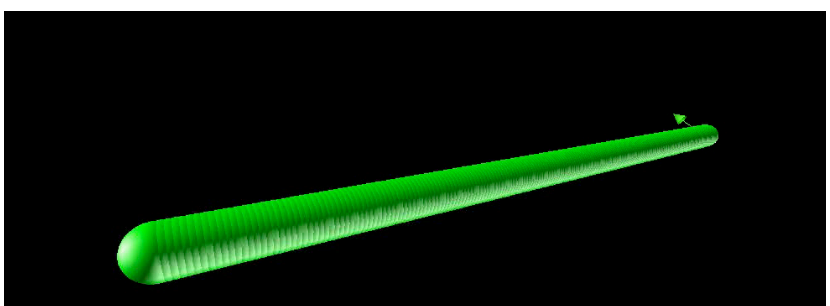
Diagram

$$Wo = \frac{d}{2}\sqrt{\frac{2\pi}{\nu T_p}}$$



- If the torsion = 0, the torque is of course 0.
- An important characteristic of this diagram is that there exists a threshold at which the sign of the torque becomes negative.

Positive feedback between aorta morphology and flow structure



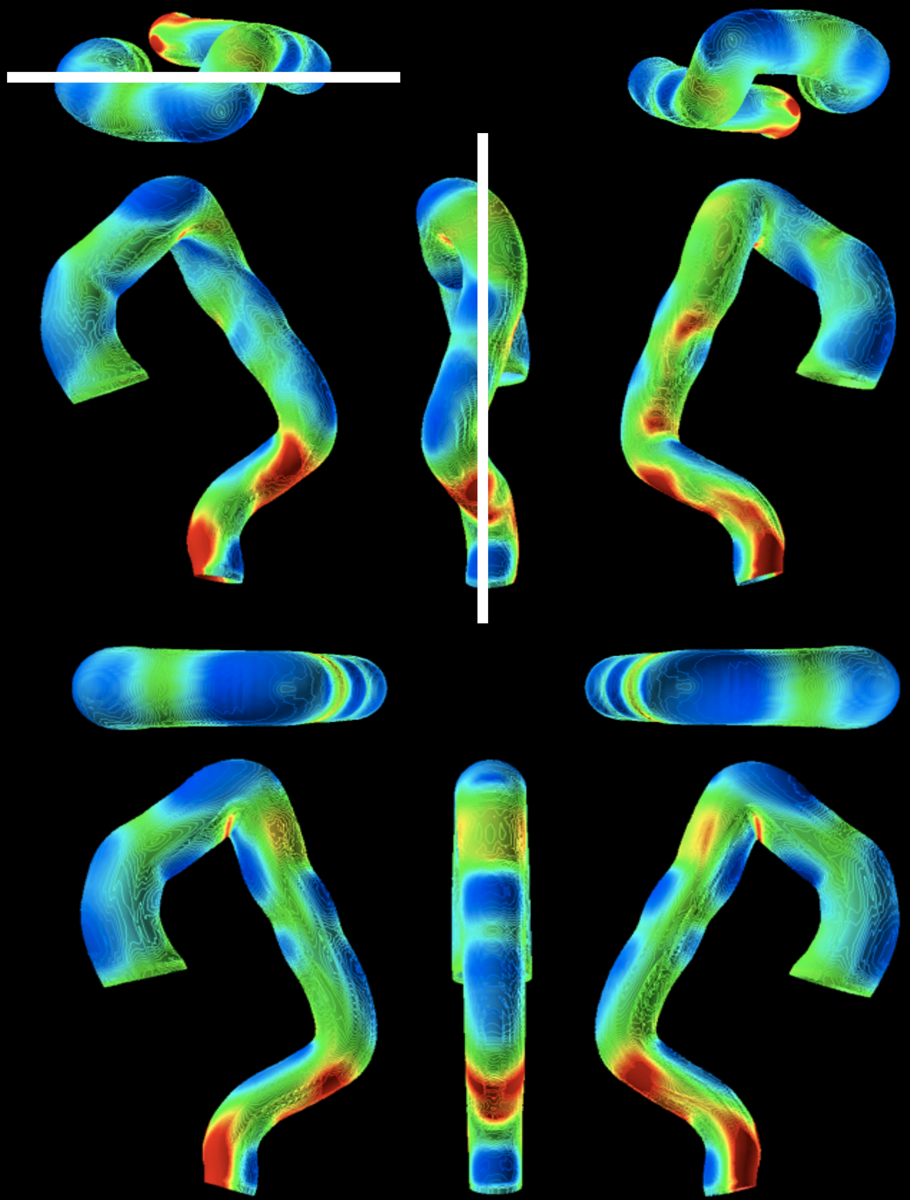
If the torsion of the tube is smaller than the threshold, the flow works to reduce the torsion. However, if the torsion is larger than the threshold, the flow-induced torque intensifies the torsion.

Examine the effects of torsion from a different perspective

Original shape

Projection onto a plane of curvature

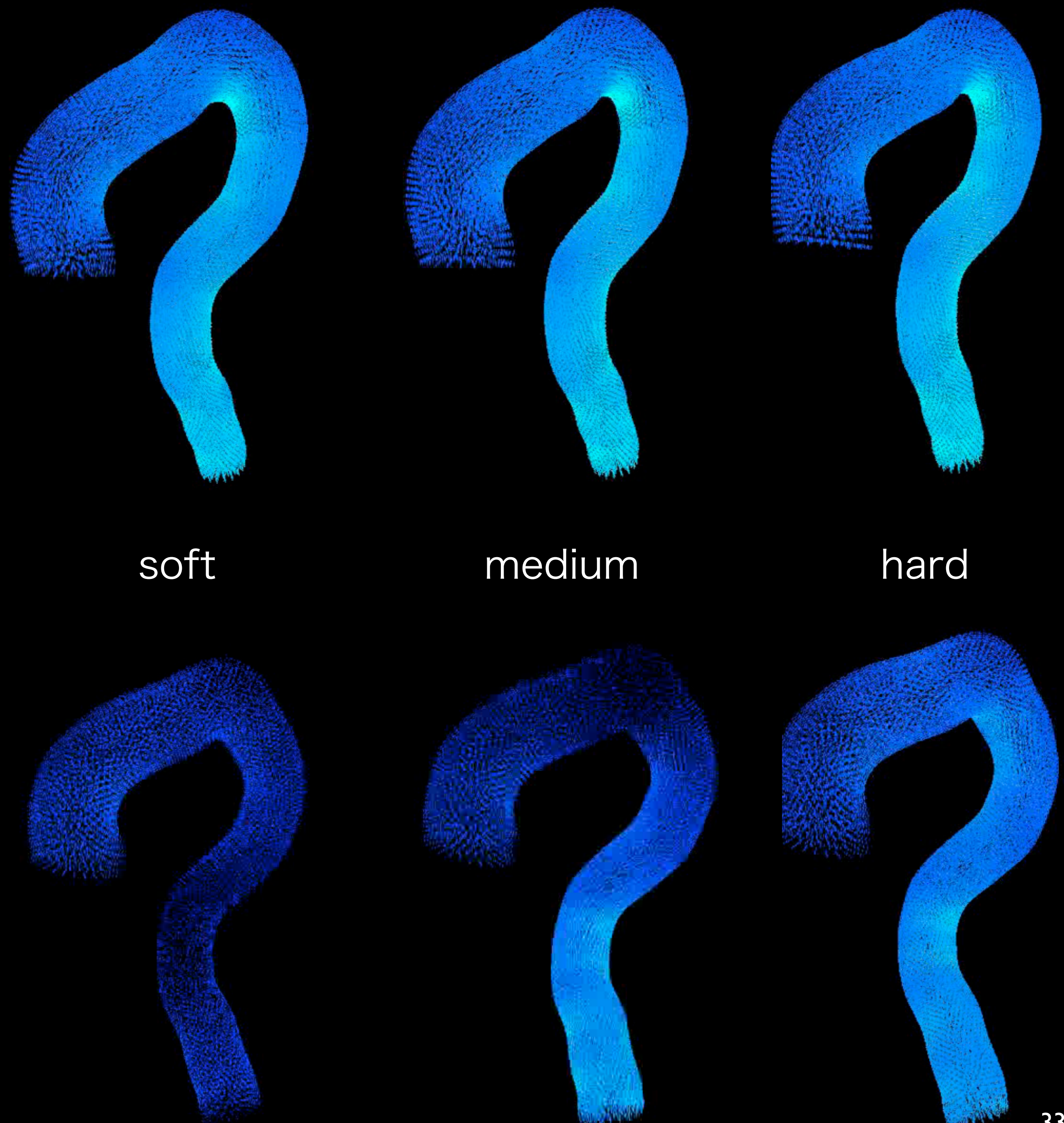
Artificial shape without torsion



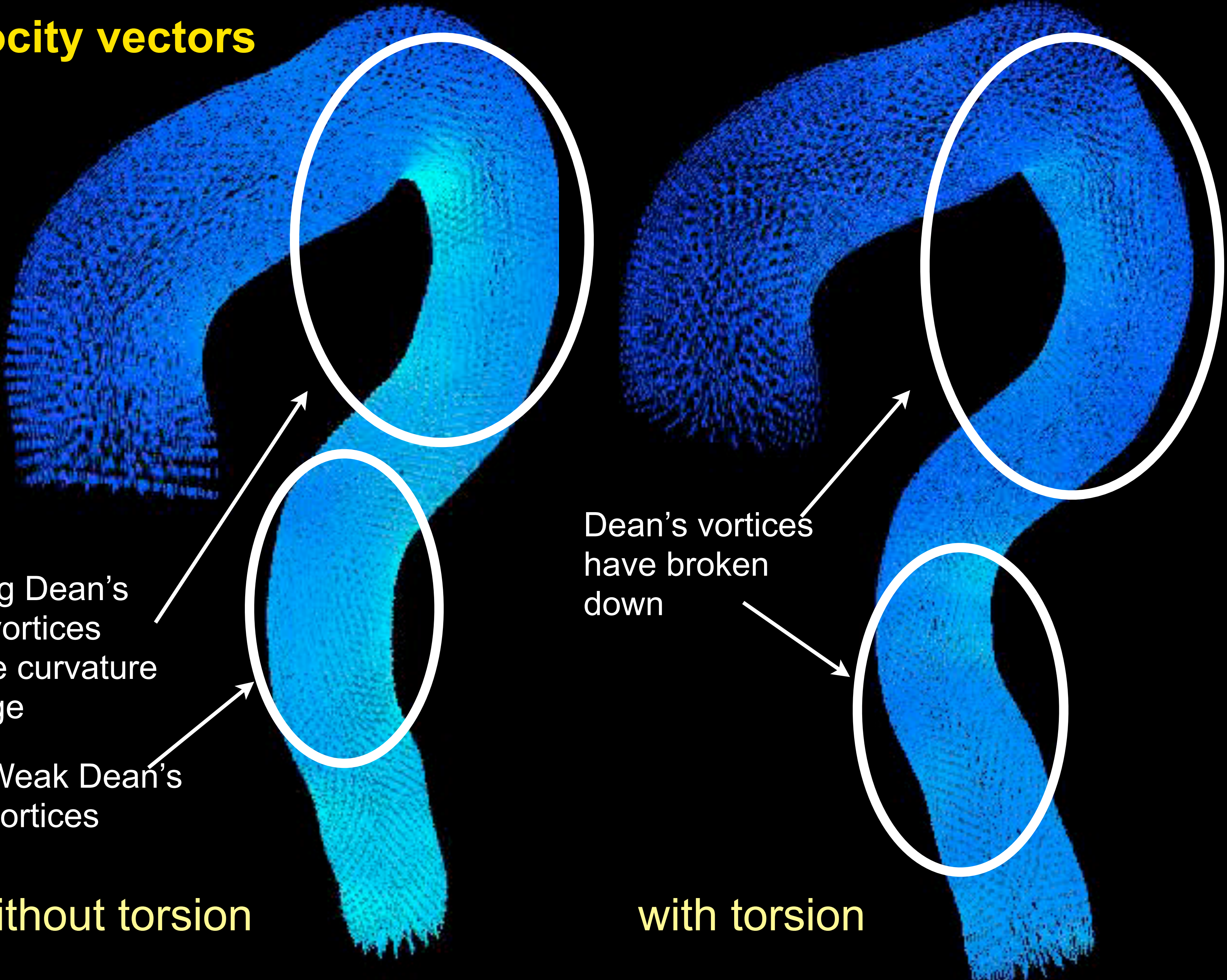
Velocity vectors
considering FSI

without torsion

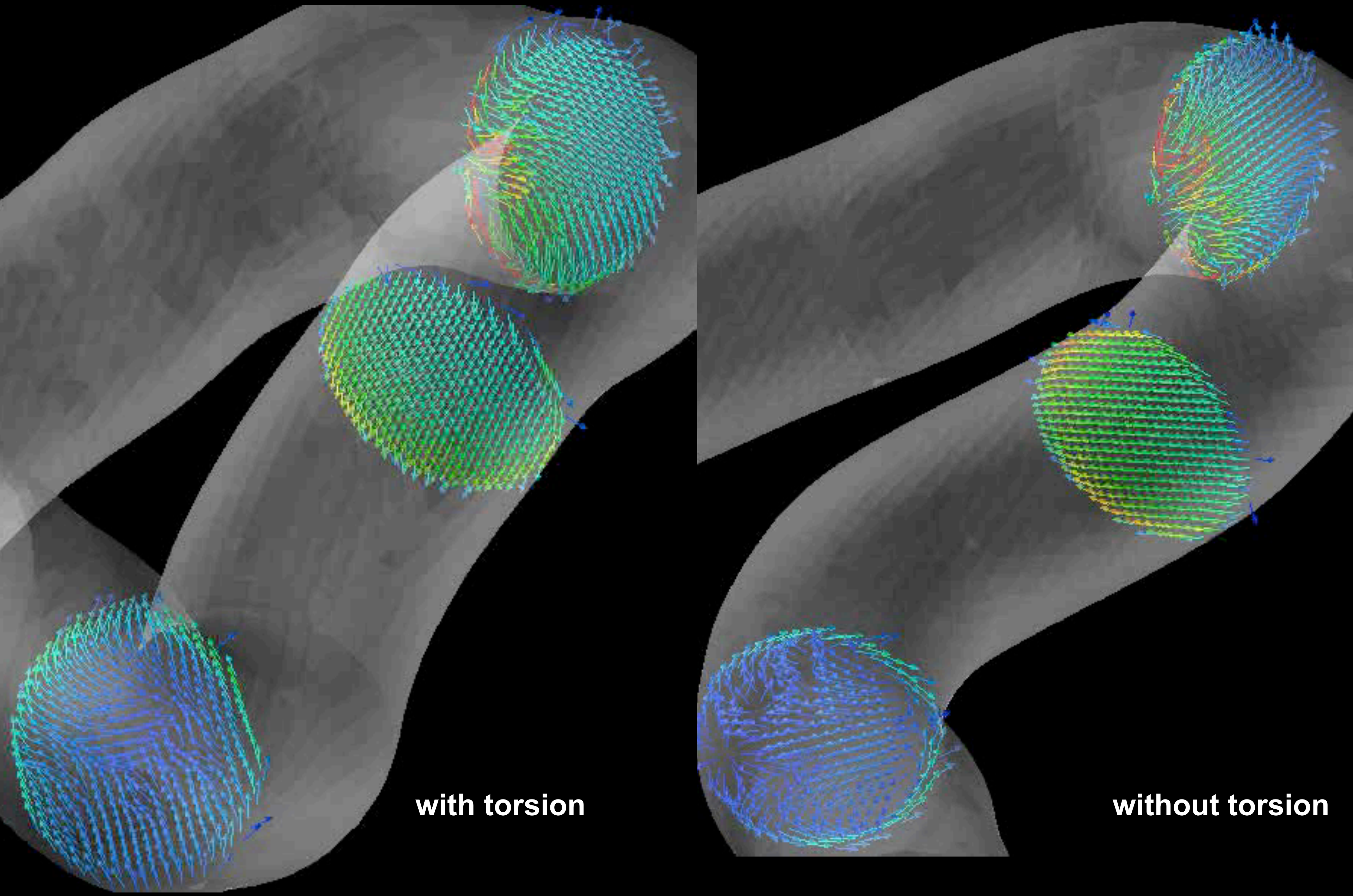
with torsion



Velocity vectors



Secondary flows

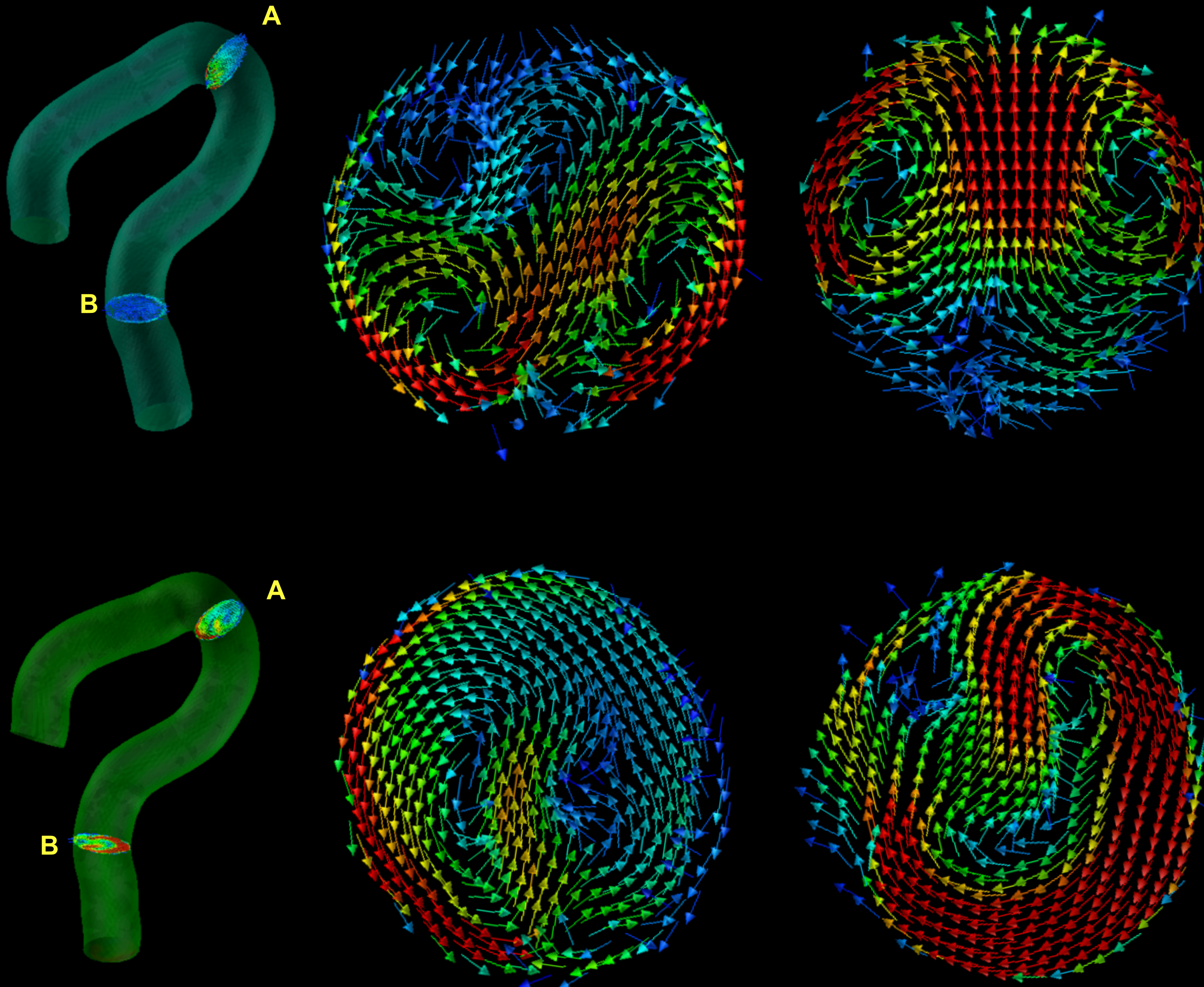


Secondary flow on the cross-section A

Secondary flow on the cross-section B

Without torsion

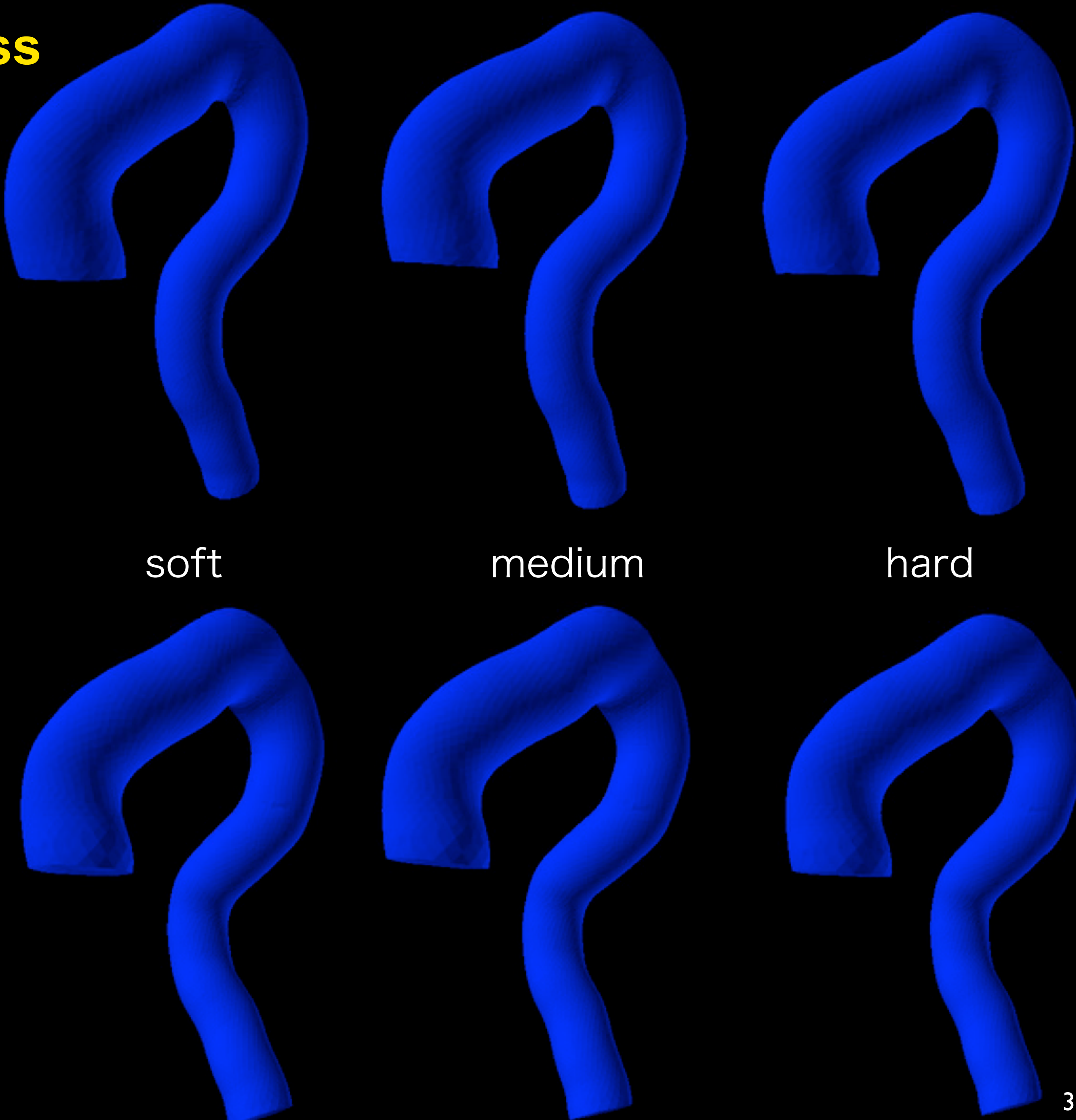
With torsion



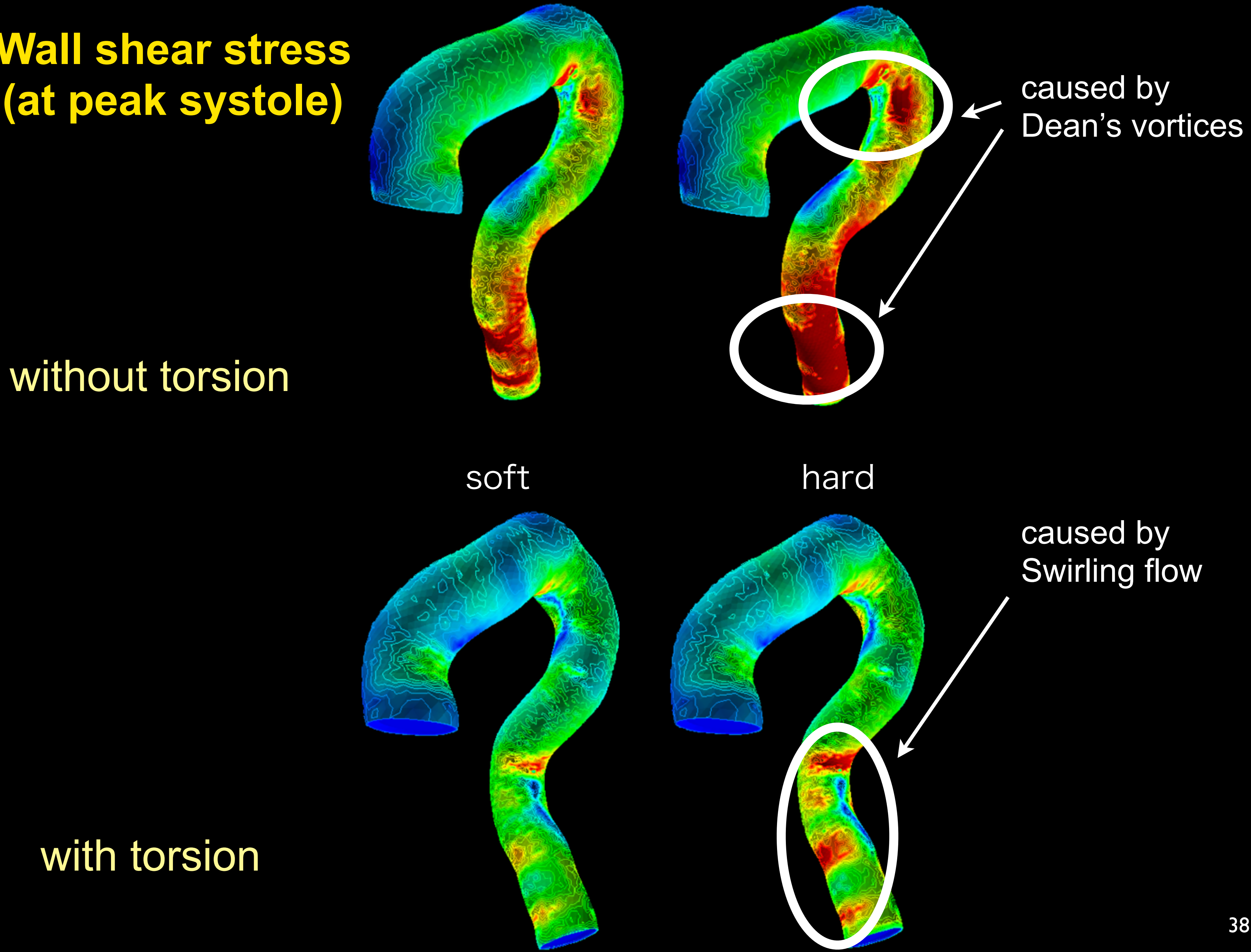
Wall Shear Stress

without torsion

with torsion



Wall shear stress (at peak systole)



As this presentation has shown up to this point

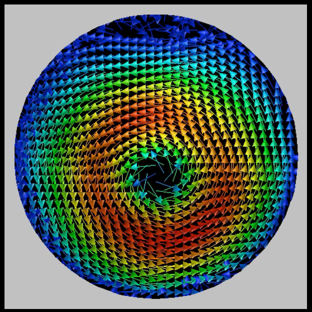
- Curvature of the aorta brings about strong Dean’s twin vortices and strong WSS in the aortic arch

Difference among individuals for curvature: small

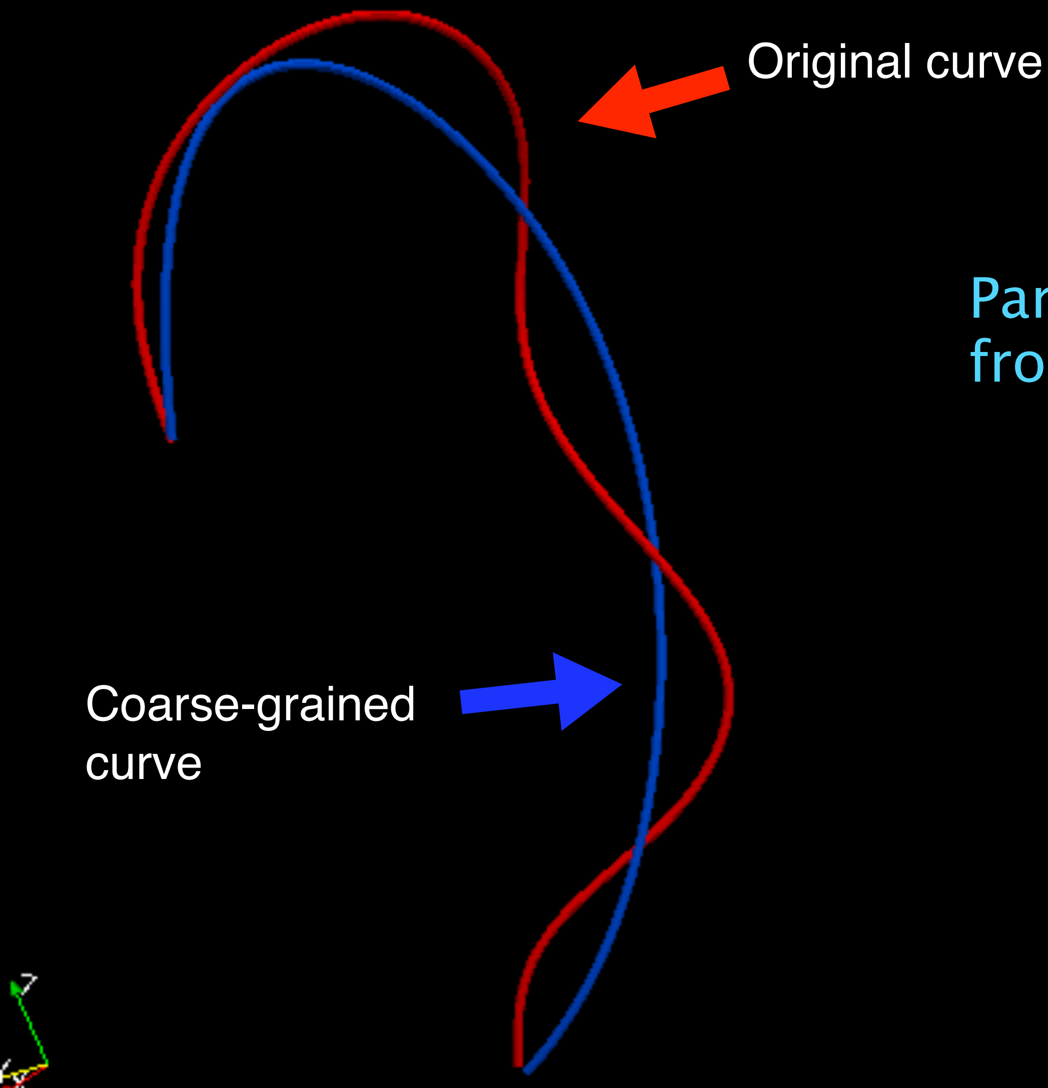
Difference among individuals for torsion: large

- Torsion in the aortic arch breaks down the Dean’s vortices, which makes WSS weaker.

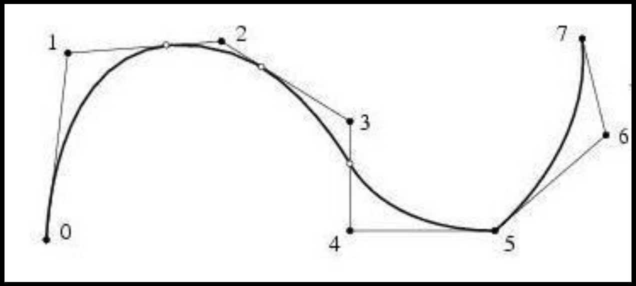
- Torsion brings about merging of Dean’s vortices and generates swirling flow, which makes WSS stronger.



Another means of understanding the characteristic difference between shapes



Parameterization using deviation from the coarse-grained curve

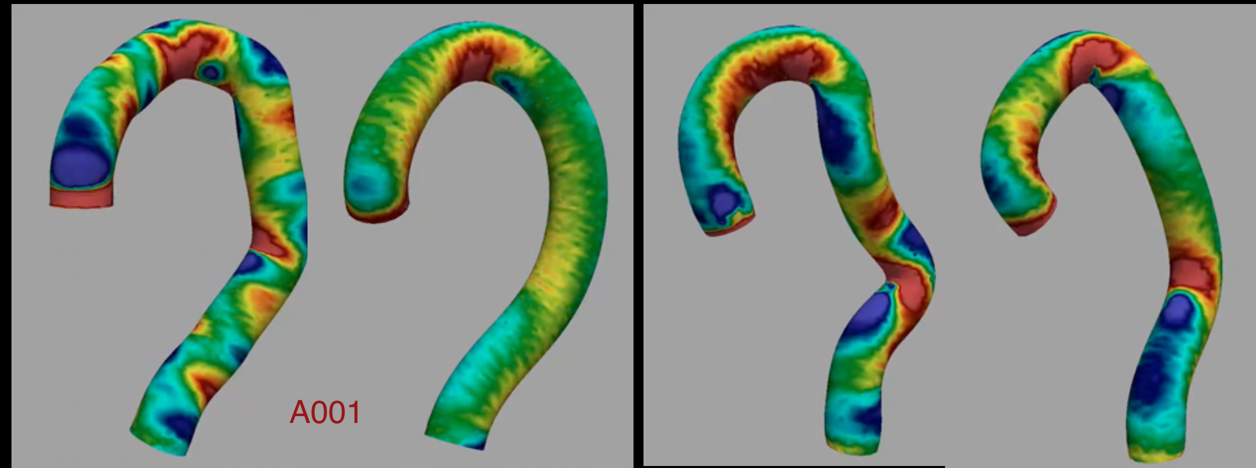


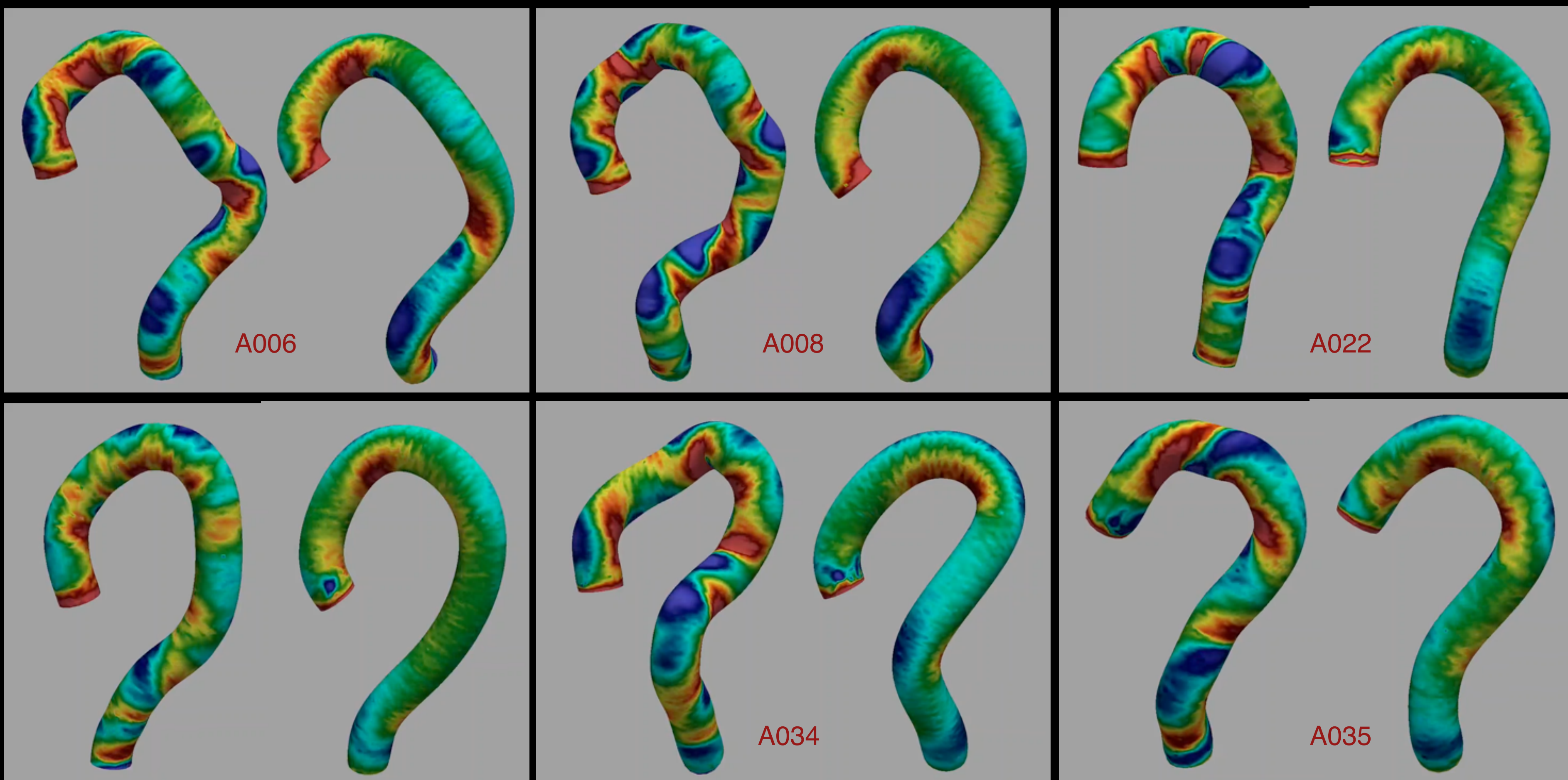
based on NURBS representation

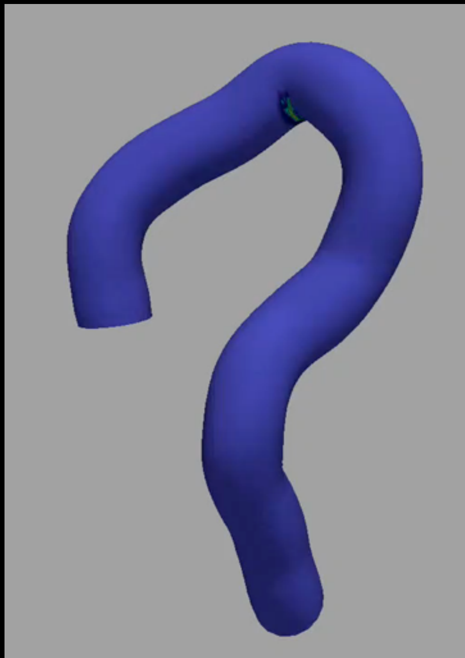
(NURBS: Non-Uniform Rational Basis Spline)

Comparison for WSS

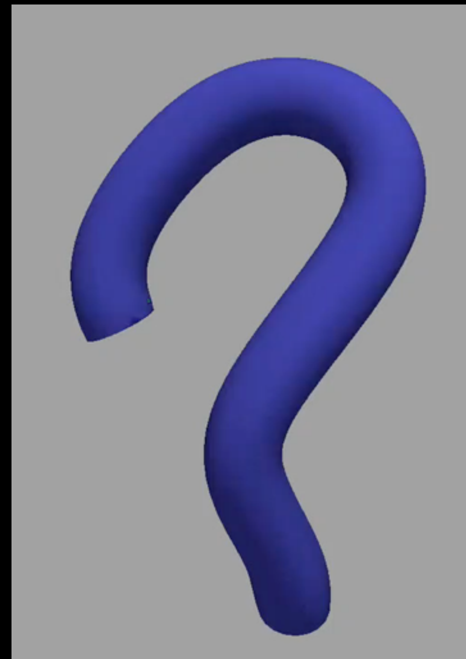
Left: original shape
Right: coarse-grained shape



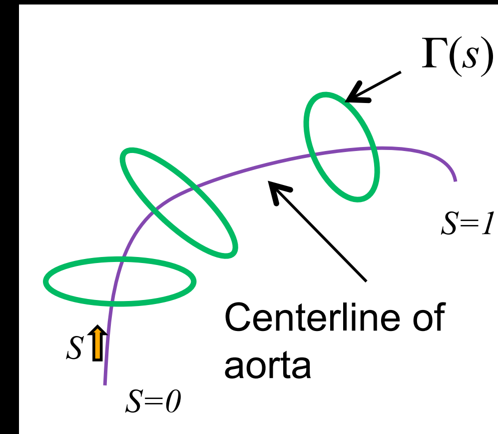




Original shape

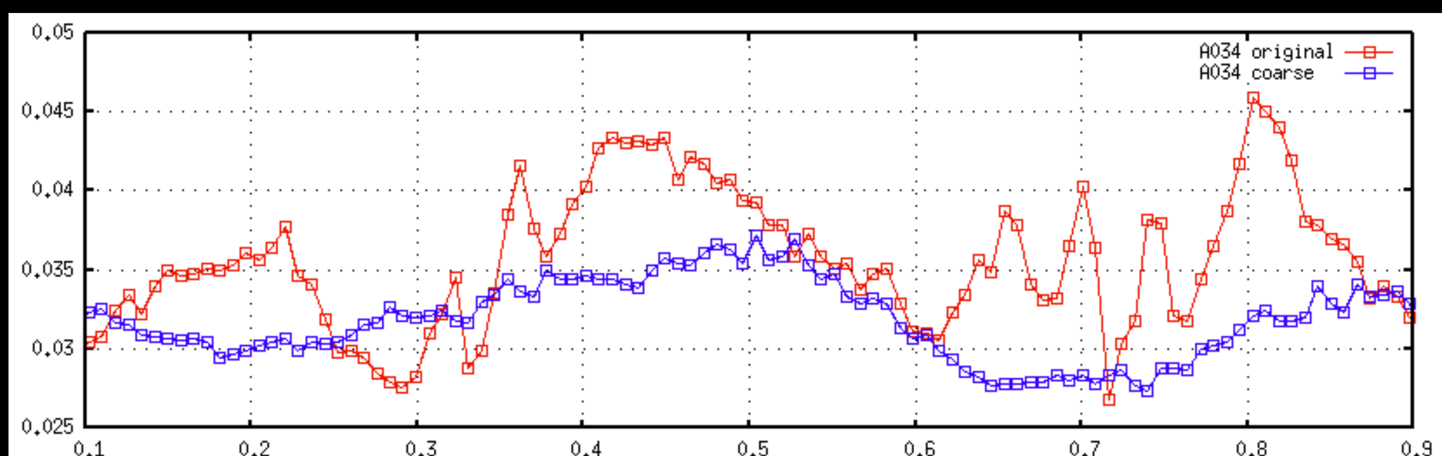


Coarse-grained shape



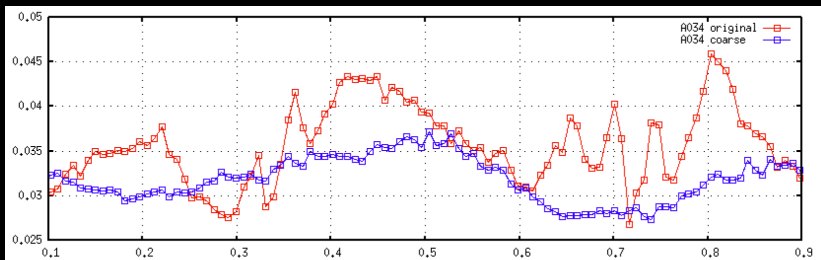
$$\tilde{\sigma}(s) = \int_{\Gamma(s)} \int_0^T |\sigma_\tau| \, dt \, d\Gamma$$

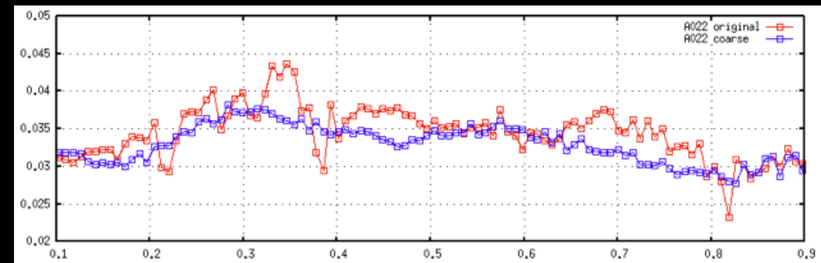
$\tilde{\sigma}(s)$

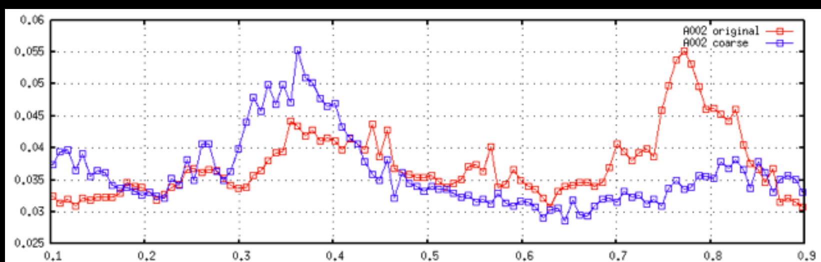


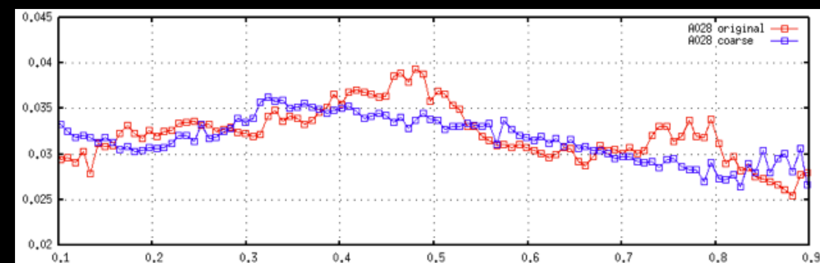
s

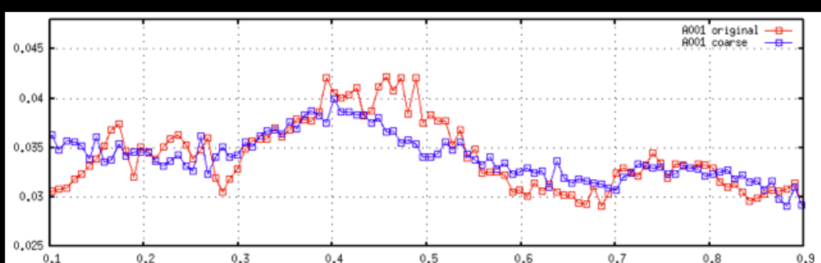
Integration of time-averaged wall shear stress on cross-sections perpendicular to the centerline

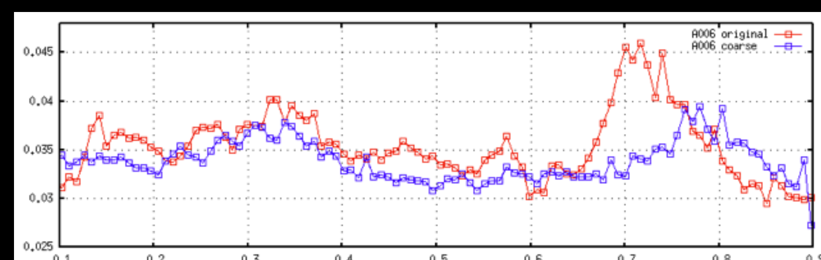


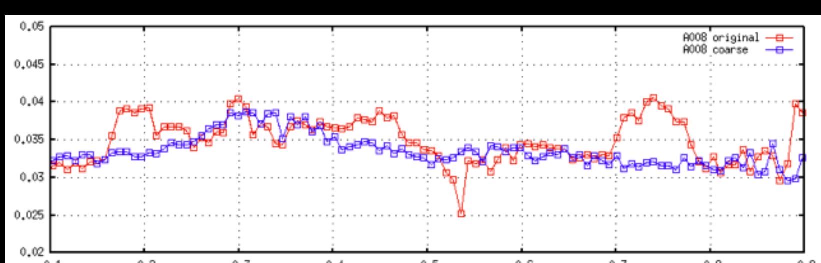


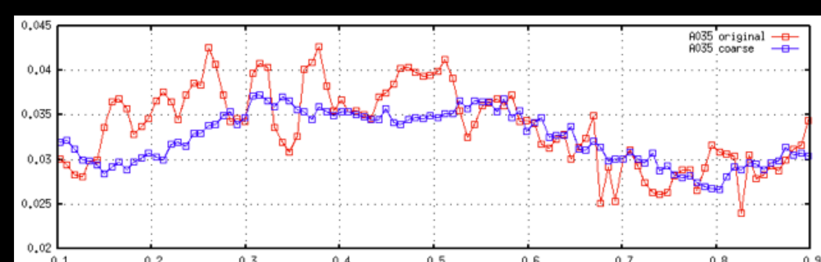




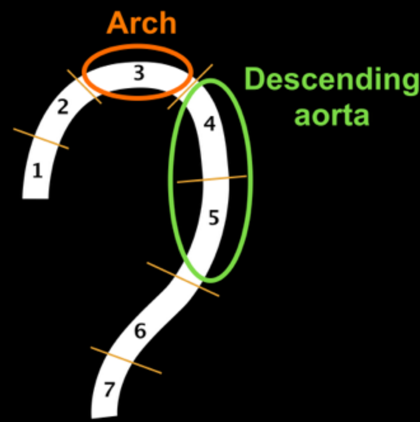


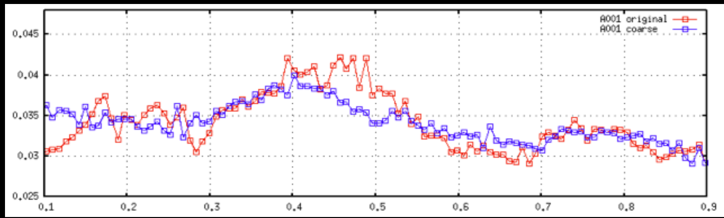


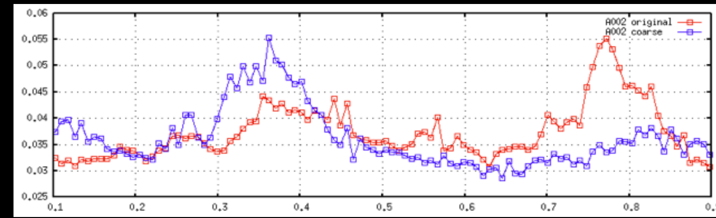


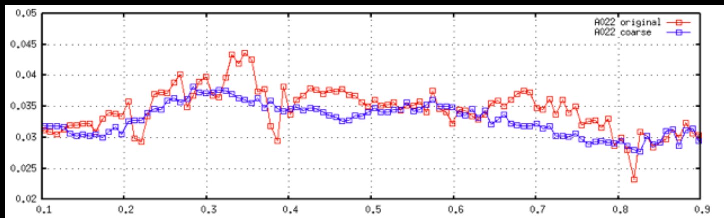


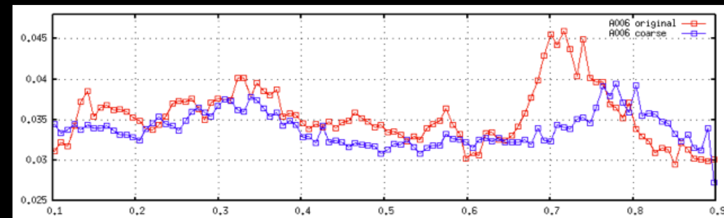
Patient cases can be classified in locations where the aneurysm developed

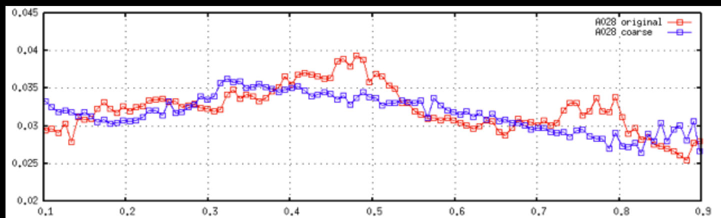


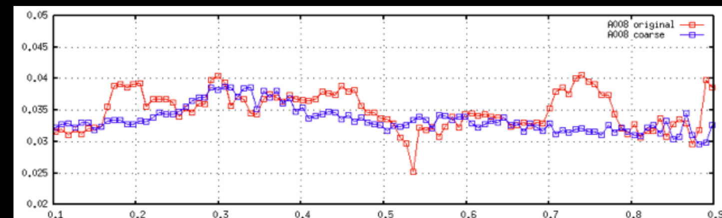


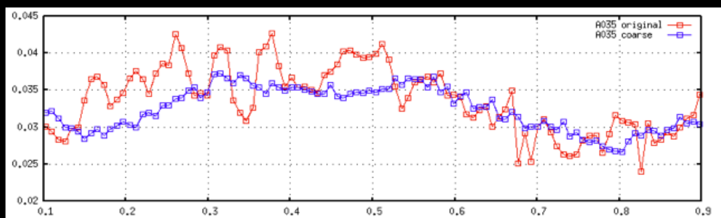


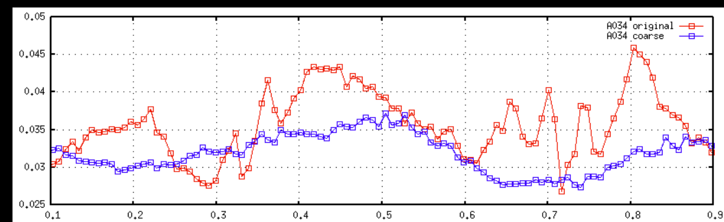










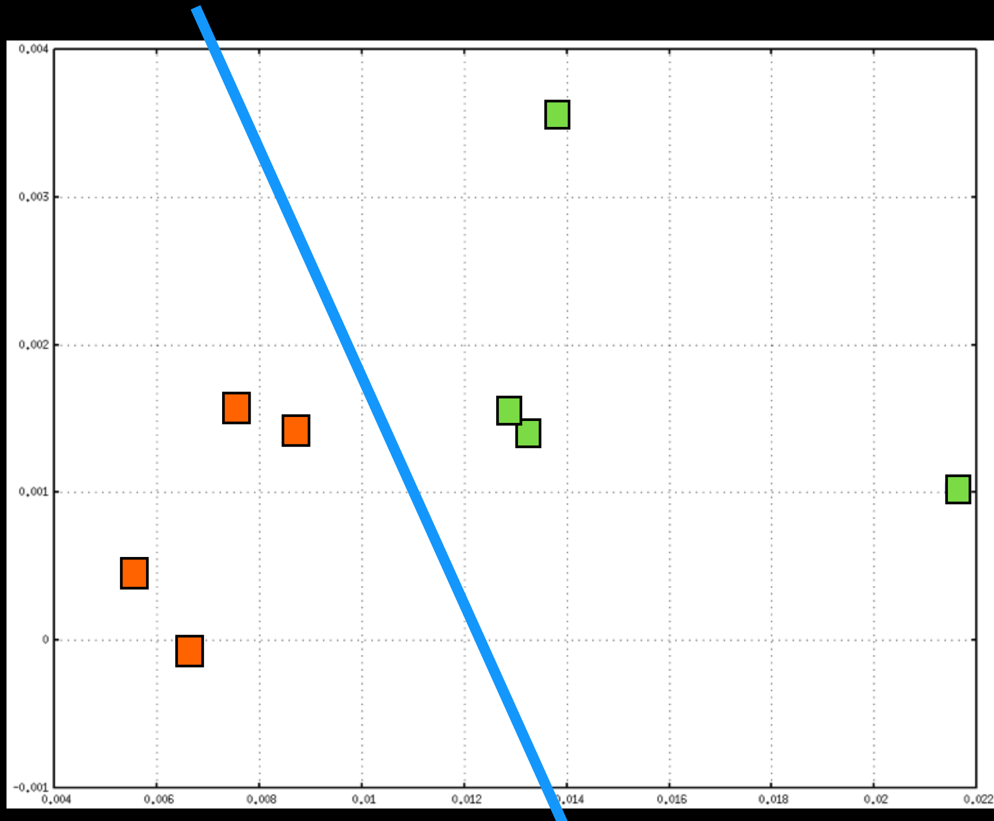


developed on aortic arch

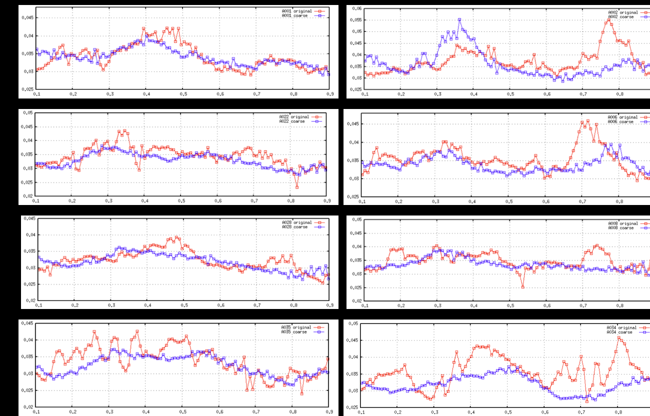
developed on descending aorta

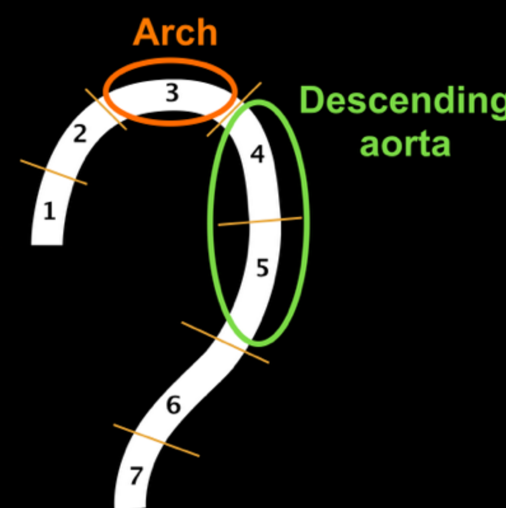
Differences in WSSs integrated along the centerlines between original and coarse-grained shapes

$$\int_0^1 \{\tilde{\sigma}_o(s) - \tilde{\sigma}_c(s)\}^2 ds$$



$$\max_{0<s<1} |\tilde{\sigma}_o(s) - \tilde{\sigma}_c(s)|$$



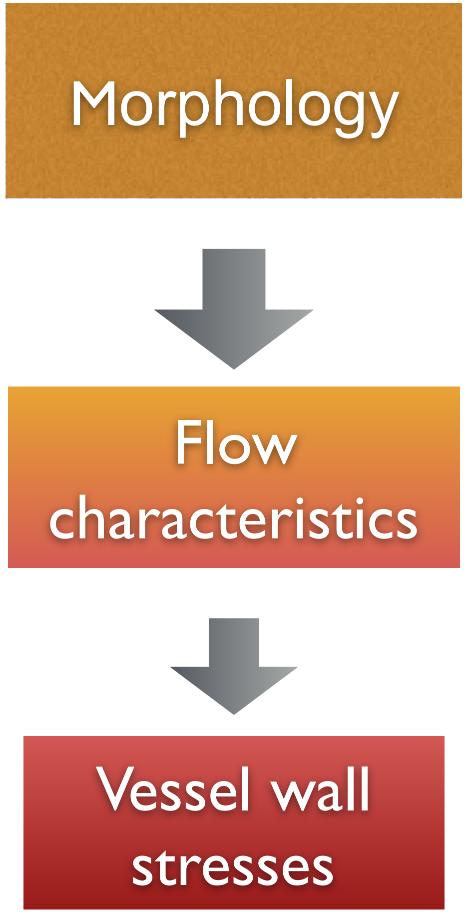


■ Patient cases with the aneurysms on the aortic arch

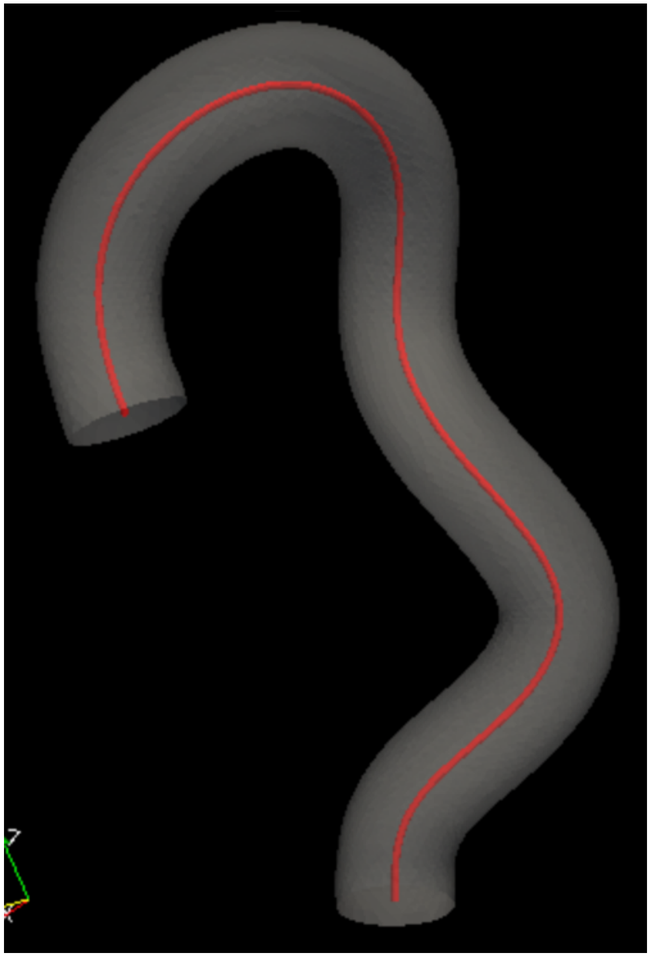
■ Patient cases with the aneurysms on the descending aorta

Should we compute blood flow for each patient to obtain force distribution on the vessel wall?

- To compute blood flow, patient-specific mesh generation, parameter selection and many other specific tasks are necessary.
- Computing blood flow for all patients is not so realistic.
- If a fundamental relation exists between morphologies and WSS/OSI distributions, then artificial intelligence might be able to learn how to estimate WSS and OSI from morphological data.



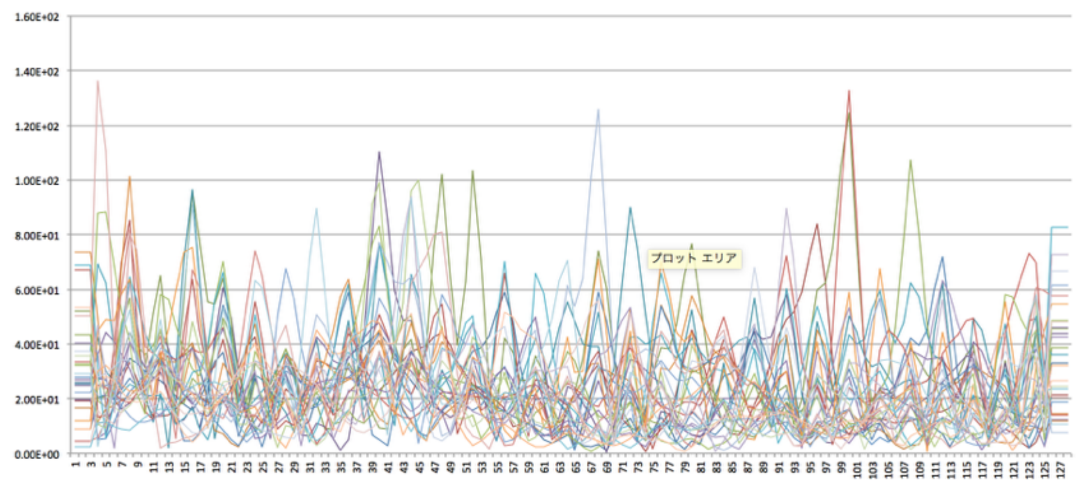
Geometrical characteristics of the centerlines



Frenet—Serret formula

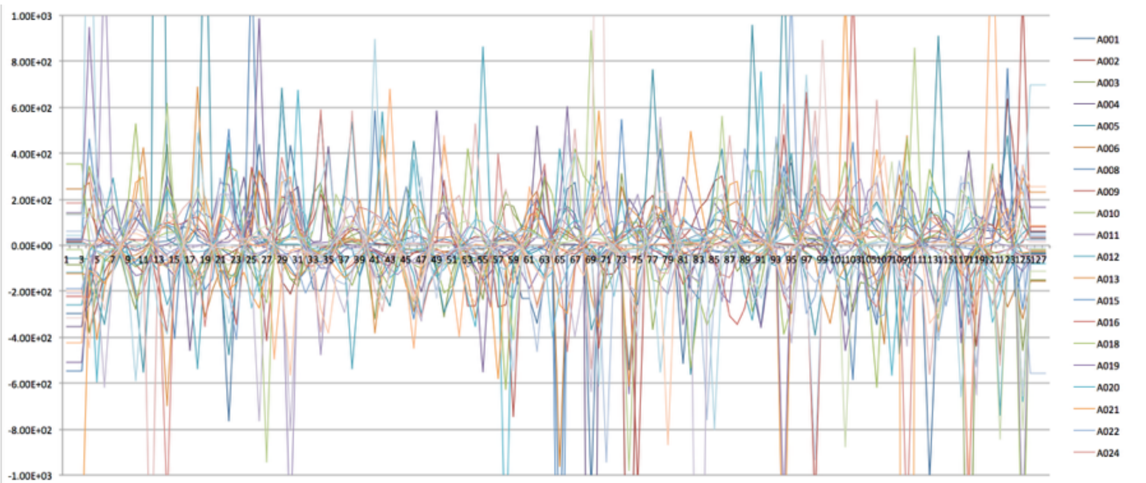
$$\frac{d}{ds}\begin{pmatrix}\boldsymbol{\tau}\\ \boldsymbol{n}\\ \boldsymbol{b}\end{pmatrix} = \begin{pmatrix}0 & Cv & 0\\ -Cv & 0 & To\\ 0 & -To & 0\end{pmatrix}\begin{pmatrix}\boldsymbol{\tau}\\ \boldsymbol{n}\\ \boldsymbol{b}\end{pmatrix}$$

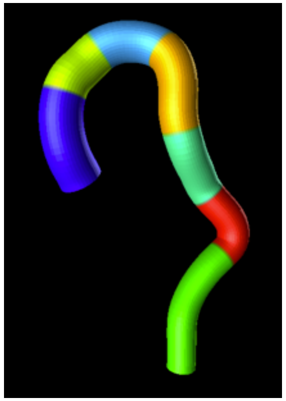
Cv: Curvature
To: Torsion



Data representation for machine learning

Thoracic aorta can anatomically be divided to seven segments.





Averaging over each segment

Machine learning for estimating WSS and OSI

Inputs

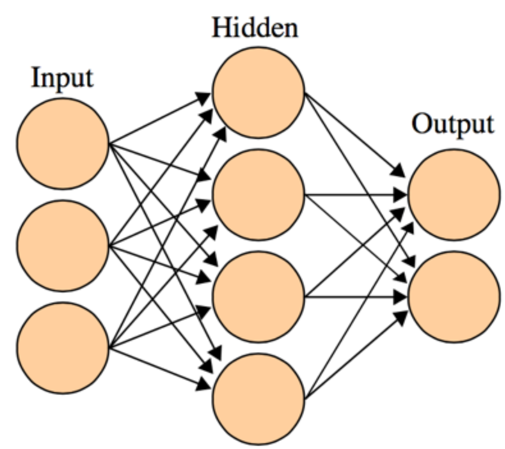
- Location of the segments
- Curvature of the centerline averaged over the segment
- Torsion of the centerline averaged over the segment

Outputs (objective variable)

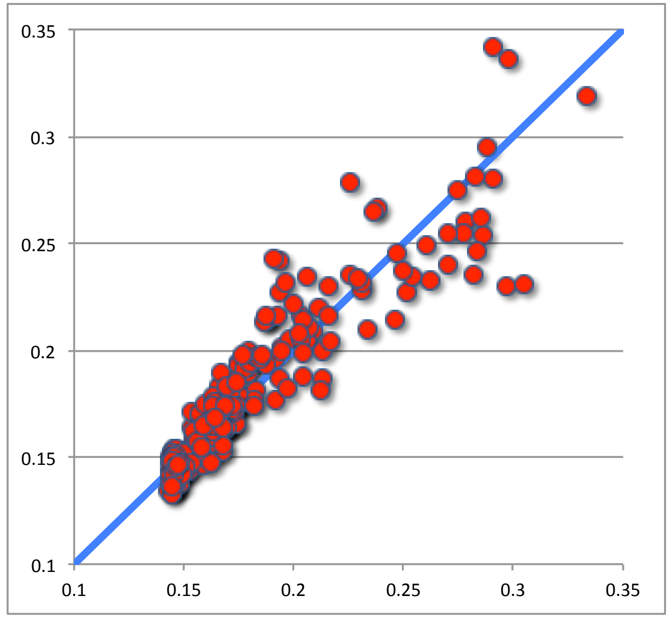
- WSS averaged over the segment
- OSI averaged over the segment

Machine learning

Number of patients = 32
Number of segments = 7
Total number of data = 224



Estimation (student) using curvature and torsion of each segment



FEM computational results (teacher)

Number of patients = 32
Number of segments = 7
Total number of data = 224

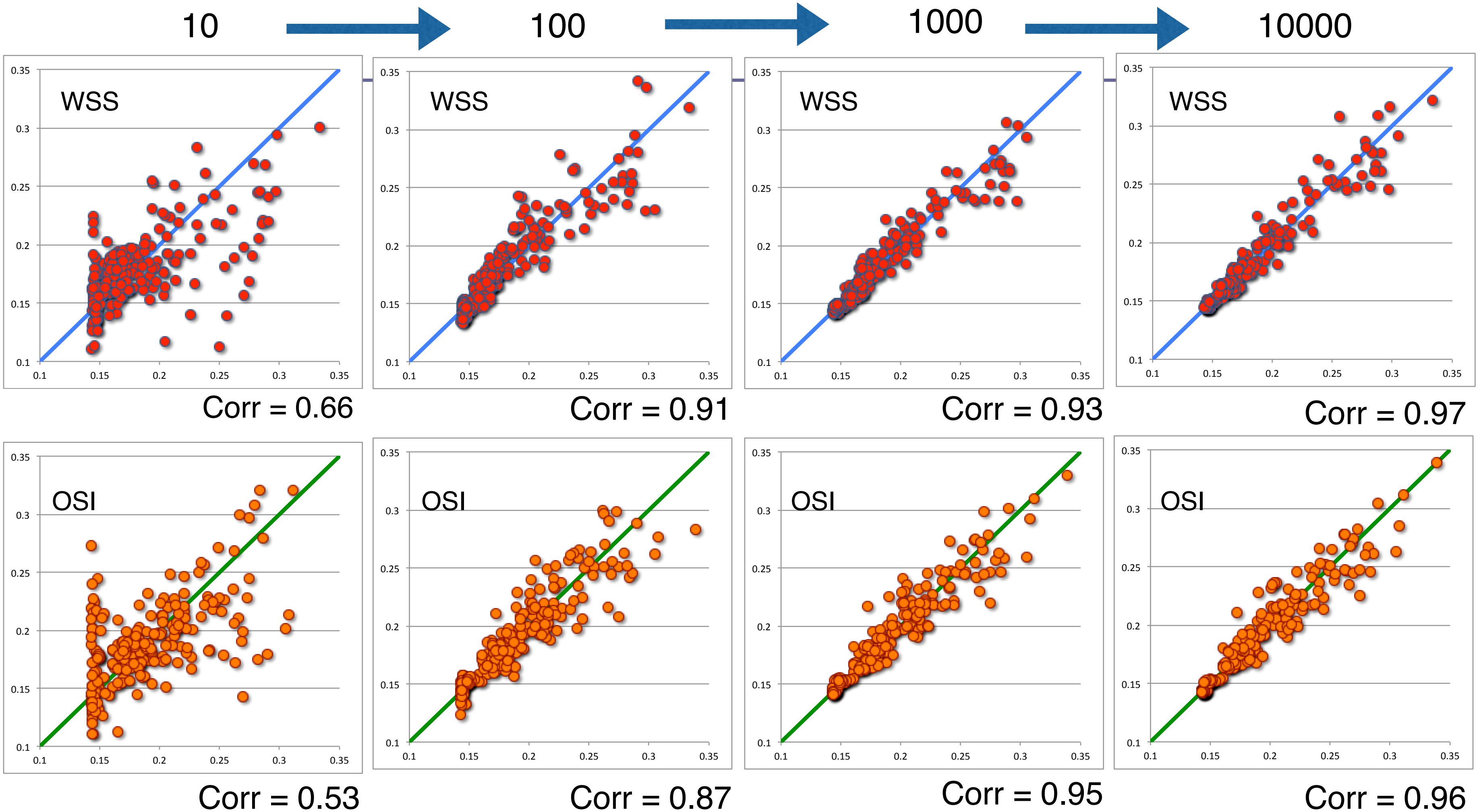
Neural network with sufficient number of hidden layers has higher prediction ability than traditional approaches, for example, linear regression analysis. However, “overfitting” problems frequently arise.

Leave-one-out cross validation procedure

1. Remove one case from the input set of N cases.
2. Learn using the N-1 remaining cases.
3. Try to estimate the objective variable of the removed case.
4. Repeat steps 1—3 for N Cases.
5. This procedure measures the ability of generalization

Leave-one-out cross validation results

Number of learning cycles



- WSS and OSI on each segment can be estimated without CFD.
- We don’t see “over-fitting” phenomena usually seen with machine learning.
- Averaging over anatomically defined segments seems to be a “good” descriptor for machine learning.

Conclusions

Morphology of individual patient's aorta

Image analysis

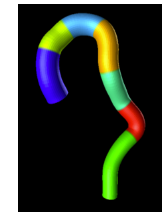
Simulation

Emulation

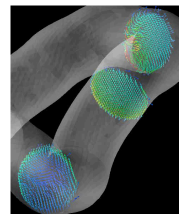
Parameterization

Simplification

Image analysis



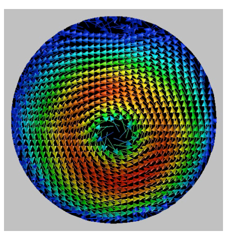
Mesh generation and CFD



Basic understanding on flow structure

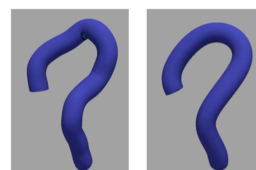
Blood flow distribution

Characteristics of morphology (curvature, torsion)

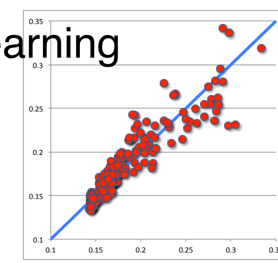


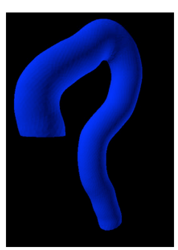
Visualization

Integration to centerlines

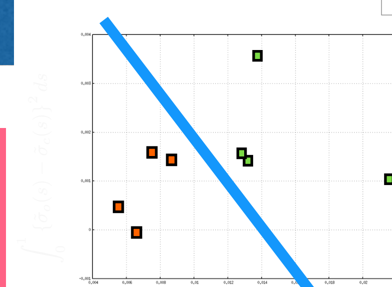


Machine learning





Characteristic quantities of the flow (WSS, OSI)



Location where aneurysm develops