ISSUES ON COMPUTATIONAL MODELING FOR COMPUTATION-AIDED DIAGNOSIS

臨床診断支援ツールのための計算力学モデリング

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Abstract. *Computational modeling of haemodynamics in cardiovascular system can be a useful means for predictive medicine, which may be implemented in a form of Computation-Aided Diagnosis (CAD) and/or Computation-Aided Surgery (CAS). A basis for such a new paradigm, in particular the CAD and CAS systems, for the coherent complexity in morphology and physiology of circulation system, requires an efficient and robust, PAtient-Specific Simulator (PASS) for haemodynamics. In this study we highlight those issues relating to the establishment of such a PASS system which is under development in RIKEN and present some preliminary results.*

1. Introduction

Blood flow under normal physiologic conditions is an important field of study, as is blood flow under disease conditions. The majority of deaths in developed country result from cardiovascular disease, most of which are associated with some from abnormal blood flow in arteries. Detection and quantification of the abnormal blood flow in arteries serve as the basis for surgical intervention.

In the Computational Biomechanics Project in RIKEN, we are aiming at providing a new paradigm of predictive medicine through development of computation-aided diagnosis and/or computation-aided surgery systems. We are working on the build-up of a patient-specific simulator for haemodynamics, which is the basis and hence the pass for the prediction of individual haemodynamic flows in any patient, the development of diagnostic tools to quantify diseases and the design of devices to mimic or alter blood flow.

The PASS system will be established under an integrated combination of the computer science, the mechanics and the medicine. It should provide an object-oriented software environment to create a specific computer model combining data input from medical-imaging sources as CT and MRI, geometry reconstruction containing automatic grid generation, solution strategies for multi-biophysics and visualization techniques. Algorithm development for solution of multi-biophysical problems in human circulatory system is very challenging because the sophisticated multi-branching network in our body extremely enhances the difficulties for computer modeling. We should solve problems as how to treat appropriate boundary conditions at inlet and outlet as well as the initial conditions; how to deal with the interactions between blood flow and compliant blood vessel; and how to validate our simulated results by means of *in vivo* and *in vitro* measurements or some self-consistent methodology. In addition, parallel architectures will be the systems for most of these modeling of arterial blood flow.

From the viewpoint of biomechanical engineering, one of the features of blood flow in arteries is the biological response to haemodynamics, which is essential to maintain normal functioning of the circulatory system and may constitute adaptation or pathological disease. We know little about the non-linear mechanics associated with this biological adaptation and it will be a challenging issue. Problem of wave propagation in a multi-branched network with compliant walls is also an important issue, which may provide adequate boundary conditions in modeling blood flow in the arterial tree structure. Mass transport, e.g., the blood cells transport which functions in nutrient and waste transport throughout the body as well as the particle transport between the vessel wall and blood is another hot

topic currently because it may provide important insight into understanding of the generation of arterial disease. Multi-scale mechanics combining the macro-haemodynamics and this micro-mechanics in an integrated way can be an important task in the future.

2. Computation-Aided Diagnosis and Computation-Aided Surgery

With the establishment of the patient-specific simulation of haemodynamics, we will be able to implement the paradigm of the predictive medicine, probably as a third tool of clinical medicine in addition with medical imaging and experience, to provide an efficient system for medical doctors to make diagnosis through computation-aided diagnosis, and for surgeon to plan their treatment or operation decision-making of cardiovascular disease by computation-aided surgery. Conventionally, this decision-making process is based largely on diagnostic imaging, experience and empirical data, which are insufficient to predict the outcome of a given treatment for an individual patient because of the multitude of therapeutic choices.

This CAD and/or CAS system may be further divided into some sub-systems of disease-specific database for diagnosis, patient-specific prediction for surgery, integrated incorporation into medical equipment and so forth, as illustrated in Fig. 1.

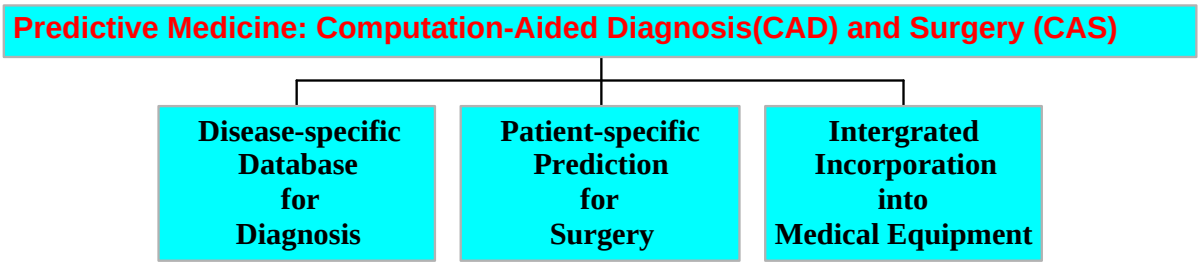

Fig. 1 Schematic diagram of the paradigm of predictive medicine

3. PAtient-Specific Simulator for haemodynamics

The patient-specific simulator for haemodynamics, i.e., the PASS is the basis and the pass for the predictive medicine. The PASS is an integrated system, as illustrated in Fig. 2, involving a medical image-based morphological realistic model, a measurement-based realistic physiological model, and a patient-specific realistic computational mechanical model.

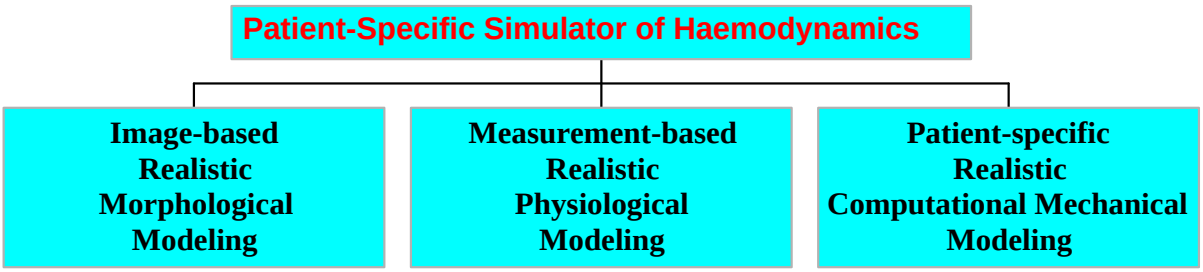

Fig. 2 Schematic diagram of the patient-specific simulator for haemodynamics

In the following, we highlight the issues, which are frequently encountered and have to be overcome when establishing these three models.

3.1 Image-based morphological modeling

The goal here is to reconstruct a complete three-dimensional geometric model for vessels and/or organs based on medical images of MR (Magnetic Resonance), US (Ultrasound), and CT X-ray. The geometric model should not be only for visualizing the object in terms of surface / volume rendering but also be specified for computational mechanical modeling of haemodynamics, i.e., involving the domain discretization (gridding). The procedure of the morphological modeling may consist of:

1) *read-in of raw medical image*, which provides 2D pixel data or 3D voxel data for 2D slice image or 3D image given by the medical equipment of MRA, US and CTA;
2) *segmentation* of the required object, which extracts configuration of the object in terms of wire frame and/or skeleton model by means of automatic, semi-automatic and manual, 2D and/or 3D image processing;
3) *smoothing and curve / surface fitting*, which is implemented for the reconstructed model as well as its geometric characteristics, e.g., curvature and torsion;
4) *modeling and domain discretization*, which involves surface or volume rendering of the reconstructed object, and domain decomposition and gridding for computation; and
5) *error analysis*, associated with the previous four processing of the morphological modeling.

3.2 Measurement-based physiological modeling

Physiological information on velocity and/or pressure in circulatory system is another issue in dominating blood flow, for the realistic patient-specific simulation of haemodynamics, as well as morphology or geometry of blood vessel. Realistic physiological model requires measurement-based physiological modeling and we may have following issues:

1) *measurement* of blood velocity and pressure by means of modern medical tools as MR, US and CT still has much to be solved associated with resolution both in space and in time;
2) *flow rate-based modeling*, which, using Doppler US techniques waveform of flow volumetric rate can be taken and transformed into boundary conditions in terms of velocity and/or pressure through simply quasi-static hydraulic modeling with consideration of mass conservation or even complicated structured tree modeling with influence of wave propagation and phase lag;
3) *pressure-based modeling*, which can define the boundary conditions at all inlets and outlets in a straightforward manner but concretely depends upon the development of medical techniques in *in-vivo* measurement of the pressure.

3.3 Patient-specific computational mechanical modeling

Characterized by the multi-branching arterial tree structure and the pulsation of heart pumping, blood flow is of four-dimensional nature, i.e., spatial 3D and 1D in time. In a sense, some local haemodynamics can be the result of interaction among different arteries upstream and even at different instants in the same artery. Aiming at development of the computation-aided diagnosis and/or computation-aided surgery systems, for establishing the PASS, we need to determine the exact blood flows in a given individual's vascular system, where models should faithfully represent individual anatomical features and simultaneously mimic the realistic physiologic flow conditions. We, therefore, have proposed a methodology of global computational modeling of blood flow in human circulatory system. We here highlight some key pointers as below.

First, the realistic morphological and physiological models as described above should be combined together in an integrated way. The *integrated model* may be superimposed synchronically into the raw medical images or a reconstructed volume rendered model so that we can check up its validation.

Then we forward to the *global computational modeling* of haemodynamics, which is designed for solving pulsatile blood flow in a multi-branched network. The basic solver is an in-house NS solver in which the incompressible, unsteady Navier-Stokes equations are discretized in a manner of finite volume method (FVM) and are solved in a time-marching manner using the pseudo-compressibility technique by adding a pseudo time derivative of pressure to the continuity equation. Since computational modeling of blood flow requires solving, in the general case, the three-dimensional transient-flow equations in deforming blood vessels the arbitrary-Lagrangian-Eulerian (ALE) description of media is employed, in which the fluid and wall domains are allowed to move to follow the distensible vessels and deforming fluid sub-domain. Boundary condition specification for multi-branched arterial networks is one of the most challenging issues in modeling blood flow. We are working on an integrated system, which involves multi-block domain with specific focus on the treatment at interface based on a multi-dimensional interpolation for velocity, pressure and flux

combine with the zonal and grid overset method. Aiming at treating the boundary conditions for velocity and pressure at all outlets and inlets in a systematic way, the physiological model as described in the preceding section is employed. The vessel walls are treated as being rigid as a first approximation though the vessel-diameter change during the cardiac cycle is often observed to be approximately 5-10% in most of the major arteries. As we extract the skeleton or centerline of each vessel during the morphological modeling we can also easily define the dynamics of each vessel in a manner of prescribed motion.

As an example of global computational modeling, we chose a prototypic cardiovascular arterial tree of the heart and proximal aorta arch involving branching arteries that supply arms and brain with blood. This computational modeling is important not only because it covers most of the important issues that will be encountered in modeling of blood flow but also the vessels (let ventricle and arteries) contained in the arterial tree exhibit flow characteristics seen in most of the arterial tree and are of great importance as they often become diseased. A realistic model combining left ventricle and aortic arch is established as shown in Fig. 3, in which the aortic arch is reconstructed based on MRI images and the left ventricle model is made using US images. Radii of the aorta is defined using an empirical formula $R=R_0e^{-As}$, where R_0=1.5*cm*, A=0.035 and s denotes the curve length of the centerline of the aorta. Note that branches are not considered here. Preliminary results using an integrated model are illustrated in Fig. 4, which supports our explanation on the features of the helical flow in aortic arch.

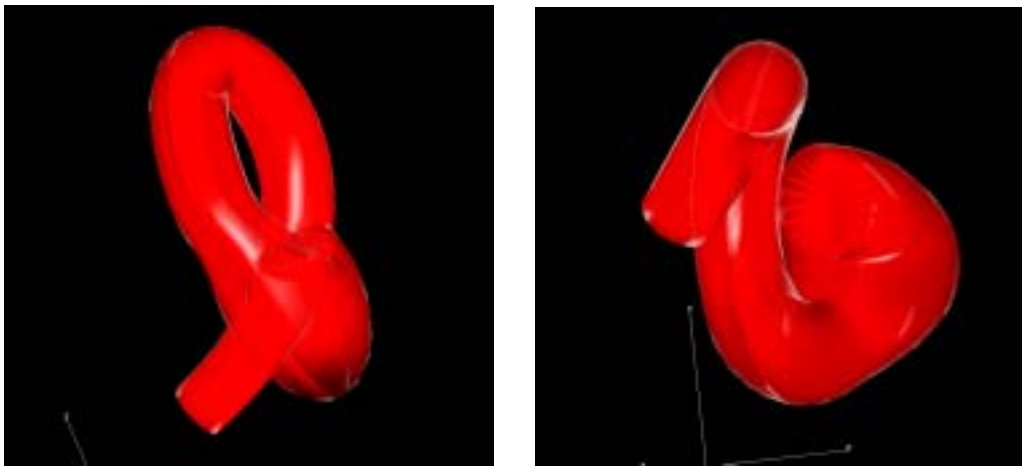

Fig. 3 A global geometric model of left ventricle and aorta

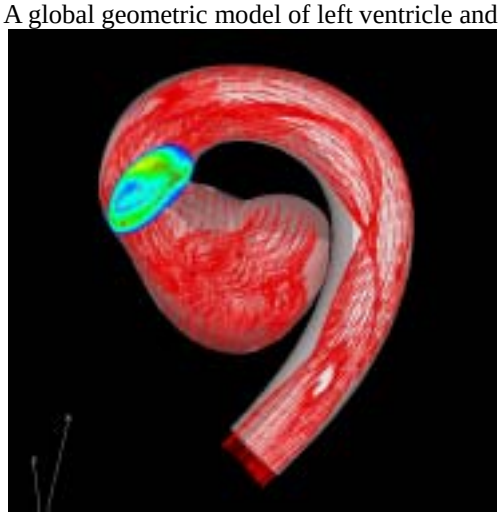

Fig. 4 Helical flow pattern in left ventricle and aortic arch

On the other hand, *verification* of the established PASS system and *validation* of the simulated

results, in particular for the complicated global computational modeling of haemodynamics, turn out to be an issue because patient-specific experimental modeling is actually not feasible. We have proposed the methodology for the so-called Verification and Validation (V&V) issue shown in Fig. 5.

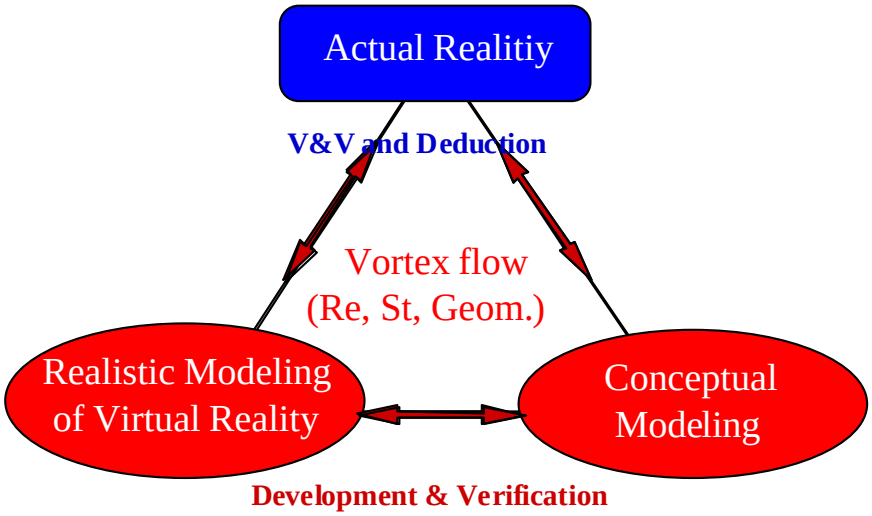

Fig. 5 Schematic diagram of the methodology for verification and validation of the PASS

The V&V issue can be firstly checked up through a conceptual model, which should work somehow as a baseline test. It may be highly idealized model such as Womersley solution in a rigid straight tube as shown in Fig. 6, and also may be some distinguished model, which can link some basic physics to physiological reality as influence of planarity or non-planarity of geometry for a bent.

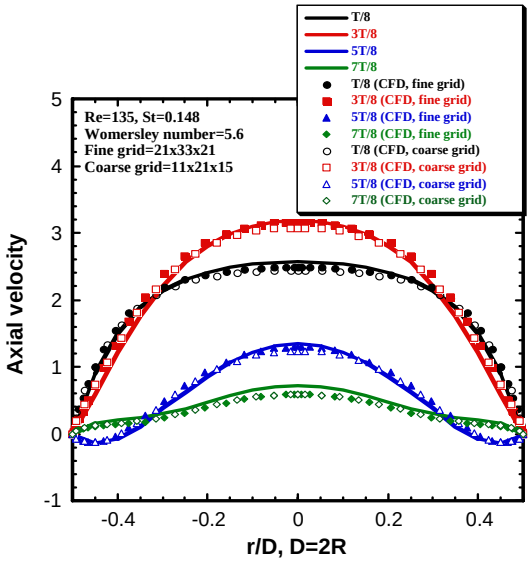

Fig. 6 Conceptual modeling of pulsatile flow in a rigid tube

Validation for the realistic simulation of the global computational modeling of haemodynamics can then be performed through comparison with *in-vivo* measurements of velocity by means of MRA and Doppler US. However, we should be very careful with the measurements because the medical equipment sometime may even output worse results compared with the simulation.

4. Conclusion

Issues on computational modeling of haemodynamics for computation-aided diagnosis and surgery are highlighted and discussed, with specific focus on the establishment of a patient-specific simulator, i.e., the PASS for haemodynanics. Aiming at clinical application of the PASS we are currently working on

three topics involving heart haemodynamics, large artery haemodynamics, and cerebral artery haemodynamics under normal and abnormal physiological conditions. Although we have much to be done in front of us, we hope that we would be able to report much more in the next Riken symposium.

5. Reference

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