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Modeling the Cardiovascular System—A Mathematical Adventure: Part II

*Using atherosclerosis as an example, the author pointed out in Part I of this article (*SIAM News*, June 2001, page 1) that effective and accurate numerical simulation tools could lead to real breakthroughs in the medical treatment of cardiovascular disease. Here, concluding the article, he points to the tremendous diversity of the human cardiovascular system, and the difficulty of coupling the different mathematical models appropriate for the different regions of the vascular system.*

Readers interested in learning more are reminded of the early fall EMS–SIAM meeting (Berlin, September 2–6), where the author will give an invited talk on modeling the cardiovascular system.

By Alfio Quarteroni

The components of the human vascular system vary tremendously, in both geometry and mechanical properties. Large vessels, like the aorta, typically have a radius of approximately 1.5 cm and a wall thickness on the order of 0.2 cm; at the other end of the spectrum are capillaries, with typical radius and wall thickness on the order of 1 μm.

Vessel wall morphologies and, correspondingly, mechanical behavior vary considerably among the vessel types. Arterial tissues are made up of elastin and collagen fibers, smooth muscle cells, and water, in amounts that vary along the arterial tree. Large arteries, such as the aorta, have thick walls with high collagen and elastin content. Elastic deformations of these vessels are rather important; elastic recoil serves to regularize blood flow during the cardiac cycle. The walls of small arteries have a large content of smooth muscle cells, which can be activated to regulate blood flow to individual organs and tissue beds. Moreover, the distinctive features of elastin and collagen that result from their substantially different stress–strain relations, together with the complex links among the fibers, make the mechanical behavior of these tissues quite complicated. Actually, arterial walls are inelastic and anisotropic or, more precisely, cylindrically orthotropic. A correct or suitable mathematical description of the behavior of these vessels is therefore a very ambitious goal.

Also varying with the type of vessel considered is the rheological behavior of blood. Blood is a suspension of different particles (red cells, white cells, platelets) in an aqueous solution (plasma). Red cells in particular, because of their tendency to aggregate into structures called roleaux, influence blood rheology. This effect is more pronounced at lower shear rates and causes an increase in the apparent flow viscosity, which explains, in part, the observation that blood is a shear thinning fluid (i.e., a fluid whose viscosity decreases as the shear rate increases), particularly in small arteries and arterioles. The governing equations are the Navier–Stokes equations

$$\begin{cases} \rho\left(\dfrac{\partial \mathbf{u}}{\partial t} + \mathbf{u}\cdot\nabla\mathbf{u}\right) - \operatorname{div}\mathbf{T}(\mathbf{u},p) = 0 \\ \operatorname{div}\mathbf{u} = 0, \end{cases}$$

to be satisfied in the fluid domain, where $\mathbf{u}$ and p represent the fluid velocity and pressure, ρ the blood density, and $\mathbf{T}$ the Cauchy stress tensor. The fluid velocity at the artery wall is determined as the (unknown) time derivative of the wall displacement.

Clearly, when the size of a vessel is comparable with that of red cells, the assumption that blood is a continuum with uniform characteristics is questionable, and it is better to resort to other models.

The tremendous diversity of geometries, physical characteristics, and fundamental behavior in the vascular system calls for the use of different mathematical models in different regions of the vascular system. In particular, the mathematical coupling of different models is important for the development of numerical schemes for simulating large parts of the cardiovascular system, if not the whole. Complex three-dimensional models of vascular flow can provide details of the flow field and quantitative information on related quantities, such as wall shear stresses. These models are computationally expensive, however, and are certainly not applicable to the circulatory system as a whole.

At the other extreme, lumped parameter models, based on an electrical network analogy, provide a computationally cheap way to obtain information about the overall behavior of the circulatory system. In these models, electric potential and current are the analogs of average pressure and mass flux, respectively. A particular vessel (or group of vessels) is described by means of its impedance, which is represented by an appropriate combination of resistors, capacitors, and, possibly, inductors. The first makes it possible to model viscous dissipation, the second accounts for vessel compliance (the ability to accumulate and release blood because of elastic deformations), and the third is used to model inertia terms. All vascular regions can then be characterized and linked in a network. The heart is represented by a generator, valves by diodes. In more genuinely mathematical terms, we are considering a system of nonlinear ordinary differential equations (more precisely of differential–algebraic equations), the nonlinearity being due mainly to the presence of the diodes whose action is described by suitable inequalities.

These lumped parameter models are able to provide only averaged data and require considerable attention to parameter settings.

Furthermore, their derivation is usually based on linearization of the flow and vessel structure dynamics. Such models are quite widely used by the medical and bioengineering communities, however, because of their low computational costs and their straightforward "physical" interpretations. Their ability to encompass the entire cardiovascular system can be exploited to supply the boundary conditions for three-dimensional, local models.

At an intermediate level of complexity, we have one-dimensional models. They are usually derived from the coupled fluid-structure problem by assuming a cylindrical-type geometry and by considering section-averaged pressure and mass flux. The result is a hyperbolic system of equations resembling the Euler equations for compressible fluids, with an additional term accounting for viscous dissipation, namely

$$\begin{cases} \dfrac{\partial A}{\partial t} + \dfrac{\partial Q}{\partial z} = 0 \\ \dfrac{\partial Q}{\partial t} + \dfrac{\partial}{\partial z}\left(\alpha \dfrac{Q^2}{A}\right) + \dfrac{A}{\rho}\dfrac{\partial p}{\partial z} + K_R \dfrac{Q}{A} = 0. \end{cases}$$

Here, t indicates the time variable and z the axial coordinate. The vessel section area A and the mass flow rate Q are the main unknowns; p is a section-averaged pressure (related to the section area A), and K_R accounts for the viscous effect. The parameter α is a function of the profile of the axial component of the velocity.

Compared with lumped parameter models, a one-dimensional model is able to give a more accurate description of wave propagation in large arteries, accounting also for nonlinear effects. The correct way to account for branching, curved geometries, and more complex vessel wall mechanics is still a matter of investigation; recent work on the subject is described in [1], [4], and [5]. A more immediate use for these models is in predicting alterations in wave patterns in large arteries as a result of pathological conditions (e.g., a stenosis) or the insertion of a prosthesis.

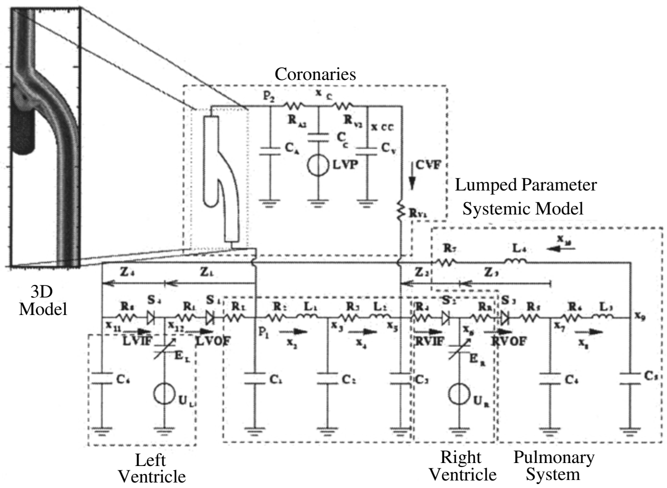

Figure 1. *Coupling of a lumped parameter model of the entire cardiovascular system, based on the electric circuit analogy, with a detailed model of a coronary bypass.*

An interesting issue—and a mathematical challenge—is the development of *multimodel simulations*, in which models of different levels of complexity are coupled in a mathematically sound way ([2], [3]). An example is shown in Figure 1; the portion corresponding to a coronary artery in a lumped parameter model of the whole cardiovascular system has been replaced by a three-dimensional local model of a bypass. The systemic model supplies the boundary conditions for the three-dimensional computations, while the computed flow and pressure fields in the bypass feed back into the global model.

More generally, lumped parameter, one- and three-dimensional models can coexist even with microscopic-scale models (based, for example, on a stochastic approach), as illustrated schematically in Figure 2. In spite of heuristic justification, these *hybrid multiscale models* need to be set on a solid mathematical basis, so that it is possible, with dimensional down-scaling, to reproduce the essential physical behavior without losing the relevant conservation properties at the interfaces.

The mathematical adventure of developing models for the numerical simulation of the cardiovascular system of a real patient is in the very early stages. Its evolution will require the tackling of several central issues in applied mathematics and numerical modeling.

Some are unique to this specific (albeit important) scientific application, such as the development of more accurate rheological models for biological tissues (heart muscle, arterial wall, capillary vessels, and blood), or the analysis of the mechanisms by which prostheses and artificial devices are assimilated and by which biological tissues degenerate.

Many other issues, however, are relevant to other families of applications as well. Chief among them are the development of fast and accurate algorithms for surface and volume reconstruction for medical images obtained by CT scanning, magnetic resonance,

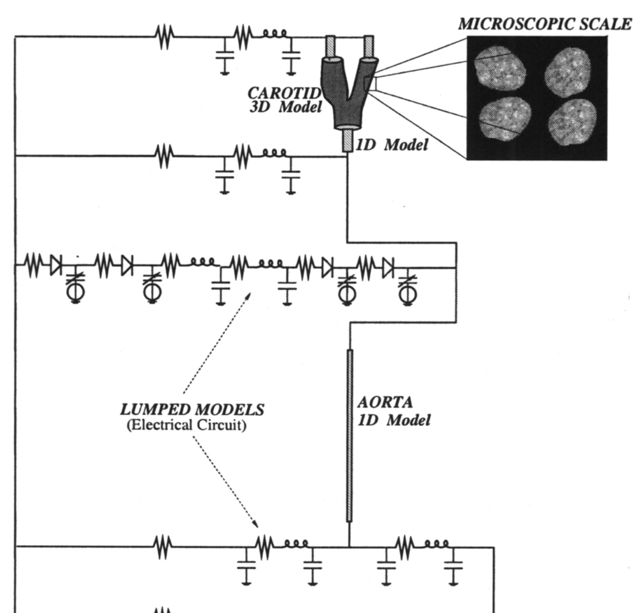

Figure 2. *Multiscale modeling of the cardiovascular system.*

digital angiography, and other emerging techniques. Other challenges include the development of parallel algorithms, the formulation of domain decomposition methods for partial differential equations in moving domains, and the formulation of splitting algorithms for multiscale models with the ability to provide accurate solutions for fast transients.

In this wide-ranging and challenging adventure, it is expected that mutually beneficial interactions with several other branches of applied mathematics will take place.

Acknowledgments

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