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Modeling the Cardiovascular System—A Mathematical Adventure: Part I

Mathematical and numerical investigations of the cardiovascular system, although a relatively new research area, will give rise to some of the major mathematical challenges of the coming decades, the author writes. In this first of two parts, he sketches some of the features that make the human blood circulatory system so challenging to model. The second part of the article (to appear in the next issue of SIAM News*) will describe research now under way, including the development of hybrid multiscale models. Quarteroni will also be presenting research in this area as one of ten invited speakers at the first EMS–SIAM meeting, "Applied Mathematics in our Changing World," which will be held in Berlin, September 2–6.*

By Alfio Quarteroni

The physiology of the cardiovascular system has been elucidated only gradually, over many centuries. Among the major actors in the lengthy process have been some of the central characters in human history.

Aristotle (384–322 B.C.), for example, identified the role of blood vessels in transferring "animal heat" from the heart to the periphery of the body (although he ignored blood circulation). In the third century B.C., Praxagoras realized that arteries and veins have different roles (believing that arteries transported air while veins transported blood). Galen (c. 130–200 A.D.) was the first to observe the presence of blood in arteries.

Much later, in the 17th century, Sir William Harvey inaugurated modern cardiovascular research with his *De Motu Cardis and Sanguinis Animalibus*, in which he wrote, "When I turned to vivisection I found the task so hard I was about to think that only God could understand the heart motion." His plaintive comment notwithstanding, Harvey observed that the morphology of valves in veins is such that they are effective only if blood is flowing toward the heart. His conclusion: "I began privately to consider if it (the blood) had a movement, as it is, it would be in a circle."

It was in studying arterial blood flow that 19th-century physician and physicist J.P. Poiseuille developed the first simplified mathematical model of fluid flow in a cylindrical pipe.

In the 18th century, the Reverend S. Hales introduced quantitative studies of blood pressure (*Hemostatics*, 1773). Later, Euler and D. Bernoulli both made great contributions to fluid dynamics research. In particular, Bernoulli, investigating the laws governing blood pressure as a professor of anatomy at the University of Basel in Switzerland, formulated his famous law relating pressure, density, and velocity: $p + 1/2\rho\,|u|^2 =$ const (vis viva equation, 1730).

In the 19th century, J.P. Poiseuille, a medical doctor and a physicist, was studying the flow of blood in arteries when he derived the first simplified mathematical model of flow in a cylindrical pipe, a model that still bears his name today.

T. Young later made fundamental contributions to research on elastic properties of arterial tissues and on the propagation of pressure: "The inquiry in what manner and at what degree the circulation of the blood depends on the muscular and the elastic powers of the heart and of the arteries, supposing the nature of these powers to be known, must become simply a question belonging to the most renowned departments of the theory of hydraulics" (from a lesson given by Young at the Royal Society of London in 1809).

At the beginning of the 20th century, 0. Frank introduced the idea that the circulatory system is analogous to an electric network. In 1955, J. Womersley, studying vascular flows, found the analytical counterpart of Poiseuille flow in pressure gradients that vary periodically in time, a situation that more closely describes actual pressure variations during the cardiac cycle.

In the second half of the 20th century, developments in mathematical modeling were limited to basic paradigms, such as flow in morphologically simple regions (e.g., Poiseuille or Womersley solutions), or to models based on electric network analogies. Exact solutions are very difficult to obtain in more general situations, because of the strong nonlinear interactions among different parts of the system and the geometric complexities of individual vascular morphologies.

Flow Patterns and Arterial Disease

As in many applied sciences, mathematical and numerical models are increasingly important in biology and medicine today. Most notably, mathematical and numerical investigations of the blood circulatory system, although energetically pursued for only a few years, are poised to become one of the major mathematical challenges of the coming decades.

During the 1970s, in vitro or animal experiments were the main mode of cardiovascular investigations (see, for example, [9]). In recent years, advances in computational fluid dynamics, together with dramatic improvements in computer performance, have resulted in significant breakthroughs that promise to revolutionize vascular research (see, for example, [2], [3], [5], [8]).

Physical quantities like shear stress, which are troublesome to measure in vivo, can be computed for real geometries with the support of modern noninvasive data-acquisition technologies (e.g., nuclear magnetic resonance, digital subtraction angiography, spiral computerized tomography) and three-dimensional geometric reconstruction algorithms (see, for example, [1], [6], [9]).

Clinical investigations have shown that plaque deposits are commonly found in regions of low shear stress. Plaque deposition, also known as atherosclerosis, is the leading cause of death in the western world. Indeed, plaque deposits in the carotid artery can lead to heart attacks or to stroke. Plaque formation in the abdominal aorta or the femoral artery can lead to insufficient blood flow to the lower limbs.

In the cardiovascular system, altered flow conditions—such as separation, flow reversal, and low or oscillatory shear stress areas—are recognized as important factors in the development of arterial disease. A detailed understanding of the local hemodynamics, of the effects of vascular wall modification on flow patterns, and of long-term adaptation of the system to surgical procedures can have useful clinical applications. Some of these phenomena are not well understood, making it difficult to foresee the short- and long-term evolution of the disease and to plan therapeutic approaches. In this context, the availability of effective and accurate numerical simulation tools could be a real breakthrough.

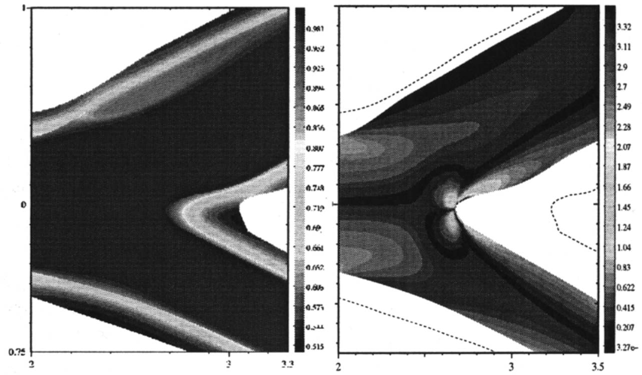

Figure 1. *Simulation of the absorption of oxygen by the arterial wall. Left, snapshot of the computed oxygen concentration field in a human carotid bifurcation, in the fluid and in the wall. Right, measure of the shear stresses in the fluid, obtained at the same time. Low shear stress values at the wall negatively affect permeability and thus wall absorption of oxygen.*

So far, such analyses have been possible only in very limited morphological regions, and under mathematical assumptions that sometimes depart from reality. The road toward realistic simulations, however, has now at least been outlined.

The Path to Virtual Surgery: Mathematical Challenges

As it flows, blood interacts both mechanically and chemically with the vessel walls, giving rise to a complex fluid–structure interaction problem that is difficult to simulate numerically. Indeed, the mechanical coupling requires algorithms that correctly describe both the macroscopic-level transfer of energy between the fluid (typically modeled by the Navier–Stokes equations) and the structure, and the microscopic-level influence of wall shear stress on cellular orientation, with possible cell damage. At the same time, the flow equations have to be coupled with appropriate models describing the absorption of involved chemicals (e.g., oxygen, lipids, drugs) by the wall and their transport, diffusion, and kinetics (see Figure 1). Numerical simulations of this type can help to clarify biochemical modifications produced by alterations in the flow field—caused, for instance, by a stenosis (i.e., a localized narrowing of a vessel lumen, normally due to fat accumulation).

Another important challenge is the modeling of the heart; here, investigations are characterized by strong interactions between fluid dynamics, structural mechanics with large deformations and displacements, and the electrical field carrying the signals that activate the heart muscle cells. Global mechanical models of the heart have been proposed and successfully tested, in particular by C. Peskin [3]. The ability to simulate the heart should have a tremendous impact on medical research and surgical planning. However, we are still a long way from having techniques that can be used for practical medical purposes.

The simulation of large and medium-sized arteries is more advanced; applications of computer models to medical research and, in a slightly longer term, to everyday medical practice can already be envisaged. Simulating the flow in a coronary bypass, for instance, can improve understanding of the effects of arterial geometry on the flow and, in turn, postsurgical evolution. Study of

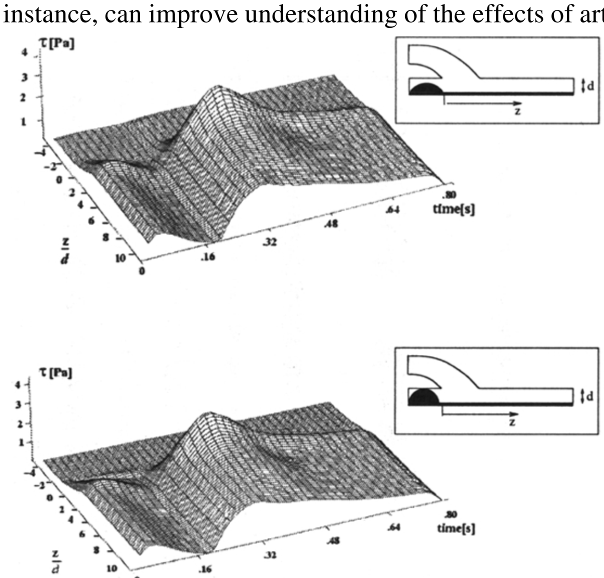

Figure 2. *Shear stress distribution calculated on a by-pass geometry for a 70% stenosis (top) and a 100% stenosis (bottom).*

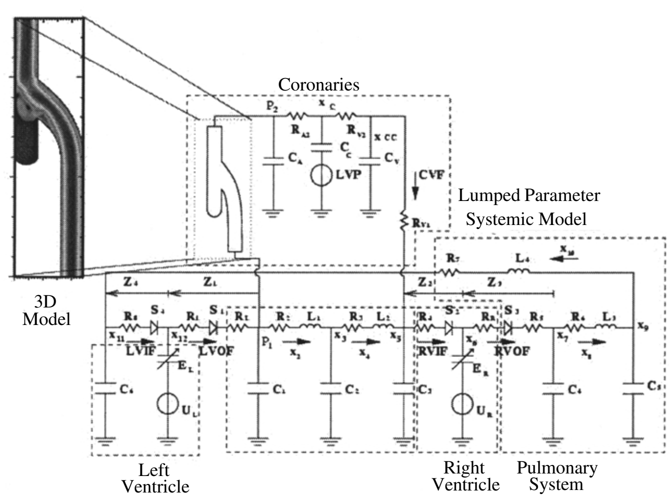

Figure 3. *Coupling of a lumped parameter model of the entire cardiovascular system, based on the electric circuit analogy, with a detailed model of a coronary bypass.*

the effects of vascular prostheses and artificial valve implants on local and global hemodynamics can be advanced by sufficiently accurate simulations of the blood flow field. Figure 2 shows the shear stress distributions calculated for a bypass geometry for two stenosis conditions. (The multiscale approach illustrated in Figure 3 was used in the computation.) Because anomalies in the shear stress distribution are believed to be linked to plaque deposition, simulations of this type should prove useful to medical researchers.

A similar perspective could provide specific design indications for surgical procedures. Figure 4, for instance, shows two ways in which a shunt (i.e., a connection between two vessels) can be realized in the pulmonary circulation of newborn infants with cardiac malformations. In this case, numerical simulations can help the surgeon understand the effects of different solutions on blood circulation and provide guidance in the selection of the most appropriate procedure for a specific patient. Different shunt procedures and different geometries, for instance, can be simulated before the surgical intervention, and quantitative data, such as pressure and flows at specific locations, can indicate the optimal configuration. In the case illustrated in Figure 4, with input data for a newborn infant, a classical Norwood procedure with a shunt diameter of 3 mm would ensure a flow rate of 0.67 and 0.50 l/min at the right pulmonary and main coronary arteries, respectively. The modified Blalock–Taussig procedure, with the same shunt diameter, would result in corresponding rates of 0.45 and 0.54 l/min.

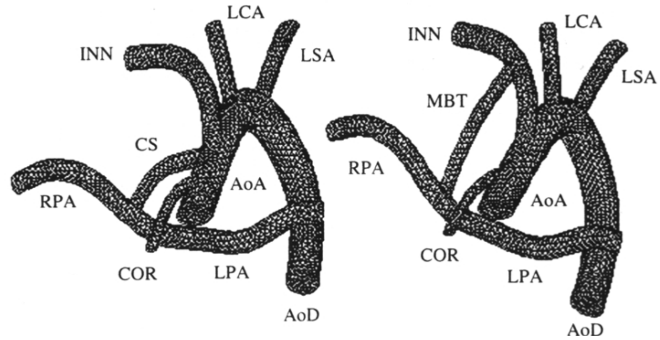

Figure 4. *Reconstructed geometries of two possible shunt surgery configurations: classical Norwood central shunt (left) and modified Blalock–Taussig procedure (right) (from [4]). AoA indicates ascending aorta; AoD, descending aorta; LSA, left subclavian artery; LCA, left carotid artery; INN, innominate artery; COR, main coronary artery; RPA, right pulmonary artery; and LPA, left pulmonary artery.*

In such a "virtual surgery" environment, the outcome of alternative treatments for an individual patient can be foreseen by simulations. This numerical approach is one aspect of a new paradigm in clinical practice known as "predictive medicine" (see [7]).

Acknowledgments

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