Mathematical Modelling of the Cardiovascular System

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Abstract

In this paper we will address the problem of developing mathematical models for the numerical simulation of the human circulatory system. In particular, we will focus our attention on the problem of haemodynamics in large human arteries.

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1. Introduction

The simulation of not only the physiological functioning of the blood circulatory system, but also of specific pathological circumstances is of utmost importance since cardiovascular diseases represent the leading cause of death in developed countries, with a tremendous medical, social and economic impact.

In the cardiovascular system, altered flow conditions, such as flow separation, flow reversal, low and oscillatory shear stress areas, are recognised as important factors in the development of arterial diseases. A detailed understanding of the local haemodynamics, the effect of vascular wall modification on flow patterns and its long-term adaptation to surgical procedures can have useful clinical applications. Some of these phenomena are not well understood, making it difficult to foresee short and long term evolution of the disease and the planning of the therapeutic approach. In this context, the mathematical models and numerical simulations can play a crucial role.

Blood flow interacts both mechanically and chemically with the vessel walls. The mechanical coupling requires algorithms that correctly describe the energy transfer between the fluid (typically modelled by the Navier-Stokes equations) and the structure of the vessel wall. On the other hand, the flow equations can be coupled with appropriate models that describe the wall absorption of bio-chemicals (e.g. oxygen, lipids, drugs, etc.) and of their transport, diffusion and kinetics. Numerical simulations of this type may help to understand

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the modifications in bio-chemical exchanges due to an alteration of the flow field caused, for instance, by a stenosis (i.e. a localised narrowing of a vessel lumen, normally due to fat accumulation).

The simulation of large and medium-size arteries is now sufficiently advanced so to envisage the applications of computer models to medical research and, in a medium range, to everyday medical practise. For instance, simulating the flow in a coronary by-pass may help understanding the extent at which its geometry influences the flow and in turn the post-surgery evolution. Also the study of the effects of a vascular prosthesis as well as the study of artificial valve implants are areas which could benefit from a sufficiently accurate simulation of blood flow field.

In this paper we review the principal mathematical steps behind the derivation of the coupled fluid-structure equations which model the blood flow motion in large and medium-sized arteries. Then we mention the way geometrical multiscale models, that combine mathematical models set up in different spatial dimensions, can be conveniently used to simulate the whole circulatory system.

2. The coupled fluid-structure problem

In this section we will treat the situation arising when the flow in a vessel interacts mechanically with the wall structure. This aspect is particularly relevant for blood flow in large arteries, where the vessel wall radius may vary up to 10% because of the forces exerted by the flowing blood stream.

We will first illustrate a framework for the Navier-Stokes equations in a moving domain which is particularly convenient for the analysis and for the set up of numerical solution methods.

2.1. The Arbitrary Lagrangian Eulerian (ALE) formulation of the Navier-Stokes equations

Navier-Stokes equations are usually derived according to the Eulerian approach where the independent spatial variables are the coordinates of a fixed Eulerian system. When considering the flow inside a portion of a compliant artery, we have to compute the flow solution in a computational domain $\Omega_t$ varying with time.

Figure 1: A simple model of a section of an artery. The vessel wall $\Gamma^w_t$ is moving. The location along the $z$ axis of $\Gamma^i_t$ and $\Gamma^o_t$ are fixed.

The boundary of $\Omega_t$ may in general be subdivided into two parts. The first part coincides with the physical fluid boundary, i.e. the vessel wall $\Gamma^w_t$ (see Fig. 1), which is moving
under the effect of the flow field. The other part of \( \partial \Omega_t \) corresponds to artificial boundaries which delimit the region of interest from the remaining part of the cardiovascular system.

The “artificial” boundaries are the inlet and outlet (or, using the medical terminology, the proximal and distal) sections, here indicated by \( \Gamma_{in}^w \) and \( \Gamma_{out}^w \), respectively. The location of these boundaries is fixed a priori. More precisely, \( \Gamma_{in}^w \) and \( \Gamma_{out}^w \) may change with time because of the displacement of \( \Gamma_t^w \), however they remain planar and their position along the vessel axis is kept fixed. In this case the Eulerian approach becomes impractical.

A possible alternative would be to use the \textit{Lagrangian approach}, where we identify the computational domain on a reference configuration \( \Omega_0 \), e.g. that at the initial time \( t = 0 \), and the corresponding domain in the current configuration will be provided by the Lagrangian mapping

\[
\Omega_t = \Omega_{\mathcal{L}_t} = \mathcal{L}_t(\Omega_0), \quad t > 0,
\]

which describes the motion of a material particle and whose time derivative is the fluid velocity. Since the fluid velocity at the wall is equal to the wall velocity, the Lagrangian mapping effectively maps \( \Gamma_0^w \) to the correct wall position \( \Gamma_t^w \) at each time \( t \). However, the artificial boundaries in the reference configuration, say \( \Gamma_0^{in} \) and \( \Gamma_0^{out} \), will now be transported along the fluid trajectories. This is unacceptable, particularly for a relatively large time interval as \( \Omega_t \) rapidly becomes highly distorted.

A more convenient situation is the one when, even if the wall is moving, one keeps the inlet and outlet boundaries at the same spatial location along the vessel axis. With that purpose, we introduce the \textit{Arbitrary Lagrangian Eulerian} (ALE) mapping \( \mathcal{A}_t : \Omega_0 \rightarrow \Omega_{\mathcal{A}_t} \), \( \mathbf{Y} \rightarrow \mathbf{x}(t, \mathbf{Y}) = \mathcal{A}_t(\mathbf{Y}) \), which provides the spatial coordinates \((t, \mathbf{x})\) in terms of the so-called \textit{ALE coordinates} \((t, \mathbf{Y})\), with the basic requirement that \( \mathcal{A}_t \) retrieves, at each time \( t > 0 \), the desired computational domain, \( \Omega_t = \Omega_{\mathcal{A}_t} = \mathcal{A}_t(\Omega_0), \quad t \geq 0 \).

The ALE mapping should be continuous and bijective in \( \Omega_0 \). Once given, we may define the \textit{domain} velocity field as

\[
\mathbf{w} = \frac{\partial \mathcal{A}_t}{\partial t} \circ \mathcal{A}_t^{-1},
\]

where the composition operator applies only to the spatial coordinates. The ALE time derivative of a function \( f : \mathcal{I} \times \Omega_t \rightarrow \mathbb{R} \), which we denote by \( \frac{D^A}{Dt} f \), is defined as

\[
\frac{D^A}{Dt} f : \mathcal{I} \times \Omega_t \rightarrow \mathbb{R}, \quad \frac{D^A}{Dt} f = \frac{\partial f}{\partial t} \circ \mathcal{A}_t^{-1}.
\]

This definition is readily extended to vector valued functions. The ALE derivative is related to the Eulerian (partial) time derivative by the relation

\[
\frac{D^A}{Dt} f = \frac{\partial f}{\partial t} + \mathbf{w} \cdot \nabla f,
\]

where the gradient is made with respect to the \( \mathbf{x} \)-coordinates.

The Navier-Stokes equations may be formulated in order to put into evidence the ALE time derivative, obtaining

\[
\frac{D^A}{Dt} \mathbf{u} + [(\mathbf{u} - \mathbf{w}) \cdot \nabla] \mathbf{u} + \nabla p - \div \mathbf{T} = \mathbf{f}, \quad \text{in } \Omega_t, \quad t > 0,
\]

\[
\div \mathbf{u} = 0,
\]

\[
in \Omega_t, \quad t > 0,
\]

\[
(2.5)
\]
where $T$ is the Cauchy stress tensor, which for Newtonian fluid is given by $T = \nu(\nabla u + \nabla u^T)$, being $\nu$ the blood kinematic viscosity.

When considering small vessels, accounting for non-Newtonian behaviour of blood becomes crucial. In that case the functional dependence of $T$ on $u$ becomes more complex, see for instance [18].

2.2. The structure model

The vascular wall has a very complex nature and devising an accurate model for its mechanical behaviour is rather difficult. Its structure is indeed formed by many layers with different mechanical characteristics [8, 11], which are usually in a pre-stressed state. Moreover, experimental results obtained by specimens are only partially significant. Indeed, the vascular wall is a living tissue with the presence of muscular cells which contribute to its mechanical behaviour. It may then be expected that the dead tissue used in the laboratory will have different mechanical characteristics than the living one. Moreover, the arterial mechanics depend also on the type of the surrounding tissues, an aspect almost impossible to reproduce in a laboratory. As we have already pointed out, the displacements cannot be considered small (at least in large arteries where the radius may vary up to a few percent during the systolic phase). Consequently, an appropriate model for the structure displacement $\eta$ reads

$$\rho_w \frac{\partial^2 \eta}{\partial t^2} - \text{div} \sigma(\eta, \frac{\partial \eta}{\partial t}) = f, \quad \text{in } \Omega_t, \; t > 0,$$

where $\Omega_t$ indicates the current configuration and $\sigma$ is the Cauchy stress tensor. The latter may depend on the structure velocity because of viscoelasticity. A full Lagrange formulation for the structure on a fixed reference configuration $\Omega_0$ may be obtained by the usual Lagrange and Piola transformation (see, e.g., [2]). A general framework to derive constitutive equations for arterial walls is reported in [11].

It is the role of mathematical modelling to find reasonable simplifying assumptions by which major physical characteristics remain present, yet the problem becomes computationally attractive. In particular, a simpler model may be obtained by considering only displacements in the radial direction and a cylindrical geometry for the vessel. Furthermore if we neglect the geometrical non-linearities (which correspond to assume small displacements), as well as the variations along the radial directions (small thickness assumption) we obtain the following “generalised string model” [16, 14] for the evolution of the radial displacement $\eta = R - R_0$,

$$\frac{\partial^2 \eta}{\partial t^2} - a \frac{\partial^2 \eta}{\partial z^2} + b \eta - c \frac{\partial^3 \eta}{\partial t^2 \partial z} = H, \quad \text{in } \Gamma_0^w, \; t > 0, \quad (2.6)$$

where $a > 0$ and $b > 0$ are parameters linked to the vessel geometry and mechanical characteristics, $c > 0$ is a viscoelastic parameter and $H$ is a forcing term which depends on the action of the fluid, as we will see in (2.7). More details as well as the derivation of this model are found in the cited references.

Here $\Gamma_0^w$ is the reference configuration for the structure

$$\Gamma_0^w = \{(r, \theta, z) : r = R_0(z), \theta \in [0, 2\pi), z \in [0, L]\}.$$
where \( L \) indicates the length of the arterial element under consideration. In our cylindrical coordinate system \((r, \theta, z)\), the \( z \) coordinate is aligned along the vessel axes and a plane \( z = \tau (= \text{constant}) \) defines an axial section.

2.3. Coupling with the structure model

We now study the properties of the coupled fluid-structure problem, using for the structure the generalised string model (2.6). We will take \( n \) always to be the outwardly vector normal to the fluid domain boundary. Furthermore we define \( g \) as the metric function so that the elemental surface measure \( d\sigma \) on \( \Gamma^w_0 \) is related to the corresponding measure \( d\sigma_0 \) on \( \Gamma^w_0 \) by \( d\sigma = g \, d\sigma_0 \).

We will then address the following problem: *For all \( t > 0 \), find \( u, p, \eta \) such that*

\[
\begin{align*}
\{ & u, p \quad \text{satisfy problem (2.5)}, \\
& \eta \quad \text{satisfies problem (2.6)}, \\
& u \circ A_t = \frac{\partial \eta}{\partial t} e_r, \quad \text{on } \Gamma^w_0, \\
& H = g \frac{\rho}{\rho_w h_0} (p - p_0) n - T(u) \cdot n \cdot e_r, \quad \text{on } \Gamma^w_0.
\end{align*}
\]

Here, \( p_0 \) is the pressure acting at the exterior of the vessel, \( e_r \) is the radial unit vector, \( \rho_w \) and \( \rho \) are the wall and fluid densities, respectively, while \( h_0 \) is the wall thickness. The system is complemented by appropriate boundary and initial conditions.

We may then recognise the sources of the coupling between the fluid and the structure models, which are twofold. In view of a possible iterative solution strategy, the fluid solution provides the value of \( H \), which is function of the fluid stresses at the wall. On the other hand, the movement of the vessel wall modifies the geometry on which the fluid equations must be solved, besides providing Dirichlet boundary conditions for the fluid velocity in correspondence to the vessel wall.

**Remark 2.1.** We may note that the non-linear convective term in the Navier-Stokes equations is crucial to obtain the well-posedness of the coupled problem, because it generates a boundary term which compensates that coming from the treatment of the acceleration term. These two contributions are indeed only present in the case of a moving boundary. See [14] and [1].

2.4. Numerical solution of the coupled fluid-structure problem

In this section we describe an algorithm that at each time-level allows the decoupling of the sub-problem related to the fluid from that related to the vessel wall. As usual, \( t^k \), \( k = 0, 1, \ldots \) denotes the \( k \)-th discrete time level; \( \Delta t > 0 \) is the time-step, while \( v^k \) is the approximation of the function (either scalar or vector) \( v \) at time \( t^k \).

The numerical solution of the fluid-structure interaction problem (2.7) will be carried out by constructing a proper finite element approximation of each sub-problem. In particular, for the fluid we need to devise a finite element formulation suitable for moving domains (or, more precisely, moving grids). In this respect, the ALE formulation will provide an appropriate framework.
To better illustrate the situation we refer to Fig. 2 where we have drawn a 2D fluid structure interaction problem (only the upper portion of the vessel is reported). For the sake of simplicity we have considered only a two-dimensional fluid structure problem, yet the algorithm here presented may be readily extended to more complex situations and three dimensional problems.

Figure 2: A simple fluid-structure interaction problem. On the left the domain definition and on the right the discretized vessel wall corresponding to a possible value of \( \eta_h \).

Figure 3: The triangulation used for the fluid problem at each time \( t \) is the the image through a map \( A_t \) of a mesh constructed on \( \Omega_0 \).

The structure on \( \Gamma^w_0 \) will be discretized by means of a grid \( \mathcal{T}^s_{t,h} \) and employing piecewise linear continuous (P1) finite elements to represent the approximate vessel wall displacement \( \eta_h \). The position at time \( t \) of the discretized vessel wall boundary, corresponding to the discrete displacement field \( \eta_h(t) \), is indicated by \( \Gamma^w_{t,h} \). Consequently, the fluid domain will be represented at every time by a polygon, which we indicate by \( \Omega_{t,h} \). Its triangulation \( \mathcal{T}^f_{t,h} \) will be constructed as the image by an appropriate ALE mapping \( A_t \) of a triangulation \( \mathcal{T}^f_{0,h} \) of \( \Omega_0 \), as shown in Fig. 3. Correspondingly, \( \Omega_{t,h} = A_t \Omega_{0,h} \), where \( \Omega_{0,h} \) is the discretisation of \( \Omega_0 \) induced by \( \mathcal{T}^f_{0,h} \). The trace of \( \mathcal{T}^f_{0,h} \) on \( \Gamma^w_{0,h} \) will coincide with the \( \mathcal{T}^s_{t,h} \) of the vessel wall, i.e. we here consider geometrically conforming finite elements between the fluid and the structure. The possibility of using geometrically non-conforming finite elements has been investigated in [10].

Having at disposal the discrete displacement field \( \eta_h^{k+1} \) at \( t = t^{k+1} \) and thus the position of the domain boundary \( \partial \Omega_{k+1,h} \), the set up of a map \( A_{t+1} \) such that \( A_{t+1}(\mathcal{T}^f_{0,h}) \)
is an acceptable finite element mesh for the fluid domain is not a simple task. However, if we can assume that \( \Omega_{t,h} \) is convex for all \( t \) and that the displacements are relatively small, the following technique, known as harmonic extension, may well serve the purpose. If \( X_h \) indicates the P1 finite element vector space associated to \( T_{f,h}^0 \) and \( g_h \): \( \partial \Omega_{0,h} \to \partial \Omega_{t,k+1,h} \) is the function describing the fluid domain boundary, we build the map by seeking \( y_h \in X_h \) such that

\[
\int_{\Omega_0} \nabla y_h : \nabla z_h = 0 \quad \forall z_h \in X_h^0, \quad y_h = g_h, \quad \text{on} \ \partial \Omega_{0,h}, \quad (2.8)
\]

and then setting \( A_{t,k+1}(Y) = y_h(Y), \quad \forall Y \in \Omega_{0,h} \). A more general discussion on the construction of the ALE mapping may be found in [5, 12] as well as in [9].

**Remark 2.2.** Adopting P1 elements for the construction of the ALE map ensures that the triangles of \( T_{h,0} \) are mapped into triangles, thus \( T_{h,1} \) is a valid triangulation, under the requirement of invertibility of the map (which is assured if the domain is convex and the wall displacements are small).

As for the time evolution, we may adopt a linear time variation within each time slab \([t^k, t^{k+1}]\) by setting

\[
A_t = \frac{t - t^k}{\Delta t} A_{t,k+1} - \frac{t - t^{k+1}}{\Delta t} A_{t,k}, \quad t \in [t^k, t^{k+1}].
\]

Then, the corresponding domain velocity \( w_h \) will be constant on each time slab.

### 2.4.1. The iterative algorithm

We are now in the position of describing an iteration algorithm for the solution of the coupled problem. As usual, we assume that all quantities are available at \( t = t^k, k \geq 0 \), provided either by previous calculations or by the initial data and we wish to advance to the new time step \( t^{k+1} \). For ease of notation we here omit the subscript \( h \), with the understanding that we are referring exclusively to finite element quantities.

The algorithm requires to choose a tolerance \( \tau > 0 \), which is used to test the convergence of the procedure, and a relaxation parameter \( 0 < \theta \leq 1 \). In what follows, the subscript \( j \geq 0 \) denotes the sub-iteration counter.

The algorithm reads:

A1 Extrapolate the vessel wall structure displacements and velocity:

\[
\eta^{k+1}(0) = \eta^k + \Delta t \dot{\eta}^k, \quad \dot{\eta}^{k+1}(0) = \dot{\eta}^k.
\]

A2 Set \( j = 0 \).

A2.1 By using \( \eta^{k+1}(j) \) compute the new grid for the fluid domain \( \Omega_t \) and the ALE map by solving the harmonic extension problem (2.8).

A2.2 Approximate the Navier-Stokes problem to compute \( u^{k+1}_{(j+1)} \) and \( p^{k+1}_{(j+1)} \), using as velocity on the wall boundary the one calculated from \( \dot{\eta}^{k+1}(j) \).

A2.3 Approximate the structure problem to compute \( \eta^{k+1}_{(j+1)} \) and \( \dot{\eta}^{k+1}_{(j+1)} \) using \( u^{k+1}_{(j+1)} \) and \( p^{k+1}_{(j+1)} \) to recover the forcing term \( H \).
A.2.4 Unless $\|\eta^{k+1}_a - \eta^{k+1}_{(j)}\|_{L^2(\Gamma^a_\omega)} + \|\eta^{k+1}_s - \eta^{k+1}_{(j)}\|_{L^2(\Gamma^s_\omega)} \leq \tau$, set

$$
\eta^{k+1}_{(j+1)} = \theta \eta^{k+1}_{(j)} + (1-\theta) \eta^{k+1}_{(j)}
$$

and $j \leftarrow j + 1$. Then return to step 2a.

A3 Set

$$
\eta^{k+1} = \eta^{k+1}_{a}, \quad \dot{\eta}^{k+1} = \dot{\eta}^{k+1}_{a},
$$

$$
u^{k+1} = u^{k+1}_{(j+1)}, \quad p^{k+1} = p^{k+1}_{(j+1)}.
$$

If the algorithm converges, then $\lim_{j \to \infty} u^{k+1}_{(j)} = u^{k+1}$ and $\lim_{j \to \infty} \eta^{k+1}_{(j)} = \eta^{k+1}$, where $u^{k+1}$ and $\eta^{k+1}$ are the approximate solution of the coupled problem at time step $t^{k+1}$.

The algorithm entails, at each sub-iteration, the computation of the equation for the structure mechanics, the Navier-Stokes equations and the solution of two Laplace equations (2.8), one for every displacement component. It is therefore quite computationally expensive. Alternatively, less implicit formulations may be adopted, see for instance [13], yet it has been found that for the problem at hand a strong coupling between fluid and structure must be maintained also at discrete level in order to have stable algorithms [12].

### 3. Multiscale modelling of the cardiovascular system

The cardiovascular system is highly integrated. In many cases, to isolate the part of interest from the rest of the system would require specification of point-wise boundary data on artificial boundary sections. These are difficult to pre-determine. To account for the effect of the global circulatory system when focusing on specific regions we propose to integrate a hierarchy of models operating at different “scales”. At the highest level we have the full three-dimensional fluid-structure interaction problem. This will be used where details of local flow fields are needed. At the lowest level, we use lumped parameter models based on the resolution of systems of non-linear ordinary algebraic-differential equations for averaged mass flow and pressure. The latter models are often described by help of an analogy with an electrical circuit, where the voltage represents blood pressure and the current the flow rate. They are well fit to supply the more sophisticated models with the effects of the circulation in small vessels, the capillary bed, the venous system, as well as the action of the heart. A transition between the two extrema could be achieved by convenient one-dimensional models expressed by a first order non-linear hyperbolic system (see Fig. 4). The derivation of the one-dimensional model and a possible numerical implementation may be found in [6, 4, 14].

An analysis of the coupling between fluid-structure models and one dimensional models may be found in [3], while the direct coupling by lumped parameter models and Navier-Stokes model is found in [15, 17], the coupling between lumped parameter models and one-dimensional models is also treated in [7].

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Figure 4: An example of multiscale simulation of blood flow, with the interplay between three-dimensional, one-dimensional and lumped parameters models. On top we show a global model of the circulatory system where a coronary by-pass is being simulated by a Navier-Stokes fluid-structure interaction model. The rest of the circulatory system is described by means of a lumped parameter model, based on the solution of a system of ODEs, is here represented by an electrical circuit analog in the bottom part of the figure.
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