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Reduced models of the cardiovascular system

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Due to the large number of vessels involved and the multitude of different length scales required to accurately represent the flow in the various regions of the cardiovascular system, simulations of the flow of blood in the entire system based on full 3D models are beyond the capability of current computers and they will be for years to come. Moreover, the huge amount of data that would be generated by such simulations is costly to process and of difficult clinical interpretation.

On the other hand, it is possible to devise simplified models exploiting specific features of blood flow, such as the basically cylindrical morphology of the vessels. Even though these models are highly simplified with respect to the local dynamics, they can provide reliable numerical results at a low computational cost. Interpretation is much straightforward, thus making them ideal as an everyday tool for use in clinical practice.

Moreover, these models are well-suited for describing systemic dynamics such as *feedback mechanisms* that play an important role in the the correct working of the vascular system. These dynamics typically involve mechanical and biochemical phenomena that can be hardly described in terms of complete 3D models.

In these notes, we address simplified models and in particular we consider:

- 1. one-dimensional (1D) models in which the space dependence is reduced only to the axial coordinate;
- 2. lumped parameter (or 0D) models, where the space dependence is discretized, by splitting the cardiovascular system into a set of compartments. The associated mathematical model is typically based on ordinary differential and algebraic equations (DAE), often represented in terms of hydraulic or electric networks.

It is worth mentioning that studies on one-dimensional models of blood flow were first presented by Leonhard Euler in his seminal article entitled *Principa pro motu sanguinis determinando* [14]. In spite of the simplifying assumptions behind these models, they are very useful and many of their analytical and numerical aspects still deserve further investigation³.

1.1 One-dimensional (1D) models

There are several ways of deriving a 1D model of an incompressible fluid flowing in a compliant pipe. One could start from the incompressible Navier-Stokes equations and perform an asymptotic analysis by assuming that the radius of the vessel, R_0 , is small compared to its length l, i.e. $\frac{R_0}{L} \ll 1$, that will permit us to simplify the governing equations by discarding the higher order terms in $\frac{R_0}{L}$ as proposed by [4]. Alternatively, the 1D model could be derived by assuming cylindrical symmetry and integrating the Navier-Stokes equations on a generic section as described in [57].

Here we will follow the approach advocated and described in [36, 37] and derive the governing equations from conservation principles. This approach is more general and it does not require any simplifying assumptions concerning the geometry of the vessel section.

1.1.1 Derivation of the governing equations

We consider a simple compliant tube, illustrated in Figure 1.1, as a model of the artery. We assume that the axis of the vessel is rectilinear and coincides with the x axis. The starting point for the derivation of the one-dimensional governing equations is Reynolds' transport theorem for an arbitrary control volume V_t with boundary ∂V_t and outer normal \boldsymbol{n} . A formal derivation of this formula can be found in [59]. It states that, for a continuous function $f = f(t, \boldsymbol{x})$, we have

$$\frac{d}{dt} \int_{V_t} f \, dV = \int_{V_t} \frac{\partial f}{\partial t} \, dV + \int_{\partial V_t} f \, \boldsymbol{u}_b \cdot \boldsymbol{n} \, d\sigma \tag{1.1}$$

where \boldsymbol{x} stands for (x, y, z) and \boldsymbol{u}_b is the velocity of the boundary of volume V_t . This is composed of the arterial wall $\partial V_{t,w}$ and the two end sections S_1 and S_2 , that are assumed normal to the axis. On S_1 and S_2 the normal component of \boldsymbol{u}_b is 0, while on $\partial V_{t,w}$ velocity \boldsymbol{u}_b does coincide with the velocity \boldsymbol{u}_w of the arterial wall, so that

$$\int_{\partial V_t} f \, \boldsymbol{u}_b \cdot \boldsymbol{n} \, d\sigma = \int_{\partial V_{t,w}} f \, \boldsymbol{u}_w \cdot \boldsymbol{n} \, d\sigma. \tag{1.2}$$

³ "Thus in explaining the motion of the blood, we come up against the same insuperable difficulties which clearly prevent us from more accurately investigating all the works of the Creator; wherein we ought constantly to admire and to venerate much more the highest wisdom conjoined with omnipotence since truly not even the greatest human ingenuity avails to understand and explain the true structure of the slightest micro-organism", L. Euler [9].



Fig. 1.1. Notation used to describe a simple compliant tube

Here u_w is taken to be different of the fluid velocity $u = (u_1, u_2, u_3)$ to allow for the presence of a permeable lumen. The relative velocity between the arterial wall and the fluid at the lumen is given by

$$w = u_w - u$$

To obtain the one-dimensional form of the conservation laws, we consider a rea-averaged values of the relevant variables. The area-averaged value of f is denoted by \bar{f} and given by

$$\bar{f} = \frac{1}{A} \int_{S} f \, d\sigma \tag{1.3}$$

where $A = A(x,t) = \int_S d\sigma$ is the area of the cross section S. Using this notation, we write a volume integral as

$$\int_{V_t} f \, dV = \int_{x_1}^{x_2} \left[\int_S f \, d\sigma \right] \, dx = \int_{x_1}^{x_2} A \bar{f} \, dx \tag{1.4}$$

where x_1 and x_2 ($x_2 > x_1$) are the x-coordinates of the cross sections S_1 and S_2 .

Given that x_1 and x_2 are independent of time, the left-hand side term of equation (1.1) can be written as

$$\frac{d}{dt} \int_{V_t} f \, dV = \int_{x_1}^{x_2} \frac{\partial}{\partial t} \left(A\bar{f} \right) \, dx \tag{1.5}$$

The presence of a permeable wall makes the evaluation of the second term of the right-hand side of equation (1.1) more involved. After (1.2), this term is calculated as

$$\int_{\partial V_{t,w}} f \boldsymbol{u}_w \cdot \boldsymbol{n} \, d\sigma = \int_{\partial V_{t,w}} f \boldsymbol{w} \cdot \boldsymbol{n} \, d\sigma + \int_{\partial V_{t,w}} f \boldsymbol{u} \cdot \boldsymbol{n} \, d\sigma$$

Observe that

$$\int_{\partial V_{t,w}} f \boldsymbol{u} \cdot \boldsymbol{n} \, d\sigma = \int_{\partial V_t} f \boldsymbol{u} \cdot \boldsymbol{n} \, d\sigma - \int_{S_1} f \boldsymbol{u}_w \cdot \boldsymbol{n} \, d\sigma - \int_{S_2} f \boldsymbol{u}_w \cdot \boldsymbol{n} \, d\sigma = \int_{\partial V_t} f \boldsymbol{u} \cdot \boldsymbol{n} \, d\sigma + \int_{S_1} f u_1 \, d\sigma - \int_{S_2} f u_1 \, d\sigma$$

where u_1 is the x-component of the velocity u. Thanks to the Gauss' theorem, we have

$$\int_{\partial V_{t,w}} f\boldsymbol{u} \cdot \boldsymbol{n} \, d\sigma = \int_{V_t} \nabla \cdot (f\boldsymbol{u}) \, dV + \int_{S_1} f u_1 \, d\sigma - \int_{S_2} f u_1 \, d\sigma$$

so that using area-averaged quantities, we finally obtain

$$\int_{\partial V_{t,w}} f \boldsymbol{u}_{w} \cdot \boldsymbol{n} d\sigma = \int_{\partial V_{t,w}} f \boldsymbol{w} \cdot \boldsymbol{n} \, d\sigma - \int_{x_{1}}^{x_{2}} \frac{\partial}{\partial x} \left[A \left(\overline{f u_{1}} \right) \right] dx + \int_{V_{t}} \nabla \cdot (f \boldsymbol{u}) \, dV$$
(1.6)

Finally, including the expressions (1.5) and (1.6) into equation (1.1) leads to

$$\int_{x_1}^{x_2} \frac{\partial}{\partial t} \left(A\bar{f} \right) \, dx = \int_{x_1}^{x_2} \left(\int_S \frac{\partial f}{\partial t} \, d\sigma \right) \, dx + \int_{x_1}^{x_2} \left(\int_{\partial S} f \boldsymbol{w} \cdot \boldsymbol{n} \, d\gamma \right) \, dx - \int_{x_1}^{x_2} \frac{\partial}{\partial x} \left[A \left(\overline{fu_1} \right) \right] \, dx + \int_{x_1}^{x_2} \left(\int_S \nabla \cdot \left(f \boldsymbol{u} \right) \, d\sigma \right) \, dx$$

and, given that this is true for any values of the coordinates of the end sections x_1 and x_2 , the final form of the one-dimensional transport theorem for a generic variable f is

$$\frac{\partial}{\partial t} \left(A\bar{f} \right) + \frac{\partial}{\partial x} \left[A \left(\overline{fu_1} \right) \right] = \int_S \left[\frac{\partial f}{\partial t} + \nabla \cdot (f\boldsymbol{u}) \right] \, d\sigma + \int_{\partial S} f\boldsymbol{w} \cdot \boldsymbol{n} \, d\gamma \quad (1.7)$$

This formula is general and applicable to both compressible and incompressible fluids. Now we will proceed to derive the governing equations by invoking the principles of conservation of mass and balance of momentum.

Conservation of mass

The equation representing the conservation of mass in the flexible tube is obtained by taking f = 1 in equation (1.7). If we further assume that the fluid is incompressible, i.e. $\nabla \cdot \boldsymbol{u} = 0$, we get

$$\frac{\partial A}{\partial t} + \frac{\partial}{\partial x} \left(A \bar{u}_1 \right) = \int_{\partial S} \boldsymbol{w} \cdot \boldsymbol{n} \, d\gamma \tag{1.8}$$

where the term in the right-hand side could be interpreted as a volumetric outflow per unit length and unit time.

Balance of momentum

Here we take $f = u_1$ in the area-averaged Reynolds' transport expression (1.7), and assume again that the fluid is incompressible, to obtain

$$\frac{\partial}{\partial t} \left(A \bar{u}_1 \right) + \frac{\partial}{\partial x} \left(A \overline{u}_1^2 \right) = \int_S \left[\frac{\partial u_1}{\partial t} + \boldsymbol{u} \cdot \nabla u_1 \right] \, d\sigma + \int_{\partial S} u_1 \boldsymbol{w} \cdot \boldsymbol{n} \, d\sigma \quad (1.9)$$

which we now write as

$$\frac{\partial}{\partial t} \left(A \bar{u}_1 \right) + \frac{\partial}{\partial x} \left(A \overline{u_1^2} \right) = \int_S \frac{D u_1}{D t} \, d\sigma + \int_{\partial S} u_1 \boldsymbol{w} \cdot \boldsymbol{n} \, d\sigma \tag{1.10}$$

where $\frac{D}{Dt} = \frac{\partial}{\partial t} + \boldsymbol{u} \cdot \nabla$ denotes the so-called material or Lagrangian derivative. To calculate the first term on the right-hand side of equation (1.10) we apply the momentum conservation for the control volume V_t in the form

$$\int_{V_t} \frac{D}{Dt}(\rho \boldsymbol{u}) \, dV = \int_{V_t} \rho \boldsymbol{f}^b \, dV + \int_{\partial V_t} \boldsymbol{T} \boldsymbol{n} \, d\sigma \tag{1.11}$$

where f^b represents the body force per unit volume and T is the Cauchy stress tensor (see e.g. [59]). Assuming that the density ρ is constant and using the divergence theorem, the balance of momentum equation (1.11) is written as

$$\int_{V_t} \frac{D\boldsymbol{u}}{Dt} \, dV = \int_{V_t} \boldsymbol{f}^b \, dV + \frac{1}{\rho} \int_{V_t} \nabla \cdot \boldsymbol{T} \, dV \tag{1.12}$$

Now, invoking the constitutive equation for the fluid, we could write the stress tensor ${\boldsymbol T}$ as

$$T = -pI + D \tag{1.13}$$

where p denotes the pressure, I is the identity tensor, and D represents the tensor of deviatoric stresses due to the viscosity of the fluid. Setting $\nabla \cdot D = d$ we also write

$$abla \cdot \boldsymbol{T} = -
abla p +
abla \cdot \boldsymbol{D} = -
abla p + \boldsymbol{d}$$

and, therefore, equation (1.12) as

$$\int_{x_1}^{x_2} \left(\int_S \frac{D\boldsymbol{u}}{Dt} \, d\sigma \right) \, dx = \int_{x_1}^{x_2} \left(\int_S \left[\boldsymbol{f}^b + \frac{1}{\rho} \left(-\nabla p + \boldsymbol{d} \right) \right] \, d\sigma \right) \, dx \qquad (1.14)$$

Since x_1 and x_2 can be arbitrarily chosen, the integrands in the left and righthand sides of equation (1.14) must be equal, therefore we could write the *x*-component of this equation as

$$\int_{S} \frac{Du_1}{Dt} \, d\sigma = \int_{S} \left[f_1^b + \frac{1}{\rho} \left(-\frac{\partial p}{\partial x} + d_1 \right) \right] \, d\sigma, \tag{1.15}$$

where d_1 is the *x*-component of *d*. Substituting this expression in equation (1.10) gives

$$\frac{\partial}{\partial t} (A\bar{u}_1) + \frac{\partial}{\partial x} \left(A\overline{u}_1^2 \right) = \int_S \left[f_1^b + \frac{1}{\rho} \left(-\frac{\partial p}{\partial x} + d_1 \right) \right] \, d\sigma + \int_{\partial S} u_1 \boldsymbol{w} \cdot \boldsymbol{n} \, d\sigma, \quad (1.16)$$

which can be expressed using area-averaged values as

$$\frac{\partial}{\partial t} \left(A \bar{u}_1 \right) + \frac{\partial}{\partial x} \left(A \overline{u_1^2} \right) = \frac{A}{\rho} \left(\rho \bar{f}_1^b - \frac{\partial \bar{p}}{\partial x} + \bar{d}_1 \right) + \int_{\partial S} u_1 \boldsymbol{w} \cdot \boldsymbol{n} \, d\sigma. \quad (1.17)$$

The term $\overline{u_1^2}$ in this equation is handled by defining a momentum-flux correction coefficient α , which is a function of the velocity profile, as

$$\overline{u_1^2} = \frac{1}{A} \int_S u_1^2 \, d\sigma = \alpha \bar{u}_1^2, \tag{1.18}$$

where α is also called the *Coriolis coefficient*. For a flat profile we have $\alpha = 1$ and for a parabolic flow $\alpha = 4/3$.

The term representing the viscous forces \bar{d}_1 is taken to be a linear function of the area-averaged velocity \bar{u}_1 of the form

$$\frac{A}{\rho}\bar{d}_1 = -K_R\bar{u}_1,\tag{1.19}$$

where K_R is a strictly positive quantity which represents the viscous resistance of the flow per unit length of tube. It is worth observing that for a proper definition of the coefficient, (1.19) is fulfilled by the well known Poiseuille flow. The final form of the balance of momentum equation is

$$\frac{\partial}{\partial t} \left(A \bar{u}_1 \right) + \frac{\partial}{\partial x} \left(\alpha \bar{u}_1^2 \right) = A \bar{f}_1^b - \frac{A}{\rho} \left(\frac{\partial \bar{p}}{\partial x} \right) - K_R \bar{u}_1 + \int_{\partial S} u_1 \boldsymbol{w} \cdot \boldsymbol{n} \, d\sigma. \quad (1.20)$$

The unknowns in the system given by (1.8) and (1.20) are p, A and \bar{u}_1 . Their number exceeds the number of equations and a common way to close the system is to explicitly provide an relationship between the pressure of the vessel p and the vessel area A. This relation will be derived from an appropriate simplification of models of wall mechanics.

Simplified models of wall mechanics

By assuming *static equilibrium* in the radial direction of a cylindrical tube, from one-dimensional models of wall mechanics (see e.g. [63]) one can derive a pressure relationship of the form

$$p = P_{ext} + \beta(\sqrt{A} - \sqrt{A_0}), \qquad (1.21)$$

where

$$\beta = \frac{\sqrt{\pi}h_0 E}{(1-\nu^2)A_0}.$$
(1.22)

Here h_0 and $A_0 = A_0(x)$ denote the vessel thickness and sectional area, respectively, at the equilibrium state $(p, Q) = (P_{ext}, 0)$, E = E(x) is the Young modulus, P_{ext} is the external pressure, assumed constant, and ν is the Poisson ratio. This ratio is typically taken to be $\nu = 1/2$ since biological tissue is practically incompressible.

The algebraic relation (1.21) assumes that the wall is instantaneously in equilibrium with the pressure forces acting on it. This approach corresponds to the so-called *independent ring model* (see [63]).

Wall inertia and viscoelasticity can be included, yielding a differential pressure law. For instance (see [63]) we may write

$$p - P_{ext} = \frac{\gamma_0}{2\sqrt{\pi A_0}} \ddot{A} + \frac{\gamma_1}{2\sqrt{\pi A_0}} \dot{A} + \Phi(A; A_0, \beta), \qquad (1.23)$$

where $\gamma_0 = \rho_w h_0$, $\gamma_1 = \frac{\gamma}{r_0^2}$ and the last term is the elastic response, modelled through equation (1.21). Here γ is the viscoelasticity coefficient. For more details, see [60].

1.1.2 Different formulations of the governing equations

In what follows, we will assume that the lumen is impermeable $(\boldsymbol{w} \cdot \boldsymbol{n} = 0)$, that body forces are neglegible $(\bar{f}_1^b = 0)$, and we will also simplify the notation by denoting the area-averaged axial velocity by u instead of \bar{u}_1 and using p instead of \bar{p} . Defining the mass flux across a section as $Q = Au = \int_S u_1 d\sigma$, the equations (1.8) and (1.20) now read

$$\begin{cases} \frac{\partial A}{\partial t} + \frac{\partial Q}{\partial x} = 0\\ \frac{\partial Q}{\partial t} + \frac{\partial}{\partial x} \left(\alpha \frac{Q^2}{A} \right) + \frac{A}{\rho} \left(\frac{\partial p}{\partial x} \right) + K_R \frac{Q}{A} = 0 \end{cases}$$
(1.24)

These equations will be referred to as the *conservation form of the governing equations* since they have been derived directly from conservation principles.

The system of equations (1.24) can be expressed alternatively in terms of the variables (A, u). By simple manipulations one gets

$$\begin{cases} \frac{\partial A}{\partial t} + \frac{\partial Au}{\partial x} = 0\\ \frac{\partial u}{\partial t} + (2\alpha - 1)u\frac{\partial u}{\partial x} + (\alpha - 1)u^2\frac{\partial A}{\partial x} + \frac{1}{\rho}\frac{\partial p}{\partial x} + K_R\frac{u}{A} = 0 \end{cases}$$
(1.25)

Both systems (1.24) and (1.25) may be written in conservation form. Let us assume that the wall mechanics is described by the algebraic pressure-wall relationship (1.21).

For the system (A, Q) we will write

$$\frac{\partial \mathbf{Q}}{\partial t} + \frac{\partial \mathbf{G}}{\partial x}(\mathbf{Q}) = \mathbf{B}(\mathbf{Q}) \tag{1.26}$$

with

$$\mathbf{Q} = \begin{bmatrix} A \\ Q \end{bmatrix}, \ \mathbf{G} = \begin{bmatrix} Q \\ \frac{Q^2}{A} + \frac{\beta}{3\rho} A^{\frac{3}{2}} \end{bmatrix} \text{ and } \mathbf{B} = \begin{bmatrix} 0 \\ -K_R \frac{Q}{A} + \frac{A}{\rho} \frac{d\beta}{dx} \left(A_0^{\frac{1}{2}} - \frac{2A^{\frac{1}{2}}}{3} \right) \end{bmatrix}.$$
(1.27)

For the (A, u) system, if for the sake of simplicity we assume $\alpha = 1$, we have

$$\frac{\partial \boldsymbol{U}}{\partial t} + \frac{\partial \boldsymbol{F}}{\partial x}(\boldsymbol{U}) = \boldsymbol{S}(\boldsymbol{U})$$
(1.28)

with

$$\boldsymbol{U} = \begin{bmatrix} A \\ u \end{bmatrix}, \quad \boldsymbol{F} = \begin{bmatrix} Au \\ p_t \end{bmatrix} \quad \text{and} \quad \boldsymbol{S} = \begin{bmatrix} 0 \\ -K_R \frac{u}{A} \end{bmatrix}. \tag{1.29}$$

Here

$$p_t = \frac{u^2}{2} + \frac{p}{\rho} \tag{1.30}$$

denotes the *total pressure* (scaled by the constant density).

In the case $\alpha = 1$ the two weak forms are equivalent for smooth solutions, in particular when A and Q are C^1 continuous functions with respect to both arguments and A is strictly positive. Nevertheless, the assumption $\alpha = 1$ is quite realistic in the problems at hand since the velocity profile is in fact almost flat (see [45]) and the solutions within each of the approaches presented in these notes will be sufficiently smooth to favour the use of the (A, u) system which has a simpler structure.

The (A, u) and the (A, Q) systems given respectively by equations (1.25) and (1.24), together with the algebraic pressure-area relationship (1.21), will be starting points of the numerical schemes discussed in the sequel.

Remark 1.1.1 Even though the values of the coefficients α , K_R and β are fixed a priori once we make assumptions on the velocity profile and on the wall mechanics, it is also possible to interpret them as parameters of the model that can be obtained by fitting the results of the 1D model to available in vivo or 3D computational data as proposed in [44].

1.1.3 Characteristic variables

Considering the pressure-area relationship (1.21) and assuming that $\beta = \beta(x)$ and $A_0 = A_0(x)$ we recall that applying the chain rule we obtain

$$\frac{\partial p}{\partial x} = \frac{\partial p}{\partial A}\frac{\partial A}{\partial x} + \frac{\partial p}{\partial \beta}\frac{\partial \beta}{\partial x} + \frac{\partial p}{\partial A_0}\frac{\partial A_0}{\partial x}$$

where

$$\frac{\partial p}{\partial A} = \frac{\beta}{2\sqrt{A}}.$$

System (1.25) can therefore be written in quasi-linear form as

$$\frac{\partial U}{\partial t} + H \frac{\partial U}{\partial x} = \begin{bmatrix} A \\ u \end{bmatrix}_t + \begin{bmatrix} u & A \\ c^2/A & u \end{bmatrix} \begin{bmatrix} A \\ u \end{bmatrix}_x = \begin{bmatrix} 0 \\ f \end{bmatrix}$$
(1.31)

where

$$c^2 = \frac{A}{\rho} \frac{\partial p}{\partial A} = \frac{\beta \sqrt{A}}{2\rho}$$
 and $f = \frac{1}{\rho} \left[K_R u - \frac{\partial p}{\partial \beta} \frac{\partial \beta}{\partial x} + \frac{\partial p}{\partial A_0} \frac{\partial A_0}{\partial x} \right].$

Under the assumption that A > 0, which is indeed a necessary condition to have a physically relevant solution, the matrix **H** has two real eigenvalues $\lambda_{1,2} = u \pm c$ and the corresponding left eigenmatrix **L** is

$$\mathbf{L} = \begin{bmatrix} \mathbf{I}_1^T \\ \mathbf{I}_2^T \end{bmatrix} = \begin{bmatrix} \frac{c}{A} & 1 \\ -\frac{c}{A} & 1 \end{bmatrix}.$$
 (1.32)

For the typical values of velocity, vessel area and elastic parameter β encountered in arteries under physiological conditions, we have that $\lambda_1 > 0$ and $\lambda_2 < 0$. Therefore our system is *strictly hyperbolic* and *subcritical* (see [42] for these definitions).

The characteristic variables can be determined by integrating the differential system $\partial_U \mathbf{W} = \mathbf{L}$. It may be shown that this is possible for our problem and that the two characteristic variables are

$$W_1 = u + 4c = u + 4A^{1/4} \sqrt{\frac{\beta}{2\rho}}$$
(1.33)

$$W_2 = u - 4c = u - 4A^{1/4} \sqrt{\frac{\beta}{2\rho}}.$$
 (1.34)

Since $\beta > 0$, we may write, as previously reported in [22], the variables (A, u) in terms of (W_1, W_2) as

$$A = \left[\frac{(W_1 - W_2)}{4}\right]^4 \left(\frac{\rho}{2\beta}\right)^2 \qquad u = \frac{(W_1 + W_2)}{2}.$$
 (1.35)

In the case where f = 0 equations (1.31) can be transformed in a decoupled system of equations for the characteristic variables, which component-wise reads

$$\begin{cases} \frac{\partial W_1}{\partial t} + \lambda_1 \frac{\partial W_1}{\partial x} = 0\\ \frac{\partial W_2}{\partial t} + \lambda_2 \frac{\partial W_2}{\partial x} = 0. \end{cases}$$
(1.36)

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Remark 1.1.2 Smoothness of the solution. We recall some of the main results regarding the hyperbolic system at hand. It has been shown in [7] that, using a pressure-area relationship of the form

$$p - P_{ext} = G_0 \left[\left(\frac{A}{A_0} \right)^{\frac{\delta}{2}} - 1 \right],$$

where $\delta > 1$ and G_0 is a constant elasticity parameter, and under some reasonable conditions on the smoothness of boundary and initial data, the solution of system (1.24) remains smooth. Two critical assumptions to reach this conclusion are the pulsatility of the inflow data and a bound on the length of the tube; both are verified for physiological flow in the human arterial tree. In the same work it is shown that, if the solution is smooth and the initial and boundary data are such that A > 0, A remains strictly positive for all times. In [17] an energy inequality was derived which bounds a measure of the energy of the hyperbolic system in terms of the initial and boundary data. Furthermore, in the same work it has been found that the quantity

$$s = \frac{1}{2}\rho A u^2 + \int_{A_0}^A (p - P_{ext}) dA$$

is an entropy function for the system with associated flux equal to $F_s = Q p_t$.

1.1.4 Boundary conditions

The characteristic analysis and the fact that for physiological conditions the flow is subcritical (i.e. $\lambda_1 > 0$ and $\lambda_2 < 0$) leads us to the conclusion that only one boundary condition has to be imposed at each end of the tube. Different type of boundary conditions may be envisaged.

Non-reflecting boundary conditions

Non-reflecting boundary conditions are those that allow the simple wave associated with the characteristics exiting the domain to leave without spurious reflections. Typically those conditions are expressed in terms of the characteristic variables. In [72] and [33] non-reflecting boundary conditions for an isolated vascular segment corresponding to an hyperbolic system like (1.26) are provided as

$$\mathbf{l}_1 \left[\frac{\partial \mathbf{Q}}{\partial t} - \mathbf{B}(\mathbf{Q}) \right]_{x=x_1} = 0, \quad \mathbf{l}_2 \left[\frac{\partial \mathbf{Q}}{\partial t} - \mathbf{B}(\mathbf{Q}) \right]_{x=x_2} = 0.$$

where \mathbf{l}_1 and \mathbf{l}_2 are given by equation (1.32).

For $\mathbf{B}(\mathbf{Q}) = \mathbf{0}$ they are equivalent to imposing a constant value for the entering characteristics, otherwise these relations account for the 'natural decay' due to the presence of the source term. With those conditions the amplitude of the incoming waves may vary only because of the source term (in particular it is constant when the source term is zero). In our case a condition of this type may be convenient at the outlet section (i.e. $x = x_2$) when one can neglect possible contributions of waves coming from the distal circulation, while at the inlet ($x = x_1$) we would like to prescribe some given values of pressure or flux data coming either from measurement or other models. When the peripheral circulation is introduced, we need specific models for the terminal vessels that will be discussed later.

Inlet conditions

The hyperbolic system at hand allows us to impose either a flux Q (or velocity u) or area A at $x = x_1$. For instance we may impose

$$A(x_1, t) = g(t), \quad t > 0$$

where g(t) is a known function obtained, for instance, from the knowledge of the pressure time variation at $x = x_1$. This type of condition is clearly of reflective type and the simple wave associated to the outgoing characteristic $(W_2 \text{ in this case})$ may be partly reflected back into the computational domain. Yet, this reflection is a physical one.

It is also possible to have available values of both pressure (and thus area) and flux variations at the inlet. For instance, measurements of pressure pulse together with flux data could be obtained from Doppler ultrasound. Clearly the hyperbolic system does not allow to impose both conditions at the same time. However, one may construct a set of allowable boundary conditions through the exact or approximate solution of a Riemann problem [28] at the boundary using the computed values and the known values at the inlet.

Terminal vessels

The human arterial system is a network of large arteries branching out into many smaller arteries, arterioles and capillaries. We are usually interested in the results in the larger arteries in the network. Blood vessels further down the arterial tree are very small and numerous. They have, all together, an important role in determining the haemodynamics in the large arteries since they offer flow resistance and pressure wave is partially reflected at each bifurcation. An accurate description of all these vessels and districts although virtually possible is unfeasible for the huge amount of data required not to mention the computational costs. For these reasons, the downstream circulation is usually described in terms of lumped parameter models. In Sect. 1.2 we will introduce extensively these kind of models and their derivation. So, in general terms, an appropriate way for accounting outflow conditions is to resort to *multiscale models*, namely coupling 1D and lumped parameter models (see the next chapter). Here we limit ourselves to some considerations when the role of the lumped parameter models is only to provide a boundary condition for the 1D model, without further details on the peripheral circulation.

Denoting by $\pi_T(\omega)$ and $\chi_T(\omega)$ the Fourier transform of $p_T(t) = p(x_{\text{out}}, t)$ and $Q_T(t) = Q(x_{\text{out}}, t)$ respectively at the end of the 1D network, the behavior of the downstream network can be represented by the *terminal impedance* (see Fig. 1.13, left) as

$$\zeta_T(\omega) = \frac{\pi(\omega)}{\chi(\omega)}.\tag{1.37}$$

An extensive discussion about the role of the impedance function in describing the vascular tree haemodynamics can be found in Chap. 13 of [45]. Here the impedance is the *transfer function* describing in a simplified way the downstream blood dynamics that actually influences the hemodynamics in the proximal district represented by our 1D model. The counterpart of (1.37) in the time domain is obtained by computing the inverse Fourier transform of the terminal impedance, $Z_T = \mathcal{F}^{-1}(\zeta_T)$ and by applying the convolution theorem

$$p_T(t) = \int_{t-H}^t Z_T(t-\tau) Q_T(\tau) d\tau,$$
 (1.38)

where H denotes the heart beat duration. Relation (1.38), possibly approximated with suitable numerical quadratures, provides the boundary condition to be used for the 1D network model in correspondence of terminal vessels.

Since possible examples of impedance functions used in the literature stem from the representation of the terminal districts by lumped parameter models, often represented in terms of electrical circuits, we postpone their description to the next section (see Sect. 1.2.4).

1.1.5 Extensions of the basic model

In the previous sections we have introduced some assumptions on the geometry of the vessel and on the smoothness of the coefficients characterizing the wall dynamics. These hypotheses are acceptable for small segments of the vascular tree, however more general models should be introduced to deal with segments with discontinuous properties, bifurcations and curved vessels. These will be discussed in the following sections.

Discontinuous material properties

In some cases, material properties of the wall are not smooth. In particular, coefficient β introduced in (1.21) features discontinuities for instance in stented arteries (Fig. 1.2) or in by-pass grafts. The Young's modulus E can exhibit jumps due to the differences between the vascular tissue and the prosthesis (see e.g. [41]). It is also possible for the area of the vessel to change abruptly due to certain pathologies, e.g. an aneurysm.

Since the derivative of the elastic coefficient β appears in the balance of momentum equation, the presence of discontinuities in β require careful treatment in our models. There are basically two approaches for handling material discontinuities.



Fig. 1.2. Discontinuity of Young's modulus in the case of a stented artery. Bottom left: regularization approach; bottom right: domain splitting

- 1. *Data regularization*: the discontinuous data are suitably replaced by smooth functions that can be differentiated and the models presented above can be used straightforwardly.
- 2. Domain splitting: the vessel with discontinuous properties is split into a set of smooth segments and the coupling between each pair of segments is accomplished through suitable *matching or interface conditions*. A reasonable choice is to assume continuity of fluxes and thus impose the continuity of mass flux and total pressure across the interface, i.e.

$$Q = u_l A_l = u_r A_r \tag{1.39}$$

$$P_r = \rho \frac{u_l^2}{2} + \beta_l (\sqrt{A_l} - \sqrt{A_{l_0}}) = \rho \frac{u_r^2}{2} + \beta_r (\sqrt{A_r} - \sqrt{A_{r_0}}) \quad (1.40)$$

This interface conditions will preserve the conservation properties of the (A, u) system.

In practice, the problem can be solved iteratively, by solving the sequence of problems on each segment. In this case, the interface conditions (possibly reformulated in terms of characteristic variables) become boundary

conditions on each segment, following a classical domain decomposition approach (see e.g. [64]).

Treatment of bifurcations

The 1D model of the compliant tube can be extended to handle the arterial tree by adopting a domain splitting technique similar to the one used for the discontinuous case. Again we require suitable interface conditions at the bifurcations or branching points of the tree (see Fig. 1.3).



Fig. 1.3. Arterial tree bifurcation: Notation

In the bifurcations the problem is only *locally* one-dimensional, in the sense that each branch is associated with its own axis (denoted by x, \overline{x} and \underline{x} in Fig. 1.3). The use of domain splitting techniques allows us to cast the global problem into a set of 1D problems (1.24) or (1.25). If we denote by x^* the branching point such that it is the right-end point x_r^p of the parent vessel Ω_p , and the left-end point \overline{x}_l^{b1} and \underline{x}_l^{b2} of the branches Ω_{b1} and Ω_{b2} , for a given function f defined over each segment we denote

$$f_l = f \big|_{\Omega_p}(x_r^p), \quad f_{b1} = f \big|_{\Omega_{b1}}(\overline{x}_l^{b1}), \quad f_{b2} = f \big|_{\Omega_{b2}}(\underline{x}_l^{b2}).$$

At the bifurcation we have six unknowns: (A_l, u_l) in the parent vessel, (A_{b1}, u_{b1}) and (A_{b2}, u_{b2}) in the branches Ω_{b1} and Ω_{b2} respectively.

The first three equations required to solve the problem are obtained by imposing that the characteristic variables at point x in each vessel should remain constant. Their values are

$$W_1 = u_l + 4A_l^{1/4} \sqrt{\frac{\beta_l}{2\rho}}$$
(1.41)

$$W_{21} = u_{b1} - 4A_{b1}^{1/4} \sqrt{\frac{\beta_{b1}}{2\rho}}$$
(1.42)

$$W_{22} = u_{b2} - 4A_{b2}^{1/4} \sqrt{\frac{\beta_{b2}}{2\rho}}$$
(1.43)

The other three equations required to close the problem are obtained from the continuity of mass flux and total pressure across the boundary of the elements at the bifurcation, i.e.

0

$$Q = u_p A_p = u_{b1} A_{b1} + u_{b2} A_{b2} \tag{1.44}$$

$$P_r = \rho \frac{u_p^2}{2} + \beta_p (\sqrt{A_p} - \sqrt{A_{p_0}}) = \rho \frac{u_{b_1}^2}{2} + \beta_{b_1} (\sqrt{A_{b_1}} - \sqrt{A_{b_1_0}}) \quad (1.45)$$

$$P_r = \rho \frac{u_p^2}{2} + \beta_p (\sqrt{A_p} - \sqrt{A_{p_0}}) = \rho \frac{u_{b2}^2}{2} + \beta_{b2} (\sqrt{A_{b2}} - \sqrt{A_{b2_0}}) \quad (1.46)$$

The six equations given by (1.41-1.46) define a non-linear system of algebraic equations which determine the values of (A_l, u_l) , (A_{r1}, u_{r1}) and (A_{r2}, u_{r2}) at the bifurcation. These values are then used to evaluate the flux at the elemental interfaces in the numerical discretization.

We have assumed that the coefficient β could be different in the three vessels, as it is to be expected from the different values of their respective areas at rest A_0 .

Remark 1.1.3 Continuity of the total pressure in (1.45, 1.46) can be modified for including pressure losses due to the bifurcation. These typically depend on the bifurcation angle. For more details see [19, 69].

Accounting for curvature in 1D models (Directors' theory)

One of the most relevant assumptions in devising the basic 1D model is that the axis of the vessel is rectilinear. Actually, if we remove this hypothesis, it is still possible to define a main flow direction in the domain, namely the curvilinear abscissa along the axis, and however the effect of the blood dynamics in the other directions on the main one is no longer negligible (see [58]). Nevertheless, there are some vessels which are significantly curved (aorta, femoral arteries, etc.). For these vessels, the basic 1D model (1.25) or (1.24) can be considered only as a rough description. A possible model relies on introducing a subdivision into subsegments sufficiently short to be considered straight and

connected one to the other with a suitable angle $\theta \neq 0$ (see Fig. 1.4). This means that a suitable pressure loss as a function of the angle needs to be introduced in the interface conditions between one segment and the other. The other interface conditions will be given by the flow conservation (see (1.39) and Remark 1.1.3).



Fig. 1.4. Splitting of a curved domain into a sequence of rectilinear segments

Alternatively, here we would like to briefly address the definition of 1D models which are able to account for the effects of the transversal dynamics on the axial one, having the computational cost of the simplified models. The task is not easy, since we want to devise a sort of 1D models for the cheap description of a genuinely 3D dynamics.

Simplified models for curved pipes can be obtained for small curvatures of the vessels with a perturbation analysis of the rectilinear model (see [12]). Let us consider the non-dimensional parameter

$$D = 2\sqrt{2}\sqrt{\frac{r_w}{r_c}} \text{Re}$$
(1.47)

where r_w is the vessel radius, r_c is the curvature radius of the vessel axis $(r_c \to \infty \text{ in the straight case})$ and Re is the Reynolds number of the rectilinear case. D is called *Dean number*. Simplified models can be obtained for small values of the Dean number, which are for instance able to correctly compute the stagnation points of the secondary motion zones. For large values of D these models need to be suitably corrected, and the analysis becomes by far more difficult: a complete description of this approach can be found in [58], Chap. 4.

A different approach relies on the *theory of Cosserat* curves considered by Green and Naghdi in [29,30] (see also [41]). If we consider the reference frame (s, \hat{y}, \hat{z}) of Fig. 1.4 right, the basic idea of the Green and Naghdi approach is to represent the velocity field $\mathbf{u}(s, \hat{y}, \hat{z}, t)$ with respect a set of *shape functions* that depend only on the coordinates in the normal section \hat{y}, \hat{z} and are given by

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$$\mathbf{u}(s,\hat{y},\hat{z},t) = \sum_{n=0}^{N} \omega_n(s,t) \boldsymbol{\varphi}(\hat{y},\hat{z}), \qquad (1.48)$$

where ω_n are the coefficients of the velocity profile. This can be considered as a generalization of the straight vessel case, where we set for the axial velocity, $u_z(x, y, z, t) = \varphi(y, z)\overline{u}(x, t)$ being $\overline{u}(x, t)$ the average velocity and $\varphi(\hat{y}, \hat{z})$ a given velocity profile. Once a basis functions set is selected the unknowns are the coefficients ω_n , that can be computed by solving a suitable set of equations derived by mass and momentum conservation principles.

In principle, the accuracy of these models can be tuned by choosing a suitably large N, i.e. having a rich enough basis functions set. However, even for small values of N, mathematical difficulties of the obtained model imply high numerical costs. For more details, see [41].

1.1.6 The numerical solution of the 1D models

The wave propagation speeds in the large arteries are typically an order of magnitude higher than the average flow speeds. As mentioned previously, the characteristic system is inherently subcritical and does not produce shock under physiological conditions. Therefore the numerical challenge is to propagate waves for many periods without suffering from excessive errors in amplitude (*dissipation*) and in phase (*dispersion*) (see e.g. [42]). If the solution remains smooth then high-order methods are particularly attractive due to the fast convergence of the dispersion and dissipation errors with the order of the scheme [68].

Here, we limit ourselves to present a possible discretization of the problems, based on a *Taylor-Galerkin approach*, which is essentially a generalization of the classical *Lax-Wendroff* scheme for systems of conservation laws (see [42]).

Another more recent approach, based on the *discontinuous Galerkin approach* is addressed in [60], Chapter 10.

Taylor-Galerkin method

In this section we describe the numerical discretisation of the (Q, A) system described by equation (1.24) recast in the conservation form (1.28) given by

$$\frac{\partial \boldsymbol{Q}}{\partial t} + \frac{\partial \boldsymbol{G}}{\partial x}(\boldsymbol{Q}) = \boldsymbol{B}(\boldsymbol{Q})$$

The expressions for Q, G and B are given in (1.27).

We proceed to discretise equation (1.28) by adopting a second-order Taylor-Galerkin scheme. To this aim, we write the Taylor expansion truncated up to the second order terms at time t^n such that $\Delta t = t^{n+1} - t^n$, yielding

$$\boldsymbol{U}^{n+1} = \boldsymbol{U}^n + \Delta t \left. \frac{\partial \boldsymbol{U}}{\partial t} \right|^n + \frac{\Delta t^2}{2} \left. \frac{\partial^2 \boldsymbol{U}}{\partial t^2} \right|^n.$$
(1.49)

and we obtain

The time derivatives will be replaced by space derivatives, by exploiting the equations (1.28). In particular, we will use the abridged notation

$$G_{U} = \frac{\partial G}{\partial U}, \quad B_{U} = \frac{\partial B}{\partial U},$$
$$\frac{\partial Q}{\partial t} = B - \frac{\partial G}{\partial x}$$
(1.50)

$$\frac{\partial^2 \mathbf{Q}}{\partial t^2} = \mathbf{B}_U \frac{\partial U}{\partial t} - \frac{\partial^2 \mathbf{G}}{\partial t \partial x} = \mathbf{B}_U \frac{\partial U}{\partial t} - \frac{\partial}{\partial x} \left(\mathbf{G}_U \frac{\partial U}{\partial t} \right) = \mathbf{B}_U \left(\mathbf{B} - \frac{\partial \mathbf{G}}{\partial x} \right) - \frac{\partial \left(\mathbf{G}_U \mathbf{B} \right)}{\partial x} + \frac{\partial}{\partial x} \left(\mathbf{G}_U \frac{\partial \mathbf{G}}{\partial x} \right)$$
(1.51)

Remark 1.1.4 The presence of a non-constant source term and the explicit dependence of the momentum flux G on the variable x through $\beta(x)$ makes the derivation of the scheme slightly more complex than the standard Lax-Wendroff formulation. In particular we stress that, in contrast to the normal derivation, we have not further developed the x derivative of the fluxes, since for our problem

$$\frac{\partial \boldsymbol{G}}{\partial x} \neq \boldsymbol{G}_{\boldsymbol{U}} \frac{\partial \boldsymbol{U}}{\partial x}$$

because of the dependence of G on x through β .

From (1.49), (1.50) and (1.51) we obtain the following time-marching scheme

$$\boldsymbol{U}^{n+1} = \boldsymbol{U}^n - \Delta t \frac{\partial}{\partial x} \left[\boldsymbol{G}^n + \frac{\Delta t}{2} \boldsymbol{G}^n_{\boldsymbol{U}} \boldsymbol{B}^n \right] - \frac{\Delta t^2}{2} \left[\boldsymbol{B}^n_{\boldsymbol{U}} \frac{\partial \boldsymbol{G}^n}{\partial x} - \frac{\partial}{\partial x} \left(\boldsymbol{G}^n_{\boldsymbol{U}} \frac{\partial \boldsymbol{G}^n}{\partial x} \right) \right] + \Delta t \left(\boldsymbol{B}^n + \frac{\Delta t}{2} \boldsymbol{B}^n_{\boldsymbol{U}} \boldsymbol{B}^n \right).$$
(1.52)

Space discretisation is carried out by using linear finite elements. To that purpose, let us subdivide the domain Ω into N_{el} finite elements Ω_e , of size h_e . We indicate by \mathbf{V}_h the space of continuous vector functions defined on Ω , linear on each element, and with \mathbf{V}_h^0 the set formed by functions of \mathbf{V}_h which are zero at $x = x_1$ and $x = x_2$. Furthermore, we omit the subscript Ω in the $\mathbf{L}^2(\Omega)$ vector product.

Using the notation

$$G_{LW} = G + (\Delta t/2)G_U B$$
$$B_{LW} = B + (\Delta t/2)B_U B$$

and

$$(\mathbf{u}, \mathbf{v})_{\Omega} = \int_{\Omega} \mathbf{u} \ \mathbf{v} \ dx$$

as the standard $\mathbf{L}^2(\Omega)$ inner product, the finite element solution of (1.52) requires, for $n \geq 0$, to find U_h^{n+1} in \mathbf{V}_h which satisfies for all $\boldsymbol{\psi}_h$ in \mathbf{V}_h^0 that

$$(\boldsymbol{U}_{h}^{n+1}, \boldsymbol{\psi}_{h}) = (\boldsymbol{U}_{h}^{n}, \boldsymbol{\psi}_{h}) + \Delta t(\boldsymbol{G}_{LW}^{n}, \frac{\partial \boldsymbol{\psi}_{h}}{\partial x}) - \frac{\Delta t^{2}}{2} (\boldsymbol{B}_{\boldsymbol{U}}^{n} \frac{\partial \boldsymbol{G}^{n}}{\partial x}, \boldsymbol{\psi}_{h}) - \frac{\Delta t^{2}}{2} (\boldsymbol{G}_{\boldsymbol{U}}^{n} \frac{\partial \boldsymbol{G}^{n}}{\partial x}, \frac{\partial \boldsymbol{\psi}_{h}}{\partial x}) + \Delta t(\boldsymbol{B}_{LW}^{n}, \boldsymbol{\psi}_{h}).$$
(1.53)

The numerical initial condition U_h^0 will be taken as the finite element interpolant of the given initial data U_0 . A possible technique for computing the boundary values U_h^{n+1} is described later on.

In (1.53) we need to numerically integrate the terms containing the fluxes and sources. For the terms involving G^n and G^n_U we have projected each component on the finite element function space V_h via interpolation. The same applies for the other vector products which involve only G^n and G^n_U .

The term $d\beta/dx$ in \mathbf{B}^n and \mathbf{B}^n_U must be approximated in a piecewise constant manner to ensure that our numerical scheme represents constant solutions of the differential problem exactly. Therefore, on each element (x_e^l, x_e^u) we have approximated $d\beta/dx$ by $[\beta(x_i^u) - \beta(x_i^l)]/h_e$. For the remaining terms we have applied the same technique adopted for the fluxes. This gives rise to a piecewise linear discontinuous representation for the source terms.

Numerical boundary conditions

The numerical scheme (1.53) need to be complemented with boundary data Q or U at the boundaries of the domain Ω . We note that knowledge of W_1 and W_2 given in (1.33, 1.34) at the boundaries would in principle enable us to compute the corresponding values of Q or U, thanks to relation (1.35). However, given that the propagation speed is subcritical, only one condition has to be assigned at each end for the well-posedness of the differential problem. More precisely, we require information about the conservative variables at the ends of the domain, i.e. $Q(x_1, t)$ and $Q(x_2, t)$. To extract this from the characteristic information $W_1(x_1,t)$ and $W_2(x_2,t)$ we require an additional expression for the other characteristic variables $W_2(x_1, t)$ and $W_1(x_2, t)$ to recover Q using equation (1.35) which must also be compatible with the original differential problem. In the current approach, we have adopted a technique based on the extrapolation of the outgoing characteristics. We make the initial assumption that, at the boundary points $x = x_1$ and $x = x_2$, $\frac{d\beta}{dx} = 0$ and that K_R is negligible. We then assume that in the vicinity of the boundary the flow is essentially governed by the characteristic system (1.36). An equivalent derivation for the (A, Q) system can be found in [22]. Let us consider the proximal boundary $x = x_1$ over a generic timestep (the distal boundary is treated in a similar fashion). We assume that U^n is known and we linearise λ_2 in the second equation in (1.36) by taking its value at time t^n and at x = a. Recalling that $\lambda_2 < 0$, the solution corresponding to this linearised problem at the time level t^{n+1} gives

$$W_2^{n+1}(x_1) = W_2^n(x_1 - \lambda_2^n(x_1)\Delta t),$$

which is, in fact, a first-order extrapolation of the outgoing characteristic variable W_2 from the previous time level (see Fig. 1.5). In the general case, when the source term is not negligible, equation for W_2 reads

$$\frac{\partial W_2}{\partial t} + \lambda_2 \frac{\partial W_2}{\partial x} = f_2(W_1, W_2)$$

that can be still used for extrapolation in the form

$$W_2^{n+1}(x_1) = W_2^n(x_1 - \lambda_2^n(x_1)\Delta t) + f_2(W_1^n(x_1), W_2^n(x_1))\Delta t,$$

which corresponds to a first-order approximation in time. Higher order extrapolations in time can also be applied as well.



Fig. 1.5. Extrapolation of the characteristic W_2 in x_1

Using the extrapolated value of $W_2^{n+1}(x_1)$ and the value of $W_1^{n+1}(x_1,t)$ provided by the boundary condition, we are able to compute the required boundary data $U^{n+1}(x_1)$ using (1.35).

Similar considerations can be applied to the right boundary x_2 . This technique may also be easily adapted to incorporate boundary conditions that are not given in terms of the characteristic variables, for instance, if a given law for the pressure $p(x_1, t) = \psi(t)$ is imposed at the proximal boundary.

1.2 Zero-dimensional (0D) or lumped models

1.2.1 Derivation of the governing equations

As for the 1D models, lumped parameters models can be derived by general conservation principles or directly by averaging 3D and 1D models. In the former case, the key concept is the *compartment*, that is a part of the system

at hand that it is worth to be considered as a homogeneous unit. Following this approach, a continuous space dependence is lost, and the emphasis is on the behavior of the unit with respect to the rest of the system (input/output relations). Actually, transfer functions can be formulated either on physical or empirical relations. We will see an example of compartmental model in Sect. 1.2.5.

Here, we follow the latter approach, since we have already derived onedimensional models to be averaged. This approach is closer to the physics of the problem, which is useful in understanding the role of the parameters of the model and in their quantification. We will start from lumped parameter models of a simple vascular districts and then, by application of conservation principles providing matching conditions among the districts, we will build more general models.

Let us consider again the simple artery Ω , illustrated in Fig. 1.1, of length $l = |x_2 - x_1|$. We define the (volumetric) mean flow rate over the whole district as the quantity

$$\hat{Q} = \frac{\rho}{l} \int_{\Omega} u_1 d\upsilon = \frac{\rho}{l} \int_{x_1}^{x_2} \left(\int_{\mathcal{S}(x)} u_x d\sigma \right) dx = \frac{\rho}{l} \int_{x_1}^{x_2} Q(x) dx.$$
(1.54)

Similarly, we define the *mean pressure and area* over the length of the compartment as

$$\hat{p} = \frac{1}{l} \int_{x_1}^{x_2} P dx, \quad \hat{A} = \frac{1}{l} \int_{x_1}^{x_2} A dx.$$
(1.55)

Starting from equations (1.24) for this domain, we integrate the continuity equation along the axial direction $(x_1 \leq x \leq x_2)$ to obtain

$$l\frac{dA}{dt} + Q_2 - Q_1 = 0 (1.56)$$

where we have set

$$Q_1(t) = Q(t, x_1), \quad Q_2(t) = Q(t, x_2).$$
 (1.57)

Observe that now \hat{A} depends only on time, so we have an ordinary time derivative.

In considering the momentum equation, we add the following simplifying assumptions:

- 1. the contribution of the convective term $\partial_x(\alpha Q^2/A)$ may be neglected; and
- 2. the variation of A (and β) with respect to x is small compared to that of P and Q.

The first assumption is particularly suited to represent the peripheral circulation, where blood flow is in general quite slow. The second assumption is

reasonable when the axial average is carried out over short segments. It basically amounts to replace A in the momentum equation with a constant value for the area that in general is assumed to be the area at rest A_0 . With these assumptions, averaging over x of $(1.24)_2$ yields

$$\frac{\rho l}{A_0} \frac{d\hat{Q}}{dt} + \frac{\rho K_R l}{A_0^2} \hat{Q} + P_2 - P_1 = 0.$$
(1.58)

where

$$P_1(t) = P(t, x_1), \quad P_2(t) = P(t, x_2).$$
 (1.59)

As for 1D models we have now the problem of closing system (1.56, 1.58), by adding a wall mechanics law. In particular, if we assume the simple law (1.21) to hold, we have

$$\int_{x_1}^{x_2} \frac{\partial p}{\partial t} dx = \int_{x_1}^{x_2} \frac{\beta}{2\sqrt{A}} \frac{\partial A}{\partial t} dx.$$

Now, if we exploit the second assumption above, we obtain

$$l\frac{d\hat{p}}{dt} = \frac{l\beta}{2\sqrt{A_0}}\frac{d\hat{A}}{dt}$$

which we write, for convenience, as

$$\frac{d\hat{A}}{dt} = k_1 \frac{d\hat{p}}{dt} \tag{1.60}$$

where $k_1 = \frac{\sqrt{A_0}}{\beta}$. Substituting (1.60) into (1.56) we obtain

$$k_1 l \frac{d\hat{p}}{dt} + Q_2 - Q_1 = 0 \tag{1.61}$$

that together with (1.58) represents the lumped parameter models for the vessel at hand.

These equations are also found in the analysis of electrical circuits. Before the related equations could be (rapidly) solved using digital computers, early simulations of flow in the vascular system were based on analog circuits mimicking its structure, see for instance [79]. In the electric network analogy, the blood flow rate is assimilated to the current, while the blood pressure corresponds to the voltage as we have summarized in Tab. 1.1.

In order to exploit this electrical analogy, we recast the system (1.58, 1.61) as

		Hydraulic	Electric	
		Pressure	Voltage	
		Flow rate	Current	
		Blood viscosity	Resistance R	
		Blood inertia	Inductance L	
		Wall compliance	Capacitance ${\cal C}$	
R		P L dO	Q P Q	$\begin{pmatrix} Q \\ \downarrow \\ \uparrow \\ \uparrow \\ dP \end{pmatrix} P$
	P = RQ	$L\frac{dQ}{dt} =$	= <i>P</i>	$C\frac{dI}{dt} = Q$

 Table 1.1. Correspondence table of the analogy between electric and hydraulic networks.

 \pm =Reference Pressure Value

Fig. 1.6. Notation used in the electrical analogy of the circulatory system

$$\begin{cases} C\frac{d\hat{p}}{dt} + Q_2 - Q_1 = 0\\ L\frac{d\hat{Q}}{dt} + R\hat{Q} + P_2 - P_1 = 0. \end{cases}$$
(1.62)

The coefficients R, L and C are associated to elements of a circuit as depicted in Fig. 1.6, where the corresponding equation is recalled at the bottom. We recall hereafter their physical significance.

- **Resistance** The coefficient $R = \frac{\rho K_R l}{A_0^2}$ in equation (1.62) represents the *resistance* induced to the flow by the blood viscosity. Different expressions for R can be obviously obtained for different velocity profiles or if a non-Newtonian rheology is introduced into the model (see e.g. [66], [79], [23]).
- **Inertia** The coefficient $L = \frac{\rho l}{A_0}$ in equation (1.58) represents the inertial term in the momentum equation and it will be called the *inductance* of the flow.
- **Compliance** It is characterized by the coefficient $C = k_1 l$ that represents the mass storage term in the mass conservation law, due to the *compliance* of the vessel.

For instance, if we assume Poisseuille flow (i.e. fully developed flow with a constant pressure gradient) and that the vessel is a cylinder of constant

circular section we have

$$R = \frac{8\pi\rho\nu l}{\pi^2 r_0^4} = \frac{8\mu l}{\pi r_0^4}; \quad L = \frac{\rho l}{\pi r_0^2}; \quad C = \frac{3\pi R_0^3 l}{2Eh_0}$$

The system of equations (1.62) involve the mean flow rate and pressure over the vascular segment at hand and the *boundary* values of pressure and flow rate Q_i, P_i , with i = 1, 2. Strictly speaking, the term *boundary* is inappropriate, since the continuous space dependence has been lost in the axial average, and they simply represent input/output quantities exchanged by the vessel with the rest of the systems. However, we will retain the term, since it is related to the physical derivation of the equations. In particular, in order to close problem (1.62), we need to introduce some *boundary conditions*. This means that we identify the *input data* of the district at hand. For instance, suppose that Q_1 and P_2 are given. Then, (1.62) represents a system of two equations for four unknowns, \hat{Q}, \hat{p}, P_1 and Q_2 . The dynamic of the system is represented by \hat{p} and \hat{Q} , i.e. by the unknowns that are under time derivative (the *state variables*). We approximate now the unknowns on the upstream and downstream sections with the state variables,

$$\hat{p} \approx P_1, \quad \hat{Q} \approx Q_2,$$

that corresponds to assume that the *output* of the district is given by the *state* variables. With these additional assumptions, which are reasonable for a short pipe, the lumped parameter model becomes:

$$\begin{cases} C\frac{dP_1}{dt} + Q_2 = Q_1 \\ L\frac{dQ_2}{dt} + RQ_2 - P_1 = P_2. \end{cases}$$
(1.63)

where the input data have been put on the right hand side. This system can be illustrated by the electric \mathcal{L} -network shown in Figure 1.7 (left).

$$\begin{array}{c} Q_1 \\ \hline P_1 \end{array} \xrightarrow{R} \begin{array}{c} L \\ \hline \\ \hline \\ \hline \\ \end{array} \end{array} \xrightarrow{Q_2} \begin{array}{c} Q_2 \\ \hline \\ P_2 \end{array} \xrightarrow{Q_1} \begin{array}{c} L \\ \hline \\ P_1 \end{array} \xrightarrow{R} \begin{array}{c} Q_2 \\ \hline \\ \hline \\ \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \\ \hline \\ \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \\ \hline \\ \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \\ \hline \\ \hline \\ \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \\ \hline \\ \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \\ \hline \\ \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \\ \hline \\ \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \\ \hline \\ \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \\ \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \end{array} \xrightarrow{Q_2} \begin{array}{c} \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \end{array} \xrightarrow{Q_2} \begin{array}{c} \hline \end{array} \xrightarrow{Q_2} \begin{array}{c} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \begin{array}{c} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \begin{array}{c} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \begin{array}{c} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \begin{array}{c} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \begin{array}{c} \end{array} \xrightarrow{Q_2} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \xrightarrow{Q_2} \xrightarrow{Q_2} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \xrightarrow{Q_2} \xrightarrow{Q_2} \end{array} \xrightarrow{Q_2} \xrightarrow{Q_2}$$

Fig. 1.7. Lumped \mathcal{L} -network (top) and \mathcal{L} -inverted network (bottom) equivalent to a short pipe

In a similar way, if the pressure P_1 and the flow rate Q_2 are prescribed, we still approximate the quantities at the upstream and downstream sections by the state variables, i.e. $\hat{p} \approx P_2$, $\hat{Q} \approx Q_1$, yielding the system represented by an electric analog, called an \mathcal{L} -inverted network, depicted in Figure 1.7(right).

If the mean pressures P_1 and P_2 are prescribed, the system can be modelled by a cascade connection of \mathcal{L} and \mathcal{L} -inverted lumped representations, yielding a \mathcal{T} -network (Figure 1.8). Similarly, if both flow rates Q_1 and Q_2 are prescribed, the vessel Ω is described by an electric π -network, obtained as a cascade connection of a \mathcal{L} -network and a \mathcal{L} -inverted network (Figure 1.9).



Fig. 1.8. Cascade connection of a \mathcal{L} -inverted and a \mathcal{L} -network (top), lumped \mathcal{T} -network (bottom)



Fig. 1.9. Cascade connection of a \mathcal{L} -network and a \mathcal{L} -inverted one (top), lumped π -network (bottom)

The four different representations arise from four different possible assumptions about the data prescribed at the upstream and downstream sections. In other words, the four different lumped models can be considered as the lumped parameter simplifications of four different "boundary" values problems.

Remark 1.2.1 An extensive analysis of the relation between 1D and 0D models of a cylindrical vessel can be found in [47]. We point out however that different ways can be pursued for devising lumped parameter models. Among the most recent, we mention the one proposed in [54] which is based on suitable approximations of the inverse Laplace transform of the axisymmetric Stokes equations in rigid vessels.

1.2.2 Lumped parameters models for the heart

The heart is subdivided into the right and the left parts, separated by the septum. The right heart supplies the pulmonary circulation, while the left pumps the blood into the systemic tree. Each side consists of two chambers, the atrium and the ventricle, separated by the atrioventricular valves (the tricuspid valve in the right side, the mitral valve in the left one). Their role is to receive fluid at low pressure and transfer it to a higher pressure region, acting as a *pump*. A possible representation of heart working is given by left ventricle pressure-volume diagrams (see [35]).

Each ventricle can be described therefore as a vessel where the most significant feature is the compliance and the compliance changes with time (see [5, 35, 38, 67]).

The starting point for a candidate mathematical model is the relation that links internal pressure with the radius of an elastic spherical ball filled with fluid. Here and in the following we take $P_{ext} = 0$. We have

$$\pi R^2 P = 2\pi E h_0 R \frac{R - R_0}{R_0},$$

where R_0 is the reference sphere radius (corresponding to P = 0), h_0 is a reference thickness of the ball surface and E denotes the Young's modulus. The contraction of the cardiac muscle may be taken into account by an increase of E (stiffening) and by a shortening of the muscle length (i.e. a reduction of R_0). It is more convenient to express this relation as a function of the volume V, instead of the radius. By recalling that $V = \frac{4}{3}\pi R^3$, a linearisation procedure leads to

$$P = \frac{E(t)h_0}{2\pi R_0^3(t)} \left(V - V_0(t)\right),$$

where we have indicated the coefficients that change in time because of the action of the muscle. This simplified model does indeed describe the major characteristic of the ventricle. If we indicate $C(t) = \frac{2\pi R_0^3(t)}{E(t)h_0}$ we may re-write the relation in the mode compact form

$$V(t) = C(t)P(t) + V_0(t).$$

By differentiating with respect to time we obtain

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$$\frac{dV}{dt} = Q = \frac{dC}{dt}P + C\frac{dP}{dt} + M_Q(t)$$
(1.64)

where Q represents the (incoming) flow rate and $M_Q = \frac{dV_0}{dt}$ is the action exerted by the contraction of the cardiac muscle.

A lumped representation (electric analog) of each ventricle⁴ is given in Fig. 1.10, where R accounts for an additional viscous resistance inside the ventricle. Here, M_Q is represented by a current generator.



Fig. 1.10. Electric analog of the lumped parameter model of a ventricle



Fig. 1.11. P - Q curve in a diode, representing the electric analog of a heart valve.

The electrical analog of the presence of heart valves has been represented in Fig. 1.10 by *diodes*. Ideally, the behaviour of a diode is described by the curve depicted in Fig. 1.11 and given by

$$\begin{cases} P = 0 \text{ if } Q > 0\\ Q = 0 \text{ if } P < 0. \end{cases}$$

This means that the diode representation does not allow flow through the valve if the pressure is higher downstream than upstream. If the upstream pressure is higher, the diode allows the flow without any pressure loss. This is an "ideal" behaviour. Real valves have a different behaviour that can be represented by the curve

⁴ A mechanical representation of the heart working based on the classical Hill's model for the muscle can be found in [39] and [82].

$$Q = Q_S \left(e^{\alpha P} - 1 \right) \tag{1.65}$$

called *Shockley equation*. In some cases, this equation has been approximated by a piecewise polynomial curve (see e.g. [46]).

The presence of diodes introduces a nonlinear term in the system. However, if we resort to the Shockley model, the nonlinear terms are smooth in terms of mathematical regularity.

1.2.3 Lumped parameters models for the circulatory system

In the previous sections we have introduced lumped parameter description of two basic compartments, a segment of vessel and the heart. A possible model for the vascular network can be derived by "connecting" these compartments by means of appropriate *matching conditions*, in a way similar to the one pursued for the 1D model of bifurcations in Sect. 1.1.5. Matching conditions will be actually driven by *continuity of flux* and *balance of momentum* at the interfaces. More precisely, since our lumped parameter models deal with the flow rate Q and the pressure P, matching conditions will essentially state the continuity of these variables at the interfaces. In the electric analog, these relations correspond to the application of the classical *Kirchhoff laws* for the nodes (conservation of current/flow rate) and the nets (conservation of the voltage/pressure). For these reasons, lumped parameter models will also be referred to as *Kirchhoff* (K) models.

A sketch of possible connections of different compartments is given in Fig. 1.12.

More detailed models for the circulation are proposed in [52, 80], where hundreds of elementary compartments are considered.

Mathematical and numerical analysis of lumped parameters models

From the mathematical viewpoint, a general representation of lumped parameters models is a system of differential-algebraic equations (DAE) of the form

$$\begin{cases} \frac{d\mathbf{y}}{dt} = \mathbf{b}(\mathbf{y}, \mathbf{z}, t) & t \in (0, T] \\ G(\mathbf{y}, \mathbf{z}) = 0 \end{cases}$$
(1.66)

together with the *initial condition vector* $\mathbf{y}|_{t=t_0} = \mathbf{y}_0$. Here, \mathbf{y} is the vector of state variables, the vector \mathbf{z} contains the other variables of the network and G represents the algebraic equations derived from the Kirchhoff laws. Differentiating the algebraic equations with respect to time we get

$$\frac{dG(\mathbf{y}, \mathbf{z})}{dt} = \mathbf{J}_{\mathbf{y}} \frac{d\mathbf{y}}{dt} + \mathbf{J}_{\mathbf{z}} \frac{d\mathbf{z}}{dt} = 0$$

where $\mathbf{J}_{\mathbf{y}} = \frac{\partial G}{\partial \mathbf{y}}$ and $\mathbf{J}_{\mathbf{z}} = \frac{\partial G}{\partial \mathbf{z}}$ are the Jacobian matrices with respect to \mathbf{y} and \mathbf{z} . Assuming that $J_{\mathbf{z}}$ is non singular, the DAE system is said to be of



Fig. 1.12. Lumped parameters model for a branched vessel as a cascade of T and π networks

index 1 (see e.g. [26]). This is the most frequent case in problems concerning lumped parameters models of the vascular system. We can then write

$$\frac{d\mathbf{z}}{dt} = -\mathbf{J}_{\mathbf{z}}^{-1}\mathbf{J}_{\mathbf{y}}\frac{d\mathbf{y}}{dt} = -\mathbf{J}_{\mathbf{z}}^{-1}\mathbf{J}_{\mathbf{y}}\mathbf{b}(\mathbf{y}, \mathbf{z}, t).$$
(1.67)

Assuming that an initial vector \mathbf{z}_0 is available, the first equation of (1.66) and (1.67) can be rewritten as the classical Cauchy problem

$$\begin{cases} \frac{d\mathbf{w}}{dt} = \mathbf{a}(\mathbf{w}, t) & t \in (0, T] \\ \mathbf{w}(t_0) = \mathbf{w}_0, \end{cases}$$
(1.68)

where $\mathbf{w} = [\mathbf{y}, \mathbf{u}]^T$ and $\mathbf{a} = [\mathbf{b}, -\mathbf{J}_{\mathbf{z}}^{-1}\mathbf{J}_{\mathbf{y}}\mathbf{b}]^T$. For the analysis of this problem we can refer to classical mathematical results, e.g. [32]. We will recall the following results:

- 1. if $\mathbf{a}(\mathbf{w}, t)$ is continuously differentiable there exists a time interval $[0, T^*]$ in which the solution of the problem exists and is unique;
- 2. if, moreover, the derivatives $\partial \mathbf{a}_i / \partial w_j$ are bound in the time interval [0, T], then the solution of the Cauchy problem exists and is unique in [0, T].

Numerical solution of Cauchy problems like (1.68) is an important branch of scientific computing. A general introduction can be found in [40].

When the DAE problem (1.66) is of index higher than one, which is not the usual situation in this kind of problems, both the mathematical and numerical analyses become more involved. We refer the interested readers to [3,26].



Fig. 1.13. Left: Terminal impedance for the peripheral circulation. Right: Lumped parameters representation (electrical networks) of possible impedances: (a) pure resistive load; (b) original windkessel model; (c) three elements windkessel; (d) four elements windkessel



Fig. 1.14. Modulus (left) and angle (right) for the transfer function of the four networks in Fig. 1.13(right)

1.2.4 Lumped parameter models for terminal vessels

By using the electrical analogy presented above, we now consider briefly some possible model for the terminal vessels to be used as stand-alone models or for computing boundary conditions to 1D networks (Sect. 1.1.4).

Pure resistive load: In some cases, the dynamics of blood in peripheral vessels is adequately represented by a simple algebraic law, see Fig. 1.13(right), given by

$$p_T(t) = RQ_T(t), \tag{1.69}$$

corresponding to the impedance $Z_T(t-\tau) = R\delta(\tau-t)$, where δ denotes the Dirac delta. This is particularly true for small vessels where the heart pulsatility has been almost completely attenuated by the larger vessel compliance and the motion is almost steady. An effective way of including this condition into the 1D model is based on the introduction of a *reflection coefficient*. The reflection coefficient, R_t , is defined in [43] as the ratio of the magnitude of change of pressure across the reflected wave, dP, to the magnitude of change of pressure in the incident wave, ΔP . It is a function of the terminal resistance at the vessel outflow and is given by

$$R_t = \frac{dP}{\Delta P} = \frac{AR - \rho c}{AR + \rho c} = \frac{R - \rho c/A}{R + \rho c/A}$$

Here, the venous pressure is assumed to be zero.

The value of R_t permits the outflow at the boundary to vary between a free outflow when $R_t = 0$ and a blockage when $R_t = 1$. Using this relationship and equation (1.35) which relates the velocity u and the characteristic variables, W_1 and W_2 , the velocity, u^* , at the boundary can be specified to be

$$u^{\star} = \left[\frac{(u_0 + u_l)}{2} + 2(c_l - c_0)\right] (1 - R_t)$$
(1.70)

where u_0 and c_0 are the undisturbed states on the right-hand side at t = 0. The characteristic variable W_1 remains unaltered at the outflow boundary and is given as

$$W_1 = u_l + 4c_l = u^* + 4c^*$$

and therefore c^* at the boundary must be

$$c^{\star} = \left[\frac{u_l - u^{\star}}{4}\right] + c_l. \tag{1.71}$$

We define the incoming wave, W_2 , as

$$W_2 = u_r - 4c_r = u^* - 4c^*. \tag{1.72}$$

Substituting equations (1.70) and (1.71) into equation (1.72) and choosing $c_l = c_r$ at the boundary, leads us to the values of u_r and A_r to be prescribed at the boundary, these are

$$u_r = (1 - R_t)[(u_0 + u_l) + 4(c_l - c_0)] - u_l$$

$$A_r = A_l.$$

The characteristic variable, W_2 , at the outflow can now be calculated using equation (1.34).

Remark 1.2.2 There is another possible definition for the reflection coefficient which is more suitable for prescribing boundary conditions based on the Riemann variables. At the terminal boundaries (subscript T), using equations (1.35) and (1.69) we have

$$\begin{cases} W_1 = \frac{p_T}{A_T(p_T)R_T} + 4A^{1/4}(p_T)\sqrt{\frac{\beta_T}{2\rho}} \\ W_2 = \frac{p_T}{A_T(p_T)R_T} - 4A^{1/4}(p_T)\sqrt{\frac{\beta_T}{2\rho}} \end{cases}$$

We define the characteristic reflection coefficient as

$$R_c = -\frac{W_2}{W_1}$$

that identifies the fraction of incident Riemann variable W_1 actually transformed into the backward propagating⁵ Riemann variable W_2 by the resistive load. By a simple linearization (see [20]) we can compute

$$R_c = \frac{R - R_a}{R + R_a}$$

with $R_a = 0.25\sqrt{2\rho/\beta_T^3\sqrt{A_0}}$. We still have that for $R_T \to \infty$, $R_c \to 1$ that implies that $W_2 = -W_1$ and thus u = 0 from their definition (1.33-1.34). Since W_1 can be easily computed by extrapolation along the characteristic curves, the condition

$$W_2 = -R_c W_1 \tag{1.73}$$

readily yields a boundary value for W_2 .

Windkessel models: A more accurate representation of the terminal load is provided by the models including some possible dynamics related to vessel compliance and blood inertia. The first model was introduced by Otto Frank in 1899 [25]. It included a peripheral resistance and a compliance (see Fig. 1.13(b)) which yields a value of the impedance

$$\zeta_T(\omega) = \frac{R}{1 + \sqrt{-1}\omega RC}$$

This model has been called *Windkessel* in analogy with the device (made of a reservoir and an air chamber) converting the alternate (periodic) water pumping of firemen into a steady flow. In order to better fit the experimental results (see [50,80]), this basic model has been successively refined by Westerhof and his co-workers with the introduction of a second resistance (see

 $^{^{5}}$ The negative sign indicates the change in propagation direction.

Fig. 1.13(c)). The model has been called a *three-element Windkessel* or also familiarly *Westkessel*, and corresponds to an impedance value of

$$\zeta_T(\omega) = \frac{R_1 + R_2 + \sqrt{-1}\omega R_1 R_2 C}{1 + \sqrt{-1}\omega R_2 C}$$

More recently (see [6,71]), it has been pointed out that the fitting of experimental data with the three elements Windkessel model requires values that are not clearly related to the physical properties of the arteries. A new improvement of the model has been therefore proposed, leading to a four-element network (Fig. 1.13 right, (d)) that includes an inductor for inertial effects. The impedance of the model is

$$\zeta_T(\omega) = \frac{R_1 R_2 - C R_1 R_2 L \omega^2 + \sqrt{\omega} (R_1 + R_2)}{R_1 - C R_2 L \omega^2 + \sqrt{\omega} (L + C R_1 R_2)}.$$

The determination of an appropriate estimate of the parameters of these models is a difficult problem. The interested reader is referred to [6, 50, 71]. An intuitive and systematic approach to estimate the parameters of a three-element model is presented in [2].

The moduli of impedances and angles of the four networks considered in Fig. 1.13 are drawn in Fig. 1.14.

Remark 1.2.3 For including this kind of conditions in the 1D model, an alternative to equation (1.38) consists in formulating a condition in the timedomain for the Riemann variables (see the previous remark). For instance, by setting $R = R_1 + R_2$, the three-element Windkessel model corresponds to the boundary condition

$$R_2 C \frac{R_a + R_1}{R_a + R} \frac{dW_2}{dt} + W_2 = R_2 C \frac{R_a - R_1}{R_a + R} \frac{dW_1}{dt} - R_c W_1$$

that generalizes (1.73) (see [20]).

Structured tree model: The dynamics spanned by family of Windkessel models is quite crude and in particular the wave propagation in the peripheral circulation is not well represented. A possible way for accounting these effects is the introduction of lumped parameters models with many elements, following the *geometrical multiscale approach* discussed in Chapter 2. A different approach, still resorting to the definition of an appropriate impedance function has been introduced in [53] and it is based on the representation of the terminal vessels as a structured tree (see Fig. 1.15).

By classical arguments in the wave theory (see e.g. [58]), the impedance at the beginning of a vessel with length l can be written as a function of the impedance at the end:

$$\zeta_{beg}(\omega) = \frac{g^{-1}\sqrt{-1}\sin(\omega l/c) + \zeta_{end}(\omega)\cos(\omega l/c)}{\cos(\omega l/c) + g\sqrt{-1}\zeta_{end}(\omega)\sin(\omega l/c)},$$
(1.74)



Fig. 1.15. Structured asymmetric tree representation of peripheral circulation

where

$$g = A_0 \sqrt{\frac{3\sqrt{A_0}K}{2E\pi h\rho}}, \quad c = \sqrt{\frac{2E\pi hK}{3\sqrt{A_0}\rho}}$$

and K is an appropriate function of the Womersley number. The basic idea of this peripheral model is therefore to apply this formula for the terminal impedance ζ_T that is expressed in this way as a function of the impedance at the end of the first peripheral vessel. The latter will be computed recursively by:

- 1. giving a model for the bifurcations in terms of impedance of parent and daughters vessels;
- 2. applying (1.74) for each branch of the vascular tree.

Continuity of pressure and flow rate at the bifurcation yields the condition linking the impedance of the parent vessel to the impedances of the daughter vessels (we assume branching with only two daughters)

$$\zeta_{parent} = \left(\frac{1}{\zeta_{d1}} + \frac{1}{\zeta_{d1}}\right)^{-1}.$$

Each branch of the tree is then scaled on the basis of the following assumptions:

1. at each bifurcation, the daughters branches scale asymmetrically with respect to the parent one with radius factors α , β that can be determined on the based of optimal branching considerations (see [53]);
2. under a certain threshold on the radius it is possible to assume that the impedance is purely a resistive load, known by experimental data.

Observe that the threshold is applied to the vessel radii and not to the number of branchings, so the number of branches is in general a function of the position of the interface with the 1D model and will be not assumed to be known a priori.

A more detailed code for this impedance modeling can be found in [57]. Results presented in [55] show that this approach for terminal outflow boundary conditions provide reliable results. In particular, it provides a closer physiological behavior than the Windkessel models, with a correct phase-lag between flow and pressure.

See also [70] for an advanced application of this approach.

1.2.5 Modeling the interaction between cardiovascular system and chemical species

In the previous sections we have assumed that the parameters of the models depend on the morphological features and are constant in time (see equation (1.58)). This is a strong simplification since daily experience indicates that these parameters change in different physiological situations. Heavy exercise requires a body's response that involves biochemical reactions, chemicals transport (oxygen in particular) and definitely adjustments in blood flow. The cardiovascular system has feedback mechanisms that regulate its working activity and are essential for life (see e.g. [35]). The dynamics underlying these phenomena is extremely heterogeneous and complex, involving different chemical species, the cardiovascular and the nervous systems from peripheral to central districts (see [57], Chap. 7). There are long-term mechanisms that are essentially driven by the renal activity. Presence of water and salt or hormones can be adjusted by the kidneys for controlling arterial pressure. Other mechanisms belong to the short term regulation effects. In the latter case, the central nervous system (CNS) is the main mediator, involving baroreceptors, mechanoreceptors and chemoreceptors. The latter are sensitive to chemicals in blood (see [60]). When the oxygen concentration drops, chemoreceptors increases cardiac strength and vasoconstriction. Baroreceptors are sensitive to the pressure alterations. They are located in the carotid sinus and the aortic arch. The role of the *baroreflex effect* is to keep the pressure within a physiological range. Mechanoreceptors are located in the atria and in the pulmonary veins and control arterial pressure by acting on the venous volume.

Other tuning dynamics are specifically present in the cardiovascular system. In particular, the *autoregulation* is a mechanism for maintaining an almost constant oxygen supply (in particular in the brain), driven by the smooth muscles in the vascular walls (see [1, 35]).

Lumped parameter models are an affordable mathematical and numerical tool for modeling these complex phenomena. Here we address some basic



Fig. 1.16. Simplifed compartment model of the circulation.

ideas for including feedback mechanisms in the models introduced so far. We essentially need

- 1. lumped parameter models for chemical species, and
- 2. constitutive equations establishing the dependence of the parameters of the cardiovascular model on the concentration of chemicals.

We present these topics by means of an example based on Chap. 1 of reference [10].

Cardiovascular model

We assume the the cardiovascular system is represented by means of a set of four compartments (see Fig. 1.16):

Right heart/lungs/left heart acting as a forcing term for the whole system. Large arteries represented by a resistance R_a and a compliance C_a .

Systemic arteries that are represented by the compliance C_s and three sub-districts

- 1. skeletal muscle represented by the resistance R_{sm} and with flow rate Q_{sm} ;
- 2. splanchnic compartment with resistance R_{sp} and flow rate Q_{sp} ;
- 3. other organs with resistance R_o and flow rate Q_o .
- The total systemic resistance will be given by

$$R_s = \left(R_{sm}^{-1} + R_{sp}^{-1} + R_o^{-1}\right)^{-1}.$$

Venous system that is represented by the compliance C_v as their deformability is the more relevant feature of the veins.

The cardiovascular system will be therefore modelled by a lumped parameter model of the form

$$\begin{cases} C_{a} \frac{dP_{a}}{dt} = Q_{a} - \frac{P_{a} - P_{s}}{R_{a}} \\ C_{s} \frac{dP_{s}}{dt} = \frac{P_{a} - P_{s}}{R_{a}} - \frac{P_{s} - P_{v}}{R_{s}} \\ C_{v} \frac{dP_{v}}{dt} = Q_{a} - C_{a} \frac{dP_{a}}{dt} - C_{s} \frac{dP_{s}}{dt} \\ Q_{sm} = \frac{P_{s} - P_{v}}{R_{sm}}, \quad Q_{sp} = \frac{P_{s} - P_{v}}{R_{sp}}, \quad Q_{o} = \frac{P_{s} - P_{v}}{R_{o}}. \end{cases}$$
(1.75)

Here Q_a is driven by the heart activity that can be simply given by

$$\begin{cases}
Q_a = \frac{V_{str}}{T} \\
V_{str} = V_{ed}(P_v) - V_{u,vent} - \frac{P_a}{E}.
\end{cases}$$
(1.76)

Here, T is the *heart period*, V_{str} is the stroke volume of the heart. The latter is assumed to be a function of the end-of-diastole volume V_{ed} , which is in turn a function of the venous pressure P_v , of the (constant) unstressed ventricular volume $V_{u,vent}$ and of the arterial pressure P_a by means of the heart *elastance* E.

Chemical model

Let us start considering only the dynamics of oxygen. We denote by $[O_2]_i$ the oxygen concentration in compartment i ($i \in (a, v, sm, sp, o)$) and by V_i is the volume of the *i* compartment. A possible law for the dynamics of oxygen in the systemic compartments (i = sm, sp, o) is

$$V_i \frac{d[O_2]_i}{dt} = -r_i([O_2]_i, t) + Q_i(t) \left([O_2]_a - \sigma_i[O_2]_i \right),$$
(1.77)

where r_i is the oxygen consumption rate and σ_i is a partition (constant) coefficient, function of the oxygen concentration in the different compartments *at rest*. The first term on the right-hand side is driven by the chemical reactions, while the second one is related to the *transport* associated to the blood flow. In the arterial compartment it is reasonable to assume that the oxygen consumption is negligible, so that $[O_2]_a$ is constant. In the venous compartment, by mass conservation, we collect the residual oxygen coming from the systemic compartments and it concentration is thus given by

$$[O_2]_v = \sum_{i=sm,sp,o} \frac{Q_i}{Q_a} \sigma_i [O_2]_i.$$

A possible generalization of this equation to the multi-chemical case is the following. We introduce a *vector* of chemical concentration \mathbf{c}_i so that c_{ki} is the concentration of the $k^t h$ species in compartment *i*. This model is given by

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$$\begin{cases} V_i \frac{d\mathbf{c}_i}{dt} = A \boldsymbol{\psi}_i(\mathbf{c}_i, t) + \mathbf{b}_i(\mathbf{c}_a, \mathbf{c}_i, Q_i, t); & i = sm, sp, o \\ \mathbf{c}_v = \sum_{i = sm, sp, o} \frac{Q_i}{Q_a} S_i \mathbf{c}_i \\ \mathbf{c}_a = \mathbf{c}_a(\mathbf{c}_a^0, \mathbf{c}_v) \end{cases}$$
(1.78)

where S_i is a diagonal matrix with entries given by the partition coefficients σ_{ki} and \mathbf{c}_a^0 is the arterial vector concentration at rest. Moreover, $\boldsymbol{\psi}_i$ is the vector of consumption rates associated to chemical reactions and A_i is the so-called *stoichiometric matrix* representing the weighed connection of the species involved in the chemical reactions. Term \mathbf{b}_i represents the convection contribution to the chemical dynamics, driven by the blood flow. It is worth pointing out that since chemical reactions can have different time scales associated with each reaction, differential systems like (1.78) can in practice be *stiff*.



Fig. 1.17. Three compartments representation of the feedback cardiovascular model

Feedback model

The dependence of chemical dynamics on fluid dynamics is clearly defined in the transport term \mathbf{b}_i of equation (1.78). Let us consider now how the chemical dynamics can affect the blood flow (see Fig. 1.17). To this aim, following [75], we introduce some new unknowns:

 f_{es} represents the efferent sympathetic activity;

 f_{ev} is the efferent vagal activity;

 f_{cs} is the *carotid sinus firing rate*, that is the action generated by pressure alterations at the level of the carotid sinus;

 f_{cm} is the chemoreflex activity;

 R_i with i = sm, sp, o the state variables determining the systemic resistances and influenced by the vagal activity;

 x_i with i = sm, sp, o the state variables determining the systemic resistances and influenced by the chemoreflex activity;

 P_n a reference pressure value.

We assume that the heart period T and the elastance E are influenced by the efferent vagal and sympathetic activities. In particular, we assume that

$$\begin{cases} \frac{dT}{dt} = \frac{1}{\tau_T} \left(T_0 - T - \sigma_{T,s}(f_{es}) - \sigma_{T,v}(f_{ev}) \right) \\ \frac{dE}{dt} = \frac{1}{\tau_E} \left(E_0 - E - \sigma_{T,s}(f_{es}) \right) \\ f_{es} = f_{es,\infty} + \left(f_{es,0} - f_{es,\infty} \right) \exp(-k_{es}f_{cs}) \\ f_{ev} = \frac{f_{ev,0} + f_{ev,\infty} \exp((f_{cs} - f_{cs,0})/k_{ev})}{1 + \exp((f_{cs} - f_{cs,0})/k_{ev}))} \\ f_{cs} = \frac{f_{min} + f_{max} \exp((P_a - P_n)/k_a)}{1 + \exp((P_a - P_n)/k_a)} \end{cases}$$
(1.79)

where σ , E_0 , T_0 , $f_{,\infty}$, $f_{,0}$, f_{min} , f_{max} and k (with their respective indices) represent appropriate functions and constants. The reference pressure P_n is driven by the chemoreflex activity and its temporal variation is given by

$$\frac{dP_n}{dt} = \frac{1}{\tau_{P_n}} \left(P_{n,0} - P_n - \sigma_{P_n,cm}(f_{cm}) \right)$$
(1.80)

The systemic resistances are influenced both by the baroreflex and chemoreflex activities. More precisely, for i = sm, sp, o we have

$$\begin{cases} \frac{dR_i}{dt} = \frac{1}{\tau_{\widetilde{R}_i}} \left(\widetilde{R}_{i,0} - \widetilde{R}_i - \sigma_{\widetilde{R}_i,s}(f_{es}) \right) \\ \frac{dx_i}{dt} = \frac{1}{\tau_{x_i}} \left(x_{i,0} - x_i - \sigma_{x_i,cm}(f_{cm}) \right) \end{cases}$$
(1.81)

where finally we "assemble" the resistances

 \sim

$$R_{sm} = \frac{\widetilde{R}_{sm}}{1 + x_{sm}}$$

$$R_{sp} = \widetilde{R}_{sp}(1 + x_{sp}) \qquad (1.82)$$

$$R_o = \frac{\widetilde{R}_o}{1 + x_o}.$$

Finally, the chemoreflex control is driven by the oxygen concentration:

$$f_{cm} = \begin{cases} 0 & \text{if } [O_2]_{sm} > [O_2]_{sm}^0 \\ k_{cm} \left([O_2]_{sm} - [O_2]_{sm}^0 \right)^2 & \text{otherwise.} \end{cases}$$
(1.83)

Equations $(1.75), \ldots, (1.83)$ represent a possible simplified model of feedback mechanisms in the cardiovascular system More details can be found in [10, 56, 74, 75].

A major concern in the devise of this kind of models is the parameter identification based on experimental data. There are different approaches for pursuing this aim. Basically, the problem is recast into the form of the minimization of the distance between an experimental data set and the corresponding results predicted by the theory, by acting on the values of the parameters to be estimated. The "optimal values" can be found by means of:

line search algorithms (see e.g. [62]), that are quite cheap and however can found local (i.e. non global) optimal values;

genetic algorithms, that compute the global optimal solution, even if with a larger computational cost. See [11] for more details.

Multiscale models of the vascular system

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There are essentially three classes of models for the vascular system: fully three dimensional models, based on the Navier-Stokes (NS) equations, one dimensional models, including the space dependence on the vessel axial coordinate, based on the Euler (E) equations, and the lumped parameter or zero-dimensional models, based on the Kirchhoff laws (K) for hydraulic networks. Navier-Stokes based models can account for many different features of blood flow problems, such as the blood rheology, the vascular wall dynamics, the interaction between blood flow and wall deformation. These models are perfectly adequate for investigating qualitatively and quantitatively the effects of the geometry on the blood flow and the possible relations between local haemodynamics and pathologies onrise. On the other hand, the high computational costs restrict their use to cover few contiguous vascular districts only.

Euler-based models provide an optimal tool for the analysis of wave propagation phenomena in the vascular tree. In particular, they are convenient when the local flow details are less relevant than the accounting for propagative phenomena on large parts of the vascular tree and the numerical results are needed in a relatively short time. These models outline the role of the vascular system as a sort of telegraph line with the task of transmitting nutrients as well as biological signals along the body. On the other hand, the space dependence still retained in these models inhibits their use in the whole vascular system. In fact, it would be impossible to follow the geometrical and rheological details of the capillary network.

On the contrary, Kirchhoff-based models can provide a representation of a large part or even the whole circulatory system, since they get rid of the explicit space dependence (see Sect. [57]). In a simple and however still quantitative way, these models can include the presence of the heart, the venous system, but also account for self-regulating and metabolic dynamics (see Sect. 1.2.5 and [60]).

If NS, E and K models provide such a different tools, reliable numerical methods for real life applications need to overcome the drawbacks and weakness of each individual class of models. This can be done by resorting to the *geometrical multiscale representation* of the circulatory system.

2.1 What do we mean with *geometrical multiscale* models?

Geometrical multiscale⁴ approach is a strategy for modeling the circulatory system, including the reciprocal interactions between local and systemic haemodynamics by exploiting the complementary features of the different possible models. Indeed, these features lead in a natural way to couple detailed local models with coarser models able to describe the dynamics over a large part or the whole system with acceptable computational costs (see Fig. 2.1).



Fig. 2.1. A schematic representation of a geometrical multiscale model

⁴ Term "multiscale" is often used with a different meaning in many fields of mathematical and numerical modeling, whenever two or more time and/or spatial scales are present. Typical examples are the modeling of turbulence or multiresolution representations. In order to avoid ambiguities, we have added the term *geometrical* for identifying the multiscale perspective illustrated in this chapter.

Multiscale modeling can be regarded as a refinement of models, or a sort of "models zoom" in a specific region of interest, moving from a rough description of the whole system (*bottom-up approach*). From a different point of view, it can be regarded as a sophisticated and reliable method for computing correct boundary conditions at the artificial boundaries of a district of interest (*top-down approach*), i.e. non-physical boundaries which however are needed to limit the computational domain. In the latter perspective, it can be considered also as a specific numerical tool for avoiding spurious effects in domains with artificial boundaries. Indeed, in a domain interested by wave propagation as a net of compliant vessels, artificial boundaries can be source of numerical errors and specific numerical techniques are in order. The geometrical multiscale approach can be regarded in this case as a new approach for solving this class of problems, whose generality goes beyond the specific bioengineering applications addressed in this book.

Despite the simplicity of the basic idea, the coupling of NS, E and K models lead to nontrivial problems at both the mathematical and the numerical level. After a quick review of possible multiscale models of the cardiovascular system and the coupling conditions based on some intuitive formulations, we will consider in more details the mathematical aspects of this approach, leading to less immediate and however more accurate solutions.

2.2 How can we get multiscale models?

2.2.1 Coupling of 3D and 1D models

According to the top-down approach introduced above, let us consider the coupling of 3D and 1D models for haemodynamics (see Fig. 2.2). This is of interest for instance when an endograft prosthesis or a stent is deployed in a specific district (abdominal aorta, carotid, etc.) and one is interested to the alterations induced by this operations on the pressure propagation over the vascular tree.

As already mentioned, from a purely mathematical point of view this is also an effective way for implementing physically based absorbing conditions, in particular for a 3D compliant model. As it has been pointed out in [17], the solution of the fluid-structure interaction problem in a compliant vessel Ω_{3D} features a propagative behavior of hyperbolic type, similar to the one of a compressible flow in a rigid pipe. The density variations in the latter problem are somehow associated in the former with the volume variations, due to the vessel compliance. To fix the ideas, let us suppose to split the pressure wave propagation into an axial forward component (from heart to periphery in the arteries, form periphery to heart in the veins) and a backward one. During the heart beat the component outgoing the domain is not in general independent of the one incoming through the same (artificial) boundaries. At each bifurcation the forward component is partially reflected, inducing



Fig. 2.2. A 3D-1D model

a backward wave (as we have seen in the previous chapter). Forward and backward components are therefore related by the structure of vascular tree. A correct mathematical model of this relation is crucial to avoid unphysical reflections in the numerical solution at the inflow/outflow boundaries induced by a wrong decomposition of incoming and outgoing waves. Coupling of 3D and 1D models is therefore a possible and reliable approach for this aim, by introducing a proper 1D representation of the vascular tree around Ω_{3D} .

Appropriate matching conditions drive the data exchange between NS and E models at the interface Γ (see Fig. 2.3). Different conditions in fact can be considered. In particular we refer to the following quantities defined on Γ (see [17])

$$A = \operatorname{meas}(\Gamma), \quad Q = \int_{\Gamma} \boldsymbol{u} \cdot \mathbf{n} d\gamma,$$

$$\overline{\boldsymbol{u}} = \frac{1}{A} \int_{\Gamma} \boldsymbol{u} \cdot \mathbf{n} d = \frac{Q}{A} \gamma, \quad \overline{p} = \frac{1}{A} \int_{\Gamma} p d\gamma.$$

(2.1)

A priori, it is reasonable to prescribe the following continuity conditions at the interface:

- [A] area: $A_{3D} = A_{1D};$
- [B] mean pressure: $\overline{p}_{3D} = \overline{p}_{1D}$;
- [C] flux: $Q_{3D} = Q_{1D};$



Fig. 2.3. 3D-1D model: detail of the coupling at the outflow of Ω_{3D}

[D] incoming characteristic:
$$\overline{\boldsymbol{u}}_{3D} + \frac{8}{\rho} \left(\sqrt{\overline{p} - p_{ext} + p^*} - \sqrt{p^*} \right) = W_{1,1D};$$

[E] mean total pressure: $\overline{p}_{3D} + \frac{1}{2} \overline{\boldsymbol{u}}_{3D}^2 = \overline{p}_{1D} \frac{1}{2} \overline{\boldsymbol{u}}_{1D}^2,$

where $W_{1,1D}$ is the incoming characteristic variable⁵ introduced in (1.33), p_{ext} is the pressure external to the vessel and p^* depends on the physical features of vascular walls (see [60]). These conditions are not all independent. For instance, [A],[B] and [D] imply conditions [C]. Similarly, conditions [A], [C] and [D] imply [B]. Moreover, it is worth observing that, following the derivation of 1D models carried out in Chap. 1, conditions [B], [D] and [E] can be replaced by similar conditions where the mean pressure on the 3D side is substituted by the averaged normal stresses (see [17]), yielding:

$$\begin{bmatrix} B1 \end{bmatrix} \overline{\sigma_{\mathbf{n}}}_{3D} = \overline{p}_{1D};$$

$$\begin{bmatrix} D1 \end{bmatrix} \overline{u}_{3D} + \frac{8}{\rho} \left(\sqrt{\overline{\sigma_{\mathbf{n}}} - p_{ext} + p^*} - \sqrt{p^*} \right) = W_{1,1D};$$

$$\begin{bmatrix} E1 \end{bmatrix} \text{ mean total pressure: } \overline{\sigma_{\mathbf{n}}}_{3D} + \frac{1}{2} \overline{u}_{3D}^2 = \overline{p}_{1D} \frac{1}{2} \overline{u}_{3D}^2.$$

⁵ The incoming characteristic variable is W_1 because we are considering an interface which is an outflow (distal) boundary for the 3D model and correspondingly an inflow (proximal) boundary for the 1D model. Should we swap the sequence of 1D and 3D models, the incoming characteristic variable would be W_2 .

In practice, we can identify different sets of independent interface conditions:

a) [A], [B], [D];b) [A], [C], [D]; c) [A], [B1], [D1]; d) [A], [C], [D1];e) [A], [E], [D]; f) [A], [E1], [D].

These have all the effect of forcing the continuity conditions listed above. However, as usual, different possible choices that are equivalent form the mathematical viewpoint can lead to different numerical schemes.

Some numerical issues

In numerical solution of multiscale models presented above it is natural to split the scheme into the iterative sequence of dimensionally homogeneous problems, namely 3D and 1D separately. In this way, we can figure out for instance the following algorithm to be carried out at each time $step^6$. We focus our attention on interface between the two models. In particular, we refer to interface conditions (b) of the previous list. The conditions on the other boundaries are assumed to be standard.

Inizialization. Set k = 0 and select an initial guess for the mean velocity $\overline{u}_{3D}^{(0)}$ and pressure $\overline{p}^{(0)}$ at the interface. Typically, this guess is given by the same quantities at the end of the previous time step.

Loop.

- 1. Solve the 1D model, using [D] as boundary condition at the interface, by computing $W_1^{(k)}$ as a function of the current guess of the mean velocity and pressure (or normal stress). The other boundaries of the 1D model will be properly managed (see Sect. 1.1.4). In this step, $A_{1D}^{(k+1)}$ and $Q_{1D}^{(k+1)}$ are computed. 2. Solve the 3D fluid-structure interaction model, with [A] as a boundary
- condition for the structure and [C] for the fluid by using $A_{1D}^{(k+1)}$ and $Q_{1D}^{(k+1)}$. At the end of this step, compute the new guess $W_1^{(k+1)}$. Set k = k + 1.
- Test. The loop ends when:

$$|W_1^{(k)} - W_1^{(k-1)}| \le \varepsilon, \quad |A^{(k)} - A^{(k-1)}| \le \varepsilon, \quad |Q^{(k)} - Q^{(k-1)}| \le \varepsilon$$
(2.2)

being ε a given tolerance.

 $^{^{6}}$ We will not put in evidence explicitly the time index for the sake of notation.

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Different algorithms can be devised, for different interface conditions.

Observe that while the boundary conditions in step (1) of the loop lead to a mathematicaly well posed problem, step (2) in this form does not, since these averaged data on the boundary are not enough to solve uniquely the 3D problem. A specific treatment of these "defective boundary data" set is required. To be more concrete, let us consider [A] used as condition for the structure at step 2. On the 3D compliant model we would need pointwise data for the wall displacement d. On the other hand, when the area of the interface A_{1D} is known from the computation of the 1D model, we have the average condition:

$$\int_{\Gamma(\boldsymbol{d}(t))} d\gamma = A_{1D}(t). \tag{2.3}$$

We need to "spread" the average data to pointwise conditions. To this aim we can assume a shape for the displacement depending on a single parameter to be tuned so to force (2.3). For instance, suppose that it is possible to identify an axis of the 3D compliant vessel and that the shape of Γ is circular with centre on the axis of coordinates (x_c, y_c, z_c) . For the sake of simplicity, let us assume that Γ belongs to the plane (x, y) identified by the equation $z = z_c$. In this way the component d_3 along z of the position d is constant and we can set:

$$d_1(x, y, z, t) = x_c + R(t)\cos\left(\tan^{-1}\left(\frac{y}{x}\right)\right) = x_c + \sqrt{\frac{A_{1D}(t)}{\pi}}\cos\left(\tan^{-1}\left(\frac{y}{x}\right)\right),$$

$$d_2(t) = y_c + R(t)\sin\left(\tan^{-1}\left(\frac{y}{x}\right)\right) = y_c + \sqrt{\frac{A_{1D}(t)}{\pi}}\sin\left(\tan^{-1}\left(\frac{y}{x}\right)\right),$$

$$d_3(t) = z_c.$$

(2.4)

With this choice the average condition has been extended to pointwise data, by assuming a priori a planar circular shape for the interface Γ .

In a similar way we can address condition [C], by assuming, for instance, a velocity profile depending on a proper parameter. To be more precise, let us assume again that Γ has a circular shape in the xy-plane. Then, we can resort to the well known Poiseuille parabolic velocity field

$$u_1 = u_2 = 0, \quad u_3(x, y, t) = \frac{2Q_{1D}(t)}{\pi\rho R^2} \left(1 - \frac{(x - x_c)^2 + (y - y_c)^2}{R^2}\right),$$
 (2.5)

where Q_{1D} is the flow rate computed by the 1D model. Again, the arbitrary selection of a velocity profile converts the average conditions into pointwise Dirichlet conditions for the fluid problem.

Numerical results (see Fig. 2.4 and 2.5) show that this approach is actually able to reduce spurious back-reflections at the boundaries, in particular when the arbitrary assumptions on the displacement shape or the chosen velocity profile are realistic. However, in general, the arbitrary selection of a shape for the displacement or the velocity profile strongly affects the numerical solution. Hence, the reliability of results obtained in this way is sometimes questionable.

More sophisticated mathematical and numerical techniques that are able to expand average data to pointwise conditions are required for ensuring better accuracy. We will address these techniques in Sect. 2.3.



Fig. 2.4. 3D simulation: pressure wave propagation along a compliant vessel. Spurious effects arise at the artificial downstream boundary(courtesy of G. Fourestey)

Another drawback of this multiscale coupling still relies on the limited capability of E models of covering the capillary network, which on the other hand is the main source of the back reflections propagating in the arterial tree and of including the action of the heart. These require more sophisticated multiscale models.

2.2.2 Coupling of 1D-0D and 3D-1D-0D models

A possible way to account for the presence of the capillary bed in the computation of travelling pressure waves and the action of the heart is to close the 3D-1D network with K models. This requires in particular the coupling of 1D and lumped parameter models, through interface conditions. A simplified version of this coupling has been already addressed in Chap. 1. In that case, lumped parameter models were represented by a simple terminal impedance for prescribing boundary conditions in the frequency domain at the downstream sections of a 1D network. Here, we want to give an insight of models and numerical issues arising from a precise and accurate inclusion of the dynamics in K models. In the multiscale framework they are described in terms of a system of differential-algebraic equations (see (1.66)) in the time variable.



Fig. 2.5. Multiscale 3D-1D simulation: pressure wave propagation along the two submodels. Spurious effects at the artificial boundary are small (courtesy of G. Fourestey)

For the sake of simplicity, we consider the multiscale model represented in Fig. 2.6, where the 1D model represents a simple cylindrical domain. More complex problems, featuring a network of 1D segments or even a coupled 3D-1D model can be considered as well within the same framework.

In the model at hand we have two interfaces, Γ_0 and Γ_1 , where it is reasonable to prescribe the continuity of:

- [A] area: $A_{1D} = A_{0D}$;
- B] pressure: $P_{1D} = P_{0D}$;
- [C] flow rate: $Q_{1D} = Q_{0D}$.

Moreover, we could force the continuity of the Riemann variables:

- [D] characteristic variable propagating from the heart to the peripheries:
- $\frac{Q_{0D}}{A_{0D}} + \frac{8}{\rho} \left(\sqrt{P_{0D} p_{ext} + p^*} \sqrt{p^*} \right) = W_{1,1D};$ [E] characteristic variable propagating from the peripheries to the heart: $\frac{Q_{0D}}{A_{0D}} \frac{8}{\rho} \left(\sqrt{P_{0D} p_{ext} + p^*} \sqrt{p^*} \right) = W_{2,1D}.$

Again, these conditions are not all independent. This is the case for instance of [A] and [B], since both the E and K models include a wall law linking together pressure and area. Should these wall laws be the same, actually continuity of the area implies continuity of the pressure and vice-versa. More in general, only one between [A] and [B] can be explicitly prescribed.



Fig. 2.6. 1D-0D model: the 1D model is given by a simple compliant straight cylinder, the 0D model is composed by the network in the cube and two bridging regions (upstream and downstream). Upstream bridging region is given by a T network, featuring the flow rate Q_0 as state variable. Downstream bridging region has the pressure P_1 as state variable. These interface compartments are compatible with the splitting scheme described in the text

Similarly, only two conditions among [B], [C], [D] and [E] can be selected, for instance:

- 1. conditions [B], [D] at the upstream interface Γ_0 ;
- 2. conditions [C], [E] at the downstream interface Γ_1 .

Some numerical issues

A possible approach for solving this multiscale model still resorts to splitting the computation into the sequence of dimensionally homogeneous problems. In the case of Fig. 2.6, this means that we solve separately the DAE system corresponding to the lumped parameter model and the Euler hyperbolic system. Let us consider preliminarily the simple case in which a 1D straight cylinder is split into a 1D-0D model as illustrated in Fig. 2.7. In particular, let us consider the multiscale model at the top of Fig. 2.7, where the 0D model is prepresented by a \mathcal{L} inverted network (see Chap. 1). The lumped parameter model is therefore described by the following equations:

$$C\frac{dP}{dt} = Q_{up} - Q,$$

$$L\frac{dQ}{dt} + RQ = P - P_{dw}.$$
(2.6)

A possible iterative scheme reads as follows. At each time step:

- Initialization. Set k = 0 and fix an initial guess for the interface flow rate $Q_{up}^{(0)}$.
- Loop. 1. Solve the 0D model (2.6), by using $Q_{up}^{(k)}$ as forcing term. This yields the estimates of $Q^{(k)}$ and $P^{(k)}$. On the basis of this computation, Riemann variable $W_2^{(k)}$ at the interface incoming to the 1D model can be computed.
 - 2. Solve the 1D model by using incoming Riemann variable $W_2^{(k)}$ as boundary condition. At the end of this step, a new guess for $Q_{up}^{(k+1)}$ is available. Set k = k + 1.
- **Test.** The loop ends when the solution fulfills an appropriate test, for instance:

$$|P^{(k)} - P^{(k-1)}| \le \varepsilon, \quad |Q_{up}^{(k)} - Q_{up}^{(k-1)}| \le \varepsilon.$$

Let us consider now multiscale model on the bottom of Fig. 2.7. Here 0D model is represented by a \mathcal{L} network, described by system

$$L\frac{dQ}{dt} + RQ = P_{up} - P,$$

$$C\frac{dP}{dt} = Q - Q_{dw}.$$
(2.7)

We can still use an iterative approach as follows.

- Initialization. Set k = 0 and fix an initial guess for interface pressure $P_{up}^{(0)}$. Loop. 1. Solve the 0D model (2.7), by using $P_{up}^{(k)}$ as forcing term. This yields the estimates of $Q^{(k)}$ and $P^{(k)}$. On the basis of this computation, Riemann variable $W_2^{(k)}$ at the interface incoming to the 1D model can be computed.
 - 2. Solve 1D model by using incoming Riemann variable $W_2^{(k)}$ as boundary condition. At the end of this step, a new guess for $P_{up}^{(k+1)}$ is available. Set k = k + 1.

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Fig. 2.7. Two simple examples of 1D-0D multiscale models. At the top, the lumped parameter model is given by a \mathcal{L} -inverted network. On the bottom, it is given by a \mathcal{L} network. The two network configurations are appropriate for different iterative solvers (see text)

Test. The loop ends when the solution fulfills an appropriate test, for instance:

 $|P_{up}^{(k)} - P_{up}^{(k-1)}| \le \varepsilon, \quad |Q^{(k)} - Q^{(k-1)}| \le \varepsilon.$

Several remarks are in order. First of all the use of characteristic variables has the advantage of prescribing (at least approximatively) absorbing boundary conditions, well suited for avoiding numerical reflections at the boundary of the E model (see Chap. 1).

Secondly, interface conditions are by definition localized in a specific position in space. On the other hand, K models have lost an explicit space dependence. Therefore, in managing matching conditions with K models:

1. interface conditions yield a forcing term in the 0D model;

2. different configurations of the 0D models are associated with different iterative schemes: in the first case the 0D model is forced by the flow rate Q_{up} and provides the pressure P; in the latter case, it is forced by the pressure P_{up} and provides the flow rate Q.

The latter item deserves some further remarks. In lumped parameter problems, interfaces between E and K models are represented by the boundary of the 1D domain and the compartments placed in the neighborhood of the 1D models⁷. The structure of the graphs of these compartments implicitly defines the interface variables that are state variables for the 0D model and the ones that are forcing terms. In the iterative scheme, the latter are related to the variables "received" by the 1D problem from the 0D one, the former are related to variabes "computed" by the K problem and "returned" to the E one (possibly in the form of the Riemann variables).

The compartments of the 0D model that play the role of the interfaces with the other models will be called *bridging regions*. The link between the graph of the bridging regions and the numerical scheme will be called *bridging region compatibility*. More precisely, we say that a numerical scheme is *bridging region compatible* if it is consistent with the topology of the bridging region.

For instance, for the multiscale model of Fig. 2.6, where the upstream bridging region is given by a T network and the downstream one is given by a π network, a bridging regions compatible scheme reads as follows.

Initialization. Set k = 0 and fix an initial guess for the upstream pressure $P_0^{(0)}$ and the donwstream flow rate $Q_1^{(0)}$.

- Loop. 1. Solve the 0D model, by using the available upstream pressure and the downstream flow rate as forcing terms. Compute in particular the upstream flow rate $Q_0^{(k)}$ and the downstream pressure $P_1^{(k)}$. After this computation, the incoming Riemann variables, $W_1^{(k)}$ upstream and $W_2^{(k)}$ downstream are available.
 - 2. Solve the 1D model by using the incoming Riemann variables as boundary conditions. At the end of this step, new guesses for the upstream pressure $P_0^{(k+1)}$ and the donwstream flow rate $Q_1^{(k+1)}$ are available.
- **Test.** The loop ends when the solution fulfills an appropriate test, for instance:

$$|P_i^{(k)} - P_i^{(k-1)}| \le \varepsilon, \quad |Q_i^{(k)} - Q_i^{(k-1)}| \le \varepsilon, \qquad i = 0, 1.$$

Remark 2.2.1 Step 1 can be regarded as a stand-alone lumped parameter model, represented by the circuit of Fig. 2.8, where input variables of the 1D model are represented by a current and a voltage generator respectively. In terms of circuit analysis bridging region compatibility in fact implies that no

 $^{^7}$ In the two oversimplified examples above they in fact corresponds to the entire 0D models.

voltage/pressure generator is in parallel with a capacitor and no current/flow rate generator is in series with an inductance. Under these assumptions it is possible to prove that the DAE system associated with this stand-alone network is of index 1 and it can be reduced to a well posed Cauchy problem for a system of ordinary differential equations (see [13, Chap.12]).



Fig. 2.8. Stand alone 0D model corresponding to step 2 of the splitting iterative algorithm (see text) $\,$

Aortic valve function

As we have pointed out, an advantage of K models is their capability of representing in relatively simple terms complex systems like the heart or the action of control dynamics. Moving from the observation that "the left ventricle and arterial circulation represent two mechanical units that are joined together to form a coupled biological system" [45, Chap.13], it makes sense to consider a 1D model for the aorta coupled with the lumped parameter model of the heart presented in Sect. 1.2.2. Since the coupling is mediated by the aortic valve, we assume that there are two possible working states for the system Heart-Aorta.

1. closed value (CV) condition: when the aortic value is closed, the two systems are actually decoupled; in particular, for the arterial tree we have at

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Fig. 2.9. Ventricular and arterial pressures during the heart beat. When the aortic valve is open, the two pressures can be assumed to be the same

the aorta inflow a null flow rate condition, resorting to the conditions on the Riemann invariants:

$$W_1 = -W_2.$$

2. open value (OV) condition: the ventricular pressure is related to the 1D problem by solving equation (1.64) which we recall here for the sake of clarity:

$$\frac{1}{E_v}\frac{dP_v}{dt} + \frac{d}{dt}\left(\frac{1}{E_v}\right)P_v = -Q_v,$$

During this phase, we assume that ventricular flow rate Q_v and pressure P_v are equal to the arterial ones at the aorta inflow (see Fig. 2.9), corresponding to conditions

$$Q_v = Q_{1D}, \quad P_v = P_{1D}.$$

Numerical implementation of these conditions by using the incoming characteristic variable in the 1D network is addressed in [20].

Transition between OV and CV conditions cannot be prescribed a priori. We assume that the valve opens under the action of a differential pressure and it closes when forced by a flow reversal. This means that in numerical coupling when the valve is closed, at each time step aortic and ventricular pressures need to be compared. If $P_v - P_{1D} < 0$ the valve is kept closed (CV conditions), otherwise we switch to OV conditions until the next closure. To determine the instant of valve closure (end of systole) we check the sign of

the flux at the aortic proximal node. At the first time step when Q_v becomes negative we "close" the valve by adopting again CV boundary condition, up to the next heart cycle (see Fig.2.10).



Fig. 2.10. Flow chart representation of the aortic valve modeling.

As an application of this model, we mention [20].

2.2.3 Coupling of 3D-0D models

In our top-down approach, we have coupled the three kind of models, moving from the finest 3D down to the coarsest 0D. In some applications a sort of *shortcut modeling* can be pursued, coupling together directly 3D and 0D models. This is, for instance, the case when the wave propagation phenomena are not of interest, and a 3D simulation needs boundary conditions that could account in a precise way the dynamics of the complete vascular tree.

Consider for instance the model obtained by coupling a 3D model of a region of interest and a lumped parameter model like in Fig. 2.11. Again, three model ingredients can be identified:

 $K \ model,$ represented by a system of ordinary differential equations in the form

$$\frac{d\mathbf{y}}{dt} + A\mathbf{y} = \mathbf{f}$$

NS model, represented by the Navier-Stokes equations with appropriate boundary conditions on the vascular walls Γ_w ;

interface conditions represented by continuity conditions.

At each interface in particular we consider the following conditions.

- $\begin{bmatrix} A \end{bmatrix} \text{ area: } A_{3D,i} = \text{meas}(\Gamma_i) = A_{0D,i};$ $\begin{bmatrix} B \end{bmatrix} \text{ mean pressure: } \overline{p}_{3D,i} = \frac{1}{A_{3D,i}} \int_{\Gamma_i} p d\gamma = P_{0D,i};$ $\begin{bmatrix} C \end{bmatrix} \text{ for party } Q = p_{0D,i} = \frac{1}{A_{3D,i}} \int_{\Gamma_i} p d\gamma = P_{0D,i};$
- [C] flow rate: $Q_{3D,i} = \rho \int_{\Gamma_i} \boldsymbol{u} \cdot \mathbf{n}_i d\gamma = Q_{0D,i}.$

As we have already pointed out for 3D-1D coupling, condition [B] can be replaced by a condition on the normal component of the stress



Fig. 2.11. Representation of a 3D rigid-0D geometrical multiscale model with three bridging regions (BR0, BR1, BR2). At the inlet of the 3D domain, the bridging region features the current/flow rate Q_0 as state variable. This is therefore computed by the 0D model. In the other bridging regions, the voltage/pressures p_i , i = 1, 2, are the state variables. The 0D model is forced by the mean pressure at the interface Γ_0 and by the flow rates at Γ_1 and Γ_2

$$[B1] \frac{1}{A_{3D,i}} \int_{\Gamma_i} (p\mathbf{n}_i - (\nabla \mathbf{u} + \nabla \mathbf{u}^T) \cdot \mathbf{n}_i) d\gamma = P_{0D,i}.$$

Possible interface conditions are therefore represented by [A], [B] and [C] or [A], [B1] and [C]. If the 3D model is assumed to be rigid, the three conditions are not independent and in particular [A] and [B] (or [B1]) cannot be prescribed explicitly together. Actually, in the 3D model interface area is constant, while in the 0D model a pressure law (see (1.21)) between area and pressure is postulated. For this reason, typical interface conditions in the 3D rigid-0D coupling are [B] (or [B1]) and [C].

Some numerical issues

To fix the ideas, we consider the problem represented in Fig. 2.11 where the 3D model is assumed to be rigid and interface conditions [B1] and [C] are

prescribed. We consider the following algorithm for the numerical coupling at each time step.

- Initialization. Select an initial guess for the pressure $P_0^{(0)} = P_0$ and the flow rates $Q_1^{(0)} = Q_1$ and $Q_2^{(0)} = Q_2$ at the interfaces. Typical choice is to take these quantities at the previous time step. Set the iteration index k = 0.
- Loop.
- p. 1. Solve the 0D model by using the forcing terms $P_0^{(k)}$, $Q_1^{(k)}$ and $Q_2^{(k)}$. This step, in particular, computes the state variables of the K model $Q_0^{(k+1)}$, $P_1^{(k+1)}$ and $P_2^{(k+1)}$. 2. Solve the 3D model by using the boundary conditions given by $Q_0^{(k+1)}$, $P_1^{(k+1)}$ and $P_2^{(k+1)}$. Compute the average normal stress on Γ_0 , $P_0^{(k+1)} = \int_{\Gamma_0} (p^{(k+1)} \mathbf{n}_0 (\nabla \mathbf{u}^{(k+1)} + \nabla \mathbf{u}^{(k+1),T}) \cdot \mathbf{n}_0) d\gamma$ and the flow rates $O_0^{(k+1)}$. rates $Q_1^{(k+1)} = \rho \int_{\Gamma_1} \mathbf{u}^{(k+1)} \cdot \mathbf{n}_1 d\gamma$ and $Q_2^{(k+1)} = \rho \int_{\Gamma_2} \mathbf{u}^{(k+1)} \cdot \mathbf{n}_2 d\gamma$. Test. The iteration continue up to the fulfillment of a convergence test, for
- instance:

$$|P_i^{(k+1)} - P_i^{(k)}| \le \varepsilon, \quad |Q_i^{(k+1)} - Q_i^{(k)}| \le \varepsilon, \quad i = 0, 1, 2.$$

Similarly to what we have pointed out in the previous sections for the other multiscale models, several remarks are in order.

- 1. Bridging regions compatibility. Since the interface in the K model is represented by a compartment, this bridging region has to be devised appropriately. More precisely, it has to be able to compute the quantities required by the splitting scheme. To be concrete, in the example of the algorithm presented above, the flow rate at Γ_0 and the pressures P_1 and P_2 must be state variables of the lumped parameter models. As we have pointed out, this ensures well posedness of the problem solved at step 1.
- 2. 3D defective boundary data problems. The K model (as well as the E model) computes averaged quantities that do not provide enough boundary data to the 3D model in step (2) of the loop. As for the coupling between 3D and 1D models, we could postulate a priori a profile for the velocity or the normal stress and use the average data for the fine tuning of the boundary conditions. For instance, we could "expand" average data into pointwise data in the following manner:
 - Flow rate conditions \rightarrow Poiseuille parabolic profile \rightarrow (Standard) Dirichlet conditions (see (2.5));
 - Average pressure conditions \rightarrow Constant normal stress \rightarrow (Standard) Neumann conditions:

$$p\mathbf{n} - \nu \nabla \boldsymbol{u} \cdot \mathbf{n} = P\mathbf{n} \tag{2.8}$$

where P is constant over the interface.

At which extent numerical results are affected by this arbitrary profile selection is a crucial question for the reliability of multiscale modeling. We will address this problem in the next sections.

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An example of this model to by-pass simulations is given in [61].

Remark 2.2.2 The same algorithm for the 3D-0D coupling can be extended to the compliant case. If the 3D compliant model refers to an algebraic model for the vascular walls, no further interface conditions are needed. In the case of a differential (in space) structure model, conditions on area should be explicitely prescribed. In the splitting scheme, they can be used as boundary conditions for the 3D problem, as we have done for the 3D-1D coupling. Again condition on area is not enough for the structure problem and can be expanded into a pointwise Dirichlet condition by assuming a priori a shape (f.i. circular) for the structure at the interface, as we have done in (2.4).

2.2.4 How can we improve multiscale models?

In this section we have proposed different coupled models, with some basic ideas for their numerical implementation. Mismatch of mathematical features of submodels to be coupled requires specific strategies for making geometrical multiscale simulations affordable. In particular, we outline the role of the characteristic variables as interface conditions in the coupling of E models. In the formulation of numerical schemes, this can allow to solve E models with absorbing boundary conditions, which guarantee a correct capturing of wave propagation dynamics at the interface. Another relevant point is the role of interface compartments or bridging regions in coupling with K models. The definition of these regions compatible with the numerical splitting method is crucial for the overall correctness of the model.

There are two further points that deserve a deeper analysis, for the improvements of multiscale modeling.

Average data expansion: when coupling 3D with 1D or 0D models, we need to convert average data into pointwise boundary conditions. We have proposed some practical strategies, which however introduce a level of arbitrariness in the final numerical solution. Indeed, numerical results in [48,77] show how the prescription of an arbitrary velocity profile can sometimes induce incorrect results (and maybe lead a medical researcher to wrong conclusions). We need therefore to understand if there is an optimal approach able to reduce the impact on the final solution of the unavoidable arbitrariness. To be precise, if we select an arbitrary parabolic profile at the inlet of a cylindrical pipe, as done in (2.5), we could expect that this choice will not affect the numerical results far away from that inlet boundary. In steady problems, it is commonly accepted that the effects of the profile chosen at the inlet are no more significant after an entry length $L \approx 0.06D$ where D is the diameter of the pipe (see [81]). However, for unsteady problems it has been verified in [65] that an entry length of 40D may be not enough to recover the analytical (Womersley) solution from a prescription of an inlet parabolic profile. Different strategies, able

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to force a given flow rate *without* the prescription of a velocity profile are then necessary to improve the reliability of multiscale results.

Efficiency of coupling iterative schemes: we have presented some possible basic iterative schemes, resorting to the successive solution of standard subproblems. The effectiveness of this kind of schemes (in terms of number of iterations required for the convergence) can be improved for instance by introducing appropriate relaxation strategies. Convenience of such splitting schemes in comparison with non-splitting or monolithic solvers is another relevant point in devising multiscale models.

We investigate these two items in the next sections. We also discuss mathematical well posedness of multiscale models.

2.3 Defective boundary data problems

Let us consider the 3D Navier-Stokes equations

$$\rho \frac{\partial \boldsymbol{u}}{\partial t} + \rho \boldsymbol{u} \cdot \nabla \boldsymbol{u} - \mu \Delta \boldsymbol{u} + \nabla p = \mathbf{f}, \qquad (2.9)$$
$$\nabla \cdot \boldsymbol{u} = 0,$$

that we assume to hold in the 3D domain Ω . The boundary $\partial \Omega$ still consists of the vascular wall Γ_w and the artificial boundaries Γ_i , with $i = 1, 2, \ldots, m$. For the moment, we assume that the vessel is rigid, i.e.

$$\boldsymbol{u}|_{\boldsymbol{\Gamma}_{w}} = \boldsymbol{0},\tag{2.10}$$

where Γ_w denotes the part of the boundary corresponding to the vascular wall. The initial conditions

$$\boldsymbol{u}(\boldsymbol{x},0) = \boldsymbol{u}_0(\boldsymbol{x}) \tag{2.11}$$

are assigned.

We will consider the two kind of averaged data encountered in the previous section, namely conditions on mean velocity or flow rates and on mean pressures.

2.3.1 Flow rate problem

Consider problem given by (2.9), (2.10), (2.11), together with boundary conditions:

$$\rho \int_{\Gamma_i} \boldsymbol{u} \cdot \boldsymbol{n} \, \mathrm{d}\boldsymbol{\gamma} = Q_i, \quad i = 0, 1, \dots, m,$$

where Q_i are given functions of time. In the case of a rigid domain, the incompressibility of the fluid implies the following constraint on the data:

$$\sum_{i=0}^{m} Q_i = 0.$$

To avoid dealing with this constraint we will consider a slightly different problem, namely

$$p\boldsymbol{n} - \nu \frac{\partial \boldsymbol{u}}{\partial \boldsymbol{n}} | = \boldsymbol{0}, \text{ on } \Gamma_0, \qquad \rho \int_{\Gamma_i} \boldsymbol{u} \cdot \boldsymbol{n} \, \mathrm{d}\boldsymbol{\gamma} = Q_i, \quad i = 1, \dots, m.$$
 (2.12)

In the analysis of this problem, we will prove however that there is no loss of generality with these conditions.

In the sequel, for the sake of simplicity, we set $\rho = 1$.

We have already pointed out that conditions (2.12) are not enough for existence of a solution. Three scalar conditions should be required for the well posedness of the problem, while (2.12) provides only a scalar value for each Γ_i , for i = 1, 2, ... m. The approach advocated in the previous section was based on a-priori selection of a velocity profile fitting the given flow rate (see for instance [8, 16]).

This approach is in fact pretty simple, since it actually reduces the defective boundary problem to a classical Dirichlet one. Nevertheless there are several limitations. Real vascular geometries are typically far from being cylindrical circular and rectilinear, that are the assumptions for the Womersley and Poiseuille solutions. Moreover, a-priori selection of a profile strongly affects the entire numerical solution.

In general, practical solution currently adopted is to expand the computational domain, such that the arbitrary velocity profile is prescribed far away from the zone of interest and the domain extensions have a circular shape at the artificial boundaries (*flow extensions*). However, this affects the computational costs, in particular for unsteady computations and as we have pointed out the effects of the arbitrary choice are sometimes still present in the region of interest.

Different approaches that do not require arbitrary prescription of a velocity profile are therefore very helpful.

A variational approach

A strategy proposed in [34] relies on the selection of an appropriate variational formulation for the problem at hand including all the available data. Variational formulation by itself will complete the boundary data set with homogeneous natural conditions. These conditions have been called sometimes *do nothing conditions*, since they are obtained spontaneously as a result of the chosen variational formulation⁸. They are indeed less perturbative (or

⁸ This denomination is effective but also a little bit misleading, since in any case these conditions "*do something*". This is the reason why we do not adopt this name here.

"invasive") with respect to the (unknown) solution, since they are natural conditions for the chosen variational formulation.

To introduce this approach for the flow rate problem, we need some functional spaces and a specific notation. Set:

$$\widehat{\mathbf{V}}_f \equiv \left\{ \mathbf{v} \in \mathbf{V}_f : \int_{\Gamma_j} \mathbf{v} \cdot \mathbf{n} = 0, \ \forall j = 1, 2, \dots, m \right\},\$$

and let us denote by \mathbf{b}_i , i = 1, ..., m the functions of V_f such that, for all j = 1, ..., m

$$\int_{\Gamma_j} \mathbf{b}_i \cdot \boldsymbol{n} \, d\gamma = \delta_{ij}, \qquad \nabla \cdot \mathbf{b}_i = 0.$$

These functions are commonly called *flux carriers* and act as a lifting of the flow rate data. We set $\boldsymbol{u} = \hat{\boldsymbol{u}} + \sum_{i=1}^{m} Q_i \mathbf{b}_i$. A possible variational formulation of the flow rate problem is the following: find $\hat{\boldsymbol{u}} \in L^2(0, T, \hat{\mathbf{V}}_f) \cap L^{\infty}(0, T, \mathbf{L}^2(\Omega))$ and $p \in L^2(0, T, Q_f)$ such that for all $\mathbf{v} \in \hat{\mathbf{V}}_f$ and $q \in Q_f$:

$$\begin{pmatrix} \partial \widehat{\boldsymbol{u}} \\ \partial t, \mathbf{v} \end{pmatrix} + a(\boldsymbol{u}, \mathbf{v}) + c\left(\widehat{\boldsymbol{u}}, \widehat{\boldsymbol{u}}, \mathbf{v}\right) + c\left(\widehat{\boldsymbol{u}}, \sum_{j=1}^{m} Q_j \mathbf{b}_j, \mathbf{v}\right) + c\left(\sum_{j=1}^{m} Q_j \mathbf{b}_j, \widehat{\boldsymbol{u}}, \mathbf{v}\right) + b(\mathbf{v}, p) = (\mathbf{f}, \mathbf{v}) - \sum_{j=1}^{m} \left(\left(\frac{\partial Q_j}{\partial t} \mathbf{b}_j, \mathbf{v}\right) + Q_j a(\mathbf{b}_j, \mathbf{v}) \right) - c\left(\sum_{j=1}^{m} Q_j \mathbf{b}_j, \sum_{j=1}^{m} Q_j \mathbf{b}_j, \mathbf{v}\right), \\ b(\widehat{\mathbf{u}}, q) = 0,$$

$$(2.13)$$

with $\widehat{\mathbf{u}}(\boldsymbol{x}, 0) = \boldsymbol{u}_0 - \sum_{j=1}^m Q_j(0) \mathbf{b}_j.$

This formulation actually forces implicitly some conditions, as it is stated by the following proposition (for the proof see [34]).

Proposition 2.3.1 The solution of the flow problems (2.13) fulfills the following boundary conditions on Γ_i , i = 1, ..., m:

$$(p\boldsymbol{n} - \mu \boldsymbol{\nabla} \boldsymbol{u} \cdot \boldsymbol{n})_{\Gamma_i} (\mathbf{x}, t) = C_i(t)\boldsymbol{n}, \quad \forall \mathbf{x} \in \Gamma_i, i = 1, \dots, m, t > 0,$$

where $C_i = C_i(t)$ are unknown functions of time.

Remark 2.3.1 In the case of a problem with flow conditions also on Γ_0 , with the constraint on the data $\sum_{i=0}^{m} Q_i = 0$, the previous proposition still holds with $C_0 = C_0(t)$ an arbitrary function of time. The case considered in (2.12) is therefore a special case where we choose $C_0 = 0$. Problem associated to conditions (2.12) is of the same type of the one with all flow boundary conditions, and there is no need of forcing explicitly the data compatibility constraint on the assigned flow rates.

Concerning the well posedness, we have the following result, proved in [34].

Proposition 2.3.2 Under suitable assumptions on the smoothness of the domain and the initial data, there exists a time interval in which the flow problem (2.13) is well posed. If $||\nabla u_0||$ and $|Q_i|$ for all i are sufficiently small the solution exists for each t > 0.

This approach has a practical drawback. The functional space $\mathbf{\hat{V}}_{f}$ is not standard. In view of the numerical approximation, the construction of finite dimensional functional subspaces and of the flux carriers functions set is rather problematic.

Different strategies have been proposed that do not suffer from these limitations even if they present other drawbacks.

Augmented formulation

A second approach, proposed in [18], considers the flux conditions as constraints for the solution, to be forced by means of Lagrange multipliers (in a way similar to the treatment of the incompressibility constraint in the mixed formulation of the Navier-Stokes). In practice, we introduce a vector function $\lambda(t)$ and resort to the following problem: find $\mathbf{u} \in L^2(0, T, \mathbf{V}_f) \cap$ $L^{\infty}(0, T, \mathbf{L}^2(\Omega)), p \in L^2(0, T, Q_f)$ and $\lambda \in (L^2(0, T))^m$ such that for all $\mathbf{v} \in \mathbf{V}_f, q \in Q_f$:

$$\left(\frac{\partial \boldsymbol{u}}{\partial t}, \mathbf{v}\right) + a(\mathbf{u}, \mathbf{v}) + c\left(\boldsymbol{u}, \boldsymbol{u}, \mathbf{v}\right) + b(\mathbf{v}, p) + \sum_{i=1}^{m} \lambda_i \int_{\Gamma_i} \mathbf{v} \cdot \boldsymbol{n} \, d\gamma = (\mathbf{f}, \mathbf{v}),$$

$$b(\boldsymbol{u}, q) = 0,$$

$$\int_{\Gamma_i} \mathbf{u} \cdot \boldsymbol{n} \, d\gamma = Q_i \qquad i = 1, 2, \dots m,$$
(2.14)

Well posedness analysis for this augmented formulation can be carried out by means of classical arguments (see [27]). In particular, moving from the well posedness result of Prop. 2.3.2, it can be shown that an inf-sup condition holds for the augmented problem, leading to the following result (see [76]).

Proposition 2.3.3 Under the same assumptions of Prop. 2.3.2, the augmented formulation (2.14) is well posed.

Moreover, the investigation of the boundary conditions forced in the augmented formulation so that the problem has a unique solution highlights the physical significance of the Lagrange multiplier. We have in fact the following Proposition (for the proof see [18]).

Proposition 2.3.4 The solution of problem (2.14) fulfills the following conditions on the artificial boundaries Γ_i , i = 1, 2, ..., m:

$$(p\boldsymbol{n} - \mu \boldsymbol{\nabla} \boldsymbol{u} \cdot \boldsymbol{n})_{\Gamma_i} (\mathbf{x}, t) = \lambda_i(t)\boldsymbol{n}, \forall \mathbf{x} \in \Gamma_i, i = 1, \dots, m, t > 0.$$
(2.15)

In other words, the Lagrange multipliers λ_i do coincide with the functions C_i and play the role of normal stresses on the artificial boundaries.

The augmented formulation is based on standard functional spaces, whose finite dimensional approximations are readily built (and present in most of the commercial packages). However the indefinite saddle point nature of the associated problem needs a specific analysis. Discretization of (2.14) leads indeed to an algebraic problem that in general is not convenient to solve in a monolithic way, i.e. with the contemporary computation of \boldsymbol{u}, p and λ_i . Indeed, from one hand the resulting linear system is in general ill conditioned, moreover problem (2.14) is not standard, since it simultaneously deals with velocity, pressure and the Lagrange multipliers. Available software packages are usually unsuitable for this kind of problems.

These remarks suggest to split apart the fluid dynamics (\boldsymbol{u}, p) from λ_i computations. Some numerical methods have been proposed in [18, 76, 78] to this aim. We limit ourselves to consider algebraic splittings of the matrix obtained after discretization/linearization of the problem at hand at each time step. This system reads $A\mathbf{y} = \mathbf{c}$, with

$$\mathbf{A} = \begin{bmatrix} \mathbf{C} \ \mathbf{D}^T \ \mathbf{L}^T \\ \mathbf{D} \ \mathbf{0} \ \mathbf{0} \\ \mathbf{L} \ \mathbf{0} \ \mathbf{0} \end{bmatrix}, \qquad \mathbf{c} = \begin{bmatrix} \mathbf{b} \\ \mathbf{0} \\ \mathbf{q} \end{bmatrix}$$
(2.16)

being the discrete counterpart of (2.14). Matrix L corresponds to the discretization of the boundary integrals on Γ_i , D is the discretization of the divergence operator and C is the result of the discretization and linearization of the operator $\left(\frac{\partial \boldsymbol{u}}{\partial t}, \mathbf{v}\right) + a(\mathbf{u}, \mathbf{v}) + c(\boldsymbol{u}, \boldsymbol{u}, \mathbf{v})$. Correspondingly, $\mathbf{y} = [\mathbf{U}, \mathbf{P}, \boldsymbol{\Lambda}]^T$, contains the nodal values of the unknowns of velocity, pressure and Lagrange multipliers respectively. Moreover **b** comes from the discretization of source terms in the momentum equation, and entries of vector **q** are the prescribed flow rates Q_i . Using the notation

$$\mathcal{C} = \begin{bmatrix} \mathbf{C} \ \mathbf{D}^T \\ \mathbf{D} \ \mathbf{0} \end{bmatrix}, \mathcal{L} = \mathbf{L},$$

matrix A can be rewritten in the form:

$$\mathbf{A} = \begin{bmatrix} \mathcal{C} \ \mathcal{L}^T \\ \mathcal{L} \ \mathbf{0} \end{bmatrix}.$$

Correspondingly, we set $\mathbf{x}_1 = [\mathbf{U}, \mathbf{P}]^T$ and $\mathbf{x}_2 = \boldsymbol{\Lambda}$. Similarly, we denote $\mathbf{f}_1 = [\mathbf{b}, \mathbf{0}]^T$ and $\mathbf{f}_2 = \mathbf{q}$.

A possible way for splitting velocity/pressure and multipliers computations is based on the following classical algebraic factorization: 2 Multiscale models of the vascular system

$$\begin{bmatrix} \mathcal{C} \ \mathcal{L}^T \\ \mathcal{L} \ \mathbf{0} \end{bmatrix} = \begin{bmatrix} \mathcal{C} & \mathbf{0} \\ \mathcal{L} & -\mathcal{L}\mathcal{C}^{-1}\mathcal{L}^T \end{bmatrix} \begin{bmatrix} I \ \mathcal{C}^{-1}\mathcal{L}^T \\ \mathbf{0} & I \end{bmatrix}$$

This yields the following three-steps

1)
$$C \widehat{\mathbf{x}}_1 = \mathbf{f}_1,$$

2) $\mathcal{L}C^{-1}\mathcal{L}^T \mathbf{x}_2 = \mathcal{L}\widehat{\mathbf{x}}_1 - \mathbf{f}_2,$
3) $C \mathbf{x}_1 = \mathbf{f}_1 - \mathcal{L}^T \mathbf{x}_2.$

Observe that

- a) steps (1) and (3) consist of solving a system for C, i.e. to solve a standard Navier-Stokes problem. Any existing CFD incompressible code can be used to this aim (see [76]);
- b) step (2) consists of solving a problem governed by matrix the $m \times m$ matrix $\mathcal{LC}^{-1}\mathcal{L}^T$, being m the number of artificial sections where the flow rate is assigned. This is typically a small number in haemodynamics problems (≤ 5). Therefore, a small number of GMRes iterations is in general enough for solving this system. However, the explicit computation of this matrix is not convenient, since the inversion of \mathcal{C} in general yields a full (i.e. non sparse) matrix, requiring a large amount (usually unaffordable) of memory storage resources. Iterative methods avoid the explicit calculation of the matrix, since they only need the application of the current matrix to a vector. This can be done in the following way ($\mathbf{v}, \mathbf{r}, \mathbf{z}$ and \mathbf{w} are vectors of proper dimension)

$$\mathbf{r} = \mathcal{L}\mathcal{C}^{-1}\mathcal{L}^T \mathbf{v} \Rightarrow \begin{cases} \mathbf{z} = \mathcal{L}^T \mathbf{v}, \\ \mathbf{w} = \mathcal{C}^{-1} \mathbf{z} \Rightarrow \mathcal{C} \mathbf{w} = \mathbf{z}, \\ \mathbf{r} = \mathcal{L} \mathbf{w}. \end{cases}$$

Second step on the right hand side requires again to solve a standard Navier-Stokes problem.

c) step (3) can be rewritten in the form:

$$\mathbf{x}_1 = \mathcal{C}^{-1} \mathbf{f}_1 - \mathcal{C}^{-1} \mathcal{L}^T \mathbf{x}_2 = \widehat{\mathbf{x}}_1 - \mathbf{r}$$

where vector $\mathbf{r} \equiv C^{-1} \mathcal{L}^T \mathbf{x}_2$ is a by-product of the last iteration of step (2), so that this step simply requires a vector sum.

This approach can still be computationally expensive, in particular in unsteady problems, since step (2) requires at each GMRes iteration to solve a Navier-Stokes problem. For this reason, some specific techniques for computing an approximate solution to $A\mathbf{y} = \mathbf{c}$ have been devised. In [77] an "approximated technique" is proposed, such that the error introduced is confined in a small neighborhood of the sections where flow rate are prescribed. In Fig. 2.12 we present an example of solution in a realistic geometrical model of a carotid bifurcation. The heuristic approach based on the prescription of an inlet velocity parabolic profile and a constant pressure profile at the outlet

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of the internal carotid (on the left) yields a different solution of the velocity field computed with the Lagrange multiplier approach (centre). Solution obtained with inexact approach [77] (on the right) is very similar to the Lagrange multiplier one, and it requires about one half of the computational time.



Fig. 2.12. Computations in a 3D carotid bifurcation (the square identifies the cutting plane). Velocity field obtained with the prescription of an inlet parabolic profile (left) the splitting augmented lagrangian scheme (centre), the inexact approach of [77] (right)



Fig. 2.13. Control approach applied to a flow rate problem in a 3D carotid bifurcation. On the left, the solution obtained by solving the minimization problem. On the right, plot of the differences with the solution obtained by the Lagrange multiplier approach. The differences are below the discretization error

Control approach

We finally address a different approach, that is in some sense "dual" to the Lagrange multiplier strategy. More precisely, in the latter method flow rate boundary conditions are regarded as a constraint to be forced by means of Lagrange multipliers to the Navier-Stokes solution. Navier-Stokes equations in this context play the role of *state equations*. A different, more versatile approach can be devised by swapping the roles. We introduce a functional to be minimized in order to force the fulfillment of the given defective boundary conditions, and use Navier-Stokes equations as a constraint for the functional minimization. Clearly, for this to work we need to make Navier-Stokes problem function of parameters, called *control variables*, over which the minimum is seeked. The defective boundary problem in this way is formulated as a *control problem* (see e.g. [31]).

For the sake of simplicity, we introduce this approach for the case of the steady Stokes problem. The extension to the unsteady Navier-Stokes problem can be found in [24].

Let us consider the following functional associated with flux conditions (2.12)

$$J_Q: \mathbf{V}_f \to \mathbb{R}^+, \quad J_Q(\mathbf{w}) = \frac{1}{2} \sum_{i=1}^m \left(\int_{\Gamma_i} \mathbf{w} \cdot \mathbf{n} d\gamma - Q_i \right)^2.$$
 (2.17)

We can formulate the defective boundary problem as follows: minimize functional (2.17) with the constraint

$$-\mu \Delta \boldsymbol{u} + \nabla \boldsymbol{p} = \mathbf{f}, \qquad \mathbf{x} \in \Omega$$

$$\nabla \cdot \boldsymbol{u} = 0, \qquad \mathbf{x} \in \Omega$$

$$\boldsymbol{u}|_{\Gamma_w} = \mathbf{0}, \qquad (2.18)$$

$$(-\boldsymbol{p}\boldsymbol{n} + \mu \nabla \boldsymbol{u}(\mathbf{k}) \cdot \mathbf{n})|_{\Gamma_0} = \mathbf{0}, \qquad (2.18)$$

$$(-\boldsymbol{p}\boldsymbol{n} + \mu \nabla \boldsymbol{u}(\mathbf{k}) \cdot \mathbf{n})|_{\Gamma_i} = -k_i \boldsymbol{n}, \ i = 1, \dots, m.$$

Here $\mathbf{f} \in \mathbf{L}^2(\mathbf{\Omega})$ is given and the control variables are taken to be the constant normal components k_i of stress on the artificial boundaries. That is, we look for the values of k_i such that the solution of (2.18) minimizes J_Q . In the sequel we will denote by \mathbf{k} the *m*-dimensional vector with entries k_i . To this aim, following e.g. [31], we introduce the constrained functional:

$$\mathcal{L}(\mathbf{w}, s; \boldsymbol{\lambda}_{\mathbf{w}}, \lambda_{s}; \boldsymbol{\eta}) = J_{Q}(\mathbf{w}) + \mu(\nabla \mathbf{w}, \nabla \boldsymbol{\lambda}_{w}) + b(s, \nabla \cdot \boldsymbol{\lambda}_{w}) + \sum_{i=1}^{m} \int_{\Gamma_{i}} \eta_{i} \boldsymbol{\lambda}_{w} \cdot \boldsymbol{n} \, d\gamma - (\mathbf{f}, \boldsymbol{\lambda}_{w}) - (\lambda_{s}, \nabla \cdot \mathbf{w}).$$

Here $\lambda_{\mathbf{w}}$ and λ_s are the so-called *adjoint* variables associated with \mathbf{w} and s respectively. Solution is seeked by looking for stationary points of \mathcal{L} . This turns to be equivalent to solve the following problem⁹, where for the sake of brevity we omit to specify that the differentials are computed in $[\mathbf{u}, \mathbf{p}; \lambda_{\mathbf{u}}, \lambda_{\mathbf{p}}; \mathbf{k}]$, while we put into evidence the dependence on the control variables.

⁹ Rigorously speaking, the problem is obtained by forcing the *Gateaux differentials* of \mathcal{L} evaluated along the direction of any test function to vanish in correspondence of the solution $[\mathbf{u}, \mathbf{p}; \boldsymbol{\lambda}_{\mathbf{u}}, \boldsymbol{\lambda}_{\mathbf{p}}; \mathbf{k}]$ (see [31]).

Given $\mathbf{f} \in \mathbf{L}^2(\Omega)$ and $\mathbf{Q} \in \mathbb{R}^m$, find $\boldsymbol{u}(\mathbf{k}) \in \mathbf{V}, \mathbf{p}(\mathbf{k}) \in \mathbf{L}^2(\Omega), \lambda_{\boldsymbol{u}} \in \mathbf{V}, \lambda_p \in L^2(\Omega)$ and $\mathbf{k} \in \mathbb{R}^m$, such that, for all $\mathbf{v} \in \mathbf{V}, q \in L^2(\Omega)$ and $\nu \in \mathbb{R}$:

$$(P)^{\leq d\mathcal{L}_{\boldsymbol{\lambda}_{\mathbf{w}}}, \mathbf{v} \rangle = \mu(\nabla \mathbf{u}, \nabla \mathbf{v}) + b(p, \nabla \cdot \mathbf{v}) + \sum_{i=1}^{m} \int_{\Gamma_{i}} k_{i} \mathbf{v} \cdot \mathbf{n} \, d\gamma - (\mathbf{f}, \mathbf{v}) = 0,$$

$$\begin{cases} < d\mathcal{L}_{\mathbf{u}}, \mathbf{v} \rangle = \mu(\nabla \mathbf{v}, \nabla \boldsymbol{\lambda}_{\boldsymbol{u}}) + b(\lambda_{p}, \nabla \cdot \mathbf{v}) - \sum_{i=1}^{m} \left(\int_{\Gamma_{i}} \boldsymbol{u} \cdot \mathbf{n} \, d\gamma - Q_{i} \right) \int_{\Gamma_{i}} \mathbf{v} \cdot \mathbf{n} \, d\gamma = 0,$$

$$(A) \sum_{i=1}^{m} \left(\int_{\Gamma_{i}} \boldsymbol{u} \cdot \mathbf{n} \, d\gamma - Q_{i} \right) \int_{\Gamma_{i}} \mathbf{v} \cdot \mathbf{n} \, d\gamma = 0,$$

$$(C_{j}) < d\mathcal{L}_{\eta_{j}}, \nu \rangle = \int_{\Gamma_{j}} \nu \boldsymbol{\lambda}_{\boldsymbol{u}} \cdot \mathbf{n} \, d\gamma = 0, \quad j = 1, \dots, m.$$

This system couples a steady Stokes problem (P), its adjoint (A) and m scalar equations (optimality conditions, denoted by (C_j)). Observe that the latter conditions force the adjoint variable λ_u to have null flux on the artificial boundaries. Well posedness of this problem is investigated in [24].

Numerical solution of this problem is not trivial. A possible approach is to resort to the *steepest descent method* applied to the minimization of the functional at hand. For more details see [24].

In Fig. 2.13 we report the computation for the same case of Figure 2.12, solved with the control approach. On the right, the differences with the solution computed with the Lagrange multiplier approach are below the discretization errors. The computational costs of this approach can be made comparable with the ones of the augmented formulation (solved by the splitting scheme) thanks to a proper selection of the iterative solver of the sequence of problems (P), (A) and (C_j) . The control approach is on the other hand more versatile, as we will see when considering the mean pressure problems.

2.3.2 Mean pressure problem

Let us consider now the following problem: look for (u, p) such that equation (2.9) is satisfied with conditions (2.10) and (2.11) and

$$\int_{\Gamma_i} p d\gamma = P_i, \qquad i = 0, 1, \dots, m, \tag{2.19}$$

where P_i are given functions of time. As for flow rate problem, conditions (2.19) are not enough for having well-posedness and some further data need to be prescribed. Let us illustrate some approaches that aim at completing these conditions in a mathematically sound way, that is affecting as little as possible the corresponding solutions.

Again, we will introduce a variational approach at first, then we will consider a possible Lagrange multiplier formulation. Both approaches are affected by some important drawbacks that the formulation based on control approach overcomes.

A variational approach

In [34] the following variational formulation of the mean pressure problem is proposed: given $P_i(t)$, i = 1, 2, ..., m, find $(\boldsymbol{u}, p) \in L^2(0, T; \mathbf{H}^1(\Omega)) \times L^2(0, T; L^2(\Omega))$ such that for all $\mathbf{v} \in \mathbf{H}^1(\Omega)$ and $q \in L^2(\Omega)$

$$\left(\frac{\partial \boldsymbol{u}}{\partial t}, \mathbf{v}\right) + a(\boldsymbol{u}, \mathbf{v}) + c\left(\boldsymbol{u}, \boldsymbol{u}, \mathbf{v}\right) + b(\mathbf{v}, p) = (\mathbf{f}, \mathbf{v}) - \sum_{j=1}^{m} P_j \int_{\Gamma_j} \mathbf{v} \cdot \mathbf{n} d\gamma,$$

$$b(\mathbf{u}, q) = 0,$$

(2.20)

with $\boldsymbol{u}(\boldsymbol{x},0) = \boldsymbol{u}_0(\boldsymbol{x}).$

Boundary conditions added by this formulation are identified in the following Proposition (see [34]).

Proposition 2.3.5 Any smooth solution of (2.20) fulfills the following boundary conditions on the artificial boundaries Γ_i , i = 0, 1, 2, ..., m:

$$(p(\mathbf{x}, \mathbf{t})\mathbf{n} - \nu \nabla \mathbf{u}(\mathbf{x}, \mathbf{t}) \cdot \mathbf{n})|_{\Gamma_i} = P_i(t)\mathbf{n}, \quad \forall \mathbf{x} \in \Gamma_i, t > 0.$$

This Proposition states that variational formulation (2.20) forces the mean pressure data by imposing a constant normal stress on the artificial boundaries. This is indeed the expected solution in special domains, like a cylindrical rectilinear pipe where Γ_i is normal to the axis. Here, formulation (2.20) actually forces the given mean pressure data.

For a generic domain, however, this techniques provides only an approximate formulation to the pressure drop problem. This is for instance the case of a rectilinear cylindrical domain with Γ_i oblique to its axis (see Fig. 2.14). We can therefore consider different approaches.

Augmented formulation

Augmented formulation for pressure drop problems still stems from regarding mean pressure data as constraints for the Navier-Stokes solution, leading to the problem: find $\mathbf{u} \in L^2(0, T, \mathbf{V}_f) \cap L^{\infty}(0, T, \mathbf{L}^2(\Omega)), p \in L^2(0, T, Q_f)$ and $\boldsymbol{\lambda} \in (L^2(0, T))^m$ such that for all $\mathbf{v} \in \mathbf{V}_f, q \in Q_f$:

$$\left(\frac{\partial \boldsymbol{u}}{\partial t}, \mathbf{v}\right) + a(\mathbf{u}, \mathbf{v}) + c(\boldsymbol{u}, \boldsymbol{u}, \mathbf{v}) + b(\mathbf{v}, p) + \sum_{i=1}^{m} \frac{1}{\Gamma_i} \int_{\Gamma_i} p d\gamma = (\mathbf{f}, \mathbf{v})$$

$$b(\boldsymbol{u}, q) + \sum_{j=0}^{m} \lambda_j \int_{\Gamma_j} q d\gamma = 0$$

$$\frac{1}{|\Gamma_i|} \int_{\Gamma_i} p d\gamma = P_i \qquad i = 1, 2, \dots m.$$
(2.21)

This problem unfortunately yields unreliable solutions. As a matter of fact, it is possible to verify (see [17]) that implicit conditions forced by this formulation read:



Fig. 2.14. A domain where variational formulation (2.20) for the mean pressure problem is not exact. τ_1 and τ_2 are the directions orthogonal to the axis *a* and **n** is the unit vector orthogonal to the artificial boundary

$$\boldsymbol{u}(\mathbf{x},t)\cdot\mathbf{n}=\lambda_i(t)$$
 on Γ_i .

In general, since λ_i are non zero constants in space and $\boldsymbol{u} = \boldsymbol{0}$ on Γ_w we have an incompatibility on $\overline{\Gamma}_i \cap \overline{\Gamma}_w$. For this reason, augmented formulation for mean pressure drop problems is not furtherly investigated.

Control approach

Approach based on control theory presented for flow rate problems can be straightforwardly extended to mean pressure problems. With this aim, we introduce the following functional.

$$J_P(s) = \frac{1}{2} \left(\sum_{i=0}^m \frac{1}{|\Gamma_i|} \int_{\Gamma_i} s \, d\gamma - P_i \right)^2 \tag{2.22}$$

and, as for the flow rate conditions, we consider a constrained minimization problem. Again, we assume that Navier-Stokes equations play the role of constraint for the solution minimizing (2.22). As control variables we still assume the constant normal stresses $\mathbf{k} = [k_i]$. It is worth remarking that this is not the only possible formulation, since other choices for the control variables can be pursued, such as flow rates (see [24]).

Still referring to steady Stokes equations for the sake of simplicity, we introduce the following Lagrange functional:

$$\mathcal{L}(\mathbf{w}, s; \boldsymbol{\lambda}_w, \lambda_s; \boldsymbol{\eta}) = J_P(s) + a(\mathbf{w}, \boldsymbol{\lambda}_w) + d(s, \boldsymbol{\lambda}_w) + \sum_{i=0}^m \int_{\Gamma_i} \eta_i \boldsymbol{\lambda}_w \cdot \mathbf{n} \, d\gamma - (\mathbf{f}, \boldsymbol{\lambda}_w) + d(\lambda_s, \mathbf{w}).$$
The stationary point of \mathcal{L} fulfills the following problem: given $\mathbf{f} \in \mathbf{L}^2(\Omega)$ and $P_j \in \mathbb{R}, j = 0, ..., m$, find $\mathbf{k} \in \mathbb{R}^m$, $\mathbf{u}(\mathbf{k}) \in \mathbf{V}_{div}, p(\mathbf{k}) \in H^1(\Omega), \lambda_u \in \mathbf{V}_{div}$ and $\lambda_p \in H^1(\Omega)$, such that, for all $\mathbf{v} \in \mathbf{V}_{div}, q \in H^1(\Omega)$ and $\nu \in \mathbb{R}$,

$$(P) \begin{cases} < d\mathcal{L}_{\boldsymbol{\lambda}_{\boldsymbol{u}}}, \mathbf{v} >= a(\mathbf{u}, \mathbf{v}) + d(p, \mathbf{v}) + \sum_{i=0}^{m} \int_{\Gamma_{i}} k_{i} \mathbf{v} \cdot \mathbf{n} \, d\gamma - (\mathbf{f}, \mathbf{v}) = \mathbf{0}, \\ < d\mathcal{L}_{\boldsymbol{\lambda}_{p}}, q >= d(q, \mathbf{u}) = \mathbf{0}, \\ < d\mathcal{L}_{\mathbf{u}}, \mathbf{v} >= a(\mathbf{v}, \boldsymbol{\lambda}_{\boldsymbol{u}}) + d(\boldsymbol{\lambda}_{p}, \mathbf{v}) = 0, \\ < d\mathcal{L}_{p}, q >= \sum_{i=0}^{m} \left(\frac{1}{|\Gamma_{i}|} \int_{\Gamma_{i}} p \, d\gamma - P_{i} \right) \frac{1}{|\Gamma_{i}|} \int_{\Gamma_{i}} q \, d\gamma + d(q, \boldsymbol{\lambda}_{\mathbf{u}}) = \mathbf{0}, \\ (C_{j}) \quad < d\mathcal{L}_{k_{i}}, \nu >= \int_{\Gamma_{i}} \nu \boldsymbol{\lambda}_{\mathbf{u}} \cdot \mathbf{n} \, d\gamma = \mathbf{0}, \quad \mathbf{i} = \mathbf{0}, \dots, \mathbf{m}. \end{cases}$$

One of the most interesting features of this approach is that functional to be minimized can be properly adjusted for including a priori informations on the behavior of the solution on artificial boundaries. For instance, for a boundary of a pipe non orthogonal to the axis (see Fig. 2.14), when as we have pointed out variational formulation (2.20) fails, the functional to be minimized can be adapted in order to include physical evidence of the prevalent axial direction of the flow. We resort therefore to the functional

$$\mathcal{L}(\mathbf{w}, s; \boldsymbol{\lambda}_w, \lambda_s; \boldsymbol{\eta}) = J_P(s) + a(\mathbf{w}, \boldsymbol{\lambda}_w) + d(s, \boldsymbol{\lambda}_w) + \sum_{i=0}^m \int_{\Gamma_i} \eta_i \boldsymbol{\lambda}_w \cdot \mathbf{n} \, d\gamma - (\mathbf{f}, \boldsymbol{\lambda}_w) + d(\lambda_s, \mathbf{w}) + \mathcal{S}(\mathbf{w}, \boldsymbol{\tau}_1, \dots, \boldsymbol{\tau}_m)$$
(2.23)

where in a problem with d space dimensions

$$\mathcal{S}(\mathbf{w}, \boldsymbol{\tau}_1, \dots, \boldsymbol{\tau}_m) = \frac{1}{2} \sum_{l=1}^{d-1} \sum_{i=0}^m \int_{\Gamma_i} |\mathbf{w} \cdot \boldsymbol{\tau}_l|^2 \, d\gamma \tag{2.24}$$

and τ_l are the orthogonal directions to the pipe axis a, that in this case do not coincide with the tangential directions to the boundary Γ_i . Perturbation S forces velocity components orthogonal to a to be small. With a proper choice of control variables, this yields good numerical results. For instance, suppose to prescribe a mean pressure $\int_{\Gamma} p d\gamma = P = 1 g/(s^2 cm)$ at the outlet Γ_{out} of the domain T (see Figure 2.15 top). Boundary Γ_{out} is supposed to be an artificial boundary in a pipe where a Poiseuille flow holds, so that vertical velocity is zero.

By minimizing functional (2.22), an undesiderable vertical velocity at the outlet occurs (Figures 2.15, centre). To avoid these effects, we minimize the penalized functional (2.23) with (2.24), using the complete stress (normal and tangential) as control variables. Figures 2.15, bottom, show that these strategies are able to strongly reduce the wrong tangential velocities.

Remark 2.3.2 Extension of the strategies presented above to the case of compliant domains is not trivial. Preliminar investigations can be found in [49, 51, 60].



Fig. 2.15. Simulations in a 2D pipe with an oblique boundary: in the centre axial and normal velocity componets by solving a mean pressure problem with the minimization of (2.22). On the bottom the same problem solved by minimizing (2.24): the velocity component along τ is strongly reduced (maximum value in the last figure is 10^{-5})

2.4 Some well posedness results

In this section we gather some theoretical properties of multiscale models. We illustrate in particular some stability results concerning the coupling of 3D and 1D models. Then we will present a general well posedness analysis of 3D/0D models and its extension to the 1D/0D case.

2.4.1 Coupling of 3D and 1D models

Referring to Fig. 2.16, let us consider the following problem, where 3D and 1D domains have an axis that for the sake of simplicity we assume to be along z direction. 3D problem for $z \in [0, a]$ is represented by the following system



Fig. 2.16. Domain for the coupled 3D/1D problem

$$\begin{aligned} \frac{\partial \boldsymbol{u}}{\partial t} + \left(\frac{1}{2}\nabla |\boldsymbol{u}|^2 + (\nabla \times \boldsymbol{u}) \times \boldsymbol{u}\right) - \nabla \cdot (2\nu \mathbf{D}(\boldsymbol{u})) + \nabla p &= \mathbf{f} \quad \mathbf{x} \in \Omega_f, t > 0, \\ \nabla \cdot \boldsymbol{u} &= 0 \qquad \mathbf{x} \in \Omega_f, t > 0, \\ \rho_w \frac{\partial^2 \boldsymbol{d}_r}{\partial t^2} + \sigma \mathbf{d}_r &= \Phi_r - \Phi_{ext} \quad \mathbf{x} \in \Gamma_w, t > 0, \end{aligned}$$

$$(2.25)$$

where ρ_w is the wall density, d_r is the radial displacement, while we assume that axial and circumferential displacements are null, and $\Phi_r - \Phi_{ext}$ is the difference of stresses in the radial direction induced by the fluid and the external organs. Observe that the structure is modelled by the *independent rings model*, while the convective term of the fluid problem has been rearranged in order to have natural conditions associated with the total pressure (see [60]).

System is completed by the initial conditions $d(\mathbf{x}, 0) = d_0$, $\frac{\partial d}{\partial t}(\mathbf{x}, 0) = \mathbf{u}_s$ for $\mathbf{x} \in \Gamma_w$ and $u(\mathbf{x}, 0) = u_0$ for $\mathbf{x} \in \Omega$. At the inlet Γ_{in} of the 3D domain we can assume both Dirichlet and Neumann conditions for the Navier-Stokes equations.

For $z \in (a, b)$ we assume E model to hold with equations (1.24) that we report here

$$\frac{\partial A}{\partial t} + \frac{\partial Q}{\partial x} = 0,$$

$$\frac{\partial Q}{\partial t} + \frac{\partial}{\partial x} \left(\alpha \frac{Q^2}{A} \right) + \frac{A}{\rho} \left(\frac{\partial p}{\partial x} \right) + K_R \frac{Q}{A} = 0.$$

We assume moreover that area and pressure are related by an algebraic law in the form (see Sect. 1.1.1)

$$P - P_{ext} = \psi(A, A_0, \beta) = \beta \frac{\sqrt{A} - \sqrt{A_0}}{A_0}.$$

On z = b we assume absorbing boundary conditions, stating that the incoming characteristic variable (W_2) vanishes.

We assume in z = a the following matching conditions

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$$\left(\left(p + \frac{1}{2} |\boldsymbol{u}|^2 \right) \mathbf{I} - 2\nu \mathbf{D}(\boldsymbol{u}) \right) \cdot \boldsymbol{n} = P_{1D} + \frac{1}{2} |\overline{\boldsymbol{u}}_{1D}|^2,$$

$$\int_{\Gamma_f} \boldsymbol{u} \cdot \boldsymbol{n} d\gamma = Q_{1D}.$$
 (2.26)

With this problem, we associate the following functionals for each t > 0:

3D problem: $\mathcal{E}_{3D} = \frac{1}{2} ||\boldsymbol{u}||_{L^2}^2 + \frac{\rho_w}{2} ||\frac{\partial \mathbf{d}}{\partial t}||_{L^2_0}^2 + \frac{b}{2} ||\mathbf{d}||_{L^2_0}^2$

where L_0^2 stands for $L^2(\Gamma_{w,0})$, being $\Gamma_{w,0}$ a reference configuration for the structure, mapping into the current one at each time instant; 1D problem: $\mathcal{E}_{1D} = \frac{1}{2} \int_a^b \frac{Q^2}{A} dz + \int_a^b \int_{A_0}^A \psi(\tau, A_0, \beta) d\tau dz.$

The following results have been proved in [49].

Proposition 2.4.1 1. If homogeneous Dirichlet conditions for the velocity are prescribed on Γ_{in} , we have (energy decay property)

$$\mathcal{E}_{3D}(t) + \nu \int_0^t ||\mathbf{D}(\boldsymbol{u})||_{L^2}^2 dt + \mathcal{E}_{1D}(t) K_r \int_0^t \int_a^b \frac{Q^2}{A^2} dz dt \le \mathcal{E}_{3D}(0) + \mathcal{E}_{1D}(0).$$

2. If non homogeneous Neumann conditions for the fluid are prescribed on Γ_{in} with data **g**, we have (energy estimate)

$$\begin{aligned} \mathcal{E}_{3D}(t) + \nu \int_0^t ||\mathbf{D}(\boldsymbol{u})||_{L^2}^2 dt + \mathcal{E}_{1D}(t) K_r \int_0^t \int_a^b \frac{Q^2}{A^2} dz dt \leq \\ \left(\mathcal{E}_{3D}(0) + \mathcal{E}_{1D}(0) + C \int_0^t ||\mathbf{g}||_{L^2(\Gamma_i n)}^2 \right) e^{2\nu t}. \end{aligned}$$

Remark 2.4.1 Previous results can be extended to more complex domains with many interfaces between 3D and 1D models. As a matter of fact, these results can be applied locally at each interface.

2.4.2 Coupling of 3D and 0D models

We consider now the multiscale 3D/0D depicted in Fig. 2.11. In particular we make the following basic assumptions.

- 1. NS model is given in terms of classical primitive variable formulation of Navier-Stokes equations. We assume that initial data and forcing terms are small enough, for the sake of well-posedness of the problem (see [34]).
- 2. Nonlinear terms of K model (introduced by the modelling of valves and of the heart action) are described by smooth functions (see Chap. 1, Fig. 1.11).

This coupled problem can be analyzed by a fixed point strategy represented in Fig. 2.17. Precisely, we regard the solution as the fixed point of an operator \mathcal{T} given by the sequence of NS and K problems (denoted respectively as \mathcal{P}_{NS}



Fig. 2.17. Splitting/fixed point reformulation of multiscale model of Fig. 2.11

and \mathcal{P}_K). Setting $\mathcal{T} = \mathcal{P}_K \cdot \mathcal{P}_{NS}$ the solution to the coupled multiscale problem satisfies

$$\overline{\mathbf{s}} = \mathcal{T}\overline{\mathbf{s}} = \mathcal{P}_K \cdot \mathcal{P}_{NS}\overline{\mathbf{s}}.$$

In this framework, we add two further assumptions.

- 3. The splitting into subproblems \mathcal{P}_{NS} and \mathcal{P}_{K} represented in Fig. 2.17 is bridging region compatible. With reference to Fig. 2.11, the role of interface variables in the splitting is given in Tab. 2.1.
- 4. Defective boundary problem \mathcal{P}_{NS} is formulated in terms of variational formulations following the variational approach advocated in Sect. 2.3.

	Input \mathcal{P}_{NS} =Output \mathcal{P}_K	Input \mathcal{P}_K = Output \mathcal{P}_{NS}
Γ_0	pressure P_0	flow rate Q_0
Γ_1	flow rate Q_1	pressure P_1
Γ_2	flow rate Q_2	pressure P_2

 Table 2.1. Role of matching data in a bridging region compatible splitting for multiscale model depicted in Fig. 2.11

By collecting classical results of calculus and results proven in [34], [13], we have that:

- 1. **NS Problem:** If initial and forcing data are small enough, \mathcal{P}_{NS} is well posed.
- 2. **K Problem:** DAE system of \mathcal{P}_K is of index 1 and can be reformulated as a well posed Cauchy problem.
- 3. **Multiscale:** There exists $T^* > 0$ such that \mathcal{T} is *compact* in $(0, T^*]$. This means that the application of \mathcal{T} to bounded sequences of arguments yields *convergent* sequences in appropriate topologies (for a more precise definition of compactness see f.i. [83]).

The latter step actually proves the existence of a fixed point, thanks to the classical *Schauder's fixed point theorem*.

2.4.3 Coupling of 1D and 0D models

Following a similar outline as for the 3D-0D coupling, in [15] the coupling between 1D and 0D models is investigated. It is assumed that the 1D model is represented in terms of characteristic variables **W** and that the DAE system of lumped parameters model is reduced to an ordinary differential system, so that the coupled model reads

$$\frac{\partial \mathbf{W}}{\partial t} + \begin{bmatrix} \mu(W_1, W_2) & 0\\ 0 & \lambda(W_1, W_2) \end{bmatrix} \frac{\partial \mathbf{W}}{\partial x} = 0, \quad \text{in } \mathbb{R}^+ \times [0, T]$$

$$\frac{d \mathbf{y}}{dt} = \mathcal{G}(\mathbf{y}, t) + \mathbf{f} \quad \text{in } [0, T].$$
(2.27)

System (2.27) is completed by initial conditions $\mathbf{w}(x,0) = \mathbf{w}_0(x), \mathbf{y}(x,0) =$ $\mathbf{y}_0(x)$ and the matching conditions:

$$W_1(a,t) = g(\mathbf{y}, W_2), \mathbf{f} = \mathbf{f}(\mathbf{W}),$$

where x = a is the interface between the two submodels, g is a suitable function relating the Riemann invariant W_1 with the entry of the state vector **y** associated with the interface condition, for instance the interface pressure, and correspondingly forcing term \mathbf{f} would depend on the interface flow rate $Q = Q(\mathbf{W}).$

Results obtained for the 3D/0D coupling can be strengthened in the case of 1D/0D problems. In fact the analysis can be carried out again by reformulating this problem in a fixed point framework. Let \mathcal{P}_K be the operator corresponding to solve the lumped parameter model for a given flow rate Qat the interfaces and \mathcal{P}_E be the operator corresponding to solve 1D model for given pressure interfaces and to compute the associated interface flow rates. Then the problem at hand can be reformulated as the search of the fixed point for the operator:

$$\mathcal{T} = \mathcal{P}_E \cdot \mathcal{P}_K.$$

Under mild assumptions on the regularity of the initial data and on λ and μ it is possible to prove that:

- 1. \mathcal{P}_K is well posed for $0 < t \leq T_0$ with $T_0 \leq T$;
- 2. \mathcal{P}_E is well posed for $0 < t \leq T_1$ with $T_1 \leq T$; 3. \mathcal{T} is a *contraction* in $0 < t \leq \hat{T} \leq \min(T_0, T_1)$, i.e.

$$||\mathcal{T}(Q_1) - \mathcal{T}(Q_2)||_{C^0[0,\hat{T}]} \le K||u_1 - u_2||_{C^0[0,\hat{T}]}$$

with K < 1, being Q_1 and Q_2 two interfaces flow rates properly selected.

The latter inequality is stronger than the compactness proved for the corresponding operator in the 3D/0D. In particular, well known Banach contraction theorem (see e.g. [83]) proves in this case that the solution to the coupled problem exists and it is unique.



Fig. 2.18. 3D/0D coupling with K models described by impedance functions ζ_1 and ζ_2 in the frequency domain. Here lumped parameters model have the role of describing terminal vessels (see Sect. 1.1.4)

2.5 Numerical techniques for the coupling

We here consider possible numerical techniques for the coupled problems. In particular we will distinguish between monolithic solvers where the coupled problem is treated as a whole and substructuring-type solvers. In the latter, the solution is seeked by an iterative procedure where each model is computed in sequence. Monolithic solvers avoid the problem of setting up a fast convergent sequence of iterates. Yet, they may be more difficult to implement and sometimes give rise to badly conditioned problems. Substructuring procedures, on the other hand, may allow to use existing software already developed for solving subproblems separately.

2.5.1 Monolithic solvers

A variational formulation

Let us start considering the case of a 3D-0D coupled problem where K models describe terminal vessels, as we have done in Sect. 1.1.4. More precisely, we assume that the presence of terminal vessels is described in the frequency domain by means of an appropriate impedance function $\zeta_i(\omega)$ for i = 1, 2, ..., m(see Chap. 1) to be coupled to the 3D problem at the *m* distal boundaries of the latter. On the proximal boundaries of the NS problem we assume for the sake of simplicity that boundary data (pressure or flow rates) are given, for instance by measurements (see Fig. 2.18, where m = 2).

If $\pi_i(\omega)$ and $\chi_i(\omega)$ represent the Fourier transform of the interface pressures $P_i(t)$ and flows $Q_i(t)$ respectively, we have in the frequency domain

$$\pi_i(\omega) = \zeta_i(\omega)\chi_i(\omega).$$

In the time domain, the latter relation reads

$$P_i(t) = \frac{1}{T} \int_{t-T}^{t} Z_i(t-\tau)Q_i(\tau)d\tau.$$
 (2.28)

Here Z_i is the inverse Fourier transform of ζ_i and T is the heart beat period. Conditions (2.28) are not mean pressure boundary conditions, since the pressure is given as a function of the (unknown) flow rate. However, we can include (2.28) in the variational formulation of the 3D NS problem in a way similar to the one pursued for variational formulation of the mean pressure problem (see (2.20)). We set (for $j = 1, \ldots, m$)

$$\int_{\Gamma_j} (p\boldsymbol{n} - \nu \mathbf{D}(\boldsymbol{u}) \cdot \boldsymbol{n}) \cdot \mathbf{v} d\gamma = P_j \int_{\Gamma_j} \boldsymbol{n} \cdot \mathbf{v} d\gamma.$$

In this way, a variational formulation of the 3D/0D coupled problem reads:

$$\left(\frac{\partial \boldsymbol{u}}{\partial t}, \mathbf{v}\right) + a(\boldsymbol{u}, \mathbf{v}) + c(\boldsymbol{u}, \boldsymbol{u}, \mathbf{v}) + b(\mathbf{v}, p) + \sum_{j=1}^{m} \left[\frac{1}{T} \int_{t-T}^{t} Z_j(t-\tau) \int_{\Gamma_j} \boldsymbol{u}(\tau) \cdot \mathbf{n} d\tau \int_{\Gamma_j} \mathbf{v} \cdot \mathbf{n} d\gamma\right] = (\mathbf{f}, \mathbf{v}), \qquad (2.29)$$
$$b(\mathbf{u}, q) = 0,$$

and we obtain Robin boundary conditions for the Navier-Stokes problem.

For instance, if space discretization is obtained by the finite element methods and time discretization by means of finite difference schemes, then velocity field at time t^n is represented as

$$oldsymbol{u}_h(oldsymbol{x},t^n) = \sum \mathbf{U}_i^n oldsymbol{arphi}_i(oldsymbol{x})$$

being φ_k the basis functions of the finite element space and \mathbf{U}_k^n the nodal values vector. The boxed term can be discretized in time by resorting to classical quadrature formulas. If the quadrature nodes do coincide with time discretization points, we have simply

$$\frac{1}{T} \int_{t^{n+1}-T}^{t^{n+1}} Z_j(t^{n+1}-\tau) \int_{\Gamma_j} \boldsymbol{u}(\tau) \cdot \mathbf{n} d\tau \int_{\Gamma_j} \mathbf{v} \cdot \mathbf{n} d\gamma \approx \frac{1}{T} \left(\sum_{k=\underline{k}}^{\overline{k}} w_k Z_j(t^{n+1}-t^k) \int_{\Gamma_j} \boldsymbol{\varphi}_j \cdot \mathbf{n} \sum_l \int_{\Gamma_j} \boldsymbol{\varphi}_l \cdot \mathbf{n} \right) \mathbf{U}_j^l,$$

where w_k are the quadrature weights and the quadrature nodes are such that $T - t^{n+1} \leq t^{\underline{k}} \leq t^{\underline{k}+1} \leq \ldots \leq t^{\overline{k}-1} \leq t^{\overline{k}} \leq t^n$.

Remark 2.5.1 In the oversimplified case of a purely resistive impedance function $Z_j(t) = R_j T \delta(t)$, being δ the Dirac generalized function, boxed terms reduce to

$$R_j \int_{\Gamma_j} \boldsymbol{u}(t) \cdot \mathbf{n} d\gamma \int_{\Gamma_j} \mathbf{v} \cdot \mathbf{n} d\gamma.$$

This approach has been adopted for instance in [16] where the relevance of an appropriate impedance function is clearly pointed out by numerical results.

An algebraic formulation

In the previous section we have given a monolithic formulation of a coupled 3D/0D problem in which however the role of K model was essentially to provide boundary conditions in a way consistent with the structure of the vascular tree. Blood dynamics in terminal vessels is computed only as far as it influences 3D solutions at the interfaces.

Let us consider now a different approach in which one is interested also to the evolution of the state variables in the lumped parameter model. We assume therefore to describe 0D problems in the time domain as a system of ordinary differential equations.

For the sake of concreteness we will refer our general formulation to an example. We consider the multiscale problem represented in Fig. 2.19, where the K model is given by a network featuring a capacitance C, three resistances and three inductors. The forcing term in the network is given by a voltage/pressure generator where $P_p(t)$ is a given function. NS model is given by Navier-Stokes equations and bridging region compatibility implies that flow rate is prescribed at the boundaries of 3D domain. A model for the compliance of the wall can be included as well. For the sake of simplicity however we assume that the pipe is rigid, so that incoming flow rate is equal to the outgoing one. Equations associated to K model are

$$L\frac{dQ}{dt} + RQ + P = P_p - P_1 + P_2,$$

$$C\frac{dP}{dt} - Q = 0,$$
(2.30)

where $L = L_1 + L_2 + L_3$ and $R = R_1 + R_2 + R_3$, P is the pressure jump associated with the capacitance C, P_1 and P_2 are computed by the 3D model, and Q is the flow rate in the circuit.

Assume that both 3D and 0D problems have been properly discretized in space (3D) and time (3D and 0D) and linearised when required. At a pretty general level, at each time step we have to solve a linear system in the form:

$$\begin{bmatrix} \mathcal{A}_{cc} \ \mathcal{A}_{cf} \\ \mathcal{A}_{fc} \ \mathcal{A}_{ff} \end{bmatrix} \begin{bmatrix} \mathbf{s}_{c}^{n+1} \\ \mathbf{s}_{f}^{n+1} \end{bmatrix} = \begin{bmatrix} \mathbf{b}_{c}^{n+1} \\ \mathbf{b}_{f}^{n+1} \end{bmatrix} + \begin{bmatrix} \mathbf{g}_{c}(\mathbf{s}_{c}^{n}, \mathbf{s}_{c}^{n-1}, \dots, \mathbf{s}_{c}^{n-p_{c}}) \\ \mathbf{g}_{f}(\mathbf{s}_{f}^{n}, \mathbf{s}_{f}^{n-1}, \dots, \mathbf{s}_{f}^{n-p_{f}}) \end{bmatrix}.$$
 (2.31)

Indexes c and f stand for coarse and fine, since they refer to discretization of K and NS models respectively. We use this notation, since most part of the following considerations can be applied to different multiscale models (including 3D/1D or 1D/0D) as well. Vectors \mathbf{g}_c and \mathbf{g}_f account for the terms due to the time advancing schemes in the two submodels, that depend on the solution \mathbf{s} at the previous time steps ($p_c + 1$ and $p_f + 1$ are the steps of the time discretization scheme for the two subproblems respectively). Let us denote by N_u and N_p the number of velocity and pressure degrees of freedom respectively in the NS domain. Suppose moreover to solve the flow boundary



Fig. 2.19. An example of 3D/0D geometrical multiscale model

problem by means of a Lagrange multiplier approach, so that $\mathbf{s}_f \in \mathbb{R}^{N_u+N_p+1}$ given by $\mathbf{s}_f = [\mathbf{U}, \mathbf{P}, \lambda]$, while the vector of the unknowns of the coarse model is given by the state variables of the network, namely $\mathbf{s}_c = [Q, P]$. Now suppose to use an implicit Euler time discretization for both the fine and the coarse models. From (2.30) we have therefore:

$$\mathcal{A}_{cc} = \begin{bmatrix} \frac{1}{\Delta t} L + R & 1\\ -1 & C \end{bmatrix}, \mathcal{A}_{ff} = \begin{bmatrix} \frac{1}{\Delta t} \mathbf{M} + \mathbf{K} & D^T & \Lambda \\ \mathbf{D} & \mathbf{0} & \mathbf{0} \\ \Lambda^T & \mathbf{0} & \mathbf{0} \end{bmatrix}, \quad (2.32)$$

where M is the mass matrix, K is the discretization of the diffusion-convection operator of the momentum equation and D is the discretization of the divergence operator in the NS problem, while the discretization of the term related to the Lagrange multiplier has been denoted here by Λ .

Once pressure in 3D model is computed for a given flow rate, mean pressures P_1 and P_2 at the interfaces are computed by means of quadrature formulas

$$P_k = \int_{\Gamma_k} p d\gamma \approx \sum_i w_{i,k} p(x_i, y_i, z_i) \qquad k = 1, 2.$$
(2.33)

It is practically convenient to assume that quadrature nodes x_i, y_i, z_i on Γ_k do coincide with nodes of the space discretization of the problem¹⁰. Then we have (see also (2.14)):

¹⁰ In general quadrature nodes will not correspond to grid nodes and interpolation procedures will be necessary.

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$$\mathcal{A}_{cf} = \begin{bmatrix} \mathbf{0}_{1 \times N_u} & a_{cf} & 0\\ \mathbf{0}_{1 \times N_u} & \mathbf{0}_{1 \times N_p} & 0 \end{bmatrix}, a_{fc,i} = \begin{cases} 0 & \text{if } (x_i, y_i, z_i) \notin \Gamma_{1,2}\\ w_{i,k} & \text{if } (x_i, y_i, z_i) \in \Gamma_{1,2} \end{cases},$$
$$\mathcal{A}_{fc} = \begin{bmatrix} \mathbf{0}_{N_u \times 1} & \mathbf{0}_{N_u \times 1}\\ \mathbf{0}_{N_p \times 1} & \mathbf{0}_{N_p \times 1}\\ -1 & 0 \end{bmatrix}.$$

Finally:

$$\mathbf{b}_{c}^{n+1} = \begin{bmatrix} P_{P}(t^{n+1}) \\ 0 \end{bmatrix}, \mathbf{b}_{f}^{n+1} = \begin{bmatrix} \mathbf{F}^{n+1} \\ 0 \\ 0 \end{bmatrix}, \mathbf{g}_{c} = \begin{bmatrix} \frac{1}{\Delta t} LQ^{n} \\ 0 \end{bmatrix}, \mathbf{g}_{f} = \begin{bmatrix} \frac{1}{\Delta t} M \mathbf{U}^{n} \\ 0 \\ 0 \end{bmatrix}$$
(2.34)

A possible solution strategy is to solve the complete system (2.31) as a whole at each time step. As already pointed out, also for simple cases as for the example at hand, this approach can have the drawback of a badly conditioned system. An alternative approach is a Schur complement decomposition of the problem. By a formal elimination of the coarse solution \mathbf{s}_{c}^{n+1} , we obtain

$$\left(\mathcal{A}_{ff} - \mathcal{A}_{fc}\mathcal{A}_{cc}^{-1}\mathcal{A}_{cf}\right)\mathbf{s}_{f}^{n+1} = \mathbf{b}_{f}^{n+1} + \mathbf{g}_{2}(\mathbf{s}_{f}^{n}) - \mathcal{A}_{fc}\mathcal{A}_{cc}^{-1}\left(\mathbf{b}_{c}^{n+1} + \mathbf{g}_{c}(\mathbf{s}_{c}^{n})\right).$$
(2.35)

In general, matrix \mathcal{A}_{cc}^{-1} is not available and appropriate techniques of solution are required (see the next section). However, in the simplest coarse models like the one at hand, matrix \mathcal{A}_{cc}^{-1} can be easily computed

$$\mathcal{A}_{cc}^{-1} = \frac{1}{(\Delta t^{-1}L + R) + 1} \begin{bmatrix} C & -1\\ 1 & \Delta t^{-1}L + R \end{bmatrix}$$
(2.36)

and problem can be solved by (2.35). In fact, by algebraic manipulation, the Schur complement is explicitly computed

$$\mathcal{A}_{ff} - \mathcal{A}_{fc} \mathcal{A}_{cc}^{-1} \mathcal{A}_{cf} = \begin{bmatrix} \frac{1}{\Delta t} M + K & D & r \\ D^T & \mathbf{0} & \mathbf{0} \\ r^T & -\frac{\Delta t C}{L + \Delta t (R+1)} a_{cf} & \mathbf{0} \end{bmatrix}.$$
 (2.37)

System (2.35) can be therefore solved, yielding the fine solution \mathbf{s}_{f}^{n+1} . Coarse solution is then recovered by solving

$$\mathbf{s}_{c}^{n+1} = \mathcal{A}_{cc}^{-1} \left(\mathbf{b}_{c}^{n+1} + \mathbf{g}_{c}(\mathbf{s}_{c}^{n}) - \mathcal{A}_{cf} \mathbf{s}_{f}^{n+1} \right).$$

2.5.2 Iterative substructuring approaches

The block gaussian elimination proposed in the previous section is seldom feasible, since matrix \mathcal{A}_{cc}^{-1} is neither easy nor convenient to compute explicitly

in general. For this reason, here we address some possible solution schemes resorting to the separate computing of the submodels that do not need the explicit computation of \mathcal{A}_{cc}^{-1} .

A first, simple method for solving the problem is following iterative scheme.

- 1. Let $\mathbf{s}_{f,0}^{n+1}$ be a time extrapolation of \mathbf{s}_{f}^{n+1} based on the previous time evaluations of \mathbf{s}_{f} .
- 2. For $k = 0, 1, 2, \dots$ solve

$$\begin{cases} \mathcal{A}_{cc} \mathbf{s}_{c,k+1}^{n+1} = \mathbf{b}_{c}^{n+1} + \mathbf{g}_{c}(\mathbf{s}_{c}^{n}, \dots, \mathbf{s}_{c}^{n-p_{c}}) - \mathcal{A}_{cf} \mathbf{s}_{f,k}^{n+1} \\ \mathcal{A}_{ff} \mathbf{s}_{f,k+1}^{n+1} = \mathbf{b}_{f}^{n+1} + \mathbf{g}_{f}(\mathbf{s}_{f}^{n}, \dots, \mathbf{s}_{c}^{n-f_{f}}) - \mathcal{A}_{fc} \mathbf{s}_{c,k+1}^{n+1} \end{cases}$$
(2.38)

up to the fulfillment of an appropriate convergence test.

Observe how this splitting approach is essentially based on the same fixed point formulation devised for well posedness analysis of multiscale problems.

The first issue is the *convergence* of the iterations. This problem can be analyzed by regarding this scheme as a *block Gauss-Seidel* scheme for solving system (2.31), or, equivalently, as a Richardson preconditioned scheme (see e.g. [62]). Upon classical arguments of numerical analysis, the convergence of the scheme is driven by the maximum ρ among the absolute values of the eigenvalues of matrix

$$\begin{bmatrix} \mathcal{A}_{cc} & \mathbf{0} \\ \mathcal{A}_{fc} & \mathcal{A}_{ff} \end{bmatrix}^{-1} \begin{bmatrix} \mathcal{A}_{cc} & \mathcal{A}_{cf} \\ \mathcal{A}_{fc} & \mathcal{A}_{ff} \end{bmatrix}$$

More precisely, if $\rho < 1$, the scheme converges. In practice, it is quite hard to compute ρ , so this convergence analysis is seldom able to give quantitative responses about convergence and it has essentially a theoretical relevance. A practical approach for driving the iterative scheme to the convergence is to introduce an arbitrary parameter to be properly tuned. In the present case, (2.38) can be modified as follows. For the sake of notation we drop time index n+1 from now on.

$$\begin{cases} \mathcal{A}_{cc} \mathbf{s}_{c,k+1} = \mathbf{b}_{c} + \mathbf{g}_{c} (\mathbf{s}_{c}^{n}, \dots, \mathbf{s}_{c}^{n-p_{c}}) - \mathcal{A}_{cf} \mathbf{s}_{f,*}^{n+1} \\ \mathcal{A}_{ff} \mathbf{s}_{f,k+1} = \mathbf{b}_{f} + \mathbf{g}_{f} (\mathbf{s}_{f}^{n}, \dots, \mathbf{s}_{f}^{n-p_{f}}) - \mathcal{A}_{fc} \mathbf{s}_{c,k}^{n+1} \\ \mathbf{s}_{f,*}^{n+1} = \theta \mathbf{s}_{f,k+1}^{n+1} + (1-\theta) \mathbf{s}_{f,k}^{n+1} \end{cases}$$
(2.39)

In the example above, this means that average pressures used as forcing terms for the coarse problem are modulated by the *relaxation parameter* θ . An appropriate selection of θ can yield or improve convergence of the iterative scheme, even if a priori it is not easy to identify its optimal value.

This scheme has been used for 3D/1D coupling illstrated in Fig. 2.20. The 3D model is rigid and mimics a stented segment of a cylindrical artery. Pressure drop problem is solved for the NS model, being pressure computed as a function of the area computed by E model. The latter receives data on

flow rate, that are formulated in terms of the incoming characteristic variables $(W_2 \text{ at interface } \Gamma_{up} \text{ and } W_1 \text{ at interface } \Gamma_{dw})$. Velocity and pressure solutions in 3D model (bottom, centre) are illustrated together with area in upstream (bottom, left) and downstream (bottom, right) of Fig. 2.20. Effects of the stent rigidity on the upstream area can be recognized. Relaxation parameter θ has been tuned in this case by a trial and error approach.

The main drawback of this approach is related to the computational costs. Iterations of these coupling algorithm are nested into the time loop, and this in general implies high computational costs. For this reason, more sophisticated algorithms can be devised to reduce the number of iterations. Possible approaches resort to a dynamical choice of relaxation parameters, or to more effective preconditioners of the coupled problem at hand.

Remark 2.5.2 Splitting schemes as (2.38) or (2.39) can be regarded as the final result of an approximation process starting from a fully accurate model of blood flow problems. If Ω denotes the cardiovascular system (a) in Fig. 2.21, we can summarize the steps performed as follows.

- Domain splitting: Ω is split into Ω_f and Ω_c subdomains ((b) in Fig. 2.21). Original problem is formulated as a set of subproblems. This is the first step of any domain decomposition method (see e.g. [64, 73]). In domain decomposition theory domain splitting can be performed with or without overlap among subdomains. Here we assume that subdomains do not overlap. Appropriate interface conditions describe the link between two subdomain solutions.
- 2. Model coarsening: Fully model in Ω_c is downscaled to a coarse model ((c) in Fig. 2.21). For lumped parameter models this step requires to keep trace of interface conditions that need to be incorporated in K problem by means of a proper selection of bridging regions.
- 3. Iterative substructuring schemes: Solution of the overall problem is pursued by a sequence of subdomain solutions suitably coupled((d) in Fig. 2.21). In particular, for coarse K models bridging region compatibility guarantees that in the downscaled problem interface conditions are correctly included.

This picture based on domain decomposition theory can be useful for the set up and analysis of effective ad hoc preconditioners.

Another approach for reducing computational costs is based on the introduction of a completely explicit splitting of subproblems.

2.5.3 Decoupled schemes

A simple way for reducing the computational costs essentially relies on the time dependent nature of the problems at hand. At each time step t^{n+1} we compute an extrapolation \mathbf{s}_f^{\star} of \mathbf{s}_f^{n+1} as a function of the fine solution at the previous time steps and we solve

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Fig. 2.20. 3D/1D multiscale problem: solution based on an iterative splitting solver with a relaxation parameter θ . Courtesy of T. Passerini



Fig. 2.21. Geometrical multiscale modelling as a domain decomposition method

$$\begin{cases} \mathcal{A}_{cc}\mathbf{s}_{c} = \mathbf{b}_{c} + \mathbf{g}_{c}(\mathbf{s}_{c}^{n}, \mathbf{s}_{c}^{n-1}, \dots, \mathbf{s}_{c}^{n-p_{c}}) - \mathcal{A}_{cf}\mathbf{s}_{f}^{\star} \\ \mathcal{A}_{ff}\mathbf{s}_{f}^{n+1} = \mathbf{b}_{f}^{n+1} + \mathbf{g}_{f}(\mathbf{s}_{f}^{n}, \mathbf{s}_{f}^{n-1}, \dots, \mathbf{s}_{f}^{n-p_{f}}) - \mathcal{A}_{fc}\mathbf{s}_{c}^{n+1} \end{cases}$$
(2.40)

In practice, we perform scheme (2.38) for one time solely. A flow-chart representation of this scheme is given in Fig. 2.22.



Fig. 2.22. Semi-implicit solver for multiscale problems

The computational advantage is clear, since in this way no nested iterations are required. However, both stability and accuracy issues need to be addressed.

1. Absolute Stability in time of the scheme is affected by the explicit treatment of the fine solution in the first equation. The region of absolute stability (see [40]) will be reduced even when unconditionally stable time advancing schemes such as implicit Euler are used for the time discretization. 86 Luca Formaggia, Alfio Quarteroni, and Alessandro Veneziani

A precise quantitative computation of these stability restrictions is in practice neither easy nor convenient. It is however worth pointing out that in many situations time advancing schemes used for solving single subproblems are explicit or semi-explicit. This is the case of 3D Navier-Stokes solver with a semi-explicit treatment of the convective term or of Lax-Wendroff schemes for 1D Euler equations (see Chap. 1). Numerical experience suggests that in many situations stability bounds associated with time advancing schemes are not significantly affected by the splitting scheme (2.40).

Another example is provided by 3D/1D model presented in [21]. In Fig. 2.23 we report the comparison between the pressure computed by a standalone 3D compliant model and a multiscale model, solved with a scheme in the form (2.40). Stand-alone model is a 10cm long tube, the multiscale one is split into two domains (3D and 1D) of 5cm. Matching conditions force the continuity of the total stresses and fluxes.



Fig. 2.23. Comparison between the pressure values of the stan-alone and the multiscale solutions at three different times (t=0.005, 0.01 and 0.015), using a 3D linear elastic model for the structure.Courtesy of Alexandra Moura

Explicit coupling scheme (2.40) has been successfully used also for the application of multiscale modeling to paediatric surgery (see [46]).

2. Time Accuracy. Time accuracy associated with scheme (2.40) is not reduced respect to the uncoupled scheme (2.38) provided that an appropriate extrapolation \mathbf{s}_{f}^{\star} is computed. More precisely, if q_{c} denotes the accuracy of the time advancing scheme for the coarse problem and q_{f} the one for the fine problem, an extrapolation of order q_{c} of \mathbf{s}_{f} is enough for maintaining an accuracy of order q_{c} to the solution of the coarse problem. The accuracy of the fine solution will depend both on q_{f} and q_{c} . More precisely, on the basis of classical results of numerical analysis (see [40]), it is possible to prove that accuracy of the fine model is given by:

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$$q = \min(q_f, q_c + 1).$$
 (2.41)

Since it is reasonable that for the fine model one would have a greater accuracy in time than for the coarse model, the interesting consequence of (2.41) is that for a desired accuracy q of the fine solution, the coarse model can be solved with a scheme of order q - 1.

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