Modeling Blood Flow in Macrocirculatory System

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Notes pertaining to mathematical models of blood flow in the macrocirculatory system. We aim to develop mathematical models describing the hemodynamics of arterial and large venous segments, then we extend our models to macrocirculation networks using a domain decomposition approach.

Keywords: *computational hemodynamics, 0D blood-flow, 1D blood-flow, 2D-blood-flow, PINN's, finite element methods, discontinous galerkin, Lax-Wendroff, fluid-structure ineraction (FSI)*

Contents

1 Preliminaries

Mathematical Notation

$\mathbb{R}$	set of real numbers
$\mathbb{R}^+$	set of positive real numbers
$\mathbb{R}^-$	set of negative real numbers
$\mathbb{R}^n$	n-dimensional real vector space
$\Omega \subset \mathbb{R}^n$	a connected open subset of $\mathbb{R}^n$
$\overline{\Omega}$	the closure of Ω
$\partial\Omega$	the boundary of Ω
dx	Lebesgue measure on $\mathbb{R}^n$
dS	surface measure on $\partial\Omega$
dV	volume measure on Ω
∇	gradient operator
Δ	Laplace operator
div	divergence of a vector field
div	divergence of a tensor
$\boldsymbol{v}_i$	i-th component of vector $\boldsymbol{v}$
$\langle \cdot, \cdot \rangle_X$	inner product on vector space X
$\langle \boldsymbol{u}, \boldsymbol{v} \rangle$	inner product of vectors $\boldsymbol{u}, \boldsymbol{v} \in \mathbb{R}^n$
$\dfrac{\partial}{\partial \hat{\boldsymbol{n}}} = \langle \nabla, \hat{\boldsymbol{n}} \rangle$	normal derivative on $\partial\Omega$
$\|\cdot\|$	L^2-norm
$C^k(\Omega)$	space of k times continuously differentiable functions on Ω
$C_0^k(\Omega)$	space of k times continuously differentiable functions with compact support in Ω
$C_0^k(\overline{\Omega})$	space of k times continuously differentiable functions which have bounded and uniformly continuous derivatives up to order k with compact support in Ω
$C_0^\infty(\Omega)$	space of smooth functions with compact support in Ω
$L^p(\Omega)$	Lebesgue space of p-integrable functions on Ω

Symbols and Abbreviations

$\therefore$	consequently
$\because$	because
$\implies$	implies
$\iff$	if and only if
$:=$	defines
$\equiv$	equivalent
s.t.	such that
w.r.t.	with respect to
m.b.s.	m.b.s.
a.e.	almost everywhere
wlog	without loss of generality
i.e.	"id est" (that means)
e.g.	"exempli gratia" (for example)
ODE	Ordinary Differential Equation
PDE	Partial Differential Equation
IC	Initial Condition
BC	Boundary Condition
0D	Zero dimensional
1D	One dimensional
2D	Two dimensional
3D	Three dimensional
FSI	Fluid-Structure Interaction
WHO	World-Health Organization
SB	Stenotic Bloodflow
bpm	beats per minute
RBC	Red Blood Cell

Parameters and Units

ρ density of blood $\left[\frac{kg}{m^3}\right]$

η dynamic viscosity $\left[Pa \cdot s\right]$

μ kinematic viscosity $\left[\frac{m^2}{s}\right]$

τ shear stress

$\dot{\gamma}$ shear rate

R radius of vessel with diameter $2R$

$\boldsymbol{u}$ velocity field

p pressure field

W_0 Womersley number $\left[\,-\,\right]$

Re Reynolds number $\left[\,-\,\right]$

Pe Péclet number $\left[\,-\,\right]$

2 Introduction

2.1 Physiological Background

The circulatory system consists of a human's heart, vascular network, lungs, and organs. The heart is the source, transporting Oxygen-rich blood to the organs and deoxygenated (and carbon dioxide-enriched) blood back to the lungs. Lungs discharge $CO2$ and enrich the blood with Oxygen. We refer to these respective processes as the *pulmonary circulation* and the *systemic circulation* (resp.). The *macrocirculatory system* consists of the heart and the large vessels in the systemic circulation. Particularly, the arteries of the macrocirculatory system transport oxygenated blood from the heart, driving the return of deoxygenated blood in large vessels back to the heart. Hemodynamics refers to the study of blood flow in the circulatory system.

Cardiovascular disease (CVD) is the leading cause of death in developed nations. According to the World Health Organization (WHO), CVD accounts for approximately 30% of all global deaths in 2012. Understanding the hemodynamics of the macrocirculatory system is crucial for diagnosing, treating, and preventing CVD. Consequently, our motivation is to simulate and analyze various cardiovascular conditions, including arterial stenosis, aneurysms, and heart valve disorders, with the aim to better enable provider treatment.

SEO for insurance companies

A single beat of the heart propels blood through the macrocirculatory system, the "lub-dub" sound. We refer to the beat and the sequence of events until the successive beat as the *cardiac cycle*. The cardiac cycle consists of two main phases: systole and diastole, during which the heart chamber is accumulating blood and releasing blood (resp.). The beat can be recognized as a pulse wave in large vessels, characterized by the Wormersley number W_0:

$$W_0 := 2R \cdot \sqrt{\frac{\omega \rho}{\eta}}$$

a dimensionless parameter comparing the frequency ω of the pulse wave to the blood's kinematic viscosity η and the vessel diameter $2R$.

Definition 1. The Reynolds number Re characterizes flow in blood vessels:

$$Re := 2R \cdot \frac{\rho U}{\eta},$$

where U is the mean flow velocity.

Low Re indicates laminar flow, while high Re suggests turbulent flow.

Observed Cardiac Cycle Characteristics

Normal resting heart rate is considered to be $\omega = 70$ bpm, so the cardiac cycle is approximately $0.86s$., consisting of:

1. Systole (ventricular contraction) ≈ 0.3 seconds.

2. Diastole (ventricular relaxation) ≈ 0.7 seconds.

The blood volume of a human is approximately 5.7-6.0 liters of blood, flowing a full cycle roughly every minute. The energy driving the flow comes from oxygen and nutrients absorbed from food, creating waste products that must be removed; the *coronary artery*'s responsibility. The buildup of waste products results in Arteriosclerosis, a narrowing of the coronary artery, leading to reduced and turbulent blood flow. (Add citations here of turbulence in the presence of stenotic arteries).

Explain Anuerysms and their hemodynamic characteristics

Explain Heart valve conditions and there hemodynamic Characteristics

Note [1, Table 1.1, p. 10, §1.1] shows $W_0 \propto 2R$ and $Re \propto (2R)^{-1}$; we observe large pulses and turbulent flow in large vessels and small pulses and laminar flow in small vessels.

2.2 Fluid Model of Blood

Let

$$\Omega(t) := \{x \in \mathbb{R}^3 \ : \ x \text{ is inside the blood vessel at time } t\},$$

our models describe the kinematics of blood on the time interval $[0, T]$ in the lumen $\Omega(t) \subset \mathbb{R}^3$ of a blood vessel.

Constituents and hematocrit. Blood consists of plasma and formed elements (cells). Red blood cells (RBCs) comprise $\approx 97\%$ of the cellular volume, and cells occupy $\approx 45\%$ of the blood volume. The remaining $\approx 55\%$ is plasma, which is $\approx 90\%$ water. The ratio of RBC volume to total blood volume is the *hematocrit value H*, an important metric describing the influence of red blood cells on the flow.

Modeling framework. In *continuum mechanics*, fluids are modeled by *continuous fields*. At *microscopic scales*, our models break down—fluids are discrete collections of molecules, not continuous fields. However, at the macroscopic scale we can hope that such models remain accurate. We adopt the continuum hypothesis and treat the heterogeneous mixture of blood as a single-constituent, homogeneous, isotropic fluid with domain $\Omega(t)$. as a single-constituent, homogeneous, isotropic fluid with domain $\Omega(t)$. Let $\boldsymbol{u} : \Omega(t) \to \mathbb{R}^n$

be the velocity, $\rho : \Omega(t) \to \mathbb{R}^+$ the density, and $p : \Omega(t) \to \mathbb{R}$ the thermodynamic pressure. Define the rate-of-deformation tensor

$$\boldsymbol{D}(\boldsymbol{u}) := \tfrac{1}{2}\big(\nabla\boldsymbol{u} + (\nabla\boldsymbol{u})^\top\big)$$

as the the symmetric part of the Jacobian of $\boldsymbol{u}$; it measures how a continuum of fluid deforms locally under the velocity field $\boldsymbol{u}$.

Definition 2. A fluid is *Newtonian* if its Cauchy stress $\boldsymbol{\sigma}$ depends linearly on the rate-of-deformation tensor $\boldsymbol{D}(\boldsymbol{u})$.

Definition 3. A fluid is *isotropic* if its constitutive response is independent of the coordinate system. Writing the Cauchy stress as $\boldsymbol{\sigma} = \boldsymbol{\sigma}(\boldsymbol{D})$, isotropy means that for every orthogonal rotator $\boldsymbol{Q} \in \mathrm{SO}(3)$,

$$\boldsymbol{Q}\,\boldsymbol{\sigma}(\boldsymbol{D})\,\boldsymbol{Q}^\top \;=\; \boldsymbol{\sigma}\big(\boldsymbol{Q}\,\boldsymbol{D}\,\boldsymbol{Q}^\top\big).$$

Definition 4 (Newtonian, isotropic constitutive law)**.** For a Newtonian, isotropic fluid the Cauchy stress is

$$\boldsymbol{\sigma} = -\,p\,\mathrm{I} + 2\,\eta\,\boldsymbol{D}(\boldsymbol{u}) + \lambda\,\mathrm{div}(\boldsymbol{u})\,\mathrm{I},$$

where $\eta > 0$ is the dynamic (shear) viscosity and λ the bulk viscosity.

Note, an isotropic fluid at rest (quiescent state $\boldsymbol{u} \equiv \boldsymbol{0}$) sustains only hydrostatic stress: $\boldsymbol{\sigma} = -p\,\mathrm{I}$.

Definition 5 (Incompressibile fluid)**.** A fluid is *incompressible* if its density is constant in space and time.

Definition 6 (Incompressible flow)**.** A flow is *incompressible* if density is materially constant in space and time. Let $D_t(\rho) := \partial_t \rho + \mathrm{div}(\rho \boldsymbol{u})$ be the material derivative, then incompressible flow means $D_t(\rho) = 0$ in $\Omega(t)$ for all time t.

Remark. By assumption that blood is an incompressible fluid, $\rho \equiv \rho_0 > 0$ constant. By mass conservation of an incompressible fluid, it may be shown that the fluid's flow is incompressible in the sense of Definition 6.

Assuming incompressibility of the fluid and flow, we have the equivalences:

$D_t \rho = 0$

$\iff \partial_t \rho + \text{div}(\rho \boldsymbol{u}) = 0$

$\iff \text{div}(\rho \boldsymbol{u}) = 0 \quad (\because \ \rho \text{ is constant})$

$\iff \nabla \cdot (\rho \boldsymbol{u}) = 0$

$\iff \langle \rho \boldsymbol{u}, \nabla \rangle = 0$

$\iff \rho \langle \boldsymbol{u}, \nabla \rangle = 0$

$\iff \langle \boldsymbol{u}, \nabla \rangle = 0 \quad (\because \ \rho > 0)$

$\iff \nabla \cdot \boldsymbol{u} = 0$

So under incompressibility of the fluid and flow, the divergence-free condition $\text{div}(\boldsymbol{u}) = 0$ of our velocity field holds in $\Omega(t)$. Consequently, the Cauchy stress simplifies to

$$\boldsymbol{\sigma} = -p\,\mathrm{I} + 2\,\eta\,\boldsymbol{D}(\boldsymbol{u})$$

Remark (Dynamic vs. Kinematic Viscosity). Throughout assume $\eta \in \mathbb{R}^+$ denote the *dynamic viscosity* of blood, and let $\mu \in \mathbb{R}^+$ denote the *kinematic viscosity*. Then:

$$\mu := \frac{\eta}{\rho} \tag{1}$$

where ρ is the blood density $\left[\frac{kg}{m^3}\right]$ (assumed constant by incompressibility). Thus:

- η quantifies the internal resistance of blood to shear deformation, i.e., $\eta := \dfrac{\tau}{\dot{\gamma}}$, with units $[Pa \cdot s]$;

- μ adjusts η by the density ρ, capturing the viscous diffusion of momentum per unit mass, with units $\left[\frac{m^2}{s}\right]$.

Intuitively, η measures how "thick" or "sticky" the fluid is, while μ measures how quickly momentum diffuses through the fluid due to viscosity.

Parameterization of viscosity (large vessels). We will model blood as Newtonian in large arteries by taking η constant (so $\mu = \eta/\rho$ constant). When diameter d and hematocrit effects are needed, we use a relative viscosity $\eta_r(H, d)$ that scales an absolute baseline η:

$$\eta_{\text{eff}} \ = \ \eta_r(H, d)\,\eta.$$

clean-up above remark. How do we conclude now that η is constant, so μ is constant?

An empirical fit (e.g. [4]) is

$$\eta_r = 1 + (\eta_{0.45} - 1)\frac{(1-H)^C - 1}{(1-0.45)^C - 1}, \qquad \begin{cases} \eta_{0.45} = 6\,e^{-0.085\,d} + 3.2 - 2.44\,e^{-0.06\,d^{0.645}}, \\[2mm] C = \left(0.8 + e^{-0.075\,d}\right)\left(-1 + \dfrac{1}{1 + 10^{-11}\,d^{12}}\right) + \dfrac{1}{1 + 10^{-11}\,d^{12}}, \end{cases}$$

(2)

where $d := 2R/(1.0\mu m)$ is the (scaled) vessel diameter. In large vessels, η_r is often constant, justifying the Newtonian assumption.

2.3   Navier Stokes System

The Navier-Stokes (NS) system in conservative form:

Definition 7 (Incompressible-Newtonian NS (Conservative Form)). We seek velocity and pressure feilds

$$\boldsymbol{u} : \Omega(t) \to \mathbb{R}^3, \ (x,y,z) \mapsto (u_1(x,y,z), \ u_2(x,y,z), \ u_3(x,y,z)),$$

$$p : \Omega(t) \to \mathbb{R}, \ (x,y,z) \mapsto p(x,y,z),$$

such that for $T \geq t > 0$ and in $\Omega(t)$,

$$\begin{cases} \rho\big(\partial_t \boldsymbol{u} + (\boldsymbol{u} \cdot \nabla)\boldsymbol{u}\big) = -\nabla p + \mathbf{div}\Big(2\,\mu(|\boldsymbol{D}|^2)\,\boldsymbol{D}\Big) + \rho\,\boldsymbol{f} \\[2mm] \mathrm{div}(\boldsymbol{u}) = 0, \end{cases}$$

where $\boldsymbol{f}$ is an external force field (e.g., gravity),

We rewrite Eq. 7 in standard form (as found in [3], [1].)

$$\rho\big(\partial_t \boldsymbol{u} + (\boldsymbol{u} \cdot \nabla)\boldsymbol{u}\big) = -\nabla p + \mathbf{div}\Big(2\,\mu(|\boldsymbol{D}|^2)\,\boldsymbol{D}\Big) + \rho\,\boldsymbol{f}$$

$$\iff \rho\big(\partial_t \boldsymbol{u} + (\boldsymbol{u} \cdot \nabla)\boldsymbol{u}\big) = -\nabla p + \mathbf{div}\Big(2\,\frac{\eta}{\rho}(|\boldsymbol{D}|^2)\,\boldsymbol{D}\Big) + \rho\,\boldsymbol{f}$$

$$\iff \rho\big(\partial_t \boldsymbol{u} + (\boldsymbol{u} \cdot \nabla)\boldsymbol{u}\big) = -\nabla p + \eta\,\mathbf{div}\Big(2\,\frac{1}{\rho}(|\boldsymbol{D}|^2)\,\boldsymbol{D}\Big) + \rho\,\boldsymbol{f} \quad (\because \eta = \frac{\mu}{\rho} = \mathrm{const.})$$

$$\iff \rho\big(\partial_t \boldsymbol{u} + (\boldsymbol{u} \cdot \nabla)\boldsymbol{u}\big) = -\nabla p + \mu\,\rho\,\mathbf{div}\Big(2\,\frac{1}{\rho}(|\boldsymbol{D}|^2)\,\boldsymbol{D}\Big) + \rho\,\boldsymbol{f}$$

$$\iff \partial_t \boldsymbol{u} + (\boldsymbol{u} \cdot \nabla)\boldsymbol{u} = -\frac{\nabla p}{\rho} + \mu\,\mathbf{div}\Big(2\,\frac{1}{\rho}(|\boldsymbol{D}|^2)\,\boldsymbol{D}\Big) + \boldsymbol{f}$$

$$\iff \partial_t \boldsymbol{u} + (\boldsymbol{u} \cdot \nabla)\boldsymbol{u} + \frac{\nabla p}{\rho} - \mathbf{div}\Big(\frac{2}{\rho}\,\mu\,(|\boldsymbol{D}|^2)\,\boldsymbol{D}\Big) = \boldsymbol{f}$$

$$\iff F\big(\partial_t \boldsymbol{u}, \nabla \boldsymbol{u}, \nabla p; \boldsymbol{u}, p, \rho, \mu\big) = \boldsymbol{f}$$

2.3.1 Existence and Uniqueness of NS

Remark (Global Regularity Problem for (NS)). *For any smooth, spatially localized initial data* $\mathbf{u}_0$, *does there exist a global smooth solution* $(\mathbf{u}, p)$ *to NS ? Such question is one of the Millennium Prize Problems posed by the Clay Mathematics Institute in 2000, with a prize of one million dollars for a correct solution.*

theorem (Local Existence and Uniqueness). Given smooth, localized initial data $\boldsymbol{u}_0$, there exists a maximal time $0 < T_* \leq \infty$ for which a unique solution exists.

If $T_* < \infty$, a **blow-up** occurs:

$$\sup_{x \in \mathbb{R}^3} |\mathbf{u}(t,x)| \to +\infty \quad \text{as} \quad t \to T_*.$$

Otherwise, if $T_* = \infty$, then $|\boldsymbol{u}| \to 0$ as $t \to \infty$. Numerical evidence suggests global regularity holds in most practical cases, but turbulent behavior can emerge for large initial data.

Heuristic Considerations and Energy Balance

Starting from the incompressibility condition:

$$\begin{aligned}
\operatorname{div}(\boldsymbol{u}) &= 0 \\
&\iff \quad \rho \text{ is constant in } \Omega(t) \\
&\iff \quad \text{chain rule applies to } \mathbf{div}\big(\frac{2}{\rho}\mu(|\boldsymbol{D}|^2)\boldsymbol{D}\big) \\
\implies \mathbf{div}\big(\frac{2}{\rho}\mu(|\boldsymbol{D}|^2)\boldsymbol{D}\big) &= \nabla \cdot \big(\frac{2}{\rho}\mu(|\boldsymbol{D}|^2)\boldsymbol{D}\big) \\
&= \langle \frac{2}{\rho}\mu(|\boldsymbol{D}|^2)\boldsymbol{D}, \nabla \rangle \\
&= \frac{2}{\rho}\langle \mu(|\boldsymbol{D}|^2)\boldsymbol{D}, \nabla \rangle \\
&= \frac{2}{\rho}\nabla \cdot \big(\mu(|\boldsymbol{D}|^2)\boldsymbol{D}\big) \\
\therefore \quad \frac{2}{\rho}\,\mathbf{div}\big(\mu(|\boldsymbol{D}|^2)\boldsymbol{D}\big) &= 0.
\end{aligned}$$

This vanishes if μ is constant (Newtonian fluid) and ρ is constant (incompressibility). So the diffusive term becomes:

$$\frac{2\eta}{\rho}\Delta\boldsymbol{u}, \quad \text{with } \eta = \mu\rho.$$

We heuristically compare dominant terms:

1. If $\eta\Delta\boldsymbol{u} \gg (\boldsymbol{u} \cdot \nabla)\boldsymbol{u}$, viscous dissipation dominates $\Rightarrow$ smooth, regular behavior.

show simplification of diffusive term to laplacian

2. If $(\boldsymbol{u} \cdot \nabla)\boldsymbol{u} \gg \eta \Delta \boldsymbol{u}$, nonlinearity dominates $\Rightarrow$ turbulence, potential blow-up.

We construct rigorous energy estimates in Section 3.

2.3.2 NS in Cylindrical Coordinates

The relation between cartesian and cylindrical coordinates is

$$(x, \ y, \ z) \ \mapsto (r\sin(\theta), \ r\cos(\theta), \ z), \quad r = \sqrt{x^2 + y^2}.$$

Add Derivation From Notes

3 Mathematical Models of Blood Flow

Mathematical models of blood flow in the macrocirculatory system can be classified into different categories based on their dimensionality and complexity. The choice of model depends on the specific application, computational resources, and desired accuracy.

Let our vessel wall $\partial\Omega$ be a surface in $\mathbb{R}^3$ that evolves in time which we refer to as the interface. Note $\overline{\Omega} = \Omega \cup \partial\Omega$. Note, an explicit representation of $\overline{\Omega}$ maps $(t, \theta, r, \theta, z) \mapsto (x, y, z)$. So the region enclosed by our interface is Ω, and we aim to model the velocity and pressure fields on Ω. Knowing the pressure and velocity for a portion of time allows us to compute stresses to which an arterial wall is subjected to due to the blood movement.

3.1 Dimension-Reduced Models of Blood Flow

In many practical applications, especially in large vessels, it is common to use dimensionally reduced models such as 1D or 0D models. The appeal of these models simplifies the Navier-Stokes equations by averaging over the cross-sectional area of the vessel, leading to equations that describe the flow along the length of the vessel.

The 1D model typically involves equations for the cross-sectional area $A(x, t)$ and the flow rate $Q(x, t)$, derived from conservation of mass and momentum. The 0D model, on the other hand, treats the vessel as a lumped parameter system, focusing on overall pressure and flow relationships without spatial resolution.

4 Numerical Methods for Blood Flow Simulation

Numerical methods play a crucial role in simulating blood flow in various vascular geometries. These methods allow for the approximation of complex fluid dynamics equations and enable the study of hemodynamics in realistic scenarios.

5 Misc

Coronary artery stenosis (CAS) is the narrowing of the coronary arteries due to the buildup of plaque. This narrowing can restrict blood flow to the heart muscle, leading to various cardiovascular problems, including chest pain (angina), heart attacks, and other serious complications. Current methods for predicting coronary artery stenosis are rudimentary; and often prediction does mean coronary artery stenosis obstruction ([2]). . There is a need for more accurate and reliable methods to predict and assess the severity of CAS. narrowing can restrict blood flow to the heart muscle, leading to various cardiovascular problems, including chest pain

Provide an overview of the different numerical methods used for blood flow simulation, including finite element methods (FEM), finite volume meth-ods

(angina), heart attacks, and other serious complications. Current methods for predicting coronary artery stenosis are rudimentary; and often prediction does mean coronary artery stenosis obstruction. . There is a need for more accurate and reliable methods to predict and assess the severity of CAS.

We perform a literature survey of arterial blood flow using known methods from the literature, with the hope of understanding the computational challenges and tradeoffs of various *mathematical models*.

Make some comment about "correct terminology for describing the types of coronary arterial stenosis is "coronary artery stenosis morphology." and ref figures in DOI: 10.1056

Understand Dr. Zhou's statement: Regarding the assumption about the absence of a vortex, I cannot definitively say whether it is correct or not. Please review the references provided. If needed, we

6 Appendix

References

[1] Luca Formaggia, Alfio Quarteroni, and Alessandro Veneziani. *Cardiovascular Mathematics. Modeling and Simulation of the Circulatory System.* Springer, 2009.

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[3] L. John, P. Pustějovská, and O. Steinbach. "On the influence of the wall shear stress vector form on hemodynamic indicators". In: *Computing and Visualization in Science* 4 (2017), pp. 113–122. DOI: 10.1007/s00791-017-0277-7.

[4] Gaehtgens P Pries AR Neuhaus D. "Blood viscosity in tube flow: dependence on diameter and hematocrit". In: *Am J Physiol.* (6 Pt 2).263 (1992 Dec). DOI: 10.1152/ajpheart.1992.263.6.H1770.

References

Code Listings

Optional Space for sumplementary code listings of computations done while investigating

Code 1: Algorithm 16.5

```
1        function foo()
2            println("Hello World)
3        end
```