

# Blood Flow in the Human Circulatory System

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Hemodynamics studies blood's motion, herein, we report mathematical models describing the kinematics of blood in the human macrocirculatory system. We review physiological, rheological, and mathematical foundations necessary for modeling blood flow in large vessels. We discuss numerical methods for solving the governing equations of blood flow, the incompressible Navier-Stokes equations. Finally, we present recent advances in computational hemodynamics, including physics-informed neural networks (PINN's) and fluid-structure interaction (FSI) models. (TODO)

**Keywords:** *computational hemodynamics, physics-informed neural networks, Deep-Riesz, discontinuous Galerkin, Lax-Wendroff, fluid-structure interaction (FSI)*

Taging conventions are as follows:

- Red Text means check accuracy (or clarity)
- Blue Text means not necessary
- Green Text means TODO

summarize  
final contribu-  
tions here  
and update  
keywords

## Work in Progress (WIP). Tips to keep in mind:

- Start w/ literature suvery, summarizing each articles contribution once. (i.e., limit repeat citation refs.), then prioritize sections by technicality
- Tag material by relevance, e.g., foundational. vs. tangential vs. speculative.
- Comparative analysis contrasting results, models, or point out contradictions across papers
- Always consist in notation: Actively managing acroynms, abrevs., notation, and preliminaries.
- Look into [Zotero] to manage refs.

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## 0.1 Acroynms and Abbreviations

a.e.	almost everywhere
e.g.	”exempli gratia” (for example)
i.e.	”id est” (that means)
s.s.	sufficiently smooth
s.t.	such that
r.t.	refers to
w.r.t.	with respect to
m.b.s.	must be shown
i.m.b.s.	it must be shown
i.r.t.s.	it remains to show
w.a.t.s.	we aim to show
bpm	beats per minute
wlog	without loss of generality
ODE	Ordinary Differential Equation
PDE	Partial Differential Equation
PDES	System of Partial Differential Equations
IC	Initial Condition
BC	Boundary Condition
0D	Zero dimensional
1D	One dimensional
2D	Two dimensional
3D	Three dimensional
FSI	Fluid-Structure Interaction
SB	Stenotic Blockage
RBC	Red Blood Cell
CVD	Cardiovascular disease & CVDs r.t. such diseases

## 0.2 Mathematical Notation

$\therefore$	consequently	
$\because$	because	
$\Rightarrow$	implies	
$\iff$	if and only if	
$:=$	defines	
$\equiv$	equivalence	
$\mathbb{R}$	real numbers	
$\mathbb{R}^+$	positive real numbers	
$\mathbb{R}^-$	negative real numbers	
$\mathbb{R}^n$	n-dimensional real vector space	
$\mathbb{N}$	natural numbers	
$\{\mathbf{v}_1, \dots, \mathbf{v}_n\}$	general basis of $\mathbb{R}^n$	
$\{\mathbf{e}_1, \dots, \mathbf{e}_n\}$	standard basis of $\mathbb{R}^n$	
$[n] \subset \mathbb{N}$	set $\{1, 2, \dots, n\}$	
$\Omega \subset \mathbb{R}^n$	bounded domain	
$\overline{\Omega}$	the closure of $\Omega$	
$\partial\Omega$	the boundary of $\Omega$	
$C^k(\Omega)$	$k$ times continuously differentiable functions in $\Omega$	
$C_0^k(\Omega)$	$k$ times continuously differentiable functions with compact support in $\Omega$	
$C_0^k(\overline{\Omega})$	$k$ times continuously differentiable functions which have bounded and uniformly continuous derivatives up to order $k$ with compact support in $\Omega$	Locally integrable, Lipschitz, Holder continuous, Sobolev spaces, weak derivatives, distributions, test functions, multi-index notation
$C_0^\infty(\Omega)$	smooth functions with compact support in $\Omega$	
$L^p(\Omega)$	Lebesgue space of $p$ -integrable functions on $\Omega$	

$dx$	Lebesgue measure on $\mathbb{R}^n$
$dS_x$	surface measure on $\partial\Omega \subset \mathbb{R}^n$
$dV$	volume measure on domain $\Omega \subset \mathbb{R}^3$
$dS$	surface measure on boundary $\partial\Omega \subset \mathbb{R}^3$
$\nabla$	gradient operator
$\Delta = \nabla^2 = \nabla \cdot \nabla(\cdot)$	Laplace operator
$\text{div}$	divergence of a vector field
$\mathbf{div}$	divergence of a tensor field
$v_i$	$i$ -th component of vector $\mathbf{v}$
$\langle \cdot, \cdot \rangle_X$	inner product on vector space $X$
$\langle \mathbf{u}, \mathbf{v} \rangle \equiv \langle \mathbf{u}, \mathbf{v} \rangle_{\mathbb{R}^n}$	inner product of vectors $\mathbf{u}, \mathbf{v} \in \mathbb{R}^n$
$\partial_{\hat{\mathbf{n}}} = \langle \nabla, \hat{\mathbf{n}} \rangle$	normal derivative on $\partial\Omega$
$\ \cdot\ $	$L^2$ -norm

### 0.3 Domain Specific Notation

$R$	radius of vessel with diameter $2R$
$\eta$	dynamic viscosity $[ Pa \cdot s ]$
$\mu$	kinematic viscosity $[ \frac{cm^2}{s} ]$
$\tau$	shear stress
$\dot{\gamma}$	shear rate
$\rho$	density field $[ \frac{kg}{cm^3} ]$
$p$	pressure field
$\mathbf{u}$	velocity field $[ \frac{cm}{s} ]$
$W_0$	Womersley number $[ - ]$
$Re$	Reynolds number $[ - ]$
$Pe$	Péclet number $[ - ]$
$c$	concentration of a material element
$D$	diffusion coefficient $[ \frac{cm^2}{s} ]$
$t$	time $[ s ]$
$T$	terminal time $[ s ], t > 0$
$\omega$	angular frequency $[ \frac{rad}{s} ]$
$\mathbf{f}_b$	body force per unit volume $[ \frac{N}{cm^3} ]$

## 0.4 Mathematical Foundations

Assume Zermelo-Fraenkel set theory with the axiom of choice (ZFC), and according to Cohen, it's consistent if we take the continuum hypothesis (CH); a necessary posulate in continuum mechanics. A *domain* r.t. an open and bounded subset of  $\mathbb{R}^n$  with nonempty interior  $\Omega^\circ$ , for  $N \in [3]$ . By the Heine-Borel theorem, every domain  $\Omega$  has a well-defined boundary  $\partial\Omega$  with compact closure  $\bar{\Omega} = \Omega \cup \partial\Omega$ . The compact domains of  $\mathbb{R}^N$  are precisely the closed and bounded subsets of  $\mathbb{R}^N$ . When every path between two points in  $\Omega$  may be continuously contracted to a point without leaving  $\Omega$ , we say that  $\Omega$  is *simply connected*.

Given domain  $\Omega$ , the function sp.  $\mathcal{F}(\Omega)$  is the vector sp.  $(F(\Omega), K)$  of scalar valued functions  $f : \Omega \rightarrow K$ . E.g.  $C^0(\Omega)$  r.t.  $(C(\Omega), \mathbb{R})$  all continuous real valued functions on  $\Omega$ . Let sp.  $C^k(\Omega)$  be the continuous and  $k$ -times continuously differentiable functions on  $\Omega$ , then  $C^k(\bar{\Omega})$  r.t.  $f \in C^k(\Omega)$  s.t.  $f$  and its derivatives up to order  $k$  may be continuously extended to the boundary  $\partial\Omega$ . The sp.  $C^\infty(\Omega)$  is the intersection of all  $C^k(\Omega)$  for  $k \geq 0$ , i.e. the infinitely differentiable functions on  $\Omega$ . And  $C^k(\Omega; \mathbb{R}^m)$  denotes the functions  $\mathbf{f} : \Omega \rightarrow \mathbb{R}^m$  with components in  $C^k(\Omega)$ , i.e.,  $\mathbf{f} = (f_i)_{i \in [m]}$  with  $f_i \in C^k(\Omega)$  for all  $i \in [m]$ .

Let  $n = \dim(\Omega)$ , then we say

$\phi : \Omega \rightarrow \mathbb{R}$  r.t. a *scalar field*,

$\mathbf{f} : \Omega \rightarrow \mathbb{R}^n$  r.t. a *vector field*,

$\mathbf{T} : \Omega \rightarrow \mathbb{R}^{n \times n}$  r.t. a *(second-order) tensor field*,

and we write  $\phi(\mathbf{x})$ ,  $\mathbf{f}(\mathbf{x})$ , and  $\mathbf{T}(\mathbf{x})$ <sup>1</sup> for the values at a point  $\mathbf{x} \in \Omega$ . When referring to a physical quantity, its measurement units are indicated as  $[ \cdot ]$ ; whereas dimensionless quantities are indicated as  $[ - ]$ . The  $k$ -th partial derivative of  $\phi$  w.r.t. coordinate  $x_i$  is

$$\partial_{x_i}^k \phi \equiv \frac{\partial^k \phi}{\partial x_i^k}.$$

The generalized derivative of order  $|\alpha|$  of scalar field  $\phi$  is

$$D^\alpha \phi \equiv \frac{\partial^{|\alpha|} \phi}{\partial x_1^{\alpha_1} \partial x_2^{\alpha_2} \dots \partial x_n^{\alpha_n}},$$

where  $\alpha = (\alpha_1, \alpha_2, \dots, \alpha_n)$  is a multi-index with  $|\alpha| = \alpha_1 + \alpha_2 + \dots + \alpha_n$ . For  $|\alpha| = 1$ ,  $D^\alpha \phi$  is a first-order partial derivative of  $\phi$ , e.g.  $\partial_{x_i} \phi$  where  $\alpha_i = 1$  and  $\alpha_j = 0 \forall j \in [n] : j \neq i$ .

For real-valued  $\phi \in C^1(\Omega)$ , the partial derivative w.r.t. coordinate  $x_i$  is

$$\partial_{x_i} \phi = \frac{\partial \phi}{\partial x_i}.$$

---

<sup>1</sup>Note, for tensor  $\mathbf{T}(\mathbf{x}) \in \mathbb{R}^{n \times n}$ ,  $\exists$  a linear map  $A : \mathbb{R}^n \rightarrow \mathbb{R}^n$  s.t.  $\mathbf{T}(\mathbf{x})(\mathbf{u}) \mapsto A \mathbf{u}$  for all  $\mathbf{u} \in \mathbb{R}^n$ .

reserve  
multi-index  
notation  
for later  
when we  
work with  
weak derivatives, distributions,  
Sobolev

In coordinate-free notation, for  $\mathbf{x} \in \Omega$  and  $\hat{\mathbf{n}} \in \mathbb{R}^n$ , the normal derivative is

$$\partial_{\hat{\mathbf{n}}} \phi(\mathbf{x}) := \langle \nabla \phi(\mathbf{x}), \hat{\mathbf{n}} \rangle_{\mathbb{R}^n}.$$

define as  
declared in  
notation sec

For Lebesgue measure  $d\mathbf{x}$  on  $\mathbb{R}^n$  the integral of  $\phi$  in  $\Omega$  is

$$\int_{\Omega} \phi(\mathbf{x}) d\mathbf{x}.$$

If  $\partial\Omega \in C^1$ , then  $\phi \in C^1(\bar{\Omega}) \supset L^1(\partial\Omega)$  and the integral at the boundary is

$$\int_{\partial\Omega} \phi(\mathbf{x}) dS_{\mathbf{x}}.$$

The gradient and Laplacian of  $\phi$  are (respectively):

$$\begin{aligned}\phi &\mapsto \nabla(\phi) \equiv \nabla\phi = (\partial_{x_1}, \dots, \partial_{x_N})^\top = (\partial_{x_i}\phi)_{\forall i[n]}. \\ \phi &\mapsto \Delta\phi \equiv \nabla \cdot \nabla\phi = \sum_{\forall i[n]} \partial_{x_i}^2 \phi.\end{aligned}$$

For vector-valued  $\mathbf{f} \in C^1(\Omega; \mathbb{R}^n)$  with components  $\mathbf{f} = (f_i)_{\forall i \in [n]}$ , the divergence is

$$\operatorname{div} \mathbf{f} := \nabla \cdot \mathbf{f} = \sum_{\forall i \in [n]} \partial_{x_i} f_i = \langle \mathbf{f}, \nabla \rangle_{\mathbb{R}^n}$$

The Laplacian and domain integral of  $\mathbf{f}$  are defined component-wise:

$$\begin{aligned}\mathbf{f} &\mapsto \Delta \mathbf{f} := (\Delta f_i)_{\forall i \in [n]} \\ \mathbf{f} &\mapsto \int_{\Omega} \mathbf{f} := \left( \int_{\Omega} f_i d\mathbf{x} \right)_{\forall i \in [n]}.\end{aligned}$$

For tensor-valued  $\mathbf{T} \in C^1(\Omega; \mathbb{R}^{n \times n})$  with entries  $\mathbf{T} = (T_{ij})_{i,j=1}^n$ , the divergence operator is

$$\begin{aligned}\operatorname{div} \mathbf{T} &:= (\operatorname{div} \mathbf{t}_i)_{\forall i \in [n]} : \mathbf{t}_i \text{ is the } i\text{th row of } \mathbf{T} \\ &= (\nabla \cdot \mathbf{t}_i)_{\forall i \in [n]} \\ &= \left( \sum_{\forall j \in [n]} \partial_{x_j} T_{ij} \right)_{\forall i \in [n]} \\ &= (\langle \mathbf{t}_i, \nabla \rangle_{\mathbb{R}^n})_{\forall i \in [n]}.\end{aligned}$$

The Laplacian and domain integral of  $\mathbf{T}$  are again defined component-wise:

$$\Delta \mathbf{T} := (\Delta T_{ij})_{\forall i,j \in [n]} \quad \text{and} \quad \int_{\Omega} \mathbf{T} := \left( \int_{\Omega} T_{ij} d\mathbf{x} \right)_{\forall i,j \in [n]}.$$

Let  $K$  be compact (e.g.  $\overline{\Omega}$ ), then the sp.  $(C^k(K), \mathbb{R})$  is complete with norm

$$\|\phi\|_{C^k(K)} := \sum_{\forall |\alpha| \in [k]} \sup_{\mathbf{x} \in K} |D^\alpha \phi(\mathbf{x})|.$$

meaning that every Cauchy sequence  $\{\phi_j\}_{\forall j \in \mathbb{N}} \subset C^k(K)$  converges to a limit in  $C^k(K)$ . So the complete normed sp.  $(C^k(K), \|\cdot\|_{C^k(K)})$  is banach, by the definition of banach sp. In particular, for  $k = 0$ , we have

$$\|\phi\|_{C(\overline{\Omega})} := \sup_{\mathbf{x} \in \overline{\Omega}} |\phi(\mathbf{x})| \equiv \max_{\mathbf{x} \in \overline{\Omega}} |\phi(\mathbf{x})| = \|\phi\|_\infty \quad (\text{since } \overline{\Omega} \text{ is compact}).$$

Let  $\phi \in L^p(\Omega)$  be a real-valued measurable function on  $\Omega$ , then the Lebesgue sp.  $L^p(\Omega)$  is defined as

$$L^p(\Omega) := \left\{ \phi : \Omega \rightarrow \mathbb{R} \mid \|\phi\|_{L^p(\Omega)} < \infty \right\} \quad \text{s.t.} \quad \|\cdot\|_{L^p(\Omega)} : \phi \mapsto \left( \int_{\Omega} |\phi(\mathbf{x})|^p d\mathbf{x} \right)^{1/p} \quad 1 \leq p < \infty.$$

For  $p = \infty$ , the sp.  $L^\infty(\Omega)$  is defined as

$$L^\infty(\Omega) := \left\{ \phi : \Omega \rightarrow \mathbb{R} \mid \|\phi\|_{L^\infty(\Omega)} < \infty \right\} \quad \text{s.t.} \quad \|\cdot\|_{L^\infty(\Omega)} : \phi \mapsto \sup_{\mathbf{x} \in \Omega} |\phi(\mathbf{x})|.$$

where sup here r.t. the essential supremum. It follows that  $\mathbf{f} \in L^p(\Omega; \mathbb{R}^m)$  denotes the functions whose components are in  $L^p(\Omega)$ , i.e.,  $\mathbf{f} = (f_i)_{i \in [m]}$  with  $f_i \in L^p(\Omega)$  for all  $i \in [m]$ . The sp.  $(L^p(\Omega), \|\cdot\|_{L^p(\Omega)})$  is complete, hence a banach sp. for all  $1 \leq p \leq \infty$ .

TODO:

- forgoe until we work with a Lipschitz boundary: Hölder spaces, then Hilbert and Sobolev spaces. defs and notation, then trace thm., Poincare inequality, Rellich-Kondrachov comp. thm., etc. Distributional derivatives, test functions, multi-index notation, weak derivatives, weak formulation, etc.
- Add def. and notation for Lipschitz continuous functions/sp.,  $Lip(\Omega)$  and it's norm.
- Add relation of  $Lip(\Omega)$  to  $C^0(\Omega)$ , brenner's book. Don't state why, just cite.

Work In Progress (WIP): Misc items.

- Write cylindrical operators
- Write material on directional derivatives and gradients
- Write material on Jacobian and Hessian matrices
- More detail on integration? Fubini's thm., change of variables, etc.
- Scaling argument for completeness of  $C^k(K)$  sp. norm and nondimensionalization
- Define metric sp, normed sp., inner-product sp. defs and notation; include stmt. that norm's induce metrics, metrics induce norms.
- Finite dim sp.s are complete, hence banach, and hilbert under a particular choice of inner-product; state such inner-product for their sp.s.

# 1 Introduction

Hemodynamics studies the kinematics of blood. Our interest is the kinematic motion of blood within the human macrocirculatory system, i.e. the flow of blood in large vessels such as arteries and veins. Blood is observed as a complex fluid of formed elements suspended in plasma, thus, the rheological behavior of blood is non-trivial. We report techniques and methodologies for modeling blood's motion in large vessels.

Our report is organized as follows.

After stating our report's motivation, Sec. 1.1 provides a brief physiological review of the human circulatory system. Then Sec. 1.2 reviews the continuum hypothesis, a necessary postulate in fluid mechanics which treats blood as a continuous medium. This framing reduces the hemodynamic problem to describing blood's motion in a continuum. Then Sec. ?? discusses rheological assumptions that lead to constitutive relations between the material properties of blood. By conservation, the kinematic-viscosity Navier–Stokes (NS) equations are obtained (Sec. 1.4). The NS equations are a system of coupled nonlinear partial differential equations (PDEs), the foundation of our hemodynamic models.

**Motivation** The World Health Organization (WHO) claims cardiovascular diseases (CVDs) resulted in  $\approx 32\%$  of all deaths in 2022, the leading cause of death globally, where  $\approx 85\%$  of the deaths were from heart attack or stroke. In such cases the underlying CVD is often coronary artery stenosis (CAS), the narrowing of a coronary vessel due to the buildup of plaque. Such plaque is r.t. as a stenotic blockage. There is a need for evidence-based tools to predict and assess the severity of SBs, as often prediction of CAS doesn't mean an obstruction [[1]] and severity assessments often use a simple 0D lumped-parameter model. Cardiological interventionists need better tools for predicting and treating CAS.

Current clinical methods for assessing the severity of a SB rely on imaging techniques such as angiography, intravascular ultrasound (IVUS), and optical coherence tomography (OCT) to visualize the arteries and identify areas of narrowing. Such methods provide valuable information about the anatomy of the arteries, but they do not provide direct information about the functional significance of the CAS. Functional assessment of CAS typically involves measuring the fractional flow reserve (FFR), which is the ratio of the blood pressure downstream of the stenosis to the blood pressure upstream of the stenosis during maximum blood flow. However, measuring FFR requires the use of a pressure wire, which can be invasive and carries some risks. Therefore, there is a need for non-invasive methods to assess the functional significance of CAS.

cleanup, add refs

## 1.1 Physiology

The circulatory system is the human heart, vascular network, lungs, and organs. The systems source is the heart, transporting oxygen-rich blood to the organs and deoxygenated (and carbon dioxide-enriched) blood back to the lungs. Lungs discharge CO<sub>2</sub> and enrich the blood with Oxygen, referred to as the *pulmonary*

*circulation* and the *systemic circulation* (resp.). The *macrocirculatory system* consists of the heart and the large vessels in the systemic circulation. 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.

A single beat of the heart propels blood through the macrocirculatory system, the "lub-dub" sound. The beat and the following sequence of events following until the successive beat is known 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.). Normal resting heart rate is considered to be  $\omega = 70 \text{ bpm}$ , so the cardiac cycle is approximately  $0.86\text{s}$ . and consists of:

1. Systole (ventricular contraction)  $\approx 0.3$  seconds.
2. Diastole (ventricular relaxation)  $\approx 0.7$  seconds.

During ventricular contraction, blood is ejected from the left ventricle into the aorta, creating a pressure wave that propagates through the arterial network. The Womersley number  $W_0$  characterizes the pulse waves in large vessels by comparing the pulse frequency  $\omega$  to the viscous effects determined by the kinematic viscosity  $\mu := \eta/\rho$  [  $\frac{\text{cm}^2}{\text{s}}$  ]:

$$W_0 := \sqrt{\frac{\rho\omega U}{\eta UL^{-2}}} = \sqrt{L^2 \cdot \frac{\omega}{\mu}} \quad [ - ] \quad \text{s.t.} \quad \begin{cases} L : \text{characteristic length scale} \quad [ \text{cm} ] \\ U : \text{characteristic velocity scale} \quad [ \frac{\text{cm}}{\text{s}} ] \\ \eta : \text{dynamic viscosity} \quad [ \text{Pa} \cdot \text{s} ] \\ \rho : \text{blood density} \quad [ \frac{\text{kg}}{\text{cm}^3} ] \end{cases}$$

High  $W_0$  indicates large, rapid pulses where inertial effects dominate viscous effects while low  $W_0$  indicates small, slow pulses where viscous effects dominate inertial effects. The Reynolds number  $Re$  characterizes flow in blood vessel

$$Re := L \cdot \frac{\rho U}{\eta} \quad [ - ].$$

Low  $Re$  indicates laminar flow while high  $Re$  suggests turbulent flow. Note [4, Table 1.1, p. 10, §1.1] shows  $W_0 \propto L$  and  $Re \propto (L)^{-1}$ ; we observe large pulses and turbulent flow in large vessels and small pulses and laminar flow in small vessels. Note, most often we set  $L = 2R$  where  $R$  is the radius of the vessel.

### Observed Cardiac Cycle Characteristics

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).

Is there a relationship between  $W_0$  and  $Re$  we can exploit to simplify our models? Appears so...

**Constituents and hematocrit.** Blood consists of plasma and formed elements which we call cells. Red blood cells (RBCs) comprise  $\approx 97\%$  of the cellular volume, and cellular volume is approximately  $\approx 45\%$  of the blood volume. The remaining  $\approx 55\%$  of blood volume is plasma, which is  $\approx 90\%$  water. The ratio of RBC volume to total blood volume is the *hematocrit value*  $H$ , a key metric governing apparent viscosity  $\eta$ : as  $H$  increases,  $\eta$  typically increases (cf. S6.5.1 [3]). The formed elements suspended in plasma include white blood cells (WBCs) and platelets.

## 1.2 Continuum of Blood

W.a.t. simulate blood flow in a time-dependent fluid domain  $\Omega_B \subset \mathbb{R}^{N+1}$ ; we'll take  $N \equiv 3$ , the natural setting for the derivations that follow. For each  $t \in I_T := [0, T] \subset \mathbb{R}$ , with  $T > 0$ , we define the fluid domain

$$\Omega_B(t) := \{\mathbf{x} \in \mathbb{R}^N : \mathbf{x} \text{ lies inside the vessel at time } t\}.$$

Formally, the fluid region is a time-dependent family of open sets  $\{\Omega_B(t)\}_{t \in I_T} \subset \mathbb{R}^N$  occupied by blood at time  $t$ . Let  $\Omega_B(0)$  denote the *reference configuration* and  $\Omega_B(t)$  the *current configuration* at time  $t$ . The fluid's computational domain refers to all possible configurations of  $\Omega_B(t)$ , i.e., the union over time of the spatial domains  $\Omega_B(t)$ , which we define by

$$\Omega_B := \{(t, \mathbf{x}) : t \in I_T, \mathbf{x} \in \Omega_B(t)\} \subset I_T \times \mathbb{R}^N.$$

For each material particle initially at  $\xi \in \Omega_B(0)$ , we assume that its motion is governed by an Eulerian velocity field  $\mathbf{u} : \Omega_B \rightarrow \mathbb{R}^N$ ,  $(t, \mathbf{x}) \mapsto \mathbf{u}(t, \mathbf{x})$ . Our aim in Sec. 1.2.1 is to derive equations describing the evolution of  $\xi$  as it moves from the reference configuration to the current configuration under the flow induced by  $\mathbf{u}$ . Precisely, we seek a map  $\mathcal{L}_t : \Omega_B(0) \rightarrow \Omega_B(t)$  that carries each particle  $\xi \in \Omega_B(0)$  to its current position  $\mathbf{x} \in \Omega_B(t)$  at time  $t$ .

### 1.2.1 Blood Dynamics

For each fixed  $t \in I_T$ , let the *Lagrangian map* be the map from the reference configuration to the current configuration, i.e.

$$\mathcal{L}_t : \Omega_B(0) \rightarrow \Omega_B(t), \quad \xi \mapsto \mathbf{x}(t, \xi)$$

where  $\mathbf{x}(t, \xi) = \mathcal{L}_t(\xi)$  is the particle  $\xi$ 's position at time  $t$ . We assume that, for each  $t \in I_T$ , the map  $\mathcal{L}_t : \Omega_B(0) \rightarrow \Omega_B(t)$  is a bijection, and that  $(t, \xi) \mapsto \mathcal{L}_t(\xi)$  is sufficiently smooth in  $t$  (e.g.,  $C^1$ ) so that  $\partial_t \mathbf{x}(t, \xi)$  is well-defined. The pairs  $(t, \mathbf{x})$  and  $(t, \xi)$  are respectively referred to as the Eulerian and Lagrangian coordinates. For fixed  $\xi \in \Omega_B(0)$ , we sometimes write  $\mathbf{x}(t; \xi)$  to emphasize the flow map of  $\xi$ , with corresponding trajectory  $T_\xi = \{(t, \mathbf{x}(t; \xi)) : t \in I_T\}$ .

*Remark 1.2.1* (Eulerian vs. Lagrangian). Informally, the Eulerian description focuses on what happens at a fixed spatial location  $\mathbf{x} \in \Omega_B(t)$  at a given time  $t$ ; fields such as  $\phi(t, \mathbf{x})$  or  $\mathbf{u}(t, \mathbf{x})$  are viewed as functions of  $(t, \mathbf{x})$ . In contrast, the Lagrangian description follows individual material particles  $\xi \in \Omega_B(0)$  along their trajectories  $t \mapsto \mathbf{x}(t; \xi)$ .

Let

$$\text{id}_{I_T} \times \mathcal{L}_t : I_T \times \Omega_B(0) \rightarrow \Omega_B, \quad (t, \xi) \mapsto (t, \mathcal{L}_t(\xi)).$$

Then (where defined) its inverse is

$$\text{id}_{I_T} \times \mathcal{L}_t^{-1} : \Omega_B \rightarrow I_T \times \Omega_B(0), \quad (t, \mathbf{x}) \mapsto (t, \mathcal{L}_t^{-1}(\mathbf{x})).$$

We define the Lagrangian velocity field by

$$\hat{\mathbf{u}}(t, \xi) := \partial_t \mathbf{x}(t, \xi) \quad \forall (t, \xi) \in I_T \times \Omega_B(0).$$

A change of coordinates in  $\hat{\mathbf{u}}$  yields the velocity field  $\mathbf{u}$  in the Eulerian frame, i.e.,

$$\begin{aligned} \mathbf{u}(t, \mathbf{x}) &= (\hat{\mathbf{u}} \circ (\text{id}_{I_T} \times \mathcal{L}_t^{-1})) (t, \mathbf{x}). \\ &= \hat{\mathbf{u}}(t, \mathcal{L}_t^{-1}(\mathbf{x})) \\ &= \hat{\mathbf{u}}(t, \xi) \quad \text{s.t. } \xi = \mathcal{L}_t^{-1}(\mathbf{x}) \quad \forall (t, \mathbf{x}) \in \Omega_B. \end{aligned}$$

If  $\hat{\mathbf{u}}$  and  $\Omega_B(0)$  are known, we arrive at the Cauchy problem for a particle trajectory in the Lagrangian

frame:

$$\begin{cases} \partial_t \mathbf{x}(t, \boldsymbol{\xi}) = \hat{\mathbf{u}}(t, \boldsymbol{\xi}), t \in I_T, \\ \mathbf{x}(0, \boldsymbol{\xi}) = \boldsymbol{\xi}. \end{cases}$$

Equivalently, if  $\mathbf{u}$  and  $\Omega_B$  are known, we arrive at the Cauchy problem for a particle trajectory in the Eulerian frame:

$$\begin{cases} \frac{d}{dt} \mathbf{x}(t; \boldsymbol{\xi}) = \mathbf{u}(t, \mathbf{x}(t; \boldsymbol{\xi})), t \in I_T, \\ \mathbf{x}(0; \boldsymbol{\xi}) = \boldsymbol{\xi}. \end{cases}$$

In other words, for each  $\boldsymbol{\xi} \in \Omega_B(0)$ , the trajectory  $t \mapsto \mathbf{x}(t; \boldsymbol{\xi})$  is an integral curve of the Eulerian velocity field  $\mathbf{u}$ .

**Theorem 1.2.2** (Well-posedness of particle trajectories (Hadamard)). *TODO: State and prove well-posedness in the sense of Hadamard (solution depends Lipschitz-continuously on initial data.)*

**Definition 1.2.3.** Let  $\phi \in C^k(\Omega_B)$  and  $\hat{\phi} := \phi \circ \mathcal{L}_t$  so that  $\hat{\phi}(t, \boldsymbol{\xi}) = \phi(t, \mathbf{x}(t, \boldsymbol{\xi}))$ , then the *material derivative*  $D_t \phi$  is the derivative of  $\phi$  w.r.t.  $t$  in the Lagrangian frame expressed as a function in the Eulerian frame, i.e.,

$$\begin{aligned} D_t(\phi(t, \mathbf{x})) &:= \partial_t \hat{\phi}(t, \boldsymbol{\xi}), \quad \text{s.t. } \boldsymbol{\xi} = \mathcal{L}_t^{-1}(\mathbf{x}) \\ &= \frac{d}{dt} \phi(t, \mathbf{x}(t, \boldsymbol{\xi})), \quad \forall \boldsymbol{\xi} \in \Omega_B(0) \quad (\because \hat{\phi}(t, \boldsymbol{\xi}) = \phi(t, \mathbf{x}(t, \boldsymbol{\xi}))). \end{aligned}$$

By the multivariable chain rule we simplify as

$$\begin{aligned} D_t(\phi(t, \mathbf{x})) &= \partial_t \phi(t, \mathbf{x}) + \nabla \phi(t, \mathbf{x}) \cdot \mathbf{u}(t, \mathbf{x}) \quad (\because \text{chain rule and since } \partial_t \mathbf{x} = \mathbf{u}) \\ &= \partial_t \phi + \langle \nabla \phi, \mathbf{u} \rangle_{\mathbb{R}^N} \quad \text{in } \Omega_B. \end{aligned}$$

By the divergence relationship  $\operatorname{div}(\phi \mathbf{u}) = \nabla \phi \cdot \mathbf{u} + \phi \operatorname{div}(\mathbf{u})$ , we rewrite as

$$D_t(\phi) = \partial_t \phi + \operatorname{div}(\phi \mathbf{u}) - \phi \operatorname{div}(\mathbf{u}) \quad \text{in } \Omega_B.$$

The material derivative 1.2.3 measures the rate of variation of  $\phi$  along trajectory  $T_{\boldsymbol{\xi}}$  expressed in the Eulerian variables. The literature also r.t.  $D_t$  as the *substantial derivative*, *advective derivative*, *lagrangian derivative*, or *convective derivative*.

Now differentiating  $\hat{\mathbf{u}}$  w.r.t.  $t$  yields the acceleration vector field  $\hat{\mathbf{a}}$  in the Lagrangian and Eulerian frame

respectively:

$$\begin{aligned}
\widehat{\mathbf{a}}(t, \boldsymbol{\xi}) &:= \partial_t \widehat{\mathbf{u}}(t, \boldsymbol{\xi}) = \partial_t^2 \mathbf{x}(t, \boldsymbol{\xi}) \quad \forall \boldsymbol{\xi} \in \Omega_B(0) \\
\iff \mathbf{a} &= D_t \mathbf{u} = \partial_t \mathbf{u} + (\mathbf{u} \cdot \nabla) \mathbf{u} \quad \text{in } \Omega_B(t) \\
\mathbf{a}(t, \mathbf{x}) &= \partial_t \mathbf{u}(t, \mathbf{x}) + (\mathbf{u}(t, \mathbf{x}) \cdot \nabla) \mathbf{u}(t, \mathbf{x}) \\
&= \partial_t \mathbf{u}(t, \mathbf{x}) + \sum_{\forall i \in [N]} u_i(t, \mathbf{x}) \partial_{x_i} \mathbf{u}(t, \mathbf{x}) \quad \forall (t, \mathbf{x}) \in I_T \times \Omega_B(t) \\
\iff \mathbf{a} &= \partial_t \mathbf{u} + \sum_{\forall i \in [N]} u_i \partial_{x_i} \mathbf{u} \\
&= \partial_t \mathbf{u} + \langle \nabla, \mathbf{u} \rangle_{\mathbb{R}^N} \mathbf{u} \quad \text{in } \Omega_B.
\end{aligned}$$

We denote the deformation gradient tensor in Lagrangian and Eulerian form by  $\widehat{\mathbf{F}}_t$  and  $\mathbf{F}_t$ , respectively, defined by

$$\begin{aligned}
\widehat{\mathbf{F}}_t(\boldsymbol{\xi}) &:= \nabla_{\boldsymbol{\xi}} \mathcal{L}_t(\boldsymbol{\xi}) \quad \forall \boldsymbol{\xi} \in \Omega_B(0). \\
\iff \mathbf{F}_t(\mathbf{x}) &= \nabla_{\boldsymbol{\xi}} \mathcal{L}_t(\mathcal{L}_t^{-1}(\mathbf{x})) = \partial_{\boldsymbol{\xi}} \mathbf{x}(t, \boldsymbol{\xi}) \quad \forall (t, \mathbf{x}) \in \Omega_B.
\end{aligned}$$

The tensor  $\mathbf{F}_t$  measures the spatial deformation of infinitesimal fluid elements as they move from the reference configuration to the current configuration under  $\mathcal{L}_t$  along trajectory  $T_{\boldsymbol{\xi}}$ . Suppose for each fixed  $t$  the mapping  $\mathcal{L}_t : \Omega_B(0) \rightarrow \Omega_B(t)$  is a  $C^1$ -diffeomorphism with  $\det \widehat{\mathbf{F}}_t(\boldsymbol{\xi}) > 0 \forall \boldsymbol{\xi} \in \Omega_B(0)$ <sup>2</sup>. Then  $\widehat{\mathbf{F}}_t(\boldsymbol{\xi})$  is invertible, and we define:

$$\begin{aligned}
\widehat{J}_t(\boldsymbol{\xi}) &:= \det(\widehat{\mathbf{F}}_t(\boldsymbol{\xi})) \quad \forall \boldsymbol{\xi} \in \Omega_B(0). \\
\iff J_t(\mathbf{x}) &= \det(\widehat{\mathbf{F}}_t(\mathcal{L}_t^{-1}(\mathbf{x}))) \quad \forall (t, \mathbf{x}) \in \Omega_B.
\end{aligned}$$

We r.t. such measure of spatial deformation  $\widehat{J}_t(\boldsymbol{\xi})$  as the Jacobian determinant of  $\mathcal{L}_t$  at time  $t$ . The following lemma shows that  $\partial_t J_t$  relates to the fluid's divergence  $\text{div}(\mathbf{u})$ .

**Lemma 1.2.4.** *The Jacobian determinant  $J_t(\mathbf{x})$  satisfies*

$$D_t J_t(\mathbf{x}) = J_t(\mathbf{x}) \text{div}(\mathbf{u}(t, \mathbf{x})) \quad \forall (t, \mathbf{x}) \in \Omega_B.$$

*Proof.* Ref [2], lemma 2.1, pg. 20, for proof. □

Literature often r.t. relation in lem. 1.2.4 as the *Euler expansion formula*, or *Jacobi's equation*.

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<sup>2</sup>Recall the  $\det \widehat{\mathbf{F}}$  may be interpreted as the signed volume change of an infinitesimal parallelepiped spanned by the column vectors of  $\widehat{\mathbf{F}}$ ; thus,  $\det \widehat{\mathbf{F}}_t(\boldsymbol{\xi}) > 0$  ensures that the orientation of fluid elements is preserved under the mapping  $\mathcal{L}_t$  at time  $t$ . Moreover, it prevents unphysical scenarios such as interpenetration of matter consisting of negative volumes.

Let  $V(t)$  denote a measurable material volume at time  $t$  that moves with the fluid flow, i.e.,

$$V(t) \subset \Omega_B(t), \quad \text{for each } t \in I_T$$

Equivalently,  $V(t)$  is the image of some reference volume  $V(0) \subset \Omega_B(0)$  under the Lagrangian mapping  $\mathcal{L}_t$ , i.e.,

$$V(t) = \mathcal{L}_t(V(0)).$$

The following theorem, known as the Reynolds Transport Theorem, relates the time derivative of an integral over the material derivative of  $V(t)$ .

**Theorem 1.2.5** (Reynolds Transport Theorem). *Let  $V(0) \subset \Omega_B(0)$  be a material volume in the reference configuration, and  $V(t) \subset \Omega_B(t)$  its image in the current configuration under  $\mathcal{L}_t$ . Then for  $\phi \in L^1(\Omega_B)$  we have*

$$\begin{aligned} \frac{d}{dt} \int_{V(t)} \phi(t, \mathbf{x}) \, d\mathbf{x} &= \int_{V(t)} D_t \phi(t, \mathbf{x}) + \phi(t, \mathbf{x}) \langle \nabla, \mathbf{u}(t, \mathbf{x}) \rangle \, d\mathbf{x} \\ &= \int_{V(t)} \partial_t \phi(t, \mathbf{x}) + \langle \nabla, \phi(t, \mathbf{x}) \mathbf{u}(t, \mathbf{x}) \rangle \, d\mathbf{x} \end{aligned}$$

*Proof.* Observe

$$\begin{aligned} \frac{d}{dt} \int_{V(t)} \phi(t, \mathbf{x}) \, d\mathbf{x} &= \frac{d}{dt} \int_{V(0)} \widehat{\phi}(t, \boldsymbol{\xi}) \widehat{J}_t(\boldsymbol{\xi}) \, d\boldsymbol{\xi} \quad (\text{by 1.2.3 and 1.2.4}). \\ &= \int_{V(0)} \partial_t \left( \widehat{\phi}(t, \boldsymbol{\xi}) \widehat{J}_t(\boldsymbol{\xi}) \right) \, d\boldsymbol{\xi} \\ &= \int_{V(0)} \partial_t \left( \widehat{\phi}(t, \boldsymbol{\xi}) \right) \widehat{J}_t(\boldsymbol{\xi}) + \widehat{\phi}(t, \boldsymbol{\xi}) \partial_t \left( \widehat{J}_t(\boldsymbol{\xi}) \right) \, d\boldsymbol{\xi} \quad (\text{chain rule}) \\ &= \int_{V(t)} D_t(\phi(t, \mathbf{x})) \, d\mathbf{x} + \int_{V(0)} \widehat{\phi}(t, \boldsymbol{\xi}) \widehat{J}_t(\boldsymbol{\xi}) \operatorname{div}(\mathbf{u}(t, \mathbf{x}(\boldsymbol{\xi}))) \, d\boldsymbol{\xi} \quad (\text{by again 1.2.3 and 1.2.4}). \\ &= \int_{V(t)} D_t(\phi(t, \mathbf{x})) \, d\mathbf{x} + \int_{V(t)} \phi(t, \mathbf{x}) \operatorname{div}(\mathbf{u}(t, \mathbf{x})) \, d\mathbf{x} \quad (\text{change of variables}) \\ &= \int_{V(t)} \partial_t \phi(t, \mathbf{x}) + \langle \nabla, \phi(t, \mathbf{x}) \mathbf{u}(t, \mathbf{x}) \rangle \, d\mathbf{x} \quad (\text{by 1.2.3}). \end{aligned}$$

□

### 1.3 NS-derivation

In the following derivations we let  $N \equiv 3$  so that  $\Omega_B(t) \subset \mathbb{R}^3$ . We assume blood fluid is a continuum that deforms continuously, i.e., at every point  $\mathbf{x} \in \Omega_B(t)$  and time  $t \in I_T$ , the blood's kinematic quantities are described by sufficiently smooth fields. At microscopic scales, this continuum hypothesis breaks down, since matter is a discrete collection of molecules, but at macroscopic scales empirical evidence suggests such models remain accurate.

Let blood's velocity, thermodynamic pressure, and density fields be

$$\begin{aligned}\mathbf{u} : \Omega_B &\rightarrow \mathbb{R}^3, (t, x, y, z) \mapsto (u_1(t, x, y, z), u_2(t, x, y, z), u_3(t, x, y, z))^\top, \quad \left[ \frac{\text{cm}}{\text{s}} \right] \\ p : \Omega_B &\rightarrow \mathbb{R}^+, (t, x, y, z) \mapsto p(t, x, y, z), \quad \left[ \frac{\text{N}}{\text{cm}^2} \right] \\ \rho : \Omega_B &\rightarrow \mathbb{R}^+, (t, x, y, z) \mapsto \rho(t, x, y, z), \quad \left[ \frac{\text{kg}}{\text{cm}^3} \right].\end{aligned}$$

For each  $t \in I_T$ , herein assume  $\Omega_B(t)$  is simply connected and boundary  $\partial\Omega_B(t) \in C^1$ , so, any closed curve in  $\Omega_B(t)$  can be continuously contracted to a point within  $\Omega_B(t)$ ; such an assumption is reasonable in a healthy vessel with a smooth wall. This regularity allows us to globally define geometric quantities such as surface differential operators on the fluids boundary  $\partial\Omega_B$ , then we may apply stokes theorem and Green's identities on the  $C^1$  boundaries, useful for obtaining weak integro-differential and variational formulations.

*Remark 1.3.1.* A weaker regularity condition is that  $\partial\Omega_B$  is Lipschitz. Here we must rely on standard trace theorems for Sobolev spaces (e.g.  $H^1(\Omega_B(t))$ ). In particular, the outward unit normal is then defined a.e. on  $\partial\Omega_B(t)$ , so we can meaningfully speak of normal and tangential components of vector fields on the boundary.

**Definition 1.3.2** (Incompressible fluid). A fluid is *incompressible* if for each material element  $V(0) \subset \Omega_B(0)$ , the density of that element remains constant in time, i.e.

$$\rho(t, \mathbf{x}(t, \boldsymbol{\xi})) = \rho_{V(0)} \in \mathbb{R}^+, \quad \forall (t, \boldsymbol{\xi}) \in I_T \times V(0),$$

where constant  $\rho_{V(0)}$  can depend on initial fluid element  $V(0)$ .

**Definition 1.3.3** (Incompressible flow). A flow is *incompressible* in  $\Omega_B$  if the material derivative of the density vanishes,

$$D_t \rho = 0 \quad \text{in } \Omega_B.$$

In our model we further assume a uniform initial density, so def 1.3.2 may be written as

$$\rho_{V(0)} = \rho_0 \in \mathbb{R}^+ \quad \forall V(0) \subset \Omega_B(0),$$

for some constant  $\rho_0$  independent of material element  $V(0)$ . Therefore uniform density in the reference configuration implies constant density along trajectory  $T_\xi$  to any current configuration, i.e.,

$$\begin{aligned}\rho(t, \mathbf{x}(t, \xi)) &= \rho_0 \in \mathbb{R}^+, \quad \forall(t, \xi) \in I_T \times \Omega_B(0). \\ \implies \rho(t, \mathbf{x}) &= \rho_0 \in \mathbb{R}^+, \quad \forall(t, \mathbf{x}) \in \Omega_B.\end{aligned}$$

Taking the material derivative yields  $D_t \rho = 0$  in  $\Omega_B$  – In summary, we've shown:

$$\text{Incompressible Fluid 1.3.2} \implies \text{Incompressible Flow 1.3.3.}$$

Note, the converse is not generally true: an incompressible flow ( $D_t \rho = 0$ ) only preserves density along  $T_\xi$ , allowing  $\rho = \rho(\mathbf{x})$  to vary spatially in the Eulerian frame. But particularly here, uniform initial density in  $\Omega_B(0)$  implies constant density in  $\Omega_B$  under the assumption of incompressible flow.

*Remark 1.3.4* (Divergence-free condition). Mass conservation for a fluid with density  $\rho$  and velocity  $\mathbf{u}$  yields the continuity equation

$$\partial_t \rho + \operatorname{div}(\rho \mathbf{u}) = 0 \iff D_t \rho + \rho \operatorname{div} \mathbf{u} = 0 \quad \text{in } \Omega_B.$$

For an incompressible fluid with constant density  $\rho \equiv \rho_0$ , Definition 1.3.2 implies  $D_t \rho = 0$ , so

$$0 = D_t \rho + \rho_0 \operatorname{div} \mathbf{u} \implies \operatorname{div} \mathbf{u} = 0 \quad \text{in } \Omega_B.$$

Combining this with Lemma 1.2.4,

$$D_t J_t = J_t \operatorname{div} \mathbf{u},$$

we obtain  $D_t J_t = 0$ , hence  $J_t(\mathbf{x})$  is constant along material trajectories. With the natural choice  $\mathcal{L}_0 = \operatorname{Id}$  we have  $J_0 \equiv 1$ , so incompressible flow is equivalent to

$$J_t(\mathbf{x}) \equiv 1 \quad \text{and} \quad \operatorname{div} \mathbf{u} = 0.$$

We refer to  $\nabla \cdot \mathbf{u} = \operatorname{div} \mathbf{u} = 0$  as the *divergence-free condition* in  $\Omega_B(t)$ .

By assumption blood is incompressible and newtonian, linear momentum balance follows from Newton's 2nd Law ( $F = ma$ ) for an infinitesimal fluid element  $V(t) \subset \Omega_B(t)$ .

**Definition 1.3.5.** The linear momentum balance for a fluid element  $V \in \Omega_B$  under flow  $\mathbf{u}$  is

$$\frac{d}{dt} \int_{V(t)} \rho \mathbf{u} dV = \int_{V(t)} \operatorname{div}(\mathbf{T}) dV + \int_{V(t)} \rho \mathbf{f}_b dV, \quad (\because \rho \equiv \rho_0)$$

where  $\mathbf{T}$  is the Cauchy stress tensor describing the fluids deformation,  $\mathbf{f}_b$  may be some body force per unit mass  $\left[ \frac{cm}{s^2} \right]$ .

By applying the Reynolds Transport Theorem 1.2.5 to linear momentum balance 1.3.5, we obtain the integral form of linear momentum balance:

$$\int_{V(t)} \rho \partial_t \mathbf{u} dV + \int_{\partial V(t)} \rho \mathbf{u} \langle \mathbf{u}, \hat{\mathbf{n}} \rangle dS := \int_{V(t)} \mathbf{div}(\mathbf{T}) dV + \int_{V(t)} \rho \mathbf{f}_b dV,$$

for any material volume  $V(t) \subset \Omega_B(t)$ . By the divergence theorem, we may rewrite the surface integral as a volume integral

$$\int_{V(t)} \rho \partial_t \mathbf{u} dV + \int_{V(t)} \mathbf{div}(\rho \mathbf{u} \otimes \mathbf{u}) dV := \int_{V(t)} \mathbf{div}(\mathbf{T}) dV + \int_{V(t)} \rho \mathbf{f}_b dV,$$

Since  $V(t)$  is arbitrary, the integrands must be equal a.e. in  $\Omega_B(t)$ , yielding differential form of linear momentum balance:

$$\rho \partial_t \mathbf{u} + \mathbf{div}(\rho \mathbf{u} \otimes \mathbf{u}) = \mathbf{div}(\mathbf{T}) + \rho \mathbf{f}_b, \quad \text{in } \Omega_B(t)$$

By incompressibility assumption of blood fluid 1.3.2 we have  $\rho \equiv \rho_0$  constant in  $\Omega_B(t)$ , so the linear momentum balance simplifies to

$$\rho \partial_t \mathbf{u} + \rho \mathbf{div}(\mathbf{u} \otimes \mathbf{u}) = \mathbf{div}(\mathbf{T}) + \rho \mathbf{f}_b, \quad \text{in } \Omega_B(t)$$

Using the vector calculus identity  $\mathbf{div}(\mathbf{u} \otimes \mathbf{u}) = (\nabla \cdot \mathbf{u}) \mathbf{u} + (\mathbf{u} \cdot \nabla) \mathbf{u}$  we have

$$\begin{aligned} \mathbf{div}(\mathbf{u} \otimes \mathbf{u}) &= (\nabla \cdot \mathbf{u}) \mathbf{u} + (\mathbf{u} \cdot \nabla) \mathbf{u} \\ &= 0 \cdot \mathbf{u} + (\mathbf{u} \cdot \nabla) \mathbf{u} \quad (\because \mathbf{div} \mathbf{u} = 0 \text{ by remark 1.3.4}) \\ \implies \rho \partial_t \mathbf{u} + \rho (\mathbf{u} \cdot \nabla) \mathbf{u} &= \mathbf{div}(\mathbf{T}) + \rho \mathbf{f}_b, \quad \text{in } \Omega_B(t) \end{aligned}$$

so the linear momentum balance 1.3.5 for incompressible fluid simplifies to the following form.

**Definition 1.3.6.** The differential form of linear momentum balance for an incompressible fluid element  $V \in \Omega_B$  under flow  $\mathbf{u}$  is

$$\rho(\partial_t \mathbf{u} + (\mathbf{u} \cdot \nabla) \mathbf{u}) = \mathbf{div}(\mathbf{T}) + \rho \mathbf{f}_b, \quad \text{in } \Omega_B(t)$$

The linear momentum balance equation above is not closed since the Cauchy stress tensor  $\mathbf{T}$  is unknown. To close the system, we need a constitutive law relating  $\mathbf{T}$  to kinematic quantities such as the velocity field  $\mathbf{u}$  and its derivatives.

Let the rate-of-deformation tensor be the symmetric part of the velocity gradient,

$$\mathbf{D}(\mathbf{u}) := \frac{1}{2}(\nabla \mathbf{u} + (\nabla \mathbf{u})^\top)$$

Note that  $\mathbf{u} \mapsto \mathbf{D}(\mathbf{u})$  captures spatial deformations of element  $V$  in  $\Omega_B$  under flow  $\mathbf{u}$ . Here  $\mathbf{D}(\mathbf{u})$  is related to the gradient deformation tensor  $\mathbf{F}_t$  via

$$\mathbf{D}(\mathbf{u}) = \frac{1}{2} D_t \mathbf{F}_t \mathbf{F}_t^{-1}$$

where  $D_t \mathbf{F}_t$  is the material derivative of  $\mathbf{F}_t$  (see ref [2], sec. 3.4, pg. 39, for derivation).

**Definition 1.3.7.** A fluid is *Newtonian* if its Cauchy stress tensor  $\mathbf{T}$  depends linearly on the rate-of-deformation tensor  $\mathbf{D}(\mathbf{u})$ .

**Definition 1.3.8.** A fluid is *isotropic* if its constitutive response is independent of the coordinate system. Writing the Cauchy stress as  $\mathbf{T} = \mathbf{T}(\mathbf{D})$ , isotropy means that for every orthogonal rotator  $\mathbf{Q} \in \text{SO}(3)$ ,

$$\mathbf{Q} \mathbf{T}(\mathbf{D}) \mathbf{Q}^\top := \mathbf{T}(\mathbf{Q} \mathbf{D} \mathbf{Q}^\top).$$

Where  $\text{SO}(3) := \{\mathbf{Q} \in \mathbb{R}^{3 \times 3} : \mathbf{Q} \mathbf{Q}^\top = \mathbf{I}, \det(\mathbf{Q}) = 1\}$  is the special orthogonal group in  $\mathbb{R}^3$ .

*Remark 1.3.9* (Isotropy implication). By 1.3.8, the Cauchy stress  $\mathbf{T}$  of an isotropic fluid depends only on the invariants of  $\mathbf{D}(\mathbf{u})$ , i.e., the eigenvalues of  $\mathbf{D}(\mathbf{u})$ .

*Remark 1.3.10* (Simple vs. complex fluids). In the terminology of continuum mechanics, a *simple* fluid is one whose constitutive response at a point depends only on the instantaneous values of kinematic quantities (such as the rate-of-deformation tensor  $\mathbf{D}(\mathbf{u})$ ), and not on their past history. The Newtonian, isotropic model in Definition 1.3.12 is a prototypical simple fluid. More complex models (e.g. viscoelastic fluids) incorporate memory effects so that the stress depends on the deformation history.

*Remark 1.3.11* (Blood isotropy justification). Blood is often modeled as an isotropic fluid since its microstructure (RBCs, WBCs, platelets) are suspended in plasma and distributed uniformly in all directions at macroscopic scales. This uniform distribution leads to isotropic mechanical properties, meaning blood's response to deformation is independent of direction. [[4], sec. 3.1] (Check source)

**Definition 1.3.12** (Newtonian, isotropic constitutive law). For a Newtonian, isotropic fluid the Cauchy stress is

$$\mathbf{T} = -p \mathbf{I} + 2\eta \mathbf{D}(\mathbf{u}) + \lambda \operatorname{div}(\mathbf{u}) \mathbf{I},$$

where the bulk viscosity  $\lambda \in \mathbb{R}^+$  is a material parameter quantifying the fluid's resistance to uniform compression.

So newtonian isotropic fluids at rest (quiescent state) sustains only hydrostatic stress:

$$\implies \mathbf{T} = -p\mathbf{I} \quad \text{when } \mathbf{u} \equiv \mathbf{0}.$$

Consequently, the constitutive law for newtonian fluids 1.3.12 simplifies under incompressibility assumption, because then  $\operatorname{div}(\mathbf{u}) = 0$  in  $\Omega_B$  (refer to 1.3.4).

**Definition 1.3.13** (Incompressible stress tensor). The Cauchy stress 1.3.12 simplifies to

$$\mathbf{T} = -p\mathbf{I} + 2\eta\mathbf{D}(\mathbf{u}).$$

*Remark 1.3.14* (Dynamic vs. Kinematic Viscosity). In our model assumptions, *dynamic viscosity*  $\eta \in \mathbb{R}^+$  and *kinematic viscosity*  $\mu \in \mathbb{R}^+$  relate as

$$\mu := \frac{\eta}{\rho} = \frac{\eta}{\rho_0} \in \mathbb{R}^+.$$

Here  $\eta$  quantifies the internal resistance of blood to shear deformation, i.e.,  $\eta := \frac{\tau}{\dot{\gamma}}$ , with units  $[Pa \cdot s]$ . Moreover  $\mu$  adjusts  $\eta$  by the density  $\rho$ , capturing the viscous diffusion of momentum per unit mass, with units  $[\frac{cm^2}{s}]$ . Intuitively,  $\eta$  measures how "thick" or "sticky" the fluid is, while  $\mu$  measures how quickly momentum diffuses through the fluid due to viscosity.

*Remark 1.3.15* (Newtonian Blood Justification). When diameter  $d$  and hematocrit effects are needed, one may use a Non-Newtonian model with relative viscosity  $\eta_r(H, d)$  that scales an absolute baseline  $\eta$ :

$$\eta_{\text{eff}} := \eta_r(H, d)\eta \quad (\text{effective viscosity})$$

An empirical fit from [5]

$$\eta_r := 1 + (\eta_{0.45} - 1) \frac{(1 - H)^C - 1}{(1 - 0.45)^C - 1} \text{ s.t. } \begin{cases} \eta_{0.45} = 6e^{-0.085d} + 3.2 - 2.44e^{-0.06d^{0.645}}, \\ C = (0.8 + e^{-0.075d}) \left( \frac{1}{1 + 10^{-11}d^{12}} - 1 \right) + \frac{1}{1 + 10^{-11}d^{12}}, \end{cases}$$

where  $d := 2R/(1.0\mu m)$  is the (scaled) vessel diameter. In large vessels,  $\eta_r$  is often constant, justifying the Newtonian assumption. [[4], sec. 3.1]

When modeling non-Newtonian effects (when  $\eta \neq$  constant), the kinematic viscosity  $\mu(\cdot)$  is often chosen by Carreau model [3]

$$2\mu(|\mathbf{D}|^2) = \eta_\infty + (\eta_0 - \eta_\infty) \cdot (1 + \kappa|\mathbf{D}|^2).$$

Where  $\eta_0$  and  $\eta_\infty$  are chosen to be the viscosity for very small and very large shear rates, resp., and  $\kappa \in \mathbb{R}^+$  and  $n \in (-0.5, 0)$  are model parameters. According to [[4], pg. 38], we often set

$$\eta_0 = 65.7 \cdot 10^{-3} \text{ Pa} \cdot \text{s}, \quad \eta_\infty = 4.45 \cdot 10^{-3} \text{ Pa} \cdot \text{s}, \quad \kappa = 212.2 \text{ s}^2, \quad \text{and } n = -0.325$$

In the Newtonian case, we choose  $\eta = \eta_\infty$  which allows us to determine  $\mu$  as  $\mu(|\mathbf{D}|^2) = \eta$ .

## 1.4 Navier-Stokes

When coupling our momentum balance equation with the divergence-free condition of  $\mathbf{u}$ , we obtain the Navier-Stokes (NS) equations. We present several equivalent forms of the NS equations below. First, we write the NS system in conservative form.

**Definition 1.4.1** (Conservative-Momentum Balance Form).

$$\begin{cases} \partial_t(\rho\mathbf{u}) + (\rho\mathbf{u} \cdot \nabla)\mathbf{u} = -\nabla p \operatorname{\mathbf{div}}(2\eta\mathbf{D}(\mathbf{u})) \rho\mathbf{f}, \\ \operatorname{\mathbf{div}}(\mathbf{u}) = 0, \quad \rho \equiv \rho_0 > 0 \text{ (constant)}. \end{cases}$$

Since  $\rho \equiv \rho_0$  and  $\eta \equiv \mu|\mathbf{D}|^2$ , the advective form follows from 1.4.1.

**Definition 1.4.2** (Generalized-Newtonian Navier-Stokes (NS)).

$$\begin{cases} \rho(\partial_t\mathbf{u} + (\mathbf{u} \cdot \nabla)\mathbf{u}) = -\nabla p + \operatorname{\mathbf{div}}(2\mu(|\mathbf{D}|^2)\mathbf{D}) + \rho\mathbf{f} \\ \operatorname{\mathbf{div}}(\mathbf{u}) = 0, \end{cases}$$

We divide  $\rho$  and obtain the kinematic-viscosity form from 1.4.2.

**Definition 1.4.3** (Kinematic-Viscosity Navier-Stokes (NS)).

$$\begin{cases} \partial_t\mathbf{u} + (\mathbf{u} \cdot \nabla)\mathbf{u} = -\frac{\nabla p}{\rho} + \operatorname{\mathbf{div}}\left(\frac{2}{\rho}\mu(|\mathbf{D}|^2)\mathbf{D}\right) + \mathbf{f}, \\ \partial_t\mathbf{u} + (\mathbf{u} \cdot \nabla)\mathbf{u} = -\frac{\nabla p}{\rho} + \operatorname{\mathbf{div}}\left(\frac{2}{\rho}\mu(|\mathbf{D}|^2)\mathbf{D}\right) + \mathbf{f}, \\ \operatorname{\mathbf{div}}(\mathbf{u}) = 0, \end{cases}$$

Finally, we write the NS system in operator form.

**Definition 1.4.4.** We write Eq. 1.4.2 in standard form

$$\begin{cases} F(\partial_t\mathbf{u}, \nabla\mathbf{u}, \nabla p, \mathbf{u}, p; \rho, \mu) = \mathbf{f}, \\ \operatorname{\mathbf{div}}(\mathbf{u}) = 0, \end{cases}$$

where  $F(\partial_t\mathbf{u}, \nabla\mathbf{u}, \nabla p, \mathbf{u}, p; \rho, \mu) := \partial_t\mathbf{u} + (\mathbf{u} \cdot \nabla)\mathbf{u} + \frac{\nabla p}{\rho} - \operatorname{\mathbf{div}}\left(\frac{2}{\rho}\mu(|\mathbf{D}|^2)\mathbf{D}\right)$

*Remark 1.4.5.* The NS equations are a non-linear coupled system of PDEs. The first equation follows from the balance of linear momentum and its terms are characterized as:

- The convective term  $\rho(\mathbf{u} \cdot \nabla)\mathbf{u} = \rho \begin{bmatrix} \langle \mathbf{u}, \nabla \mathbf{u}_1 \rangle \\ \langle \mathbf{u}, \nabla \mathbf{u}_2 \rangle \\ \langle \mathbf{u}, \nabla \mathbf{u}_3 \rangle \end{bmatrix}$  governs acceleration of fluid (non-linear).
- The diffusive term  $\text{div}(2\mu(|\mathbf{D}|^2) \mathbf{D})$  describes the viscoelastic behavior (linear since  $\mu$  is constant).

The second equation is the continuity equation, a consequence of the assumed fluid properties of blood that lead to the divergence-free condition on  $\mathbf{u}$ . The total system comprises of four equations in four unknowns: the three components of the velocity field  $\mathbf{u}$  and the pressure field  $p$ .

If pressure  $p$  and the velocity  $\mathbf{u}$  are given, the Cauchy stress  $\mathbf{T}$  is computed from Eq. 1.3.13. It follows that the wall shear stress (WSS) at the vessel wall is:

$$\text{WSS} := \langle \mathbf{t}_{blood}, \mathbf{T} \hat{n} \rangle : \begin{cases} \mathbf{t}_{blood} \text{ is tangent of a flow line through a cross-sectional area} \\ \hat{n} \text{ is outer normal of the cross-sectional area} \end{cases}$$

Forgoing the rigid-wall assumption allows us to model the relationship between the vessel wall and blood flow. Applicable models are referred to as fluid-structure interaction (FSI) models.

discuss in a later section

#### 1.4.1 NS in Cylindrical Coordinates

Let our vessel wall  $\partial\Omega = [0, T] \times \partial\Omega(t)$  be a surface in  $\mathbb{R}^4$  that evolves in time which we refer to as the interface. Let  $\bar{\Omega} = \partial\Omega \cup \Omega$  be the closed and compact region enclosed by our interface. So the region enclosed by our interface is  $\Omega$ , and we aim to model the velocity and pressure fields on  $\Omega$ .

The relationship between cartesian and cylindrical coordinates is

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

Assume a vessel of length  $L$  is aligned with the z-axis whose cross-section is circular with radius  $R(z, t)$  at axial position  $z$  and time  $t$ . Our fluid domain becomes

$$\Omega(t) = \{(r, \theta, z) \in \mathbb{R}^3 : r \in [0, R(z, t)], \theta \in [0, 2\pi], z \in [0, l]\}$$

where  $R(z, t)$  is the vessel radius at axial position  $z$  and time  $t$ .

Ref. notes for further details on deriving the transformation rules for vector calculus operators, or, notes where I do the derivation directly. Then discuss simplifications for axisymmetric flow.

## 2 Blood Flow Models

We seek solutions to initial and boundary value problems of Eq. 1.4.2. Let  $\mathbf{u}_0 : \Omega_B(0) \rightarrow \mathbb{R}^3$  be the initial velocity field at  $t = 0$ . Then the initial condition is given by

$$\mathbf{u}(\mathbf{x}, 0) = \mathbf{u}_0(\mathbf{x}) \quad \forall \mathbf{x} \in \Omega_B(0).$$

In practice,  $\mathbf{u}_0(z)$  may be prescribed or determined from sensor data. For the boundary conditions, we consider the following:

**Definition 2.0.1** (Inlet Boundary Condition). Let  $\mathbf{u}_0(z) : [0, \ell] \rightarrow \mathbb{R}^3$  be a prescribed velocity profile at the inlet boundary of  $\Omega_B(t)$  along the  $z$ -axis.

**Definition 2.0.2** (Outlet Boundary Condition). Let  $p_{out}(t) : [0, T] \rightarrow \mathbb{R}$  be a prescribed pressure profile at the outlet boundary of  $\Omega_B(t)$ .

We start our discussion with 1D and 0D models, reducing the d.o.f. in the NS system 1.4.2 by imposing further simplifying assumptions. Namely, w.a.t. compute average pressures and velocities after a relatively short simulation time by solving the 1D NS system in a compliant vessel with suitable side conditions. Because our model averages pressure and velocity over a surface-area, we obtain a uniform distribution of WSS on the vessel. Then, we discuss 2D and 3D models, which resolve spatial variations in pressure and velocity fields by solving the full NS system.

### 2.1 0D Models

### 2.2 1D Models

### 2.3 2D Models

### 2.4 3D Models

## 3 Appendix

### Bibliography

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## Code Listings

Code listings

**Code 1:** Algorithm 16.5

```

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

```