Triphasic Thrombosis Model: A Computational Study of Type B Aortic Dissection

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Abstract

Thrombosis refers to the formation of a thrombus, or a blood clot, within the body, which can occur either partially or completely. It serves as a crucial indicator of the severity of a patient's medical condition, with the location and characteristics of thrombosis dictating its clinical implications. Hence, accurate diagnosis and effective management of thrombosis are paramount.

In our current investigation, we incorporate the porous attributes of a thrombus using the Theory of Porous Media. This involves dividing the aggregate into solid, liquid, and nutrient phases and utilising volume fractions to capture microstructural details. Fluid flow through the porous media is modelled using a modified Darcy-Brinkman type equation, with interaction terms within balance equations facilitating the modelling of the mass exchange and other phase interactions.

We present a comprehensive framework of equations and assumptions governing the behaviour of a strongly coupled multiphasic porous medium problem. Additionally, we introduce scenarios involving type B Aortic Dissection and false lumen geometries, providing a detailed outline of the problem setup. We examine three distinct cases with varying entry and exit tear sizes. The simulation results validate the anticipated thrombi growth, with velocity plots aligning with Magnetic Resonance Imaging (MRI) data. Consequently, our proposed model offers a promising and reasonable approach for numerically simulating thrombosis and gaining insights into the underlying growth mechanics.

Keywords: thrombosis, porous media, triphasic model, aortic dissection, multiphasic, biomechanics

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1 Introduction

1.1 Motivation

Thrombosis is the process of forming a spatial structure known as a thrombus (blood clot). The formation of a thrombus involves a complex sequence of biochemical reactions. Humans possess an inbuilt system by which blood remains fluid and protects against the dangers of haemorrhage (bleeding). However, an injury to a blood vessel initiates haemostasis. Haemostasis is a mechanism which prevents and stops bleeding from a blood vessel by forming a thrombus. The process of thrombosis can be divided into two major parts: primary haemostasis and secondary haemostasis [28, 34]. We briefly overview these parts as:

• Primary Haemostasis: It involves the activation of platelets. The small blood cells (platelets) and various clotting factors are always present in the blood in their inactive form, ready to be activated within seconds of an injury. Once blood is exposed to components of the injured wall (collagen, subendothelial collagen, von Willebrand factor), platelets become activated. The von Willebrand factor acts as a glue and mediates the linking of platelets to collagen. As a result, activated platelets change their shape dramatically (from small rounded disks to flat plates with a moderately increased surface area). The platelets accumulate at the injury site and form a platelet plug.

• Secondary Haemostasis: Clotting factors (I to XIII) interact in a complicated series of chemical reactions and activate one another in a multistep pathway known as coagulation, cf. Figure 1. The coagulation cascade involves two main pathways. The intrinsic pathway is activated by trauma inside the vascular system, and the extrinsic pathway is initiated by external trauma that causes blood to escape from the vascular system. These pathways converge to a common pathway that ultimately leads to the formation of long and insoluble fibrin fibres. The fibrin fibres, along with the platelets, create a stable, permanent plug called a thrombus.

Thrombosis can be partial or complete and is a crucial indicator of the severity of a medical condition. On the one hand, it can save a life by healing an injury, such as in the case of a skin laceration or an Aortic Dissection (AD). On the other hand, it can endanger life by blocking blood vessels, as seen in cases of venous or arterial thrombosis. Moreover, some patients can be at risk of both thrombosis and bleeding simultaneously, as in the case of Disseminated Intravascular Coagulation (DIC), which is a widespread hypercoagulable state. Thrombosis can occur in any part of the body, and the clinical consequences depend on the location and nature of the thrombosis. As a result, the diagnosis and management of thrombosis is crucial [28]. For this study, we choose the case of AD for the model development process. In this context, we will briefly introduce AD and the nature of thrombosis in this condition.

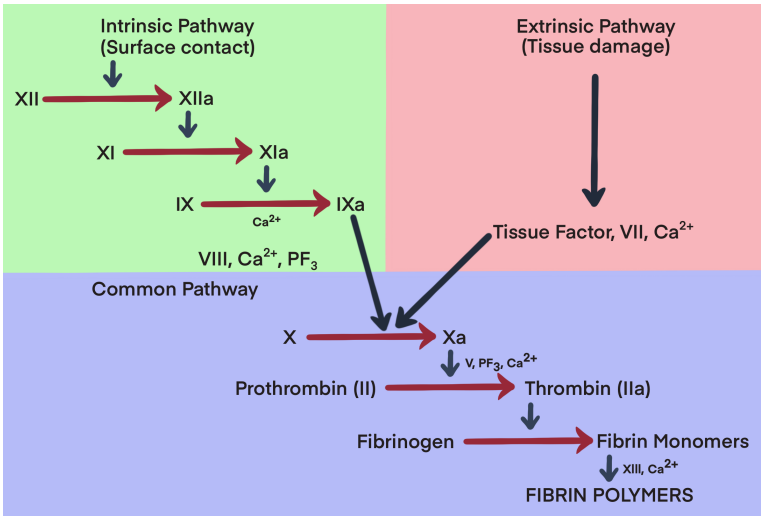
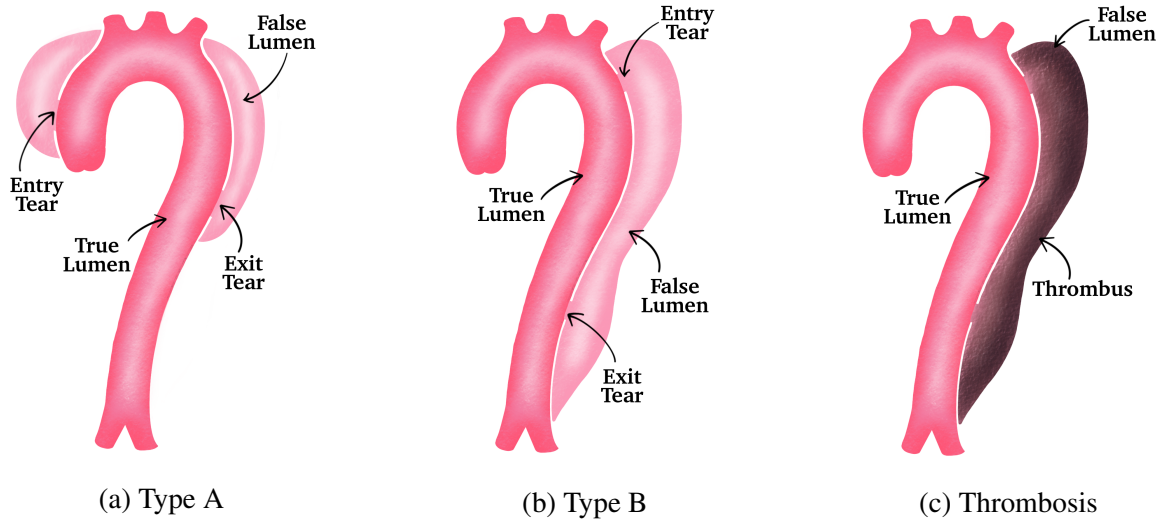


Figure 1 Schematic representation of the coagulation mechanism's intrinsic, extrinsic, and common pathways [17, 34].

1.2 Aortic Dissection

Aorta is the largest blood vessel in the body and serves as the main artery carrying blood from the heart to the entire body. The heart pumps the blood from the left ventricle into the aorta via the aortic valve, which opens and closes with each heartbeat to allow a one-way blood flow. One of the most common forms of acute aortic syndrome is AD. It begins when a tear occurs in the inner layer (intima) of the aortic wall. This tear allows the blood to flow between the inner and middle layers causing them to separate (dissect). This second blood-filled channel is called the false lumen. This condition can lead to aortic rupture or decreased blood flow to the organs, causing short- or long-term damage. AD is a severe condition that can be fatal if not treated early. The risk and nature of AD complications are highly dependent on the affected area of the aorta. There are two types of AD depending on the location of the dissection, cf. Figure 2. In type A AD, dissection occurs in the ascending part of the aorta, where the expansion of the false lumen can compress other branches of the aorta and reduce blood flow. On the contrary, dissection occurs in the descending part of the aorta in type B AD, which may extend to the abdomen. Complete or partial thrombosis in the false lumen is a significant predictor of mortality in patients [28, 49].

AD is a severe condition that may arise due to various risk factors. High blood pressure leading to increased stress on the aortic wall is the most common risk factor. Other factors include weakening of the wall, pre-existing aneurysm or defects in the aortic valve. AD primarily affects two epidemiological groups. The first group is men aged 40 to 60 years with pre-existing hypertension, and the second is younger patients with systemic or localised connective tissue abnormalities affecting the aorta. The estimated occurrence of AD is 3 to 6 cases per 100,000 people annually in Europe and the United States [21]. Moreover, in the instance of type B AD, the mortality rate is excessively high in the first seven days due to severe complications, such as malperfusion or rupture in the aorta. Approximately 40% of the patients die immediately from AD. Moreover, only 50% to 70% live 5 years after the surgery depending on the age and underlying complications [26]. This has boosted the importance of early diagnosis and treatment, which is critical for survival. Even though a general agreement exists on the need for immediate surgical repair for patients with acute type A AD, the optimal treatment of type B AD remains a matter of debate [48, 31, 16]. This led to an interest in computational methods to help with the decision-making process for treatment. Our current understanding of optimal medical care can expand by increasing insights into the progression and nature of the disease. A model for thrombosis prediction in patient-specific cases can help doctors make informed decisions and analyse the dangers



(a) Type A (b) Type B (c) Thrombosis

Figure 2 Illustrations of the entry tear, exit tear, true lumen, and false lumen in (a) type A AD, (b) type B AD, and (c) formation of thrombi in type B AD [17, 49]

involved.

1.3 State of the Art

The mathematical modelling of thrombosis first emerged in the late 1980s by Khanin et al. [24]. This research focused mainly on the coagulation network, which is a part of secondary haemostasis. Since then, the models have improved considerably. A cell-based model for haemostasis was presented by Hoffman et al. [22] which was a set of Ordinary Differential Equations (ODEs). This model was further enhanced by Lobanov et al. [30]. Ovanesov et al. [35] introduced a reaction-diffusion model based on Partial Differential Equations (PDEs), which was further developed using Computational Fluid Dynamics (CFD) with increased complexity by Leiderman et al. [29], involving more than 50 PDEs. Chen et al. [8] reduced the complexity of the model by using 8 ODEs, although these excluded platelet aggregation. Anand et al. [2] provide a detailed review of haemostasis models.

Moreover, various methodologies were employed to develop models in the context of thrombosis. Storti et al. [45] introduced a coupled solid mechanics and Fluid-Structure Interaction (FSI) model focusing on platelet plug formation. Chen et al. [7] presented another model based on FSI with simplified geometry, capable of predicting blood flow velocity and volumes of true and false lumen. Cheng et al. [9] introduced a CFD model for blood flow, treating blood as a Newtonian and incompressible fluid, specifically for the case of AD. Biasetti et al. [5] developed a CFD model for thrombi formation mechanisms in abdominal aortic aneurysms. Sousa et al. [43] and Malaspinas et al. [32] focused on the impact of haemodynamic parameters on initial thrombi formation using CFD models. Xu et al. [52] presented a 2D multiscale model for thrombi development based on CFD. Menichini et al. [33] proposed a CFD model with mass transfer equations and idealised geometries, demonstrating good agreement with clinical data. Despite certain limitations of these models, these models do validate the applicability of computational models in thrombosis prediction.

Modelling a thrombus is a continuum-mechanical problem that cannot be uniquely classified within well-known solid or fluid mechanics disciplines. Instead, it is necessary to consider a multiphasic aggregate along with the associated characteristics of its constituents. During thrombosis, evolving tissues undergo changes in their internal structure and properties other than their shape and size. As platelets cohere into a platelet aggregate, they do not immediately form a solid mass. Instead, they create a porous network with voids and channels. Following numerous reactions, the thrombus undergoes a transition to a stiff solid state. The porous nature of a thrombus makes the use of a macroscopic continuum-

mechanical approach like the Theory of Porous Media (TPM) more suitable for modelling. It provides an excellent framework to describe the overall behaviour of the multiphasic thrombus.

Various models based on TPM have been proposed to characterise the mechanical behaviour, growth, and remodelling processes of biological tissues. A biphasic model was proposed by Ehlers & Markert [14] for describing the mechanical behaviour of hydrated soft tissues and by Wagner & Ehlers [50] for describing the behaviour of brain tissue. Furthermore, Karajan [23] introduced a biphasic model to describe the mechanical behaviour of the Intervertebral Disc (IVD). Ricken et al. [41] presented a biphasic model for liver perfusion remodelling. Moreover, multiphasic models for growth and remodelling have been proposed by Ricken & Bluhm [38] and Ricken et al. [40, 39] for isotropic and transversely isotropic biological tissues. Preziosi & Tosin [37] presented multiphasic tumour growth models. Krause [25] proposed a model for tumour growth and bone remodelling using the growth energy concept. The application of TPM to describe the behaviour and growth of soft biological tissues has been well summarised by Athesian et al. [3]. The recent works employing TPM for modelling biological growth further motivate its use and highlight its relevance for modelling thrombosis.

In a recent study, we introduced a multiphasic model for thrombosis using both idealised and realistic 2D geometries [19, 18, 17]. However, in this investigation, we improve and extend the model to incorporate the viscous properties of the fluid, which become significant at high velocities. Additionally, we use actual 3D geometries to investigate the case of type B Aortic Dissection. Furthermore, we validate the simulation outcomes by comparing them with MRI scans. Additionally, we assess the model's performance across various dimensions of the entry and exit tears of the false lumen. Nonetheless, it is crucial to recognise that modelling the growth of living tissues poses inherent challenges, as well summarised by Ambrosi et al. [1].

2 The Theory of Porous Media

Within the developed framework of the Theory of Porous Media, we can obtain a macro-model to describe the complicated microstructure by using the homogenisation procedure over a Representative Elementary Volume (REV) of a thrombus, cf. Figure 3. We can split the whole constituent φ into three phases φ^α, where $\alpha = \{S, L, N\}$, leading to a triphasic model

$$\varphi = \bigcup_\alpha \varphi^\alpha = \varphi^S \cup \underbrace{\varphi^L \cup \varphi^N}_{\varphi^B}. \tag{1}$$

These three phases comprise the solid φ^S, the liquid φ^L, and the nutrient φ^N. The solid phase φ^S consists of subendothelial collagen, activated platelets (which move to the injury site), fibrin fibres (formed during the coagulation cascade), and wall cells. The solid phase is saturated with fluid blood φ^B. The blood itself consists of the nutrient phase φ^N, containing deactivated platelets (activated upon injury) and clotting factors (part of the coagulation cascade, cf. Figure 1), and the liquid phase φ^L, representing blood excluding the nutrients. For further insights into TPM, the reader is referred to Ehlers & Bluhm [12].

The concept of volume fractions n^α allows us to characterise the microstructure. It is defined as a ratio of the respective partial volume element $\mathrm{d}v^\alpha$ to the bulk volume element $\mathrm{d}v$ of the multiphasic aggregate

$$n^\alpha := \frac{\mathrm{d}v^\alpha}{\mathrm{d}v}. \tag{2}$$

Furthermore, the partial density ρ^α of a constituent is defined as the ratio of the mass element of the constituent $\mathrm{d}m^\alpha$ to the bulk volume element $\mathrm{d}v$. Similarly, the realistic density $\rho^{\alpha R}$ of a constituent is the ratio of the mass element of the constituent $\mathrm{d}m^\alpha$ to the constituent's volume element $\mathrm{d}v^\alpha$

$$\rho^\alpha = \frac{\mathrm{d}m^\alpha}{\mathrm{d}v} \qquad \text{and} \qquad \rho^{\alpha R} = \frac{\mathrm{d}m^\alpha}{\mathrm{d}v^\alpha}. \tag{3}$$

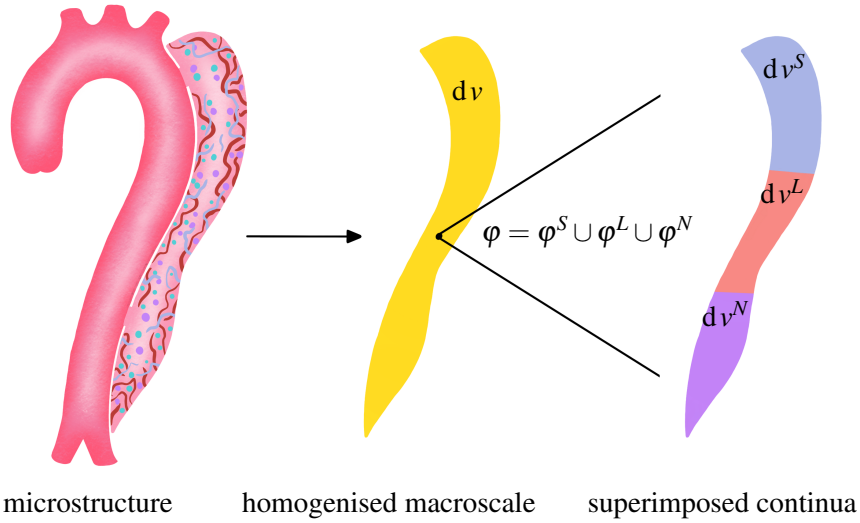


Figure 3 Illustration of the microstructure of the false lumen (left), macro-model obtained by volumetric homogenisation (centre), and superimposed continua (right)

By substituting equation (2) into (3), we obtain the relation between the densities as

$$\rho^\alpha = n^\alpha \rho^{\alpha R}. \tag{4}$$

This implies that the material's incompressibility ($\rho^{\alpha R} =$ constant) does not guarantee bulk incompressibility ($\rho^\alpha =$ constant) because the volume fraction can change owing to the deformation or mass exchange between phases.

2.1 Kinematics

In the context of the superimposed and interacting porous continua, particles P^α of all the constituents φ^α simultaneously occupy each spatial point $\mathbf{x}$ of the current configuration at any time t, cf. Figure 4. Since the particles at $\mathbf{x}$ proceed from the different reference positions $\mathbf{X}_\alpha$ at time t_0, each constituent is assigned its own motion and velocity functions

$$\mathbf{x} = \boldsymbol{\chi}_\alpha(\mathbf{X}_\alpha, t), \qquad \mathbf{x}'_\alpha = \frac{\mathrm{d}\boldsymbol{\chi}_\alpha(\mathbf{X}_\alpha, t)}{\mathrm{d}t}, \tag{5}$$

where $(\cdot)'_\alpha$ is a material time derivative defined as $\gamma_\alpha{}'(\mathbf{x}, t) = \frac{\partial \gamma}{\partial t} + \operatorname{grad}\gamma \cdot \mathbf{x}'_\alpha$ for an arbitrary scalar-valued field function γ_α. A unique inverse motion function $\boldsymbol{\chi}_\alpha^{-1}$ must exist to have a unique reference

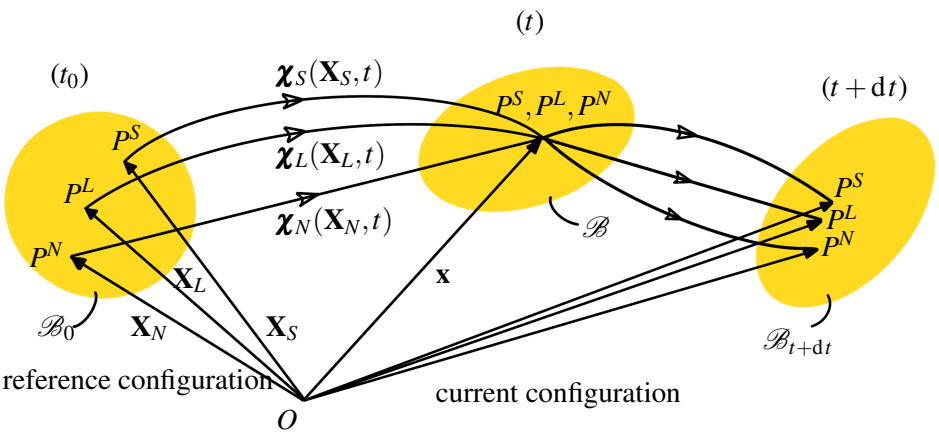


Figure 4 Motion of a triphasic aggregate [17]

position $\mathbf{X}_\alpha$ at time t_0 for each material point P^α at $\mathbf{x}$. The necessary and sufficient condition for this is the existence of a non-singular Jacobian J_α

$$\mathbf{X}_\alpha = \boldsymbol{\chi}_\alpha^{-1}(\mathbf{x},t), \qquad \text{if} \qquad J_\alpha := \det \frac{\partial \boldsymbol{\chi}_\alpha}{\partial \mathbf{X}_\alpha} \neq 0, \tag{6}$$

where $\det(\cdot)$ denotes the determinant operator. Furthermore, the deformation gradient and its inverse can be defined as

$$\mathbf{F}_\alpha = \mathrm{Grad}_\alpha\, \mathbf{x} =: \frac{\partial \boldsymbol{\chi}_\alpha(\mathbf{X}_\alpha,t)}{\partial \mathbf{X}_\alpha}, \qquad \text{and} \qquad \mathbf{F}_\alpha^{-1} = \mathrm{grad}\, \mathbf{X}_\alpha =: \frac{\partial \boldsymbol{\chi}_\alpha^{-1}(\mathbf{x},t)}{\partial \mathbf{x}}. \tag{7}$$

The right Cauchy-Green deformation tensor $\mathbf{C}_\alpha$ is defined as $\mathbf{C}_\alpha = \mathbf{F}_\alpha^T \mathbf{F}_\alpha$ and the left Cauchy-Green tensor $\mathbf{B}_\alpha$ is defined as $\mathbf{B}_\alpha = \mathbf{F}_\alpha \mathbf{F}_\alpha^T$. Moreover, the spatial velocity gradient $\boldsymbol{l}_\alpha = (\mathbf{F}_\alpha)'_\alpha \mathbf{F}_\alpha^{-1}$ can be additively decomposed into the symmetric and skew-symmetric parts

$$\boldsymbol{l}_\alpha(\mathbf{x},t) = \mathbf{d}_\alpha(\mathbf{x},t) + \mathbf{w}_\alpha(\mathbf{x},t), \tag{8}$$

where

$$\begin{aligned} \mathbf{d}_\alpha &= \frac{1}{2}(\boldsymbol{l}_\alpha + \boldsymbol{l}_\alpha^T) = \frac{1}{2}(\mathrm{grad}\, \mathbf{x}'_\alpha + \mathrm{grad}^T\, \mathbf{x}'_\alpha) = \mathbf{d}_\alpha^T, \\ \mathbf{w}_\alpha &= \frac{1}{2}(\boldsymbol{l}_\alpha - \boldsymbol{l}_\alpha^T) = \frac{1}{2}(\mathrm{grad}\, \mathbf{x}'_\alpha - \mathrm{grad}^T\, \mathbf{x}'_\alpha) = -\mathbf{w}_\alpha^T. \end{aligned} \tag{9}$$

$\mathbf{d}_\alpha$ is the symmetric part and is referred to as the rate of deformation tensor (rate of strain tensor), and the skew-symmetric part $\mathbf{w}_\alpha$ is known as the spin tensor (rate of rotation tensor or vorticity tensor).

2.2 Balance Relations

After a brief introduction to the TPM and the kinematic quantities, we introduce the local balance relations for the constituents φ^α. The mass balance is given by:

$$(\rho^\alpha)'_\alpha + \rho^\alpha\, \mathrm{div}\, \mathbf{x}'_\alpha = \hat{\rho}^\alpha, \tag{10}$$

where $\hat{\rho}^\alpha$ is the mass production term of the constituent φ^α. The volume balance can be obtained using the above equation and the equation (2) as

$$(n^\alpha)'_\alpha + n^\alpha\, \mathrm{div}\, \mathbf{x}'_\alpha = \frac{\hat{\rho}^\alpha}{\hat{\rho}^{\alpha R}}. \tag{11}$$

The balance of momentum for quasi-static conditions is read as

$$\mathbf{0} = \mathrm{div}\, \mathbf{T}^\alpha + \rho^\alpha \mathbf{b}^\alpha + \hat{\mathbf{p}}^\alpha, \tag{12}$$

where $\mathbf{T}^\alpha$ is the partial Cauchy stress tensor and $\hat{\mathbf{p}}^\alpha = \hat{\mathbf{s}}^\alpha - \hat{\rho}^\alpha \mathbf{x}'_\alpha$ is the direct momentum production term. $\hat{\rho}^\alpha \mathbf{x}'_\alpha$ represents the momentum production due to the mass exchange and $\hat{\mathbf{s}}^\alpha$ is the total momentum production. The moment of momentum balance leads to symmetric stress tensors

$$\mathbf{T}^\alpha = (\mathbf{T}^\alpha)^T. \tag{13}$$

The total production terms are restricted by the summation constraints

$$\hat{\rho}^S + \hat{\rho}^L + \hat{\rho}^N = 0, \qquad \hat{\mathbf{s}}^S + \hat{\mathbf{s}}^L + \hat{\mathbf{s}}^N = \mathbf{0}. \tag{14}$$

2.3 Assumptions

Thereafter, we present meaningful assumptions to simplify the model to a reasonable scope and adapt the model according to the theoretical background of thrombosis.

- The aggregate is assumed to be fully saturated. This condition has to be permanently fulfilled to avoid the formation of any vacant space

$$\sum_{\alpha} n^{\alpha} = n^S + n^L + n^N = 1. \tag{15}$$

- The constituents are assumed to be materially incompressible but it does not lead to bulk incompressibility

$$\rho^{\alpha R} = \text{constant}, \quad (\rho^{\alpha R})'_{\alpha} = 0. \tag{16}$$

- Isothermal conditions are assumed. Therefore, it is not needed to use the energy balance explicitly

$$\Theta^{\alpha} \equiv \Theta = \text{constant}. \tag{17}$$

- Body forces are neglected

$$\mathbf{b}^{\alpha} = \mathbf{0}. \tag{18}$$

- Both the nutrient and the liquid phases are a part of the blood phase. Therefore, both phases are assumed to have the same velocity

$$\mathbf{x}'_N = \mathbf{x}'_L = \mathbf{x}'_B. \tag{19}$$

- Furthermore, the mass exchange occurs between the nutrient and the solid phases from the physiological understanding. The liquid phase is not involved in the mass transfer

$$\hat{\rho}^L = 0 \quad \rightarrow \quad \hat{\rho}^S = -\hat{\rho}^N. \tag{20}$$

Additionally, the internal structure of a thrombus is considered to be isotropic, quasi-static conditions are assumed, and the diffusion velocity is neglected.

3 Constitutive Modelling

Thereafter, we follow the principles of determinism, equipresence, local action, and material frame indifference. Further information regarding these principles specific to this application can be found in the thesis by Gupta [17]. Moreover, to restrict the complexity of the model to a reasonable scope, the dependencies of the Helmholtz free energy are chosen as

$$\psi^S = \psi^S\{n^S, \mathbf{C}_S\}, \qquad \psi^L = \psi^L\{n^L\}, \qquad \psi^N = \psi^N\{n^N\}. \tag{21}$$

It is essential to recognise that the solid volume fraction n^S is dependent on $\det\mathbf{F}$ and $\hat{\rho}^S$ in the cases of incompressible constituents with mass exchange. This results from the time integration of the solid volume balance. However, we choose n^S as an independent constitutive variable to provide an additional degree of freedom for analysing the growth process. With n^S as the primary unknown variable, the saturation condition (15) also leads to n^N as an unknown variable. The splitting of n^B into n^L and n^N allows us to differentiate between the nutrients (deactivated platelets and clotting factors) and the liquid phase (blood excluding the nutrients) despite the velocity assumption (19). This helps to use the physiological understanding for modelling that the mass exchange occurs between the solid and the nutrient phases without altering the fluid content. The weak formulations of the governing equations for unknowns n^S and n^N will be presented in section 4.

Furthermore, the invariance condition and the polyconvexity are satisfied by representing the solid Helmholtz free energy function as

$$\psi^S = \psi^S(n^S, I_1, I_2, J_S), \tag{22}$$

where I_1 and I_2 are principal invariants of $\mathbf{C}_S$. For a detailed discussion on convexity conditions, the reader is referred to Dacorogna [11]. Thereafter, the Helmholtz free energy function can be constructed as a modified Neo-Hookean material [40, 18, 17]:

$$\psi^S = \left(\frac{n^S}{n^S_{0S}}\right)^n \frac{1}{\rho^S_{0S}} \underbrace{\left\{\frac{\mu^S}{2}(I_1 - 3) - \mu^S \ln J_S + \lambda^S \frac{1}{2}(\ln J_S)^2\right\}}_{\psi^S_{neo}}, \tag{23}$$

where ψ^S_{neo} is the Neo-Hookean material law. μ^S and λ^S are the macroscopic Lam*é* constants. $I_1 = \operatorname{tr}\mathbf{C}_S$ is the first principal invariant of $\mathbf{C}_S$. $(\cdot)_{0S}$ represents the initial value concerning the reference configuration of the solid at time t_0. The ratio of the volume fractions in the front accounts for the change in solid rigidity corresponding to changes in solid volume fractions. This helps to adapt the solid properties as the porosity changes. The material parameter n was identified to be 3 by Carter and Hayes [6] and has been used in multiple TPM-based growth models [40, 38, 39, 18].

The earlier sections lead to a reduction in process variables. This simplifies the evaluation of the entropy inequality to

$$\sum_\alpha \left[\mathbf{T}^\alpha : \mathbf{d}_\alpha - \rho^\alpha (\psi^\alpha)'_\alpha - \hat{\mathbf{p}}^\alpha \cdot \mathbf{x}'_\alpha - \hat{\rho}^\alpha (\psi^\alpha + \frac{1}{2}\mathbf{x}'_\alpha \cdot \mathbf{x}'_\alpha)\right] \geq 0. \tag{24}$$

The detailed process of the entropy inequality can be found in our previous work [18, 17]. However, it's important to note that in this study, we specifically consider the dissipation effects of fluids. As a result, the restrictions obtained from evaluating the entropy inequality and the constitutive relations are presented in the following sections.

3.1 Stress Equations

We follow the procedure outlined by Coleman and Noll [10] to evaluate the entropy inequality and incorporate considerations of fluid frictional stresses. This yields the following restrictions for stresses

$$\begin{aligned}
&\mathbf{T}^S = -n^S p\mathbf{I} - (n^S)^2 \rho^{SR} \frac{\partial \psi^S}{\partial n^S}\mathbf{I} + 2\rho^S \mathbf{F}_S \frac{\partial \psi^S}{\partial \mathbf{C}_S}\mathbf{F}_S^T, \\
&\mathbf{T}^L + n^L p\mathbf{I} + (n^L)^2 \rho^{LR} \frac{\partial \psi^L}{\partial n^L}\mathbf{I} \propto \mathbf{d}_L, \\
&\mathbf{T}^N + n^N p\mathbf{I} + (n^N)^2 \rho^{NR} \frac{\partial \psi^N}{\partial n^N}\mathbf{I} \propto \mathbf{d}_N,
\end{aligned} \tag{25}$$

where $\propto$ signifies proportional relation, $\mathbf{T}^S_E$ is the effective solid Cauchy stress and the Lagrangean multiplier p is identified as an unspecified pore pressure. Furthermore, we assume the blood to be a Newtonian and a homogeneous fluid. Therefore, considering $\varphi^B = \varphi^L + \varphi^N$ with $\partial\psi^B/\partial n^B = 0$ yields

$$\begin{aligned}
\mathbf{T}^S = -n^S p\mathbf{I} - (n^S)^2 \rho^{SR} \frac{\partial \psi^S}{\partial n^S}\mathbf{I} + \mathbf{T}^S_E, \qquad &\text{where} \qquad \mathbf{T}^S_E = 2\rho^S \mathbf{F}_S \frac{\partial \psi^S}{\partial \mathbf{C}_S}\mathbf{F}_S^T \\
\mathbf{T}^B = \mathbf{T}^L + \mathbf{T}^N = -n^B p\mathbf{I} + \mathbf{T}^B_E \qquad &\text{where} \qquad \mathbf{T}^B_E = 2n^B \mu^{BR} \mathbf{d}_B,
\end{aligned} \tag{26}$$

where $\mathbf{I}$ is the second-order identity tensor, $\mathbf{T}^B_E$ is the effective blood stress, and μ^{BR} $[N/m^3]$ is the dynamic viscosity of blood. Here, the fluid stress $\mathbf{T}^B$ is described as a sum of a pressure term $-n^B p\mathbf{I}$ and

the deviatoric stress $2n^B\mu^{BR}\mathbf{d}_B$. Utilising equations (23) and (26), the relations for the effective solid Cauchy stress $\mathbf{T}_E^S$ and the total solid Cauchy stress $\mathbf{T}^S$ can be expressed as

$$\begin{aligned}
\mathbf{T}_E^S &= \left(\frac{n^S}{n_{OS}^S}\right)^{(n+1)} \Big\{\mu^S(\mathbf{B}_S - \mathbf{I}) + \lambda^S(\ln J_S)\mathbf{I}\Big\}, \\
\mathbf{T}^S &= -n^S p\mathbf{I} - n\left(\frac{n^S}{n_{OS}^S}\right)^{n+1} \Big\{\frac{\mu^S}{2}(I_1 - 3) - \mu^S \ln J_S + \lambda^S \frac{1}{2}(\ln J_S)^2\Big\}\mathbf{I} \\
&\quad + \left(\frac{n^S}{n_{OS}^S}\right)^{(n+1)} \Big\{\mu^S(\mathbf{B}_S - \mathbf{I}) + \lambda^S(\ln J_S)\mathbf{I}\Big\},
\end{aligned} \tag{27}$$

This gives the total Cauchy stress $\mathbf{T}$ as

$$\mathbf{T} = \mathbf{T}^S + \mathbf{T}^B = \mathbf{T}_E^S - (n^S)^2\rho^{SR}\frac{\partial \psi^S}{\partial n^S}\mathbf{I} + 2n^B\mu^{BR}\mathbf{d}_B - p\mathbf{I}. \tag{28}$$

3.2 Filter Velocity

The blood velocity $\mathbf{x}_B'$ can be defined in relation to the solid velocity $\mathbf{x}_S'$ using the seepage velocity $\mathbf{w}_{BS} = \mathbf{x}_B' - \mathbf{x}_S'$. This seepage velocity characterises the fluid motion relative to the solid. The restriction obtained from the entropy inequality for the momentum production term $\hat{\mathbf{p}}^B$ can be expressed in terms of the seepage velocity for an isotropic material as

$$\hat{\mathbf{p}}^B = p\,\mathrm{grad}\,n^B - \alpha_{BS}\mathbf{w}_{BS} - \hat{\rho}^S\mathbf{x}_S', \tag{29}$$

where α_{BS} can be described by using initial intrinsic permeability of solid $K_{0S}^S\,[m^2]$ and dynamic blood viscosity $\mu^{BR}\,[Ns/m^2]$ as

$$\frac{(n^B)^2}{\alpha_{BS}} = \left(\frac{n^B}{n_{0S}^B}\right)^m \frac{K_{0S}^S}{\mu^{BR}}. \tag{30}$$

Thereafter, inserting the equations (29) and (30) in the fluid momentum balance (12), we obtain the Navier Stokes equation for quasi-static conditions extended to the porous media as

$$\mathbf{0} = -n^B\,\mathrm{grad}\,p + \mathrm{div}\,\mathbf{T}_E^B + n^B\rho^{BR}\mathbf{b}^B + \hat{\mathbf{p}}^B. \tag{31}$$

Using the equations $(9)_1$, $(26)_2$, and (31), the filter velocity $n^B\mathbf{w}_{BS}$ can be formulated as

$$n^B\mathbf{w}_{BS} = -\left(\frac{n^B}{n_{0S}^B}\right)^m \frac{K_{0S}^S}{\mu^{BR}}\left(\mathrm{grad}\,p - \underbrace{\rho^{BR}\mathbf{b}}_{:=0(18)} - \frac{\mathrm{div}\,\mathbf{T}_E^B}{n^B}\right), \tag{32}$$

where

$$\mathrm{div}\,\mathbf{T}_E^B = n^B\mu^{BR}\Big(\mathrm{div}(\mathrm{grad}\,\mathbf{x}_B') + \mathrm{grad}(\mathrm{div}\,\mathbf{x}_B')\Big). \tag{33}$$

Here, $(n^B/n_{0S}^B)^m K_{0S}^S = K_E^S$ is termed as the effective permeability which considers the change of permeability due to evolving porosity. The porosity-dependent permeability was introduced by Eipper [15], where $m \geq 0$ is a material parameter. n_{0S}^B is the initial volume fraction of blood and ρ^{BR} is the realistic density of blood. Furthermore, equations (32) and (33) result in a modified version of a non-linear Darcy-Brinkman type equation

$$\mathrm{grad}\,p = -\frac{n^B\mu^{BR}}{K_E^S}\mathbf{w}_{BS} + \mu^{BR}\Big(\mathrm{div}(\mathrm{grad}\,\mathbf{x}_B')\Big) + \mu^{BR}\Big(\mathrm{grad}(\mathrm{div}\,\mathbf{x}_B')\Big). \tag{34}$$

It is important to highlight that when considering a non-deforming solid ($\mathbf{x}_S' \equiv \mathbf{0}$) and no mass exchange ($\hat{\rho}^S = 0$), the aforementioned equation reduces to the Darcy-Brinkman equation. Ehlers [13] has extensively reviewed the classical hydromechanical equations within the framework of TPM, providing valuable insights into their application and significance.

3.3 Mass Production

Based on the assumptions outlined in subsection 2.3, the mass exchange takes place between the solid and the nutrient phases, characterised by $\hat{\rho}^S = -\hat{\rho}^N$. Subsequently, in accordance with the constraints derived from the entropy inequality, the chemical potential functions $\overline{\Psi}^\alpha$ governing the solid growth process are related as

$$\hat{\rho}^S \geq 0 \qquad \longrightarrow \qquad \overline{\Psi}^N \geq \overline{\Psi}^S. \tag{35}$$

In consideration of the thrombus growth, we formulate the mass production based on the physiological understanding of the process. Virchow's triad describes three physiological factors that influence the process of thrombosis. These factors are endothelial injury, hypercoagulability of blood and stasis of blood flow [27]. Endothelial injury refers to a vessel wall injury and triggers the platelet activation and coagulation process. Hypercoagulability means an increased tendency of coagulation in the body, and stasis of the blood flow refers to the condition of slow blood flow. These factors are considered extremely important to predict the growth of a thrombus [44]. Motivated by Virchow's triad, we dedicate our efforts to include all three factors in this model. An injury is already represented in the model through a false lumen. Also, the effects of the blood velocity and the nutrients on the thrombus growth are well researched and can be used to account for hypercoagulability and blood stasis [56, 4, 36]. Therefore, the solid mass production $\hat{\rho}^S[kg/m^3\,s]$ is postulated as a function of seepage velocity $\mathbf{w}_{BS}$ and nutrient volume fraction n^N. Furthermore, it is understood that an initial porous thrombus forms rapidly at the injury site. The rate of the thrombus growth decreases as the solid thrombus increases. This decrease primarily occurs due to the reduced permeability, the restoration of normal blood velocity, and the decrease in blood stasis. The secondary haemostasis process continues for an extended duration, resulting in the gradual transformation into a solid thrombus over time. Thus, the solid mass production $\hat{\rho}^S[kg/m^3\,s]$ is postulated also as a function of the solid volume fraction. This leads to

$$\begin{aligned}
&\hat{\rho}^S = \hat{\rho}^S(\mathbf{w}_{BS}, n^N, n^S) = \mathscr{C}\,\hat{\rho}^S_{\mathbf{w}_{BS}}(\mathbf{w}_{BS})\,\hat{\rho}^S_{n^N}(n^N)(1-n^S),\\
&\hat{\rho}^S_{\mathbf{w}_{BS}}(\mathbf{w}_{BS}) = \exp\{-\|\mathbf{w}_{BS}\|^2/\beta_1\},\\
&\hat{\rho}^S_{n^N}(n^N) = -\exp\{-(n^N)^2\beta_2\} + 1,
\end{aligned} \tag{36}$$

where $\mathscr{C}$ represents the maximum mass exchange. $\hat{\rho}^S_{\mathbf{w}_{BS}}$ denotes the increased solid mass production during low fluid velocities, reflecting the stasis of blood. The material parameter β_1 determines the dependence of mass exchange on fluid velocity, cf. Figure 5. Furthermore, $\hat{\rho}^S_{n^N}$ signifies the solid mass production in the presence of nutrients. The material parameter β_2 can be used to adapt the model to various hypercoagulability scenarios. Additionally, a linear relation for the solid volume fraction n^S is added to the formulation to regulate the growth rate with an increase in solid volume fraction n^S. However, obtaining data for the parameters in this approach can be challenging. Therefore, we opt for parameters that yield reasonable results.

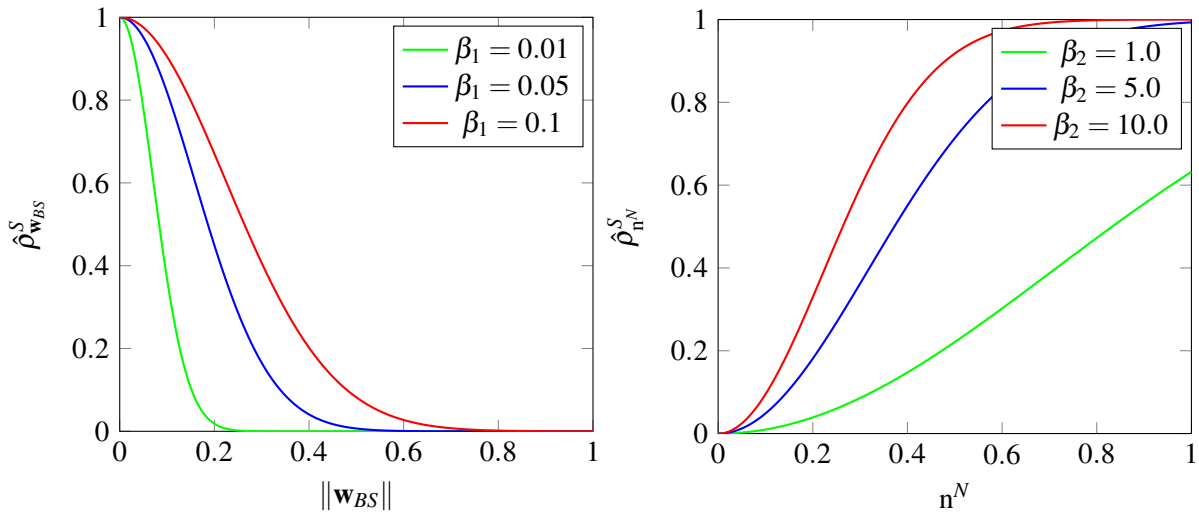


Figure 5 Variation in mass exchange rate dependence on the seepage velocity $\mathbf{w}_{BS}$ and nutrient volume fraction n^N influenced by the values of β_1 and β_2

4 Numerical Treatment

Considering the assumptions, balance equations, and constitutive relations discussed in the preceding sections, we arrive at a set of five unknown variables:

$$\mathscr{U} = \mathscr{U}(\mathbf{x},t) = \left\{\mathbf{u}_S, \mathbf{w}_{BS}, p, n^N, n^S\right\}. \tag{37}$$

The next step is to formulate the weak formulation of the governing PDEs in the framework of the standard Galerkin procedure (Bubnov-Galerkin). Therefore, we introduce the weak forms of the momentum balance of the mixture, the momentum balance of the blood, the volume balance of the mixture, the volume balance of the solid, and the volume balance of the nutrients by multiplying them with respective test functions. Thereafter, we integrate the equations over the spatial domain Ω, occupied by the body $\mathscr{B}$ at time t. We use the integration by parts and the divergence theorem to introduce the Neumann (natural) boundary terms. This yields a weak formulation of the governing equations.

• Momentum balance of mixture:

$$\begin{aligned}\mathscr{G}_{\mathbf{u}_S} = &\int_\Omega (\mathbf{T}) : \operatorname{grad} \delta\mathbf{u}_S \,\mathrm{d}v - \int_\Omega \hat{\rho}^S \mathbf{w}_{BS} \cdot \delta\mathbf{u}_S \,\mathrm{d}v \\ &- \int_{\Gamma_\mathbf{t}} \mathbf{t} \cdot \delta\mathbf{u}_S \,\mathrm{d}a = 0.\end{aligned} \tag{38}$$

• Momentum Balance of blood:

$$\begin{aligned}\mathscr{G}_{\mathbf{w}_{BS}} = &\int_\Omega \left(n^B \mathbf{w}_{BS} + \frac{K_E^S}{\mu^{BR}} \operatorname{grad} p\right) \cdot \delta\mathbf{w}_{BS} \,\mathrm{d}v \\ &+ \int_\Omega \frac{K_E^S}{n^B \mu^{BR}} \left(\mathbf{T}_E^B\right) : \operatorname{grad} \delta\mathbf{w}_{BS} \,\mathrm{d}v - \int_{\Gamma_{\mathbf{t}^B}} \underbrace{\frac{K_E^S}{n^B \mu^{BR}} \bar{\mathbf{t}}}_{:=\mathbf{t}^B} \cdot \delta\mathbf{w}_{BS} \,\mathrm{d}a = 0.\end{aligned} \tag{39}$$

• Volume balance of mixture:

$$\begin{aligned}\mathscr{G}_p = &\int_\Omega \operatorname{div}\mathbf{x}'_S\,\delta p\,\mathrm{d}v - \int_\Omega n^B\mathbf{w}_{BS}\cdot\operatorname{grad}\delta p\,\mathrm{d}v\\ &+\int_\Omega \hat{\rho}^S\left(\frac{1}{\rho^{NR}}-\frac{1}{\rho^{SR}}\right)\delta p\,\mathrm{d}v + \int_{\Gamma_q}\underbrace{n^B\mathbf{w}_{BS}\cdot\mathbf{n}}_{:=q}\,\delta p\,\mathrm{d}a = 0.\end{aligned} \tag{40}$$

• Volume balance of nutrients:

$$\begin{aligned}\mathscr{G}_{n^N} = &\int_\Omega \left((n^N)'_S + n^N\operatorname{div}\mathbf{x}'_S - \frac{\hat{\rho}^N}{\rho^{NR}}\right)\delta n^N\,\mathrm{d}v + \underbrace{\int_\Omega \operatorname{grad}n^N\cdot\operatorname{grad}\delta n^N\,\mathrm{d}v}_{:=r}\\ &-\int_\Omega n^N\mathbf{w}_{BS}\cdot\operatorname{grad}\delta n^N\,\mathrm{d}v + \int_{\Gamma_\upsilon}\underbrace{n^N\mathbf{w}_{BS}\cdot\mathbf{n}}_{:=\upsilon}\,\delta n^N\,\mathrm{d}a = 0.\end{aligned} \tag{41}$$

• Volume balance of solid:

$$\mathscr{G}_{n^S} = \int_\Omega (n^S)'_S\,\delta n^S\,\mathrm{d}v + \int_\Omega n^S\operatorname{div}\mathbf{x}'_S\,\delta n^S\,\mathrm{d}v - \int_\Omega \frac{\hat{\rho}^S}{\rho^{SR}}\,\delta n^S\,\mathrm{d}v = 0. \tag{42}$$

In the above set of weak formulations, $\mathbf{t}$ is the external load vector on the Neumann boundary $\Gamma_{\mathbf{t}}$, $\mathbf{t}^B$ is the external fluid load vector on the Neumann boundary $\Gamma_{\mathbf{t}^B}$, q is the fluid mass efflux on the Neumann boundary Γ_q, and υ is the nutrient mass efflux on the Neumann boundary Γ_υ, where $\mathbf{n}$ is the outward-oriented unit surface normal. It is well-recognised that the equation (41) tends to oscillate significantly unless stabilised or the mesh size is extremely small. Therefore, an artificial diffusion r is added to the volume balance of nutrients. The reader is referred to Santos et al. [42] and the references therein for further details on mass transport equations and stabilisation schemes.
Furthermore, we need a mixed formulation for the spatial discretisation because the unknowns have to be approximated simultaneously. Therefore, we choose quadratic shape functions for the solid displacement $\mathbf{u}_S$, and linear shape functions for the pressure p, the seepage velocity $\mathbf{w}_{BS}$, the solid volume fraction n^S, and the nutrient volume fraction n^N. This combination of the shape functions leads to the mixed formulation known as Taylor-Hood elements [46]. We use the same basis functions for the geometry as for the solid displacements $\mathbf{u}_S$ leading to the isoparametric mapping with respect to the solid displacements. Moreover, we use an implicit Euler scheme based on the backward Taylor-series expansion for the time discretisation. This gives a nonlinear system of equations which is solved using the Newton-Raphson scheme.

5 Modelling of thrombosis in type B Aortic Dissection

In this section, we demonstrate the application of the developed model for thrombosis using 3D real geometries for type B AD. The weak formulation of the triphasic model is discussed in the preceding chapter. Additionally, the constitutive relations and assumptions establish the remaining thrombosis-specific relations.
Initially, we acquired the geometry of the type B AD of a 25-year-old female patient from the Vascular Model Repository [51], as shown in Figure 6. The left image depicts the aorta with a false lumen in the case of type B AD. Upon rotating the geometry, we observe the true lumen as well, cf. Figure 6 (centre). As our focus is on modelling thrombosis in the false lumen, we extract only the false lumen from the complete geometry. This is achieved by making a perpendicular cut to the entry and exit tears. This gives us only the false lumen required for the simulation, cf. Figure 6 (right).

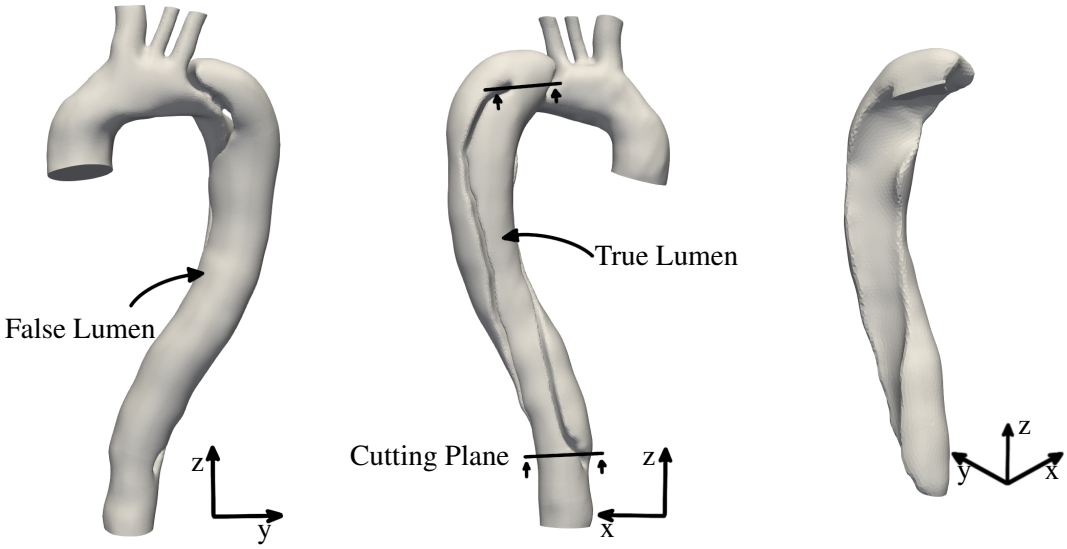


Figure 6 3D geometry of the aorta with type B AD showing the false lumen (left), true lumen and cutting planes (centre), and extracted false lumen (right)

Furthermore, we discretize the 3D false lumen using Gmsh, consisting of approximately 65,000 elements. This false lumen geometry represents a solid matrix saturated with the blood, comprising the liquid and the nutrient constituents. The entry tear at the top allows the blood to flow in. The Neumann boundary condition for the fluid volume efflux is set to $q = 0.2$ m/s, as shown in Figure 7. A Dirichlet boundary condition is applied for the nutrient volume fraction, setting $n^N = 0.4$ at the entry tear. The exit tear is treated as a drained surface, with a pressure boundary condition set to $p = 0.0$ N/m^2, allowing a free flow. Additionally, to promote thrombi growth at the walls, the seepage velocity $\mathbf{w}_{BS}$ is set to a small value of 0.01 m/s at the false lumen walls. In reality, the false lumen geometry is connected to the true lumen at the entry and exit tears, and to replicate this, we constrain the geometry at these tears in all directions. Furthermore, the simulation is performed using the parameters listed in Table 1, with a time step size of 100 seconds. For simplicity and due to a lack of material data, we assume a zero Poisson's ratio ($\lambda^S = 0$) for the solid skeleton [54, 47, 53].

Table 1 Parameters for modelling thrombosis [18]

Parameter	Value	Unit	Parameter	Value	Unit
λ^S	0.0	N/m^2	ρ^{SR}	2×10^3	kg/m^3
μ^S	1×10^5	N/m^2	ρ^{LR}	1×10^3	kg/m^3
μ^{BR}	1×10^{-3}	Ns/m^2	ρ^{NR}	2×10^3	kg/m^3
K^S_{OS}	1×10^{-6}	m^2	n^S_{OS}	0.2	-
$\mathscr{C}$	5×10^{-2}	kg/m^3s	n^N_{OS}	0.4	-
β_1	0.05	s^2/m^2	β_2	5.0	-
m	3.0	-			

Furthermore, we define three planes (P1, P2, P3) passing through the false lumen to analyse the results, as illustrated in Figure 8 (left). Upon performing the simulation with the specified setup and parameter values, we obtain solid volume fraction plots at time $t = 84$ hours, as depicted in Figure 8 (centre). The cross-sectional views at pre-defined planes indicate the formation of the thrombus and the flow of blood in certain parts of the false lumen. The solid volume fraction plots in Figure 8 (right) show that the thrombus is formed on the walls of the lumen which are the sites of injury. These observations align with

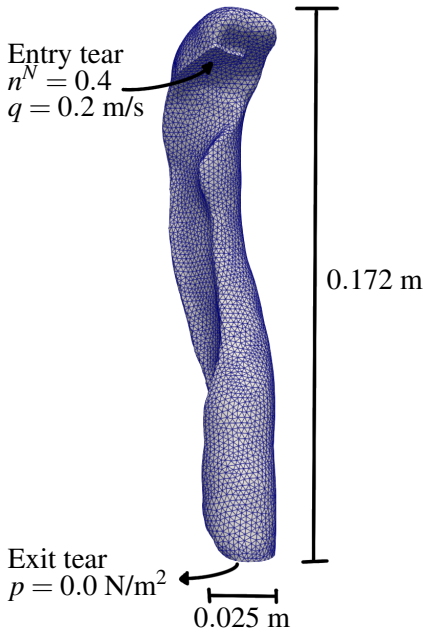


Figure 7 Discretisation and boundary conditions of the false lumen

our physiological understanding of thrombosis. Furthermore, the model demonstrates its capability to represent blood pressure, a major risk factor for Aortic Dissection, which significantly impacts thrombi growth. To investigate this, we assign three different values to the fluid volume efflux q: (a) 0.08 m/s, (b) 0.2 m/s, and (c) 0.4 m/s. The results of these three cases at plane P1 are shown in Figure 9. The varying values of the entry tear boundary condition q represent the range of blood pressure. A higher value of q corresponds to higher blood pressure, thereby making thrombi formation more challenging, and vice versa, aligning well with physiological expectations.

However, validating thrombi growth is currently challenging due to the lack of data for the presented geometry of type B Aortic Dissection. Nonetheless, a study conducted by Zimmermann et al. [55] provides 4D-flow MRI results for the geometry used in this investigation, offering an opportunity to validate the velocity results. To facilitate this comparison, we selected two more geometries from the Vascular Model Repository [51], which were also used by Zimmermann et al. [55]. This brings the total number of geometries to three for comparison of the velocity results with the 4D-flow MRI data. We denote the original geometry as Case I. Case II features an exit tear area of approximately 25% of Case I, while Case III presents an entry tear area of approximately 25% of Case I. Figure 10 shows the entry and exit tear areas in all three cases. For the simulations, we assumed a constant inflow volume. The seepage velocities obtained in these cases are presented in Figure 11. The top row displays the results of the developed triphasic model, while the bottom row showcases the velocity fields from the 4D-flow MRI from the study conducted by Zimmermann et al. [55]. The comparison shows that the magnitudes of the velocities obtained from the simulation closely match the MRI velocity profiles. Moreover, Figure 12 shows the evolution of the velocity field in time for Case I. It can be observed that the fluid velocity increases with time as more thrombi form, restricting the fluid flow.

6 Conclusion

The proposed triphasic model presents a promising approach to simulate thrombosis numerically. It offers the advantage of incorporating the mass exchange between the nutrient and the solid phases without altering the liquid volume, aligning well with the physiological understanding of thrombosis. Our analysis of the results reveals initial thrombi formation along the walls of the false lumen which is consistent

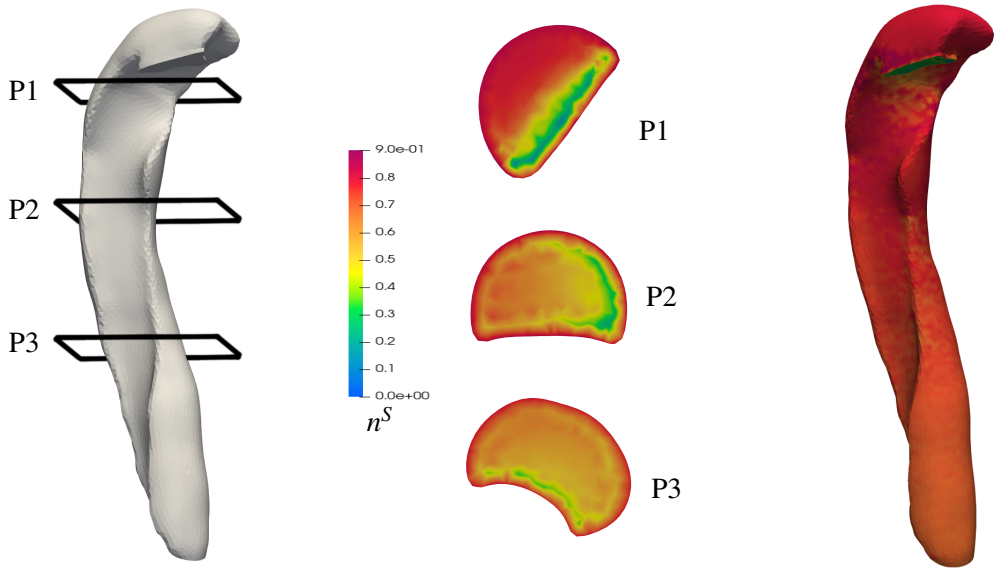


Figure 8 Geometry of the false lumen with three planes named P1, P2, and P3 (left), solid volume fraction plots illustrating the thrombus at the cross sections of the designated planes (center), and the visualisation of the thrombus formation along the walls of the false lumen (right)

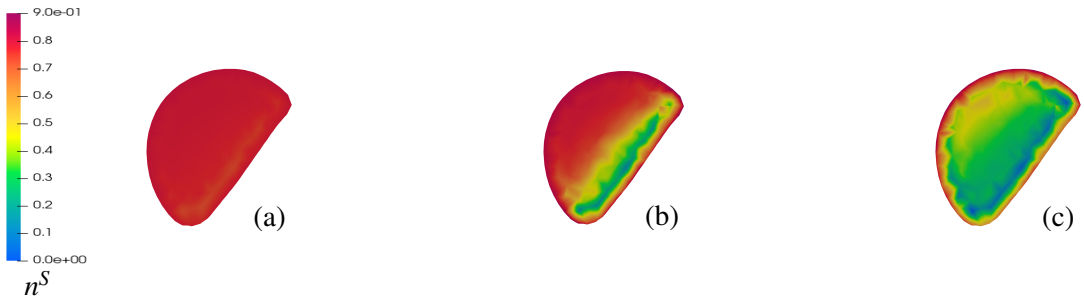


Figure 9 Visualisation of the thrombus at plane P1 demonstrates the impact of various values of the boundary condition q at the entry tear with q set to (a) 0.08 m/s, (b) 0.2 m/s, and (c) 0.4 m/s

with the process of platelet plug formation at injury sites. Over time, thrombi growth progressively restricts the blood flow through the cross-section of the false lumen.

Moreover, we have integrated the representation of Virchow's triad factors, alongside material parameters β_1 and β_2, enabling adaptation for various hypercoagulability and blood stasis scenarios. Additionally, the model can effectively capture blood pressure, a significant risk factor in Aortic Dissection. The model demonstrates its utility in real-world scenarios such as type B AD. However, further enhancements are necessary before clinical applications.

Furthermore, we have successfully validated the fluid flow magnitudes in the false lumen, although with minor discrepancies. The growth process needs to be improved to capture all the essential features comprehensively. To fully model the thrombosis process, it is necessary to incorporate the chemical reactions involved in haemostasis and account for the non-Newtonian nature of blood. Additionally, assigning physical significance to the parameters is essential for the practical application.

The development of biomechanical models presents challenges due to the lack of data and the biological complexity. Access to extensive medical and experimental data, including CT/MRI scans, is necessary for model validation, parameter determination, and refinement, leading to a more accurate representation of the growth process. Furthermore, the model's extension to other medical conditions, such as arterial or venous thrombosis and DIC, holds the potential for revolutionising medical device design, personalised medicine, and disease prognosis. Understanding the mechanics of growth

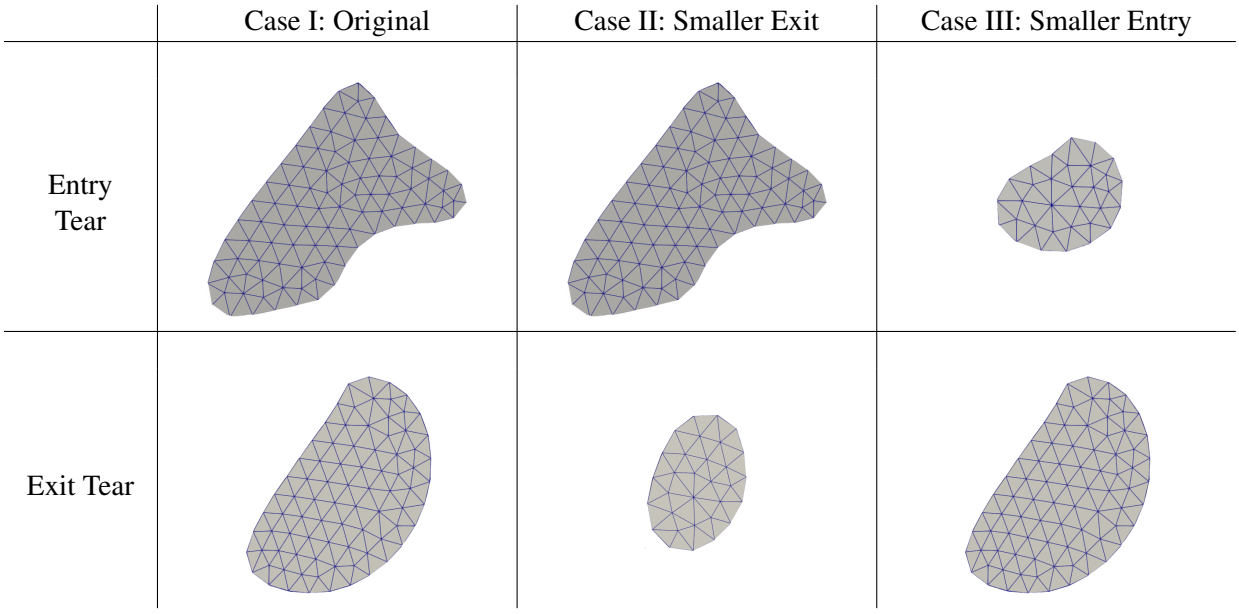


Figure 10 The 2D entry and exit tear areas for all three cases

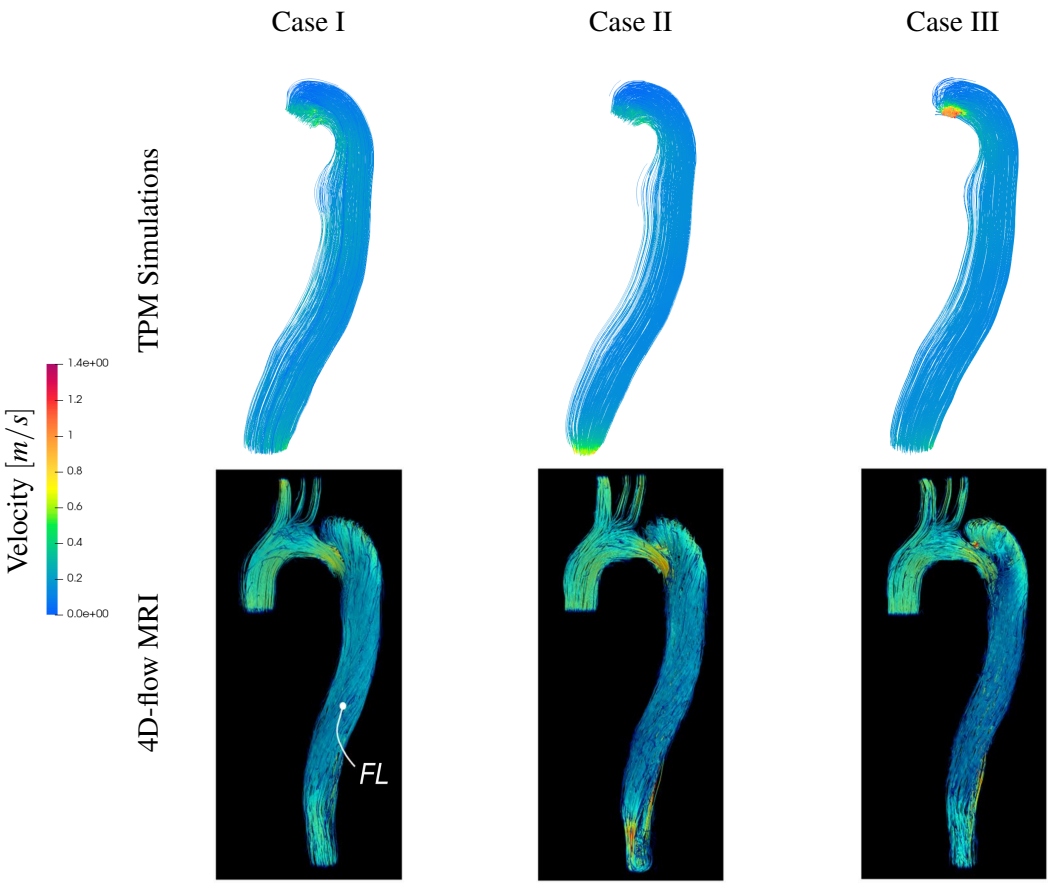


Figure 11 Comparison of velocity profiles: The top row displays the seepage velocity acquired from simulations employing the developed triphasic model. The bottom row shows the velocity obtained from the 4D-flow MRI with FL representing the false lumen (Adapted from [55] and used under CC BY 4.0)

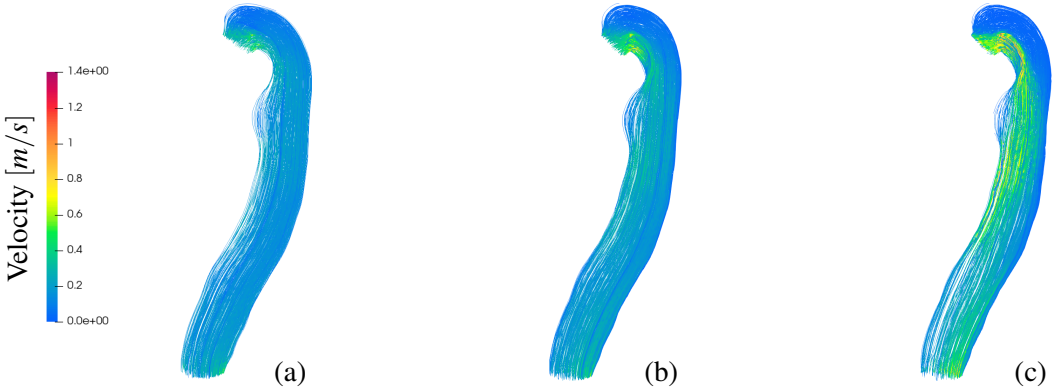


Figure 12 Evolution of seepage velocity at time $t =$ (a) 0 hours, (b) 42 hours, and (c) 84 hours

in chronic conditions could facilitate effective disease progression control and improve patient outcomes.

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Statements and Declarations

- Competing interests: The authors have no relevant financial or non-financial interests to disclose.
- Data availability: The MSH files for the three false lumen geometries used in this research are available in the repository of Graz University of Technology [20].

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