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Supplementary: Mapping Computational Thrombosis Modelling to Shear Regimes: An Application to Post-Stenotic Platelet Aggregation

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Text S1: supplementary methods and derivations.

1. Present Formulation Limitation

The present model distinguishes three platelet populations: free-flowing platelets c_f, rolling/translocating platelets c_r, and stabilised platelets c_s. Free platelets are captured at either the thrombogenic substrate or the surface of an existing aggregate, enter the rolling population, and subsequently become permanently incorporated. Only stable incorporation produces aggregate growth through the level-set update.

$$c_f \overset{J_w, R_b}{\rightarrow} c_r \overset{J_S}{\rightarrow} c_s. \tag{S1}$$

Here, J_w is the thrombogenic-wall capture flux and R_b is the diffuse-interface capture term at the clot–lumen surface. The rolling-layer saturation factor

$$\phi_{\text{sat}}(c_r) = \left(1 - \frac{c_r}{c_{\max}}\right)_+ \tag{S2}$$

limits temporary local crowding of rolling platelets. It does not quantify residual coating, ligand occupancy, or the probability that a rolling platelet becomes stably incorporated. The existing rolling-to-stable conversion rate is

$$k_{\text{adh}}^{\text{Col}}(\dot{\gamma}) = a_{\text{low}}(1 - \chi) + a_{\text{high}}\chi, \tag{S3}$$

where χ is the existing shear-dependent switching function. The coefficients a_{low} and a_{high} were fitted using collagen-coated experiments. They therefore represent effective stabilisation on a collagen-competent surface, including collagen-dependent platelet activation and the platelet–platelet growth enabled after firm arrest; they are not substrate-independent platelet constants.

2. Effect of Wall Chemistry on Initial Platelet Capture

The thrombogenic wall adhesion rate k_w controls the transition from free platelets to rolling platelets at the thrombogenic wall. Its influence on the observed deposition rate depends on the relative rates of intrinsic surface capture and hydrodynamic platelet delivery to the wall. For a reactive patch of streamwise length L subject to an approximately linear near-wall velocity profile,

$$u(y) \approx \dot{\gamma}_w y, \tag{S4}$$

the Lévêque scaling [1] gives the characteristic delivery velocity

$$k_m = C_{\mathrm{Lev}} \left(\frac{D^2 \dot{\gamma}_w}{L} \right)^{1/3}, \tag{S5}$$

where D is the effective platelet diffusivity, $\dot{\gamma}_w$ is wall shear rate, and C_{Lev} is an order-one coefficient. This is the standard high-Péclet-number scaling for delivery to a reactive wall in shear flow [2]. The capture Damköhler number is

$$\mathrm{Da}_w = \frac{k_w}{k_m}. \tag{S6}$$

When $\mathrm{Da}_w \ll 1$, surface capture is reaction-limited and changes in k_w strongly affect platelet capture. When $\mathrm{Da}_w \gg 1$, the surface captures platelets rapidly once they arrive, and the observable flux is predominantly limited by platelet delivery (see our earlier study [3]). For the present high-shear configuration, the model uses

$$D = 2 \times 10^{-11}\ \mathrm{m^2\ s^{-1}}, k_w = 10^{-3}\ \mathrm{m\ s^{-1}}. \tag{S7}$$

With $L = 50\text{–}500\mu\,\mathrm{m}$ and $\dot{\gamma}_w = 2000\text{–}8000\ \mathrm{s^{-1}}$, Equation (S5) gives a delivery velocity of order $10^{-5}\ \mathrm{m\ s^{-1}}$, and hence Da_w is of order $30\text{–}100$. Initial capture is therefore expected to be predominantly delivery-limited in this geometry. Aggregate growth is consequently more sensitive to the resolved flow field, near-wall platelet supply, effective platelet dispersion and margination, rolling-platelet residence time, and rolling-to-stable conversion than to the precise value of k_w [4], [5]. This conclusion does not mean that surface capture is universally irrelevant. For a ligand-specific or biomaterial wall, define the local reactive velocity as

$$k_{\mathrm{rxn},\ell} = k_{w,\ell} \eta_\ell(\dot{\gamma}_w)(1 - \theta_\ell), \tag{S8}$$

where $k_{w,\ell}$ is the intrinsic surface-capture velocity, η_ℓ is the ligand-specific shear response, and θ_ℓ is the fraction of surface rendered effectively inaccessible by persistent platelet coverage [6]. The corresponding local Damköhler number is

$$\mathrm{Da}_{w,\ell} = \frac{k_{\mathrm{rxn},\ell}}{k_m}. \tag{S9}$$

3. Extension of the Current Formulation for rh-VWF-Coated Surfaces

Collagen: After GPIb α tethers the platelet to collagen-bound VWF, GPVI engages collagen and signals through FcRγ (ITAM) to PLCγ2 [7]. The resulting rise in Ca^{2+} and PKC activity secretes ADP and TXA_2 and converts $\alpha\mathrm{IIb}\beta3$ and $\alpha2\beta1$ to their high-affinity forms (inside-out) [8]. Ligand occupancy then triggers outside-in signalling, which spreads the platelet and stabilises the contact [9]. Arrest is therefore rapid. GPVI is the dominant activating collagen receptor; without it, rolling persists and firm adhesion is lost or limited to a residual monolayer [10]. **Recombinant VWF:** GPIbα–A1 still captures efficiently. GPIb can signal, but only weakly and slowly, and isolated A1 or rh-VWF provides no GPVI ligand [11]. Under anticoagulation thrombin is absent, and autocrine ADP and TXA_2 remain low because secretion is poor [12]. Inside-out activation of $\alpha\mathrm{IIb}\beta3$ is therefore infrequent, outside-in signalling does not develop, and the platelet typically continues to translocate and detaches [11].

The two surfaces share tethering and differ in arrest. That asymmetry is the biological content of the coating comparison [13]. In this study k_{adh} is identified on collagen, which supplies the strong inside-out and subsequent outside-in signal for αIIbβ3, and is not transferable to rh-VWF. Functional blockade of αIIbβ3 on collagen preserves a single-platelet monolayer while abolishing thrombus buildup [14]. Primary capture (GPIb/GPVI/α2β1) remains intact; what is lost is recruitment of incoming platelets onto the first layer.

Because initial platelet tethering to immobilised rh-VWF is mediated by the same high-shear GPIbα–VWF interaction represented in the current capture and rolling formulation, those components are retained unchanged. However, the subsequent conversion of rolling platelets into stably incorporated platelets is expected to be less efficient on an rh-VWF-only surface than on the collagen-coated surfaces used to calibrate the original model. We therefore introduce a single dimensionless stabilisation-efficiency factor, indexed by wall chemistry. The stable-incorporation flux is:

$$J_{\mathrm{s},\ell} = f_{\ell} k_{\mathrm{adh}}^{\mathrm{Col}}(\dot{\gamma}) c_r. \tag{S10}$$

For the original collagen-calibrated model,

$$f_{\mathrm{Col}} = 1. \tag{S11}$$

For an immobilised rh-VWF coating,

$$0 < f_{\mathrm{rhVWF}} < 1. \tag{S12}$$

Thus,

$$J_{\mathrm{s,rhVWF}} = f_{\mathrm{rhVWF}} \left[a_{\mathrm{low}} (1-\chi) + a_{\mathrm{high}} \chi\right] c_r. \tag{S13}$$

The factor f_{rhVWF} represents the reduced probability that a platelet already tethered and rolling through GPIbα–VWF interaction becomes permanently incorporated on an rh-VWF-only coating, relative to a collagen surface. It does not represent a change in platelet delivery, wall coverage, rolling velocity, VWF density, or aggregate-surface capture. The corresponding modified platelet balances are

$$\frac{\partial c_r}{\partial t} + \nabla \cdot (\mathbf{u}_r c_r) = \nabla \cdot (D \nabla c_r) + R_b - J_{\mathrm{s},\ell}, \tag{S14}$$

$$\frac{\partial c_s}{\partial t} = J_{\mathrm{s},\ell}. \tag{S15}$$

All other components of the existing model remain unchanged in this extension, including the wall-capture flux J_w, aggregate-interface capture R_b, aggregate-capture coefficient β_0, rolling velocity $\mathbf{u}_r$, tether-layer thickness l_t, and high-shear growth cap.

Table S1. Parameters of the proposed extension model.

Quantity	Acts on	Interpretation
f_{rhVWF}	$c_r \rightarrow c_s$	Probability of firm arrest after VWF-mediated rolling
θ_{rhVWF}	$c_f \rightarrow c_r$	Progressive loss of productive first-tether access to the rh-VWF wall
Γ_{rhVWF}	Evolution of $\theta_{\mathrm{rh\,VWF}}$	Effective platelet coverage required to mask the wall

A weakly adhesive ligand, receptor blockade, a low-reactivity biomaterial, or progressive wall coverage can reduce $k_{\mathrm{rxn},\ell}$ until $\mathrm{Da}_{w,\ell}$ approaches unity. In that regime, surface chemistry becomes rate-limiting and the capture coefficient must be calibrated on the relevant coating rather than inherited from a transport-limited collagen fit. Accordingly, the rh-VWF extension retains the existing VWF-mediated capture description in the first instance and applies surface specificity primarily through f_{rhVWF}. An additional wall-accessibility state is required only if experiments demonstrate that the rate of new platelet tethering decreases as stable platelet coverage develops on the rh-VWF coating. Let

$$\theta_{\mathrm{rhVWF}} \in [0,1] \tag{S16}$$

denote the fraction of the original rh-VWF surface effectively masked by persistent platelets. The wall flux is then

$$J_{w,\,\mathrm{rhVWF}} = k_w H(\dot{\gamma}_w - \dot{\gamma}_{\mathrm{th}}) c_f \phi_{\mathrm{sat}}(c_r)(1 - \theta_{\mathrm{rhVWF}}), \tag{S17}$$

with

$$\frac{\partial \theta_{\mathrm{rhVWF}}}{\partial t} = \frac{J_{\mathrm{lock,rhVWF}}}{\Gamma_{\mathrm{rhVWF}}}(1 - \theta_{\mathrm{rhVWF}}). \tag{S18}$$

The parameter Γ_{rhVWF} is an effective stable-platelet coverage capacity. The state θ_{rhVWF} represents platelet spreading and steric masking of productive access to the original coating; it does not represent chemical consumption of rh-VWF. The accessibility layer should be activated only when the arrest correction alone cannot reproduce a measured late plateau, or when separate experiments show a reduction in first tethering events as wall coverage increases.

4. **Calibration and Scope**

For the rh-VWF experiment, calibration should proceed as follows:

1. Retain the existing flow solver, platelet transport parameters, rolling-velocity reduction, tether-layer thickness, β_0, and high-shear growth cap.
2. Retain the existing wall-capture function unless early-time rh-VWF tethering data are available.
3. Fit f_{rhVWF} to the early stable aggregate-growth phase.
4. Validate the fitted value against late-time aggregate growth and morphology across the expansion geometries.
5. Add θ_{rhVWF} and fit Γ_{rhVWF} only if the reduced arrest efficiency does not capture the measured plateau.

For simulations of platelet deposition on rh-VWF-coated surfaces, the proposed extension is deliberately restricted to the rolling-to-stable platelet transition. The hydrodynamic solver, platelet-transport formulation, rolling kinematics, tether-layer thickness, aggregate-interface capture mechanism, and high-shear growth constraint are retained without modification. In the absence of independent measurements resolving the early rh-VWF-mediated tethering response, the original wall-capture formulation is likewise preserved. The rh-VWF-specific stabilisation efficiency is estimated from the early phase of stable aggregate development and subsequently evaluated against late-time aggregate growth and morphological evolution across the expansion geometries. An additional wall-accessibility mechanism is introduced only if this minimal, mechanistically targeted modification cannot account for a reproducible late-time deposition plateau, or if experimental observations demonstrate that accumulation of a stable first platelet monolayer progressively

occludes the underlying rh-VWF coating, thereby reducing productive access to the coating and suppressing subsequent platelet tethering.

5. Numerical Setting

In the present study, time integration was performed using an implicit BDF method of order 1–2 with adaptive time-step control. The initial time step was 0.2 s, with an automatically controlled maximum time step, and the global scaled absolute tolerance was set to 0.01. A segregated solution strategy was used, with up to 10 iterations per time step among the level-set, flow, and platelet-transport subproblems. Solution-based convergence was assessed using a tolerance factor of 0.1.

6. Cartesian components

For clarity, the incompressible Navier–Stokes–Brinkman formulation of Equation (1) is written below in Cartesian component form. Let the velocity field be $\mathbf{u} = (u, v, w)$, where u, v, and w are the velocity components in the spanwise (x), streamwise (y), and wall-normal (z) directions, respectively.

The incompressibility condition is

$$\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} = 0 \tag{S19}$$

The momentum balance in the x-direction is

$$\rho\left(\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x} + v\frac{\partial u}{\partial y} + w\frac{\partial u}{\partial z}\right) = -\frac{\partial p}{\partial x} + \frac{\partial \tau_{xx}}{\partial x} + \frac{\partial \tau_{xy}}{\partial y} + \frac{\partial \tau_{xz}}{\partial z} - \mu K^{-1} u. \tag{S20}$$

The momentum balance in the y-direction is

$$\rho\left(\frac{\partial v}{\partial t} + u\frac{\partial v}{\partial x} + v\frac{\partial v}{\partial y} + w\frac{\partial v}{\partial z}\right) = -\frac{\partial p}{\partial y} + \frac{\partial \tau_{yx}}{\partial x} + \frac{\partial \tau_{yy}}{\partial y} + \frac{\partial \tau_{yz}}{\partial z} - \mu K^{-1} v. \tag{S21}$$

The momentum balance in the z-direction is

$$\rho\left(\frac{\partial w}{\partial t} + u\frac{\partial w}{\partial x} + v\frac{\partial w}{\partial y} + w\frac{\partial w}{\partial z}\right) = -\frac{\partial p}{\partial z} + \frac{\partial \tau_{zx}}{\partial x} + \frac{\partial \tau_{zy}}{\partial y} + \frac{\partial \tau_{zz}}{\partial z} - \mu K^{-1} w. \tag{S22}$$

Here, p is pressure, ρ is blood density, and $\mu K^{-1}\mathbf{u}$ is the Brinkman resistance exerted by the porous platelet aggregate. In the lumen, $K^{-1} = 0$; within the aggregate, $K^{-1} = K_{\text{clot}}^{-1}$.

For the incompressible Newtonian fluid assumed in this study, the extra-stress tensor is

$$\boldsymbol{\tau} = 2\mu\mathbf{D} = \mu(\nabla\mathbf{u} + \nabla\mathbf{u}^T), \qquad \mathbf{D} = \frac{1}{2}(\nabla\mathbf{u} + \nabla\mathbf{u}^T), \tag{S23}$$

where μ is the constant dynamic viscosity and $\mathbf{D}$ is the rate-of-deformation tensor. The normal stress components are

$$\tau_{xx} = 2\mu\frac{\partial u}{\partial x}, \tau_{yy} = 2\mu\frac{\partial v}{\partial y}, \tau_{zz} = 2\mu\frac{\partial w}{\partial z}, \quad (S24)$$

and the shear stress components are

$$\tau_{xy} = \tau_{yx} = \mu\left(\frac{\partial u}{\partial y} + \frac{\partial v}{\partial x}\right) \quad (S25)$$

$$\tau_{xz} = \tau_{zx} = \mu\left(\frac{\partial u}{\partial z} + \frac{\partial w}{\partial x}\right) \quad (S26)$$

$$\tau_{yz} = \tau_{zy} = \mu\left(\frac{\partial v}{\partial z} + \frac{\partial w}{\partial y}\right) \quad (S27)$$

The scalar shear-rate magnitude used in the shear-regulated platelet kinetics is calculated from the second invariant of the rate-of-deformation tensor:

$$\dot{\gamma} = \sqrt{2\mathbf{D}:\mathbf{D}}. \quad (S28)$$

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