Mathematical Biosciences and Engineering

MBE, 21(12): 7707–7739.
DOI: 10.3934/mbe.2024339
Received: 04 September 2024
Revised: 07 November 2024
Accepted: 20 November 2024
Published: 04 December 2024

https://www.aimspress.com/journal/MBE

Review

Integrating biomarkers for hemostatic disorders into computational models of blood clot formation: A systematic review

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Supplementary

1. Supplementary material (SM) file organization

We have created this supplementary file to organize the mathematical equations of the computational models analyzed in our systematic review.

In the “S2: Searching terms” section, we present the search terms used in various search engines (PubMed, Embase, The Cochrane Library, Scopus). It is important to note that each engine has its own conventions for using logical operators like “OR” and “AND”.

The “S3: Abbreviations” section includes a table containing the abbreviations used throughout the manuscript and this supplementary file, along with their meanings.

The "S4: Variables description" section presents a table containing the variables that appeared throughout the mathematical expressions of the computational models. This table presents the symbol, meaning of the variable, the unit of measurement, and values range, when applicable. Notably, in some studies analyzed, variables emerged that did not provide a sufficient description of their meaning. In these cases, such variables were not included in this table. We recommend that if the variable is not found in this table, readers look for its meaning in the original reference.

Sections "S5" through "S9" contain tables presenting mathematical equations for various components of interest, such as Antithrombin III, blood factor VIII, PC, fibrin(ogen), and vWF. Each table includes the reference, mathematical expression, kinetic parameter values, a brief description of the model used (if applicable), and original references.

2. Searching terms

2.1. PUBMED

("mathematical model" OR "mathematical model"[MeSH Terms] OR "mathematical modeling" OR "mathematical modeling"[MeSH Terms] OR "computational modeling" OR "computational modeling"[MeSH Terms] OR "computational simulation" OR "computational simulation"[MeSH Terms] OR "computer simulation" OR "computer simulation"[MeSH Terms] OR "model simulation" OR "model simulation"[MeSH Terms]) AND ("blood clot" OR "blood clot"[MeSH Terms] OR "thrombus" OR " thrombus"[MeSH Terms] OR "blood coagulation" OR "blood coagulation"[MeSH Terms] OR "blood plug" OR " blood plug"[MeSH Terms]) AND ("d-dimer" OR " d-dimer"[MeSH Terms] OR "fibrinogen" OR "fibrinogen"[MeSH Terms] OR "von willebrand factor" OR "von willebrand factor"[MeSH Terms] OR "factor VIII" OR "factor VIII"[MeSH Terms] OR "p-selectin" OR "p-selectin"[MeSH Terms] OR "prothrombin time" OR "prothrombin time"[MeSH Terms] OR "activated partial thromboplastin time" OR "activated partial thromboplastin time"[MeSH Terms] OR "antithrombin" OR "antithrombin "[MeSH Terms] OR "protein C" OR " protein C"[MeSH Terms] OR "protein S" OR "protein S"[MeSH Terms])

2.2. EMBASE

('mathematical model'/exp OR 'mathematical model' OR 'mathematical modeling'/exp OR 'mathematical modeling' OR 'computational modeling'/exp OR 'computational modeling' OR 'computational simulation'/exp OR 'computational simulation' OR 'computer simulation'/exp OR 'computer simulation' OR 'model simulation') AND ('blood clot'/exp OR 'blood clot' OR 'thrombus'/exp OR 'thrombus' OR 'blood coagulation'/exp OR 'blood coagulation' OR 'blood plug') AND ('d-dimer'/exp OR 'd-dimer' OR 'fibrinogen'/exp OR 'fibrinogen' OR 'von willebrand factor'/exp OR 'von willebrand factor' OR 'factor viii'/exp OR 'factor viii' OR 'p-selectin'/exp OR 'p-selectin' OR 'prothrombin time'/exp OR 'prothrombin time' OR 'activated partial thromboplastin time'/exp OR 'activated partial thromboplastin time' OR 'antithrombin'/exp OR 'antithrombin' OR 'protein c'/exp OR 'protein c' OR 'protein s'/exp OR 'protein s')

2.3. The cochrane library

(‘mathematical model’ OR ‘mathematical modeling’ OR ‘computational modeling’ OR ‘computational simulation’ OR ‘computer simulation’ OR ‘model simulation’) AND (‘blood clot’ OR ‘thrombus’ OR ‘blood coagulation’ OR ‘blood plug’) AND (‘d-dimer’ OR ‘fibrinogen’ OR ‘von willebrand factor’ OR ‘factor viii’ OR ‘p-selectin’ OR ‘prothrombin time’ OR ‘activated partial thromboplastin time’ OR ‘antithrombin’ OR ‘protein c’ OR ‘protein s’)

2.4. SCOPUS

ALL ((“Mathematical model” OR “Mathematical modeling” OR “Computational modeling” OR “computational simulation” OR “Computer Simulation” OR “model simulation”) AND (“Blood clot” OR “Thrombus” OR “Blood Coagulation” OR “blood plug”) AND (“d-dimer” OR “fibrinogen” OR “vol willebrand factor” OR “factor VIII” OR “p-selectin” OR “prothrombin time” OR “activated partial thromboplastin time” OR “antithrombin” OR “protein C” OR “protein S”)) AND (LIMIT-TO (DOCTYPE , “ar”) OR LIMIT-TO (DOCTYPE , “re”))

3. Abbreviations

Table S1. Abbreviation list.

Abbreviations	Meaning
PC	Protein C
PCA	Activated protein C
ATIII	Antithrombin III
Ba	A sum of factors IXa and Xa
Fg	Fibrinogen
Fn	Fibrin
H	Heparin
H’	Surface-bound heparin with a length of 5 saccharides
H”	Surface-bound heparin with a length of 26 saccharides
H”’	Surface-bound heparin with a length of 70 saccharides
HC	Heparin cofactor
mIIa	Intermediate meizothrombin
PLS	plasmin
TF	Tissue factor
TFPI	Tissue factor pathway inhibitor
TM	thrombomodulin
W	Prothrombinase
II	Blood factor II
IIa	Blood factor IIa

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Abbreviations	Meaning
V	Blood factor V
Va	Blood factor Va
VII	Blood factor VII
VIIa	Blood factor VIIa
VIII	Blood factor VIII
IX	Blood factor IX
IXa	Blood factor IXa
Xa	Blood factor Xa
XIa	Blood factor XIa
XIIa	Blood factor XIIa
α_1AT	Alpha-1 antitrypsin

Table S2. Abbreviations and studies frequency of the ten biomarkers.

Biomarker	Abbreviation	Frequency
D-dimer	–	1
Fibrin(ogen)	–	30
Von Willebrand Factor	vWF	9
P-selectin	–	1
Prothrombin time	PT	1
Activated partial thromboplastin time	APTT	1
Antithrombin III	ATIII	32
Protein C	PC	19
Protein S	PS	0
Blood factor VIII	FVIII	22

4. Variables description

Table S3. List of variables, description, the unit, and values range.

Variable	Description	Unit	Range
C_{APC}	Concentration of APC	M	N/A
C_{ATIII}	Concentration of ATIII	M	N/A
$C_{ATIII}(t=0)$	The initial concentration of ATIII	M	1.566×10^{-6} M [18] - 3.44×10^{-6} M [18]
$C_{ATIII,up}$	Concentration of ATIII upstream	M	N/A
C_{B_a}	The concentration of the sum of factors IXa and Xa	M	N/A
C_{F_n}	Concentration of fibrin	M	N/A
$C_{F_n}(t=0)$	The initial concentration of Fibrin	M	0 M [18,29]–3.5×10^{-7} M [18,29]

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Variable	Description	Unit	Range
$C_{F_{n,d}}$	Concentration of deposited fibrin	M	N/A
$C_{F_n\equiv II_a}$	Concentration of Fn≡IIa	M	N/A
C_{F_g}	Concentration of fibrinogen	M	N/A
$C_{F_g}(t=0)$	The initial concentration of fibrinogen	M	5.4×10^{-6} M [44]– 1.8×10^{-5} M [3]
$C_{F_{g,d}}$	Concentration of deposited fibrinogen	M	N/A
$C_{F_g}^{sat}$	Maximum local concentration of fibrin polymer due to saturation	M	N/A
$C_{F_g\equiv II_a}$	Concentration of Fg≡IIa	M	N/A
C_{F_p}	Concentration of fibrin polymer	M	N/A
C_H	Concentration of Heparin	M	N/A
$C_{H\equiv ATIII}$	Concentration of H≡ATIII	M	N/A
$C_{H'\equiv ATIII}$	The concentration of surface-bound heparin with a length of 5 saccharides	M	N/A
$C_{H''\equiv ATIIII}$	The concentration of surface-bound heparin with a length of 26 saccharides	M	N/A
$C_{H'''\equiv ATIII}$	The concentration of surface-bound heparin with a length of 70 saccharides	M	N/A
C_{HC}	Concentration of Heparin cofactor	M	N/A
$C_{HC\equiv ATIII}$	Concentration of HC≡ATIII	M	N/A
C_{mII_a}	Concentration of mIIa	M	N/A
C_{PC}	Concentration of PC	M	N/A
$C_{PC}(t=0)$	The initial concentration of PC	M	6.0×10^{-8} M [34]
C_{PCA}	Concentration of PCA	M	N/A
$C_{PCA}(t=0)$	Initial concentration of PCA	M	0 [29]– 1.59×10^{-10} M [29]
C_{TFPI}	Concentration of TFPI	M	N/A
$C_{TF\equiv VII_a}$	Concentration of the complex $TF\equiv VII_a$	M	N/A
$C_{TM\equiv II_{a,s}}$	Concentration of TM≡IIa,s	M	N/A
C_W	Concentration of prothrombinase	M	N/A
C_{II}	Concentration of II	M	N/A
C_{II_a}	Concentration of IIa	M	N/A
$C_{II_a^s}$	Concentration of II_a^s	M	N/A
$C_{II_a{}^F}$	Concentration of free factor IIa	M	N/A
$C_{II_a\equiv F_g}$	Concentration of IIa≡Fg	M	N/A
$C_{II_a\equiv F_n}$	Concentration of IIa≡Fn	M	N/A
C_V	Concentration of V	M	N/A
$C_{V\equiv II_a}$	Concentration of V≡IIa	M	N/A
C_{V_a}	Concentration of Va	M	N/A
C_{VII}	Concentration of VII	M	N/A

Continued on next page

Variable	Description	Unit	Range
$C_{VII\equiv X_a}$	Concentration of VII≡Xa	M	N/A
C_{VIII}	Concentration of VIII	M	N/A
$C_{VIII}(t=0)$	The initial concentration of VIII	M	1.0×10^{-10} M [42]– 7.0×10^{-10} M [56]
C_{VIII}^{up}	Concentration of VIII up-stream	M	N/A
C_{VIII^m}	The concentration of factor VIII on activated platelet	M	N/A
$C_{VIII_{a1L}}$	Concentration of $VIIIa_{1L}$	M	N/A
$C_{VIII_{a2}}$	Concentration of $VIIIa_2$	M	N/A
C_{VIII}^{mtot}	Concentration of platelet-bound factor VIII	M	N/A
C_{VIII_a}	Concentration of VIIIa	M	N/A
$C_{VIII_a}(t=0)$	The initial concentration of VIIIa	M	0 M [31]– 1.0×10^{-10} M [56]
$C_{VIII_a}^{up}$	Concentration of blood factor VIIIa up-stream	M	N/A
$C_{VIII_a}^{mtot}$	Concentration of platelet-bound factor VIIIa	M	N/A
$C_{VIII_a\equiv IX_a}$	Concentration of VIIIa≡IXa	M	N/A
$C_{VIII\equiv II_a}$	Concentration of VIII≡IIa	M	N/A
C_{IX}	Concentration of IX	M	N/A
$C_{IX\equiv XI_a}$	Concentration of IX≡XIa	M	N/A
C_{IX_a}	Concentration of IXa	M	N/A
$C_{IX_a^s}$	Concentration of IX_a^s	M	N/A
$C_{IX_a^{s*}}$	Concentration of IX_a^{s*}	M	N/A
C_{X_a}	Concentration of Xa	M	N/A
$C_{X_a^s}$	Concentration of X_a^s	M	N/A
$C_{X_a{}^F}$	Concentration of free factor Xa	M	N/A
$C_{X_a\equiv V_a{}^B}$	Concentration of $X_a\equiv V_a$ bond with platelet	M	N/A
$C_{X_a\equiv V_a{}^e}$	Concentration of prothrombinase complex, assembled on the exogenous phospholipids	M	N/A
$C_{X_a\equiv V_a{}^v}$	Concentration of prothrombinase complex, assembled on the endogenous lipids	M	N/A
$C_{XI\equiv XI_a}$	Concentration of XI≡XIa	M	N/A
C_{XI_a}	Concentration of XIa	M	N/A
$C_{XI_a^h}$	Concentration of XI_a^h	M	N/A
$C_{XI_a^{s*}}$	Concentration of XI_a^{s*}	M	N/A
$C_{XI_a{}^F}$	Concentration of free factor XIa	M	N/A
$C_{XI_a\equiv ATIII}$	Concentration of XIaXI_a ≡ATIII	M	N/A
C_{XII_a}	Concentration of XIIa	M	N/A
D_{ATIII}	Diffusion coefficient of ATIII	$m^2.s^{-1}$	3.49×10^{-11} $m^2.s^{-1}$ [6,36–40]– 6.68×10^{-1} $m^2.s^{-1}$ [6,36–40]

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Variable	Description	Unit	Range
D_{F_n}	Diffusion coefficient of fibrin	$m^2.s^{-1}$	0 $m^2.s^{-1}$ [50]– 2.47×10^{-11} $m^2.s^{-1}$ [14,24]
D_{F_g}	Diffusion coefficient of fibrinogen	$m^2.s^{-1}$	2.0×10^{-11} $m^2.s^{-1}$ [50]– 3.1×10^{-11} $m^2.s^{-1}$ [14,24]
D_{PC}	Diffusion coefficient of PC	$m^2.s^{-1}$	5.0×10^{-11} $m^2.s^{-1}$ [34]– 5.44×10^{-11} $m^2.s^{-1}$ [14]
D_{PCA}	Diffusion coefficient of PCA	$m^2.s^{-1}$	5.0×10^{-11} $m^2.s^{-1}$ [34]– 5.5×10^{-11} $m^2.s^{-1}$ [14]
D_{VIII}	Diffusion coefficient of VIII	$m^2.s^{-1}$	4.67×10^{-11} $m^2.s^{-1}$ [12]– 4.4×10^{-12} M [31]
D_{VIII_a}	Diffusion coefficient of VIIIa	$m^2.s^{-1}$	3.5×10^{-11} $m^2.s^{-1}$ [31]– 6.167×10^{-11} $m^2.s^{-1}$ [27]
f_{emb}	Platelet embolization rate	N/A	N/A
N_{VIII}^{b}	Surface binding sites for VIII on bounded platelet	N/A	450 [42]
N_{VIII}^{se}	Surace binding sites for VIII on endothelium-bounded platelet	N/A	450 [42]
p_{VIII}	The volume concentration of binding sites for factor VIII	M	N/A
p_{VIII}^{avail}	Available factor VIII binding sites	N/A	N/A
$P^{b,a}$	Bounded platelet	PLT/mm^3	N/A
$P^{se,a}$	subendothelial bounded platelet	PLT/mm^3	N/A
S_{ATIII}	Reaction source term of ATIII	$M.s^{-1}$	N/A
S_{F_n}	Reaction source term of Fn	$M.s^{-1}$	N/A
S_{F_g}	Reaction source term of Fg	$M.s^{-1}$	N/A
S_{PC}	Reaction source term of PC	$M.s^{-1}$	N/A
S_{PCA}	Reaction source term of PCA	$M.s^{-1}$	N/A
S_{II_a}	Reaction source term of IIa	$M.s^{-1}$	N/A
S_{VIII}	Reaction source term of VIII	$M.s^{-1}$	N/A
S_{VIII_a}	Reaction source term of VIIIa	$M.s^{-1}$	N/A
S_{IX_a}	Reaction source term IXa	$M.s^{-1}$	N/A
S_{X_a}	Reaction source term Xa	$M.s^{-1}$	N/A
S_{XI_a}	Reaction source term XIa	$M.s^{-1}$	N/A
K_{ATIII}	Second-order kinetic constant associated with ATIII, Fn and Fg	$M^{-1}.s^{-1}$	1.0×10^4 $M^{-1}.s^{-1}$ [35]
K_{AT}	The dissociation rate constant of heparin/ATIII of Griffith's template model	M	1.0×10^5 M [6,36–40]
K_T	The dissociation rate constant of heparin/thrombin of Griffith's template model	M	3.5×10^4 M [6,36–40]
$k_{1,T}$	The first-order rate constant of Griffith's template model	s^{-1}	13.333 s^{-1} [6,36–40]
$k_{B_a/ATIII}^{++}$	The second-order inhibition rate constant of Ba by ATIII	$M^{-1}.s^{-1}$	2.223 $M^{-1}.s^{-1}$ [9,10]

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Variable	Description	Unit	Range
k_{flow}	A constant for convection-diffusion transport	s^{-1}	N/A
$k^{+}_{F_g/II_a}$	First-order rate constant of conversion of fibrinogen into fibrin by IIa	s^{-1}	1.383×10^{-4} s^{-1} [27]
$k^{++}_{F_g/II_a}$	The second-order rate constant of conversion of fibrinogen into fibrin by IIa	$M^{-1}.s^{-1}$	4.0×10^{7} $M^{-1}.s^{-1}$ [35]
$-k^{++}_{F_g/II_a m}$	The second-order rate constant of conversion of fibrinogen into fibrin by IIa bound to platelet	$M^{-1}.s^{-1}$	1.16×10^{7} $M^{-1}.s^{-1}$ [44]
$k^{+}_{F_g\equiv II_a}$	The first-order rate constant of deactivation of Fg	s^{-1}	200 s^{-1} [35]
$k^{++}_{F_g\equiv II_a/ATIII}$	The second-order rate constant of the formation of Fg≡IIa≡ATIII	$M^{-1}.s^{-1}$	1.0×10^{4} $M^{-1}.s^{-1}$ [35]
$k_{F_{g,d}}$	Constant rate of fibrinogen deposition	s^{-1}	N/A
$k_{F_{n,d}}$	Constant rate of fibrin deposition	s^{-1}	N/A
$k^{cat}_{F_g/II_a}$	The michaelis-menten catalytic rate constant of conversion of fibrinogen into fibrin by IIa	s^{-1}	59 s^{-1} [9,10] - 84 s^{-1} [50]
$k^{m}_{F_g/II_a}$	The michaelis-menten rate constant of conversion of fibrinogen into fibrin by IIa	M	3.16×10^{-6} M [9,10] - 7.2×10^{-6} M [56]
$k^{cat}_{F_g/PLA}$	The michaelis-menten catalytic rate constant of fibrin breakdown	s^{-1}	25 s^{-1} [14,17–21,24,29]
$k^{m}_{F_g/PLA}$	The michaelis-menten rate constant of fibrin breakdown	M	2.5×10^{-4} M [14,17–21,24,29]
$k^{+}_{F_p/F_n}$	First-order rate constant of fibrin polymerization	s^{-1}	0.1 s^{-1} [9,10]– 1.833×10^{-3} s^{-1} [27]
$k^{++}_{F_n/II_a}$	Second-order rate constant of fibrin polymerization	$M^{-1}.s^{-1}$	2.0×10^{7} $M^{-1}.s^{-1}$ [35]
$k^{+}_{F_n\equiv II_a}$	The first-order rate constant of deactivation of Fn	s^{-1}	200 s^{-1} [35]
$k^{++}_{F_n\equiv II_a/ATIII}$	The second-order rate constant of formation of Fn≡IIa≡ATIII	$M^{-1}.s^{-1}$	1.0×10^{4} $M^{-1}.s^{-1}$ [35]
$k^{++}_{H/ATIII}$	Second-order on-rate of Heparin and ATIII	$M^{-1}.s^{-1}$	1 $M^{-1}.s^{-1}$ [49] – 1.0×10^{8} $M^{-1}s^{-1}$ [34]
$k^{+}_{H\equiv ATIII}$	First-order off-rate of H≡ATIII	s^{-1}	2.77×10^{7} s^{-1} [49]
$k^{+}_{H'\equiv ATIII/ATIII}$	First-order off-rate of ATIII and surface-bound heparin with a length of 5 saccharides	s^{-1}	2.3 s^{-1} [34]
$k^{+}_{H''\equiv ATIII/ATIII}$	First-order off-rate of ATIII and surface-bound heparin with a length of 26 saccharides	s^{-1}	0.5 s^{-1} [34]
$k^{+}_{H'''\equiv ATIII/ATIII}$	First-order off-rate of ATIII and surface-bound heparin with a length of 70 saccharides	s^{-1}	0.5 s^{-1} [34]
$k^{++}_{HC/ATIII}$	The second-order on-rate constant of HC and ATIII	$M^{-1}.s^{-1}$	3.0×10^{4} $M^{-1}.s^{-1}$ [35]
$k^{+}_{HC\equiv ATIII/ATIII}$	The first-order dissociation rate constant of $HC\equiv ATIII$	s^{-1}	1.3 s^{-1} [35]
k_{p}	Empirical constant for fibrin polymerization	$M.s^{-1}$	8.2×10^{-1} [56]
k^{+}_{PC}	The first-order rate constant of consumption of PC	s^{-1}	0.05 s^{-1} [1]
k^{+}_{PCA}	First-order rate constant of consumption of PCA	s^{-1}	0.05 s^{-1} [1]
$k^{cat}_{PC/TM\equiv II_{a,s}}$	Michaelis-Menten kinetic constant of activation of PC by the TM≡IIa,s complex	s^{-1}	5.58 s^{-1} [34]

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Variable	Description	Unit	Range
$k^{m}_{PC/TM\equiv II_{a,s}}$	Michaelis-Menten kinetic constant of activation of PC by the TM≡IIa,s complex	M	7×10^{-7} M [34]
k^{cat}_{PC/II_a}	The Michaelis-Menten catalytic rate constant of activation of PC by IIa	s^{-1}	0.65 s^{-1} [14]
k^{m}_{PC/II_a}	The Michaelis-Menten kinetic constant of activation of PC by IIa	M	3.19×10^{-6} M [14]
$k^{++}_{PCA/W}$	The second-order rate constant for the activation of PC by W.	$M^{-1}.s^{-1}$	3.67×10^{4} $M^{-1}.s^{-1}$ [29]
$k^{++}_{PCA/\alpha_1 AT}$	The second-order rate constant of the activation of PCA by $\alpha_1 AT$	$M^{-1}.s^{-1}$	1.1×10^{1} $M^{-1}.s^{-1}$ [29]
$k^{++}_{PCA,V_a,m}$	The second-order rate constant of the formation of PCA≡$V_{a,m}$ complex	$M^{-1}.s^{-1}$	1.2×10^{8} $M^{-1}.s^{-1}$ [42]
$k^{+}_{PCA\equiv V_a,m}$	The first-order rate constant of the dissociation of PCA≡$V_{a,m}$ complex	s^{-1}	1.0 s^{-1} [42]
$k^{cat}_{PCA\equiv V_a,m}$	The rate constant of the reaction between PCA and $V_{a,m}$	s^{-1}	0.5 s^{-1} [42]
$k^{++}_{PCA,VIII_a,m}$	The second-order rate constant of the formation of PCA≡$VIII_{a,m}$ complex	$M^{-1}.s^{-1}$	1.2×10^{8} $M^{-1}.s^{-1}$ [42]
$k^{+}_{PCA\equiv VIII_a,m}$	The first-order rate constant of the dissociation of PCA≡$VIII_{a,m}$ complex	s^{-1}	1.0 s^{-1} [42]
$k^{cat}_{PCA\equiv VIII_a,m}$	The rate constant of the reaction between PCA and $VIII_{a,m}$	s^{-1}	0.5 s^{-1} [42]
$k^{++}_{W/ATIII}$	The second-order inhibition rate constant of W by ATIII	$M.s^{-1}$	1.67×10^{5} $M^{-1}.s^{-1}$ [18,29]
$k^{++}_{II_a/ATIII}$	The second-order inhibition rate constant of IIa by ATIII	$M^{-1}.s^{-1}$	4.816×10^{3} $M^{-1}.s^{-1}$ [24] - 1.19×10^{7} $M^{-1}.s^{-1}$ [17–22]
$k^{+}_{II_a/ATIII}$	The first-order inhibition rate constant of IIa by ATIII	s^{-1}	2.17×10^{-2} s^{-1} [14] - 0.2 s^{-1} [42–44]
$k^{++}_{II_a{}^F}$	The second-order inhibition rate constant of free factor IIa by ATIII	$M^{-1}.s^{-1}$	6.83×10^{3} $M^{-1}.s^{-1}$ [50]
$k^{++}_{II^s_a/ATIII}$	Second-order inhibition rate constant of IIa on platelet surface by ATIII	$M^{-1}.s^{-1}$	1.4×10^{4} $M^{-1}.s^{-1}$ [49]
$k^{++}_{VIII,m}$	Rate constant which plasma-phase factor VIII binds to the surface of an activated platelet	$M^{-1}.s^{-1}$	5.0×10^{7} $M^{-1}.s^{-1}$ [30]
$k^{++}_{VIII_a,m}$	Rate constant which plasma-phase factor VIIIa binds to the surface of an activated platelet	$M^{-1}.s^{-1}$	5.0×10^{7} $M^{-1}.s^{-1}$ [30]
$k^{+}_{VIII,m}$	The rate constant of dissociation of factor VIII from a platelet surface	s^{-1}	0.17 s^{-1} [30]
$k^{+}_{VIII_a,m}$	The rate constant of dissociation of factor VIIIa from a platelet surface	s^{-1}	0.17 s^{-1} [30]
k^{+}_{VIII/II_a}	First-order rate constant for the activation of factor VIII by factor IIa	s^{-1}	1.67×10^{-7} s^{-1} [27]
k^{++}_{VIII/II_a}	Second-order rate constant for the activation of factor VIII by factor IIa	$M^{-1}.s^{-1}$	2.0×10^{7} $M^{-1}.s^{-1}$ [56] - 2.64×10^{7} $M^{-1}.s^{-1}$ [47,49]
k^{++}_{VIII/mII_a}	The second-order rate constant for the activation of factor VIII by factor mIIa	$M^{-1}.s^{-1}$	2.0×10^{7} $M^{-1}.s^{-1}$ [64]

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Variable	Description	Unit	Range
$k^{+}_{VIII\equiv II_a}$	First-order dissociation constant of the complex VIII≡IIa	s^{-1}	1 s^{-1} [42]
$k^{cat}_{VIII\equiv II_a}$	The kinetic constant of the dissociation of the complex VIII≡IIa	s^{-1}	0.9 s^{-1} [42]
k^{cat}_{VIII/II_a}	The Michaelis-Menten catalytic rate constant for the activation of factor VIII by IIa	s^{-1}	0.9 s^{-1} [42] - 3.24 s^{-1} [14,17–21,24]
K^{m}_{VIII/II_a}	The Michaelis-Menten rate constant for the activation of factor VIII by IIa	M	1.47×10^{-7} M [50] - 1.12×10^{-4} M [14,17–21,24]
$k^{cat}_{VIII,APC}$	The Michaelis-Menten rate catalytic constant for the activation of factor VIII by APC	s^{-1}	0.17 s^{-1} [14,17–21,24]
$k^{m}_{VIII,APC}$	The Michaelis-Menten rate constant for the activation of factor VIII by APC	M	1.46×10^{-8} M [14,17–21,24]
k^{++}_{VIII/X_a}	Second-order rate constant for the activation of factor VIII by factor Xa	$M^{-1}.s^{-1}$	1.0×10^{7} $M^{-1}.s^{-1}$ [56] - 1.0×10^{8} $M^{-1}.s^{-1}$ [70]
$k^{+}_{VIII\equiv X_a}$	First-order dissociation rate of the complex VIII≡Xa	s^{-1}	2.1 s^{-1} [70]
$k^{+}_{VIII_a}$	First-order consumption rate constant of VIIIa	s^{-1}	3.7×10^{-3} s^{-1} [14,17–21,24] - 5.83×10^{-3} s^{-1} [35]
$k^{+}_{VIII_{a1L}}$	The first-order rate constant for the formation of $VIII_{a1L}$	s^{-1}	2.2×10^{-5} s^{-1} [31] - 6.0×10^{-3} s^{-1} [70]
$k^{++}_{VIII_{a1L}/VIII_{a2}}$	The second-order rate constant for VIIIa	$M^{-1}.s^{-1}$	2.2×10^{4} $M^{-1}.s^{-1}$ [30] - 6.0×10^{6} $M^{-1}.s^{-1}$ [31]
$k^{++}_{VIII_a/APC}$	Second-order rate constant of formation of VIIIa≡APC complex	$M^{-1}.s^{-1}$	1.2×10^{8} $M^{-1}.s^{-1}$ [47,49]
$k^{+}_{VIII_a\equiv APC}$	First-order rate constant of dissociation of VIIIa≡APC complex	s^{-1}	1.0 s^{-1} [47,49]
$k^{+}_{VIII_a/VIII_a}$	The first-order rate constant for the consumption of factor VIIIa	s^{-1}	5.17×10^{-3} s^{-1} [27]
$k^{++}_{VIII_a/IX_a}$	The second-order rate constant for the formation of complex VIIIa≡IXa	$M^{-1}.s^{-1}$	1.0×10^{7} $M^{-1}.s^{-1}$ [56] - 1.0×10^{8} $M^{-1}.s^{-1}$ [34]
$k^{+}_{VIII_a\equiv IX_a}$	First-order dissociation rate of the complex VIIIa≡IXa	s^{-1}	5.0×10^{-3} s^{-1} [31] - 0.01 s^{-1} [34]
$k^{++}_{IX_a/ATIII}$	The second-order inhibition rate constant of IXa by ATIII	$M^{-1}.s^{-1}$	1.36×10^{2} $M^{-1}.s^{-1}$ [50] - 2.7×10^{5} $M^{-1}.s^{-1}$ [17–22]
$k^{+}_{IX_a/ATIII}$	The first-order inhibition rate constant of IXa by ATIII	s^{-1}	3.33×10^{-3} s^{-1} [14] - 0.1 s^{-1} [47]
$k^{++}_{IX^s_a/ATIII}$	The second-order inhibition rate constant of IXa on platelet surface by ATIII	$M^{-1}.s^{-1}$	4.8×10^{2} $M^{-1}.s^{-1}$ [49]
$k^{++}_{IX^{s*}_a/ATIII}$	Second-order inhibition rate constant of IXa on platelet surface on specific binding sites by ATIII	$M^{-1}.s^{-1}$	4.8×10^{2} $M^{-1}.s^{-1}$ [49]

Continued on next page

Variable	Description	Unit	Range
$k^{++}_{X_a/ATIII}$	The second-order inhibition rate constant of Xa by ATIII	$M^{-1}.s^{-1}$	2.5×10^3 $M^{-1}.s^{-1}$ [35] - 5.783×10^6 $M^{-1}.s^{-1}$ [17–22]
$k^{+}_{X_a/ATIII}$	The first-order inhibition rate constant of Xa by ATIII	s^{-1}	1.17×10^{-2} s^{-1} [14] - 0.1 s^{-1} [42–44]
$k^{++}_{X_a{}^F}$	The second-order inhibition rate constant of free factor Xa by ATIII	$M^{-1}.s^{-1}$	2.5×10^3 $M^{-1}.s^{-1}$ [50]
$k^{++}_{X_a^s/ATIII}$	Second-order inhibition rate constant of Xa on platelet surface by ATIII	$M^{-1}.s^{-1}$	3.5×10^3 $M^{-1}.s^{-1}$ [49]
$k^{++}_{X_a\equiv V_a{}^B}$	The second-order inhibition rate constant of $X_a \equiv V_a$ bound to activated platelet by ATIII	$M^{-1}.s^{-1}$	3.67×10^2 $M^{-1}.s^{-1}$ [50]
$k^{++}_{X_a\equiv V_a{}^e/ATIII}$	The second-order inhibition rate constant of $X_a \equiv V_a{}^e$ by ATIII	$M^{-1}.s^{-1}$	1.4×10^2 $M^{-1}.s^{-1}$ [35]
$k^{++}_{X_a\equiv V_a{}^v/ATIII}$	The second-order inhibition rate constant of $X_a \equiv V_a{}^v$ by ATIII	$M^{-1}.s^{-1}$	1.4×10^2 $M^{-1}.s^{-1}$ [35]
$k^{++}_{XI_a/ATIII}$	The second-order inhibition rate constant of XIa by ATIII	$M^{-1}.s^{-1}$	8.0 $M^{-1}.s^{-1}$ [35] - 1.0×10^3 $M^{-1}.s^{-1}$ [24]
$k^{++}_{XI_a{}^F}$	Second-order inhibition rate constant of free factor XIa by ATIII	$M^{-1}.s^{-1}$	3.16×10^2 $M^{-1}.s^{-1}$ [50]
$k^{++}_{XI_a^{s*}/ATIII}$	Second-order inhibition rate constant of XIa on platelet surface on specific binding sites by ATIII	$M^{-1}.s^{-1}$	2.4×10^2 $M^{-1}.s^{-1}$ [49]
$k^{++}_{XI_a^h/ATIII}$	Second-order inhibition of XI_a^h by ATIII	$M^{-1}.s^{-1}$	2.4×10^2 $M^{-1}.s^{-1}$ [49]
$k^{++}_{XI_a\equiv ATIII/ATIII}$	Second-order inhibition rate constant of XIa≡ATIII by ATIII	$M^{-1}.s^{-1}$	2.4×10^2 $M^{-1}.s^{-1}$ [49]
$k^{++}_{XII_a/ATIII}$	The second-order inhibition rate constant of XIIa by ATIII	$M^{-1}.s^{-1}$	3.645×10^1 $M^{-1}.s^{-1}$ [24]
α	Factor to model a variation in the affinity of heparin for ATIII when it is bound to thrombin or for thrombin when it is bound to ATIII	N/A	1 [6,36–40]
α_5	Kinetic coefficient	s^{-1}	58.8 [93]
β	Reaction term coefficient	N/A	N/A
η_5	Effectiveness factor	N/A	0.05 [93]

5. Mathematical equations representing Antithrombin III

Table S4. List of Equations representing ATIII.

Reference	Mathematical expression	Values used	Brief description
[1–3]	$S_{ATIII} = -k^{++}_{II_a/ATIII}C_{ATIII}C_{II_a}$ **(S4.1)**	D_{ATIII} = 5.0×10^{-11} m^2.s^{-1} [1]; 3.49×10^{-11} m^2.s^{-1} [2]; 5.57×10^{-11} m^2.s^{-1}. $C_{ATIII}(t=0)$ = 2.844×10^{-6} M [2]; 1.665×10^{-6} M [3]. $k^{++}_{II_a/ATIII}$ = 7.1×10^3 M^{-1}.s^{-1} [1]; 7.083×10^3 M^{-1}.s^{-1} [2]; 7.79×10^3 M^{-1}.s^{-1} [3].	- [1–3]: Modeled ATIII using CDR equations. C_{ATIII} influences the dynamics of both ATIII and IIa. - The value of $k^{++}_{II_a/ATIII}$ referenced in [1] was taken from Hockin's model [4]. - The original reference is [5]. The value of $k^{++}_{II_a/ATIII}$ referenced in [2] was taken from Sorensen's model [6]. The original reference is [7]. - The value of $k^{++}_{II_a/ATIII}$ referenced in [3] was taken from [8].
[9,10]	$S_{ATIII} = -C_{ATIII}\left(k^{++}_{II_a/ATIII}C_{II_a} + k^{++}_{B_a/ATIII}C_{B_a}\right)$ **(S4.2)**	D_{ATIII} = 5.0×10^{-11} m^2.s^{-1} [9,10]. $C_{ATIII}(t=0)$ = 3.4×10^{-6} M [9]; 3.0×10^{-6} M [10]. $k^{++}_{II_a/ATIII}$ = 4.817×10^3 M^{-1}.s^{-1} [9,10]. $k^{++}_{B_a/ATIII}$ = 2.223 M^{-1}.s^{-1} [9,10].	- [9,10]: Modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, IXa and Xa. - The value of $k^{++}_{II_a/ATIII}$ referenced in [9,10] was taken from [11]. - The value of $k^{++}_{B_a/ATIII}$ referenced in [9,10] was taken from [11].
[12]	$S_{ATIII} = -C_{ATIII}\left(k^{++}_{II_a/ATIII}C_{II_a} + k^{++}_{IX_a/ATIII}C_{IX_a} + k^{++}_{X_a/ATIII}C_{X_a}\right)$ **(S4.3)**	D_{ATIII} = 6.68×10^{-11} m^2.s^{-1} [12]. $C_{ATIII}(t=0)$ = 2.4×10^{-6} M [12]. $k^{++}_{II_a/ATIII}$ = 6.8×10^3 M^{-1}.s^{-1} [12]. $k^{++}_{IX_a/ATIII}$ = 2.6×10^3 M^{-1}.s^{-1} [12]. $k^{++}_{X_a/ATIII}$ = 2.6×10^3 M^{-1}.s^{-1} [12].	- [12]: modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, IXa and Xa. - The values of $k^{++}_{II_a/ATIII}$, $k^{++}_{IX_a/ATIII}$, and $k^{++}_{X_a/ATIII}$ referenced in [12] was taken from [13].
[14]	$S_{ATIII} = -k^{+}_{II_a/ATIII}C_{II_a} - k^{+}_{IX_a/ATIII}C_{IX_a} - k^{+}_{X_a/ATIII}C_{X_a}$ **(S4.4)**	D_{ATIII} = 5.57×10^{-11} m^2.s^{-1} [14]. $C_{ATIII}(t=0)$ = 2.4×10^{-6} M [14]. $k^{+}_{II_a/ATIII}$ = 2.17×10^{-2} s^{-1} [14]. $k^{+}_{IX_a/ATIII}$ = 3.33×10^{-3} s^{-1} [14]. $k^{+}_{X_a/ATIII}$ = 1.17×10^{-2} s^{-1} [14].	- [14]: modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, IXa and Xa. - The values of $k^{+}_{II_a/ATIII}$, $k^{+}_{IX_a/ATIII}$, and $k^{+}_{X_a/ATIII}$ were developed based on [15,16].

Continued on next page

Reference	Mathematical expression	Values used	Brief description
[17–22]	$S_{ATIII} = -C_{ATIII}(k^{++}_{II_a/ATIII}C_{II_a} + k^{++}_{IX_a/ATIII}C_{IX_a} + k^{++}_{X_a/ATIII}C_{X_a} + k^{++}_{XI_a/ATIII}C_{XI_a})$ **(S4.5)**	D_{ATIII} = 5.57× 10^{-11} m^2.s^{-1} [17,18,21]. $C_{ATIII}(t = 0)$ = 2.41× 10^{-6} M [17,19–21]; 1.566 × 10^{-6} M (in clot), 3.44 × 10^{-6} M (circulating blood) [18]. $k^{++}_{II_a/ATIII}$ = 1.19× 10^7 M^{-1}.s^{-1} [17–22]. $k^{++}_{IX_a/ATIII}$ = 2.7× 10^5 M^{-1}.s^{-1} [17–22]. $k^{++}_{X_a/ATIII}$ = 5.783× 10^6 M^{-1}.s^{-1} [17–22]. $k^{++}_{XI_a/ATIII}$ = 2.17× 10^2 M^{-1}.s^{-1} [17–22].	- [17,18,20,22]: modeled ATIII using CDR equations. - [19,21]: modeled ATIII using tDPD equations. - [17,19–22]: C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, IXa, Xa and XIa. - [18]: C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, IXa, Xa, XIa and $\alpha_1 AT$. - The values of $k^{++}_{II_a/ATIII}$, $k^{++}_{IX_a/ATIII}$, $k^{++}_{X_a/ATIII}$, and $k^{++}_{XI_a/ATIII}$ referenced in [17–22] was taken from Anand's model [16]. - Citation of $k^{++}_{II_a/ATIII}$: [11]. - Citation of $k^{++}_{IX_a/ATIII}$: [11]. - Citation of $k^{++}_{X_a/ATIII}$: [11]. Citation of $k^{++}_{XI_a/ATIII}$: [23].
[24]	$S_{ATIII} = -C_{ATIII}(k^{++}_{II_a/ATIII}C_{II_a} + k^{++}_{IX_a/ATIII}C_{IX_a} + k^{++}_{X_a/ATIII}C_{X_a} + k^{++}_{XI_a/ATIII}C_{XI_a} + k^{++}_{XII_a/ATIII}C_{XII_a})$ **(S4.6)**	D_{ATIII} = 5.57× 10^{-11} m^2.s^{-1} [24]. $C_{ATIII}(t = 0)$ = 2.41× 10^{-6} M [24]. $k^{++}_{II_a/ATIII}$ = 4.816× 10^3 M^{-1}.s^{-1} [24]. $k^{++}_{IX_a/ATIII}$ = 2.223× 10^2 M^{-1}.s^{-1} [24]. $k^{++}_{X_a/ATIII}$ = 3.05× 10^3 M^{-1}.s^{-1} [24]. $k^{++}_{XI_a/ATIII}$ = 1.0× 10^3 M^{-1}.s^{-1} [24]. $k^{++}_{XII_a/ATIII}$ = 3.645× 10^1 M^{-1}.s^{-1} [24].	- [24]: modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, IXa, Xa,XIa and XIIa. - [24]: Model based on the studies of [16,25]. - The original source of the values of $k^{++}_{II_a/ATIII}$, $k^{++}_{IX_a/ATIII}$, $k^{++}_{X_a/ATIII}$ referenced in [24] is [11]. - The original source of the value $k^{++}_{XI_a/ATIII}$ is [23]. - The original source of the value $k^{++}_{XII_a/ATIII}$ is [26].
[27]	$S_{II_a} = f(C_{X_a}, C_{V_a}, C_{II}, C_{II}(t = 0)) - k^{++}_{II_a/ATIII}C_{ATIII}C_{II_a}$ **(S4.7)**	D_{ATIII} = 6.17× 10^{-11} m^2.s^{-1} [27]. $k^{++}_{II_a/ATII}$ = 9.45× 10^4 M^{-1}.s^{-1} [27].	- The diffusion-reaction model incorporates convection with a parabolic speed profile. - The unit of the constant. $k^{++}_{II_a}$ was converted under the assumption that the molecular weight of thrombin is equal to 36,000 g/mol [28].

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Reference	Mathematical expression	Values used	Brief description
[18,29]	$S_{ATIII} = -C_{ATIII}\left(k^{++}_{II_a/ATIII}C_{II_a} + k^{++}_{W/ATIII}C_W\right)$ **(S4.8)**	D_{ATIII} = 5.57×10^{-11} m².s⁻¹ [18,29]. $C_{ATIII}(t=0)$ = 1.566×10^{-6} M (in clot), 3.44×10^{-6} M (in circulating blood) [18,29]. $k^{++}_{II_a/ATIII}$ = 1.19×10^{7} $M^{-1}.s^{-1}$ [18,29]. $k^{++}_{W/ATIII}$ = 1.67×10^{5} $M^{-1}.s^{-1}$ [18,29].	- [18,29]: modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, and prothrombinase. - The value of $k^{++}_{II_a/ATIII}$ referenced in [18,29] was taken from Anand's model [16]. The original source is [11].
[30,31]	$S_{ATIII} = -C_{ATIII}\left(k^{++}_{II_a/ATIII}C_{II_a} + k^{++}_{mII_a/ATIII}C_{mII_a} + k^{++}_{IX_a/ATIII}C_{IX_a} + k^{++}_{X_a/ATIII}C_{X_a} + k^{++}_{TF\equiv VII_a/ATIII}C_{TF\equiv VII_a}\right)$ **(S4.9)**	D_{ATIII} = 3.49×10^{-11} m².s⁻¹ [30,31]; $C_{ATIII}(t=0)$ = 2.844×10^{-6} M [30,31]; $k^{++}_{II_a/ATIII}$ = 7.1×10^{3} $M^{-1}s^{-1}$ [30,31]. $k^{++}_{mII_a/ATIII}$ = 7.1×10^{3} $M^{-1}s^{-1}$ [30,31]. $k^{++}_{IX_a/ATIII}$ = 4.9×10^{2} $M^{-1}s^{-1}$ [30,31]. $k^{++}_{X_a/ATIII}$ = 1.5×10^{3} $M^{-1}s^{-1}$ [30,31]. $k^{++}_{TF\equiv VII_a/ATIII}$ = 2.3×10^{2} $M^{-1}s^{-1}$ [30,31].	[30,31]: modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, mIIa, IXa, Xa, $TF\equiv VII_a$, $II_a\equiv ATIII$, $mII_a\equiv ATIII$, $IX_a\equiv ATIII$, $X_a\equiv ATIII$ and $TF\equiv VII_a\equiv ATIII$. - The kinetic parameters were taken from Hockin's model [4]. - The original citation of the values of $k^{++}_{II_a/ATIII}$ and $k^{++}_{mII_a/ATIII}$ is [5]. - The original citation of the values of $k^{++}_{IX_a/ATIII}$ and $k^{++}_{X_a/ATIII}$ is [32]. - The original citation of the value of $k^{++}_{TF\equiv VII_a/ATIII}$ is [33].
[34]	$S_{ATIII} = -C_{ATIII}\left(k^{+}_{II_a/ATIII}C_{II_a} + k^{++}_{IX_a/ATIII}C_{IX_a} + k^{++}_{X_a/ATIII}C_{X_a} + k^{++}_{H/ATIII}C_H\right) + k^{+}_{H'\equiv ATIII/ATIII}C_{H'\equiv ATIII} + k^{+}_{H''\equiv ATIII/ATIII}C_{H''\equiv ATIII} + k^{+}_{H'''\equiv ATIII/ATIII}C_{H'''\equiv ATIII}$ **(S4.10)**	D_{ATIII} = 5.11×10^{-11} m².s⁻¹ [34]. $C_{ATIII}(t=0)$ = 2.4×10^{-6} M [34]. $k^{++}_{II_a/ATIII}$ = 6.8×10^{3} $M^{-1}s^{-1}$ [34]. $k^{++}_{IX_a/ATIII}$ = 2.6×10^{3} $M^{-1}s^{-1}$ [34]. $k^{++}_{X_a/ATIII}$ = 2.6×10^{3} $M^{-1}s^{-1}$ [34]. $k^{++}_{H/ATIII}$ = 1.0×10^{8} $M^{-1}s^{-1}$ [34]. $k^{+}_{H'\equiv ATIII/ATIII}$ = 2.3 s^{-1} [34]. $k^{+}_{H''\equiv ATII\ /ATIII}$ = 0.5 s^{-1} [34]. $k^{+}_{H'''\equiv ATIII/ATIII}$ = 0.5 s^{-1} [34].	- [34]: modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII, IXa, Xa and Heparin (H). - The kinetic values were taken from [13].

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Reference	Mathematical expression	Values used	Brief description
[35]	$S_{ATIII} = -C_{ATIII}\Big(k^{++}_{IIa/ATIII}C_{IIa} + k^{++}_{IXa/ATIII}C_{IXa} + k^{++}_{Xa/ATIII}C_{Xa} + k^{++}_{XIa/ATIII}C_{XIa} + k^{++}_{Xa\equiv Va^{e}/ATIII}C_{Xa\equiv Va^{e}} + k^{++}_{Xa\equiv Va^{v}/ATIII}C_{Xa\equiv Va^{v}} + k^{++}_{HC/ATIII}C_{HC} + K_{ATIII}\big(C_{IIa\equiv F_g} + C_{IIa\equiv F_n}\big)\Big) + k^{+}_{HC\equiv ATIII/ATIII}C_{HC\equiv ATIII}$ **(S4.11)**	D_{ATIII} = 5.11× 10^{-11} m^2.s^{-1} [35]. $C_{ATIII}(t=0)$ = 2.4× 10^{-6} M [35]. $k^{++}_{IIa/ATIII}$ = 5.6× 10^{3} M^{-1}.s^{-1} [35]. $k^{++}_{IXa/ATIII}$ = 2.2× 10^{2} M^{-1}.s^{-1} [35]. $k^{++}_{Xa/ATIII}$ = 2.5× 10^{3} M^{-1}.s^{-1} [35]. $k^{++}_{XIa/ATIII}$ = 8.0 M^{-1}.s^{-1} [35]. $k^{++}_{Xa\equiv Va^{e}/ATIII}$ = 1.4× 10^{2} M^{-1}.s^{-1} [35]. $k^{++}_{Xa\equiv Va^{v}/ATIII}$ = 1.4× 10^{2} M^{-1}.s^{-1} [35]. K_{ATIII} = 1.0× 10^{4} M^{-1}.s^{-1} [35]. $k^{++}_{HC/ATIII}$ = 3.0× 10^{4} M^{-1}.s^{-1} [35]. $k^{+}_{HC\equiv ATIII/ATIII}$ = 1.3 s^{-1} [35].	- [35]: modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII, IIa, IXa, Xa, XIa, $X_a \equiv V_a{}^{e}$, $X_a \equiv V_a{}^{v}$, HC, $C_{IIa\equiv F_g}$ and $II_a \equiv F_n$.
[6,36–40]	$S_{ATIII} = -\frac{k_{1,T}C_H C_{ATIII}}{\alpha.K_{AT}.K_T+\alpha.K_{AT}.C_{IIa}+C_{ATIII}C_{IIa}}C_{IIa}$ (In the presence of Heparin) **(S4.12a)** $S_{ATIII} = -k^{++}_{IIa/ATIII}C_{ATIII}C_{IIa}$ (In the absence of Heparin) **(S4.12b)**	D_{ATIII} = 3.49× 10^{-11} m^2.s^{-1} [6,36–40]. $C_{ATIII}(t=0)$ = 2.844× 10^{-6} M [6,36–40]. $k^{++}_{IIa/ATIII}$ = 7.083× 10^{3} M^{-1}s^{-1} [6,36–40]. $k_{1,T}$=13.333 s^{-1} [6,36–40]. K_T=3.5× 10^{4} M [6,36–40]. K_{AT}=1.0× 10^{5} M [6,36–40]. α=1 [6,36–40].	- modeled ATIII using CDR equations. C_{ATIII} is incorporated into the mathematical expression of ATIII and IIa. - The kinetics values were taken from Griffith's template model [41].
[42–44]	$S_{IIa} = f\big(C_{IIa}, C_V, C_{V\equiv IIa}, C_{VII}, C_{VII\equiv IIa}, C_{VIII}$ $k^{+}_{IIa/ATIII}C_{IIa}$ **(S4.13a)** $S_{IXa} = f\big(C_{IXa}\big) - k^{+}_{IXa/ATIII}C_{IXa}$ **(S4.13b)** $S_{Xa} = f\big(C_{Xa}, C_{TFPI}, C_{VII}, C_{VII\equiv Xa}\big) - k^{+}_{Xa/ATIII}C_{IXa}$ **(S4.13c)**	$k^{+}_{IIa/ATIII}$ = 0.2 s^{-1} [42–44]. $k^{+}_{IXa/ATIII}$ = 0.1 s^{-1} [42–44]. $k^{+}_{Xa/ATIII}$ =0.1 s^{-1} [42–44].	- First-order inhibition term that is not dependent on ATIII concentration. It inhibits IIa, IXa, and Xa. - The value of $k^{+}_{IIa/ATIII}$ used in [42–44] where based in the equilibrium constant reported by [45]. - The values of $k^{+}_{IXa/ATIII}$ $k^{+}_{Xa/ATIII}$ used in [42–44] where based in the equilibrium constant reported by [46].

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Reference	Mathematical expression	Values used	Brief description
[47]	$S_{II_a} = f(C_{II_a}, C_V, C_{V\equiv II_a}, C_{VII}, C_{VII\equiv II_a}, C_{VIII}$ $k^+_{II_a/ATIII} C_{II_a}$ **(S4.14a)** $S_{IX_a} = f(C_{IX_a}) - k^+_{IX_a/ATIII} C_{IX_a}$ **(S4.14b)** $S_{X_a} = f(C_{X_a}, C_{TFPI}, C_{VII}, C_{VII\equiv X_a}) - k^+_{X_a/ATIII} C_{IX_a}$ **(S4.14c)** $S_{XI_a} = f(C_{XI_a}, C_{IX}, C_{IX\equiv XI_a}, C_{XI\equiv XI_a}) - k^+_{XI_a/ATIII} C_{XI_a}$ **(S4.14d)**	$k^+_{II_a/ATIII}$ = 0.2 s^{-1} [47]. $k^+_{IX_a/ATIII}$ = 0.1 s^{-1} [47]. $k^+_{X_a/ATIII}$ =0.1 s^{-1} [47]. $k^+_{XI_a/ATIII}$ =0.2 s^{-1} [47].	- First-order inhibition term that is not dependent on ATIII concentration, due to high concentration of ATIII in the plasma. It inhibits IIa, IXa,, Xa and XIa. - The value of $k^+_{II_a/ATIII}$ used in [42–44] where based in the equilibrium constant reported by [45]. - The values of $k^+_{IX_a/ATIII}$ $k^+_{X_a/ATIII}$ used in [42–44] where based in the equilibrium constant reported by [46]. - The value of $k^+_{XI_a/ATIII}$ used in [47] where based in the equilibrium constant reported by [48].
[49]	$\frac{dC_{ATIII}}{dt} = -k^{++}_{IX_a/ATIII} C_{IX_a} C_{ATIII} - k^{++}_{IX^s_a/ATIII} C_{IX^s_a} C_{ATIII} + k^{++}_{IX^{s*}_a/ATIII} C_{IX^{s*}_a} C_{ATIII} - k^{++}_{X_a/ATIII} C_{X_a} C_{ATIII} + k^{++}_{X^s_a/ATIII} C_{X^s_a} C_{ATIII} - k^{++}_{II_a/ATIII} C_{II_a} C_{ATIII} - k^{++}_{II^s_a/ATIII} C_{II^s_a} C_{ATIII} - k^{++}_{XI_a/ATIII} C_{XI_a} C_{ATIII} - k^{++}_{XI_a\equiv ATIII/ATIII} C_{XI_a\equiv ATIII} C_{ATIII} - k^{++}_{XI^{s*}_a/ATIII} C_{XI^{s*}_a} C_{ATIII} - k^{++}_{XI^h_a/ATIII} C_{XI^h_a} C_{ATIII} + k_{flow}(C_{ATIII,up} - C_{ATIII}) - k^{++}_{H/ATIII} C_H C_{ATIII} + k^+_{H\equiv ATIII} C_{H\equiv ATIII}$ **(S4.15)**	$k^{++}_{IX_a/ATIII}$ = 4.8× 10^2 $M^{-1}.s^{-1}$ [49]. $k^{++}_{IX^s_a/ATIII}$ = 4.8× 10^2 $M^{-1}.s^{-1}$ [49]. $k^{++}_{IX^{s*}_a/ATIII}$ = 4.8× 10^2 $M^{-1}.s^{-1}$ [49]. $k^{++}_{X_a/ATIII}$ = 3.5× 10^3 $M^{-1}.s^{-1}$ [49]. $k^{++}_{X^s_a/ATIII}$ = 3.5× 10^3 $M^{-1}.s^{-1}$ [49]. $k^{++}_{II_a/ATIII}$ = 1.4× 10^4 $M^{-1}.s^{-1}$ [49]. $k^{++}_{II^s_a/ATIII}$ = 1.4× 10^4 $M^{-1}.s^{-1}$ [49]. $k^{++}_{XI_a/ATIII}$ = 2.4× 10^2 $M^{-1}.s^{-1}$ [49]. $k^{++}_{XI_a\equiv ATIII/ATIII}$ = 2.4× 10^2 $M^{-1}.s^{-1}$ [49]. $k^{++}_{XI^{s*}_a/ATIII}$ = 2.4× 10^2 $M^{-1}.s^{-1}$ [49]. $k^{++}_{XI^h_a/ATIII}$ = 2.4× 10^2 $M^{-1}.s^{-1}$ [49]. $k^{++}_{H/ATIII}$ = 1 $M^{-1}.s^{-1}$ [49]. $k^+_{H\equiv ATIII}$ = 2.77× 10^7 s^{-1} [49].	- Modeled as a system of ordinary differential equations.

Continued on next page

Reference	Mathematical expression	Values used	Brief description
		D_{ATIII} = 3.3× 10^{-11} m[2].s[-1] [50].	
[50]	$S_{ATIII} = -k^{++}_{II_a{}^F} C_{ATIII} C_{II_a{}^F} - k^{++}_{IX_a/ATIII} C_{ATIII} C_{IX_a} - k^{++}_{X_a{}^F} C_{ATIII} C_{X_a{}^F} - k^{++}_{XI_a{}^F} C_{ATIII} C_{XI_a{}^F} - k^{++}_{X_a \equiv V_a{}^B} C_{ATIII} C_{X_a \equiv V_a{}^B}$ **(S4.16)**	$C_{ATIII}(t=0)$ = 3.4× 10^{-6} M [50]. $k^{++}_{II_a{}^F}$ = 6.83× 10^3 M[-1].s[-1] [50]. $k^{++}_{IX_a/ATIII}$ = 1.36× 10^2 M[-1].s[-1] [50]. $k^{++}_{X_a{}^F}$ = 2.5× 10^3 M[-1].s[-1] [50]. $k^{++}_{XI_a{}^F}$ = 3.16× 10^2 M[-1].s[-1] [50]. $k^{++}_{X_a \equiv V_a{}^B}$ = 3.67× 10^2 M[-1].s[-1] [50].	- The value of $k^{++}_{II_a{}^F}$ referenced in [50] was taken from [51]. - The value of $k^{++}_{IX_a/ATIII}$ referenced in [50] was taken from [52]. - The value of $k^{++}_{X_a{}^F}$ referenced in [50] was taken from [51]. - The value of $k^{++}_{XI_a{}^F}$ referenced in [50] was taken from [53]. - The value of $k^{++}_{X_a \equiv V_a{}^B}$ referenced in [50] was taken from [54].

6. Mathematical equations representing blood factor VIII

Table S5. List of Equations representing blood factor VIII and VIIIa.

Reference	Mathematical expression	Values used	Brief description
[27]	$S_{VIII_a} = -k^{+}_{VIII_a/VIII_a} C_{VIII_a} + k^{+}_{VIII/II_a} C_{II_a}$ **(S5.1)**	D_{VIII_a} = 6.167× 10^{-11} m[2].s[-1] [27]. $k^{+}_{VIII_a/VIII_a} = 5.17 \times 10^{-3}$ s[-1] [27]. k^{+}_{VIII/II_a} = 1.67× 10^{-7} s[-1] [27].	- Modeled the system as CDR. - C_{VIII_a} influences the dynamics of Xa and VIIIa. - The values of $k^{+}_{VIII_a/VIII_a}$ and k^{+}_{VIII/II_a} used in [27] were taken from [55].
[56]	$S_{VIII} = -k^{++}_{VIII/II_a} C_{VIII} C_{II_a} - k^{++}_{VIII/X_a} C_{VIII} C_{X_a}$ **(S5.2a)** $S_{VIIIa} = k^{++}_{VIII/II_a} C_{VIII} C_{II_a} + k^{++}_{VIII/X_a} C_{VIII} C_{X_a} - k^{++}_{VIII_a/IX_a} C_{VIII_a} C_{IX_a} + k^{+}_{VIII_a \equiv IX_a} C_{VIII_a \equiv IX_a}$ **(S5.2b)**	$C_{VIII}(t=0)$ = 7.0 × 10^{-10} M [56]. $C_{VIII_a}(t=0) = 1.0 \times 10^{-10}$ M [56]. k^{++}_{VIII/II_a} = 2.0× 10^7 M[-1].s[-1] [56]. k^{++}_{VIII/X_a} = 1.0× 10^7 M[-1].s[-1] [56]. $k^{++}_{VIII_a/IX_a}$ = 1.0× 10^7 M[-1].s[-1] [56]. $k^{+}_{VIII_a \equiv IX_a}$ = 5.0× 10^{-3} s[-1] [56].	- Modeled the system as CDR. - C_{VIII_a} influences the dynamics of VIIIa, IXa and VIIIa≡IXa. - C_{VIII} influences the dynamics of VIII and VIIIa. - Based on the model of Jones and Mann [57], with rate constants determined based on the study of Lawson et al. [58].

Continued on next page

Reference	Mathematical expression	Values used	Brief description
[31]	$S_{VIII} = -k^{++}_{VIII/II_a} C_{VIII} C_{II_a}$ **(S5.3a)** $S_{VIIIa} = k^{++}_{VIII/II_a} C_{VIII} C_{II_a} - k^{++}_{VIII_a/IX_a} C_{VIII_a} C_{IX_a} + k^{+}_{VIII_a \equiv IX_a} C_{VIII_a \equiv IX_a} - k^{+}_{VIII_{a1L}} C_{VIII_a} + k^{++}_{VIII_{a1L}/VIII_{a2}} C_{VIII_{a1L}} C_{VIII_{a2}}$ **(S5.3b)**	$C_{VIII}(t = 0) = 7.0 \times 10^{-10}$ M [31]. $C_{VIII_a}(t = 0) = 0$ M [31]. $D_{VIII} = 4.4 \times 10^{-12}$ m^2.s^{-1} [31]. $D_{VIII_a} = 3.5 \times 10^{-11}$ m^2.s^{-1} [31]. $k^{++}_{VIII/II_a} = 2.0 \times 10^{7}$ M^{-1}.s^{-1} [31]. $k^{++}_{VIII_a/IX_a} = 1.0 \times 10^{7}$ M^{-1}.s^{-1} [31]. $k^{+}_{VIII_a \equiv IX_a} = 5.0 \times 10^{-3}$ s^{-1} [31]. $k^{+}_{VIII_{a1L}} = 2.2 \times 10^{-5}$ s^{-1} [31]. $k^{++}_{VIII_{a1L}/VIII_{a2}} = 6.0 \times 10^{6}$ M^{-1}.s^{-1} [31].	- Modeled the system as CDR. - [31] used the Hockin's model of blood coagulation [59]. - The original citation of k^{++}_{VIII/II_a} value is [60]. - The original citation of $k^{++}_{VIII_a/IX_a}$ and $k^{+}_{VIII_a \equiv IX_a}$ is [61]. - The original citation of $k^{+}_{VIII_{a1L}}$ and $k^{++}_{VIII_{a1L}/VIII_{a2}}$ are [62,63].
[64]	$S_{VIII} = -C_{VIII}\left(k^{++}_{VIII/II_a} C_{II_a} + k^{++}_{VIII/mII_a} C_{mII_a} + k^{++}_{VIII/X_a} C_{X_a}\right)$ **(S5.4a)** $S_{VIII_a} = C_{VIII}\left(k^{++}_{VIII/II_a} C_{II_a} + k^{++}_{VIII/mII_a} C_{mII_a} + k^{++}_{VIII/X_a} C_{X_a}\right) - k^{++}_{VIII_a/IX_a} C_{IX_a} C_{VIII_a} + k^{+}_{VIII_a \equiv IX_a} C_{VIII_a \equiv IX_a}$ **(S5.4b)**	$k^{++}_{VIII/II_a} = 2.0 \times 10^{7}$ M^{-1}.s^{-1} [64]. $k^{++}_{VIII/mII_a} = 2.0 \times 10^{7}$ M^{-1}.s^{-1} [64]. $k^{++}_{VIII/X_a} = 1.0 \times 10^{7}$ M^{-1}.s^{-1} [64]. $k^{++}_{VIII_a/IX_a} = 1.0 \times 10^{7}$ M^{-1}.s^{-1} [64]. $k^{+}_{VIII_a \equiv IX_a} = 5.0 \times 10^{-3}$ s^{-1} [64].	- Modeled the system as CDR. - [64] used the model of Jones and Mann [57], with rate constants determined based on the study of Lawson et al. [58].
[12]	$S_{VIII} = -\frac{k^{cat}_{VIII/II_a} C_{VIII} C_{II_a}}{K^{m}_{VIII/II_a} + C_{VIII}}$ **(S5.5a)** $S_{VIII_a} = \frac{k^{cat}_{VIII/II_a} C_{VIII} C_{II_a}}{K^{m}_{VIII/II_a} + C_{VIII}}$ **(S5.5b)**	$C_{VIII}(t = 0) = 7.0 \times 10^{-10}$ M [12]. $C_{VIII_a}(t = 0) = 0$ M [12]. $D_{VIII} = 4.67 \times 10^{-11}$ m^2.s^{-1} [12]. $D_{VIII_a} = 4.70 \times 10^{-11}$ m^2.s^{-1} [12]. $k^{cat}_{VIII/II_a} = 0.9$ s^{-1} [12]. $K^{m}_{VIII/II_a} = 2.0 \times 10^{-7}$ M [12].	- [12] modeled as a system of CDR. - The values of k^{cat}_{VIII/II_a} and K^{m}_{VIII/II_a} were taken from [62,65].

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Reference	Mathematical expression	Values used	Brief description
[50]	$S_{VIII} = -\frac{k^{cat}_{VIII/II_a} C_{VIII} C_{II_a}}{k^m_{VIII/II_a} + C_{VIII}}$ **(S5.6a)** $S_{VIII_a} = \frac{k^{cat}_{VIII/II_a} C_{VIII} C_{II_a}}{k^m_{VIII/II_a} + C_{VIII}} - k^+_{VIII_a} C_{VIII_a}$ **(S5.6b)**	$C_{VIII}(t=0) = 7.0 \times 10^{-10}$ M [50]. $C_{VIII_a}(t=0) = 0$ M [50]. $D_{VIII} = 0$ m^2.s^{-1} [50]. $D_{VIII_a} = 3.50 \times 10^{-11}$ m^2.s^{-1} [50]. $k^{cat}_{VIII/II_a} = 0.9$ s^{-1} [50]. $k^m_{VIII/II_a} = 1.47 \times 10^{-7}$ M [50]. $k^+_{VIII_a} = 5.83 \times 10^{-3}$ s^{-1} [50].	- The values k^{cat}_{VIII/II_a} and k^m_{VIII/II_a} were taken from [66]. - The value $k^+_{VIII_a}$ were taken from [62].
[34]	$S_{VIII} = -\frac{k^{cat}_{VIII/II_a} C_{VIII} C_{II_a}}{K^m_{VIII/II_a} + C_{VIII}}$ **(S5.7a)** $S_{VIII_a} = \frac{k^{cat}_{VIII/II_a} C_{VIII} C_{II_a}}{K^m_{VIII/II_a} + C_{VIII}} -$ $k^{++}_{VIII_a/IX_a} C_{VIII_a} C_{IX_a} +$ $k^+_{VIII_a \equiv IX_a} C_{VIII_a \equiv IX_a}$ **(S5.7b)**	$C_{VIII}(t=0) = 7.0 \times 10^{-10}$ M [34]. $C_{VIII_a}(t=0) = 1.0 \times 10^{-10}$ M [34]. $k^{cat}_{VIII/II_a} = 0.9$ s^{-1} [34]. $K^m_{VIII/II_a} = 1.8 \times 10^{-7}$ M [34]. $k^{++}_{VIII_a/IX_a} = 1.0 \times 10^{8}$ M^{-1}.s^{-1} [34]. $k^+_{VIII_a \equiv IX_a} = 0.01$ s^{-1} [34].	- [34] modeled as a system of CDR. - The values of k^{cat}_{VIII/II_a} and K^m_{VIII/II_a} were taken from [65,66]. - The values of $k^{++}_{VIII_a/IX_a}$ and $k^+_{VIII_a \equiv IX_a}$ were taken from [67].
[14,17–21,24]	$S_{VIII} = -\frac{k^{cat}_{VIII/II_a} C_{VIII} C_{II_a}}{K^m_{VIII/II_a} + C_{VIII}}$ **(S5.8a)** $S_{VIII_a} = \frac{k^{cat}_{VIII/II_a} C_{VIII} C_{II_a}}{K^m_{VIII/II_a} + C_{VIII}} -$ $k^+_{VIII_a} C_{VIII_a} - \frac{k^{cat}_{VIII/APC} C_{VIII_a} C_{APC}}{k^m_{VIII/APC} + C_{VIII_a}}$ **(S5.8b)**	$C_{VIII}(t=0) = 7.0 \times 10^{-10}$ M [14,24]. $C_{VIII_a}(t=0) = 0$ M [14,24]. $D_{VIII} = 3.12 \times 10^{-11}$ m^2.s^{-1} [14,24]. $D_{VIII_a} = 3.92 \times 10^{-11}$ m^2.s^{-1} [14,24]. $k^{cat}_{VIII,II_a} = 3.24$ s^{-1} [14,17–21,24]. $K^m_{VIII,II_a} = 1.12 \times 10^{-4}$ M [14,17–21,24]. $k^+_{VIII_a} = 3.7 \times 10^{-3}$ s^{-1} [14,17–21,24]. $k^{cat}_{VIII,APC} = 0.17$ s^{-1} [14,17–21,24]. $k^m_{VIII,APC} = 1.46 \times 10^{-8}$ M [14,17–21,24].	- The studies [14,17–21,24] used the Anand model for blood coagulation [16]. - The values of k^{cat}_{VIII,II_a} and K^m_{VIII,II_a} of Anand's model were taken from [68]. - The value of $k^+_{VIII_a}$ of Anand's model was taken from [69]. - In Anand's model, it was assumed that the kinetics and the rate constants controlling the depletion of VIIIa by APC ($k^{cat}_{VIII,APC}$ and $K^m_{VIII,APC}$) mirror those governing the reduction of Va by APC (See A6 in [16]).

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Reference	Mathematical expression	Values used	Brief description
[70]	$S_{VIII} = -k^{++}_{VIII/II_a} C_{VIII} C_{II_a} - k^{++}_{VIII/X_a} C_{VIII} C_{X_a} + k^{+}_{VIII\equiv X_a} C_{VIII\equiv X_a}$ **(S5.9a)** $S_{VIII_a} = k^{++}_{VIII/II_a} C_{VIII} C_{II_a} + k^{++}_{VIII/X_a} C_{VIII} C_{X_a} - k^{++}_{VIII_a/IX_a} C_{VIII_a} C_{IX_a} + k^{+}_{VIII_a\equiv IX_a} C_{VIII_a\equiv IX_a} - k^{+}_{VIII_{a1L}} C_{VIII_a} + k^{++}_{VIII_{a1}/VIII_{a2}} C_{VIII_{a1L}} C_{VIII_{a2}}$ **(S5.9b)**	$C_{VIII}(t=0) = 7.0 \times 10^{-10}$ M [70]. $C_{VIII_a}(t=0) = 1.0 \times 10^{-10}$ M [70]. k^{++}_{VIII/II_a} = 2.0× 10^7 $M^{-1}.s^{-1}$ [70]. k^{++}_{VIII/X_a} = 1.0× 10^8 $M^{-1}.s^{-1}$ [70]. $k^{+}_{VIII\equiv X_a}$ = 2.1 s^{-1} [70]. $k^{++}_{VIII_a/IX_a}$ =1.0× 10^7 $M^{-1}.s^{-1}$ [70]. $k^{+}_{VIII_a\equiv IX_a}$ = 5.0× 10^{-3} s^{-1} [70]. $k^{+}_{VIII_{a1L}}$ = 6.0× 10^{-3} s^{-1} [70]. $k^{++}_{VIII_{a1}/VIII_{a2}}$ = 2.2× 10^4 $M^{-1}.s^{-1}$ [70].	- Was adopted from the kinetic model of Chatterjee et al. [71]. - The values k^{++}_{VIII/X_a} and $k^{+}_{VIII\equiv X_a}$ of Chatterjee et al. model [71] were taken from [65,72,73]. - The values $k^{++}_{VIII_a/IX_a}$ and $k^{+}_{VIII_a\equiv IX_a}$ of Chatterjee et al. model [71] were taken from [73,74]. - The values $k^{+}_{VIII_{a1L}}$ and $k^{++}_{VIII_{a1}/VIII_{a2}}$ of Chatterjee et al. model [71] were taken from [63,75].
[35]	$S_{VIII} = -k^{++}_{VIII/PL^e} C_{VIII} C_{PL^e} + k^{+}_{VIII/B^e} C_{VIII,B^e} - k^{++}_{VIII/PL^v} C_{VIII} C_{PL^v} + k^{+}_{VIII/B^v} C_{III,B^v}$ **(S5.10a)** $S_{VIII_a} = -k^{+}_{VIII_a} C_{VIII_a} - k^{++}_{VIII_a/PL^e} C_{VIII_a} C_{PL^e} + k^{+}_{VIII_a/B^e} C_{VIII_a,B^e} - k^{++}_{VIII_a/PL^v} C_{VIII_a} C_{PL^v} + k^{+}_{VIII_a/B^v} C_{VIII_a,B^v}$ **(S5.10b)**	k^{++}_{VIII/PL^e} = 6.3× 10^5 $M^{-1}.s^{-1}$ [35]. k^{+}_{VIII/B^e} =1.3× 10^{-3} s^{-1} [35]. k^{++}_{VIII/PL^v} = 6.3× 10^1 $M^{-1}.s^{-1}$ [35]. k^{+}_{VIII/B^v} =1.3× 10^{-3} s^{-1} [35]. $k^{+}_{VIII_a}$ = 5.83× 10^{-3} s^{-1} [35]. $k^{++}_{VIII_a/PL^e}$ = 7.8× 10^5 $M^{-1}.s^{-1}$ [35]. $k^{+}_{VIII_a/B^e}$ = 2.8× 10^{-4} s^{-1} [35]. $k^{++}_{VIII_a/PL^v}$ = 7.8× 10^1 $M^{-1}.s^{-1}$ [35]. $k^{+}_{VIII_a/B^v}$ =2.8× 10^{-4} s^{-1} [35].	- The superscript "e" denotes the factors assembled on the exogenous phospholipids. - The superscript "v" denotes the factors assembled on the endogenous phospholipids. - For a better understanding of the nomenclature, see the supplementary file of the study by Pisaryuk et al. [35].
[30]	$S_{VIII} = -k^{++}_{VIII,m} C_{VIII} (p_{VIII} - C^{mtot}_{VIII_a} - C^{mtot}_{VIII}) + k^{+}_{VIII,m} C_{VIII^m} - k^{++}_{VIII/II_a} C_{VIII} C_{II_a}$ **(S5.11a)** $S_{VIII_a} = -k^{++}_{VIII_a,m} C_{VIII_a} (p_{VIII} - C^{mtot}_{VIII_a} - C^{mtot}_{VIII}) + k^{+}_{VIII_a,m} C_{VIII^m} - k^{+}_{VIII_{a1L}} C_{VIII_a} + k^{++}_{VIII_{a1L}/VIII_{a2}} C_{VIII_{a1L}} C_{VIII_{a2}}$ **(S5.11b)**	$k^{++}_{VIII,m}$ = 5.0× 10^7 $M^{-1}.s^{-1}$ [30]. $k^{+}_{VIII,m}$ = 0.17 s^{-1} [30]. k^{++}_{VIII/II_a} = 2.0× 10^7 $M^{-1}.s^{-1}$ [30]. $k^{++}_{VIII_a,m}$ = 5.0× 10^7 $M^{-1}.s^{-1}$ [30]. $k^{+}_{VIII_a,m}$ = 0.17 s^{-1} [30]. $k^{+}_{VIII_a,L}$ =6.0× 10^{-3} s^{-1} [30]. $k^{++}_{VIII_{a1L}/VIII_{a2}}$ =2.2× 10^4 $M^{-1}.s^{-1}$ [30].	- The kinetics parameters were taken from Hockin's model. - The values of - The original citation of k^{++}_{VIII/II_a} value is [60]. - The original citation of $k^{+}_{VIII_{a1L}}$ and $k^{++}_{VIII_{a1L}/VIII_{a2}}$ are [62,63].

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Reference	Mathematical expression	Values used	Brief description
[42]	$S_{VIII} = -k^{++}_{VIII,m} C_{VIII}\left(N^{b}_{VIII} P^{b,a} + N^{se}_{VIII} P^{se,a} - C^{mtot}_{VIII_a} - C^{mtot}_{VIII}\right) + k^{+}_{VIII,m} C_{VIII^m} - k^{++}_{VIII/II_a} C_{VIII} C_{II_a} + k^{+}_{VIII\equiv II_a} C_{VIII\equiv II_a}$ **(S5.12a)** $S_{VIII_a} = -k^{++}_{VIII_a,m} C_{VIII_a}\left(N^{b}_{VIII} P^{b,a} + N^{se}_{VIII} P^{se,a} - C^{mtot}_{VIII_a} - C^{mtot}_{VIII}\right) + k^{+}_{VIII_a,m} C_{VIII^m_a} + k^{cat}_{VIII\equiv II_a} C_{VIII\equiv II_a}$ **(S5.12b)**	$C_{VIII}(t=0) = 1.0 \times 10^{-10}$ M [42]. D_{VIII} = 5.0×10^{-11} m^2.s^{-1} [42]. D_{VIII_a} = 5.0×10^{-11} m^2.s^{-1} [42]. $k^{++}_{VIII,m}$ = 5.0× 10^7 M^{-1}.s^{-1} [42]. $k^{+}_{VIII,m}$ =0.17 s^{-1} [42]. k^{++}_{VIII/II_a} = 2.64× 10^7 M^{-1}.s^{-1} [42]. $k^{+}_{VIII\equiv II_a}$ = 1 s^{-1} [42]. $k^{++}_{VIII_a,m}$ = 5.0× 10^7 M^{-1}.s^{-1} [42]. $k^{+}_{VIII_a,m}$ = 0.17 s^{-1} [42]. $k^{cat}_{VIII\equiv II_a}$ = 0.9 s^{-1} [42].[65,66]	- The value of $k^{cat}_{VIII\equiv II_a}$ was taken from [66]. - The values of $k^{++}_{VIII,m}$, $k^{++}_{VIII_a,m}$, $k^{+}_{VIII,m}$ and $k^{+}_{VIII_a,m}$ were based on the study of [76]. - The value of $k^{+}_{VIII\equiv II_a}$ was estimated from [65].
[47,49]	$\frac{dC_{VIII}}{dt} = k_{flow}\left(C^{up}_{VIII} - C_{VIII}\right) - k^{++}_{VIII,m} C_{VIII} p^{avail}_{VIII} + k^{+}_{VIII,m} C_{VIII^m} - k^{++}_{VIII/II_a} C_{VIII} C_{II_a} + k^{+}_{VIII\equiv II_a} C_{VIII\equiv II_a}$ **(S5.13a)** $\frac{dC_{VIII_a}}{dt} = k_{flow}\left(C^{up}_{VIII_a} - C_{VIII_a}\right) - k^{++}_{VIII_a,m} C_{VIII_a} p^{avail}_{VIII} + k^{+}_{VIII_a,m} C_{VIII^m_a} + k^{cat}_{VIII\equiv II_a} C_{VIII\equiv II_a} - 0.005 C_{VIII_a} - k^{++}_{VIII_a/APC} C_{VIII_a} C_{APC} + k^{+}_{VIII_a\equiv APC} C_{VIII_a\equiv APC}$ **(S5.13b)**	$C_{VIII}(t=0) = 1.0 \times 10^{-10}$ M [47,49]. D_{VIII} = 5.0×10^{-11} m^2.s^{-1} [47,49]. D_{VIII_a} = 5.0×10^{-11} m^2.s^{-1} [47,49]. $k^{++}_{VIII,m}$ = 5.0× 10^7 M^{-1}.s^{-1} [47,49]. $k^{+}_{VIII,m}$ = 0.17 s^{-1} [47,49]. k^{++}_{VIII/II_a} = 2.64× 10^7 M^{-1}.s^{-1} [47,49]. $k^{+}_{VIII\equiv II_a}$ = 1 s^{-1} [47,49]. $k^{++}_{VIII_a,m}$ = 5.0× 10^7 M^{-1}.s^{-1} [47,49]. $k^{+}_{VIII_a,m}$ = 0.17 s^{-1} [47,49]. $k^{+}_{VIII\equiv II_a}$ = 0.9 s^{-1} [47,49]. $k^{++}_{VIII_a/APC}$ = 1.2× 10^8 M^{-1}.s^{-1} [47,49]. $k^{+}_{VIII_a\equiv APC}$ = 1.0 s^{-1} [47,49]. $k^{cat}_{VIII\equiv II_a}$ = 0.9 s^{-1}. [47,49].	- The values $k^{++}_{VIII,m}$, $k^{+}_{VIII,m}$, $k^{++}_{VIII_a,m}$ and $k^{+}_{VIII_a,m}$ were based in the equilibrium constant taken from [76]. - The values of k^{++}_{VIII/II_a}, $k^{+}_{VIII\equiv II_a}$, $k^{++}_{VIII_a,m}$, $k^{+}_{VIII_a,m}$ and $k^{cat}_{VIII\equiv II_a}$ were calculated based on the studies of [65,66]. - The values of $k^{++}_{VIII_a/APC}$ and $k^{+}_{VIII_a\equiv APC}$ were chosen based on the study of [77].

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Reference	Mathematical expression	Values used	Brief description
[44]	$S_{VIII} = -k^{++}_{VIII,m} C_{VIII} \left(N^{b}_{VIII} P^{b,a} + N^{se}_{VIII} P^{se,a} - C^{mtot}_{VIII_a} - C^{mtot}_{VIII} \right) + k^{+}_{VIII,m} C_{VIII^m} - k^{++}_{VIII/II_a} C_{VIII} C_{II_a}$ **(S5.14a)** $S_{VIII_a} = -k^{++}_{VIII_a,m} C_{VIII_a} \left(N^{b}_{VIII} P^{b,a} + N^{se}_{VIII} P^{se,a} - C^{mtot}_{VIII_a} - C^{mtot}_{VIII} \right) + k^{+}_{VIII_a,m} C_{VIII^m_a} + k^{++}_{VIII/II_a} C_{VIII} C_{II_a}$ **(S5.14b)**	$C_{VIII}(t=0) = 6.0 \times 10^{-10}$ M [44]. $k^{++}_{VIII,m}$ = 5.0× 10^{7} $M^{-1}.s^{-1}$ [44]. $k^{+}_{VIII,m}$ = 0.17 s^{-1} [44]. k^{++}_{VIII/II_a} = 2.64× 10^{7} $M^{-1}.s^{-1}$ [44]. $k^{++}_{VIII_a,m}$ = × 10^{7} $M^{-1}.s^{-1}$ [44].	The kinetics parameters used were the same of [42].

7. Mathematical equations representing PC

Table S6. List of Equations representing PC and PCA.

Reference	Mathematical expression	Values used	Brief description
[1,9]	$S_{PC} = -k^{+}_{PC} C_{PC}$ **(S6.1a)** $S_{PCA} = -k^{+}_{PCA} C_{PCA}$ **(S6.1b)**	k^{+}_{PC} = 0.05 s^{-1} [1]. k^{+}_{PCA} =0.05 s^{-1} [1].	- Modeled as a system of CDR.
[34]	$S_{PC} = -\frac{k^{cat}_{PC/TM\equiv II_{a,s}} C_{TM\equiv II_{a,s}} C_{PC}}{k^{m}_{PC/TM\equiv II_{a,s}} + C_{PC}}$ **(S6.2)**	D_{PC} = 5.0× 10^{-11} $m^2.s^{-1}$ [34]. D_{PCA} = 5.0× 10^{-11} $m^2.s^{-1}$ [34]. $C_{PC}(t=0)$ = 6.0× 10^{-8} M [34]. $k^{cat}_{PC/TM\equiv II_{a,s}}$ = 5.58 s^{-1} [34]. $k^{m}_{PC/TM\equiv II_{a,s}}$ = 7× 10^{-7} M [34].	- The values of $k^{cat}_{PC/TM\equiv II_{a,s}}$ and $k^{m}_{PC/TM\equiv II_{a,s}}$ were taken from [78].
[14]	$S_{PC} = -\frac{k^{cat}_{PC/II_a} C_{II_a} C_{PC}}{k^{m}_{PC/II_a} + C_{PC}}$ **(S6.3a)** $S_{PCA} = \frac{k^{cat}_{PC,II_a} C_{II_a} C_{PC}}{k^{m}_{PC,II_a} + C_{PC}}$ **(S6.3b)**	D_{PC} = 5.44× 10^{-11} $m^2.s^{-1}$ [14]. D_{PCA} = 5.5× 10^{-11} $m^2.s^{-1}$ [14]. $C_{PC}(t=0)$ = 6.0× 10^{-8} M [14]. $C_{PCA}(t=0)$ = 0 M [14]. k^{cat}_{PC/II_a} = 0.65 s^{-1} [14]. k^{m}_{PC/II_a} = 3.19× 10^{-6} M [14].	- Modeled as a system of CDR equations.

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Reference	Mathematical expression	Values used	Brief description
[17–21,24]	$S_{PCA}=\frac{k_{PC/II_a}^{cat}C_{II_a}C_{PC}}{k_{PC/II_a}^{m}+C_{PC}}-k_{PCA/\alpha_1AT}^{++}C_{PCA}C_{\alpha_1AT}$ **(S6.4a)** $S_{PC}=-\frac{k_{PC/II_a}^{cat}C_{II_a}C_{PC}}{k_{PC/II_a}^{m}+C_{PC}}$ **(S6.4b)**	D_{PC} = 5.44× 10^{-11} m^2.s^{-1} [24]. D_{PCA} = 5.5× 10^{-11} m^2.s^{-1} [24]. $C_{PC}(t=0)$ = 6.0× 10^{-8} M [19,24]; 5.99 × 10^{-8} M (initial clot concentration), 6.0 × 10^{-8} M (circulating blood concentration) [18] $C_{PCA}(t=0)$ = 6.0× 10^{-11} M [19]; 0 M [18,24]. k_{PC/II_a}^{cat} = 0.65 s^{-1} [18–21,24]. k_{PC/II_a}^{m} = 3.19× 10^{-6} M [18–21,24]. k_{PCA/α_1AT}^{++} = 1.1× 10^{1} M^{-1}.s^{-1} [18–21,24].	- Biochemistry reactions were modeled with Anand's model of blood coagulation [16]. - The original reference of the values of k_{PC/II_a}^{cat} and k_{PC/II_a}^{m} is [79]. - The original reference of the value of k_{PCA/α_1AT}^{++} is [79].
[29]	$S_{PCA}=\frac{k_{PC/II_a}^{cat}C_{II_a}C_{PC}}{k_{PC/II_a}^{m}+C_{PC}}-k_{PCA/\alpha_1AT}^{++}C_{PCA}C_{\alpha_1AT}-k_{PCA/W}^{++}C_{PCA}C_{W}$ **(S6.5a)** $S_{PC}=-\frac{k_{PC/II_a}^{cat}C_{II_a}C_{PC}}{k_{PC/II_a}^{m}+C_{PC}}$ **(S6.5b)**	$C_{PC}(t=0)$ = 5.99 × 10^{-8} M (initial clot concentration), 6.0 × 10^{-8} M (circulating blood concentration) [29]. $C_{PCA}(t=0)$ = 1.59 × 10^{-1} M (initial clot concentration), 0 M (circulating blood concentration) [29]. k_{PC/II_a}^{cat} = 0.65 s^{-1} [29]. k_{PC/II_a}^{m} = 3.19× 10^{-6} M [29]. k_{PCA/α_1AT}^{++} = 1.1× 10^{1} M^{-1}.s^{-1} [29]. $k_{PCA/W}^{++}$ = 3.67× 10^{4} M^{-1}.s^{-1} [29].	- Biochemistry reactions were benchmarked with Anand's blood coagulation model [16]. - The original reference of the values of k_{PC/II_a}^{cat} and k_{PC/II_a}^{m} is [79]. - The original reference of the value of k_{PCA/α_1AT}^{++} is [79].
[42,43]	$S_{PCA}=-k_{PCA,V_a,m}^{++}C_{PCA}C_{V_a,m}+\left(k_{PCA\equiv V_a,m}^{+}+k_{PCA\equiv V_a,m}^{cat}\right)C_{PCA\equiv V_a,m}-k_{PCA,VIII_a,m}^{++}C_{PCA}C_{VIII_a,m}+\left(k_{PCA\equiv VIII_a,m}^{+}+k_{PCA\equiv VIII_a,m}^{cat}\right)C_{PCA\equiv VIII_a,m}$ **(S6.6)**	$k_{PCA,V_a,m}^{++}$ = 1.2 × 10^{8} M^{-1}.s^{-1} [42]. $k_{PCA\equiv V_a,m}^{+}$ = 1.0 s^{-1} [42]. $k_{PCA\equiv V_a,m}^{cat}$ = 0.5 s^{-1} [42]. $k_{PCA,VIII_a,m}^{++}$ = 1.2 × 10^{8} M^{-1}.s^{-1} [42]. $k_{PCA\equiv VIII_a,m}^{+}$ = 1.0 s^{-1} [42]. $k_{PCA\equiv VIII_a,m}^{cat}$ = 0.5s^{-1} [42].	- The kinetics were determined based on the study of Solymoss et al. [77].
[12]	$S_{PC}=0$ **(S6.7)**		
[44]	$S_{PCA}=\left(k_{PCA\equiv V_a,m}^{cat}+k_{PCA\equiv V_a,m}^{+}\right)C_{APC\equiv V_a,m}-k_{PCA\equiv V_a,m}^{++}C_{V_a,m}$ **(S6.8)**	$k_{PCA\equiv V_a,m}^{cat}$ = 0.5 s^{-1} $k_{PCA\equiv V_a,m}^{+}$ = 1.0 s^{-1} $k_{PCA\equiv V_a,m}^{++}$ = 1.2× 10^{8} M^{-1}.s^{-1}	- The kinetic parameter values were estimated based on [77].

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Reference	Mathematical expression	Values used	Brief description
[49]	$\frac{dC_{PCA}}{dt} = \left(k^{cat}_{PCA\equiv V_a,m} + k^{+}_{PCA\equiv V_a,m}\right)C_{APC\equiv V_a,m} - k^{cat}_{PCA\equiv V_a,m}C_{V_a,m} + \left(k^{cat}_{PCA\equiv VIII_a,m} + k^{+}_{PCA\equiv VIII_a,m}\right)C_{PCA\equiv VII_a,m} - k^{++}_{PCA,VIII_a,m}C_{PCA}C_{VIII_a,m} + k_{flow}\left(C^{up}_{PCA} - C_{PCA}\right) - k_{diff}\left(C_{PCA} - C^{ec}_{PCA}\right) - k^{++}_{PCA,V_a}C_{PCA}C_{V_a} + \left(k^{+}_{PCA\equiv V_a} + k^{cat}_{PCA\equiv V_a}\right)C_{PCA\equiv V_a} - k^{++}_{PCA,VIII_a}C_{PCA}C_{VIII_a} + \left(k^{+}_{PCA\equiv VIII_a} + k^{cat}_{PCA\equiv VIII_a}\right)C_{PCA\equiv VIII_a} - k^{++}_{PCA,V^{hm}_a}C_{PCA}C_{V^{hm}_a} + k^{+}_{PCA\equiv V^{hm}_a}C_{PCA\equiv V^{hm}_a} + k^{cat}_{PCA\equiv V^{hm}_a}C_{PCA\equiv V^{hm}_a} - k^{++}_{PCA,V^{h}_a}C_{PCA}C_{V^{h}_a} + k^{+}_{PCA\equiv V^{m}_a}C_{PCA\equiv V^{m}_a} + k^{cat}_{PCA\equiv V^{m}_a}C_{PCA\equiv V^{m}_a}$ **(S6.9)**	$k^{cat}_{PCA\equiv V_a,m}$ = 0.5 s^{-1} $k^{+}_{PCA\equiv V_a,m}$ = 1.0 s^{-1} $k^{cat}_{PCA\equiv VIII_a,m}$ = 0.5 s^{-1} $k^{+}_{PCA\equiv VIII_a,m}$ = 1.0 s^{-1} $k^{++}_{PCA,VIII_a,m}$ = 1.2× 10^8 M^{-1}.s^{-1} k^{++}_{PCA,V_a} = 1.2× 10^8 M^{-1}.s^{-1} $k^{+}_{PCA\equiv V_a}$ = 1.0 s^{-1} $k^{cat}_{PCA\equiv V_a}$ = 0.5 s^{-1} $k^{++}_{PCA,VIII_a}$ = 1.2× 10^8 M^{-1}.s^{-1} $k^{+}_{PCA\equiv VIII_a}$ = 1.0 s^{-1} $k^{cat}_{PCA\equiv VIII_a}$ = 0.5 s^{-1} k^{++}_{PCA,V^{hm}_a} = 1.2× 10^8 M^{-1}.s^{-1} $k^{+}_{PCA\equiv V^{hm}_a}$ = 1.0 s^{-1} $k^{cat}_{PCA\equiv V^{hm}_a}$ = 0.5 s^{-1} k^{++}_{PCA,V^{h}_a} = 1.2× 10^8 M^{-1}.s^{-1} $k^{+}_{PCA\equiv V^{m}_a}$ = 1.0 s^{-1} $k^{cat}_{PCA\equiv V^{m}_a}$ = 0.5 s^{-1} k^{++}_{APC,V^{h}_a} = 1.2× 10^8 M^{-1}.s^{-1} $k^{+}_{APC\equiv V^{m}_a}$ = 1.0 s^{-1} $k^{cat}_{APC\equiv V^{m}_a}$ = 0.5 s^{-1}	- The kinetic parameter values were estimated based on [77].

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Reference	Mathematical expression	Values used	Brief description
[47]	$\frac{dC_{PCA}}{dt} = k_{flow}(C_{PCA}^{up} - C_{PCA}) - k_{diff}(C_{PCA} - C_{PCA}^{ec}) + (k_{PCA\equiv V_a,m}^{cat} + k_{PCA\equiv V_a,m}^{+})C_{APC\equiv V_a,m} - k_{PCA/V_a,m}^{++}C_{PCA}C_{V_a,m} + (k_{PCA\equiv V_a}^{cat} + k_{PCA\equiv V_a}^{+})C_{APC\equiv V_a} - k_{PCA/V_a}^{++}C_{PCA}C_{V_a} + (k_{PCA\equiv VIII_a,m}^{cat} + k_{PCA\equiv VIII_a,m}^{+})C_{APC\equiv VIII_a,m} - k_{PCA/VIII_a,m}^{++}C_{PCA}C_{VIII_a,m} + (k_{PCA\equiv VIII_a}^{cat} + k_{PCA\equiv VIII_a}^{+})C_{APC\equiv VIII_a} - k_{PCA/VIII_a}^{++}C_{PCA}C_{VIII_a}$ **(S6.10)**	$k_{PCA\equiv V_a,m}^{cat}$ = 0.5 s^{-1} $k_{PCA\equiv V_a,m}^{+}$ = 1.0 s^{-1} $k_{PCA/V_a,m}^{++}$ = 1.2× 10^8 $M^{-1}.s^{-1}$ $k_{PCA\equiv V_a}^{cat}$ = 0.5 s^{-1} $k_{PCA\equiv V_a}^{+}$ = 1.0 s^{-1} k_{PCA/V_a}^{++} = 1.2× 10^8 $M^{-1}.s^{-1}$ $k_{PCA\equiv VIII_a,m}^{cat}$ = 0.5 s^{-1} $k_{PCA\equiv VIII_a,m}^{+}$ = 1.0 s^{-1} $k_{PCA/VIII_a,m}^{++}$ = 1.2× 10^8 $M^{-1}.s^{-1}$ $k_{PCA\equiv VIII_a}^{cat}$ = 0.5 s^{-1} $k_{PCA\equiv VIII_a}^{+}$ = 1.0 s^{-1} $k_{PCA/VIII_a}^{++}$ = 1.2× 10^8 $M^{-1}.s^{-1}$	- The kinetic parameter values were estimated based on [77].
[30]	$S_{PCA} = -k_{PCA/V_a,m}^{++}C_{PCA}C_{V_a,m} + (k_{PCA\equiv V_a,m}^{cat} + k_{PCA\equiv V_a,m}^{+})C_{APC\equiv V_a,m} = -k_{PCA/VIII_a,m}^{++}C_{PCA}C_{VIII_a,m} + (k_{PCA\equiv VIII_a,m}^{cat} + k_{PCA\equiv VIII_a,m}^{+})C_{APC\equiv VIII_a,m}$ **(S6.11)**	$k_{PCA/V_a,m}^{++}$ = 1.2× 10^8 $M^{-1}.s^{-1}$ $k_{PCA\equiv V_a,m}^{cat}$ = 0.5 s^{-1} $k_{PCA\equiv V_a,m}^{+}$ = 1.0 s^{-1} $k_{PCA/VIII_a,m}^{++}$ = 1.2× 10^8 $M^{-1}.s^{-1}$ $k_{PCA\equiv VIII_a,m}^{cat}$ = 0.5 s^{-1} $k_{PCA\equiv VIII_a,m}^{+}$ = 1.0 s^{-1}	- Kinetics parameter values were taken from [80].
[50]	$S_{PC} = -\frac{k_{PC/II_a,f}^{cat}C_{PC}C_{II_a,f}}{k_{PC/II_a,f}^{m}+C_{PC}} - \frac{k_{PC/II_a,Tm}^{cat}C_{PC}C_{II_a,Tm}}{k_{PC/II_a,Tm}^{m}+C_{PC}} - k_{PC/PCA}^{++}C_{PC}C_{PCA}$ **(S6.12a)** $S_{PCA} = \frac{k_{PC/II_a,f}^{cat}C_{PC}C_{II_a,f}}{k_{PC/II_a,f}^{m}+C_{PC}} + k_{PC/PCA}^{++}C_{PC}C_{PCA} - (k_{PCA/\alpha_2M}^{++}C_{\alpha_2M} + k_{PCA/\alpha_2AP}^{++}C_{\alpha_2AP} + k_{PCA/\alpha_1AT}^{++}C_{\alpha_1AT} + k_{PCA/PCI}^{++}C_{PCI})C_{PCA}$ **(S6.12b)**	$k_{PC/II_a,f}^{cat}$ = 0.02 s^{-1}. $k_{PC/II_a,f}^{m}$ = 6.0× 10^{-5} M $k_{PC/II_a,Tm}^{cat}$ = 0.02 s^{-1} $k_{PC/II_a,Tm}^{m}$ = 6.0× 10^{-5} M $k_{PC/PCA}^{++}$ = 4.7× 10^3 $M^{-1}\cdot s^{-1}$ k_{PCA/α_2M}^{++} = 1.0× 10^2 $M^{-1}\cdot s^{-1}$ k_{PCA/α_2AP}^{++} = 1.0× 10^2 $M^{-1}\cdot s^{-1}$ k_{PCA/α_1AT}^{++} = 1.167× 10^1 $M^{-1}\cdot s^{-1}$ $k_{PCA/PCI}^{++}$ = 5.83× 10^{-3} s^{-1}	- The values $k_{PC/II_a,f}^{cat}$, $k_{PC/II_a,f}^{m}$, $k_{PC/II_a,Tm}^{cat}$ and $k_{PC/II_a,Tm}^{m}$ were taken from [81]. - The value $k_{PC/PCA}^{++}$ was taken from [82]. - The values k_{PCA/α_2AP}^{++} and k_{PCA/α_2M}^{++} were taken from [83]. The value k_{PCA/α_1AT}^{++} was taken from [84]. The value $k_{PCA/PCI}^{++}$ was taken from [85].

8. Mathematical equations representing fibrin(ogen)

Table S7. List of equations representing fibrinogen and fibrin.

Reference	Mathematical expression	Values used / Variable description	Brief description
[1,27]	$\frac{\partial C_{F_g}}{\partial t} + \nabla \cdot \left(VC_{F_g}\right) = D\Delta C_{F_g} - k^{+}_{F_g/II_a} C_{II_a} C_{F_g}$ **(S7.1a)** $\frac{\partial C_{F_n}}{\partial t} + \nabla \cdot \left(VC_{F_n}\right) = D\Delta C_{F_n} k^{++}_{F_g/II_a} C_{II_a} C_{F_g} - k^{+}_{F_p/F_n} C_{F_n}$ **(S7.1b)** $\frac{\partial C_{F_p}}{\partial t} = k^{+}_{F_p,F_n} C_{F_n}$ **(S7.1c)**	$k^{+}_{F_g/II_a}$ = 1.383× 10^{-4} s^{-1} [27]. $k^{+}_{F_p/F_n}$ = 1.833× 10^{-3} s^{-1} [27].	- Modeled as a system of CDR equations. - The kinetics parameters were taken from [55,86].
[35]	$\frac{\partial C_{F_g}}{\partial t} + \nabla \cdot \left(VC_{F_g}\right) = D\Delta C_{F_g} - k^{++}_{F_g/II_a} C_{F_g} C_{II_a} + k^{+}_{F_g\equiv II_a} C_{F_g\equiv II_a} +$ $k^{++}_{F_g\equiv II_a/ATIII} C_{F_g\equiv II_a} C_{ATIII}$ **(S7.2a)** $\frac{\partial C_{F_n}}{\partial t} + \nabla \cdot \left(VC_{F_n}\right) = D\Delta C_{F_n} - k^{++}_{F_n/II_a} C_{F_n} C_{II_a} + k^{+}_{F_n\equiv II_a} C_{F_n\equiv II_a} +$ $k^{++}_{F_n\equiv II_a/ATIII} C_{F_n\equiv II_a} C_{ATIII}$ **(S7.2b)**	$k^{++}_{F_g/II_a}$ = 4.0× 10^{7} M^{-1}.s^{-1} [35]. $k^{+}_{F_g\equiv II_a}$ = 200 s^{-1} [35]. $k^{++}_{F_g\equiv II_a/ATIII}$ = 1.0× 10^{4} M^{-1}.s^{-1} [35]. $k^{++}_{F_n/II_a}$ = 2.0× 10^{7} M^{-1}.s^{-1} [35]. $k^{+}_{F_n\equiv II_a}$ = 200 s^{-1} [35]. $k^{++}_{F_n\equiv II_a/ATIII}$ = 1.0× 10^{4} M^{-1}.s^{-1} [35].	- Modeled as a system of CDR equations.
[9,10]	$\frac{\partial C_{F_g}}{\partial t} + \nabla \cdot \left(VC_{F_g}\right) = D\Delta C_{F_g} - \frac{k^{cat}_{F_g/II_a} C_{II_a} C_{F_g}}{k^{m}_{F_g/II_a} + C_{F_g}}$ **(S7.3a)** $\frac{\partial C_{F_n}}{\partial t} + \nabla \cdot \left(VC_{F_n}\right) = D\Delta C_{F_n} + \frac{k^{cat}_{F_g/II_a} C_{II_a} C_{F_g}}{k^{m}_{F_g/II_a} + C_{F_g}} - k^{+}_{F_p/F_n} C_{F_n}$ **(S7.3b)** $\frac{\partial C_{F_p}}{\partial t} = k^{+}_{F_p/F_n} C_{F_n}$ **(S7.3c)**	$C_{F_g}(t = 0)$ = 7× 10^{-6} M. $k^{cat}_{F_g/II_a}$ = 59 s^{-1} [9,10]. $k^{m}_{F_g/II_a}$ = 3.16× 10^{-6} M [9,10]. $k^{+}_{F_p,F_n}$ = 0.1 s^{-1} [9,10].	- The values $k^{cat}_{F_g,II_a}$ and $k^{m}_{F_g/II_a}$ were taken from [79].
[50]	$S_{F_g} = -\frac{k^{cat}_{F_g/II_a} C_{II_a} C_{F_g}}{k^{m}_{F_g/II_a} + C_{F_g}}$ **(S7.4a)** $S_{F_n} = \frac{k^{cat}_{F_g/II_a} C_{II_a} C_{F_g}}{k^{m}_{F_g/II_a} + C_{F_g}}$ **(S7.4b)**	$C_{F_g}(t = 0)$ = 7.6× 10^{-6} M [50]. $C_{F_n}(t = 0)$ = 0 M [50]. D_{F_g} = 2.0× 10^{-11} m^{2}.s^{-1} [50]. D_{F_n} = 0 m^{2}.s^{-1} [50]. $k^{cat}_{F_g/II_a}$ = 84 s^{-1} [50]. $k^{m}_{F_g/II_a}$ = 7.2× 10^{-6} M [50].	The values $k^{cat}_{F_g,II_a}$ and $k^{m}_{F_g,II_a}$ were taken from [87].

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Reference	Mathematical expression	Values used / Variable description	Brief description
[14,17–21,24,29,88]	$S_{F_g}=-\frac{k^{cat}_{F_g/II_a}C_{II_a}C_{F_g}}{k^{m}_{F_g/II_a}+C_{F_g}}$ **(S7.5a)** $S_{F_n}=\frac{k^{cat}_{F_g/II_a}C_{II_a}C_{F_g}}{k^{m}_{F_g/II_a}+C_{F_g}}-\frac{k^{cat}_{F_g/PLA}C_{PLA}C_{F_n}}{k^{m}_{F_g/PLA}+C_{F_n}}$ **(S7.5b)**	$C_{F_g}(t=0)$ = 7.0×10^{-6} M [14,19,24]; 6.654×10^{-6} M (clot), 7.0×10^{-6} M (circulating blood) [18,29]. $C_{F_n}(t=0)$ = 3.5×10^{-7} M (clot), 0 M (circulating blood) [18,29]; 7.0×10^{-9} M [19]; 0 M [14,24]. D_{F_g} = 3.1×10^{-11} m^2.s^{-1} [14,24]. D_{F_n} = 2.47×10^{-11} m^2.s^{-1} [14,24]. $k^{cat}_{F_g/II_a}$ = 59 s^{-1} [14,17–21,24,29]. $k^{m}_{F_g/II_a}$ = 3.16×10^{-6} M [14,17–21,24,29]. $k^{cat}_{F_g/PLA}$ = 25 s^{-1} [14,17–21,24,29]. $k^{m}_{F_g/PLA}$ = 2.5×10^{-4} M [14,17–21,24,29].	- Biochemistry reactions of the coagulation cascade of studies [14,17–21,24,29,88] were modeled via Anand's model [16]. The values $k^{cat}_{F_g/II_a}$ and $k^{m}_{F_g/II_a}$ were taken from [79]. The values $k^{cat}_{F_g/PLA}$ and $k^{m}_{F_g/PLA}$ were taken from [89].
[44]	$\frac{\partial C_{F_g}}{\partial t}=-\nabla\cdot\left(VC_{F_g}-D\nabla C_{F_g}\right)-k^{++}_{F_g/II_am}C_{F_g}C_{II_am}$ **(S7.6a)** $\frac{\partial C_{F_n}}{\partial t}=\nabla\cdot\left(D\nabla C_{F_n}\right)+k^{++}_{F_g/II_am}C_{F_g}C_{II_am}$ **(S7.6b)**	$C_{F_g}(t=0)$ = 5.4×10^{-6} M [44]. $k^{++}_{F_g/II_am}$ = 1.16×10^{7} M^{-1}.s^{-1} [44].	- Modeled as a system of PDEs.
[56]	$\frac{\partial C_{F_g}}{\partial t}+(V\cdot\nabla)C_{F_g}-D_{F_g}\nabla^2 C_{F_g}=-\frac{k^{cat}_{F_g/II_a}C_{II_a}C_{F_g}}{k^{m}_{F_g/II_a}+C_{F_g}}$ **(S7.7a)** $\frac{\partial C_{F_n}}{\partial t}+(V\cdot\nabla)C_{F_n}-D_{F_n}\nabla^2 C_{F_n}=\frac{k^{cat}_{F_g/II_a}C_{II_a}C_{F_g}}{k^{m}_{F_g/II_a}+C_{F_g}}+k_p\left(C_{F_n}\right)^2$ **(S7.7b)**	$k^{cat}_{F_g/II_a}$ = 84 s^{-1} [56]. $k^{m}_{F_g/II_a}$ = 7.2×10^{-6} M [56]. k_p = 8.2×10^{-1} M.s^{-1} [56].	- The values $k^{cat}_{F_g/II_a}$ and $k^{m}_{F_g/II_a}$ were taken from [57].
[90]	$\frac{\partial C_{F_n}}{\partial t}=D_{F_n}\Delta C_{F_n}-\nabla\cdot\left(vC_{F_n}\right)+\beta C_{F_n}(1-C_{F_n})$ **(S7.8)**	$\beta =$ 0.01 – 0.7 (Reaction term coefficient)	
[91,92]	$\frac{\partial C_{F_g}}{\partial t}=v\cdot\nabla C_{F_g}=D_{F_g}\Delta C_{F_g}-k^{++}_{F_g/II_a}C_{II_a}C_{F_g}\left(C^{sat}_{F_g}-C_{F_g}\right)$ **(S7.9a)** $\frac{\partial F_p}{\partial t}=k^{++}_{F_g/II_a}C_{II_a}C_{F_g}\left(C^{sat}_{F_g}-C_{F_g}\right)$ **(S7.9b)**	$C^{sat}_{F_g}$ = 1 (non-dimensional) $k^{++}_{F_g/II_a}$ = 0.1 s^{-1}	

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Reference	Mathematical expression	Values used / Variable description	Brief description
[3]	$S_{F_n} = f_{emb} C_{F_{g,d}} - \alpha_1 \frac{k^{cat}_{F_g/II_a} C_{II_a} C_{F_g}}{k^m_{F_g/II_a} + C_{F_g}}$ **(S7.10a)** $S_{F_n} = f_{emb} C_{F_{n,d}} - k_{F_{n,d}} C_{F_{n,d}} + \alpha_1 \frac{k^{cat}_{F_g/II_a} C_{II_a} C_{F_g}}{k^m_{F_g/II_a} + C_{F_g}}$ **(S7.10b)** $S_{F_{g,d}} = k_{F_{g,d}} C_{F_g} - \alpha \frac{k^{cat}_{F_g/II_a} C_{II_a} C_{F_{gd}}}{k^m_{F_g/II_a} + C_{F_{gd}}} - f_{emb} C_{F_{g,d}}$ **(S7.10c)** $S_{F_{n,d}} = k_{F_{g,d}} C_{F_n} - \alpha \frac{k^{cat}_{F_g/II_a} C_{II_a} C_{F_{gd}}}{k^m_{F_g/II_a} + C_{F_{gd}}} - f_{emb} C_{F_{n,d}}$ **(S7.10d)**	$C_{F_g}(t = 0) = 1.8\times 10^{-5}$ M [3]. $k^{cat}_{F_g/II_a} = 80$ s^{-1} [3]. $k^m_{F_g/II_a} = 6.5\times 10^{-6}$ M^{-1}.s^{-1} [3].	The values $k^{cat}_{F_g/II_a}$ and $k^m_{F_g/II_a}$ were taken from [93].
[93]	$\frac{dC_{F_n}}{dt} = \eta_5 \alpha_5 C_{II_a}$ **(S7.11)**	$\eta_5 = 0.05$ [93] $\alpha_5 = 58.8$ s^{-1} [93].	- Coagulation cascade and fibrin(ogen) modeled as a system of ODEs.
[94]	$\frac{\partial C_{F_g}}{\partial t} = -k_g C_{F_g} C_\theta - \epsilon_g \left(C_{F_g} - C^0_{F_g}\right) - \nabla \cdot (\vec{V} C_{F_g} - D_g \nabla C_{F_g})$ **(S7.12a)** $\frac{\partial M_1}{\partial t} = k_g C_{F_g} C_\theta - k_T M_1 - \nabla \cdot \left(b_p \vec{V} M_1 - D_f \nabla M_1\right)$ **(S7.12b)** $\frac{\partial M_2}{\partial t} = k_g C_{F_g} C_\theta + 4k_p (M_2 + M_1)^2 - \frac{k_b}{3}\left(\frac{M_2^2}{M_1} - M_1\right) - k_T M_2 - \nabla \cdot \left(b_p \vec{V} M_2 - D_f \nabla M_2\right)$ **(S7.12c)**	$k_g = 5.0\times 10^3$ M^{-1}.s^{-1} $\epsilon_g = 1.66\times 10^{-6}$ s^{-1} $C^0_{F_g} = 9.0\times 10^{-6}$ M $k_b = 1.67\times 10^{-3}$ s^{-1}	- θ is concentration of the activation of the biochemical network of blood coagulation. - Models the first and second fibrin moments (M_1 and M_2). - Modeled as PDEs.
[95]	$F(r_{ij}) = \chi(\lvert r_{ij}\rvert - a_{ij})$ **(S7.13a)** $F(r_{ij}) = \pi\left(1 - \frac{r_{ij}}{R_{cut}}\right)$ **(S7.13a)** $q = 1 - q_0 H(r_{ij}) and\ if\ r_{ij} > R_{cut}$ **(S7.13a)**	χ: elasticity of the red blood cell r_{ij}: separation distance between particles *i* and *j*. a_{ij}: Bonding distance. $F(r_{ij})$: Force between two bounded particles *i* and *j*. R_{cut}: cut-off radius. q: Probability of bound break. q_0: Constant. $H(r_{ij})$: intersection volume between two fluid particles.	
[64]	$\frac{\partial C_{F_n}}{\partial t} = k^+_{F_n,II_a} C_{II_a}$ **(S7.14)**	$k^+_{F_n,II_a} = 1$ s^{-1} [64].	

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Reference	Mathematical expression	Values used / Variable description	Brief description
[96]	$\frac{dL}{dt} = k_{cat} S_{PLS} \gamma$ **(S7.15)**	L : amount of fibrin lysed. k_{cat}: reaction rate constant. S_{PLS}: Adsorbed plasmin. γ: solubilization rate.	
[97]	$F_2(r) = 0 \; for \; R \le \frac{r}{a} \le L$ **(S7.16)**	a: Platelet radius. r: Distance from the center of the platelet to the wall or the surface of the other platelet.	
[98]	$\frac{dB_{high,F_n}}{dt} = -k^{++}_{B_{high,F_n}/II_a} C_{B_{high,F_n}} C_{II_a} + k^{+}_{B_{high,F_n} \equiv II_a} C_{B_{high,F_n} \equiv II_a}$ **(S7.17a)** $\frac{dB_{low,F_n}}{dt} = -k^{++}_{B_{low,F_n}/II_a} C_{B_{low,F_n}} C_{II_a} + k^{+}_{B_{low,F_n} \equiv II_a} C_{B_{low,F_n} \equiv II_a}$ **(S7.17b)**	$k^{++}_{B_{high,F_n}/II_a}$ = 1.0× 10^6 $M^{-1}.s^{-1}$ [98]. $k^{+}_{B_{high,F_n} \equiv II_a}$ = 0.15 s^{-1} [98]. $k^{++}_{B_{low,F_n}/II_a}$ = 1.0× 10^6 $M^{-1}.s^{-1}$ [98]. $k^{+}_{B_{low,F_n} \equiv II_a}$ = 2.8 s^{-1} [98].	
[99]	$f_{GPIIb/III-} \begin{cases} k_{GPIIb/III-fg}\left(\left\|r_{ij}^{GPIIb/III-fg}\right\| - I_0\right) n_{ij}^{GPIIb/III-fg} \; \left(\left\|r_{ij}^{GPIIb/III}\right.\right. \\ 0 \; \left(\left\|r_{ij}^{GPIIb/III-f}\right\| > d_a\right) \end{cases}$ **(S7.18)**	$k_{GPIIb/III-fg}$ = 1.0× 10^{-4} N/m The spring constant for interactions between GPIIb/III and fibrinogen.	
[100]	$\alpha_{AA} = K^{aa}_{AA}(n^{max}_{AA}\phi_a)^2 + K^{ab}_{AA} n^{max}_{AA} \phi_a (n^{max}_{AA}\phi_{ba} - 2z_{AA}) + K^{bb}_{AA}(n^{max}_{AA}\phi_{ba} - 2z_{AA})^2$ **(S7.19)**	K^{aa}_{AA} = 1.6 × 10^5 $M^{-1}.s^{-1}$ ($\alpha_{IIb}\beta_3$ -fibrinogen bound formation rate) K^{ab}_{AA} = 1.6 × 10^5 $M^{-1}.s^{-1}$ ($\alpha_{IIb}\beta_3$ -fibrinogen bound formation rate) n^{max}_{AA} = 50000 (maximum number of $\alpha_{IIb}\beta_3$ receptors on a platelet surface)	
[101]	$k_D(R_f, n_s^*) = R_f^2 (16[n_s^*]^{1.5}[1 + 56[n_s^*]^3])^{-1}$ **(S7.20)**	R_f = 140 (fibrin fiber radius) n_s^* : relative volume occupied by the fibres.	

9. Mathematical equations representing vWF.

Table S8. List of Equations representing vWF.

Reference	Mathematical expression	Variables description
[99]	$N_{GPIb/IX/V-vWF} = \begin{cases} 1, if\ (\gamma < \gamma_{crit}) \\ int(\alpha(\gamma - \gamma_{crit}) + 1), if\ (\gamma_{crit} < \gamma) \end{cases}$ **(S8.1a)** $f_{GPIb/IX/V-vWF} = \begin{cases} k_{GPIb/IX/V-vWF}(\lvert \boldsymbol{r}_{ij}^{GPIb/IX/V-vWF} \rvert - l_0)\boldsymbol{n}_{ij}^{GPIb/IX/V-vWF}, if\ (\lvert \boldsymbol{r}_{ij}^{GPIb/IX/V-vWF} \rvert < d_a) \\ 0, if\ (\lvert \boldsymbol{r}_{ij}^{GPIb/IX/V-v} \rvert > d_a) \end{cases}$ **(S8.1b)** $N_{GPIIb/III-vWF} = \begin{cases} 1, if\ (\gamma < \gamma_{crit}) \\ int(\alpha(\gamma - \gamma_{crit}) + 1), if\ (\gamma_{crit} < \gamma) \end{cases}$ **(S8.1c)** $f_{GPIIb/III-vWF} = \begin{cases} k_{GPIIb/III-vWF}(\lvert \boldsymbol{r}_{ij}^{GPIIb/III-v} \rvert - l_0)\boldsymbol{n}_{ij}^{GPIIb/III-v}, if\ (\lvert \boldsymbol{r}_{ij}^{GPIIb/III-vWF} \rvert < d_a) \\ 0, if\ (\lvert \boldsymbol{r}_{ij}^{GPIIb/III-v} \rvert > d_a) \end{cases}$ **(S8.1d)**	$N_{GPIb/IX/V-vWF}$: Number of springs that express interactions between GPIb/IX/V and vWF. $f_{GPIb/IX/V-vWF}$: Force of interactions between GPIb/IX/V and vWF. γ: Shear rate. γ_{crit}: Critical threshold of the shear rate. α: Proportional constant. $k_{GPIb/IX/V-vWF}$: Spring constant of interactions between GPIb/IX/V and vWF.. l_0: Natural length. $\boldsymbol{n}_{ij}^{GPIb/IX/V-vWF}$: Unit vector between particle *i* (adhered) and *j* (wall) of interactions between GPIb/IX/V and vWF. $\boldsymbol{r}_{ij}^{GPIb/IX/V-vWF}$: Distance between particle *i* (adhered) and *j* (wall) of interactions between GPIb/IX/V and vWF. $N_{GPIIb/III-vWF}$: Number of springs that express interactions between GPIIb/III and vWF. $f_{GPIIb/III-vWF}$: Force of interactions between GPIIb/III and vWF. $k_{GPIIb/III-vWF}$: Spring constant of interactions between GPIIb/III and vWF. $\boldsymbol{r}_{ij}^{GPIIb/III-vWF}$: Distance between particle *i* (adhered) and *j* (wall) of interactions between GPIIb/III and vWF. $\boldsymbol{n}_{ij}^{GPIIb/III-vWF}$: Unit vector between particle *i* (adhered) and *j* (wall) of interactions between GPIIb/III and vWF.

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Reference	Mathematical expression	Variables description
[102]	$K_1 = \frac{1}{2}\rho v^2 A(B + C \cdot tanh(D \cdot S)^2)$ **(S8.2a)** $K = \chi + \beta + \alpha + K_1$ **(S8.2b)**	K_1: Spring constant between GPIbα and vWF. ρ: Density of blood. v: Blood flow velocity. A,B,C,D: runable constants. S: Stretch of the platelet/platelet bond. χ, β, α: Adjustable parameters. K: Spring constant between GPIIa/IIIa and VWF.
[100]	$\alpha_{GG} = K_{GG}^{ab}[n_{GG}^{max}(\phi_a + \phi_u)n_{GG}^{max}(\phi_{ba} + \phi_{bu}) - 2z_{GG}] + K_{GG}^{bb}[n_{GG}^{max}(\phi_{ba} + \phi_{bu}) - 2z_{GG}]^2$ **(S8.3)**	α_{GG}: Formation of GG bonds n_{GG}^{max}: total number of GPIba receptors on the platelet surface. K_{GG}^{ab}: Second order rate constant. K_{GG}^{bb}: Second order rate constant. ϕ_a: Mobile active platelet. ϕ_u: Mobile unactive platelet. ϕ_{ba}: Bound activated platelet. ϕ_{bu}: Bound unactivated platelet. z_{GG}: number density of platelet-platelet bonds mediated by platelet GPIbalpha.
[39]	$f_{vWF} = \frac{C_{vWF}}{1+exp\left[-\left(\tau-\tau_{\frac{1}{2}}\right)/\Delta\tau\right]}$ **(S8.4)**	f_{vWF}: Amplification function. C_{vWF}: Maximum achievable value. $\tau_{\frac{1}{2}}$: Shear stress when half of the vWF multimers are fully unfolded. $\Delta\tau$: Shear stress duration of the transition. τ: Shear stress.

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Reference	Mathematical expression	Variables description
[103]	$\vec{F}_{ij}^{GPIb}(\lvert\vec{r}_{ij}\rvert) = A_{GPIb-det}e^{-\lambda_{GPIb-det}(\lvert\vec{r}_{ij}\rvert-2R)}\left(e^{-\lambda_{GPIb-det}(\lvert\vec{r}_{ij}\rvert-2R)}-1\right)\frac{\vec{r}_{ij}}{\lvert\vec{r}_{ij}\rvert}$ **(S8.5a)** $\vec{F}_{ij}^{sotch.} = \sigma_{ij}\vec{F}_{ij}^{GPIb}k_{st}\left(\lvert\vec{l}_{ij}\rvert - L_0\right)\frac{l_{ij}}{\lvert\vec{l}_{ij}\rvert}$ **(S8.5b)** $k_{0,as} = k_0[(1-\delta)\beta_i+\delta]\left[(1-\delta)\beta_j+\delta\right]$ **(S8.5c)**	$A_{GPIb-det}$: Constant. $\lambda_{GPIb-det}$: Constant. $\vec{r}_{ij}$: Distance between particles i and j. R: Platelet radius. $\vec{F}_{ij}^{GPIb}$: Interaction force between GPIb and platelet mediated by vWF. $\vec{F}_{ij}^{sotch.}$: Force by GPIb-mediated platelet interaction. k_{st}: Spring coefficient. $\lvert\vec{l}_{ij}\rvert$: Length of the spring. L_0: Equilibrium spring length. σ_{ij}: Stochastic coefficient. k_0: Maximum rate. $k_0\delta^2$ Minimum rate.
[104]	$K_{on} = \frac{K_{on}^m}{1+exp\left(\frac{\Delta G - F_t\Delta x}{k_BT}\right)}$ **(S8.6)**	K_{on}: On-rate of the binding of GP1b-A1 onto Vwf. K_{on}^m: Maximum on-rate. F_t: vWF internal tension force. ΔG: Energy barrier. Δx: displacement along the tension axis.
[105]	$F_{ad} = \frac{1}{Dis_{ad}+1}F_{ad\_max}n_{ad}$ **(S8.7a)** $F_{ag} = \frac{1}{Dis_{ag}+1}F_{ag\_max}n_{ag}$ **(S8.7b)**	F_{ad}: Adhesion force. F_{ag}: Aggregation force. Dis_{ad} and Dis_{ag}: distance from the platelet to the surface of the injured endangium and thrombus, respectively. n_{ad} and n_{ag}: unit vector distance between the points of the bounds. F_{ad_max} and F_{ag_max} : maximal magnate of the adhesion and aggregation forces, respectively.
[36]	$S_{vWF_c} = -k_{c-s}C_{vWF_c} + k_{s-c}C_{vWF_s}$ **(S8.8a)** $S_{vWF_s} = k_{c-s}C_{vWF_c} - k_{s-c}C_{vWF_s}$ **(S8.8b)**	S_{vWF_c}: Reaction source term for collapsed vWF. S_{vWF_s}: Reaction source term for stretched vWF. k_{c-s}: Conversion rate of collapsed-to-stretched vWF. k_{s-c}: Conversion rate of stretched-to-collapsed Vwf.

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