Table S1: Extended reactions and parameter values used in this coagulation model. The mode consists of 193 protein or protein complexes and 301 interactions. This model is an extension of the published extrinsic pathway model (38). New reactions, e.g., the activation of platelet by thrombin through PARs, the release of ADP and TXA2 from activated platelets, platelet activation by ADP and TXA2, the intrinsic pathway reactions, were added to the model. The kinetics of binding and reaction interactions are assumed to follow mass action rate laws where k^+ denotes the on-rate constant, k^- denotes the off-rate constant and k_c denotes the catalytic rate constants. All binding interactions are assumed to be reversible. Values for the kinetic parameters and network structure were taken from the literature, see (20, 30, 62, 66–70, 72–74, 76, 77, 83–115).

Reaction	k^+ $(AU^{-1}s^{-1})$	k^- (s^{-1})	k_c (s^{-1})	Source
VII+TF ⇌ VII-TF	$3.50 \times 10^{-2} \pm 2.24 \times 10^{-2}$	$4.91 \times 10^{-3} \pm 1.03 \times 10^{-3}$	–	(73)
VIIa+TF ⇌ VIIa-TF	$4.59 \times 10^{-2} \pm 9.26 \times 10^{-3}$	$5.28 \times 10^{-3} \pm 1.82 \times 10^{-3}$	–	(73)
Xa+VII-TF ⇌ Xa-VII-TF	$4.45 \times 10^{-3} \pm 1.23 \times 10^{-3}$	$8.14 \times 10^{-1} \pm 3.44 \times 10^{-1}$	–	(73)
Xa-VII-TF→ VIIa-TF + Xa	–	–	$3.35 \times 10^{-3} \pm 1.42 \times 10^{-3}$	(73)
IIa+VII-TF ⇌ IIa-VII-TF	$3.11 \times 10^{-4} \pm 1.26 \times 10^{-4}$	$8.46 \times 10^{-1} \pm 4.74 \times 10^{-1}$	–	(73)
IIa-VII-TF → VIIa-TF +IIa	–	–	$3.52 \times 10^{-4} \pm 6.92 \times 10^{-5}$	(73)
X+VII-TF ⇌ X-VIIa-TF	$9.35 \times 10^{-2} \pm 2.42 \times 10^{-2}$	6.19 ± 1.53	–	(86)
X-VII-TF → VIIa-TF + Xa	–	–	$1.50 \pm 4.20 \times 10^{-1}$	(86)
IX+VIIa-TF ⇌ IX-VIIa-TF	$1.53 \times 10^{-1} \pm 9.02 \times 10^{-2}$	$2.12 \pm 3.94 \times 10^{-1}$	–	(86)
IX-VII-TF → VIIa-TF + IXa	–	–	$3.30 \times 10^{-1} \pm 1.14 \times 10^{-1}$	(86)
VII+Xa ⇌ VII-Xa	$1.90 \times 10^{-1} \pm 1.20 \times 10^{-1}$	$8.07 \times 10^{-1} \pm 3.01 \times 10^{-1}$	–	(73, 77)
VII-Xa → VIIa + Xa	–	–	$5.74 \times 10^{-1} \pm 2.02 \times 10^{-1}$	(73, 77)
VII+IIa ⇌ VII-IIa	$7.75 \times 10^{-2} \pm 4.13 \times 10^{-2}$	$1.04 \times 10^{1} \pm 2.06$	–	(73, 77)
VII-IIa → VIIa + IIa	–	–	$4.66 \times 10^{-1} \pm 8.30 \times 10^{-2}$	(73, 77)
V+IIa ⇌ V-IIa	$7.99 \times 10^{-2} \pm 5.09 \times 10^{-2}$	4.31 ± 1.80[1]	–	(86)
V-IIa → Va + IIa	–	–	$3.34 \times 10^{-1} \pm 2.04 \times 10^{-1}$	(86)
VIII+IIa ⇌ VIII-IIa	$8.58 \times 10^{-2} \pm 1.62 \times 10^{-2}$	6.84 ± 3.95[2]	–	(86)
VIII-IIa → VIIIa + IIa	–	–	$3.37 \pm 3.70 \times 10^{-1}$	(86)
Xa + IX ⇌ Xa-IX	$7.37 \times 10^{-2} \pm 2.96 \times 10^{-2}$	$1.11 \pm 4.59 \times 10^{-1}$	–	(74)
Xa-IX → Xa + IXa	–	–	$2.92 \times 10^{-2} \pm 3.32 \times 10^{-3}$	(74)
Xa + V ⇌ Xa-V	$9.72 \times 10^{-2} \pm 1.18 \times 10^{-2}$	1.57 ± 1.15	–	(74, 86)
Xa-V → Xa + Va	–	–	$4.06 \times 10^{-2} \pm 7.67 \times 10^{-3}$	(74, 86)
Xa + VIII ⇌ Xa-VIII	$9.77 \times 10^{-2} \pm 2.00 \times 10^{-2}$	$1.63 \pm 8.04 \times 10^{-1}$	–	(74, 86)
Xa-VIII → Xa + VIIIa	–	–	$2.18 \times 10^{-2} \pm 5.35 \times 10^{-3}$	(74, 86)
Xa + II ⇌ Xa-II	$7.70 \times 10^{-6} \pm 2.19 \times 10^{-6}$	$1.09 \times 10^{-9} \pm 1.51 \times 10^{-10}$	–	(77)
Xa-II ⇌ IIa + Xa	–	–	$4.98 \times 10^{-6} \pm 2.65 \times 10^{-6}$	(77)
IX + P9s ⇌ IX-P9s	$8.71 \times 10^{-3} \pm 4.86 \times 10^{-3}$	$2.23 \times 10^{-2} \pm 7.63 \times 10^{-3}$	–	(73, 84)
IXa + P9s ⇌ IXa-P9s	$3.27 \times 10^{-5} \pm 1.06 \times 10^{-5}$	$4.74 \times 10^{-3} \pm 1.30 \times 10^{-3}$	–	(73, 84)
IXa + P9s* ⇌ IXa-P9s*	$2.84 \times 10^{-5} \pm 5.78 \times 10^{-6}$	$4.27 \times 10^{-3} \pm 1.63 \times 10^{-3}$	–	(73, 84)
X + P10s ⇌ X-P10s	$8.93 \times 10^{-2} \pm 4.44 \times 10^{-2}$	$2.48 \times 10^{-2} \pm 7.30 \times 10^{-3}$	–	(73, 84)
Xa + P10s ⇌ Xa-P10s	$7.90 \times 10^{-2} \pm 2.97 \times 10^{-2}$	$8.09 \times 10^{-3} \pm 5.85 \times 10^{-3}$	–	(73, 84)
V + P5s ⇌ V-P5s	6.33 ± 1.77	$1.42 \times 10^{-1} \pm 4.21 \times 10^{-2}$	–	(73, 83)
Va + P5s ⇌ Va-P5s	5.51 ± 1.07	$1.10 \times 10^{-1} \pm 3.29 \times 10^{-2}$	–	(73, 83)
VIII + P8s ⇌ VIII-P8s	$1.59 \times 10^{-1} \pm 1.08 \times 10^{-1}$	$1.22 \times 10^{-1} \pm 3.48 \times 10^{-2}$	–	(73, 85)
VIIIa + P8s ⇌ VIIIa-P8s	$2.07 \times 10^{-2} \pm 1.25 \times 10^{-2}$	$1.58 \times 10^{-1} \pm 9.01 \times 10^{-2}$	–	(73, 85)
II + P2s ⇌ II-P2s	$8.65 \times 10^{-3} \pm 3.12 \times 10^{-3}$	$1.06 \times 10^{1} \pm 4.96$	–	(73)
IIa + P2s ⇌ IIa-P2s	$3.40 \times 10^{-4} \pm 1.58 \times 10^{-4}$	1.53 ± 1.28	–	(73)
PL + Psub → AP-Psub	–	–	$9.31 \times 10^{-1} \pm 3.99 \times 10^{-1}$	(73)
PL + Psub → PL-Psub	$1.76 \times 10^{1} \pm 5.00$	–	–	(73)
AP + Psub → AP-Psub	–	–	$1.63 \times 10^{-1} \pm 6.26 \times 10^{-2}$	(73)
PL + AP ⇌ PL-AP	$5.14 \times 10^{-7} \pm 1.41 \times 10^{-7}$	$1.09 \pm 4.17 \times 10^{-1}$	–	(73)
PL-AP ⇌ 2AP	–	–	$5.97 \times 10^{-7} \pm 1.43 \times 10^{-7}$	(73)
PL + AP-Psub ⇌ PL-AP-Psub	$4.31 \times 10^{-7} \pm 1.71 \times 10^{-7}$	$1.62 \pm 9.73 \times 10^{-1}$	–	(73)
PL-AP-Psub → AP+ AP-Psub	–	–	$8.05 \times 10^{-7} \pm 4.50 \times 10^{-7}$	(73)
V-P5s + Xa-P10s ⇌ V-P5s-Xa-P10s	$2.70 \times 10^{-1} \pm 2.37 \times 10^{-1}$	$8.31 \times 10^{-1} \pm 4.61 \times 10^{-1}$	–	(73, 86)
V-P5s-Xa-P10s → Va-P5s + Xa-P10s	–	–	5.58 ± 1.09	(73, 86)
V-P5s + IIa-P2s ⇌ V-P5s-IIa-P2s	$1.39 \times 10^{-2} \pm 1.02 \times 10^{-2}$	$7.73 \times 10^{-1} \pm 5.28 \times 10^{-1}$	–	(73, 86)
V-P5s-IIa-P10s → Va-P5s + IIa-P10s	–	–	$1.23 \times 10^{1} \pm 9.74$	(73, 86)
X-P10s+tenase ⇌ X-P10s-tenase	$7.49 \times 10^{-2} \pm 2.43 \times 10^{-2}$	$1.39 \times 10^{-2} \pm 4.56 \times 10^{-3}$	–	(73, 86)
X-P10s-tenase → Xa-P10s + tenase	–	–	$2.05 \times 10^{1} \pm 3.70$	(73, 86)
X-P10s+tenase* ⇌ X-P10s-tenase*	$7.78 \times 10^{-2} \pm 3.06 \times 10^{-2}$	$1.15 \times 10^{-2} \pm 3.19 \times 10^{-3}$	–	(73, 86)
X-P10s-tenase* → Xa-P10s + tenase*	–	–	$2.17 \times 10^{1} \pm 6.59$	(73, 86)
VIII-P8s + Xa-P10s ⇌ VIII-P8s-Xa-P10s	$1.03 \times 10^{-1} \pm 2.42 \times 10^{-2}$	$1.71 \pm 8.09 \times 10^{-1}$	–	(73, 86)
VIII-P8s-Xa-P10s → VIIIa-P8s + Xa-P10s	–	–	$1.63 \times 10^{-2} \pm 6.08 \times 10^{-3}$[2]	(73, 86)
VIII-P8s + IIa-P2s ⇌ VIII-P8s-IIa-P2s	$9.81 \times 10^{-2} \pm 3.20 \times 10^{-2}$	$1.28 \times 10^{1} \pm 2.95$[2]	–	(73, 86)

Continued on next page

Reaction	k^+ $(AU^{-1}s^{-1})$	k^- (s^{-1})	k_c (s^{-1})	Source
VIII-P8s-IIa-P10s → VIIIa-P8s + IIa-P10s	–	–	$8.76 \times 10^{-1} \pm 1.39 \times 10^{-1}$	(73, 86)
II-P2s + prothrombinase ⇌ II-P2s-prothrombinase	$1.64 \times 10^{-1} \pm 1.18 \times 10^{-1}$	$4.13 \times 10^{-2} \pm 1.40 \times 10^{-21}$	–	(73, 86)
II-P2s-prothrombinase → IIa-P2s + prothrombinase	–	–	$1.20 \times 10^{1} \pm 8.07^{1}$	(73, 86)
VIIIa-P8s + IXa-P9s ⇌ tenase	$8.82 \times 10^{-2} \pm 5.02 \times 10^{-2}$	$2.80 \times 10^{-1} \pm 1.88 \times 10^{-1}$	–	(73, 86)
VIIIa-P8s + IXa-P9s* ⇌ tenase*	$9.16 \times 10^{-2} \pm 1.55 \times 10^{-2}$	$3.06 \times 10^{-1} \pm 1.63 \times 10^{-1}$	–	(73, 86)
Va-P5s + Xa-P10s ⇌ prothrombinase	$1.07 \pm 3.10 \times 10^{-1}$	$8.83 \times 10^{-1} \pm 2.89 \times 10^{-1}$	–	(73, 86)
Xa-P10s + IX-P9s ⇌ Xa-P10s-IX-P9s	$7.29 \times 10^{-4} \pm 2.11 \times 10^{-4}$	4.05 ± 3.82	–	(74)
Xa-P10s-IX-P9s → Xa-P10s + IXa-P9s	–	–	$2.05 \times 10^{-2} \pm 5.62 \times 10^{-3}$	(74)
APC + VIIIa-P8s ⇌ APC-VIIIa-P8s	$9.31 \times 10^{-2} \pm 4.03 \times 10^{-2}$	$1.51 \pm 5.84 \times 10^{-1}$	–	(73)
APC-VIIIa-P8s → APC+VIIIa-P8s-i	–	–	$5.68 \times 10^{-1} \pm 1.28 \times 10^{-1}$	(73)
APC + Va-P8s ⇌ APC-Va-P8s	$1.63 \times 10^{-1} \pm 7.45 \times 10^{-2}$	$1.31 \pm 4.51 \times 10^{-1}$	–	(73)
APC-Va-P8s → APC+Va-P8s-i	–	–	$3.46 \times 10^{-1} \pm 1.69 \times 10^{-3}$	(73)
APC + prothrombinase ⇌ APC-prothrombinase	$8.26 \times 10^{-2} \pm 4.55 \times 10^{-2}$	$1.19 \pm 4.47 \times 10^{-1}$	–	(73, 76)
APC-prothrombinase → APC + prothrombinase-i	–	–	$3.78 \times 10^{-1} \pm 1.70 \times 10^{-1}$	(73, 76)
APC + tenase ⇌ APC-tenase	$1.32 \times 10^{-1} \pm 2.42 \times 10^{-2}$	$8.69 \times 10^{-1} \pm 4.55 \times 10^{-1}$	–	(73, 76)
APC-tenase → APC + tenase-i	–	–	$4.66 \times 10^{-1} \pm 8.94 \times 10^{-2}$	(73, 76)
APC + tenase* ⇌ APC-tenase*	$1.55 \times 10^{-1} \pm 1.55 \times 10^{-2}$	$9.10 \times 10^{-1} \pm 2.98 \times 10^{-1}$	–	(73, 76)
APC-tenase* → APC + tenase*-i	–	–	$4.17 \times 10^{-1} \pm 1.63 \times 10^{-1}$	(73, 76)
TFPI + Xa ⇌ TFPI-Xa	$2.04 \times 10^{-3} \pm 6.29 \times 10^{-4}$	$8.18 \times 10^{-4} \pm 7.55 \times 10^{-4}$	–	(73, 86)
TFPI-Xa + VIIa-TF ⇌ TFPI-Xa-VIIa-TF	$9.78 \times 10^{-4} \pm 1.34 \times 10^{-4}$	$1.01 \times 10^{-3} \pm 3.36 \times 10^{-4}$	–	(73)
TFPI + X-VIIa-TF ⇌ TFPI-X-VIIa-TF	$8.25 \times 10^{-4} \pm 1.82 \times 10^{-4}$	$2.11 \times 10^{-4} \pm 1.52 \times 10^{-4}$	–	(77)
IIa → IIa-i	–	–	$4.76 \times 10^{-4} \pm 1.25 \times 10^{-4}$	(77)
ATIII + IXa ⇌ ATIII-IXa	$7.12 \times 10^{-7} \pm 4.50 \times 10^{-7}$	$8.45 \times 10^{-10} \pm 3.35 \times 10^{-10}$	–	(73, 77)
ATIII-IXa →ATIII+IXa-i	–	–	$3.71 \times 10^{-7} \pm 1.55 \times 10^{-7}$	(73, 77)
ATIII + Xa ⇌ATIII-Xa	$1.52 \times 10^{-4} \pm 5.94 \times 10^{-5}$	$6.58 \times 10^{-10} \pm 4.30 \times 10^{-10}$	–	(73, 77)
ATIII-Xa → ATIII+Xa-i	–	–	$3.76 \times 10^{-5} \pm 5.52 \times 10^{-6}$	(73, 77)
ATIII + IIa ⇌ ATIII-IIa	$2.27 \times 10^{-6} \pm 4.98 \times 10^{-7}$	$1.00 \times 10^{-9} \pm 2.08 \times 10^{-10}$	–	(73, 77)
ATIII-IIa → ATIII+IIa-i	–	–	$2.90 \times 10^{-5} \pm 2.04 \times 10^{-5}$	(73, 77)
ATIII + VIIa-TF ⇌ VIIIa-TF-ATIII	$2.34 \times 10^{-7} \pm 8.72 \times 10^{-8}$	$8.14 \times 10^{-10} \pm 3.49 \times 10^{-10}$	–	(77)
PC + IIa ⇌ PC-IIa	$5.70 \times 10^{-7} \pm 3.69 \times 10^{-7}$	$1.60 \times 10^{-9} \pm 8.05 \times 10^{-10}$	–	(76, 87)
PC-IIa → APC + IIa	–	–	$3.10 \times 10^{-4} \pm 2.06 \times 10^{-4}$	(76, 87)
IIa + TM ⇌ IIa-TM	$2.70 \times 10^{-2} \pm 8.06 \times 10^{-3}$	$8.56 \times 10^{-2} \pm 7.92 \times 10^{-2}$	–	(87)
IIa-TM + PC ⇌ IIa-TM-PC	$9.08 \times 10^{-5} \pm 5.56 \times 10^{-5}$	$3.31 \times 10^{-1} \pm 1.93 \times 10^{-1}$	–	(87)
IIa-TM-PC → IIa-TM + APC	–	–	$3.08 \times 10^{1} \pm 1.69 \times 10^{1}$	(87)
IIa + PAR1-PL ⇌ IIa-PAR1-PL	$6.15 \times 10^{-1} \pm 1.69 \times 10^{-1}$	8.51 ± 2.69	–	(66, 67)
IIa + PAR1-PL-Psub ⇌ IIa-PAR1-PL-Psub	$1.48 \times 10^{-1} \pm 6.63 \times 10^{-2}$	3.68 ± 2.52	–	(66, 67)
IIa-PAR1-PL → AP + IIa	–	–	$1.71 \times 10^{-2} \pm 1.27 \times 10^{-2}$	(66, 67)
IIa-PAR1-PL-Psub → AP-Psub + IIa	–	–	$3.62 \times 10^{-2} \pm 1.08 \times 10^{-2}$	(66, 67)
IIa + PAR4-PL ⇌ IIa-PAR4-PL	$1.87 \times 10^{-1} \pm 2.70 \times 10^{-2}$	$4.39 \pm 8.28 \times 10^{-1}$	–	(66, 67)
IIa + PAR4-PL-Psub ⇌ IIa-PAR4-PL-Psub	$5.97 \times 10^{-1} \pm 2.19 \times 10^{-1}$	$1.97 \pm 6.77 \times 10^{-1}$	–	(66, 67)
IIa-PAR4-PL → AP + IIa	–	–	$2.75 \times 10^{-1} \pm 7.35 \times 10^{-2}$	(66, 67)
IIa-PAR4-PL-Psub → AP-Psub + IIa	–	–	1.81 ± 1.18	(66, 67)
AP → APs + ADP	–	–	$1.39 \times 10^{-6} \pm 7.78s \times 10^{-7}$	(68)
AP → APs + TXA2	–	–	$1.10 \times 10^{-6} \pm 2.73 \times 10^{-7}$	(68)
AP → APs + I	–	–	$8.49 \times 10^{-7} \pm 2.96 \times 10^{-7}$	(68)
AP-Psub → APs + ADP	–	–	$1.33 \times 10^{-3} \pm 6.85 \times 10^{-4}$	(68)
AP-Psub → APs + TXA2	–	–	$2.94 \times 10^{-3} \pm 2.70 \times 10^{-3}$	(68)
AP-Psub → APs + I	–	–	$7.88 \times 10^{-4} \pm 1.55 \times 10^{-4}$	(76)
ADP + PL ⇌ ADP-PL	$2.68 \times 10^{-7} \pm 6.25 \times 10^{-8}$	$7.45 \times 10^{-1} \pm 3.92 \times 10^{-1}$	–	(68)
ADP-PL → AP + ADP	–	–	$1.95 \times 10^{-7} \pm 1.04 \times 10^{-7}$	(68)
TXA2 + PL ⇌ TXA2-PL	$3.11 \times 10^{-1} \pm 4.34 \times 10^{-1}$	$1.53 \pm 7.98 \times 10^{-1}$	–	(68)
TXA2-PL → AP + TXA2	–	–	$2.20 \times 10^{-2} \pm 6.72 \times 10^{-3}$	(68)
ADP + PL-Psub ⇌ ADP-PL-Psub	$2.75 \times 10^{-2} \pm 6.88 \times 10^{-3}$	$7.16 \times 10^{-3} \pm 4.10 \times 10^{-3}$	–	(68)
ADP-PL-Psub → AP-Psub + ADP	–	–	$2.49 \times 10^{-3} \pm 9.97 \times 10^{-4}$	(68)
TXA2 + PL-Psub ⇌ TXA2-PL-Psub	$1.23 \times 10^{-2} \pm 5.92 \times 10^{-3}$	$6.28 \times 10^{-1} \pm 2.24 \times 10^{-1}$	–	(68)
TXA2-PL-Psub → AP-Psub + TXA2	–	–	$1.95 \times 10^{-2} \pm 6.52 \times 10^{-3}$	(68)
IIa + I ⇌ IIa-I	$1.66 \times 10^{-2} \pm 5.52 \times 10^{-3}$	$1.06 \pm 2.71 \times 10^{-1}$	–	(76)
IIa-I → IIa + Ia	–	–	$4.06 \times 10^{-3} \pm 1.85 \times 10^{-3}$	(76)
XII+Surface ⇌ XII-Surface	$1.12 \times 10^{-1} \pm 4.98 \times 10^{-2}$	$1.19 \times 10^{-1} \pm 5.32 \times 10^{-2}$	–	(62)
XII-Surface → XIIa+Surface	–	–	$1.14 \times 10^{-1} \pm 3.07 \times 10^{-2}$	(62)
XIIa+PK ⇌ XIIa-PK	$1.07 \times 10^{-1} \pm 4.52 \times 10^{-2}$	$9.63 \times 10^{-2} \pm 2.16 \times 10^{-2}$	–	(62)
XIIa-PK → XIIa+ K	–	–	$2.11 \times 10^{-1} \pm 1.74 \times 10^{-1}$	(62)
XII+K ⇌ XII-K	$9.56 \times 10^{-2} \pm 3.24 \times 10^{-2}$	$9.30 \times 10^{-2} \pm 2.50 \times 10^{-2}$	–	(62)
XII-K → XIIa+ K	–	–	$8.52 \times 10^{-2} \pm 1.85 \times 10^{-2}$	(62)
XIIa+ XII ⇌ XIIa-XII	$7.63 \times 10^{-2} \pm 5.59 \times 10^{-2}$	$3.00 \times 10^{-1} \pm 3.13 \times 10^{-1}$	–	(62)
XIIa-XII → 2XIIa	–	–	$1.61 \times 10^{-1} \pm 8.58 \times 10^{-2}$	(62)
XIIa+ XI ⇌ XIIa-XI	$3.10 \times 10^{-3} \pm 1.25 \times 10^{-3}$	$1.18 \times 10^{-1} \pm 4.77 \times 10^{-2}$	–	(62)
XIIa-XI → XIIa+XIa	–	–	$3.62 \times 10^{-1} \pm 8.72 \times 10^{-2}$	(62)
XIa + XI ⇌ XIa-XI	$1.64 \times 10^{-3} \pm 6.35 \times 10^{-4}$	$8.02 \times 10^{-2} \pm 3.13 \times 10^{-2}$	–	

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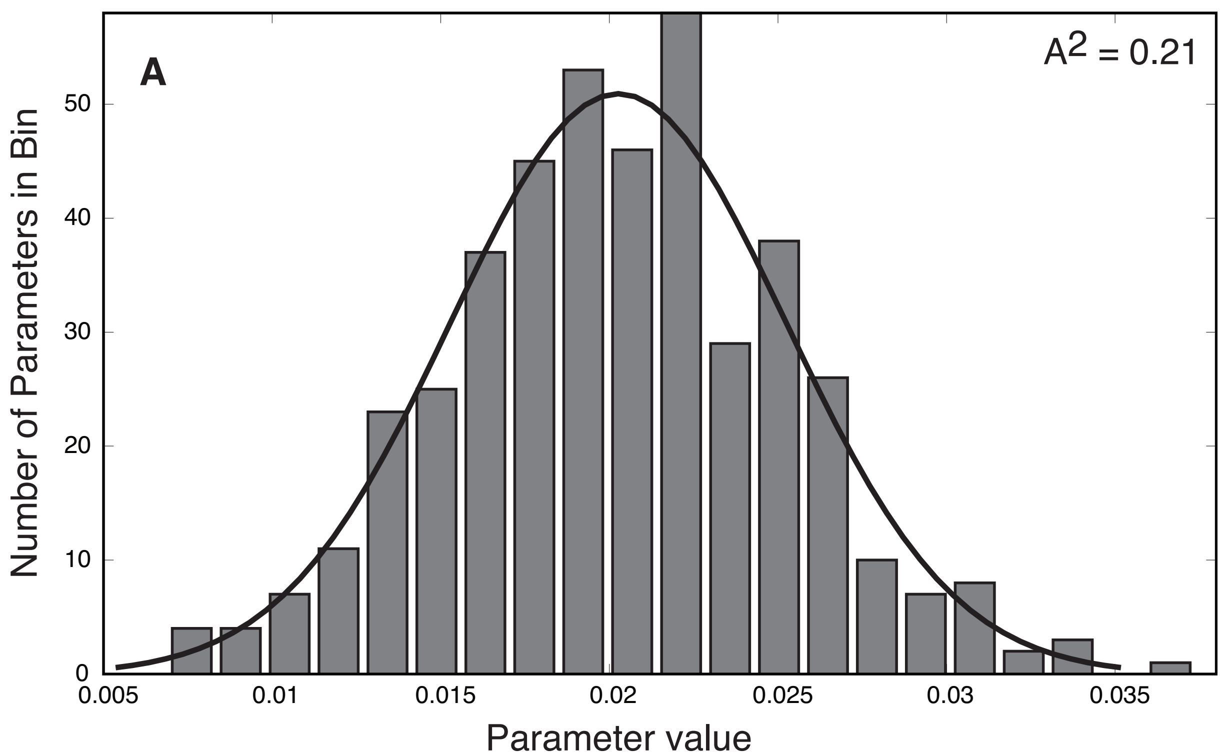
Reaction	k^+ $(AU^{-1}s^{-1})$	k^- (s^{-1})	k_c (s^{-1})	Source
XIa-XI → 2*XIa	–	–	$1.27 \times 10^{-1} \pm 2.26 \times 10^{-2}$	
XI + P11s ⇌ XI-P11s	$7.01 \times 10^{-2} \pm 3.73 \times 10^{-3}$	$6.62 \times 10^{-1} \pm 2.63 \times 10^{-1}$	–	(69, 70)
XIa + P11s* ⇌ XIa-P11s*	$1.59 \times 10^{-1} \pm 1.63 \times 10^{-1}$	$7.70 \times 10^{-2} \pm 2.71 \times 10^{-2}$	–	(69, 70)
IIa-P2s + XI-P11s ⇌ IIa-P2s-XI-P11s	$9.69 \times 10^{-3} \pm 2.77 \times 10^{-3}$	$2.76 \times 10^{-1} \pm 2.51 \times 10^{-1}$	–	(72, 88)
IIa-P2s-XI-P11s → IIa-P2s + XIa-P11s*	–	–	$1.63 \pm 3.90 \times 10^{-1}$	(72, 88)
XIa + IX ⇌ XIa-IX	$1.23 \times 10^{-2} \pm 7.91 \times 10^{-3}$	$7.39 \times 10^{-2} \pm 4.19 \times 10^{-2}$	–	(70)
XIa-IX → XIa + IXa	–	–	8.19 ± 1.45	(70)
XIa-P11s* + IX ⇌ XIa-P11s*-IX	$1.28 \times 10^{-2} \pm 5.24 \times 10^{-3}$	$1.38 \times 10^{-1} \pm 5.53 \times 10^{-2}$	–	(70)
XIa-P11s*-IX → XIa-P11s* + IXa	–	–	$1.11 \times 10^{1} \pm 4.93$	(70)
tPA+PAI1 ⇌ tPA-PAI1	$1.62 \times 10^{-2} \pm 7.62 \times 10^{-3}$	$8.83 \times 10^{-3} \pm 1.05 \times 10^{-2}$	–	(89–92)
uPA+PAI1 ⇌ uPA-PAI1	$2.16 \times 10^{-2} \pm 6.70 \times 10^{-3}$	$1.43 \times 10^{-3} \pm 8.02 \times 10^{-4}$	–	(89, 90)
tPA+PAI2 ⇌ tPA-PAI2	$1.23 \times 10^{-4} \pm 4.13 \times 10^{-5}$	$1.34 \times 10^{-6} \pm 4.64 \times 10^{-7}$	–	(91, 93)
uPA+PAI2 ⇌ uPA-PAI2	$1.46 \times 10^{-3} \pm 6.23 \times 10^{-4}$	$7.50 \times 10^{-6} \pm 3.28 \times 10^{-6}$	–	(93)
PLG+tPA ⇌ PLG-tPA	$1.43 \times 10^{-2} \pm 4.91 \times 10^{-3}$	$7.46 \times 10^{-2} \pm 3.68 \times 10^{-2}$	–	(92, 94, 95)
PLG-tPA → PLA+tPA	–	–	$2.08 \pm 5.20 \times 10^{-1}$	(92, 94, 95)
PLG+uPA ⇌ PLG-uPA	$4.05 \times 10^{-3} \pm 1.51 \times 10^{-3}$	$1.17 \times 10^{-1} \pm 3.92 \times 10^{-2}$	–	(96)
PLG-uPA → PLA+uPA	–	–	$5.37 \times 10^{1} \pm 3.50 \times 10^{1}$	(96)
PLA+A2AP ⇌ PLA-A2AP	$3.54 \times 10^{-2} \pm 9.55 \times 10^{-3}$	$6.63 \times 10^{-3} \pm 1.98 \times 10^{-3}$	–	(97–102)
PLA-A2AP → PLA+A2AP-inactive	–	–	$4.84 \times 10^{-3} \pm 1.77 \times 10^{-3}$	(97–102)
PLA+A2M ⇌ PLA-A2M	$5.58 \times 10^{-4} \pm 1.98 \times 10^{-4}$	$1.11 \times 10^{-5} \pm 2.82 \times 10^{-6}$	–	(101–103)
PLA-A2M → PLA+A2M-inactive	–	–	$1.05 \times 10^{-5} \pm 2.96 \times 10^{-6}$	(101–103)
FDPs+PLA ⇌ FDPs-PLA	$8.62 \times 10^{-3} \pm 2.64 \times 10^{-3}$	$8.52 \times 10^{-2} \pm 3.93 \times 10^{-2}$	–	(104, 105)
IIa+TAFI ⇌ IIa-TAFI	$8.92 \times 10^{-4} \pm 5.71 \times 10^{-4}$	$8.74 \times 10^{-2} \pm 4.65 \times 10^{-2}$	–	(106, 107)
IIa-TAFI → IIa+TAFIa	–	–	$5.79 \times 10^{2} \pm 7.50 \times 10^{2}$	(106, 107)
Ia+PLA ⇌ Ia-PLA	$6.26 \times 10^{-5} \pm 2.57 \times 10^{-5}$	$1.71 \times 10^{-1} \pm 9.54 \times 10^{-2}$	–	(108)
Ia-PLA → Ddimer+FDPs+PLA	–	–	$2.39 \times 10^{-4} \pm 1.73 \times 10^{-4}$	(108)
Ia+FDPs-PLA ⇌ Ia-FDPs-PLA	$4.98 \times 10^{-5} \pm 2.29 \times 10^{-5}$	$1.17 \times 10^{-1} \pm 4.42 \times 10^{-2}$	–	(108)
Ia-FDPs-PLA → Ddimer+FDPs+FDPs-PLA	–	–	$1.06 \times 10^{-3} \pm 3.16 \times 10^{-4}$	(108)
TAFIa+FDPs ⇌ TAFIa-FDPs	$8.40 \times 10^{1} \pm 3.04 \times 10^{1}$	$1.04 \times 10^{-4} \pm 2.87 \times 10^{-5}$	–	(104, 105)
H5+ATIII ⇌ H5-ATIII	$3.35 \times 10^{-2} \pm 1.29 \times 10^{-2}$	$8.83 \times 10^{-1} \pm 3.55 \times 10^{-1}$	–	(109, 110)
H5-ATIII+Xa ⇌ H5-ATIII-Xa	$2.02 \times 10^{-2} \pm 4.84 \times 10^{-3}$	$7.26 \times 10^{-10} \pm 4.68 \times 10^{-10}$	–	(109, 110)
H5-ATIII-Xa → H5-ATIII+Xa-inactive	–	–	$5.27 \times 10^{-4} \pm 2.48 \times 10^{-4}$	(109, 110)
H5-ATIII+IIa ⇌ H5-ATIII-IIa	$1.70 \times 10^{-5} \pm 5.70 \times 10^{-6}$	$1.65 \times 10^{-9} \pm 8.89 \times 10^{-10}$	–	(109, 110)
H5-ATIII-IIa → H5-ATIII+IIa-inactive	–	–	$4.96 \times 10^{-6} \pm 1.47 \times 10^{-6}$	(109, 110)
HCII+IIa ⇌ HCII-IIa	$2.77 \times 10^{-7} \pm 1.17 \times 10^{-7}$	$7.12 \times 10^{-10} \pm 4.07 \times 10^{-10}$	–	(111–113)
HCII+IIa-P2s ⇌ HCII-IIa-P2s	$7.63 \times 10^{-7} \pm 4.52 \times 10^{-7}$	$1.46 \times 10^{-9} \pm 6.76 \times 10^{-10}$	–	(111–113)
HCII+DER ⇌ HCII-DER	$9.14 \times 10^{-1} \pm 1.43 \times 10^{-1}$	$1.04 \times 10^{-9} \pm 3.00 \times 10^{-10}$	–	(111–113)
HCII-DER+IIa ⇌ HCII-DER-IIa	$2.76 \times 10^{-2} \pm 1.06 \times 10^{-2}$	$7.06 \times 10^{-10} \pm 2.52 \times 10^{-10}$	–	(111–113)
HCII-DER+IIa-P2s ⇌ HCII-DER-IIa-P2s	$3.46 \times 10^{-2} \pm 2.40 \times 10^{-2}$	$7.72 \times 10^{-10} \pm 2.30 \times 10^{-10}$	–	(111–113)
ARG +IIa ⇌ ARG-IIa	$2.91 \times 10^{-2} \pm 8.23 \times 10^{-3}$	$2.65 \times 10^{-1} \pm 5.51 \times 10^{-2}$	–	(111, 112)
ARG +IIa-P2s ⇌ ARG-IIa-P2s	$7.87 \times 10^{-2} \pm 5.44 \times 10^{-2}$	$3.14 \times 10^{-1} \pm 1.42 \times 10^{-1}$	–	(111, 112)
BIV+IIa ⇌ BIV-IIa	$6.47 \times 10^{-1} \pm 3.13 \times 10^{-1}$	$5.59 \times 10^{-1} \pm 2.10 \times 10^{-1}$	–	(111, 112)
BIV-IIa → BIV-inactive+IIa	–	–	$1.89 \times 10^{-2} \pm 1.37 \times 10^{-2}$	(111, 112)
BIV+IIa-P2s ⇌ BIV-IIa-P2s	$5.07 \times 10^{-1} \pm 1.23 \times 10^{-1}$	$7.08 \times 10^{-1} \pm 2.70 \times 10^{-1}$	–	(111, 112)
BIV-IIa-P2s → BIV-inactive+IIa-P2s	–	–	$7.49 \times 10^{-3} \pm 2.90 \times 10^{-3}$	(111, 112)
LEP+IIa ⇌ LEP-IIa	$3.57 \times 10^{-1} \pm 8.50 \times 10^{-2}$	$1.20 \times 10^{-5} \pm 4.44 \times 10^{-6}$	–	(111, 112)
LEP+IIa-P2s ⇌ LEP-IIa-P2s	$3.28 \times 10^{-1} \pm 8.56 \times 10^{-2}$	$1.50 \times 10^{-5} \pm 6.45 \times 10^{-6}$	–	(111, 112)
H5-ATIII+VIIa ⇌ H5-ATIII-VIIa	$2.06 \times 10^{-7} \pm 5.98 \times 10^{-8}$	$3.20 \times 10^{-9} \pm 3.68 \times 10^{-9}$	–	(114)
H5-ATIII+VIIa-TF ⇌ H5-ATIII-VIIa-TF	$2.36 \times 10^{-6} \pm 2.42 \times 10^{-6}$	$7.37 \times 10^{-10} \pm 4.49 \times 10^{-10}$	–	(114)
X+VIIa ⇌ X-VIIa	$3.33 \times 10^{-5} \pm 1.23 \times 10^{-5}$	$9.52 \times 10^{-2} \pm 3.43 \times 10^{-2}$	–	(20, 30)
X-VIIa → Xa+VIIa	–	–	$7.01 \times 10^{-5} \pm 2.75 \times 10^{-5}$	(20, 30)
IX+VIIa ⇌ IX-VIIa	$5.79 \times 10^{-5} \pm 1.89 \times 10^{-5}$	$1.67 \times 10^{-1} \pm 1.26 \times 10^{-1}$	–	(20, 30)
IX-VIIa → IXa+VIIa	–	–	$1.44 \times 10^{-5} \pm 2.84 \times 10^{-6}$	(20, 30)
APC+PCI ⇌ APC-PCI	$5.20 \times 10^{-6} \pm 1.47 \times 10^{-6}$	$2.19 \times 10^{-9} \pm 1.51 \times 10^{-9}$	–	(115)
IIa+PCI ⇌ IIa-PCI	$5.50 \times 10^{-6} \pm 1.00 \times 10^{-6}$	$1.84 \times 10^{-9} \pm 1.40 \times 10^{-9}$	–	(115)
Xa+PCI ⇌ Xa-PCI	$1.81 \times 10^{-5} \pm 4.21 \times 10^{-6}$	$7.49 \times 10^{-10} \pm 2.33 \times 10^{-10}$	–	(115)
XIa+PCI ⇌ XIa-PCI	$1.23 \times 10^{-4} \pm 4.58 \times 10^{-5}$	$1.58 \times 10^{-9} \pm 8.79 \times 10^{-10}$	–	(115)
uPA +PCI ⇌ uPA-PCI	$1.62 \times 10^{-6} \pm 9.00 \times 10^{-7}$	$1.99 \times 10^{-9} \pm 1.30 \times 10^{-9}$	–	(115)
tPA +PCI ⇌ tPA-PCI	$6.29 \times 10^{-7} \pm 1.77 \times 10^{-7}$	$9.13 \times 10^{-10} \pm 1.74 \times 10^{-10}$	–	(115)
K +PCI ⇌ K-PCI	$7.06 \times 10^{-5} \pm 1.88 \times 10^{-5}$	$1.10 \times 10^{-9} \pm 3.03 \times 10^{-10}$	–	(115)

Table S2: Nomenclature for model symbols.

fI/I	fibrinogen
FIa/Ia	fibrin
fII/II	prothrombin
FIIa/IIa	thrombin
fVII/VII	factor VII
FVIIa/VIIa	activated factor VII
fV/V	factor V
FVa/Va	activated factor V
fVIII/VIII	factor VIII
FVIIIa/VIIIa	activated factor VIII
fIX/IX	factor IX
FIXa/IXa	activated factor IX
fX/X	factor X
FXa/Xa	activated factor X
fXI/XI	factor X
FXIa/XIa	activated factor X
fXII/XII	factor X
FXIIa/XIIa	activated factor X
PK	prekallikrein
K	kallikrein
TF	tissue factor
TFPI	tissue factor pathway inhibitor
ATIII	antithrombin III
PC	protein C
APC	activated protein C
TM	thrombomodulin
PL	resting platelets
AP	activated platelets
Pxs	activated platelets surface binding sites for factor x
tPA	tissue plasminogen activator
uPA	urokinase
PLG	plasminogen
PLA	plasmin
A2AP	alpha-2-antiplasmin precursor
A2M	alpha-2-macroglobulin
FDPs	fibrin degradation products
TAFI	thrombin-activatable fibrinolysis inhibitor
H5	heparin
HCII	heparin cofactor II
ARG	argatroban
BIV	bivalirudin
LEP	lepirudin
PCI	protein C inhibitor



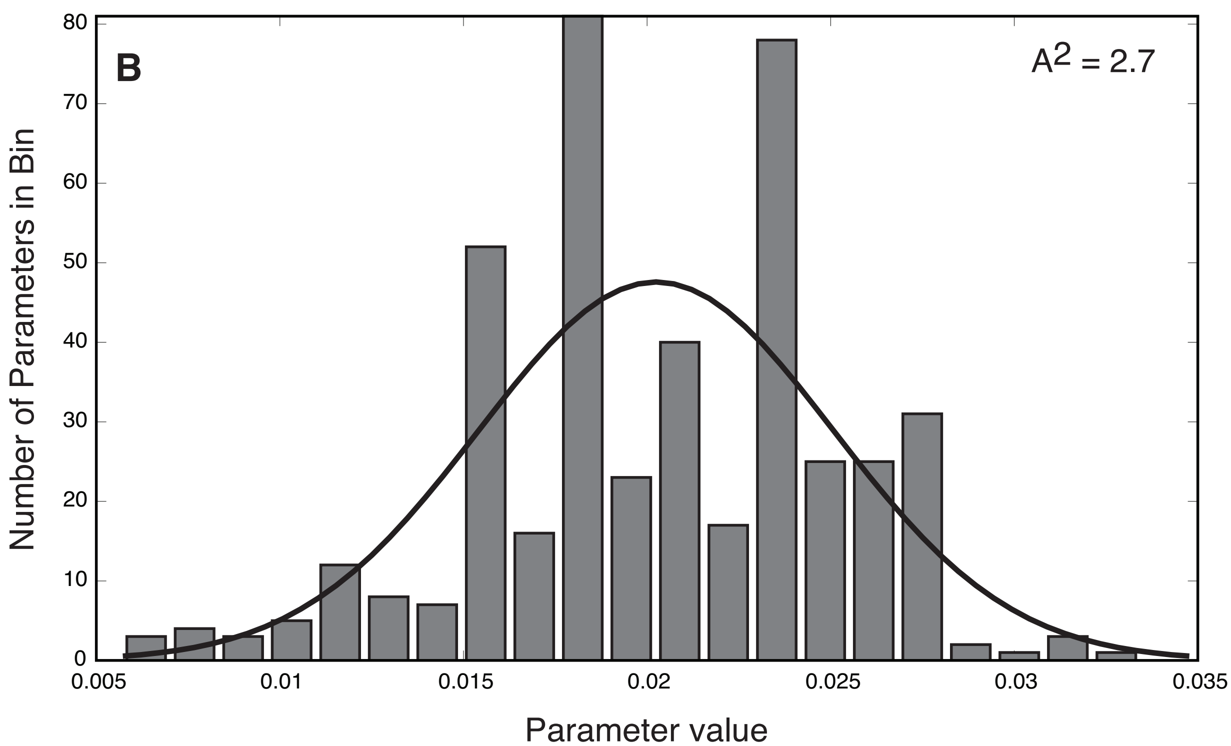


Fig. S1: The parameter distributions estimated from the training data were not normal. We performed an Anderson–Darling test on each parameter across all 437 elements of the ensemble. No parameters were normally distributed. **A:** We performed the Anderson–Darling test on a normal distribution constructed using with the mean and variance of the *most normal* parameter from the ensemble. The Anderson–Darling test classified this test distribution as normal, thus, the algorithm was correct. **B:** The most normal distribution had an A^2 statistic equal to 2.7, which is far away from normal. Even when corrected for sample size, the A^2 statistic suggested the distributions were not normal.

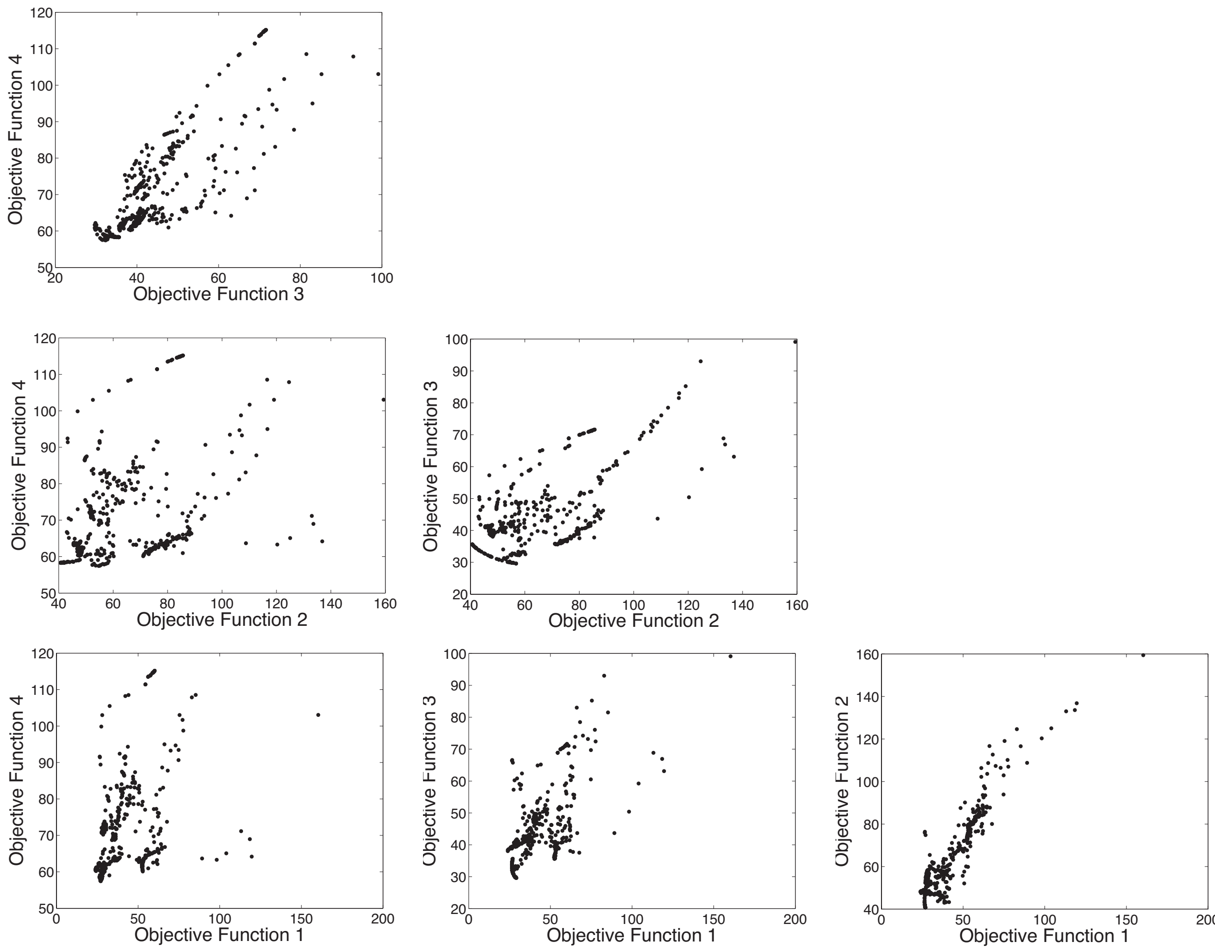


Fig. S2: Comparison of the objective function values for the training data used to estimate the model parameters. Objective 1,2,3 and 4 denote Fig. 1A, 1B, 1C and 1D from the Allen *et al.* (22). We compared the values of the four objective functions across the ensemble. For certain objective functions, e.g., O1 and O2 there was a linear relationship. Thus, models that performed well relative to O1 also performed well relative to O2. However, this was not universally true. There was a clear trade-off between O2 and O4. Models that performed well with O2 performed poorly relative to O4. Similarly, O1 versus O4 also showed a trade-off. Taken together, these results suggest that different models performed best relative to individual training data sets. Assembling these models into an ensemble allowed a single model family to describe more data.

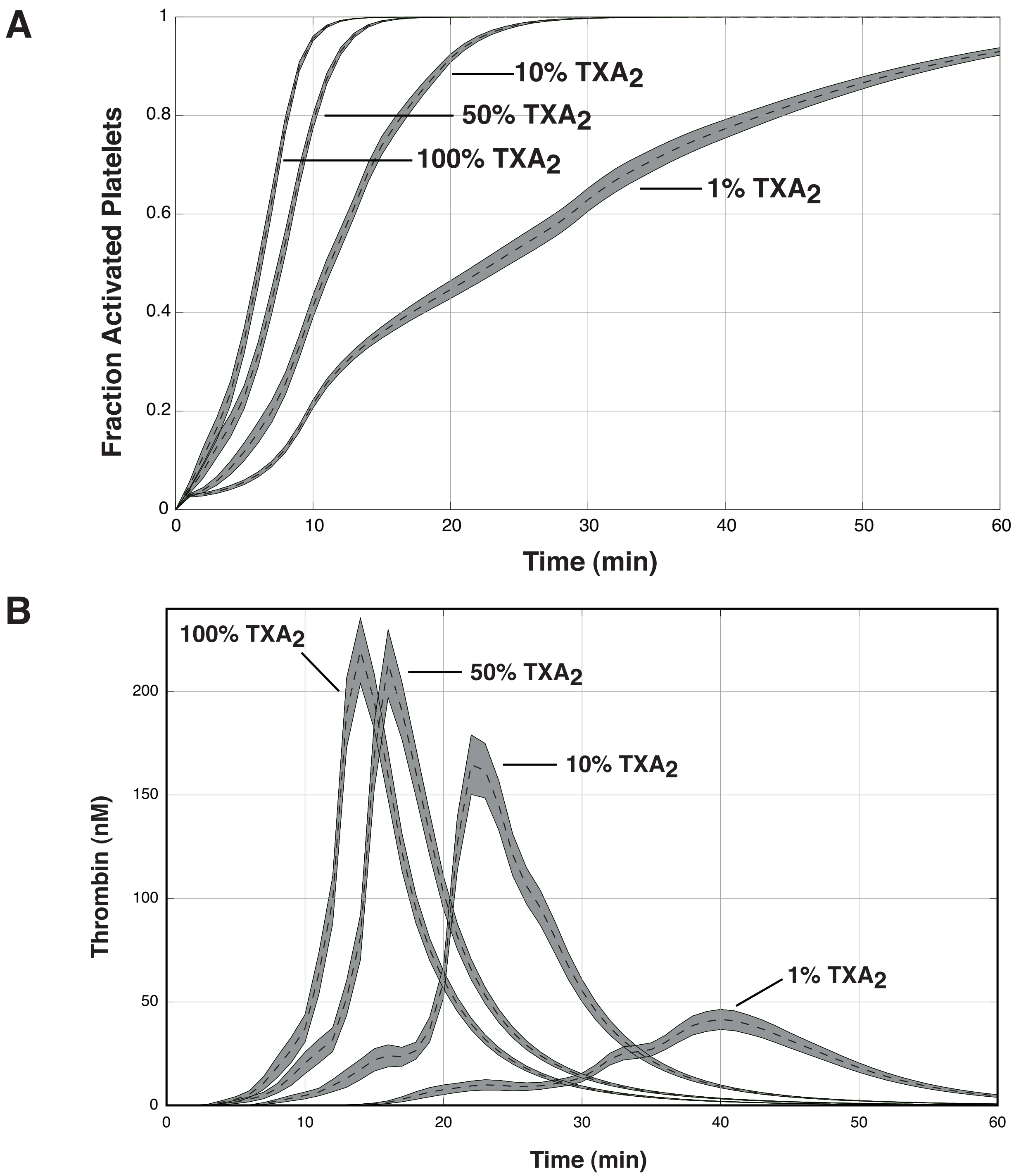


Fig. S3: Simulation of the effect of aspirin on platelet activation. for the CAD patient samples. **A:** Fraction of activated platelets versus time as a function of the level of TXA2 secretion inhibition. **B:** Thrombin concentration versus time as a function of the level of TXA2 secretion inhibition. To simulate the effect of aspirin, the rate of TXA2 secretion from platelets was reduced all other parameters held constant. The fraction of the nominal secretion rate constant is shown along with the 95% confidence estimate of the value of the mean. Significant reduction in the production of TXA2 reduced the rate of platelet activation and thrombin formation. However, moderate levels of TXA2 reduction, while non-negligible, do not qualitatively alter the thrombin or platelet activation profile.