

**Table S1: List of model parameters and initial conditions**

Name	Interpretation	Value	Units	Reference*
<b>basal<sub>T</sub></b>	Basal rate of TPO production	0.23	ng/(ml day)	15,16
<b>kP<sub>J2</sub></b>	Maximum rate of TPO production via JAK2 pathway	0.01	ng/(ml day)	8
<b>K</b>	Aged platelet concentration for half maximal uptake	47	nl <sup>-1</sup>	8
<b>γ</b>	Hill coefficient for aged platelet uptake by AMR	2		Fixed
<b>kP<sub>J1</sub></b>	Max rate of TPO production via JAK1 pathway	0.03	nl <sup>-1</sup>	9,10
<b>K<sub>J1</sub></b>	IL-6 concentration for half maximal TPO production	0.3	ng/ml	9,10
<b>k<sub>T1</sub></b>	TPO transit rate constant from liver to blood compartment	7.1	day <sup>-1</sup>	Fit
<b>d<sub>TB</sub></b>	TPO decay rate constant in blood	0.25	day <sup>-1</sup>	13,14
<b>d<sub>T</sub></b>	TPO decay rate constant in liver	0.005	day <sup>-1</sup>	13,14
<b>d<sub>TBM</sub></b>	TPO decay rate constant in bonemarrow	0.05	day <sup>-1</sup>	13,14
<b>k<sub>T2</sub></b>	TPO transit rate constant from blood to bone marrow compartment	0.34	day <sup>-1</sup>	15,16
<b>k<sub>Tc</sub></b>	Rate constant of TPO consumption by platelets	0.15	ng/day	11,12
<b>K<sub>TP</sub></b>	TPO concentration for half maximal consumption by platelets	3	ng/ml	11,12
<b>β</b>	Hill coefficient for TPO consumption	2		Fixed
<b>w<sub>T</sub></b>	Fraction of aged platelets consuming TPO	0.06		Fixed
<b>k<sub>TcM</sub></b>	Rate constant of TPO consumption by precursors	0.5	ng/day	11,12
<b>K<sub>TM</sub></b>	TPO concentration for half maximal consumption by precursors	0.04	ng/ml	11,12
<b>f</b>	Fraction of precursors consuming TPO	0.1		Fixed
<b>basal<sub>MB</sub></b>	Basal rate of megakaryoblast (MB) production from stem cells	0.05	1/(nl day)	Fit
<b>g<sub>J1</sub></b>	Max rate of MB production through JAK1 pathway	0.06	1/(nl day)	1,2
<b>K<sub>BJ1</sub></b>	IL-6 concentration for half maximal MB production	0.1	ng/ml	1,2
<b>g<sub>J2</sub></b>	Max rate of MB production through JAK2 pathway	0.2	1/(nl day)	1,2
<b>K<sub>BJ2</sub></b>	TPO concentration for half maximal MB production	0.12	ng/ml	1,2
<b>α</b>	Hill coefficient for MB production via JAK2 pathway	1		Fit
<b>k<sub>MB</sub></b>	MB transit rate constant	0.4	day <sup>-1</sup>	3,4
<b>g<sub>MK</sub></b>	MK proliferation rate constant	0.2		7
<b>Δ<sub>MK</sub></b>	TPO concentration for half maximal MK proliferation	0.03	ng/ml	7
<b>δ</b>	Hill coefficient for MK proliferation	2		Fixed
<b>d<sub>MK</sub></b>	MK decay rate constant	0.1325	day <sup>-1</sup>	Fit
<b>E<sub>max</sub></b>	Rate constant of MK differentiation under the influence of TPO	1		Fixed
<b>k<sub>MK</sub></b>	Megakaryocyte(MK) transit rate constant	0.5	day <sup>-1</sup>	4,5

<b>k<sub>d</sub></b>	MK differentiation rate constant	2	day <sup>-1</sup>	4,5
<b>K<sub>BM</sub></b>	TPO concentration for half maximal MK differentiation	0.09	ng/ml	4-6
<b>ε</b>	Hill coefficient for MK differentiation	2		Fixed
<b>P<sub>MK</sub></b>	Number of platelets produced per MK per day (corrected for volume)	350		4,5
<b>dP<sub>aging</sub></b>	Rate constant of platelet aging	0.4	day <sup>-1</sup>	Fixed
<b>d<sub>AMR</sub></b>	Rate of aged platelet uptake by hepatic AMR	0.3	1/(nl day)	8
<b>dP<sub>immune</sub></b>	Rate constant of immune clearance of platelets	0.4	day <sup>-1</sup>	5,8
<b>basal<sub>IL6</sub></b>	Basal rate of IL-6 production	0.01	ng/(ml day)	Fixed
<b>d<sub>IL6</sub></b>	IL-6 decay rate constant	0.033	day <sup>-1</sup>	Fixed

<b>Species category</b>	<b>Species names</b>	<b>Initial Values</b>	<b>Units</b>
Megakaryoblasts	MB,MB1,MB2	0.1,0.1,0.1	cells/nl
Megakaryocytes	MK,MK1,MK2	0.25,0.25,0.25	cells/nl
Platelets	Pnew, Paged	120,140	cells/nl
Thrombopoietin	TL,TB,TBM	0.05,0.2,0.12	ng/ml
Interleukin	IL-6	0.3	ng/ml

\*These references are the sources for initial values of system parameters. Final estimates are obtained by optimizing to literature data.