

SUPPORTING MATERIAL FOR “MATHEMATICAL MODELLING INDICATES THAT LOWER ACTIVITY OF THE HAEMOSTATIC SYSTEM IN NEONATES IS PRIMARILY DUE TO LOWER PROTHROMBIN CONCENTRATION”

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1. VARIABILITY BETWEEN INDIVIDUALS WITHIN THE SAME AGE GROUP

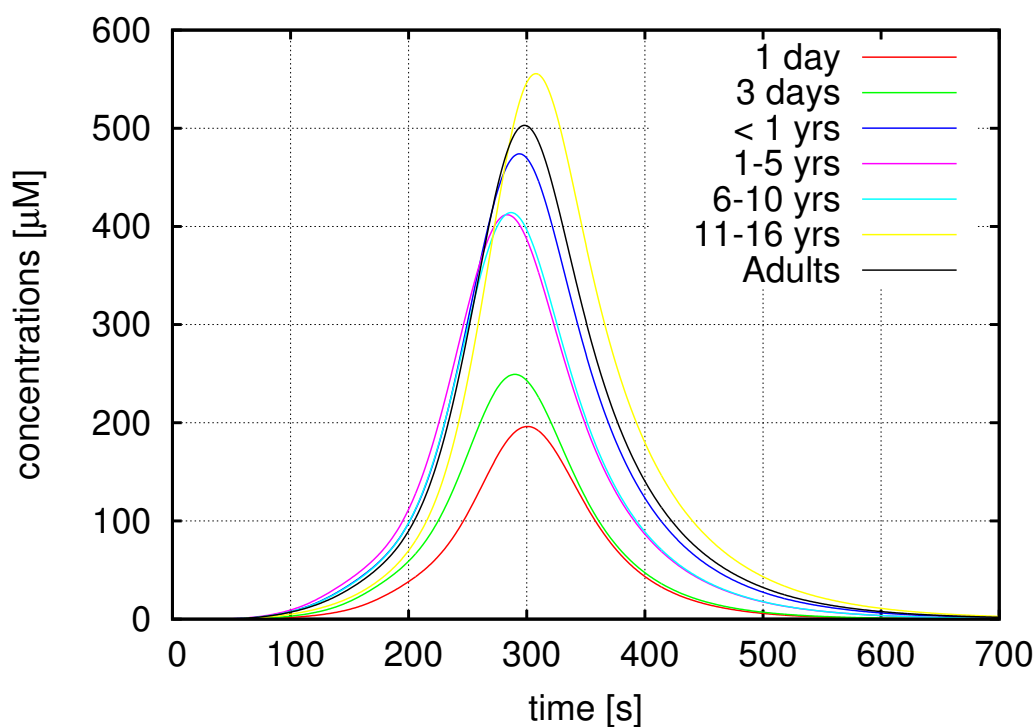


FIGURE S1. Age-dependent thrombin generation curves (TGC) calculated from the Hockin-Mann model [2] parameterised with the mean values of each age group from the data of Attard et al. [1]

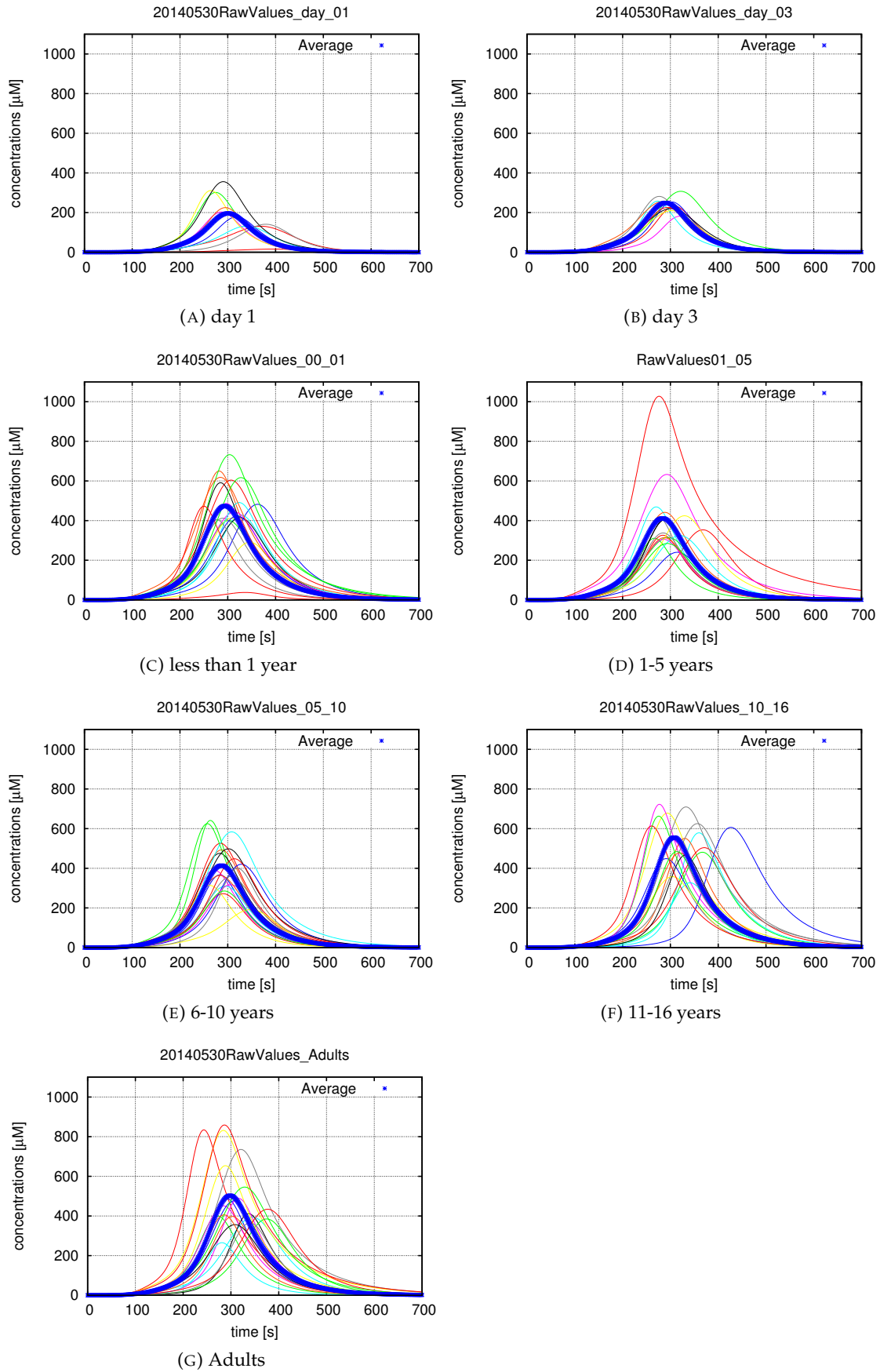


FIGURE S2. TGCs calculated from the Hockin-Mann model [2] parametrised with data from individual patients [1].

2. SCATTER PLOTS FOR ALL COMBINATIONS OF FACTOR CONCENTRATIONS FROM [1]

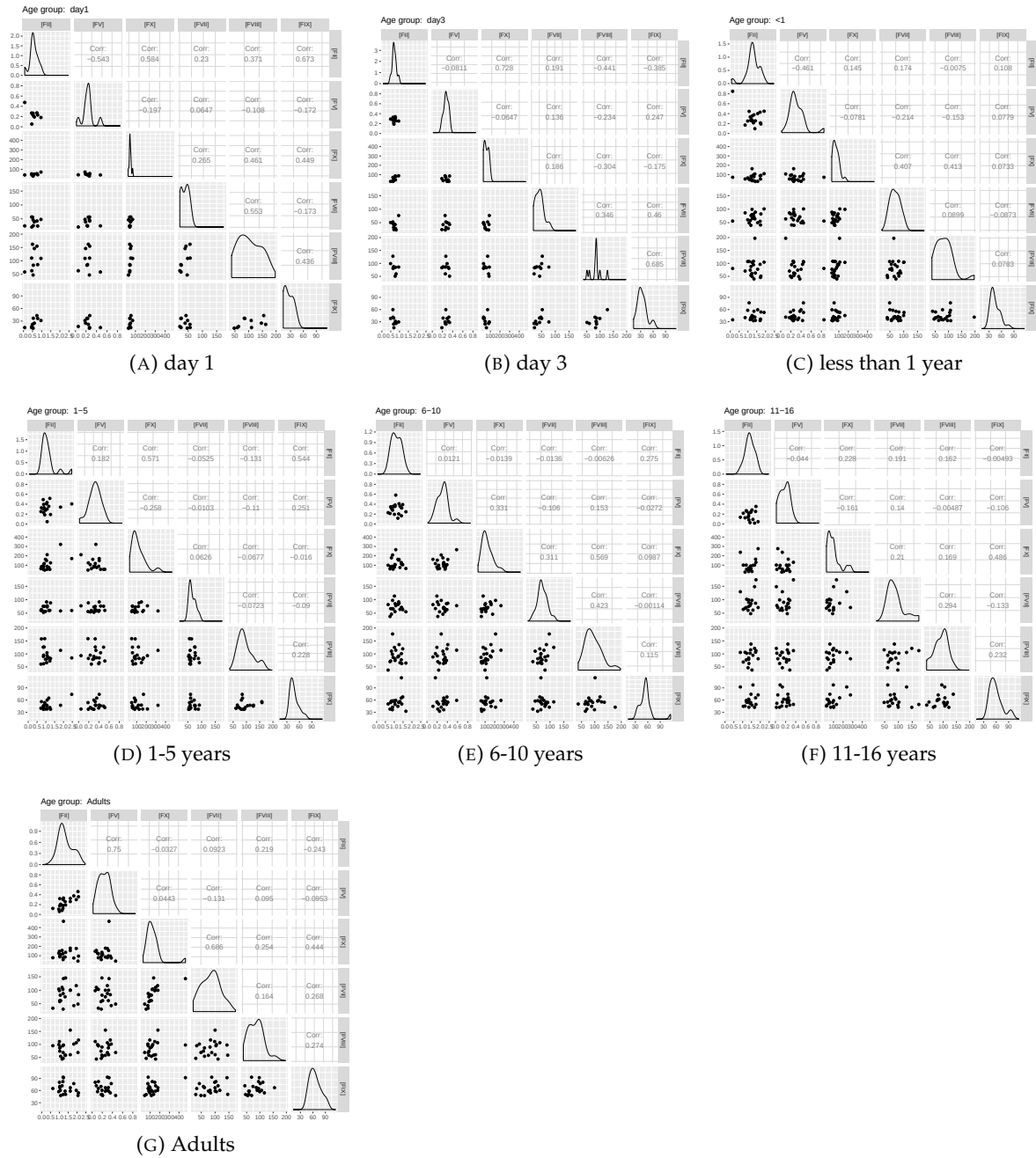


FIGURE S3. Scatter plots for all combinations of coagulation factors from the data collected by Attard et al. [1].

3. EQUATIONS OF THE MODEL BY HOCKIN ET AL. [2]

$$\begin{aligned}
\frac{d[TF]}{dt} &= -k_2[TF][VII] + k_1[TF.VII] - k_4[TF][VIIa] + k_3[TF.VIIa] \\
\frac{d[VII]}{dt} &= -k_2[TF][VII] + k_1[TF.VII] - k_5[TF.VIIa][VII] - k_6[Xa][VII] - k_7[IIa][VII] \\
\frac{d[TF.VII]}{dt} &= +k_2[TF][VII] - k_1[TF.VII] \\
\frac{d[VIIa]}{dt} &= -k_4[TF][VIIa] + k_3[TF.VIIa] + k_5[TF.VIIa][VII] + k_6[Xa][VII] + k_7[IIa][VII] \\
\frac{d[TF.VIIa]}{dt} &= +k_4[TF][VIIa] - k_3[TF.VIIa] - k_9[TF.VIIa][X] + k_8[TF.VIIa.X] - k_{12}[TF.VIIa][Xa] + k_{11}[TF.VIIa.Xa] - k_{14}[TF.VIIa][IX] + k_{13}[TF.VIIa.IX] \\
&\quad + k_{15}[TF.VIIa.IX] - k_{37}[TF.VIIa][Xa.TFPI] - k_{42}[TF.VIIa][ATIII] \\
\frac{d[Xa]}{dt} &= -k_{12}[TF.VIIa][Xa] + k_{11}[TF.VIIa.Xa] + k_{22}[IXa.VIIIa.X] - k_{28}[Xa][Va] + k_{27}[Xa.Va] \\
&\quad - k_{34}[Xa][TFPI] + k_{33}[Xa.TFPI] - k_{38}[Xa][ATIII] \\
\frac{d[IIa]}{dt} &= +k_{16}[Xa][II] + k_{32}[Xa.Va][mIIa] - k_{41}[IIa][ATIII] \\
\frac{d[X]}{dt} &= -k_9[TF.VIIa][X] + k_8[TF.VIIa.X] - k_{21}[IXa.VIIIa][X] + k_{20}[IXa.VIIIa.X] + k_{25}[IXa.VIIIa.X] \\
\frac{d[TF.VIIa.X]}{dt} &= +k_9[TF.VIIa][X] - k_8[TF.VIIa.X] - k_{10}[TF.VIIa.X] \\
\frac{d[TF.VIIa.Xa]}{dt} &= +k_{12}[TF.VIIa][Xa] - k_{11}[TF.VIIa.Xa] - k_{36}[TF.VIIa.Xa][TFPI] + k_{35}[TF.VIIa.Xa.TFPI] + k_{10}[TF.VIIa.X] \\
\frac{d[IX]}{dt} &= -k_{14}[TF.VIIa][IX] + k_{13}[TF.VIIa.IX] \\
\frac{d[TF.VIIa.IX]}{dt} &= +k_{14}[TF.VIIa][IX] - k_{13}[TF.VIIa.IX] - k_{15}[TF.VIIa.IX] \\
\frac{d[IXa]}{dt} &= +k_{15}[TF.VIIa.IX] - k_{19}[VIIIa][IXa] + k_{18}[IXa.VIIIa] - k_{40}[IXa][ATIII] + k_{25}[IXa.VIIIa.X] + k_{25}[IXa.VIIIa] \\
\frac{d[II]}{dt} &= -k_{16}[Xa][II] - k_{30}[Xa.Va][II] + k_{29}[Xa.Va.II] \\
\frac{d[VIII]}{dt} &= -k_{17}[IIa][VIII] \\
\frac{d[VIIIa]}{dt} &= +k_{17}[IIa][VIII] - k_{19}[VIIIa][IXa] + k_{18}[IXa.VIIIa] + k_{23}[VIIIa1.L][VIIIa2] - k_{24}[VIIIa] \\
\frac{d[IXa.VIIIa]}{dt} &= +k_{19}[VIIIa][IXa] - k_{18}[IXa.VIIIa] - k_{21}[IXa.VIIIa][X] + k_{20}[IXa.VIIIa.X] + k_{22}[IXa.VIIIa.X] - k_{25}[IXa.VIIIa] \\
\frac{d[IXa.VIIIa.X]}{dt} &= +k_{21}[IXa.VIIIa][X] - k_{20}[IXa.VIIIa.X] - k_{22}[IXa.VIIIa.X] - k_{25}[IXa.VIIIa.X] \\
\frac{d[VIIIa1.L]}{dt} &= -k_{23}[VIIIa1.L][VIIIa2] + k_{24}[VIIIa] + k_{25}[IXa.VIIIa.X] + k_{25}[IXa.VIIIa] \\
\frac{d[VIIIa2]}{dt} &= -k_{23}[VIIIa1.L][VIIIa2] + k_{24}[VIIIa] + k_{25}[IXa.VIIIa.X] + k_{25}[IXa.VIIIa] \\
\frac{d[V]}{dt} &= -k_{26}[IIa][V] \\
\frac{d[Va]}{dt} &= +k_{26}[IIa][V] - k_{28}[Xa][Va] + k_{27}[Xa.Va] \\
\frac{d[Xa.Va]}{dt} &= +k_{28}[Xa][Va] - k_{27}[Xa.Va] - k_{30}[Xa.Va][II] + k_{29}[Xa.Va.II] + k_{31}[Xa.Va.II] \\
\frac{d[Xa.Va.II]}{dt} &= +k_{30}[Xa.Va][II] - k_{29}[Xa.Va.II] - k_{31}[Xa.Va.II] \\
\frac{d[mIIa]}{dt} &= +k_{31}[Xa.Va.II] - k_{32}[Xa.Va][mIIa] - k_{39}[mIIa][ATIII] \\
\frac{d[TFPI]}{dt} &= -k_{34}[Xa][TFPI] + k_{33}[Xa.TFPI] - k_{36}[TF.VIIa.Xa][TFPI] + k_{35}[TF.VIIa.Xa.TFPI] \\
\frac{d[Xa.TFPI]}{dt} &= +k_{34}[Xa][TFPI] - k_{33}[Xa.TFPI] - k_{37}[TF.VIIa][Xa.TFPI] \\
\frac{d[TF.VIIa.Xa.TFPI]}{dt} &= +k_{36}[TF.VIIa.Xa][TFPI] - k_{35}[TF.VIIa.Xa.TFPI] + k_{37}[TF.VIIa][Xa.TFPI] \\
\frac{d[ATIII]}{dt} &= -k_{38}[Xa][ATIII] - k_{39}[mIIa][ATIII] - k_{40}[IXa][ATIII] - k_{41}[IIa][ATIII] - k_{42}[TF.VIIa][ATIII] \\
\frac{d[Xa.ATIII]}{dt} &= +k_{38}[Xa][ATIII] \\
\frac{d[mIIa.ATIII]}{dt} &= +k_{39}[mIIa][ATIII] \\
\frac{d[IXa.ATIII]}{dt} &= +k_{40}[IXa][ATIII] \\
\frac{d[IIa.ATIII]}{dt} &= +k_{41}[IIa][ATIII] \\
\frac{d[TF.VIIa.ATIII]}{dt} &= +k_{42}[TF.VIIa][ATIII]
\end{aligned}$$

REFERENCES

- [1] Attard, C., T. van der Straaten, V. Karlaftis, P. Monagle, and V. Ignjatovic (2013). Developmental hemostasis: age-specific differences in the levels of hemostatic proteins. *Journal of Thrombosis and Haemostasis* 11, 1850–1854.
- [2] Hockin, M. F., K. C. Jones, S. J. Everse, and K. G. Mann (2002). A model for the stoichiometric regulation of blood coagulation. *Journal of Biological Chemistry* 277(21), 18322–18333.