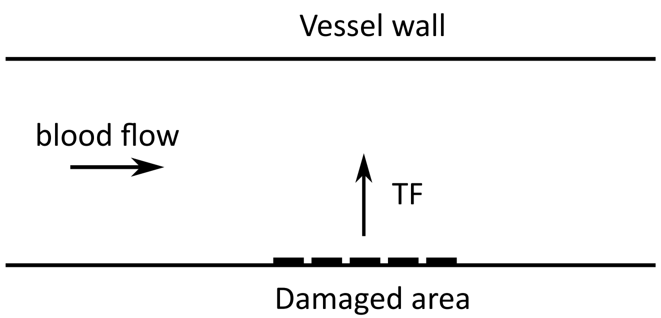
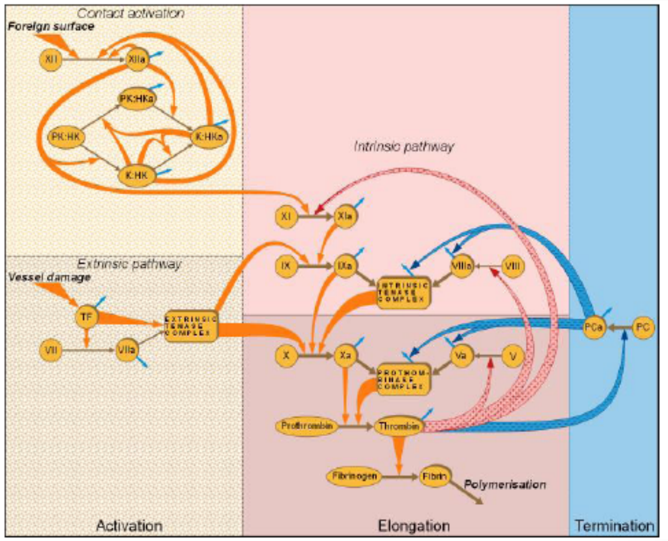
Existence, stability and speed of the travelling wave solutions in the mathematical model of blood coagulation

T. Galochkina, A. Bouchnita, V. Volpert

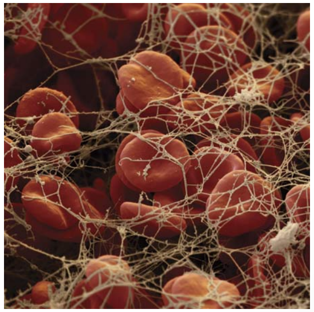
Fibrin clot growth: distribution of blood factors

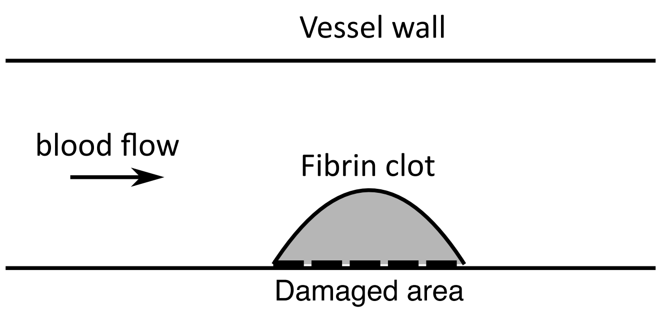


Coagulation cascade

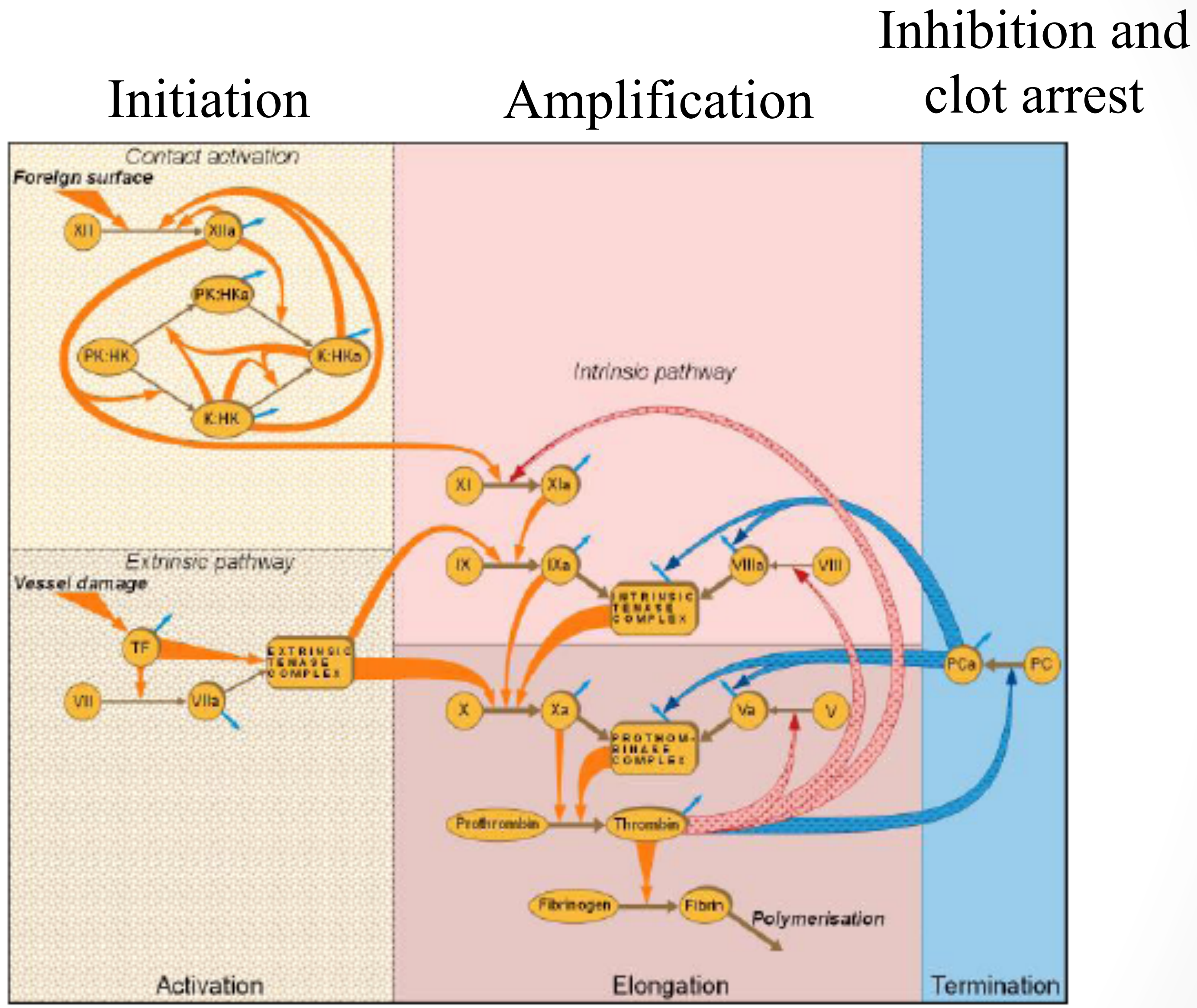


Fibrin polymer

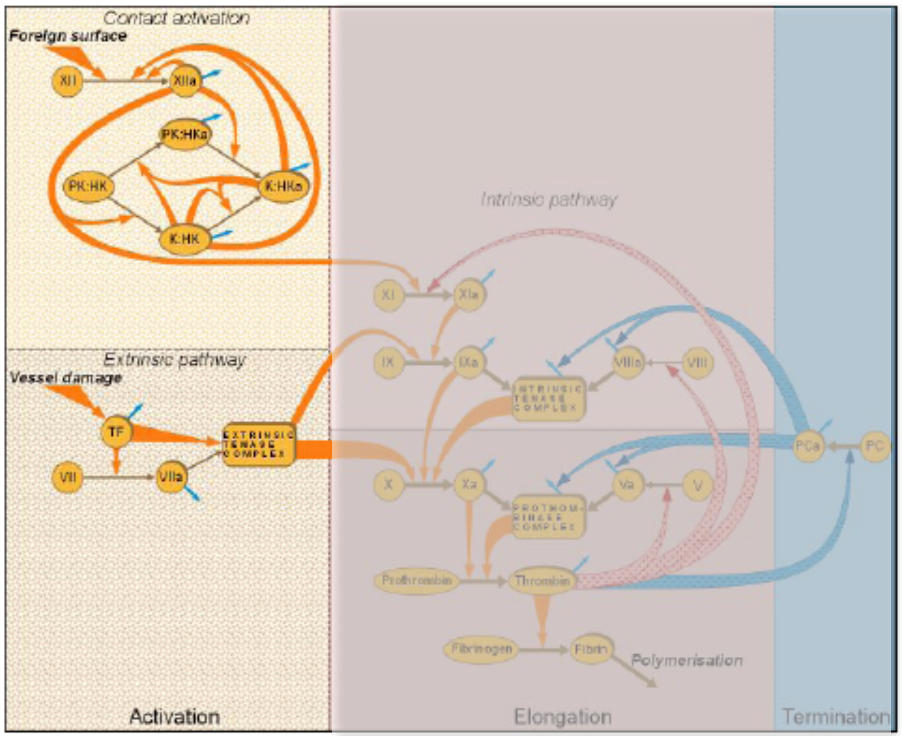




Coagulation cascade



Initiation



intrinsic pathway

↑

XIa

XIIa

negatively charged surface

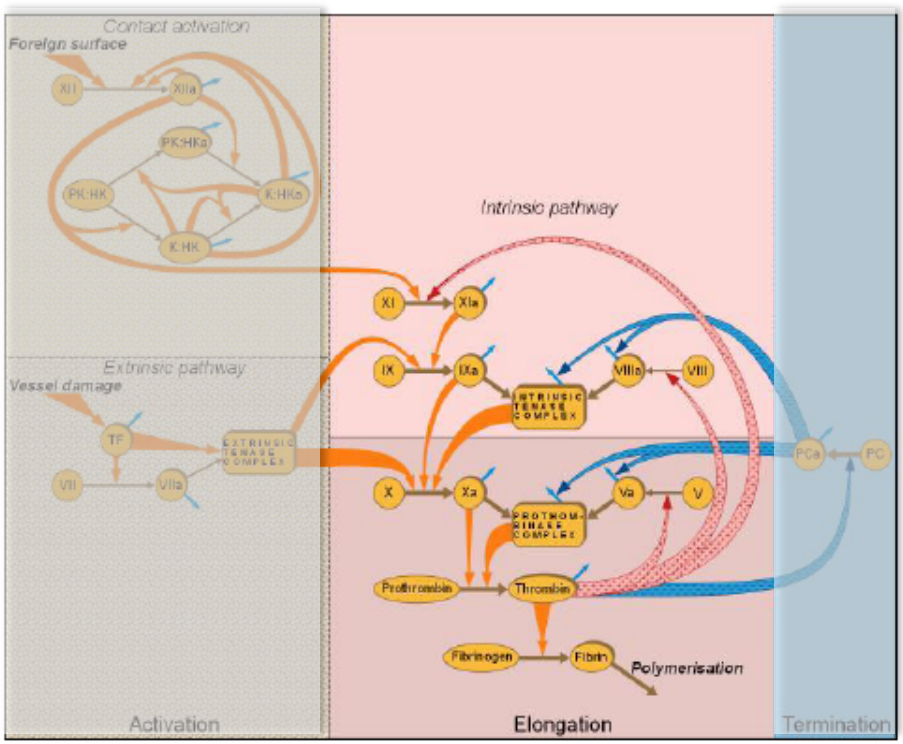
IX IXa X Xa

VII

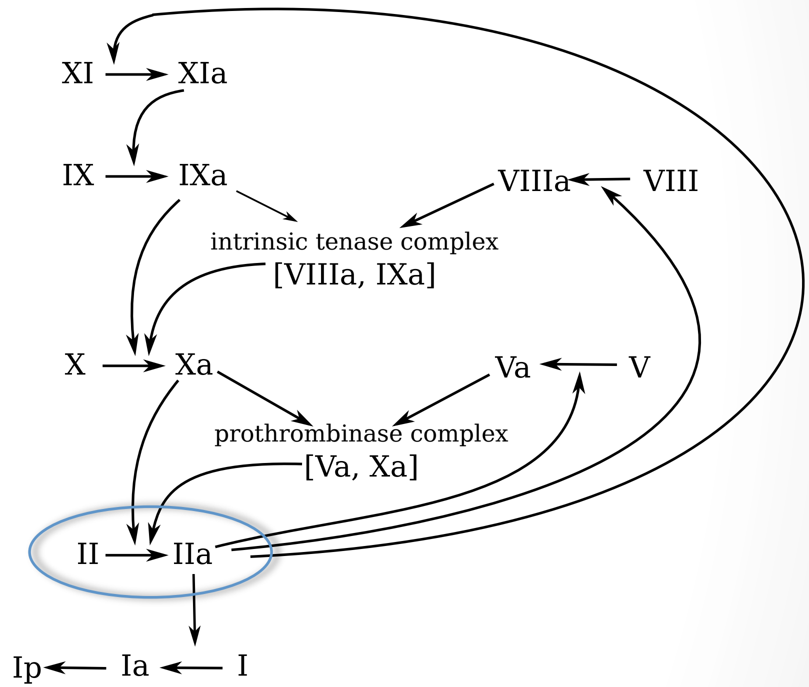
TF+VIIa

vessel wall damage

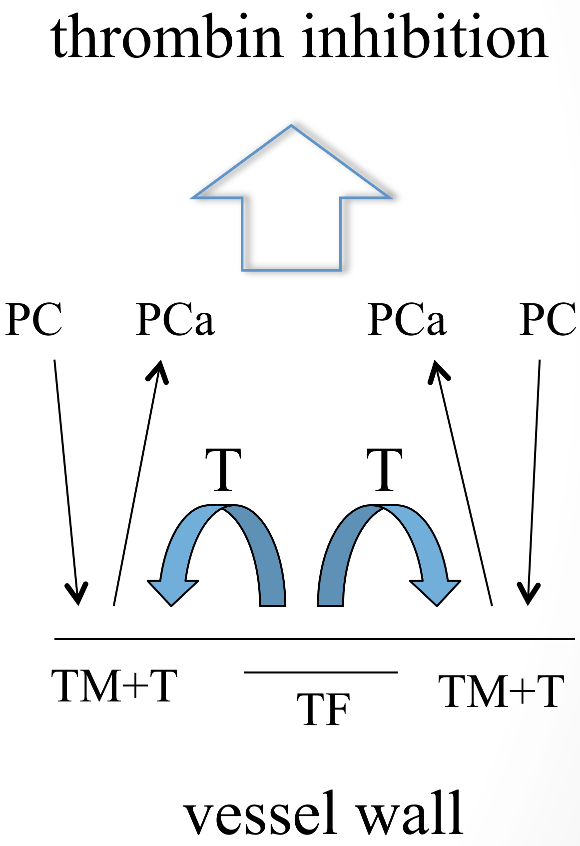
Amplification



Intrinsic pathway: production of thrombin

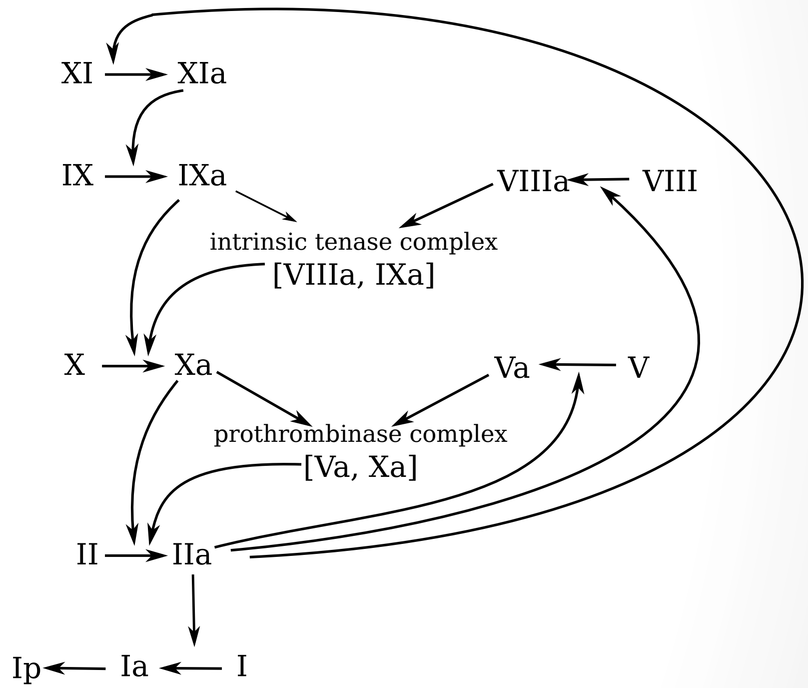


Clot growth arrest: role of the activated protein C

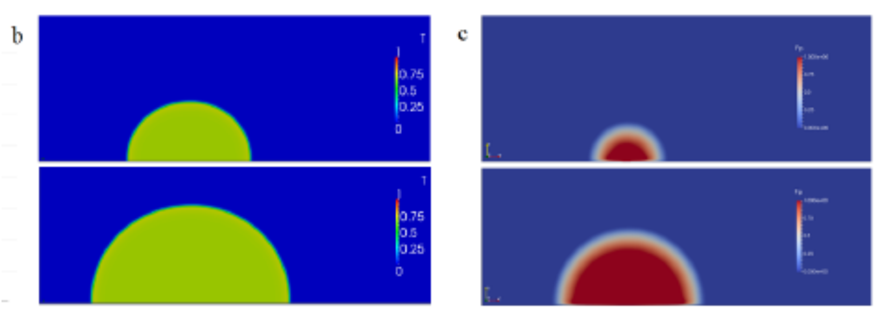


Intrinsic pathway: mathematical model

$$
\begin{aligned}
\frac{\partial U_{11}}{\partial t} &= D\Delta U_{11} + k_{11}T - h_{11}U_{11}, \\
\frac{\partial T}{\partial t} &= D\Delta T + \left(k_2 U_{10} + \overline{k_2}\frac{k_{510}}{h_{510}}U_{10}U_5\right)\left(1 - \frac{T}{T_0}\right) - h_2 T, \\
\frac{\partial U_9}{\partial t} &= D\Delta U_9 + k_9 U_{11} - h_9 U_9, \\
\frac{\partial U_{10}}{\partial t} &= D\Delta U_{10} + k_{10}U_9 + \overline{k_{10}}\frac{k_{89}}{h_{89}}U_9 U_8 - h_{10}U_{10}, \\
\frac{\partial U_8}{\partial t} &= D\Delta U_8 + k_8 T - h_8 U_8, \\
\frac{\partial U_5}{\partial t} &= D\Delta U_5 + k_5 T - h_5 U_5.
\end{aligned}
$$



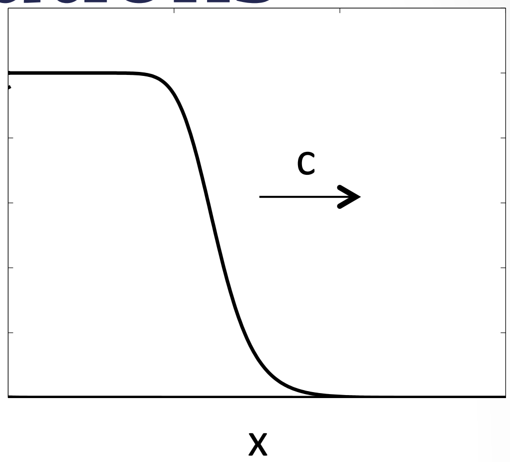
Thrombin Fibrin

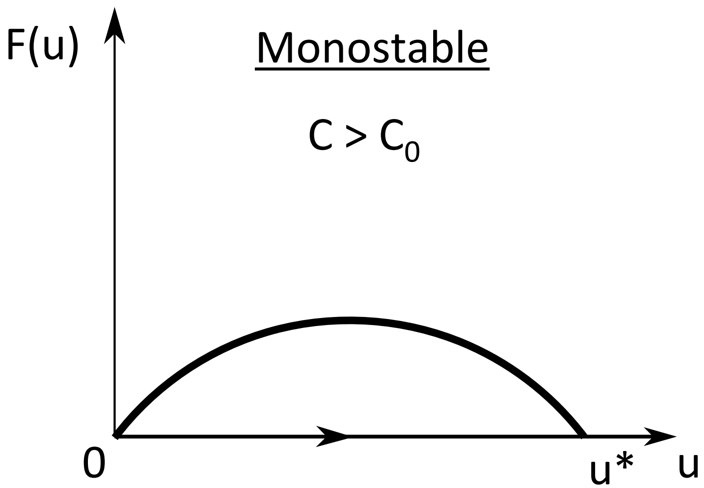


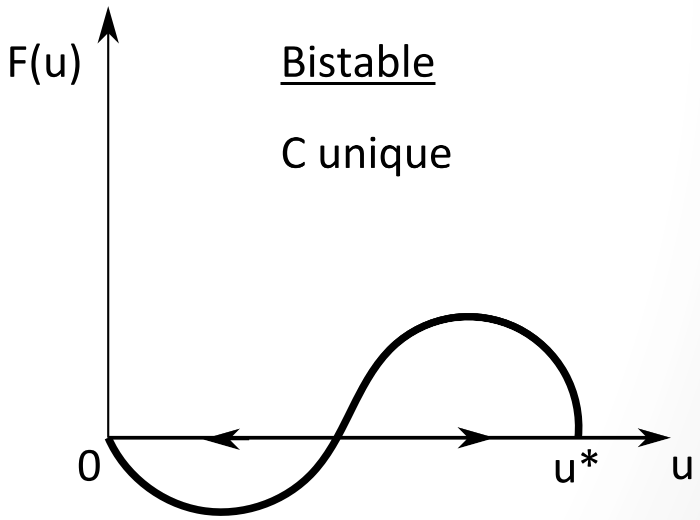
Thrombin propagation: traveling wave solutions

$$u(x,t) = w(x - ct),\ w(-\infty) = w_*,\ w(+\infty) = 0$$

$$\frac{\partial u}{\partial t} = D\Delta u + F(u),\ \frac{\partial F_i}{\partial u_j} \geq 0,\ \forall i \neq j.$$







Existence and stability of the traveling wave solutions

Complete system

$$\frac{\partial T}{\partial t} = D\Delta T + \left(k_2 U_{10} + \overline{k_2}\frac{k_{510}}{h_{510}} U_{10} U_5\right)\left(1 - \frac{T}{T_0}\right) - h_2 T,$$
$$\frac{\partial U_{11}}{\partial t} = D\Delta U_{11} + k_{11} T - h_{11} U_{11},$$
$$\frac{\partial U_9}{\partial t} = D\Delta U_9 + k_9 U_{11} - h_9 U_9,$$
$$\frac{\partial U_{10}}{\partial t} = D\Delta U_{10} + k_{10} U_9 + \overline{k_{10}}\frac{k_{89}}{h_{89}} U_9 U_8 - h_{10} U_{10},$$
$$\frac{\partial U_8}{\partial t} = D\Delta U_8 + k_8 T - h_8 U_8,$$
$$\frac{\partial U_5}{\partial t} = D\Delta U_5 + k_5 T - h_5 U_5.$$

One-equation model

$$\frac{\partial T}{\partial t} = \Delta T + P(T),$$

$$P(T) = kT^3(T^0 - T) - \sigma T$$

$$U_{11} = \frac{k_{11}}{h_{11}} T,\ U_9 = \frac{k_9 k_{11}}{h_9 h_{11}} T,\ U_5 = \frac{k_5}{h_5} T,\ U_8 = \frac{k_8}{h_8} T,$$
$$U_{10} = \frac{k_9 k_{11}}{h_{10} h_9 h_{11}}\left(k_{10} T + \overline{k_{10}}\frac{k_{89}}{h_{89}} T^2\right)$$

System reduction: minimax method

$$u'' + cu' + F(u,v) = 0$$
$$v'' + cv' + \frac{1}{\varepsilon}(au - bv) = 0$$

Formal transition:

$$\varepsilon \to 0, \qquad v = \frac{a}{b}u$$
$$u'' + cu' + F\left(u, \frac{a}{b}u\right) = 0$$

Minimax representation of the wave speed:

$$\min_x \frac{\rho_1'' + F(\rho_1, \rho_2)}{-\rho_1'} \le c \le \max_x \frac{\rho_1'' + F(\rho_1, \rho_2)}{-\rho_1'},$$
$$\min_x \frac{\rho_2'' + \frac{1}{\varepsilon}(\rho_1 - \rho_2)}{-\rho_2'} \le c \le \max_x \frac{\rho_2'' + \frac{1}{\varepsilon}(\rho_1 - \rho_2)}{-\rho_2'}.$$

Test functions:

$$\rho_1 = u_0,$$
$$\rho_2 = u_0 + \varepsilon F\left(u_0, \frac{a}{b}u_0\right)\frac{a}{b^2},$$

Estimates and convergence:

$$c_0 + \varepsilon \max\left\{\min_x \varphi, \min_x \psi\right\} \le c \le c_0 + \varepsilon \min\left\{\max_x \varphi, \max_x \psi\right\}$$

Analytical estimate for the thrombin wave propagation speed!

Blood disorders and speed of thrombin propagation

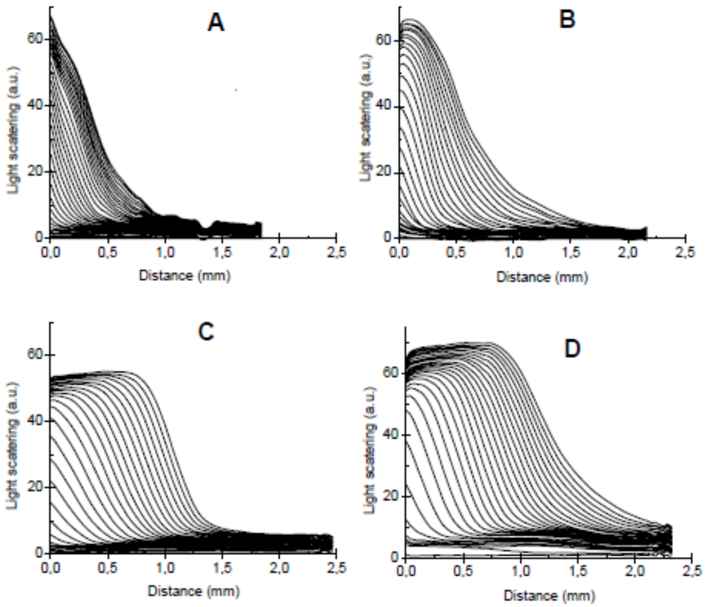
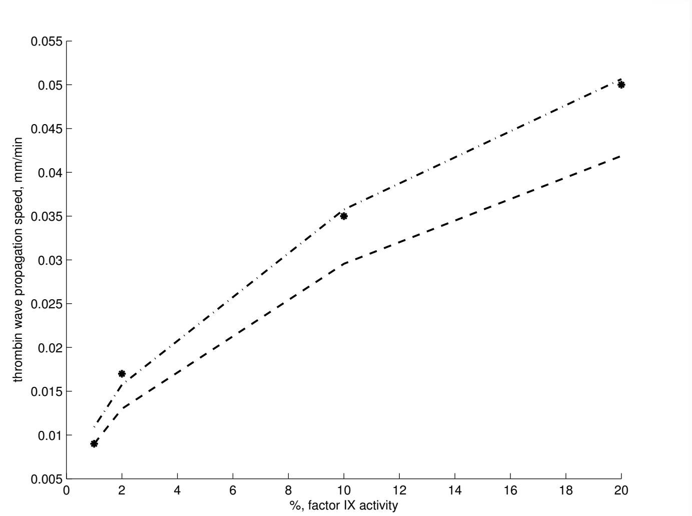


Figure 5. Clot growth from the glass surface in plasma of patients with (A) less than 1%, (B) 1.8%, (C) 2.8%, and (D) 5.5% of normal FIX clotting activity. The first curve was recorded in less than 1 minute after the start of the experiment; all other curves were recorded at a 2-minute intervals.



$$\hat{c}_1 = \sqrt{D}\frac{bII_0^2 - \frac{4}{5}bII_0^3 - 2h_2}{\sqrt{2\left(bII_0^2 - \frac{4}{5}bII_0^3\right)}}$$

$$b = \frac{k_9 k_{11} \overline{k_{10}} k_8 k_{89} \overline{k_2} k_5 k_{510} II_0^2}{h_9 h_{10} h_{11} h_8 h_{89} h_5 h_{510}}$$

Spatial Dynamics of Contact-Activated Fibrin Clot Formation *in vitro* and *in silico* in Haemophilia B: Effects of Severity and Ahemphil B Treatment

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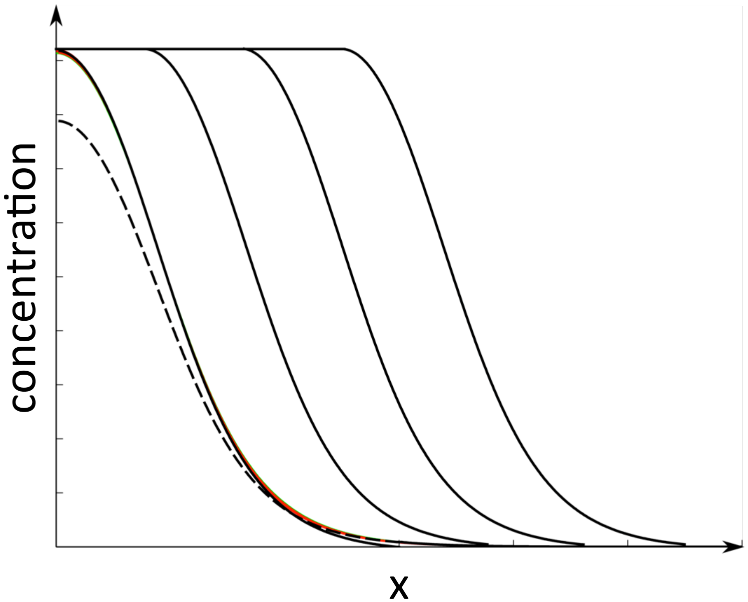
Conditions on thrombin wave propagation

<u>Pulse solution:</u> $Dw'' + F(w) = 0, \; w'(0) = 0, \; w(+\infty) = 0$

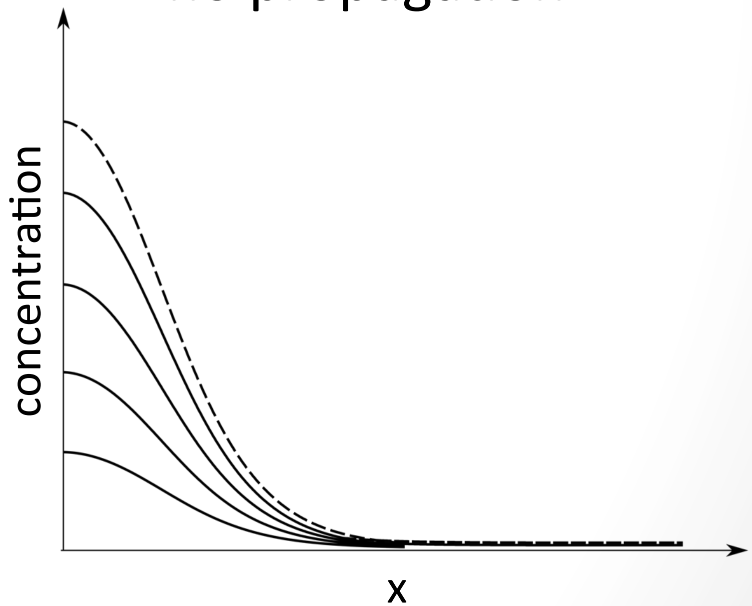
I.c. > pulse solution

propagation

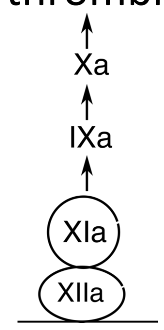


I.c. < pulse solution

no propagation



Initiation of thrombin formation near the contact surface



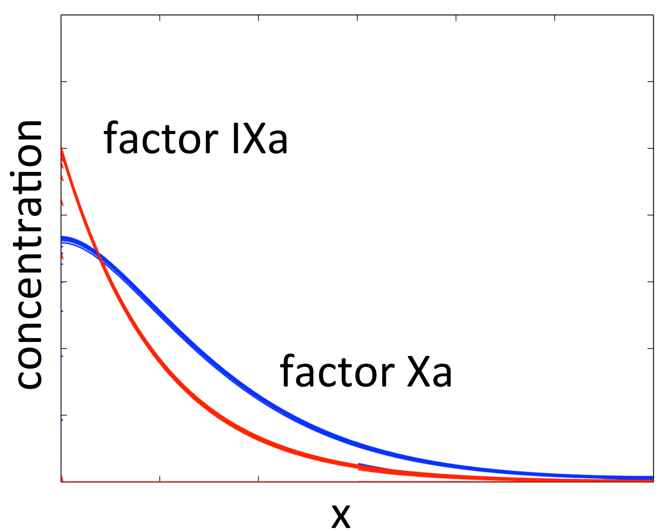
$$\frac{\partial U_9}{\partial t} = D\frac{\partial^2 U_9}{\partial x^2} - h_9 U_9, \quad \left.\frac{\partial U_9}{\partial n}\right|_{x=0} = P,$$

$$\frac{\partial U_{10}}{\partial t} = D\frac{\partial^2 U_{10}}{\partial x^2} + k_{10} U_9 - h_{10} U_{10},$$

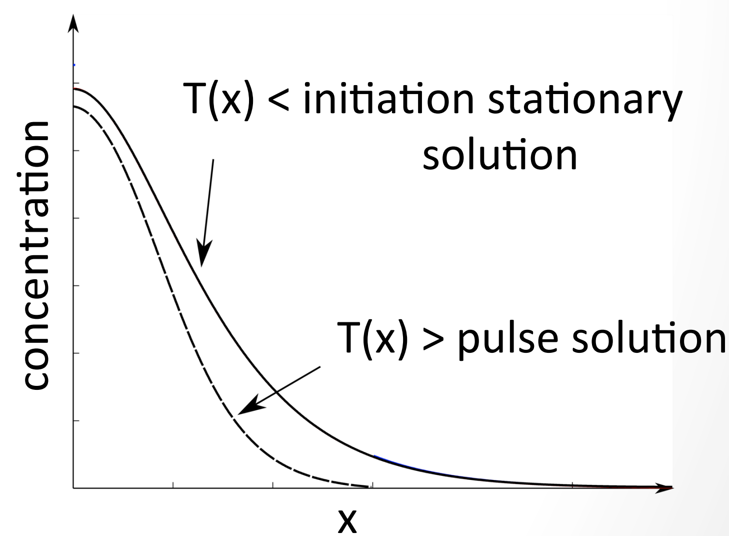
$$\frac{\partial T}{\partial t} = D\frac{\partial^2 T}{\partial x^2} + K U_{10}\left(1 - \frac{T}{T_0}\right) - h_2 T$$

$$\frac{\partial T}{\partial t} = \Delta T + P(T),$$

$$P(T) = kT^3(T^0 - T) - \sigma T$$



Condition on wave propagation



What do we get from theoretical analysis of 1D problem?

- Proof the existence and stability of the traveling wave solutions
- Wave speed estimate
- Analytical conditions on the thrombin wave propagation

Thank you for your attention!