# Modeling Blood Clotting Mechanisms

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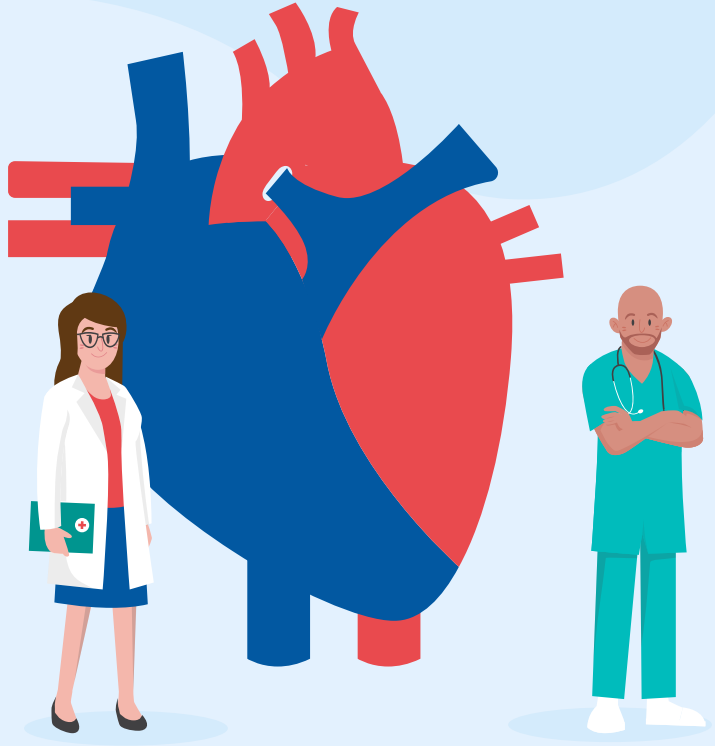

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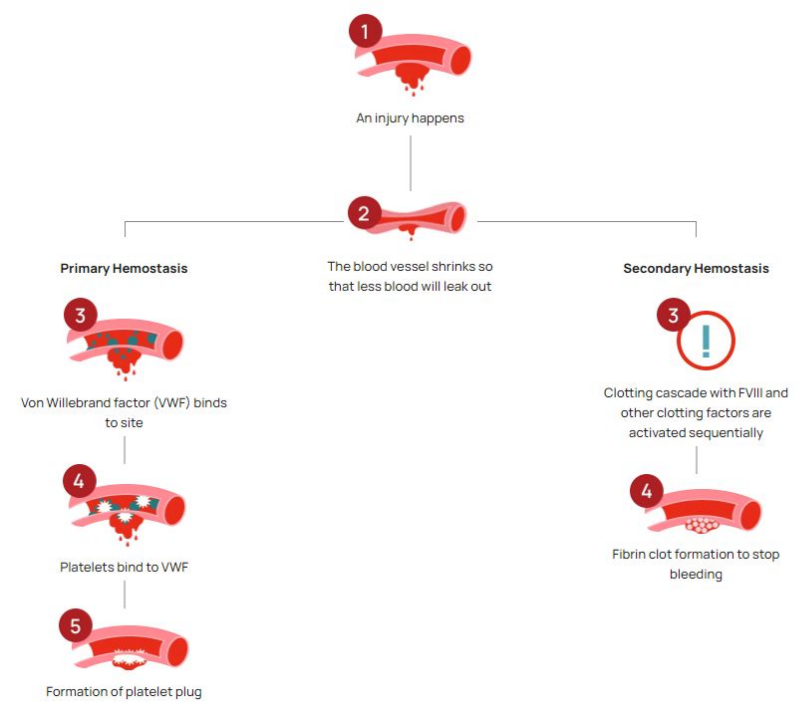
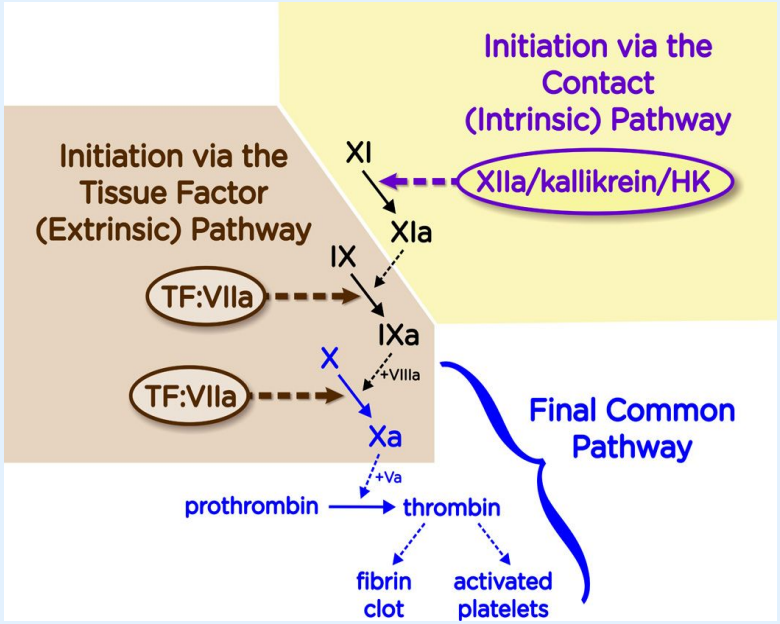
# Introduction

# Background

- Blood coagulation is an essential body process used to combat inflammatory stimuli
- Platelets and plasma in the blood combine to form clots over injuries
- For more superficial soft tissue injuries, it serves as a **negative feedback response** to prevent excessive bleeding



# Blood Coagulation Pathways




- The cascade can be simplified as two separate pathways that activate clotting factor Xa:
  - Intrinsic
  - Extrinsic
- Factor Xa transforms prothrombin to thrombin transforms prothrombin to fibrin which makes a formal clot to cease bleeding
- Anticoagulants such as heparin can boost antithrombin which essentially inhibits the cascade

**Our project models the blood clotting cascade, a sequential process responding to vessel injury by orchestrating platelets, clotting factors, and feedback mechanisms.**

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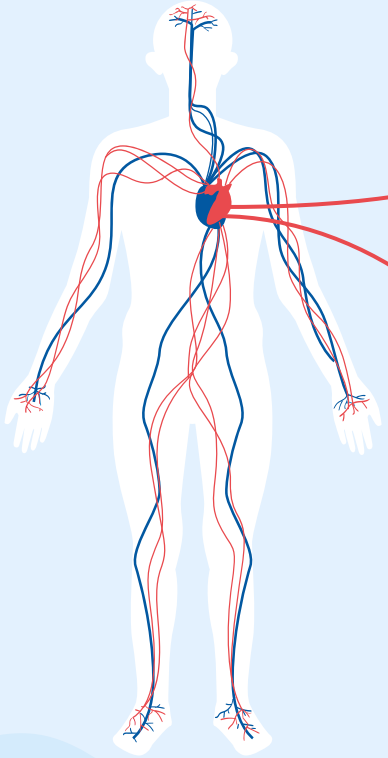
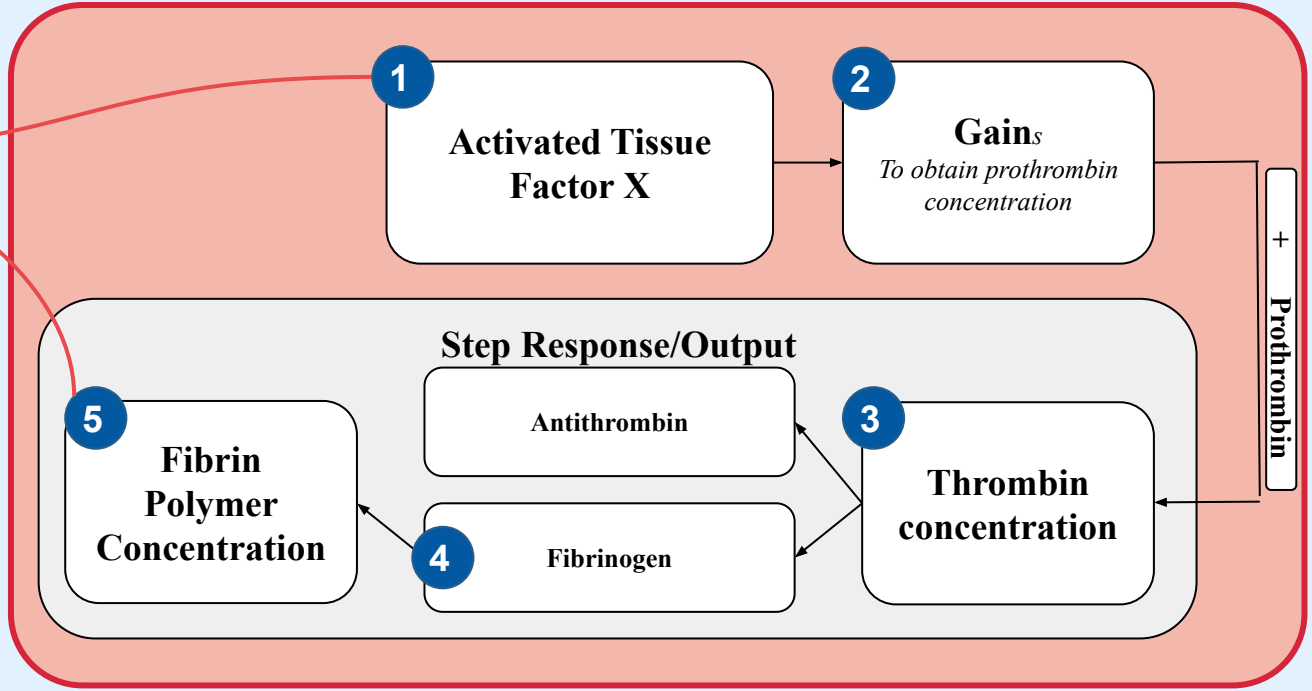
# Methods

# Blood Coagulation Biosystem Schematic





# Assumptions

- **Simplified Model**
  - Utilizing a condensed model with three equations and 9 kinetic constants to represent the intricate blood coagulation process.

- **Neglect of Spatial Variation or Diffusion Processes**
  - PDEs explicitly include spatial dependence through the variable, x
  - The (∂^2P/∂x^2, ∂^2T/∂x^2, ∂^2u/∂x^2) terms account for the spread/diffusion of the blood components in space

- **Initial concentrations of prothrombin(P) and thrombin(T) are equal**

# ODE system for Blood Coagulation (simple)

$$\frac{dP}{dt} = -(k_5 u + k_6 T + k_7 T^2 + k_8 T^3) P, \quad (1)$$

$$\frac{dT}{dt} = (k_5 u + k_6 T + k_7 T^2 + k_8 T^3) P - k_9 T, \quad (2)$$

[3]

$$\frac{du}{dt} = (k_1 + k_2 T + k_3 T^2)(u^0 - u) - k_4 u. \quad (3)$$

| | | |
|---|---|---|
| $k_1$ | 4.802e-05 | |
| $k_2$ | 1.111e-05 | |
| $k_3$ | 2.448e-07 | |
| $k_4$ | 0.000479 | |
| $k_5$ | 1.859e-05 | |
| $k_6$ | 3.762e-06 | |
| $k_7$ | 1.285e-10 | |
| $k_8$ | 4.066e-10 | |
| $k_9$ | 0.0202 | |
| $P_0$ | 1400 | |
| $X_0$ | 135 | |
| $D$ | Diffusion coefficient | 5e-5 |

- **P (Prothrombin)**
  - concentration of prothrombin in the blood plasma
  - inactive precursor of T, and its activation is a key step in the coagulation cascade
- **T (Thrombin)**
  - concentration of thrombin in the blood plasma
  - enzyme in blood coagulation
  - catalyzes conversion of fibrinogen to fibrin, leading to blood clot formation
- **u (Activated Factor X)**
  - concentration of activated factor X in the blood plasma
  - catalyzes conversion of prothrombin to thrombin

# ODE System for Blood Coagulation (complex)

$$\frac{\partial P}{\partial t} = D\frac{\partial^2 P}{\partial x^2} - \left(k_5 u + k_6 T + k_7 T^2 + k_8 T^3\right) P, \quad (4)$$

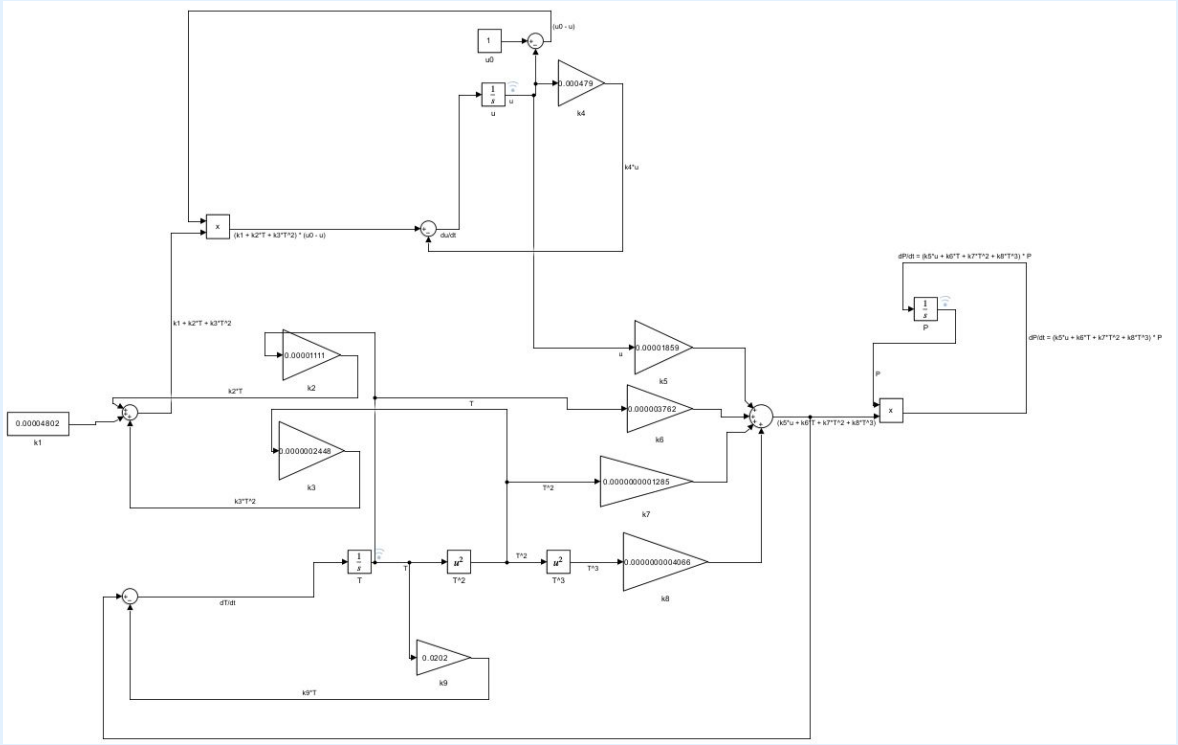
$$\frac{\partial T}{\partial t} = D\frac{\partial^2 T}{\partial x^2} + \left(k_5 u + k_6 T + k_7 T^2 + k_8 T^3\right) P - k_9 T, \quad (5)$$

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} + \left(k_2 T + k_3 T^2\right)\left(u^0 - u\right) - k_4 u, \quad (6)$$

[3]

- Extends the framework to consider spatial variations in addition to temporal dynamics
- The diffusion terms account for movement of substances in space
- Takes into account things such as the propagation of reaction-diffusion waves.

# Simulink Model



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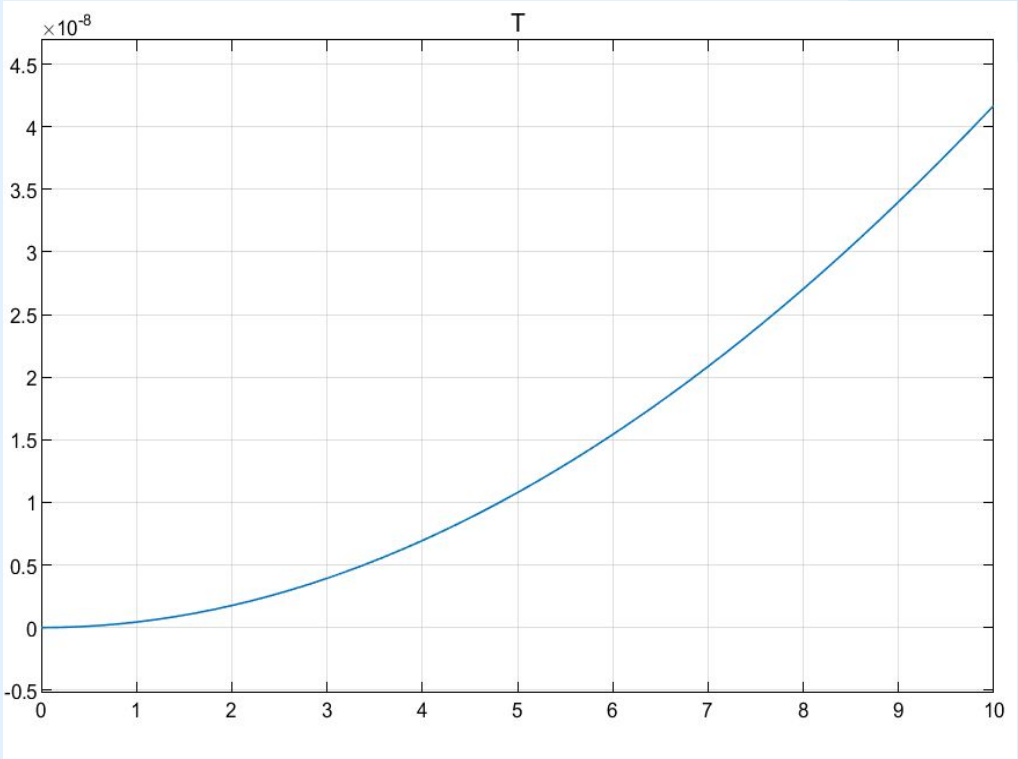
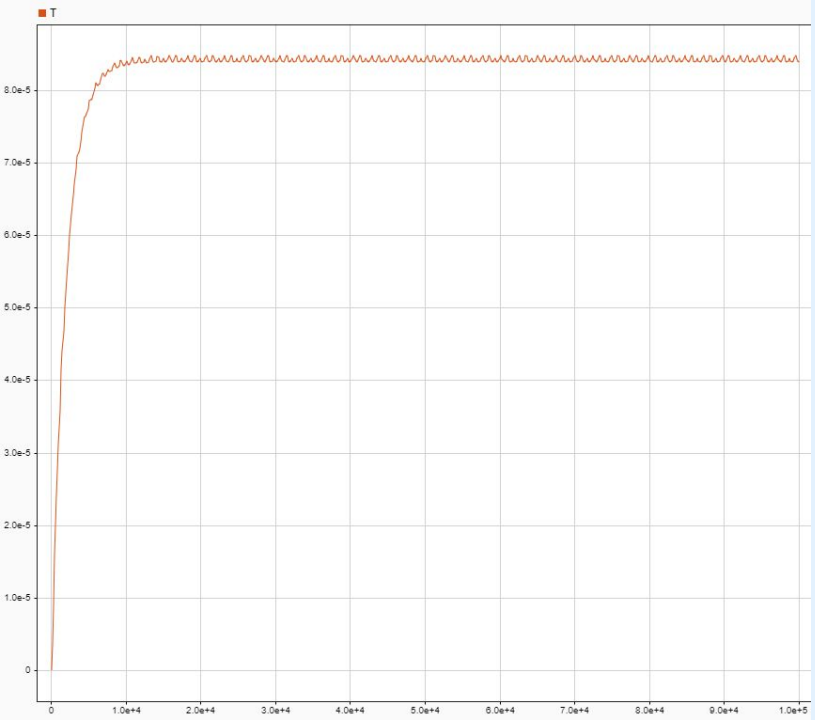
# Results

# Frequency Response




Thrombin Concentrations when Initial Conditions are Applied

# Frequency Response




Thrombin Concentrations when Initial Conditions are 0

# Analysis:

- Initiation & Exponential Growth Phase
  - When wounds open (slide 13)
  - Thrombin levels increase rapidly
  - Makes an exponential shape (typical in biosystems)
- Plateau Phase
  - Thrombin levels gradually plateau (slide 14)
  - Wounds close → Less need for coagulation
  - Dilution as blood continues to flow

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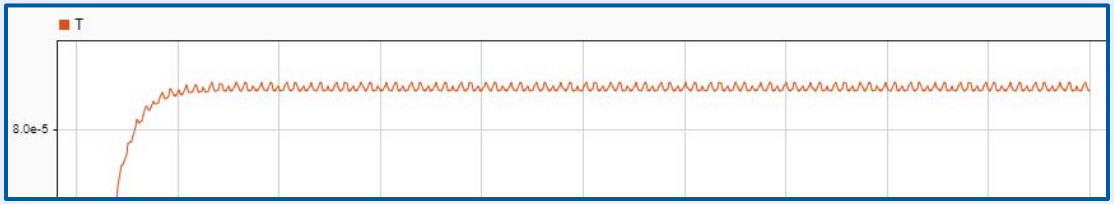
# Conclusion

# Interpretations

- Thrombin concentration plateaus, but does not reach steady state, therefore it is an unstable system
  - Waveforms observed after plateau

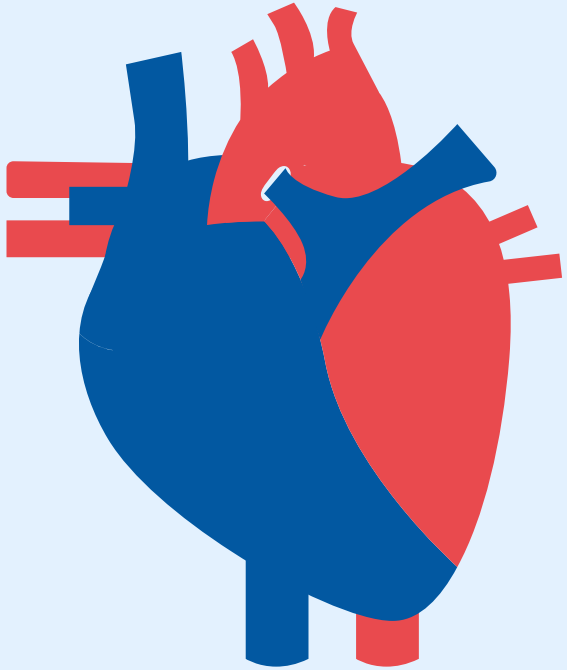



- Our system is a simplified version of reality
  - Did not model the output of prothrombin
  - If we include more interactions between biosignals, we can attain more accurate signals that represent coagulation.

# Future Steps/Clinical Applications

- Simplified model can be used by physicians to diagnose those with blood clotting disorders (e.g. hemophilia)

- Surgical applications - modeling the coagulation cascade can help monitor potential blood loss or excess clotting during surgery



## Special Thanks

- Dr. Gert Cauwenberghs
- Benjamin Balster

# References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