

A Mathematical Model for Blood Clotting

Sumanth Swaminathan David A. Edwards

Department of Mathematical Sciences; University of Delaware; Newark, DE 19716

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1 Introduction

Many biological phenomena are characterized by extensive fluid mechanical and chemical reactionary systems. As such, it is necessary to understand the manner in which these processes develop and the role that they play in a given system. Vascular blood flow is characterized by convective, diffusive, and reactive processes. Specifically, blood clot formation involves platelet convection within the blood stream, diffusion through the L ev eque boundary layer of the blood vessel, and binding to vascular breaches. Accordingly, in order to understand blood clotting, the fluid mechanics of blood flow as well as the reaction mechanism of platelet adhesion are relevant. In this study, we formulate a mathematical model for blood clotting and associated processes.

2 Governing Equations

2.1 Conservation of Mass

We start by considering blood flow in a uniform tube; that is to say there is no variation in the θ -direction, and there is no narrowing from blood clotting in the \tilde{z} -direction.

Conservation of mass in a cylindrical tube is modelled as follows:

$$\frac{1}{\tilde{r}} \frac{\partial(\tilde{r}\tilde{u}_{\tilde{r}})}{\partial\tilde{r}} + \frac{1}{\tilde{r}} \frac{\partial\tilde{u}_{\theta}}{\partial\theta} + \frac{\partial\tilde{u}_{\tilde{z}}}{\partial\tilde{z}} = 0. \quad (1)$$

where $(\tilde{u}_{\tilde{r}}, \tilde{u}_{\theta}, \tilde{u}_{\tilde{z}})$ is the velocity in the radial, angular, and downstream directions.

Examining (1), the following can be noted.

- (a) If we remove the radial and angular velocity terms, we are left with $\partial\tilde{u}_{\tilde{z}}/\partial\tilde{z} = 0$. This means that $u_{\tilde{z}}$ is not a function of \tilde{z} . We can remove the radial and angular velocity terms from this equation because we are assuming that the blood vessel is significantly small enough so that the flow of blood proceeds in a straight line and does not move in the radial direction. Also, we assume no rotation of the blood against the walls of the vessel, so there is no movement in any direction except the z -direction.
- (b) We have also assumed that there is no turbulence or churning in the tube, so $u_{\tilde{z}}$ is functionally independent of θ . Consequently, $u_{\tilde{z}}$ is solely a function of \tilde{r} .

2.2 Conservation of Linear Momentum/Steady Flow Case

We now wish to model conservation of linear momentum in the tube for our system. This is derived from the Navier-Stokes equations presented in cylindrical coordinates as follows:

$$\rho \left(\frac{\partial \tilde{u}_r}{\partial t} + \tilde{u}_r \frac{\partial \tilde{u}_r}{\partial \tilde{r}} + \frac{\tilde{u}_\theta}{\tilde{r}} \frac{\partial \tilde{u}_r}{\partial \theta} - \frac{\tilde{u}_\theta^2}{\tilde{r}} + \tilde{u}_z \frac{\partial \tilde{u}_r}{\partial \tilde{z}} \right) = -\frac{\partial \tilde{p}}{\partial \tilde{r}} + \mu \left\{ \frac{\partial}{\partial \tilde{r}} \left[\frac{1}{\tilde{r}} \frac{\partial(\tilde{r}\tilde{u}_r)}{\partial \tilde{r}} \right] + \frac{1}{\tilde{r}^2} \frac{\partial^2 \tilde{u}_r}{\partial \theta^2} - \frac{2}{\tilde{r}^2} \frac{\partial \tilde{u}_\theta}{\partial \theta} + \frac{\partial^2 \tilde{u}_r}{\partial \tilde{z}^2} \right\}, \quad (2)$$

$$\rho \left(\frac{\partial \tilde{u}_\theta}{\partial t} + \tilde{u}_r \frac{\partial \tilde{u}_\theta}{\partial \tilde{r}} + \frac{\tilde{u}_\theta}{\tilde{r}} \frac{\partial \tilde{u}_\theta}{\partial \theta} + \frac{\tilde{u}_\theta \tilde{u}_r}{\tilde{r}} + \tilde{u}_z \frac{\partial \tilde{u}_\theta}{\partial \tilde{z}} \right) = -\frac{1}{\tilde{r}} \frac{\partial \tilde{p}}{\partial \theta} + \mu \left\{ \frac{\partial}{\partial \tilde{r}} \left[\frac{1}{\tilde{r}} \frac{\partial(\tilde{r}\tilde{u}_\theta)}{\partial \tilde{r}} \right] + \frac{1}{\tilde{r}^2} \frac{\partial^2 \tilde{u}_\theta}{\partial \theta^2} + \frac{2}{\tilde{r}^2} \frac{\partial \tilde{u}_r}{\partial \theta} + \frac{\partial^2 \tilde{u}_\theta}{\partial \tilde{z}^2} \right\}, \quad (3)$$

$$\rho \left(\frac{\partial \tilde{u}_z}{\partial t} + \tilde{u}_r \frac{\partial \tilde{u}_z}{\partial \tilde{r}} + \frac{\tilde{u}_\theta}{\tilde{r}} \frac{\partial \tilde{u}_z}{\partial \theta} + \tilde{u}_z \frac{\partial \tilde{u}_z}{\partial \tilde{z}} \right) = -\frac{\partial \tilde{p}}{\partial \tilde{z}} + \mu \left[\frac{1}{\tilde{r}} \frac{\partial}{\partial \tilde{r}} \left(\tilde{r} \frac{\partial \tilde{u}_z}{\partial \tilde{r}} \right) + \frac{1}{\tilde{r}^2} \frac{\partial^2 \tilde{u}_z}{\partial \theta^2} + \frac{\partial^2 \tilde{u}_z}{\partial \tilde{z}^2} \right], \quad (4)$$

where ρ represents the pressure, μ the viscosity, and \tilde{P} the pressure.

Since we know that there is no radial or angular velocity and that $\partial \tilde{u}_z / \partial \tilde{z} = 0$ and $\partial \tilde{u}_z / \partial \theta = 0$, equation (5) can be reduced to the following:

$$\rho \left(\frac{\partial \tilde{u}_z}{\partial t} \right) = -\frac{\partial \tilde{p}}{\partial \tilde{z}} + \mu \left[\frac{1}{\tilde{r}} \frac{\partial}{\partial \tilde{r}} \left(\tilde{r} \frac{\partial \tilde{u}_z}{\partial \tilde{r}} \right) \right].$$

Rearranging this equation, we can represent conservation of linear momentum in our system as

$$\frac{\partial \tilde{p}}{\partial \tilde{z}} = \frac{\mu}{\tilde{r}} \frac{\partial}{\partial \tilde{r}} \left(\tilde{r} \frac{\partial \tilde{u}_z}{\partial \tilde{r}} \right) - \rho \left(\frac{\partial \tilde{u}_z}{\partial t} \right). \quad (5)$$

We can analyze this result in a couple different ways. We begin by assuming steady flow, which implies no change in velocity over time. Equation (5) for this case then becomes

$$\frac{\partial \tilde{p}}{\partial \tilde{z}} = \frac{\mu}{\tilde{r}} \frac{\partial}{\partial \tilde{r}} \left(\tilde{r} \frac{\partial \tilde{u}_z}{\partial \tilde{r}} \right). \quad (6)$$

Now, since the left side is a function of only \tilde{z} , and the right side is a function of only \tilde{r} , we can say that both sides of the equations are constant, and we can now represent $\partial \tilde{p} / \partial \tilde{z}$ as the average pressure gradient across the length (L) of the tube. First, we establish boundary conditions on the pressure:

$$\tilde{p}(\tilde{r}, \theta, 0, \tilde{t}) = P_0 + \Delta P, \quad \tilde{p}(\tilde{r}, \theta, L, \tilde{t}) = P_0.$$

Given these boundary conditions, the average pressure across the tube is

$$\frac{\partial \tilde{p}}{\partial \tilde{z}} = \frac{\tilde{p}(\tilde{r}, \theta, L, \tilde{t}) - \tilde{p}(\tilde{r}, \theta, 0, \tilde{t})}{L} = \frac{P_0 - (P_0 + \Delta P)}{L} = -\frac{\Delta P}{L}.$$

Now equation (6) evolves as follows:

$$\begin{aligned}
-\frac{\Delta P}{L} &= \frac{\mu}{\tilde{r}} \frac{\partial}{\partial \tilde{r}} \left(\tilde{r} \frac{\partial \tilde{u}_{\tilde{z}}}{\partial \tilde{r}} \right) \\
\frac{\partial}{\partial \tilde{r}} \left(\tilde{r} \frac{\partial \tilde{u}_{\tilde{z}}}{\partial \tilde{r}} \right) &= -\frac{\tilde{r} \Delta P}{\mu L}.
\end{aligned} \tag{7}$$

Because we are modelling a system that has surface reactions as the fluid flows, it is common to accept a no-slip convention. This means that the fluid sticks to the wall and, there is no flow there. Consequently, one boundary condition that arises for this system is $\tilde{u}_{\tilde{z}}(R) = 0$ (R represents the radius of the tube).

2.3 The Convection-Diffusion System/Boundary Layer

The convection-diffusion equation accounts for the change in the concentration of reactant in fluid over time due to its convection across the cylinder and its diffusion through the boundary layer. It is modelled in cylindrical coordinates as follows:

$$\frac{\partial \tilde{C}}{\partial \tilde{t}} = \tilde{D} \left[\frac{1}{\tilde{r}} \frac{\partial}{\partial \tilde{r}} \left(\tilde{r} \frac{\partial \tilde{C}}{\partial \tilde{r}} \right) + \frac{1}{\tilde{r}^2} \frac{\partial^2 \tilde{C}}{\partial \theta^2} + \frac{\partial^2 \tilde{C}}{\partial \tilde{z}^2} \right] - (\tilde{u}_{\tilde{r}}, \tilde{u}_{\theta}, \tilde{u}_{\tilde{z}}) \cdot \nabla \tilde{C}, \tag{8}$$

where \tilde{D} represents the molecular diffusivity. This equation will be simplified and scaled in later passages. The boundary conditions on the system are as follows:

- (a) The input concentration is set to be the initial concentration of platelets in the blood, so $\tilde{C}(\tilde{r}, \theta, 0, \tilde{t}) = C_T$.
- (b) At the reacting surface of the boundary layer ($\tilde{r} = R$) the flux through the surface is equal to the rate of change of the bound receptor concentration (denoted by $\tilde{B}(\theta, \tilde{z}, \tilde{t})$).

2.4 The Surface Reactions

Initially, we consider a two step reaction that produces two complexes. First, the reactant in the fluid (L) binds to a receptor (R) to form a ligand (platelet) receptor complex (LR). Second, this complex reacts with more ligand to produce a new complex (L₂R). Although it is plausible to consider more reactions of this type and also consider reversible reactions, for now we consider just this simple case. Furthermore, we consider only first order kinetics in the reactants. The reactions are modelled in the following manner:



If we consider the concentration of each species as

- (a) $[L_i R] = \tilde{B}^{(i)}$ (for $i > 0$),
- (b) $[R] = R_T - \tilde{B}^{(1)} - \tilde{B}^{(2)} = \tilde{B}^{(0)}$,

(c) $[L]=\tilde{C}$,

then we can write the rate law for this pair of reactions in differential form assuming first order kinetics. This takes the following form:

$$\frac{\partial \tilde{B}^{(1)}}{\partial \tilde{t}} = \tilde{k}_1 \left(R_T - \tilde{B}^{(1)} - \tilde{B}^{(2)} \right) \tilde{C}(R, \tilde{z}, \tilde{t}) - \tilde{k}_2 \tilde{B}^{(1)} \tilde{C}(R, \tilde{z}, \tilde{t}), \quad (11)$$

$$\frac{\partial \tilde{B}^{(2)}}{\partial \tilde{t}} = \tilde{k}_2 \tilde{B}^{(1)} \tilde{C}(R, \tilde{z}, \tilde{t}), \quad (12)$$

where \tilde{k}_i are the reaction rate constants.

We consider the relationship between the flux through the surface and the rate of change of the total bound receptor concentration in the following manner:

$$-\tilde{D} \frac{\partial \tilde{C}}{\partial \tilde{r}}(R, \tilde{t}) = \frac{\partial \tilde{B}^{(1)}}{\partial \tilde{t}} + \frac{\partial \tilde{B}^{(2)}}{\partial \tilde{t}}. \quad (13)$$

The motivation of this equation is essentially a mass balance. We account for the accumulation or depletion of $\tilde{B}(\theta, \tilde{z}, \tilde{t})$ over time with whatever is left over in the tube after particles enter and exit. In this case, because diffusion is dominating, particles would be diffusing in and out of the boundary layer.

3 Scalings

All quantities having a physical dimension are scaled against some characteristic quantity. These quantities often represent maximum values, and on occasion are merely terms that simplify algebra. Characteristic quantities are denoted as x_c , and the dimensionless scaled terms are represented by the following:

$$x = \frac{\tilde{x}}{x_c}. \quad (14)$$

3.1 The velocity

To simplify and solve equation (8), we choose a scaling for the velocity in order to make equation (8) look like the following:

$$\frac{\partial}{\partial r} \left(r \frac{\partial u}{\partial r} \right) = -4r. \quad (15)$$

Choosing the characteristic radius (r_c) to be the radius of the blood vessel (R), and scaling equation (8), we get the following:

$$\begin{aligned} \frac{\partial}{\partial (r \cdot r_c)} \left[(r \cdot r_c) \left(\frac{\partial (u \cdot u_c)}{\partial (r \cdot r_c)} \right) \right] &= -\frac{(r \cdot r_c) \Delta P}{\mu L}. \\ u_c \left[\frac{\partial}{\partial r} \left(r \frac{\partial u}{\partial r} \right) \right] &= -4r \left(-\frac{R^2 \Delta P}{4\mu L} \right) \\ u_c &= \left(\frac{R^2 \Delta P}{4\mu L} \right). \end{aligned} \quad (16)$$

Of course, having now chosen the characteristic radius to be the radius of the blood vessel (R), the boundary condition on the velocity is

$$u_z(1) = 0. \quad (17)$$

3.2 The Convection-Diffusion System

In the case of the convection-diffusion equation, the scaling for time and the length of the tube are still not chosen. Time will be scaled later when scaling the boundary layer equation. Of course, an appropriate scaling for the independent variable z would be the length of the tube as that would be the maximum distance blood would ever travel. The length scaling will be denoted: ($z_c = L$). Plugging these scalings into the convection-diffusion equation and simplifying, we get the following:

$$\frac{\partial(C_b \cdot C_c)}{\partial(t \cdot t_c)} = \tilde{D} \left[\frac{1}{(r \cdot R)} \frac{\partial}{\partial(r \cdot R)} \left((r \cdot R) \frac{\partial(C_b \cdot C_c)}{\partial(r \cdot R)} \right) + \frac{1}{(r^2 \cdot R^2)} \frac{\partial^2(C_b \cdot C_c)}{\partial\theta^2} \right. \\ \left. + \frac{\partial^2(C_b \cdot C_c)}{\partial(z \cdot z_c)^2} \right] - u_z \left(\frac{C_c u_c}{z_c} \right) \frac{\partial C_b}{\partial z} \quad (18)$$

$$\frac{1}{u_c t_c} \frac{\partial C_b}{\partial t} = \frac{\tilde{D}}{u_c R^2} \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial C_b}{\partial r} \right) \right] + \left(\frac{\tilde{D}}{L^2 u_c} \right) \frac{\partial^2 C_b}{\partial z^2} - \left(\frac{u_z}{L} \right) \frac{\partial C_b}{\partial z}$$

$$\frac{L}{u_c t_c} \frac{\partial C_b}{\partial t} = \frac{\tilde{D} L}{u_c R^2} \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial C_b}{\partial r} \right) \right] + \left(\frac{\tilde{D}}{L u_c} \right) \frac{\partial^2 C_b}{\partial z^2} - u_z \frac{\partial C_b}{\partial z}$$

$$\frac{L}{u_c t_c} \frac{\partial C_b}{\partial t} = \frac{\tilde{D} L}{u_c R^2} \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial C_b}{\partial r} \right) + \left(\frac{R^2}{L^2} \right) \frac{\partial^2 C_b}{\partial z^2} \right] - u_z \frac{\partial C_b}{\partial z}$$

$$\frac{L}{u_c t_c} \frac{\partial C_b}{\partial t} = \frac{\tilde{D} L}{u_c R^2} \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial C_b}{\partial r} \right) + \epsilon^2 \frac{\partial^2 C_b}{\partial z^2} \right] - u_z \frac{\partial C_b}{\partial z} \quad (19)$$

where

$$\epsilon = \frac{R}{L}. \quad (20)$$

In this case, because the diffusivity constant (\tilde{D}) is small, the coefficient of the first term on the right hand side of equation (19) is also small. Thus, we scale the radius again by this coefficient in such a way as to blow up the region around the walls where the reactions take place. We do this because we assume that at this point, the effects of convection and diffusion balance and we can analyze the change in the concentration of reactant due to the reactions with the wall. First, we let

$$y = \text{Pe}^\alpha (1 - r),$$

where

$$\text{Pe} = \frac{u_c u'_z(1) R^2}{\tilde{D} L}.$$

The definition for the Peclét number closely resembles the inverse of the coefficient of the first term on the right side of equation (19). Thus, its inverse is also a small number and is an appropriate

scaling factor for the radius. The use of the extra derivative term is for algebraic simplicity and becomes more clear in later passages when we discuss the solution to the velocity equation and how it affects the convection-diffusion system. The absolute value of the derivative term is used because the velocity profile decreases as it approaches the wall, so the derivative of the velocity at the wall is negative. This is more mathematically obvious later when we show the solution for the velocity profile. Next we do a two-term Taylor series expansion of u_z about the boundary of the blood vessel at $r = 1$. Here $u_z(1)$ is zero because of the no-slip condition imposed at the wall.

$$u_z = u_z(1) + (r - 1)u'_z(1) = \text{Pe}^{-\alpha}u'_z(1)y.$$

Now we can re-scale equation (19).

$$\begin{aligned} \frac{L}{u_c t_c} \frac{\partial C}{\partial t} = & \text{Pe}^{-1}u'_z(1) \left[\frac{-\text{Pe}^\alpha}{1 - y\text{Pe}^{-\alpha}} \left[\frac{\partial}{\partial y} \left((1 - y\text{Pe}^{-\alpha})(-\text{Pe}^\alpha) \left(\frac{\partial C}{\partial y} \right) \right) \right] + \epsilon^2 \frac{\partial^2}{\partial y^2} \right] \\ & - (\text{Pe}^{-\alpha}u'_z(1)y) \frac{\partial C}{\partial z}. \end{aligned} \quad (21)$$

We eliminate the ϵ^2 term because it is small, so the equation becomes

$$\begin{aligned} \frac{L}{u_c t_c} \frac{\partial C}{\partial t} &= \text{Pe}^{-1}u'_z(1) \left[\frac{\text{Pe}^{2\alpha}}{1 - y\text{Pe}^{-\alpha}} \left[\frac{\partial}{\partial y} \left((1 - y\text{Pe}^{-\alpha}) \left(\frac{\partial C}{\partial y} \right) \right) \right] \right] - \text{Pe}^{-\alpha} (u'_z(1)y) \frac{\partial C}{\partial z} \\ \frac{L}{u_c t_c} \frac{\partial C}{\partial t} &= \text{Pe}^{-1}u'_z(1) \left[\frac{\text{Pe}^{2\alpha}}{1 - y\text{Pe}^{-\alpha}} \left(-\text{Pe}^{-\alpha} \frac{\partial C}{\partial y} + (1 - y\text{Pe}^{-\alpha}) \frac{\partial^2 C}{\partial y^2} \right) \right] - \text{Pe}^{-\alpha} (u'_z(1)y) \frac{\partial C}{\partial z} \\ \frac{L}{u_c t_c} \frac{\partial C}{\partial t} &= \text{Pe}^{-1}u'_z(1) \left[\frac{-\text{Pe}^\alpha}{1 - y\text{Pe}^{-\alpha}} \frac{\partial C}{\partial y} + \text{Pe}^{2\alpha} \frac{\partial^2 C}{\partial y^2} \right] - \text{Pe}^{-\alpha} (u'_z(1)y) \frac{\partial C}{\partial z} \\ \frac{L}{u_c u'_z(1) t_c} \frac{\partial C}{\partial t} &= \text{Pe}^{(2\alpha-1)} \frac{\partial^2 C}{\partial y^2} - \text{Pe}^{-\alpha} y \frac{\partial C}{\partial z}. \end{aligned} \quad (22)$$

Here, we recognize that both terms on the right side of equation (22) should be important. To ensure this, we equate the powers of the Peclét number in both terms and determine that $\alpha = 1/3$. Equation (22) then reduces to

$$\frac{L\text{Pe}^{-\frac{1}{3}}}{u_c |u'_z(1)| t_c} \frac{\partial C}{\partial t} = \frac{\partial^2 C}{\partial y^2} - y \frac{\partial C}{\partial z}. \quad (23)$$

3.3 The Surface Reactions

The rate laws associated with the reactions at the boundary layer introduce several new variables that all need to be scaled. Ideally, after scaling, the equations should look nearly the same and all of the dimensional quantities unique to this problem would be eliminated. Thus, if we choose the following scalings:

$$t_c = \frac{1}{\tilde{k}_1 C_c}, \quad B_c^{(1)} = B_c^{(2)} = R_T, \quad k_2 = \frac{\tilde{k}_2}{\tilde{k}_1},$$

then equations (11) and (12) transform as follows:

$$\frac{\partial \tilde{B}^{(1)}}{\partial \tilde{t}} = \tilde{k}_1 \left(R_T - \tilde{B}^{(1)} - \tilde{B}^{(2)} \right) \tilde{C}(R, \tilde{z}, \tilde{t}) - \tilde{k}_2 \tilde{B}^{(1)} \tilde{C}(R, \tilde{z}, \tilde{t})$$

$$\begin{aligned} \frac{\partial (B^{(1)} \cdot R_T)}{\partial (t \cdot t_c)} = & \tilde{k}_1 \left(R_T - B^{(1)} \cdot R_T - B^{(2)} \cdot R_T \right) C(0, z, t) \cdot C_c \\ & - \tilde{k}_2 \left(B^{(1)} \cdot R_T \right) C(0, z, t) \cdot C_c \end{aligned} \quad (24)$$

$$\begin{aligned} \frac{\partial B^{(1)}}{\partial t} = & \tilde{k}_1 t_c C_c \left(1 - B^{(1)} - B^{(2)} \right) C(0, z, t) - \tilde{k}_2 C_c t_c B^{(1)} C(0, z, t) \\ \frac{\partial B^{(1)}}{\partial t} = & \left(1 - B^{(1)} - B^{(2)} \right) C(0, z, t) - k_2 B^{(1)} C(0, z, t), \end{aligned} \quad (25)$$

$$\begin{aligned} \frac{\partial (B^{(2)} \cdot R_T)}{\partial (t \cdot t_c)} = & \tilde{k}_2 C_c R_T B^{(1)} C(0, z, t) \\ \frac{\partial B^{(2)}}{\partial t} = & k_2 B^{(1)} C(0, z, t). \end{aligned} \quad (26)$$

We further scale equation (13) using all of our previously chosen scalings to get the following:

$$\begin{aligned} -\tilde{D} \frac{\partial \tilde{C}}{\partial \tilde{r}}(R, \tilde{t}) &= \frac{\partial \tilde{B}^{(1)}}{\partial \tilde{t}} + \frac{\partial \tilde{B}^{(2)}}{\partial \tilde{t}} \\ -\frac{\tilde{D} C_c}{R} \frac{\partial C}{\partial r} &= \frac{R_T}{t_c} \left[\frac{\partial B^{(1)}}{\partial t} + \frac{\partial B^{(2)}}{\partial t} \right] \\ \frac{\tilde{D} C_c}{R} \left(-\text{Pe}^{\frac{1}{3}} \right) \frac{\partial C}{\partial y} &= \frac{R_T}{t_c} \left[\frac{\partial B^{(1)}}{\partial t} + \frac{\partial B^{(2)}}{\partial t} \right] \\ \frac{\partial C}{\partial y}(0, z, t) &= \frac{R R_T \text{Pe}^{-\frac{1}{3}}}{\tilde{D} C_c t_c} \left[\frac{\partial B^{(1)}}{\partial t} + \frac{\partial B^{(2)}}{\partial t} \right] \\ \frac{\partial C}{\partial y}(0, z, t) &= \text{Da} \left[\frac{\partial B^{(1)}}{\partial t} + \frac{\partial B^{(2)}}{\partial t} \right], \end{aligned} \quad (27)$$

where

$$\text{Da} = \frac{R \tilde{k}_1 R_T \text{Pe}^{-\frac{1}{3}}}{\tilde{D}}. \quad (28)$$

Da is referred to as the Damköhler number. The important terms in the definition are the reaction rate constant (\tilde{k}_1) and the diffusion coefficient (\tilde{D}). The ratio here gives a comparison between the rate of reaction and the rate of diffusion. For high Da, the reaction rate dominates whereas for low Da, diffusion dominates.

Summary of Scalings
Scalings:

$$r_c = R, \quad z_c = L, \quad y = \text{Pe}^{\frac{1}{3}}(1-r), \quad C_c = C_T, \quad (29)$$

$$t_c = \frac{1}{\tilde{k}_1 C_c}, \quad B_c^{(1)} = B_c^{(2)} = R_T, \quad k_2 = \frac{\tilde{k}_2}{\tilde{k}_1}.$$

Scaled Equations:

$$\frac{\partial}{\partial r} \left(r \frac{\partial u}{\partial r} \right) = -4r,$$

$$\frac{L\text{Pe}^{\frac{1}{3}}}{u_c|u'_z(1)|t_c} \frac{\partial C}{\partial t} = \frac{\partial^2 C}{\partial y^2} - y \frac{\partial C}{\partial z},$$

$$\frac{\partial B^{(1)}}{\partial t} = k_1 \left(1 - B^{(1)} - B^{(2)} \right) C(1, z, t) - k_2 B^{(1)} C(1, z, t),$$

$$\frac{\partial B^{(2)}}{\partial t} = k_2 B^{(1)} C(1, z, t),$$

$$\frac{\partial C}{\partial y}(0, z, t) = \text{Da} \left[\frac{\partial B^{(1)}}{\partial t} + \frac{\partial B^{(2)}}{\partial t} \right].$$

4 Solutions/Results

4.1 The velocity

As previously stated, the no-slip condition sets up the following boundary condition on the velocity:

$$u_z(1) = 0.$$

With this boundary condition, we solve equation (15) for the velocity as follows:

$$\frac{\partial}{\partial r} \left(r \frac{\partial u}{\partial r} \right) = -4r$$

$$r \frac{du_z}{dr} = -2r^2 + \gamma_1$$

$$du_z = \left(-2r + \frac{\gamma_1}{r} \right) dr$$

$$u_z = -r^2 + \gamma_1 \ln(r) + \gamma_2.$$

The natural log function is not continuous at the origin, so we let $\gamma_1 = 0$. Using the boundary condition, we find that $\gamma_2 = 1$. Thus,

$$\underline{u_z(r) = 1 - r^2}. \quad (30)$$

Now, equation (23) and the value of the Peclet number are fully discernible because

$$u'_z(1) = 2.$$

Thus,

$$\begin{aligned} \text{Pe} &= \frac{2u_c R^2}{\tilde{D}L}, \\ \frac{L\text{Pe}^{-\frac{1}{3}}}{2u_c t_c} \frac{\partial C}{\partial t} &= \frac{\partial^2 C}{\partial y^2} - y \frac{\partial C}{\partial z}. \end{aligned} \quad (31)$$

Note that the left side of equation (31) is very small due to the size of the inverse Peclet number. This allows us to simplify (31) to:

$$y \frac{\partial C}{\partial z} = \frac{\partial^2 C}{\partial y^2}. \quad (32)$$

4.2 The Convection-Diffusion System

We know that convection happens far quicker than diffusion. Thus, we can represent the concentration of the unbound platelets and that of the bound receptor sites in a couple ways. One way is to assume the concentration of the unbound platelets never changes and say that only the empty receptors react to create a product. Another way is to account for the small change in platelet concentration due to diffusion. We accomplish both of these tasks by representing the concentration of the platelets and the bound receptors as a series expansion in orders of Da (the Damköhler number):

$$C(y, z, t; \text{Da}) = C_0(y, z, t) + \text{Da}C_1(y, z, t) + o(\text{Da}), \quad (33)$$

$$B(z, t; \text{Da}) = B_0^{(i)}(z, t) + \text{Da}B_1^{(i)}(z, t) + o(\text{Da}). \quad (34)$$

First, we look at the concentration of unbound platelets. If we plug (33) into (32) and expand to leading two orders, we observe the following:

$$y \frac{\partial C_0}{\partial z} = \frac{\partial^2 C_0}{\partial y^2}, \quad (35)$$

$$y \frac{\partial C_1}{\partial z} = \frac{\partial^2 C_1}{\partial y^2}. \quad (36)$$

Now, the solution to the leading order equation is obtained by observing the flux condition specified by (27). We know that to leading order, (27) specifies that there is no radial gradient in C at the boundary layer. Thus,

$$\frac{\partial C_0}{\partial z} = 0 \quad (37)$$

$$C_0(z) = \text{constant}, \quad (38)$$

but, by the boundary condition specified at the entrance of the blood vessel (at all radii), we know that $C_0(r, 0, t) = 1$. Since equation (38) indicates that C_0 is constant in z ,

$$C_0(r, z, t) = 1. \quad (39)$$

This then becomes the one unique solution to (35). The solution for the leading second order equation is, however, more complicated.

4.3 The Surface Reactions

The reaction equations for the bound state are expanded upon substitution of (34) as follows.

$$\frac{\partial B_0^{(1)}}{\partial t} + \text{Da} \frac{\partial B_1^{(1)}}{\partial t} = \left[1 - \left(B_0^{(1)} + \text{Da} B_1^{(1)} \right) - \left(B_0^{(2)} + \text{Da} B_1^{(2)} \right) \right] [C_0 + \text{Da} C_1] - k_2 \left(B_0^{(1)} + \text{Da} B_1^{(1)} \right) (C_0 + \text{Da} C_1) \quad (40)$$

$$\begin{aligned} \frac{\partial B_0^{(1)}}{\partial t} + \text{Da} \frac{\partial B_1^{(1)}}{\partial t} &= \left(C_0 - C_0 B_0^{(1)} - \text{Da} C_0 B_1^{(1)} - C_0 B_0^{(2)} - \text{Da} C_0 B_1^{(2)} \right) + \\ &\left(\text{Da} C_1 - \text{Da} C_1 B_0^{(1)} - \text{Da}^2 C_1 B_1^{(1)} - \text{Da} C_1 B_0^{(2)} - \text{Da}^2 C_1 B_1^{(2)} \right) - \\ &k_2 \left(B_0^{(1)} C_0 + \text{Da} C_1 B_0^{(1)} + \text{Da} C_0 B_1^{(1)} + \text{Da}^2 C_1 B_1^{(1)} \right) \end{aligned} \quad (41)$$

If we include only the leading order terms, we get the following:

$$\frac{\partial B_0^{(1)}}{\partial t} = k_1 \left(1 - B_0^{(1)} - B_0^{(2)} \right) - k_2 B_0^{(1)}, \quad (42)$$

$$\frac{\partial B_0^{(2)}}{\partial t} = k_2 B_0^{(1)}, \quad (43)$$

where we have used (39). If we include only second-order terms, we conclude:

$$\begin{aligned} \frac{\partial B_1^{(1)}}{\partial t} &= -B_1^{(1)} - B_1^{(2)} + C_1(1, z, t) - C_1(1, z, t) B_0^{(1)} - C_1(1, z, t) B_0^{(2)} - k_2 C_1(1, z, t) B_0^{(1)} - k_2 B_1^{(1)} \\ \frac{\partial B_1^{(1)}}{\partial t} &= -B_1^{(1)} (1 + k_2) + C_1(1, z, t) \left(1 - B_0^{(1)} (1 + k_2) - B_0^{(2)} \right) - B_1^{(2)}. \end{aligned} \quad (44)$$

Equation (26) simplifies more easily into:

$$\frac{\partial B_1^{(2)}}{\partial t} = k_2 \left[B_0^{(1)} C_1(1, z, t) + B_1^{(1)} \right]. \quad (45)$$

If we solve the rate laws to leading order of Da, we ignore the correction and achieve a solution, but if we wish to account for the correction, we may do so by solving the rate laws to the next order. The following are the leading order solutions to first, the governing equation for the evolution of unbound ligand (equation (27)), and second, the reaction rate laws (equations (25) and (26)).

In order to solve the reaction rate laws for the bounded complexes, we rely on the following boundary conditions:

$$B_0^{(1)}(z, 0) = 0, \quad B_0^{(2)}(z, 0) = 0.$$

Additionally, we find the differential boundary conditions on $B_0^{(i)}$ by plugging the above boundary conditions into (42) and (43):

$$\frac{\partial B_0^{(1)}}{\partial t}(z, 0) = k_1 \left(R_T - B_0^{(1)}(z, 0) - B_0^{(2)}(z, 0) \right) - k_2 B_0^{(1)}(z, 0),$$

$$\frac{\partial B_0^{(2)}}{\partial t}(z, 0) = k_2 B_0^{(1)}(z, 0).$$

Thus,

$$\frac{\partial B_0^{(1)}}{\partial t}(z, 0) = 1, \quad \frac{\partial B_0^{(2)}}{\partial t}(z, 0) = 0.$$

Note that all four of the above boundary conditions are initially constant for all z . Accordingly, equations (42) and (43) can be treated as a system of two second order, linear, *ordinary* differential equations. We proceed to solve this system by first differentiating (42):

$$\ddot{B}_0^{(1)} = -\dot{B}_0^{(1)}(1 + k_2) - \dot{B}_0^{(2)}.$$

Plugging this result into (26):

$$\ddot{B}_0^{(1)} + \dot{B}_0^{(1)}(1 + k_2) + k_2 B_0^{(1)} = 0, \quad B_0^{(1)}(0) = 0, \quad \dot{B}_0^{(1)}(0) = 1,$$

we find a characteristic equation: $r^2 + r(1 + k_2) + k_2 = 0$, the solutions of which are

$$r = \frac{-(1 + k_2) \pm \sqrt{(1 + k_2)^2 - 4k_2}}{2} = \frac{(-1 - k_2) \pm (k_2 - 1)}{2} = -k_2, -1.$$

Thus, our general solution is

$$B_0^{(1)}(t) = \sigma_1 e^{-k_2 t} + \sigma_2 e^{-t}.$$

Plugging in the boundary conditions, we have

$$B_0^{(1)}(0) = \sigma_1 + \sigma_2 = 0, \quad \dot{B}_0^{(1)}(0) = -k_2 \sigma_1 - \sigma_2 = 1$$

$$\sigma_1 = \frac{1}{1 - k_2}, \quad \sigma_2 = \frac{1}{k_2 - 1}.$$

Hence,

$$B_0^{(1)}(t) = \frac{e^{-k_2 t} - e^{-t}}{1 - k_2}. \quad (46)$$

Having an expression for $B_0^{(1)}(t)$ simplifies the process of solving for $B_0^{(2)}(t)$. Substituting for $B_0^{(1)}(t)$ in equation (26), we get:

$$\begin{aligned} \dot{B}_0^{(2)} &= k_2 \left[\frac{e^{-k_2 t} - e^{-t}}{1 - k_2} \right] \\ B_0^{(2)} &= k_2 \left[\frac{-e^{-k_2 t}}{k_2(1 - k_2)} + \frac{e^{-t}}{1 - k_2} \right] + \varsigma \\ B_0^{(2)} &= \frac{-e^{-k_2 t} + k_2 e^{-t}}{1 - k_2} + \varsigma. \end{aligned}$$

Substituting the boundary conditions, $B_0^{(2)}(0) = 0$, we determine ς as

$$0 = \frac{-1 + k_2}{1 - k_2} + \varsigma, \quad \varsigma = 1.$$

Hence,

$$B_0^{(2)}(t) = \frac{k_2 e^{-t} - e^{-k_2 t}}{1 - k_2} + 1. \quad (47)$$

Note: Both solutions satisfy their predicted initial and long term behavior. Both vanish for $t = 0$, and for $t \rightarrow \infty$, all of the reactants go to producing the complex $B_0^{(2)}$. Thus, from a surface perspective, the solutions look valid.

5 Special Cases

5.1 Correction for Non-Newtonian Flow

Physically, one characterizes a Newtonian fluid as one in which the stress response invoked upon the application of some external force is directly proportional to that applied force. Now, in order to correct for the possibility that a fluid does not behave like a Newtonian fluid, we introduce the factor β into the equation for the velocity:

$$u_z(r) = 1 - r^\beta. \quad (48)$$

This factor then easily filters through the convection-diffusion equations because for this velocity profile: $u'_z(1) = \beta$. This is why the Peclét number was defined the way it was. This way, the unknown factor β in the velocity profile is accounted for. Now, introducing this variation in the velocity profile into the convection-diffusion equation, we find that (23) evolves to:

$$\frac{LPe^{\frac{1}{3}}}{u_c t_c \beta} \frac{\partial C_b}{\partial t} = \frac{\partial^2 C_b}{\partial y^2} - y \frac{\partial C_b}{\partial z}. \quad (49)$$

Of course, β is merely a constant, so the intention of simplifying the convection-diffusion equations to the form of (48) would be to obtain an equation that, once scaled completely, would be easy to solve or **has been previously solved**.

5.1.1 Agreement With Grabowski's Paper

Grabowski [1] uses several parameters and constants in his paper that could be useful for ours. In order to use his numbers, we must first find the relationship between his scalings and ours. We start by considering the velocity. We scale our velocity against a constant u_c which we would be considered the maximum velocity in the tube. If we examine his definition of velocity, we can find a relationship between our u_c and his U .

Grabowski's definition of velocity is as follows (a is the radius of the tube, and r is the independent variable representing the radius):

$$u = \frac{3n+1}{n+1} U \left[1 - \left(\frac{r}{a} \right)^{\frac{n+1}{n}} \right]. \quad (50)$$

The average velocity could then be calculated by integrating over the radius of the tube and then dividing that value by the cross sectional area. Examine the following:

$$\bar{u} = \frac{3n+1}{n+1} (U) \left[\int_0^a \left(1 - \left(\frac{r}{a} \right)^{\frac{n+1}{n}} \right) r dr d\theta \right] \frac{1}{\pi a^2}$$

$$\begin{aligned}
\bar{u} &= \frac{3n+1}{n+1} (U) \left[\int_0^a \left(r - \left(r^{\frac{2n+1}{n}} \right) \left(\frac{1}{a^{\frac{n+1}{n}}} \right) \right) dr \right] \frac{2}{a^2} \\
\bar{u} &= \frac{3n+1}{n+1} (U) \left[\frac{a^2}{2} - a^{\frac{3n+1}{n}} \left(\frac{n}{3n+1} \right) \left(\frac{1}{a^{\frac{n+1}{n}}} \right) \right] \frac{2}{a^2} \\
\bar{u} &= \frac{3n+1}{n+1} (U) \left[1 - a^{\frac{n+1}{n}} \left(\frac{2n}{3n+1} \right) \left(\frac{1}{a^{\frac{n+1}{n}}} \right) \right] \\
\bar{u} &= \frac{3n+1}{n+1} (U) \left(1 - \frac{2n}{3n+1} \right) \\
\bar{u} &= \frac{3n+1}{n+1} (U) \left(\frac{n+1}{3n+1} \right) = U.
\end{aligned}$$

Thus, Grabowski's U represents his average velocity. Now, our dimensionless velocity profile is given by equation (48). Our scaling can be compared to his by examining the definition of each scaled variable. Our equation looks as follows:

$$\tilde{u}_z(r) = u_c \left(1 - \left(\frac{\tilde{r}}{R} \right)^\beta \right). \quad (51)$$

Comparing (51) to (50), we can show that our variables and Grabowski's variables have the following relationships:

$$u_c = \left(\frac{3n+1}{n+1} \right) U, \quad \beta = \frac{n+1}{n}.$$

This expression for u_c is encouraging because just from a surface look at Grabowski's velocity, we can tell that the maximum velocity occurs in the middle of the tube at $r = 0$. Setting $r = 0$ gives us exactly the expression shown above for u_c .

5.2 Unsteady Flow

Initially, because we assumed steady flow we were able to make extensive simplifications on equation (5) which we derived from the conservation of linear momentum.

Now, in this case, we can still make some important simplifications. First, because the left hand side is a function of only z and t , and the right hand side is a function of only r and t , we can say that the entire equation is a function of only t . This may not seem relevant now, but it is important when simplifying the equation after we choose a new form for the velocity.

We wish to model the flow of the blood with pulsations instead of steady flow. The most reasonable way to do this would be to represent the velocity as the steady flow plus some term that gives periodic deviation from the norm. Thus, we redefine u_z as follows:

$$\tilde{u}_{\tilde{z}}(\tilde{r}, \tilde{t}) = \tilde{u}_s(\tilde{r}) + \tilde{u}_{\tilde{r}}(\tilde{r}) \cos \omega t. \quad (52)$$

For algebraic simplicity, this can also be written as:

$$\tilde{u}_{c\tilde{z}}(\tilde{r}, \tilde{t}) = \tilde{u}_s(\tilde{r}) + \tilde{u}_c(\tilde{r}) e^{i\omega t}. \quad (53)$$

where:

$$\tilde{u}_{\tilde{r}}(\tilde{r}) \cos \omega t = \text{Re} \left(\tilde{u}_c(\tilde{r}) e^{i\omega t} \right), \quad (54)$$

$$\tilde{u}_{\tilde{z}}(\tilde{r}, \tilde{t}) = \text{Re}(\tilde{u}_{c\tilde{z}}(\tilde{r}, \tilde{t})). \quad (55)$$

Equation (5) can be simplified by grouping like powers of t upon substitution of (53). First, we scale the equation using our previous scalings for u_z , r , z , and p .

$$\frac{\partial(p \cdot \Delta P)}{\partial(z \cdot L)} = \left(\frac{\mu}{r \cdot R}\right) \frac{\partial}{\partial(r \cdot R)} \left((r \cdot R) \frac{\partial(u_z \cdot u_c)}{\partial(r \cdot R)} \right) - \rho \left(\frac{\partial(u_z \cdot u_c)}{\partial t} \right).$$

Now we substitute (16) for u_z and simplify to get

$$4 \left(\frac{\partial p}{\partial z} \right) = \frac{\mu}{r} \frac{\partial}{\partial r} \left(r \frac{\partial u_{\tilde{z}}}{\partial r} \right) - \rho \left(\frac{\partial u_{\tilde{z}}}{\partial t} \right).$$

The scaled equation can now be manipulated in combination with (53) to solve for the pressure gradient down the length of the blood vessel:

$$\begin{aligned} 4 \left(\frac{\partial p}{\partial z} \right) &= \frac{\mu}{r} \frac{\partial}{\partial r} [r (u'_s(r) + u'_c(r)e^{i\omega t})] - \left(\frac{\rho i \omega u_c \mu}{R^2} \right) e^{i\omega t} \\ 4 \left(\frac{\partial p}{\partial z} \right) &= \frac{\mu}{r} [(u'_s(r) + u'_c(r)e^{i\omega t}) + r u''_s(r) + r u''_c(r)e^{i\omega t}] - \left(\frac{\rho i \omega u_c \mu}{R^2} \right) e^{i\omega t} \\ 4 \left(\frac{\partial p}{\partial z} \right) &= e^{i\omega t} \left[(\mu) u''_c(r) + \frac{\mu}{r} u'_c(r) - \frac{\rho i \omega u_c \mu}{R^2} \right] + [(\mu) u''_s(r) + \frac{\mu}{r} u'_s(r)] \\ \frac{\partial p}{\partial z} &= -(1 + p e^{i\omega t}), \end{aligned} \quad (56)$$

where

$$p = \left[\mu u_c''(r) + \frac{\mu}{r} u_c'(r) - \frac{\rho i \omega u_c \mu}{R^2} \right].$$

This result is important because when we plug it back into equation (5), we are able to group powers of $e^{i\omega t}$ and isolate the steady part (u_s) and the pulsating part (u_c) of the velocity. The steady part of course matches the previous work, but the pulsating part is more interesting. After scaling and simplifications, we obtain a second order ODE for u_c as follows.

Plugging (56) into (5), we get:

$$-4(1 + p e^{i\omega t}) = e^{i\omega t} \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial u_c}{\partial r} \right) - \frac{\rho i \omega u_c \mu}{R^2} \right] + \frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial u_s}{\partial r} \right)$$

Isolating u_c and u_s , the following can be concluded. In the steady case, we have

$$\frac{\partial}{\partial r} \left(r \frac{\partial u_s}{\partial r} \right) = -4r,$$

while for the unsteady case we have

$$-4p = \frac{d^2 u_c}{dr^2} + \frac{1}{r} \frac{du_c}{dr} - i \alpha^2 u_c, \quad (57)$$

where:

$$\alpha = \frac{\sqrt{\rho \omega \mu}}{R}$$

Of course, the no-slip condition holds for this case as well, so the same boundary condition holds: $u_c(1) = 0$.

Equation (57) is a Bessel equation, which upon solving, yields Bessel functions of order zero. The following solution accepts one Bessel function and eliminates another. We eliminate the Y_0 because it is not continuous at the origin and therefore, physically unreasonable.

$$-4p = \frac{d^2 u_c}{dr^2} + \frac{1}{r} \frac{du_c}{dr} - i\alpha^2 u_c$$

Homogeneous Solution:

$$\frac{d^2 u_c}{dr^2} + \frac{1}{r} \frac{du_c}{dr} - i\alpha^2 u_c = 0$$

Let:

$$-i\alpha^2 = \lambda^2, \quad \xi = \lambda r$$

$$\frac{d^2 u_c}{dr^2} + \frac{1}{r} \frac{du_c}{dr} + \lambda^2 u_c = 0$$

$$\lambda^2 \frac{d^2 u_c}{d\xi^2} + \frac{\lambda^2}{\xi} \frac{du_c}{d\xi} + \lambda^2 u_c = 0$$

$$\xi^2 \frac{d^2 u_c}{d\xi^2} + \xi \frac{du_c}{d\xi} + \xi^2 u_c = 0$$

$$u_c = \tau_1 J_0(\xi) + \tau_2 Y_0(\xi)$$

$$u_c = \tau_1 J_0(\alpha r \sqrt{-i})$$

$$u_c = \tau_1 J_0(\alpha r e^{-\frac{\pi i}{4}}).$$

Particular Solution:

$$\frac{d^2 u_c}{d\xi^2} + \frac{1}{\xi} \frac{du_c}{d\xi} + u_c = -\frac{4p}{\lambda^2}$$

$$\xi \frac{d^2 u_c}{d\xi^2} + \frac{du_c}{d\xi} + \xi u_c = -\frac{4p}{\lambda^2} (\xi)$$

let:

$$Y(\xi) = A, \quad (A \text{ is constant}) \text{ Then:}$$

$$A\xi = -\frac{4p}{\lambda^2} (\xi)$$

$$A = -\frac{4p}{\lambda^2}.$$

Final Solution:

$$u_c = \tau_1 J_0(\alpha r e^{-\frac{\pi i}{4}}) - \frac{4p}{\lambda^2}.$$

Now we substitute our boundary condition ($u_c(1) = 0$):

$$\tau_1 = \frac{4p}{\lambda^2} \left[\frac{1}{J_0(\alpha e^{-\frac{\pi i}{4}})} \right]$$

$$u_c = \frac{4p}{i\alpha^2} \left[\frac{J_0(\alpha r e^{-\frac{\pi i}{4}})}{J_0(\alpha e^{-\frac{\pi i}{4}})} - 1 \right]$$

$$u_c(r) = \frac{4pi}{\alpha^2} \left[1 - \frac{J_0(\alpha r e^{-\frac{\pi i}{4}})}{J_0(\alpha e^{-\frac{\pi i}{4}})} \right]. \quad (58)$$

6 Conclusions

The leading order perturbation of the reaction system, developed subject to first order, irreversible kinetics, yields solutions of expected physical behavior. Further work is necessary to develop the solution profiles subject to first order perturbation. Additional refinement could also be done on the assumed reaction kinetics. For example, solution profiles could be generated for any number of reversible reactions. These are yet to be developed.

We further develop velocity profiles for blood flow in both the steady and the unsteady case. The steady case demonstrates standard Poiseuille flow profiles while the unsteady case, subject to periodic pulsations, yields Bessel Function profiles. Further studies should be conducted to show the impact of the unsteady velocity profiles, as compared with the steady profiles, on the convection-diffusion system. The resulting system, combined with new reaction kinetics, would likely yield more interesting results.

References

- [1] E.F. Grabsowski, L.I. Friedman and E.F. Bankoff, Effects of shear rate on the diffusion and adhesion of blood platelets to a foreign surface. *Ind. Eng. Chem. Fund.* 11 (1972) pp. 931-980.