Modeling, Computation and simulation of non-linear soft-tissue interaction with flow dynamics with application to biological systems*

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Abstract

In this work, a computational model for the interaction of blood flow with the wall of an intracranial saccular aneurysm that is surrounded by cerebral spinal fluid is considered. The coupled fluid-structure interaction model presented includes growth and remodeling effects within the soft-tissue by incorporating elastin and collagen dynamics which are two of the main layers in the arterial wall. The resulting nonlinear system of coupled differential equations are solved numerically using implicit finite difference methods coupled with the Newton's method. The linearized version of the nonlinear system was also considered and solved both analytically using Laplace transformation and numerically using implicit finite difference methods. The nonlinear effects on rupture was studied and compared for benchmark studies and the computational results indicate that the model proposed is robust and reliable.

Keywords: Mechanics, Computation, Aneurysm, Rupture, bio-mechanics.

Introduction

Over the last three decades there has been a lot of efforts to study intracranial saccular aneurysms which are focal dilatation of the arterial wall that are found in the Circle of Willis. The specific mechanisms responsible for their genesis, enlargement, and rupture has been a prominent area of research during these years. There have been competing hypothesis in the literature on the pathogenesis and lesion development involving limit point instabilities, [12, 1, 7], equilibrium wall stress and wall strength comparisons [2] and instability of the wall in response to pulsatile blood flow [8, 18, 13, 17, 19, 11].

Intracranial Saccular aneurysm which is a soft tissue interacts with a variety of flows including blood as well as the Cerebral spinal fluid. Based on the influence of various bio-mechanical factors, the growing aneurysm can be potentially ruptured and that leads to either a neurological disorder or death. About 80% to 90% of ruptured aneurysms leads to death [21].

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In the last two decades, several researchers have tried to investigate different aspects of biomechanics of aneurysms [14, 15, 16, 20]. Different groups of researchers had identified the elastodynamics of the arterial wall interaction with the blood flow to be the main reason for the rupture of an aneurysm [8, 18, 13]. A coupled fluid-structure model to understand the elastodynamics better was studied more extensively in the past few years [17, 19, 4, 11]. These models introduced mathematical models of increasing complexity for intracranial saccular aneurysms that described the coupled interaction between blood, arterial wall, and Cerebral Spain Fluid (CSF). In [19], the CSF was modeled using simplified Navier-Stokes equations, whereas the arterial wall structure was modeled using a spring mass system. A Fourier series was used to model the interaction between blood pressure and inner wall. While the model developed yielded good insight into understanding rupture, there was a great need to incorporate the growth and remodeling effects of the soft-tissue that will help to introduce important attributes and constituent of the arteries wall which will be the focus of this work. There are three main constituents of the artery wall, namely, the elastin, the collagen, and the smooth muscle [9, 5]. The elastin is a stable protein and is considered the most load bearing element that functions as resistance to the formation of an anuerysm, whereas the collagen is the protein that is responsible for preventing rupture after formation of an aneurysm. The growth of the aneurysm is associated with deficiency of elastin and weakening of the artery wall [6]. Hence, elastin and collagen should be incorporated into the modeling of arterial wall in order to obtain an accurate biological model of the aneurysm that can lead to better interpretation and prediction for this disease. This is one of the main contributions of this work.

In Section 2, we will describe the mathematical model that we will consider to solve a coupled fluid structure problem. Section 3 describes the implicit finite difference implementation of the coupled system. In section 4 we include some results from our computational experiments indicating the influence of collagen and elastin. Finally in section 5, we conclude and present some future work.

Mathematical Models and Background

The current work will build on models developed in [19] which helped to develop a very simple mathematical model of a thin-walled, spherical intracranial aneurysm surrounded by cerebral spinal fluid which is referred to as CSF (See Figure 1). This model involved solving coupled partial differential equations for fluids (modeling blood and cerebral spinal fluid) interacting with elastic structures modeling aneurysms using novel approaches. These models in [19, 4] were validated using analytical techniques and computational tools.

Next we describe briefly the models that were proposed which will be considered in this

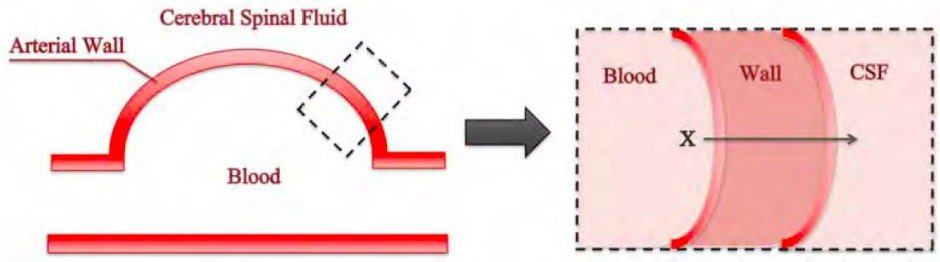

Figure 1: Model of an aneurysm in an arterial wall with blood inside and CSF outside

work and how they will be enhanced in this work using effects of growth and remodeling.

Model of the Cerebral Spinal Fluid

The model of Cerebral Spinal Fluid (CSF) considered in this paper is the simplified one dimensional Navier-stokes equation. Assuming the CSF is inviscid and slightly compressible with negligible non-linear effects, one can derive the following wave equation [19]:

$$v_t = c^2 u_{xx} \tag{1}$$

$$u_t = v \tag{2}$$

Here $u(x,t)$ is assumed to be the displacement of the CSF with $v(x,t)$ as the velocity. Since we are looking to find the movement of outer wall due to the interaction with CSF, we consider $x = 0$ to denote the outer wall (See Figure 1) and therefore we are interested in finding the solution to equations (1) and (2) at $x = 0$ that will describe the movement of the wall at any time $t \geq 0$. In order to solve the system, we will assume that the displacement and velocity of the CSF is zero initially. This is given by the initial conditions:

$$u(x,0) = v(x,0) = 0. \tag{3}$$

The boundary conditions will be described later after the discussion of the modeling of the blood pressure and the arterial wall which are discussed next.

Model of the Blood Pressure

The blood pressure is modeled using Fourier series since we consider the behavior to be pulsatile [3, 10, 17]. This relation can be described as:

$$P_B(t) = P_m + \sum_{n=1}^{N}(A_n \cos(nwt) + B_n \sin(nwt)) \tag{4}$$

where P_m is the mean blood pressure, A_n, B_n are Fourier coefficients, and w is the fundamental circular frequency [10].

Model of the Arterial Wall

We consider the arterial wall to be modeled using a simple spring-mass system that incorporates the elastin and collagen effects in the outer wall of the arteries. The force of this system maybe denoted by F_S which is given by $F_O - F_I$ where F_O and F_I are the forces of outer and inner wall respectively. This maybe expressed as:

$$F_S = K_E A_E(t)\sigma_E(\epsilon_E) + K_C A_C(t)\sigma_C(\epsilon_C) - aP_B(t) \tag{5}$$

where K_E, K_C are the scaling coefficients, $A_E(t), A_C(t)$ are the cross-sectional areas, and $\sigma_E(\epsilon_E)$, $\sigma_C(\epsilon_C)$ are the stresses for elastin and collagen respectively. These stresses are related to the respective strains through nonlinear constitutive laws given by:

$$\epsilon_E = (((L + u(0,t))/L)^2 - 1)/2 \qquad \epsilon_C = (\epsilon_E + (1 - r^2)/2)/r^2$$

where L denotes the length of the unstrained tissue, u its extension, and r is the stretched factor of unstrained tissue of collagen fiber.

Governing Equations of Motion

In order to solve the system (1)-(2), we need two boundary conditions. The first boundary condition is at point $x = 0$, and it can be derived from the model of blood pressure and the arterial wall that we have discussed. Note that the force balance equation at $x = 0$ maybe written as:

$$F_T = F_F - F_S. \tag{6}$$

where $F_T = mv_t(0,t)$ which is the inertial term corresponding to the product of mass of the wall m and acceleration, $F_F = \rho c^2 u_x(0,t)a$ is the fluid force, with a is the cross-sectional area and ρ, the density of the CSF.

Substituting equation (5) into (6) we obtain the following boundary condition at $x = 0$:

$$\begin{aligned} mv_t(0,t) = aP_m &- K_E A_E(t)\sigma_E(\epsilon_E) - K_C A_C(t)\sigma_C(\epsilon_C) + \rho c^2 a u_x(0,t) \\ &+ \sum_{n=1}^{N}(aA_n \cos(nwt) + aB_n \sin(nwt)) \end{aligned} \tag{7}$$

The second boundary condition can be obtained using the plane wave approximation that states that the waves from the wall will die down some fixed distance away from the wall. If this can be applied at point $x = L$, then the second boundary condition becomes [19]:

$$v(L,t) = -cu_x(L,t) \tag{8}$$

Combining (1), (2), (3), (7) and (8), we obtain the following system of coupled fluid-structure interaction problem:

$$\begin{aligned} v_t &= c^2 u_{xx} \\ u_t &= v \\ u(x,0) = v(x,0) &= 0 \\ mv_t(0,t) &= aP_B(t) - K_E A_E(t)\sigma_E(\epsilon_E) \\ &\qquad -K_C A_C(t)\sigma_C(\epsilon_C) + \rho c^2 a u_x(0,t) \\ v(L,t) &= -cu_x(L,t) \end{aligned} \tag{9}$$

For simplicity, we will assume that the cross-sectional areas are constant and a materially linear constitutive relationship between stress and strain is considered. In particular, we consider $A_E(t) = \gamma_E, A_C(t) = \gamma_C$, and $\sigma_E(\epsilon_E) = \epsilon_E$, $\sigma_C(\epsilon_C) = \epsilon_C$. Note that we still consider the soft-tissue to be geometrically non-linear which is the relation between the strains and the respective displacements. Given that system (9) is a coupled nonlinear system, it requires a numerical solution which will be discussed next.

An Implicit Finite Difference Solution Method

In order to solve system (9), we use an implicit finite difference method wherein we will replace the derivatives of the terms in the system by their corresponding finite difference approximations in a discretized domain. We employ the following second order finite difference approximation:

$$
\begin{aligned}
u'(y_i) &= \frac{u(y_i+\Delta y)-u(y_i-\Delta y)}{2\Delta y}+O(\Delta y^2), && \Delta y \le y_i \le Y-\Delta y \\
u''(y_i) &= \frac{u(y_i+\Delta y)-2u(y_i)+u(y_i-\Delta y)}{\Delta y^2}+O(\Delta y^2) && \Delta y \le y_i \le Y-\Delta y \\
u'(0) &= \frac{-3u(0)+4u(\Delta y)-u(2\Delta y)}{2\Delta y}+O(\Delta y^2) && (y_i=0) \\
u'(Y) &= \frac{u(Y-2\Delta y)-4u(Y-\Delta y)+3u(Y)}{2\Delta y}+O(\Delta y^2) && (y_i=Y)
\end{aligned}
$$

where $\Delta x = \dfrac{L}{M},\ \Delta t = \dfrac{tF}{N}, 0 \le x \le L$, and $0 \le t \le tF$

Then the system (9) can be rewritten implicitly as:

$$
\begin{aligned}
\frac{v_i^{j+1}-v_i^{j-1}}{2\Delta t} &= \frac{c^2(u_{i+1}^{j+1}-2u_i^{j+1}+u_{i-1}^{j+1})}{\Delta x^2}+O(\Delta x^2,\Delta t),\ 1 \le i \le M-1 && (10)\\
\frac{u_i^{j+1}-u_i^{j-1}}{2\Delta t} &= v_i^{j+1}+O(\Delta t),\ 0 \le i \le M && (11)\\
\frac{m(v_0^{j+1}-v_0^{j-1})}{2\Delta t} &= aP_B(t(j+1))+\frac{\rho c^2 a(-3u_0^{j+1}+4u_1^{j+1}-u_2^{j+1})}{2\Delta x}-\frac{K_E\gamma_E}{L}u_0^{j+1} \\
&\quad -\frac{K_E\gamma_E}{L}(u_0^{j+1})^2-\frac{K_C\gamma_C}{Lr^2}u_0^{j+1} && (12)\\
&\quad -\frac{K_C\gamma_C}{2L^2r^2}(u_0^{j+1})^2-\frac{K_C\gamma_C(1-r^2)}{2r^2}+O(\Delta x^2,\Delta t) \\
v_M^{j+1} &= \frac{-c(u_{M-2}^{j+1}-4u_{M-1}^{j+1}+3u_M^{j+1})}{2\Delta x}+O(\Delta x^2) && (13)
\end{aligned}
$$

Rewriting this nonlinear system as $F(\mathbf{u})=\mathbf{0}$ after dropping the higher order terms we get:

$$
\left(\frac{2c^2}{\Delta x^2}\right)u_i^{j+1}-\left(\frac{c^2}{\Delta x^2}\right)(u_{i-1}^{j+1}+u_{i+1}^{j+1})+\left(\frac{1}{2\Delta t}\right)v_i^{j+1}-\left(\frac{1}{2\Delta t}\right)v_i^{j-1}=0 \qquad (14)
$$

$$
u_i^{j+1}-2\Delta t v_i^{j+1}-u_i^{j-1}=0 \qquad (15)
$$

$$\left(\frac{K_E\gamma_E}{2L^2}+\frac{K_C\gamma_C}{2L^2r^2}\right)(u_0^{j+1})^2+\left(\frac{3\rho c^2 a}{2\Delta x}+\frac{K_E\gamma_E}{L}+\frac{K_C\gamma_C}{Lr^2}\right)u_0^{j+1}-\left(\frac{4\rho c^2 a}{2\Delta x}\right)u_1^{j+1}+\left(\frac{\rho c^2 a}{2\Delta x}u_2^{j+1}\right)$$
$$+\left(\frac{m}{2\Delta t}v_0^{j+1}\right)-\left(\frac{m}{2\Delta t}\right)v_0^{j-1}-aP_B(t(j+1))+\frac{K_C\gamma_C(1-r^2)}{2r^2}=0 \quad (16)$$

$$cu_{M-2}^{j+1}-4cu_{M-1}^{j+1}+3cu_M^{j+1}+2\Delta x v_M^{j+1}=0 \quad (17)$$

The system can be solved at each time step $J+1$ for $J \geq 1$ using the Newton's method for solving nonlinear system:

$$\mathbf{u}^{n+1}=\mathbf{u}^n-J(\mathbf{u})^{-1}F(\mathbf{u}) \quad (18)$$

where $J(\mathbf{u})$ is the Jacobian matrix of the system, n is the Newton iteration number, and $F(\mathbf{u})$ is the system above. Here,

$$J(\mathbf{u})=\begin{bmatrix} B(\mathbf{u}) & C \\ D & E \end{bmatrix}$$

$$B(\mathbf{u})=\begin{bmatrix}
\frac{3\rho c^2 a}{2\Delta x}+\frac{K_E\gamma_E}{L}+\frac{K_C\gamma_C}{Lr^2}+\left(\frac{K_E\gamma_E}{L^2}+\frac{K_C\gamma_C}{L^2r^2}\right)u_0^{j+1} & \frac{-4\rho c^2 a}{2\Delta x} & \frac{\rho c^2 a}{2\Delta x} & 0 & \dots & 0 \\
-\frac{c^2}{\Delta x^2} & 2\frac{c^2}{\Delta x^2} & -\frac{c^2}{\Delta x^2} & 0 & \dots & 0 \\
0 & -\frac{c^2}{\Delta x^2} & 2\frac{c^2}{\Delta x^2} & -\frac{c^2}{\Delta x^2} & \dots & 0 \\
\vdots & \ddots & \ddots & \ddots & & \vdots \\
\vdots & & \ddots & \ddots & \ddots & \\
0 & \dots & 0 & -\frac{c^2}{\Delta x^2} & 2\frac{c^2}{\Delta x^2} & -\frac{c^2}{\Delta x^2} \\
0 & \dots & 0 & c & -4c & 3c
\end{bmatrix}$$

$$C=\begin{bmatrix}
\frac{m}{2\Delta t} & 0 & 0 & & \dots & 0 \\
0 & \frac{1}{2\Delta t} & 0 & 0 & \dots & 0 \\
0 & 0 & \frac{1}{2\Delta t} & 0 & \dots & 0 \\
\vdots & & \ddots & \ddots & & \vdots \\
0 & \dots & 0 & 0 & \frac{1}{2\Delta t} & 0 \\
0 & \dots & 0 & 0 & 0 & 2\Delta x
\end{bmatrix}$$

$$D = \begin{bmatrix} 1 & 0 & \dots & 0 \\ 0 & 1 & \dots & 0 \\ \vdots & & \ddots & \vdots \\ 0 & \dots & 0 & 1 \end{bmatrix}$$

$$E = \begin{bmatrix} -2\Delta t & 0 & \dots & 0 \\ 0 & -2\Delta t & \dots & 0 \\ \vdots & & \ddots & \vdots \\ 0 & \dots & 0 & -2\Delta t \end{bmatrix}$$

To solve using the Newton's method, we require a guess which we will use from the solution at first two time steps.

For $1 \leq i \leq M-1$,

$$\frac{v_i^1 - v_i^0}{\Delta t} = \frac{c^2(u_{i+1}^1 - 2u_i^1 + u_{i-1}^1)}{\Delta x^2} + O(\Delta x^2, \Delta t) \tag{19}$$

for $0 \leq i \leq M$,

$$\frac{u_i^1 - u_i^0}{\Delta t} = v_i^1 + O(\Delta t) \tag{20}$$

$$\frac{m(v_0^1 - v_0^0)}{\Delta t} = aP_{Blood}(t) + \frac{\rho c^2 a(-3u_0^1 + 4u_1^1 - u_2^1)}{2\Delta x} - \frac{K_E\gamma_E}{L}u_0^1 - \frac{K_E\gamma_E}{2L^2}(u_0^1)^2 - \frac{K_C\gamma_C}{Lr^2}u_0^1 - \frac{K_C\gamma_C}{2L^2r^2}(u_0^1)^2 - \frac{K_C\gamma_C(1-r^2)}{2r^2} + O(\Delta x^2, \Delta t) \tag{21}$$

$$v_M^1 = \frac{-c(u_{M-2}^1 - 4u_{M-1}^1 + 3u_M^1)}{2\Delta x} + O(\Delta x^2) \tag{22}$$

Then substituting the initial condition and drooping higher order terms, we get:

$$\left(\frac{1}{\Delta t}\right)v_i^1 - \left(\frac{c^2}{\Delta x^2}\right)u_{i+1}^1 + \left(\frac{2c^2}{\Delta x^2}\right)u_i^1 - \left(\frac{c^2}{\Delta x^2}\right)u_{i-1}^1 = 0 \tag{23}$$

for $0 \leq i \leq M$,

$$u_i^1 - \Delta t v_i^1 = 0 \tag{24}$$

$$\left(\frac{m}{\Delta t}\right)v_0^1 + \left(\frac{3\rho c^2 a}{2\Delta x} + \frac{K_E\gamma_E}{L} + \frac{K_C\gamma_C}{Lr^2}\right)u_0^1 + \left(\frac{K_E\gamma_E}{2L^2} + \frac{K_C\gamma_C}{2L^2r^2}\right)(u_0^1)^2 - \frac{4\rho c^2 a}{2\Delta x}u_1^1 + \frac{\rho c^2 a}{2\Delta x}u_2^1 + \frac{K_C\gamma_C(1-r^2)}{2r^2} - aP_{BLOOD}(t) = 0 \quad (25)$$

$$cu_{M-2}^1 - 4cu_{M-1}^1 + 3cu_M^1 + (2\Delta x)v_M^1 = 0 \quad (26)$$

Computational Experiments

In this section, we perform some computational studies to validate the numerical solution to the geometrically nonlinear model that introduces the effects of the elastin and collagen. Since this nonlinear system can only be solved numerically using nonlinear solvers, the following steps are applied in order to validate this solution. First, the nonlinear model is linearized using Taylor series expansion, and this linearized version of the model was solved both analytically using Laplace transform and numerically using implicit finite difference approximation. The behavior of numerical solution against the analytical solution was validated. After the validation, the influence of various parameters on the displacement of the wall $u(0,t)$ was investigated. Secondly, the numerical solution for the linear model is used as initial guess for the nonlinear model to solve system numerically using Newton's method with implicit finite difference approximation. Finally the influence of some parameters on the displacement of wall is also considered.

In this experiment, the following realistic values are utilized. For the CSF, $p = 1000kg/m^3$, $c = 1500m/s$ are used. For the Wall, $a = 0.01m^2$, $k_E = 800\ N/m$, $k_C = 3.52N/m$, $A_E = 20\ m^2$, $A_C = 10\ m^2$, $r = 2\ m$, and $L = 1.5m$ are used. Finally, $Pm = 8759.279403mmHg$, $w = 1rad/s$ are used for the blood pressure model, and for the harmonics, $A_1 = -7.13, A_2 = -3.08, A_3 = -0.130, A_4 = -0.205, A_5 = 0.0662, B_1 = 4.64, B_2 = -1.18, B_3 = -0.564, B_4 = -0.346, B_5 = -0.120$, all in mmHg.

First, in Figure 2, we compare the linear solution without growth and remodeling obtained in [19] in comparison to both the analytical solution obtained by linearization of coupled non-linear system with growth and remodeling (9) as well as the numerical solution to (9) obtained via the implicit finite difference method. The figure shows that the inclusion of growth and remodeling does have an effect even though the solution seems to have the same shape. Their inclusion yields a decreased displacement of the outer wall which seems to suggest that including elastin and collagen can help prevent rupture.

The Influence of length of unstrained tissues

Next, we wanted to investigate the effect of the length of the column where the CSF lives on the displacement of the outer wall. As Figure 3 illustrates, we noted that as the length

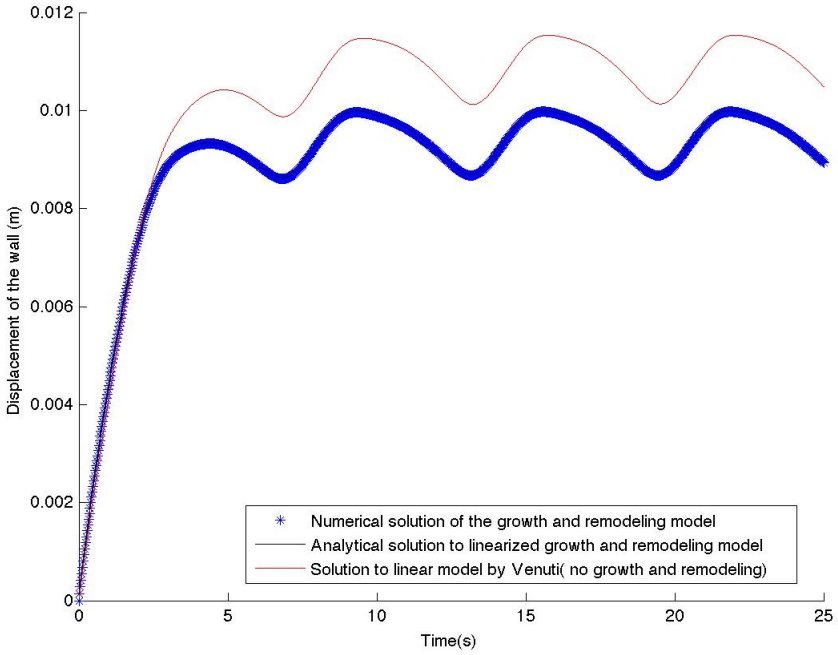

Figure 2: Nonlinear Growth and Remodeling solution VS Linear Solutions

is reduced, the movement of the wall declines dramatically. Figure 3 illustrates the motion of the wall for decreasing length from $L = 1.5\ m$ to $L = 0.1\ m$. The results seem to agree with what is expected intuitively.

Influence of Elastin and Collagen parameters

The elastic and collagen parameters (K_E,K_C) seem to play an important role in the modeling of the arterial wall since they are responsible for the elasticity and strength of wall tissue. Figure 4 shows the solution for different values of K_E starting from $300N/M$ till $800N/M$ while figure 5 represent the solution for different values of K_C starting from $1.52N/M$ till $6.52N/M$. Figure 4 suggests that the displacement increases and takes longer to stabilize into a periodic motion as K_E decreases. However, Figure 5 shows that the displacement increases in a steady periodic motion as K_C increases. Both these computational observations seem to correspond to what has been observed in the literature.

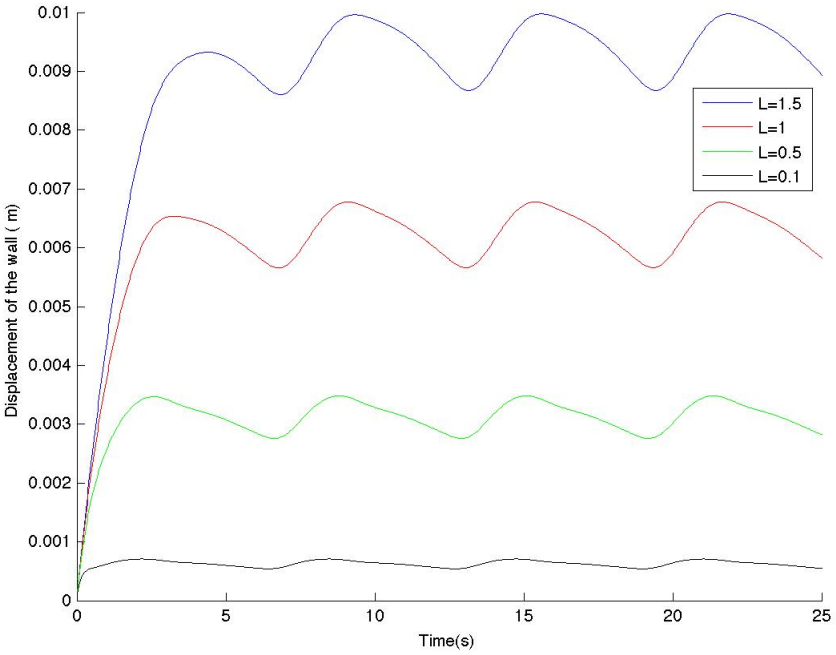

Figure 3: Influence of Length of Unstrained Tissues

Conclusions and Future work

The model developed in this work studies the influence of growth and remodeling on the rupture of an aneurysm In this model, three important components of aneurysm modeling that were considered include the blood pressure,the CSF, and arterial wall. The specific contribution of this paper was to expand on an earlier work to incorporate more relevant features of the arterial wall to stimulate the complex biological structure of the human arteries. The collagen and elastin are the most important fibers located in the wall layers that are incorporated herein in the model of the wall. This new incorporation results in a new nonlinear system that is solved numerically using implicit finite difference approximation and Newton's method for solving system of nonlinear equations. The results obtained in this work is encouraging to understand and provides a better insight into the rupture of an aneurysm. The model for the fluid considered herein is a linear model and we hope to expand our work to incorporate non-linearities in the fluid as well as develop similar models in higher dimensions which are aspects that will be considered in forthcoming papers.

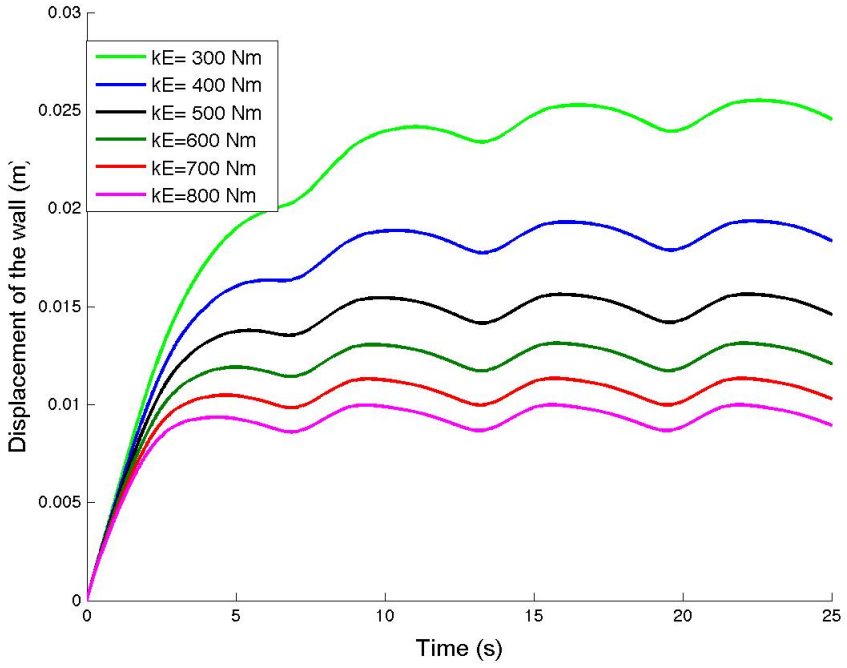

Figure 4: Influence of parameter k_E on the displacement of the outer-wall

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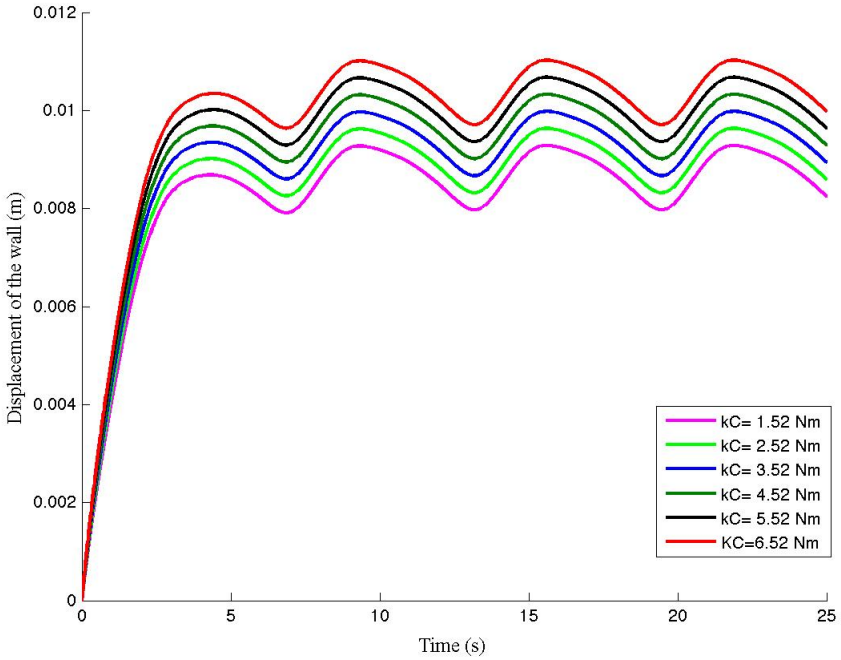

Figure 5: Influence of parameter k_C on the displacement of the outer-wall

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