MATHEMATICAL PROBLEMS IN MODELING ARTIFICIAL HEART

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In this paper we discuss some problems arising in mathematical modeling of artificial hearts. The hydrodynamics of blood flow in an artificial heart chamber is governed by the Navier-Stokes equation, coupled with an equation of hyperbolic type subject to moving boundary conditions. The flow is induced by the motion of a diaphragm (membrane) inside the heart chamber attached to a part of the boundary and driven by a compressor (pusher plate). On one side of the diaphragm is the blood and on the other side is the compressor fluid. For a complete mathematical model it is necessary to write the equation of motion of the diaphragm and all the dynamic couplings that exist between its position, velocity and the blood flow in the heart chamber. This gives rise to a system of coupled nonlinear partial differential equations; the Navier-Stokes equation being of parabolic type and the equation for the membrane being of hyperbolic type. The system is completed by introducing all the necessary static and dynamic boundary conditions. The ultimate objective is to control the flow pattern so as to minimize hemolysis (damage to red blood cells) by optimal choice of geometry, and by optimal control of the membrane for a given geometry. The other clinical problems, such as compatibility of the material used in the construction of the heart chamber, and the membrane, are not considered in this paper. Also the dynamics of the valve is not considered here, though it is also an important element in the overall design of an artificial heart. We hope to model the valve dynamics in later paper.

1. MATHEMATICAL MODEL OF ARTIFICIAL HEART

In this section we develop the dynamic models of each of the components of an artificial heart and finally combine them to form the complete model.

1.1. Membrane Dynamics

We use the Lagrange principle to develop the dynamics of the diaphragm. Let ρ denote the mass density of the membrane, z the distance of the membrane from the base D where it is attached. Here we call the set $D \subset R^2$, which may be either circular or elliptic in shape, the base of the heart chamber.

Energy Densities. The kinetic and potential energy densities of the membrane are given by $(K \cdot E)_m \equiv (1/2)(\rho) \, z_t^2$ and $(P \cdot E)_m \equiv (1/2)(\Sigma \, \nabla z, \, \nabla z)$, respectively, where

$$\Sigma = \begin{pmatrix} \sigma_{11} & \sigma_{12} \\ \sigma_{21} & \sigma_{22} \end{pmatrix},$$

is the stress tensor.

The Lagrangian is given by

$$l(z, z_t, z_x, z_y) \equiv \int_D l^0 dx dy.$$

where

$$l^0 \equiv (1/2)\{(\rho)\, z_t^2 - (\sigma_{11}\, z_x^2 + 2\sigma_{12}\, z_x z_y + \sigma_{22}\, z_y^2)\}.$$

Using D'Alembert's principle of least action we obtain the differential equation for the membrane

$$\rho z_{tt} - Lz = f \tag{1}$$

where

$$Lz \equiv (\sigma_{11}\, z_{xx} + 2\sigma_{12} z_{xy} + \sigma_{22} z_{yy})$$

and

$$f \equiv p_i - p(t, x, y, z(t, x, y))$$

is the force driving the membrane, with p_i being the internal compressor pressure, and $p(t, x, y, z(t, x, y))$ is the fluid pressure on the surface of the membrane inside the heart chamber. This equation is to be completed by defining the boundary and initial conditions as follows.

Boundary Condition. Since the membrane is attached to the boundary of the base D, z must satisfy the Dirichlet boundary condition:

$$z(t, x, y)\, \big|_{(x,y)\in \partial D} = 0. \tag{2}$$

Initial Conditions.

$$z(0, x, y) = z_0(x, y), \qquad (x, y) \in D$$

$$z_t(0, x, y) = z_1(x, y) \qquad (x, y) \in D. \tag{3}$$

Complete Membrane Dynamics. Thus the complete membrane dynamics is given by

$$\begin{cases} \rho z_{tt} - Lz \\ \qquad = p_i - p(t, x, y, z(t, x, y)), (x, y) \in D \\ z\,|_{S=\partial D} = 0, \\ z(0, x, y) = z_0, \qquad (x, y) \in D \\ z_t(0, x, y) = z_1, \qquad (x, y) \in D \end{cases} \tag{4}$$

1.2. Fluid Dynamics of Heart Chamber

Basic equation. Let

$$u = \begin{pmatrix} u_1 \\ u_2 \\ u_3 \end{pmatrix} \tag{5}$$

denote the velocity field of the fluid in the heart chamber. From the principle of conservation of momentum and the incompressibility condition we know that fluid motion is governed by the well-known Navier-Stokes equation:

$$\rho_0 \, \partial u/\partial t + \rho_0(u.\nabla)u - \gamma \triangle u + \nabla p = \rho_0 g, \qquad t > 0, \xi \in \Omega, \, div(u) = 0 \qquad (6)$$

where ρ_0 is the mass density of the fluid and g denotes the force per unit mass due to gravity and γ the kinematic viscosity and p the pressure and $\xi \equiv (x, y, z) \in \Omega \subset R^3$. The set Ω is the heart chamber having ports and solid boundaries.

Boundary Conditions. The boundary consists of four parts as described below:

$$\partial\Omega \equiv \Gamma_r \cup \Gamma_m \cup \Gamma_0 \cup \Gamma_i$$

$$\Gamma_i \equiv \text{inlet port}, \Gamma_r \equiv \text{rigid boundary} \qquad (7)$$

$$\Gamma_o \equiv \text{outlet port}, \Gamma_m \equiv \text{flexible membrane boundary}$$

$$\text{area } \Gamma_i = \text{area } \Gamma_o \equiv a.$$

Let ν denote the outward normal to the boundary $\partial\Omega$. Assuming, for simplicity, uniform velocity throughout the cross section of the inlet and outlet ports having cross sectional area a, we have

$$\begin{cases} u.\nu \mid_{\Gamma_r} = 0, u.\nu \mid_{\Gamma_m} = u(t, x, y, z(t, x,y)).\nu = - \, \tilde{z}_t.\nu \\ u.\nu \mid_{\Gamma_i} = u.\nu \mid_{\Gamma_o} = (1/a) \int_D z_t(t, x, y) \, dxdy, \end{cases} \qquad (8)$$

where $\tilde{z}_t = col(0, 0, z_t)$.

Define the boundary operator

$$\tau u \equiv u.\nu \mid_{\Gamma_s}, \qquad s = \{r, m, o, i\}. \qquad (9)$$

Introducing the operator C, this can be written compactly as

$$\begin{cases} \tau u \equiv X_r.0 + I_{T/2}.X_i.(1/a) \int_D z_t \, dxdy - X_m.\tilde{z}_t.\nu + I_T.X_o.(1/a) \int_D z_t \, dxdy. \\ \equiv Cz_t, \end{cases} \qquad (10)$$

where $\chi_s(\xi) = \begin{cases} 1, \xi \in \Gamma_s \\ 0, \xi \notin \Gamma_s, \end{cases}$

and $I_{T/2}$ and I_T are the indicator functions of the intervals $[0, T/2]$ and $[T/2, T]$, respectively. So the dynamics of the fluid (blood) in the heart chamber is given by the nonhomogeneous boundary value problem as presented below

$$\begin{cases} \rho_0 \partial u/\partial t + \rho_0(u.\nabla)u - \gamma \triangle u + \nabla p = \rho_0 g, \qquad t > 0, \xi \in \Omega \\ div(u) = 0; \\ \tau u \equiv u.\nu \mid_{\Gamma} = v \equiv C \, z_t \\ u(0) = u(0, \xi) \equiv u_0, \text{ where } \xi \equiv (x, y, z). \end{cases} \qquad (11)$$

For simplicity, in the development of the above model we have tacitly assumed that blood is a Newtonian fluid.

2. COMPLETE DYNAMICS OF ARTIFICIAL HEART

Strictly speaking, equation (11) is not complete. The domain of fluid motion Ω is variable and it is given by $\Omega_t \equiv \{\xi \in \Omega : \xi = (x, y, z), z \geq z(t, x, y), (x, y) \in D\}$ which represents the part of the domain that lies on one side of the membrane surface. Thus the complete dynamics of the artificial heart driven by a compressor is given by:

$$\begin{cases} \rho z_{tt} - Lz \\ \qquad = p_i - p(t, x, y, z(t, x, y)), (x, y) \in D \\ z\,|_{S=\partial D} = 0, \\ z(0, x, y) = z_0, \qquad (x, y) \in D \\ z_t(0, x, y) = z_1, \qquad (x, y) \in D \end{cases} \tag{12}$$

$$\begin{cases} \rho_0 \partial u/\partial t + \rho_0 (u.\nabla)u - \gamma \triangle u + \nabla p = \rho_0 g, \quad t > 0, \\ \xi \in \Omega_t \equiv \{\xi \in \Omega : \xi = (x, y, z), z \geq z(t, x, y)\}, \\ div(u) = 0, \\ \tau u = v \equiv C\, z_t \\ u(0) = u(0, x, y, z) \equiv u_0. \end{cases} \tag{13}$$

This is a nonhomogeneous moving boundary value problem and is notoriously difficult both theoretically and computationally. This model is closer to the actual physical situation than the model presented in [1].

3. FORMULATION OF CONTROL PROBLEM

It is known that hemolysis is caused largely by excessive shear stresses and vortices. Blood clot may be caused by recirculation and stagnation. Hence an artificial heart must be designed and controlled so as to minimize shear stresses, vortices and stagnation. We present here two different formulations of the control problem.

(F1): Let $(u^d.v)|\Gamma_0((u^d.v)|\Gamma_i)$ denote the outward normal velocity distribution across the outlet (inlet) port required to empty (fill) the heart chamber during systolic (diastolic) phase of the cardiac cycle $[0, T] \equiv I$. Define

$$Q_1(t, \nabla u), \equiv \int_{\Omega_t} (Q_1(\nabla u), \nabla u))d\xi$$

$$Q_2(t, curl\, u) \equiv \int_{\Omega_t} (Q_2 curl\, u, curl\, u)d\xi,$$

$$Q_3^s(t, u - u^d) \equiv \lambda_3 \int_{\Gamma_s} |(u(t, \xi) - u^d(t, \xi)).v|^2 d\xi, s = i, o.$$

The first quadratic form Q_1 is a measure of shear stress and the second form Q_2 is a measure of recirculation and stagnation and Q_3^s, $s = i, o$ is a measure of discrepancy

between the desired and the actual flow at the outlet or the inlet ports. Let $Q_4(p_i)$ denote any nonnegative possibly quadratic functional of the compressor pressure operating the heart. Using these components we can construct the following objective functional given by

$$J(p_i) \equiv (1/2) \int_I \{Q_1(t, \nabla u) + Q_2(t, curl\ u)$$

$$+ I_{T/2}Q_3^i(t, u - u^d) + I_T Q_3^o(t, u - u^d) + Q_4(p_i)\}\ dt. \tag{14}$$

The problem is to find a control policy describing the input pressure p_i that minimizes the functional $J(p_i)$ subject to the dynamic constraints (12) and (13).

(F2): An alternate formulation is given as follows: Find a control policy that minimizes the functional

$$J(p_i) \equiv (1/2) \int_I \{Q_1(t, \nabla u) + Q_2(t, curl\ u) + Q_4(p_i)\}dt \tag{15}$$

subject to the dynamic constraints (12) and (13) and the equality constraint

$$\rho_0 \int_0^{T/2} \int_D z_t(t, \eta)d\eta dt = M_{T/2} = \rho_0 \int_{T/2}^T \int_D z_t(t,\eta)d\eta dt \tag{16}$$

where $M_{T/2}$ is a known constant representing the total mass of fluid (blood) that must be sucked in and pumped out during the half cycles $[0, T/2]$ and $[T/2, T]$, respectively. Unfortunately the necessary conditions developed by Abergel and Temam [2] and those developed by Ahmed [1] do not apply in the present situation.

4. A SIMPLIFIED ABSTRACT MODEL

Recall that the domain of fluid motion Ω is variable, in fact, a function of the position of the membrane, that is, $\Omega(z)$. This makes it difficult to construct an abstract model. Assuming that the membrane displacement is so small that it is negligible, we can write an abstract evolution equation. Later we shall discuss the modification necessary to relax this assumption.

For membrane dynamics define operator A_1 as

$$\begin{cases} D(A_1) \equiv \{\phi \in L_2(D) : L\phi \in L_2(D), \phi \mid_{s=\partial D} = 0\} \\ A_1\phi = -(1/\rho)L\phi \text{ for } \phi \in D(A_1). \end{cases} \tag{17}$$

Define

$$w_1 \equiv z, w_2 \equiv z_t. \tag{18}$$

For the fluid dynamics, the standard function spaces required are as follows:

$$\begin{cases} V \equiv c\ell^{H^1}\{\phi \in C_0^\infty(\Omega, R^n) : div\ \phi = 0, \phi.\nu = 0\}, \\ H \equiv c\ell^{L_2}\{\phi \in C_0^\infty(\Omega, R^n) : div\ \phi = 0, \phi.\nu = 0\}. \end{cases} \tag{19}$$

where V is given by the closure, in the topology of the standard Sobolev space H^1, of divergence free vector fields from the class of C^∞—functions whose outward normal component vanish on the boundary. Similarly H is defined with reference to L_2 in place of H^1.

Then we obtain the well-known Gelfand triple

$$V \hookrightarrow H = H^* \hookrightarrow V^* \ (\equiv \text{dual of } V), \tag{20}$$

where the embeddings are continuous.

Consider the Dirichlet problem

$$\begin{cases} M\phi \equiv \gamma \triangle \phi = 0 \\ \tau \phi = v. \end{cases} \tag{21}$$

It is known that this equation has a unique solution $\phi = Rv$, where R is the Dirichlet map given by $R = (\tau|_{KerM})^{-1}$.

Let P denote the projection of L_2 to H.

Define

$$\begin{cases} A_2\phi \equiv -(\gamma/\rho_0)P(\triangle \phi) \\ b(\phi, \psi) \equiv P((\phi.\nabla)\psi) \\ B(\phi) \equiv b(\phi,\phi) \\ \tilde{g} \equiv P(g). \end{cases} \tag{22}$$

Then the membrane equation (12) and the fluid dynamics equation (13) can be combined to form an evolution system

$$\begin{cases} du/dt + A_2u + B(u) = A_2RCw_2 + \tilde{g} \\ dw_1/dt = w_2 \\ dw_2/dt + A_1w_1 = (1/\rho)(p_i - p(t, w_1)); \end{cases} \tag{23}$$

with the initial conditions

$$u(0) = u_0, w_1(0) = w_{10} = z_0, w_2(0) = w_{20} = z_1,$$

where w_1 and w_2 represent respectively the instantaneous position $z(t,.,.)$ and velocity $z_t(t,.,.)$ profiles of the membrane.

Defining

$$\psi \equiv \begin{pmatrix} u \\ w \end{pmatrix} \text{ a five vector,}$$

$$A \equiv \begin{pmatrix} A_2 & 0 & -A_2RC \\ 0 & 0 & -1 \\ 0 & A_1 & 0 \end{pmatrix};$$

$$F(y) \equiv \begin{pmatrix} B(u) \\ 0 \\ (1/(\rho))\, p\,(t, w_1) \end{pmatrix};$$

$$G \equiv \begin{pmatrix} \tilde{g} \\ 0 \\ (1/\rho)p_i \end{pmatrix};$$

we have the abstract evolution equation

$$\begin{cases} d\psi/dt + A\psi + F(\psi) = G \\ \psi(0) = \psi_0. \end{cases} \tag{24}$$

Note that the domain of the operator A is given by

$$D(A) \equiv H_\sigma^2\,(\Omega) \times (H^2\,(D) \cap H_0^1\,(D)) \times L_2(D),$$

where H_σ^2 denotes the class of divergence free-vector fields contained in the standard Sobolev space H^2. Equation (24) can be solved in the weak sense in the Hilbert space

$$X \equiv H \times D\,(\sqrt{(A_1}\,)) \times L_2(D). \equiv H \times H_0^1(D) \times L_2(D).$$

The control here is the internal compressor pressure p_i as applied to the membrane.

5. CORRECT ABSTRACT MODEL

Here we present a more complete abstract model. Let $\eta \in H_0^1(D) \cap H^2(D)$ and define

$$\Omega(\eta) \equiv \{\xi = (x, y, z) \in \Omega : z \geq \eta(x, y), (z, y) \in D\}.$$

Since the membrane is not allowed to stretch beyond certain limits inside Ω, this set is nonempty. By Sobolev embedding theorem, $\eta \in C^\alpha(D)$ for $\alpha \in (0, 1)$. Thus $\Omega(\eta)$ is sufficiently smooth. Replacing the set Ω of expression (19) by $\Omega(\eta)$, we obtain the parameterized family of Gelfand triples

$$V(\eta) \hookrightarrow H(\eta) \hookrightarrow V(\eta)^*,$$

parameterized by η. We redefine the operators A_2 and B of the expression (22) as follows. Let P_η denote the projection of $L_2(\Omega(\eta))$ to $H(\eta)$. Define

$$\begin{cases} A_2(\eta)\phi \equiv -\,(\gamma/\rho_0)P_\eta(\triangle \phi) \\ b(\eta, \phi, \psi) \equiv P_\eta((\phi.\nabla)\psi) \\ B(\eta, \phi) \equiv b(\eta, \phi, \phi) \\ \tilde{g} \equiv P_\eta(g). \end{cases} \tag{25}$$

Thus the correct evolution equation for the controlled artificial heart may be written as

$$\begin{cases} du/dt + A_2(w_1)u + B(w_1, u) = A_2(w_1)RCw_2 + \tilde{g} \\ dw_1/dt = w_2 \\ dw_2/dt + A_1w_1 = (1/\rho)(p_i - p(t, w_1)). \end{cases} \qquad (26)$$

In this case the evolution equation (24) takes the form

$$\begin{cases} d\psi/dt + A(\psi) + F(\psi) = G \\ \psi(0) = \psi_0. \end{cases} \qquad (27)$$

which is fully nonlinear or more precisely, quasi-linear. Here the operator A which was linear in case of (24), is no more linear since A_2 and B are both dependent on w_1.

The question of existence and regularity properties of solutions of this equation is completely open. We expect that the semigroup technique developed by Kato (see [3], p. 174] for quasi-linear systems may work. Once this problem is resolved we can undertake the questions of optimal controls of artificial heart on a rigorous basis.

Another difficulty with equation (26) is that even though the pressure term disappears from the abstract Navier-Stokes equation, it remains in the membrane equation. This difficulty can be partially overcome by reformulating the control problem as follows: Let $F \subset L_\infty(I, L_2(D))$ be a w^* compact set. Find $f \in$ so that

$$J(f) \equiv \int_I (Q_1 + Q_2 + Q_3)\, dt \to Inf,$$

subject to the dynamic constraint

$$\begin{cases} du/dt + A_2(w_1)u + B(w_1, u) = A_2(w_1)RCw_2 + \tilde{g} \\ dw_1/dt = w_2 \\ dw_2/dt + A_1w_1 = f. \end{cases} \qquad (28)$$

Once an optimal f^0 is determined, one can choose $p_i^0 = \rho f^0 + p(.,w_1^0)$, where

$$\psi^0 \equiv \begin{pmatrix} u^0 \\ w^0 \end{pmatrix}, p^0 \equiv p(., w_1^0)$$

is the optimal state trajectory.

6. SIMPLIFIED CONTROL PROBLEM

Recently a simplified version of this problem has been solved in [1] where the membrane dynamics is omitted. In that the boundary condition in equation (11) is replaced simply by $\tau u \equiv v$ where v is considered to be the basic control to be chosen so as to minimize the objective functional given by equation (14) with p_i replaced by v. The question of existence of solutions of the nonhomogeneous boundary value problem is treated by use of semigroup theory [3]. Existence of optimal controls is based on weak lower

semi-continuity and compactness arguments. Also several necessary conditions of optimality were given in [1]. We reproduce here one of the necessary conditions [see 1, Theorem 4, p. 114] which is closer to the problem considered here.

Necessary Conditions of Optimality

THEOREM 1   *In order that the pair $\{u^0, v^0\}$ be optimal, it is necessary that the following equations and the inequality hold*:

$$
\begin{cases}
(i): du^0/dt + A_2 u^0 + B(u^0) = A_2 R v^0 + \tilde{g}, \, u^0(o) = u_0 \\
(ii): -dz^0/dt + \beta^* z^0 = \ell_u(u^0, v^0), \, z^0(T) = 0 \\
(iii): \int_0^T \{< (AR)^* z^0(t), v^0(t) >_{E^*,E} + \ell(u^0(t), v^0(t))\} dt \\
\qquad \leq \int_0^T \{< (AR)^* z^0(t), v(t) >_{E^*,E} + \ell(u^0(t), v(t))\} dt \\
\qquad for \, all \, v \in U_{ad}
\end{cases}
\tag{29}
$$

where β^* is the adjoint of the operator B given by $Bz = A_2 z + b(u^0, z) + b(z, u^0)$, and ℓ is the cost integrand as in (14).

In case ℓ is Frechet differentiable in the control variable v one can present a simple algorithm for computing the optimal control.

$$
\begin{cases}
J'(v^n) \equiv (AR)^* z^n + \ell_v(u^n, v^n) \\
v^{n+1} \equiv v^n - \epsilon \Lambda^{-1} J'(v^n) \\
J(v^{n+1}) = J(v^n) - \epsilon \| \Lambda^{-(1/2)} J'(v^n) \|^2_{L_2(\Gamma)} + 0(\epsilon),
\end{cases}
\tag{30}
$$

where $\Lambda = (-\Delta_\Gamma)^{1/2}$ and Δ_Γ is the Laplace-Beltrami operator corresponding to the boundary Γ.

This algorithm has been successfully tried on 2-d Navier-Stokes equation [4, 5]. Currently 3-d codes are being written. One of the difficulties in developing numerical codes for optimal control problems as given above is that commercially available Navier-Stokes solver can not be adapted to this problem because of the requirement that the adjoint equation must be solved backward in time simultaneously. Thus an independent code was developed right from the scratch.

7. CONCLUSION

In this paper we have presented a complete dynamic model for the artificial heart. We have also given a correct formulation of an optimal control problem with a performance functional that takes into account all the potential flow related causes of hemolysis. However we have not been able to develop a sound theoretical basis concerning the questions of existence and regularity properties of solutions of these general equations. This remains an open problem. For a simplified problem, we have developed necessary conditions of optimality which have been used by our Control and Systems group in Ottawa University to develop numerical codes modifying standard CFD codes. Very interesting numerical results have been reported in several conferences [1,4,5]. Based on the results of the simplified problem we are convinced that a solution of the complete problem as presented here would be of great value to the designers of artificial hearts.

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