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# On the Constitutive Models for Heart Valve Leaflet Mechanics

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Large-strain constitutive modeling of biological tissues has grown enormously as a field in the past decade. This paper investigates the viability of the existing models for describing heart valve leaflet mechanics. The properties of the leaflet tissue are discussed, and a variety of constitutive models are addressed. Models based on continuum and unit cell approaches are highlighted as being suited to leaflet modeling.
**Key words:** heart valve; leaflet; constitutive; mechanics.

## INTRODUCTION

In the past decade, finite element based computational modeling and mechanical analysis of heart valves have greatly aided planning and evaluation of heart valve surgery, design of bioprosthetic valve replacements, and general understanding of healthy and abnormal cardiac function. Such models must be based on an accurate description of the mechanical behavior of the valve material under physiological conditions. Numerous constitutive models have been developed to describe heart valve tissue and other similar biological tissues. This paper addresses the derivation of a variety of models and discusses their applicability to heart valve tissue.

### Basic Properties of Heart Valve Tissue

The basic physical properties of heart valve tissue govern the assumptions that can be made in the formulation of a constitutive model. Heart valve tissue consists of a fibrous tissue network, mainly collagen and elastin, saturated with a fluid that is mostly water. SEM of leaflet tissue shows that the fibrous network is wavy and uniaxially aligned (see Fig. 1).

The aligned fibers of the leaflet tissue make the stress-strain response highly anisotropic. Tensile testing (Billiar and Sacks 2000) shows that the aortic leaflets are significantly stiffer in the circumferential direction than the radial direction, and similar results have been recorded for mitral valve tissue (Clark, 1973). Data for mitral valve tensile testing is shown in Fig. 2.

A material supported by uniaxially aligned fibers can be described by a special case of anisotropy known as transverse isotropy. In transverse isotropy, the material has one preferred direction parallel to the fiber direction, and the responses in every direction perpendicular to the preferred direction are identical to each other.

The waviness of the fibers also significantly affects the stress-strain response. Generally, less force is required to stretch a wavy fiber than a straight fiber. At low strains, the fibers in heart valve tissue are wavy, and the tissue can be extended by relatively low stresses. As strains increase, the fibers are straightened, and the stress required to extend the tissue increases dramatically. This nonlinear response is evidenced in Fig. 2, as the slope of the stress-strain curve increases with increasing strain.

Water comprises between 60 and 70% of a collagenous tissue by weight (Weiss *et al*., 1996). This volume of water appears to be tightly bound to the fibrous network, as evidenced by fact that it is difficult to exude any significant amount of fluid by compression (Hvidberg, 1960). Thus, models should consider the tissue to be nearly or completely incompressible.

Since the tissue consists of a combination of solid of fluid components, it would be natural to assume that

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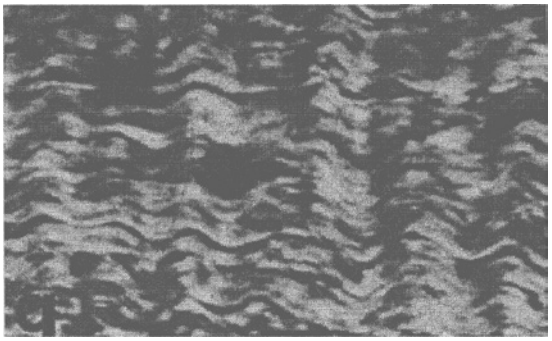

**Figure 1.** SEM of tricuspid valve leaflet material. From Broom (1978), showing characteristic aligned waviness.

the solid component would contribute an elastic response to loading and the fluid component would contribute a viscous response, so that the overall response would be viscoelastic. Fung (1967, 1993) has shown, however, that biological tissues can be preconditioned by repeatedly loading and unloading the specimen. After a number of cycles, the response will reach a steady state where that involves one non-linear response for the loading phase and a separate non-linear response for the unloading cycle. Once this steady state has been reached, both phases are insensitive to the loading rate: the viscous effect disappears after preloading. A material with this response can be treated as one hyperelastic material in loading, and a separate material in unloading. Such behavior, known as pseudoelasticity, has been shown to apply to heart valve tissue (May-Newman and Yin, 1995).

A constitutive model for heart valve tissue must incorporate all of the features listed above: it should describe a pseudoelastic, incompressible, anisotropic, nonlinear material. While relatively few models have been formulated specifically for heart valve tissue, a number of models exist for biological soft tissues in general and for similar tissues.

## Constitutive Models

This section surveys a few different derivations for the stress-strain behavior of heart valve and similar tissues. These derivations include a range of information about the structure of the tissue, from phenomological models that include no information about the structure to unit-cell models that are derived completely from network structure.

Many constitutive models for biological tissues are derived by extending theories developed for rubber deformation. Rubber models apply generally to large-strain, isotropic, hyperelastic materials, therefore extending these models to include anisotropic, pseudoelastic behavior creates models appropriate for biological tissues. The essential concept of this class of theory is that the energy density in the material can be determined as a function of the strain state. Once the strain-energy function $W$ is known, the stress state can be determined by taking the derivative of $W$ with respect to a strain measure, such as

$$\sigma = \frac{\partial W}{\partial \varepsilon}, \tag{1}$$

where $\sigma$ the Cauchy (true) stress tensor and $\varepsilon$ is the Green strain tensor. The most common form used to determine

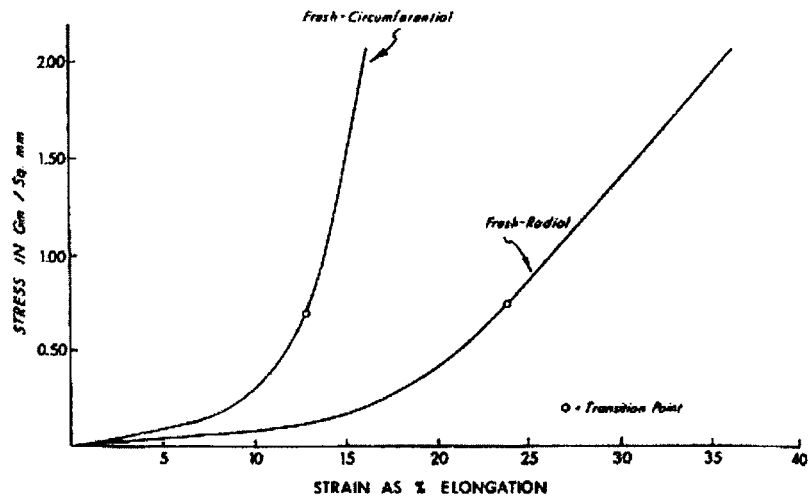


**Figure 2.** Uniaxial stress-strain data for fresh human mitral leaflet tissue From Clark (1973), showing highly nonlinear and anisotropic response.

stresses for the materials considered here is

$$\sigma = -pI + 2F\frac{\partial W}{\partial C}F^T, \tag{2}$$

where $F$ is the deformation gradient, $C$ is the left Cauchy-Green strain tensor, $p$ is a Lagrange multiplier to enforce incompressiblilty, and $I$ is the identity tensor (Holzapfel, 2001).

## PHENOMOLOGICAL MODELS

A phenomological model is typically developed by guessing either a form of the stress strain response or of the strain-energy function. The resulting stress-strain response is then fit to experimental stress-strain data.

A large-strain constitutive model can be formulated by extension of one of the many well-known models for linear elastic materials. Li *et al*. have created a model for heart valve tissue by extending the linear transversely isotropic model (Li *et al*., 2001). The stress-strain relation for the linear transversely isotropic model is

$$\sigma = [E]\varepsilon, \tag{3}$$

where the stiffness matrix $[E]$ is a function of two Young's moduli $E_x$ and $E_y$, two Poisson's ratios $V_{xy}$ and $\mathrm{v}_{yx}$, and a shear modulus $G_{xy}$. Here the nonlinear material behavior is accounted for by letting the Young's moduli with an effective strain $\bar{\varepsilon}$,

$$\bar{\varepsilon} = \frac{\sqrt{(\varepsilon_x - \varepsilon_y)^2 + (\varepsilon_z - \varepsilon_y)^2 + (\varepsilon_x - \varepsilon_z)^2 + \frac{3}{2}(\gamma_{xy}{}^2 + \gamma_{yz}{}^2 + \gamma_{xz}{}^2)}}{\sqrt{2}(1+\nu)}. \tag{4}$$

$E_x$ and $E_y$ are assumed to have exponential forms, and fitting to uniaxial strain data gives:

$$E_x = 1927.2e^{9.827\varepsilon_x},$$
$$E_y = 118.34e^{13.20\bar{\varepsilon}}. \tag{5}$$

with $E_x >> E_y$, $G_{xy}$ can be calculated in the linear elastic sense from

$$G_{xy} = \frac{E_y}{2(1+\nu_{xy})}, \tag{6}$$

and the two Poisson's ratios are assumed to be equal 0.45 at all strains for nearly incompressible tissue. This model is reported to achieve a good fit with uniaxial data from porcine aortic heart valve. This is the only model known to the authors intended to model heart valve tissue by extension of linear elastic theory.

Many models exist that involve assuming a strain-energy function for the tissue. Based on observations for rat mesentery, Fung and co-workers (Tong and Fung, 1974) proposed that the strain energy should be exponentially related to the strain,

$$W = \frac{c}{2}(e^Q - 1), \tag{7}$$

where $c$ is a constant and $Q$ is a function of the strain state such as

$$Q = c_{ijk;}\ E_{ij}E_{kl}, \tag{8}$$

where all $c$'s are constants and $E_{xy}$ is the $x - y$ term of the Green strain.

A similar function can be written including only planar tension terms

$$W = B_0\left[\exp\left(\frac{b_1E_{11}^2}{2}\right) + \exp\left(\frac{b_2E_{22}^2}{2}\right) + \exp\left(\frac{b_3E_{11}E_{22}}{2}\right) - 3\right], \tag{9}$$

where $B_0$, $b_1$, $b_2$, and $b_3$ are constants. This function fits well with canine pericardium biaxial data (Choi and Vito, 1990). When the coupling terms is removed to leave

$$W = \frac{c}{2}\left[\exp\left(A_1\varepsilon_{11}^2 + A_2\varepsilon_{22}^2\right) - 1\right], \tag{10}$$

where $A_1$ and $A_2$ are constants, only a poor fit could be achieved with biaxial human aortic tissue data (Billiar and Sacks, 2000).

## TRANSVERSELY ISOTROPIC MODELS

The models in this section determine strain-energy functions based on the assumption of transverse isotropy and in terms of strain invariants. Transverse hyperelasticity can be completely described by the three strain invariants and two pseudo-invariants (Holzapfel, 2001). The three basic invariants are

$$I_1 = tr(C),\ I_2 = \frac{1}{2}\left[(trC)^2 - tr(C)^2\right],\ I_3 = \det(C), \tag{11}$$

and the two pseudo-invariants are

$$I_4 = N\cdot C\cdot N,\ I_5 = N\cdot C^2\cdot N, \tag{12}$$

where $N$ is a tensor describing the local fiber direction.

Stress-strain data suggests that the strain-energy function of passive myocardium depends strongly on $I_4$ and $I_4$, and is independent of the other invariants (Humphrey and Yin, 1989). Thus, a subclass of transversely isotropic materials is defined by $I_1$ and $\alpha$, where $\alpha$ is the stretch in the fiber direction,

$$\alpha^2 = I_4. \tag{13}$$

The strain strain-energy function may be broken into two independent isotropic and anisotropic contributions,

$$W = W_1 + W_A, \tag{14}$$

where each term is represented by a Fung-like exponential,

$$W = W_I + W_A = c\{\exp[b(I_1 - 3)] - 1\} + A\left\{\exp\left[a(\alpha - 1)^2\right] - 1\right\}. \tag{15}$$

This function mimics the biaxial myocardium data reasonably well (Humphrey and Yin, 1989).

Other functions of $I_1$ and $\alpha$ have been proposed, such as

$$W = c_1(\alpha - 1)^2 + c_2(\alpha - 1)^3 + c_3(I_1 - 3) + c_4(I_1 - 3)(\alpha - 1) + c_5(I_1 - 3)^2. \tag{16}$$

This function was formulated to fit one specific set of data, but also achieved fairly accurate predictions of biaxial data that was not included in the formulation (Humphrey *et al.*, 1990).

A transversely isotropic strain-energy function can be written with analogy to the exponential form of Eq. 7,

$$Q = c_1(I_1 - 3)^3 + c_2(\alpha - 1)^4. \tag{17}$$

This equation achieved favorably agreed with biaxial data from both mitral valve leaflets (May-Newman and Yin, 1998). It should be noted that this formulation requires only three coefficients, $c_1$ and $c_2$ from Equation 20 and $c$ from Equation 7. The works described here have determined constants only for loading behavior of the tissue, and not the unloading. A pseudoelastic model would have different constants for the unloading phase.

## ALIGNED FIBER MODELS

The models in this section take a variety of approaches to tie the overall tissue behavior to the behavior of a single fiber or bundle of fibers. A strain-energy function or stress function may be proposed for a single fiber or group of fibers, then geometric assumptions are used to extrapolate the stress-strain or strain-energy model for the whole tissue.

Again the strain-energy function can be broken into components. In this case (Humphrey and Yin, 1987), it is assumed that the fluid matrix, collagen, and elastin each contribute independent terms to the strain-energy,

$$W = W_m + \sum |W^c + \sum |W^e, \tag{18}$$

where $W_m$ is the strain-energy function of the fluid matrix, and $W^c$ and $W^e$ are the collagen and elastin components, respectively. The fiber components must be summed to represent fibers oriented in different directions. Elastin behaves generally as a linear spring, so its behavior is represented by

$$W^e = b[\gamma - \ln\gamma - 1], \tag{19}$$

where $b$ is a constant and $\gamma$ is the stretch ratio in the direction of the elastin fiber, and represents the net effect of the collagen fibers by

$$W^c = A\{\exp a(\beta - 1)^2 - 1\}, \tag{20}$$

where $A$ and $a$ are constants and $\beta$ the stretch ratio in the direction of the collagen fiber. The summation of the fiber strain energy terms for a transversely isotropic material is evaluated as

$$W = \sum W^c + \sum W^e = \int_0^\pi (W^c + W^e)\, d\phi, \tag{21}$$

where $\varphi$ represents an angle in the plane of the tissue. The fluid matrix is assumed to contribute only a hydrostatic pressure, which is incorporated into the Lagrange multiplier in Equation 2. This function was shown to fit pleura data reasonably well (Humphrey and Yin, 1987).

Separate models have been proposed for collagen and elastin fibers (Lanir, 1979). The force to extend an elastin fiber is

$$F_e = K_e[\lambda - 1], \tag{22}$$

where $K_e$ is the spring constant for an elastin fiber and $\lambda$ is the stretch ratio of the fiber. A crimped collagen fiber is assumed to stretch with zero force until it is straightened, and once it is straightened acts as a linear spring,

$$F_c \begin{cases} 0, & \lambda < \lambda_c \\ K_c[\lambda - \lambda_c], & \lambda > \lambda_c, \end{cases} \tag{23}$$

where $\lambda_c$ is the critical stretch needed to straighten the fiber and $K_c$ is the spring constant for a straightened collagen fiber. This work also proposed that, rather than calculating exactly when each collagen fiber reaches its straightening stretch, a probability function can be used to determine what percentage of fibers are straight for any tissue strain state (Lanir, 1979). Subsequent models generally ignore the elastin component to model the network entirely in terms of probabilistic collagen fibers (Lanir, 1982).

One such model based on the previous work represents the fiber stress-strain relationship with

$$\sigma_f(\varepsilon_f) = K_2 \int_0^{\varepsilon_f} D(x) \frac{\varepsilon_f - x}{1 + 2x}\, dx, \tag{24}$$

where $\sigma_f$ and $\varepsilon_f$ are the stress and strain in the fiber, respectively, $x$ is the variable of integration, and $D(x)$ is defined by a Gamma distribution,

$$D(x) = \frac{1}{\beta^\alpha \Gamma(\alpha)} x^{\alpha-1} \exp\left(-\frac{x}{\chi}\right), \tag{25}$$

where $\alpha$ and $\beta$ are positive constants. The tissue stress-strain relationship can then be found by

$$\sigma = \int_{-\pi/2}^{\pi/2} R(\theta)\sigma_f(\varepsilon_f)[N \otimes N]\, d\theta, \tag{26}$$

where $R$ represents the angular distribution of the fibers. The fiber stress-strain relation can also be represented by

$$\sigma_f(\varepsilon_f) = A[\exp(B\varepsilon_f) - 1], \tag{27}$$

where $A$ and $B$ are constants, and both Equation 24 and Equation 27 have good fit and predictive ability for bovine pericardium biaxial data (Sacks, 2003). Equation 27 has been found to give a good fit and predictive behavior for biaxial aortic valve cusp samples (Billiar and Sacks, 2000).

## UNIT-CELL MODELS

A common approach in the constitutive modeling of rubber and elastomer materials is to derive the entire model from knowledge of the material's microstructure. Entropy-based models are used to predict the behavior of a single fiber and a unit-cell approach is used to determine the bulk tissue properties. Many such models have been presented for modeling of rubber; for a review the reader is directed to Boyce and Arruda, 2000. Rubber models are generally isotropic, so modeling of heart valve tissue and the like requires extension to anisotropy. Unit cell models can be readily extended to orthotropy, and the derivation of one such model is followed here.

The strain-energy equation for a single fiber can be determined using a freely-jointed or wormlike chain model. Using a Langevin freely-jointed chain model appropriate for large strains gives the increase in strain energy from undeformed length $R$ to deformed length $r$ for a chain of total length $L$,

$$\Delta w = k_B \Theta N \left[ \left( \frac{\rho}{N}\beta_\rho + \ln \frac{\beta_\rho}{\sinh \beta_\rho} \right) - \left( \frac{P}{N}\beta_P + \ln \frac{\beta_P}{\sinh \beta_P} \right) \right], \tag{28}$$

where $k_B$ is Boltzmann's constant, $\Theta$ is the absolute temperature, $N$ is the number of links in a single chain, and $\rho$ and $P$ are the normalized chain lengths $r/L$ and $R/L$, respectively (Bischoff *et al.*, 2002). $\beta$ is defined by the inverse Langevin function so that $\beta_\rho \mathcal{L}^{-1}(\rho/L)\beta_R = \mathcal{L}^{-1}(R/L)$. Using an eight chain unit-cell model, as shown in Fig. 3, the strain energy needed to stretch the chains within the cell is

$$w_{\text{chains}} = w_0 + 2k_B\Theta N \sum_{i=1}^{4} \left[ \frac{\rho^{(i)}}{N} \beta_\rho{}^{(i)} + \ln \frac{\beta_\rho^{(i)}}{\sinh \beta_\rho{}^{(i)}} \right], \tag{29}$$

where $i$ sums over half of the chains.

There also exists a strain energy due to repulsion between the chains,

$$w_{\text{repulsion}} = \frac{8k_B\Theta\sqrt{N}\beta_P}{a^2 + b^2 + c^2} \ln(\lambda_a \lambda_b \lambda_c), \tag{30}$$

where $a$, $b$, and $c$ are the dimensions shown in Fig. 3 and $\lambda_a, \lambda_b$, and $\lambda_a$ are the stretches in the directions along the principal material axes. Assuming the

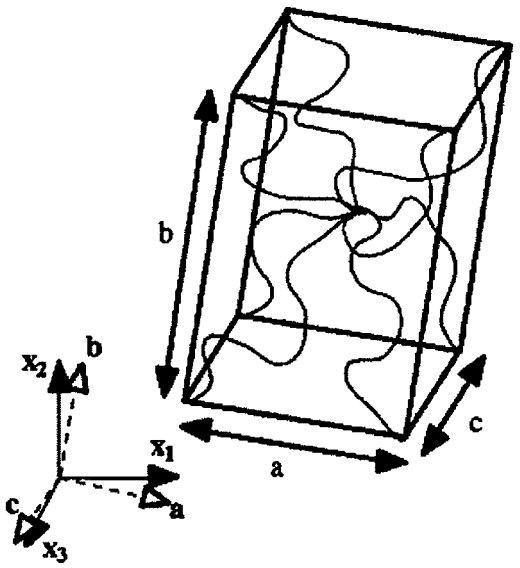


**Figure 3.** Eight chain unit-cell model. From Bischoff (2002).

material is incompressible, the complete strain energy function is given by

$$W = \sum_{n/8} \frac{n}{8}(w_{\text{chain}} + w_{\text{repulsion}}), \tag{31}$$

where $n$ is the chain density. $N$ can be directly related to $a$, $b$, and $c$, so this model is applicable with four free variables: $n$, $a$, $b$, and $c$. This function provides a good fit to uniaxial skin data (Bischoff *et al*., 2002).

## DISCUSSION

The main challenge in constructing a constitutive model for heart valve leaflet tissue is that the tissues are thin, and experimentally can only be rigorously tested in states of planar tension. In normal heart valve function, however, the leaflets are subjected to significant out-of-plane and compressive stresses. The researcher's task is to create a model from two-dimensional data that will predict three-dimensional behavior.

While heart valve tissue cannot be readily tested in three-dimensions, results from other materials show that the some of the models presented here apply in three-dimensional states. Microstructural unit-cell models have been verified in three-dimensional stress states in rubber (Boyce and Arruda, 2000) and transversely isotropic models have been similarly verified in artificial (Kominar *et al*., 1995) and biological materials (DiSilvestro *et al*., 2001). No such verification is known for the phenomological model described here (Equations 3–7), and some models are not intended for use in three-dimensional stress states: the simplifications of Fung's exponential given in Equation 9 and Equation 10, for example, include only in-plane strain terms and are not intended for use in three dimensions.

The unit-cell and transversely isotropic models seem equally applicable to describing the behavior of heart valve tissue, and researchers have achieved similar results fitting either model to biaxial data. There are some differences between the two classes of models that may help in deciding which to use. Equation 17 has the advantage that its constants can be determined in a relatively straightforward fashion through constant-invariant tests, while finding the constants of a unit-cell model requires fitting curves to multiple sets of data. a unit-cell model includes data on the microstructure of the material, and therefore may be preferred when the microstructural features are of interest.

There are a few important effects that none of these models incorporate. First, heart valve leaflets are composed of three layers known to have different mechanical properties from each other (Vesely and Noseworthy, 1992) while all of these models assume that the material is homogonous through the thickness. A better model would either include the three different layers as one laminated body or provide three separate regions, each with a different constitutive model. All three of the layers are structurally similar, so the model for each layer can be in the same form as the homogenous models shown in this paper. Moreover, while the tissue is known to be pseudoelastic and have significantly different loading from unloading curves, all of the models here either give only the loading curve of one general curve.

## CONCLUSIONS

We have reviewed a number of various models proposed for heart valve leaflet or similar biological tissue. Of these, the unit-cell microstructural models and the transversely isotropic models are most applicable to describing a general three-dimensional stress-strain state. The simplified transversely isotropic models, formulated in terms of two strain invariants, are most easily fit to biaxial experimental data. The unit-cell models cannot be fit to data as easily, but capture more of the material's microstructure. Either of these models could be significantly improved by including the layered characteristic of heart valve tissue and by providing separate curves for the loading and unloading phases.

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