Constitutive Modeling of Biological Soft Tissues

Attila P. Nagy[1], David J. Benson[1], Vikas Kaul[2], Mark Palmer[2]
[1]*Livermore Software Technology Corporation, Livermore, CA 94551, USA*
[2]*Medtronic plc, Minneapolis, MN 55432, USA*

Abstract

In the present communication, we introduce a class of material models primarily aimed at simulating the elastic and viscous behavior of biological soft tissues in LS-DYNA®. The constitutive law is modular and each module may comprise of different models. Consequently, the analyst may easily change models in a module and also include additional modules to account for more complex material behaviors within the same keyword. In its most general form, the material is considered nearly incompressible, anisotropic, and hyperelastic with the passive behavior defined using a decoupled strain energy function. The contractile and viscoelastic behavior of the tissue may be considered by invoking extra modules. The models are verified using a wide range of recently published results and show excellent agreement.

Introduction

Computational constitutive modeling of biological soft tissues is of paramount importance in modeling realistic device-tissue interaction during the design and development of medical devices. Almost all biological soft tissues are complex composite materials in which fibers are embedded in a fluid-like matrix. While soft tissues possess distinct multi-scale characteristics, an efficient numerical framework is facilitated by continuum-based constitutive relations that describe an averaged or homogenized behavior of the material. Generally, these material models can be classified as morphological or structural, phenomenological, and hybrid. Morphological models are derived from considering the underlying microstructure of the tissue. On the other hand, phenomenological models invoke material parameters with no direct morphological basis. Hybrid models aim to combine the best of the previous classes to define a more generic material response. For a detailed overview of constitutive models of biological tissues, the reader is referred to [9], [5], [3], [4] and the references therein.

In the past decades there has been a significant growth in interest in understanding the behavior of biological soft tissues. Recent advances in experimental techniques, medical imaging, and computer science enable the development and continuous improvement of accurate and efficient continuum material models. The present paper is aimed at describing recent constitutive modeling efforts in LS-DYNA focusing on biological soft tissues. The remaining part of the paper is organized as follows. A modular keyword is introduced in Section 1. An overview of currently available constitutive models and features is presented in Section 2. Selected example problems and future developments are discussed in Sections 3 and 4, respectively.

Modular Keyword Design

A new class of material models aimed at describing the mechanical behavior of biological soft tissues is introduced in `*MAT_295`. The constitutive laws introduced therein are implemented in a modular fashion. Each module may comprise of different models. Consequently, the analyst may easily change models in a module and include additional modules to account for more complex material behavior within the same keyword. A couple of things are worth noting at this point. Firstly, extending an existing module with a new model or even including a new module does not require the developer to add a new material keyword. Secondly, some of the material models may also be used to model a wider class of materials including fiber-reinforced elastomers, stretchable fabrics, *etc.*

Currently, there are four material modules available that describe the passive isotropic and anisotropic, active, and viscous nature of the material. The isotropic module is mandatory whereas the others are optional, and each module may be invoked once for a specific material. An excerpt of the corresponding keyword is depicted in Figure 1.

```
*MAT_295
$#     mid       rho      aopt
        16   1.04E-6       2.0
$#  module      mtyp      beta        nu
ISO              3      -2.0       &nu
$#     ic1       ic2
      1.36      1.75
$#  module      mtyp        nf
ANISO            1         2
$# fiber family #1
$#   alpha         A         B
       10.       .08       .76
$#    mfbr     flcid        k1        k2
         1         0       .49      9.01
$# fiber family #2
$#   alpha         A         B
      -10.       .08       .76
$#    mfbr     flcid        k1        k2
         1         0       .49      9.01
$#  module      mtyp     alcid      adir
ACTIVE           2         0         1
$#       b       ca2+   ca2+max         n        l0         l    taumax         f
      4.75       1.8      4.35        2.      1.58       1.6      100.        .0
$#      t0     gamma
        0.      1.45
$#      xp        yp        zp        a1        a2        a3      macf      ihis
                                     1.0       0.0       0.0       1.0
$#      v1        v2        v3        d1        d2        d3      beta       ref
                                     0.0       1.0       0.0
```

*Figure 1 Sample keyword for *MAT_295*

Constitutive Models

A brief overview of the finite strain constitutive models implemented as part of `*MAT_295` is provided in this section. In what follows, passive, active, and viscoelastic material behaviors are discussed separately.

Passive Models. Most soft tissues possess an oriented architecture of collagen fibril bundles conferring to both anisotropy and nonlinearity to their elastic response [3]. Since the material is assumed to be nearly incompressible and hyperelastic, we can postulate the existence of a decoupled Helmholtz free energy or elastic potential energy function $\Psi(\boldsymbol{F}, \boldsymbol{A}_i)$ where $\boldsymbol{F}$ is the deformation gradient, $\boldsymbol{A}_i$, with $i = 1, \dots, n$, where n is the number of fiber families, is the (mean) unit reference orientation of the *i*th fiber bundle or fiber family included in the model. To ensure material stability as well as a stable numerical computational scheme, the elastic potential needs to be polyconvex by construction.

The isotropic behavior of the non-collagenous matrix material is formulated in terms of the isotropic invariants or the principal stretches and an appropriate set of material parameters. Currently, the neo-Hookean, Mooney-Rivlin, Ogden, see *e.g.* [5], and Holzapfel-Ogden [10] models may be used to describe the isotropic behavior of the continua.

Anisotropy is introduced by collagen fibers ubiquitous in different soft tissues, *e.g.* arterial walls, skin, and skeletal muscle. Experimental studies of their microstructure suggest that the embedded fibers are highly dispersed or, in other words, follow a spatially varying distribution. To this end, accounting for fiber dispersion in the constitutive model is imperative. Generally, there are two methods to incorporate fiber dispersion in continuum constitutive laws, namely the angular integration [15] and the generalized structure tensor-based approaches [3], [10]. It has recently been shown that the two methods yield virtually the same results [12]; however, in view of numerical implementation, accuracy, and efficacy, the latter formulation is more attractive. Consequently, all currently available models in LS-DYNA invoke the generalized structure tensor. The structure tensor, in its most generic form, is based on a non-symmetric fiber dispersion model that allows us to distinguish between the dispersions in the tangential and normal directions [11]. The structure tensor associated with an arbitrary fiber family is written as

$$\boldsymbol{H}_i = \boldsymbol{A}\boldsymbol{I} + B\boldsymbol{A}_i \otimes \boldsymbol{A}_i + (\boldsymbol{1} - \boldsymbol{3}\boldsymbol{A} - \boldsymbol{B})\boldsymbol{N} \otimes \boldsymbol{N}, \tag{1}$$

where $\boldsymbol{I}$ is the second order identity tensor, $\boldsymbol{N}$ is the unit reference normal vector, and the parameters A and B quantify fiber dispersion and can be computed from a normalized probability density function. Note that appropriate choice of these parameters allows us to recover several special cases including (transversely) isotropic and planar (isotropic) dispersions as well as perfect alignment along $\boldsymbol{A}_i$.

The mechanical behavior of the fibers may be defined using the phenomenological models introduced by Holzapfel *et al.* [9] and extended by Holzapfel and Ogden [10] and Eriksson *et al.* [1], or the morphological model of Freed and Doehring [2]. Alternatively, the fiber stress versus stretch curve may be defined using the `*DEFINE_CURVE` keyword which allows for the direct use of experimental data. To allow even greater flexibility, fiber dispersion, *i.e.* the general structure tensor, and fiber model properties are defined for each fiber family separately.

Active Models. The contractile or active behavior of the material defines the relationship between cytosolic calcium concentration and tension developed in heart muscle. The active behavior may be modeled using the modified Hill equation governing chemical equilibria in dilute solutions. Hence, the active fiber stress is given by the scaled isometric tension development

$$\tau = c(\lambda)\tau_{max} \frac{[\mathrm{Ca}^{2+}]^m}{[\mathrm{Ca}^{2+}]^m + [\mathrm{Ca}_{50}^{2+}]^m}, \tag{2}$$

where $c(\lambda)$ is a fiber stretch dependent internal variable, τ_{max} is the maximum stress generated at reference length *i.e.*, $\lambda = 1$, $[\mathrm{Ca}^{2+}]$ is the cytosolic calcium concentration, $[\mathrm{Ca}_{50}^{2+}]$ is the calcium concentration at $\tau = \tau_{max}/2$, and m is the Hill coefficient. Depending on the choice of the stretch-dependent internal variable, one may recover the elastance model [6] or the model originally proposed by Hunter *et al.* [14].

Viscoelastic Models. To date, a linear and a quasi-linear, or also known as separable nonlinear viscoelasticity, originally introduced by Fung [4], is implemented in LS-DYNA. These models rarely represent the true rate-dependent behavior of biological soft tissues and the inclusion of more advanced generalized nonlinear viscoelastic models is required in the future.

Numerical Examples

Constrained uniaxial stretch. We first consider a constrained stretch of a unit cube such that $\lambda_1 = \lambda_3 = 1$ and $\lambda_2 > 1$. An example for this simple homogeneous deformation is when, for instance, a blood vessel undergoes large circumferential but little or no axial and radial strains [16]. A single family of perfectly aligned fibers is embedded in the cube. The reference fiber orientation vector $\boldsymbol{A}_1$ is defined within the 1-2 plane with a relative orientation of θ with respect to the first axis. Multiple reference orientations are considered with the intent to highlight some differences between the Holzapfel-Gasser-Ogden (HGO) model, as outlined in Gasser *et al.* [4], and its modified form proposed by Nolan *et al.* [16].

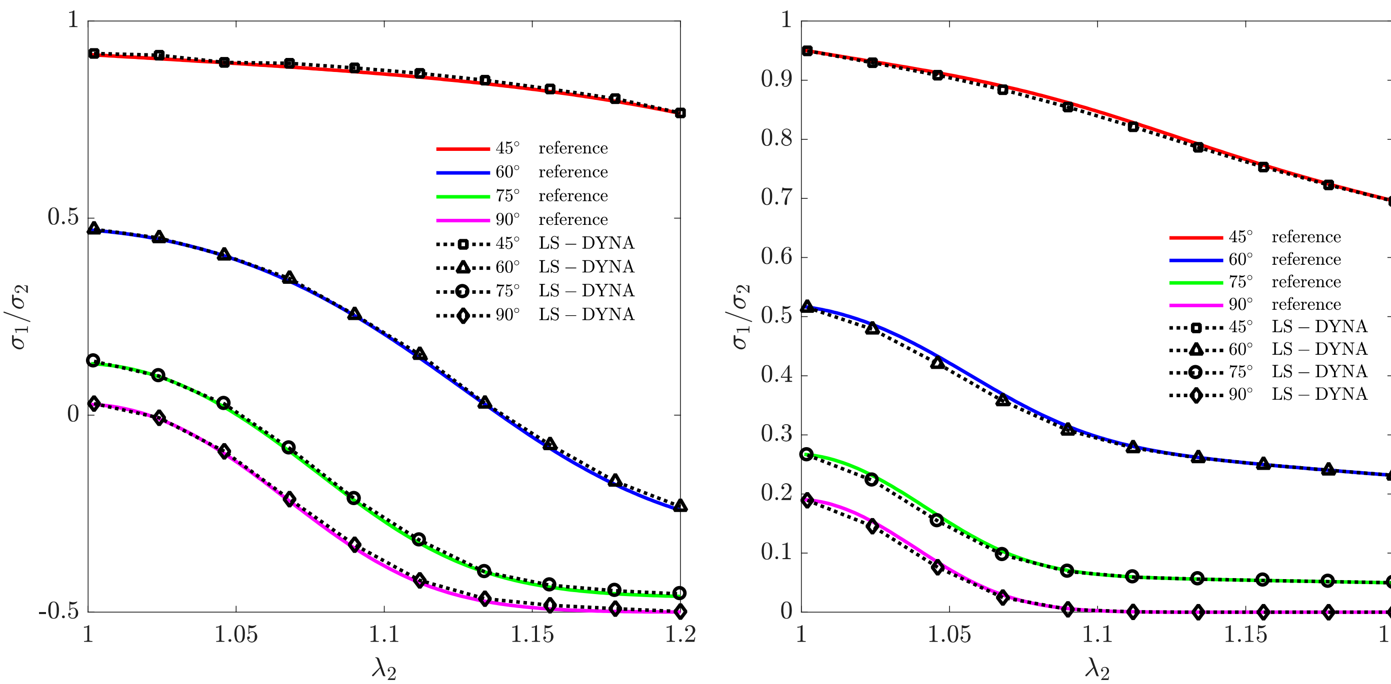

Figure 2 Ratio of lateral and axial Cauchy stresses versus stretch invoking the (a) Holzapfel-Gasser-Ogden model [4] and (b) its modified form proposed by Nolan et al. [16]

The ratio of lateral and axial Cauchy stresses σ_1/σ_2 is depicted in Figure 2. Results obtained using the HGO model indicate an auxetic material response if the fibers are aligned closer to the direction of the stretch. In fact, if the fiber is oriented along the second axis, *i.e.* $\theta = 90°$, one may observe the most profound compressive lateral stresses. In contrast, the modified model yields tensile lateral stresses for all fiber orientations, a behavior which one would expect from a transversely isotropic material.

Active stress development under uniaxial tension. In what follows, we consider a unit cube discretized using seven elements of irregular shape under uniaxial tension. The active model is given by Hunter *et al.* [14] and active stresses are computed for two distinct levels of calcium concentration. The active stresses computed using LS-DYNA nicely match the corresponding analytical solutions as shown in Figure 3.

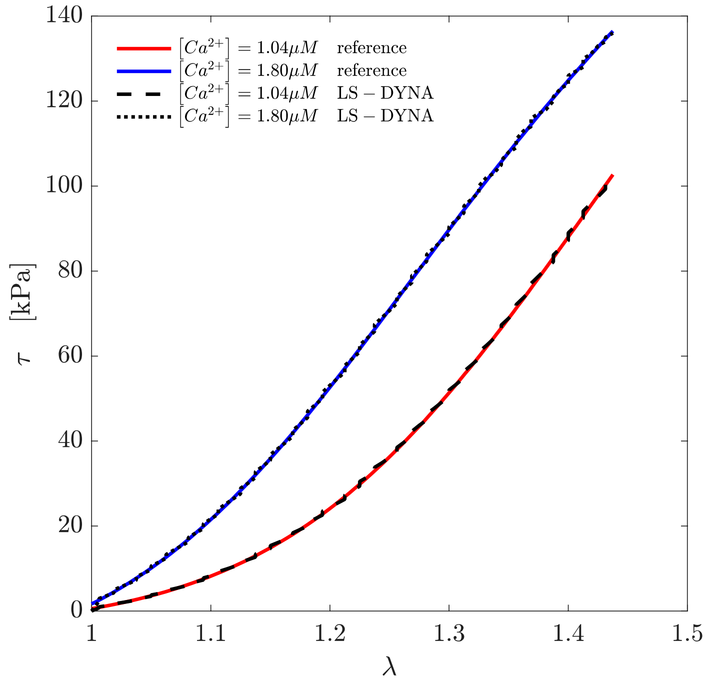

Figure 3 Active stress versus fiber stretch at two concentrations of cytosolic calcium

Conclusions and Future Developments

A brief overview of novel biological soft tissue modelling features in LS-DYNA was presented. In particular, we introduced and discussed the new modular `*MAT_295` which represents a collection of material models frequently used in computational biomechanics. The presented example problems demonstrate the accuracy of LS-DYNA compared to reference solutions published in the literature.

Several distinct development directions need to be pointed out. First of all, we envision the gradual expansion of `*MAT_295` with both new modules and models. Secondly, we are working on the interface of solid mechanics, electromagnetics, as well as incompressible fluid solvers to investigate more complex coupled problems in the near future. Thirdly, we are enhancing capabilities that enable material parameter identification for the class of materials included in `*MAT_295` within LS-OPT®. Finally, we remark that `*MAT_295` is currently only available for solid elements and its applicability for shell elements needs to addressed in the future.

References

[1] Eriksson TSE, Prassl AJ, Plank G, Holzapfel GA (2013) *Modeling the dispersion in electro-mechanically coupled myocardium* International Journal for Numerical Methods in Biomedical Engineering 29:1267-1284

[2] Freed AD, Doehring TC (2005) *Elastic response of crimped collagen fibrils* Journal of Biomechanical Engineering 127:587-593

[3] Freed AD, Einstein DR, Vesely I (2005) *Invariant formulation for dispersed transverse isotropy in aortic heart valves.* Biomechanics and Modeling in Mechanobiology 4:100-117

[4] Fung YC (1981) *Biomechanics: mechanical properties of living tissues* New York, NY USA: Springer

[5] Gasser TC, Ogden RW, Holzapfel GA (2006) *Hyperelastic modeling of arterial layers with distributed collagen fibre orientations.* Journal of the Royal Society Interface 3:15-35

[6] Guccione JM, Waldman LK, McCulloch AD (1993) *Mechanics of active contraction in cardiac muscle: Part II – Cylindrical Models of the systolic left ventrice* Journal of Biomechanical Engineering 115:82-90

[7] Gültekin O, Sommer G, Holzapfel GA (2016) *An orthotropic viscoelastic model for the passive myocardium: continuum basis and numerical treatment* Computer Methods in Biomechanics and Biological Engineering 15:1647-1664

[8] Holzapfel GA, (2000) *Nonlinear solid mechanics. A continuum approach for engineering* Chichester, UK: Wiley.

[9] Holzapfel GA, Gasser TC, and Ogden RW (2000) *A new constitutive framework for arterial wall mechanics and a comparative study of material models* Journal of Elasticity and the physical science of solids 61:1-48

[10] Holzapfel GA, Ogden RW (2009) *Constitutive modelling of passive myocardium: a structurally based framework for material characterization* Philosophical Transactions of the Royal Society A 367:3445-3475

[11] Holzapfel GA, Niestrawska JA, Ogden RW, Reinisch AJ, and Schriefl AJ (2015) *Modelling non-symmetric collagen fibre dispersion in arterial walls* Journal of the Royal Society Interface 12:1-14

[12] Holzapfel GA, Ogden RW (2017) *Comparison of two model frameworks for fiber dispersion in the elasticity of soft biological tissues* European Journal of Mechanics – A/Solids 66:193-200

[13] Holzapfel GA, Ogden RW (2017) *On fiber dispersion models: exclusion of compressed fibers and spurious model comparisons* Journal of Elasticity 129:49-68

[14] Hunter PJ, Nash MP, Sands GB (1997) *Computational electromechanics of the heart* In Computational biology of the heart (eds Panfilov AV, Holden AV), Chichester, UK: Wiley

[15] Lanir Y (1983) *Constitutive equations for fibrous connective tissues* Journal of Biomechanics 16:1-12

[16] Nolan DR, Gower AL, Destrade M, Ogden RW, McGarry JP (2014) *A robust anisotropic hyperelastic formulation for the modeling of soft tissue.* Journal of the Mechanical Behavior of Biomedical Materials 29:48-60