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RATE-TYPE ELASTICITY AND VISCOELASTICITY OF AN ERYTHROCYTE MEMBRANE

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The rate-type constitutive theory of elastic and viscoelastic response of an erythrocyte membrane is presented. The results are obtained for an arbitrary isotropic strain energy function, and for its particular Evans–Skalak form. The explicit representations of the corresponding fourth-order tensors of elastic moduli are derived, with respect to principal axes of stress, and an arbitrary set of orthogonal axes. The objective rate-type viscoelastic constitutive equations of the cell membrane are then derived, based on the Maxwell and Kelvin models of viscoelastic behavior.

1. Introduction

The study of the mechanical response of a red blood cell (erythrocyte) membrane has received a great amount of attention from both classical mechanics and bio-chemo-mechanical points of view [Evans and Skalak 1980; Fung 1993; Agre and Parker 1989; Boal 2002]. Recent studies have addressed the evolution of mechanical properties of the cell membrane, associated with dynamic remodeling and reorganization of the membrane structure during large deformations of the cell, in response to mechanical, thermal, and chemical forces [Gov 2007; Li et al. 2007; Park et al. 2010]. Once the evolution equations for such structural changes are constructed, their incorporation in the constitutive theory can be accomplished through the rate-type constitutive equations, analogous to the existing theories of biological remodeling or growth of soft tissues [Lubarda and Hoger 2002; Garikipati et al. 2006; Taber 2009]. Since the rate-type constitutive theories relate the rates of stress and deformation, an essential ingredient of such theories is the elastic constitutive expression in the rate-type (incremental) form. The objective of this paper is to develop such rate-type constitutive expression, corresponding to an arbitrary isotropic strain energy function, and its Evans–Skalak particular form. The explicit expressions are derived for the components of the fourth-order tensor of elastic moduli, which relate the objective rates of the conjugate stress and strain tensors. The derived rate-type elasticity equations are then used to construct the objective rate-type viscoelastic constitutive equations for erythrocyte membrane, based on the Maxwell and Kelvin viscoelastic models.

Since the red blood cell membrane is only about 100 Å thick, it is assumed that the model of continuum mechanics applies only within the plane of the membrane. The applied forces are thus considered to be distributed along the length, with the membrane stresses defined by the force/length ratios. The upper bound on the in-plane Poisson ratio is equal to 1, rather than $\frac{1}{2}$, as in the three-dimensional isotropic elasticity. When modeled as infinitesimally thin, the erythrocyte membrane has no buckling resistance, and thus can support only noncompressive loadings, which give rise to nonnegative principal stresses

Keywords: elastic modulus, erythrocyte, membrane elasticity, rate theory, viscoelasticity.

[Lubarda and Marzani 2009; Lubarda 2010]. The incorporation of small, but finite bending stiffness (proportional to the square of the membrane thickness) is needed to address other features of the membrane response, such as the size and shape of membrane wrinkles which may form during large deformations [Haughton 2001; Géminard et al. 2004], the membrane adhesive interactions [Agrawal and Steigmann 2009], or the resting shape of the cell and the skeleton/bilayer interactions in optical tweezer stretching and micropipette aspiration tests [Peng et al. 2010].

The content of the paper is as follows. Section 2 contains the kinematics and kinetics of the membrane in-plane deformation. The Evans–Skalak form of the elastic strain energy is adopted, as in most other recent work on the mechanics of red blood cell, (e.g., [Mills et al. 2004; Zhu et al. 2007]). The rate-type elasticity equations, which relate the Jaumann rate of the Kirchhoff stress to the rate of deformation tensor, are derived in Section 3. The explicit representation of the elastic moduli tensor is given for an arbitrary isotropic strain energy function, and for its special Evans–Skalak form. The results are given for the coordinate axes parallel to the principal axes of stress, and for the arbitrary set of orthogonal axes. Since the areal modulus of the erythrocyte cell is several orders of magnitude higher than the shear modulus, for some applications it may be appropriate to model the membrane as infinitely stiff to its area change; in Section 4 we accordingly present the rate-type elastic constitutive analysis for isoareal membranes. The derived rate-type elasticity equations are used in Section 5 to derive the objective rate-type viscoelasticity equations, corresponding to the Maxwell and Kelvin viscoelastic models. The results are given explicitly for an arbitrary isotropic strain energy function and for its particular Evans–Skalak form. Concluding remarks are given in Section 6. For completeness of the analysis, the appendices contain the results of the rate-type elastic analysis based on the Lagrangian strain and its conjugate Piola–Kirchhoff stress (Appendix A), and the deformation gradient and its conjugate nominal stress (Appendix B).

2. Kinematic and kinetic preliminaries

The deformation gradient associated with in-plane deformation of a thin plane membrane is

$$\boldsymbol{F} = \lambda_1\, \boldsymbol{n}_1 \otimes \boldsymbol{N}_1 + \lambda_2\, \boldsymbol{n}_2 \otimes \boldsymbol{N}_2, \tag{1}$$

where λ_1 and λ_2 are the principal stretches, $\boldsymbol{N}_i$ are the unit vectors along the principal directions of the right stretch tensor $\boldsymbol{U}$ in the undeformed configuration, and $\boldsymbol{n}_i = \boldsymbol{R}\cdot\boldsymbol{N}_i$ are the unit vectors in the deformed configuration, along the principal directions of the left stretch tensor $\boldsymbol{V}$. The polar decomposition of the deformation gradient is $\boldsymbol{F} = \boldsymbol{V}\cdot\boldsymbol{R} = \boldsymbol{R}\cdot\boldsymbol{U}$, where $\boldsymbol{R} = \boldsymbol{n}_1 \otimes \boldsymbol{N}_1 + \boldsymbol{n}_2 \otimes \boldsymbol{N}_2$ is the rotation tensor. The dyadic product of two vectors is denoted by $\otimes$.

The strain energy (per unit initial area) of an isotropic membrane is a function of the principal stretches, $\phi = \phi(\lambda_1, \lambda_2)$. An infinitesimal change of the strain energy is equal to the work done by the true (Cauchy) stress components σ_1 and σ_2 on the incremental stretches $\mathrm{d}\lambda_1$ and $\mathrm{d}\lambda_2$, which gives

$$\mathrm{d}\phi = \sigma_1\lambda_2\, \mathrm{d}\lambda_1 + \sigma_2\lambda_1\, \mathrm{d}\lambda_2. \tag{2}$$

By taking the differential of $\phi = \phi(\lambda_1, \lambda_2)$, the comparison with (2) establishes the constitutive expressions

$$\sigma_1 = \frac{1}{\lambda_2}\frac{\partial\phi}{\partial\lambda_1}, \quad \sigma_2 = \frac{1}{\lambda_1}\frac{\partial\phi}{\partial\lambda_2}. \tag{3}$$

The corresponding Kirchhoff stress components, $\tau_i = (\det \boldsymbol{F})\,\sigma_i = (\lambda_1\lambda_2)\,\sigma_i$, are

$$\tau_1 = \lambda_1 \frac{\partial\phi}{\partial\lambda_1}, \quad \tau_2 = \lambda_2 \frac{\partial\phi}{\partial\lambda_2}. \tag{4}$$

2.1. ***Evans–Skalak form of the strain energy.*** The strain energy of an isotropic membrane must be a symmetric function of λ_1 and λ_2. Evans and Skalak [1980] proposed that $\phi = \phi(\alpha, \beta)$, where the deformation measures

$$\alpha = \lambda_1\lambda_2 - 1, \quad \beta = \frac{1}{2}\left(\frac{\lambda_1}{\lambda_2} + \frac{\lambda_2}{\lambda_1}\right) - 1 \tag{5}$$

are constructed so that $\alpha = \beta = 0$ in the undeformed configuration. The parameter α is the area change per unit undeformed area, while β is a measure of the distortional deformation. The Evans–Skalak model of a nonlinear elastic membrane corresponds to $\phi = \frac{1}{2}\kappa\alpha^2 + \mu\beta$, i.e.,

$$\phi = \tfrac{1}{2}\,\kappa(\lambda_1\lambda_2 - 1)^2 + \mu\left[\frac{1}{2}\left(\frac{\lambda_1}{\lambda_2} + \frac{\lambda_2}{\lambda_1}\right) - 1\right], \tag{6}$$

where κ and μ are the areal (bulk) modulus and the shear modulus of the membrane, respectively. From (3), the stress components are

$$\sigma_{1,2} = \kappa(\lambda_1\lambda_2 - 1) \pm \tfrac{1}{2}\,\mu(\lambda_2^{-2} - \lambda_1^{-2}), \tag{7}$$

$$\sigma_1 + \sigma_2 = 2\kappa(\lambda_1\lambda_2 - 1), \quad \sigma_1 - \sigma_2 = \mu(\lambda_2^{-2} - \lambda_1^{-2}). \tag{8}$$

Numerous experiments have been conducted in the past to measure the elastic and viscous properties of the human erythrocyte membrane. For example, from the micropipette aspiration tests of red blood cells, it has been estimated that the shear modulus (μ) of the erythrocyte membrane is in the range $4 - 10$ μN/m, while the areal modulus (κ) is on the order $10^3 - 10^4$ higher than that [Evans and Skalak 1980; Boal 2002]. Such a large difference in two stiffnesses is because the areal modulus of the cell membrane is controlled mostly by the phospholipidic bilayer, while the shear modulus is determined by the elastic properties of the cytoskeleton, a two-dimensional network of spectrin strands bound to the bilayer. The viscous properties of the cell are due to glycoproteins, lipid integral and peripheral membrane proteins, lipid rafts, and transmembrane cholesterol. Based on the measurements of the characteristic time for relaxation, the shear viscosity has been estimated to be in the range 0.6–2.7 μN·s/m [Hochmuth 1987].

If the Kirchhoff stress components are used, the expressions (7)–(8) can be rewritten as

$$\tau_1 + \tau_2 = 2\kappa\lambda_1\lambda_2(\lambda_1\lambda_2 - 1), \quad \tau_1 - \tau_2 = \mu\left(\frac{\lambda_1}{\lambda_2} - \frac{\lambda_2}{\lambda_1}\right). \tag{9}$$

For the later purposes of the rate-type theory of viscoelasticity and the incremental solution of the boundary value problems, it is important to invert (9), and express $\lambda_1\lambda_2$ and λ_1/λ_2 in terms of stress components. The resulting expressions are

$$\begin{gathered}\lambda_1\lambda_2 = \frac{1}{2}\left[1 + \left(1 + 2\,\frac{\tau_1+\tau_2}{\kappa}\right)^{1/2}\right], \\ \frac{\lambda_1}{\lambda_2} = \frac{\tau_1-\tau_2}{2\mu} + \left[1 + \left(\frac{\tau_1-\tau_2}{2\mu}\right)^2\right]^{1/2}, \quad \frac{\lambda_2}{\lambda_1} = -\frac{\tau_1-\tau_2}{2\mu} + \left[1 + \left(\frac{\tau_1-\tau_2}{2\mu}\right)^2\right]^{1/2}.\end{gathered} \tag{10}$$

The sum and difference of the Kirchhoff stress components can be expressed in terms of the Cauchy stress components as

$$\tau_1 \pm \tau_2 = \left(1 + \frac{\sigma_1 + \sigma_2}{2\kappa}\right)(\sigma_1 \pm \sigma_2), \tag{11}$$

because, from (9), $\lambda_1\lambda_2 = 1 + (\sigma_1 + \sigma_2)/2\kappa$, and $\tau_i = (\lambda_1\lambda_2)\sigma_i$, for $i = 1, 2$.

2.2. ***Stress response on arbitrary axes.*** The strain energy of an isotropic membrane can be expressed as a function of two independent invariants of the left Cauchy–Green deformation tensor $\boldsymbol{B} = \boldsymbol{V}^2$, i.e.,

$$\phi = \phi(I_B, II_B), \quad I_B = \operatorname{tr}\boldsymbol{B} = \lambda_1^2 + \lambda_2^2, \quad II_B = \det\boldsymbol{B} = \lambda_1^2\lambda_2^2. \tag{12}$$

where I_B is the trace, and II_B the determinant of $\boldsymbol{B}$. Since $\dot{I}_B = \dot{B}_{kk} = 2B_{ij}D_{ij}$, $\dot{II}_B = 2II_B D_{kk}$, and $\dot{\phi} = \tau_{ij}D_{ij}$, by taking the time-rate of (12), if follows that

$$\tau_{ij} = 2\left(\frac{\partial\phi}{\partial I_B}\, B_{ij} + II_B\,\frac{\partial\phi}{\partial II_B}\,\delta_{ij}\right), \tag{13}$$

where δ_{ij} is the Kronecker delta. The invariants I_B and II_B are related to the invariants α and β by

$$\alpha = II_B^{1/2} - 1, \quad \beta = \frac{I_B}{2II_B^{1/2}} - 1; \qquad I_B = 2(1+\alpha)(1+\beta), \quad II_B = (1+\alpha)^2. \tag{14}$$

Consequently,

$$\frac{\partial\phi}{\partial I_B} = \frac{1}{2}\, II_B^{-1/2}\,\frac{\partial\phi}{\partial\beta}, \quad \frac{\partial\phi}{\partial II_B} = \frac{1}{4}\, II_B^{-1/2}\left(2\,\frac{\partial\phi}{\partial\beta} - I_B II_B^{-1}\,\frac{\partial\phi}{\partial\beta}\right), \tag{15}$$

and the substitution into (13) gives an alternative representation of the stress response

$$\sigma_{ij} = \frac{\partial\phi}{\partial\alpha}\,\delta_{ij} + \frac{1}{\det\boldsymbol{B}}\,\frac{\partial\phi}{\partial\beta}\, B'_{ij}, \tag{16}$$

where $B'_{ij} = B_{ij} - B_{kk}\delta_{ij}/2$ is the deviatoric part of B_{ij}.

If ϕ is given by the Evans–Skalak form $\phi = \frac{1}{2}\kappa\alpha^2 + \mu\beta$, (16) reduces to

$$\sigma_{ij} = \kappa\alpha\,\delta_{ij} + \frac{\mu}{\det\boldsymbol{B}}\, B'_{ij}. \tag{17}$$

The first term on the right-hand side of (16) and (17) is the spherical part, $\sigma_{kk}\delta_{ij}/2$, and the second term is the deviatoric part of the stress, σ'_{ij}. If the coordinate axes are parallel to the principal axes of $\boldsymbol{B}$, (17) reduces to (7).

3. Rate-type constitutive analysis

In this section we derive the rate-type form of the elastic constitutive equations, expressed with respect to the principal axes of stress and the constitutive structure (4), and with respect to arbitrary set of orthogonal axes and the constitutive structure (13) or (16).

3.1. ***Rate of deformation and spin tensors.*** For the rate-type constitutive analysis, the rates of deformation need to be considered. To that goal, we first introduce the spin tensors

$$\boldsymbol{\Omega} = \Omega(\boldsymbol{N}_1 \otimes \boldsymbol{N}_2 - \boldsymbol{N}_2 \otimes \boldsymbol{N}_1), \quad \boldsymbol{\omega} = \omega(\boldsymbol{n}_1 \otimes \boldsymbol{n}_2 - \boldsymbol{n}_2 \otimes \boldsymbol{n}_1), \tag{18}$$

such that $\dot{\boldsymbol{N}}_i = \boldsymbol{\Omega} \cdot \boldsymbol{N}_i$ and $\dot{\boldsymbol{n}}_i = \boldsymbol{\omega} \cdot \boldsymbol{n}_i$ $(i = 1, 2)$. In particular,

$$\dot{\boldsymbol{N}}_1 = -\Omega\, \boldsymbol{N}_2, \quad \dot{\boldsymbol{N}}_2 = \Omega \boldsymbol{N}_1, \qquad \dot{\boldsymbol{n}}_1 = -\omega\, \boldsymbol{n}_2, \quad \dot{\boldsymbol{n}}_2 = \omega \boldsymbol{n}_1, \tag{19}$$

where $-\Omega$ is the rate of the counterclockwise rotation of the dyad $(\boldsymbol{N}_1, \boldsymbol{N}_2)$, while $-\omega$ is the rate of the counterclockwise rotation of the dyad $(\boldsymbol{n}_1, \boldsymbol{n}_2)$. Consequently, by differentiating (1), and by using (19), the rate of the deformation gradient becomes

$$\dot{\boldsymbol{F}} = \dot{\lambda}_1\, \boldsymbol{n}_1 \otimes \boldsymbol{N}_1 + \dot{\lambda}_2\, \boldsymbol{n}_2 \otimes \boldsymbol{N}_2 + (\lambda_2\omega - \lambda_1\Omega)\boldsymbol{n}_1 \otimes \boldsymbol{N}_2 - (\lambda_1\omega - \lambda_2\Omega)\boldsymbol{n}_2 \otimes \boldsymbol{N}_1. \tag{20}$$

Since the inverse of the deformation gradient is

$$\boldsymbol{F}^{-1} = \frac{1}{\lambda_1}\boldsymbol{N}_1 \otimes \boldsymbol{n}_1 + \frac{1}{\lambda_2}\boldsymbol{N}_2 \otimes \boldsymbol{n}_2, \tag{21}$$

the substitution of (20) and (21) into the expression for the velocity gradient $\boldsymbol{L} = \dot{\boldsymbol{F}} \cdot \boldsymbol{F}^{-1}$ gives

$$\boldsymbol{L} = \frac{\dot{\lambda}_1}{\lambda_1}\boldsymbol{n}_1 \otimes \boldsymbol{n}_1 + \frac{\dot{\lambda}_2}{\lambda_2}\boldsymbol{n}_2 \otimes \boldsymbol{n}_2 + \omega(\boldsymbol{n}_1 \otimes \boldsymbol{n}_2 - \boldsymbol{n}_2 \otimes \boldsymbol{n}_1) - \Omega\left(\frac{\lambda_1}{\lambda_2}\boldsymbol{n}_1 \otimes \boldsymbol{n}_2 - \frac{\lambda_2}{\lambda_1}\boldsymbol{n}_2 \otimes \boldsymbol{n}_1\right). \tag{22}$$

Its symmetric and antisymmetric parts are the rate of deformation tensor

$$\boldsymbol{D} = \frac{\dot{\lambda}_1}{\lambda_1}\boldsymbol{n}_1 \otimes \boldsymbol{n}_1 + \frac{\dot{\lambda}_2}{\lambda_2}\boldsymbol{n}_2 \otimes \boldsymbol{n}_2 + \Omega\,\frac{\lambda_2^2 - \lambda_1^2}{2\lambda_1\lambda_2}(\boldsymbol{n}_1 \otimes \boldsymbol{n}_2 + \boldsymbol{n}_2 \otimes \boldsymbol{n}_1), \tag{23}$$

and the spin tensor

$$\boldsymbol{W} = \left(\omega - \Omega\,\frac{\lambda_1^2 + \lambda_2^2}{2\lambda_1\lambda_2}\right)(\boldsymbol{n}_1 \otimes \boldsymbol{n}_2 - \boldsymbol{n}_2 \otimes \boldsymbol{n}_1). \tag{24}$$

The components of the rate of deformation and spin tensors, on the current axes $\boldsymbol{n}_i$, are

$$D_{11} = \frac{\dot{\lambda}_1}{\lambda_1}, \quad D_{22} = \frac{\dot{\lambda}_2}{\lambda_2}, \quad D_{12} = \Omega\,\frac{\lambda_2^2 - \lambda_1^2}{2\lambda_1\lambda_2} \tag{25}$$

and

$$W = \omega - \Omega\,\frac{\lambda_1^2 + \lambda_2^2}{2\lambda_1\lambda_2}, \tag{26}$$

so that

$$\boldsymbol{D} = \sum_{i,j=1}^{2} = D_{ij}\, \boldsymbol{n}_i \otimes \boldsymbol{n}_j, \quad \boldsymbol{W} = W(\boldsymbol{n}_1 \otimes \boldsymbol{n}_2 - \boldsymbol{n}_2 \otimes \boldsymbol{n}_1). \tag{27}$$

3.2. ***Rate-type constitutive equations.*** A comprehensive treatment of the three-dimensional rate-type (incremental) elasticity can be found in Haughton and Ogden [1978] and Ogden [1984]. Some of the results in this section can be deduced from this theory directly, but some require a separate analysis. The rate of the Kirchhoff stress $\boldsymbol{\tau} = \tau_1 \boldsymbol{n}_1 \otimes \boldsymbol{n}_1 + \tau_2\, \boldsymbol{n}_2 \otimes \boldsymbol{n}_2$ is

$$\dot{\boldsymbol{\tau}} = \dot{\tau}_1\, \boldsymbol{n}_1 \otimes \boldsymbol{n}_1 + \dot{\tau}_2\, \boldsymbol{n}_2 \otimes \boldsymbol{n}_2 - \omega(\tau_1 - \tau_2)(\boldsymbol{n}_1 \otimes \boldsymbol{n}_2 + \boldsymbol{n}_2 \otimes \boldsymbol{n}_1), \tag{28}$$

from which we conclude that

$$\dot{\tau}_{12} = \dot{\tau}_{21} = -\omega(\tau_1 - \tau_2). \tag{29}$$

Observing, from (25) and (26), that

$$\omega = W - \frac{\lambda_1^2 + \lambda_2^2}{\lambda_1^2 - \lambda_2^2}\, D_{12}, \tag{30}$$

the expression (29) can be rewritten as

$$\overset{\circ}{\tau}_{12} = (\tau_1 - \tau_2)\, \frac{\lambda_1^2 + \lambda_2^2}{\lambda_1^2 - \lambda_2^2}\, D_{12}. \tag{31}$$

The Jaumann rate $\overset{\circ}{\boldsymbol{\tau}}$ is defined by $\overset{\circ}{\boldsymbol{\tau}} = \dot{\boldsymbol{\tau}} - \boldsymbol{W}\cdot\boldsymbol{\tau} + \boldsymbol{\tau}\cdot\boldsymbol{W}$. Since, instantaneously, on the axes $\boldsymbol{n}_i$, the shear stress $\tau_{12} = 0$, the components of the Jaumann rate of the Kirchhoff stress are

$$\overset{\circ}{\tau}_{11} = \dot{\tau}_{11}, \quad \overset{\circ}{\tau}_{22} = \dot{\tau}_{22}, \quad \overset{\circ}{\tau}_{12} = \dot{\tau}_{12} + W(\tau_1 - \tau_2), \tag{32}$$

which was used in the transition from (29) to (31).

Having regard to constitutive expressions (4), the rates of the Kirchhoff stress components are

$$\dot{\tau}_1 = \left(\frac{\partial\phi}{\partial\lambda_1} + \lambda_1\,\frac{\partial^2\phi}{\partial\lambda_1^2}\right)\dot{\lambda}_1 + \left(\lambda_1\,\frac{\partial^2\phi}{\partial\lambda_1\partial\lambda_2}\right)\dot{\lambda}_2, \quad \dot{\tau}_2 = \left(\lambda_2\,\frac{\partial^2\phi}{\partial\lambda_1\partial\lambda_2}\right)\dot{\lambda}_1 + \left(\frac{\partial\phi}{\partial\lambda_2} + \lambda_2\,\frac{\partial^2\phi}{\partial\lambda_2^2}\right)\dot{\lambda}_2. \tag{33}$$

Consequently, by using (25), the objective rate-type constitutive expressions for elastic deformations of a thin membrane are

$$\begin{aligned}
\overset{\circ}{\tau}_{11} &= \lambda_1\left(\frac{\partial\phi}{\partial\lambda_1} + \lambda_1\,\frac{\partial^2\phi}{\partial\lambda_1^2}\right)D_{11} + \left(\lambda_1\lambda_2\,\frac{\partial^2\phi}{\partial\lambda_1\partial\lambda_2}\right)D_{22},\\
\overset{\circ}{\tau}_{22} &= \left(\lambda_1\lambda_2\,\frac{\partial^2\phi}{\partial\lambda_1\partial\lambda_2}\right)D_{11} + \lambda_2\left(\frac{\partial\phi}{\partial\lambda_2} + \lambda_2\,\frac{\partial^2\phi}{\partial\lambda_2^2}\right)D_{22},\\
\overset{\circ}{\tau}_{12} &= \left(\lambda_1\,\frac{\partial\phi}{\partial\lambda_1} - \lambda_2\,\frac{\partial\phi}{\partial\lambda_2}\right)\frac{\lambda_1^2 + \lambda_2^2}{\lambda_1^2 - \lambda_2^2}\, D_{12}.
\end{aligned} \tag{34}$$

3.3. ***Elastic moduli tensor.*** The tensor representation of the constitutive expressions (34) is

$$\overset{\circ}{\boldsymbol{\tau}} = \boldsymbol{\mathcal{L}} : \boldsymbol{D}, \quad \overset{\circ}{\tau}_{ij} = \mathcal{L}_{ijkl} D_{kl}, \tag{35}$$

where the components of the fourth-order tensor of the elastic moduli

$$\begin{aligned}
\boldsymbol{\mathcal{L}} = \mathcal{L}_{1111}\, &\boldsymbol{n}_1\otimes\boldsymbol{n}_1\otimes\boldsymbol{n}_1\otimes\boldsymbol{n}_1 + \mathcal{L}_{2222}\,\boldsymbol{n}_2\otimes\boldsymbol{n}_2\otimes\boldsymbol{n}_2\otimes\boldsymbol{n}_2\\
&+ \mathcal{L}_{1122}\,(\boldsymbol{n}_1\otimes\boldsymbol{n}_1\otimes\boldsymbol{n}_2\otimes\boldsymbol{n}_2 + \boldsymbol{n}_2\otimes\boldsymbol{n}_2\otimes\boldsymbol{n}_1\otimes\boldsymbol{n}_1)\\
&+ \mathcal{L}_{1212}\,(\boldsymbol{n}_1\otimes\boldsymbol{n}_2 + \boldsymbol{n}_2\otimes\boldsymbol{n}_1)\otimes(\boldsymbol{n}_1\otimes\boldsymbol{n}_2 + \boldsymbol{n}_2\otimes\boldsymbol{n}_1)
\end{aligned} \tag{36}$$

are

$$\begin{aligned}\mathcal{L}_{1111} &= \lambda_1\left(\frac{\partial\phi}{\partial\lambda_1}+\lambda_1\,\frac{\partial^2\phi}{\partial\lambda_1^2}\right), \quad \mathcal{L}_{2222}=\lambda_2\left(\frac{\partial\phi}{\partial\lambda_2}+\lambda_2\,\frac{\partial^2\phi}{\partial\lambda_2^2}\right),\\ \mathcal{L}_{1122} &= \lambda_1\lambda_2\,\frac{\partial^2\phi}{\partial\lambda_1\partial\lambda_2}, \quad \mathcal{L}_{1212}=\frac{1}{2}\left(\lambda_1\,\frac{\partial\phi}{\partial\lambda_1}-\lambda_2\,\frac{\partial\phi}{\partial\lambda_2}\right)\frac{\lambda_1^2+\lambda_2^2}{\lambda_1^2-\lambda_2^2},\end{aligned} \tag{37}$$

with the obvious symmetry properties

$$\mathcal{L}_{1122}=\mathcal{L}_{2211}, \quad \mathcal{L}_{1212}=\mathcal{L}_{2121}=\mathcal{L}_{1221}=\mathcal{L}_{2112}. \tag{38}$$

The components of the tensor $\boldsymbol{\mathcal{L}}$, as well as the components of the tensors $\mathring{\boldsymbol{\tau}}$ and $\boldsymbol{D}$, relative to the fixed base vectors, can be easily obtained by the tensor transformation rules. An alternative, direct derivation is presented in section 3.4.

If the strain energy is given by (6), the elastic moduli become

$$\begin{aligned}\mathcal{L}_{1111} &= \mathcal{L}_{2222}=\kappa\lambda_1\lambda_2(2\lambda_1\lambda_2-1)+\mu\,\frac{\lambda_1^2+\lambda_2^2}{2\lambda_1\lambda_2},\\ \mathcal{L}_{1122} &= \kappa\lambda_1\lambda_2(2\lambda_1\lambda_2-1)-\mu\,\frac{\lambda_1^2+\lambda_2^2}{2\lambda_1\lambda_2}, \quad \mathcal{L}_{1212}=\mu\,\frac{\lambda_1^2+\lambda_2^2}{2\lambda_1\lambda_2}.\end{aligned} \tag{39}$$

3.4. ***Elastic compliances tensor.*** The inverted form of (35), giving the rate of deformation tensor in terms of the Jaumann rate of the Kirchhoff stress, is

$$D_{ij}=\mathcal{M}_{ijkl}\mathring{\tau}_{kl}. \tag{40}$$

The nonvanishing components of the elastic compliances tensor are

$$\mathcal{M}_{1111}=\frac{\mathcal{L}_{2222}}{\Delta}, \quad \mathcal{M}_{2222}=\frac{\mathcal{L}_{1111}}{\Delta}, \quad \mathcal{M}_{1122}=\mathcal{M}_{2211}=-\frac{\mathcal{L}_{1122}}{\Delta}, \quad \mathcal{M}_{1212}=\frac{1}{4\mathcal{L}_{1212}}, \tag{41}$$

where

$$\Delta=\mathcal{L}_{1111}\mathcal{L}_{2222}-\mathcal{L}_{1212}^2. \tag{42}$$

If the strain energy is given by the Evans–Skalak form (6), the determinant Δ is

$$\Delta=2\kappa\mu(2\lambda_1\lambda_2-1)(\lambda_1^2+\lambda_2^2), \tag{43}$$

while the elastic moduli $\mathcal{L}_{ijkl}$ (on the principal axes of stress) are given by (39).

3.5. ***Rate-type elasticity on arbitrary axes.*** The objective rate form of the constitutive expression (13) can be obtained directly by applying to it the Jaumann derivative. Since $\mathring{\boldsymbol{B}}=\boldsymbol{B}\cdot\boldsymbol{D}+\boldsymbol{D}\cdot\boldsymbol{B}$, $\dot{I}_B=2\boldsymbol{B}:\boldsymbol{D}$, and $\dot{II}_B=2II_B\,\mathrm{tr}\,\boldsymbol{D}$, it readily follows that

$$\mathring{\tau}_{ij}=\mathcal{L}_{ijkl}D_{kl}, \tag{44}$$

where

$$\mathcal{L}_{ijkl}=c_1\delta_{ij}\delta_{kl}+c_2(\delta_{ij}B_{kl}+B_{ij}\delta_{kl})+c_3B_{ij}B_{kl}+c_4(\delta_{ik}B_{jl}+B_{ik}\delta_{jl}+\delta_{jk}B_{il}+B_{jk}\delta_{il}) \tag{45}$$

are the components of the fourth-order tensor of elastic moduli with respect to arbitrary orthogonal axes, and

$$c_1 = 4II_B\left(\frac{\partial\phi}{\partial II_B} + II_B\,\frac{\partial^2\phi}{\partial II_B^2}\right), \quad c_2 = 4II_B\,\frac{\partial^2\phi}{\partial I_B \partial II_B}, \quad c_3 = 4\,\frac{\partial^2\phi}{\partial I_B^2}, \quad c_4 = \frac{\partial\phi}{\partial I_B}. \tag{46}$$

If the strain energy is expressed in terms of the invariants α and β, rather than I_B and II_B, the parameters c_i become

$$\begin{aligned} c_1 &= (1+\alpha)^2\,\frac{\partial^2\phi}{\partial\alpha^2} + (1+\beta)^2\,\frac{\partial^2\phi}{\partial\beta^2} - 2(1+\alpha)(1+\beta)\,\frac{\partial^2\phi}{\partial\alpha\partial\beta} + (1+\alpha)\,\frac{\partial\phi}{\partial\alpha} + (1+\beta)\,\frac{\partial\phi}{\partial\beta},\\ c_2 &= \frac{\partial^2\phi}{\partial\alpha\partial\beta} - \frac{1}{1+\alpha}\left[(1+\beta)\,\frac{\partial^2\phi}{\partial\beta^2} + \frac{\partial\phi}{\partial\beta}\right],\\ c_3 &= \frac{1}{(1+\alpha)^2}\,\frac{\partial^2\phi}{\partial\beta^2}, \quad c_4 = \frac{1}{2(1+\alpha)}\,\frac{\partial\phi}{\partial\beta}. \end{aligned} \tag{47}$$

In the case of the Evans–Skalak strain energy, this simplifies to

$$c_1 = \kappa(1+\alpha)(1+2\alpha) + \mu(1+\beta), \quad c_2 = -\mu(1+\alpha)^{-1}, \quad c_3 = 0, \quad c_4 = -c_2/2. \tag{48}$$

If the coordinate axes are parallel to the principal axes of $\boldsymbol{B}$, (45) with (48) reduces to (39). In this case, $\mathcal{L}_{1111} = \mathcal{L}_{2222} = c_1$, $\mathcal{L}_{1122} = c_1 - 2\mathcal{L}_{1212}$, and $\mathcal{L}_{1212} = \mu(1+\beta)$.

4. Isoareal membranes

As discussed in the introduction, the areal modulus of the red blood cell is several orders of magnitude higher than the shear modulus, and for some applications it may be appropriate to model the membrane as infinitely stiff to the area change ($\kappa \to \infty$, $\nu = 1$). In this case, there is a deformation constraint $\lambda_1\lambda_2 - 1 = 0$, so that $D_{11} + D_{22} = 0$. The rate of work is $\dot\phi = (\sigma_1 - \sigma_2)\dot\lambda_1/\lambda_1$, and by differentiation $\phi = \phi(\lambda_1)$ with respect to time, there follows

$$\sigma_1 - \sigma_2 = \lambda_1\,\frac{\mathrm{d}\phi}{\mathrm{d}\lambda_1}. \tag{49}$$

The average normal stress is undetermined by the constitutive analysis, and denoting it by $-p_0$, we can write

$$\sigma_1 + \sigma_2 = -2p_0. \tag{50}$$

Therefore, the principal stresses are

$$\sigma_1 = \frac{1}{2}\,\lambda_1\,\frac{\mathrm{d}\phi}{\mathrm{d}\lambda_1} - p_0, \quad \sigma_2 = -\frac{1}{2}\,\lambda_1\,\frac{\mathrm{d}\phi}{\mathrm{d}\lambda_1} - p_0. \tag{51}$$

The function $p_0 = p_0(x_1, x_2)$ is determined by solving a specific boundary-value problem under consideration. If the strain energy is

$$\phi = \mu\beta = \mu\big(\tfrac{1}{2}(\lambda_1^2 + \lambda_1^{-2}) - 1\big), \tag{52}$$

the stresses become

$$\sigma_1 = \tfrac{1}{2}\,\mu(\lambda_1^2 - \lambda_1^{-2}) - p_0, \quad \sigma_2 = -\tfrac{1}{2}\,\mu(\lambda_1^2 - \lambda_1^{-2}) - p_0. \tag{53}$$

4.1. ***Rate theory for isoareal membranes.*** For isoareal membranes the Cauchy and Kirchhoff stress are equal to each other, so that (31) becomes

$$\overset{\circ}{\sigma}_{12} = \lambda_1 \frac{\mathrm{d}\phi}{\mathrm{d}\lambda_1} \frac{\lambda_1^2 + \lambda_1^{-2}}{\lambda_1^2 - \lambda_1^{-2}} D_{12}. \tag{54}$$

Furthermore, by differentiating (50) and (51),

$$\overset{\circ}{\sigma}_{11} + \overset{\circ}{\sigma}_{22} = -2\dot{p}_0, \quad \overset{\circ}{\sigma}_{11} - \overset{\circ}{\sigma}_{22} = \left(\lambda_1 \frac{\mathrm{d}\phi}{\mathrm{d}\lambda_1} + \lambda_1^2 \frac{\mathrm{d}^2\phi}{\mathrm{d}\lambda_1^2}\right) D_{11}. \tag{55}$$

If ϕ is given by (52), the rate-type constitutive expressions, on the principal stress axes, become

$$\overset{\circ}{\sigma}_{ij} = -\dot{p}_0 \delta_{ij} + \mu(\lambda_1^2 + \lambda_1^{-2}) D_{ij}. \tag{56}$$

4.2. ***Expressions on arbitrary axes.*** The strain energy of an isotropic isoareal membrane is a function of only one strain of stretch invariant, e.g., $\phi = \phi(I_B)$. Its rate is

$$\dot{\phi} = 2 \frac{\mathrm{d}\phi}{\mathrm{d}I_B} B'_{ij} D_{ij}, \tag{57}$$

because $\dot{I}_B = 2B'_{ij} D_{ij}$, the rate of deformation being deviatoric, so that $B_{ij} D_{ij} = B'_{ij} D_{ij}$. Since the rate of work is $\dot{\phi} = \sigma_{ij} D_{ij} = \sigma'_{ij} D_{ij}$, again because $D_{kk} = 0$, the comparison with (57) gives

$$\sigma'_{ij} = 2 \frac{\mathrm{d}\phi}{\mathrm{d}I_B} B'_{ij}, \tag{58}$$

and thus the stress response is

$$\sigma_{ij} = -p_0 \delta_{ij} + 2 \frac{\mathrm{d}\phi}{\mathrm{d}I_B} B'_{ij}, \tag{59}$$

To derive the rate-type form of (59), it is convenient to first rewrite (59) as

$$\sigma_{ij} = -\left(p_0 + I_B \frac{\mathrm{d}\phi}{\mathrm{d}I_B}\right) \delta_{ij} + 2 \frac{\mathrm{d}\phi}{\mathrm{d}I_B} B_{ij}. \tag{60}$$

The application of the Jaumann derivative to (60), having regard to $\dot{I}_B = 2B_{ij} D_{ij}$ and $\overset{\circ}{B}_{ij} = B_{ik} D_{kj} + D_{ik} B_{kj}$, then yields

$$\overset{\circ}{\sigma}_{ij} = -\dot{p}_0 \, \delta_{ij} + \left[c_0 \delta_{ij} B_{kl} + c_3 B_{ij} B_{kl} + c_4 (\delta_{ik} B_{jl} + B_{ik} \delta_{jl} + \delta_{jk} B_{il} + B_{jk} \delta_{il})\right] D_{kl}. \tag{61}$$

The parameters c_0, c_2, and c_4 are

$$c_0 = -2\left(\frac{\mathrm{d}\phi}{\mathrm{d}I_B} + I_B \frac{\mathrm{d}^2\phi}{\mathrm{d}I_B^2}\right), \quad c_3 = 4 \frac{\mathrm{d}^2\phi}{\mathrm{d}I_B^2}, \quad c_4 = \frac{\mathrm{d}\phi}{\mathrm{d}I_B}. \tag{62}$$

If the strain energy is of the Evans–Skalak form

$$\phi = \mu\beta = \mu\left(\tfrac{1}{2} I_B - 1\right), \tag{63}$$

the parameters (62) reduce to $c_0 = -\mu$, $c_3 = 0$, and $c_4 = \mu/2$, while (61) simplifies to

$$\overset{\circ}{\sigma}_{ij} = -\dot{p}_0 \, \delta_{ij} + \tfrac{1}{2} \mu \left(\delta_{ik} B_{jl} + B_{ik} \delta_{jl} + \delta_{jk} B_{il} + B_{jk} \delta_{il} - 2\delta_{ij} B_{kl}\right) D_{kl}. \tag{64}$$

When coordinate axes coincident with the principal directions of $\boldsymbol{B}$ are used, (64) reduces to (56).

5. Rate theory of viscoelasticity

To study the time-dependent aspiration of an erythrocyte cell membrane into a micropipette [Evans and Hochmuth 1976], or the cell recovery upon its deformation by optical tweezers [Dao et al. 2003; Mills et al. 2004], viscoelastic constitutive models have been employed. In this section, we extend the constitutive models their considered by constructing the objective rate type viscoelastic constitutive equations of both Maxwell and Kelvin type, based on an arbitrary isotropic strain energy function, and its special Evans–Skalak form. For an integral type of viscoelastic constitutive equations for thin membranes, we refer to [Tözeren et al. 1982; Wineman 2007].

5.1. ***Maxwell viscoelastic model.*** In the Maxwell viscoelastic model, the rate of deformation is assumed to be the sum of the elastic and viscous parts, i.e.,

$$D_{ij} = D^{\mathrm{e}}_{ij} + D^{\mathrm{v}}_{ij}. \tag{65}$$

The elastic part is related to the objective Jaumann rate of the Kirchhoff stress by the constitutive expression (36), in which $\phi = \phi^{\mathrm{e}}(I^{\mathrm{e}}_B, II^{\mathrm{e}}_B)$, so that

$$\mathring{\tau}_{ij} = \mathcal{L}^{\mathrm{e}}_{ijkl} D^{\mathrm{e}}_{kl}, \quad D^{\mathrm{e}}_{ij} = \mathcal{M}^{\mathrm{e}}_{ijkl} \mathring{\tau}_{kl}. \tag{66}$$

The viscous part is assumed to be deviatoric and governed by the Newton viscosity law

$$D^{\mathrm{v}}_{ij} = \frac{1}{2\eta}\,\sigma'_{ij}, \quad \sigma'_{ij} = \sigma_{ij} - \frac{1}{2}\,\sigma_{kk}\delta_{ij}. \tag{67}$$

The coefficient of membrane viscosity η is assumed to be constant, although it could vary with the amount of stretching [Evans and Hochmuth 1976]. The experimentally reported values for η are in the range between 0.6 and 2.7 μN·s/m, being strongly influenced by the concentration of hemoglobin in the cytoplasm, which binds to the membrane of the cell [Hochmuth 1987; Hochmuth and Waugh 1987]. By substituting (66) and (67) into (65), there follows

$$\mathring{\tau}_{ij} = \mathcal{L}^{\mathrm{e}}_{ijkl}\left(D_{kl} - \frac{1}{2\eta}\,\sigma'_{kl}\right), \quad D_{ij} = \mathcal{M}^{\mathrm{e}}_{ijkl}\mathring{\tau}_{kl} + \frac{1}{2\eta}\,\sigma'_{ij}. \tag{68}$$

When expressed on the principal axes of the current stress, $\mathcal{L}^{\mathrm{e}}_{ijkl}$ is given by (37), and (68) becomes

$$\mathring{\tau}_{ij} = \mathcal{L}^{\mathrm{e}}_{ijkl} D_{kl} - \frac{1}{4\eta}(\mathcal{L}^{\mathrm{e}}_{ij11} - \mathcal{L}^{\mathrm{e}}_{ij22})(\sigma_1 - \sigma_2). \tag{69}$$

If the elastic response is governed by the Evans–Skalak form of the elastic strain energy, the elastic moduli $\mathcal{L}^{\mathrm{e}}_{ijkl}$ are given by (39), in which λ_1 and λ_2 are replaced by λ^{e}_1 and λ^{e}_2. Since the viscous part of the rate of deformation is assumed to be deviatoric, the membrane area change is entirely due to elastic deformation, so $\lambda_1\lambda_2 = \lambda_1^{\mathrm{e}}\lambda_2^{\mathrm{e}}$. Consequently, from Equations (10)–(11),

$$
\begin{gathered}
\lambda_1^{\mathrm{e}}\lambda_2^{\mathrm{e}} = \frac{1}{2}\left[1+\left(1+2\,\frac{\tau_1+\tau_2}{\kappa}\right)^{1/2}\right] = 1+\frac{\sigma_1+\sigma_2}{2\kappa},\\
\frac{\lambda_1^{\mathrm{e}}}{\lambda_2^{\mathrm{e}}} = \frac{\tau_1-\tau_2}{2\mu}+\left[1+\left(\frac{\tau_1-\tau_2}{2\mu}\right)^2\right]^{1/2}, \quad \frac{\lambda_2^{\mathrm{e}}}{\lambda_1^{\mathrm{e}}} = -\frac{\tau_1-\tau_2}{2\mu}+\left[1+\left(\frac{\tau_1-\tau_2}{2\mu}\right)^2\right]^{1/2},
\end{gathered}
\tag{70}
$$

where $\tau_1 \pm \tau_2$ is given in terms of stress by (11). This specifies the components of the elastic moduli tensor $\mathcal{L}^{\mathrm{e}}_{ijkl}$ in terms of the current stress state, as needed in the incremental procedure of solving the path-dependent viscoelastic boundary value problems.

If the membrane is modeled as an isoareal membrane, by using (56), we obtain (on the current principal axes of stress)

$$
\mathring{\sigma}_{ij} = -\dot{p}_0\delta_{ij} + 2\mu\left[1+\left(\frac{\sigma_1-\sigma_2}{2\mu}\right)^2\right]^{1/2}\left(D_{ij}-\frac{1}{2\eta}\,\sigma'_{ij}\right) \tag{71}
$$

and

$$
D'_{ij} = \frac{1}{2\mu}\left[1+\left(\frac{\sigma_1-\sigma_2}{2\mu}\right)^2\right]^{-1/2}\mathring{\sigma}'_{ij} + \frac{1}{2\eta}\,\sigma'_{ij}. \tag{72}
$$

5.2. *Kelvin viscoelastic model.* An alternative, Kelvin-type viscoelastic model can be constructed by assuming that the deviatoric part of stress is the sum of the elastic and viscous contributions, $\sigma'_{ij} = \sigma'^{\mathrm{e}}_{ij} + \sigma'^{\mathrm{v}}_{ij}$. By using the elastic constitutive expression (16) and the Newton viscosity law, this gives

$$
\sigma'_{ij} = \frac{1}{\det \boldsymbol{B}}\,\frac{\partial\phi}{\partial\beta}\,B'_{ij} + 2\eta D'_{ij}. \tag{73}
$$

The average normal stress is assumed to be due to elastic deformation only, so that, from (16),

$$
\sigma_{kk} = 2\,\frac{\partial\phi}{\partial\alpha}. \tag{74}
$$

The total stress is

$$
\sigma_{ij} = \frac{\partial\phi}{\partial\alpha}\,\delta_{ij} + \frac{1}{\det \boldsymbol{B}}\,\frac{\partial\phi}{\partial\beta}\,B'_{ij} + 2\eta D'_{ij}. \tag{75}
$$

When expressed on the principal stress axes, this is

$$
\begin{aligned}
\sigma_1 &= \frac{\partial\phi}{\partial\alpha} + \frac{1}{2}\,\frac{\partial\phi}{\partial\beta}\,(\lambda_2^{-2}-\lambda_1^{-2}) + \eta\left(\frac{\dot\lambda_1}{\lambda_1}-\frac{\dot\lambda_2}{\lambda_2}\right),\\
\sigma_2 &= \frac{\partial\phi}{\partial\alpha} + \frac{1}{2}\,\frac{\partial\phi}{\partial\beta}\,(\lambda_1^{-2}-\lambda_2^{-2}) + \eta\left(\frac{\dot\lambda_2}{\lambda_2}-\frac{\dot\lambda_1}{\lambda_1}\right).
\end{aligned}
\tag{76}
$$

A version of (76), corresponding to an isoareal Evans–Skalak model with $\phi = \mu\beta$, was used by [Mills et al. 2004] in their finite-element evaluation of cell stretching by optical tweezers.

We next determine the expressions for the components of the rate of deformation tensor, which is particularly important if the Kelvin model is combined in series with the Maxwell model to obtain a more complex or capable viscoelastic model. The deviatoric part of the rate of deformation follows from

(73) as

$$D'_{ij} = \frac{1}{2\eta}\left(\sigma'_{ij} - \frac{1}{\det \boldsymbol{B}}\,\frac{\partial\phi}{\partial\beta}\,B'_{ij}\right). \tag{77}$$

For a prescribed history of stress, it remains to determine the rate of the area change, i.e., $D_{kk} = \mathrm{d}(\ln \mathrm{d}A)/\mathrm{d}t$. This can be accomplished by differentiating (74), which gives

$$\dot{\sigma}_{kk} = 2\left(\frac{\partial^2\phi}{\partial\alpha^2}\,\dot{\alpha} + \frac{\partial^2\phi}{\partial\alpha\partial\beta}\,\dot{\beta}\right). \tag{78}$$

It can be readily shown that

$$\dot{\alpha} = II_B^{1/2} D_{kk}, \quad \dot{\beta} = II_B^{-1/2}\,B'_{ij} D_{ij}, \tag{79}$$

so that the substitution into (78) yields

$$\dot{\sigma}_{kk} = 2\,\frac{\partial^2\phi}{\partial\alpha^2}\,II_B^{1/2} D_{kk} + 2\,\frac{\partial^2\phi}{\partial\alpha\partial\beta}\,II_B^{-1/2} B'_{ij} D'_{ij}. \tag{80}$$

The trace product $B'_{ij} D'_{ij}$ can be eliminated from (80) by using (77), with the result

$$B'_{ij} D'_{ij} = \frac{1}{\eta}\left(\tfrac{1}{2}\,\sigma_{ij} B'_{ij} - \beta(\beta+2)\,\frac{\partial\phi}{\partial\beta}\right). \tag{81}$$

In the derivation, the Frobenius norm of $\boldsymbol{B}'$ is expressed as $B'_{ij} B'_{ij} = \frac{1}{2} I_B^2 - 2II_B$. The substitution of (81) into (80) gives the desired expression for D_{kk} in terms of the current stress and its rate. This is

$$D_{kk} = \frac{II_B^{-1}}{2\partial^2\phi/\partial\alpha^2}\left[II_B^{1/2}\dot{\sigma}_{kk} - \frac{1}{\eta}\,\frac{\partial^2\phi}{\partial\alpha\partial\beta}\left(\sigma_{ij} B'_{ij} - 2\beta(\beta+2)\,\frac{\partial\phi}{\partial\beta}\right)\right]. \tag{82}$$

If the strain energy is given by the Evans–Skalak form $\phi = \frac{1}{2}\kappa\alpha^2 + \mu\beta$, (77) and (82) reduce to

$$D'_{ij} = \frac{1}{2\eta}\left(\sigma'_{ij} - \frac{\mu}{\det \boldsymbol{B}}, B'_{ij}\right), \quad D_{kk} = \frac{1}{(\det \boldsymbol{B})^{1/2}}\,\frac{\dot{\sigma}_{kk}}{2\kappa}. \tag{83}$$

On the principal stress axes, this becomes

$$D_1 - D_2 = \frac{1}{2\eta}\big(\sigma_1 - \sigma_2 + \mu(\lambda_1^{-2} - \lambda_2^{-2})\big), \quad D_1 + D_2 = \frac{1}{2\kappa\lambda_1\lambda_2}\,(\dot{\sigma}_1 + \dot{\sigma}_2). \tag{84}$$

If the membrane is modeled as isoareal, with $\phi = \phi(\beta)$, then

$$D'_{ij} = \frac{1}{2\eta}\left(\sigma'_{ij} - \frac{\mathrm{d}\phi}{\mathrm{d}\beta}\,B'_{ij}\right), \quad D_{kk} = 0. \tag{85}$$

In this case, the average normal stress $\sigma_{kk}/2 = -p_0$ is unspecified by the constitutive analysis.

6. Conclusion

We have presented in this paper the rate-type constitutive analysis of erythrocyte membrane undergoing large elastic and viscoelastic deformations. The results are obtained for an arbitrary isotropic strain energy function, and for its special Evans–Skalak form, commonly used to study the mechanical response of red blood cells. The explicit representation of the fourth-order tensor of elastic moduli, which relates the objective rate of the Kirchhoff stress to the rate of the deformation tensor, is derived with respect to the principal axes of stress, and an arbitrary set of orthogonal axes, used as the background axes in the numerical treatment of the boundary-value problems. Since the areal modulus of the erythrocyte membrane is several orders of magnitude higher than the shear modulus, the rate-type equations are also derived for an isoareal membrane. The viscoelastic constitutive equations are then derived by adopting either the Maxwell or the Kelvin viscoelastic model, i.e., by adopting the additive decomposition of the rate of deformation, or the stress tensor, into its elastic and viscous parts. More involved viscoelastic models can also be considered, such as those used in [Lubarda and Marzani 2009] in the context of small strains. The obtained constitutive equations may be readily implemented in the incremental (numerical) treatments of the path-dependent boundary-value problems, such as those associated with large deformation and shape recovery of an erythrocyte passing through and exiting from narrow capillaries [Pozrikidis 2003], or excessive aspiration of the cell membrane into micropipette, which may lead to membrane necking followed by formation of a vesicle [Peng et al. 2010]. Other potential application of derived equations is in a related study of the mechanics of nuclear membranes, bounding the nucleus of eukaryotic cells [Vaziri and Mofrad 2007].

The elastic properties of a healthy cell during its lifetime of about 120 days are essential for its main function to deliver the oxygen, while squeezing through capillaries. The degradation of elastic properties and the gradual loss of the membrane elasticity are therefore an important extension of the present work. From the mechanics point of view, this extension may proceed in the spirit of the rate-type theory of damage elasticity [Lubarda and Krajcinovic 1995], provided that the appropriate specification of the parameters which account for biochemical and physical processes of membrane damage and fatigue, and their evolution equations, are available. This, together with the description of active topological remodeling of the membrane structure during large deformations, is a challenging avenue for future research.

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Appendix A: Rate-type elasticity with respect to symmetric Piola–Kirchhoff stress

If the initial configuration is used as the reference configuration in the formulation and the solution of the boundary value problem, the rate-type constitutive expressions are needed with respect to the Lagrangian strain

$$\boldsymbol{E} = \tfrac{1}{2}\,(\lambda_1^2 - 1)\,\boldsymbol{N}_1 \otimes \boldsymbol{N}_1 + \tfrac{1}{2}\,(\lambda_2^2 - 1)\,\boldsymbol{N}_2 \otimes \boldsymbol{N}_2,$$

and its conjugate symmetric Piola–Kirchhoff stress $\boldsymbol{S}$. The components of the stress $\boldsymbol{S} = S_1 \boldsymbol{N}_1 \otimes \boldsymbol{N}_1 + S_2 \boldsymbol{N}_2 \otimes \boldsymbol{N}_2$ are

$$S_1 = \frac{1}{\lambda_1}\frac{\partial \phi}{\partial \lambda_1}, \qquad S_2 = \frac{1}{\lambda_2}\frac{\partial \phi}{\partial \lambda_2},$$

such that $\dot{\phi} = S_{ij}\dot{E}_{ij}$. Omitting details of the derivation, the corresponding rate-type constitutive expression is

$$\dot{S}_{ij} = \Lambda_{ijkl}\dot{E}_{kl},$$

where

$$\Lambda_{1111} = \frac{1}{\lambda_1^2}\left(\frac{\partial^2\phi}{\partial\lambda_1^2} - \frac{1}{\lambda_1}\frac{\partial\phi}{\partial\lambda_1}\right), \quad \Lambda_{2222} = \frac{1}{\lambda_2^2}\left(\frac{\partial^2\phi}{\partial\lambda_2^2} - \frac{1}{\lambda_2}\frac{\partial\phi}{\partial\lambda_2}\right),$$

$$\Lambda_{1122} = \frac{1}{\lambda_1\lambda_2}\frac{\partial^2\phi}{\partial\lambda_1\partial\lambda 2}, \quad \Lambda_{1212} = \frac{1}{\lambda_1^2-\lambda_2^2}\left(\frac{1}{\lambda_1}\frac{\partial\phi}{\partial\lambda_1} - \frac{1}{\lambda_2}\frac{\partial\phi}{\partial\lambda_2}\right),$$

with the obvious symmetries $\Lambda_{1212} = \Lambda_{2121} = \Lambda_{1221} = \Lambda_{2112}$ and $\Lambda_{1122} = \Lambda_{2211}$. The well-known relationship [Hill 1978] between the moduli $\mathcal{L}_{ijkl}$, appearing in the constitutive structure $\mathring{\tau}_{ij} = \mathcal{L}_{ijkl}D_{kl}$, and the moduli Λ_{ijkl}, appearing in the constitutive structure $\dot{S}_{ij} = \Lambda_{ijkl}\dot{E}_{kl}$, is

$$\mathcal{L}_{ijkl} = F_{im}F_{jn}\Lambda_{mnpq}F_{kp}F_{lq} + \frac{1}{2}(\tau_{ik}\delta_{jl} + \tau_{jk}\delta_{il} + \tau_{il}\delta_{jk} + \tau_{jl}\delta_{ik}).$$

If the strain energy is given by the Evans–Skalak form (6), the elastic moduli become

$$\Lambda_{1111} = \frac{1}{\lambda_1^4}\left(\kappa\lambda_1\lambda_2 + \mu\,\frac{3\lambda_2^2-\lambda_1^2}{2\lambda_1\lambda_2}\right), \quad \Lambda_{1122} = \frac{1}{\lambda_1^2\lambda_2^2}\left(\kappa\lambda_1\lambda_2(2\lambda_1\lambda_2-1) - \mu\,\frac{\lambda_1^2+\lambda_2^2}{2\lambda_1\lambda_2}\right),$$

$$\Lambda_{2222} = \frac{1}{\lambda_2^4}\left(\kappa\lambda_1\lambda_2 + \mu\,\frac{3\lambda_1^2-\lambda_2^2}{2\lambda_1\lambda_2}\right), \quad \Lambda_{1212} = \frac{1}{\lambda_1^2\lambda_2^2}\left(\kappa\lambda_1\lambda_2(1-\lambda_1\lambda_2) + \mu\,\frac{\lambda_1^2+\lambda_2^2}{2\lambda_1\lambda_2}\right).$$

Appendix B: Rate-type elasticity with respect to nominal stress

The nominal stress $\boldsymbol{P} = \boldsymbol{F}^{-1}\cdot\boldsymbol{\tau}$ appears in the variational formulation of the boundary value problems, when the differential equations of motion are expressed in terms of the displacement components. The rate of work is then $\dot{\phi} = P_1\dot{\lambda}_1 + P_2\dot{\lambda}_2$, and the components of $\boldsymbol{P} = P_1\boldsymbol{N}_1\otimes\boldsymbol{n}_1 + P_2\boldsymbol{N}_2\otimes\boldsymbol{n}_2$ are

$$P_1 = \frac{\partial\phi}{\partial\lambda_1}, \quad P_2 = \frac{\partial\phi}{\partial\lambda_2}.$$

Again omitting details of the derivation, it follows that $\dot{P}_{ji} = \hat{\Lambda}_{jilk}\dot{F}_{kl}$, where

$$\hat{\Lambda}_{1111} = \frac{\partial^2\phi}{\partial\lambda_1^2}, \quad \hat{\Lambda}_{2222} = \frac{\partial^2\phi}{\partial\lambda_2^2}, \quad \hat{\Lambda}_{1122} = \hat{\Lambda}_{2211} = \frac{\partial^2\phi}{\partial\lambda_1\partial\lambda_2},$$

$$\hat{\Lambda}_{1212} = \hat{\Lambda}_{2121} = \frac{1}{\lambda_1^2-\lambda_2^2}\left(\lambda_1\frac{\partial\phi}{\partial\lambda_1} - \lambda_2\frac{\partial\phi}{\partial\lambda_2}\right),$$

$$\hat{\Lambda}_{1221} = \hat{\Lambda}_{2112} = \frac{1}{\lambda_1^2-\lambda_2^2}\left(\lambda_2\frac{\partial\phi}{\partial\lambda_1} - \lambda_1\frac{\partial\phi}{\partial\lambda_2}\right).$$

Since $\dot{\boldsymbol{P}} = \dot{\boldsymbol{S}}\cdot\boldsymbol{F}^T + \boldsymbol{P}\cdot\boldsymbol{L}^T$, the relationship between the pseudomoduli $\hat{\Lambda}_{ijkl}$ and the moduli Λ_{ijkl} from Appendix A is $\hat{\Lambda}_{jilk} = \Lambda_{jmln}F_{im}F_{kn} + S_{jl}\delta_{ik}$.

If the strain energy is given by (6), the elastic pseudomoduli become

$$\hat{\Lambda}_{1111} = \kappa\lambda_2^2 + \mu\,\frac{\lambda_2}{\lambda_1^3}, \quad \hat{\Lambda}_{2222} = \kappa\lambda_1^2 + \mu\,\frac{\lambda_1}{\lambda_2^3},$$
$$\hat{\Lambda}_{1122} = \hat{\Lambda}_{2211} = \kappa(2\lambda_1\lambda_2 - 1) - \mu\,\frac{\lambda_1^2+\lambda_2^2}{2\lambda_1^2\lambda_2^2},$$
$$\hat{\Lambda}_{1212} = \hat{\Lambda}_{2121} = \mu\,\frac{1}{\lambda_1\lambda_2},$$
$$\hat{\Lambda}_{1221} = \hat{\Lambda}_{2112} = \kappa(1-\lambda_1\lambda_2) + \mu\,\frac{\lambda_1^2+\lambda_2^2}{2\lambda_1^2\lambda_2^2}.$$

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