



Elastic Reaction-Diffusion Solver Theory Manual Version 1.0

Last Updated: September 13, 2024

Contributors

Steven LaBelle(steven.labelle@utah.edu)

Steve Maas (steve.maas@utah.edu)

Dr. Jeffrey Weiss (jeff.weiss@utah.edu)

Contact address

Musculoskeletal Research Laboratories, University of Utah

72 S. Central Campus Drive, Room 2646

Salt Lake City, Utah

Website

MRL: <http://mrl.sci.utah.edu>

FEBio: <http://febio.org>

Forum

<https://forums.febio.org/index.php>

Acknowledgments

Development of the FEBio project is supported in part by a grant from the U.S. National Institutes of Health (R01GM083925) and NSF (OAC Award No. 2246911).



Contents

1	Continuum Mechanics of Elastic Reaction-Diffusion Analyses	3
1.1	Introduction	3
1.2	Elastic Reaction-Diffusion Analyses	3
1.2.1	Governing Equations	4
1.3	Chemical Reactions	5
1.3.1	Solutes	5
1.3.2	Mass Action Chemical Kinetics	6
1.3.3	Hill-Type Chemical Kinetics	6
1.4	Kinematic Growth	7
2	Linearization and Discretization of the Nonlinear FE Method	9
2.1	Weak Formulation for Elastic Reaction-Diffusion Materials	9
2.1.1	Linearization along $\Delta \mathbf{u}$	10
2.1.2	Linearization along Δc^γ	11
2.1.3	Linearization of External Virtual Work	11
2.1.4	Discretization	12
2.2	Linearization and Discretization of Kinematic Growth Materials	14
2.2.1	Linearization of Kinematic Growth materials along $\Delta \mathbf{u}$	14
2.2.2	Linearization of Kinematic Growth materials along Δc^γ	15
2.2.3	Discretization of Kinematic Growth materials	16
2.3	Tangents for Linearization and Discretization of Chemical Reactions	16
2.3.1	Tangents that arise during the linearization along $\Delta \mathbf{u}$	16
2.3.2	Tangents that arise during the linearization along Δc^γ	17
2.3.2.1	Tangents for mass action reaction kinetics	17
2.3.2.2	Tangents for Hill-type reaction kinetics	17
A	Tensor Calculus	18
A.1	Tensor dyadic products and contraction	18
A.2	Useful derivatives	18
	Bibliography	19

Chapter 1

Continuum Mechanics of Elastic Reaction-Diffusion Analyses

1.1 Introduction

This document details the theoretical background for the elastic reaction-diffusion solver plugin in FEBio. This plugin was developed to simplify aspects of the biphasic, triphasic, and multiphasic solvers in FEBio. The plugin was specifically motivated to model kinematic growth where growth is driven by the production of chemical species.

Chapter 1 details the theoretical background, assumptions, and governing equations for the physics solved by this plugin. Chapter 2 details the linearization and discretization of the governing equations for implementation in finite element code. An appendix is included that details mathematical prerequisites for the tensor algebra and calculus.

1.2 Elastic Reaction-Diffusion Analyses

This manual details the theory behind the elastic reaction-diffusion solver plugin for FEBio. This document builds on the main FEBio manual (in particular, the multiphasic module). Elastic reaction-diffusion materials represent a simplification of the biphasic-solute and multiphasic materials, where there is no explicitly modeled porous media or fluid phase. Solid mechanics and chemical reaction-diffusion kinetics are formulated to be nearly independent of each other aside from additional user-defined constitutive relations where implicit feedback between stress/strain and chemical processes are defined. This approach is justified when there is a large difference in time scales between displacements associated with solid mechanics and those associated with solute transport and chemical kinetics (a common assumption of kinematic growth theory [1]). Additionally, this approach introduces the assumption that the entire solid mass may turn over at each new time step, resulting in a new reference configuration defined by new extensive material properties (volume, shape, etc.) but constant intensive material properties (solid density, solute concentration and diffusivity, etc.).

Elastic reaction-diffusion analyses deviate from biphasic-solute and multiphasic analyses by assuming that solute concentrations c^α , fluxes j^α , diffusivities d^α , and kinetic parameters $k_f, k_r, \hat{\zeta}$ are tracked only in an intensive sense (i.e., volumetric changes due to strain do not affect the apparent concentration or related parameters). This treatment introduces implicit sources of extensive quantities such as mass and energy which either 1) have negligible contributions when

volumetric changes occur at a much longer time scale than chemical transport and kinetics, and/or 2) may be accounted for by implicit variables. Similar reasoning is used to justify the removal of porosity, hydraulic permeability, and fluid pressure (p). In the absence of fluid field variables, only isotropic diffusivity is introduced for the time being. One last distinction from biphasic and multiphasic materials is that standard thermodynamic conditions are assumed throughout the analysis (i.e., solutes behave ideally). Any deviations from standard conditions may be implicitly accounted for when specifying the average material and constitutive behaviors during an analysis. Charged species are similarly not accounted for in this framework.

This analysis should not be used when modeling electrochemistry or short-time mechanochemical phenomena (e.g. osmotic pressure, non-negligible solute volume fractions, convection). The user is responsible for ensuring that these assumptions are appropriate for a given problem.

1.2.1 Governing Equations

The governing equations adopted in this finite element implementation of neutral solute transport in porous media are based on the framework of mixture theory [3, 7]. The fundamental modeling assumptions adopted in this treatment are quasi-static conditions for momentum balance (negligible effects of inertia), intrinsic incompressibility of all constituents (invariant true densities), isothermal conditions, negligible volume fraction of solute relative to the solid and solvent, and negligible effects of solute viscosities (friction between similar and dissimilar solutes) relative to frictional interactions between solutes and the solid matrix. These assumptions are often made in studies of biological tissues and cells with the additional simplification that frictional interactions do not arise between the solutes and the solvent (in contrast to biphasic, biphasic-solute, triphasic, and multiphasic material formulations).

Chemical species are treated as solutes that do not contribute directly to the solid matrix properties (as solid bound molecules do in the multiphasic module). Non-diffusing species may be modeled by setting the diffusivity $d^\alpha \approx 0$ (as of now, numerical errors emerge when setting 0 diffusivity so low values are recommended instead). The motion of the solid matrix is described by the displacement vector \mathbf{u} while solute concentrations are described by c^α . The solid stress is described by the Cauchy stress tensor $\boldsymbol{\sigma}$. Under the established assumptions, it is common to solve the equations of motion associated with the solid mechanics and chemical kinetics separately before superimposing the chemical solution onto the mesh solved by the elastic equations of motion. The conservation of mass and linear momentum for the solid respectively reduce to

$$\frac{D\rho}{Dt} = \rho \operatorname{div} \mathbf{v}, \quad (1.2.1)$$

$$\rho \frac{D\mathbf{v}}{Dt} = \operatorname{div} \boldsymbol{\sigma} = \mathbf{0}. \quad (1.2.2)$$

The balance of mass and linear momentum for a solute α is given by

$$\frac{\partial \rho^\alpha}{\partial t} + \operatorname{div} (\rho^\alpha \mathbf{v}^\alpha) = \hat{\rho}^\alpha, \quad (1.2.3)$$

$$-\rho^\alpha \operatorname{grad} \tilde{\mu}^\alpha - \mathbf{f}^{\alpha\sigma} \cdot (\mathbf{v}^\alpha - \mathbf{v}^\sigma) - \mathbf{f}^{\alpha w} \cdot (\mathbf{v}^\alpha - \mathbf{v}^w) = \mathbf{0}. \quad (1.2.4)$$

where $\rho^\alpha = M^\alpha c^\alpha$ is the density, M^α is the (invariant) molecular weight, $\tilde{\mu}^\alpha$ is the mechanochemical potential, \mathbf{v}^α is the velocity, and $\mathbf{f}^{\alpha w}, \mathbf{f}^{\alpha\sigma}$ are the diffusive drag tensors representing momentum exchange via frictional interactions between a given solute and the solid (σ , not bolded) and implicit solvent (w) ([4]). We assume that diffusive drag terms between solutes are negligible.

The mechano-chemical potential is the sum of the mechanical and chemical potentials. The chemical potential μ^α represents the rate at which the mixture free energy changes with increasing mass of α . From classical physical chemistry, the general form of a constitutive relation for the chemical potential is $\mu^\alpha = \mu_0^\alpha(\theta) + (R\theta/M^\alpha) \ln a^\alpha$ [6], where R is the universal gas constant, θ is the absolute temperature, M^α is the molecular weight (invariant) and a^α is the activity of constituent α (a non-dimensional quantity); $\mu_0^\alpha(\theta)$ is the chemical potential at some arbitrary reference state, at a given temperature. As previously outlined in the FEBio manual (Biphasic-Solute governing equations), $a^\alpha = \gamma^\alpha c^\alpha / \kappa^\alpha c_0^\alpha = c^\alpha / \tilde{\kappa}^\alpha c_0^\alpha$ where c_0^α is the solute concentration in some standard reference state (an invariant, typically $c_0^\alpha = 1$ M), γ^α is the non-dimensional activity coefficient (deviation from ideal physico-chemical behavior [6]), and solubility due to the fraction of the pore space which is accessible to the solute. For the elastic-solute materials, we assume both ideal physico-chemical behavior, and no exclusion of the interstitial space of the porous solid matrix throughout the analysis (i.e., $\forall t \geq 0 \tilde{\kappa}^\alpha = \kappa^\alpha = \gamma^\alpha = 1$).

In an elastic solute material, the mechano-electrochemical potential of each solute is simplified to

$$\tilde{\mu}^\alpha = \mu_0^\alpha(\theta) + \frac{R\theta}{M^\alpha} \left(\ln \frac{c^\alpha}{c_0^\alpha} \right). \quad (1.2.5)$$

The gradient of the mechano-chemical potential gives

$$\begin{aligned} \text{grad } \tilde{\mu}^\alpha &= \frac{R\theta}{M^\alpha c^\alpha} \text{grad } c^\alpha \\ &= \frac{R\theta}{\rho^\alpha} \text{grad } c^\alpha. \end{aligned} \quad (1.2.6)$$

For elastic-solute analyses, we assume that the fluid convection over the timescale of solid deformation is negligible (i.e., $\mathbf{w} = \mathbf{v}^w - \mathbf{v}^\sigma \approx \mathbf{0}$) which implies $\mathbf{v}^\sigma = \mathbf{v}^w$ (which is justified when assuming that \mathbf{v}^w represents the average solvent velocity over large time-scales). Thus, the resulting balance of linear momentum becomes

$$-R\theta \text{grad } c^\alpha - (\mathbf{f}^{\alpha\sigma} + \mathbf{f}^{\alpha w}) \cdot (\mathbf{v}^\alpha - \mathbf{v}^s) = \mathbf{0}. \quad (1.2.7)$$

This expression can be formulated in terms of the solute molar flux ($\mathbf{j}^\alpha = c^\alpha (\mathbf{v}^\alpha - \mathbf{v}^\sigma)$) and the effective diffusivity $\mathbf{d}^\alpha = R\theta c^\alpha (\mathbf{f}^{\alpha\sigma} + \mathbf{f}^{\alpha w})^{-1}$. Fick's first law is recovered by multiplying $c^\alpha (\mathbf{f}^{\alpha s})^{-1}$ into the above expression:

$$\mathbf{j}^\alpha = -\mathbf{d}^\alpha \text{grad } c^\alpha. \quad (1.2.8)$$

This form of the mass balance for the solute is convenient for a finite element formulation where the mesh is defined on the solid matrix.

1.3 Chemical Reactions

Chemical reactions are incorporated into the mixture through the mass supply term $\hat{\rho}^\alpha$ (and thus \hat{c}^α). This section details the treatment of chemical species and their kinetics.

1.3.1 Solutes

In chemistry, solute content is often represented in units of molar concentration (moles per fluid volume). It follows that solute molar concentration c^α and molar supply \hat{c}^α are related to ρ^α and $\hat{\rho}^\alpha$ via

$$c^\alpha = \frac{\rho^\alpha}{M^\alpha}, \quad \hat{c}^\alpha = \frac{\hat{\rho}^\alpha}{M^\alpha}. \quad (1.3.1)$$

The molar flux of constituent α relative to the solid is given by

$$\mathbf{j}^\alpha = c^\alpha (\mathbf{v}^\alpha - \mathbf{v}) . \quad (1.3.2)$$

1.3.2 Mass Action Chemical Kinetics

Productions rates are described by constitutive relations which are functions of the state variables. In a biological mixture under isothermal conditions, the minimum set of state variables needed to describe reactive mixtures that include a solid matrix are: the (uniform) temperature θ , the solid matrix deformation gradient \mathbf{F} (or related strain measures), and the molar content c^α of the various constituents. This set differs from the classical treatment of chemical kinetics in fluid mixtures by the inclusion of \mathbf{F} (of which we treat differently here than in the multiphasic module).

Consider a general chemical reaction,

$$\sum_{\alpha} \nu_R^\alpha c^\alpha \rightarrow \sum_{\alpha} \nu_P^\alpha c^\alpha , \quad (1.3.3)$$

where ν_R^α and ν_P^α represent stoichiometric coefficients of the reactants and products, respectively. Since the molar supply of reactants and products is constrained by stoichiometry, it follows that all molar supplies \hat{c}_i^α due to chemical reactions $i \in r$ may be related to production rates $\hat{\zeta}_i$ according to

$$\hat{c}_i^\alpha = \nu_i^\alpha \hat{\zeta}_i , \quad (1.3.4)$$

where ν_i^α represents the net stoichiometric coefficient for α :

$$\nu_i^\alpha = \nu_{P,i}^\alpha - \nu_{R,i}^\alpha . \quad (1.3.5)$$

The production rate $\hat{\zeta}_i$ for mass-action forward reactions is given by :

$$\hat{\zeta}_i = k_i \prod_{\alpha} (c^\alpha)^{\nu_i^\alpha} . \quad (1.3.6)$$

The total molar supply is given by the summation

$$\hat{c}^\alpha = \sum_i \nu_i^\alpha \hat{\zeta}_i \quad (1.3.7)$$

From the main FEBio theory manual, it follows in general that $c_i^\alpha = \nu_i^\alpha \hat{\zeta}_i$.

1.3.3 Hill-Type Chemical Kinetics

An alternate set of chemical kinetics is introduced with Hill-type equations where species α is activated (denoted by Boolean operator \rightarrow) by species β . The Hill-type equation has the form:

$$f_{\rightarrow\beta}^\alpha = \frac{B (c^\beta)^n}{K^n + (c^\beta)^n} , \quad (1.3.8)$$

$$B = \frac{EC_{50}^{n-1} - 1}{2EC_{50}^{n-1} - 1} , \quad (1.3.9)$$

$$K = (B - 1)^{1/n} , \quad (1.3.10)$$

where n is the Hill coefficient and EC_{50}^{n-1} is the concentration or activity level c^β at which the production of c^α becomes half maximal. Inhibition of species α by a tertiary species γ is given through the Boolean NOT operation, i.e.,:

$$f_{\neg\gamma}^\alpha = 1 - f_{\rightarrow\gamma}^\alpha. \quad (1.3.11)$$

When a species α is simultaneously activated and/or inhibited by multiple species, the net Hill equation is achieved through the Boolean AND operation (denoted by Boolean operator \wedge):

$$f_{\rightarrow\beta\wedge\neg\gamma}^\alpha = f_{\rightarrow\beta}^\alpha f_{\neg\gamma}^\alpha. \quad (1.3.12)$$

The (normalized) molar production rate for a chemical species is given by setting $\nu_i^\alpha = 1$, $\hat{\zeta}_i = k_H f_i^\alpha$, i.e.,:

$$\hat{c}_i^\alpha = k_H f_i^\alpha. \quad (1.3.13)$$

1.4 Kinematic Growth

The motivation to develop the elastic reaction-diffusion solver plugin was to model kinematic growth driven by chemical species production without considering fluid pressure, poroelasticity/permeability, or electrochemistry. Kinematic growth (KG) theory is a framework to model tissue expansion and contraction which may be related directly to any state variable. This is an alternative framework to constrained mixture theory (CMT) which is included in the main FEBio release. Unlike CMT, KG may be modeled as an open system where supplies and sinks of mass or energy may be implicitly available (or negligible on the time scale of growth which occurs over days to years). Kinematic growth is computationally simpler than CMT as it does not require tracking of multiple reference configurations, pre-stretches, and generations of each mixture constituent. Instead, KG assumes that the deformation gradient \mathbf{F} may be multiplicatively decomposed into a growth contribution \mathbf{F}^g and elastic contribution \mathbf{F}^e :

$$\mathbf{F} = \mathbf{F}^e \mathbf{F}^g. \quad (1.4.1)$$

The growth deformation tensor maps the reference configuration Ω_0 into an intermediate “stress-free” configuration Ω_* in which material elements (points, lines, areas, volumes) may overlap. The elastic deformation tensor then maps from the intermediate configuration into the current configuration Ω which accounts for both the residual stresses needed to resolve overlaps between adjacent material elements, as well as any externally imposed boundary conditions that occur in a traditional solid analysis. The growth tensor is postulated as a function of a state variable and is often constrained to assume an orthogonal, symmetric positive definite tensor with a growth stretch ϑ_i along each principal direction:

$$\mathbf{F}^g = \sum_{i=1}^N \vartheta_i \mathbf{n}_{0,i} \otimes \mathbf{n}_{0,i}, \quad (1.4.2)$$

where $\mathbf{n}_{0,i}$ is the orientation of each principal direction in the reference configuration. Typically, growth is modeled as line-type, area-type, or volume-type given by:

$$\mathbf{F}^g = \begin{cases} \mathbf{I} + [\vartheta - 1] \mathbf{n}_{\parallel} \otimes \mathbf{n}_{\parallel} & \text{line-type: } (N = 1), \vartheta_1 = \vartheta; \mathbf{n}_{\parallel} = \mathbf{n}_{0,1} \\ \sqrt{\vartheta} \mathbf{I} + [1 - \sqrt{\vartheta}] \mathbf{n}_{\perp} \otimes \mathbf{n}_{\perp} & \text{area-type: } (N = 2), \vartheta_1, \vartheta_2 = \vartheta; \mathbf{n}_{\perp} = \mathbf{n}_{0,3} \\ \vartheta^{1/3} \mathbf{I} & \text{volume-type: } (N = 3), \vartheta_1, \vartheta_2, \vartheta_3 = \vartheta \end{cases}. \quad (1.4.3)$$

Note that we only consider “isotropic growth” where the growth stretch along any growing direction is the same but is 1 for non-growing directions. The stretch may be defined as a function of time or as a function of another variable. Often, the rate of growth is posited instead of the growth stretch which is solved by iterative methods. The rate of growth has the general form

$$\dot{\vartheta} = k(\vartheta)\phi(\bullet), \quad (1.4.4)$$

where $k(\vartheta)$ is a function that bounds the solution to prevent uncontrollable growth/contraction and $\phi(\bullet)$ is the function that depends on the posited variable of interest. We implement $k(\vartheta)$ as the bandpass function:

$$k(\vartheta) = \vartheta_{\min} + \vartheta_{\max} \left(\frac{1}{1 + \exp\left(-\frac{\vartheta - \vartheta_a}{\gamma}\right)} + \frac{1}{1 + \exp\left(-\frac{\vartheta - \vartheta_a}{\gamma}\right)} \right), \quad (1.4.5)$$

where ϑ_a determines the width of the bandpass, and γ controls the rate of transition from the lower bound ϑ_{\min} to the upper bound ϑ_{\max} . Most commonly, $\phi(\bullet)$ has been formulated as a function of stress, strain, or one of their invariants. We focus instead on $\phi(\dot{c}^\alpha)$ such that growth emerges from changes in chemical a species α while accounting for its history since the reference configuration. Currently, a simple relation is supported:

$$\phi(\dot{c}^\alpha) = g \frac{dc^\alpha}{dt}, \quad (1.4.6)$$

where g is a constant scalar.

The unknown deformation gradients \mathbf{F} and \mathbf{F}^g are solved by postulating \mathbf{F}^g , solving the elastic stress \mathbf{S}^e due to \mathbf{F}^e in the intermediate configuration Ω_* that results from an increment in nodal displacements \mathbf{u} , and then performing the appropriate push-pull operations. It is useful to note the following quantities that are derived from the deformation gradients:

$$J = \det \mathbf{F} = J^e J^g, \quad J^e = \det \mathbf{F}^e, \quad J^g = \det \mathbf{F}^g, \quad (1.4.7)$$

$$\mathbf{C} = \mathbf{F}^T \mathbf{F} = \mathbf{F}^{gT} \mathbf{F}^{eT} \mathbf{F}^e \mathbf{F}^g, \quad \mathbf{C}^e = \mathbf{F}^e \mathbf{F}^{eT}, \quad \mathbf{C}^g = \mathbf{F}^g \mathbf{F}^{gT}, \quad (1.4.8)$$

where J, J^e, J^g are volume ratios and $\mathbf{C}, \mathbf{C}^e, \mathbf{C}^g$ are right Cauchy-Green deformation tensors. The elastic stress is determined from:

$$\mathbf{S}^e = 2 \frac{\partial W^e}{\partial \mathbf{C}^e}. \quad (1.4.9)$$

A pull-back operation provides the (referential) 2nd Piola-Kirchhoff stress:

$$\mathbf{S} = J^g \mathbf{F}^{g-1} \cdot \mathbf{S}^e \cdot \mathbf{F}^{g-T}, \quad (1.4.10)$$

while a push-forward operation provides the Cauchy stress:

$$\boldsymbol{\sigma} = \frac{1}{J} \mathbf{F} \cdot \mathbf{S} \cdot \mathbf{F}^T = \frac{1}{J^e} \mathbf{F}^e \cdot \mathbf{S}^e \cdot \mathbf{F}^{eT}. \quad (1.4.11)$$

Chapter 2

Linearization and Discretization of the Nonlinear FE Method

The chapter begins with a short introduction to the weak formulation for the physics described in 1. The linearization and discretization of the general weak form are demonstrated in 2.1. Next, tangents for kinematic growth analyses are introduced in 2.2. Finally, the tangents for chemical kinetics are presented in 2.3.

2.1 Weak Formulation for Elastic Reaction-Diffusion Materials

The virtual work integral for a mixture of intrinsically incompressible constituents combines the balance of momentum for the mixture, the balance of mass for the mixture, and the balance of mass for each of the solutes.

For the elastic reaction-diffusion materials, it is assumed that there is a large difference in time scales between displacements and solute transport and kinetics (such as during some growth and remodeling simulations). The first consequence of this is that solute c^α concentrations, solute flux \mathbf{j}^α , and diffusivity \mathbf{d}^α are unaffected by volumetric changes (i.e., J) or rotation. Thus, unlike the multiphasic module, interactions between solid displacements and concentration displacements $\left(\frac{\partial \mathbf{k}}{\partial \mathbf{E}}, \hat{\zeta}_\varepsilon, \mathcal{D}^\alpha, \frac{\delta c^\alpha}{J}, \frac{\partial \tilde{\mathbf{k}}}{J}, \mathbf{j}'_u, \text{etc.}\right)$ are not evaluated unless otherwise stated. The second consequence is that fluid pressure (p, \tilde{p}) and solute convection are assumed to be negligible (as are $\mathcal{K}, \tilde{\mathcal{K}}, \tilde{\mathbf{k}}'_c, \frac{\partial \tilde{\mathcal{K}}}{\partial c^\alpha}, \mathbf{w}'_u, \mathbf{w}'_c$). Finally, standard thermodynamic conditions are assumed throughout the analysis such that the activity coefficient, effective solubility, partition coefficient, osmotic coefficient, and diffusivities are constant (i.e., $\gamma^\alpha, \hat{\kappa}^\alpha, \tilde{\kappa}^\alpha = 1, \Phi = 0, \frac{\partial \mathbf{d}^\alpha}{\partial \tilde{c}^\alpha}, \frac{\partial \mathbf{d}^\alpha}{\partial \tilde{\kappa}^\alpha}, \mathbf{d}'_c, \frac{\partial d_0}{\partial \theta} = \mathbf{0}$). We leave the possibility that the stress/strain and solute concentrations may contain interaction terms (e.g., $\sigma'_c, \frac{\partial \mathbf{S}}{\partial c}, \frac{\partial c}{\partial \sigma}, \frac{\partial \mathbf{k}}{\partial \mathbf{E}}, \hat{\zeta}_\varepsilon$) may be non-zero under certain kinematic growth relations. This analysis should not be used if modeling electrochemistry or short-time mechano-chemical phenomena are desired (e.g. osmotic pressure, non-negligible solute volume fractions, convection).

The virtual work integral simplifies to:

$$\begin{aligned} \delta W &= \delta G \\ &+ \int_b \delta \mathbf{v} \cdot \operatorname{div} \boldsymbol{\sigma} \, dv \\ &+ \sum_{\alpha} \int_b \delta c^{\alpha} \left[\frac{D}{Dt} c^{\alpha} + \operatorname{div} \mathbf{j}^{\alpha} \right] \, dv, \end{aligned} \quad (2.1.1)$$

where $\delta \mathbf{v}$ is the virtual velocity of the solid, δc^{α} is the virtual molar energy of solute α , and δG is the Gibb's free energy (due to chemical reactions). Here, b represents the mixture domain in the spatial frame and dv is an elemental volume in b . The Gibb's free energy is given by

$$\delta G = \sum_{\alpha} \sum_i \int_b \delta c^{\alpha} \hat{c}_i^{\alpha} \, dv. \quad (2.1.2)$$

Applying the divergence theorem, δW may be split into internal and external contributions to the virtual work, $\delta W = \delta W_{\text{ext}} - \delta W_{\text{int}}$, where

$$\begin{aligned} \delta W_{\text{int}} &= \delta G \\ &+ \int_b \boldsymbol{\sigma} : \delta \mathbf{d}^s \, dv \\ &+ \sum_{\alpha} \int_b \left[\mathbf{j}^{\alpha} \cdot \operatorname{grad} \delta c^{\alpha} - \delta c^{\alpha} \frac{D}{Dt} c^{\alpha} \right] \, dv, \end{aligned} \quad (2.1.3)$$

and the external work is given by

$$\delta W_{\text{ext}} = \int_{\partial b} \left[\delta \mathbf{v} \cdot \mathbf{t} + \sum_{\alpha} \delta c^{\alpha} j_n^{\alpha} \right] \, da. \quad (2.1.4)$$

In these expressions, $\delta \mathbf{d}^s = (\operatorname{grad} \delta \mathbf{v} + \operatorname{grad}^T \delta \mathbf{v}) / 2$ (not to be confused with diffusivity tensors \mathbf{d}^{α}), ∂b is the boundary of b , and da is an elemental area on ∂b . In this finite element formulation, \mathbf{u} and c^{α} are used as nodal variables, and essential boundary conditions may be prescribed on these variables. Natural boundary conditions are prescribed to the mixture traction, $\mathbf{t} = \boldsymbol{\sigma} \cdot \mathbf{n}$ and normal solute flux $j_n^{\alpha} = \mathbf{j}^{\alpha} \cdot \mathbf{n}$, where \mathbf{n} is the outward unit normal to ∂b .

2.1.1 Linearization along $\Delta \mathbf{u}$

Linearization of the elastic reaction-diffusion module is symbolically given by

$$\delta W + D\delta W [\Delta \mathbf{u}] + \sum_{\alpha} D\delta W [\Delta c^{\alpha}] \approx 0. \quad (2.1.5)$$

The linearization of the first term in δW_{int} along $\Delta \mathbf{u}$ yields

$$D \left(\mathbf{S} : \delta \dot{\mathbf{E}} \right) [\Delta \mathbf{u}] \, dV = \left[\delta \mathbf{d}^s : \boldsymbol{\mathcal{C}} : \Delta \boldsymbol{\varepsilon} + \boldsymbol{\sigma} : (\operatorname{grad}^T \Delta \mathbf{u} \cdot \operatorname{grad} \delta \mathbf{v}) \right] \, dv, \quad (2.1.6)$$

where $\boldsymbol{\mathcal{C}}$ is the spatial elasticity tensor of the solid,

$$\boldsymbol{\mathcal{C}} = J^{-1} [\mathbf{F} \otimes \mathbf{F}] : \mathbb{C} : [\mathbf{F}^T \otimes \mathbf{F}^T], \quad (2.1.7)$$

where \mathbb{C} is the material elasticity tensor of the mixture.

The second term is given by

$$D(\mathbf{J}^\alpha \cdot \text{Grad } \delta c^\alpha) [\Delta \mathbf{u}] dV = 0, \quad (2.1.8)$$

where it is assumed that concentration is unaffected by deformation and molar flux is unaffected by rotation.

The third and fourth terms are given by:

$$D\left(\delta c^\alpha \frac{\partial c^\alpha}{\partial t}\right) [\Delta \mathbf{u}] dV = 0, \quad (2.1.9)$$

$$D\delta G [\Delta \mathbf{u}] dV = 0. \quad (2.1.10)$$

2.1.2 Linearization along Δc^γ

The linearization of the first term in δW_{int} along Δc^γ yields

$$D(\mathbf{S} : \delta \dot{\mathbf{E}}) [\Delta c^\gamma] dV = 0. \quad (2.1.11)$$

The second term is

$$D(\mathbf{J}^\alpha \cdot \text{Grad } \delta c^\alpha) [\Delta c^\gamma] dV = \delta_{\alpha\gamma} \text{grad } \delta c^\alpha \cdot \mathbf{d}^\alpha \cdot \text{grad } \Delta c^\gamma dv, \quad (2.1.12)$$

where $\delta_{\alpha\gamma}$ is the Kronecker delta such that $\alpha = \gamma \rightarrow \delta = 0, \alpha \neq \gamma \rightarrow \delta = 0$.

The third term is

$$D\left(\frac{\partial c^\alpha}{\partial t} \delta c^\alpha\right) [\Delta c^\gamma] dV = \delta c^\alpha \frac{\delta_{\alpha\gamma}}{\Delta t} \Delta c^\gamma dv. \quad (2.1.13)$$

where we similarly used a backward difference scheme to discretize the time derivative.

The final term is

$$D\delta G [\Delta c^\gamma] dV = \sum_\alpha \sum_i \int_b \delta c^\alpha \frac{\partial \hat{c}_i^\alpha}{\partial c^\gamma} \Delta c^\gamma dv, \quad (2.1.14)$$

where the terms $\partial \hat{c}_i^\alpha / \partial c^\gamma$ depends on the specific reaction kinetics (see 2.3).

2.1.3 Linearization of External Virtual Work

The linearization of δW_{ext} depends on whether natural boundary conditions are prescribed as area densities or total net values over an area. Thus, in the case when $\mathbf{t} da$ (net force) or $j_n^\alpha da$ (net molar flow rate) are prescribed over the elemental area da , there is no variation in δW_{ext} and it follows that $D\delta W_{\text{ext}} = 0$. Alternatively, in the case when \mathbf{t} or j_n^α are prescribed, the linearization may be performed by evaluating the integral in the parametric space of the boundary surface ∂b , with parametric coordinates (η^1, η^2) . Accordingly, for a point $\mathbf{x}(\eta^1, \eta^2)$ on ∂b , surface tangents (covariant basis vectors) are given by

$$\mathbf{g}_\alpha = \frac{\partial \mathbf{x}}{\partial \eta^\alpha}, \quad (\alpha = 1, 2) \quad (2.1.15)$$

and the outward unit normal is

$$\mathbf{n} = \frac{\mathbf{g}_1 \times \mathbf{g}_2}{|\mathbf{g}_1 \times \mathbf{g}_2|}. \quad (2.1.16)$$

The elemental area on ∂b is $da = |\mathbf{g}_1 \times \mathbf{g}_2| d\eta^1 d\eta^2$. Consequently, the external virtual work integral may be rewritten as

$$\delta W_{\text{ext}} = \int_{\partial b} \left(\delta \mathbf{v} \cdot \mathbf{t} + \sum_{\alpha \neq s, w}^{\alpha_s} \delta c^\alpha j_n^\alpha \right) |\mathbf{g}_1 \times \mathbf{g}_2| d\eta^1 d\eta^2, \quad (2.1.17)$$

The directional derivative of δW_{ext} may then be applied directly to its integrand, since the parametric space is invariant [2].

If we restrict traction boundary conditions to the special case of normal tractions, then $\mathbf{t} = t_n \mathbf{n}$ where t_n is the prescribed normal traction component. Then it can be shown that the linearization of δW_{ext} along $\Delta \mathbf{u}$ produces

$$D(\delta W_{\text{ext}})[\Delta \mathbf{u}] = \int_{\partial b} \left(t_n \delta \mathbf{v} + \sum_{\alpha \neq s, w}^{\alpha_s} \delta c^\alpha j_n^\alpha \mathbf{n} \right) \cdot \left(\frac{\partial \Delta \mathbf{u}}{\partial \eta^1} \times \mathbf{g}_2 + \mathbf{g}_1 \times \frac{\partial \Delta \mathbf{u}}{\partial \eta^2} \right) d\eta^1 d\eta^2. \quad (2.1.18)$$

The linearizations along Δc^γ reduces to zero, $D(\delta W_{\text{ext}})[\Delta c^\gamma] = 0$.

2.1.4 Discretization

To discretize the virtual work relations, let

$$\begin{aligned} \delta \mathbf{v} &= \sum_{a=1}^m N_a \delta \mathbf{v}_a, & \Delta \mathbf{u} &= \sum_{b=1}^m N_b \Delta \mathbf{u}_b, \\ \delta c^\alpha &= \sum_{a=1}^m N_a \delta c_a^\alpha, & \Delta c^\gamma &= \sum_{b=1}^m N_b \Delta c_b^\gamma, \end{aligned} \quad (2.1.19)$$

where N_a represents the interpolation functions over an element, $\delta \mathbf{v}_a$, δc_a^α , $\Delta \mathbf{u}_a$, and Δc_a^γ respectively represent the nodal values of $\delta \mathbf{v}$, δc^α , $\Delta \mathbf{u}$, and Δc^γ ; m is the number of nodes in an element.

The discretized form of δW_{int} may be written as

$$\delta W_{\text{int}} = \sum_{e=1}^{n_e} \sum_{k=1}^{n_{\text{int}}^{(e)}} W_k J_\eta \sum_{a=1}^m \begin{bmatrix} \delta \mathbf{v}_a & \delta c_a^\alpha & \cdots & \delta c_a^\gamma \end{bmatrix} \cdot \begin{bmatrix} \mathbf{r}_a^u \\ r_a^\alpha \\ \vdots \\ r_a^\gamma \end{bmatrix}, \quad (2.1.20)$$

where n_e is the number of elements in b , $n_{\text{int}}^{(e)}$ is the number of integration points in the e -th element, W_k is the quadrature weight associated with the k -th integration point, and J_η is the Jacobian of the transformation from the current spatial configuration to the parametric space of the element. In the above expression,

$$\begin{aligned} \mathbf{r}_a^u &= \boldsymbol{\sigma} \cdot \text{grad } N_a, \\ r_a^\alpha &= \mathbf{j}^\alpha \cdot \text{grad } N_a - N_a \frac{\partial c^\alpha}{\partial t} + N_a \sum_i \hat{c}_i^\alpha, \end{aligned} \quad (2.1.21)$$

and it is understood that J_η , \mathbf{r}_a^u , and $r_a^\alpha \cdots r_a^\gamma$ are evaluated at the parametric coordinates of the k -th integration point. Since the parametric space is invariant, time derivatives are evaluated

in a material frame. For example, the time derivative $DJ(\mathbf{x}, t)/Dt$ becomes $\partial J(\eta_k, t)/\partial t$ when evaluated at the parametric coordinates $\eta_k = (\eta_k^1, \eta_k^2, \eta_k^3)$ of the k -th integration point. All time derivatives are discretized using a backward difference scheme.

Similarly, the discretized form of $D\delta W_{\text{int}} = D\delta W_{\text{int}}[\Delta \mathbf{u}] + \sum_{\gamma} D\delta W_{\text{int}}[\Delta c^{\gamma}]$ may be written as

$$D\delta W_{\text{int}} = \sum_{e=1}^{n_e} \sum_{k=1}^{n_{\text{int}}^{(e)}} W_k J_{\eta} \sum_{a=1}^m \sum_{b=1}^m \begin{bmatrix} \delta \mathbf{v}_a & \delta c_a^{\alpha} & \cdots & \delta c_a^{\gamma} \end{bmatrix} \cdot \begin{bmatrix} \mathbf{K}_{ab}^{uu} & \mathbf{k}_{ab}^{u\alpha} & \cdots & \mathbf{k}_{ab}^{u\gamma} \\ \mathbf{k}_{ab}^{\alpha u} & k_{ab}^{\alpha\alpha} & \cdots & k_{ab}^{\alpha\gamma} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{k}_{ab}^{\gamma u} & k_{ab}^{\gamma\alpha} & \cdots & k_{ab}^{\gamma\gamma} \end{bmatrix} \cdot \begin{bmatrix} \Delta \mathbf{u}_b \\ \Delta c_b^{\alpha} \\ \vdots \\ \Delta c_b^{\gamma} \end{bmatrix}, \quad (2.1.22)$$

where the terms in the first column are the discretized form of the linearization along $\Delta \mathbf{u}$:

$$\mathbf{K}_{ab}^{uu} = \text{grad } N_a \cdot \mathbf{C} \cdot \text{grad } N_b + (\text{grad } N_a \cdot \boldsymbol{\sigma} \cdot \text{grad } N_b) \mathbf{I}, \quad (2.1.23)$$

$$\mathbf{k}_{ab}^{\alpha u} = 0, \quad (2.1.24)$$

The terms in the remaining columns of the stiffness matrix are the discretized form of the linearization along Δc^{γ} :

$$\mathbf{k}_{ab}^{u\alpha} = N_b \boldsymbol{\sigma}'_{\alpha} \cdot \text{grad } N_a, \quad (2.1.25)$$

$$k_{ab}^{\alpha\gamma} = -\delta_{\alpha\gamma} \text{grad } N_a \cdot \mathbf{d}^{\alpha} \cdot \text{grad } N_b - N_a N_b \frac{1}{\Delta t} + N_a N_b \sum_{\alpha} \sum_i \frac{\partial \hat{c}_i^{\alpha}}{\partial c^{\gamma}}, \quad (2.1.26)$$

The discretization of δW_{ext} has the form

$$\delta W_{\text{ext}} = \sum_{e=1}^{n_e} \sum_{k=1}^{n_{\text{int}}^{(e)}} W_k J_{\eta} \sum_{a=1}^m \begin{bmatrix} \delta \mathbf{v}_a & \delta c_a^{\alpha} & \cdots & \delta c_a^{\gamma} \end{bmatrix} \cdot \begin{bmatrix} N_a t_n \mathbf{n} \\ N_a j_n^{\alpha} \\ \vdots \\ N_a j_n^{\gamma} \end{bmatrix}, \quad (2.1.27)$$

where $J_{\eta} = |\mathbf{g}_1 \times \mathbf{g}_2|$. The summation is performed over all surface elements on which these boundary conditions are prescribed. The discretization of $-D\delta W_{\text{ext}}$ has the form

$$-D\delta W_{\text{ext}} = \sum_{e=1}^{n_e} \sum_{k=1}^{n_{\text{int}}^{(e)}} W_k J_{\eta} \sum_{a=1}^m \sum_{b=1}^m \begin{bmatrix} \delta \mathbf{v}_a & \delta c_a^{\alpha} & \cdots & \delta c_a^{\gamma} \end{bmatrix} \cdot \begin{bmatrix} \mathbf{K}_{ab}^{uu} & \mathbf{k}_{ab}^{u\alpha} & \cdots & \mathbf{k}_{ab}^{u\gamma} \\ \mathbf{k}_{ab}^{\alpha u} & k_{ab}^{\alpha\alpha} & \cdots & k_{ab}^{\alpha\gamma} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{k}_{ab}^{\gamma u} & k_{ab}^{\gamma\alpha} & \cdots & k_{ab}^{\gamma\gamma} \end{bmatrix} \cdot \begin{bmatrix} \Delta \mathbf{u}_b \\ \Delta c_b^{\alpha} \\ \vdots \\ \Delta c_b^{\gamma} \end{bmatrix}, \quad (2.1.28)$$

where

$$\mathbf{K}_{ab}^{uu} = t_n N_a \mathcal{A} \left\{ \frac{\partial N_b}{\partial \eta^1} \mathbf{g}_2 - \frac{\partial N_b}{\partial \eta^2} \mathbf{g}_1 \right\}, \quad (2.1.29)$$

$$\mathbf{k}_{ab}^{\alpha u} = 0.$$

In this expression, $\mathcal{A}\{\mathbf{v}\}$ is the antisymmetric tensor whose dual vector is \mathbf{v} (such that $\mathcal{A}\{\mathbf{v}\} \cdot \mathbf{q} = \mathbf{v} \times \mathbf{q}$ for any vector \mathbf{q}).

2.2 Linearization and Discretization of Kinematic Growth Materials

2.2.1 Linearization of Kinematic Growth materials along $\Delta \mathbf{u}$

For kinematic growth, additional linearization since the stress may be considered a function of \mathbf{F} and \mathbf{F}^g (i.e., $\mathbf{S}(\mathbf{F}, \mathbf{F}^g)$). The material elasticity tensor of the mixture now becomes:

$$\mathbb{C} = 2 \frac{d\mathbf{S}}{d\mathbf{C}} = \mathbb{C}^e + \mathbb{C}^g. \quad (2.2.1)$$

The elastic contribution is given by:

$$\mathbb{C}^e = 2 \frac{\partial \mathbf{S}(\mathbf{F}, \mathbf{F}^g)}{\partial \mathbf{C}} \bigg|_{\mathbf{F}^g} = J^g [\mathbf{F}^{g-1} \oslash \mathbf{F}^{g-1}] : \mathbb{L}^e : [\mathbf{F}^{g-T} \oslash \mathbf{F}^{g-T}], \quad (2.2.2)$$

where \mathbb{L}^e is the elasticity tensor that arises due to elastic deformation when observed from the stress-free intermediate configuration given by:

$$\mathbb{L}^e = 2 \frac{\partial \mathbf{S}^e}{\partial \mathbf{C}^e} \bigg|_{\vartheta}. \quad (2.2.3)$$

The growth contribution is given by [5]:

$$\mathbb{C}^g = 2 \left[\frac{\partial \mathbf{S}(\mathbf{C}, \vartheta)}{\partial \mathbf{F}^g} \bigg|_{\mathbf{C}} : \frac{\partial \mathbf{F}^g}{\partial \vartheta} \right] \otimes \frac{\partial \vartheta}{\partial \mathbf{C}}. \quad (2.2.4)$$

The first term is given by

$$\frac{\partial \mathbf{S}}{\partial \mathbf{F}^g} = \mathbf{S} \otimes \mathbf{F}^{g-T} - [\mathbf{F}^{g-1} \oslash \mathbf{S} + \mathbf{S} \oslash \mathbf{F}^{g-1}] - J^g [\mathbf{F}^{g-1} \oslash \mathbf{F}^{g-1}] : \frac{1}{2} \mathbb{L}^e : [\mathbf{F}^{g-T} \oslash \mathbf{C}^e + \mathbf{C}^e \oslash \mathbf{F}^{g-T}]. \quad (2.2.5)$$

The second term is given by

$$\frac{\partial \mathbf{F}^g}{\partial \vartheta} = \begin{cases} \mathbf{n}^{\parallel} \otimes \mathbf{n}^{\parallel} & \text{line-type growth} \\ \frac{1}{2\sqrt{\vartheta}} [\mathbf{I} - \mathbf{n}^{\perp} \otimes \mathbf{n}^{\perp}] & \text{area-type growth} \end{cases}. \quad (2.2.6)$$

The third term involves evaluating the growth scalar ϑ . When the evolution of the growth scalar is formulated as $\dot{\vartheta} = d\vartheta/dt$, the growth stretch is evaluated in a local Newton iteration with the residual R and its tangent K :

$$R = \vartheta - \vartheta_n - \dot{\vartheta} \Delta t, \quad (2.2.7)$$

$$K = \frac{\partial R}{\partial \vartheta} = 1 - \Delta t \frac{\partial \dot{\vartheta}}{\partial \vartheta}, \quad (2.2.8)$$

$$\frac{\partial \dot{\vartheta}}{\partial \vartheta} = \phi(\dot{\epsilon}^\alpha) \frac{\partial k(\vartheta)}{\partial \vartheta} + k(\vartheta) \frac{\partial \phi(\dot{\epsilon}^\alpha)}{\partial \vartheta}. \quad (2.2.9)$$

The function $\phi(\dot{\epsilon}^\alpha)$ is independent of ϑ . Thus, the tangent simplifies to:

$$K = 1 - \Delta t \phi(\dot{\epsilon}^\alpha) \frac{\partial k(\vartheta)}{\partial \vartheta}. \quad (2.2.10)$$

The residual is evaluated w.r.t. \mathbf{C} and rearranged to solve for $\frac{\partial \vartheta}{\partial \mathbf{C}}$:

$$\frac{\partial R}{\partial \mathbf{C}} = \frac{\partial \vartheta}{\partial \mathbf{C}} - \frac{\partial \dot{\vartheta}}{\partial \mathbf{C}} \Delta t = \mathbf{0}, \quad (2.2.11)$$

$$\frac{\partial \vartheta}{\partial \mathbf{C}} = \frac{\partial \dot{\vartheta}}{\partial \mathbf{C}} \Delta t = \left[\phi(\dot{c}^\alpha) \frac{\partial k(\vartheta)}{\partial \vartheta} \frac{\partial \vartheta}{\partial \mathbf{C}} + k(\vartheta) \frac{\partial \phi(\dot{c}^\alpha)}{\partial \dot{c}^\alpha} \frac{\partial \dot{c}^\alpha}{\partial \mathbf{C}} \right] \Delta t, \quad (2.2.12)$$

$$\frac{\partial \vartheta}{\partial \mathbf{C}} = \frac{k(\vartheta) \Delta t}{K} \frac{\partial \phi(\dot{c}^\alpha)}{\partial \dot{c}^\alpha} \frac{\partial \dot{c}^\alpha}{\partial \mathbf{C}}. \quad (2.2.13)$$

Here, we define the terms

$$\frac{\partial \phi(\dot{c}^\alpha)}{\partial \dot{c}^\alpha} = \begin{cases} \frac{\partial \phi(\dot{c}^\alpha)}{\partial \dot{c}^\alpha} & \alpha = \text{growth species} \\ 0 & \alpha \neq \text{growth species} \end{cases}, \quad (2.2.14)$$

$$\frac{\partial k(\vartheta)}{\partial \vartheta} = \frac{\vartheta_{\max}}{\gamma} \left(\frac{\exp\left(-\frac{\vartheta + \vartheta_a}{\gamma}\right)}{\left(1 + \exp\left(-\frac{\vartheta + \vartheta_a}{\gamma}\right)\right)^2} + \frac{\exp\left(-\frac{\vartheta - \vartheta_a}{\gamma}\right)}{\left(1 + \exp\left(-\frac{\vartheta - \vartheta_a}{\gamma}\right)\right)^2} \right), \quad (2.2.15)$$

$$\frac{\partial \dot{c}^\alpha}{\partial \mathbf{C}} = \frac{J}{2} \mathbf{F}^{-1} \cdot \hat{\mathbf{c}}_\varepsilon^\alpha \cdot \mathbf{F}^{-T}, \quad (2.2.16)$$

$$\hat{\mathbf{c}}_\varepsilon^\alpha = \frac{\partial \hat{c}^\alpha}{\partial \boldsymbol{\varepsilon}} = \sum_i \nu_i^\alpha \hat{\boldsymbol{\zeta}}_{\varepsilon,i}^\alpha, \quad (2.2.17)$$

$$\hat{\boldsymbol{\zeta}}_{\varepsilon,i}^\alpha = \frac{\partial \hat{\zeta}_i^\alpha}{\partial \boldsymbol{\varepsilon}} = \begin{cases} \mathbf{0} & \text{Morphoelastic growth} \\ \frac{\partial \hat{\zeta}_i^\alpha}{\partial \text{tr}(\boldsymbol{\sigma})} & \text{Mechanosensitive growth} \end{cases}. \quad (2.2.18)$$

Terms pertaining to chemical reactions are expanded in 2.3.

The linearization of the first term in δW_{int} along $\Delta \mathbf{u}$ yields:

$$D \left(\mathbf{S} : \delta \dot{\mathbf{E}} \right) [\Delta \mathbf{u}] dV = [\delta \mathbf{d}^s : \mathcal{C}^e : \Delta \boldsymbol{\varepsilon} + \boldsymbol{\sigma} : (\text{grad}^T \Delta \mathbf{u} \cdot \text{grad} \delta \mathbf{v})] dv, \quad (2.2.19)$$

The second and third terms remain unchanged. The final term is given by

$$D \delta G [\Delta \mathbf{u}] dV = \sum_a \int_b \delta c^\alpha [\hat{\mathbf{c}}_\varepsilon^\alpha : \Delta \boldsymbol{\varepsilon}] dv = \sum_\alpha \sum_i \nu_i^\alpha \int_b \delta c^\alpha [\hat{\boldsymbol{\zeta}}_{\varepsilon,i}^\alpha : \Delta \boldsymbol{\varepsilon}]. \quad (2.2.20)$$

The formulations for $\hat{\mathbf{c}}_{\varepsilon,i}$ and $\hat{\boldsymbol{\zeta}}_{\varepsilon,i}$ depend on the reaction kinetics as detailed in 2.3.

2.2.2 Linearization of Kinematic Growth materials along Δc^γ

The linearization of the first term in δW_{int} along Δc^γ yields

$$D \left(\mathbf{S} : \delta \dot{\mathbf{E}} \right) [\Delta c^\gamma] dV = \Delta c^\gamma (\boldsymbol{\sigma}'_\gamma : \delta \mathbf{d}^s) dv, \quad (2.2.21)$$

where $\boldsymbol{\sigma}'_\gamma$ is generally zero except for cases where chemical kinetics are mechanosensitive (dependent on the stress or strain). In this case,

$$\boldsymbol{\sigma}'_\gamma = J^{-1} \mathbf{F} \cdot \frac{\partial \mathbf{S}}{\partial c^\gamma} \cdot \mathbf{F}^T. \quad (2.2.22)$$

where symmetric growth tensors yield the expression

$$\frac{\partial \mathbf{S}}{\partial c^\gamma} = \frac{\partial \mathbf{S}}{\partial \mathbf{F}^g} : \frac{\partial \mathbf{F}^g}{\partial \vartheta} \frac{\partial \vartheta}{\partial c^\gamma}, \quad (2.2.23)$$

$$\frac{\partial \vartheta}{\partial c^\gamma} = \frac{\partial \vartheta}{\partial \dot{\vartheta}} \frac{\partial \dot{\vartheta}}{\partial \dot{c}^\gamma} \frac{\partial \dot{c}^\gamma}{\partial c^\gamma} = k(\vartheta) \frac{\partial \phi(\dot{c}^\gamma)}{\partial c^\gamma}. \quad (2.2.24)$$

The remaining terms are unchanged.

2.2.3 Discretization of Kinematic Growth materials

The discretization for kinematic growth materials requires altering a few terms from the elastic reaction-diffusion discretization in 2.1.4.

The discretized form of previously zero-valued stiffness matrix contributions become:

$$\mathbf{k}_{ab}^{\alpha u} = N_a \sum_i \hat{\mathbf{c}}_{\varepsilon,i}^\alpha \cdot \text{grad } N_b \, dv, \quad (2.2.25)$$

and

$$\mathbf{k}_{ab}^{u\alpha} = N_b \boldsymbol{\sigma}'_\alpha \cdot \text{grad } N_a. \quad (2.2.26)$$

2.3 Tangents for Linearization and Discretization of Chemical Reactions

2.3.1 Tangents that arise during the linearization along $\Delta \mathbf{u}$

For the case of stress-dependent concentration kinetics we have

$$D\delta G[\Delta \mathbf{u}] = \sum_\alpha \int_b \delta c^\alpha [\hat{\mathbf{c}}_i^\alpha : \Delta \boldsymbol{\varepsilon}] \, dv = \sum_\alpha \sum_i \nu_i^\alpha \int_b \delta c^\alpha [\hat{\boldsymbol{\zeta}}_{\varepsilon,i} : \Delta \boldsymbol{\varepsilon}] \, dv \quad (2.3.1)$$

where

$$\hat{\mathbf{c}}^\alpha = \sum_i \nu_i^\alpha \hat{\boldsymbol{\zeta}}_{\varepsilon,i}, \quad (2.3.2)$$

$$\hat{\boldsymbol{\zeta}}_{\varepsilon,r} = \frac{\partial \hat{\zeta}_r}{\partial \boldsymbol{\varepsilon}}, \quad (2.3.3)$$

are the tangent of the reaction rate to the strain which depend on the specific reaction. This tangent is zero unless there is a stress- or strain-dependent relationship. For stress-dependent kinetics the tangent becomes

$$\hat{\boldsymbol{\zeta}}_{\varepsilon,r} = \frac{\partial \hat{\zeta}_r}{\partial \boldsymbol{\varepsilon}} = \frac{\partial \hat{\zeta}_r}{\partial \boldsymbol{\sigma}} : \boldsymbol{\mathcal{C}}, \quad (2.3.4)$$

where the specific reaction kinetics dictate $\partial \hat{\zeta}_r / \partial \boldsymbol{\sigma}$. For reactions where the reaction rate is proportional to the trace of stress as bounded by a sigmoidal function, i.e.,

$$\hat{\zeta}_r(\boldsymbol{\sigma}) = k_F s(\boldsymbol{\sigma}) = k_F \left(1 + \frac{a_{amp}}{1 + \exp\left(-\frac{\text{tr}(\boldsymbol{\sigma}) - s_0}{b}\right)} \right), \quad (2.3.5)$$

the tangent is

$$\frac{\partial \hat{\zeta}_r}{\partial \boldsymbol{\sigma}} = \frac{\partial \hat{\zeta}_r}{\partial s(\boldsymbol{\sigma})} \frac{\partial s(\boldsymbol{\sigma})}{\partial \text{tr}(\boldsymbol{\sigma})} \cdot \mathbf{I} : \mathcal{C}, \quad (2.3.6)$$

$$\frac{\partial \hat{\zeta}_r}{\partial s(\boldsymbol{\sigma})} = k_F, \quad (2.3.7)$$

$$\frac{\partial s(\boldsymbol{\sigma})}{\partial \text{tr}(\boldsymbol{\sigma})} = \frac{a \exp\left(-\frac{\text{tr}(\boldsymbol{\sigma}) - s_0}{b}\right)}{b \left(1 + \exp\left(-\frac{\text{tr}(\boldsymbol{\sigma}) - s_0}{b}\right)\right)^2}. \quad (2.3.8)$$

2.3.2 Tangents that arise during the linearization along Δc^γ

2.3.2.1 Tangents for mass action reaction kinetics

Mass-action forward reactions are linearized as:

$$\frac{\partial \hat{c}_i^\alpha}{\partial c^\beta} = \hat{\zeta}_i \frac{(\nu_i^\alpha)^2}{c^\alpha}. \quad (2.3.9)$$

2.3.2.2 Tangents for Hill-type reaction kinetics

Hill-type activation reactions $f_{\rightarrow\beta}^\alpha$ are linearized as:

$$\frac{\partial \hat{c}_{\rightarrow\beta}^\alpha}{\partial c^\beta} = k_H \frac{\partial f_{\rightarrow\beta}^\alpha}{\partial c^\beta}, \quad (2.3.10)$$

$$\frac{\partial f_{\rightarrow\beta}^\alpha}{\partial c^\beta} = \frac{n K^n f_{\rightarrow\beta}^\alpha}{c^\beta (K^n + (c^\beta)^n)}. \quad (2.3.11)$$

Hill-type inhibition reactions $f_{\neg\gamma}^\alpha$ are linearized as:

$$\frac{\partial \hat{c}_{\neg\gamma}^\alpha}{\partial c^\gamma} = k_H \frac{\partial f_{\neg\gamma}^\alpha}{\partial c^\gamma} = k_H \frac{\partial (1 - f_{\rightarrow\gamma}^\alpha)}{\partial c^\beta} = -k_H \frac{\partial f_{\rightarrow\gamma}^\alpha}{\partial c^\gamma}. \quad (2.3.12)$$

When a chemical species α is activated by β AND simultaneously inhibited by γ the Hill-type function $f_{\rightarrow\beta\wedge\neg\gamma}^\alpha$ is linearized as:

$$\frac{\partial \hat{c}_{\rightarrow\beta\wedge\neg\gamma}^\alpha}{\partial c^\beta} = k_H f_{\neg\gamma}^\alpha \frac{\partial f_{\rightarrow\beta}^\alpha}{\partial c^\beta}, \quad (2.3.13)$$

$$\frac{\partial \hat{c}_{\rightarrow\beta\wedge\neg\gamma}^\alpha}{\partial c^\gamma} = -k_H f_{\rightarrow\beta}^\alpha \frac{\partial f_{\rightarrow\gamma}^\alpha}{\partial c^\gamma}. \quad (2.3.14)$$

Appendix A

Tensor Calculus

A.1 Tensor dyadic products and contraction

We indicate tensor order as

Order	Function	Style	Symbolic	Indicial
0	scalar	lower-case, italicized	a	a
1	column vector	lower-case, italicized, bold	\mathbf{a}	a_i
2	matrix	upper-case, italicized, bold	\mathbf{A}	A_{ij}
3	matrix	upper-case, calligraphic, bold	\mathcal{A}	A_{ijk}
4	matrix	upper-case, double-struck, bold	\mathbb{A}	A_{ijkl}

The fourth-order dyadic products of two second order tensors are given as

$$(\mathbf{A} \otimes \mathbf{B})_{ijkl} = \mathbf{A}_{ij} \mathbf{B}_{kl} , \quad (\text{A.1.1})$$

$$(\mathbf{A} \oslash \mathbf{B})_{ijkl} = \mathbf{A}_{ik} \mathbf{B}_{jl} , \quad (\text{A.1.2})$$

$$(\mathbf{A} \ominus \mathbf{B})_{ijkl} = \mathbf{A}_{il} \mathbf{B}_{jk} , \quad (\text{A.1.3})$$

$$(\mathbf{A} \odot \mathbf{B})_{ijkl} = \frac{1}{2} (\mathbf{A} \oslash \mathbf{B} + \mathbf{A} \ominus \mathbf{B}) = \frac{1}{2} (\mathbf{A}_{ik} \mathbf{B}_{jl} + \mathbf{A}_{il} \mathbf{B}_{jk}) . \quad (\text{A.1.4})$$

Contraction of two tensors is given by

$$(\mathbf{A} : \mathbf{B}) = A_{ij} B_{ij} = B_{ij} A_{ij} , \quad (\text{A.1.5})$$

$$(\mathbb{A} : \mathbf{B})_{ij} = A_{ijkl} B_{kl} , \quad (\mathbf{B} : \mathbb{A})_{kl} = B_{ij} A_{ijkl} , \quad (\text{A.1.6})$$

$$(\mathbb{A} : \mathbb{B}) = A_{ijkl} B_{ijkl} . \quad (\text{A.1.7})$$

A.2 Useful derivatives

Below are useful derivatives

$$\left(\frac{\partial \mathbf{A}}{\partial \mathbf{A}} \right)_{ijkl} = \mathbf{I} \oslash \mathbf{I} = \delta_{ik} \delta_{jl} , \quad (\text{A.2.1})$$

$$\left(\frac{\partial \mathbf{A}^T}{\partial \mathbf{A}} \right)_{ijkl} = \mathbf{I} \ominus \mathbf{I} = \delta_{il} \delta_{kj} , \quad (\text{A.2.2})$$

$$\left(\frac{\partial \mathbf{A}^{-1}}{\partial \mathbf{A}}\right)_{ijkl} = -\mathbf{A}^{-1} \oslash \mathbf{A}^{-T} = -A_{ik}^{-1} A_{lj}^{-1}, \quad (\text{A.2.3})$$

$$\left(\frac{\partial \mathbf{A}^{-T}}{\partial \mathbf{A}}\right)_{ijkl} = -\mathbf{A}^{-T} \oslash \mathbf{A}^{-1} = -A_{ki}^{-1} A_{jl}^{-1} \quad (\text{A.2.4})$$

$$\left(\frac{\partial \text{tr}(\mathbf{A})}{\partial \mathbf{A}}\right)_{ij} = \mathbf{I} = \delta_{ij}, \quad (\text{A.2.5})$$

$$\left(\frac{\partial \det(\mathbf{A})}{\partial \mathbf{A}}\right)_{ij} = \det(\mathbf{A}) \mathbf{A}^{-T} = \det(\mathbf{A}) A_{ij}, \quad (\text{A.2.6})$$

Bibliography

- [1] Gerard A. Ateshian, Steven A. LaBelle, and Jeffrey A. Weiss. Continuum Growth Mechanics: Reconciling Two Common Frameworks. *Journal of Biomechanical Engineering*, 146(10):101003, 05 2024.
- [2] Javier Bonet and Richard D. Wood. *Nonlinear continuum mechanics for finite element analysis*. Cambridge University Press, 1997.
- [3] R.M. Bowen. Theory of mixtures. *Continuum physics*, 3(Pt I), 1976.
- [4] W. Y. Gu, W. M. Lai, and V. C. Mow. A mixture theory for charged-hydrated soft tissues containing multi-electrolytes: passive transport and swelling behaviors. *J Biomech Eng*, 120(2):169–80, 1998.
- [5] Serdar Göktepe, Oscar John Abilez, Kevin Kit Parker, and Ellen Kuhl. A multiscale model for eccentric and concentric cardiac growth through sarcomerogenesis. *Journal of Theoretical Biology*, 265(3):433–442, 2010.
- [6] I. Tinoco Jr., K. Sauer, and J. C. Wang. *Physical chemistry : principles and applications in biological sciences*. Prentice Hall, 1995.
- [7] C. Truesdell and R. Toupin. *The classical field theories*, volume III/1 of *Handbuch der physik*. Springer, Heidelberg, 1960.