Numerical methods for strongly coupled simulations of cardiac electro-mechanics

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This presentation has three main parts

1. Operator splitting for strongly coupled electro-mechanics
2. Linearization of active tissue stress
3. Mechano-electric feedback in an infarcted heart
Operator splitting for strongly coupled simulations
Cardiac electro-mechanics is described by a system of ODEs and PDEs

\[ \nabla \cdot (FS) = 0 \]
\[ F = I + \nabla u \]
\[ S = S^p + JF^T \sigma^a (s, \lambda, \dot{\lambda}) F^{-T} \]
\[ S^p = \partial \Psi / \partial E \]
\[ \Psi = \frac{1}{2} K(e^W - 1) + C_{compr} (J \ln J - J + 1) \]
\[ W = b_{ff} E_{ff}^2 + b_{xx} (E_{nn}^2 + E_{ss}^2 + E_{sn}^2 + E_{ns}^2) + b_{fx} (E_{fn}^2 + E_{nf}^2 + E_{fs}^2 + E_{sf}^2) \]
\[ \frac{\partial s}{\partial t} = f \left( s, v, \lambda, \frac{\partial \lambda}{\partial t} \right) \]
\[ \frac{\partial v}{\partial t} + I_{ion} (v, s, \lambda) = \nabla \cdot (M_i \nabla v) + \nabla \cdot (M_i \nabla u_e) \]
\[ 0 = \nabla \cdot (M_i \nabla v) + \nabla \cdot \left( \left( M_i + M_e \right) \nabla u_e \right) \]
Splitting methods are attractive for handling the complexity of the models

System of ODEs

\[ \frac{\partial v}{\partial t} = -I_{\text{ion}}(v,s,\lambda_{n-1}) \]
\[ \frac{\partial s}{\partial t} = f(s,v,\lambda_{n-1},\dot{\lambda}_{n-1}) \]

System of linear PDEs

\[ \frac{\partial v}{\partial t} = \nabla \cdot (M_i \nabla v) + \nabla \cdot (M_i \nabla u_e) \]
\[ 0 = \nabla \cdot (M_i \nabla v) + \nabla \cdot ((M_i + M_e) \nabla u_e) \]

Nonlinear elasticity

\[ \nabla \cdot (FS) = 0 \]
\[ F = I + \nabla u \]
\[ S = S^p + J F^T \sigma^d(s_n,\lambda,\dot{\lambda}) F^{-T} \]
\[ S^p = \partial \Psi / \partial E \]
Different challenges are associated with each sub-problem

• Cell model ODE system:
  • Complexity poses a challenge for verification and debugging
  • Small computational challenge because of parallelism

• Bidomain model
  • High resolution requirements lead to huge linear systems; a considerable bottleneck for research

• Elasticity
  • Passive mechanics fairly standard hyper-elasticity
  • Strong coupling leads to problems of stability and convergence
The intimate coupling of active stress and cell model ODEs is a challenge for operator splitting.

\[ \nabla \cdot (FS) = 0 \]

\[ F = I + \nabla u \]

\[ S = S^p + JF^T \sigma^a (s, \lambda, \dot{\lambda}) F^{-T} \]

\[ S^p = \partial \Psi / \partial E \]

\[ \frac{\partial s}{\partial t} = f(s,v,\lambda,\dot{\lambda}) \]
Spatial discretization gives rise to a system of non-linear DAEs

$$\nabla \cdot (FS) = 0$$

$$F = I + \nabla u$$

$$S = S^p + JF^T \sigma^a(s, \lambda, \dot{\lambda}) F^{-T}$$

$$S^p = \partial \Psi / \partial E$$

$$\frac{\partial s}{\partial t} = f(s, v, \lambda_n, \dot{\lambda}_n)$$

$$A(u, s) = 0$$

$$\frac{\partial s}{\partial t} = f(s, u)$$
The ODE/DAE literature includes a large choice of solvers for index 1 DAEs

- **Half-explicit methods**
  - Integrate ODEs over one time step to obtain $s_{n+1}$, then solve algebraic constraint for $u_{n+1}$
  - Unstable for coupled cardiac mechanics

- **Brute force methods**
  - Solve the constraint $A(u,s) = 0$ with Newton’s method, re-integrate ODE systems inside every Newton iteration
  - Used in the cardiac modeling community

- **Fully implicit methods (impl. Euler, RK, BDF etc)**
  - Good stability and accuracy
  - Challenging to handle multiscale nature of cardiac electro-mechanics
The stability problems of half-explicit methods is limited to a small fraction of the state variables

An intermediate approach:

1. Identify strongly coupled components $s_{\text{strong}}$

2. Use a half-explicit method for $s_{\text{weak}}$, fully implicit for $s_{\text{strong}}$

\[
A(u,s) = 0
\]

\[
\frac{\partial s_{\text{strong}}}{\partial t} = f(s,u)
\]

\[
\frac{\partial s_{\text{weak}}}{\partial t} = f(s,u_{n-1})
\]

Coupled model of Winslow et al (1999) and Rice et al (2008);
$s_{\text{strong}}$ has 2 out of 40 components
A local linearization of the ODE systems enables semi-analytical solution and explicit update formulas (generalized Rush-Larsen method)

\[ A(u,s) = 0 \]

\[ \frac{\partial s}{\partial t} = f(s,v,u) \approx \frac{(s_{\infty}(u,s_n) - s)}{\tau(u,s_n)} \]

\[ A(u,s_{n+1}) = 0 \]

\[ s_{n+1} = s_{\infty}(u) + (s_{\infty}(u) - s_n)e^{-\Delta t/\tau(u)} \]
The mechanics problem is reduced to a quasi-static equilibrium problem which is solved without considering ODEs

\[ \nabla \cdot (FS) = 0 \]

\[ F = I + \nabla u \]

\[ S = S^p + JF^T \sigma^a (s_{weak}^{n+1}, u) F^{-T} \]

\[ S^p = \partial \Psi / \partial E \]
The three sub-problems can be solved in sequence for each time step

- **Cell model ODE system:**
  - Generalized Rush-Larsen or SDIRK with adaptive step

- **Bidomain model**
  - Fully implicit backward Euler time discretization
  - Finite Element spatial discretization
  - Block preconditioner based on geometric multigrid

- **Elasticity**
  - FE on coarse mesh (from GMG grid hierarchy)
  - Newton’s method for solving non-linear equations
Linearization of active tissue mechanics
The “standard” method is to linearize 2nd Piola-Kirchoff stress wrt Green-Lagrange strain

\[ \nabla \cdot (FS) = 0 \]

\[ F \approx F^n + \frac{\partial F}{\partial u} \Delta u = F^n + \nabla(\Delta u) \]

\[ S \approx S^n + \frac{\partial S}{\partial u} \Delta u = S^n + D\Delta E \]

leads to the following FE stiffness matrix formulation

\[ B_{ij} = \int_\Omega (\nabla \phi_i : \nabla \phi_j S + F^T \nabla \phi_i : D : F^T \nabla \phi_j ) dV \]
The classic approach is well suited for hyper-elasticity, but not for the active stress component

\[
S_{ij}^{n+1} \approx S^n + D_{ijkl} \Delta E_{kl}
\]

\[
D_{ijkl} = \frac{\partial S_{ij}}{\partial E_{kl}} = \frac{\partial^2 W}{\partial E_{ij} \partial E_{kl}} + \frac{\partial S^a_{ij}}{\partial E_{kl}} \left\{ \begin{array}{l}
\frac{\partial^2 W}{\partial E_{ij} \partial E_{kl}} \\
\frac{\partial}{\partial E_{kl}} (JF^T \sigma^a (s, \lambda, \dot{\lambda}) F^{-T})
\end{array} \right\}
\]

\[
E = \frac{1}{2} (F^T F - I)
\]
We can also linearize the 1st PK stress with respect to the deformation gradient

\[ \nabla \cdot P = 0 \quad P = FS \]

\[ P^{n+1} \approx P^n + A \Delta F \]

We get an alternative stiffness matrix, based on the first elasticity tensor:

\[ B_{ij} = \int_{\Omega} (\nabla \phi_i : A : \nabla \phi_j) dV \]
The *first elasticity tensor* is convenient for linearizing the active stress

\[ P_{ij} = \frac{\partial W}{\partial F_{ij}} \]

\[ P_{ij}^{n+1} \approx P^n + A_{ijkl} \Delta F_{kl} \]

\[ A_{ijkl} = \frac{\partial P_{ij}}{\partial F_{kl}} = \frac{\partial^2 W}{\partial F_{ij} \partial F_{kl}} + \frac{\partial P_i^a}{\partial F_{kl}} \]

\[ = \frac{\partial^2 W}{\partial F_{ij} \partial F_{kl}} \left\{ + \frac{\partial}{\partial F_{kl}} (J \sigma^a (s, \lambda, \dot{\lambda}) F^{-T}) \right\} \]
The two linearization methods can also be combined

\[ B_{ij} = \int_{\Omega} (\nabla \phi_i : \nabla \phi_j S^p + F^T \nabla \phi_i : D^p : F^T \nabla \phi_j + \nabla \phi_i : A^a : \nabla \phi_j) dV \]

We use the 2\textsuperscript{nd} elasticity tensor wherever possible, and resort to the more numerically based 1\textsuperscript{st} elasticity tensor only when needed.
To summarize, we investigate the performance of three different linearization methods

1. Applying the product rule for differentiation of $FS$, then compute the final steps numerically. This is standard in hyper-elasticity and yields a FE stiffness matrix involving the second elasticity tensor

2. Applying numerical differentiation directly on $P=FS$, to yield a stiffness matrix based on the first elasticity tensor

3. A mixed approach using the second elasticity tensor for the passive stress and the first elasticity tensor for the active stress
The three linearization methods are applied to three different test cases:

1) Free contraction of tissue slab
2) Passive inflation of bi-v mesh
3) Dynamic simulation on bi-v mesh
Efficiency and robustness improves with consistent linearization

<table>
<thead>
<tr>
<th>Method</th>
<th>1st</th>
<th>2nd</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free contraction (HMT)</td>
<td>144 (1.0)</td>
<td>282 (1.55)</td>
<td>144 (1.19)</td>
</tr>
<tr>
<td>Free contr. (Rice et al)</td>
<td>174 (2.22)</td>
<td>227 (2.42)</td>
<td>174 (2.39)</td>
</tr>
<tr>
<td>Passive inflation</td>
<td>144 (87.3)</td>
<td>144 (87.3)</td>
<td>144 (103.6)</td>
</tr>
<tr>
<td>PV loop (Rice et al)</td>
<td>2326 (1168)</td>
<td>3416 (1562)</td>
<td>2184 (1345)</td>
</tr>
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Total number of iterations (normalized CPU time)
Ongoing work; replace linearization by hand with symbolic, automatic differentiation

def strain_energy(self, K, C_compr, b_ff, b_xx, b_fx):
    F = self.F
    I = self.I
    E = 0.5*(F.T*F - I)
    J = det(F)
    W = (b_ff*E[f,f]**2
         + b_xx*(E[n,n]**2 + E[s,s]**2 + E[n,s]**2)
         + b_fx*(E[f,n]**2 + E[n,f]**2 + 2*E[f,s]**2))
    psi = 0.5*K*(exp(W) - 1) + C_compr*(J*ln(J) - J + 1)
    return psi

    # Total potential energy
Pi = psi*dx - dot(B, u)*dx - dot(T, u)*ds

    # Compute first variation of Pi (directional derivative about u in the direction of v)
F = derivative(Pi, u, v)

    # Compute Jacobian of F
dF = derivative(F, u, du)
Mechano-electric feedback in an infarcted heart
MR images are used to build the FE model of an LV with a large anteroapical infarct
Cardiac electro-mechanics is described with a strongly coupled model


- Bidomain model for signal conduction

- Slightly compressible Fung-type model for passive tissue mechanics

- Linear SAC current:

\[ I_{sac} = m_{sac} (v - E_{sac}), \quad E_{sac} = -6mV \]

\[ m_{sac} = g_{sac} (\lambda - 1) \]
Computed strains are compared with data from tagged MRI
A steady state is reached in 3-4 cardiac cycles

PV Loops

Ca\(^{2+}\) transients

Action potentials
The full cycle simulation clearly reveals the mechanical dysfunction around the infarct.
Simulations reveal severe mechanical changes in the infarct border zone
The effect of SACs is only visible with reduced tissue connectivity in the BZ.
Increasing SAC conductance has opposite effect in remote and border zone region
The ongoing activities are supported by three focused grants from the Research Council of Norway:

- “In Silico Heart Failure – tools for accelerating biomedical research” (J Sundnes et al)
  - Software tools for strongly coupled simulations
  - Fundamental mechanisms of heart failure and mechano-induced arrhythmias

- “Modeling the engineered heart” (S Wall)
  - Investigations of HF therapies based on tissue engineering

- “Center for cardiological innovation” (T Edvardsen, M Maleckar et al)
  - Clinical innovations based on cardiac ultrasound and computational models
  - Assessment of SCD risk, HF therapy planning, etc…