Spatial Scaling in Multiscale Models: A Method for Coupling Agent-based and Finite-element Models of Tissue Remodeling

BiomedicalEngineering
University of Virginia

Jia-Jye Lee[1], Lee Talman[1], Shayn M. Peirce[1, 2], and Jeffrey W. Holmes[1, 2, 3]

[1] Department of Biomedical Engineering, [2] Cardiovascular Research Center, and [3] Department of Medicine, University of Virginia, Charlottesville, VA, USA

Cardiac Biomechanics Group

Introduction

- Cellular activities, extracellular matrix (ECM) homeostasis and remodeling, and tissue mechanics form a mechanobiological feedback loop.
- Multi-scale models that couple agent-based modeling (ABM) to represent cell behaviors and finite element modeling (FEM) to represent tissue mechanics have been used to explore cell-ECM-mechanics interactions in healing myocardial infarcts (Rouillard and Holmes, 2012 and 2014).
- However, one of the challenges in coupling an ABM to an FEM is spatial scaling.
- Furthermore, the two modeling frameworks typically employ different coordinate systems that may be related through nonlinear mappings.

Objective: This study aims to develop a general approach to ABM-FEM coupling that accounts for different spatial scaling in the two model components while allowing the user flexibility to adjust the mesh density of each component independently.

Methods

Agent-based model:

- The agent-based model of cell migration and ECM remodeling was constructed in Repast Simphony (2.3.1).
- A 1-cm square slice of tissue was represented using a 100-by-100 array of GridPoints.

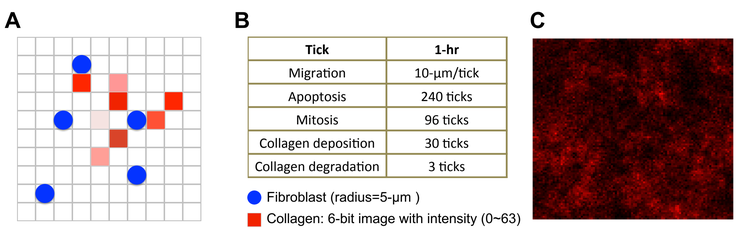

Figure 1: (A) Fibroblasts were modeled as agents with a radius of 5-μm that each occupy one discrete point on an ABM grid and remodel collagen (red). (B) Fibroblasts migrate and replicate without overlapping, deposit and degrade collagen, apoptose after a specified lifetime, and produce (C) a heterogeneous distribution of collagen.

Finite element model:

- A 1-cm square and 2.5-μm thick slab of tissue was simulated as a neo-Hookean material with material properties that varied with local collagen fraction (F_{cf}) using FEBio (v 2.4.2).

$$W = C_1(I_1 - 3),\ C_1 = 2.6\big(1 + 4(F_{cf} - 0.03)/0.27\big).$$

- The slab was loaded in the x direction with a prescribed traction force.

Methods

Coupled simulation procedure:

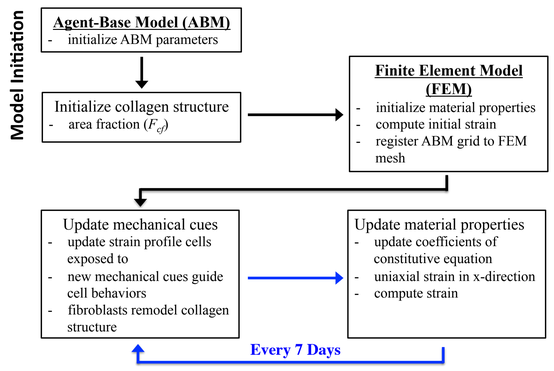

Figure 2: ABM-FEM coupling ran for a total time of 42 days. After every 7 days of simulation, ABM exported collagen amount at each GridPoint to a file that was used to compute new material parameters for each element and FE simulations repeated with strains passed back to the ABM.

Registration of ABM grid to FE mesh:

- The mapping between element coordinates (ξ_1,ξ_2,ξ_3) and physical (i.e., 'real-world') coordinates (x_1,x_2,x_3) is specified by interpolation functions and nodal parameters n_{jk}:

$$\boldsymbol{x_1 = f_1(\xi_i, n_{jk})},\ \boldsymbol{x_2 = f_2(\xi_i, n_{jk})},\ \boldsymbol{x_3 = f_3(\xi_i, n_{jk})}.$$

- Two possible approaches: (1) to establish regularly spaced GridPoints in the ABM and invert equations to identify the corresponding points in element coordinates, or (2) to select evenly spaced points in the FE mesh that correspond to nonuniform physical spacing in the ABM.

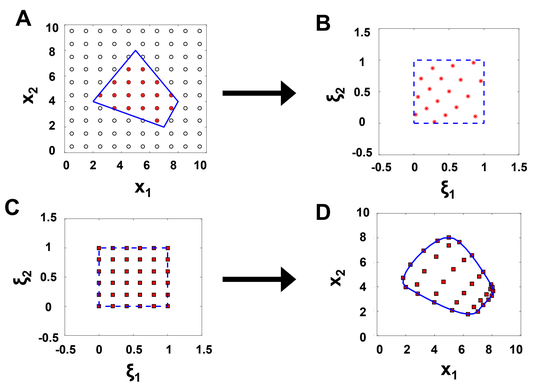

Figure 3: (A) An ABM grid with GridPoints (black hollow circles) in (x_1,x_2) was mapped to a bi-linear FE mesh (blue solid line. (B) (ξ_1,ξ_2) corresponding to each GridPoint inside the element (red dots) were identified. (C) An array of evenly-spaced points within the FE mesh (ξ_1,ξ_2) were selected, and mapped to (D) their nonuniform physical spacing in (x_1,x_2) with a bi-cubic Hermite interpolation.

Case study of FE mesh refinement:

- Spatial correspondence between an ABM and FEM with variable grid/mesh densities (2-by-2 to 50-by-50 elements).

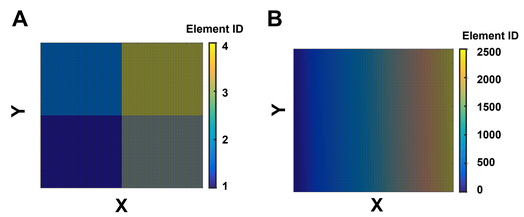

Figure 4: A 100x100 ABM grid was overlaid with (A) 2x2 and (B) 50x50 FE mesh (color code shows element ID).

Results

- Collagen fraction increased from 0.03 at 0 days to 0.28 at 42 days; as collagen accumulated, material stiffness increased, reducing mean strains from 0.08 to approximately 0.02.
- Mesh refinement produced spatial heterogeneity in collagen content and material properties.

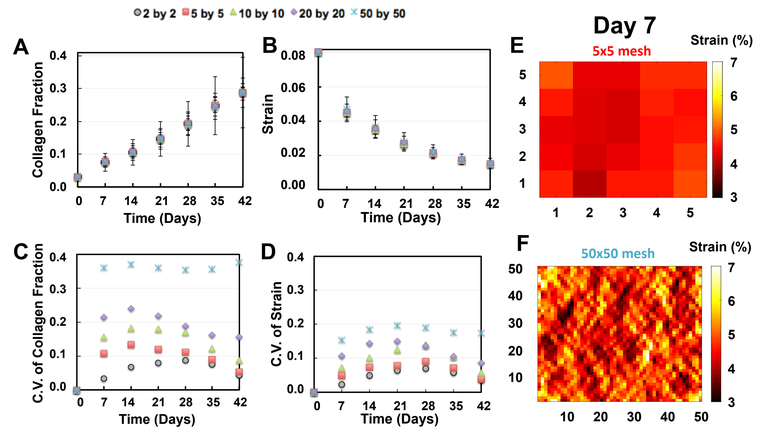

Figure 5: Coupling models with varying FE mesh densities yielded similar (A) overall collagen fraction and (B) strain over a time course of 0-42 days but produced higher variability in (C) collagen content and (D) strain and more spatial heterogeneity in strain (E, 5x5 mesh, F 50x50 mesh at Day 7) as the number of elements increased.

Summary and Future Works

- A general approach was developed to establish spatial correspondence between an agent-based model grid and a finite-element model mesh.
- Refining the FE mesh actually increased strain differences between adjacent elements in the FEM.
- This heterogeneity will have significant nonlinear effects in our coupled model once strain is allowed to feed back on collagen deposition and degradation in the ABM.

References

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