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Numerical Modeling of Mechanobiological Remodeling and Fibrotic Progression in Soft Tissues Under Repeated Mechanical Trauma

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1. Introduction

Soft-tissue fibrosis is a pathological remodeling occurring in dermis, skeletal muscle, fascia, myocardium, and connective tissues following chronic injury or repeated trauma. Fibrosis is frequently described in organ-specific contexts. Its underlying mechanobiological cascade remains largely universal, and characterized by persistent inflammatory signaling involving cytokine release, fibroblast recruitment, excessive collagen deposition, progressive tissue stiffening, with Young's modulus (E) typically increasing by a factor of 2 to 10, ultimately impairing physiological function (Tschumperlin et al., 2018). Repeated trauma due to cyclic loading are increasingly recognized as key determinants of pathological tissue repair. Mechanical impacts activate mechanosensitive cellular pathways, and alter extracellular matrix (ECM) turnover. However, fibrotic progression has not yet been quantitatively related to the trauma frequency because of the lack of longitudinal data. The objective is here to develop a generic computational framework for describing fibrotic remodeling in soft tissues subjected to repeated mechanical deformation. A mechanobiological reaction–diffusion model of cytokines, fibroblasts, and collagen is coupled with a finite element mechanical model, enabling local collagen accumulation to progressively alter tissue stiffness.

2. Methods

Fibrotic remodeling was modeled using three coupled biological fields: cytokine concentration C, fibroblast density F, and collagen concentration *Coll* within a $1\,cm^3$ cube of soft tissue.

Cytokine equation

$$\frac{\partial C}{\partial t} = D_C \nabla^2 C + p_C\, C \frac{F}{F + s_F} - d_C\, C$$

Fibroblast equation

$$\frac{\partial F}{\partial t} = D_F \nabla^2 F + p_F\, C\left(1 - \frac{F}{s_F}\right) - d_F\, F - \chi \nabla\left(\frac{F}{1 + F.s_F} \nabla C\right)$$

Collagen equation

$$\frac{\partial Coll}{\partial t} = D_{Coll} \nabla^2 Coll + p_{Coll}\, F\left(1 - \frac{Coll}{s_{Coll}}\right) - d_{Coll}\, Coll$$

Boundary conditions

$$\frac{\partial C}{\partial n} = 0, \quad \frac{\partial F}{\partial n} = 0, \quad \frac{\partial Coll}{\partial n} = 0 \quad \text{on } \textit{cube faces}$$

The parameter values are reported in Table 1.

A quasi-static deformation of 10% was applied to the cube through a central 0.5 cm×0.5 cm area located on the z=1 face, while the opposite face was fixed. This loading condition was selected based on experimental evidence showing that strain levels of this magnitude are

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sufficient to trigger inflammation and ECM remodeling (Anloague et al., 2020; Guo et al., 2022).

To focus mainly on the underlying mechanobiological processes, the tissue was here represented as a linear elastic material whose stiffness, E=3kPa at t=0, could evolve linearly with collagen content: $E_{new} = E_{old} + aColl$, with $a = 100$.

We simulate various cyclic deformation frequencies: 1/y, 2/y and 1/m.

Biochemical equations were discretized using a custom finite-difference solver based on an explicit time integration scheme. Mechanical response was computed using FEbio. Weak coupling strategy solve sequentially biochemical and mechanical subproblems.

Table 1. Parameter values used in the model (Avner & Wenrui, 2017; Hillen & Painter, 2009).

Parameters		Value	Unit
C_0	Cytokine concentration at t=0	0	g/cm^3
F_0	Fibroblast concentration at t=0	4.75E-3	g/cm^3
$Coll_0$	Collagen concentration at t=0	3.26E-3	g/cm^3
D_C	Cytokine Diffusion Coeff	1.08E-2	cm^2/d
D_F	Fibroblast Diff. Coeff	1.47E-7	cm^2/d
D_{Coll}	Collagen Diffusion Coeff	4.59E-12	cm^2/d
p_C	Cytokine production rate	9.64E-2	d^{-1}
p_F	Fibroblaste production rate	5.0E-4	d^{-1}
p_{Coll}	Collagen production rate	6.0E-5	d^{-1}
d_C	Cytokine degradation rate	2.376E-1	d^{-1}
d_F	Fibroblast apoptosis rate	1.66E-2	d^{-1}
d_{Coll}	Collagene degradation rate	6.0E-5	d^{-1}
s_F	Fibroblaste saturation	3.0E-2	g/cm^3
S_{Coll}	Collagen saturation	1.0E-1	g/cm^3

3. Results and discussion

Simulations of a single mechanical deformation show an immediate cytokine response (fig.1) lasting approximately 48 hours. Fibroblast density peaks between 2 and 5 days before progressively decreasing as cytokine levels fall below the activation threshold. In contrast, collagen accumulation occurs over much longer timescales, reaching its maximum after approximately 3 months and slowly returning toward baseline over more than one year. Repeated trauma applied every month maintain cytokine levels, fibroblast activation, sustained collagen synthesis and leads to tissue stiffening (fig.1). Impacted area exhibits severe fibrotic stiffening (E=14kPa) while most of the domain converges toward a moderately elevated stiffness level (E=6kPa), indicating diffuse fibrotic remodeling. By contrast, simulations with trauma applied every 6 months show substantially reduced collagen accumulation and lower final stiffness values, suggesting partial biological recovery between trauma events. Annual trauma simulations further support this trend, with collagen concentration beginning to decrease over long timescales, consistent with partial tissue repair. These results suggest that some trauma frequencies by maintaining inflammatory could be a primary driver of pathological fibrotic progression with irreversible scar collagen deposition. The current model captures a

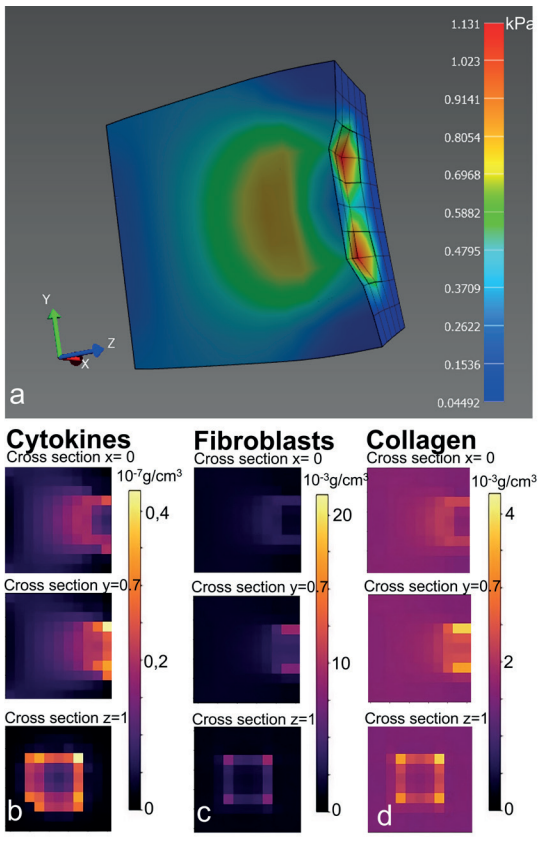

Figure 1. (a) Cubic soft-tissue volume illustrating the effective stress (kPa) state at the 9th impact, after previous impacts applied at a rate of one every month. Cross-section views of distributions in tissue, of cytokines (b) following the first impact, and of fibroblasts (c) and collagen (d) 60 days after the first impact.

plausible post-traumatic remodeling dynamic consistent with current mechanobiological understanding.

Building on this in silico proof of concept, the model is currently being extended to cardiac tissue to investigate how stretch-induced fibrosis may alter subsequent contractile function.

4. Conclusions

This study presents a generic mechanobiological computational framework for post-traumatic fibrosis in soft tissues. The coupled biological–mechanical model reproduces key features of fibrotic progression, including persistent cytokine activation, fibroblast recruitment, collagen accumulation, and localized tissue stiffening. The simulations highlight the major role of trauma frequency in determining whether tissue remodeling remains reversible or progresses toward chronic fibrosis. This framework provides a foundation for predictive modeling of post-traumatic soft-tissue degeneration and could support future clinically informed diagnostic tools. As a future perspective, a visco-hyperelastic constitutive model combined with high-rate dynamic loading conditions could be implemented to better capture the mechanical response of soft tissues during impact events.

Contributor Roles

CD: Conceptualization, Methodology, Writing original draft; Validation: JLM: Conceptualization, Supervision, Writing – review & editing, Funding acquisition.

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