Modeling Fluid-Structure Interaction of Biodegradation in Engineered Tissue Scaffolds

Priyanka Patki
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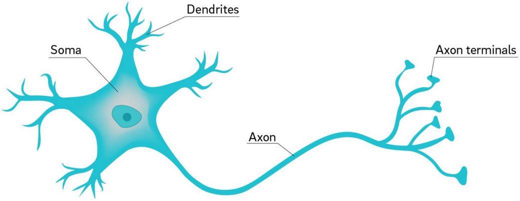
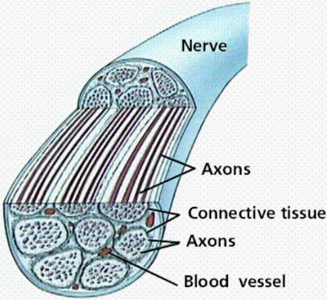
Overview

Introduction

Neurons and nerves



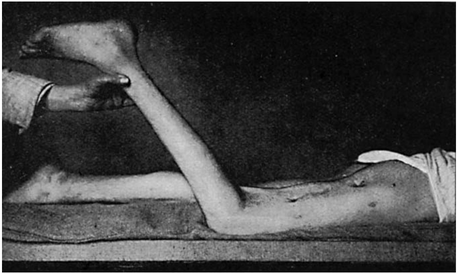


- A neuron [1]
- Carries messages brain ↔ body

- Cross section of a nerve [2]
- Bundle of axons

[1] https://ucsdnews.ucsd.edu/pressrelease/why_are_neuron_axons_long_and_spindly
[2] Purves *et al.*, Life: The Science of Biology, 4th Edition

Nerve injuries



[1]Zochodne, Douglas W. Neurobiology of peripheral nerve regeneration. Cambridge, UK: Cambridge University Press, 2008

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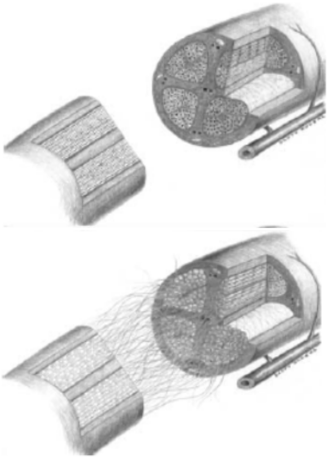
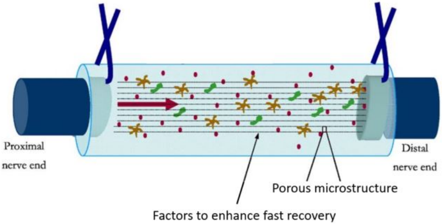


- Loss of sensation or motor control
- Large gap: Mis-alignment of regrowing fibres

[1] Zochodne, Douglas W. Neurobiology of peripheral nerve regeneration. Cambridge, UK: Cambridge University Press, 2008

Tissue Engineered Nerve Guidance Channels

A typical nerve regeneration scaffold [1]



- Biocompatible
- Porous
- Mechanical strength
- Biodegradable

Chemo-mechanical coupling

[1] Bellamkonda, R.V., Biomaterials, 27(19):3515-3518, 2006.

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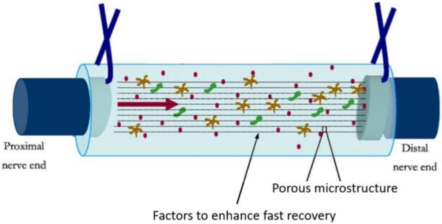

Components:

- Porous degrading solid
- Base fluid
- Product of degradation (Monomer)

Reactive Fluid-Structure Interaction (FSI)

[1] Bellamkonda, R.V., Biomaterials, 27(19):3515-3518, 2006.

Modelling of degrading porous scaffolds

Incompressibility, Saturation and Mass balance:

- Mixture theory

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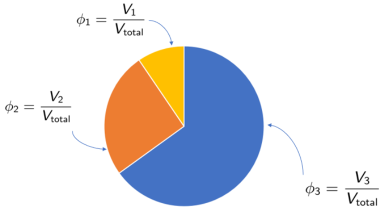
$$\frac{\partial \rho_a}{\partial t} + \nabla \cdot (\rho_a \mathbf{v}_a) = \hat{c}_a$$

- Saturation condition: $\sum_{a=1}^{N} \phi_a = 1$



Momentum balance

After deriving constitutive relationships, we get:

- Balance of momentum - solid

$$-\nabla \cdot \mathrm{T}^e - \rho_s \mathbf{b}_s + \phi_s \nabla p - \phi_1^2 \frac{\mu_1}{\kappa_s}(\mathbf{v}_1 - \mathbf{v}_s) - \phi_2^2 \frac{\mu_2}{\kappa_s}(\mathbf{v}_2 - \mathbf{v}_s) = \mathbf{0},$$

- Balance of momentum - fluid (f=1,2)

$$-\rho_f \mathbf{b}_f + \phi_f \nabla p + \phi_f^2 \frac{\mu_f}{\kappa_s}(\mathbf{v}_f - \mathbf{v}_s) = \mathbf{0},$$

- Fluid-Solid interaction: Non-linear, Darcy flow-like term
  - μ_f: viscosity of fluid
  - κ_s: permeability of porous solid
- Non-linear PDEs

COMSOL Implementation

FEM Implementation

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FEM Implementation

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- 8 variables...
  - Three velocities: $\mathbf{v}_s,\ \mathbf{v}_1,\ \mathbf{v}_2$
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  - Volume fractions: $\phi_s,\ \phi_1,\ \phi_2$
  - Pressure: p

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Eulerian strong form

$\longrightarrow$ ALE strong form

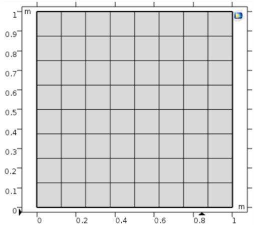
$\longrightarrow$ ALE weak form

$\longrightarrow$ Descretized weak form $\longrightarrow$ COMSOL Multiphysics

COMSOL Implementation

COMSOL Multiphysics $\longrightarrow$ Mathematics Module $\longrightarrow$ Weak form PDE

Choice of finite elements



- Square domain, side = 1 m.
- Descretized into square cells
- "Swept mesh": element size = $\frac{1}{h}$ m.

- Lagrange polynomial interpolation for all variables
- In order to satisfy the *inf-sup* or *Brezzi-Babuska* condition:
  - Degree of interpolation of scalars is one less that of vectors:
  - Lagrange quadratic elements for vectors, linear for scalars
  - Lagrange cubic and quadratic elements for vectors and scalars respectively.

Numerical Scheme - Method of Manufactured Solutions

- FEM implementation tested using Method of Manufactured Solutions:
  1. Impose a known solution for all variables
  2. Derive force fields and boundary conditions
  3. Solve the problem and compare solution with the imposed manufactured solution
- Basically, we check if our numerical scheme gives us correct solutions of a problem with known solutions

Numerical Scheme - Method of Manufactured Solutions

- Example: Velocity of fluid
  1. Imposed 'Solution' - radially varying sinusoidal function:
     $v_x = v_0 \cos\left(2\pi \frac{t}{t_0}\right) \sin\left(2\pi \frac{x^2+y^2}{L^2}\right)$
  2. Derive force fields and boundary conditions by substituting into governing equations
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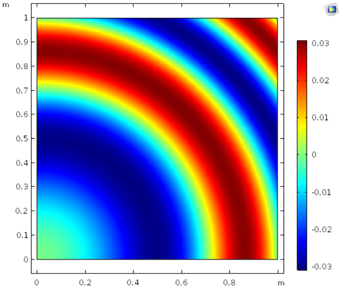
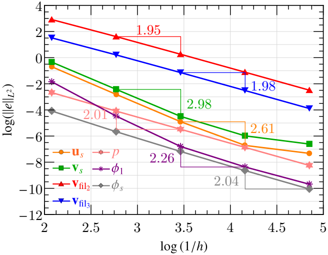
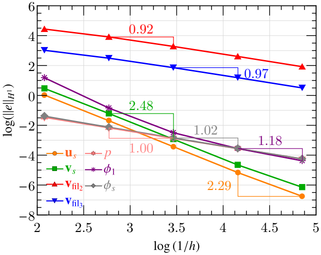


Convergence analysis

- Convergence analysis carried out by performing parametric sweep over mesh size: $h = 1/8, 1/16, 1/32, 1/64, 1/128m$
- Postprocessing: "Global integration" feature
  - L^2 error norm: $\log(||e||_{L^2}) = \frac{||a_{sol} - a_{MS}||}{||a_{MS}||}$
  - H^1 error semi-norm: $\log(||e||_{H^1}) = \frac{||\nabla a_{sol} - \nabla a_{MS}||}{||\nabla a_{MS}||}$





Convergence rates when quadratic elements for vectors and linear elements for scalars are used.

Closing remarks

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- Summary
  - Mixture theoretic model to study chemistry-mechanical property evolution of degrading scaffolds developed
  - COMSOL implementation of the FEM model tested using Method of Manufactured Solutions for stability and accuracy
- Ongoing and future work
  - Experimental validation of numerical model for degradation mechanisms of actual TENG materials

- We gratefully acknowledge the support by the National Science Foundation grants CMMI 1537008 and CBET 1705854.

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Appendix

Parameter	Value
m_s	$3e3kg/ms^2$
μ_2	$1e-3kg/sm$
μ_3	$1.5e-3kg/sm$
κ_s	$1e-3m^2$

$$\mathbf{u}_s = \bar{u}_s \sin\left(\frac{2\pi t}{t_0}\right) \left[\cos\left(2\pi\frac{x+y}{L}\right)\imath + \sin\left(2\pi\frac{x-y}{L}\right)\jmath\right], \tag{1}$$

$$\mathbf{v}_{\text{fil}_2} = \bar{v}_{\text{fil}_2} \cos\left(\frac{2\pi t}{t_0}\right) \left[\sin\left(2\pi\frac{x^2+y^2}{L^2}\right)\imath + \cos\left(2\pi\frac{x^2-y^2}{L^2}\right)\jmath\right], \tag{2}$$

$$\mathbf{v}_{\text{fil}_3} = \bar{v}_{\text{fil}_3} \cos\left(\frac{2\pi t}{t_0}\right) \left[\cos\left(2\pi\frac{x^2}{L^2}\right)\sin\left(2\pi\frac{y^2}{L^2}\right)\imath + \sin\left(2\pi\frac{x^2-y^2}{L^2}\right)\jmath\right], \tag{3}$$

$$p = \bar{p}\sin\left(\frac{2\pi t}{t_0}\right)\sin\left(2\pi\frac{x+y}{L}\right), \tag{4}$$

$$\phi_2 = \check{\phi}_2 + \bar{\phi}_2\cos\left(\frac{2\pi t}{t_0}\right)\cos\left(2\pi\frac{x+y}{L}\right), \tag{5}$$

$$\phi_s = \check{\phi}_s + \bar{\phi}_s\sin\left(\frac{2\pi t}{t_0}\right)\sin\left(2\pi\frac{x+y}{L}\right), \tag{6}$$

Constant	Value
$\bar{u}_s$	$0.001m$
$\bar{v}_{\text{fil}_1}$	$0.1m/s$
$\bar{v}_{\text{fil}_2}$	$0.1m/s$
$\bar{p}$	$1Pa$

Constitutive Relations for $\hat{\mathbf{p}}_a$ and T_a

- Mass balance:

$$\frac{\partial \phi_a}{\partial t} + \nabla \cdot (\phi_a \mathbf{v}_a) = \frac{\hat{c}_a}{\gamma_a}$$

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- Second law of thermodynamics:

$$-\sum_{a=1}^{N} \grave{\Psi}_a - \sum_{a=1}^{N} \mathrm{tr}\left((\Psi_a \mathrm{I} - \mathrm{T}_a^{\mathrm{T}})\nabla \mathbf{v}_a\right) - \sum_{a=1}^{N} (\hat{\mathbf{p}}_a + \frac{1}{2}\hat{c}_a(\mathbf{v}_a - \mathbf{v}_1))\cdot(\mathbf{v}_a - \mathbf{v}_1) \geq 0,$$

- $(\hat{\mathbf{p}}_a, \mathrm{T}_a, \Psi_a)$ are assumed to be functions of $(\mathrm{C}_s, \phi_a, \mathbf{v}_a)$ and their gradients

Ψ_a: Helmholtz free energy

Constitutive Relations for $\hat{\mathbf{p}}_a$ and T_a

- Combining the two, we get a 'Variational inequality' and a Lagrange multiplier, P,

$$
-\sum_{a=1}^{N} \dot{\Psi}_a - \sum_{a=1}^{N} \mathrm{tr}\left((\Psi_a \mathsf{I} - \mathsf{T}_a^{\mathrm{T}})\nabla \mathbf{v}_a\right) - \sum_{a=1}^{N}(\hat{\mathbf{p}}_a + \frac{1}{2}\hat{c}_a(\mathbf{v}_a - \mathbf{v}_1)) \cdot (\mathbf{v}_a - \mathbf{v}_1)
$$

$$
+P\left(\frac{\partial \phi_a}{\partial t} + \nabla \cdot (\phi_a \mathbf{v}_a) - \frac{\hat{c}_a}{\gamma_a}\right) \geq 0
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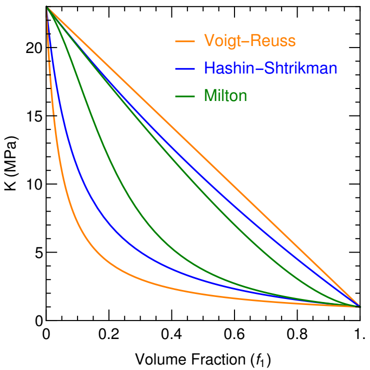
  - Constitutive relations for T_a and $\hat{\mathbf{p}}_a$
  - P, the Lagrange multiplier, represents the 'base' pressure in the system.

Elastic properties

($K_1 = 1\ MPa,\ K_2 = 23\ MPa, G_1 = 1\ MPa$ and $G_2 = 50\ MPa$)



[1]Voigt, L., Lehrbuch der Kristallphysik. (mit Ausschluss der Kristalloptik), 1910
[2]Reuss, A., ZAMM - Journal of Applied Mathematics and Mechanics, 9(1):49-58, 1929
[3]Hashin *et al.*, Journal of the Mechanics and Physics of Solids, 10(4):343-352, 1962
[4]Milton, G. W., Physical Review Letters, 46(8):542-545, 1981

Transport properties

- **Effective diffusion coefficient**[1]
  Brownian motion of fluid particles hindered by porous structure
  - Hashin-Shtrikman (Volume fraction only)

$$\frac{D_e}{D_1} = \frac{2}{2 + f_2},$$

  - Ogston - low density approximation (Volume fraction only)

$$\frac{D_e}{D_1} = 1 - \frac{2}{3} f_2,$$

  - Torquato approximation (S_2 and higher order functions)

$$\frac{D_e}{D_1} = \frac{1}{1 - f_2} \frac{(1 + \frac{1}{2}\frac{\gamma_2}{\xi_2} - \frac{1}{2}\xi_2) + (-1 + \frac{1}{2}\frac{\gamma_2}{\xi_2} - \frac{1}{2}\xi_2) f_2}{(1 + \frac{1}{2}\frac{\gamma_2}{\xi_2} - \frac{1}{2}\xi_2) + (\frac{1}{2} + \frac{1}{2}\frac{\gamma_2}{\xi_2} + \frac{1}{4}\xi_2) f_2}$$

    - f_2 - Volume fraction of solid phase
    - $\xi_i, \ \gamma_i$ - parameters derived using $S_2, \ S_3, \ S - 4$

[1] Jiao *et al.*, Physical Biology, 9(3):1-13, 2012