Modeling and simulation of tissue dynamics
ECMI Modelling Week 2024

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**Introduction**

Tissues are formed by a mixture of cells, liquid with dissolved chemicals, and a matrix that keeps the cells together.

► **Goal**: simulate water absorption in a simple geometry driven by cell death due to some kind of damage (mechanical or chemical).

► **Idea**: use volume fractions to describe the amount of alive and dead cells at each location and the flow of water.
Applications

Swelling is any abnormal enlargement of a body part, result of inflammation or a buildup of fluid. Edema describes swelling in the tissue outside of the joint, and effusion describes swelling that is inside a joint, such as a knee.
Variables

Let introduce some useful variables:

- $\varphi_a$ is the volume fraction of alive cells;
- $\varphi_d$ is the volume fraction of dead cells;
- $\varphi_f$ is the volume fraction of fluid;
- $c_n$ is the concentration of nutrients;
- $c_p$ is the concentration of toxicant;
- $c_m$ is the concentration of medicine;
- $v_b$ is the velocity of biomass (dead and alive cells);
- $v_f$ is the velocity of fluid (water);
- $p$ is the pressure.

Note: $\varphi_b + \varphi_f = 1$, where $\varphi_b = \varphi_a + \varphi_d$, $0 \leq \varphi_b, \varphi_f \leq 1$. 
Our model

Remind the volume fractions $\varphi_a, \varphi_d, \varphi_f$, the concentrations $c_n, c_p$ and the velocities $\mathbf{v}_b, \mathbf{v}_f$

\[
\begin{align*}
\partial_t \varphi_a + \text{div}(\varphi_a \mathbf{v}_b) &= k_b \frac{c_n}{c_n + K_n} \varphi_a - k_d \frac{c_p}{c_p + K_p} \varphi_a \\
\partial_t \varphi_d + \text{div}(\varphi_d \mathbf{v}_b) &= k_d \frac{c_p}{c_p + K_p} \varphi_a \\
\partial_t \varphi_f + \text{div}(\varphi_f \mathbf{v}_f) &= -k_b \frac{c_n}{c_n + K_n} \varphi_a \\
\partial_t c_n + \text{div}(\mathbf{v}_f c_n) - \text{div}(D_n \nabla c_n) &= -k_n \frac{c_n}{c_n + \hat{K}_n} \varphi_a \\
\partial_t c_p + \text{div}(\mathbf{v}_f c_p) - \text{div}(D_p \nabla c_p) &= -k_p \frac{c_p}{c_p + \hat{K}_p} \varphi_a
\end{align*}
\]

with positive constants $k_b, k_d, k_n, k_p$ (rates of birth, death, nutrient and toxicant absorption), $K_n, K_p, \hat{K}_n, \hat{K}_p$ (half saturations), $D_n, D_p$ (diffusivities).
Goal: Check that a concentration of poison increases the volume fraction of dead biomass. Let’s consider:

- \( \Omega = [0, 1] \times [0, 1] \);
- \( c_n \) as a constant;
- \( c_p \) equal to a narrow gaussian centered at the middle point of the lower boundary;
- \( \varphi_f = 0.5, \varphi_a = 0.5, \varphi_d = 0 \) as initial conditions;
- zero Neumann boundary conditions where needed\(^1\);
- the two velocities small and constant at the beginning.

\(^1\)zero Neumann boundary conditions are needed where the scalar product of the normal and the velocity has the right sign
Solution
**Goal:** Check that water can enter the poisoned region where cells are dying driven by poison and death. Let’s consider:

- $\Omega = [0, 1]$ (discard the $x$-dimension by symmetry);
- $c_p$ equal to a decreasing hyperbolic branch;
- $c_n$ equal to a constant;
- $\varphi_d(y, 0)$ decreasing function;
- nonzero boundary conditions at the bottom for $\varphi_d$ because of the condition $v_f \cdot n < 0$. 
Remind the volume fractions $\varphi_a, \varphi_d, \varphi_f$, the concentrations $c_n, c_p$, the velocities $v_b, v_f$ and the pressure $p$. We have the elliptic problem:

$$
\nu' \partial_y^2 v_{b,2} = P' \partial_y p + \Pi' \partial_y c_p
$$

$$
\frac{\rho}{T} k_h(\epsilon) P' \partial_y^2 p = \partial_y v_{b,2} + \frac{\rho}{T} k_h(\epsilon) \Pi' \partial_y^2 c_p
$$

$$
v_{f,2} = v_{b,2} - P' \frac{\rho}{T} k_h(\epsilon) \frac{1}{\epsilon} \partial_y p
$$

$$
\partial_t \varphi_f + \partial_y (\varphi_f v_{f,2}) = -k'_b \frac{c_n}{c_n + 1} (1 - \varphi_f - \varphi_d)
$$

with $k_h(\epsilon) = \epsilon^2 a$ and $\nu', P', \Pi', \rho, T, a$ constants. Let $v_{b,2}(0) = 0 = v_{b,2}(1) = 0$ and $\varphi_f(y, 0) = \epsilon > 0$ small. Boundary conditions for $p$ should be Dirichlet.
Test 2

\[ \phi_a \]

\[ \phi_d \]

\[ \phi_f \]

\[ c_p \]
We wanted to get the excess water out the tissue by removing the toxicant and applying a concentration of a medicine.
Conclusion

- Multi phase flow-model for tissues, including volume fractions of alive and dead cells, concentrations of toxicants and medicines.

- Test cases addressed:
  - cell death by toxicity
  - water intake by tissues to diminish toxic effects
  - medicine usage to extract excess water

- Need to improve results considering tissue / channel system to be addressed by FEM.
Thank you for your attention