Boundary Integral Method for Coupled Biofilm Gel/Fluid Problems

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Outline

- Background
- Motivating Experiments
- Mathematical Model - Fixed Domain
- Mathematical Model - Viscous Fluid
- Mathematical Model - Gel

What is a Biofilm?

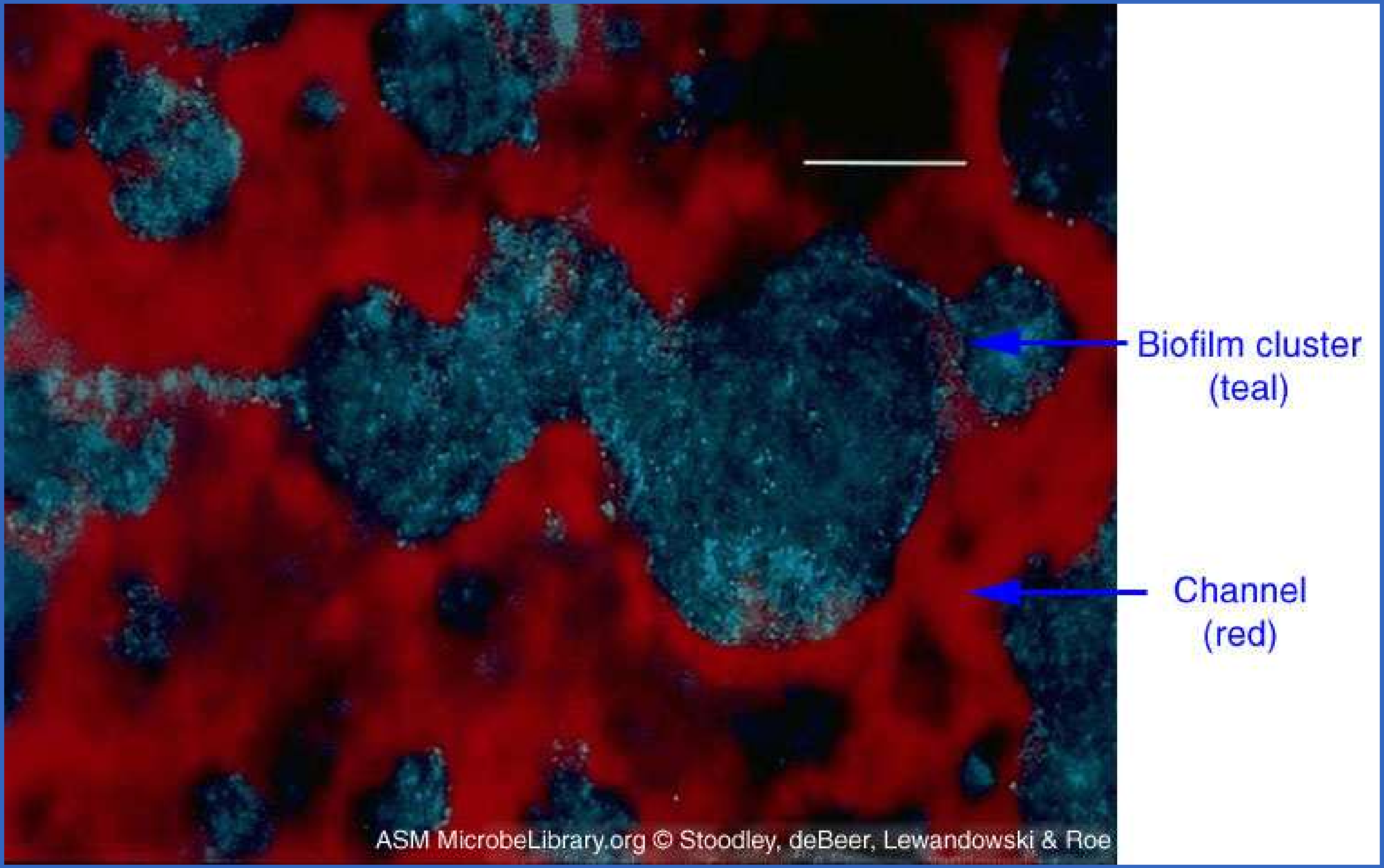
Basics:

- An aggregate of polymer-producing bacteria
- Polymer (EPS)
  - Primary organic matter (50 - 90 %)
  - Composed of polysaccharide, proteins, nucleic acids
  - forms a hydrogel
- Typically multiple species of bacteria and growth limiting substrates

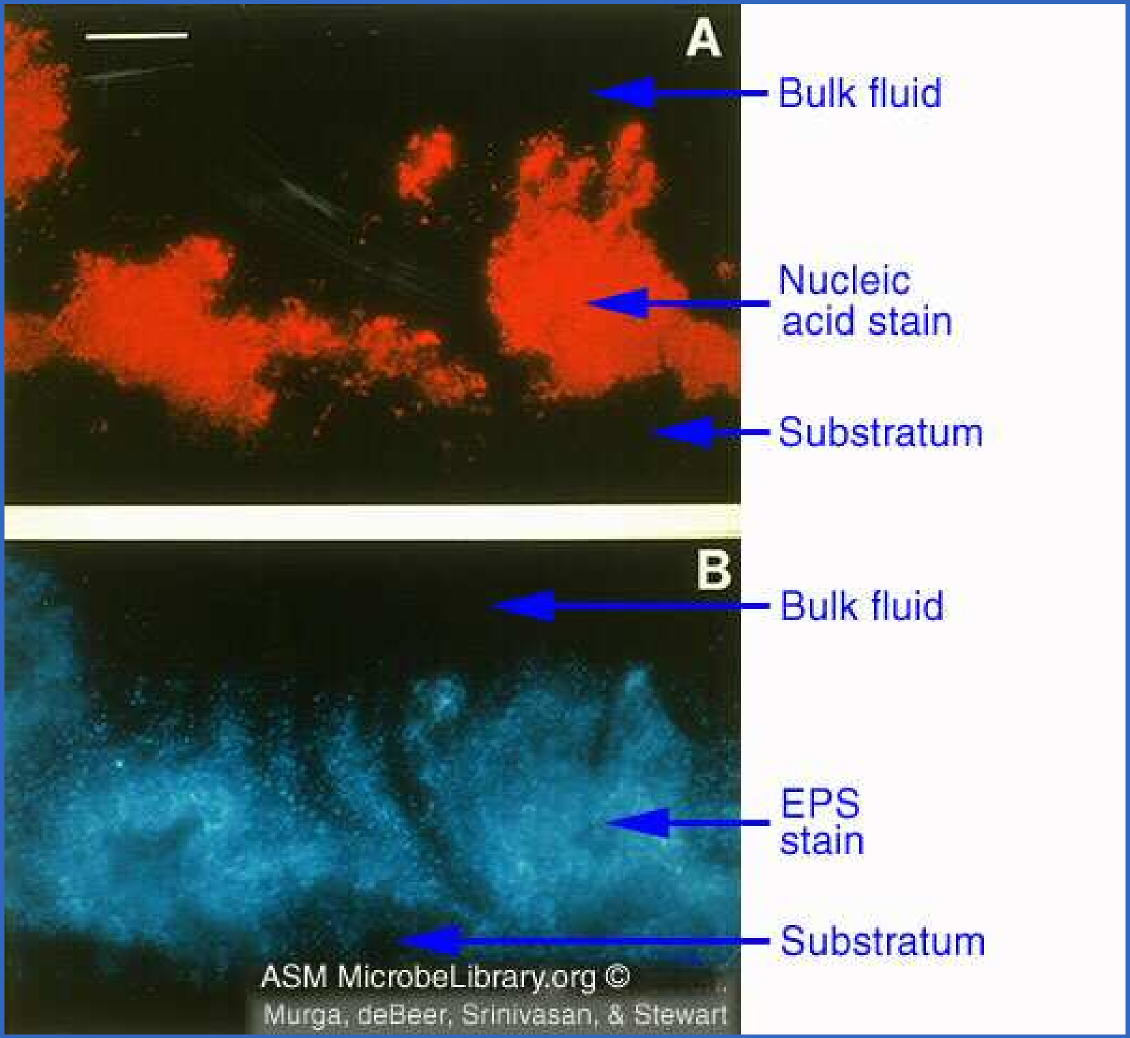
Multiple Scales

- Length scales
  - Bacteria $\approx$ 10 μ m
  - Cluster $\approx$ 100 μ m
  - Thickness $\approx$ 1000 μ m
  - Fluid Domain $\approx$ mm - cm
- Time Scales
  - Diffusion $\approx$ seconds
  - Relaxation time $\approx$ minutes
  - Growth $\approx$ hours

Experimental View I



Experimental View II



Motivating Experiment - Deformation

movie

This time-lapse video sequence shows Staphylococcus aureus biofilm cell clusters in a glass flow cell stretching and contracting as the flow rate of the nutrient feed is turned up and down between 0 and 9.3 ml/min.

Plan of Attack

- Short time - Fixed Interface:
  - Slowed Penetration: Degradation, adsorption or synthesis
  - Disinfection: Physiological Resistance - Non-respiring $\Longrightarrow$ lowered susceptibility
  - Negligible Growth
  - Fixed Domain
  - **Compare with viability data**

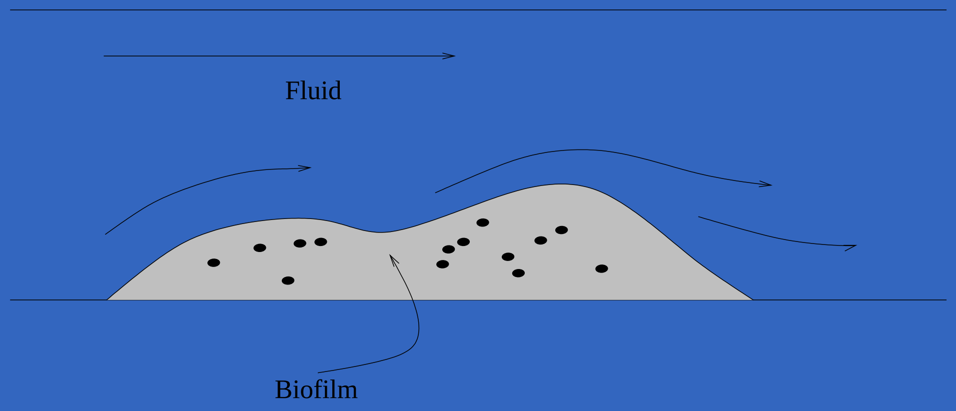
Plan of Attack cont’d

- Intermediate time - Free Interface
  - Negligible Growth
  - Fluid induced deformation of the biofilm
  - Viscous motion (time-scale longer than relaxation time-scale)
  - **Stress profiles**

Plan of Attack Cont'd

- Long time - Free Interface and gel structure
  - Osmotic Pressure
  - Include growth of the domain
  - **Multi-species competition**

Short time - Fixed Domain Equations

- 

- Fluid Dynamics

$$\mu \Delta \mathbf{U} = \nabla p - \mathbf{F}$$
$$\nabla \cdot \mathbf{U} = 0$$

Equations - cont'd

- Substrate

$$\frac{D}{Dt}S(\mathbf{x},t) = \underbrace{\nabla \cdot (D_s \nabla S(\mathbf{x},t))}_{\text{Diffusion}} - \underbrace{\mu_s \frac{S}{K_s + S} B(\mathbf{x},t)}_{\text{Consumption}}$$

- Biocide

$$\frac{D}{Dt}A(\mathbf{x},t) = \underbrace{\nabla \cdot (D_a \nabla A(\mathbf{x},t))}_{\text{Diffusion}} - \underbrace{H_a(A,N)}_{\text{Reaction}}$$

Mathematical Model: Equations cont'd

- Neutralizer

$$\frac{\partial N(\mathbf{x},t)}{\partial t} = -k_r Y_n A N$$

- Bacteria

$$\frac{\partial B}{\partial t} = -\kappa Y \mu_s A \frac{S}{K_s + S} B$$

Mathematical Issue: Fluid Dynamics

Main challenge - irregular geometry

- Standard finite difference discretization prone to errors
- Other possible methods: Finite elements, non-standard stencils
- Looking ahead to moving interface

Regularized Stokeslets

- Begin with a background flow

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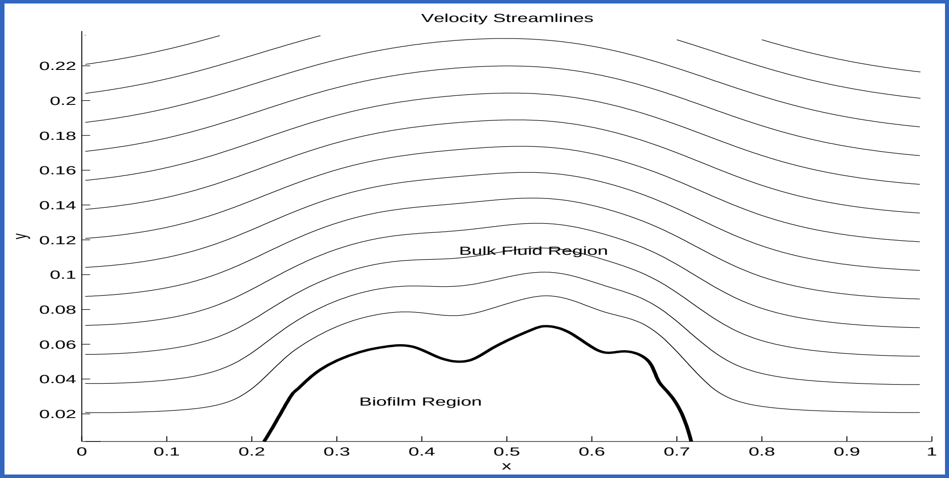
- Flow around obstacles is the sum of background flow and those due to forces

Regularized Stokeslets

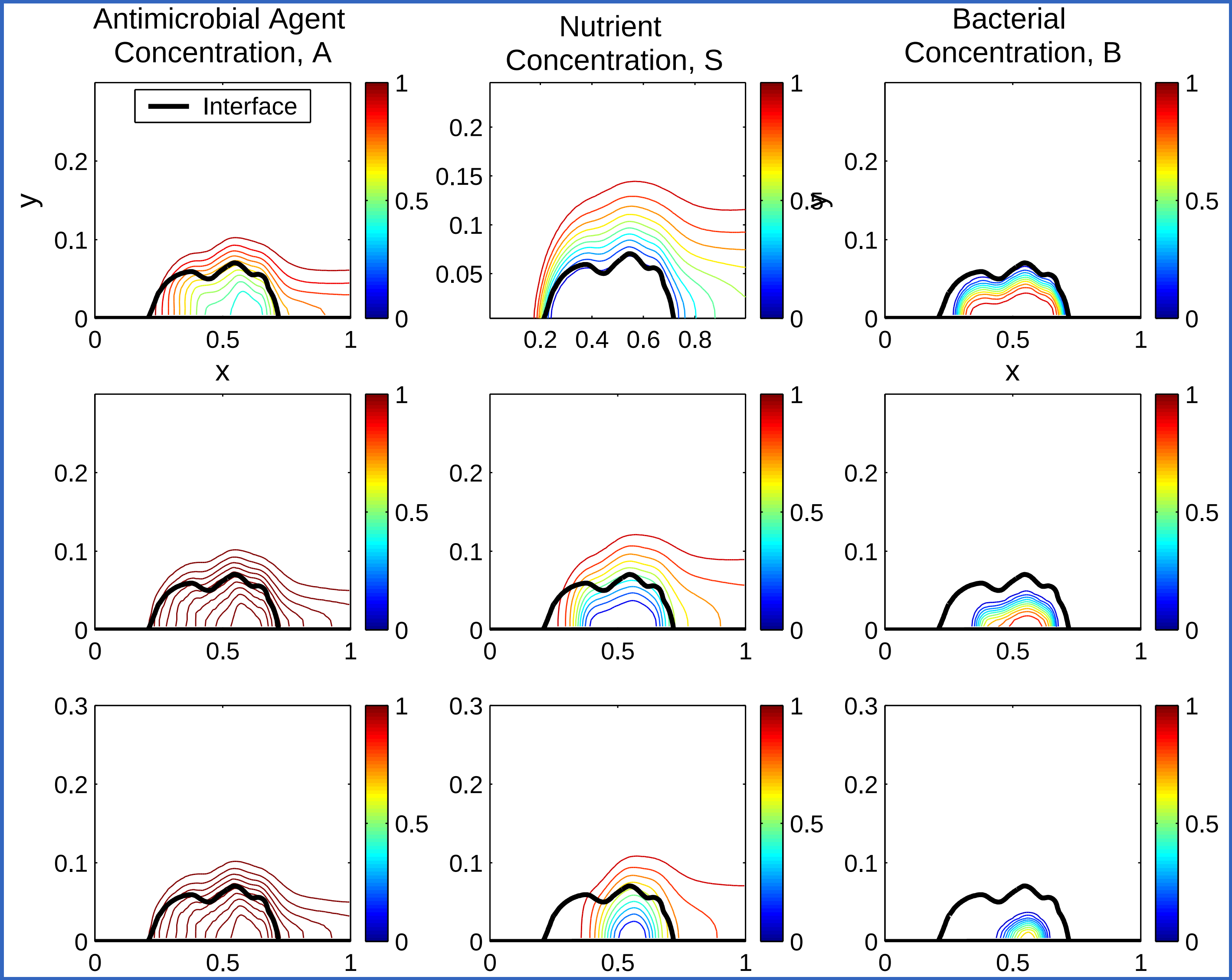
- Begin with a background flow
- Stokeslet - Fundamental solution to Stokes with singular force
- Choose force so the velocity is zero
- Flow around obstacles is the sum of background flow and those due to forces
- Regularize all forces to get analytic approximation of the flow

Example

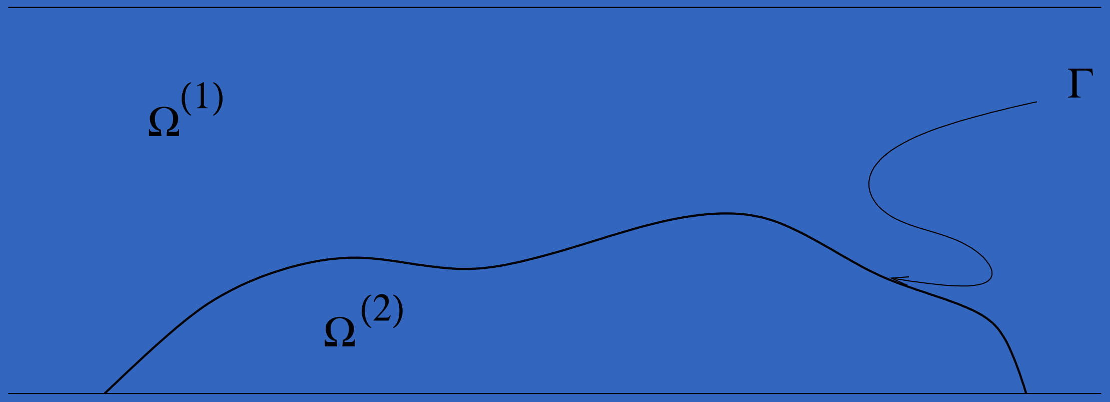


movie

Simulation Results



Short time - Evolving Interface

- Fixed domain method discretized integral equation
- Focus on coupled motion of two viscous fluids (creeping bulk flow and viscous biofilm)
- 

Comparison Flows - Short Time

Bulk Flow:

$$\begin{aligned} \nabla \cdot \sigma^{(\mathbf{1})} &= 0 \\ \nabla \cdot \mathbf{U}^{(\mathbf{1})} &= 0 \end{aligned}$$

Biofilm Flow:

$$\begin{aligned} \nabla \cdot \sigma^{(\mathbf{2})} &= 0 \\ \nabla \cdot \mathbf{U}^{(\mathbf{2})} &= 0 \end{aligned}$$

Fundamental:

$$\begin{aligned} \nabla \cdot \sigma' &= \mathbf{f}\delta(\mathbf{x} - \mathbf{x_0}) \\ \nabla \cdot \mathbf{U}' &= 0 \end{aligned}$$

Reciprocal Relations - Short Time

$$\nabla \cdot (\mathbf{U}^{(*)}\sigma') - \nabla \cdot (\mathbf{U}'\sigma^{(*)}) \; = \; \mathbf{f}\delta(\mathbf{x} - \mathbf{x_0})\mathbf{U}$$

- Analogous to Green's Theorem
- $\mathbf{U}'$ - Single layer potential (Stokeslet)
- σ' - Double layer potential

Boundary Integral Formulation - Short Time

- Flow in $\Omega^{(1)}$ due to singular force in $\Omega^{(1)}$

$$
\begin{aligned}
U_j^{(1)}(\mathbf{x_0}) &= -\frac{1}{4\pi\mu^{(1)}}\int_\Gamma \sigma_{ik}^{(1)}\eta_k(\mathbf{x})\mathbf{G}_{ij}(\mathbf{x},\mathbf{x_0})\;dl(\mathbf{x}) \\
&\quad +\frac{1}{4\pi}\int_\Gamma U_i(\mathbf{x})\mathbf{T}_{ijk}(\mathbf{x},\mathbf{x_0})\eta_k(\mathbf{x})\;dl(\mathbf{x})
\end{aligned}
$$

- Flow in $\Omega^{(2)}$ due to singular force in $\Omega^{(1)}$

$$
\begin{aligned}
0 &= \int_\Gamma \sigma_{ik}^{(2)}\eta_k(\mathbf{x})\mathbf{G}_{ij}(\mathbf{x},\mathbf{x_0})dl(\mathbf{x}) \\
&\quad -\mu^{(2)}\int_\Gamma U_i(\mathbf{x})\mathbf{T}_{ijk}(\mathbf{x},\mathbf{x_0})\eta_k(\mathbf{x})dl(\mathbf{x})
\end{aligned}
$$

Integral Equations - Short Time

Combine these:

$$\begin{aligned} U_j^{(1)}(\mathbf{x_0}) &= -\frac{1}{4\pi\mu^{(1)}}\int_\Gamma \Delta\sigma_{ik}\eta_k \mathbf{G}_{ij}(\mathbf{x},\mathbf{x_0})\,dl(\mathbf{x}) \\ &\quad +\frac{1-\lambda}{4\pi}\int_\Gamma U_i(\mathbf{x})\mathbf{T}_{ijk}(\mathbf{x},\mathbf{x_0})\eta_k(\mathbf{x})\,dl(\mathbf{x}) \end{aligned}$$

Integral Equations - Short Time cont'd:

The same for the biofilm flow:

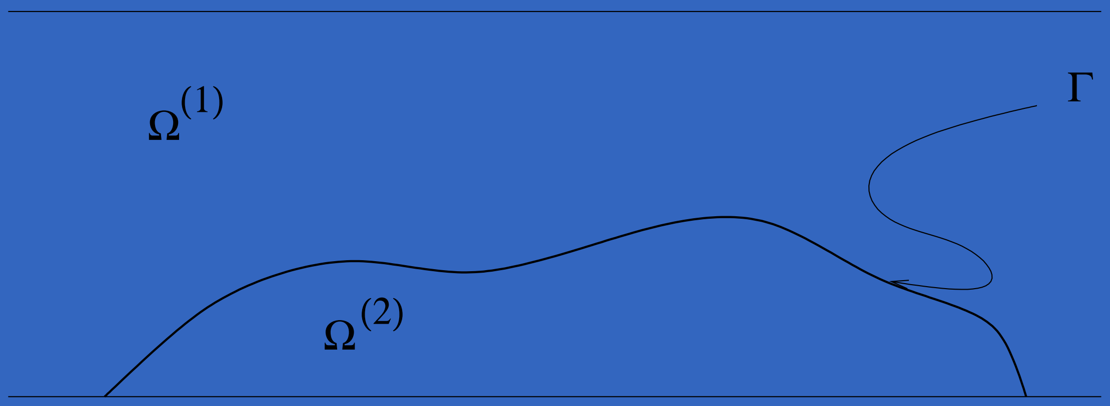
$$\begin{aligned} U_j^{(2)}(\mathbf{x_0}) &= -\frac{1}{4\pi\mu^{(2)}}\int_\Gamma \Delta\sigma_{ik}\eta_k \mathbf{G}_{ij}(\mathbf{x},\mathbf{x_0})\ dl(\mathbf{x}) \\ &+\frac{1-\frac{1}{\lambda}}{4\pi}\int_\Gamma U_i(\mathbf{x})\mathbf{T}_{ijk}(\mathbf{x},\mathbf{x_0})\eta_k(\mathbf{x})\ dl(\mathbf{x}) \end{aligned}$$

What's the point?

- Reduces to previous case if $\mu^{(2)} \longrightarrow \infty$
- Can include extra stresses (i.e. osmotic pressure and contribution from growth)
- Reduced Dimensionality
- Evolution of the interface is straightforward
- Regularized Stokeslet's

Long time - Osmotic Pressure

- Biofilm Motion due to growth (osmotic pressure)and fluid forces



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Fundamental:

$$\begin{aligned}\nabla \cdot \sigma' &= \mathbf{f}\delta(\mathbf{x} - \mathbf{x_0}) \\ \nabla \cdot \mathbf{U}' &= 0\end{aligned}$$

$$\begin{aligned}\sigma^{(2)} &= -(P^{(2)} - \Psi(\theta) - \frac{2}{3}\mu R(S, \mathbf{x}))\mathbf{I} \\ &\quad + \mu^{(2)}(\nabla \mathbf{U}^{(2)} + \nabla {\mathbf{U}^{(2)}}^T)\end{aligned}$$

Reciprocal Relations - Short Time

$$
\begin{aligned}
\nabla \cdot (\mathbf{U}\sigma') - \nabla \cdot (\mathbf{U}'\sigma) &= \mathbf{f}\delta(\mathbf{x} - \mathbf{x_0})\mathbf{U} \\
&\quad + R(S, \mathbf{x})\nabla(\frac{1}{r})
\end{aligned}
$$

Boundary Integral Formulation - Long Time

- External Flow:

$$U_j^{(1)}(\mathbf{x_0}) = -\frac{1}{4\pi\mu^{(1)}}\int_\Gamma \sigma_{ik}^{(1)}\eta_k(\mathbf{x})\mathbf{G}_{ij}(\mathbf{x},\mathbf{x_0})\;dl(\mathbf{x}) + \frac{1}{4\pi}\int_\Gamma U_i(\mathbf{x})\mathbf{T}_{ijk}(\mathbf{x},\mathbf{x_0})\eta_k(\mathbf{x})\;dl(\mathbf{x})$$

- Internal Flow

$$0 = \int_\Gamma \sigma_{ik}^{(2)}\eta_k(\mathbf{x})\mathbf{G}_{ij}(\mathbf{x},\mathbf{x_0})dl(\mathbf{x}) - \mu^{(2)}\int_\Gamma U_i(\mathbf{x})\mathbf{T}_{ijk}(\mathbf{x},\mathbf{x_0})\eta_k(\mathbf{x})dl(\mathbf{x}) - \int_\Omega R(S,\mathbf{x})\nabla\frac{1}{r}\;dV$$

Integral Equations - Long Time

Combine these (internal Flow):

$$
\begin{aligned}
0 &= \int_\Gamma \sigma_{ik}^{(2)} \eta_k(\mathbf{x}) \mathbf{G}_{ij}(\mathbf{x}, \mathbf{x_0}) dl(\mathbf{x}) \\
&\quad -\mu^{(2)} \int_\Gamma U_i(\mathbf{x}) \mathbf{T}_{ijk}(\mathbf{x}, \mathbf{x_0}) \eta_k(\mathbf{x}) dl(\mathbf{x}) - \int_\Omega R(S, \mathbf{x}) \nabla
\end{aligned}
$$

Integral Equations - Short Time cont'd:

The same for the biofilm flow:

$$U_j^{(2)}(\mathbf{x_0}) = -\frac{1}{4\pi\mu^{(2)}}\int_\Gamma \Delta\sigma_{ik}\eta_k \mathbf{G}_{ij}(\mathbf{x},\mathbf{x_0})\,dl(\mathbf{x})$$
$$+\frac{1-\frac{1}{\lambda}}{4\pi}\int_\Gamma U_i(\mathbf{x})\mathbf{T}_{ijk}(\mathbf{x},\mathbf{x_0})\eta_k(\mathbf{x})\,dl(\mathbf{x}) - \int_\Omega$$

Summary

- Introduced a framework for interface problems
- Derived equations of motion: fixed, viscous and gel
- Numerical implementation (fixed, Regularized Stokeslet’s)
- Implement viscous and gel