Session 13

SIMPLE LIPID SYSTEMS
Micropipette Aspiration

- Measure non-adherent cells
  - Exhibit liquid-like flow behavior
    - Rate of entry depends on pressure
  - Exhibit surface tension behavior
    - Recovers shape upon release
- Is a fluid droplet model appropriate?
  - What is cellular viscosity?
  - What is mechanical coupling to cortex?
Newtonian Liquid Drop Model

- **Model:**
  - Cortical layer enclosing a Newtonian liquid

- **Core:**
  - Cytoplasm viscosity: $\mu$
  - Newtonian fluid: Stress ($\tau$) vs. velocity gradient is linear: $\tau = \mu \frac{du}{dy}$

- **Cortex:**
  - Anisotropic viscous fluid layer
  - Negligible bending stiffness
  - Two viscosity terms
    - $\kappa$ is dilation viscosity
    - $\eta$ is shear viscosity

- **Pipet:**
  - Frictionless interaction
  - Reaction force at pipet orifice
Approach

- Define constitutive relationship for liquid core
  - Equations of motion for Newtonian fluid with creeping flow

- Determine boundary conditions
  - Equations of motion for cortical shell (cortex)
  - Equations of viscous deformation for cortical shell
  - No slip condition at core-cortex interface
Approach

- Not an easy task to obtain numerical solution to this problem
  - Discontinuities
  - Inversion difficulties

- Yeung & Evans’ approach
  - Spherical solutions exist for cell exterior to pipet
  - Course approximation used for flow inside pipet
  - Coupling provided by pressure difference:
    \[ \Delta P = (p_o - p_{orif}) + (p_{orif} - p_i) \]
Core: Creeping Flow

Equations of motion

By means of indicial notation, this is

\[ \sigma_{ij} = -p \cdot \delta_{ij} + \mu \left[ \frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i} \right], \quad (1) \]

\[ \sigma_{11} = -p + \mu \left( \frac{\partial u_1}{\partial x_1} + \frac{\partial u_1}{\partial x_1} \right) = -p + 2\mu \frac{\partial u_1}{\partial x_1} \]

\[ \sigma_{12} = \mu \left( \frac{\partial u_1}{\partial x_2} + \frac{\partial u_2}{\partial x_1} \right) = \sigma_{21} \]

\[ \sigma_{13} = \mu \left( \frac{\partial u_1}{\partial x_3} + \frac{\partial u_3}{\partial x_1} \right) = \sigma_{31} \]

\[ \sigma_{22} = -p + 2\mu \frac{\partial u_2}{\partial x_2} \]

\[ \sigma_{23} = \mu \left( \frac{\partial u_2}{\partial x_3} + \frac{\partial u_3}{\partial x_2} \right) = \sigma_{32} \]

\[ \sigma_{33} = -p + 2\mu \frac{\partial u_3}{\partial x_3} \]
Core

- In rectilinear coordinates

\[
\begin{align*}
\sigma_{11} &= -p + 2\mu \frac{\partial u_1}{\partial x_1} \\
\sigma_{12} &= \mu \left( \frac{\partial u_1}{\partial x_2} + \frac{\partial u_2}{\partial x_1} \right) = \sigma_{21} \\
\sigma_{13} &= \mu \left( \frac{\partial u_1}{\partial x_3} + \frac{\partial u_3}{\partial x_1} \right) = \sigma_{31} \\
\sigma_{22} &= -p + 2\mu \frac{\partial u_2}{\partial x_2} \\
\sigma_{23} &= \mu \left( \frac{\partial u_2}{\partial x_3} + \frac{\partial u_3}{\partial x_2} \right) = \sigma_{32} \\
\sigma_{33} &= -p + 2\mu \frac{\partial u_3}{\partial x_3}
\end{align*}
\]

\[
\begin{align*}
\sigma_x &= -p + 2\mu \frac{\partial u}{\partial x} \\
\tau_{xy} &= \mu \left( \frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} \right) = \tau_{yx} \\
\tau_{xz} &= \mu \left( \frac{\partial u}{\partial z} + \frac{\partial w}{\partial x} \right) = \tau_{zx} \\
\tau_{yz} &= \mu \left( \frac{\partial v}{\partial z} + \frac{\partial w}{\partial y} \right) = \tau_{zy} \\
\sigma_y &= -p + 2\mu \frac{\partial v}{\partial y} \\
\tau_{yz} &= \mu \left( \frac{\partial v}{\partial z} + \frac{\partial w}{\partial z} \right) = \tau_{zy} \\
\sigma_z &= -p + 2\mu \frac{\partial w}{\partial z}
\end{align*}
\]
Incompressibility condition for a fluid

By means of indicial notation

\[ \sum \frac{\partial u_k}{\partial x_k} = 0. \tag{2} \]

Consider one-dimensional flow \((x,u)\). If gradient exists, then fluid density would have to expand or compress to satisfy.
Core

- Mechanical equilibrium

\[ \sum_k \frac{\partial \sigma_{ik}}{\partial x_k} = 0 \]

- By means of indicial notation

\[ \frac{\partial \sigma_{11}}{\partial x_1} + \frac{\partial \sigma_{12}}{\partial x_2} + \frac{\partial \sigma_{13}}{\partial x_3} = 0 \]
\[ \frac{\partial \sigma_{21}}{\partial x_1} + \frac{\partial \sigma_{22}}{\partial x_2} + \frac{\partial \sigma_{23}}{\partial x_3} = 0 \]
\[ \frac{\partial \sigma_{31}}{\partial x_1} + \frac{\partial \sigma_{32}}{\partial x_2} + \frac{\partial \sigma_{33}}{\partial x_3} = 0 \]

\[ \frac{\partial \sigma_x}{\partial x} + \frac{\partial \tau_{xy}}{\partial y} + \frac{\partial \tau_{xz}}{\partial z} = 0 \]
\[ \frac{\partial \tau_{yx}}{\partial x} + \frac{\partial \sigma_y}{\partial y} + \frac{\partial \tau_{yz}}{\partial z} = 0 \]
\[ \frac{\partial \tau_{zx}}{\partial x} + \frac{\partial \tau_{zy}}{\partial y} + \frac{\partial \sigma_z}{\partial z} = 0 \]
Core

- By taking derivative of each equation (1), e.g.

\[
\frac{\partial \sigma_{11}}{\partial x_1} = -\frac{\partial p}{\partial x_1} + 2\mu \frac{\partial^2 u_1}{\partial x_1^2}
\]

\[
\frac{\partial \sigma_{12}}{\partial x_2} = \mu \left( \frac{\partial^2 u_1}{\partial x_2^2} + \frac{\partial^2 u_2}{\partial x_1 \partial x_2} \right)
\]

\[
\frac{\partial \sigma_{13}}{\partial x_3} = \mu \left( \frac{\partial^2 u_1}{\partial x_3^2} + \frac{\partial^2 u_3}{\partial x_1 \partial x_3} \right)
\]

- Can sum together to get

\[
\frac{\partial \sigma_{11}}{\partial x_1} + \frac{\partial \sigma_{12}}{\partial x_2} + \frac{\partial \sigma_{13}}{\partial x_3} = -\frac{\partial p}{\partial x_1} + \mu \left( \frac{\partial^2 u_1}{\partial x_1^2} + \frac{\partial^2 u_1}{\partial x_2^2} + \frac{\partial^2 u_1}{\partial x_1 \partial x_2} + \frac{\partial^2 u_1}{\partial x_3^2} + \frac{\partial^2 u_1}{\partial x_1 \partial x_3} \right)
\]
Core

- **Simplifying by mechanical equilibrium**

\[
\begin{align*}
\frac{\partial \sigma_{11}}{\partial x_1} + \frac{\partial \sigma_{12}}{\partial x_2} + \frac{\partial \sigma_{13}}{\partial x_3} &= - \frac{\partial p}{\partial x_1} + \mu \left( \frac{\partial^2 u_1}{\partial x_1^2} + \frac{\partial^2 u_1}{\partial x_2^2} + \frac{\partial^2 u_1}{\partial x_1 \partial x_2} + \frac{\partial^2 u_1}{\partial x_3^2} + \frac{\partial^2 u_1}{\partial x_1 \partial x_3} \right) \\
0 &= - \frac{\partial p}{\partial x_1} + \mu \left( \frac{\partial^2 u_1}{\partial x_1^2} + \frac{\partial^2 u_1}{\partial x_2^2} + \frac{\partial^2 u_1}{\partial x_1 \partial x_2} + \frac{\partial^2 u_2}{\partial x_3^2} + \frac{\partial^2 u_1}{\partial x_1 \partial x_3} \right)
\end{align*}
\]

- **Simplifying by incompressibility condition**

\[
\begin{align*}
0 &= - \frac{\partial p}{\partial x_1} + \mu \left( \frac{\partial}{\partial x_1} \left( \frac{\partial u_1}{\partial x_1} + \frac{\partial u_2}{\partial x_2} + \frac{\partial u_3}{\partial x_3} \right) + \frac{\partial^2 u_1}{\partial x_1^2} + \frac{\partial^2 u_1}{\partial x_2^2} + \frac{\partial^2 u_1}{\partial x_3^2} \right) \\
0 &= - \frac{\partial p}{\partial x_1} + \mu \left( \frac{\partial^2 u_1}{\partial x_1^2} + \frac{\partial^2 u_1}{\partial x_2^2} + \frac{\partial^2 u_1}{\partial x_3^2} \right)
\end{align*}
\]

- **Have creeping flow eqs.**

\[
\frac{\partial p}{\partial x_i} - \mu \cdot \sum_k \frac{\partial^2 u_i}{\partial x_k^2},
\]
Cortex

- Stress Resultants ($\tau_m$, $\tau_\phi$)
  - For thin shell, stresses integrated by thickness
    \[ \tau = \int \sigma_{ij} d\delta \]
  - Units [N/m]
  - Types: lateral, bending, torque, transverse
Cortex

- Coordinate system: (s, θ)
  - Axisymmetry yields in-plane stress resultants
    - Meridional \( \tau_m : \quad \tau_m \approx \sigma_m \delta \)
    - Circumferential \( \tau_\phi : \quad \tau_\phi \approx \sigma_\phi \delta \)
Cortex

- Balance of forces in normal direction

\[ \Delta \sigma_n = \sigma_n - \sum_{i,j} n_i \cdot \sigma_{ij} \cdot n_j = \tau_m \cdot \frac{d\theta}{ds} + \tau_\phi \cdot \frac{\sin \theta}{r}, \quad (4) \]

where \( \sigma_n = p_0 \) the outside pressure, \( n_i \) are unit vectors normal to the surface, and \( \sum n_i \sigma_{ij} n_j \) are normal tractions on the interior surface by the liquid core.
Balance of forces in tangential direction

\[
\Delta \sigma_t = -\sigma_t + \sum_{i,j} t_i \cdot \sigma_{ij} \cdot n_j = \frac{d \tau_m}{ds} + \left[ \frac{\tau_m - \tau_\phi}{r} \right] \cos \theta. \quad (5)
\]

where \( \sigma_t = 0 \) on the outside, \( t_i \) are unit vectors tangential to the surface, and \( \sum t_i \sigma_{ij} n_j \) are tangential tractions on the interior surface by the liquid core.
Cortex

- For BCs, we need constitutive relationships
- Cortex deforms by planar dilation and shear
  - $\kappa$ is viscosity for surface area dilation
  - $\eta$ is viscosity for shear shear
  - Units: $[\text{dyne} \cdot \text{s/cm}^2] \cdot [\text{cm}] = [\text{dyne} \cdot \text{s/cm}]$
Cortex

- First order model: stress resultants are proportional to rate of dilation and shear

\[ \bar{\tau} = (\tau_m + \tau_\phi)/2 = \bar{\tau}_o + \kappa \cdot V_\alpha \]
\[ \tau_s = (\tau_m - \tau_\phi)/2 = 2\eta \cdot V_s, \quad (6) \]

where \( \bar{\tau}_o \) is static in-plane tension corresponding to zero rate of shearing and dilation

- Rotation of c.s. for principal shear stresses
Cortex

- Kinematics of flow in the shell (curved surface)

\[ V_a = \frac{d v_s}{ds} + \frac{v_s}{r} \cdot \cos \theta + v_n \left( \frac{d \theta}{ds} + \frac{\sin \theta}{r} \right) \]
\[ 2V_s = \frac{d v_s}{ds} - \frac{v_s}{r} \cdot \cos \theta + v_n \left( \frac{d \theta}{ds} - \frac{\sin \theta}{r} \right). \tag{7} \]

where \( v_s, v_n \) are velocity fields derived from normal and tangential projections of fluid core velocities at the interface

\[ v_n = \sum_k n_k \cdot v_k \]
\[ v_s = \sum_k t_k \cdot v_k. \tag{8} \]

i.e., motion of cortical layer specified by liquid core’s fluid velocities at the interface with a no-slip assumption
Solution Approach

- Yeung and Evan use a general solution for axisymmetric creeping flow for exterior region

\[ v_R(R, \theta) = - \sum_{n=2}^{\infty} (A_n \cdot R^{n-2} + C_n \cdot R^n) P_{n-1}(\cos \theta) \]

\[ v_\theta(R, \theta) = \sum_{n=3}^{\infty} (nA_nR^{n-2} + (n+2)C_nR^n) \frac{I_n(\cos \theta)}{\sin \theta} \]

\[ p(R, \theta) = \Pi - \mu \sum_{n=2}^{\infty} \frac{2(2n+1)}{(n-1)} C_n R^{n-1} P_{n-1}(\cos \theta), \quad (9) \]

- Course approximation used for inside the pipet
Additional models

- Compound liquid drop model
  - Incorporates the higher viscosity and stiffness of the smaller nucleus
Additional Models

- Shear thinning liquid drop model
  - Approximates the apparent viscosity decrease with aspiration pressure

- Positive feedback: increase in shear rate leads to decreased viscosity, which in turn further increases shear rate...
Additional Models

- Maxwell Liquid Drop
  - Large deformations satisfied by Newton liquid drop model but not for small deformations

- Accounts for initial elastic-like entry during aspiration