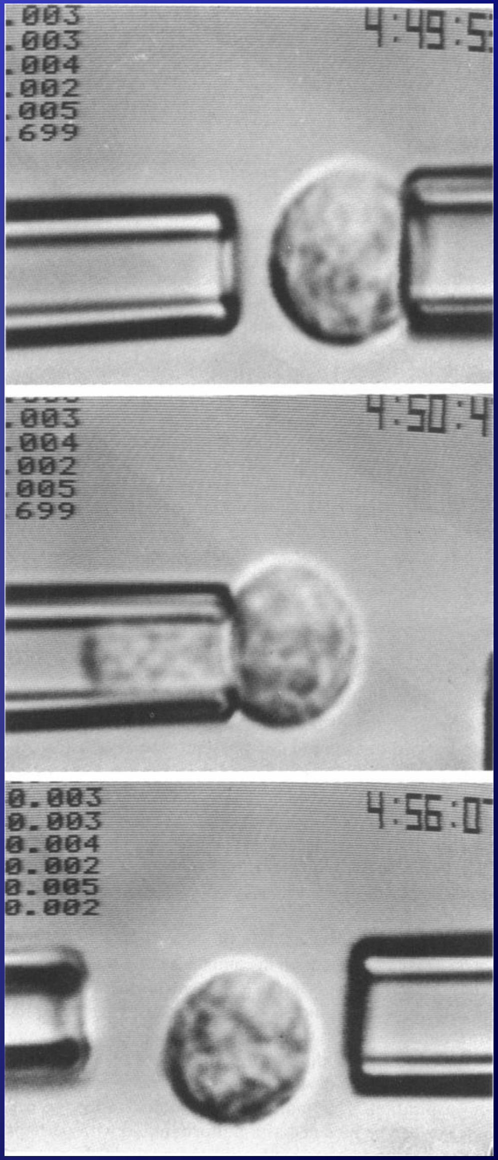
Session 13

SIMPLE LIPID SYSTEMS

Micropipette Aspiration

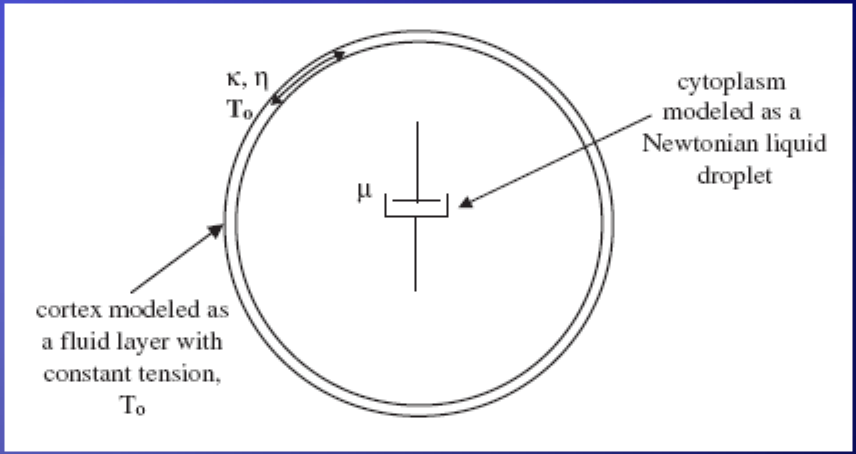
- Measure non-adherent cells
  - Exhibit liquid-like flow behavior
    - Rate of entry depends on pressure
  - Exhibit surface tension behavior
    - Recovers shape upon release
- Is a fluid droplet model appropriate?
  - What is cellular viscosity?
  - What is mechanical coupling to cortex?



Newtonian Liquid Drop Model

- Model:
  - Cortical layer enclosing a Newtonian liquid
- Core:
  - Cytoplasm viscosity: μ
  - Newtonian fluid: Stress (τ) vs. velocity gradient is linear:

    $$\tau = \mu\ (du/dy)$$



- Cortex:
  - Anisotropic viscous fluid layer
  - Negligible bending stiffness
  - Two viscosity terms
    - κ is dilation viscosity
    - η 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

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

- By means of indicial notation, this is

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

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

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

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

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

$$\sigma_{33} = -p + 2\mu\frac{\partial u_3}{\partial x_3}$$

Core

- In rectilinear coordinates

$$\sigma_{11} = -p + 2\mu \frac{\partial u_1}{\partial x_1}$$

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

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

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

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

$$\sigma_{33} = -p + 2\mu \frac{\partial u_3}{\partial x_3}$$

$$\Rightarrow$$

$$\sigma_x = -p + 2\mu \frac{\partial u}{\partial x}$$

$$\tau_{xy} = \mu \left(\frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} \right) = \tau_{yx}$$

$$\tau_{xz} = \mu \left(\frac{\partial u}{\partial z} + \frac{\partial w}{\partial x} \right) = \tau_{zx}$$

$$\sigma_y = -p + 2\mu \frac{\partial v}{\partial y}$$

$$\tau_{yz} = \mu \left(\frac{\partial v}{\partial z} + \frac{\partial w}{\partial z} \right) = \tau_{zy}$$

$$\sigma_z = -p + 2\mu \frac{\partial w}{\partial z}$$

Core

- Incompressibility condition for a fluid

$$\sum_k \frac{\partial v_k}{\partial x_k} = 0. \qquad (2)$$

- By means of indicial notation

$$\frac{\partial u_1}{\partial x_1} + \frac{\partial u_2}{\partial x_2} + \frac{\partial u_3}{\partial x_3} = 0$$

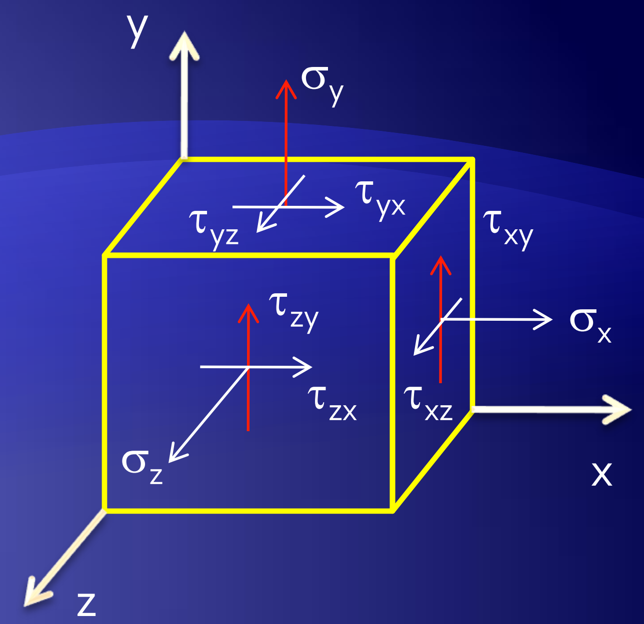
$$\left(\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} = 0 \right)$$

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

Core

- Mechanical equilibrium

$$\sum_k \frac{\partial \sigma_{ik}}{\partial x_k} = 0$$



- By means of indicial notation

$$\frac{\partial \sigma_{11}}{\partial x_1} + \frac{\partial \sigma_{12}}{\partial x_2} + \frac{\partial \sigma_{13}}{\partial x_3} = 0 \qquad \frac{\partial \sigma_x}{\partial x} + \frac{\partial \tau_{xy}}{\partial y} + \frac{\partial \tau_{xz}}{\partial z} = 0$$

$$\frac{\partial \sigma_{21}}{\partial x_1} + \frac{\partial \sigma_{22}}{\partial x_2} + \frac{\partial \sigma_{23}}{\partial x_3} = 0 \quad \Rightarrow \quad \frac{\partial \tau_{yx}}{\partial x} + \frac{\partial \sigma_y}{\partial y} + \frac{\partial \tau_{yz}}{\partial z} = 0$$

$$\frac{\partial \sigma_{31}}{\partial x_1} + \frac{\partial \sigma_{32}}{\partial x_2} + \frac{\partial \sigma_{33}}{\partial x_3} = 0 \qquad \frac{\partial \tau_{zx}}{\partial x} + \frac{\partial \tau_{zy}}{\partial y} + \frac{\partial \sigma_z}{\partial z} = 0$$

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

$$\frac{\partial \sigma_{11}}{\partial x_1} + \frac{\partial \sigma_{12}}{\partial x_2} + \frac{\partial \sigma_{13}}{\partial x_3} = -\frac{\partial p}{\partial x_1} + \mu\left(\frac{\partial^2 u_1}{\partial {x_1}^2} + \frac{\partial^2 u_1}{\partial {x_1}^2} + \frac{\partial^2 u_1}{\partial {x_2}^2} + \frac{\partial^2 u_2}{\partial x_1 \partial x_2} + \frac{\partial^2 u_1}{\partial {x_3}^2} + \frac{\partial^2 u_3}{\partial x_1 \partial x_3}\right)$$

Core

- Simplifying by mechanical equilibrium

$$\frac{\partial\sigma_{11}}{\partial x_1}+\frac{\partial\sigma_{12}}{\partial x_2}+\frac{\partial\sigma_{13}}{\partial x_3}=-\frac{\partial p}{\partial x_1}+\mu\left(\frac{\partial^2 u_1}{\partial x_1{}^2}+\frac{\partial^2 u_1}{\partial x_1{}^2}+\frac{\partial^2 u_1}{\partial x_2{}^2}+\frac{\partial^2 u_2}{\partial x_1\partial x_2}+\frac{\partial^2 u_1}{\partial x_3{}^2}+\frac{\partial^2 u_3}{\partial x_1\partial x_3}\right)$$

$$0=-\frac{\partial p}{\partial x_1}+\mu\left(\frac{\partial^2 u_1}{\partial x_1{}^2}+\frac{\partial^2 u_1}{\partial x_1{}^2}+\frac{\partial^2 u_1}{\partial x_2{}^2}+\frac{\partial^2 u_2}{\partial x_1\partial x_2}+\frac{\partial^2 u_1}{\partial x_3{}^2}+\frac{\partial^2 u_3}{\partial x_1\partial x_3}\right)$$

- Simplifying by incompressibility condition

$$0=-\frac{\partial p}{\partial x_1}+\mu\left(\frac{\partial}{\partial x_1}\left(\frac{\partial u_1}{\partial x_1}+\frac{\partial u_2}{\partial x_2}+\frac{\partial u_3}{\partial x_3}\right)+\frac{\partial^2 u_1}{\partial x_1{}^2}+\frac{\partial^2 u_1}{\partial x_2{}^2}+\frac{\partial^2 u_1}{\partial x_3{}^2}\right)$$

$$0=-\frac{\partial p}{\partial x_1}+\mu\left(\frac{\partial^2 u_1}{\partial x_1{}^2}+\frac{\partial^2 u_1}{\partial x_2{}^2}+\frac{\partial^2 u_1}{\partial x_3{}^2}\right)$$

- Have creeping flow eqs.

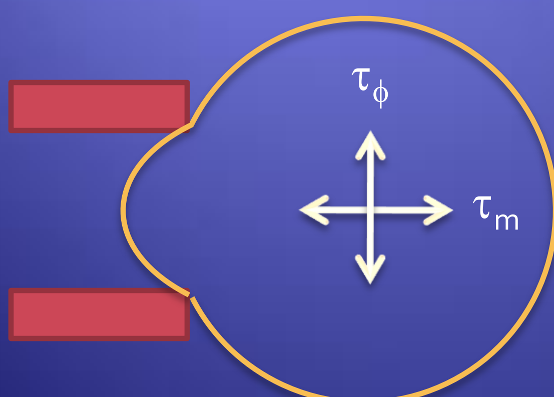
$$\frac{\partial p}{\partial x_i}=\mu\cdot\sum_k\frac{\partial^2 v_i}{\partial x_k^2}, \qquad (3)$$

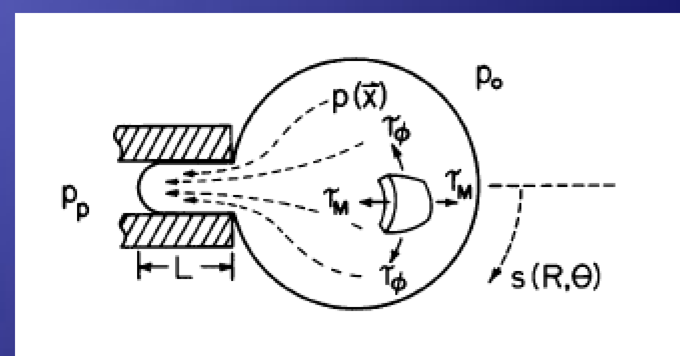
Cortex

- Stress Resultants (τ_m , τ_ϕ)
  - For thin shell, stresses integrated by thickness

$$\tau = \int \sigma_{ij} d\delta$$

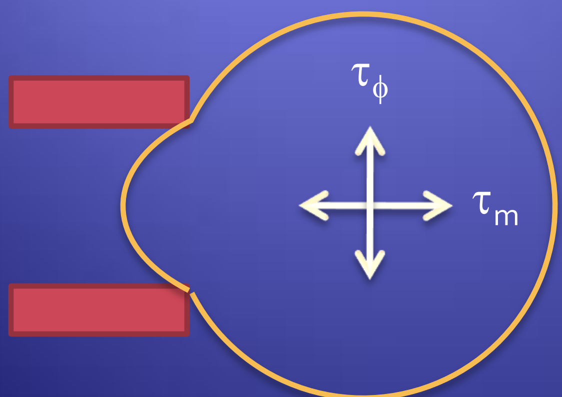
  - Units [N/m]
  - Types: lateral, ~~bending~~, torque, transverse

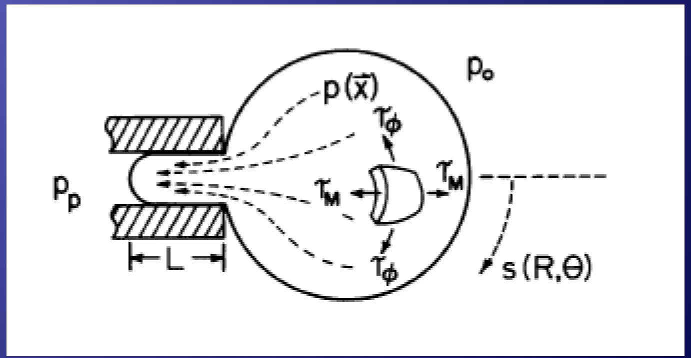




Cortex

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



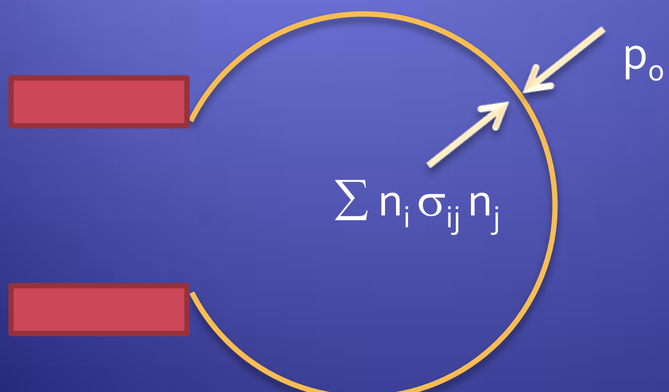


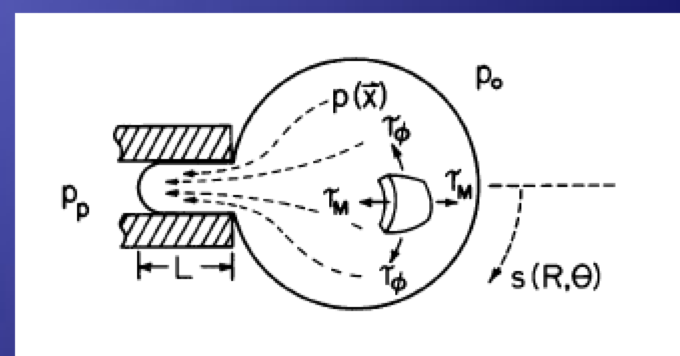
Cortex

- Balance of forces in normal direction

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

where $\sigma_n = p_o$ 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



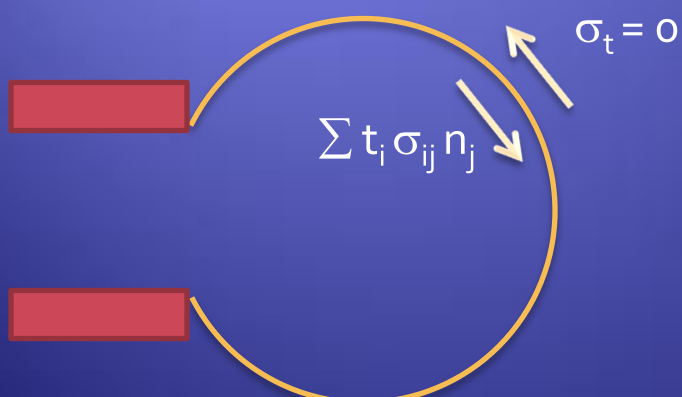


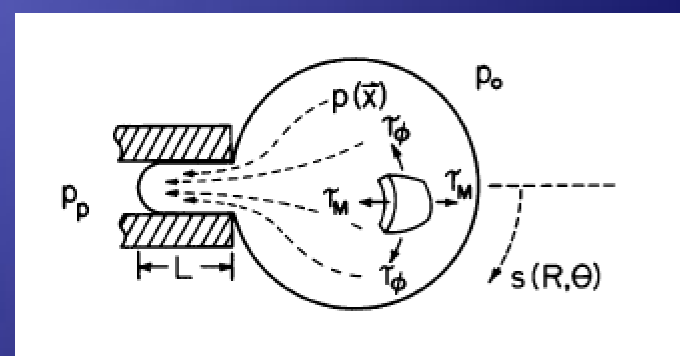
Cortex

- Balance of forces in tangential direction

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

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
  - κ is viscosity for surface area dilation
  - η is viscosity for surface shear
  - Units: [dyne·s/cm^2]*[cm] = [dyne·s/cm]

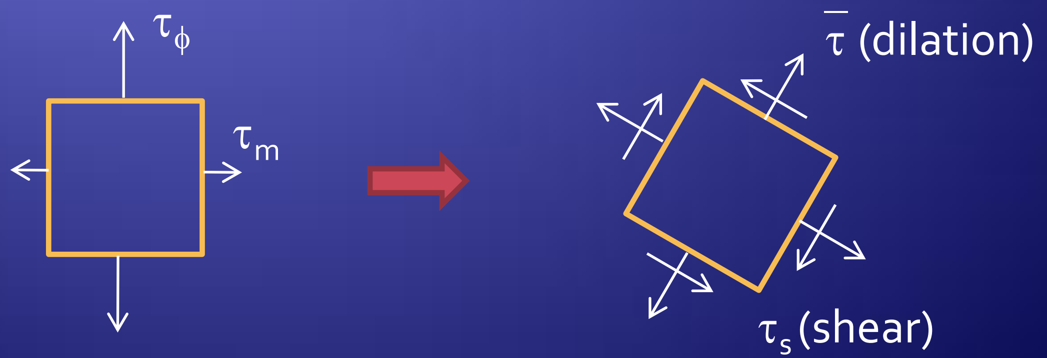
Cortex

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

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

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)

$$V_\alpha = \frac{dv_s}{ds} + \frac{v_s}{r}\cdot\cos\theta + v_n\left(\frac{d\theta}{ds} + \frac{\sin\theta}{r}\right)$$

$$2V_s = \frac{dv_s}{ds} - \frac{v_s}{r}\cdot\cos\theta + v_n\left(\frac{d\theta}{ds} - \frac{\sin\theta}{r}\right). \qquad (7)$$

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

$$v_n = \sum_k n_k \cdot v_k$$

$$v_s = \sum_k t_k \cdot v_k. \qquad (8)$$

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

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

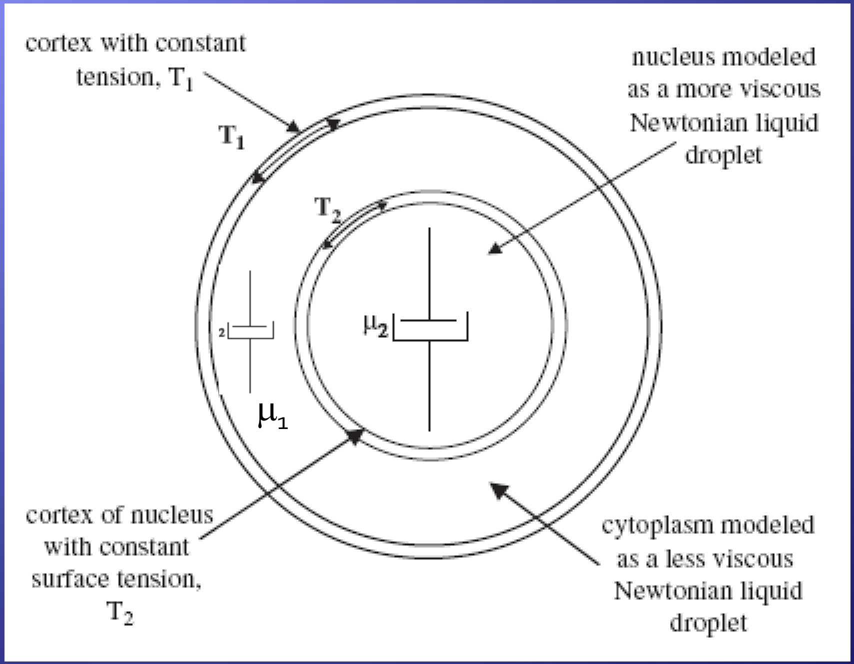
$$v_\theta(R,\theta) = \sum_{n=2}^{\infty} (nA_nR^{n-2} + (n+2)C_nR^n)\, \frac{I_n(\cos\theta)}{\sin\theta}$$

$$p(R,\theta) = \Pi - \mu \sum_{n=2}^{\infty} \frac{2(2n+1)}{(n-1)} C_nR^{n-1}\, P_{n-1}(\cos\theta), \qquad (9)$$

- Course approximation used for inside the pipet

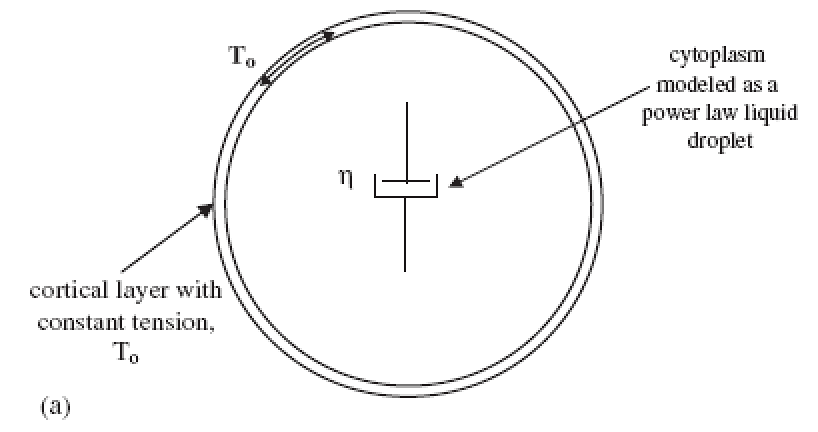
Additional models

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



Additional Models

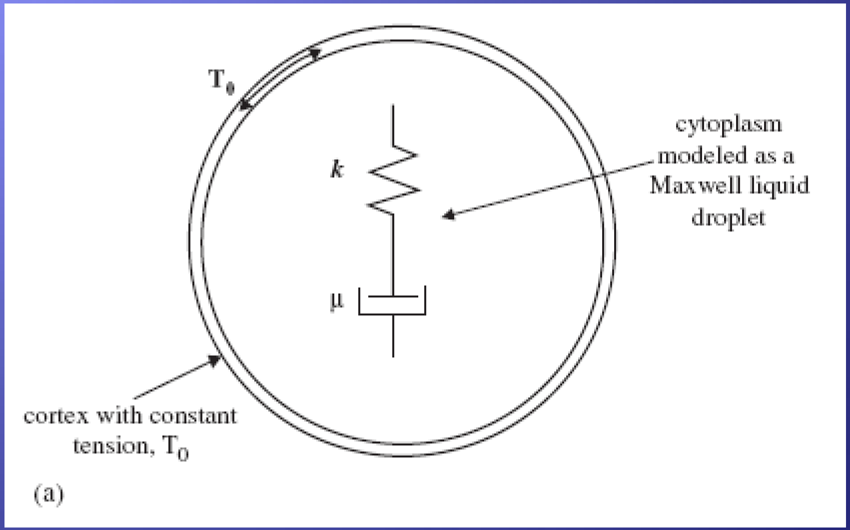
- Shear thinning liquid drop model
  - Approximates the apparent viscosity decrease with aspiration pressure



  - Positive feedback: increase in shear rate leads to decreased viscosiy, 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