Biological moving boundary problems

John King

Centre for Mathematical Medicine and Biology

University of Nottingham

England

+ Vanessa Styles, Chandrasekhar Venkataraman

School of Mathematical and Physical Sciences

University of Sussex

Scales (+ multiscale)	Example
• Molecular	Protein folding
• Subcellular	Organelles
• Cellular	Cell motility
• Tissue	In a minute
• Population	Ecology
• Galactic	Interstollar diffusion

Tissue-level

- Tumour growth
- Tissue engineering
- Biofilm growth
- Developmental biology ...

Early work includes:

Tumour growth – Burton 1966, Greenspan 1972;

Oxygen consumption – Crank & Gupta 1972.

Minimal modelling

$$\frac{\partial n}{\partial t} + \nabla \cdot (\underset{\sim}{v}\, n) = k n \qquad , \; n \in [0,1] \text{ volume fraction of cells.}$$

Two immediate issues : (i) this is one equation for N+1 unknowns ;

(ii) the model needs to be compatible with $n \leq 1$.

The main continuum-level approaches are (I) reaction-diffusion:

$$\frac{\partial n}{\partial t} = D \Delta n + k n (1-n)$$

and variants thereof and (II) mechanics-based moving boundary problems (these are not mutually exclusive).

Simplest cases

(a) Uniform packing, $n = \theta$ (constant). Suffices for radial symmetry

$$\frac{1}{r^{N-1}} \frac{\partial}{\partial r} \left(r^{N-1} V \right) = k \qquad \text{in } 0 \le r < S$$

$$\dot{S} = V \qquad \text{on } r = S$$

$$V = \frac{k}{N} r \quad , \quad \dot{S} = \frac{k}{N} S \quad \Rightarrow \quad S = S_0 \, e^{kt/N}$$

(Malthusian growth for k constant).

(b) Darcy + prescription of intercellular pressure $P(n)$.

$$\underset{\sim}{v} = -\kappa(n) \nabla P(n) \qquad \Rightarrow \qquad \frac{\partial n}{\partial t} = \nabla \cdot (\kappa P' \nabla n) + kn.$$

Requires P to be singular at $n = 1$, also (c).

(c) Complementarity problem

(b) for $n < 1$ together with

$$\nabla . (\kappa_1 \nabla p) = -k \qquad \text{where } n \equiv 1, \ \kappa_1 = \kappa(1), \ p > P_1 \equiv P(1).$$

with

$$n|_- = 1, \quad p|_+ = P_1, \quad \frac{\partial p}{\partial \nu}\Big|_- = \frac{\partial p}{\partial \nu}\Big|_+$$

at the moving boundary that separates the two.

Two-phase Darcy : elliptic solution for $N=2$

$$\Delta p_+ = 0$$

$$p_- = p_+ , \quad q_\nu = -K_- \frac{\partial p_-}{\partial \nu} = -K_+ \frac{\partial p_+}{\partial \nu} \qquad \text{(Muskat)}$$

$$\Delta p_- = -k_-$$

$$F(x,y,t) = 0$$

$$x = s(t) \cosh u \cos v$$

$$y = s(t) \sinh u \sin v$$

$$F = 0 \iff u = U(t)$$

- $$\Delta p = \frac{2}{s^2(\cosh 2u - \cos 2v)} \left(\frac{\partial^2 p}{\partial u^2} + \frac{\partial^2 p}{\partial v^2} \right) ;$$

- $$\frac{\partial F}{\partial t} = k \nabla F . \nabla p \quad \Rightarrow \quad -(\cosh 2u - \cos 2v)\, \dot{U} - \frac{\dot{s}}{s} \sinh 2u = \frac{2k}{s^2} \frac{\partial p}{\partial u} .$$

$$\Rightarrow \quad p_- = -\frac{s^2 k_-}{8} (\cosh 2u + \cos 2v) + \alpha_-(t) \cosh 2u \cos 2v + \beta_-(t) ,$$

$$p_+ = \alpha_+(t)\, e^{-2u} \cos 2v + \beta_+(t)\, u .$$

$$\Rightarrow \quad -\frac{s^2 k_-}{8} + \alpha_- \cosh 2U = \alpha_+ e^{-2U} , \quad -\frac{s^2 k_-}{8} \cosh 2U + \beta_- = \beta_+ U ,$$

$$\dot{U} = \frac{4\kappa_-\alpha_-}{s^2} \sinh 2U = -\frac{4\kappa_+\alpha_+}{s^2} e^{-2U},$$

$$-\dot{U}\cosh 2U - \frac{\dot{s}}{s}\sinh 2U = -\frac{k_-\kappa_-}{2}\sinh 2U = \frac{2\kappa_+}{s^2}\beta_+ .$$

$$\Rightarrow \boxed{\dot{U} = \frac{k_-\kappa_-\kappa_+ \sinh 2U}{2(\kappa_-\sinh 2U + \kappa_+\cosh 2U)}, \quad \dot{s} = \frac{k_-\kappa_-^2 \sinh 2U}{2(\kappa_-\sinh 2U + \kappa_+\cosh 2U)} s .}$$

$$\Rightarrow \frac{d}{dt}(s^2 \sinh 2U) = k_-\kappa_- s^2 \sinh 2U$$

✓ (exponential growth in area).

One-phase cases:

$\kappa_+ = \infty$ (exterior inviscid) $\Rightarrow \dot{U} = \frac{k_-\kappa_-}{2}\tanh 2U$, $\dot{s} = 0$ (tends to circle);

$\kappa_+ = 0$ (interior inviscid) $\Rightarrow \dot{U} = 0$, $\dot{s} = \frac{k_-\kappa_-}{2} s$ (fixed eccentricity).

For $\kappa_+ > 0$ tends to circle, but for $\kappa_- > \kappa_+$ expect Saffman-Taylor instability.

Linear stability of circular solution

Perturb about ($r=s(t)$ now denotes leading-order moving boundary)

$$p_- = -\frac{1}{4}k_- r^2 + \frac{k_- K_-}{2K_+} s^2 \ln s + \frac{1}{4}k_- s^2, \quad p_+ = -\frac{k_- K_-}{2K_+} s^2 \ln r, \quad \dot{s} = \frac{1}{2}k_- K_- s$$

via $p_\pm + \delta P_\pm$, $s + \delta S$ with

$$P_- = \alpha_-(t) r^n \cos n\theta, \quad P_+ = \alpha_+(t) r^{-n} \cos n\theta, \quad S = \sigma(t) \cos n\theta, \quad n = 1, 2, \ldots .$$

$$\Rightarrow \alpha_- s^n - \frac{1}{2}k_- s\sigma = \alpha_+ s^{-n} - \frac{1}{2}\frac{k_- K_-}{K_+} s\sigma,$$

$$\dot{\sigma} = -K_-\left(n\alpha_- s^{n-1} - \frac{1}{2}k_-\sigma\right) = -K_+\left(-n\alpha_+ s^{-n-1} + \frac{1}{2}\frac{k_- K_-}{K_+}\sigma\right).$$

$$\Rightarrow \boxed{\dot{\sigma} = -\frac{k_- K_-}{2(K_- + K_+)}(n-1)(K_+ - K_-)\sigma.}$$

For $K_+ > K_-$ all modes with $n>1$ decay; for $K_+ < K_-$ they grow, but grow faster than $s(t)$ only for $(n-2)K_- > nK_+$, consistent with the above.

Nutrient-limited Darcy (c is nutrient concentration)

$$\Delta p = -k(c), \qquad D \Delta c = \beta k(c) \qquad \text{in } \Omega(t)$$

$$p = 0, \quad c = c_*, \quad q_\nu = -\frac{\partial p}{\partial \nu} \qquad \text{on } \partial\Omega(t)$$

$$\Rightarrow \beta p + Dc = D c_*$$

$$\Rightarrow \boxed{\begin{array}{ll} D \Delta c = \beta k(c) & \text{in } \Omega(t) \\ c = c_*, \quad q_\nu = \dfrac{D}{\beta} \dfrac{\partial c}{\partial \nu} & \text{on } \partial\Omega(t) \end{array}}$$

Special case : $\Delta c = \lambda^2 c$

$k = \frac{D\lambda^2}{\beta} c$

- 'Moments' $\frac{d}{dt} \int_{\Omega(t)} \Phi(\underset{\sim}{x})\, e^{-\frac{D\lambda^2 c_* t}{\beta}} \, d\underset{\sim}{x} = 0$ wherever $\Delta \Phi = \lambda^2 \Phi$.

- Baiocchi transform (moving boundary now $t = \omega(\underset{\sim}{x})$)

$$w = e^{\frac{D\lambda^2 c_* t}{\beta}} \int_{\omega}^{t} e^{-\frac{D\lambda^2 c_* t'}{\beta}} \left(c_* - c(\underset{\sim}{x}, t')\right) dt'$$

$$\Rightarrow \quad \Delta w = \lambda^2 w + \frac{\beta}{D} \qquad \text{in } \Omega(t) \setminus \Omega(0)$$

$$w = \frac{\partial w}{\partial \nu} = 0 \qquad \text{on } \partial\Omega(t)$$

(cf. quadrature domains etc.).

<u>Stokes flow</u>

$$\nabla \cdot \underset{\sim}{v} = 0 \quad , \quad \frac{\partial \sigma_{ij}}{\partial x_j} = 0 \quad ,$$

$$\sigma_{ij} = -p\,\delta_{ij} + \mu \left(\frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i} \right) + \lambda \frac{\partial v_k}{\partial x_k} \delta_{ij} .$$

$N=2$

$$\underset{\sim}{v} = \left(\frac{\partial \psi}{\partial y} - \frac{\partial \phi}{\partial x} \, , \, -\frac{\partial \psi}{\partial x} - \frac{\partial \phi}{\partial y} \right) \qquad \text{(Helmholtz)}$$

$$\sigma_{11} = \frac{\partial^2 A}{\partial y^2} \, , \quad \sigma_{12} = -\frac{\partial^2 A}{\partial x \partial y} \, , \quad \sigma_{22} = \frac{\partial^2 A}{\partial x^2} \qquad \text{(Airy)}$$

$$\Rightarrow \qquad \Delta \phi = -k$$

$$\frac{\partial^2 A}{\partial y^2} - \frac{\partial^2 A}{\partial x^2} = 4\mu \frac{\partial^2 \psi}{\partial x \partial y} + 2\mu \left(\frac{\partial^2 \phi}{\partial y^2} - \frac{\partial^2 \phi}{\partial x^2} \right),$$

$$-\frac{\partial^2 A}{\partial x \partial y} = \mu \left(\frac{\partial^2 \psi}{\partial y^2} - \frac{\partial^2 \psi}{\partial x^2} - 2 \frac{\partial^2 \phi}{\partial x \partial y} \right),$$

$$\Rightarrow \quad \Delta^2 A = 2\mu \Delta^2 \phi , \qquad \Delta^2 \psi = 0 ,$$

with

$$p = -\frac{1}{2} \Delta \left(A + (\lambda + 2\mu) \phi \right) = -\frac{1}{2} \Delta A + \underbrace{\frac{1}{2}(\lambda+2\mu) k}_{\text{proliferation pressure}} .$$

Moving boundary conditions

$$q_\nu = -\left(\frac{\partial\psi}{\partial s} + \frac{\partial\phi}{\partial\nu}\right), \quad A = \frac{\partial A}{\partial\nu} = 0.$$

For k constant, $\phi = -\frac{1}{4}k(x^2+y^2)$ w.l.o.g. and introducing

$$X = x/e^{\frac{1}{2}kt}, \quad Y = y/e^{\frac{1}{2}kt}, \quad T = \frac{1}{k}(1-e^{-kt})$$

transforms the problem to standard Stokes flow.

For $k = k(c)$, $D\Delta c = \beta k(c)$ then $\phi = -\frac{D}{\beta}c$ w.l.o.g.,

but little further simplication may be available.

$1\frac{1}{2}$ - phase Darcy

(m volume fraction of dead cells)

$$\frac{\partial n}{\partial t} + \nabla \cdot (\underset{\sim}{v}\, n) = k(c)\, n - \gamma K(c)$$

$$\frac{\partial m}{\partial t} + \nabla \cdot (\underset{\sim}{v}\, m) = \gamma K(c) n - \lambda m$$

$n + m = 1$

$$\nabla \cdot \left(D(n) \nabla c \right) = \phi\, k(c)\, n$$

$$\underset{\sim}{v} = - \frac{1}{\mu(n)} \nabla p$$

$$k(c) = \frac{c}{1+c}, \quad K(c) = \frac{1}{1+c}, \quad D(n) = D, \quad \mu(n) = e^{\xi n}.$$