Department of Mathematics

Modelling and simulation of cell membrane dynamics

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Motivation

The study of cell membrane dynamics is part of a more general study of cell behaviour. Cell dynamics plays a critical role in many biological processes such as

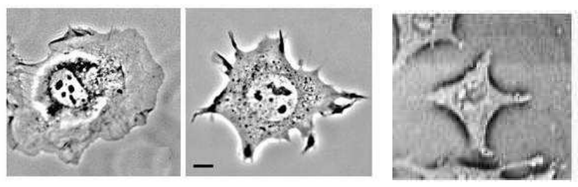
- wound healing, embryogenesis, immune response and

pathological processes such as

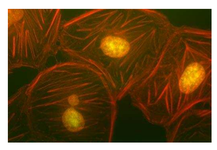
- formation of primary and secondary tumours.

Our model which describes the membrane dynamics is an extension of the model by Stephanou et al in [1].

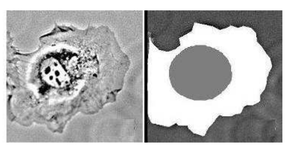
An Eukaryotic cell



Typical cell morphologies



Actin filaments in red.



Right: Cell cytoplasm in white.

Modelling hypothesis

- The Actin filaments (F-actin) is a viscoelastic gel in the cell cytoplasm.
- Actin and myosin forms a contractile network which increases pressure in the cell.
- This pressure pushes the membrane outwards at locations where the membrane is not firmly linked to the actin network.
- We model the membrane as a free moving boundary.

The cytomechanical model

Let $\Omega_t \subset \mathbf{R}^2$ be a simply connected bounded continuously deforming domain.

- $t \in I = [0, T_f]$, $T_f > 0$ and $\partial\Omega_t$ is the boundary of the continuously changing domain.
- Let $a = a(\mathbf{x}(t), t)$ denotes the f-actin concentration, and
- $\mathbf{u} = (u(\mathbf{x}(t), t), v(\mathbf{x}(t), t))^T$ the displacement of actin at position $\mathbf{x} = (x(t), y(t)) \in \Omega_t \subset \mathbf{R}^2$ such that

$$-\nabla \cdot (\sigma_v + \sigma_e + \sigma_c + \sigma_p) = \mathbf{0} \qquad \text{in} \quad \Omega_t \tag{1a}$$

$$\frac{\partial a}{\partial t} - D\Delta a + \nabla \cdot (a\frac{\partial \mathbf{u}}{\partial t}) - k_a(a_c - a) = \mathbf{0} \qquad \text{in} \quad \Omega_t \tag{1b}$$

$$a(\mathbf{x}, t) = a_0, \qquad \mathbf{u}(\mathbf{x}, t) = \mathbf{u}_0 \quad \text{for } x \in \Omega_t,\ t = 0 \tag{1c}$$

$$\sigma_v \cdot \hat{\mathbf{n}} = \sigma_e \cdot \hat{\mathbf{n}} = \hat{\mathbf{n}}.\nabla a = 0 \quad \text{for } x \in \partial\Omega_t,\ t \in I \tag{1d}$$

where σ_v, σ_e, σ_c and σ_p are the viscous, elastic, contractile and pressure induced stress tensors respectively given by:

$$\sigma_v = \mu_1\dot{\epsilon} + \mu_2\dot{\varphi}\mathbf{I}, \qquad \sigma_e = E'[\epsilon + V'\varphi\mathbf{I}], \qquad \sigma_c = \psi a^2 e^{-a/a_{sat}}\mathbf{I},$$
$$\sigma_p = \frac{p}{1+\varphi}\Big(1 + \frac{2}{\pi}\delta(l)\arctan a\Big)\mathbf{I}.$$

Semi-discrete finite element model

We approximate our model by the classical Galerkin method, in the framework of the finite element method such that we obtain:

$$\begin{bmatrix} [A^{11}] & [A^{12}] \\ [A^{12}]^T & [A^{22}] \end{bmatrix} \begin{Bmatrix} \{\dot{u}\} \\ \{\dot{v}\} \end{Bmatrix} + \begin{bmatrix} [B^{11}] & [B^{12}] \\ [B^{12}]^T & [B^{22}] \end{bmatrix} \begin{Bmatrix} \{u\} \\ \{v\} \end{Bmatrix} = \begin{Bmatrix} \{F^1\} \\ \{F^2\} \end{Bmatrix} \tag{2}$$

$$\frac{d}{dt}\Big(M(t)a(t)\Big) + \Big(DK(t) + k_aM(t) + H(t;\beta) - R(t;\dot{\mathbf{x}})\Big)a(t) = k_a a_c S, \tag{3}$$

where

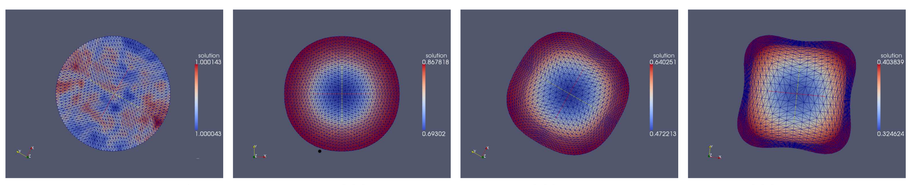
- $M(t)$ is a mass matrix.
- $K(t)$, A and B are stiffness matrices.
- F is a generalized force vector and $\beta := \frac{\partial \mathbf{u}}{\partial t}$.
- H and R are the flow and mesh velocity dependent element matrices respectively.

Time discretization and mesh updating technique

- We discretize both (2) and (3) in time using the implicit Euler scheme.
  - This scheme is unconditionally stable.
- At each time $t \in I$, $t > 0$, we update the boundary nodes of our mesh.
- Then deform the internal nodes using the spring analogy.

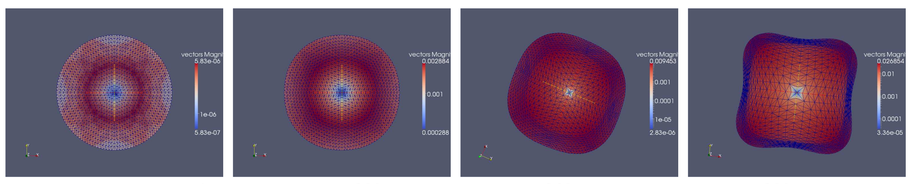
Numerical results

The parameter values used in the numerical simulations are [2] : $\mu_1 = 4.6 \times 10$, $\mu_2 = 2.41 \times 10^2$, $p = 4.6154$, $V' = 0.75$, $\psi = 2.6 \times 10^3$, $D = 2.8 \times 10^{-3}$, $k_a = 0.2$, $a_c = 1.0$ and $a_{sat} = 1.1$.



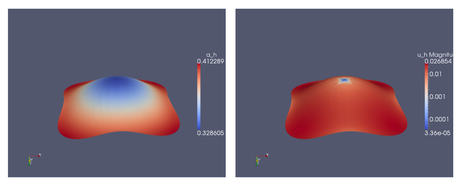
$n = 4$ $n = 200$ $n = 260$ $n = 300$

a_h solutions



$n = 4$ $n = 200$ $n = 260$ $n = 300$

u_h solutions



Solution profiles at $n = 300$: left (a_h), right (u_h)

Conclusion

We modelled cell dynamics by considering both mechanical and biochemical properties of actin filaments and its concentrations. With this model we were able to describe various shapes and movements of protrusion and retraction of the membrane. Our results agree qualitatively with those observed in experiments.

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Literature:

1). Stephanou,A. & Chaplain, M.A.J. A mathematical model for the dynamics of large membrane deformations of isolated fibroblasts. *Bulle. Math. Biol.*, **66**, 1119-1154, (2004).

2). Holmes, M. J. & Sleeman, B. N. A mathematical model of tumour angiogenesis incorporating cellular traction and viscoelastic effects. *J. Theor. Biol.*, **202**, 95-112, (2000).