Diffusion of calcium in biological tissues and accompanied mechano-chemical effects

Zbigniew Peradzyński & Bogdan Kaźmierczak

Institute of Applied Mathematics and Mechanics, University of Warsaw
Banacha 2. 0-097 Warsaw. E-mail zperadz@mimuw.edu.pl and
Institute of Fundamental Technological Research, Polish Academy of Sciences Świętokrzyska 21, 0-049 Warsaw

---

Diffusion of calcium and accompanying mechanical effects in three basic structures:

- In the bulk tissue – mathematically in a 3-dimentional space,
- In a thin tissue layer (basically 2-dimensional space)
- In an infinite thin cylindrical volume (basically 1 – dimensional space).

The diffusion of calcium plays an important role in the living cells. It is mainly manifested in the existence of waves of calcium concentration:

1. intracellular waves
2. across the tissue -extracellular waves.
   - They are responsible for the coordination of the response to the local changes of the conditions.
   - Variation of calcium concentration can serve as a mechanism of movement of cells (e.g. crawling motility of keratocytes)

In supporting calcium waves the nonlinear, autocatalytic mechanism, represented by a bi-stable source term in the respective diffusion equation

$$c_t = D\Delta c + f(c)$$

plays an important role.

Example: $f = -A(c - c_1)(c - c_2)(c - c_3)$

where $0 \leq c_1 < c_2 < c_3$,

The calcium wave represents a travelling front joining the two stable equilibriums.

Experiments: calcium waves can be generated by local mechanical stimulation. So, there must be some coupling between the chemical (change of calcium concentration) and mechanical processes (deformation). Since the deformations induced by traction are rather small, we assume that the tissue can be treated as a visco-elastic material, whose stress tensor has the following form:

$$\sigma_{ij} = \lambda\theta\delta_{ij} + 2\mu\epsilon_{ij} + \nu_1\dot{\theta}\delta_{ij} + \nu_2\dot{\epsilon}_{ij} + \tau_{ij} \ ,$$

where λ and μ are the Lame coefficients, $\hat{\epsilon} = (\epsilon_{ij})$ is the infinitesimal strain tensor, $\theta = Tr\hat{\epsilon}$ is the dilation, v_1 and v_2 are the viscosities and $\hat{\tau} = \hat{\tau}(c)$ is the symmetric traction tensor representing traction forces, generated by the sol- gel transition of the cytoplasm. This transition is caused by the change of calcium concentration.

The diffusion of calcium is rather slow (e.g. the speed of calcium waves is of the order of tens microns per second), therefore the inertial forces can neglected and the equation of motion of the medium reduces to the quasi-static balance of forces:

$$\frac{\partial}{\partial x^j}\sigma_{ij} + F_i = 0$$

In the case of tissue F can represent forces exerted on the cytogel by extracellular matrix consisting of a net of actin fibers.

E.g. we can assume that F is a restoring force proportional to the displacement vector-field u(x).

$$F = -ku$$

Diffusion in the whole $\mathbb{R}^3$

Mechanical part. We assume that the traction tensor is isotropic, $\tau_{ij} = \tau\delta_{ij}$. Expressing the strain tensor in terms of the displacement vector field $\bar{u}(x)$,

$$\epsilon_{ij} \stackrel{\text{def}}{=} \frac{1}{2}(u_{i,j} + u_{j,i}),$$

we can write balance of forces as

$$\nabla\left\{(\mu+\lambda)\theta + \nu_1\dot{\theta} + \frac{1}{2}\nu_2 div\dot{\bar{u}} + \tau\right\} + \mu\Delta\bar{u} + \frac{1}{2}\nu_2\Delta\dot{\bar{u}} = \mathrm{k}\bar{u}$$

To solve this equation we can introduce the potential for the displacement vector-field $\bar{u}$ i.e. $\bar{u}(x) = grad\psi$. Then, denoting

$$\nu \stackrel{\text{def}}{=} \nu_1 + \nu_2$$

and noticing that $\theta = \Delta\psi$ we obtain:

$$\nabla\{(2\mu+\lambda)\theta + \nu\dot{\theta} + \tau - k\psi\} = 0$$

Assuming that the stresses are vanishing at infinity we have

$$(2\mu+\lambda)\theta + \nu\dot{\theta} + \tau = k\psi$$

By the definition of θ we obtain the following linear evolutionary equation for the displacement potential

$$\nu\frac{\partial}{\partial t}\Delta\psi + (2\mu+\lambda)\Delta\psi - k\psi + \tau(c) = 0$$

In general the viscous forces are much smaller than the elastic ones, so they can treated as a perturbation, thus writing

$$\epsilon_{ij} = \epsilon_{ij}^{(0)} + \nu\epsilon_{ij}^{(1)} + \cdots,$$

and consequently

$$\theta = \theta^{(0)} + \nu\theta^{(1)} + \cdots \quad \text{and} \quad \psi = \psi^{(0)} + \nu\psi^{(1)} + \cdots$$

For the first approximation we obtain (case k=0)

$$(2\mu + \lambda)\theta^{(0)} + \tau = k\psi^{(0)},$$

which is equivalent by definition of θ to the following Helmholtz equation

$$\Delta\psi^{(0)} - \frac{k}{2\mu+\lambda}\,\psi^{(0)} = -\frac{1}{2\mu+\lambda}\,\tau$$

whereas for the first correction terms we obtain

$$(2\mu + \lambda)\theta^{(1)} - k\psi^{(1)} + \nu\dot{\theta}^{(0)} = 0, \quad \text{so}$$

$$\theta^{(1)} - \frac{k}{2\mu+\lambda}\,\psi^{(1)} = -\frac{1}{(2\mu+\lambda)^2}\dot{\tau}$$

Similarly as before we obtain the Helmholtz equation for the first correction for

$$\Delta\psi^{(1)} - \frac{k}{2\mu+\lambda}\,\psi^{(1)} = \frac{1}{(2\mu+\lambda)^2}\dot{\tau}$$

The asymptotic analysis of equations (10) and (12) for large and small k is possible.

Here we consider here mainly the case of k=0. In this case we have

$$\theta^{(0)} = -\frac{\tau}{2\mu+\lambda} \qquad \text{and} \qquad \theta^{(1)} = \frac{1}{(2\mu+\lambda)^2}\dot{\tau}$$

2.2 Reaction diffusion equation. The calcium diffusion equation with incorporated mechanical effects is

$$c_t = D\Delta c + f(c,\theta)$$

The experimental determination of the source function f(c,θ) seems to be very difficult, especially that the proposed mathematical model should be treated as an approximation of much more complex reality. The source term *f*(*c*,θ) should satisfy some physical restrictions e.g. it should be nonnegative when concentration c approaches zero. In [1] f is proposed as a sum:

$$f(c,\theta) = f(c) + \gamma\theta,$$

which can be thought of as a first term in the power series of f with respect to the dilation θ. This form for large values θ can however lead to unphysical behavior- the source term can become negative for c=0, thus leading to unphysical negative values of calcium concentrations. Still it can be useful in explaining some interesting features of the mechno-chemical coupling. The experiments in which calcium waves are generated by squeezing locally the tissue or part of a cell see[ ], can be explained in the frame of discussed here mechano-chemical model if the coupling constant γ is negative. Indeed squeezing induces negative θ, therefore if initially the system was in the lower stable state C_1

(ground state) then when θ decreases during the gradual squeezing, the ground state $C_1(\theta)$ increases till the moment where the minimum of the function $f(c,\theta)+\gamma\theta$ with respect to c becomes equal to zero. At this moment the stable and unstable states merge and C_1 becomes unstable for positive perturbations of c. When θ is still increasing the state C_1 (as well as C_2) cease to exist and the system is jumping to the upper stable state. In this way the local concentration becomes high enough to start the propagation of travelling wave supported in its further evolution by the autocatalytic mechanism, encoded in the model by bistability of f(c).

In our appr. $\theta = \theta^0 + \theta^1$. Assuming that, $\theta^0(c) = -\frac{\tau(c)}{2\mu+\lambda}$ is already encoded In the form of f ; that is assuming that $f(c,\theta) = f(c) + \gamma\theta^0(c) + \gamma\theta^{(1)} = g(c) + \gamma\theta^{(1)}$ we obtain

$$c_t = D\Delta c + g(c) + \gamma\theta^{(1)} \qquad \text{or}$$

$$c_t = D\Delta c + g(c) + \gamma\frac{\nu}{(2\mu+\lambda)^2}\dot{\tau}$$

Noticing that $\dot{\tau} = \tau_{,c}\, c_t$ we finally arrive at a single reaction diffusion equation

$$\beta(c)c_t = D\Delta c + g(c),$$

where $\beta = (1 - \gamma \frac{\nu}{(2\mu+\lambda)^2} \tau_{,c})$.

The existence of travelling waves solutions follows immediately from the appropriate theorem for a single reaction diffusion equation, provided that g(c) is of a bi-stable type. In the case when β is a non-vanishing constant or does not change much, the viscosity influences only the speed of the wave leaving the wave profile unchanged.

For very large k, when other terms except of ψ and τ can be neglected we have $\psi = -k^{-1}\tau$ and then the reaction diffusion equation for calcium concentration becomes

$$c_t = \left(D - \gamma k^{-1}\tau_{,c}\right) \Delta c + f(c) - \gamma k^{-1}\tau_{,cc}(\nabla c)^2.$$

3.Diffusion in a thin layer of a visco-elastic material

Consider a thin layer of visco-elastic material; $(x^1, x^2, x^3) \in \Re^2 \times [-d, d]$ with free, unloaded upper and lower surfaces. Under the influence of internal stresses such layer can in principle undergo buckling. This possibility, however, will not be analyzed here. In this Section we assume that the traction tensor $\hat{\tau}$ can be somewhat anisotropic, i.e. it can be of the following form

$$\hat{\tau} = \begin{bmatrix} \tau & 0 & 0 \\ 0 & \tau & 0 \\ 0 & 0 & \tau_{33} \end{bmatrix}$$

Together with x^1, x^2, x^3 we use here x, y, z and $\bar{x} = (x^1, x^2)$ for the convenience.

Since the layer is thin we can expand the displacement vector-field in powers of z (=x^3) up to second order terms (the dependence on t is suppressed for the convenience)

$$u_i = a_i^0(\bar{x}) + a_i^{(1)}(\bar{x})z + a_i^{(2)}(\bar{x})z^2$$

The plane $(x^1, x^2, 0)$ is assumed to be a symmetry plane, so we have

$$\begin{cases} u_\alpha(\bar{x}, z) = u_\alpha(\bar{x}, z), \ \alpha = 1{,}2 \\ u_3(\bar{x}, -z) = -u_3(\bar{x}, z) \end{cases}$$

This implies: $u_3 = a_3^1 z$ and $u_\alpha^1 \equiv 0$, so finally

$$\begin{cases} u_\alpha = a_\alpha^0(\bar{x}) + a^2(\bar{x})z^2 \\ u_3 = a_3^1(\bar{x})z \end{cases}$$

Consequently the strain tensor is given by:

$$\epsilon_{\alpha\beta} = \frac{1}{2}\{a_{\alpha,\beta}^0 + a_{\alpha,\beta}^2 z^2 + a_{\beta,\alpha}^0 + a_{\beta,\alpha}^2 z^2\}$$

$$\epsilon_{\alpha 3} = \frac{1}{2}\{2a_\alpha^2 + a_{3,\alpha}^1\}z$$

$$\epsilon_{33} = a_3^1$$

Boundary conditions. Since the top and bottom surfaces are free unloaded surfaces the following relations must be satisfied for $z = \pm d$:

1. $\sigma_{\alpha 3} = 0 :\ ,\ 2\mu\epsilon_{\alpha 3} + \nu_2\dot{\epsilon}_{\alpha 3} = 0$
2. $\sigma_{33} = 0 \ :\ \ \lambda\theta + 2\mu\epsilon_{33} + \nu_1\dot{\theta} + \nu_2\dot{\epsilon}_{33} + \tau_{33} = 0$

Balance of forces , $\phi(t, x, y)$ potential:

$$(\lambda + \mu)\theta - \mu\epsilon_{33} + \nu\dot{\theta} - \nu_2\dot{\epsilon}_{33} + \tau - k\phi = 0$$

Boundary conditions: If $z=\pm d$ (free unloaded surfaces) we require that for i= *1,2,3,* σ_{i3} =0; thus for i=α=1,2 we arrive at

$$\epsilon_{\alpha 3}|_{z=\pm\delta} = 0 \quad \Rightarrow \quad 2a_2^{(2)} + a_{3,\alpha}^{(1)} = 0 \quad \Rightarrow \quad \epsilon_{\alpha 3} = 0 \qquad \text{(23a)}$$

Whereas for i=3 we have

$$\lambda\theta + 2\mu a_3^{(1)} + \tau_{33} = 0 \qquad \text{(23b)}$$

Let us note that If we do the averaging of Eqs (22) over the layer thickness 2d, we obtain similar results

$$\epsilon_{\alpha\beta} = \frac{1}{2}(a_{\alpha,\beta} + a_{\beta,\alpha}) + \frac{1}{2}(a_{\alpha,\beta}^{(2)} + a_{\beta,\alpha}^{(2)})\frac{d^2}{3} \qquad \text{(24a)}$$

$$\epsilon_{\alpha 3} = 0 \quad , \quad \epsilon = a_3^{(1)} \qquad \text{(24b)}$$

Now we can proceed in a similar way as previously, assuming that $\hat{\tau}$ depends only on c, whereas c can be a function of t,x,y, but not z, we introduce the two-dimensional potential ψ, $u_\alpha = \frac{\partial}{\partial x^\alpha}\psi$,

ale $\theta = \epsilon_{11} + \epsilon_{22} + \epsilon_{33} = a_{11} + a_{22} + a_3^1$

So in zero order approximation:

$$\boxed{\lambda(a_{11} + a_{22}) + (2\mu + \lambda)a_3^{(1)} + \tau_{33} = 0}$$

Propagation in thin layers – plane stress state assumption.

$$\sigma_{ij} = \{\sigma_{\alpha\beta}, \sigma_{\alpha 3}, \sigma_{33}\} \qquad \alpha, \beta = 1,2$$

$$\theta = \tilde{\theta} + \epsilon_{33} \qquad \text{gdzie} \qquad \tilde{\theta} = \epsilon_{11} + \epsilon_{22},$$

Boundary conditions. Since the top and bottom surfaces are free unloaded surfaces the following relations must be satisfied for $z = \pm d$:

1. $\sigma_{\alpha 3} = 0$, which implies $2\mu\epsilon_{\alpha 3} = 0$ ( )
2. $\sigma_{33} = 0$ which implies $\lambda\theta + 2\mu\epsilon_{33} + \tau_{33} = 0$ at $z = \pm d$ ( )

Let us note that:

1. If the calculations are made up to main, i.e. zero order terms in d, then the coefficients of the strain tensor are depending only x and y. Indeed we have
   $$\epsilon_{\alpha\beta} = \frac{1}{2}(a_{\alpha,\beta} + a_{\beta,\alpha}) \qquad \epsilon_{\alpha 3} = 0 \quad , \quad \epsilon_{33} = a_3^{(1)}$$
2. If second order terms in d are preserved, then as it can be easily verified, the averaging over the layer thickness in the mechanical equilibrium equations, denoted here by $< >$, commutes with differentiation

$$< \frac{\partial}{\partial x^j}\sigma_{ij} >= \frac{\partial}{\partial x^j} < \sigma_{ij} >$$

Therefore, mechanical equilibrium equations

$$\sigma_{ij,j} = \hat{k}u, \qquad \text{where } \hat{k} = \begin{bmatrix} k & 0 & 0 \\ 0 & k & 0 \\ 0 & 0 & 0 \end{bmatrix}, \qquad \text{are}$$

reduced to $\sigma_{\alpha\beta,\beta} = ku_\alpha$, with $\alpha, \beta = 1{,}2$. Now it is convenient to introduce a 2-dimensional dilation, $\tilde{\theta} = \epsilon_{11} + \epsilon_{22}$, related to the two-dimensional strain tensor $\epsilon_{\alpha\beta}$, $\alpha, \beta = 1{,}2$. The boundary condition $\sigma_{33} = 0$ gives us

$$\lambda\tilde{\theta} + (2\mu + \lambda)\epsilon_{33} + \tau_{33} = 0 \qquad \Rightarrow \qquad \epsilon_{33} = -\frac{1}{2\mu+\lambda}\{\tau_{33} + \lambda\tilde{\theta}\}$$

Proper b-dry condition is:

$$\lambda\tilde{\theta} + (2\mu + \lambda)\epsilon_{33} + \nu_1\dot{\tilde{\theta}} + \nu_2\dot{\epsilon}_{33} + \tau_{33} = 0$$

A. Mechanical equilibrium equations

$$\sigma_{ij,j} = 0 \qquad \Rightarrow \qquad \sigma_{\alpha j,j} = 0 \qquad \Rightarrow \qquad \sigma_{\alpha\beta,\beta} = 0$$

Since all quantities in the above equations are independent of z, i.e. they depend on x^1, x^2 and t then

$$\left(\lambda\theta\delta_{\alpha\beta} + 2\mu\epsilon_{\alpha\beta} + \tau_{\alpha\beta}\right)_{,\beta} = 0$$

Full equation of mechanical equilibrium (with viscous terms) is

$$\left(\lambda\theta\delta_{\alpha\beta} + 2\mu\epsilon_{\alpha\beta} + \nu_1\dot{\theta}\delta_{\alpha\beta} + \nu_2\dot{\epsilon}_{\alpha\beta} + \tau_{\alpha\beta}\right)_{,\beta} = 0,$$

$$\left(\lambda\tilde{\theta}\delta_{\alpha\beta} + \lambda\epsilon_{33}\delta_{\alpha\beta} + 2\mu\epsilon_{\alpha\beta} + \nu_1\dot{\tilde{\theta}}\delta_{\alpha\beta} + \nu_1\dot{\epsilon}_{33}\delta_{\alpha\beta} + \nu_2\dot{\epsilon}_{\alpha\beta} + \tau_{\alpha\beta}\right)_{,\beta} = 0$$

which can be transformed to (nie jest dobrze bo eps33 jest policz niedokl)

$$(\lambda + \mu)\tilde{\theta} + \lambda\epsilon_{33} + \nu\dot{\tilde{\theta}} + \nu_1\dot{\epsilon}_{33} + \tau - k\psi = 0$$

$$\left[\frac{2\mu\lambda}{2\mu+\lambda}\tilde{\theta}\delta_{\alpha\beta} + 2\mu\epsilon_{\alpha\beta} + \nu_1\dot{\tilde{\theta}}\delta_{\alpha\beta} + \nu_2\dot{\epsilon}_{\alpha\beta} - \frac{\nu_1}{2\mu+\lambda}\dot{\tau}_{33} + (\tau - \frac{\lambda}{2\mu+\lambda}\tau_{33})\right]_{,\beta} = ku_\alpha$$

Using the potential for u, and denoting as before $\nu = \nu_1 + \nu_2$, we obtain after integration we again arrive at a Helmholtz equation for the potential $\psi(t, x, y)$

$$(\frac{2\mu\lambda}{2\mu+\lambda} + \mu)\Delta\psi + \nu\Delta\dot{\psi} - k\psi + \left(\tau - \frac{\lambda}{2\mu+\lambda}\tau_{33} - \frac{\nu_1}{2\mu+\lambda}\dot{\tau}_{33}\right) = 0$$

From now on we assume k=0, and expand the potential as before

$$\mu\frac{2\mu+\lambda}{2\mu+\lambda}\Delta\psi + \nu\Delta\dot{\psi} - k\psi + \left(\tau - \frac{\lambda}{2\mu+\lambda}\tau_{33} - \frac{\nu_1}{2\mu+\lambda}\dot{\tau}_{33}\right) = 0$$

$$\left(\frac{2\mu\lambda}{2\mu+\lambda}\tilde{\theta}\delta_{\alpha\beta} + 2\mu\epsilon_{\alpha\beta} + (\tau - \frac{\lambda}{2\mu+\lambda}\tau_{33})\right)_{,\beta} = 0$$

$$\left[\frac{2\mu\lambda}{2\mu+\lambda}\tilde{\theta}\delta_{\alpha\beta} + 2\mu\epsilon_{\alpha\beta} + \left(\tau - \frac{\lambda}{2\mu+\lambda}\tau_{33}\right)\delta_{\alpha\beta} \right]_{,\beta} = ku_\alpha$$

where $\theta = \tilde{\theta} + \epsilon_{33}$.Introducing (2-dimensional) potential: $u_\alpha = \phi_{,\beta}$ we arrive at

$$\nabla_\alpha \left\{ 4\mu\frac{\lambda+\mu}{2\mu+\lambda}\Delta\phi + \left(\tau - \frac{\lambda}{2\mu+\lambda}\tau_{33}\right) - k\phi \right\} = 0,$$

which after integration gives

$$4\mu\frac{\lambda+\mu}{2\mu+\lambda}\Delta\phi + \left(\tau - \frac{\lambda}{2\mu+\lambda}\tau_{33}\right) - k\phi = 0$$

4 Diffusion in a long thin fiber.

In this case we assume that traction tensor is symmetric with respect to x (= x^1) axis

$$\hat{\tau} = \begin{bmatrix} \tau_{11} & 0 & 0 \\ 0 & \tau & 0 \\ 0 & 0 & \tau \end{bmatrix}$$

By the axial symmetry of the problem we have

$$\sigma_{ij} = \{\sigma_{11}, \sigma_{1\alpha}, \sigma_{\alpha\beta}\} \qquad \alpha, \beta = 2{,}3$$

Z symetrii $\epsilon_{22} = \epsilon_{33}$, a więc $\theta = \tilde{\theta} + 2\epsilon_{22}$ $\theta = \epsilon_{11} + 2\epsilon_{22}$

Warunki brzegowe $\sigma_{i2} = 0$, $\sigma_{i3} = 0$

i=2 $\qquad \lambda\theta + 2\mu\epsilon_{22} + \tau = 0 \qquad \theta = \tilde{\theta} + 2\epsilon_{22}$ stąd

$$\lambda\tilde{\theta} + 2(\lambda+\mu)\epsilon_{22} + \tau_{22} = 0 \quad \rightarrow \quad \lambda\epsilon_{11} + 2(\lambda+\mu)\epsilon_{22} + \tau_{22} = 0$$

Równania równowagi:

$$\lambda\theta_{,1} + 2\mu\epsilon_{11,1} + \tau_{11,1} = 0$$
$$\lambda\theta + 2\mu\epsilon_{11} + \tau_{11} = 0$$

stąd

$$\begin{cases} (2\mu+\lambda)\epsilon_{11} + 2\lambda\epsilon_{22} + \tau_{11} = 0 \\ \lambda\epsilon_{11} + 2(\lambda+\mu)\epsilon_{22} + \tau_{22} = 0 \end{cases}$$

$$\epsilon_{22} = \frac{\lambda\tau_{11} - (\lambda+2\mu)\tau}{2\mu(2\mu+3\lambda)} = -\frac{1}{2\mu+3\lambda}\tau$$

$$\epsilon_{11} = \frac{\lambda\tau - (\lambda+\mu)\tau_{11}}{\mu(2\mu+3\lambda)} = -\frac{1}{2\mu+3\lambda}\tau$$

In the case of isotropic traction tensor $\tau_{11} = \tau$, we have $\epsilon_{11} = \epsilon_{22} = \epsilon_{33}$ and

$$\theta = 3\epsilon_{11} = -3\frac{1}{2\mu+3\lambda}\tau$$

Uwaga: można oczywiście postulować równanie

$f = f(c.\theta,\dot{\theta})$ *wtedy* $\dot{\theta}$ *- wylicza się przez c.*

……

$$\nabla\left\{(\mu+\lambda)\theta + \nu_1\dot{\theta} + \frac{1}{2}\nu_2 div\dot{U} + \tau\right\} + \mu\Delta u + \frac{1}{2}\nu_2\Delta\dot{u} = 0$$

Thus to solve this equation we can introduce the potential for $\bar{u}$ i.e. $\bar{u}(x) = grad\psi$. Then noticing that $\theta = \Delta\psi$ we obtain:

$$\nabla\{(2\mu+\lambda)\theta + (\nu_1+\nu_2)\dot{\theta} + \tau\} = 0$$

Thus we have:

1. $(2\mu+\lambda)\theta^{(0)} + \tau = 0$

   $\Delta\psi^{(0)} = -\dfrac{\tau}{2\mu+\lambda}$
2. $(2\mu+\lambda)\theta^{(1)} + \nu\dot{\theta} = 0$

So $\quad \Delta\psi^{(1)} = \frac{\nu}{(2\mu+\lambda)^2}\dot{\tau}$

and $\quad \theta^{(1)} = -\frac{\nu}{2\mu+\lambda}\dot{\theta}^{(0)}$

………

By taking the trace of the last equation we obtain

$(3\lambda+2\mu)\theta^{(1)} + (3\nu_1+\nu_2)\dot{\theta}^{(0)} = 0$ *and consequently*

$\theta^{(1)} = -\frac{3\nu_1+\nu_2}{3\lambda+2\mu}\dot{\theta}^{(0)}.$

By taking the traceless part of equation 2. we arrive at

$2\mu\left(\epsilon^{(1)} - \frac{1}{3}\theta^{(1)}\delta_{ij}\right) + \nu_2\left(\dot{\epsilon}_{ij}^{(0)}\delta_{ij}\right) = 0,$

which finally allows us to find the correction to the strain tensor due to the viscosity

$$\epsilon_{ij}^{(1)} = \frac{\nu_2}{2\mu}\left(\frac{1}{3}\dot{\theta}^{(0)}\delta_{ij} - \dot{\epsilon}_{ij}^{(0)}\right) - \frac{1}{3}\frac{3\nu_1 + \nu_2}{3\lambda + 2\mu}\dot{\theta}^{(0)}\delta_{ij}$$

In the case of isotropic traction tensor, $(\tau_{ij} = \tau\delta_{ij})$, Eq.(1) after introducing the displacement vector-field **u**(x) gives us

$(\mu + \lambda)\nabla\theta^{(0)} + \mu\Delta\boldsymbol{u} + \nabla\tau = 0$

for the zero-order approximation. In general the displacement **u**(**x**) can be decomposed into the sum of the gradient of a potential and the curl of a certain vector-field. As all other terms in the equation are gradient-like and the material in the infinity is assumed to be undisturbed, then it is sufficient to introduce the displacement potential $\boldsymbol{u} = \nabla\psi$. In this way we come to

$$\boldsymbol{\nabla\{(2\mu + \lambda)\Delta\psi + \tau\} = 0}$$

So, up to a constant we have

$$\Delta\boldsymbol{\psi} = -\frac{\boldsymbol{\tau}}{\boldsymbol{2\mu + \lambda}}$$

Noticing that $\Delta\psi = \theta$ we have $\theta^{(0)} = -\frac{\tau}{2\mu+\lambda}$.

Developing the potential Ψ similarly as the strain tensor

$$\psi = \psi^{(0)} + \psi^{(1)} + \cdots$$

we have $\Delta\psi^{(1)} = -\theta^{(1)}$

………………………………………………………………………………………………………

we have $\Delta\psi^{(1)} = \theta^{(1)}$

where the zero-part of the strain tensor corresponds to the vanishing viscosities. Comparing the terms of the same order we obtain

1. $\sigma^{(0)} = \lambda\theta^{(0)}\delta_{ij} + 2\mu\epsilon_{ij}^{(0)} + \tau_{ij}$
2. $\sigma^{(1)} = \sigma\lambda\theta^{(1)}\delta_{ij} + 2\mu\epsilon_{ij}^{(1)} + \nu_1\dot{\theta}^{(0)}\delta_{ij} + \nu_2\dot{\epsilon}_{ij}^{(0)}$

……………………………………

[1] J.D. Murray, Mathematical Biology, Springer, Berlin, 2nd edition, 1993.
[2] J. Keener, J. Sneyd, Mathematical Physiology, Springer 1998.

[4] Kevin Burton,* Jung H. Park, and D. Lansing Taylor "Keratocytes Generate Traction Forces in Two Phases" Molecular Biology of the Cell, Vol. 10, 3745–3769, November 1999
[1] L.F. Jaffe, The path of calcium in cytosolic calcium oscillations: a unifying hypothesis, Proc. Natl. Acad. Sci. USA, 88 (1991), pp. 9883-9887.
[2] Y.C. Fung, Foundations of Solid Mechanics, Prentice-Hall, 1965.
[3] J.D., 2nd Murray, Mathematical Biology, Springer, Berlin edition, 1993.
[4] G. C. Cruywagen, J. D. Murray, On a tissue interaction model for skin pattern formation, Journal of Nonlinear Science, 2 217-240, (1992),

[5] P. Fife, Mathematical Aspects of Reacting and Diffusing Systems, Lecture Notes in Biomath., vol.28, Springer, New York, 1979.
[6] O. Diekmann, N. M. Temme, Nonlinear Diffusion Problems, Mathematisch Centrum, Amsterdam, (1976).
[7] H. Engler, Relations between travelling wave solutions of quasilinear parabolic equations, Proc. AMS 93 (1985), 287-302.
[8] B. Kazmierczak, K. Piech´or, Some Heteroclinic Solutions of a Model of Skin Pattern Formation, Math. Meth. Appl. Scien. 27 (2004), No 13.
[9] A. Volpert, V. Volpert, V. Volpert, Traveling Wave Solutions of Parabolic Systems, AMS, Providence 1994.
[10] J. Tsai, J. Sneyd, Existence and stability of traveling waves in buffered systems, SIAM J. Appl. Math., 66 (2005), pp. 237-265
[11] M. Falcke, Reading the patterns in living cells - the physics of Ca^{2+} signaling, Advances in Physics, 53, 2004, pp. 255-440
[12] J. Shenq Guo, J. Tsai, The asymptotic behavior of solutions of the buffered bistable system, J. Math. Biol. (2006).
[13] A. Doyle, W. Marganski and J. Lee, Calcium transients induce spatially coordinated increases in traction force during the movement of fish keratocytes, Journal of Cell Science 117 (2004), pp. 2203-2214
[14] B. Kazmierczak, Existence of Travelling Wave Solutions for Reaction-Diffusion Convection Systems via the Conley Index Theory, Top. Meth. in Nonl. Anal. 17(2) (2001), 359-403.
[15] B. Kazmierczak, Z. Peradzy´nski, Heteroclinic solutions for a system of strongly coupled ODEs, Math. Meth. Appl. Scien.19(1996), 451-461.
[16] B. Kazmierczak, V. Volpert, Existence of Heteroclinic Orbits for Systems Satisfying Monotonicity Conditions, Nonlinear Analysis TM &A 55 (2003), 467-491.
[17] J. Sneyd, P.D. Dalez & A. Duffy, Traveling Waves in Buffered Systems: Applications to calcium waves, SIAM J. Appl. Math. 58 (1998), pp. 1178-1192.
[18] R. Kupferman, P. P. Mitra, P. C. Hohenberg, S. S. Wang, Analytical Calculation of Intracellular Calcium Wave Characteristics Biophys. J., 72 (1997), p. 2430-2444.

[19] B. Kazmierczak, V. Volpert, Calcium waves in systems with immobile buffers as a limit of waves for systems with non zero diffusion, submitted.
[20] J. Sneyd, Calcium Oscilations and Waves, Proceedings of Symposia in Applied Mathematics, 59(2002), 83-118.
[21] J. Keener, J. Sneyd, Mathematical Physiology, Springer 1998.
[22] F. R. Gantmaher, Teoria Matric (in Russian), Nauka, 1988.
[23] K.J.Palmer, Exponential dichotomies and transversal homoclinic points, J. Diff. Equat., 20 (1984), pp. 225-256.
[24] E.C.M. Crooks, On the Vol'pert theory of travelling wave solutions for parabolic equations, Nonlinear Analysis TM &A, 26 (1996), 1621-1642.
[25] A.E. Taylor, Introduction to functional analysis, J.Wiley and Sons, New York, 1958.
[26] N. R. Jorgensen, S. C. Teilmann, Z. Henriksen, R. Civitelli, O. H. Sorensen, T. H. Steinberg, Activation of L-type Calcium Channels Is Required for Gap Junction-mediated Intercellular Calcium Signaling in Osteoblastic Cells, J. Biological Chemistry, 278 (2003), pp. 40824086.
[27] S. H. Young, H. S. Ennes, J. A. McRoberts, V. V. Chaban, S. K. Dea, E. A. Mayer Cure, Calcium waves in colonic myocytes produced by mechanical and receptor-mediated stimulation, Am. J. Physiol. Gastrointest. Liver Physiol. 276 (1999), pp. 1204-1212.
[28] Mutungi, K. W. Ranatunga, The viscous, viscoelastic and elastic characteristics of resting fast and slow mammalian (rat) muscle fibres, Journal of Physiology (1996), 496, pp.827-836
[29] Yun-Bi Lu, Kristian Franze, Gerald Seifert, Christian Steinhuser, Frank Kirchhoff, Hartwig Wolburg, Jochen Guck, Paul Janmey, Er-Qing Wei, Josef Kas and Andreas Reichenbach, Viscoelastic properties of individual glial cells and neurons in the CNS, PNAS, 103 (2006), pp. 1775917764.
[30] D. Bia, R. Armentano, D. Craiem, J. Grignola, F. Gines, A. Simon, J. Levenson, Smooth muscle role on pulmonary arterial function during acute pulmonary hypertension in sheep, Acta Physiol.

Scand. 181 (2004), pp. 359366).
[31] P.B. Dobrin, J. M. Doyle, Vascular Smooth Muscle and the Anisotropy of Dog Carotid Artery, Circ. Res. 27(1970), pp. 105-119.
[32] D. Liao, C. Sevcencu, K. Yoshida, H. Gregersen, Viscoelastic properties of isolated rat colon smooth muscle cells, Cell Biology International 30 (2006), pp. 854-858.
[33] M. Sato, N. Ohshima & R. M. Nerem, Viscoelastic properties of cultured porcine aortic endothelial cells exposed to shear stress,