Modeling Durotaxis using Mechanical Bidomain model

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Analytical treatment - 10/03/2018

The equations formulated below consider a gradient in the extracellular stiffness in a 1-d strand of tissue using the mechanical bidomain model.

Consider u_x and w_x as the intra- and extra-cellular displacements of the bidomain layer. x being the principal direction of the one-dimensional tissue strand, T being the tension, p and q being the intra- and extra-cellular pressure contributions arising mostly from hydrostatic forces.

The standard equations of the bidomain model are as follows [1]:

$$-\frac{\partial p}{\partial x} + \nu(\frac{\partial^2 u_x}{\partial x^2} + \frac{\partial^2 u_x}{\partial y^2}) + \gamma\frac{\partial^2 u_x}{\partial x^2} + \frac{\partial T}{\partial x} = K(u_x - w_x) \tag{1}$$

$$-\frac{\partial q}{\partial x} + \mu(\frac{\partial^2 w_x}{\partial x^2} + \frac{\partial^2 w_x}{\partial y^2}) = -K(u_x - w_x) \tag{2}$$

For this problem we consider:

- $\mu = \mu_0 + gx$
- No contributions along the y axis
- p,q and T are constant and hence their gradients are zero along the x axis
- Slope of μ is a constant
- K is same for intra- and extra-cellular displacements

$$\nu\frac{\partial^2 u_x}{\partial x^2} + \gamma\frac{\partial^2 u_x}{\partial x^2} = K(u_x - w_x) \tag{3}$$

$$\mu_0\frac{\partial^2 w_x}{\partial x^2} + gx\frac{\partial^2 w_x}{\partial x^2} = -K(u_x - w_x) \tag{4}$$

Simplifying the above expression, replacing u_x in equation (2) from (1):

$$u_x = w_x + \frac{\nu}{K}\frac{\partial^2 u_x}{\partial x^2} + \frac{\gamma}{K}\frac{\partial^2 u_x}{\partial x^2} + \gamma\frac{\partial^2 u_x}{\partial x^2} \tag{5}$$

$$\therefore \frac{\mu_0}{K}\frac{\partial^2 w_x}{\partial x^2} + x\frac{g}{k}\frac{\partial^2 w_x}{\partial x^2} = -(\frac{\nu}{K}\frac{\partial^2 u_x}{\partial x^2} + \frac{\gamma}{K}\frac{\partial^2 u_x}{\partial x^2}) \tag{6}$$

Final form the equation can be written as:

$$\frac{\partial^2 w_x}{\partial x^2}(\frac{\mu_0}{K} + \frac{gx}{K}) + \frac{\partial^2 u_x}{\partial x^2}(\frac{\nu}{K} + \frac{\gamma}{K}) = 0 \tag{7}$$

Analytical treatment - 10/04/2018

The equations formulated below consider a gradient in the extracellular stiffness in a 1-d strand of tissue using the mechanical bidomain model.

Consider u_x and w_x as the intra- and extra-cellular displacements of the bidomain layer. x being the principal direction of the one-dimensional tissue strand, T being the tension, p and q being the intra- and extra-cellular pressure contributions arising mostly from hydrostatic forces.

The intra and extra-cellular stresses arising in the 1-d strand of tissue can be expressed as [2]:

$$\tau_{ix} = -p + 2\nu\epsilon_{ix} + T \tag{8}$$

$$\tau_{ex} = -q + 2\mu(x)\epsilon_{ex} \tag{9}$$

Relationship between the strains and displacement can be written as:

$$\frac{\partial\tau_{ix}}{\partial x} = K(u_x - w_x) \tag{10}$$

$$\frac{\partial\tau_{ex}}{\partial x} = -K(u_x - w_x) \tag{11}$$

Using equation (8) and (9) in (10) and (11) the resulting intra- and extra-cellular equations are:

$$\frac{\partial}{\partial x}(-p + 2\nu\frac{\partial u_x}{\partial x}) = K(u_x - w_x) \tag{12}$$

$$\frac{\partial}{\partial x}(-q + 2\mu(x)\frac{\partial w_x}{\partial x}) = -K(u_x - w_x) \tag{13}$$

For the problem we have assumed $\mu = \mu_0 + gx$, where g is a constant. Rewriting (12) and (13) we have:

$$-\frac{\partial p}{\partial x} + 2\nu\frac{\partial^2 u_x}{\partial x^2} = K(u_x - w_x) \tag{14}$$

$$-\frac{\partial q}{\partial x} + 2(g\frac{\partial w_x}{\partial x} + \frac{\partial^2 w_x}{\partial x^2}\mu(x)) = -K(u_x - w_x) \tag{15}$$

Analytical treatment - 11/13/2018

In order to obtain an analytical solution for the problem initially we consider g = 0. The boundary limits of the 1-dimensional problem assume the length of the domain spanning form x=-L to x=+L. The stresses are taken to be zero at each of the boundaries. We begin by implementing a trial solution for u_x and w_x.

$$u_x = Ax + Bsinh\Big(\frac{x}{\sigma}\Big) \tag{16}$$

$$w_x = Cx + Dsinh\Big(\frac{x}{\sigma}\Big) \tag{17}$$

For estimating the values of A,B,C,D we assume additionally p=q=0. Rewriting (12):

$$2\nu\frac{\partial^2}{\partial x^2}\Big(Ax + Bsinh\Big(\frac{x}{\sigma}\Big)\Big) = K\Big(Ax + Bsinh\Big(\frac{x}{\sigma}\Big) - Cx - Dsinh\Big(\frac{x}{\sigma}\Big)\Big) \tag{18}$$

$$2\nu\frac{\partial}{\partial x}\Big(A + \frac{B}{\sigma}cosh\Big(\frac{x}{\sigma}\Big)\Big) = K\Big((A-C)x + (B-D)sinh\Big(\frac{x}{\sigma}\Big)) \tag{19}$$

$$2\nu\frac{B}{\sigma^2}sinh\Big(\frac{x}{\sigma}\Big) = K\Big((A-C)x + (B-D)sinh\Big(\frac{x}{\sigma}\Big)\Big) \tag{20}$$

and (13)

$$2\mu(x)\frac{\partial^2}{\partial x^2}\Big(Cx + Dsinh\Big(\frac{x}{\sigma}\Big)\Big) = -K\Big(Ax + Bsinh\Big(\frac{x}{\sigma}\Big) - Cx - Dsinh\Big(\frac{x}{\sigma}\Big)\Big) \tag{21}$$

$$2\mu(x)\frac{\partial}{\partial x}\Big(C + \frac{D}{\sigma}cosh\Big(\frac{x}{\sigma}\Big)\Big) = -K\Big((A-C)x + (B-D)sinh\Big(\frac{x}{\sigma}\Big)) \tag{22}$$

$$2\mu(x)\frac{D}{\sigma^2}sinh\Big(\frac{x}{\sigma}\Big) = -K\Big((A-C)x + (B-D)sinh\Big(\frac{x}{\sigma}\Big)\Big) \tag{23}$$

From (20) and (23) we have:

$$D = -\frac{\nu}{\mu(x)}B \tag{24}$$

Comparing coefficients of hyperbolic sine terms we see that (20) and (23) is satisfied only when the coefficient of the linear term is zero. Therefore,

$$A = C \tag{25}$$

Hence the length constant[1] σ has the value[2]

$$\sigma = \sqrt{\frac{2\nu\mu}{K(\nu+\mu)}} \tag{26}$$

To obtain the values of the unknown parameters B and C, we impose boundary conditions. At the edge (x = ±L) we have, normal stresses τ_{ix} and τ_{ex} as zero. As a result we get,

$$C + \frac{D}{\sigma}cosh\Big(\frac{x}{\sigma}\Big) = 0 \tag{27}$$

$$A + \frac{B}{\sigma}cosh\Big(\frac{x}{\sigma}\Big) = -\frac{T}{2\nu} \tag{28}$$

[1] This might also be a variable since μ is a function of x for the problem

[2] $\mu(x)$ is also written as μ

Solving (27) and (28) using (24)-(26) we have:

$$A = C = -\frac{T}{2(\nu + \mu)} \tag{29}$$

$$B = -\frac{T}{2\nu}\Big(\frac{\mu}{\nu + \mu}\Big)\frac{\sigma}{cosh(\frac{L}{\sigma})}\ , D = \frac{T}{2(\mu + \nu)}\frac{\sigma}{cosh(\frac{L}{\sigma})} \tag{30}$$

Using this we get the intra and extracellular displacement in terms of T as:

$$u_x = -\frac{T}{2(\nu + \mu)}\Big(x + \frac{\mu}{\nu}\sigma\frac{sinh(\frac{x}{\sigma})}{cosh(\frac{L}{\sigma})}\Big) \tag{31}$$

$$w_x = -\frac{T}{2(\nu + \mu)}\Big(x - \sigma\frac{sinh(\frac{x}{\sigma})}{cosh(\frac{L}{\sigma})}\Big) \tag{32}$$

Since μ is variable for the problem we now write it as: $\mu = \mu_0 + gx$. Remaining derivation of u_x and w_x along with its derivatives and double derivatives has been attached separately.

Bibliography

[1] Bradley J Roth *The Mechanical Bidomain Model: A Review* ISRN Tissue Eng. 2013

[2] Sharma, Kharananda; Al-Asuoad, Nofe; Shillor, Meir; Roth, Bradley J. *Intracellular, extracellular, and membrane forces in remodeling and mechanotransduction: The mechanical bidomain model* Journal of Coupled Systems and Multiscale Dynamics, Volume 3, Number 3, September 2015, pp. 200-207(8)