

Modeling Durotaxis using Mechanical Bidomain model

Prof Brad Roth, Debabrata Auddya

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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]:

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

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

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

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

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

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

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

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

Final form the equation can be written as:

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

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]:

$$\tau_{ix} = -p + 2\nu\epsilon_{ix} + T \quad (8)$$

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

Relationship between the strains and displacement can be written as:

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

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

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

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

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

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

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

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

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 from $x=-L$ 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 .

$$u_x = Ax + B \sinh\left(\frac{x}{\sigma}\right) \quad (16)$$

$$w_x = Cx + D \sinh\left(\frac{x}{\sigma}\right) \quad (17)$$

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

$$2\nu \frac{\partial^2}{\partial x^2} \left(Ax + B \sinh\left(\frac{x}{\sigma}\right) \right) = K \left(Ax + B \sinh\left(\frac{x}{\sigma}\right) - Cx - D \sinh\left(\frac{x}{\sigma}\right) \right) \quad (18)$$

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

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

and (13)

$$2\mu(x) \frac{\partial^2}{\partial x^2} \left(Cx + D \sinh\left(\frac{x}{\sigma}\right) \right) = -K \left(Ax + B \sinh\left(\frac{x}{\sigma}\right) - Cx - D \sinh\left(\frac{x}{\sigma}\right) \right) \quad (21)$$

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

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

From (20) and (23) we have:

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

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,

$$A = C \quad (25)$$

Hence the length constant¹ σ has the value²

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

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

$$C + \frac{D}{\sigma} \cosh\left(\frac{L}{\sigma}\right) = 0 \quad (27)$$

$$A + \frac{B}{\sigma} \cosh\left(\frac{L}{\sigma}\right) = -\frac{T}{2\nu} \quad (28)$$

¹This 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:

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

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

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

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

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

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.

Analytical treatment - 12/21/2018

We are considering plane stress conditions for the model. Nothing depends on y.

$$\begin{aligned}\tau_{exx} &= -q + 2\mu\epsilon_{exx} \\ \tau_{eyy} &= -q \\ \tau_{ezz} &= -q + 2\mu\epsilon_{ezz}\end{aligned}$$

Since $\tau_{ezz} = 0$ so

$$-q + 2\mu\epsilon_{ezz} = 0$$

or, $q = 2\mu\epsilon_{ezz}$, but, $\epsilon_{exx} + \epsilon_{ezz} = 0$, so

$$q = -2\mu\epsilon_{exx}$$

Therefore the stresses along the principal directions can be written as:

$$\tau_{exx} = 4\mu\epsilon_{exx} \quad \tau_{eyy} = 2\mu\epsilon_{exx} \quad \tau_{ezz} = 0 \quad \tau_{exy} = 0$$

The final partial differential form of the equations look like:

$$\begin{aligned}\frac{\partial\tau_{exx}}{\partial x} + \frac{\partial\tau_{exy}}{\partial y} &= -K(u_x - w_x) \\ \text{or, } 4\left(\frac{\partial\mu}{\partial x}\epsilon_{exx} + \mu\frac{\partial\epsilon_{exx}}{\partial x}\right) &= -K(u_x - w_x)\end{aligned}$$

For the intracellular layer the principal stress is the same except that Tension T along the principal direction (x) is also taken into account. Thus the final set of working equations are, considering μ has a gradient along x and ν is a constant for the problem.

$$\begin{aligned}4\mu\frac{\partial^2 w}{\partial x^2} + 4\frac{\partial w}{\partial x}\frac{\partial\mu}{\partial x} &= -K(u_x - w_x) \\ 4\nu\frac{\partial^2 u}{\partial x^2} &= K(u_x - w_x)\end{aligned}$$

$\mu = \text{constant}$

$$\begin{aligned}4\mu\frac{\partial^2 w}{\partial x^2} &= -K(u_x - w_x) \\ 4\nu\frac{\partial^2 u}{\partial x^2} &= K(u_x - w_x)\end{aligned}$$

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 .

$$\begin{aligned}u_x &= Ax + B\sinh\left(\frac{x}{\sigma}\right) \\ w_x &= Cx + D\sinh\left(\frac{x}{\sigma}\right)\end{aligned}$$

For estimating the values of A,B,C,D we assume: Rewriting (12):

$$\begin{aligned} 4\nu \frac{\partial^2}{\partial x^2} \left(Ax + B \sinh\left(\frac{x}{\sigma}\right) \right) &= K \left(Ax + B \sinh\left(\frac{x}{\sigma}\right) - Cx - D \sinh\left(\frac{x}{\sigma}\right) \right) \\ 4\nu \frac{\partial}{\partial x} \left(A + \frac{B}{\sigma} \cosh\left(\frac{x}{\sigma}\right) \right) &= K \left((A - C)x + (B - D) \sinh\left(\frac{x}{\sigma}\right) \right) \\ 4\nu \frac{B}{\sigma^2} \sinh\left(\frac{x}{\sigma}\right) &= K \left((A - C)x + (B - D) \sinh\left(\frac{x}{\sigma}\right) \right) \end{aligned}$$

and (13)

$$\begin{aligned} 4\mu(x) \frac{\partial^2}{\partial x^2} \left(Cx + D \sinh\left(\frac{x}{\sigma}\right) \right) &= -K \left(Ax + B \sinh\left(\frac{x}{\sigma}\right) - Cx - D \sinh\left(\frac{x}{\sigma}\right) \right) \\ 4\mu(x) \frac{\partial}{\partial x} \left(C + \frac{D}{\sigma} \cosh\left(\frac{x}{\sigma}\right) \right) &= -K \left((A - C)x + (B - D) \sinh\left(\frac{x}{\sigma}\right) \right) \\ 4\mu(x) \frac{D}{\sigma^2} \sinh\left(\frac{x}{\sigma}\right) &= -K \left((A - C)x + (B - D) \sinh\left(\frac{x}{\sigma}\right) \right) \end{aligned}$$

From (20) and (23) we have:

$$D = -\frac{\nu}{\mu} B \quad (33)$$

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,

$$A = C \quad (34)$$

Length constant σ remains as:

$$\sigma = \sqrt{\frac{4\nu\mu}{K(\nu + \mu)}} \quad (35)$$

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

$$C + \frac{D}{\sigma} \cosh\left(\frac{L}{\sigma}\right) = 0 \quad (36)$$

$$A + \frac{B}{\sigma} \cosh\left(\frac{L}{\sigma}\right) = -\frac{T}{4\nu} \quad (37)$$

Solving the equations using given by (33) - (35) and using them in (36) and (37) we have: Solving (27) and (28) using (24)-(26) we have:

$$A = C = -\frac{T}{4(\nu + \mu)} \quad (38)$$

$$B = -\frac{T}{4\nu} \left(\frac{\mu}{\nu + \mu} \right) \frac{\sigma}{\cosh\left(\frac{L}{\sigma}\right)}, D = \frac{T}{4(\mu + \nu)} \frac{\sigma}{\cosh\left(\frac{L}{\sigma}\right)} \quad (39)$$

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

$$u_x = -\frac{T}{4(\nu + \mu)} \left(x + \frac{\mu}{\nu} \sigma \frac{\sinh\left(\frac{x}{\sigma}\right)}{\cosh\left(\frac{L}{\sigma}\right)} \right) \quad (40)$$

$$w_x = -\frac{T}{4(\nu + \mu)} \left(x - \sigma \frac{\sinh\left(\frac{x}{\sigma}\right)}{\cosh\left(\frac{L}{\sigma}\right)} \right) \quad (41)$$

$$\mu = \mu_0 + g x$$

For this condition the set of equations which we need to consider for obtaining an analytical solution are:

$$4\mu \frac{\partial^2 w}{\partial x^2} + 4 \frac{\partial w}{\partial x} \frac{\partial \mu}{\partial x} = -K(u_x - w_x) \quad (42)$$

$$4\nu \frac{\partial^2 u}{\partial x^2} = K(u_x - w_x) \quad (43)$$

Replacing unknowns term by term from the previous solutions and given data we have an expression for the difference between u_x and w_x :

$$\left[\frac{-4}{K}(\mu_0 + gx) \frac{\partial^2}{\partial x^2} \left(-\frac{T}{4(\nu + \mu)} \left(x - \sigma \frac{\sinh(\frac{x}{\sigma})}{\cosh(\frac{L}{\sigma})} \right) \right) - \frac{4g}{K} \frac{\partial}{\partial x} \left(-\frac{T}{4(\nu + \mu)} \left(x - \sigma \frac{\sinh(\frac{x}{\sigma})}{\cosh(\frac{L}{\sigma})} \right) \right) \right]$$

Mathematica Code

The code below returns the value of the above expression. f(x) returns the value of $u_x - w_x$

```
sigma[x_] = ((4*(muz + gx)*nu)/(K*(nu+muz+gx)))^0.5
g[x_] = -(Tx/(4*(nu+muz+gx))) +
  ((T*sigma[x]*sinh[x/sigma[x]])/(4*(nu+muz+gx)*cosh[L/sigma[x]]))
g'[x_]
g''[x_]
f[x_] = (-4/K)*(muz+gx)*g''[x] + (-4*g/K)*g'[x]
```

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)