In cell biology, proteins are transported in a bidirectional way along molecular motors. In a 1-D model, the density of motors is modeled by a reaction-advection system of the form:

\[ \frac{\partial \rho}{\partial t} = M \rho + \frac{1}{\varepsilon} A \rho \quad \text{on } 0 < x < 1, \ t > 0 \]

where

\[ M = \begin{pmatrix} -v_{L} & 0 & 0 \\ 0 & v_{L} & 0 \\ 0 & 0 & D_{0} \end{pmatrix}, \quad \rho = \begin{pmatrix} \rho_{R} \\ \rho_{L} \\ \rho_{u} \end{pmatrix} \]

and \( A \) is a 3x3 transition matrix of the form:

\[ A = \begin{pmatrix} -\nu_{u} & 0 & \nu_{b} \\ 0 & -\nu_{u} \left( 1-\gamma \right) \nu_{b} \\ \nu_{u} & \nu_{u} - \nu_{b} \end{pmatrix} \]

**Remarks**

(i) In dimensionless model, \( \varepsilon = \frac{V}{L \Gamma} \)

where \( V \) is typical speed of motors, \( L \) is domain length

and \( \Gamma \) is a typical binding rate (dimensional version of \( \nu_{b} \) or \( \nu_{u} \)).

Typically, \( L = 100 \mu m \), \( V \approx 1-2 \mu m/sec \), \( \Gamma \approx 0.1 - 0.5/sec \)

so we have \( \varepsilon \ll 1 \), "strong binding" approximation.

(ii) \( v_{L}, v_{R} \) are non-dimensional motor speeds and \( D_{0} \) is a non-dimensional diffusivity.

(iii) \( \nu_{u} \) is transition rate from either of the two motors (left and right) to cytoplasm. \( \nu_{b} \) with \( 0 < \gamma < 1 \) binding rate to right-moving state while \( (1-\gamma) \nu_{b} \) binding rate to left-moving state.
NOW DERIVE CONSERVATION PRINCIPLE. WE OBSERVE THAT THE COLUMN SUM OF
A VANISHES, AND SO IF WE ADD THE THREE EQUATION, WE GET
\[ d_t (p^R + p^L + p^U) = -V_R p^R_x + V_L p^L_x + D_0 p^U_{xx}. \]
NOW INTEGRATING OVER THE DOMAIN
\[ \frac{d}{dt} \int_0^1 (p^R + p^L + p^U) \, dx = \int_0^1 \left( -V_R p^R_x + V_L p^L_x + D_0 p^U_{xx} \right) \, dx. \]

TO IMPOSE MASS CONSERVATION AND FIX THE DENSITY AT \( x = 0 \) \& \( x = 1 \)
\[ -V_R p^R_x + V_L p^L_x + D_0 p^U_{xx} = 0 \text{ at } x = 0; \quad p^R_x = 0 \text{ at } x = 0; \quad p^L_x = 0 \text{ at } x = 1. \]

IN THIS WAY, THE SUM \( p^R + p^L + p^U \) IS PRESERVED IN TIME.

WE NOW SEEK TO DERIVE AN EQUATION FOR \( y(x, t) \) DEFINED BY
\[ y(x, t) = p^R + p^L + p^U. \]

WE OBSERVE THAT \( \psi^T A = 0 \) WHERE \( \psi = \left( \begin{array}{c} 1 \\ 1 \end{array} \right) \). THIS \( \psi \) IS IN NULLSPACE
OF \( A^T \), SO THAT \( A^T \psi = 0 \). (1)

NOW LET \( \phi \) BE EIGENVector OF \( A \) CORRESPONDING TO A ZERO
EIGENVALUE
\[ A \phi = 0. \] (2)

WE ASSUME THAT \( \dim \lambda(A) = 1 \) AND WE NORMALIZE EIGENFUNCTION
SO THAT
\[ \psi^T \phi = 1. \] (3)

WE THEN WRITE OUR SYSTEM AS
\[ p_t = \frac{1}{\varepsilon} A p + M p \] (*)

AND WE LOOK FOR A SOLUTION TO (*) IN THE FORM
\[ p = y \phi + w \] (4)
Now multiplying by \( \psi^T \) and using \( \gamma = \psi^T p \) and \( \psi^T \psi = I \) we obtain
\[
\psi^T p = \gamma \psi^T \psi + \psi^T w \rightarrow \gamma = \gamma + \psi^T w \rightarrow \psi^T w = 0. \quad (5)
\]

Thus \( w \perp \psi \). Recall that \( \Lambda(A^T) \) and \( R(A) \) are orthogonal complements.

This yields that \( w \in R(A) \).

We would like now to derive a PDE for \( y(x,t) \) and \( \psi(x,t) \).

We first multiply (4) by \( \psi^T \) to obtain
\[
\psi^T \psi_t = \frac{1}{\varepsilon} \psi^T \psi A \psi + \psi^T \psi M \psi
\]

But \( \psi_t = \gamma_t \psi + \psi_t \psi \), so that
\[
\psi^T \left[ \gamma_t \psi + \psi_t \psi \right] = \frac{1}{\varepsilon} \psi^T \psi A \left[ \gamma \psi + \psi \right] + \psi^T \psi M \left[ \gamma \psi + \psi \right]. \quad \text{But} \quad A \psi = 0,
\]

so that
\[
\gamma_t \psi^T \psi + \psi_t \psi = \frac{1}{\varepsilon} \psi^T \psi A \psi + \psi^T \psi M \left[ \gamma \psi + \psi \right]
\]

Using \( \psi^T \psi = 0 \) and \( \psi^T \psi = 1 \) we get with \( \psi^T \psi A = (A^T \psi)^T = 0 \) that
\[
\gamma_t = \psi^T M \left[ \gamma \psi + \psi \right] \quad (6)
\]

Now we derive a PDE for \( \psi \): we put (4) into (7) to get
\[
\psi^T \psi_t = \frac{1}{\varepsilon} \psi^T \psi A \psi + \psi^T \psi M \psi
\]

With \( A \psi = 0 \) we get
\[
\psi_t = \frac{1}{\varepsilon} \psi A \psi + \psi^T M \psi
\]

Combining this with (6) yields
\[
\psi_t = \frac{1}{\varepsilon} \psi A \psi + \left( I - \psi^T \psi \right) M \psi + \psi^T M \psi
\]

With
\[
\gamma_t = \psi^T M \psi
\]

\[
(7)
\]
Remark: The system (7) is an exact reformulation of (4) and couples the slow manifold $y$ to the dynamics of $w$.

The solution for the three components, apart from boundary layers near $x=0,1$, is

$$ p(x,t) = y(x,t) \tilde{\phi} + w(x,t). $$

We now carry out an asymptotic expansion for $w$ to decouple (7).

We recall that

$$ y^T \tilde{w} = 0 \text{ to all orders in } \varepsilon. $$

We expand

$$ w = w_0 + \varepsilon w_1 + \cdots $$

To leading order we obtain from first equation of (7) that

$$ w_0 = 0 $$

and at next order

$$ A w_1 = w_0 - (I - \tilde{\phi} y^T) M[y \tilde{\phi} + w_0]. $$

From (9), $w_0 = \alpha \tilde{\phi}$ and $y^T w_0 = 0 \Rightarrow \alpha y^T \tilde{\phi} = 0$ but $y^T \tilde{\phi} = 1$

so that $\alpha = 0$. Thus, $w_0 = 0$.

At next order

$$ A w_1 = - (I - \tilde{\phi} y^T) M[y \tilde{\phi]}. $$

We now claim that (11) has a unique solution. To show that $\exists$ a solution

we must show that the right hand side of (11) is in the range of $A$,

or equivalently has no component in $\Lambda(A^T)$. We multiply (11) by $y^T$ and get

$$ y^T A w_1 = y^T (I - \tilde{\phi} y^T) M[y \tilde{\phi] = -(y^T - \tilde{\phi} y^T) M[y \tilde{\phi] = 0 $$

since $\tilde{\phi} y^T = 1$. Thus, $(I - \tilde{\phi} y^T) M[y \tilde{\phi] \in \Lambda(A)$. 


This (11) has a solution, and we make it unique by setting $\psi^+ w_i = 0$ as required by expanding (15) in $\varepsilon$.

In this way we obtain that, from (17),

$$y_t = \psi^+ M \left[ y \tilde{\phi} + \varepsilon w_i + \ldots \right] \quad (12).$$

**Leading-Order Solution**

If we neglect the $O(\varepsilon)$ term in (12) we have

$$y_t = \psi^+ M \left( y \tilde{\phi} \right) \quad (13).$$

We then solve

$$A \tilde{\phi} = 0 \rightarrow \begin{pmatrix} -K_u & 0 & R/K_b \\ 0 & -K_u & (1-\gamma)K_b \\ K_u & K_u & -K_b \end{pmatrix} \begin{pmatrix} \tilde{\phi}_1 \\ \tilde{\phi}_2 \\ \tilde{\phi}_3 \end{pmatrix} = 0$$

We obtain in terms of a scaling factor $\frac{1}{\chi}$ that

$$\tilde{\phi} = \frac{1}{\chi} \begin{pmatrix} R/K_b/K_u \\ (1-\gamma)K_b/K_u \\ 1 \end{pmatrix} \quad (14)$$

which chosen so that $\psi^+ \tilde{\phi} = 1 \rightarrow \frac{1}{\chi} \begin{pmatrix} R/K_b + (1-\gamma)K_b + 1 \\ K_u/K_u \\ K_u/K_u \end{pmatrix} = 1$.

This yields that $\chi = \frac{K_u + K_b}{K_u}$ and so

$$\tilde{\phi} = \frac{K_u}{K_u + K_b} \begin{pmatrix} R/K_b/K_u \\ (1-\gamma)K_b/K_u \\ 1 \end{pmatrix} \quad (15)$$

How to leading order from (13) we have

$$y_t = (1 \ 1 \ 1) \begin{pmatrix} -V_A \delta x & 0 & 0 \\ 0 & V_L \delta x & 0 \\ 0 & 0 & D_0 \delta xx \end{pmatrix} \begin{pmatrix} y \tilde{\phi}_1 \\ y \tilde{\phi}_2 \\ y \tilde{\phi}_3 \end{pmatrix}$$

$$y_t \approx -V_b \frac{\delta}{\delta x} (y \tilde{\phi}_1) + V_L \frac{\delta}{\delta x} (y \tilde{\phi}_2) + D_0 \frac{\delta}{\delta xx} (y \tilde{\phi}_3) \quad (16)$$

Now putting (16) into (15) we obtain that

$$y_t \approx -V_b \frac{K_b/K_u}{K_u + K_b} (y \phi)_x + \frac{V_L (K_b/K_u)K_u}{K_u + K_b} [(1-\gamma) y]_x + \frac{D_0 K_u}{K_u + K_b} \frac{y}{xx}$$
\[ \frac{V_t}{V_x} = - \frac{K_b}{K_u + K_b} (y \phi)_x + \frac{K_b V_L}{K_u + K_b} [(1 - \phi) y]_x + \frac{D_0}{K_u + K_b} \phi \phi_x. \quad (17) \]

Notice that this is a convection-diffusion equation for \( \sqrt{V_t} \).

Here we have allowed for \( P = P(x) \) in \( 0 < P(x) < 1 \), that chance of binding to either left or right motor depends on \( x \).

Now in the special case where \( P \) is a constant, independent of \( x \), then (17) can be written as

\[ V_t = \sqrt{v_{\text{eff}}} \phi \phi_x + D_{\text{eff}} \phi \phi_x \]

where

\[ \sqrt{v_{\text{eff}}} = \frac{K_b}{K_u + K_b} (V_R P + V_L (1 - P)) \]

\[ D_{\text{eff}} = \frac{D_0}{1 + K_b/K_u} \]

Notice that \( K_b/K_u \) measure amount of time (in relative terms) that the carbo remain in free state as compared to being attached to a motor. If \( V_R = V_L = V \), then \( \sqrt{v_{\text{eff}}} = \frac{K_b}{K_u + K_b} V (1 - 2P) \)

which vanishes if \( P = 1/2 \) as expected.

Remark: One can go to higher order to calculate \( \phi \). For an interpretation and generalization of the methodology see:

For an extension of the analysis to the case of nonlinear binding, where the model has the form

\[ \rho_t = \frac{1}{\epsilon} \mathbf{F}(\rho) + \mathbf{M} \rho \quad \text{with} \quad \mathbf{M} = \begin{pmatrix} -V_1 \partial_x & 0 & 0 \\ 0 & V_2 \partial_x & 0 \\ 0 & 0 & D_0 \partial_{xx} \end{pmatrix} \]

and \( \rho = \begin{pmatrix} \rho_1 \\ \rho_2 \\ \rho_3 \end{pmatrix}, \quad \mathbf{F} = \begin{pmatrix} F_1 \\ F_2 \\ F_3 \end{pmatrix} \) with \( F_1 + F_2 + F_3 = 0 \)

See Section 3 of the paper


on my webpage.