A mathematical model for the axonal cargo transport

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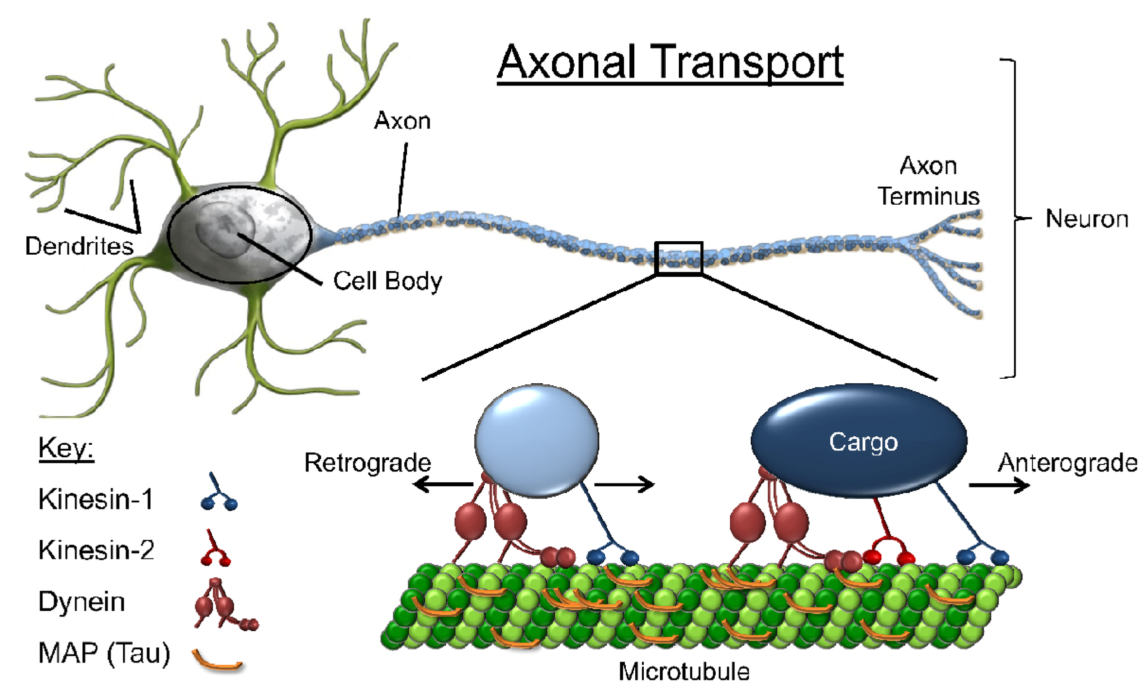
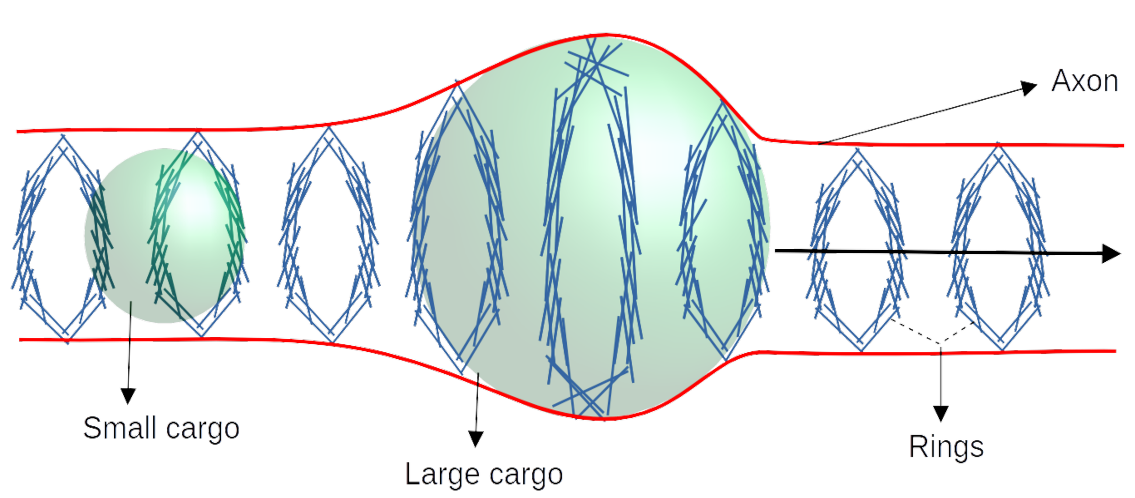
Introduction:

Axonal transport is the process whereby motor proteins actively navigate microtubules to deliver diverse cargoes.



Gregory J. Hoeprich, The Role Of Kinesin-2 In Navigating Microtubule Obstacles: Implications For The Regulation Of Axonal Transport, 2016

Actin-myosin rings are wrapped around the circumference of axons. The rings are evenly spaced along axonal shafts.



Cargo vesicles of different sizes are moving through the axon. The transport speed of cargoes is inversely correlated with their size[1].

During cargo transport a number of forces arise. We formulate a physical model to describe this phenomenon.

Mathematical Model:

- Force due to motor proteins:

$$F = NF_s\left(1 - \frac{V}{V_m}\right)$$

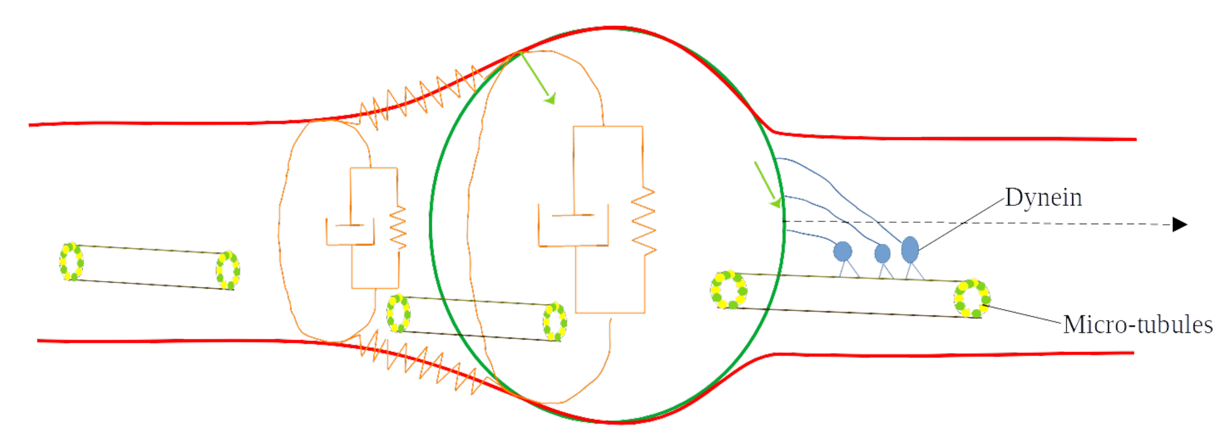
- Spring force describing elasticity of actomyosin rings:

$$F = -k(r_j - R_a)$$

- Drag (dashpot) representing viscosity of actomyosin rings:

$$F = -\eta\, r_j'$$

- Spring force coupling neighbouring rings
- Steric interaction force actomyosin rings – cargo vesicle



Different forces are acting on the cargo

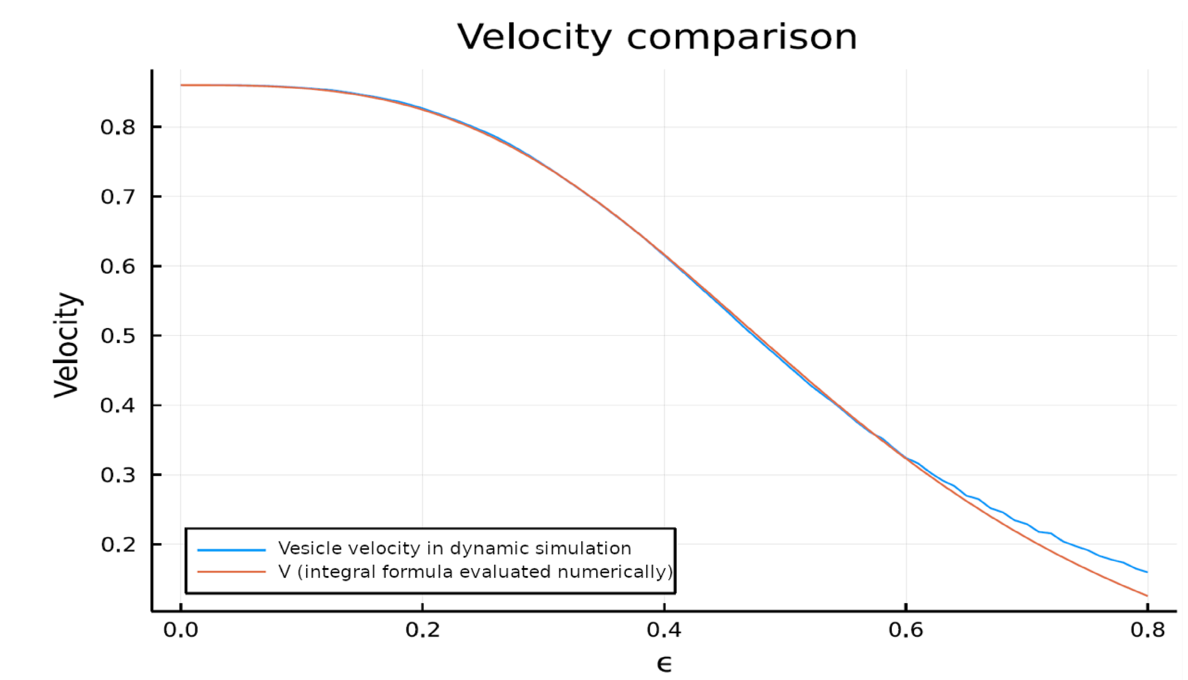
Combining all forces and written as the Energy functional, we get

$$E(x, r_j) = \left(\frac{(x - x^{n-1})^2}{2\,\Delta t}\right) N \frac{F_s}{V_m} - NF_s\, x + k \sum_{j=1}^{n} \frac{(r_j - R_A)^2}{2} + \eta \sum_{j=1}^{n} \frac{(r_j - r_j^{n-1})^2}{2\,\Delta t}$$
$$+ \frac{\alpha}{2} \sum_{j=1}^{n} (r_{j+1} - r_j)^2 + \frac{1}{2\epsilon} \sum_{j=1}^{n} \left(h(x - y_j) - r_j\right)_+^{2}$$

The Euler Lagrange Equations (after homogenization $\Delta y \to 0$ and $\Delta t \to 0$ and non-dimensionalisation)

$$\begin{cases} V_\epsilon = V_m - \dfrac{1}{F_s} \displaystyle\int_{A_\epsilon}^{B_\epsilon} \lambda_\epsilon(t, y)\ \eta'_\epsilon(y)\,dy \\ \dot{\rho_\epsilon} = -\rho_\epsilon + \lambda_\epsilon(t, y) + \alpha\, \rho_\epsilon'' \\ \rho_\epsilon \geq \eta_\epsilon\,. \end{cases}$$

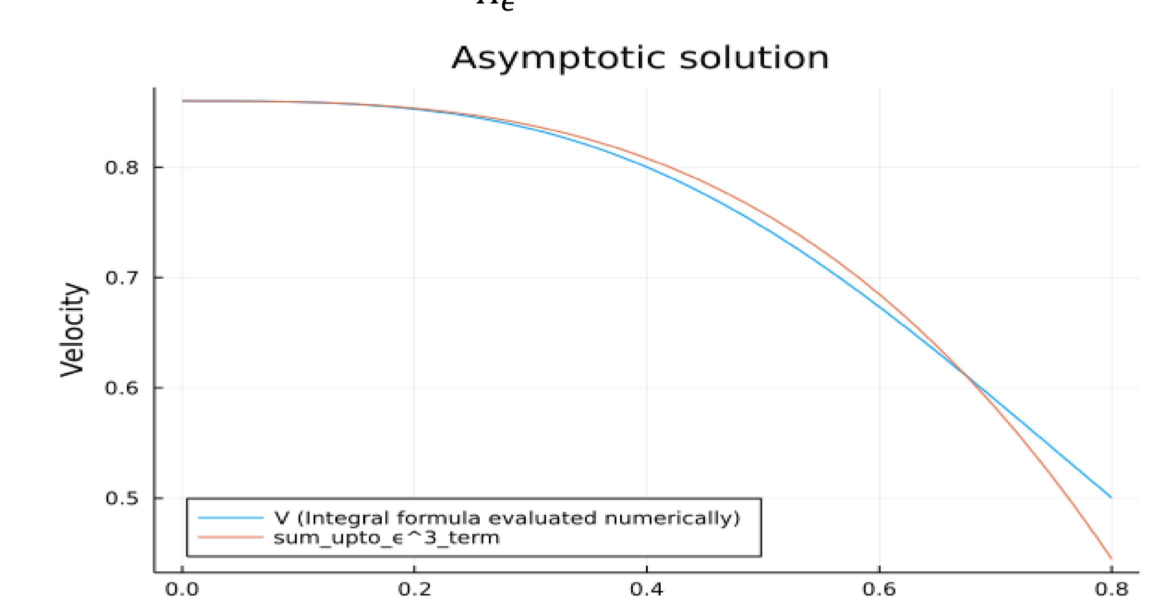
Results:



Here the free moving velocity[2] is $V_m = 0.86\ \mu m\ s^{-1}$ and number of motor protein $N = 5$.

We solve the problem as an obstacle problem[2]. We compute the cargo moving velocity V_ϵ by

$$V_\epsilon = V_m + \int_{A_\epsilon}^{B_\epsilon} \lambda_\epsilon(t, y)\ \eta'_\epsilon(y)\,dy$$



The velocity in asymptotic approximation is

$$V_\epsilon = V_m - \frac{2\sqrt{2}\,V_m}{3\,F_s}\epsilon^3 + O(\epsilon^3)$$

We write the velocity in dimensional quantities as

$$V = V_m \left(1 - \frac{2\sqrt{2}}{3} \left(\frac{R_v - R_A}{R_A}\right)^{\frac{3}{2}} \left(\frac{R_A\, \eta\, V_m}{\Delta y\, N\, F_s}\right)\right).$$

Acknowledgement: The University of Queensland and CSIRO

References:

1. Tong Wang et al., Radial contractility of actomyosin rings facilitates axonal trafficking and structural stability, JCB,2020
2. Donatella Danielli, An Overview of the Obstacle Problem, AMS, 2020