Modeling transport of a pulse of radiolabeled organelles in a *Drosophila* unipolar motor neuron

A. V. Kuznetsov

Received: 15 January 2012 / Accepted: 15 October 2012 / Published online: 18 November 2012
© Springer Science+Business Media Dordrecht 2012

Abstract Based on published experimental evidence, this paper develops a model for the transport of a pulse of radiolabeled organelles in a unipolar *Drosophila* motor neuron. In particular, since published data indicate that no microtubules (MTs) travel from the primary neurite into the dendrite, it is investigated how organelles are transported into the dendrite. Analytical solutions describing concentrations of kinesin- and dynein-driven organelles in the primary neurite, axon, and dendrite are obtained. The effects of increasing the width of the pulse and increasing the rate of organelle transition rate from the kinesin-driven to the dynein-driven state are investigated.

Keywords Unipolar neurons • Branch point • Intracellular transport • Axonal and dendritic cargos • Mathematical modeling

1 Introduction

Understanding organelle trafficking and its regulation in neurons is of great importance because malfunctioning of organelle transport machinery is linked to many devastating neurological diseases, such as Alzheimer's disease (Bean [1], Stokin et al. [2]). In axons and dendrites, transport of organelles toward MT plus-ends is powered by kinesin motors while transport toward MT minus-ends is powered by dynein motors (Goldstein and Yang [3]).

A. V. Kuznetsov (✉)
Department of Mechanical and Aerospace Engineering, North Carolina State University,
Campus Box 7910, Raleigh, NC 27695–7910, USA
e-mail: avkuznet@ncsu.edu

Despite some differences between mammalian and fly neurons, *Drosophila* is becoming an emerging model system to use for the study of neurophysiology (Gouwens and Wilson [4], Tuthill [5]). This research has already brought some interesting insights. Recently, Rolls et al. [6] and Stone et al. [7] (see also Baas and Lin [8]) investigated microtubule orientation in *Drosophila* neurons and reported that in axons all MTs have plus-end-out orientation while in dendrites more than 90% of MTs have minus-end-out orientation. This is different from mammalian dendrites where MTs have mixed polarity orientation, with approximately 50% having their plus-ends directed outward and 50% having their minus-ends directed outward (Baas et al. [9], Stepanova et al. [10]). According to Stone et al. [7], this suggests that minus-end-out rather than mixed MT polarity orientation may be a signature of the dendritic cytoskeleton. There are also some interesting studies on the ability of *Drosophila* neurons to regenerate after trauma, such as after complete axon removal (Stone et al. [11]). It has been shown that regeneration in this case involves complete MT polarity reversal in one dendrite that is later converted to an axon.

Drosophila motor neurons are unipolar. In such neurons, the neuron body (soma) gives rise to a single process (a primary neurite) that after some distance bifurcates into one axonal and one dendritic arbor, see Fig. 1a (Tuthill [5], Stone et al. [7]). The purpose of an axon is to transmit signals while the purpose of a dendrite is to receive signals [12]. Understanding transport of organelles in unipolar neurons is challenging. Indeed, as noted in Rolls [13], it is not clear how dendrites receive any cargo, as it was shown in Stone et al. [7], no microtubules travel from the primary neurite into the dendrite. The purpose of this paper is to investigate this situation theoretically and test the hypothesis that when the dendrite-destined organelles enter the axon, they detach from kinesin and reattach to dynein motors. This allows them to use minus-end-out MTs going into the dendrite. This hypothesis is based on the map of endosome transport in *Drosophila* unipolar neurons reported in Stone et al. [7] and the ideas about concerted switching of motors expressed in Rolls [13]. Steady-state transport in unipolar neurons has been investigated by Kuznetsov [14].

In writing the governing equations, the effects associated with MT dynamic instability [15] were neglected. There is experimental evidence indicating that the suppression of MT dynamic instability did not interfere with the delivery of new membrane material to the growth cone region of a neurite [16]. This justifies the assumption that dynamic instability is not the primary factor in organelle transport in neurites.

2 Governing equations

Figure 1 displays a sketch of a unipolar *Drosophila* neuron cell with a primary neurite (region 1), axon (region 2), and dendrite (region 3). According to the results reported in Stone et al. [7], in the primary neurite and in the axon of a unipolar neuron MTs have plus-end-out orientation while in the dendrite they have minus-end-out orientation. Also, imaging endosome transport indicated that 41.1% of endosomes traveled between the cell body to axon, 53.3% moved between the dendrite and axon, and only a small amount (5.6%) moved between the cell body to axon [7]. This suggests that in order to get to the dendrite, organelles (transported by kinesin motors) must first travel to the axon, then (while in the axon) change their association to dynein motors, and only then travel from the axon to dendrite by using MTs with minus-end-out orientation. Figure 1b displays a kinetic diagram showing two populations of organelles (kinesin and dynein-driven) in the axon and possible

Fig. 1 **a** Sketch of a unipolar *Drosophila* neuron cell with a primary neurite (region 1), axon (region 2), and dendrite (region 3); the percentages of endosomes that move through the branch point are from [7]. **b** Kinetic diagram showing two populations of organelles (kinesin and dynein-driven) in the axon and possible transition from the kinesin-driven to the dynein-driven state. **c** Inlet condition at the base of the primary neurite

transition from the kinesin-driven to the dynein-driven state. It is possible to develop a more sophisticated model by adding the third kinetic state that describes organelles detached from MTs [17] (such organelles can diffuse in the cytoplasm). However, that would elevate the complexity of the model such that no analytical solution would be possible any more.

Figure 1c shows the inlet condition at the base of the primary neurite. It is assumed that radiolabeled organelles enter the primary neurite as a pulse; initially the concentration of radiolabeled organelles in the primary neurite is zero, then (at $t_1^* = 0$) the concentration of kinesin-driven organelles at $x_1^* = 0$ is suddenly increased to n_{in}^* and remains at this level until $t_1^* = t_c^*$ and then it is suddenly dropped to zero.

According to Carter and Cross [18] and Vale et al. [19], kinesin-1 (conventional kinesin) walks to the MT plus-ends with an average velocity of $1 \mu\text{m/s}$ while according to King and Schroer [20] and Toba et al. [21], cytoplasmic dynein walks to the MT minus-ends with approximately the same average velocity of $1 \mu\text{m/s}$; therefore, for the ease of comparison between transport in axons and dendrites it is assumed that $v_{kin}^* = v_{dyn}^* = v^*$.

2.1 Primary dendrite (region 1)

Kinesin-driven transport in the primary neurite is governed by the following equation [22]:

$$\frac{\partial n_+^*}{\partial t_1^*} = -v^* \frac{\partial n_+^*}{\partial x_1^*} \quad (1)$$

where n_+^* is the number density of organelles transported by kinesin motors (particles/ μm^3), v^* is the kinesin (or dynein) motor velocity ($\mu\text{m/s}$), x_1^* is the linear coordinate along the primary neurite (μm) (at the branch point $x_1^* = 0$), and t_1^* is the time measured from the moment when the pulse of organelles has entered the primary neurite (s). Asterisks denote dimensional variables.

The situation when a pulse of radiolabeled organelles is injected at the base of a primary neurite is modeled. This implies that the initial concentration of radiolabeled organelles is zero and the boundary condition describing the pulse of duration t_c^* with the amplitude n_{in}^* is

$$n_+^*(0, t_1^*) = n_{in}^* [1 - H(t_1^* - t_c^*)] \quad (2)$$

The dimensionless form of (1) is

$$\frac{\partial n_+}{\partial t_1} = -\frac{\partial n_+}{\partial x_1} \quad (3)$$

where

$$n_+ = \frac{n_+^*}{n_{in}^*}, \quad x_1 = \frac{x_1^* \gamma^*}{v^*}, \quad t_1 = t_1^* \gamma^* \quad (4)$$

The dimensionless form of boundary condition (2) is

$$n_+(0, t_1) = 1 - H(t_1 - t_c) \quad (5)$$

where $t_c = t_c^* \gamma^*$.

The Laplace transform of (3) (subject to a zero initial condition) is

$$s\bar{n}_+ = -\frac{\partial \bar{n}_+}{\partial x_1} \quad (6)$$

and the Laplace transform of boundary condition (5) is

$$\bar{n}_+(0, s) = \frac{1 - e^{-st_c}}{s} \quad (7)$$

The solution of subsidiary (6) subject to boundary condition (7) is

$$\bar{n}_+(x_1, s) = \frac{\exp[-s(t_c + x_1)](-1 + \exp[st_c])}{s} \quad (8)$$

Calculating the inverse Laplace transform [23] of (8), the solution describing concentration pulse propagation in the primary neurite is obtained as:

$$n_+(x_1, t_1) = H[t_1 - x_1] - H[t_1 - t_c - x_1] \quad (9)$$

Equation (9) shows that in the primary dendrite the initial pulse propagates without changing its shape with a velocity equal to that of the kinesin motor.

2.2 Axon (region 2)

Organelles enter the axon driven by kinesin motors and then, while in the axon, some of them switch to dynein motors and reverse the direction of their motion. Transport in the axon is governed by the following equations [24]:

$$\frac{\partial n_-^*}{\partial t_2^*} = v^* \frac{\partial n_-^*}{\partial x_2^*} + \gamma^* n_+^* \quad (10)$$

$$\frac{\partial n_+^*}{\partial t_2^*} = -v^* \frac{\partial n_+^*}{\partial x_2^*} - \gamma^* n_+^* \quad (11)$$

where n_-^* is the number density of organelles transported by dynein motors (particles/ μm^3), γ^* is a first-order rate constant describing the probability of organelle transition from the kinesin-driven to the dynein-driven state (1/s), x_2^* is the linear coordinate along the axon (μm) (at the branch point $x_2^* = 0$), and t_2^* is the time measured from the moment when the pulse of organelles has entered the axon (s). t_2^* and t_1^* are related by the following equation:

$$t_2^* = t_1^* - \frac{L^*}{v^*} \quad (12)$$

where L^* is the length of the primary neurite (μm).

Since the concentration pulse does not change its shape as it propagates down the primary neurite, the pulse entry into the axon is modeled by the following boundary condition, which is similar to (2):

$$n_+^*(0, t_2^*) = n_{in}^* [1 - H(t_2^* - t_c^*)] \quad (13)$$

Equation (10) also requires a boundary condition at the axon terminal. As the diameter of the axon is much smaller than its length, the axon is modeled as semi-infinite in length. This assumption will break down very close to the axon terminal, but will be valid over most of the axon length. Therefore, instead of imposing a boundary condition at the end of the axon, a condition postulating that n_-^* is finite when $x_2^* \rightarrow \infty$ is imposed.

At the moment when the pulse enters the axon, $t_2^* = 0$, the initial concentration of radiolabeled organelles in the axon is also zero.

The dimensionless forms of (10) and (11) are

$$\frac{\partial n_-}{\partial t_2} = \frac{\partial n_-}{\partial x_2} + n_+ \quad (14)$$

$$\frac{\partial n_+}{\partial t_2} = -\frac{\partial n_+}{\partial x_2} - n_+ \quad (15)$$

where additional dimensionless variables are defined as follows:

$$n_- = \frac{n_-^*}{n_{in}^*}, x_2 = \frac{x_2^* \gamma^*}{v^*}, t_2 = t_2^* \gamma^*. \quad (16)$$

The Laplace transforms of (14) and (15) with zero initial conditions are

$$s\bar{n}_- = \frac{\partial \bar{n}_-}{\partial x_2} + \bar{n}_+ \quad (17)$$

$$s\bar{n}_+ = -\frac{\partial \bar{n}_+}{\partial x_2} - \bar{n}_+ \quad (18)$$

and the Laplace transform of boundary condition (13) is given by (7).

The solutions of subsidiary (17) and (18) subject to boundary condition (7) and the condition that $\bar{n}_-(x_2, s)$ remains finite as $x_2 \rightarrow \infty$ are

$$\bar{n}_+(x_2, s) = \frac{\exp[-x_2 - s(t_c + x_2)](-1 + \exp[st_c])}{s} \quad (19)$$

$$\bar{n}_-(x_2, s) = \frac{\exp[-x_2 - s(t_c + x_2)](-1 + \exp[st_c])}{s(1 + 2s)} \quad (20)$$

Calculating the inverse Laplace transforms of (19) and (20) leads to the following solutions:

$$n_+(x_2, t_2) = \exp[-x_2] \{H[t_2 - x_2] - H[t_2 - t_c - x_2]\} \quad (21)$$

$$n_-(x_2, t_2) = \exp[-x_2] \left\{ \left(1 - \exp\left[\frac{1}{2}(-t_2 + x_2)\right] \right) H[t_2 - x_2] - \left(1 - \exp\left[\frac{1}{2}(-t_2 + t_c + x_2)\right] \right) H[t_2 - t_c - x_2] \right\} \quad (22)$$

According to (22), the concentration of dynein-driven organelles at the branch point (leaving the axon en route to the dendrite) is

$$n_-(0, t_2) = \left(1 - \exp\left[-\frac{t_2}{2}\right] \right) H[t_2] + \left(-1 + \exp\left[\frac{1}{2}(-t_2 + t_c)\right] \right) H[t_2 - t_c] \quad (23)$$

2.3 Dendrite (region 3)

Dynein-driven transport in the dendrite is governed by the following equation:

$$\frac{\partial n_-^*}{\partial t_2^*} = -v^* \frac{\partial n_-^*}{\partial y^*} \quad (24)$$

where y^* is the linear coordinate along the dendrite (μm) (at the branch point $y^* = 0$). The sign change before the term on the right-hand side of (24) in comparison with (10) is due to the opposite MT orientation in a dendrite compared to the axon, so dynein motors transport organelles into the dendrite (while they were transporting organelles out of the axon).

The dimensionless form of (24) is

$$\frac{\partial n_-}{\partial t_2} = -\frac{\partial n_-}{\partial y} \quad (25)$$

where

$$y = \frac{y^* v^*}{v^*} \quad (26)$$

The Laplace transform of (25) (subject to a zero initial condition) is

$$s\bar{n}_- = -\frac{\partial \bar{n}_-}{\partial y} \quad (27)$$

Equation (23) is used as the boundary condition for (25). The Laplace transform of (23) is

$$\bar{n}_-(0, s) = \frac{1 - e^{-st_c}}{s + 2s^2} \quad (28)$$

Finding the solution of subsidiary (27) subject to boundary condition (28) and calculating the inverse Laplace transform of the result give

$$\begin{aligned} n_-(y, t_2) = & \left(1 - \exp\left[\frac{1}{2}(-t_2 + y)\right]\right) H[t_2 - y] \\ & + \left(-1 + \exp\left[\frac{1}{2}(-t_2 + t_c + y)\right]\right) H[t_2 - t_c - y] \end{aligned} \quad (29)$$

3 Results and discussion

The only parameter involved in (9), (21), (22), and (29) giving concentrations of organelles in a primary neurite, axon, and dendrite is the dimensionless duration of the pulse, $t_c = t_c^* \gamma^*$. The rate characterizing transition of cargos from one kinetic state to another can range widely; for example, according to the estimates reported in Jung and Brown [25], the orders of magnitude of various kinetic constants involved in their models of slow axonal transport varied between 10^{-6} and 10^{-1} s^{-1} . The kinetic constants for fast axonal transport are expected to be at the high end of this range. Indeed, the average detachment rate from MTs for kinesin-1 is estimated to be 1 s^{-1} (Schnitzer et al. [26], Vale et al. [19]) while the average attachment rate for cytoplasmic dynein is estimated to be 1.5 s^{-1} (Carter and Cross [18], Vale et al. [19]). However, the transition rate is expected to be smaller than these estimates because the transition involves detachment from MTs with plus-end-out orientation, switching of kinesin to dynein molecular motors, and then attachment to MTs with minus-end-out orientation. Lacking definitive experimental measurements, 10^{-2} s^{-1} is used as a reasonable order of magnitude estimate for γ^* . If the pulse duration is 1 s, the value of t_c is estimated at 0.01. The velocity of kinesin and dynein motors (this parameter is involved in scaling the coordinates x_1^* and x_2^* , see (4) and (16)) is assumed to be $1 \mu\text{m/s}$.

Figure 2 displays the number density of organelles transported by kinesin motors in the primary neurite for three different pulse durations: Fig. 2a is computed for $t_c^* = 1 \text{ s}$, Fig. 2b is computed for $t_c^* = 2 \text{ s}$, and Fig. 2c is computed for $t_c^* = 3 \text{ s}$. As one would expect, the increase of the pulse duration increases the width of the pulse in the primary neurite.

Figure 3 is computed for $t_c^* = 1 \text{ s}$. Figure 3a displays the concentration pulse of organelles transported by kinesin motors in the axon; it shows that the amplitude of the pulse decreases as the pulse propagates down the axon. The decrease is due to organelle transition to the dynein-driven state. Figure 3b displays the number density of organelles transported by dynein motors in the axon. This figure shows that the transition from the kinesin-driven to the dynein-driven state results in a tail of dynein-driven organelles distributed all the way between the branch point and the edge of the pulse in Fig. 3a. The tail of dynein-driven organelles thus follows the pulse of kinesin-driven organelles. The concentration of dynein-driven organelles slightly decreases as x_2^* increases and then drops sharply to zero at the edge of the kinesin-driven pulse.

Fig. 2 Number density of organelles transported by kinesin motors in the primary neurite.

$v^* = 1 \mu\text{m/s}$, $\gamma^* = 10^{-2} \text{s}^{-1}$.

a $t_c^* = 1 \text{s}$; **b** $t_c^* = 2 \text{s}$; **c** $t_c^* = 3 \text{s}$

Fig. 3 **a** Number density of organelles transported by kinesin motors in the axon. **b** Number density of organelles transported by dynein motors in the axon. **c** Number density of organelles transported by dynein motors in the dendrite. $t_c^* = 1$ s, $v^* = 1$ $\mu\text{m/s}$, $\gamma^* = 10^{-2}\text{s}^{-1}$

Fig. 4 Similar to Fig. 3, but now for $t_c^* = 3$ s

Fig. 5 Similar to Fig. 3, but now for $\gamma^* = 3 \times 10^{-2} \text{ s}^{-1}$

Figure 3c displays the concentration of organelles transported by dynein motors in the dendrite. Dynein-driven organelles enter the dendrite from the axon and then propagate deeper into the dendrite. The concentration of these organelles in the dendrite slightly increases as y^* increases (this happens because the concentration of dynein-driven organelles entering the dendrite at the branch point decreases as time increases, and thus organelles that got into the dendrite earlier have a larger concentration than those that entered later) and then sharply drops to zero.

Figure 4 is similar to Fig. 3, but it is computed for $t_c^* = 3$ s, three times the value of the pulse duration used for Fig. 3. As a result of this change, the pulse of kinesin-driven organelles in Fig. 4a became three times wider, and concentrations of dynein-driven organelles in the axon (Fig. 4b) and dendrite (Fig. 4c) increased by approximately a factor of three.

Figure 5 is similar to Fig. 3, but it is computed for $\gamma^* = 3 \times 10^{-2} \text{s}^{-1}$, three times the value of the kinetic rate constant used for Fig. 3. Since the kinetic rate constant describes the probability of organelle transition from the kinesin-driven to the dynein-driven state, its increase resulted in a faster decay of kinesin-driven organelle concentration in the axon in Fig. 5a compared to the case displayed in Fig. 3a. Since kinesin-driven organelles transition to the dynein-driven state more intensively, the concentrations of dynein-driven organelles in the axon (Fig. 5b) and dendrite (Fig. 5c) in this case are larger than those displayed in Fig. 3b and c.

4 Conclusions

The question of how organelles get into dendrites of unipolar *Drosophila* neurons is investigated. Since experimental results reported in Stone et al. [7] indicate that there are no MTs that travel from the primary neurite into dendrite, based on [13] it is hypothesized that kinesin-driven organelles, upon entering the axon, lose their attachment to kinesin motors and reattach to dynein motors. This makes it possible for these organelles to use minus-end-out MTs and enter a dendrite. It is assumed that a pulse of microinjected organelles enters a primary neurite. These organelles are transported by kinesin motors. Once the pulse enters the axon, organelles start transitioning to the dynein-driven state. The solutions describing the evolutions of concentrations of kinesin-driven and dynein-driven organelles in the primary neurite, axon, and dendrite in response to the initial pulse of kinesin-driven organelles entering the primary neurite are obtained. In the primary neurite, the pulse of kinesin-driven organelles retains its shape as it propagates toward the branch point. In the axon, the amplitude of the kinesin-driven pulse decays as organelles detach from kinesin motors and reattach to dynein motors. The concentration of dynein-driven organelles in the axon is distributed all the way between the branch point and edge of the pulse of kinesin-driven organelles. The concentration decreases slightly as the pulse propagates deeper into the axon because dynein-driven organelles are constantly removed from the axon at the branch point and are transported into the dendrite. Since the concentration of dynein-driven organelles at the branch point decreases as time increases, organelles that entered the dendrite earlier have a larger concentration than those that entered the dendrite later.

Increasing the width of the pulse (by a factor of three) increases the concentrations of dynein-driven organelles in the axon and dendrite by approximately the same amount. Increasing the rate of organelle transition from the kinesin-driven to the dynein-driven state (by a factor of three) results in a faster decay of the kinesin-driven pulse in the axon and in an increase of concentrations of dynein-driven organelles (by approximately a factor of two).

The model thus makes some testable predictions. Testing these predictions by experimentation can help elucidate transport mechanisms in unipolar neurons.

References

1. Bean, A.J. (ed.): Protein Trafficking in Neurons. Elsevier/Academic, Amsterdam (2007)
2. Stokin, G.B., Lillo, C., Falzone, T.L., Brusch, R.G., Rockenstein, E., Mount, S.L., Raman, R., Davies, P., Masliah, E., Williams, D.S., Goldstein, L.S.B.: Axonopathy and transport deficits early in the pathogenesis of Alzheimer's disease. *Science* **307**, 1282–1288 (2005)
3. Goldstein, L.S.B., Yang, Z.H.: Microtubule-based transport systems in neurons: the roles of kinesins and dyneins. *Annu. Rev. Neurosci.* **23**, 39–71 (2000)
4. Gouwens, N.W., Wilson, R.I.: Signal propagation in *Drosophila* central neurons. *J. Neurosci.* **29**, 6239–6249 (2009)
5. Tuthill, J.C.: Lessons from a compartmental model of a *Drosophila* neuron. *J. Neurosci.* **29**, 12033–12034 (2009)
6. Rolls, M.M., Satoh, D., Clyne, P.J., Henner, A.L., Uemura, T., Doe, C.Q.: Polarity and intracellular compartmentalization of *Drosophila* neurons. *Neural Dev.* **2**, 7 (2007)
7. Stone, M.C., Roegiers, F., Rolls, M.M.: Microtubules have opposite orientation in axons and dendrites of *Drosophila* neurons. *Mol. Biol. Cell* **19**, 4122–4129 (2008)
8. Baas, P.W., Lin, S.: Hooks and comets: the story of microtubule polarity orientation in the neuron. *Developmental Neurobiology* **71**, 403–418 (2011)
9. Baas, P.W., Deitch, J.S., Black, M.M., Banker, G.A.: Polarity orientation of microtubules in hippocampal neurons: Uniformity in the axon and nonuniformity in the dendrite. *Proc. Natl. Acad. Sci. USA* **85**, 8335–8339 (1988)
10. Stepanova, T., Slemmer, J., Hoogenraad, C.C., Lansbergen, G., Dortland, B., De Zeeuw, C.I., Grosveld, F., van Cappellen, G., Akhmanova, A., Galjart, N.: Visualization of microtubule growth in cultured neurons via the use of EB3-GFP (end-binding protein 3-green fluorescent protein). *J. Neurosci.* **23**, 2655–2664 (2003)
11. Stone, M.C., Nguyen, M.M., Tao, J., Allender, D.L., Rolls, M.M.: Global up-regulation of microtubule dynamics and polarity reversal during regeneration of an axon from a dendrite. *Mol. Biol. Cell* **21**, 767–777 (2010)
12. Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., Walter, P.: In: *Molecular Biology of the Cell*, 5th edn. Garland Science, New York (2008)
13. Rolls, M.M.: Neuronal polarity in *Drosophila*: sorting out axons and dendrites. *Developmental Neurobiology* **71**, 419–429 (2011)
14. Kuznetsov, A.V.: Modelling active transport in *Drosophila* unipolar motor neurons. *Comput. Methods Biomech. Biomed. Eng.* **14**, 1117–1131 (2011)
15. Janulevicius, A., van Pelt, J., van Ooyen, A.: Compartment volume influences microtubule dynamic instability: a model study. *Biophys. J.* **90**, 788–798 (2006)
16. Zakharenko, S., Popov, S.: Dynamics of axonal microtubules regulate the topology of new membrane insertion into the growing neurites. *J. Cell Biol.* **143**, 1077–1086 (1998)
17. Smith, D.A., Simmons, R.M.: Models of motor-assisted transport of intracellular particles. *Biophys. J.* **80**, 45–68 (2001)
18. Carter, N.J., Cross, R.A.: Mechanics of the kinesin step. *Nature* **435**, 308–312 (2005)
19. Vale, R.D., Funatsu, T., Pierce, D.W., Romberg, L., Harada, Y., Yanagida, T.: Direct observation of single kinesin molecules moving along microtubules. *Nature* **380**, 451–453 (1996)
20. King, S.J., Schroer, T.A.: Dynactin increases the processivity of the cytoplasmic dynein motor. *Nat. Cell Biol.* **2**, 20–24 (2000)
21. Toba, S., Watanabe, T.M., Yamaguchi-Okimoto, L., Toyoshima, Y.Y., Higuchi, H.: Overlapping hand-over-hand mechanism of single molecular motility of cytoplasmic dynein. *Proc. Natl. Acad. Sci. USA* **103**, 5741–5745 (2006)
22. Kuznetsov, A.V.: Modeling of organelle entry in an axon and dendrite. *J. Mech. Med. Biol.* (2012, in press). doi:[10.1142/S0219519412500261](https://doi.org/10.1142/S0219519412500261)
23. Abramowitz, M., Stegun, I.A. (eds.): *Handbook of Mathematical Functions, with Formulas, Graphs, and Mathematical Tables*. Dover Publications, Mineola (1965)

24. Kuznetsov, A.V.: Modelling of axonal cargo rerouting in a dendrite. *Math. Med. Biol.* (2012, in press). doi:[10.1093/imammb/dqs021](https://doi.org/10.1093/imammb/dqs021)
25. Jung, P., Brown, A.: Modeling the slowing of neurofilament transport along the mouse sciatic nerve. *Phys. Biol.* **6**, 046002 (2009)
26. Schnitzer, M.J., Visscher, K., Block, S.M.: Force production by single kinesin motors. *Nat. Cell Biol.* **2**, 718–723 (2000)