Surfing at the wave fronts: the bidirectional movement of cargo particles driven by molecular motors

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Abstract

The collective behavior of molecular motor proteins have been investigated in the literature using models to describe the long-time dynamics of a unidimensional continuum motor distribution. Here, we consider the phenomena related to the transport of particles (vesicles, organelles, virus, etc) in the realm of these continuum motor systems. We argue that cargo movement may result from its ability to perturb the existing motor distribution and to surf at the resulting shock waves separating regions of different motor densities within the transient regime. In this case, the observed bidirectionality of cargo movement is naturally associated with reversals of shocks directions. Comparison of the quantitative results predicted by this model with available data for cargo velocity allows us to suggest that geometrical characteristics of the transported particle shall determine the extension and intensity of the perturbation it produces and thus, its dynamics. Possible implications of these ideas to virus movement at the cell body are discussed in connection with their distinguished morphological characteristics.

Key words: collective effects of molecular motors; cargo transport; non-linear partial differential equations; shock waves.

1 Introduction

The intracellular active transport of particles, including organelles, vesicles and virus is mediated by motor proteins such as myosin, kinesins and dyneins [1]. The unidirectional motion of a single motor along protein filaments is well characterized experimentally and it was first modeled at a microscopic level by a stochastic dynamics describing the behavior of a Brownian particle in the presence of a time-dependent asymmetric potential field [2],[3],[4],[5]. The idea is based on the mechanism of ”ratchet and paw ” introduced by Feynmann to discuss the meaning of the second
law of thermodynamics [6]. Since then, this model has been used as a prototype to explain why and in what conditions Brownian particles are able to do work against external potential gradients. Also if particles can bind directly to motors, the transport of cargo follows as a direct consequence of motor movement.

More recently, it appeared in the literature attempts to describe the movement of interacting Brownian motors, since it was realized that collective effects emerging from this situation may be relevant to explain certain characteristics of cellular transport and, in particular, the observed property of bidirectionality of cargo movement [7],[8],[9],[10]. This non-diffusive type of process is characterized by inversions of cargo direction after processive runs \(^1\) that may be preceded by relative large resting times (intervals within which the particles remain at the same microtubule site).

Attempts to describe the observed bidirectional movement of extensive objects (filaments) mediated by motor proteins use essentially the same ideas of the original microscopic models [11]. Numerical results indicate that some of the observed characteristics of bidirectional movement are captured in this way provided that the number of motors attached simultaneously to the filament, arranged in a periodic way, be no less than a certain critical number \(N_{\text{min}}\). Because of this, it is not clear how such models could be extended to describe the observed bidirectional movement of small particles, as vesicles or virus.

The most accepted explanation in these cases is referred in the literature as the coordination model [7]. According to this, the bidirectional movement would result from the coordinated action of two type of motors - a plus-ended and a minus-ended motor - attached simultaneously to cargo (filament). The reversal of its direction would just reflect the fact that one or other type of motor, but not both simultaneously, shall be active during the respective time intervals. The motor coordination, that is, the control of motors activity would be accomplished by an external non-motor protein complex that should be able to coordinate the movement and timing of many motors of different nature and distinct characteristics - certainly a very non-trivial job. Such an external complex has never been identified in any in vivo experiment [12].

At certain scales of interest, phenomena related to the collective behavior of interacting Brownian motors can also be approached by models that are intended to describe dynamic aspects of continuum media. Such description, referred in the following as macroscopic model, is generally justified upon evaluation of the characteristic sizes and time scales where the molecules operate at very low Reynold's numbers [13]. Usually, the approach is based on the continuum versions of the "asymmetric exclusion processes" (ASEP) [14],[15],[16],[17] for studying the long-time behavior of motors interacting through volume excluded [13] [18] [19] [20]. From this perspective, the individual microscopic asymmetric movement of motors is assumed a priori and for open boundary conditions the problem consists in analyzing the steady-state behavior of a defined motor density as the solutions to the corresponding non-linear differential equation - the non-viscous Burgers equation - that describes the dynamics of the system in these limits. It is also possible to superimpose to the ASEP a non-conservative Langmuir process to allow the system exchange motors with the bulk at any position of the microtubule [19]. Apparently, however, questions related to cargo transport, have not been considered in this context.

Here, we make a proposal in this direction based on considerations about the interactions

\(^1\)Processive run in this context is referred to the movement accomplished in one definite direction before inversion or detachment from filament.
between cargo and motor molecules. It relies on the idea that the arrival of a cargo particle may perturb the motor system in such a way to produce local changes onto the existing motor density.

Thereafter cargo may take advantage of the gradients induced by this initial perturbation to move along microtubule by surfing at the density shock waves formed as the motor system relaxes back to the situation before interaction with cargo. Shock waves separate regions of different motor densities and evolve according to the transient solutions to the corresponding Burgers equation for the considered initial conditions (perturbation). Within this view, bidirectional movement of cargo particles follows naturally as a consequence of the reversals of shocks propagation direction.

From a more quantitative perspective, we use data from the movement of vesicles in Drosophila embryo [21] to perform a phenomenological analysis of the model considering the explicit expressions obtained for shock velocities. As we shall see, this allows us to associate geometrical characteristics of cargo with the extension and magnitude of the perturbation it produces. We then discuss on the possibility to make a connection between these results with the properties of the observed movement of virus at the cell body.

2 From the microscopic potential models to the macroscopic motor density profile

We consider the continuum limit of the mean field approximation (the macroscopic limit) of an ASEP discrete model representing the stochastic dynamics of particle motors moving in a one-dimensional space. Within this view, the diffusion process is not accounted for explicitly; its effects on the movement of each motor under the time-dependent asymmetric potential, are assumed a priori. Yet, the parameters that define the asymmetry of the potential, can be incorporated into the parameters of the considered ASEP.

Consider the time-dependent asymmetric and periodic microscopic potential shown in Fig. 1. The position of each minimum may be associated to the position of a one-dimensional lattice site; the distance between sites being \( l = a + b \) coincides with the spacial period of the potential. The difference between parameters \( a \) and \( b \) define the strength of the asymmetry. The time dependence is such that it alternates between an ”off” state (flat potential), when the particle feels no forces, and an state ”on” - the sawtooth profile shown. If the potential is turned off and the particle starts to diffuse from a local minimum corresponding to the site \( i \) of the lattice, it shall diffuse around this position up to the instant when the potential is turned on again, after a time interval \( \tau \). At this instant, the particle is supposed to fall immediately into the nearest minimum (adiabatic approximation). Because \( a > b \), and considering a regime of relative slow diffusion, it is more likely that the nearest minimum achieved by the particle be that at site \( i+1 \). This prototype mechanism was conceived to explain from a microscopic point of view the observed unidirectional movement of a Brownian motor [3], [4], [5].

ASEP models have been introduced more recently in this context as a way to account for collective effects of many motors moving on the same lattice model ([18], [20]). At these scales, motors are self-driven and the interactions among them are that of volume excluded, i.e. a motor can not occupy a site already occupied by another motor. Let us now consider a stochastic description of the process at this scale. The time unit being the interval \( \tau \) within which a particle can execute one movement to a neighbor site with (transition) probability \( p_i \) to move from site \( i \) to site \( i + 1 \)
and (transition) probability \(q_i\) to move from site \(i\) to site \(i-1\). Neglecting correlations (mean-field approximation) the average density \(\rho_i(t+\tau)\) of motors at site \(i\), at time \(t+\tau\) satisfies the following recurrence relation:

\[
\rho_i(t+\tau) = \rho_i(t) + \rho_{i+1}(t)q_{i+1}(t) + \rho_{i-1}(t)p_{i-1}(t) - \rho_i(t)(p_i(t) + q_i(t))
\]  

Excluded volume interaction is introduced into the model by attributing to \(p_i\) and \(q_i\) an explicit dependence on the occupation of the target sites:

\[
p_i(t) = p(1 - \rho_{i+1}(t))
\]

and

\[
q_i(t) = q(1 - \rho_{i-1}(t))
\]

Here, \(p\) and \(q\) are dimensionless constants such that \(p, q < 1\). Now, let \(N\) be the total number of lattice sites and let \(L \equiv 1\) be its total length. As in Ref. [19], the discrete model can be coarse-graining with lattice constant \(l = 1/N\) to a continuum such that for \(N \to \infty\) the density \(\rho_i(t)\) becomes a function \(\rho(x, t)\) of a continuum variable \(x = i/N\). In this limit, \(\rho_{i\pm 1}\) can be expanded in powers of \(l\):

\[
\rho_{i\pm 1}(t) = \rho(x \pm l, t) = \rho(x, t) \pm l\partial_x \rho(x, t) + \frac{1}{2} l^2 \partial_x^2 \rho(x, t) + O(l^3)
\]

and the recurrence in (1) becomes

\[
\frac{\rho(x, t+\tau) - \rho(x, t)}{\tau} = \gamma \left[ \frac{(p + q)}{2} l^2 \partial_x^2 \rho(x, t) + (p - q)(2\rho(x, t) - 1)\partial_x \rho(x, t) \right] + O(l^2)
\]

where we have defined

\[
\gamma = \frac{l}{\tau}
\]

For \(\tau \to 0\) and \(l \to 0\) keeping \(\gamma\) in (6) finite and neglecting terms of \(O(l)\), Eq. (5) converges to the non-viscous Burgers equation

\[
\partial_t \rho + \gamma(p - q)(1 - 2\rho)\partial_x \rho = 0.
\]

Now, a connection between the above description and the microscopic model can be made by setting

\[
p = a/l \quad \text{and} \quad q = b/l
\]

so that Eq. (7) is rewritten as

\[
\partial_t \rho + K \partial_x (\rho(1 - \rho)) = 0
\]

where we have defined \(K \equiv \gamma(a - b)N\) positive. This can also be expressed as \(\partial_t \rho + \partial_x j = 0\) with the particle current given by

\[
j(x, t) = K \rho(x, t)(1 - \rho(x, t)).
\]

Notice that to keep \(K\) finite as \(N \to \infty\), parameters \(a\) and \(b\) must scale as \(1/N\). The same behavior is expected for the Langmuir rates in the model of Ref. [19]. In these conditions, and with no lost of generality, we can set \(K = 1\).
The nonequilibrium steady-state solutions to this equation have already been explored in the references mentioned above to study the long-time behavior of molecular motor traffic with open boundary conditions. This allows one to make important predictions on the stationary density profiles related to the concentrations gradients of motors at the microtubule ends. In particular, the emergence of stable domain walls separating regions of different motor densities, predicted in these conditions, have indeed been observed in recent experiments [22]. Here, we consider periodic boundary and study the short-time behavior of the system described by Eq. (9), after being perturbed with respect to the motor density steady-state $\rho(x,t) = 1/2$. The results we obtain for a particular choice of initial conditions are shown in the next section.

3 Results

It is known that perturbations around the steady state solutions of Burgers equation (9) may create shocks due to encounters of particles at different velocities ([23],[24]). This leads us to speculate that cargo may use these shock waves, by *surfing* at the wave fronts, in order to reach target sites.

To illustrate these ideas, we can generally conceive that the approach of cargo induces a perturbation on motor density such as to create at the cargo neighborhood regions where motor density becomes lower and others where density becomes higher than the steady state $\rho = 1/2$. As an example, we choose

\[
\begin{align*}
\rho(x,0) &= 1/2 \quad \text{for} \quad x < 0 \\
\rho(x,0) &= 1/2 - \varepsilon \quad \text{for} \quad 0 < x < 2a \\
\rho(x,0) &= 1/2 \quad \text{for} \quad 2a < x < 3a \\
\rho(x,0) &= 1/2 + \varepsilon \quad \text{for} \quad 3a < x < 4a \\
\rho(x,0) &= 1/2 \quad \text{for} \quad x > 4a
\end{align*}
\]

(11)

to represent such perturbation (see Fig(2a)). Parameters $a$ and $\varepsilon$ are related, respectively, to the extension and magnitude of this perturbation.

We then use the method of characteristics to find the transient solutions to Eq. (9) that reveal the time evolution of shocks for these initial conditions (IC) (11), which is our main interest here. This is performed in the Appendix.

The results for the density profile are represented in Fig.(2) at various instants of time. The behavior of each shock front, namely, distance traveled up to an eventual encounter with other shock fronts - which are identified here with the processive runs - the time spent within each of these runs, and the corresponding expressions for average shock velocities are compiled in Table1.

In the next Section, we use these results to examine the consequences of the hypothesis made above.

4 Discussion
4.1 the surfing

The model proposed here offers rather simple explanations to a few but essential phenomena related to motor-driven cargo transport. In particular, it suggests an alternative to interpret data showing that cargo executes a non-diffusive bidirectional movement before it arrives at its final destination.

In general the main difficulty to explain the bidirectional movement of cargo relies precisely on the fact that the existing models have been conceived to explain the unidirectional movement of motors. Because of this, the original idea that the cargo movement shall be put into effect by its attachment to a single or a few identical motor proteins has been reviewed in the literature.

The alternative mechanism proposed here does not exclude the possibility that eventually, the presence of two types of motors may contribute to explain the reversals of particle direction. However, it does not use this as a necessary condition as does the coordination model mentioned above. Within such an alternative context, cargo is driven by shocks and this is independent of the nature of motors involved provided they offer an assessable density background. That is, in order to move and eventually change direction, cargo must be able to perturb this background and follow gradients of motor density right after perturbation, just like the putative microscopic ”second class particles” introduced in the context of many-particle asymmetric exclusion processes (ASEP) to study the nature of shocks at these scales [14], [15].

Although we do not offer here any direct evidence that would support these ideas we can test for their compatibility by confronting some experimental data with the results shown in Table 1 for the considered initial conditions. For example, it is shown there that a cargo particle accompanying the wave front referred here as wave front 2, or second shock, would perform a backward movement within a time interval $T_1 = a/2\varepsilon$ that depends on the model parameters. Within the subsequent time interval $T_2 = a/4\varepsilon$, the particle would remain at rest up to the instant $3a/4\varepsilon$ when it reverses the direction of movement. Thereafter, the particle would proceed eventually changing the magnitude of its velocity though not direction anymore (in this specific case (11) the reversal happens just once) until the motor density recovers its steady state profile $\rho(x,t) = 1/2$ and the particle reaches its final destination at the one of the microtubule ends, as expected. Therefore, at least qualitatively, the phenomenological aspects of the observed movement, as reversals of direction, processivity in both directions and resting times are accounted for by this model.

Evidently, if one considers other initial conditions, for example by introducing additional parameters to characterize the perturbation, it is expected a great variety of time intervals and corresponding distances traveled in both directions, differing in processivity and velocity. Therefore, a relevant aspect of this proposal is the possibility to attribute primarily to cargo the task for creating such gradients, thus inducing its own surfing movement. This is discussed below in connection to a more quantitative analysis of available data from real biological systems.

4.2 phenomenological analysis

Consider for instance the data in the literature on the movement of lipid vesicles on Drosophila embryo [21]. We can check for their compatibility with the results in Table 1 all expressed in terms of just two parameters $a$ and $\varepsilon$. To accomplish this, we observe that data analysis obtained from the transport of vesicles in the referred experiment identifies two typical runs in both directions: one that is short (average distance $d_{short} \sim 100nm$) and slow (average velocity $v_{slow} \sim 200 nm/s$) and
another that is long (average distance $d_{\text{long}} \sim 1000\,\text{nm}$) and fast (average velocity $v_{\text{fast}} \sim 400\,\text{nm/s}$). We shall use these data to estimate the values of $a$ and $\varepsilon$. We proceed by identifying $v_{\text{slow}}$, taken from experimental data, with the average velocity of the 4th shock front $v_4 = 2\,\varepsilon/7$. It results $\varepsilon \sim 700$. We can now use this to predict the magnitude of the average shock front velocity for the 5th shock $v_5 = \varepsilon/2 \sim 350$ which approaches very well the values (absolute values) observed for $v_{\text{fast}} \sim 400\,\text{nm/s}$.

On the other hand, these results must be compatible with the predictions for the distances traveled by the corresponding shocks. This complements the analysis by estimating possible values for parameter $a$. Accordingly, the predicted distance $d_5$ must be approximately one order of magnitude greater than $d_4$. This is in fact accomplished by the results shown in Table 1 since from there $d_5/d_4 = 8$.

We shall now perform a slight different analysis of the data by redefining the constant $a$ such that

$$a \equiv 500p(\text{nm}) \quad (12)$$

where $p$ is a numerical factor. From this, $d_4 = 80p(\text{nm})$ and $d_5 = 650p(\text{nm})$. Therefore, if we choose $p = 1.2$, it results $d_4 \sim 100(\text{nm})$ and $d_5 \sim 800(\text{nm})$. These can be compared to the results for $d_{\text{short}}$ and $d_{\text{long}}$ given above to conclude that the characteristic times and distances traveled by shock fronts 4 and 5 can be related in a very direct way with the typical values obtained in experiments for short and long runs, respectively.

More interesting, however, is the fact that this approach to the experimental data is made possible with the choice in (12) for $p \sim O(1)$. First, notice that $500\,\text{nm}$ is the average diameter of the vesicles transported in the referred experiments. Thus, if the nature of interactions between cargo and motors are of short range, this implies that the magnitude and extension of the perturbation should be related to the geometrical characteristics (typical sizes) of the cargo. Therefore, if the nature of interaction of different cargos with motors is the same, but cargo differ from each other in morphological aspects, these differences would be reflected in the specific way (size, magnitude) each of them perturb the equilibrium motor distribution and consequently, in the diversity of movements. Such diversity is indeed observed in experiments using different motor/cargo systems and/or under different conditions [7].

The above considerations seem specially attractive to explain the behavior of virus particles moving within the cellular environment observed more recently using confocal microscopy technique ([25], [26], [27]). According to the authors of these experiments, virus appear surfing along filopodia in such a way to perform a bidirectional motor-driven process in the presence of a single type of motor protein, unidirectional myosin II. From these observations the authors then discuss on the possibility that, in these experiments, virus might have been able to create the conditions to induce their own movement. These observations support the idea that virus use (hijack) existing cell transport machinery to invade the cell [27]. The model presented here suggests a mechanism to explain how this can be accomplished without external and specific mechanisms of coordination. Such explanation has a focus on the morphological aspects of cargo - which, of course, is a distinguished characteristic of virus. In our view, this complements the suggestions made in Ref. [25].

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2It must be remembered that the parameter $\varepsilon$ was defined adimensional and that the velocities are expressed in units of the parameter $K$ that have been defined equal to one.
relative to the existence of a common mechanism that drives different virus particles to their targets in cells, in spite of their morphological differences. We propose that this common mechanism is just related to their ability to interact with the system by perturbing the existing motor profile. Specific geometries, however, would be used by virus to create a variety of movements, possible necessary for their efficiency. We thus believe that these ideas may be helpful for studying the mechanisms of virus infection and also for designing drugs that must be directed to the cell body.

5 Appendix

Here we obtain the properties of shock waves shown in Table 1 within the transient regime, after the motor system is perturbed by interaction with cargo. We apply the method of characteristics to find the transient solutions to the equation (9). For this, we follow the texts by Habermann ([23]) and that by Evans ([24]).

\[ \frac{\partial \rho(x, t)}{\partial t} + (1 - 2\rho(x, t)) \frac{\partial \rho(x, t)}{\partial x} = 0 \]  

(13)

for the chosen initial conditions (IC) (11). In turn, these solutions define the properties of shocks depicted in Table 1 which is our main concern in this work. For each pair \((\rho(x_0), x_0)\) there corresponds a characteristic curve for (9) given by

\[ x(t) = (1 - 2\rho(x_0))t + x_0 \]  

(14)

Thus, the IC in (11) define the different characteristic families:

\[ x_1(t) = x_0 \quad \text{for} \quad x_0 < 0 \]  

(15)

\[ x_2(t) = x_0 + 2\varepsilon t \quad \text{for} \quad 0 < x_0 < 2a \]

\[ x_3(t) = x_0 \quad \text{for} \quad 2a < x_0 < 3a \]

\[ x_4(t) = x_0 - 2\varepsilon t \quad \text{for} \quad 3a < x_0 < 4a \]

\[ x_5(t) = x_0 \quad \text{for} \quad 4a < x_0 \]

These are represented in Fig.(3) where one observes the occurrence of shocks dividing regions of different density values. There are six shocks. There are also shown in this figure the rarefaction regions that are localized between any two characteristic families that get apart from each other as the time evolves. The exact determination of the origin of each of these shocks (time and space) - and rarefaction regions and the course of their time evolution allows us to describe the evolution of \(\rho(x, t)\).

At the initial time \((t = 0)\) there are two shocks:

- **shock 1** \((x_{s1}(t))\) at position \(x_{s1}(0) = 2a\), between the families defined by \(x_2(t)\) and \(x_3(t)\). The velocity of this shock front is determined by mass conservation conditions:

\[ \frac{dx_{s1}}{dt} = \frac{j(\rho(x_3)) - j(\rho(x_2))}{\rho(x_3) - \rho(x_2)} = \varepsilon \]
where the current $j(\rho)$ is defined by (10). We then have

$$x_{s1}(t) = 2a + \varepsilon t$$

that gives the shock position as a function of time.

- **shock 2** ($x_{s2}(t)$) at $x_{s2}(0) = 3a$, between the families defined by $x_3(t)$ and $x_4(t)$. The velocity of this shock is given by

$$\frac{dx_{s2}}{dt} = \frac{j(\rho(x_4)) - j(\rho(x_3))}{\rho(x_4) - \rho(x_3)} = -\varepsilon$$

from which

$$x_{s2}(t) = 3a - \varepsilon t$$

Still at $t = 0$, there originate two rarefaction regions

- **rarefaction 1** ($x_{r1}(t)$) at $x_{r1}(0) = 0$, evolving in the region between families $x_1(t)$ and $x_2(t)$. The requirement of entropic solutions drive us to look for the corresponding family of characteristic curves $x_{r1}(t)$ defined by the density $\rho_{r1}$ at each point in this region:

$$x_{r1}(t) = (1 - 2\rho_{r1})t \quad \text{for} \quad 1/2 - \varepsilon < \rho_{r1} < 1/2$$

which are also represented in Fig. 2. Conversely, one can write the solutions to $\rho_{r1}(x_{r1}, t)$ for density profile at each position $x_{r1}$ in this region as

$$\rho_{r1}(x_{r1}, t) = 1/2 - \frac{x_{r1}}{2t} \quad \text{for} \quad 0 < x_{r1} < 2\varepsilon t$$

- **rarefaction 2** ($x_{r2}(t)$) at $x_{r2}(0) = 4a$, evolving in the region between families $x_4(t)$ and $x_5(t)$. The characteristics in this region are given by

$$x_{r2}(t) = 4a + (1 - 2\rho_{r2})t \quad \text{for} \quad 1/2 < \rho_{r2} < 1/2 + \varepsilon$$

thus

$$\rho_{r2}(t, x_{r2}) = 1/2 + \frac{4a - x_{r2}}{2t} \quad \text{for} \quad 4a - 2\varepsilon t < x_{r2} < 4a$$

- **shock 3** ($x_{s3}(t)$) The third shock occurs at time $t_3^0$ when the two families $x_{s1}(t)$ and $x_{s2}(t)$ cross. Thus, $t_3^0$ is determined by the condition: $x_{s1}(t_3^0) = x_{s2}(t_3^0)$, which gives

$$t_3^0 = a/2\varepsilon.$$  

The velocity of the shock is given by

$$\frac{dx_{s3}}{dt} = \frac{j(\rho(x_4)) - j(\rho(x_2))}{\rho(x_4) - \rho(x_2)} = 0$$

meaning that the shock front is stationary at $x_{s3}(t_3^0) = x_{s1}(t_3^0) = 5a/2$.  

9
• shock 4 \((x_{s4}(t))\) occurs at time \(t^0_4\) when the family \(x_4\) with origin at \(x_0 = 4a\) reaches the second region of rarefaction and also cross the characteristics from family \(x_2\). Thus, \(t^0_4\) is determined by the relation \(x_{s3}(t^0_4) = x_{r2}(\rho = 1/2 + \varepsilon; t^0_4)\), which gives
\[
t^0_4 = 3a/4\varepsilon
\] (23)
The (continuity) condition, in this case reads
\[
\frac{dx_{s4}}{dt} = \frac{j(\rho_{r2}(x_{s4})) - j(\rho(x_4))}{\rho_{r2}(x_{s4}) - \rho(x_4)}
\]
that is
\[
\frac{dx_{s4}}{dt} = \frac{\varepsilon - (4a - x_{s4})}{2t}
\] (24)
then \(x_{s4}\) is given by the solutions to the above differential equation for initial condition \(x_{s4}(t^0_4)\) such that \(x_{s3}(t^0_4) = x_{s4}(t^0_4)\). The result is [28]
\[
x_{s4}(t) = 4a - 2\sqrt{3a\varepsilon t + 2\varepsilon t}
\] (25)
The dependence on time of the corresponding shock velocity can now be found
\[
\frac{dx_{s4}}{dt} = 2\varepsilon - \sqrt{\frac{3a\varepsilon}{t}}
\] (26)
• shock 5 \((x_{s5}(t))\), occurs between the two rarefaction regions, at the time \(t^0_5\), when the characteristic from the family \(x_2\) that originates at \(x_0 = 0\) encounters \(x_{s4}\)
\[
x_{r2}(\rho_{r1} = 1/2 - \varepsilon; t^0_5) = x_{s4}(t^0_5)
\] (27)
resulting
\[
t^0_5 = \frac{4a}{3\varepsilon}
\] (28)
The mass conservation conditions in this case (see 21 and 19) reads
\[
\frac{dx_{s5}}{dt} = \frac{j(\rho_{r2}(x_{s5})) - j(\rho_{r1}(x_{s5}))}{\rho_{r2}(x_{s5}) - \rho_{r1}(x_{s5})} = \frac{x_{s5} - 2a}{t}
\]
Considering that \(x_{s4}(t^0_5) = x_{s5}(t^0_5)\) this can be integrated to find
\[
x_{s5}(t) = 2a + (\varepsilon/2)t
\] (29)
thus
\[
\frac{dx_{s5}}{dt} = \varepsilon/2
\] (30)
• shock 6 \((x_{s6}(t))\), occurs at \(t^0_6\) when shock 5 encounters the characteristics from family \(x_5\) that starts at \(x_0 = 4a\). Then, \(t^0_6\) results from the relation \(x_{s5}(t^0_6) = 4a\). Using the above derived expression for \(x_{s5}(t)\) one gets
\[
t^0_6 = 4a/\varepsilon
\] (31)
The mass conservation conditions impose that
\[
\frac{dx_{s6}}{dt} = \frac{j(\rho(x_5)) - j(\rho_{r1}(x_{s5}))}{\rho(x_5) - \rho_{r1}(x_{s5})} = \frac{x_{s6}}{2t}
\]
whose solution for the initial condition $x_{s6}(t_0^0) = 4a$ becomes

$$x_{s6}(t) = 2\sqrt{a\varepsilon t}$$

from which one can find the shock velocity:

$$\frac{dx_{s6}}{dt} = \sqrt{\frac{a\varepsilon}{t}}$$

The fact that this velocity is always positive, implies that for $t > t_0^0 = 4a/\varepsilon$ the solutions to Eq. (9) for the considered initial conditions (11) are

$$\rho(x, t) = \frac{1}{2} \quad \text{for} \quad x < 0 \quad (34)$$

$$\rho(x, t) = \frac{1}{2} - \frac{x}{2t} \quad \text{for} \quad 0 < x < 4a + \sqrt{\frac{a\varepsilon}{t}} \quad (35)$$

$$\rho(x, t) = \frac{1}{2} \quad \text{for} \quad 4a + \sqrt{\frac{a\varepsilon}{t}} < x \quad (36)$$

From these, one sees that for long times, i.e. for $t > t_0^0 = 4a/\varepsilon$, the density profile returns to its uniform steady state profile, $\rho(x, t) = 1/2$. This corresponds to the situation before perturbation imposed by cargo particles. The solutions discussed above refer to behavior of $\rho(x, t)$ within the transient regime soon after being perturbed by cargo. The properties of shocks derived here are compiled in Table 1.
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References

[1] For a review, see: Howard J., Mechanics of Motor Proteins and the Cytoskeleton (Sinauer Associates, MA (2001))

[2] Astumian, R. D. and M. Bier, Fluctuation Driven Rachets: Molecular Motors. Phys. Rev. Lett., 72 (1994) 1766 – 1769.

[3] Astumian, R. D. Adiabatic Theory of Fluctuation-Induced Transport on a Periodic Potential. J. Phys. Chem., 100 (1996) 19075 – 19081.

[4] Adjari, A., J. Prost, . Mouvement Induit par un Potentiel Périodique de Basse Symétrie: Dielectrophorèse Pulsée. C. R. Acad. Sci. Paris, t. 315 Série II (1992) 1635 – 1639.

[5] Magnasco, M. O. Forced Thermal Ratchets Phys. Rev. Lett., 71 (1993) 1477 – 1481

[6] Feynman, R. P., R. B. Leighton, and Sands., The Feynman Lectures on Physics. Vol. I. Reading MA: Addison-Wesley, 1963. Chapter 46 p. 46-1 – 46-9. ISBN 0-201-02116-1

[7] Gross, S. P. Hilther and Yon: A Review of bi-Directional Microtubule-Based Transport, Phys. Biol., 1 (2004) R1 – R11.

[8] Murray, J. W., E. Bananis, and A. W. Wolkoff, Reconstitution of ATP-dependent Movement of Endocytic Vesicles Along Microtubules In Vitro: An Oscillatory Bidirectional Process, Mol. Biol. Cell, 11 (2000) 419 – 433.

[9] Welte, M. A. Bidirectional Transport along microtubules. Curr. Biol., 14 (2004) R525 – R537.

[10] Ross, J. L., K. Wallace, H. Shuman, Y. E. Goldman, E. L. F. Holzbaur, Processive bidirectional motion of dynein-dynactin complexes in vitro. Nat. Cell Biol., 8 (2006) 562 – 570.

[11] a) Jülicher F., J. Prost, Cooperative Molecular Motors, Phys. Rev. Lett 75 (1995), 2618 , b) Jülicher F., J. Prost, Spontaneous Oscillations of Collective Molecular Motors, Phys. Rev. Lett 78 (1997) 2618 ; c) Badoual M., F. Jülicher , J. Prost, Bidirectional cooperative motion of molecular motors, Proc. Natl. Acad. Sci. USA 6696 - 6701 (2002);

[12] Gross, S. P., M. A. Welte, S. M. Block, and E. F. Wieschaus, E. F. Coordination of opposite-polarity microtubule motors, J. Cell Biol., 156 (2002) 715 – 724.

[13] Chowdhury, D. Traffic Flow of Interacting Self-Driven Particles: Rails and Trail, Vehicles and Vesicles. Physica Scripta, T106 (2003) 13 – 18.
[14] Andjel, E. D., M. Bramson, T. M. Liggett, Shocks in the asymmetric exclusion process. *Prob. Theor. Rel. Fields*, 78 (1988) 231

[15] Ferrari, P., C. Kipnis, E. Saada, Microscopic Structure of Travelling Waves in the Asymmetric Simple Exclusion Process. *Ann. Prob.*, 19 (1991) 226.

[16] Krug, J. Boundary-Induced Phase Transitions in Driven Diffusive Systems. *Phys. Rev. Lett.*, 76 (1991) 1882 – 1885

[17] Derrida, B., E. Domany, D. Mukamel, An Exact Solution of a One-Dimensional Asymmetric Exclusion Model with Open Boundaries. *J. Stat. Phys.* 69 (1992) 667 – 687.

[18] Parmeggiani, A., T. Franosch, and E. Frey, Phase Coexistence in Driven One-Dimensional transport. *Phys. Rev. Lett.*, 90 (2003) 086601-1 – 086601-4.

[19] Parmeggiani, A., T. Franosch, and E. Frey, E. Totally Asymmetric Simple Exclusion Process with Langmuir Kinetics, *Phys. Rev. E*, 70 (2004) 046101-1 – 046101-20;

[20] Klumpp, S., R. Lipowsky,., Traffic of Molecular Motors Through Tube-Like Compartments, *J. Stat. Phys.* 113 (2003) 233 -268.

[21] Welte, M. A., S. P. Gross, M. Postner, S. M. Block, and E. F. Wieschaus, Developmental Regulation of Vesicle Transport in *Drosophila* Embryos: Forces and Kinetics, *Cell*, 92 (1998) 547 – 557.

[22] Nishinari, K., Y. Okada, A. Schadschneider, and D. Chowdhury, Intracellular Transport of Single-Headed Molecular Motors KIF1A. *Phys. Rev. Lett.*, 95 (2005) 118101-1 – 118101-4.

[23] Haberman, R. *Elementary Applied Partial Differential Equations*. Third edition. Prentice Hall, 1998. Chapter 11: The Method of characteristics for Linear and Quasi-Linear Wave Equations, p. 417 – 447. ISBN 0-13-263807-X.

[24] Evans, L. C., *Partial Differential Equations* (Graduate Studies in Mathematics Vol. 19), American Mathematical Society, Providence, Rhode Island (1999).

[25] Lehmann, M.J., N. M. Sherer, C. B. Marks., M. Pypaert, W. Mothes, Actin- and myosin driven movement of viruses along filopodia precedes their entry into cells, *J. Cell Biol.* 170 (2005) 317 - 325;

[26] Ploubidou, A., M. Way, Viral transport and the cytoskeleton, *Curr. Opin. Cell Biol.* 13 (2001) 97 - 105.

[27] Kerstin, R., K. Döhner, B. Sodeik, Viral interactions with the cytoskeleton: a hitchhiker’s guide to the cell, *Cell. Microb.* 8 (2006), 387 - 400.

[28] Apostol, T. M. *Calculus*. Vol. I. Second Edition. New York: John Wiley & Sons, Inc. 1967. Chapter 8: Introduction to Differential Equations. p 305 – 357. ISBN 0-471-00005-1.
Table 1 - Kinematic properties of shock fronts formed within the course of time evolution of the initial density profile in (11). The average velocity is calculated from the ratio between traveled distance (column 4) and the corresponding time interval (column 3) for each processive movement.

| shock number | initial time | time interval | travel distance | average velocity | instant velocity |
|--------------|--------------|---------------|-----------------|------------------|-----------------|
| 1            | 0            | a/2ε          | a/2             | ε                | ε               |
| 2            | 0            | a/2ε          | a/2             | −ε               | −ε              |
| 3            | a/2ε         | a/4ε          | 0               | 0                | 0               |
| 4            | 3a/4ε        | 7a/12ε        | a/6             | 2ε/7             | 2ε − √(3aε/τ)   |
| 5            | 4a/3ε        | 8a/3ε         | 4a/3            | ε/2              | ε/2             |
| 6            | 4a/ε         | ∞             | ∞               | −                | √(aε/τ)         |
6 Figure Caption

Figure 1 - The asymmetrical potential field introduced in Refs. ([3], [4], [5]).
This is defined by parameters $a$ and $b$ and we chose $a > b$.

Figure 2 - The motor density profile at different instants of time. The cargo is represented by the circle and at each instant, its position is adjacent to the shock front, the arrows pointing to the direction of the movement. Fig.2(a) shows that the considered initial condition (11) corresponds to a local perturbation on motor density with respect to its steady state $\rho(x, t) = 1/2$.

Figure 3 - Characteristics to Eq.(9) for the initial conditions given by (11).