Collective transport of weakly interacting molecular motors with Langmuir kinetics

SAMEEP CHANDEL¹, ABHISHEK CHAUDHURI¹ and SUDIPTO MUHURI²

¹ Indian Institute of Science Education and Research Mohali - Knowledge City, Sector 81, SAS Nagar - 140306, Punjab, India
² Department of Physics, Savitribai Phule Pune University - Ganeshkhind, Pune 411007, India

received 8 January 2015; accepted in final form 25 March 2015
published online 23 April 2015

PACS 87.16.A – Theory, modeling, and simulations
PACS 87.16.dj – Dynamics and fluctuations
PACS 87.16.Nn – Motor proteins (myosin, kinesin dynein)

Abstract – Filament-based intracellular transport involves the collective action of molecular motor proteins. Experimental evidences suggest that microtubule (MT) filament bound motor proteins such as kinesins weakly interact among themselves during transport and with the surrounding cellular environment. Motivated by these observations we study a driven lattice gas model for collective unidirectional transport of molecular motors on open filament. This model incorporates short-range next-nearest-neighbour (NNN) interactions between the motors and couples the transport process on filament with surrounding cellular environment through adsorption-desorption Langmuir kinetics (LK) of the motors. We analyse this model within the framework of a mean-field (MF) theory in the limit of weak interactions between the motors. We point to the mapping of this model with the non-conserved version of the Katz-Lebowitz-Spohn (KLS) model. The system exhibits rich phase behavior with a variety of inhomogeneous phases including localized shocks in the bulk of the filament. We obtain the steady-state density and current profiles, analyse their variation as a function of the strength of interaction and construct the non-equilibrium MF phase diagram. We compare these MF results with Monte Carlo simulations and find that the MF analysis shows reasonably good agreement with simulation results as long as the motors are weakly interacting. For sufficiently strong NNN interaction between the motors, the mean-field results deviate significantly, and for very strong NNN interaction in the absence of LK, the current in the lattice is determined solely by the NNN interaction parameter and it becomes independent of entry and exit rates of motors at the filament boundaries.

Motor proteins play a crucial role in various intracellular processes. Their collective action is involved in host of functions ranging from intracellular trafficking to the organization of the complex cytoskeletal network [1]. Individual motor proteins such as kinesin and myosin hydrolyze ATP to actively move along the cellular filaments [1,2]. While single-molecule experiments have shed light on the mechano-chemical properties and functioning of individual motor proteins [2], it has been established that many of the cellular functions such as cell division and intracellular transport are achieved by the collective effect of many motors. Many motors working in unison not only generate large forces that are required for many cellular processes but they are also responsible for long-distance regulated transport inside the cell [3]. Thus, it is of considerable interest to understand how the interaction between individual motor proteins affects the collective transport within the cell.

Experimental studies on transport of kinesin motors on MT filament suggest that the individual motors interact weakly with their neighbours on the MT and that this attractive interaction manifests as a propensity of the motors to cluster during their transport on cellular filaments [4–6]. It has also been widely observed that the spatial organization of the motors and the cellular cargo that they transport on the filaments is sensitive to the surrounding cellular environment. For example, experiments done to study the spatial distribution of pigment granules in extracts of melanophore cell has illustrated that altering the cellular environment by specific biochemical means affects the binding affinity of the motors to the filaments and which, in turn, can lead to spatial reorganization of...
the pigment granules [3,7,8]. Further, since cellular cargoes carried by the motors are loaded and offloaded at the filament ends, the role of the boundary processes at the filament ends also plays a significant role in determining the spatial organization of the motors on individual filaments [3].

In light of these experimental findings, we study a minimal lattice gas model for unidirectional transport on a single filament which takes into account the weak interaction between the motors and their interaction with the surrounding environment at the microscopic scales within a simplified framework. The proposed framework provides a natural means to qualitatively understand some of the aspects of collective behaviour of motors and their spatial organization, that emerges at macroscopic cellular scales. We study this model within a mean-field (MF) theory and compare the results with Monte Carlo (MC) simulation results.

The minimal model that we analyse, is a variant of the totally asymmetric exclusion process (TASEP) and belongs to the broad class of one-dimensional driven diffusive systems [9]. Driven diffusive systems in one dimension have been studied extensively from a theoretical perspective [9–17] and they exhibit a variety of interesting features and rich phase behaviour which includes boundary-induced phase transitions [12,13,18–20]. Such boundary-induced phase transitions in these driven systems are in contrast to one-dimensional equilibrium systems where the boundaries do not affect the macroscopic phase of the system [12]. These models have proved to be particularly useful in modeling a variety of processes such as transport across biomembrane channels [21], cellular cargo transport [19,20,22–24], stochastic pumps [25,26], fungal growth [27,28] as well as the collective dynamics of interacting molecular motors [29–31].

Our lattice gas model, which incorporates both Langmuir kinetics (LK) and next-nearest-neighbour (NNN) interactions between molecular motors, shows significant dependence of density and current profiles not only on the interaction strength and boundary entry/exit rates but also on the attachment-detachment rates associated with the LK process. In the weakly interacting limit, the MF theory works well and shows reasonable agreement with MC results. However, unlike the system of usual TASEP (with simple excluded-volume effect) coupled to the LK process [19], where MF works very well, in our model with NNN interactions, the simple MF theory breaks down even for moderate NNN interaction strengths. For very strong NNN interactions in the absence of LK process, current in the system is controlled solely by the rate at which motors unbind from a cluster on the filament. Now we proceed to describe the details of the model.

The cytoskeletal filament on which the molecular motors move is represented as a one-dimensional lattice of length $L$. The motors bound to the filament are the “particles” in this description. The total number of lattice sites is $N$ so that the lattice spacing $\varepsilon = L/N$. The occupation number of a lattice site $i$ is denoted by $n_i$ which assumes values $n_i = 1$ if occupied and $n_i = 0$ otherwise. Particles hop unidirectionally to the right on this lattice with excluded-volume interactions preventing two particles from occupying a given site as in the usual TASEP model as long as the particles are free (not part of any cluster). The short-range attractive interaction between the motors is incorporated by including next-nearest-neighbour (NNN) interaction. Due to the attractive interaction, the motors exhibit an enhanced tendency to form a cluster while the propensity to detach from a cluster is diminished. We include this effect by choosing a hop rate for a free particle (not part of a cluster) to jump into a cluster as $q$, with $q > 1$ while its hop rate out of the motor cluster is chosen to be $r \equiv \frac{1}{q}$ [31]. Otherwise if a free particle hops to the right and remains free, then the hop rate is 1. We also choose a hop rate of 1 if a particle which is part of a cluster jumps into another cluster. At the filament ends, particles enter the left boundary site with a rate $\alpha$ if the particle does not join a cluster, i.e. if the neighbouring site on the right of the boundary site is unoccupied, while the entry rate is $q\alpha$ if the particle enters the boundary and the adjacent site is occupied by a particle. For the boundary site at the filament end, the particles leave the lattice with a rate $\beta$ as long as the neighbouring site to the left of the right boundary site is unoccupied, while the exit rate of the particles is $\beta/q$ if the particle at boundary site is part of a cluster. The effect of the embedding environment is incorporated by allowing for stochastic attachment and detachment process of motors on the filaments. This process breaks the particle conservation of the motors in the bulk of the filament. The introduction of Langmuir kinetic process of attachment and detachment is done such that a particle in the bulk can detach from a lattice site with a rate $\omega_D$ while a particle could attach to a vacant lattice site with rate $\omega_A$.

The various processes are summarized in fig. 1. With all the various processes taken under consideration, the evolution equations for the occupation number operators $n_i = \{0,1\}$ are given by:

$$\frac{dn_i}{dt} = q_i n_{i-1} - q_{i+1} n_i + q_{i-1} n_i - q_i n_{i+1} + \alpha_i n_{i+1} - \alpha_i n_i + \beta_i n_i - \beta_i n_{i-1}$$

where

- $q_i = \frac{1}{q}$ for $i = 1, N$;
- $q_i = q$ for $i = 2, \ldots, N-1$;
- $\alpha_i = \alpha$ for $i = 1$;
- $\beta_i = \beta$ for $i = N$;
- $\alpha_i = \beta_i = 0$ for $i = 2, \ldots, N-1$.

These equations describe the population of clusters at the boundary sites and the detachment and attachment rates at the boundary sites.
the bulk and the two boundaries are given by the following equations, respectively:

\[
\frac{\partial n_i}{\partial t} = \frac{1}{q} \left[ \left( n_{i-1} - 1 \right) n_{i} + n_{i+1} \right] + \omega_A (1 - n_i)
\]

(1)

\[
\frac{\partial n_i}{\partial t} = \frac{1}{q} \left[ n_i (1 - n_{i-1}) - n_{i+1} \right] + \omega_D (1 - n_i)
\]

(2)

\[
\frac{\partial n_N}{\partial t} = \frac{1}{q} \left[ n_N (1 - n_{N-1}) - n_1 \right] + \omega_N (1 - n_i)
\]

(3)

We restrict ourselves to the regime where the boundary processes of particle input and output compete with the bulk process of stochastic attachment and detachment. Thus, we define the bulk attachment rate \( \Omega_A = \omega_A N \) and the bulk detachment rate \( \Omega_D = \omega_D N \) and hold the bulk attachment and detachment rates fixed as \( N \to \infty \) [19,20]. We normalize the total length of the lattice \( L \) to 1. The continuum mean-field (MF) evolution equation of the mean density of particles is obtained by taking the expectation value of the site occupation number operators, \( \rho = \langle n_i \rangle \), invoking the usual procedure of factorizing the two-point correlators arising out of different combinations of site occupation numbers, \( \langle n_i n_j \ldots n_k \rangle = \langle n_i \rangle \langle n_j \rangle \ldots \langle n_k \rangle \) and then expressing the resultant equations in terms of continuum variables of relative position \( x = i \epsilon / L \) along the filament lattice [19,20,22]. The continuum MF evolution equation in the bulk reads as

\[
\frac{\partial \rho}{\partial t} = -\varepsilon \left[ \frac{\partial}{\partial x} J(\rho) + \Omega_A (1 - \rho) - \Omega_D \rho \right],
\]

(4)

where the current has the form

\[
J(\rho) = \rho (\rho_0 + \rho_1)(1 - \rho)^2 + \left( \frac{1}{q} + \frac{1}{q - 1} \right) \rho^2 (1 - \rho)^2.
\]

(5)

Here we have displayed terms up to the leading order in \( \varepsilon \).

The corresponding equation for the steady-state density profile \( \rho(x) \) is obtained by simply setting the time derivatives of \( \rho \) in eq. (4) to zero. For satisfying the left boundary condition at \( x = 0 \), the density profile has to satisfy the conditions \( \rho(0) = \alpha \) and for the density profile satisfying the right boundary condition, \( \rho(1) = 1 - \beta \).

It is worthwhile pointing out all the different limits of this model. In the absence of next-nearest-neighbour (NNN) interaction and Langmuir kinetics (LK) of particle attachment and detachment, the dynamics of the model reduces to the usual TASEP. In this limit, which is obtained by setting \( q = 1 \) and \( \Omega_D, \Omega_A = 0 \), we obtain the steady-state MF equation which corresponds to the MF steady-state solution for TASEP. For the situation in which LK is present, while the NNN interaction is absent, the steady-state equation reduces to the steady-state equation for the model discussed in [19,20], wherein the steady state allows for phase coexistence and shocks localized in the bulk. Finally when the Langmuir kinetics is absent while the NNN interaction is included, then the MF steady-state solution is same as the steady-state density solution discussed in [32]. In this limit, the model maps on to the Katz-Lebowitz-Spohn (KLS) model [33,34]. For the KLS model particle hopping is independent on \( N \) and is defined by the rules \( 1011 \to 1100, 1010 \to 1000, 0010 \to 0100 \) and \( 0011 \to 0101 \), where 1 corresponds to a particle occupancy at a lattice site while 0 corresponds to a vacancy, and where these processes occur in general with different rates [33,34]. In the absence of LK, the model discussed in this letter exactly maps to the dynamics of the KLS model, by replacing particles of the KLS model by vacancies and vacancies of the KLS model by particles for our case. While for the KLS model it has been shown that the MF analysis breaks down for strong NNN interaction, we restrict ourselves to the situation in which the NNN interaction is weak, as is the case for motor interactions on cytoskeletal filaments. In this limit the MF picture can fairly accurately describe the steady-state behaviour as confirmed by Monte Carlo simulations.

Further, unlike the KLS model, here the interplay of the bulk translational dynamics on the lattice with the Langmuir kinetic processes gives rise to a qualitatively new scenario, wherein we find that phase coexistence and localized shocks in the bulk which are also controlled by attachment-detachment rates associated with the LK process apart from the NNN coupling strength and the boundary entry and exit rates. Thus, the model discussed in this letter can be considered as a non-conserved version of the KLS model.

In order to simplify the analysis and construct the entire MF phase diagram in the weak motor interaction limit, we restrict our analysis for a special choice of Langmuir kinetic processes wherein the attachment rate \( \Omega_D = \Omega_A = \Omega \), the steady-state differential equation for density is

\[
(1 - 2\rho) \left[ (1 - \rho)^2 + 2 \left( \frac{1}{q} + \frac{1}{q - 1} \right) \rho (1 - \rho) \right] \frac{d\rho}{dx} = \Omega (1 - 2\rho).
\]

(6)

Like in case of TASEP, one of the possible solutions of eq. (6) is the homogeneous solution, \( \rho(x) = \frac{1}{2} \). This corresponds to the maxima of current in the lattice. The
corresponding expression for the current in this maximal current (MC) phase is \( J_M = \frac{1}{2} + \frac{1}{16}(q + 1/q) \) and the density profile becomes independent of the boundary densities. Unlike TASEP, the maximal current in the lattice for this case is \( J_M < 1/4 \) for \( q \neq 1 \). Apart from this homogeneous solution for the density, the other possible solution is obtained by integrating eq. (6) and it is in the form of a form a cubic equation in \( \rho \),

\[
\rho^3 - \frac{3}{2} \rho^2 - \frac{3}{A} \rho + \frac{3}{A} (\Omega x + C) = 0, \tag{7}
\]

where \( A = 2(q+1/q) - 4 \) and \( C \) is a constant which is fixed by appropriate boundary condition. Using the mean-field boundary conditions in the steady state, \( \rho(0) = \alpha \) and \( \rho(1) = 1 - \beta \), we can determine \( C \) from eq. (7). Substituting \( C \) back in eq. (7), we can then solve for the cubic equation to determine the physically relevant solutions which will give the density profile \( \rho(x) \). This is then used in eq. (5), to calculate the current in the different phases. When the density profile satisfies the boundary condition at the left boundary at \( x = 0 \), \( \rho(0) = \alpha \) is substituted in eq. (7) to obtain the corresponding expression for \( C \) and the entire density profile in the range \( 0 \leq x \leq 1 \) is subsequently obtained by solving eq. (7). This corresponds to the low-density (LD) solution. Similarly the high-density (HD) solution for the density profile is obtained by using the boundary condition \( \rho(1) = 1 - \beta \). It is important to note that eq. (6) is a first-order differential equation which has to satisfy two boundary conditions. Therefore, the problem is overdetermined and the two solutions that respect the two boundary conditions will in general not match and will give rise to a shock in the bulk. The position of the shock is determined by the continuity of the current \( J \) for the two different solutions. In general three different density profiles may coexist on the filament lattice, e.g., the LD, HD and the MC phase. For any two phases to coexist, the current \( J \) corresponding to the two different phases at a particular location \( x = x_o \) on the lattice must be equal for the domain range \( 0 < x < 1 \), \( x_o \) being the position of the domain wall separating the two phases. While the density profile is continuous across a domain wall separating a LD or HD phase region with a MC phase region, the density change across a domain wall separating a LD phase with a HD phase is discontinuous and results in a shock localized in the bulk (fig. 2). The location of the domain wall coincides with the position where the current is maximum, the current increasing and decreasing monotonically with \( x \) on either side of it. With increasing interaction (increasing \( q \)), the domain wall shifts to the left. For very strong interaction, the domain wall disappears as the system enters into the HD phase, the density profile being larger than 1/2. As expected, the mean-field results no longer hold for large \( q \).

In general the possible phases in the bulk of the filament are the pure LD, HD and MC phases, two-phase coexistence of LD with MC (LD-MC), HD with MC (HD-MC) and LD with HD (LD-HD), and three-phase coexistence of LD with MC and HD (LMH). The LD-HD phase is characterized by density discontinuity and shock localized in the bulk of the lattice. The phase boundaries separating the different possible phases are determined by setting the domain wall position to the left or the right end of the filament lattice. We now discuss the conditions which determine the MF phase boundaries that separate the different possible phases.

**Phase coexistence boundary between LD and LD-HD**: Starting from eq. (7), the density profile corresponding to the LD phase is obtained by using the boundary condition \( \rho(0) = \alpha \). The corresponding current profile \( J(x) \) is obtained by using eq. (5). Similarly the current solution for the HD phase is obtained by using the boundary condition \( \rho(1) = 1 - \beta \). To obtain the phase boundary, the current
solution corresponding to the LD phase $J_{LD}$ is equated with the current solution corresponding to the HD phase $J_{HD}$ at $x = 1$, i.e., $J_{LD}(x = 1) = J_{HD}(x = 1)$.

**Phase coexistence boundary between HD and LD-HD:**
For obtaining the phase boundary, the current solution corresponding to the LD phase $J_{LD}$ is equated with the current solution corresponding to the HD phase $J_{HD}$ at $x = 0$, i.e., $J_{LD}(x = 0) = J_{HD}(x = 0)$.

**Phase coexistence boundary between LD and LD-MC:**
For obtaining the phase boundary in this case, the density solution for the low-density phase $\rho_{LD}$ is equated to 1/2 at the right boundary, i.e., $\rho_{LD}(x = 1) = \frac{1}{2}$. The resultant phase boundary has the equation of a straight line.

**Phase coexistence boundary between MC and LD-MC:**
Here the phase boundary is determined by equating the density solution for the LD phase $\rho_{HD}$ to 1/2 at the left boundary of the filament, i.e., $\rho_{LD}(x = 0) = \frac{1}{2}$. This is simply an equation of a straight line $\alpha = 1/2$.

**Phase coexistence boundary between MC and HD-MC:**
For obtaining the phase boundary in this case, the density solution for the high-density phase $\rho_{HD}$ is equated to 1/2 at the right boundary, i.e., $\rho_{HD}(x = 1) = \frac{1}{2}$. Thus, the resultant phase boundary is a straight line $\beta = 1/2$.

**Phase coexistence boundary between HD and HD-MC:**
For obtaining the phase boundary in this case, the density solution for the high-density phase $\rho_{HD}$ is equated to 1/2 at the left boundary, i.e., $\rho_{HD}(x = 0) = \frac{1}{2}$. The resultant phase boundary is a straight line.

In fig. 3 we display the MF phase diagram for different values of $q$. When $q$ is sufficiently small, the topology of the phase diagram is very similar to that of the TASEP-LK phase diagram as in ref. [20]. With increasing value of $q$ the location of the phase boundaries changes. Further, unlike TASEP-LK, the phase boundary curve separating the LD-HD phase with HD and the phase boundary curve separating the LD-HD phase with LD is not a straight line. For high values of $q$ corresponding to strong NNN interaction, the MF predictions significantly deviates from the actual density and current profiles and the corresponding phase boundaries. In the limit of $q \gg 1$, the MF picture completely breaks down. In the absence of LK process, the current in the lattice in this limit is controlled solely by the slowest process in the lattice, i.e., the rate at which the particles leave the cluster, $J \simeq 1/q$, for large $q$. Figure 4 shows this variation.

In summary, we have studied a driven lattice gas model for the transport of molecular motors which not only have short-range next-nearest-neighbour interaction but also interact with the cellular environment through adsorption-desorption Langmuir kinetics. We showed that the resulting phase diagram is extremely rich, with a variety of inhomogeneous phases, including localized shocks in the bulk. Our mean-field results match reasonably well with the Monte Carlo simulations for weak interactions. For strong interaction (large $q$) between motors, our MF approach breaks down completely unlike TASEP with Langmuir kinetics. In this limit and in the absence of LK process, the current in the lattice becomes independent of the boundary rates and depends only on $q$. We show that
our model maps to the non-conserved version of the KLS model.

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SM acknowledges DBT RGYI Project No. BT/PR6715/GBD/27/463/2012 for financial support.

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