The dynamics of cargo driven by molecular motors in the context of asymmetric simple exclusion processes.

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Abstract

We consider the dynamics of cargo driven by a collection of interacting molecular motors in the context of an asymmetric simple exclusion processes (ASEP). The model is formulated to account for i) excluded volume interactions, ii) the observed asymmetry of the stochastic movement of individual motors and iii) interactions between motors and cargo. Items (i) and (ii) form the basis of ASEP models and have already been considered in the literature to study the behavior of motor density profile [4]. Item (iii) is new. It is introduced here as an attempt to describe explicitly the dependence of cargo movement on the dynamics of motors. The steady-state solutions of the model indicate that the system undergoes a phase transition of condensation type as the motor density varies. We study the consequences of this transition to the properties of cargo velocity.

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1 Introduction

Asymmetric simple exclusion processes (ASEP) are specially convenient for describing general properties of dynamical systems consisting on a collection of many-interacting particles in situations for which the physicochemical characteristics of the components and thus the nature of interactions, need not to be described in details [1], [2]. Because of this, ASEP models have been used to study the collective movement of molecular motors that happen at the microtubules within cellular environment [3], [4], [5], [6]. These are models that can be defined in one-(spacial)-dimension and incorporate the asymmetry of the motion of individual motors.

Since the initial proposal pointing out to ASEP as a possibility to describe the collective dynamics of molecular motors [3], the general interests are mainly focused on the properties of the system at different boundary conditions that allow to make predictions on the stationary currents or on the average motor velocities as function of external loading forces [7]. Also, the effects of motor coordination onto the process of pulling on fluid membranes [8] have been studied in the literature in the context of discrete ASEP models with disorder [9], [10]. It shall be interesting then to investigate whether this type of description can be extended to describe directly the movement of cargo driven by motors to understand some of its characteristics observed in experiments.

Cargo transport by motors happens at the cellular environment where simple diffusion of vesicles or nutrients is severely limited by the presence of innumerable structures inside the cytoplasm. Besides, it is known that virus particles can take advantage of the existing transport mechanisms using molecular motors as carriers to reach the interior of the cell [11], [12]. Therefore, by studying the properties of a model that leads to quantitative predictions on the movement of both motor and cargo might be helpful to understand mechanisms to prevent cell infection and/or to design more efficient drug carriers [13].

We have already worked on this problem to investigate the movement of cargo in connection to the short-time behavior of the motor density profile defined in the context of the continuum limit of an ASEP with periodic boundary conditions [14]. Here, we present an alternative to describe the long-time regime (steady-state) of the movement of cargo using a discrete version of the model. The
elementary dynamical processes, that is, the processes at the level of individual particles moving on a defined one-dimensional lattice with periodic boundary conditions are such to account for two kinds of particles - the motors and the cargoes. Other processes that take place on a lattice and involve two kinds of particles with exclusion have already been explored in the literature to describe diverse phenomena. The presence of the seminal second class particle, for example, has been considered to study the microscopic properties of shock fronts exhibited by the system due to density inhomogeneities [15]. This kind of model can also be used to study the properties of the density profile in the presence of defects [16].

The important point we want to notice is that, up to the present, all kinds of particles in the ASEP models presented in the literature are, in all cases, provided with their own (intrinsic) dynamics. As a rule, an encounter of a particle with another is just supposed to change their original dynamics, or even to impede their movement (excluded-volume interactions), by inducing modifications on the rates of the original stochastic movement. This is the case, for example of the model cited above containing second class particles. The elementary processes in this case are

\[
10 \rightarrow 01 \\
12 \rightarrow 21 \quad \text{first and second class} \\
20 \rightarrow 02
\]

that is, either particles of first (1) and second (2) classes can move by their own if the target neighboring site is unoccupied (0). They can also move if interacting with other particles by interchanging occupancy sites as in 12 → 21. This is also the case of another ASEP-like model for which the particles with different dynamics simulate the presence of cars (1) and trucks (2) on a same traffic road [17], [18]. For this model, the direction of the intrinsic movement of particle (2) is opposed to that in the previous case:

\[
10 \rightarrow 01 \\
12 \rightarrow 21 \quad \text{cars and trucks} \\
02 \rightarrow 20
\]

As we want to describe the movement of cargo driven by motors using an ASEP-like model, we
need first to think on possible ways cargo may use the motors to move and up to what extent the presence of cargo can affect the intrinsic dynamics of motors. The first idea that occurred to us is that the elementary processes in this case should be such to attribute exclusively to one kind of particles - the motors - the ability to move independently, i.e. motors should be able to hop from site to site the only restriction being excluded volume interactions with other motors. The other kind of particles - the cargoes - should move only if assisted by motors. Therefore, the dynamics must, in addition, incorporate explicitly a form for the motor/cargo interactions at this particle level. We want to examine how such interactions affect the long-time average properties of both cargoes and motors.

Based on the above considerations we present in Section 2 what we conceived as a minimum model that is able to account explicitly for the dynamics of both cargo and motors expected as a result from their mutual interactions. This is presented as an ASEP model that incorporates a few common characteristics of this biological system, but avoids details of motor/cargo interactions. It turns out that this model is exactly solvable, that is, the steady-state configurations can be determined. Using the matrix approach proposed and developed by Derrida, Lebowitz, Evans, among others [2], [19], these states are conveniently represented as products of certain non-commuting matrices which can be used to calculate the properties of interest as the average cargo velocity discussed in Sec.3. The analytical results obtained in this way are used in Section 4 to discuss the phenomenological consequences of the model.

2 An ASEP model for motors and cargo

There are a few proposals in the literature to characterize the origins and the role of the components involved in the cargo/motor interactions at a microscopic level [20]. Data suggest that such interactions are mediated by certain proteins - dynactin is the most studied - but apparently there is consensus about their short-range nature as a general characteristic. In terms of the scales involved, this is equivalent to say that such cargo/motor interactions happen by "direct contact" among individual components. Moreover, although the experiments indicate that the number
of motors attached simultaneously to cargo may be large [21], there is limited information on
the typical times each motor, or group of motors, remains attached to cargo in the course of its
movement. Therefore, in building up our model, we avoid details of the processes associated to
such microscopic interactions and simply account for these as stochastic processes. We suppose
that the time scales associated to the motor/cargo interactions are very short if compared with
observation time so the events that happen within such intervals need not to be described as we
treat the problem at a larger time scale.

The ASEP model considered here consists on a collection of $M$ motors, and $K$ cargoes, referred
in the following as particles of type 1 and particles of type 2 respectively, distributed among the $N$
sites of a one dimensional cyclic lattice. Each particle occupies a single site and $N - M - K > 0$
sites remain empty (Fig.1). The total number of particles of each species is conserved. We consider
the case $K = 1$ so that at the steady state, all configurations of the system are equally likely (1).

Each site is identified by its position on the lattice $j = 1, 2, \ldots N$ and occupation at each site is
specified by a corresponding site variable $\sigma_j$ that assumes integer values 0, 1 or 2, if the site is
empty (0), occupied by a motor (1), or occupied by cargo (2). A state $C$ of the system is specified
by the set \{ $\sigma_1 \sigma_2 \ldots \sigma_N$ \}. As usual, in this kind of description the stochastic dynamics is defined
through a Poissonian process taking place at the lattice such that at each time interval $dt$, a pair of
consecutive sites $i$ and $i+1$ is selected at random and the system is updated depending on whether
it is possible to exchange particles between these two sites. We choose the following possibilities

$10 \rightarrow 01$ with rate $k$, probability $kdt$

$12 \rightarrow 21$ with rate $w$, probability $w dt$ \hspace{1cm} (3)

$21 \rightarrow 12$ with rate $p$, probability $pdt$

where the pair of sites $(i, i+1)$ is being represented by the values assumed by the variables $(\sigma_i, \sigma_{i+1})$.

According to these rules a cargo is allowed to move only if ”assisted” by a motor at a neighbor
site. We see this as a possibility to describe the fact that the movement of cargo is conditioned to
that of motors, as observed in real systems. At this level of description one must consider that if

\[1\] In the presence of more than one particle of type 2 obeying the algebra [8], the system loses ergodicity. In these
more general cases, an invariant measure should be assigned to each subspace of configurations that preserve the
number of empty sites between each pair of these particles.
motors affect the movement of cargo then cargo must have influence on the movement of motors. In the present model this is incorporated into the dynamics [3] both explicitly, by the processes that involve cargo/motor exchanging positions in both directions and implicitly, by modifying the motors hopping rates that assume distinct values depending whether a jump occurs towards an empty site or by interchanging position with particle 2.

Here, we are concerned with the kinematics of the cargo at long-time regimes. For this, we use the matrix-approach [1], [2] to represent any configurations of the system of $N$ sites by a product of $N$ matrices, so that the probability of occurrence of a particular configuration $C$ is given by

$$P_{N,M}(C) = \frac{1}{Z_{N,M}} Tr \prod_{i=1}^{N} (\delta_{\sigma_i,1} D + \delta_{\sigma_i,2} A + \delta_{\sigma_i,0} E)$$  \hspace{1cm} (4)

where the Kronecker delta symbols select the correct occupancy and

$$Z_{N,M} = \sum_{\{\sigma_i\}} Tr \prod_{i=1}^{N} (\delta_{\sigma_i,1} D + \delta_{\sigma_i,2} A + \delta_{\sigma_i,0} E)$$  \hspace{1cm} (5)

is the normalization. The sum extends over all allowed configurations for which $\sum_i \delta_{\sigma_i,1} = M$ and $\sum_i \delta_{\sigma_i,2} = K = 1$. In the product above, site $i$ is represented by matrix $D$ if it is occupied by a motor (particle 1), by matrix $A$ if it is occupied by the cargo (particle 2) or by matrix $E$ if it is empty (not-occupied).

In the stationary state, the probabilities $P_{N,M}(C)$ for all configurations $C$ satisfy the condition [19]:

$$\sum_{C'} P_{N,M}(C') W(C' \rightarrow C) - P_{N,M}(C) W(C \rightarrow C') = 0$$  \hspace{1cm} (6)

where $W(C' \rightarrow C)$ is the rate at which the exchange of particles occur between neighboring sites so that all nonzero terms in the above sum are those for which configurations $C$ and $C'$ differ from each other at most by the occupancy of a pair of sites.

As an example, we consider for $N = 4$, $K = 1$, $M = 2$ the following configuration $C = 1201$. There is just one way to leave this configuration that is through the process: $12 \rightarrow 21$ with $W(C \rightarrow C') = w$. On the other hand, there are two ways to reach this configuration, either by exchanging particle positions (i) by the process $10 \rightarrow 01$ in configuration $C' = 1210$ with $W(C' \rightarrow C) = k$ or (ii) by the process $21 \rightarrow 12$ in configuration $C' = 2101$, with $W(C' \rightarrow C) = p$. 

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So, in this case, equation (6) reads:

\[ wTr(\text{DAED}) = kTr(\text{DADE}) + pTr(\text{ADED}) \] (7)

As a general rule, the main difficulty in using this method to determine the probabilities \( P_{N,M}(C) \) for each configuration \( C \) is to find the algebra, if any, that must be satisfied by the corresponding matrices of a given ASEP model in order to satisfy condition (6) for a given dynamics as in (3). In the present case, we conjecture that if \( D, A \) and \( E \) are such that

\[
\begin{align*}
DA - xAD &= E - D \\
DE &= E \\
EA &= E \\
EE &= E
\end{align*}
\] (8)

for

\[ x = \frac{k + p}{w} \] (9)

then, Eq. (8) is satisfied. This can be tested using explicit examples, as the one considered in (7). Using (8) to evaluate the traces, one can easily check that the identity holds trivially. In the following, we study properties of this model that are of interest for examining the consequences of the model regarding the characteristics of cargo movement.

3 Average cargo velocity

For \( K = 1 \) i.e. just one cargo, in the presence of \( M \) motors distributed along a cyclic lattice of \( N \) sites, we consider \( N > M + 1 \), to ensure that at least one site in the system remains empty. In this case, the average cargo velocity \( \langle v \rangle \) at steady state is expressed as

\[
\langle v \rangle = \frac{1}{Z_{N,M}} \left( p \sum_{\{\sigma_i\}} Tr \prod_{i=1}^{N-2} (\delta_{\sigma_i,1}D + \delta_{\sigma_i,0}E)AD - w \sum_{\{\sigma_i\}} Tr \prod_{i=1}^{N-2} (\delta_{\sigma_i,1}D + \delta_{\sigma_i,0}E)DA \right) \] (10)

where the sums in the numerator extends over all configurations of \( M - 1 \) motors distributed among \( N - 2 \) sites. The first sum in the RHS accounts for all configurations in which the site at the
immediate right of cargo is occupied by a motor. The second sum accounts for all configurations in which there is a motor at immediate left of cargo at a lattice position. Notice that due to the invariance of the trace the normalization factor $Z_{N,M}$ can be written as

$$Z_{N,M} = \sum_{\{\sigma_i\}} Tr \prod_{i=1}^{N-1} (\delta_{\sigma_i,1} D + \delta_{\sigma_i,0} E) A$$

(11)

where the sum extends over all configurations of $M$ motors distributed among $N - 1$ sites.

In order to make reference to the above traces over products of matrices, it is convenient to introduce the functions $W_{\sigma_{j-1}, \sigma_j, \sigma_{j+1}, ...}$ to indicate the configurations having the n-uple $(j - 1, j, j + 1, ...)$ fixed, the corresponding sites occupied by particles or holes assigned by the variables $\sigma_{j-1}, \sigma_j, \sigma_{j+1}, ...$. Using these definitions, we write

$$\langle v \rangle = \frac{1}{Z_{N,M}} \left( p \sum_{\{\sigma_i\}} W_{21} - w \sum_{\{\sigma_i\}} W_{12} \right)$$

(12)

where

$$Z_{N,M} = \sum_{\{\sigma_i\}} W_{21} + \sum_{\{\sigma_i\}} W_{20}$$

(13)

for $W_{12} = \prod_{i=2}^{N-2} (\delta_{\sigma_i,1} D + \delta_{\sigma_i,0} E) DA$ and analogous definitions for $W_{21}, W_{20}$ and $W_{02}$. Alternatively, due to the cyclic property of the trace, $Z_{N,M}$ can also be calculated from

$$Z_{N,M} = \sum_{\{\sigma_i\}} W_{12} + \sum_{\{\sigma_i\}} W_{02}.$$  

(14)

These two expressions (13) and (14) are equivalent and both will be used below, at convenience. Notice that we can rewrite the sum over configurations in $W_{20}$ as

$$\sum_{\{\sigma_i\}} W_{20} = \sum_{\{\sigma_i\}} W_{120} + \sum_{\{\sigma_i\}} W_{020}$$

(15)

where the first (second) sum on the RHS extends over all configurations of $M - 1$ motors with the triplet 120 fixed ($M$ motors with the triplet 020 fixed) distributed among $N - 3$ lattice sites. Making use of the decompositions in (13) and (15), the average cargo velocity (12) is expressed as

$$\langle v \rangle = p - \frac{1}{Z_{N,M}} \left\{ p \left( \sum_{\{\sigma_i\}} W_{120} + \sum_{\{\sigma_i\}} W_{020} \right) + w \left( \sum_{\{\sigma_i\}} W_{12} \right) \right\}$$

(16)
We compute $Z_{N,M}$ as it is expressed in Eq. (14).

A convenient way to perform the calculations indicated above is to replace the sums over site variables $\{\sigma_i\}$ by sums over blocks defined by the integers $\{m_i\}$ and $\{q_i\}$ for $i = 1, 2, \ldots, k$. (see for example, ref. [17]). In this representation,

$$
\sum_{\{\sigma_i\}} W_{12} = \sum_{\{m_i\}; \{q_i\}} tr(E^{q_1} D^{m_1} \ldots E^{q_{k-1}} D^{m_{k-1}} E^{q_k} D^{m_k} A)
$$

with $m_k \geq 1$;

$$
\sum_{\{\sigma_i\}} W_{02} = \sum_{\{m_i\}; \{q_i\}} tr(E^{q_1} D^{m_1} \ldots E^{q_{k-1}} D^{m_{k-1}} E^{q_k} A)
$$

with $q_k \geq 1$;

$$
\sum_{\{\sigma_i\}} W_{120} = \sum_{\{m_i\}; \{q_i\}} tr(E^{q_1} D^{m_1} \ldots E^{q_{k-1}} D^{m_{k-1}} E^{q_k} D^{m_k} A)
$$

with $q_1 \geq 1$ and $m_k \geq 1$;

$$
\sum_{\{\sigma_i\}} W_{020} = \sum_{\{m_i\}; \{q_i\}} tr(E^{q_1} D^{m_1} \ldots E^{q_{k-1}} D^{m_{k-1}} E^{q_k} A)
$$

with $q_1 \geq 1$ and $q_k \geq 1$.

From the algebra in (8), it follows that $D^m A E = x^m A E$. This identity is needed in the evaluation of the above traces for general configurations of the variables $\{\sigma_i\}$. The results are

$$
\begin{align*}
W_{12} &\equiv tr(E^{q_1} D^{m_1} \ldots E^{q_{k-1}} D^{m_{k-1}} E^{q_k} D^{m_k} A) = x^{mk} tr(E) \\
W_{02} &\equiv tr(E^{q_1} D^{m_1} \ldots E^{q_{k-1}} D^{m_{k-1}} E^{q_k} A) = tr(E) \\
W_{120} &\equiv tr(E^{q_1} D^{m_1} \ldots E^{q_{k-1}} D^{m_{k-1}} E^{q_k} D^{m_k} A) = x^{mk} tr(E) \\
W_{020} &\equiv tr(E^{q_1} D^{m_1} \ldots E^{q_{k-1}} D^{m_{k-1}} E^{q_k} A) = tr(E)
\end{align*}
$$

Notice that $W_{12}$ and $W_{120}$ are functions of the size $m_k$ of the block, i.e. of the number of particles of type 1 (motors) that precede particle 2 (cargo). Because of this, the evaluation of the respective sums over $\{q_i\}$ and $\{m_i\}$ in configurations of the type $W_{12}$ (or $W_{120}$), excluding $m_k$, is equivalent to account for the number of ways for distributing $M - m_k$ motors into $N - m_k - 2$ (or into $N - m_k - 3$) sites. The factor 2 in the first case comes from the exclusion of two sites from the total: one occupied by the cargo and another that must remain empty to define the limits of the cluster of $m_k$ motors behind the cargo. Then,

$$
S_1 \equiv \sum_{\{\sigma_i\}} W_{12} = \sum_{m=1}^{M} \binom{N - m - 2}{M - m} x^m tr(E)
$$

(22)
and
\[ S_2 \equiv \sum_{\{\sigma_i\}} W_{120} = \sum_{m=1}^{M} \left( \frac{N - m - 3}{M - m} \right) x^m \text{tr}(E) \tag{23} \]

\( W_{02} \) and \( W_{020} \) correspond to configurations that do not present motors behind the cargo. In the sum over configurations of the type \( W_{02} \) one must account for the number of ways to distribute \( M \) motors into \( N - 2 \) sites (from the total of \( N \) sites, there must be excluded 2, one to fix the cargo and the other to fix an empty site). Then,
\[ \sum_{\{\sigma_i\}} W_{02} = \left( \frac{N - 2}{M} \right) \text{tr}(E) \tag{24} \]
and
\[ \sum_{\{\sigma_i\}} W_{020} = \left( \frac{N - 3}{M} \right) \text{tr}(E) \tag{25} \]

We now proceed by computing the sum over integer \( m \) in (22) and (23).

### 3.1 Approximate expression for the average velocity of the cargo in the limit of very large systems

Our intention is to obtain an expression for the average velocity \(< v >\) of cargo in the limit for which both the number of sites and the number of motors (which are conserved by the dynamics) are taken very large, that is \( N \to \infty \) and \( M \to \infty \). These limits are supposed to be taken in such a way to ensure that the ratio between these two quantities
\[ \lim_{N \to \infty} \frac{M}{N} = \rho \tag{26} \]
converges to a defined density of motors \( \rho \), such that \( 0 < \rho < 1 \). These same limits have already been considered in Ref. [17] to calculate the average velocity of trucks in a related traffic problem. Here, we proceed along the same lines sketched by these authors.

First, we use Stirling formula \( N! \sim \sqrt{2\pi NN^N} \exp(-N) \) for very large \( N \), to approximate the combinatorial coefficients in (22) and (23). It results
\[ C_{02} \equiv \lim_{N \to \infty} \left( \frac{N - 2}{M} \right) \sim \lim_{N \to \infty} \frac{(1 - \rho)^2 \exp[-N(\rho \ln \rho + (1 - \rho) \ln(1 - \rho))] \sqrt{2\pi N \rho(1 - \rho)}}{\sqrt{2\pi N \rho(1 - \rho)}} \tag{27} \]
and

\[ C_{020} \equiv \lim_{N \to \infty} \lim_{M \to \infty} \left( \frac{N-3}{M} \right) \sim \lim_{N \to \infty} \frac{(1-\rho)^3 \exp[-N(\rho \ln \rho + (1-\rho) \ln(1-\rho))]}{\sqrt{2\pi N \rho(1-\rho)}} \tag{28} \]

In order to evaluate the sums \( S_1 \) and \( S_2 \) in (22) and (23), we follow the procedure used in Ref. [22]. There, sums involving factorials of this kind are approximated by integrals and the asymptotic regimes are obtained using Laplace’s method [23]. Considering then the limit of very large systems and defining \( z = m/N \), we calculate

\[ \lim_{N \to \infty} \lim_{M \to \infty} S_1 \simeq \lim_{N \to \infty} \frac{\sqrt{N(1-\rho)^2}}{2\pi(1-\rho)} \int_0^\rho \frac{1}{(1-z)^{1/2}} \frac{e^{Nf(z)}}{(1-z)^2} \, dz \tag{29} \]

where we have defined the function \( f(z) \) of a single variable \( z \) as

\[ f(z) = (1-z) \ln(1-z) - (\rho - z) \ln(\rho - z) - (1-\rho) \ln(1-\rho) + z \ln x \tag{30} \]

and used the fact that in the specified limit, the sum in \( m \) converges to the integral as \( \frac{1}{N} \sum_{m} \to \int_0^\rho dz \).

Now observe that \( f(z) \) has a maximum at

\[ z_{\text{max}} = \frac{1-x\rho}{1-x}, \tag{31} \]

so in order to apply Laplace’s method in the present case, one must distinguish between two possibilities, namely

- if \( x\rho \geq 1 \) \((x > 1)\) then, \( 0 \leq z_{\text{max}} \leq \rho \) i.e. \( z_{\text{max}} \) belongs to the integration interval. In this case, Laplace’s method gives

\[ \lim_{N \to \infty} S_1 \sim \left( \frac{x-1}{x} \right) \exp[-N(-\ln x + (1-\rho) \ln(x-1))] \tag{32} \]

or

- if \( x\rho \leq 1 \) either for \( x > 1 \) or \( x < 1 \), then \( z_{\text{max}} < 0 \). Therefore, in this case \( z_{\text{max}} \) does not belong to the integration interval. Since \( f(z) \) is a monotone decreasing function of \( z \), the integral is dominated by the value of the integrand at \( z = 0 \), and application of Laplace’s method results

\[ \lim_{N \to \infty} S_1 \sim -\frac{(1-\rho)^2}{\sqrt{2\pi N \rho(1-\rho) \ln(x-1)}} \exp[-N(\rho \ln \rho + (1-\rho) \ln(1-\rho))] \tag{33} \]
Analogously, the asymptotic behavior of the sum $S_2$ \(^{(23)}\) must be analyzed according to the range of $x\rho$:

- If $x\rho \geq 1$ ($x > 1$), then
  \[
  \lim_{N \to \infty} S_2 \sim \left( \frac{x - 1}{x} \right)^2 \exp[-N(-\ln x + (1 - \rho) \ln(x - 1))] \tag{34}
  \]
  
or
  \[
  \lim_{N \to \infty} S_2 \sim -\frac{(1 - \rho)^3}{\sqrt{2\pi N\rho(1 - \rho)}} \frac{1}{\ln(\rho x)} \exp[-N(\rho \ln \rho + (1 - \rho) \ln(1 - \rho))] \tag{35}
  \]

From these results, one concludes that if $x\rho \geq 1$ then both $S_1$ and $S_2$ are the dominant factors in the expression for $<v>$ both in the numerator and in the denominator. In this regime,

\[
< v > \sim \lim_{N \to \infty} \left[ p - \frac{1}{S_1} (pS_2 + wS_1) \right] \sim -\frac{kw}{k + p} \quad \text{for} \quad x\rho \geq 1 \tag{36}
\]

On the other hand, if $x\rho \leq 1$, all factors in the expression \(^{(16)}\) for $<v>$ are of the same order of magnitude and then,

\[
< v > \sim \lim_{N \to \infty} \left\{ p - \frac{1}{(S_1 + C_{02})} \left[ p(S_2 + C_{020}) + wS_1 \right] \right\} \sim p\rho + \frac{w}{\ln(\rho x) - 1} \quad \text{for} \quad x\rho \leq 1 \tag{37}
\]

The consequences of these results to the phenomenology of cargo movement will be analyzed in the next section.

### 4 Discussion and concluding remarks

The aim of the present work is to study the consequences of introducing cargo into certain lattice models where there is also present a set of biased molecular motors interacting through excluded-volume interactions. We consider an ASEP-like model specially designed to account for both kinds of particles. Therefore, the model includes an assumption about the stochastic nature of the movement of cargo and its dependence on the dynamics of motors. To our knowledge, this is the
first attempt to include in the same framework, at the particle level, the effects on the movement of motors due to the presence of cargo and vice-versa.

We look for the probabilities associated to the configurations of the system at the stationary state which are represented by products of certain noncomuting matrices [1]. Using this representation, we were able to make quantitative predictions on the average properties that characterize the movement of cargo. We focus on the computation of the average velocity of cargo \(< v >\) whose behavior predicted by the model suggests that the system displays a phase transition under variation of the parameters. Fig. 2 shows \(< v >\) plotted according to the results in Eqs. (36) and (37) as a function of \(\rho\), at different values of \(p\) for fixed \(w\) and \(k\). Observe that for sufficiently high values of \(p\) the function \(< v >\) displays a change in its behavior at values of \(\rho\) for which \(x\rho = 1\), as \(< v >\) becomes independent of \(\rho\).

In order to interpret these results, it shall be easier first to discuss on the kind of movement one would expect for cargo in the context of the considered ASEP. The mechanisms in (3) that define its elementary movements within each unit interval of time correspond to those of exchanging positions with a neighbor motor. The assigned hopping rates are such to promote, at a first moment, an accumulation of motors at one side (at the left side) of the cargo. Then cargo would be able to move backwards by exchanging position with these accumulated motors. By doing this, the motors end up transposed to the cargo’s front. Because motors are assigned with an intrinsic dynamics - they move preferentially to the right - these motors at cargo’s front will tend to disperse. Since the vesicle depends on such clusters of motors to develop a measurable velocity, it ends up moving mostly due to the motors accumulated at its back.

The dependence of \(< v >\) on \(\rho\) in Fig.2 confirms these expectations showing that \(< v >\) assumes only negative values, at all ranges of parameters. One could expect, in principle, that at high values of \(\rho\) there would be a balance between a tendency for maintenance of motors in front of the cargo, as excluded-volume become more important and eventually would be responsible for expressive motor accumulation at cargo’s front. So, in principle, one could think that for sufficient high values of \(p\) there would be a chance for the cargo to develop a macroscopic movement towards the plus end of the microtubule, that is to the forward direction as well, \(< v >\) eventually displaying positive
values for $\rho > x^{-1}$. According to the results, however, this does not happen either. The behavior of $\langle v \rangle$ predicted for high values of $\rho$ can be understood by recognizing the formation of an "infinite" (macroscopic) cluster of motors behind the cargo with which it can always exchange positions. The formation of such infinite cluster would be a consequence of the phase transition (of condensation type) predicted for this system. The average velocity in this region of density becomes constant probably due to the uniformity of motor distribution along this cluster.

We can then summarize these results by saying that the single cargo in this system of many motors develops, a backwards movement at any value of the hopping rates $k, p$ and $w$, or density $\rho$. The magnitude of such velocity, however, is highly dependent on $\rho$ and becomes constant at such values of $\rho$ greater than a critical value $\rho_c = x^{-1}$. It would be interesting then to test these predictions using data from experiment in vivo by monitoring the behavior of the motor density as cargo moves.

Actually, data from Drosophila embryos [21, 24] show that cargo velocity presents distinct behaviors depending on the stage of embryo development. It remains to investigate whether these changes could be associated to corresponding changes in the density of motors available at each of these stages. To our knowledge, there is limited information about the possible changes on the motor distribution along the microtubules due to the movement of cargo. The present study suggests that any investigation in this direction might be relevant to find ways to control cargo movement.

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Figure Caption

- Fig.1 - A configuration of the one-dimensional (discrete) ASEP model for interacting motors (gray) and cargo (black). Each particle, occupies a single site at each instant of time. The non-occupied (empty) sites are represented by line segments. The random processes are such that each motor is allowed to hop at rate $k$ to its nearest neighbor on the right if it is empty. The motors and cargo can exchange places at a rate $p$ (motor jumping to nearest neighbor at the right) or $q$ (motor jumping to the nearest neighbor at the left).

- Fig.2 - Average velocity of cargo as a function of motor density $\rho$, at various values of parameter $p$, for fixed $w = 3$ and $k = 1$, as indicated. The predicted phase transition is illustrated by the change in the behavior of $<v>$ that assume a constant value for $\rho > \rho_c = 1/x$. 