

Collective Phenomena in Intracellular Processes

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Abstract

Intracellular transport and cytoskeletal organization are the result of an interaction between elastic filaments and force generation by motor proteins. The observed phenomena are still too complex for a complete theoretical description. Studies on simple model systems reveal interesting collective phenomena which can be understood on the basis of driven stochastic processes far from equilibrium.

Keywords: molecular motors, intracellular transport, driven systems

1 Introduction

Eucariotic cell functions like mitosis, intracellular transport, cell movement and growth are complex phenomena based on a cooperative action of cellular components such as enzymes, cytoskeletal filaments, membranes and related regulatory proteins. It is only fair to say that we are still quite far from understanding such highly integrated many component systems regulating intracellular processes. For reaching this ambitious goal, several approaches are possible and necessary. In addition to experimental studies, theoretical work can either try to model the whole complexity of many interacting components by a numerical analysis or try to unravel some generic principles starting from only a few components and adding additional features successively. In the present contribution we take the latter route to study some aspects of intracellular transport. An important class of intracellular transport

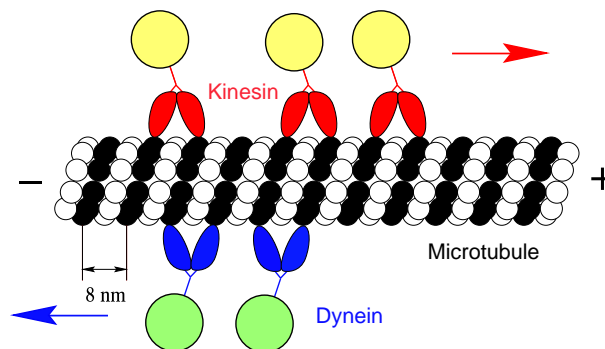


Figure 1: Illustration of intracellular transport. Kinesin, a molecular motor, is moving along a protofilament towards the plus end of the microtubule, while dyneins move in the opposite direction.

is mediated by molecular motors like myosin, kinesin and dynein which move along cytoskeletal filaments (F-actin and microtubules) [4]. This motion is driven by the free energy released in the chemical

hydrolysis reaction of ATP (adenosine-triphosphate). It drives conformational changes of the protein and at the same time switches the affinity to the cytoskeletal filaments. The detailed mechanisms are still a matter of debate and intensive research [11]. They do not concern us here, since we are not interested in the principles governing the chemo-mechanics of individual enzymes, but in the possible cooperativity in the intracellular transport resulting from the concerted action of a large assembly of such engines. Figure 1 illustrates the problem for kinesin and dynein moving along microtubules. We would like to ask how molecular motors cooperate at high densities and what role is played by interactions between them and other microtubule associated proteins (MAP's). Conventional kinesin, powering axonal transport of vesicles towards the synapse in neurons, can stay attached to its track over several hundred hydrolysis cycles, a property called "processivity". Then, for sufficiently high densities, interactions between these engines will become of importance, the simplest being the mutual blockage of binding sites. There is also some indication for attractive interaction between molecular motors [13].

Another closely related biological process, where collective phenomena are expected to be of importance is mRNA translation in eucaryotes, which involves unidirectional motion of ribosome complexes along mRNA strands. Theoretical investigations go back to the pioneering work by MacDonald *et al.* [7]. More recent work tries to understand feedback mechanisms and cooperative effects [1]. Yet another cellular process is filopod growth in eukaryotic cells produced by motor proteins interacting within actin filaments [6], where again cooperativity is supposed to play an essential role. An even broader range of questions arises when one tries to understand how cells organize their interior to fulfill their various duties. Internal organization processes include physical separation of molecules or molecular aggregates, definition of distinct functional regions, and the active transport of molecules between these regions. In addition to biochemical regulation, such processes are also strongly influenced by physical principles of self-assembly, mechanical forces generated by the action of motor proteins. The interplay between both gives rise to complex cellular processes. In this respect microtubules and motors have been used as *in vitro* model systems. For example, it has been shown that the localization of centrosomes and mitotic spindles is to a large extent a physical self-organization process. In recent work it is found that microtubules form asters even in absence of the centrosome [8]. We believe that the pattern formation observed in these simple *in vitro* systems are only first examples of what will be a much broader range of self-tuned or regulated structural and temporal organization in biological systems. In this contribution we will study a novel class of cooperativity resulting from the non-equilibrium dynamics of intracellular transport. We will learn how the density as well as the current along the molecular tracks can be regulated by varying the density of proteins at the ends of the molecular tracks, as well as by the bulk concentration of motor proteins and ATP.

2 Theoretical Model Systems

Actual biological systems are in general far too complex to be analyzed by taking into account all molecular details. A successful strategy is to build the complex systems starting with a few components hoping that they already capture some of the main features of the process. Additional components are added one at a time to find out which one may be crucial or of minor importance only. We will take such an approach. The purpose of this section is to introduce some simple model systems and important paradigms of stochastic particle systems.

2.1 Binding Kinetics

We begin with a discussion of the kinetics of some macromolecular assembly processes relevant for the formation of functional structures in cells. In particular, we are interested in the dynamics of ligand-substrate binding, where the substrate is a one- or two-dimensional lattice and the ligands are dimers or oligomers.

Langmuir kinetics (LK) is the simplest paradigm of binding kinetics of enzymes to some substrate. One considers the adsorption-desorption kinetics of particles on a lattice coupled to a bulk reservoir. The particles are assumed to adsorb at an empty site or desorb from an occupied one with rates ω_A and ω_D , respectively; see Fig. 2. All interactions between the particles other than the hard-core repulsion are neglected. Then, the rate equation for the average occupation number $\rho(t)$ reads

$$\frac{d\rho(t)}{dt} = -\omega_D\rho(t) + \omega_A(1 - \rho(t)). \quad (1)$$

Microscopic reversibility demands that the kinetic rates obey detailed balance such that the system evolves into an equilibrium steady state, which is well described within standard concepts of equilibrium statistical mechanics. The equilibrium density $\rho_{\text{eq}} = K/(1 + K)$ is solely determined by the ratio of the two kinetic rates, the binding constant $K = \omega_A/\omega_D$.

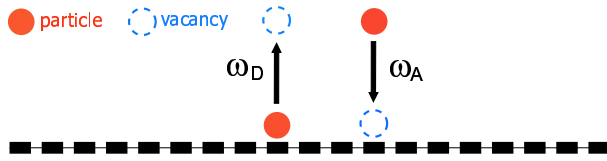


Figure 2: Illustration of Langmuir kinetics. Particles from a reservoir can attach and detach at rates ω_A and ω_D , respectively. Each binding site can only be occupied by one particle.

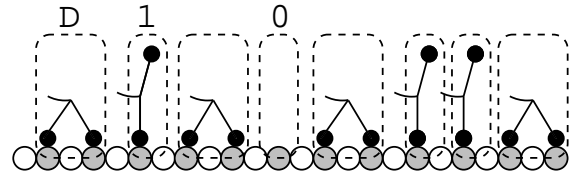


Figure 3: Configuration of kinesin on a protofilament. Each site may be empty (0) or occupied by kinesin dimers bound with both (D) or only one (1) head.

Binding kinetics becomes considerably more complicated if the ligands are dimers or oligomers [2]. An example of particular relevance for intracellular transport is the binding kinetics of kinesin dimers and tubulin. Kinesin dimers can either attach with one or two heads along a single protofilament; see Fig. 3. The equilibrium stoichiometry is now characterized by two binding constants. Again, one finds that detailed balance fully determines the equilibrium stoichiometry in terms of these binding constants. The crucial differences to simple Langmuir kinetics is not in the stoichiometry but in how an initial configuration relaxes towards the equilibrium state. Whereas for monomers one finds simple exponential decay (Langmuir kinetics), for dimers there are different scenarios depending on the value of the equilibrium binding constants. If the probability for the second head to bind after the first one has attached is low, there will be comparatively few double-bonded dimers in the steady state. Consequently cooperative effects and correlations are less important implying that the equilibration process is exponential. The dynamics is drastically different if the second head binds immediately after the first one. Then, the equilibrium state will mainly consist of dimers bound with both heads. Their positions are correlated at a length scale given by the average distance between defects in the periodic pattern which can either be vacancies or single-bonded dimers. These correlations lead to a dynamics which is slowed down drastically as compared to the kinetics of individual dimers [2].

2.2 Molecular Motors and Active Transport. The Poisson Stepper

A large variety of theoretical models for motor proteins have been defined and explored in recent years (for a review see e.g. Ref. [4, 11]). These models differ in the level of detail in describing the interaction between molecular motors and their molecular tracks, the internal structure and dynamics of the motor proteins, and the complexity of the chemical kinetics taken into account. In essence, they model the molecular motors by rather complex stochastic processes coupling chemical and mechanical degrees of freedom. Here, we are interested in collective phenomena resulting from the interaction of

many molecular motors. We take the liberty to use the simplest possible model, the Poisson stepper, which still captures the most essential features of motor proteins, stochasticity and uni-directionality. There are mainly two reasons for taking such an approach. The first one is that we would like to isolate the collective effects from the complexity of the stochastic dynamics of a single motor. The second reason is based on the experience from studies of related driven non-equilibrium systems, where it is found that collective phenomena are not sensitive to the details of the dynamics of the individual components. At a later stage one certainly has to come back to this point and examine its validity; this is the topic of ongoing research [3].

The “Poisson enzyme” is defined as the following stochastic process. An object is assumed to move step-wise and only uni-directionally along a one-dimensional periodic array of binding sites such that the displacement of the enzyme is given by $x(t) = a \cdot n(t)$. Here a is the stepsize and $n(t)$ is the random variable of the Poisson process with values $n(t)$ a growing sequence of integers. Each step forward occurs stochastically with a constant rate r . This corresponds to the assumption that every biochemical cycle leads to a single step-wise displacement.

The master equation for the probability $P_n(t)$ to find the enzyme at site number n at time t reads

$$\frac{dP_n(t)}{dt} = r P_{n-1}(t) - r P_n(t). \quad (2)$$

The dynamics of the Poisson enzyme has the following well known characteristics. There is an exponential waiting time distribution for the enzyme to proceed by one step. The average time an enzyme waits to make this step is known as the *dwell time* τ , which is simply related to the rate as $\tau = 1/r$. The waiting time between successive steps is exponentially distributed. The enzyme moves on average with a constant velocity, i.e. the mean displacement grows linear with time $\langle n(t) \rangle = rt + n_0$, where $n_0 = 0$ is the initial position of the enzyme at time $t = 0$. Finally, the probability to find the enzyme at site n after time t is given by the Poisson distribution, $P_n(t) = ((t/\tau)^n/n!) e^{-t/\tau}$. An important quantity for characterizing the stochastic process is the randomness parameter R , defined as the ratio between mean $\langle n(t) \rangle$ and variance $\Delta n = \langle n^2(t) \rangle - \langle n(t) \rangle^2$. Since mean and average are identical for a Poisson process, $\langle n(t) \rangle = \Delta n = t/\tau$, the randomness parameter is simply $R = 1$. As compared to an actual motor this is too high indicating that there is more than one rate limiting step necessary to describe such stochastic engines [4, 11].

2.3 A Minimal Model for Collective Phenomena in Intracellular Transport

A minimal model for the collective dynamics of motor proteins has to account for the following experimental facts. The binding sites along the one-dimensional molecular tracks are spaced periodically. Each site can only bind a single enzyme, since double occupancy is sterically excluded. Each enzyme moves uni-directionally from one end to the other. The stepping process itself is a rather complicated stochastic process involving many chemical and mechanical states. As argued above, we reduce this process to its bare essential, a uni-directional step-wise process with a single effective hopping rate (“Poisson enzyme”). Each molecular track has a finite length, and in general one would like to allow for the enzyme reservoirs at both ends to have different densities and/or the attachment rate at the left and right end to be different from each other and different from the hopping rate in the bulk. All this taken together defines the totally asymmetric simple exclusion process (TASEP), a stochastic model which has been introduced by MacDonald *et al.* [7] to describe the kinetics of biopolymerization on nucleic acid templates. The model also serves as a playground for the discussion of some fundamental aspects of non-equilibrium statistical mechanics [12]. For it to be a proper minimal model for intracellular transport it also has to account for the fact that microtubules are embedded in a cellular environment with a reservoir of motors in solution. This allows for motors to attach from the solution to the molecular track or detach from it and become part of the reservoir again. Then one arrives at the TASEP with Langmuir kinetics introduced in Ref. [9]; for an illustration see Fig. 4.

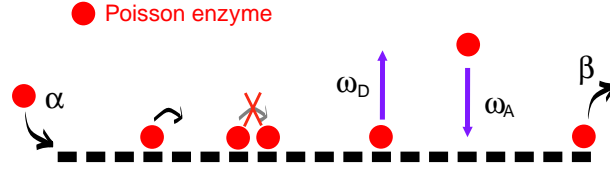


Figure 4: Schematic drawing of the totally asymmetric simple exclusion process with bulk attachment and detachment [9]. The entrance and exit rates at the left and right end of the track are given by α and β , respectively; ω_A and ω_D denote the local attachment and detachment rates.

The model is defined as follows. We consider a one-dimensional lattice with sites labeled $i = 1, \dots, N$ and lattice spacing $a = L/N$, where L is the total length of the lattice. The site $i = 1$ ($i = N$) defines the left (right) boundary, while the collection $i = 2, \dots, N - 1$ is referred to as the bulk. The microscopic state of the system is characterized by a distribution of identical particles on the lattice, i.e. by configurations $\mathcal{C} = \{n_i\}_{i=1, \dots, N}$, where each of the occupation numbers n_i can only be zero (vacancy) or one (particle). The statistical properties of the model are given in terms of the probabilities $\mathcal{P}(\mathcal{C}, t)$ to find a particular configuration \mathcal{C} at time t . The evolution of the probabilities \mathcal{P} is described by a master equation:

$$\frac{d\mathcal{P}(\mathcal{C}, t)}{dt} = \sum_{\mathcal{C}' \neq \mathcal{C}} [\mathcal{W}_{\mathcal{C}' \rightarrow \mathcal{C}} \mathcal{P}(\mathcal{C}', t) - \mathcal{W}_{\mathcal{C} \rightarrow \mathcal{C}'} \mathcal{P}(\mathcal{C}, t)]. \quad (3)$$

Here, $\mathcal{W}_{\mathcal{C} \rightarrow \mathcal{C}'}$ is a non-negative transition rate from configuration \mathcal{C} to \mathcal{C}' .

The TASEP and LK can be considered as two of the simplest paradigms which contrast equilibrium and non-equilibrium dynamics and stationary states. Langmuir kinetics evolves into a steady state well described in terms of standard concepts of equilibrium statistical mechanics. Driven lattice gases like the TASEP evolve into a stationary non-equilibrium state carrying a finite current. Whereas such non-equilibrium steady states are quite sensitive to changes in the boundary conditions, equilibrium steady states are very robust to such changes and dominated by the bulk dynamics. In the TASEP new particles can enter or leave the system only at the system boundaries, whereas in the bulk there are no sources or sinks. This is different in LK, where particles can enter or leave the system at any site. Depending on whether we consider a canonical or grand canonical ensemble the lattice is connected to a finite [5] or infinite [9] particle reservoir. Unlike the steady state of the TASEP, the equilibrium steady state of LK does not have any spatial correlations.

Combining both of these processes may at first sight seem as a trivial exercise since one might expect bulk effects to be predominant in the limit of large system sizes. This is indeed the case for detachment and attachment rates, ω_A and ω_D , which are independent of the system size N . However, one can expect interesting effects from the competition between bulk and boundary dynamics if the *gross rates* $\Omega_A = \omega_A N$ and $\Omega_D = \omega_D N$ are comparable with the hopping rates and the entrance and exit rates, i.e. are kept fixed as one considers larger and larger systems. To see this consider the following heuristic argument. A given particle will typically spend a time $\tau \sim 1/\omega_D$ on the lattice before detaching. During this “residence time” the number of sites n explored by the particle is of the order of $n \sim \tau$. Hence, for fixed ω_D , the fraction $n/N \sim 1/(\omega_D N)$ of sites visited by a particle during its walk on the lattice would go to zero as $N \rightarrow \infty$. Only if we introduce a “total” detachment rate by $\Omega_D = N\omega_D$ and keep it constant instead of ω_D as $N \rightarrow \infty$, the particle will travel a finite fraction of the total lattice size. In other words, competition will be expected only if the particles live long enough such that their internal dynamics or the external driving force transports them a finite fraction along the lattice before detaching. Then, particles spend enough time on the lattice to “experience” their mutual interaction and, eventually, produce collective effects. Similar arguments hold for holes due to the particle-hole symmetry of the dynamics. Such competition between bulk and boundary effects are

to be expected in intracellular transport and other biological processes. Processive molecular motors like Kinesin advance along cytoskeletal filaments while attachment and detachment of motors between the cytoplasm and the filament occur [4]. Typically kinetic rates are such that these motors walk a finite fraction along the molecular track before detaching. This falls well into the regime where we expect novel stationary states.

The stochastic dynamics defined above can in general not be solved exactly. Hence, we take the following approach: we solve the full stochastic dynamics using Monte Carlo simulations and in parallel develop an approximation scheme which still captures the main features of the problem. For the analytical treatment we neglect the discrete nature of the occupation numbers and write down a set of *rate equations* for the average occupation numbers $\rho_i(t) = \langle n_i(t) \rangle$,

$$\frac{d\rho_i}{dt} = \rho_{i-1}(1 - \rho_i) - \rho_i(1 - \rho_{i+1}) + \omega_A(1 - \rho_i) - \omega_D\rho_i \quad (4)$$

for any site in the bulk, while for sites at the boundaries one obtains: $d\rho_1/dt = \alpha(1 - \rho_1) - \rho_1(1 - \rho_2)$, and $d\rho_N/dt = \rho_{N-1}(1 - \rho_N) - \beta\rho_N$. Note that these rate equations are only approximate. They neglect density correlations and assume that correlation functions factorize as $\langle n_i(t)n_j(t') \rangle = \rho_i(t)\rho_j(t')$. These rate equations can certainly be solved numerically. It will, however, be instructive to consider the continuum version of these equations, i.e. the limit where $\varepsilon = L/N$ becomes small. Then, one finds to leading order in ε the following non-linear differential equation for the average profile at the stationary state [9]:

$$\frac{\varepsilon}{2}\partial_x^2\rho + (2\rho - 1)\partial_x\rho + \Omega_A(1 - \rho) - \Omega_D\rho = 0. \quad (5)$$

with the boundary conditions $\rho(0) = \alpha$ and $\rho(1) = 1 - \beta$; this can be interpreted as if the system at both ends is in contact with particle reservoirs of respective fixed densities α and $1 - \beta$. Note also that from now on we are measuring all lengths in units of the filament length L .

3 Density Regulation and Cooperativity in Active Systems

The purpose of this section is to explain the physical principles underlying density and current regulation in active transport along linear molecular tracks. For simplicity we only discuss the simplest possible case with a binding constant $K = 1$; the analysis of the general scenario can be found in a forthcoming publication [10]. Then, $\Omega = \Omega_A = \Omega_D$ and the stationary density profile (in the continuum limit $\varepsilon \rightarrow 0$) is determined by a rather simple first order differential equation,

$$(2\rho - 1)(\partial_x\rho - \Omega) = 0, \quad (6)$$

with the boundary conditions $\rho(0) = \alpha$ and $\rho(1) = 1 - \beta$. This equation has only three basic solutions corresponding to a maximal current (MC), a high density (HD) and a low density (LD) phase. There is a constant solution with $\rho_l(x) = \frac{1}{2}$, identical both to the equilibrium stoichiometry in Langmuir kinetics and the density of the maximal current phase in the TASEP. There are two linear profiles $\rho_{\alpha,\beta} = \Omega x + C_{\alpha,\beta}$ with $C_\alpha = \alpha$ and $C_\beta = 1 - \beta - \Omega$, matching the density at the left and the right boundary, respectively. For $\alpha < \frac{1}{2}$ and $\beta < \frac{1}{2}$ they describe the density profiles of the low and high density phases, respectively. The full density profile for a given set of parameters is obtained by concatenating the three basic solutions such that the current is continuous along the molecular tracks [10]. Depending on how the three solutions $\rho_\alpha(x)$, $\rho_\beta(x)$ and $\rho_l(x)$ can be matched, different scenarios arise for the full density profile $\rho(x)$.

Let's consider values for the entrance and exit rate such that the densities at the left and right boundary are below and above the value of the Langmuir isotherm, $\rho_l = \frac{1}{2}$. If the densities at the boundaries are sufficiently close to ρ_l one can have 3-phase coexistence with a continuous density

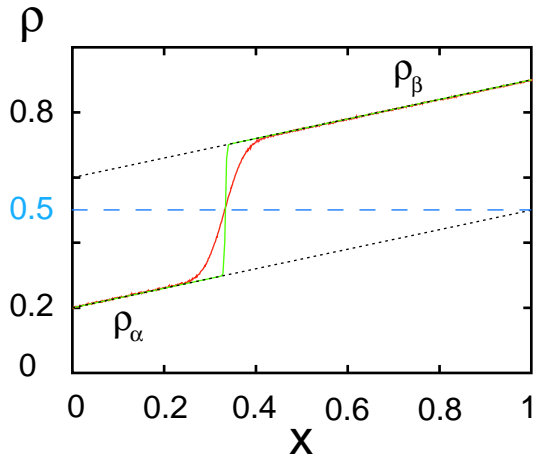


Figure 5: Average density profile $\rho(x)$ for $\alpha = 0.2$, $\beta = 0.1$ and $\Omega = 0.3$. In this parameter range one observes a 2-phase coexistence: a low and a high density phase are separated by a domain wall. The profiles are computed analytically with Eq. 6 (dashed), within a mean-field approximation (green/light), and from Monte-Carlo simulations (red/dark). Only in proximity of the domain wall the results from the mean-field approximation show deviations from the density profile obtained by Monte-Carlo simulation.

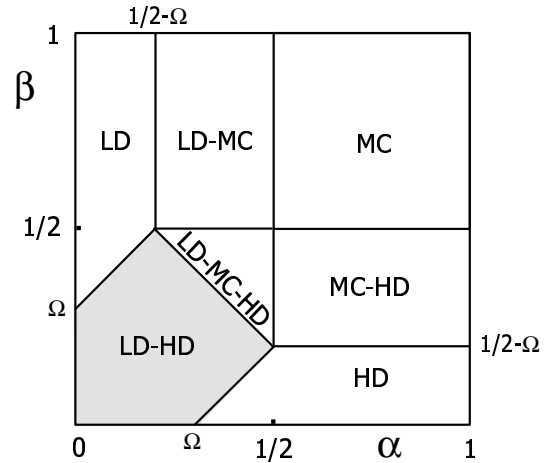


Figure 6: Phase diagram for $\Omega = 0.3$. In the high density (HD) and low density (LD) phase, the density profiles are linear and regulated by the right and left boundary, respectively. In contrast, the bulk density in the maximal current phase (MC) is constant and independent of the boundaries, i.e. solely determined by bulk properties. There are several mixed phases with coexistence between various homogeneous phases. The most interesting one (grey area) is the LD-HD phase where the LD and HD regions are separated by a density discontinuity.

profile, where the constant density of ρ_l (MC) intervenes between the two linear solutions emerging from the left (LD) and right (HD) boundaries. Upon lowering both the entrance and exit rates, or in other words upon increasing the density difference between the left and the right boundary, the width of the intervening maximal current phase becomes smaller and eventually shrinks to zero. Then one is in a 2-phase coexistence region where low and high density phases are separated by a density discontinuity, located at a point where the currents corresponding to the right and left solutions match; compare Fig. 5. Similar to the TASEP the domain wall may be located in the bulk or at the boundaries of the system, such that we can have parameter regimes with 2-phase coexistence (LD-HD) or homogeneous LD and HD phases. In addition, one can also find parameter regimes where the MC phase coexists with the LD and HD phase. The results are summarized in the phase diagram, Fig. 6.

These results have a series of important implications on how one can regulate the density and current along microtubules and in related cellular processes such as the syntheses of DNA and RNA or even proteins. The MC current phase has a bulk density of $\rho_l = \frac{1}{2}$ which is completely independent of the magnitude of the entrance and exit rates. This phase is referred to as bulk dominated. It can neither be regulated by changing the protein reservoirs at the boundaries nor by altering the ATP content in the solution or changing the attachment rates Ω of the motor proteins. We have here an example of a stationary density and current which is insensitive or robust against external

perturbations. These conclusions remain valid even in multi-phase regimes for those sections along the microtubules with a constant density equal to ρ_l . This behavior has to be contrasted with the LD and HD phases. They are very sensitive to changes in the attachment rate Ω and the exit and entrance rates α and β , respectively. Indeed, they determine the slope and the boundary values of the density profiles, which in turn uniquely determines the stationary current profiles. All of these conclusions are rather obvious for the present case due to the simplicity of the mathematical expressions. They remain valid for binding constants $K \neq 1$, and constitute a generic principle of cooperativity in intracellular transport.

4 Kinesin Density and Current Profiles along Microtubules

Finally, let us be specific and give predictions for the density and current profiles using realistic parameters for kinesin on microtubules. For this we have to come back to the more general model described by Eq. 5. It can be solved similar to Eq. 6 but the mathematics is considerably more complicated; for details see Ref. [10]. Here we restrict ourselves to a discussion of numerical solution of Eq. 5 for a range of binding constants $K = \Omega_A/\Omega_D$.

From single-molecule motility assays we know that the whole kinesin dimer moves forward by one tubulin dimer ($a = 8$ nm) in one step, ending up in the same physical conformation from which it started. This corresponds to the elementary step of our Poisson process. Kinesin is a processive motor, i.e. it can stay attached to its track over about 100 ATP hydrolysis cycles. The speed of kinesin is limited by the chemical turnover rate of a single motor multiplied with the step produced per ATP hydrolyzed. Typical values are velocities of $1 \mu\text{m/s}$ (for a review see e.g. Ref. [4, 11]). Hence we can take for typical detachment rates $\Omega_D \approx 1$ Hz. Finally, typical filament length are $L \approx 5 - 10 \mu\text{m}$, such that the number of sites is $N \approx 1000$. In many instances there is no particular reason why motors should preferentially enter at the left end (though one could think of situations where we have a large reservoir there). This gives $\alpha = 0$ for the entrance rate. The plus end of the microtubule may or may not block the motor molecules. For illustration we take the two extreme cases of “open” and “blocked” ends, corresponding to exit rates of $\beta = 0$ and $\beta = 1$, respectively. The case of blocked ends may also correspond to a particular site along the microtubule which is blocked by some microtubule associated protein (MAP). Figures 9 and 10 show these two extreme situations for a series of binding constants K . Note that one can vary the binding constant K by changing the concentration of kinesin molecules in solution or/and the ATP concentration.

For open ends (Fig. 8) the density profile changes upon increasing the binding constant K from a LD phase density profile to a density profile showing phase coexistence between the LD and MC phase and finally to a completely flat profile corresponding to the stoichiometry of the Langmuir isotherm. The main control parameter is the binding constant, the presence of the open end shows only minor modifications of the density profile which become pronounced only in the immediate vicinity of the right end, where the density has to drop to zero due to the open boundary condition. Similarly, there is a boundary layer at the left end where the density drops to zero since $\alpha = 0$. For blocked ends (Fig. 7), the right boundary has a strong effect on the density profile which even increases with increasing binding constant K . Again, it is only when the binding constant becomes very large that Langmuir kinetics starts to dominate and one arrives at a density profile which for most parts of the microtubule is very similar to the case with open ends. Note that Figs. 8 and 7 show the density profiles as obtained from the rate equations in the continuum limit, Eq. 5. The actual profiles obtained from the full stochastic dynamics look indeed very similar [10].

Due to the non-linearities in the dynamics a density profile alone is not sufficient to discuss the mass transport along the filaments. In Figs. 9 and 10 the current profiles are shown for the same parameters as the density profiles. Again, we only show the results obtained from the solution of the rate equations in the continuum limit; the deviations from the Monte-Carlo results are even smaller than for the corresponding density profiles. There are two main features of these current profiles. In

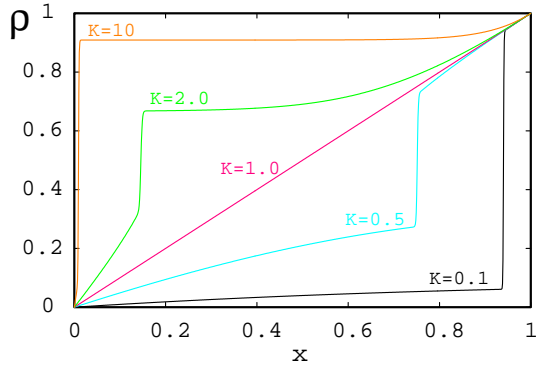


Figure 7: Density profile of kinesin motors along a microtubule for blocked ends ($\beta = 0$) and a series of binding constants K indicated in the graph. The entrance rate is taken as $\alpha = 0$.

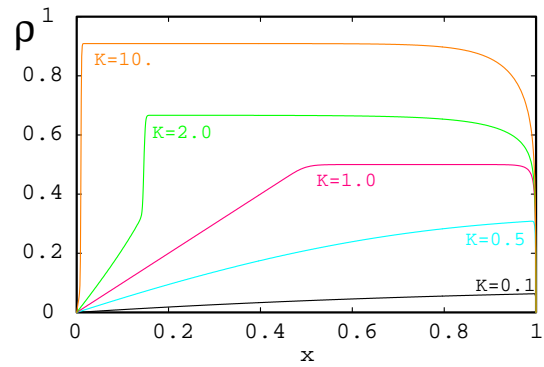


Figure 8: Density profile of kinesin motors along a microtubule for open ends ($\beta = 1$) and a series of binding constants K indicated in the graph. The entrance rate is taken as $\alpha = 0$.

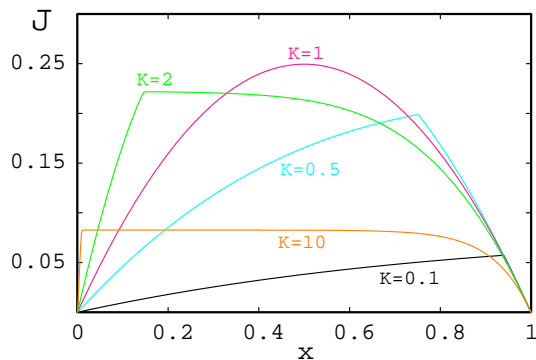


Figure 9: Current profile of kinesin motors along a microtubule for blocked ends ($\beta = 0$) and a series of binding constants K indicated in the graph. The entrance rate is taken as $\alpha = 0$.

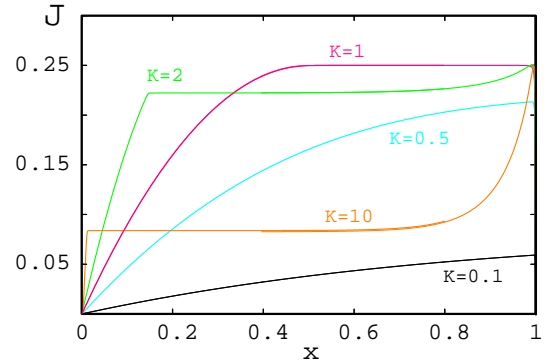


Figure 10: Current profile of kinesin motors along a microtubule for open ends ($\beta = 1$) and a series of binding constants K indicated in the graph. The entrance rate is taken as $\alpha = 0$.

both cases we find an optimal value for the binding constant. At roughly $K = 1$ the current seems to be maximal for most parts of the filament, and it is greatly reduced for both raising and lowering the binding constant. For low binding constants a low density is the reason for a low current. For high binding constants the increased density does not lead to a higher but a lower current due to jamming effects similar to our experience with vehicular traffic at rush hours. The difference between open and blocked ends are mainly close to the right end. For blocked ends the motors can not pass the right end and hence the current must decrease upon approaching the right end, quite similar to a red traffic light. In contrast, a blocked end allows free passage of the current such that the current increases and is maximal at the right end.

5 Summary and Outlook

We have seen that a minimal model for collective intracellular transport shows a surprisingly rich phenomenology including a multitude of different phases. Some of these phases are bulk dominated and robust to any changes in the environment, others respond quite sensitively to protein or ATP concentration in the bulk or/ and changes in the chemical rates at the boundaries of the system. This may serve as a paradigm for a broad range of cellular processes including filopod growth, protein synthesis and protein translocation. Future research will now need to study additional features of the model. One could think of including more molecular details of the stochastic processes governing the dynamics of individual molecular motors, interaction of different species of motors, regulation by microtubule associated proteins, and many other things.

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