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Phase transitions in systems with two species of molecular motors

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Abstract. – Systems with two species of active molecular motors moving on (cytoskeletal) filaments into opposite directions are studied theoretically using driven lattice gas models. The motors can unbind from and rebind to the filaments. Two motors are more likely to bind on adjacent filament sites if they belong to the same species. These systems exhibit i) continuous phase transitions towards states with spontaneously broken symmetry, where one motor species is largely excluded from the filament, ii) hysteresis of the total current upon varying the relative concentrations of the two motor species, and iii) coexistence of traffic lanes with opposite directionality in multi-filament systems. These theoretical predictions should be experimentally accessible.

Cytoskeletal motors which convert chemical free energy into directed movements along filament tracks have been studied extensively during the last decade. Many different motor molecules have been identified and much insight has been gained into their motor mechanisms and their functions within cells [1]. Much of the present knowledge about motor mechanisms has been obtained from *single*-molecule experiments, which have been performed under a variety of different conditions [2].

Cooperative effects, on the other hand, arising from motor-motor interactions have hardly been explored experimentally so far. Most of the available information about these interactions is due to decoration experiments where the binding patterns of inactive (non-moving) motors to immobilized filaments are examined by electron microscopy and X-ray scattering. Decoration experiments clearly demonstrate mutual exclusion from binding sites of the filaments. In addition, there is evidence for an effectively attractive motor-motor interaction mediated via the filament. Such an interaction is implied by the coexistence of decorated and bare filaments, which has been observed both for the decoration of actin filaments by myosin [3,4] and for the decoration of microtubules by kinesin [5]. In the case of actin decoration, the motor-motor interaction depends on the internal conformation of the actin filaments [4]. This observation as well as experimental results on active kinesin in the presence of ATP [6] suggest that a bound motor leads to a localized deformation of the filament which promotes the binding of further motors on adjacent binding sites.

A convenient way to study interacting motors theoretically is to model the motor movements as walks on a lattice [7, 8]. In these models, the directed walks along filaments are described as biased random walks, whereas the unbound motors undergo symmetric random walks corresponding to diffusive motion. Interactions can be taken into account by hopping rates which depend on the presence of motors on adjacent lattice sites. These models are new variants of driven lattice gas models or exclusion processes, where the driving is localized to the filaments. Other variants of driven lattice gas models have been previously studied for a variety of transport processes, see, *e.g.*, [9–11].

In this letter, we will address the cooperative behavior of two species of motors moving along the same filament, but into opposite directions. In both the kinesin and myosin motor families, motors moving into opposite direction have been identified, *e.g.* myosin V and VI or conventional kinesin and ncd [1]. The directionality of motors can also be engineered by genetic methods, *e.g.* [12, 13]. The two species of motors compete for the same binding sites along the filament [14]. In order to incorporate the effectively attractive motor-motor interactions as deduced from the decoration experiments [3–6], a bound motor is taken to increase the adsorption rate onto adjacent binding sites for motors of the same species. We will show that these models exhibit states of spontaneously broken symmetry, hysteresis of current and motor densities, and, in multi-filament systems, the coexistence of traffic lanes with opposite directionality. In contrast to the non-equilibrium phase transitions of the asymmetric simple exclusion process [9] or the "bridge" model [11], the transitions discussed here are *not* induced by the boundaries, but by the binding and unbinding dynamics of the active particles. This implies that they can be simply controlled by the bulk concentrations of the two motor species.

To proceed, let us consider a one-dimensional lattice representing a filament on which two species of motor particles move. We will denote the two species by "plus" and "minus". Plus-motors attempt to hop to the right with a rate $\alpha = v_{\rm b}/\ell$, which depends on the motor velocity $v_{\rm b}$ in the absence of other motors and on the filament repeat distance ℓ, while minus-motors move to the left with the same rate α. Backward steps are neglected, because they are rare for cytoskeletal motors. Hopping attempts are only successful if the target site is not occupied by another motor. This incorporates the mutual exclusion of the motors and prevents, in particular, that bound plus- and minus-motors pass each other.

In general, the filament is located within a larger volume such as a tube with a certain amount of unbound motors which can bind to an empty filament site. Likewise, bound motors have a small probability to unbind at each step. In order to model this system, we replace the solution surrounding the filament by a reservoir which is characterized by the two concentrations ρ_+ and ρ_- of the unbound plus- and minus-motors. Very similar behavior is found for a refined model as in [8], where the unbound motors undergo symmetric random walks within a tube and the number of particles is locally conserved.

The rates for binding and unbinding depend on the state of adjacent lattice sites. If no other motors are close, an unbound plus- or minus-motor binds to an empty filament site with rate $\pi_{\rm ad}\rho_\pm$, where $\pi_{\rm ad}$ is the adsorption rate and $\rho_\pm$ are the concentrations of unbound plus- and minus-motors in the solution, and a bound motor unbinds with rate ϵ(1). A typical value for ϵ is $\alpha/100$, as follows from the observed walking distances [7](2).

If the motors interact *only* via their mutual exclusion, *no* phase transition occurs in the system as one varies the bulk motor concentrations. Such transitions are found, however, if one incorporates the previously mentioned filament-mediated interaction which will affect, in

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(1)As in [7, 8], we do *not* scale the detachment/attachment rates with the system size L, in contrast to [15].

(2)For motor complexes or cargo particles with n active motors, one would have $\epsilon \sim \epsilon_1^n$ with the detachment rate ϵ_1 of a single motor. In addition, the velocity, and thus α, are reduced for such a particle due to the mutual hindrance of the active motors.

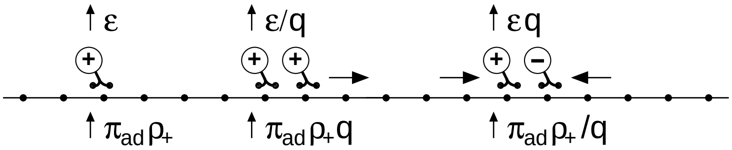

Fig. 1 – "Plus" and "minus" motors which move on the filament to the right and to the left, respectively. The rates for attachment to and detachment from the filament depend on the state of the forward neighbor site on the filament. Left: at sites with a vacant forward neighbor, motors unbind and bind with rates ϵ and $\pi_{\rm ad}\rho_\pm$. Middle: a motor of the same species at the forward neighbor site enhances binding and reduces unbinding by factors $q > 1$ and $1/q$, respectively. Right: a motor of the other species reduces binding and enhances unbinding.

general, both the binding and the unbinding rates, $\pi_{\rm ad}$ and ϵ, in the direction perpendicular to the filament and the forward rate α for steps parallel to the filament.

Let us assume that the binding rate $\pi_{\rm ad}$ is increased by a factor q and that the unbinding rate ϵ is decreased by a factor $1/q$ if another motor of the same species already occupies the forward neighbor site on the filament, see fig. 1(3). These binding and unbinding processes obey detailed balance [8]. For steps along the filament, on the other hand, detailed balance is broken since these active steps are coupled to ATP hydrolysis, and the corresponding rate α will, in general, change to α/q' with $q' \neq q$ if a motor of the same species is present on the forward neighbor of the target site. We find that the system undergoes a phase transition for fixed q' and sufficiently large values of q. In order to eliminate one parameter, we will focus in the following on the situation with $q' = 1$. For an effectively attractive interaction between two motors of the same species, we have $q > 1$. In the presence of a bound motor of the other species at the forward neighbor site the unbinding rate is enhanced by a factor q, while the adsorption rate is reduced by a factor $1/q$.

In order to suppress all effects arising from the two ends of the filament, we will first consider periodic boundary conditions in the longitudinal direction parallel to the filament. Therefore, the phase transitions found here can*not* be induced by the boundary conditions imposed on the system, in contrast to [9, 11].

For large q, motors bound to the filament strongly attract other motors of the same type to the filament, but repel those of the other type. Now, if the bound concentration of one motor species is much higher than the one of the other species, the second species is basically excluded from the binding sites of the filament. On the other hand, the motors of the majority species on the filament are unlikely to unbind, since they are effectively attracted by their neighbors. In fact, these interactions lead to a *non-equilibrium phase transition* induced by the active movements of the motors with a critical point at $q = q_{\rm c}$ for $\rho_+ = \rho_- = \rho/2$, *i.e.*, for equal bulk concentrations of plus- and minus-motors. We have found these phase transitions both from Monte Carlo (MC) simulations and analytical mean-field calculations, compare fig. 2.

For $\rho_+ = \rho_- = \rho/2$ and $q < q_{\rm c}$, motors of both species are bound to the filament and the densities of bound motors, $\rho_{{\rm b},+}$ and $\rho_{{\rm b},-}$, are equal for both types. The total current vanishes as the motor currents with opposite directionality, J_+ and J_-, balance each other. For $q > q_{\rm c}$, on the other hand, we observe spontaneous symmetry breaking. Motors of one species are bound to the filament, while those of the other species are largely excluded from it, resulting in a non-zero value of the density difference $m_{\rm b} \equiv \rho_{{\rm b},+} - \rho_{{\rm b},-}$ as shown in fig. 2(a) and (c). Likewise, the total current $J \equiv J_+ + J_-$ is also finite for $q > q_{\rm c}$. The current decreases for

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(3)Interactions involving nearest neighbors in both forward and backward direction lead to similar results.

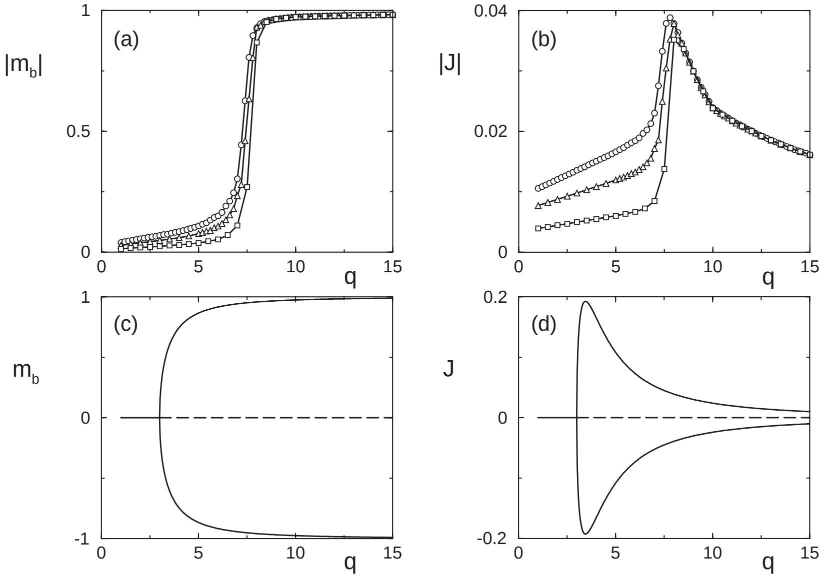

Fig. 2 – Density difference $m_\mathrm{b} = \rho_{\mathrm{b},+} - \rho_{\mathrm{b},-}$ and total current $J = J_+ + J_-$ as functions of the interaction parameter q as obtained from MC simulations (a, b) and analytical mean-field calculations (c, d). In (a, b) the absolute values of m_b and J are shown for different filament lengths $L = 200$ (○), $L = 400$ (△), and $L = 1600$ (□), see text. The mean-field solutions (c, d) show a symmetric solution $m_\mathrm{b} = 0$ and $J = 0$ and two branches with broken symmetry for $q > q_\mathrm{c}$. The hopping rates are $\alpha = 1$, $\epsilon = 0.01$, $\pi_\mathrm{ad} = 0.1$, and the unbound motor concentrations are $\rho = 2\rho_+ = 2\rho_- = 0.1$.

large q as the filament becomes overcrowded. The MC simulations exhibit strong finite-size effects. We sometimes observe reversal of the direction of the current at $q > q_\mathrm{c}$, as the system flips from one broken-symmetry state to the other. In addition, for values of q close to q_c, the total current J and the difference m_b of bound densities exhibit strong fluctuations. Because of these fluctuations, we plotted the absolute values of m_b and J in fig. 2(a) and (b). These quantities exhibit non-zero values for finite system size L, but decrease to zero for large L.

The critical interaction parameter q_c as determined by simulations depends on L, see fig. 3(a). Extrapolation of these data leads to the estimate $q_\mathrm{c} = 7.9 \pm 0.1$ for infinite L and to $q_\mathrm{c}(\infty) - q_\mathrm{c}(L) \sim 1/L^{1/2}$. In addition, we find that the time between subsequent flips from one ordered state to the other at $q > q_\mathrm{c}$ increases exponentially with L [16]. These observations strongly indicate that symmetry breaking persists in the thermodynamic limit.

We have determined the critical interaction parameter q_c as a function of the overall motor concentration $\rho \equiv \rho_+ + \rho_-$ in the solution. The resulting phase diagram as obtained from MC simulations and mean-field calculations is shown in fig. 3(b).

In systems with several parallel filaments, the symmetry breaking leads to the coexistence of traffic lanes with opposite directionality. We have performed simulations for the case of two parallel filaments which are placed within a cylindrical tube, parallel to the cylinder axis [16]. In this case, the particle number is locally conserved. Therefore, if one motor species starts to decorate one filament, the other motor species attains a larger bulk concentration and is, thus, more likely to bind to the other filament. Indeed, for $q > q_\mathrm{c}$, we observe that the two filaments are covered by different motor species which then form two traffic lanes with opposite directionality. Thus, the symmetry breaking provides a simple mechanism for

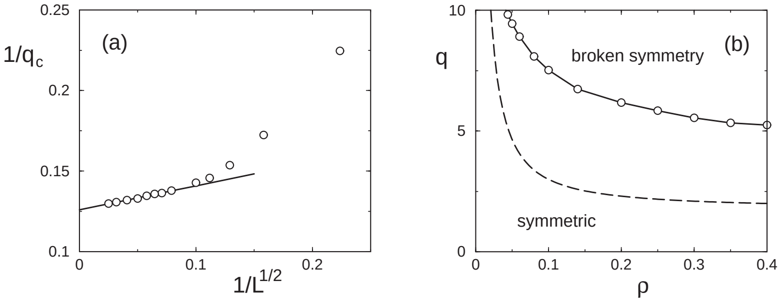

Fig. 3 – (a) The inverse critical interaction strength $1/q_\mathrm{c}$ as obtained from simulations for different system sizes L with $20 \le L \le 1600$. The line is a linear fit to the data which leads to $q_\mathrm{c} = 7.9 \pm 0.1$ at infinite L. (b) Phase diagram as a function of the interaction parameter q and the concentration of unbound motors $\rho = 2\rho_\pm$, as obtained from simulations with $L = 400$ (data points) and from mean-field theory (dashed line). Parameters are as in fig. 2.

efficient transport between two reservoirs of cargo particles.

Within mean-field theory, the time evolution of the densities of bound motors $\rho_{\mathrm{b},+}$ and $\rho_{\mathrm{b},-}$ is given by

$$\frac{\partial}{\partial t}\rho_{\mathrm{b},\pm} + \frac{\partial}{\partial x}J_\pm = I_\pm(q), \tag{1}$$

with the currents

$$J_\pm \equiv \pm v_\mathrm{b}\rho_{\mathrm{b},\pm}(1-\rho_\mathrm{b}) - D_\mathrm{b}\left(\frac{\partial\rho_{\mathrm{b},\pm}}{\partial x} + \rho_{\mathrm{b},\pm}\frac{\partial\rho_{\mathrm{b},\mp}}{\partial x} - \rho_{\mathrm{b},\mp}\frac{\partial\rho_{\mathrm{b},\pm}}{\partial x}\right) \tag{2}$$

and the attachment/detachment terms

$$\begin{aligned} I_\pm(q) \equiv & -\epsilon\rho_{\mathrm{b},\pm}(1-\rho)\left[(1-\rho_\mathrm{b}) + q\rho_{\mathrm{b},\mp} + \frac{1}{q}\rho_{\mathrm{b},\pm}\right] + \\ & + \pi_\mathrm{ad}\rho_\pm(1-\rho_\mathrm{b})\left[(1-\rho_\mathrm{b}) + \frac{1}{q}\rho_{\mathrm{b},\mp} + q\rho_{\mathrm{b},\pm}\right]. \end{aligned} \tag{3}$$

Here the parameters v_b and D_b are the velocity and the diffusion coefficient of single bound motors and $\rho_\mathrm{b} \equiv \rho_{\mathrm{b},+} + \rho_{\mathrm{b},-}$. The factor $(1-\rho)$ in the detachment term describes crowding of motors in the solution with $(1-\rho) \approx 1$ for typical experimental conditions. It follows from (1)-(3) that the stationary and spatially homogeneous states satisfy $I_+ = I_- = 0$. For the symmetric case with $\rho_+ = \rho_- = \rho/2$, this leads to a critical point at $q = q_\mathrm{c}$ as given by

$$q_\mathrm{c} \equiv \eta + \sqrt{\eta^2+3} \qquad \text{with} \qquad \eta \equiv \frac{\epsilon(1-\rho)}{\pi_\mathrm{ad}\rho}. \tag{4}$$

The corresponding order parameter $m_\mathrm{b} \equiv \rho_{\mathrm{b},+} - \rho_{\mathrm{b},-}$ vanishes for $q < q_\mathrm{c}$, but attains the finite value

$$m_\mathrm{b} = \pm\sqrt{\frac{(q^2-2\eta q-3)(q^2-2\eta q+1)}{(q-1)^2(q-2\eta+1)^2}} \sim \pm(q-q_\mathrm{c})^{1/2} \tag{5}$$

for $q > q_\mathrm{c}$. Likewise, the total current $J = v_\mathrm{b}m_\mathrm{b}(1-\rho_\mathrm{b})$ also vanishes as $(q-q_\mathrm{c})^{1/2}$. The analysis of the MC data indicates that $m_\mathrm{b} \sim (q-q_\mathrm{c})^\beta$ with $\beta \simeq 0.35$.

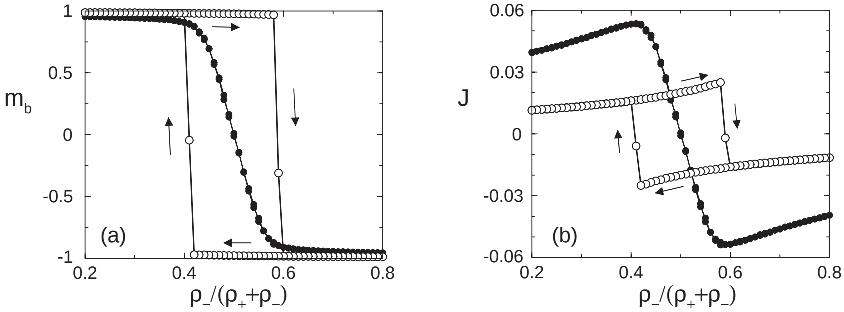

Fig. 4 – (a) The density difference $m_\mathrm{b} = \rho_{\mathrm{b},+} - \rho_{\mathrm{b},-}$ and (b) the total current $J = J_+ + J_-$ as a function of the fraction of minus-motors ρ_-/ρ for fixed overall concentration, $\rho = \rho_+ + \rho_- = 0.1$. The white and black data points correspond to $q = 12 > q_\mathrm{c} \simeq 7.5$ and $q = 6 < q_\mathrm{c}$, respectively. For $q < q_\mathrm{c}$, no hysteresis is observed. Data points have been obtained by simulating 10^6 MC steps for each value of ρ_-. The rates are as in fig. 2 and the filament length $L = 400$.

Linear stability analysis shows that the symmetric solution with $m_\mathrm{b} = 0$ is stable for $q < q_\mathrm{c}$ and becomes unstable for $q > q_\mathrm{c}$, while the solution with broken symmetry is stable in the range of q where it exists(4).

Varying the difference $\rho_+ - \rho_-$ of the unbound motor concentrations for constant overall concentration $\rho = \rho_+ + \rho_-$, we observe a discontinuous transition with hysteresis at $q > q_\mathrm{c}$, see fig. 4. It is interesting to note that the total current, $J = J_+ + J_-$, increases as the concentration of minority motors, which are excluded from the filament, is increased, and thus adopts its maximal value in the region of metastability. To observe hysteresis, it is, however, not necessary to keep the overall concentration ρ constant. In an experiment, one could start with $\rho_- < \rho_+$, add first minus-motors until $\rho_- > \rho_+$ and then add plus-motors, thereby increasing the overall concentration ρ. Such an experiment will again show hysteresis since q_c decreases with increasing ρ, as shown in fig. 3.

The systems discussed so far were characterized by periodic boundary conditions in the longitudinal direction parallel to the filament. These boundary conditions are useful from a theoretical point of view since they suppress all boundary effects which can dominate the relatively small systems accessible to computer simulations. In principle, one could study such systems experimentally if one combined several filaments to ring-like arrangement. In practice, essentially straight filaments of finite length with two "open" ends are simpler to prepare. Thus, let us finally consider such systems consisting of one or several straight filaments in contact with a solution of plus- and minus-motors, again with the concentrations ρ_+ and ρ_-, respectively. Motors can attach to the filament and unbind from it with the same rates as before with the exception of the last binding sites at the filament ends, where unbinding occurs with rate ϵ_end. If the filament is sufficiently long with length $L \gg v_\mathrm{b} q/\epsilon$ and $L \gg v_\mathrm{b} q/\epsilon_\mathrm{end}$, the bound density along the filament will be determined by the bulk dynamics, while the dynamics at the filament ends leads to the formation of boundary layers, so that the phase transitions described above for the periodic case also occur for the case with "open" ends. In order to see whether these phase transitions could be observed in experiments where the typical filament length is tens of micrometers, we performed simulations for this open case with $L = 1000$ and motor parameters as in fig. 2. In these simulations, symmetry breaking

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(4)Our mean-field equations also imply a spurious "blocking transition" for small q and large v_b which is *not* observed in our MC simulations, compare [17].

and hysteresis are clearly observed for an intermediate range of the unbinding rate at the filament end ϵ_{end} as given by $0.03 \lesssim \epsilon_{\mathrm{end}} \lesssim 0.5$, with approximately the same value of q_{c} as for the periodic case(5). Since ϵ_{end} can be expected to lie within this range for cytoskeletal motors, this implies that these phase transitions should be accessible in *in vitro* experiments with two species of motors and filaments of length $L \gtrsim 10\,\mu\mathrm{m}$.

In summary, we have discussed models for two species of interacting molecular motors. Binding to a filament is promoted by bound motors of the same, but suppressed by bound motors of the other species. These systems exhibit active, non-equilibrium phase transitions with spontaneous symmetry breaking, hysteresis and (in the case of many filaments) the formation of lanes with opposite directionality. On the one hand, these systems represent new lattice gas models, which exhibit phase transitions between two ordered states induced by active particles. On the other hand, these novel phase transitions should also be accessible to experiments with cytoskeletal motors.

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(5) For smaller or larger ϵ_{end}, the boundary layers become quite large and the density difference m_{b} fluctuates strongly at intermediate q. For small ϵ_{end}, plus-motors crowd at the plus-end and minus-motors at the minus-end. For large ϵ_{end}, plus-motors are depleted at the plus-end, which is then dominated by minus-motors, and vice versa at the minus-end.