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Active Pattern Formation in One and Two Dimensions

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Active pattern formation in one and two dimensions

by

Hui-Shun Kuan

B.S., National Taiwan University, 2008

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Date ________________

The final copy of this thesis has been examined by the signatories, and we find that both the content and the form meet acceptable presentation standards of scholarly work in the above mentioned discipline.
In this thesis, we studied active systems in one or two dimensions in which particles are self-propelled and repel each other. In one-dimensional models, we considered driven particles on single lanes or in anti-parallel overlaps with both binding/unbinding and switching between the lanes. These models are inspired by experiments on kinesin proteins walking on microtubules or anti-parallel overlaps. In the single-lane case, we focused on length regulation controlled by end concentration or flux. In the anti-parallel overlap case, we used a phase space flow method to determine the density profiles and compared the analytic results with kinetic Monte Carlo simulations. In calculating the phase diagram, we also found a phase, the low density-high density phase, which was not found previously. In two dimensional systems, we studied high-aspect-ratio self-propelled rods with a repulsive potential over a wide range of packing fraction and driving to determine the nonequilibrium state diagram and dynamic behavior. Flocking and nematic-laning states occupy much of the parameter space. In the flocking state, the average internal pressure is high and structural and mechanical relaxation times are long, suggesting that rods in flocks are in a translating glassy state despite overall flock motion. In contrast, the nematic-laning state shows fluid-like behavior. The flocking state occupies regions of the state diagram at both low and high packing fraction separated by nematic-laning at low driving and a history-dependent region at higher driving; the nematic-laning state transitions to the flocking state for both compression and expansion. We propose that the laning-flocking transitions are a type of glass transition which, in contrast to other glass-forming systems, can show fluidization as density increases. The fluid internal dynamics and ballistic transport of the nematic-laning state may promote collective dynamics of rod-shaped microorganisms.
Dedication

To my beloved sister, Wen-Hui Kuan.
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4.1 Nonequilibrium state diagram and snapshots of self-propelled rods of aspect ratio 40. (a) State diagram as a function of Peclet number and packing fraction. Points indicate parameter sets of simulations. Solid lines indicate boundaries of regions of stability of different initial conditions. I (orange), isotropic state; F (purple) flocking state; NL (green) nematic-laning state; C (pink) crystalline state. Green-purple striping indicates region where both flocking and nematic-laning initial conditions are stable. (b-g) Simulation snapshots at indicated packing fraction and Peclet number. Rods are colored by orientation according to the colorwheel. (b) Isotropic. (c) Nematic. (d) Crystal. (e) Flocking. (f) Nematic–laning. (g) Flocking.

4.2 The pair distribution function (a), polar orientational correlation function (b), and nematic orientational correlation function (c) as a function of the separation $r_{\perp}$ perpendicular to the rod long axis in the flocking state ($\phi = 0.3$, blue) and the nematic-laning state ($\phi = 0.4$, red). 

4.3 An example flock identification using distributions of local polar order parameter and contact number, for a simulation with $\phi = 0.1$ and $Pe = 320$. (a) The joint distribution of local polar order parameter and contact number. (b) A snapshot of the flocking state where green indicates flock boundary rods, blue denotes flock interior rods, and red denotes vapor.

4.4 Illustration of determination of isotropic and flocking state boundary. Flock size distributions for $\phi = 0.05$, where systems with $Pe < 20$ are identified as isotropic and $Pe \geq 20$ are identified as flocking.

4.5 Left, the exponent of power-law decay in structure factor auto-correlation function at $Pe= 160$, where the fitting equation is $At^{-\alpha}$. Right, the effective shear viscosity as the function of packing fraction for $Pe= 160$. 
4.6 Hysteresis in simulations under expansion, compression, and with an applied field.

(a) Simulation snapshots of an expansion run initially in the nematic-laning state at $\phi = 0.5$ (far left). When the packing fraction reaches 0.4 the system transitions to the flocking state. (b) Simulation snapshots of a compression run initially in the flocking state at $\phi = 0.34$ (far right). The system remains in the flocking state when compressed. (c) Simulation snapshots of run with applied nematic aligning field beginning in the flocking state at $\phi = 0.44$ (far left). The applied field breaks up the flock and allows a return to the nematic-laning state after the field is removed (far right). (d) Internal pressure for systems shown in (a-c). Blue, initial nematic-laning state as shown in (a); red initial flocking state as shown in (b); black, system with nematic aligning field as shown in (c).

4.7 Mechanical and structural properties of the nematic-laning and flocking states. (a,b) Internal pressure as a function of packing fraction during expansion (left-handed triangles) and compression (right-handed triangles) runs for simulations with varying Peclet number. The black arrows and open circles indicate the initial state of each run. (c) Structure-factor autocorrelation as a function of time for $\text{Pe}=160$ and systems in the laning ($\phi = 0.44$, red) and flocking ($\phi = 0.34$, blue) states for the peak nearest wave number $k = 2\pi/\sigma$. The autocorrelation exhibits exponential decay in the nematic-laning state with characteristic time $\tau_c = 0.10$ and power-law decay in the flocking state with the exponent $\alpha = 0.27$ as indicated. Inset, semi-log plot. (d) Stress-tensor autocorrelation as a function of time for $\text{Pe}=160$ and systems in the nematic-laning ($\phi = 0.4 - 0.48$) and flocking ($\phi = 0.36 - 0.38$) states. Inset, zoomed view of long-time tail.
4.8 Comparison of self-propelled rod and sphere nonequilibrium state diagrams. (a) SPR state diagram from this study as a function of the translational Peclet number. Blue dashed lines show limits of stability of the nematic-laning state characterized by ballistic transport along the lane. (b) Self-propelled sphere state diagram as a function of the rotational Peclet number, adapted from Fily, Henkes, and Marchetti (5).
Chapter 1

Introduction

Many natural phenomena exhibit external driving or internal self-propelled force. Examples include motor proteins walking along biopolymers (6) and swarms of bacteria (7). These non-equilibrium systems constantly consume and dissipate energy, which makes their dynamics and steady states different from thermal equilibrium systems. Significant differences from equilibrium systems that we study include long range boundary effects and an anomalous fluid–jamming transition. In addition to their fundamental interest in the study of active pattern formation, these phenomena play important roles in biological responses such as filament length regulation and wound healing.

To investigate how non-equilibrium driving affects pattern formation in one and two dimensions, I developed models of driven particle motion and corresponding interactions which mimic biological systems. In Chapter II, I discuss models of motor proteins walking along a microtubule that contribute to length regulation. In Chapter III, I study motion of motor proteins in anti-parallel microtubule overlaps, motivated by length regulation of overlaps in the mitotic spindle. Because of the additional filament, motors can switch to another lane, which causes a local jamming pattern in the bulk of the overlap. In Chapter IV, I discuss a two dimensional system of self-propelled rods, inspired by schools of fish and swarms of bacteria. Due to the symmetry breaking of the moving objects, a variety of novel phases appear.
1.1  Kinetic Monte Carlo simulations

In Chapter II and III, I study motor proteins walking along a microtubule (fig. 1.1), using both analytical methods and kinetic Monte Carlo (kMC) simulation methods. Here I describe the basic model and the kMC simulation approach common to both problems. In the model of motors moving on a single filament, each motor can hop forward one site if the site is empty with a probability $v \Delta t$. At each site, a motor can bind with probability $k_{on} c \Delta t$ from the bulk solution if the site is empty, or a motor can unbind probability $k_{off} \Delta t$ if the site is occupied.

In the extended model of motor motion on antiparallel overlaps (figure 1.1 right), motors can switch between the two filaments at rate $s$. Therefore, for a given motor-occupied site, the motor can switch to the corresponding site on the neighboring filament if it is empty, with probability $s \Delta t$.

1.2  Brownian dynamics simulations

In Chapter IV, we adopt a minimal model of self-propelled spherocylinders evolving under Brownian dynamics similar to that used previously (8). To simulate the Brownian motion of rods, we adopt the computational scheme of Tao et al. (9), which has been used successfully in simulations of concentrated solutions of high aspect ratio rod-shaped particles.
The center-of-mass equation of motion for rod $i$ with center-of-mass position $r_i$ and orientation $u_i$ is

$$ r_i(t + \delta t) = r_i(t) + \Gamma_i^{-1}(t) \cdot F_i(t) \delta t + \delta r_i(t), \quad (1.1) $$

where $\delta t$ is the integration timestep and the random displacement $\delta r_i(t)$ is Gaussian-distributed and anisotropic, with variance

$$ \langle \delta r_i(t) \delta r_i(t) \rangle = 2k_B T \Gamma_i^{-1}(t) \delta t. \quad (1.2) $$

Here, $k_B$ is Boltzmann’s constant, $T$ is the absolute temperature, and $F_i(t)$ is the systematic (deterministic) force on particle $i$. The inverse friction tensor is

$$ \Gamma_i^{-1}(t) = \gamma_{||}^{-1} u_i(t) u_i(t) + \gamma_{\perp}^{-1} [I - u_i(t) u_i(t)], \quad (1.3) $$

where $\gamma_{||}$ and $\gamma_{\perp}$ are the parallel and perpendicular friction coefficients of the rod.

The orientational equation of motion is

$$ u_i(t + \delta t) = u_i(t) + \frac{1}{\gamma_r} T_i(t) \times u_i(t) \delta t + \delta u_i(t), \quad (1.4) $$

where $\gamma_r$ is the rotational friction coefficient, $T_i(t)$ is the systematic torque on particle $i$, and the random reorientation $\delta u_i(t)$ is Gaussian-distributed, with variance

$$ \langle \delta u_i(t) \delta u_i(t) \rangle = 2k_B T \frac{1}{\gamma_r} [I - u_i(t) u_i(t)] \delta t. \quad (1.5) $$

For spherocylinders of length $L$ and diameter $\sigma$, the friction coefficients are (10)

$$ \gamma_{||} = \frac{2\pi \eta (L + 1)}{\ln a - 0.207 + 0.980/a - 0.133/a^2}, \quad (1.6) $$

$$ \gamma_{\perp} = \frac{4\pi \eta (L + 1)}{\ln a + 0.839 + 0.185/a + 0.233/a^2}, \quad (1.7) $$

$$ \gamma_r = \frac{\pi \eta (L + 1)^3}{\ln a - 0.662 + 0.917/a - 0.050/a^2}, \quad (1.8) $$

where $a = L/\sigma + 1$ and $\eta$ is the fluid viscosity. Note that $\gamma_{||} \approx \gamma_{\perp}/2$ for high aspect ratio rods.

The deterministic forces and torques acting on rods have two contributions: an active driving force acting along the particle axis, $F_i^{\text{drive}} = F_D u_i$, and excluded-volume interactions between
particles modeled by the WCA potential (11). The WCA pair potential is a Kihara-type interaction that depends on the minimum distance $s_{ij}$ between the two finite line segments of length $L$ that define the axes of particles $i$ and $j$,

$$u_{ij}^{\text{wca}}(s_{ij}) = \begin{cases} 
4\epsilon \left[ \left( \frac{\sigma}{s_{ij}} \right)^{12} - \left( \frac{\sigma}{s_{ij}} \right)^{6} \right] + \epsilon, & s_{ij} < 2^{1/6} \sigma \\
0, & s_{ij} \geq 2^{1/6} \sigma.
\end{cases} \tag{1.9}$$

Here, $\sigma$ is the effective rod diameter and $\epsilon$ sets the energy scale of the potential. Note that $s_{ij}$ is an implicit function of the center of mass positions and orientations of the two interacting rods, $s_{ij}(u_i, u_j, r_{ij})$, where $r_{ij} = r_j - r_i$. In this study we set $\epsilon/(k_BT) = 1$. For this value of $\epsilon$, the typical distance of closest approach between rods is comparable to $\sigma$, and the thermodynamic properties in the absence of driving closely resemble those of hard rods with aspect ratio $L/\sigma$, a model that is well-characterized both in 2D (12) and 3D (13, 14).

Because the Brownian dynamics scheme involves random particle displacements and rotations, close contacts between rods that produce very large forces and torques occasionally occur, leading to instabilities in the dynamics. Such instabilities are avoided by softening the WCA potential at short distances to keep the resulting forces and torques within reasonable bounds (9). At the same time, we adjust the integration timestep to ensure that pairs of interacting particles probe the softened region of the potential infrequently, so that excluded volume effects are properly accounted for.

We nondimensionalize using the rod diameter $\sigma$ and characteristic thermal energy $k_BT$ as the units of length and energy. The unit of time is chosen to be the diffusive time scale $\tau = \sigma^2/D$, where $D$ is the diffusion coefficient of a sphere of diameter $\sigma$, $D = k_BT/(3\pi \eta \sigma)$. The system is then characterized by three dimensionless parameters: (1) the packing fraction $\phi = Na_{\text{rod}}/A_{\text{system}}$, where $N$ is the number of rods, $a_{\text{rod}} = L\sigma + \pi \sigma^2/4$ is the rod area, and $A_{\text{system}}$ is the system area; (2) the rod aspect ratio $R = L/\sigma$; and (3) the Peclet number $\text{Pe} = FDL/(k_BT)$. We studied aspect ratio 40 rods and varied the other two parameters over a wide range to determine the dynamic state behavior of the system: $\phi$ was varied between 0.01 and 1.04, and $\text{Pe}$ between 0 and 320. All
of the simulated systems described here consisted of \( N = 4000 \) rods in a square, periodic box, and the typical duration of simulations was \( 10^7 \tau \). The simulation time step was \( \Delta t = 0.25\tau \).
Chapter 2

Filament length regulation by molecular motors (1)

2.1 Introduction

A fundamental question in biology is how organisms control the size of subcellular structures, cells, organs, and whole organisms. The physical principles underlying the sensing and control of size in biology are not well understood; indeed, whether there are general principles or mechanisms in size control is unclear (15–17). In particular, the regulation of polymer length is important for the organization of the cellular cytoskeleton. Regulation of cytoskeletal filaments affects both the size of subcellular organelles such as the mitotic spindle (18, 19) and the structure of cells themselves (20, 21). This paper focuses on the regulation of microtubule length. Microtubules are an important cytoskeletal filament that contribute to cell structure, affect the distribution of other cytoskeletal filaments, move chromosomes during cell division, and serve as tracks for transport within the cell.

Microtubules undergo complex, nonequilibrium polymerization dynamics, known as dynamic instability, characterized by stochastic switching between distinct growing and shrinking states. When dynamic microtubules polymerize in vitro from purified tubulin protein, dynamic instability leads to a broad distribution of polymer lengths (22). However, in cells other proteins are also present which modify microtubule dynamics, particularly at the plus ends of microtubules (23). This allows cells to control tubulin polymerization dynamics to give microtubules of regulated length. A relatively well-studied example of length regulation of microtubule-based structures is the control of flagellar length in Chlamydomonas reinhardtii, where the assembly and disassembly
of the flagellum is controlled to give a fixed flagellar length (24). However, in general it is not well understood how cells control the length of their microtubules.

Recently an example of physically-based microtubule length detection and control was proposed, based on motor proteins that walk with directional bias on a microtubule and shorten a stabilized (non-polymerizing) microtubule from its plus end (25–27). If the motors are processive (unbinding slowly from the microtubule), then a long filament can accumulate large numbers of motors at its end, and the shortening rate is high; for a short filament fewer motors reach the end, and shortening slows. This length-dependent depolymerization has been demonstrated for the kinesin-8 protein Kip3p moving on stabilized microtubules. The physical interactions of motors moving on the filament allow a physical process (the rate of depolymerization) to vary with the filament length, thereby allowing “sensing” of the length (26–28). By coupling this length-sensitive decrease in filament length with other processes (for example, a constant filament growth rate) a specific filament length or narrow filament-length distribution could in principle be achieved (26).

To understand the biological relevance of length-dependent depolymerization, it is important to make a connection between the biophysically measured effects of purified proteins on stabilized microtubules and the more complex situation in cells. Stabilized microtubules have little or no intrinsic length dynamics, while in cells microtubules undergo dynamic instability. Other proteins can also modify microtubule dynamics. Therefore, the kinesin-8 length-dependent depolymerization process will be affected by microtubule length fluctuations and the presence of other proteins at microtubule tips. In general, any biophysical mechanism of length regulation must be robust to noise in the cellular environment.

Recent work suggests that length-dependent depolymerization per se may not be occurring in cells. Kinesin-8 proteins may act to promote catastrophe (the transition from growing to shrinking) rather than direct depolymerization. Extensive experiments have demonstrated that deletions or knockdowns of kinesin-8 proteins in cells result in longer microtubules and mitotic spindles as well as an increase in chromosome loss in mitosis (25, 29–35). Other work has shown that kinesin-8 activity is associated with destabilization of microtubules and other alterations in microtubule
dynamics (25–27, 29, 34, 36–49). While the molecular mechanisms of kinesin-8 protein function are not clear, it appears that not all kinesin-8 proteins are able to depolymerize stabilized microtubules (40, 49, 50). Instead, experimental evidence (25, 39, 43, 49) and modeling work (51) suggest that in cells kinesin-8 proteins may act to promote catastrophe of dynamic microtubules. Therefore, it is necessary to understand the consequences of length-dependent changes in microtubule dynamic instability to predict the effects of these motors in cells. This addresses the general question of how length-sensing mechanisms are altered by fluctuations and dynamics in biological systems.

Previous theory and modeling work has addressed aspects of kinesin 8 behavior and length regulation. Several papers have focused on modeling the physical effects important to describe the length-dependent depolymerization of otherwise static filaments (27, 28, 52) or filaments with simplified polymerization kinetics (53–55). Previous work has not examined the effect of catastrophe-promoting motors on the length distribution of microtubules undergoing dynamic instability. Tischer et al. used a similar formalism to that in this paper in a model for how length-dependent microtubule catastrophe and rescue rates affect the density of cargo-carrying motors along microtubules, an effect that could be used to target cargo delivery to specific cellular locations (56).

In this paper, we develop a simplified physical theory to compare two scenarios for length regulation: for length regulation by depolymerization we calculate the steady-state length that is reached by a constantly growing filament balanced by depolymerizing motors, while for length regulation by altering catastrophe we consider filaments undergoing dynamic instability with alterations in the dynamics due to motors. We consider two possible mechanisms of motor action at the microtubule tip, both the minimal model in which motor effects (depolymerization or catastrophe) increase in proportion to the motor density (28, 52, 55) and the cooperative model in which motor effects (depolymerization or catastrophe) increase in proportion to the flux of motors to the filament end (27). These two models show important differences in their effects on length regulation, suggesting that cellular length regulation could be sensitive to the precise mechanism. We find consistent qualitative agreement between mean-field theory and stochastic simulation; in some parameter regimes the two approaches agree quantitatively.
Figure 2.1: Schematic of the model. Left, model of length regulation by depolymerization. Filament growth is balanced by motor-induced depolymerization. Motors bind to and unbind from the filament, move toward the filament plus end, and catalyze removal of filament subunits from the plus end. This leads to a length-dependent depolymerization rate, so a single filament length is favored, depending on the model parameters. Right, model of length regulation by altering catastrophe. The filament undergoes dynamic instability at its plus end, characterized by stochastic transitions between growing (blue) and shrinking (green) states. Motors bind to and unbind from the filament, move toward the filament plus end, and catalyze catastrophe (transition from the growing to the shrinking state) at the filament plus end. Now the catastrophe frequency is length dependent, which leads to a broad distribution of filament lengths determined by the properties of the motors.

2.2 Motor dynamics along filament

The mean-field density of the motors along the filament, \( \rho(x,t) \), in units of motors per unit length is described by (57)

\[
\frac{\partial \rho}{\partial t} = -v \frac{\partial}{\partial x} \left[ \rho \left( 1 - \frac{\rho}{\rho_{\text{max}}} \right) \right] + k_{\text{on}} c \left( 1 - \frac{\rho}{\rho_{\text{max}}} \right) - k_{\text{off}} \rho. \tag{2.1}
\]

On the right hand side, the first term describes biased motion of the motors with speed \( v \), where crowding effects reduce the motor flux (57) and \( \rho_{\text{max}} \) is the maximum possible motor density. The second term describes binding of motors to unoccupied sites at rate per unit length \( k_{\text{on}} c \). The third term describes unbinding of motors from occupied sites at rate \( k_{\text{off}} \). This formulation assumes a continuum limit in which the lattice spacing \( a \to 0 \) so that the motor density can be treated as continuous in \( x \). The bulk motor concentration \( c \) is assumed constant, i.e., the binding of motors to the filament is assumed not to deplete the pool of motors in the bulk. Note that we
do not consider protofilament interactions within a microtubule, so we are effectively considering a single protofilament microtubule (figure 2.1).

For relatively low motor density, we neglect crowding effects in the drift term, which makes the density equation linear. In addition, we work with the motor fractional occupancy \( p(x,t) = \rho(x,t)/\rho_{\text{max}} \), so the density equation can be written
\[
\frac{\partial p}{\partial t} = -v \frac{\partial p}{\partial x} + \frac{k_{\text{on}} c}{\rho_{\text{max}}} (1 - p) - k_{\text{off}} p.
\] (2.2)

With the initial condition \( p(x,t) = 0 \) at time \( t = 0 \) and the boundary condition \( p(x=0,t) = 0 \), the solution to this equation is
\[
p(x,t) = \begin{cases} p_0(1 - e^{-t/\tau}), & x \geq vt \text{ (short time)} \\ p_0(1 - e^{-x/\lambda}), & x < vt \text{ (long time)} \end{cases}
\] (2.3)

Here the steady-state occupancy away from the filament ends is \( p_0 = k_{\text{on}} c/(k_{\text{off}} \rho_{\text{max}} + k_{\text{on}} c) \), the time scale \( \tau = 1/(k_{\text{off}} + k_{\text{on}} c/\rho_{\text{max}}) \), and the length scale \( \lambda = v/(k_{\text{off}} + k_{\text{on}} c/\rho_{\text{max}}) = v\tau \). At long time, the density approaches the steady state profile which is constant away from the filament end but has a boundary layer for small \( x \) where transport effects and boundary conditions change the motor density away from \( p_0 \) (53, 57, 58).

### 2.3 Length regulation by depolymerization

Here we study the regulation of filament length assuming the motors directly depolymerize the filament, an effect which is balanced by a constant rate of filament growth (figure 2.1A). This approach neglects fluctuations due to microtubule dynamic instability, and so the resulting length is deterministically reached. We suppose that a filament grows with constant speed \( u \).

We consider two simple models for the dynamics of the end. For **density-controlled depolymerization**, the motor-induced depolymerization rate is proportional to the motor occupancy at the end (as introduced by Hough et al. (28) and also considered in refs (52, 55)). For **flux-controlled depolymerization**, the motor-induced depolymerization rate is proportional to the
motor flux to the end (as introduced by Varga et al. (27), and also considered in ref (52)). We assume that the motors move faster than the growth \((v > u)\), so the motors track the end as observed experimentally. We therefore assume that the motor occupancy away from the filament end reaches the steady-state value \(p(x) = p_0(1 - e^{-x/\lambda})\).

Dimensional analysis suggests that the filament length reached should be related the boundary layer length scale \(\lambda = v/(k_{\text{off}} + k_{\text{on}}c/\rho_{\text{max}}) = v\tau\), the obvious length scale that can be constructed from the rates in the problem. However, the steady-state filament length is quite different from \(\lambda\) and is controlled by the dynamics at the end of the filament.

This model is related to recent work that also considered the balance between depolymerizing motors and filament kinetics described by constant growth (53, 55) or treadmilling (54). The model here is simplified compared to the previous work, to allow the derivation of analytic expressions for the length achieved and to allow comparison to the results for filaments undergoing dynamic instability.

2.3.1 Density-controlled depolymerization

In the density-controlled model, we assume that the depolymerization rate is proportional to the motor density at the terminal site of the microtubule (28). We assume that only the motor occupancy at the last site of the filament is important for depolymerization, i.e., we neglect possible cooperative effects. Define \(p_e(t)\) to be the average motor occupancy at the last site on the filament, and the filament length is \(L(t)\). The mean-field density-dependent depolymerization model is:

\[
\dot{p}_e = \left(\frac{v - \dot{L}}{a}\right) p(L - a, t)(1 - p_e) - k_{\text{off}}^\text{end} p_e, \tag{2.4}
\]

\[
\dot{L} = u - wp_e. \tag{2.5}
\]

The first term on the right side of equation (2.4) represents the stepping of motors from the site adjacent to the end to the terminal site on the filament, at rate \((v - \dot{L})/a\). The density at the penultimate site on the filament is \(p(L - a, t)\), where \(a\) is the lattice spacing, assumed small. If the motor dynamics at the end are faster than the typical time scale of density changes in the bulk
Figure 2.2: Filament dynamics and steady-state filament length as a function of bulk motor concentration for length regulation by depolymerization. Blue (top), density-controlled depolymerization; red (bottom), flux-controlled depolymerization. Left, example trace of filament length versus time in the stochastic simulation for $c = 10 \text{nM}$. Middle, normalized filament length distribution in the stochastic simulation for $c = 10 \text{nM}$, averaged from 10 stochastic simulations after removal of the initial transient. Right, steady-state filament length predictions of mean-field theory and the stochastic simulation (error bars are standard deviations of steady-state length distributions). The steady-state length varies rapidly with the bulk motor concentration. The two models give similar predictions, and the approximate expressions for the steady-state length are within a factor of two of the exact expressions except for very low bulk motor concentrations. This mean-field theory uses the parameters $v = 3 \mu \text{m min}^{-1}$, $k_{\text{on}} = 2 \text{nM}^{-1} \mu \text{m}^{-1} \text{min}^{-1}$, $k_{\text{off}} = 0.25 \text{ min}^{-1}$, $k_{\text{off}}^{\text{end}} = 1.45 \text{ min}^{-1}$, $w = 1.025 \mu \text{m min}^{-1}$, $a = 8 \text{ nm}$, $\delta = 8 \text{ nm}$, and $\rho_{\text{max}} = 125 \mu \text{m}^{-1}$; for the density-controlled model $u = 1.0 \mu \text{m min}^{-1}$ while for the flux-controlled model $u = 0.5 \mu \text{m min}^{-1}$. The stochastic simulation uses the same parameters except $w = 1.5 \mu \text{m min}^{-1}$ and $k_{\text{off}}^{\text{end}} = 1 \text{ min}^{-1}$ for the density-controlled model.

of the filament, we can treat the motor density away from the end quasi-statically assuming it is unaffected by the end dynamics. Thus, we write $p(L-a, t) \approx p(L, t)$, where $p(x, t)$ is the motor occupancy for a region far from the filament end. Because the kinetics of motor removal may be different at the end of the filament, we include crowding effects at the last site even though they are neglected elsewhere along the microtubule. The second term on the right side of equation (2.4) describes unbinding of the motor at the end. In equation (2.5), the filament lengthens at constant speed $u$ and shortens at a rate proportional to the motor density at the end, with a maximum
speed \( w \).

Note that in this model the unbinding of the motor from end of the filament (controlled by the term with rate \( k_{\text{off}}^{\text{end}} p_{e} \) in equation (2.4)) is decoupled from the depolymerization rate (controlled by the term with rate \( w p_{e} \) in equation (2.5)). This means that we allow processive depolymerization, with a single motor able to remove an average of \( w/k_{\text{off}}^{\text{end}} \) monomers from the filament.

The steady-state length in the density-controlled model \( L_{\text{den}} \) is reached when \( \dot{L} = 0 \) and \( \dot{p}_{e} = 0 \), which implies \( p_{e} = u/w \) and

\[
L_{\text{den}} = -\lambda \ln \left( 1 - \frac{u a k_{\text{off}}^{\text{end}}}{p_{0} v (w - u)} \right)
\]

\[
\approx \frac{u}{k_{\text{on}} c} \left( \frac{p_{\text{max}} a k_{\text{off}}^{\text{end}}}{w - u} \right)
\]

The approximate solution in equation (2.7) applies when the second term inside the logarithm of equation (2.6) is small. Note that there is no steady-state solution if either \( w < u \) (in this case the motors can never remove dimers quickly enough to keep up with the growth) or \( u a k_{\text{off}}^{\text{end}} / (p_{0} v (w - u)) \geq 1 \). Therefore the motor occupancy must be larger than the critical value \( p_{0e} = u a k_{\text{off}}^{\text{end}} / (v (w - u)) \) for a steady-state length to occur, implying a minimum bulk motor concentration of \( c_{c} = k_{\text{off}} p_{\text{max}} a k_{\text{off}}^{\text{end}} / (k_{\text{on}} [w(u/w - 1) - a k_{\text{off}}^{\text{end}}]) \). In practice given measured motor parameters, reasonable values of the steady-state length require \( w \) quite similar to \( u \); the requirement for such fine-tuning of the depolymerization rate suggests that this length-regulation mechanism is not highly robust (figure 2.2).

We show the dependence of the steady-state length on the bulk motor concentration in figure 2.2. We use parameters similar to those found in experiments (25, 27). The results of stochastic simulation of density-controlled depolymerization agree qualitatively with the predictions of the mean-field theory (figure 2.2, details of the simulations are described in section 2.5). The best agreement occurs when the stochastic simulation uses a slightly larger motor-induced depolymerization speed \( w \) and a slightly lower motor unbinding rate from the filament end \( k_{\text{off}}^{\text{end}} \) than the mean-field theory. In this case the mean filament lengths reached in the two models are similar, but the stochastic simulation shows large fluctuations about the mean length. This is intuitively
reasonable since in this model depolymerization is controlled by the motor occupancy at the terminal site of the filament, which undergoes significant fluctuations.

2.3.2 Flux-controlled depolymerization

Varga et al. found that their experimental data for depolymerization of stabilized microtubules by Kip3p are consistent with filament depolymerization being determined by the flux of motors to the end (27). In this model, a motor would in principle remain bound to the filament end forever, unless displaced from the tip by the arrival of another motor. When unbinding, each motor is assumed to shorten the microtubule by a length \( \delta \) (where \( \delta \) could equal the lattice spacing \( a \) if each motor removes exactly one tubulin dimers, but could differ from \( a \) depending on the motor depolymerization processivity). Therefore the depolymerization speed is \( w = \delta J(L) \), where \( J(L) = p(L)\rho_{\text{max}}(v - \dot{L}) \) is the flux of motors to the end of the filament. Note that steric interactions between motors that decrease the flux are neglected here. The length of the microtubule changes in time according to

\[
\dot{L} = u - w = u - \delta \rho_{\text{max}} p(L) \left( v - \dot{L} \right)
\]

At steady state, \( \dot{L} = 0 \) and the motor occupancy is the steady-state value. Therefore \( u = \delta \rho_{\text{max}} v p(L_{ss}) \), and the steady-state length in the flux-controlled model is

\[
L_{\text{flux}} = -\lambda \ln \left[ 1 - \frac{u}{\rho_0 \delta \rho_{\text{max}}} \right] 
\approx \frac{u}{k_{\text{on}} c} \left( \frac{1}{\delta} \right).
\]

As above, the approximate solution applies when the second term inside the logarithm is small. Note that there is no steady-state solution if \( u/(v\delta \rho_0 \rho_m) \geq 1 \). This implies that the motor density must be larger than the critical value \( \rho_{0c} = u/(v\delta \rho_{\text{max}}) \) for a steady-state length to occur; this corresponds to a critical bulk motor density \( c_c = k_{\text{off}} \rho_{\text{max}} u/(k_{\text{on}} (v\delta \rho_{\text{max}} - u)) \). This requires \( v\delta \rho_{\text{max}} > u \); in practice, for parameters for the budding-yeast motor Kip3 \( v\delta \rho_{\text{max}} \) must be a few times \( u \) to get steady-state lengths of a few microns.
We show the dependence of the steady-state length on the bulk motor concentration in figure 2.2. The results of stochastic simulation of flux-controlled depolymerization agree quantitatively with the predictions of the mean-field theory for identical parameters (figure 2.2, details of the simulations are described in section 2.5). Compared to the density-controlled depolymerization model, the flux-controlled depolymerization model shows decreased fluctuations and a relatively narrow length distribution. This may occur because in this model depolymerization is controlled by the motor flux to end of the filament, which is a collective property of multiple motors.

The structures of the steady-state solutions are similar in the two models, having the approximate form (equations (2.7) and (2.10)) \( L \sim u/k_{\text{on}}c \) times a factor with units of inverse length related to how motors are removed from the end. These approximations to \( L \) make clear the strong dependence of the steady-state length on the bulk motor concentration, implying that length regulation by this mechanism requires tight regulation of the motor concentration \( c \). In the density-controlled model the motor unbinding rate from the end of the filament and the difference \( w - u \) between the maximum speed of depolymerization and the filament growth rate are important in controlling the length reached. In the flux-controlled model the steady-state length takes a simple form, depending primarily on \( u, k_{\text{on}}c, \) and \( \delta \).

In both cases, there is a minimum motor occupancy required to reach a steady-state length, as expected, because a minimum number of motors is required for depolymerization to balance polymerization. The steady-state filament length is quite different from the dimensional length scale \( \lambda \) which characterizes the motor density profile.

### 2.4 Length regulation by altering catastrophe

In cells, microtubule filaments typically don’t grow constantly as in the simple model above, but instead undergo dynamic instability, characterized by long-lived growing and shrinking regimes with transitions between these two states. Studies of Kip3p in cells (25) and \textit{in vitro} (43) and of other kinesin-8 motors (39, 49), as well as modeling work (51) suggest that in cells these proteins may act to promote catastrophe (the transition from growing to shrinking) of dynamic microtubules.
Therefore, it is necessary to understand the consequences of length-dependent changes in filament
dynamics (rather than merely shortening) to predict the effects of these motors in cells.

Here we develop a theory of motors that promote filament catastrophe in a length-dependent
manner. The number probability density \( n(L) = n_G(L) + n_S(L) \) for filaments of length \( L \)
are made up of two populations, growing (G) and shrinking (S) filaments. The total number of filaments
is \( N = \int n(L) \, dL \). In this model, we neglect pauses (neither growth nor shrinkage) exhibited by
dynamic microtubules in cells. The distributions evolve according to

\[
\frac{\partial n_G}{\partial t} = -u \frac{\partial n_G}{\partial L} - f_c n_G + f_r n_S \tag{2.11}
\]
\[
\frac{\partial n_S}{\partial t} = w \frac{\partial n_S}{\partial L} + f_c n_G - f_r n_S \tag{2.12}
\]

The terms in the first equation represent filament growth with speed \( u \), catastrophe with frequency
\( f_c \), and rescue with frequency \( f_r \). The terms in the second equation represent filament shortening
with speed \( w \), catastrophe, and rescue. At steady state, \( u \frac{\partial n_G}{\partial L} = w \frac{\partial n_S}{\partial L} \). The solution to this
equation (consistent with the boundary condition that the number of filaments drops to zero as
\( L \to \infty \)) is \( n_S = (u/w)n_G \). Then the steady-state equation for the total number of filaments
\( n = n_G + n_S \) simplifies to

\[
\frac{\partial n}{\partial L} = -\left( \frac{f_c}{u} - \frac{f_r}{w} \right) n \tag{2.13}
\]

If the catastrophe and rescue rates are spatially constant, the microtubule length distribution is
exponential, \( n(L) = n_0 \exp(-(f_c/u - f_r/w)L) \), so the distribution is a bounded exponential if
\( f_c/u > f_r/w \) and has characteristic length \( uw/(f_c w - f_r u) \).

In the case of length-dependent rates, we have the formal solution

\[
\ln n = - \int dL \left( \frac{f_c}{u} - \frac{f_r}{w} \right) \tag{2.14}
\]

Here, we assume that only the catastrophe rate \( f_c(L) \) varies with length (as observed for the
kinesin-8 motors Klp5/6 in fission yeast cells (39)), and other rates are all constant. Then

\[
n = n_0 e^{f_r L/w} \exp \left( -\frac{1}{u} \int dL \, f_c(L) \right) \tag{2.15}
\]
Figure 2.3: Dynamics of length regulation by altering catastrophe. Top, density-controlled model. Bottom, flux-controlled model. Left, example trace of filament length versus time in the stochastic simulation. Middle, catastrophe frequency as a function of filament length, comparing mean-field theory (line) and stochastic simulation (points). Right, length distribution of dynamic filaments for the model with and without motors, comparing mean-field theory and stochastic simulation. The presence of the motors leads to a significant decrease in the mean filament length. This figure uses the parameters $v = 3 \mu m \ min^{-1}$, $u = 1 \mu m \ min^{-1}$, $w = 7 \mu m \ min^{-1}$, minimum catastrophe frequency $f_c = 0.2 \ min^{-1}$, rescue frequency $f_r = 0.05 \ min^{-1}$, $a = 8 \ nm$, and $\rho_{\text{max}} = 125 \mu m^{-1}$. For the density-controlled model the parameters are $k_{\text{on}} = 1 \ nM^{-1} \mu m^{-1} \ min^{-1}$, $k_{\text{off}} = 0.25 \ min^{-1}$, $k_{\text{end-off}} = 1.5 \ min^{-1}$, bulk motor concentration $c = 2 \ nM$, and $\alpha = 0.35 \ min^{-1}$. The simulation of the density-controlled model has the same parameters except $k_{\text{off}} = 1 \min^{-1}$ and $\alpha = 0.38$. For the flux-controlled model the parameters are $k_{\text{on}} = 3 \ nM^{-1} \mu m^{-1} \ min^{-1}$, $k_{\text{off}} = 0.25 \ min^{-1}$, bulk motor concentration $c = 4 \ nM$, and $\alpha = 7 \times 10^{-3}$. The simulation of the flux-controlled model has the same parameters as the corresponding mean-field theory except $k_{\text{on}} = 1.5 \ nM^{-1} \mu m^{-1} \ min^{-1}$ and $\alpha = 2 \times 10^{-3}$.

### 2.4.1 Density-controlled catastrophe

As above, we assume that the motors move faster than the filament growth, so the motors track the end and the motor density is at steady state. In the density-controlled catastrophe model, we assume that the catastrophe frequency increases linearly with the motor occupancy at the end of the filament:

$$f = f_c + \alpha p_e.$$ (2.16)
The motor occupancy at the end is determined, as before, by equation (2.4). At steady state, this gives that the occupancy at the end of the growing filament is

\[ p_e = \frac{b(1 - e^{-L/\lambda})}{k_{\text{end}}^{\text{off}} + b(1 - e^{-L/\lambda})}, \]

(2.17)

with \( b = (v - u)p_0/a \). Using the integral

\[ \int_0^L dL \frac{1 - e^{-L/\lambda}}{k_{\text{end}}^{\text{off}} + b(1 - e^{-L/\lambda})} = \frac{L}{k_{\text{end}}^{\text{off}} + b} \ln \left( 1 + \frac{b}{k_{\text{end}}^{\text{off}}}(1 - e^{-L/\lambda}) \right), \]

(2.18)

the length distribution is

\[ n(L) = n_0 e^{-((f_c + \Delta f)/u - f_r/w) L} \left( 1 + \frac{(v - u)p_0}{ak_{\text{end}}^{\text{off}}} (1 - e^{-L/\lambda}) \right) \left( \frac{\alpha k_{\text{end}}^{\text{off}}}{u(k_{\text{end}}^{\text{off}} + (v - u)p_0/a)} \right), \]

(2.19)

where \( \Delta f_{\text{den}} = \alpha(v - u)p_0/(ak_{\text{end}}^{\text{off}} + (v - u)p_0) \) is the maximum possible increase in the catastrophe frequency in the density-controlled model. We see two effects due to motors: first, there is an effective increase in the catastrophe rate of \( \Delta f_{\text{den}} \). Second, there is an additional multiplicative factor in the length distribution. This factor approaches one in the limit of short filaments \( (L \ll \lambda) \) and for typical experimental parameters varies slowly with \( L \).

Note that in this model the unbinding of the motor from end of the filament is controlled by the rate constant \( k_{\text{end}}^{\text{off}} \). This means that a motor can processively track the end of a depolymerizing filament, and this processivity tends to increase motor concentration at the end of the filament and therefore enhance the filament-shortening effects of motors.

### 2.4.2 Flux-controlled catastrophe

In the flux-controlled catastrophe model, we assume that the catastrophe frequency increases linearly with the flux of motors to the end:

\[ f = f_c + \alpha J. \]

(2.20)

The flux to the end of the microtubule is \( J = p(L)\rho_{\text{max}}(v - u) \). Note that steric interactions between motors that decrease the flux are neglected here. The length distribution is then

\[ n = n_0 e^{-(f_c/u + \Delta f/\rho_{\text{max}}(v - u)/w) L} \exp \left( \frac{\alpha(v - u)\rho_{\text{max}} p_0 \lambda}{u} (1 - e^{-L/\lambda}) \right), \]

(2.21)
where $\Delta f_{\text{flux}} = \alpha (v - u) \rho_{\text{max}} p_0$ is the maximum possible increase in the catastrophe frequency in the flux-controlled model. Again, we see two effects from the length-dependent catastrophe: there is an effective increase in the catastrophe rate of $\Delta f_{\text{flux}}$, and there is an additional multiplicative factor in the length distribution which is an exponential of an exponential of the length. This factor approaches 1 in the limit of short microtubules ($L \ll \lambda$) and approaches the constant factor $\exp \left( \frac{\alpha (v - u) \rho_{\text{max}} p_0}{u} \lambda \right)$ as $L \to \infty$; for typical experimental parameters this factor is of order 1.

We show simulations of filament length as a function of time, calculations of the variation of catastrophe frequency with filament length and filament length distributions in figure 2.3. We chose parameters from experiments on the increase in catastrophe frequency associated with the kinesin-8 motor Klp5/6 in fission yeast (39), which found a catastrophe frequency $f_c = 0.2 \ \text{min}^{-1}$ in cells lacking kinesin-8 motors and a length-dependent increase in the catastrophe frequency up to a maximum of $0.5 \ \text{min}^{-1}$ for filaments 8 $\mu$m long in cells containing motors. With the correct choice of parameters, the length-dependent increase in catastrophe frequency due to motors is qualitatively similar to that measured by Tischer et al. (39).

The results of stochastic simulation are shown for comparison with mean-field theory. For density-controlled catastrophe, there is excellent agreement between stochastic simulation results and mean-field theory if the parameters $k_{\text{end off}}$ and $\alpha$ are slightly modified. The flux-controlled catastrophe model predictions of the dependence of catastrophe frequency on filament length show only rough qualitative agreement with mean-field theory; the shapes of the curves are quite different. Even this level of agreement requires modification of the parameters $k_{\text{on}}$ and $\alpha$.

### 2.4.3 Mean filament length

The length-dependent catastrophe induced by motors changes the microtubule length distribution in two ways: the effective catastrophe frequency increases, and the length distribution is multiplied by an additional function. When the additional change in the functional form due to this multiplication can be neglected, including only the effective increase in the catastrophe frequency gives a simple result for the change in mean filament length. The approximate length distribution
Figure 2.4: Mean filament length and changes in filament length as a function of motor parameters. Left, variation as a function of bulk motor concentration. Center, variation as a function of motor speed. Right, variation as a function of $k_{\text{end}}$ in the density-controlled model. This figure uses the same parameters as figure 2.3 except where noted in varying the bulk motor concentration and motor speed: $v = 3 \mu \text{m min}^{-1}$, $u = 1 \mu \text{m min}^{-1}$, $w = 7 \mu \text{m min}^{-1}$, minimum catastrophe frequency $f_c = 0.2 \text{ min}^{-1}$, rescue frequency $f_r = 0.05 \text{ min}^{-1}$, $a = 8 \text{ nm}$, and $\rho_{\text{max}} = 125 \mu \text{m}^{-1}$. For the density-controlled model the parameters are $k_{\text{on}} = 1 \text{ nM}^{-1} \mu \text{m}^{-1} \text{ min}^{-1}$, $k_{\text{off}} = 0.25 \text{ min}^{-1}$, $k_{\text{end}} = 1.5 \text{ min}^{-1}$, $\mu \text{m}^{-1}$, bulk motor concentration $c = 2 \text{ nM}$, and $\alpha = 0.35 \text{ min}^{-1}$. The simulation of the density-controlled model has the same parameters except $k_{\text{end}} = 1 \text{ min}^{-1}$ and $\alpha = 0.38$. For the flux-controlled mean-field model the parameters are the same as for the density-controlled mean-field model except $k_{\text{on}} = 3 \text{ nM}^{-1} \mu \text{m}^{-1} \text{ min}^{-1}$ and $\alpha = 7 \times 10^{-3}$. The simulation of the flux-controlled model has the same parameters as the corresponding mean-field theory except $k_{\text{on}} = 1.5 \text{ nM}^{-1} \mu \text{m}^{-1} \text{ min}^{-1}$ and $\alpha = 2 \times 10^{-3}$.

The mean length is

$$n(L) = n_0 e^{-\left[(f_c + \Delta f)/u - f_r/w\right]L}.$$  \hspace{1cm} (2.22)

We define $\bar{L}_0 = uw/(f_cw - f_ru)$, the mean filament length in the absence of motors, and the mean length including motor effects is $\bar{L} = \bar{L}_0 - \Delta L$. The mean length is

$$\bar{L} = \bar{L}_0 \left( \frac{f_c - \frac{u}{w} f_r}{f_c - \frac{u}{w} f_r + \Delta f} \right)$$  \hspace{1cm} (2.23)

The fractional change in the mean length is

$$\frac{\Delta L}{\bar{L}_0} = \frac{\Delta f}{f_c - \frac{u}{w} f_r + \Delta f}$$  \hspace{1cm} (2.24)
This expression is an approximation that typically overestimates the change in filament length due to motors, but has the advantage that it has a simple analytical form that can be used to understand which parameters control the mean length. The mean filament length is related to the maximum increase in catastrophe frequency that can be achieved by the motors. In the density-controlled model $\Delta f_{\text{den}} = \alpha (v-u)p_0/(ak_{\text{off}} + (v-u)p_0)$, and in the flux-controlled model $\Delta f_{\text{flux}} = \alpha (v-u)p_{\text{max}}p_0$.

The change in the mean filament length varies with the bulk motor concentration (through the occupancy $p_0$), the difference between the filament growth speed and the motor walking speed, and the motor unbinding rate from the filament end in the density-controlled model (figure 2.4). This suggests that in cells length regulation could be tuned by altering motor concentration, motor/filament velocity, or motor off rate at the end of the filament in the density-controlled model. For typical experimental parameters, the fractional change in mean filament length varies from 0.1 to 0.9 with changes in these parameters. While changes in bulk motor concentration can alter the mean filament length, relatively large changes in the concentration (over two orders of magnitude) lead to only modest changes in mean filament length. We find that in comparison to stochastic simulation the approximate expressions calculated above tend to overstate the changes in mean filament length achievable through bulk motor density changes. Particularly for the flux-controlled model, mean filament length is more sensitive to alterations in motor speed. Varying motor speed over a factor of 4 allows approximately factor of 10 change in the mean filament length. Comparison to stochastic simulations shows that mean filament length changes due to variation in motor speed are accurately captured by the approximate model.

In the density-controlled model, the rate constant $k_{\text{off}}$ controls the residence time of a motor at the end of a filament. In the limit that this rate becomes large compared to other rates in the problem, the motors rapidly unbind upon reaching the filament end and the changes in filament length due to motors become smaller.

The increase in catastrophe due to motors can shift the filament length distribution from the unbounded growth regime to the bounded growth regime. If $f_r/w > f_c/u$, the filament dynamics
are in the unbounded growth regime, with no defined mean filament length. If the increase in catastrophe due to motors $\Delta f$ is large enough, the presence of motors can shift the distribution back to the bounded growth regime characterized by an exponential length distribution and a well-defined mean filament length. This requires that $\Delta f > f_{ru}/w - f_c$. This relationship implies a minimum motor concentration to shift from the unbounded to bounded growth regime.

2.5 Stochastic simulation

We developed a kinetic Monte Carlo simulation of the model as shown in figure 2.1. The model considers a single filament (equivalent to representing a microtubule by a single protofilament) made up of a varying number of monomers. Each motor occupies a single filament monomer. Typical time scales of motor and filament processes are of order seconds to minutes, so we chose a simulation time step of 0.01 s. At each time step a number of monomers equal to the total number of monomers currently in the filament is randomly sampled and one step of the polymerization dynamics at the end of the filament is performed. Each site on the filament except the last site has the same rules: a motor can bind to an empty site, if the next site forward is empty a motor can step forward, and a motor can unbind to create an empty site.

The behavior of the last site (the end of the filament) varies depending on the model considered. In the model of length regulation by depolymerization (figure 2.1A), the filament can grow by addition of a monomer. Growth is independent of motor occupancy at the last site. The filament can shrink by one monomer depending on the motor occupancy at the end of the filament. In the density-controlled depolymerization model, removal of the terminal monomer can occur if the terminal site is occupied by a motor. In this model the motor can processively track the depolymerizing filament: if the penultimate site is empty, the motor at the last site steps backward when the terminal monomer is removed. If the second-to-last site is occupied, the motor on the terminal site is removed when the terminal monomer is removed. The motor at the terminal site can also directly unbind from the filament without removal of a monomer. In the flux-controlled depolymerization model, removal of the terminal monomer occurs when the last and penultimate
sites are both occupied by motors and the motor at the penultimate site attempts a forward step. In this case the terminal motor and monomer are both removed.

In the model of length regulation by catastrophe (figure 2.1B), the filament stochastically switches between growing and shrinking states. Speeds of growth and shrinkage as well as the rescue frequency are independent of motor occupancy at the last site. The catastrophe frequency is increased depending on the motor occupancy at the end of the filament. In the density-controlled catastrophe model, the catastrophe frequency is increased by $\alpha$ if the terminal site is occupied by a motor. In this model the motor can processively track the depolymerizing filament: if the filament is shortening and the penultimate site is empty, the motor at the last site steps backward when the terminal monomer is removed. If the second-to-last site is occupied, the motor on the terminal site is removed when the terminal monomer is removed. The motor at the terminal site can also directly unbind from the filament without removal of a monomer. In the flux-controlled catastrophe model, the increase in the catastrophe frequency by $\alpha$ occurs when the last and penultimate sites are both occupied by motors and the motor at the penultimate site attempts a forward step. In this case the terminal motor is removed independent of whether or not a catastrophe occurs.

In all versions of the model, if the filament fully depolymerizes (0 sites remain) a new filament is nucleated containing 1 site. For each parameter set we performed 5-10 simulations of $10^6 - 10^8$ time steps.

2.6 Conclusion

We have considered an example of biophysical length regulation by motors that walk along a filament and promote filament shortening, inspired by experiments on the effects of kinesin-8 motor proteins on microtubule dynamics. The motors bind to microtubules and move toward their plus ends, and the presence of motors at the filament end alters microtubule polymerization dynamics.

The first mechanism we considered is a simplified model of length regulation, in which the motors directly catalyze depolymerization of the filament from its plus end. When the action of the motors is balanced by a constant filament polymerization rate, a steady-state filament length
can be reached. This mechanism neglects any fluctuating filament dynamics: only a single steady-state length is reached. In the stochastic simulation, fluctuations due to stochastic motor/filament dynamics lead to a spread about the mean length but the distribution of filament lengths remains strongly peaked. There is a minimum bulk motor concentration on the filament to reach a steady-state length, because if there are too few motors, motor-induced depolymerization can never be fast enough to balance the intrinsic polymerization. In addition, inequalities involving the motor motion constrain the parameter regime where steady-state solutions are possible. The steady-state filament length differs from the length scale $\lambda$ which characterizes the motor density profile. The steady-state filament length depends sensitively on the bulk motor concentration, implying that this mechanism of length regulation requires tight control of total motor number to operate successfully.

Other recent theory work has addressed length regulation due to depolymerizing motors and filament kinetics described by constant growth (53, 55) or treadmilling (54). Govindan et al. considered a similar model for motor motion, but used an absorbing boundary condition for motors at the filament plus end, an approximation that doesn’t apply to filaments with biologically realistic growth and shrinkage rates. Their work found an exponential filament length distribution for typical parameter values corresponding to Kip3 (53). Melbinger et al. improved the model of Govindan et al. by studying in detail how effects of motor crowding near the microtubule end control the depolymerization dynamics. They discovered a parameter regime in which filament length is well regulated, and how the length depends on motor kinetics (55). Johann et al. considered the related problem of how length regulation can be achieved by depolymerizing motors on filaments that undergo treadmilling dynamics (addition of subunits at one end and removal at the other) (54).

In the model of length regulation by depolymerization we have discussed, constant growth is balanced by length-dependent depolymerization. In the balance-point model of flagellar length regulation in *Chlamydomonas*, a constant rate of flagellar disassembly is balanced by a length-dependent rate of flagellar assembly, leading to a fixed flagellar length (24, 59). While the underlying microscopic mechanisms of flagellar length regulation differ from those discussed here, the conceptual
similarity is striking. Perhaps this basic idea of regulating length by making assembly or disassembly length-dependent while the other process (disassembly or assembly) is length independent could be a general paradigm for length regulation, at least of microtubule-based structures.

A more biologically relevant model for the length regulation of dynamic microtubules is length regulation by altering catastrophe, in which the filament undergoes dynamic instability characterized by long-lived growing and shrinking states with transitions between growth and shrinkage. The effect of the motors at the end is then not to directly depolymerize the filament but to increase the catastrophe frequency (the frequency of transitions from growing to shrinking). We calculate how the filament length distribution is altered by the motor-dependent increase in catastrophe frequency, and derive a simple approximate expression that relates the mean filament length to the maximum increase in catastrophe frequency that can be achieved by the motors. The mean filament length varies modestly with bulk motor concentration but is sensitive to the difference between the filament growth speed and the motor walking speed.

The increase in catastrophe frequency associated with the kinesin-8 motor Klp5/6 in fission yeast cells was measured by Tischer et al. (39), who found a catastrophe frequency $f_c = 0.2 \text{ min}^{-1}$ in cells lacking Klp5/6 and a length-dependent increase in the catastrophe frequency up to a maximum of $0.5 \text{ min}^{-1}$ for filaments $8 \mu m$ long in cells containing motors. With the correct choice of parameters, our model displays a length-dependent increase in catastrophe frequency due to motors which is qualitatively similar to that measured by Tischer et al. Using these parameters in our model, changes in the mean length of a factor of 2 can be achieved by this mechanism.
Chapter 3

Motor protein accumulation on anti-parallel microtubule overlaps (2, 3)

3.1 Introduction

Motor protein motion along biological polymers is important in many biological processes (60). Examples include kinesin walking along microtubules and ribosomes moving along mRNA (61, 62). These filaments act as one-dimensional lanes that allow proteins to move over long distances and accumulate at the correct location for their biological function. Physical models of motor protein motion often incorporate two main features: directional motion along a filament and binding/unbinding.

The directional motion of motor proteins is a remarkable implementation of a classic model of divergent-diffusive transport, the totally asymmetric simple exclusion process (TASEP) (63, 64). In the TASEP, particles move unidirectionally along a one-dimensional lattice and experience excluded volume interactions. The TASEP and its variants have been applied to one-dimensional nonequilibrium transport problems ranging from molecular motors to vehicular and pedestrian traffic. In contrast to thermodynamic systems, the non-equilibrium steady-state solution of the TASEP is sensitive to the boundary conditions, even in the bulk of the lane (6, 63, 65, 66). The TASEP has been solved exactly by Derrida et al. (67). Three phases can occur, the low-density, high-density, and maximum current states. Kolomeisky et al. (68) analyzed the formation of the steady-state phases in the mean-field equation by analyzing the dynamics of domain walls that can appear when two phases coexist in the same lane. This work also found that the boundary conditions are not
always satisfied and there is no steady localized domain wall in the pure TASEP\(^1\).

Because binding kinetics are important for most motor proteins, biophysical models have extended the TASEP to include motor binding and unbinding (Langmuir kinetics, LK). Parmeggiani, Franosch, and Frey (PFF) developed a single-lane TASEP plus LK model and determined the mean-field solutions (57, 69). They discovered a new phase with low density-high density coexistence in this model, implying that domain wall localization can occur due to LK. Experimental work measured kinesin-8 motor protein traffic jams on stabilized microtubules, and found good agreement with the density profiles predicted by PFF (70).

TASEP-inspired models have been applied to motor proteins that move on cytoskeletal filaments and affect filament length. Motors can affect the lengths of microtubules (27), antiparallel microtubule overlaps (71), and the microtubule-based the mitotic spindle (19, 72). Kinesin-8 motors walk with directional bias and promote microtubule plus-end shortening (25–27). These experiments have inspired theory to describe how length-dependent depolymerization affects otherwise static microtubules (27, 28, 52), microtubules with simplified polymerization kinetics, (53–55, 73), and dynamic microtubules (1, 56, 74).

The bipolar structure of the mitotic spindle leads to overlapping antiparallel microtubules at the center of the spindle. Control of microtubule overlaps is therefore important for mitosis and cytokinesis. Microtubule crosslinking (by PRC1/Ase1/MAP65) and motion of kinesin-4 motors (chromokinesins) stabilize microtubule antiparallel overlaps (75–77), along with other motors and proteins (78, 79). Bieling, Telley, and Surrey (BTS) reconstituted a minimal system of stable antiparallel MT overlaps in which the crosslinking protein PRC1 bound preferentially to overlapping regions of antiparallel MTs (71). PRC1 recruited the kinesin-4 motor Xklp1 to the overlap. Xklp1 motors could bind to and unbind from the MTs, walk toward the plus end of each MT, and switch between the two MTs at a relatively high rate (71). Motors present near the MT plus ends slowed the polymerization speed, consistent with earlier work showing that Xklp1 inhibits dynamic

\(^1\) More precisely, there is a possibility for a localized domain wall to appear when the inward current and outward currents are equal. However, the domain wall can appear at any point. Thus, the average density profile becomes a line instead of the high density-low density coexistence phase.
instability (80) and affects spindle MT mass (81). As a result, antiparallel MT overlaps reached a constant length that depended on the bulk concentration of motors. This work demonstrated that motor-dependent regulation of dynamics and length can occur not just for single MTs, but for overlapping MT pairs.

Recently we developed a model inspired by the BTS experiments in which we studied antiparallel lanes with TASEP, LK, and lane switching for fixed-length lanes (2). Our work is related to previous generalizations of the TASEP to multiple lanes and coupling between lanes. Multi-lane systems with two or more species have been studied (82, 82–87). Reichenbach et al. (88) studied parallel and Juhász (89) anti-parallel lanes without LK; both derived analytic solutions. In these models, even though LK is absent, domain wall localization can occur due to switching events which balance the flux (in the work of PFF, this is called the matching condition (57)). Multi-lane models that included LK were studied by Gupta and Dhiman (84) (parallel lanes), and Levine and Willmann (85) (antiparallel lanes). This work found that multiple phases appear and that analytic solutions can be derived in some limites. Other related work includes that of Chai et al. (86), who studied multiple species on one lane with some non-moving species, and Nowak et al. (58), who studied fluctuating boundary conditions. Pierobon et al. (90) considered the case in which the lane has a defect, which makes a singular point in the density profile, causing new bottleneck phases to appear.

First of all, we compared steady-state density profiles of our model to those determined experimentally (2), and discussed how the appearance of a localized domain wall can be understood a using total binding constraint. Then, we extend our the work by analyzing the density-density phase plane to solve the steady-state mean-field equations and determine the phase boundaries. Analyzing the model’s phase-space flows and fixed points, as well as their changes with parameters, allows us to calculate the phase diagram. Some previous work has discussed fixed-points of TASEP models (57, 85). Yadav et al. used phase-plane analysis of a fixed-point-based boundary layer method to study multi-lane TASEP models (91). Here we undertake a detailed study of the model’s phase-space flows and fixed points and along with an analytic phase-plane solution. This allows us
both to develop intuition and calculate the mean-field phase diagram with minimal assumptions. We explain why high motor switching rate between the two lanes leads to a new low density-high density-low density-high density coexistence phase, for which multiple domain walls occur in the bulk of the system. We also extend our previous work, which only considered symmetric boundary conditions (2), to the case of asymmetric boundary conditions.

In sec. 3.2, we describe the discrete model and derive the mean-field approximation. Using the random phase approximation and Taylor expansion, we derive the steady-state mean-field differential equations. Then in sec. 3.3, we develop a method to derive key features of the density profiles using phase-space flows. This is a different approach from determining the position-dependent density profiles that was done in previous work (57, 82–85, 85, 86, 88). In sec. 3.4, we determine the nonlinear phases of the model with symmetric boundary conditions. We also derive an analytic approximation to the position-dependent solution and two ways to determine domain wall positions and phase boundaries. In sec. 3.5, we determine the phase diagram for symmetric boundary conditions, and in sec. 3.6 discuss the general case of asymmetric boundary conditions. Sec. 3.7 is the conclusion.

3.2 Model

Our model of motor motion on antiparallel lanes (2) is based on the BTS experiments (71). Motors move toward lane plus ends, bind to and unbind from each lane, and switch between lanes (fig. 3.1). We study lanes with fixed number of sites $N$. At each site, motor binding occurs with binding rate $k_{\text{on}}c$, where $k_{\text{on}}$ is the binding rate constant per site and $c$ the bulk motor concentration, and motor unbinding occurs with rate $k_{\text{off}}$. Each bound motor steps at rate $v$ to the next site toward the MT plus end (if the next site is unoccupied), and switches at rate $s$ to the site on the adjacent MT (if that site is unoccupied). Nontrivial competition between the motor stepping (TASEP) and Langmuir kinetics occurs when the overall binding rate to one filament in the overlap $K_{\text{on}}c = Nk_{\text{on}}c$ and unbinding rate $K_{\text{off}} = Nk_{\text{off}}$ are of similar magnitude to the motor speed $v$ (57).

The discrete model is based on the occupation number $\hat{n}_i$, which is 1 (0) if site $i$ is occupied
Figure 3.1: Schematic of the antiparallel two-lane TASEP with Langmuir kinetics and lane switching. Two lanes (green and blue) have their plus ends (indicating the direction of motor motion) oppositely oriented. The blue lane (R) has plus end to the right; the green lane (L) has plus end to the left. Motors (red) bind to empty lattice sites with rate $k_{\text{on}}$ and unbind with rate $k_{\text{off}}$. Bound motors step toward the lane plus end with rate $v$ (if the adjacent site toward the plus end is empty) or switch to the other filament with rate $s$ (if the corresponding site on the adjacent filament is empty). At minus ends, motors are inserted at rate $\alpha_{R,L}v$. At plus ends, motors are removed at rate $\beta_{R,L}v$.

(1) For bulk sites ($2 < i < N - 1$) on lanes with plus end (corresponding to the direction of motor motion) to the right ($R$) and left ($L$), the equations are

$$\frac{d\hat{n}_{R,i}(t)}{dt} = v\hat{n}_{R,i-1}(t)[1 - \hat{n}_{R,i}(t)] - v\hat{n}_{R,i}(t)[1 - \hat{n}_{R,i+1}(t)] + k_{\text{on}}c[1 - \hat{n}_{R,i}(t)] - k_{\text{off}}\hat{n}_{R,i}(t) - s\hat{n}_{R,i}(t)[1 - \hat{n}_{L,i}(t)] + s\hat{n}_{L,i}(t)[1 - \hat{n}_{R,i}(t)], \quad (3.1)$$

$$\frac{d\hat{n}_{L,i}(t)}{dt} = v\hat{n}_{L,i+1}(t)[1 - \hat{n}_{L,i}(t)] - v\hat{n}_{L,i}(t)[1 - \hat{n}_{L,i-1}(t)] + k_{\text{on}}c[1 - \hat{n}_{L,i}(t)] - k_{\text{off}}\hat{n}_{L,i}(t) - s\hat{n}_{L,i}(t)[1 - \hat{n}_{R,i}(t)] + s\hat{n}_{R,i}(t)[1 - \hat{n}_{L,i}(t)]. \quad (3.2)$$

The boundary site equations include fluxes into and out of the lanes. The entering flux is $v\alpha_{R,L}[1 - \hat{n}_{1}(t)]$, and the exiting flux is $v\beta_{R,L}\hat{n}_{N}(t)$, where the $R,L$ subscript denotes either the right- or left-pointing lane. We neglect binding and switching kinetics at the boundary sites. Then we have

$$\frac{d\hat{n}_{R,1}(t)}{dt} = v\alpha_{R}[1 - \hat{n}_{R,1}(t)] - v\hat{n}_{R,1}(t)[1 - \hat{n}_{R,2}(t)], \quad (3.3)$$

$$\frac{d\hat{n}_{R,N}(t)}{dt} = v\hat{n}_{R,N-1}(t)[1 - \hat{n}_{R,N}(t)] - v\beta_{R}\hat{n}_{R,N}(t), \quad (3.4)$$

$$\frac{d\hat{n}_{L,1}(t)}{dt} = v\hat{n}_{L,2}(t)[1 - \hat{n}_{L,1}(t)] - v\beta_{L}\hat{n}_{L,1}(t), \quad (3.5)$$

$$\frac{d\hat{n}_{L,N}(t)}{dt} = v\alpha_{L}[1 - \hat{n}_{L,N}(t)] - v\hat{n}_{L,N}(t)[1 - \hat{n}_{L,N-1}(t)]. \quad (3.6)$$
These boundary conditions fix the motor densities to be $\alpha_{R,L}$ at the minus end and $1 - \beta_{R,L}$ at the plus end of each lane.

We performed kinetic Monte Carlo (kMC) simulations of the discrete model with time step $\Delta t$. We applied the following rules for an overlap with $N$ sites per lane.

1. Randomly choose a lane ($R/L$) and site $i$.

2. If the site is empty, attach a motor with probability $k_{on}c\Delta t$. If the site is occupied, detach the motor with probability $k_{off}\Delta t$.

3. If the site is occupied and the adjacent site toward the plus end is empty, move the motor forward with probability $v\Delta t$.

4. If the site is occupied and the corresponding site on the neighboring lane is empty, switch the motor to the other lane with probability $s\Delta t$.

5. Enforce the boundary conditions: site 1 on lane $R$ and site $N$ on lane $L$ are occupied with probability $\alpha_{R,L}$, while site $N$ on lane $R$ and site 1 on lane $L$ are occupied with probability $(1 - \beta_{R,L})$.

6. Repeat steps 1-5 $2N$ times total to sample all sites on both lanes.

We chose $\Delta t$ to give a characteristic time for motor binding/unbinding of about $10^5$ time steps. For the reference parameter set and a bulk motor concentration of 200 nM, we used $\Delta t = 5 \times 10^{-4}$. Approximately $4 \times 10^7$ time steps were used to reach steady state, then $2 \times 10^6$ time steps were used to collect data. To determine the average motor concentration, we averaged $10^4$ samples separated by 200 time steps. The reference parameter set was obtained from the BTS measurements (71) or estimated based on comparison of our kMC simulations to the BTS data (2). These parameter values are summarized in table 3.1.
Symbol & Parameter & Reference value & Notes \\
--- & --- & --- & --- \\
v & Motor speed & $0.5 \, \mu m \, s^{-1}$ & Measured by Bieling et al. (71); varied up to $8 \, \mu m \, s^{-1}$ to study effect of varying speed on density profiles \\
k_{on} & Binding rate constant & $2.7 \times 10^{-4} \, nM^{-1} \, s^{-1}$ & Estimated based on motor density profiles and kymographs in Kuan and Betterton (2) \\
c & Bulk motor concentration & $1$–$200$ nM & Varied by Bieling et al. (71) \\
k_{off} & Unbinding rate & $0.169 \, s^{-1}$ & Measured by Bieling et al. (71) \\
s & Switching rate & $0.44 \, s^{-1}$ & Measured by Bieling et al. (71) \\
\alpha & Motor flux constant into overlap from MT minus end & 0 & Motors bind primarily inside the overlap; see discussion in Kuan and Betterton (2). We varied $\alpha$ between 0 and 1 to determine the model phase diagram \\
\beta & Motor flux constant out of overlap from MT plus end & 0 & An upper bound on the end motor unbinding rate is $\beta = 2.7 \times 10^{-3}$; see Kuan and Betterton (2). We varied $\beta$ between 0 and 1 to determine the model phase diagram \\
$N$ & Number of sites & 1000 & We used $N = 1000$ unless otherwise specified \\

Table 3.1: Parameter values for the reference parameter set, taken from experimental measurements or estimated as noted.
3.2.1 Mean-field continuum model

We derived the mean-field continuum approximation to the model (2) as in previous work (57). We applied the stationary average \( \langle \hat{n}_i \rangle \equiv \rho_i \), the random phase approximation \( \langle \hat{n}_i \hat{n}_{i+1} \rangle = \langle \hat{n}_i \rangle \langle \hat{n}_{i+1} \rangle \), and assumed motor commutation during switching \( \langle \hat{n}_{R,i} \hat{n}_{L,i} \rangle = \langle \hat{n}_{L,i} \rangle \langle \hat{n}_{R,i} \rangle \). We then Taylor expanded to take the continuum limit and nondimensionalized by choosing the length of the overlap, \( L \), as the unit of length and \( L/v \) as the unit of time. Capital letters denote the nondimensionalized parameters (\( S = sL/v \) and so on). With \( x = 0 \) the center of the overlap, the boundary conditions become \( \rho_R(x = -\frac{1}{2}) = \alpha_R \), \( \rho_L(x = \frac{1}{2}) = \alpha_L \) and \( \rho_R(x = \frac{1}{2}) = 1 - \beta_R \), \( \rho_L(x = -\frac{1}{2}) = 1 - \beta_L \). The steady-state continuum mean-field equations are then

\[
0 = (2\rho_R - 1) \frac{\partial \rho_R}{\partial x} + K_{on} c (1 - \rho_R) - K_{off} \rho_R - S \rho_R + S \rho_L, \tag{3.7}
\]
\[
0 = (1 - 2\rho_L) \frac{\partial \rho_L}{\partial x} + K_{on} c (1 - \rho_L) - K_{off} \rho_L + S \rho_R - S \rho_L. \tag{3.8}
\]

Because the equations are first order differential equations, only one boundary condition is required for each. However, since each end of the lane has two boundary conditions, the equations are overdetermined. The nonlinearities in these equations have a similar form to those of Burgers’ equation in fluid dynamics. Burgers’ equation also becomes overdetermined in the inviscid limit in which terms with second-order derivatives are neglected, which leads to the formation of shocks or domain walls which match solutions satisfying the two different boundary conditions (57, 92, 93).

Here we denote \( x_w \) the domain wall position where the solution that obeys the left boundary condition matches the solution that obeys the right boundary condition. The matching condition at the domain wall is continuity in the flux \( j(x) = \rho(x)(1 - \rho(x)) \), which can be written \( j(x_w - \epsilon) = j(x_w + \epsilon) \), where \( \epsilon \) is infinitesimal. Since at the domain wall the density is not continuous, fulfilling the matching condition requires a density jump (57) of the form \( \rho(x_w - \epsilon) = 1 - \rho(x_w + \epsilon) \).

3.2.2 Total binding constraint, central density, and boundary layer length

These equations satisfy a total binding constraint at steady state found by summing over all sites on both lanes. In the discrete equations, the flux terms of the form \( \hat{n}_{i-1}(t)[1 - \hat{n}_i(t)] \) sum to
Figure 3.2: Total binding constraint. Points show the integral of the motor density on a single filament as described by Eqn. 3.11. The dashed line is $\rho_0$. For all simulations performed, the total binding constraint is satisfied.

zero and only the binding and boundary terms remain:

$$\sum_{i=2}^{N-1} [2k_{on}c - (k_{on}c + k_{off})(\hat{n}_{R,i} + \hat{n}_{L,i})] + v\alpha_R[1 - \hat{n}_{R,1}(t)] + v\alpha_L[1 - \hat{n}_{L,N}(t)] - v\beta_R\hat{n}_{R,N}(t) - v\beta_L\hat{n}_{L,1}(t) = 0.$$  

(3.9)

This gives a constraint on the summed motor occupancy

$$\sum_{i=1}^{N} \hat{n}_{R,i} + \hat{n}_{L,i} = 2N\rho_0 + \frac{v[\alpha_R(1 - \alpha_R) + \alpha_L(1 - \alpha_L) - \beta_R(1 - \beta_R) - \beta_L(1 - \beta_L)]}{k_{on}c + k_{off}},$$  

(3.10)

where we have defined the Langmuir density $\rho_0 = k_{on}c/(k_{on}c + k_{off})$. Therefore, at steady state an effective binding equilibrium that reflects binding, unbinding, and the lane-end boundary conditions must be reached on average for the entire system. This is related to the zero-current condition found in previous work on the two-lane antiparallel TASEP without binding kinetics (87, 89).

In the continuum mean-field model, the total binding constraint becomes

$$\int_{-\frac{1}{2}}^{\frac{1}{2}} dx \rho_R(x) + \rho_L(x) = 2\rho_0 + \frac{\alpha_R(1 - \alpha_R) - \beta_R(1 - \beta_R) + \alpha_L(1 - \alpha_L) - \beta_L(1 - \beta_L)}{K_{on}c + K_{off}}.$$  

(3.11)

Besides the total binding constraint, the overlap central density, and boundary layer length are important in biological systems. To derive the analytic form of these quantities, we assume the motor densities vary linearly near the filament ends (equations 3.34 and 3.35), and that the domain walls are infinitely thin so that we can neglect them in integrating the density. A filament can be
divided it into three regions separated by the symmetric boundary layer ends are \( \pm x_{bl} \) (fig. 3.3). The density is approximately

\[
\rho_R(x) = \begin{cases} 
(K_{on}c + S)(x + \frac{1}{2}) & -\frac{1}{2} \leq x \leq -x_{bl} \\
\rho_0 + A \cosh \lambda x + B \sinh \lambda x & -x_{bl} \leq x \leq x_{bl} \\
(K_{off} + S)(x - \frac{1}{2}) + 1 & x_{bl} \leq x \leq \frac{1}{2}
\end{cases}
\] (3.12)

The middle formula in equation 3.12 is the solution of equations 3.7 and 3.8 if we neglect the nonlinear terms, which is a good approximation since the density profile doesn’t change much with position in the central region. The constant \( \lambda \) is defined by

\[
\lambda^2 = (K_{on}c + K_{off} + 2S)(K_{on}c + K_{off})
\]

and \( \rho_0 \) is the Langmuir density. The coefficients \( A \) and \( B \) are derived by using continuity in the density at left end, \((K_{on}c + S)(\frac{1}{2} - x_{bl})\), and continuity in the flux at the right end, \(1 - ((K_{off} + S)(x_{bl} - \frac{1}{2}) + 1) = (K_{off} + S)(\frac{1}{2} - x_{bl})\). Then we find

\[
A = \frac{(\frac{1}{2} - x_{bl})(K_{on}c + K_{off} + 2S) - 2\rho_0}{2 \cosh(\lambda x_{bl})}
\] (3.13)

\[
B = \frac{(\frac{1}{2} - x_{bl})(K_{off} - K_{on}c)}{2 \sinh(\lambda x_{bl})}
\] (3.14)

For the reference parameter set that we study here, the motor speed is large compared to the other rates, making the dimensionless rates small and therefore \( \lambda x \ll 1 \). We can then approximate \( \cosh(\lambda x) \approx 1 \) and \( \sinh(\lambda x) \approx \lambda x \).

We then find the approximate form of the density profile

\[
\rho_R(x) = \begin{cases} 
(K_{on}c + S)(x + \frac{1}{2}) + \alpha & -\frac{1}{2} \leq x \leq -x_{bl} \\
\frac{x}{x_{bl}} \left(\frac{1}{2} - x_{bl}\right)(K_{off} - K_{on}c) - \alpha + \beta \right] + & x_{bl} \leq x \leq \frac{1}{2} \\
\frac{1}{2}(\frac{1}{2} - x_{bl})(K_{on}c + K_{off} + 2S) + \frac{\alpha + \beta}{2} & -x_{bl} \leq x \leq x_{bl} \\
(K_{off} + S)(x - \frac{1}{2}) + 1 - \beta & x_{bl} \leq x \leq \frac{1}{2}
\end{cases}
\] (3.15)

Plugging this approximation to the density into the total binding constraint (Eqn. 3.11), we find

\[
-
\frac{1}{8}(2x_{bl} - 1)(4 + K_{off}(6x_{bl} - 1) + K_{on}c(2x_{bl} + 1) + 8Sx_{bl}) = \rho_0,
\] (3.16)
Figure 3.3: Motor occupancy and boundary layer ends. Motor density profile $\rho_R(x)$ for rightward-moving motors. Red: kMC simulation results; blue: the linear approximation of Eqn. 3.15. The ends of the boundary layers are labeled $\pm x_{bl}$. This simulation used the reference parameter set with bulk concentration $c = 200$ nM.

or

$$x_{bl} = \frac{16(S + K_{off} - 1) \pm \sqrt{4(1 - K_{off} - S)^2 + (3K_{off} + K_{on}c + 4S)(4 - 8\rho_0 - K_{off} + K_{on}c)}}{16(3K_{off} + K_{on}c + 4S)}.$$

(3.17)

The motor density in the center of the overlap is then

$$\rho_c = \frac{(1 - 2x_{bl})(K_{on}c + K_{off} + 2S)}{4}.$$

(3.18)

This result shows that the motor density at the center of the overlap is not simply $\rho_0$, even when the overlap is long. Instead the center density depends on the motor speed and filament switching rate in addition to binding parameters. In fig. 3.3 we show the comparison of the approximate density profile and positions of the ends of the boundary layers. In fig. 3.4 we compare the analytic predictions for the boundary layer length to results from simulations.

3.3 Phase plane solution

One solution to the steady-state mean field equations (3.7) and (3.8) is the constant solution at the Langmuir density $\rho_0 = K_{on}c/(K_{on}c + K_{off})$. To study spatially varying solutions, we define
Figure 3.4: Length of boundary layer overlap ends where motors accumulate, as a fraction of the total overlap length. Left: variation with bulk motor concentration; right: variation with motor speed. Points indicate simulation results and dashed lines predictions from Eqn. 3.17.

The differences of the densities from \( \frac{1}{2} \), \( \sigma_{R,L}(x) = \rho_{R,L}(x) - \frac{1}{2} \). The equations can then be written

\[
\frac{d\sigma_R}{dx} = \frac{k}{2} - \frac{\gamma}{4\sigma_R} - \frac{S\sigma_L}{2\sigma_R},
\]

(3.19)

\[
\frac{d\sigma_L}{dx} = \frac{k}{2} + \frac{\gamma}{4\sigma_L} + \frac{S\sigma_R}{2\sigma_L},
\]

(3.20)

where we have defined the rate combinations \( k = K_{on}c + K_{off} + S \) and \( \gamma = K_{on}c - K_{off} \), and equations (3.19) and (3.20) are well defined for \( \sigma_{R,L} \neq 0 \). We have not determined \( x \)-dependent expressions for \( \sigma_R(x) \) and \( \sigma_L(x) \) by solving these equations. Instead, we determined an implicit solution by first defining the sum and difference of the densities, \( \phi(x) = \sigma_R + \sigma_L \) and \( \omega(x) = \sigma_R - \sigma_L \). The equations become

\[
\frac{d\phi}{dx} = \frac{\gamma\omega + 2S\phi\omega}{\phi^2 - \omega^2},
\]

(3.21)

\[
\frac{d\omega}{dx} = \frac{(k - S)\phi^2 - \gamma\phi - (k + S)\omega^2}{\phi^2 - \omega^2},
\]

(3.22)

which combine to give

\[
\omega \frac{d\omega}{d\phi} = \frac{(k - S)\phi^2 - \gamma\phi - (k + S)\omega^2}{\gamma + 2S\phi}.
\]

(3.23)

Defining \( \eta(\phi) = \omega^2(\phi) \), this can be rewritten

\[
\frac{1}{2} \frac{d\eta}{d\phi} = \frac{(k - S)\phi^2 - \gamma\phi - (k + S)\eta}{\gamma + 2S\phi},
\]

(3.24)
or
\[
\frac{\gamma + 2S\phi}{2} d\eta + \left[\gamma \phi - (k - S)\phi^2 + (k + S)\eta\right] d\phi = 0. \tag{3.25}
\]
This inexact ODE can be made exact through multiplication by the integrating factor \((\gamma + 2S\phi)^{k/S}\).

We then obtain the solution by direct integration,
\[
C_1 = \int d\eta \left(\frac{\gamma + 2S\phi}{2}\right) + \int d\phi \left[\gamma \phi \right] + \int d\phi \left[\gamma \phi - (k - S)\phi^2 + (k + S)\eta\right], \tag{3.26}
\]
which gives the solution
\[
\omega^2(\phi) = \frac{C}{(\gamma + 2S\phi)^{1+k/S}} + \frac{2(k + S)\gamma \phi - (k - S)(k + 2S)\phi^2 - \gamma^2}{2(k + 2S)(k + 3S)}. \tag{3.27}
\]
Here \(C_1\) and \(C\) denote integration constants. Equation (3.28) gives solutions for the density profiles in the \(\omega-\phi\) or \(\sigma_R-\sigma_L\) plane.

The integration constant \(C\) can be obtained by plugging in the boundary conditions: \(\sigma_R(x = -\frac{1}{2}) = \alpha_R - \frac{1}{2}, \sigma_R(x = \frac{1}{2}) = \frac{1}{2} - \beta_R, \sigma_L(x = -\frac{1}{2}) = \frac{1}{2} - \beta_L, \) and \(\sigma_L(x = \frac{1}{2}) = \alpha_L - \frac{1}{2}\). In much of this paper, we focus on the symmetric case for which \(\alpha_R = \alpha_L = \alpha\) and \(\beta_R = \beta_L = \beta\). Later in section 3.6 we discuss the general case when \(\alpha_R \neq \alpha_L\) and \(\beta_R \neq \beta_L\).

### 3.3.1 Position-dependent approximate solutions

In equations (3.19) and (3.20), position-dependent solutions can be derived by integrating
\[
\frac{d\sigma_R}{dx} = \frac{2k\sigma_R - \gamma - 2S\sigma_L(x)}{4\sigma_R(x)}, \quad \Rightarrow \quad dx = \frac{2k\sigma_R - \gamma - 2S\sigma_L(x)}{4\sigma_R} d\sigma_R. \tag{3.29}
\]
Since \(\sigma_L\) depends on \(x\), this equation is difficult to integrate directly. However, since equation (3.28) gives the relationship between \(\sigma_R\) and \(\sigma_L\), we can rewrite \(\sigma_L(x) = \sigma_L(\sigma_R)\). If we define \(Y_R = \sigma_R - \frac{\gamma}{2k}\), the equation (3.29) can be written
\[
dx = \frac{4}{2k} \left(\frac{Y_R + \gamma}{Y_R - \frac{\gamma}{2k}\sigma_L(Y_R)}\right) dY_R. \tag{3.30}
\]
This allows us to perform direct integration with an appropriate expansion of \(\sigma_L(Y_R)\).
3.3.2 Phase space flow and fixed points

We can determine important features of the density profiles by treating studying equations (3.19) and (3.20) in the $\sigma_R-\sigma_L$ phase plane and determining the phase space flows. In the phase plane, equations (3.19) and (3.20) define an effective velocity field that shows the local change in $\sigma_R$ and $\sigma_L$ at each point in the plane (fig. 3.5). Note that because the equations are unchanged under the operation $R \rightarrow L, x \rightarrow -x$, the phase field is symmetric under reflection about the line $\sigma_L = \sigma_R$.

The flow trajectories are controlled by the fixed points in the phase plane. There can be as many as three fixed points: the Langmuir isotherm (LI), and two transition points (TP) that appear for sufficiently high switching rate. Figure 3.5 shows the fixed points for low switching rate (left) and high switching rate (right). To determine the fixed points, we rearrange equation (3.28) to solve for the integration constant:

$$C = (\gamma + 2S\phi)^{1+k/S} \left[ \omega^2 + \frac{2(k + S)\gamma \phi - (k - S)(k + 2S)\phi^2 - \gamma^2}{(k + 2S)(k + 3S)} \right].$$  (3.31)
The transition line and points can be determined by the trajectories with $C = 0$. In this case, either the first term $(\gamma + 2S\phi)^{1+k/S}$ or the second term in square brackets is zero. If the first term is zero, we find that $\gamma + 2S(\sigma_R + \sigma_L) = 0$. This is a line with slope $-1$ in the $\sigma_R$-$\sigma_L$ plane that intercepts the line $\sigma_L = 0$ at the point $\sigma_R = (K_{\text{off}} - K_{\text{on}}c)/(2S)$. This line can also be derived by setting equation (3.21) to zero. This is equivalent to requiring that the total density $\phi = \sigma_R + \sigma_L$ be independent of $x$; in this case $\omega(\gamma + 2S\phi)/\phi^2 = 0$, leading to $\gamma + 2S(\sigma_R + \sigma_L) = 0$ as above. Physically, this means that the switching and binding terms balance. This line is called the transition line, and the transition points occur where this line crosses the $\sigma_R = 0$ and $\sigma_L = 0$ lines. Since the flow values are ill-defined at the transition points (one of $d\sigma_{R,L}/dx$ is ill-defined), they can only lie on $\sigma_{R,L} = 0$ lines.

If the second term in square brackets is zero, the solution is a hyperbola that satisfies
\[
\omega^2 - \frac{k - S}{k + 3S} \left[ \phi - \frac{\gamma(k + S)}{(k - S)(k + 2S)} \right]^2 + \frac{\gamma^2 S}{(k - S)(k + 2S)^2} = 0.
\] (3.32)
The line and hyperbola solutions are shown in figs. 3.5 and 3.6. The hyperbola intersects the transition line at the transition points.

The position of the transition line and points allows us to define two critical switching rates. When $S$ increases to the value $S_{\text{low}} = (K_{\text{off}} - K_{\text{on}}c)/2$, the transition line first intersects $(\sigma_R, \sigma_L) = (\frac{1}{2}, \frac{1}{2})$. This allows the H_n phase to appear for $S_{\text{low}} < S < S_{\text{high}}$ (as discussed below in sec. 3.5). When $S > S_{\text{high}} = K_{\text{off}} - K_{\text{on}}c$, the transition points appear. This upper critical switching rate occurs when the transition line first intersects $(\sigma_R, \sigma_L) = (\frac{1}{2}, 0)$ and $(0, \frac{1}{2})$. This allows appearance of the LHLH phase (as discussed below in sec. 3.5).

The general case in equation (3.31) is can be understood as a exponential-like term (because the term $(\gamma + 2S\phi)^{1+k/S}$ reduces to an exponential if $S \to 0$) times a hyperbola term. The hyperbola has foci and, in general, two intersections on the $\sigma_R = \sigma_L$ line. The exponential term won’t change these properties qualitatively, if it remains real. For the special value
\[
C_{L1} = \frac{\gamma S^{\gamma(k+S)^{2+k/S}}}{(k-S)(k+2S)(k+3S)^3},
\] (3.33)
Figure 3.6: Changes in trajectories and fixed points with varying switching rate. Curves with $s = 0$ s$^{-1}$, black; $s = \frac{3(k_{\text{off}} - k_{\text{on}c})}{4} \approx 0.0862$ s$^{-1}$, purple; $s = s_{\text{high}} \approx 0.1150$ s$^{-1}$, blue; $s = 0.5$ s$^{-1}$, green. The red point labels $s_{\text{low}}$. The arrow indicates how the curve with $C_{\text{LI}}$ changes as $s$ increases. The bulk motor concentration is $c = 200$ nM and motor speed is $5$ µm s$^{-1}$; other parameters are the reference values of table 3.1.

The two intersections of the curves with the $\sigma_R = \sigma_L$ line become one intersection$^2$. The intersection is the LI. At the Langmuir isotherm, the density on each lane is the Langmuir density set by binding/unbinding equilibrium. As a result, $\frac{d\sigma_R}{dx} = \frac{d\sigma_L}{dx} = 0$. We note that in the limit $S \to 0$, these curves merge with the $C = 0$ curves discussed above. In this limit, $C_{\text{LI}} = 0$.

3.3.3 Linear solution near overlap ends

Near the ends of the overlap, the variation of density becomes approximately linear. Consider the left end of the overlap near $x = -1/2$, where $\rho_R \approx 0$ and $\rho_L \approx 1$. This implies that $\sigma_R \approx -1/2$ and $\sigma_L \approx 1/2$, so $\sigma_R \approx -\sigma_L$. Then equations 3.19 and 3.20 become approximately

\begin{align*}
\frac{d\sigma_R}{dx} &= K_{\text{on}c} + S \\
\frac{d\sigma_L}{dx} &= -(K_{\text{off}} + S).
\end{align*}

\footnote{This is analogous to the standard hyperbola equation $\frac{x^2}{a^2} - \frac{y^2}{b^2} = r^2$. The curve intersects the x-axis at $(\pm ar, 0)$. These reduce to only one intersection when $r = 0$.}
Therefore, near the overlap ends the motor density varies linearly. We can achieve a better approximation to the motor density near the overlap ends by including the density dependence of the term inversely proportional to density. Then the approximate equations are

\[
\frac{d\sigma_R}{dx} = \frac{k + S}{2} - \frac{\gamma}{2\sigma_R} \tag{3.36}
\]

\[
\frac{d\sigma_L}{dx} = -\frac{k + S}{2} + \frac{\gamma}{2\sigma_L} \tag{3.37}
\]

An implicit solution for the densities as a function of \(x\) is

\[
x - x_0 = \frac{2\sigma_R(k + S) + \gamma \log(\gamma - 2(k + S)\sigma_R)}{(k + S)^2} \tag{3.38}
\]

\[
x - x_0 = -\frac{2\sigma_L(k + S) + \gamma \log(\gamma - 2(k + S)\sigma_L)}{(k + S)^2} \tag{3.39}
\]

We plot these approximate solutions on the phase plane in fig. 3.8 and superimposed on the density profiles in fig. 3.7. As expected, the approximations agree well with simulation results near the overlap ends.

### 3.3.3.1 Domain walls

In principle, the phase-plane density profile can be determined by following the local velocity field, connecting the two points on the plane that correspond to the lane end boundary conditions.
Indeed, if the boundary points both lie in the same quadrant of the plane, the solution follows the local flow. However, in many cases the boundary points lie in different quadrants. In this case, the boundary points cannot be connected without crossing the lines $\sigma_R = 0$ or $\sigma_L = 0$ where equations (3.19) or (3.20) are ill defined. Then the solution will contain a domain wall at position $x_w$ that must be satisfied the matching condition $\sigma(x_w - \epsilon) = -\sigma(x_w + \epsilon)$ (as discussed in sec. 3.2.1). In the phase plane, a domain wall therefore appears as sign change of one of the densities (fig. 3.8).

### 3.3.3.2 Finite-size constraint

The solutions are also affected by the finite-size constraint. If, for example, each lane has 1000 sites, the correct trajectory should connect the boundary points with exactly 1000 sites. The number of sites controls the effective magnitude of $dx$, and is therefore analogous to time in the flow. Thus, the faster the effective flow, the smaller the number of sites traversed in position space.

At the Langmuir isotherm, the number of sites can be infinite since this point has zero flow velocity $^3$. As the total number of sites increases, the trajectory will approach closer to the LI, because this point is the only one which can contain an infinite number of sites (fig. 3.8). The finite-size constraint can prevent the solution from exactly following the phase-space flow. As a result, the boundary conditions are not always satisfied. This is discussed further in sec. 3.4.

### 3.4 Nonequilibrium phases for symmetric boundary conditions

The nonequilibrium steady-state solution of TASEP models sensitively depends on the boundary conditions $\alpha$ and $1 - \beta$ (63). Because the flux $\rho(1 - \rho)$ is maximized for an occupancy of $\frac{1}{2}$, the phase with bulk density of $\frac{1}{2}$ is called the maximum-current phase. The high-density phase has bulk density $> \frac{1}{2}$ and the low-density phase has bulk density $< \frac{1}{2}$. In the single-lane TASEP with LK, PFF found a low density-high density coexistence phase and a Meissner phase, but no maximum current phase (57).

---

$^3$ Because the nondimensionalization depends on the motor speed, the connection between the phase-space effective velocity and the number of sites also depends on the motor speed.
Figure 3.8: Effects of domain walls and finite size on density profiles. Left, determination of domain wall positions. Red points show kMC simulation results. The boundary points are \((\sigma_R, \sigma_L) = (-\frac{1}{2}, \frac{1}{2})\) and \((\sigma_R, \sigma_L) = (\frac{1}{2}, -\frac{1}{2})\). The solution locally follows the flow, which cannot connect the boundary points without crossing the lines with \(\sigma_R = 0\) and \(\sigma_L = 0\) where the velocity is ill-defined. Crossing these lines uses the matching condition to connect to another exact solution curve, introducing a domain wall. Right, finite-size constraint. The blue points are kMC simulation results for \(N = 1000\), and the green \(N = 500\). For a larger number of sites, the dimensionless motor speed is smaller, moving the solution closer to the LI. The switching rate is \(0.44 \text{ s}^{-1}\), the bulk motor concentration \(c = 200 \text{ nM}\), the motor speed \(5 \mu\text{m s}^{-1}\), the binding rate constant \(k_{on}c = 2.7 \times 10^{-5} \text{ nM}^{-1} \text{s}^{-1}\) (left), \(2.7 \times 10^{-5} \text{ nM}^{-1} \text{s}^{-1}\) (right), the unbinding rate \(k_{off} = 0.0169 \text{ s}^{-1}\) (left), and \(= 0.169 \text{ s}^{-1}\) (right); other parameters are the reference values of table 3.1.

In our antiparallel two-lane model with binding and switching kinetics, we find the same phases that appear in the single lane case. In addition, we find a new four-phase coexistence low density-high density-low density-high density (LHLH) phase, as discussed below. In addition, the non-zero switching rate in our model that couples the two lanes means that the central density is not only attracted to the Langmuir isotherm and repelled from the maximum current lines, but also attracted by the transition line. This competition can cause either a local maximum or minimum of the density at the overlap center \((x = 0)\). If the total density \(\rho_R(x) + \rho_L(x)\) has a local maximum (minimum) at \(x = 0\), we denote it a local maximum (minimum) phase. The occurrence of local maxima/minima also occurs in the single lane case (57), though PFF didn’t treat it as separate feature of the phase since it has a less pronounced effect there than in the antiparallel lane case.
Figure 3.9: Illustration of the 4 regions of the central density. The switching rate is $0.5 \text{s}^{-1}$, the bulk motor concentration $c = 200 \text{nM}$, and the motor speed is $5 \mu\text{m s}^{-1}$; other parameters are the reference values of table 3.1.

where the overall density is the sum of the two single-lane densities.

Here we focus on the case of symmetric boundary conditions with $\alpha_R = \alpha_L = \alpha$ and $\beta_R = \beta_L = \beta$. We first discuss the stability of the boundary conditions and properties of the central density. Then, we describe each phase and how we determine the phase boundaries. We focus on the case $LI < \frac{1}{2}$. Because the system has particle-hole symmetry, the case $LI > \frac{1}{2}$ can be understood by the transformation $\rho \rightarrow 1 - \rho$. 
3.4.1 Domain wall motion

The non-equilibrium steady-state solution of the TASEP highly depends on boundary conditions $\alpha$ and $1 - \beta$ (the inward flux or outward flux). However, the boundary conditions are not always satisfied at the boundary sites (or continuously approaching at the boundary sites). The stability of the boundary density values was determined for the single-lane TASEP by Kolomeisky et al. (68), who worked out the speed at which a domain wall moves. When $\alpha$ and $\beta < \frac{1}{2}$, the domain wall velocity is $V = \frac{j_r - j_l}{\rho_r - \rho_l}$, where $j_{r,l}$ denotes the current at the right and left boundaries. If we take $\rho_l = \alpha$, $j_l = \alpha(1 - \alpha)$, $\rho_r = \beta$, and $j_r = \beta(1 - \beta)$, the domain wall velocity is $\beta - \alpha$. Therefore if $\beta > \alpha$ the domain wall moves to the right end of the system and the right boundary condition is not satisfied, while if $\beta < \alpha$ the left boundary condition is not satisfied.

A similar relation can be determined for matching a high-density region to a maximum-current region with a domain wall (68). Suppose $\alpha > \frac{1}{2}$ and $\beta < \frac{1}{2}$, but a maximum-current phase appears on the left so that $j_l$ becomes $\frac{1}{4}$. The domain wall velocity becomes $V = \frac{j_r - j_l}{\rho_r - \rho_l} = \frac{\beta(1 - \beta) - \frac{1}{4}}{1 - \beta - \frac{1}{2}} = \beta - \frac{1}{2} < 0$, which gives an unstable left boundary condition. Similar behavior occurs if $\alpha < \frac{1}{2}$ and $\beta > \frac{1}{2}$.

These relations no longer strictly hold when binding kinetics or switching between multiple lanes are added to the model. However, they are a valuable starting point to gain intuition about the stability of domain walls due to the TASEP.

3.4.2 Properties of the central density

When the boundary conditions are symmetric, the total density is symmetric about $x = 0$. Therefore, $\rho_R(0) = \rho_L(0)$ and the density in the center of the system must lie on the $\sigma_R = \sigma_L$ line. The $\sigma_R = \sigma_L$ line can be separated into four regions, which correspond to four different possible behaviors of the central density (fig. 3.5 and 3.9).

Region I occurs where $\sigma_R = \sigma_L$ and the density is less than the Langmuir isotherm. In this region, the flow makes the density approach the LI. At the isotherm, the rates of change of both
\( \sigma_R \) and \( \sigma_L \) are zero, and as the flow approaches the LI, these rates of change decrease. Therefore, the density remains less than or equal to the Langmuir isotherm. This makes the central density a local maximum, which we denote a local maximum phase. Region II occurs where \( \sigma_R = \sigma_L \) and the density is greater than the Langmuir isotherm, but less than 0. In this region, the flow makes the density approach the LI, decreasing the density. The density remains greater than or equal to the Langmuir isotherm. This makes the central density a local minimum, which we denote a local minimum phase.

Regions III and IV occur where \( \sigma_R = \sigma_L \) and the density is greater than 0 but less than the transition line (for region III), and greater than the transition line (for region IV). The transition line occurs where the effects of switching and binding kinetics balance. In region III, binding kinetics are more important, while in region IV, switching kinetics are more important. In both of these regions, the central density is > \( \frac{1}{2} \) on a single lane. Because the density is greater than LI, the mean-field binding and unbinding terms in equations (3.7) and (3.8) are net negative. As a result, the flux term \(-(2\rho_R - 1) \frac{\partial \rho_R}{\partial x} = \frac{\partial}{\partial x} (\rho_R(1 - \rho_R)) = (\rho_R(x_{out})(1 - \rho_R(x_{out}))) \) become negative. Therefore, the flux decreases as the density increases. Another way to see this is to note that the flux has a maximum for \( 0 \leq \rho \leq 1 \) when \( \rho = \frac{1}{2} \). For \( \rho < \frac{1}{2} \), the flux increases as density increases, while if \( \rho < \frac{1}{2} \), the flux decreases as density increases. The net effect is to cause the density to increase approaching the \( \sigma_R = \sigma_L \) line in region III. Therefore the central density has a local maximum in region III. However, in region IV, \( \sigma_R \) and \( \sigma_L \) are larger, causing the switching terms to contribute significantly to the flow. This gives a positive contribution in equations (3.7) and (3.8). Therefore, the flow changes the sign in region IV (compared with region III). The central density has a local minimum in region IV.

3.4.3 Nonequilibrium phases

Here we discuss the nonequilibrium phases that occur in our model, as illustrated in figs. 3.10, 3.11. There are 5 possible phases: low density, high density, low density-high density, low density-high density-low density-high density, and Meissner. As mentioned above, we focus on the case
Figure 3.10: Examples of the nonlinear phases for low switching rate. Upper left: trajectories in the $\sigma_R$-$\sigma_L$ plane. Upper right: trajectories in the $\phi$-$\omega$ plane, where $\phi = \sigma_R + \sigma_L$ and $\omega = \sigma_R - \sigma_L$, illustrating the local maxima and minima of the central density. Lower left: the density in lane R, $\rho_R(x)$. Lower right: the total density as a function of position. The boundary conditions are $(\alpha, 1 - \beta) = (0.05, 0.1)$, red, $(0.1, 0.95)$, purple, $(0.3, 0.4)$, grey, $(0.6, 0.4)$, yellow $(0.3, 0.95)$, green, $(0.6, 0.95)$, blue, and $(0.95, 0.99)$, cyan. The switching rate is $0.1 \text{ s}^{-1}$, the bulk motor concentration $c = 200 \text{ nM}$, and the motor speed $5 \mu \text{m s}^{-1}$; other parameters are the reference values of table 3.1.

with $LI < \frac{1}{2}$.

**Low density (L):** The density in each lane remains $< \frac{1}{2}$. The L phase occurs when $\alpha < \frac{1}{2}$ and the right boundary condition cannot be satisfied. According to the properties of the local maxima and minima derived above in sec. 3.4.2, if $\alpha < LI$, the central density is local maximum; if $\alpha > LI$, the central density is a local minimum (fig. 3.12 right).

**High density (H):** The density in each lane remains $> \frac{1}{2}$. The H phase occurs when $\alpha > \frac{1}{2}$.
Figure 3.11: Examples of the nonlinear phases for high switching rate. Upper left: trajectories in the $\sigma_R-\sigma_L$ plane. Upper right: trajectories in the $\phi-\omega$ plane, where $\phi = \sigma_R + \sigma_L$ and $\omega = \sigma_R - \sigma_L$, illustrating the local maxima and minima of the central density. Lower left: the density in lane R, $\rho_R(x)$. Lower right: the total density as a function of position. The boundary conditions are $(\alpha, 1 - \beta) = (0.05, 0.6)$, red, $(0.3, 0.9)$, green, $(0.3, 0.95)$ blue, and $(0.9, 1.0)$, cyan. The switching rate is $0.5 \text{ s}^{-1}$, the bulk motor concentration $c = 200 \text{ nM}$, and the motor speed $5 \text{ \mu m s}^{-1}$; other parameters are the reference values of table 3.1.

and $\beta < \frac{1}{2}$ so that the left boundary condition cannot be satisfied. There is a critical concentration we denote $\rho_c$ which corresponds to the density where the transition line crosses the $\sigma_R = \sigma_L$ line.

If $1 - \beta < \rho_c$, the central density is a local maximum, while if $1 - \beta > \rho_c$, the central density is a local minimum (fig. 3.12 left).

**Low density-high density coexistence (LH):** In this phase, the steady-state density on each lane has both low-density and high-density regions. A domain wall occurs where the low-
Figure 3.12: Example phase-plane trajectories of L and H phases. Left: L phases. The starting and ending points are $(\sigma_R, \sigma_L) = (-0.45, -0.4)$ and $(-0.4, -0.45)$, blue, $(-0.4, -0.45)$ and $(-0.45, -0.4)$, green, $(-0.2, -0.1)$ and $(-0.1, -0.2)$, red, and $(-0.1, -0.2)$ and $(-0.2, -0.1)$, purple. The dashed lines show that the L phase obeys the left boundary conditions, where the positions are $\sigma_R = -0.45$, blue, $\sigma_R = -0.4$, green, $\sigma_R = -0.2$, red, and $\sigma_R = -0.1$, purple. Right: H phases. The starting and ending points are $(\sigma_R, \sigma_L) = (0.3, 0.45)$ and $(0.45, 0.3)$, blue, $(0.2, 0.49)$ and $(0.49, 0.2)$, green. The dashed lines show that the H phase obeys the right boundary conditions, where the positions are $\sigma_L = 0.45$, blue, and $\sigma_L = 0.49$, green. The black dashed line $\sigma_L = \rho_c - \frac{1}{2} \approx 0.4567$, the critical density $\rho_c$ (see text) of the local minimum and local maximum phases. The switching rate is $0.1 \text{ s}^{-1}$, bulk motor concentration $c = 200 \text{ nM}$, and motor speed $5 \mu\text{m s}^{-1}$; other parameters are the reference values of table 3.1.

and high-density phases meet; we call the length of the high-density region the boundary-layer length (2). We discuss how the domain wall position is determined in more detail in sec. 3.5. The boundary layer length determines whether the overlap shows greater motor accumulation at the center or at the ends: if the boundary layer length is greater than half the overlap length, the overall density is higher at the overlap center (since we set our LI = $\frac{k_{\text{off}} c}{k_{\text{on}} c + k_{\text{off}}} < \frac{1}{2}$). We note that this condition is distinct from whether or not a local maximum or minimum occurs at the overlap centers, as discussed above. The local extremum is identified using the derivative $d(\sigma_R + \sigma_L)/dx$ at the overlap center.

**Low density-high density-low density-high density (LHLH):** For sufficiently high switching rate, a multi-phase coexistence region can appear in the LH region (fig. 3.11). To
understand why the LHLH phase occurs, note that the transition line (fig. 3.5 left) divides the phase plane into two regions. If a boundary point is above the transition line in the upper left quadrant, the flow does not reach the $\sigma_L = 0$ line, where a jump into Region II is possible (fig. 3.9) in order to complete the connection\(^4\). Thus, the only allowed domain wall involves a jump to the upper right quadrant (outside of the hyperbola) to flow, and then jump to the Region II. This is because the flow outside the hyperbola will not pass the $\sigma_R = \sigma_L$ line. These multiple jumps cause multiple domain walls to appear. We note that the LHLH phase is reminiscent of LD-BP-HD multi-phase coexistence found by Pierobon et al. (90), which arises from a point defect on a single lane.

**Meissner (M):** In the pure TASEP the maximum current phase, when the bulk density profile is independent of the boundary conditions (63); the analogous phase in the TASEP with LK is the Meissner phase (57). Neither of the boundary conditions is satisfied in this phase.

### 3.5 Phase diagram for symmetric boundary conditions

Figure 3.13 shows typical phase diagrams, showing the regions where the five phases (L, H, M, LH, and LHLH) appear as a function of the boundary conditions $\alpha$ and $1 - \beta$. These boundary motor densities define the boundary points in the phase plane (fig. 3.5). To determine the phase diagram, it is convenient to determine trajectories on the phase plane. The phase regions are the collection of all the boundary points which show the same physical behavior (fig. 3.10 and 3.11). As noted above, we study $LI < \frac{1}{2}$. The phase boundaries are determined as follows:

**Boundary between L and M phases:** The phase boundary between L and M phases occurs where $\alpha = \frac{1}{2}$, because the boundary conditions cannot be satisfied when $\alpha > \frac{1}{2}$ and $\beta > \frac{1}{2}$. The phase in which none of the boundary conditions are satisfied defines the Meissner phase (57).

**Boundaries of the LH phase:** The low density-high density coexistence phase contains a

\(^4\) The reason why we mention Region II is because: first, it is not possible to jump to Region I for the high value, because of the matching condition $\sigma(x_w - \epsilon) = -\sigma(x_w + \epsilon)$. To jump from the upper left quadrant to the lower left quadrant, $\sigma_R$ should be the same. However, the region which is above the transition line and in the upper left quadrant might have higher $\sigma_R$ value than the highest possible $\sigma_R$ value in region I. Second, if jumping to Region III and IV, the trajectory cannot be completed with the correct total number of sites.
Figure 3.13: The phase diagrams for low (left, 0.1 s\(^{-1}\)) and high (right, 0.5 s\(^{-1}\)) switching rate. The phases are L, low density, M, Meissner, H, high density, LH, low density-high density coexistence, and LHLH, low density-high density-low density-high density coexistence. The green dashed line indicates where the domain wall position \(x_w = 0\), which separates regions with a local maximum of the central density (x) or local minimum (n). The red dashed lines indicate boundaries between local maximum and minimum phases. For low switching rate, the left parts of the L and LH phases are local maximum phases, and the right are local minimum phases. The upper part in the H phase is local minimum phase. For high switching rate, the left parts of the L and LH phases are local maximum phases, and the right parts are local minimum phases. The bulk motor concentration is \(c = 200\) nM, and the motor speed 5 \(\mu m s^{-1}\); other parameters are the reference values of table 3.1.

domain wall, where the density is not continuous but the flux \(\rho(1 - \rho)\) is remains continuous (57). Across the domain wall, the matching condition \(\rho(x_w - \epsilon) = 1 - \rho(x_w + \epsilon)\) must be satisfied, which is equivalent to \(\sigma(x_w - \epsilon) = -\sigma(x_w + \epsilon)\). The boundaries of the LH phase occur when the domain wall position \(x_w\) moves outside the lane, that is, when \(|x_w| > \frac{1}{2}\).

To determine the domain wall position, we integrate the density profile back from the center \((x = 0)\) to \(x = -\frac{1}{2}\), thereby determining \(\sigma_R(x = -\frac{1}{2})\). Because system is symmetric, the central density \(\sigma_{R,L}(x = 0)\) must lie on the line \(\sigma_R = \sigma_L\) (fig. 3.5). By integrating the density to \(x = -\frac{1}{2}\), we can map the line of slope 1 to the set of points \(\sigma_R(x = -\frac{1}{2})\) (fig. 3.14, black arrows to blue solid lines). If we apply the matching condition to this set of points to jump them to positive values of \(\sigma_L\), we have found the set of points for which the domain wall occurs at \(x_w = \frac{1}{2}\) (it can be treated
Figure 3.14: Illustration of calculation of the LH phase boundary. The red line indicates the central density, which lies on the $\sigma_R = \sigma_L$ line for symmetric boundary conditions. Backward integration from this line (black arrows) to $x = -\frac{1}{2}$ gives the thick blue and green, where the blue line corresponds to $\sigma < 0$ and green line $\sigma > 0$. Applying the matching condition to $\sigma_L$ and $\sigma_R$ (green arrows) gives the dashed blue and green lines, respectively. These are the phase boundaries of the LH phase. The switching rate is $0.1 \text{ s}^{-1}$, bulk motor concentration $c = 200 \text{ nM}$, and motor speed $5 \mu\text{m s}^{-1}$; other parameters are the reference values of table 3.1.

as an L phase that extends to the right end of the lane, fig. 3.14, green arrow to blue dashed lines). This defines the phase boundary of the LH phase (fig. 3.14, blue dashed line). Using the same analysis, we draw another phase boundary of the LH phase when the domain wall position is at $x_w = -\frac{1}{2}$, which is equivalent to the boundary for which the high-density phase extends to the left end of the system (fig. 3.14, green dashed line).

In the upper right quadrant of the phase plane ($\sigma_{R,L} > 0$), the left boundary condition cannot be satisfied, so the LH phase boundaries are the horizontal lines which define the upper boundary of the M phase. If the domain wall position is greater than $\frac{1}{2}$, the right boundary condition is no longer satisfied, and vice versa for $x_w < -\frac{1}{2}$ case. Thus, the region under the lower boundary of the LH phase and $\alpha > \frac{1}{2}$ does not satisfy the right boundary condition. In addition, $\alpha > \frac{1}{2}$ means that the left boundary condition is not satisfied. Therefore, this region is the Meissner phase.

Since the phase boundaries depend on assuming that the points $\sigma_{R,L}(x = 0)$ lie on the
\( \sigma_R = \sigma_L \) line, the width of the phases and the shape of the phase boundaries depend on the number of sites in the lanes and the motor speed. The faster the speed or the lower the number of sites, the smaller the dimensionless values of \( K_{\text{on}}c, K_{\text{off}}, \) and \( S \). This leads to a smaller magnitude of the phase plane flow velocity. Since the integration of the densities from \( x = 0 \) to \( x = -\frac{1}{2} \) is inversely proportional to the flow velocity \( \frac{\partial \sigma_{R,L}}{\partial x} \), decreases in motor speed make the phase boundary lines closer to the line \( \sigma_R = \sigma_L \). However, the line dividing the L and LH phases always passes through the Langmuir isotherm \( \sigma_R = \rho_0 - \frac{1}{2}, \sigma_L = -\rho_0 + \frac{1}{2} \), since the phase plane flow velocity is zero at the Langmuir isotherm. Similarly, slower motor speed or higher number of sites in the overlap makes the set of points obtained by integrating backward move closer to the trajectory line that passes through the Langmuir isotherm (fig. 3.15) \(^5\).

Once the domain wall position decreases to \( x_w < 0 \), the longer length of the high-density region makes the overall central density greater than the end density. This determines whether the center of the lanes has a local maximum or local minimum; these two cases are distinguished by the thick dashed line in the phase diagram (fig. 3.13 left). If \( x_w = 0 \), then the central density must lie on the line \( \sigma_R = -\sigma_L \), because then by the matching condition the density can jump to the line \( \sigma_R = \sigma_L \) and then jump to \( \sigma_R = -\sigma_L \). Therefore, the set of starting points that correspond to domain wall positions with \( x_w = 0 \) is calculated by integrating backwards from the \( \sigma_R = -\sigma_L \) line to determine \( \sigma_{R,L}(x = -\frac{1}{2}) \).

The weak dashed line in the LH phase indicates whether a local maximum or minimum occurs (fig. 3.13). If the domain wall is in region I, the central density is a local maximum, while if domain wall is in Region II, the central density is a local minimum. By integrating backwards from \( \sigma_R = \rho_0 - \frac{1}{2}, \sigma_L = -\rho_0 + \frac{1}{2} \), (the point at which the domain wall position overlaps with the Langmuir isotherm), we can determine the dividing line between the local maximum/minimum regions \(^6\).

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\(^5\) A larger number of sites means a lower nondimensional motor speed. The magnitude of arrows in the phase plane represent the velocity, so slower speed requires more steps to reach the same point, making the flow trajectory closer to a lower velocity one.

\(^6\) We note that the H phase has a local maximum or minimum due to the transition line. However, there is no local maximum and minimum due to the transition line in LH phase, because the boundary of the local maximum
Boundaries of the LHLH phase: When we integrate backwards from the $\sigma_R = \sigma_L$ line, it is not possible to reach the $\sigma_R = 0$ line if the switching rate is high (fig. 3.16). The transition line then separates the set of backwards integrated points into two regions (see region III and IV in sec. 3.4.2, fig. 3.17). The LHLH phase appears in the region between $\sigma_R = 0$ and the LH phase boundary.

Boundaries of the H phase: The region in the phase diagram with high values of $1 - \beta$ (small $\beta$) above the LH phase corresponds to the high-density phase. In the H phase, the lane left-end boundary condition is not satisfied. This phase is divided into two regions in which the central density has a local maximum or local minimum, controlled by the transition line. We determine and minimum due to the transition line in the LH phase is outside of the phase boundary. In other words, this case only occurs when the domain wall position is outside of the lane.
Figure 3.16: Illustration of calculation of the LHLH phase boundary. The red line indicates the central density, which lies on the $\sigma_R = \sigma_L$ line for symmetric boundary conditions. The thick black lines are the line and hyperbola determined from the equation (3.28) with $C = 0$. The dashed black lines are trajectories determined by backward integration the from $\sigma_R = \sigma_L$ line. The blue curves show the flow directions. The switching rate is 0.5 s$^{-1}$, bulk motor concentration $c = 200$ nM, and motor speed 5 $\mu$m s$^{-1}$; other parameters are the reference values of table 3.1.

the separation between these two behaviors by determining where the set of points $\sigma_{R,L} = x = -\frac{1}{2}$ integrated backwards from the $\sigma_R = \sigma_L$ line intercept the transition line (fig. 3.18).

The method to determine the local maximum and minimum phases boundary (black dashed line).

3.5.1 Approximate phase boundaries using the total binding constraint

Phases that include domain walls mean that the density profile does not always exactly satisfy the first-order mean-field steady-state equations (3.7), (3.8), and (3.28). The density is separated into several regions (fig. 3.19). In principle, there could be multiple possible trajectories which satisfy the boundary conditions and locally satisfy the differential equations (fig. 3.19 right). Despite the possibility of multiple solutions for the same boundary conditions, our kMC simulation results typically find just one stable steady-state solution for each set of boundary conditions.

To understand this, we consider the number of equations and unknowns. We focus on a
Figure 3.17: Illustration of calculation of phase boundaries. The red line indicates the central density, which lies on the $\sigma_R = \sigma_L$ line for symmetric boundary conditions. Backward integration from this line (black arrows) to $x = -\frac{1}{2}$ gives the thick blue and green, where the blue line corresponds to $\sigma < 0$ and green line $\sigma > 0$. Applying the matching condition to $\sigma_L$ and $\sigma_R$ (blue and green arrows) gives the dashed blue and green lines, respectively. These are the phase boundaries of the LH phase. The green dashed line stops around $\sigma_R = -0.1386$ and won’t extend to $\sigma_R = 0$ line. The switching rate is $0.5 \text{ s}^{-1}$, bulk motor concentration $c = 200 \text{ nM}$, and the motor speed $5 \mu\text{m s}^{-1}$; other parameters are the reference values of table 3.1.

single lane, e.g., the R lane. From equation (3.30), we can derive the density profile starting from the left end and the left boundary condition $\alpha_R$. We integrate to the domain-wall position $x_L$; the corresponding density profile is $\rho(x_L)$. We have two unknowns ($x_L$ and $\rho(x_L)$) and one equation (3.30). Using the same argument beginning from the right end of the lane, we have two unknowns ($x_R$ and $\rho(x_R)$) and one equation (3.30). Then we can determine the density profile between $x_L$ and $x_R$ using equation (3.28) or (3.30) with boundary conditions $\rho(x_L)$ and $1 - \rho(x_R)$\footnote{Note that the boundary condition $1 - \rho(x_R)$ is due to the domain-wall matching condition.}. This adds no new variables and one equation (3.30). Thus, there are four unknown variables: $x_R$, $x_L$, $\rho(x_R)$, and $\rho(x_L)$, and three equations. We need one more equation in order to uniquely determine the density profile. As discussed above in sec. 3.3.2, this can be done numerically using the finite-size constraint. Alternatively, we can use the total binding constraint of equation (3.11), as discussed in our previous work (2). Satisfying one of these constraints automatically satisfies the other.
Figure 3.18: Illustration of calculation of phase boundaries of local maximum and minimum phases. The dashed green line is obtained from backward integration of the $\sigma_R = \sigma_L$ line to $x = -\frac{1}{2}$. The green line indicates the LH phase boundary determined by the matching condition, where the right of the line is the H phase. The red line is the transition line. Since the H phase satisfies the right boundary condition, the starting point of the density profile depends on $\sigma_L$ value. Therefore, the phase boundary of the local maximum and minimum phase is a horizontal line that intersects the green dashed line and the transition line. The local minimum phase is above the black dashed line.

The switching rate is $0.1 \text{ s}^{-1}$, bulk motor concentration $c = 200 \text{ nM}$, and motor speed is $5 \mu\text{m s}^{-1}$; other parameters are the reference values of table 3.1.

The total binding constraint is useful because it can be combined with analytic approximations to the position-dependent density profile (equation (3.30)).

Here we illustrate how to use the total binding constraint to derive analytic estimates for the LH phase boundaries for symmetric boundary conditions. Therefore the domain-wall positions are also symmetric, so $x_r = -x_{bl}$ and $x_l = x_{bl}$. If we consider the limit of large motor speed, equations (3.19) and (3.20) can be approximated by a piecewise linear form (3.15). Using the total binding constraint of equation (3.11), the integral of the density is

$$\frac{1}{8} \left[ 4 - K_{off} + K_{on}c - 4x_{bl}^2(3K_{off} + K_{on}c + 4S) + 4\alpha - 4\beta + 8x_{bl}(-1 + K_{off} + S + 2\beta) \right] = \rho_0 + \frac{\alpha(1 - \alpha) - \beta(1 - \beta)}{K_{on}c + K_{off}}. \quad (3.40)$$

The phase boundary between the LH and L phases occurs when the domain wall position is $x_{bl} = \frac{1}{2}$. 
Figure 3.19: Illustration of the density profile (left) and hypothetical phase-plane trajectories (right) in the LH phase. Right: the purple curves indicate the density profile starting from the boundary conditions, and the blue and red curves are two different hypothetical trajectories which locally obey equations (3.7), (3.8), and (3.28). The parameters are $s = 0.44 \text{ s}^{-1}$, $c = 200 \text{ nM}$, $v = 5 \mu \text{m s}^{-1}$, $k_{\text{on}} = 2.7 \times 10^{-6} \text{ nM}^{-1} \text{ s}^{-1}$, and $k_{\text{off}} = 0.00169 \text{ s}^{-1}$; other parameters are the reference values of table 3.1.

Then, equation (3.40) simplifies to

$$\frac{\alpha + \beta}{2} = \rho_0 + \frac{\alpha(1 - \alpha) - \beta(1 - \beta)}{K_{\text{on}}c + K_{\text{off}}},$$ \hspace{1cm} (3.41)

or

$$\beta = \frac{1}{4}[K_{\text{off}} + K_{\text{on}}c + 2 \pm \sqrt{(K_{\text{off}} + K_{\text{on}}c + 2)^2 + 8(K_{\text{off}} + K_{\text{on}}c)\alpha - 16\alpha(1 - \alpha) - 16(K_{\text{off}} + K_{\text{on}}c)\rho_0}].$$ \hspace{1cm} (3.42)

Similarly, the phase boundary between the LH and H phases is found by considering a piecewise-linear density profile like that above, but with a jump to high density at $x_l$. In this case, the approximate density profile is:

$$\rho_R(x) = \begin{cases} 
(K_{\text{on}}c + S)(x + \frac{1}{2}) + \alpha & -\frac{1}{2} \leq x \leq -x_{\text{bl}} \\
-x_{\text{bl}} \frac{x}{2} \left(\frac{1}{2} - x_{\text{bl}}\right)(K_{\text{off}} - K_{\text{on}}c) - \alpha + \beta & -x_{\text{bl}} \leq x \leq x_{\text{bl}} \\
-(\frac{1}{4} - \frac{x_{\text{bl}}}{2})(K_{\text{on}}c + K_{\text{off}} + 2S) + \frac{2-\alpha-\beta}{2} & x_{\text{bl}} \leq x \leq \frac{1}{2} \\
(K_{\text{off}} + S)(x - \frac{1}{2}) + 1 - \beta & x_{\text{bl}} \leq x \leq \frac{1}{2}
\end{cases}$$ \hspace{1cm} (3.43)
Figure 3.20: Comparison of determination of the L boundaries using total binding constraint with linear approximation (green curves, equations (3.15) and (3.43)) and the finite-size constraint without any approximation (blue curves). The switching rate is 0.1 s\(^{-1}\), bulk motor concentration \(c = 200\) nM, and motor speed 5 \(\mu\)m s\(^{-1}\); other parameters are the reference values of table 3.1.

As above, the phase boundary between the LH and H phases occurs when the domain wall position is \(x_{bl} = \frac{1}{2}\) (note that \(x_{bl}\) is positive in our convention), giving a relation from the total binding constraint of

\[
1 - \frac{\alpha + \beta}{2} = \rho_0 + \frac{\alpha(1 - \alpha) - \beta(1 - \beta)}{K_{on}c + K_{off}},
\]

or

\[
\beta = \frac{1}{4}[-K_{off} - K_{on}c + 2 \pm [(K_{off} + K_{on}c - 2)^2 + 16(K_{off} + K_{on}c)]^{1/2} - 8\alpha(K_{off} + K_{on}c) - 16\alpha(1 - \alpha) - 16\rho_0(K_{off} + K_{on}c)]^{1/2}.
\]

Figure 3.20 shows the result of determining the LH phase boundaries using this approximation and the total binding constraint. It agrees well with the numerically determined boundaries, particularly for small \(\alpha\).
3.6 Nonequilibrium phases for general boundary conditions

In general, the boundary conditions might not symmetric for the two lanes: \( \alpha_R \neq \alpha_L \) and \( \beta_R \neq \beta_L \). In this case, we cannot determine the density profile using the symmetry argument that the central density lies on the \( \sigma_R = \sigma_L \) line. However, we can still use the properties of the analytic solution to the mean-field steady-state equations and the phase space flow to determine properties of the solutions. The density profile locally follows the phase space flow, and is connected by a curve with the correct number of sites that link the left boundary condition \( \sigma_R(x = -\tfrac{1}{2}) = \alpha_R - \tfrac{1}{2} \), \( \sigma_L(x = -\tfrac{1}{2}) = \tfrac{1}{2} - \beta_L \) to the right boundary condition \( \sigma_R(x = \tfrac{1}{2}) = \tfrac{1}{2} - \beta_R \), \( \sigma_L(x = \tfrac{1}{2}) = \alpha_L - \tfrac{1}{2} \). The matching condition for the domain wall can be applied, if necessary. We can describe the possible behaviors based on whether or not each of the four boundary conditions if satisfied. This gives \( 2^4 = 16 \) possible cases, which can be grouped into ten classes and are illustrated in figs. 3.21 and 3.22.

The location of the boundary conditions in the phase plane determine the types of behavior that can occur. We will therefore consider which quadrant in the phase plane (upper right, upper left, lower left, lower right) contain left boundary condition \( (\alpha_R, 1 - \beta_L) \) and the right boundary condition \( (1 - \beta_R, \alpha_L) \).

**All boundary conditions satisfied:** This case is analogous to the LH phase in the symmetric phase diagram. It often occurs when the left boundary condition \( (\alpha_R, 1 - \beta_L) \) is in the upper left quadrant of the phase plane and the right boundary condition \( (1 - \beta_R, \alpha_L) \) is in the lower right quadrant. A domain wall occurs either in the upper right or lower left quadrant.

**No boundary conditions satisfied:** This case is analogous to the M phase in the symmetric phase diagram. It often occurs when the left boundary condition is in the lower right quadrant and the right boundary condition is in the upper left quadrant. The density profile is independent of the boundary conditions.

**Both lane minus-end boundary conditions satisfied:** Thus case is analogous to the L phase in the symmetric phase diagram. It often occurs when the left boundary condition and the
right boundary condition are in the lower left quadrant. The density profile follows a trajectory which obeys $\sigma_R(x = -\frac{1}{2}) = \alpha_R - \frac{1}{2}$, $\sigma_L(x = \frac{1}{2}) = \alpha_L - \frac{1}{2}$, and contains the correct number of sites (fig. 3.21A).

**Both lane plus-end boundary conditions satisfied:** This case is analogous to the H phase in the symmetric phase diagram. It often occurs when the left boundary condition and the right boundary condition are in the upper right quadrant. The density profile follows a trajectory which obeys $\sigma_R(x = \frac{1}{2}) = \frac{1}{2} - \beta_R$, $\sigma_L(x = -\frac{1}{2}) = \frac{1}{2} - \beta_L$, and contains the correct number of sites (fig. 3.21B).

**Both lane minus-end and one plus-end boundary conditions satisfied:** This case is analogous to a semi-LH phase. It can occur two ways, depending on whether lane L or R has its plus-end boundary condition satisfied. The L case often occurs when the left boundary condition is in the upper left quadrant and the right boundary condition is in the lower left quadrant. This phase occurs when the right boundary point moves from the lower right quadrant (where all boundary conditions can be satisfied) to the lower left quadrant. The domain wall of the R lane moves beyond $x_w = \frac{1}{2}$, so that the right boundary condition for the R lane is not satisfied.

The R case is symmetric with the L case. It occurs when the left boundary condition is in the lower left quadrant and the right boundary condition is in the lower right quadrant. This phase occurs when the left boundary point moves from the the upper left quadrant (where all boundary conditions can be satisfied) to the lower left quadrant. The domain wall of the L lane moves beyond $x_w = -\frac{1}{2}$, so that the left boundary condition for the L lane is not satisfied.

**Left or right boundary conditions satisfied:** This case is analogous to a semi-LH phase. First we consider when the left boundary condition is satisfied. This often occurs when both the left and right boundary conditions are in the upper left quadrant. This case can be treated as moving the right boundary condition from the lower left quadrant to the upper left quadrant. Once the right boundary condition passes the $\sigma_L = 0$ line, the flow cannot reach the right boundary condition, even with a domain wall. Therefore, the density profile is dominated by the left boundary condition only.
The case in which right boundary condition is satisfied is symmetric. This often occurs when both boundary conditions are in the lower right quadrant. This case can be treated as moving the left boundary condition from the lower left quadrant to the lower right quadrant. Once the right boundary condition passes the $\sigma_R = 0$ line, the flow cannot reach the left boundary condition, even with a domain wall. Therefore, the density profile is dominated by the right boundary condition only.

**Only one minus-end boundary condition satisfied:** This case is analogous to a semi-LH phase. The case in which right lane minus-end boundary condition $\alpha_R$ is satisfied often occurs when the left boundary condition is in the lower left quadrant and the right boundary condition is located in the upper left quadrant. This case can be treated as moving the left boundary condition from the upper left quadrant to the lower left quadrant. Once the domain wall position in the left lane is less than $-\frac{1}{2}$, the left boundary condition of the left lane is not satisfied. Therefore, the density profile is dominated by the R lane minus-end boundary condition only.

The case in which the left-lane minus-end boundary condition $\alpha_L$ is satisfied is symmetric. This often occurs when the left boundary condition is in the lower right quadrant and the right boundary condition is in the lower left quadrant. This case can be treated as moving the right boundary condition from the lower right quadrant to the lower left quadrant. Once the domain wall position in the right lane is greater than $\frac{1}{2}$, the right boundary condition of the right lane is not satisfied. Therefore, the density profile is dominated by the L lane minus-end boundary condition only.

**Both lane plus-end and one minus-end boundary conditions satisfied:** This case is analogous to a semi-LH phase. The case in which all but $\alpha_L$ is satisfied often occurs when the left boundary condition is in the upper left quadrant and the right boundary condition is in the upper right quadrant. This case can be treated as moving the right boundary condition from the lower right quadrant to the upper right quadrant. Once the domain wall position in the left lane is greater than $\frac{1}{2}$, the right boundary condition of the left lane is not satisfied.

The case in which all but $\alpha_R$ is satisfied is symmetric. This case often occurs when the left
boundary condition is in the upper right quadrant and the right boundary is in the lower right
quadrant. This case can be treated as moving the left boundary condition from the upper left
quadrant to the upper right quadrant. Once the domain wall position in the right lane is less than
$-\frac{1}{2}$, the left boundary condition of the right lane is not satisfied.

**Both boundary conditions on one lane satisfied:** The case in which the R lane boundary
conditions are satisfied often occurs when the left boundary condition is in the lower left quadrant
and the right boundary condition is in the upper right quadrant. The density profile follows a
trajectory which obeys $\sigma_R(x = -\frac{1}{2}) = \alpha_R - \frac{1}{2}$, $\sigma_R(x = \frac{1}{2}) = \frac{1}{2} - \beta_R$, and contains the correct
number of sites (fig. 3.21C).

The case in which the L lane boundary conditions are satisfied is symmetric. This case often
occurs when the left boundary condition is in the upper right quadrant and the right boundary
condition is in the lower left quadrant. The density profile follows a trajectory which obeys $\sigma_L(x =
-\frac{1}{2}) = \frac{1}{2} - \beta_L$, $\sigma_L(x = \frac{1}{2}) = \alpha_L - \frac{1}{2}$, and contains the corred number of sites (fig. 3.21D).

**Only one plus-end boundary condition satisfied:** First we consider when the R lane
plus-end boundary condition is satisfied. This case often occurs when the left boundary condition
is in the upper right quadrant and the right boundary condition is in the upper left quadrant.
This case can be treated as moving the right boundary condition from the upper right quadrant to
the upper left quadrant. Once the right boundary condition crosses $\sigma_R = 0$, the L lane plus-end
boundary condition is not satified.

The case when the L lane plus-end boundary condition is satisfied is symmetric. This case
often occurs when the left boundary condition is in the lower right quadrant and the right boundary
condition is in the upper right quadrant. This case can be treated as moving the left boundary
condition from the upper right quadrant to the lower right quadrant. Once the right boundary
condition crosses $\sigma_L = 0$, the R lane plus-end boundary condition cannot be satisfied.
Figure 3.21: Example phase-plane trajectories and density profiles (inset) for general boundary conditions. Insets show $\rho_R + \rho_L$ (blue), $\rho_R$ (red), and $\rho_L$ (green). Red dots are kMC simulation results. The blue dot indicates the left boundary condition and the green dot the right boundary condition. A: The blue line is $\sigma_R = \alpha_R$, and the green line is $\sigma_L = \alpha_L$. B: The blue line is $\sigma_L = 1 - \beta_R$, and the green line is $\sigma_R = 1 - \beta_L$. C: The blue line is $\sigma_R = \alpha_R$, and the green line is $\sigma_R = 1 - \beta_L$. D: The blue line is $\sigma_L = 1 - \beta_L$, and the green line is $\sigma_L = \alpha_L$. The switching rate is 0.1 s$^{-1}$, bulk motor concentration $c = 200$ nM, and motor speed 5 $\mu$m s$^{-1}$; other parameters are the reference values of table 3.1.

3.7 Conclusion

In this chapter, we firstly studied a model of motor motion on antiparallel MT overlaps that incorporates motor binding and unbinding, plus-end directed motor motion, and switching between
Figure 3.22: Example phase-plane trajectories and density profiles for general boundary conditions, illustrating how altering the right boundary condition changes the density profile. A: Colored dots indicate the right boundary condition. Red curve satisfies all four boundary conditions, green, blue, and brown curves do not satisfy $\beta_R$, and the purple curve satisfies $\alpha_R$ and $\beta_L$. B, C: corresponding density profiles on the R lane (B) and L lane (C). The switching rate is $0.1 \text{ s}^{-1}$, bulk motor concentration $c = 200 \text{ nM}$, and motor speed $5 \mu\text{m s}^{-1}$; other parameters are the reference values of table 3.1.

filaments (fig. 3.1) with symmetric boundary conditions, and solve the general case secondly. Our model is inspired by the experiments of Bieling, Telley, and Surrey on the motion of the kinesin-4 motor Xklp1 on antiparallel MT overlaps (71). Our model is an extension of previous theory that studied motor motion on a single MT with binding kinetics (57, 69), or motor motion on two antiparallel filaments with lane switching, but no binding kinetics (87, 89). To our knowledge, this is the first theoretical study of a two-lane TASEP model with oppositely oriented lanes, switching, and binding/unbinding.
Figure 3.23: Comparison of motor density profiles for zero and small $\beta$. Left: motor density $\rho_R(x)$ for $\beta = 0$. Right: motor density $\rho_R(x)$ for $\beta = 2.7 \times 10^{-3}$. Other parameters are the reference parameters with motor concentrations as shown in the legend.

To compare to the BTS experiments, we used measured or estimated parameters (table 3.1). Because PRC1 recruits motors directly into the overlap and motor binding to single MTs is much weaker, we neglect motor binding to MTs outside of the overlap and set the minus-end flux parameter $\alpha = 0$. Using the bulk motor unbinding rate $k_{\text{off}}$ as an upper bound on the plus-end unbinding rate, we find $\beta \leq 2.7 \times 10^{-3}$. This value is sufficiently small that it gives motor density profiles indistinguishable from those with $\beta = 0$ (fig. 3.23). Therefore no-flux boundary conditions with $\alpha = \beta = 0$ are used to model the experiments. Simulated images of the motor distribution in an overlap and simulated kymographs of motor trajectories are similar to those found experimentally (fig. 3.1).

We derived analytical and approximate solutions of the continuum steady-state equations and compared them to kMC simulation results (fig. 3.25). Since the steady-state mean-field equations are nonlinear and strongly coupled (for sufficiently high switching rate), we study their solutions in the density-density phase plane (sec. 3.3). We find an analytical solution in the phase plane and an expansion to determine position-dependent approximate solutions. Studying the phase space flow and fixed points of the model (fig. 3.5) gives intuition for the phases and how they change with parameters. In particular, both the number and location of the phase-plane fixed points (fig. 3.6) change with switching rate: for sufficiently high switching rate, two additional fixed points appear,
Figure 3.24: Control of boundary layer length. Left: boundary layer length as a fraction of total overlap length, shown as a function of bulk motor concentration and motor speed. Right: boundary layer length as a function of overlap length for the reference parameter set and varying bulk motor concentration. The boundary layer length is the distance at each end of the overlap where significant motor accumulation occurs and is determined by Eqn. 3.17.

leading to qualitative changes in the behavior of the model. In particular, for sufficiently high switching rate a new multi-phase coexistence low density-high density-low density-high density (LHLH) phase appears. In the mean-field model, we can calculate exactly the critical switching rates at which these changes occur. In addition, phase plane analysis allows us to determine domain wall positions using the finite-size constraint (fig. 3.8).

We then use the phase-plane analysis to determine the nonlinear phases that can occur for the case of symmetric boundary conditions (sec. 3.4). The fixed points divide the lanes’ central density into 4 regions (fig. 3.9) with different flow properties. These determine the phases that can occur. For low switching rate, the low-density (L), high-density (H), low density-high density coexistence (LH), and Meissner (M) phases previously studied by PFF for the single-lane case (57) occur (fig. 3.10). For high switching rate, the LHLH phase appears (fig. 3.11). We also determine
which boundary conditions are satisfied in different phases (fig. 3.12).

The analysis of the phase-space flows and fixed points allow us to determine the phase diagram for the biophysically relevant case of symmetric boundary conditions (sec. 3.5). Fig. 3.13 illustrates the phase diagrams for low and high switching rate. We then discuss the calculation of the boundaries of each phase, particularly using backward integration from the lanes’ center to determine the LH phase boundaries (fig. 3.14), its changes with motor speed (fig. 3.15), and the LHLH phase boundaries (figs. 3.16, 3.17). A similar method can be used to determine whether there is a local maximum or minimum at the lanes’ center (fig. 3.18). Additionally, we discuss an alternate method for determining approximate phase boundaries of the LH phase using an analytic approximation to the density profile (fig. 3.19) and the total binding constraint. The approximate phase boundaries computed in this way are close to those determined from the phase-plane analysis (fig. 3.20).

We then considered the general case of asymmetric boundary conditions (sec. 3.6). There are 10 cases corresponding to different possibilities for which boundary conditions are satisfied; we
Figure 3.26: Motor density profiles for the large-$S$ parameter set. Left: motor density $\rho_R(x)$ on MT with rightward-moving motors. Right: total motor density $\rho_R(x) + \rho_L(x)$ on both MTs in the overlap.

show some examples in fig. 3.21. Changes in the location of the boundary point in the phase plane cause predictable changes (fig. 3.22). To sum up of the phase-plane analysis, it is useful because the analytic solution to the mean-field steady-state equations allows us to determine the trajectories and fixed points. This approach may be useful in the future for the study of other multi-lane TASEP models.

Finally, we studied the model in more detail both for the reference parameters and a high-switching-rate parameter set (table 3.1). Results of kMC simulations (fig. 3.27, 3.26) agree well with exact and approximate solutions of the continuum steady-state equations (fig. 3.25, 3.7). In contrast to systems in which motors move on single filaments (1, 27, 28, 52–55, 73), we find that antiparallel overlaps with no-flux boundary conditions have total zero current. This leads to a total binding constraint that the integral of the total motor density on a single filament must equal $\rho_0$, the motor density set by binding/unbinding equilibrium (fig. 3.2).

For the experimentally relevant low density-high density coexistence phase, the density profiles are approximately piecewise linear (fig. 3.3). This motivates an analytic approximation to determine the density profiles consistent with the total binding constraint and gives analytic expressions for the overlap center motor density and the length of the boundary layer in which motors accumulate near the overlap ends. We find that as a result of the total binding constraint, the motor
Figure 3.27: Motor density profiles for the reference parameter set. Left: motor density $\rho_R(x)$ on MT with rightward-moving motors. Right: total motor density $\rho_R(x) + \rho_L(x)$ on both MTs in the overlap. Parameters are the reference parameter set of table 3.1 with the bulk motor concentrations indicated in the legend.

density at the center of the overlap is not determined solely by the motor binding equilibrium, but is also controlled by the overlap length, motor speed, and filament switching rate (fig. 3.28, 3.29). These same parameters control the length of the boundary layer at the overlap ends where motors accumulate (fig. 3.4).

The mitotic spindle contains arrays of overlapping antiparallel MTs to which multiple motors and crosslinkers bind (78). The surprising differences in motor density profiles between single filaments and the antiparallel overlaps we study here are therefore of interest in the study of the spindle midzone. For antiparallel overlaps, both the motor density far from the overlap ends and the number of motors near the overlap ends can be tuned not just by motor binding kinetics but also by motor speed, filament switching rate, and overlap length (fig. 3.24). The antiparallel filament geometry gives biological systems additional handles to control motor density, its spatial distribution, and therefore motor function. Motor density can affect recruitment of other proteins
Figure 3.28: Motor density at the center of the overlap. Left: variation with bulk motor concentration; right: variation with motor speed. Points indicate simulation results and dashed lines theoretical prediction from Eqn. 3.18. The red line shows the value of the Langmuir density $\rho_0$ for the same parameters.

and MT dynamics. Therefore, this previously undescribed mechanism of regulation of motor density along MTs may offer advantages to the control of motor activity.

For single MTs, length regulation by the kinesin-8 motor Kip3 depends on a functional form of motor density that is independent of MT length (26, 27). The physics we describe here means that the motor density and extent of motor accumulation at the overlap ends depends on overlap length. Therefore, length regulation of antiparallel MT overlaps must occur differently.
Figure 3.29: Dependence of density profiles on motor speed. Left: motor density $\rho_R(x)$ on MT with rightward-moving motors. Right: total motor density $\rho_R(x) + \rho_L(x)$ on both MTs in the overlap. Varying motor speed can significantly alter the motor density at the center of the overlap. These simulations use the large-$S$ parameter set of table 3.1 with bulk motor concentration $c = 200$ nM and the motor speeds indicated in the legend.
Chapter 4

Active phases in two dimensions (4)

4.1 Introduction

Active matter made up of self-driven particles exhibits novel physical properties include collective motion, nonequilibrium order-disorder transitions, and anomalous fluctuations and mechanical response (94, 95). Understanding active matter may aid the development of new technologies including autonomously motile and self-healing synthetic materials. Examples of active matter include animal flocks (96), crawling and swimming cells (97–100), vibrated granular materials (101, 102), self-propelled colloidal particles (103, 104), and the cellular cytoskeleton and cytoskeletal extracts (105, 106).

Among active matter, self-propelled rods (SPR) provide a useful minimal model system. Self-propulsion and excluded volume interactions via a short-range repulsive potential are the only ingredients; rod alignment occurs through collisions. Experiments which may be approximated as SPR include vibrated granular rods (107), motion of cytoskeletal filaments on a motor-bound surface (106, 108), and surface or film swarming of rod-like bacteria (99, 100, 109, 110). Because of their simplicity SPR are attractive to simulation study (8, 110–116) and have also been the focus of analytic theory (115, 117, 118). SPR display a rich variety of dynamic states, including collective motion (102, 119–132) and formation of dynamic clusters (8, 108, 112, 113, 116, 132–134).

For SPR, rod shape, density, and driving are important in determining the dynamic behavior (8, 110, 112–118). For low driving, equilibrium-like isotropic and nematic liquid crystal phases are recovered (116–118). For higher driving, dynamic states characterized by the appearance of flocks,
stripes, and swirls appear (8, 110, 112, 115–118). Baskaran and Marchetti derived a hydrodynamic model from the kinetics of SPR with two-rod collisions and determined a state diagram from linear stability analysis of homogeneous states, finding that activity lowers the isotropic-nematic transition density (117, 118). Previous simulation work has observed flocking and laning states similar to those we study here (8, 115, 116), but did not measure on dynamic state transitions, hysteresis, or structural and mechanical properties. In this work, by studying the state diagram over a broader range of parameters with extensive expansion and compression simulations and mechanical and structural characterization, we demonstrate strong hysteresis, the emergence of glassy dynamics in the flocking state, and reentrant fluidization.

We studied self-propelled 2D spherocylinders with Brownian dynamics, as in previous work (8), using the computational scheme of Tao et al. (9) developed for equilibrium simulations of concentrated solutions of high-aspect-ratio particles. Rods have length $L$ and diameter $\sigma$. The center-of-mass and orientational equations of motion for rod $i$ with center-of-mass position $\mathbf{r}_i$ and orientation $\mathbf{u}_i$ are

$$
\mathbf{r}_i(t + \delta t) = \mathbf{r}_i(t) + \Gamma_i^{-1}(t) \cdot \mathbf{F}_i(t) \delta t + \delta \mathbf{r}_i(t), \quad (4.1)
$$

$$
\mathbf{u}_i(t + \delta t) = \mathbf{u}_i(t) + \frac{1}{\gamma_r} \mathbf{T}_i(t) \times \mathbf{u}_i(t) \delta t + \delta \mathbf{u}_i(t), \quad (4.2)
$$

where the random displacements $\delta \mathbf{r}_i(t)$ and $\delta \mathbf{u}_i(t)$ are Gaussian-distributed, $\Gamma_i^{-1}(t)$ is the inverse friction tensor, $\gamma_r$ is the rotational drag coefficient, and $\mathbf{F}_i(t)$ and $\mathbf{T}_i(t)$ are the deterministic force and torque on particle $i$. Excluded-volume interactions between particles are modeled by the WCA potential as a function of the minimum distance $s_{ij}$ between the two finite line segments of length $L$ that define the axes of particles $i$ and $j$ (11). The self-propulsion force is directed along the particle axis with $\mathbf{F}_{\text{drive}}^i = F_D \mathbf{u}_i$. In the absence of nonequilibrium driving, this model has been well-characterized both in 2D (12) and 3D (13, 14).

We nondimensionalize using the length $\sigma$, energy $k_B T$, and time $\tau = D/\sigma^2$, where $D$ is the diffusion coefficient of a sphere of diameter $\sigma$. The three dimensionless parameters are the rod aspect ratio $R = L/\sigma$, fixed at 40, the packing fraction $\phi = A_{\text{rods}}/A_{\text{system}}$, and the translational
Figure 4.1: Nonequilibrium state diagram and snapshots of self-propelled rods of aspect ratio 40. (a) State diagram as a function of Peclet number and packing fraction. Points indicate parameter sets of simulations. Solid lines indicate boundaries of regions of stability of different initial conditions. I (orange), isotropic state; F (purple) flocking state; NL (green) nematic-laning state; C (pink) crystalline state. Green-purple striping indicates region where both flocking and nematic-laning initial conditions are stable. (b-g) Simulation snapshots at indicated packing fraction and Peclet number. Rods are colored by orientation according to the colorwheel. (b) Isotropic. (c) Nematic. (d) Crystal. (e) Flocking. (f) Nematic–laning. (g) Flocking.

Peclet number $\text{Pe} = F_D L / (k_B T)$. We varied $\phi$ between 0.01 and 1.04 (where $\phi > 1$ is possible due to the slight softness of the repulsive potential), and $\text{Pe}$ between 0 and 320. We simulated $N = 4000$ rods in a square, periodic box. Most simulations were initialized in an equilibrium isotropic, nematic, or crystalline initial condition, then nonequilibrium activity was turned on and the system was allowed to run for $10^7 \tau$. The simulation measurement run was $10^7 \tau$, and the time step $\Delta t = 0.25 \tau$. 
4.2 Measurements

To fully characterize the dynamical states of systems of self-propelled rods we measure a variety of structural, dynamical, and mechanical properties, described below.

4.2.1 Mechanical and thermodynamic properties

The osmotic pressure (stress) tensor for a periodic system of $N$ interacting particles at temperature $T$ in a 2D volume $A$ is given by

$$\Pi = \frac{N k_B T}{A} I + \frac{1}{A} W,$$

(4.3)

where the first and second terms on the right-hand side represent the ideal gas and interaction contributions, respectively, $I$ is the unit tensor, and $W$ is the virial tensor,

$$W = \sum_{i<j} N r_{ij} F_{ij}^{\text{wca}},$$

(4.4)

where the sum ranges over all interacting pairs of particles, and $F_{ij}^{\text{wca}} = -\nabla s_{ij} u_{ij}^{\text{wca}}$.

From the stress tensor we can calculate the equation of state, i.e., the isotropic internal pressure

$$\langle P_0 \rangle = \frac{1}{2} \langle \Pi_{xx} + \Pi_{yy} \rangle.$$  

(4.5)

The nature of the pressure in active systems has been the subject of recent work (135–137); here we consider the internal pressure determined by the virial only. The off-diagonal component of the stress tensor is the shear stress,

$$\langle \Pi_{xy}(t) \rangle = \frac{1}{2} \langle \Pi_{xy}(t) + \Pi_{yx}(t) \rangle,$$

(4.6)

where the shear viscosity can be measured via the Green-Kubo relation (138)

$$\eta_{\text{eff}} = \frac{1}{k_B T A} \int_0^\infty \langle \Pi_{xy}(t) \Pi_{xy}(0) \rangle dt,$$

(4.7)

and $A$ is the volume of the system.
4.2.2 Structural properties

To assess orientational order, we compute the vectorial polar order parameter

$$ P = \frac{1}{N} \sum_{i=1}^{N} \mathbf{u}_i $$

and the traceless, symmetric 2D nematic ordering tensor

$$ Q = \frac{1}{N} \sum_{i=1}^{N} (2 \mathbf{u}_i \mathbf{u}_i - \mathbf{I}), $$

where $\mathbf{I}$ is the unit tensor. Most of the states studied here have some degree of local polar order but are globally non-polar, so $P$ is typically small in magnitude. Nematic order is characterized by the largest eigenvalue $S$ of the ordering tensor $Q$ and the corresponding eigenvector defines the nematic director orientation.

To measure positional correlations we calculate the pair distribution function $g(r)$ using

$$ g(r) = \frac{1}{\rho N} \left\langle \sum_{i=1}^{N} \sum_{j \neq i}^{N} \delta(r - r_{ij}) \right\rangle, $$

where $\rho = N/V$ is the number density of rods and $r_{ij} = r_j - r_i$ is the center-to-center separation of particles $i$ and $j$. Orientational correlations are characterized by the polar orientational correlation function

$$ g_1(r) = \left\langle \frac{\sum_{i=1}^{N} \sum_{j \neq i}^{N} \mathbf{u}_i \cdot \mathbf{u}_j \delta(r - r_{ij})}{\sum_{i=1}^{N} \sum_{j \neq i}^{N} \delta(r - r_{ij})} \right\rangle, $$

and the nematic orientational correlation function

$$ g_2(r) = \left\langle \frac{\sum_{i=1}^{N} \sum_{j \neq i}^{N} [2 \mathbf{u}_i \cdot \mathbf{u}_j]^2 - 1 \delta(r - r_{ij})}{\sum_{i=1}^{N} \sum_{j \neq i}^{N} \delta(r - r_{ij})} \right\rangle. $$

Positional and orientational correlations are measured in a filament-fixed reference frame where the $+y$ axis coincides with rod orientation vector $\mathbf{u}$. Examples of correlation functions from our simulations are shown in fig. 4.2.

We define an order parameter that measures the degree of local polar ordering in the neighborhood of particle $i$,

$$ p_i = \frac{\sum_{j \neq i}^{N} \mathbf{u}_i \cdot \mathbf{u}_j e^{-\alpha s_{ij}^2}}{\sum_{j \neq i}^{N} e^{-\alpha s_{ij}^2}}. $$
Figure 4.2: The pair distribution function (a), polar orientational correlation function (b), and nematic orientational correlation function (c) as a function of the separation $r_{\perp}$ perpendicular to the rod long axis in the flocking state ($\phi = 0.3$, blue) and the nematic-laning state ($\phi = 0.4$, red).

We chose the parameter $\alpha = 1$ so that only near neighbors of particle $i$ contribute significantly to the sums in Equation 4.13, and we defined the summation of the Gaussian weighting factor as the contact number, $c_i = \sum_{i \neq j} e^{-s_{ij}^2}$.

The polar order parameter $p_i$ ranges from $-1$ (particle $i$ surrounded by neighbors of opposite polarity) to 1 (particle $i$ surrounded by neighbors of opposite polarity). The distribution $f(p_i)$ of local order parameters $p_i$ is used to identify and count particles belonging to sub-populations with distinct local polar environments (fig. 4.3). This is useful for measuring the contributions of distinct sub-populations to dynamical properties such as the mean squared displacement and to mechanical properties such as the internal pressure tensor. The polar order parameter $p_i$ is also useful for direct identification of polar domains (e.g., flocks or lanes), defined as contiguous domains of rods with a polar order parameter that exceeds a threshold, taken to be $p_i = 0.5$ here. Any pair of rods for which $s_{ij} < r_c = 3\sigma$ and the angle $< 30$ degrees is considered a nearest-neighbor pair for the purpose of defining contiguous domains. Flock boundary and interior particles are determined by the contact number in the contiguous domains of rods (fig. 4.3). We set the critical contact number $c_i^* = 0.5$ is this study: boundary rods have the contact number smaller than 0.5, while interior rods have the contact number greater than 0.5.
Figure 4.3: An example flock identification using distributions of local polar order parameter and contact number, for a simulation with $\phi = 0.1$ and $Pe = 320$. (a) The joint distribution of local polar order parameter and contact number. (b) A snapshot of the flocking state where green indicates flock boundary rods, blue denotes flock interior rods, and red denotes vapor.

Figure 4.4: Illustration of determination of isotropic and flocking state boundary. Flock size distributions for $\phi = 0.05$, where systems with $Pe < 20$ are identified as isotropic and $Pe \geq 20$ are identified as flocking.

4.2.3 Dynamical properties

To characterize particle transport, we calculate the mean-squared displacement,

$$\Delta r^2(t) = \frac{1}{N} \sum_{i=1}^{N} \langle [r_i(t) - r_i(0)]^2 \rangle,$$

(4.14)
where the angle brackets denote an average over all time origins. In anisotropic states (e.g., the nematic-laning state) we separately measure the mean-squared displacements parallel and perpendicular to the nematic director, $\Delta r^2_\parallel(t)$ and $\Delta r^2_\perp(t)$. More generally (e.g., for isotropic states), we measure the mean squared displacements parallel and perpendicular to the initial particle orientation (at the time origin). Transport is typically power-law,

$$\Delta r^2(t) \sim t^\alpha$$

with $\alpha = 1$ at equilibrium (diffusion) and $\alpha > 1$ under driving (superdiffusion). The overall dynamics are complex, and the exponent $\alpha$ is a function of time lag. In the flocking state, for example, superdiffusive transport is observed at short to intermediate timescales, crossing over to diffusive behavior for times large compared to the characteristic timescale for flock reorientation.

Similarly, for orientational dynamics, the mean squared angular displacement is

$$\Delta \theta^2(t) = \frac{1}{N} \sum_{i=1}^{N} \left\langle [\theta_i(t) - \theta_i(0)]^2 \right\rangle,$$  

where $\theta_i = \cos^{-1}(u_i \cdot \hat{y})$. Note that $\theta_i$ in this equation is defined on the interval $-\infty < \theta_i < \infty$.

To characterize mechanical relaxation in the flocking and laning states, we compute the effective shear viscosity of the system from the stress autocorrelation function via a Green-Kubo relation (see equation 4.7). Note that $\eta_{\text{eff}}$ is the effective shear viscosity of the system of interacting rods, which should not be confused with the fluid viscosity $\eta$ defined above.

Structural relaxation is characterized by measuring the autocorrelation function for fluctuations in the angle-averaged structure factor,

$$C_S(k,t) = \langle \delta S(k,t) \delta S(k,0) \rangle,$$  

where $k$ is the magnitude of the wavevector, the average is over all time origins, and

$$\delta S(k,t) = S(k,t) - \langle S(k,t) \rangle$$

is the fluctuation in the the angle-averaged structure factor. The angle-averaged structure factor is given by

$$S(k,t) = \frac{1}{2\pi} \int_0^{2\pi} d\phi S(k,t),$$

(4.19)
where $\phi$ is the orientation of wavevector $k$ in the $k_x, k_y$ plane. The instantaneous structure factor $S(k, t)$ is

$$S(k, t) = \frac{1}{N} \rho(k, t) \rho(-k, t)$$

(4.20)

where $\rho(k, t)$ is the spatial Fourier transform of the density,

$$\rho(k, t) = \int d\mathbf{r} \ e^{-i\mathbf{k} \cdot \mathbf{r}} \rho(\mathbf{r}, t) = \sum_{i=1}^{N} e^{-i\mathbf{k} \cdot \mathbf{r}_i(t)}.$$  (4.21)

We chose to work with the angle-averaged structure factor because it is rotationally invariant, and so its autocorrelation probes internal structural relaxation of flocks and lanes but is insensitive to reorientation. We measured $C_S(k, t)$ for $k$ values corresponding to the two primary peaks in $\langle S(k, t) \rangle$, namely $k \approx 2\pi/L$ and $k \approx 2\pi/\sigma$. To determine the $k$ value of the peak, we compute the 2D static structure factor and determine the location of the maximum by averaging the peaks along the $k_x$ and $k_y$ axes. To compute the angle-averaged structure factor, we use

$$S(k, t) = \frac{1}{2\pi} \int_{0}^{2\pi} \frac{1}{N} \rho(k, t) \rho(-k, t) \ d\theta$$

$$= \frac{1}{2\pi} \int_{0}^{2\pi} \frac{1}{N} \sum_{i,j}^{N} \ e^{-i(k \cos \theta (x_i(t) - x_j(t)) + k \sin \theta (y_i(t) - y_j(t)))} \ d\theta$$

(4.22)

$$= \frac{1}{2\pi N} \sum_{i,j=1}^{N} J_0(k |\mathbf{r}_i(t) - \mathbf{r}_j(t)|),$$  (4.23)

where $\mathbf{r}_i = (x_i, y_i)$, and $J_0$ is the Bessel function of the first kind. Therefore the particle positions at time $t$ and $k$ are sufficient to compute the angle-averaged structure factor.

The flocking state shows power-law decay in the structure factor auto-correlation function (detailed state criteria are described in the next section), and the corresponding exponent increases as the packing fraction increases. The exponents approach a plateau for large packing fractions, greater than 0.5 (fig. 4.5).

### 4.3 Results

At zero or low driving, we find equilibrium isotropic, nematic, and crystalline states (fig. 4.1a-d). While we did not map the equilibrium phase transitions in detail, our observations are consistent with previous work (12). As the Peclet number increases, lower packing fractions roughly
corresponding to the equilibrium isotropic phase typically show flocking behavior characterized by collective motion of clusters of various sizes coexisting with a low-density vapor (fig. 4.1e), as observed previously (8, 112, 113, 132–134). While the flocking state remains globally isotropic (consistent with previous predictions (117)), the formation of dense aligned clusters is characterized by short-range density correlations that lead to peaks in the pair distribution function and the emergence of polar and nematic orientational correlations that persist over a cluster-size length scale (fig. 4.2, and other data not shown). Rod mean-squared displacements are ballistic at short times, turning over to diffusive at long times due to flock reorientation. The long-time angular mean-squared displacement is diffusive.

4.3.1 State diagram

We identified four different states in our simulations: isotropic, flocking, nematic–laning, and crystal, where the green–purple shaded region indicates the corresponding states are initial condition dependent. The following sections are the definition we used in order to determined the state boundaries.

4.3.1.1 Isotropic–nematic

The state boundary between isotropic and nematic states is determined by nematic order parameter, $S$, where the nematic has the value $S > 0.5$ and the isotropic has the value $S < 0.5$.

4.3.1.2 Isotropic–flocking

For each simulation in the isotropic–flocking region, we computed the flock size distribution and fit it to a power-law with exponential cutoff, $p(n) \sim n^\alpha \exp(-n/n_c)$, where $p(n)$ is the probability of finding a flock of size $n$. A system is designated flocking if the exponent $\alpha$, is greater than $-3.0$, and typically the corresponding critical flock size, $n_c$, is greater than $100$ indicating nearly power law decay (fig. 4.4). We identified rods as members of flocks or vapor using the local polar order parameter $p_i$. If a rod has $p_i < 0.5$, we labeled it a vapor particle. In addition, two rods belong
to the same flock if both have local polar order $\geq 0.5$, the minimum distance between them $\leq 3\sigma$, and the angle between them is $< 30$ degrees.

## 4.3.1.3 Flocking–laning

The state boundaries between the flocking and laning states are determined via internal pressure measurements. The flocking state has relatively high pressure, while the laning state has relatively low pressure, and the state boundary between these two states has a suddenly increasing/decreasing pressure during expansion/compression simulations.

### 4.3.1.4 Expansion simulations from high density flocking state

To further study hysteresis in our system, we performed expansion simulations from the high density flocking state, $\phi = 1.0$, to the low density flocking state, $\phi = 0.28$, with Pe= 160, and 40. The system remains flocking during expansion for Pe = 160, while for Pe=40 lanes re-emerge upon expansion, and then transition back to flocks at low density. This confirms the reentrance.
4.3.2 Flocking–Nematic-laning state transition

The flocking state shows large density heterogeneity suggestive of two-phase coexistence between dense orientationally ordered clusters and low-density isotropic rods. In previous work on self-propelled spheres or disks, two-phase coexistence of a dense cluster and a dilute vapor was observed that appears qualitatively similar to what we observe here (5, 104, 139–147). However, flocks are dynamic and are constantly merging, breaking up, and exchanging particles with the dilute region (112, 133, 134). We identified flocks based on measurements of the contact number $c_i = \sum_{i \neq j} e^{-s_{ij}^2}$ and local polar order parameter $p_i = \sum_{i \neq j} \mathbf{u}_i \cdot \mathbf{u}_j e^{-s_{ij}^2} / c_i$ of rod $i$. Two-dimensional histograms show peaks in the density for large $p_i$ over a range of $c_i$ (fig.4.3); individual flocks were defined as collections of neighboring flock particles (fig.4.3). We identified flocks and isolated them...
in a box empty of other rods; this led the isolated flock to break up, demonstrating that flocks are not stable as isolated clusters. Flock size distributions are stable in time and power law in form with an exponential cutoff, as observed previously (99, 112, 134, 148, 149) (fig.4.4).

As the Peclet number increases, higher packing fractions driven from an equilibrium nematic or crystal typically show nematic-laning behavior characterized by the formation of polar lanes of upward- and downward-moving particles (fig. 4.1f,g). The density is approximately uniform and the orientational order is globally nematic in most cases with polar correlations on the scale of the system size in the alignment direction and on the scale of a typical lane width perpendicular to the alignment direction (fig.4.2 and data not shown). Rod mean-squared displacements are ballistic in the alignment direction and diffusive perpendicular, while the angular mean-squared displacement is bounded due to the the maximum angular deviation of rods. The emergence of lanes in SPR and related models has been observed in previous simulation studies (8, 110, 115, 116, 150), and laning has been studied previously for spherical particles both in experiments (151–153) and theory/simulation (154–158). Laning occurs because of the differences in collisions experienced by rods as a function of their polar environment: a rod moving surrounded by opposite polarity rods will experience more collisions, and therefore more momentum transfer, than when surrounded by rods of similar polarity. A rod surrounded by others of similar polarity will therefore experience reduced lateral movement and be less likely to leave the polar lane (8, 154).

To characterize the transitions between nematic-laning and flocking states, we performed expansion and compression runs in which the packing fraction was changed by $\Delta \phi = 0.02$, the simulation was run for $10^7 \tau$ to reach a dynamic steady state, and then measurements were performed over an additional $10^7 \tau$. The appearance of the nematic-laning state is dependent on initial conditions; lanes with equal numbers of up- and down-moving rods result from initialization with an equilibrium nematic state and the high rod packing fraction which prevents rod reorientation. Upon expansion, the system undergoes an abrupt transition to the flocking state (fig. 4.6a), while compression simulations subsequently started in the flocking typically remain in the flocking state (fig. 4.6b). If we apply a nematic aligning field to a compressed flocking state, the induced
rod reorientation can break up the flock and allow a transition back to the nematic-laning state (fig. 4.6c). This strong hysteresis is another signature of an abrupt dynamic transition between the laning and flocking states. While previous work has examined the nonequilibrium state diagram of SPR(8, 110, 112, 115–118), to our knowledge this is the first study to demonstrate strong hysteresis in this system.

McCandlish et al. found the laning state to be unstable to break up (8). While the strong hysteresis we observe makes it difficult to guarantee that any nonequilibrium state is stable for infinite time, our expansion and compression simulations effectively extended our simulation times up to $2 \times 10^8 \tau$ in the nematic-laning state, and upon reaching the transition boundary we typically see break up of the lanes into flocks within the $10^7 \tau$ equilibration run. Therefore in our system the laning phase appears to be stable, consistent with other work (110, 115, 116). The instability observed by McCandlish et al. may be related to the reentrance we observe if the simulations were performed near the upper limit of stability of the nematic-laning state.

During expansion runs, the isotropic internal pressure $P_o$, measured by the virial, abruptly changes by a factor of 2–10 at the transitions between nematic-laning and flocking states (fig. 4.6d). (The nature of the pressure in active systems has been the subject of recent work (135–137); here we consider the internal pressure determined by the virial only.) At the highest packing fractions the internal pressure approaches a plateau value near 10 for all systems, suggesting that a pure dense flocking state has been reached. The internal pressure of the flocking state lies along an envelope that decreases with decreasing packing fraction as the rod flocking/isotropic fraction varies. Nematic-laning systems undergo transitions to flocking upon both expansion and compression (fig. 4.7a,b, open circles labeled by arrows indicate starting simulations of expansion/compression runs). Flocking systems, typically remain flocking upon compression, but for low packing fractions a transition back to the nematic-laning state upon compression can occur (fig. 4.7b, open circles labeled by downward-pointing arrows indicate starting simulations of compression runs).

The dense clusters and high pressure in the flocking state suggest that the clusters may
Figure 4.7: Mechanical and structural properties of the nematic-laning and flocking states. (a,b) Internal pressure as a function of packing fraction during expansion (left-handed triangles) and compression (right-handed triangles) runs for simulations with varying Peclet number. The black arrows and open circles indicate the initial state of each run. (c) Structure-factor autocorrelation as a function of time for Pe=160 and systems in the laning ($\phi = 0.44$, red) and flocking ($\phi = 0.34$, blue) states for the peak nearest wave number $k = 2\pi/\sigma$. The autocorrelation exhibits exponential decay in the nematic-laning state with characteristic time $\tau_c = 0.10$ and power-law decay in the flocking state with the exponent $\alpha = 0.27$ as indicated. Inset, semi-log plot. (d) Stress-tensor autocorrelation as a function of time for Pe=160 and systems in the nematic-laning ($\phi = 0.4 - 0.48$) and flocking ($\phi = 0.36 - 0.38$) states. Inset, zoomed view of long-time tail.

have slow internal dynamics. To characterize structural relaxation we measured the normalized structure-factor autocorrelation function $C(t)/C(0)$, where $C(t) = \langle \delta S(k,t)\delta S(k,0) \rangle$, $k$ is the magnitude of the wavevector and $\delta S(k,t) = S(k,t) - \langle S(k,t) \rangle$ is the fluctuation in the the angle-averaged structure factor $S(k,t) = \frac{1}{2\pi N} \int_{0}^{2\pi} d\phi \rho(k,t)\rho(-k,t)$. Because the angle-averaged structure factor is rotationally invariant, its autocorrelation probes internal structural relaxation of flocks and lanes.
but is insensitive to flock reorientation. We determined the location of the peak nearest to wave number \( k = \frac{2\pi}{\sigma} \), corresponding to side-by-side filaments separated by approximately one diameter. In the nematic-laning state, the structure-factor autocorrelation exponentially decays (fig. 4.7c, red curve). However in the flocking state, the structure-factor autocorrelation has a power-law tail, indicating slow structural relaxation (fig. 4.7c, blue curve). Expansion to lower packing fractions has little effect on the power-law exponent, indicating that slow relaxation of dense clusters controls the decay of the structure-factor autocorrelation. Compression leads to a density-dependent exponent (fig.4.5).

Mechanical relaxation was measured by the autocorrelation function of the off-diagonal internal stress tensor \( \langle \Pi_{xy}(t)\Pi_{xy}(0) \rangle \). In the nematic-laning state, the stress autocorrelation drops to zero around \( t = 1 \) (fig. 4.7d, blue, red, and purple curves). In the flocking state, the stress autocorrelation function relaxes to a small but long-lived plateau (fig. 4.7d, yellow-green and grey curves). Consistent with this, the effective shear viscosity measured via the Green-Kubo relation shows a factor of \( 10^3 \) increase upon transition from the nematic-laning to the flocking state for \( \text{Pe}=80 \) (fig.4.5).
4.4 Conclusion

The large increases in pressure and shear viscosity and slowed structural and mechanical relaxation that occurs upon transition from nematic-laning to flocking suggest that this is a type of glass transition in which flocks, although collectively moving, have an internally glassy, solid-like structure. Related observations were made in an experimental system with self-propelled colloids, for which nonequilibrium driving promoted formation of small, mobile crystalline clusters (104). Related phase separation between a low-density gas and high-density liquid, glassy clusters or crystals has been observed both in experiments (104, 139, 140) and theory and simulations (5, 141–147). In contrast to both recent active jamming work and classic granular jamming (159, 160), in our self-propelled rod system the increased importance of aligning interactions means that the transition to the translating glassy flocking state can occur both as density is raised and lowered. This reentrant fluidization appears to be a novel feature of this transition in systems of self-propelled rods.

Self-propelled rods couple shape anisotropy to directional polarity, in contrast to self-propelled spheres. This enables a rich state diagram for SPR with important implications for transport (fig. 4.8). Orientational ordering allows SPR to form a nematic-laning state at high packing fraction characterized by fluid internal dynamics and ballistic transport along the lanes. Much of the same region of parameter space of self-propelled spheres consists of phase-separated liquid-liquid coexistence (fig. 4.8)(5, 141–147) for which particle dynamics are diffusive(5) and the formation of dense clusters limits particle motion. Perhaps the physics of laning is important for collective motion of rod-shaped microorganisms such as *Myxococcus xanthus*, which during fruiting-body formation assemble into dense streams qualitatively similar to the lanes we observe(100). Ballistic transport through coupling of orientational order and self propulsion may give an advantage to rod-shaped rather than spherical bacteria.
Chapter 5

Summary and future directions

In this thesis, I studied the dynamics and steady states of 1D and 2D driven systems, using both analytic and numerical methods. In chapter II, I considered the density controlled or flux controlled models to solve single filament length regulation with depolymerization or dynamic instability assumptions of microtubule growing/shrinking. The analytic solutions agree well with kMC simulations even under only considering the steady states assumptions of the microtubule length and the linear order of the totally asymmetric simple exclusion process on a filament with Langmuir kinetics. In chapter III, I analytically solved the mean-field description of the steady-state totally asymmetric simple exclusion process on antiparallel lanes with Langmuir kinetics and switching between lanes. Unlike for equilibrium systems, the totally asymmetric simple exclusion process inherently contains long-range boundary effects which play an important role in biological systems. The non-linearity of the TASEP makes the equations hard to solve in real space; however, using phase space flow and fixed points, we can easily understand the real space solutions and characterize the phase boundaries. The understanding of the motor density profile will serve as a foundation for future work to address overlap length regulation in mitosis.

Chapter IV discusses two-dimensional active rods. The numerical modeling results show several phases which do not occur for equilibrium systems. I found anomalous dynamics, including power law decay of stress correlations and a fluid–jamming transition with reentrant fluidization. These results might be important in understanding how rod-shaped bacteria such as *Myxococcus xanthus* assemble into dense clusters.
5.1 Future directions

Biological systems usually have steady inward and outward energy or density currents which show novel non-equilibrium steady-state phenomena. These phenomena are important in maintaining the lives and poorly understand. One of the main questions is the motion under different dimensions or switching between different dimensions, for example, proteins inside a cell can move along a microtubule (1D motion), move on a nucleus membrane (2D motion), diffuse in the cytoplasm (3D motion), or switch between these media. Thus, what are the biophysical properties? And, is there any biological reason for this type of complex dynamics? Moreover, the active systems contain some interesting but unsolved questions from the pure physics point of view. How do biological patterns or structures form and do people find all of the biological patterns or structures? Do active systems form a well-defined steady state, and is there any good description analogous to the concept of free energy in equilibrium statistical mechanics?
Bibliography


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