Asters, Spirals and Vortices in Mixtures of Motors and Microtubules: The Effects of Confining Geometries on Pattern Formation

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Abstract

We model the effects of confinement on the stable self-organized patterns obtained in the non-equilibrium steady states of mixtures of molecular motors and microtubules. In experiments [Nédélec et al. Nature, 389, 305 (1997); Surrey et al., Science, 292, 1167 (2001)] performed in a quasi-two-dimensional confined geometry, microtubules are oriented by complexes of motor proteins. This interaction yields a variety of patterns, including arrangements of asters, vortices and disordered configurations. We model this system via a two-dimensional vector field describing the local coarse-grained microtubule orientation and two scalar density fields associated to molecular motors. These scalar fields describe motors which either attach to and move along microtubules or diffuse freely within the solvent. Transitions between single aster, spiral and vortex states are obtained as a consequence of confinement, as parameters in our model are varied. We also obtain other novel states, including “outward asters”, distorted vortices and lattices of asters on confined systems. We calculate the steady state distribution of bound and free motors in aster and vortex configurations of microtubules and compare these to our simulation results, providing qualitative arguments for the stability of different patterns in various regimes of parameter space. We also study the role of crowding or “saturation” effects on the density profiles of motors in asters, discussing the role of such effects in stabilizing single asters.

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I. INTRODUCTION

The mitotic spindle in a dividing eukaryotic cell is comprised of several millions of interacting protein molecules [1]. Remarkably, these molecular constituents self-organize to yield patterns at the scale of microns. The existence of such self-organized non-equilibrium structures at the sub-cellular scale is a common feature of biological systems. Such structures include the endoplasmic reticulum and the Golgi complex, membrane-bound organelles which participate in intra-cellular trafficking. They also include the cytoskeleton, a cell-spanning network of polymers such as microtubules, actin filaments and intermediate filaments [1].

The mitotic spindle consists of two interpenetrating arrays of microtubules [2]. Each such array originates from a microtubule organizing centre formed at the two ends of the dividing cell. Microtubules are semi-flexible polymers formed by polymerizing an asymmetric dimeric unit [3]. An individual microtubule is a polar object: microtubule ends, labelled as − and +, grow and shrink at different rates. This polarity dictates the direction of motion of a class of molecular motor proteins on microtubules. Motor proteins such as kinesins use energy derived from adenosine tri-phosphate (ATP) hydrolysis to exert forces and to translocate along microtubules [4]. The direction of motion is dictated by the filament polarity – both plus-end and minus-end directed motors exist [1, 4].

The principal microtubule organizing centre in most animal cells is the centrosome. In a dividing cell, the centrosome first duplicates to form the two poles of a mitotic spindle. Each centrosome nucleates a radial array of microtubules called an aster [5]. The two asters move apart to opposite ends of the cell as mitosis proceeds. Microtubules in the region between them then preferentially elongate, forming the spindle [5].

Interestingly, experiments on centrosome-free fragments of the cytosol containing both motors and microtubules also obtain self-organized aster-like structures [6]. Asters, in addition to other complex patterns such as vortices and disordered aster-vortex mixtures, are also seen in vitro, in experiments on mixtures of molecular motors and microtubules [7]. Features of spindle formation are reproduced in mixtures of motors, microtubules and gold beads coated with DNA [8]. The fact that such experiments are able to mimic the complex self-organized states seen in living cells indicates that simple mesoscale models which work with fewer components may be useful in capturing some aspects of cellular pattern formation [9].
This paper presents a theory of pattern formation in mixtures of molecular motors and microtubules in a confined geometry. We motivate hydrodynamic equations of motion for a coarse-grained field representing the local orientation of microtubules as well as for local motor density fields \[10\]. In our theoretical description, as well as in the experiments, microtubules are oriented by complexes of bound motors, yielding patterns at large scales \[11, 12\].

The experimental work of relevance to this paper is the following: Nédélec and collaborators study pattern formation in mixtures of complexes of conventional kinesins with microtubules in a confined quasi-two-dimensional geometry \[7\]. The later experiments of Surrey \textit{et al.} investigate pattern formation in larger systems where the effects of boundaries appear negligible \[13\]. The experiments are supplemented by simulations which reproduce many features of the experiments \[7, 13, 15, 16, 17\].

Our approach is closest in spirit to that of Lee and Kardar (LK) \[18\]. The LK model is a hydrodynamic description of two coupled fields. One of these is a two-dimensional vector field describing the coarse-grained orientation of the microtubule. The other is a conserved scalar field representing the local motor density. The LK model captures two prominent features of the experiments of Nédélec \textit{et al.:} the presence of stable vortices formed by microtubules and the instability of an aster formed in the early stages of pattern formation to a single, stable vortex at large motor densities. However, despite this success of the LK model, several features of the experiments are incompletely understood. The transition between a single aster and a single vortex seen in the experiments appears to be driven primarily by confinement. (When a growing microtubule hits the wall of the confining region, it bends and distorts. The elastic energy cost of this distortion can be relaxed in part if the microtubules assume a vortex configuration.) In the LK model, confinement does not appear to play a vital role, and the single aster to single vortex transformation is a generic feature even for large system sizes, provided the motor density is sufficiently large.

Experiments obtain a variety of stable steady states on larger systems as a function of motor density. These include a “lattice of asters” state in which asters are the only stable structures, a “lattice of vortices” state, in which individual vortices are stable while asters are absent, as well as an intermediate “aster-vortex mixture” state. The LK approach predicts that a single vortex should be the stable state at large motor densities even for very large systems. Experiments, however, always see a “lattice of asters” in this regime.

The LK model predicts that motor density profiles in asters are always simple decaying
exponentials, independent of the rates at which motors hop on and off the filament. However, experiments and theoretical work suggest more complex decays. Such decays include the intriguing possibility of power-laws with exponents which vary continuously as a function of the on-off hopping rates. Nédélec, Surrey and Maggs (NSM) derive equations for motor profiles around a single preformed aster, showing analytically that such profiles are pure power-law in nature \[19\]. The NSM equations describe motors as either freely diffusing in the solvent or as bound to and moving along a microtubule. These states are allowed to interconvert. The densities of bound and free motors are governed by separate equations. LK, in contrast, use a single equation for the full motor density field which is effectively the “sum” of these equations but ignore the dynamics of the difference field.

The NSM equations describe a single aster configuration composed of a fixed number of inward (or outward) pointing microtubules. As a consequence, the density of microtubule decreases radially outward from the aster core. Since the free motors become bound only in the presence of microtubule, the conversion rate should be proportional to the local microtubule density. This yields a non-trivial space dependence for this conversion rate, which is responsible for the power-law decay of motor densities. However, NSM do not address issues of pattern formation. We suggest here, in contrast to NSM, that at the length scales appropriate to a coarse-grained hydrodynamic description of pattern formation and at the densities of microtubules in the experiments, it is appropriate to ignore fluctuations in the local density of microtubule. The relevant fluctuating field is then the orientation field for the microtubule at fixed density, as in the LK model \[20, 21\].

Detailed information regarding the ordering of microtubules in the presence of molecular motors has come from the extensive simulations of Nédélec and collaborators \[7, 13, 15, 16\]. These simulations, performed in a two-dimensional geometry, obtain asters and vortices, in addition to relatively disordered configurations in which both asters and vortices are present. The best simulations require as many as 19 parameters to be specified; these include fluid viscosities, motor diffusion constants, binding strengths and microtubule bending rigidities. However, the uncertainties in these parameters are large, often of an order of magnitude or more.

The hydrodynamic approach used here involves far fewer free parameters \[22\]. Since structures obtained in the simulations are appropriate to specific parameter values simulated, it is hard a priori, to guess at what patterns would result on changing one or more of them.
However, one might expect several microscopic interactions to yield the same hydrodynamic description, provided it is general enough. Simulating hydrodynamic equations is often far faster and more efficient computationally than direct molecular dynamics simulations. This makes efficient scans of parameter space possible. Finally, simpler descriptions in terms of a small set of model equations enable analytic progress in some limits.

We summarize our results here: In a regime of parameter space for our model which is closest to that for the LK model, we obtain a single vortex as a stable final state for large motor densities. Our results here coincide with the LK results. However, in other regimes, asters are favoured. A “lattice of asters” state is stabilized in our model through a low-order relevant term in the equation of motion for the microtubule orientation. On small systems, constraints due to confinement favour a small number of asters, whose number can be increased systematically as parameters are varied. We provide qualitative arguments for the stability of different patterns in varied regimes of parameter space.

We calculate the distribution of free and bound motors in asters and vortices obtained in our model. Our results for motor profiles about asters differ from both the LK result and the NSM one. We derive an exponential decay of bound motor densities away from aster cores, modulated by a power-law in which the exponent of the power law depends in a non-universal way on dynamical parameters. The associated decay length for the exponential can become very large in some regimes of parameter space, yielding what would appear to be pure power-law decays close to the aster core. In contrast, LK would predict a pure exponential decay, whereas the NSM result is a pure power law. For vortices, we obtain results equivalent to the LK results.

We obtain, numerically, the solutions to our equations when “crowding” effects due to the interactions of motors moving on microtubules are accounted for in a simple way. Such effects distribute the motor density more uniformly along the microtubules. We argue that the inclusion of such “crowding effects” should further act to favour asters over vortices in finite systems. We suggest that the term “spiral” as opposed to “aster” or “vortex” is a more generic description of the microtubule configuration. We adduce simulational evidence for such spiral structures favoured by confinement and point out that the microtubule configurations seen in experiments do resemble spirals in many cases.

Our results relating to pattern formation in systems where the effects of boundaries can be neglected appear elsewhere. To summarize these briefly, we show in Ref. that our
FIG. 1: Qualitative “phase diagram” illustrating how different states, the disordered state, the aster-vortex mixture state, the lattice of vortices state, the single vortex, the lattice of asters, dominate in different regimes of parameter space; for a definition of parameters see text. The parameter $\epsilon$ is plotted on the $y$ axis, with the total motor density $m$ plotted on the $x$ axis. The parameter $S$ extends out of the plane of the figure.

model generates all the patterns seen in experiments, such as the aster-vortex mixture, the “lattice of asters” and the “lattice of vortices” [24]. We show how these states are linked in a non-equilibrium “phase diagram”, reproduced in Fig. 1, demonstrating how smooth trajectories in parameter space can connect the states observed, in agreement with the experiments [25]. Fig. 1 is relevant to experimental data in that it shows how a relatively small number of parameters may suffice to fix the macroscopic state of the system.

The outline of this paper is the following: In Section II, we describe the details of our model. We discuss and justify each term which appears in our equations of motion for microtubule and motor fields. Section III describes our numerical methods. Section IV presents results from our numerical simulation of the equations of motion for different boundary conditions. In Section V, we present analytic results for the profile of motor densities in
single vortex and aster configurations. In a subsection, these analytic results are compared with results from direct simulations of the hydrodynamic equations. Section VI discusses how saturation effects resulting from the interactions of bound motors affects motor density profiles. Section VII combines the results of Sections V and VI in a discussion of the relative stability of aster and vortex configurations. We provide a simple intuitive argument for the stability of different patterns as parameters in our model are changed. The concluding section, Section VIII, summarizes the results of this study and outlines possibilities for further work.

II. MODEL

Our model treats motors attached to microtubules differently from motors which diffuse freely in solution. Motors which move on microtubules are referred to as “bound” motors, while those which diffuse in the ambient solvent are referred to as “free” motors. These are described by coarse-grained fields denoted by $m_b$ and $m_f$ respectively and obey different equations of motion. In the absence of interconversion terms changing a bound motor to a free motor, $m_b$ obeys a continuity equation involving the current of motors transported along the microtubules. The free motor field $m_f$ obeys a diffusion equation with a diffusion constant $D$. These two fields are coupled through mechanisms which convert “free” motors to “bound” motors and vice versa. The equations they obey have the form

$$\partial_t m_f = D \nabla^2 m_f - \gamma'_{f \rightarrow b} m_f + \gamma'_{b \rightarrow f} m_b$$

$$\partial_t m_b = -A \nabla \cdot (m_b \mathbf{T}) + \gamma'_{f \rightarrow b} m_f - \gamma'_{b \rightarrow f} m_b$$

$\gamma'_{f \rightarrow b}$ and $\gamma'_{b \rightarrow f}$ are the rates at which free motors become bound motors (“on” rate) and vice-versa (“off” rate). These rates have dimensions of inverse time. Note that the total motor density field $m = m_b(r) + m_f(r)$ is a conserved field.

The term $A \nabla \cdot (m_b \mathbf{T})$ describes the motion of bound motors along microtubules with velocity $A$. One could, as we will do later, make the velocity itself density dependent. (This is natural when modeling motor motion in terms of the one-dimensional driven diffusive dynamics of interacting particles for which the current $J(\rho)$ is a non-linear function of the density $\rho$.) While the rate $\gamma'_{f \rightarrow b}$ should depend on the local density of microtubule, we will assume that microtubule density fluctuations are suppressed at the scales relevant
to a hydrodynamic description and retain only the orientational degree of freedom of the local microtubule field. We work in two dimensions throughout, since the experiments were performed in a quasi-two dimensional geometry [12].

The dynamics of the microtubules, given by the equation below, incorporates the terms used by Lee and Kardar in specific limits. It also includes one completely new term. As in the LK model, we ignore fluctuations in the density of microtubules, concentrating on their orientational degrees of freedom. The hydrodynamic equation includes terms which reflect the dynamics of individual microtubules. We take these to be stabilized at unit length. It also includes motor-independent and motor-dependent orientation terms. In principle, for a non-equilibrium problem, all symmetry allowed terms must figure here. Of these terms, we will incorporate only the lowest-order symmetry allowed terms whose contributions can be justified transparently on physical grounds.

Our equation then reads,

$$\partial_t T = T(\alpha - \beta T^2) + \gamma m_b \nabla^2 T + \gamma' \nabla m_b \cdot \nabla T + \kappa' \nabla^2 T + S' \nabla m_b$$  

(3)

The first term, $T(\alpha - \beta T^2)$, governs the stabilization of the microtubules at a preferred length of $\alpha/\beta$, which we will normalize to unity. The second and third terms, $\gamma m_b \nabla^2 T + \gamma' \nabla m_b \cdot \nabla T$, are alignment terms, reflecting the alignment of microtubules due to the action of bound motors. The third term is also interpretable as a “convective” term, in which the local velocity which convects fluctuations in the $T$ field is proportional to the gradient of bound motor density.

The fourth term, $\kappa' \nabla^2 T$, describes an intrinsic stiffness against distortions, allowing tubules to form an ordered phase in the absence of thermal noise. (This term was dropped by LK, where it was assumed that the orientation of the tubules was solely driven by the motor current. We include it here because it is certainly symmetry allowed, is linear in the field $T$ and thus should appear at lowest order. It is also useful in maintaining the local smoothness of the patterns generated).

The last term is completely new; it is a symmetry allowed term of linear order in the fields. Note that a few terms allowed by symmetry have been intentionally excluded. These include the term $m_b \nabla(\nabla \cdot T)$; such a term has an effect equivalent to the $\nabla m_b$ term of the equation above which is lower order in gradients.

In the LK model the coefficients $\gamma$ and $\gamma'$ are taken to be equal. Thus, the second
and third terms can be interpreted in terms of the functional derivative of a “free energy” term. In general however, away from thermal equilibrium, these two coefficients differ and we may explore the regimes of parameter space in which their relative strengths vary. For convenience we choose \( \gamma' = \epsilon \gamma \) and vary the parameter \( \epsilon \) to tune the ratio of these two terms.

The following transformation simplifies the equations considerably: scale length in units of \( D/A\sqrt{\beta/\alpha} \), time in units of \( \beta D/(\alpha A^2) \), motor density in units of \( D/\gamma \) and the tubule density in units of \( \sqrt{\alpha/\beta} \). The equations then reduce to

\[
\frac{\partial}{\partial t} m_f = \nabla^2 m_f - \gamma_{f\rightarrow b} m_f + \gamma_{b\rightarrow f} m_b \tag{4}
\]

\[
\frac{\partial}{\partial t} m_b = -\nabla \cdot (m_b \mathbf{T}) + \gamma_{f\rightarrow b} m_f - \gamma_{b\rightarrow f} m_b \tag{5}
\]

\[
\frac{\partial}{\partial t} T = C T (1 - T^2) + m_b \nabla^2 T + \epsilon \nabla m_b \cdot \nabla T + \kappa \nabla^2 T + S \nabla m_b \tag{6}
\]

The parameter \( C \) given by \( \beta D/A^2 \) is the growth constant. \( \gamma_{f\rightarrow b} \) and \( \gamma_{b\rightarrow f} \) are scaled in units of inverse time (i.e. \( (\beta D/(\alpha A^2))^{-1} \)). \( \kappa' \) is appropriately scaled to \( \kappa = \kappa'/D \) and \( S = S'(\beta D)/(\alpha \gamma A) \). Note that the scaled equations for the free and bound motors (Eqns. 4, 5) are invariant when the motor densities are multiplied by a constant. We will use this invariance in Section V(C) to compare analytic results for motor density profiles with results from numerical simulations.

We relate our scaled parameters to typical experimental values in the following way: The tubule density, scaled in terms of \( \sqrt{\alpha/\beta} \), is chosen to be unity. The diffusion constant \( D \) is about \( 20 \mu m^2/s \) and \( A \sim 1 \mu m/s \), defining basic units of length and time as \( 20 \mu m \) and 20 seconds respectively. A tubule density of 1 implies that over a coarse-graining length of \( 400 \mu m^2 \), there are around 400 microtubules, a value close to that used in the simulations \[13\]. Our choice for \( \gamma_{f\rightarrow b} \) and \( \gamma_{b\rightarrow f} \) corresponds to physical rates of \( 0.005 s^{-1} \) to \( 0.05 s^{-1} \), slightly smaller than those in the simulations \[16\]; using larger rates does not affect our conclusions here.

III. NUMERICAL METHODS

We solve Equations 4, 5 and 6 numerically on an \( L \times L \) square grid indexed by \((i, j)\) with \( i = 1, \ldots L \) and \( j = 1, \ldots L \). The equation for the free motor density is evolved through an Euler scheme,

\[
m_f(t + \Delta t) = m_f(t) - \Delta t \nabla \cdot J(m_f) - \gamma_{f\rightarrow b} m_f + \gamma_{b\rightarrow f} m_b, \tag{7}
\]
where

\[ J_x(m_f(i,j)) = (m_f(i+1,j) - m_f(i-1,j))/2\delta, \tag{8} \]
\[ J_y(m_f(i,j)) = (m_f(i,j+1) - m_f(i,j-1))/2\delta. \tag{9} \]

The grid spacing is \( \delta x = \delta y = \delta = 1 \) and the time step \( \Delta t = 0.1 \). At the boundaries, we impose the boundary condition that no current (either of free or bound motors) flows into or out of the system. This condition is easily imposed by setting the appropriate current to zero.

A related discretization is used for the bound motor density equation

\[ \partial_t m_b = -\nabla \cdot (m_b \mathbf{T}) + \gamma_{f \rightarrow b} m_f - \gamma_{b \rightarrow f} m_b, \tag{10} \]

where, in the bulk, partial derivative terms are discretized as

\[ \partial_x(m_b \mathbf{T}) = (m_b(i+1,j)T_x(i+1,j) - m_b(i-1,j)T_x(i-1,j))/2\delta. \tag{11} \]

with a similar equation used for the \( y \)-component.

The \( T \) equation is differenced through the Alternate Direction Implicit (ADI) operator splitting method in the Crank-Nicholson scheme. At the first half time-step

\[ (rI - \mathcal{L}_x)T_x^{n+1/2} = (rI + \mathcal{L}_y)T_x^n, \tag{12} \]

where \( r = 2\delta^2/\delta t \) and \( I \) is the identity matrix. The superscripts on \( T_x \) indicate the time-step at which these quantities are calculated. The operators \( \mathcal{L}_x \) and \( \mathcal{L}_y \) are given by

\[ \mathcal{L}_x = m_b \partial_x^2 + (\partial_x m_b)\partial_x + S(\partial_x m_b), \tag{13} \]
\[ \mathcal{L}_y = 2C(1 - T^2) + m_b \partial_y^2 + (\partial_y m_b)\partial_y + S(\partial_y m_b). \tag{14} \]

The first and second derivatives evaluated for a function \( f(i,j) \) on a lattice point \((i,j)\) in the bulk are

\[ \partial_x f(i,j) = (f(i+1,j) - f(i-1,j))/2\delta, \tag{15} \]
\[ \partial_x^2 f(i,j) = (f(i+1,j) - 2f(i,j) + f(i-1,j))/\delta^2, \tag{16} \]

with similar equations for the \( y \)-derivatives.

At the second half time step

\[ (rI - \mathcal{L}_y)T_x^{n+1} = (rI + \mathcal{L}_x)T_x^{n+1/2}, \tag{17} \]
where

\[ \mathcal{L}_x = m_b \partial_x^2 + (\partial_x m_b) \partial_x + S(\partial_x m_b), \]  
(18)

\[ \mathcal{L}_y = m_b \partial_y^2 + (\partial_y m_b) \partial_y + S(\partial_y m_b). \]  
(19)

A similar scheme is used for differencing the equation for the \( T_y \) component. Our simulations are on lattices of several sizes, ranging from \( L = 30 \) to \( L = 200 \). We vary the motor density in the range 0.01 to 5 in appropriate dimensionless units. We work with two different types of boundary conditions on the \( T \) field. In the first, which we refer to as reflecting boundary conditions, the microtubule configuration at the boundary sites is fixed to point along the inward normal. In the second, which we refer to as parallel boundary conditions, microtubule orientations at the boundary are taken to be tangential to the boundary. In both these sets of boundary conditions, the state of the boundary \( T \) vectors is fixed and does not evolve. The total number of motors, initially divided equally between free and bound states and distributed randomly among the sites, is explicitly conserved.

We add weak noise, primarily in the \( T \) equation of motion, to ensure that true steady states are reached in our simulations. Large noise strengths wipe out patterns, yielding homogeneous states. We have also experimented with a variety of initial states to ensure that the qualitative features of the patterns we obtain as stable steady states are, indeed, robust.

IV. RESULTS AND DISCUSSION: NUMERICAL

This section presents the results of our simulations in different regimes of parameter space for the boundary conditions discussed above. The simulations discussed here are on systems of size \( L = 30 \), corresponding to physical length scales of about 60\( \mu \)m. Our results on somewhat larger systems (\( L = 50 \)) are intermediate in character between the results for \( L = 30 \) presented here and our results on systems of much larger sizes (\( L \geq 100 \)), where boundary effects are negligible.

We work at a fixed large motor density of \( m = m_b + m_f = 0.5 \). We work at fixed values of \( \gamma_{\text{b} \to \text{f}} = \gamma_{\text{f} \to \text{b}} = 0.5 \) here but have checked that making the motors more or less processive does not alter our results qualitatively. For motors with very small “on” and “off” rates, we see disordered states best described as aster-vortex mixtures. The patterns obtained here
FIG. 2: Steady-state configurations of microtubules with reflecting boundary conditions. The parameters are $m = 0.5$ and $\gamma_{f \rightarrow b} = \gamma_{b \rightarrow f} = 0.5$. Patterns are shown at different $\epsilon$ at (a) $S = 0$, (b) $S = 0.05$, (c) $S = 0.5$ and (d) $S = 2$.

emerge at still higher motor densities for low values of the processivity. We work with a small value of $\kappa$, ($\kappa = 0.05$ here), such that the magnitude of the self alignment term $\kappa \nabla^2 T$ is small compared to $m_b \nabla^2 T$.

A. Reflecting boundary conditions

Our results for reflecting boundary conditions are shown in Fig. 2(a) – (d). Each column represents a different value of $S$ : i.e. (a) $S = 0$, (b) $S = 0.05$ (c) $S = 0.5$ and (d) $S = 2$. We vary the parameter $\epsilon$ in these scans, with $\epsilon$ taking the values $\epsilon = 0.0, 0.5, 1.0$ and 5 as shown.
FIG. 3: Steady-state bound motor density profiles with reflecting boundary conditions. The parameters are $m = 0.5$ and $\gamma_{f \rightarrow b} = \gamma_{b \rightarrow f} = 0.5$. Profiles are shown at different $\epsilon$ at (a) $S = 0$, (b) $S = 0.05$, (c) $S = 0.5$ and (d) $S = 2$. The darker regions indicate regions of lower motor density.

In Figs. 2(a) – (d), the effects of varying $\epsilon$ with reflecting boundary conditions are the following: In Fig. 2(a), $S = 0$ and the steady state configuration at $\epsilon = 0$ is an aster with tubules directed radially inward towards the core. When $\epsilon$ is increased to 0.5, the configuration resembles a “spiral”. As $\epsilon$ is increased further the spiral distorts into a vortex. In Fig. 2(b), we show configurations at small but non-zero $S$, $S = 0.05$. The single aster is stable for $\epsilon = 0$ and 0.5, but yields to a single vortex for larger $\epsilon$. A general observation is that the core of the vortex is increasingly distorted as $\epsilon$ is increased further.

Fig. 2(c) shows steady state configurations at $S = 0.5$. A tendency towards the formation of a lattice of asters is apparent, as $\epsilon$ is increased at these values of $S$. This is consistent with our earlier results on large systems, where we observed that non-zero $S$ always promoted the lattice of asters. At large $\epsilon$ e.g. $\epsilon = 5$, there is a pronounced tendency towards alignment, yielding a steady state pattern of a vortex with a highly distorted core. Fig. 2 (d) shows configurations at $S = 2$, where the lattice of asters is present at all values of $\epsilon$ shown. At
FIG. 4: Steady-state configurations of microtubules with parallel boundary conditions. The parameters are $m = 0.5$ and $\gamma_{f\rightarrow b} = \gamma_{b\rightarrow f} = 0.5$. Patterns are shown at different $\epsilon$ at (a) $S = 0$, (b) $S = 0.05$, (c) $S = 0.5$ and (d) $S = 2$.

At large $\epsilon$, the tendency towards parallel alignment competes with the tendency towards aster formation. At still larger values of $\epsilon$, we obtain an aligned phase in the bulk (not shown), reminiscent of the “bundles” seen in the experiments at large motor concentration.

Figures 3(a) – (d) show bound motor density profiles corresponding to the microtubule arrangements of Figs. 2(a) – (d). Lighter regions of the figure indicate regions of larger density. Note that the bound motor density is concentrated at the centres of asters. In vortex configurations, the motor density profiles for bound motors are far smoother. In the “lattice of asters” configuration, the bound motor density profiles peaks at the centres of the asters, decaying to a small value at intermediate points far away from aster cores. The profiles of free motor densities are visually very similar to those for bound motors and are
FIG. 5: Steady-state bound motor density profiles with parallel boundary conditions. The parameters are $m = 0.5$ and $\gamma_{f \to b} = \gamma_{b \to f} = 0.5$. Profiles are shown at different $\epsilon$ at (a) $S = 0$, (b) $S = 0.05$, (c) $S = 0.5$ and (d) $S = 2$. The darker regions indicate regions of lower motor density. Not shown here.

B. Parallel boundary conditions

We now discuss pattern formation in finite systems with parallel boundary conditions, see Figs. 4(a)–(d). These are to be contrasted to Figs. 2(a)–(d). Note that qualitatively different sequences of patterns are stabilized at identical values of other parameters, depending on the boundary conditions. This illustrates the sensitivity to boundary conditions which obtains for sufficiently small system sizes $L$.

Fig. 4(a) shows pattern formation with parallel boundary conditions at $S = 0$. A single vortex is obtained as a steady state at all values of $\epsilon$ shown i.e. $\epsilon = 0.0, 0.5, 1.0$ and 5. Fig. 4(b) shows patterns for $S = 0.05$. The steady state here is a single aster with tubules pointing
outwards at the core, but aligned with the configurations at the boundary. (We term such configurations as “outward asters”.) Clearly these arise as a consequence of the boundary conditions which favour vortices and the parameter regime which favours asters. At $\epsilon = 5$, the steady state is a well-formed, clean vortex. Fig 4(c) illustrates pattern formation at $S = 0.5$, as a function of $\epsilon$. We see a tendency towards the formation of the lattice of asters phase expected for large $S$ for sufficiently large $\epsilon$, although indications of this are seen even for small $\epsilon$.

At very high $\epsilon$, we obtain an unusual configuration which we term a “flag”. In this configuration, tubules point radially outward near the core while merging with the imposed parallel microtubule configuration near the boundary. However, the configuration appears to have a four-fold axis, in which the axis lines are along the diagonal. Across this axis, the microtubule orientation changes sharply. This 4-fold symmetry reflects the four-fold symmetry of the simulation box. Finally, Fig. 4(d) shows patterns formed at $S = 2$. In this regime, the lattice of asters is the stable steady state for all values of $\epsilon$.

Figures 5(a) – (d) shows bound motor density profiles corresponding to the microtubule arrangements of Figs 4(a) – (d). Note that the density distribution in single vortices varies smoothly, consistent with theoretical expectations. The profiles appear sensitive to the boundary and a four-fold rotation axis can be seen in several of the patterns which involve a single vortex. The patterns for non-zero and large $S$ are very similar to those obtained for reflecting boundary conditions with similar values of parameters. The profiles of free motor densities are again visually very similar to those for bound motors and are not shown here.

C. Discussion

Our results for the cases outlined in the previous sub-section are summarized as follows. For reflecting boundary conditions, we obtain the general sequence aster → spiral → vortex at $S = 0$. This sequence is obtained at fixed motor density, as a function of the non-equilibrium parameter $\epsilon$. With parallel boundary conditions, the patterns formed are generically vortices, although the region surrounding the core is progressively distorted as $\epsilon$ is increased. Finite $S$ favours the formation of a lattice of asters, as in large systems. We observe some novel configurations such as the “flag” configuration, reflecting the four-fold symmetry of the simulation box and the outward aster.
We commented earlier that the configurations obtained in experiments appear to represent states intermediate between asters and vortices in the most general case. We expand on this here: A spiral configuration is described by the unit vector field \( \mathbf{T} = T_r \hat{r} + T_\theta \hat{\theta} \) in which \( T_r \) and \( T_\theta \) take the forms,

\[
T_r = \cos(\alpha), \quad T_\theta = \sin(\alpha), \quad (20)
\]

where \( \alpha \) is a constant. This contains both asters and vortices in appropriate limits: In the limit \( \alpha = 0 \), this equation describes an aster, while in the limit \( \alpha = \pi/2 \), the configuration is a vortex. Thus asters and vortices are particular limiting cases of more general spiral states.

In our simulations, spirals arise as a consequence of the competition between the vortex configurations favoured locally for intermediate and large values of \( \epsilon \) and reflecting boundary conditions, which favour asters. Spirals offer the best compromise between these and it is reasonable to expect that such states should be more generically seen than either asters or vortex states. Indeed, inspection of the configurations associated to the “lattice of vortices” in Ref. [13] provides strong visual evidence for generic spiral states.

The bound and free motor profiles we obtain in the simulations are consistent with expectations from our theoretical analysis (see below). The characteristic sharp peaks in motor density profiles associated with asters are replaced by far more slowly varying profiles for vortices. The lattice of asters, therefore has strong signals in the motor distribution function. Appropriate experimental labelling of motors in this phase should yield patterns and profiles closely similar to those displayed here.

V. ANALYTIC RESULTS FOR MOTOR PROFILES IN ASTER AND VORTEX CONFIGURATIONS

We now present an analytic calculation of free and bound motor density profiles in vortex and aster configurations. We fix single vortex and aster configurations of microtubules and solve for steady state free and bound motor densities in the presence of the fixed microtubule configuration.

We find steady state solutions of Eqns. 4 and 5 by setting the time derivatives to zero i.e. \( \partial_t m_f = \partial_t m_b = 0 \). Adding and subtracting these equations, we obtain

\[
\nabla^2 m_f - \nabla \cdot (m_b \mathbf{T}) = 0, \quad (21)
\]
The first of these equations implies that
\[ \nabla m_f = m_b T + C, \]  
where \( C \) is an arbitrary vector whose divergence \( \nabla \cdot C = 0 \).

A. Single vortex i.e. \( T = \hat{\theta} \)

Assuming radial symmetry, we may write \( m_f = m_f(r) \) and \( m_b = m_b(r) \). Let \( C = c_r \hat{r} + c_\theta \hat{\theta} \).

Eqn. \( 21 \) then implies
\[ \partial_r m_f \hat{r} = m_b \hat{\theta} + c_r \hat{r} + c_\theta \hat{\theta}. \]  
Hence,
\[ c_r = \partial_r m_f \text{ and } c_\theta = -m_b. \]

The constraint of zero divergence for \( C \) yields
\[ \partial_r c_r + \frac{c_r}{r} + \frac{1}{r} \partial_\theta c_\theta = 0. \]  
Since \( c_\theta = -m_b(r) \) is purely radial
\[ \partial_\theta c_\theta = 0. \]

Eqn. \( 26 \) then becomes a radial equation
\[ \partial_r c_r + \frac{c_r}{r} = 0. \]  
Using \( c_r = \partial_r m_f \), we obtain
\[ \nabla^2 m_f = 0, \]  
which supports solutions of the form
\[ m_f(r) = c_1 + c_2 \ln(r), \]  
where \( c_1 \) and \( c_2 \) are constants to be determined by boundary conditions and normalization.

Eqn. \( 22 \) now simplifies to
\[ \gamma_{b \rightarrow f} m_b - \gamma_{f \rightarrow b} m_f = 0 \]  

\[ \nabla^2 m_f + (\gamma_{b \rightarrow f} m_b - \gamma_{f \rightarrow b} m_f) = 0. \] (22)
which yields
\[ m_b(r) = \frac{\gamma_{f \to b}}{\gamma_{b \to f}} (c_1 + c_2 \ln(r)) \tag{32} \]

We must determine the constants \( c_1 \) and \( c_2 \). There is no radial current of motors (bound or free) in the vortex configuration. The condition of no radial current of free motors at the boundary implies
\[ \partial_r m_f(r) = 0 \text{ at } r = L, \tag{33} \]

therefore implying that \( c_2 = 0 \). The constant \( c_1 \) is determined by normalization
\[ \int d^2r (m_f(r) + m_b(r)) = N. \tag{34} \]

In the vortex configuration
\[ \int d^2r (1 + \frac{\gamma_{f \to b}}{\gamma_{b \to f}}) c_1 = N, \tag{35} \]

which gives
\[ c_1 = \frac{n}{2\pi} \frac{1}{(1 + \frac{\gamma_{f \to b}}{\gamma_{b \to f}})}, \tag{36} \]

with \( n \) the density of motor \( N/L^2 \).

The result above holds for purely tangential boundary conditions, consistent with the symmetry of the vortex. It will be modified \textit{vis. a vis} the simulation results both as a consequence of the (cartesian) latticization used to discretize the equations as well as by the four-fold symmetry of the simulation box. Both these factors will lead to a combination of the logarithmic and constant solutions above.

\[ \text{B. Single aster solution i.e. } T = -\hat{r} \]

We again assume radial symmetry for the bound and free motor densities. We choose \( \mathbf{C} = f(r)\hat{r} \), with \( f(r) \) such that \( \mathbf{C} \) is divergenceless \( i. e. \ \nabla \cdot \mathbf{C} = 0 \). We thus obtain \( f(r) = c_0/r \), with \( c_0 \) a constant. The radial current of free motors is \( -\partial_r m_f \hat{r} \) while the radial current of bound motors is \( -m_b \hat{r} \). The boundary condition that the total motor current vanishes at the boundary implies
\[ \partial_r m_f + m_b = c_0/r = 0 \text{ at } r = L. \tag{37} \]

This ensures that \( c_0 = 0 \) and therefore
\[ \partial_r m_f(r) = -m_b(r). \tag{38} \]
Eqn. 22 becomes
\[ \partial_r^2 r_m f + \left( \frac{1}{r} - \gamma_{b\rightarrow f} \right) \partial_r m_f - \gamma_{f\rightarrow b} m_f = 0. \]  
(39)

This is a second order differential equation whose solution is completely specified if the value of the function and of its derivative at the boundary are supplied. Given these boundary conditions, the free motor density can be obtained via a numerical solution using the Runge-Kutta method. The bound motor density is also easily determined via a radial derivative of the free motor density.

We now derive exact and asymptotic expressions for motor densities in the aster geometry. The general solution to the equation above is a combination of confluent hypergeometric functions and has the form
\[ m_f(r) = e^{\frac{1}{2}(\gamma_{b\rightarrow f}/r - \sqrt{\gamma_{b\rightarrow f}^2 + 4\gamma_{f\rightarrow b}^2} r)} \left[ c_1 F_1 \left( \frac{1}{2} - \frac{\gamma_{b\rightarrow f}}{2\sqrt{\gamma_{b\rightarrow f}^2 + 4\gamma_{f\rightarrow b}^2}}, 1, \sqrt{\gamma_{b\rightarrow f}^2 + 4\gamma_{f\rightarrow b}^2} r \right) + c_1 U \left( \frac{1}{2} - \frac{\gamma_{b\rightarrow f}}{2\sqrt{\gamma_{b\rightarrow f}^2 + 4\gamma_{f\rightarrow b}^2}}, 1, \sqrt{\gamma_{b\rightarrow f}^2 + 4\gamma_{f\rightarrow b}^2} r \right) \right]. \]  
(40)

The functions \( F_1 \) and \( U \) are the two solutions of the confluent hypergeometric Kummer equation. It is useful to define a quantity \( p \) given by
\[ p = \frac{1}{2} \left( 1 - \frac{\gamma_{b\rightarrow f}}{\sqrt{\gamma_{b\rightarrow f}^2 + 4\gamma_{f\rightarrow b}^2}} \right). \]  
(41)

Note that
\[ 0 \leq p \leq 0.5, \]  
(42)
with \( \gamma_{b\rightarrow f}, \gamma_{f\rightarrow b} \geq 0 \). The argument of the exponent in Eq. (40) is always negative for all \( \gamma_{b\rightarrow f}, \gamma_{f\rightarrow b} \geq 0 \). The coefficients \( c_1 \) and \( c_2 \) are determined by boundary and normalization conditions.

The boundary condition is that there is no total motor current at the boundary. i.e.
\[ \partial_r m_f(r) + m_b(r) = 0 \text{ at } r = L, \]  
(43)
since the radial current of bound motors in the aster configuration is \( J = -m_b(r) \hat{r} \). This can be used to determine \( c_2 \) in terms of \( c_1 \). We find that on imposing the no-current boundary condition, \( c_2 \) is very small compared to \( c_1 \) and is significant only when the system size is of
order the “correlation” length over which the density decays. We will assume (see below) that we can set $c_2 = 0$ to yield physically admissible solutions.

The constant $c_1$ can now be fixed by the normalization condition which requires the total number of motors (bound+free) be constant,

$$\int_0^L d^2r (m_b(r) + m_f(r)) = N.$$  \hspace{1cm} (44)

where $N$ is the total number of motors.

A physical argument for neglecting the $\gamma / (\gamma^2 + 4\gamma f + f^2) \gamma f / (\gamma^2 + 4\gamma f + f^2)$ term in comparison with the $U(1/2 - \gamma / (\gamma^2 + 4\gamma f + f^2))$ term which is clearly untenable on physical grounds. On the other hand, $U(1/2 - \gamma / (\gamma^2 + 4\gamma f + f^2))$ decreases monotonically with increasing $r$. Hence we retain only the $U(1/2 - \gamma / (\gamma^2 + 4\gamma f + f^2))$ part of the solution for $m_f(r)$.

To derive the asymptotics we begin with the integral representation

$$U(p, q, x) = \frac{1}{\Gamma(p)} \int_0^\infty e^{-xt} t^{p-1} (1 + t)^{q-p-1} dt.$$  \hspace{1cm} (46)

We relabel $(\gamma^2 + 4\gamma f + f^2) r = z$ and $1/2 (1 - \gamma / (\gamma^2 + 4\gamma f + f^2)) = p$ for notational convenience. We then obtain

$$U(p, 1, z) = \frac{1}{\Gamma(p)} \int_0^\infty e^{-zt} t^{p-1} (1 + t)^{q-p} dt.$$  \hspace{1cm} (47)

We now change variables to $u = zt$. The integral is then

$$\frac{1}{\Gamma(p)} \frac{1}{z^p} \int_0^\infty e^{-u} u^{p-1} (1 + u/z)^{q-p} du.$$  \hspace{1cm} (48)

Since $p$ is a small number between 0 and 0.5 we may expand the denominator binomially. The first term gives $\Gamma(p)$ and subsequent terms converge. Hence in the large $z$ (asymptotic limit), the integral is just $\Gamma(p)$. Therefore,

$$m_f(r) = c_1 \frac{e^{-r/\xi}}{\sqrt{\gamma^2 + 4\gamma f + f^2} r^p} \left( \frac{p}{r} + 1 \right),$$

$$m_b(r) = c_1 \frac{e^{-r/\xi}}{\sqrt{\gamma^2 + 4\gamma f + f^2} r^p} \left( \frac{p}{r} + 1 \right).$$
FIG. 6: Density profiles for bound motor densities. The profiles are shown for an aster in the regime $\gamma_{f\rightarrow b} = \gamma_{b\rightarrow f} = 0.5$, with $S = 0$. The density is chosen to be 0.5.

where the inverse of the “correlation” length is defined as

$$\xi^{-1} = \left| \frac{\gamma_{b\rightarrow f} - \sqrt{\gamma_{b\rightarrow f}^2 + 4\gamma_{f\rightarrow b}}}{2} \right| = \left| \frac{P\gamma_{b\rightarrow f}}{2p - 1} \right|. \quad (49)$$

The correlation length $\xi$ and the power-law exponent $p$ depend on $\gamma_{f\rightarrow b}$ and $\gamma_{b\rightarrow f}$. We see that the bound motor density in the aster case has an exponential fall modulated by a power-law tail instead of the pure exponential falloff predicted in the LK model.

Another limit in which an exact answer can be obtained is the following: If there is no interconversion between the two species of motors (i.e. $\gamma_{b\rightarrow f} = \gamma_{f\rightarrow b} = 0$), the equations of motion for free motors and bound motors decouple. The number of free motors and bound motors in the system are then conserved independently. The free motor density equation supports solutions of the form $m_f(r) = c_1 + c_2 \ln(r)$, where $c_1$ and $c_2$ are constants of integration. Imposing a vanishing current of free motors at the boundary constrains $c_2 = 0$. The other constant $c_1$ can be fixed from the condition that the total number of free motors is constant. The bound motor density then has the simple power-law behavior $m_b(r) \sim 1/r$. 
C. Comparison of the analytic results with simulations

These analytic results can now be compared to the results of direct simulations of the dynamical equations for single aster and vortex structures. We choose $T = \dot{r}$ in the full equations of motion for the motor densities given in Eqns. (4) and (5) to represent the aster. We then evolve these equations in time till the steady state is reached. We compare the motor profiles obtained in such simulations to profiles obtained from solving the ODE at steady state (Eq. 39) by a 4th order Runge-Kutta method. Free and bound motor densities at the boundary of the system are obtained by solving the full time-dependent equations (Eqns. 4 and 5). These are used as boundary value input to the Runge-Kutta procedure to facilitate direct comparison between simulation and analytic results.

Using the symmetry of the scaled equations Eqns. 4 and 5 discussed in Section II, we normalize the densities obtained by these two methods to the same constant value before comparing them. Figure 6 shows a plot of the distribution of bound motors in a single aster obtained from (i) the direct simulation (ii) the Runge-Kutta method and (iii) the exact solution outlined in the previous section. The parameter values are $\gamma_{f \to b} = \gamma_{b \to f} = 0.5$ and $m = 0.5$. Fig. 7 shows the comparison between simulations, the Runge-Kutta method and the exact solution for the free motor density profiles. While the data is noisy, particularly for

![Graph showing density profiles compared to simulations and exact solutions.](image)
FIG. 8: Density profiles for bound motor densities. The profiles are shown for a vortex in the regime $\gamma_{f\rightarrow b} = \gamma_{b\rightarrow f} = 0.5$ and $S = 0$. The density is chosen to be 0.5.

the bound motor densities, the agreement with the theoretically predicted result is satisfying.

Fig. 8 shows the distribution of bound motors in a vortex configuration obtained by fixing $T = \hat{T}$ in the full equations of motion for the motor densities given in Eqns. 4 and 5. The plot, of $m_b(r)$ vs. $r$, illustrates the slow, essentially logarithmic variation of the motor densities in such configurations, consistent with the analytic approach of this paper and of earlier work.

VI. SATURATION EFFECTS AND THE STABILIZATION OF ASTERS

So far, in our analysis, we have ignored the effects of interactions between bound motors. These motors, in their physical setting, have a finite size and move on a one-dimensional track, the microtubule. It is thus reasonable to expect that interactions between bound motors should become increasingly important at large motor densities. One can account for these interactions by simply requiring that more than one motor cannot occupy the same volume in space at the same time. Such “excluded volume” interactions have been used in earlier models for collective effects in molecular motor transport.

At the simplest level, accounting for such interactions leads to a non-linear (in general, also non-monotonic) dependence of the motor current on the density. This can be incorpor-
rated in our calculation by choosing a motor current of the form

\[ J_{mb} = A m_b f(m_b) T. \]  

(50)

The function \( f(m_b) \) should, in principle, be calculated from an underlying microscopic model. We will circumvent this necessity by simply assuming a convenient form purely for illustrative purposes which is (a) consistent with the requirement that \( A \) (the velocity) is density independent for small \( m_b \) densities and (b) saturates for large \( m_b \). One such choice is

\[ f(m_b) = 1 - \tanh(m_b/m_{sat}). \]  

(51)

The value \( m_{sat} \) limits the current of bound motors. When \( m_{sat} \gg m_b \) then \( f(m_b) \to 1 \) and we recover results discussed earlier. When \( m_{sat} \ll m_b \), the current reduces as \( f(m_b) \to 0 \). In the aster case \((T = \hat{r})\), Eq. 38 becomes

\[ \partial_r m_f(r) = -m_b(r)f(m_b). \]  

(52)

Therefore, the free motors obey

\[ \partial_r^2 m_f + \left( \frac{1}{r} - \gamma_{b \to f} f(m_b) \right) \partial_r m_f - \gamma_{f \to b} m_f = 0. \]  

(53)

This equation can now be solved as a boundary value problem using the methods described earlier.

Figure 9 shows bound motor densities \( m_b(r) \) as a function of \( r \) for different values of \( m_{sat} \). We have normalized each of the plots to the same value at the origin. We choose \( m_{sat} = 0.001, 0.1, 1 \) and 1000. An increased \( m_{sat} \) implies smaller saturation effects. The plots shown in Fig. 9 are normalized to unity at \( r = 1 \). Observe that reducing \( m_{sat} \) leads to far smoother variations of the bound motor density. Data for the associated free motor densities are similar and are not shown here.

VII. RELATIVE STABILITY OF ASTERS AND VORTICES

As we have seen in Section IV, single asters are unstable to single vortices for large systems, provided \( S = 0 \). This is surprising because both asters and vortices are equivalent topological defects – an aster can be transformed into a vortex by rotating all \( T \) vectors through \( 90^\circ \). However, motor density profiles in aster and vortex configurations are different.
FIG. 9: Effect of saturation on the motor density profile. As the effect of saturation is increased, the profile is smoother. The curves are labeled from left to right as $m_{\text{sat}} = 1000, 1.0, 0.1, 0.001$.

It is thus natural to seek an explanation for the relative stability of asters and vortices at $S = 0$ which proceeds from this observation.

Lee and Kardar rationalize the stability of vortices vis. a vis asters in the simulations in the following way: If $\epsilon = 1$, the right-hand-side of the tubule equation derived by LK can be interpreted as the functional derivative of a “free energy”. The motor density profile plays the role of a spatially modulated stiffness. This enables the calculation of the relative “free energies” of aster and vortex states. Smoother motor density profiles lead to lower “free energies”. The reduced energy of the vortex configuration, in which motor density profiles decay logarithmically, implies its increased stability as compared to asters, for which motor density profiles decay exponentially away from the core.

The competition between strain energies of asters and vortices thus implies a system-size dependence of “energies” and a cross-over length scale at which the energies of the two are comparable. For system sizes smaller than this length, asters are favoured while vortices are favoured for larger system sizes. This simple argument rationalizes the relative stability of aster and vortex states. We will use it to explain an intriguing feature of our data – the presence of stable asters for fairly large system sizes e.g. $L = 50$, in the $S = 0$ limit. At these scales and for equivalent parameter values, the LK model would have yielded a single vortex in steady state.
FIG. 10: A plot of the difference in energies of a single vortex and a single aster versus the system size $L$. The parameter values are $m = 1, \epsilon = 1$ and $S = 0$. The y-axis is plotted with a logarithmic scale. The point at which the energy of the vortex becomes lower than the energy of the aster shows up as the minimum in this curve. In the Lee–Kardar model the length scale at which the vortex becomes lower in energy is about four times smaller than in our model.

We adapt the Lee-Kardar argument to our model, using our analytic results for bound motor density profiles in asters and vortices. In Fig. 10, we show the modulus of the difference in energy of a single vortex and a single aster as a function of the system size for our model and for the Lee-Kardar model. We work at the same value of total motor density $m$ in each case, setting $\epsilon = 1$. Since the magnitude of “energy” scales in the two models differs, the behaviour of the energy difference is most clearly seen using a logarithmic scale for the $y$–axis. The point at which the vortex energy is reduced below the aster energy appears as the minimum in the curve. From the position of this minimum, we see that the crossover length scale above which asters are unstable to vortices is smaller in the Lee-Kardar model as compared to our model.

The fact that this crossover length scale lies between 50 and 100 in our units for length rationalizes our observation that the stable asters we obtain for $L = 50$ are replaced by stable vortices for $L = 100$. These results support, and add further credence to, the Lee-Kardar argument, at least in the $S = 0$ case. With finite $S$, of course, vortices are disfavoured altogether and generating stable aster structures is no longer an issue.
We now provide a qualitative explanation of three basic features of motor and microtubule arrangements at zero and non-zero \( S \). These are (i) the absence of vortices at non-zero \( S \), (ii) the presence of a small number of large asters at small \( S \) vs. (iii) the presence of a large number of small asters which increases as \( S \) for larger \( S \). Our approach is approximate and qualitative, based on “free energy” type arguments, analogous to those of Lee and Kardar.

Consider the limit in which \( \epsilon = 1 \) and the \( \nabla m \) term is obtained through a functional differentiation of the “free-energy” term

\[
E_S = \int d^2 x (\alpha \nabla \cdot \mathbf{T} + \frac{S}{\alpha} m_b)^2. \tag{54}
\]

A functional derivative of \( F \) with respect to the \( \mathbf{T} \) field generates the terms \( \alpha^2 \nabla(\nabla \cdot \mathbf{T}) \) and \( S \nabla m_b \). In the limit that \( \alpha \to 0 \), we obtain the \( \nabla m_b \) term of our equation of motion. (We prefer to work with a non-vanishing, although infinitesimal, value of \( \alpha \) and to consider the effects of varying \( S \), to avoid the singular behaviour which arises in the \( \alpha = 0 \) limit.) Our introduction of the term in \( S \) was, in fact, motivated by the observation that motors moving along two initially parallel microtubule configurations, act to bring them together, favouring a non-zero divergence. This physics, though incorporated in the simulations of Nédéléc et al., is ignored in the LK model.

The full “free energy” for the \( \mathbf{T} \) field is

\[
E = \int d^2 x \left[ -\frac{1}{2} \alpha |\mathbf{T}|^2 + \frac{1}{4} \beta |\mathbf{T}|^4 + \frac{1}{2} m_b(r)(\nabla \mathbf{T})^2 + \frac{1}{2} (\alpha \nabla \cdot \mathbf{T} + \frac{S}{\alpha} m_b)^2 \right]. \tag{55}
\]

We fix the modulus of \( \mathbf{T} \), thereby eliminating the first two terms, and concentrate on the relative energetics of states governed by the last two terms of the equation.

For the Lee-Kardar model, with \( S = 0 \), the stability of vortices over asters can be understood from simple comparisons of the relative energies of vortices and asters. First consider the case of a single aster. We choose a simplified profile for bound motors, assuming,

\[
m_b = A \quad r \leq \xi \]
\[
m_b = 0 \quad r > \xi. \tag{56}
\]

This represents, although approximately, the fact that microtubule densities are significant only over distances of order \( \xi \) from the core of the aster. The factor \( A \) is a normalization factor which ensures a fixed number of motors \( N \) in a system of typical size \( L \). We will work with a fixed overall density of motors \( \sim N/L^2 \) and examine the limit in which \( L \to \infty \).
In the $S = 0$ limit, the energy $E_A$ of the aster is dictated by

$$E_A^0 \sim \int_a^L d^2 r \ m_b(r)(\nabla T)^2 \sim A \log(\xi/a)$$

where we cut the integral off at a lower limit $a$ corresponding to a microscopic coarse-graining scale and have used the fact that $(\nabla T)^2 = 1/r^2$ for both asters and vortices. We now fix $A$ by normalization: since $\int_a^L m(r)d^2r = N = nL^2 \sim A\xi^2$, we obtain $E_A^0 \sim nL^2 \log(\xi/a)/\xi^2$. (Accounting for a more complex decay of the bound motor density does not change this result qualitatively.) Thus, for a system of size $L$ ($L \gg \xi$), imposing a fixed density of motor yields a quadratic increase of the energy with system size $L$.

We now repeat the same argument with a single vortex. Here, the relatively slower variation $m_b(r) \sim C_1 + C_2 \log(r/\lambda)$ yields $E_v^0 \sim \int_a^L (m_b(r)/r^2)rdr \sim \log(L/a)$, upto further logarithmic corrections. The prefactor is then independent of system size, leading to an overall logarithmic increase of energy with system size, a far weaker function than the quadratic dependence on $L$ of the aster. This implies that for sufficiently large $L$, the energy of the isolated vortex falls below that of a single aster, as first suggested by Lee and Kardar, in systems of sufficiently large sizes.

How are these arguments modified at finite $S$? Since simulations indicate that the state obtained at finite positive $S$ is a “lattice of asters” with the scale of the aster decreasing as $S$ is increased, we will compare the energies of single vortex configurations with energies for an assembly of asters (“mini-asters”) of typical size $\sigma$. We imagine that the $L \times L$ system is subdivided into $\sigma \times \sigma$ units and place an aster in each one of these sub-units. For a system of linear size $L$, the number density of such asters is $\phi$. For inward pointing asters, as obtained in our calculation, the divergence $\nabla \cdot \mathbf{T} = -1/r$. Consider first the term

$$E_S \sim \int d^2 x \left[ \alpha \nabla \cdot \mathbf{T} + \frac{S}{\alpha} m_b(r) \right]^2.$$  (58)

Now mini-asters are (i) assumed small and (ii) obey boundary conditions which differ from the case of the single system-size spanning aster. Bound motor profiles are then, in general, combinations of the two solutions obtained earlier rather than the single one which yielded the exponentially damped form used in our earlier analysis. Also, the close proximity of the many mini-asters formed indicates a slower than exponential variation of the bound motor densities about each one. Let us assume that motor densities in such mini-asters adjust in order that the following motor density profile is obtained: $m_b(r) \sim \alpha^2/Sr(r \leq \sigma)$ and
$m_b(r) \sim 0(r > \sigma)$. This ensures that the contribution of the term above is cancelled. Note that the bulk of the contribution to the energy of a mini-aster comes from the region $r \leq \xi$; the contributions from larger regions is negligible provided $\xi \sim \sigma$.

We first calculate the energy $E_{1mA}$ of a single such mini-aster configuration. This is obtained from the integral

$$E_{1mA} = \int_{a}^{L} d^2r m_b(r)(\nabla T)^2 \sim \frac{\alpha^2}{S} \int_{a}^{\sigma} dr \frac{1}{r^2} \sim \frac{\alpha^2}{Sa}$$

The number of motors in a single mini-aster is obtained from

$$N_{1mA} \sim \int_{a}^{\sigma} m(r) dr \sim \frac{\alpha^2 \sigma}{S}$$

The total energy $E_{mA}^T$ of the system of miniasters is then

$$E_{mA}^T \sim \frac{\alpha^2}{Sa} \phi L^2$$

The constraint $n = \phi N_{1mA}$ yields

$$\phi \sim \frac{S}{\alpha^2 \sigma}$$

illustrating how the number of asters increases as $S$ is increased. The total energy corresponding to a fixed areal density of motors $n$ is then easily derived as

$$E_{mA}^T \sim \frac{n L^2}{\sigma a}$$

We now compare this with the energy of a single vortex at non-zero $S$, computed assuming that the motor density profiles are the same as in the case in which $S$ was zero. This is obtained as $E_v \sim S^2 n^2 L^2 / \alpha^2$, yielding the ratio

$$\frac{E_{mA}^T}{E_{mA}^T} \sim \frac{n S^2 \sigma a}{\alpha^2}$$

We may also compare the energy of an assembly of mini-asters with the energy of a single aster. Arguments similar to those above yield $E_A \sim n^2 S^2 L^2 / \alpha^2$, and thus

$$\frac{E_A}{E_{mA}^T} \sim \frac{n S^2 \sigma a}{\alpha^2}$$

Note that both these arguments indicate that as $\alpha$ is reduced towards zero (or $S$ is increased from a non-zero value), both single asters and single vortices are unstable to an array of mini-asters. At infinitesimal $\alpha$, provided $S$ is non-zero, our results indicate that the number density of mini-asters increases with $S$ (linearly in the simple argument given here), with the size of each aster decreasing in proportion. The arguments given here rest on the assumption that the motor distribution in asters adjusts so as to minimize the cost for the term involving $S$. No such adjustment can lower the energy of single vortex configurations.
VIII. CONCLUSIONS

This paper presents a hydrodynamic theory of pattern formation in motor-microtubule mixtures, accounting for the effects of confinement. We show that the influence of the boundaries on pattern formation can be considerable, by illustrating how either asters or vortices can be formed depending on how the orientation of microtubules is fixed at the boundary. We have explored the parameter space of $\epsilon, m$ and $S$ systematically, describing the variety of configurations obtained. We obtain density distributions of free and bound motors corresponding to the final microtubule configurations. Such plots may be compared directly to experiments. We have also compared analytic predictions for motor density profiles in isolated vortices and asters with simulation data. Our results presented here complement our earlier work on pattern formation on much larger systems, in which the effects of boundaries were minimal[11].

One technical improvement would be to account for variations in the local density of microtubule, as opposed to only their orientation. We could then account for the density dependence of quantities such as $\gamma_{f \rightarrow b}$. More information from experiments, performed in confined geometries using motors with a range of different processivities would also be useful in clarifying some of the issues which relate to the simulations described here. It would also be interesting to search for the novel configurations we obtain here in different regimes of parameter space, such as the “flag”, the distorted vortex and the “outward aster”.

As we have emphasized here and in earlier work[10, 11], the set of hydrodynamic equations we motivate and use allow for a minimal yet complete description of the patterns formed in mixtures of motors and microtubules. We have suggested elsewhere[10] that it may be useful to think of spindle formation itself as a pattern formation problem which can be modelled using continuum hydrodynamical equations in a small number of variables. Further work relating to this program is in progress.

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[1] Molecular Biology of the Cell, 4th ed., B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts,
Microtubules in vitro undergo an alternating process of rapid, stochastic polymerization and depolymerization unless stabilized.

Since the experiments are performed in a confined geometry, the otherwise long-ranged hydrodynamic interaction is screened because the boundaries of the system act as a sink for momentum. Neglecting the role played by hydrodynamics is therefore justified.

Conventional kinesins are +end directed i.e. they move towards the + end of microtubules, whereas NCD’s are − end directed.
The nature of the states obtained in this calculation are very similar to the ones obtained by Lee and Kardar. Our critique of the Lee-Kardar model above applies to these results as well.

[22] K. Kruse and F. Julicher, Phys. Rev. Lett. 85, 1778 (2000); Phys. Rev. E 67, 051913 (2003); K. Kruse, S. Camalet, and F. Julicher, Phys. Rev. Lett. 87, 138101 (2001).

[23] J. Toner and Y. Tu, Phys. Rev. E 58, 4828 (1998); J. Toner and Y. Tu, Phys. Rev. Lett. 75, 4326 (1995).

[24] We only fail to obtain “bundles”, a disordered phase obtained at still higher densities of motors.

[25] We find it convenient to refer to the distinct states seen in the experiments and our simulations as “phases”, insofar as quantitative distinctions can be made between them and they are well contrasted from the point of view of the experiments. However such terminology is, strictly speaking, inaccurate since we believe that sharp qualitative distinctions between several of these states, such as the disordered phase, the aster-vortex mixture and the lattice of vortices cannot be made – a more generic name would be a disordered/aster-vortex mixture dominated by arrested states at low motor density[18] in this regime.

[26] W. Press, S. Teukolsky, W. Vellerling and B. Flannery, Numerical Recipes in C, Cambridge University Press (1998).

[27] Y. Aghababaie, G.I. Menon and M. Plischke, Phys. Rev. E, 59, 2578 (1999).