Chapter 1

Introduction

If living cells were machines built from a framework of struts and diverse material components, driven by an internal Carnot engine, then our well established laws of mechanics and thermodynamics of small, open systems would have sufficed to describe its dynamical state and mechanical response [1, 2]. The living cell (Fig. 1.1) is much more complex: its architecture is self-organised, reconstructing continually in response to a variety of internal and external cues [2, 4]. This is facilitated by an incredible array of protein machines which have evolved to perform a range of tasks such as (i) *catalysts*, which facilitate or inhibit biochemical reactions, (ii) *motors*, which facilitate transport of *material*, e.g., proteins and lipids, across the cell and (iii) *signaling molecules*, which facilitate the *transfer of information* [4, 5]. Some of these protein machines are agents for construction (and deconstruction) of supramolecular structures such as protein filaments and lipid membranes. Lipid membranes partition specific chemicals into morphologically distinct organelles within the cell, as well as encapsulate chemicals for transport between organelles [5]. Protein filaments provide scaffolding and structural stability to the cell and its organelles; in addition they also serve as *tracks* for the transport of material within the cell [5, 6, 7].

What lies at the heart of this uniquely regulated behaviour of the living state is *activity*. The living cell is maintained in a state far from chemical equilibrium, by producing high levels of stored chemical energy in the form of Adenosine triphosphate (ATP) or Guanosine triphosphate (GTP) [6]. This stored chemical energy is the source for activity, fuelling protein machines, which when recruited to precise locations on filaments or membranes, produce local mechanical stresses. These active mechanical stresses can give rise to (i) local deformations or changes in the state of the filaments or membranes, (ii) directed transport and (iii) local sources of noise [8]. The change in the state of filaments and membranes resulting from activity, in turn influence the active process. This tight coupling between local state change of the filaments and membranes, mechanical stress, and chemical reactions is a hallmark of active processes [8].

In formal terms, active systems are simply a collection of ‘particles’ (filaments + motors, membranes + pumps), *driven* by internal energy sources, as a result of which they give rise to local mechanical stresses [8], which in turn affects the configuration of particles. The formal study of the physical consequences of activity constitutes a special example of non-equilibrium statistical mechanics of driven states of matter. Thus one may study both single particle and collective behaviour of active particles: the steady state patterns [9, 10, 11, 12, 13], hydrodynamics [14, 15] and rheology [15, 16, 17] are unique and show

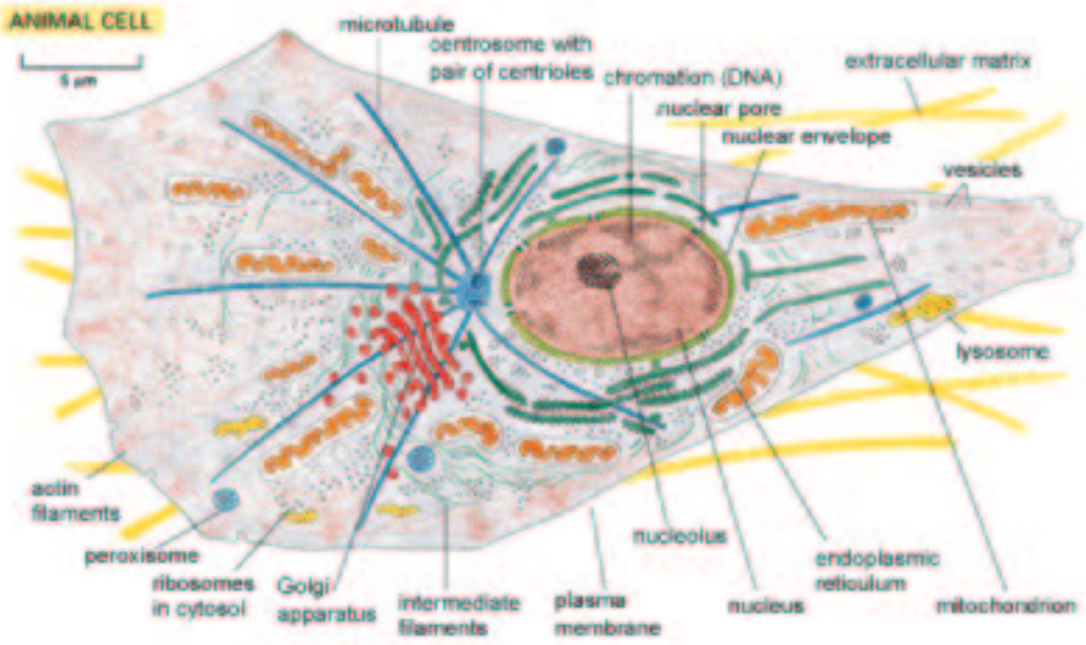

Figure 1.1: Schematic of a typical animal cell, showing the organization of the filaments [3].

qualitative differences from their passive counterparts [15, 16, 17, 18]. Indeed one of the most dramatic consequences of activity is movement : active systems exhibit *moving steady states* [13, 15, 19]. It is hoped that the study of the physical consequences of active systems will provide the framework to understand complex cellular processes such as intracellular trafficking, cell mechanics and cell motility, among others.

In this thesis, we focus on cellular *filaments*, both passive and active. We will study their mechanics and transport with particular emphasis on the coupling between mechanics and chemistry. In chapter 2, we take the example of DNA-protein (un)binding kinetics, to illustrate that the chemical kinetics of (un)binding of the protein is affected by the scale-dependent mechanical stiffness of the DNA heteropolymer. In chapter 3, we study the collective behaviour of active filaments and see how activity manifests through the organization and the novel mechanical response of a suspension of filaments. In chapters 4 and 5, we develop a theoretical framework to understand active transport of cargo vesicles on static filaments. We first discuss bidirectional transport of a single vesicle driven by processive motors on a filament (chapter 4). The transport properties are regulated by the chemical (un)binding kinetics of motor proteins. In chapter 5, we study collective transport of interacting vesicles

on a filament, within a new 4-species model belonging to the class of interacting lattice gas models.

1.1 Brief description of cellular filaments : DNA, actin and microtubules

In this brief description of three cellular filaments, Deoxyribonucleic acid (DNA), actin and microtubules, we will only focus on their structural, dynamic and mechanical aspects. These polymers are built from monomeric units, some with the aid of ATP/GTP. They are typically semiflexible, a feature characterised by a persistence length [20], defined as the typical length over which tangent vectors to the curve representing the polymer are uncorrelated due to thermal fluctuations. In *in-vivo* conditions, they typically organize into mesoscale structures, by coupling to specific proteins [2, 5]. Being polar, they can form tracks on which motor proteins can transport cargo vesicles and organelles in a directed manner [5, 7, 21, 22].

Deoxyribonucleic acid (DNA) is a semiflexible heteropolymer whose monomeric units are the four nucleic acids: Adenine(A), Cytosine(C), Guanine(G) and Thymine(T). It is a double helix formed by two complimentary strands. The complimentary strands comprise of a sugar phosphate backbone held together by hydrogen bonds between the G-C and A-T base pairs [5]. The bend persistence length of the DNA is $\simeq 53\ nm = 156$ bp (base pairs) [23, 24] and its Young's modulus is around 1 GPa [4]. Nuclear processes such as transcription and replication involve attachment of specific proteins to the DNA-strand in a site specific manner. The binding typically leads to a local distortion of the DNA [25, 26], which changes its elastic properties.

Actin filaments are generated by the polymerisation of monomeric actin to form tight helical strands of diameter 5-9 nm. They are polar and semi-flexible, with a persistence length of 17 μm [27]. They are highly dynamic - their polymerisation and depolymerisation is regulated by the hydrolysis of ATP. *In-vivo*, they can organize into a variety of structures - linear bundles, two-dimensional networks, branched networks and three-dimensional gels - by means of temporary and permanent crosslinkers [2, 5, 6]. In conjunction with myosin, they apply contractile forces on the cell. They are involved in a variety of cellular functions, such as providing mechanical support to the cell, cell motility, determining cell shape and serving as tracks for intra-cellular transport [2, 5, 6].

Microtubule filaments are formed by the polymerisation of $\alpha - \beta$ tubulin dimers. The dimers are 8 *nm* long and under *in-vivo* conditions, they assemble to form a polarized tubule

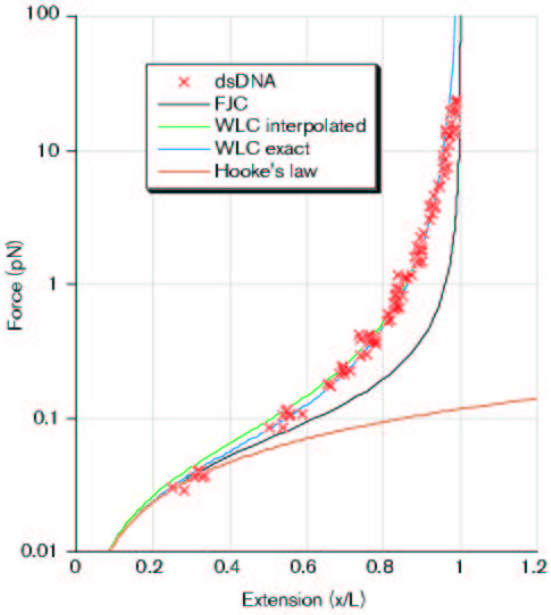

Figure 1.2: Force versus extension data (red crosses) for DNA λ phage DNA (48502 *bp*) pulled by magnetic beads in 10mM Na^+ buffer. The data are fit to a WLC model solved numerically (WLC exact), using persistence length $L_p = 53nm$. The corresponding Freely Jointed Chain (FJC) curve, WLC interpolation (using an approximate interpolation formula [30]) curve and Hooke's law force curve, assuming the same persistence length are also shown [23].

with a 25 *nm* diameter [5, 28]. *In-vivo* microtubules are highly dynamic objects - their polymerisation and depolymerisation is regulated by the hydrolysis of GTP. They are intrinsically asymmetric, with the (+) end chemically and morphologically distinct from the (−) end. This polarity is recognized by the motor proteins, which move along this track in a directed manner, carrying vesicle cargo along with it [7]. In cells, they are organized roughly radially, with the (+) end pointing towards the periphery and the (−) end being at the microtubule organizing center (MTOC) located near the nucleus (Fig. 1.1) [7]. The persistence length of a microtubule is ~ 1 *mm* [4] and thus suitable for long distance intracellular transport. Its Young's modulus is ~ 2 *GPa* [4], similar to that of hard plastic.

1.2 'Single-Particle' description of filaments

1.2.1 Passive Filaments

At scales much larger than its intrinsic pitch ($\simeq 3.4$ *nm* = 10 bp for DNA), the mechanical properties of passive, semiflexible filaments such as DNA and actin are governed primarily

by bending, twisting and stretching [29, 30, 31]. Single molecule experiments, such as those using optical tweezers, measure the force-extension curves of these filaments. For a DNA, free to swivel at one end, the force-extension curves (Fig. 1.2), show an initial Hookean regime, arising from entropic elasticity, before rising sharply. A successful model that explains a whole variety of force-extension curves of DNA is the Worm like chain (WLC) model, which represents the DNA by an inextensible continuous curve of total length L, parametrized by an arc length, s. In this model, the elastic energy (in units of thermal energy k_BT) stored in a particular conformation is written in terms of its local curvature, twist and stretch, as,

$$\begin{aligned}\frac{\mathcal{H}}{k_BT} &= \frac{1}{2}\int_0^L ds\left[A(\Omega_1^2+\Omega_2^2)+C(\Omega_3-\omega_0)^2+B\omega_0^2\alpha^2+2D\omega_0(\Omega_3-\omega_0)\alpha\right.\\ &+ \left. 2G(\Omega_3-\omega_0)\Omega_2+2K\omega_0\Omega_2\alpha\right]. \qquad (1.1)\end{aligned}$$

Here, $\Omega_{1,2}$ are the bending strains, $\Omega_3-\omega_3$ is the twist strain and α is stretching strain. The coefficients A and C are the bend and twist persistence lengths, ω_0 is the unstressed filament's helix density and B reflects the intrinsic stretchability of DNA. The parameter G is the twist-bend coupling, D is the stretch-twist coupling and K measures the coupling between stretch and bend [31, 32, 33].

The curve in Fig. 1.2 can be fit by one parameter, the bend persistence length [23, 24]. The bend persistence length for DNA measured this way is about 53 nm [23, 24] while the twist persistence length is about 75 nm [29, 34]. The bend persistence length of actin is around 17 μm [27].

1.2.2 Active Filaments

Active filaments, such as cellular actin and microtubules are maintained singly and collectively out of equilibrium, both by processive motors [2, 4] and continuous polymerization and depolymerisation [6]. Motors, driven by ATP hydrolysis, move along filaments, producing active forces and torques on the filaments which result in directed translational and rotational movement. On the other hand, it is not obvious how polymerisation - depolymerisation processes in cellular filaments are active. To see why this constitutes an active non-equilibrium process, consider the dynamics of an equilibrium 'living' polymer. For an equilibrium 'living' polymer undergoing polymerisation-depolymerisation, the length fluctuates in a diffusive manner. The diffusion coefficient, $D = k_{on}$ c δ^2, where k_{on} is the on-rate for polymerization, c is the monomer concentration, and δ is the increase in length due to

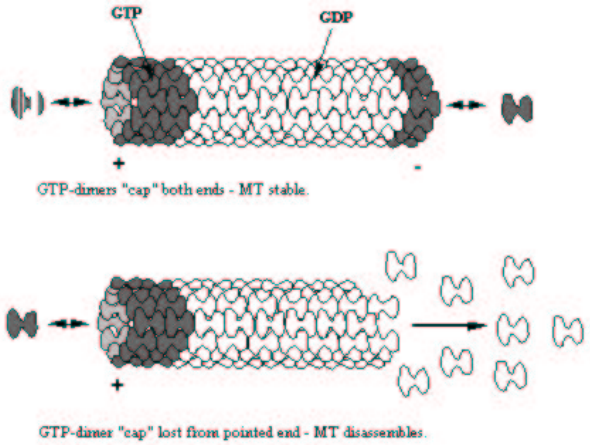

Figure 1.3: Treadmilling in microtubules: (a) When both the plus and minus ends of the microtubule has GTP-containing subunits, then the microtubule is stable with polymerisation at both ends. (b) During treadmilling, the rate hydrolysis of GTP to GDP at the minus end is faster than GTP containing subunit addition, leading to loss of the "cap" and depolymerization at the minus end. At the plus end the GTP containing cap keeps on adding new subunits, so that there is a net polymerisation at plus end and a net depolymerisation at minus end [37].

the addition of a monomer [6, 35]. For a microtubule filament, $k_{on} = 5 \times 10^6\ mole^{-1}\ s^{-1}$, c = 10 μM and $\delta = 0.6\ nm$. If one uses the expression for equilibrium diffusion coefficient to compute the standard deviation of the length of the filament, then it turns out that the standard deviation of the length over 1 *min* is 46 *nm* and over one week it is only 4.7 μm. This is to be contrasted with what actually happens with individual microtubules in the cell. Microtubules can switch between a growing phase (with rate $\simeq 1\ \mu m/min$) and a shrinking phase (with rate $\simeq 10\ \mu m/min$) on timescales of minutes [6, 36]. It is seen that neighbouring microtubules can be in different phases indicating that length fluctuations in microtubules is not due to fluctuations in monomer concentration.

In general, activity affects individual cellular filament properties in three different ways:

(i) Activity affects the polymerisation-depolymerisation kinetics of the filaments, such that there is net polymerisation at one end of the filament and net depolymerisation at the other end, in a process called *treadmilling* (Fig. 1.3) [6]. This results in the generation of non-equilibrium stresses. (ii) These active stresses, in general, produces movement. For instance, the coupling of polymerising actin with the cell membrane results in cell motility [38, 39]. (iii) Activity drives motor proteins, which bind to filaments and generate forces and torques between the filaments, inducing relative motion [6, 17].

1.3 Collective description of active filaments

The collective properties of passive and active filaments at large scales is best described within a hydrodynamic framework. The hydrodynamics of passive filaments is well understood [20]; in this section we will describe only those features of the hydrodynamics which bring out differences between active and passive filaments. This is highlighted by the *in-vitro* experiments described below.

In-vitro experiments done on actin-myosin solutions have revealed the role of motor activity in generating contractile forces in filaments. Myosin's motor domain binds to actin filaments and uses ATP hydrolysis to generate force to move along the polar actin filaments. This force induces collective sliding of the filaments and produces local stresses [17].

In-vitro experiments on a suspension containing tubulin, kinesin and ATP have revealed a whole range of dynamic phases and pattern formation [9]. Tubulin polymerises to form dynamic microtubule filaments. The kinesin motors attach to the microtubules and in presence of ATP, move towards the microtubule plus ends and form dynamic crosslinks between the microtubules. In a confined cylindrical geometry, microtubules polymerizing from an initial homogenous solution of tubulin monomers, first organize into a symmetric aster. As the microtubules continue to grow, the finite geometry causes them to buckle. The centre of the aster becomes unstable and a vortex structure is formed. In an unconfined geometry, further self-organization of previously formed structures of asters and vortices are seen. The final patterns depend on the initial concentration of the molecular components. At low concentration of motors, a lattice of vortices forms, but at slightly higher concentration, a lattice of asters can be observed. Finally at even higher motor concentration, the microtubules form bundles [9]. In the cellular context however, the occurence of different organizations is not necessarily triggered by precise variations of the protein concentration, but rather on a variety of regulatory processes such as binding of associated proteins [40]. Thus, the collective behaviour of filaments lead to the formation of various kinds of structures, regulated by activity through ATP or GTP hydrolysis.

In-vitro experiments done with actin-myosin II and ATP showed that myosin II has a significant effect on the network rheology — activity reduces the stress relaxation time in a concentrated polymer solution [17]. Rheological measurements show that the storage modulus (G') is decreased by around 40%, on addition of ATP, as compared to the solution without ATP. Most of the filaments displayed sliding in the presence of ATP and were immobilized under ADP conditions. Thus, the macroscopic rheological and transport properties of active

filaments are controlled and regulated by activity and are very different from a collection of passive filaments.

Activity also plays a role in intracellular transport by the motor proteins. The motors use the filament track to transport cargo and organelles, whose spatial distribution is regulated by motor-filament binding kinetics driven by activity [7, 21].

To understand these different driven phases that active particle suspensions exhibit and their rheological response, we resort to a hydrodynamic description, as developed in [10, 14, 16]. The idea is to write down equations of motion to describe the large-scale, long-time dynamics of the active particle systems, similar in spirit, to the equations of passive hydrodynamics. This approach, in principle, can describe the behaviour of a wide class of active systems, such as actin-myosin complex, bacterial suspensions, moving flocks of birds and swimming fishes [13, 15]. In analogy with equilibrium hydrodynamics, active particle systems exhibit distinct phases, which can be classified on the basis of their symmetries. As with passive systems, their hydrodynamics can be described by a small number of hydrodynamic variables. The fluid is described in terms of coarse grained number density $\rho(\mathbf{r}, t)$ and velocity $\mathbf{v}(\mathbf{r}, t)$ fields. The Navier-Stokes equation describing the hydrodynamics of a simple incompressible fluid [41], is given by,

$$\frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v}.\nabla)\mathbf{v} = -\frac{1}{\rho}\nabla p + \frac{\eta}{\rho}\nabla^2\mathbf{v} \tag{1.2}$$

In addition, for an incompressible fluid, $\boldsymbol{\nabla} \cdot \mathbf{v} = 0$. Using the incompressibility condition, the pressure, p can be eliminated. The microscopic features of the fluid are represented by a single phenomenological parameter, the dynamic viscosity η. Once this parameter is determined from experiments or from more microscopic models, one can solve equation (1.2), to predict the velocity profile at all times.

This hydrodynamic description is appropriate to phenomenan at length scales much larger than the mean free path and time scales much larger than the average collision time. To identify the relevant hydrodynamical variables, we simply look at those variables which survive at late times. These correspond to variables which obey conservation laws like the number density, momentum density and broken symmetry variables [13]. The relevant terms which appear in the continuum equations for these hydrodynamic variables are terms which are important at large length scales and long time scales and which are not ruled out by symmetries and conservation laws. For instance, the symmetries which appear in the Navier-Stokes equation are rotational invariance, space and time translation invariance and invari-

ance under Galilean transformations. At large length and time scales, it suffices to keep the lowest order terms in space and time derivatives, consistent with symmetry.

Early theoretical modelling of the collective behaviour of large number of active particles focussed on the phenomenon of flocking among organisms, e.g., flocking of birds [13, 19]. In particular these models noted the striking analogy between flocking and ferromagnetism. The velocity vectors of individual birds resemble the individual spins in a ferromagnet, which on an average point in the same direction. In the ordered flocking state, the average centre of mass velocity of the flock acquires a nonzero value, producing spontaneously symmetry broken moving steady state. This spontaneous symmetry breaking happens in all dimensions, $d \geq 2$. This is to be contrasted with the absence of long range order in equilibrium spin systems in 2-dimensions [42].

In describing the collective behaviour of a suspension of cellular filaments or bacteria, one needs to include the dynamics of the fluid medium. The total momentum of the system (particles + fluid) is a conserved hydrodynamic variable. Thus to describe the collective behaviour of such systems, one has to formulate hydrodynamic equations for the variables : c, the concentration of the filaments, **p**, the broken symmetry variable associated with average drift velocity of the active filaments with respect to the solvent, and **g**, the total momentum density. An active particle, on long time scale acts like a permanent force dipole. A collection of such active filaments gives rise to active stresses. The deviatoric part of this active stress, to leading order, is given by [14],

$$\sigma^a(\mathbf{r},t) = Wc(\mathbf{r},t)\left(\frac{\mathbf{p}\,\mathbf{p}}{p^2} - \frac{1}{3}\mathbf{I}\right), \tag{1.3}$$

where the magnitude and *sign* of W characterises the nature of the elementary force dipoles [14, 16].

Thus activity generates flow. For a suspension of polar filaments it can lead to an average drift velocity of the active filaments with respect to the surrounding fluid medium [16]. In chapter 3, we will derive the equations of motion for an active-filament suspension, from which we will obtain steady state patterns, hydrodynamic flows and rheology of the active suspension.

1.4 Prelude to chapters

1.4.1 Chapter 2 : Sequence-dependent DNA elasticity - Implications for DNA-protein binding

A variety of proteins such as RNA polymerase and transcription factors, bind to DNA in order to initiate and perform tasks such as transcription and replication. In each instance, the protein locally distorts the DNA in the process of binding. Experiments on the binding of 434 repressor (involved in transcription) [26], showed that it distorts the DNA over a scale of 12 bps upon binding.

In this chapter, we ask whether this elastic deformation of the DNA filament is sensitive to the sequence of the base-pairs over that scale. We answer in the affirmative. This implies that the (un)binding kinetics of a DNA-binding protein depends on the elastic properties of DNA *in a sequence dependent manner*. This suggests that even for non-specific binding, the kinetics of DNA-protein binding is sequence dependent. Thus far from being a passive substrate wherein biological function happens, we believe that the underlying filament may regulate the process itself.

We study the 'sequence'- distribution of thermally averaged global and local elastic properties of a DNA random heteropolymer of a fixed length N, within the simple WLC model. Using a mapping to the disordered Heisenberg chain, we arrive at a number of qualitative results, on the form of the distribution function of the thermally averaged end-to-end distance $\langle R^2 \rangle$, and its moments. For long, $N \to \infty$ chains, this distribution is Gaussian; for shorter chains, there is a crossover to an exponential distribution, with the most probable end-to-end distance deviating significantly from the mean. Further, the distribution of local quantities related to the thermally averaged tangent-tangent correlator are typically broad, even in the thermodynamic limit, *i.e., they do not self average*. We argue that this scale dependent 'sequence' sensitivity should have important biological implications, specifically for the binding of proteins to DNA — we present a simple model calculation of the binding/unbinding kinetics of DNA-binding proteins and give numerical estimates for the human DNA-repair enzyme HOGG1.

1.4.2 Chapter 3 : Active oriented filaments — shear stabilization and rheology

In this chapter we study the collective behaviour and mechanical response of active fila-

ments such as actin-myosin and motor-microtubule complexes.

Theoretical studies focussing on the rheological properties have looked at the interplay between activity, flow and order [16]. These studies have predicted novel behaviour of such systems and sharp departures from the rheological behaviour of their passive counterparts. For instance, for active suspensions there is an active enhancement or reduction of viscosity on approaching the transition to the orientationally ordered phase from an isotropic phase. This in turn can lead to a mitigation of shear thinning effects and in some cases to shear thickening [16]. This is in contrast to the passive system, where the onset of orientational order invariably leads to shear thinning. The question we ask is, what is the rheological response of this active suspension when it is driven across the orientational transition.

However it has been shown that the orientationally ordered phase of such active particle suspension is hydrodynamically unstable [14].

In this chapter we study the effect of an externally imposed planar shear on the stability of the orientationally ordered active phase. We proceed by setting up coarse-grained equations governing the hydrodynamic velocity, broken symmetry variable associated with the polarization vector defining the average drift velocity with respect to the fluid and the concentration of the active filaments. We then look at the stability of the homogeneous oriented steady state in the presence of the imposed shear flow.

We find that a sufficiently large shear rate can overcome the instability caused by the active stresses and stabilize the orientationally ordered phase. We show that a dimensionless *active* Peclet number, the ratio of the active stress to the externally applied shear stress, determines the phase stability. We obtain the non-equilibrium stability diagram as a function of this dimensionless number and alignment parameter. The rheology of the stabilized active oriented phase exhibits interesting behaviour; the orientationally ordered state has a non-zero, anisotropic prestress in contrast to equilibrium nematics.

1.4.3 Chapter 4 : Active bidirectional transport of vesicles on microtubules

In chapter 4, we study the role of activity in the transport of cargo vesicles on cellular filaments. More specifically, we focus on bidirectional transport of vesicles and organelles on microtubules.

One of the striking features of the cell is that its constituents, the organelles and the innumerable transport vesicles are spatially organized. This heterogenous organization within the

cell is maintained actively and dynamically, employing different mechanisms [6, 7]. Much attention has been focussed on the two related questions,

How is this spatial organization (often polarized) achieved?

How is transport regulated ?

In-vitro studies done using melanophore cell extracts, have exhibited bidirectional transport of pigment granules on microtubules by multiple oppositely directed motors. Similar nature of experiments have been done to study axonal transport in nerve cells. It has been observed that regulation of the activity and (un)binding of motors lead to a change in the macroscopic organization of the vesicles and organelles within the cell, which under certain physiological conditions can lead to a polarized distribution of vesicles.

In this chapter, we develop a 'single-particle'(vesicle) transition rate model [43] for bidirectional transport. In this model, the state of the vesicle is described by the number of plus-end directed motors (kinesin) and minus-end directed motors (dyenin), carried by the vesicle cargo, which are attached to the filament. We then derive the general master equation governing the time evolution of the state of the vesicle. Next, we consider microscopic models for the form of the velocity of the vesicle and the (un)binding rates of the motors in a given state. With these inputs, we determine the steady state solutions of the master equation and various macroscopic transport properties, such as, distribution of the velocity of the vesicles, the distribution of reversal times of the vesicles, the first passage time of unbinding of the vesicle from the filament and the average number of the motors attached to the microtubule.

We quantitatively predict how motor binding affinity of kinesin and dyenin would lead to changes in the macroscopic distribution of the vesicles and their velocities. We see that increasing the efficiency of binding of one kind of motor relative to the other, can lead to polarized distribution of the cargo vesicles and a skewed distribution of velocities. Similar efficiency of binding for both kinesin and dyenin results in no net directional transport of vesicles. We make qualitative comparisons of our predictions with experimental data obtained from tracking individual vesicle trajectories [44] and find broad agreement of certain gross features such as occurence of multiple peaks in the distribution of the velocities of the vesicles.

Our hope is that such models, in conjunction with vesicle tracking experiments, would be able to shed light on the microscopic mechanisms of (un)binding and movement of vesicles by motor activity.

1.4.4 Chapter 5 : Collective transport of interacting vesicles on microtubules

Many macroscopic features of vesicle transport in controlled *in-vitro* experiments may be understood in terms of single-particle models. However, in the over-crowded environment of the cell, one cannot ignore interactions between vesicles. Further, the effect of finite boundaries on the transport properties can be significant, as cargo vesicles are loaded and off-loaded at specific locations within the cell.

We present a simple minimal model for the collective transport of vesicles, which incorporates both the interaction between vesicles and the effects of finite boundaries. In this minimal model, we restrict the maximum number of attached motors of either kind to 1. We incorporate the effects of the boundaries and the interaction between the vesicles through excluded volume effects. The dynamics consists of; (i) the translation of the vesicles on 1-d lattice, and (ii) the inter-conversion between the states of the vesicles. We derive equations of motion with these dynamical rules, and obtain the steady state solution and the corresponding phases in a specific limit - when the inter-conversion dynamics is much faster than translation- using a mean-field analysis. We obtain phase boundaries and the entire phase diagram using a domain wall approach [45], and find good agreement with Monte-Carlo simulations done in this limit. We illustrate qualitatively how (un)binding kinetics, effects of excluded volume and finite boundaries can influence the macroscopic phases characterizing collective state of the vesicles. We believe that this 4-species model, is a minimal model for the dynamics of interacting vesicles undergoing bidirectional transport.

1.5 Conclusions

In this thesis, we look at the mechanics of and transport on cellular filaments. Our study reveals the crucial role played by activity in determining individual filament behaviour and shaping the collective response of these filaments. It also highlights the contrast in the behaviour of active filaments and their passive counterparts. While the mechanics and transport within the living cell is enormously complex, we have, in this thesis, attempted to construct *primitive* models which highlight *basic* mechanisms and principles underlying the workings of this intricate ‘machine of life’. For doing this we have liberally taken recourse to our familiar laws and techniques of non-equilibrium statistical mechanics, with the hope that such an exercise will shed some light on the *actual* processes occuring within the cell.

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