Semiflexible Filaments in Entangled Solution

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Abstract

Dense environment (entangled state) of filaments constrains their thermal movement. In particular, for a semiflexible filament, the transverse motility is highly limited to its axial direction, with the result the fluctuation of normal modes of the conformation of the filament is also largely suppressed. In this paper, we study how the motility of a semiflexible filament in entagled solution is modified by comparing it to that in dilute solution based on a simple model. We also expect to experimetntally demonstrate that the thermal fluctualtion of normal modes of a semiflexible filament, such as single-walled carbon nanotubes (SWNTs), is modified by the entaglement of other filaments. This helps us understand complex behaviors of semiflexible filaments observed in cellular systems.

I. Introduction

Filaments inside a cell have varied stiffness and serve many functions including rigidity of cell membrane, cellular motility, as well as muscle contraction. Among them, actin is a semiflexible filament and serves in maintaining the cell membrane and promoting cellular transportation by collaborating with molecular motors such as myosin, kinesin and dynein. Actin filaments, even without any motor proteins, show very unique behavior at both single filament scale and global collective scale. In very dilute solution they independently fluctuate while in dense solution they interfere with each other's path and gradually shift to the nematic phase, where filaments are collectivelly lined up in one direction in much denser solution. Those two different regimes unique to actin are caused by their semiflexibility where the countour length is shorter but still comparable to its persistence length, l_p, as listed in the Table 1.

In this paper, we assume the situation whrere there are no myosins, thus, filaments only thermally fluctuate. The study about their behaviors even without myosins are still important because thermal fluctuation itself plays an indespensible role in living system such varied forms of cellur motility.

We explore the thermal fluctuation of semiflexible filaments without any molecular motors in entagled state, as we mentioned above, where their motility is highly constrained in the axial direction (reptation) by surrounding filaments. We will see in later section entanglement leads to viscoelastic regime, where non-Markovianity (memory) of the system plays an important role that cannot seen in purely viscous system. In experimentally investigating semiflexible filaments, single-walled carbon nanotubes (SWNTs) are very detectable candidates as trackers instead of direclty tracking actin itself [1]. SWNTs are very long-lasting fluorecent tracers in actin solution under near-infrared light and can have their mechanical property (e.g. stiffness, diameter, as well as countour length) comparable to that of actin, as can be seen in Table 1.

Name	Typical Length (L)	Persistence Length (l_p)	Motors
Actin	$10\mu m$	$17 \pm 2\mu m$	Myosin
SWNT	$10\mu m$	$30\mu m$	-
Microtubles	$1mm$	$4 - 8mm$	Kinesins / Dynein
DNA [1]	$2m$	$40nm$	-
Uncooked spagetti	$30cm$	$10^{18}m$	-

Table 1: *Mechanical property of filaments*

II. Theory

i. Viscous system [2]

We can start from purely viscous where filaments are sparsely distributed and friction forces acting on them are totally determined by the product of the drag and velocity in instantatenous frame. The corresponding warm-like chain (WLC) model is wrriten as

$$\mathcal{H}[\vec{r}](t) = \kappa/2 \int_0^L ds'(\partial^2\vec{r}/\partial s^2)^2(s',t) \qquad (1)$$

where s denotes arclength of a filament and κ is bending stiffenss. Basically, this Hamiltonian is interpreted as the bending energy stored over the filament. The equivalent expression in terms of Frenet-Serret tangent vector $\partial\vec{r}/s = \vec{t}$, as can be seen in Figure 1, would be

$$\mathcal{H}[\vec{r}](t) = \kappa/2 \int_0^L ds'(\partial\vec{t}/\partial s)^2(s',t) \qquad (2)$$
$$-f_{||}(s,t)(\vec{t}^T \cdot \vec{t} - 1)$$

In the above equation, we assume local inextensibility by a Lagrangain multiplier $f_{||}(\vec{t}^T \cdot \vec{t} - 1)$, which is fair requirement unless all relevant forces (e.g. thermal fluctuation, interaction with other filaments or motors) are strong enough to dissemble the chemical bonds between neighboring monomers consisting of the filaments. We will look only at the tranverse fluctuation. To this end, we project the coordinate of backbones $\vec{r}(s,t)$ into $(\vec{r}_{||}, \vec{r}_\perp)(s,t)$ as depiceted in Figure 1, then the resultant Hamiltonian's equation (Lanvegin equation) is

[1] For human genomes

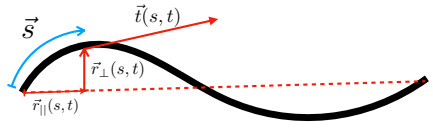

Figure 1

obtained (see supplementary) as

$$\frac{\gamma_\perp}{L}\frac{\partial r_\perp}{\partial t} = -\kappa(\frac{\partial^4 r_\perp}{\partial s^4})(s,t) + \xi(s,t) \qquad (3)$$

where ξ is thermal noise and safely assumed to be white ($< \xi(t)\xi(t') > \propto \delta(t-t')$) and $\gamma_\perp$ is the Stokes' friction for the transverse motion of a filamend and given as

$$\gamma_\perp = \frac{4\pi\eta L}{log(\frac{L}{d})}$$

By plugging the Fourier form $r_\perp = \sum_{k,w} a_k(\bar{w})e^{i(\omega t - ks)}$ (Figure 2) in the eq. (3) and average over time, an important relation for purely viscous system is obtained as

$$\omega(k) = \frac{\kappa k^4}{\gamma_\perp}, \quad < a_k^2 > = < a_k^2 >_c = \frac{2k_B T}{L\kappa k^4} \qquad (4)$$

The plot can be found in Figure 2

ii. Viscoelastic system [3]

Now we extend the equation of motion (3), which works only for purely viscous solution,

into the entangled state where dynamical force from surrounding fluid are no longer negligible. To this end, following the treatment [], we can write instead

$$\int_{-\infty}^{t} dt' \alpha_{\perp}(t-t')\gamma_{\perp}(t') = -\kappa(\frac{\partial^4 r_{\perp}}{\partial s^4})(s,t) + \xi(s,t) \tag{5}$$

The new variable $\alpha_{\perp}$ above is called as *viscoelastic memory kernel* and genrated by surrounding medium through the *Generalized Stokes-Theorem*. The only modification between equation (5) from (3) is the left hand side and it literally reflects the viscoelastic effects: the information (energy) stored in the medium in the past (not only the most recent past) affects the motion in the current time frame as can be seen in the integral over time. The important note here is that viscoelastic regime, thermal force is no longer white as the elastic components exert forces on sufficiently slow time scale and we can require it to obey $< \xi(\omega)\bar{\xi}(\omega) > \propto Im(\alpha_{\perp}(\omega))$, thus no longer $< \xi(t)\xi(t') > \propto \delta(t-t')$ holds.

As done in viscous equation of motion, we use the Fourier transformation $r_{\perp}(s,t) = \sum_k a_k(t)v_k(s)$ to see the equation for each kth mode. This Fourier representation in a filament is equivalent to the projection of transverse displacement onto the orthonormal eigenmodes $v_k(s)$. Plugging this into the equation (5) with the orthogonality $\int_0^L ds y_k(s)y_{k'}(s) = \delta_{k,k'}$, we can decompose it in the equation of motion for each normal modes,

$$\int_{-\infty}^{t} dt' \alpha_{\perp}(t-t')a_k(t') = -\kappa k^4 a_k(t) + \xi_k(t) \tag{6}$$

The appropriate boundary condition for free-end filament should be

$$(No\ Torque) \quad \frac{\partial^2 r_{\perp}}{\partial s^2}(t, 0\ and\ L) = 0 \tag{7}$$

$$(No\ Shear) \quad \frac{\partial^3 r_{\perp}}{\partial s^3}(t, 0\ and\ L) = 0 \tag{8}$$

which gives the expression for the Fourier components for free-end as

$$v_k(s) = \frac{1}{\sqrt{L}} \times \begin{cases} \frac{cosh(\frac{k}{L}(s-\frac{L}{2}))}{cosh(\frac{k}{2})} + cos(\frac{k}{L}(s-\frac{L}{2}))cos(\frac{k}{2}), & \text{n odd} \\ \frac{sinh(\frac{k}{L}(s-\frac{L}{2}))}{sinh(\frac{k}{2})} + sin(\frac{k}{L}(s-\frac{L}{2}))sin(\frac{k}{2}), & \text{n even} \end{cases}$$

where wavenumber is discretized as $k = (n + \frac{1}{2})\pi$, $n \in \mathbb{N}$. To obtain the Fluctuation-Dissipation theorem for the mode amplitude, we exert the Fourier transformation for time componet in (6) and find

$$\hat{a}_k(\omega) = \frac{\hat{\xi_k}(w)}{\hat{\alpha}_{\perp}(\omega) + \kappa k^4} \tag{9}$$

and based on the Kelvin-Voigt model $\hat{a}_k(\omega) = \hat{a}_0 + i\frac{\gamma\omega}{L}$, where the 1st term represents the elastic force acting without time delay and the 2nd term does the viscostic force. Finally, applying the Wiener-Khinchin theorem to $\hat{a}_k(\omega)\bar{\hat{a}}_k(\omega)$ yields from equation(9),

$$< a_k^2 > = < a_k^2 >^c = \frac{k_B T \tau_k}{L\gamma_{\perp}} \tag{10}$$

$$\tau_k = \frac{\gamma_{\perp}}{\kappa L k^4 + L\alpha_0} \tag{11}$$

As seen in equation (4), (10) and plotted in figure 2, viscoelasticity modifies the fluctuation of mode amplitudes, which is the main claim of this paper. Again, this is one of the direct of the viscoelastic effects as can be seen in the difference of left hand side between equation (3) and (5).

III. Experiments (data not shown)

We can possibly do the experiment under the G-actin concentration of $1\mu g/ml$ with the inducer for polymerization of actin filaments and SWNTs are also added to it as a tracers. The information of SWNTs with varied length fluctuation is stored as coordinates of each beads along the backbone using near-infrared microscopy. The data subsequently converted into analyzable form in MATLAB by such software as ImageJ (NIH) and FIESTA.

IV. Results

The mode fluctuation of transverse motion of a filament in purely viscous system is characterized as the power-law: the amplitude vairiance

is inverse proportional to the fourth power of wavenumber. On the pther hand, we expect that filaments in viscoelastic system does not show the direct the fourth power law, instead, have smller power dependence for small wavenumber due to the elasticity (shear modulus) factor α_0 seen in the denominator in (11).

V. Discussion

As shown in the figure 2, the first several transverse modes are more strongly suppressed by the elastic effect rather than with larger mode k . This is very naturally speculated because as the index number of the mode goes down, the typical size of the tranversal deviation is larger amd larger and would be more tightly constrained by surrounding filaments while small transversal deviation (large mode k) are relatively freely fluctualting even in very dense envrionment. Moreover, increasing the ratio of shear modulas to the bending capacit results in the large suppression and this indicates that either increasing density of filamens or decreasing the bending capacity (more flexible filamets are) leads to elasticity-dominant regime. These are also easily undertood by effective tube regime, tha is, the effective (snaking cylindrical) region in the entangled state. The effective radius of such a tube is given as the decreasing function of density (shear modulas0 and bending capacity (persistence length), thus, the story above can be easily rephrased.

As a future suggestion, if we change the flexibility of a filament (filexible filamnet or stiff filament) we might see something exotic or the moxture of them can be next interesting step. Also, incorporating myosyn (molecular motor) activity into the system can be expected to change how filaments are fluctuating.

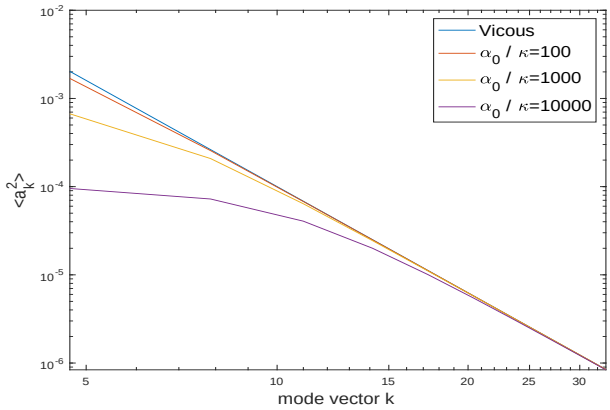

Figure 2: *Mode amplitude variance with mode vector k. In this plot, we only look at the power-law between mode vector k and mode amplitude with tuning the ratio of the shear modulas to bending capacity and thus, other parameters irrelavant are arbitralily chosen. Therefore, the unit of y-axis is also arbitrary unit.*

References

[1] Nikta Fakhri, Alok D. Wessel, Charlotte Willms, Matteo Pasquali, Dieter R. Klopfenstein, Frederick C. MacKintosh and Christoph F. Schmidt *High-resolution mapping of intracellular fluctuations using carbon nanotubes* Science **344**, 6187 (2014)

[2] C. P. Broedersz and F. C. MacKintosh *Modeling semiflexible polymer networks* Rev. Mod. Phys. **86**, 995 (2014)

[3] Jannes Gladrow, Master's thesis