A Langevin dynamics approach for analyzing the mechanical response of bio-polymers

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A Langevin dynamics based formulation is proposed to describe the shape fluctuations of extended objects like bio-filament and cell membrane. We show that, for simple problems, solutions of the resulting stochastic partial differential equation (SPDE) asymptotically reduce to predictions from classical modal analysis. In addition, methodologies are developed to implement this formulation in finite element (FEM) simulations where, besides entropy, the finite deflection of filament itself has also been taken into account. The validity of the proposed finite element-Langevin dynamics approach is verified by comparing numerical results with various theoretical predictions. Our formulation can serve as a computational framework for future studies on realistic biological structures like the cytoskeleton.

Introduction-Accumulating lines of evidence suggest that bio-filaments like F-actin and microtubule, as major components of cytoskeleton, are largely responsible for maintaining cell shape, driving cell movement, and mechanosensing. For this reason, extensive finite element (FEM) simulations [1, 2] and constitutive modelling [3] have been conducted to determine how networks composed by these bio-polymers resist deformation. However, on a fundamental level, a theoretical framework, taking into account thermal undulations of individual filament, that can easily be implemented in direct numerical simulations is still lacking. In this paper, a Langevin dynamics based formulation is proposed to describe the shape fluctuations of bio-polymers. We show that, solutions of the resulting stochastic partial differential equation (SPDE) asymptotically reduce to predictions from classical modal analysis for simple problems and hence unambiguously prove the validity of this approach. This formulation is then implemented in finite element (FEM) simulations and we demonstrated that numerical results from this method match well with various theoretical predictions.

Formulation-According to Langevin [4], the effects of collisions with surrounding fluid molecules on the motion of any particle can be represented by (i) a viscous force $v\xi$, with v and ξ being the particle velocity and the medium viscosity respectively, thwarting the movement of the object, and (ii) a random force f driving the Brownian motion of that particle. Furthermore, the random force must follow a Gaussian distribution with zero mean and, in the one dimensional case, have a correlation function $\langle f(t)\ f(\tau)\rangle = 2\xi k_B T\delta(t-\tau)$, where t and τ represent time, δ corresponds to the Dirac delta function, and k_BT is the thermal energy. The same line of reasoning can be applied to analyzing thermal undulations of extended objects. The only difference is that, for a filament (treated as a beam here), f must be interpreted as a distributed load causing the beam to deflect and ξ should represent the viscous coefficient per unit length of the filament. In addition, the relationship between f and ξ becomes

$$\langle f(\vec{x},t)\ f(\vec{y},\tau)\rangle = 2\xi k_B T\delta(\vec{x}-\vec{y})\delta(t-\tau). \tag{1}$$

Hence, neglecting any inertia effects, the thermal fluctuations of an initially straight filament can be described by

$$\xi\frac{\partial w}{\partial t} + EI\frac{\partial^4 w}{\partial x^4} = f(x,t) \tag{2}$$

with *EI* being the bending rigidity of the filament and *w* being the deflection of the beam, refer to Fig. 1. We want to point out that (2) is a stochastic partial differential equation (SPDE) as f is random here. If both ends of the filament (with length L) are hinged as shown in Fig. 1, then the solution of (2), satisfying the initial condition $w(x,0)=0$, can be found as

$$w(x,t) = \frac{2}{L\xi}\sum_n \sin\frac{n\pi x}{L}\int_0^L \sin\frac{n\pi s}{L}\int_0^t f(s,\tau)e^{-\pi^4 n^4 EI(t-\tau)/\xi L^4}\,d\tau ds \tag{3}$$

from which, in conjunction with (1), the correlation function of w can be found as

$$\langle w(x,t)\ w(y,\eta)\rangle = \frac{2k_BTL^3}{\pi^4 EI}\sum_n \frac{\sin(n\pi x/L)\sin(n\pi y/L)}{n^4}\left[e^{-\pi^4 n^4 EI(\eta-t)/\xi L^4} - e^{-\pi^4 n^4 EI(\eta+t)/\xi L^4}\right] \tag{4}$$

in which it has been assumed that $\eta \geq t$. In the special case where $y=x,\ \eta=t,$ and $t\to\infty$, (4) reduces to $\lim_{t\to\infty}\langle w(x,t)\ w(x,t)\rangle = \sum_n \frac{2k_BTL^3}{\pi^4 n^4 EI}\sin^2\left(\frac{n\pi x}{L}\right)$, a relationship that can also be arrived if we express the deflection profile as $w(x,t)=\sum_n a_n(t)\cdot\sin\frac{n\pi x}{L}$, with a_n being a set of random variables, and then invoke the theorem of equipartition in evaluating $\langle w(x,t)\ w(x,t)\rangle$. However, unlike traditional modal analysis which produces relationships that are valid only when thermodynamic equilibrium is reached, i.e. over long time periods, the Langevin dynamics approach adopted here can provide temporal as well as spatial correlation functions, like (4), which fully capture the dynamics of the system.

Implementation in FEM simulations-The Langevin dynamics formulation also provides a viable solution to the outstanding question of how to take into account thermally-induced deformations of soft objects in finite element

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(FEM) simulations. Following typical procedures in FEM, we divide a filament into numerous segments and the first thing we need to determine is what kind of load should be applied on each element. The simplest choice is to assume that the load acting on element i over the time interval $[t_j\ t_{j+1}]$ is uniform, denoted as f_i^j. To be self-consistent, f_i^j should satisfy $f_i^j = \frac{1}{(x_{i+1}-x_i)(t_{j+1}-t_j)}\int_{x_i}^{x_{i+1}}\int_{t_j}^{t_{j+1}} f(x,t)\,dtdx$, where x_i and x_{i+1} are the coordinates of the two ends of the element. Obviously, we have $\langle f_i^j\rangle = 0$. In addition, the auto correlation function of this force can be found as

$$\langle f_i^j\ f_i^j\rangle = \frac{2\xi k_B T}{(x_{i+1}-x_i)(t_{j+1}-t_j)}. \tag{5}$$

Hence, the effective transverse force acting on each element follows a Gaussian distribution with a mean of 0 and a variance given by (5). In order to take into account possible finite deflection of filament, we also need to include its displacement along the axial direction, i.e. $u(x,t)$ as illustrated in Fig. 1, in the calculation. In this case, the elastic energy stored in element i takes the form $U_{elem}^i = \int_{x_i}^{x_{i+1}}\left[\frac{EA}{2}\left(\frac{\partial u}{\partial x}+\frac{1}{2}\left(\frac{\partial w}{\partial x}\right)^2\right)^2 + \frac{EI}{2}\left(\frac{\partial^2 w}{\partial x^2}\right)^2\right]dx$, where the first term in the bracket represents the stretching energy, adopting the so-called the von Karman strain, with EA being the stretching rigidity of the filament and the second term corresponds to the conventional bending energy. In addition, it is reasonable to believe that the frictional force (along the longitudinal direction of filament) induced by the bombardments of liquid molecules is much smaller than the normal one causing the filament to deflect. As such, the viscous coefficient associated with axial motion should be much smaller than ξ, suggesting that u is a fast variable when compared with w. Based on these considerations, a numerical scheme was developed as follow: (i) at the beginning of any time interval $[t_j\ t_{j+1}]$, assume that w is fixed and calculate u by enforcing equilibrium in the axial direction; (ii) calculate $\partial w(x,\ t_j)/\partial t$ using u obtained in (i); (iii) update w as $w(x,\ t_{j+1}) = w(x,\ t_j) + (t_{j+1}-t_j)\frac{\partial w(x,\ t_j)}{\partial t}$. Starting from a given initial state, the whole calculation is carried out by repeating the three steps listed above. As an example, the compressive response of a simply supported filament in the presence of thermal fluctuations is considered by using cubic and linear interpolations of w and u, respectively, in each element. Calculations were conducted by fixing one end of the filament and assigning an axial displacement of $-\Delta$ to the other end, i.e. $u(L) = -\Delta$. Based on eight independent simulations, the average compressive axial force, i.e. $\langle F\rangle$, as a function of the nominal compressive strain $\varepsilon = \Delta/L$ is shown in Fig. 2 by the circular symbols. Notice that the force is normalized by the classic Euler buckling load $F_{c0} = \pi^2 EI/L^2$ and ε is normalized by the corresponding Euler buckling strain $\varepsilon_{c0} = \pi^2 EI/EAL^2$. Our results suggest that filament force reaches its maximum at certain moderate $\varepsilon/\varepsilon_{c0}$ value, ~ 3 in Fig. 2, and then gradually drops to F_{c0} as ε continues to increase. Actually, the same problem has been considered recently via modal analysis approach [5] and prediction from that study is represented by the solid line in Fig. 2. Clearly, simulation results here match with theoretical prediction very well. Similar calculations have also been conducted for a filament in 3d by introducing a new variable representing filament deflection in the third direction and then taking into account its contribution (similar to that of w) to the bending and stretching energies. The 3d simulation results and corresponding prediction from [5] are shown in Fig. 2 by the square symbols and the dashed line. Unlike two dimensional cases, now the filament force asymptotically approaches F_{c0} but can never exceed it.

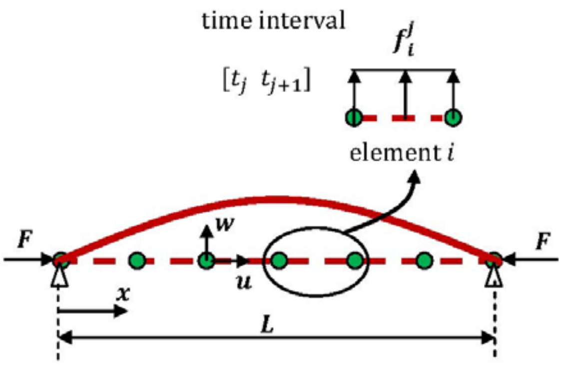

Figure 1. Schematic plot of a simply supported filament. The solid line corresponds to the deformed beam while the un-deformed filament is represented by the dashed line.

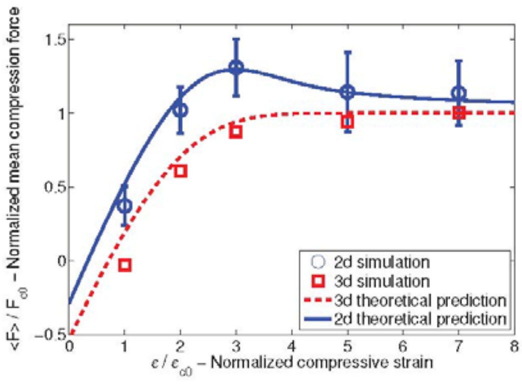

Figure 2. Filament force as a function of nominal compressive strain. Calculations are conducted by dividing the filament into 10 equal-sized elements and choosing $EI/k_BTL = 100$ and $EAL/k_BT = 10^6$.

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