Applications of nonlinear analysis to cell biology: assembly kinetics, mechanical properties and coupled dynamics of molecular motors and biopolymers

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This paper discusses the role of nonlinearities in the physical description of several key biomolecules that participate in a number of crucial subcellular processes, namely actin, microtubules and motor proteins (especially kinesin). We show that the assembly kinetics of actin is a nonlinear process that requires not only a mechanism of saturation but also annealing and fragmentation that are governed by coupled nonlinear equations involving monomer concentration and filament number as the key dynamical variables. The observed dendritic growth of actin networks in cell motility phenomena is subsequently described by the coupling of actin filaments to the protein called Arp 2/3. We then investigate the role of nonlinear dynamics in the formation of microtubules. First of all, high concentration of the constituent protein tubulin leads to self-sustained oscillations in the assembly and disassembly dynamics of microtubules. We propose a biophysics-based model that describes these oscillations. Furthermore, space-flight laboratory experiments have shown that the in vitro and in vivo self-organization of microtubules is sensitive to gravitational conditions. We propose a model of self-organization of microtubules in a gravitational field. The model is based on the dominant chemical kinetics. The pattern formation of microtubule concentration is obtained: 1) in terms of a moving kink in the limit when the disassembly rate is negligible, and 2) for the case of no free tubulin and only assembled microtubules present. The results of our simulations are in good quantitative agreement with experimental data. Finally, we present a recently proposed model of molecular and bulk elastic properties of microtubules that include macroscopic estimates of the anisotropic elastic moduli of microtubules, accounting for the molecular forces between tubulin dimers: for a longitudinal compression, for a lateral force and for a shearing force. At the level of large bending motions of microtubule filaments, a continuous medium model is proposed describing a microtubule as an elastic rod. Keeping the dominant nonlinear terms in the bending dynamics equation, we found that when the microtubule is subjected to bending forces, the deviation angle satisfies a Sine-Gordon equation. Particular analytical solutions of this equation are found which describe kink and anti-kink bending modes that may propagate at a range of velocities along the length of the microtubule. Kinetic energies and characteristic damping times of these modes are calculated for different propagation velocities and compared with thermal and ATP hydrolysis energies. Finally, we discuss how coupled dynamical equations in at least two spatial and one temporal dimension can successfully describe the behavior of motor proteins such as kinesin. Our focus is placed on directionality of motion that we claim is a direct result of the torsional springs that are loaded in the processes of binding between kinesin motor domains and the microtubule filament. The mathematical formulation of this important biophysical problem involves the use of coupled Langevin equations.

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