Thermal Response of Protein Microtubules: A Nonlocal Elasticity Perspective on Cellular Mechanics

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Abstract:

This study delves into the dynamic behavior and thermal effects on isolated protein microtubules. Microtubules, pivotal as bio-beam structures, form an essential component of the cytoskeleton in eukaryotic cells. Modeling microtubules as beam elements is crucial for accurately capturing their dynamic characteristics. To this end, the equation of motion is formulated, accompanied by parametric analyses to examine the influences of shear deformation, thermal effects, and the length scale coefficient. The findings are then juxtaposed with classical systems and existing literature, demonstrating that the approach adopted in this research yields results that are not only more precise but also align more closely with experimental data, underscoring the superiority of the proposed system in capturing the nuanced behavior of microtubules.

Keywords: Nonlocal Elasticity Theory; Microtubule Dynamics; Comparative Modeling; Biomechanics; Parametric Analysis.

1. Introduction

In the field of cattle practice, the findings from this study on protein microtubules and their dynamic responses under thermal effects have significant implications, especially for cellular stability and function in biological processes essential for animal health and reproduction. Here are some key applications:

1. **Improving Disease Resistance**: Understanding the thermal sensitivity of microtubules at the cellular level could aid in the development of cattle vaccines or treatments that target cellular stability during diseases, particularly those affecting cell division or intracellular transport, which are crucial in immune responses.

2. **Enhancing Fertility**: The role of microtubules in mitosis is integral to reproductive biology. Insights into their behavior under thermal stress can inform strategies for better embryo development and reproductive health in cattle, optimizing conditions for in vitro fertilization or other breeding technologies.
3. **Heat Stress Management**: As heat stress impacts cattle productivity, knowing how cellular structures respond to temperature changes can contribute to new management strategies that protect cellular health and maintain cattle productivity in hot climates.
4. **Antimicrobial Strategies**: Thermal sensitivity data on microtubules may help in developing antimicrobials that disrupt cellular processes in pathogens but not in the host, improving animal health and reducing disease transmission in livestock.

These applications demonstrate how cellular-level research can translate into advances in cattle health, reproductive efficiency, and resilience, contributing to the broader field of veterinary science.

Microtubules (MTs) are one of the essential elements that make up the cytoskeleton in eukaryotic cells. They play a significant character in several biological developments, like cell division, cell motility, motor protein movements, intracellular transport, and mobile nuclei formation of the eyelashes and flagella [1-5]. MTs are made up of both α-tubulin and β-tubulin (see Fig. 2). They are flexible and stiffer, around one hundred times to other filaments. These properties have a composite structure, and the molecular shuttle is also considered an anisotropic structure. MTs possess the structure of a hollow cylinder and are generally obtained through 13 parallel protofilaments in vivo, but the variation of this number can vary around the range of 9-16 in vitro [6-10]. Generally, MTs are found with external and internal diameters of 25nm and 15 nm, along with lengths around 10 nm to 100 μm [11].

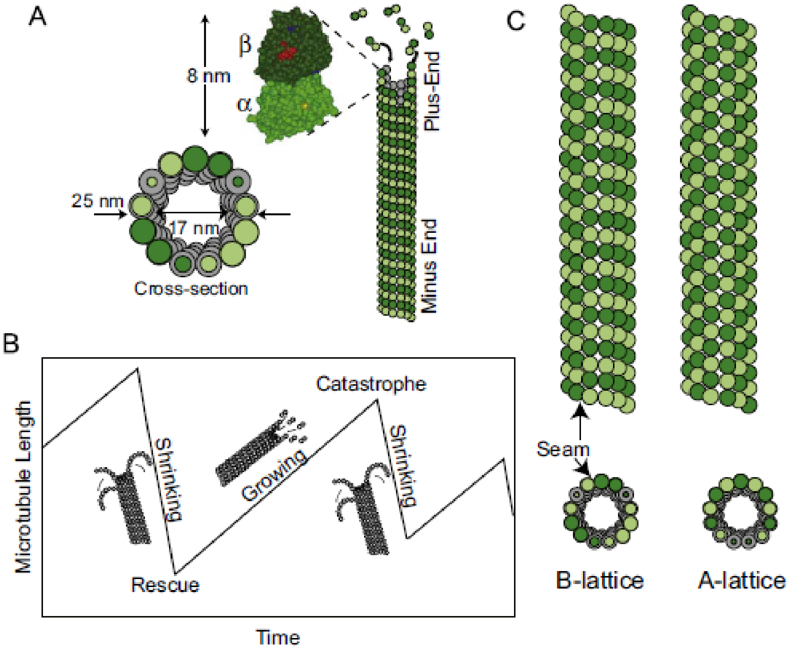

Fig. 1: MT dynamics and structure. (A) MTs indicate polymer filaments design through tubulin dimers. The tubulin-based heterodimer is designed through alpha and beta, which are light and dark green. Some of the dimers bind together to check the polymer, and each dimer is added to the ends to grow the MTs. The plus-end is one of the shrinking, rapidly growing, and dynamic ends. In contrast, the minus-end represents the less dynamic. MTs have outer and inner diameters around 25 nm and 17 nm. (B) MTs shrink and grow by the dimers' loss and dimers' addition, respectively. Stochastic transitions are called catastrophes and rescue obtained from growing to shrinking and shrinking to growing, respectively. MTs show more stability by reducing catastrophes and increasing the frequencies. (C) Microtubule A-lattice and B-lattice. In A-lattice, light green (α) touches the dark green (β) all through the lattice. In the A-lattice, no seam is found, while in the B-lattice, the light green traces a neighboring α excluding the seam [12].

The mechanical performances of MTs are complex in environmental circumstances like viscoelastic/elastic temperature and medium. Many investigations have been performed based on the temperature inflexibility of MTs. The flexural inflexibility of taxol-free MTs is reduced by increasing the temperature [13]. The flexural inflexibility reduces at one end by increasing the temperature from 20 °C-35 °C. The flexural inflexibility data of MTs are obtained with 8-

12 mm length ranges under the temperature 20 °C- 35 °C. Hence, it is noticed that the influences of temperature have impacts on the mechanical characteristics as the natural vibration frequencies and critical buckling force of MTs. However, the simulation reports of the mechanical performances of temperature-dependent based on MTs are unusual. A few limited experiments using these test samples have been performed, and limited values have been found through these tests. Hence, it is useful to investigate the buckling vibration descriptions of MTs using computational mechanical techniques through the temperature properties [14].

The simulations through the mechanical temperature of MTs are stimulated by the condition and current investigations through the mechanical performances of MTs to consider the effects of environmental temperature. A constitutive relationship using the atomistic continuum is incorporated and developed into a computational mesh-free structure by including the effects of temperature. In the expansion of the mechanical mesh-free simulation structure, the temperature impacts on the microtubule rigidity are considered together with experimental trials [15-16]. Hence, the temperature-based mechanical MTs' performances with vibration frequencies and critical buckling forces are exploited by means of developing the atomistic-continuum mesh-free structure. Several investigations [17-19] have been presented to study the vibration microtubule behavior, but no one has worked on the behavior of temperature changes.

In this article, the vibration behaviors of MTs are considered, and the cytoskeleton, which is an important element in living cells, is studied. present the microtubule model like a beam, the nonlocal Timoshenko beam theory is proposed. The specific form of the transverse wave spreading in MTs is examined along with the effects of both temperature changes and small-scale parameters using the Timoshenko beam nonlocal system. The developed model in this study will attract the large community of biophysicists investigating the field of mechanical filament rather than to the community of engineering.

2. Analysis of elastic microtubules systems in nonlocal continuum mechanics

In this section, the nonlocal elasticity theory with the rate of stress at a reference point x is proposed in the field of strain function at each point throughout the body. These statements are related to the atomic theory of experimental observations and lattice dynamics on phonon dispersal. In these bounds, the strain effects other than x are neglected, and one gets the local/classical elasticity theory. Using the theory of the Timoshenko beam, the generic form of the transverse sensations using an elastic beam with thermal impacts is provided as [20-22]:

$$\frac{\partial V}{\partial x} - \rho A \frac{\partial^2 \omega}{\partial t^2} + N_t \frac{\partial^2 \omega}{\partial x^2} = 0, \qquad (1)$$

$$\frac{\partial M}{\partial x} + V = \rho I \frac{\partial^2 \psi}{\partial t^2}, \qquad (2)$$

Where *M(x, t)* and *V(x, t)* are the bending moments and resultant shear force, respectively, *A* denotes the cross-section area, ρ is the protein microtubules mass density, *w(x, t)* shows the beam's flexural deflection, ψ and *I* indicate the rotation angle of the protein microtubules cross-section and moment of inertia. N_t is the additional axial force that depends on the temperature θ along with thermal coefficient α based on the protein microtubules; the resultant force is given as:

$$N_t = -\alpha E A \theta. \qquad (3)$$

In the nonlocal elasticity, the uniaxial constitutive law for linear, homogeneous, isotropic, in absent of body force is expressed as [23]

$$\sigma - (e_0 a)^2 \frac{\partial^2 \sigma}{\partial x^2} = E\varepsilon, \qquad (4)$$

$$\tau - (e_0 a)^2 \frac{\partial^2 \tau}{\partial x^2} = G\gamma, \qquad (5)$$

Where ε and σ are the axial strain and stress, e_0 shows the constant value for the protein microtubules, and *a* represents a typical internal length, i.e., granular distance, C–C bond length, and lattice arrangement. Furthermore, it is noted that e_0 values need to be found through matching dispersion plane wave curves or experiments with the dynamics of the atomic frame. *G* shows the shear modulus, τ, γ are the shear stress and strain. The impacts of $e_0 a$, i.e., small scale coefficient, on the shear force are not mentioned in the preceding research [24-25]. The identical e_0 values at the transverse directions and in-plane are provided in Eqs (4) and (5) due to the stress tensor symmetry $\tau_{xy} = \tau_{yx}$ are in-plane as well as transverse directions. The resultant bending moment *M* and cross-sectional shear force *V* are derived as:

$$M = \int_A y\sigma \, dA, \qquad V = \int_A \tau \, dA. \qquad (6)$$

The γ and ε strains using the Timoshenko beam system are written as:

$$\varepsilon = y\frac{\partial \psi}{\partial x}, \tag{7}$$

$$\gamma = \frac{\partial \omega}{\partial x} - \psi. \tag{8}$$

The explicit terminologies of the shear force V and bending nonlocal moment M are provided as:

$$M = EI\frac{\partial \psi}{\partial x} + (e_0 a)^2\left[\rho I\frac{\partial^3 \psi}{\partial x\,\partial t^2} - \rho A\frac{\partial^2 \psi}{\partial t^2} + N_t\frac{\partial^2 w}{\partial x^2}\right] \tag{9}$$

$$V = \beta GA\left(\frac{\partial w}{\partial x} - \psi\right) + (e_0 a)^2\left[\rho A\frac{\partial^3 w}{\partial x\,\partial t^2} - N_t\frac{\partial^3 w}{\partial x^3}\right] \tag{10}$$

Where β represents the shear-dependent form factor on the cross-sectional shape, β is the recommended value, and the adjustment coefficient value is 10⁄9 for the cross-area circular shape [27]. By substituting the above Eqs (9)-(10) into (1)- (2), the obtained form of motion based on the Timoshenko beam nonlocal system along with thermal impacts on displacement form is obtained as:

$$EI\frac{\partial^2 \psi}{\partial x^2} + \beta GA\left(\frac{\partial w}{\partial x} - \psi\right) = \rho I\frac{\partial^2}{\partial t^2}\left[\psi - (e_0 a)^2\frac{\partial^2 \psi}{\partial x^2}\right] \tag{11}$$

$$\beta GA\frac{\partial}{\partial x}\left(\frac{\partial w}{\partial x} - \psi\right) + N_t\frac{\partial^2}{\partial t^2}\left[w - (e_0 a)^2\frac{\partial^2 \psi}{\partial x^2}\right] = \rho A\frac{\partial^2}{\partial t^2}\left[w - (e_0 a)^2\frac{\partial^2 w}{\partial x^2}\right] \tag{12}$$

It is observed that the Timoshenko beam local system using the thermal impact is improved when the e_0 parameter goes to zero.

3. Wave propagation in protein microtubules using thermal impacts.

finding an analytical outcome for simply maintained boundary conditions (BCs) of the current model, the protein microtubules beam is simply assumed. Consequently, the BCs take the form:

$$w(x,t) = \bar{W}e^{i\omega t}\cos(\lambda x), \qquad \psi(x,t) = \bar{\psi}e^{i\omega t}\cos(\lambda x) \tag{13}$$

where $\overline{w}$ shows the protein microtubules deflection amplitude $\lambda_n = \frac{n\pi}{L}$ and $\overline{\psi}$ are the slope amplitudes of the protein microtubules because of bending deformation. In addition, ω is the frequency of the wave motion. The updated form of the frequencies via the Timoshenko beams nonlocal system using Eq (11), (12), and (13) is given as:

$$(\omega_n^2)NT = \frac{1}{2}\left(\alpha_n \pm \sqrt{\alpha_n^2 - 4\beta_n}\right), \tag{14}$$

$$\alpha_n = \frac{N_t\lambda_n^2}{\rho A} + \frac{\beta IG\lambda_n^2 + \beta AG + EI\lambda_n^2}{\rho I}\frac{1}{1+(e_0a)^2\lambda_n^2}, \tag{15}$$

$$\beta_n = \frac{E\beta G\lambda_n^4}{\rho^2(1+(e_0a)^2\lambda_n^2)^2} + N_t\lambda_n^2\frac{(EI\lambda_n^2 + \beta AG)}{\rho^2 IA(1+(e_0a)^2\lambda_n^2)} \tag{16}$$

Based on the formulations obtained above with the nonlocal Timoshenko beam theory for protein MT, the thermal vibration properties of protein MT are discussed here. To examine the temperature change and scale parameter effects on the protein microtubules vibrations, the comparison of the including/excluding results using the thermal effects along with the nonlocal parameter is present. It shows that the result ratios with the change/without change of temperature are respectively provided as:

$$\chi_N = \frac{(\omega_n)_{NT}}{(\omega_n)_{LT}}, \qquad \chi_{th} = \frac{(\omega_n)_{NT}}{(\omega_n)_{NT}^0}, \tag{11}$$

where $(\omega_n)_{LT}$ and $(\omega_n)_{NT}^0$ are the Euler beam local system frequencies with and without the thermal impacts at θ = 0. In the comparison of dynamic lattice results with nonlocal theory, it is observed that e_0 is taken as 0.39. Hence, e_0 values need to be measured in the experimental investigations.

4. Results and discussions

In the present section, we delineate the execution of numerical simulations designed to probe the vibrational frequencies of microtubules, with a specific focus on the implications of thermal variations. The simulations contemplate various boundary conditions, explicitly the simply supported (S-S) and clamped-free (C-F) configurations, to encapsulate the spectrum of potential mechanical constraints. Figures 2 through 4 exhibit the modal frequency curves of microtubules across an environmental temperature range extending from 5°C to 50°C. This assortment of data provides a comprehensive analysis of two quintessential boundary condition types, C-F and S-S, under the influence of thermal fluctuations. These analytical explorations are critical for understanding the thermo-mechanical behavior of microtubules within the cellular milieu, offering valuable insights into their biomechanical stability and functionality. Figure 2 provides a quantitative depiction of the vibrational frequency behavior of protein microtubules under thermal stress, as a function of microtubule length, in a simply-supported boundary condition. The graph plots frequency against microtubule length, showcasing three distinct thermal environments, represented by the temperatures 15°C, 25°C, and 50°C. The data suggest a negative correlation between the microtubule length and its frequency, which is consistent with the principles of vibrational analysis in elastic media. At an increased length, the microtubule exhibits lower frequencies, indicative of a softer structure susceptible to larger deformations.

Furthermore, the graph demonstrates a temperature-dependent decrease in frequency, implying that thermal fluctuations contribute to the softening of the microtubule structure, which in turn affects its vibrational characteristics. This decrease in frequency with temperature is a manifestation of the increased thermal agitation at the molecular level, which reduces the stiffness of the microtubules.

This data is pivotal for understanding the biomechanical properties of microtubules and their functional adequacy in various cellular processes. It provides insights into the fundamental aspects of microtubule mechanics that could be critical for cellular integrity and mechanics at physiological temperatures. The implications of this study are significant for the field of cellular biomechanics and could influence the understanding of cellular responses to thermal stress, which is relevant in the context of diseases where temperature regulation is disrupted.

Figure 3 illustrates the relationship between the natural frequency of microtubules (MTs) and their length, for varying geometrical parameters, within the framework of the nonlocal Timoshenko beam theory. The graph plots the frequency on the y-axis against the microtubule length on the x-axis. Three curves correspond to different values of a geometrical parameter, possibly related to the microtubule's diameter or another characteristic dimension that affects its stiffness and, consequently, its vibrational properties.

The solid line represents the smallest geometrical parameter value (0.003), the dashed line represents an intermediate value (0.006), and the dotted line represents the largest value (0.009). As the geometrical parameter increases, which could be interpreted as an increase in the microtubule's cross-sectional area or a modification of its stiffness, there is a noticeable decrease in the natural frequency for a given length. This is consistent with physical intuition and mechanical principles: larger or stiffer structural dimensions typically result in lower frequencies of vibration due to higher inertia or reduced elasticity.

The nonlocal Timoshenko beam theory accommodates for the effect of shear deformation and rotational inertia, which are particularly relevant at the microscale, where classical beam theories may not capture the behavior of such slender structures accurately. The data presented in this graph provides crucial insights into how the intrinsic geometrical properties of microtubules influence their dynamic response, which is essential for the design of experiments and the development of accurate predictive models in cellular biomechanics.

Figure 4 presents a graphical analysis of how the shear modulus ratio affects the natural frequency of microtubule (MT) proteins, at two different physiological temperatures, within a surrounding filament network. The shear modulus ratio, plotted on the x-axis, likely represents the relative stiffness of the microtubule to the surrounding matrix or the influence of the shear modulus on the MT's mechanical properties. The y-axis measures the frequency of the microtubule, which is related to its vibrational behavior.

The solid line indicates the frequency response at a body temperature of 37°C, and the dashed line represents the response at 34°C, slightly below normal body temperature. It can be observed that as the shear modulus ratio increases, indicating an increase in relative stiffness, the frequency of the microtubules also increases. This trend is consistent with mechanical theory, which suggests that stiffer materials tend to vibrate at higher frequencies. Notably, the frequency at the higher temperature of 37°C is consistently below that at 34°C across the entire range of shear modulus ratios. This could imply that the thermal energy at the higher temperature may be causing the microtubules to soften, hence they vibrate at a lower frequency compared to when they are at the cooler temperature. This observation may be important for understanding how temperature variations within physiological ranges can influence the mechanical stability and functions of microtubules in cellular processes.

Overall, the temperature impacts, rotary inertia reduces in the vibrational frequencies, transverse shear deformation, the reduction is noticed at higher vibration levels and the ratio of the small length-to-diameter. It is noticed that by taking small ratios of length-to-diameter along with high vibration factors, the Timoshenko beam nonlocal theory is observed for better prediction frequencies as an alternative to the Euler-Bernoulli beam system that ignores the rotary inertia and shear transverse deformation effects. The preceding parametric investigation represents that the small-scale impact, rotary inertia reduces in the vibrational frequencies, and transverse shear deformation, especially for short protein microtubules, and for higher vibration systems.

Absolutely, the applications of this research are transformative. In biotechnology and nanotechnology [28-30], understanding the vibrational behavior of protein microtubules can lead to significant advancements. The development of nano-electromechanical systems (NEMS) and micro-electromechanical systems (MEMS) [31-35] benefits greatly from these insights, particularly in the realms of drug delivery and biomedical device precision. Furthermore, this research enhances our comprehension of cellular mechanics, a key aspect of biological sciences. The implications in materials science are also profound [36-41]. By improving our understanding of the mechanical properties of nanoscale materials and structures, the study paves the way for innovative applications in diverse fields such as electronics, robotics, and aerospace. This interdisciplinary impact underscores the importance of such research in driving technological and scientific progress.

5. Conclusion

This comprehensive study has elucidated the intricate interplay between temperature and the dynamic mechanical behavior of protein microtubules within living cells, through the lens of nonlocal elasticity theory. The application of the Timoshenko beam model, in contrast to the classical Euler beam theory, has provided a more refined analysis of microtubules' vibrational characteristics, accounting for shear deformation and rotational inertia effects. Our results have conclusively demonstrated that thermal effects induce a reduction in the vibrational frequency of microtubules, which is further modulated by changes in the number of vibrational modes, the length-to-diameter ratio, and the intrinsic temperature of the cellular environment. Specifically, an increase in the shear modulus ratio correlates with a heightened frequency response, emphasizing the significance of microtubule geometry in their mechanical response. Notably, at physiological temperatures, the thermal impact is non-linear, with frequency values increasing at lower temperatures under thermal loading but decreasing at higher temperatures. This nuanced thermal sensitivity is critical for the stability and function of microtubules in various cellular processes, including mitosis and intracellular transport. The findings of this study provide valuable insights into the design of targeted therapeutics and the development of synthetic microtubules, potentially impacting the field of nanobiotechnology and the treatment of diseases linked to cytoskeletal dysfunction.

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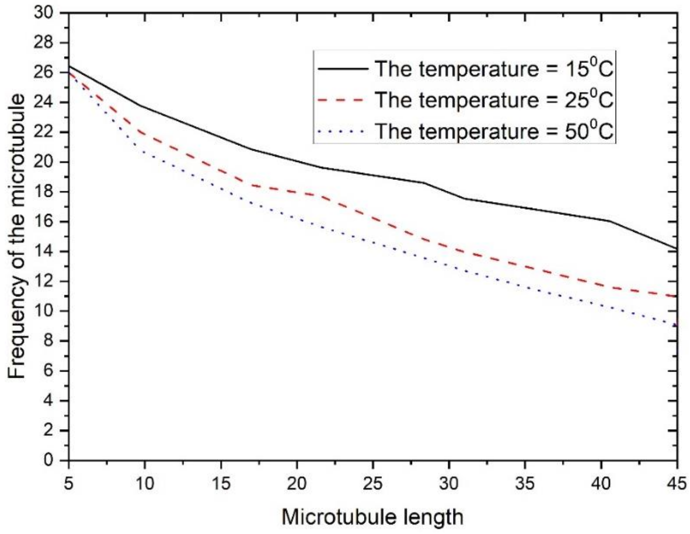

Figure 2: Relationship between the vibrational frequency of protein microtubules and their length across different temperature settings, with a simply-supported boundary condition. The frequency demonstrates a decreasing trend with increased microtubule length, and a reduction in frequency is observed with rising temperatures, indicative of the thermal sensitivity of microtubule dynamics..

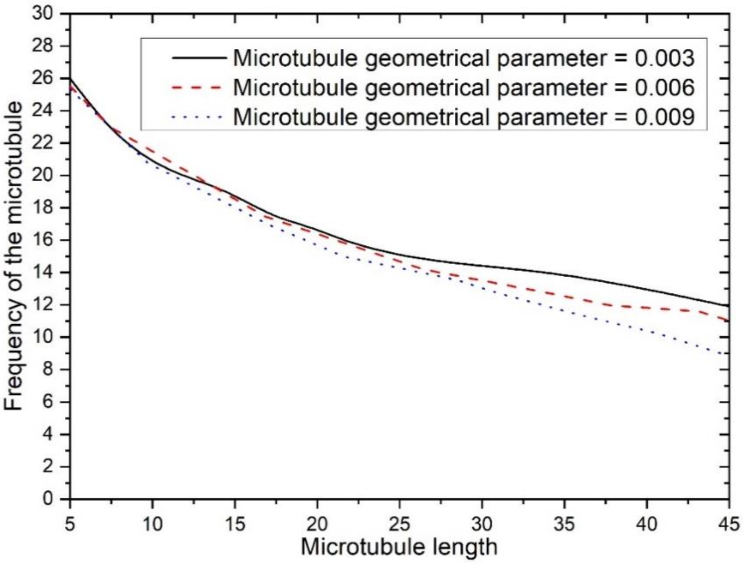

Figure 3: Frequency versus microtubule length for varying microtubule geometrical parameters, analyzed within the nonlocal Timoshenko beam theoretical framework. Each curve depicts the change in natural frequency with microtubule length for a distinct geometrical parameter value, demonstrating the sensitivity of vibrational characteristics to microtubule geometry.

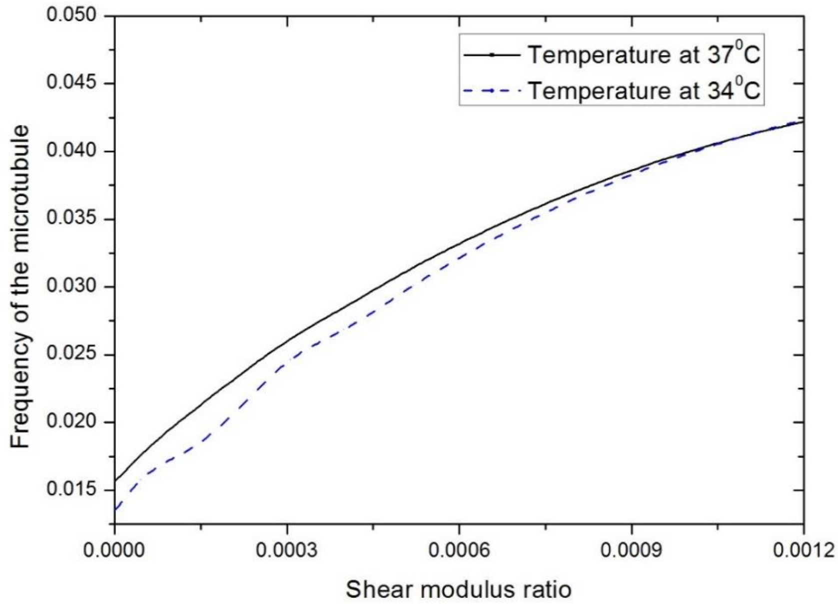

Figure 4: The influence of the shear modulus ratio on the vibrational frequency of microtubule proteins at two physiological temperatures, within a cytoskeletal filament network. The data indicates that an increase in the shear modulus ratio correlates with an increase in frequency, and the overall frequency is lower at 37°C compared to 34°C, suggesting temperature-dependent changes in microtubule mechanics.

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