BIOMECHANICAL CHARACTERISTICS OF MICROTUBULES DURING DEFORMATION AND VIBRATION

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Abstract

Due to their potential use as sensors, actuators, drug delivery systems, and other devices, microtubules (MT) have significant technical significance. It is crucial to comprehend the biological function of the MTs since their characteristics and mechanics are significantly influenced by their biomechanical environment. Although static microtubule mechanics has received a great deal of attention, only a small number of studies have focused on the biomechanical characteristics of microtubules that are deforming and vibrating. In this work, we use 3D finite element analysis to examine the biomechanical characteristics of the microtubule under bending deformation and free vibration. Finite element analysis results for force-deformation, vibration frequencies, and mode shapes are shown. According to the results, over longer time intervals, the force-deformation characteristics become non-linear and change with time and phase. Higher modes will exhibit coupled bending, torsion, and axial deformations and have MT vibration modes with frequencies in the GHz range. The deformation of these higher modes and forms changes, which may have effects on biological and physiological activity, particularly in terms of sensing, actuation, and communication with cells. Understanding the bending force-deformation properties, vibration modes, and frequency of self-assembled microtubules should be made easier.

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1. Introduction

The fundamental building blocks for microtubules (MTs), which are long filamentous intracellular structures with a diameter of 25 nm and are fairly lengthy, are tubulin dimers (and tubulins). MTs are in charge of a number of biological processes, including flagellar motility, intracellular structure and transport organisation, and cell division (Johnson et al., 2002). Living cells regularly experience bending, stress, torsion, vibration, and these behaviours are crucial to the biomechanical behaviour of microtubules. Moreover, microtubules include individual tubulins that may exist in many states and undergo changes on various time scales, displaying the multifunctional features of MTs.

Both straight and curved microtubules show anisotropic characteristics(Valdman et al., 2012) as well as length-dependent mechanical characteristics(Dogterom & Surrey, 2013). Moreover, the mechanical properties of MTs are significantly influenced by the binding of microtubule association proteins (MAPs). The aforementioned mix of features enables MTs to perform a variety of tasks, including cargo delivery, mitosis, flagella and cilia movement, and regulating cell shape. In order to further understand the mechanical characteristics of MTs, several papers were published to further explain these traits shown in tests.

Many studies have been conducted on the static and molecular causes of individual MT mechanics (Hawkins et al., 2010). In the effort to comprehend the relationship between the material qualities of microtubules and their capacity to perform a variety of roles in cells, there has been substantial investigation on the vibration dynamics and fluctuations of microtubules. Several research on MT vibrations have been done because of how important and influential they are for intracellular functions. Using 3D models, (Pampaloni et al., 2006) examined the beam-like bending vibration of microtubules. They also looked on the use of microtubule electromechanical vibration in sensors (Verhey & Gaertig, 2007). In an electric field, MTs' transverse vibration ranges from 18.4 to 240.3 MHz, and the variations in vibrational properties may be caused by interactions between tubulins, which might make them useful as sensors for observing physiological processes. In their research of the buckling and vibration responses of microtubules in axons, (Bachand et al., 2015) employed a nonlocal strain gradient model and discovered some intriguing features of softening and hardening at higher vibrational frequencies. In their mini-review, (Liew et al., 2015; Tang et al., 2009) analysed models of microtubule vibration dynamics and outlined the drawbacks of their inability to effectively predict physiological or biological activity. An atomistic investigation of the deformation pattern of vibrating microtubules by (Kis et al., 2002) revealed that anisotropy caused by bonds between tubulins has a significant impact on the vibration frequencies. Microtubules' mechanical characteristics (Young's modulus) were calculated using dynamic simulation and the finite element technique and their results were compared to those from previously published research. In order to examine microtubule characteristics under free vibration, (Kabir et al., 2014) created an orthotropic shell model. They also demonstrated the significance of vibrational models in both longitudinal and circumferential orientations.

Straight protofilaments were modelled using a finite element method by (Li et al., 2017), who also looked at the impact of various loadings on the mechanical behaviour of the protofilaments. They discovered that under tension and torsion, the protofilament acts nonlinearly, yet linearly under bending. Curvature has a significant impact on the mechanical behaviour, particularly the stress-strain correlations, according to research by (Li et al., 2019) on the mechanical characteristics of microtubule protofilaments that are curved. The references (Li et al., 2019; Liew et al., 2015; Tang et al., 2009) make it clear that microtubule/protofilament stiffness under successive loadings is significantly influenced by both deformation and stiffness. Moreover, the stiffness and maximum stresses in the MTs are two ways that the protofilament/MT curvature affects mechanical behaviour. More research into the vibrational behaviour of tubulins is critical given the significant role they play in microtubule self-assembly and the interactions between them.

By 3D finite element analysis, we examined the microtubules' vibrational frequencies and mode morphologies in this work. Bending deformation and free vibrational evaluations were performed following the creation of the MT shape and assignment of the attributes. Finite element analysis findings for force-deformation and free vibration characteristics are given and analysed.

2. Computational Approach

In the calculations, a protofilament-based microtubule arrangement that consists of a hollow cylindrical tube fused together in parallel to one another along the circumferential direction was considered. A microtubule typically consists of 8–13 protofilaments and measures 15.4–25 nm in diameter on the inside and outside, respectively. Tens of nanometers to hundreds of microns are the possible ranges for MT length. In Figure 1, you can see that we made 8 protofilaments along the circumferential direction, each of which was made up of 10 spherical tubulins, with -tubulin and -

tubulin forming a dimer. The inner and outer microtubule diameters of each tubulin are estimated to be 12 nm and 24 nm, respectively, with a tubulin diameter of 6 nm. ANSYS DesignModuler was used to create the microtubules, and to reflect the elasticity of MT proteins, one tubulin was linked to the other via a spring at the contact site. Figure 1 also displays the microtubule's finite element model (FEM).

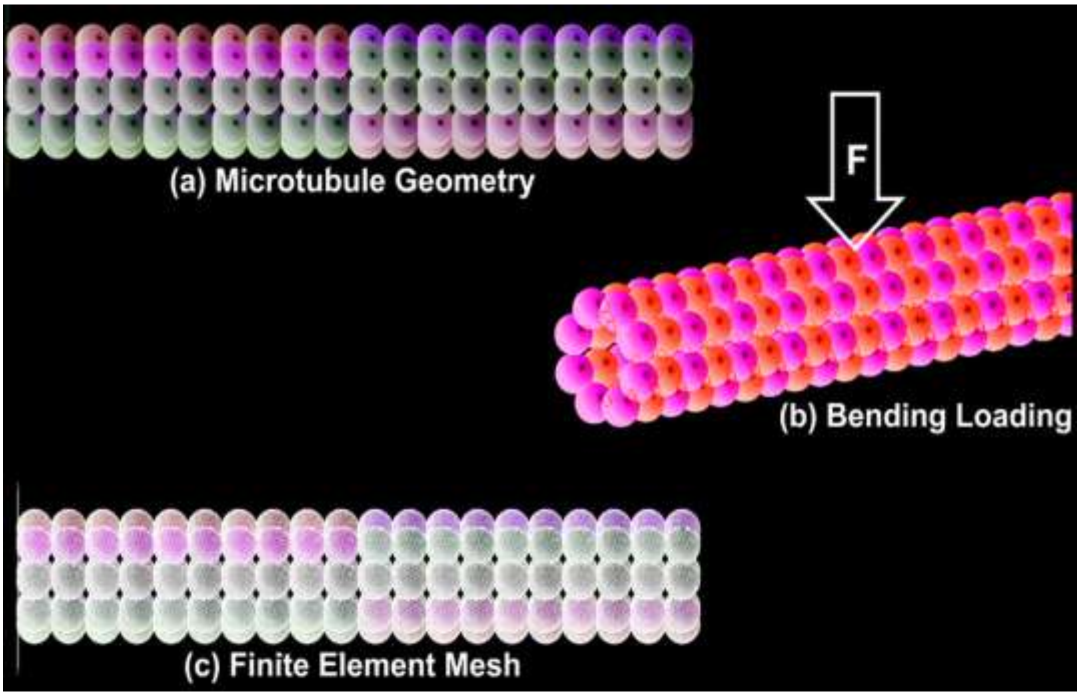

Figure 1: In the analysis of microtubules, (a) geometry, (b) bending loads, and (c) finite element mesh were taken into account

The literature is where we found the spring constants and material characteristics we used in our investigation. According to a molecular dynamics (MD) research, each individual tubulin has a stiffness of around 11 N/m, but a whole tubulin has a stiffness of about 15.6 N/m. The spherical shell model's shear modulus is set at 400 MPa. Our model does not distinguish between tubulins and tubulins because of their structural resemblance and comparable mechanical capabilities. Table 1 contains a collection of these facts.

Table 1: FE model parameters for microtubule construction

Parameter	Value
Microtubulin radius	12.5 nm
Microtubulin surface area	157 nm^2
Microtubulin volume	8.2 μm^3
Each contract area	3.6 nm^2
Initial shear modulus	400 MPa
Microtubule spring constant	47.1 nN/nm

ANSYS 16.0 Mechanical package software was used to run all simulations. Our 3D finite element model was created using ANSYS Workbench, and it was examined using a nonlinear material condition. The computational model used here has 103,350 shell components and 104,000 nodes. With a typical curvature of roughly 0.4 rad/nm in fibroblast cells, experimental studies have demonstrated that MTs commonly bend in live cells. In order to evaluate the bending deformations, the bending of MT was explored in a manner akin to the research employing a

nanoindentation technique. Here are the findings of the analyses of the force-deformation and free vibration modes.

3. Results and Discussion

3.1. Characteristics of Force-Deformation in Bending

The force-deformation properties were investigated using finite element modelling, and the results were compared to those from in-silico and nanoindentation experiments. Using the finite element analysis, Figure 2 depicts the bending deformation of the MT at four distinct phases (times). As can be observed, bending distortion gets worse as time goes on. Figure 3 displays the force-deformation properties with time. The MT is initially stiff and gradually starts to soften and become non-linear with time and further deformation.

Figure 4 displays the findings of maximum displacement and maximum stresses at various times/phases. Figure 4 shows that during the bending loading on the MT, the maximum displacements and stresses grow with increasing times. It's noteworthy to note that the computational model is validated by the fact that the MT bending deformation is within the range (5–25 nm) of results from molecular dynamics simulations. Moreover, the force-deformation properties change from linear to non-linear with various bending deformation phases. This demonstrates how the MT may change its shape to accommodate different loading scenarios.

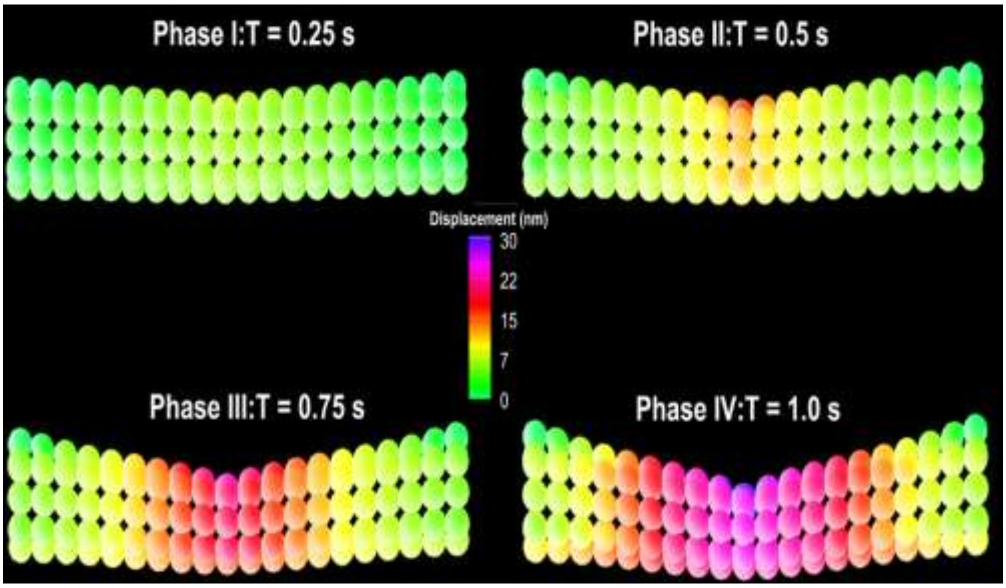

Figure 2: Deformation of microtubules at four distinct intervals and phases

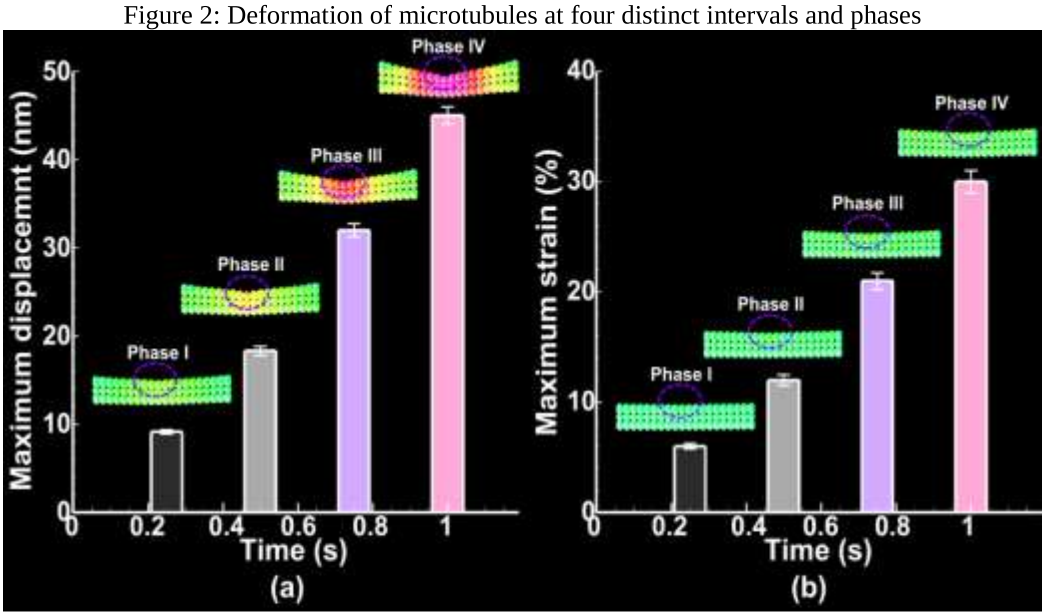

Figure 4: Maximum displacement (a) and maximum strains (b) of microtubule under bending at four different times

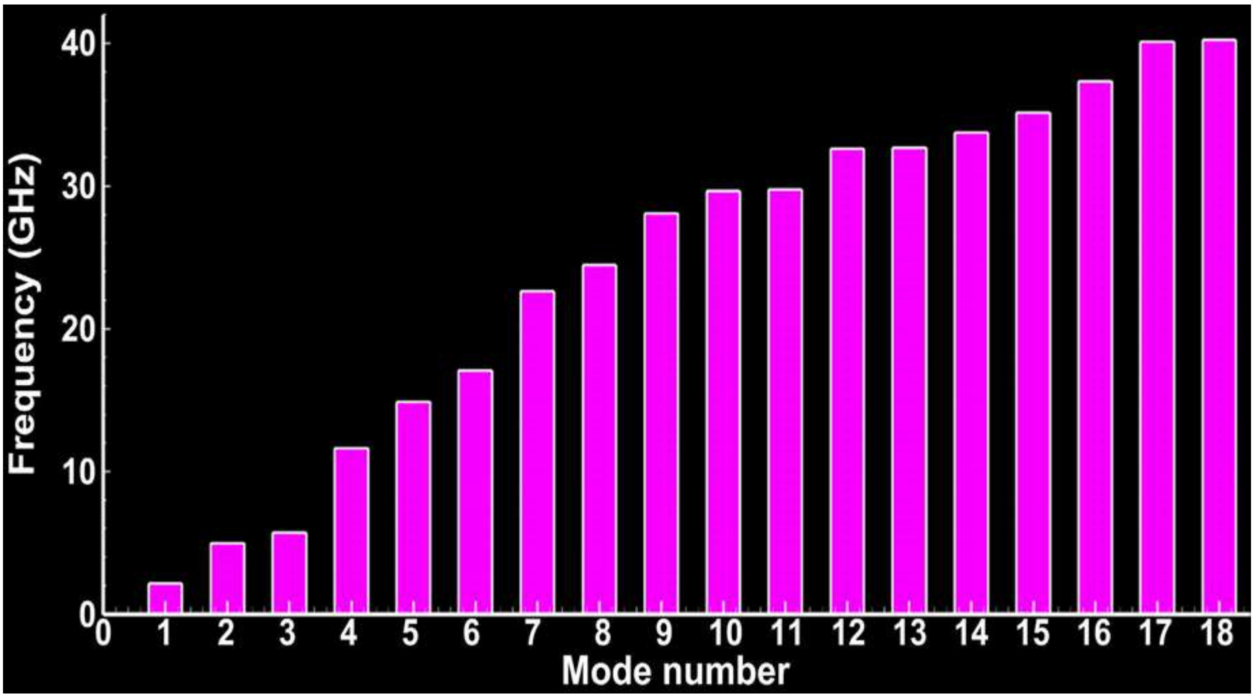

Figure 5: The study revealed the first 18 microtubule vibration frequencies

3.2. Features of Free Vibration

Figure 5 displays the vibration frequency findings for the MT configuration from the finite element study. The first 18 modes of vibration for the MT under consideration have frequencies in the GHz range. This result is in line with findings from earlier research. Figure 6 displays the mode forms for these 18 frequencies. The main modes include linked axial and bending (mode 8), coupled bending and torsion (mode 7), and bending (mode 4). (mode 11). Higher modes include higher bending, twisting, and axial forces (modes 14, 16, 17).

It's fascinating to observe how the MT can support many vibration modes and their fusion. This is crucial for MT performance because it may behave as a multifunctional unit with capabilities for shape organization, nanomaterial, sensing, and actuation. In Figure 7, the vibration modes are also qualitatively compared to those discovered using molecular dynamics simulations. There is a pretty strong consensus. In order to create the MT self-assembly, tubulin and their binding sites cause deformations, which are reflected in these vibration modes.

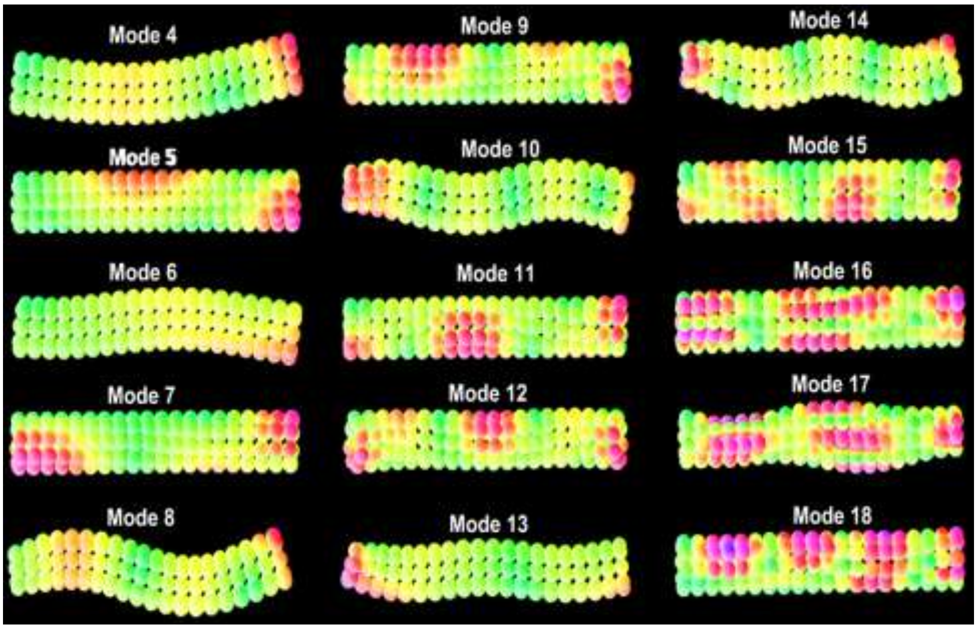

Figure 6: After investigation, the microtubule's mode shapes were determined

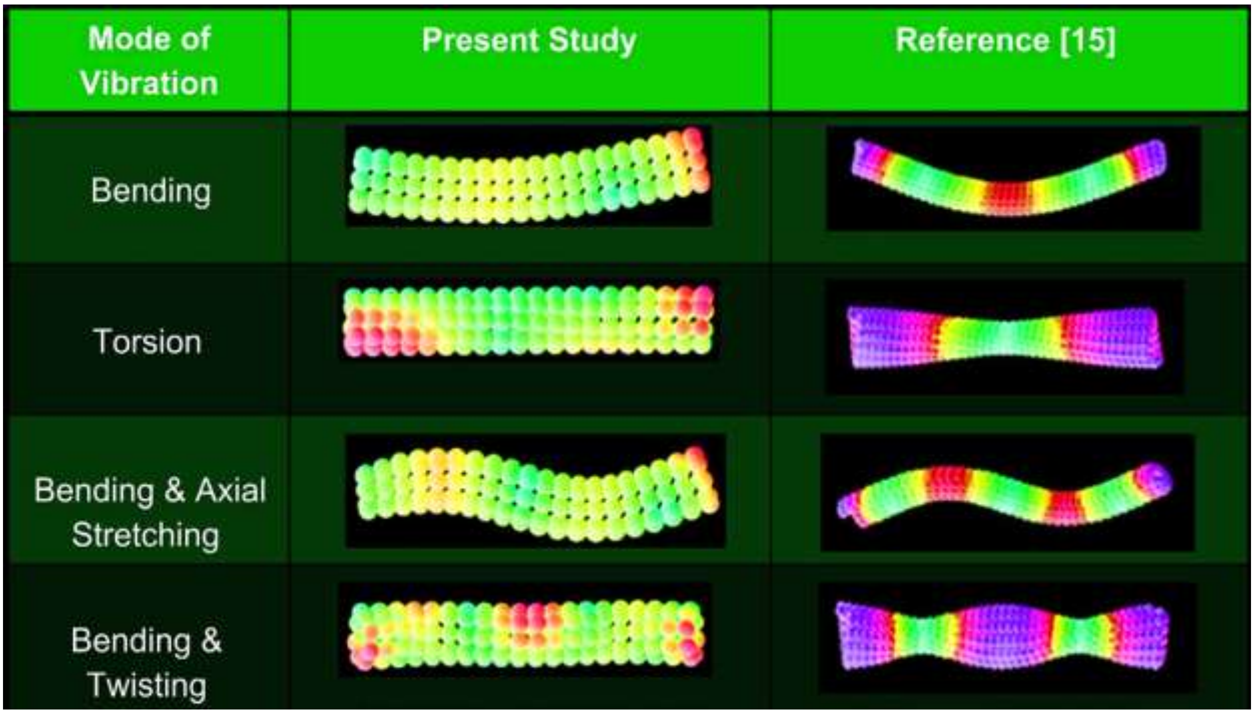

Figure 7: Comparison of the microtubule's first few fundamental mode shapes with those found using molecular dynamics

4. Conclusion and future scope

In this work, bending deformation and free vibration evaluations were carried out using a 3D finite element model for microtubules that was based on molecular level data. The deformations were discovered to be within the range of 5 - 30 nm when the findings of bending deformation characteristics with increasing time were compared with molecular dynamics analysis results. The findings of vibration frequencies and modes also compared favorably in terms of frequency ranges and vibration modes. In addition, bending, axial, and torsion modes were mixed in the higher vibration modes. Our findings show the versatility of MT in tolerating coupled deformations and raise the possibility of MT applications as sensors and actuators.

5. Reference

Bachand, G. D., Spoerke, E. D., & Stevens, M. J. (2015). Microtubule-based nanomaterials: Exploiting nature's dynamic biopolymers. *Biotechnology and Bioengineering*, *112*(6), 1065–1073.

Dogterom, M., & Surrey, T. (2013). Microtubule organization in vitro. *Current Opinion in Cell Biology*, *25*(1), 23–29.

Hawkins, T., Mirigian, M., Yasar, M. S., & Ross, J. L. (2010). Mechanics of microtubules. *Journal of Biomechanics*, *43*(1), 23–30.

Johnson, A., Lewis, J., Raff, M., Roberts, K., & Walter, P. (2002). Molecular biology of the cell. *Garland Science*, *4*.

Kabir, A. M. R., Inoue, D., Hamano, Y., Mayama, H., Sada, K., & Kakugo, A. (2014). Biomolecular motor modulates mechanical property of microtubule. *Biomacromolecules*, *15*(5), 1797–1805.

Kis, A., Kasas, S., Babić, B., Kulik, A. J., Benoit, W., Briggs, G. A. D., Schönenberger, C., Catsicas, S., & Forro, L. (2002). Nanomechanics of microtubules. *Physical Review Letters*, *89*(24), 248101.

Li, S., Wang, C., & Nithiarasu, P. (2017). Three-dimensional transverse vibration of microtubules. *Journal of Applied Physics*, *121*(23), 234301.

Li, S., Wang, C., & Nithiarasu, P. (2019). Electromechanical vibration of microtubules and its application in biosensors. *Journal of the Royal Society Interface*, *16*(151), 20180826.

Liew, K. M., Xiang, P., & Zhang, L. W. (2015). Mechanical properties and characteristics of microtubules: a review. *Composite Structures*, *123*, 98–108.

Pampaloni, F., Lattanzi, G., Jonáš, A., Surrey, T., Frey, E., & Florin, E.-L. (2006). Thermal fluctuations of grafted microtubules provide evidence of a length-dependent persistence length. *Proceedings of the National Academy of Sciences*, *103*(27), 10248–10253.

Tang, Y., Liu, L., Li, W., Shen, B., & Hu, W. (2009). Interface characteristics and mechanical properties of short carbon fibers/Al composites with different coatings. *Applied Surface Science*, *255*(8), 4393–4400.

Valdman, D., Atzberger, P. J., Yu, D., Kuei, S., & Valentine, M. T. (2012). Spectral analysis methods for the robust measurement of the flexural rigidity of biopolymers. *Biophysical Journal*, *102*(5), 1144–1153.

Verhey, K. J., & Gaertig, J. (2007). The tubulin code. *Cell Cycle*, *6*(17), 2152–2160.