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# Nonlocal frequency analysis of nanoscale biosensors

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ABSTRACT

As a first endeavor, we propose nonlocal elasticity theory for carbon nanotube based cantilever biosensors. By using the frequency-shift of the fundamental vibration mode, we develop new nonlocal frequency sensor equations utilizing energy principles. Two physically realistic configurations of the added mass, namely, point mass and distributed mass are considered. Exact closed-form expressions relating the frequency-shift and the added mass have been derived for both the cases. The proposed nonlocal sensor-equations are general in nature and depend on three non-dimensional calibration constants namely, the stiffness calibration constant, the mass calibration constant and the nonlocal calibration constant. Explicit analytical expressions of these calibration constants are derived. An example of a single wall carbon nanotube with attached multiple strands of deoxythimidine is considered to illustrate the analytical results. Molecular mechanics simulation is used to validate the new nonlocal sensor equations. The optimal values of nonlocal parameter are obtained from the molecular mechanics simulation results. The nonlocal approach generally predicts the frequency shift accurately compared to the local approach. Numerical results show the importance of considering the distributed nature of the added mass while using the nonlocal theory.



## 1. Introduction

From nanoscale experiments [1–3], it has been observed that the mechanical properties of nano dimensional materials are much influenced by the 'size-effects'. The influence of size-effects on the magnitudes of resonance frequency and buckling load of nanoscale objects (viz. nanotubes and graphene) by atomistic simulations has also been reported [4]. Size-effects are related to atoms and molecules that constitute the materials. Though molecular dynamic (MD) simulation is justified for the analysis of nanostructures [4], the approach is computationally exorbitant for nanostructures with large numbers of atoms. This calls for the use of conventional continuum mechanics [5] in analysis of nanostructures. However classical continuum models are considered scale-free and it lacks the accountability of the effects arising from the small-scale where 'size-effects' are prominent. The application of classical continuum models may be questionable in the analysis of nanostructures such as carbon nanotubes and graphene sheets. One widely promising size-dependant continuum theory is the nonlocal elasticity theory pioneered by Eringen [6] which bring in the scale-effects and underlying physics within the formulation. In the nonlocal elasticity theory, the small-scale effects are captured by assuming that the stress at a point is a function of the strains at all points in the domain. Nonlocal theory considers long-range inter-atomic interaction and yields results dependent on the size of a body [6]. Some drawbacks of the classical continuum theory could be efficiently avoided and the size-dependent phenomena can be reasonably explained by nonlocal elasticity. From the literature it has been found that nonlocal elasticity has been used in various mechanical studies of nanostructures viz. nanobeams [7,8], nanoplates [9,10], carbon nanotubes [11,12], graphenes [13,14], microtubules [15,16] and nanorings [17].

Nanoscale sensors are a significant application area of nanotechnology. Significant growth is expected in this section over the next decade. Nanosensors are simple engineered device used to detect and convey information about nanoparticles and biomolecules to the macroscopic world. Nanoscale sensors are crucial for future biomedical technologies [18–21]. Nanosensors are broadly classified as chemical nanosensors [22] and biosensors [23–25]. The general role of chemical nanosensors is to detect the properties of gaseous molecules such as its speed and wavelength. One example of synthetic biosensors is by attaching particular nanoparticle or biomolecule to the end of carbon nanotubes (CNT) and calculating the vibration frequency of CNT with or without the particle periodically. Recently CNTs are delivering promises as functional materials for the development of advanced biosensors with such novel features. The concept of developing nano biosensors by utilizing CNTs [26–29] are thus becoming increasingly popular. The application of CNTs in ultrasensitive nanobiosensors [20,21] is the main theme of this paper.

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From the experimental evidence the biological entities such as DNA, proteins, enzymes, bacteria can be immobilized either in the hollow cavity through supramolecular inclusion or on the surface of carbon nanotubes and at the end-caps [30–34]. Biological entities such as carbohydrates [35,36], nucleic acids [37,38], peptides [39,40], and proteins [41,42], are non-covalently adsorbed on the carbon nanotube surfaces through hydrophobic, π–π stacking, and electrostatic interactions. This has motivated the development of nano biosensors [43] and nanoscale bioreactor systems based on CNTs. Further randomly entangled CNTs are physically coated onto conventional electrodes for many electrochemical biosensing applications [31].

Resonance based sensors offer the deeper potential of achieving the high-fidelity requirement of many sensing applications [44]. The principle of mass detection using resonators is based on the fact that the resonant frequency is sensitive to the resonator mass, which includes the self-mass of the resonator and the attached mass. The change of the attached mass on the resonator causes a shift to the resonant frequency. The key issue of mass detection is in quantifying the change in the resonant frequency due to the added mass.

Recognising the fact that the frequency shift based approach is a promising way forward for the nano-scale bio sensors and the nonlocal theory is a valid efficient theory for a wide range of nano-scale objects, in this paper we aim to put these together. In particular, we develop a new analytical approach for nano biosensors using nonlocal elasticity theory [6]. Recently Lee et al. [45] calculated the frequency shift of carbon-nanotube based mass sensor using nonlocal elasticity theory. This aim of this paper is to take the next step, which is to develop sensor equations based on the frequency shift. We consider the interaction of a biomolecule resting on the single-walled carbon nanotube. Employing Euler–Bernoulli beam theory [8] and molecular mechanics simulation we report a simple approach for modeling and calibrating nanoscale biosensors. The nanoscale-effects in the biosensor engineering model are handled by the nonlocal elastic approach which is in accordance with lattice dynamics. Closed-form nonlocal frequency expression is derived to detect the mass of biomolecule from the nonlocal frequency-shift. Both point mass and distributed mass attached to single-walled carbon nanotube is considered. The nonlocal effects on the frequency shift are analysed and discussed. Comparing with the molecular mechanics results, optimised values of the nonlocal parameters are found for the biosensor models. A numerical example of a single walled CNT based biosensor to detect the mass of several strands of deoxythimidine is considered. It is shown that the new sensor equations obtained using the proposed nonlocal theory can provide more accurate prediction of the attached mass compared to the same using the classical theory.

## 2. Review of nonlocal elasticity theory

For sake of completeness we provide a brief review of nonlocal elasticity theory. According to nonlocal elasticity, the basic equations for an isotropic linear homogenous nonlocal elastic body neglecting the body force are given as [6,12–14].

$$\begin{aligned} &\sigma_{ij,j} = 0, \\ &\sigma_{ij}(\boldsymbol{x}) = \int_{\boldsymbol{V}} \phi(|\boldsymbol{x} - x'|, \alpha) t_{ij} d\boldsymbol{V}(x'), \ \forall x \in \boldsymbol{V} \\ &t_{ij} = H_{ijkl}\varepsilon_{kl}, \\ &\varepsilon_{ij} = \frac{1}{2}(u_{i,j} + u_{j,i}) \end{aligned} \tag{1}$$

The terms $\sigma_{ij}$, $\varepsilon_{kl}$, $H_{ijkl}$ are the stress, strain and fourth-order elasticity tensors respectively. The above equation (Eq. (1)) couples the stress due to nonlocal elasticity and the stress due to classical elasticity. The kernel function $\phi(|\boldsymbol{x} - \boldsymbol{x}'|, \alpha)$ is the nonlocal modulus. The nonlocal modulus acts as an attenuation function incorporating into constitutive equations the nonlocal effects at the reference point $\boldsymbol{x}$ produced by local strain at the source $\boldsymbol{x}'$ $|\boldsymbol{x} - \boldsymbol{x}'|$ represents the distance in the Euclidean form and $\alpha$ is a material constant that depends on the internal (e.g. lattice parameter, granular size, distance between the C–C bonds) and external characteristics lengths (e.g. crack length, wave length). Material constant $\alpha$ is defined $\alpha = e_0 a/\ell$. Here $e_0$ is a constant for calibrating the model with experimental results and other validated models [6]. The parameter $e_0$ is estimated such that the relations of the nonlocal elasticity model could provide satisfactory approximation to the atomic dispersion curves of the plane waves with those obtained from the atomistic lattice dynamics. $a$ and $\ell$ are the internal (e.g. lattice parameter, granular size, distance between C–C bonds) and external characteristic lengths (e.g. crack length, wave length) of the nanostructure.

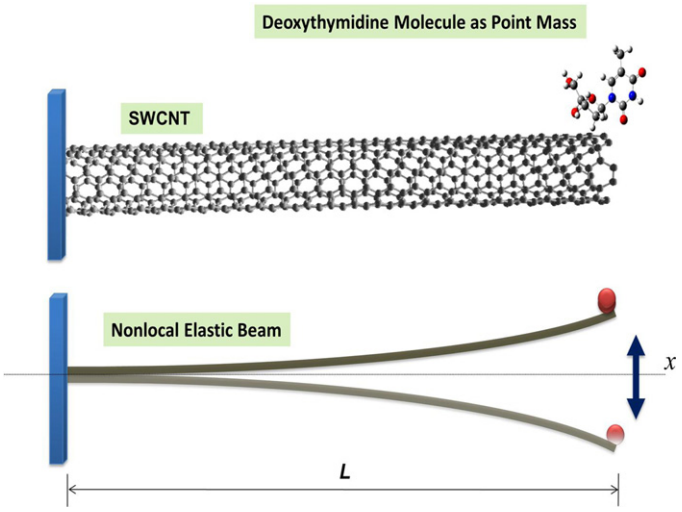



**Fig. 1.** Idealisation of a single-walled carbon nanotube (CNT)-deoxythymidine molecule as nonlocal elastic continuum beam with a point mass.

## 3. Nonlocal resonance frequency of CNT with attached biomolecule

We consider the frequency of single-walled carbon nanotubes (SWCNT) with an attached bio-mass, for example, a deoxythymidine molecule (Fig. 1). The continuum models based on nonlocal beam as well as shell have been used extensively for single- and multi-walled carbon nanotubes [11,12]. In order to obtain simple analytical expressions for sensor design, we model a SWCNT using a rod based on the nonlocal Euler–Bernoulli beam theory [12]. The equation of motion of free vibration is given as

$$EI\frac{\partial^4 w}{\partial x^4} + \left[1 - (e_0 a)^2 \frac{\partial^2}{\partial x^2}\right] \rho A \frac{\partial^2 w}{\partial t^2} = 0 \tag{2}$$

where $E$ is Young's modulus, $I$ the second moment of the cross sectional area $A$, and $\rho$ the density of the material. Suppose the length of the SWCNT is $L$. Depending on the boundary condition of the SWCNT and the location of the attached mass, the resonant frequency of the combined system can be derived.

We consider only the fundamental frequency $f_n$ of the vibrating systems as:

$$f_n = \frac{1}{2\pi}\sqrt{\frac{k_{eq}}{m_{eq}}} \tag{3}$$

where $k_{eq}$ and $m_{eq}$ are the equivalent stiffness and mass of the vibrating system. In the fundamental mode of vibration, the vibration mode shape is similar to that of the bending deformation of a nonlocal cantilever beam under a point load at the free edge.

Considering the deformation of the free edge, the stiffness of the SWCNT is assumed as [44]

$$k_{eq} = \frac{3EI}{L^3} \tag{4}$$

It is known that the static bending solutions of integral-based nonlocal elastic beams are identical to the classical (local) solution, i.e. the small scale effect is not explicitly present [7]. However, it should be noted that Challamel and Wang [46] has proposed a gradient elastic model as well as an integral non-local elastic model combining the local and the non-local curvatures in the constitutive elastic relation; and consequently small-scale effects are reflected in the analysis. In the present analysis we assume general bending solutions of integral-based non-local elastic beams identical to the classical (local) solution.

The deflection shape of the SWCNT with a point load is given in [45] as

$$W(x) = \frac{x^2(3L-x)}{2L^3} \tag{5}$$

The kinetic energy $T$ considering nonlocal effects [6] with added biomolecule mass is expressed as [47]:

$$T = \frac{1}{2}\int_0^L \rho A\left(\frac{\partial w(x,t)}{\partial t}\right)^2 dx + \frac{1}{2}M\left(\frac{\partial w(L)}{\partial t}\right)^2 + \frac{1}{2}\int_0^L (e_0a)^2\rho A\left(\frac{\partial^2 w(x,t)}{\partial x \partial t}\right)^2 dx \tag{6}$$

When the nonlocal effects are ignored ($e_0a = 0$) we obtain the classical expression of kinetic energy.

Assuming harmonic motion, we have

$$w(x,t) = W(x)e^{i\omega t} \tag{7}$$

where $\omega$ is the circular frequency and $i$ is the conventional imaginary number $i = \sqrt{-1}$. Substituting this into the expression of the kinetic energy one obtains

$$\begin{aligned} T &= \frac{\omega^2}{2}\int_0^L \rho A W(x)^2 dx + \frac{1}{2}MW(L)^2 \\ &+ \frac{\omega^2}{2}\int_0^L (e_0a)^2\rho A\left(\frac{dW(x)}{dx}\right)^2 dx \\ &= \rho A\frac{\omega^2}{2}\int_0^L W(x)^2 dx + \frac{\omega^2}{2}MW(L)^2 \\ &+ \rho A(e_0a)^2\frac{\omega^2}{2}\int_0^L \left(\frac{dW(x)}{dx}\right)^2 dx \end{aligned} \tag{8}$$

Using the displacement function in Eq. (5) and carrying out the integrals we have

$$T = \frac{\omega^2}{2}\left(\frac{33}{140}\rho AL + M + \left(\frac{e_0a}{L}\right)^2\frac{6}{5}\rho AL\right) \tag{9}$$

Therefore the equivalent mass of the combined system is given as

$$m_{eq} = \frac{33}{140}\rho AL + M + \left(\frac{e_0a}{L}\right)^2\frac{6}{5}\rho AL \tag{10}$$

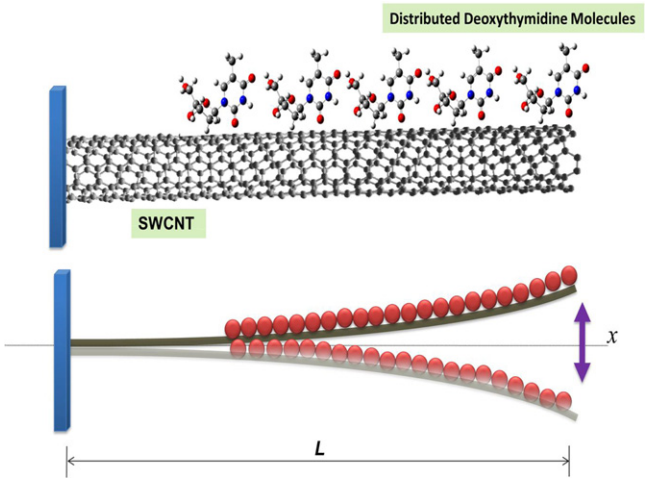



**Fig. 2.** Idealisation of a single-walled carbon nanotube (CNT) and several strands of deoxythymidine molecules as s nonlocal elastic continuum beam with distributed mass.

Using Eqs. (4) and (9) the approximate resonance frequency can be obtained as

$$f_n = \frac{1}{2\pi}\sqrt{\frac{k_{eq}}{m_{eq}}} = \frac{1}{2\pi}\sqrt{\frac{(3EI/L^3)}{(33/140)\rho AL + M + (e_0a/L)^2(6/5)\rho AL}} \tag{11}$$

Since we derive the frequency equations base on the energy methods [47], the nonlocal effect is introduced in the equivalent mass. The frequency expression can be represented in terms of three calibration constants, $C_k$, $C_{nl}$ and $C_m$ such that

$$f_n = \frac{1}{2\pi}\frac{C_k\beta}{\sqrt{1 + C_{nl}\theta^2 + C_m\Delta M}} \tag{12}$$

where

$$\beta = \sqrt{\frac{EI}{\rho AL^4}} \tag{13}$$

$$\Delta M = \frac{M}{\rho AL} \tag{14}$$

$$\theta = \frac{e_0a}{L} \tag{15}$$

The stiffness calibration constant, mass calibration constant and the nonlocal calibration constant are respectively given by

$$C_k = \sqrt{\frac{140}{11}}, \quad C_m\frac{140}{33}, \text{ and } C_{nl} = \frac{56}{11} \tag{16}$$

These calibration constants will be used to derive the sensor equations.

## 4. Nonlocal resonance frequency with attached distributed biomolecules

Here we consider biosensors with CNT when the attached mass (biomolecules) is distributed in nature (Fig. 2). This is the more general case compared to what considered in the previous section (Section 3). A nano biosensor with distributed mass is shown in the Fig. 2, where a CNT is loaded with distributed deoxythymidine molecules. The biosensor is modelled as a nonlocal beam with attached distributed mass. Suppose the added mass occupies a length $\gamma L$and its mass per unit length is $M$. Therefore we have the total mass $m = M \times \gamma L$.

The kinetic energy of the SWCNT with the added distributed mass can be written as

$$T = \frac{\omega^2}{2}\int_0^L \rho A W(x)^2 dx + \frac{\omega^2 M}{2\gamma L}\int_{\xi=L-\gamma L}^{L} W(\xi)^2 d\xi + \frac{\omega^2}{2}\int_0^L (e_0 a)^2 \rho A\left(\frac{dW(x)}{dx}\right)^2 dx \quad (17)$$

Using Eq. (17) and a similar procedure as the case of point mass, the three calibration constants, namely the stiffness calibration constant, the mass calibration constant and the nonlocal calibration constant, can be evaluated.

The fundamental frequency for attached distributed mass can be expressed as

$$f_n = \frac{1}{2\pi}\frac{C_k\beta}{\sqrt{1 + C_{nl}\theta^2 + C_m(\gamma)\Delta M}} \quad (18)$$

where $C_k$ and $C_{nl}$ are same as Eq. (16), that is $C_k = 3.5675$ and $C_{nl} = 5.0909$. The mass calibration constant $C_m(\gamma)$ for distributed case is calculated as

$$C_m(\gamma) = \frac{140 - 210\gamma + 105\gamma^2 + 35\gamma^3 - 42\gamma^4 + 5\gamma^6}{33} \quad (19)$$

The mass calibration constant is a function of the length of the attached mass as expected. In the special case the length of the mass ($\gamma$) approaches to 0, the calibration constant in Eq. (19) reduces to the point mass cases derived before.

The values of the mass calibration constants $C_m(\gamma)$for different selected values of $\gamma$ are shown in Table 1. It can be seen that with the increase in the value of $\gamma$, the value of the mass calibration constant decreases. Therefore, according to Eq. (19), this in turn will make the sensor less sensitive even when the amount of total added mass is the same. Practically Eq. (19) suggests that, in order to design a sensitive CNT based biosensor, one need to maximise the length of the CNT relative to the length of the biomolecule. The effective length of the biomolecule would also refer to number of molecules consecutively attached to the nanotube with respect to length of the CNT.

## 5. Nonlocal sensor equations

In this section we present the sensor equations based on nonlocal elasticity. We will derive the general expression of the added mass of biomolecule based on the frequency-shift of the CNT.Using Eq. (12), the resonance frequency without the added mass and nonlocal effects is given by

$$f_{0n} = \frac{1}{2\pi}C_k\beta \quad (20)$$

Combining Eqs. (18) and (20) we obtain

$$f_n = \frac{f_{0n}}{\sqrt{1 + C_{nl}\theta^2 + C_m\Delta M}} \quad (21)$$

The frequency shift of the biosensor can be written as

$$\Delta f = f_{0n} - f_n = f_{0n} - \frac{f_{0n}}{\sqrt{1 + C_{nl}\theta^2 + C_m\Delta M}} \quad (22)$$

From this we deduce

$$\frac{\Delta f}{f_{0n}} = 1 - \frac{1}{\sqrt{1 + C_{nl}\theta^2 + C_m\Delta M}} \quad (23)$$

Rearranging the equations gives the expression of the relative added mass as

$$\Delta M = \frac{1}{C_m(1 - (\Delta f/f_{0n}))^2} - \frac{C_{nl}}{C_m}\theta^2 - \frac{1}{C_m} \quad (24)$$

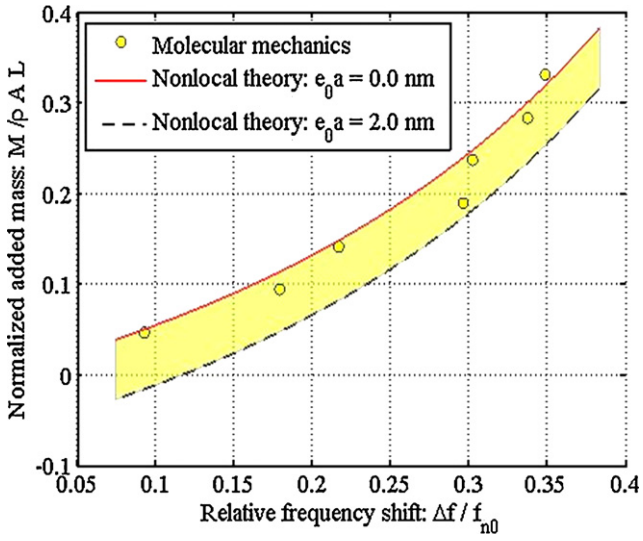



**Fig. 3.** Normalized mass vs. relative frequency shift for the SWCNT with point mass. The band covers the complete range of nonlocal the parameter $0\,\text{nm} \le e_0 a \le 2.0\,\text{nm}$. It can be seen that the molecular mechanics simulation results reasonably fall within this band (except at ($\Delta f/f_{n0} = 0.35$)).

This equation (Eq. (24)) completely relates the change in mass with the frequency shift using the mass calibration constant and the nonlocal calibration constant. The actual value of the added mass can be obtained from (24) as

$$M = \frac{\rho AL}{C_m}\frac{C_k^2\beta^2}{(C_k\beta - 2\pi\Delta f)^2} - \frac{C_{nl}}{C_m}\theta^2\rho AL - \frac{\rho AL}{C_m} \quad (25)$$

This is the general equation which completely relates the added mass and the frequency shift using the calibration constants. These calibration constants change depending on the boundary conditions and geometry of the added mass.

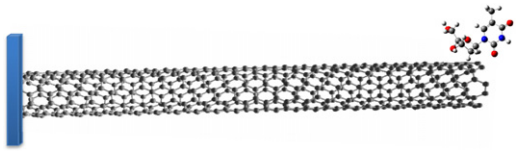
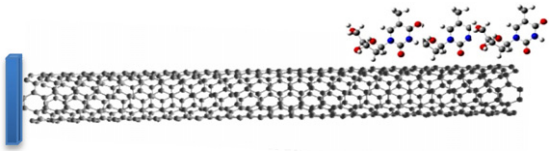
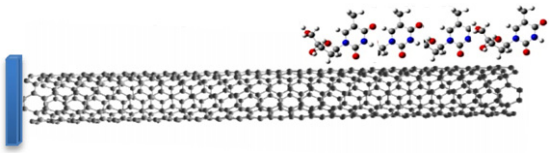
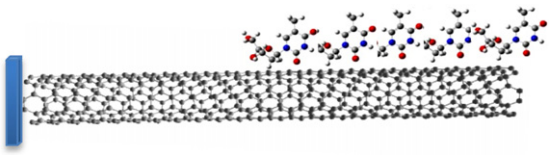
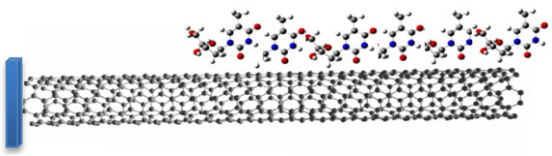
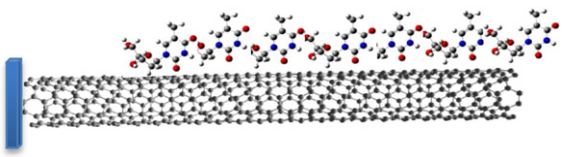
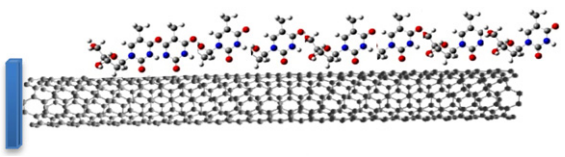
## 6. Results and discussions

### 6.1. SWCNT with deoxythymidine as a point biomolecule

We use a zigzag (5, 0) single-walled carbon nanotube (SWCNT) as a biosensor. The length of SWCNT is considered as 8.52 nm. The added mass is considered to be deoxythymidine, a nucleotide that is found in DNA. The added mass and the corresponding frequency shift are determined from the molecular mechanics simulation results carried out in Ref. [48]. For the details of molecular mechanics simulation one may refer to Ref. [48]. The added mass is considered in normalized form. The frequency shifts are considered in dimensionless form and is defined as the ratio of the difference between the fundamental frequency of a nanotube with and without attached mass to that without the attached mass (Eq. (21)). The values of frequencies shift are used in Eq. (24). These frequency shifts due to the added biomolecules can be considered as 'experimental results'. The value of the mass predicted by this equation is then compared with the known values used in the molecular mechanics simulations. The identified mass determined from the frequency shift in a cantilevered SWCNT is shown in Fig. 3. It is observed that with the increase in the added mass, the frequency shifts also increase.

We have used the nonlocal elastic approach to derive the sensor equations. The applicability of nonlocal elasticity theory in the analysis of single nanostructures (e.g., nanotubes and graphene sheet) has been established in various previous works [7–17]. While applying the classical elasticity, the small scale effects are ignored and thus may be inadequate for the present analysis. It can be seen

**Table 1**
Mass calibration constants $C_m$ for CNT based biosensor.

| Pictorial representation | Mass size | $C_m$ |
|---|---|---|
|  | $\gamma = 0.1$ | 3.6388 |
|  | $\gamma = 0.2$ | 3.1034 |
|  | $\gamma = 0.3$ | 2.6381 |
|  | $\gamma = 0.4$ | 2.2420 |
|  | $\gamma = 0.5$ | 1.9114 |
|  | $\gamma = 0.6$ | 1.6409 |
|  | $\gamma = 0.7$ | 1.4230 |
|  | $\gamma = 0.8$ | 1.2493 |

that the frequency shift of the sensor increases (Fig. 3) with the increasing attached mass when the nonlocal effects are considered.

The exact value of the nonlocal parameter for hybrid structures such as the SWCNT-deoxythymidine based nano biosensor is still unknown. Generally for carbon nanotubes it is observed that nonlocal parameter $(e_0a)$ is considered within the range $0\,\text{nm} \le e_0a \le 2.0\,\text{nm}$ [8,49]. The band of added mass with frequency shift for nonlocal parameters within the range $0\,\text{nm} \le e_0a \le 2.0\,\text{nm}$ is illustrated in the Fig. 3.

It is seen that this 'band' of nonlocal analysis reasonably covers the frequency shifts obtained via the molecular mechanics simulation. In other words, nonlocal elasticity considers size-effects at the nanoscale and imparts results that are size dependent. We have developed the nonlocal sensor equations based on energy principles. Consequently we see that the absolute frequencies of a cantilever SWCNT decreases with increasing nonlocal parameter (Eq. (12)). For the same relative frequency shift, it is observed that the predictions of mass of the added deoxythymidine with nonlocal sensor equations are smaller compared to that with 'local or classical' sensor equations. Next we have carried out analysis to predict the best value of nonlocal parameter $(e_0a)$ based on the results of molecular mechanics simulations. We have found that $e_0a = 0.65\,\text{nm}$ yields the best value for nonlocal sensor equations. The plot of the curve with nonlocal elasticity theory is shown in Fig. 4. From Fig. 4 it can be observed that the nonlocal sensor equations with $(e_0a = 0.65\,\text{nm})$ predicts better resemblance with

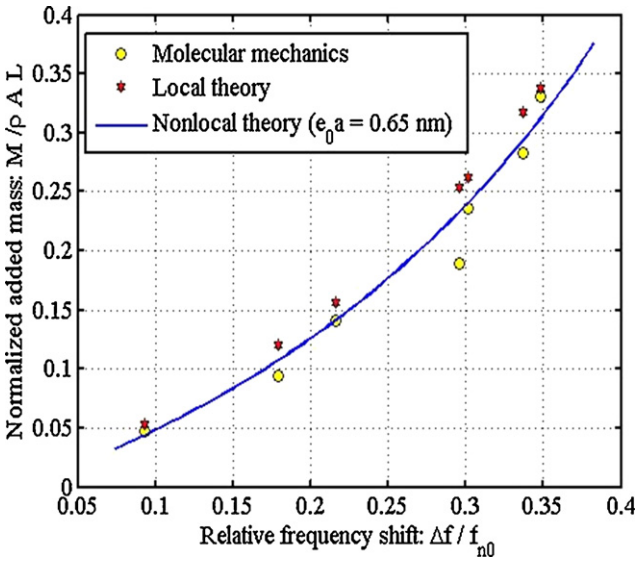



**Fig. 4.** Normalized mass vs. relative frequency-shift for the point mass system. Results from nonlocal and local theory are compared. Nonlocal parameter $e_0a = 0.65$ nm fits the molecular mechanics results very well.

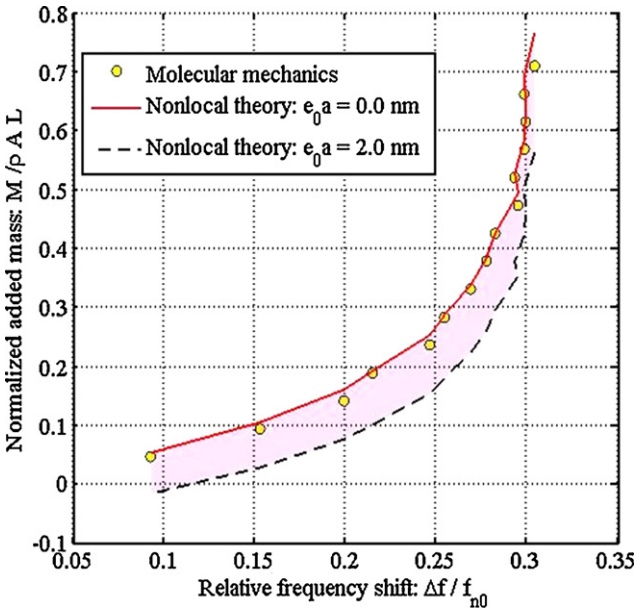



**Fig. 5.** Normalized mass vs. relative frequency shift for the SWCNT with distributed biomolecule. The band covers the complete range of nonlocal parameter, i.e. $0\text{ nm} \le e_0a \le 2.0$ nm. It can be seen that the molecular mechanics simulation results fall within this band.

molecular mechanics results; and is better than the classical sensor equations ($e_0a = 0$).

The goodness of fit value corresponding to local and nonlocal theory has been calculated as $R^2 = 0.9990$ and $R^2 = 0.9995$ respectively. This demonstrates that overall the nonlocal theory is more accurate with respect to molecular mechanics simulation. The percentage error in the mass detection using cantilevered SWCNT based nano biosensor for single biomolecule is listed in Table 2. The error is calculated with respect to the molecular mechanics simulation results. The percentage errors are shown for both local sensor equations ($e_0a = 0$) and nonlocal sensor equations ($e_0a = 0.65$ nm). From the Table it can be observed that the percentage errors for different frequency shifts are smaller with nonlocal sensor equations $e_0a = 0.65$ nm. The average errors for local elastic and nonlocal elastic sensor equations are, respectively, 16.1520% and 7.8185%. No particular pattern with respect to the frequency shift is observed.

### 6.2. SWCNT with strands of deoxythymidine as distributed biomolecules

The case of distributed mass is considered here (Fig. 2). The development of nonlocal sensor equations is extended to that of SWCNT with attached distributed deoxythymidine biomolecules. A nano biosensor with distributed added mass is shown in the Fig. 2. The sensor equations are developed based on Eq. (17). Fig. 5 shows the variation of frequency shift and added mass for distributed biomolecules in SWCNT. For the results plotted here, the value of $\gamma$ varies between 0 and 0.8. Here it is observed that the frequency shift is very sensitive to added mass in comparison to point biomolecule mass sensors.

Similar to previous study, we have considered nonlocal parameter ($e_0a$) within the range $0\text{ nm} \le e_0a \le 2.0$ nm for nonlocal sensor equations. The band of added distributed mass with frequency shift for nonlocal parameters within the range $0\text{ nm} \le e_0a \le 2.0$ nm is illustrated in the Fig. 5. It is seen that this 'band' of nonlocal analysis reasonably covers the frequency shifts via molecular mechanics simulation for lower values of nonlocal parameter ($e_0a$). As the values of nonlocal parameter increases within the band $0\text{ nm} \le e_0a \le 2.0$ nm the prediction shifts from the molecular mechanics simulations.

For distributed mass, we have carried out analysis to predict the best value of nonlocal parameter ($e_0a$) based on the results of molecular mechanics simulations. We have found that $e_0a = 0.50$ nm yields the best value for nonlocal sensor equations. The plot of the curve with nonlocal elasticity theory is shown in Fig. 6. From Fig. 6 it can be observed that the nonlocal sensor equations with ($e_0a = 0.50$ nm) predicts better resemblance with molecular mechanics results; and is better than the classical sensor equations ($e_0a = 0$). However the sensitivity of nonlocal effects is much more than point mass system.

The percentage error using the proposed local and nonlocal elastic method in the mass detection using cantilevered CNT based biosensor for distributed biomolecules is listed in Table 3. The percentage errors are shown for both local sensor equations ($e_0a = 0$) and nonlocal sensor equations ($e_0a = 0.50$ nm). Different normalized length of the added distributed bio mass is also taken into consideration. From the table it can be observed that the percentage errors for different frequency shifts are smaller with nonlocal sensor equations ($e_0a = 0.50$ nm). One can observe that average maximum errors considering local elastic and nonlocal elastic sensor equations are, respectively, 5.3581% and 2.7566%. Similar to previous study [48] no particular pattern with respect to the frequency shift is observed.

**Table 2**
Percentage error in the mass detection using cantilevered CNT based biosensors for single biomolecule. The errors are shown for both local and nonlocal elastic theories (with optimised nonlocal parameter $e_0a = 0.65$ nm).

| Relative frequency shift | Percentage error | |
|---|---|---|
| | Local elasticity | Nonlocal elasticity |
| 0.0929 | 13.9879 | 7.3226 |
| 0.179 | 28.1027 | 13.3841 |
| 0.2165 | 11.1765 | 0.1131 |
| 0.2956 | 34.2823 | 22.9147 |
| 0.3016 | 10.9296 | 1.6392 |
| 0.3367 | 12.4422 | 3.5486 |
| 0.3477 | 2.1427 | 5.807 |

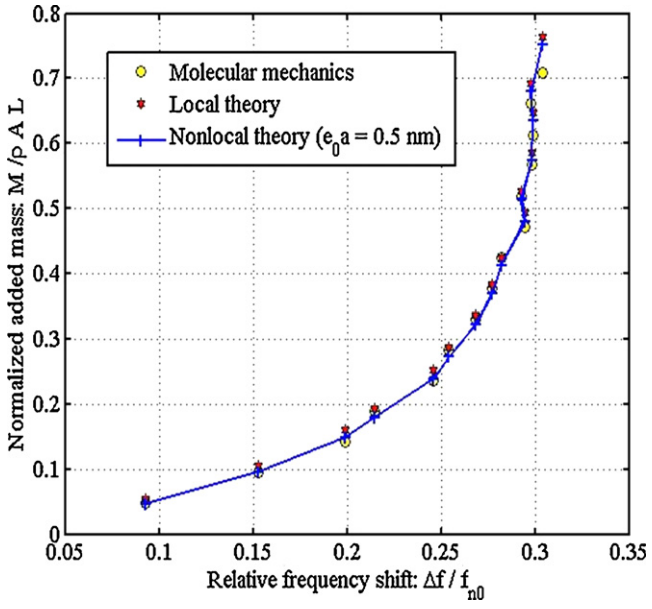



**Fig. 6.** Normalized mass vs. relative frequency-shift for the distributed mass system. Results from nonlocal and local theory are compared. Nonlocal parameter $e_0a = 0.5$ fits the molecular mechanics results very well.

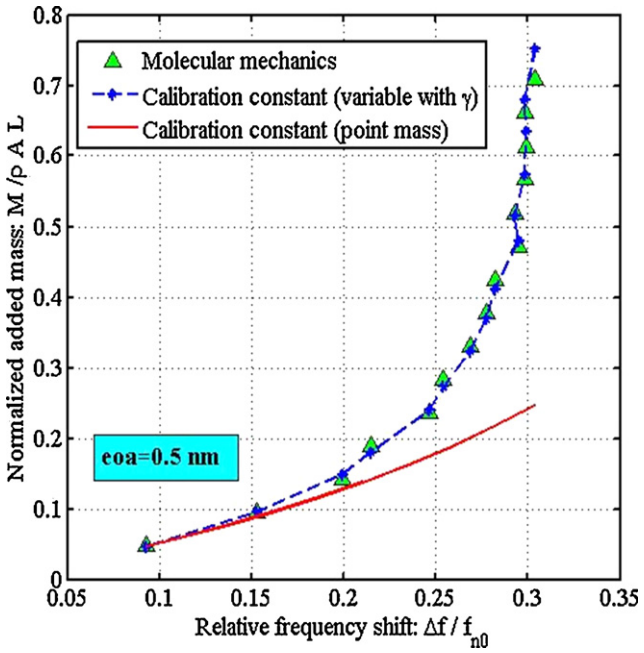



**Fig. 7.** Identified attached masses of biomolecules from the frequency shift in a cantilevered CNT biosensors. The point mass assumption often used in cantilevered sensors can result in significant error when the mass is distributed in nature.

### 6.3. Nonlocal sensors: point mass vs. distributed mass

The frequency shift curves using the point mass assumption in comparison with the distributed mass assumption are shown in Fig. 7. Nonlocal sensor equations are considered using $e_0a = 0.50$ nm. The importance of using the calibration constant varying with the length of the mass is clear from this comparative study.

The proposed nonlocal calibration constant based approach is validated using data from the molecular mechanics simulations. The importance of using the calibration constant varying with the length of the mass can be seen. The point mass assumption [50,51] often used in cantilevered sensors or resonators can result in significant error when the mass is distributed in nature.

In summary in this paper an analytical method for calculating the frequency shift in a CNT based resonator is shown using nonlocal elasticity. The trend in resonating biosensors is to increase the sensitivity by making the resonators smaller. But there are many technological problems still, such as manufacturability, readout and functionalization. The work presented here could act as an input to understand such small biosensors once they become realizable. This is a case where the theory might be ahead of the fabrication capabilities, but it will be a valuable model to have for evaluating future cantilever nanosensors.

**Table 3**
Percentage errors in the mass detection using cantilevered CNT based biosensor for distributed added biomolecules. The errors are shown for both local and nonlocal elastic theories (with optimised nonlocal parameter $e_0a = 0.5$ nm).

| Relative frequency shift | Normalized length | Percentage error | |
|---|---|---|---|
| | | Local elasticity | Nonlocal elasticity |
| 0.0929 | 0 | 13.9879 | 1.2813 |
| 0.153 | 0.05 | 11.8626 | 1.4132 |
| 0.1991 | 0.1 | 13.7038 | 5.171 |
| 0.2148 | 0.15 | 1.7865 | 4.9412 |
| 0.2462 | 0.2 | 7.0172 | 1.0914 |
| 0.2542 | 0.25 | 1.3278 | 3.6149 |
| 0.2687 | 0.3 | 1.9943 | 2.2774 |
| 0.2773 | 0.35 | 1.2631 | 2.4081 |
| 0.2821 | 0.4 | 0.1653 | 3.0046 |
| 0.2948 | 0.45 | 4.515 | 1.7056 |
| 0.2929 | 0.5 | 1.3776 | 1.0761 |
| 0.2983 | 0.55 | 3.2275 | 1.0155 |
| 0.2989 | 0.6167 | 5.524 | 3.4922 |
| 0.2981 | 0.6667 | 4.6735 | 2.7585 |
| 0.3039 | 0.7167 | 7.9455 | 6.0986 |

## 7. Conclusion

The possibility of using CNT as a nanoscale biosensor is explored using the shift in the nonlocal resonance frequencies. Nonlocal elasticity is utilized for the development of the sensor equations. CNTs are modelled by continuum based nonlocal approach. Nonlocal effects are introduced using the energy based methods. The single-walled CNT resonators are assumed in cantilevered configuration. Two types of physically realistic mass loadings, namely, point mass and distributed mass, have been considered. A general closed-form nonlocal sensor-equation has been derived for the detection of the mass of biological objects attached to the CNT. It is shown that the sensor-equation can be calibrated by three non-dimensional calibration constants, namely the stiffness calibration constant, the mass calibration constant and the nonlocal calibration constant. Numerical values and analytical expressions of these calibration constants are derived in closed-form using energy principles.

A molecular mechanics based approach is proposed to validate the nonlocal calibration constant based sensor equations. UFF model have been used, wherein, the force field parameters are estimated using the general rules based on the element, its hybridization and its connectivity. Acceptable agreements between the proposed nonlocal approach and the molecular mechanics simulations have been observed. However the sensor equations are dependent on nonlocal parameters. It is found that the nonlocal parameter values of 0.65 nm and 0.50 nm are the best values for point mass and distributed mass assumption, respectively. Our results indicate that the distributed nature of the mass has considerable influence on the performance of the sensor. Using the nonlocal sensor equations, the point mass assumption may lead to significant error when the true mass is distributed in nature.

Results reveal that the nonlocal approach is able to predict the frequency shift much accurately compared to local approach. The present nonlocal elastic method is expected to give accurate results if the location and distribution of the added mass are known with reasonable accuracy.

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