Computational design and multiscale modeling of a nanoactuator using DNA actuation

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Abstract
Developments in the field of nano-biodevices coupling nanostructures and biological components are of great interest in medical nanorobotics. As the fundamentals of bio/non-bio interaction processes are still poorly understood in the design of these devices, design tools and multiscale dynamics modeling approaches are necessary at the fabrication pre-project stage. This paper proposes a new concept of optimized carbon nanotube based servomotor design for drug delivery and biomolecular transport applications. The design of an encapsulated DNA-multi-walled carbon nanotube actuator is prototyped using multiscale modeling. The system is parametrized by using a quantum level approach and characterized by using a molecular dynamics simulation. Based on the analysis of the simulation results, a servo nanoactuator using ionic current feedback is simulated and analyzed for application as a drug delivery carrier.

1. Introduction

Nanometer scale actuators that can provide motion and measurement with nanometer-order resolution are currently being investigated for nanorobotic systems. One major application concerns in vivo surgery of individual human cells. However, nanorobotic systems for performing surgery require the ability to build precise structures, actuators and tools [1, 2]. In the last decade, progress has been made in artificial nanoscale actuators due to the discovery of carbon nanotubes (CNTs). Baughman et al were the first to demonstrate the actuator property of CNTs by using actuators based on sheets of single-walled carbon nanotubes (SWNT) [3]. As an example, these actuators can be constructed by taking advantage of bond length changes induced by charge ejection in order to build up rotation bearings [4]. New and exciting phenomena have been observed in multi-walled carbon nanotubes (MWNTs), including field emission [5], quantum conductance [6] or constant-force nanosprings [7]. Based on these effects, several proposals for MWNT based nanoactuators have been proposed. Gao et al were the first to show an electromechanical actuator based on a multi-walled nanotube (MWNT) [8]. More recently, a telescoping nanotube servomotor with integrated position sensing based on field emission has been reported [9]. Such nanotube actuators have mainly been designed for solid-state nanorobot actuation where manipulation and assembly of nanoscale objects are required. For applications in nanomedicine [22, 23], such as novel drug delivery nanorobots capable to perform controlled and targeted drug delivery into cells, performances of nanotube actuators are limited due to the operation of high electrostatic fields in liquid mediums.

Proteins represent fertile territory for nanoscale machines that produce linear motions in liquid environments. Recent years have seen substantial progress in DNA actuation nanomechanical devices. DNA undergoes substantial conformational changes in response to environmental stimuli (temperature, acidic concentration, salt, ionic level) which facilitate controlled mechanical motion. Unusual DNA motifs [10, 11, 27] can be used to construct molecular building blocks by virtue of the fact that the sticky-ended association of DNA molecules occurs with a very high specificity. Branched DNA molecules with sticky ends are promising for assembling robotic based DNA nanostructures. Simmel [12] reported the
construction of a mechanical DNA based device that might serve as the basis for a nanoscale robotic actuator. The mechanism has two rigid double-stranded DNA arms, a few nanometers long, that can be made to rotate between fixed positions by introducing a positively charged cobalt compound into the solution surrounding the molecules. Applying the same idea, Hamdi et al [13] proposed a controllable DNA based nanogripper. It is composed of a ds-DNA protein with two single carbon nanotubes (SWNT) as nano-arms. Fully reversible structural conversion allowed the simulation of a gripper opening and closing. Reil et al [14] proposed X-shaped DNA tiles linking a square grid with some DNA strands that can lengthen or shorten by few nanometers like tiny pistons.

Bridging the fields of biology and nanotechnology, we propose in this paper a novel concept of an encapsulated DNA molecule acting as a nanoscale actuator inside carbon nanotubes in a water solute environment. We report molecular dynamics simulations of the dynamic processes towards the prototyping of biological servo nanoactuators (termed, DNA@MWNT). The results indicated spontaneous insertion and confinement of a double-stranded Z-DNA molecule under a combined action of van der Waals and hydrophobic interaction forces. Under the temperature-dependent conformational relaxation of DNA encapsulated in a double-walled carbon nanotube, a controllable and reversible linear motion has been investigated using molecular dynamics simulation. Dynamics atomistic-continuum modeling of the forces and energies involved in the driving mechanism has been investigated in order to optimize its displacement–force characteristics. To improve the precision of the DNA@MWNT nanoactuator, in situ position biosensing feedback in the water environment is necessary. Molecular dynamics simulations revealed the molecular transport dynamics of single-walled carbon nanotubes (SWNT) channels conducting water [15, 20], ions [16] or nucleic acids [17, 21]. Based on these biological channel concepts, a current based position biosensing system is thus made possible. We investigated a new method of ionic position feedback through the dependence of chloride ion diffusion ($\text{Na}^+$) by thermal fluctuations on the interelectrode distance. The results pave the way for future applications of a linear nanotube servomotor acting as a controlled miniature needle for selective cancer cell destruction.

In the following, the optimized design of an encapsulated DNA-nanotube actuator is introduced in section 2. Bio-nanoactuator modeling is then proposed through an atomistic-continuum approach [28] in section 3. In section 4, a concept of nanotube servomotor with integrated ionic current based position sensing is described.

2. Design of encapsulated DNA-double-walled carbon nanotube actuator (DNA@MWNT)

This section develops the design and optimization methodologies of the nanotube actuator based on molecular computational studies.
potential and the corresponding exerted force for this system are of the form:

\[ U = -k(x - x_0)^2/2 \quad F = k(x - x_0). \] (1)

Table 1 shows the main DNA characteristics with respect to the maximum force \( F_{\text{max}} \), the maximum displacement \( D_{\text{max}} \) and the melting point temperature \( T \). First, we notice that the melting point temperature leading to the opening of ds-DNA branches is very similar. Secondly, the A-DNA molecule presents a larger force slope during denaturation compared to Z-DNA and B-DNA molecules but it is limited by its small denaturation displacement. Third, the motive force produced by denaturation of the B-DNA is too small to counteract the sum of the interlayer van der Waals interaction\( (f_{\text{vdw}}) \), electrostatic force \( (f_{\text{elec}}) \) and the total intershell sliding resistance force \( (f_r) \). Finally, the Z-DNA molecule is chosen as the nanoactuator because of its powerful and controllable driving performances.

3. DNA@MWNT nanoactuator modeling

3.1. Multiscale approach

The limitations of purely atomistic or purely continuum simulations have motivated research in multiscale simulations that bridge atomistic simulation and continuum modeling. In order to make the computations selective, multiscale models usually decomposes the domain into coarse/fine subregions. We have developed a design and modeling platform that couples different frameworks. We use different physics for particular length and timescales to characterize and treat aspects of nanostructure phenomena that operate only over those scales (figure 3). Through quantum mechanics calculation, we optimized the geometry of the single-walled CNT. As the ds-DNA is attached to single-walled CNT by a –COOH-group a novel nonstandard group is created and must be parametrized.

3.2. Atomistic modeling

By using the density functional theory method we calculated the bond length, angles, electrostatic potential (ESP), charges and vibrational frequencies of these linkage groups. These parameters are then used at the molecular dynamics level for nanoactuator optimization.

3.3. Molecular dynamics modeling

To predict the dynamic performance of a designed nanodevice (i.e., energy and force calculation), we perform molecular dynamics (MD) simulations based on the calculation of the free energy that is released during the transition from the native to fusogenic state. We used MD software called NAMD (Chemistry at Harvard Molecular Mechanics) [16]. In MD, the feasibility of a particular conformation of the biomolecule in question is dictated by the energy constraints. Hence, a transition from one given state to another must be energetically
favorable, unless there is an external impetus that helps the molecule overcome the energy barrier. When a macromolecule changes conformation, the interactions of its individual atoms with each other as well as with the solvent compose a very complex force system.

3.4. Continuum approach modeling

The micro-forces acting on the slider carbon nanotube (CNT) can be represented by the scheme of figure 4. The continuum model of the DNA based nanoactuator is illustrated in figure 5. By assuming the dynamics along the \( z \)-axis, the Newtonian mechanics equation can be written in the steady state as:

\[
f_{\text{DNA}} + f_{\text{elec}} - f_{\text{vdw}} - f_{\text{sub}} = 0
\]

where \( f_{\text{DNA}} \) represents the force delivered by DNA during denaturation, \( f_{\text{elec}} \) represents electrostatic repulsive force between the stator CNT and slider CNT, \( f_{\text{vdw}} \) represents the van der Waals forces between the two CNTs and \( f_{\text{sub}} \) represents the non-bonded forces applied by the substrate on the slider carbon nanotube, this force is the total of electrostatic and van der Waals interactions. We assume the mechanical interlayer sliding force \( f_t \) to be negligible.

3.4.1. The electrostatic force. According to the Coulomb’s law, the resultant electrostatic force between the two CNTs can be calculated by the following equations:

\[
f_{\text{elec}} = \sum_{i=1}^{n} \frac{q_i q_j}{4\pi \varepsilon_0 \varepsilon_r \delta_{ij}^2}
\]

where \( q_i \) and \( q_j \) are magnitudes of the charges of two nucleotides; \( \delta_{ij} \) is their separation distance; \( \varepsilon_0 \) is the permittivity of free space; and \( \varepsilon_r \) is the relative dielectric constant of the medium in which the charges are placed. The line of action of the electrostatic force is assumed to be along the direction of motion of the inner tube.

3.4.2. The van der Waals force. The van der Waals force is a short-range force caused by instantaneous dipole interactions. The force is comparatively larger in air than in a liquid media, and is proportional to the Hamaker constant, which is one of the leading parameters to accurately estimate the van der Waals forces. The van der Waals forces is included by using the Lennard-Jones potential as:

\[
f_{\text{vdw}} = \sum_{\text{excl}(i,j)=1} \varepsilon_{ij} \left( \left( \frac{R_{ij}}{r_{ij}} \right)^{12} - 2 \left( \frac{R_{ij}}{r_{ij}} \right)^{6} \right)
\]

where \( \varepsilon_{ij} \) represents the energy of the minimum (deepest) point on the van der Waals curve for the atom pair \( i-j \), \( R_{ij} \) is the separation distance between the atom pair \( i-j \) at the energy
4. Simulations results

4.1. Encapsulation of DNA inside carbon nanotubes

Here we report molecular dynamics simulations of the dynamic processes of encapsulating DNA inside CNTs in a solute environment. The nanotube/DNA interaction experiences a strong attractive force from each other when their separation is about 1 nm [20]. On this basis, we investigated a DNA-encapsulated SWNT procedure when applying simultaneously direct current (DC) and radio frequency (RF) electric fields to a substrate coated with open-ended SWNTs. Such a non-organic interaction occurs when immersed in an electrolyte plasma. By Raman spectroscopy and HR-TEM analysis, the encapsulation of DNA inside SWNTs is enhanced when both the DC and RF electric fields are simultaneously superimposed. These results indicate that the process of superimposing an RF electric field upon a DC electric field plays a decisive role in the DNA-encapsulated SWNT formation in this solution phase procedure, just as in the electrolyte plasma [19]. We simulate the molecular dynamics of the DNA encapsulation inside a SWCNT. A direct electric field is applied to the electrolyte plasma containing DNA negative ions in order to irradiate the single-walled carbon nanotubes with DNA ions. The designed DNA–CNT system consists of a homogeneous single-strand DNA oligonucleotide with 8 adenine bases and an uncapped armchair (16, 16) carbon nanotube (5.84 nm long and 2.14 nm in diameter). As initial configurations, CNT and DNA were aligned along the nanotube axis and separated by 0.65 nm. The CNT–DNA complex was solvated in a water reservoir and its dynamics was simulated for 2 ns at a temperature of 355 K. The nanotube charge distribution on the single-walled carbon nanotube is obtained by an atomistic moment method based on classic electrostatics theory. A time-step of 2 fs was used and full-precision trajectory was recorded every 1 ps. The snapshots of the oligonucleotide–nanotube system, shown in figure 6, indicated a very fast insertion process of the oligonucleotide into the nanotube. These simulation results are similar to those of Gao et al [20]. At \( t = 30 \) ps, the first base of the oligonucleotide has begun to enter the nanotube. After 500 ps, five of the eight DNA bases are fully inside the nanotube and the first base has reached the opposite end of the tube. The derived van der Waals energy between the nanotube and the first DNA base entering the nanotube decreases greatly with distance. Correspondingly, the center of mass distance between the oligonucleotide and carbon nanotube rapidly decreases with time up to 500 ps (see figure 7). As shown in (figure 8), the non-bonded energy interaction increases greatly with respect to the DNA insertion due to the strong attractive van der Waals interaction. At the equilibrium point, the DNA is in a stable sustentation state inside the nanotube.
Figure 9. Force balance of the nanoactuator. (a) Forces when the inner CNT is far from the substrate and (b) forces when the effector is close to substrate.

4.2. Bio-nanoactuator behavior simulation

Figures 9(a) and (b) show the simulation characteristics of the forces involved in the driving mechanism. The set of curves in figure 9(a) shows the linear region of control of the nanoactuator. The DNA force $F_m$ increases gradually as the sliding nanotube moves until saturation is reached. It should be noticed that the electrostatic repulsive force $F_{\text{elec}}$ decreases with respect to the slider motion. On the contrary, the van der Waals force $f_{\text{vdw}}$ presents two distinct states: a repulsive interaction and attractive interaction. The set of curves in figure 9(b) shows the force variation when the DNA actuation is saturated. Close to the substrate, we can see a drastic decrease of the electrostatic repulsive force and van der Waals interaction. Regarding the binding and reversible denaturation of double-stranded DNA [24, 25] we
characterized by molecular dynamics the eventual reversibility of DNA inside the carbon nanotube. Figure 10 show the trajectories of the DNA terminus during forward and backward motion.

5. Position control of nanoactuator using ionic current feedback sensor

To improve the precision of the DNA@MWNT nanoactuator, in situ position biosensing feedback in water environment is necessary. Molecular dynamics simulations revealed the molecular transport dynamics of single-walled carbon nanotube channels conducting water [20], ions [16] or nucleic acids [17]. The activation energy barrier for entry of ions through hydrophobic carbon nanotubes is caused by the fact that water molecules being immobilized inside the tube require considerable energy to reorient them around the ions as they do in the bulk. This energy corresponds to the free energy of solvation allowing ion permeation [16]. This additional energy can be provided by (1) an external electric field or (2) the presence of charged atoms on the nanotube.

As shown in figure 11, we investigated the former solution in order to simulate a biological current sensor. We investigated a new ionic position feedback through the dependence of sodium ion diffusion (Na\(^{+}\)) by thermal fluctuations on the interelectrode distance. Even though an electrical field alone would drive ions into the nanotube, the partial charge on the substrate strongly increases the sensitivity of permeation. Furthermore, it can be used to control the rate of the ionic flow into the slider nanotube. An electric field of 0.15 V nm\(^{-1}\) was used to drive the ions through the CNTs.

Figure 12 shows clearly some snapshots of the permeation of (Na\(^{+}\)) ions and water molecules through the double-walled inner CNT. It can be explained by the fact that when the temperature increased during denaturation of Z-DNA, the thermal fluctuation of the nanochannel increased, the rate of ion injection into the nanochannel slightly increased and then the injected ions easily moved toward the other side without disturbance. A closer view shown in figure 13 visualizes the directional water and ion flow under a hydrostatic pressure difference induced through the application of an attractive electrostatic force. The occupancy of ions in the tube depends strongly on the current position of the slider nanotube.

To characterize ion transport through the nanotube for a given electric voltage \(V\), we calculated the electrolytic current \(I_e\) (from the ionic electric charges \(q_i\)) as a function of time \(t\).
The current expression is given by:

\[
I_t = \frac{1}{\delta_t L_z} \sum_{i=1}^{n} q_i (z_i(t + \delta_t) - z_i(t))
\]  

(5)

where \( z_i \) and \( q_i \) are the \( z \) coordinate and the charge of atom \( i \), respectively; \( L_z \) is the length of the simulated system.

By measuring the ionic current, we can achieve an efficient position control of the CNT effector as shown in figure 14. We notice that current decreases gradually (after \( t = 50 \) ps) as the sliding tube approaches the substrate. By filtering the ionic current, a linear current–distance calibration has been simulated.

The main idea presented here consists of using ionic current feedback to measure the effector displacement. By measuring the ionic current, as shown in figure 11, it will be possible to get the end effector position. Figure 13 shows the simulated relationship between the end effector position and the ionic current. Experimentally, the plasma ion irradiation method [29] allows the measurement of the ionic current. For the \textit{in vivo} application, the actuator looks like a switch, the state of the motor (closed or opened) will be determined from the control parameter, such as DNA denaturation temperature.

Figure 11(b), adopted from [29], illustrates a schematic of an experimental setup for the DNA based nanoactuator in the electrolyte plasma. The DC is superimposed upon Al electrodes which are covered with DNA motor (right) and graphite substrate (left electrode). A direct current (DC) is applied to the electrolyte plasma by supplying DC (VDC) voltages to aluminum (Al) electrodes (anode and cathode) immersed in the electrolyte plasma. When the DC electric field is applied, the DNA@CNT molecule is considered to be irradiated to the cathode electrode like an electrophoresis, the substrate is considered to be irradiated to the anode. Further work on the implementation of the ionic current sensor in a position feedback system is under investigation. Modeling and simulations allow the choice of a suitable control method for the DNA actuation. The controller can be implemented in the experimental setup.

6. Conclusion

Nanoscale linear servomotors actuated by DNA molecule with integrated position sensing have been investigated from the design, modeling and simulation perspectives. As the fundamentals of bio/non-bio interaction processes are still poorly understood in the design of these bio-nanodevices, we presented in this study different design tools and a multiscale dynamics modeling approach: atomistic-continuum models. These tools permit the optimized design of an encapsulated DNA-double-walled carbon nanotube (DNA@MWNT) actuator from its initial design stage to its control stage. Experiments are currently carried out at the Laboratoire de Biologie Moléculaire of Orléans in order to validate the proposed servo nanoactuator design with integrated ionic feedback current.

References

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