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Design and Computational Analysis of a Linear Nanotube Servomotor 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 (DNA@MWNT) actuator is prototyped using a molecular dynamics simulator. Then, a multiscale dynamics model from the mechanics point of view is proposed through an atomistic-continuum approach. 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.**

I. INTRODUCTION

Nanometer scale actuators that can provide motion and measurement with nanometer-order resolution are currently 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 evidence the actuator property of CNTs by using actuators based on sheets of single walled carbon nanotubes (SWNT) [3]. As example, these actuators can be constructed by taking advantage on bond-length changes induced by charge ejection in order to built up rotation bearings [4]. New and exciting phenomena have been observed in multiwalled 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 multiwalled nanotube (MWNT) [8]. More recently, a telescoping nanotube servomotor with integrated position sensing based on field emission [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 nanomedecine 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.

It is the reason why 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 responses to environmental stimuli (temperature, acidic concentration, salt, ionic level) which facilitate controlled mechanical motion. Unusual DNA motifs [10],[11] can be used to construct molecular building blocks by virtue of the fact that the sticky-ended association of DNA molecules occurs with 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. In the same idea, Hamdi *et al.* [13] proposed a controllable DNA based-nanogripper. It is composed of a dsDNA protein with two single carbon nanotubes (SWNT) as nano arms. Fully reversible structural conversion allowed to simulate a gripper opening and closing. Reil *et al* [14] proposed a X-shaped DNA tiles linking a square grid with some DNA strands that can lengthen or shorten few nanometers like tiny pistons.

Bridging the fields of biology and nanotechnology, we propose in this paper a novel concept of encapsulated DNA molecule acting as 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 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-

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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 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 nanotubes (SWNT) channels conducting water [20], ions [16] or nucleic acids [17]. Based on these biological channels concepts, a current-based position sensing system is made thus possible. We investigated a new ionic position feedback through the dependence of chlorure ion diffusion (Na^+) by thermal fluctuations on interelectrode distance. The results paves the way for future applications of linear nanotube servomotor acting as a controlled miniature needle for selective cancer cell destruction.

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

II. 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.

A. Design Concept

The discovery of multi walled carbon nanotubes offers many scientific challenges for their adaption to a wide variety of nanometer scale actuators. The low-frictional effect for a sliding inner tube inside multi-walled carbon nanotubes have been exploited to create gigahertz oscillation [18], rotational actuators with a nanotube as rotation bearing [8] or telescoping MWNT linear nanomotors using field emission [9]. Fig.1 shows a new concept of open ended double-walled carbon nanotube actuator working in a biological medium. In the proposed design, the sliding inner tube is actuated by an encapsulated double stranded deoxyribonucleic acid (ds-DNA) connected to a support electrode. The structure is like an hairpin composed of two coils, having each C-terminal connected to the sliding inner nanotube. The inner nanotube slides when undergoing a conformational change induced by temperature variation (increase or decrease) in mildly acidic medium (pH=5.5). The design optimization and performance analysis of the DNA@MWNT actuator performances is performed by design software with molecular computational package.

B. Choice of DNA actuation

Chemically, DNA is a long polymer made up of a linear series of subunits known as nucleotides. Structurally, DNA molecule is usually found as a double helix, with two strands wrapped around one another. However, DNA molecule can adopt other configurations and can exist in single-stranded forms. Double-stranded DNA (ds-DNA) has sparked the renewed interest in the force versus extension of polymers for controllable biomolecular springs. As shown in Fig.2, three crystallized states of DNA have been studied:(a) A-DNA, (b) Z-DNA and (c) C-DNA.

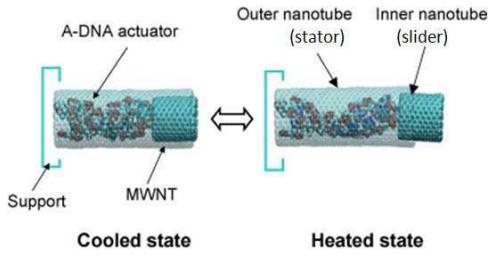

Fig. 1. Basic concept of a linear encapsulated DNA-MWNT nanoactuator controlled by temperature parameter.

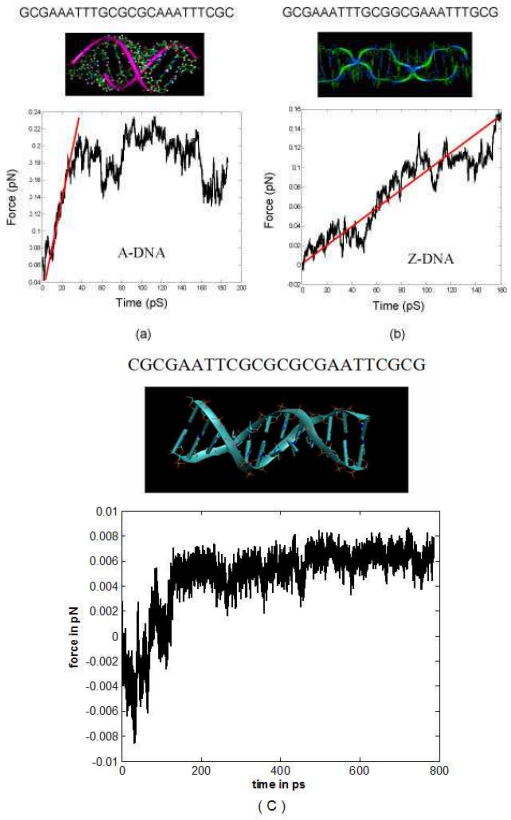

Fig. 2. Chemical structure and mechanical force delivered by DNA denaturation for (a) A-DNA (b) Z-DNA structures and (c) B-DNA.

We studied the mechanical properties of the three models in order to choose the best candidate for our nanoactuator structure. We use a modified steered molecular dynamics (SMD) technique to measure the motive force produced by denaturation of the DNA. to perform this measure we run a molecular dynamics simulation of the DNA denaturation with an applied external constraint to the

TABLE I

TABLE1: CHARACTERISTICS OF DNA ACTUATION WHEN DENATURED BY TEMPERATURE.

DNA model	Fmax(pN)	Dmax(nm)	T(K)
A-DNA	0.234	0.81	345
B-DNA	0.0082	0.02	337.2
Z-DNA	0.16	1.81	338

DNA terminus. This constraint was applied in the form of a harmonic spring of known stiffness k, attached to the center of mass of the the terminus nucleic acid. the harmonic guiding potential and the corresponding exerted force for this system are of the form:

$$U = -k(x-x_0)^2/2 \quad F = k(x-x_0)$$

Table1 shows the main DNA characteristics with respect to the maximum force $Fmax$, the maximum displacement $Dmax$ and the melting temperature point T. First, we notice that the melting temperature point leading to the opening of ds-DNA branchs is very similar. Secondly, the A-DNA molecule presents 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 in order to counteract the sum of the interlayer van der Waals interaction(f_{vdw}), electrostatic force (f_{elec}) and the total intershell sliding resistance force (f_r). Finally, the Z-DNA molecule is chosen as nanoactuator with respect to its powerful and controllable driving performances.

C. 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 strong attractive force from each other when interesting their separation is about 1 nm [20]. On this basis, we investigated a DNA-encapsulated SWNTs procedure when applying simultaneously direct current (DC) and radio frequency (RF) electric fields to a substrate coated with open-ended SWNTs. Such 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 a 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 such 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

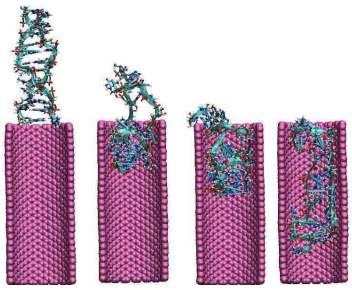

Fig. 3. Simulation snapshots of a DNA insertion inside SWCNT. Water molecules are not displayed for clarity.

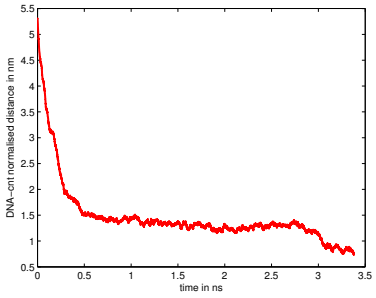

Fig. 4. Normalized center-of-mass distances between the oligonucleotide and carbon nanotube as function of simulation time.

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 temperature 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 Fig.3 indicated a very fast insertion process of oligonucleotide into nanotube. These simulation results are similar to those of Gao *etal*. [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 oligonucleotide and carbon nanotube rapidly decreases with time up to 500 ps (see Fig.4). As shown in (Fig.5), 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.

III. DNA@MWNT NANOACTUATOR MODELING

A. Multi-Scale Approach

The limitations of purely atomistic or purely continuum simulations, have motivated research in multi-scale sim-

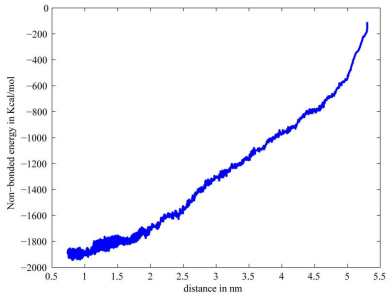

Fig. 5. Non-bonded energy interaction between the oligonucleotide and carbon nanotube as function of center-of-mass distance.

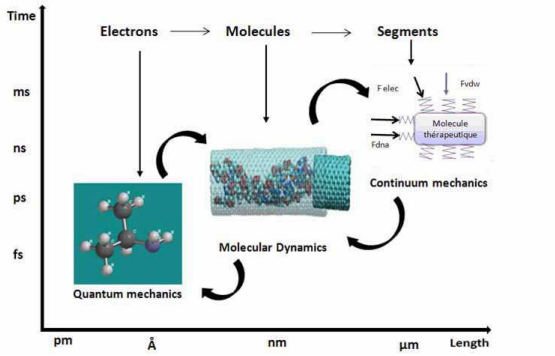

Fig. 6. Illustration of Multiscale approach for the design of Bio-Nanorobotics structure.

ulations that bridge atomistic simulation and continuum modeling. In order to make the computations selective, multi-scale models usually decomposes the domain into coarse/fine subregions. We have developed a design and modeling platform that couple different frameworks. We use several physics for particular length and time scales to characterize and treat aspects of nanostructure phenomena that operates only over those scales (Fig.6). Through quantum mechanics calculation (Spartan Software), we optimized the geometry of the single walled CNT. As the ds-DNA is attached to single walled CNT by -COOH-group a novel nonstandard group becomes created and must be parameterized. By using Density functional theory method we calculated the bond length, angles, electrostatic potential (ESP), charges and vibrational frequencies of theses linkage groups. These parameters are then used at the molecular dynamics level (NAMD sofware) for nanoactuator optimization.

B. Atomistic and molecular modeling of DNA encapsulated CNTs

The dynamics of the slider carbon nanotube (CNT) can be represented by the scheme of Fig.6. By assuming the dynamics along the z-axis, the Newtonian mechanics equation can be written in a steady-state:

$$f_{DNA} + f_{elec} - f_{vdw} - f_{sub} = 0 \tag{1}$$

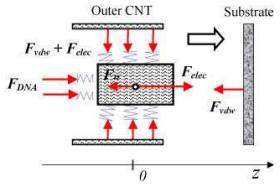

Fig. 7. Dynamics model of the nanomotor actuated by DNA molecule.

where f_{DNA} represents the force delivered by DNA during denaturation, f_{elec} represents electrostatic repulsive force between the stator CNT and slider CNT, f_{vdw} represents the van der Waals forces between the two CNTs and f_{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 to be negligible the mechanical interlayer sliding force f_r.

1) The electrostatic force: According to the Coulombs law, the resultant electrostatic force between the two cnt's can be calculated by the following equations:

$$f_{elec} = \sum_{j=i+1}^{n} \frac{q_i q_j}{4\pi\varepsilon_0\varepsilon_r\delta_{ij}^2} \tag{2}$$

where and q_i and q_j are magnitudes of the charges of two nucleotides; δ_{ij} is their separation distance; ε_0 is the permittivity of free space; and ε_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 applies.

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:

$$f_{vdw} = \sum_{excl(i,j)=1} \varepsilon_{ij} \left((\frac{R_{ij}}{r_{ij}})^{12} - (\frac{R_{ij}}{r_{ij}})^{6} \right) \tag{3}$$

where ε_{ij} represents the energy of the minimum (deepest) point on 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 minima, and r_{ij} is the current actual distance between atom i and atom j. The attractive forces between two proximal atoms are proportional to r_{ij}^{-6} and the repulsive forces due to their nuclear repulsions are proportional to r_{ij}^{-12}

The Fig.8(a)-(b) visualizes the simulation characteristics of the forces involved in the driving mechanism. The set of curves in Fig.8(a) shows the linear region of control of the nanoactuator. The DNA force F_m increases gradually as the sliding nanotube is moving until to saturate. It should be noticed that the electrostatic repulsive force F_{elec} decreases with respect to the slider motion. On contrary, the van der Waal force f_{vdw} present two distinct states:

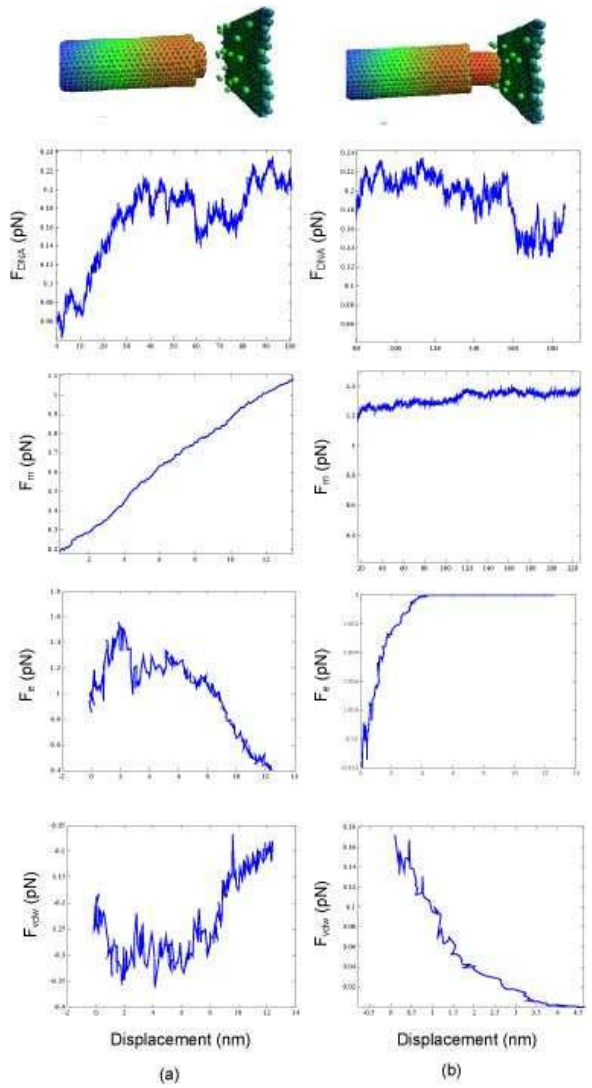

Fig. 8. Force balance of the nanoactuator. (a) forces when the inner CNT is far from the substrate and (b) forces when the effector is closed to susbstate.

repulsive interaction and attractive interaction. The set of curves in Fig.8(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 de Waals interaction. It should be noticed that the nanoactuator is fully reversible as shown in Fig.8.

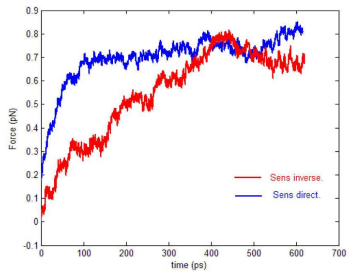

Fig. 9. Motion force for a forward and backard motion.

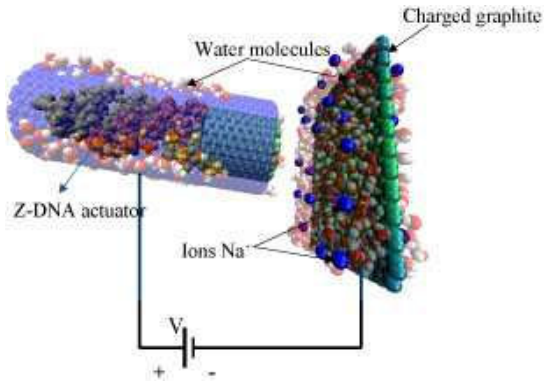

Fig. 10. Structure of the servo nanoactuator with ionic current feedback for position measurement.

IV. Servo Nanoactuators using ionic current feedback

To improve the precision of 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 nanotubes 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 would 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 Fig.10, we investigated the former solution in order to simulate biological current sensor. We investigated a new ionic position feedback through the dependence of sodium ion diffusion (Na^+) by thermal fluctuations on interelectrode distance. Even though an electrical field alone would drive ions into the nanotube, the partial charge on the substrate increases strongly 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 was used to drive the ions through the CNTs.

Fig.11 shows clearly some snapshots of 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 Fig.12 visualizes the directional water and ions flow under a hydrostatic pressure difference induced through the application of attractive electrostatic force. The occupancy of ions in the tube depends strongly of the current position of the slider nanotube.

To characterize ion transport through the nanotube for a

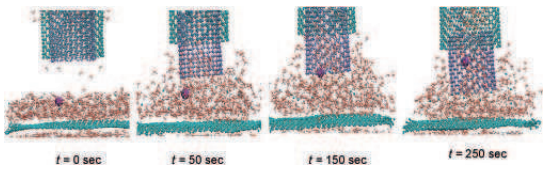

Fig. 11. Snapshots of permeation of Na^+ ions through the double walled carbon nanotube. Water molecules are also shown during permeation.

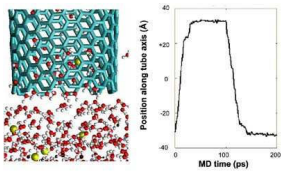

Fig. 12. Position trajectory of Na^+ ions during transport.

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 equation (4).

$$I_t = \frac{1}{\delta_t L_z} \sum_{i=1}^{n} q_i (z_i(t+\delta_t) - z_i(t)) \qquad (4)$$

where zi and qi are the z coordinate and the charge of atom i, respectively; Lz is the length of the simulated system.

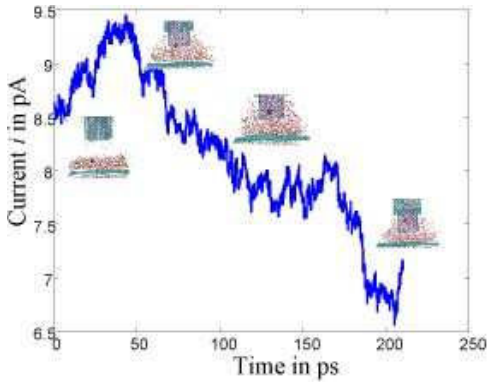

Fig. 13. Current-time characteristic.

By measuring the ionic current, we can achieve an efficient position control of the CNT effector as shown in Fig.13. We can 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. Further work on the implementation of the ionic current sensor in a position feedback system is under investigation.

V. Conclusion

Nanoscale linear servomotors actuated by DNA molecule with integrated position sensing has been investigated from 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 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 Molculaire of Orlans in order to validate the proposed servo nanoactuator design with integrated ionic feedback current.

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