

Computational modeling of transport in synthetic nanotubes: a review

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Abstract

Synthetic nanotubes which have the ability to broadly mimic the function of biological ion channels have extraordinary potential for various applications, from ultra-sensitive biosensors to efficient water purification devices. As a result of their immense potential the design and fabrication of such synthetic nanotubes is rapidly gaining momentum. We briefly review recent theoretical and experimental studies on nanoscale, cylindrical, hollow tubes constructed from carbon, boron and nitrogen atoms which are able to selectively transport water molecules, cations (positively charged ions) or anions (negatively charged ions) similar to various biological ion channels.

Key words: Nanotubes; synthetic ion channels; Ion-selectivity; Biomedical applications; Filtration

Background

Nanotubes are cylindrical, hollow tubes similar in diameter to biological ion channels (a few nanometers). They can be fabricated from a range of materials, from the more commonly studied carbon to boron nitride and silicon carbide. In recent years, there have been rapid advances in technologies for synthesizing nanotubes made from various materials and modifying their surface chemistry. An excellent summary of current techniques of fabricating nanotubes is given by Harris [1].

Nanotube length can be precisely controlled [2, 3] so as to target cells with a specific membrane thickness. For example, certain gram negative bacterial cell membranes are thinner than human cell membranes and therefore may be a suitable target for tailored nanotubes. The

surface chemistry of nanotubes can also be modified [4] to make the tubes soluble [5] or to target specific cells [6]. During fabrication carbon nanotubes will acquire hydrophilic ends (such as -OH, -COOH, -H) and, if desired, they can be further modified such that other functional groups are covalently attached to the partially-charged termini. Moreover, the sidewalls of nanotubes can be modified either by covalently bonding functional groups [7] or by wrapping a molecule around the surface [8, 9]. A recent review by Karousis *et al.* [10] outlines various approaches used to modify carbon nanotubes by covalently bonding functional groups on their external surface or otherwise.

There is a general consensus that pristine carbon nanotubes, or nanotubes with no functional groups attached at their ends or to their surface, are toxic to cells [11], whereas boron nitride nanotubes are considered non-cytotoxic [12]. The cytotoxicity of pristine carbon nanotubes is largely due to their insolubility in aqueous solutions, hydrophobicity and tendency to aggregate. The cytotoxicity of nanotubes, however, can be reduced [13] by rendering them soluble by modifying their surface chemistry [5].

It may be possible that synthetic nanotubes can be rendered selectively permeable to specific ionic species, thus mimicking one of the key features of biological membrane ion channels. Current theoretical and experimental findings suggest that there is a real possibility of assembling ion-selective nanotube-based pores in novel ways, creating practical nanodevices. These engineered, nanoscale pores, once successfully designed and fabricated, could lead to a host of pharmaceutical products, such as antimicrobial agents and drugs to combat certain human diseases, in addition to having potential applications as ultra-sensitive biosensors and water purification devices. The feasibility of utilizing carbon nanotubes as efficient water purification devices [14, 15] or single-ion detectors [16] has already been demonstrated experimentally.

These biology-inspired nanotubes will lead to a new generation of products which are more efficient than their current counterparts. For example, nanotube-based water channels are shown to conduct water an order of magnitude faster than commercially available reverse osmosis membranes [17, 18]. Studies on carbon nanotubes which sieve water molecules from seawater have been summarized in a number of excellent review articles [19-24]. Moreover, Hilder and Chung [25] have designed a nanotube which can mimic the antibiotic gramicidin but with potassium conductance six times larger. This suggests that a nanotube-based drug, more potent in destroying microorganisms than the naturally occurring one, could be engineered. Nanotubes have also been shown to embed into a cell membrane and conduct ions much faster than biological channels [26-28]. As a result of their immense potential, artificial ion channels constructed from synthetic nanotubes is a unique field of research which has recently begun to gain momentum. For a number of years synthetic ion channels based on molecular structures other than nanotubes, such as cucubituril macrocycles [29], have been investigated. For further details on synthetic channels made from organic molecules, the reader is referred to a review by Sakai *et al.* [29].

Here, we briefly review some of the recent studies carried out on cylindrical nanotubes, which broadly replicate the dynamics of ion permeation across membrane ion channels. Many of these investigations aim to theoretically demonstrate the feasibility of creating synthetic, ion-selective, carbon or boron nitride nanotubes. As the technology of fabricating nano-devices advances in the near future, these nanotubes conceived at the proof-of-principle level may be eventually manufactured and brought into practical use.

The paper is organized as follows. We first survey the computational studies on the interaction between engineered nanotubes and cell membranes. For nanotubes to be useful in a

biological setting, they must remain stable in a cell membrane, which is composed of two hydrophilic outer layers separated by the inner hydrophobic core. We next highlight some of the ground-breaking experimental and computational work on water-conducting, ion-rejecting pores. These devices have obvious uses for water purification and desalination, as well as potential biological applications. Finally, we review some of the recent investigations on nanopores which are selectively permeable to either positively charged particles or negatively charged particles. It is of theoretical, as well as practical interest to explore how a simple nano-device made from one or two atomic species can mimic some of the functions of complex biological ion channels made of bulky membrane proteins.

Stability of synthetic nanotubes in lipid bilayer

Potential biological applications of engineered tubes as nanosyringes or artificial ionic channels mandate that they be stable in the lipid bilayer. Therefore, it is important to determine whether or not synthetic nanotubes will incorporate into a cell membrane, align vertically across it and remain stable, similar to the polypeptide gramicidin and other membrane proteins, including ion channels. There are several computational studies which examine the interaction between nanotubes and lipid bilayers using coarse-grained or steered molecular dynamics [26, 27, 30, 31]. The results of these calculations reveal that carbon nanotubes with hydrophilic ends are potentially stable in a lipid bilayer.

Lopez *et al.* [26, 31] first demonstrated, using coarse-grained molecular dynamics, that small diameter carbon nanotubes approximately 1.3 nm in diameter, 3 nm in length and functionalized with hydrophilic termini, can spontaneously insert into and align across a lipid bilayer. Their nanopores are terminated at each end with generic hydrophilic units constructed

from coarse-grain water sites. The hydrophilic ends are crucial to stability, as close matching to the hydrophobic and hydrophilic domains of the bilayer is necessary to avoid pore blocking [26, 31]. Insertion of a purely hydrophobic nanotube results in the nanotube remaining in the hydrophobic core of the bilayer, parallel to the bilayer plane [31]. Lopez *et al.* observe a lipid-assisted mechanism for the passive insertion of these hydrophilic terminated carbon nanotubes, as shown in Figure 1. An animation of the lipid-assisted mechanism is available as supplementary information in Ref. [26].

Subsequently, Shi *et al.* [27] investigated single-walled carbon nanotubes with diameters from 1 to 1.5 nm and lengths of 6 nm. Their nanotubes are purely hydrophobic, as they are not terminated with hydrophilic functional groups. They found that small diameter tubes enter the membrane via a piercing mechanism and for larger diameter nanotubes the bilayer changes shape to wrap around the tube.

According to a coarse-grained molecular dynamics study by Nielsen *et al.* [30], close matching to the hydrophobic and hydrophilic domains is crucial for stability in the bilayer. The bilayer thickness thins as it approaches contact with a nanotube, and as the ratio of nanotube radius to length decreases tilting of the tube in the bilayer becomes more pronounced. These findings are in accord with those reported previously by Lopez *et al.* [26, 31].

Wallace and Sansom [32], on the other hand, used steered coarse-grained molecular dynamics to investigate bilayer penetration by a hydrophobic nanotube. They simulated nanotubes with diameters from 1.4 to 6.1 nm and lengths of 5 and 10 nm. Their simulation results are in broad agreement with a recent experimental study [33], in which the force required to push large diameter nanotubes into a living cell is measured using atomic force microscopy. As expected, the force required to penetrate the bilayer is shown to monotonically increase with

an increase in nanotube diameter [32]. Moreover, they found that there is no apparent effect on bilayer integrity following nanotube penetration.

Similar to Wallace and Sansom [32], Hilder *et al.* [28] used steered molecular dynamics this time using an all-atom force field. They investigated the stability of a carbon nanotube 0.9 nm in diameter and with a length of 3.4 nm in a lipid bilayer. Since all atoms were explicitly represented, rather than a generic hydrophilic termini their nanotubes were terminated with carbonyl groups (C=O). In agreement with Lopez *et al.* [26, 31], they determined a deep energy well of 250-300 kcal mol⁻¹ suggesting that the nanotube is likely to be confined to the centre of the lipid bilayer.

Studies on water flow across nanotubes

The flow of water through synthetic nanotubes has been extensively investigated using computer simulations. These studies have illustrated that synthetic nanotubes are capable of conducting water molecules exceptionally fast, whilst rejecting charged particles. The results of these theoretical studies indicate that membranes embedded with nanotubes may one day be used for water purification or desalination. Given the exciting possibilities presented by these nanotube-based membranes, researchers are beginning to focus on their fabrication and testing. By functionalizing their ends or external surface, a synthetic nanotube can be embedded in various membranes. Recent techniques have enabled the arrangement of aligned carbon nanotubes within membranes such as polymers [24, 34] and silicon nitride [14, 15, 35]. Figure 2 illustrates a schematic of a carbon nanotube-silicon nitride membrane. Such a membrane exhibits an enhanced mechanical strength [35, 36], thus enabling it to withstand large applied pressures. However, these experimental studies [14, 34, 35] have predominantly focused on the flow of

water molecules only. In agreement with theoretical studies, experiments have demonstrated exceptionally fast water flow rates [14, 34, 35] which have been attributed to the near frictionless surface of the nanotube wall [34]. Recently, due to the increasing interest in these nanotube-based membranes for desalination, Fornasiero *et al.* [15] investigated their ion exclusion capability. Their sub-2-nm diameter carbon nanotubes embedded in silicon nitride could achieve ion exclusion as high as 98%, but at salt concentrations of 10 mM ions were no longer excluded. In more recent work, Fornasiero *et al.* [37] demonstrate experimentally that the ion permeability and exclusion through these nanotubes can be controlled by adjusting the solution pH which affects the ionized carboxylic groups at the nanotube opening.

Water flow across nanotubes has been extensively investigated theoretically. In their molecular dynamics simulations, Hummer *et al.* [38] observe spontaneous and continuous filling of a carbon nanotube 0.8 nm in diameter with a single-file chain of water molecules, illustrated in Figure 3. In the absence of an applied pressure, and with no ions present, water is found to flow in both directions at a rate of 17 water molecules per ns. Moreover, the filling or emptying of these nanotubes occurs by sequential adding or removing of water molecules to or from the single-file hydrogen bonded chain, and this is shown to occur rapidly [39]. As a comparison, aquaporin-1 conducts at a rate of 3 water molecules per ns [40]. This initial finding, that a carbon nanotube is populated with a single-file chain of water molecules, has been confirmed in *ab initio* simulations [41]. Mann and Halls [41] observe a single-file chain of water inside a carbon nanotube 0.8 nm in diameter. In contrast to the biological water channel aquaporin [40, 42], proton conduction can occur across carbon nanotubes 0.8 nm in diameter under the influence of an applied electric field [41]. Similar results have been obtained by Garate *et al.* [43]. Aquaporin

allows the rapid flow of water with no proton transport, which is postulated to result from the transient reversal of the water chain due to residues lining the pore [40].

Kalra *et al.* [44] study, using molecular dynamics simulations, the osmotically driven transport of water through a hexagonally packed array of 0.8 nm diameter carbon nanotubes, as illustrated in Figure 4. They too obtain a single-file water chain with a flow rate of 5.8 water molecules per ns, twice that of aquaporin-1. Their simulations reveal that the water flow rate is independent of nanotube length, suggesting that permeant water molecules encounter virtually no friction. The rate-limiting step appears to be the barrier presented to the water at the entry and exit of the pore. Similarly, the transport of water through arrays of carbon nanotubes ranging in diameter from 0.6 to 1.1 nm was investigated by Corry [17]. He finds that ions face a large energy barrier and do not enter 0.68 and 0.8 nm diameter carbon nanotubes. However, as the diameter increases above 0.95 nm ions can pass through. In contrast, water molecules conduct through all nanotubes studied, with the conductance increasing with increasing diameter. Similar to Kalra *et al.* [44], the conduction is independent of nanotube length. This work suggests that 0.95 nm diameter carbon nanotubes could obtain 95% salt rejection with a water flow rate much faster than existing semi-permeable membranes used in desalination.

In recent work Corry [45] examined water and ion transport through carbon nanotube based membranes. This work aimed to investigate whether larger diameter (1.1 nm) nanotubes could be made to reject ions by attaching various charged and polar functional groups to the nanotube ends. Although the addition of charges is shown to prevent the passage of ions, it also reduces the flow of water through the membrane. Despite this the performance of these membranes was shown to be many times better than existing desalination membranes.

Alternatively, double-walled carbon nanotubes have been proposed as artificial water channels by Liu *et al.* [46]. This would enable functionalization to be included along the length of the inner nanotube while avoiding hydrophobic mismatch of the hydrophobic and hydrophilic domains of the lipid bilayer. The structure outside the nanotube has been shown to greatly affect water permeation across the channel [47]. Thus, use of a double-walled carbon nanotube enables protection of the inner tube from the disturbance of the membrane environment [46].

It is possible to fabricate nanotubes from a range of materials, such as from boron and nitrogen atoms to form a boron nitride nanotube. As yet there are no experimental studies which investigate the flow of water through boron nitride nanotubes. However, theoretical studies have shown boron nitride nanotubes to have superior water permeation properties when compared to carbon nanotubes [18, 48-50]. Water molecules encounter a lower energy barrier at the pore entrance of a boron nitride nanotube as a result of the stronger van der Waals interaction between the boron nitride nanotube and water [50]. For example, a boron nitride nanotube with a diameter of 0.69 nm can conduct water, whereas a similar sized carbon nanotube has only intermittent filling of water [48, 49]. Similarly, Suk *et al.* [50] finds a higher water flux exists through a boron nitride nanotube as compared to a carbon nanotube, and both nanotubes had significantly higher flux than that of a polymethyl methacrylate (PMMA) pore.

Water conduction and salt rejection through boron nitride nanotubes embedded in a silicon nitride membrane was investigated by Hilder *et al.* [18]. They find that a boron nitride nanotube 0.69 nm in diameter embedded in a silicon nitride membrane can, in principle, obtain 100% salt rejection at concentrations of seawater (500 mM) whilst allowing water to flow at rates as high as 10.7 water molecules per ns. Moreover, ions continue to be rejected at hydrostatic pressures as high as 612 MPa. When the nanotube diameter is increased above 0.83

nm ions can enter the tube. By assuming a pore density of $2.5 \times 10^{11} \text{ cm}^{-2}$ [14, 35] and at an operating pressure of 5.5 MPa the authors [18] predict water flow rates approximately 4 times that of a commercially available reverse osmosis element.

Most computational studies on these synthetic nanotubes are conducted using a non-polarizable force field. This has been shown to be a reasonable approximation since the effect of water on a polarizable nanotube is negligible [51, 52], and never accounts for more than 8% of the total interaction energy [51]. In contrast, in the biological channel gramicidin the polarization of water is important in calculating the interaction energy [53].

Mimicking ion-selective biological ion channels

Although most research has focused on the use of synthetic nanotubes as water channels, increasing attention has been given to the design of ion-selective synthetic nanotube channels which could potentially be useful in unique devices such as ultra-sensitive biosensors, and may help to gain insight into complex biological ion channel processes. Due to the relatively recent interest in ion-selective nanotubes and the degree of difficulty in fabricating such tubes there are very few related experimental studies. Therefore, initial theoretical studies may prove to be useful to facilitate further experimental studies. In this section we first highlight recent studies which have demonstrated the potential of nanotubes to non-selectively exclude or conduct ions. Following this, we review research which have achieved exclusive selectivity to positively charged (cations) and negatively charged (anions) ions.

Peter and Hummer [54] illustrate using molecular dynamics simulations that non-polar pores less than 0.5 nm in diameter block ions, but increasing the pore diameter to 1 nm allows the passage of ions. They observe a drastic increase in the diffusion coefficient of ions once the

tube diameter is above this critical value, and this critical diameter can also be linked to changes in the water structure within the nanotube. This critical diameter has also been noted in a study by Beu [55] which included a polarizable model for water and solute ions. Beu found that polarizability has a negligible influence on the ionic currents through carbon nanotubes 6 nm in length with diameters ranging from 1 to 1.6 nm. Ions are thought to move through the tube almost frictionlessly, but as ions enter the nanotube they encounter an energy barrier which increases as the pore radius decreases [55]. As a result, ion currents show a strong dependence on pore radius. In recent experiments, Yu *et al.* [56] report on the gated ionic diffusion through densely packed carbon nanotube membranes with both 3 nm nanotube and 3 nm interstitial pore diameters. At a temperature of 298 K ions become trapped in the membrane due to discontinuous water clusters. However, by increasing the temperature, or exposing the membrane to ultrasound, ion diffusion rates were shown to increase. Although the membrane is able to gate the flow of ions, it is not selective to a particular ion type.

It is possible to increase ion occupancy within a carbon nanotube by placing a rim of partial charges at the nanotube ends [57]. In molecular dynamics simulations Joseph *et al.* [57] demonstrate a 4-fold increase in ion occupancy in a carbon nanotube, 2.2 nm in diameter and 1.3 nm long, using a partial charge of $\pm 0.38 e$ placed at the nanotube rim atoms. Fornasiero *et al.* [37] were able to control ion transport through fabricated carbon nanotube pores 0.8 to 2.6 nm in diameter embedded in a silicon nitride matrix. Following Joseph *et al.* [57] their nanotube ends were terminated with negatively charged carboxylic groups. By varying the solution pH they were able to modulate the nanotube tip charges so that the membrane would either reject ions or permeate ions. In addition, they found that an increase in the number of multivalent ions in the solution decreased the rejection capability towards monovalent ions.

The above research illustrates the potential of nanotubes to exclude or conduct ions depending on diameter and environmental factors but these studies are not selective to a particular ion type. In other words, cations will flow in one direction and anions in the opposite direction across these tubes under the influence of an applied field. In the following sections we outline research in which exclusive cation- and anion-selectivity is achieved. For example, Park *et al.* [58] design a novel ion separator using a Y-junction carbon nanotube, illustrated in Figure 5. They demonstrate, using molecular dynamics, the ability to separate potassium and chloride ions from KCl solution by applying a negative and positive surface charge density to the two branches, respectively. Park *et al.* suggest that a Y-junction carbon nanotube could be used as a fluidic component in complex fluid networks and nanoscale lab-on-chip applications.

Cation-selective channels

Majumder *et al.* [59] fabricate membranes constructed from vertically aligned carbon nanotubes approximately 7 nm in diameter embedded in a polystyrene matrix and investigate the effect of anionically charged functional groups at the nanotube open ends. They show that these charged groups increase the flux of cationic species approximately 4-fold compared to their unmodified carbon nanotube membrane. The effects of an applied voltage across the nanotube-embedded membrane are investigated in subsequent work [60]. Their membranes exhibit voltage gated control of ionic transport through the cores of the nanotubes. For example, at a positive bias the tethered tips are drawn into the nanotube, occluding the pore. They demonstrate the effectiveness of such a device using a relatively large cation, ruthenium bi-pyridine ($\text{Ru}(\text{bipy})_3^{2+}$). For example, increasing the voltage from 0 mV to 50 mV reduces the flux of $\text{Ru}(\text{bipy})_3^{2+}$ to approximately 25%.

In a molecular dynamics computational study by Yang and Garde [61], a negative charge density of $-n e$ is uniformly distributed to all atoms of a carbon nanotube 0.67 nm in diameter and 1.1 nm in length (comprising 100 carbon atoms) so that each atom carries a charge of $-n/100 e$. When the surface charge is $-5 e$ the nanotube interior becomes favorable to all three investigated cations, namely potassium, cesium and sodium. In contrast, when the surface charge is reduced to $-2 e$ no cations enter the tube. At a charge of $-3 e$, sodium ions take 25 times longer to enter the nanotube than potassium and cesium ions. Studies such as these may aid better design of high energy storage devices.

Again using molecular dynamics, Liu *et al.* [62] demonstrate that a hexagonal array of non-charged carbon nanotubes, each with an effective diameter of 0.44 nm, is able to discriminately select potassium ions over sodium in the presence of an applied pressure of 5 MPa. They suggest that the key to this ion selectivity is the higher binding energy of water molecules in the first hydration shell of sodium which renders it more stable and therefore sodium has a higher desolvation energy making it more difficult to permeate through a narrow nanotube. The flexibility of the hydration shell of a potassium ion enables it to maintain better coordination within the nanotube [62-64]. Similarly, Song and Corry [65] show that narrow carbon nanotubes with no functionalization have intrinsic ion selectivity. Dehydration energy plays a dominant role in determining selectivity in narrow pores since in narrow pores all ions have to be largely dehydrated; for example, as sodium has a larger dehydration energy it faces a steeper barrier to enter the tube. Although the work of Liu *et al.* [62] presents interesting possibilities the simulation times of only 0.35 ns are too small to have confidence in the result. In similar work, they find that positive or negative ions will exit the nanotube only when one or two other ions of

the same charge are present in the tube, suggesting that the permeation mechanism involves the presence of multiple ions and Coulomb repulsion [66].

A single-walled carbon nanotube of 1.2 nm diameter and 1.34 nm length is shown to discriminate Na^+ over K^+ or vice versa, depending on the patterns of carbonyl oxygens placed on its interior surface [67]. The positions of the carbonyl oxygens in the molecular dynamics study by Gong *et al.* [67] are chosen such that they mimic the arrangement of amino acids in the selectivity filter of the biological potassium channel. Unfortunately, the investigated nanotubes are not exclusively selective so that although preference will result for one ion type the other will also traverse the nanotube.

Recently, Lee *et al.* [16] fabricated single-walled carbon nanotube ion channels with negatively charged ends approximately 1.5 nm in diameter which conduct protons and are blocked by cations present in the surrounding electrolyte solution. Moreover, they observe complete rejection of ions for voltages less than 100 mV. Once the electric field is large enough the larger cations move across the channel and this blocks the flow of protons. These synthetic nanopores are therefore capable of single-ion detection.

For the first time, it has been demonstrated theoretically that a functionalized carbon nanotube embedded in a lipid bilayer can selectively allow cations to move across under the influence of an applied electric field [25]. The nanotube, 0.91 nm in diameter and 3.6 nm in length, is functionalized with hydrogen at the ends and in two thin circular rings near the entrances of the nanotube, as illustrated in Figure 6. This nanotube is selectively permeable to monovalent cations, binds divalent cations and rejects anions. The characteristics of this channel resemble the antibiotic gramicidin-A, one of the first antibiotics used clinically, but the potassium current is six times larger. Moreover, Hilder *et al.* [68] designed a carbon nanotube 1

nm in diameter and 3.6 nm in length which is functionalized with carboxylic acid at the ends. In the presence of an electric field the nanotube exhibits the ability to selectively conduct cations by an ion chaperoning mechanism, whereby a chloride ion ferries a sodium ion across the channel.

Anion-selective channels

A number of studies have demonstrated the ability of synthetic nanotubes to be selective to cations. In comparison, few have demonstrated anion-selectivity. Combining density functional theory and molecular dynamics simulations, Won and Aluru [69] design a single-walled boron nitride nanotube with a diameter of 1.36 nm which demonstrates selectivity of chloride over potassium ions. They find that although both ions can enter the nanotube, chloride ions are 10 times more likely to be observed inside the nanotube. In contrast, they find that a similar sized carbon nanotube selectively transports potassium ions. Water within the boron nitride nanotube was shown to orient such that there exists a net positive charge at the centre of the nanotube, facilitating the attraction for negatively charged chloride ions.

In recent studies which combine molecular and stochastic dynamics, Hilder *et al.* [28] design carbon nanotubes with an effective diameter of 0.9 nm and terminated with carbonyl functional groups that are shown to be exclusively selective to chloride ions. Figure 7 illustrates schematically the carbonyl terminated carbon nanotube embedded in a lipid bilayer. Moreover, these nanotubes broadly mimic the functions of biological chloride channels but with a chloride conductance four and two times larger than through the CIC-1 and GABA_A biological chloride channels, respectively.

Future perspectives

Synthetic nanotubes show enormous potential as artificial ion channels in both theoretical and experimental work. It is now possible to fabricate and design synthetic nanotubes that are selectively permeable to water molecules, cations or anions. Although research into mimicking biological ion channels has recently gained momentum it is still very much in its infancy and much work needs to be done before practical applications will be realized. With the work of Fornasiero *et al.* [15] the development of desalination membranes incorporating nanotubes is closer to being achieved than any other application. For the application of these synthetic ion channels in a biological setting to be realized it is vital that there be more studies confirming theoretical work and confirming their lack of toxicity. It is hoped that this review will facilitate interest and expedite progress in this unique field of research.

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Figure Legends

Figure 1: Lipid assisted mechanism observed by Lopez *et al.* [26]. Hydrophilic terminated carbon nanotube (a) spontaneously adsorbs onto the membrane, (b) is partially immersed with

the nanotube axis essentially parallel to the membrane plane, (c) lipids form salt bridges with the hydrophilic termini, and (d) assist the nanotube across the membrane so that it forms (e) a transmembrane pore which can conduct water. Reprinted with permission from [26]. Copyright 2004 National Academy of Sciences, USA.

Figure 2: Cross-section schematic of a carbon nanotube-silicon nitride membrane platform which includes silicon support chip, aligned double-walled carbon nanotubes, the filling silicon nitride matrix, and the carbon nanotube tips functionalized with carboxylic groups. Reprinted in part with permission from [15]. Copyright 2008 National Academy of Sciences, USA.

Figure 3: Schematic illustration of a typical nanotube with a single-file chain of water molecules.

Figure 4: Carbon nanotube membrane formed from hexagonally packed array of carbon nanotubes in a periodic cell. Reprinted with permission from [17]. Copyright 2008 American Chemical Society.

Figure 5: Schematic of ion separation using a Y-junction carbon nanotube. Reproduced in part with permission from [57]. Copyright 2006 IOP Publishing Ltd.

Figure 6: Schematic of the 0.91 nm diameter carbon nanotube with hydrogen terminated ends and exohydrogenated surface (outside surface) shown in blue. Potassium ions (shown in pink) are located at the two binding sites. Reprinted in part from [25], copyright 2010, with permission from Elsevier.

Figure 7: Schematic of the 0.9 nm diameter carbon nanotube with carbonyl terminated ends [28] shown in red. Chloride ions (shown in green) are located at the two binding sites.