Dramatic transport properties of carbon nanotube membranes for a robust protein channel mimetic platform

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ABSTRACT

Carbon nanotube (CNT) membranes offer an exciting opportunity to mimic natural protein channels due to (1) a mechanism for dramatically enhanced fluid flow, (2) ability to place 'gatekeeper' chemistry at the entrance to pores, and (3) being electrically conductive to localize electric field or perform electrochemical transformations. The transport mechanisms through CNT membranes are primarily (1) ionic diffusion near bulk expectation, (2) gas flow enhanced 1–2 orders of magnitude primarily due to specular reflection, and (3) fluid flow 4–5 orders of magnitude faster than conventional materials due to a nearly ideal slip-boundary interface. Transport can be modulated by 'gatekeeper' chemistry at the pore entrance using steric hindrance, electrostatic attraction/repulsion, or biochemical state. Electroosmotic flow is seen to be highly power efficient and can act as a pump through regions of chemical selectivity. The fundamental requirements of mimicking protein channels are present in the CNT membrane system. This membrane structure is mechanically far more robust than lipid bilayer films, allowing for large-scale chemical separations, delivery or sensing based on the principles of protein channels. Applications ranging from water purification, energy generation and bio-separations are highlighted.

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1. Introduction

Nature's pumps, biological protein channels, have the ability to selectively pump necessary chemicals through cell walls at rates orders of magnitude faster than simple diffusion or Newtonian fluid flow. Mimicking this function in large-area robust man-made structures can have broad application in water purification, chemical separations, drug delivery and sensing. The key to nature's protein channels are (1) selective receptor chemistry at the pore entrance, (2) a mechanism for fast fluid flow or mass-transport, and (3) signal chemistry at the exit side of protein to activate the channel [1,2]. The mass transport through proteins is so selective and enhanced that it seemingly defies the laws of continuum physics where, by chemisorption or kinetic scattering, the boundary condition of surface flow velocity is zero. Nature achieves this feet by a large superstructure of folded polypeptides that through hydrogen bonding form channels of precise atomic distance. In the case of aquaporin, the placement of the functional groups with either unscreened charge or hydrogen bonding precisely orientates the dipoles of molecules as small as water allowing them to flow in concerted motion without kinetic scattering. In the case of proton channels the proton shuttles down chains or hydrogen bond ordered water with dramatic mobility. Mimicking the complete protein superstructure is an extremely daunting challenge and requires the use of fragile micelles to form the membrane. It would be ideal to mimic the key steps of chemical selectivity, to the level of orientating water dipoles, at the entrance to a rigid nm-scale pore. This 'gatekeeper' would ideally be a monolayer thick and be able to actively pump chemicals through the pore. However this mimetic approach would require a nearly frictionless conduit, on the length scale of microns for mechanical support, that does not suffer from the non-slip boundary condition of Newtonian flow found in the nm-scale pores of conventional materials.

Fluid flow through the cores of carbon nanotubes (CNTs) is predicted to show dramatically enhanced transport of hydrocarbon gases and water [3]. An early molecular dynamics (MD) study [4] predicted that water flow through 'hydrophobic' single-walled CNTs (SWCNTs) should be not only possible but be dramatically enhanced. This is because the process of water entering CNT can induce H-bond ordering in a chain of water molecules. This can make-up for the energy cost to lose 2 of the 4 weak hydrogen bonds as the water molecules separates from the bulk water into the hydrophobic CNT core. In order to preserve the H-bond ordering of the water chain, it is critical to have nearly frictionless interaction with the CNT graphite sheets to not scatter or even rotate the quickly flowing water. The large van der Waals distance ($\sim$2 Å) and flat ordering of graphite sheets were predicted to allow this. Using the study's theoretical volume-rate (which is comparable to

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that of the protein channel *aquapourin-1*) divided by the CNT cross sectional area, a water flow velocity of ∼90 cm/s is predicted, which is *5 orders of magnitude faster* than would be for conventional materials of similar pore size (0.6 nm). High flow velocities of molecules through CNTs were also predicted due to the nearly frictionless nature of the CNT walls [5] as well as the fast diffusion rates for hydrocarbons [6,7]. In the latter case, favorable interactions of the methane with the CNT wall predict the molecule will 'skate' down the tube wall and not scatter in random directions, as would conventionally happen in the case of Knudsen diffusion. The flow velocity of gaseous methane is predicted to be ∼260 cm/s at 1 bar [7]. In all models, the atomically flat nature of graphite sheets inherent to the CNT microstructure makes the enhanced flow possible over long length scales. In fact, if an atomic step edge is placed inside CNT core, MD simulation predict a dramatic drop in flow rates due to scattering [8]. Thus CNT cores, with atomically smooth and inert surfaces are theoretically predicted to have dramatic flow enhancements rivaling that of protein channels.

The pinnacle requirement for the protein mimetic system is the ability to orient small molecules for selective transport through the channel. For instance, enzymes are active due to the fact that the substrate molecule is precisely oriented as it reacts with catalytic site to break even C–C bonds at room temperature in aqueous environments. In proton channels hydronium ion can travel down ordered water channels with high mobility, which would have important application in hydrogen fuel cells. In the aquaporin channel there is a flip in water dipole that prevents proton transport, allowing only pure water transport. Though it is known, by the observed transport properties of proteins, that it is possible to orientate molecules in channels, MD simulations can give insight into the minimum required charge to orientate water with meaningful probability through CNT. The Fang group [9] in a controversial [10,11] paper predicted the net pumping of water with full point charge near the entrance of the membrane and distributed charge near the middle. It appeared from this simulation, that by ordering water at the entrance (and a required second ordering point within the tube) faster bursts of coupled water transport

were allowed, but was not possible from the reverse direction, thereby giving net pumping. This simulation was done on a short time scale to not allow the second law of thermodynamics to be realized and there was issue with the simulation step size to get net pumping [10]. However the work does show induced order can be transmitted down CNT cores and sets a charge length scale requirement of ∼1.2 Å outside the tube to see dipole orientation effects. This short distance of charge outside the CNT wall is primarily due to the large van der Waals distance (∼2 Å) within the CNT core. This predicted distance is less than even a C–F bond, hence is it is difficult to achieve the required charge on the outside of CNTs. To reach the desired distance of charge, functional chemistry will have to be placed at the entrances to CNT pores to act as ordering 'gatekeepers'.

2. Experimental CNT fabrication and flow properties

Since the popularized discovery in 1991 the field of carbon nanotubes had largely focused on the superb mechanical strength and nearly ballistic electron conduction properties. However several groups [12–14] early on recognize the potential interest of fluid flow through CNTs. The Crooks group had isolated single CNT by a microtome method and measured electroosmotic flow rates [14], primarily using polystyrene beads blocking ionic current through the CNT via Coulter counting method. The flow values were close to conventional expectations; however the CNT was ∼200 nm in diameter and had an amorphous carbon coating that would interfere with the perfect slip conditions. With the large diameter, it is difficult to observe any enhanced flow rates due to the r^4 dependence on flow rate using Haagen–Poiseuille equation of conventional Newtonian flow. Another pivotal early study was from the Martin group where porous anodized aluminum oxide (AAO) was coated with carbon giving largely amorphous CNTs (a-CNT) membranes. Elegant elephoretic and osmotic studies [15–17] showed that the flow rates were improved but comparable to conventional expectations. However these CNTs were amorphous
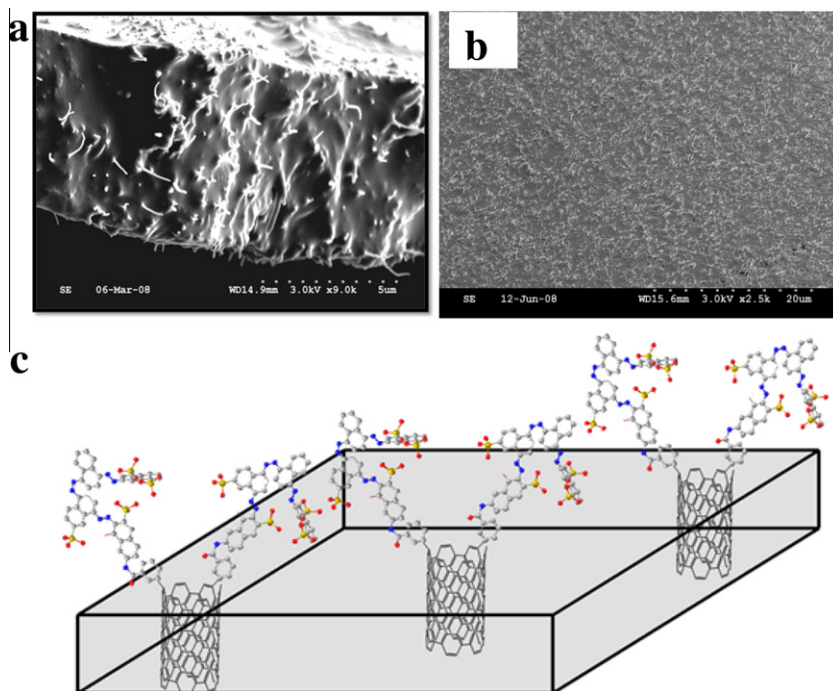
Fig. 1. SEM images of microtome-cut CNT membrane (a) cross-sectional view and (b) top view; (c) schematic shows the molecular structure of the anionic dye covalently functionalized on the surface of CNTs (gray: C; red: O; blue: N; yellow: S). Figure reproduce with permission of Ref. [39].
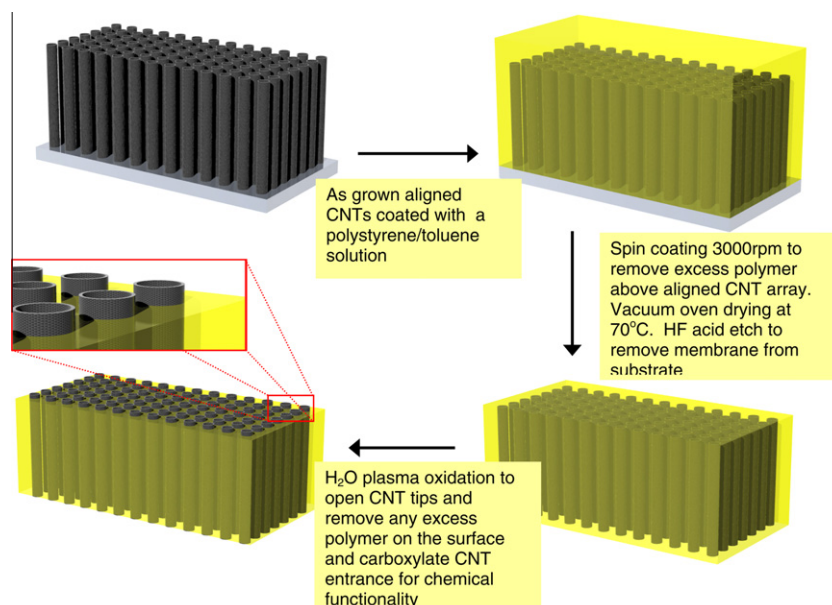
Fig. 2. Processing steps involved in aligned CNT membrane fabrication process for large areas [24]. Alternatively microtoming of CNT/epoxy composite can be used for laboratory scale studies [39].

samples and the diameter were ~100 nm making it difficult to detect any flow enhancement. To observe fast fluid flow properties within CNT cores ordered graphitic CNT membranes with small diameters (1–10 nm) were needed.

Aligned growth of dense arrays of multi-walled CNTs has been demonstrated at the University of Kentucky [18,19] and elsewhere [20–22]. Although the outer diameters have significant variance (30 ± 10 nm), the hollow inner core diameter is well controlled to 7 ± 1 nm. Since this is a thermal chemical vapor deposition (CVD) process using readily available xylene/ferrocene, it is an industrially scalable process with an estimated cost of $0.60/m^2. The primary goal is to form a membrane structure taking advantage of the as-deposited alignment of multi-walled CNTs to form a well-controlled nano-porous membrane structure [23]. If the space between CNTs could be filled with a polymer barrier, then a membrane with a rigid pore structure, high porosity, and small pore size dispersion could be synthesized as diagrammed in Fig. 1.

Fig. 2 diagrams the process to form CNT membranes. First a 50 wt% solution of polystyrene (PS) and toluene is spun coat over the surface of the aligned CNT array. PS is known to have a high wet-ability with CNTs and thus can impregnate into a CNT array without disrupting the alignment of the CNT forest [24,25]. Excess polymer on top of the structure is removed during the spin coating process due to the high viscous drag within the CNT array. HF acid is then used remove CNT/PS composite from the quartz substrate. To remove any thin layer of excess polymer on the top surface and open the normally closed CNT tips a H$_2$O plasma enhanced oxidation process [26] is used. Importantly this process removes the Fe nanocrystal catalysts from the tips of CNTs and leaves the tips CNTs functionalized with carboxylic acid that are readily functionalized with selective receptors [27].

Recently, a simpler fabrication method was reported by the Hinds' group [39] based on microtoming method that was a modification of the early report from the Crooks group [14]. A 1–5 wt% CNT/triton is mixed into epoxy hardener/resin by high shear velocity mixer (Thinky AR-100) and then formed into 5 mm diameter composite dies and cured. Commercially available CNT powders with inner diameter ranging from 10 to 1.5 nm can be easily mixed into these polymer composites. Thin 5 μm slices are made by microtome and plasma oxidation is used to remove any polymer

residue and functionalize the CNT tips. Though small in area, and thus difficult for large-scale production, the technique is particularly useful for laboratory studies and can be widely adapted by the membrane research community.

3. Major mechanisms of mass transport through CNTs

With such dramatic theoretical predictions, it was necessary to confirm the fast transport phenomena experimentally. Additionally the unique geometry of the cut CNTs allows chemistry to be placed precisely at the pore entrances, allowing for gate keeper activity. The term gate keeper is used here as a chemical layer only at the pore entrance that selectively allows chemicals to pass into and through the pores of the membrane, much how natural protein channels work. Both enhanced transport *and* gate keeper selectivity are key elements for mimicking natural protein channels. Success with this approach would allow for fast transport and high selectivity, which is not attainable for conventional membrane systems at the performance level of natural protein channels.

3.1. Ionic diffusion and gatekeeper activity

The plasma oxidation process to open CNTs results in carboxylate groups at the pore entrances that can be used to form covalently bonded carboimide linkages. Most any ligand with a primary amine can be covalently attached to the tips of CNTs and act as a chemically selective gatekeeper. The first systematic study [28] to prove that 'gatekeeper' chemistry can be formed on CNT membranes was with a series of four chemically distinct gatekeepers: short chained alkane, long chained alkane, long polypeptide, and highly charged dye molecule. In this study, IR data was consistent with the formation of carboimide linking chemistry at the surface which was confirmed by later electrochemical studies [29]. The simultaneous diffusional transport of ionic dyes through the membrane was measured. To demonstrate gatekeeper activity we looked at the ratio of small dyemolecule methyl viologen^{2+} (MV) and large dye Ru(bipyr)$_3^{2+}$ (Ru) permeation through the membrane, where the larger dye should be more hindered. With longest molecule (polypeptide) covalently tethered to entrance of the 7 nm diameter pore, the ratio of small to large molecule (MV/Ru) passing

through the membrane was ∼3.6. This is significantly higher than the ∼1.6 to ratio of bulk water diffusivity hence showing modest gatekeeper activity. With the long and short alkanes, only modest separations were seen but overall flux of aqueous ionic dyes decreased due to the tip becoming hydrophobic. The observed transport effects were a combination of both steric bulk and hydrophobic/phylic nature of the CNT tip chemistry. The observed separations were modeled with hindered diffusion in small pores, calculated by the Renkin equation, occurring only at the tip gatekeeper region and with bulk diffusivity through the long length of the CNT core. This is consistent with the oxidation process that cut the CNT tips and placed functional chemistry at the pore entrances. An interesting point in this study was that the negatively charge dye molecule tethered to CNT entrance increased the flux (5-fold) of the positively charged dyes by electrostatic attraction. The effect could be screened by spectator ions (KCl) in solutions of high ionic strength. Thus electrostatics can be a strong force in enhancing flow rates or manipulating charged gatekeepers.

3.2. Biological gating

With the relatively large pore diameters of 7 nm, the multi-walled CNT (MWCNT) membranes are a natural choice for examining large biological molecules as gate keepers. In the first report of graphitic CNT membranes [23], biotin was tethered to CNT entrances and irreversibly bound to streptavidin protein to block the pores. In a subsequent study [30] reversible desthiobiotin was covalently tethered to CNT entrances. In the presence of large streptavidin protein, the pore was blocked with a corresponding drop in flux of a dye across the membrane. With the addition of the much stronger biotin molecule to the solution, the tethered desthiobiotin is displaced from the protein by solution phase biotin, opening the membrane pores and returning to original flux values. This is an important experiment on several levels. The first is that the streptavidin protein is of well defined size ∼4 nm that can block only CNT pores (radius) but not large macroscopic cracks. The fact that that blockage was removed by chemistry to displace the four binding sites shows that this was not a physisorption phenomena, but due to selective surface chemistry binding. On a practical level, this system provides two sensor routes: (1) large proteins selectively blocking CNT pores or (2) proper release chemistry opening pores. In another biological gating study, the primary hypothesis was to see if known bio-catalytic (enzymatic) activity could occur at the tips of CNTs and affect the mass transport through membrane structures [31]. A peptide sequence G-R-T-G-R-R-N-S-I-NH2, specific to protein kinase, was covalently bound to CNT tip. The serin was pholated by protein kinase A/ATP and subsequently dephospholated by Alkaline Phosphatase. The state of the tethered peptide ligand (phosphylated or not) was detected by monoclonal anti-phosphoserine antibody binding to the tethered peptide in the phospylated state. The diffusional flux through the CNT membrane was modulated by these events showing that enzymatic catalysis (ATP cycle) could be performed at the tips of CNTs. This has important implications for drug delivery where natural biological process can open pores for drug delivery when the chemistry requires it. Sensors can also be developed by monitoring ionic diffusion to an electrode through CNT membrane in the presence or absence of bound bio-chemistry at CNT tips.

3.3. Gas and fluid flow

Molecular dynamics simulation had predicted very rapid fluid and gas flow within CNTs due to a nearly atomically flat surface with minimal scattering or chemical attraction. The phenomenon was experimentally observed with pressure induced solvent flow [32] and gas flow [33]. In the initial report, flow through the

Table 1
Pressure driven liquid flow through MWCNT membranes as a function of solvent in order of decreasing polarity [32].

Liquid	Flow velocity normalized at 1 bar (cm/s)	Calculated Newtonian flow velocity at 1 bar (cm/s)	Enhancement factor	Slip length (μm)
Water	26	5.7×10^{-4}	4.5×10^4	54
EtOH	4.5	1.4×10^{-4}	3.2×10^4	28
IPA	1.12	7.7×10^{-4}	1.5×10^4	13
Hexane	5.6	5.16×10^{-4}	1.1×10^4	9.5
Decane	0.67	1.72×10^{-4}	3.9×10^3	3.4

aligned CNT membrane was measured in a syringe-pump pressure cell apparatus [32], where mass (hence volume) of the solvent passing through the membrane area is directly measured on a pan balance as a function of time. Flow data summarized in Table 1. There is a remarkable *4–5 orders of magnitude* increase in water flow over what would be seen in conventional nanoporous structures. For gas flow there is a 1–2 order of magnitude increase in flux over Knudsen diffusion [33] in 2 nm pores. For our larger multiwalled CNTs with 7 nm inner diameter, the gas flow enhancement is about 20. Both studies are consistent with specular reflection, where gas molecules keep their forward momentum (i.e. no back scattering). The result of such fast transport of liquids has important practical applications since less than one thousandth the membrane area will be needed for the same amount of chemical separation from conventional membranes. The enhanced liquid flow is also one of the three critical components for mimicking protein channels.

The flow flux rate of liquids (J) through conventional porous membranes can be predicted using the well known Haagen–Poiseuille equation [34] given by:

$$J = (\varepsilon r^2 \Delta P)/(8\mu\tau L)$$

In this formula, ε is the relative porosity, r is pore radius (7 nm for our system), P is pressure applied, μ is dynamic viscosity, τ is tortuosity (1.1) and L is the length of the pore. The basic assumptions of this equation are laminar flow and 'no-slip' at the boundary layer, i.e. the velocity of the liquid at the CNT wall is zero. This zero velocity at pore walls is the physical origin of low flow velocities in conventional membrane pores. For Newtonian liquids in pores the velocity goes from zero at the wall to a maximum 'core' velocity at the pore center based on the viscous shear from applied pressure. However in nm-scale pores this core velocity is exceedingly small. Needed are high velocities along pore walls, referred to as slip conditions. Protein channels have ideal slip conditions with single file pumping of solvent or permeate. A useful convention for slip boundary is slip length that can be calculated from the equation [35]:

$$V(\lambda)/Vns = 1 + 4\lambda/r$$

In this formula, $V(\lambda)$ is the experimentally observed flow velocity (cm/s), Vns is the 'no-slip' flow velocity calculated from the Haagen–Poiseuille equation, λ is the slip length and r is the radius of the nanotube. For water dramatic slip lengths of 50–100 μm, compared to the CNT radius of 3.5 nm, are experimentally seen for water. This means that the surface velocity on the CNT wall is nearly identical to that of the pore center, or a nearly ideal slip condition. The longest slip lengths were observed for the polar molecules (i.e. water and MeOH) that are expected to have the weakest interactions with hydrophobic CNTs. Both for the polar and non-polar liquids, the slip lengths decrease with the longer hydrocarbon chain length. This is consistent with the concept of more interaction with the CNT wall will decrease the slip lengths and hence the flow

enhancement. However, even for long chain alkanes, flow rates are still dramatically enhanced compared to conventional materials.

In general, the transport through the CNT core shows nearly no enhancement in ionic diffusion, about a factor of 20–100 for gas flow, and a remarkable enhancement (4–5 orders of magnitude) of fluid flow. In the former case of ionic diffusion, the non-interacting CNTs offer no advantages for transport; essentially acting like a mirror for ions and molecules to bounce off of. Brownian scattering of ions within the solvent inside of CNT cores would dominate and thus follow Fick's law of diffusion. Experimental measurements of ionic transport across the CNT membrane closely correlates with bulk diffusivity. For gasses, scattering is only off of the smooth CNT walls and the retention of forward momentum gives significant enhancement. However the rate limiting step becomes the gas molecule entering the pore entrances, which are a very low percent of surface area. Since pore size cannot yet be controlled to sub-angstrom precision, chemical selectivity is given only by differences in gas velocity ($v \propto \text{mass}^{1/2}$). Placing highly selective chemistry at pore entrances (i.e. gatekeeper) would, by necessity slow, the gas molecule to zero velocity and thus completely negate the fast flow phenomena of forward scattering off of CNT wall. In the case of the much denser liquid flow, dramatic enhancement is observed because of the nearly frictionless interface of the liquid and the CNT. This allows for very high wall velocity ($\sim$10 cm/s at 1 atm) whereas in conventional materials (atomically rough and short van der Waals distances) have zero net velocity at pore walls. *However a significant intellectual puzzle emerges*: How to selectively let chemicals into CNT cores while maintaining enhanced flow rates that are based on a nearly ideal non-interaction phenomenon. Adding selective chemistry to the pore entrances or along CNT cores ruins the enhanced liquid flow effect that is based on atomically flat non-interacting CNT wall. The flow enhancement dropped from 46,000 to 220 to <5-fold enhancement over Haagen–Poiseuille flow with the sequential hydrophilic/bulky functionalization of (1) as-made CNT, (2) tip functionalization, and (3) core functionalization respectively [36]. This experiment on the same membrane proves the flow phenomena is based on smooth CNT surface but also unfortunately shows that it is not possible to get both high selectivity and high flow rate by simple chemical functionalization at the pore entrance. What is needed is a *pumping mechanism at the location of selective chemistry*. The velocity or momentum developed at this region can be transmitted down the nearly frictionless CNT core as plug flow. Promising methods to induce pumping at the CNT tip region are by molecular motion or by electric field induced electro-osmosis and electrophoresis.

4. Electrostatic gatekeeping and electroosmotic pumping

The concept of an active 'gatekeeper' that can be pulled into and out of the pore entrance can be the basis of a pump or the active element of a drug delivery system. To prove the concept of an electrostatically actuated gatekeeper, a long quadra-charged dye molecule was tethered to the entrances of CNTs as shown in Fig. 1c [37]. Importantly, we needed a very high density of molecules on the CNT surface to be effective gatekeepers in the pore. To achieve this, electrochemical grafting of highly reactive diazonium salt onto CNT surfaces [36,38] was performed. The diazonium salts are highly reactive and can react with the basal planes of CNT, not just the more reactive cut tips. To avoid this aggressive reaction inside of the CNT, a continuous flow of inert water, at the previously mentioned remarkably high velocities, is passed through the CNT core. This prevents the diazonium reaction inside the CNT core but allows the reaction only at the CNT tips exposed to the diazonium solution. This is referred to as 'flow grafting', which is a powerful tool to place chemistry only at the tips of CNTs to act

as 'gatekeepers'. At 0 V bias, selectivity between the two permeate molecules across the membrane is close to the ratio of bulk diffusivity ($\sim$1.6). After application of positive bias, the separation factor increases to about 10, significantly higher than what had been achieved in the earlier study [32] without bias applied. The applied bias evidently gives enough electrostatic force to the tethered charged gatekeeper molecule in the channel to effectively block the CNT pore entrance. In the case of 'flow grafted' chemistry at the top tip surface, positive bias attracts the negatively charged tethers into the pore blocking the larger permeate. With negative bias the tethers are repelled, opening the pore. However this study did not prove effective blocking for smaller molecules such as nicotine and clonidine that would be required for drug delivery applications. A more effective blocking method or active pumping mechanism is needed for drug delivery therapies, where a delivery device will require on/off ratios greater than 10.

Electroosmotic flow (EOF) is the phenomena where a membrane pore has covalently bound charge, usually anionic, that allows cations to flow under electric field but rejects anions traveling in the opposite direction. The moving cations induce a net flow of solvent and neutral molecules. Generally this is a very inefficient process limited by the Debye screening lengths within the first nm of the pore surface. Ideally one can have charge at CNT entrances to exclude anionic charge and allow cation to pump liquid efficiently down the fast CNT core. This pumping can occur through regions of chemical selectivity, thereby solving the problem of how to achieve fast flux and selective chemistry in the CNT system. Electroosmosis had been studied in the a-CNT membranes [15] showing moderately enhanced performance compared to conventional materials. However, it is expected that the fast slip boundary conditions of graphitic CNT cores can allow for more efficient EOF. EOF was recently studied [39] in CNT membranes and found to be 40-fold more power efficient than comparable conventional materials. This power efficiency is gained by both low applied voltages and efficient pumping by ions in the small diameter CNTs. Using large cation complexes, such as Ru(bipyr)$_3^{2+}$ ($\sim$1.1 nm diameter), and single walled CNTs (SWCNTs), less than 1.5 nm in diameter, a 1:1 ratio of cations to neutral small molecule is achieved through EOF at equal concentrations in the feed solution. This compares very well to the 200-40:1 ratio found in conventional materials. With these SWCNTs, the case of ideal electroosmosis is nearly realized; where a single ion can pump a column of solution through the length of a CNT. The power efficiency of EOF is particularly important for biomedical devices. The EOF driven transdermal drug delivery system was recently demonstrated [40] to delivery nicotine at the fluxes used in commercially available skin patches. Fig. 3 shows the electroosmotic pumping of nicotine in the *on* and *off* states and the test cell for *in vitro* skin studies. In particular the flux could be switched by EOF between that of high dose and low dose commercially available patches, thus allowing programmable treatment regiments after counseling. This allows a mixture of psychological counseling and chemical stimuli to optimize addiction treatment. The 40-fold improvement in EOF power efficiency of the CNT membrane system allows the device to operate for 10 days on a single standard watch battery which is critical for compact medical devices.

5. Recent progress in CNT membrane applications

Several research groups have succeeded in synthesizing graphitic CNT membranes and demonstrating interesting flow phenomena or separation applications. A semiconductor fabrication approach to small diameter CNTs, $\sim$1.5 nm inner diameter (i.d.) imbedded in Si_3N_4 showed dramatic gas and liquid flow [33]. As shown in Fig. 4, these membranes subsequently showed 40% ion
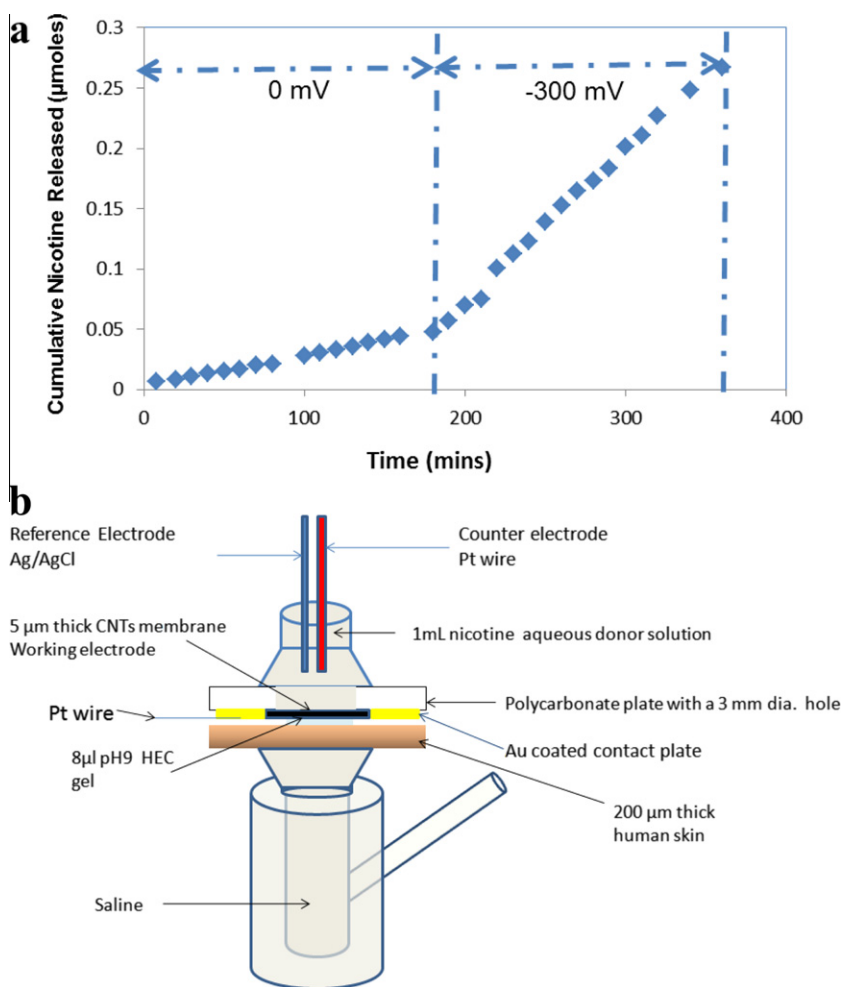
Fig. 3. (a) Flux of nicotine through CNT membrane with/without applying a −300 mV bias. The ratio of −300 mV to 0 mV nicotine flux is 5.5. Donor solution is a pH8 220 mM (35 mg/ml) nicotine aqueous solution; (b) schematic for switchable transdermal drug delivery (skin/gel/CNT membrane). Active area of CNT membrane is 0.07 cm². Reproduced permission of Ref. [39].

rejection at ~1 mmol KCl concentrations and greater than 90% rejection for ~1 mmol $K_3Fe(CN)_6$ [41]. Desalination is one of the most important potential applications for CNT membranes that can have enormous impact on future water shortage needs [42,43]. A polymer of just a few weight percent of CNTs can have the same volume rate as commercial reverse osmosis (RO) polymer membranes using 1/100th the area giving dramatic capital cost and energy savings. However demonstration of ion exclusion at sea water concentrations (~0.6 M) remains an elusive challenge for CNT membranes. In the case of ~1.6 nm i.d. tubes with carboxylic acid functionality larger multivalent anions ($Fe(CN)_6^{3-}$) give reasonable rejection due to Donnan rejection mechanism of tighter rejection of multivalent species at the anionic CNT entrances [33]. However of concern is that at ~1 mmol ion concentration, significant screening effects are seen by a drop in rejection. At this concentration the Debye screening length is about 9.4 nm, significantly longer than CNT radius (~0.8 ± 0.2 nm), suggesting that it would be difficult to increase charge-based rejection by just further reduction in CNT diameter. A difficulty with nanofiltration [44] is the reduction of ion rejection as flow rate increases due to mass transport increasing the screening of charge along pore walls, allowing ions to flow through the core. This kinetic screening is further exasperated in the CNT case since the charged region is only at the tips (<1 nm length), which is required for rapid flow rates, instead of the entire length the pore as in nanofiltration membranes. MD simulations of high charge density at entrances
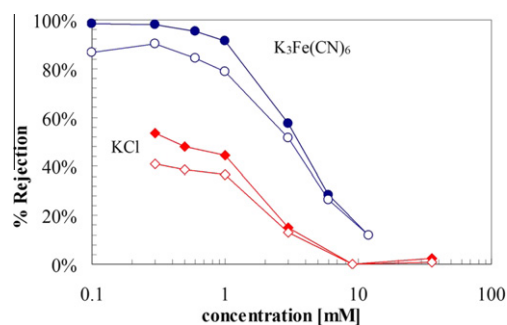

Fig. 4. Ionic rejection of $K_3Fe(CN)_6$ and KCl as a function of feed solution concentration through carboxyl functionalized DWCNT membranes (~1.6 nm i.d.) for desalination applications. Debye screening length at 1 mM is approximately 9 nm. Figure reproduced permission of Ref. [40].

to CNT can show significant ion rejection at moderate flows [45] and is important to verify experimentally if the ion rejection is possible. Efforts to increase the charge density by the previously mention diazonium grafted SWCNT membranes (from microtome method) in this laboratory have not produced results significantly improved over prior reports [32] and studies are ongoing. At this time a more likely method of desalination is to use SWCNT with inner diameter smaller than the hydrated radius of ions [46] with 8,8

CNTs being the optimal diameter predicted from MD simulation [47]. Size sieving is widely considered the mechanistic basis for RO in conventional polymer systems, but the CNTs can afford orders of magnitude improvements in flow rates not possible in solid state diffusion through the free volume of polymers. Our experience [38] is that even CNTs near 1 nm i.d. can support ionic current, so the key challenge then becomes to experimentally grow CNTs of precise diameter near 0.8 ± 0.1 nm. Other routes to desalinization by pervaporation are also proposed and may offer energy saving transport at temperatures below boiling [48]. It worth mentioning that conventional RO membranes materials have been modified with CNTs to improve mechanical strength and chloride resistance which are meaningful parameters in large-scale application [49].

CNT membranes can also be used for gas separations since gas flow also shows enhanced transport. The Marand group reported a simple fabrication technique that was commonly used to make Buckey paper [50] by filtration could be applied to CNT membranes. In this case a significant number of CNTs can be oriented down the filter and the proper amount of polymer added to form a continuous film. Gases followed the expected $(mass^{-1/2})$ flow rate dependence and modest separations of CO_2 from CH_4 through the membrane were observed [51]. The Lin group has also made aligned CNT membranes on durable ceramic supports and demonstrated initial gas separations [52]. CNT membranes have also been made by taking advantage of the outer CNT walls showing oil separations [53]. The as grown CNT arrays are relatively sparse (~5% volume) but can be compressed by capillary forces [54] resulting in dense membrane structures. These compressed membranes structures surprisingly showed dramatically fast transport [55] on the smooth outer walls of MWCNTs. By using applied bias, they were also able to move the liquid/air interface for gated ionic transport [56]. Recently magnetic field has been able to align CNTs within lyotropic polymers that are later crosslinked by UV radiation as a potential new CNT membrane fabrication technique [57]. CNT membranes are also ideal platforms for energy applications. With the successful development of RO membranes in desalination, the process can be reversed to generate electricity in regions where fresh water goes into the ocean. This process of pressure retarded osmosis (PRO) [58] is being vigorously pursued by Statkraft corporation in Norway. CNTs can also act as catalyst supports [59] with high mass activity for thin uniform layers of Pt catalyst by diazonium grafting pretreatment of CNT surfaces [60] for MeOH fuel cells. The most ideal use of an expensive catalyst, from the perspective of cost efficiency, would be to have a narrow stream of MeOH flowing over an atomically thick catalyst surface at the exit or entrance of a CNT. Particularly intriguing is that MeOH in flowing aqueous solutions is seen to partition to the hydrophobic walls of CNTs [61] and to thus efficiently flow over the catalytic site at the exit of CNTs [62]. Inside 1 nm i.d. CNTs, 1 molar $MeOH/H_2O$ solutions flowing at the rapid velocities of ~10 cm/s result in ~90% efficiency in terms of transporting MeOH to the reactive Pt catalyst site by partitioning to the sidewalls of CNTs. Particularly promising about this geometry is that we can start to consider controlling the orientation of reactants while hitting metallic catalyst centers, which is mechanistically similar to what is done within enzyme proteins.

CNT membranes have also shown useful separations. In the case of the Wu group, a polymer/MWCNT composite ultrafiltration membrane was used separate poultry products. In going from 0% to 5% MWCNT loading, significant improvement in water flux from ~200 L m^2 h to ~500 L/m^2 h were seen with 94% membrane rejection rate to egg albumin [63]. Another important bioseparation demonstration [64] with MWCNTs was the test case of Bovine Serum Antibody (~10 nm diameter) and lysosome (~4 nm diameter). By using electrophoretic pumping between 0 and 300 mV, the lysosome was seen to have mobilities two orders of magnitude lower than its mobility in bulk water. However it should be noted that in conventional nanoporous materials mobility is typically five orders of magnitude slower due to strong protein interactions with pore surfaces. The CNT interior core is relatively inert to proteins thereby allowing for chemical separation applications and conduits for intercellular injection. At higher voltages (>0.5 V) the conformation of lysosome changes allowing mobilities through CNTs to approach that of small molecule $Ru(bipyr)_3^{2+}$. BSA is completely size excluded to the detection limit of the system thereby demonstrating biomolecule separations.

Perhaps the most interesting recent developments in CNT membranes are the reports of ionic conductivity through CNT cores. Electrosmosis through chemically modified double walled CNTs, with 40-fold power consumption improvements, was the basis for a programmable transdermal device with 10 day lifetime using conventional watch battery [39]. The Strano group recently reported [65] dramatic proton and K^+ mobilities through SWCNTs that are 10^8 and 10^2 faster than bulk solution respectively. The reported proton velocities through the channel were approaching a staggering 10^4 m/s. Proton mobilities are known to be high in protein channels and are based on protons shuttling down ordered water chains. If verified, this discovery will have enormous application in fuel cells where selective proton conductive membranes are a common requirement. The currently used Nafion has many technical limitations including temperature stability and humidity control. However this fast ionic mobility was indirectly measured using the analysis of signal fluctuation lifetimes through a small numbers of CNTs (~10–20). The mechanistic source of the signal fluctuation was a fundamental assumption could not be confirmed by independent experiments. Membranes, with large numbers of CNT channels, offer a method to directly measure macroscopic quantities of ions injected into the permeate solution. Using ~1 nm diameter SWCNTs [66] in microtomed CNT membranes showed K^+ mobilities close (within a factor of 5) to bulk value while inducing electroosmotic flow [38]. Certainly the measurement of ion and proton conduction will be an important line of inquiry for CNT membranes and has exciting potential in fuel cell applications.

6. Conclusions and future prospects

CNT membranes offer an exciting opportunity to mimic natural protein channels due to (1) a mechanism of dramatically enhanced liquid flow, (2) ability to place 'gatekeeper' chemistry at the entrance to pores, and (3) the ability to electroosmotically pump chemicals through regions of chemical selectivity that would otherwise slow the flow. The structure is mechanically far more robust than lipid bilayer films and does not require expensive protein expression and separations to form the active channels. All these unique features allow for large-scale chemical separations, chemical delivery or chemical sensing based on the principles of protein channels. Initial studies show ion-rejection at low salt concentrations which is promising for water desalination or forward osmotic power generation applications. CNTs are conductive and can act as electrochemical catalyst supports. Initial bioseparations and oil filtrations have also been reported. Interesting ionic and proton conduction studies have been recently reported and could dramatically enhance fuel cell performance.

The transport mechanisms through CNT membranes are primarily (1) ionic diffusion near bulk expectation, (2) gas flow enhanced 1–2 orders of magnitude primarily due to specular reflection off of smooth graphite core, and (3) liquid flow 4–5 orders of magnitude faster than conventional materials due an ideal slip-boundary interface. The transport can be modulated by

'gatekeeper' chemistry at the pore entrance that can block by steric hindrance, electrostatic attraction/repulsion, or biochemical state. The density of gatekeeper chemistry can be enhanced by electrochemical grafting at only the tip region. A more general intellectual puzzle is that the dramatic flow enhancement is negated if one places high density of selective chemistry along the CNT walls. Important is to develop systems, such as electroosmotic flow, that can actively pump selected chemicals through the region of chemical functionality so that they can continue down the length of CNT cores at dramatic flow rates. With properly placed charge, dipoles of molecules as small as water could be oriented to induce a state coupled flow that would be truly following the elegant examples given by the natural protein channels.

Acknowledgements

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