**Electro-osmotic flow through carbon nanotube membranes for programmed transdermal drug delivery.**

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Carbon nanotubes have three key attributes that make them of great interest for novel membrane applications 1) atomically flat graphite surface allows for ideal fluid slip boundary conditions 2) the cutting process to open CNTs inherently places functional chemistry at CNT core entrance and 3) CNT are electrically conductive allowing for electrochemical reactions and application of electric fields gradients at CNT tips. To explore the hypothesis of 'Gatekeeper' membrane selectivity, the entrances to CNT's cores were functionalized with aliphatic amines of different lengths, charged dye molecule and poly-peptides. Anionic charged functional groups are seen to sharply increase flux of cationic permeates. This effect is reduced at higher solution ionic strength consistent with shorter Debye screening length screening attractive charge at the CNT core entrance. A hindered diffusion model with a geometry of CNT tip functionalization, not along the length of CNT core, was consistent with the experimentally observed selectivities. Functionality can be forced to occur at the CNT tip entrances by fast fluid flow of an inert solvent through the core during electrochemical functionalization. Changes in the flux and selectivity support a model where charged tethered molecules at the tips are drawn into the CNT core at positive bias hindering/gating flux across the membrane. In general, the transport mechanisms through CNT membrane are a) ionic diffusion is near bulk expectation with no enhancement from CNT b) gas flow is enhanced by ~1-2 order of magnitude due to specular reflection off of flat graphitic surface c) and pressure driven flux of a variety of solvents (H2O, hexane, decane ethanol, methanol) are 4-5 orders of magnitude than conventional Newtonian flow due to atomically flat graphite planes inducing nearly ideal slip conditions. However the act of placing selective functional chemistry at pore entrance or along the core, dramatically/completely eliminates the enhanced flow effects by eliminating the near perfect slip condition. Needed is a mechanism to pump chemicals through the pore where selective chemistry is. The CNT membrane, with tips functionalized with charged molecules, is a nearly ideal platform to induce electro-osmotic flow with high charge density at pore entrance and a nearly frictionless surface for the propagation of plug flow. Through diazonium electrochemical modification we have successfully bound anionic surface charge to CNT tips and along CNT cores. Both cationic and neutral fluxes through the CNT membrane are observed as a function of bias. High electro-osmotic flows of 0.05 cm/s at negative 300mV bias are seen. The analysis of charged dye molecules (Ru(bpy)3^2+) showed a factor of 50 enhancement in on state (-300mV) and of state (+300mV) primarily due to electrophoretic effects. Neutral molecules (caffeine) within ionic solutions showed a factor of 10 enhancement in on state (-300mV) and of state (+300mV). The enhanced transport of neutral species under bias is the primary proof of the existence of an electro-osmotic processes. The optimization of this process occurred after 2 steps; 1) use of CNTs with diameter under 2nm to avoid the effects of screening (Debye length ~1nm) and 2) use of quad-valent charged dye tethered to CNT entrance and core. Electrochemical grafting of diazonium salts with carboxylate groups is also necessary to achieve the necessary charge density. Use of the electro-osmotic phenomenon for responsive/programmed transdermal drug delivery devices is discussed with the voltage gated delivery of clonidine and nicotine across CNT membrane at therapeutically useful fluxes.

[1] "Aligned Multiwalled Carbon Nanotube Membrane" Hinds, B.J.*; Chopra, N.; Andrews, R.; Gavalas, V.; Bachas L. *Science* **2004** 303 62-65.
[2] "Effect of Tip Functionalization on Transport through Vertically Oriented Carbon Nanotube Membranes" Majumder, M.; Chopra, N.; Hinds, B.J * *J. Amer. Chem. Soc.* **2005**; 127, 9062-9070.
[3] "Voltage Gated Carbon Nanotube Membranes" Majumder, M.; Zhan, X; Andrews, R; Hinds, B.J * *Langmuir* **2007**; 23(16); 8624-8631.
[4] "Nanoscale hydrodynamics: Enhanced flow in carbon nanotubes" Majumder, M.; Chopra, N.; Andrews, R; Hinds, B.J * *Nature* **2005**, 438, 44.

Summary

Carbon Nanotube (CNT) membranes have demonstrated dramatic fluid flow enhancements due to nearly frictionless cores. Entrances to CNTs can be chemically modified to become anionic thereby allowing only cation flow under applied bias generating efficient electro-osmotic flows. Programmed transdermal delivery at therapeutically useful fluxes is demonstrated.