Nanoparticles and Their Role in Medicine, Engineering and Agriculture

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Around 2001, the idea of nanotechnology began to explode and was seen everywhere.


Scientists are re-creating our world in the realm of the intensely tiny. The potential payoff: denser hard drives, smaller chips, better medicine.
The possibilities are remarkable, because the scale is thousands of times smaller than that embodied in the very best contemporary computer chips.
Jean-Pierre Sauvage
Sir J. Fraser Stoddart
Bernard L. Feringa

2016
FAST FORWARD TO 2016

- The Nobel Prize for Chemistry
- molecular machines
- “miniaturised machines and taken chemistry to a new dimension.”
What is a nanoparticle?

- 1-100nm
- Behaves differently
- Different types – C-based

Ceramic

Metal
Why does size matter?

- Things begin to behave differently

Melting point of Bulk gold 1064°C.
But, at nanoscale gold melts at 300°C !!!

Source: TATA Consulting Engineers Limited
## Silver

<table>
<thead>
<tr>
<th>Microscale</th>
<th>Nanoscale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coins, Jewellery, silverware</td>
<td>Conductive inks for printed electronics to produce printed circuit boards – flexible and printable electronics</td>
</tr>
<tr>
<td>Melting point about 960 oC</td>
<td>Melting point 530 (Due to ratio of surface atoms to the total number of particles)</td>
</tr>
<tr>
<td></td>
<td>Highest electrical conductivity per unit volume</td>
</tr>
</tbody>
</table>
An example

Source: https://www.nano.gov/nanotech-101/special
Shortfalls/Gaps in Current ME

1. Acceptor Loss
2. Single Solvent Systems
3. Need for field portable analysis
4. Lack of comprehensive schemes
5. Need for improved membrane materials
Carbon nanotubes
LLME

- Hydrophobic, non-polar compounds
- Limited by the partition coefficient
Advantages

• Easily automated
• Can be done in a few minutes
• Uses microlitres of organic solvent
• Inexpensive
Carbon nanotubes
(a) Photograph of NIM; (b) photograph of pure polypropylene; (c) SEM of polypropylene surface; (d) SEM of NIM surface; (e) Confocal Raman Microscope Image pure microporous polypropylene; (f) Confocal Raman Microscope Image of NIM.
Raman spectra of pure polypropylene and NIM. The NIM spectra (taken at 780nm with 1mW power) showing characteristic SWNT peaks in the high-energy mode (red); pure polypropylene membrane spectra (taken at 532nm with 100mW power) has no CNT peaks (green).
ABSTRACT

The present disclosure provides an improved membrane or substrate having carbon nanotubes introduced and/or immobilized therein, and an improved method for introducing and/or immobilizing carbon nanotubes in membranes or substrates. More particularly, the present disclosure provides for improved systems and methods for fabricating membranes or substrates having carbon nanotubes immobilized therein. In one embodiment, the present disclosure provides for systems and methods for introducing and/or immobilizing functionalized carbon nanotubes into a pore structure of a polymeric membrane or substrate, thereby dramatically improving the performance of the polymeric membrane or substrate. In exemplary embodiments, the present disclosure provides for systems and methods for the fabrication of nanotube immobilized membranes by incorporating CNTs in a membrane or substrate.

$\text{Conc. } H_2SO_4 + HNO_3$  \rightarrow  \text{Microwave}  \rightarrow  \text{MWCNTS}$
CARBON NANOTUBE MEDIATED MEMBRANE EXTRACTION

Inventors: Kamila Hylton, Tasom (JM); Somnath Mitra, Bridgewater, NJ (US)

Assignee: New Jersey Institute of Technology, Newark, NJ (US)

Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 508 days.

Appl. No.: 12/437,789
Filed: May 8, 2009

Prior Publication Data

Related U.S. Application Data

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B01D 61/36 (2006.01)
B01D 71/02 (2006.01)

U.S. Cl.
CPC B01F 11/10 (2013.01); B01D 67/0079 (2013.01); B01D 69/141 (2013.01);

Field of Classification Search
CPC B01D 67/0044; B01D 67/0099; B01D 67/0093; B01D 67/0079; B01D 69/141; B01D 69/148; B01D 71/021; B01D 71/82; B01D 61/00; B01D 61/36; B01D 53/22; B01D 53/223; B01D 71/02; C01H 31/022; C01H 31/0226; C01H 31/0253;

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18 Claims, 18 Drawing Sheets
## Membrane Performance

<table>
<thead>
<tr>
<th></th>
<th>Plain Membrane</th>
<th>NIM with MWNT</th>
<th>% improvement</th>
<th>NIM with SWNT</th>
<th>% improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>μ-LLME</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toluene</td>
<td>3673</td>
<td>5281</td>
<td><strong>44</strong></td>
<td>5746</td>
<td><strong>56</strong></td>
</tr>
<tr>
<td>Naphthalene</td>
<td>221</td>
<td>731</td>
<td><strong>231</strong></td>
<td>446</td>
<td><strong>102</strong></td>
</tr>
<tr>
<td><strong>μ-SLME</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCAA</td>
<td>221</td>
<td>273</td>
<td><strong>24</strong></td>
<td>401</td>
<td><strong>81</strong></td>
</tr>
<tr>
<td>BCAA</td>
<td>381</td>
<td>1296</td>
<td><strong>240</strong></td>
<td>931</td>
<td><strong>144</strong></td>
</tr>
</tbody>
</table>

Table showing variation of EF with membrane material
Nanotechnology and Medicine

Applications of multifunctional self-assembled nanoparticles (credit: Yuanpei Li et al./Nature Communications)

- Imaging sensitivity for tumour detection through background suppression in blood, as well as preferential accumulation and signal amplification in tumours

APPLICATIONS

- Photodynamic therapy (PDT)/Photothermal therapy (PTT)
- NIRF imaging (NIRFI)
- PET
- MRI
- Chemo-PDT
- Drugs

$^{64}$Cu

Gd(III)
Nanotechnology and Medicine

• The surface/volume ratio of particles is very large
  nanoparticles have a huge surface suitable for chemical interactions with biomolecules

• shorter (bio)chemical reaction times
  analytical devices are faster and more sensitive.

Using nanoparticles (nano pillars, nano beads) on sensing part of an analytical device 
miniaturisation.

Smaller devices  
1. reduced sample size
2. reduced invasiveness
Nanotechnology and Medicine

Three main areas being explored:

1. Diagnostics – both in vitro and in vivo - *In vitro*, synthesized particles and manipulation or detection devices allow recognition, capture, concentration of biomolecules. *In vivo*, synthetic molecular assemblies are essentially designed as a contrast agent for imaging.

2. Therapeutics – synthetic nanoparticles are designed for the vectorization and delivery of pharmaceutical active ingredients.

3. Regenerative medicine – looking at designing biocompatible materials intended to support the growth of cells used in cell therapy.
Diagnostics

Smaller samples required

less invasive and less traumatic methods of extraction required.

Produces more complete (and more accurate) biological data from a single measurement.

Enables further refinement of diagnostic techniques, leading to high throughput screening (to test one sample for numerous diseases, or screen large numbers of samples for one disease)

Faster

The detection of diseases at an earlier stage than current techniques.

In check™ lab on chip platform. Credit: ST-Micro.
Diagnostics

Researchers at Worcester Polytechnic Institute are using **antibodies attached to carbon nanotubes** in chips to detect cancer cells in the bloodstream. The researchers believe this method could be used in simple lab tests that could provide early detection of cancer cells in the bloodstream.

Researchers at MIT have developed a sensor using carbon nanotubes embedded in a gel; that can be injected under the skin to **monitor the level of nitric oxide** in the bloodstream. The level of nitric oxide is important because it indicates inflammation, allowing easy monitoring of inflammatory diseases. In tests with laboratory mice the sensor remained functional for over a year. Researchers have demonstrated a way to use nanoparticles for **early diagnosis of infectious disease**. The nanoparticles attach to molecules in the bloodstream indicating the start of an infection. When the sample is scanned for Raman scattering the nanoparticles enhance the Raman signal, allowing detection of the molecules indicating an infectious disease at a very early stage.

A test for early detection of kidney damage is being developed. The method uses **gold nanorods** functionalized to attach to the type of protein generated by damaged kidneys. When protein accumulates on the nanorod the color of the nanorod shifts. The test is designed to be done quickly and inexpensively for early detection of a problem.
Diagnostics

• **NanoFlares** - detecting cancer cells in the bloodstream is being developed using nanoparticles called.

• designed to bind to genetic targets in cancer cells, and generate light when that particular genetic target is found.

• When the nanoparticles attach to a cancer tumors the *nanoparticles release* peptides.

• The idea is that since each nanoparticle carries several peptides a high concentration of these biomarkers will occur even at very early stages of cancer,
Diagnostics

• In-vivo diagnostics refers in general to imaging techniques

• Nanoimaging includes several approaches using techniques for the study of in-vivo molecular events and molecules manipulation.

• Imaging techniques cover advanced optical imaging and spectroscopy, nuclear imaging with radioactive tracers, magnetic resonance imaging, ultrasound, optical and X-ray imaging, all of which depend on identifying tracers or contrast agents that have been introduced into the body to mark the disease site

• Creation of highly sensitive, highly reliable detection agents that can also deliver and monitor therapy.
Therapeutics

The usual drug particle size is in the range of $10^{-4}$m, which is around 10 times larger than RBC, and therefore, majority of drug is wasted, decreases its efficacy, leads to its distribution to non-target areas, increasing unwarranted side effects.
Therapeutics

Aim therapies directly and selectively at diseased tissues or cells,

The main use of nanoparticle medicinal products (NMP) is vectorisation of active compounds, corresponding to several products already marketed like Doxil™ or more recently Abraxane™.

Nanocarriers present several advantages over conventional chemotherapy.

• Protect drugs from being degraded in the body before they reach their target

• Enhance drug absorption into tumors and the cancerous cells themselves;

• Allow for better control over the timing and distribution of drugs to the tissue, making it easier for oncologists to assess how well they work;

• Prevent drugs from interacting with normal cells, thus avoiding side effects.
Generally three vector generations are considered:

• First generation vectors: nanospheres and nanocapsules (the best known and most accessible);

• Second generation vectors: nanoparticles coated with hydrophilic polymers such as polyethylene glycol (PEG), PEGylated nanoparticles; eg. Cimzia used to treat Crohn’s disease and rheumatoid arthritis

• Third generation vectors, still under development, combining a biodegradable core and a polymer envelope (PEG) with a membrane recognition ligand.
Researchers at the Wyss Institute are testing nanoparticles that release drugs when subjected to sheer force, such as occurs when passing through a section of artery that is mostly blocked by a clot. Lab tests on animals have shown that this method is effective in delivering drugs used to dissolve clots.

Researchers at the Houston Methodist Research Institute have demonstrated a targeted drug delivery method in mice using silicon nanoparticles that degrade inside a tumor, releasing polymer strands that form a nanoparticle containing the drug to be delivered. This polymer nanoparticle dissolves inside the cancer cell, delivering the drug to the cancer cell.
Therapy techniques

Researchers have developed "nanosponges" that absorb toxins and remove them from the bloodstream. The nanosponges are polymer nanoparticles coated with a red blood cell membrane. The red blood cell membrane allows the nanosponges to travel freely in the bloodstream and attract the toxins.

Researchers are investigating the use of bismuth nanoparticles to concentrate radiation used in radiation therapy to treat cancer tumors. Initial results indicate that the bismuth nanoparticles would increase the radiation dose to the tumor by 90 percent.
Drug delivery (mechanical) devices

Implanted drug delivery devices – DDD – Examples are DebioStar or Nanopump™, fabricated by the Swiss company Debiotech

The Nanopump™ is a miniaturised drug delivery pump based on MEMS chips which can be implanted for accurate dosing of various therapeutic compounds with dedicated delivery profiles.

Designed with reservoirs, actuators, pumps to control accurately the release of pharmaceutical ingredients.

These drug delivery devices can be implanted within the body, even in the brain.
Therapeutics

Surgical nanorobotics – A nanorobotic device could be introduced into the human body either via a natural opening or surgically. It could act as a homing device, searching for pathology, diagnosing it, and even curing it by nanomanipulation, all the while coordinated by an onboard computer, maintaining contact with the supervising surgeon via coded ultrasound signals.

Source: Le voyageur Temps / Indian Heart Journal 68 (2016) 437–439
Engineering

Nanodiagnostics
construction of nanoelectronic devices that could detect the concentrations of biomolecules in real time for use as medical diagnostics.

Biological sensors/nanosensors – These are miniaturized nanoelectronic devices that could interact with single cells, undertake in vivo proteomic sensing, and could be used not only in basic biological research but also health monitoring.

lab-on-a-chip and lab-on-paper serve as new platforms for diagnosis of diseases and low-cost multi-analyte sensing
Agriculture

- Agriculture:
  - Banana, Coconut, Coffee

- is a major cause of climate change and ecosystem degradation.

- Involves significant use of fertilizers to utilize to supplement soil nutrients, to promote plant growth and to increase crop productivity and food quality is prevalent in modern agriculture.
Nanoagriculture involves the employment of Nano particles in agriculture with the chief aim being improvements in quality, pest resistance and yield.

Ref: Srilatha, J Nanomedic Nanotechnol 2011, 2:7 http://dx.doi.org/10.4172/2157-7439.1000123

ars.els-cdn.com/content/image/1-s2.0-S1748013214001340-fx1_lrg.jpg
Agriculture

Sustainable intensification is a concept related to a production system aiming to increase the yield without adverse environmental impact while cultivating the same agricultural area.

They can find application, as an example, for the development of intelligent nanosystems for the immobilization of nutrients and their release in soil. Such systems have the advantage to minimize leaching, while improving the uptake of nutrients by plants, and to mitigate eutrophication by reducing the transfer of nitrogen to groundwater.

Four types of nanomaterials in agriculture:
1. macronutrient nanofertilizers,
2. micronutrient nanofertilizers,
3. nutrient-loaded nanofertilizers, and
4. plant-growth-enhancing nanomaterials.
Macronutrient nanofertilizers

N, P, K, Mg, Ca

Currently – high application + low efficiency → ground and surface water
Potential applications of nanotechnology in agriculture. (A) Increase the productivity using nanopesticides and nanofertilizers; (B) Improve the quality of the soil using nanozeolites and hydrogels; (C) Stimulate plant growth using nanomaterials (SiO$_2$, TiO$_2$, and carbon nanotubes); (D) Provide smart monitoring using nanosensors by wireless communication devices.
<table>
<thead>
<tr>
<th>Purpose</th>
<th>Material</th>
<th>Findings</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smart agrochemical delivery system via plant roots of sunflower, tomato, pea and wheat</td>
<td>Magnetic carbon coated nanoparticles</td>
<td>Nanoparticles moved through plant xylem and phloem within 24 h</td>
<td>Cifuentes et al., 2010</td>
</tr>
<tr>
<td>Controlled release herbicide delivery system for atrazine</td>
<td>Polyhydroxybutyrate-co-hydroxyvalerate microspheres with atrazine (~13 nm)</td>
<td>Good affinity of herbicide with polymer, decreased genotoxicity and increased biodegradability</td>
<td>Grillo et al., 2010</td>
</tr>
<tr>
<td>Nanocomposite based controlled release of herbicide, 2,4-dichlorophenoxyacetate (2,4-D)</td>
<td>Inorganic Zn–Al layered double hydroxide (ZAL) as release agent</td>
<td>Initial burst of 2,4-D followed by sustained release that depended on type of anions and their concentrations in release medium</td>
<td>Hussein et al., 2005</td>
</tr>
<tr>
<td>Controlled delivery system for water-soluble pesticide (validamycin)</td>
<td>Porous hollow silica nanoparticles (PHSNs)</td>
<td>Pesticide was loaded into PHSNs (36 wt % loading capacity) and the release was in two stages: initial burst followed by sustained release</td>
<td>Liu et al., 2006</td>
</tr>
<tr>
<td>Reduce the bean rust disease severity</td>
<td>CNT conjugated with INF24 oligonucleotides</td>
<td>Treatment reduced the rust severity</td>
<td>Corrêa et al., 2010</td>
</tr>
<tr>
<td>Control of lentil pathogen and wilting</td>
<td>Silver nanoparticles-AgNPs (0.5–1000 ppm)</td>
<td>Faster plant growth compared to control; AgNPs did not reduce the plant wilting</td>
<td>Ashrafi et al., 2010</td>
</tr>
<tr>
<td>Physical and biological changes of Brassica oleracea in presence of nanomaterials</td>
<td>TiO₂ (5–8 nm) 0.05–2 mL of TiO₂ in 500 mL of Hoagland solution</td>
<td>Higher concentrations had negative impact on shoot length whereas positive impact on root length</td>
<td>Singh et al., 2010</td>
</tr>
<tr>
<td>Effect of carbon nanostructures on tomato germination</td>
<td>MWCNTs</td>
<td>Seed germination was not related to MWNCTs (observed up to 7 days)</td>
<td>Lima et al., 2010</td>
</tr>
<tr>
<td>Treatment of fungal pathogens in vitro and in chickpea and wheat plants</td>
<td>Amphotericin B nanodisks (AMB-NDs) 0.1–2 μg/mL (in vitro), 0.1–10 μg/L (plants)</td>
<td>AMB-NDs inhibited fungi at 0.1 μg/mL (in vitro); effective chickpea fusarium wilt control (preventive dosage of 0.1 μg/L), wheat leaf rust control by foliar treatment</td>
<td>Perez-de-Luque et al., 2012</td>
</tr>
</tbody>
</table>

Source: Applications of nanomaterials in agricultural production and crop protection: A review
Lav R.Khot, Sindhuja Sankaran, Joe Mari Maja, Reza Ehsani, Edmund W. Schuster
THANK YOU