

RECENT ADVANCES IN CARBON NANOTUBES A PROMISING APPROACHES IN CANCER THERAPY

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ABSTRACT

The carbon nanotube's structure can be thought of as a sheet of graphite which has been rolled into a cylinder. A nanotube can also contain multiple cylinders of different diameters nested inside one another. This type is called a multi-wall nanotube (MWNT). A nanotube with just one cylinder is referred to as a single-wall nanotube (SWNT). Other varieties of nanotubes include ropes, bundles and arrays. Over the past two years, researchers have demonstrated repeatedly that certain types of carbon nanotubes are among the most effective materials known for transporting proteins, genes, and drug molecules across the cell membrane. Now, an attempt to better understand this process has found that virtually any type of carbon nanotube can enter a wide variety of cell types. Significant progress in interfacing carbon nanotubes with biological materials has been made in key areas such as aqueous solubility, chemical and biological functionalization for biocompatibility and specificity, and electronic sensing of proteins. This article reviews the current trends in biological functionalization of carbon nanotubes and their potential applications for cancer diagnostics. The present work compiles the review on carbon nanotubes and its efficacy in treatment of cancer and also reports the mechanism and properties.

Key-words: Nanotubes, biological events, cancer, nanomedicine

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INTRODUCTION

Carbon nanotubes (CNTs) are allotropes of carbon with a cylindrical nanostructure. Nanotubes have been constructed with length-to-diameter ratio of up to 28,000,000:1, which is significantly larger than any other material. These cylindrical carbon molecules have novel properties that make them potentially useful in many applications in nanotechnology, electronics, optics and other fields of materials science, as well as potential uses in architectural fields. They exhibit extraordinary strength and unique electrical properties, and are efficient conductors of heat. Their final usage, however, may be limited by their potential toxicity.

Nanotubes are members of the fullerene structural family, which also includes the spherical buckyballs. The ends of a nanotube might be capped with a hemisphere of the buckyball structure. Their name is derived from their size, since the diameter of a nanotube is on the order of a few nanometers (approximately 1/50,000th of the width of a human hair), while they can be up to several millimeters in length (as of 2008). Nanotubes are categorized as single-walled nanotubes (SWNTs) and multi-walled nanotubes (MWNTs).

The nature of the bonding of a nanotube is described by applied quantum chemistry, specifically, orbital hybridization. The chemical bonding of nanotubes is composed entirely of sp^2 bonds, similar to those of graphite. This bonding structure, which is stronger than the sp^3 bonds found in diamonds, provides the molecules with their unique strength. Nanotubes naturally align themselves into "ropes" held together by Van der Waals forces. Under high pressure, nanotubes can merge together, trading some sp^2 bonds for sp^3 bonds, giving the possibility of producing strong, unlimited-length wires through high-pressure nanotube linking.

Carbon nanotubes (CNTs) are allotropes of carbon. A single-walled carbon nanotube (SWNT) is a one-atom thick sheet of graphite (called graphene) rolled up into a seamless cylinder with diameter of the order of a nanometer. This results in a nanostructure where the length-to-diameter ratio exceeds 10,000. Such cylindrical carbon molecules have novel properties that make them potentially useful in many applications in nanotechnology, electronics, optics and other fields of materials science. They exhibit extraordinary strength and unique electrical properties, and are efficient conductors of heat. Inorganic nanotubes have also been synthesized. Nanotubes are members of the fullerene structural family, which also includes buckyballs. Whereas buckyballs are spherical in shape, a nanotube is

cylindrical, with at least one end typically capped with a hemisphere of the buckyball structure. Their name is derived from their size, since the diameter of a nanotube is in the order of a few nanometers (approximately 50,000 times smaller than the width of a human hair), while they can be up to several millimeters in length. There are two main types of nanotubes: single-walled nanotubes (SWNTs) and multi-walled nanotubes (MWNTs).

CARBON NANOTUBES: CLASSIFICATION

- 1. Single-walled**
- 2. Multi-walled**
- 3. Fullerite**
- 4. Torus**
- 5. Nanobud**

Single-walled nanotubes (SWNT)

It have a diameter of close to 1 nanometer, with a tube length that can be many thousands of times longer. The structure of a SWNT can be conceptualized by wrapping a one-atom-thick layer of graphite called graphene into a seamless cylinder. The way the graphene sheet is wrapped is represented by a pair of indices (n,m) called the chiral vector. The integers n and m denote the number of unit vectors along two directions in the honeycomb crystal lattice of graphene. If $m=0$, the nanotubes are called "zigzag". If $n=m$, the nanotubes are called "armchair". Otherwise, they are called "chiral".

Single-walled nanotubes are a very important variety of carbon nanotube because they exhibit important electric properties that are not shared by the multi-walled carbon nanotube (MWNT) variants. Single-walled nanotubes are the most likely candidate for miniaturizing electronics beyond the micro electromechanical scale that is currently the basis of modern electronics. The most basic building block of these systems is the electric wire, and SWNTs can be excellent conductors. One useful application of SWNTs is in the development of the first intramolecular field effect transistors (FETs). The production of the first intramolecular logic gate using SWNT FETs has recently become possible as well. To create a logic gate you must have both a p-FET and an n-FET. Because SWNTs are p-FETs when exposed to oxygen and n-FETs when unexposed to oxygen, they were able to protect half of a SWNT from oxygen exposure, while exposing the other half to oxygen.

The result was a single SWNT that acted as a NOT logic gate with both p and n-type FETs within the same molecule.

Multi-walled

Multi-walled nanotubes (MWNT) consist of multiple layers of graphite rolled in on themselves to form a tube shape. There are two models which can be used to describe the structures of multi-walled nanotubes. In the *Russian Doll* model, sheets of graphite are arranged in concentric cylinders, e.g. a (0,8) single-walled nanotube (SWNT) within a larger (0,10) single-walled nanotube. In the *Parchment* model, a single sheet of graphite is rolled in around itself, resembling a scroll of parchment or a rolled up newspaper. The interlayer distance in multi-walled nanotubes is close to the distance between graphene layers in graphite, approximately 3.3 Å. The special place of double-walled Carbon Nanotubes (DWNT) must be emphasized here because they combine very similar morphology and properties as compared to SWNT, while improving significantly their resistance to chemicals. This is especially important when functionalisation is required (this means grafting of chemical functions at the surface of the nanotubes) to add new properties to the CNT. In the case of SWNT, covalent functionalisation will break some C=C double bonds, leaving "holes" in the structure on the nanotube and thus modifying both its mechanical and electrical properties. In the case of DWNT, only the outer wall is modified. DWNT synthesis on the gram-scale was first proposed in 2003 by the CCVD technique, from the selective reduction of oxides solid solutions in methane and hydrogen.

Fullerite

Fullerites are the solid-state manifestation of fullerenes and related compounds and materials. Being highly incompressible nanotube forms, polymerized single-walled nanotubes (P-SWNT) are a class of fullerites and are comparable to diamond in terms of hardness. However, due to the way that nanotubes intertwine, P-SWNTs don't have the corresponding crystal lattice that makes it possible to cut diamonds neatly. This same structure results in a less brittle material, as any impact that the structure sustains is spread out throughout the material.

Torus

A nanotorus is a theoretically described carbon nanotube bent into a torus (donut shape). Nanotori have many unique properties, such as magnetic moments 1000 times

larger than previously expected for certain specific radii. Properties such as magnetic moment, thermal stability, etc. vary widely depending on radius of the torus and radius of the tube.

Nanobud

Carbon NanoBuds are a newly discovered material combining two previously discovered allotropes of carbon: carbon nanotubes and fullerenes. In this new material fullerene-like "buds" are covalently bonded to the outer sidewalls of the underlying carbon nanotube. This hybrid material has useful properties of both fullerenes and carbon nanotubes. In particular, they have been found to be exceptionally good field emitters.

PROPERTIES

Strength

Carbon nanotubes are the strongest and stiffest materials yet discovered in terms of tensile strength and elastic modulus respectively. This strength results from the covalent sp^2 bonds formed between the individual carbon atoms. In 2000, a multi-walled carbon nanotube was tested to have a tensile strength of 63 gigapascals (GPa). (This, for illustration, translates into the ability to endure weight of 6300 kg on a cable with cross-section of 1 mm^2 .) Since carbon nanotubes have a low density for a solid of 1.3 to $1.4 \text{ g}\cdot\text{cm}^{-3}$,^[5] its specific strength of up to $48,000 \text{ kN}\cdot\text{m}\cdot\text{kg}^{-1}$ is the best of known materials, compared to high-carbon steel's $154 \text{ kN}\cdot\text{m}\cdot\text{kg}^{-1}$.

Under excessive tensile strain, the tubes will undergo plastic deformation, which means the deformation is permanent. This deformation begins at strains of approximately 5% and can increase the maximum strain the tubes undergo before fracture by releasing strain energy.

CNTs are not nearly as strong under compression. Because of their hollow structure and high aspect ratio, they tend to undergo buckling when placed under compressive, torsional or bending stress.

Comparison of Mechanical Properties

Material	<u>Young's Modulus</u> (TPa)	Tensile Strength (GPa)	Elongation at Break (%)
SWNT	~1 (from 1 to 5)	13–53 ^E	16
Armchair SWNT	0.94 ^T	126.2 ^T	23.1

Zigzag SWNT	0.94 ^T	94.5 ^T	15.6–17.5
Chiral SWNT	0.92		
MWNT	0.8–0.9 ^E	150	
Stainless Steel	~0.2	~0.65–1	15–50
Kevlar	~0.15	~3.5	~2
Kevlar ^T	0.25	29.6	

^EExperimental observation; ^TTheoretical prediction

The above discussion referred to axial properties of the nanotube, whereas simple geometrical considerations suggest that carbon nanotubes should be much softer in the radial direction than along the tube axis. Indeed, TEM observation of radial elasticity suggested that even the van der Waals forces can deform two adjacent nanotubes^[18]. Nanoindentation experiments, performed by several groups on multiwalled carbon nanotubes, indicated Young's modulus of the order of several GPa confirming that CNTs are indeed rather soft in the radial direction.

Kinetic

Multi-walled nanotubes, multiple concentric nanotubes precisely nested within one another, exhibit a striking telescoping property whereby an inner nanotube core may slide, almost without friction, within its outer nanotube shell thus creating an atomically perfect linear or rotational bearing. This is one of the first true examples of molecular nanotechnology, the precise positioning of atoms to create useful machines. Already this property has been utilized to create the world's smallest rotational motor. Future applications such as a gigahertz mechanical oscillator are also envisaged.

Electrical

Because of the symmetry and unique electronic structure of graphene, the structure of a nanotube strongly affects its electrical properties. For a given (n,m) nanotube, if $n = m$, the nanotube is metallic; if $n - m$ is a multiple of 3, then the nanotube is semiconducting with a very small band gap, otherwise the nanotube is a moderate semiconductor. Thus all armchair ($n = m$) nanotubes are metallic, and nanotubes (5,0), (6,4), (9,1), etc. are semiconducting. In theory, metallic nanotubes can carry an electrical current density of 4×10^9 A/cm² which is more than 1,000 times greater than metals such as copper.

Thermal

All nanotubes are expected to be very good thermal conductors along the tube, exhibiting a property known as "ballistic conduction," but good insulators laterally to the tube axis. It is predicted that carbon nanotubes will be able to transmit up to $6000 \text{ W}\cdot\text{m}^{-1}\cdot\text{K}^{-1}$ at room temperature; compare this to copper, a metal well-known for its good thermal conductivity, which transmits $385 \text{ W}\cdot\text{m}^{-1}\cdot\text{K}^{-1}$. The temperature stability of carbon nanotubes is estimated to be up to $2800 \text{ }^\circ\text{C}$ in vacuum and about $750 \text{ }^\circ\text{C}$ in air.

Defects

As with any material, the existence of a crystallographic defect affects the material properties. Defects can occur in the form of atomic vacancies. High levels of such defects can lower the tensile strength by up to 85%. Another form of carbon nanotube defect is the Stone Wales defect, which creates a pentagon and heptagon pair by rearrangement of the bonds. Because of the very small structure of CNTs, the tensile strength of the tube is dependent on its weakest segment in a similar manner to a chain, where the strength of the weakest link becomes the maximum strength of the chain.

Crystallographic defects also affect the tube's electrical properties. A common result is lowered conductivity through the defective region of the tube. A defect in armchair-type tubes (which can conduct electricity) can cause the surrounding region to become semiconducting, and single monoatomic vacancies induce magnetic properties.

Crystallographic defects strongly affect the tube's thermal properties. Such defects lead to phonon scattering, which in turn increases the relaxation rate of the phonons. This reduces the mean free path and reduces the thermal conductivity of nanotube structures. Phonon transport simulations indicate that substitutional defects such as nitrogen or boron will primarily lead to scattering of high-frequency optical phonons. However, larger-scale defects such as Stone Wales defects cause phonon scattering over a wide range of frequencies, leading to a greater reduction in thermal conductivity.

One-dimensional transport

Due to their nanoscale dimensions, electron transport in carbon nanotubes will take place through quantum effects and will only propagate along the axis of the tube. Because of this special transport property, carbon nanotubes are frequently referred to as "one-dimensional" in scientific articles.

Toxicity

Determining the toxicity of carbon nanotubes has been one of the most pressing questions in nanotechnology. Unfortunately such research has only just begun and the data is still fragmentary and subject to criticism. Preliminary results highlight the difficulties in evaluating the toxicity of this heterogeneous material. Parameters such as structure, size distribution, surface area, surface chemistry, surface charge, and agglomeration state as well as purity of the samples, have considerable impact on the reactivity of carbon nanotubes. However, available data clearly show that, under some conditions, nanotubes can cross membrane barriers, which suggests that if raw materials reach the organs they can induce harmful effects such as inflammatory and fibrotic reactions.

A study led by Alexandra Porter from the University of Cambridge shows that CNTs can enter human cells and accumulate in the cytoplasm, causing cell death. Results of rodent studies collectively show that regardless of the process by which CNTs were synthesized and the types and amounts of metals they contained, CNTs were capable of producing inflammation, epithelioid granulomas (microscopic nodules), fibrosis, and biochemical/toxicological changes in the lungs. Comparative toxicity studies in which mice were given equal weights of test materials showed that SWCNTs were more toxic than quartz, which is considered a serious occupational health hazard when chronically inhaled. As a control, ultrafine carbon black was shown to produce minimal lung responses.

The needle-like fiber shape of CNTs, similar to asbestos fibers, raises fears that widespread use of carbon nanotubes may lead to mesothelioma, cancer of the lining of the lungs often caused by exposure to asbestos. A recently-published pilot study supports this prediction. Scientists exposed the mesothelial lining of the body cavity of mice, as a surrogate for the mesothelial lining of the chest cavity, to long multiwalled carbon nanotubes and observed asbestos-like, length-dependent, pathogenic behavior which included inflammation and formation of lesions known as granulomas. Authors of the study conclude:

"This is of considerable importance, because research and business communities continue to invest heavily in carbon nanotubes for a wide range of products under the assumption that they are no more hazardous than graphite. Our results suggest the need for further research and great caution before introducing such products into the market if long-term harm is to be avoided."

Synthesis



Powder of carbon nanotubes

Techniques have been developed to produce nanotubes in sizeable quantities, including arc discharge, laser ablation, high pressure carbon monoxide (HiPCO), and chemical vapor deposition (CVD). Most of these processes take place in vacuum or with process gases. CVD growth of CNTs can occur in vacuum or at atmospheric pressure. Large quantities of nanotubes can be synthesized by these methods; advances in catalysis and continuous growth processes are making CNTs more commercially viable.

Arc discharge

Nanotubes were observed in 1991 in the carbon soot of graphite electrodes during an arc discharge, by using a current of 100 amps, that was intended to produce fullerenes. However the first macroscopic production of carbon nanotubes was made in 1992 by two researchers at NEC's Fundamental Research Laboratory.^[34] The method used was the same as in 1991. During this process, the carbon contained in the negative electrode sublimates because of the high discharge temperatures. Because nanotubes were initially discovered using this technique, it has been the most widely-used method of nanotube synthesis. The yield for this method is up to 30 percent by weight and it produces both single- and multi-walled nanotubes with lengths of up to 50 micrometers with few structural defects.

Laser ablation

In the laser ablation process, a pulsed laser vaporizes a graphite target in a high-temperature reactor while an inert gas is bled into the chamber. Nanotubes develop on the

cooler surfaces of the reactor as the vaporized carbon condenses. A water-cooled surface may be included in the system to collect the nanotubes.

This process was developed by Dr. Richard Smalley and co-workers at Rice University, who at the time of the discovery of carbon nanotubes, were blasting metals with a laser to produce various metal molecules. When they heard of the existence of nanotubes they replaced the metals with graphite to create multi-walled carbon nanotubes. Later that year the team used a composite of graphite and metal catalyst particles (the best yield was from a cobalt and nickel mixture) to synthesize single-walled carbon nanotubes.

The laser ablation method yields around 70% and produces primarily single-walled carbon nanotubes with a controllable diameter determined by the reaction temperature. However, it is more expensive than either arc discharge or chemical vapor deposition.

Chemical vapor deposition (CVD)



Nanotubes being grown by plasma enhanced chemical vapor deposition

The catalytic vapor phase deposition of carbon was first reported in 1959, but it was not until 1993 that carbon nanotubes were formed by this process. In 2007, researchers at the University of Cincinnati (UC) developed a process to grow aligned carbon nanotube arrays of 18 mm length on a FirstNano ET3000 carbon nanotube growth system.

During CVD, a substrate is prepared with a layer of metal catalyst particles, most commonly nickel, cobalt, iron, or a combination. The metal nanoparticles can also be produced by other ways, including reduction of oxides or oxides solid solutions. The diameters of the nanotubes that are to be grown are related to the size of the metal particles. This can be controlled by patterned (or masked) deposition of the metal, annealing, or by plasma etching of a metal layer. The substrate is heated to approximately 700°C. To initiate the growth of nanotubes, two gases are bled into the reactor: a process gas (such as ammonia, nitrogen or hydrogen) and a carbon-containing gas (such as acetylene, ethylene, ethanol or methane). Nanotubes grow at the sites of the metal catalyst; the carbon-containing gas is broken apart at the surface of the catalyst particle, and the carbon is transported to the edges of the particle, where it forms the nanotubes. This mechanism is still being studied. The catalyst particles can stay at the tips of the growing nanotube during the growth process, or remain at the nanotube base, depending on the adhesion between the catalyst particle and the substrate.

CVD is a common method for the commercial production of carbon nanotubes. For this purpose, the metal nanoparticles are mixed with a catalyst support such as MgO or Al₂O₃ to increase the surface area for higher yield of the catalytic reaction of the carbon feedstock with the metal particles. One issue in this synthesis route is the removal of the catalyst support via an acid treatment, which sometimes could destroy the original structure of the carbon nanotubes. However, alternative catalyst supports that are soluble in water have proven effective for nanotube growth.

If a plasma is generated by the application of a strong electric field during the growth process (plasma enhanced chemical vapor deposition*), then the nanotube growth will follow the direction of the electric field.^[43] By adjusting the geometry of the reactor it is possible to synthesize vertically aligned carbon nanotubes^[44] (i.e., perpendicular to the substrate), a morphology that has been of interest to researchers interested in the electron emission from nanotubes. Without the plasma, the resulting nanotubes are often randomly

oriented. Under certain reaction conditions, even in the absence of a plasma, closely spaced nanotubes will maintain a vertical growth direction resulting in a dense array of tubes resembling a carpet or forest.

Of the various means for nanotube synthesis, CVD shows the most promise for industrial-scale deposition, because of its price/unit ratio, and because CVD is capable of growing nanotubes directly on a desired substrate, whereas the nanotubes must be collected in the other growth techniques. The growth sites are controllable by careful deposition of the catalyst. In 2007, a team from Meijo University demonstrated a high-efficiency CVD technique for growing carbon nanotubes from camphor.^[45] Researchers at Rice University, until recently led by the late Dr. Richard Smalley, have concentrated upon finding methods to produce large, pure amounts of particular types of nanotubes. Their approach grows long fibers from many small seeds cut from a single nanotube; all of the resulting fibers were found to be of the same diameter as the original nanotube and are expected to be of the same type as the original nanotube. Further characterization of the resulting nanotubes and improvements in yield and length of grown tubes are needed.

CVD growth of multi-walled nanotubes is used by several companies to produce materials on the ton scale, including NanoLab, Bayer, Arkema, Nanocyl, Nanothinx, Hyperion Catalysis, Mitsui, and Showa Denko.

Natural, incidental, and controlled flame environments

Fullerenes and carbon nanotubes are not necessarily products of high-tech laboratories; they are commonly formed in such mundane places as ordinary flames, produced by burning methane, ethylene, and benzene, and they have been found in soot from both indoor and outdoor air. However, these naturally occurring varieties can be highly irregular in size and quality because the environment in which they are produced is often highly uncontrolled. Thus, although they can be used in some applications, they can lack in the high degree of uniformity necessary to meet many needs of both research and industry. Recent efforts have focused on producing more uniform carbon nanotubes in controlled flame environments. Nano-C, Inc of Westwood, Massachusetts, is producing flame synthesized single-walled carbon nanotubes. This method has promise for large-scale, low-cost nanotube synthesis, though it must compete with rapidly developing large scale CVD production.

FUTURE PROSPECTS

Application of Nanotechnology in Electronic Devices

Nanomaterials are produced by two methods, the bottom up and top down. The bottom up method has been successfully used for self assembly by researchers through out the world. The bottom up method especially is therefore useful for ionic and electronic applications, however top down method plays a major role in research in many US universities and companies.

One of the important applications of nanotechnology is in advance architecture level of the Si-LSI technology. One method of constructing an electronic device is using bottom up method and combining it with top down method.

Many researchers has used bottom up method to fabricate a DRAM capacitor. DRAM comprises a pair of transistor and capacitor. Scientists at University of California have successfully fabricated a two-layered dielectric film. The dielectric film contains a self assembled monolayer and electrolyte. The redox reduction between SAM and electrolyte controls the capacitance and electromotive force within the dielectric film.

Flash memeory is another important application of nanotechnology. In conventional flash memory, a unit of single transistor is used. Highly integrated flash memory, a major non-volatile memory is in high demand for portable devices such as mobile phones. A floating gate stores the charge in the flash memory and these floating gates are being replaced by number of nanodots. These nanodots are non-continuous film and work smoothly even when the film contains certain amount of defects. So, the flash memory is far better than the conventional semiconductor memory.

Nanomedicine: current status and future prospects

Applications of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems has recently been referred to as "nanomedicine" by the National Institutes of Health. Research into the rational delivery and targeting of pharmaceutical, therapeutic, and diagnostic agents is at the forefront of projects in nanomedicine. These involve the identification of precise targets (cells and receptors) related to specific clinical conditions and choice of the appropriate nanocarriers to achieve the required responses while minimizing the side effects. Mononuclear phagocytes, dendritic cells, endothelial

cells, and cancers (tumor cells, as well as tumor neovasculature) are key targets. Today, nanotechnology and nanoscience approaches to particle design and formulation are beginning to expand the market for many drugs and are forming the basis for a highly profitable niche within the industry, but some predicted benefits are hyped. This article will highlight rational approaches in design and surface engineering of nanoscale vehicles and entities for site-specific drug delivery and medical imaging after parenteral administration.

Nanoparticles with inherent diagnostic properties

Nanotechnology is an area of science devoted to the manipulation of atoms and molecules leading to the construction of structures in the nanometer scale size range (often 100 nm or smaller), which retain unique properties. Indeed, the physical and chemical properties of materials can significantly improve or radically change as their size is scaled down to small clusters of atoms. Small size means different arrangement and spacing for surface atoms, and these dominate the object's physics and chemistry. Colloidal gold, ironoxide crystals, and quantum dots (QDs) semiconductor nanocrystals are examples of nanoparticles, whose size is generally in the region of 1–20 nm, and have diagnostic applications in biology and medicine. Gold nanoparticles have application as quenchers in fluorescence resonance energy transfer measurement studies. For example, the distance-dependent optical property of gold nanoparticles has provided opportunities for evaluation of the binding of DNA-conjugated gold nanoparticles to a complementary RNA sequence. Iron oxide nanocrystals with superparamagnetic properties are used as contrast agents in magnetic resonance imaging (MRI), as they cause changes in the spin-spin relaxation times of neighboring water molecules, to monitor gene expression or detect pathologies such as cancer, brain inflammation, arthritis, or atherosclerotic plaques. QDs can label biological systems for detection by optical or electrical means in vitro and to some extent in vivo. The fluorescence emission wavelength (from the UV to the near-IR) of QDs can be tuned by altering the particle size, thus these nanosystems have the potential to revolutionize cell, receptor, antigen, and enzyme imaging. Indeed, a recent report demonstrated the use of QDs for tracking metastatic tumor cell extravasation (20). Their large surface area-to-volume ratio offers potential for designing multifunctional nanosystems. Undoubtedly, application of such multi-wavelength optical nanotools may eventually aid our understanding of the

complex regulatory and signaling networks that govern the behavior of cells in normal and disease states.

Nanovehicles and drug carriers

In addition, there are numerous engineered constructs, assemblies, architectures, and particulate systems, whose unifying feature is the nanometer scale size range (from a few to 250 nm). These include polymeric micelles, dendrimers, polymeric and ceramic nanoparticles, protein cage architectures, viral-derived capsid nanoparticles, polyplexes, and liposomes. First, therapeutic and diagnostic agents can be encapsulated, covalently attached, or adsorbed on to such nanocarriers. These approaches can easily overcome drug solubility issues, particularly with the view that large proportions of new drug candidates emerging from high-throughput drug screening initiatives are water insoluble. But some carriers have a poor capacity to incorporate active compounds (e.g., dendrimers, whose size is in the order of 5–10 nm). There are alternative nanoscale approaches for solubilization of water insoluble drugs. One approach is to mill the substance and then stabilize smaller particles with a coating; this forms nanocrystals in size ranges suitable for oral delivery, as well as for intravenous injection. Thus, the reduced particle size entails high surface area and hence a strategy for faster drug release. Pharmacokinetic profiles of injectable nanocrystals may vary from rapidly soluble in the blood to slowly dissolving. Second, by virtue of their small size and by functionalizing their surface with synthetic polymers and appropriate ligands, nanoparticulate carriers can be targeted to specific cells and locations within the body after intravenous and subcutaneous routes of injection. Such approaches, may enhance detection sensitivity in medical imaging, improve therapeutic effectiveness, and decrease side effects. Some of the carriers can be engineered in such a way that they can be activated by changes in the environmental pH, chemical stimuli, by the application of a rapidly oscillating magnetic field, or by application of an external heat source. Such modifications offer control over particle integrity, drug delivery rates, and the location of drug release, for example within specific organelles. Some are being designed with the focus on multifunctionality; these carriers target cell receptors and delivers simultaneously drugs and biological sensors. Some include the incorporation of one or more nanosystems within other carriers, as in micellar encapsulation of QDs; this delineates the inherent nonspecific adsorption and aggregation of QDs in biological environments. In addition to

these, nanoscale-based delivery strategies are beginning to make a significant impact on global pharmaceutical planning and marketing (market intelligence and life-cycle management)

Carbon Nanotube Membrane for controlled transportation

Various researchers have already studied fluid flow in micrometer level carbon nanotube channels. These open-ended carbon nanotube offer various possibilities as conduits for flow especially for low surface tension fluid as these nanomaterials have excellent rigid cylindrical pores. Selected microfabrication technique can enhance the possibilities for development of various small-scale-devices. These small-scale devices or lab-on-a-chip can play a key role in chemical analysis or synthesis.

Actually modifying their surfaces, scientists can enhance the molecular selectivity of carbon nanotubes. Researchers has already established various applications of nanotubes or nanopores such as molecule detection, storage and delivery of encapsulation media, biocatalysis, biomolecule separation devices and for selective and rapid gas flow. Researchers have studied and fabricated a well-ordered membrane structure by aligning array of carbon nanotubes impregnated in polystyrene matrix.

The open tips of carbon nanotube in the membrane structure are attached with carboxylate that can be easily functionalized. This functionalization especially with a bulky receptor can subsequently be used to open or close the pore. Thus the membrane structure is suitable for the gas flow or ionic transport. Recently researchers have fabricated functionalized carbon nanotube at the end and its application as ionic transport has been achieved. Researchers could achieve this by releasing receptor in controlled fashion.

Scientists have also developed an inner-coated carbon nanotube. Here the inside walls of carbon nanotubes within the carbon nanotube membrane contains the redox-active polymer film. The specifically selected polymer film can be reversibly switched electrochemically and therefore it controls both the direction and magnitude of electroosmotic flow through carbon nanotube membrane.

RECENT RESEARCHES

The procedure, which used DNA-encased, multi-walled carbon nanotubes (MWCNTs) to treat human prostate cancer tumors in mice, left only a small burn on the

skin that healed within days. The researchers envision using the particles not only to kill tumors through heating, but also to target cancer drugs to the diseased area in patients.

"The long-term goal in the project is to be able to use the DNA-encased MWCNTs in multi-modality fashion for a variety of types of tumors," Gmeiner said.

Carbon nanotubes are sub-microscopic particles that have been the subject of intense cancer research. The MWCNTs used in the current study consist of several nanotubes that "fit inside one another like Russian dolls," Gmeiner said. The MWCNTs are injected into a tumor and then heated with laser-generated near-infrared radiation. For this study, the tubes were injected into human prostate cancer tumors being grown in mice. The radiation causes the tubes to vibrate, creating heat. That heat kills the cancer cells near the nanotubes. If there are enough nanotubes, the amount of heat generated can kill whole tumors.

For this study, researchers used MWCNTs encased with DNA, which prevented them from bunching up in the tumor, allowing them to heat more efficiently at a lower level of radiation and leaving the surrounding tissue virtually unharmed.

With funding from the National Cancer Institute and the North Carolina Biotechnology Center, researchers grew 24 prostate cancer tumors in 12 mice. They then separated the mice into groups receiving treatment with DNA-encased MWCNTs and laser, laser only, non-DNA-encased MWCNTs only, or no treatment.

The eight tumors treated with a single injection of DNA-encased MWCNTs and zapped with a 70-second burst from a three-watt laser were gone within six days after treatment. While a minor surface burn appeared at the site of laser treatment, it healed within a few days with antibiotic ointment, Gmeiner said.

The tumors in the other treatment groups showed no distinguishable reduction.

Using the DNA-encased MWCNTs increased heat production two- to threefold – allowing researchers to use fewer nanotubes and a less powerful laser to kill tumors – an important consideration as scientists determine potential issues with the toxicity of nanotubes, since they remain in the body after treatment, Gmeiner said.

Current thermal ablation, or heat therapy, treatments for human tumors include radiofrequency ablation, which causes regional heating between two electrodes implanted in tissue but cannot be used to selectively distinguish cancer cells from healthy cells, like researchers hope they will be able to do with MWCNTs. In addition to the DNA-encased

MWCNTs used in this study, other nanomaterials, such as single-walled carbon nanotubes and gold nanoshells, are also currently undergoing experimental investigation as cancer therapies.

Before treatment with MWCNTs can be tested in humans, studies need to be done to test the toxicity and safety, looking to see if the treatment causes any changes to organs over time, as well as the pharmacology of the treatment, to see what happens to the nanotubes, which are synthetic materials, over time.

Carbon nanotubes, long, thin cylinders of carbon, were discovered in 1991 by S. Iijima. These are large macromolecules that are unique for their size, shape, and remarkable physical properties. They can be thought of as a sheet of graphite (a hexagonal lattice of carbon) rolled into a cylinder. These intriguing structures have sparked much excitement in the recent years and a large amount of research has been dedicated to their understanding. Currently, the physical properties are still being discovered and disputed. What makes it so difficult is that nanotubes have a very broad range of electronic, thermal, and structural properties that change depending on the different kinds of nanotube (defined by its diameter, length, and chirality, or twist). To make things more interesting, besides having a single cylindrical wall (SWNTs), nanotubes can have multiple walls (MWNTs)--cylinders inside the other cylinders.

Scientists involved in cancer research are showing a lot of interest in carbon nanotubes (CNTs) to be used in basically three cancer-fighting areas. CNTs are being developed as targeted delivery vehicles for anticancer drugs right into cancer cells - think of really, really tiny injection needles. They are also used as the therapeutic agent itself; there is research that shows that CNTs can act as nanoscale bombs that literally blow apart a cancer cell. A third area of application is using CNTs as imaging agents. Particularly single-walled CNTs (SWCNTs) are under active development for various biomedical applications. One of the issues in using CNTs for therapeutic applications is the question of how to get them to the desired place within the organism, say a tumor cell. Another significant problem in applying CNTs for biological applications is that the nanotubes do not stay suspended as discrete nanotubes in aqueous solutions. Coupling the CNT with biomolecules, such as proteins, is a good method for targeting specific sites but has the disadvantage of either reducing protein activity or CNT absorption or both. A novel

method demonstrates that it is possible to achieve complete retention of enzymatic activity of adsorbed proteins as well as retention of a substantial fraction of the near-infrared (NIR) absorption of SWCNTs.

Previous research already attempted to adsorb different proteins on single-walled carbon nanotubes. In one ("Structure and Function of Enzymes Adsorbed onto Single-Walled Carbon Nanotubes"), a solvent displacement method was used to adsorb two proteins. For one protein (soybean peroxidase), only 28% of the native enzyme activity was retained. For the other protein (alpha-chymotrypsin), no greater than 1% of the enzyme activity was retained. In another ("Selectivity of water-soluble proteins in single-walled carbon nanotube dispersions"), nanotubes and protein were sonicated in aqueous solution, which resulted in temperatures up to 60-70°C. The nanotubes could not be dispersed for two of the proteins (papain and pepsin). For the other two proteins (lysozyme and albumin), the nanotubes could be dispersed, but there was a significant change in the structure of both proteins after adsorption, as measured by circular dichroism.

Nanotechnology may help revolutionize medicine in the future with its promise to play a role in selective cancer therapy. City of Hope researchers hope to boost the brain's own immune response against tumors by delivering cancer-fighting agents via nanotubes. A nanotube is about 50,000 times narrower than a human hair, but its length can extend up to several centimeters.

The Nano and Micro Systems Group at JPL, which has been researching nanotubes since about 2000, creates these tiny, cylindrical multi-walled carbon tubes for City of Hope. City of Hope researchers, who began their quest in 2006, found good results: The nanotubes, which they used on mice, were non-toxic in brain cells, did not change cell reproduction and were capable of carrying DNA and siRNA, two types of molecules that encode genetic information.

Carbon nanotubes are extremely strong, flexible, heat-resistant, and have very sharp tips. Consequently, JPL uses nanotubes as field-emission cathodes -- vehicles that help produce electrons -- for various space applications such as x-ray and mass spectroscopy instruments, vacuum microelectronics and high-frequency communications.

"Nanotubes are important for miniaturizing spectroscopic instruments for space applications, developing extreme environment electronics, as well as for remote sensing,"

said Harish Manohara, the technical group supervisor for JPL's Nano and Micro Systems Group.

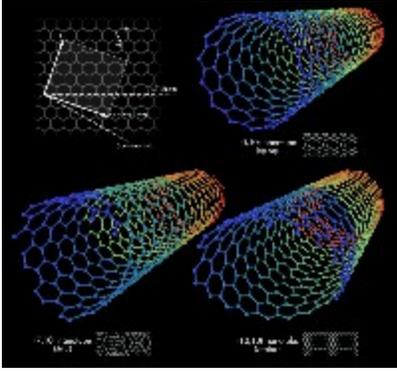
A team led by U-M chemical engineering professor Walter J. Weber Jr. tagged multi-walled carbon nanotubes—one of the most promising nanomaterials developed to date—with the carbon-14 radioactive isotope, which enabled the nanotubes to be tracked and quantified as they were absorbed into living cells. Researchers used cancer cells called HeLa cells, and also measured nanotube uptake in an earthworm and an aquatic type of worm.

In tagging the nanotubes with the isotope, researchers found that about 74 percent of the nanotubes added to a culture of cancer cells were assimilated by the cells after 15 minutes, and 89 percent of nanotubes assimilated after six hours, according to the paper. And the uptake was nearly irreversible, with only about 0.5 percent of the nanotubes releases from the cell after 12 hours.

More importantly, carbon nanotubes are able to deliver the drug to a specific cancer cell type and avoid other cells. In an earlier issue of Nature Nanotechnology, Liu et al. tested the biodistribution of carbon nanotubes in mice and demonstrated that carbon nanotubes are able to efficiently target tumors.

SmartBombingTumors

First, Liu and collaborators attach a tumor cell-specific peptide to the carbon nanotube. This peptide then guides the nanotube to a tumor cell. The cell then swallows the nanotube, loaded with doxorubicin, and dies. Dai explains the phenomenon by hypothesizing that the tumor cell membranes are permeable to the designed amphiphilic carbon nanotubes. Although the structure of the nanotube itself is hydrophobic, hydrophilic groups decorating the macromolecule create an overall amphiphilic nature which allows for passage through a cell membrane. However, the detailed molecular mechanisms remain unknown. 



3-D simulation of (top) tumor-binding peptide-poly(ethylene glycol)-functionalized carbon nanotube loaded with (right) cancer drug doxorubicin.

GoodCarriersbyDesign

Liu excitedly recounts the group's reaction when they discovered that carbon nanotubes could enter living cells: "You could imagine how many things you can do in the cells with carbon nanotubes." Nanotubes provide ideal surfaces for interacting with many cancer therapy drugs because the nanotubes' electron structure is able to form non-covalent bonds to the aromatic groups that characterize many of these drugs. Additionally, single-walled carbon nanotubes are estimated to have ultrahigh surface areas up to 2600 m²/g. This feature confers upon carbon nanotubes the ability to load drugs in large quantities.

SafetyConcerns

Despite promising research, there are potential caveats associated with carbon nanotube-mediated drug delivery such as the nanotubes' potential toxicity and possible negative effects on human organs. Nanotubes are very stable molecules and are therefore likely to persist in the body after initial treatment. Experiments in living cells and mice have shown that there is no apparent toxic effect in the short term. A latest study in collaboration with Stanford Medical School revealed that carbon nanotubes were safe in mice for up to six months.

However, whether there are longer-term effects and whether nanotubes can be used in humans are still unknown. Liu and collaborators have observed high levels of carbon nanotubes in the mouse reticuloendothelial system (RES), which includes the liver and spleen, implying that the nanotubes may be accumulating in these areas. Their latest experiments suggest that nanotubes trapped in these organs would be slowly excreted from mice within a few months (unpublished work). However, even if the nanotubes themselves

are safe, chemotherapy drugs carried into RES organs by nanotubes may still have toxic effects.

SmallTubes,BigPotential

In addition to toxicity studies, the Stanford researchers have also been working on getting nanotubes to carry small interference RNAs (siRNAs), proteins and plasmids into living cells. Early experiments have shown that carbon nanotubes can achieve a higher success rate in penetrating living cells and lower toxicity as compared to traditional liposome-mediated methods. This success could lead to new alternatives in RNAi for biomedical research and possible solutions in gene therapy.

“You can attach a combination of drugs or peptides on the nanotube surface,” Liu further stressed, “which could create a higher order of specificity and effects in cancer therapy.” Liu is confident that they can “also target nanotubes to specific organs or tissues if there exists signal ligands for specific targeting.” This would open other avenues for nanotube-mediated drug delivery.

Due to their ability to non-covalently interact with a wide range of important molecules, carbon nanotubes are unique and exciting among nanomaterials. By loading cancer drugs onto carbon nanotubes and delivering them to tumors, the work done by Dai and other researchers at Stanford opens up a new door to in vivo cancer therapy. While we may have to wait a little longer for carbon nanotubes to enter clinical applications, nanotube biotechnology will undoubtedly aid our understandings of the life sciences and provide new approaches in chemistry, biology and medicine.

CONCLUSION

Carbon nanotubes have remarkable electronic and mechanical properties and have been shown to exhibit very interesting mesoscopic phenomena. We study electronic transport across individual single-wall carbon nanotubes

Carbon nanotubes are molecular-scale tubes of graphitic carbon with outstanding properties. They are among the stiffest and strongest fibres known, and have remarkable electronic properties and many other unique characteristics. For these reasons they have attracted huge academic and industrial interest, with thousands of papers on nanotubes

being published every year. Commercial applications have been rather slow to develop, however, primarily because of the high production costs of the best quality nanotubes.

Big markets, apart from materials, in which nanotubes may make an impact, include flat panel displays (near-term commercialization is promised here), lighting, fuel cells and electronics. This last is one of the most talked-about areas but one of the farthest from commercialization, with one exception, this being the promise of huge computer memories (more than a thousand times greater in capacity than what you probably have in your machine now) that could, in theory, put a lot of the \$40 billion magnetic disk industry out of business. Companies like to make grand claims, however, and in this area there is not just the technological hurdle to face but the even more daunting economic one, a challenge made harder by a host of competing technologies.

Despite an inevitable element of hype, the versatility of nanotubes does suggest that they might one day rank as one of the most important materials ever discovered. In years to come they could find their way into myriad materials and devices around us and quite probably make some of the leaders in this game quite rich.

REFERENCES

Yildirim, T.; *et al.* (2000). "Pressure-induced interlinking of carbon nanotubes". *Physical Review B* 62: 19.

Monthieux, Marc; Kuznetsov, Vladimir L. (2006). "Who should be given the credit for the discovery of carbon nanotubes?". *Carbon* 44. Retrieved on 2007-07-26.

[<http://carbon.phys.msu.ru/publications/1952-radushkevich-lukyanovich.pdf>

Radushkevich-Lukyanovich (1952) in russian

Oberlin, A.; M. Endo, and T. Koyama, J. Cryst. Growth (March 1976). "Filamentous growth of carbon through benzene decomposition" 32: 335 - 349. Retrieved on 2007-07-28.

Endo, Morinobu & Dresselhaus, M. S. (October 26, 2002),

<<http://web.mit.edu/tinytech/Nanostructures/Spring2003/MDresselhaus/i789.pdf>>.

Retrieved on July 26, 2007

Izvestiya Akademii Nauk SSSR, Metals. 1982, #3, p.12-17 [in Russian]

US patent 4663230, "Carbon fibrils, method for producing same and compositions containing same", granted 1987-05-05

Iijima, Sumio (1991). "Helical microtubules of graphitic carbon". *Nature* 354: 56 - 58.

Bethune, D. S.; et al. (17 June 1993). "Cobalt-catalysed growth of carbon nanotubes with single-atomic-layer walls". *Nature* 363: 605–607. DOI:10.1038/363605a0.

Iijima, Sumio (1993). "Single-shell carbon nanotubes of 1-nm diameter". *Nature* 363: 603 - 605.

The Discovery of Single-Wall Carbon Nanotubes at IBM. IBM. Retrieved on 2007-07-26.

Krättschmer, W. (1990). "Solid C60: a new form of carbon". *Nature* 347: 354 - 358.

Kroto, H. W. (1985). "C60: Buckminsterfullerene". *Nature* 318: 162 - 163.

Dekker, Cees (May 1999). "Carbon nanotubes as molecular quantum wires". *Physics Today* 52 (5): 22 - 28. Retrieved on 2007-07-28.

Martel, R.; V. Derycke, C. Lavoie, J. Appenzeller, K. K. Chan, J. Tersoff, and Ph. Avouris (December 2001). "Ambipolar Electrical Transport in Semiconducting Single-Wall Carbon Nanotubes". *Physical Review Letters* 87 (25). Retrieved on 2007-07-28.

Collins, Philip G.; Phaedon Avouris (December 2000). "Nanotubes for Electronics". *Scientific American*: 67, 68, and 69.

Carbon Solutions, Inc.. Retrieved on 2007-07-28.

CarboLex. Retrieved on 2007-07-28.

Flahaut, E.; Bacsá R, Peigney A, Laurent C. (2003). "Gram-Scale CCVD Synthesis of Double-Walled Carbon Nanotubes". *Chemical Communications* 12: 1442 - 1443. Retrieved on 2007-07-28.

Liu, Lei; Guo, G. Y.; Jayanthi, C. S.; and Wudate, S. Y. (2002). "Colossal Paramagnetic Moments in Metallic Carbon Nanotubes". *Physical Review Letters* 88 (21). Retrieved on 2007-07-28.

Huhtala, Maria; Kuronen, Antti; Kaski, Kimmo (2002). "Carbon nanotube structures: molecular dynamics simulation at realistic limit". *Computer Physics Communications* 146. Retrieved on 2007-07-28.

Yu, Min-Feng (2000). "Strength and Breaking Mechanism of Multiwalled Carbon Nanotubes Under Tensile Load". *Science* 287: 637 - 640.

(2002) *Science and Application of Nanotubes (chapter: Electronic and Mechanical Properties of Carbon Nanotubes)*. Springer US, 297 - 320. ISBN 978-0-306-47098-1.

Qian, Dong; Gregory J Wagner; Wing Kam Liu; Min-Feng Yu; Rodney S Ruoff (November 2002). "Mechanics of carbon nanotubes". *Applied Mechanics Reviews* 55 (6): 495 - 533.

Easy Slider, Science Magazine, July 28, 2000. Retrieved on 2007-07-30.

Curnings, John (2000). "Low-Friction Nanoscale Linear Bearing Realized from Multiwall Carbon Nanotubes". *Science* 289: 602 - 604.

Fennimore, A. M. (2003). "Rotational actuators based on carbon nanotubes". *Nature* 424: 408 - 410.

Curnings, John (2004). "Localization and Nonlinear Resistance in Telescopically Extended Nanotubes". *Physical Review Letters* 93.

Curnings, John (2002). "Nanotubes in the Fast Lane". *Physical Review Letters* 88.

Sammalkorpi, M. (2004). "Mechanical properties of carbon nanotubes with vacancies and related defects". *Physical Review B* 70.

Resselhaus, M.S.. "Carbon nanotubes", Jan 1, 1998.

Harris, Peter J.F. (1999). *Carbon Nanotubes and Related Structures*. Cambridge, UK: Cambridge University Press.

Inman, Mason. "Legendary Swords' Sharpness, Strength From Nanotubes, Study Says", National Geographic, November 16, 2006. Retrieved on 2007-05-26.

"Secret's out for Saracen sabres", NewScientistTech, November 15, 2006.

Iijima, Sumio (1991). "Helical microtubules of graphitic carbon". *Nature* 354: 56 - 58.

Ebbesen, T. W.; Ajayan, P. M. (1992). "Large-scale synthesis of carbon nanotubes". *Nature* 358: 220 - 222.

Guo, Ting (1995). "Self-Assembly of Tubular Fullerenes". *J. Phys. Chem.* 99: 10694 - 10697.

Guo, Ting (1995). "Catalytic growth of single-walled nanotubes by laser vaporization". *Chem. Phys. Lett.* 243: 49 - 54.

Walker Jr., P. L. (1959). "Carbon Formation from Carbon Monoxide-Hydrogen Mixtures over Iron Catalysts.I. Properties of Carbon Formed". *J. Phys. Chem.* 63: 133.

José-Yacamán, M. (1993). "Catalytic growth of carbon microtubules with fullerene structure". *Appl. Phys. Lett.* 62: 657.

Beckman, Wendy. "UC Researchers Shatter World Records with Length of Carbon Nanotube Arrays", University of Cincinnati, April 27, 2007.

Eftekhari, A.; Jafarkhani, Parvaneh; Moztafzadeh, Fathollah (2006). "High-yield synthesis of carbon nanotubes using a water-soluble catalyst support in catalytic chemical vapor deposition". *Carbon* 44: 1343.

Ren, Z. F. (1998). "Synthesis of Large Arrays of Well-Aligned Carbon Nanotubes on Glass". *Science* 282: 1105.

Carbon Nanotubes from Camphor: An Environment-Friendly Nanotechnology. *Journal of Physics*. Retrieved on 2007-08-15.

Boyd, Jade. "Rice chemists create, grow nanotube seeds", Rice University, November 17, 2006.

Singer, J.M.; Grumer, J. (1959). "Carbon formation in very rich hydrocarbon-air flames. I. Studies of chemical content, temperature, ionization and particulate matter". *Seventh Symposium (International) on Combustion*.

Yuan, Liming; Kozo Saito, Chunxu Pan, F.A. Williams, and A.S. Gordon (2001). "Nanotubes from methane flames". *Chemical physics letters* 340: 237–241. DOI: 10.1016/S0009-2614(01)00435-3.

Yuan, Liming; Kozo Saito, Wenchong Hu, and Zhi Chen (2001). "Ethylene flame synthesis of well-aligned multi-walled carbon nanotubes". *Chemical physics letters* 346: 23–28. DOI:10.1016/S0009-2614(01)00959-9.

Duan, H. M.; and J. T. McKinnon (1994). "Nanoclusters Produced in Flames". *Journal of Physical Chemistry* 98 (49): 12815–12818. DOI:10.1021/j100100a001.

Murr, L. E.; J.J. Bang, E.V. Esquivel, P.A. Guerrero, and D.A. Lopez (2004). "Carbon nanotubes, nanocrystal forms, and complex nanoparticle aggregates in common fuel-gas combustion sources and the ambient air". *Journal of Nanoparticle Research* 6: 241–251. DOI:10.1023/B:NANO.0000034651.91325.40.

Vander Wal, R.L. (2002). "Fe-catalyzed single-walled carbon nanotube synthesis within a flame environment". *Combust. Flame* 130: 37 - 47.

Saveliev, A.V.; Merchan-Merchan, W.; Kennedy, L.A. (2003). "Metal catalyzed synthesis of carbon nanostructures in an opposed flow methane oxygen flame". *Combust. Flame* 135: 27 - 33.

Height, M.J.; Howard, J.B.; Tester, J.W.; Vander Sande, J.B. (2004). "Flame synthesis of single-walled carbon nanotubes". *Carbon* 42: 2295 - 2307.

Sen, S.; Puri, I.K. (2004). "Flame synthesis of carbon nanofibres and nanofibre composites containing encapsulated metal particles". *Nanotechnology* 15: 264 - 268.

Yu, Min-Feng (2000). "Strength and Breaking Mechanism of Multiwalled Carbon Nanotubes Under Tensile Load". *Science* 287: 637 - 640.

Inman, Mason. "Legendary Swords' Sharpness, Strength From Nanotubes, Study Says", National Geographic News, November 16, 2006.

"Secret's out for Saracen sabres", New Scientist, November 15, 2006.

Edwards, Brad C. (November 2003). *The Space Elevator*. BC Edwards. ISBN 0974651710.

Zhang, Mei (2005). "Strong, Transparent, Multifunctional, Carbon Nanotube Sheets". *Science* 309 (5738): 1215 -1219.

Dalton, Alan B. (2003). "Super-tough carbon-nanotube fibres". *Nature* 423 (6941): 703.

Kanellos, Michael. "Carbon nanotubes enter Tour de France", CNET News, July 7, 2006.

Postma, Henk W. Ch.; Teepen, Tijs; Yao, Zhen; Grifoni, Milena; Dekker, Cees (2001). "Carbon Nanotube Single-Electron Transistors at Room Temperature". *Science* 293 (5527).

Collins, Philip G.; Arnold, Michael S.; Avouris, Phaedon (April 27, 2001). "Engineering Carbon Nanotubes and Nanotube Circuits Using Electrical Breakdown". *Science* 292 (5517): 706 - 709.

Song, Jin; Dongmok, Whang; McAlpine, Michael C.; Friedman, Robin S.; Yue, Wu; Lieber, Charles M. (2004). "Scalable Interconnection and Integration of Nanowire Devices Without Registration". *Nano Letters* 4 (5): 915 - 919.

Tesng, Yu-Chih (2004). "Monolithic Integration of Carbon Nanotube Devices with Silicon MOS Technology". *Nano Letters* 4 (1): 123 - 127.

Singh, Ravi (2005). "Binding and condensation of plasmid DNA onto functionalized carbon nanotubes : Toward the construction of nanotube-based gene delivery vectors". *J. Am. Chem. Soc.* 127 (12): 4388 - 4396.

Simmons, Trevor (2007). "Large Area-Aligned Arrays from Direct Deposition of Single-Wall Carbon Nanotubes". *J. Am. Chem. Soc.*