

CARBON NANOTUBES FOR MEDICAL APPLICATIONS

[A.R. Harutyunyan](#)¹, B.K. Pradhan¹, G.U. Sumanasekera¹, [E.Yu. Korobko](#)²,
[A.A. Kuznetsov](#)³

¹ Dept. of Physics, The Pennsylvania State University, University Park, PA 16802, USA

² Dept. of Pharmacy, People Friendship University of Russia, Moscow, 117513 Russia

³ Institute of Biochemical Physics RAS, Moscow V-334, 117977, Russia

INTRODUCTION: Recent discoveries of various forms of carbon nanostructures have stimulated research on their applications in diverse fields. They hold promise for applications in medicine, drug and gene delivery areas [1]. For instance, carbon nanotubes have the potential to carry drugs in the organism as they are hollow and much smaller than the blood cells. The methods were developed for attaching DNA and protein molecules to the inside and outside of the nanotubes. This gives one the ability to target and destroy individual cells that may be cancerous or infected by a virus. Nanotubes with attached enzymes might, in the long term, be used as enzymatic biosensors that could simultaneously detect and measure a variety of biological molecules [2]. Carbon nanotubes arrays can play a key role in the artificial cochlea development (JPL in Pasadena, CA). It has been established that growing of the carbon nanotubes requires use of small metal catalyst particles (~5-100 nm). Usually 3d metals (Fe, Co, Ni) or their combinations with other metals are very effective as catalysts. Carbon nanofibers/nanotubes grow through or from the surface of such metal catalyst particles. A combination of carbon nanotubes and the magnetic, metal catalyst particles may allow one using carbon nanofibers/nanotubes for the magnetically guided drug delivery purposes.

A successful application of such a nanotube-magnetic particle combination depends significantly on the physical, chemical and biological properties of the material. The particles must be biologically inert and biodegradable, they must have high sorption capacity, the sorption selectivity must be adjustable, convenient binding with antibodies must be possible, and high magnetization and magnetic susceptibility in the relatively weak magnetic fields should also be achievable (particularly if such particles are designed for the guided drug delivery). Iron particles with combination of different carbon nanostructures meet all these requirements. Therefore, they are likely candidates for medical applications. Proposed medical applications of the carbon nanotubes require pure nanotube material. However, it has been established that beside nanotubes, the reaction product contains a mixture of different carbon forms, such as

amorphous carbon (which covers the nanotubes), multi-shell carbon, as well as metal catalyst residues. The impurities affect the properties of the carbon nanotube reaction product and make its application problematic. Therefore, a controlled synthesis of different kinds of carbon nanofibers/nanotubes, their purification and the property modification became a very important object of materials research investigations.

The growing interest in basic research on carbon nanotubes and in their applications require new, flexible approaches to their synthesis. Many researchers consider chemical vapor decomposition (CVD) method as the only viable approach to a controlled, large-scale production of carbon nanotubes, and in particular, the single wall nanotubes. In this work we present CVD synthesis of different forms of carbon nanofibers and nanotubes, their purification and modification by filling the nanotubes with different metals and large molecules like the fullerene (a "peapod" structure). Also we discuss problems that can become a serious barrier to the nanotubes applications.

METHODS: The catalyst powders for synthesis of carbon nanofibers (CNFs) were prepared by the conversion of metal carbonates to oxides with further reduction of pure metal particles. The precipitate of the metal carbonates was obtained from the solution of calculated amounts of analytical-grade reagents in the form of respective metal nitrates, using ammonium bicarbonate. After drying in the oven at 105-110°C for 24 hours, the precipitate was sintered in the air for 4 hours at a 400°C to convert the carbonate to oxides. The apparatus used in this work consisted of a quartz flow reactor (38 mm i.d. and 90 cm long) located in a horizontal tube furnace. After reduction of catalyst (Fe) powders in a 10% H₂/He gas at 500°C, the temperature was raised to 600°C and carbon fibers were grown by passing a mixture of C₂H₄ and H₂ gases over the catalysts for 90 min.

In the case of growing single wall carbon nanotubes (SWNTs), the aluminum oxide-supported iron catalyst particles were prepared by adding iron nitrite aqueous solution into methanol solution containing ~2 μm diameter Al₂O₃ particles. After reduction of the aluminum oxide-supported Fe ox-

ide catalyst in the H₂ gas at 500°C, the gas was replaced by argon and the temperature was raised to the nanotube growth temperature. SWNTs were grown by passing a mixture of CH₄ diluted in Ar over the catalyst at a temperature in the range 700-900°C for ~60 min. The reactor was then allowed to cool to room temperature with the Ar gas flowing

The “peapod” structures were prepared by a diffusion of C₆₀ molecules inside the preliminary purified SWNTs with opened ends at 420° C in an evacuated (10⁻⁶ Torr) and sealed glass ampoule. SWNTs were first subjected to selective oxidation to remove amorphous carbon, which covers the SWNTs and the metal catalyst particles, followed by refluxing of nitric acid, which digests the residual metal and opens the tube ends; it also creates defects or a hole on the sidewall of SWNTs. With the opening of the nanotube ends, and the creation of the hole in the nanotube wall, the internal pore or channel is accessible to foreign materials such as C₆₀.

The inclusion of iron oxide nanoparticles into template-synthesized carbon nanotubes was also possible when MOCVD (metal organic chemical vapor deposition) technique was employed. A carbon-deposited film was subjected to MOCVD of ferrocene Fe(C₅H₅)₂ in the following manner.

Ferrocene was vaporized at 90 °C (corresponding to the vapor pressure of 0.1 kPa) and the vapor was introduced into the film in the quartz reactor with H₂ gas (50% in N₂) at a total flow rate of 100 cm³ (STP)/min. The feed line was wrapped with heating tapes and maintained at a high temperature (150°C) to avoid the condensation of ferrocene vapor. In order to prepare Ni/carbon nanocomposites, metal-organic chemical vapor deposition (MOCVD) of nickelocene Ni(C₅H₅)₂ was employed in the following manner. Nickelocene was vaporized at 105 °C (corresponding to the vapor pressure of 0.6 kPa) and the film was exposed to the vapor with H₂ gas (50% in N₂) at a total flow rate of 100 cm³ (STP)/min at 275 °C for 0.25 or 1 h. After the metal loading, the films were treated with 10 M NaOH solution at 150 °C in an autoclave for 6 h to dissolve the anodic aluminum oxide. Metal/carbon nanotube composites were obtained as an insoluble fraction.

RESULTS & DISCUSSION: From the first derivative of the temperature programmed oxidation (TPO) profile (50-100°C, rate 3°C/min, under dry air), the preferential oxidation temperatures of the different phases of carbon in the sample were determined. Existence of a more than one peak is connected with the inhomogeneity of the sample

(with amorphous carbon and different morphologies of carbon fibers present); this was also correlated with the microscopic measurement results. The mild HCl acid treatment and selective oxidation were carried out to remove the catalyst particles not connected with fibers and the undesirable carbon structures. The DTPO profile after post synthesis treatment showed mainly one peak, which we associate with certain carbon structure. In Fig. 1a the TEM image of the “herringbone” fiber is shown after post synthesis treatments. TEM studies have shown that after selective oxidation, the amorphous carbon phases are removed from carbon nanofibers, and as a result, the BET surface area increases (for given sample from 170 to 580 g/m²). The studies of the BET surface area modification showed that by changing the synthesis conditions (H₂/C₂H₄ ratio) and the subsequent oxidation procedure, it is possible to control pore size distribution and to achieve a relatively high surface area of ~ 800g/m². By changing the catalyst particle size (from 20-150nm) and its composition (e.g. Fe/Ni with different ratio), we were able to synthesize different morphologies of carbon nanofibers (“tubular”, “spiral”, “platelet”) with modified magnetic properties (H_c~120-300G and M_s~20-30 emu/g). The resulting GNFs have a potential for applications as magnetic adsorbents.

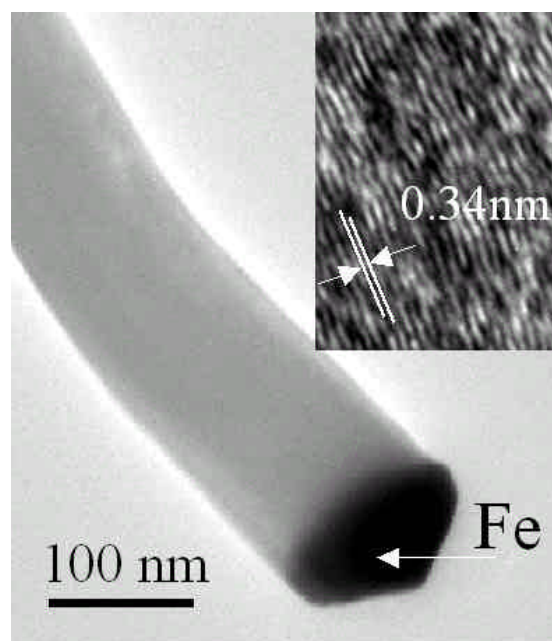


Fig 1: TEM images of carbon nanofiber.

TEM studies of raw samples showed that the SWNTs are a minority constituent in the reaction product. Also present, for example, was amorphous carbon, which coated the bundle walls, the residual metal catalyst, and the multi-shell sp² carbon, which covered the metal catalyst residue. The images of SWNTs bundles exhibit an average bun-

dle diameter of 10 nm; also, many individual SWNTs with average diameter of ~1.5nm were observed. Further application of SWNTs in medicine requires purification of the reaction product. Aluminum oxide powders were removed after HF acid treatment of the raw sample. Initial selective oxidation to remove amorphous carbon, followed by a reflux in HNO₃ acid to remove the metal catalyst (Fe) particles, was conducted. In Fig. 2 the TEM image of the SWNTs after purification is shown.

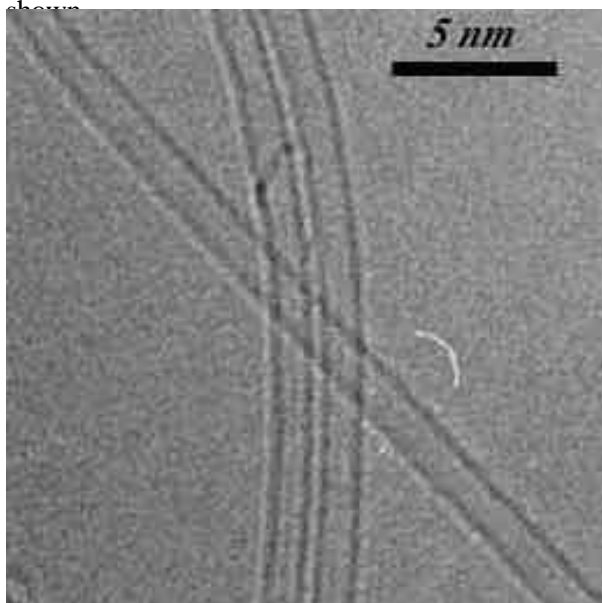


Fig. 2: TEM image of purified SWNTs.

It is important to mention that the refluxing in HNO₃ acid can induce wall damage in the tubes, which changes the electronic structure of the SWNT; this, in turn, can affect the binding energy and can limit the proposed applications in the medicine. Also, as a result of the purification procedure, most of the Fe particles were removed (<0.2wt%), which made it impossible to use these tubes for the magnetically guided drug delivery. Moreover, one must consider the potential interaction of the purified SWNTs with certain gases and chemical species, which adds additional limitations on their medical applications. Electrical and thermal transport studies reveal that the raw SWNTs are extrinsically p-type due to O₂ doping. By stripping O₂ molecules from the nanotube walls with high temperature degassing in vacuum, the nanotubes become n-type (as determined by thermoelectric power measurements) and considered to be intrinsic. The intrinsically n-type SWNTs show measurable, reversible changes in their transport properties when exposed to gases like He, N₂, and H₂. Gases like O₂, NH₃ induce irreversible changes implying charge transfer reactions leading to changes in electronic structure of the nanotubes. More interestingly, chemical vapors such as alcohol and aromatics in contact with nanotube walls

induce huge swings in transport/electronic properties and thus modify the binding energy.

TEM image of the “peapod” structure is shown in Fig. 3. As one can see, the C₆₀ molecules formed a chain inside the SWNTs.

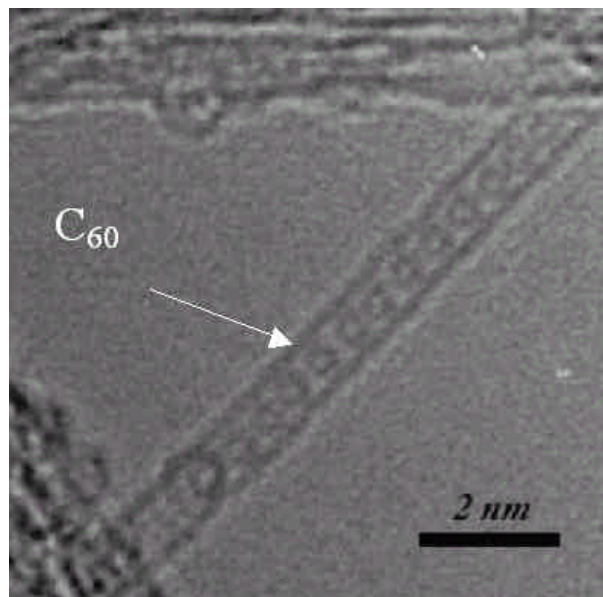


Fig. 3: TEM image of C₆₀@SWNT.

Therefore, it is possible to fill SWNTs with relatively large molecules, which may lead to applications of some specific properties of such molecules, in combination with SWNTs, to particular problems in medicine.

Figure 4a shows the TEM bright field image of the Fe/carbon tube composites prepared by the MOCVD at 400 °C for 3 h with 0.1 kPa ferrocene vapor. These images exhibit the presence of uniform carbon nanotubes with the outer diameter of 30 nm and the wall thickness of about 5 nm. Although some of the tubes are empty, the others contain many dark particles. It should be noted that there are no metal deposits on the outside wall of the nanotubes. The high magnification image shows that the shape of some particles looks like a cube, implying high crystallinity of these particles. Figure 4b shows a TEM bright field image of the nickel/carbon nanotube composite prepared by the MOCVD of nickelcene for 1 h. The image exhibits a carbon nanotube with a diameter of about 30 nm, containing a single nanowire of 500 nm in length and 4 nm in diameter. Energy dispersive X-ray spectrum taken from this nanowire confirms the presence of nickel element with no signal corresponding to oxygen. Silver, platinum and gold filling are also possible by an impregnation method.

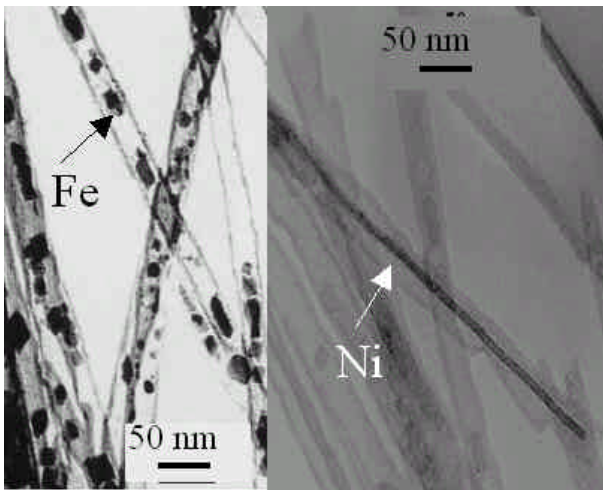


Fig. 4: TEM images of MWNTs filled with Fe (left) and Ni (right).

CONCLUSIONS: Carbon nanotubes (purified/modified) have a high potential of finding unique applications in wide areas of medicine. Also, the encapsulation of other materials in the carbon nanotubes would open up a possibility for their applications in medicine. There remains a number of fundamental issues that need to be resolved, however, such as homogeneity of the material that contains different nanostructures, wide distribution of the nanotube's diameters, presence of residual metals; separation of the individual nanotubes; and a sensitivity to the different gases and species. Also, purification of the nanotubes without inducing wall defects remains a challenging problem.

REFERENCES: ¹C. N. R. Rao and A. K. Cheetham (2001), *J. of Materials Chemistry*, **11**, 2887-94, ²M. Freemantle (1996) *Chem. & Eng. News*, **July 15**, 62-64.