LE NANOTECNOLOGIE PER BIOLOGIA E LA MEDICINA

S. Bellucci

NEXT Nanotechnology Laboratory

INFN-Laboratori Nazionali Frascati

MATINEES DELLA SCIENZA 25 Febbraio 2016

INFN
Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Frascati

The National Institute of Nuclear Physics (INFN - Istituto Nazionale di Fisica Nucleare) is an organization for research in nuclear physics. There are different divisions in Italy. The Frascati National Laboratories (LNF) is the largest and one of the most important ones. The research here is primarly concentrated on particle physics.

e-mail: bellucci@lnf.infn.it

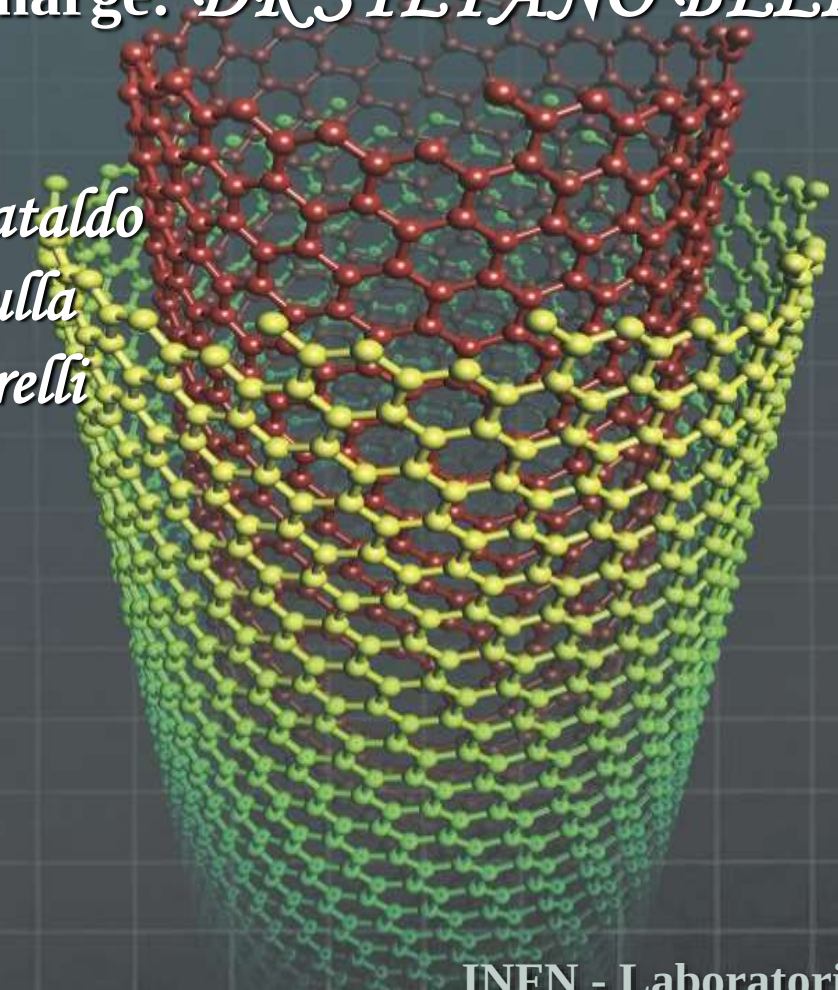
Laboratori Nazionali di Frascati

NEXT

Nano Technology Laboratories

NanoscienE eXperiments for Technology

Lab in charge: *DR STEFANO BELLUCCI*



Phd St. Antonino Cataldo

Ing. Federico Micciulla

Phd St. Silvia Bistarelli

Matteo Mastrucci

Roberto Baldini

e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati


Il MONDO della SCUOLA, della RICERCA e dell'IMPRESA insieme per l'INNOVAZIONE:
NANOSCIENZA E NANOTECNOLOGIA
I.T.I.S. "G.Galilei" di Arezzo, 11 e 12 marzo 2013

NEXT

NANOTECHNOLOGY LABORATORIES

NANOSCIENCE EXPERIMENTS FOR TECHNOLOGY

Activity 360° on NanoTechnology

"L' Inventore" delle nanotecnologie

Nel 1959 **Richard Feynman** (*Nobel '65, Fisica*), in un celebre discorso intitolato "There's Plenty of Room at the Bottom", di fatto diede inizio alla ricerca mondiale nel campo della nanoscienza.

Cosa sono le nanotecnologie?

Le nanotecnologie sono l'insieme di metodi e tecniche per la manipolazione della materia su scala atomica e molecolare e hanno l'obiettivo di costruire materiali e prodotti con speciali e superiori caratteristiche chimico-fisiche

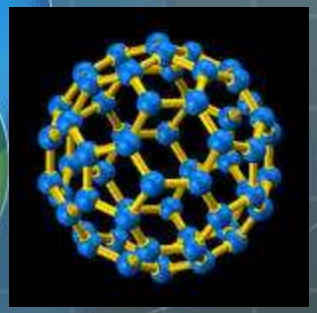
***TAPPE DELLA NANORICERCA*:**

1959: R. Feyman prevede la nascita della nanotecnologia
1974: Primo dispositivo elettronico molecolare brevettato (IBM)
1981: Invenzione del microscopia ad effetto tunnel (IBM-Zurigo)
1985: Scoperta dei fullereni
1988: La Dupont progetta la prima proteina artificiale
1989: D.M. Eigler (IBM) scrive il nome della sua azienda con 35 atomi di Xenon
1991: S. Iijima scopre i nanotubi di carbonio
1993: Nasce alla Rice University (USA) il primo laboratorio di Nanotecnologie

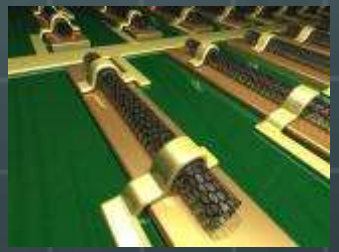
Nanotecnologia

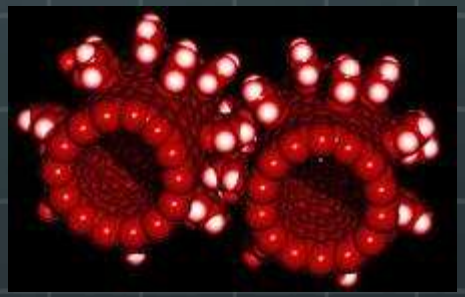
La Nanotecnologia e' la capacita' di realizzare oggetti e strutture con precisione atomica, letteralmente atomo per atomo.

Speculare alle capacita' delle cellule viventi, che fanno esattamente lo stesso, sebbene basandosi sull'evoluzione e non sulla progettazione.



Applicazioni se*mplici* involvono la creazione di nuovi e potenti materiali, diamanti perfetti in grandi quantitativi e strumenti per manipolare oggetti su qualsivoglia scala dimensionale.





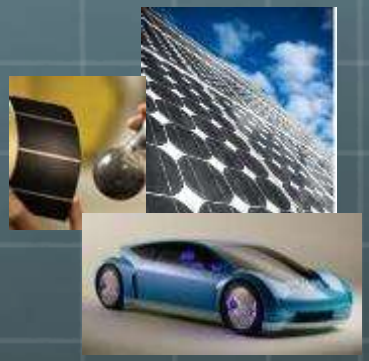
Applicazioni piu' *avanzate* involveranno nanocomputers massicciamente paralleli, auto-replicazione e nanodispositivi intelligenti, capaci di interagire col loro ambiente.

Nanotechnology

The science of manipulating matter at the atomic and molecular level to obtain materials with specifically enhanced chemical and physical properties.

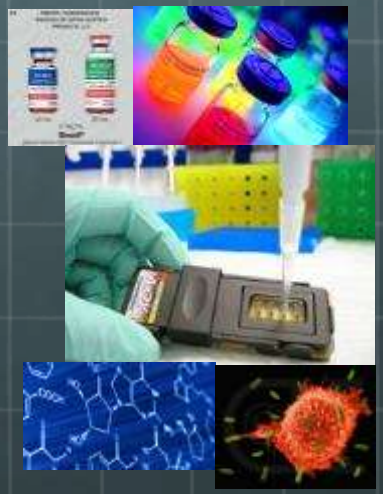
Information Technology

- Smaller, faster, more energy efficient and powerful computing and other IT-based systems



Energy

- More efficient and cost effective technologies for energy production
  - Solar cells
  - Fuel cells
  - Batteries
  - Bio fuels



Medicine

- Cancer treatment
- Bone treatment
- Drug delivery
- Appetite control
- Drug development
- Medical tools
- Diagnostic tests
- Imaging

Consumer Goods

- Foods and beverages
  - Advanced packaging materials, sensors, and lab-on-chips for food quality testing
- Appliances and textiles
  - Stain proof, water proof and wrinkle free textiles
- Household and cosmetics
  - Self-cleaning and scratch free products, paints, and better cosmetics

Le basi delle Nanotecnologie

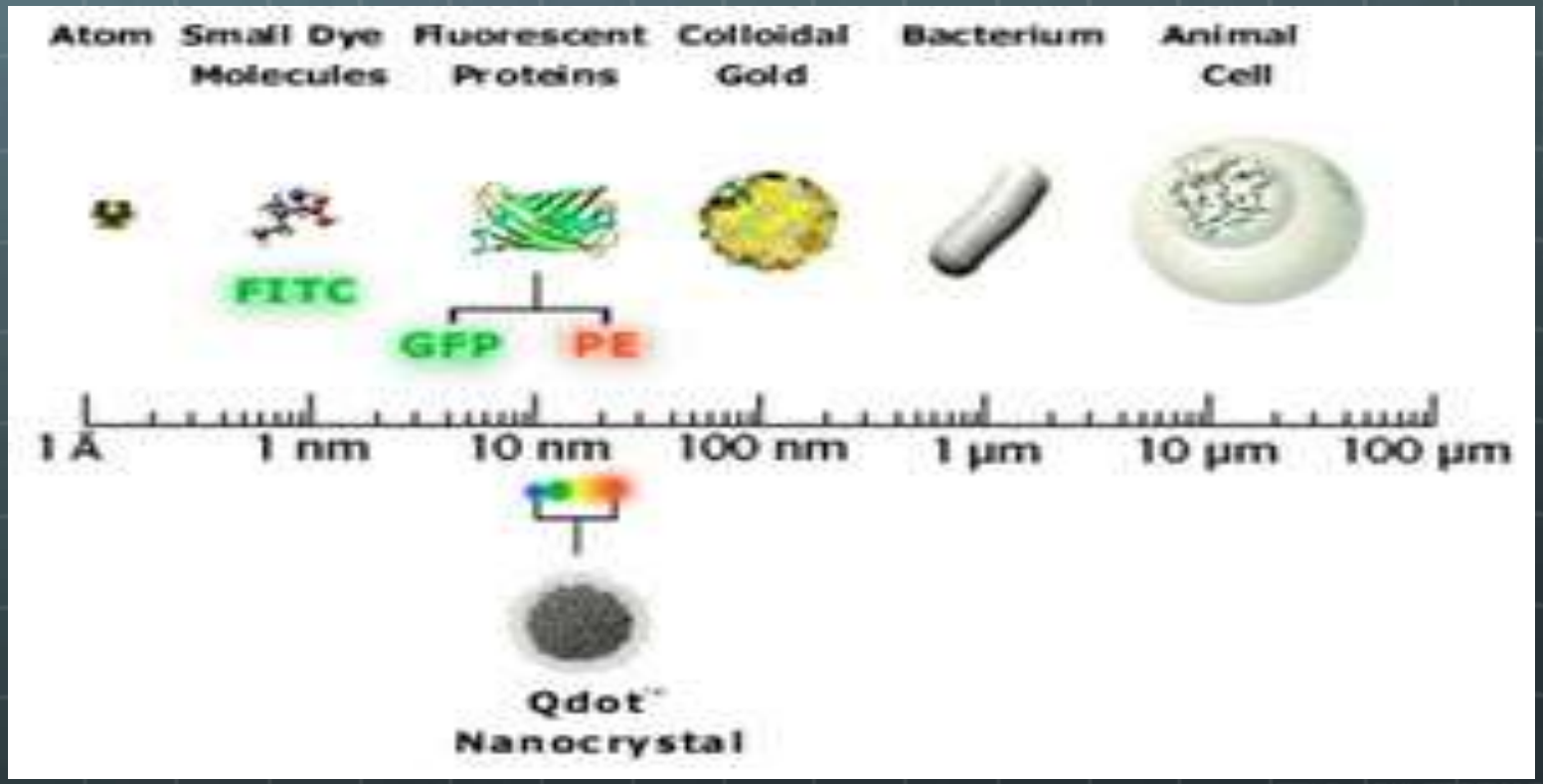
- Si lavora ai livelli atomico, molecolare, e sopramolecolare
- La scala delle lunghezze coinvolte è approssimativamente tra 1 e 100 nm
- Lo scopo è la creazione e l'utilizzo di materiali, dispositivi, sistemi dotati di proprietà e di funzioni fondamentalmente innovative, a causa della loro struttura piccolissima (nanoscopica).

e-mail: bellucci@lnf.infn.it

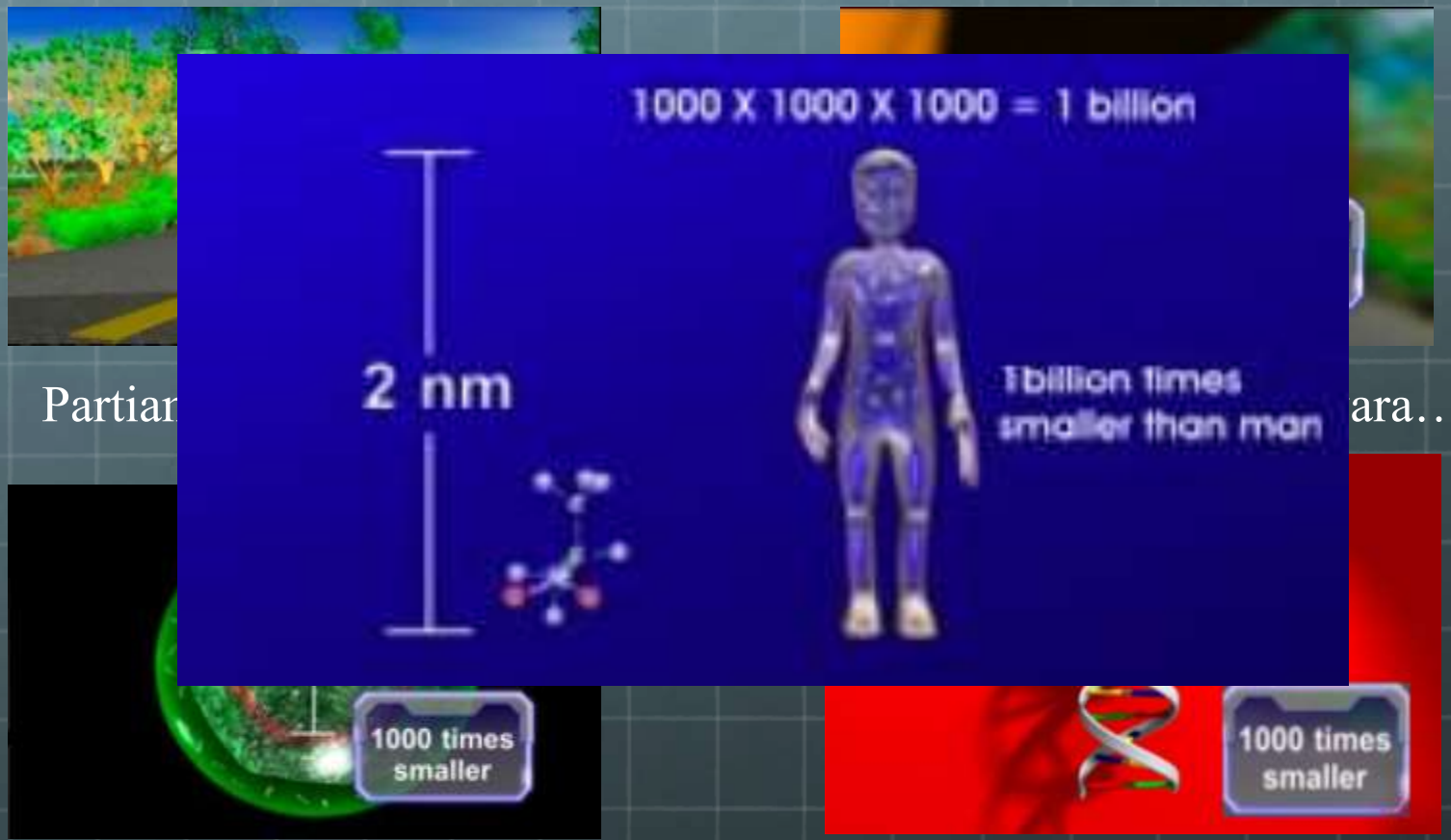
INFN - Laboratori Nazionali di Frascati

Scala nanoscopica

- Nanometro = 1 milionesimo di millimetro
- Un Nanometro è grande come uno strato 3-5 atomi



Nano? Capiamo le dimensioni…



Partiar… …ara…

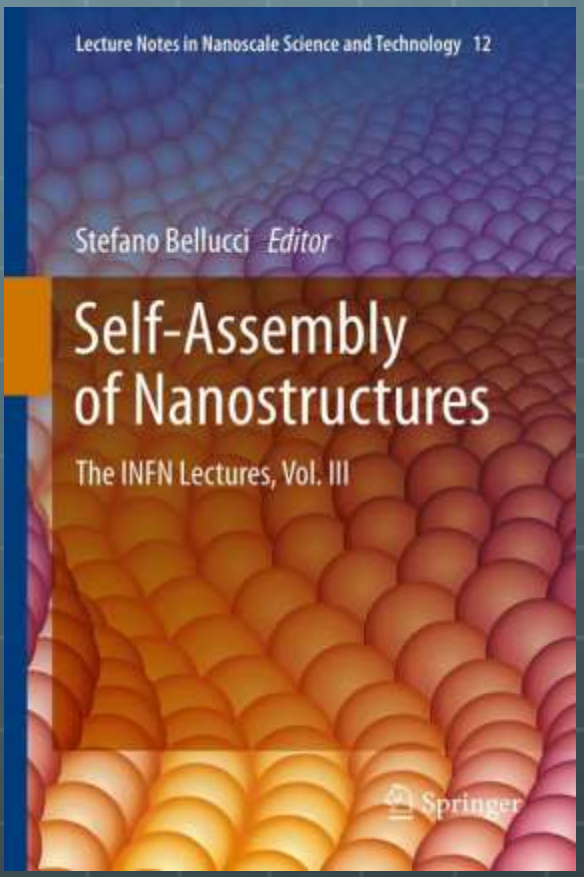
…arriviamo ai suoi occhi…

…e finalmente arriviamo al nanometro!!!

e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati

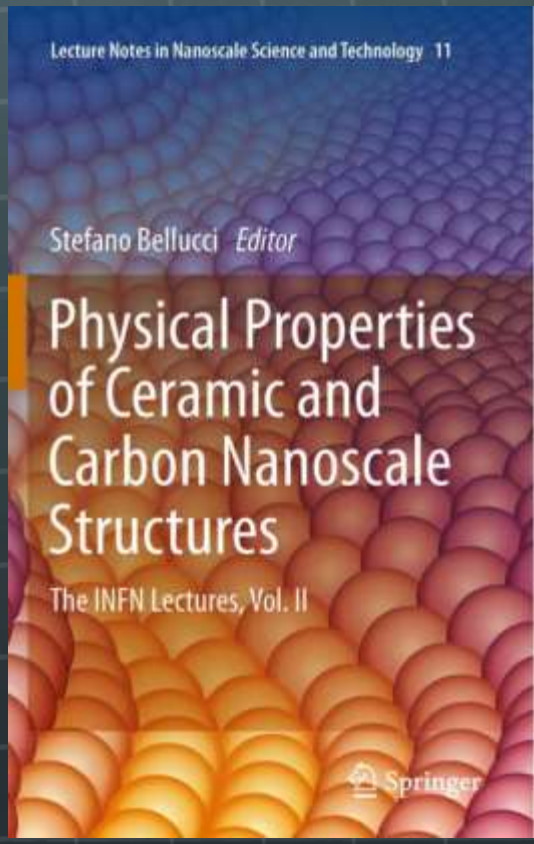
Approccio “Bottom-Up”



- Concetto introdotto da Eric Drexler
- Processo di costruire i sistemi atomo per atomo, allo scopo

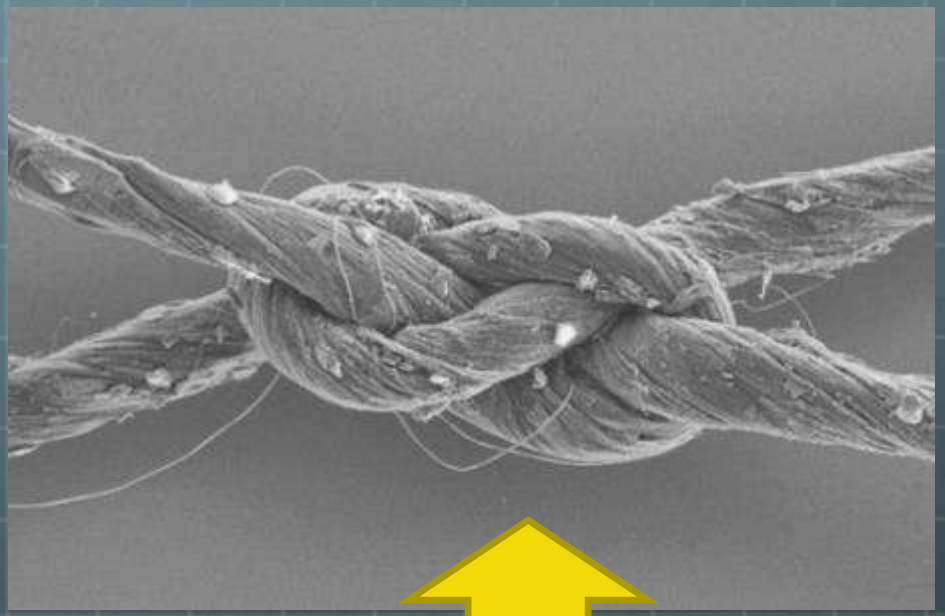
di minimizzare lo scarto

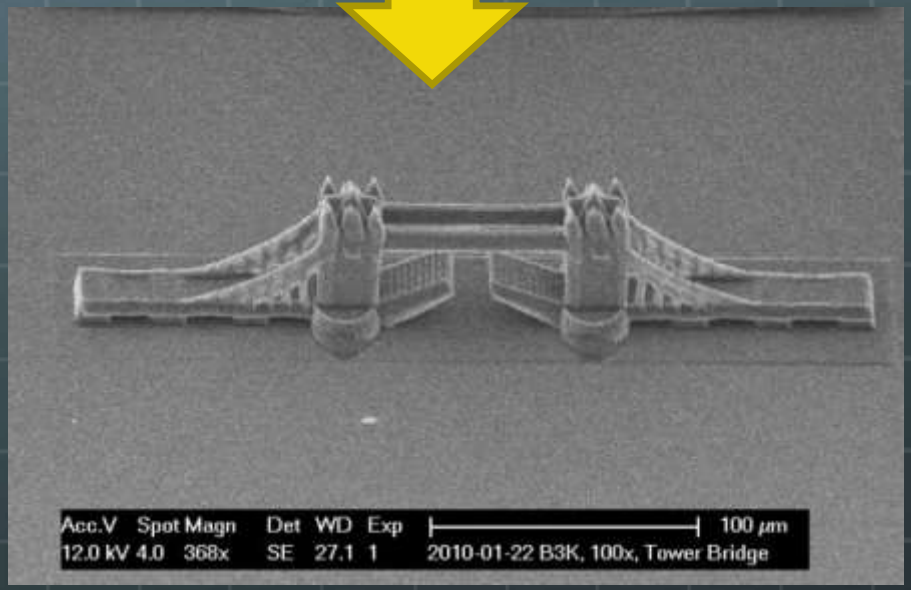
e aumentare la reattività



e-mail: bellucci@lnf.infn.it

"Top – Down Bottom- Up"





e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati

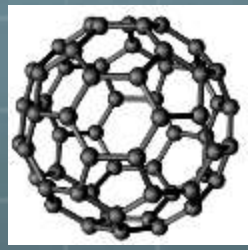
Usi delle Nanotecnologie

- Tecnologia pervasiva (oltre che abilitante)
- Usi delle Nanotecnologie sono presenti ovunque
- Energia solare, batterie, armi, progettazione e manufattura di strumentazione… in qualsivoglia area applicativa, le nano- tecnologie potrebbero avere un ruolo nel futuro
- Data la molteplicità dei loro usi, dobbiamo necessariamente interessarci del loro impatto sull'ambiente e sulla salute umana, in particolare dei soggetti professionalmente esposti

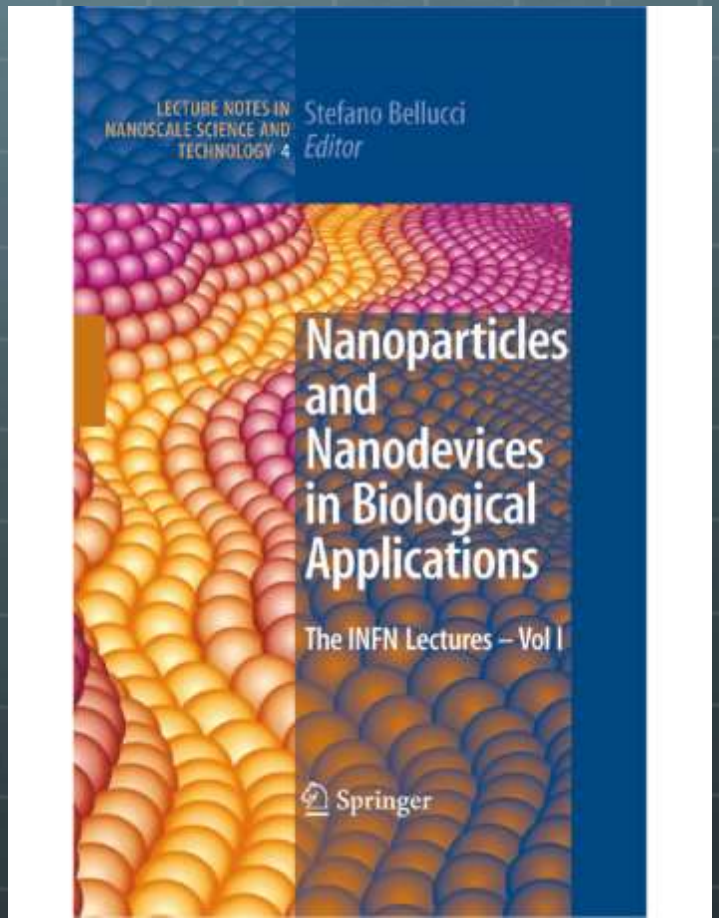
e-mail: bellucci@lnf.infn.it

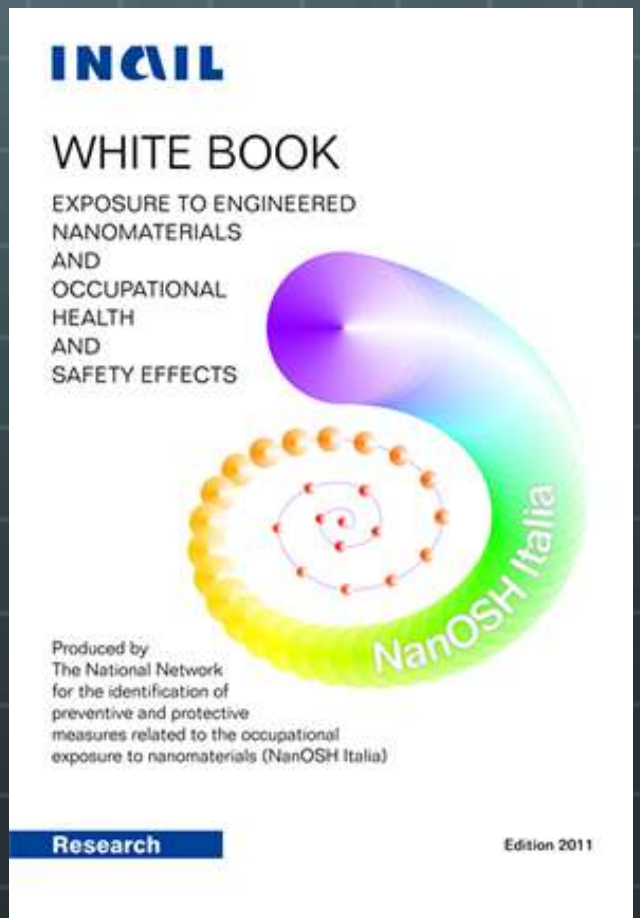
INFN - Laboratori Nazionali di Frascati

Impatto su ambiente e salute



- Possibile instabilità di alcune nanostrutture
  - Ad es. problema potenziale del “fullerene” dissolto in acqua nel legarsi al DNA, influenzando struttura, stabilità e funzioni biologiche delle molecole di DNA.





Possibili Problemi con le Nanotecnologie

- Modifiche radicali nella struttura economica
  - I prodotti al livello nano potrebbero diventare poco costosi da realizzare e richiedere una quantità minima di forza lavoro umana
  - Perdita di valore delle risorse materiali ed umane
- Problemi di Sicurezza
  - Dispositivi estremamente piccoli con piena funzionalità potrebbero diventare una causa di preoccupazione nella lotta contro il terrorismo
  - Possibile una corsa agli armamenti nanotech

http://www.crnano.org/dangers.htm#economy

Grandi Sfide alla Nanotecnologia

- I materiali sono difficili da manipolare ed è difficile mantenerli stabili
- Comprendere le caratteristiche dei nano materiali
  - Una singola particella di silicio non si comporta come il silicio bulk
  - Dipendenza da dimensioni, forma, e da ciò che circonda la particella

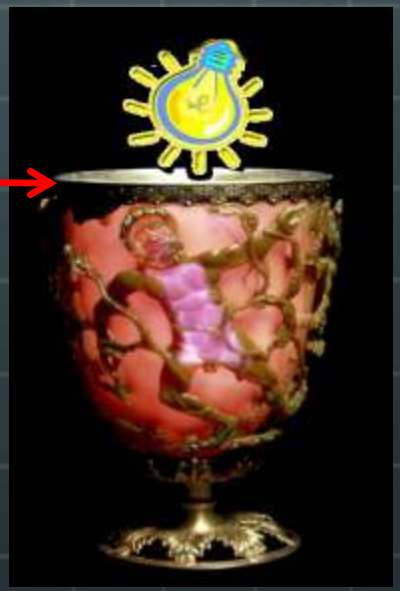
e-mail: bellucci@lnf.infn.it

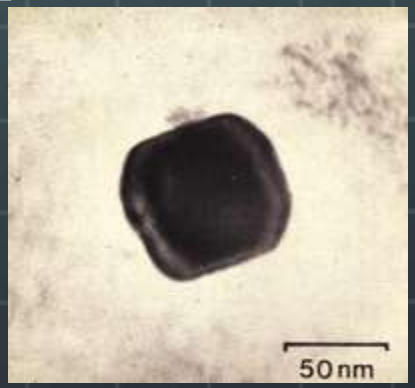
INFN - Laboratori Nazionali di Frascati

Un primo esempio di nanotecnologie!

Vaso di Licurgo
(IV sec. d.C., British Museum)

Presenta una diversa colorazione se osservato in **riflessione**, verde, o in **trasmissione**, rosso, per la presenza di nanoparticelle di oro e di argento.

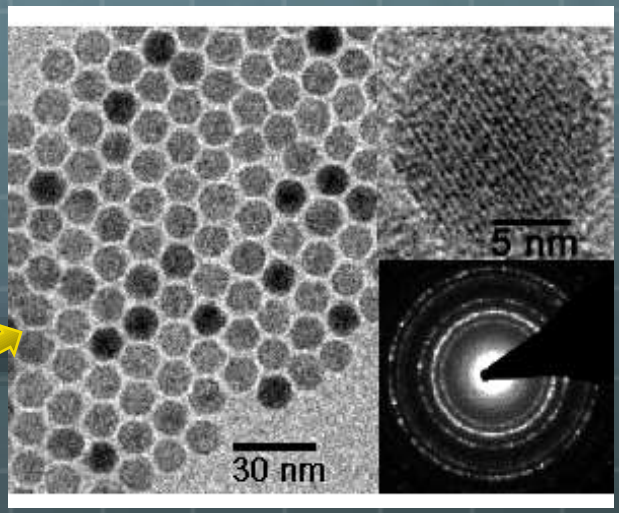


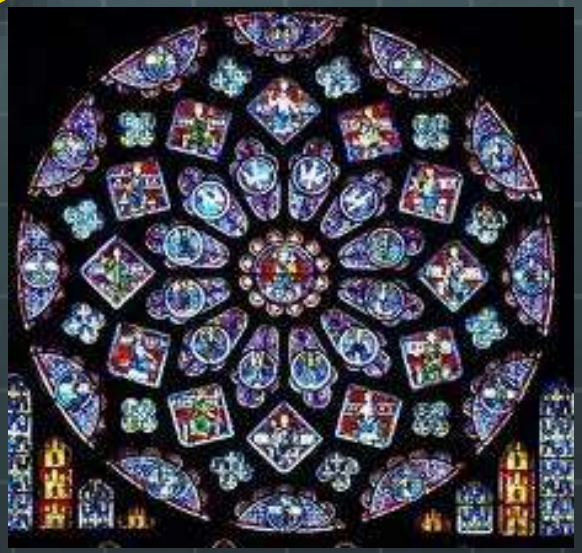


e-mail: bellucci@lnf.infn.it

Un altro esempio di nanotecnologie!

Nanoparticelle metalliche di diversa specie
Nelle vetrate delle chiese medioevali.



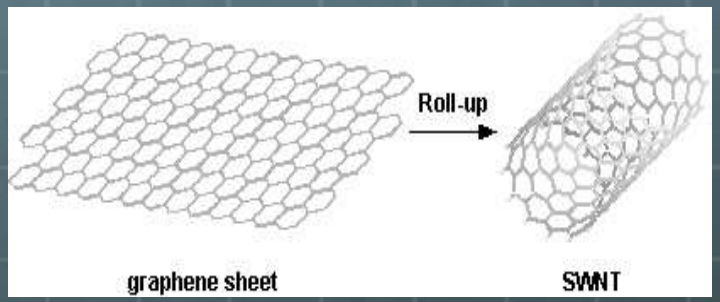


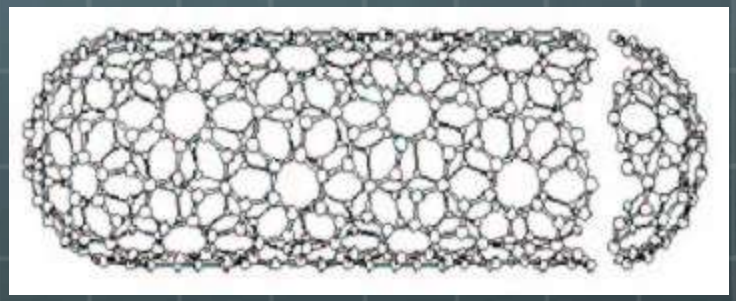
INFN - Laboratori Nazionali di Frascati

e-mail: bellucci@lnf.infn.it

Nanotubi di carbonio

- Scoperti nel 1991 da **Sumio Iijima**, un ricercatore dei Nec Labs di Tsukuba in Giappone.
- Sono cilindri cavi, ottenuti arrotolando su se stesso un foglio di grafene ossia un singolo piano di grafite (un reticolo esagonale di atomi di carbonio) e chiuso alle estremità da due semisfere di fullerene



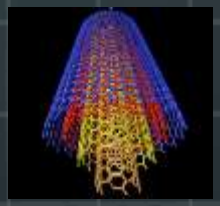


Si distinguono in:

SWNT
(Single wall Nanotubes)

Φ=1÷3 nm
L= 0.5÷10⁴ µm

MWNT
(Multi wall Nanotubes)

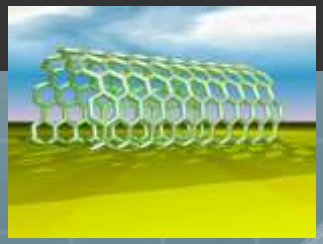


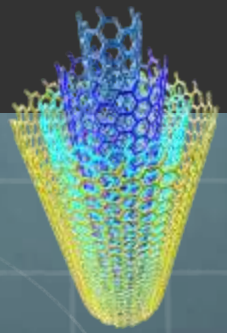
Φ=5÷200 nm
L= 0.5÷200 µm

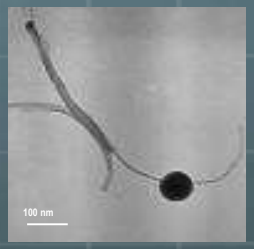
e-mail: bellucci@lnf.infn.it

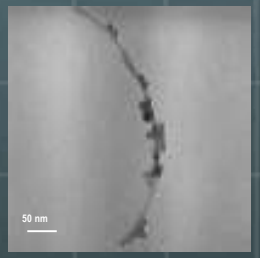
INFN - Laboratori Nazionali di Frascati

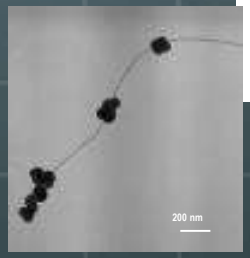
Nanotubi di Carbonio

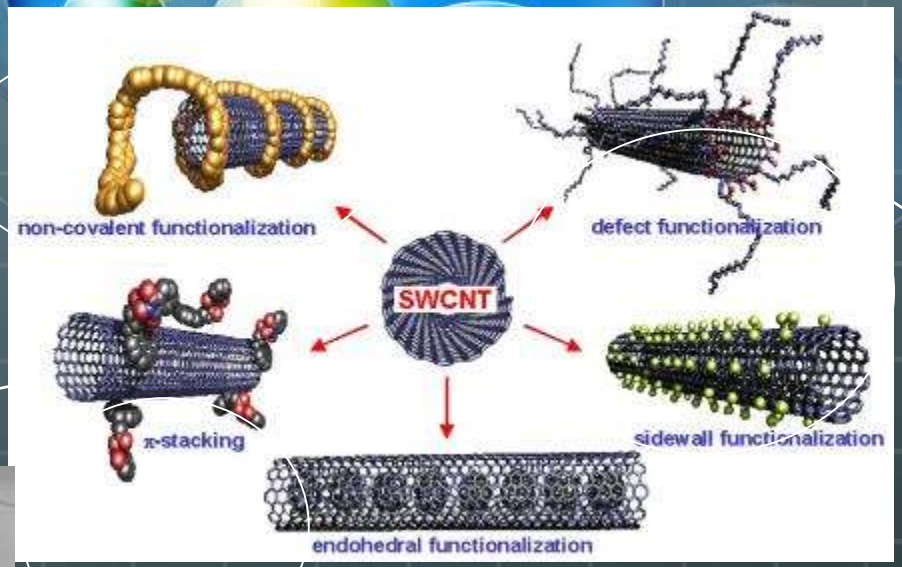


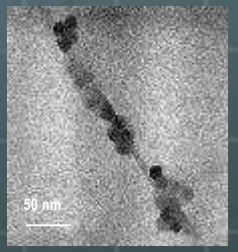


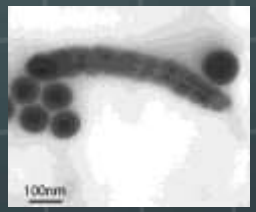












I nanotubi di Carbonio sono caratterizzati da proprieta' strutturali, meccaniche, elettriche e chimiche e sono stati studiati e utilizzati per la realizzazione di nanomateriali compositi.

MA COSA HA DI SPECIALE UN NANOTUBO?

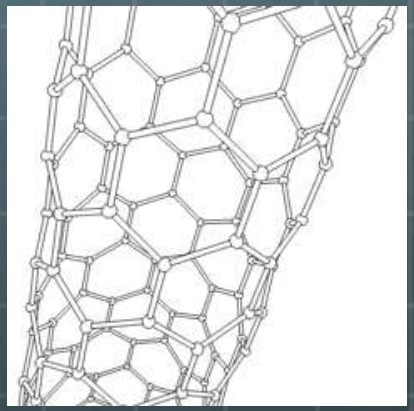
Presenta un aspect ratio (L/Φ) alto ⇒struttura monodimensionale.

Capacità di trasportare correnti elevate, senza surriscaldarsi (densita' di corrente di 10^9 A/cm^2).

Elevata conducibilità termica ad elevate temperature e a temperatura ambiente (1800-6000W/m*K).

E' 50000 volte più sottile di un capello umano.

Presenta elevato *modulo elastico* (fino a 1 Tpa) ed elevata resistenza a trazione (150 Gpa).



e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati

Materiali nanocompositi

Matrice

- Resina epossidica

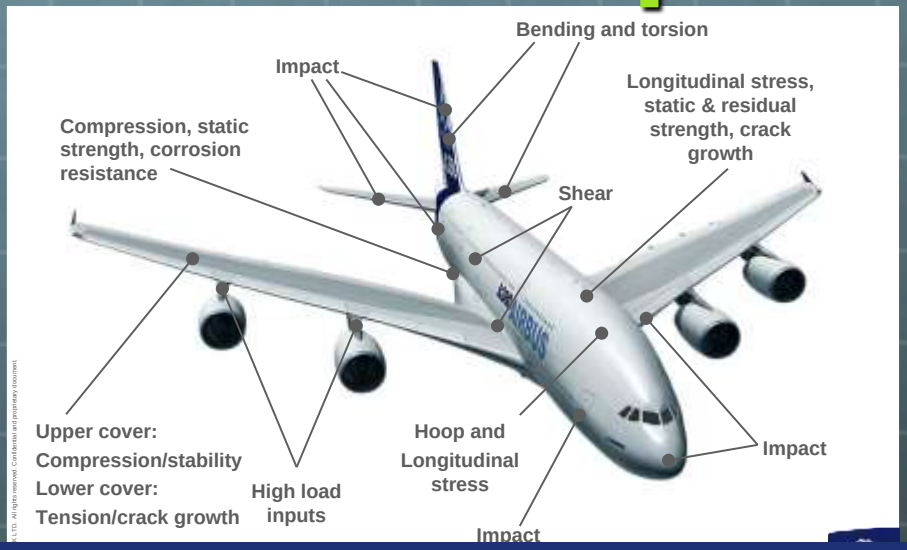
Filler

- Nanotubi di carbonio
- GNPs

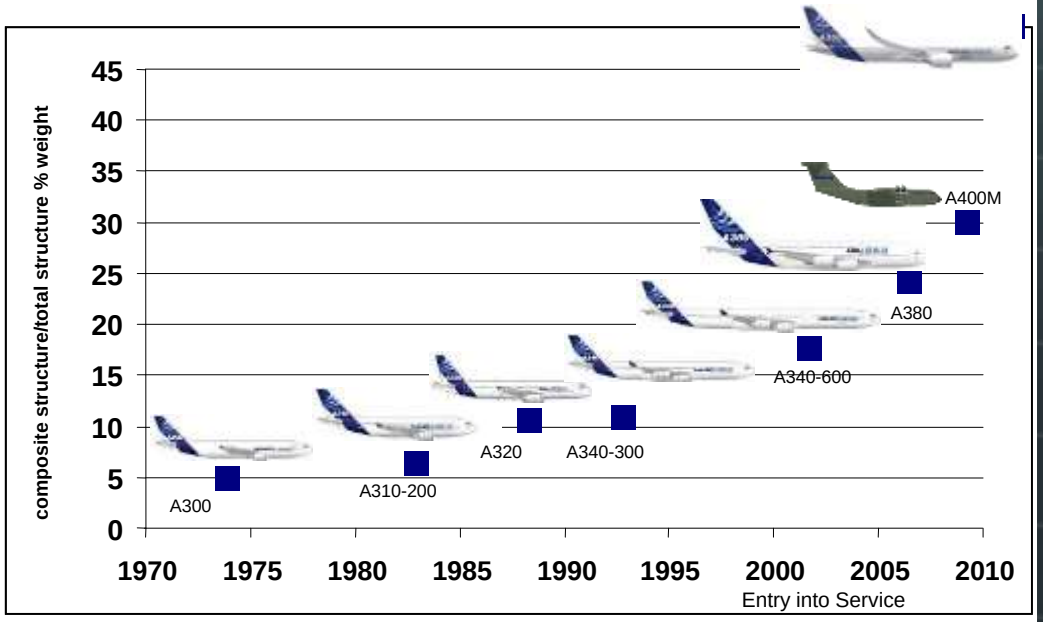
Una delle due fasi ha dimensioni nanometriche

Realizzazione di un nanocomposito con funzione di rivestimento contro le EMI.

Applicazioni dei nanocompositi

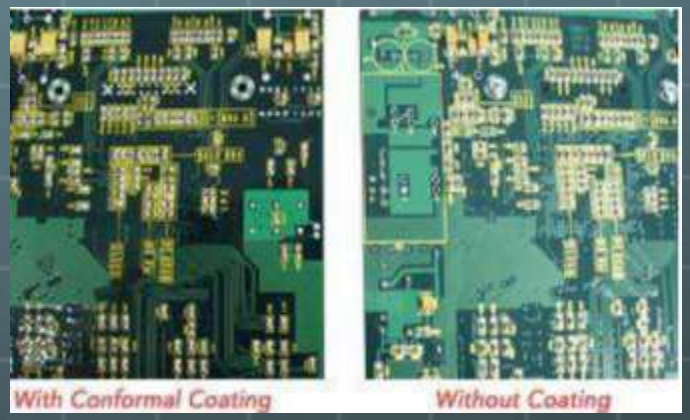


Composites introduction on Airbus aircraft



Fonti Airbus 2007

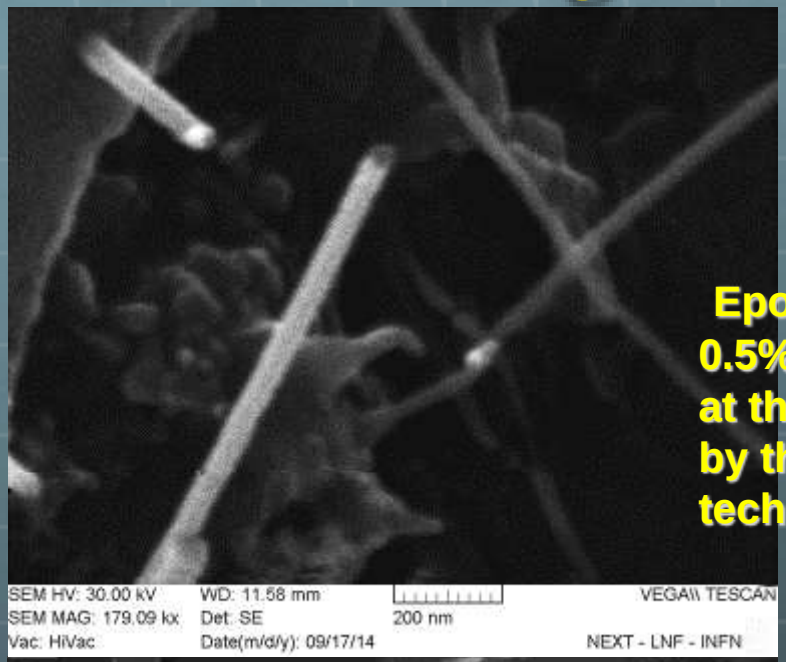
Applicazioni dei nanocompositi



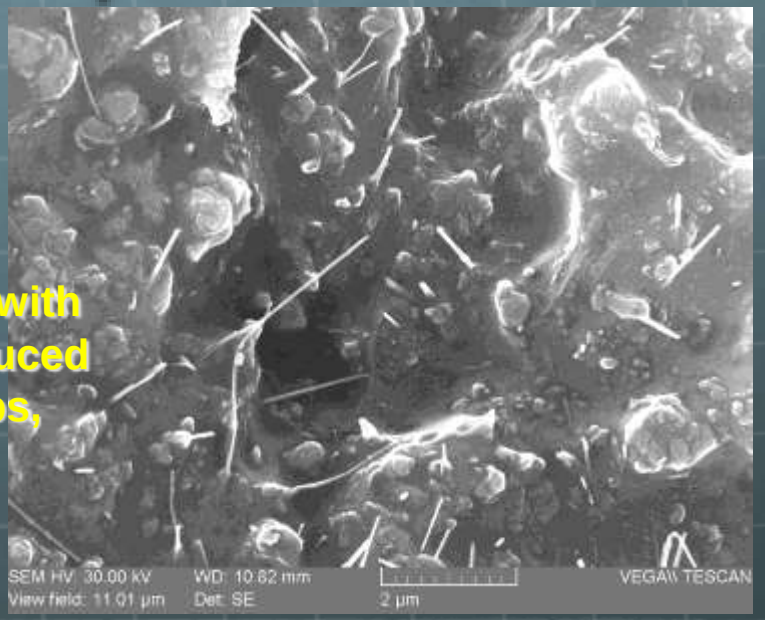
e-mail: bellucci@lnf.infn.it

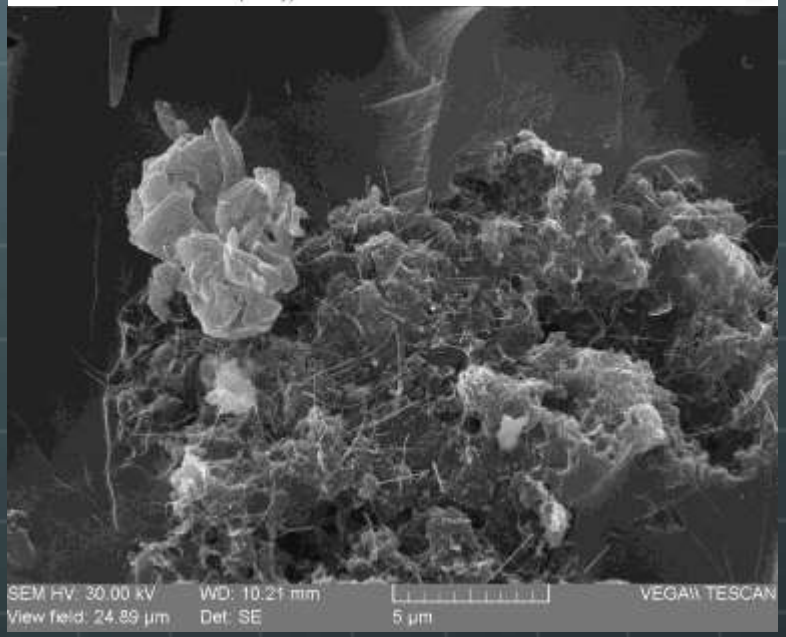
INFN - Laboratori Nazionali di Frascati

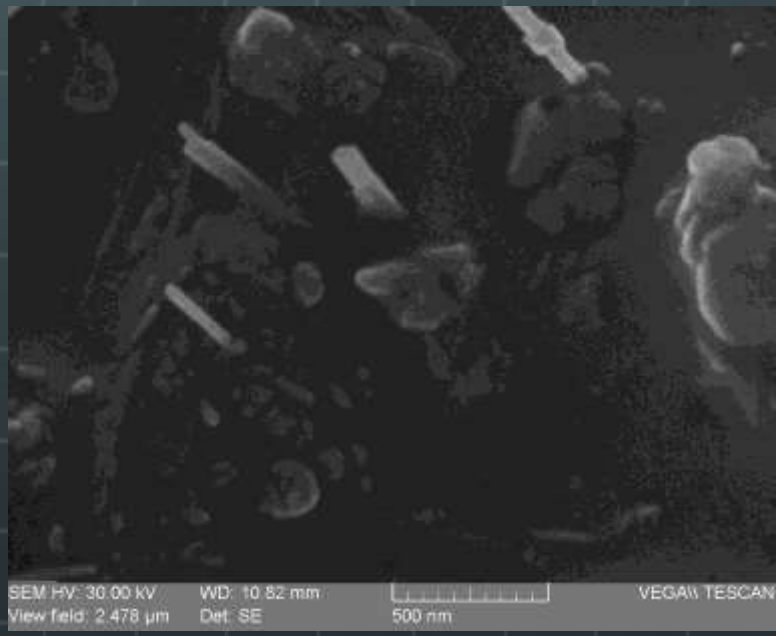
Images of Nanocomposites



Epoxy Resin loaded with 0.5%wt MWCNT produced at the NEXT – LNF labs, by the arc discherge technique



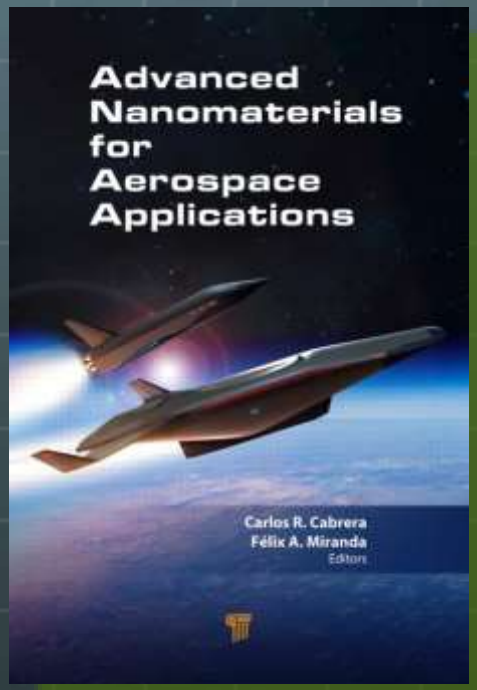




Shielding Effectiveness

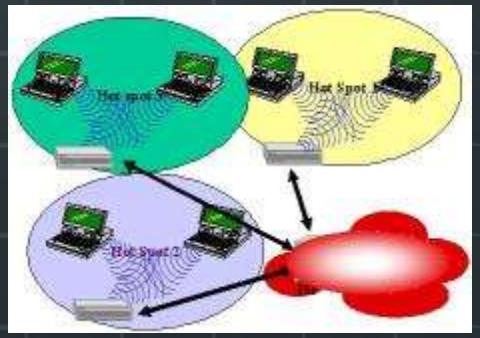
- ✓ Innovative Materials with a high efficiency in electromagnetic shielding effectiveness and suitable mechanical & chemical properties (low weight, resistence against corrosion, *etc*) can significantly enhance Electromagnetic Compatibility; preventing unauthorized access to networks informations; reducing impact on electronic setups due to attacks carried out by EM pulses.

- ✓ Designing an electromagnetic coating with controlled properties

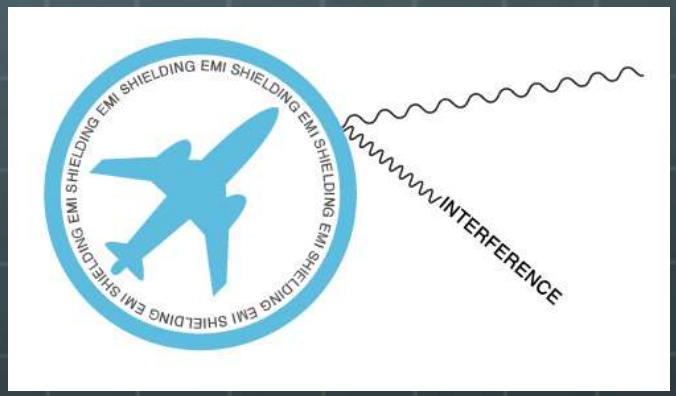


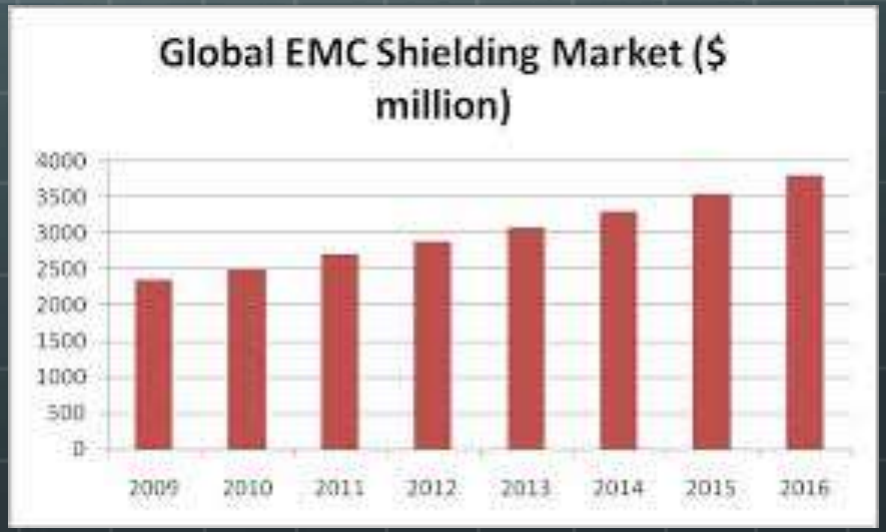
Information Technology Shielding

Wireless Handset Shielding



Shielding Effectiveness





Nano for Future Transportation & Mobile

Symbiosis Car

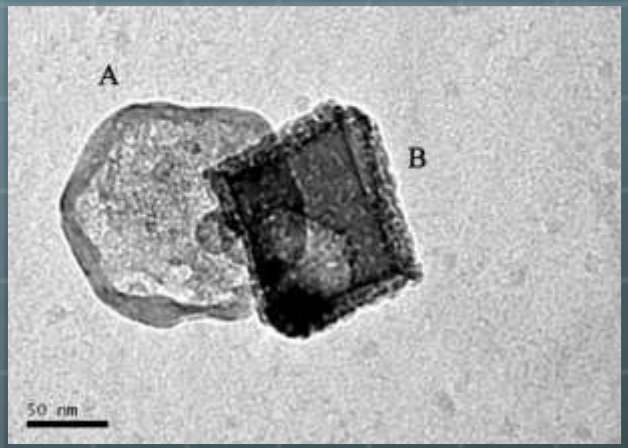
Samsung Flexible Mobile

e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati

Nanotecnologie nel Restauro!

Immagini TEM di due particelle in sospensione di dimensioni nanometriche:
$Ca(OH)_2$ di forma esagonale (A),
$CaCO_3$ di forma prismatica (B)

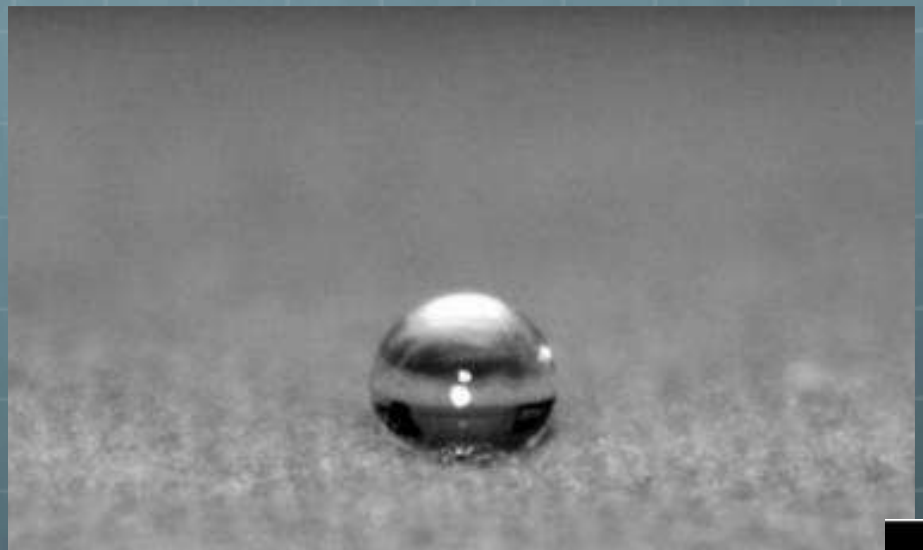


Affresco del Beato Angelico Abbazia di San Marco a Firenze

INFN - Laboratori Nazionali di Frascati

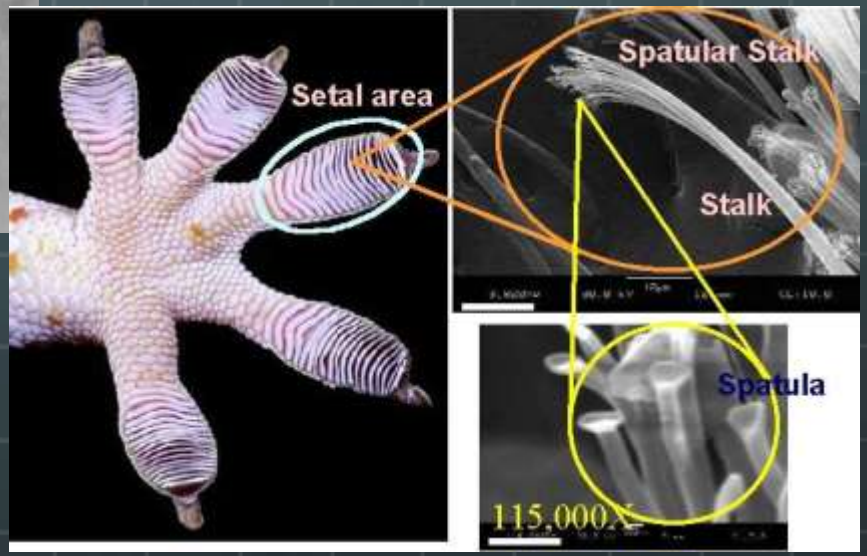
e-mail: bellucci@lnf.infn.it

Nano – Bio mometic !



Goccia di acqua su nano composito ricoperto da uno strato di cotone

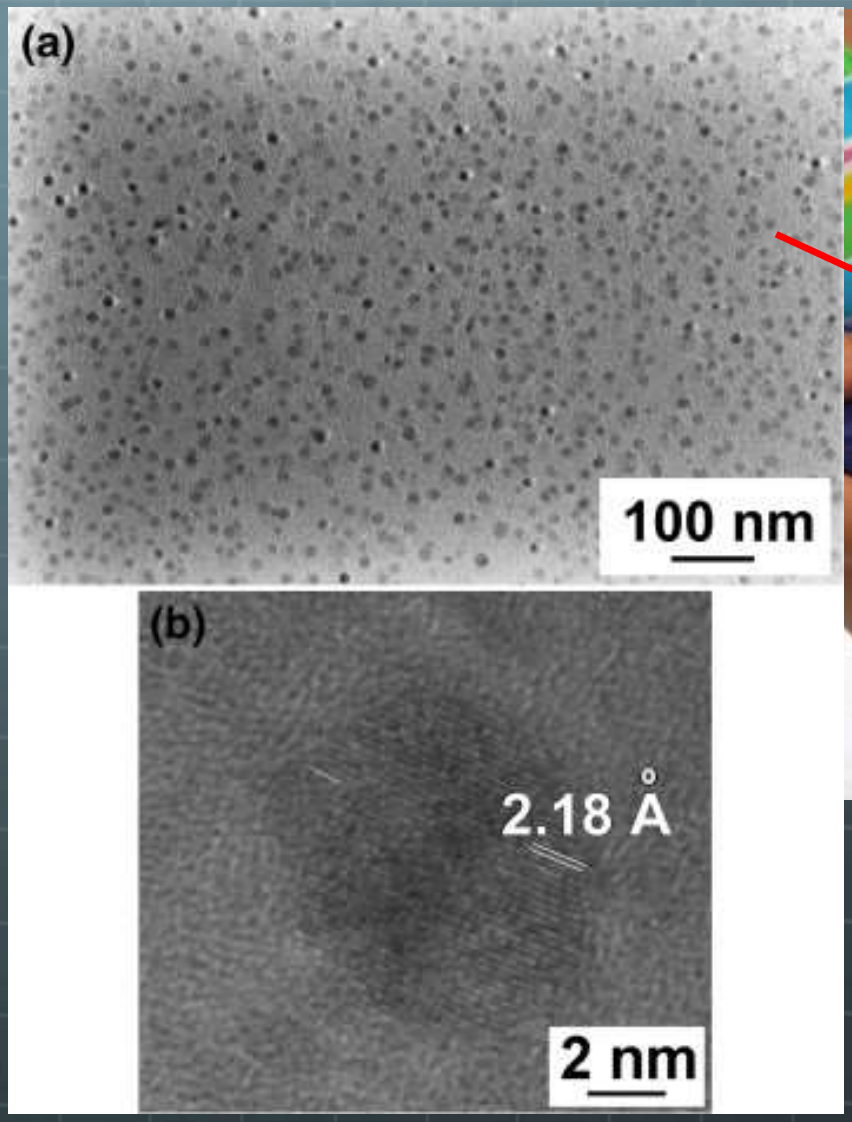
Tokay gecko foot-hair images: gecko foot bottom view (left image); zooming into one of the stalks under SEM (right upper image, bar indicates 10 μm), and zooming into spatulae and spatular stalks at the end of a stalk under SEM (right lower image, bar indicates 300 nm) (courtesy of Kellar Autumn)



INFN - Laboratori Nazionali di Frascati

e-mail: bellucci@lnf.infn.it

Nano –Cosmetici !



INFN - Laboratori Nazionali di Frascati

e-mail: bellucci@lnf.infn.it

Fonti energia, impatto ambientale

Table I: Average Lifecycle CO_2 Emissions from Different Energy Sources.	
Energy Source	**Lifecycle CO_2 Emissions (g per kWh)**
Coal	1,000
Oil	800
Natural gas	400–500
Solar	13–730
Wind	7–124
Nuclear	2–60

Bollettino MRS 2008

e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati

Soluzione alla Sicurezza Energetica e al Riscaldamento Globale

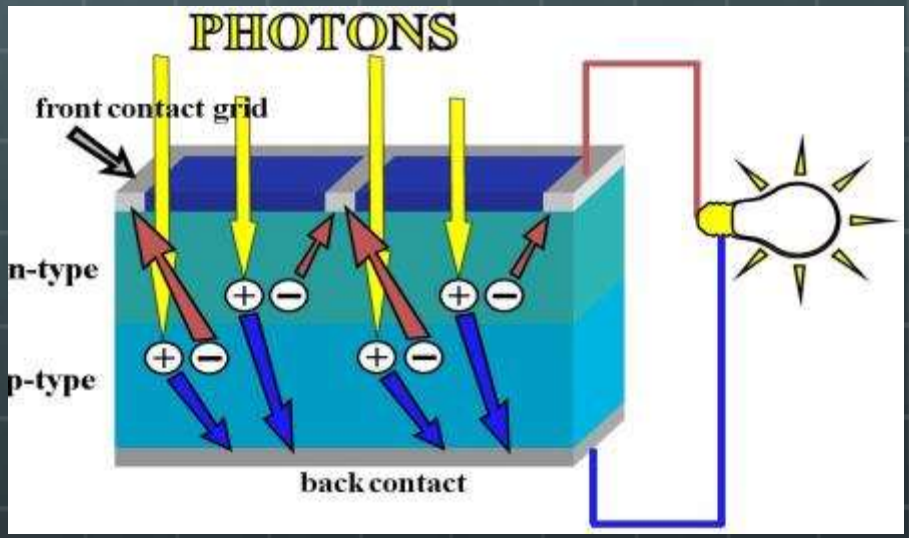
Non è necessario un Passo Indietro in Tecnologia, Velocità e Comfort!

e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati

Potenzialità delle nano tecnologie per l'energia solare

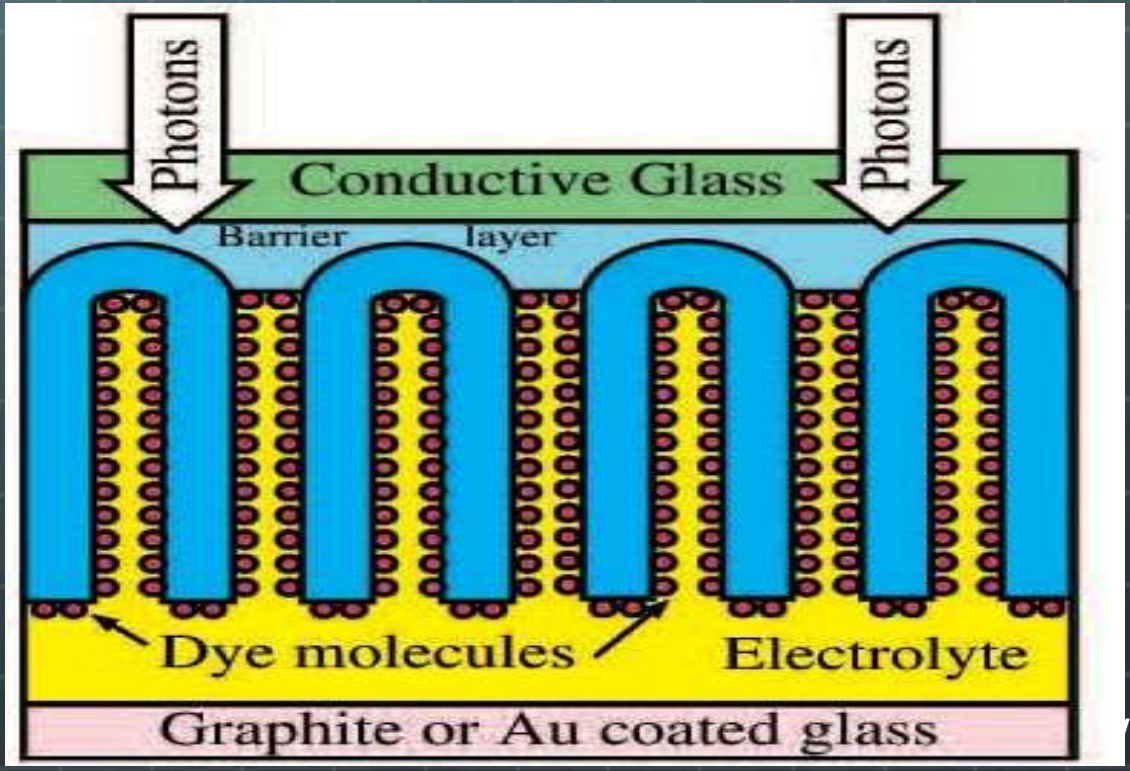
- Il problema principale degli attuali sistemi di energia solare è la loro limitata efficienza
  - Le celle solari più avanzate utilizzano solo tra il 10 e il 30 percento dell'energia solare disponibile che colpisce le celle



technologynewsdaily.com

Dye Sensitive Solar Cells con rivestimento ai Nanotubi

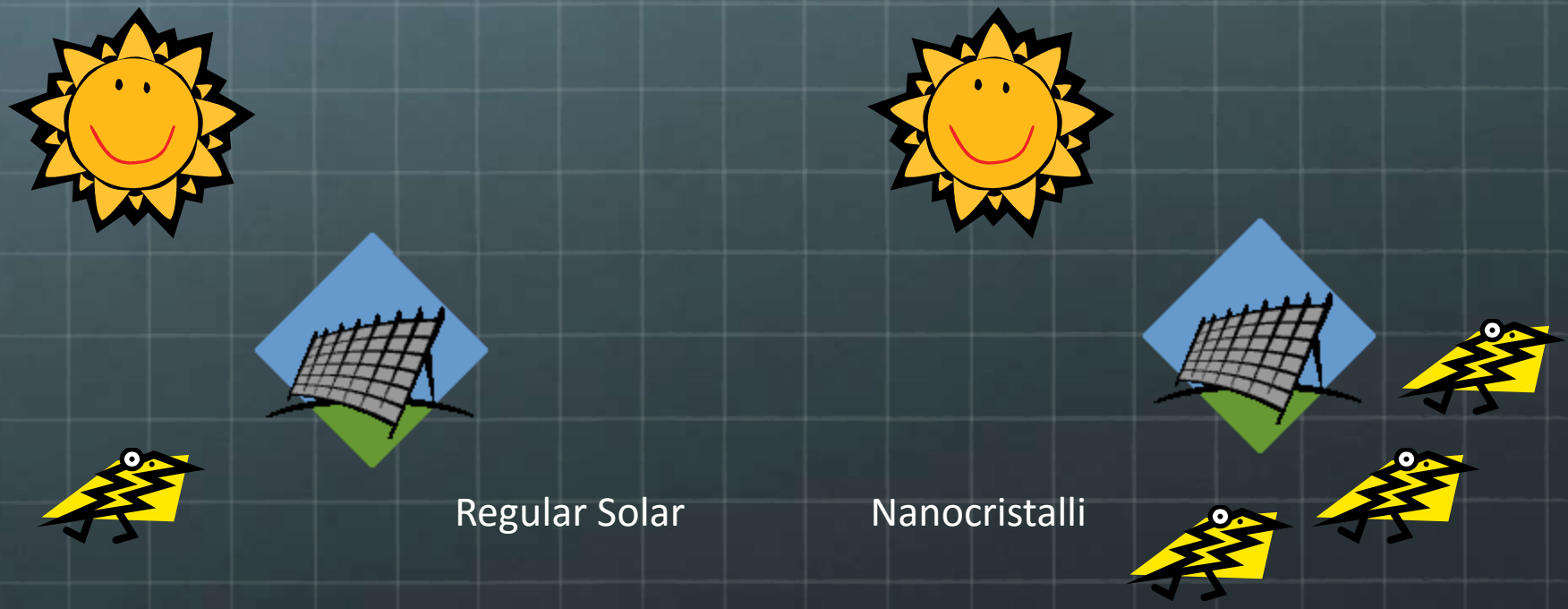
- Alla Penn State University si usano nanotubi di titania e dye naturale per cercare di ottenere energia solare più cost-effective



www.physorg.com

Maggiore Efficienza delle Nanotecnologie

- Nanocristalli
  - Maggior numero di elettroni – 3 a 1
  - Maggiore quantità di energia prodotta

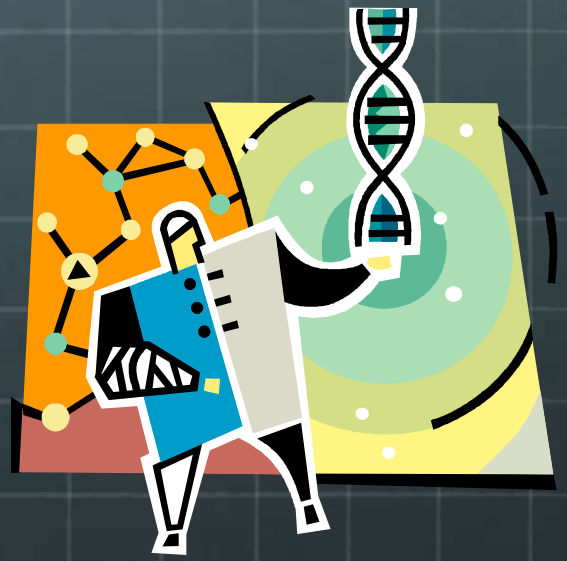


Regular Solar

Nanocristalli

Migliori capacità di raccogliere la luce

- Antenne alla Nanoscala
  - DNA “scaffold”
  - Incremento dell’assorbimento fotonico
- Problema
  - Perdita di energia nel transporto
    - Possibile soluzione
      - Posizionamento delle antenne controllato col DNA

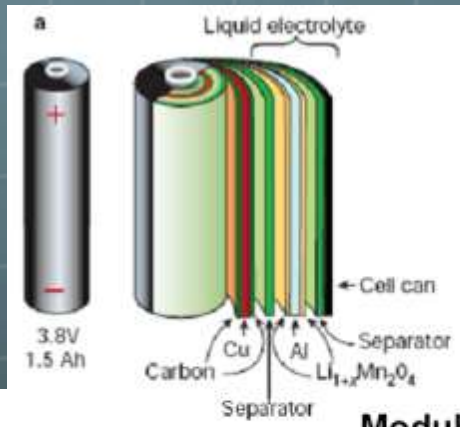


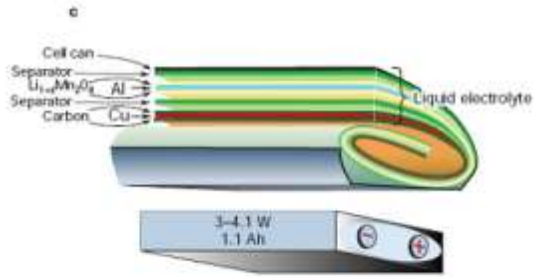
http://www.technologynewsdaily.com/node/4856

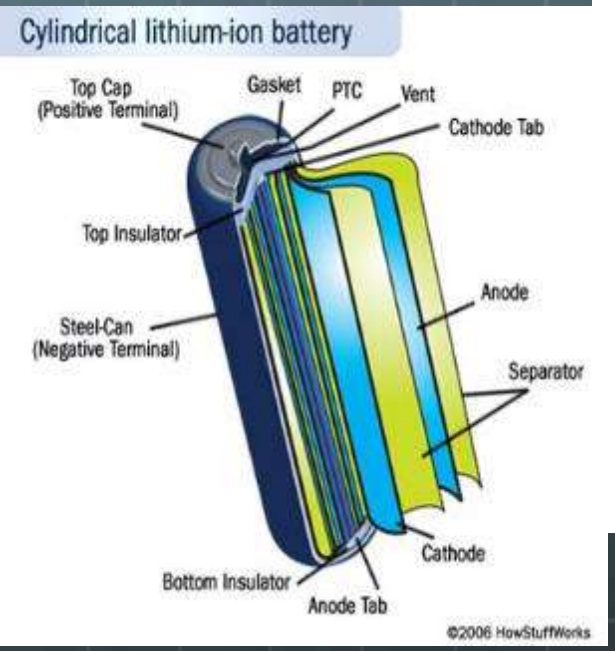
Progresso attuale nel Solar Nanotech

- 6% efficienza nelle plastic solar cells
  - Benefici delle plastic cells
    - Flessibilità
    - Arrotolabili
    - Uso domestico
- Possibili utilizzi
  - Rivestimento di tetti
  - Automobili
  - Personale militare

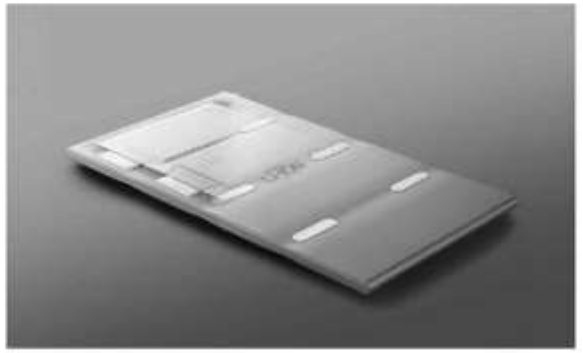
Batterie a ioni Litio, i fondamenti







Module of compact Li-ion battery



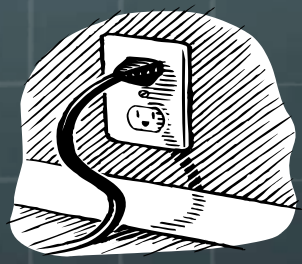
Tarascon et. al, Nature (2001)

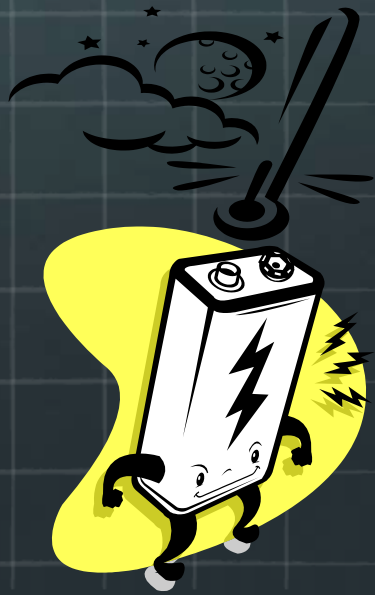
http://electronics.howstuffworks.com/lithium-ion-battery1.htm

Nano Possibilities

Altair Technology NanoSafe Battery

- Battery Life Lunga
  - Potenzialmente 20+ anni
- Ricarica veloce
  - Potenzialmente ricarica in minuti
- Temperature operative estese
  - Da -50° C a 75° C
- Elevato Power Output
  - Potentialmente 4 volte di più delle batterie ricaricabili a ioni litio attuali

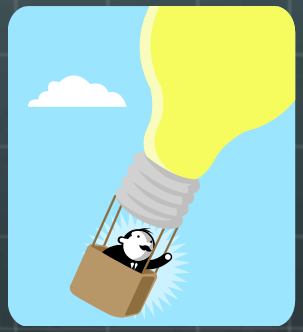




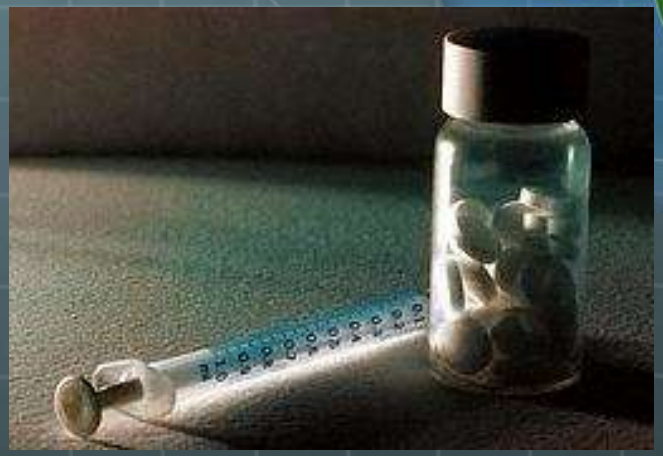
Conclusione

La Nanotecnologia ha il potenziale per revoluzionare il sistema energetico in Italia e nel Mondo. Dalle celle a combutibile, alle batterie dei telefoni cellulari, allo equipaggiamento spaziale, la nanotecnologia può essere utilizzata

Tuttavia, molta ricerca è necessaria e vi sono molti ostacoli da superare per rendere questa tecnologia commercialmente praticabile



Nanomedicina & Citotossicita’



Si sta studiando da una decina di anni l’impatto potenziale sull’ambiente e la salute dei nanotubi di carbonio, che si presentano in molte forme differenti and possono venire modificati chimicamente e/o funzionalizzati per mezzo di biomolecole.

La nanomedicina e’ la preservazione e il miglioramento della salute umana usando strumenti e conoscenza molecolari del corpo umano

L'UNIVERSO DELL'ESPOSIZIONE A NANOMATERIALI

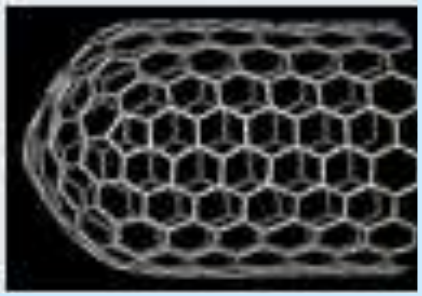
Esposizione accidentale a NP derivate da processi di combustione

NP diesel, fumi di saldatura, termodegradazione m. plastiche

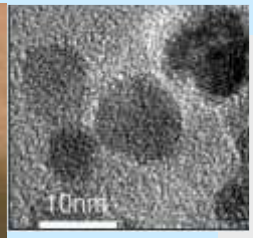
Carbon black, TiO_2

Esposizione accidentale a materiali di nuova sintesi

Esposizione accidentale a NP di nuova sintesi e NP modificate



Nanotubi di carbonio



Dendrimeri, fullereni, PMP, *quantum dots*

Esposizione deliberata a NM in ambito biomedico

e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati

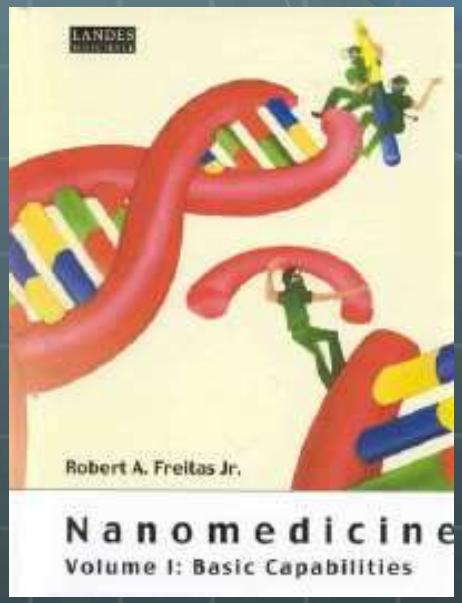
NANOPARTICELLE ARTIFICIALI "INVOLONTARIE"…

«Golfo del Messico, incendio di una piattaforma petrolifera»

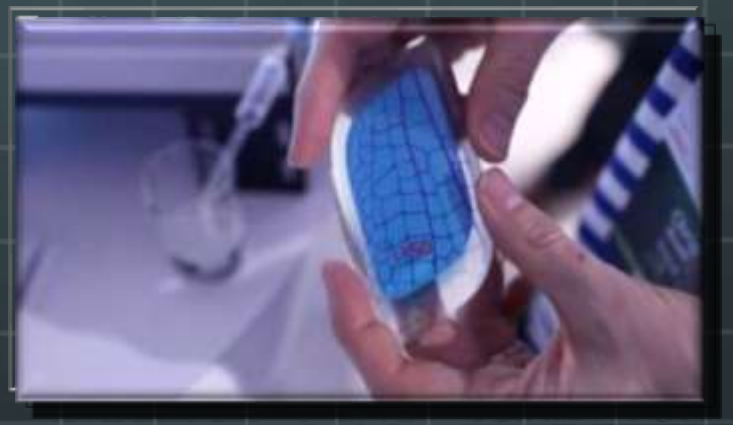
«Bari, 2006: implosione del complesso residenziale di Punta Perotti»

NANOPARTICELLE INGEGNERIZZATE (ENMs)…

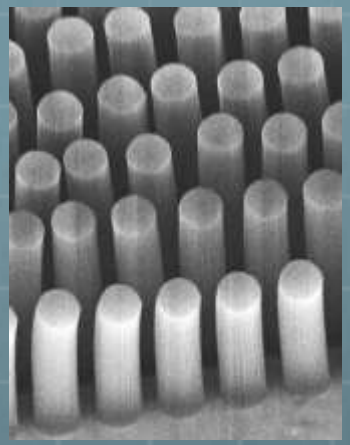
…niente più tergicristalli…

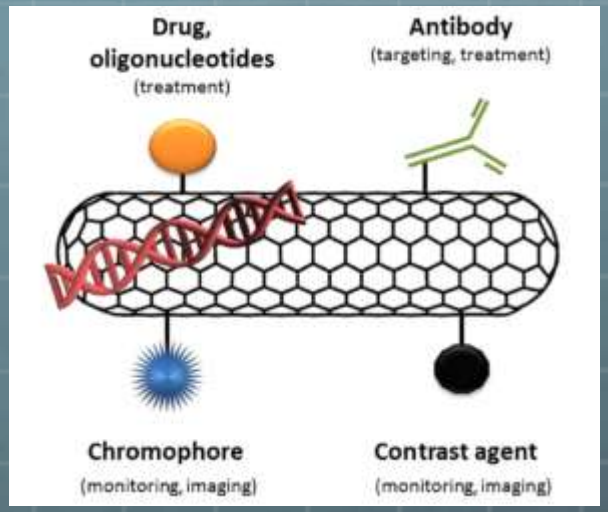


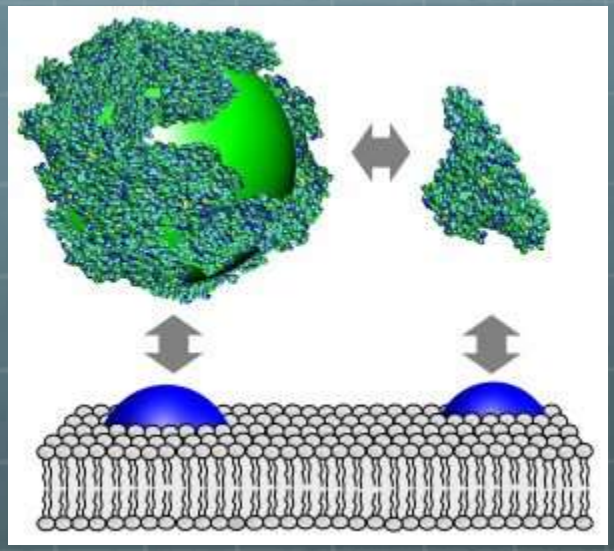
Nanomedicina: medicina della singola cellula

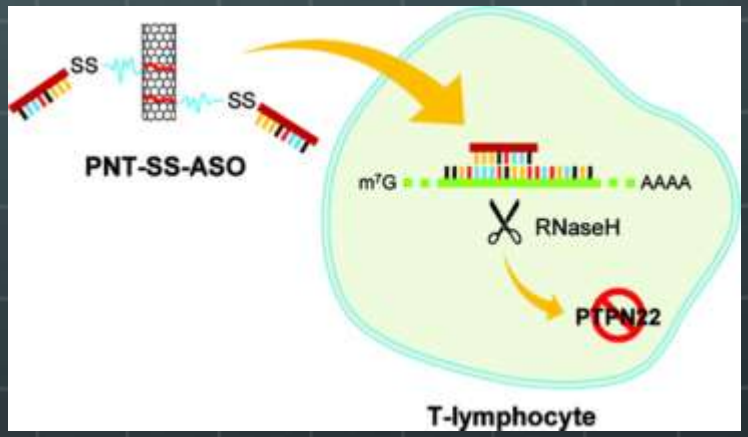


…o «ditate» sui display…









I nanotubi visti dal fisico

Modificati dal farmacologo

Studiati dal biologo

Visti dal medico

Nanoparticelle prodotte durante fenomeni di combustione

- Epidemiologia
- Tossicologia

Nanoparticelle utilizzate nell'industria

Nanotecnologie

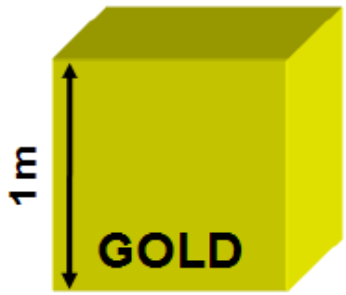
Quali pericoli?

Proprietà fisico-chimiche

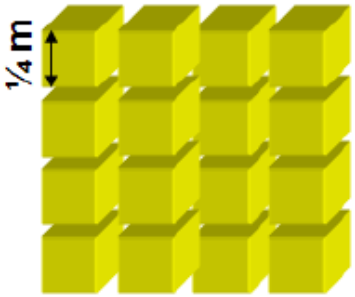
1. Rapporto superficie/volume: area superficiale estremamente estesa;

2. Elevato numero di atomi in superficie (Una particella di 300 nm ha il 5% degli atomi in superficie, una di 30 il 50%).

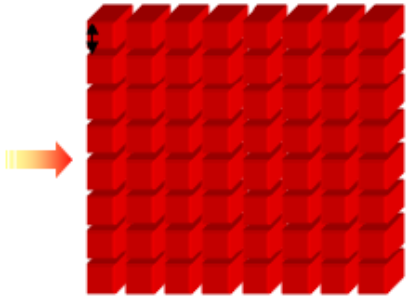
New Properties of Matter Based on Size and Surface Area



Each side=1 M
Mass≈43,000 lb
Surface Area (SA)=6 m^2
≈ 8 ft x 8 ft room

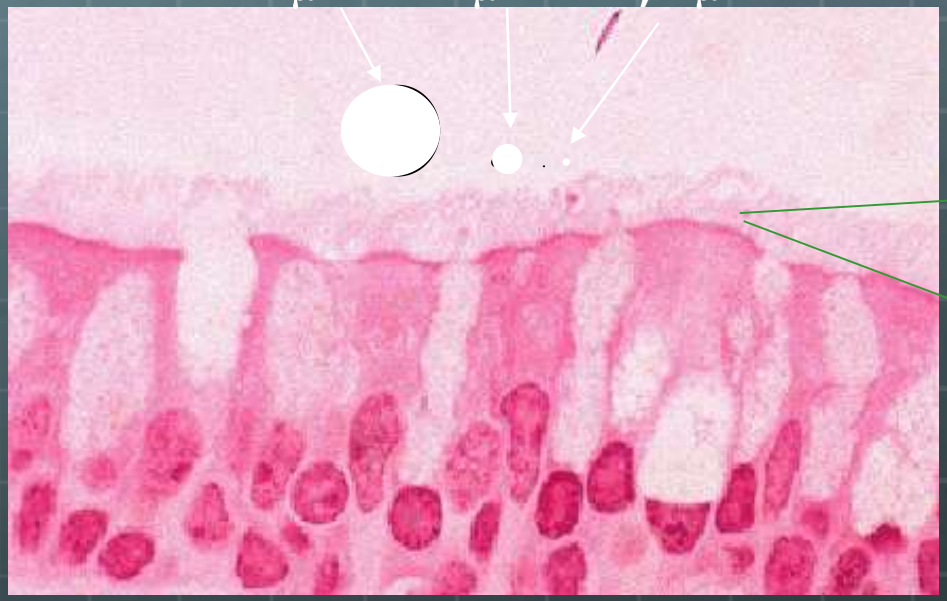


Each side=1/4 M
Mass≈43,000 lb
SA=24 m^2



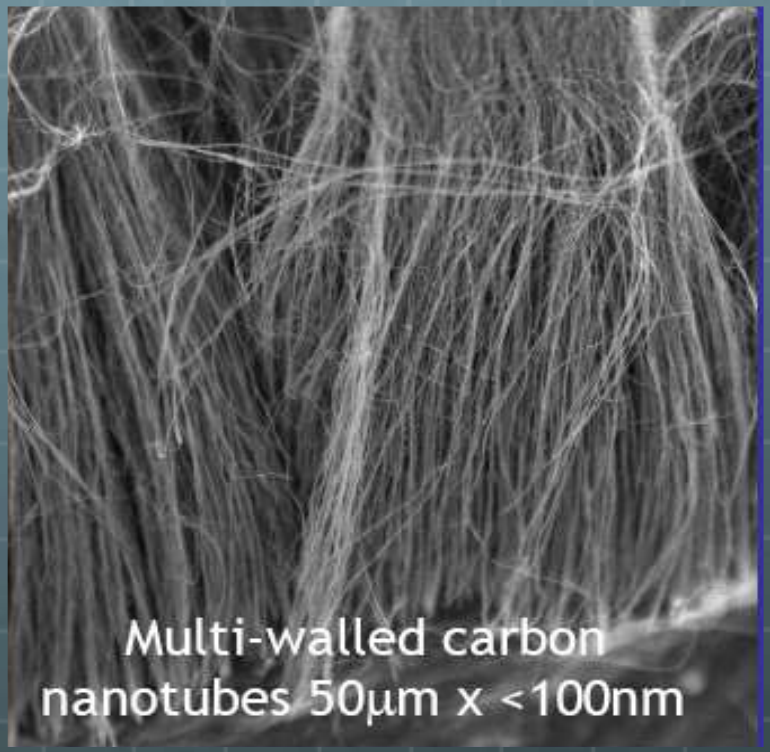
Each side=1 nM
Mass≈43,000 lb
SA=6 billion m^2 ≈ 2500 $miles^2$
State of Delaware= 2490 $miles^2$

Le caratteristiche dimensionali influiscono sulle possibilità di interazione



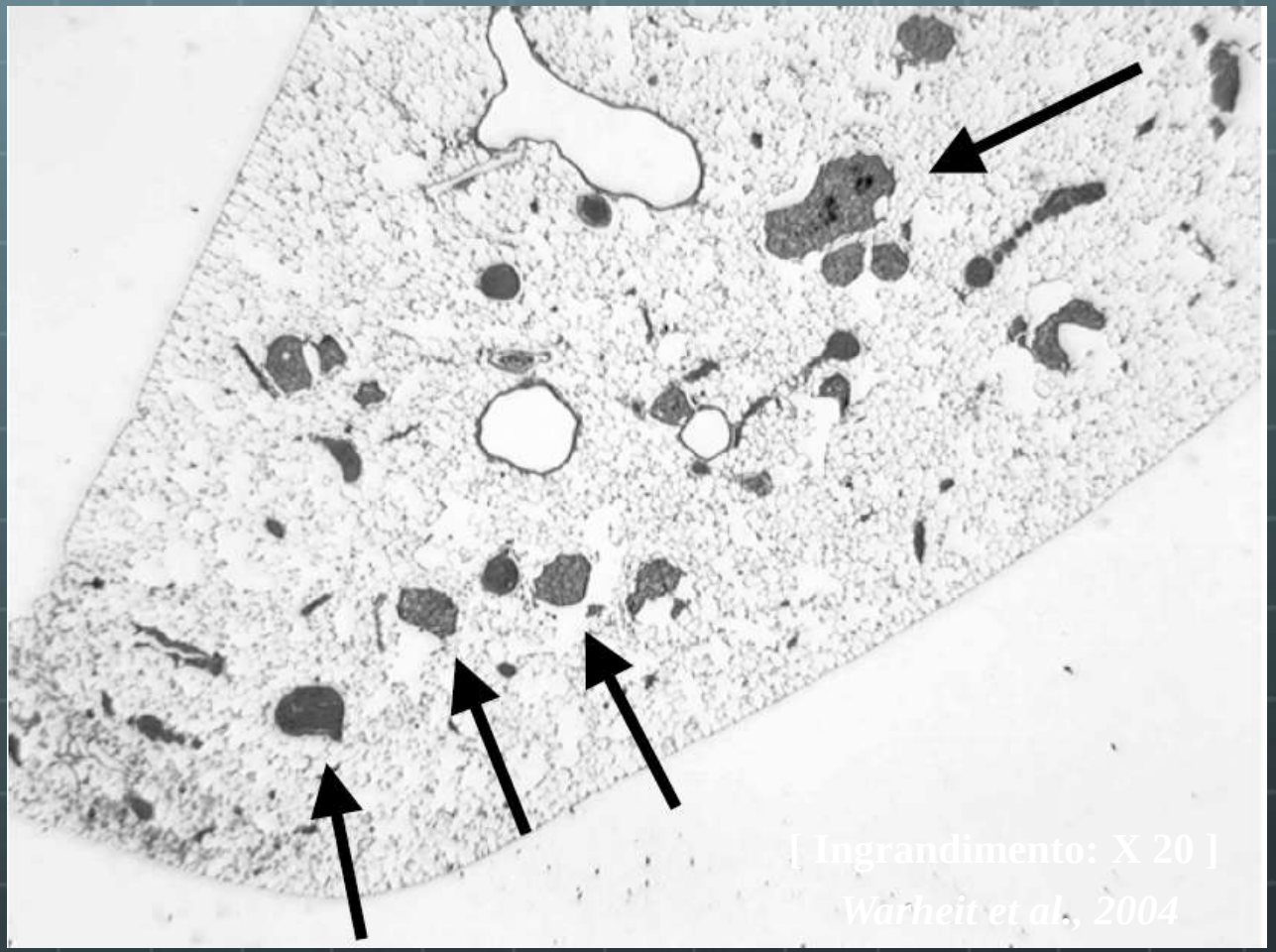
EPITELIO BRONCHIALE

Nanotubi ed asbesto

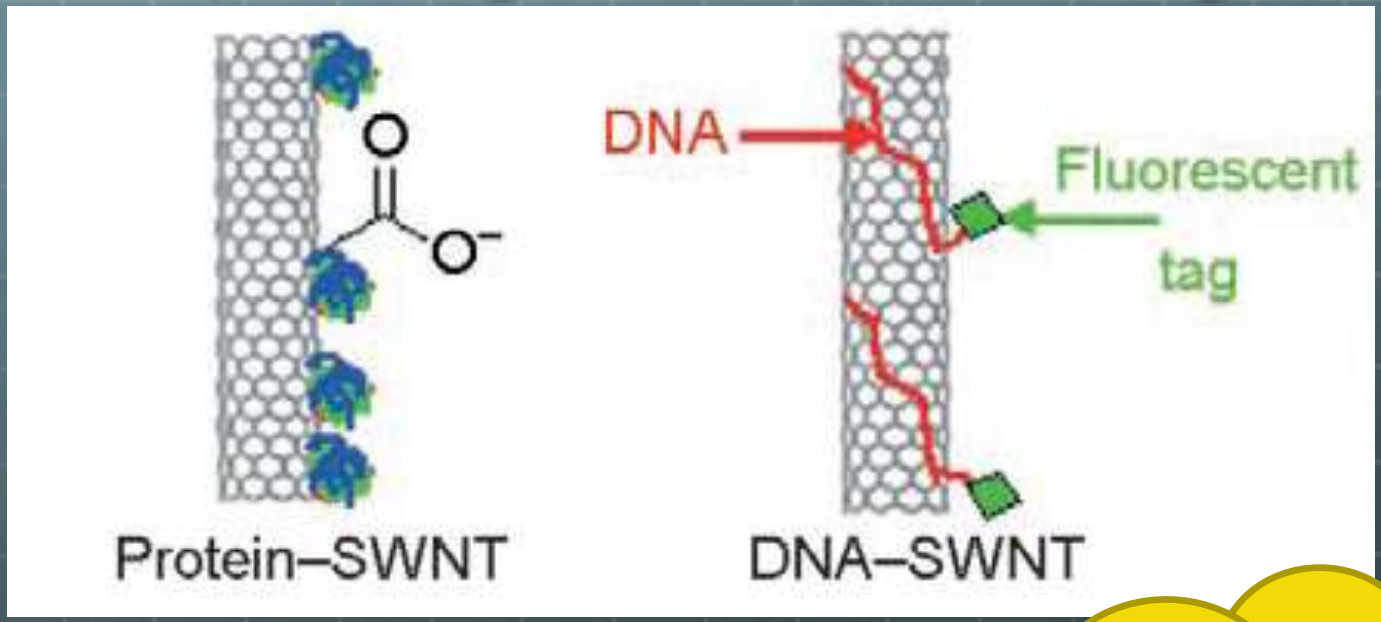


- **da 0,1 μm a centinaia di μm di lunghezza**
- **diametro da 1 nm (SW) a 200 nm (MW)**
- **aghiformi, comportamento simile ad asbesto**
- **idrofobici, resistenti alla frammentazione**

Tessuto polmonare di ratto esposto a NTC a parete singola (1 mg/Kg) 30gg dopo l'instillazione. Si nota la presenza di lesioni granulomatose (frecce) con distribuzione parenchimale non uniforme, probabilmente dovuta alle modalità di esposizione (*macroaggregati*)



I nanomateriali possono essere costituiti da parti organiche e parti inorganiche ….



Ma allora le possibilità divengono infinite ……

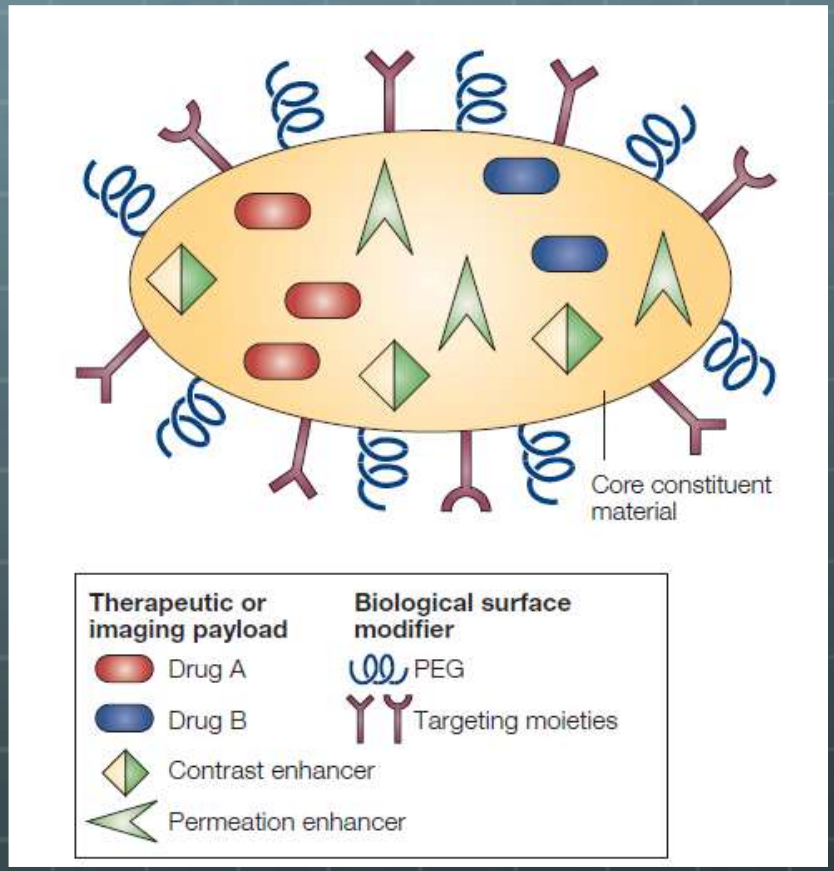
Nanoparticella multifunzionale.

- la capacità di trasportare uno o più agenti terapeutici;

- molecole per il targeting (anticorpi coniugati o altri agenti di riconoscimento);

- elementi per l'amplificazione del segnale e per il riconoscimento;

- elementi per la stabilizzazione (conservazione in circolo) e per l'aumento della capacità di penetrazione



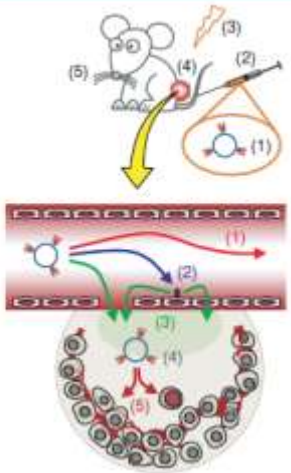
Review

Journal of Nanoscience and Nanotechnology
Vol. 14, 1–17, 2014
www.aspbs.com/jnn

Targeted Nanodrugs for Cancer Therapy: Prospects and Challenges

Massimo Bottini[1, 2, 3, *], Cristiano Sacchetti[1, 4], Antonio Pietroiusti[5], Stefano Bellucci[3], Andrea Magrini[5], Nicola Rosato[2], and Nunzio Bottini[4, *]

[1] *Inflammatory and Infectious Disease Center, Sanford-Burnham Medical Research Institute, 10901 North Torrey Pines Road, La Jolla, CA 92037, USA*
[2] *Department of Experimental Medicine and Surgery, University of Rome Tor Vergata, Via Montpellier 1, 00133 Rome, Italy*
[3] *INFN, National Laboratory of Frascati, Via Enrico Fermi 40, 00044 Frascati, Rome, Italy*
[4] *Division of Cellular Biology, La Jolla Institute for Allergy and Immunology, 9420 Athena Circle, La Jolla, CA 92037, USA*
[5] *Department of Biomedicine and Prevention, University of Rome Tor Vergata, Via Montpellier 1, 00133 Rome, Italy*



(1) Targeted-nanodrug
- nanocarrier type and properties
- ligand-receptor pair
- ligand type and affinity
- bioconjugation technique

(2) Route of administration
(3) Stimuli
- environmental (pH, enzymes,...)
- external

(4) Tumor type
(5) Host

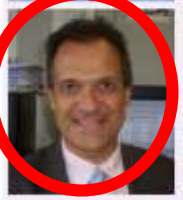
(1) Pharmacokinetic profile
(2) Tumor targeting
(3) Tumor penetration
- passive (EPR)
- active (iRGD)

(4) Tumor trafficking
(5) Cell targeting & trafficking

Massimo Bottini holds a degree in Electronic Engineering and a Ph.D. in Sensorial Systems. He received postdoctoral research training at the Sanford-Burnham Medical Research Institute in La Jolla, California, and he was appointed as an Assistant Professor at the University of Rome Tor Vergata (Rome, Italy) in 2009 and as an Adjunct Assistant Professor at the Sanford-Burnham Medical Research Institute (La Jolla, CA) in 2012. He was awarded a John Vaughan Scholar by the Arthritis National Research Foundation in 2011 and 2012. His research is focused on the investigation of the biological performance of carbon nanotube-based nanoparticles and their use as targeted drug delivery systems for the therapy of cancer and autoimmune diseases.

Cristiano Sacchetti received a M.S. degree in Medical Biotechnology in 2007 and a Ph.D. in Medical Biotechnology and Molecular Medicine in 2011 from the University of Rome Tor Vergata (Rome, Italy). He has been working in the group of Dr. M. Bottini at the Sanford-Burnham Medical Research Institute (La Jolla, CA) as a postdoctoral associate since 2011. His research includes the fabrication and characterization of nanoscopic particles for the targeting of immune cell populations in various tumor and arthritic model systems.

Antonio Pietroiusti is an Assistant Professor of Occupational Medicine at the University of Rome Tor Vergata (Rome, Italy). He is a partner in the FP7-MARINA, a project focusing on reference methods for risk management of nanomaterials, in the COST action MODENA, aimed at quantitative nanostructure-toxicity-relationship modeling to facilitate risk assessment of novel nanomaterials, and in the NanoReg, focused on delineating regulatory measure for the use of nanomaterials.

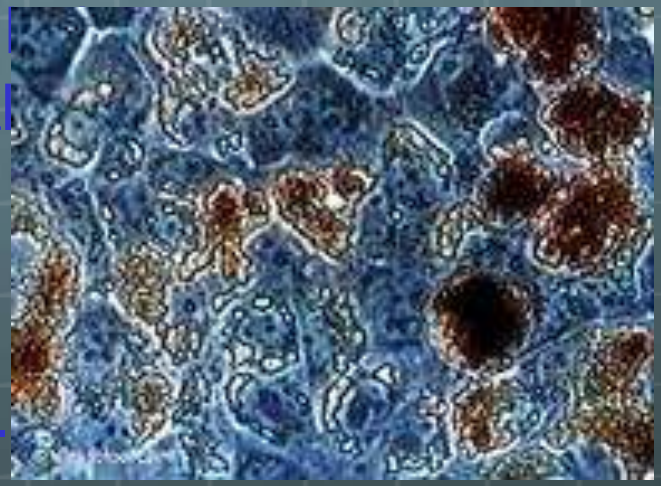


Stefano Bellucci obtained his Ph.D. in the physics of elementary particles at SISSA (Trieste, Italy) in 1986. He worked in the USA (1983–1988) as a Research Associate at Brandeis University and as visiting researcher at M.I.T., University of Maryland, and University of California at Davis. He returned to Italy as a Tenured Researcher (Research Staff) at INFN (Istituto Nazionale di Fisica Nucleare) Laboratori Nazionali di Frascati (LNF) in 1987. He was appointed as INFN First Researcher (Senior Research Staff) in 2005. His research interests include theoretical physics, condensed matter, nanocarbon-based composites and biomedical applications. He is INFN scientist in charge of EU projects "BY-NanoERA—Institutional Development of Applied Nanoelectromagnetics: Belarus in ERA Widening," "NAnoceMC—Nano-thin and micro-sized carbons: Toward electromagnetic compatibility application," and "FAEMCAR—Fundamental and Applied Electromagnetics of Nano-Carbons."

Andrea Magrini is an Associate Professor at the University of Rome Tor Vergata (Rome, Italy). He is head of the Unit of Occupational Medicine, Director of the School of Occupational Medicine and Vice-President of the Ph.D. in Prevention Techniques in the Environment and at Worksites at the University of Rome Tor Vergata. He is also chief of the Division of Occupational Medicine at the Tor Vergata University Hospital and Secretary of the Italian Society of Occupational Medicine and Industrial Hygiene. His primary scientific interest is the health effects of nanoparticles.

Nanotech per Terapia Tumorale

Iron oxide nanoparticles, with diameters 10,000 times smaller than that of a human h can easily penetrate cancer cells and wreak significant damage once inside, to fight a particularly aggressive form of brain cancer called glioblastoma, but which can be used to treat other forms of the disease.



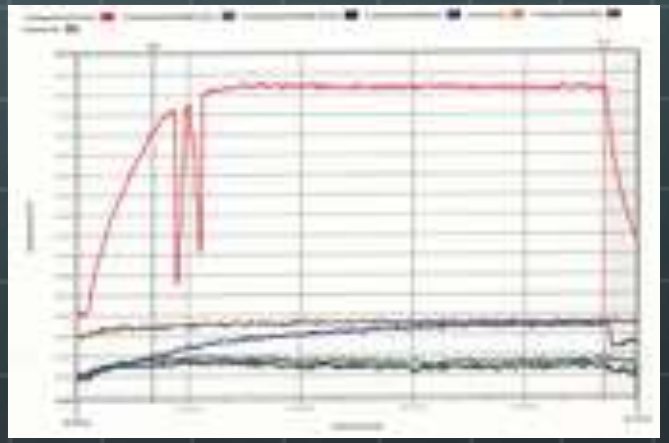
The image shows nanoparticles surrounding cancer cells.

The new procedure involves coating the tiny iron oxide particles with an organic substance, such as the sugar glucose, and injecting them into a malignant tumor. The tumor, which has a fast metabolism and correspondingly high energy needs, greedily sucks up the little particles masquerading as sugar pellets of a sort. Healthy cells, instead, show little interest.

Nanotech per Terapia Tumorale

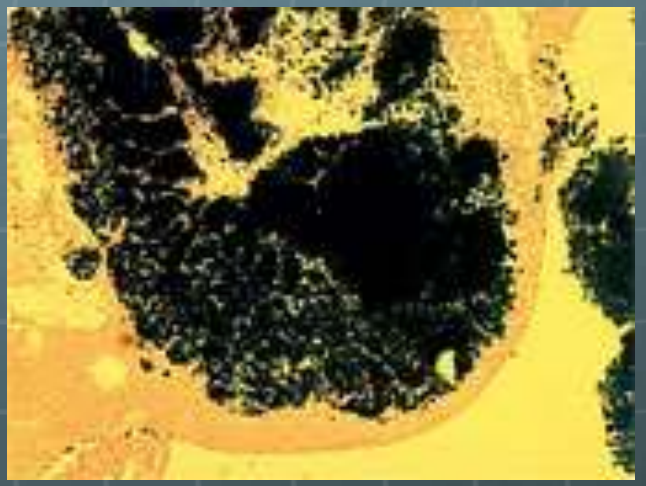
- The magnetic field heats up nanoparticles in the malignant tissue to temperatures up to 45 degrees Celsius. Heat destroys many of the cancer cells in and around the tumor or weakens them to a point that they are more effectively treated with radiation or chemotherapy.

The treatment is automatically recorded. Herein the temperature of the tumor (red) and other body-temperatures are registered.



Nanotech per Terapia Tumorale

In many pre-clinical tests the characteristics of nano-particles were optimized. Here: Accumulation of nano-particles in tumor tissue (RG-2 glioblastoma of the rat).



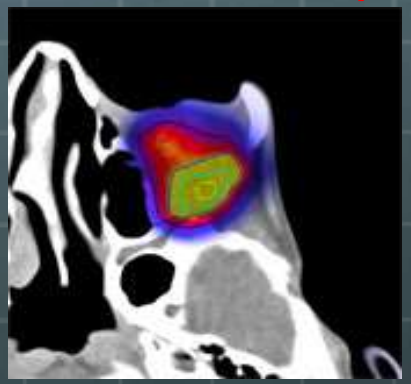
- The treatment, known as magnetic fluid hyperthermia, was successfully used in 2003 for extending the lives of laboratory rats which were implanted with malignant brain tumors. The rats receiving the nanotherapy lived four times as long as rats receiving no treatment.

Images source: MFH Hyperthermiesysteme GmbH and MagForce Applications GmbH, Berlin, Germany

Nanotech per Terapia Tumorale

- Subsequently the new technique was applied on 15 patients suffering from *Glioblastoma mutiforme,* the most common primary brain tumor and the most aggressive form of brain cancer (life expectancy prognosis in humans: 6-12 months).

A precise thermotherapy of target areas in almost every region of the body is possible (here: Thermotherapy of the orbita up to a maximum temperature of 49° C).



- The treatment is particularly attractive to doctors working with tumors in the brain since the nanoparticles are placed in the malignant tissue by means of an extremely precise electronic navigation system. So they can reach tumors that lie outside the reach of conventional surgical treatment, such as those situated deep in the brain or in regions that are responsible for essential tasks like speech or motor functions.

Biosensor Composites

Using these procedures, we obtained new CNT–nanocomposites with covalently attached silica nano-beads. Non-oxidized CNT (with negligible COOH content) do not support any composite formation.

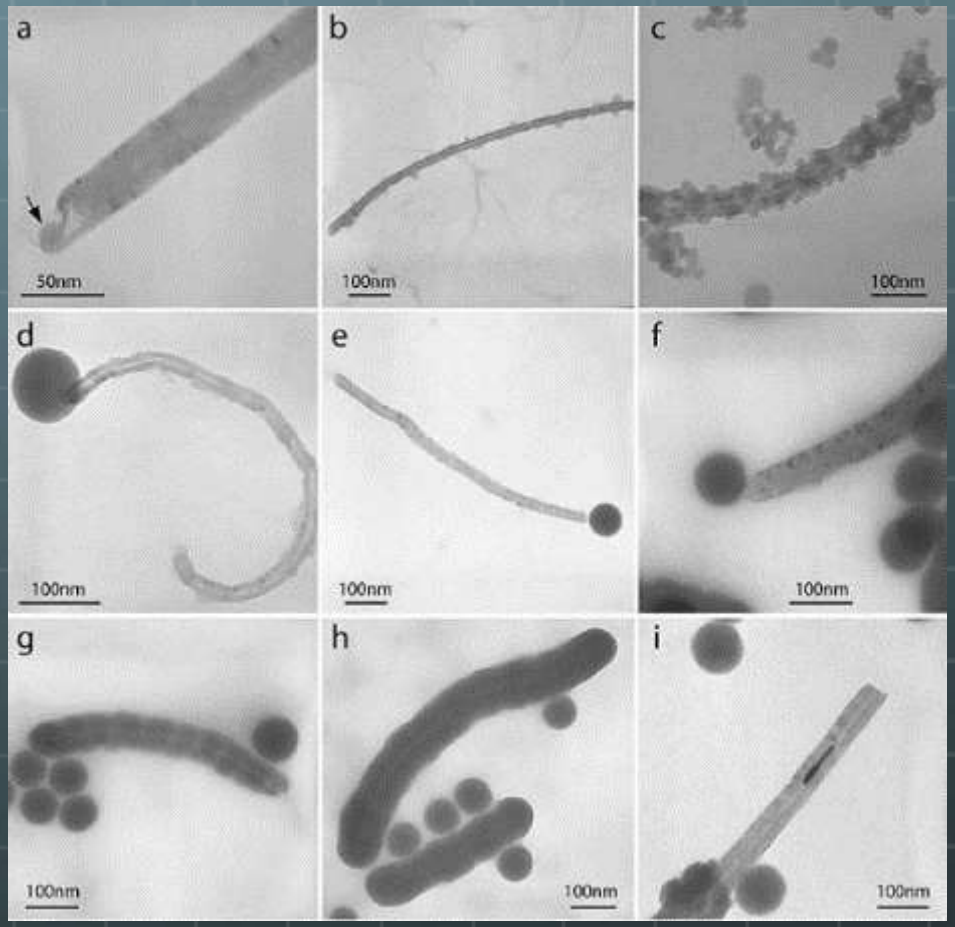
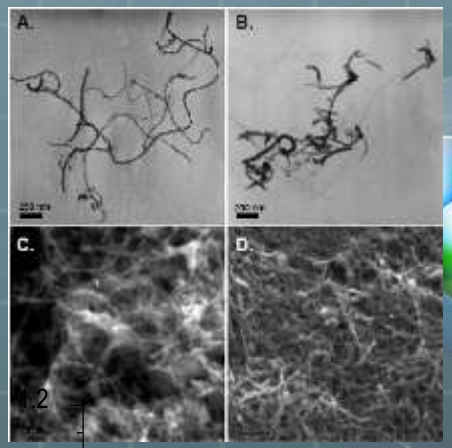


Fig. 3: Transmission electron microscopic images of the CNT–nanocomposites prepared using conditions for small (a–c) or large (d–i) silica nanobeads.

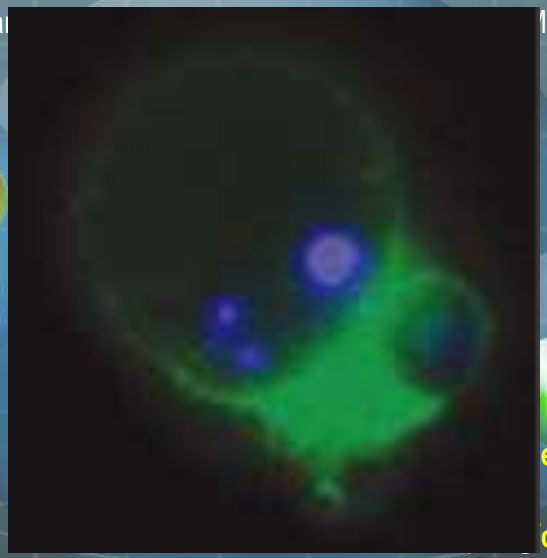
The arrow in panel (a) indicates a nanobead at the tip of the CNT.

The arrow in panel (i) indicates a polymerized silica inside a CNT.

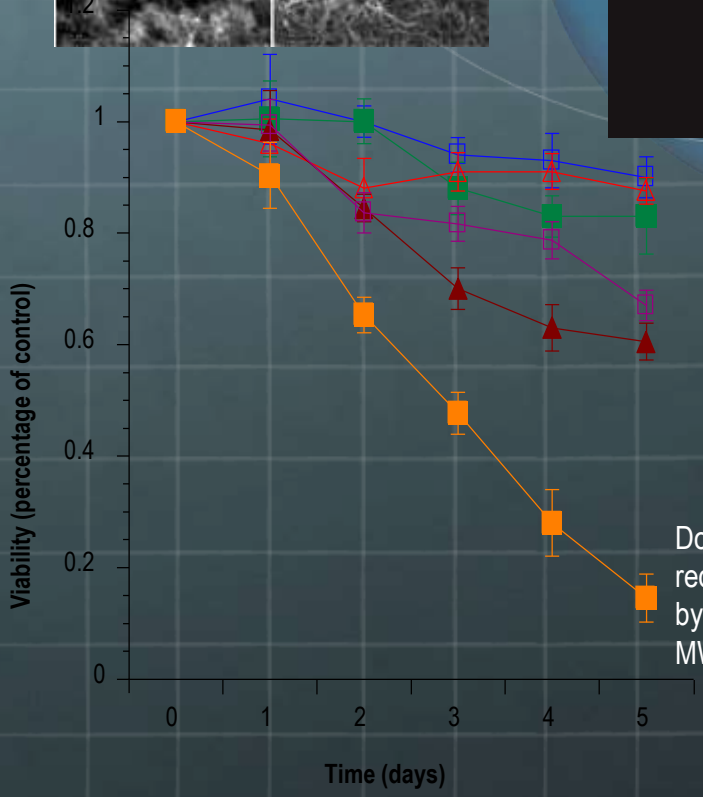
Citotossicita' dei MWNT su cellule Jurkat



TEM (A a… …WNT (A and C) and MWNT-COOH (B and D).

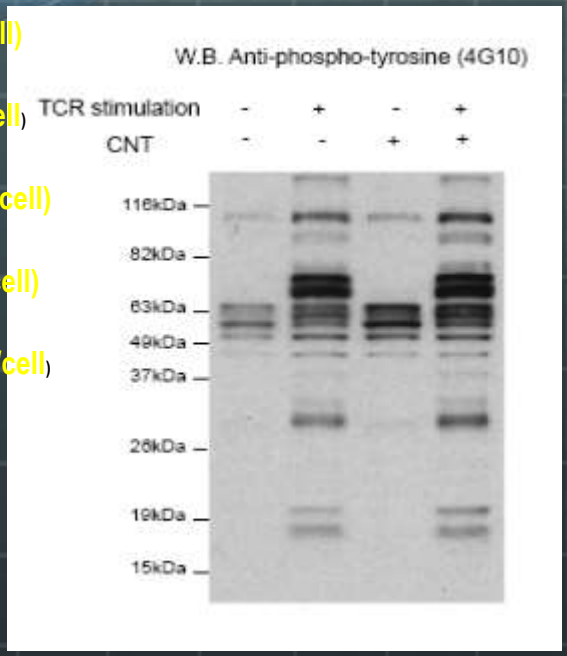


Annexin V positive Jurkat cells show pyknotic nuclear DNA condensation and membrane blebbing, two typical features of apoptotic cells.



Dose- and time-dependent reduction in Jurkat cell viability by carbon black, pristine MWNT and oxidized MWNT.

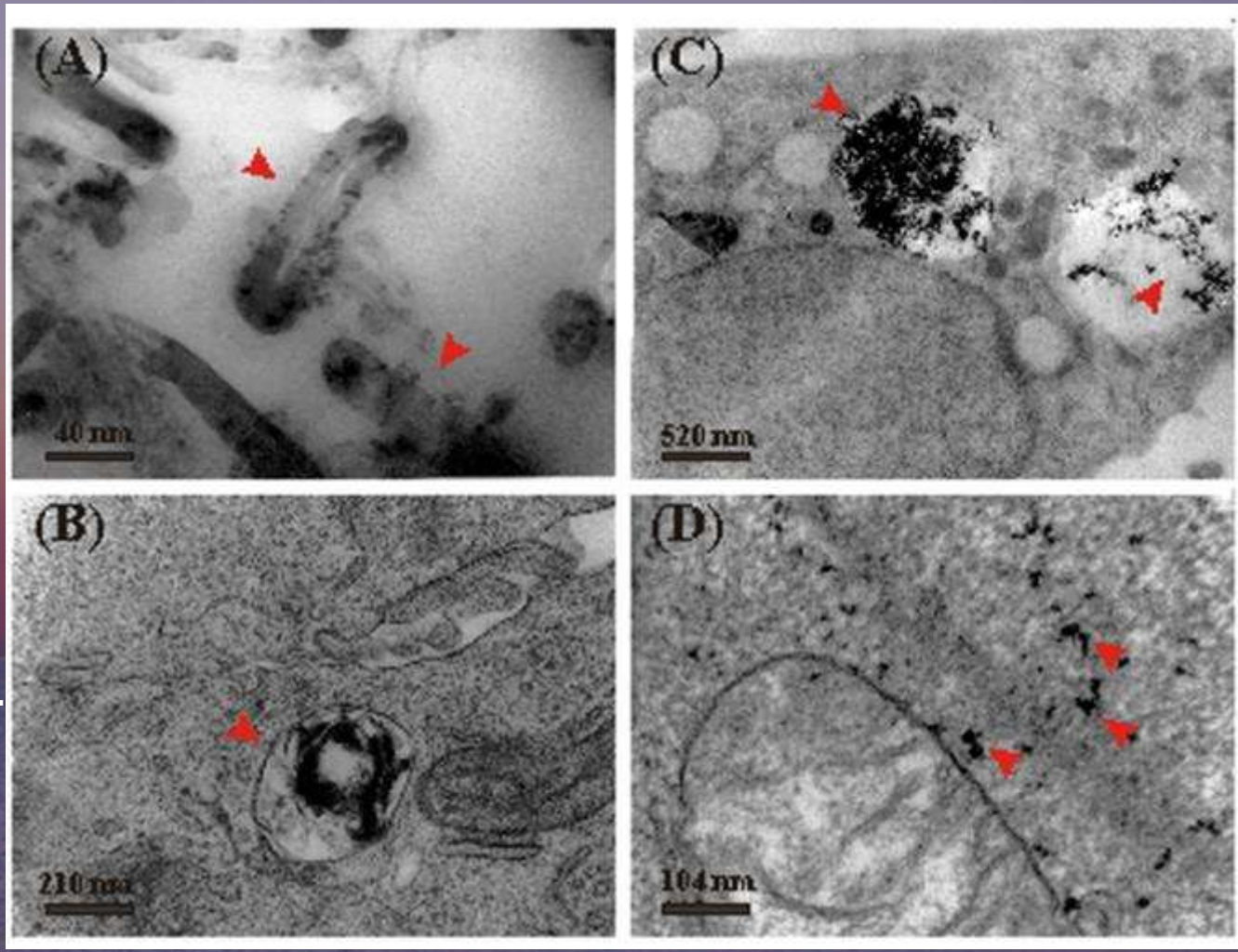
Effects of MWNT-COOH on T cell antigen receptor signaling.



e-mail: bellucci@lnf.infn.it
INFN - Laboratori Nazionali di Frascati

To better understand how MWCNTs functionalized and not could exert their biological effects in MCF-7 cells, we observed their cellular localization by transmission electron microscopy (Fig.)

After 24 hours of treatment all types of MWCNTs showed a low efficiency of cellular internalization. Differences in MWCNTs cellular distribution: MWCNTs were present into the cytosol both as scattered particles and in vesicules while MWCNTs-COOH and MWCNTs-OH were mainly found in vesicles. After 72 hours of treatment the efficiency of cellular internalization of all types of MWCNTs was really increased. MWCNTs were still present into the cytosol both as scattered particles and in vesicules; MWCNTs-COOH were detected only in vesicles as aggregates, whereas MWCNTs-OH were detected only as scattered particles in the cytosol and did not form any aggregate:



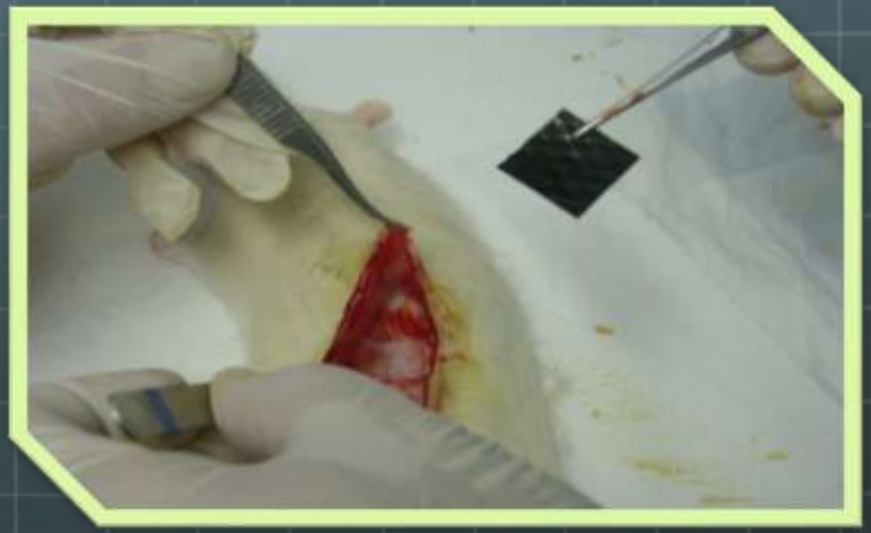
consistent with the above remark that MWCNTs-OH do not form (large) aggregates in acqueous suspension, after sonication.

.

Transmission electron microscopy of (A) MWCNTs; (B) MWCNTs inside MCF-7 cellular vesicle; (C) MWCNTs-COOH inside MCF-7 cellular vesicles; (D) cytosolic distribution of MWCNTs-OH in MCF-7 cells. Red arrowheads indicate MWCNTs functionalized and not.

Experimental

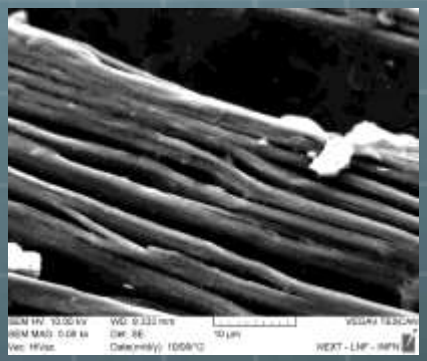
Shiny side of Buckypaper sticks less on the biology tissue than rough face!



@INFN: a novel fabrication technique

Istituto Nazionale di Fisica Nucleare (INFN), LNF-Frascati (Rome), Italy - NEXT Nanotec. group

INTERCALATION OF A GRAPHITE CRYSTAL

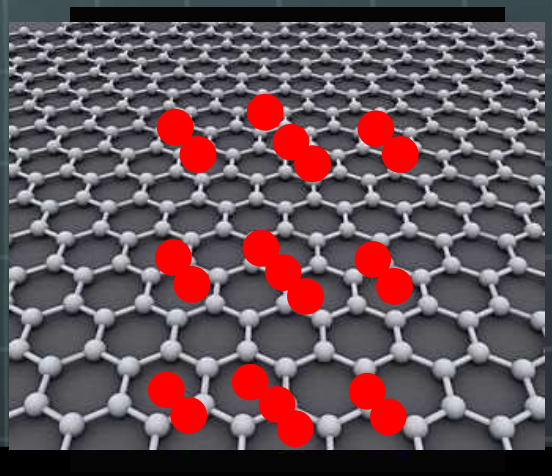


- **Thermal expansion by MICROWAVE OVEN**
- **Cheap** (homemade microwave oven)
- **Fast** (10 sec of irradiation)
- **Eco-friendly** (solvent-free)

Multilayered structure with **intercalant agents** (**sulfates, nitrates**) between graphite planes

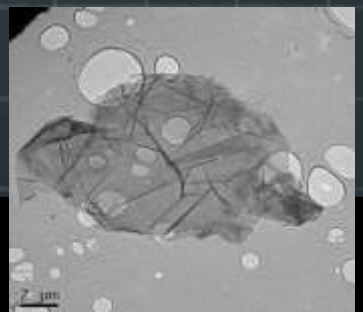
- Intercalated agents
- Vaporized Intercalated agents

- Mechanism of expansion
- **Thermal shock** induced by irradiation **vaporize** the intercalated agents
- Vapor produce a **pressure** among planes
- **Expansion** of **graphene plates**



After expansion

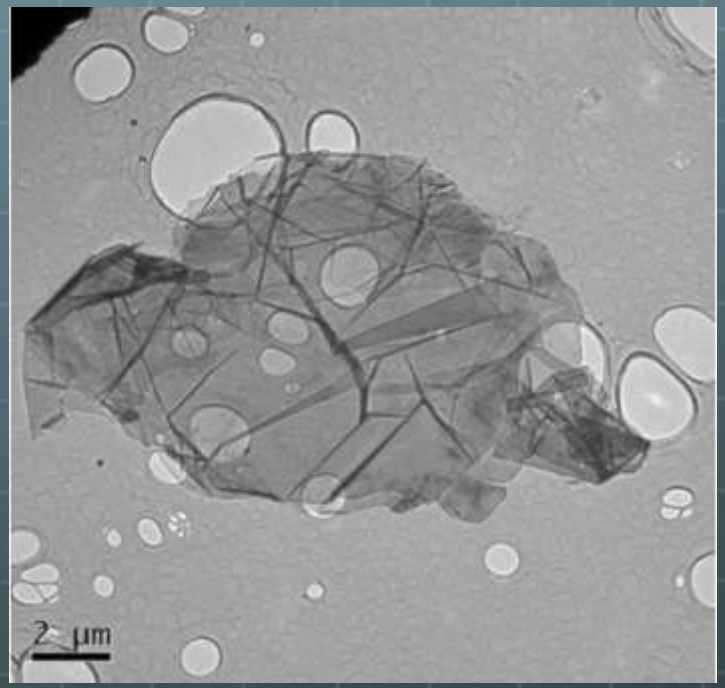
- **Large graphene plates**
- **with: 6±5 layers**

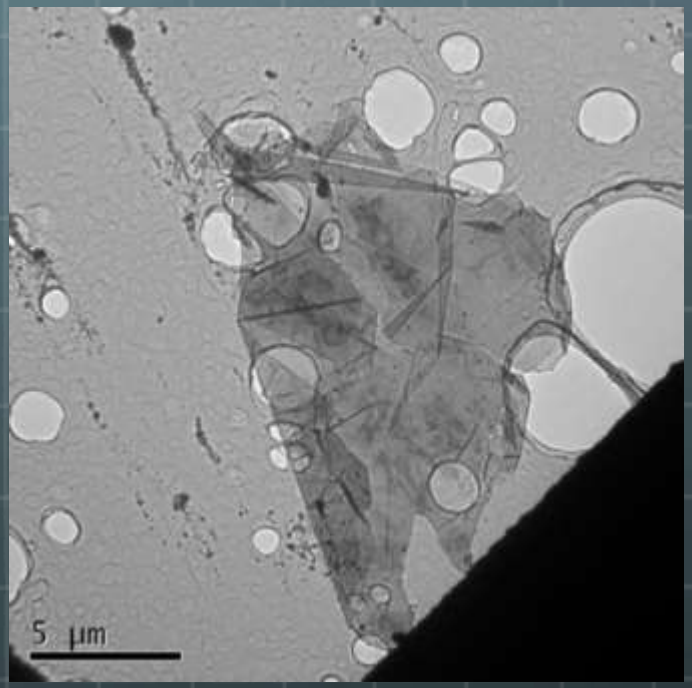


e-mail: bellucci@lnf.infn.it

@INFN: a novel fabrication technique

Few Layer Graphene (FLG)





TEM images show particles with the two dimensional lateral sides having sizes about tens **micrometers** and a thickness some **2 nm**

- **Very large particle area**
- **Thickness: 6±5 planes**

e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati

Delivery and imaging of miRNAs by multifunctional carbon nanotubes and circulating miRNAs as innovative therapeutic and diagnostic tools for pediatric pulmonary hypertension

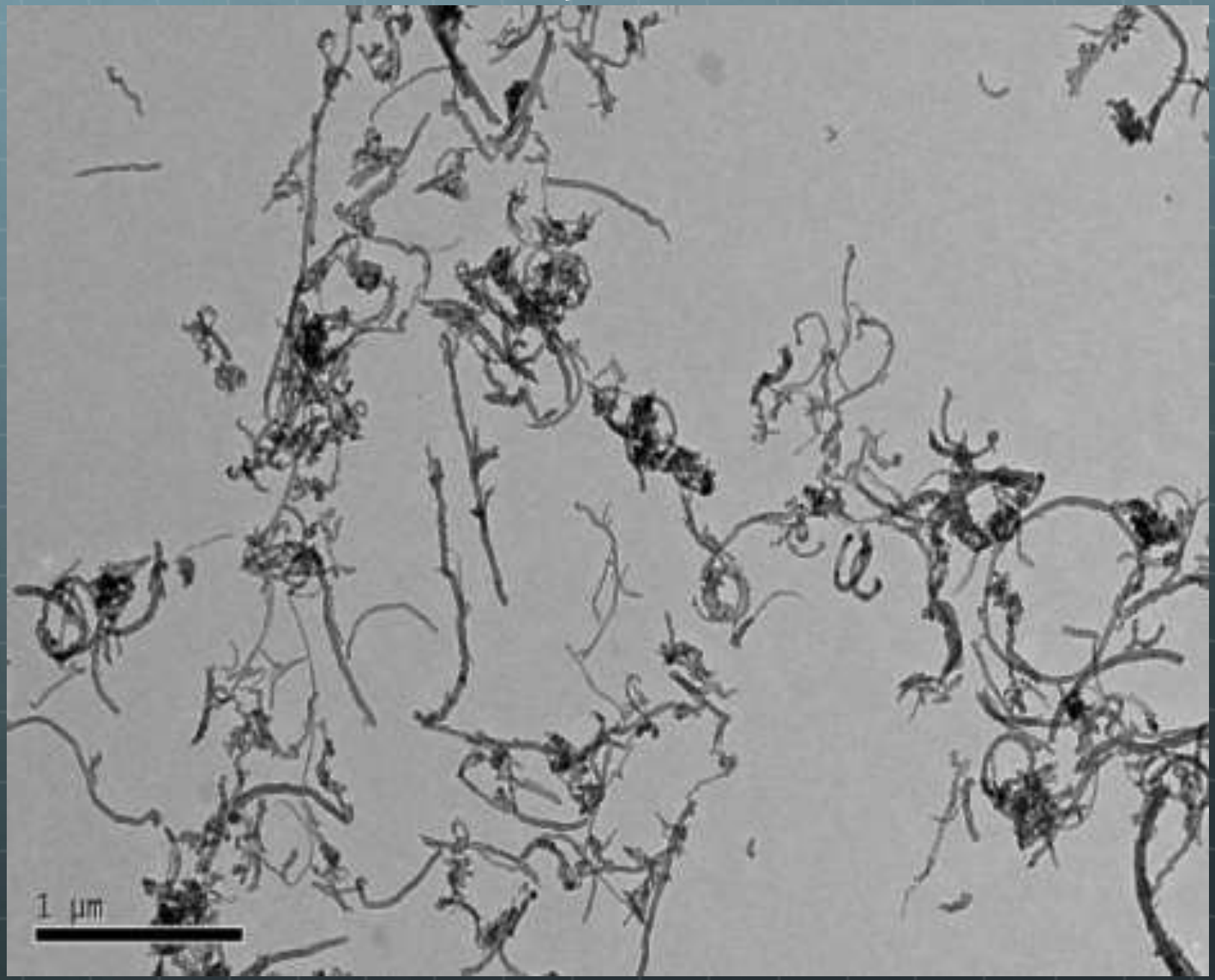
Ricerca Finalizzata

Lab. Microarrays

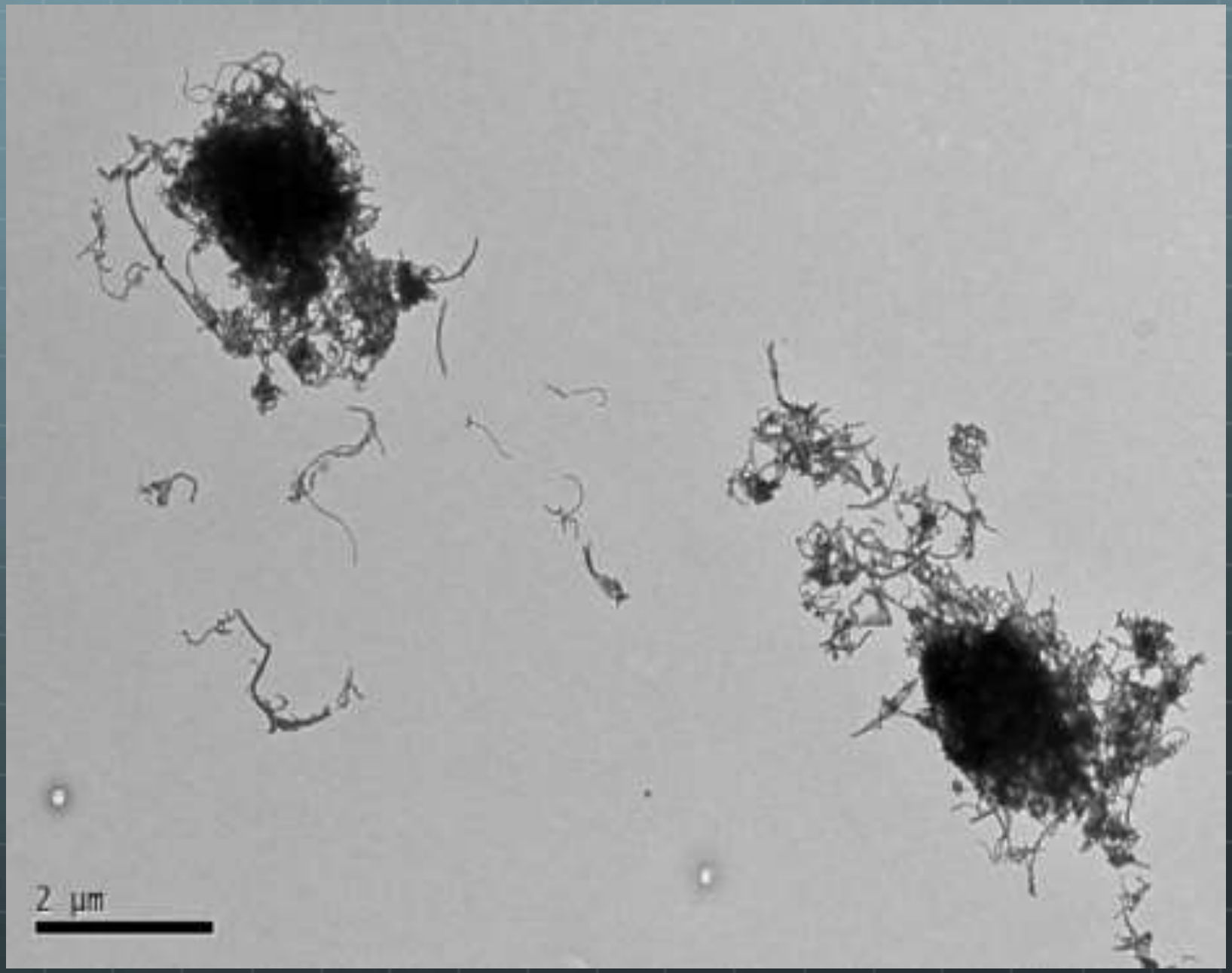
STEFANO BELLUCCI
INFN-Laboratori Nazionali di Frascati.

ANDREA CAPORALI
University of Edinburgh, UK.

PEI25-CNT

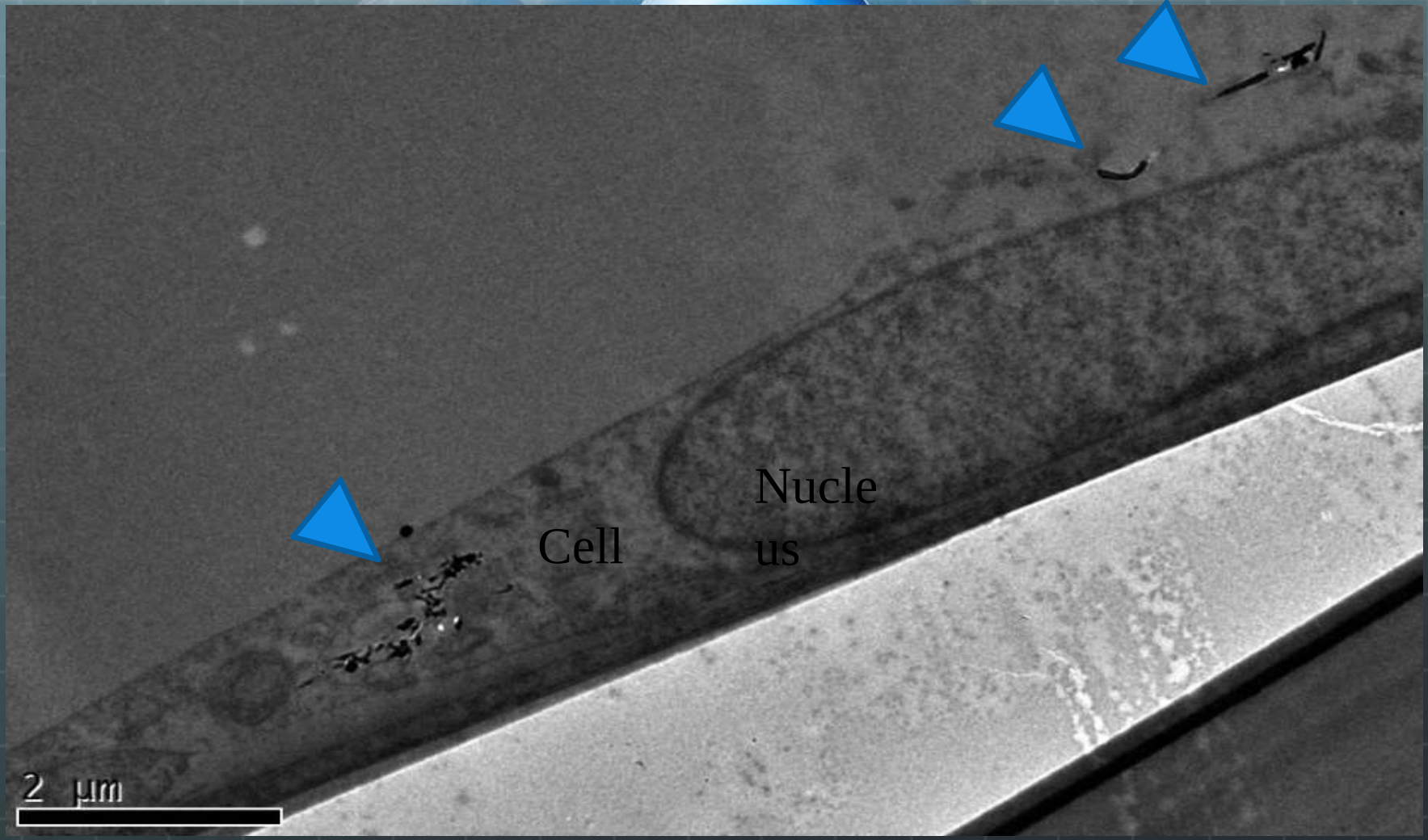


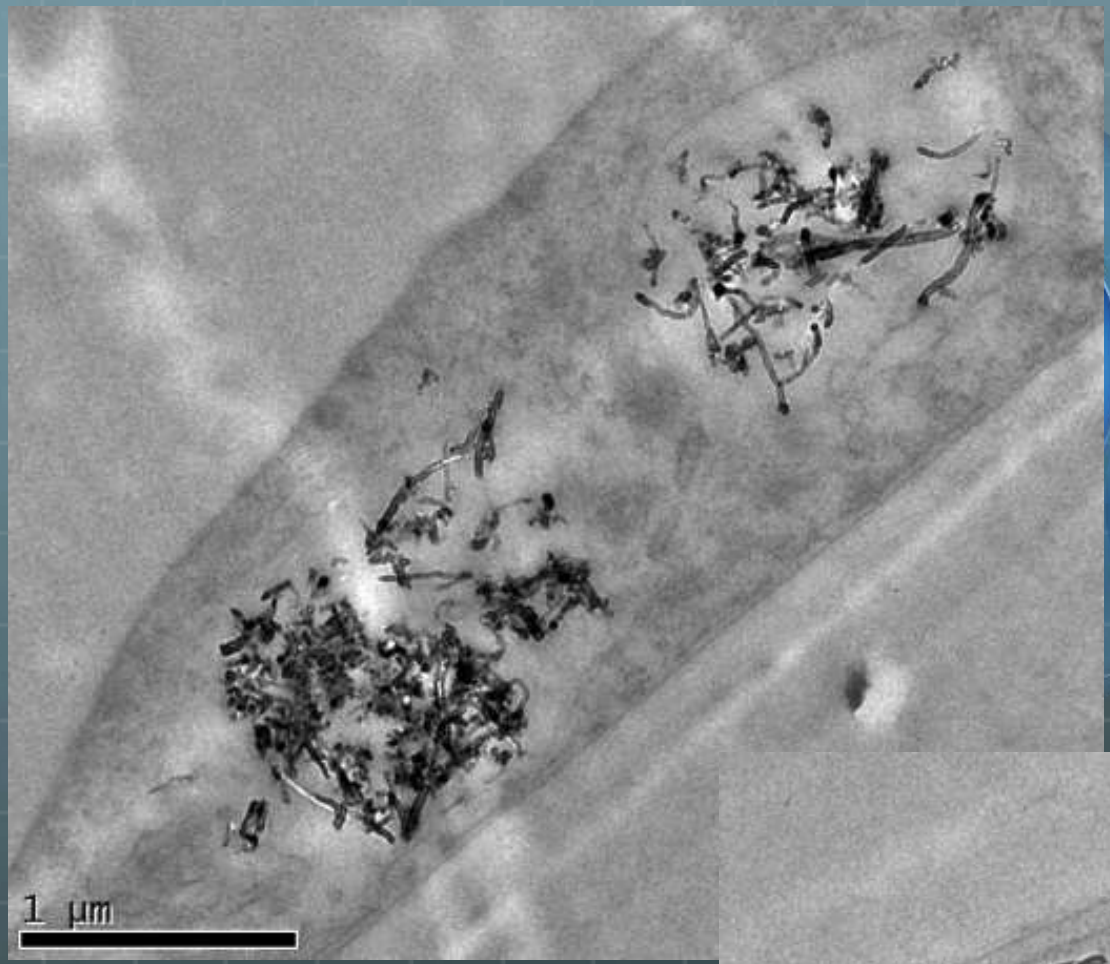
PAMAM-CNT

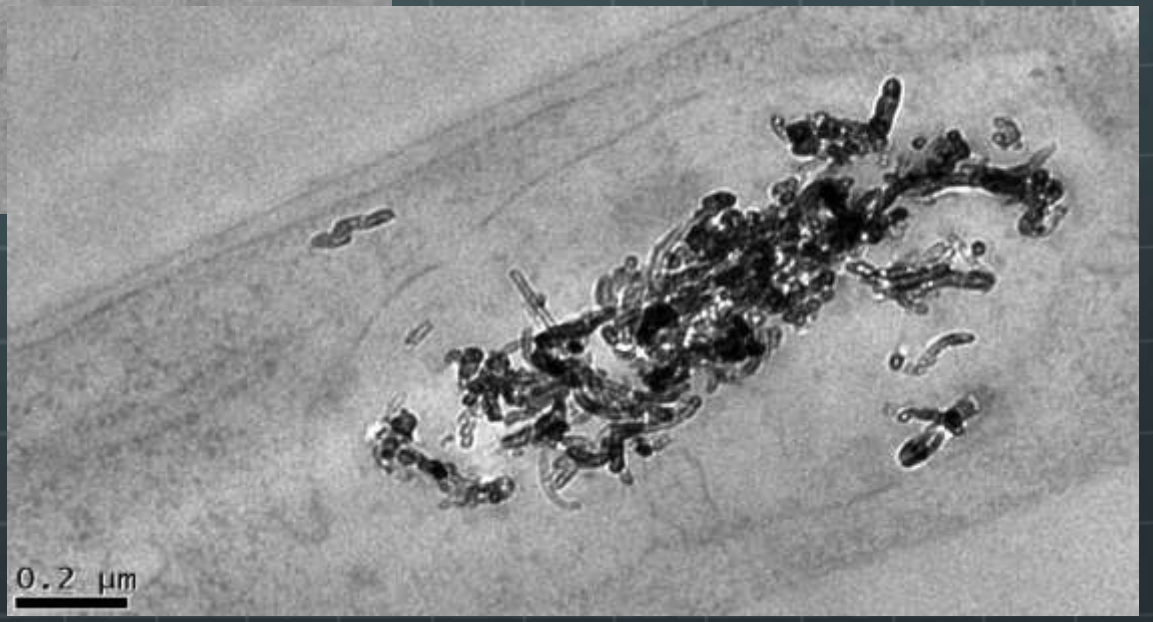


Internalization of CNTs

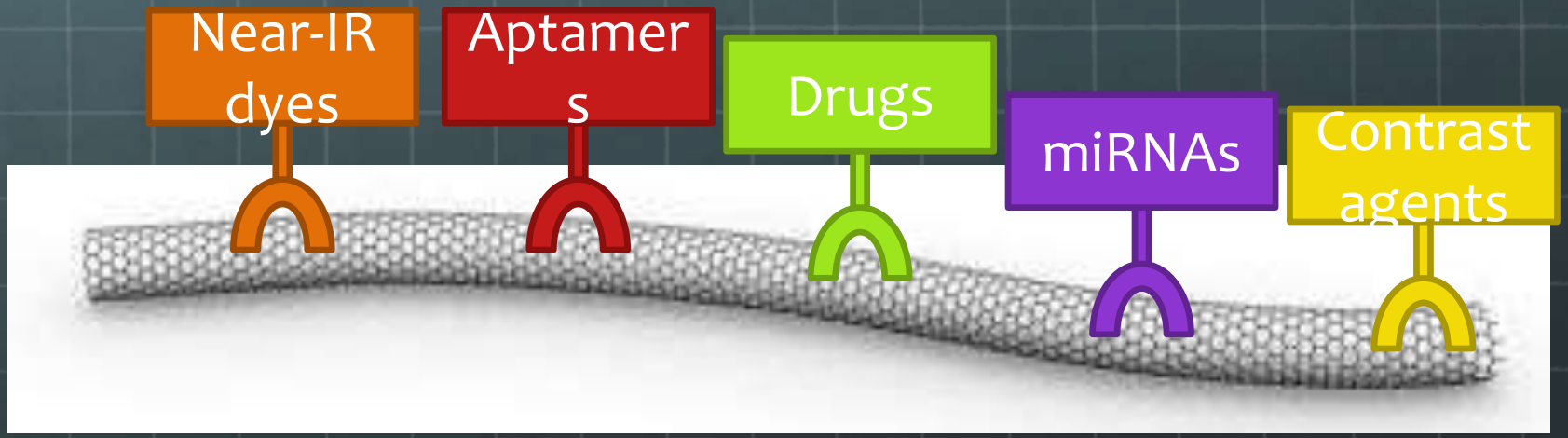
CNTs both inside and outside cells.



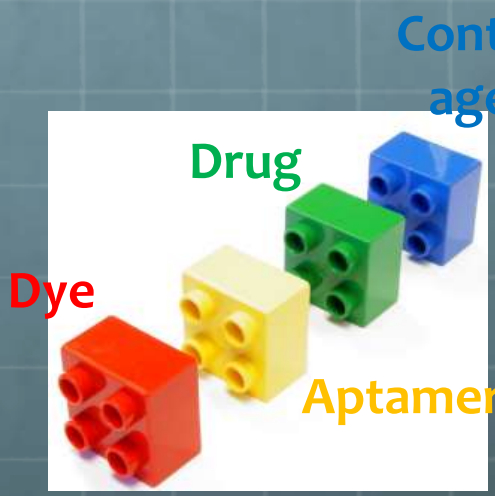

1 µm


0.2 µm

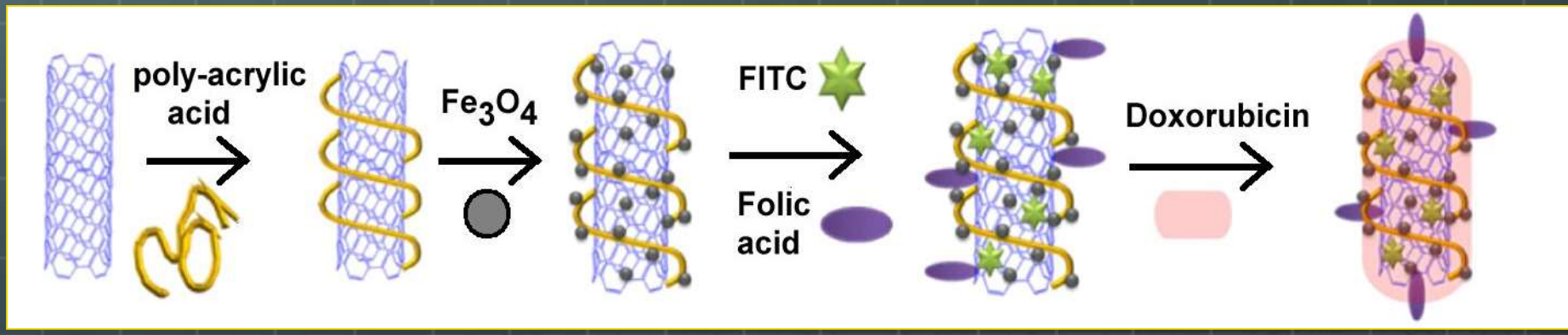
Looking forward



Looking forward



Multifunctional Drug Delivery Vector



Lu, Y. J et al. 2012. Colloids Surf. B Biointerfaces, 89, 1-9.

Grazie
per la vostra attenzione!

e-mail: bellucci@lnf.infn.it

INFN - Laboratori Nazionali di Frascati