NANOMATERIALS FOR BIO-MEDICINE

Stefano Bellucci, PhD, Habil. Prof., First Researcher, Head of NEXT Group

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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 primarily concentrated on particle physics.
Carbon nanotubes synthesis
Graphene synthesis
Microscopy SEM / AFM Raman/FTIR
Structural & Transport Modelling & simulation
Toxicology & Drug delivery
Interconnects
Field Emission
Nanocomposites
(Bio) sensors

ACTIVITY 360° ON NANOTECHNOLOGY
INTRODUCTION TO NANOPARTICLES AND THEIR USES
APPLICATIONS OF NANOPARTICLES

- Heat retaining textiles
- Self-cleaning textiles
- Anti-stain textiles
- Wound dressing
- Dental ceramics
- Bone growth
- Bio-composites
- Molecular tagging
- Drug delivery
- MRI contrast agents
- Imaging
- Antibacterial
- Nutraceuticals
- Antioxidants
- Fungicides
- Interactive food
- Food processing catalysts
- Food quality/safety analysis sensors
- Gas-barrier coatings
- Antifouling coatings
- UV blocking coatings
- Antimicrobial coatings

- Hydrogen storage materials
- Lithium ion battery electrodes
- Medical textiles
- Drug delivery
- Cancer therapy
- Hyperthermic treatment
- Drug delivery
- MRI contrast agents
- Imaging
- Antibacterial
- Nutraceuticals
- Antioxidants
- Fungicides
- Interactive food
- Food processing catalysts
- Food quality/safety analysis sensors
- Gas-barrier coatings
- Antifouling coatings
- UV blocking coatings
- Antimicrobial coatings

- Fuel cell catalysts
- Environmental catalysts
- Waste water treatment
- Quantum computers
- High density data storage
- Ferro fluids
- Nanoscale patterning of electronic circuits
- Industrial Catalysts
- Functional nanocomposites
- Food packaging
- Food processing catalysts
- Food quality/safety analysis sensors
- Gas-barrier coatings
- Antifouling coatings
- UV blocking coatings
- Antimicrobial coatings

- Paint-on solar cells
- Dye sensitised solar cells
- Automotive catalysts
- Pollutant scavengers
- Pollution monitoring sensors
- Quantum lasers
- High power magnets
- Single electron transistors
- High sensitive sensors
- Chemical sensors
- Gas sensors
- Nano-inks
- Transparent conductive polymer films
- Transparent conductive polymer films
- Nano-phosphors for display
- Wear-resistant coatings
- Self-cleaning building surface
- UV blocking coatings
- Antimicrobial coatings

- Hydrogen production photocatalysts
- Fuel additive catalysts
- Environmental catalysts
- Waste water treatment
- Quantum computers
- High density data storage
- Ferro fluids
- Nanoscale patterning of electronic circuits
- Industrial Catalysts
- Functional nanocomposites
- Food packaging
- Food processing catalysts
- Food quality/safety analysis sensors
- Gas-barrier coatings
- Antifouling coatings
- UV blocking coatings
- Antimicrobial coatings

- Textiles
- Renewable Energy
- Biomedical
- Environment
- Electronics
- Industrial
- Food Agriculture
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
THE BASICS OF NANOTECHNOLOGIES

• You work at the atomic, molecular, and supramolecular levels...

• The scale of lengths involved is approximately between 1 and 100 nm

• The aim is the creation and use of materials, devices, systems with fundamentally innovative properties and functions, due to their very small (nanoscopic) structure.
Physical-chemical properties

1. Surface to volume ratio: extremely large surface area;

2. High number of surface atoms (a particle of 300 nm has 5% of the surface atoms, one of 30 nm has got 50%).
New Properties of Matter Based on Size and Surface Area

Each side = 1 M
Mass ≈ 43,000 lb
Surface Area (SA) = 6 m²
≈ 8 ft x 8 ft room

Each side = 1/4 M
Mass ≈ 43,000 lb
SA = 24 m²

Each side = 1 nM
Mass ≈ 43,000 lb
SA = 6 billion m² ≈ 2500 miles²
State of Delaware = 2490 miles²
NANOSCOPIC SCALE

- Nanometer = 1 million-th of millimeter
- One Nanometer is as big as a layer of 3-5 atoms
Let's start with a man... we get to a mosquito... we come to his eyes... and we finally get to the nanometer!!!
“Top – Down”

“Bottom – Up”
“BOTTOM-UP” APPROACH

- A concept introduced by Eric Drexler
- Process of constructing systems atom by atom, to the aim of
  - minimizing waste
  - increasing reactivity

e-mail: bellucci@lnf.infn.it
First example of nanotechnology!

Lycurgus Cup
(IV sec. CE, British Museum)

It has a different coloration when observed in reflection, or in transmission, owing to the presence of nanoparticles of gold and silver.

e-mail: bellucci@lnf.infn.it
Another example of nanotechnology

Metal nanoparticles of different species
In the stained glass windows of medieval churches.

e-mail: bellucci@lnf.infn.it
In 1931, Max Knoll and Ernst Ruska invented the transmission electron microscope (TEM), nearly 34 years after the discovery of the electron by J. J. Thomson. M. Von Ardenna built the first prototype of Scanning Electron Microscope in 1938, followed soon by the first commercial TEM, built by Siemens in 1939. The first commercial SEM was commercialized by Cambridge Instrument Company Inc. in 1965.
Gerd Binnig and Heinrich Rohrer at IBM Zürich introduced a new microscope that is not dependent on wavelength: Scanning Tunneling Microscope (STM), 1981.

Binnig, Quate, and Gerber invented the atomic force microscope for the specific purpose of investigating surfaces on the atomic scale, 1985.

Binnig, Quate, and Gerber in 1990 and formally ushered in the field of atomic force microscopy, 1990.

2013 – The Smallest Film in the World
THE CARBON FAMILY

- C Nanotube
- Graphene
- Diamond
- Graphite
- Fullerene
CARBON NANOTUBES

- Discovered in 1991 by Sumio Iijima, a researcher at Nec Labs in Tsukuba, Japan.
- Hollow cylinders, long and thin; they can be thought of a sheet of graphite (a hexagonal lattice of carbon atoms) rolled up into a cylinder, closed by two fullerene emispheres.

We can distinguish:
- SWNT (Single wall Nanotubes)
  - \( \Phi = 1 \pm 3 \text{ nm} \)
  - \( L = 0.5 \pm 10^4 \mu\text{m} \)
- MWNT (Multi wall Nanotubes)
  - \( \Phi = 5 \pm 200 \text{ nm} \)
  - \( L = 0.5 \pm 200 \mu\text{m} \)
WHAT’S SO SPECIAL IN A C NANOTUBE?

High aspect ratio ($L/\Phi$) $\Rightarrow$ one-dimensional structure

High elastic modulus (up to 1 Tpa) and high tensile strength (150 Gpa).

Ability to carry high currents, without overheating (current density $10^9$ A/cm$^2$).

50000 times thinner than a human hair

High thermal conductivity both at high and at room temperature (1800-6000 W/m*K).

50000 times thinner than a human hair
<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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<tbody>
<tr>
<td>Very simple process. CNTs of high quality and purity, with few defects.</td>
<td>Dispersion in CNTs size. Low amount of CNTs achievable Need for purification from unwanted forms of C (onions, amorphous).</td>
</tr>
<tr>
<td>Long CNTs. Controllable pipe diameters.</td>
<td>Low amount of CNTs achievable.</td>
</tr>
<tr>
<td>Possibility to grow CNTs oriented and according to predefined geometries. High amount of CNTs.</td>
<td>Need for a catalyst for decomposition of hydrocarbons. High density of both local and topological defects.</td>
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**Arc discharge:**

**Laser ablation:**

**Chemical vapour deposition:**

e-mail: bellucci@lnf.infn.it
Synthesis
La Ferrari F2007 was a concentrate of nanotechnology:

• Carbon nanotube brakes
• Car body made of ultra-light material obtained using carbon nanotubes
• Special tyre compound using C nanotubes composites
Nano for Future Transportation & Mobile

Symbiosis Car: Symbiosis Vehicle Runs on Solar Piezoelectric Energy

Samsung Flexible Mobile: display technology known as an OLED (organic light emitting diode) (active matrix light emitting diode) screen. As the OLED pixels create their own light source, they don’t need a back light like LCD screen technology, but the circuitry to control the pixels is fused into glass.
Nanotechnology in Restoration!

Calcium hydroxide nanodispersions used for nanocleaning; TEM Images of two nano-sized particles in suspension: Ca(OH)2 hexagonal (A), CaCO3 prismatic (B)

Beato Angelico’s fresco at San Marco’s Abbey in Florence

INFN - Laboratori Nazionali di Frascati
Water droplet on nano material coating a cotton layer

Nanoparticles having diameter smaller than 100 nm are coating the matrix.
Nano – ENERGY!

thermoelectric power generation

Wake Forest University’s Center for Nanotechnology and Molecular Materials
High UV protection through nanoparticles’ dispersion
USES OF NANOTECHNOLOGIES

• Pervasive and enabling technology

• Utilization of Nanotechnology is found everywhere (ubiquitous technology)

• Solar energy, batteries, weapons, instrumentation design and manufacture... in any application area, nano-technologies could play a role in the future.

• Given the multiplicity of their uses, we must necessarily be concerned about their impact on the environment and human health, in particular on professionally exposed workers.
IMPACT OF NANO ON HEALTH AND ENVIRONMENT
IMPACT ON ENVIRONMENT AND HEALTH

- Possible instability of certain nanostructures
- E.g. potential problem from “fullerene” dissolved in water which can bind to DNA, hence affecting structure, stability and biological functions of DNA molecules
GRAND CHALLENGES OF NANOTECHNOLOGY

• The materials are difficult to handle and it is difficult to keep them stable.

• Understanding the characteristics of nano materials
  • A single particle of silicon does not behave like bulk silicon
  • Dependence on size, shape, and surroundings of the particle (e.g. bio corona)
at synthesis in living organism biological barrier(s)
NANOPARTICLES PRODUCED DURING COMBUSTION PROCESSES

- Epidemiology
- Toxicology

Nanoparticles in use in industry

Nanotechnology
FOR NANOTECHNOLOGIES CURRENTLY .....
**Toxicity**

![Graph showing cell proliferation](image)

**Effects of MWCNTs on the proliferation of the human arterial smooth muscle cells** (hSMCs). The cells were treated with MWCNTs at concentrations from 0.001 to 0.1 mg ml⁻¹ for 24 and 72 h. Cell proliferation was determined by a count performed by a particle count and size analyzer. Each column represents the mean value ± SD of three separate experiments performed in duplicate. * p < 0.01 versus CTRL.

**Carbon nanotubes toxicology and effects on metabolism and immunological modification in vitro and in vivo**

The cytoxicity evaluation of MWCNT buckypaper treatment on human and cancer cells was carried out on human colorectal, breast and leukemic cancer cell lines in vitro, while having no effect on proliferation and viability of normal human arterial smooth muscle cells and human dermal fibroblasts in vitro.

Growth inhibition, cell-cycle alteration and apoptosis in stimulated human peripheral blood lymphocytes by multiwalled carbon nanotube buckypaper, O Zeni, A Sannino, S Romeo, F Micciulla, S Bellucci, MR Scarfi Nanomedicine, 1-10 (2014)

Cytotoxicity of Multiwalled Carbon Nanotube Buckypaper in Human LymphocytesO Zeni, A Sannino, S Romeo, MR Scarfi, L Coderoni, F Micciulla, I Sacco, ... Sensors and Microsystems, 489-493 (2011)

Nanomedicine & Cytotoxicity

Nanomedicine is the preservation and improvement of human health using molecular tools and molecular knowledge of the human body.

Since over two decades the potential environmental and occupational impact is studied of carbon nanotubes, which exist in many different forms and can be chemically modified and/or functionalized with biomolecules.
«ACCIDENTAL» ARTIFICIAL NANOPARTICLES

«Traffic jams, LA California»

«Gulf of Mexico, off-shore oil well burning»

«Bari, Italy, 2006: implosion of Punta Perotti residential complex»
Accidental Exposure to NP originating in combustion processes

Accidental Exposure to newly synthetized materials

Accidental Exposure to newly synthetized and modified/functionalized NP

Deliberate Exposure to NM in biomedicine

THE UNIVERSE OF EXPOSURE TO NANOMATERIALS

NP diesel, soldering fume, termodegradation of plastics

Carbon black, TiO₂

Carbon nanotubes

Dendrimers, fullerenes, quantum dots
ENGINEERED NANOPARTICLES (ENMs)

Nanomedicine as a single cell medicine

...no more windshield wipers...

...or «fingerprints» on displays
Nanotubes as seen by a physicist/chemist

Modified by a pharmacologist

Studied by a biologist

Seen by a physician
NANOMATERIALS CAN BE ALSO MADE BY ORGANIC AND INORGANIC PARTS ....

Possibilities become infinitely many ....
MULTIFUNCTIONAL NANOPARTICLES.

- CAPABILITY TO CARRY ONE OR MORE THERAPEUTIC AGENTS;

- MOLECULES FOR TARGETING (CONJUGATED ANTIBODIES OR OTHER AGENTS FOR RECOGNITION);

- ELEMENTS FOR SIGNAL AMPLIFYING AND FOR RECOGNITION;

- ELEMENTS FOR STABILIZATION (CONSERVATION IN CIRCLE) AND FOR ENHANCING CAPABILITY TO PENETRATE
Synthesis and characterization

Fig 1: Multi-walled carbon nanotubes before (a) and after (b) oxidation in nitric acid.

The oxidized CNT (CNT-COOH) were shorter and straighter (Fig. 1b).
Their carboxylic acid groups greatly facilitated their dispersion in aqueous solutions, as well as their further functionalization (Fig. 2a).

Synthesis and characterization

Fig. 2: Scheme for preparing the CNT–nanoparticle composite.

(a) Oxidation and preparation of the CNT-APTEOS precursor.

(b) Formation of silica nanobeads in reverse micelles in a water-in-oil microemulsion. Nanobeads are covalently linked to the CNT only at locations functionalized with triethoxy-silane groups (dots inside the micelles), while the bare graphitic wall of the pristine CNT did not associate with reverse micelles.
Synthesis and characterization

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.
Cytotoxicity of MWNT: apoptosis on PBL

CNTs induce apoptosis of human T cells.

A. Immunofluorescence images of untreated Jurkat cells (upper panels) and cells treated 24 h with oxidized MWNT.

B. At higher magnification annexin V positive Jurkat cells show pyknotic nuclear DNA condensation and membrane blebbing, two typical features of apoptotic cell death.

C. Time course of Jurkat cell apoptosis after treatment with 1 ng/cell (open triangles) or 10 ng/cell (filled triangles) of oxidized MWNT.

D. Time course of human peripheral blood lymphocytes (PBL) apoptosis after treatment with 1 ng/cell (open) or 10 ng/cell (filled) of pristine (squares) or oxidized (triangles) MWNT.
SAFE USE OF NANOTECH IN HEALTH
EXAMPLE BIOCEMENT 4 BONES

Microfractures: skull, vertebrae
BIOCEMENT: DENTAL APPLICATIONS

Graphical representation; the illustration purposes only.
Iron oxide nanoparticles, with diameters 10,000 times smaller than that of a human hair, 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 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.
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.
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
Subsequently the new technique was applied on 15 patients suffering from *Glioblastoma multiforme*, 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.
TERANOSTICS

a) Magnetic induction coil
b) Untreated control, Core-shell nanoparticle, Feridex, Doxorubicin
Before treatment, 18 days after treatment
c) Tumour volume (V/V₀) over time
Core-shell nanoparticle hyperthermia, Feridex hyperthermia, Doxorubicin hyperthermia, a.c. field only, Core-shell nanoparticle only, Untreated control

d) Core-shell nanoparticle hyperthermia
50µm, Untreated control

e) Tumour volume (V/V₀) 18 days after treatment
Core-shell nanoparticle hyperthermia, Doxorubicin hyperthermia, Feridex hyperthermia

ROS, photosensitizer, magnetic nanoparticles, tumor depletion
DIAGNOSTICS: LAB ON CHIP
LAB ON CHIP

Traditional Lab vs. On-chip lab

Fusion and sorting of two trains of droplets

Railroad-like channel Guiding track
SENSORS BASED ON RAMAN SPECTROSCOPY
Wireless biosensors for homeland security

Analyte Detection
BIOSENSORS: DNA CHIP

Elements of a Biosensor

Samples
- Cell Cultures
- Human Samples (Blood, Urine, Saliva)
- Food Samples
- Environmental Samples (Air, Water, Soil, Vegetation)

Transducers
- Nucleic Acids
- Cells
- Antibodies
- Enzymes
- Nanowire Array
- Nanoparticles
- Electrodes
- a) Bioreceptor(s)
- b) Electrical Interface(s)

Electronic System
- FET Devices
- c) Signal Amplifier
- d) Signal Processor
- e) Display

Graph showing Hybridization Time vs. Signal Output

Switch to TE buffer

100
200
300
400
50
10
15
20
Hybridization Time (min)
Sensing

Electrochemical sensing using composite coatings based on carbon nanostructures

Cyclic Voltammetry and SEM images of nanocomposite Epoxy-CNT 10%

Modification of screen printed electrodes (SPE) with nanocomposite materials

CV and SEM images of nanocomposite Epoxy-GNP 10%

CV and –SEM images of nanocomposite Epoxy-CNT-NH$_2$ 10%

SPE modified with Epoxy-CNT-NH$_2$ 10% and Epoxy-CNT-NH$_2$ 10% most sensitive than SPE unmodified
Nanocomposite based photonic crystal sensors of biological and chemical agents

NEXT group @INFN Frascati, in collaboration with the National Academy of Science of Kiev and the Lviv Polytechnic in Ukraine and with the Fraunhofer Institute of Potsdam-Golm in Germany, proposed developing cheap, yet effective photonic crystal (PC) structures, formed by a periodic distribution of nanoparticles (NP) in polymer matrix for PC powered sensor applications and fluorescent and Raman spectroscopy, for highly sensitive detection of chemical and biological agents. The volume PC structures will be fabricated using holographic method in original photopolymer nanocomposites.

Figure 1 – White light diffraction by polymer gratings—Ag NP (a), LaPO$_4$ NP (b), TiO$_2$ NP (c)
NANOVECTORS FOR DRUG DELIVERY
Targeted Nanodrugs for Cancer Therapy: Prospects and Challenges

Massimo Bottini1,2,3, Cristiano Sacchetelli1,4, Antonio Pietroistiti5, Stefano Bellucci3, Andrea Magrini5, Nicola Rosato5, and Nunzio Bottini6,7

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

Targeted Nanodrugs for Cancer Therapy: Prospects and Challenges

Massimo Bottini holds a degree in Electronic Engineering and a Ph.D. in Sensory 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 Sacchetelli 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. Romiti 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 Pietroistiti 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 MOODENA, aimed at quantitative nanomaterial-toxity-relationship modeling to facilitate risk assessment of novel nanomaterials, and in the NanoLeg, 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 (1981-1988) 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 in 1997 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-NanoER—Institutional Development of Applied Nanoelectromechanics: Silicon in ERA- Widening,” “Nanomic” “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-Dean 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.
DRUG DELIVERY SYSTEMS

Liposomes
- Encapsulated hydrophilic drugs
- Lipid Bilayer

Nanosphere
- Encapsulated Drug
- Lipophilic drugs

Nanostructure & Linear polymers
- Conjugated Drug

Dendrimer
- Drug molecule
- Targeting entity or linking agent
When a drug is swallowed, this is absorbed by the digestive apparatus and reversed inside the systemic circulation (blood) that carries it for the entire body. This cannot reach the brain, owing to the screening effect of the blood-brain barrier (BBB) that allows the passage of very few molecules.
WHAT IF THE DRUG IS FOR CURING NEUROLOGICAL DISEASES?

THE DRUG CROSSES THE MEMBRANE AND REACHES THE BRAIN

IT TAKES CARE OF THE PATHOLOGY INDIRECTLY BY NOT USING THE APPROPRIATE DRUG

COLLATERAL EFFECTS

INVASIVE CARE:
- LUMBAR INJECTION
- OPEN THE HEAD

OUCH!!
AN ALTERNATIVE WAY THAT WOULD ALLOW TO DELIVER ANY TYPE OF DRUG TO THE BRAIN EXISTS. PASSING THROUGH THE NOSE, EXPLOITING THE AXONIC TERMINATIONS OF THE OLFACTORY BULB.

USING 2 TRANSPORT ROUTES:
• AXONAL TRANSPORT
• TRANSPORT BETWEEN SUPPORT CELLS
USING AEROSOL IT IS POSSIBLE TO OBTAIN A SELF-ADMINISTRATION

STEP 1: DENDRITES ABSORPTION
STEP 2: AXONALLY PASS
STEP 3: STREAM INTO THE BRAIN

GRAPHICAL REPRESENTATION OF AXONALLY-MEDIATED TRANSPORT
THE MOLECULES IN THE NOSE ARE QUICKLY ELIMINATED BY MUCOCILIAR CLEARENCE. THE CELLS OF THE NOSE ARE COVERED BY CILIA THAT MOVE IN A SYNCHRONOUS WAY, TO ELIMINATE THE DRUG TOWARDS THE RHINOPHARYNX.

MUCOADHESIVE NANOVECTORS CAN BE USED TO ENCAPSULE THE DRUG. THIS PERMITS TO INCREASE THE RETENTION TIME IN THE NASAL CAVITY, THUS ALLOWING THE DRUG TO REACH THE TARGET.
Delivery and imaging of miRNAs by multifunctional carbon nanotubes and circulating miRNAs as innovative therapeutic and diagnostic tools for pediatric pulmonary hypertension
Current applications (use of bulk nanotubes):
- As composite fibers embedded in polymers to improve the mechanical, thermal and electrical properties of the bulk product.
- As tips for atomic force microscope probes.

In the biomedical field the use of CNTs is further limited by their insolubility in aqueous solutions, by their intrinsic toxicity and in some cases by safety regulations.

AIM: Develop novel non-toxic CNT-based vectors for nucleic acid delivery in human cells (i.e. endothelial cells).
Delivery of miRNAs in endothelial cells

PEI-CNT-pre-miR-Cy3

HUVEC

PAMAM-CNT-pre-miR-Cy3

HUVEC
Intracellular localization

(i) 
Nucleus
Cytoplasm

(ii) 
Nucleus
Cytoplasm

(iii) 
Vacuole

(iv) 
Vacuole
In vivo Delivery

Sponge implant model. The sponge-induced inflammatory angiogenesis consists of the implantation (in mice) of a synthetic polymer in subcutaneous sites. This model can be used as controlled sustained-release delivery system of therapeutic agents.

PERSPECTIVES
- Therapeutic angiogenesis
- Vascular Remodeling
QUESTIONS?

Thanks for your attention

bellucci@lnf.infn.it

QUESTIONS?

Changes
NEXT EXIT

Laboratory of Nanotechnology

NEXT

QUESTIONS?

Thanks for your attention

bellucci@lnf.infn.it