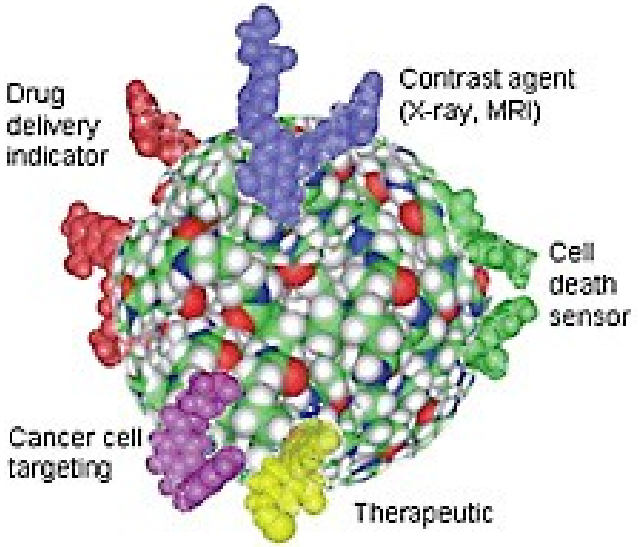
Lectures on Medical Biophysics

Department of Biophysics, Medical Faculty,
Masaryk University in Brno

Nanomedical Devices

(a lecture for future)



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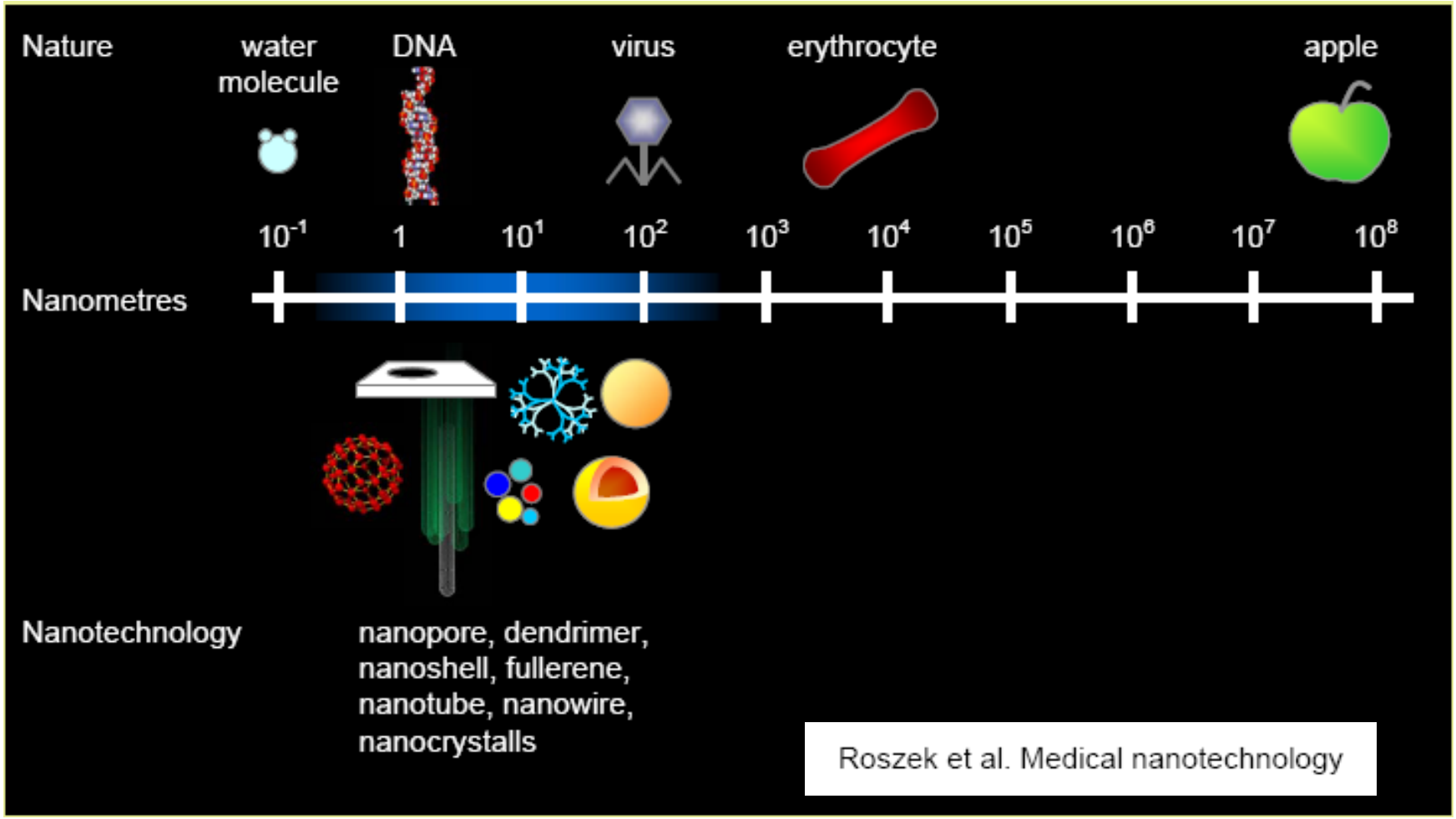
Basics

- Nanomedical devices - definition: biomedical devices at the scale 1 - 100nm
- Very multidisciplinary
- Promise:
  - New methods for prevention, diagnosis, therapy
  - Daily screening of health (very fast Point Of Care – POC - testing)
  - Therapy tailored to the individual patient

How much is a nanometer?



Notice much smaller than RBC

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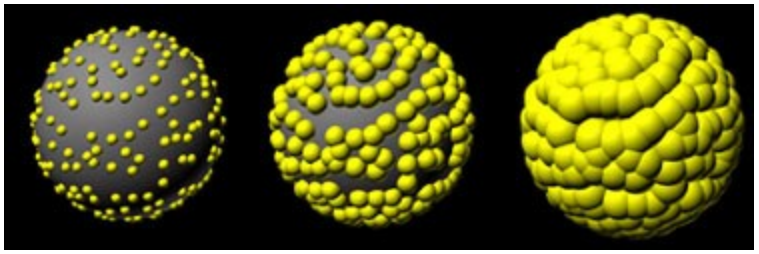
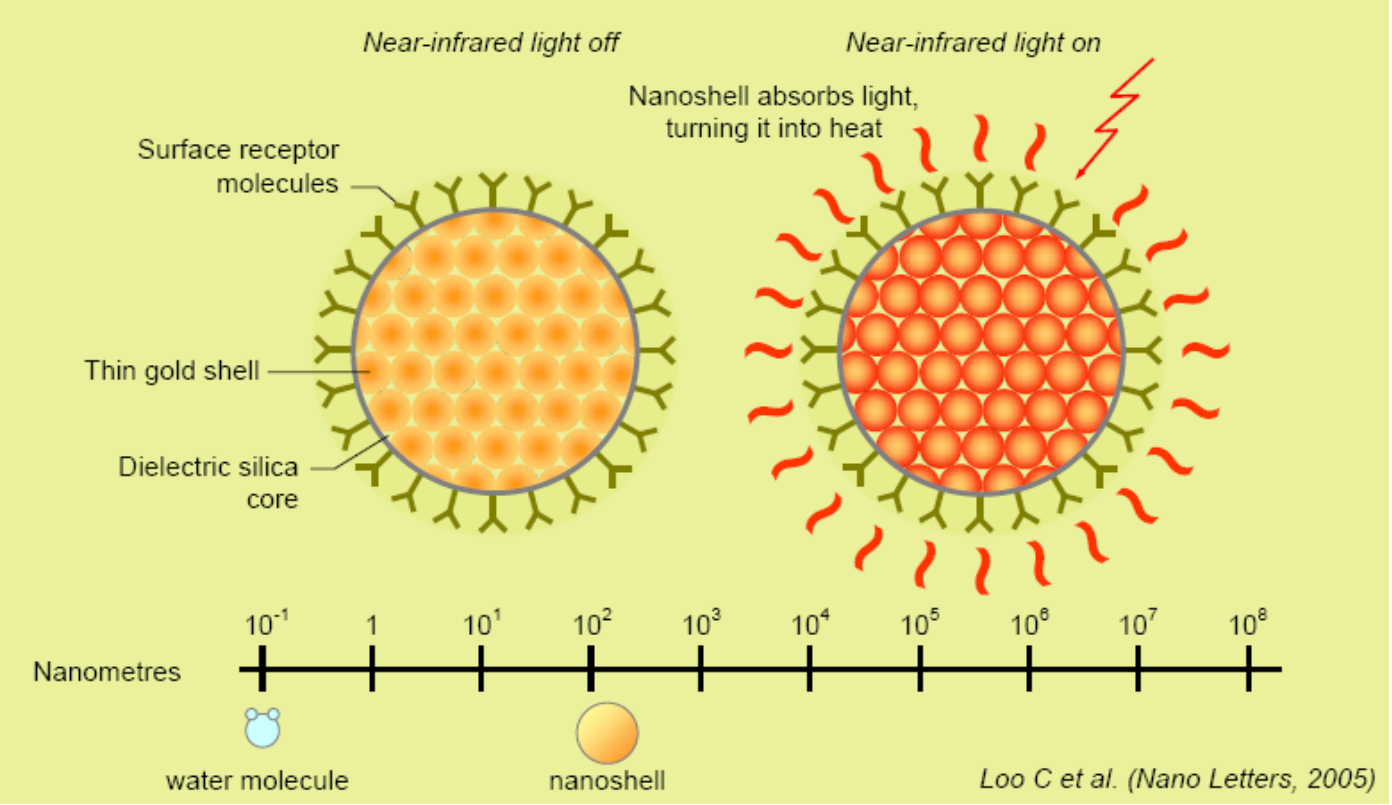
Nanoshell

- A nanoshell is composed of a spherical hollow shell of insulator surrounded by a conducting shell of a few nanometer in thickness.
- By varying the thickness of the conducting shell one can precisely tune the electric and optical properties of nanoshells e.g., make them absorb a certain wavelength of light



Computer simulation depicts growth of gold nanoshell: a silica (glass) spherical core covered with a layer of gold. Gold is a biocompatible compound, making it a useful material for medical applications.

Courtesy N. Halas



Nanoshells: Medical Applications - Photothermal Tumor Ablation

- The nanoshells are coated with receptors that bind to tumor cells and are simply injected into the bloodstream. Once delivered to a tumor, near infrared light is shone through the skin (near IR is not attenuated much by tissue). The nanoshells absorb the IR and convert it to heat with incredible efficiency. This raises the temperature of the local environment of the tumor cells by 10-20 degrees and the cells die. Advantage: zero toxic effects (unlike chemotherapy) no ionizing radiation (like radiotherapy).

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Nanoshells: Medical Applications - Single Molecule Raman Spectroscopy

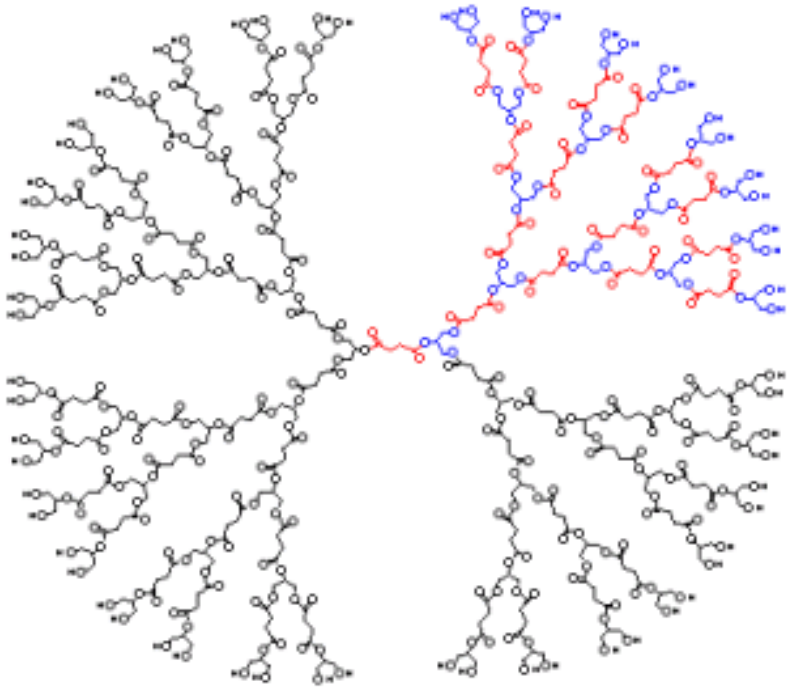
- Scientists have long known that they could boost the Raman light emissions from a sample by the addition of colloidal particles to a sample. Nanoshells are colloids and can increase the Raman signal by *1000 million* times. In this way it is possible to characterize *single* molecules (such as environmental contaminants, chemical or biological toxins and even viruses).
- Advantages: very high sensitivity, high levels of multiplexing (simultaneous measurement of many biomolecules), ability to perform detection in blood and other biological matrices.

Nanoshells: Medical Applications - Delivering Insulin

- Nanoshells loaded with insulin would be injected under the skin, where they would stay for months. To release the drug, patients would use a pen-sized IR laser over the skin at the injection site.

Dendrimers

- Dendrimers are globular shaped polymers composed of branched repeating units emitting from a central core (like a tree, snowflake).
- Biodendrimers are dendrimers comprised of repeating units known to be biocompatible or biodegradable in vivo to natural metabolites.
- The cavities present in dendrimers can be used as binding sites for smaller molecules - effectively the dendrite becomes a nanosized ‘container’ for various molecules.



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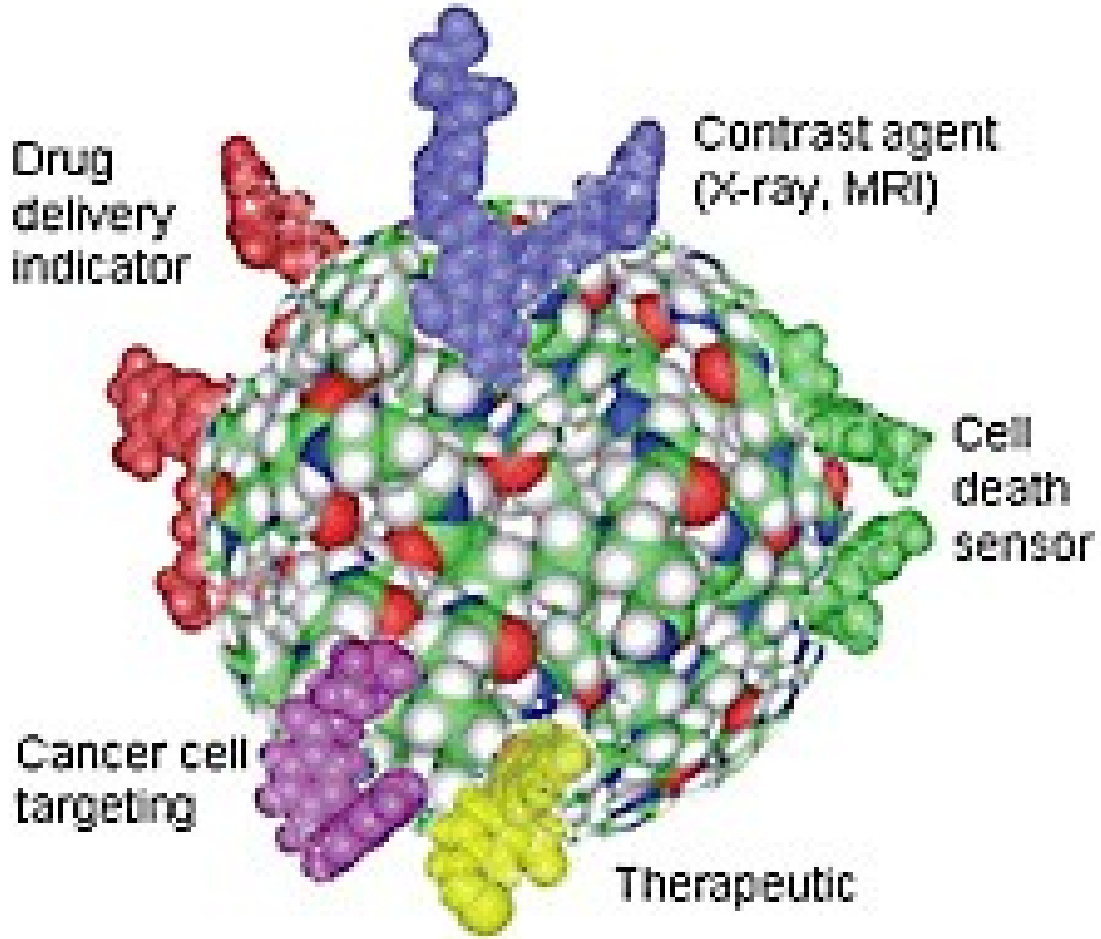
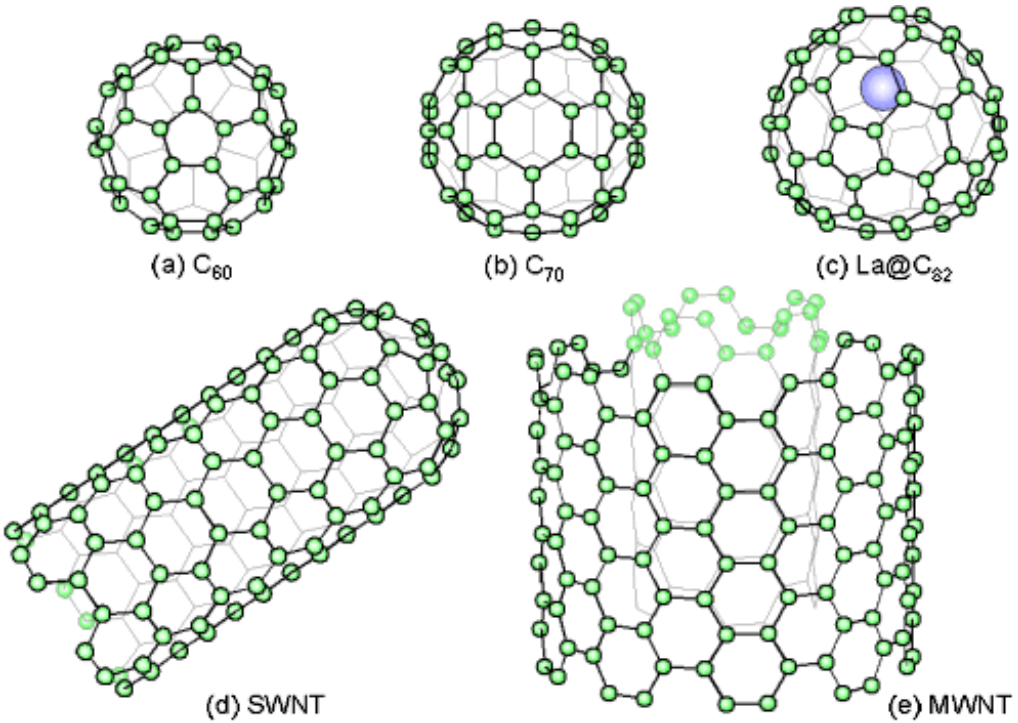
Dendrimers: Medical Applications – Multifunctional nanosized containers ('Platforms')



Fullerenes (and nanotubes)

- Carbon molecules in the shape of a hollow sphere, ellipsoid, tube or ring.
- Cylindrical fullerenes are often called nanotubes.
- The smallest fullerene is C_{60} (i.e., 60 C atoms)
- Other atoms can be trapped inside fullerenes e.g., $La@C_{82}$
- SWNT - single walled nanotubes
- MWNT - multiwall carbon nanotube



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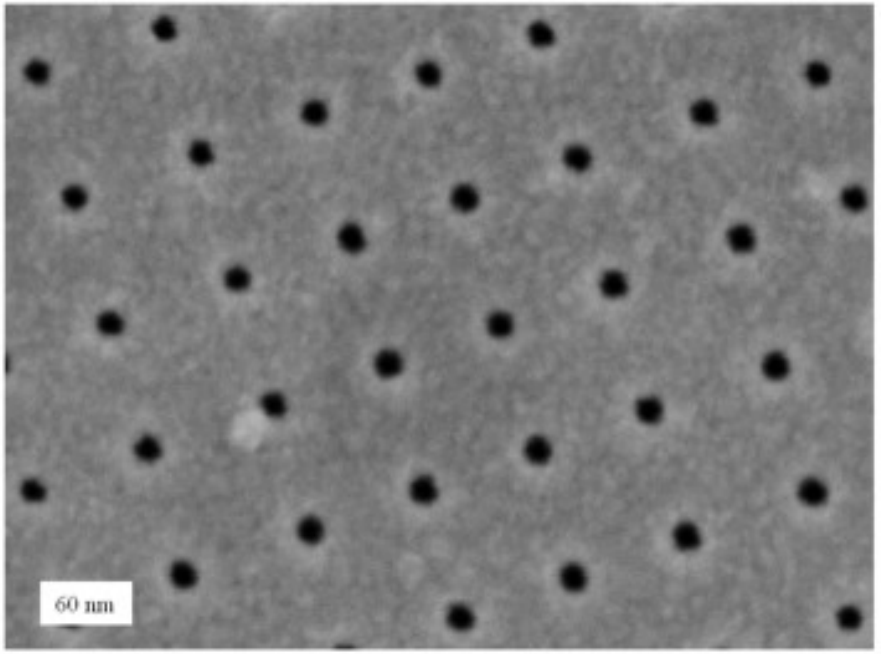
Fullerenes: Medical Uses

- Carbon nanotube reinforced catheters (nanotubes have a Young's modulus 5 times that of steel!)
- Nanotube-based "cold" cathodes (give up electrons freely without need for thermionic emission). Will change conventional x-ray tube technology as do not need a high power source and are exceptionally durable. Nanotube based small X-ray tubes for radiation therapy inside the body (brachytherapy).
- Fullerenes with Gd are 5 times better contrast agents than those used presently.
- Multifunctional platforms: binding specific antibiotics to the fullerene to target resistant bacteria and cancer cells. Fullerenes are not very reactive and are insoluble in many solvents.

Nanopores

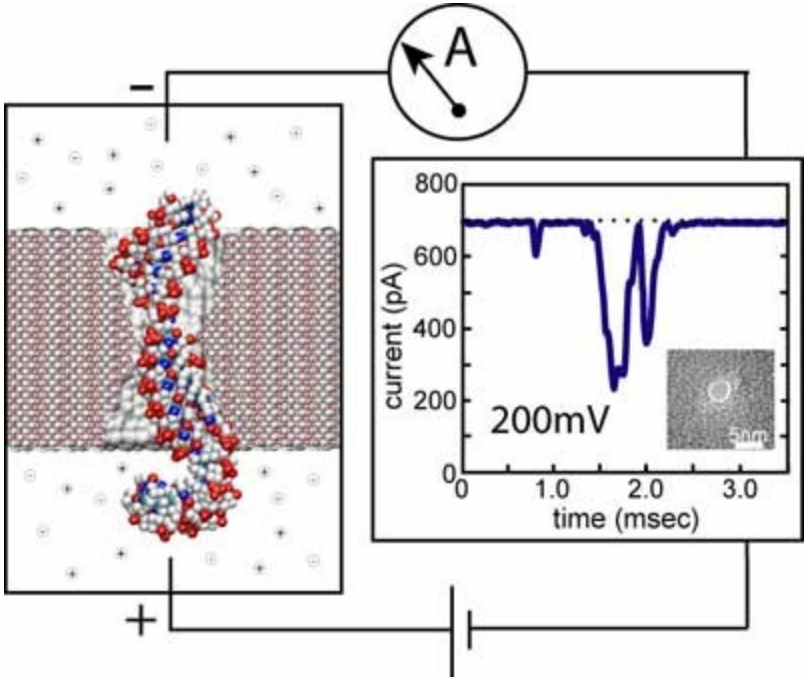
- Nanometer diameter pores pervade biology. They are used to regulate the flow of ions or molecules through the otherwise impermeable, nanometer-thick membranes that surround cells or organelles.



Solidstate nanopores drilled by a focused-ion-beam in a 10 nm thick silicon nitride membrane. The scale bar is 60 nm.
Ref: H.D. Tong, H.V. Jansen, V.J. Gadgil, C.G. Bostan, J.W. Berenschot, C.J.M. van Rijn, and M. Elwenspoek, Nano Lett. 4, 283, (2004).

Nanopores: Medical Applications: DNA sequencing

- As the DNA molecule passes through the nanopore, different bases lead to different drops in the current and hence can be identified.
- Such sequencing, could revolutionize the field of genomics, as sequencing could be carried out in a matter of seconds.
- Other applications of this technique include separation of single stranded and double stranded DNA in solution, and the determination of length of biopolymers.



http://www.ks.uiuc.edu/Research/nanopore/

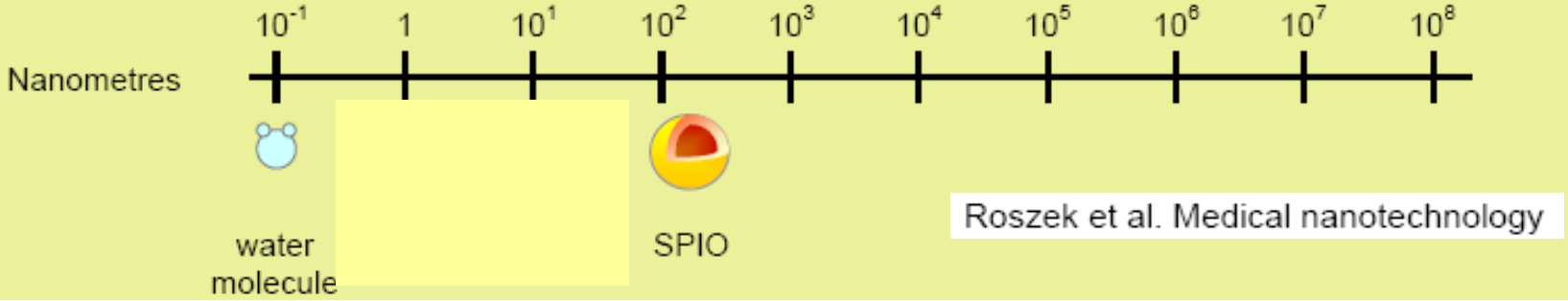
Nanocrystal

- A nanocrystal is a crystalline particle with at least one dimension less than 100 nm.
- Semiconductor nanocrystals in the sub-10nm size range are often referred to as ‘quantum dots’. A quantum dot has a discrete quantized energy spectrum not energy bands like bigger size of solids.

Nanocrystal: Medical applications: Contrast Media for MRI Imaging

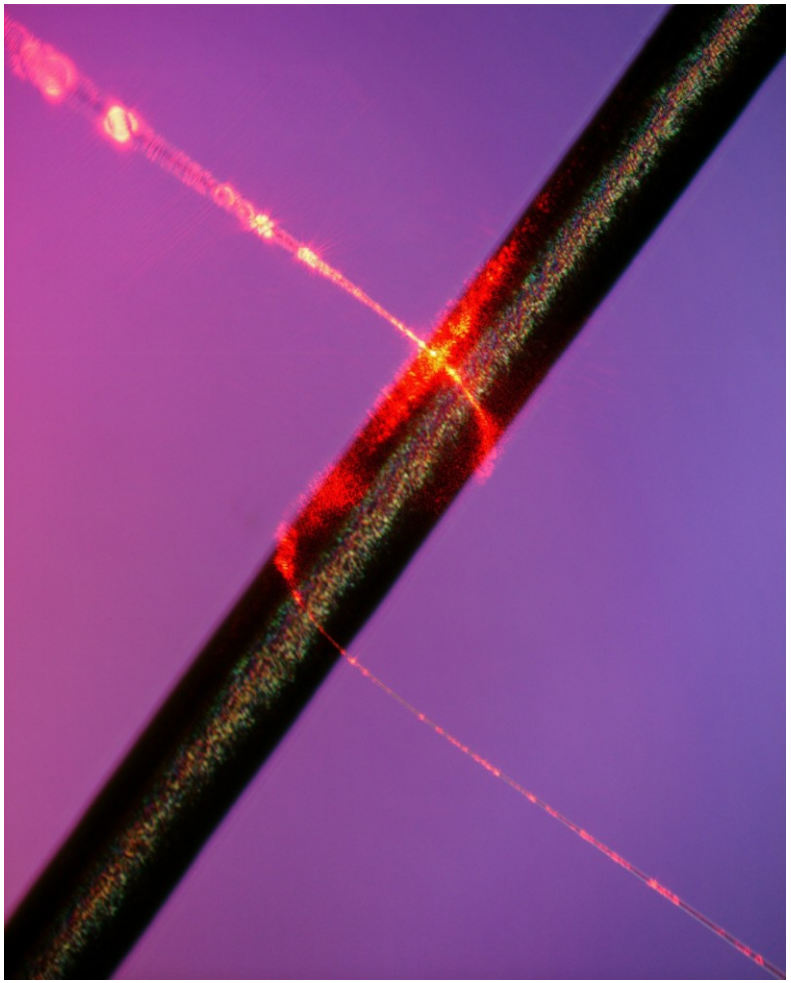
Magnetic resonance imaging

- Superparamagnetic nanocrystalls (**dark** contrast effect in images)
  - Superparamagnetic iron oxide (SPIO) (50-500 nm) – *on the market*
    - Lumirem® and Endorem™, Advanced Magnetics Inc, USA
  - Ultrasmall superparamagnetic iron oxide (USPIO) (<50nm) – *clin. investigation*
    - Supravist™, Schering AG, Germany
    - Sinerem®, Guerbet SA, France



Nanowires

- A nanowire is a wire of diameter of the order of nm.
- Photo: A light-conducting silica nanowire wraps a beam of light around a strand of human hair. The nanowires are flexible and can be as slender as 50 nanometers in width, about one-thousandth the width of a hair.
- This is far smaller than the smallest capillary in the body! That means nanowires could, in principle, be threaded through the circulatory system to any point in the body without blocking the normal flow of blood or interfering with the exchange of gases and nutrients through the blood-vessel walls



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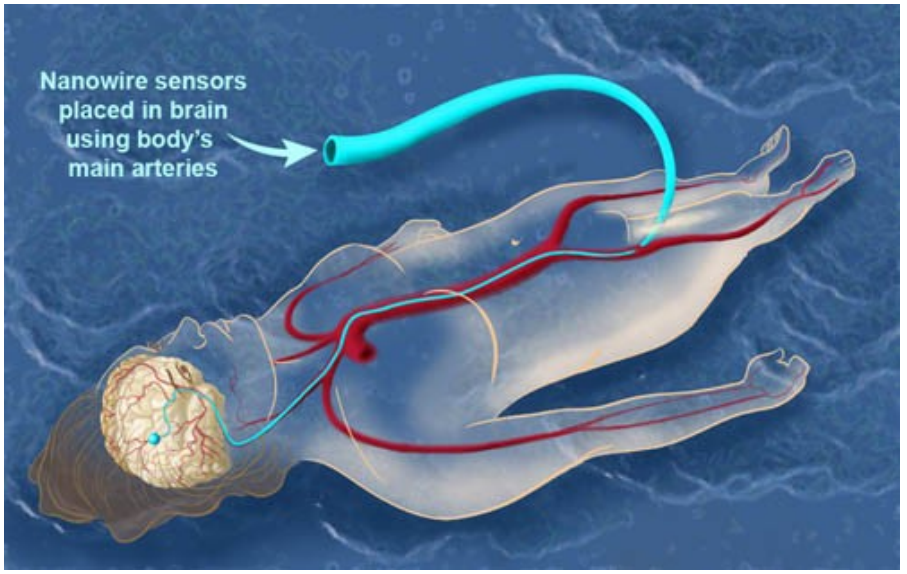
Nanowires: Medical Applications – Brain studies and therapy

- Bunch of nanowires being guided through the circulatory system to the brain. Once there, the nanowires would spread out branching into tinier and tinier blood vessels. Each nanowire would then be used to record the electrical activity of a single nerve cell, or small groups of nerve cells (better than PET or fMRI!) giving the ability to pinpoint damage from injury and stroke, localize the cause of seizures, and other brain abnormalities. It's long been known that people with Parkinson's disease can experience significant improvement from direct stimulation of the affected area of the brain with electrical pulses. Indeed, that is now a common treatment for patients who do not respond to medication. But the stimulation is currently carried out by inserting wires through the skull and into the brain, a process that causes scarring of brain tissue. The hope is, by stimulating the brain with nanowires threaded through pre-existing blood vessels, doctors could give patients the benefits of the treatment without the damaging side effects.



Nanowires: Medical Applications – Environmental Molecular Sensors

- Compared to ordinary fiber optic cable, which appears to the naked eye as a uniform glowing line, nanowires have a beaded appearance when viewed under magnification. That's because unlike a normal fiber, which confines light within its walls, minuscule particles of dust along the nanowires' surface can scatter the light beam. This sensitivity to surface contaminants could lead to use of the nanowires as molecular sensors.
- One could fit the surface of the wire with receptors for environmental molecules. If those target molecules are present, they'll attach to the receptors and blobs of tiny lights will be seen when the wires are illuminated.

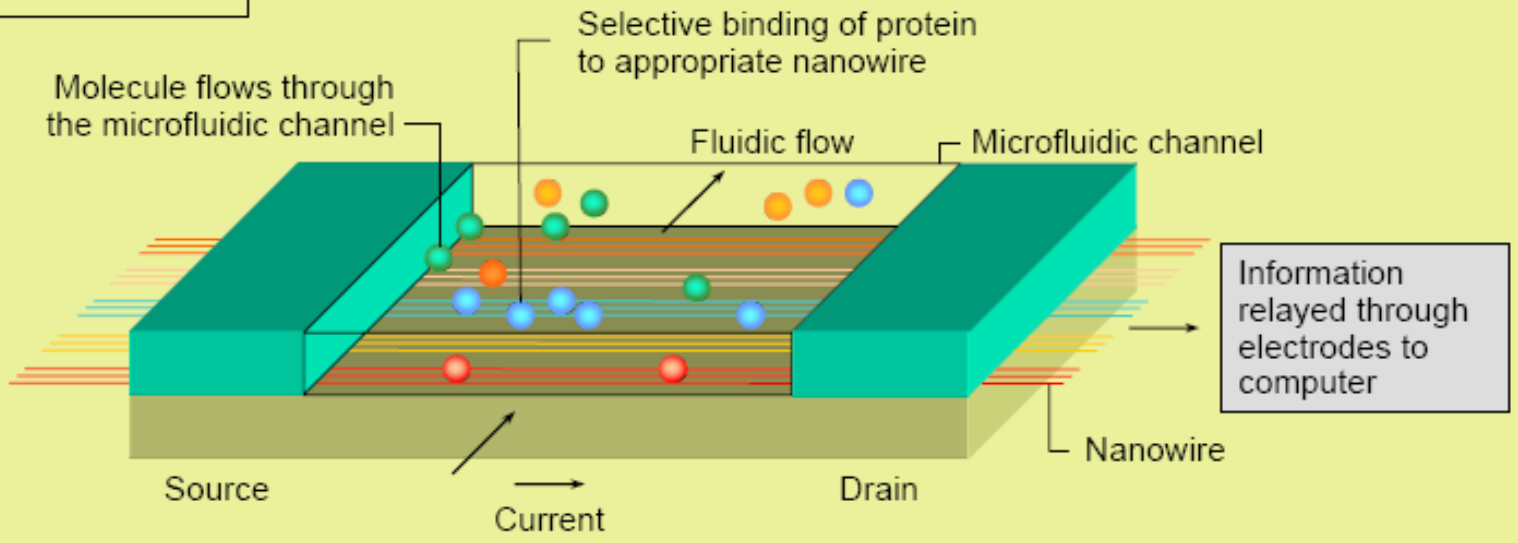
Nanowires: Medical Applications: Biomolecular Sensors

Silicon nanowire-based field-effect transistor

Electrical detection technology

Roszek et al.
Medical Nanotechnology

Applications:
Virus detection
Cancer markers
Cystic fibrosis



Health Risks

- Nanoparticles are able to cross biological membranes and access cells, tissues and organs that larger-sized particles normally cannot. They can gain access to the blood stream following inhalation or ingestion. At least some can penetrate the skin. Once in the blood stream, they can be transported around the body and are taken up by organs and tissues including the brain, heart, liver, kidneys, spleen, bone marrow and nervous system. Unlike larger particles, they may be taken up by cell mitochondria and the cell nucleus. Studies demonstrate the potential for DNA mutation and induce major structural damage to mitochondria, even resulting in cell death.
- Hundreds of consumer products incorporating nanoparticles are now on the market, including cosmetics, sunscreens, sporting goods, clothing, electronics, baby and infant products, and food and food packaging.

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