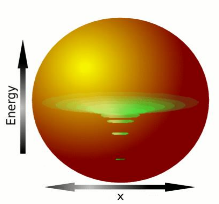

Laser for NANO (bio-medical)

Pioneering pulsed laser synthesis of colloids
Advanced Nanoparticle Generation and Excitation by Lasers in Liquids.

Důmyslné formy hmoty otvírající široký prostor převratnému vývoji vědy a novým technologiím

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Institute of Engineering Physics for Biomedicine, Moscow, RU
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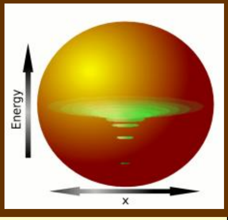

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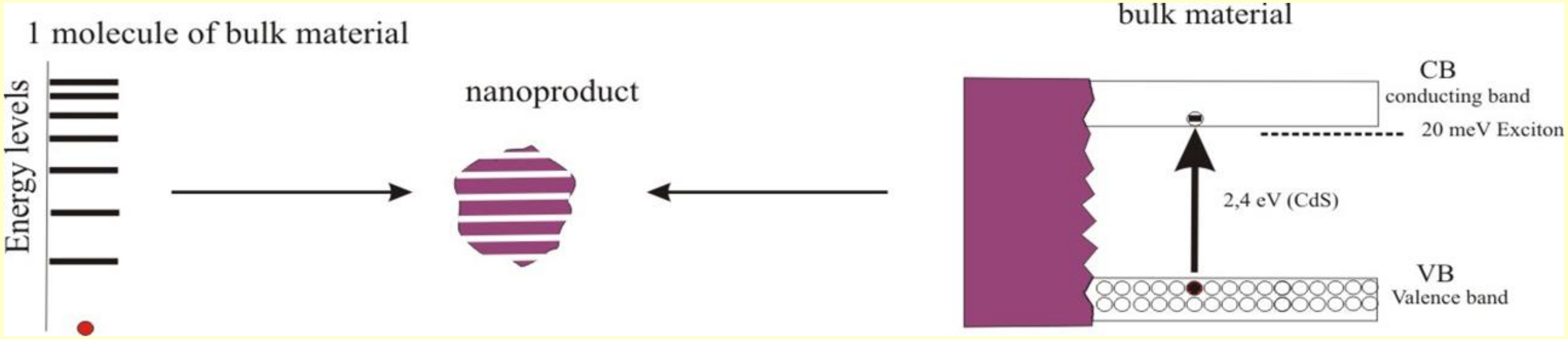
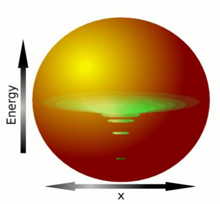
During the past several decades, "small-particle" research has become quite popular in various fields of physics and chemistry. By "small particles" are meant clusters of atoms or molecules of metals, semiconductors and others materials, ranging in size between
single atoms or molecules and bulk materials.



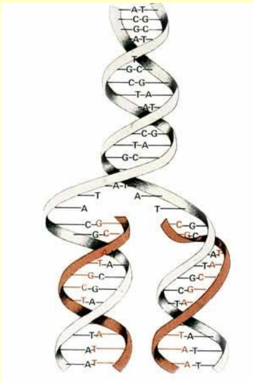
Contemporary science reached the level
which makes possible to peep into very tiny pieces of matter
to observe natural processes taking place inside. (nano size)

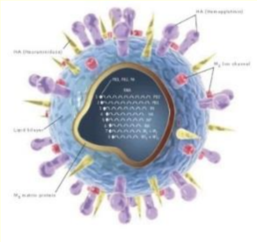


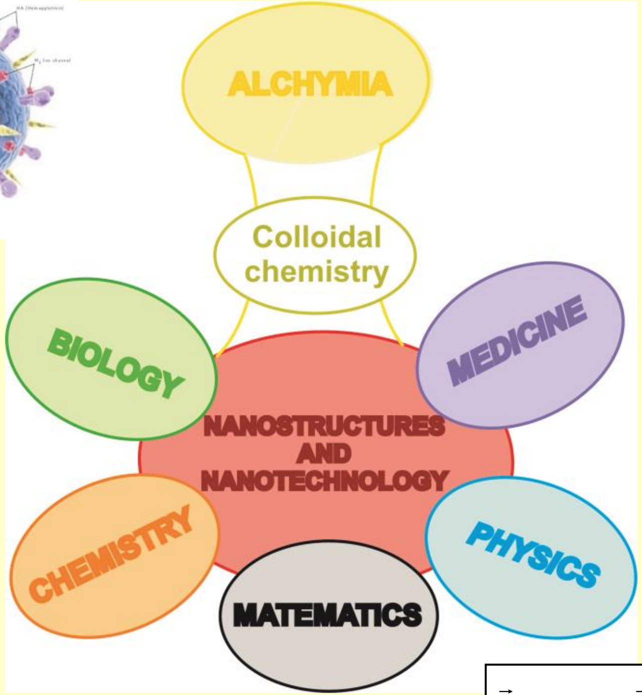
Nanotechnology is an inter-disciplinary branch of science

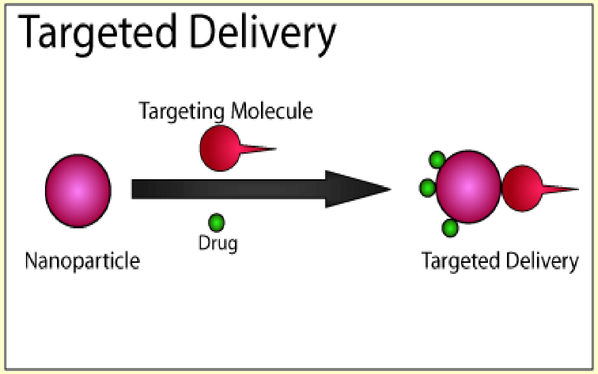
Problems of nanostructures belong to an inter-disciplinary field of research, where chemistry, physics, biology and mathematics, and perhaps some other branches of science as well, overlap in creating possibility to describe, study and employ these directions.

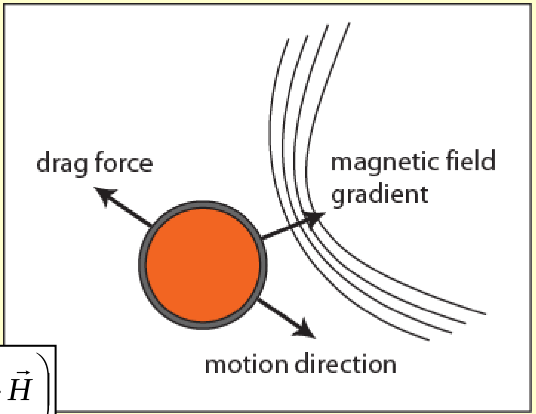
Nanophysics, nanochemistry, nanomedicine, nanobiology, and particle nanostructures are categories of current nanoscience

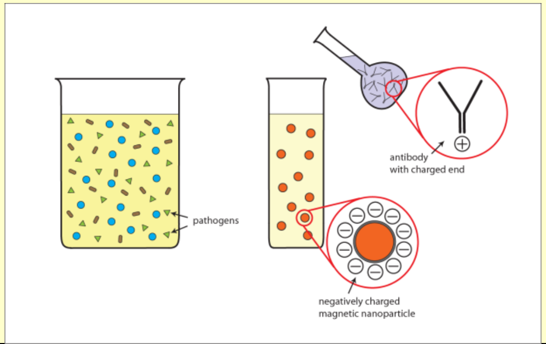












$$\vec{F}_m = V_m \Delta\chi \vec{\nabla}\left(\frac{1}{2}\vec{B}\cdot\vec{H}\right)$$

Example of unusually properties of nanomaterials

very small nano-material objects have
unsually physical and chemical properties for example

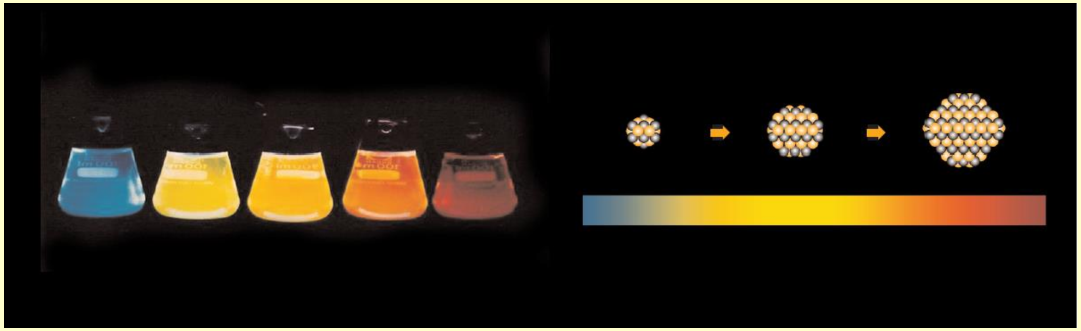
- Black semiconductor like Cd_3As_2 is red (can be also yellow), exhibits strong luminescence, and is soluble.
- Carbon C is red and soluble.
- Iron Fe is soluble and yellow.
- Silicon Si is yellowish, exhibits strong luminescence, soluble in organic solvents.

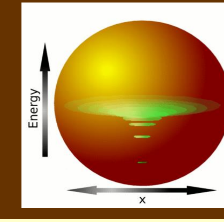
Nanoceramics last temperatures up to 3000°C (Space shuttle) and so on.
Kelvar Liberec
Carbone-fiber composites 14x lighter than steel , 10 stronger than steel

Luminescence of nanoparticles

Cd_3As_2 in aqueous solutions in UV light

Increasing particles size from left to right





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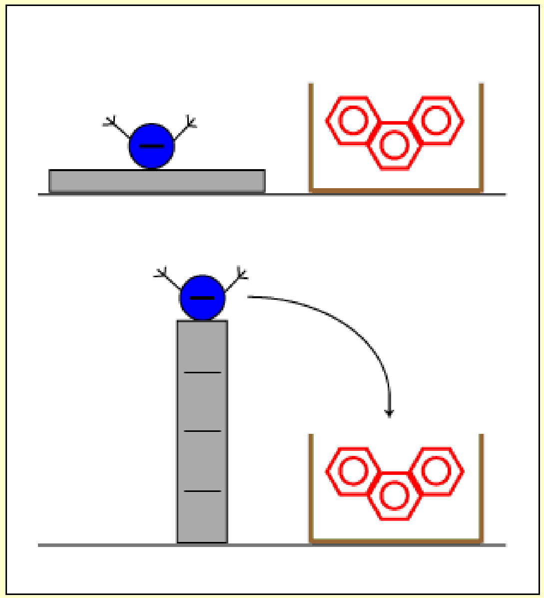
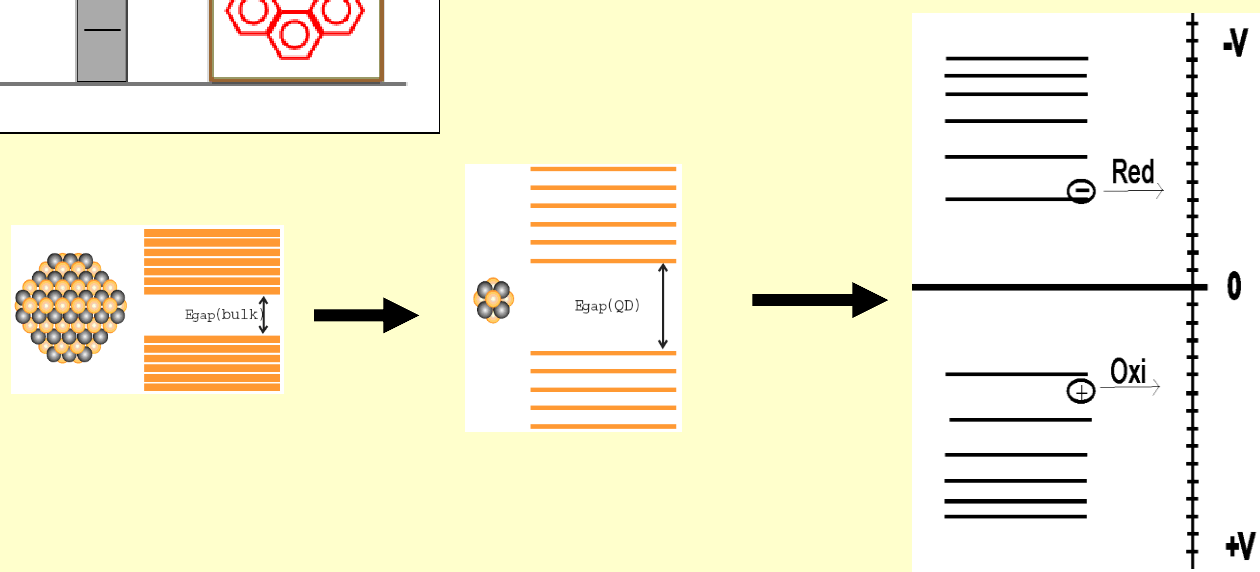
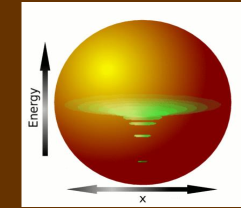
Powder TiO_2 (big particles)

Nanoparticles TiO_2







Energy and wavelength of free electron

Maxwell-Boltzmann

$$E = \frac{3}{2}kT \qquad E_{300K} \doteq 0.04\,\text{eV}$$

where E is the kinetic energy of the carrier,
T is temperature in K , and *k* = 1.38×10-23 JK-1.

DeBroglie - duality of particles

$$\lambda = \frac{h}{\sqrt{2mE}} \Rightarrow \lambda = \frac{h}{\sqrt{3mkT}}$$

where□ *l* is the wavelength of the carrier with mass *m* and *h* = 6.63×10^{-34} Js.
In case of thermal electron *m* = 9.1×10$^{-31\ \text{kg}}$. at 300 K

$$\lambda \doteq 62\,\text{Å}$$

Laser for NANO (bio-medical)

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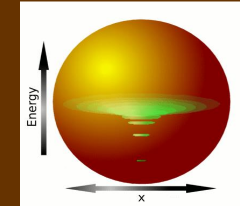
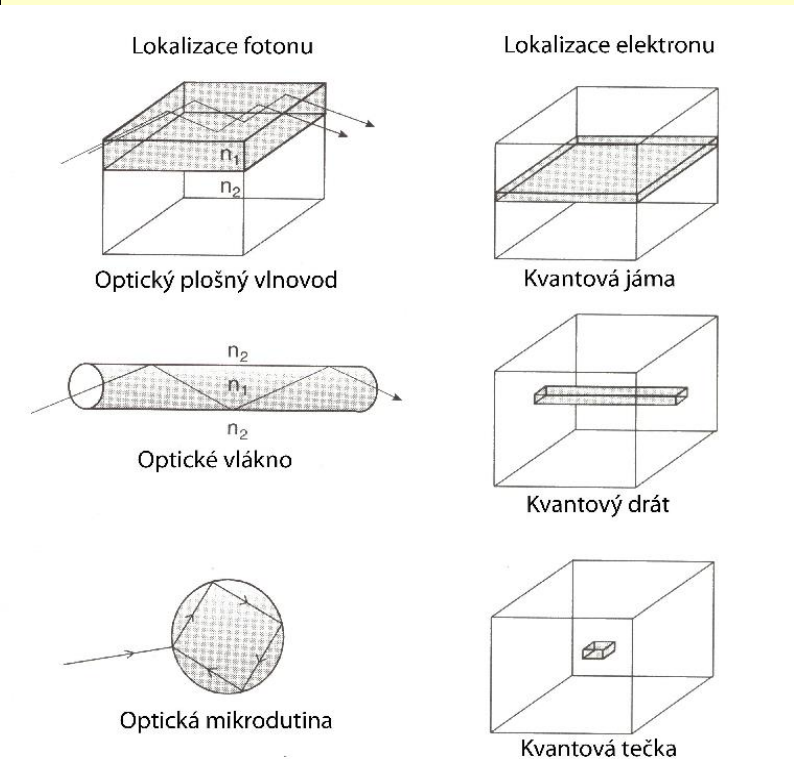




Similarities in Characteristics of Photons and Electrons

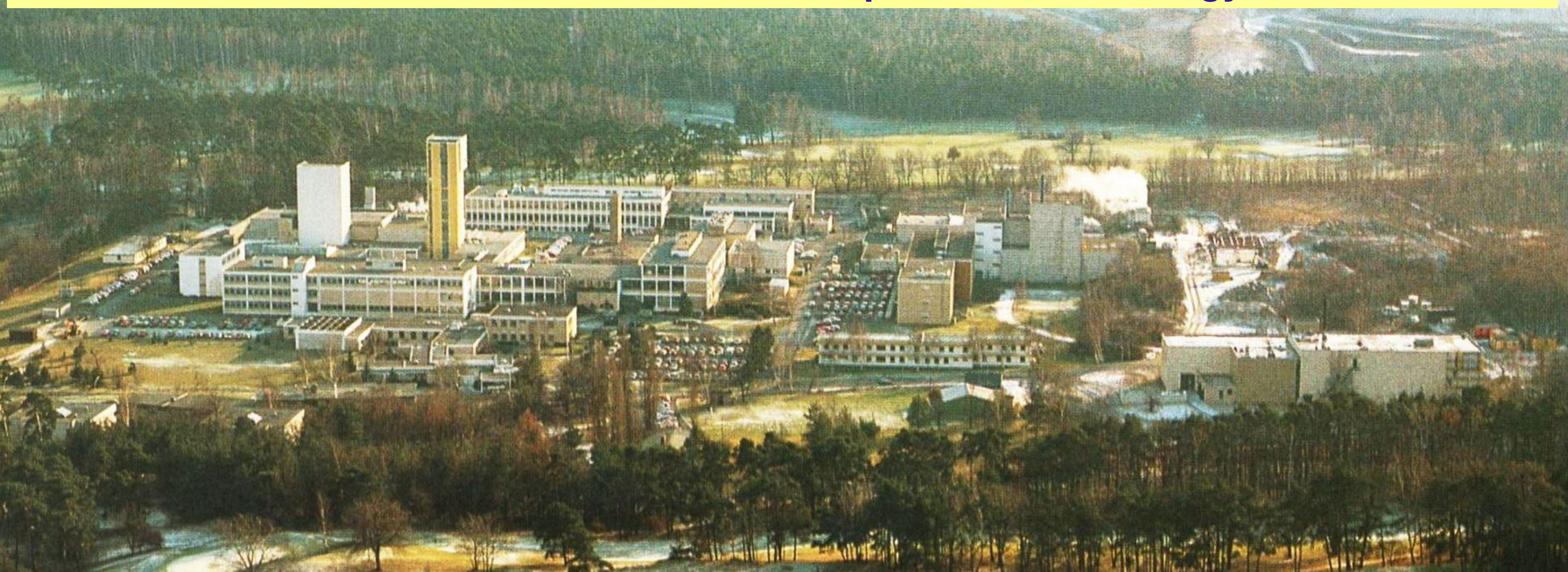
Photons **Fotonické struktury**	Electrons **Elektronické struktury**
Wavelength	
$\lambda = \frac{h}{p} = \frac{c}{\nu}$	$\lambda = \frac{h}{p} = \frac{h}{mv}$
Eigenvalue (Wave) Equation	
$\left\{\nabla \times \frac{1}{\varepsilon(r)} \nabla \times\right\}\mathbf{B}(r) = \left(\frac{\omega}{c}\right)^2 \mathbf{B}(r)$	$\hat{H}\psi(r) = -\frac{\hbar^2}{2m}(\nabla \cdot \nabla + V(r))\psi(r) = E\psi$
Maxwellovy rovnice	**Schrödingerova rovnice**
Free-Space Propagation	
Plane wave $\mathbf{E} = (\frac{1}{2})\mathbf{E}^\circ(e^{i\mathbf{k}\cdot\mathbf{r}-\omega t} + e^{-i\mathbf{k}\cdot\mathbf{r}+\omega t})$ $\mathbf{k}$ = wavevector, a real quantity	Plane wave: $\Psi = c(e^{i\mathbf{k}\cdot\mathbf{r}-\omega t} + e^{-i\mathbf{k}\cdot\mathbf{r}+\omega t})$ $\mathbf{k}$ = wavevector, a real quantity
Interaction Potential in a Medium	
Dielectric constant (refractive index)	Coulomb interactions
Propagation Through a Classically Forbidden Zone	
Photon tunneling (evanescent wave) with wavevector, **k**, imaginary and hence amplitude decaying exponentially in the forbidden zone	Electron-tunneling with the amplitude (probability) decaying exponentially in the forbidden zone
Localization	
Strong scattering derived from large variations in dielectric constant (e.g., in photonic crystals)	Strong scattering derived from a large variation in Coulomb interactions (e.g., in electronic semiconductor crystals)
Cooperative Effects	
Nonlinear optical interactions	Many-body correlation Superconducting Cooper pairs Biexciton formation

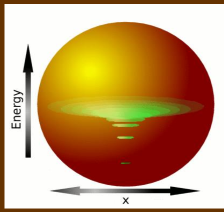
1980

Ambitious objective of project EUREKA (EU and Germany1980) was to end the domination of U.S. and Japan in the field of chip technology (1 Mb/cm2).

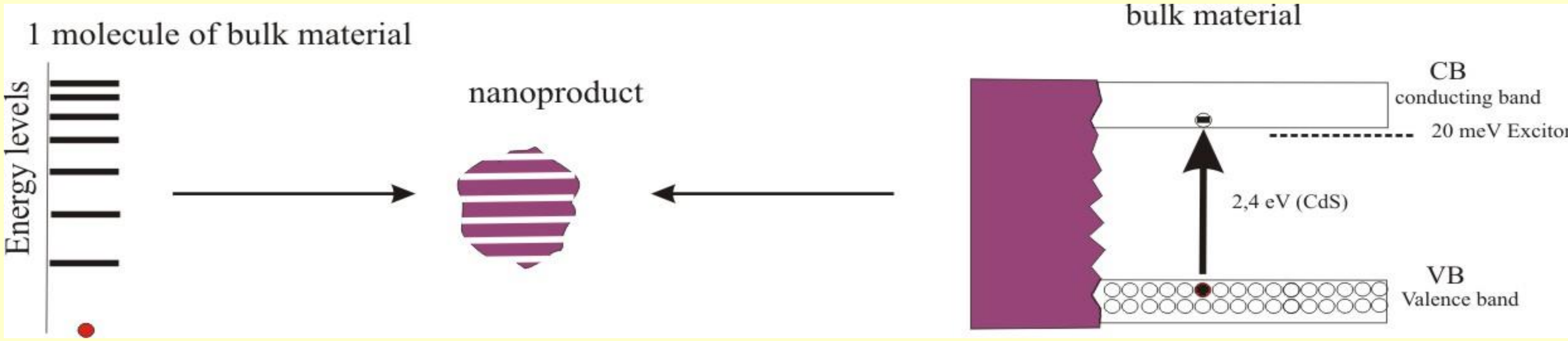
To obtain chip units with a density record 10 ÷ 100 Mb/cm2 was to ensure necessary material base.

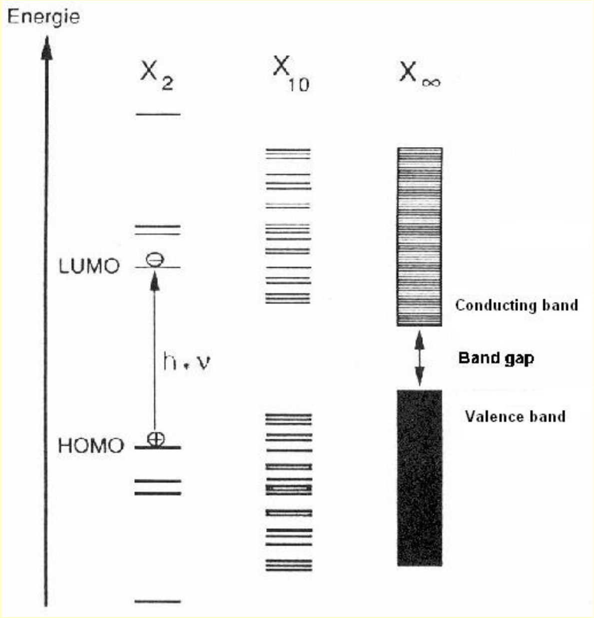
HMI in Berlin has become in the being a major centre for research and training materials for miniaturisation particles technology.

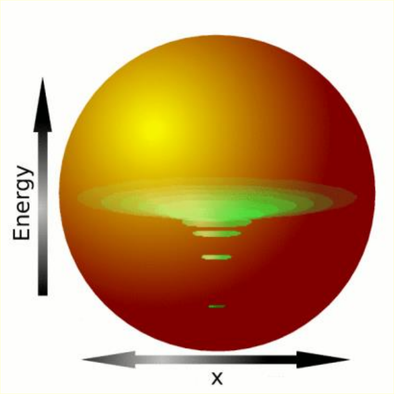


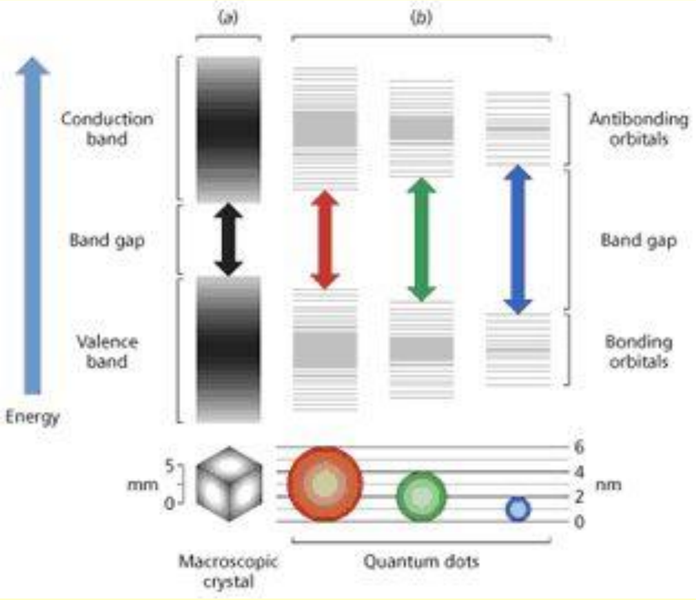


APPROACH TO NANOSTRUCTURES





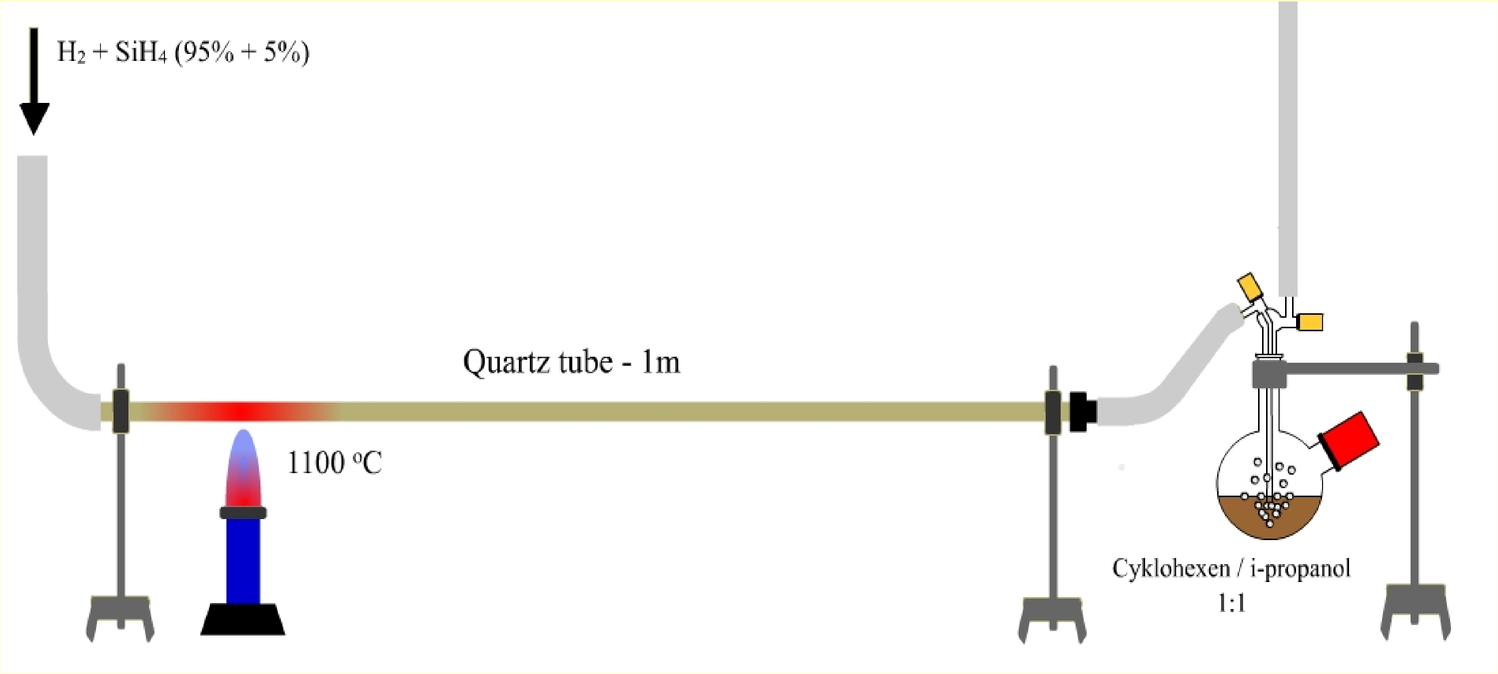




Si nanoparticles as markers for bio-applications. Creep effect.

Thermolysis, Thermal decomposition

Thermal decomposition, also called **thermolysis**, is defined as a chemical reaction in which a compound breaks up into at least two other substances when heated. The reaction is usually endothermic as heat is required to break chemical bonds in the compound undergoing decomposition. The *decomposition temperature* of a substance is the temperature at which the substance decomposes into smaller substances or into its constituent atoms. When taken place it needs to be supervised as it can be dangerous.



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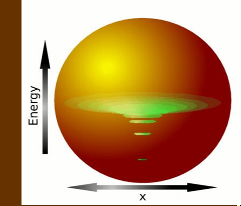
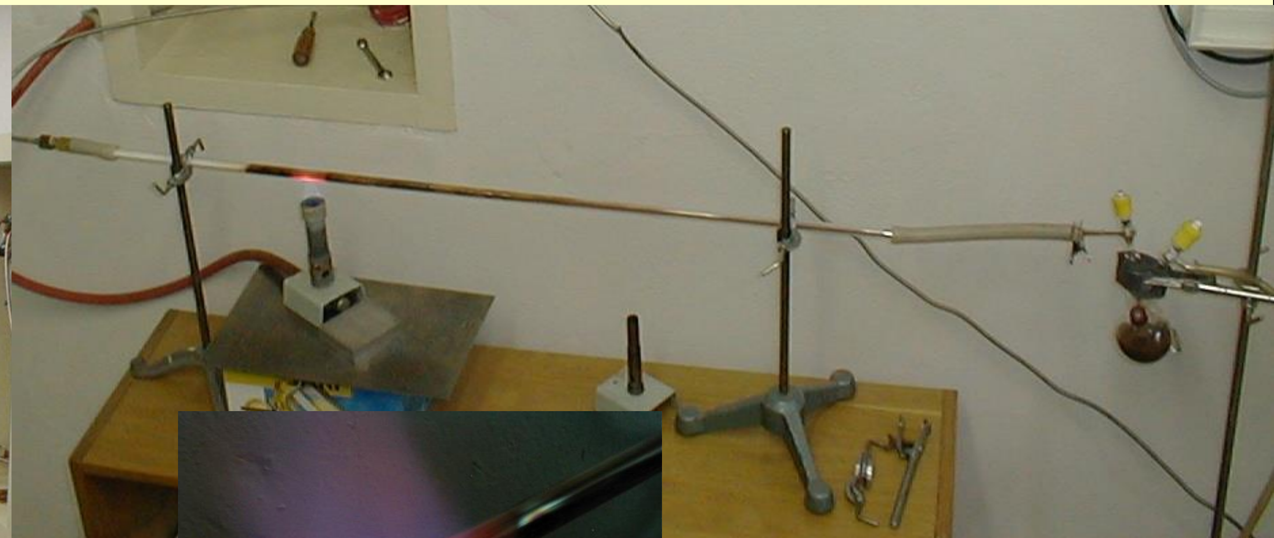
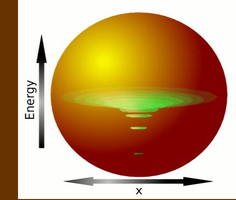
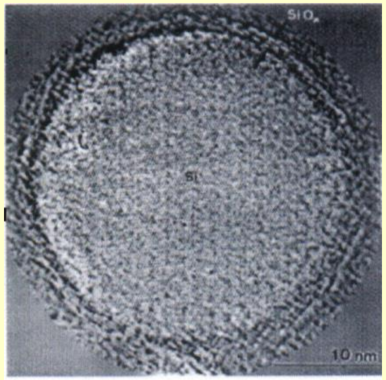




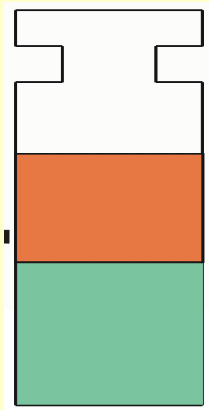


Silicon nanoparticles

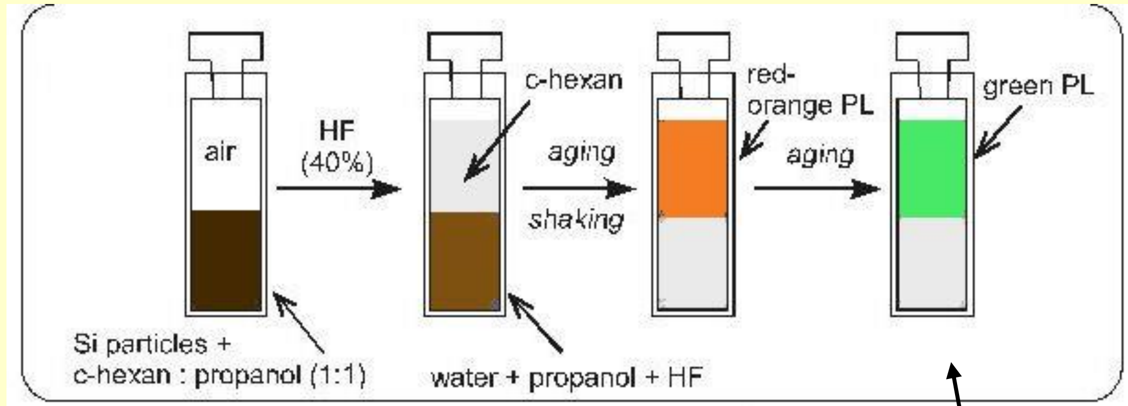


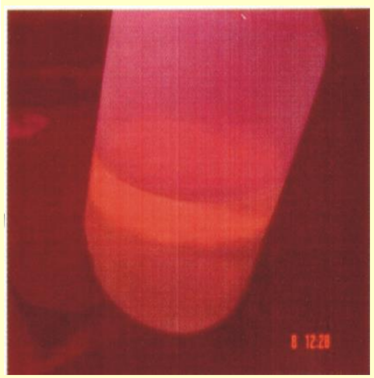
~ 10 nm size

SiO_2 surface shell
silicon nanoparticle

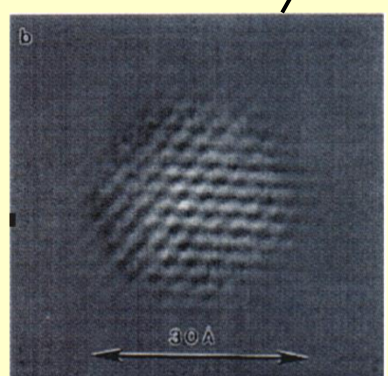


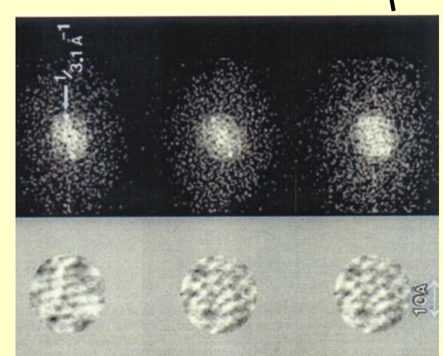
Chemical etching





Photoluminiscence Si nanoparticles in cyclohexane

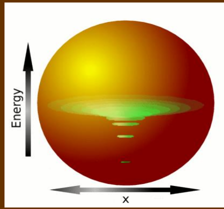




Fojtik A.,Giersig M.,Henglein A.:
Formation of Nanaometer-Size Silicon particles in a Laser Induced Plasma i SiH4.
Ber.Buns.Phys.Chem. Vo1.97,No.11 (1993)p.1493

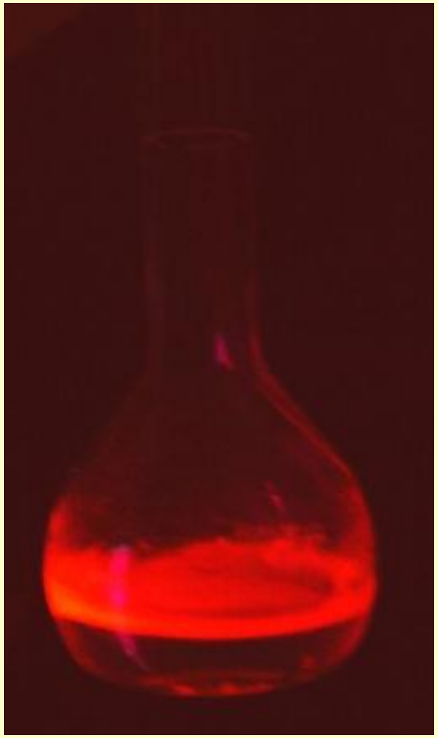
Fojtik A.,Henglein A.:
Luminiscent Colloidal Silicon Particles.
Chem.Phys.Letters 221 (1994)p.363

FojtikA.,HengleinA.:
Luminescece of Colloidal Silicon Suspendions: Quantum Yield,Quenching,and Surface Phenomena
J.Phys.Chem. B, Vo.110,No 5,2006, p.1994-1998



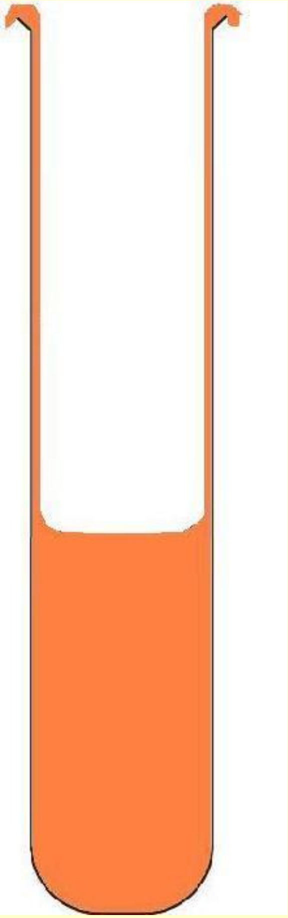
CREEP EFFEKT

0 sec

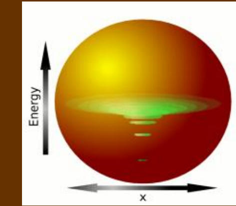


5 sec

30 sec



Simulace supratekutosti (vzlínaní)



Could lasers be put to a good use?

Attempts were made, but without any particular breakthrough...

At that time, we aimed to new type of nanostructures and we really had not expected that usage of lasers could bring us something revolutionary.

But there was a surprise waiting around the corner...

Laser for NANO (bio-medical)

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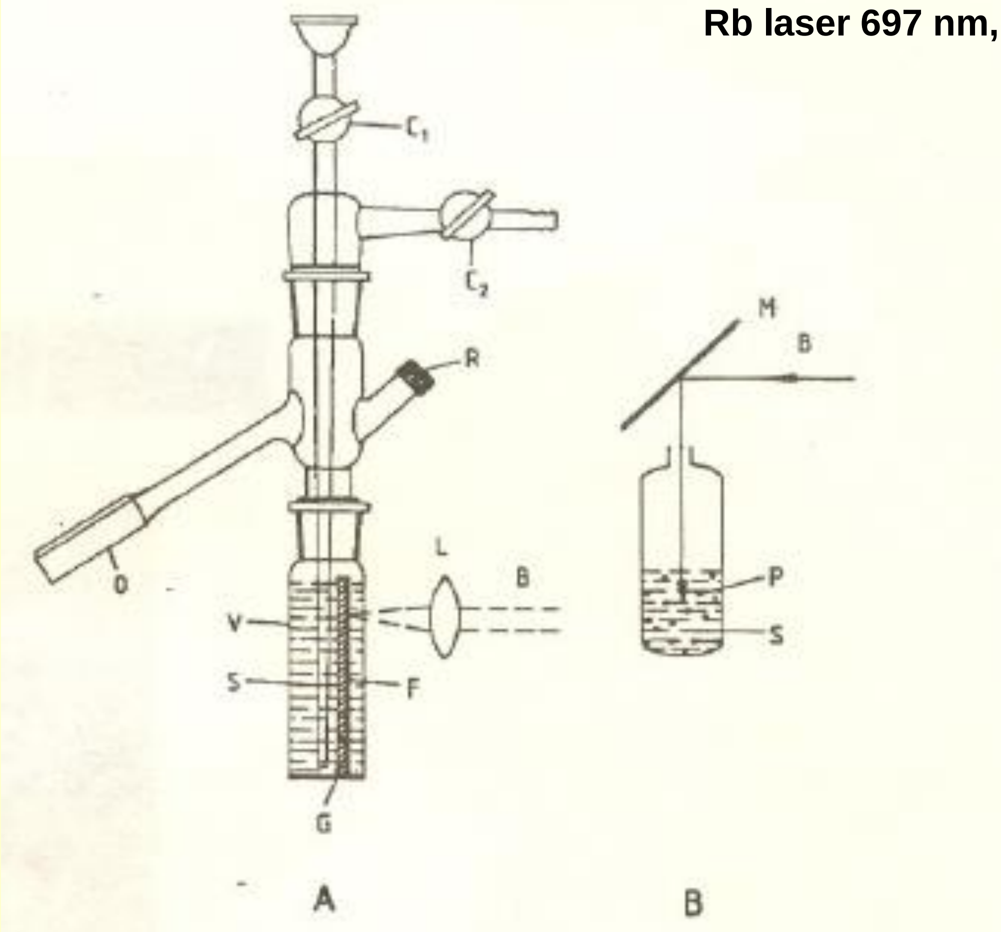
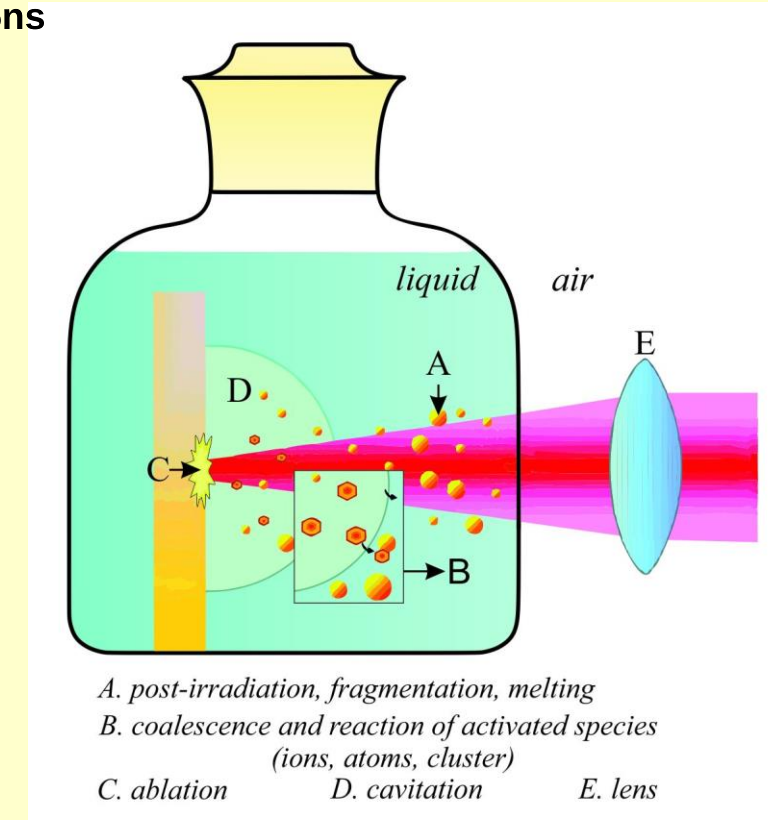
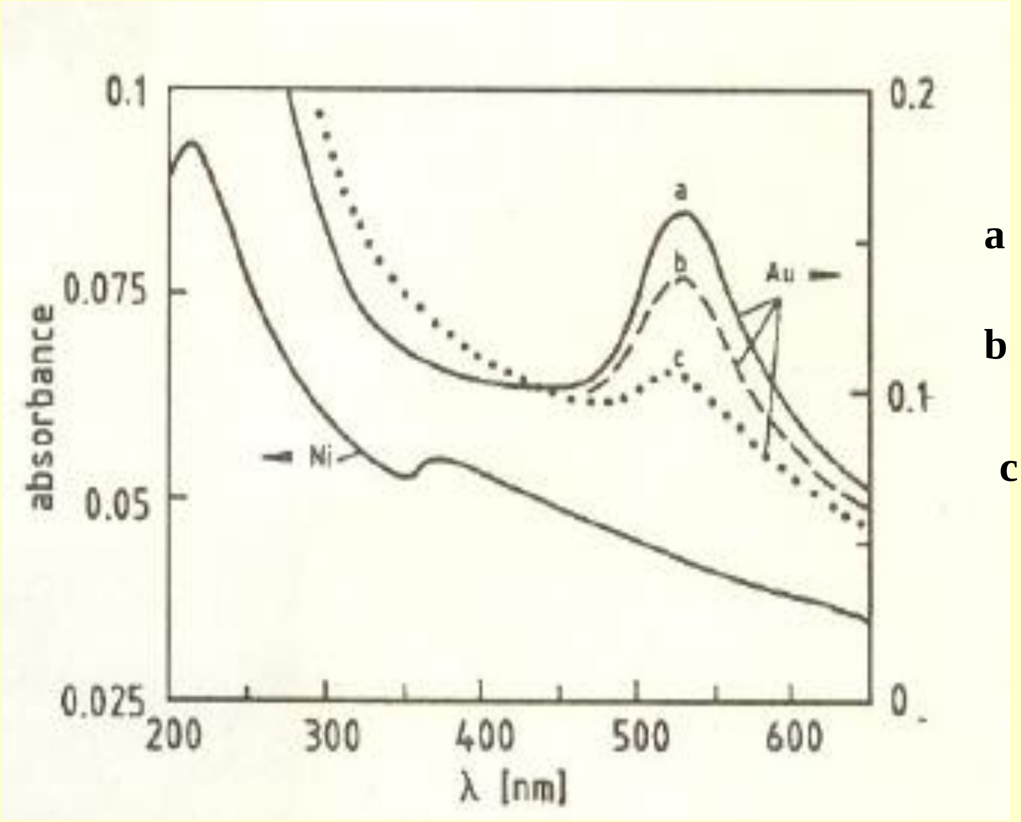
Rb laser 697 nm, 3-5ns





A: Experimental arrangement for ablation of films in liquid by a strong laser beam
V: glass vessel, F: film on glass support **G**, **L:** lens, **B:** laser beam, **O:** optical cuvette
R: rubber septum, **C_1, C_2:** stopcocks, **B:** Method for the ablation of suspended particles in a liquid, **B:** laser beam, **M:** mirror, **S:** solvent, **P:** suspended particles.

of_gold-in-water.mp4



Plasmon, Au metal

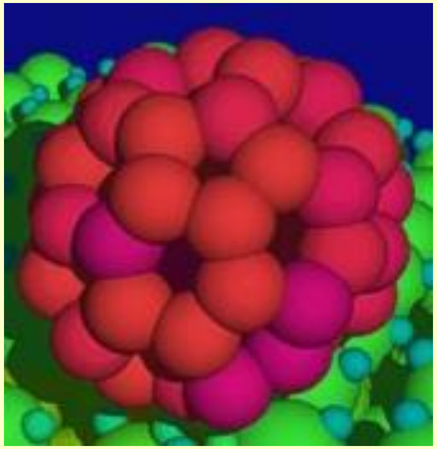
a 2,3 J/cm^2

b 7,0 J/cm^2

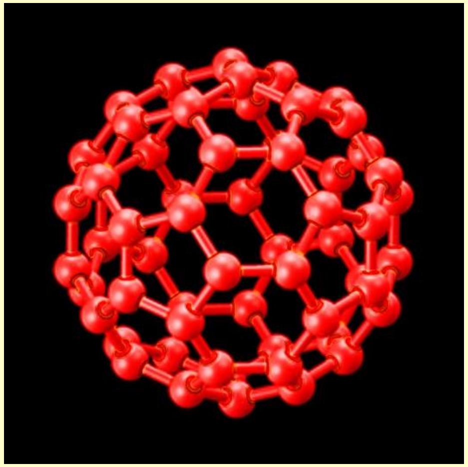
c 27 J/cm^2

Absorption spectra of the colloidal gold solutions obtained at different laser intensities.
The golg film was 500A thick and illuminated in 2-propanol without stabilizer.
Laser intensity: a: 2.3, b: 7.0, c: 27 J/cm^2. The figure also contain the absorption spectrum of a nickel sol obtained by ablation of nickel film (on glass) in aqueous 10^{-3}M sodium polyacrylate.

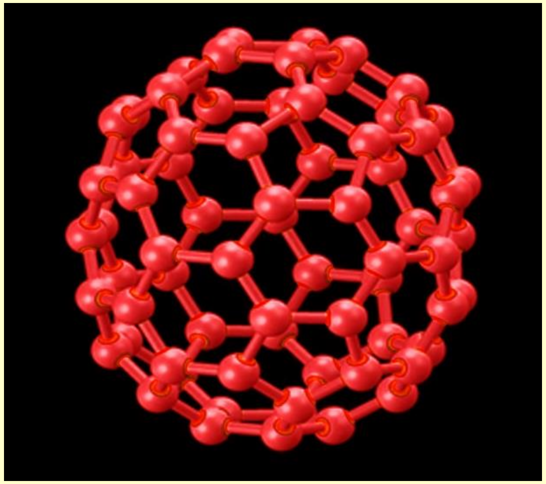
C 60



C 60



C 90



Laser for NANO (bio-medical)

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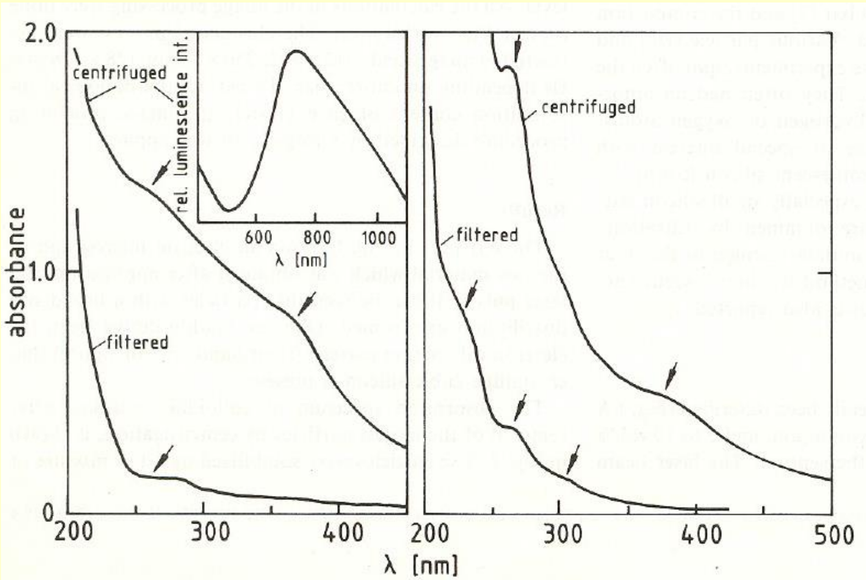
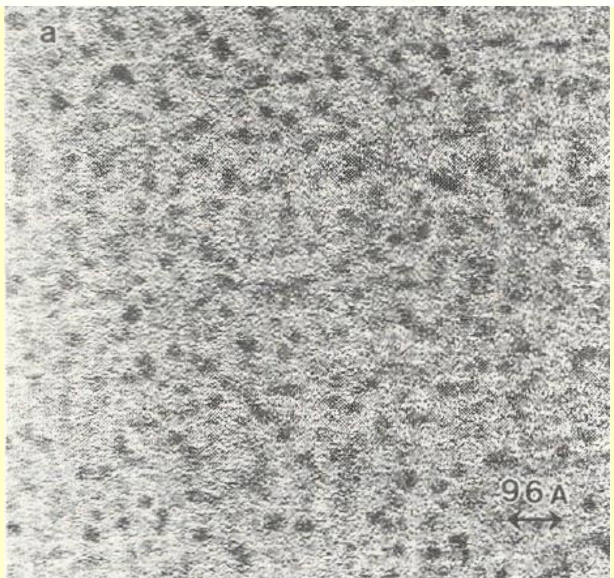
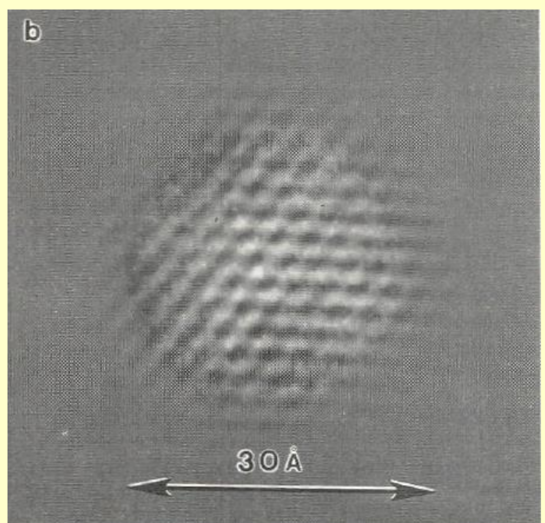
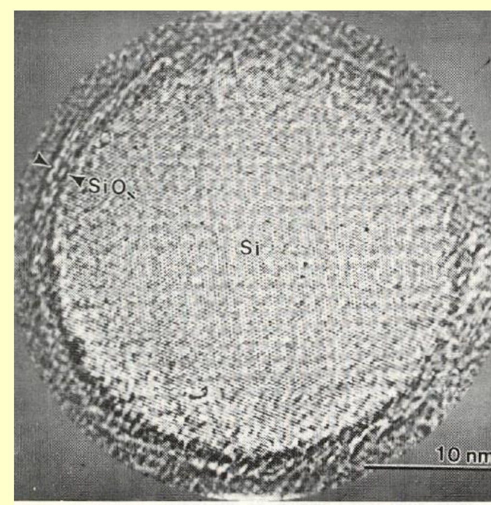
Formation of Nanometer-Size Silicon Particles in a Laser Induced Plasm in SiH_4



Absorption spectra of centrifuged and filtered silicon particles. Right: thiol-stabilizer present in the cyclohexane-propanol solvent mixture. The spectra of solution were taken towards blanks containing the solvent mixture (plus stabilizer).Insert: luminescence spectra of the etched particles in solution; excitation wavelength: 360nm.







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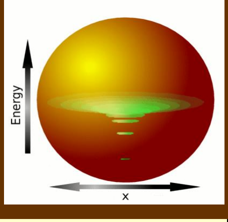
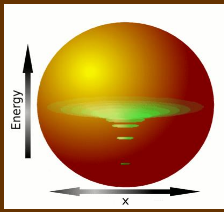




New approach

Biological Application of

Laser-generated Nanoparticles

Stephan Barcikowski

For biomedical applications, purity matters.

Purity of "Gold Colloid" (Material Safety Data Sheet)

SIGMA®

3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone 800-325-5832 • (314) 771-5765
Fax (314) 286-7828
email: techserv@sial.com
sigma-aldrich.com

ProductInformation

Gold Colloid, 5 nm (G1402)
Gold Colloid, 10 nm (G1527)
Gold Colloid, 20 nm (G1652)

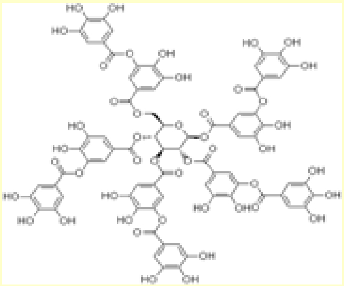
Storage Temperature 2-8 °C

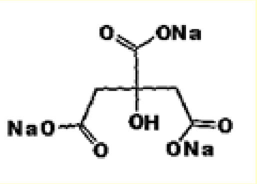
Product Description
Colloidal gold is a discrete, electron dense, non-fading, red colored marker useful as a probe in electron microscopy, light microscopy, and blotting procedures.[1] It requires no additional processing for detection, but in certain applications, the signal can be dramatically enhanced by reaction with silver (Silver Enhancer Kit, Product Code SE-100).

All unconjugated gold colloids contain approximately 0.01% $HAuCl_4$ suspended in 0.01% tannic acid with 0.04% trisodium citrate, 0.26 mM potassium carbonate, and 0.02% sodium azide as a preservative.

Precautions and Disclaimer
Due to the sodium azide content a material safety sheet (MSDS) for this product has been sent to the attention

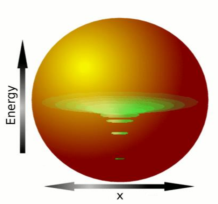
All unconjugated gold colloids contain approximately 0.01% $HAuCl_4$ suspended in 0.01% tannic acid with 0.04% trisodium citrate, 0.26 mM potassium carbonate, and 0.02% sodium azide as a preservative.



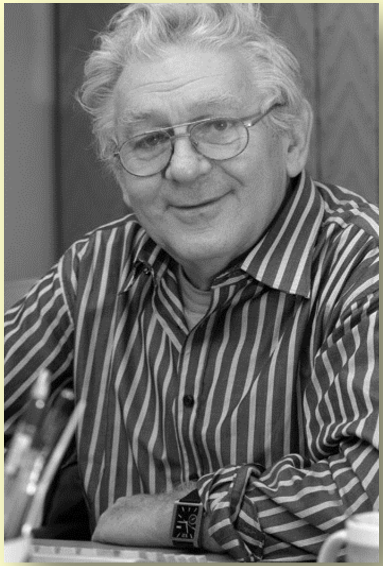


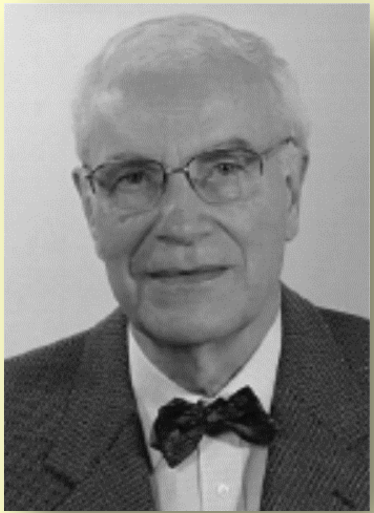
NaN_3

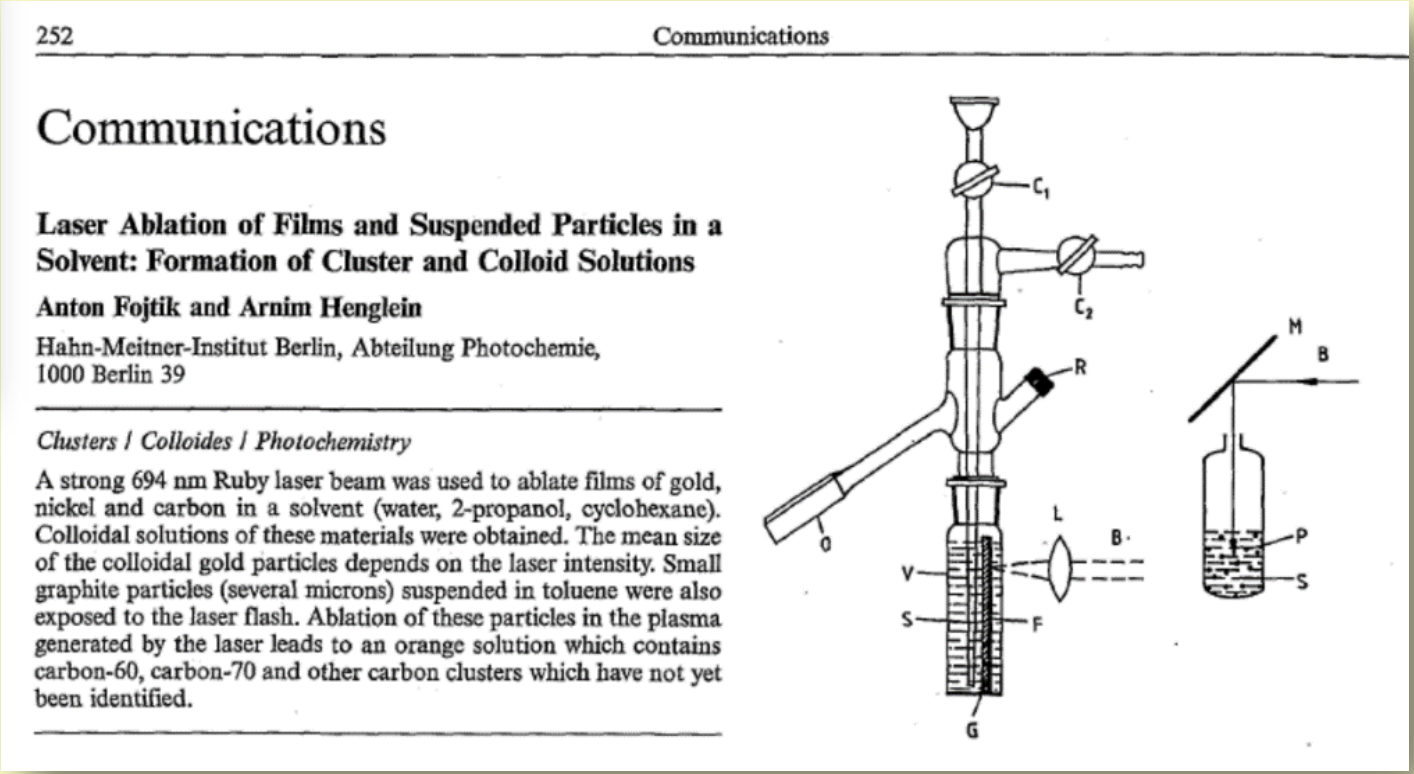
Ligand-free Nanoparticles from Laser Ablation in Liquids



When it begun …


Anton Fojtik


Arnim Henglein, † 2012



Communications

Laser Ablation of Films and Suspended Particles in a Solvent: Formation of Cluster and Colloid Solutions

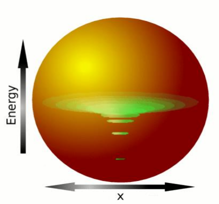
Anton Fojtik and Arnim Henglein

Hahn-Meitner-Institut Berlin, Abteilung Photochemie, 1000 Berlin 39

Clusters / Colloides / Photochemistry

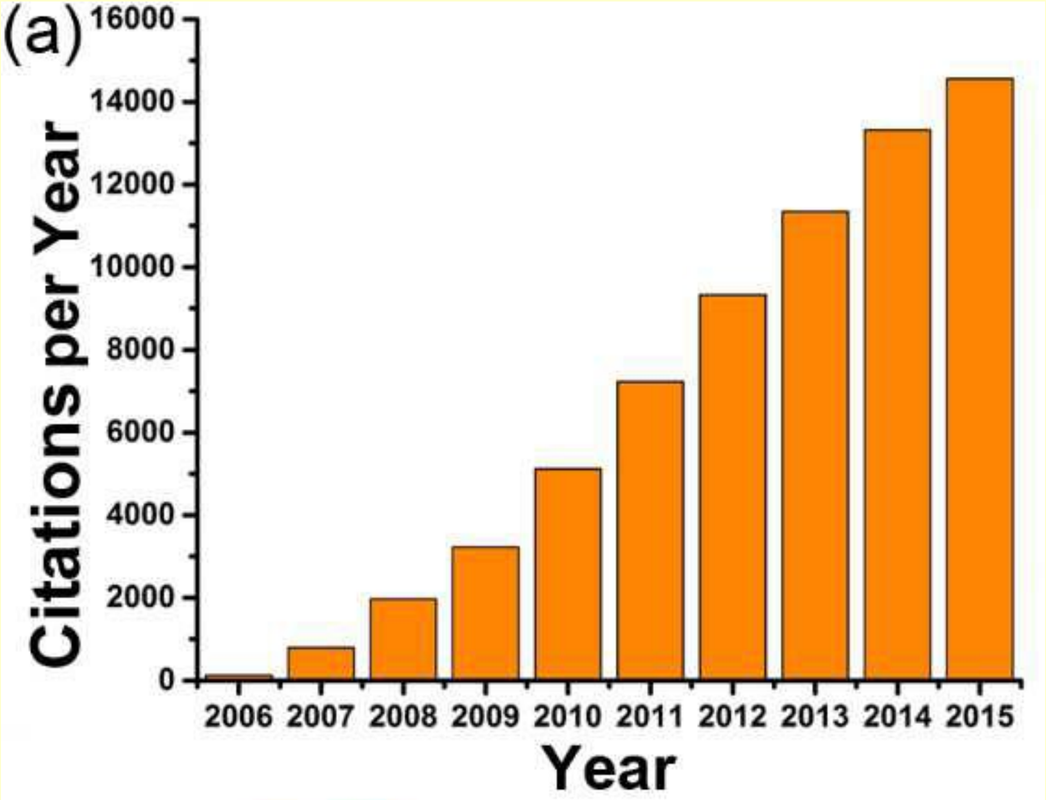
A strong 694 nm Ruby laser beam was used to ablate films of gold, nickel and carbon in a solvent (water, 2-propanol, cyclohexane). Colloidal solutions of these materials were obtained. The mean size of the colloidal gold particles depends on the laser intensity. Small graphite particles (several microns) suspended in toluene were also exposed to the laser flash. Ablation of these particles in the plasma generated by the laser leads to an orange solution which contains carbon-60, carbon-70 and other carbon clusters which have not yet been identified.

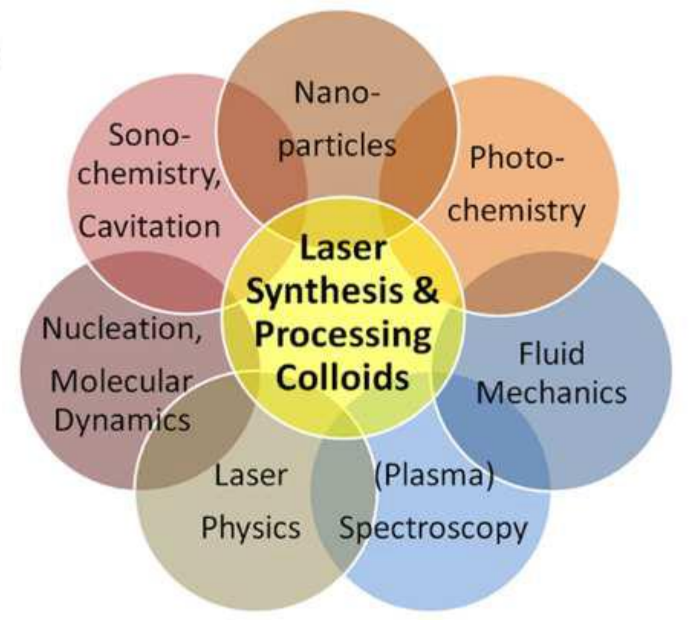
Ber. Bunsenges. Phys. Chem. 97 (**1993**) 2, 252-254



Biomedical Application

… to grow rapidly within connected disciplines

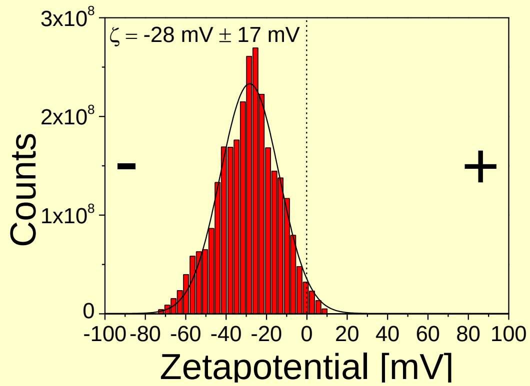




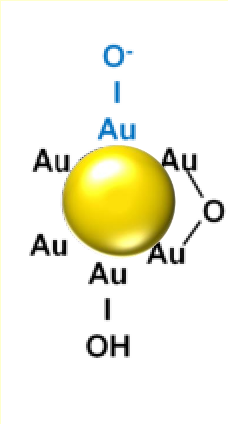
D. Zhang, B. Gökce, S. Barcikowski. Chem Rev. (2016), in revision

Surface Charge of laser-generated nanoparticles

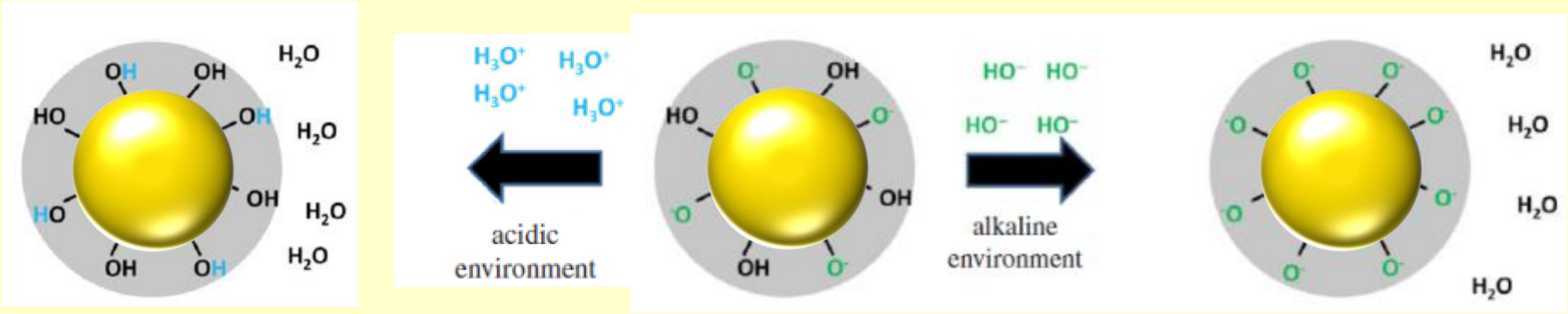
Noble metal nanoparticle surface is partially oxidized



adsorption of anions

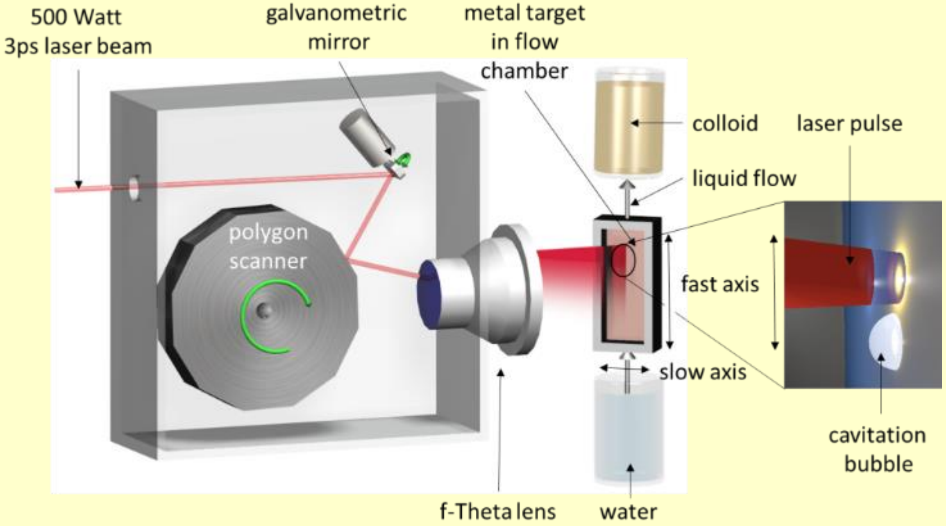


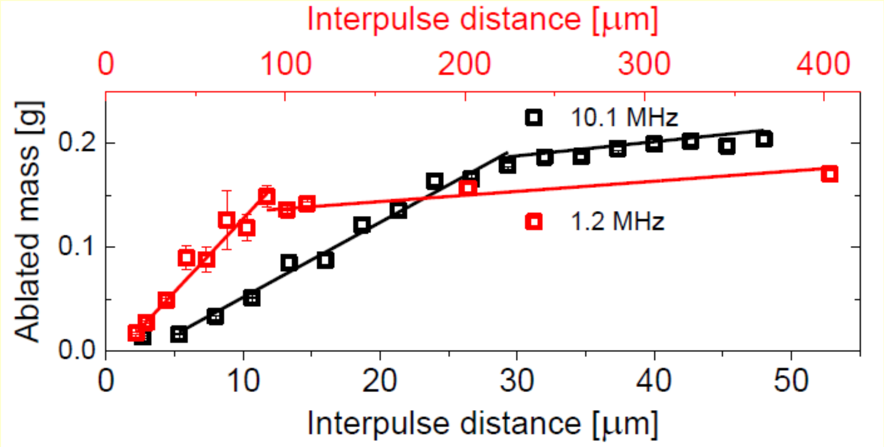
negative zeta potential (pH-dependent)

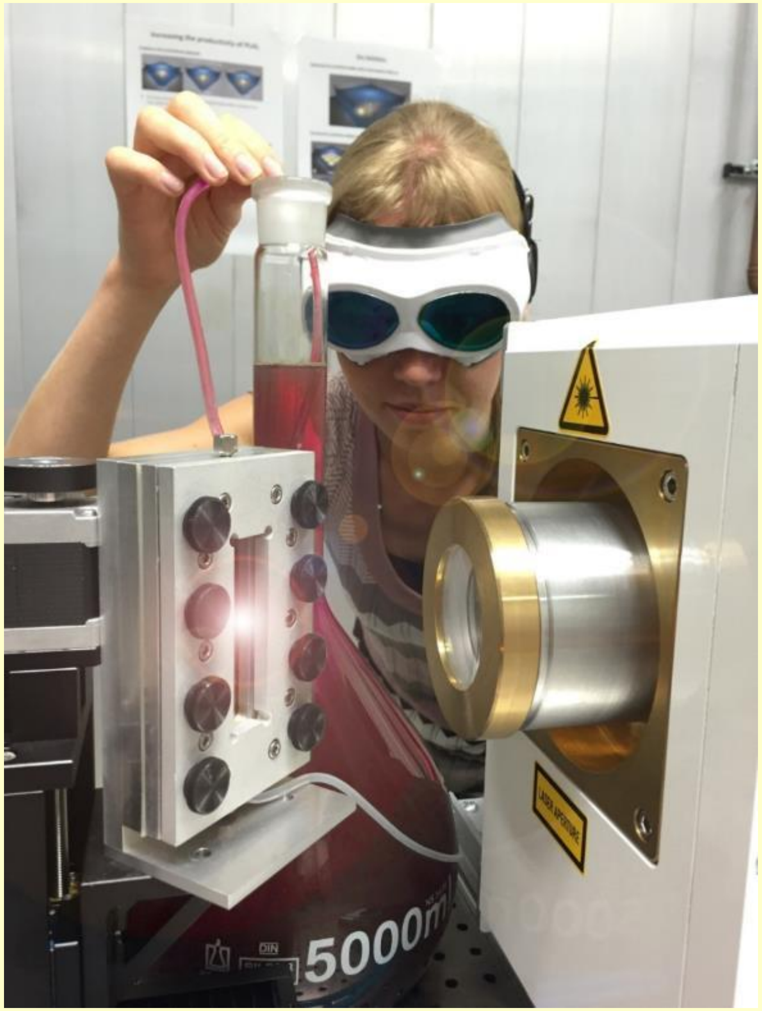


Rehbock; Barcikowski et al.; ***PCCP 2013***, *15 (9), 3057-3067.*
Pfeiffer, Barcikowski, Parak et al.,, ***J. R. Soc. Interface 2014***,*11, 20130931*

500 W, MHz, ps Laser Ablation at High-Speed (500 m/s)





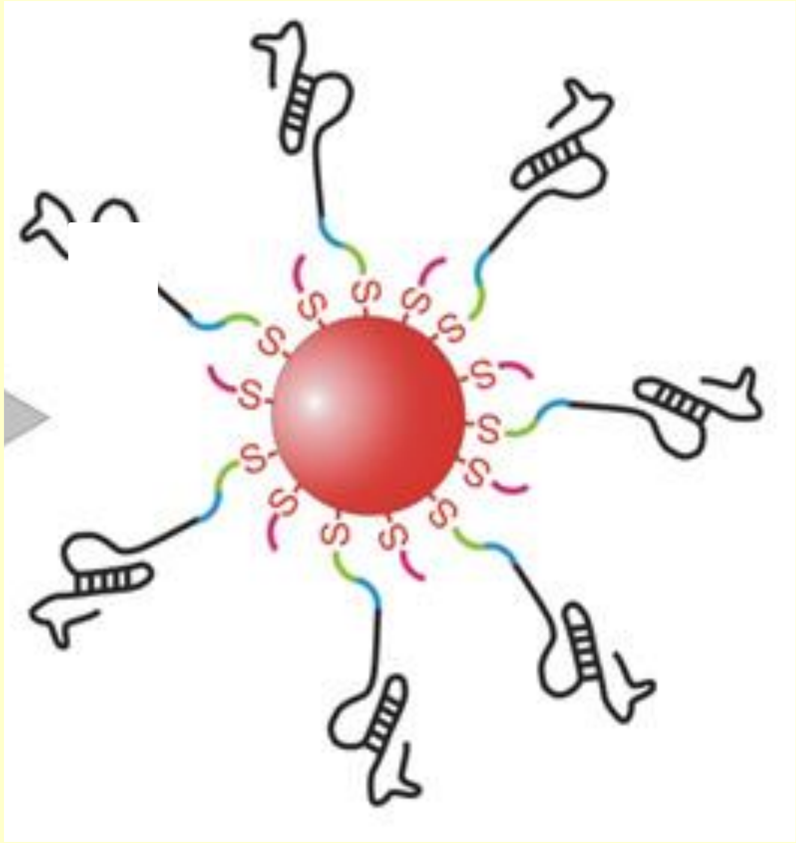


R. Streubel, S. Barcikowski, B. Gökce, Optics Letters 41 (2016), 1486

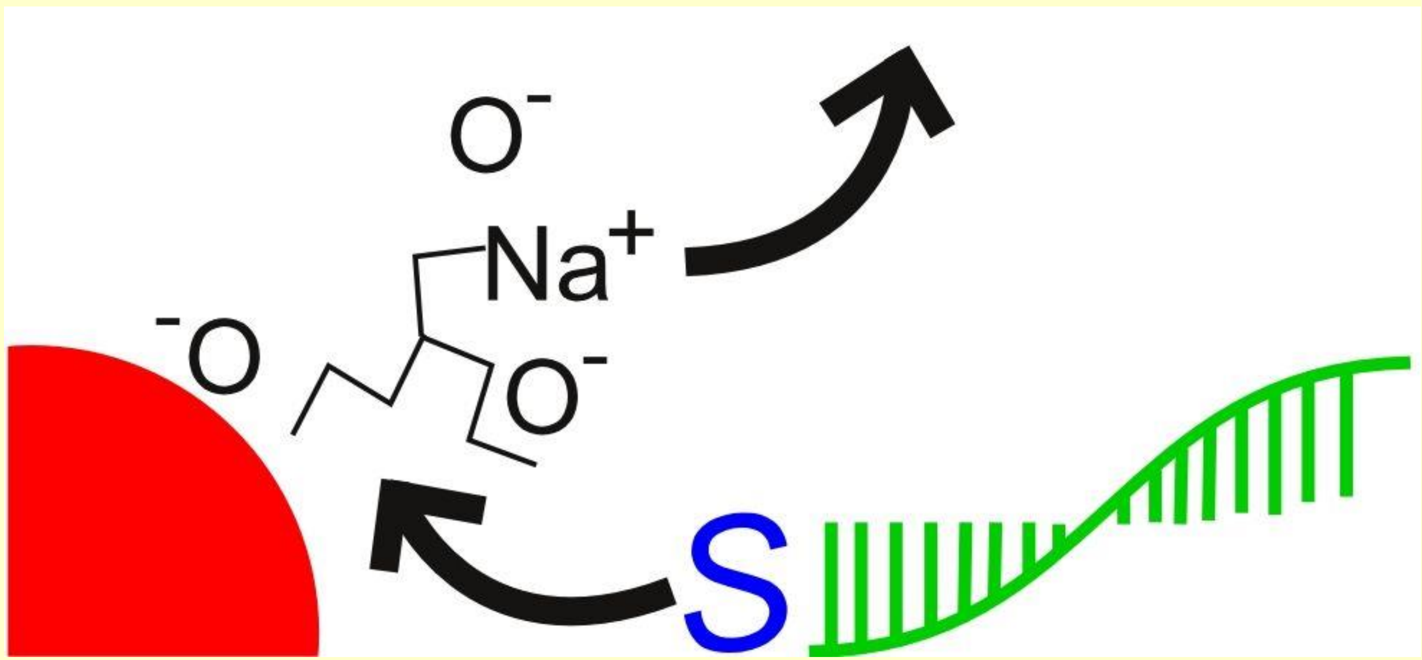
Laser for NANO (bio-medical)
ČVUT FJFI Praha 21.12.2017

Nanoparticle Targeting & Binding

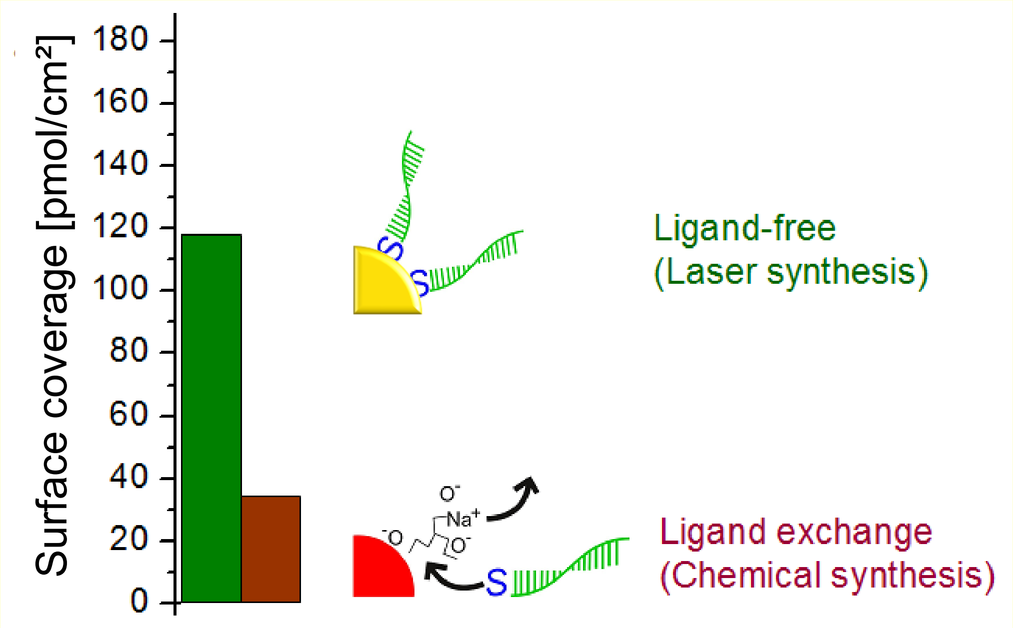
Bioconjugation of Nanoparticles



Ligand Exchange

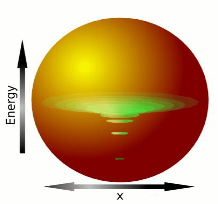


Conjugation Efficiency



Chemical reactants block the surface

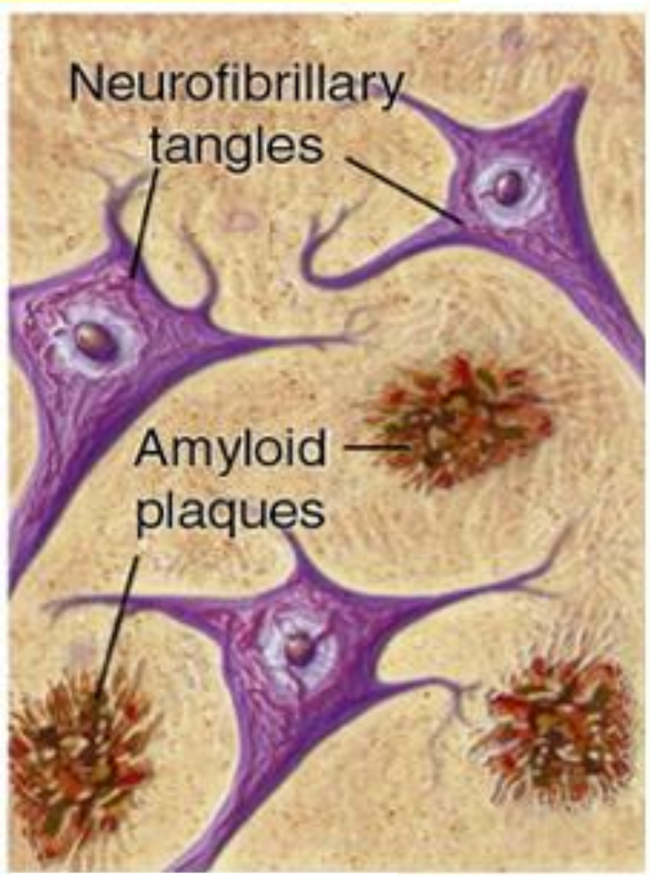
Laser-generated NP → **4 x higher surface coverage**

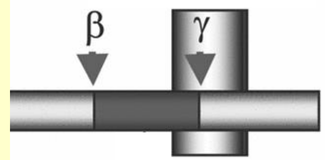


Morbus Alzheimer

Morbus Alzheimer

Alzheimer's brain

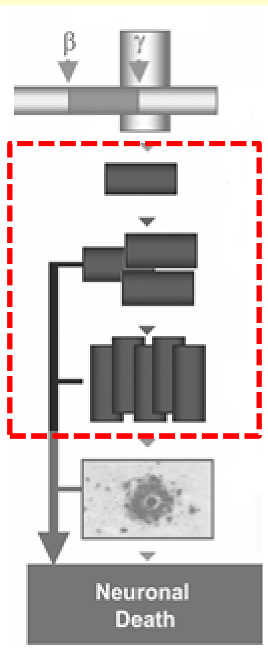




APP (amyloid precursor protein)

Biochemical Society Transactions (2005) 33, 553-558

How to counteract protein misfolding with nanoparticles?

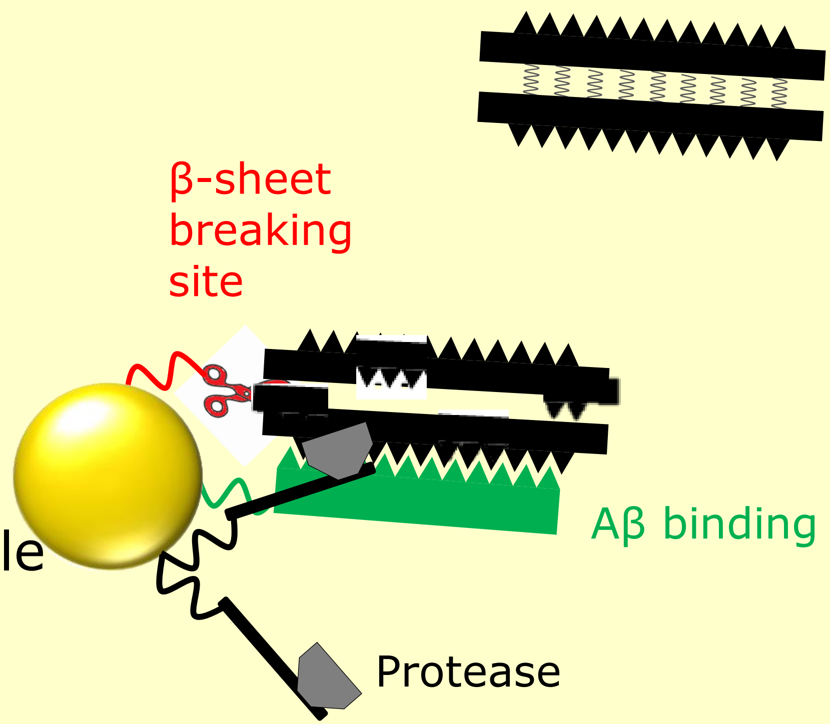


Aβ oligomers

Aβ fibrils

β-sheet rich aggregates of Aβ

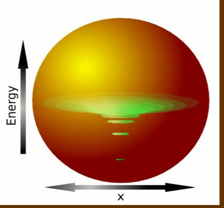
β-sheet breaking site



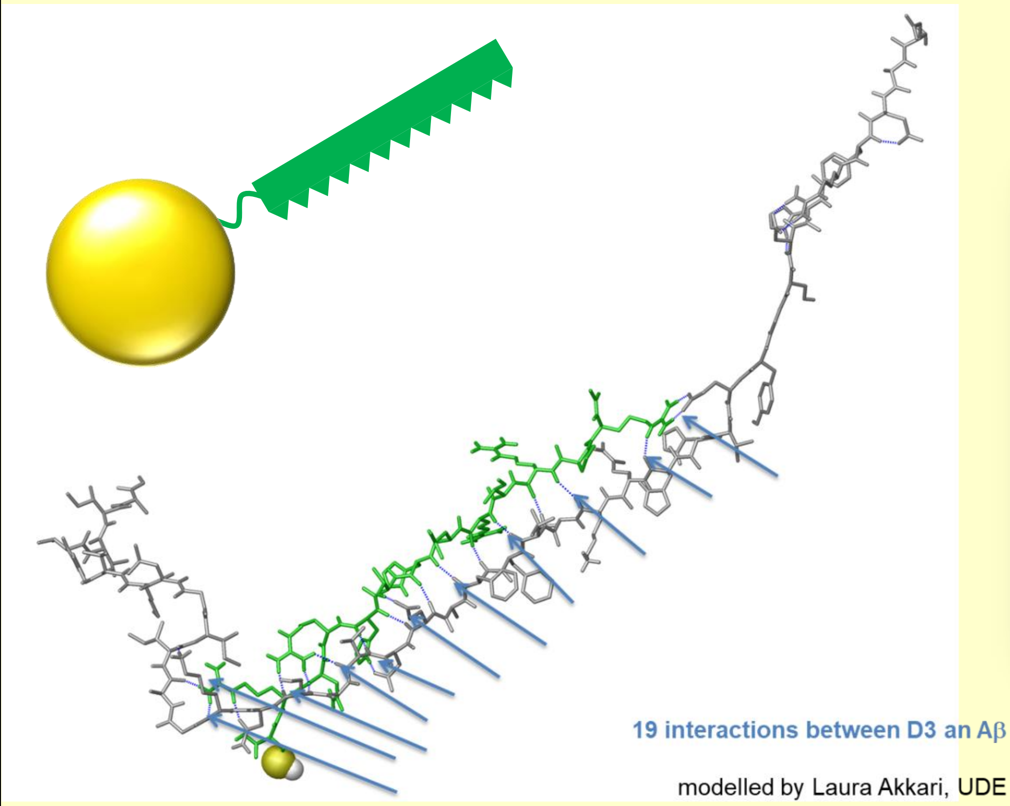
Nanoparticle

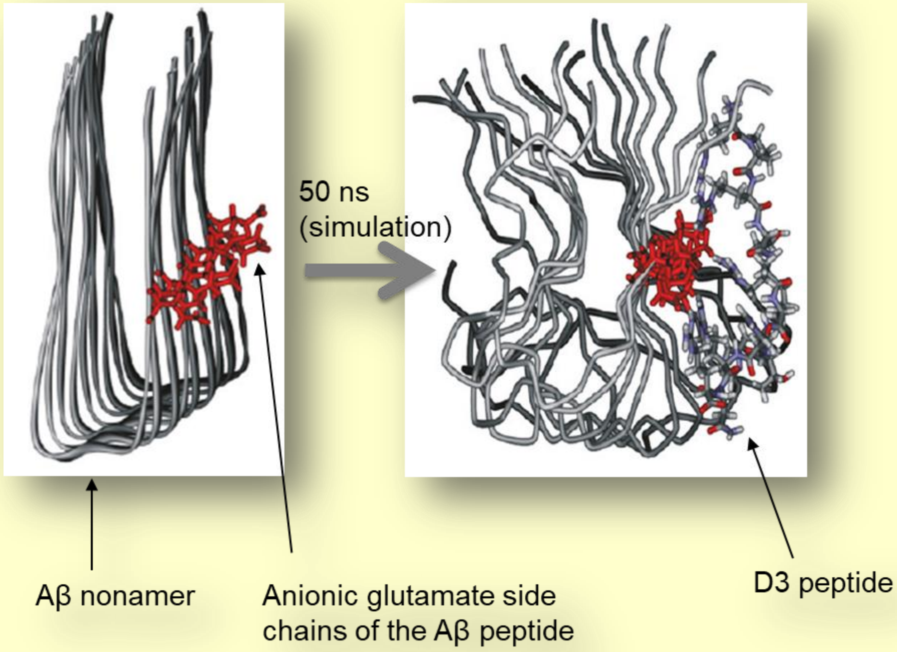
Aβ binding site

Protease



Molecular Design for Abeta-Targeting and Binding



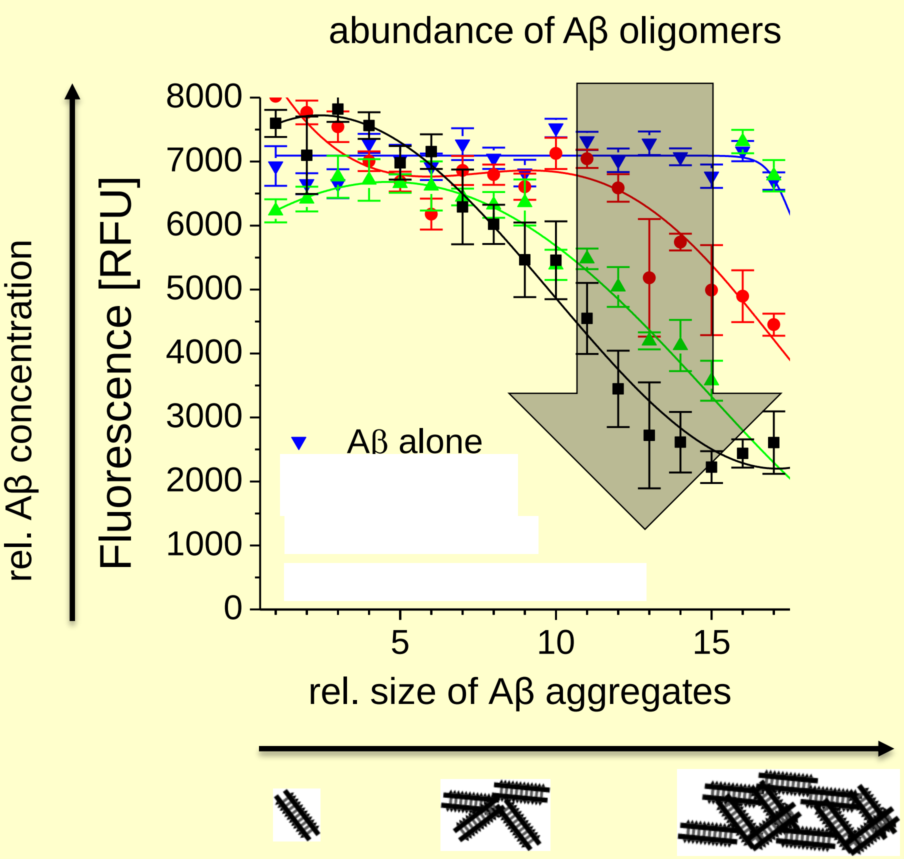


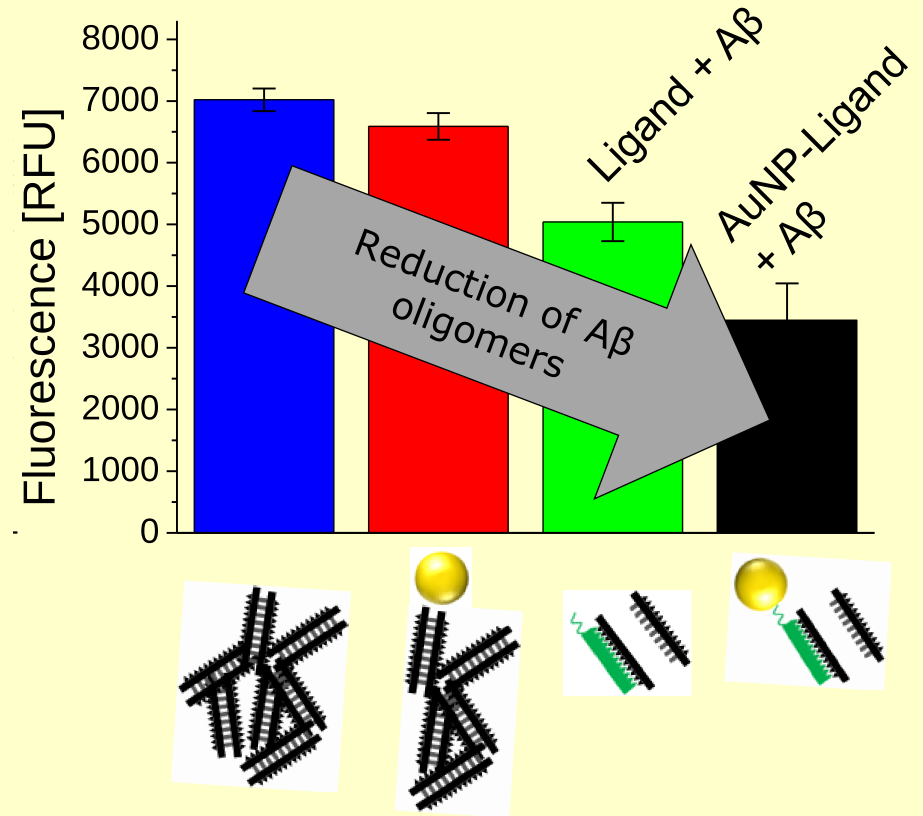
Funke et al., ACS Chem. Neurosci. (2010), 1, 639–648

Hochdoerffer, …Schrader: J. Am. Chem. Soc. 2011

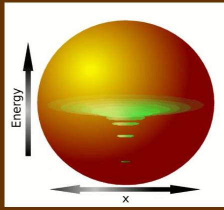
Müller-Schiffmann et al., Angew. Chem. Int. Ed. 2010

Inhibition of Alzheimer protein aggregation

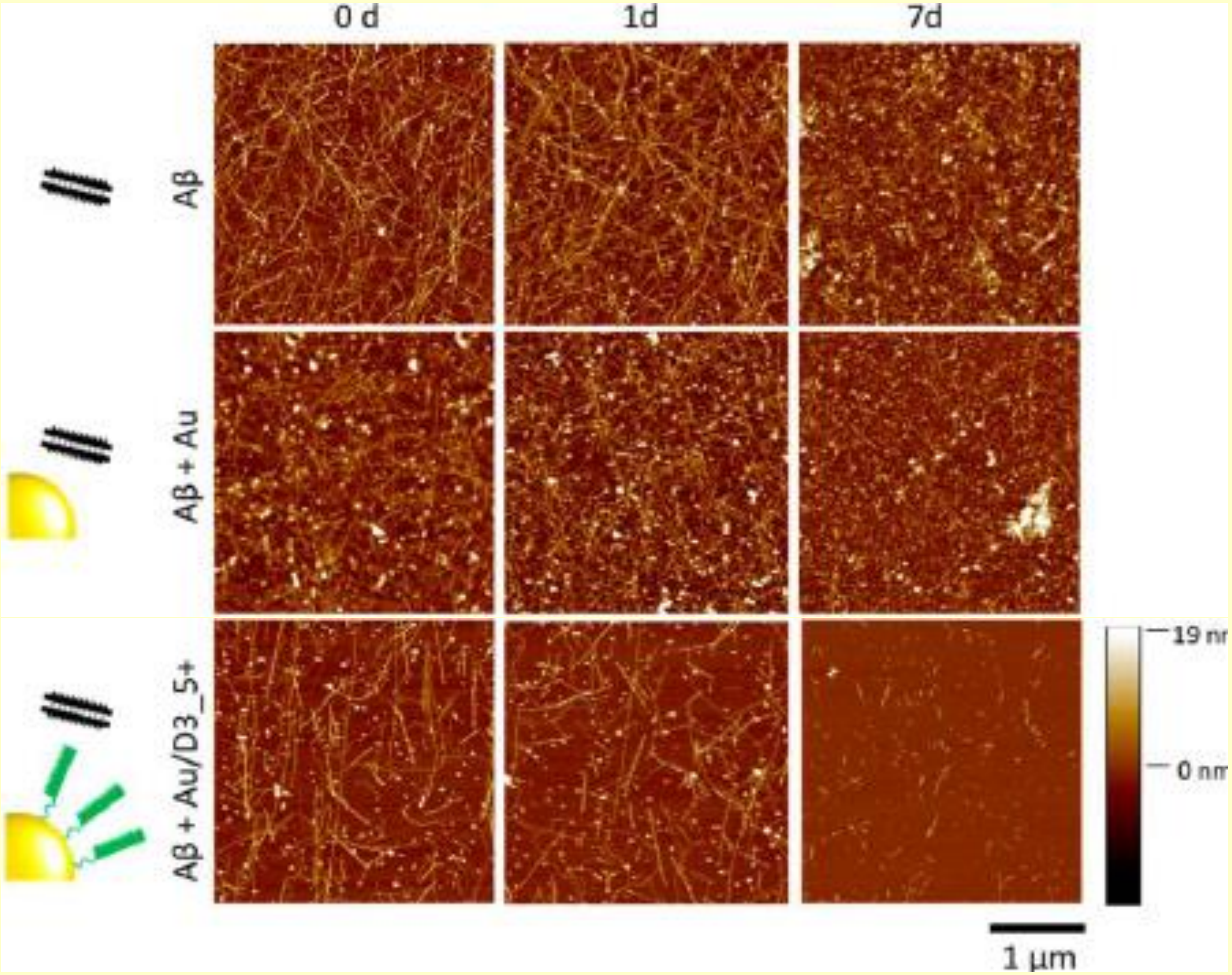




C. Streich, L. Akkari….T. Schrader, S. Barcikowski. ACS Nano, 2016, 10, 7582-7597



Inhibition of Alzheimer protein aggregation



C. Streich, L. Akkari….T. Schrader, S. Barcikowski. ACS Nano, 2016, 10, 7582-7597

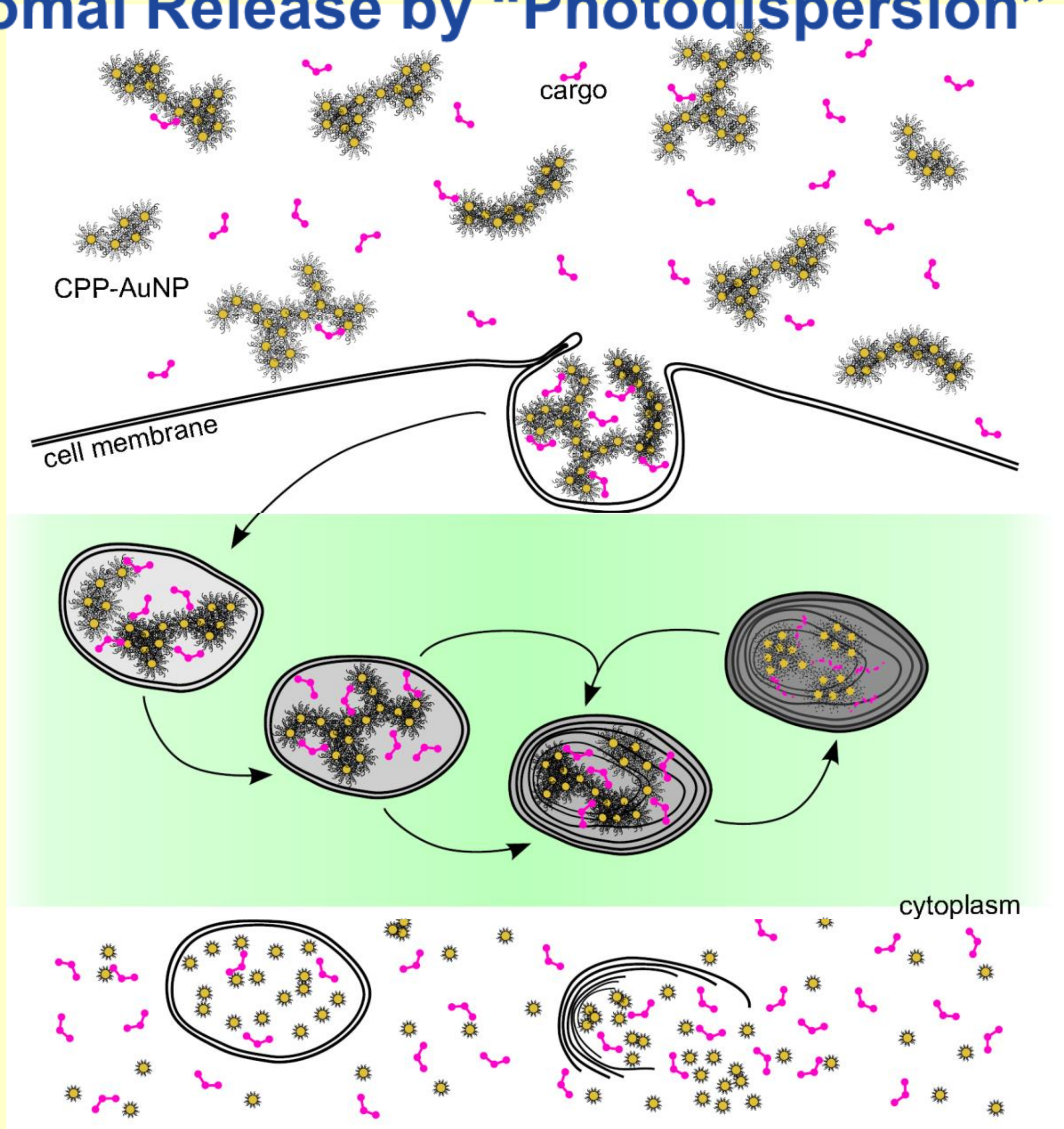
Endosomal Release by "Photodispersion"

Incubation of AuNP-NLS agglomerates

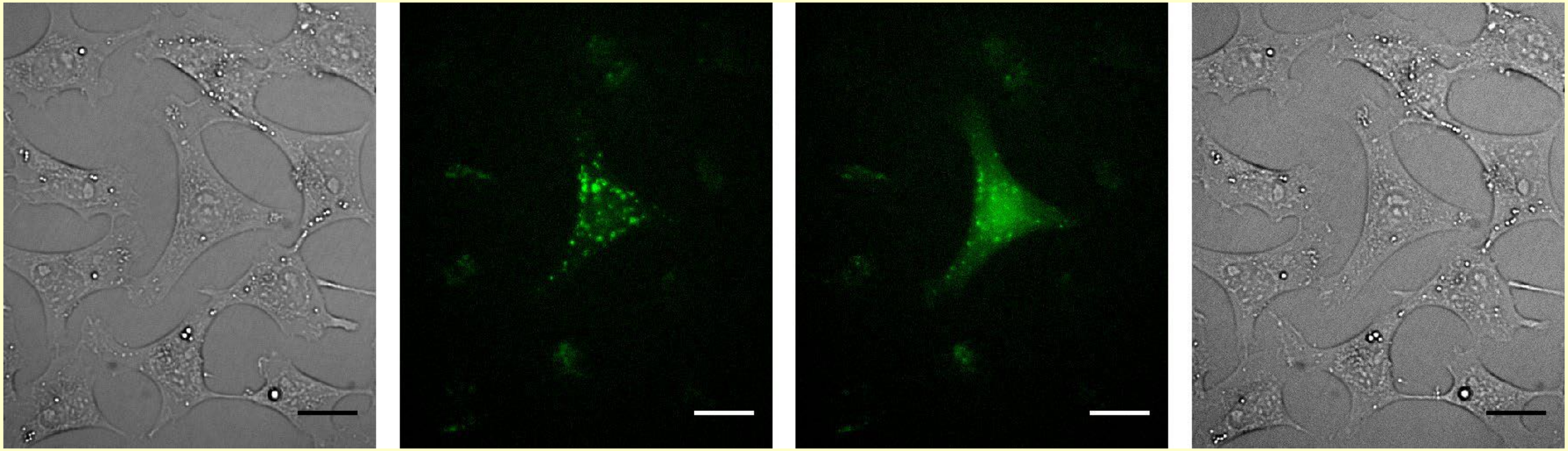
Endosomale uptake

Laser irradiation of enclosed agglomerates

Intracellular release



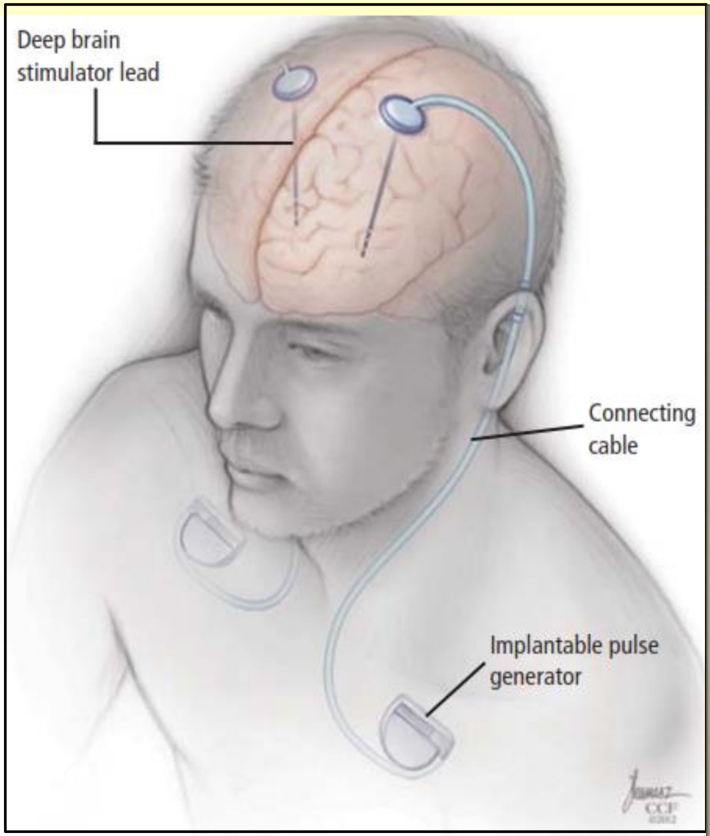
Endosomal Release by Photodispersion



Krawinkel *et al. J Nanobiotechnol (2016) 14:2*

Implants for Parkinson Therapy

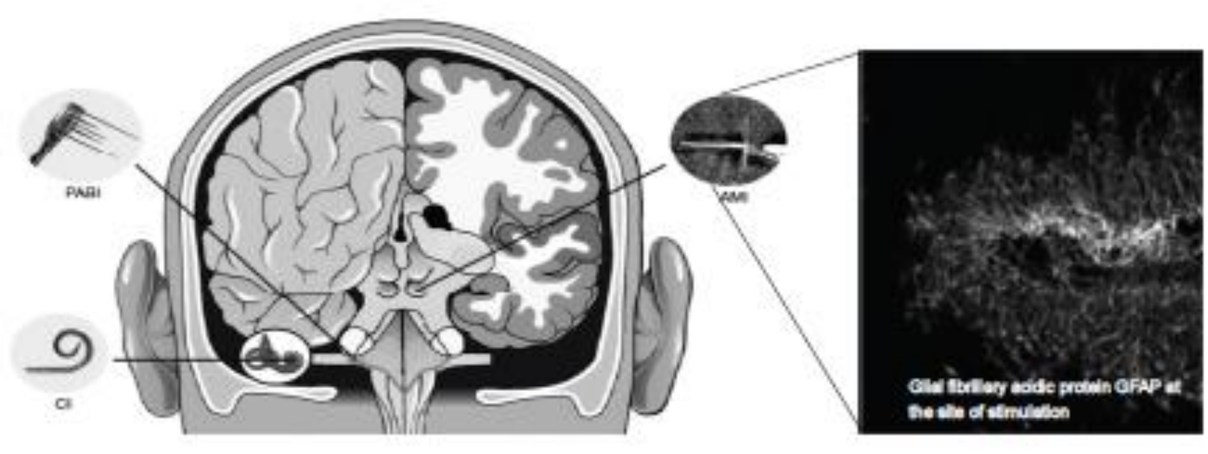
Deep Brain Stimulation (DBS)



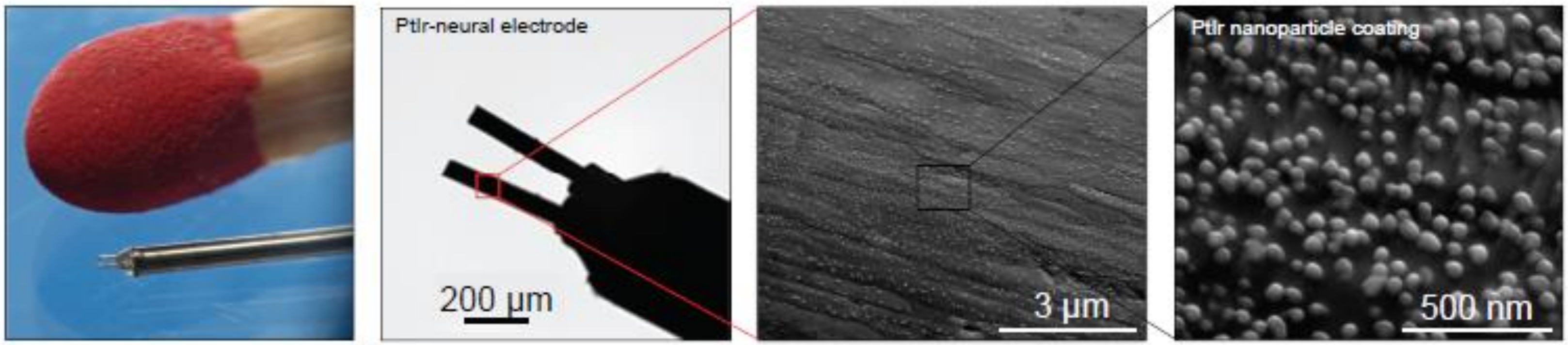
H. Fernandez, *Cleveland Clinic Journal of Medicine* **2012**, *79*, 28

Andrew Johnson, on: youtu.be./uBh2LxTW0s0

Nanoparticle Coating of Neural Electrodes (Parkinson Disease)



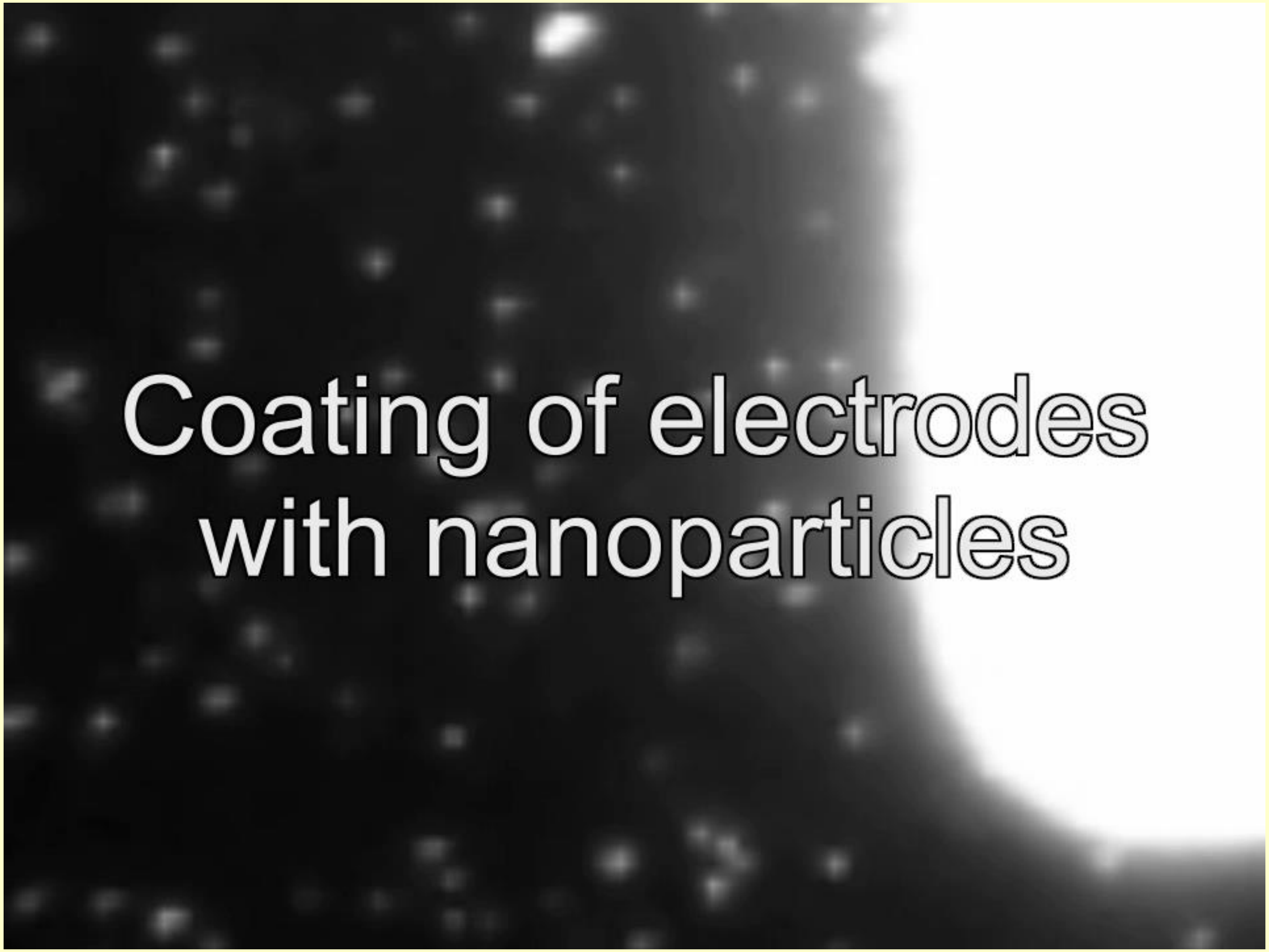
Unwanted electrode encrustation. Coronal cross-section of rat brain with glial reaction around electrode tip.



Neural Pt_9Ir electrode coated with monolayer of laser-generated Pt_9Ir nanoparticles after annealing.

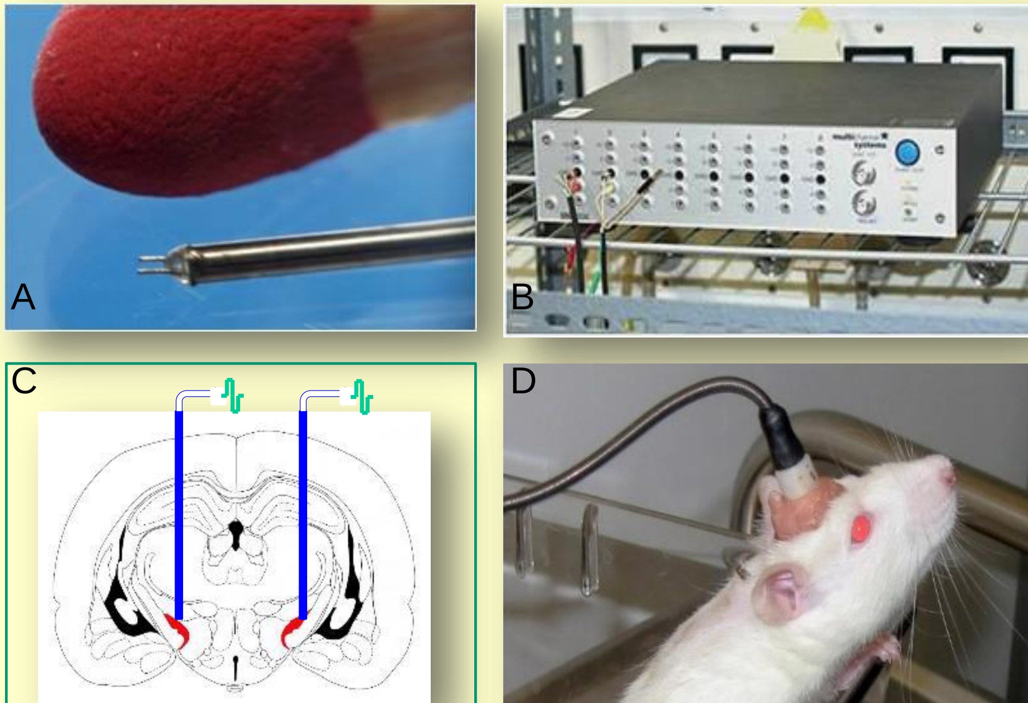
J. Jakobi et al. *Nanotechnology* (2011)

Deposition of Ligand-Free Nanoparticles on Neural Electrode Surfaces

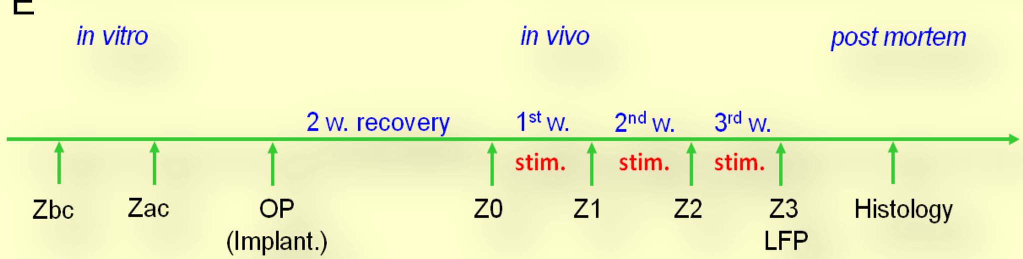


YouTube-Channel: http://youtube.com/nanofunction

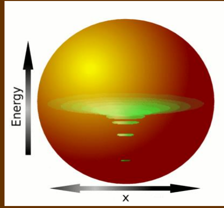
Clinical Testing of Neural Electrodes



E



Angelov, Koenen, Jakobi, Heissler, Alam, Schwabe, Barcikowski, Krauss, *J Nanobiotechnol (2016)*



**Presently, situation for such a field of research,
i.e., „Nanoparticle Generation by Lasers in Liquids",
is becoming a much hotter topic due to availability
of picosecond and femtosecond lasers.**

Shorter time for energy deposition causes less problems:
-with high temperature,
-narrowing the size distribution,
-with possible applications in biological systems.

Prof. Stephan Barcikowski, University Essen-Duisburg Gernany
Prof. Vincenzo Amendola, University of Padova, Padova, Italy

of_gold-in-water.mp4