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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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 other 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.
Example of unusually properties of nanomaterials

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

• Black semiconductor like Cd$_3$As$_2$ 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$_3$As$_2$ in aqueous solutions in UV light Increasing particles size from left to right
Powder TiO$_2$ (big particles)

Nanoparticles TiO$_2$
Energy and wavelength of free electron

Maxwell-Boltzmann  \[ E = \frac{3}{2} kT \quad E_{300K} \approx 0.04 \text{ eV} \]

where \( E \) is the kinetic energy of the carrier, \( T \) is temperature in K, and \( k = 1.38 \times 10^{-23} \text{ JK}^{-1} \).

DeBroglie - duality of particles

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

where \( \lambda \) is the wavelength of the carrier with mass \( m \) and \( h = 6.63 \times 10^{-34} \text{ Js} \).

In case of thermal electron \( m = 9.1 \times 10^{-31} \text{ kg} \), at 300 K

\[ \lambda \approx 62 \text{ Å} \]
### Similarities in Characteristics of Photons and Electrons

<table>
<thead>
<tr>
<th>Photons</th>
<th>Fotonické struktury</th>
<th>Electrons</th>
<th>Elektronické struktury</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wavelength</strong></td>
<td></td>
<td></td>
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<tr>
<td>$\lambda = \frac{\hbar}{p} = \frac{c}{\nu}$</td>
<td>$\lambda = \frac{\hbar}{p} = \frac{\hbar}{mv}$</td>
<td></td>
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<tr>
<td><strong>Eigenvalue (Wave) Equation</strong></td>
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<tr>
<td>$\left{ \nabla \times \frac{1}{\varepsilon(r)} \nabla \times \right} B(r) = \left( \frac{\omega}{c} \right)^2 B(r)$</td>
<td>$\hat{\mathcal{H}}\psi(r) = \frac{\hbar^2}{2m} (\nabla \cdot \nabla + V(r))\psi(r) = E\psi$</td>
<td></td>
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<tr>
<td><strong>Maxwellovy rovnice</strong></td>
<td><strong>Free-Space Propagation</strong></td>
<td><strong>Schrödingerova rovnice</strong></td>
<td></td>
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<tr>
<td>Plane wave</td>
<td>Plane wave:</td>
<td>Plane wave:</td>
<td></td>
</tr>
<tr>
<td>$E = (\frac{1}{2})E_0(e^{ik \cdot r - \omega t} + e^{-ik \cdot r + \omega t})$</td>
<td>$\Psi = c(e^{ik \cdot r - \omega t} + e^{-ik \cdot r + \omega t})$</td>
<td>$\Psi = c(e^{ik \cdot r - \omega t} + e^{-ik \cdot r + \omega t})$</td>
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<tr>
<td>$k = $ wavevector, a real quantity</td>
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<tr>
<td><strong>Interaction Potential in a Medium</strong></td>
<td><strong>Coulomb interactions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dielectric constant (refractive index)</td>
<td>Coulomb interactions</td>
<td></td>
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</tbody>
</table>

### Propagation Through a Classically Forbidden Zone
- Photon tunneling (exponentially decaying 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
Ambitious objective of project EUREKA (EU and Germany 1980) 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 $10 \div 100$ 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

1 molecule of bulk material

nanoproduct

Energy levels

bulk material

CB conducting band
20 meV Exciton

2.4 eV (CdS)

VB Valence band

Energie

X∞

X10

X2

LUMO

hν

HOMO

Conducting band

Band gap

Valence band
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.
Laser for NANO (bio-medical)
ČVUT FJFI Praha 21.12.2017
Silicon nanoparticles

~ 10 nm size

SiO₂ surface shell
silicon nanoparticle

Chemical etching

Photoluminescence Si nanoparticles in cyclohexane


CREEP EFFEKT

Simulace supratekutosti (vzlínání)

0 sec  5 sec  30 sec
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...
A: Experimental arrangement for ablation of films in liquid by a strong laser beam

V: glass vessel,  F: film on glass support, G: lens,  B: laser beam,  O: optical cuvette

Rb laser 697 nm, 3-5ns

A. post-irradiation, fragmentation, melting
B. coalescence and reaction of activated species (ions, atoms, cluster)
C. ablation
D. cavitation
E. lens
Absorption spectra of the colloidal gold solutions obtained at different laser intensities. The gold film was 500Å thick and illuminated in 2-propanol without stabilizer. Laser intensity: a: 2.3 J/cm², b: 7.0 J/cm², c: 27 J/cm². 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.
Formation of Nanometer-Size Silicon Particles in a Laser Induced Plasm in SiH₄

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.
Laser for NANO (bio-medical)
ČVUT FJFI Praha 21.12.2017
New approach
Biological Application of Laser-generated Nanoparticles
For biomedical applications, purity matters.
Purity of "Gold Colloid" (Material Safety Data Sheet)

All unconjugated gold colloids contain approximately 0.01% HAuCl₄ suspended in 0.01% tannic acid with 0.04% trisodium citrate, 0.26 mM potassium carbonate, and 0.02% sodium azide as a preservative.
Ligand-free Nanoparticles from Laser Ablation in Liquids
When it begun ...

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.

Biomedical Application
... to grow rapidly within connected disciplines

Surface Charge of laser-generated nanoparticles

Noble metal nanoparticle surface is partially oxidized

\[ \zeta = -28 \text{ mV} \pm 17 \text{ mV} \]

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
Nanoparticle Targeting & Binding
Bioconjugation of Nanoparticles
Ligand Exchange

obtained coverage
surface coverage of ssO [pmol cm$^{-2}$]

particle mean diameter [nm]

Au$^+$, Au$^{3+}$
in situ ex situ

BSA conjugation (multi layer formation)
calculated saturation conjugation by ligand exchange

non specific binding (no thiol)
Conjugation Efficiency

Chemical reactants block the surface

Laser-generated NP $\rightarrow 4 \times$ higher surface coverage
Morbus Alzheimer
Morbus Alzheimer

Alzheimer’s brain

Neurofibrillary tangles

Amyloid plaques

APP (amyloid precursor protein)

β

γ

BIOCHEMICAL SOCIETY TRANSACTIONS (2005) 33, 553-558
How to counteract protein misfolding with nanoparticles?

- β-sheet rich aggregates of Aβ
- β-sheet breaking site
- Aβ fibrils
- Aβ oligomers
- Neuronal Death
- Nanoparticle
- Aβ binding site
- Protease
Molecular Design for Abeta-Targeting and Binding

19 interactions between D3 an Aβ
modelled by Laura Akkari, UDE

Aβ nonamer
Anionic glutamate side chains of the Aβ peptide
D3 peptide

Funke et al., ACS Chem. Neurosci. (2010), 1, 639–648
Müller-Schiffmann et al., Angew. Chem. Int. Ed. 2010
Inhibition of Alzheimer protein aggregation

Fluorescence [RFU] vs. rel. size of Aβ aggregates

- Aβ alone
- AuNP + Aβ
- Ligand + Aβ
- AuNP-Ligand + Aβ

Reduction of Aβ oligomers

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

Endosomal 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
Nanoparticle Coating of Neural Electrodes (Parkinson Disease)

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

Neural Pt₉Ir electrode coated with monolayer of laser-generated Pt₉Ir nanoparticles after annealing.

J. Jakobi et al. Nanotechnology (2011)
Deposition of Ligand-Free Nanoparticles on Neural Electrode Surfaces

Coating of electrodes with nanoparticles
Clinical Testing of Neural Electrodes

A

B

C

D

E

in vitro

in vivo

post mortem

2 w. recovery

1st w.

2nd w.

3rd w.

Zbc

Zac

OP (Implant.)

Z0

Z1

Z2

Z3

LFP

Histology

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 Germany
Prof. Vincenzo Amendola, University of Padova, Padova, Italy