

Nanotechnology

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- 1.5 Properties of Nanoscale Matter**

2. Preparation of Nanostructures

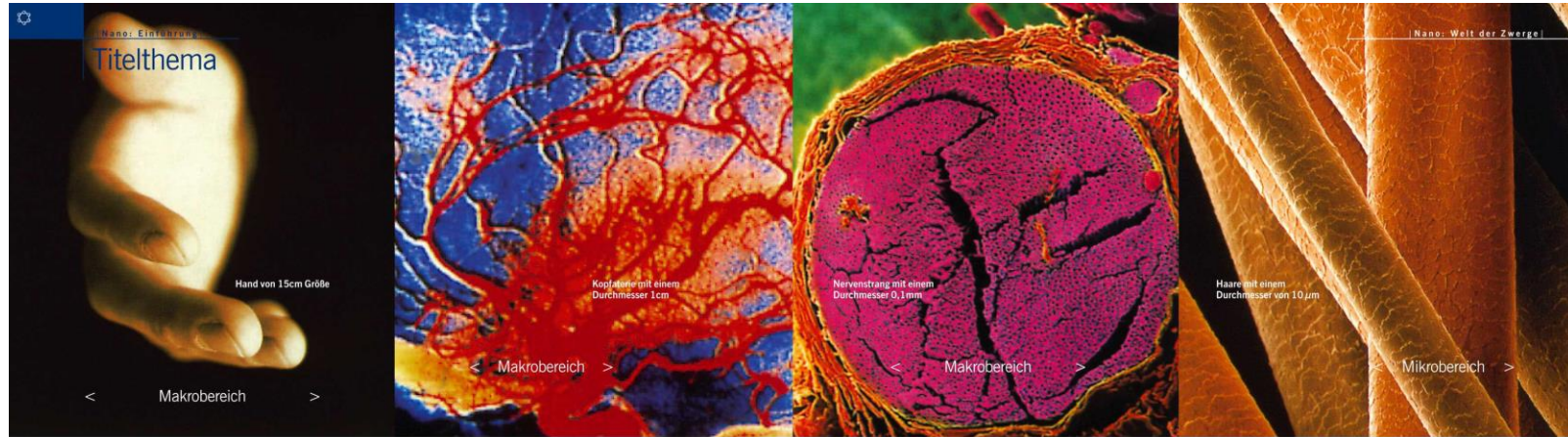
- 2.1 Approaches to Nanoscale Structures**
- 2.2 Ball Milling**
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- 3.4 Medical Therapy**
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- 3.6 Biosensors and -assays**

1.1 Motivation

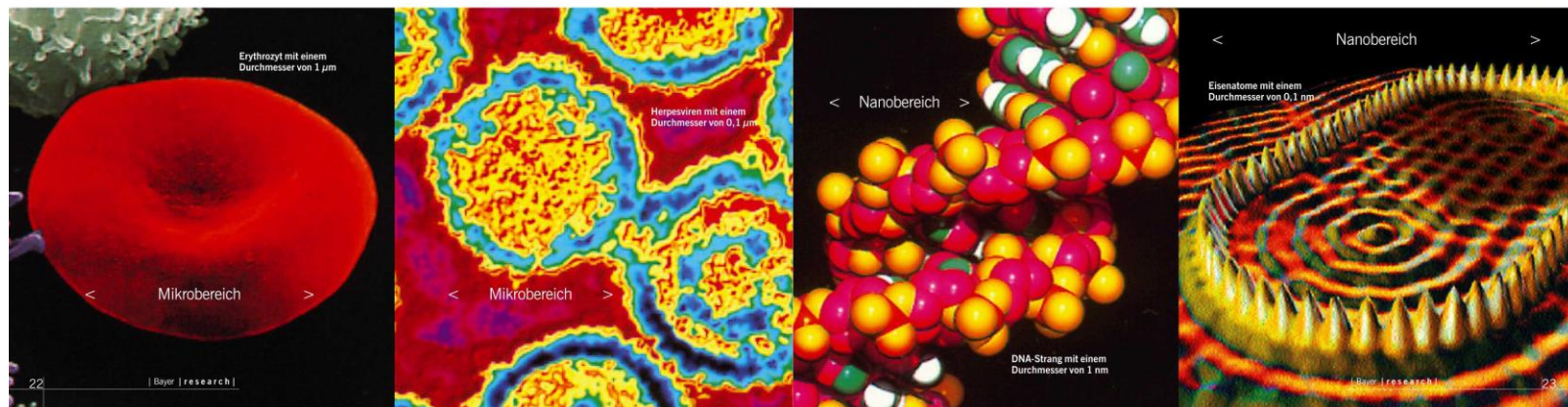
Many Application Areas, e.g. Chemistry, Electronic, Materials, Medicine, Photonic



BAYER-FORSCHER EROBERN DEN NANOKOSMOS

Aufbruch in den Nanokosmos

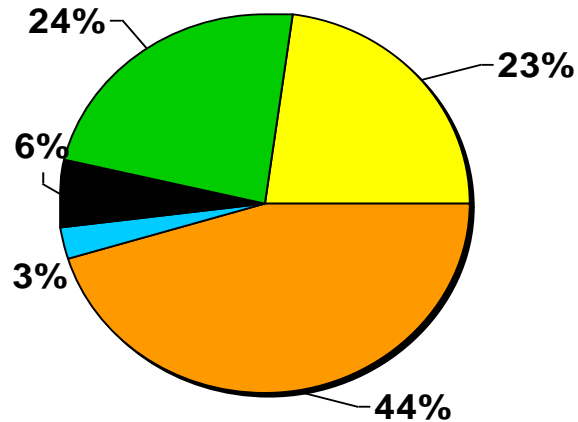
DER WEG IN DEN NANOKOSMOS erschließt Forschern völlig neue Welten. Die winzigen Dimensionen übersteigen die menschliche Vorstellungskraft und lassen neue Kräfte wirksam werden. →



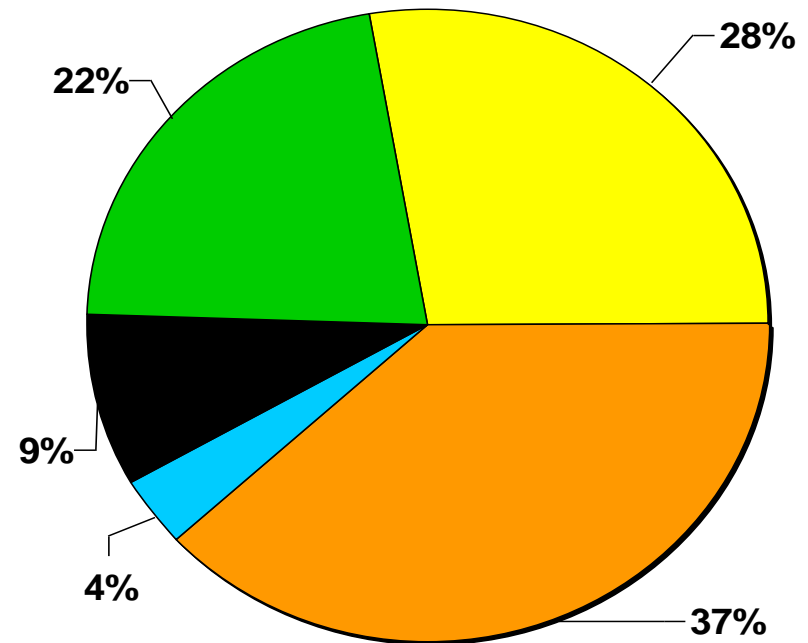
1.2 Economical Relevance






World market for nanotechnology in percent

2001: 54 Bill. €



2010: 220 Bill. €

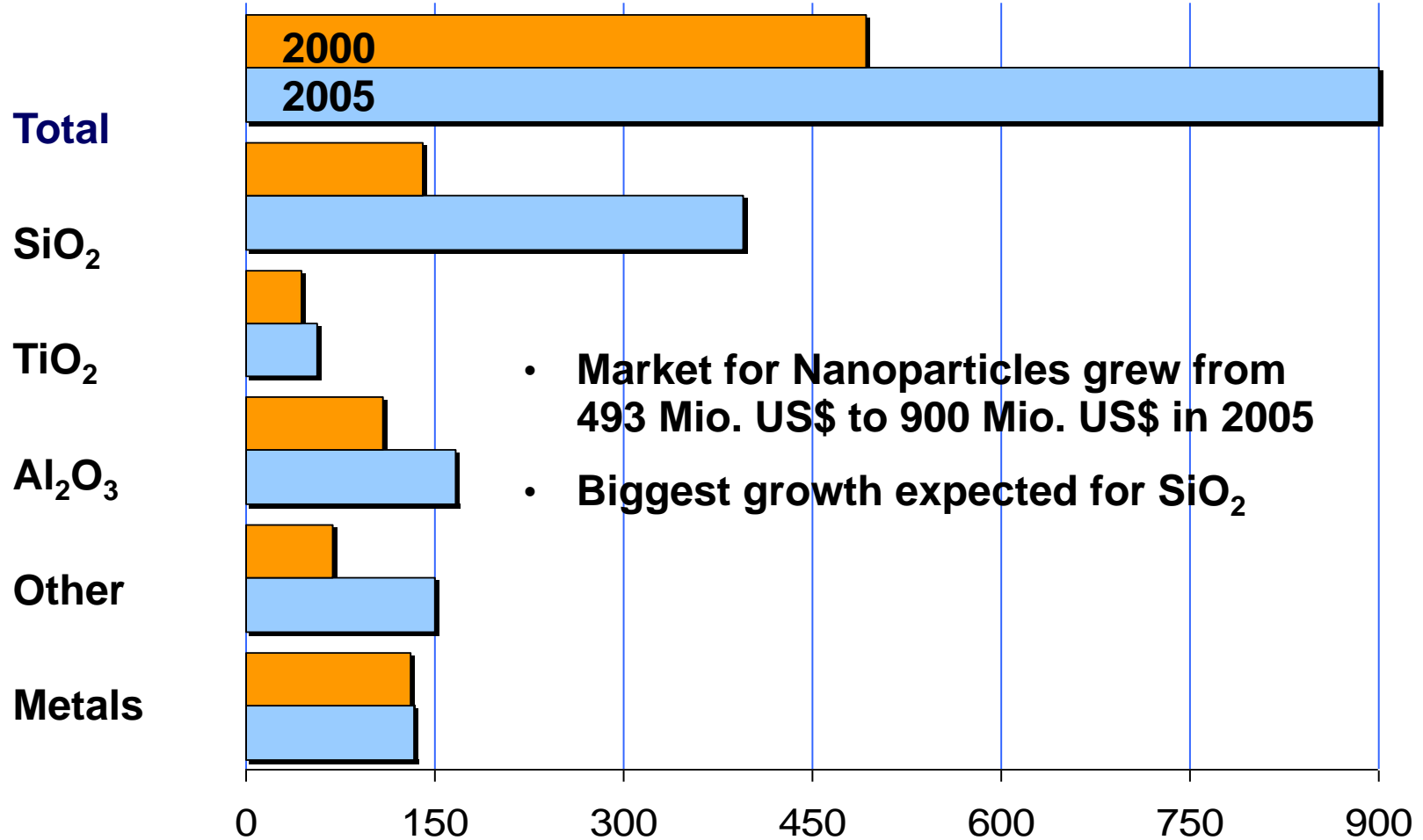


-  Nanoparticles and nanocomposites
-  Ultrathin layers
-  Analysis of nanostructures
-  Ultraprecise modification of surfaces
-  Lateral Nanostructures

Source: DG Bank

1.2 Economical Relevance

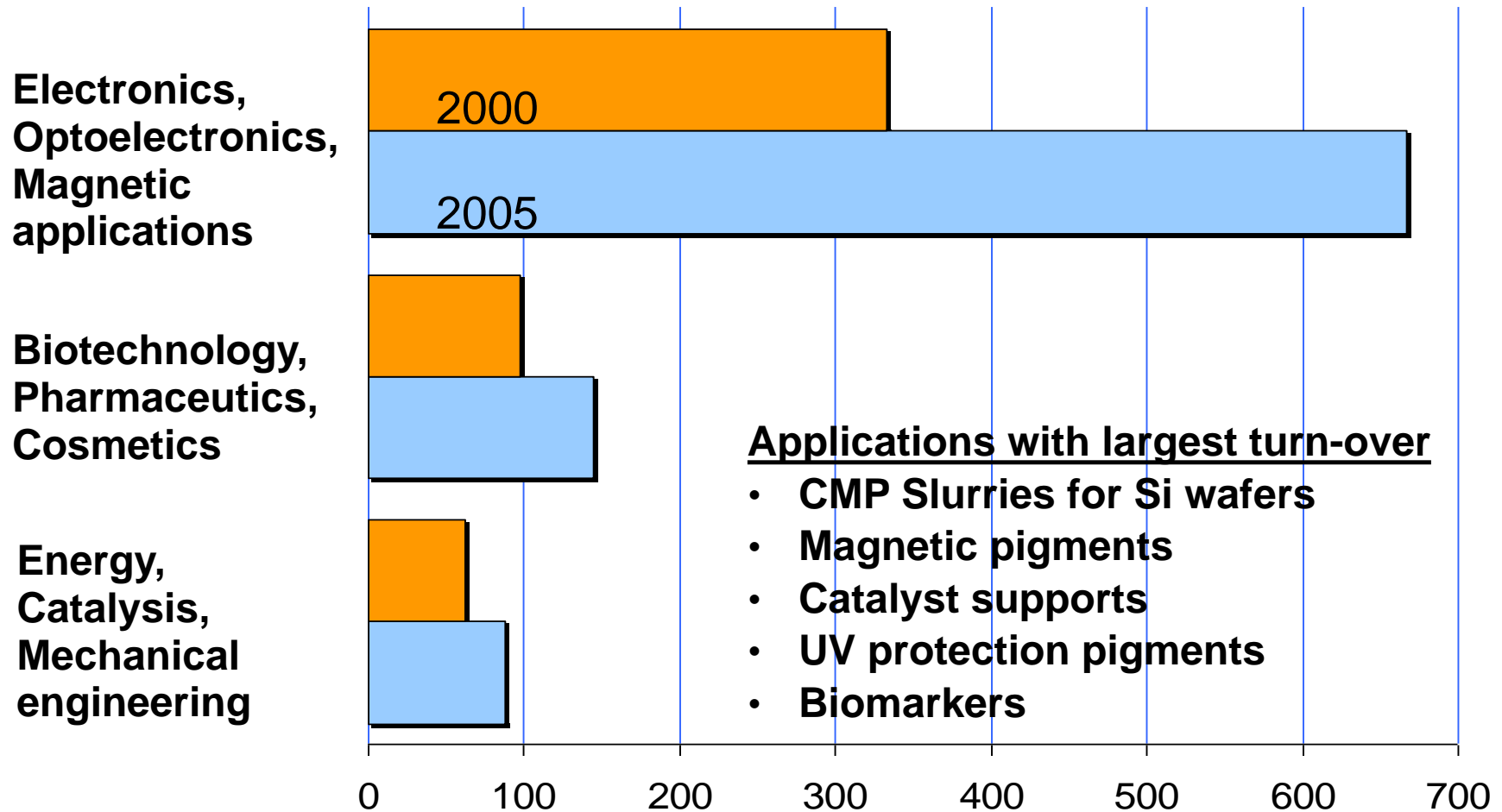
World market for nanoparticles in Mill. US\$ by material



Source: BCC 2002

1.2 Economical Relevance

World market for nanoparticles in Mill. US\$ by application area



Applications with largest turn-over

- CMP Slurries for Si wafers
- Magnetic pigments
- Catalyst supports
- UV protection pigments
- Biomarkers

Source: BCC Inc. 2002

1.3 Definition

What is Nanotechnology?

Nano: Greek prefix which means dwarf

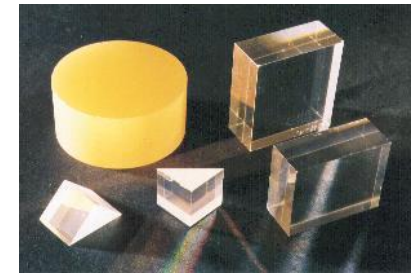
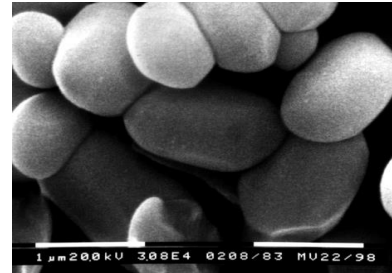
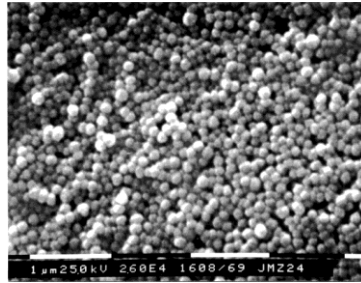
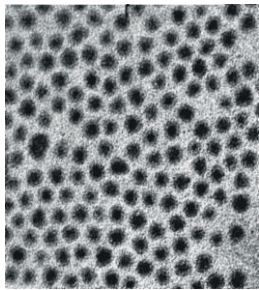
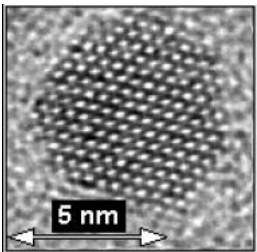
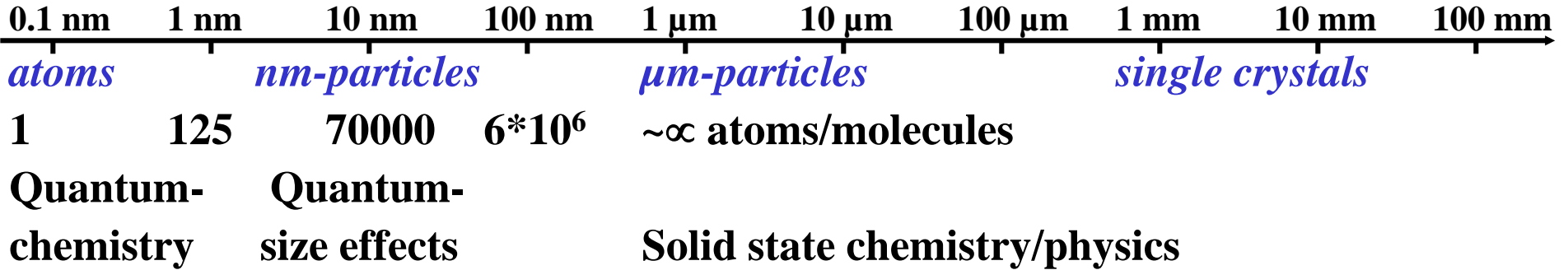
Nanotechnology can be defined as

- 1. Research and technology development at the atomic, molecular or macromolecular levels, in the length scale of approximately 1 -100 nanometer**
- 2. Creating and using structures, devices and systems that have novel properties and functions because of their small and/or intermediate size**
- 3. Ability to control or manipulate on the atomic scale**

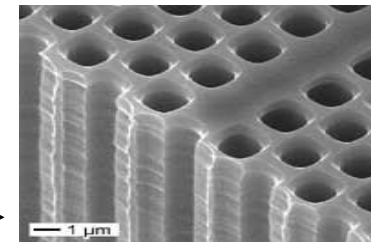
According to the NNI, USA (<http://www.nano.org>)

1.3 Definition

Nanoscale particles have an average particle size smaller than ~ 100 nm

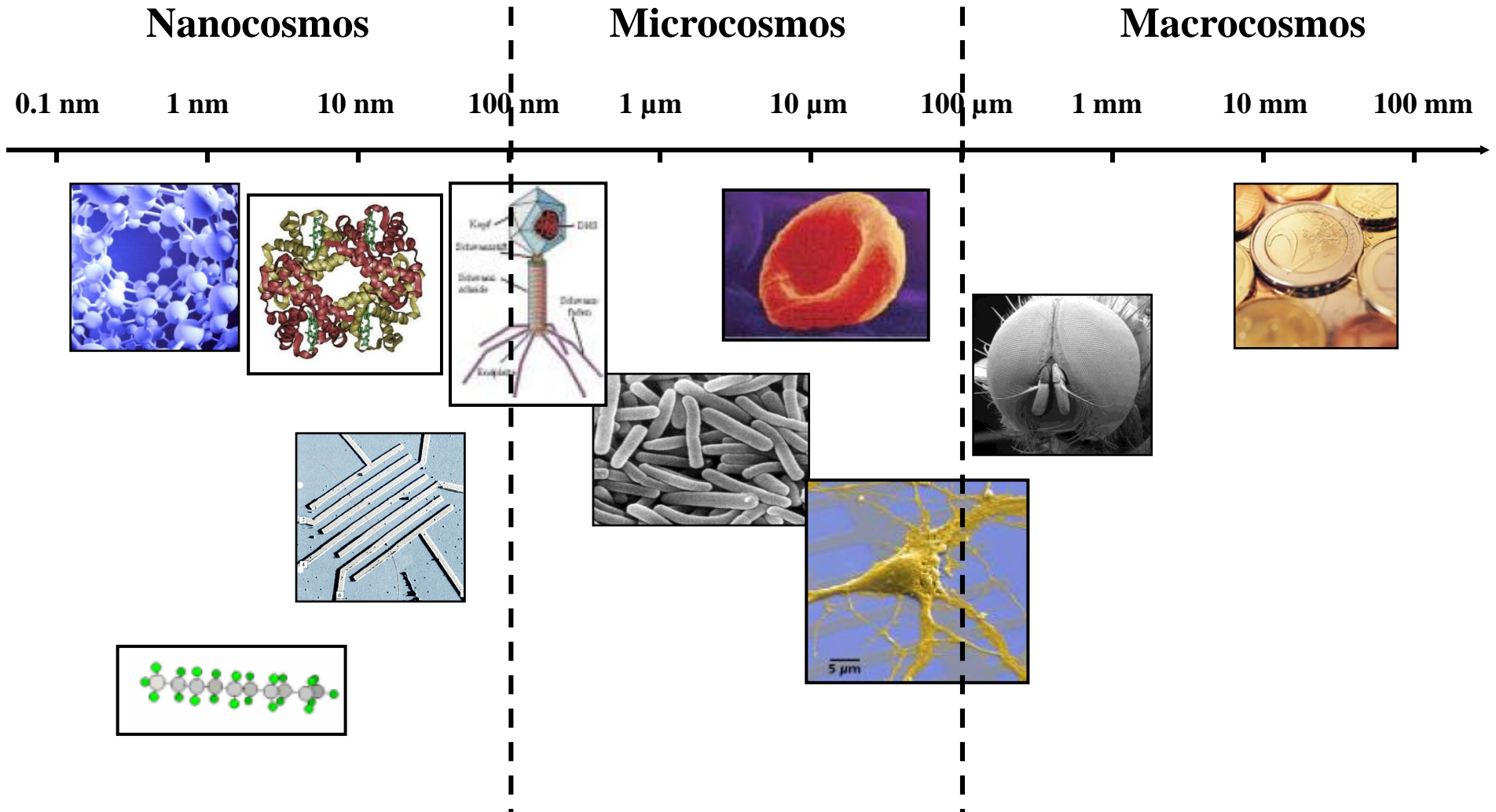


- 0-dim. Quantum dots luminescence marker
- 1-dim. Quantum wires field emission electrodes
- 2-dim. Quantum wells active layer in LEDs
- 3-dim. Bulk photonic crystals



1.3 Definition

Dimensions of structures in biochemistry and material science



1.4 Historical Milestones

3.5 Mrd. Years	Procaryontic cells with nano machines
400 B.C.	Demokrit: Reasoning about atoms and matter
1905 A.D.	Albert Einstein: Calculate molecular diameter
1931	Max Knoll & Ernst Ruska: Electron microscope
1959	Richard Feynman: „There’s Plenty of Room at the Bottom“
1968	Alfred Y. Cho & John Arthur (Bell Labs): MBE (atomic layer growth)
1974	Norio Taniguchi: Nanotechnology for fabrication methods below 1 μm
1981	Gerd Binnig & Heinrich Rohrer: Nobel Prize for Scanning Tunneling Microscope
1985	Robert F. Curl, Harold W. Kroto, Richard Smalley: Buckminsterfullerenes (Bucky balls)
1986	K. Eric Drexler: Engines of Creation
1989	M. Eigler: Writing with a STM tool

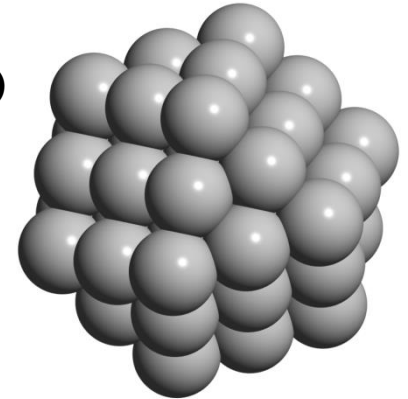
1.4 Historical Milestones

- 1991** Sumio Iijima (NEC): Carbon nanotubes
- 1993** Warren Robinett, R. Stanley Williams: Combination of SEM and VR (virtual reality system)
- 1998** Cees Dekker et al.: Carbon nano tube transistor
- 1999** James M. Tour & Mark A. Read: Single molecule switch
- 2000** Eigler et al.: Construction of quantum corrals and quantum mirrors
- 2001** Florian Bamberg: Soldering of nanotubes with e-beam
- 2004** Intel launches the Pentium IV “Prescott” processor based on 90 nm technology
- 2006** Yi Lu et al.: Smart nanomaterials with DNA molecules

1.5 Properties of Nanoscale Matter

Nanoscale materials behave as surface matter

Au-Cluster (55 atoms)



Aus "Allgemeine und Anorganische Chemie" (Steinle, Jockel, Wilbur, Rappert-Carlson), erschienen bei Spektrum Akademischer Verlag, Heidelberg. © 2004 Elsevier GmbH München. Abbildung 14-7.jpg

n	Atoms/Cluster	Percentage surface atoms	Cluster size
1	13	92 %	0.58 nm
2	55	76 %	1.4 nm
3	147	63 %	2.1 nm
4	309	52 %	2.8 nm
5	561	45 %	3.5 nm
7	1415	35 %	5 nm
9	2869	28 %	6.5 nm

Consequences for

Reactivity

Defect density

Band gap

solid state chemistry

+

+

-/+

catalysis

+

+

-

optical properties

-

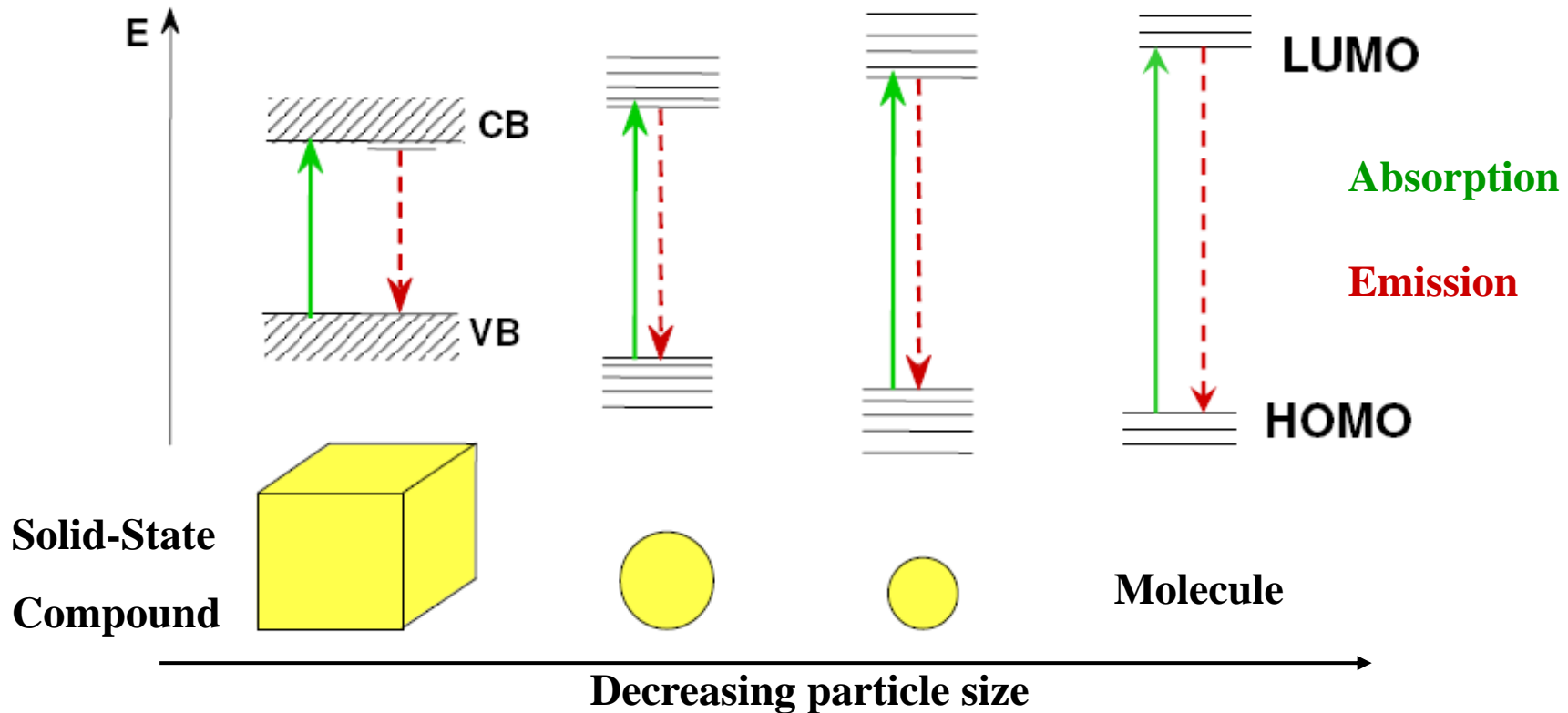
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1.5 Properties of Nanoscale Matter

Nanoscale materials can show quantum confinement effects

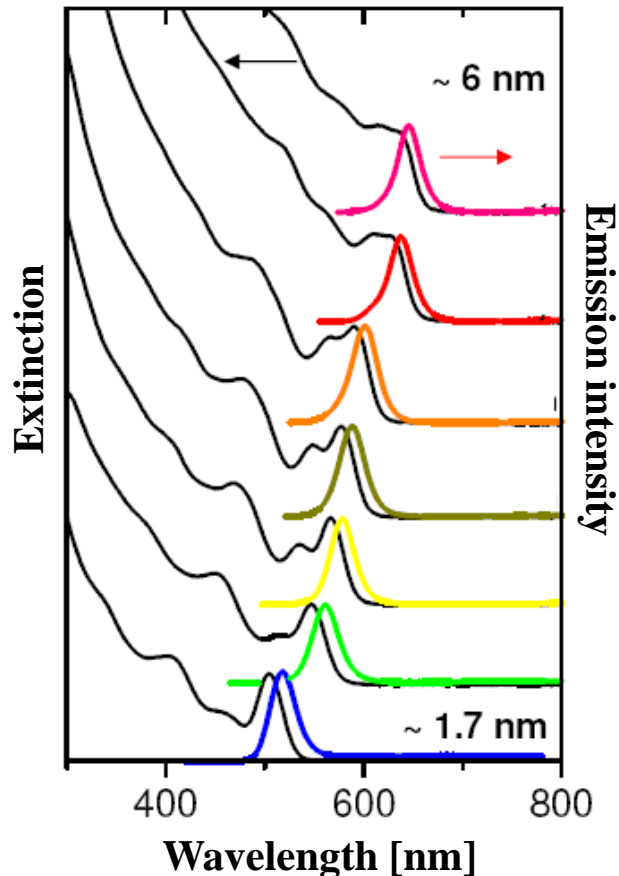
Very small nanoparticles show strong confinement of excitons (weakly bound electron-hole pairs) and thus dependence of absorption and luminescence on particle size



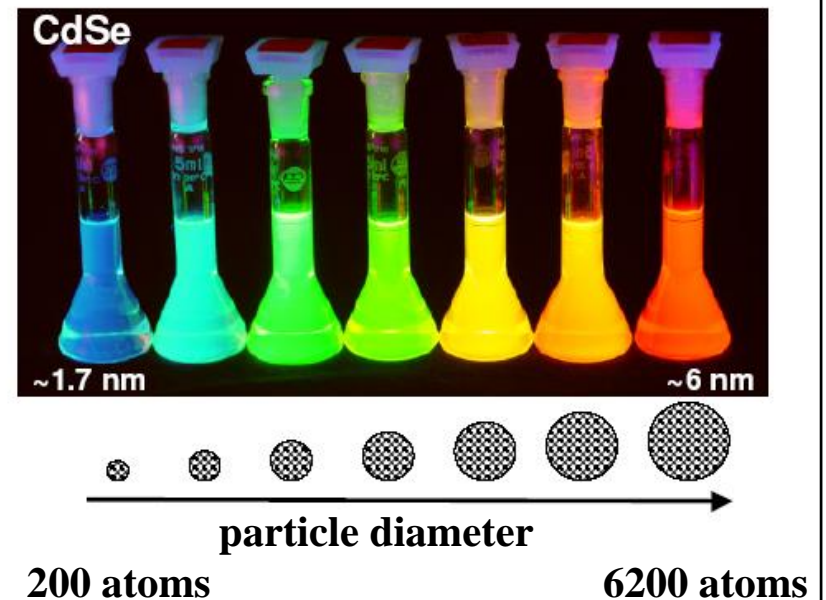
1.5 Properties of Nanoscale Matter

CdSe Nanocrystals

Absorption and luminescence spectra

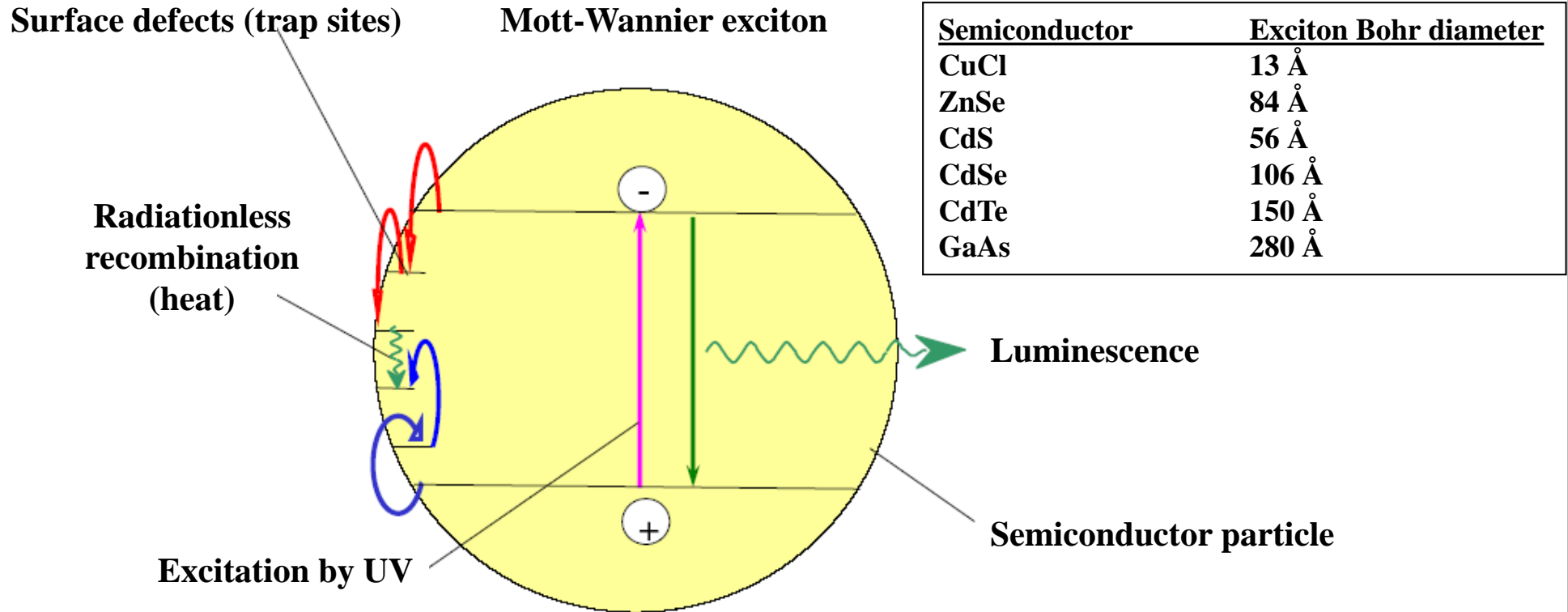


Colour under UV-A Excitation



1.5 Properties of Nanoscale Matter

Nanoscale luminescent materials are mostly less efficient than microscale materials

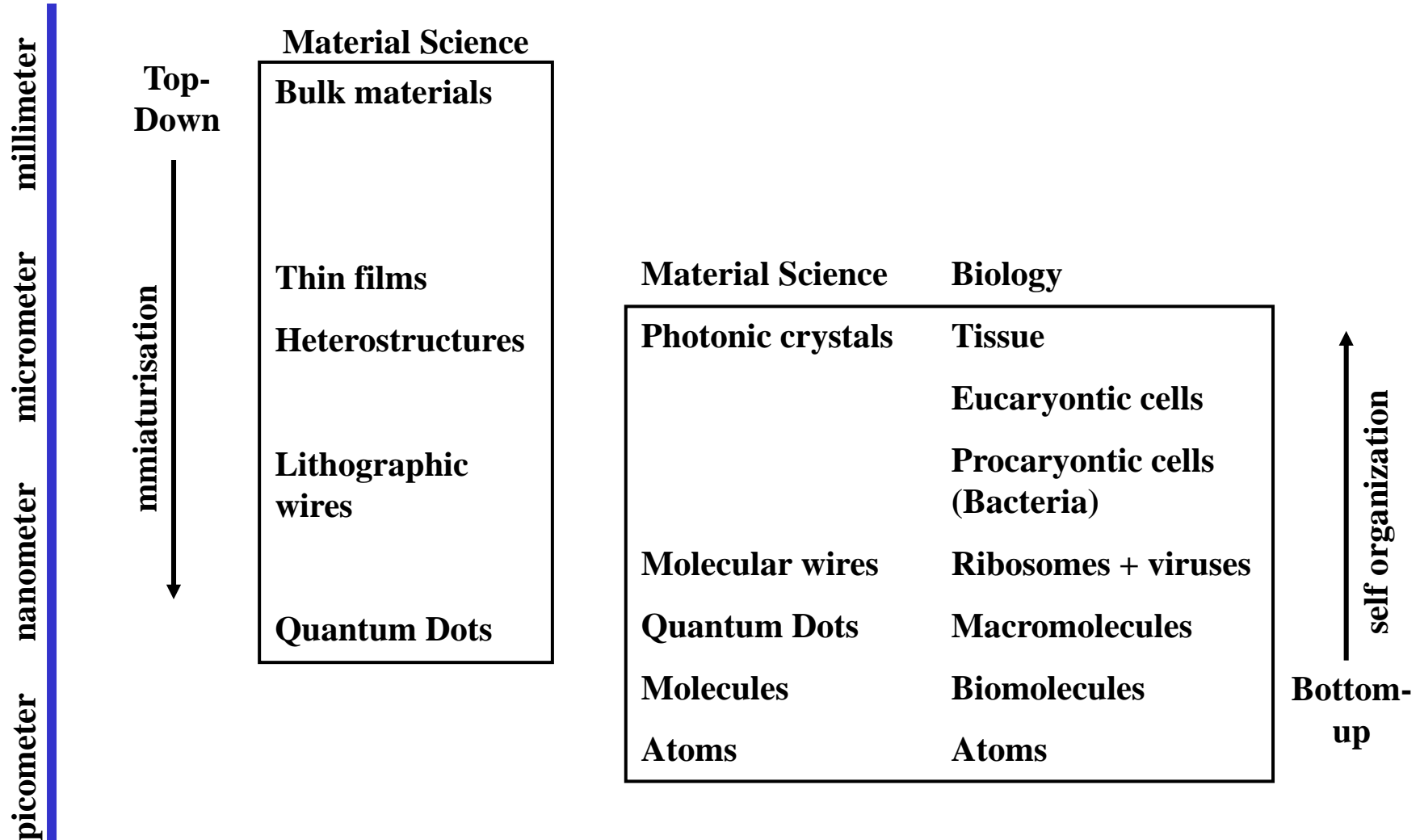


Result: Quenching of luminescence

Problem solution: Epitactical growth of a material with a higher band gap onto the surface

2.1 Approaches to Nanoscale Structures

Top-down or Bottom-up



2.1 Approaches to Nanoscale Structures

Methods to achieve nanostructures

Zero dimensional structures → nanoparticles, quantum dots

- **Precipitation in confined structures**
- **Physical treatment of targets**

One dimensional structures → tubes, wires

- **Electro deposition**
- **Chemical Vapour Deposition**

Two dimensional structures → wells, layers

- **Chemical Vapour Deposition**
- **Photolithography**

Three dimensional structures → photonic crystals, superlattices

- **Replacement reactions**
- **Crystallisation of nanocrystals**
- **DNA based assembly**

2.1 Approaches to Nanoscale Structures

Driving force for particle growth

Gibbs energy minimization by reducing the surface/volume ratio

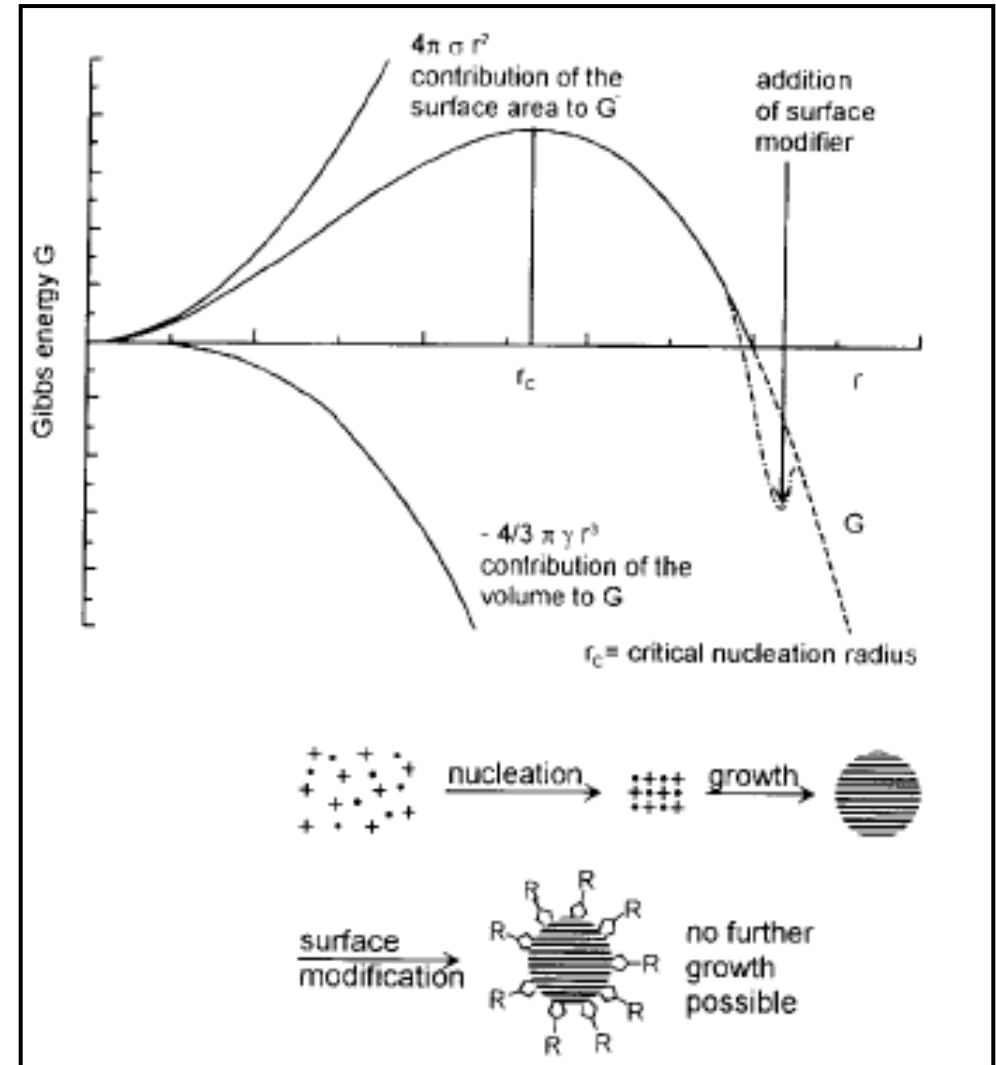
Surface energy increases quadratically, but volume energy decreases cubically

Very small particles (r_c) are highly reactive, due to their high chemical potential

Comment

5 nm particles ~ 50% surface atoms

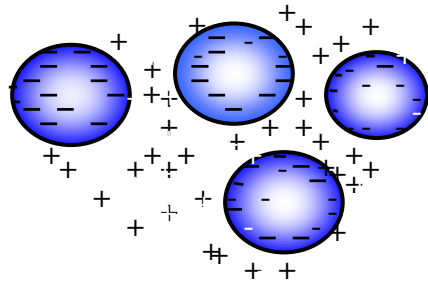
1 μm particles ~ 0.6% surface atoms



2.1 Approaches to Nanoscale Structures

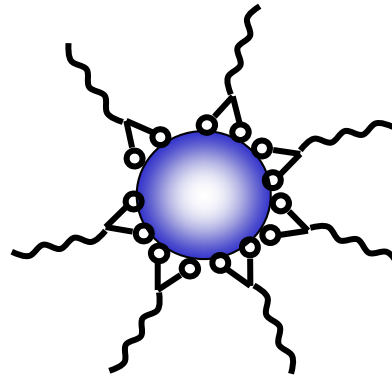
Stabilisation of small colloidal particles

a) electrostatic



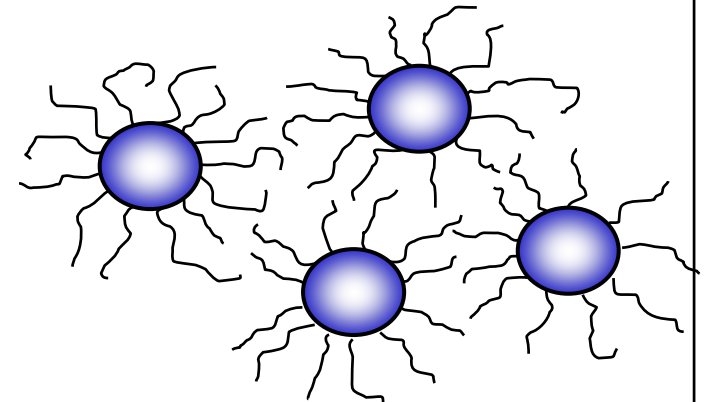
Surface charging

b) thermodynamic



**Surface complexation
(modification)**

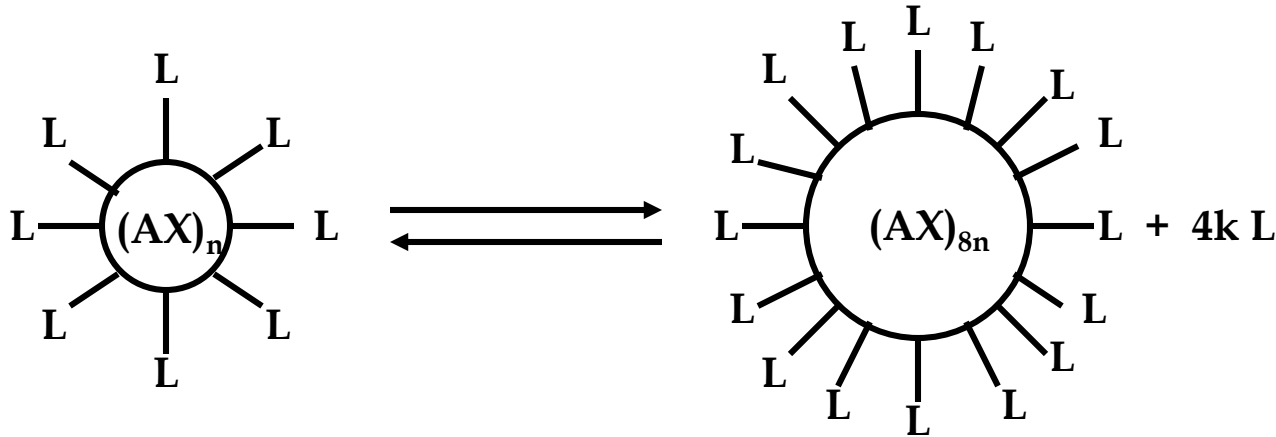
c) static



**Adsorption of polymer
molecules by the surface**

2.1 Approaches to Nanoscale Structures

b) Thermodynamic stabilisation of nanoparticles



Ligandmoleküle fest an der Oberfläche gebunden

Energie-Bilanz bei der Verdopplung des Teilchenradius:

$(AX)_n L_k \rightarrow (AX)_{8n} L_{4k} + 4k L$ (free Ligands) \Rightarrow Cleavage of the metal-ligand bond required for particle growth

- Strong metal-ligand bond small cluster
- Weak metal-ligand bond large cluster

\Rightarrow Cluster size scales with metal-ligand bond strength

2.2 Ball Milling

Top-down: Mechanical crushing of solids into nanocrystallites

L

Advantages

- Inexpensive
- Large scale process
- Old well-established process
- Down to 2 – 20 nm possible

Disadvantages

- Irregular nanoparticles
- Introduction of defects
- Introduction of impurities from balls and milling additives



A ball mill being used as part of a gold mining operation in Peru

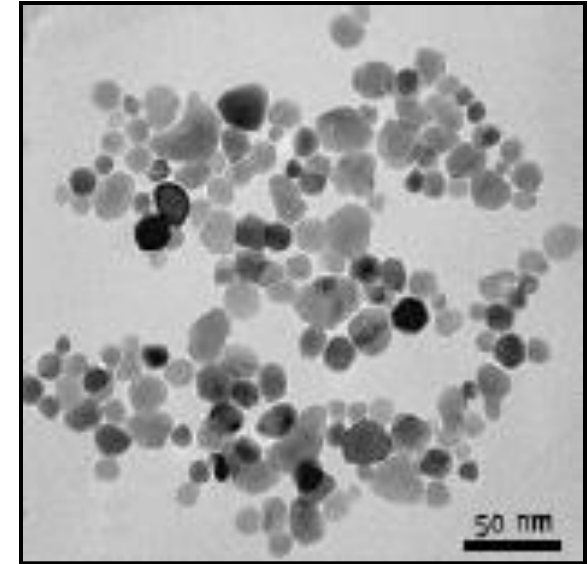
2.2 Ball Milling

Top-down: Mechanical crushing of solids into nanocrystallites

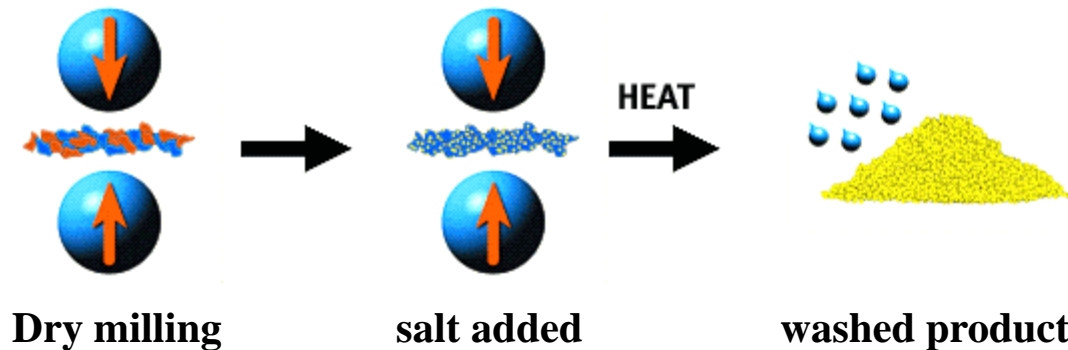
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Milling process

- Dry
- Dry + solid additive (salt)
- Wet (slurry)



ZnO nanoscale particles from a milling process

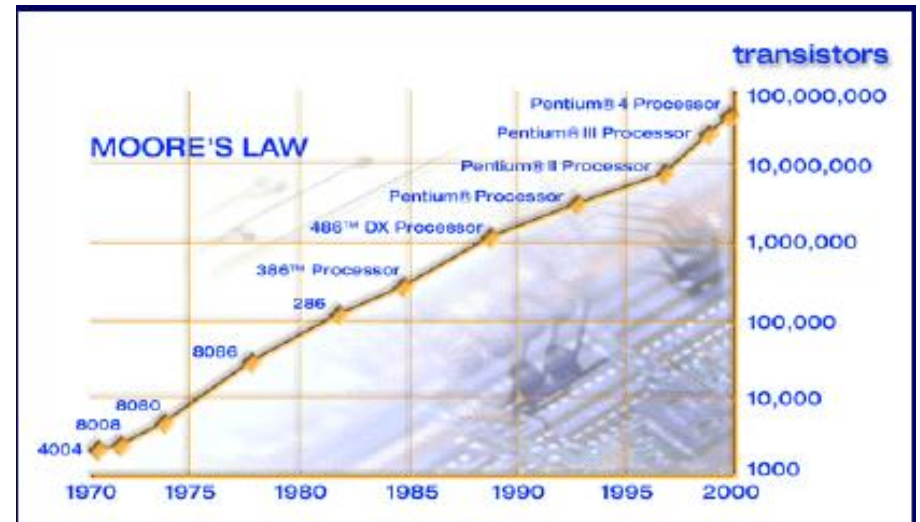
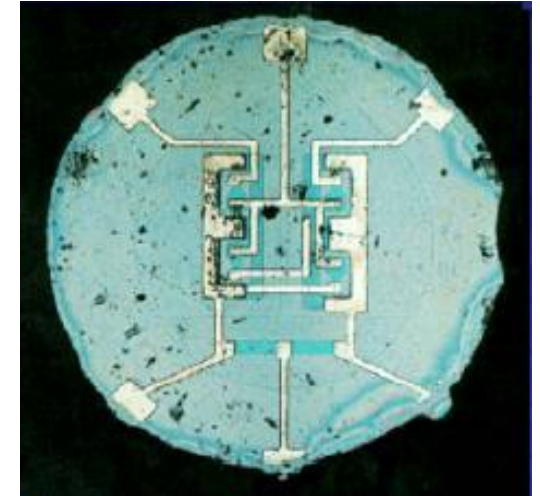


2.3 Photolithography

Top-down: Photochemical manufacturing of micro- and nanostructures for integrated circuits

History of integrated circuit development

- 1947 Invention of the transistor
- 1961 First integrated circuit
- 1965 Moore's law published
- 1975 Intel 8080 chip: 4500 transistors
- 1981 „640 kByte ought to be enough for anybody“ (Bill Gates)
- 1993 Pentium I: 3.1 Mio. transistors
- 1997 Pentium II: 7.5 Mio. transistors
250 nm line width
- 2000 180 nm line width
- 2002 130 nm structures
- 2005 45 nm technology

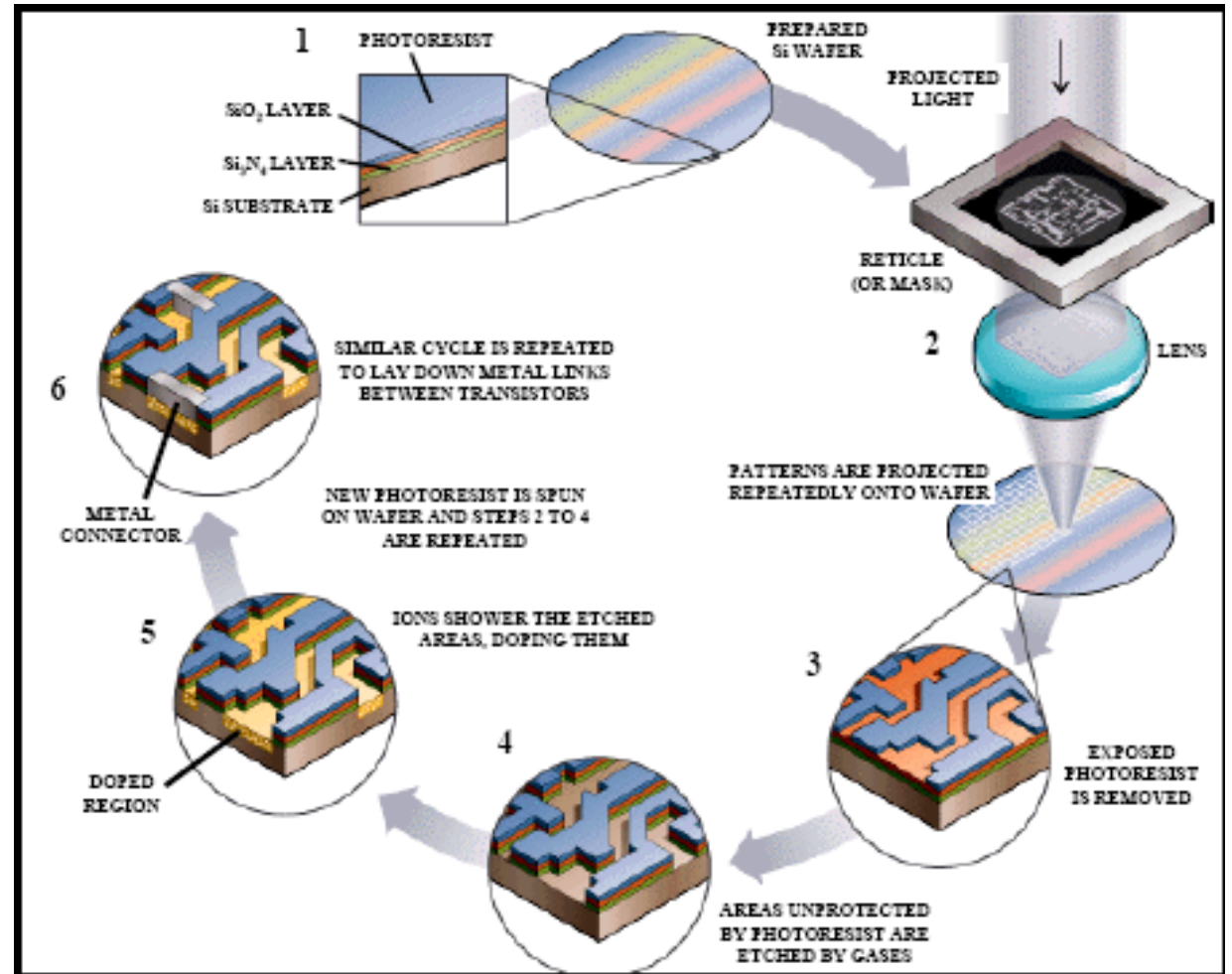


2.3 Photolithography

Top-down: Photolithography

Process

1. Photoresist layer deposition by spin coating
2. Exposure to UV Radiation
3. Removal of photoresist
4. Etching of unprotected areas
5. Doping by ion implantation
6. Repeat cycle to deposit metal connector



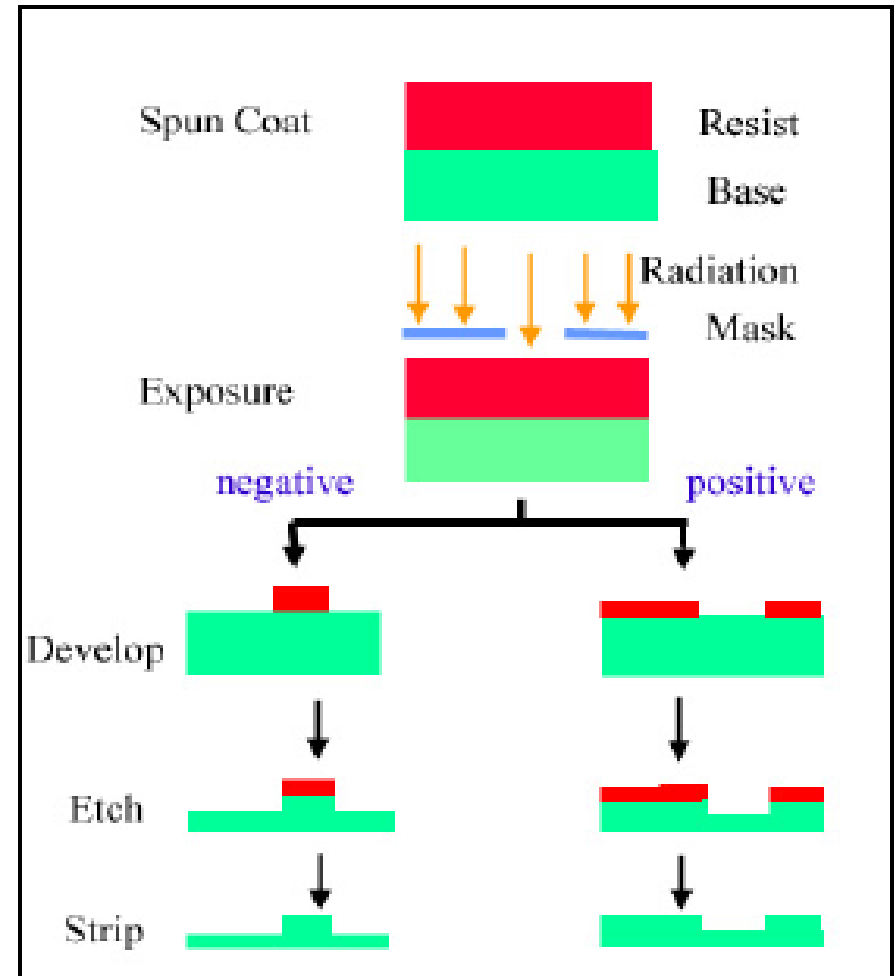
2.3 Photolithography

Top-down: Photolithography

Evolution of the lithography process

Stepper	λ [nm]	Radiation source
Visible g-line	436	high-pressure Hg
Visible i-line	365	high-pressure Hg
High deep UV	248	KrF Excimer LASER
Deep UV	193	ArF Excimer LASER
Deep UV	157	F ₂ Excimer LASER
Extreme UV	13.7	
Electron beam		

Schematic process flow



2.3 Photolithography

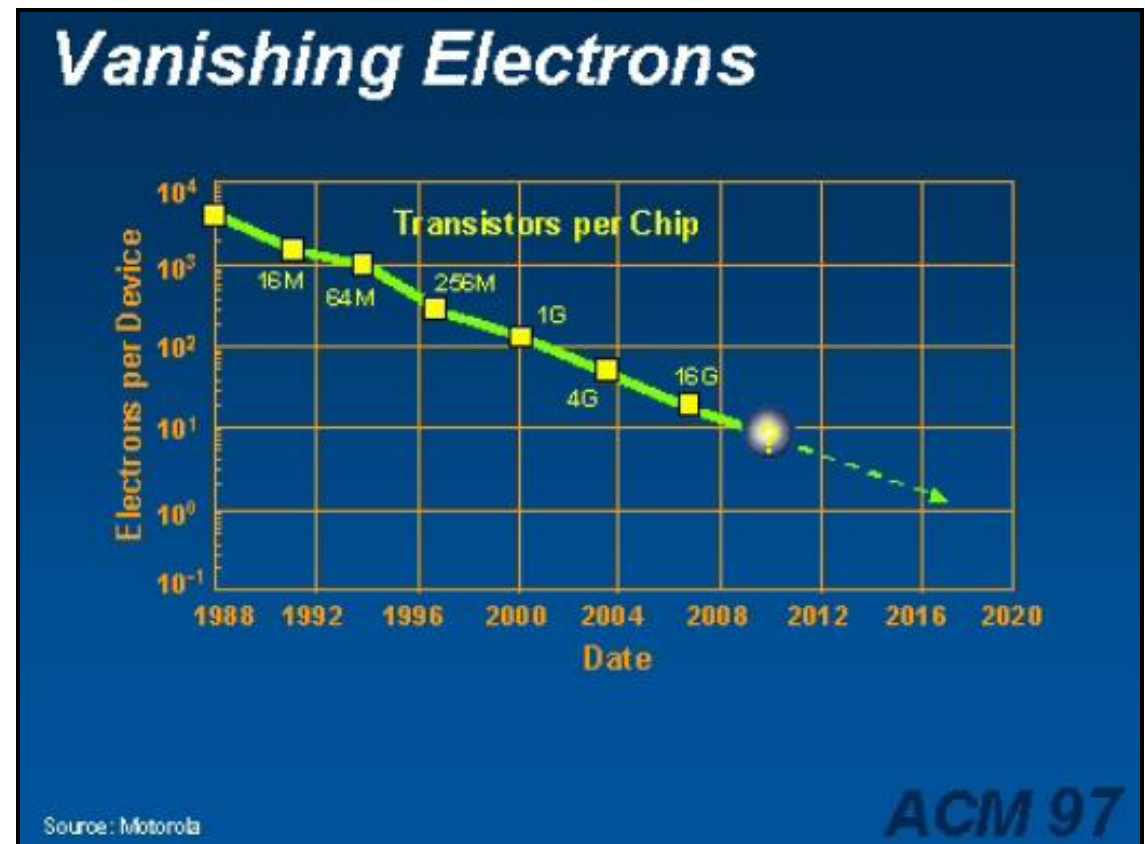
Limitations of photolithography and miniaturisation of transistors

Technical limitations

- Wavelength of radiation source
- Focussing of radiation

Fundamental limitation

- Typically a semiconductor of 1000 nm^3 comprises one free electron
- Extrapolation of the present development shows that “single electron transistors” will be reality at ~ 2020



2.4 Gas Phase Processes

Top-down: LASER-Ablation for the synthesis of Carbon Nano Tubes (CNTs)

The vaporization of a target at a fixed temperature by a continuous CO₂ laser beam ($\lambda = 10.6 \mu\text{m}$) is shown in the bottom figure.

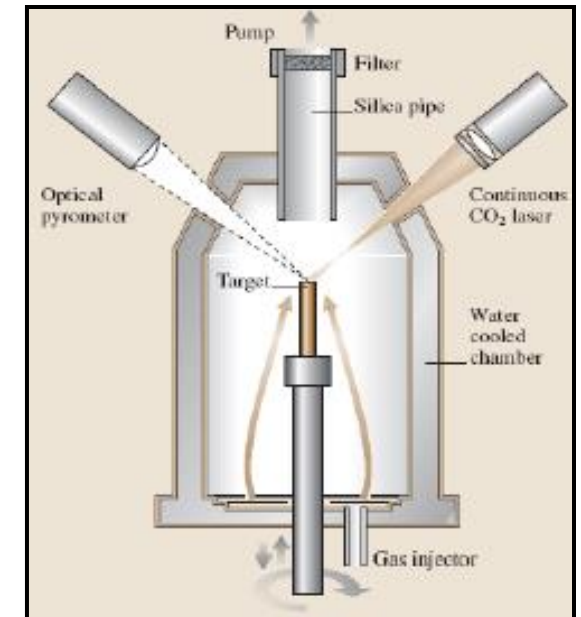
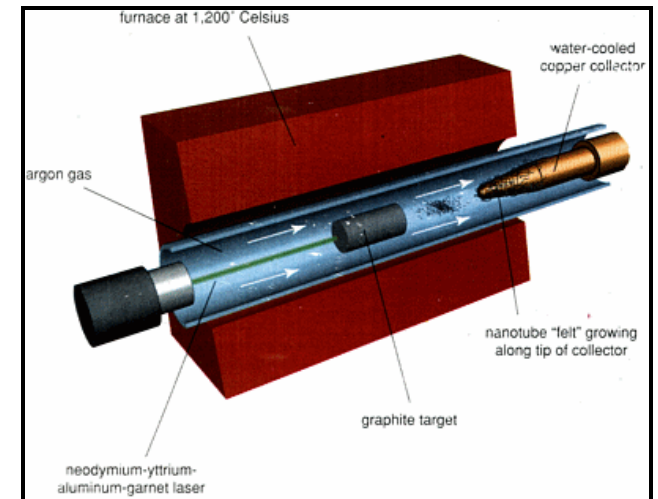
The power can be varied from 100 W to 1600 W.

The temperature of the target is measured with an optical pyrometer.

These measurements are used to regulate the laser power to maintain a constant vaporization temperature.

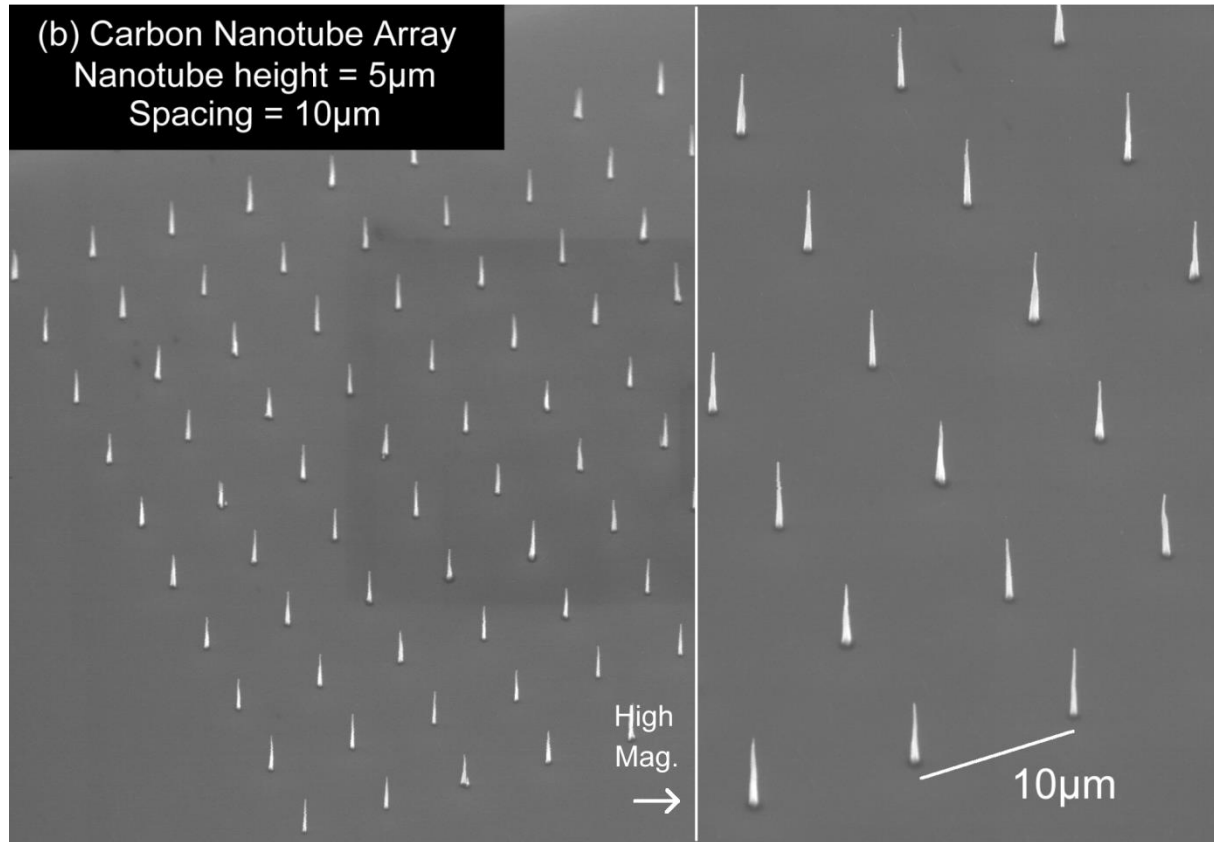
The gas, heated by the contact with the target, acts as a local furnace and creates an extended hot zone, making an external furnace unnecessary.

The gas is extracted through a silica pipe, and the solid products formed are carried away by the gas flow through the pipe and then collected on a filter.



2.4 Gas Phase Processes

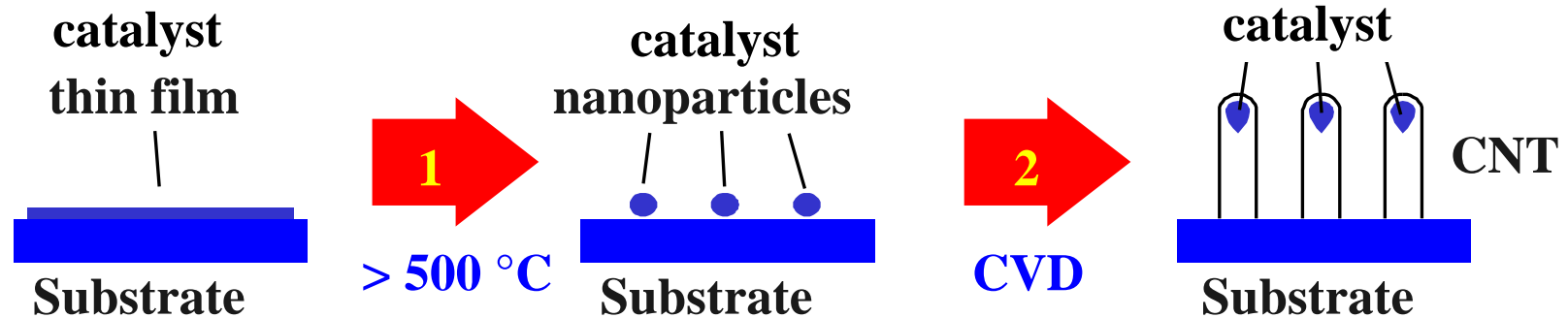
Bottom-up: CNT growth synthesis by DC Plasma Chemical Vapour Deposition



W. Milne, J. Robertson, K. Teo, Cambridge U. UK
(FP5-EU-Program CARDECOM Partner)

2.4 Gas Phase Processes

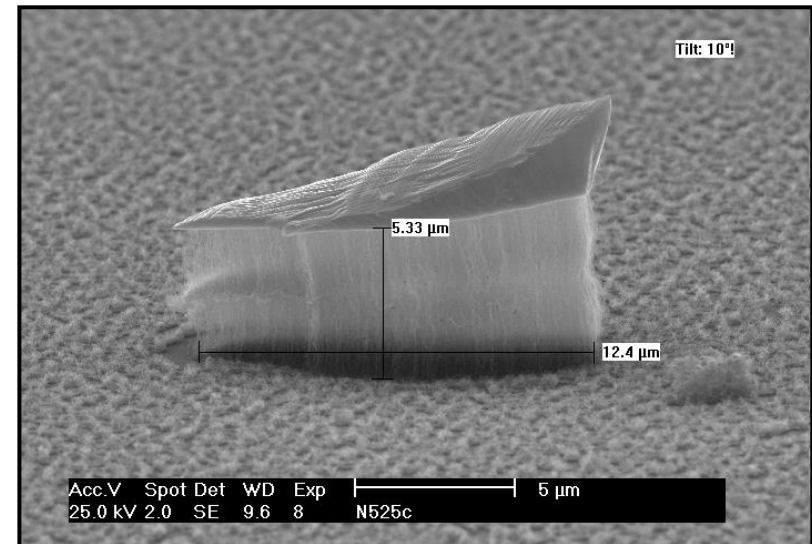
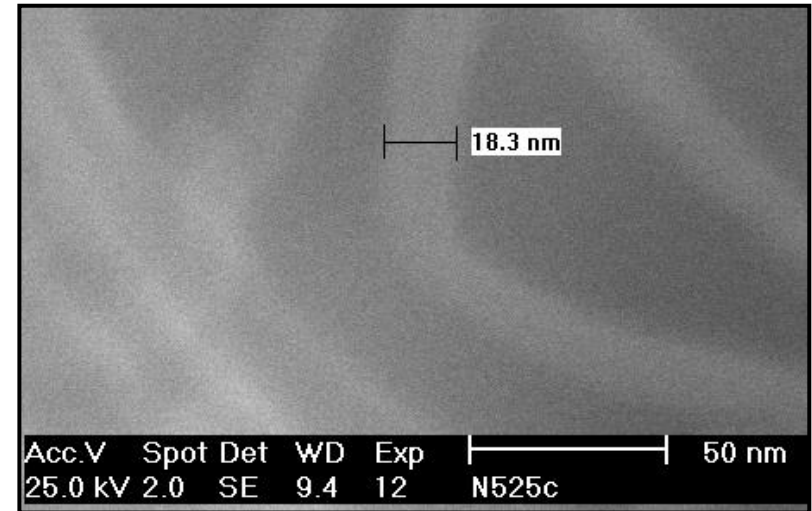
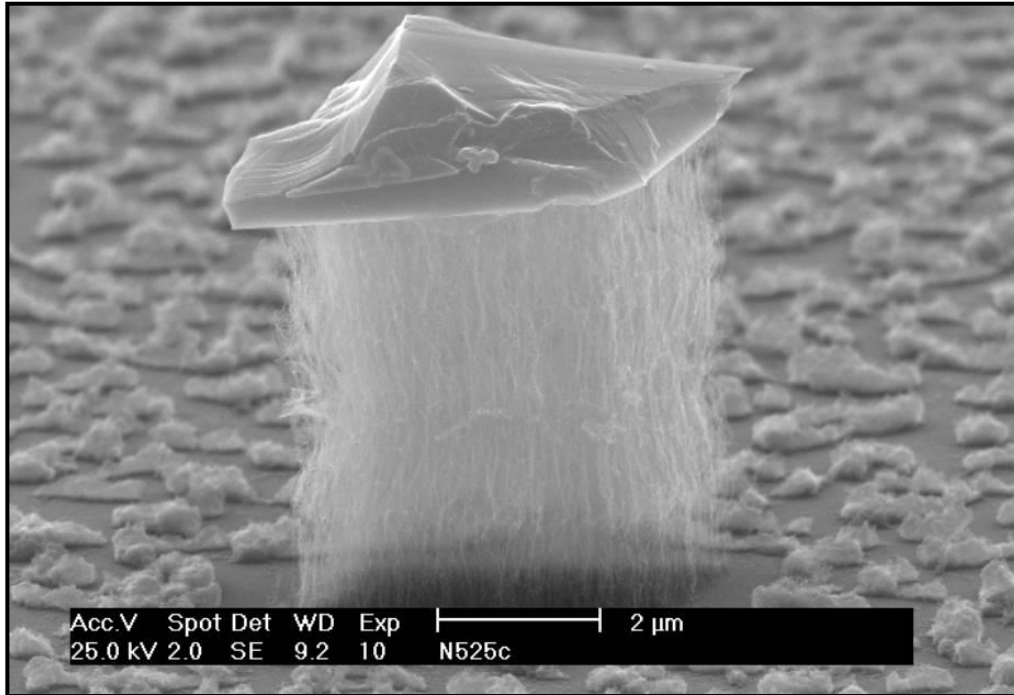
Bottom-up: CNT growth synthesis by DC Plasma CVD



1. **Deposition of a catalyst film (Ni, Fe, Co)**
2. **Formation of catalyst nanoparticles at 500 – 900 °C (growth temp.): Catalyst film breaks into nanoparticles**
3. **Plasma CVD: C-carrier (CH_4 , C_2H_2) provides C for tube growth, etchant (NH_3 , N_2 , H_2) removes unwanted amorphous carbon**

2.4 Gas Phase Processes

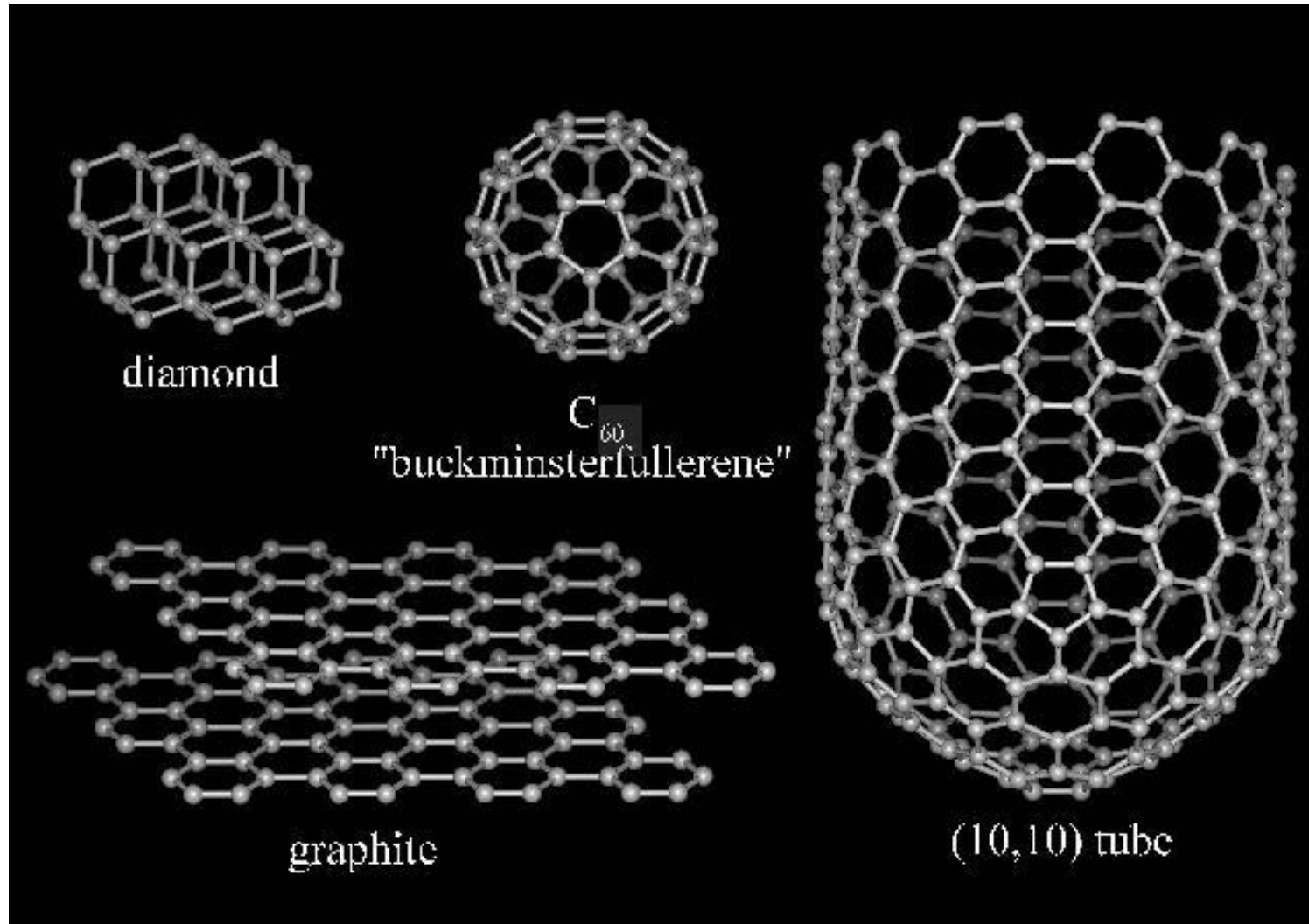
Bottom-up: CNTs grown by DC Plasma CVD



Source: Peter K. Bachmann
Philips Research Laboratories Aachen

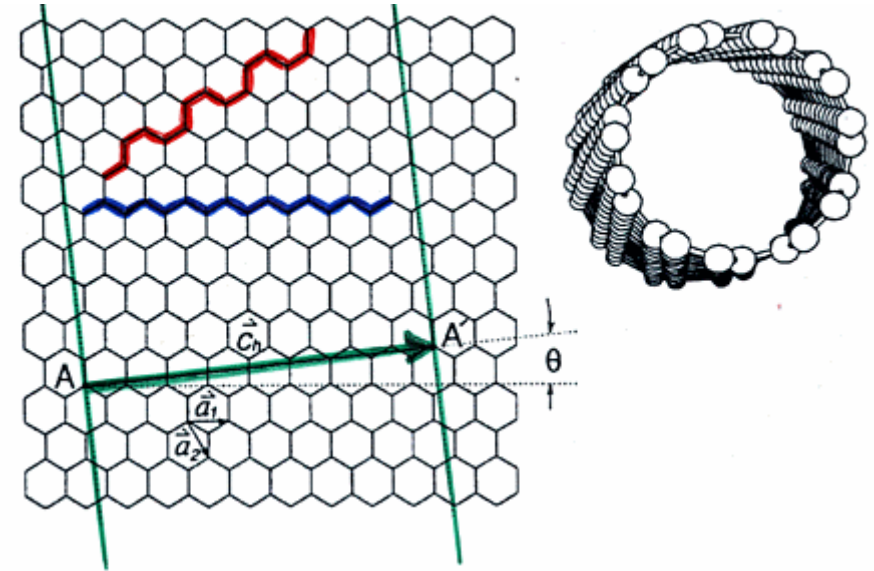
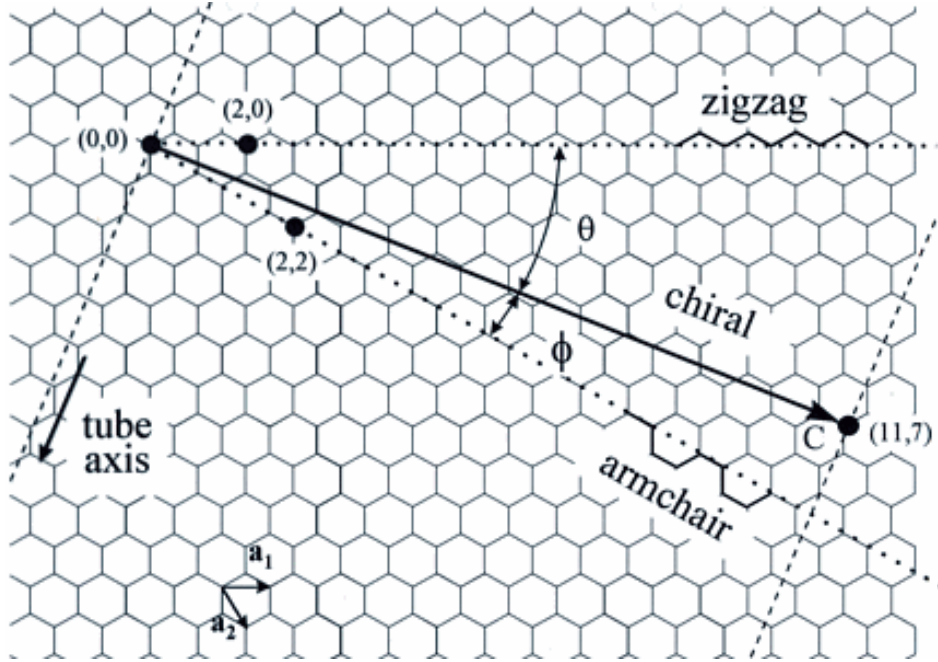
2.4 Gas Phase Processes

Allotropic forms of elemental carbon



2.4 Gas Phase Processes

Carbon Nano Tubes: Structures and properties



n and m determine the chirality and thus conductance, density, lattice structure, etc.

Metallic

(n,n) armchair

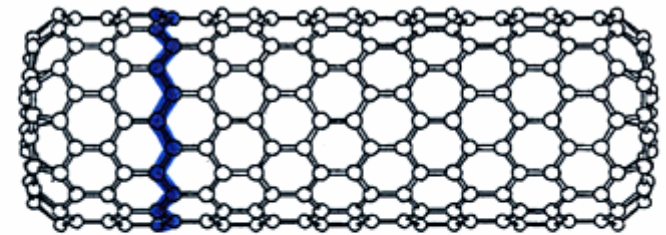
(n,m) where $n-m = 3x$

Semiconducting

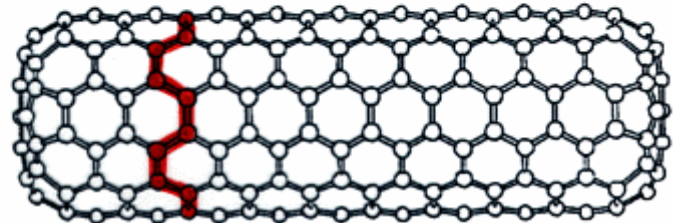
$(n,0)$ zigzag

(n,m) where $n-m \neq 3x$
band gap ~ 0.5 eV

'zigzag'

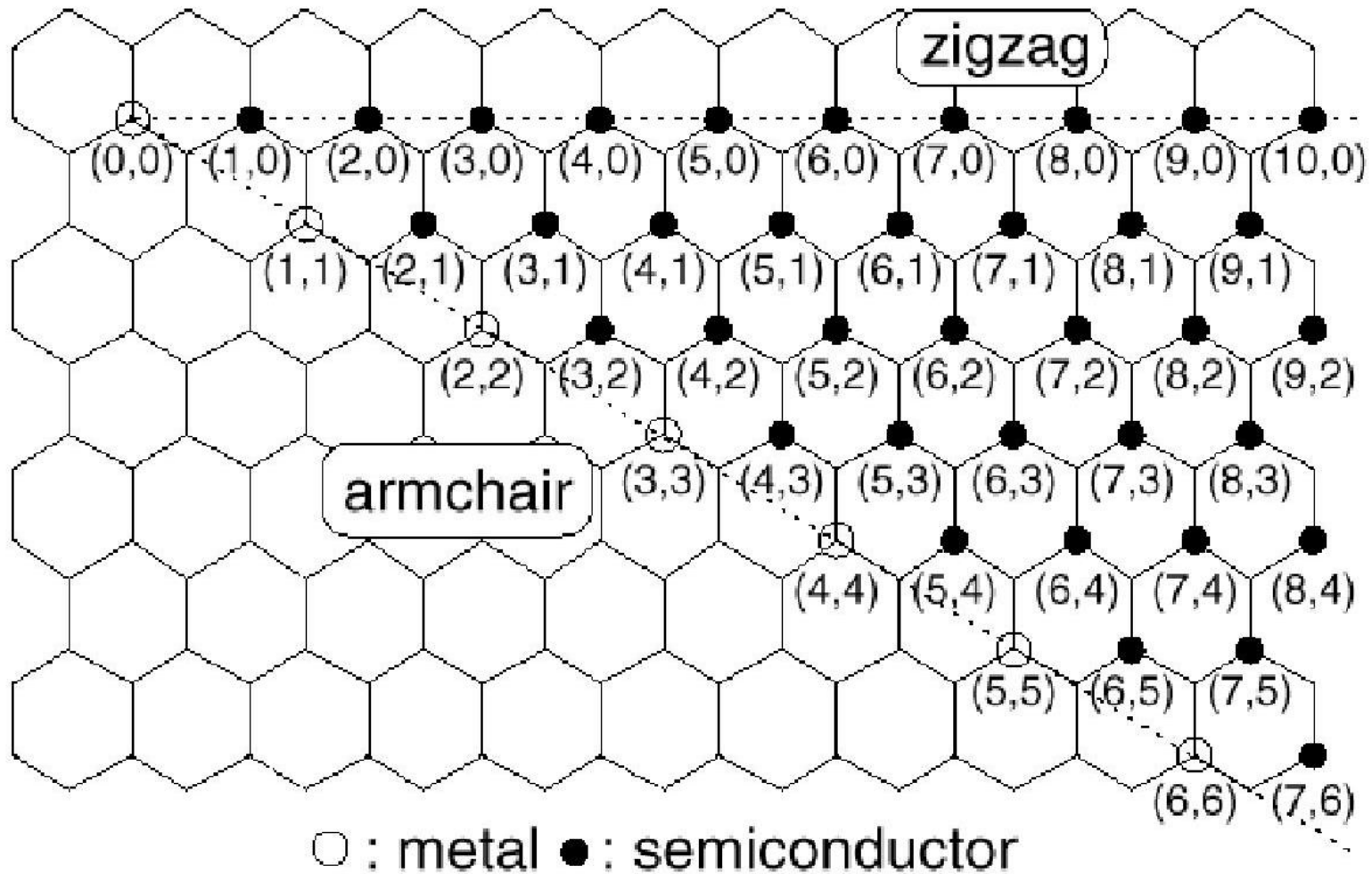


'armchair'



2.4 Gas Phase Processes

Carbon Nano Tubes: Structures and properties



2.4 Gas Phase Processes

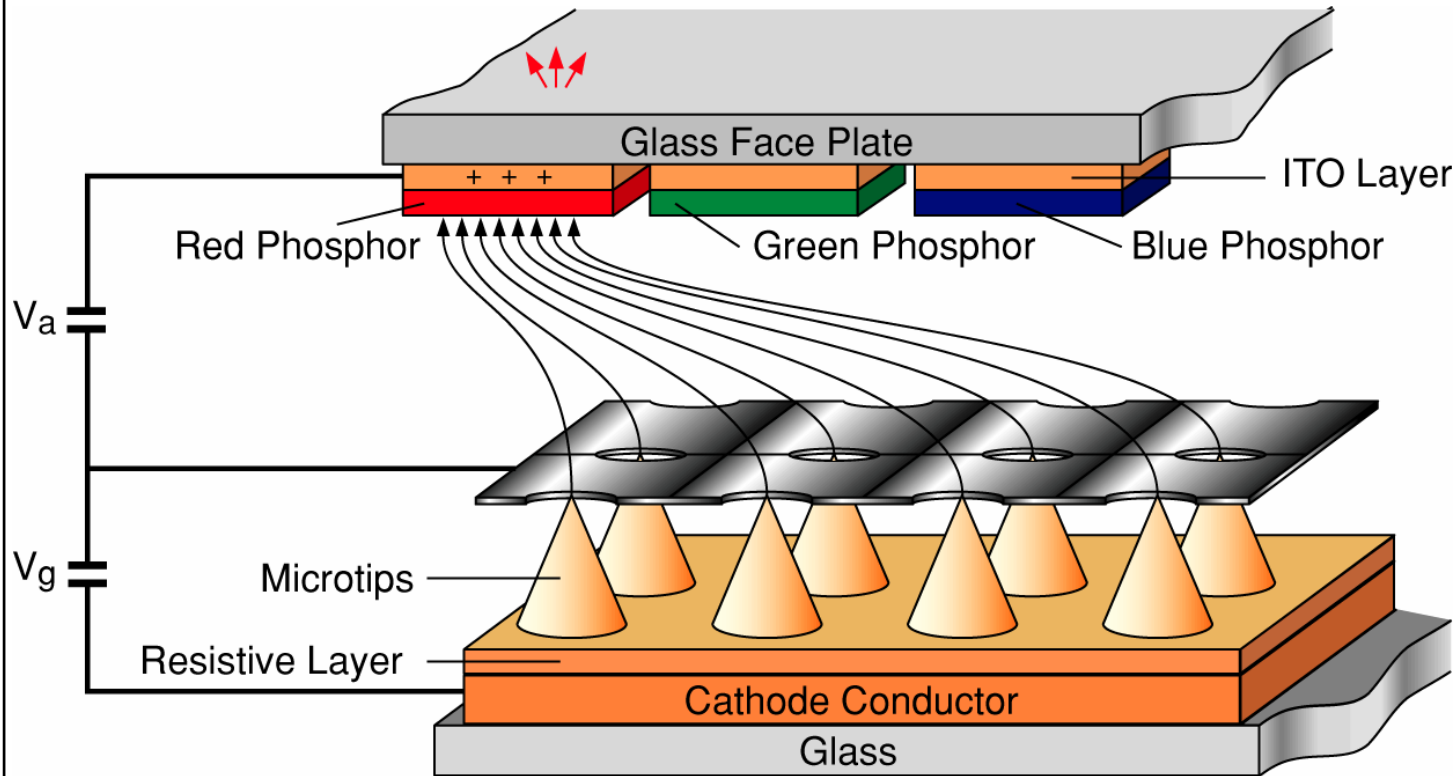
Carbon Nano Tubes: Physical properties

Average diameter of Single Wall Nano Tubes (SWNTs)	1.2 - 1.4 nm
Lattice parameter	
(10,10) Armchair	16.78 Å
(17,0) Zigzag	16.52 Å
Density	
(10,10) Armchair	1.33 g/cm³
(17,0) Zigzag	1.34 g/cm³
(12,6) Chiral	1.40 g/cm³
Optical band gap	
For (n,m): n-m is divisible by 3 (metallic)	0.0 eV
For (n,m): n-m is not divisible by 3 (semi-cond.)	~ 0.5 eV
Electrical transport	
Conductance quantization	(12.9 kΩ)⁻¹
Resistivity	10⁻⁴ Ωcm
Maximum current density	10¹³ A/m²
Thermal transport	
Thermal conductivity	~ 2000 W/m·K
Elastic behavior	
Young's modulus (SWNTs)	~ 1 TPa
Young's modulus (MWNTs)	1.28 TPa
Maximum tensile strength	~ 100 GPa

2.4 Gas Phase Processes

Carbon Nano Tubes: Application in Field Emission Displays (FEDs)

Standard field-emission display set-up

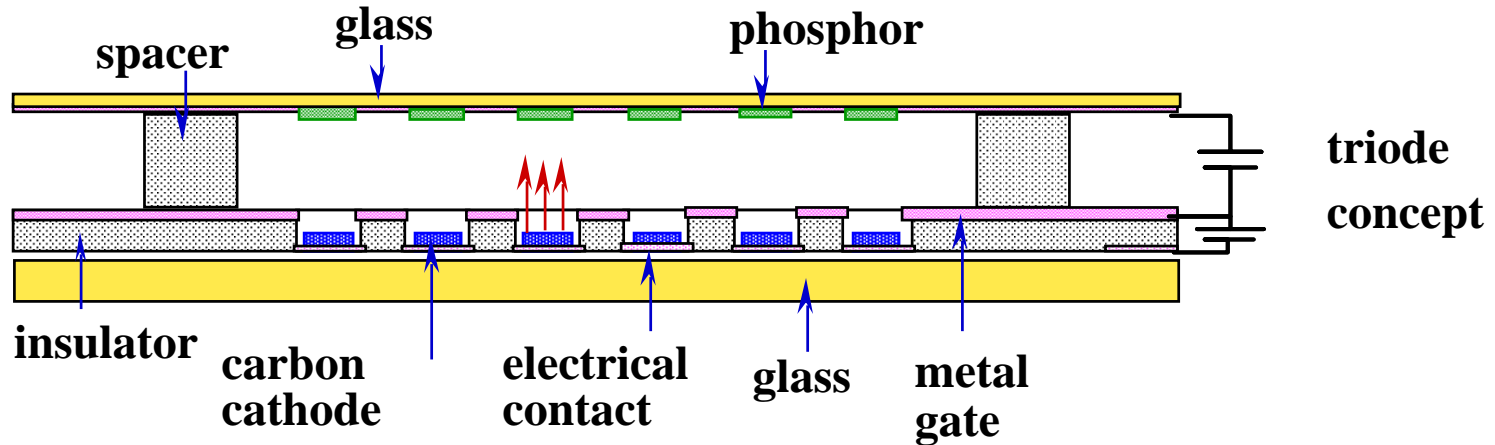


RGB Phosphors

- **Blue**
 $\text{Y}_2\text{SiO}_5:\text{Ce}$
- **Green**
 $\text{Y}_2\text{SiO}_5:\text{Tb}$
- **Red**
 $\text{Y}_2\text{O}_3:\text{Eu}$

2.4 Gas Phase Processes

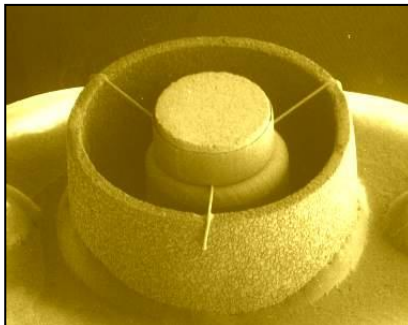
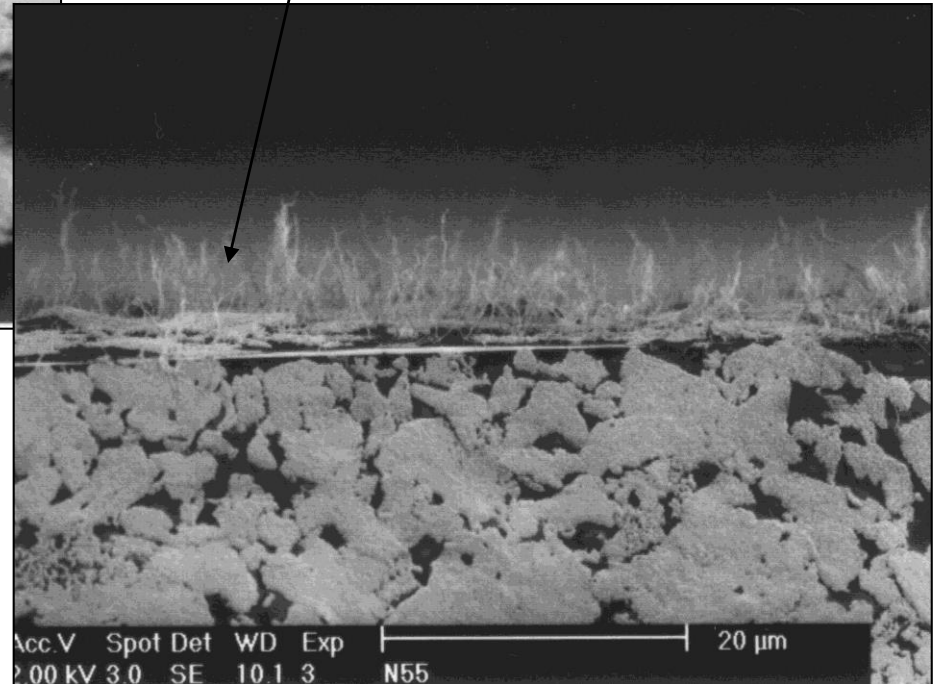
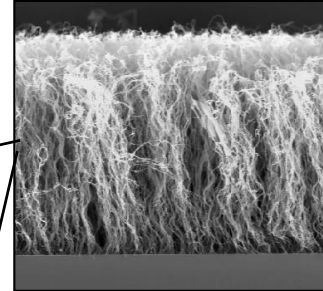
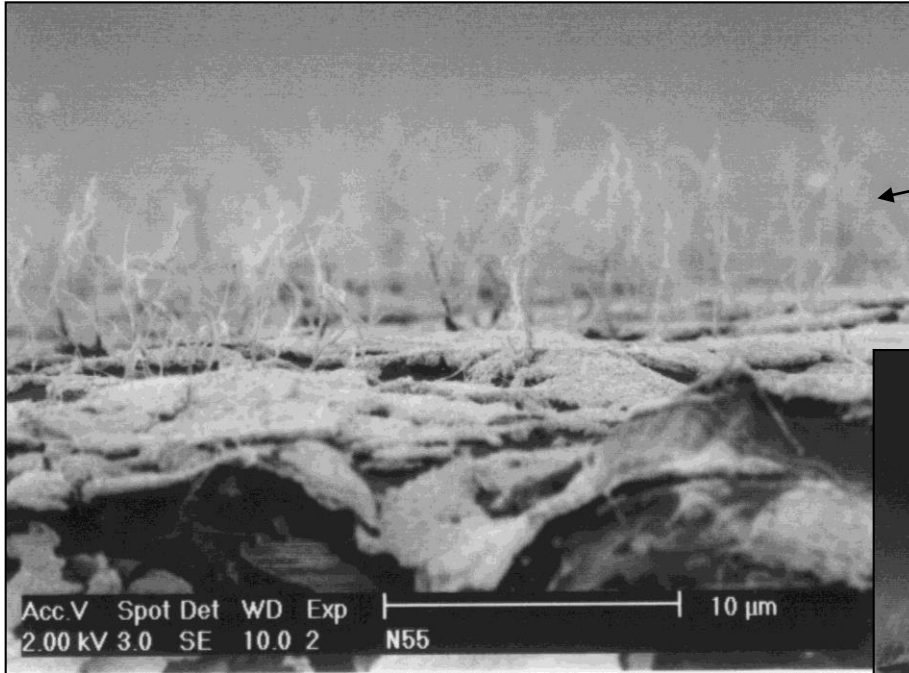
Carbon Nano Tubes: Application in Field Emission Displays (FEDs)



Source:
PixTech Inc.

2.4 Gas Phase Processes

Carbon Nano Tubes: Application in electron guns of Cathode Ray Tubes (CRTs)



2.4 Gas Phase Processes

Bottom-up: Chemical Vapour Deposition (CVD)

Chemical process for depositing thin solid films of various materials onto a substrate

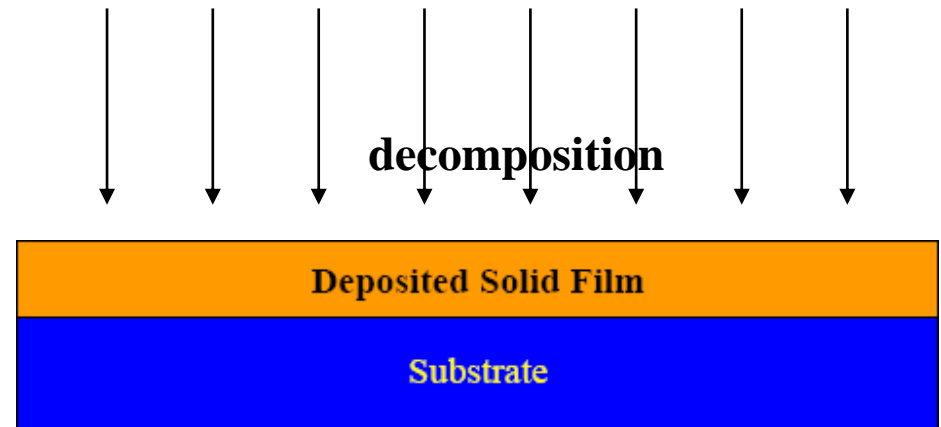
Deposition material: Diamond, metals, oxides, nitrides, borides, carbides ...

Substrate: Si, SiO₂, Si₃N₄, Al₂O₃ ...

Application areas

- Coating of tools (W, Diamond)
- Metal contacts on semiconductors (Cu, Ag)
- Transparent conductors onto glass (ITO)
- Insulation layers (SiO₂)
- Composite materials (Al)
- Preparation of semiconductors
 - (Al,In,Ga)N
 - (Al,In,Ga)P
 - Ga(As,P)

Gaseous (metal organic) precursor



2.4 Gas Phase Processes

Bottom-up: Chemical Vapour Deposition (CVD)

Advantages of CVD

- Ease of control of layer thickness
- Good layer homogeneity
- „Universal“ process

CVD parameters

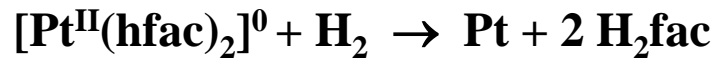
- Volatility of precursor
- Ease of decomposition & volatility of fragments
- Relative concentration
- Catalyst on target surface (e.g. Ni or Co)
- Crystallographic arrangement of surface
- Process temperature
- Gas pressure
-

2.4 Gas Phase Processes

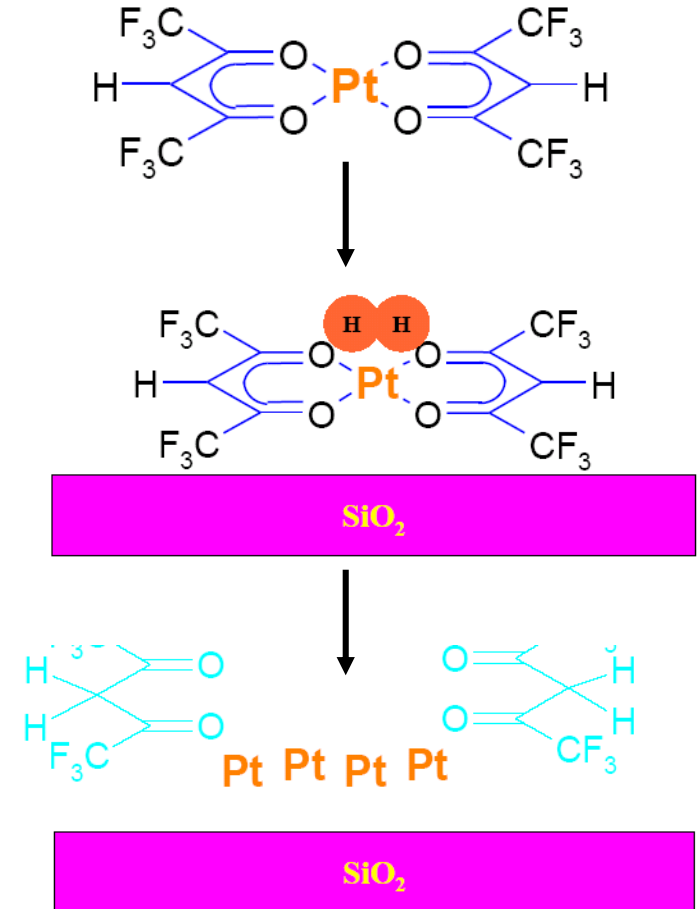
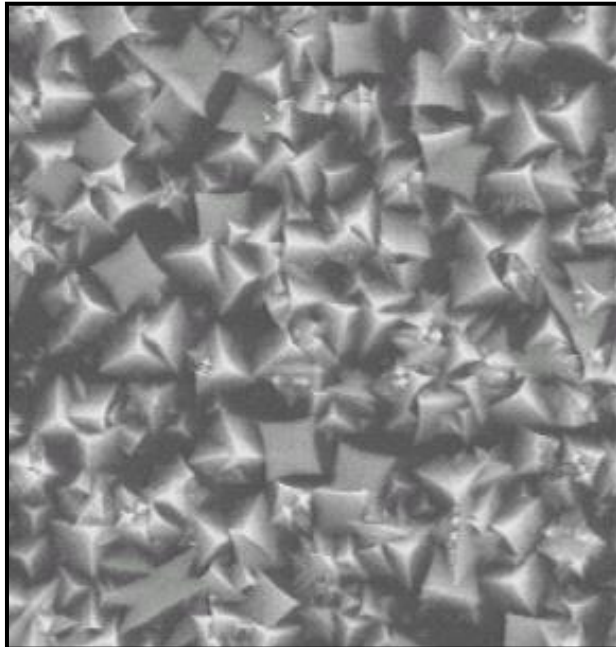
Bottom-up: Chemical Vapour Deposition (CVD) of Platinum layers

Precursor: $[\text{Pt}^{\text{II}}(\text{hfac})_2]^0$ hfac = hexafluoroacetylacetonate

Reductive thermal decomposition:



Result



2.4 Gas Phase Processes

Bottom-up: Other CVD Methods

Decomposition due to

LASER beam

(Microwave) plasma

High temperature

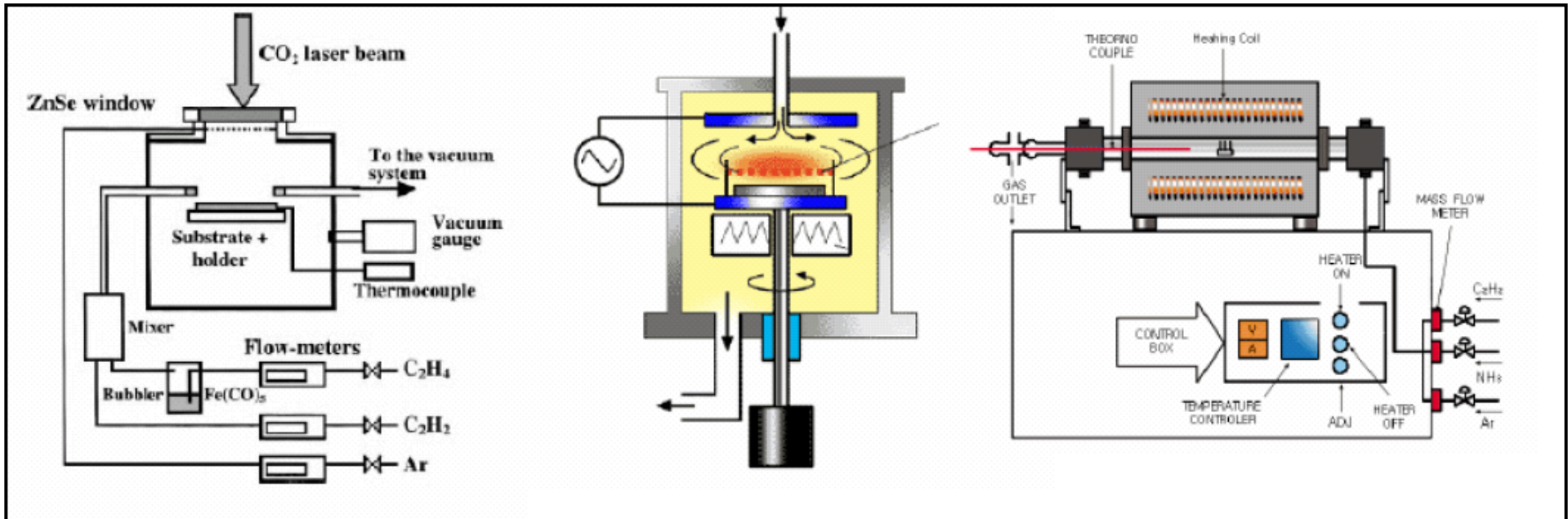
Method

Laser assisted CVD

Plasma enhanced CVD

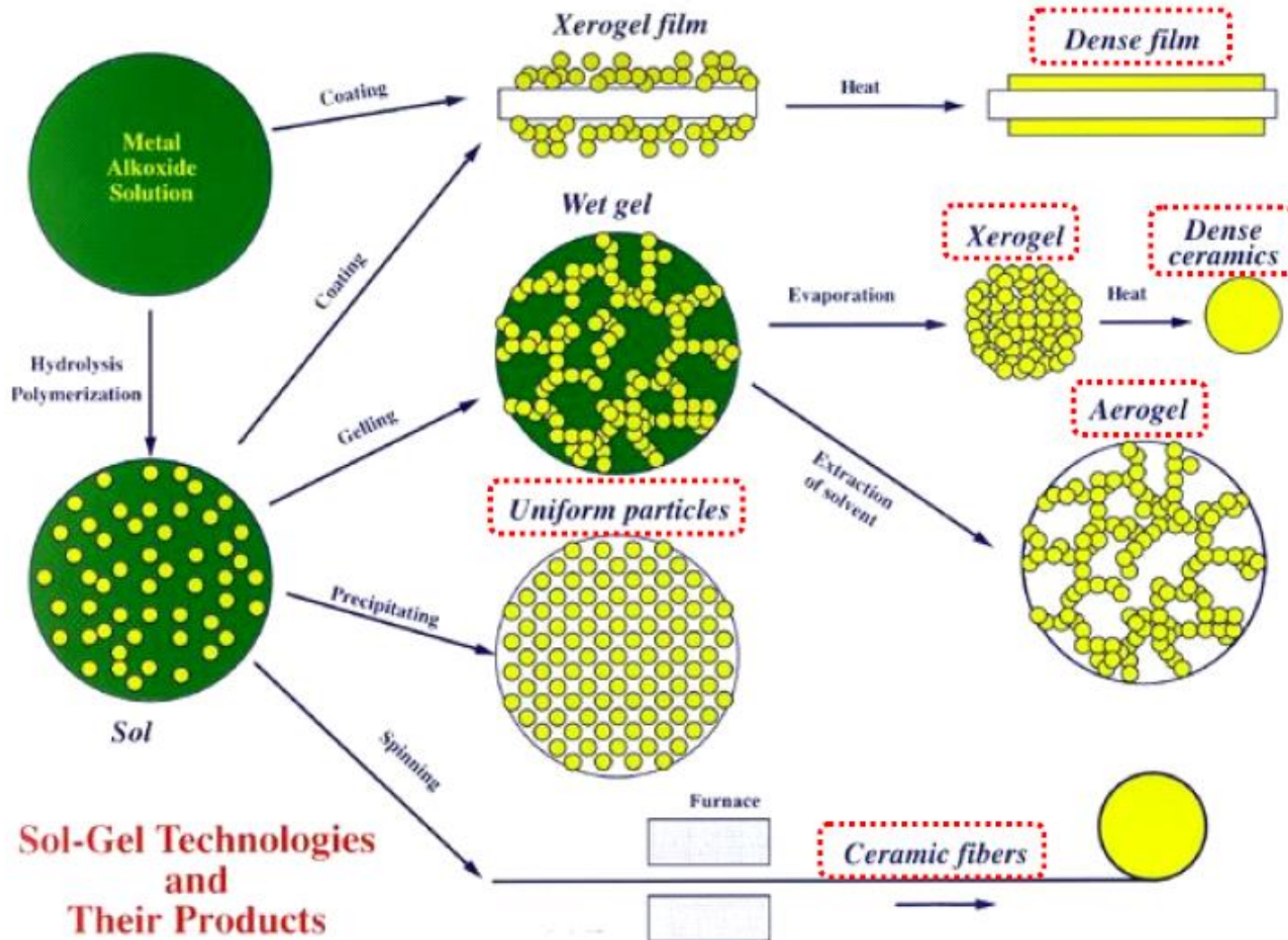
Thermal CVD, fluid bed CVD

.....



2.5 Liquid Phase Processes

Bottom-up: Sol-Gel Process



2.5 Liquid Phase Processes

Bottom-up: Sol-Gel Process

Advantages

- **Ease of production of large area coatings**
- **Scalable**
- **Precise composition control**
- **Low temperature synthesis**
- **High homogeneity**
- **Tunable layer composition**

Disadvantages

- **Sensitivity for atmosphere condition**
- **Cost of raw materials**
- **Use of toxic solvent system**

2.5 Liquid Phase Processes

Bottom-up: Sol-Gel Process

Optical Coating



Optical Coating



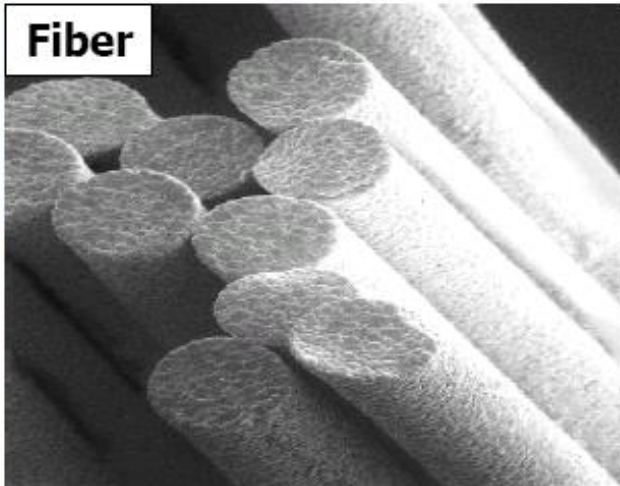
Dense Ceramics



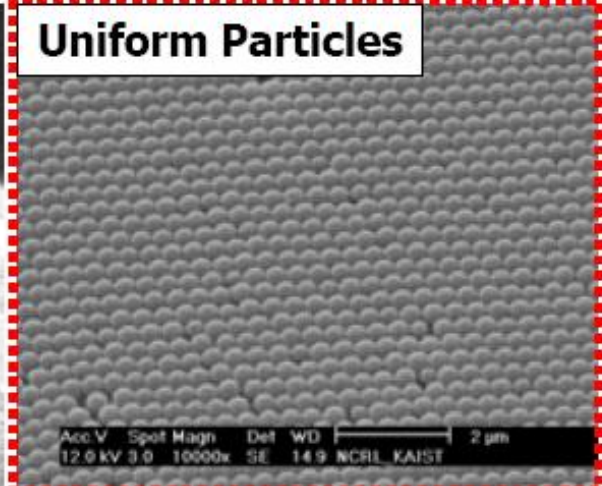
Thin Films



Fiber

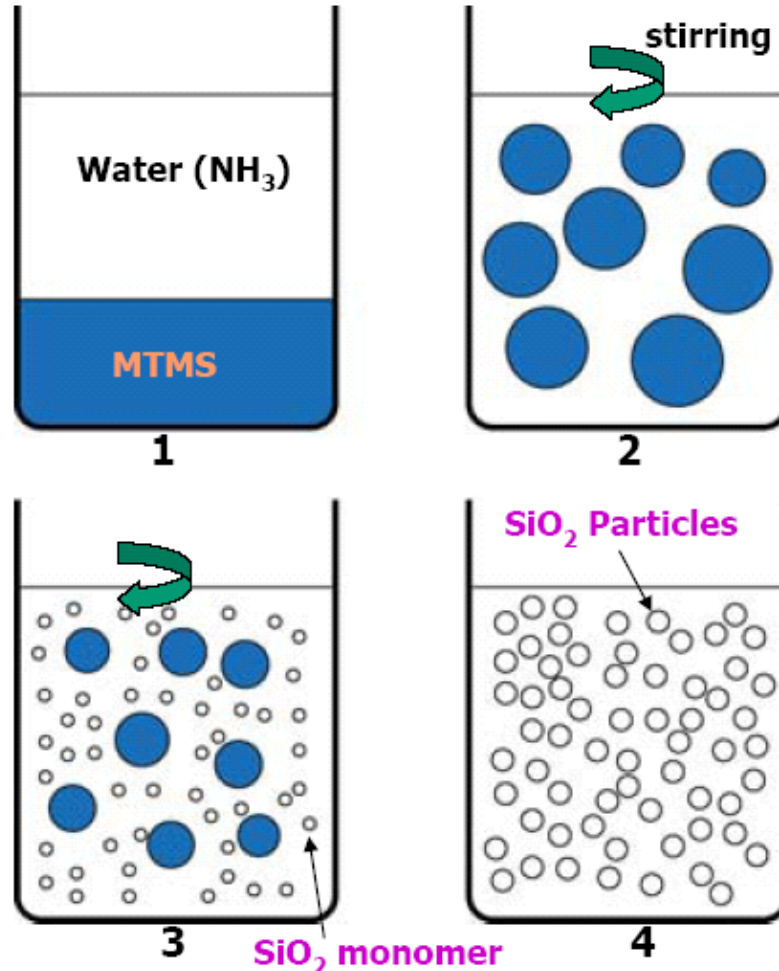


Uniform Particles

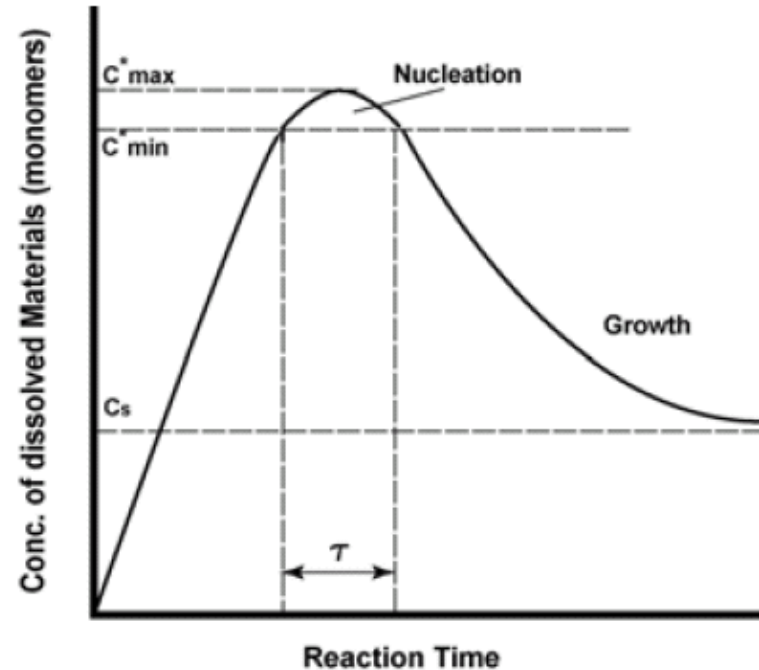


2.5 Liquid Phase Processes

Bottom-up: Sol-Gel Process



Lamer diagram

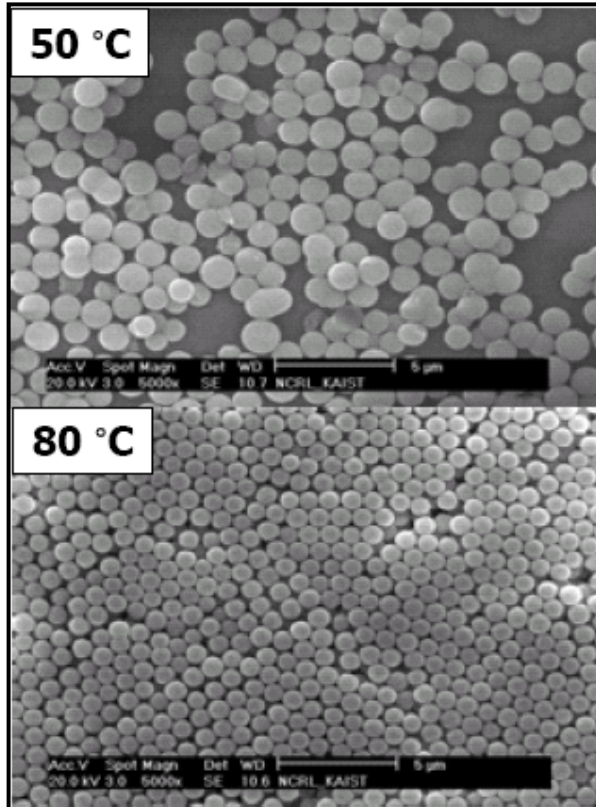


► To make monodispersed Particles, the time τ should be decreased.

MTMS = Methyltrimethoxysilane

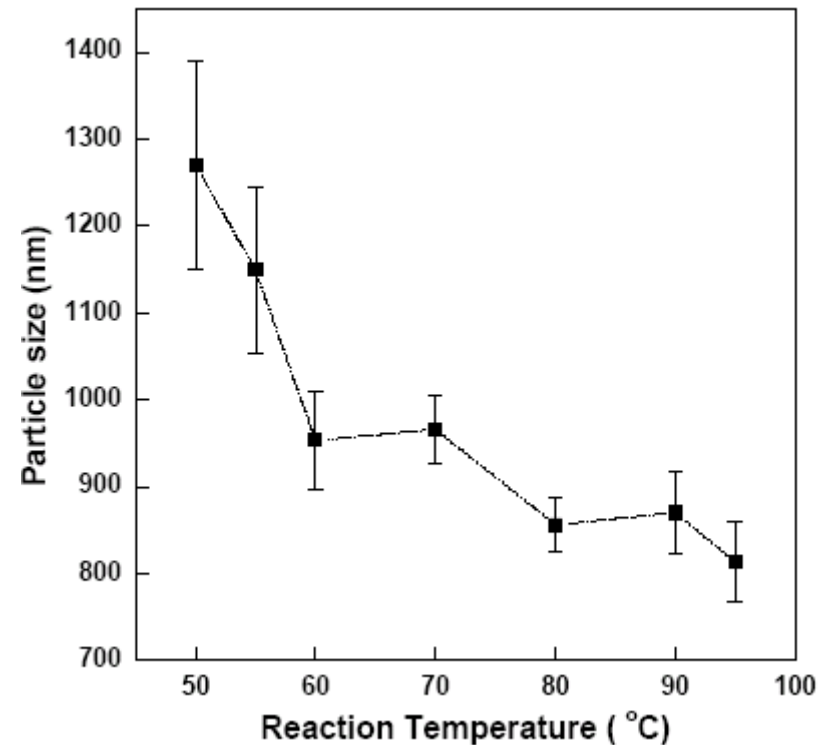
2.5 Liquid Phase Processes

Bottom-up: Sol-Gel Process



0.6 M MTMS, 1 M NH₃

Particle size vs. reaction temperature

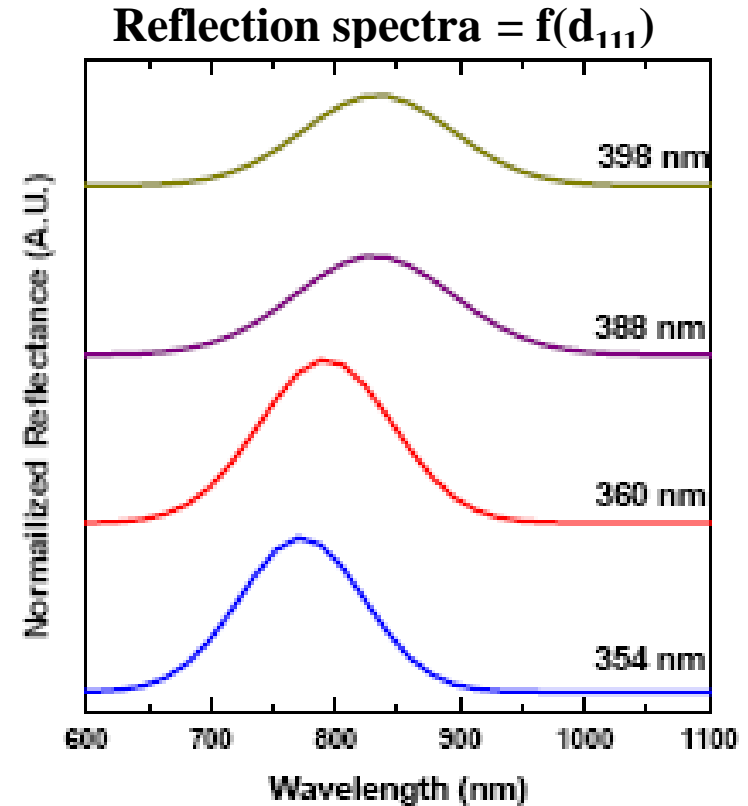
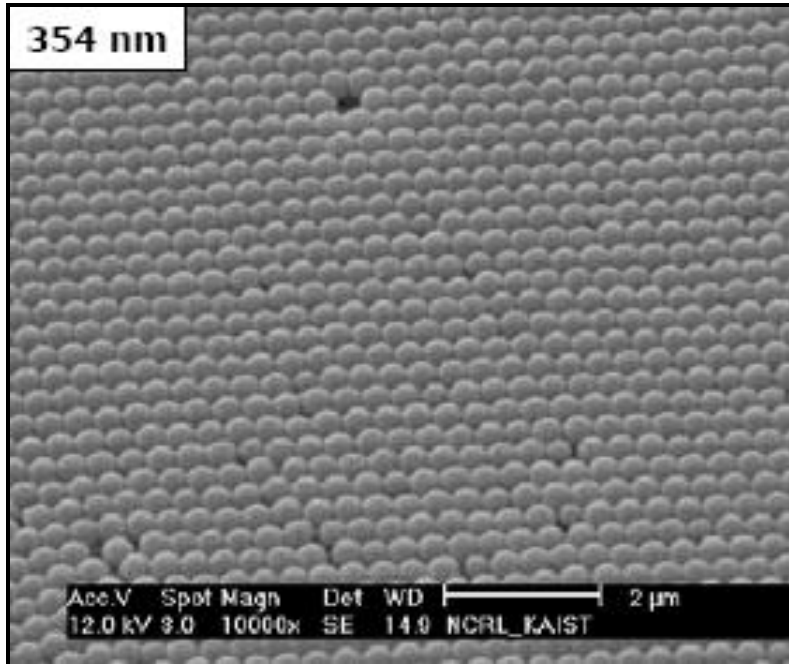


Temperature↑ ⇒ Reaction rate↑ ⇒ Nucleation time↓ ⇒ Size Distribution↓

2.5 Liquid Phase Processes

Bottom-up: Sol-Gel Process „Stöber Process“

Photonic crystal out of SiO₂ spheres (Opal)



Bragg's law: $\lambda_{\text{Bragg}} = 2n_{\text{eff}} \cdot d_{111}$

with $n_{\text{eff}} = \sqrt{n_{\text{SiO}_2}^2 \cdot f + n_{\text{air}}^2 \cdot (1-f)}$

and $d_{111} = (2/3)^{1/2} \cdot D$, f = filling ratio

2.5 Liquid Phase Processes

Bottom-up: Synthesis of metal nanoparticles

Application of metal nanoparticles

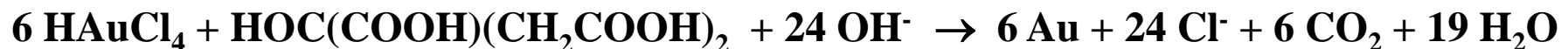
- Electronic materials, e.g. Ni
- Magnetic materials, e.g. Fe
- Catalysts, e.g. Pt
- Explosives, e.g. Al
- Powder metallurgy, e.g. Cr
- Photographic films, e.g. Ag

Synthesis approach: Reduction of metal salts

a) In organic solvents (non noble metals)



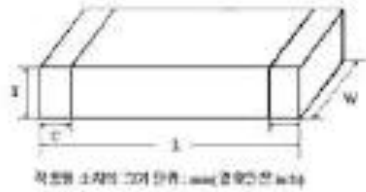
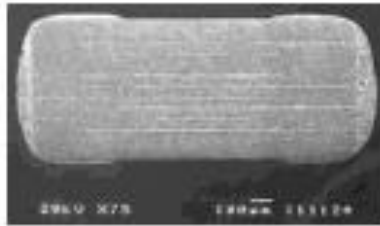
b) In water (noble metals, i.e. Rh, Ir, Pd, Pt, Cu, Ag, Au)



2.5 Liquid Phase Processes

Bottom-up: Synthesis of metal nanoparticles

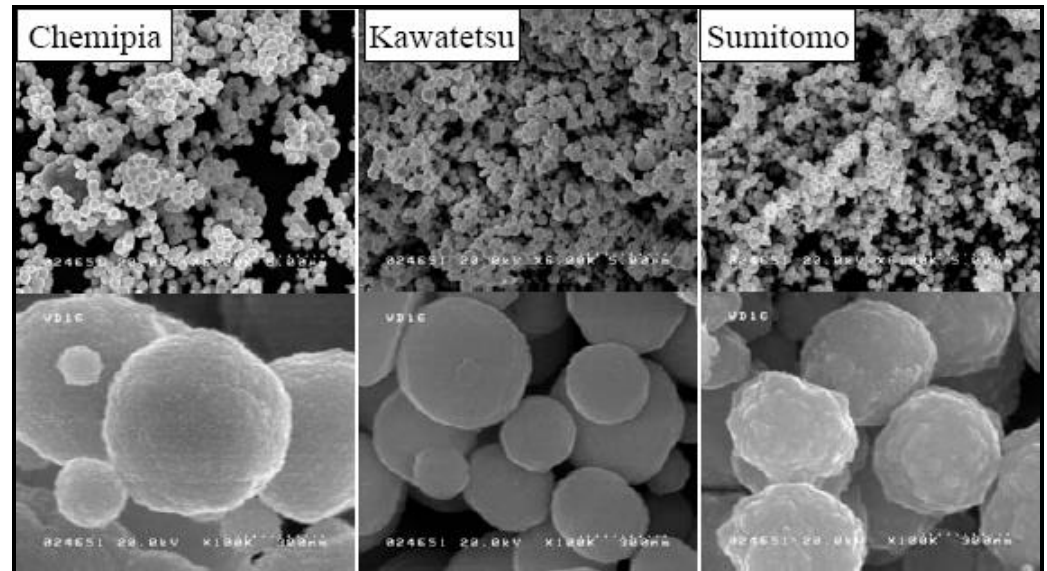
Example: Manufacturing of multi-layer ceramic capacitors (MLCCs)



Ongoing improvement of small high capacitance MLCCs require a continuous reduction of

- dielectric layer thickness
- **internal Ni electrode layer thickness (80 ± 20 nm Ni particles)**

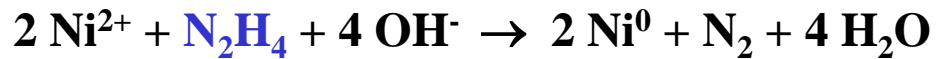
Commercial Ni nanoscale powders



2.5 Liquid Phase Processes

Bottom-up: Synthesis of metal nanoparticles

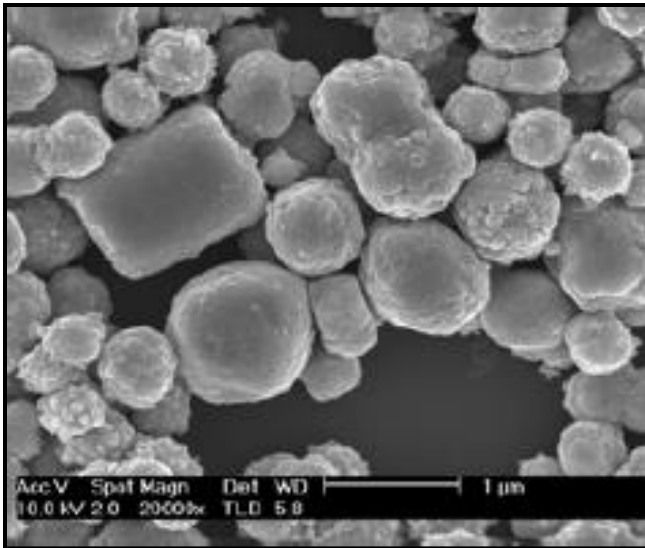
Reduction of Ni²⁺ in solution



Hydrazine = Reducing agent

Result

Particles with Random shape and size and a broad broad size distribution



Advanced precipitation processes

- Application of an additive (dispersant, complex agent)
- Heterogeneous nucleation (seed)

2.5 Liquid Phase Processes

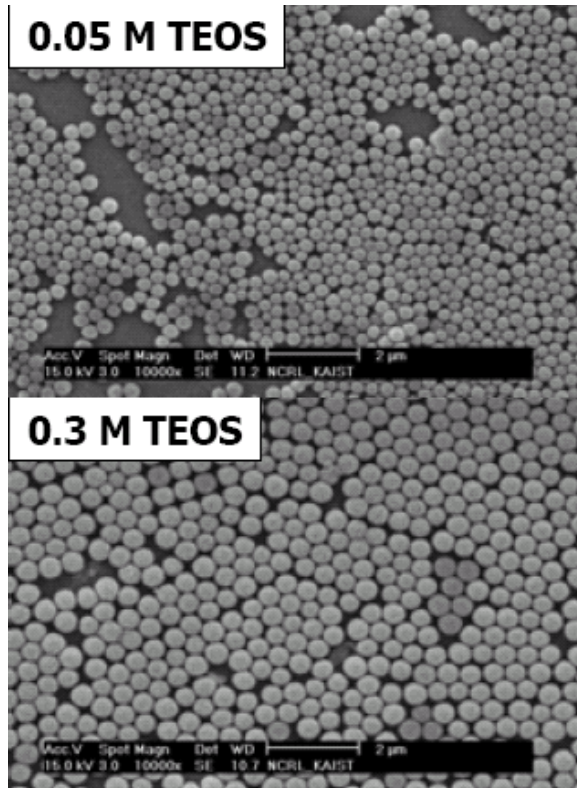
Bottom-up: Synthesis of metal nanoparticles

Guideline for the reducing agent

Metal	E^0 [V] vs. SHE	Reducing agent	Conditions
Au, Pd, Pt, Ag	$> + 0.7$	organic acids, ROH, polyols	$> 70\text{ }^\circ\text{C}$
Rh, Ir, Hg		aldehyds, sugars	$< 50\text{ }^\circ\text{C}$
		hydrazine, H_2SO_3, H_3PO_2	ambient temp.
		NaBH_4, boranes, hydrated e^-	ambient temp.
Cu, Re, Ru	$< + 0.7 > 0.0$	polyols	$> 120\text{ }^\circ\text{C}$
		aldehydes, sugars (Fehling sol.!)	$> 70\text{ }^\circ\text{C}$
		hydrazine, hydrogen	$< 70\text{ }^\circ\text{C}$
		NaBH_4	ambient temp.
Cd, Co, Ni, Fe	$< 0.0 > - 0.6$	polyols	$> 180\text{ }^\circ\text{C}$
In, Sn, Mo, W		hydrazine, hydroxylamine	$70 - 100\text{ }^\circ\text{C}$
		NaBH_4, boranes, hydrated e^-	ambient temp.
Cr, Mn, Ta, Y	$< - 0.6$	NaBH_4, boranes	T, p $>$ ambient
		hydrated e^-	ambient temp.

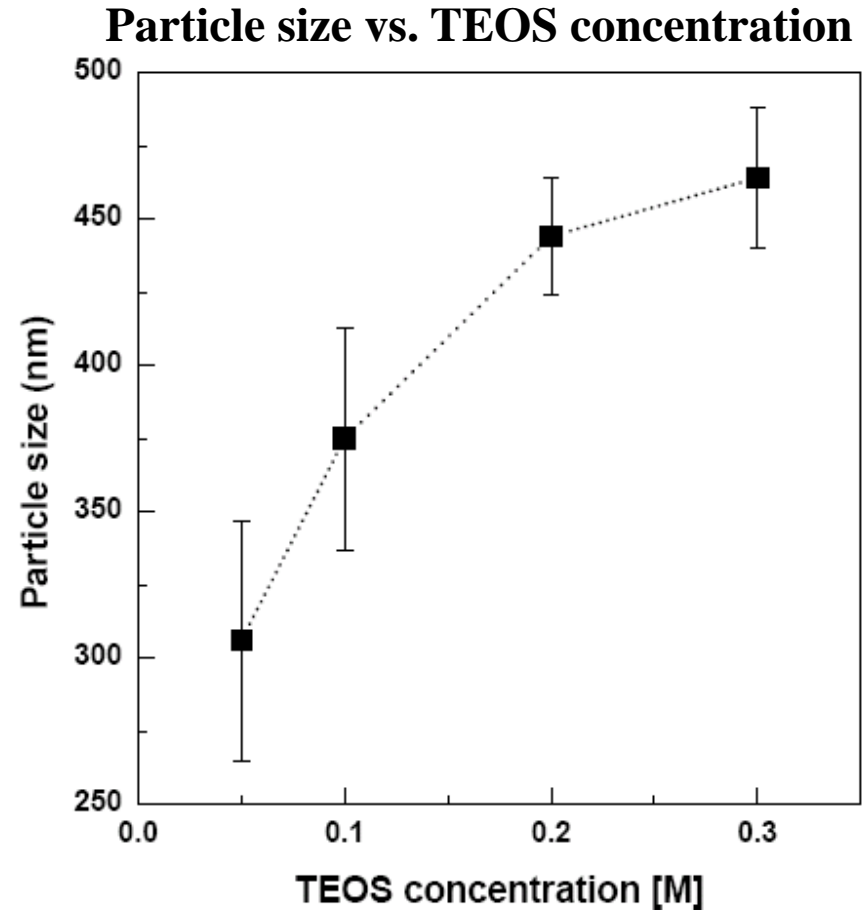
2.5 Liquid Phase Processes

Bottom-up: Sol-Gel Process „Stöber Process“



$\text{H}_2\text{O}/\text{EtOH} = 0.2$, 0.7 M NH_3 , $22 \text{ }^\circ\text{C}$

TEOS Concentration $\uparrow \Rightarrow$ Particle size \uparrow



2.5 Liquid Phase Processes

Bottom-up: Synthesis of metal nanoparticles

How to control metal particle size?

- **Processing parameter**
 - Temperature, pressure, concentration, pH, ultrasound application, ...
- **Seed (heterogeneous nucleation)**
 - Type and concentration of applied seed
- **Complex agent**
 - Complex stability

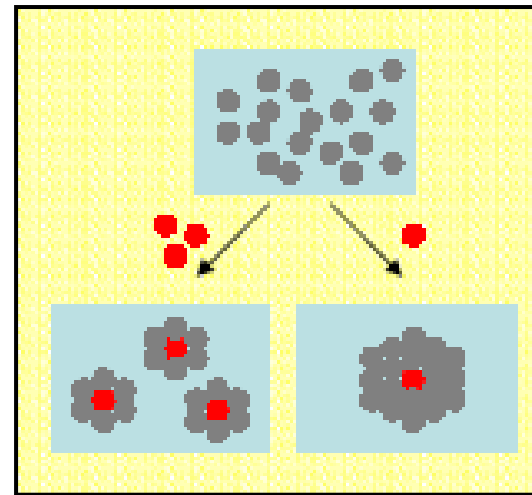
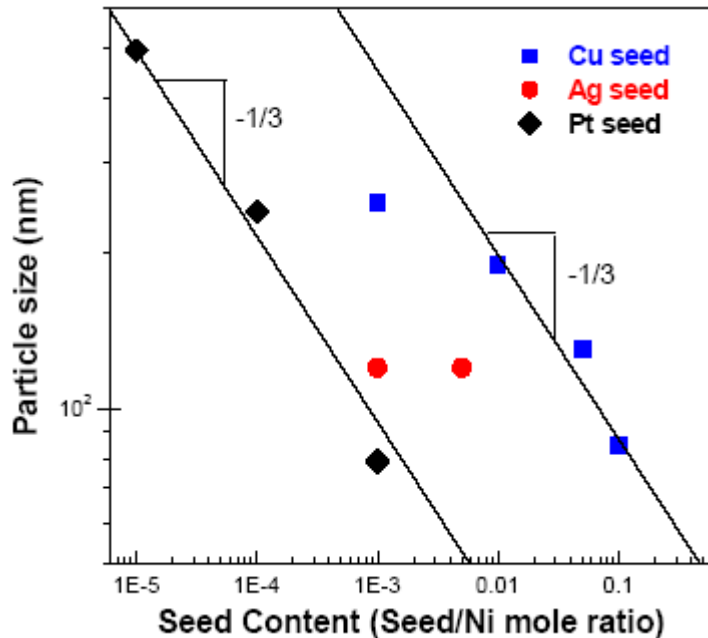
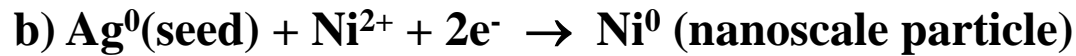
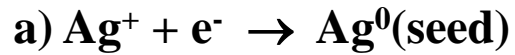
Redox potential of Ag^+ as function of the presence of a complexing agents

Redox system	$-\log K_B$	E^0 [V] vs. SHE
$\text{Ag}^+ + e^- \rightarrow \text{Ag}^0$	-	+ 0.799
$[\text{Ag}(\text{NH}_3)_2]^+ + e^- \rightarrow \text{Ag}^0 + 2 \text{NH}_3$	7.2	+ 0.38
$[\text{Ag}(\text{SO}_3)_2]^{3-} + e^- \rightarrow \text{Ag}^0 + 2 \text{SO}_3^{2-}$	8.7	+ 0.29
$[\text{Ag}(\text{S}_2\text{O}_3)_2]^{3-} + e^- \rightarrow \text{Ag}^0 + 2 \text{S}_2\text{O}_3^{2-}$	13.4	+ 0.01
$[\text{AgI}_4]^{3-} + e^- \rightarrow \text{Ag}^0 + 4 \text{I}^-$	15.0	- 0.09
$[\text{Ag}(\text{CN})_3]^{2-} + e^- \rightarrow \text{Ag}^0 + 3 \text{CN}^-$	22.2	- 0.51

2.5 Liquid Phase Processes

Bottom-up: Synthesis of metal nanoparticles

Heterogeneous nucleation

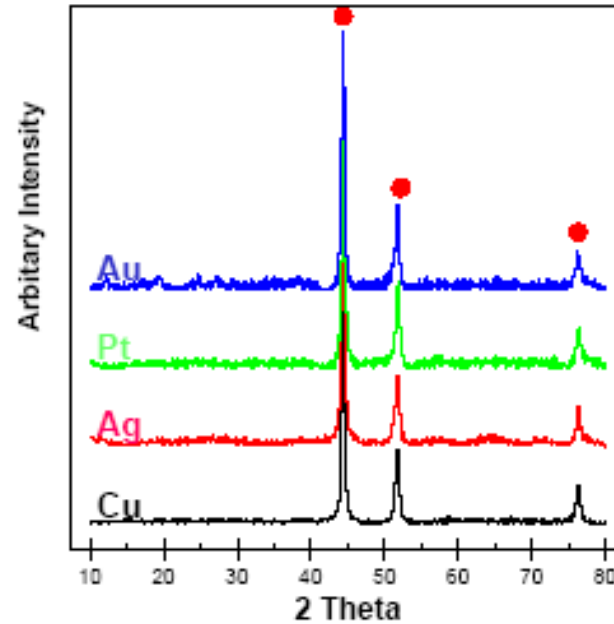
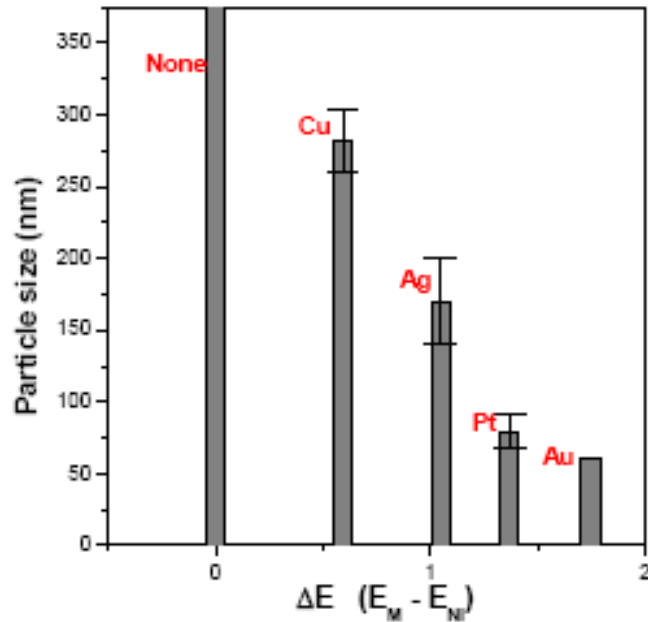


$$d_m = A \cdot [\text{Seed}]^{-1/3}$$

2.5 Liquid Phase Processes

Bottom-up: Synthesis of metal nanoparticles

Heterogeneous nucleation



Seed	E^0 [V] vs. SHE	Ni particle size [nm]
Cu	+0.34	282
Ag	+0.80	170
Pt	+1.18	90
Au	+1.50	60

2.5 Liquid Phase Processes

Bottom-up: Synthesis of metal nanoparticles

Formation mechanism of seed-mediated growth for Ag and Au rods

a) Ag- or Au-salt + NaBH_4 + citrate \rightarrow seed

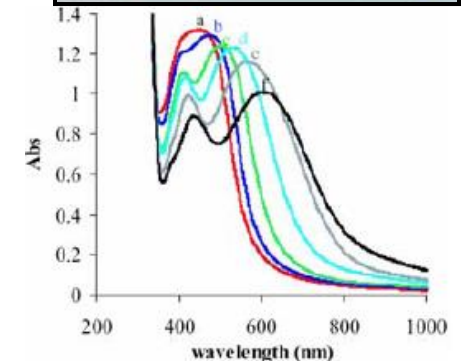
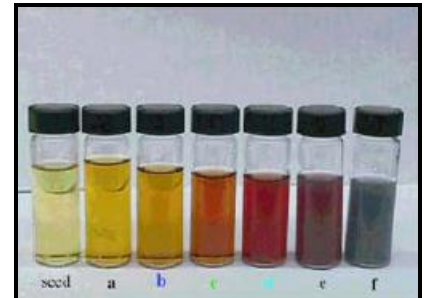
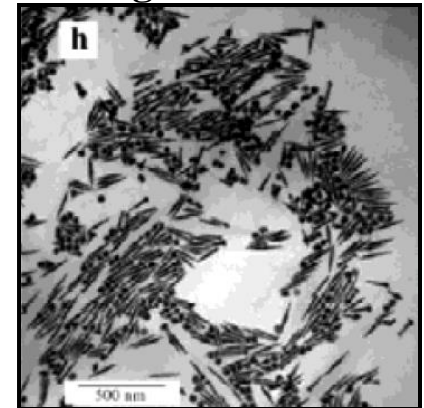
b) seed + metal salt + ascorbic acid + CTAB \rightarrow nanorods
(CTAB = Cetyltrimethylammonium bromide)

Chemical	Role
NaBH_4	strong reducing agent
Citrate	capping agent
Ascorbic acid	weak reducing agent
CTAB	rod like template

Decreasing the seed concentration increases the aspect ratio and the color (absorption edge) of nanorods

Aspect ratio increases from 1:1 to 1:10 (left graphs)

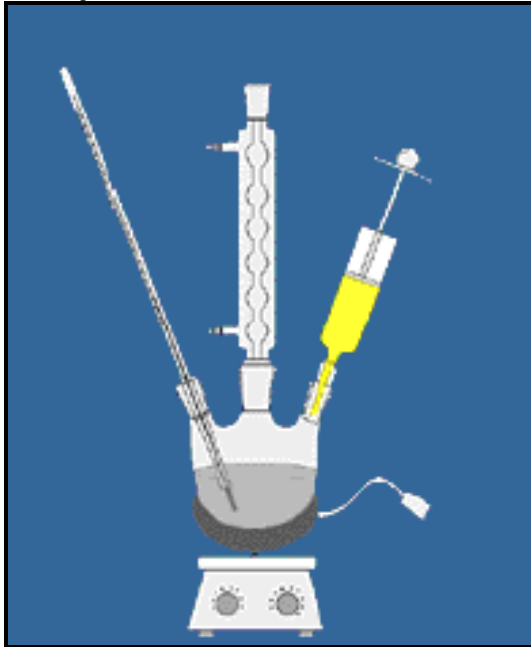
Ag nanorods



2.5 Liquid Phase Processes

Bottom-up: Synthesis of metal nanoparticles

Polyol method



boiling point $> 120^{\circ}\text{C}$

e.g. ethylen glycol

Synthesis pathway

1. Dissolve soluble metal salts, e.g. acetates in pure alcohol (reducing agent) with a rather high boiling point

2. Boil for several hours

3. Separate by centrifugation

4. Wash by alcohol

→ Au, Pt, Pd, Ag, Rh, Hg, Ir, Cu, Re, Ru, Cd, Co, Ni, Fe, In, Sn, Mo, W, ...

2.5 Liquid Phase Processes

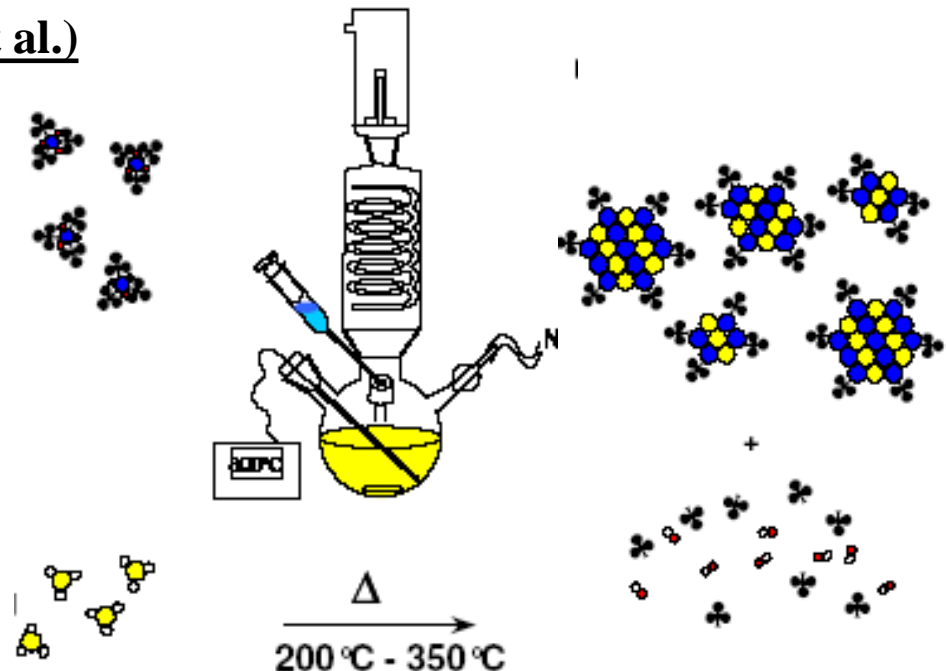
Bottom-up: Synthesis of phosphate nanoparticles

Synthesis in alcohols (van Veggel)

1. LnCl_3 and trisalkylphosphate in methanol
 2. Addition of H_3PO_4
 3. Addition of trioctylamine to deprotonate phosphoric acid
- ⇒ Formation of LnPO_4 nanoscale particles with alkyl phosphate capping

Synthesis in highly boiling polyols (Haase et al.)

1. $\text{Ln}(\text{ac})_3$ in ethylen glycol
 2. Addition of trioctylphosphin oxide
 3. Addition of Na_2HPO_4
 4. Boiling
- ⇒ Formation of LnPO_4 nanoscale particles with TOPO capping



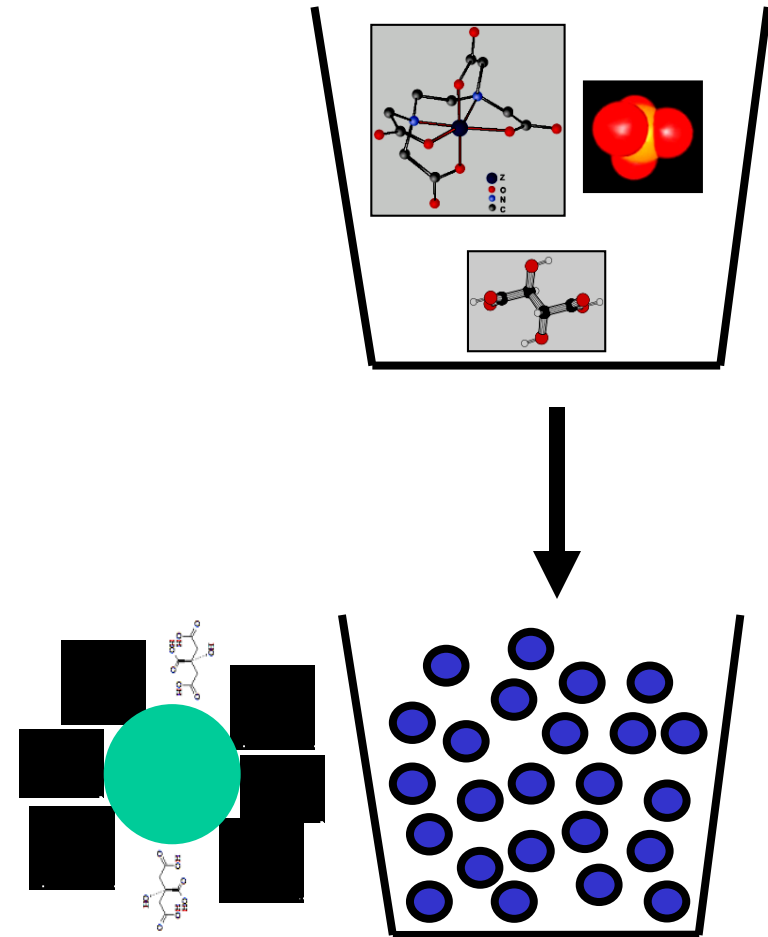
2.5 Liquid Phase Processes

Bottom-up: Synthesis of phosphate nanoparticles

Synthesis in water (Merikhi, Bachmann, Jüstel et al.)

1. $\text{Ln}(\text{ac})_3$ in acidic water
2. Addition of complexing agent
3. Addition of an excess of citric acid
4. Addition of H_2PO_4^-
5. Enhance pH to 9 – 10 and temper at 80 – 90 °C

⇒ Formation of LnPO_4 nanoscale particles with citric acid capping

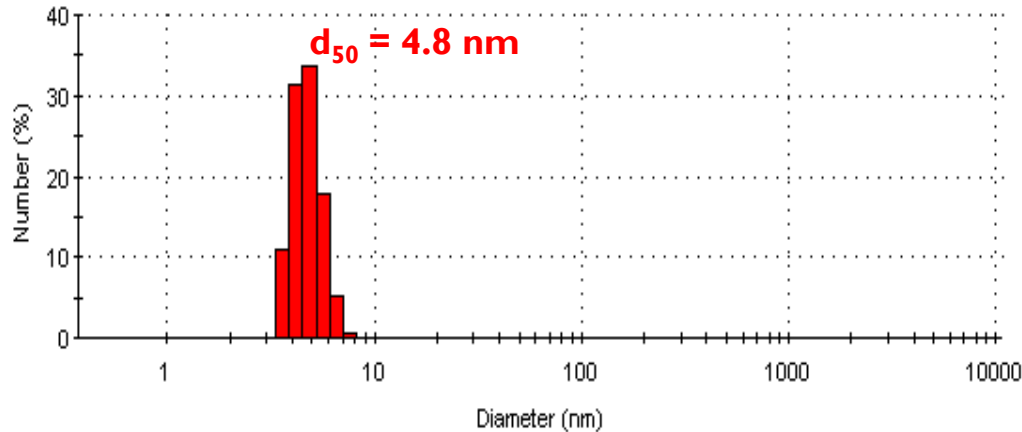


2.5 Liquid Phase Processes

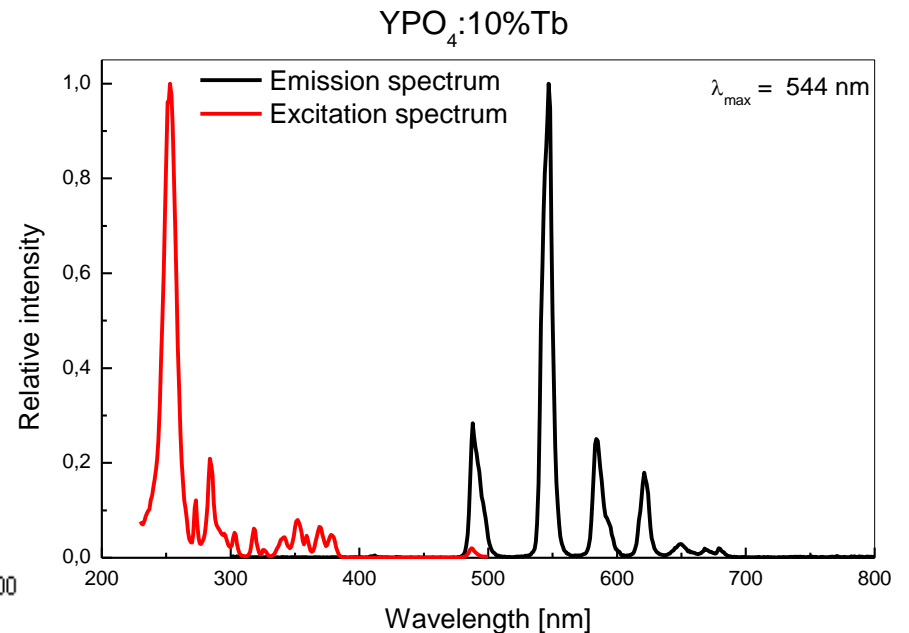
Bottom-up: Synthesis of phosphate nanoparticles

Example: Colloidal $\text{YPO}_4:\text{Tb}^{3+}$ nanoscale particles in aqueous solution

Particle size distribution by dynamic light scattering (Malvern Nanosizer)



Emission and excitation spectrum

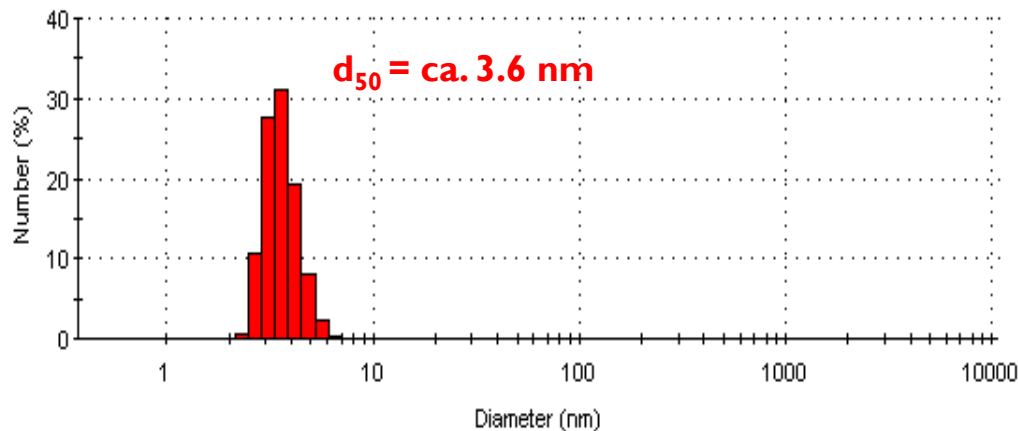


2.5 Liquid Phase Processes

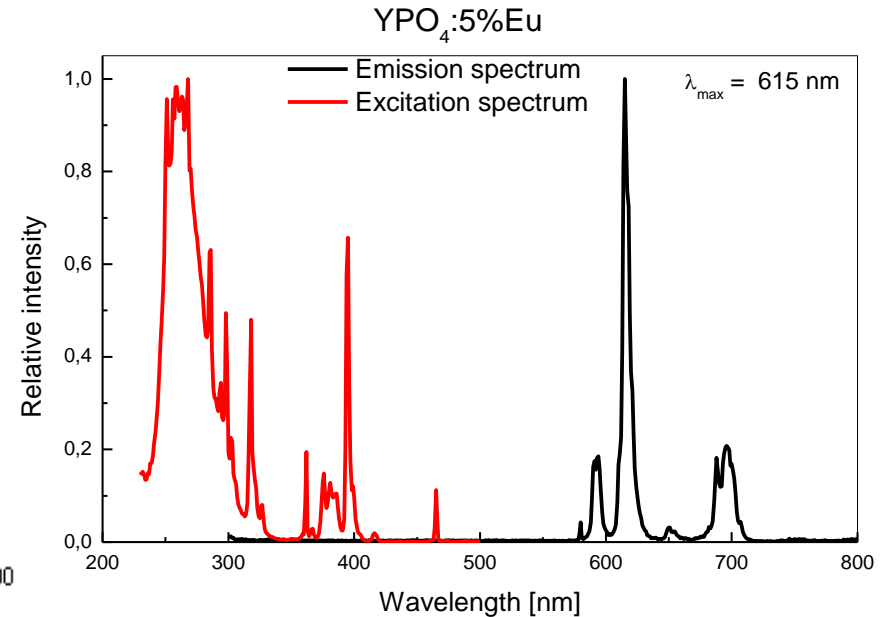
Bottom-up: Synthesis of phosphate nanoparticles

Example: Colloidal $\text{YPO}_4:\text{Eu}^{3+}$ nanoscale particles in aqueous solution

Particle size distribution by dynamic light scattering (Malvern Nanosizer)



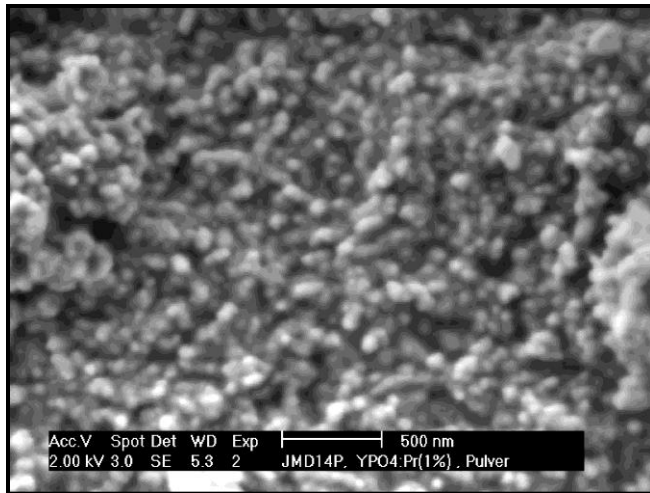
Emission and excitation spectrum



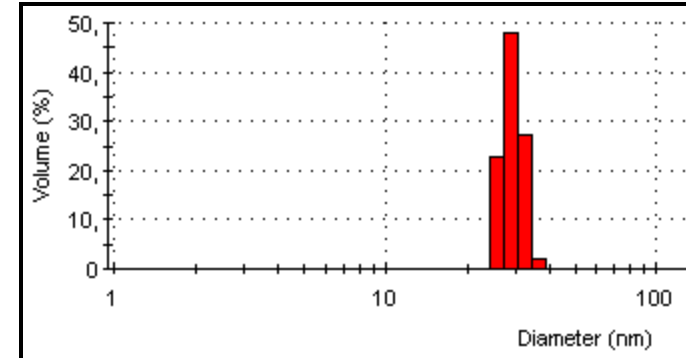
2.5 Liquid Phase Processes

Bottom-up: Synthesis of phosphate nanoparticles

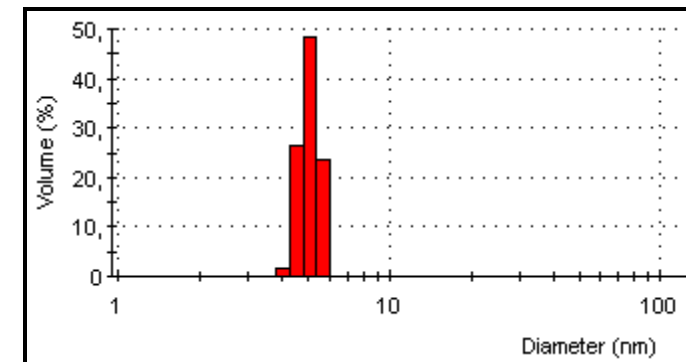
YPO₄:Pr and LuPO₄:Pr as 235 nm emitter



YPO₄:Pr (30 nm particles)



LuPO₄:Pr (5 nm particles)

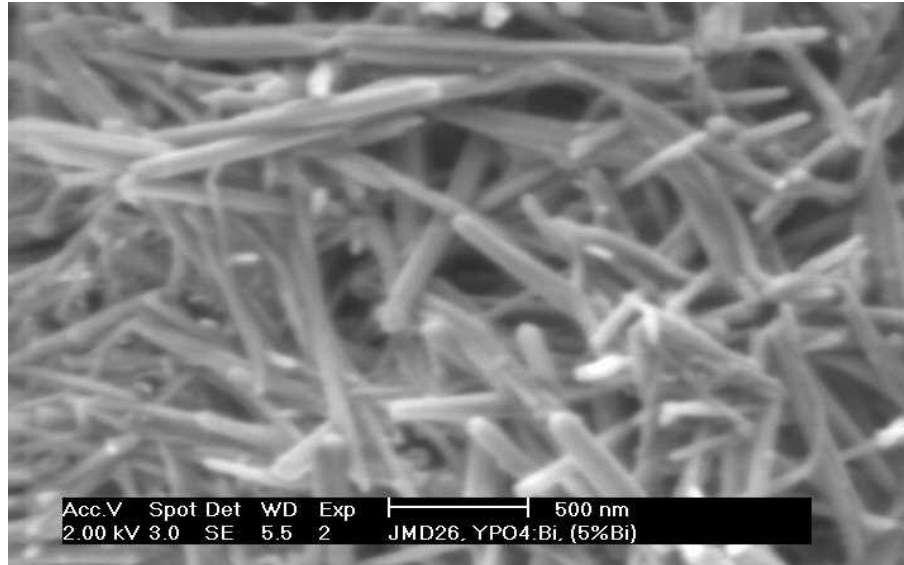


Further examples: GdPO₄:Pr, LaPO₄:Pr, YPO₄:Ln (Ln = Ce, Gd, Nd)

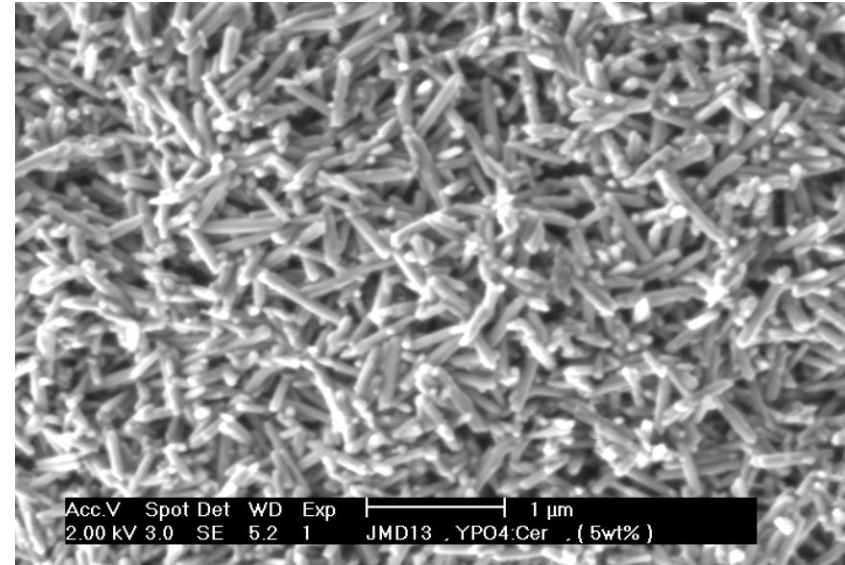
2.5 Liquid Phase Processes

Bottom-up: Synthesis of phosphate nanoparticles using rod like template

YPO₄:Bi Nanorods



YPO₄:Ce Nanorods



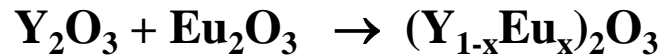
Application areas

- Precursor for phosphor syntheses
- Precoatings of lamp glass
- Phosphors for UV emitting discharge lamps

3.1 Material Synthesis

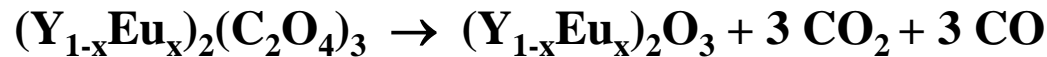
Synthesis pathways to $Y_2O_3:Eu$ powder

1. Ceramic method

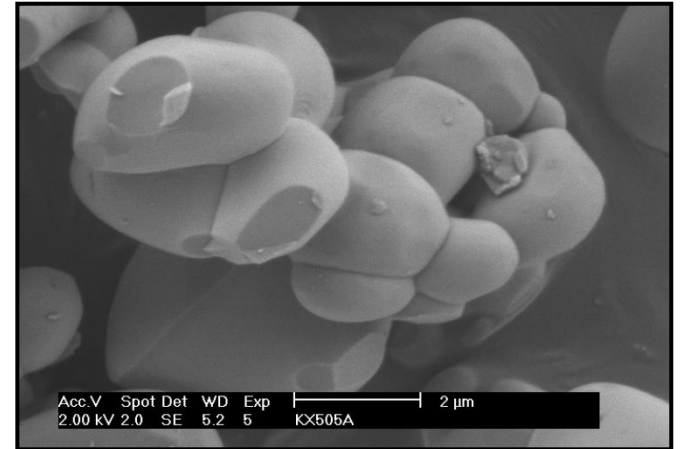
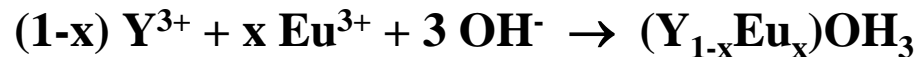
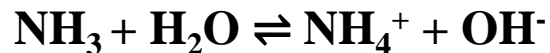


2. Precipitation methods

a) Oxalate route (non-homogeneous precipitation)



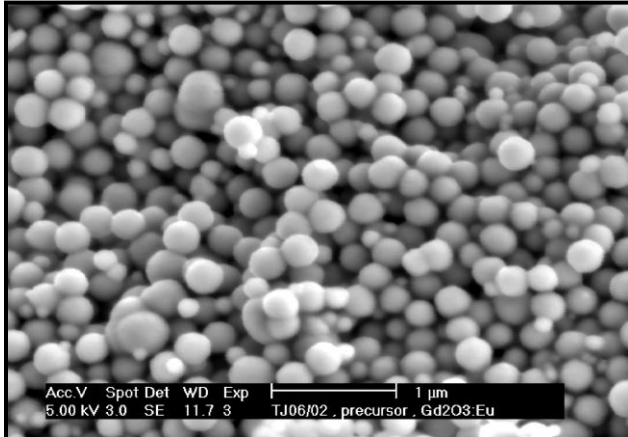
b) Hydroxide route (homogeneous precipitation)



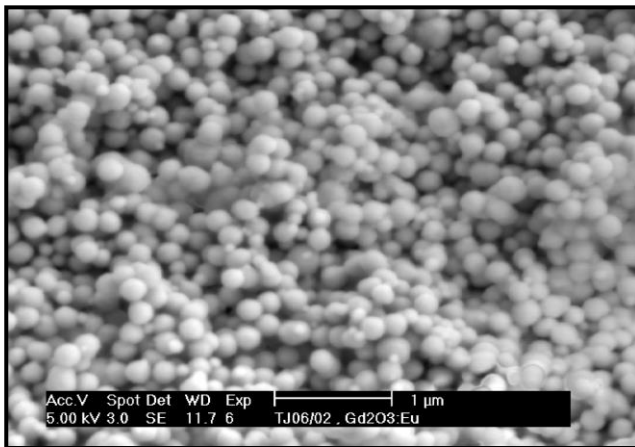
3.1 Material Synthesis

Synthesis of $\text{Y}_2\text{O}_3:\text{Eu}$ nanoscale powder

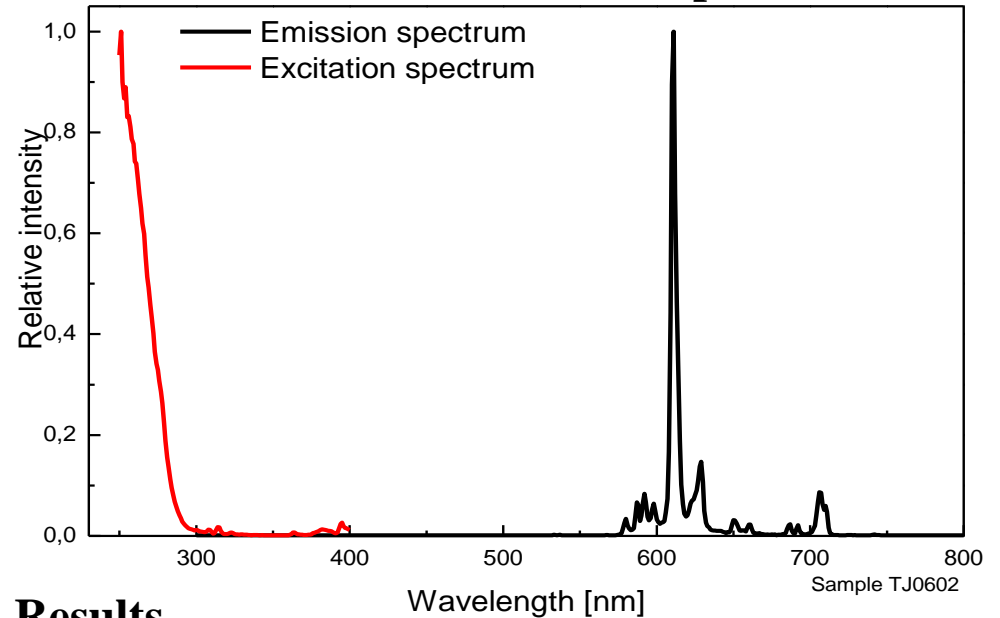
Hydroxide precursor



$\text{Y}_2\text{O}_3:\text{Eu}$ phosphor



Emission and excitation spectrum



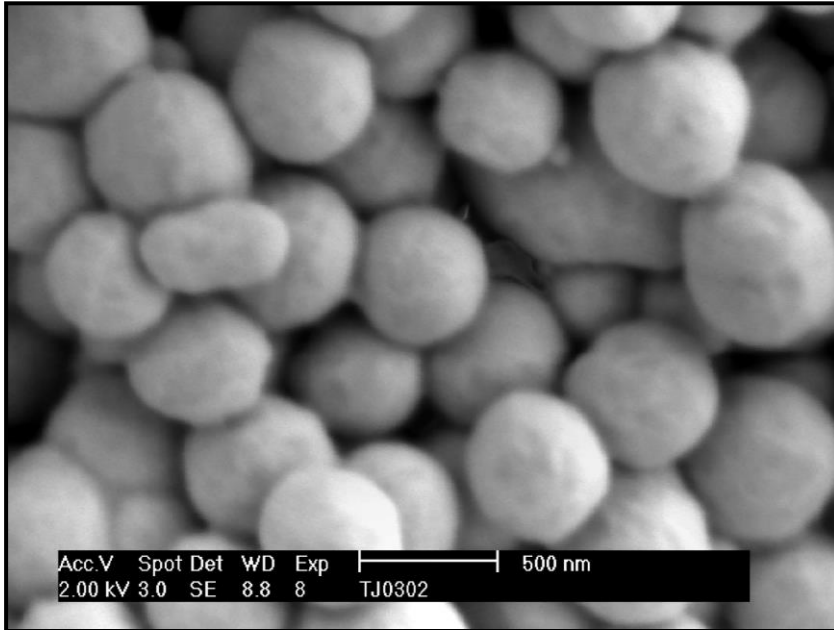
Results

- 200 nm particles
- Narrow particle size distribution
- Homogeneous particle morphology
- Quantum efficiency > 65%

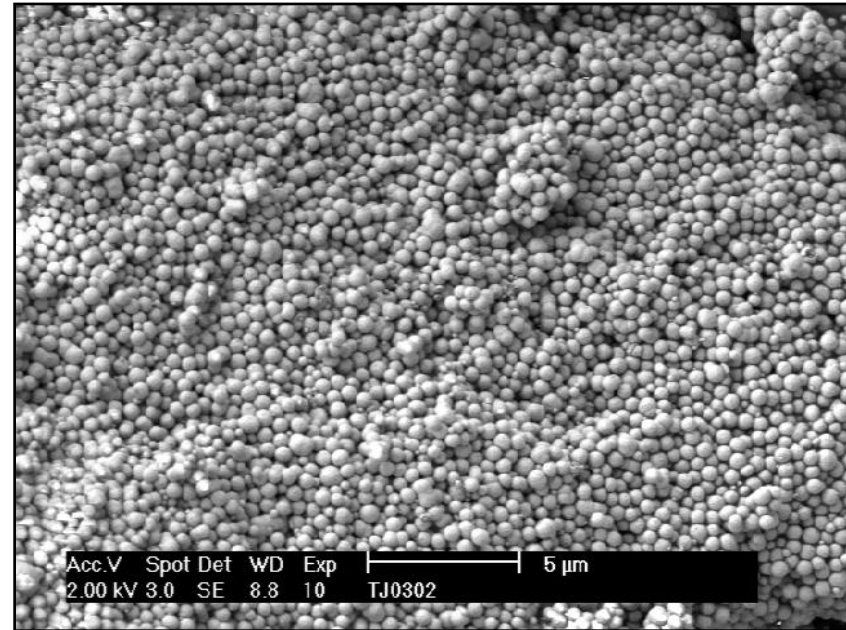
3.1 Material Synthesis

Synthesis of $(\text{Y,Gd})_2\text{O}_3:\text{Eu}$ nanoscale powder

Homogeneous particle morphology



⇒ homogeneous layer morphology



- $(\text{Y,Gd})_2\text{O}_3$ particle diameter ~ 200 – 500 nm
- Thin and dense layer, e.g. as a reflector layer

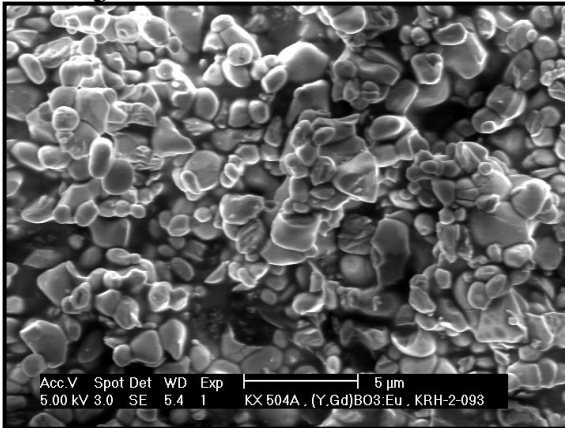
3.1 Material Synthesis

Synthesis of homogeneous (Y,Gd)BO₃:RE powder for PDPs

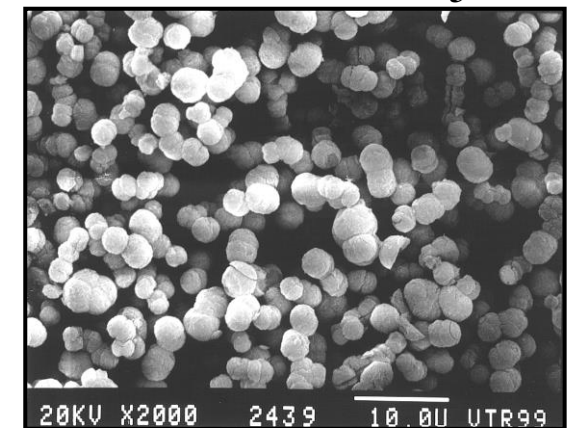
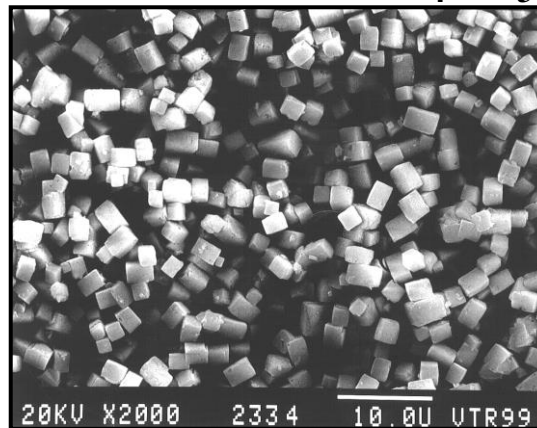
- a) Synthesis of an insoluble precursor LnB(OH)₄CO₃
⇒ 0.6 - 7.0 μm particles
- b) Conversion into the phosphor by annealing: Ln = Y, La, Gd, Lu
 - Blue LnBO₃:Ce, LnBO₃:Tm
 - Green LnBO₃:Tb, LnBO₃:Er
 - Red LnBO₃:Eu, LnBO₃:Sm

“Precursor route”

LnBO₃:Eu (solid state synthesis)



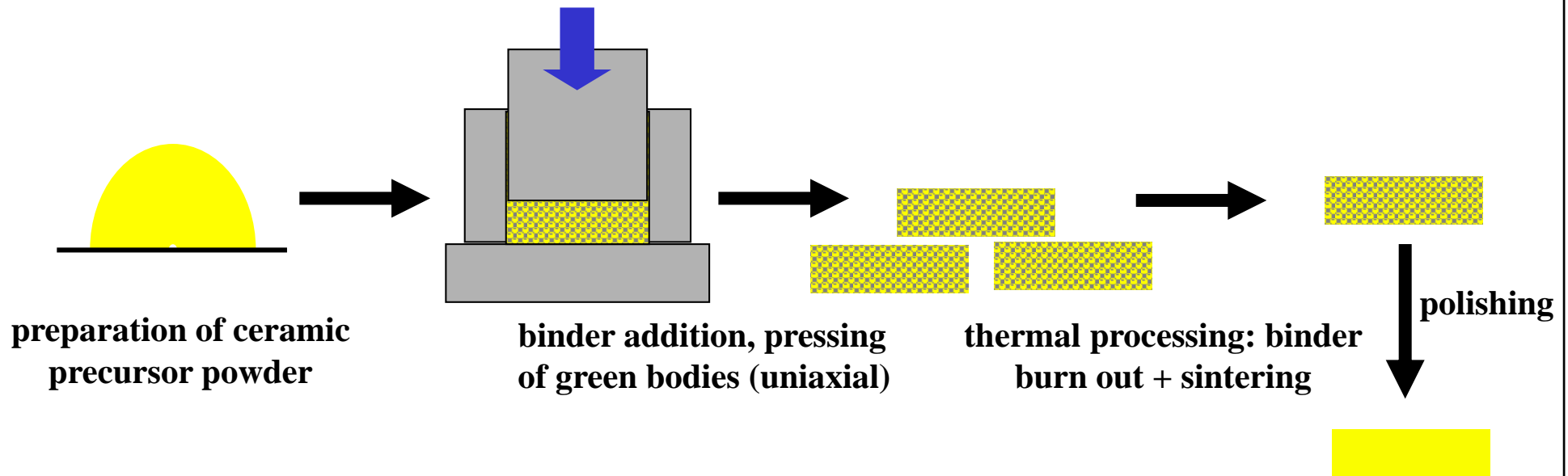
Precursor LnB(OH)₄CO₃ → Phosphor LnBO₃



3.1 Material Synthesis

Synthesis of optically transparent ceramics

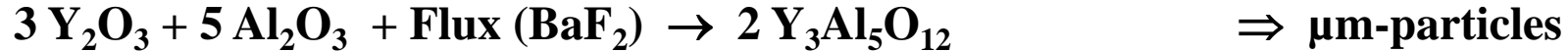
- **Optical transmission:** $I/I_0 = (1-R)^2 \exp(-\mu x)$
R: reflectivity, **μ :** absorption coefficient, **x:** sample thickness
- $\mu = a + S_{im} + S_{op}$
a: electronic absorption, **S_{im} :** impurity scattering, **S_{op} :** optical anisotropy scattering
- **Requirements for transparency:** optically isotropic host lattice, no pores or second phases



3.1 Material Synthesis

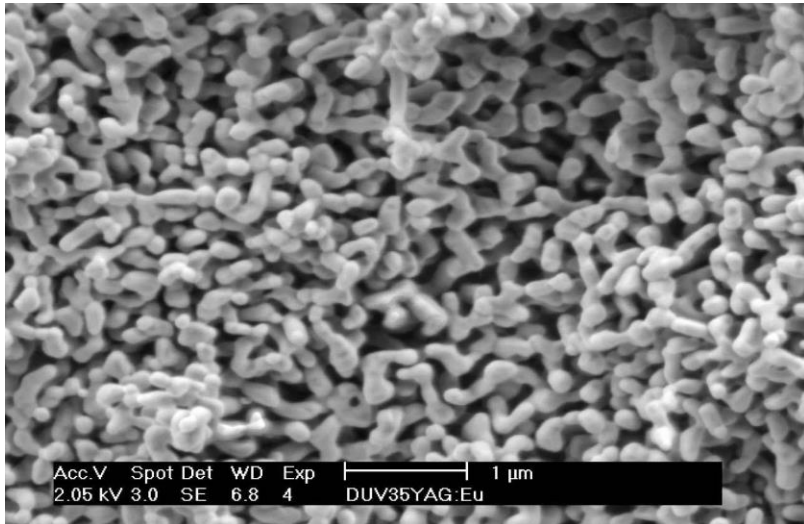
Synthesis of $Y_3Al_5O_{12}:Ce$ (cubic) powder for ceramic processing

1. Ceramic method

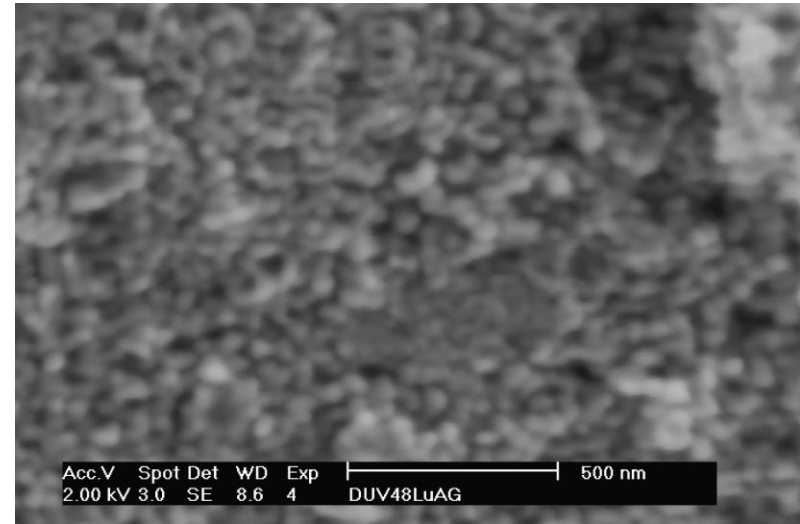


2. Homogeneous precipitation of hydroxycarbonates + surfactants, e.g. sodium dodecylsulfate

\Rightarrow Reduction in particle size and improvement of homogeneity \Rightarrow nm-particles



method according to
Konoshima Chemical

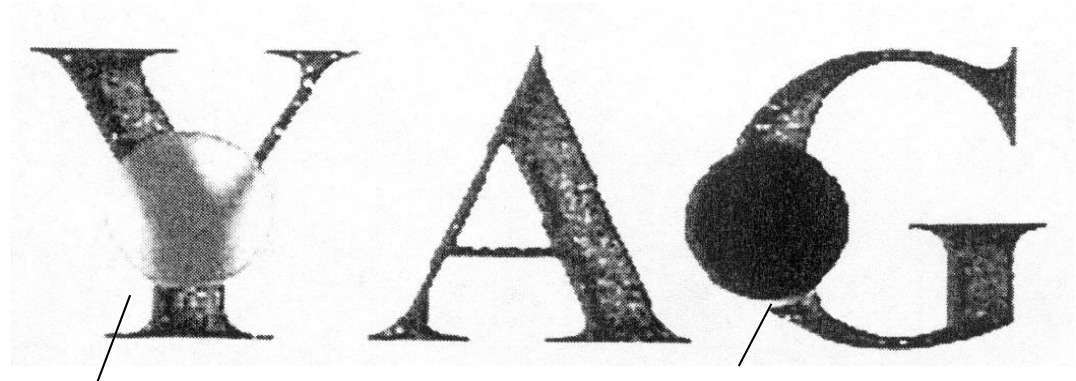
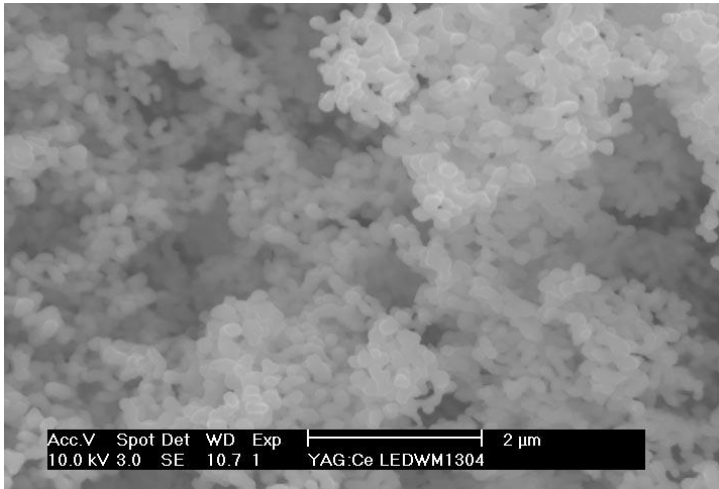


method according to
D. Uhlich, Diploma thesis (2004)

3.1 Material Synthesis

Synthesis of transparent $\text{Y}_3\text{Al}_5\text{O}_{12}:\text{Ce}$ „Yellow phosphor for LEDs“

1. Precipitation of nanopowder
 $\text{Al}(t\text{-BuO})_3 + \text{Y}(\text{NO}_3)_3$ in ethyl acetate
2. Sintering: 1000 °C in air
3. Pellets pressing (PVA binder) in SiC pit
4. Microwave treatment (400 W, 35 min.) + polishing



microwave sintered

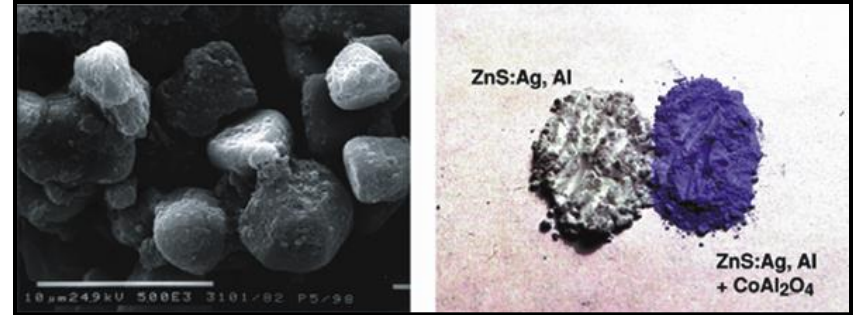
1400 °C, 4 h

3.2 Functional Coatings and Layers

Application areas

Nanoparticle coatings

- Pigmentation of display phosphors, e.g. applied in CRTs or PDPs
- Protective coatings onto μ -scale pigments and μ -scale phosphors
- Dielectric coatings onto electroluminescence phosphors (EL)



Nanoparticle layers

- Colour filter, e.g. onto incandescent lamps (Philips Blue Vision)
- Interference filter onto display glass + light bulbs
- Transparent converter layer in LEDs
- Lamp production: Improvement of layer morphology and adhesion

3.2 Functional Coatings and Layers

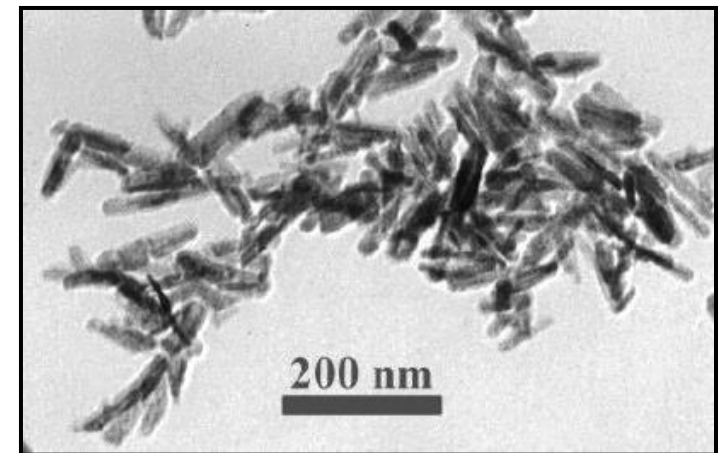
Coating materials

Requirements

- (photo)chemical and thermal stability
- high transparency

Protective materials		Band gap [eV]	PZC [pH]
• LaPO_4		8.7	7.8
• SiO_2		8.4	2-3
• MgO		8.0	12.0
• $\gamma\text{-Al}_2\text{O}_3$		7.5	9.0
• Y_2O_3		5.6	9.1
• La_2O_3		5.5	10.5
• C (diamond) “DLC”		5.4	?
• SnO_2		3.6	4.5
• ZnO		3.4	10.5
Colour filter			
• $\alpha\text{-Fe}_2\text{O}_3$	rot	1.9	6.7
• CoAl_2O_4	blau	?	9 - 10

$\alpha\text{-Fe}_2\text{O}_3$ Nanoparticles



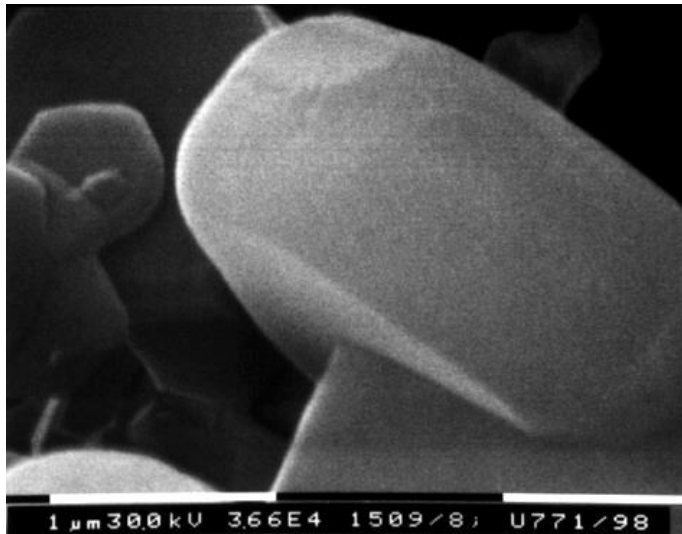
3.2 Functional Coatings and Layers

Protective MgO coating on BaMgAl₁₀O₁₇:Eu (BAM) “Blue Phosphor for PDPs”

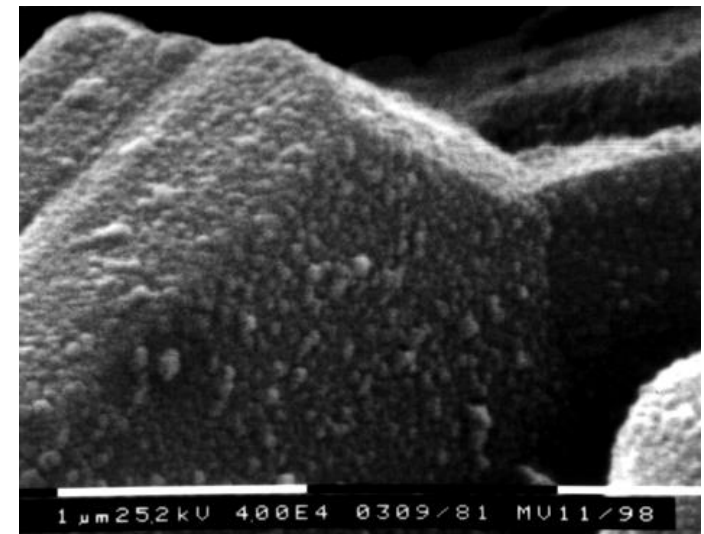
Process

- Mg(NO₃)₂ + urea + BAM in H₂O
- Homogeneous pH value enhancement:
$$\text{H}_2\text{N-CO-NH}_2 + \text{H}_2\text{O} \rightarrow 2 \text{NH}_3 + \text{CO}_2$$
$$\text{NH}_3 + \text{H}_2\text{O} \rightleftharpoons \text{NH}_4^+ + \text{OH}^-$$
$$\text{Mg}^{2+} + 2 \text{OH}^- \rightarrow \text{Mg(OH)}_2$$
- Sintering at 600 °C: Mg(OH)₂ → MgO + H₂O ⇒ MgO nm particles onto BAM particles

SEM image BaMgAl₁₀O₁₇:Eu



SEM image BaMgAl₁₀O₁₇:Eu (MgO)



3.2 Functional Coatings and Layers

Protective La_2O_3 coating on $\text{BaSi}_2\text{O}_5:\text{Pb}$ (BSP) “UV-A Phosphor for tanning lamps”

Application problem

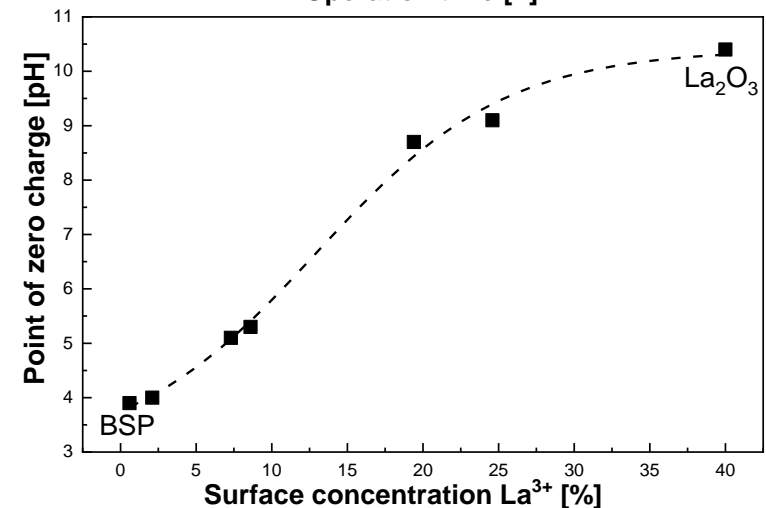
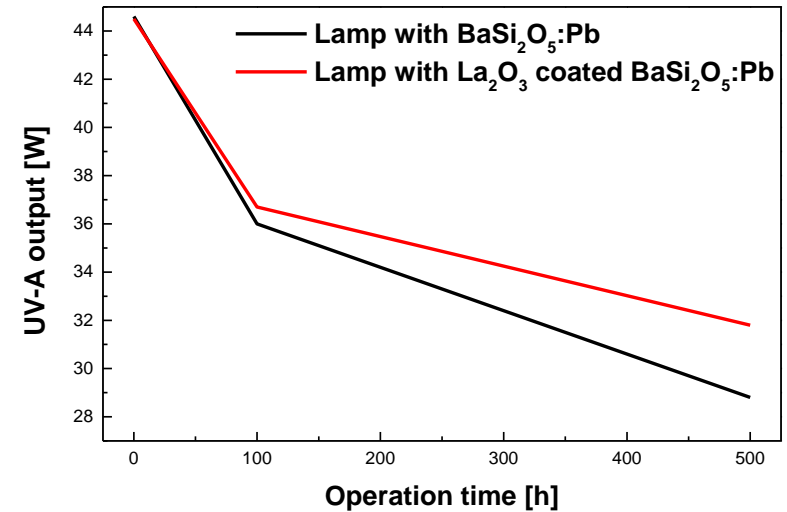
BSP has a low PZC and thus shows fast Hg^+ take-up in fluorescent lamps, which results in strong light output decrease

Solution

Coating by a high PZC material as e.g. La_2O_3 or Al_2O_3

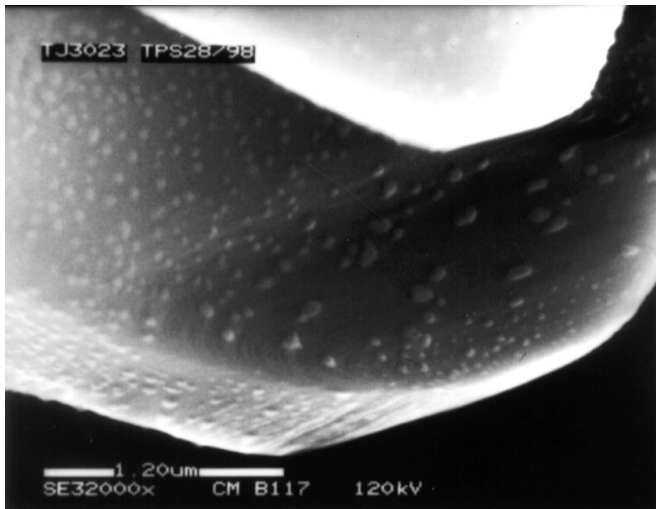
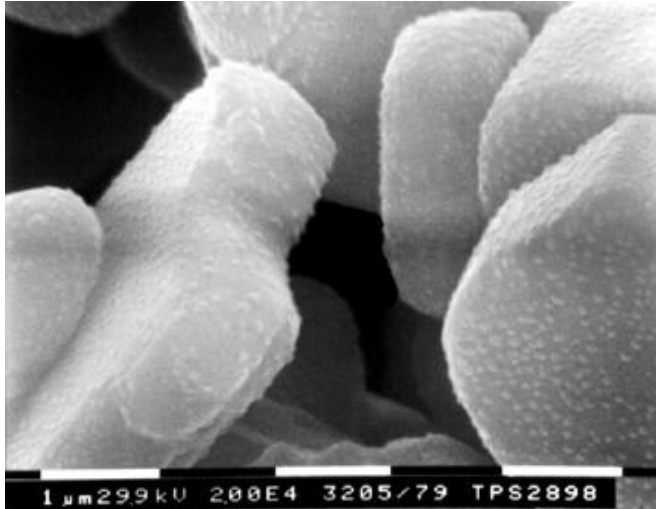
Coating process

- Neutral to alkaline suspension pH 7 - 10
- Stabilisation of La^{3+} required, e.g. by complexation with EDTA

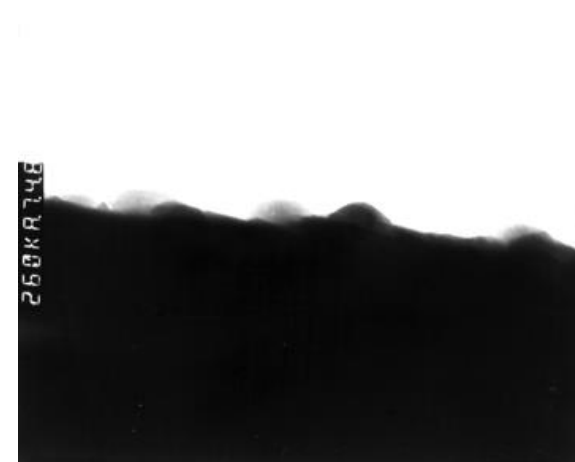


3.2 Functional Coatings and Layers

SEM images



TEM images



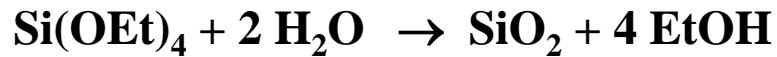
3.2 Functional Coatings and Layers

Protective SiO₂ coating on (Ca,Sr)S:Eu “Red LED phosphor”

Application problem

- (Ca,Sr)S:Eu is highly sensitive towards H₂O and CO₂
- (Ca,Sr)S:Eu is highly refractive (n > 2.0)

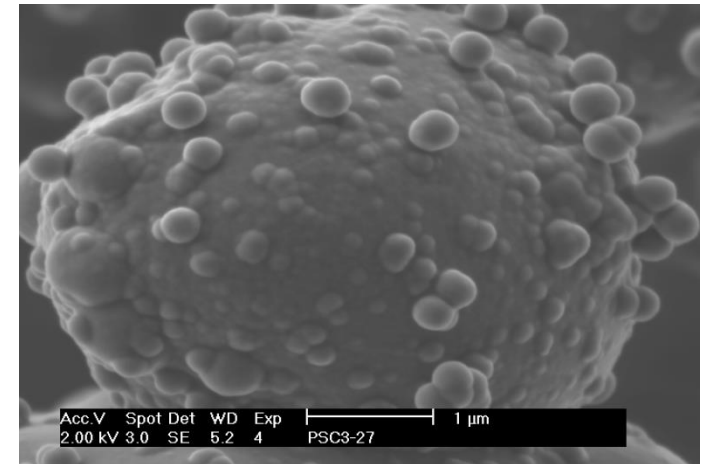
Coating process



“Hydrolysis of TEOS in EtOH”

SiO₂ coated (Ca,Sr)S:Eu

- Coating reduces diffusion of H₂O and CO₂ to the particle surface
- Coating is nano structured which results in refractive index gradient layer (anti-reflective surface)

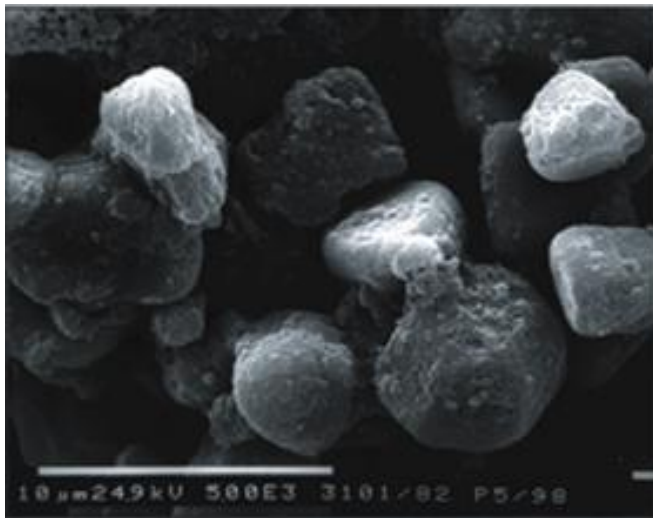


„Moth eye coating“

3.2 Functional Coatings and Layers

Pigmentation of ZnS:Ag by CoAl_2O_4

- Co-precipitation of Co^{2+} and Al^{3+} by Hydrolysis of $\text{Co}(\text{CH}_3\text{COO})_2$ und $\text{Al}(\text{CH}_3\text{COO})_3$ in aqueous solution:
$$\text{Co}^{2+} + \text{Al}^{3+} + 5 \text{OH}^- \rightarrow \text{Co}(\text{OH})_2 + \text{Al}(\text{OH})_3$$
- Sintering: Hydroxides $\rightarrow \text{CoAl}_2\text{O}_4$

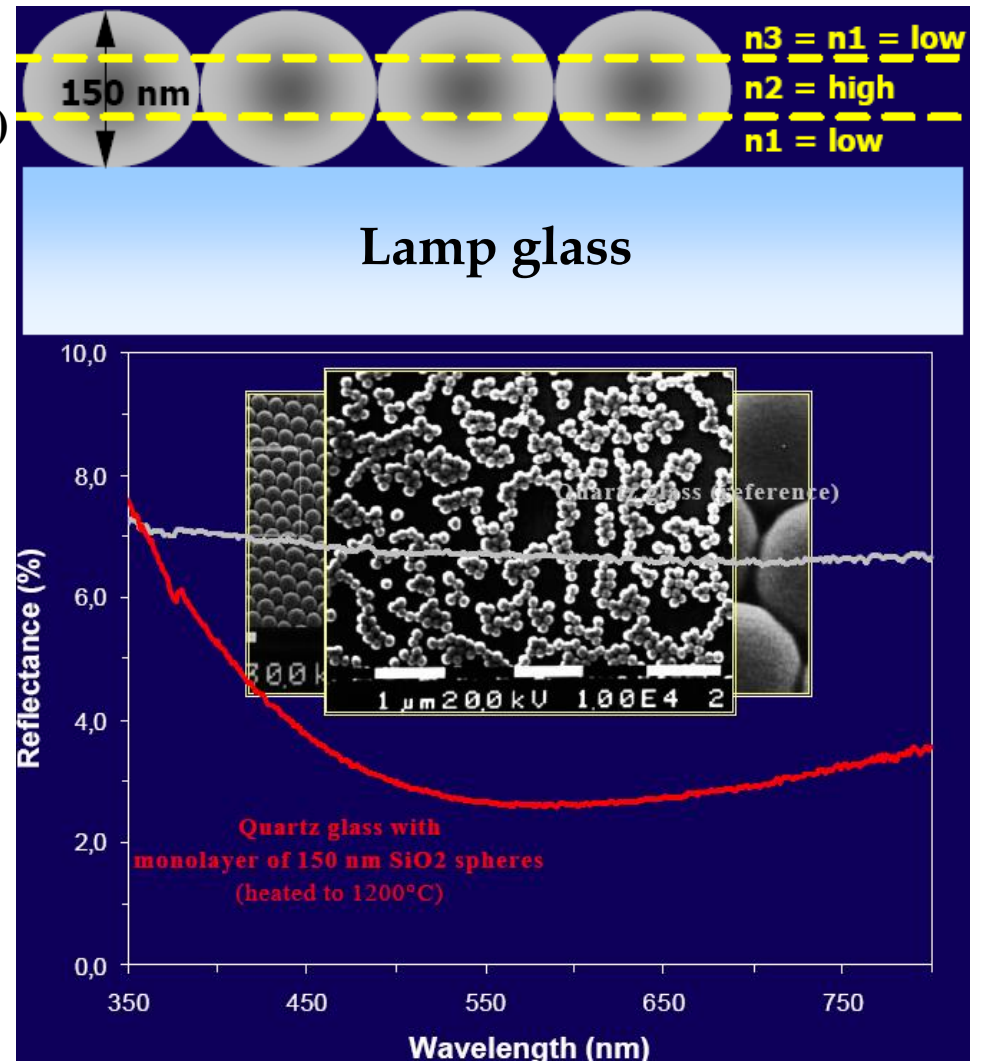


3.2 Functional Coatings and Layers

Interference layers

⇒ Anti-reflective coatings (light outcoupling)

- stacks of layers (high and low index of refraction)
- monolayer of monodisperse spherical particles

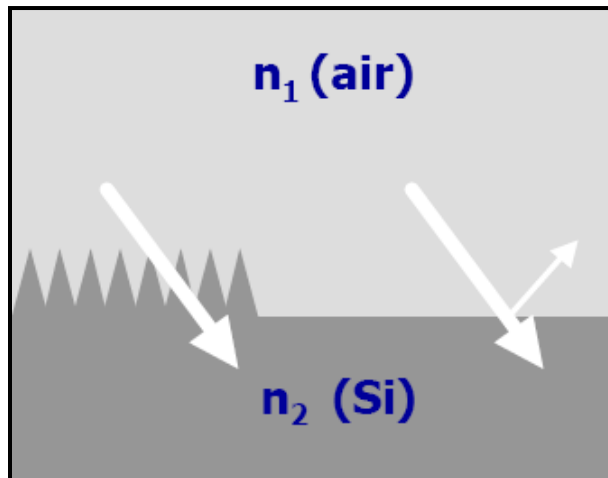


3.2 Functional Coatings and Layers

Interference layers

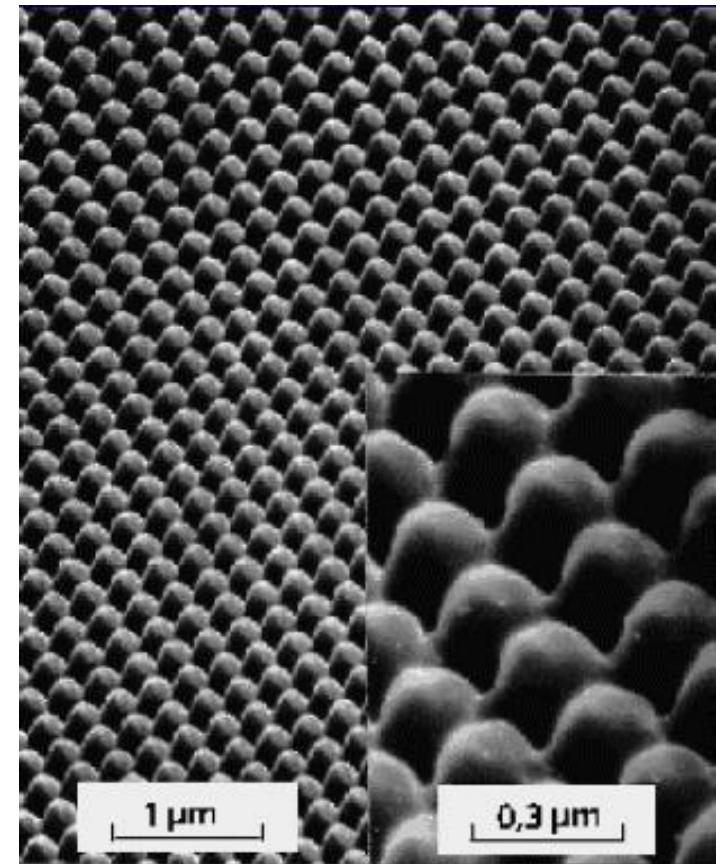
⇒ Moth eye coatings (light incoupling)

Solar cells with enhanced efficiency



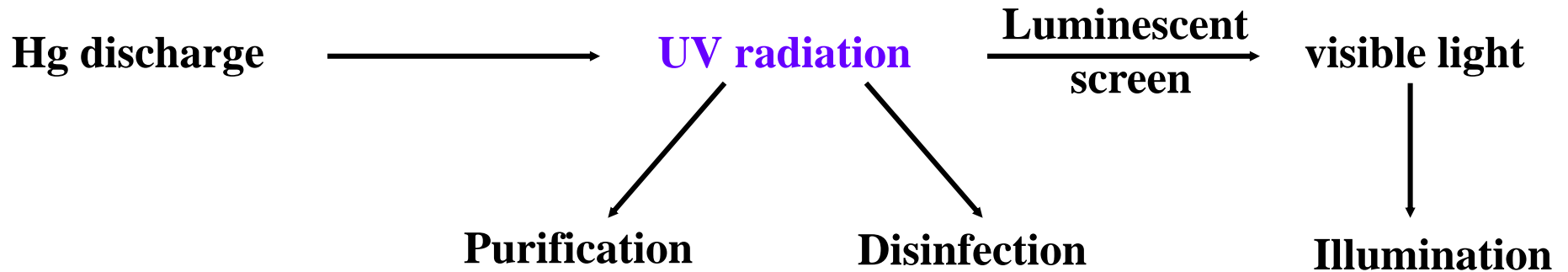
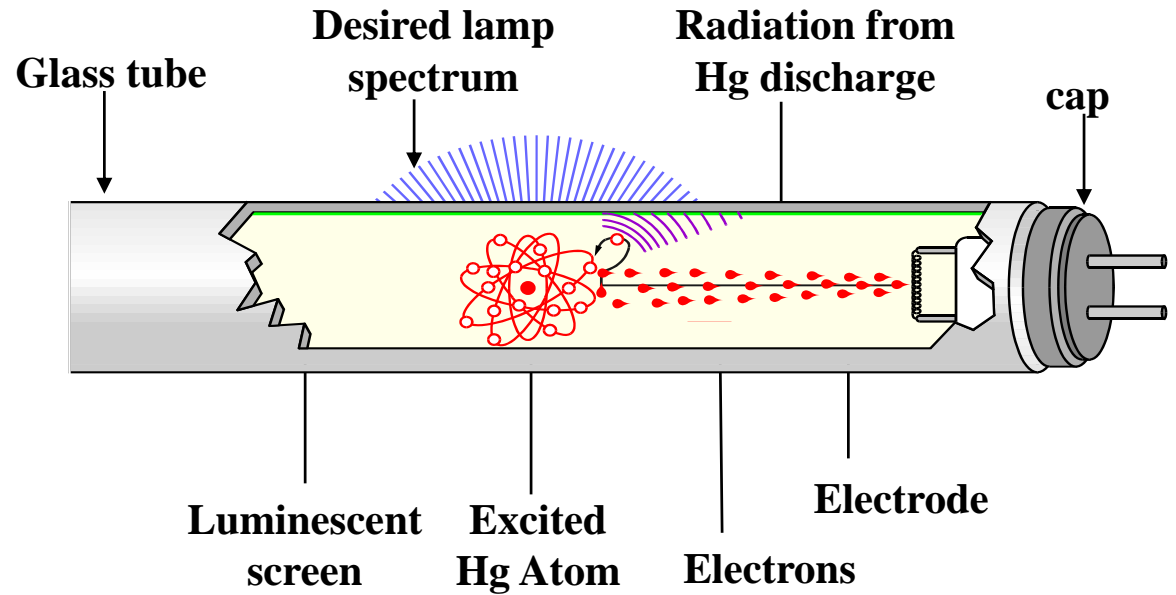
Porous refractive gradient layer
Periodic surface structure

Fraunhofer Institute Freiburg



3.2 Functional Coatings and Layers

Luminescent screen in fluorescent lamps



3.2 Functional Coatings and Layers

Nanoparticle filler (5 – 50 nm Al_2O_3 or $\text{Ca}_2\text{P}_2\text{O}_7$)

Effect of alon-c filler

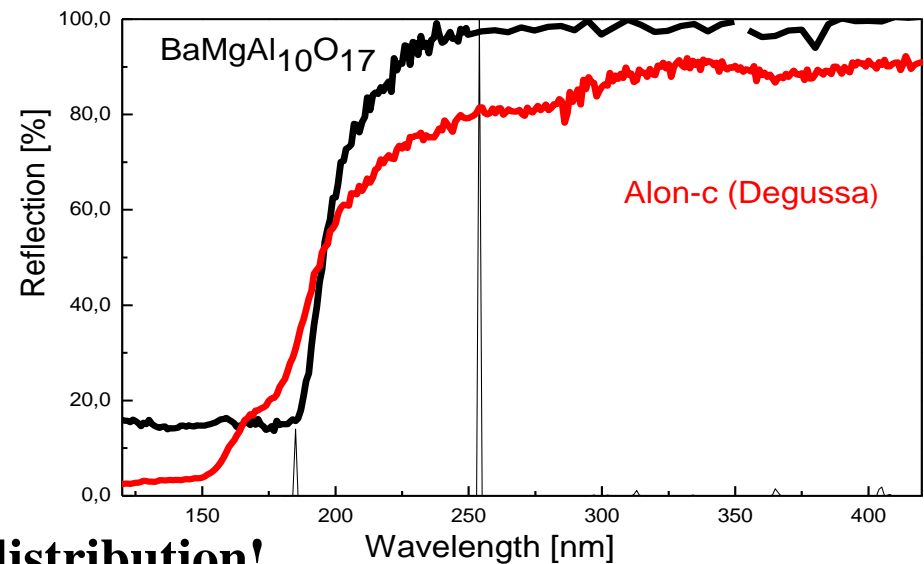
- Improves adhesion
- Improves lamp lifetime (reduces Hg take-up)
- Reduces initial light output
due to absorption of 185 and 254 nm line

Alternative wide band gap materials

- Y_2O_3
- MgO
- AlPO_4
- MgAl_2O_4
- $\text{AEMgAl}_{10}\text{O}_{17}$ (AE = Ca, Sr, Ba)

Scattering power depends on particle size distribution!

Reflection spectra

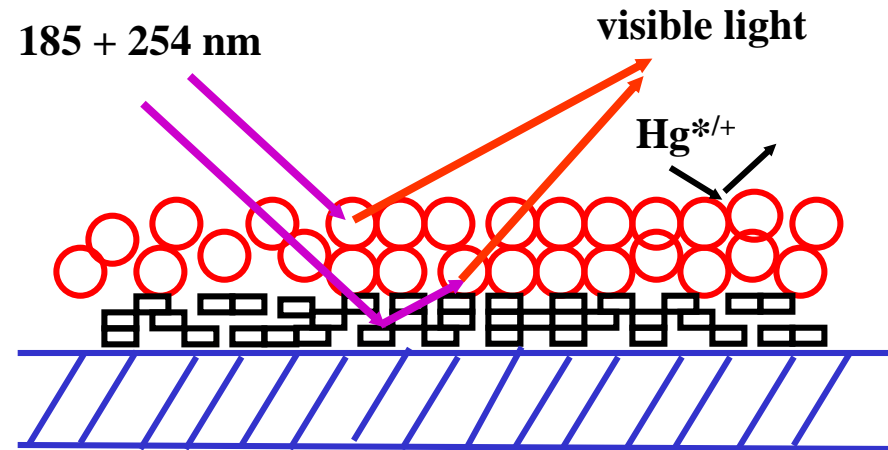


3.2 Functional Coatings and Layers

Precoating layers (20 - 50 nm Al_2O_3 or Y_2O_3)

Schematic build-up of a luminescent screen in fluorescent lamps

1. Luminescent material + filler
2. Precoating
3. Glass substrate



Functions of pre-coating layer

- Protection of glass from Hg discharge
- Backscattering of transmitted UV photons

GE, US: “Star coating”

Today: Nanoparticles of Al_2O_3 (alon-c)

3.3 MR Contrast Enhancement and Hyperthermia

Improvement of diagnostic methods, e.g. ^1H NMR (tomography)

Physics

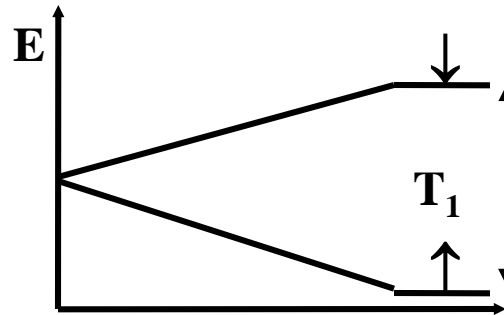
Protons ($^1\text{H}^+$) have a spin

$\Rightarrow I = 1/2$

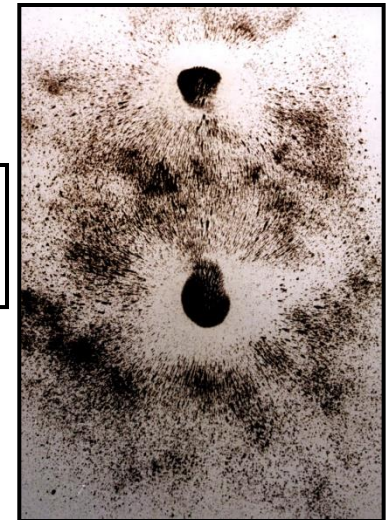
$\Rightarrow m_I = +1/2$ and $m_I = -1/2$

\Rightarrow energy separation ΔE by a magnetic field B

\Rightarrow monitored are T_1 spin-lattice relaxation rates



$$\Delta E = h\nu = \gamma \frac{h}{2\pi} B_0$$



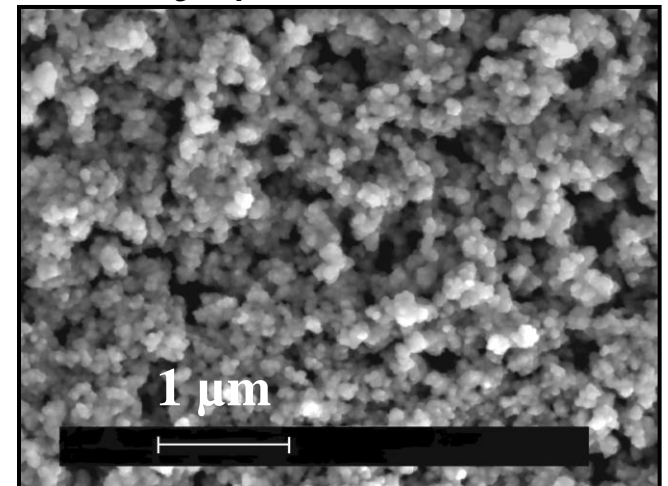
Requirements on materials for MR contrast enhancement

- “Single-domain” magnetic nano particles, e.g. $\gamma\text{-Fe}_2\text{O}_3$, Fe_3O_4 , Fe , CrO_2
- Paramagnetic compounds, e.g. Gd-complexes or Gd^{3+} in nano vesicles
- $\text{\O} \sim 10$ nm, spherical morphology

Diagnostic advantages

- Higher image resolution
- Little impact by external magnetic fields
- Coupling of imaging with therapy

Fe_3O_4 Nanoparticles



3.3 MR Contrast Enhancement and Hyperthermia

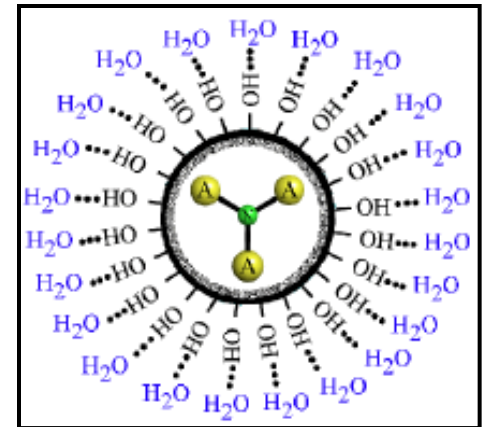
Improvement of diagnostic methods, e.g. ^1H NMR (tomography)

Physics: Gd^{3+} comprising MR contrast enhancement pharmaceuticals

Association of Gd^{3+} ($[\text{Xe}]4f^7$ $S = 7/2$) cations to the the ^1H nuclei (H_2O) results in accelerated relaxation of protons due to magnetic interaction

Approaches

- a) Application of Gd^{3+} complexes with coordination sites accessible towards H_2O molecules, e.g. $[\text{Gd}(\text{DTPA})]$
- b) Application of Gd^{3+} comprising vesicles, e.g. $\text{Gd}_2\text{HoN}@C_{80}(\text{OH})_n$ (Shinohara et al. have reported a significant increase (>20) in the ^1H MR T_1 spin-lattice relaxation rate)



3.3 MR Contrast Enhancement and Hyperthermia

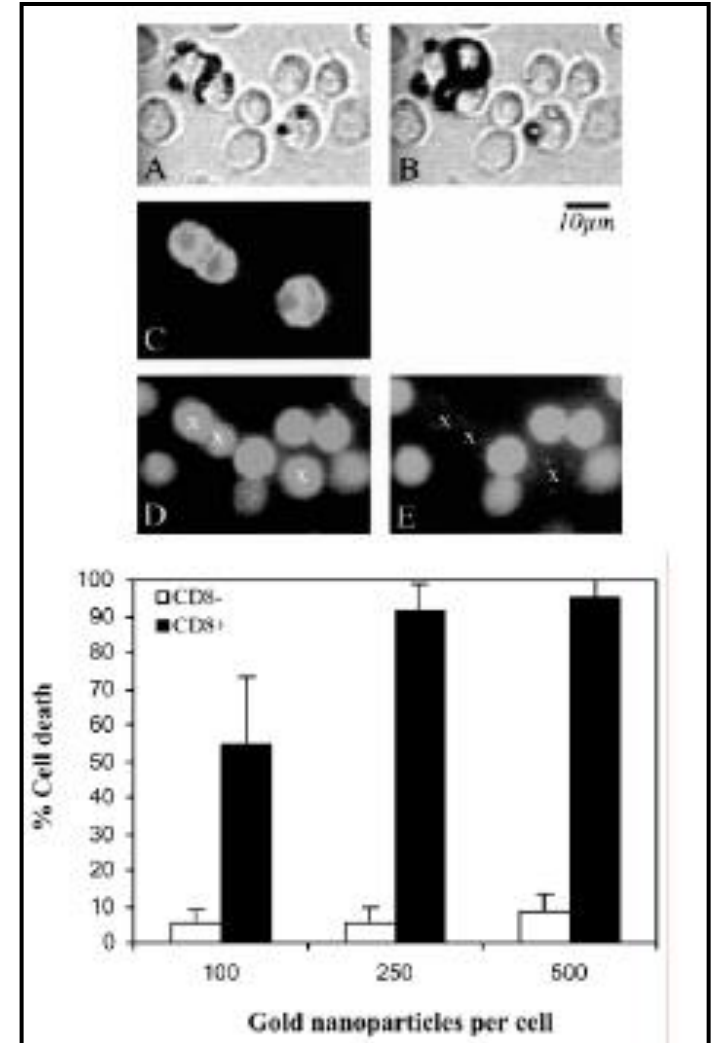
Hyperthermia - Thermal cancer therapy

Idea

Cancer cell death induced by strong magnetic AC field or LASER irradiation

Method

- Surface modification of magnetic nanoparticles (Fe_2O_3 , FePt, or Au) to achieve selective up-take into cancer cells (antigen-antibody approach)
- Inject into blood or cancer tissue
- Apply AC field (oscillation) or LASER radiation (absorption) to heat up cancer cells
- Cell death for $T > 44\text{ }^\circ\text{C}$



3.4 Medical Therapy

Drug delivery

Motivation

- a) **A major problem in pharmaceutical research is the formulation of the active ingredients. Substances have to be transported to the target cells (and only there) and release or activate the drug there in the desired concentration over time.**
Nanoparticle can function as a protective shell to prevent the immune system to destroy the drug, function as an envelope to ensure the correct delivery to the target cells or act as an ingredient deposit.
- b) **Nanoparticles and nanocrystalline materials are already commercialized as antimicrobial and antifungal agents. The health care industry needs for improved protection against bacteria in the face of growing antibiotic resistance.**

Some examples

- **Radiation therapy**
- **Photodynamic therapy**
- **Ag has antibiotic properties and is being used to made into crystalline nanoparticles, which increase solubility and potency**

3.4 Medical Therapy

Radiative cancer therapy

1. Irradiation by x-rays

- Application of keV to few MeV radiation
- Problems:
 - Low cross-section of absorbing material requires relatively high dose
 - No healthy/diseased tissue contrast

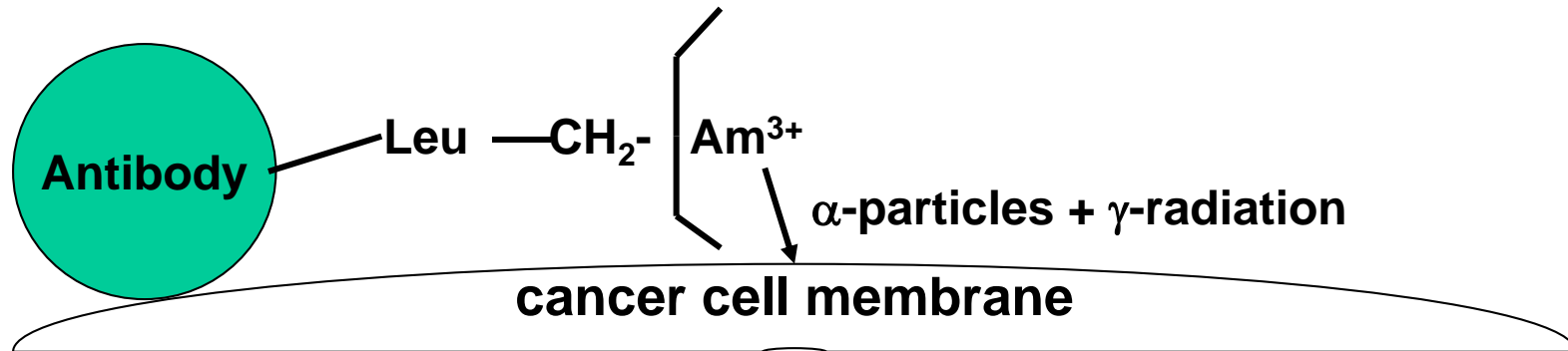
2. Application of radionuclides

- $^{212}\text{Bi} \rightarrow \alpha + ^{208}\text{Tl}$ (half life ~ 1 h, 13.3 h for ^{123}I , 7 h for ^{212}At)
- To achieve high specificity to cancer cells, the radionuclide cations are chelated by organic moieties, e.g. edta, which is conjugated to an antibody with high specificity to cancer cells
- Problems:
 - Toxicity of the agents
 - Short half-life of useful radionuclides

3.4 Medical Therapy

Radiative cancer therapy

Radiation therapy by application of radionuclides



Coupling towards nanoparticle occurs e.g. by the application of the biotine-avidine system

References

- Photogen Inc., US 6331286
- Light Sciences Limited Partnership, WO 99/52565

3.4 Medical Therapy

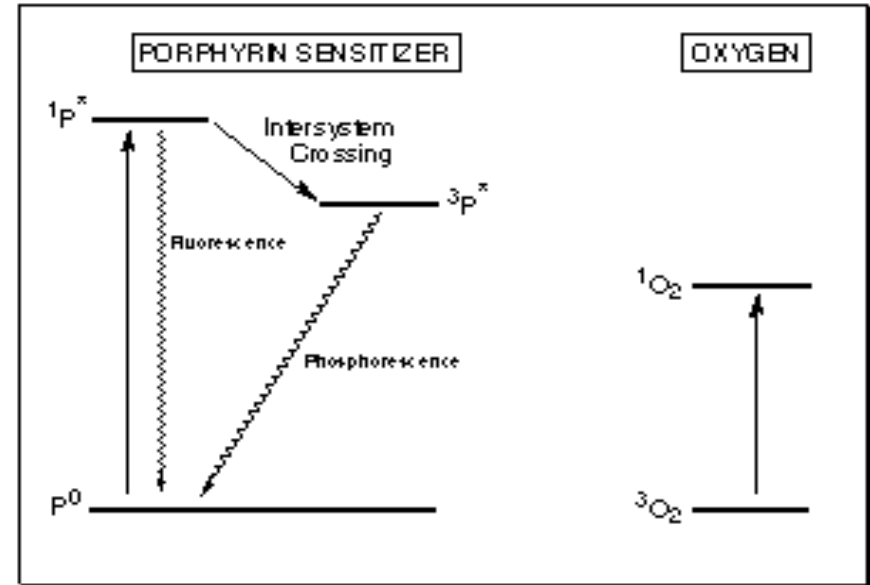
Photodynamic cancer therapy

Principle

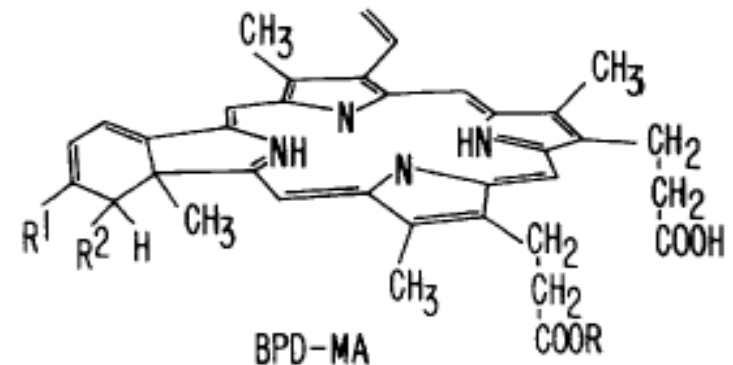
- Administration of a photosensitive drug to an affected area (e.g. cancer tissue)
- Subsequent irradiation with light
- Light sources (50 mW/cm², 600 – 800 nm)
 - LASER
 - AlInGaP LEDs
 - Low-pressure discharge lamps

Application areas

- Skin cancer treatment: Basal cell cancer, melanoma
- Blood cancer treatment: Leukemia
- Rheumatoid arthritis
- Bio stimulation: Wound healing
- Cosmetic skin treatment: Stain removal



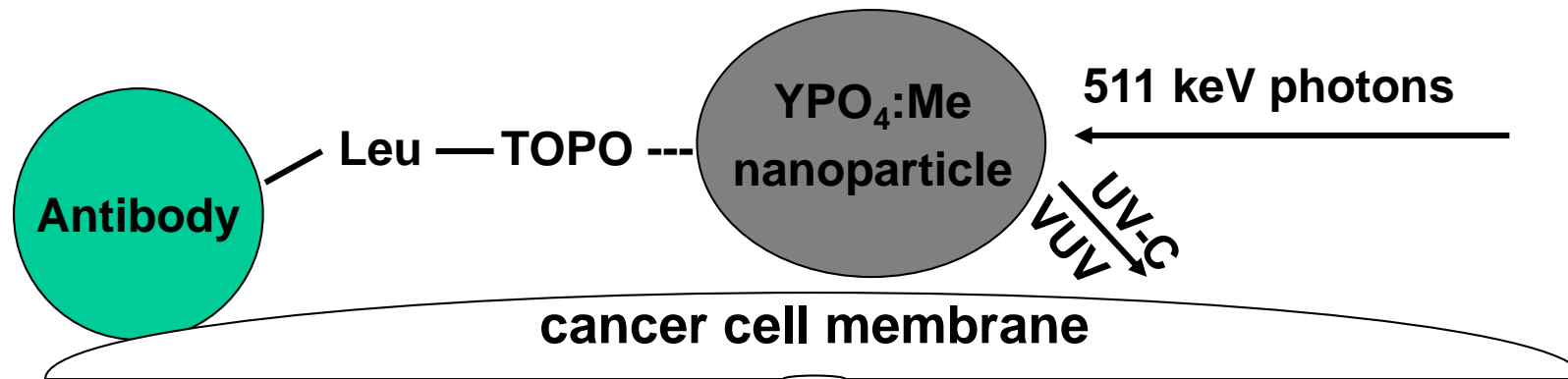
Structure of a porphyrin sensitizer



3.4 Medical Therapy

Photodynamic cancer therapy

Idea: Application of UV-C or VUV emitting nanoscale materials



Excitation of the nanoscale material

- Internally: Doping with a (positron emitting) radionuclide
- Externally: Irradiation by x-rays, e.g. 511 keV (large contrast!)

Reference

Philips, EP 03047566

3.4 Medical Therapy

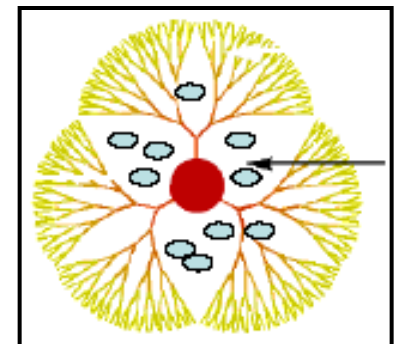
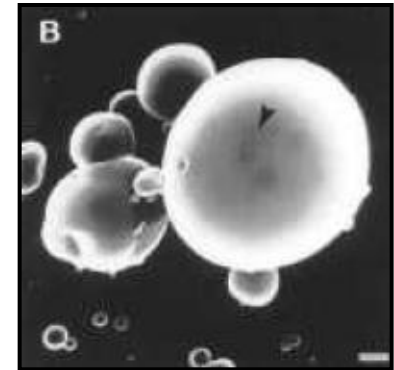
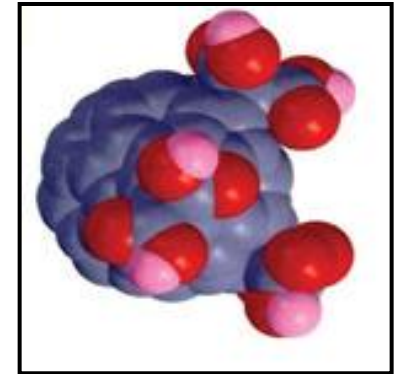
Site selective delivery of pharmaceuticals

Vehicles

- C_{60} or C_{70} surface modified by antigen moieties
- Polymeric nanoparticles, e.g. as delivery system for influenza virus glyco proteins
(Source: http://www.md.ucl.ac.be/pharma/pub_farm_stat.htm)
- Dendrimer conjugates

Controlled release of pharmaceuticals by

- “Biochemistry”
- Heat
- Radiation

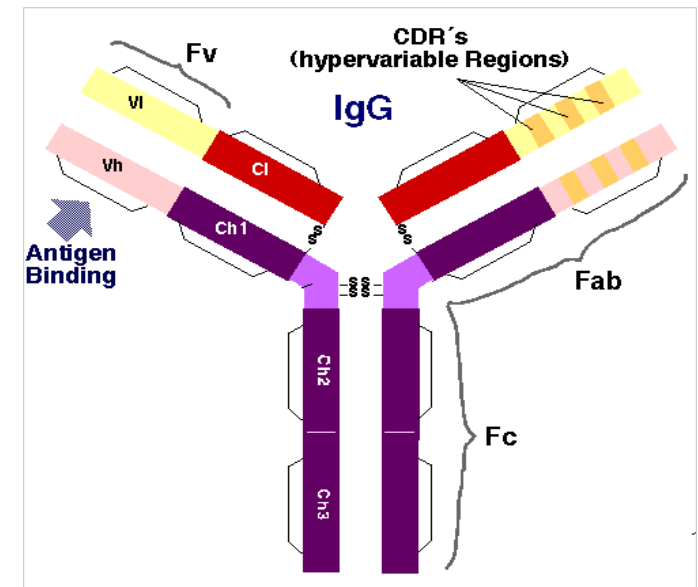
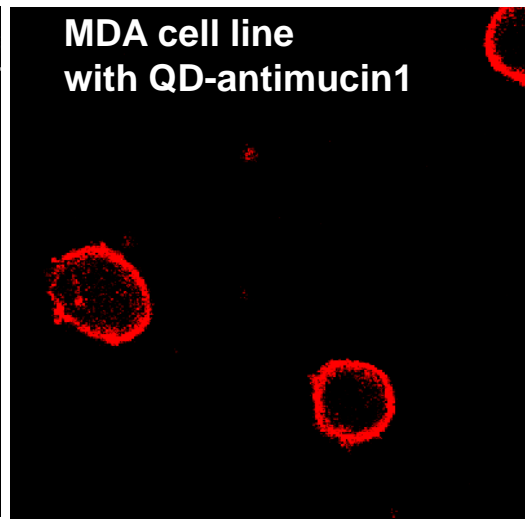
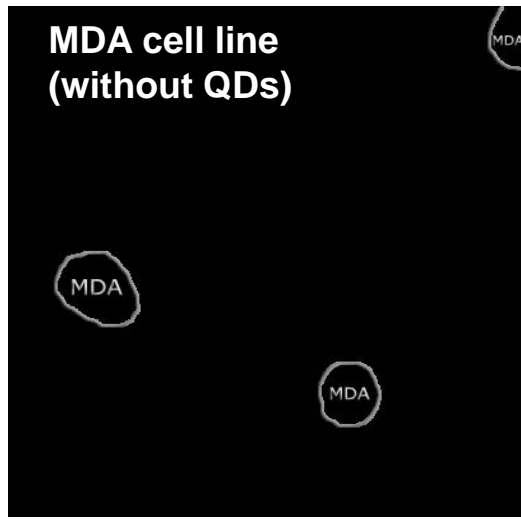
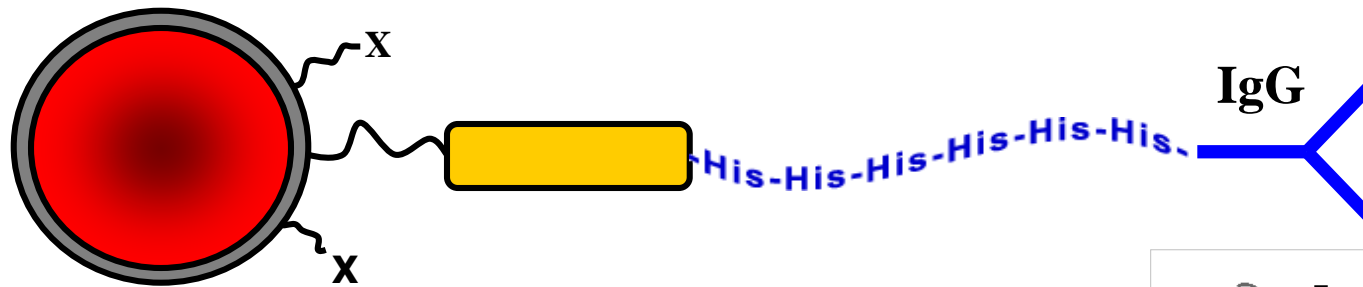


3.5 Optical Imaging

Principle of the application of nanoscale particles for contrast enhancement

Core-shell nanoscale particles, e.g. CdS coated by ZnS, are modified by bio molecules

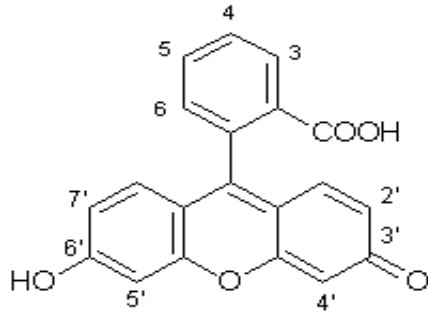
⇒ antigen-antibody reaction



3.5 Optical Imaging

Applied materials for optical contrast enhancement

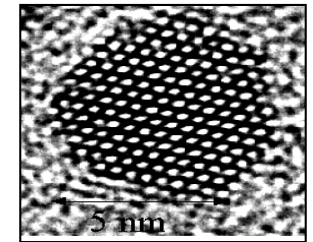
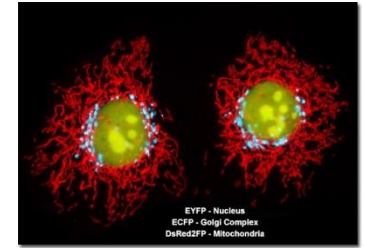
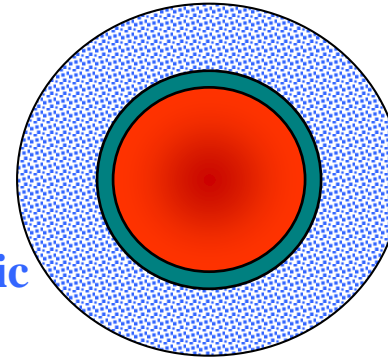
Fluorescent dyes



Organic fluorophores, e.g. Fluoresceine

Quantum dots

Core
Shell
Hydrophilic Coating



TEM image of an inorganic Quantum Dot

Properties

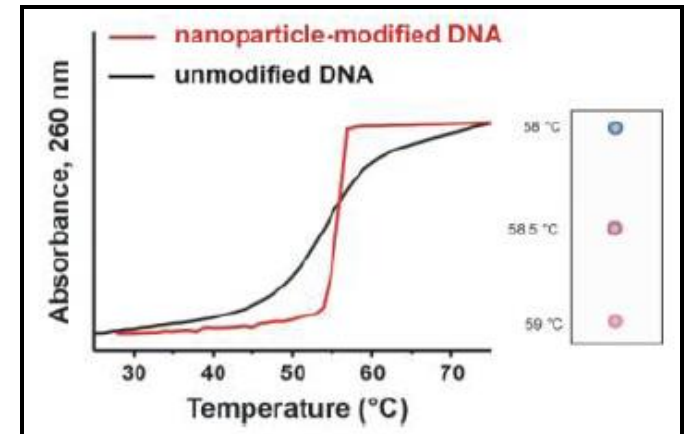
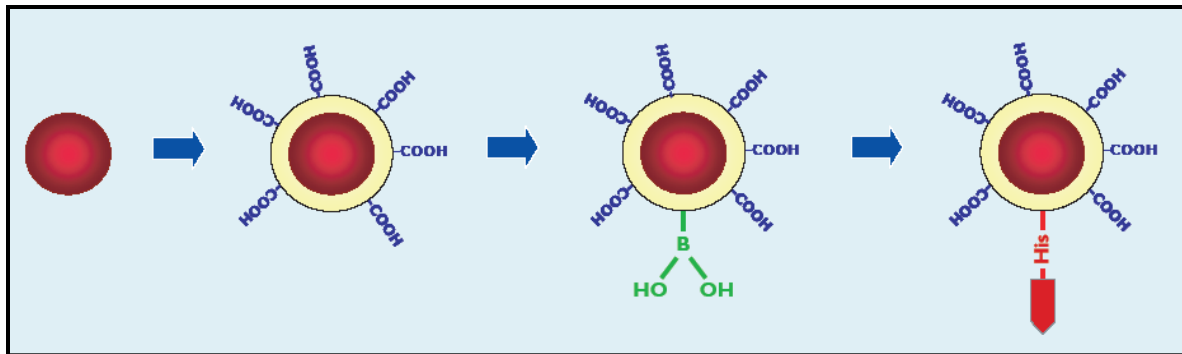
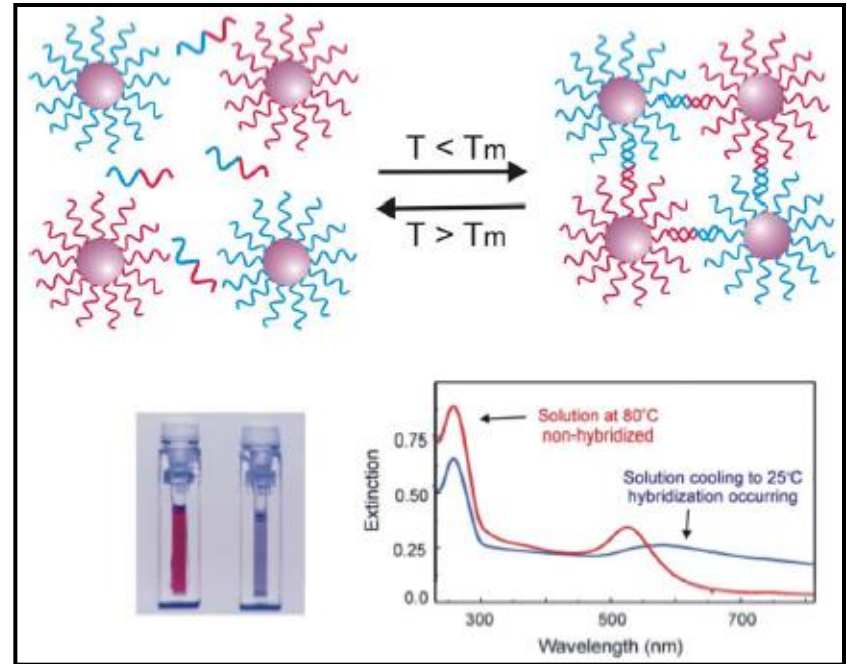
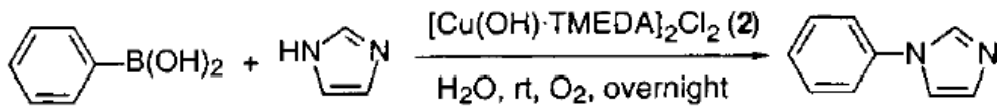
Broadband excitation	+	+
Narrow band emission	-	+
Multicolor	+	+
Photochemical stability	-	+
Thermal stability	-	+

3.5 Optical Imaging

Bioconjugation

a) Assembly of DNA-modified quantum dots by DNA hybridization results in color change

b) Linkage to proteins, e.g. via histidin (His)
Chemical reaction between boron acid and imidazol:

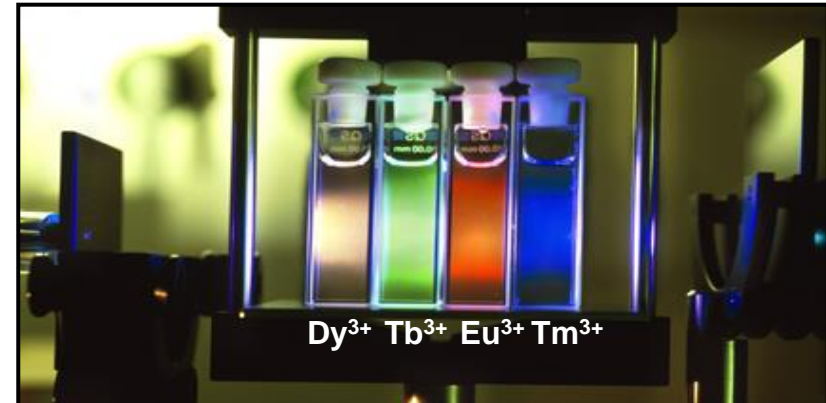


3.5 Optical Imaging

Nanoscale rare earth ortho-phosphates

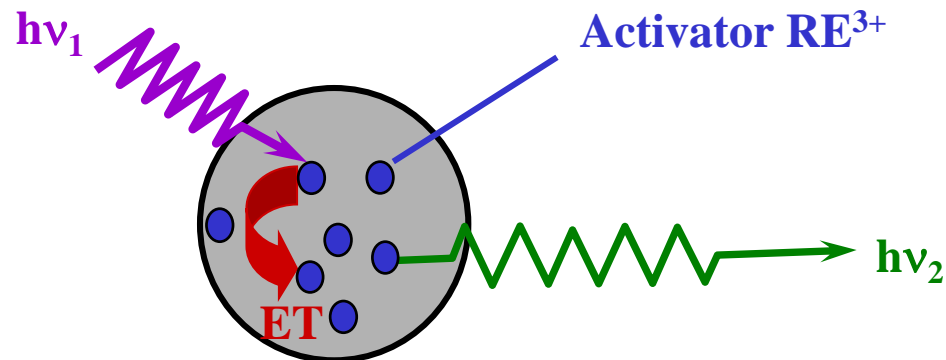
Advantages

- narrow band emission
- many different colors
- up conversion
- high photo stability
- high chemical stability
- small size (1 – 10 nm)
- non or minor toxicity expected



Colloidal solutions of (Y,Gd)PO₄:RE
upon UV-A excitation

Working principle



3.5 Optical Imaging

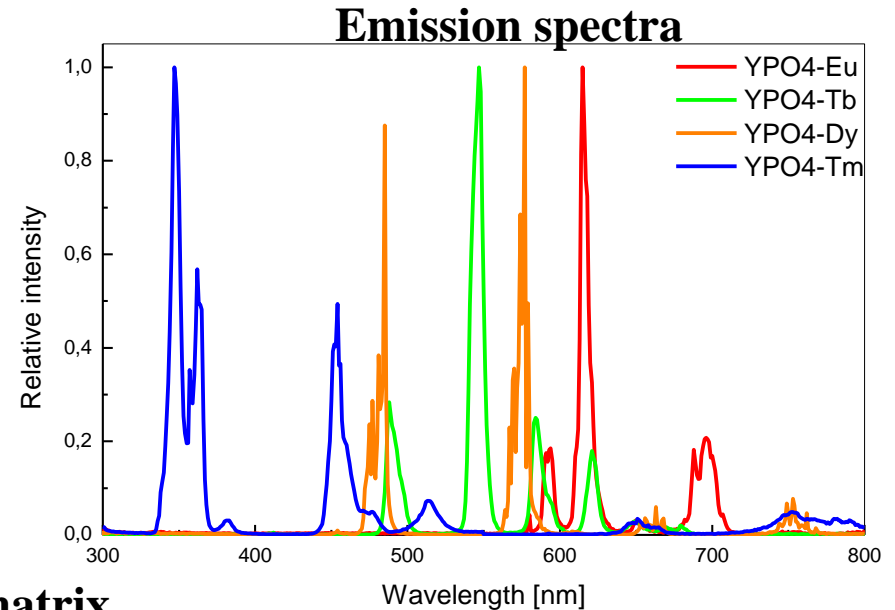
Nanoscale rare earth ortho-phosphates

Optical properties

- **Line emitters**
- **Emission spectra are independent of particle size**
- **Several emission lines can be combined e.g. Tb^{3+} with Eu^{3+}**
- **Slow decay (1 – 10 ms), i.e. easy discrimination from fluorescence of organic matrix**

Chemical properties

- **High photo stability**
- **Low solubility product: $K_L = c(Ln^{3+}) * c(PO_4^{3-}) \sim 10^{-30} \text{ mol}^2/l^2$**
- **Particle size (1 - 10 nm) comparable to organic dyes**
- **Buffer effect: $PO_4^{3-} \rightarrow HPO_4^{2-} \rightarrow H_2PO_4^-$**



3.5 Optical Imaging

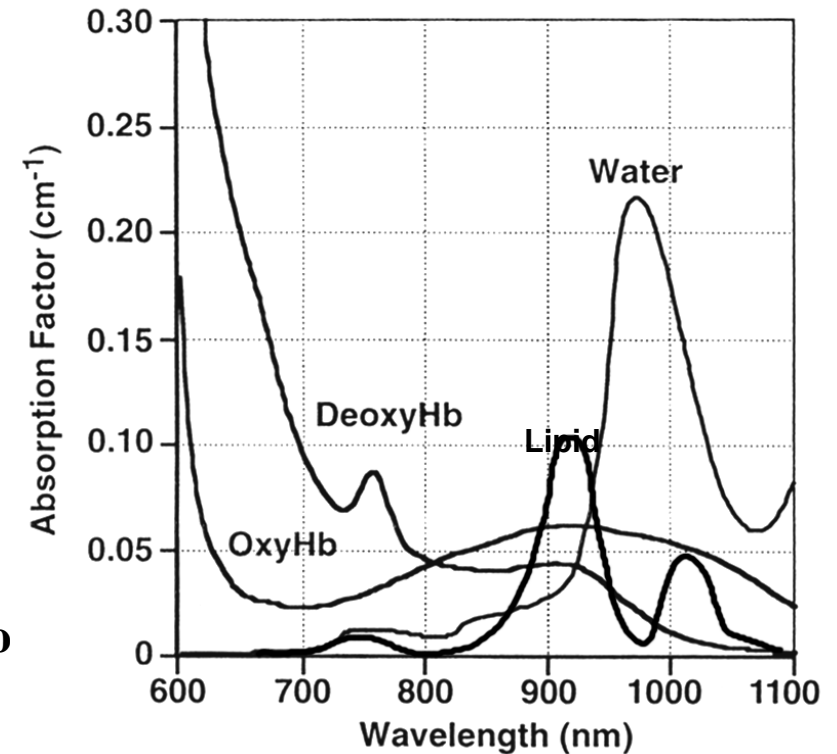
Nanoscale rare earth ortho-phosphates

Optical imaging in-vivo

- Excitation and emission in the IR-A range (700 – 900 nm)
- Pr^{3+} , Nd^{3+} , Yb^{3+} , (Eu^{3+}), Cr^{3+} , Fe^{3+}

Applications

- Visualization of nano structures in cells
⇒ ion channels, ribosome, ...
- OMR: Simultaneous optical and magnetic diagno
⇒ Gd^{3+} doped nano scale particles



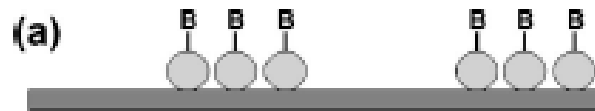
NIR Window

From Chance, Ann N Y Acad Sci, 1998. 838: 29-45, with the addition of lipid data from Conway et al., Am J Clin Nutr, 1984. 40: 1123-30, scaled appropriately

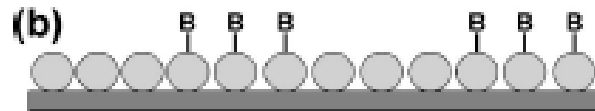
3.5 Optical Imaging

In-vitro optical imaging on chips

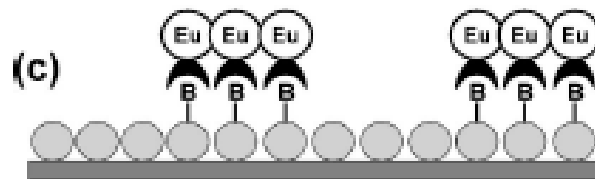
Application: Visualization of protein (BSA)-micro structures (BSA = blood serum albumin)






Coating of a Si wafer by biotin(B)-BSA

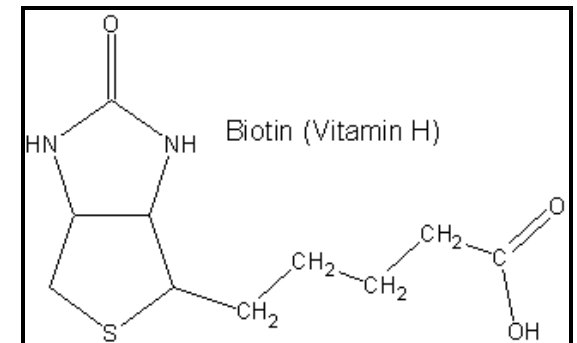


Blocking of free Si-"Sites" by BSA



Hybridisation with avidin labeled nano scale particles, e.g. $Gd_2O_3:Eu$

-  - printed BSA-Biotin
-  - blocking BSA
-  - avidin labeled with $Eu:Gd_2O_3$



3.6 Biosensors and -assays

Definition

Biosensor

A device that uses specific biochemical reactions mediated by isolated enzymes, immunosystems, tissues, organelles or whole cells to detect chemical compounds, usually by electrical, thermal or optical signals.

Bioassay

A bioassay is a procedure for determining the concentration, purity, or biological activity of a substance by measuring the biological response that it produces compared to a standard

- Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA)
- Hormones (steroids)
- Proteins (polypeptides)
- Immune globulins IgG, IgM, IgA, IgD, IgE ⇒ immunoassays (antibody-antigen reaction)

Determination of

- a single analyt ⇒ Single analyt assays
- several analyts ⇒ Multi analyt assays

3.6 Biosensors and -assays

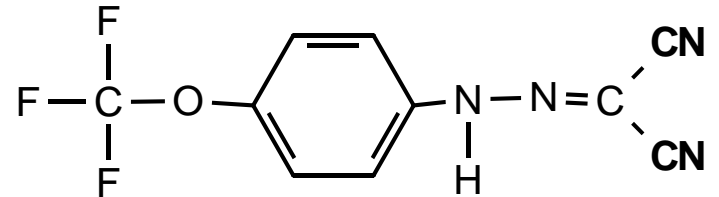
Application areas

Biosensors

- Glucose in blood
- Cancer markers in blood
- Penicillin in fungi bioreactors
- Urea in urine

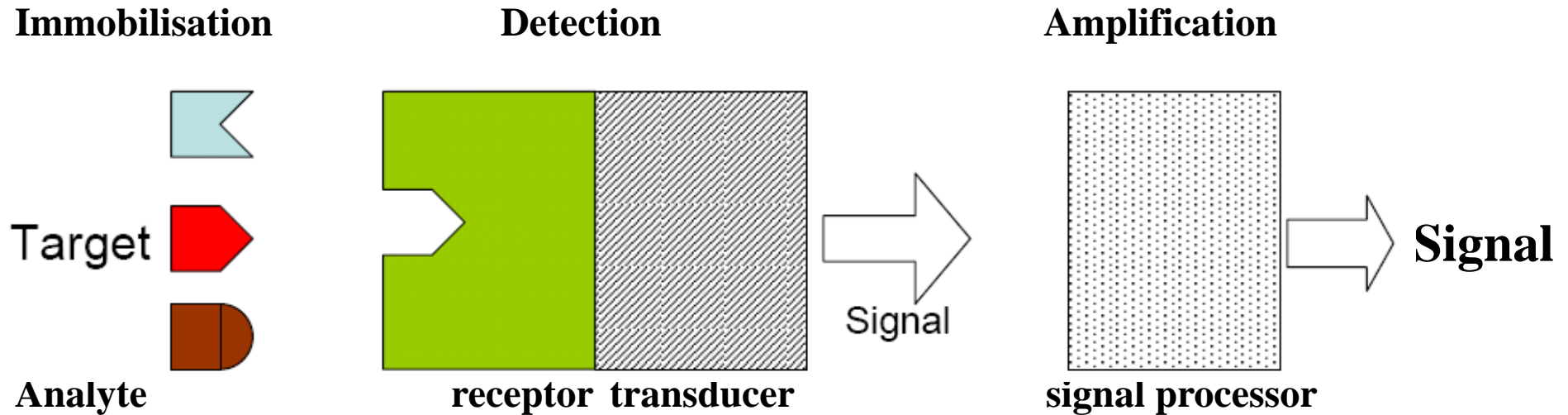
Environmental sensors

- Detection of gaseous molecules
 - NO
 - CO
 - ethylene (plant stress signal)
 - cis-3-hexen-ol (plant odorous substance)
 - α -pyrene, 3-carene, 2-methoxyphenol (early fire detection by electro antennographic detector (antenna of the jewel beetle))
- Detection of poisonous substances in soil
 - 2,4-Dinitrophenol
 - Pentachlorophenol
 - FCCP →



3.6 Biosensors and -assays

Principle of operation



Analyte

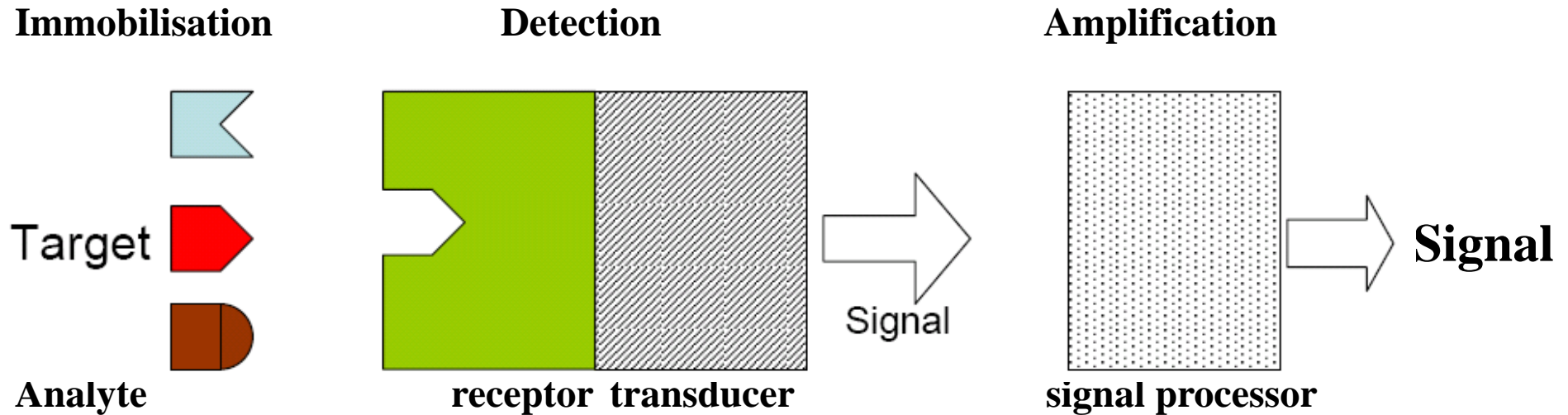
- The substances to be measured
- **Small molecules:** Sugars, urea, cholesterol, glutamic acid, phosphate, ..
- **Macro molecules:** Nucleic acids (DNA, RNA), poly peptides (protein, antibody, enzyme)

Receptor

- A sensing element that responds to the substances being measured
- The interaction must be highly selective \Rightarrow Enzyme, Antibody, Nucleic acids, Cells

3.6 Biosensors and -assays

Principle of operation



Transducer

A device that converts the physical or chemical changes due to analyte receptor reaction to another form of physical signal (in general, electronic signals) whose magnitude is proportional to the amount of the analyte

Electrochemical detection Potentiometric, Voltammetric, Conductimetric

Optical detection Fluorescence, Absorbance, Light scattering, Refractive index

Electrical detection Field effect transistor (FET)

Mechanical, Thermal, Piezoelectric, Surface acoustic waves, Magnetical,

3.6 Biosensors and -assays

Performance factors

Sensitivity

- **Minimum amount of analyte that are able to be detected above the background**
- **Units: Concentration, number of analyte, density, weight**

Specificity/Selectivity

- **The ability to discriminate between substrates. This is function of biological component, principle, although sometimes the operation of the transducer contributes to selectivity**
- **Molecular recognition**
- **Separation scheme**
- **Signal overlap**

Speed/Response Time

- **Sample preparation + Biological/Chemical reaction + Signal Processing**
- **Bench process : hours to weeks**
- **Chip process: minutes to hours**
- **Ultra-high temporal resolution, 10 ns, for real-time measurement of molecular kinetics**

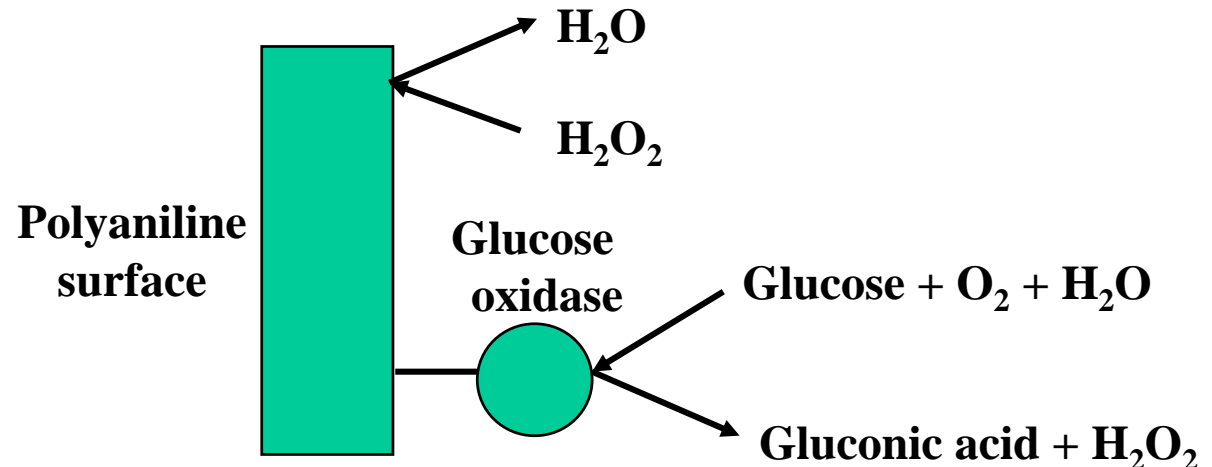
Moreover: Accuracy, Simplicity, Cost, Lift time, ...

3.6 Biosensors and -assays

Examples

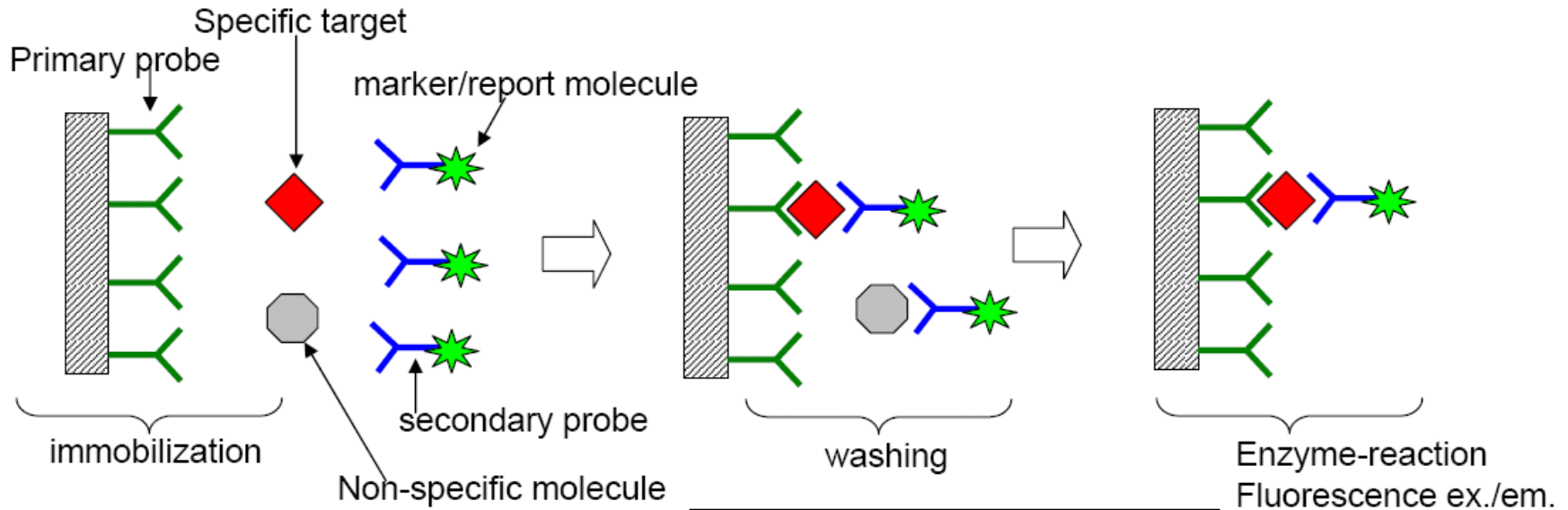
Conversion of bio molecules by an enzyme bound to a surface (e.g. polyaniline)

<u>Enzyme</u>	<u>Reaction</u>
GOD	glucose + O ₂ → gluconic acid + H ₂ O ₂
Urease	(NH ₂) ₂ CO + H ₂ O → 2 NH ₃ + CO ₂
Catalase	H ₂ O ₂ → H ₂ O + O ₂
Trypsin	polypeptide → amino acids
Amylase	starch → glucose
Uricase	uric acid + H ₂ O → NH ₃ + CO ₂



3.6 Biosensors and -assays

Biosensing of macromolecules



Steps

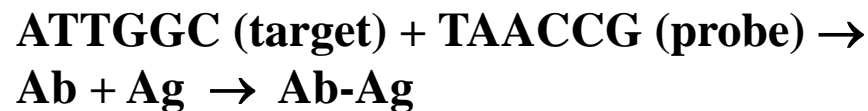
- (1) Immobilization of primary probes
- (2) Mixing/incubation of the mixtures
- (3) Washing the non-specific bindings
- (4) Signal transduction

Markers/Report molecules

- (1) Enzymes
- (2) Fluorescence tags
nanoparticles
fluorescent dyes
- (3) Radioactive tags

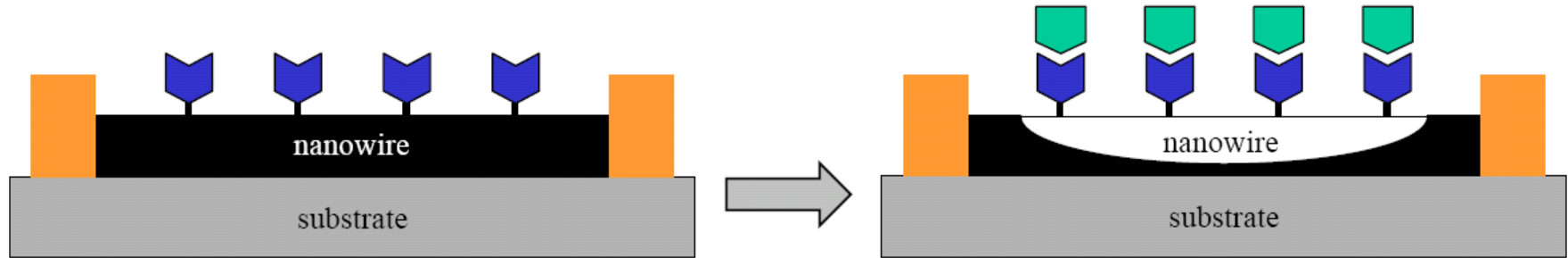
Molecular recognition

- (1) Watson-Crick base pairing
- (2) Antibody-antigen binding



3.6 Biosensors and -assays

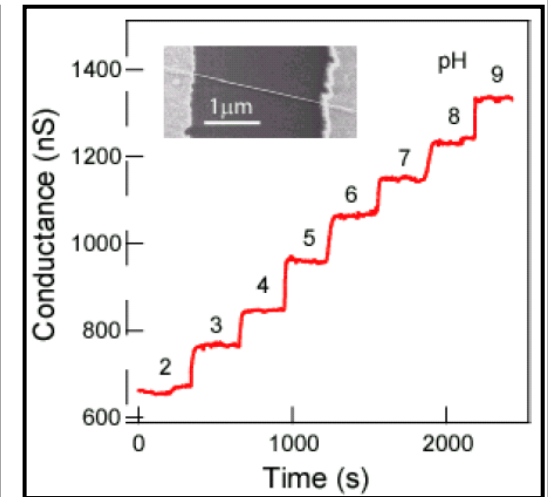
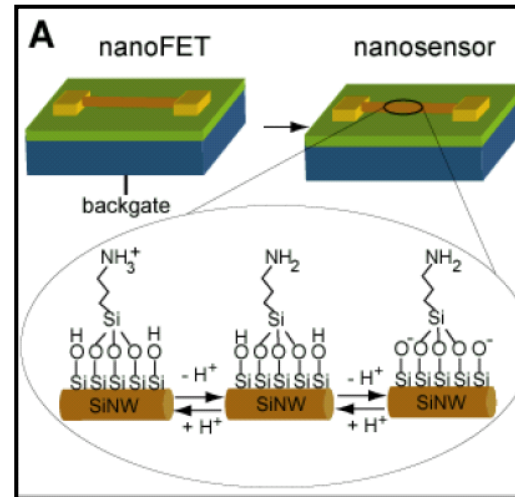
Nanowire nanosensor



Binding of chemical or biological species to the surface of a nanowire will result in depletion or accumulation of carriers.

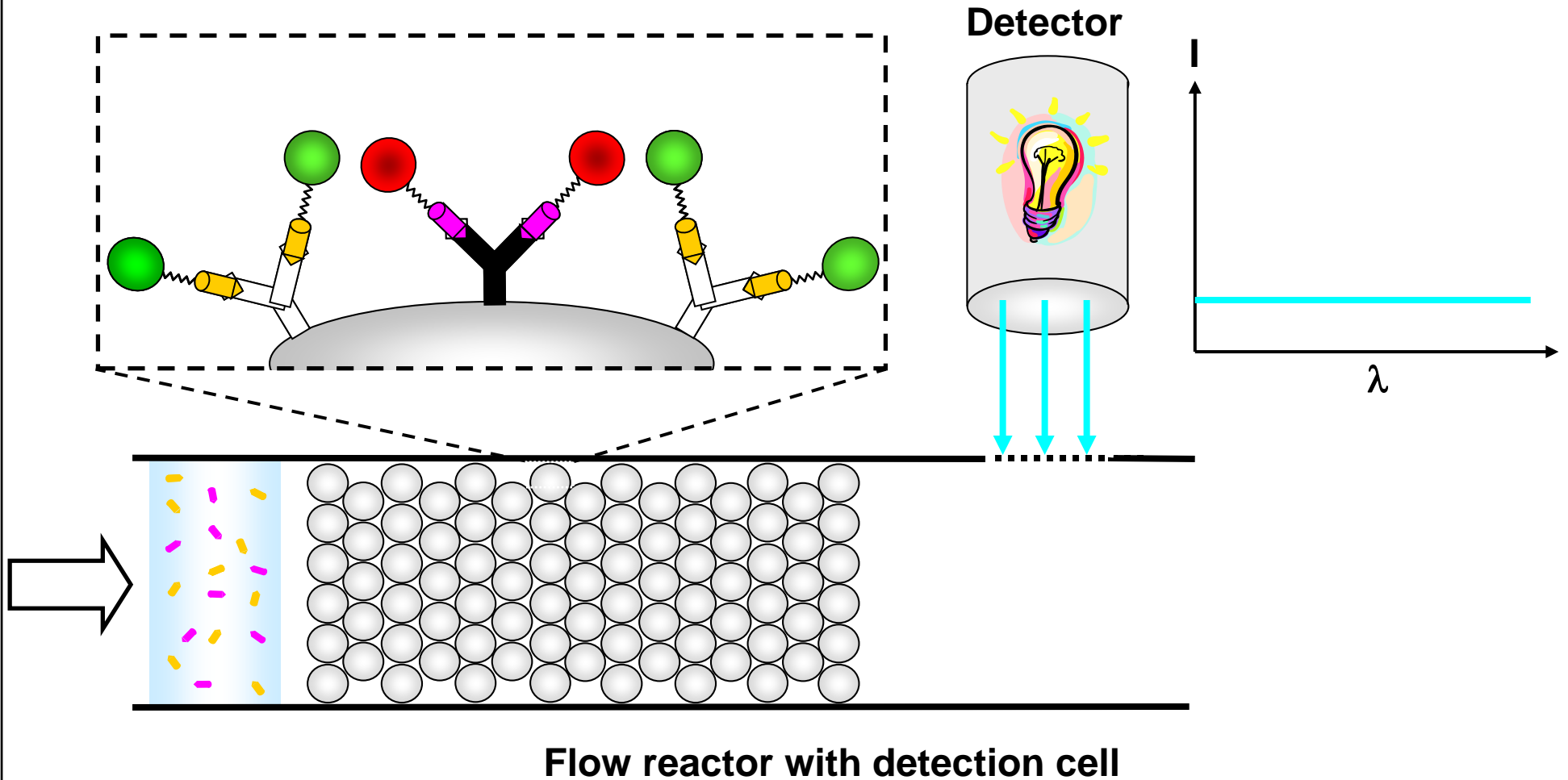
The change in carrier concentration due to binding can be directly monitored by measuring the nanowire conductance.

A solid state FET, whose conductance is modulated by an applied gate, is transformed into a nanosensor by modifying the silicon oxide surface. The conductance of modified Si-NWs increases stepwise with discrete changes in pH from 2 to 9. Changes in the surface charge can chemically-gate the Si-NW.



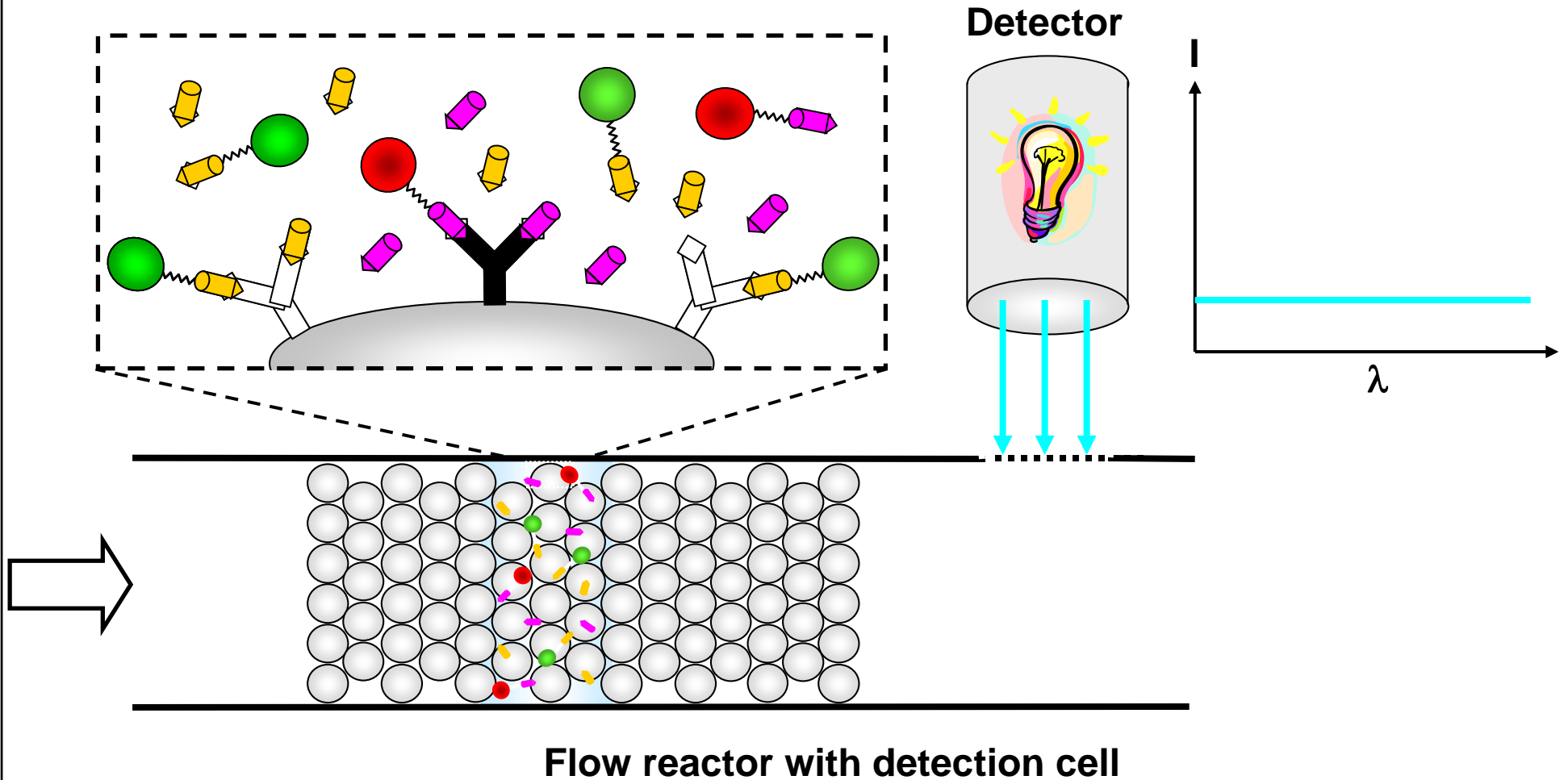
3.6 Biosensors and -assays

Multi analyte nanoparticle release bioassay



3.6 Biosensors and -assays

Multi analyte nanoparticle release bioassay



3.6 Biosensors and -assays

Multi analyte nanoparticle release bioassay

