Safety-relevant Properties of Nanoparticles

PSAM 2008

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Contents

Chances

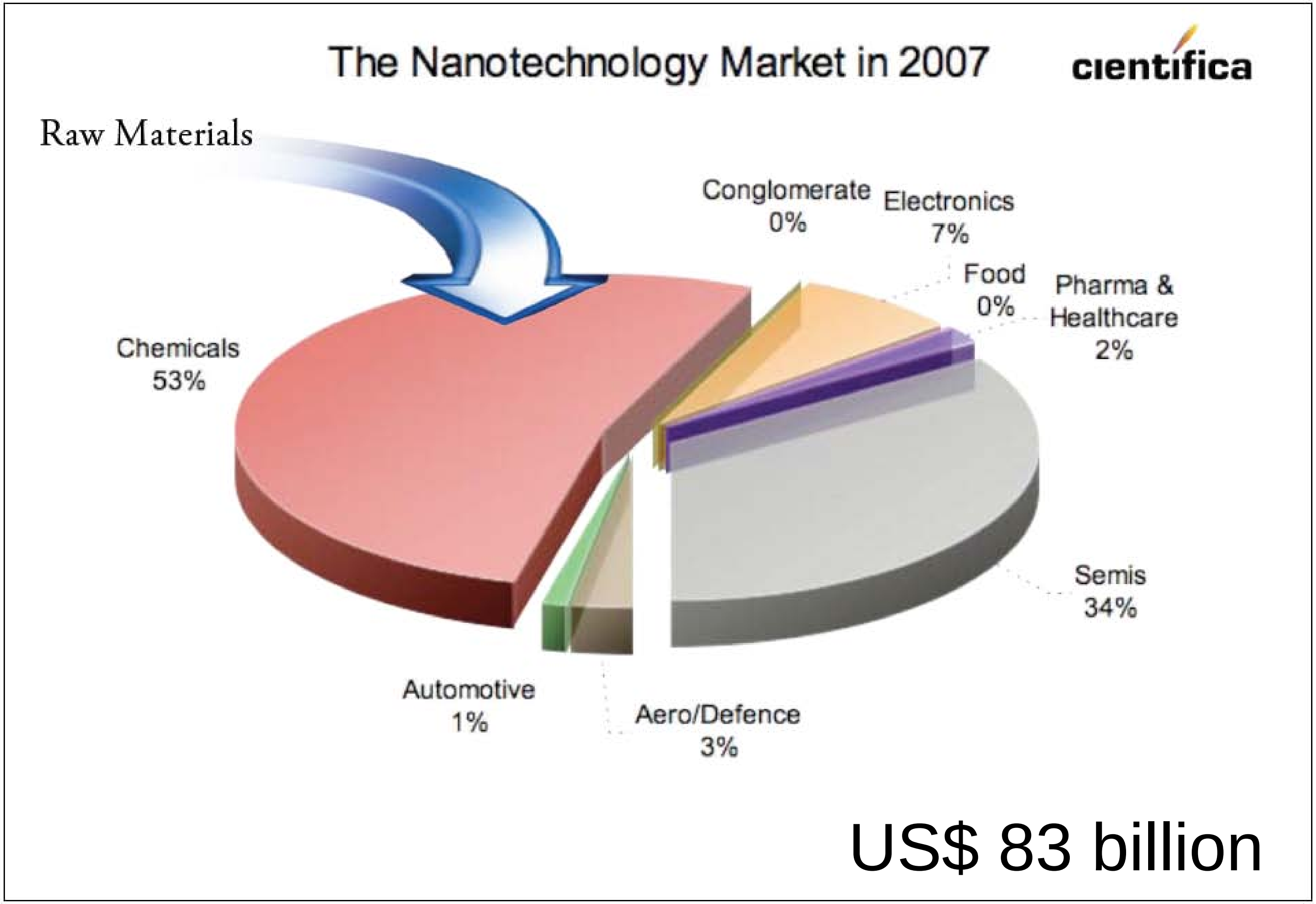

Figure 2 The Nanotechnology Market in 2007

Source: Cientifica Ltd., April 2007

Definition Nanomaterial acc. to ISO TC 229

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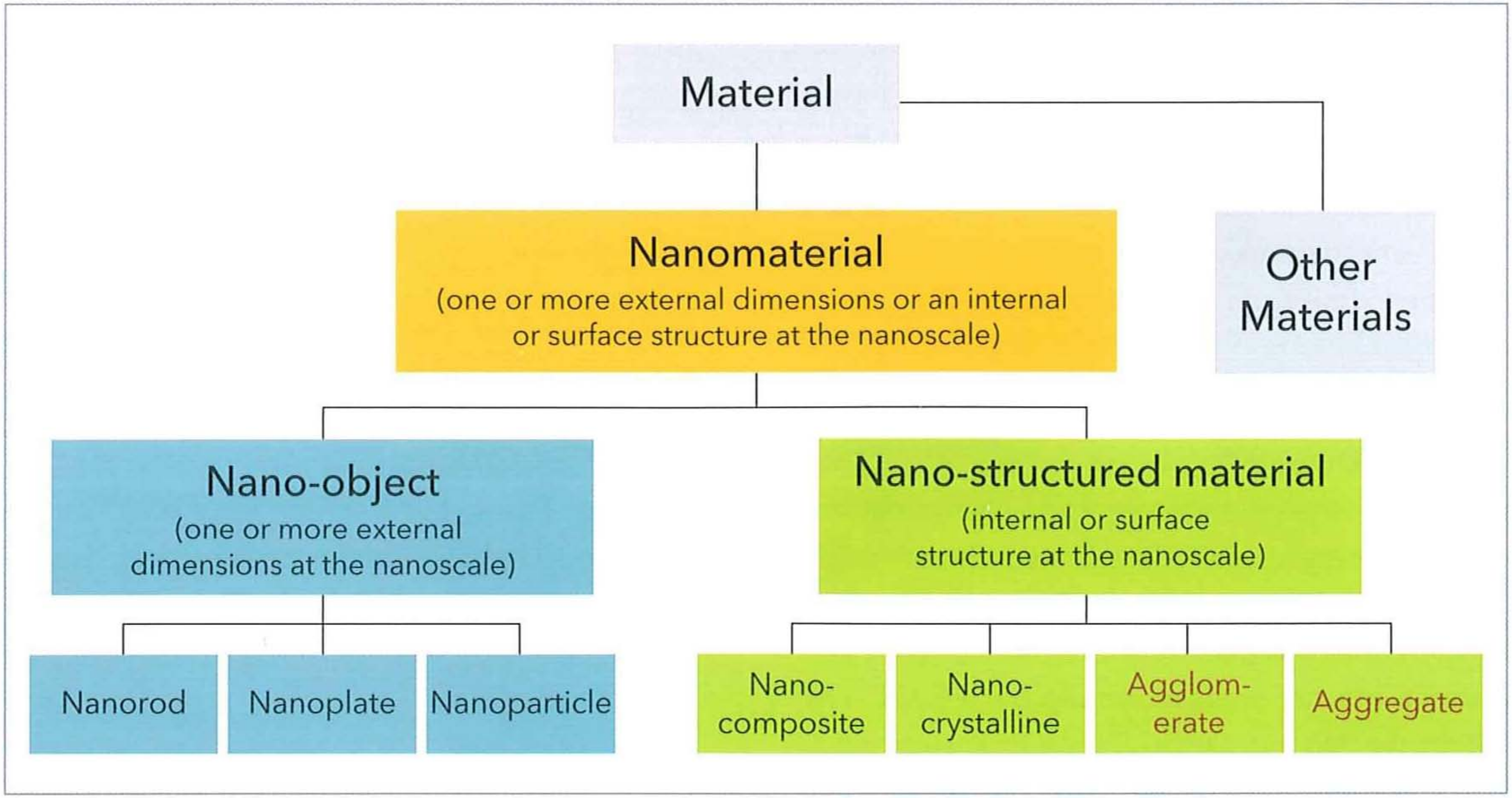

nanoscale: size from about 1nm up to 100nm

Source: Pridöhl, Evionik Degussa

Nanoobjects

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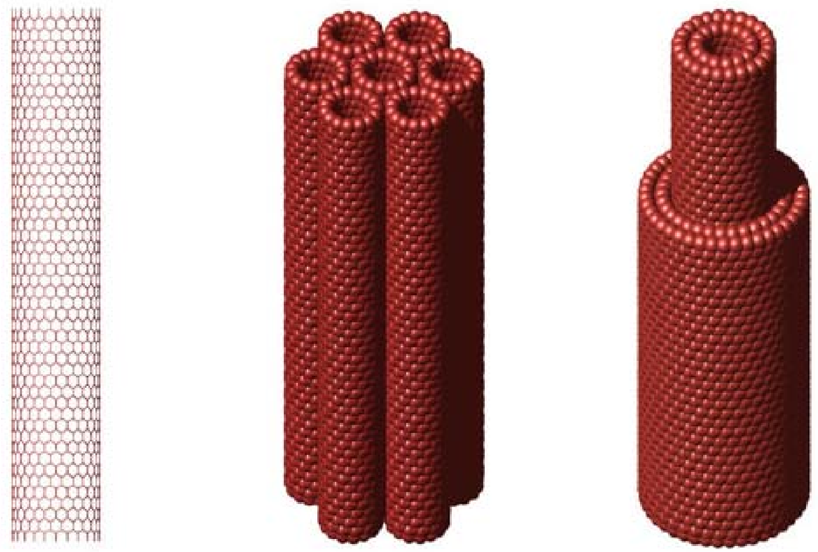
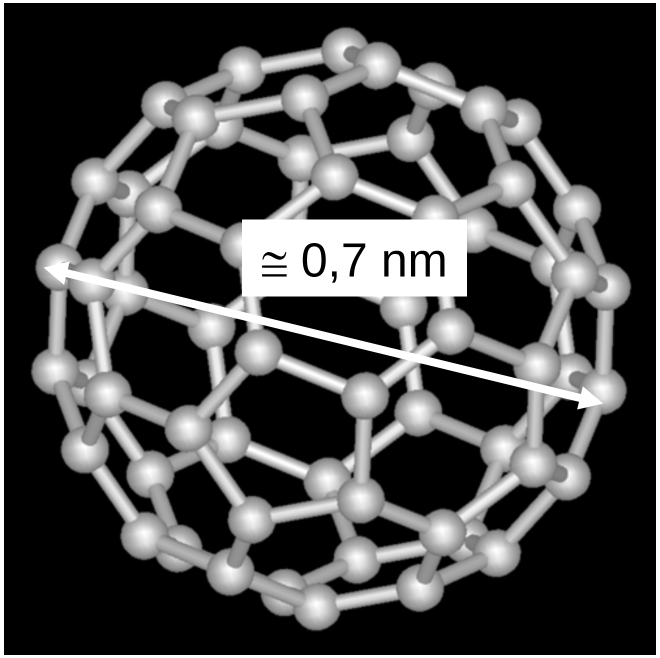


Carbon Nano Tubes (CNT), an example of nanorods

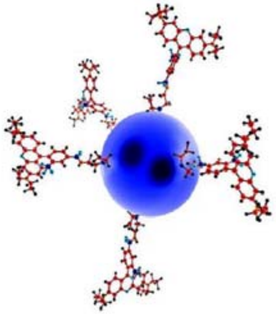
Fullerene, a nanoparticle



Exposure to nanoparticles

Sources of nanoparticles:

- **natural** (forest fires, volcanic eruptions,...)
- **anthropogenic**
  (byproduct of industrial activities
  like welding, polishing,...)
- **targeted** chemical engineering



Nanorisks?

First indications of health damages:

Agricola (1494-1555), Paracelsus (1493-1541) report about lung diseases of miners in Bohemia and Austria

Nanorisks?

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1) It could be shown in the last decades that such **diseases** of miners like pneumoconiosis (includes asbestosis and silicosis) are correlated with the **concentration of ultrafine particulate matter** (UFP) in the air inhaled. (UFP ≅ particles with a diameter of equal or less than 0,1 μm = 100 nm)

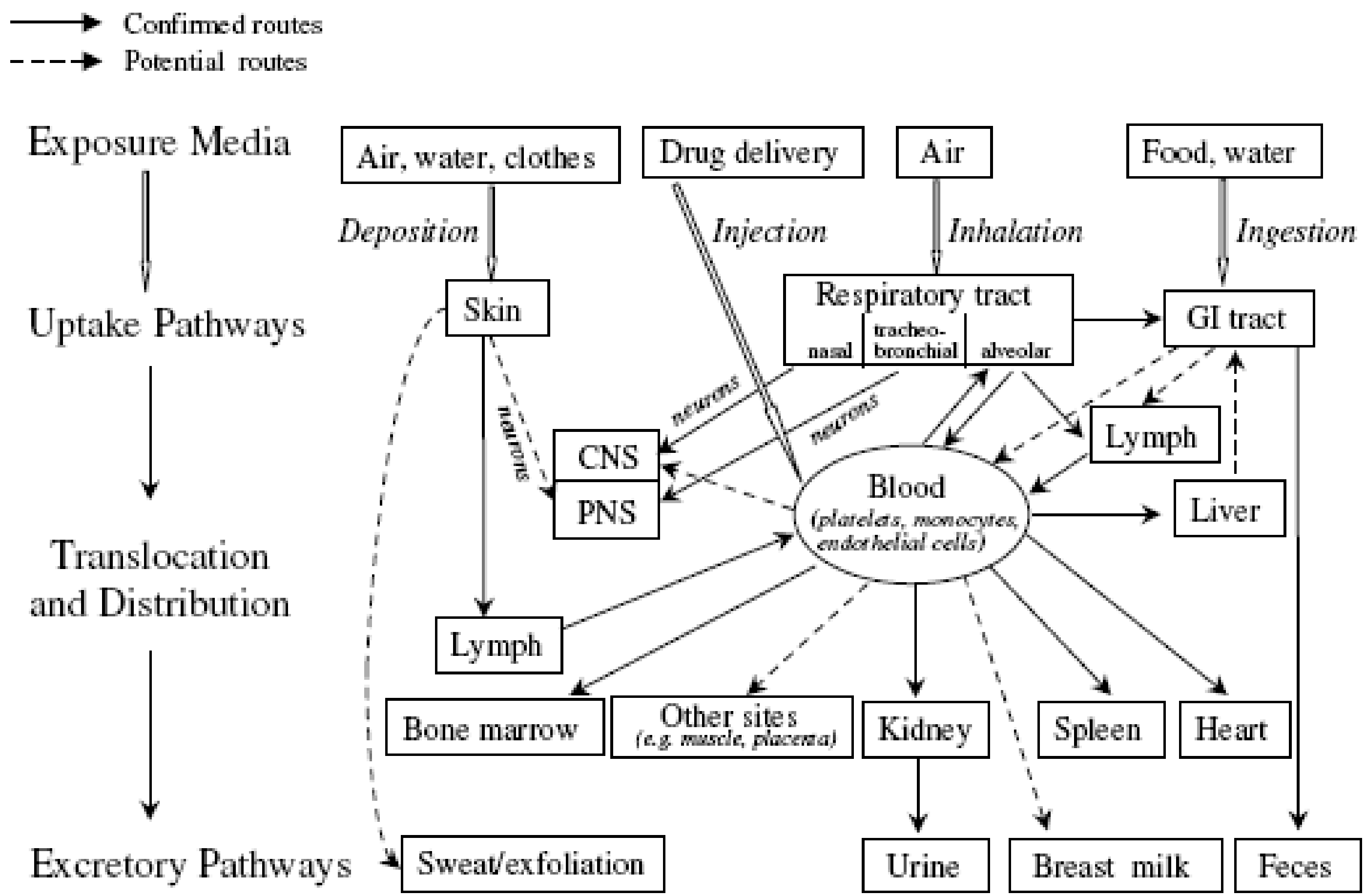
2) Further investigations demonstrated the correlation of **UFP in ambient air** with negative effects on human health (lung and cardiovascular diseases, Alzheimer). This happened even at far lower concentrations that were expected due to experiences with occupational exposure!

3) Due to these epidemiological studies numerous **in-vivo- and in-vitro-experiments** have been and are still performed. They prove the potential of (some) nanomaterials to cause detrimental or adverse health effects in humans and the environment.

Nanomaterial in consumer products

www.nanotechproject.org/consumerproducts

How can nanomaterial be incorporated?



Source: Oberdörster et. al., Particle and Fibre Toxicology, 2:8, 2005

Safety relevant properties acc. to literature

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- Shape
- Surface charge
- Porosity
- Surface area
- Crystal structure
- Heterogeneity
- Size (distribution)
- Solubility
- Chemical composition
- Surface chemistry
- Agglomeration/Aggregation
- Dispersibility
- Reactivity

No generally agreed metrics
No dose-response relationships

following Maynard, A. D., Woodrow Wilson International Center for Scholars ICON Research Need Assessment, January 9 207, Bethesda, MD

Safety relevant properties?

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Key questions:

Are these properties independent?
What are the fundamental properties, which one are derived?

Theoretical implications:

What determines the hazardousness of nanomaterial?

Practical implications:

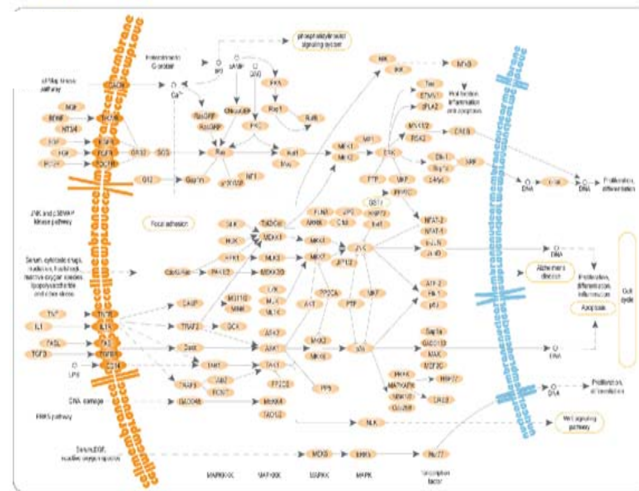
How must nanomaterial be characterized?
What are the main operational quantities to be measured?

Why is size decisive?

The reductionistic approach

Toxic effects are results of reactions of an organism to chemical substances.

These reactions are based on very complex cellular responses to substances (which may be transformed during the translocation process in the body).



Cellular responses are all again based on biochemical reactions which are governed by thermodynamics and kinetics – like all chemical processes.

$$aA + bB \rightleftarrows cC + dD$$

$$\Delta\mu^{\bullet} = -RT \ln K_a$$

$$K_a = \frac{a_C^c \cdot a_D^d}{a_A^a \cdot a_B^b}$$

“Thermodynamics of Nanoparticles” - Gibb‘s Free Energy

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$$G = U - TS - \sum_j X_j Y_j = \sum_{i=1}^{n} \mu_i n_i$$

$$dG = -SdT - \sum_j X_j dY_j + \sum_{i=1}^{n} \mu_i \, dn_i$$

U	Inner Energy
S	Entropy
T	Temperature
X	generalized displacement (volume, area, polarization,…)
Y	generalized force (negative pressure, surface tension, electrical field,…)
μ_i	Chemical potential of substance i
n_i	number of moles of substance i

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Chemical potential μ^σ of a substance at surface σ, compared with it’s bulk value μ (at const. T, p)

$$\mu^\sigma := \left(\frac{\partial G^\sigma}{\partial n^\sigma}\right)_{p,T} = \gamma\left(\frac{dA}{dn^\sigma}\right)_{p,T} + \mu$$

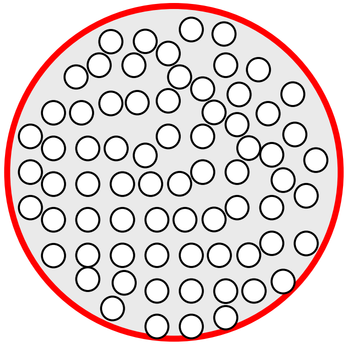
Kelvin‘s equation for spherical particles with radius r describes the difference of their chemical potential and of bulk material (same substance); V_m = mole volume of that substance

$$\mu^\sigma - \mu = \gamma\left(\frac{dA}{dn^\sigma}\right) = \frac{2\gamma V_m}{r}$$

γ = surface tension

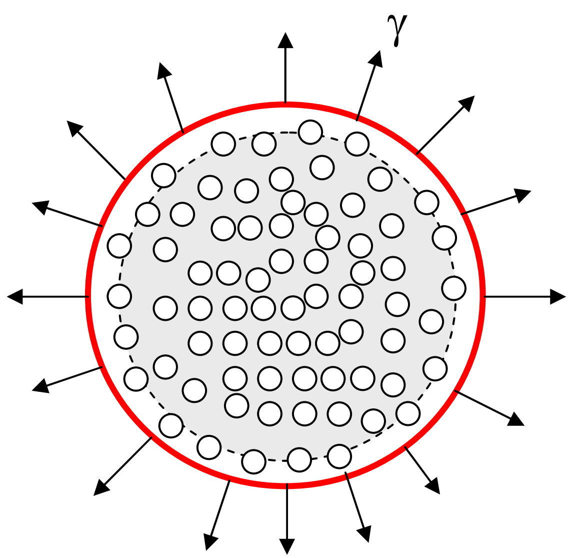
Deriving γ (1)

Surface A_1



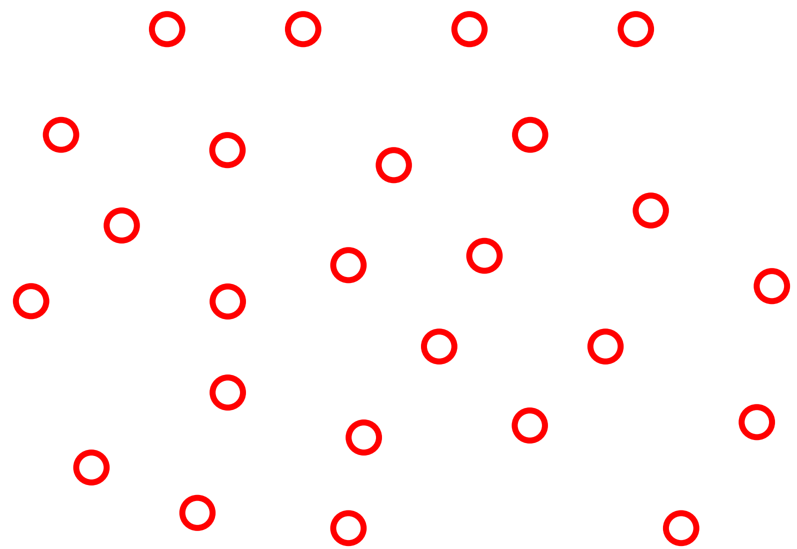
Nanoparticle of radius r_1

Surface $A_2 > A_1$



Nanoparticle of radius $r_2 > r_1$;
γ: surface tension

Deriving γ (2)



Ideal Gas, surface $A_3 >> A_1, A_2$

Complete separation of the molecules/ion-pairs/atoms forming the nanoparticle creates the „maximum surface area“. The particles have now the diameter r_{min}

At standard condition (index 0,
(T = 298.2 K, p = 1 atm),
r_{min} = radius of gaseous material

$$\mu^0_{Gas} - \mu^0_{Bulk} = \frac{2\gamma V_m}{r_{\min}}$$

An estimation of γ can be derived from fundamental thermodynamic data of a given substance
(taking standard free energies of formation for bulk/gaseous material)

The effect of size (1)

For nanoparticle in the gas phase with partial pressure p_{nano}
(T = 298.2 K, p = 1 atm),
r = radius of nanoparticle

$$\mu^{nano} \cong \mu^{0}_{Bulk} + \frac{2\gamma V_m}{r} + RT \ln p_{nano}$$

For nanoparticle with radius r in arbitrary state (in a physiological fluid, e.g.) with activity a

$$\mu = \mu^{\bullet}_{Bulk} + \frac{2\gamma V_m}{r} + RT \ln a$$

or

$$\boxed{\mu = \mu^{\bullet}_{Bulk} + RT \ln\left(a\, e^{\frac{2\gamma V_m}{RT\, r}} \right)}$$

(the dot stands for the standard state a = 1 and r = ∞ in a biological system, e.g. – this standard state is different from the "ordinary thermodynamic standard state"!!)

The effect of size (2)

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Therefore, one can formally make the following substitution of the activity a for nanoparticles with radius r :

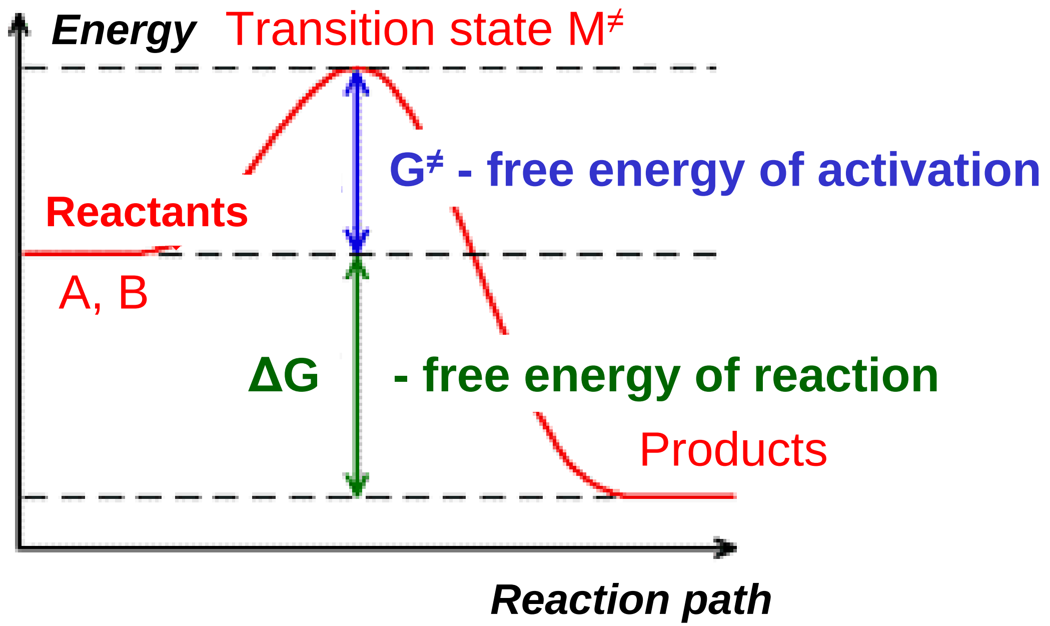
$$a \Rightarrow a e^{\frac{2\gamma V_m}{RT r}}$$

This has an important effect on chemical reactions:

According to Eyring's theory, a reaction of two partners A and B starts with the formation of a transition state $M^{\neq}$ which then decays to the products:

$$A + B \rightleftarrows M^{\neq} \longrightarrow \text{Products}$$

The effect of size (3)



The rate constant of this reaction (k) is then given by

$$k = \frac{k_B T}{h} e^{-\frac{\Delta G^{\neq}}{RT}}$$

where k_B is Boltzmann‘s constant, h is Planck’s constant and $\Delta G^{\neq}$ is the free energy of activation which is necessary to create $M^{\neq}$ from A and B.

The effect of size (4)

For a reaction in real solutions we have the following relation for the rate of reaction

$$rate \sim k\, a_A\, a_B$$

If A is a nanoparticle, we can make the substitution derived above

$$a_A \Rightarrow a_A\, e^{\frac{2\gamma V_m}{RT\, r}}$$

This leads to an increase of the rate constant of the reaction:

$$k \Rightarrow k = \frac{k_B T}{h} e^{-\frac{\Delta G^{\neq}}{RT}} e^{\frac{2\gamma V_m}{RT\, r}} = \frac{k_B T}{h} e^{-\frac{(\Delta G^{\neq} - \frac{2\gamma V_m}{r})}{RT}}$$

So the free energy of activation is decreased compared to the "non-nano-case" – the reaction can speed up considerably.

The effect of size - example

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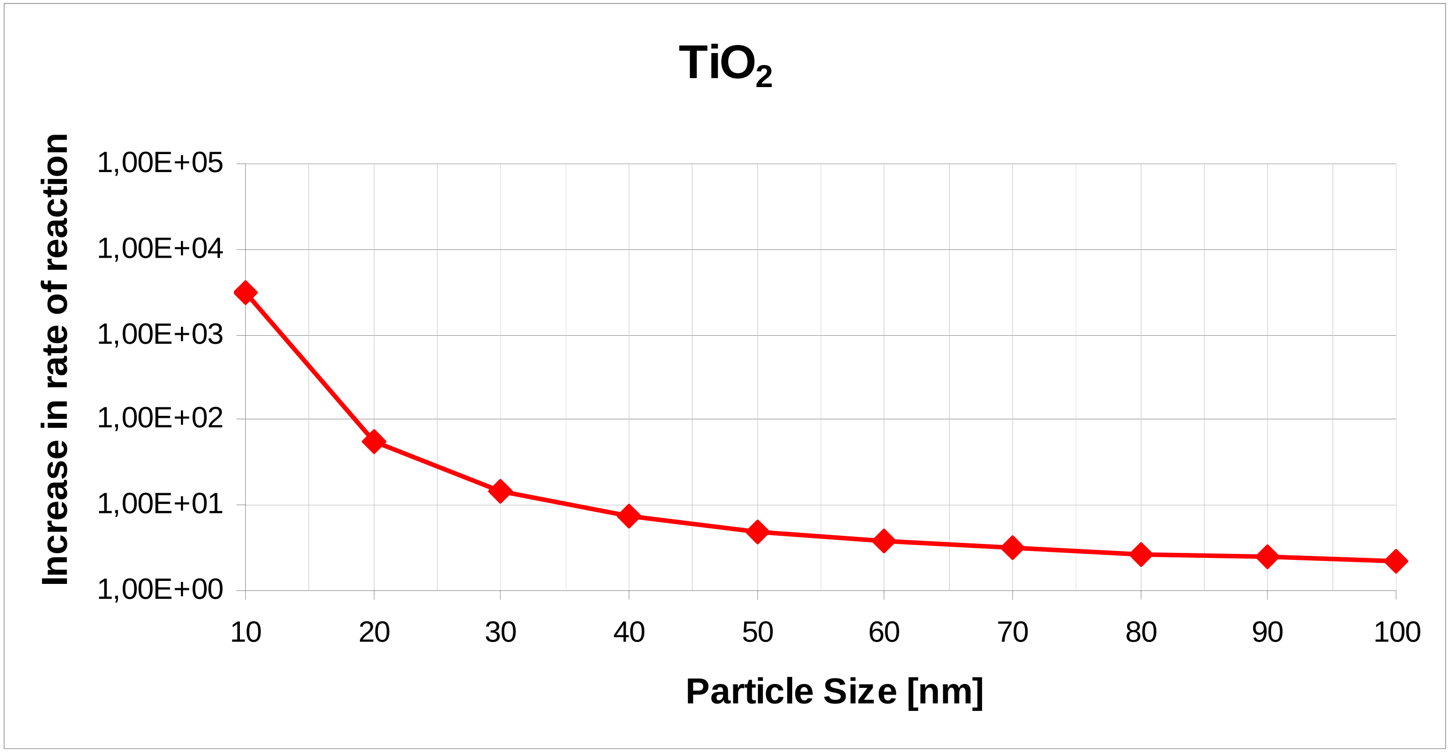

Increase of k by factor 2 and more at particle sizes < 120nm

The effect of size - example

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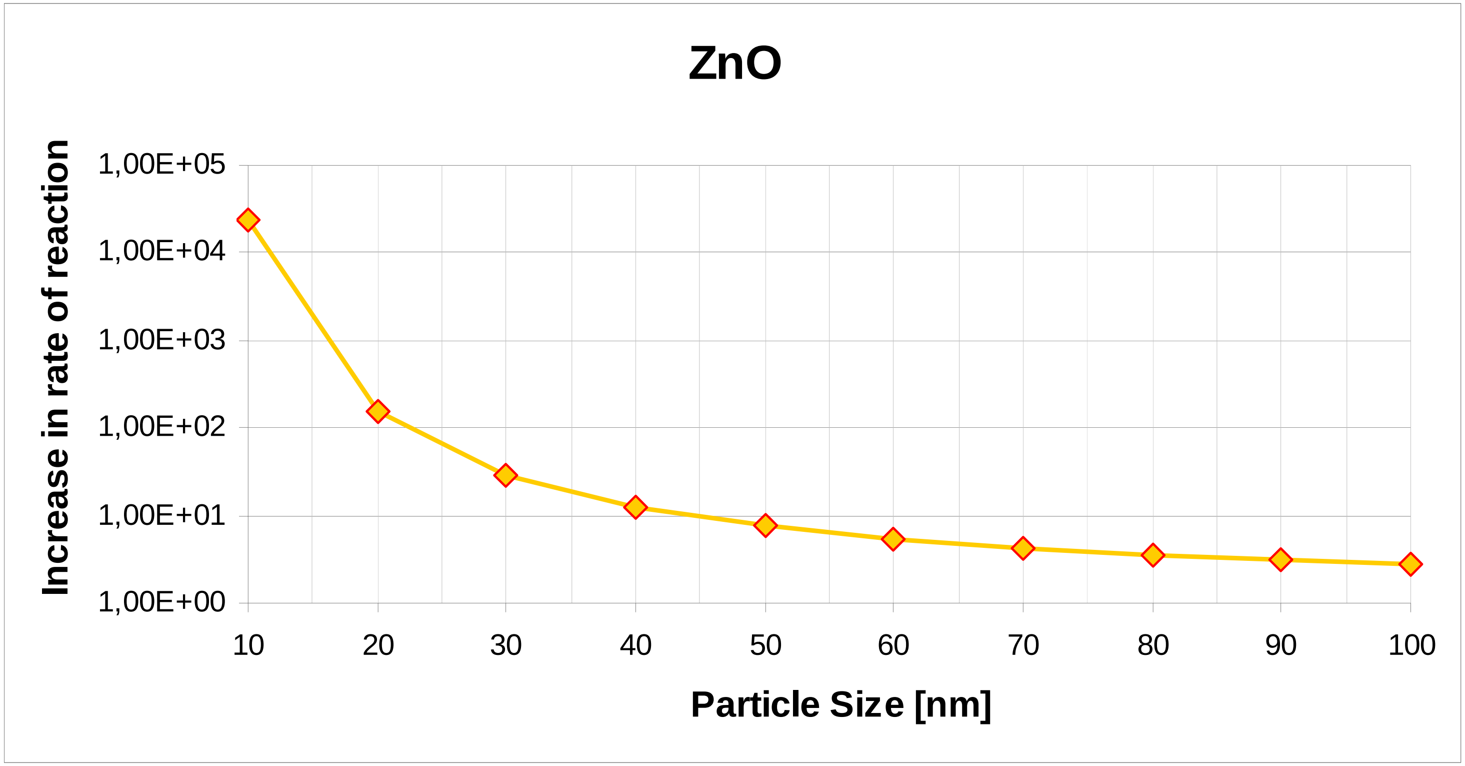

Increase of k by factor 2 and more at particle sizes < 150nm

The effect of size - example

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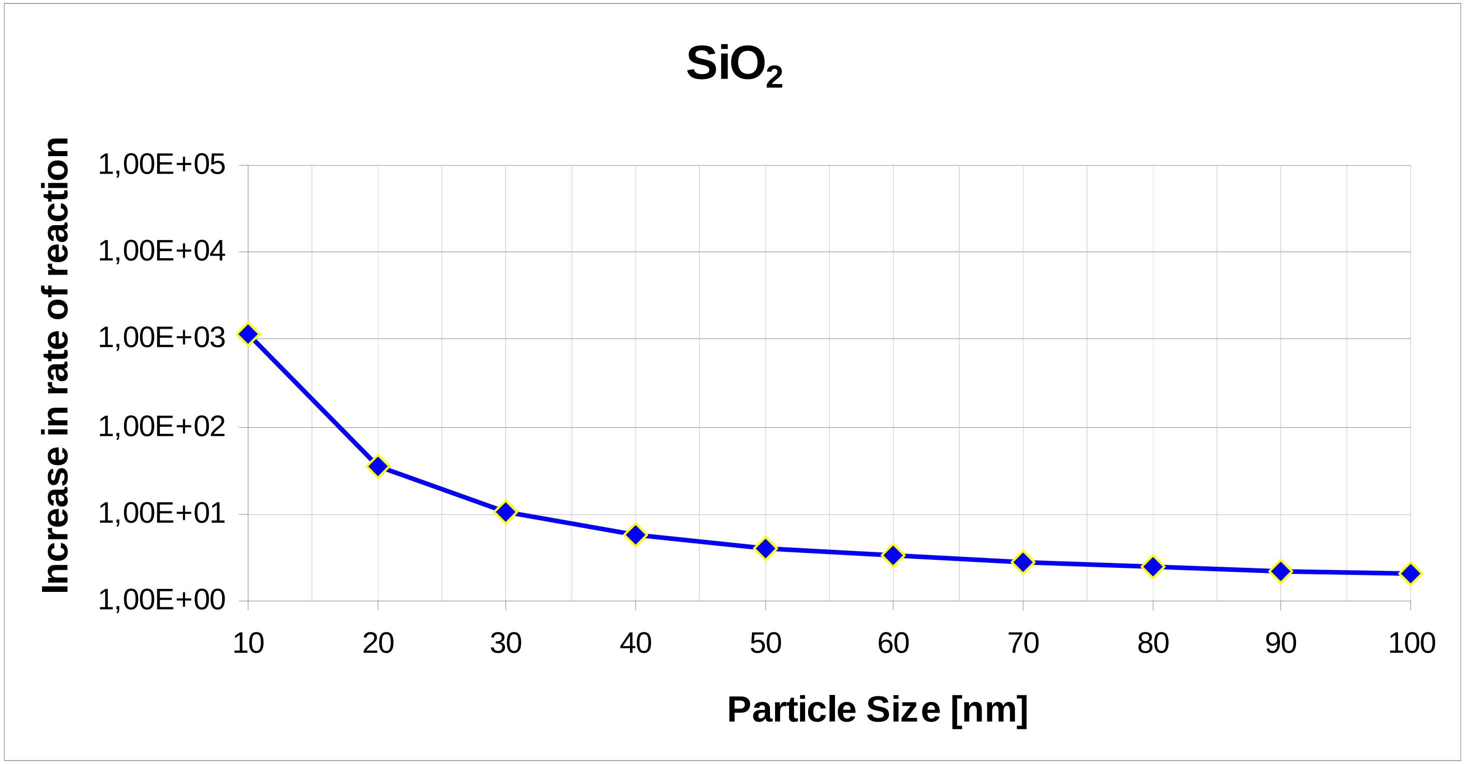
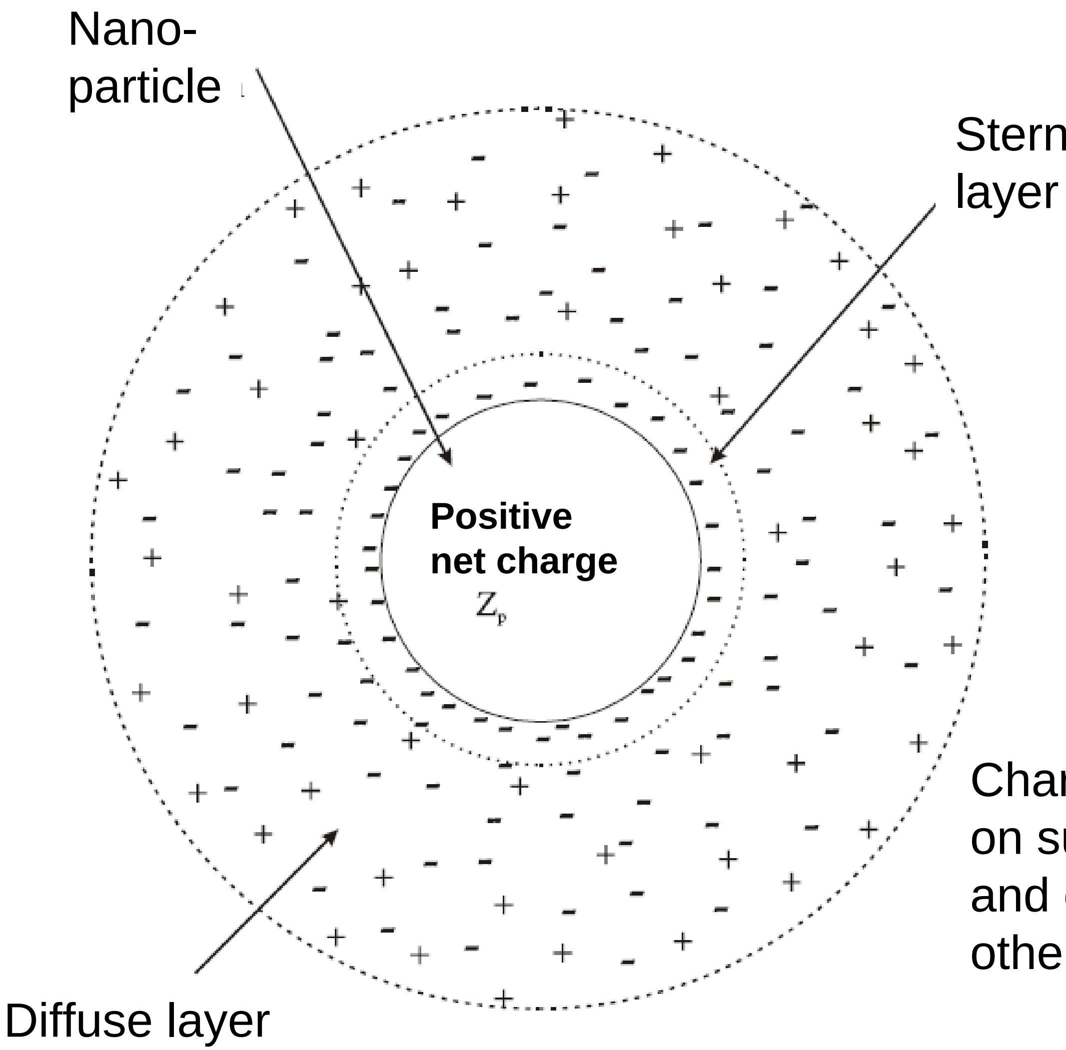


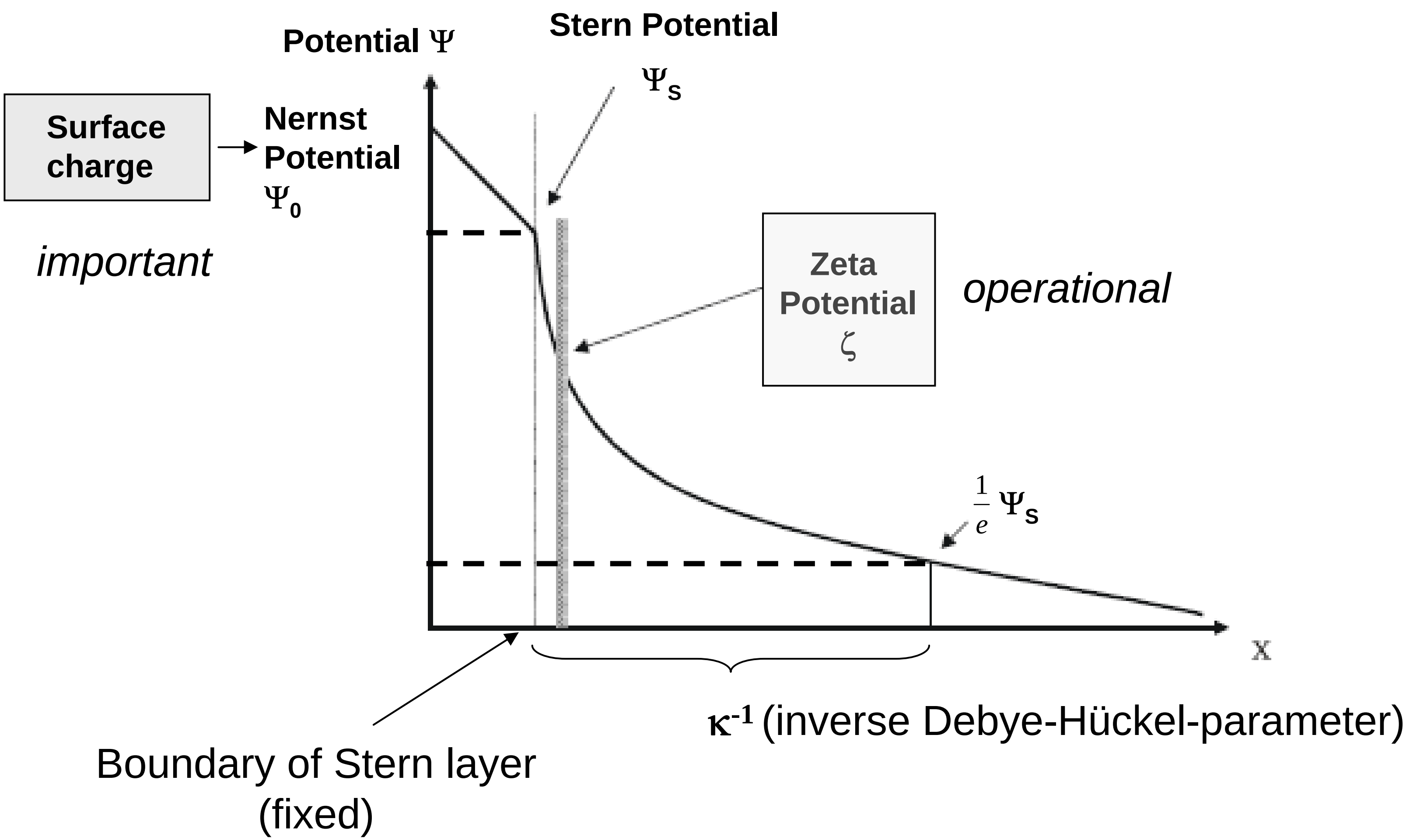
Increase of k by factor 2 and more at particle sizes < 100nm

Interaction of charged nanoparticles (1)

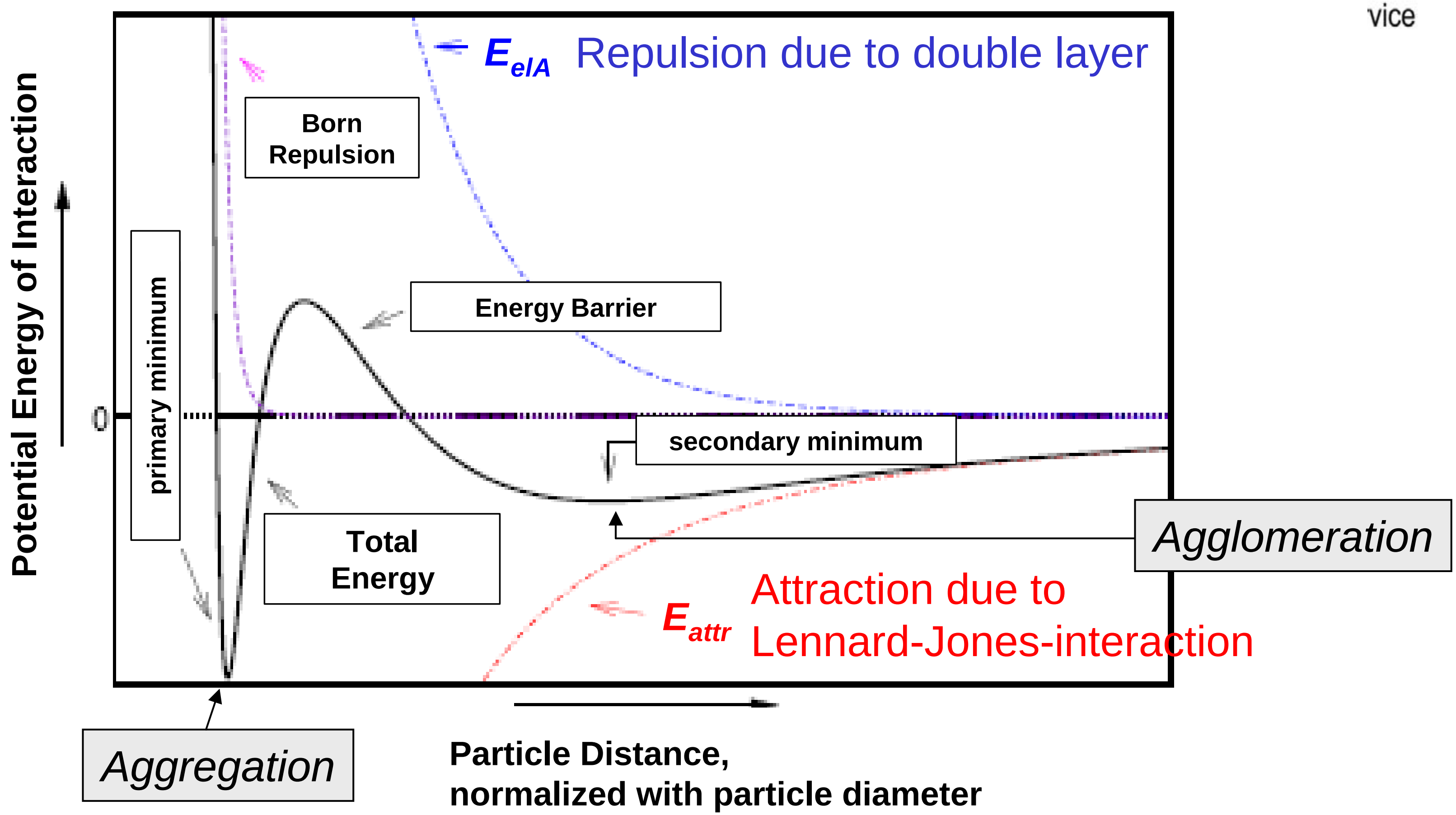


Charge depends on surface chemistry and environment (pH, other cations/anions…)

Interaction of charged nanoparticles (2)



Interaction of charged nanoparticles (3)



The total energy of **interaction of charged nanoparticles** depends also critically on the **size** of the particle and on the medium.

Conclusion: What are Safety relevant properties?

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- Shape
- Surface charge
- Porosity
- Surface area
- Crystal structure
- Heterogeneity

- Size (distribution)
- Solubility
- Chemical composition
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following Maynard, A. D., Woodrow Wilson International Center for Scholars ICON Research Need Assessment, January 9 207, Bethesda, MD

Conclusion: What are Safety relevant properties?

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“Chemical composition” and **“crystal structure”**:
Essential, but not completely independent; remember the distinction between (non-)stoichiometric *compositions* and modification or phase/homogeneity/purity/defects in the *crystal*.
Some defects are again due to thermodynamics (e. g. $Zn_{1+x}O$ and Ti_nO_{2n-1})

“Surface chemistry”:
Fundamental; it influences surface structure, charge, “reactivity”, **solubility** and agglomeration/aggregation.

“Reactivity”:
Better: Chemical potential; it influences the equilibrium of any chemical reaction. The increase of the chemical potential with decreasing particle size makes size the obviously important parameter when talking about “nanos”.

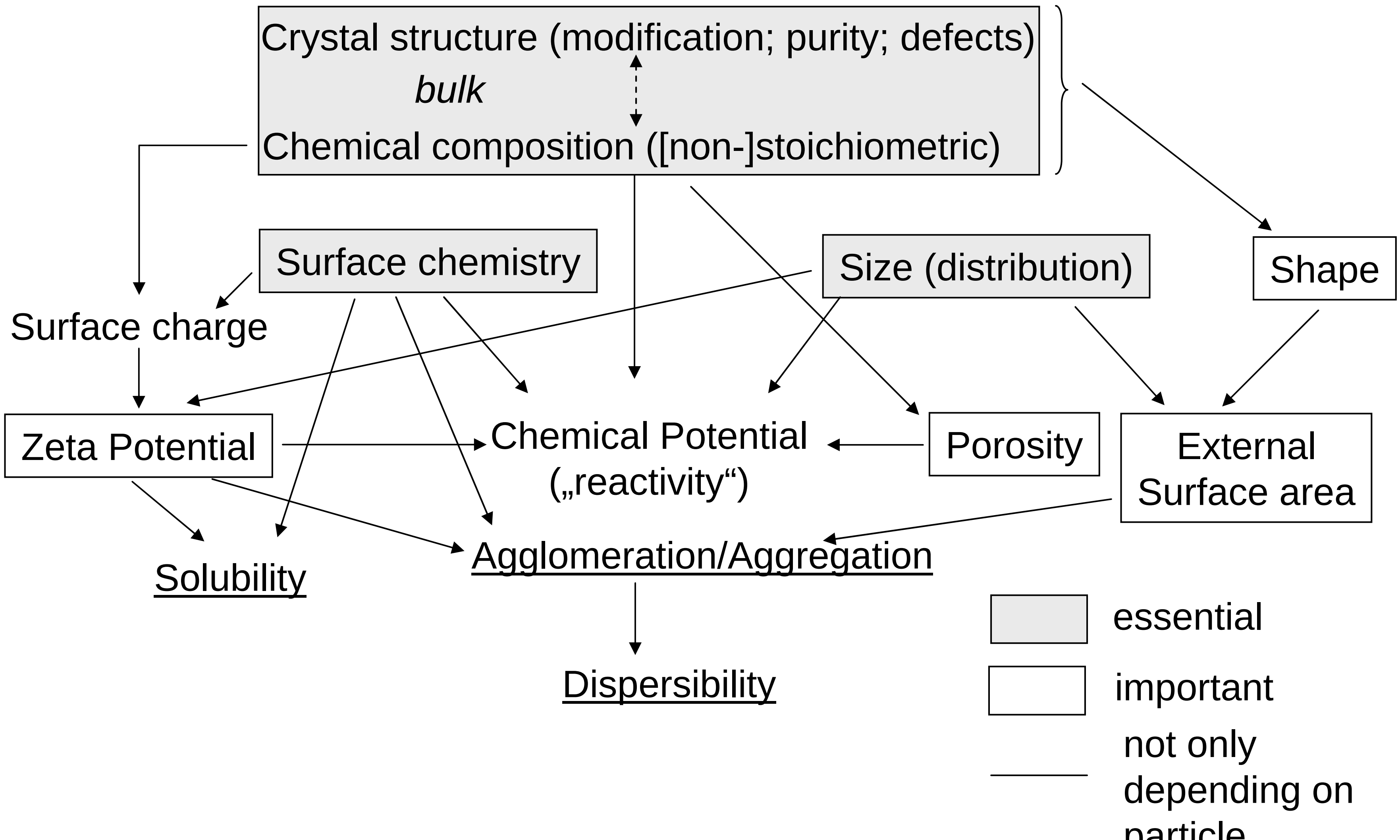
Conclusion: What are Safety relevant properties?

“Surface charge”:
Fundamental, but not an operational parameter

“Agglomeration” and “aggregation”:
Not fundamental parameters; since they determine **“dispersibility”** in turn, that quantity is also not fundamental.

“Surface area”:
Determined by **“size”** and **“shape”** of the particle. Distinction of ‘external’ surface (= surface area) and ‘internal’ surface (**“porosity”**) seems to make sense.

Conclusion: Hierarchy of safety relevant properties



Thanks for your attention!!