

NANOMATERIALS

and

Toxicological Risk

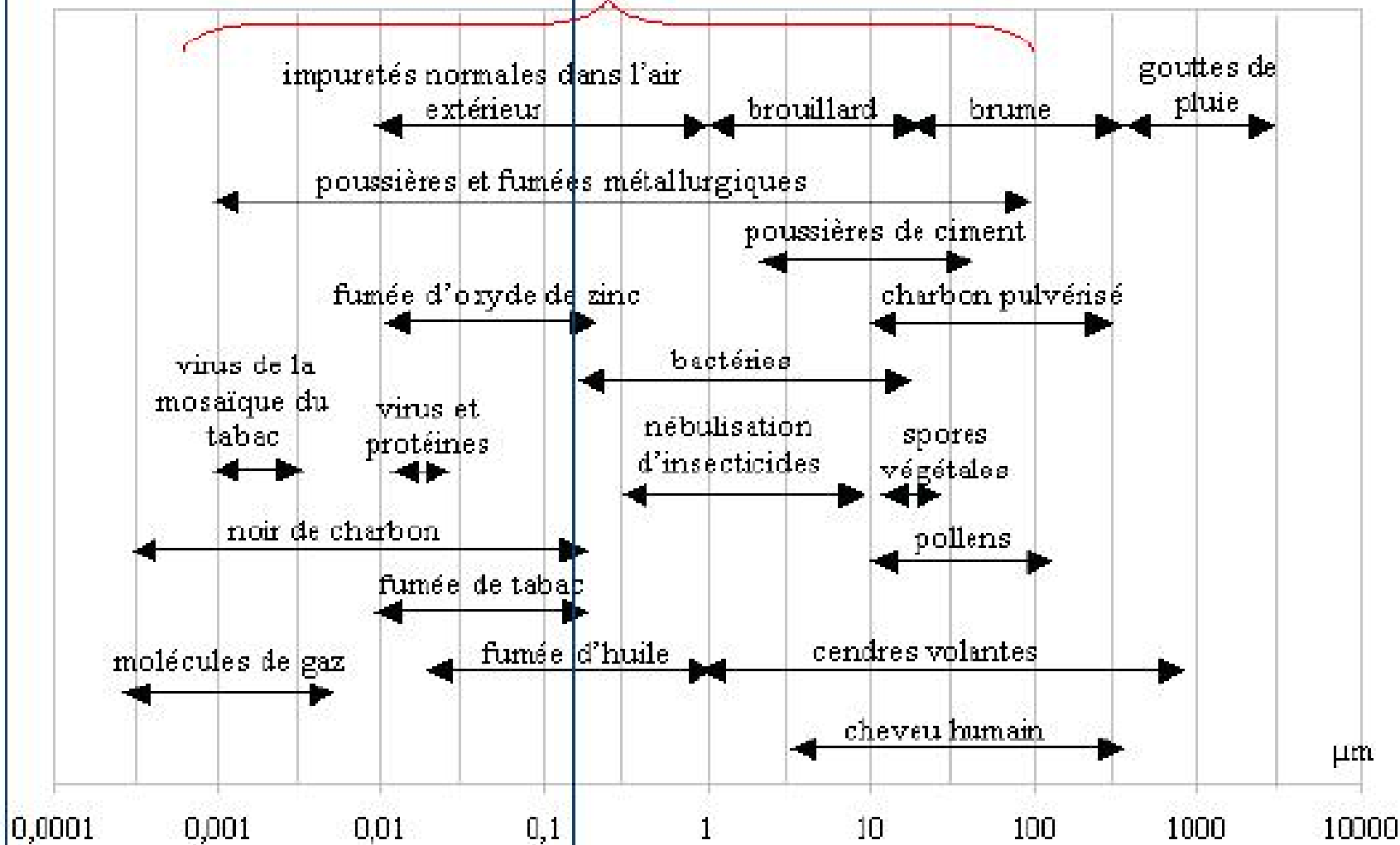
A.LOMBARD

Consultant Toxicologist & IPRP



Nanomonde

aérosols



diâmes des particules de différentes substances

Nanoworld



Dust mite
200 μm



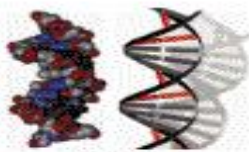
Ant
 $\sim 5 \text{ mm}$



Human hair
 $\sim 10\text{-}50 \mu\text{m}$
wide

Red blood cells with white cell

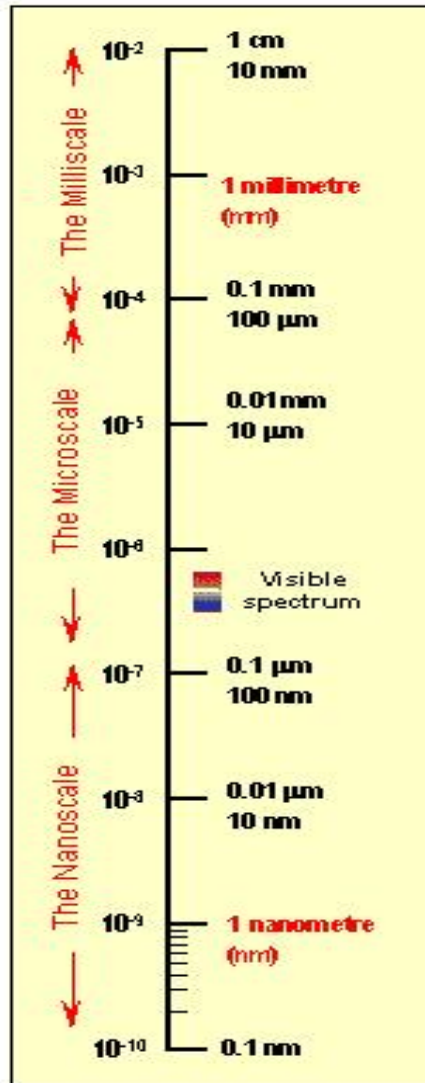
$\sim 2\text{-}5 \mu\text{m}$



DNA
 $\sim 2\text{-}1/2 \text{ nm}$



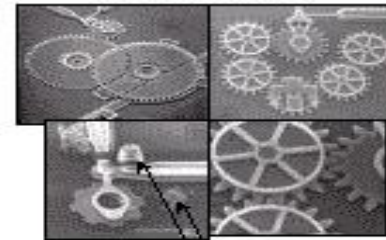
5 Atoms of silicon
1 nm



Head of a pin
1-2 mm

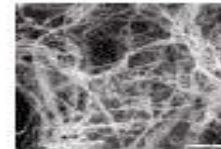
Micro Electro Mechanical Devices

10 -100 μm wide

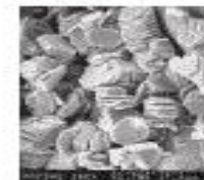


Pollen grain

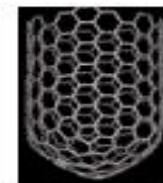
Red blood cells



Cellulose nanofibrils
20-100nm wide

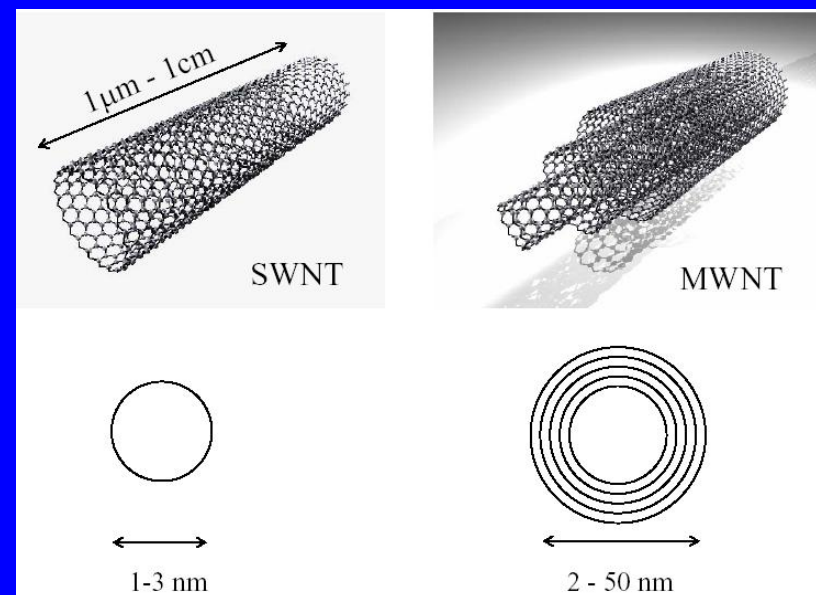
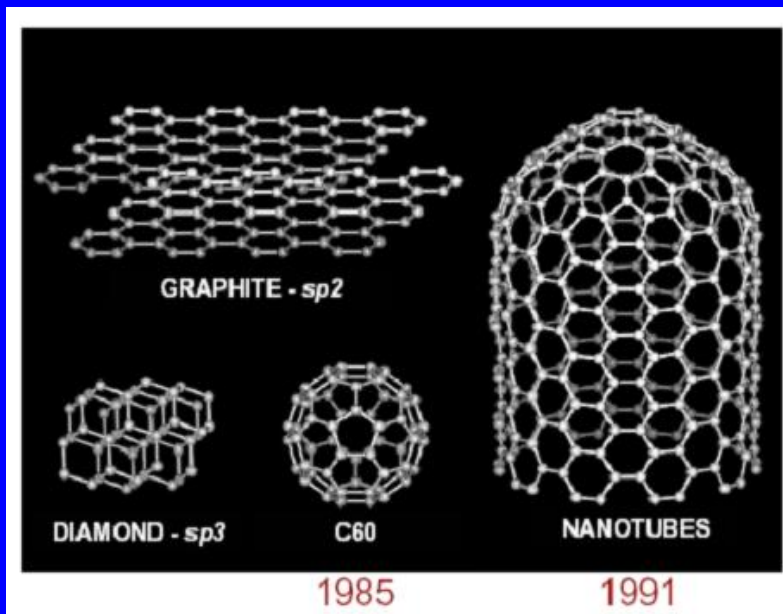
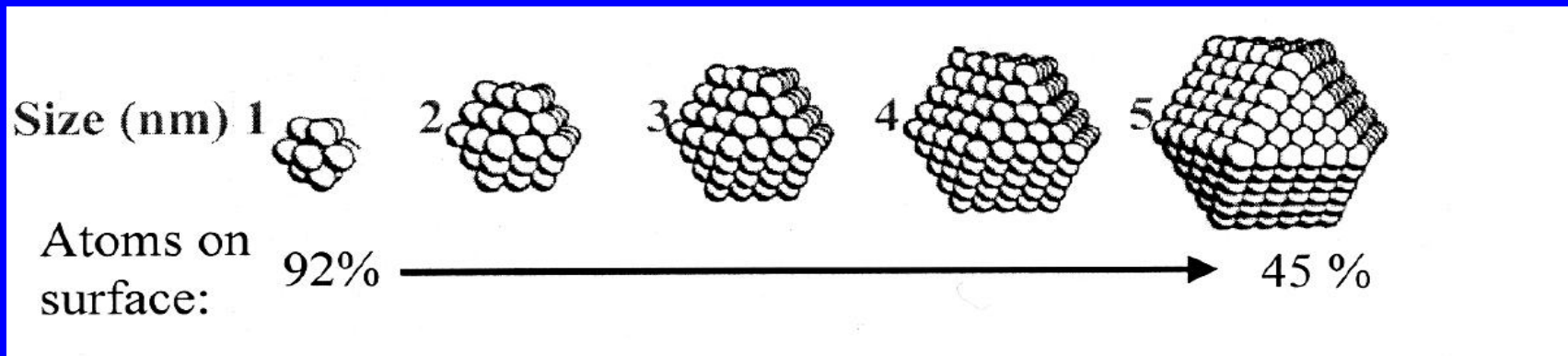


Stacks of clay mineral platelets, each platelet with $\sim 1 \text{ nm}$ thickness



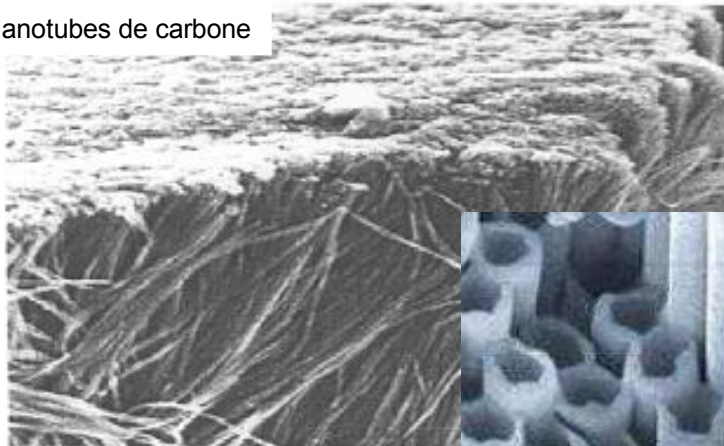
Carbon nanotube
 $\sim 2 \text{ nm}$ diameter

Nanoparticles and carbon nanotubes

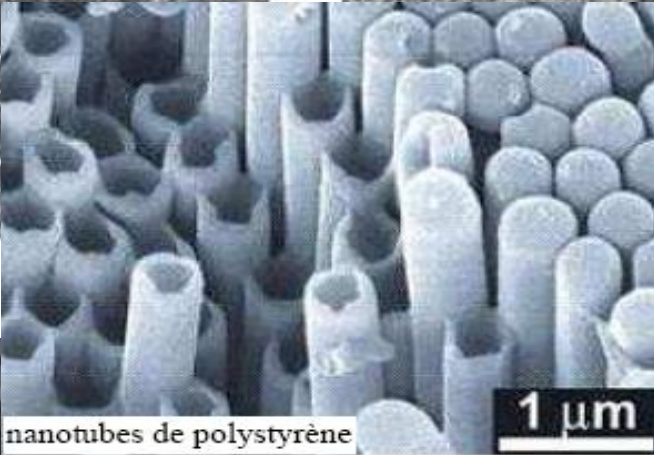
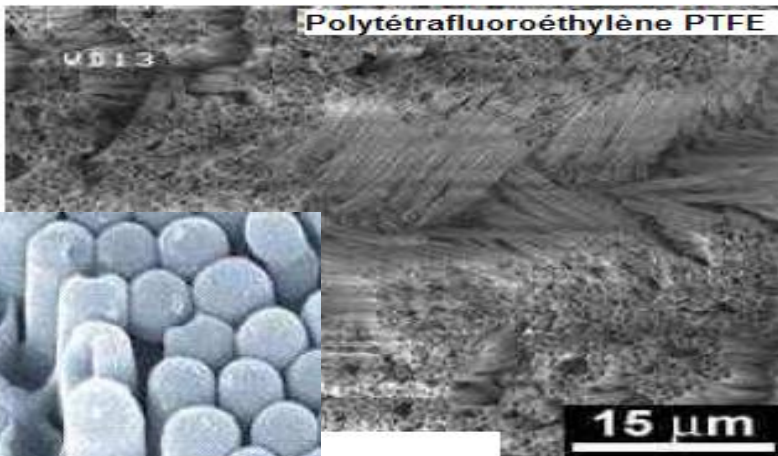


Nanotubes / Nanofibers

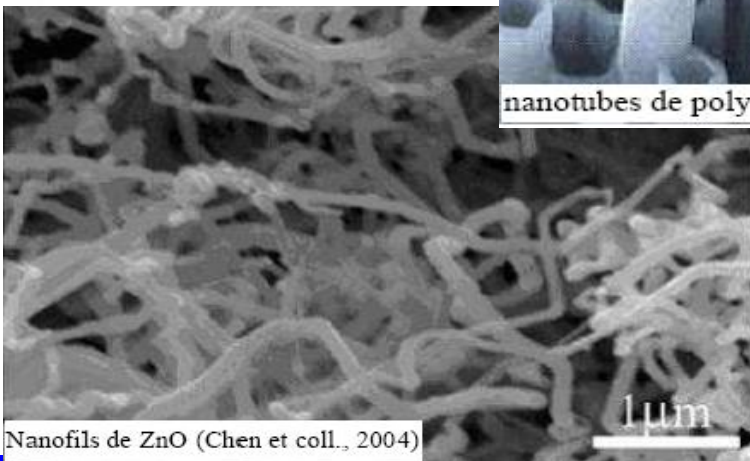
Nanotubes de carbone



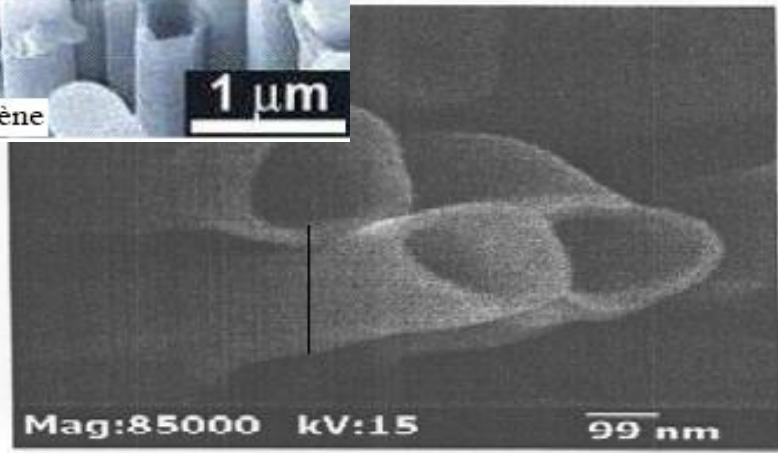
Polytétrafluoroéthylène PTFE



nanotubes de polystyrène



Nanofils de ZnO (Chen et coll., 2004)



Exposures to nanoparticles

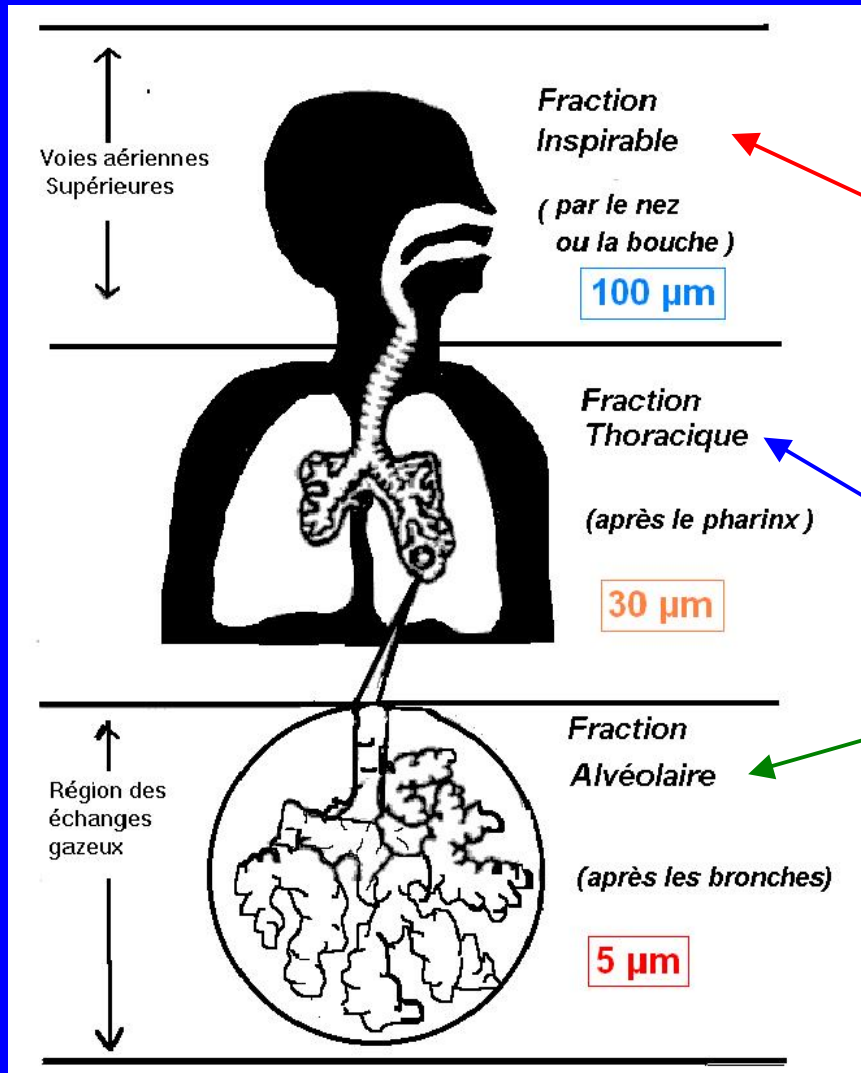
Exposure to nanoparticles is as long as humanity.

ambient air = more than 10 000 / 1 cm³ for particles >10 nm

Most of the nanoparticles just go through the body without any interaction and are rapidly excreted.

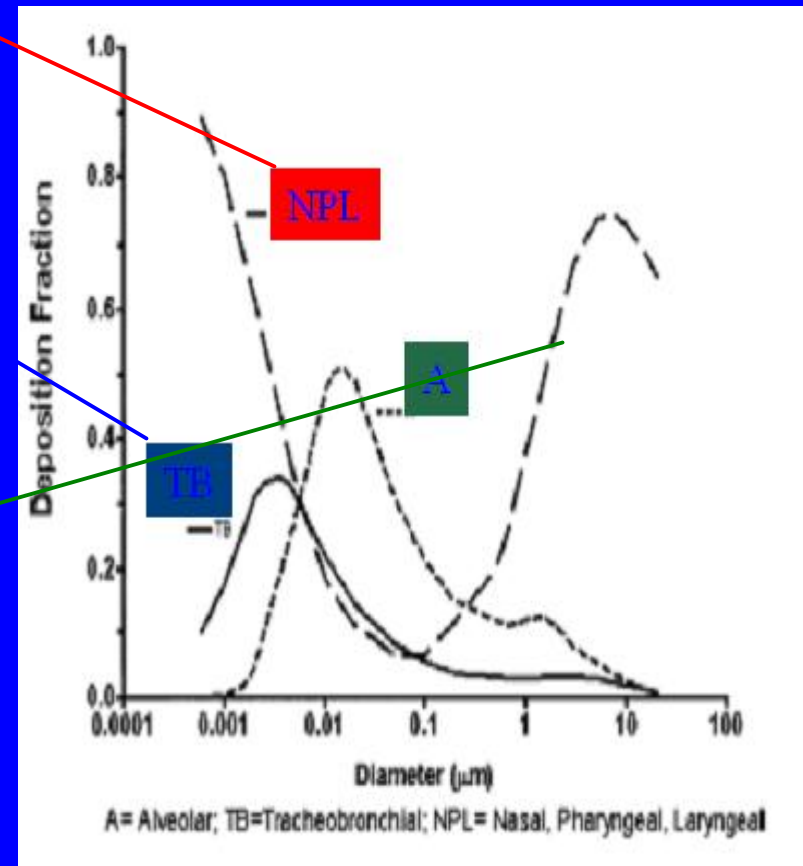
- The nanoparticles from natural origin seems to be well accepted by the human and animal organisms during the species evolution.
- Human made nanoparticles with specific physico-chemical properties may combine with other particles or organic components like proteins or even DNA to disturb the cells

Particles penetration into the Respiratory Tract

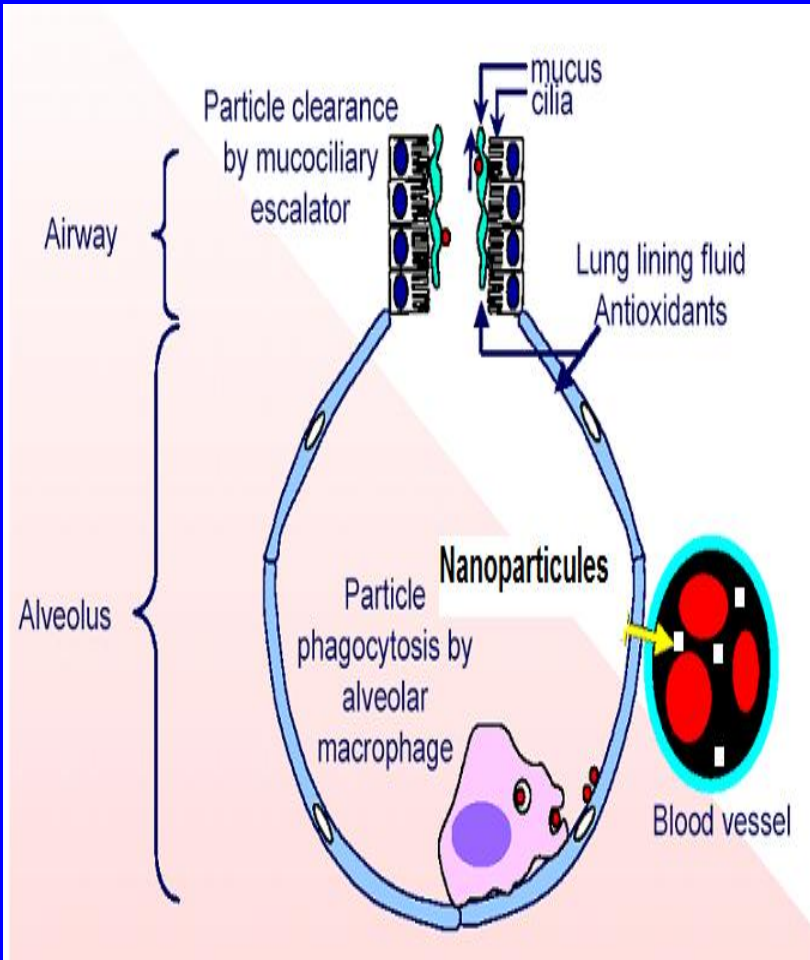


Nanoparticles deposition

Oberdorster G et al. *Inhal. Toxicol.* 2004, 16:437-445



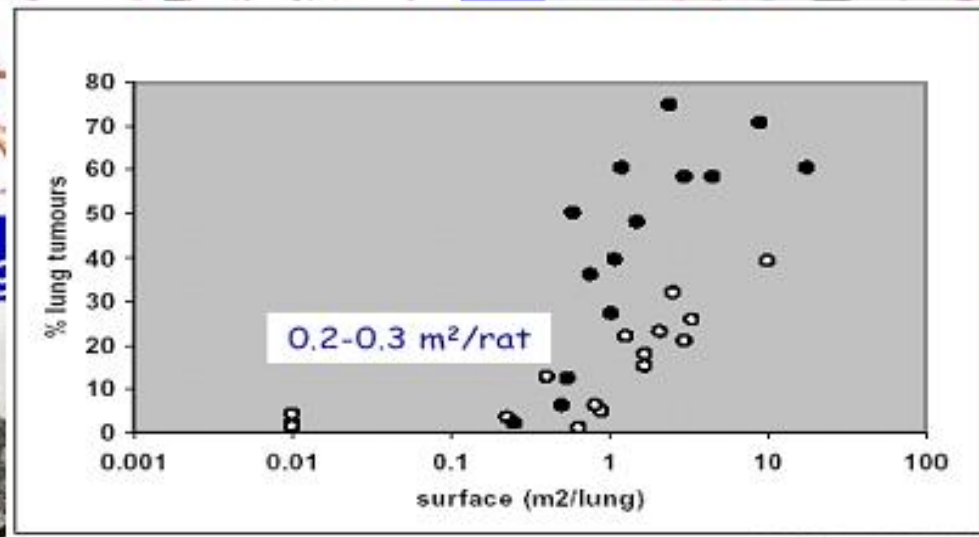
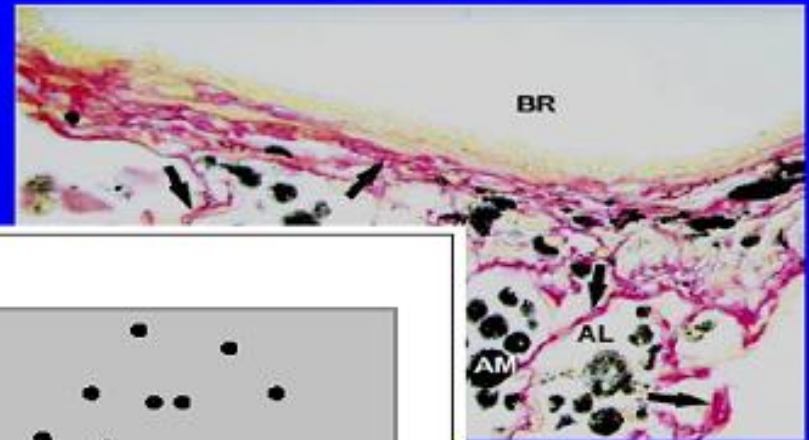
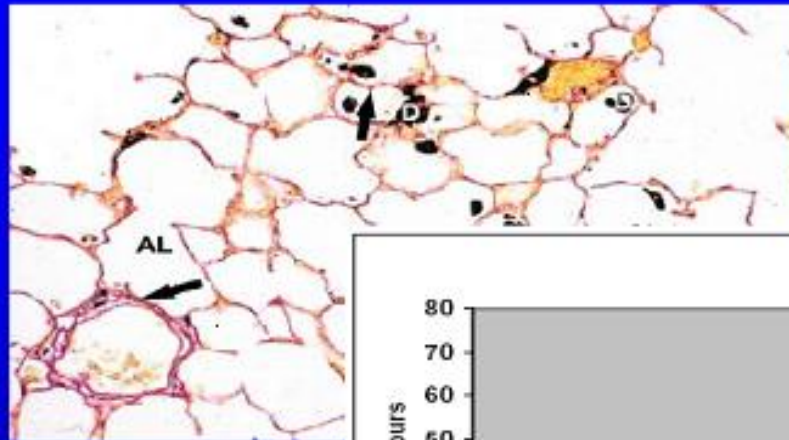
Alveolar and cellular translocation



Particle size (nm)	Type	Translocation	Localization/Effect	Reference
5-20 nm	Gold, albumin coated	yes	via caveolae	Mehta <i>et al.</i> , 2004
8 nm	Gold, albumin coated	yes	via "vesicles"	König <i>et al.</i> , 1993
8 nm	Gold, albumin coated	yes	via caveolae	Heckel <i>et al.</i> , 2004
18 nm	Iridium	yes ^A	Extrapulm. org.	Kreyling <i>et al.</i> , 2002
30 nm	Gold	yes	Platelet	Berry <i>et al.</i> , 1977
35 nm	Carbon	yes	Liver	Oberdörster <i>et al.</i> , 2002
60 nm	Polystyrene,	yes ^B	Thrombus, early	Nemmar <i>et al.</i> , 2002, Silva <i>et al.</i> , 2005
60 nm	Polystyrene	?	No thrombus	Nemmar <i>et al.</i> , 2002
80 nm	Iridium	yes ^A	Extrapulm. org.	Kreyling <i>et al.</i> , 2002
240 nm	Polystyrene, lecithin	yes	Monocyte	Kato <i>et al.</i> , 2003
240 nm	Polystyrene, uncoated	no		Kato <i>et al.</i> , 2003
400 nm	Polystyrene	no	Thrombus, late	Nemmar <i>et al.</i> , 2004

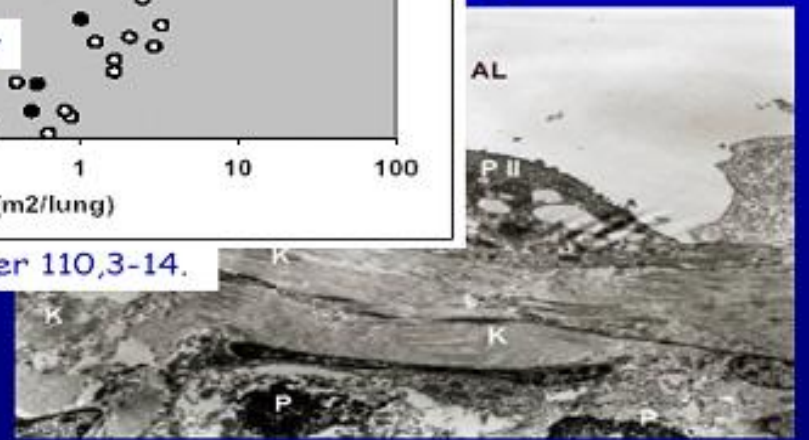
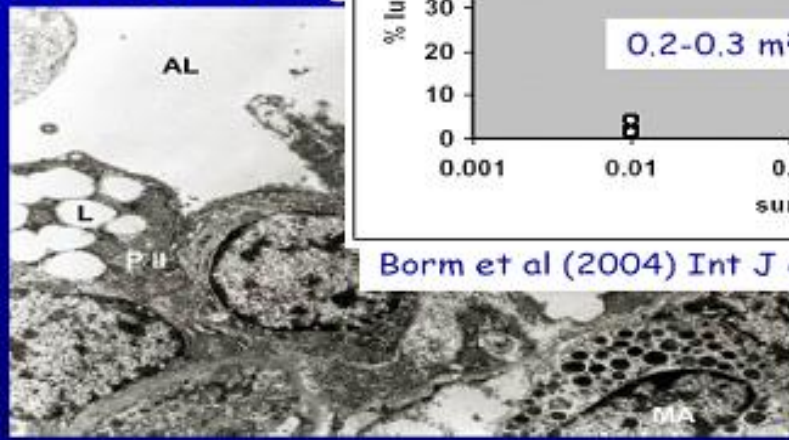
A = minimal; B = indirect evidence

Intra cellular translocation of diesels nanoparticles

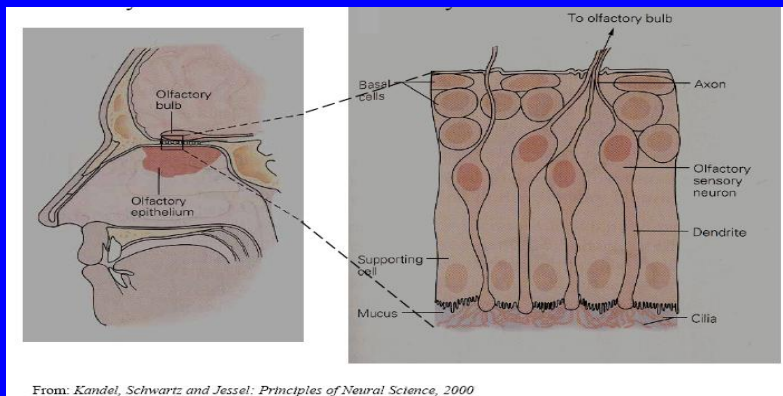


Borm et al (2004) Int J cancer 110,3-14.

Diesel 15 mg

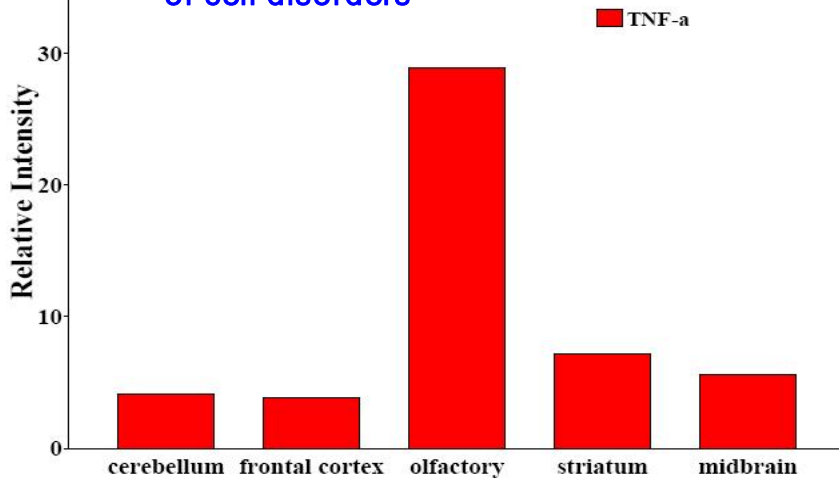


Translocation through olfactory l'epithelium ?



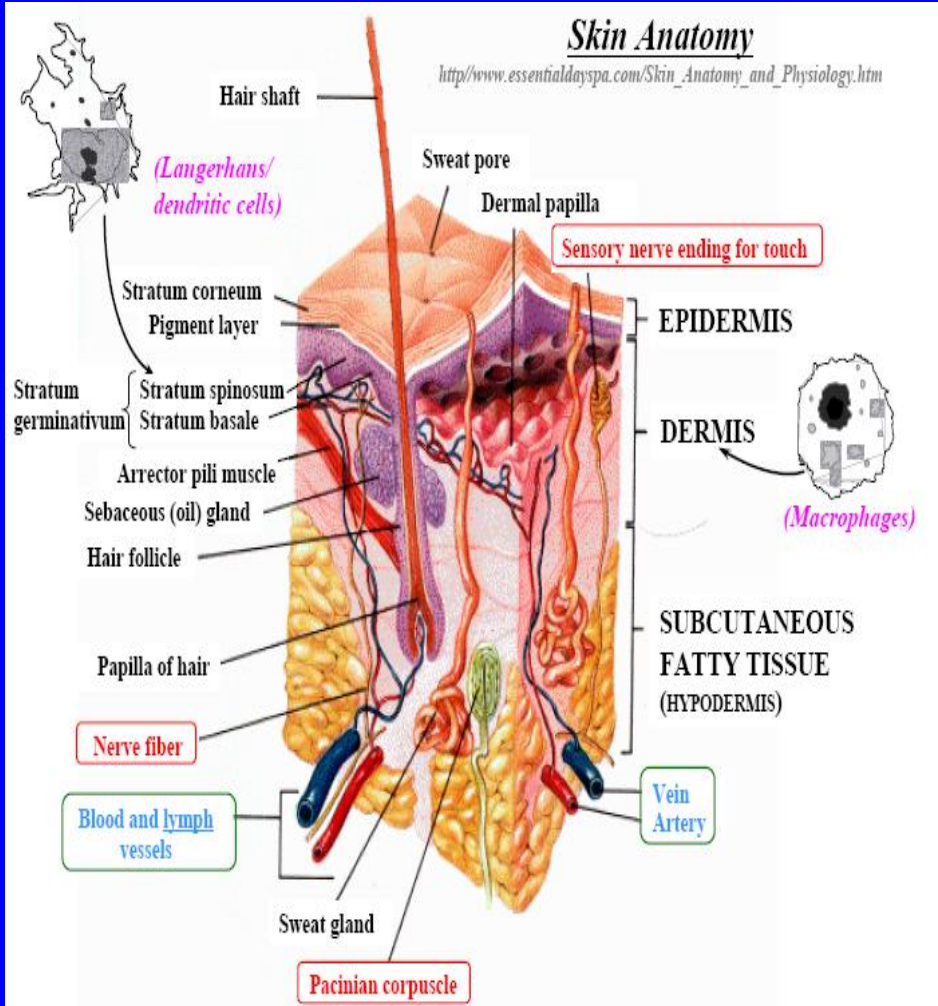
From: Kandel, Schwartz and Jessel: Principles of Neural Science, 2000

TNF: Tumor Necrotic Factor = indicator of cell disorders

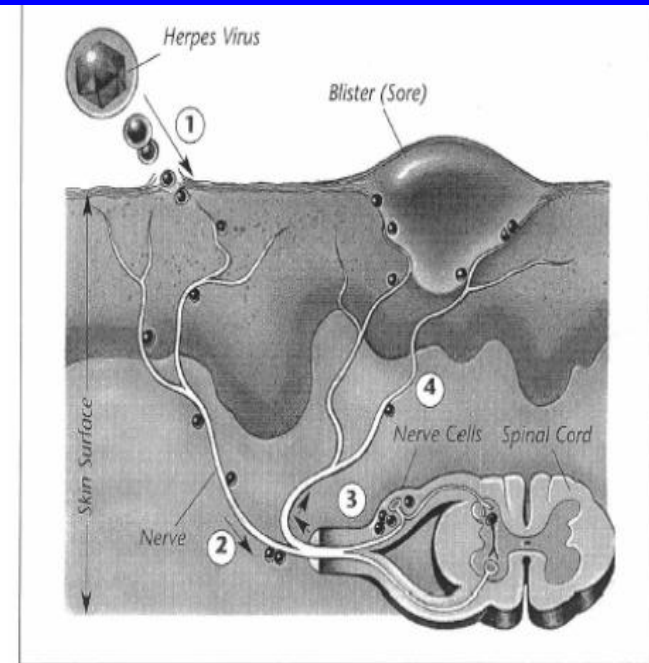


- 1941: *Bodian and Howe*: **Olfactory** axonal transport of Polio-virus (30 nm) after intranasal instillation in chimpanzee. Transport velocity: **2.4 mm/h**
- 1970: *de Lorenzo*: **Olfactory** axonal transport of 50 nm colloidal gold after intranasal instillation in squirrel monkey. Transport velocity: **2.5 mm/h**
- 1998: *Hunter and Udem*: Rhodamine-labelled 40 nm microspheres translocation via sensory nerves of **TB region** to ganglion nodosum in hamster after intratracheal instillation.
- 1999: *Hunter and Dey*: Retrograde tracing of **trigeminal** neurons from nasal epithelium with Rhodamine-labelled ~40 nm microspheres after intratracheal instillation.
- 2004: *Oberdörster et al.*: ¹³C particles (CMD ~36 nm) translocation to **olfactory** bulb after inhalation exposure in rats.
- 2006: *Elder et al.*: Mn-oxide particles (CMD ~30 nm) inhalation exposure in rats; increased Mn and inflammatory response in **olfactory** bulb.

Translocation of nanoparticles through the skin ?



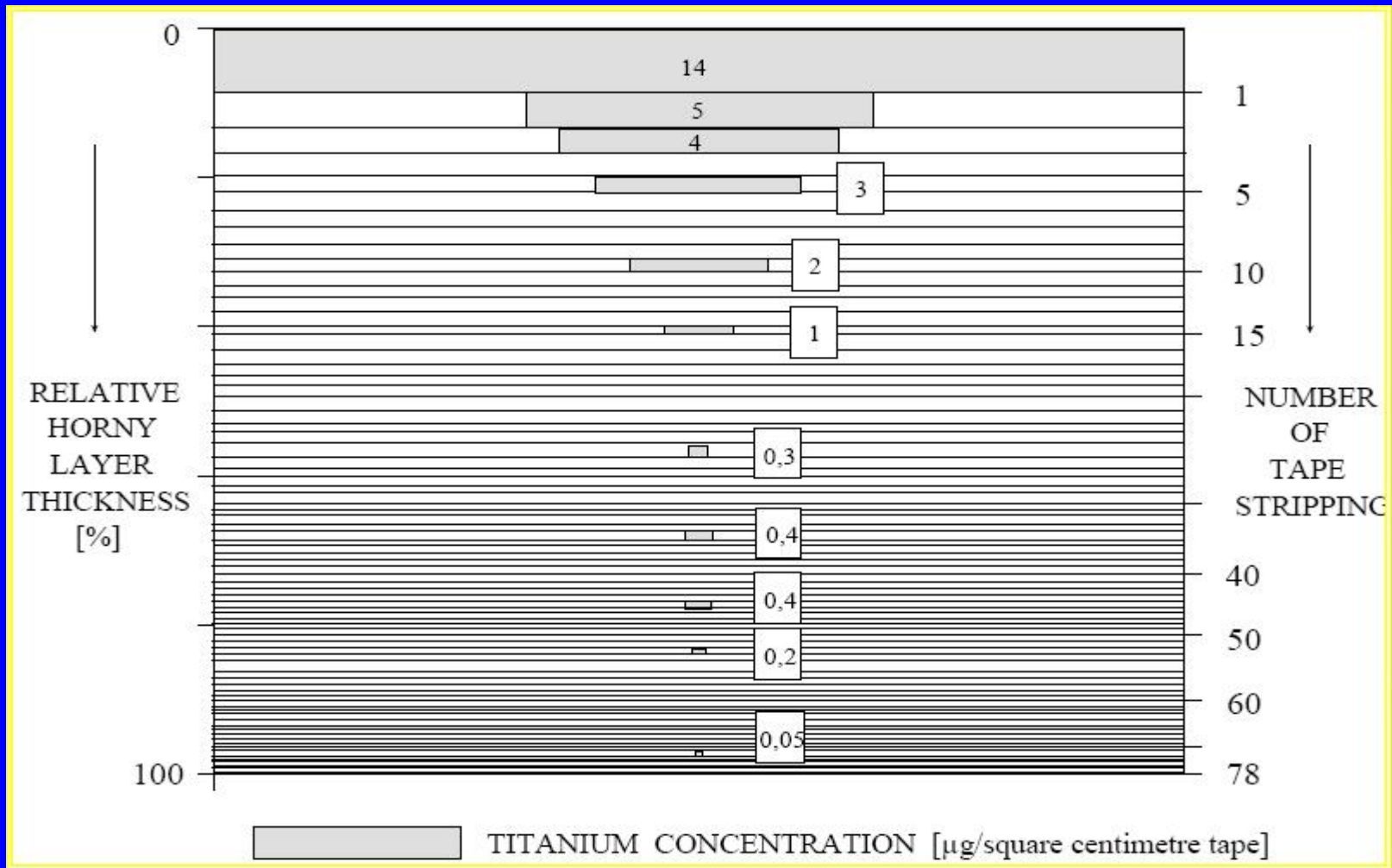
Is translocation of nanoparticles using the same ways than virus ?



The herpes virus passes through your skin (1). It travels through your body (2) and settles at nerve cells near your spine (3). When something triggers a new bout of herpes, the virus leaves its resting place and travels along the nerve, back to the surface of the skin (4).

from: "Planning your Pregnancy and Birth" 3rd Ed. American College of OB/GYN

No percutaneous penetration of TiO₂



Lademann et al., 1999

Dispute on the percutaneous penetration of nanoparticles

→ No passive percutaneous translocation « in vivo » in human.

(Pflücker et al 2001, Alvarez-Roman et al., 2004), and Stracke et al. (2006)

→ Possible percutaneous translocation (Hoet et al., 2004; Oberdörster, 2005, Shim et al. (2004)

- minimum by mechanical action

(Tinkle et al. 2003, Cormier et al., 2001;Teichmann et al., 2006)

- minimum on abraded skin (Gopee et al. (2006)

- minimum through hair follicles (Lademann et al., 1999)

Conclusion : necessity of further investigations for passive percutaneous translocation through human skin of nanoparticles (size <10 nm) like quantum dot

According to exposure conditions.(Ryman-Rasmussen et al (2006)

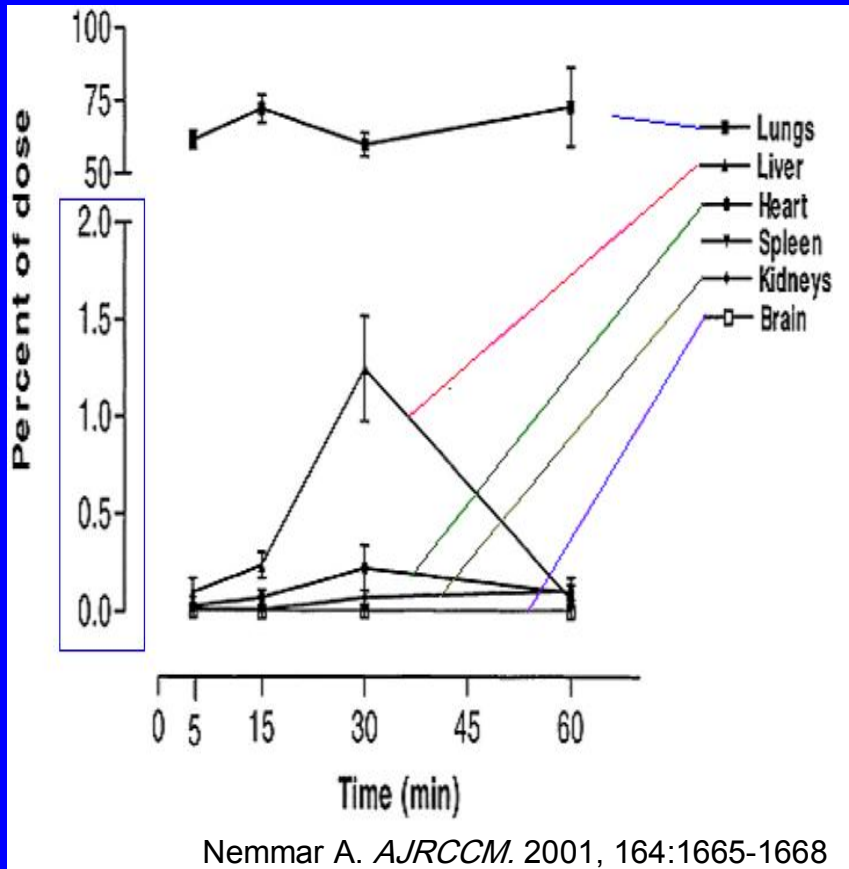
Digestive absorption of nanoparticles

- High daily absorption of nanoparticles and microparticles (0.1-3 μm) through the digestive tract.
- Estimation de 10^{12} - 10^{14} particles per day in occidental world mainly silicates and titanium dioxide from food and toothpaste (Lomer et al. 2004).
- Translocation through the digestive mucosa :
 - by M cells covering Peyer's patches,
 - by the lymphoid follicles, and by the intestinal epithelium

Systemic translocation through the lung

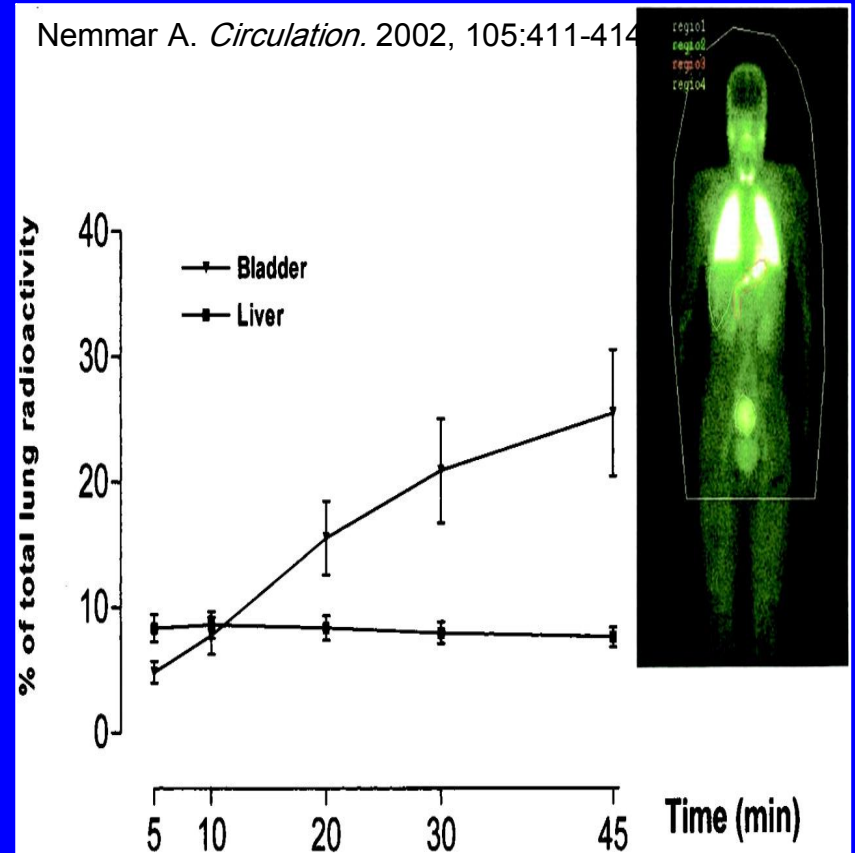
In hamsters

Albumine particles (diamètre < 80 nm)
labelled ^{99m}Tc Intra Tracheal administration



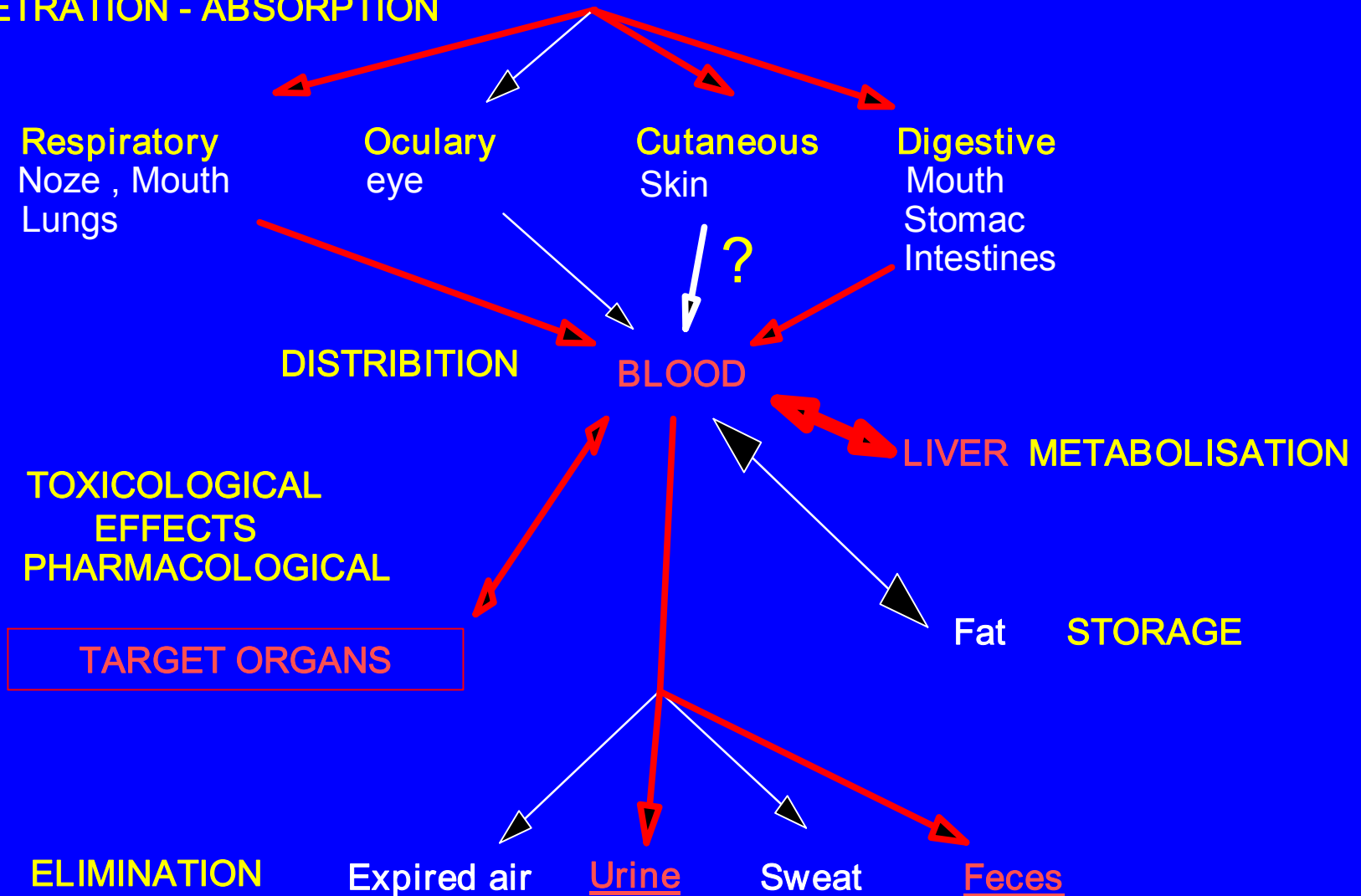
In Human volunteers

Carbon black particles (diameter 5 - 10 nm)
labelled ^{99m}Tc Technetium



Nanoparticles body cycle?

PENETRATION - ABSORPTION



Questions in Hygiene & Environment

- How to characterise the nanoparticles ?
 - Composition, structure, size distribution, surface , weigh , ???
- What are the biological and toxicological effects ?
- How to control the exposures ?
- What type of exposure protection is safe ?
 - Adaptation of the todays procedures ?
 - Total confinement of the plants and laboratories ?
- Are the downstream users exposed ?
- How to handle the wastes ?
- How to protect the environment ?

Impact of the physical properties of nanoparticles

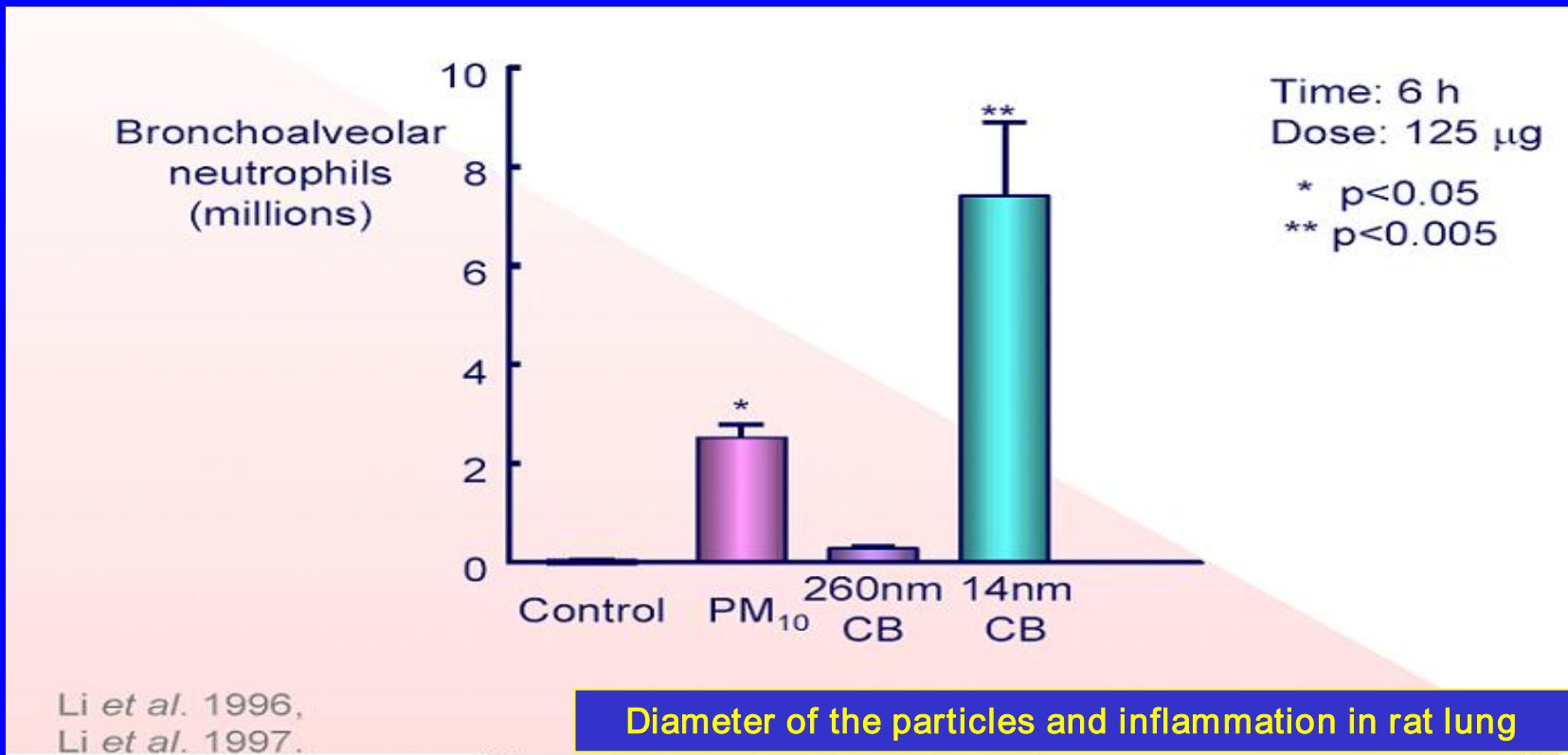
Size :Fines and ultrafines



Respiratory tract
penetration

Shape: (balls or fibers)

Cell transfert



Impact of the composition of the particles

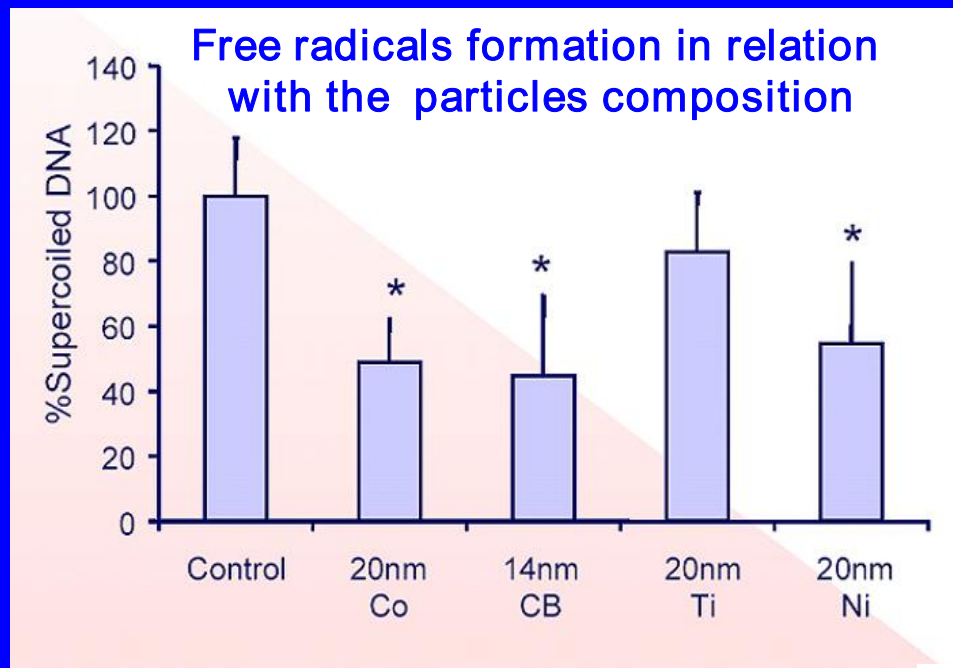
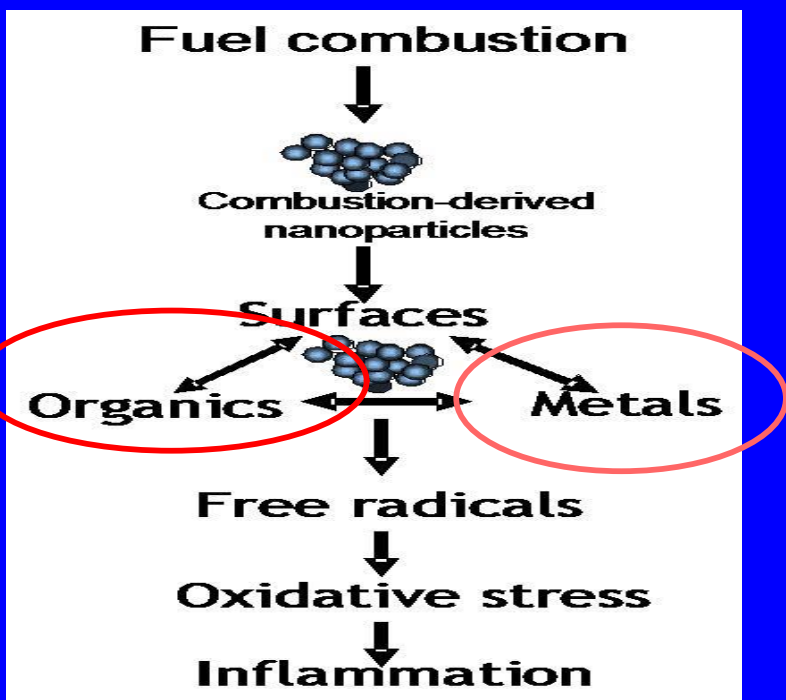
Composition :

organic components (endotoxines, bactéria) →
inorganic components : Fe, V, Zn
biological components (s, pollens)

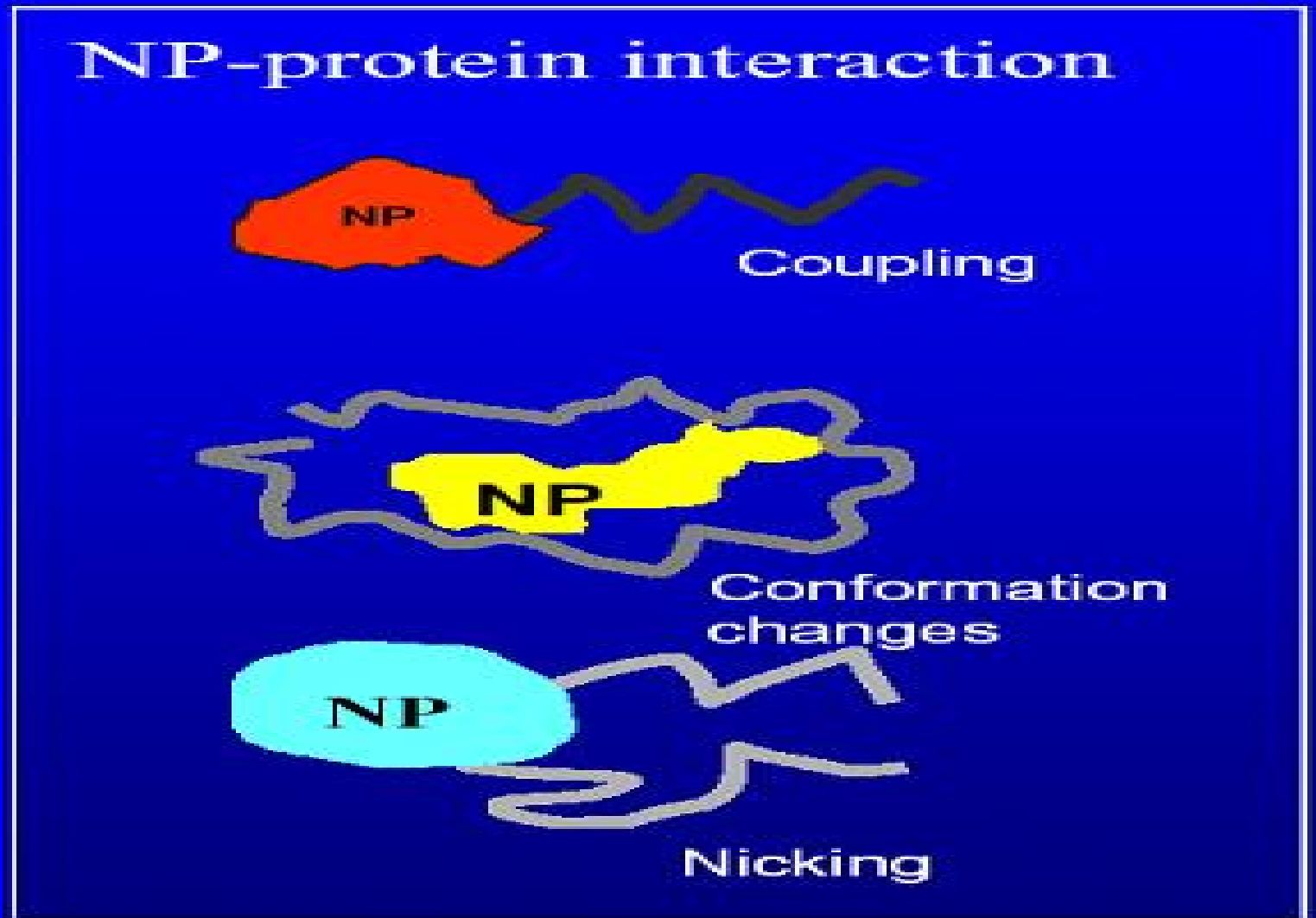
Oxydative Stress

Inflammation

Cytotoxicité



Nanoparticles and intracellular proteins Interactions



Immunotoxicity ?

- Manmade nanoparticles in ambient air :
 - high adjuvant properties → increase the lung reactivity to allergenes in relation with the decreased size of the particles
- Studies in human volunteers:
 - The lung inflammatory reaction caused by nanomatériaux, influences the severity of allergic reactions
 - Severity of the reactions depending of the exposed individuals (atopics / non-atopics).

(De Haar et al. 2006, Steerenberg et al. 2006, Granum and Lovik 2002, Nygaard et al. 2004, Alessandrini et al. 2006),

→ Similar question for cutaneous allergy

Cardiovascular Toxicity ?

The translocation of nanoparticles from the lung to the blood may

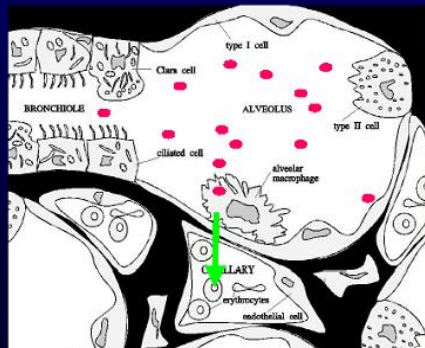
- increase of the blood viscosity
- create blood vessel's walls inflammation
- thrombosis
- Impairment of the cardiac function
- **Infarctus risk**

Hypothesis 1

HOET

inhaled particles:

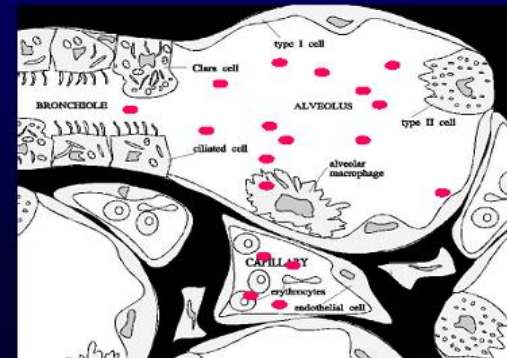
- pulmonary inflammation
- + systemic release of mediators



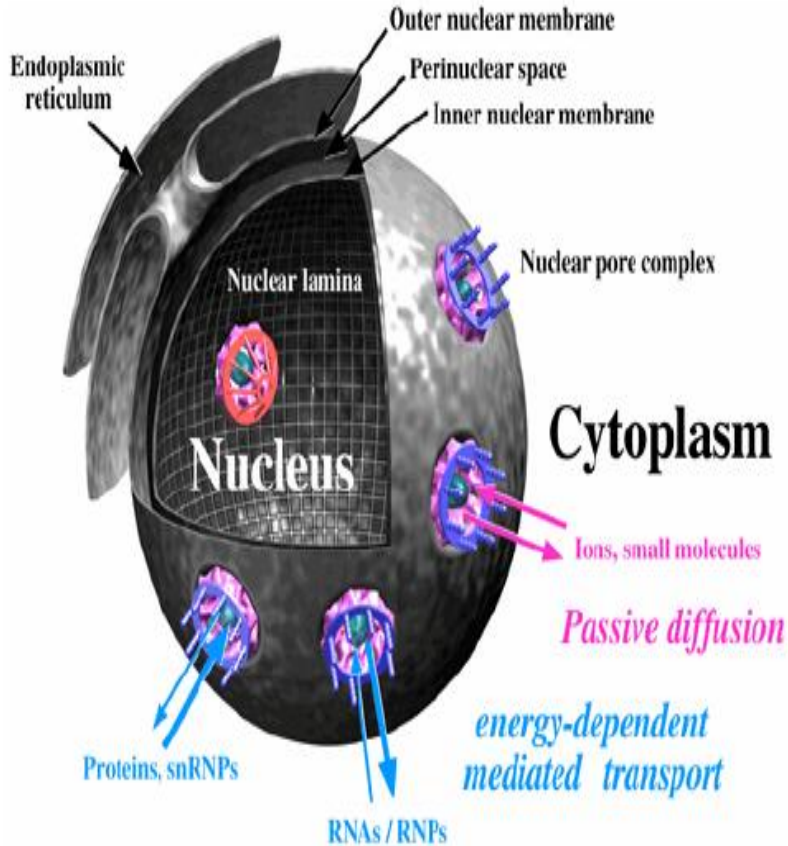
Inflammatory mediators

Hypothesis 2

- inhaled ultrafine particles ($\text{Ø} < 0.1 \mu\text{m}$)
- pass into the circulation
- “direct” effects on cardiovascular endpoint



Translocation into the cell's nucleus ?



Stoffler et al, 1999

Nuclear Import of Nucleoplasmin-coated Gold Particles into Oocyte nuclei via NPC

From: Panté and Kam, 2002

Functional Diameter of NPC:

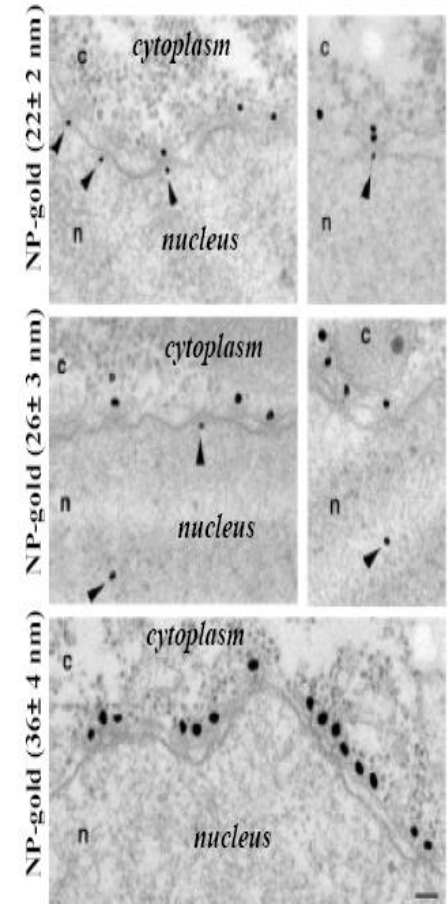
32.4 nm

38.4 nm

46.4 nm

Functional Nucleopore Diameter:

39nm

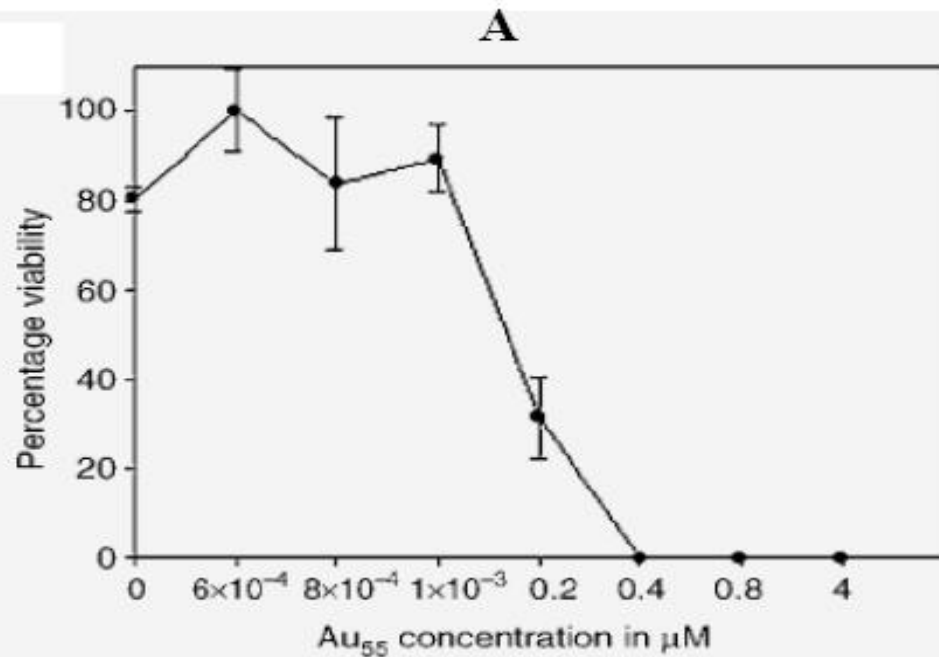


(Bar 100 nm)

DNA adducts of gold nanoparticles

Cellular Uptake and Toxicity of Au₅₅ Nanoparticles (1.4nm)

(Tsoli et al., 2005)

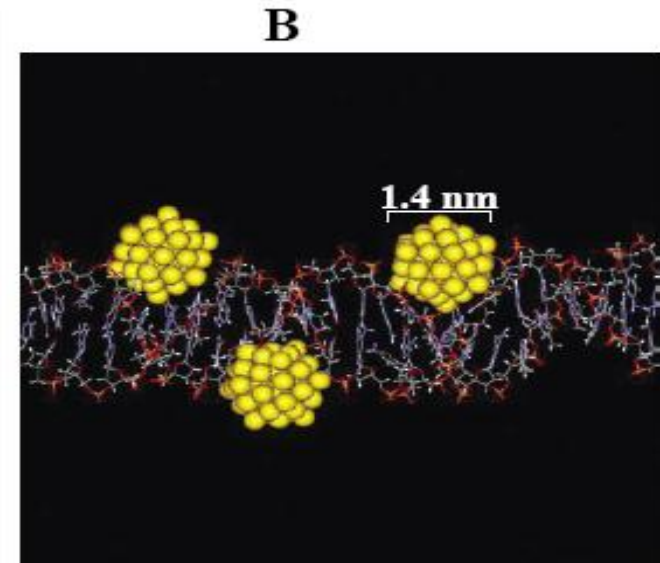


A: Cytotoxicity of Au₅₅ particles in BLM melanoma cells, 72h incubation

Cellular gold distribution:

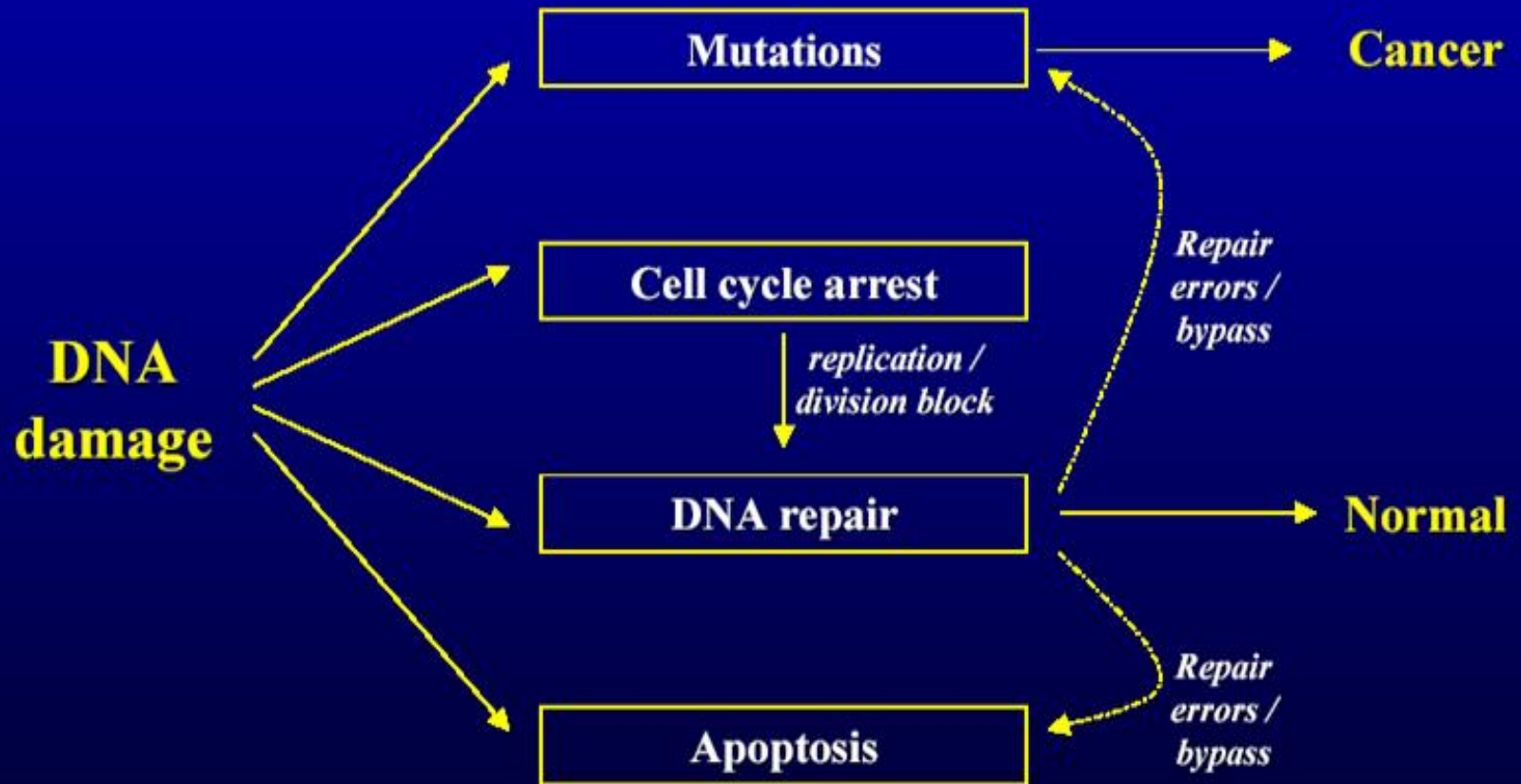
57.5% cytoplasm

42.5% cell nucleus (50% DNA)



B: Au₅₅ particles irreversibly attached to major grooves of B-DNA

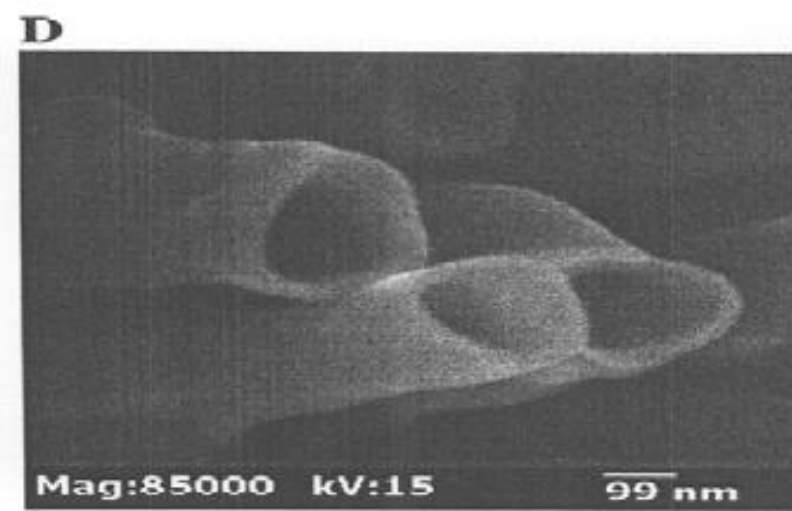
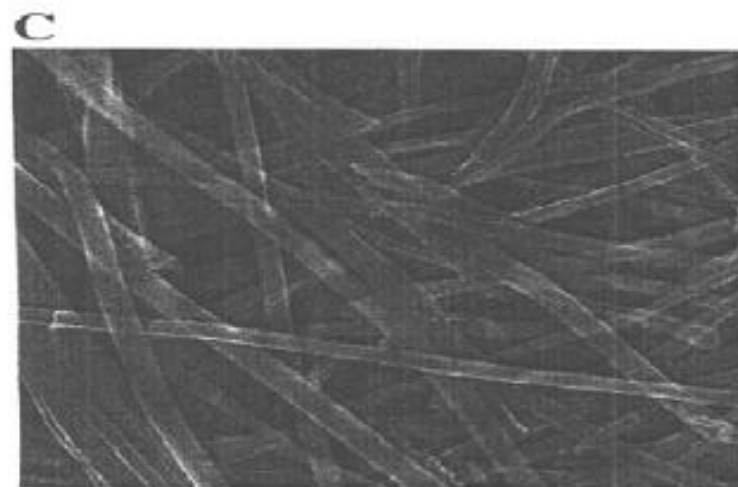
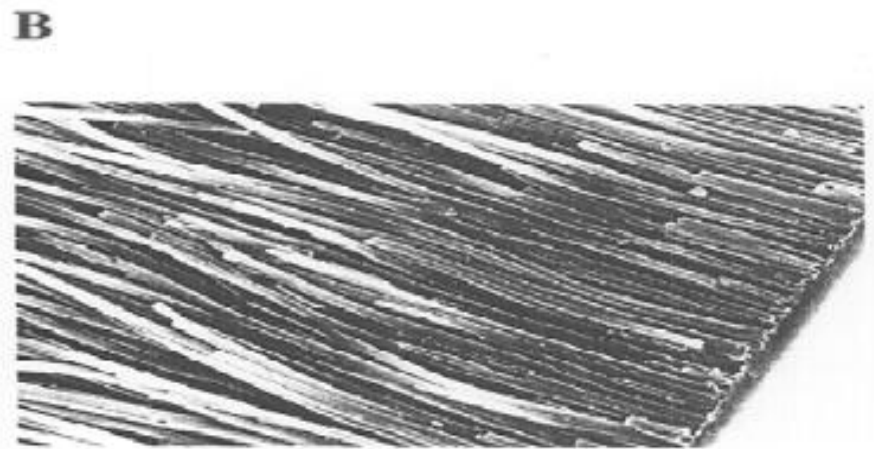
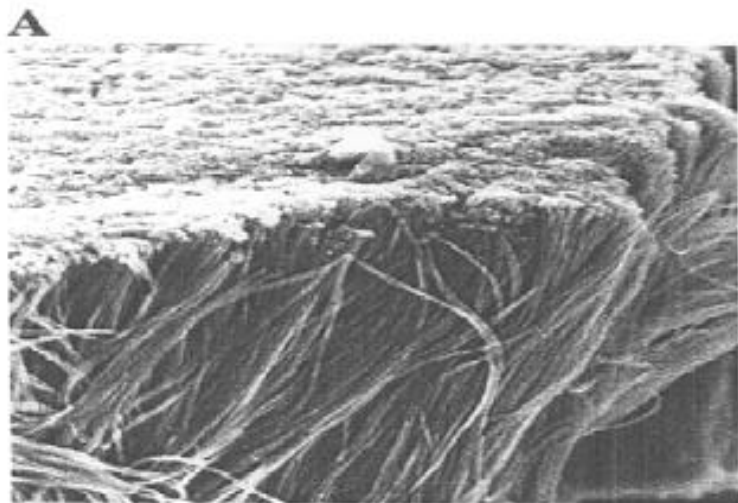
Cellular responses and/or consequences of DNA damage



Mutagenicity

- Penetration of the nanoparticles into sub-cellular structures
 - Into the mitochondrions (Li et al. 2003)
 - Into the nucleus (Chen and von Mücke 2005)
 - perturbation of cellular respiratory cycle
 - increase of the oxidative stress
 - interference with DNA replication and repair .
-
- DNA adducts of diesel or carbon black combustion produced nanoparticles (Borm et al. 2004)

Nanotubes / Nanofibers



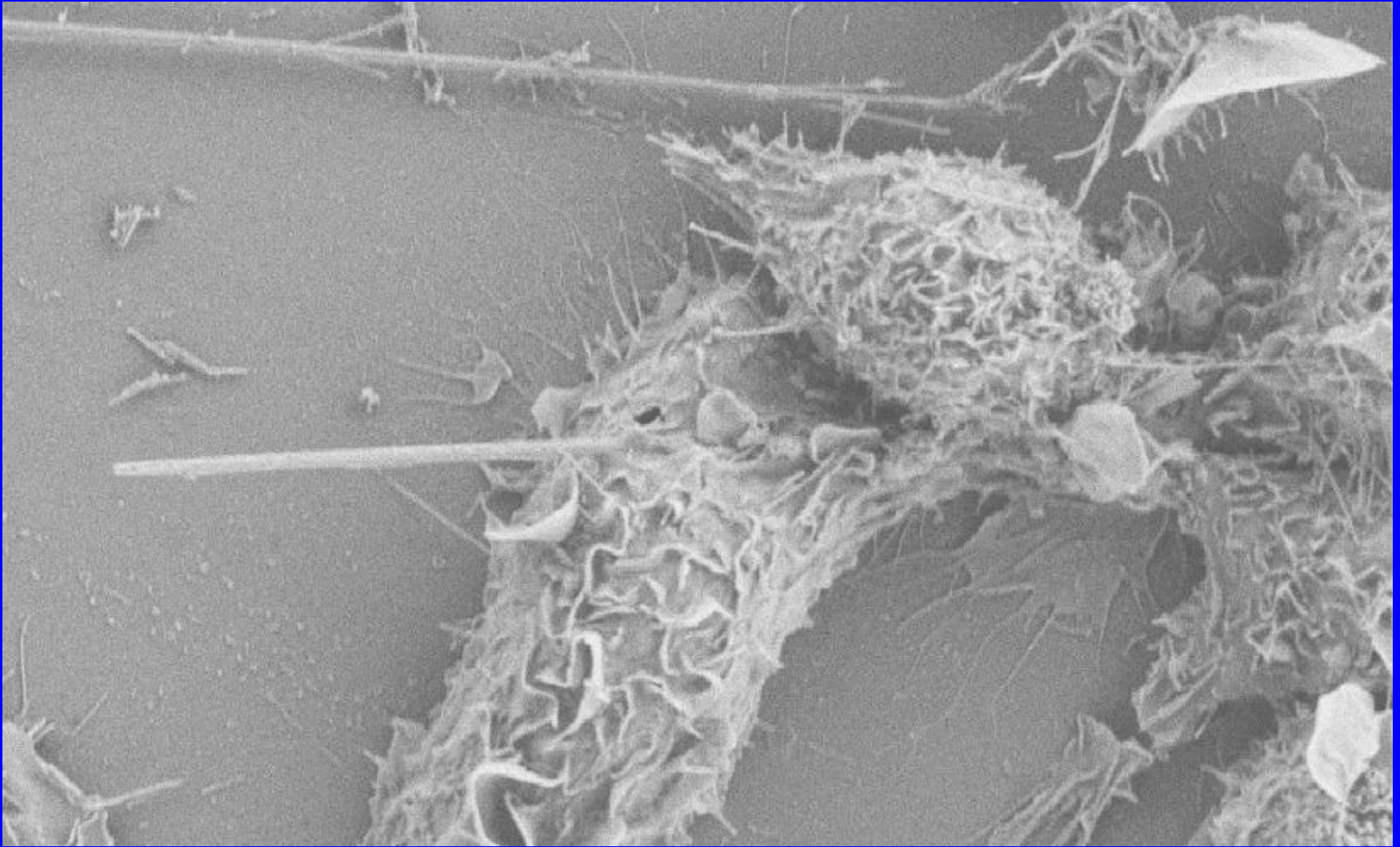
Questions on the nanotubes and the nanofibers

The nanofibers and the nanotubes have similarities in dimensions and physical properties than asbestos fibers

Are they a potential risk for human health ?

Sample	Diameter (nm)	Length (nm)	Aspect Ratio	Toxicity	Carcinogenicity
TiO ₂	120	-	-	No	No
Carbon black	75	-	-	No	No
Crocidolite asbestos	1000	14,000	14:1	Yes	Yes
Carbon fiber	150	60,000	400:1	Yes	?

Macrophage and Asbestos fiber



Pulmonary effects of carbone nanotubes

intra-tracheal Instillation in rat

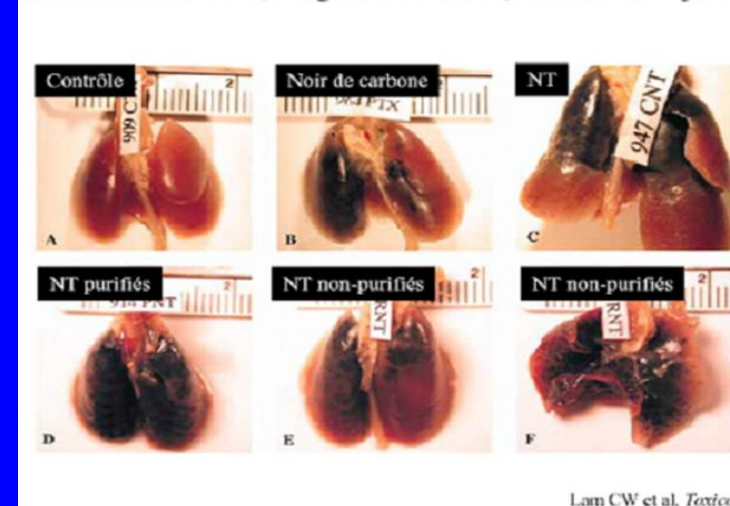
Non purified carbon Single wall nanotubes

- inflammation, épithelioïd granulomas and fibrosis formation.
(Warheit et coll. 2004 et Lam et coll. 2004)
- Fibrosis mechanism resulting of the direct activation of pulmonary fibrocytes.
(A.Shvedova 2005)
- No trans-alveolar transfer

- Purified Nanotubes soluble in water

- No cytotoxic effects (Isobe et coll 2006)
- Inflammatoiry effects due to
chemical impureties (nanofibers,
carbon nanoparticles, catalytic metals) (JT. James 2005)

Inoculation IT de 0,5 mg de nanotubes, examen à 90 jours In Mice



Lam CW et al. *Toxicol. Sci.* 2004, 77:126-134

Carbon Nanotubes / Asbestos

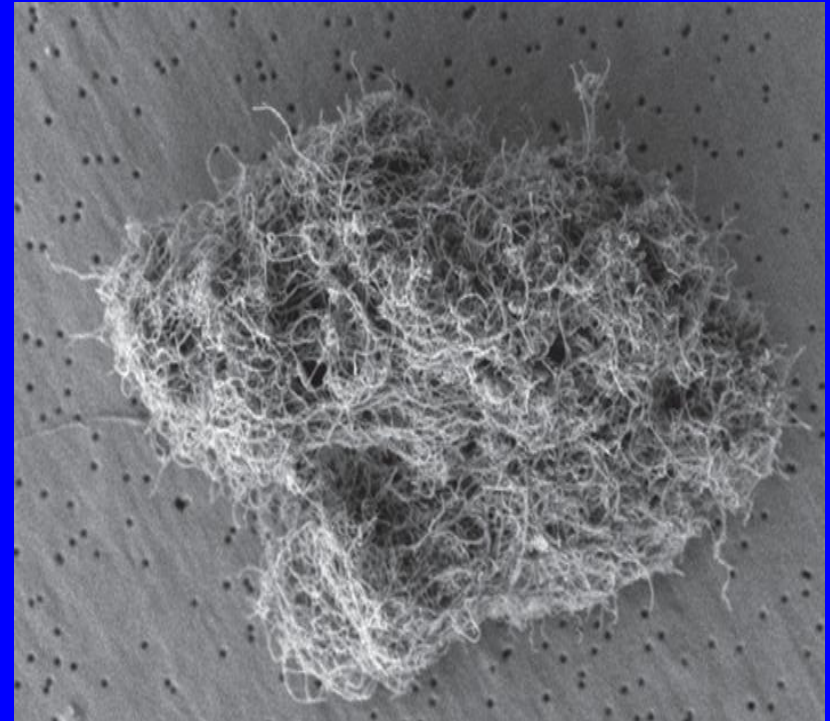
The nanotubes are flexibles

→ Impossibility to transfert through the alveolis into the la pleura.

Agglomeration in balls in the alveoly

→ Increase of the pulmonary persistence

→ Alvéolar fibrosis

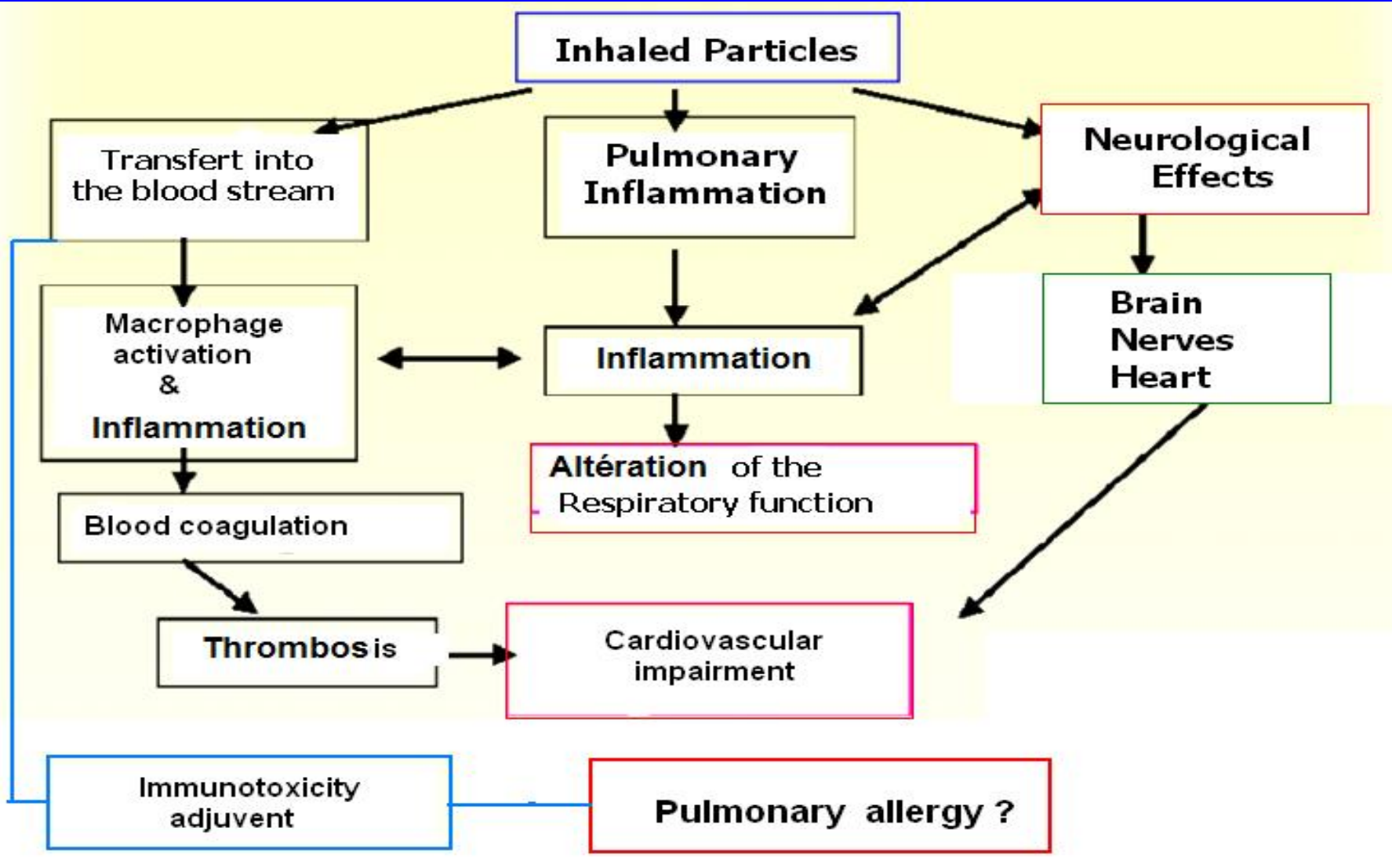


Agrégates of purified SWNT (134 nm) dispersed in water are 10 times less cytotoxic than silica particles (Isobe et coll 2006)

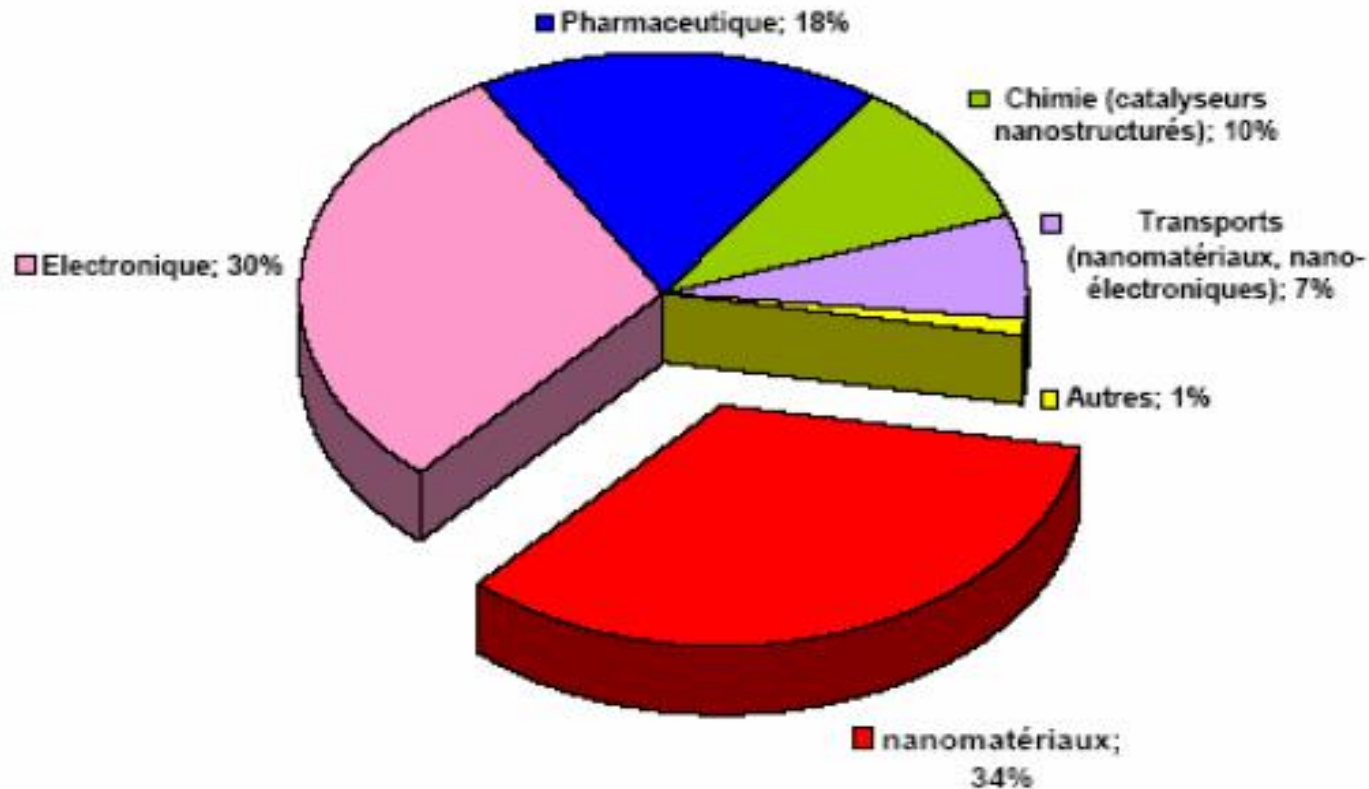
Summary of the biological effects of the Nanomaterials

- May be responsible of the increased mortality rate in population exposed to Ultra fines particles
- May induce pulmonary inflammation by ROS formation
- May transfer through the alveoli and migrate into the blood and lymph
 - Into the liver and the spleen
 - Into the kidneys
 - Into the brain
- Increase of the blood viscosity
- May provoke blood vessels thrombosis
- May be Ecotoxic

Summary of the biological effects of Nanoparticles



% of economic impact of nanotechnologies in 2010



(Développement et Conseil, 2004)

Metallic nanoparticles utilisation

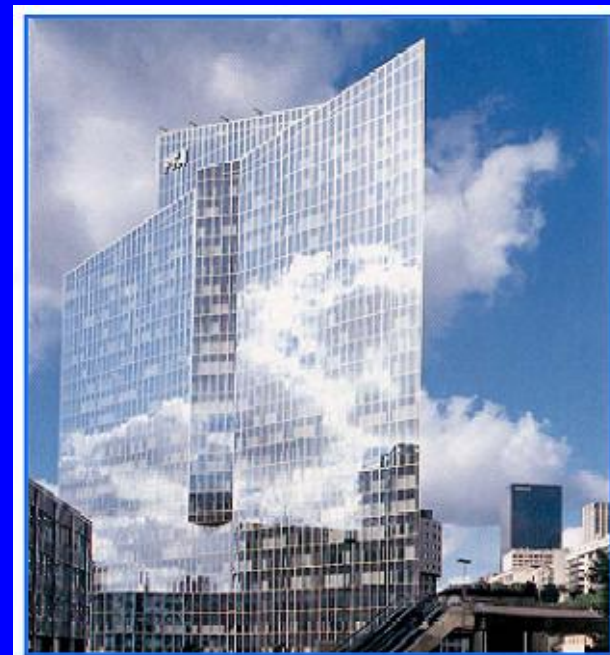
TiO₂ depollution



Insulation

Couche d'argent (<20nm)

verre



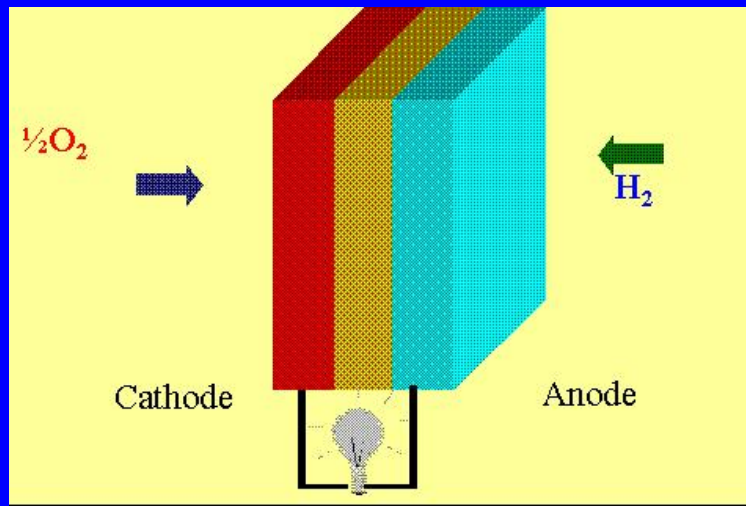
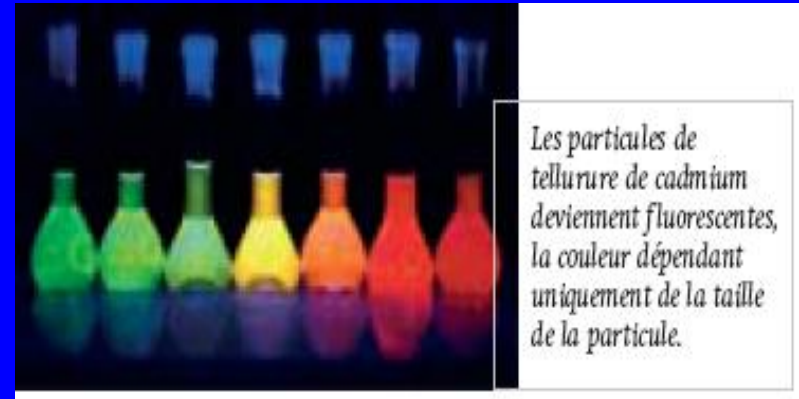
Gold nanoparticles



Nanomaterials utilisation

This way, Nanofuturism looks good...

- Catalysts and nano membranes for better fuel cells
- Nanofilms for water-repelling windshields
- Distributed solar cells using conformable photovoltaics
- Ceramics with improved catalysts for reduced emissions
- High-brightness nano-enhanced polymer displays
- Tens of sensors incl. oxygen, temp., pressure, magnetic field, acceleration
- Nanopowders and coatings for more durable paint
- Fast-charge batteries for hybrid cars
- Lighter, tougher tires; nanoclays to improve tire gas barriers
- Carbon nanotube alloys for lighter, tougher frames
- Polymer composite panels for greater stiffness and toughness

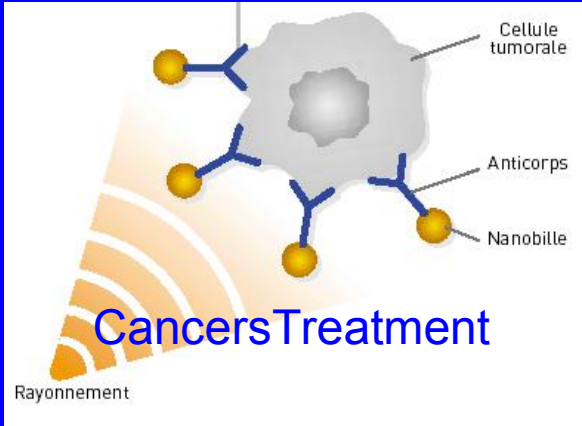


Energy Technologies

Medical Utilisation



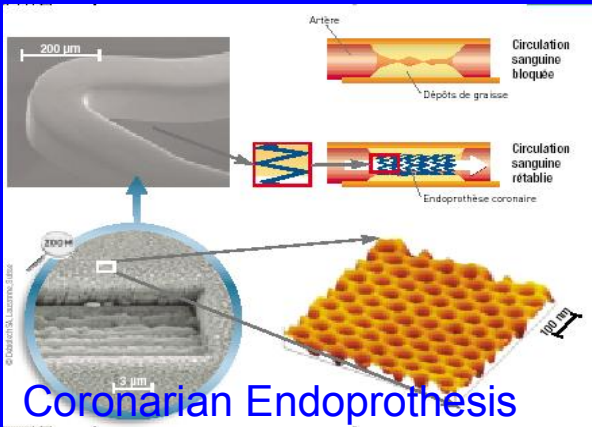
Prothesis



Cancers Treatment



Nanodrugs

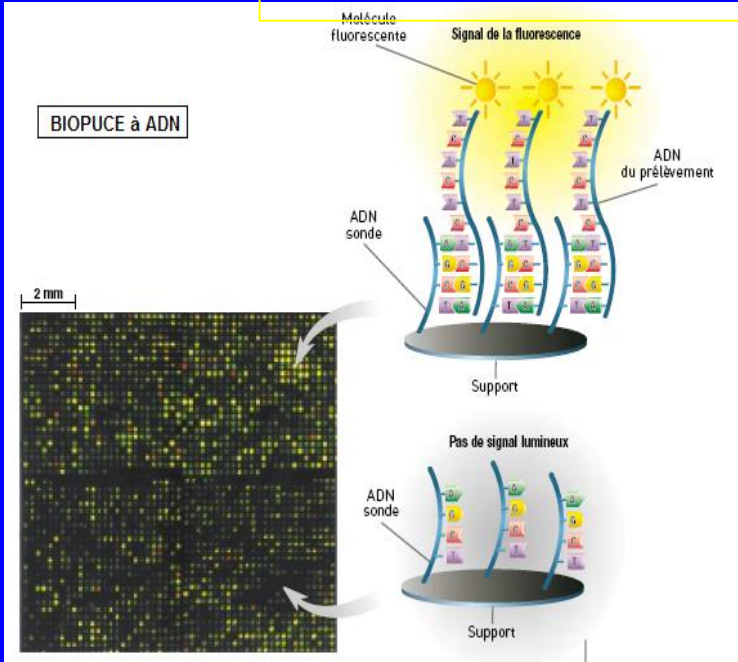


Coronarian Endoprothesis

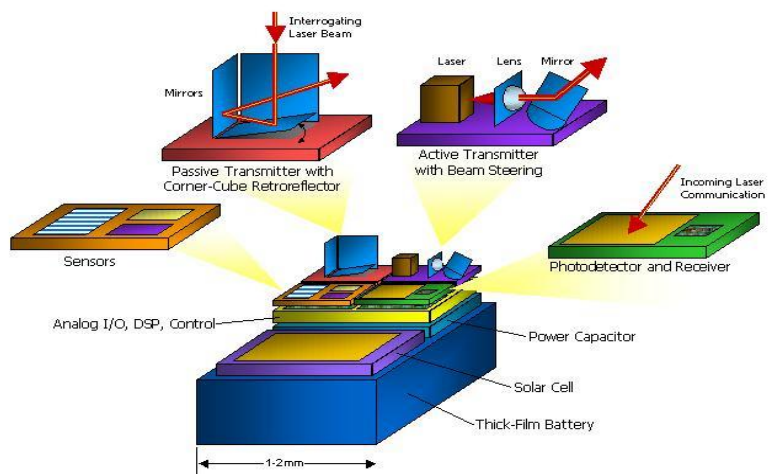
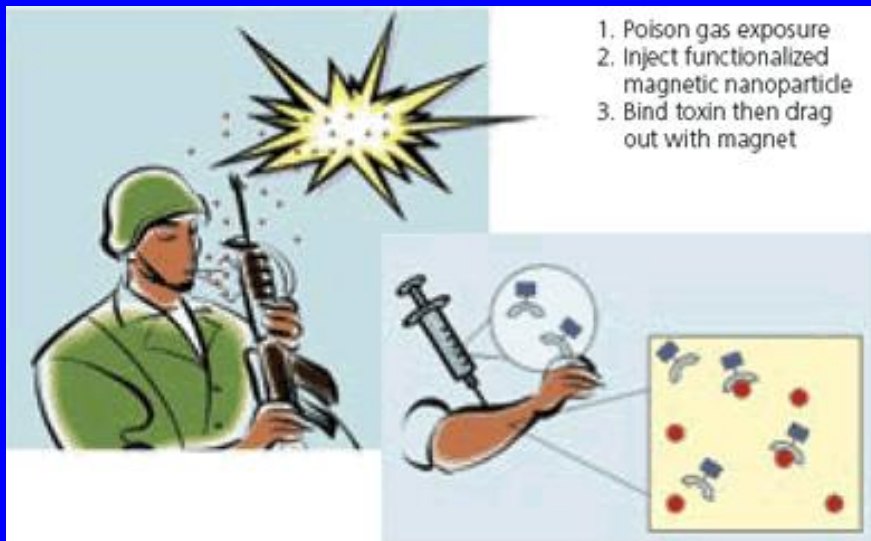
Non-viral genique therapy



Micro laboratories



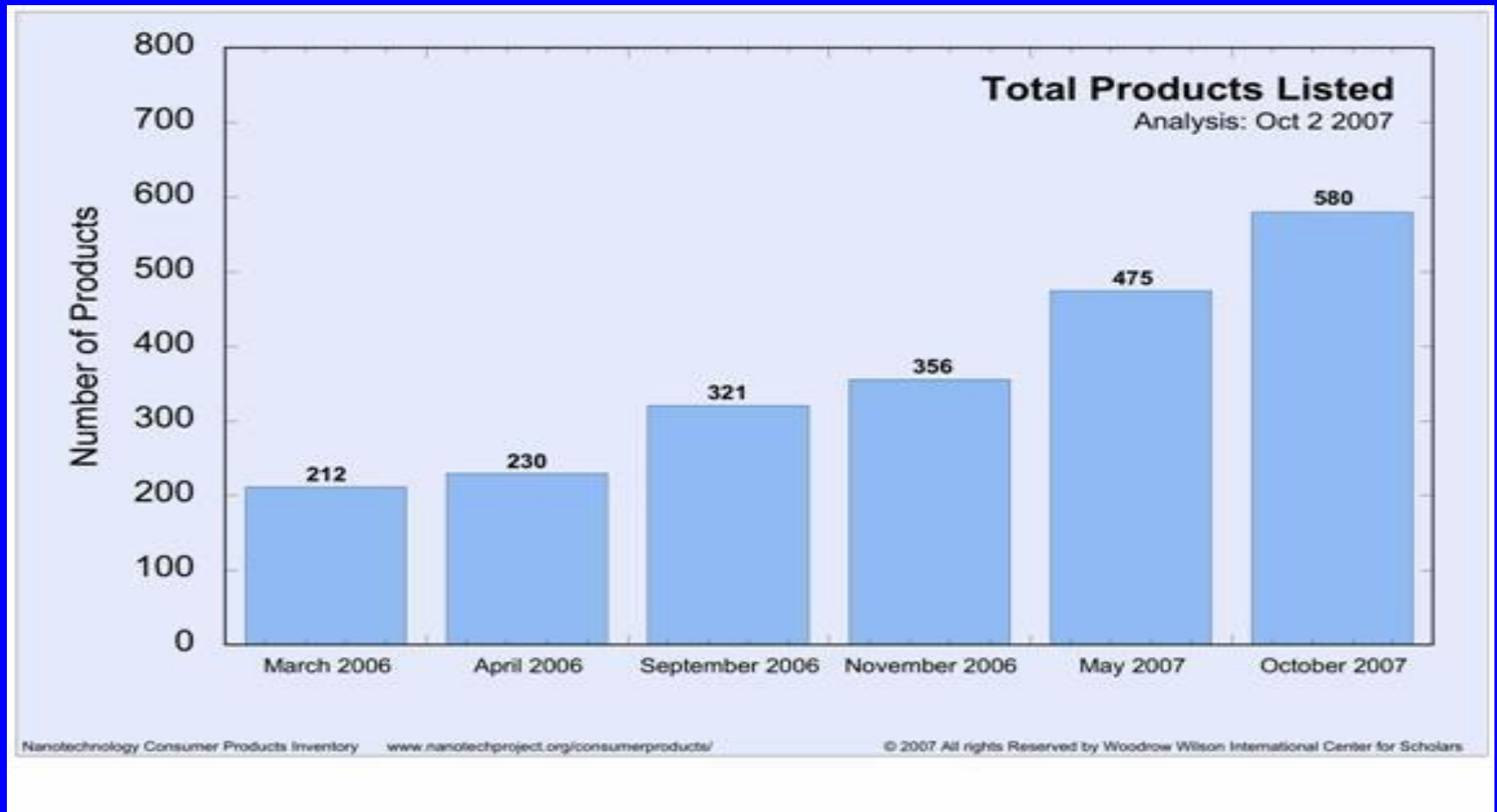
Military utilisation



Smart dusts



Consumer products



Source: Nanotechnology Consumer Products Inventory, Woodrow Wilson International Center for Scholars. www.nanotechproject.org/consumerproducts

Nanotechnologies by products categories

Source: Nanotechnology Consumer Products Inventory, Woodrow Wilson International Center for Scholars. www.nanotechproject.org/consumerproducts

Consumer products with nanomaterials in EU 2006

Category	Sub category	Examples of products
Textiles and shoes	Clothing	<i>Socks, pants, shirts, pullovers, vests, shorts (also water shorts), jackets, elbow and knee guards, underwear, gloves, cap, ear bands, earmuffs, scarf's, ties, heal cushions</i>
	Other textiles	<i>Sheets, bedding and mattresses, pillows and cushions, umbrellas, suitcases and bags, plush toys, other fabrics</i>
	Shoes	<i>Insoles, shoes</i>
Filtration, purification, neutralisation and sanitisation	Air or water filtration and purification	Air filtrations and purification devices, masks and respirators, water filtration or purification devices
	Air conditioning	<i>Air Conditioning and heating systems</i>
	Sanitizers and neutralisers	Air Sanitizers or neutralizers, chemical (gas/liquid) neutralisers
Miscellaneous	Coatings	<i>Anti fogging coatings, self-cleaning coatings, water and dirt repellent and antibacterial, waxes, lubricants, protective layers for displays (anti-scratch)</i>
	Others	Diamonds, watch chain (anti-bacterial), sunglasses

* Products printed in italic are known or expected to be available on the European market

Category	Sub category	Examples of products
Electronics and computers	Mobile (audio) devices	<i>MP3 players, mobile phones</i>
	Large household appliances	<i>Refrigerators, washing machines, irons, vacuum cleaners</i>
	Computer hardware	<i>Processors and chips (e.g. game consoles), memory- and hard disks, cooling fans, computer mouse</i>
	Displays	<i>LEDs in flashlights, OLEDs in displays</i>
	Energy related	<i>Solar cells, batteries</i>
	Ink and paper	<i>Ink for electronic applications, photo paper</i>

Motor vehicles	Exterior	<i>Glass and windshields, painted or coated exteriors, tyres</i>
	Other	<i>Engine oils, fuels and catalysts</i>
Sporting goods	Rackets and sticks	<i>Rackets, bats, golf clubs, hockey sticks, skis, snowboards, bicycle frames and other bicycle parts</i>
	Balls	<i>Bowling balls, tennis balls, golf balls</i>
	Other	<i>Wetsuit, fishing lure, horse shoes</i>

Category	Sub category	Examples of products
Household products and home improvement	Cleaning products	Dish, hand and fruit washing emulsions, rubber gloves, <i>disinfectant sprays or liquids</i> , fabric softeners, <i>lens, display and optics cleaners</i> , odour removers
	Cooking utensils and kitchenware	<i>Cutting boards, table-, cooking and kitchen ware</i> , teapots, porcelain, baby mugs, baby milk bottles, bottle brushes, frying oil reforming catalytic devices, bowls (also for pets), food storage containers (anti-bacterial), food storage bags, <i>plastic or aluminium wrappings</i>
	Construction materials	Locks, door knobs, handles, water taps (anti-bacterial), <i>glass (self-cleaning)</i> , wooden floors, <i>cement and concrete products</i> , toilets, tiles
	Paint	<i>Paint (kitchen, bath, insulation, radio frequency blocking)</i>
Personal care products and cosmetics	Sun cosmetics	<i>Sunscreen lotions, sunscreen creams, sunscreen oils, sunscreen powder, hair protection spray</i>
	Baby care products	Baby sunscreen, pacifiers
	Hair care	Shampoo, conditioner, hair gel/styling products, hair re-growth products
	Skin care	<i>Razors, facial masks, facial steamers, skin creams/lotions/oils/sprays/powders</i> , deodorant, whitening lotions, <i>fragrances</i> , wet wipes, soaps, body wash, shower gels, etc.
	Oral hygiene	<i>Tooth paste</i> , teeth cleaner, tooth brush
	Make-up and nail care	Make-up instruments and brushes, make-up removal and cleaning products, lipstick, mascara, make-up base and foundations, blush
	Over the counter health products	<i>(Sticking)plasters, home pregnancy tests, thermal patches, joint and muscle pain relief cream, condoms, mosquito repellent</i>

Carbon nanotubes utilisation



NanoSolve™ in Easton Sports bike components



BABOLAT

Matériaux composites
Renfort de polymères



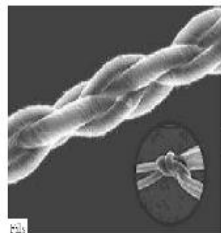
CEA - LETI

écrans plats à émission
de champ

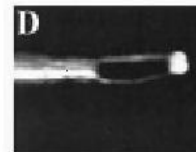
BMC Pro Machine SLC 01



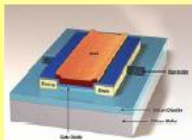
BMC's new full carbon bicycle frame uses Easton's Carbon Nanotube technology and beefy tubes to create a stiff and comfortable ride. Story at VeloGoGo



Nano-conteneurs
Transport de médicaments



NEMS



Électronique souple
Nano-électronique



Pointes de microscope AFM

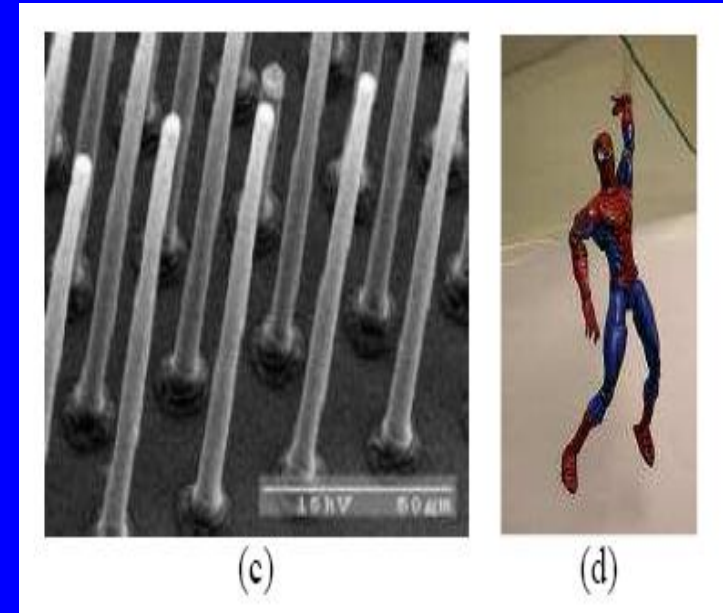
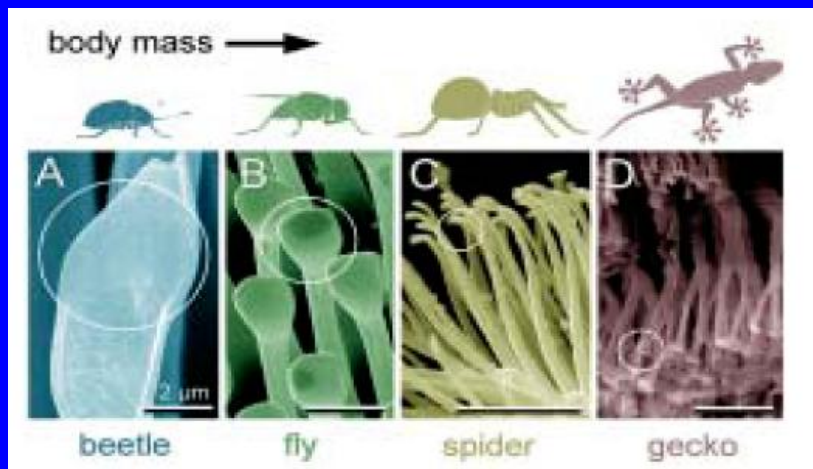


LifeStraw Offers Clean Water to Thirsty World

Nanotechnologies and nature



Effet lotus



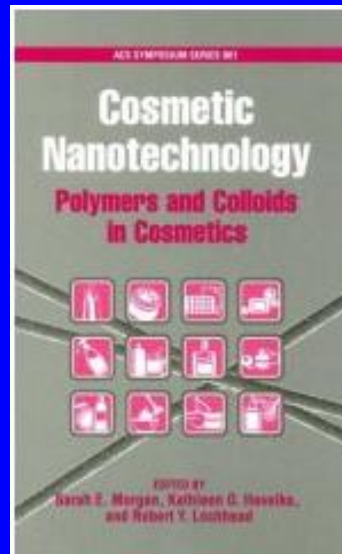
Les pattes du lézard Gecko (figure a) comportent 2 millions de filaments d'un diamètre de 5 micromètres, eux-mêmes constitués de 100 à 1000 nanofibres (figure b) d'un diamètre de 0,2 micromètres, soit 100 millions à un milliards de tels objets par animal. La figure c présente la structure artificielle biomimétique et la figure d, présente un jouet commercialisé aux Etats-Unis (masse 100g, 15 cm haut) – (Carnegie Mellon University)

Nanotechnologies and cosmetics

Plasma TiO₂ Compounded Multi-functional Cosmetics



Plasma TiO₂ Compounded Multi-functional Cosmetics



HAIR +POWER

Nanotechnology in the hair cosmetics with the use of nanospheres.

Hair +Power is a healing line with nanospheres which has been developed especially for people with head skin and hair problems (dandruff, seborrhea and thinning hair).

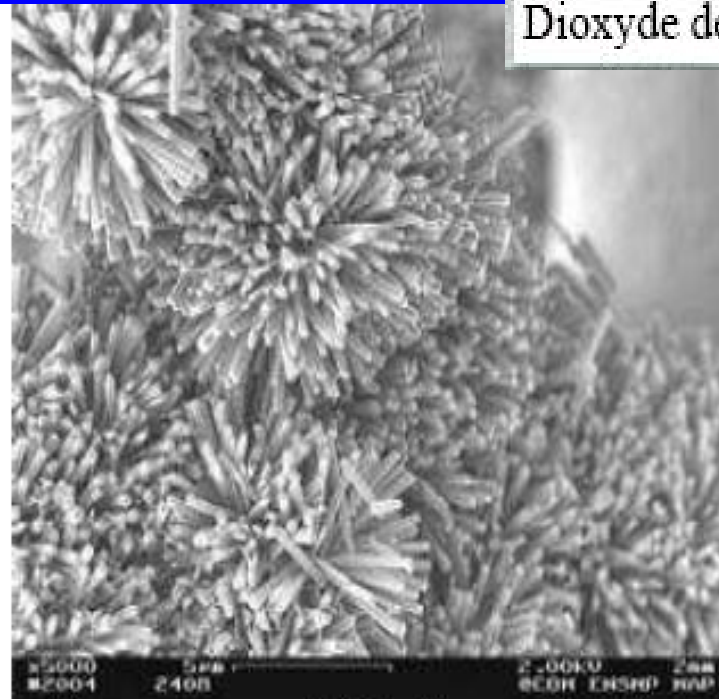
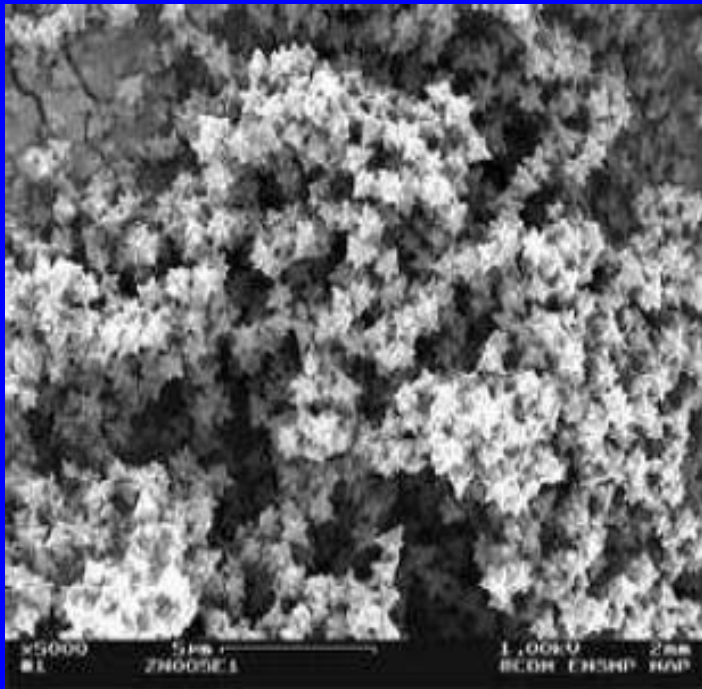
Nanospheres are nanometric carriers, which act on the cellular level bringing a strong, vital power of the vitamins and helping in cell regeneration at the same time as well as balancing physic properties of the head skin.

top

Cosmetic Industry

Nanostructured agrégats of 250 à 500 nm composed by Nanoparticles of 135 à 20nm

Surface 30 à 60m² per gram



Particules d'oxyde de zinc en forme d'étoiles et de pompons pour l'industrie cosmétique

Transparency of TiO₂ Nanoparticle Dispersions



10nm TiO₂ produces transparent dispersions for all skin types.

(Slide made available by KOBO, www.koboproducts.com)

Q3N - 5/2007

Food including nanostructured components



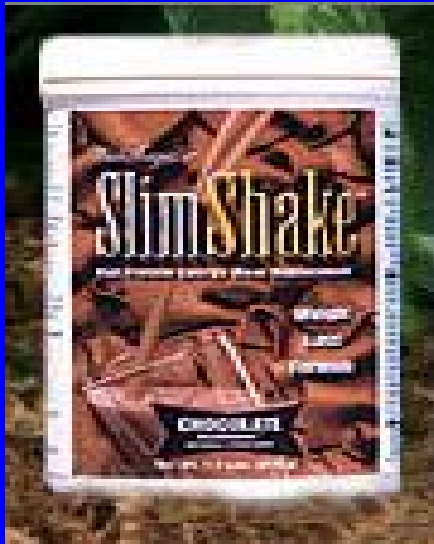
Nanotechnologies in
the Food Industry

Cientifica
August 2006

Choco'la™ Chocolate Gum



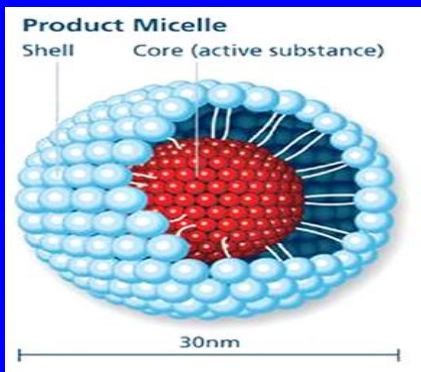
Canola Active Oil



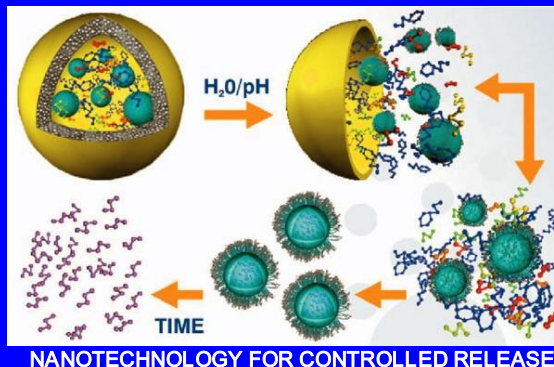
Alimentation and food packaging



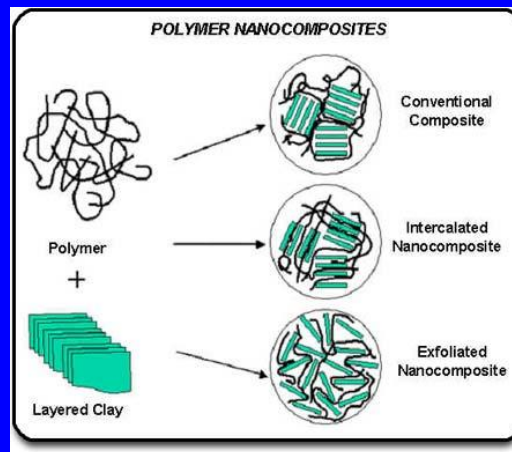
At the BASF Beverage Lab in Ludwigshafen, Germany, Andreas Hasse, left, and Clemes Sambale assess drinks that were made with synthetic beta-carotene, a nanoparticle used to add color and health benefits.



Nanotechnology active ingredient delivery systems such as this by AQUANOVA offer the promise of enhanced food performance in the future.



NANOTECHNOLOGY FOR CONTROLLED RELEASE



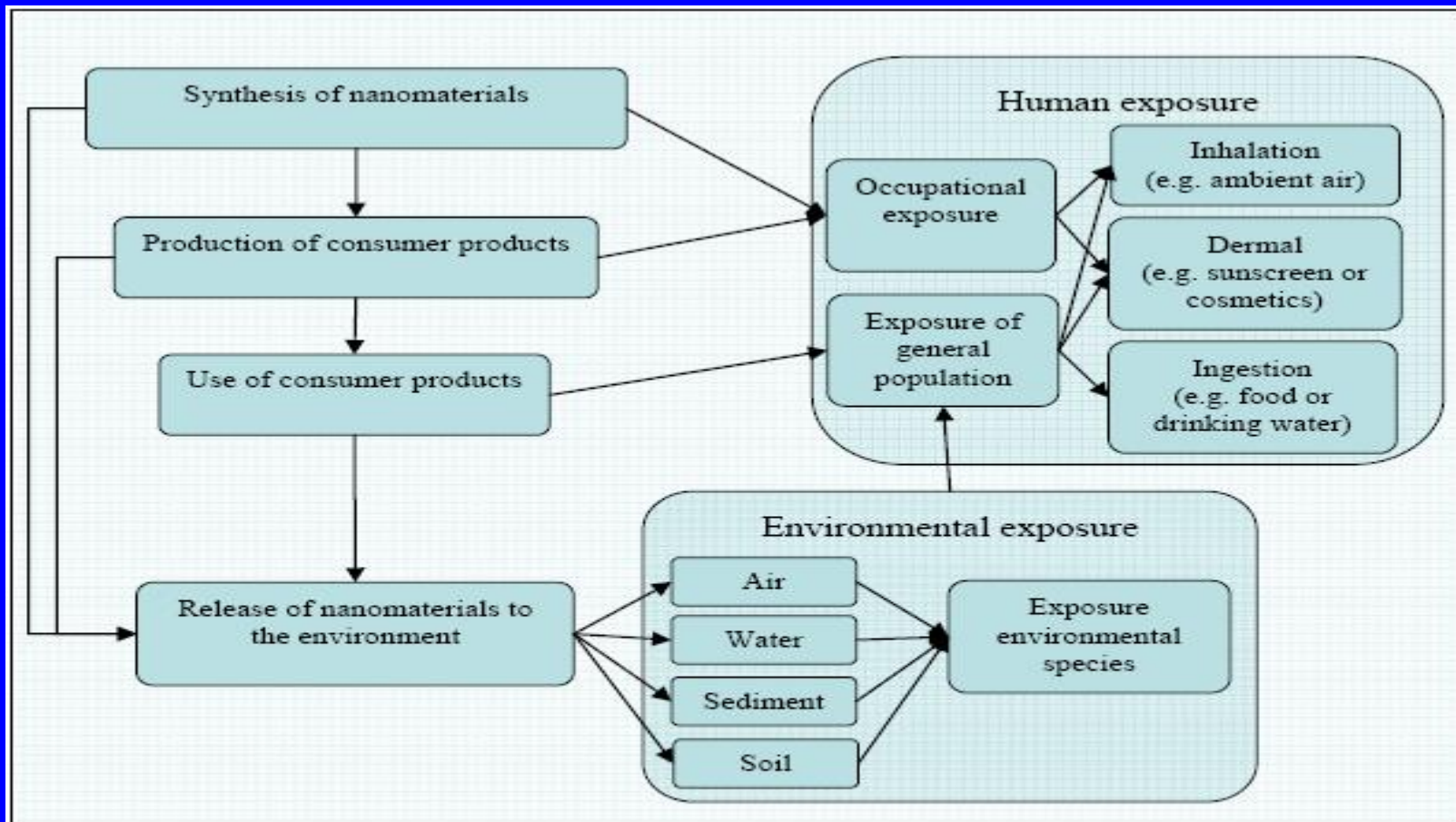
Samsung Silver Nano Fridge



Samsung's SILVER WASH



Potential exposures



Potential exposure in the different life cycle phases of nanomaterials used in consumer products (Modified from Tsuji et al., 2006 and Wiesner et al., 2006).

AFSSET 2006

Professional Exposure Sources

Procédé	Concentration totale dans la gamme de mesure 14-673 nm (particules/cm ³)	Maximum de concentration en nombre (nm)
En plein air, au bureau	> 10 000	
Fonderie de silicium	100 000	280-520
Broyage de métal	> 130 000	17-170
Soudure (au fil à souder)	> 400 000	36-64
Réduction plasma	> 500 000	120-180
Boulangerie	> 640 000	32-109
Terrain d'aéroport	> 700 000	< 45
Soudure (autogène)	De 100 000 à plus de 40 000 000	40-600

Comparaison des concentrations de nanoparticules dans l'atmosphère des lieux de travail (Möhlmann, 2004)

Detection of nanoparticles in air

No apparatus or methodologies validated in 2007

Some apparatus in test

- TSI 3080 series Electrostatic Classifier
- TSI Model 3007 Condensation Particle Counter
- TSI 3090 Engine Exhaust Particle Sizer Spectrometer
- DEKATI
- GRIMM SMPS
- Low pressure impactor bernier type (>21 nm)
- TSI FMPS
- NSAM
- TEOM



Respiratory Protections



No efficacy for the nanoparticles



Best protection for the producers and users of nanoparticles



Masks N95 approved by NIOSH

→ non filtration of 5% of the particles size 40 nm

(publication The ISRP Journal du 10/ 2007)

→ Best masks FFP3 and HEPA

Potential exposure to Nanomaterials

Free Nanoparticles

→ Biodisponibility + + +

Exposition + + +



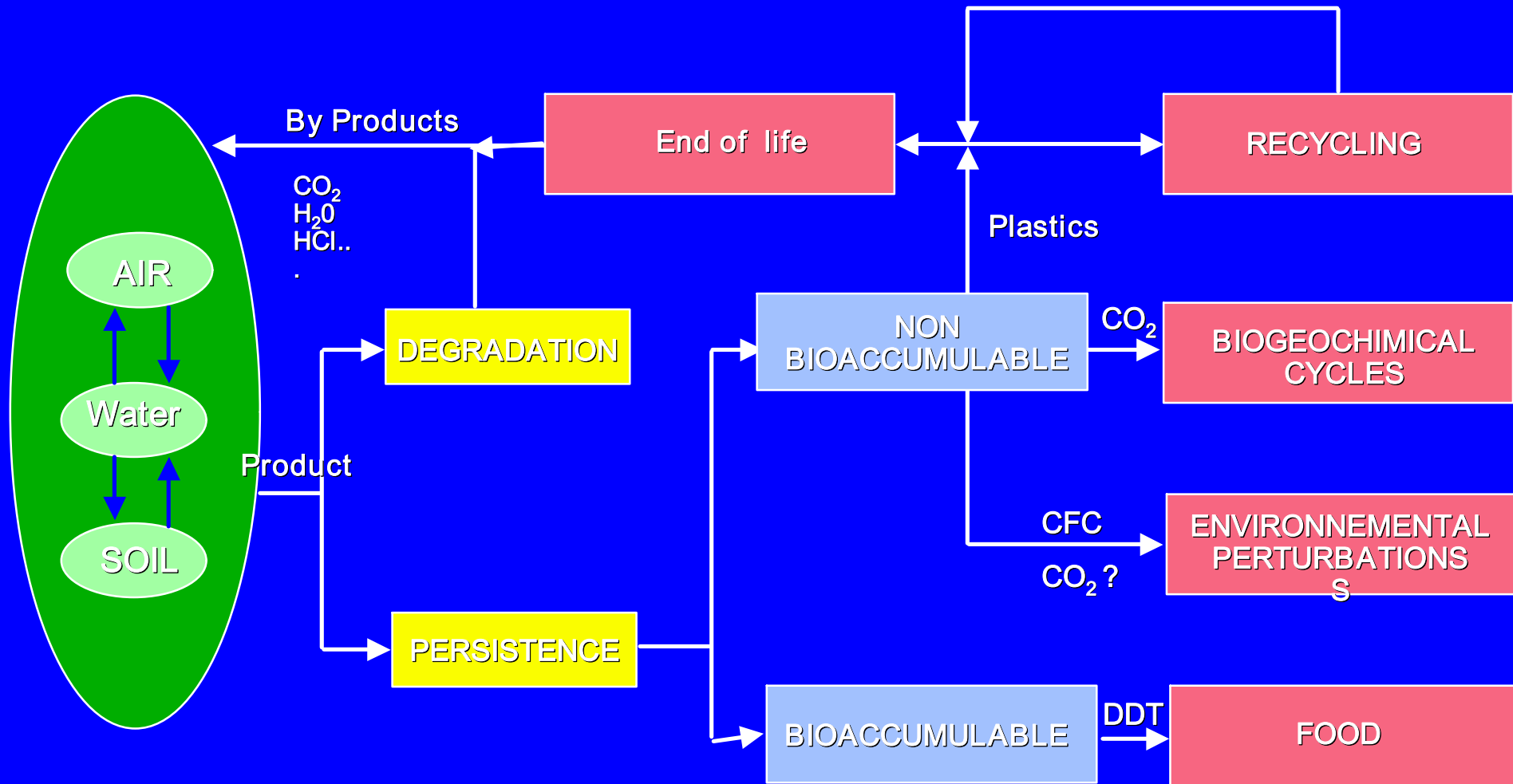
Nanoparticles included
in a solid or liquid matrice

→ No immediate
biodisponibility

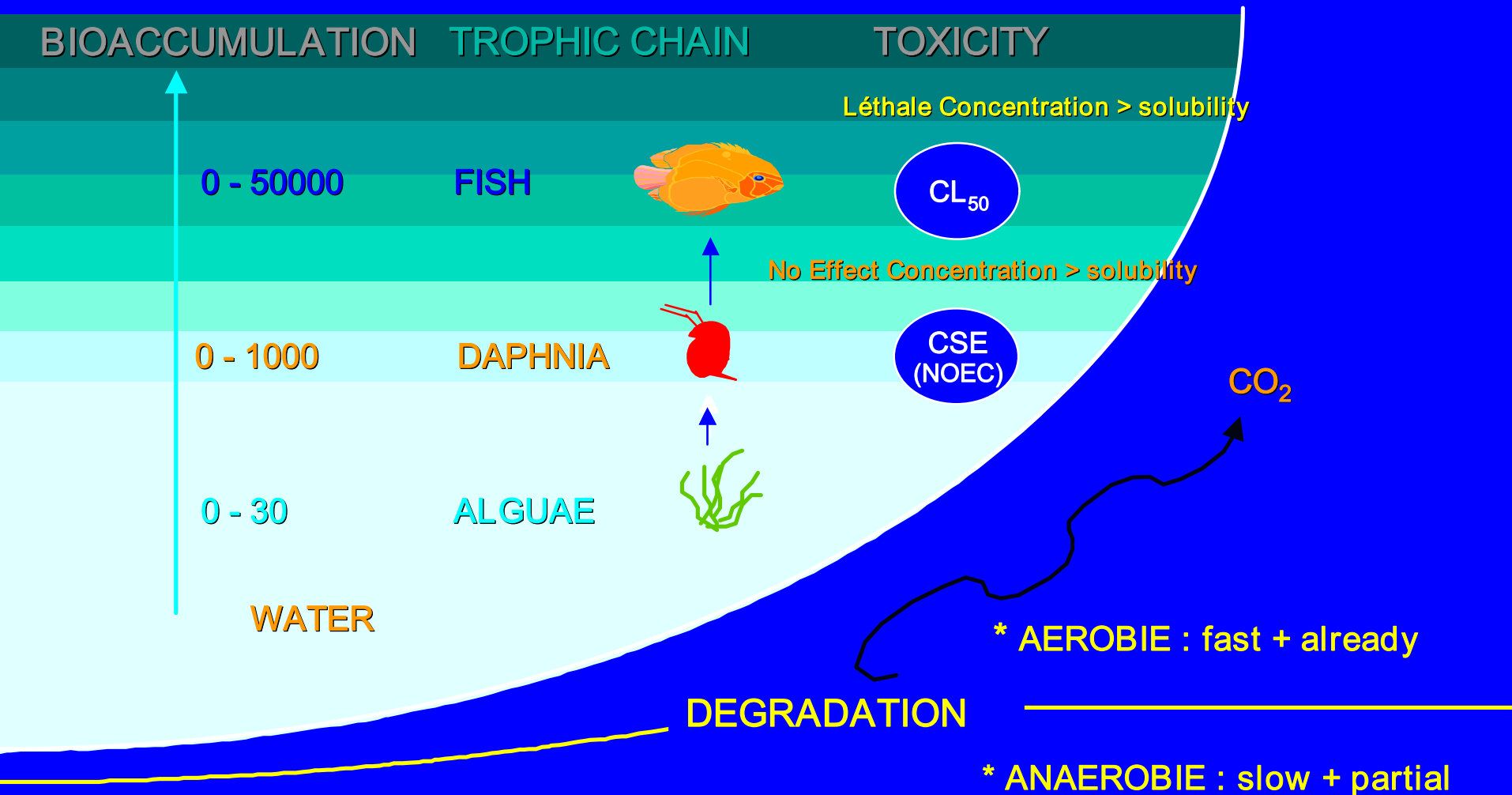
Exposition ? or +/-



From cradle to grave cycle



ENVIRONMENT Fate and : *Bioconcentration*



Conclusions of the européen project Nanosafe 1

→ No relevant information en 2005 !

Fate in human and in the environment ?

- Toxicological Mécanisms
- Peneration routes, metabolisation and distribution in the body
- Transport, persistence and accumulation in the environment ?



Potential Risks



Production volumes ?

- Confidentiality of the processes and of the production volumes
- Volume of particles release into the environment during production and destruction.



Technical Controls ?

- Parameters for risk assessment
- At the work place,
- In the environment
- Standardisation of methodologies

Answers from Nanosafe 2 in 2008 ?

Programme européen Nanosafe 2

This project is complementary and necessary for future and running programs on nanomaterials such as: Nanoderm, Nabucco, Nanocare, etc.

NANOSAFE2 will develop innovative detection, traceability and characterization techniques for engineered nanoparticles covering the whole chain of some reference particles including production, conditioning, storage, transportation, transformation into final product, during product life and at the end of product life (disposal). Both air and liquid media will be investigated.

NANOSAFE2 will provide a framework for obtaining conclusive toxicity data of generic interest of the reference particles. This includes the development of new and cheaper rapid screening methods using *in vitro* techniques and *in silico* (computer simulation) models. These new techniques will be evaluated and validated against *in vivo* exposure experiments, the only existing "gold standard". This will allow working towards risk assessment guidelines for reference materials. The results will be published in an open manner and available to the total community through the web portal.

NANOSAFE2 will develop advanced technologies to limit both exposition to nanoparticles and leaks to environment by designing safe production equipment, handling automation, dynamic confinement, individual protection devices, filtration, etc. New procedures developed in this program will then be qualified at 3 industrial sites in the frame of the global risk management strategy proposed in NANOSAFE2.

NANOSAFE2 will evaluate both societal and environmental impacts and propose new legislation and standardization measures relevant for nanoparticles by involving regulatory bodies (HSL, HVBG-BIA which are members of CEN). This project will insure a large dissemination of knowledge for nanoparticle safety by organizing workshops with world wide standards organizations, promote population awareness and training activities.



STUDY

Policy Department
Economic and Scientific Policy

NANOMATERIALS IN CONSUMER PRODUCTS

Availability on the European market and
adequacy of the regulatory framework
RIVM/SIR Advisory report 11014

(IP/A/ENVI/IC/2006-193)

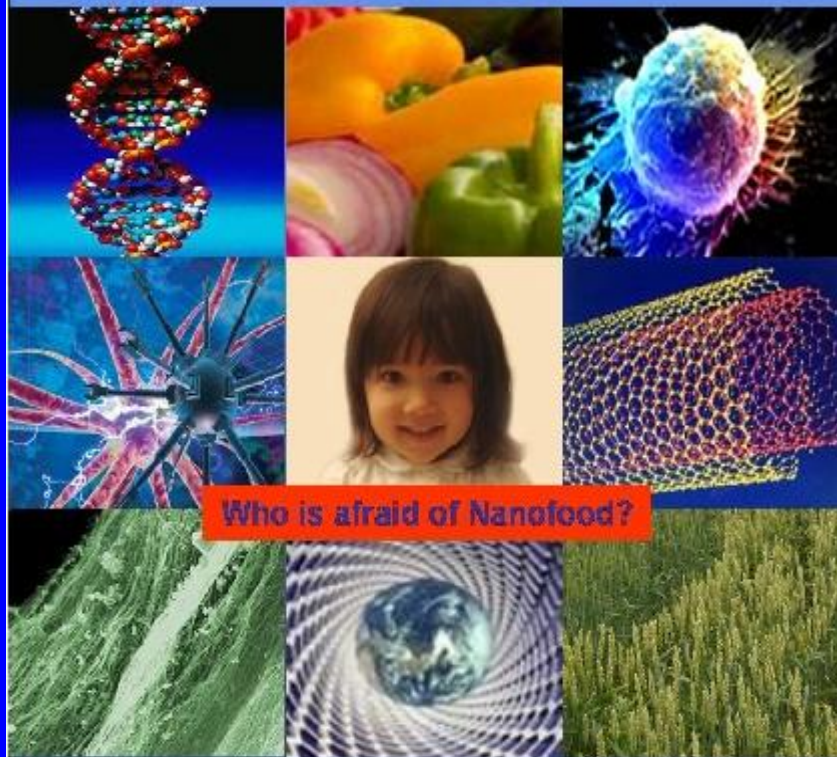
IP/A/ENVI/ST/2006-41

PE 085.628

Nano food 2040

Nanotechnology In Food, Food Processing, Agriculture, Packaging
and Consumption

*State of Science, Technologies, Markets, Applications and
Developments to 2015 and 2040*

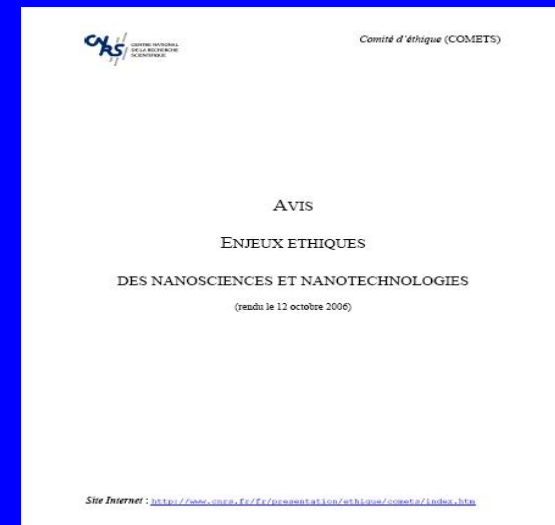
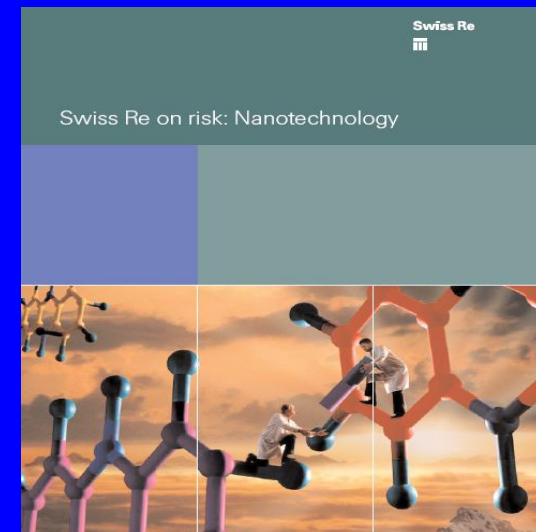
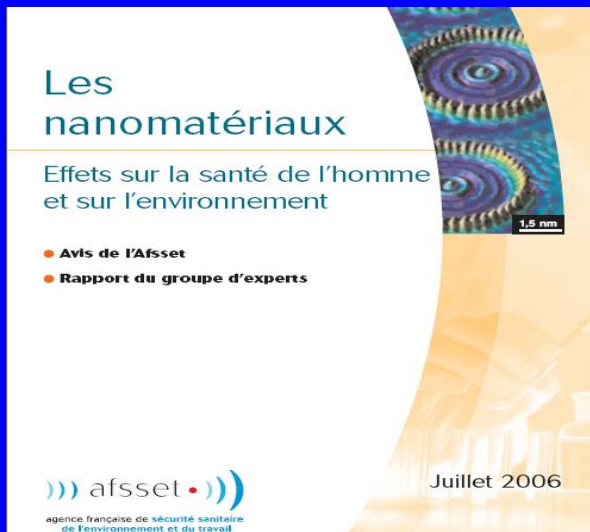


Who is afraid of Nanofood?

Helmut Kaiser

HKC22

Some references



Some references

Déterminants des effets des nanoparticules sur la santé

Jorge Boczkowski
Unité INSERM 408 et Université Paris 7

Alain Lombard
Arkema

Journée ECRIN; Paris 9 novembre 2004

Cardio-pulmonary effects of inhaled particulates

Peter HOET
Pneumologie, Longtoxicologie
Arbeids- Milieu- en Verzekeringsgeneeskunde
K.U. Leuven
Belgium

Toxicological effects of nanoparticles *in vitro* and *in vivo*

Vicki Stone

Biomedicine Research Group
School of Life Sciences
Napier University
Edinburgh

LEGI



Are Nanomaterials a Potential Human Health Hazard?

Agnes B. Kane, M.D., Ph.D.
Department of Pathology and Laboratory Medicine
Brown University
Providence, Rhode Island 02912 USA

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Mechanisms of genotoxicity of ambient particulate matter


Roel Schins

Partiele Research

Institut für umweltmedizinische Forschung (IUF)
Heinrich-Heine University
Düsseldorf, Germany.



From asbestos to nanoparticles, 28-30 June 2004, Torino, Italy.



RESEARCH REPORT

HEALTH EFFECTS INSTITUTE

Acute Pulmonary Effects of Ultrafine Particles in Rats and Mice

Günter Oberdörster, Jacob N Finkelstein, Carl Johnston, Robert Gelein, Christopher Cox, Raymond Baggs, and Alison C P Elder


Number 96
August 2000

Final Version


Nanoparticles:
health impacts?

by David B. Warheit

OPPORTUNITIES AND RISKS OF NANOPARTICLES



Paul J.A. Borm



Heerlen (NL) Düsseldorf (GE)

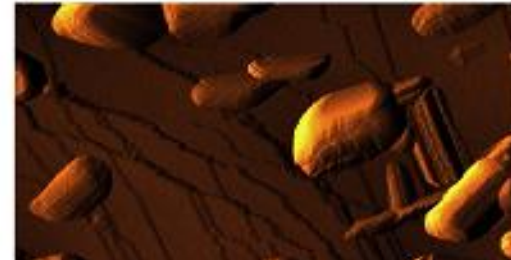
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Nanoparticles: An occupational hygiene review

Prepared by the **Institute of Occupational Medicine**
for the Health and Safety Executive 2004

**NANOTECHNOLOGIES: A PRELIMINARY RISK ANALYSIS ON
THE BASIS OF A WORKSHOP ORGANIZED IN BRUSSELS ON
1–2 MARCH 2004 BY THE HEALTH AND CONSUMER
PROTECTION DIRECTORATE GENERAL OF THE EUROPEAN
COMMISSION**



BIA-Report 7/2003

BIA-Workshop „Ultrafeine Aerosole an Arbeitsplätzen“

veranstaltet am 21. und 22. August 2002
im Berufsgenossenschaftlichen Institut
für Arbeitsschutz – BIA, Sankt Augustin

NATIONAL
NANOTECHNOLOGY
INITIATIVE



Research Needs on Environmental Safety and Health Issues for Nanotechnology

NNI-ChI Consultative Board for Advancing Nanotechnology
ESH Working Group

Chemical Industry
VISION2020
Technology Partnership

Some references

This Provisional PDF corresponds to the article as it appeared upon acceptance. Copyedited and fully formatted PDF and full text (HTML) versions will be made available soon.

The potential risks of nanomaterials: a review carried out for ECETOC

Particle and Fibre Toxicology 2006, **3**:11 doi:10.1186/1743-8977-3-11

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