NTNU

Norwegian University of Science and Technology

TMT4320 Nanomaterials
November 9th, 2016

- Nanotoxicology

  Oberdörster *et al*. – Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles

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FORSKNINGSNYHETER FRA NTNU OG SINTEF

GEMINI

Nano på godt og vondt

Små byggeklosser – stor uvisshet. Ingen vet hvor nanopartiklene blir av til slutt.

s. 30

SLANGEROBOT-FAMILIEN

PiKo, Kulko, Anna Konda og Aiko går i lære

MINERAL-RIKET

Norsk kvarts er gull verdt

ASIATISK INNERSVING

Hvem er flinkest i landet her?

Forsker på mulige skader av nanopartikler

Sintef-forskere skal finne ut hvordan nanopartikler virker på krepsdyr og plankton. Det er en mulighet for at nanopartikler kan klatre i næringskjeden og komme i maten vår.

Sintef-forsker og miljøkjemiker Andy Booth understreker at ikke alle nanopartikler er farlige. Mange typer nanopartikler finnes naturlig i naturen og har eksistert siden jorda ble dannet. Aske er for eksempel et stoff som har slike ørsmå partikler i seg.

Nytt på jorda

Det nye er at vi kan fremstille nanopartikler industrielt og designe dem med ulike egenskaper. Det finnes i dag slike partikler i over 1000 produkter, for eksempel i undertøy, solkrem og kjøkkenredskaper. Industrielle nanopartikler kan være forskjellig fra dem som allerede finnes i naturen. Problemet er at vi ikke vet nok om hvordan de vil oppføre seg, skriver forskningsmagasinet Gemini i kommende utgave.

Andy Booth har interessert seg for om nanopartikler kan være giftige og Sintef investerer nå av egne midler for å forske på det. Forskerne skal se på hvordan partiklene oppfører seg, og hvordan de påvirker organismer når de slippes ut i det marine miljøet. Et av målene er å finne ut om partiklene blir tatt opp av små krepsdyr og zooplankton - og om de er giftige for dem. Senere skal man studere hvordan torskelarver og andre større organismers tåler partiklene.

Blir i kroppen?

– Kan nanopartiklene tas opp i organismen, for eksempel hos mennesket?

– Det foreligger mye data som indikerer at de går gjennom organismen uten å bli tatt opp. Det store problemet er at de er så forskjellige og oppfører seg ulikt. Forsøkene våre vil fortelle oss om partiklene skilles ut, eller om de vil forblir inne i organismen. Eventuelt hvordan de vil oppføre seg der, sier Booth.

Han antar at noen av partiklene kan være giftige, men sier at det avhenger av mange faktorer, blant annet av konsentrasjonen og kombinasjonen av nanopartiklene.

Det finnes millioner av potensielle varianter av nanopartikler.

Vet lite

– Har industrien gode nok tester til å sikre at nanoproduktene de slipper på markedet er trygge?

– Et godt spørsmål. Vi har standard tester som forteller oss om et stoff er giftig eller ikke. Men i dag har vi ingen slike tester som fungerer ett hundre prosent på nanopartikler. Å utvikle nye tester er noe forskerne jobber med internasjonalt, sier Booth. Han tror produsentene er ekstra varsomme og at det er vanskelig å sende produkter på markedet som er helseskadelige.

Andy Booth og Sintef-teamet på tolv personer har startet et møysommelig arbeid. En av de største utfordringene er å finne metoder som gjør det mulig å undersøke hvordan de ørsmå partiklene oppfører seg i naturen – og hvordan de eventuelt påvirker den.

Nano ut i naturen

Industrielt fremstilte nanopartikler kan komme ut i naturen på mange måter. Gjennom utslipp i industrien, under transport og gjennom bruken av nanoprodukter. For eksempel vil nanopartikler i solkrem bli med i avløpsvannet etter en dusj. Når produktene med nanomaterialer til slutt blir søppel, vil en del av dem komme ut i naturen.

At Sintef studerer mulige skadevirkninger er ikke så rart, Sintef driver nemlig selv med forskning og utvikling på nanofeltet.

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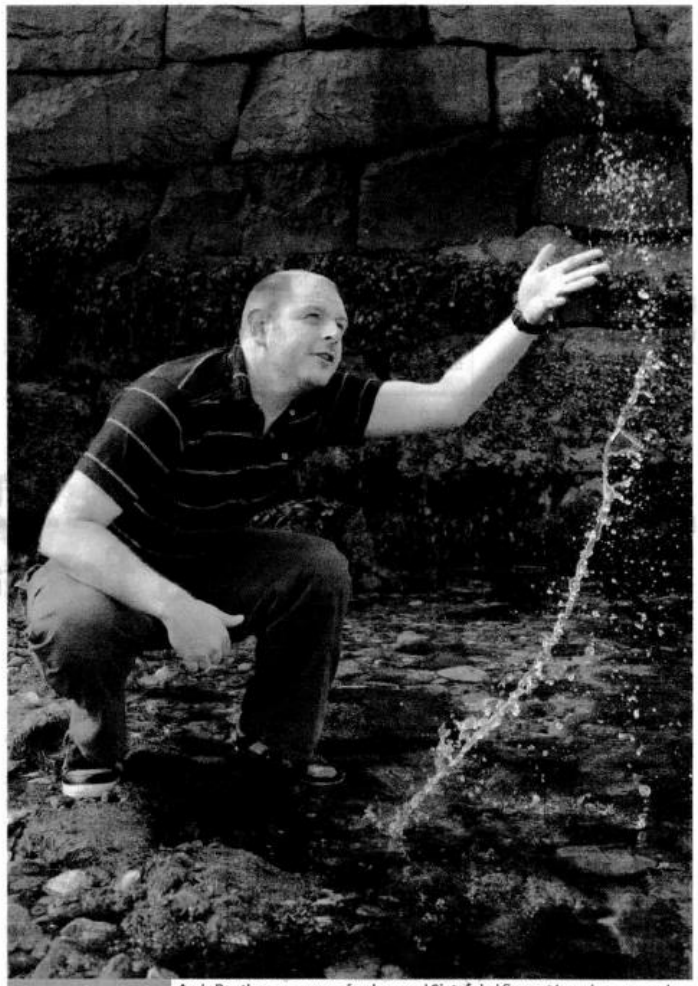


Nano på avveie Andy Booth og en gruppe forskere ved Sintef skal finne ut hvordan menneskeskapte nanopartikler påvirker livet i havet. Foto: THOR NIELSEN/NTNU/Sintef

Nanoparticles in everyday life

Table 1. UFPs/NPs (< 100 nm), natural and anthropogenic sources.

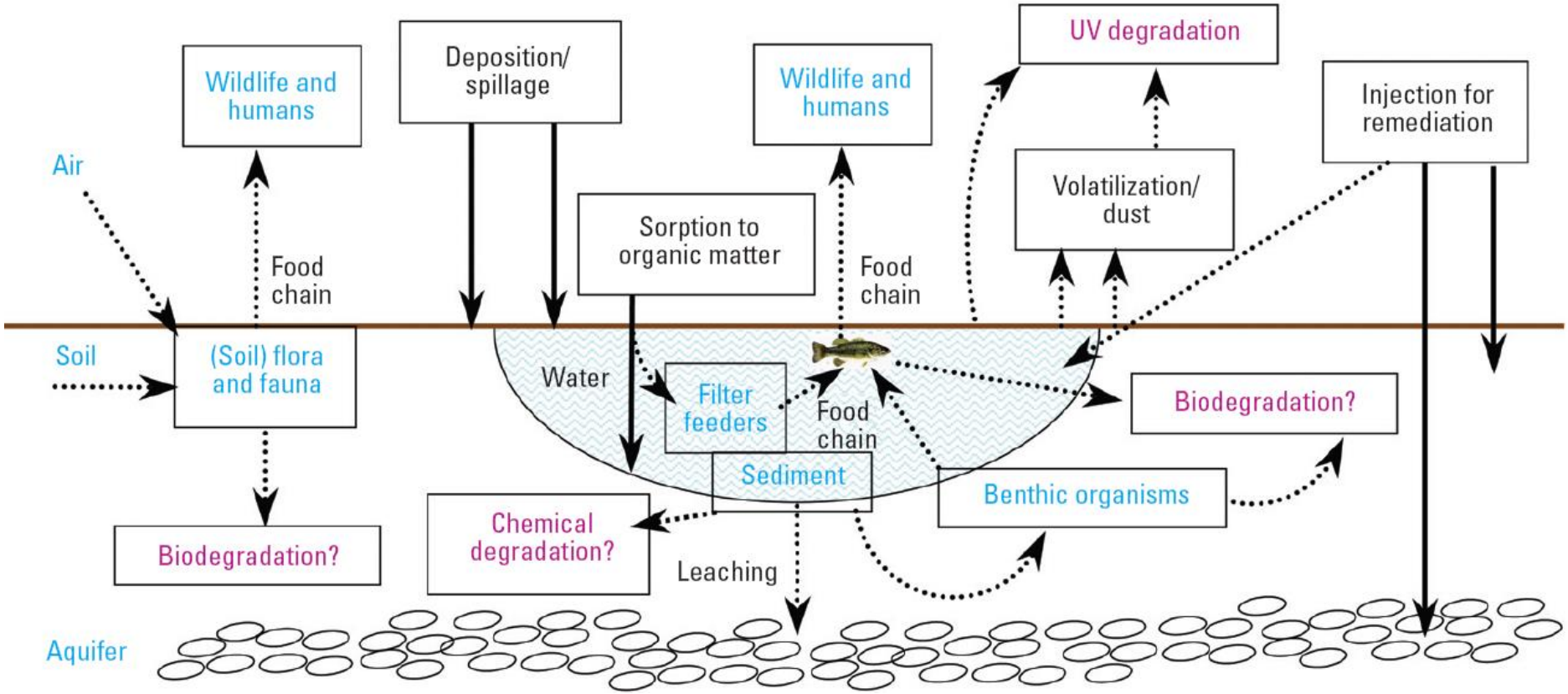
Natural	Anthropogenic	
	Unintentional	Intentional (NPs)
Gas-to-particle conversions	Internal combustion engines	Controlled size and shape, designed for functionality
Forest fires	Power plants	
Volcanoes (hot lava)	Incinerators	Metals, semiconductors, metal oxides, carbon, polymers
Viruses	Jet engines	
Biogenic magnetite: magnetotactic bacteria protoctists, mollusks, arthropods, fish, birds human brain, meteorite (?)	Metal fumes (smelting, welding, etc.)	Nanospheres, -wires, -needles, -tubes, -shells, -rings, -platelets
	Polymer fumes	
	Other fumes	Untreated, coated (nanotechnology applied to many products: cosmetics, medical, fabrics, electronics, optics, displays, etc.)
Ferritin (12.5 nm)	Heated surfaces	
Microparticles (< 100 nm; activated cells)	Frying, broiling, grilling	
	Electric motors	

– Anthropogenic = menneskeskapt (man-made)

Nanoparticle vs nanocomposites

- Nanoparticles in free form versus materials containing nanoparticles or nanostructures
- Concerns regarding composites containing nanoparticles
  - Production
  - Waste or byproducts
  - Accidents and leakages
  - Recycling and disposal
- Nanoparticles in consumer goods can easily leak out into the environment
- Very little research on how nanoparticle will affect the environment including soil, flora, small fauna, large wildlife and humans

Routes of NP exposure in the environment



→ Routes demonstrated in the laboratory or field or are currently in use

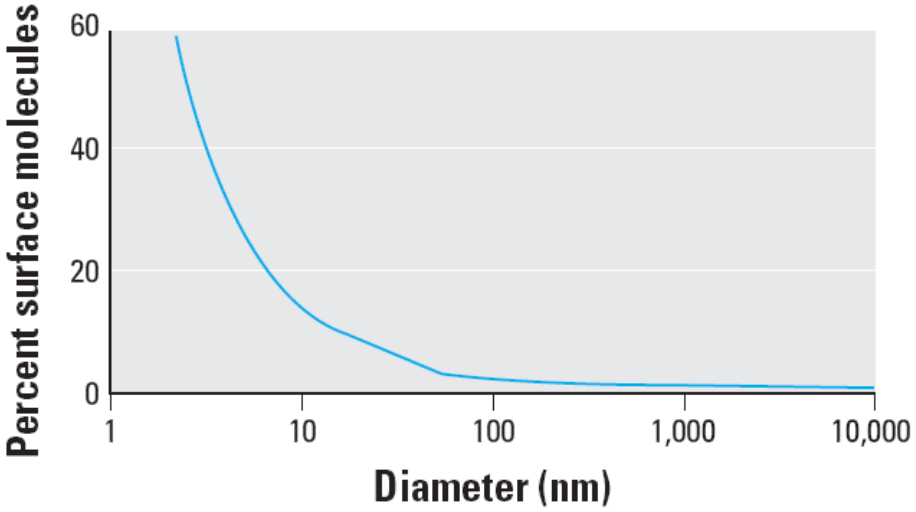
⇢ Possible exposure, uptake, distribution and degradation routes

– Possible degradation routes

– Possible sinks and sources

Nanotoxicology

- Research effects of engineered nanomaterials on living organisms
- Small size is what gives nanoparticles and nanostructured materials their specific properties and make them useful
- Size can be harmful due to large area/volume ratio (reactivity)



Important parameter

- Nanoparticles are small:
  - High surface/volume ratio – reactivity increases
  - Can get access where other particles cannot
- Other parameters are also influential:
  - Surface chemistry (solubility, reactivity)
  - Surface coating
  - Morphology
  - Size distribution (mono/polydisperse)
  - Electrostatic charge
- Human/environment exposure
  - Dose + exposure time is important
  - Degradation mechanisms

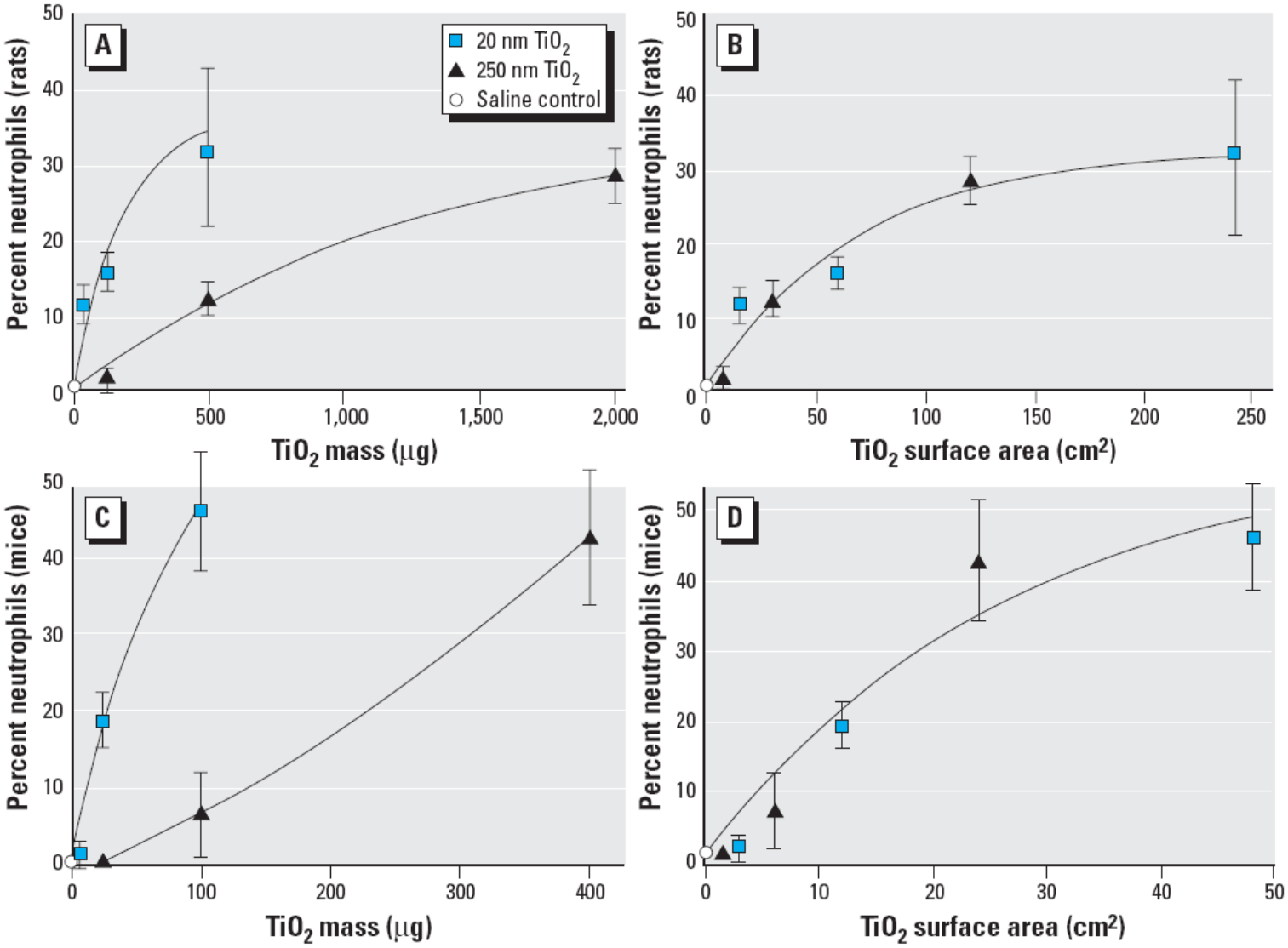


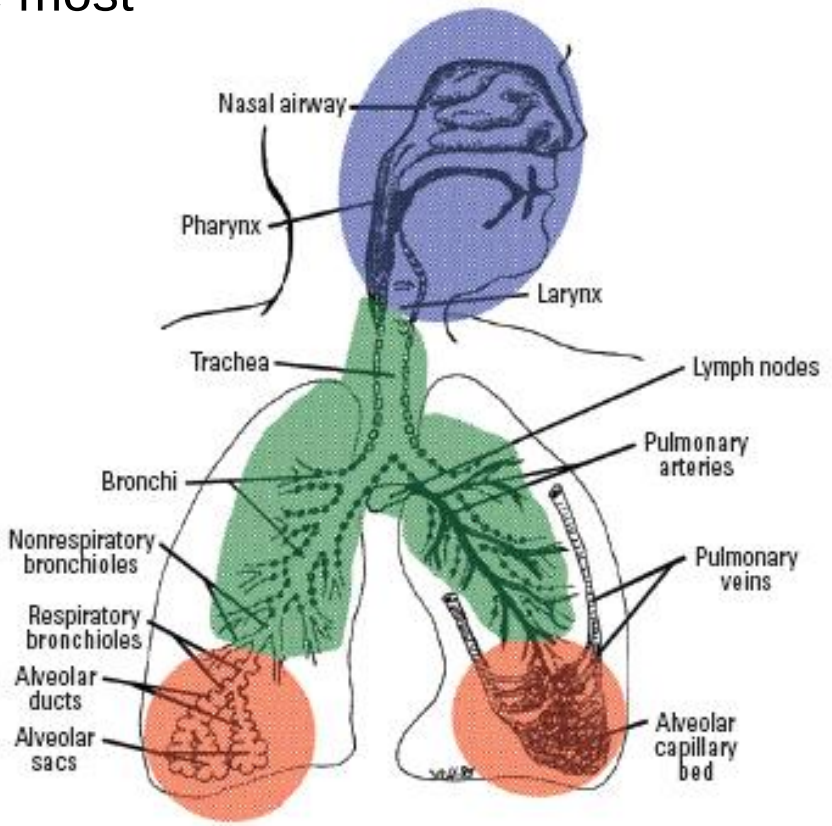
Figure 4. Percentage of neutrophils in lung lavage of rats (*A,B*) and mice (*C,D*) as indicators of inflammation 24 hr after intratracheal instillation of different mass doses of 20-nm and 250-nm TiO_2 particles in rats and mice. (*A,C*) The steeper dose response of nanosized TiO_2 is obvious when the dose is expressed as mass. (*B,D*) The same dose response relationship as in (*A,C*) but with dose expressed as particle surface area; this indicates that particle surface area seems to be a more appropriate dosemetric for comparing effects of different-sized particles, provided they are of the same chemical structure (anatase TiO_2 in this case). Data show mean ± SD.

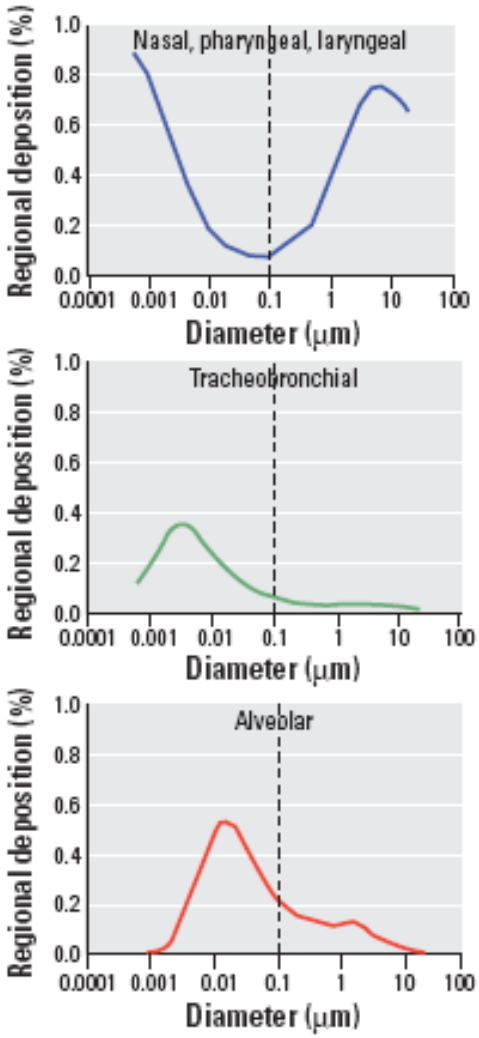
Exposure paths

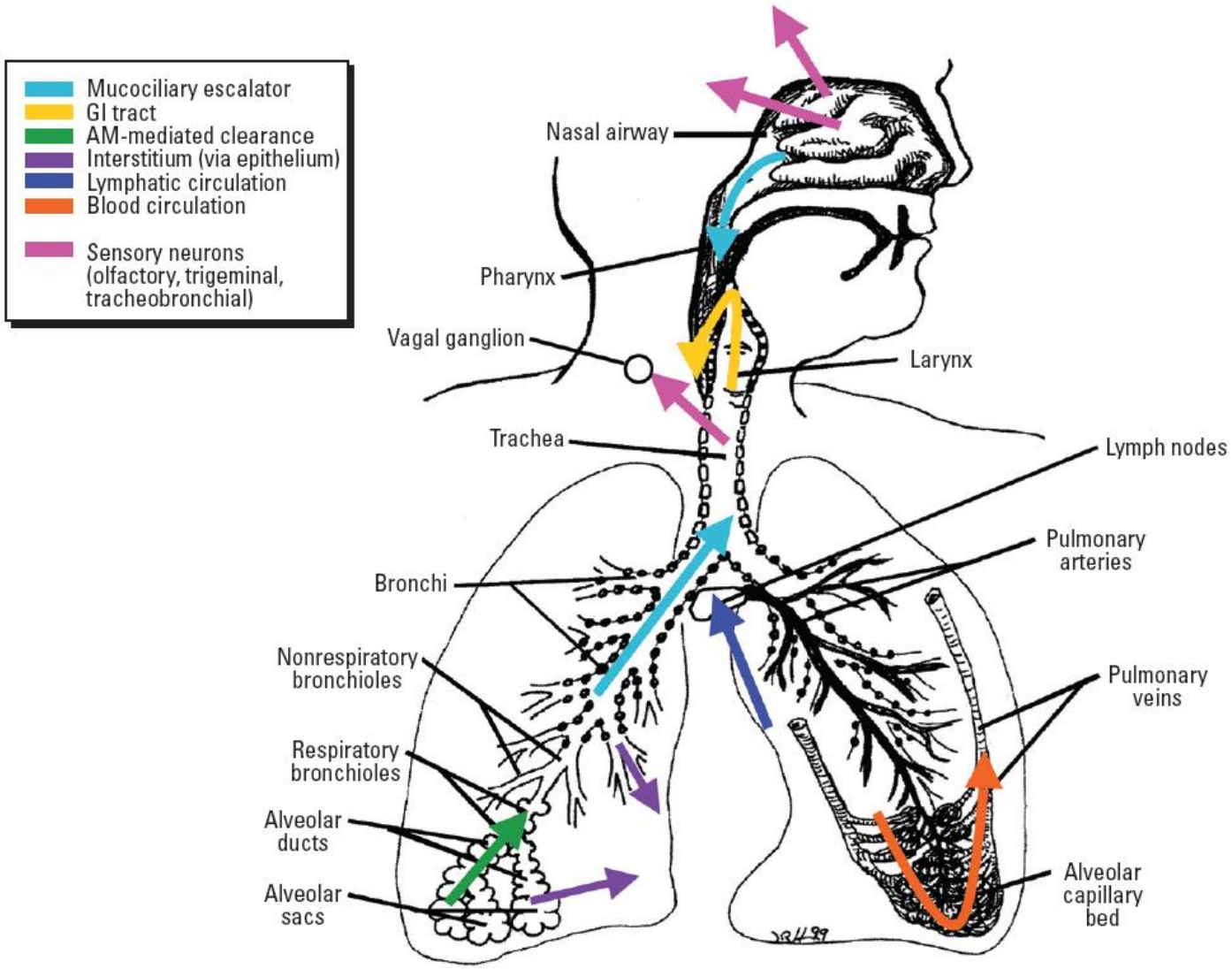
- Exposure paths include:
  - Inhalation (respiratory tract)
    - Airborne particles
  - Dermal uptake (skin)
    - Cosmetics, sunscreens
    - Clothes
    - (Airborne particles)
  - Ingestion (gastrointestinal tract)
    - Food
    - Water
    - Drug / drug delivery devices
    - (Airborne particles)
  - Injection (blood circulation)

Respiratory system

- Nature of interaction depends on size, shape and surface reactivity
- Inhalation is the major route of exposure and uptake through respiratory tract has been studied the most

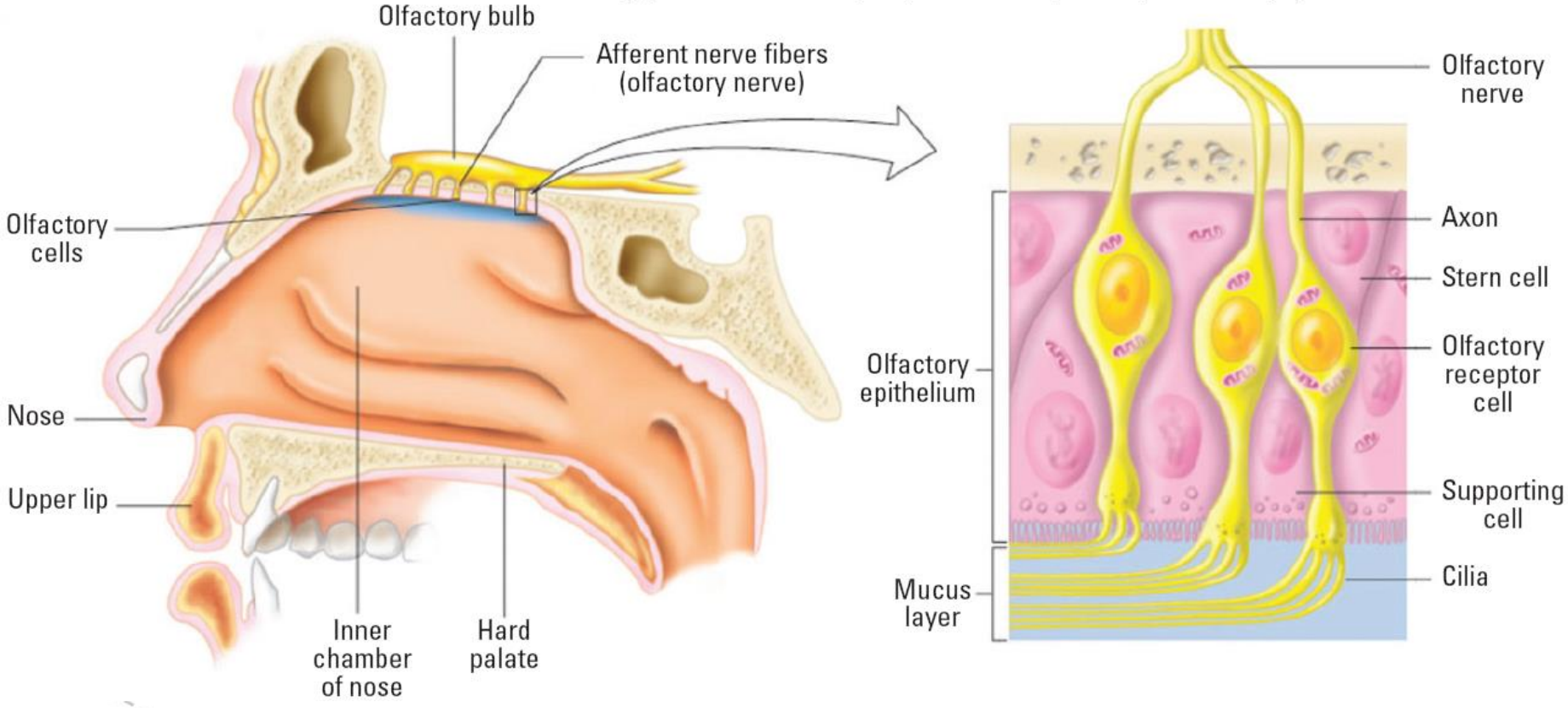






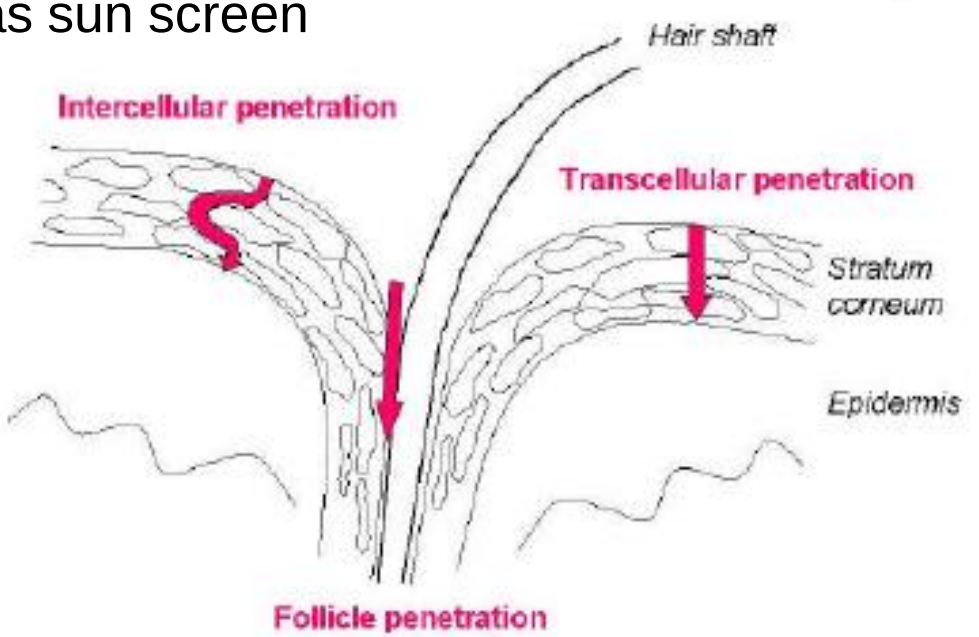
Pathways of particle clearance (disposition) in and out of the respiratory tract. There are significant differences between NSPs and larger particles for some of these pathways.

Neuronal uptake and translocation



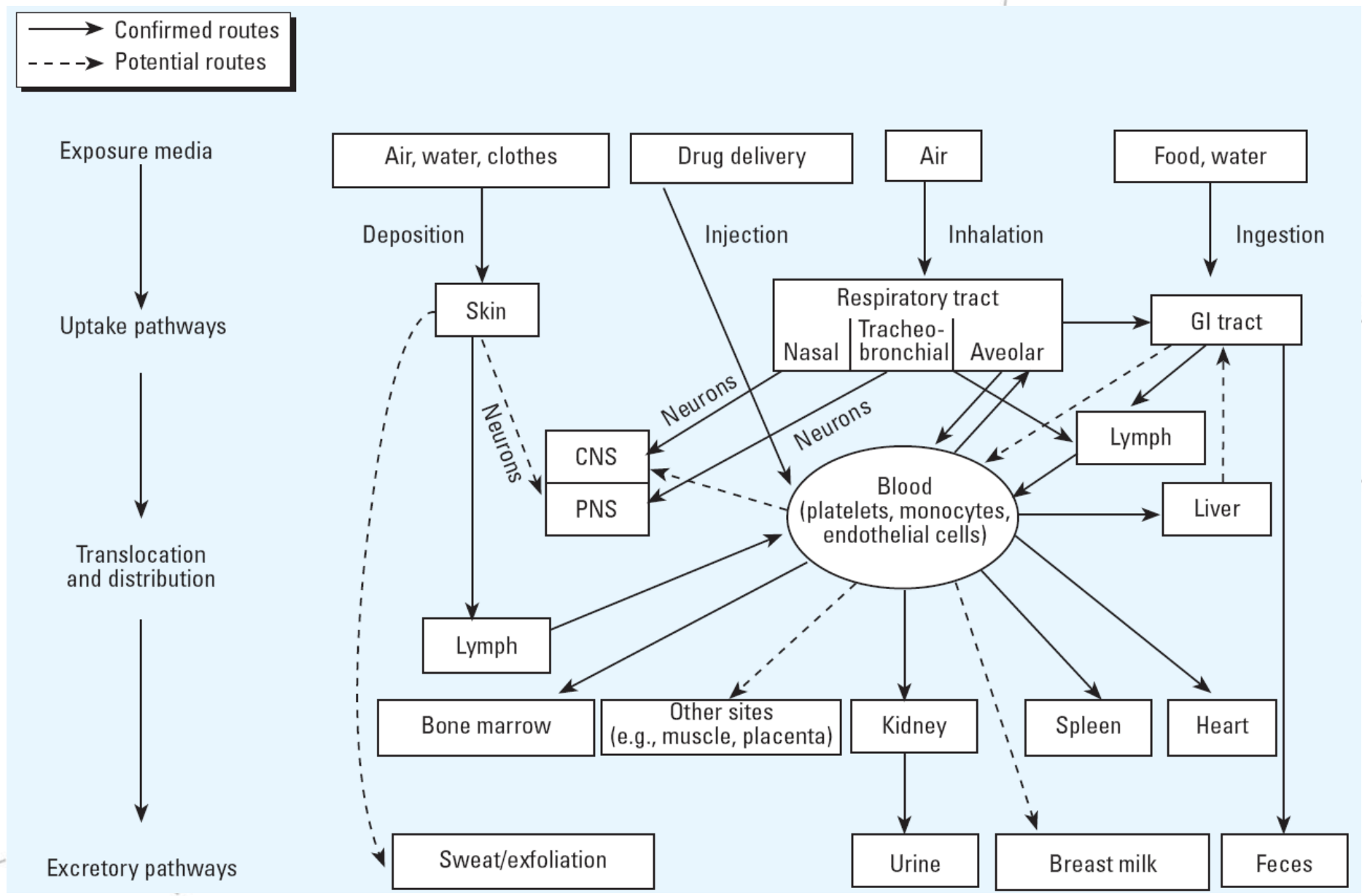
Dermal uptake

- Nanoparticle penetration through skin can occur through three different routes:
  - Intercellular
  - Intracellular
  - Through hair follicles
- After penetration translocation to the blood circulation or the nervous system has been shown
- Many cosmetic products such as sun screen contain nanoparticles
  - Unlikely that these are small enough to penetrate skin
  - What happens if these are applied to broken skin?



Ingestion

- Gastrointestinal tract (GI) [N: mage/tarm]
- Only a few studies have investigated the uptake and disposition of nanomaterials by the GI tract, and most have shown that nanoparticles pass through the GI tract and are eliminated rapidly


Confirmed routes
Potential routes
Exposure media
Uptake pathways
Translocation and distribution
Excretory pathways
Air, water, clothes
Drug delivery
Air
Food, water
Deposition
Injection
Inhalation
Ingestion
Skin
Respiratory tract
Nasal
Tracheo-bronchial
Aveolar
GI tract
Neurons
Neurons
Neurons
CNS
PNS
Lymph
Blood (platelets, monocytes, endothelial cells)
Liver
Lymph
Bone marrow
Other sites (e.g., muscle, placenta)
Kidney
Spleen
Heart
Sweat/exfoliation
Urine
Breast milk
Feces

Nanotoxicology studies

- The doses in laboratory studies are often way above real values
- The mechanistic pathways that operate at low realistic doses are likely to be different from those operating at very high doses when the cell's or organism's defenses are overwhelmed
- Study designs should include doses that most closely reflect the expected exposure levels

Risk assessment

- The lack of toxicology data on engineered NPs does not allow for adequate risk assessment
- Because of this, some may even believe that engineered NPs are so risky that they call for a precautionary halt in NP-related research
- However, the precautionary principle should not be used to stop research related to nanotechnology and NPs
- Instead, we should strive for a sound balance between further development of nanotechnology and the necessary research to identify potential hazards in order to develop a scientifically defensible database for the purpose of risk assessment

Risk assessment contd.

- For nanomaterial producers, it will be important to demonstrate that what they may perceive as a new and potentially harmless form of a familiar material has, indeed, an acceptable risk profile
- If such proactive steps are not taken, nanomaterials may be regarded as dangerous by the public and regulators, which could lead to inappropriate categorization and unnecessarily burdensome regulations
- Such action (or inaction on the side of producers), in turn, could result in significant barriers to commercialization and the widespread acceptance of otherwise useful nanotechnology materials

Summary

- Very little has been done to assess and systematically map the effects and possible dangers of nanomaterials and nanoparticles vs their larger counterparts
- Initial research has found that nanoparticles do penetrate and attack parts of living organisms that large particles cannot reach
- There are possible health issues with nanoparticles
  - Higher toxicity
  - Higher reactivity
  - Properties different from bulk materials
- Exposure to nanoparticles increases exponentially but no one quite knows what the consequences might be
- What about animals, plants, soil, etc.…?

Table S-1

Airborne Ultrafine/Nano Particles: Workplace and Environment

Sources → Exposure → Dose → Response

What are they?

Indoors
heated surfaces
frying
broiling
grilling
electric motors

Outdoors
urban air
internal combustion
power plants
incinerators
gas-to-particle convers.
forest fires
airplane jets
recreation (ski waxing)

Workplace
metallurgy (fumes)
welding
polymer fumes
nanotechnology
(biomed. electronics)
nanotubes

What levels?

Exposure Routes
inhalation
ingestion
dermal

Concentration
ng/m^3 - mg/m^3
10^2 - $>10^6$ part./cm^3

Duration
minutes
hours
days
continuous/peak

Location
distance from source
wind direction

How much is retained?

Dosemetric
mass
number
surface

Deposition
respiratory tract:
ventilatory and
anatomic parameters

Disposition
within respiratory tract
extrapulmonary organs
disease state

Physico-chemical Properties
organics, inorganics
metals
crystalline, amorphous
surface area
solubility (water, lipid)

Physiological or adverse?

Epidemiologic Studies
ambient UFP
susceptibles only?
mortality/morbidity
(respiratory, cardiovascular)

Clinical Studies
lab. generated UFP
ambient UFP
healthy/susceptibles
(respiratory, cardiovascular)

Animal Studies
lab. generated UFP
Ambient and occupational UFP
compromised animal models
(respiratory, cardiovascular, CNS)
mechanisms

***In vitro* Studies**
mechanisms
oxidative stress
cellular/molecular

Learning objectives - Nanotoxicology

- Could discuss issues related to the toxicity of nanoparticles
  - Why CAN nanoparticles be harmful?
  - Exposure paths

- Nanoparticles are small:
  - High surface/volume ratio – reactivity increases
  - Can get access where other particles cannot