Challenges to ensuring the safety of emerging nanomaterials

Tutorial

AAAR Annual Conference
October 20 2000, Orlando FL

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Chief Science Advisor, Project on Emerging Nanotechnologies
Woodrow Wilson International Center for Scholars (in partnership with the Pew Charitable Trusts)

AAAR conference, Orlando FL, 10/20/08

The

art and science

of building stuff

that does stuff

at the nanometer scale

Richard Smalley

Nanotechnology can... *Make better products*

I wish my sunscreen wasn't so unsightly

I wish my socks didn't smell so much!

I wish my tennis racquet was lighter and stronger

I wish I could keep leftovers for longer, before they go off

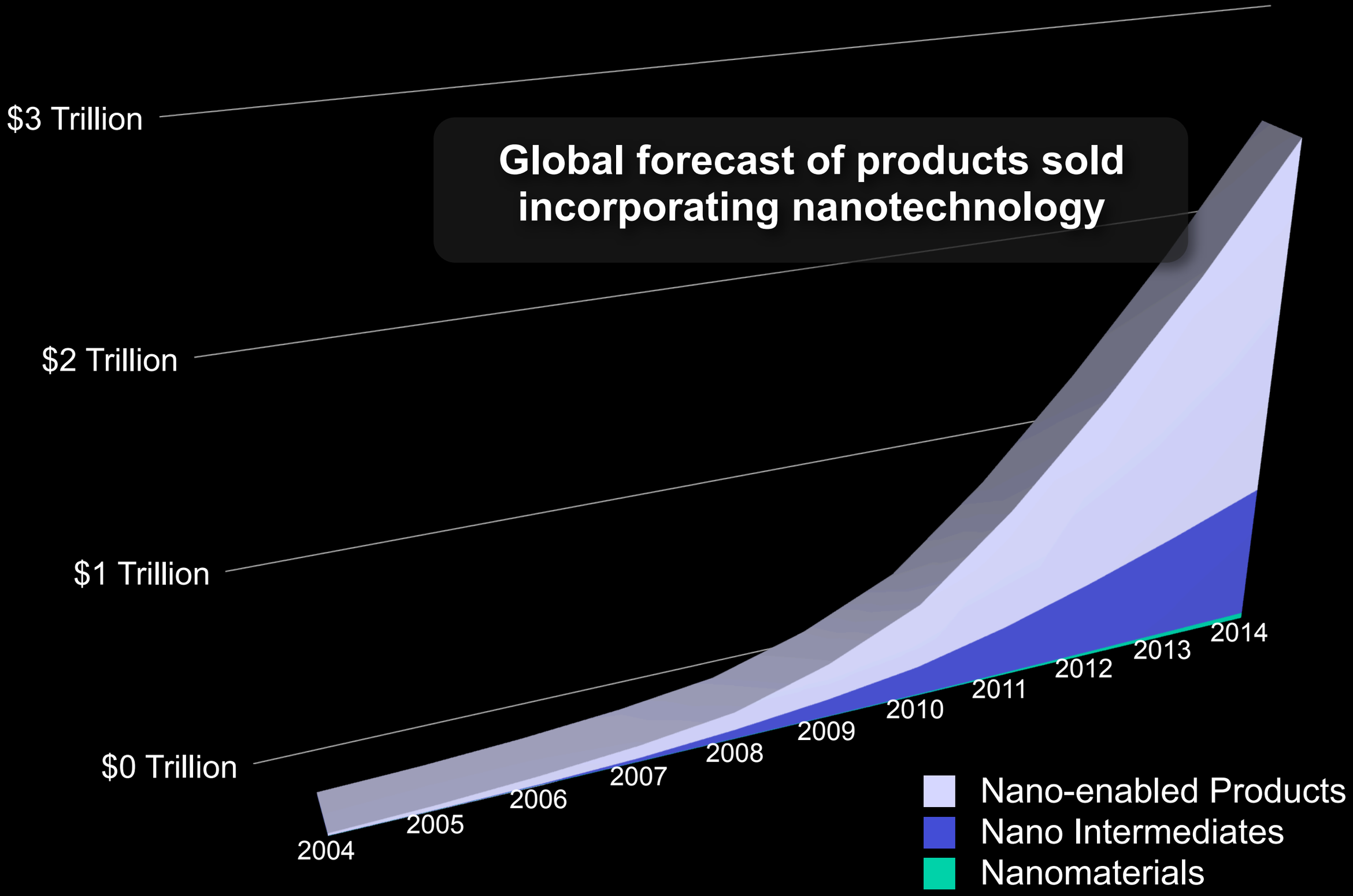
I wish spilt red wine would run off my pants without staining

I wish I could get more songs on my iPod

Over 800 listed manufacturer-identified nanotech consumer products:
www.nanotechproject.org/consumerproducts

Nanotechnology can... *Generate Wealth*

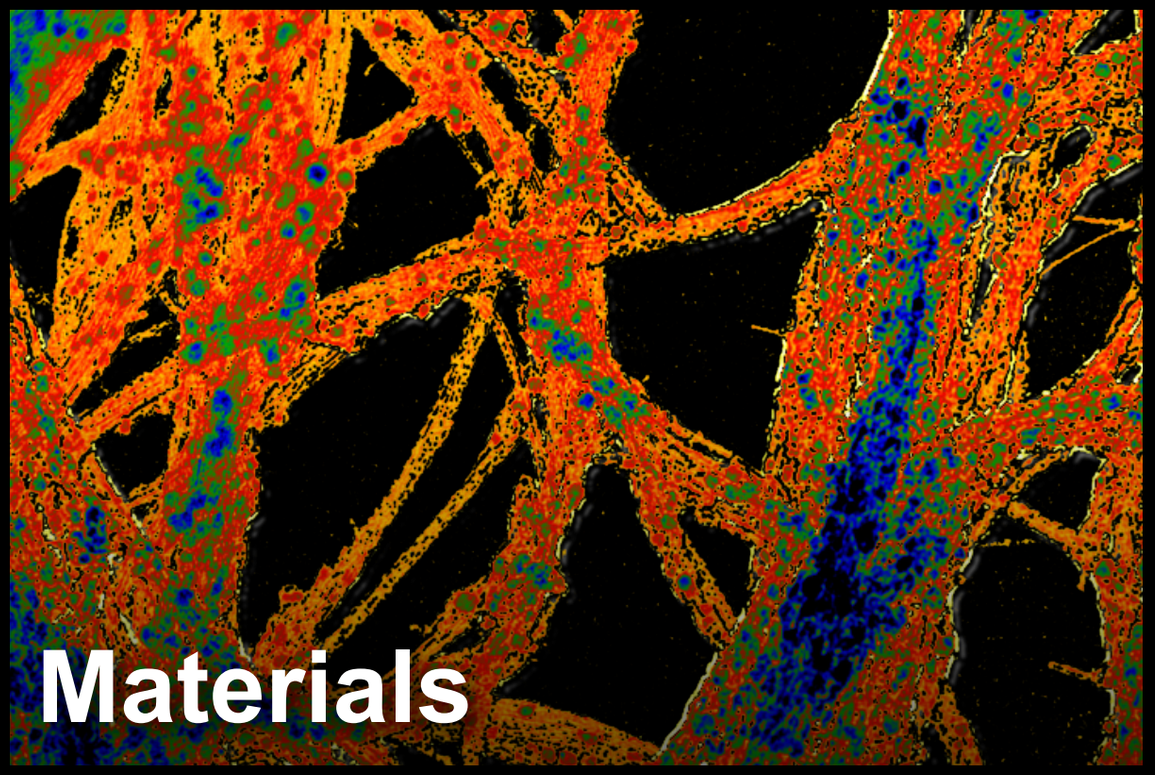
Global forecast of products sold incorporating nanotechnology



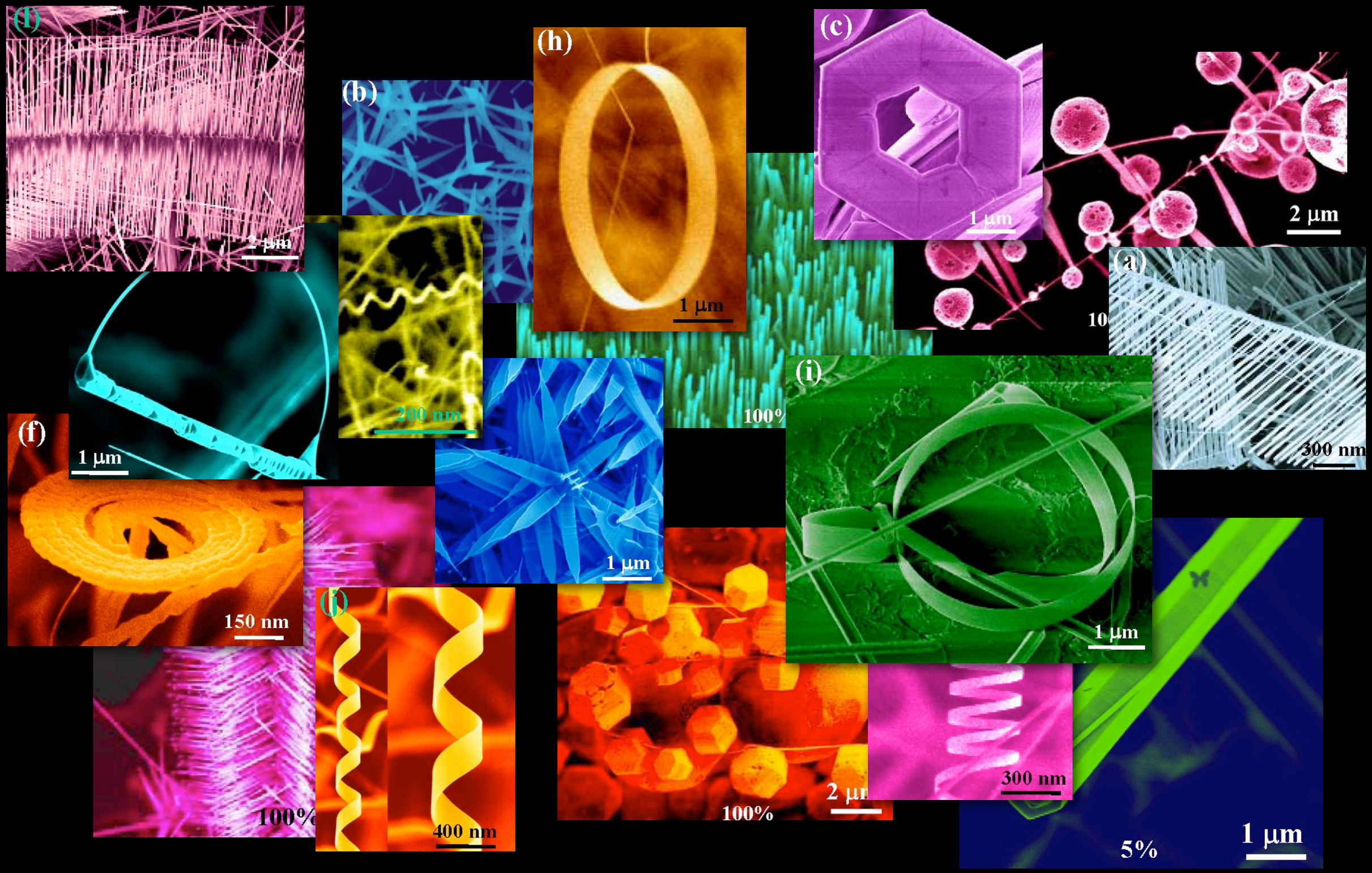
Source: 2004 Lux Research Report: "Sizing nanotechnology's value chain"

Nanotechnology can...

Make A Difference



Does the ***added value*** that nanotechnology brings to products, lead to ***unconventional*** potential to cause harm?

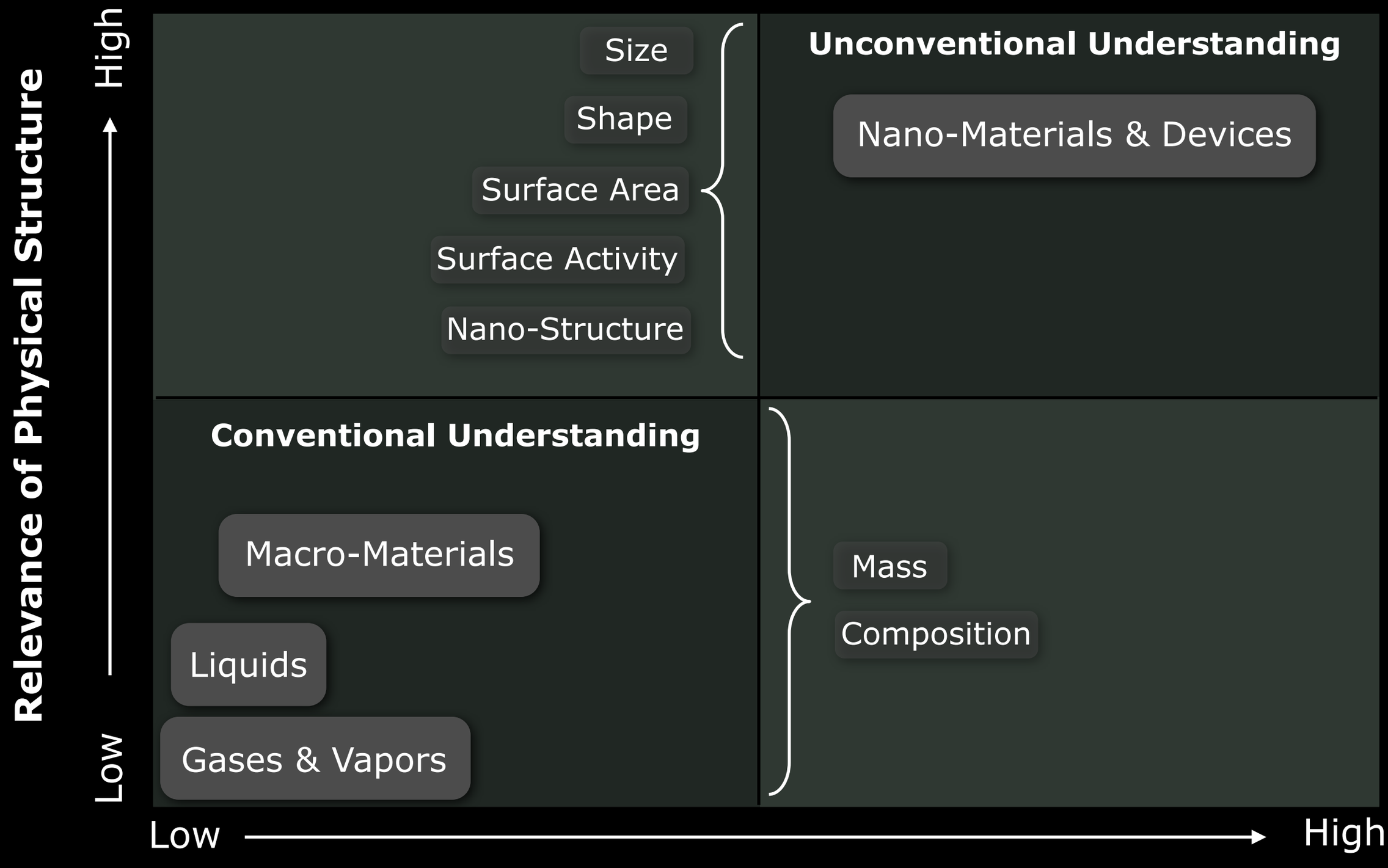


Nano-ZnO: One chemistry, many shapes

Courtesy of Prof. Z.L. Wang, Georgia Tech

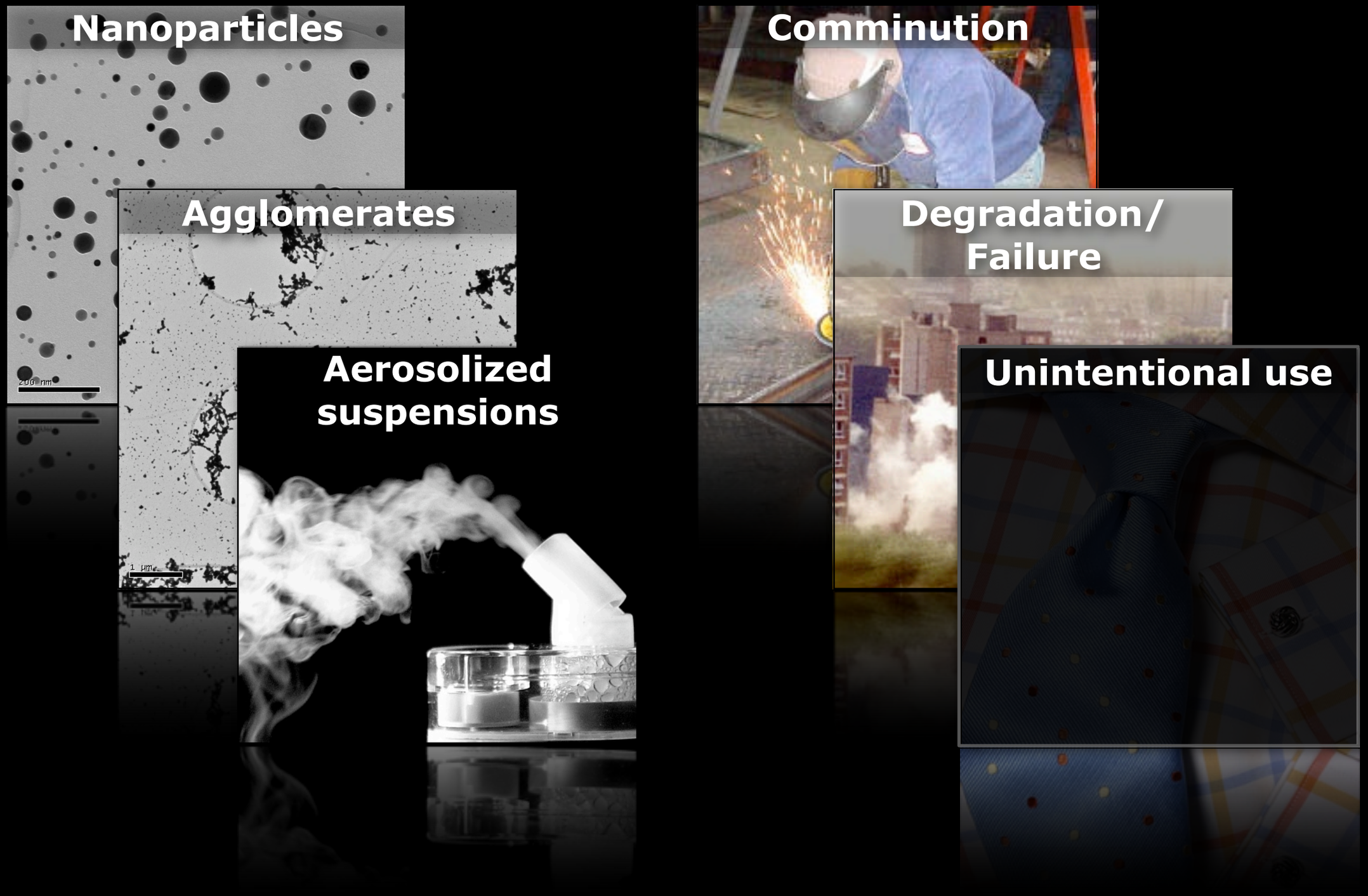
A thought experiment

The potential significance of structure on nanomaterial impact



Setting Boundaries

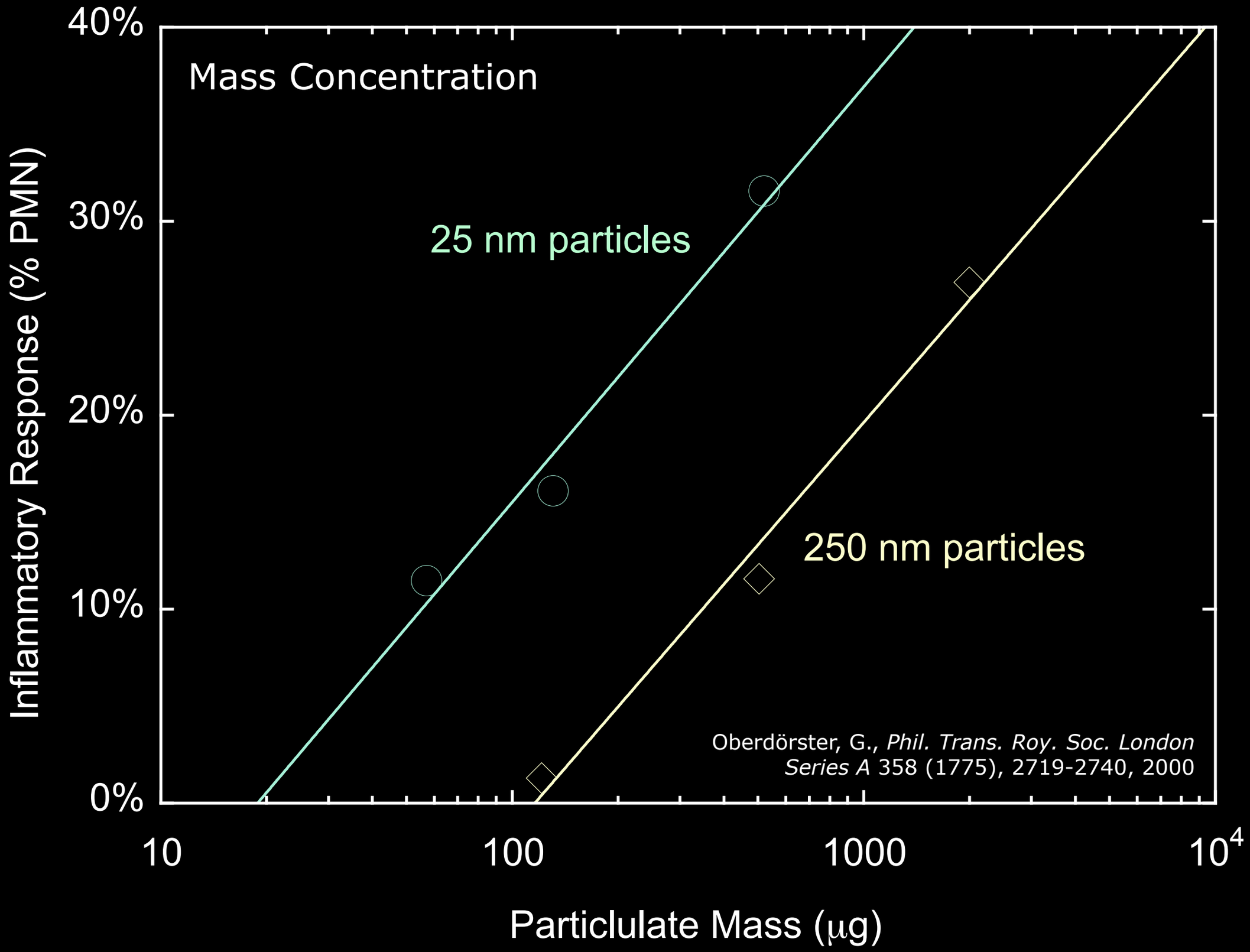
Engineered nanomaterials which potentially present new challenges



Maynard and Kuempel (2005), *J. Nanopart. Res.* 7(6) 587-614

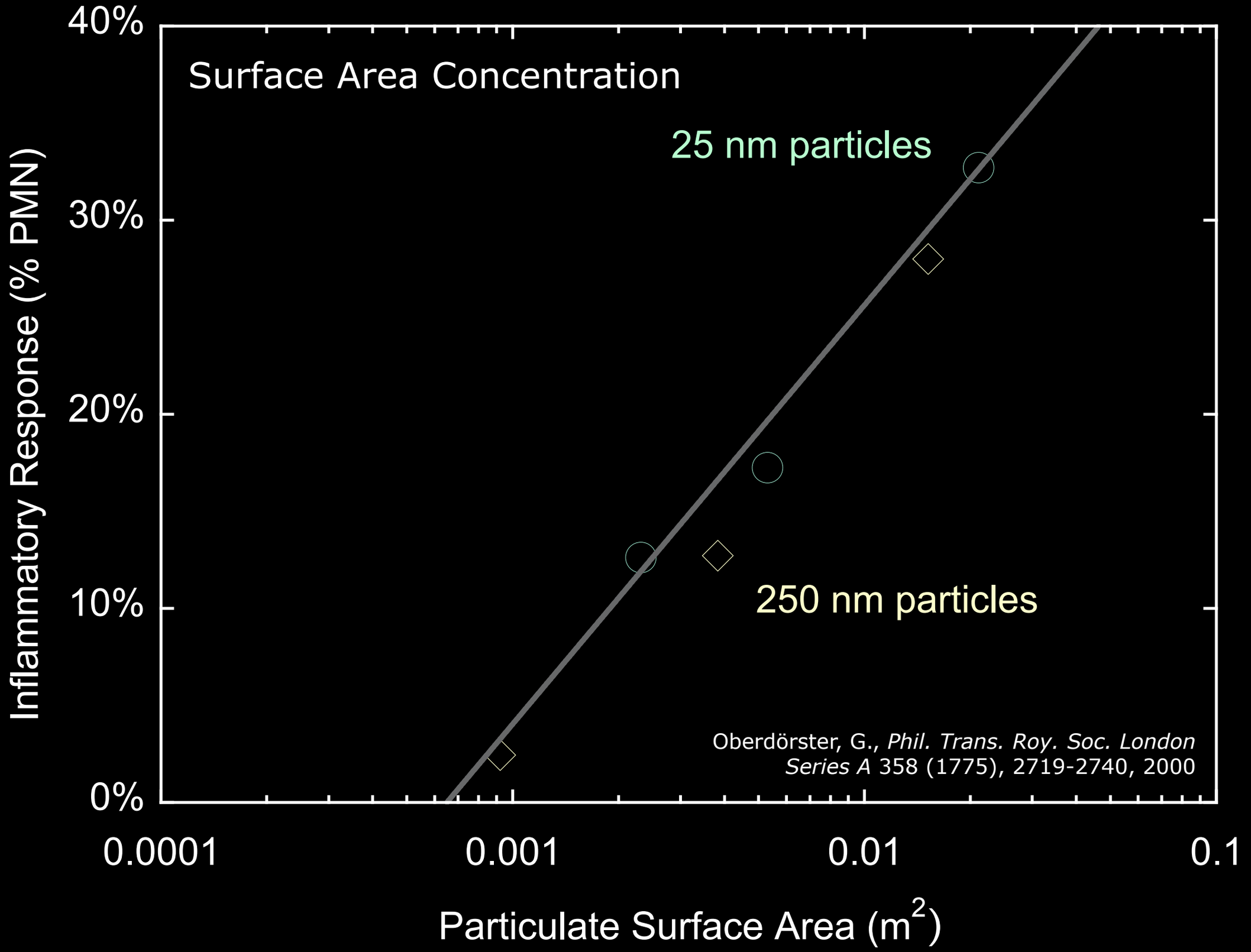
Structure-related hazard: Particle Size

TiO_2 Instillation in Rats



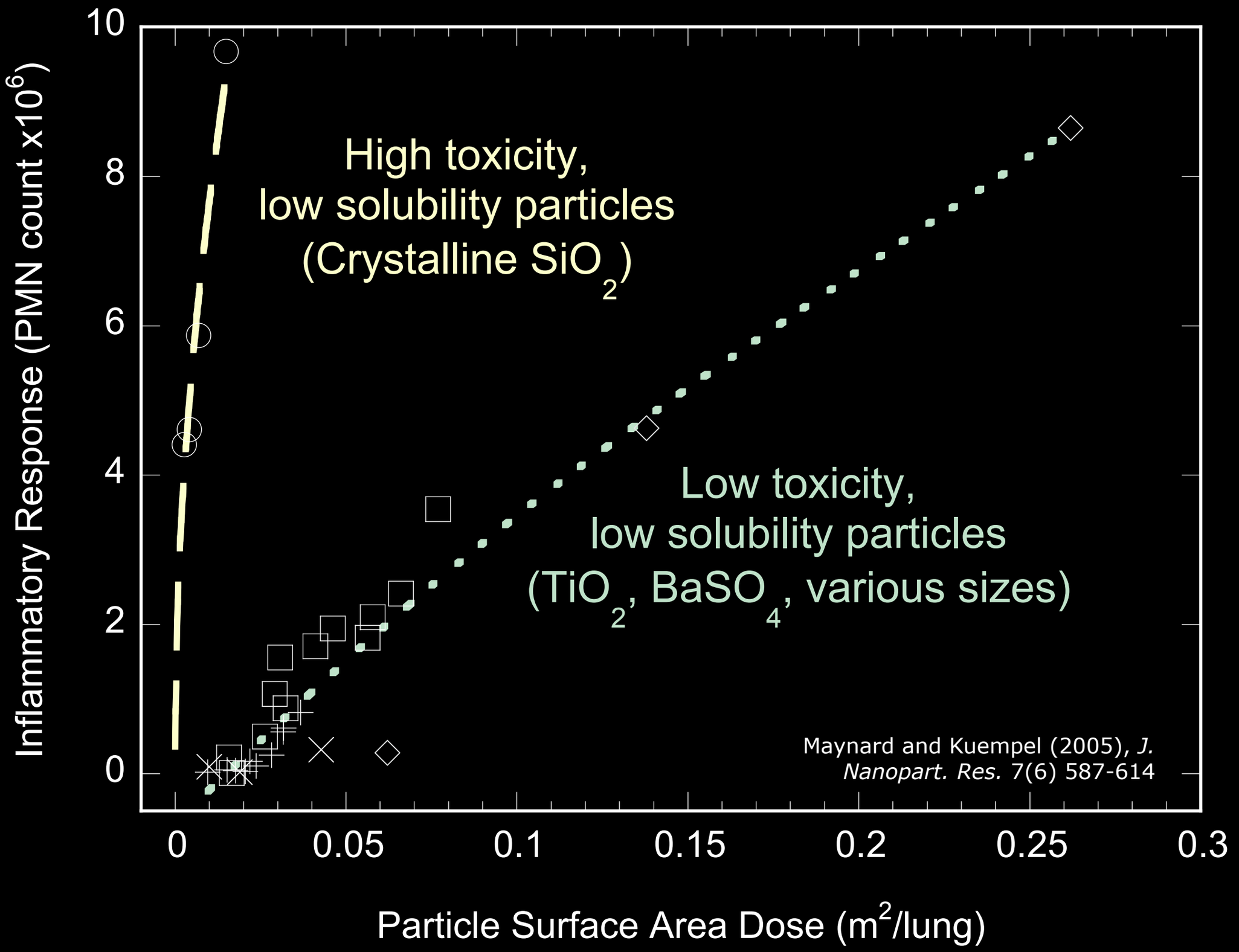
Structure-related hazard: Surface Area

TiO_2 Instillation in Rats



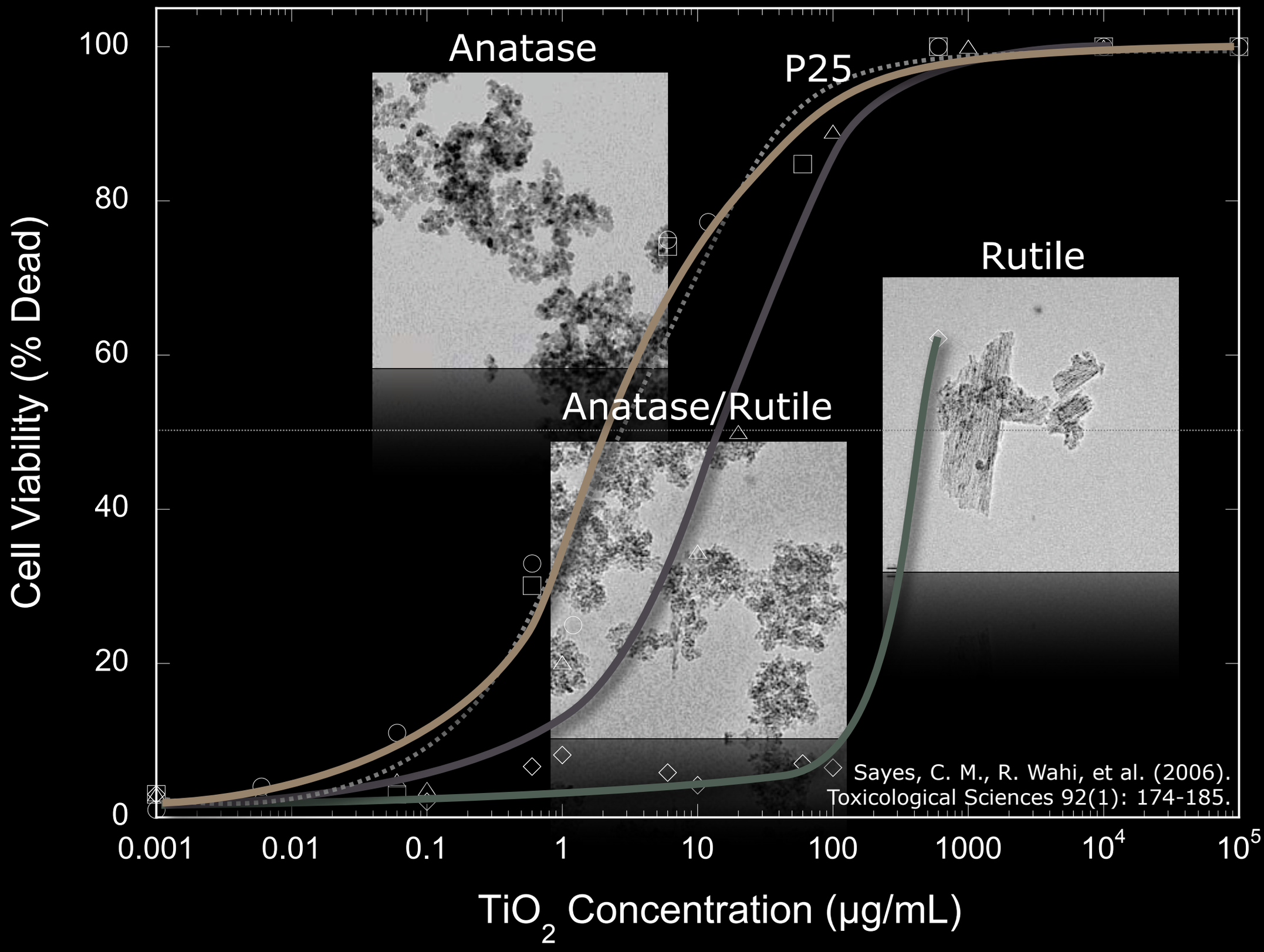
Structure-related hazard: Surface Chemistry

Rats



Structure-related hazard: Crystallinity

In vitro studies - Human Dermal Fibroblasts



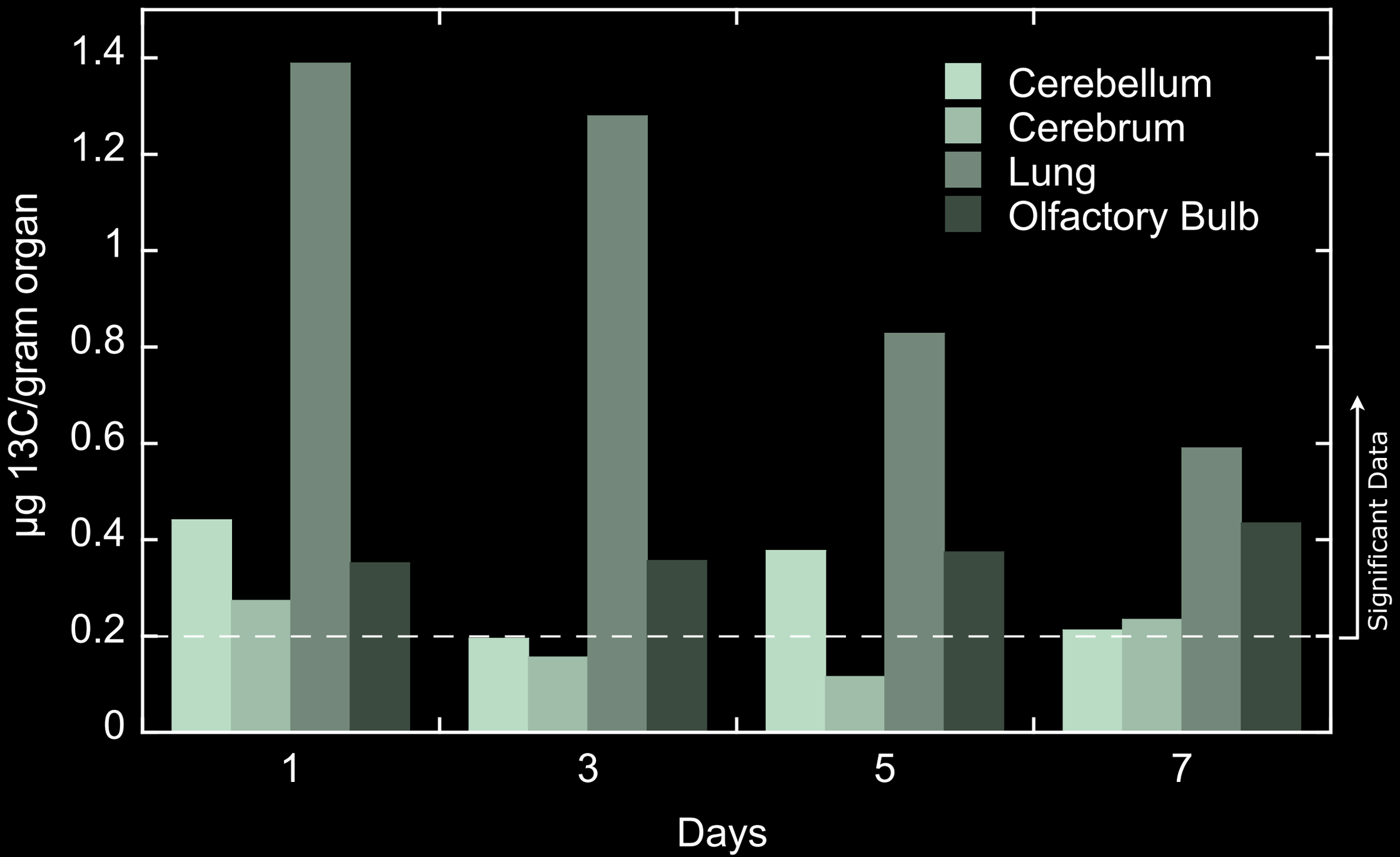
Structure-related hazard: Translocation

Translocation following inhalation - Nose to Brain

(Based on Oberdörster, G., *et al. (2004)*, *Inhal. Toxicol.* 16 (6-7), 437-445)

Structure-related hazard: Translocation

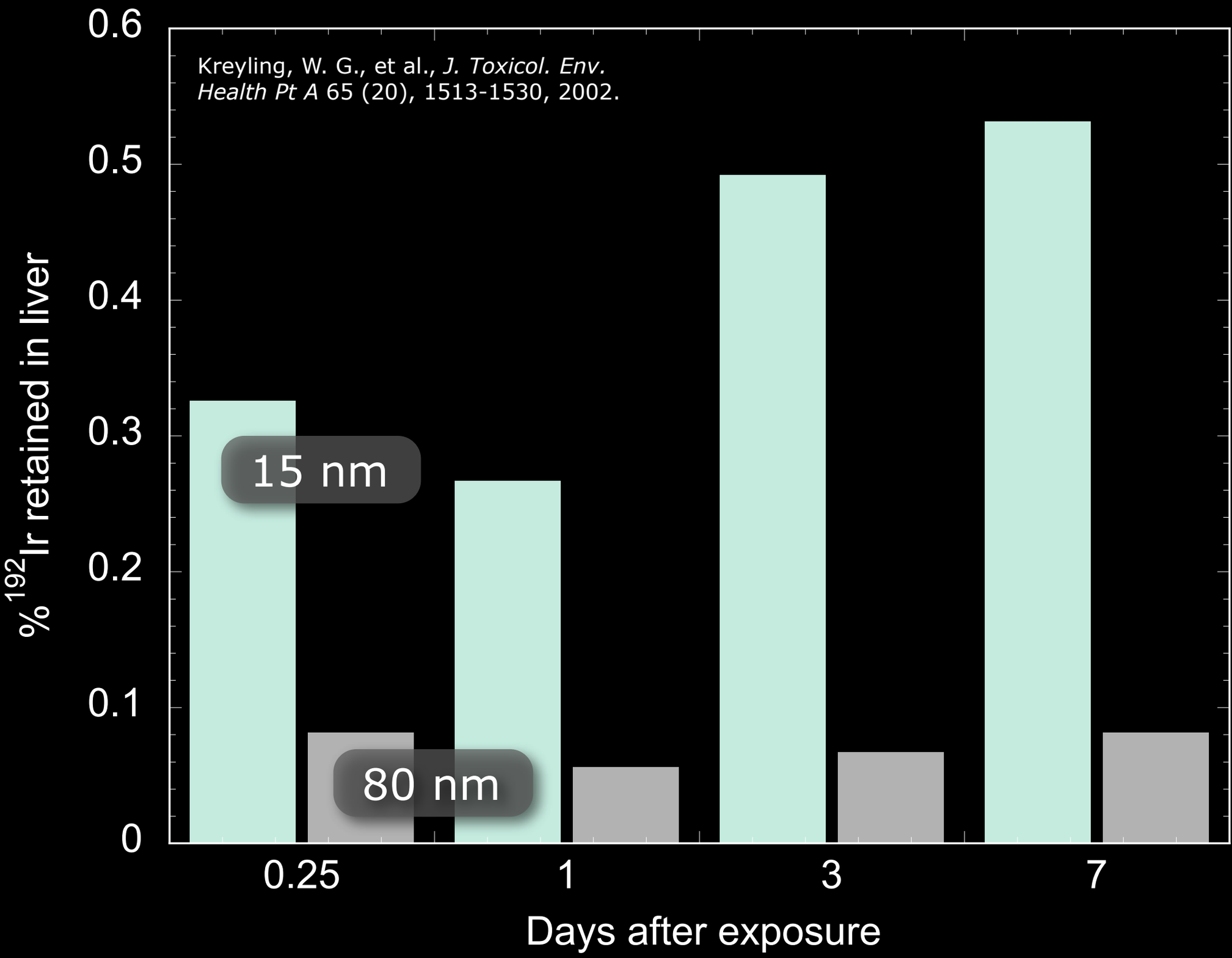
Translocation following inhalation - Nose to Brain



(Based on Oberdörster, G., *et al. (2004)*, *Inhal. Toxicol.* 16 (6-7), 437-445)

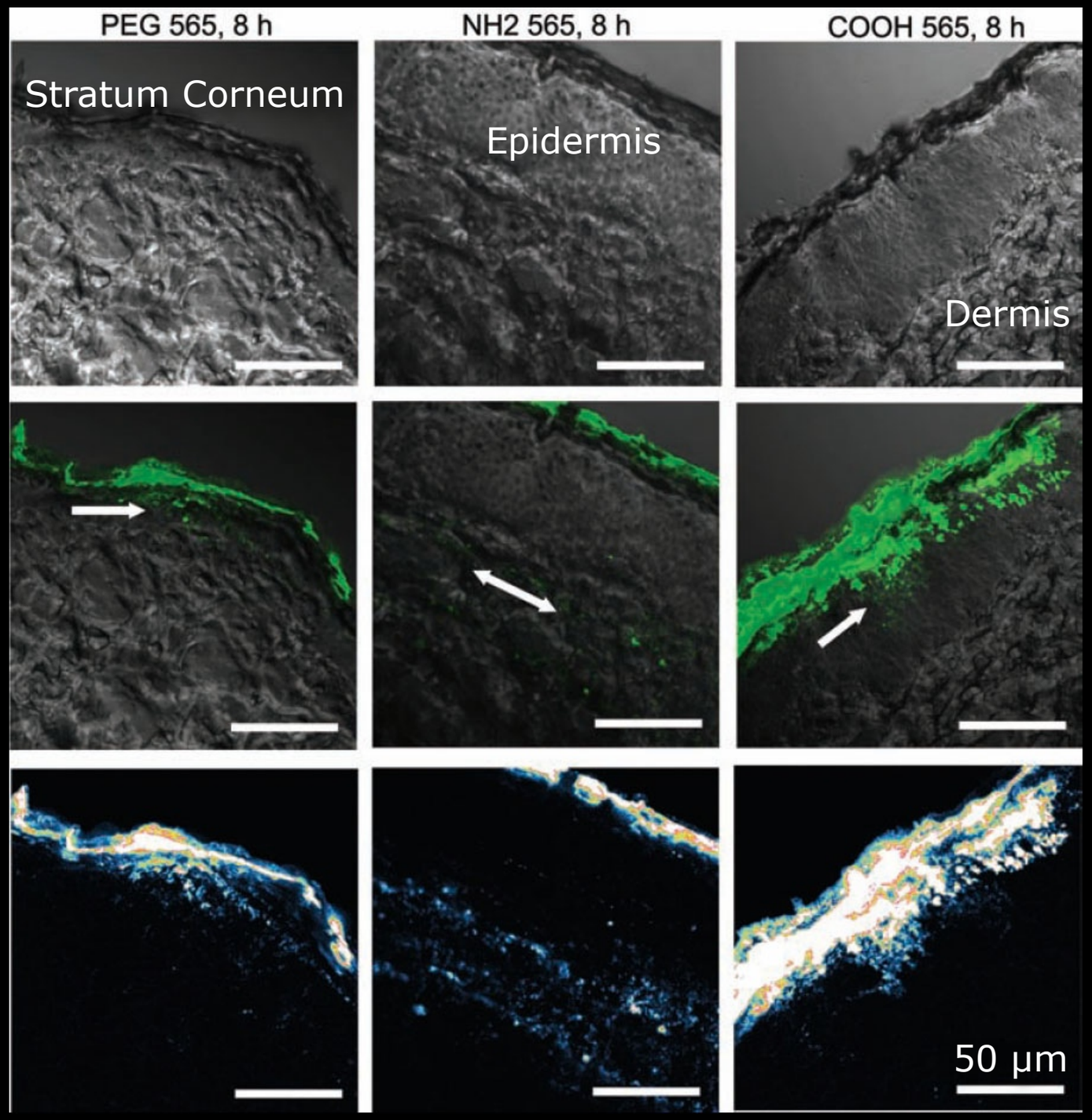
Structure-related hazard - Translocation

Translocation following inhalation - Lungs to Liver



Scale-specific hazard: Skin Penetration

4.6 nm spherical Quantum dots in porcine skin flow-through cell



Confocal Scanning Microscope images

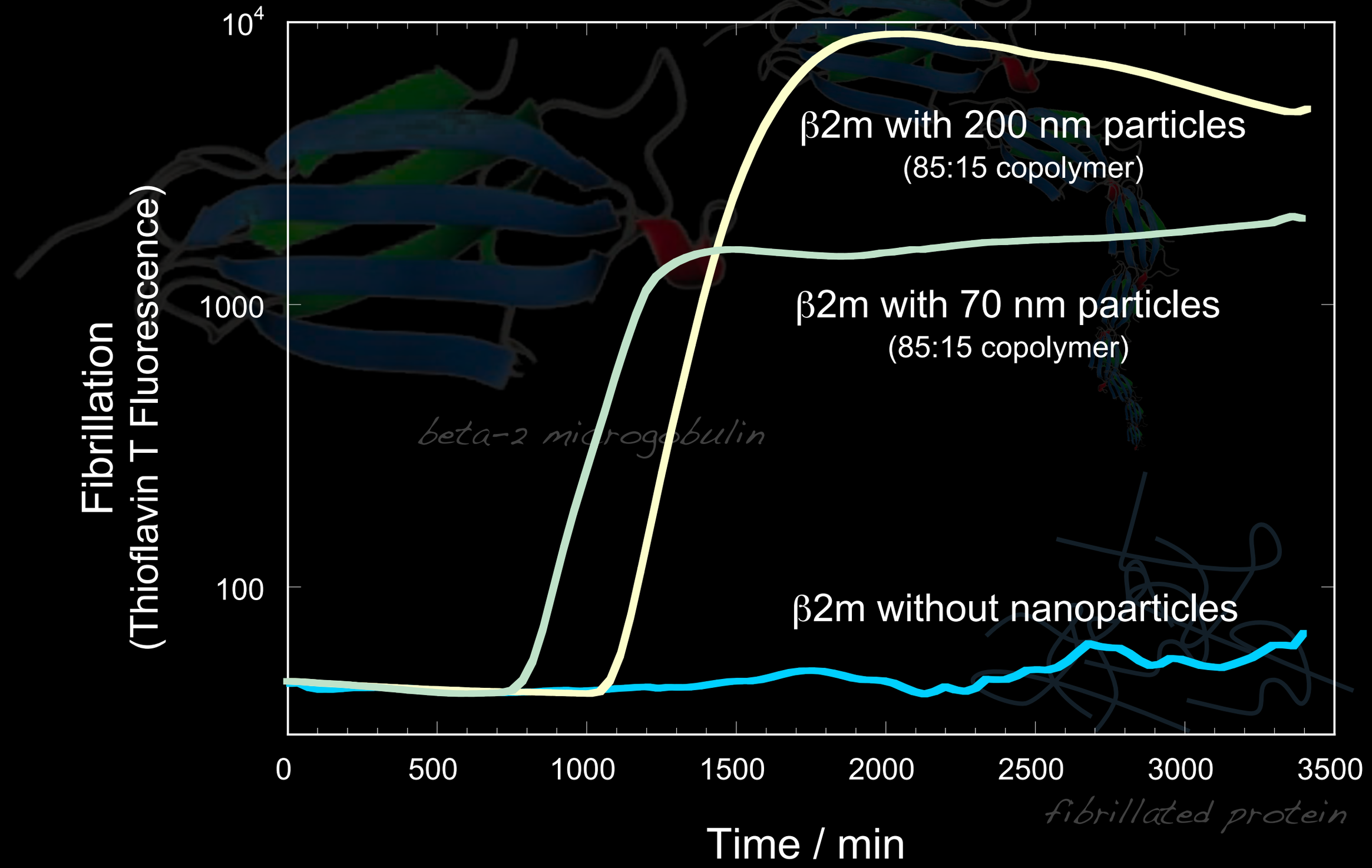
Quantum Dot fluorescence channel

Fluorescence intensity scan

Ryman-Rasmussen, J. P., J. E. Riviere and N. A. Monteiro-Riviere (2006). Tox. Sci. 91:159-165

Scale-specific hazard: Form

Interfering with biology at the nanoscale

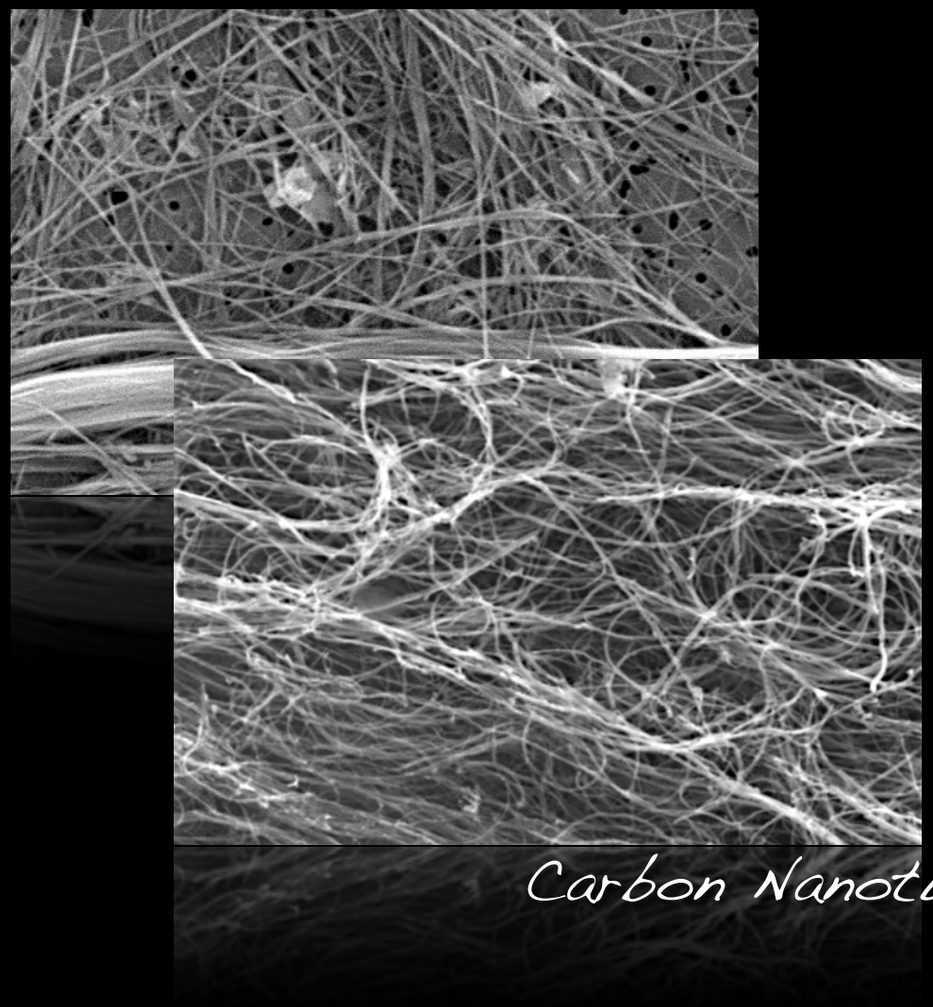


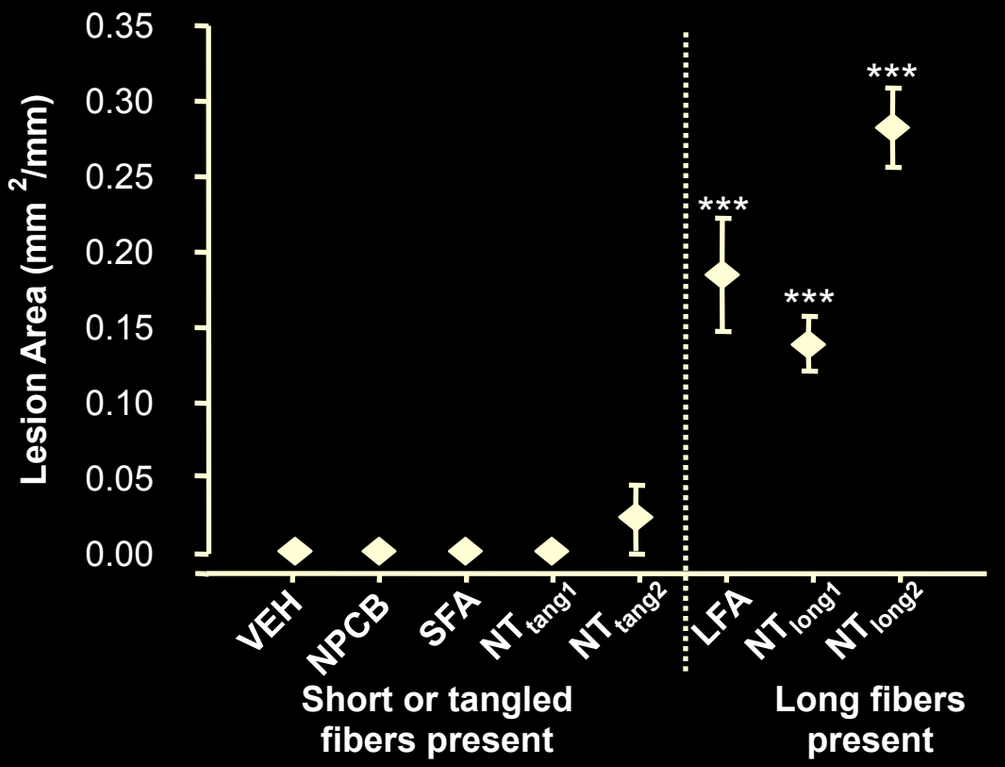
Linse, S., C. Cabaleiro-Lago, W.-F. Xue, I. Lynch, S. Lindman, E. Thulin, S. E. Radford and K. A. Dawson (2007). "Nucleation of protein fibrillation by nanoparticles." Proc. Natl. Acad. Sci. U. S. A. 104: 8691-8696.

Structure-related hazard: Shape

Influence of shape on a material's risk profile

Asbestos

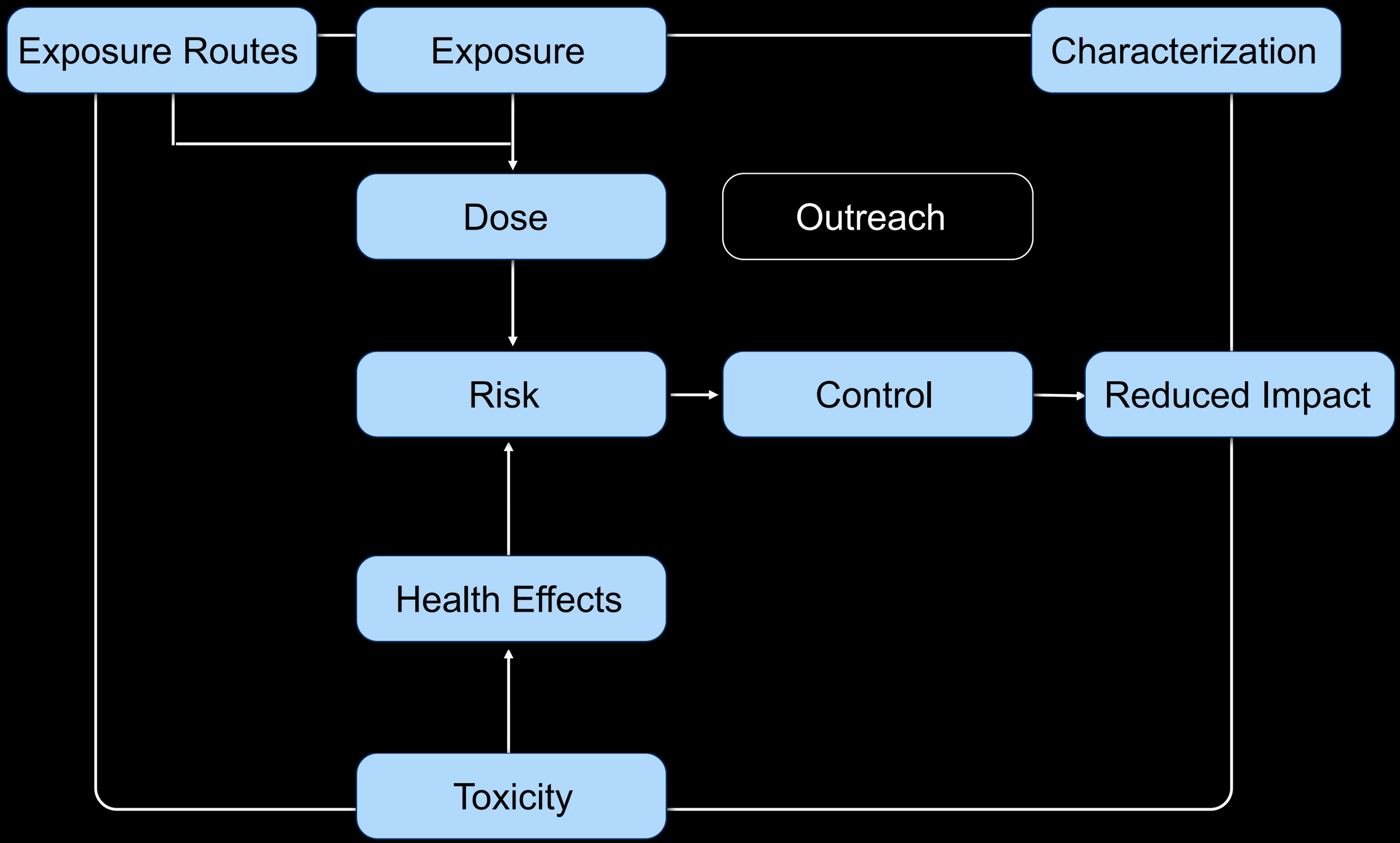


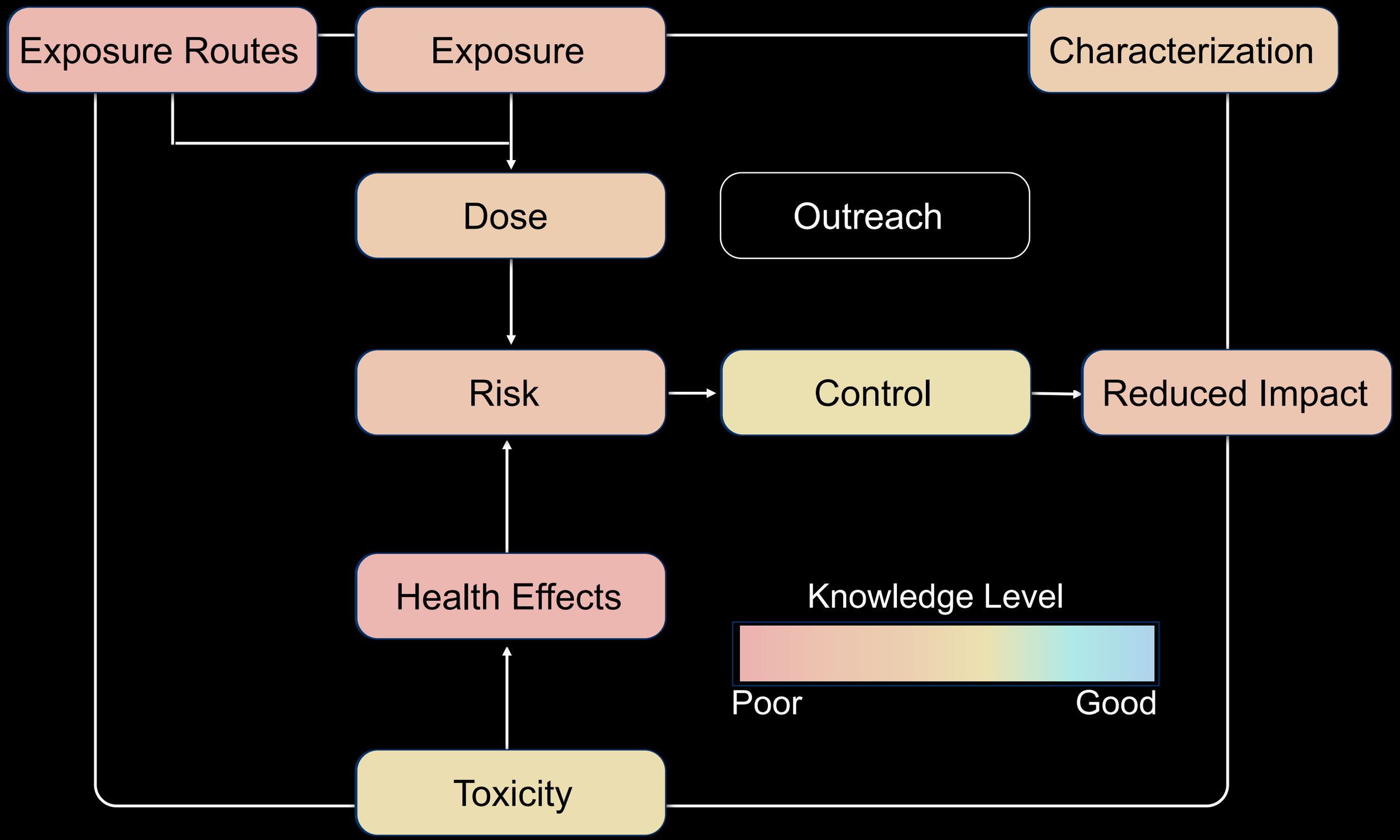


Carbon nanotubes that look like harmful asbestos fibers, behave like harmful asbestos fibers

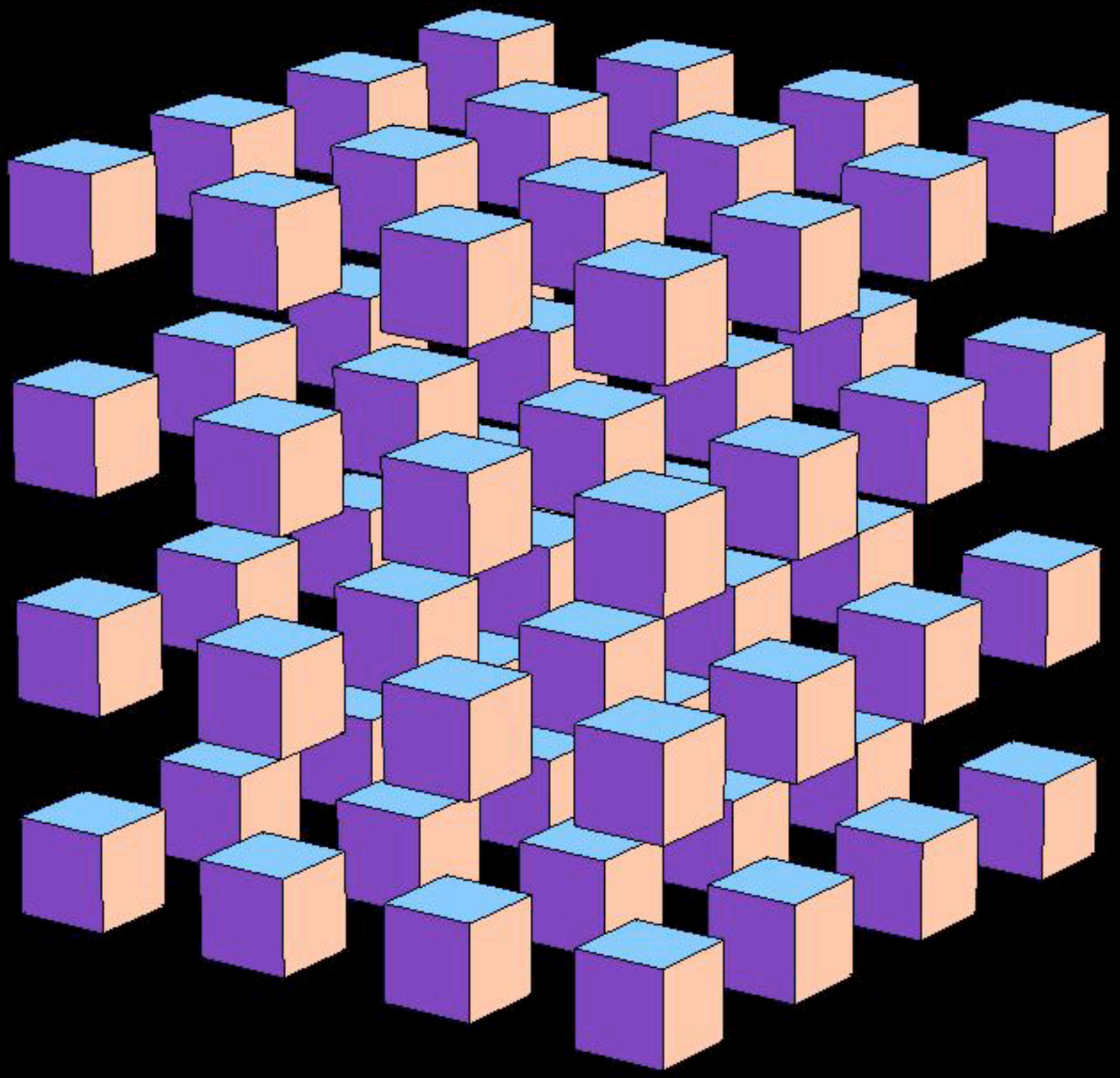
Source: Craig Poland

Poland, C. A., R. Duffin, I. Kinloch, A. Maynard, W. A. H. Wallace, A. Seaton, V. Stone, S. Brown, W. MacNee and K. Donaldson (2008). "Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study." Nature Nanotechnology doi:10.1038/nnano.2008.111.


Exposure Routes
Exposure
Characterization
Dose
Outreach
Risk
Control
Reduced Impact
Health Effects
Toxicity

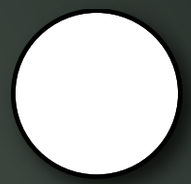

Exposure Routes
Exposure
Characterization
Dose
Outreach
Risk
Control
Reduced Impact
Health Effects
Knowledge Level
Poor
Good
Toxicity

Nanoparticles do not play by the rules



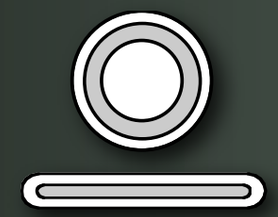
www.youtube.com/watch?v=gcOzMRFO0I4

Classifying diverse nanoparticles



Compact/Sphere
Homogeneous

Heterogeneous
Core-surface

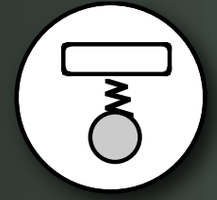


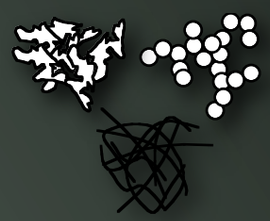
High aspect ratio
Homogeneous

Heterogeneous
Distributed

Complex non-spherical
Homogeneous

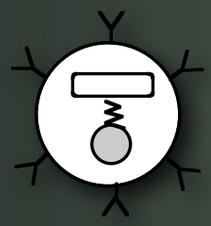
Active
External stimuli

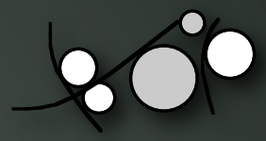




Homogeneous agglomerates
Single particle class

Multifunctional
Complex responses





Heterogeneous aggregates
Many particle classes

Maynard, A. D. and R. J. Aitken (2007). Nanotoxicology 1(1): 26-41.

Potentially significant attributes

- Differentiated component release
- Shape
- Core-surface Heterogeneity
- Charge
- Response to environment
- Porosity
- Response to stimulus
- Surface Area
- Surface Chemistry
- Crystal Structure
- Composition
- Distributed Heterogeneity
- Solubility
- Propensity to change structure

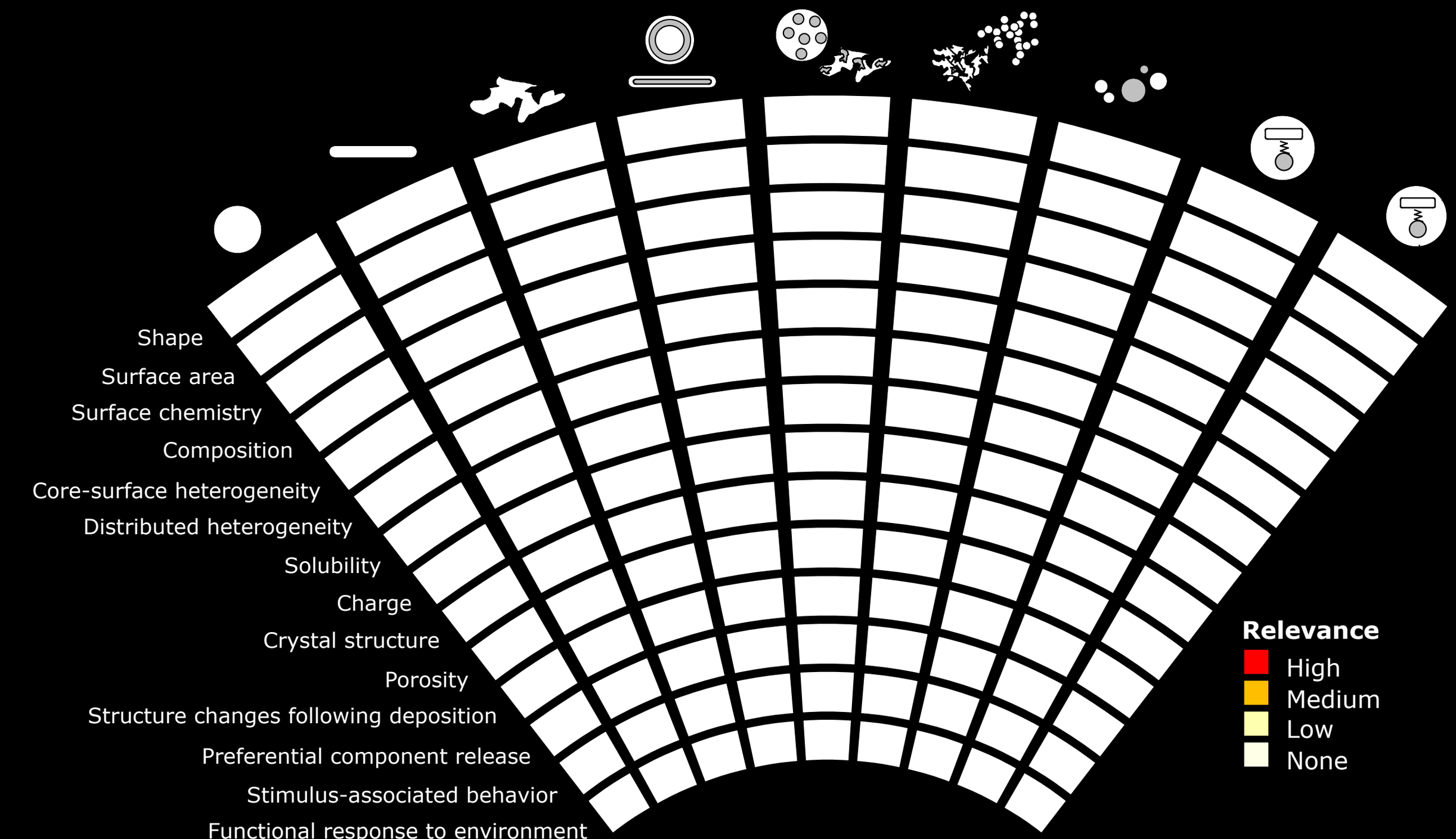
Maynard, A. D. and R. J. Aitken (2007). Nanotoxicology 1(1): 26-41.

Monitoring nanoscale aerosol exposures

Options

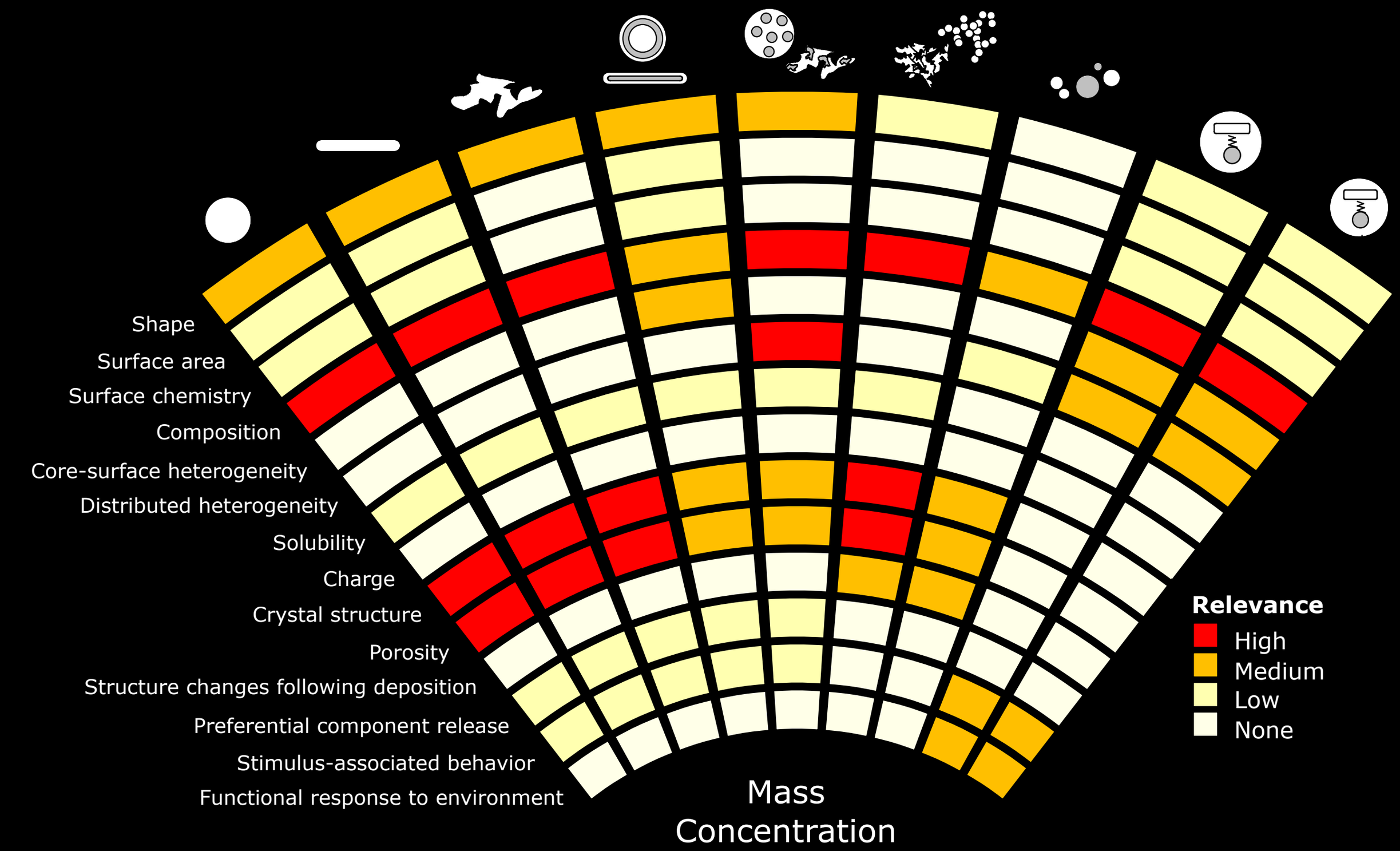
Or…

Assessing the relevance of different exposure metrics

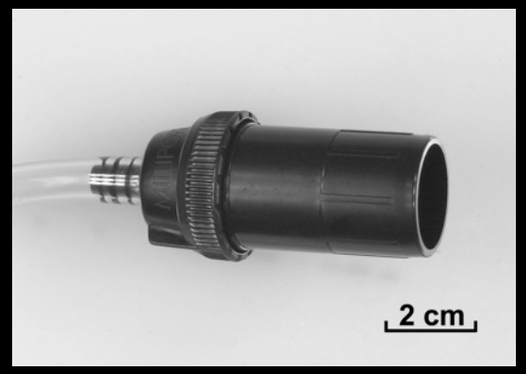


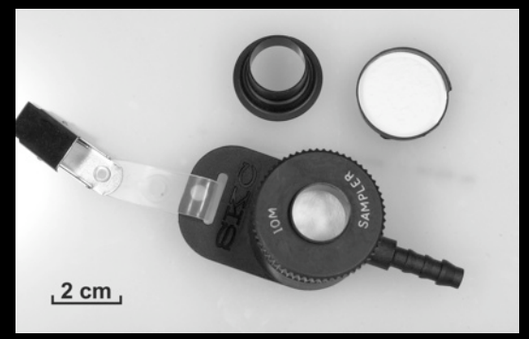
Maynard, A. D. and R. J. Aitken (2007). Nanotoxicology 1(1): 26-41.

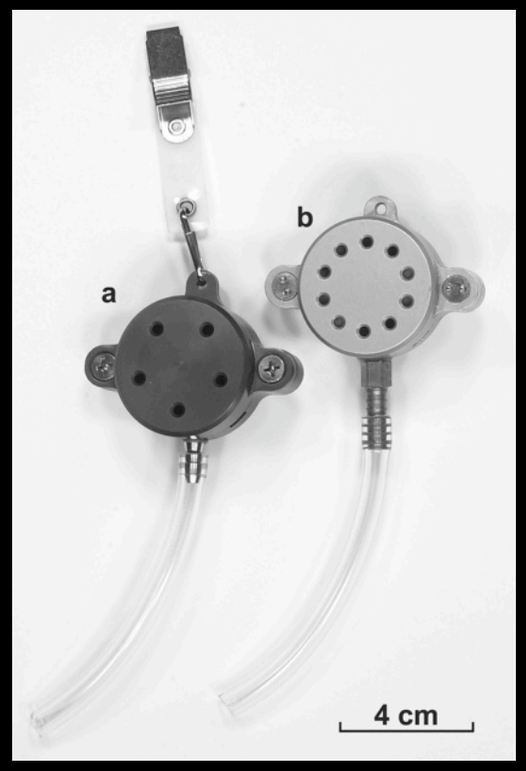
Mass



Maynard, A. D. and R. J. Aitken (2007). Nanotoxicology 1(1): 26-41.


2 cm


SKC
10M
SAMPLER
2 cm

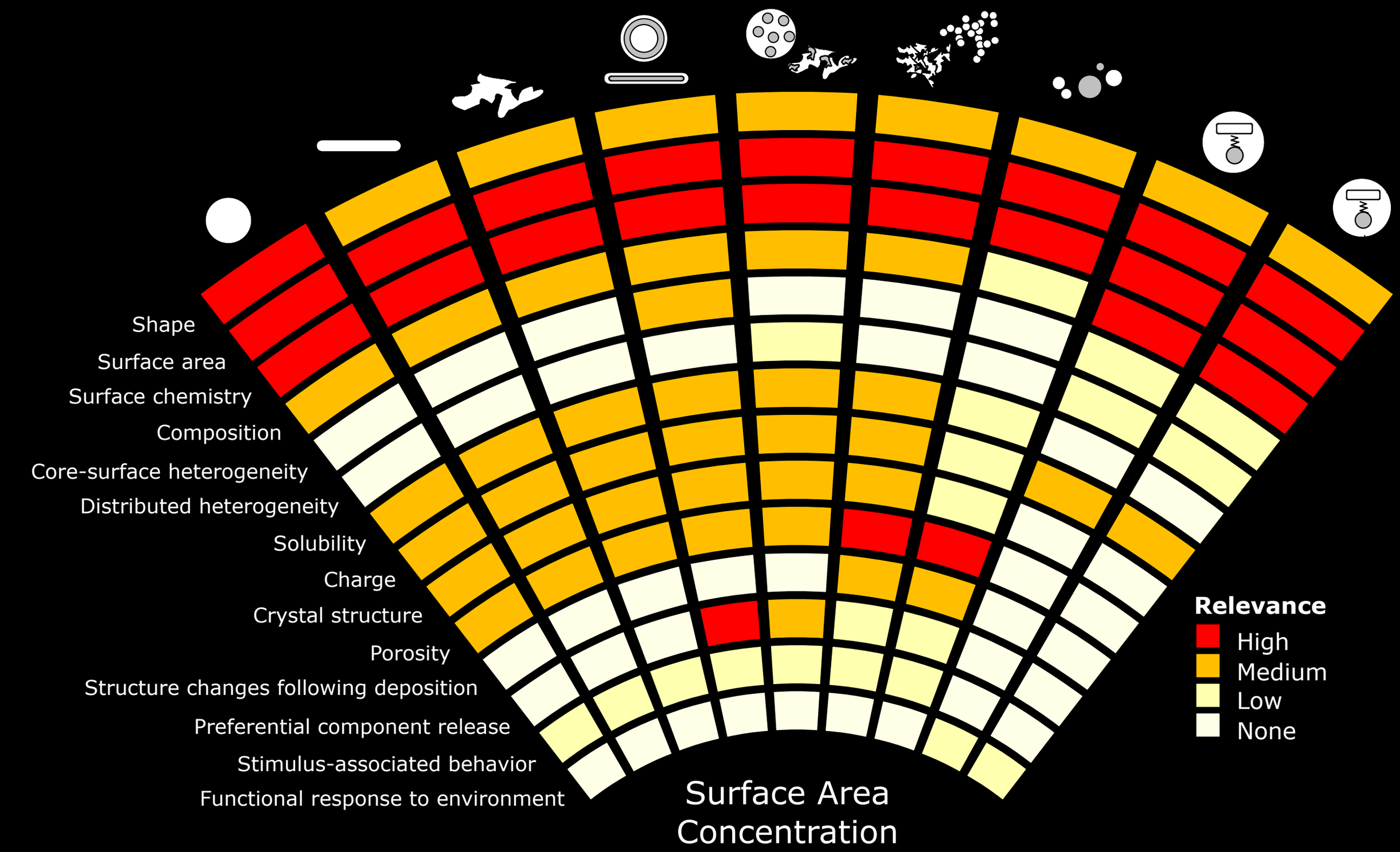

a
b
4 cm


4 cm


CASELLA
LONDON
ISLEWORTH
GRAVIMETRIC DUST SAMPLER
4 cm


4 cm

Surface Area



Maynard, A. D. and R. J. Aitken (2007). Nanotoxicology 1(1): 26-41.

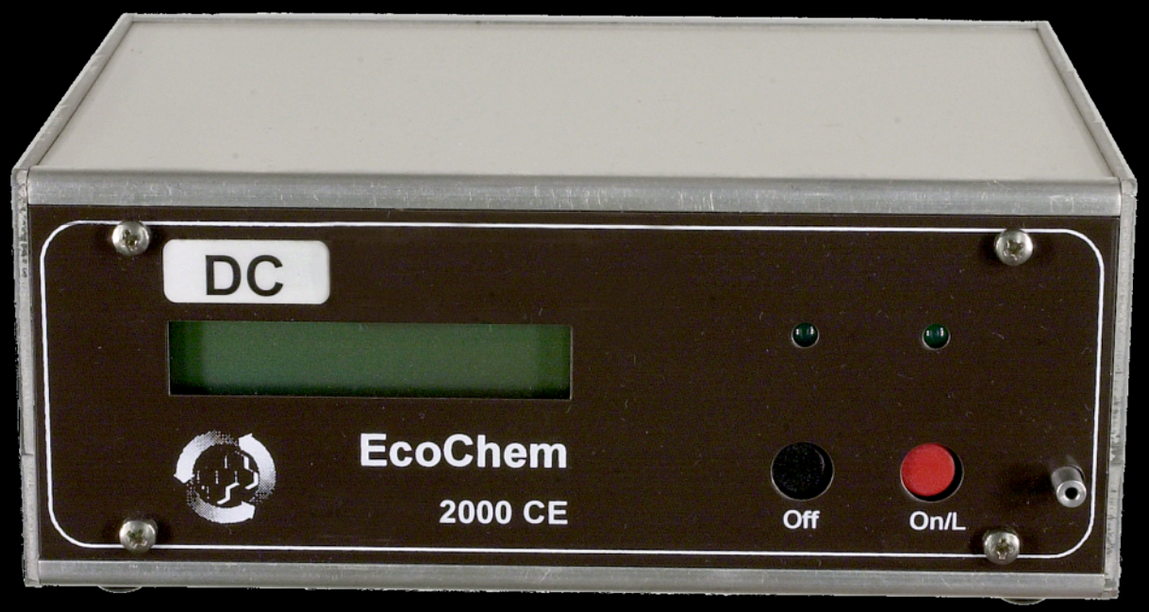
Aerosol Surface Area Measurement

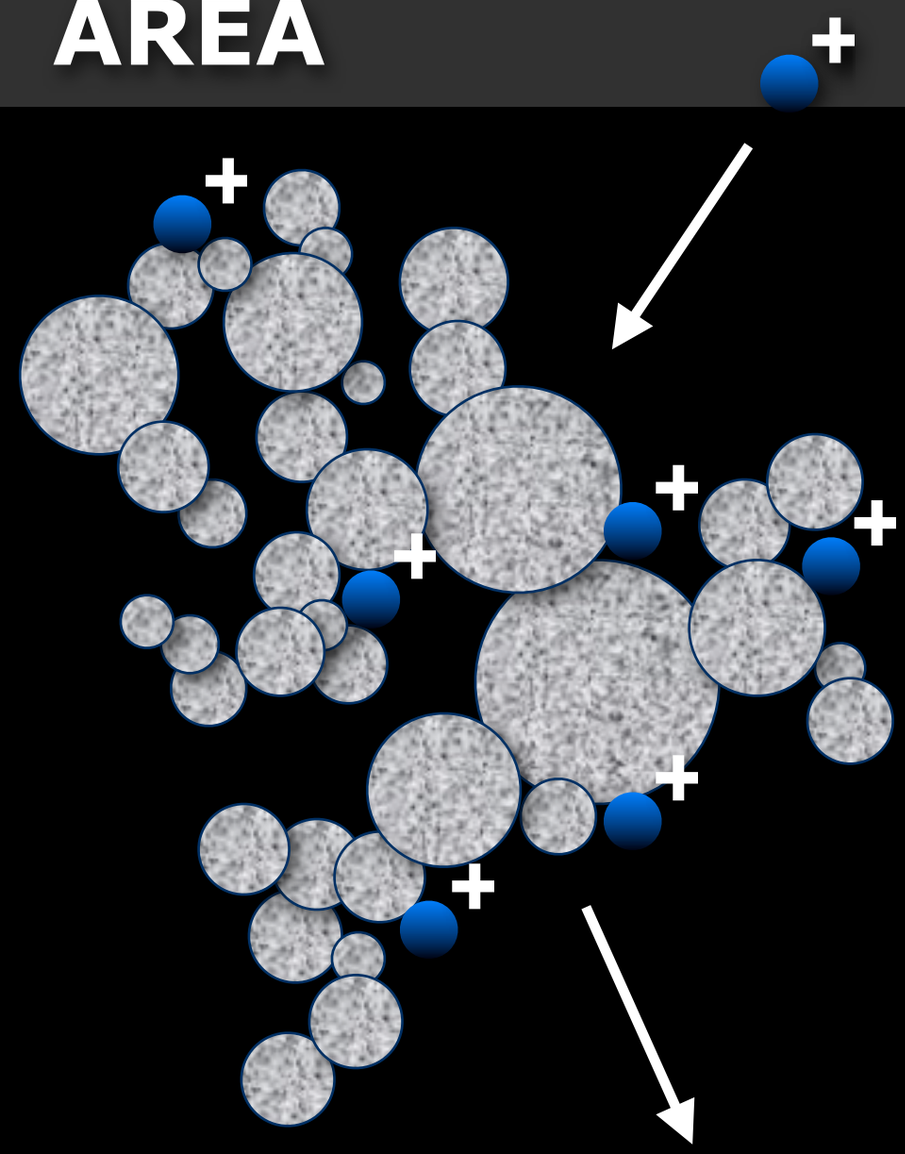
Using Attachment Rate

AEROSOL CHARGE $\propto$ **SURFACE AREA**

DC2000 CE Diffusion Charger

EcoChem

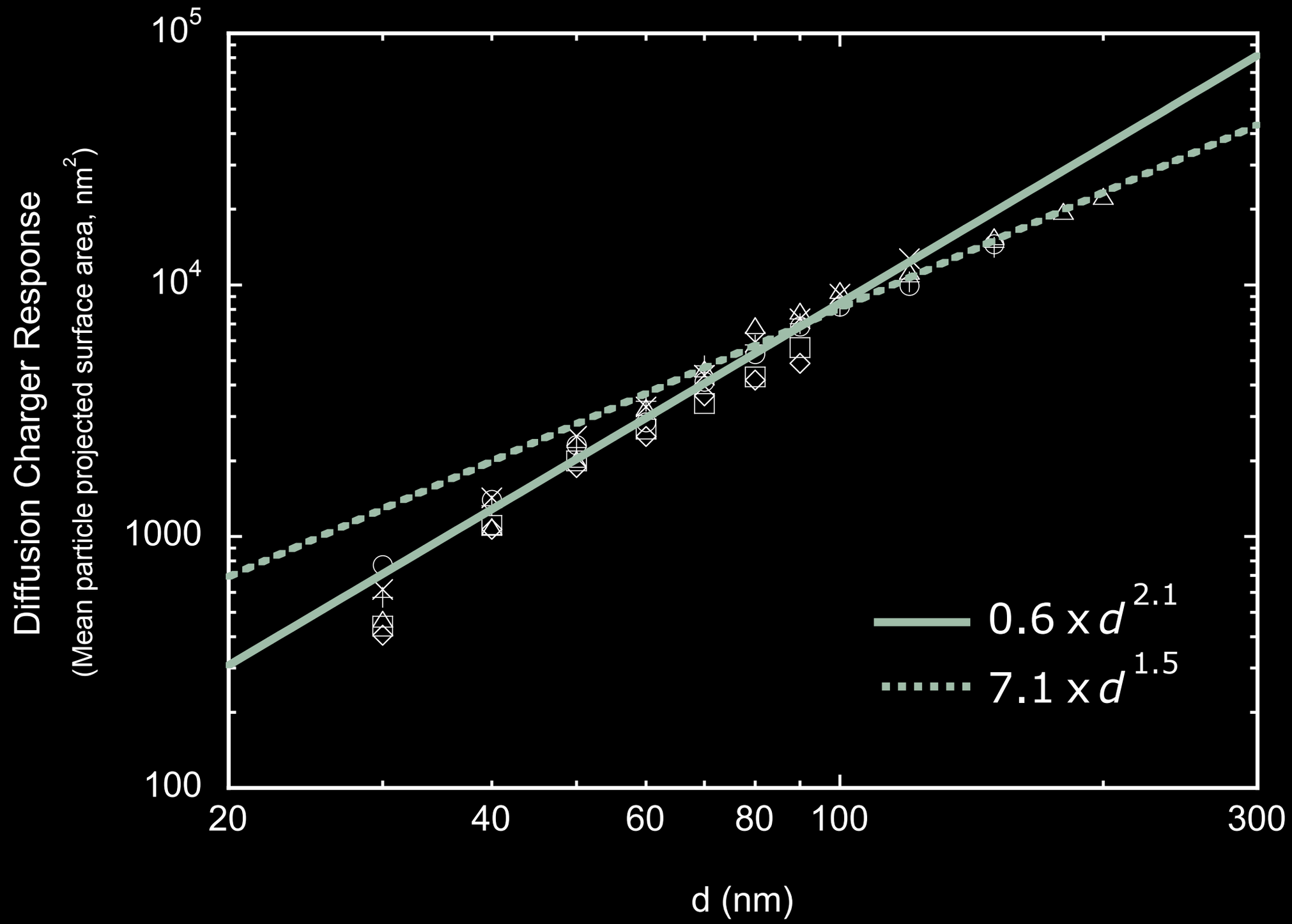




ELECTROMETER

Aerosol Surface Area Measurement

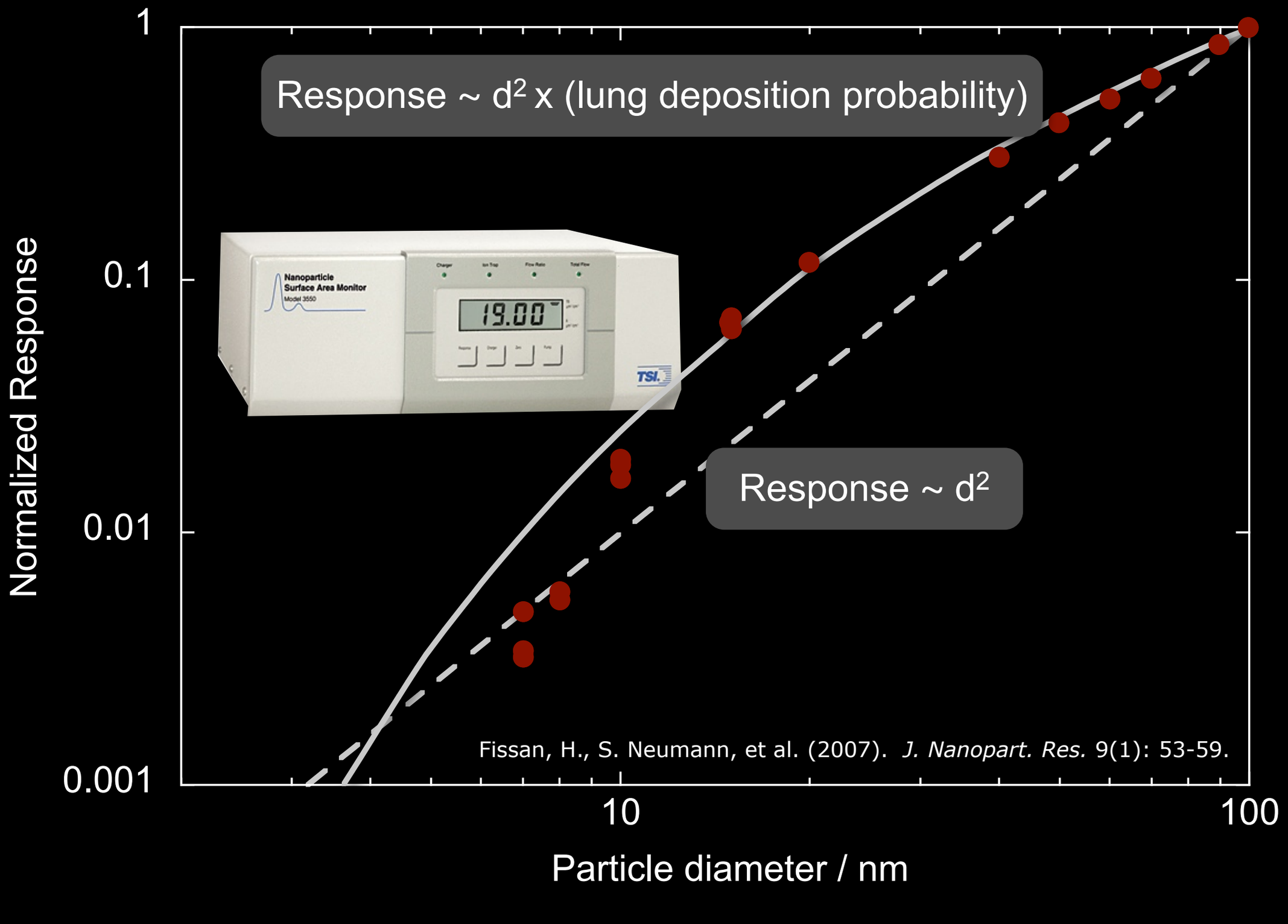
Diffusion Charger Response



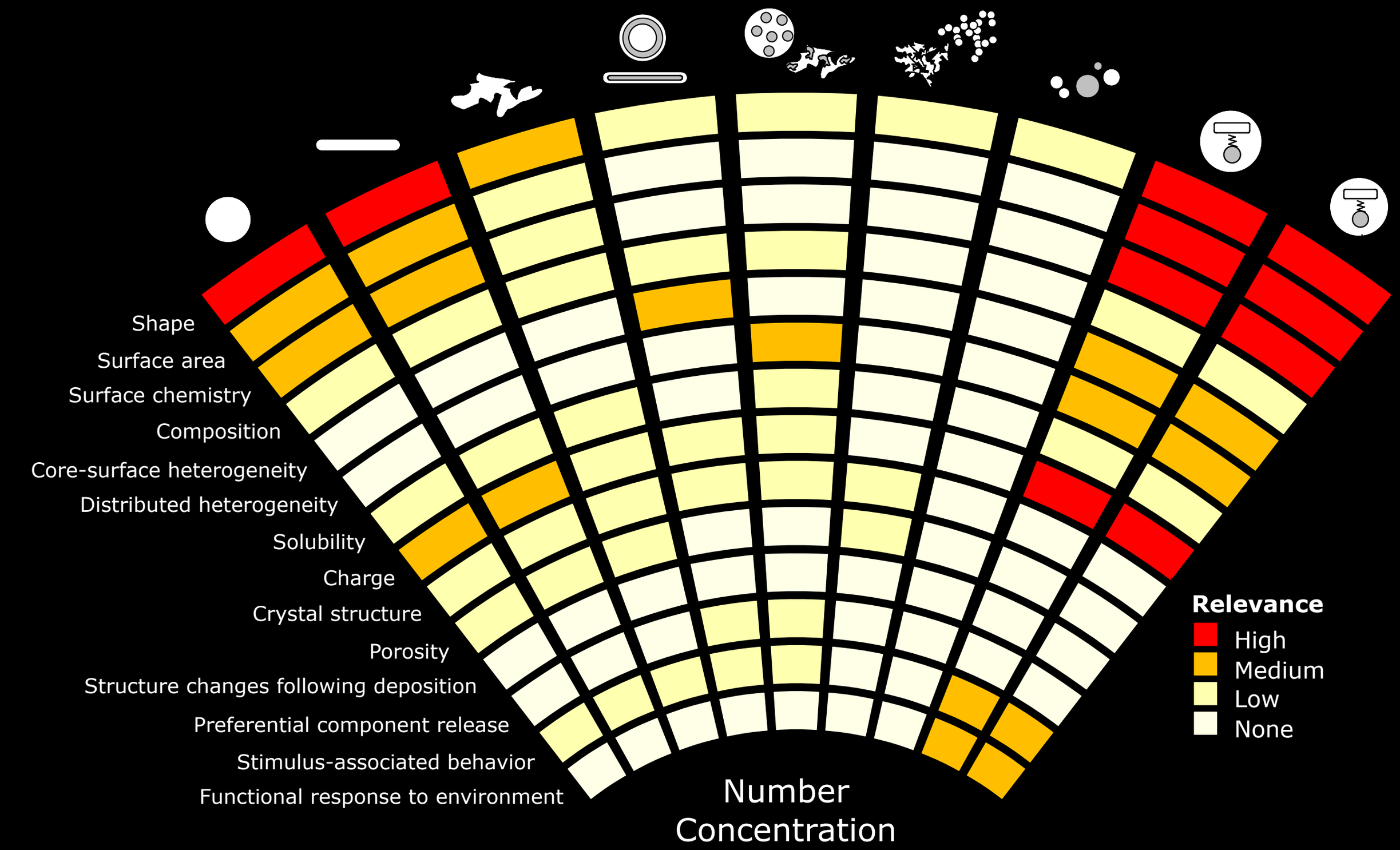
Ku, B. K. and Maynard, A. D. J. Aerosol Sci. 36 (9), 1108-1124, 2005.

Aerosol Surface Area Measurement

Measuring deposited surface area



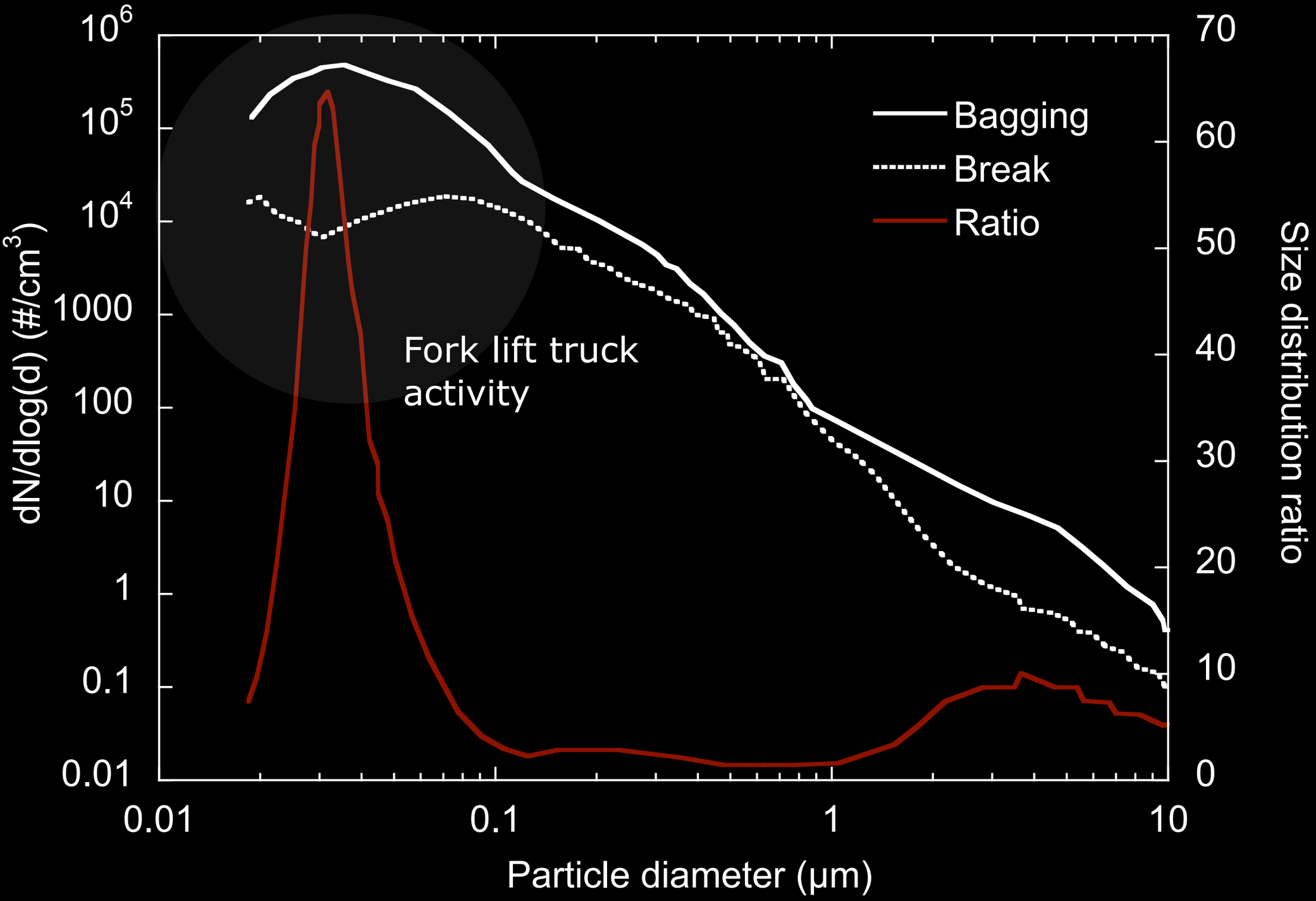
Particle Number



Maynard, A. D. and R. J. Aitken (2007). Nanotoxicology 1(1): 26-41.

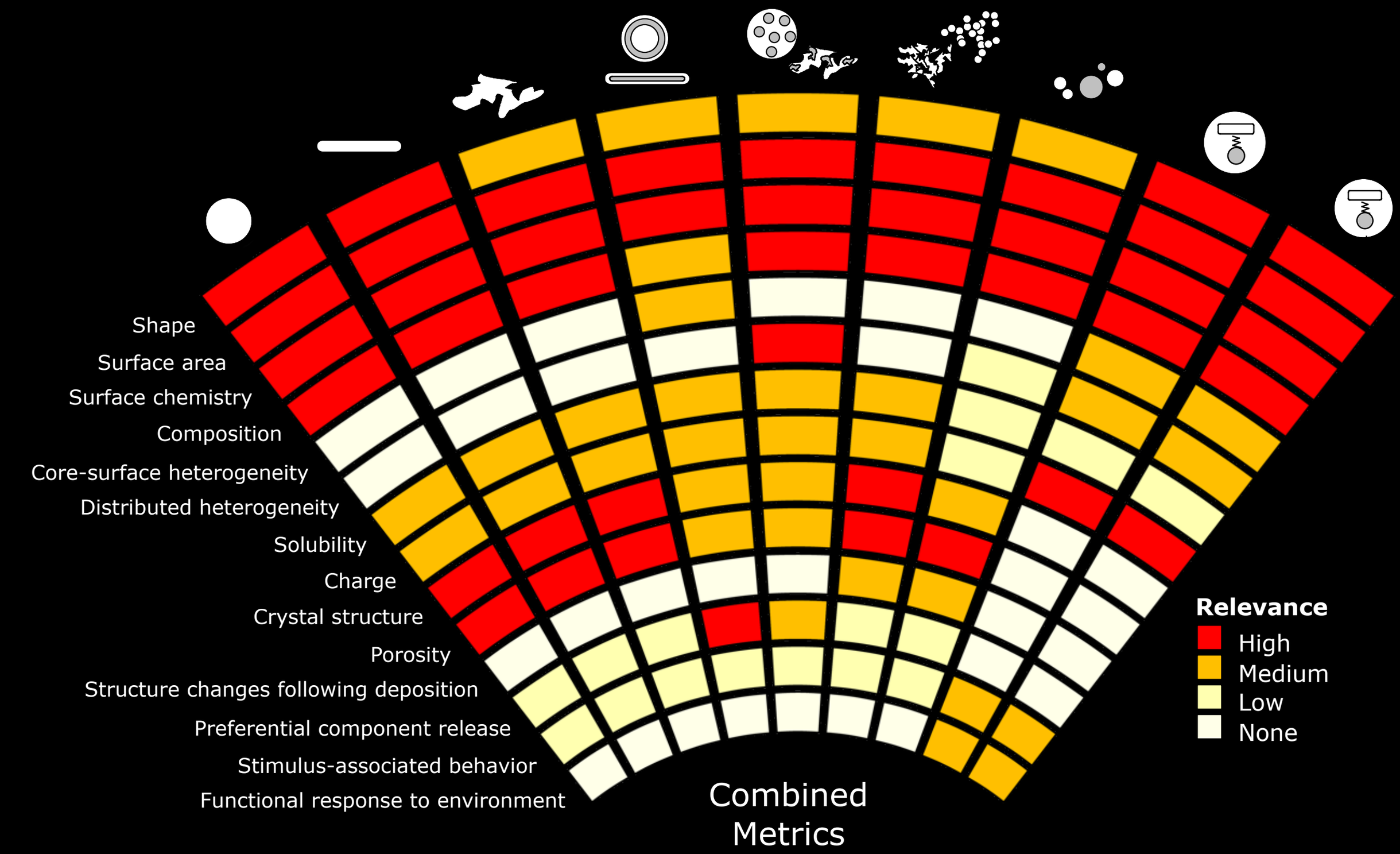
Particle size-resolved exposure measurements

Aerosol exposure during carbon black bagging



Kuhlbusch, T. A. J., S. Neumann, et al. (2004). *J. Occup. Environ. Hyg.* 1(10): 660-671.

Number, Mass or Surface Area



Maynard, A. D. and R. J. Aitken (2007). Nanotoxicology 1(1): 26-41.

COMMENTARY

Safe handling of nanotechnology

The pursuit of responsible nanotechnologies can be tackled through a series of grand challenges, argue Andrew D. Maynard and his co-authors.

When the physicist and Nobel laureate Richard Feynman challenged the science community to think small in his 1959 lecture 'There's Plenty of Room at the Bottom', he planted the seeds of a new era in science and technology. Nanotechnology, which is about controlling matter at near-atomic scales to produce unique or enhanced materials, products and devices, is now maturing rapidly with more than 300 claimed nanotechnology products already on the market[1]. Yet concerns have been raised that the very properties of nanostructured materials that make them so attractive could potentially lead to unforeseen health or environmental hazards[2].

D. RAMSEY

Nature Vol. 444/16 November 2006

2 Assess whether fibre-shaped nanoparticles present a unique health risk

3 Models for predicting engineered-nanomaterial behaviour in the environment

2 Validated alternatives for *in vivo* nanomaterial toxicity tests

5 Strategic research programmes

2 High-throughput toxicity-testing protocols

1 'Smart sensors' that indicate potential harm

2006 2008 2010 2012 2014 2016 2018 2020 2022

1 A universal aerosol sampler for airborne nanostructure materials

1 Instruments to monitor waterborne engineered nanomaterials

4 The ability to evaluate the impact of engineered nanomaterials from cradle to grave

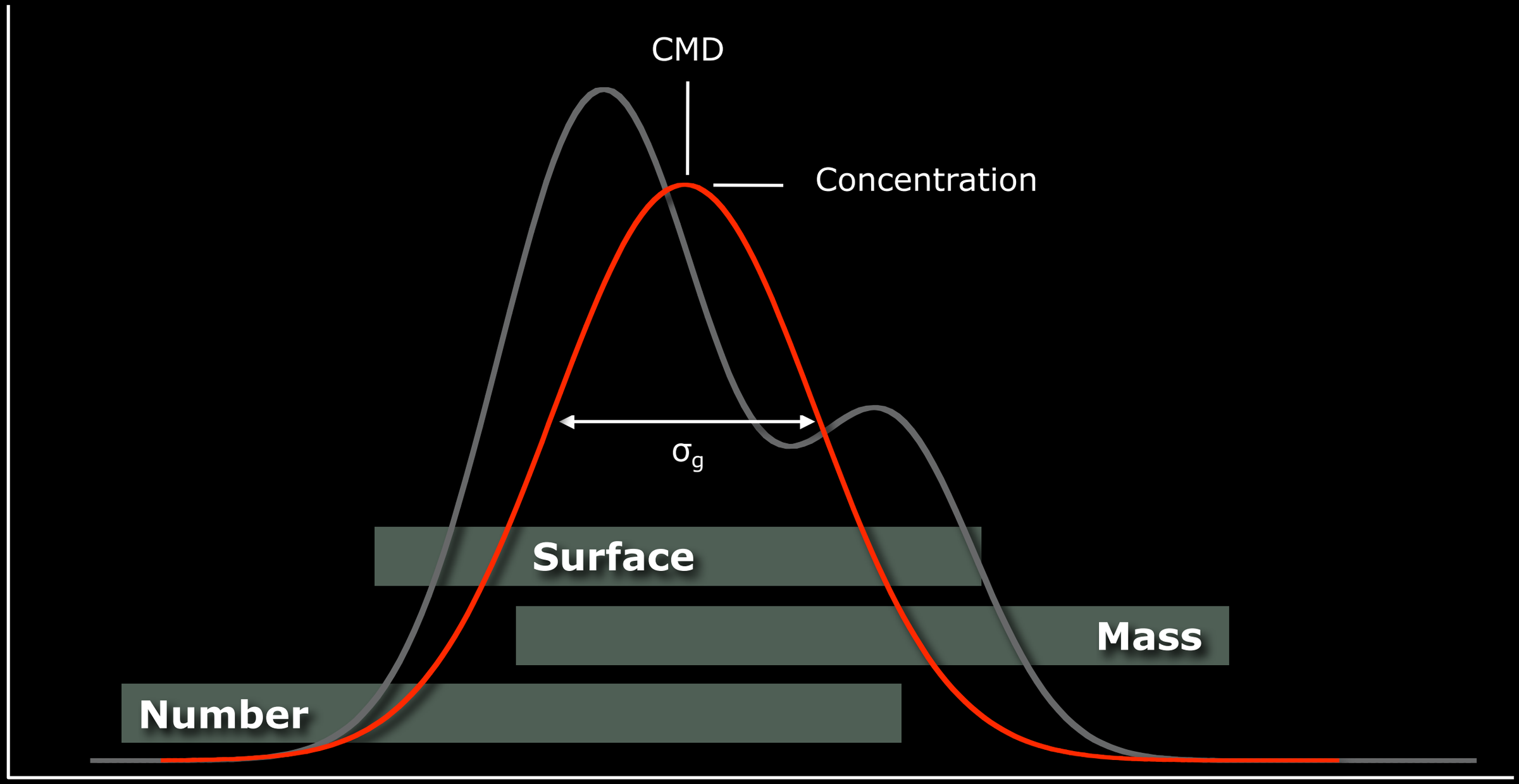
3 Methods for engineering nanomaterials that are safe-by-design

3 Models for predicting engineered-nanomaterial behaviour in the body

FIVE GRAND CHALLENGES

Developing safe nanotechnologies through sound science

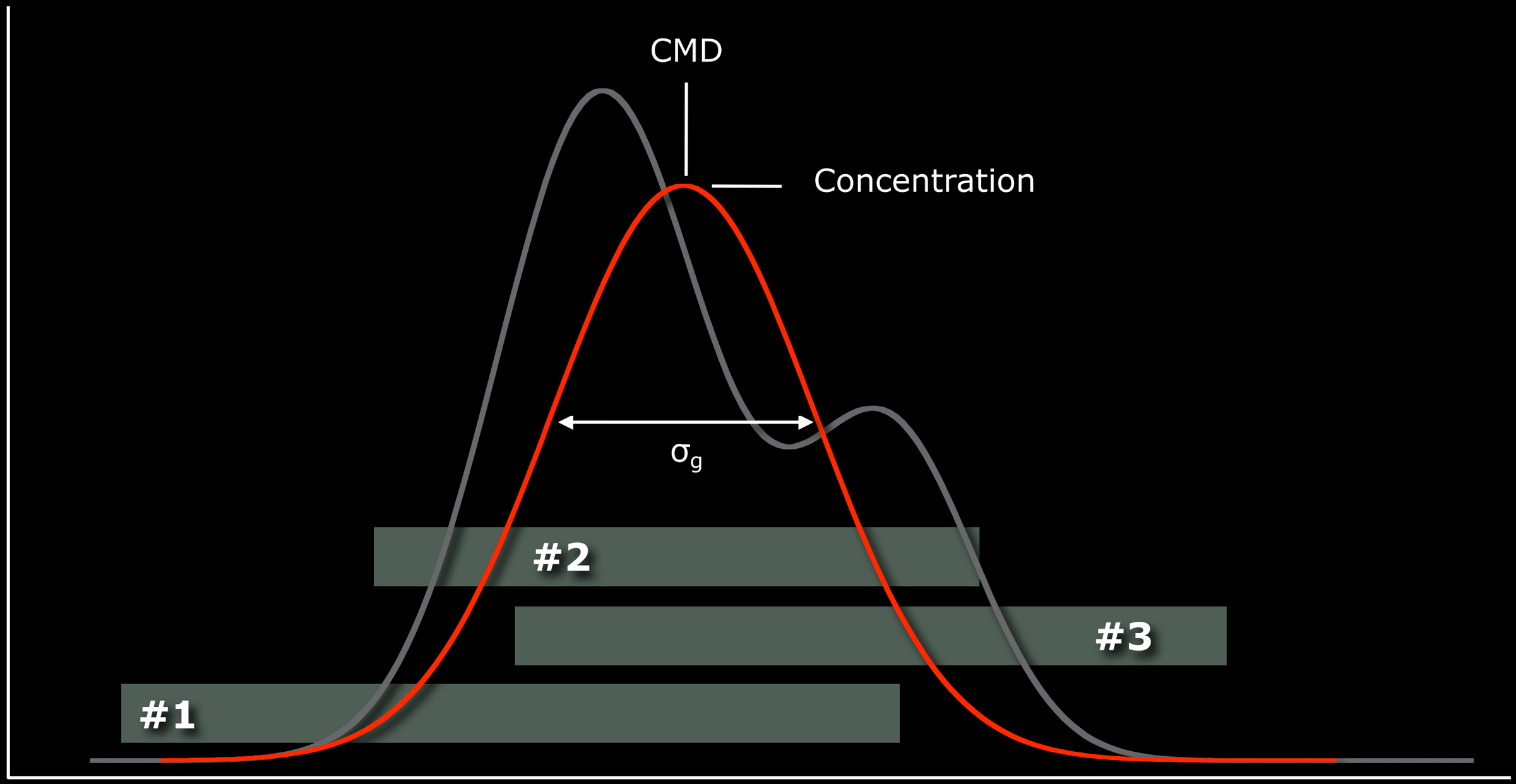
Sophisticated data inversion can offer insight into nano-aerosol exposure from relatively few measurements



Woo, K.-S., Chen, D.-R., Pui, D. Y. H. and Wilson, W. E. (2001). Use of continuous measurements of integral aerosol parameters to estimate particle surface area. Aerosol Sci. Tech. 34:57-65.

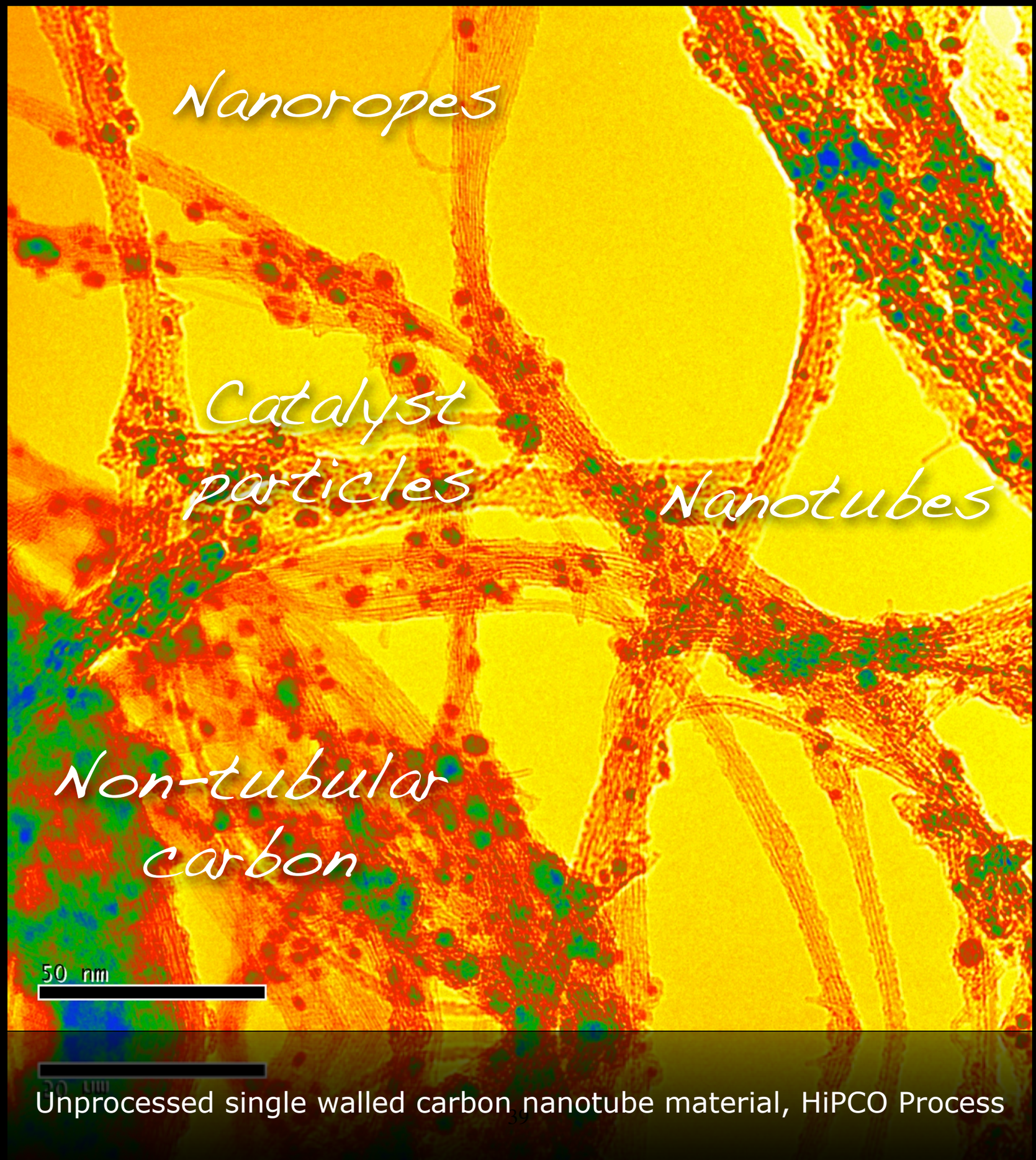
Maynard, A. D. (2003). Estimating aerosol surface area from number and mass concentration measurements. Ann. Occup. Hyg. 47:123-144.

Sophisticated data inversion can offer insight into nano-aerosol exposure from relatively few measurements



Woo, K.-S., Chen, D.-R., Pui, D. Y. H. and Wilson, W. E. (2001). Use of continuous measurements of integral aerosol parameters to estimate particle surface area. Aerosol Sci. Tech. 34:57-65.

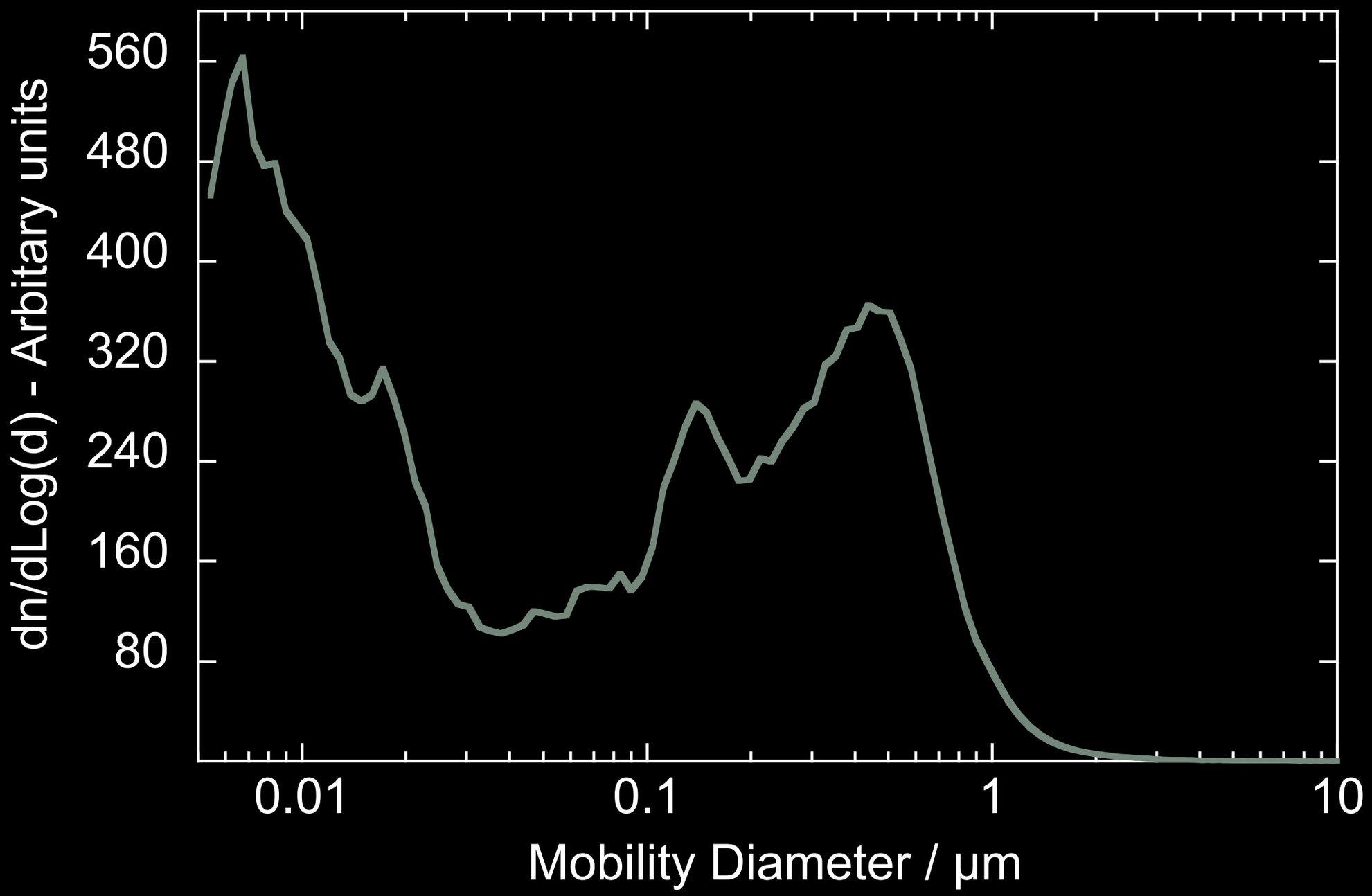
Maynard, A. D. (2003). Estimating aerosol surface area from number and mass concentration measurements. Ann. Occup. Hyg. 47:123-144.



Unprocessed single walled carbon nanotube material, HiPCO Process

SWCNT Aerosol

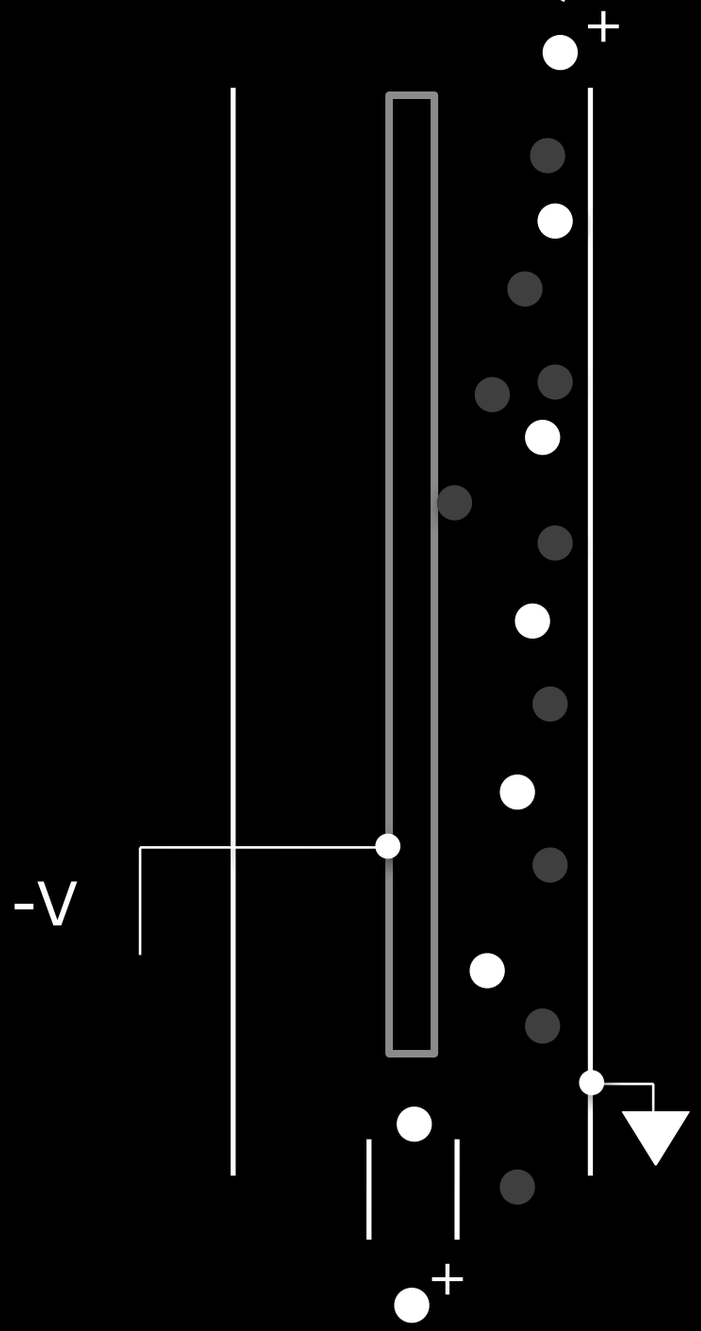
Generated from dry material through energetic agitation



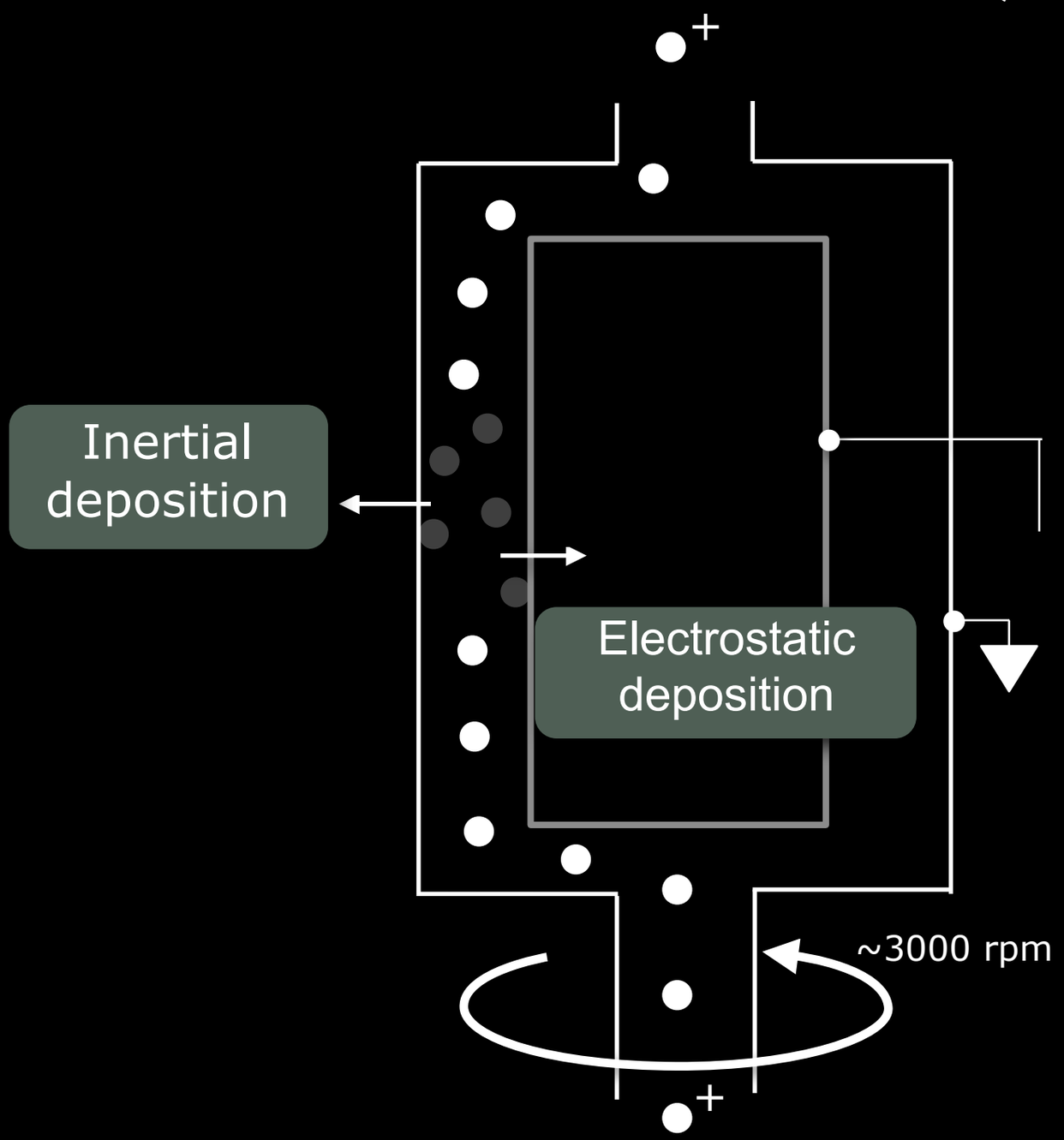
Maynard, A. D., P. A. Baron, et al. (2004). J. Toxicol. Environ. Health 67(1): 87-107.

Characterizing airborne carbon nanotubes

Differential Mobility Analysis



Aerosol Particle Mass Analysis



Maynard, A. D., B. K. Ku, M. Emery, M. Stolzenburg and P. H. McMurry (2007). J. Nanopart. Res. 9(1): 85-92.

Structural Parameter

Proportional to specific surface area

$$Selection_{DMA} \propto \pi \bar{d}_m^2 \quad \text{- units of surface area}$$

$$Selection_{APM} \propto qE \frac{\bar{r}}{\omega^2} \quad \text{- units of mass}$$

$$\Gamma = \frac{\pi \bar{d}_m^2}{q\bar{r}} \frac{\omega^2}{E}$$

Maynard, A. D., B. K. Ku, M. Emery, M. Stolzenburg and P. H. McMurry (2007). J. Nanopart. Res. 9(1): 85-92.

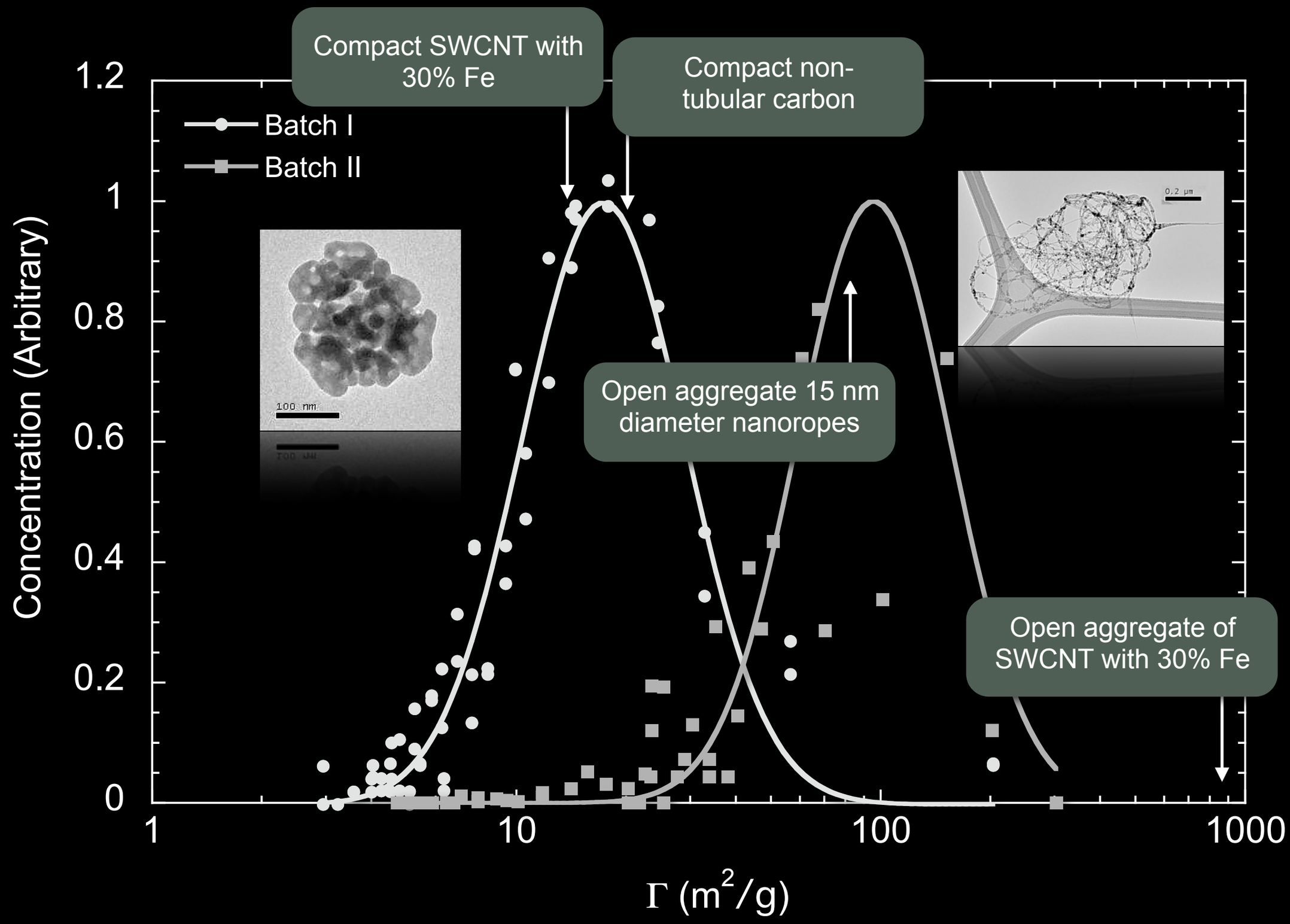
Structural Parameter

Predicted Values

Particle description	Mobility Diameter	Predicted value of Gamma (m^2/g)
Compact non-tubular carbon particles	150 nm	20
Open agglomerate of single walled carbon nanotube with 30% Fe	150 nm	860
Open agglomerate of 5 nm diameter Fe particles	150 nm	150
Compact single walled carbon nanotubes with 30% Fe	31 nm	58
Open agglomerate of 5 nm diameter nanoropes with 30% Fe	31 nm	240

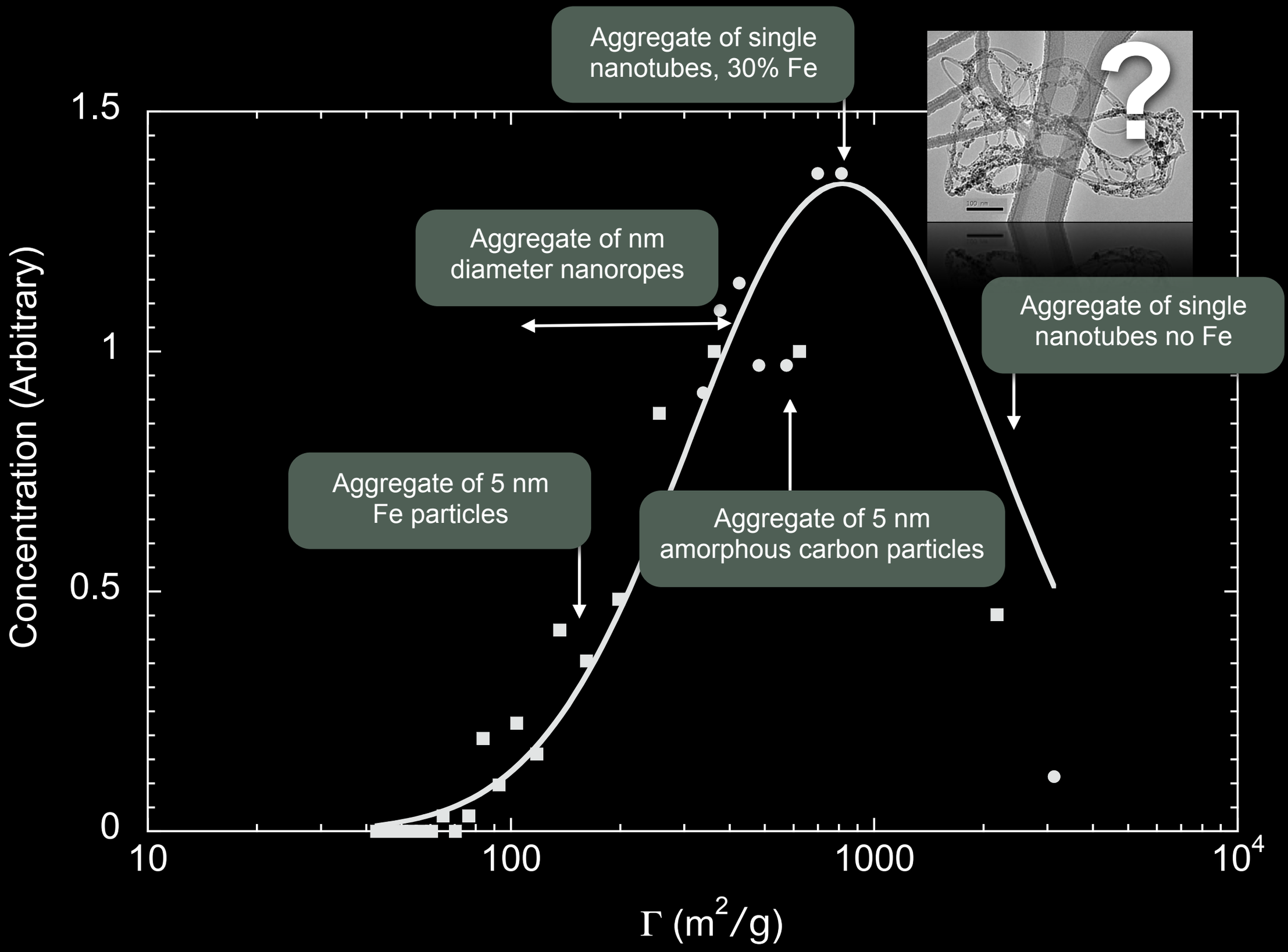
Maynard, A. D., B. K. Ku, M. Emery, M. Stolzenburg and P. H. McMurry (2007). J. Nanopart. Res. 9(1): 85-92.

150 nm mobility diameter particles

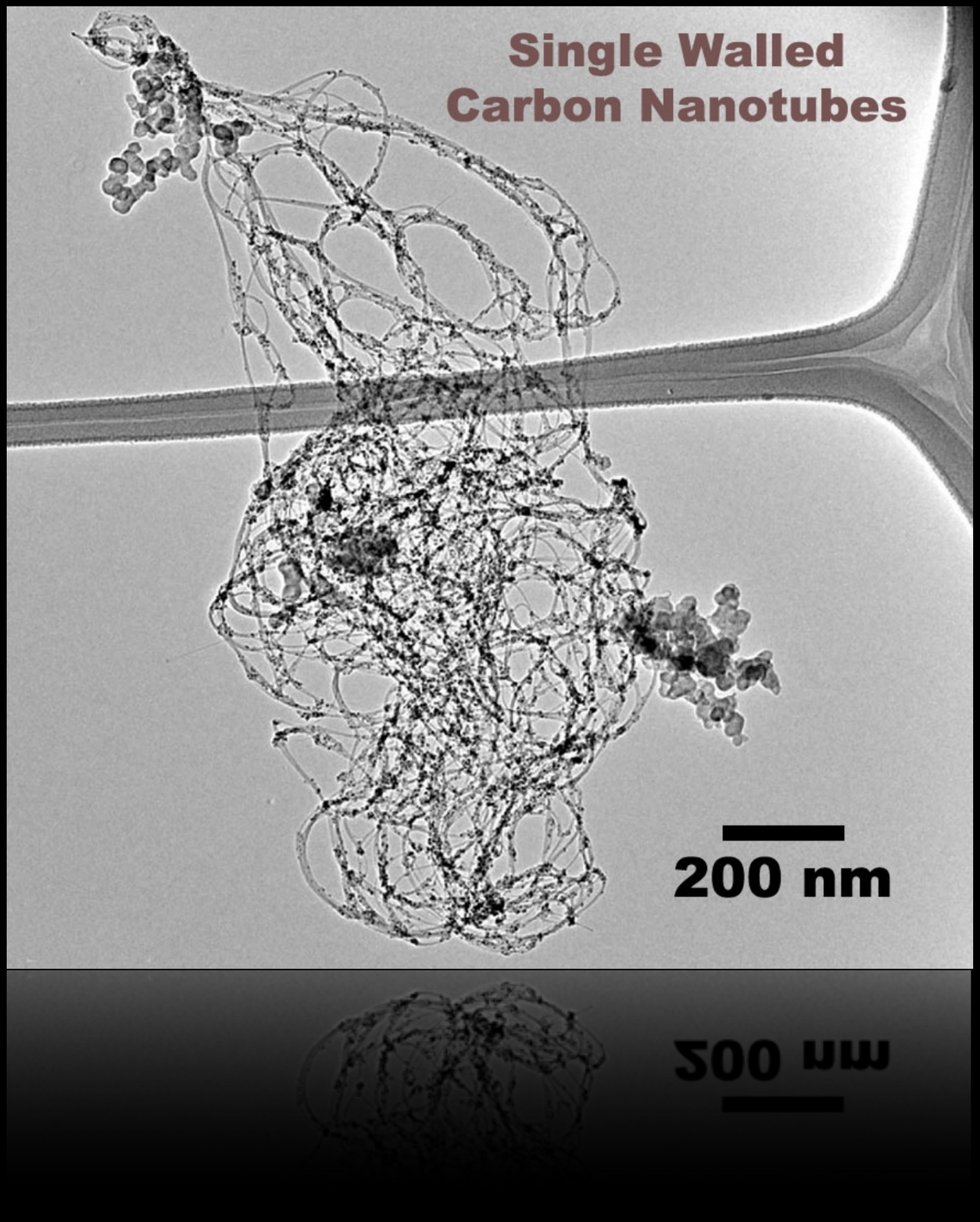


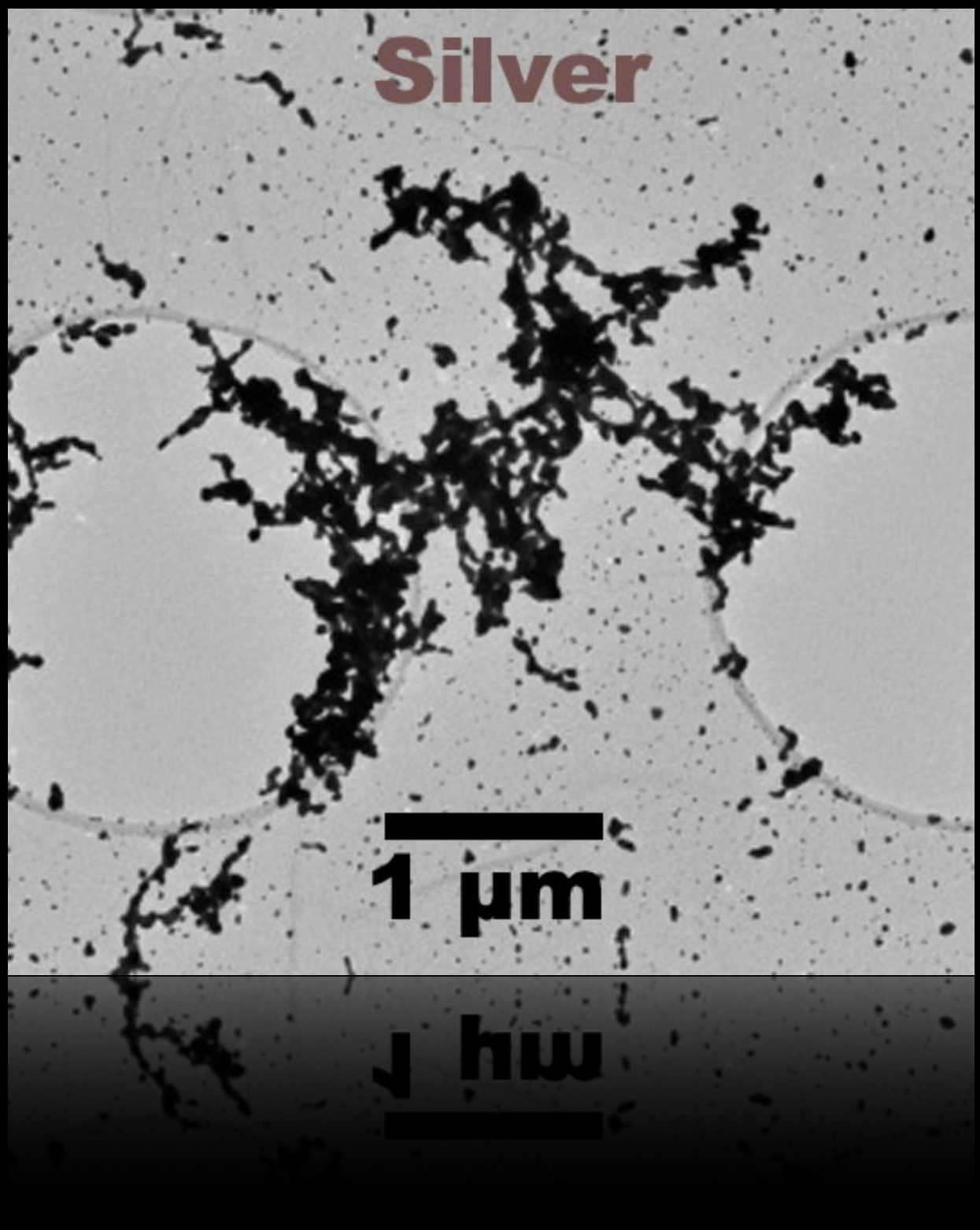
Maynard, A. D., B. K. Ku, M. Emery, M. Stolzenburg and P. H. McMurry (2007). J. Nanopart. Res. 9(1): 85-92.

31 nm mobility diameter particles

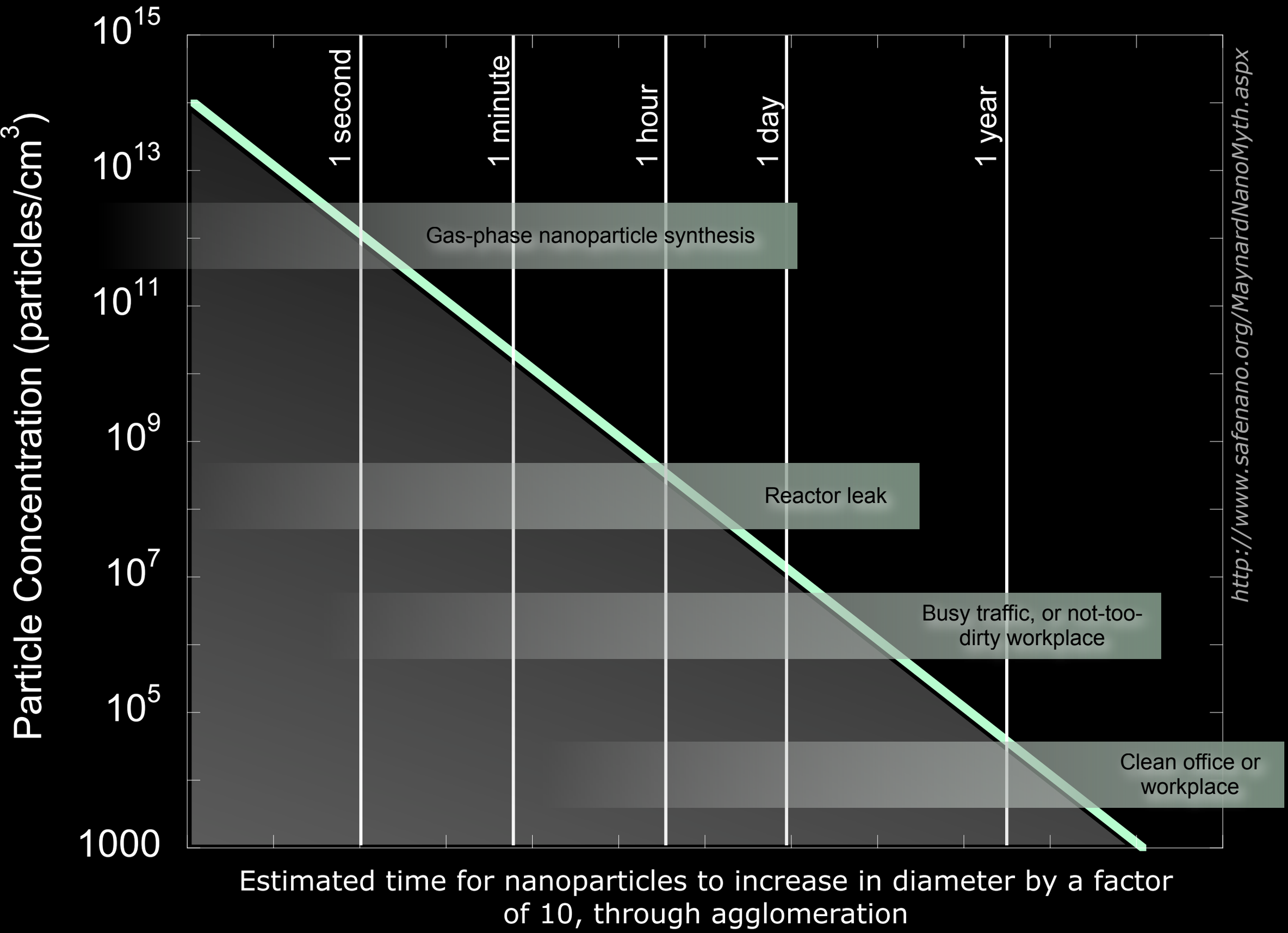


Maynard, A. D., B. K. Ku, M. Emery, M. Stolzenburg and P. H. McMurry (2007). J. Nanopart. Res. 9(1): 85-92.


Single Walled
Carbon Nanotubes
200 nm

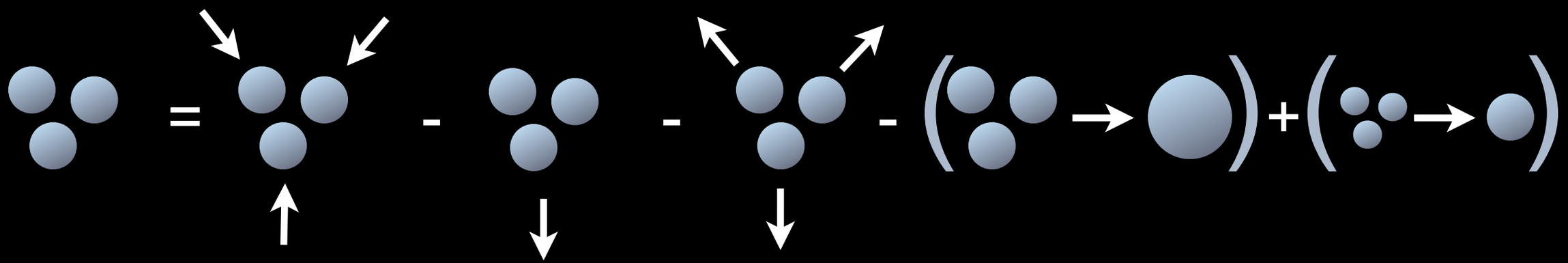

Silver
1 µm

Agglomeration - simple model



Agglomeration - complex model

Using the General Dynamic Equation



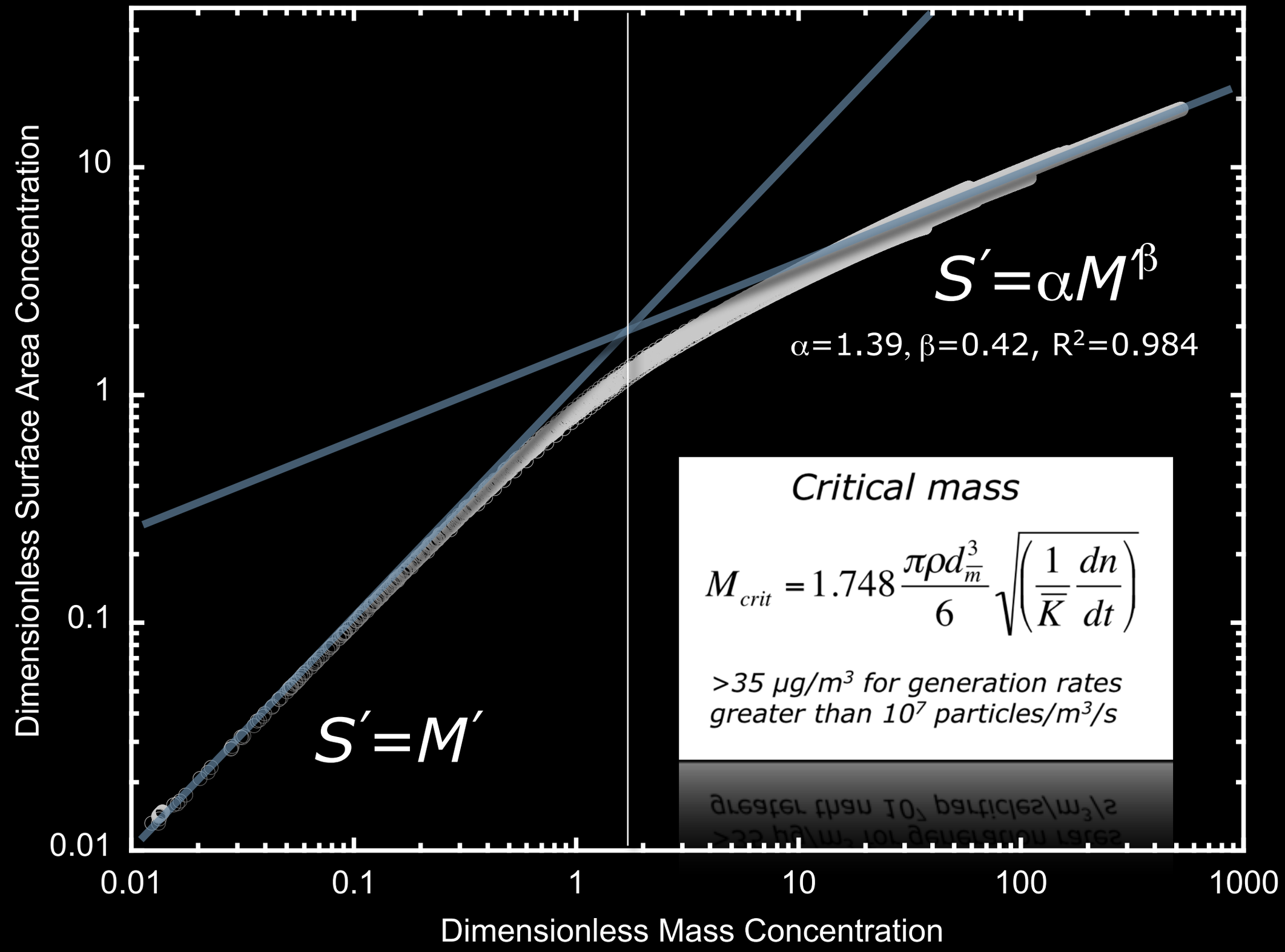
$$\frac{dn(d)}{dt}$$

Generation

Gravitational Settling

Diffusion

Coagulation

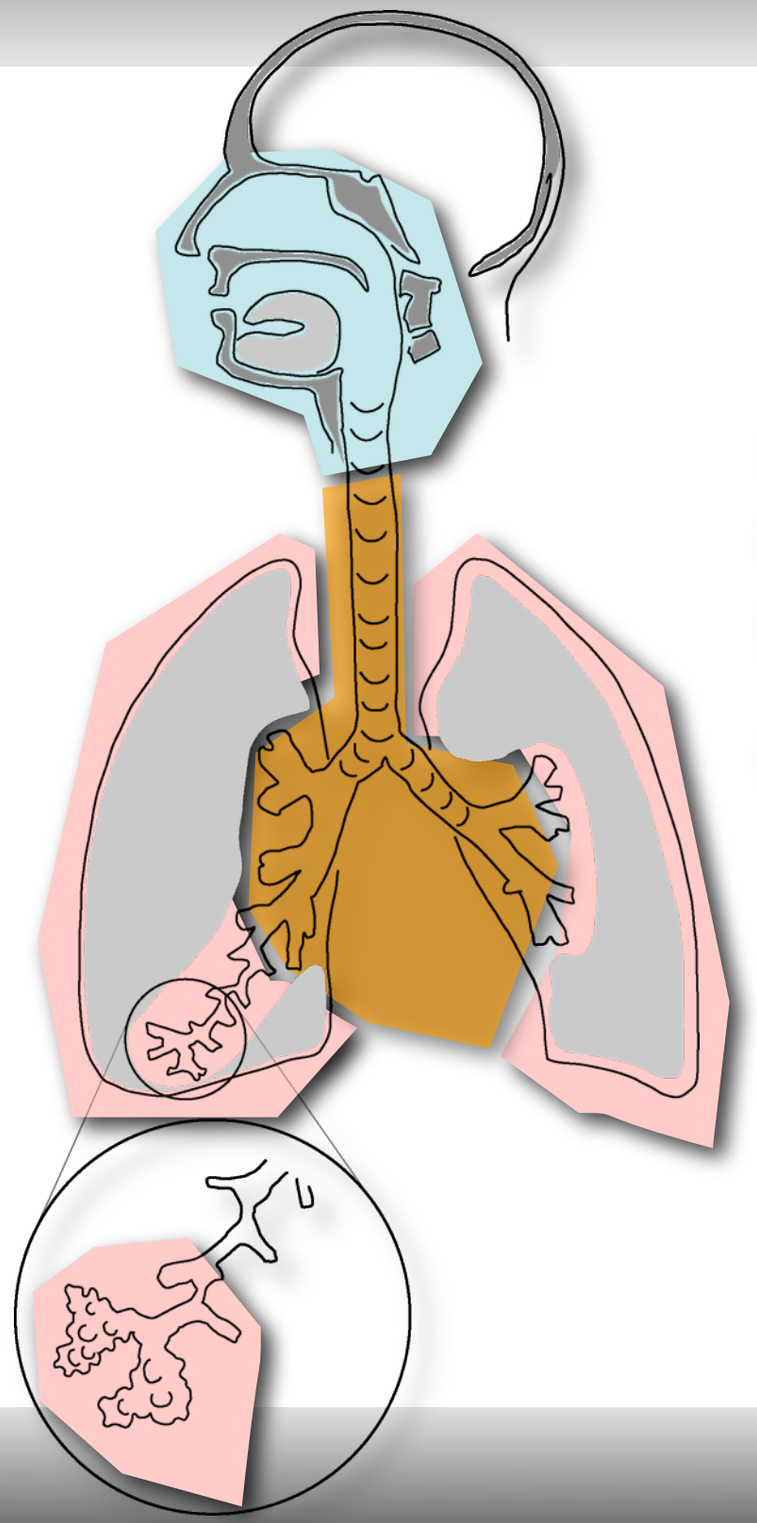


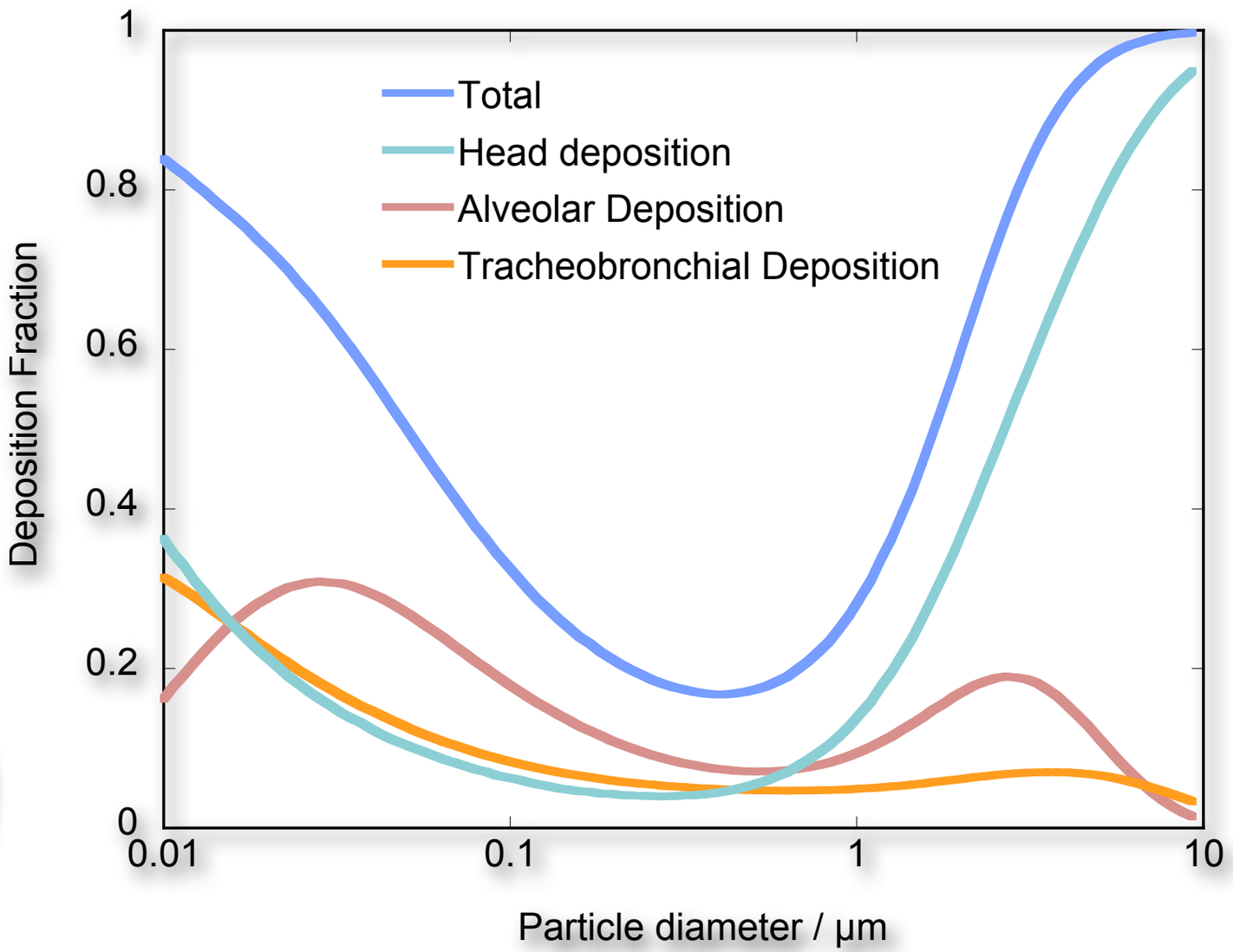
Maynard, A. D. and Maynard, R. L. (2002). A derived association between ambient aerosol surface area and excess mortality using historic time series data. Atmos. Env. 36:5561-5567.


Silver
1 µm
hω

Particle deposition in the lungs

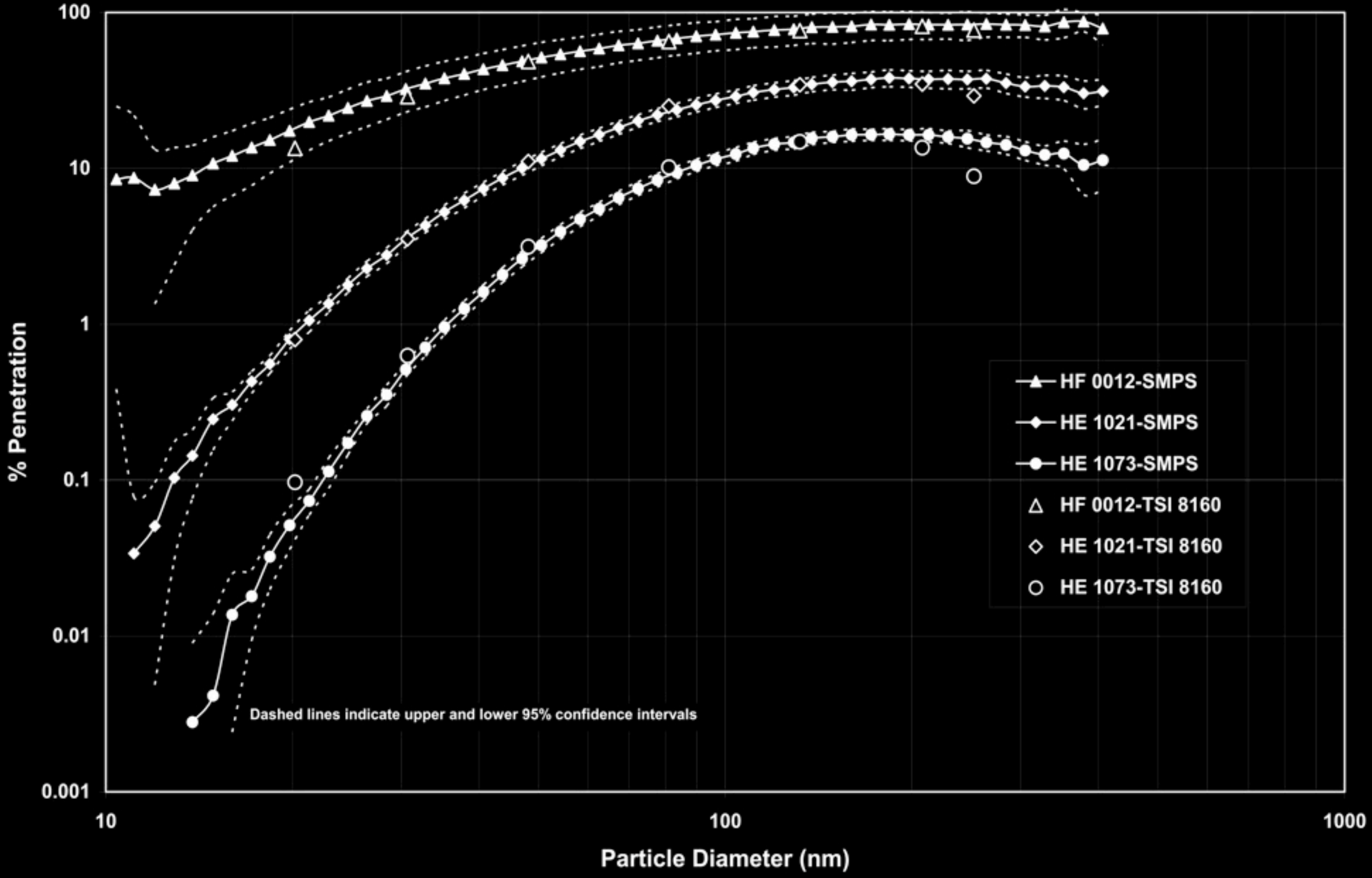
Modeled lung deposition. Mouth and nose breathing, person at rest.



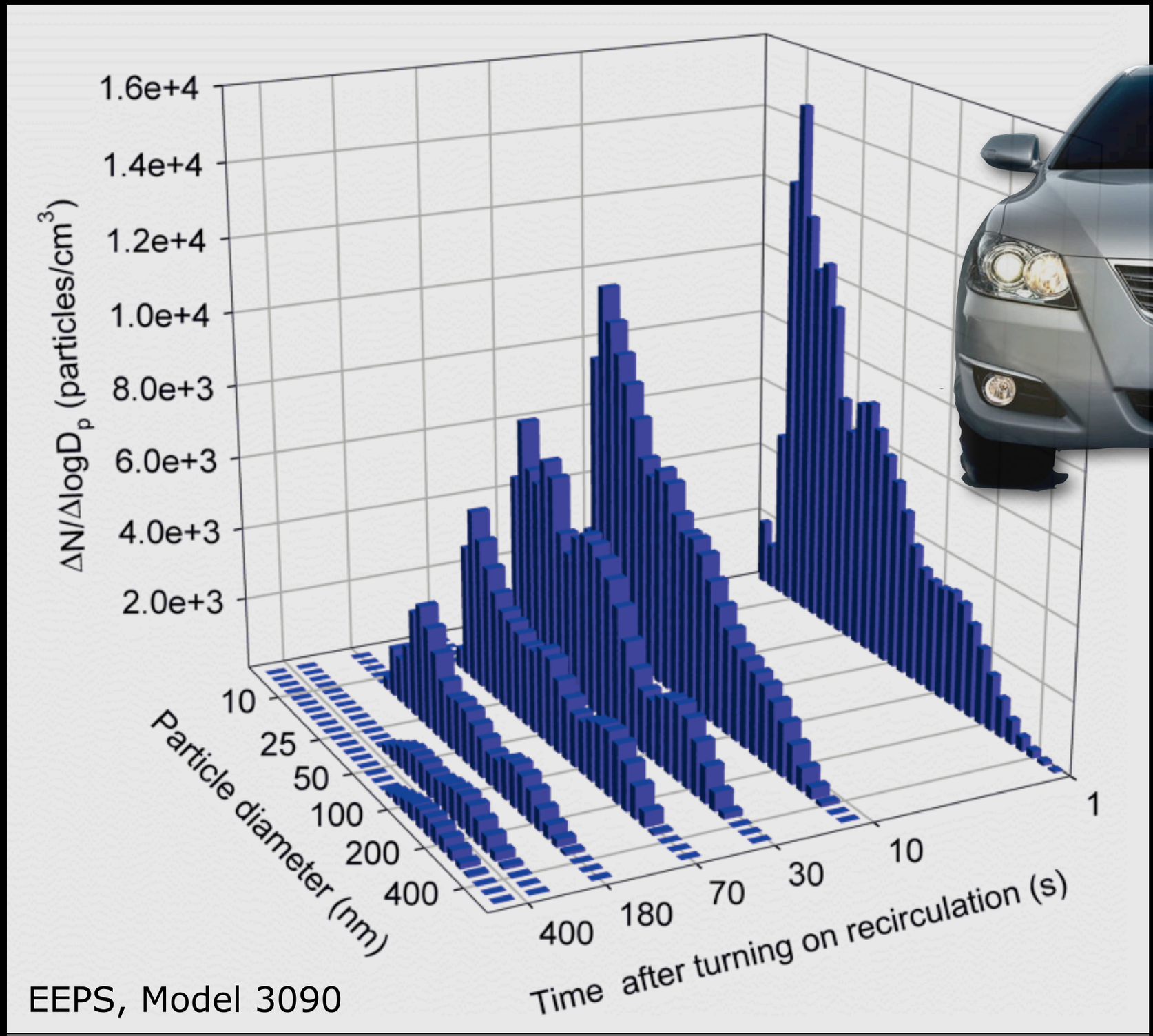


Source: Multiple Pathway Deposition Model (MDEP), CIIT

Filter penetration



Japuntich, D. A., L. M. Franklin, et al. (2007). J. Nanopart. Res. 9(1) 93-107



EEPS, Model 3090

Min efficiency ~ 20%

Driving in heavy traffic, air recirculation on.

In-cabin aerosol < 4000 particles/m3 within 3 minutes

Pui, D. Y. H., Qi, C., Stanley, N., Oberdörster, G. and Maynard, A. (2008). Recirculating Air Filtration Significantly Reduces Exposure to Airborne Nanoparticles. Environ Health Perspect doi:10.1289/ehp.11169.

Exposure Management

Control Banding - Concept

Amount Used	Low Dustiness	Medium Dustiness	High Dustiness
Hazard Group A			
Small	1	1	1
Medium	1	1	2
Large	1	2	2
Hazard Group B			
Small	1	1	1
Medium	1	2	2
Large	1	3	3
Hazard Group C			
Small	1	1	2
Medium	2	3	3
Large	2	4	4
Hazard Group D			
Small	2	2	3
Medium	3	4	4
Large	3	4	4
Hazard Group E			
For all hazard group E substances, choose control approach 4			

Parameters

Hazard Group

Dustiness

Amount Used

Control Approach

- General Ventilation
- Engineering Control
- Containment
- Specialist Advice

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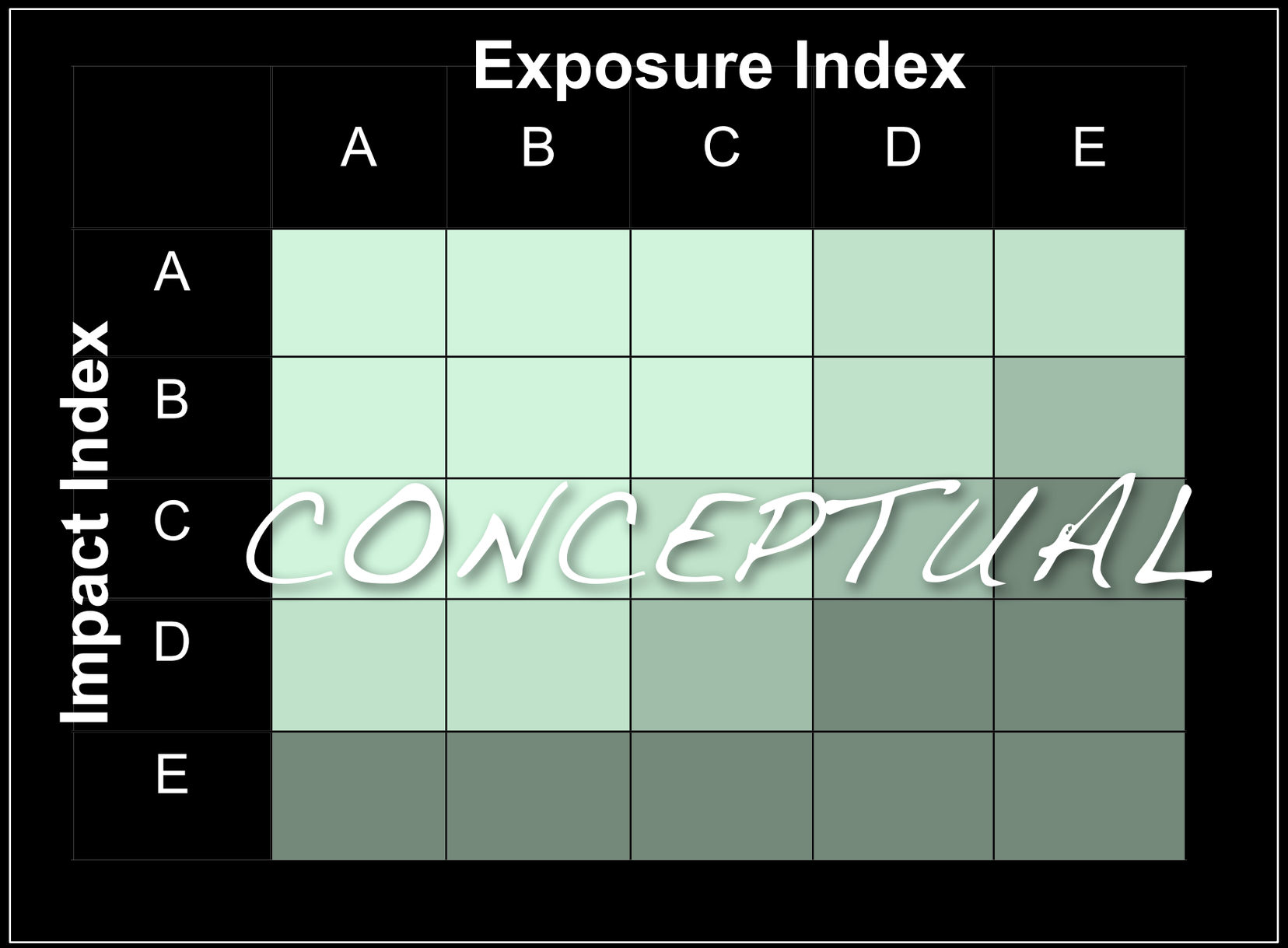
Creative Risk Management

Can we learn from control banding?



Exposure Index

Dustiness

Amount Used

Impact Index

Bulk hazard

Surface Area

Surface Activity

Shape

Size

Control Approach

- General Ventilation
- Engineering Control
- Containment
- Specialist Advice

Maynard, A., D. (2007). Nanotechnology: The next big thing, or much ado about nothing? Ann. Occup. Hyg. 51:1-12.

Novel Materials

Unconventional material behavior leads to unconventional risks

Knowledge of aerosol behavior provides insight into "new" mechanisms of impact

Understanding aerosol behavior can help monitor and reducing potential impact

Aerosol science can contribute to the development of new products and processes that are "safe by design"

Responsible Development

ETC Group

Additional Reading
(Selected)

Pui, D. Y. H., Qi, C., Stanley, N., Oberdörster, G. and Maynard, A. (2008). Recirculating Air Filtration Significantly Reduces Exposure to Airborne Nanoparticles. Environ Health Perspect doi:10.1289/ehp.11169.

Poland, C. A., Duffin, R., Kinloch, I., Maynard, A., Wallace, W. A. H., Seaton, A., Stone, V., Brown, S., MacNee, W. and Donaldson, K. (2008). Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. Nature Nanotechnology 3:423-428.

Hansen, S. F., Maynard, A., Baun, A. and Tickner, J. A. (2008). Late lessons from early warnings for nanotechnology. Nature Nanotechnology 3:444-447.

Maynard, A. D., Ku, B. K., Emery, M., Stolzenburg, M. and McMurry, P. H. (2007). Measuring particle size-dependent physicochemical structure in airborne single walled carbon nanotube agglomerates. J. Nanopart. Res. 9:85-92.

Maynard, A., D. (2007). Nanotechnology: The next big thing, or much ado about nothing? Ann. Occup. Hyg. 51:1-12.

Oberdörster, G., Stone, V. and Donaldson, K. (2007). Toxicology of nanoparticles: A historical perspective. Nanotoxicology 1:2 - 25.

Maynard, A. D., Aitken, R. J., Butz, T., Colvin, V., Donaldson, K., Oberdörster, G., Philbert, M. A., Ryan, J., Seaton, A., Stone, V., Tinkle, S. S., Tran, L., Walker, N. J. and Warheit, D. B. (2006). Safe handling of nanotechnology. Nature 444:267-269.

Elder, A., Gelein, R., Silva, V., Feikert, T., Opanashuk, L., Carter, J., Potter, R., Maynard, A., Finkelstein, J. and Oberdorster, G. (2006). Translocation of inhaled ultrafine manganese oxide particles to the central nervous system. Environ. Health Perspect. 114:1172-1178.

Ku, B. K. and Maynard, A. D. (2006). Generation and investigation of airborne silver nanoparticles with specific size and morphology by homogeneous nucleation, coagulation and sintering. J. Aerosol Sci. 37:452-470.

Oberdörster, G., Maynard, A., Donaldson, K., Castranova, V., Fitzpatrick, J., Ausman, K., Carter, J., Karn, B., Kreyling, W., Lai, D., Olin, S., Monteiro-Riviere, N., Warheit, D. and Yang, H. (2005). Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy. Part. Fiber Toxicol. 2:doi:10.1186/1743-8977-1182-1188.

Maynard, A. D. and Kuempel, E. D. (2005). Airborne nanostructured particles and occupational health. Journal Of Nanoparticle Research 7:587-614.

Ku, B. K. and Maynard, A. D. (2005). Comparing aerosol surface-area measurement of monodisperse ultrafine silver agglomerates using mobility analysis, transmission electron microscopy and diffusion charging. J. Aerosol Sci. 36:1108-1124.

Maynard, A. D., Baron, P. A., Foley, M., Shvedova, A. A., Kisin, E. R. and Castranova, V. (2004). Exposure to Carbon Nanotube Material: Aerosol Release During the Handling of Unrefined Single Walled Carbon Nanotube Material. J. Toxicol. Environ. Health 67:87-107.

Pui, D. Y. H., Flagan, R. C., Kaufman, S. L., Maynard, A. D., de la Mora, J. F., Hering, S. V., Jimenez, J. L., Prather, K. A., Wexler, A. S. and Ziemann, P. J. (2004). Experimental methods and instrumentation. Journal Of Nanoparticle Research 6:314-315.

Brown, L. M., Collings, N., Harrison, R. M., Maynard, A. D. and Maynard, R. L., eds. (2003). Ultrafine Particles in the Atmosphere. Imperial College Press, London, UK.

Maynard, A. D. and Brown, L. M. (2000). Overview of methods for analysing single ultrafine particles. Philosophical Transactions of the Royal Society of London Series a-Mathematical Physical and Engineering Sciences 358:2593-2609.

Preining, O. (1998). The physical nature of very, very small particles and its impact on their behavior. J. Aerosol Sci. 29:481-495.

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