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Dosimetry models to align nanoparticle dose across systems for better risk assessment

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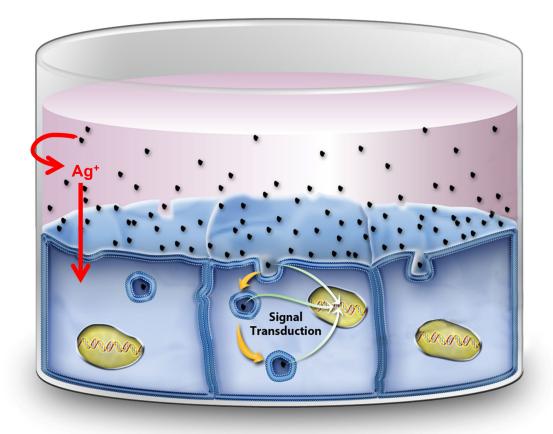
The dose makes the poison





In vitro nanotoxicology

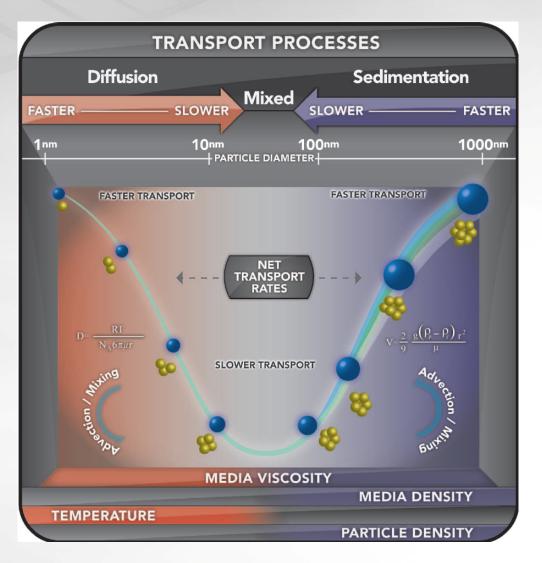




Nanoparticle transport processes



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Teeguarden *et al.* 2007. *Toxicol. Sci.* 95(2): 300-312 DeLoid *et al.* 2014. *Nat. Commun.* 5, 3514

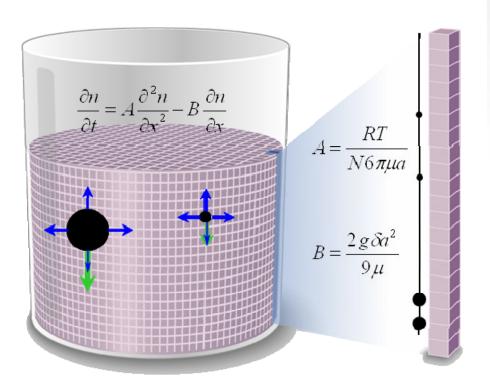
In vitro sediment diffusion and dosimetry (ISDD) model



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https://nanodose.pnnl.gov/default.aspx?topic=ISDD

Hinderliter *et al.* 2010. *Part Fibre Toxicol.* 7(1) 36 Cohen *et al.* 2014 *Part Fibre Toxicol.* (11) 20



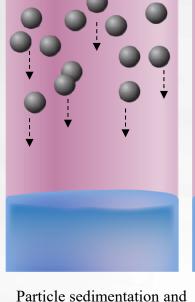
ISD3: Implications of dissolution



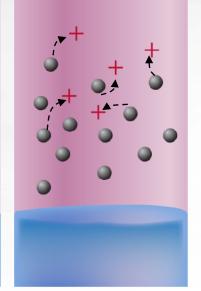
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Time

Liquid column height



diffusion



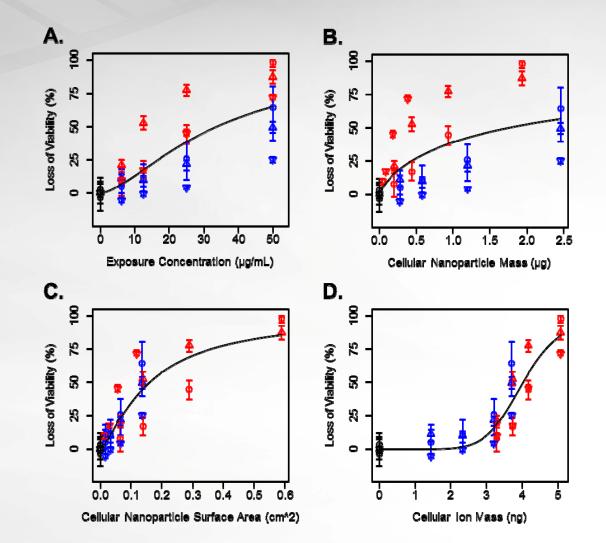
Particle dissolution and ion release

Particle and ion uptake by cells

https://nanodose.pnnl.gov/default.aspx?topic=ISD3

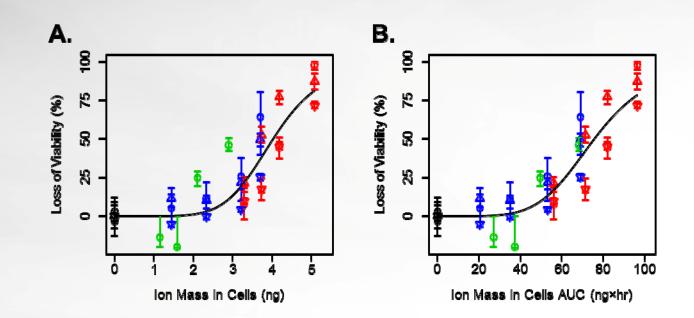
Enables dose response analysis with various dose metrics





Including ion only exposures





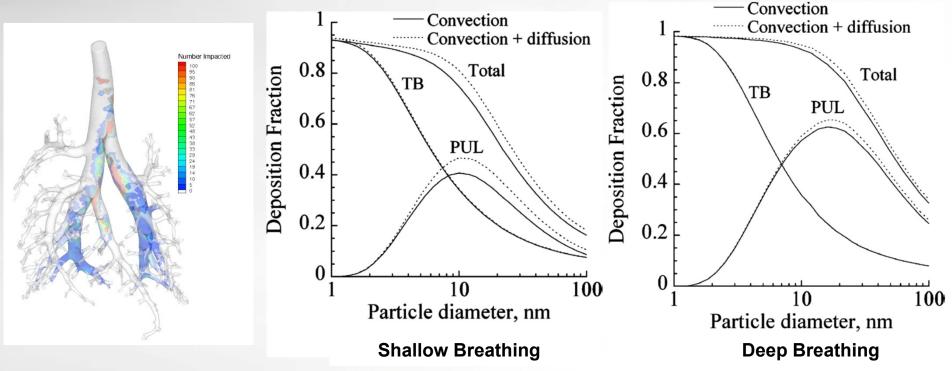
Animal models and humans



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https://www.ara.com/products/multiplepath-particle-dosimetry-model-mppd-v-304



Anjilvel *et al.* 1995. *Fundam. Appl. Toxicol.* 28, 41-50. Asgharian *et al.* 2001 *Aerosol Sci and Tech* 34:4, 332-339. Asgharian and Price 2007 *Inhal. Toxicol.* 19: 1045-1054. Miller et al. 2016. *J. Aerosol Sci.* 99, 14-26.

Conclusions



- Dose makes the poison
- In order to realize Tox 21 vision, we need to understand nanoparticle dose
- Dosimetry models exist to predict nano dose
 - Conventional cell cultures
 - MPPD version needed for air liquid interface assays?
 - Animal models
 - Humans
 - Includes children geometries
- Models can be used to design toxicity in vitro assays based on exposure assessments
- Aligning dose across systems is essential for successful risk assessment

Questions?



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