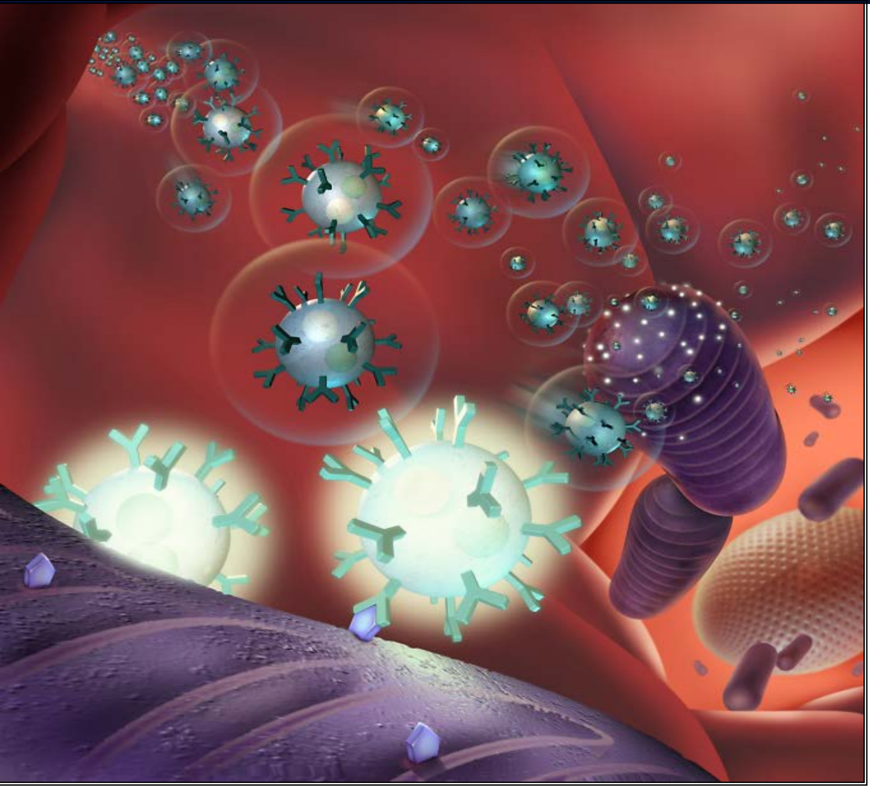
Integrating fate and toxicity of engineered nanoparticles into LCIA



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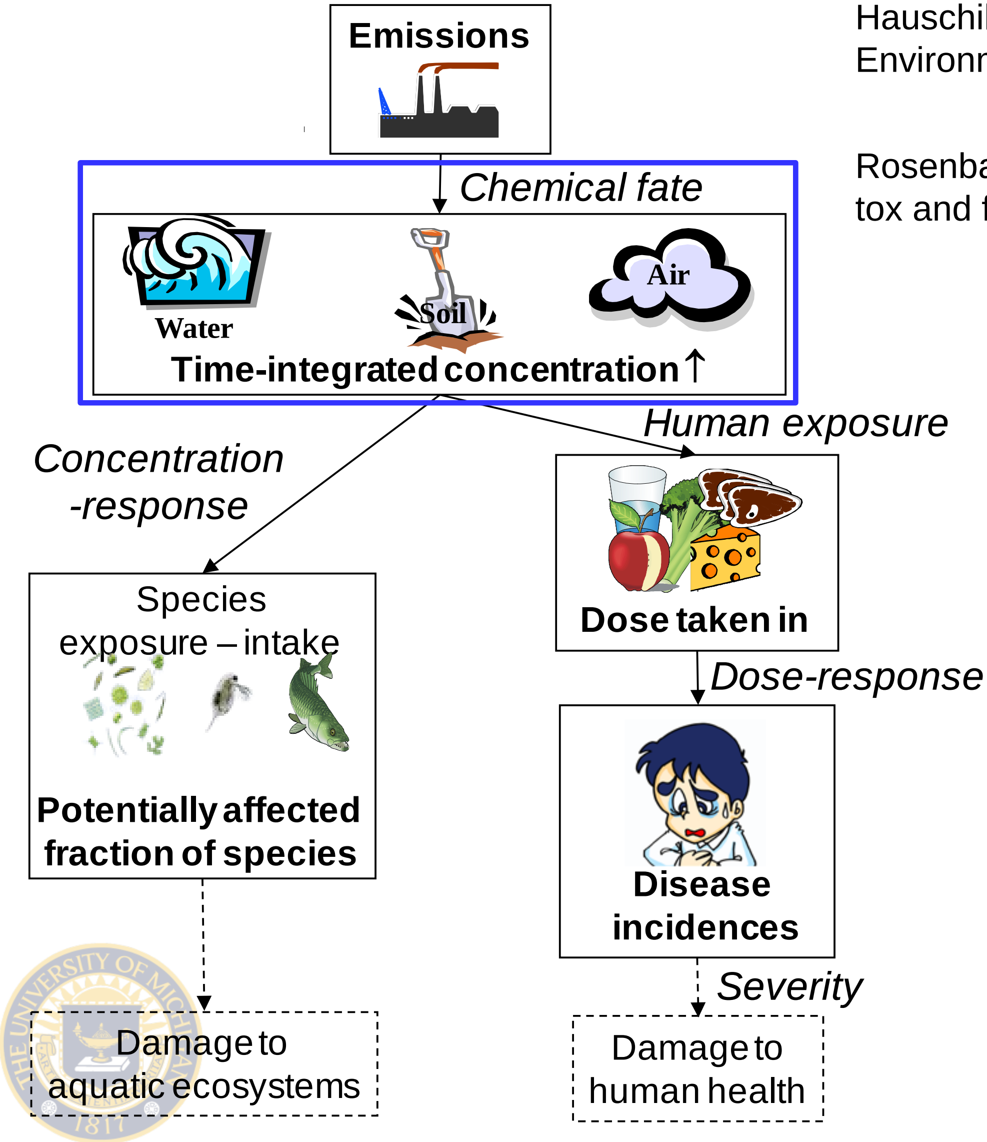
Workshop on Life Cycle of nanotechnologies: EPA-EU 2-3 October 2006, Wilson center

- There is no generic LCA of nanomaterials, just as there is no generic LCA of chemicals.
- The ISO-framework for LCA (ISO 14040:2006) is suitable.
- Processes are under development and may be rapidly evolving. This is a very similar situation to e.g. electronic industry.
- Try to characterize the main manufacturing pathways/ technologies (lithography, precipitation, SPM, depositions).
- Main challenge and gap: direct toxicity of nanoparticle. Start now!

USEtox framework for human toxicity and ecotoxicity of chemicals and nanoparticles



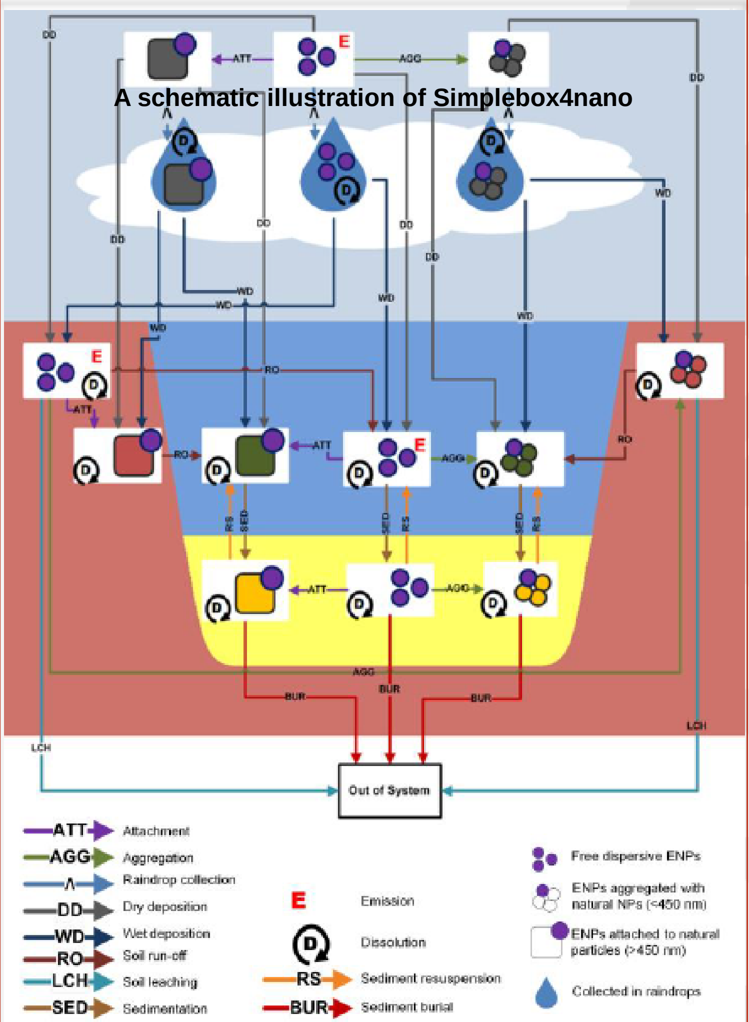
Hauschild et al., 2008. The Search for Harmony and Parsimony. Environmental Science &Technology, 42(19), 7032-7036

Rosenbaum et al., 2008: USEtox factors for factors for human tox and freshwater ecotox, Int J LCA, 13(7)532-546.

USEtox framework is Valid for nanoparticles, but fate, exposure and effect factors need to account for nano-specific mechanisms

Fate Factor (FF)
Application of Simpleboxnano4 to nano TiO2

A schematic illustration of Simplebox4nano



A schematic illustration of SimpleBox4nano's model matrix 'A'

Simplebox4nano residence time In the environment for nano-TiO2

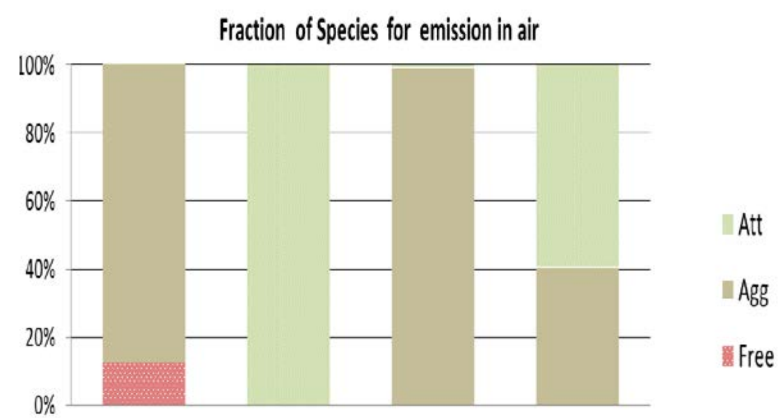
Residence time [day]	Air	Water	soil
Free	0.5	0.06	0.0001
Aggregated	7.2	41	15
Attached	1.8	41	58

Factor 650 between free and aggregated !

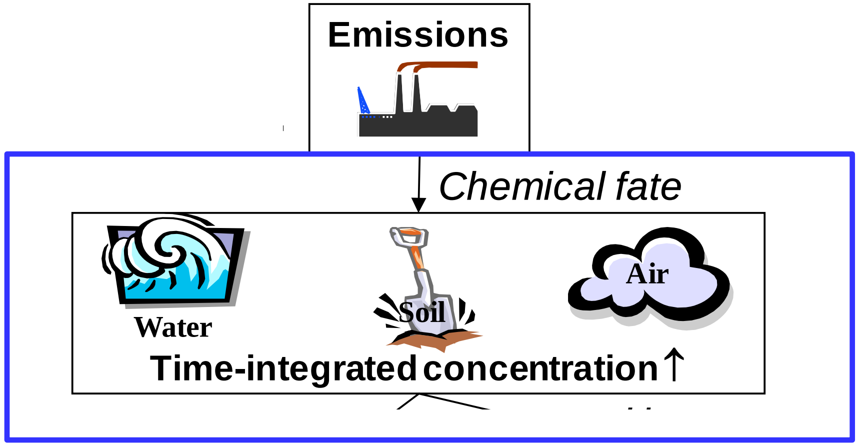
Salieri & Jolliet - Simplebox4nano/USEtox From 15 to 4 compartments

k (day-1)	Free in atmosphere	Agg in atmosphere	Att in atmosphere	Free in rain	Agg in rain	Att in rain	Free in soil pore water	Agg in soil pore water	Att to solids soil	Free in water	Agg in water	Att in water	Free in sediment	Agg in sediment	Att in sediment
Free in atmosphere	-3.486	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Agg in atmosphere	1.854	-1.498	0	0	0	0	0	0	0	0	0	0	0	0	0
Att in atmosphere	0.004	0	-1.691	0	0	0	0	0	0	0	0	0	0	0	0
Free in rain	0.039	0	0	-9.460	0	0	0	0	0	0	0	0	0	0	0
Agg in rain	0	0.016	0	0	-9.460	0	0	0	0	0	0	0	0	0	0
Att in rain	0	0	0.153	0	0	-9.460	0	0	0	0	0	0	0	0	0
Free in soil pore wat	0.119	0	0	7.760	0	0	-1591.804	0	0	0	0	0	0	0	0
Agg in soil pore wat	0	0.021	0	0	7.760	0	1372.478	-0.008	0	0	0	0	0	0	0
Att to solids in soil	0	0	0.076	0	0	7.760	219.317	0	-8.22E-07	0	0	0	0	0	0
Free in water	0.009	0	0	0.240	0	0	0.008	0	0	-29.320	0	0	0.001	0	0
Agg in water	0	0.001	0	0	0.240	0	0	0.008	0	27.261	-0.009	0	0	0.001	0
Att in water	0	0	0.002	0	0	0.240	0	0	8.22E-07	2.052	0	-1.023	0	0	0.004
Free in sediment	0	0	0	0	0	0	0	0	0	2.43E-05	0	0	-45.738	0	0
Agg in sediment	0	0	0	0	0	0	0	0	0	0	0.002	0	27.744	-0.001	0
Att in sediment	0	0	0	0	0	0	0	0	0	0	0	1.016	17.992	0	-0.004

Total Fate factor [days]	Free in air	Free in soil	Free in water	Free in sediment
Total in air	3	0	0	0
Total in soil	28,642	167,684	0	0
Total in water	14	73	128	117
Total in sediment	46	246	433	741



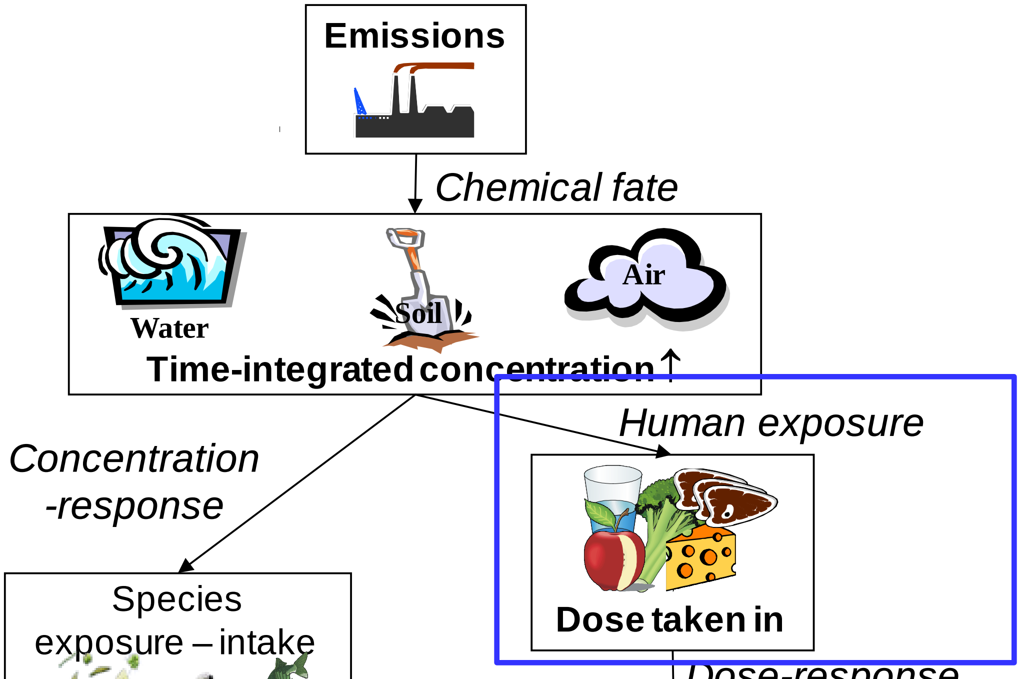
Fate factor – comparison



Fate factor
Residence time of TiO2

Fate Factor	Free in water [days]	Agg in water [days]	Ratio Agg/Free [-]
Salieri & Jolliet 15 x 15	0.034	127-137	4029
Salieri & Jolliet 4x4	0.034	127	3735
Ettrup & Laurent	0.63	45	71
	Factor [-]	Factor [-]	
Ratio Ettrup/Salieri	0.05	3.0	

Exposure factor – Fish bioconcentration factor

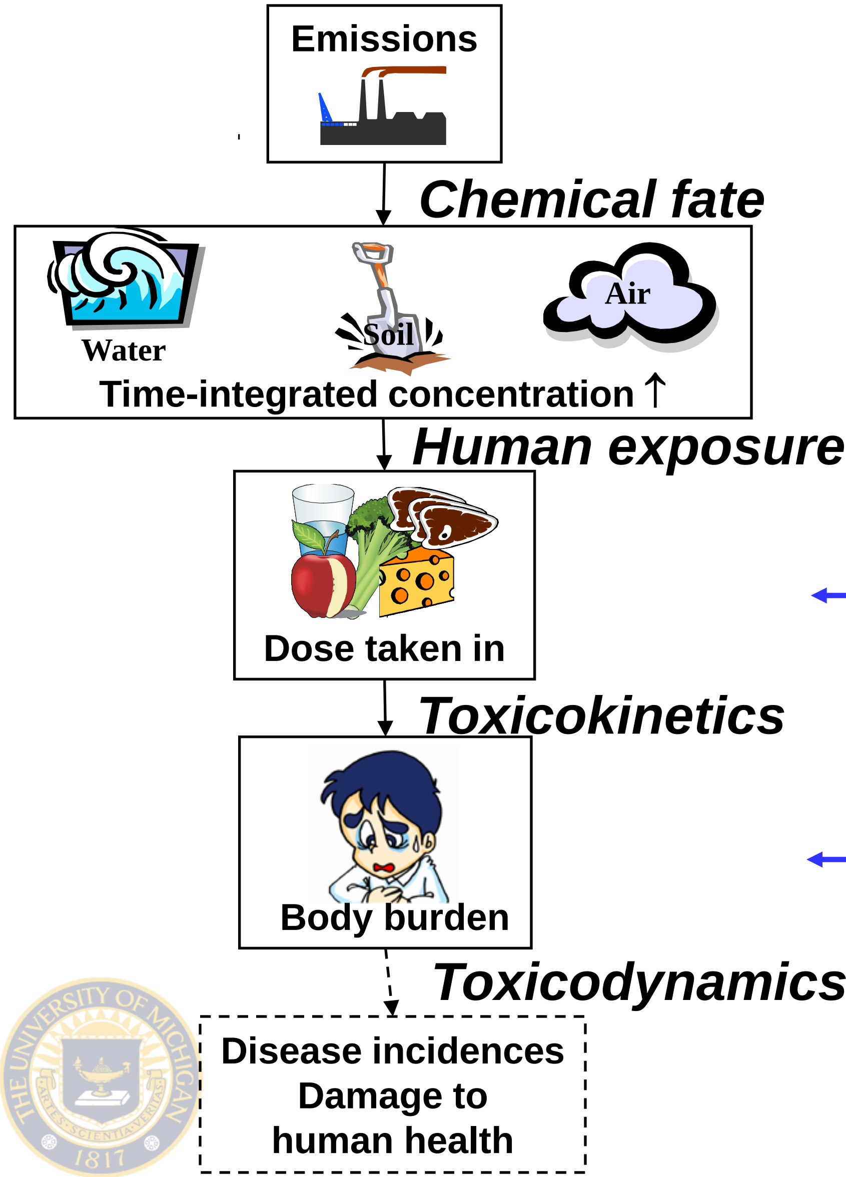


Ettrup et al., 2017.
ES&T 51, 4027−4037

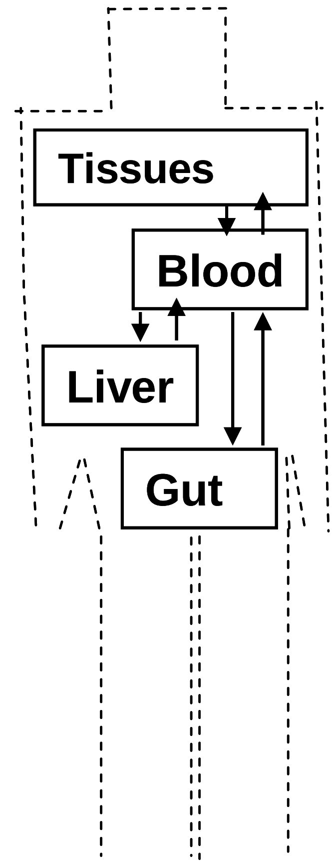
Fish & below ground plant bioconcentration factors (BCF), geomean of experimental data!

Bioconcentration factor	BCF Fish [l/kg]	BCF Plant [-]
Geomean	21.4	3.0
Range	1.3 - 180	0.7 - 18

Biodistribution of nanoparticles in humans → enables the link to in-vitro measurements



Half-life
[day]



Generic Physiologically based PharmacoKinetic Model framework for NPs

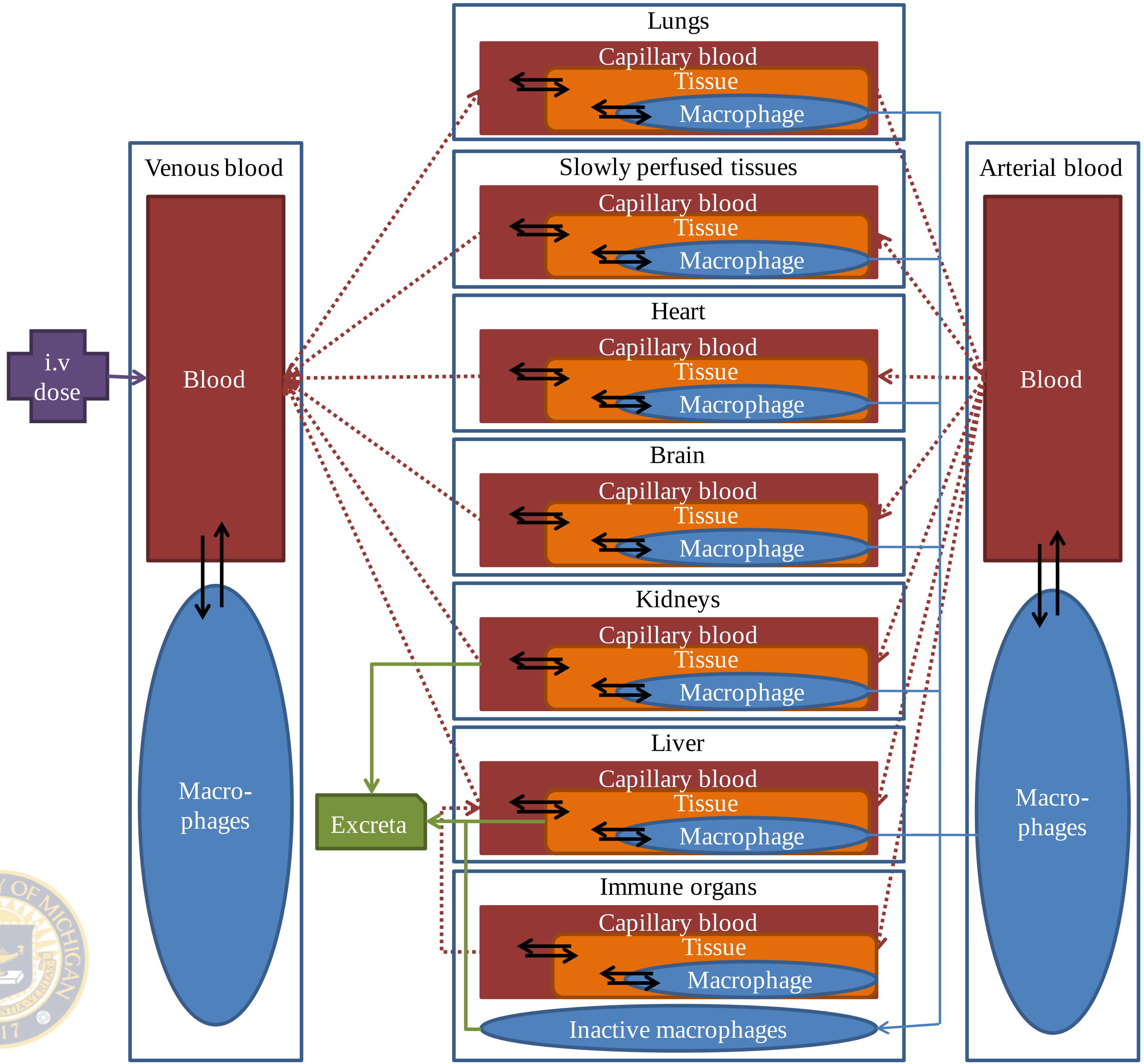


Fig 1. Framework of the PBPK model

Generalized Physiologically Based PharmacoKinetic model (PBPK)

Li et al., 2014, Nanotoxicology, 8, Issue SUPPL. 1, 128-137.

Carlander et al., International Journal of Nanomedicine, 11, 625–640

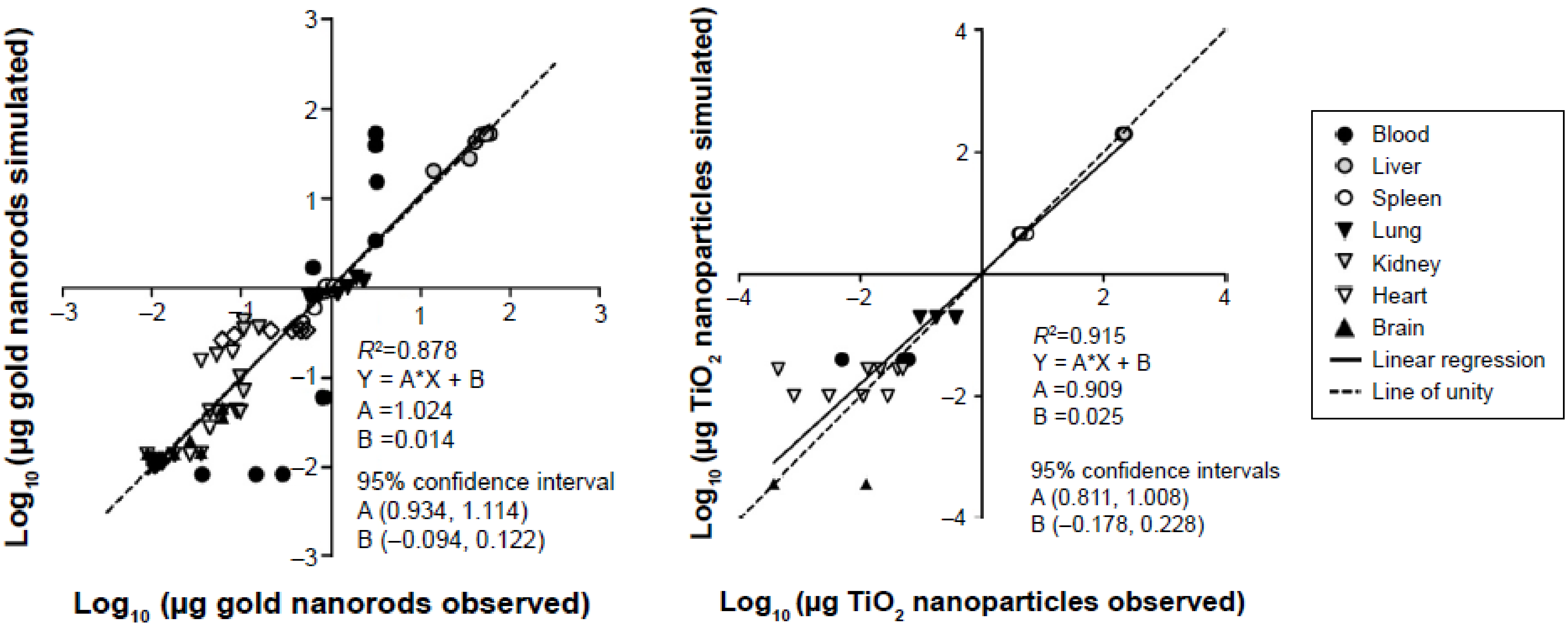
Table 5 Nanoparticle-specific parameters of our physiologically-based pharmacokinetic model

Parameter	Unit	PAA-PEG	PAA	Gold	TiO_2
CL_u	mL/h	1	2.4	0.2	N/A
CL_f	mL/h	1	1.7	1.2	N/A
k_{ab0}	1/h	1	2.9	0.7	82
k_{sab0}	1/h	1	1.5	8.8	57
M_{cap}	µg	1	1.9	0.2	0.5
P	Unitless	1	0.5	0.5	3.8
X_{fast}	Unitless	1	0.7	910	111
X_{rest}	Unitless	1	1.3	1.7	0.2
X_{brain}	Unitless	1	1.0	103	21.1

Notes: Optimized values expressed relative to the corresponding values for PAA-PEG.

as few adjusted parameters as possible

Generalized PBPK model



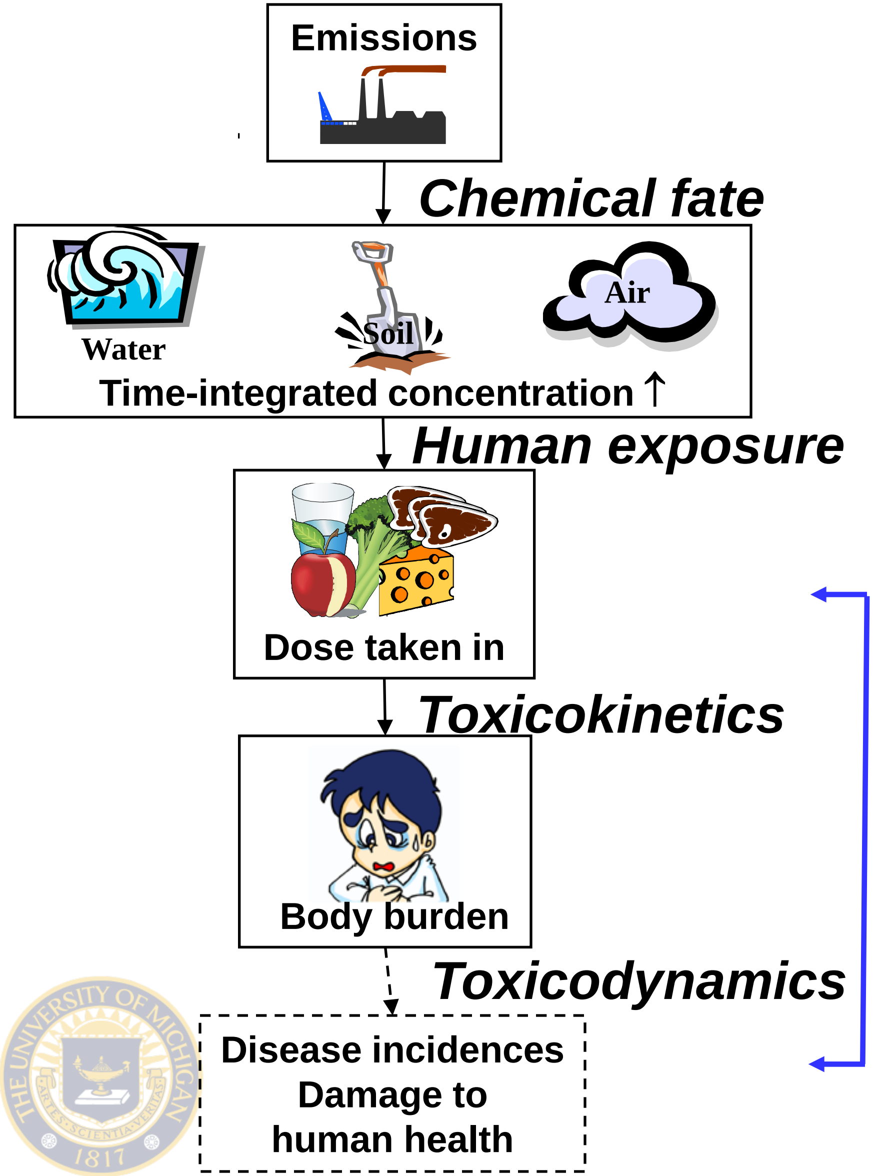
The model explains 97% of the observed variation in polyacrylamide NPs amounts across organs, between 68% and 95% for NanoCeO2, 88% for gold NPs and 92% for TiO2 NPs.

Also runs for

PLGA-mPEG (114 nm)	BVP-PLA (319 nm)	Ag (20 nm)	Ag (80 nm)	Ag (110 nm)	CeO_2 (instilled, 13 nm)

Carlander et al., International Journal of Nanomedicine, 11, 625–640

Framework for human toxicity and ecotoxicity of chemicals and nanoparticles



Effect factor
Impact/kg$_{in}$

based on NOAEL

J Nanopart Res (2017) 19:130
DOI 10.1007/s11051-017-3816-8

CrossMark

RESEARCH PAPER

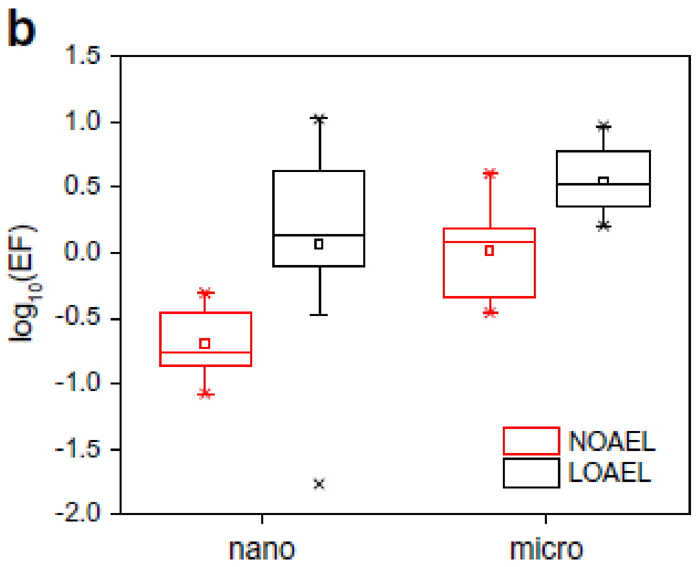
Human health no-effect levels of TiO_2 nanoparticles as a function of their primary size

Alexis Laurent · Jack R. Harkema · Elisabeth W. Andersen · Mikołaj Owsianiak · Eldbjørg B. Vea · Olivier Jolliet

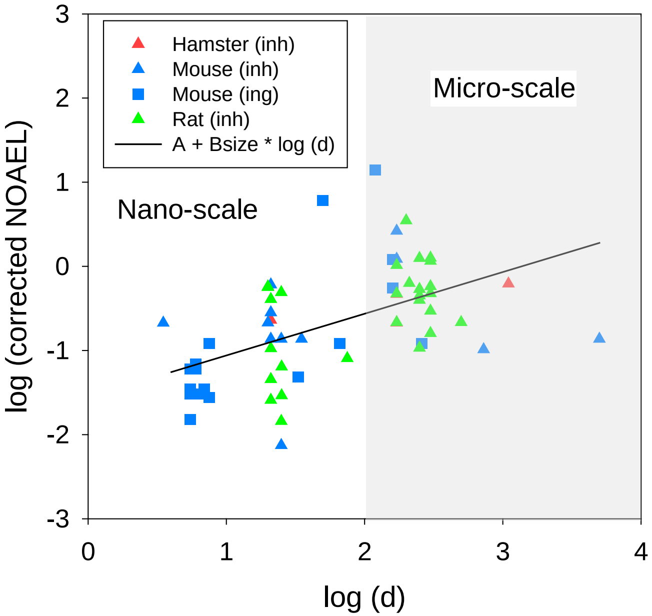
Table 1 Summary of reviewed in vivo studies with ranges of NOAEL and LOAEL for TiO_2 particles

Exposure routes	Number of studies (papers)[a]	Number of tests[a]	Number of left-censored NOAEL data	Number of right-censored LOAEL data	Number of interval-censored NOAEL/LOAEL data	NOAEL (LOAEL) ranges (mg/kg-bw/d)
Ingestion	6 (6)	15	3	5	1/1	40–24,000 (8–1000)
Inhalation	15 (26)	45	7	14	6/6	0.0836–4.05 (0.0171–10.5)
Total retrieved	21 (32)	60	10	19	7/7	–

No Observed Adverse Effect Level NOAEL for TiO2 a data rich chemical, most studies in East Asia



Laurent et al., 2017. J Nanopart Res 19:130

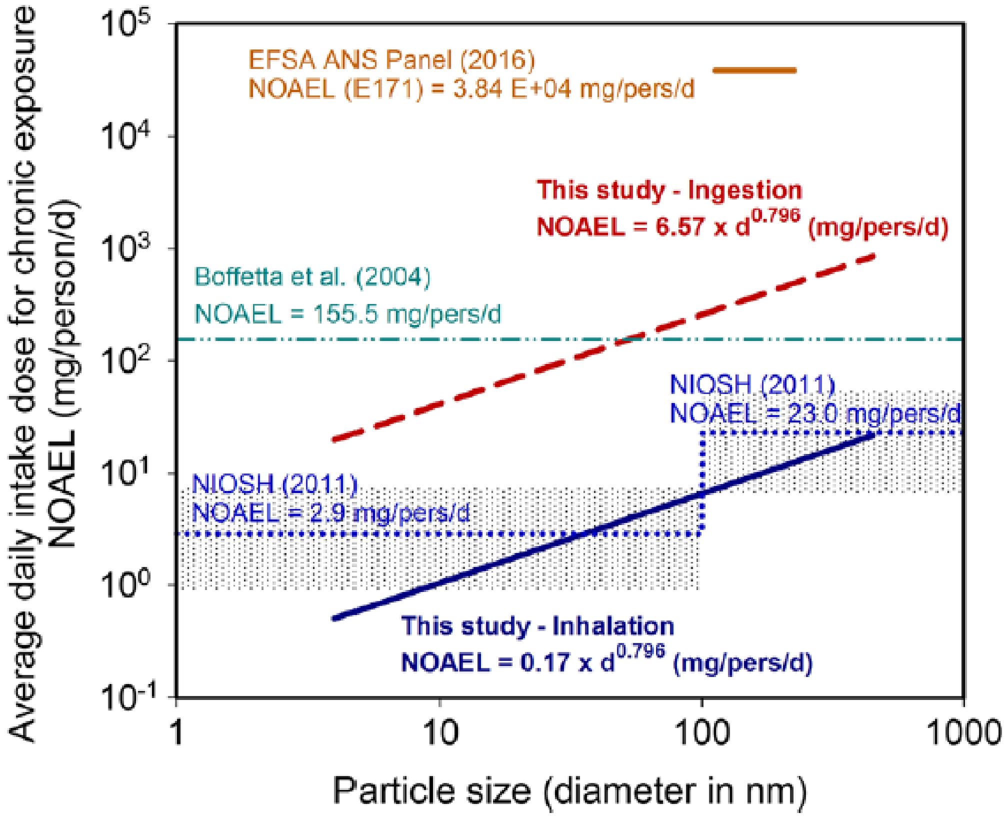


$$\log(NOAEL) = \alpha + \beta_{size} \log(d) + \beta_{species,\,route}\, I_{species,\,route} + \beta_{LOAEL}\, I_{LOAEL}$$

Supplementary Table S6. Regression analysis (MLR) on interval-censored data converted to human equivalent doses for inhalation and ingestion exposure to TiO_2 (n=14) [a]

Parameter	Estimate (95% CI)	Std. Err.	P values
Intercept	-2.228 (-3.36; -1.87)	0.335	1.42E-5 **
Log Size	0.796 (0.43; 1.16)	0.163	6.43E-4 **
Inhalation	0 (reference, see intercept)	-	-
Ingestion	1.592 (1.15; 2.04)	0.199	1.20E-5 **
LOAEL	0.725 (0.42; 1.03)	0.137	3.46E-4 **
Adj. R2	0.911		
Q^2 (LOO)	0.886		
p-value for model	3.98E-6 **		

log (NOAEL) as a function of log (d) R2 = 0.52, 0.76 on restricted set



NOAEL to ED50 to EF

EF in
Cases of non-cancer / kg_{in}

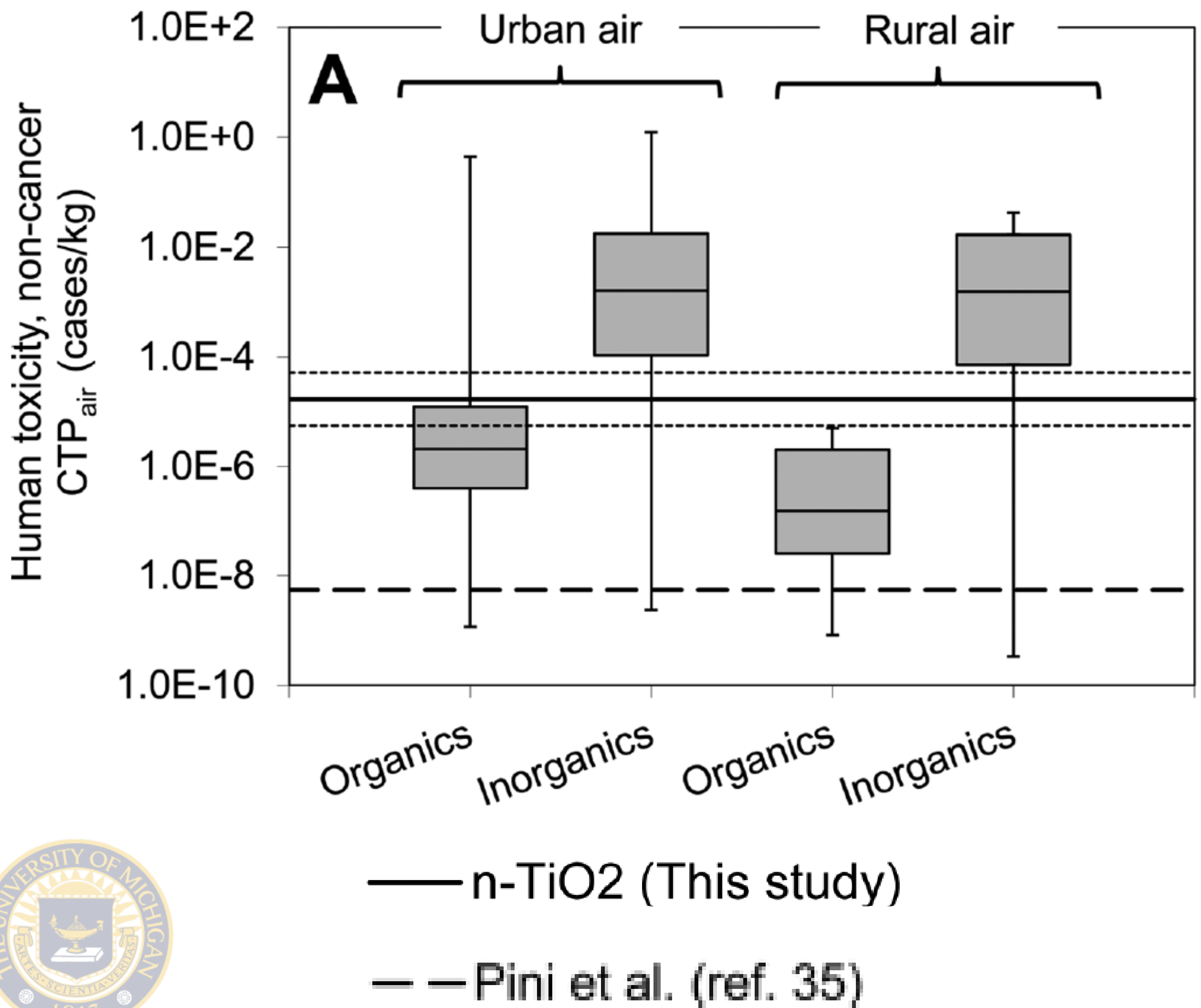
$$EF_{hum}^{inh} = 1.29 \times 10^{1} \times d^{-0.796}$$

$$EF_{hum}^{ing} = 3.31 \times 10^{-1} \times d^{-0.796}$$

Laurent et al., 2017.
J Nanopart Res 19:130

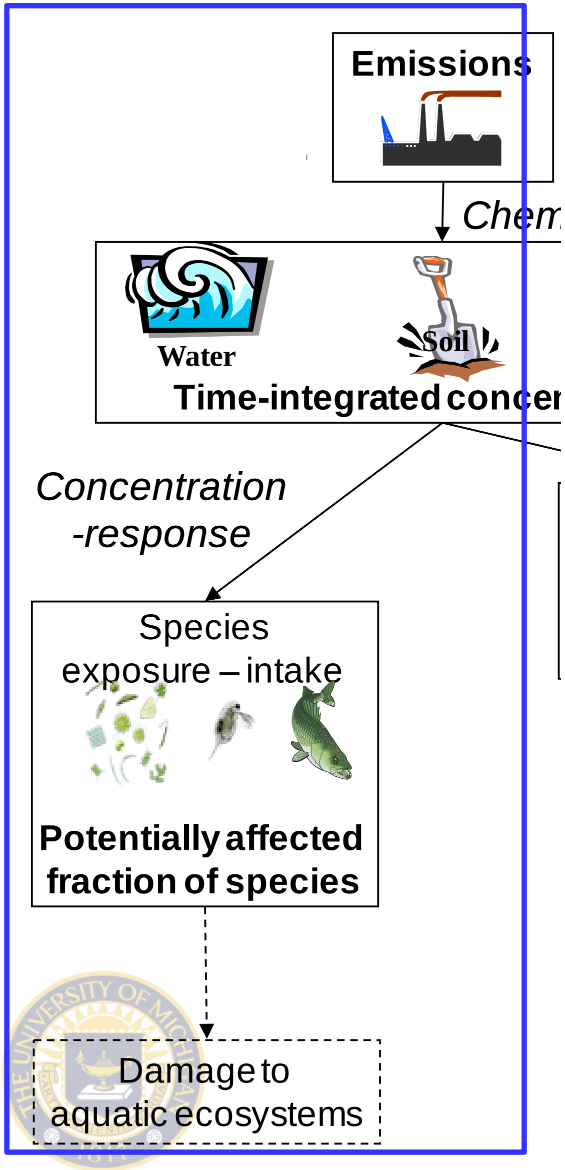
Characterization factors for freshwater human non cancer – comparison with USEtox CFs

CFs non-cancer for emissions into air



Ettrup et al., 2017.
ES&T 51, 4027−4037

Framework for human toxicity and ecotoxicity of chemicals and nanoparticles



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Ecotoxicity: LC50s → HC50

Particle type	Endpoint [mgTiO²/L]	Specie	Exposure	Size (pristine) [nm]
				Bacteria
Nanocrystaline	>112.5	*V. fischeri*	30-min EC50	6
Sigma Aldrich	>100	*V. fischeri*	15-min EC50	40
Sigma Aldrich	>11987	*V. fischeri*	30-min EC50	47.5

HC50 and effect Factor	Free & Agg water [days]
HC50 mg/L	18.6
EF PAF m3/kg	26.9

Ecotoxicological effect factor

- **Ecotoxicological impacts may already be incorporated in LCA, as soon as EC50 are available**

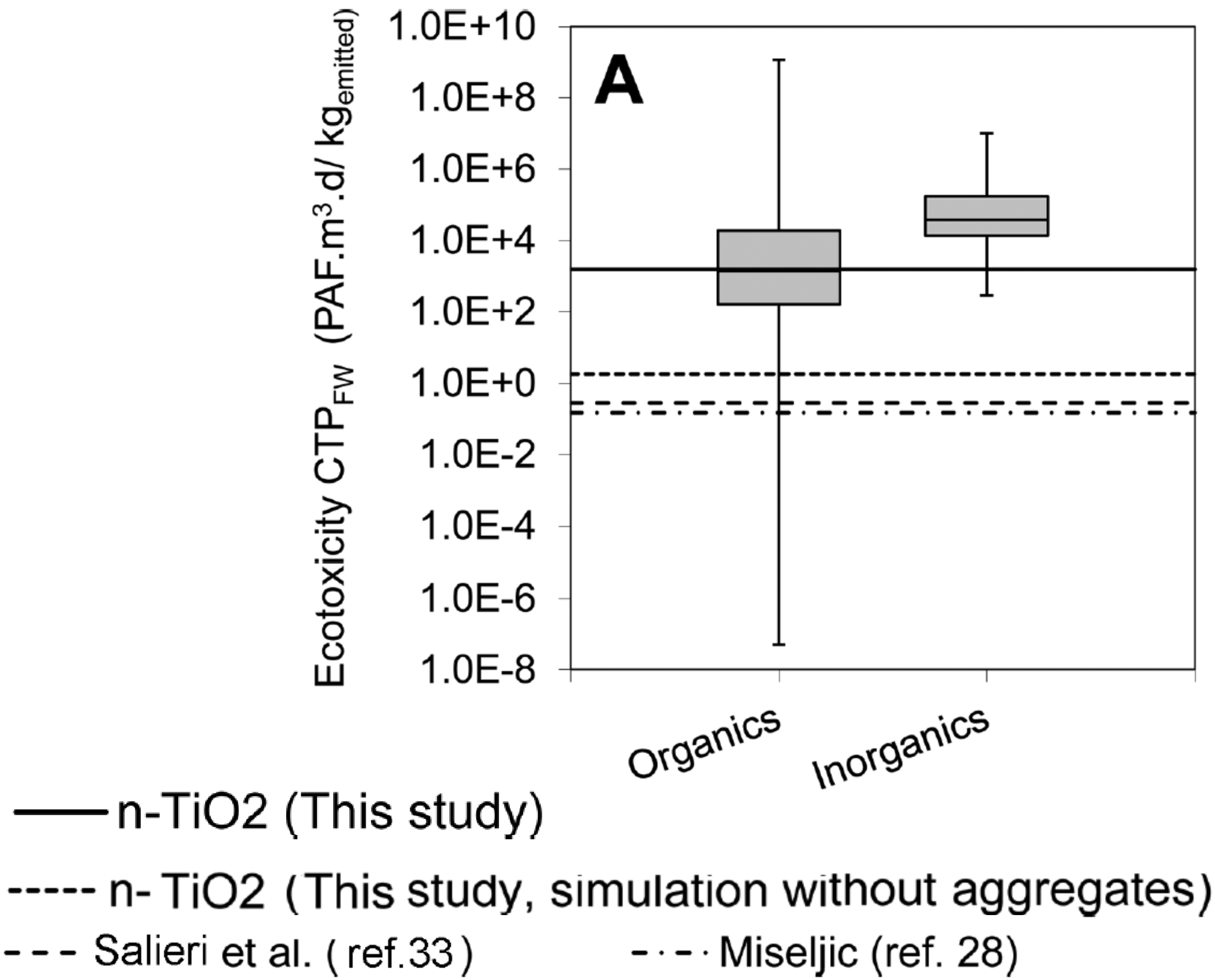
- **For comparative assessment, use the HC50, the concentration at which 50% of the species are affected = geometric mean of the EC50s of all species tested (not the PNEC):**

$$CF = F_w \cdot \frac{\tau_{1/2w}}{\ln(2)} \cdot \frac{0.5}{HC_{50}}$$

- **Bioavailability modeling (e.g. sulfides)**

Characterization factors for ecotoxicity – comparison with USEtox & other studies

CFs Ecotox for emissions into freshwater



Ettrup et al., 2017. ES&T 51, 4027−4037

Conclusions

- **Possible to adapt USEtox to nano speciation based on compartment specific ratios between free / agg and at**
- **First human and ecotox effect factors + characterization factors available based on literature review for TiO2 or silver**
- **Need to extend to a larger number of nanoparticles, in particular BAFs and human tox**
- **Some of the nanoparticles have been extensively studied**