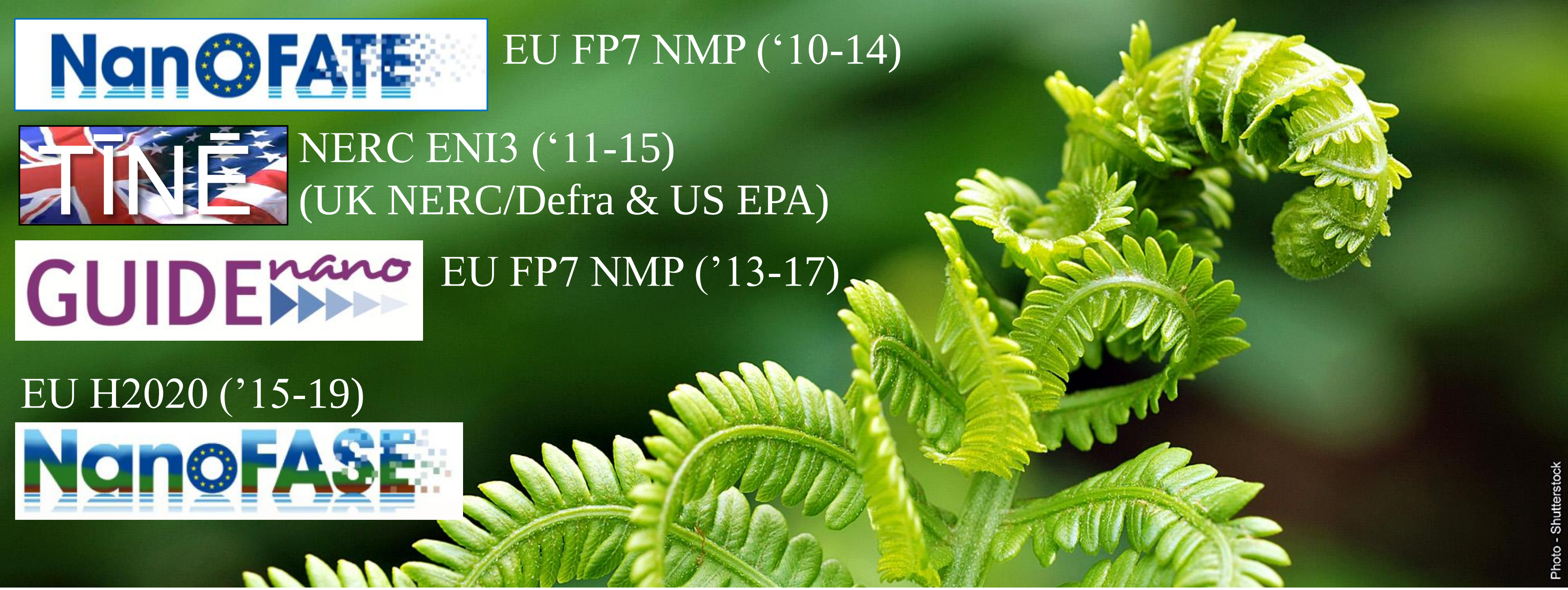


What is the meaning of pristine nanoparticles, their lifecycle and fate? An overview and forward look

Claus Svendsen[1], Elma Lahive[1], Marianne Matzke[1], Carolin Schultz[1], Ana Romero-Freire[1,2], Soco Vazquez[3], Maria Diez Ortiz[1,3], Alan Lawlor[4], Daniel Starnes [5], Olga Tsyusko[5], Jason Unrine[5], Greg Lowry[6], David Spurgeon[1] and Steve Lofts[4]

[1]NERC-CEH, Wallingford, United Kingdom
[2]Soil Science Department. University of Granada, Spain
[3] NanoHealth & Safety group, LEITAT, Barcelona, Spain
[4]NERC-CEH, Lancaster, United Kingdom
[5]Department of Plant and Soil Sciences, University of Kentucky, Lexington, USA
[6]Carnegie Mellon University, Pittsburgh, USA

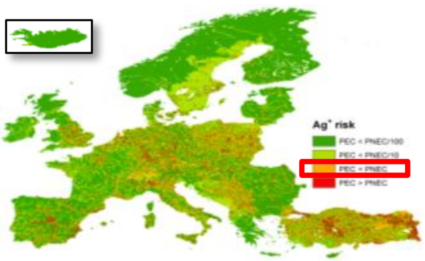
Behaviour and Fate is environment dependent

Most "entities" change behaviour when moved from one compartment to another or between different Phys Chem. parameters.

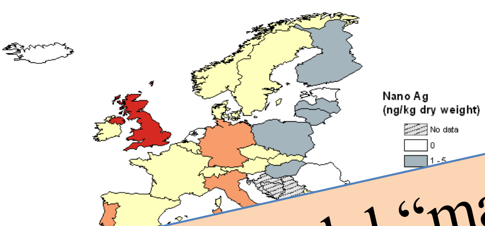
Data needs for environmental RA of nano

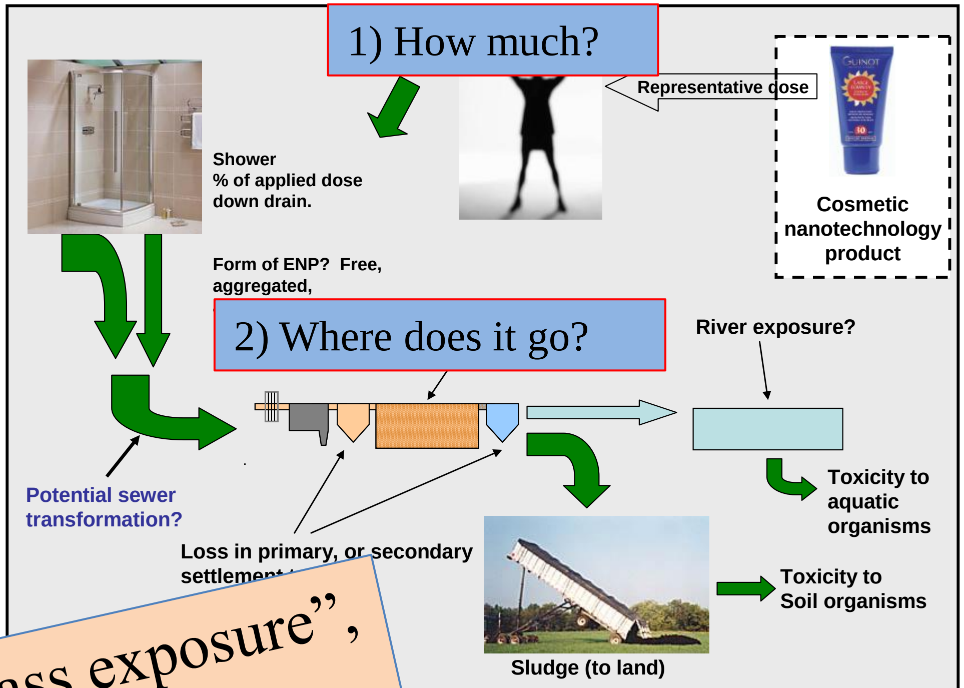
PECs:

Water:



Soil:

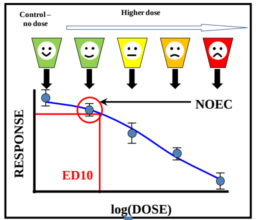




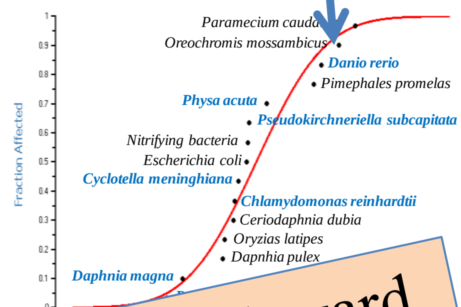
3) Will it cause effects?

PNECs:

2-5x



Ag ENPs



Can model “mass exposure”, even spatially resolved.

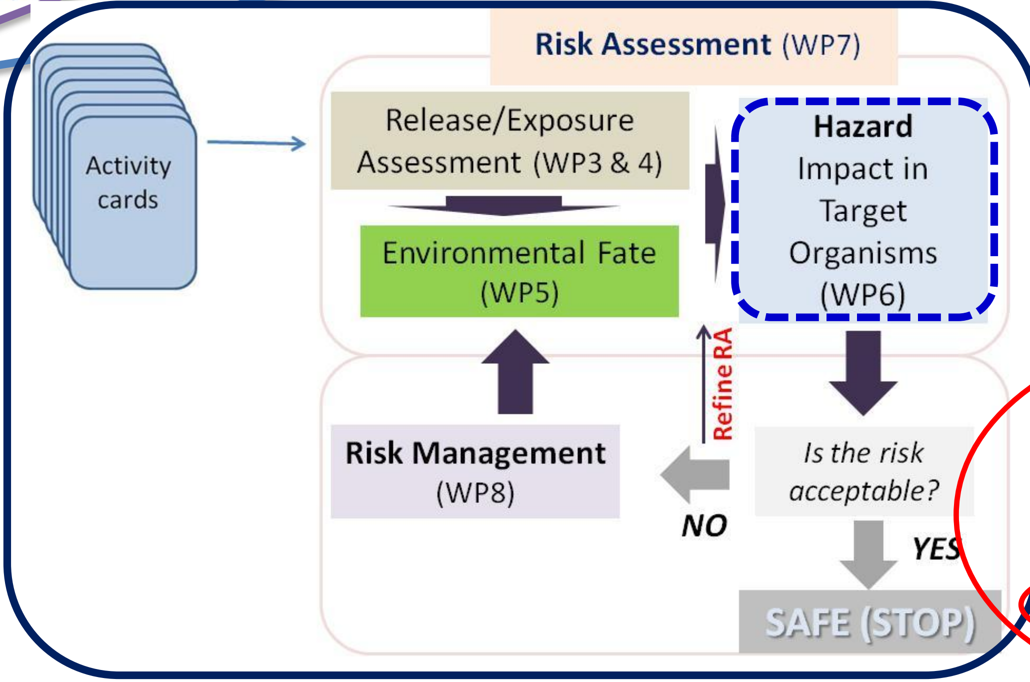
Can’t test all NMs for hazard. What is “the right” Haz data?

“Tools for mapping environmental … ope from commercial nanoparticles used in … nsumer products”

NanOFATE

SEVENTH FRAMEWORK PROGRAMME

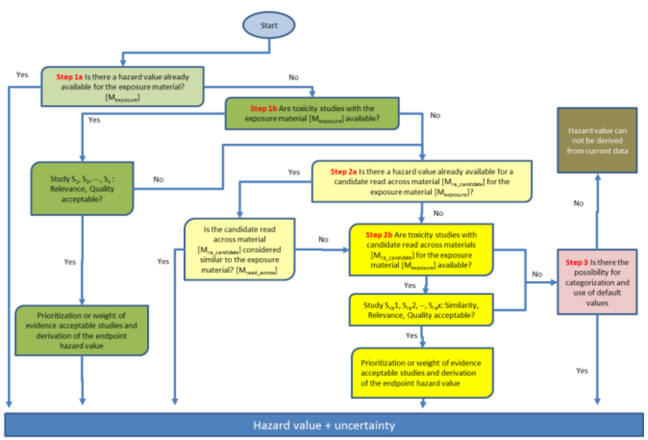
Hazard data selection



Aim: to generate Hazard estimates using as much of existing data and methods as possible.

Data selection:
- Quality (of test)
- Relevance (of test)
- Similarity (of NM)

Decision-trees



Predictive models, data & assumptions

$Ag^{+}_{tox} > Ag^{PVP}NP_{tox} > AgSNP_{tox}$

High dissolution => high ion tox

etc, etc

Decision tables

	Data entry question or decision table	Answer	Action	DNEL	Uncertainty
1	Are there regulatory binding or provisional OELs/DNELs for the exposure relevant test material?	Yes	go to 2		
		No	go to 3		
2	Which is the OELs/DNELs value:	DNEL_VALUE	DNEL is defined. Finish.	Is DNELinh, long-term	low
3	Are there valid inhalation studies with the exposure relevant test material or a similar one?	Yes	go to 4		
		No	go to 7		
4	Launches decision tree on relevance of test	Valid inhalation study	go to 5	defined in test relevance table	defined in test relevance table
		Not valid inhalation study	go to 7		

Similarity

Step 1 of “read across”

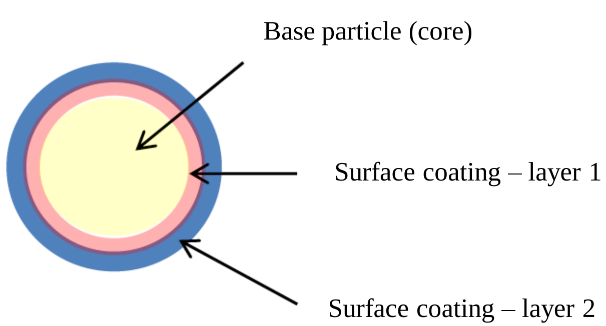
Comparing “Nano Forms”

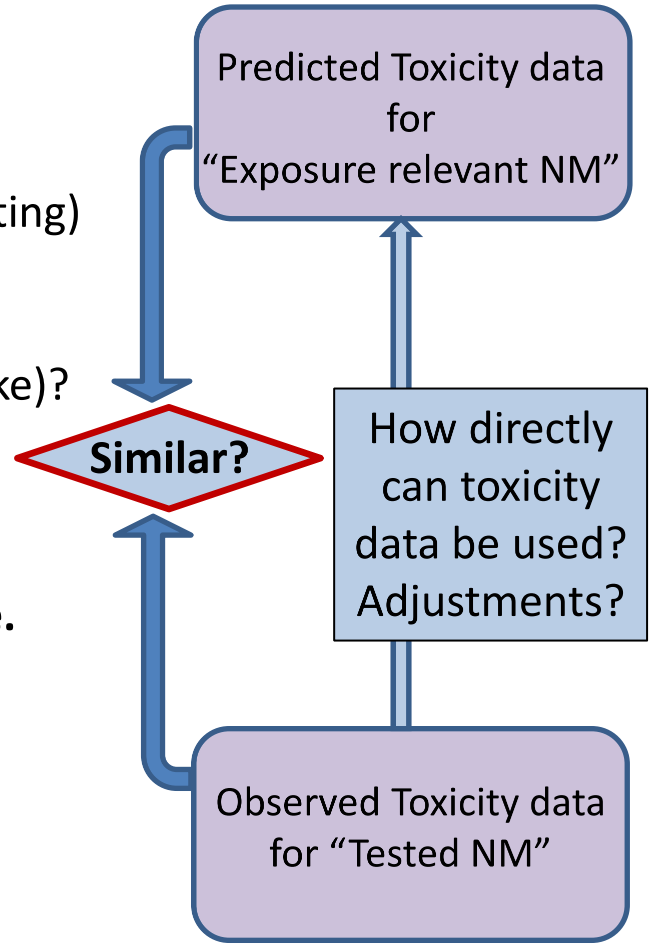
- OECD/ECHA workshop on this
- ECHA consultation on this
  (Adopted US EPA – includes coating)

Key issues:

- Where does it go (fate and uptake)?
- What does it look like?
- What does it do?

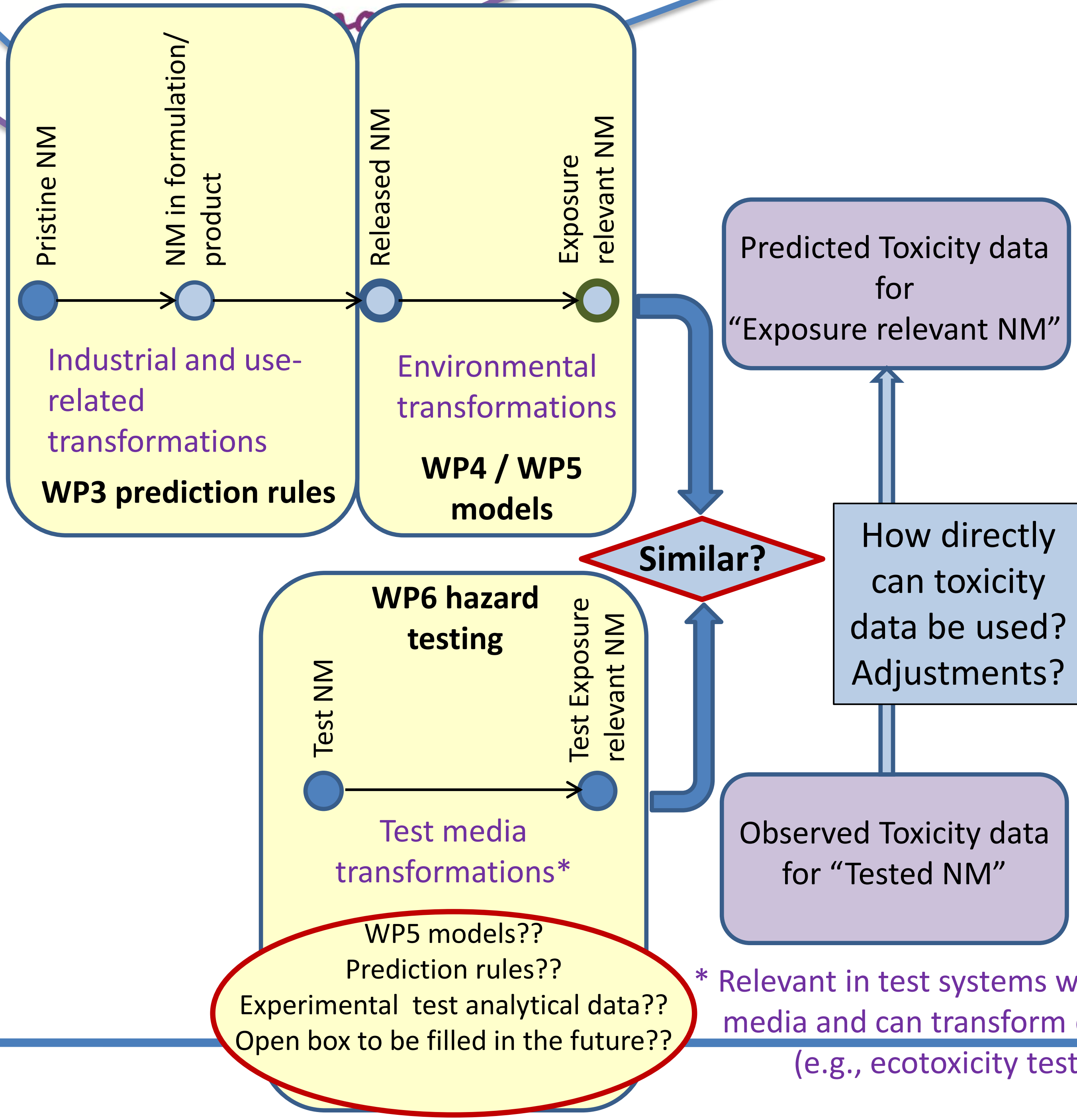
Need to agree on what to compare.



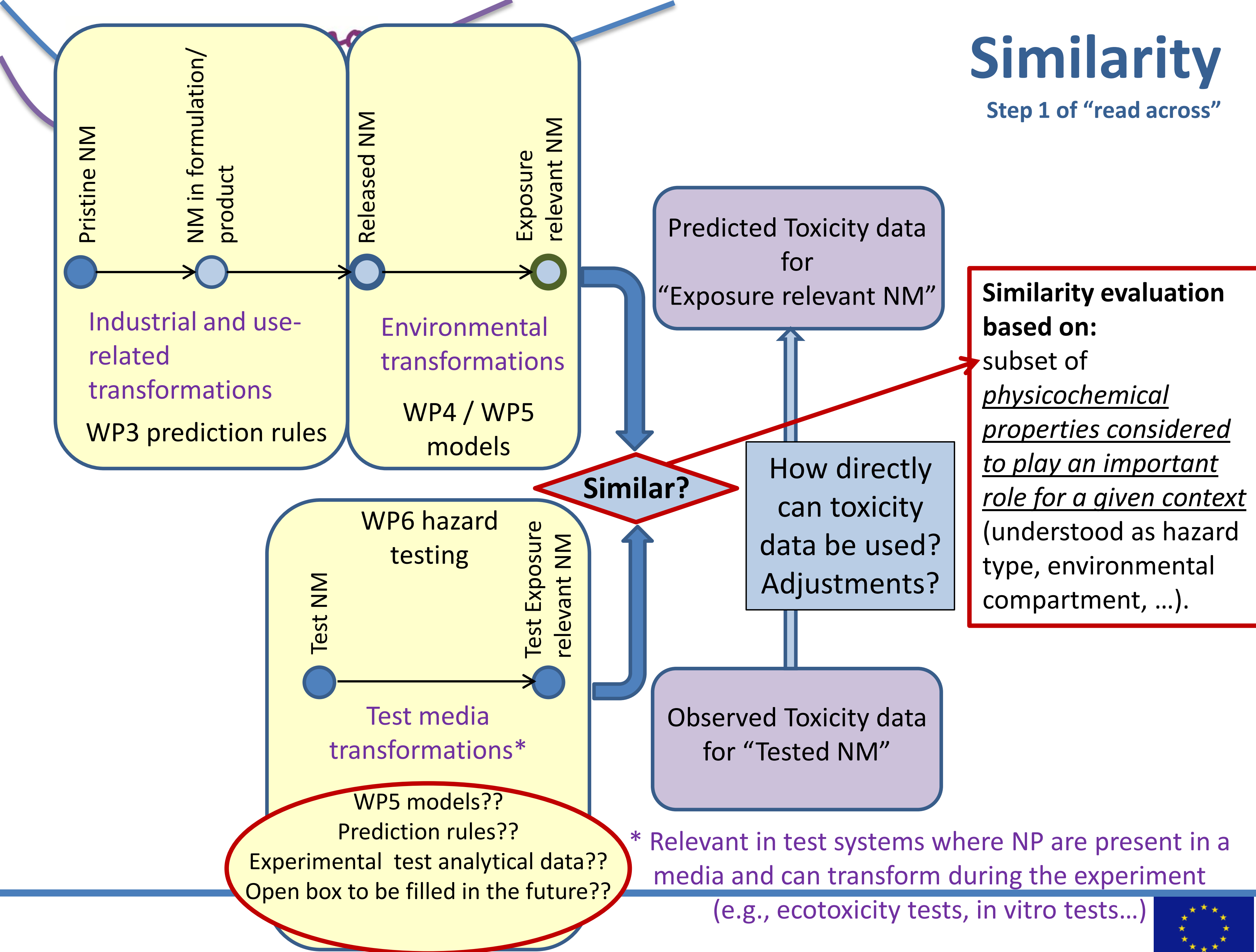


Similarity

Step 1 of "read across"



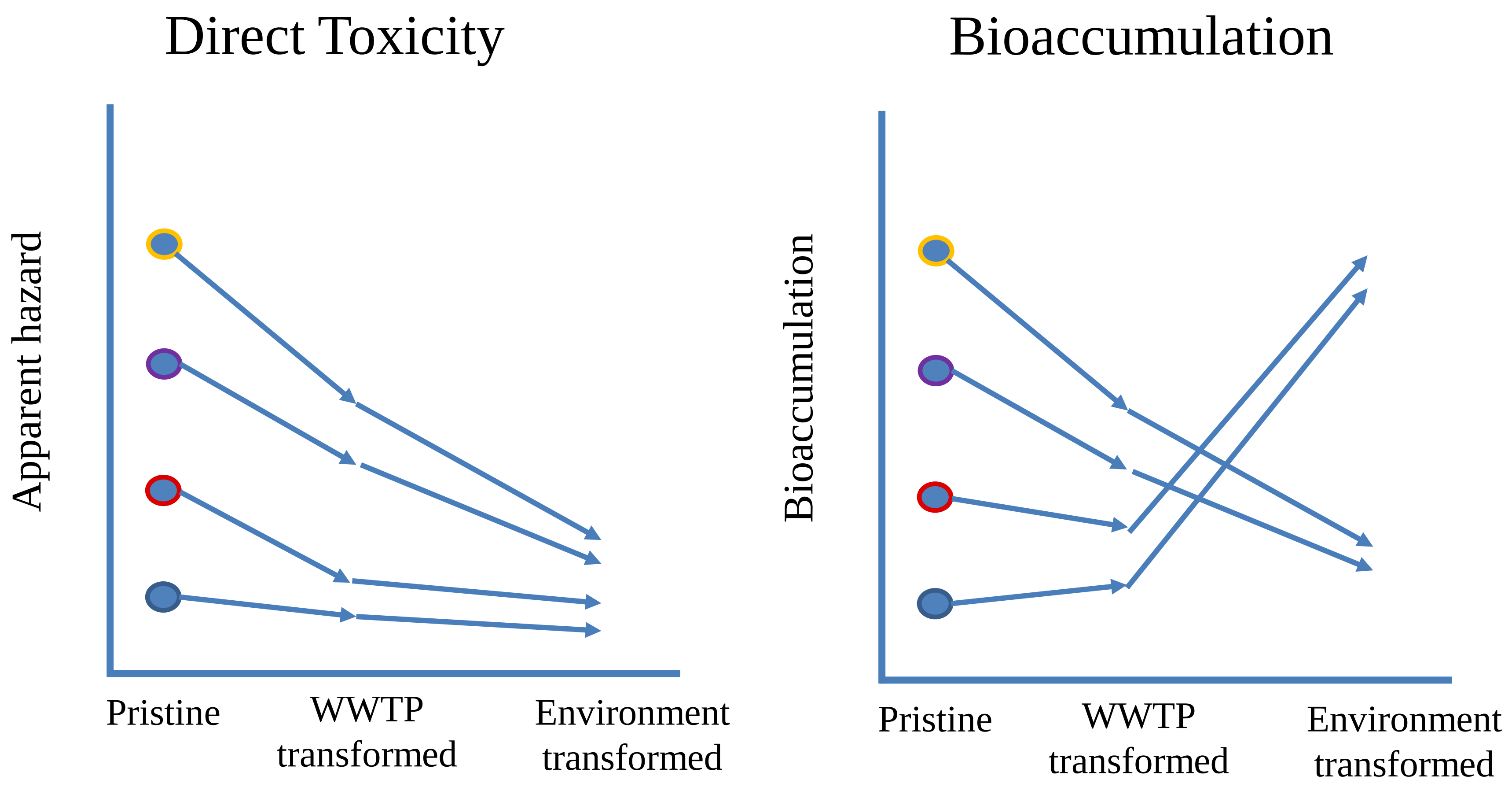
* Relevant in test systems where NP are present in a media and can transform during the experiment (e.g., ecotoxicity tests, in vitro tests…)


Similarity
Step 1 of "read across"
Pristine NM
NM in formulation/ product
Released NM
Exposure relevant NM
Industrial and use-related transformations
WP3 prediction rules
Environmental transformations
WP4 / WP5 models
Predicted Toxicity data for "Exposure relevant NM"
Similarity evaluation based on:
subset of physicochemical properties considered to play an important role for a given context (understood as hazard type, environmental compartment, …).
Similar?
How directly can toxicity data be used? Adjustments?
WP6 hazard testing
Test NM
Test Exposure relevant NM
Test media transformations*
Observed Toxicity data for "Tested NM"
WP5 models??
Prediction rules??
Experimental test analytical data??
Open box to be filled in the future??
* Relevant in test systems where NP are present in a media and can transform during the experiment (e.g., ecotoxicity tests, in vitro tests…)

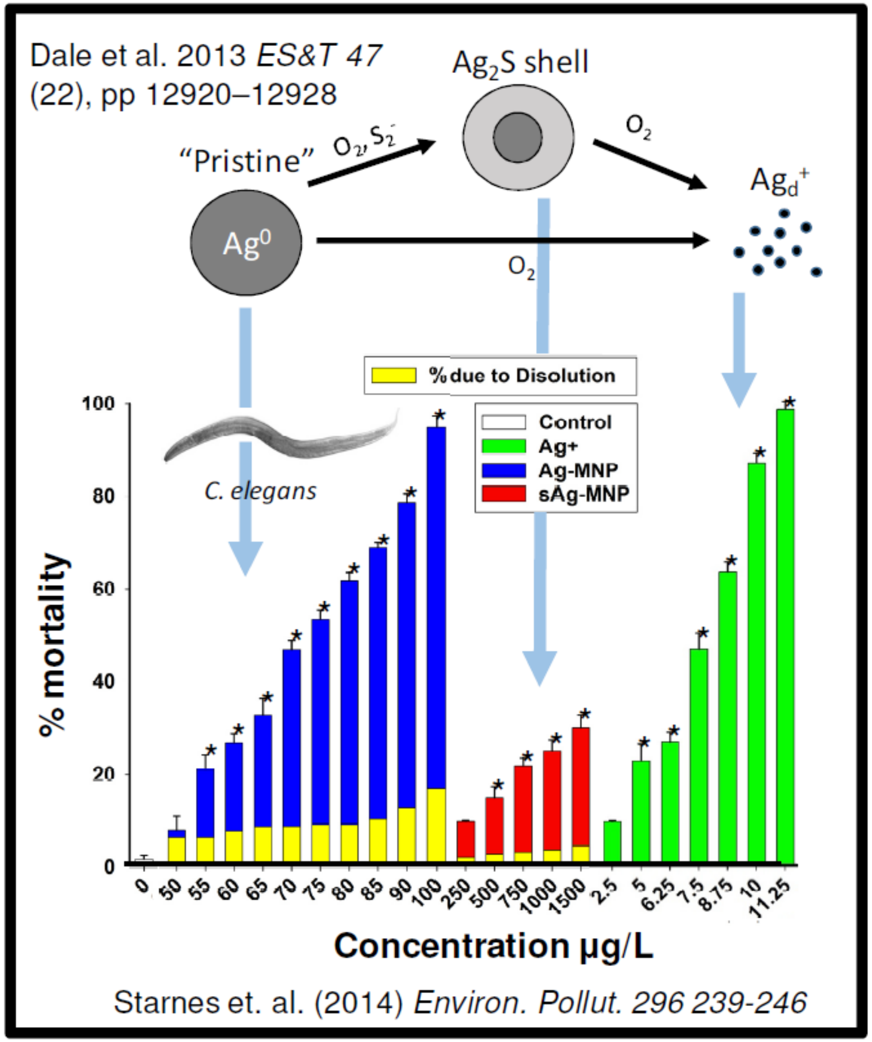
“Read across” assumptions in the environment

Reactive nano materials in reactive environments => Transformations

“Context”



“Read across” assumptions in the environment



Hazard ranking:

=>

Mass exposure (PEC)/
Ion Hazard (PNEC)
based RA
Should be conservative and protective.

But what if:

Ag_2S accumulates
in hotspots (biota) and
dissolves late
(e.g. post ingestion)

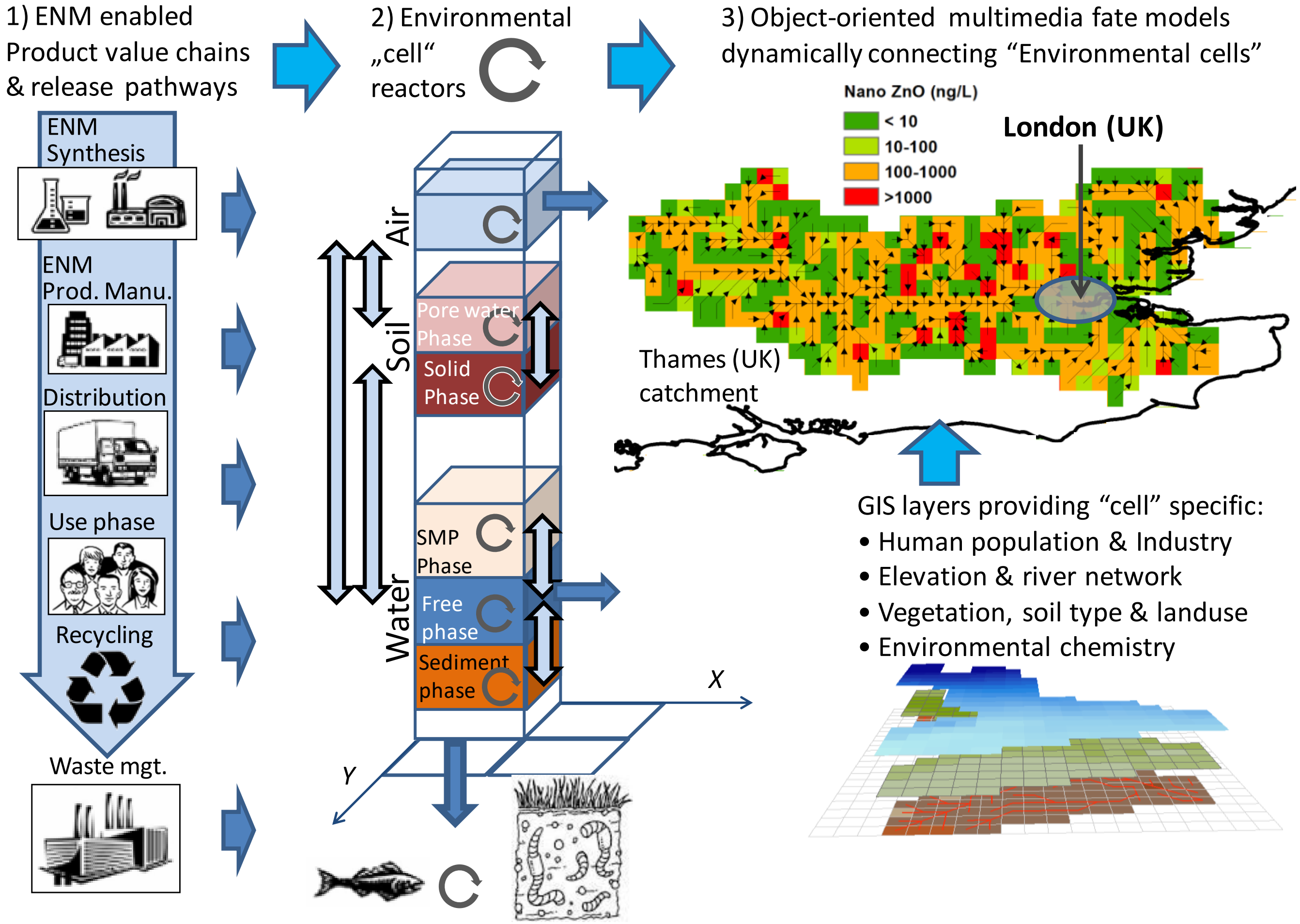
=>

Need to understand Exposure

NanoFASE

Exposure - Nanomaterial fate in the environment:

Where, what and for how long?



- **“Reactors” and relevant ENMs** (using the right starting materials at each step)
- **Functional fate groups** a tool to understand and reduce complexity
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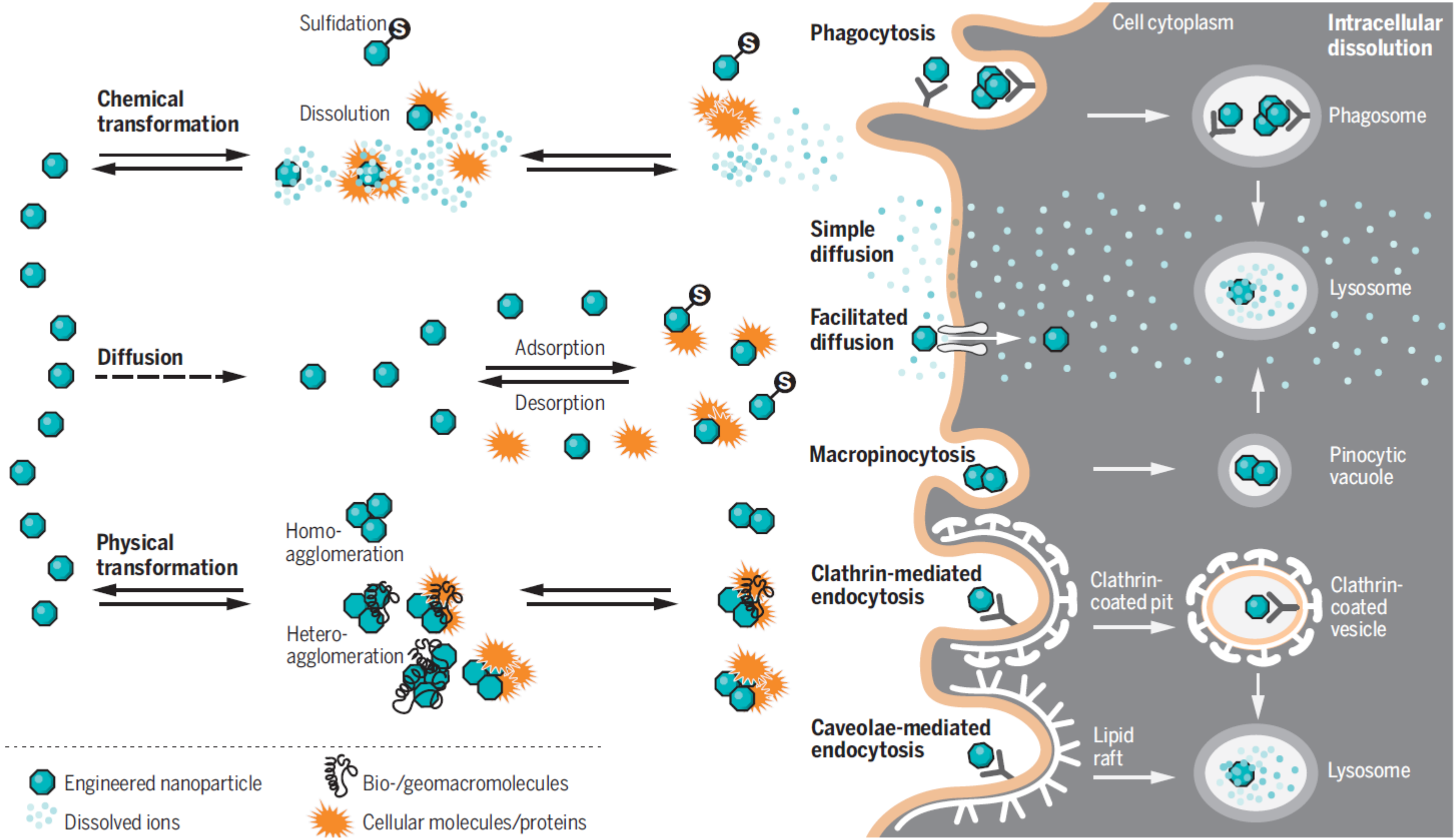
Conceptual workflow for a framework to deliver dynamic multimedia fate prediction both in a generalised model environment and GIS enabled mode.

NanoFASE

Environmental reactors: Complex, but may they help?

Reactive nano materials in reactive environments => Transformations

Valsami-Jones and Lynch (2015) Science

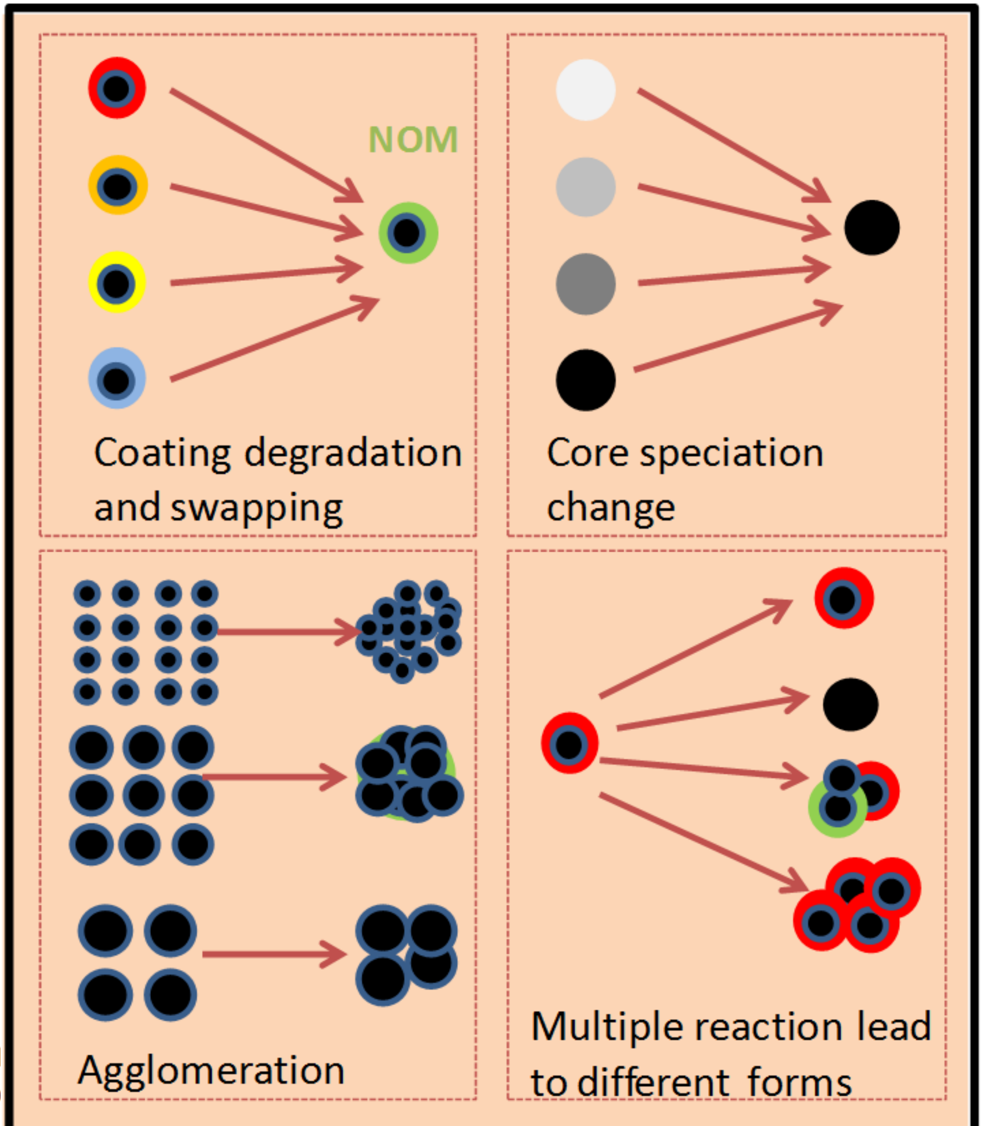


Nanoparticle complexity. Schematic illustration of the competing environmental transformation and organismal uptake processes that occur for a nanomaterial in aquatic environments, illustrated using a silver nanoparticle.

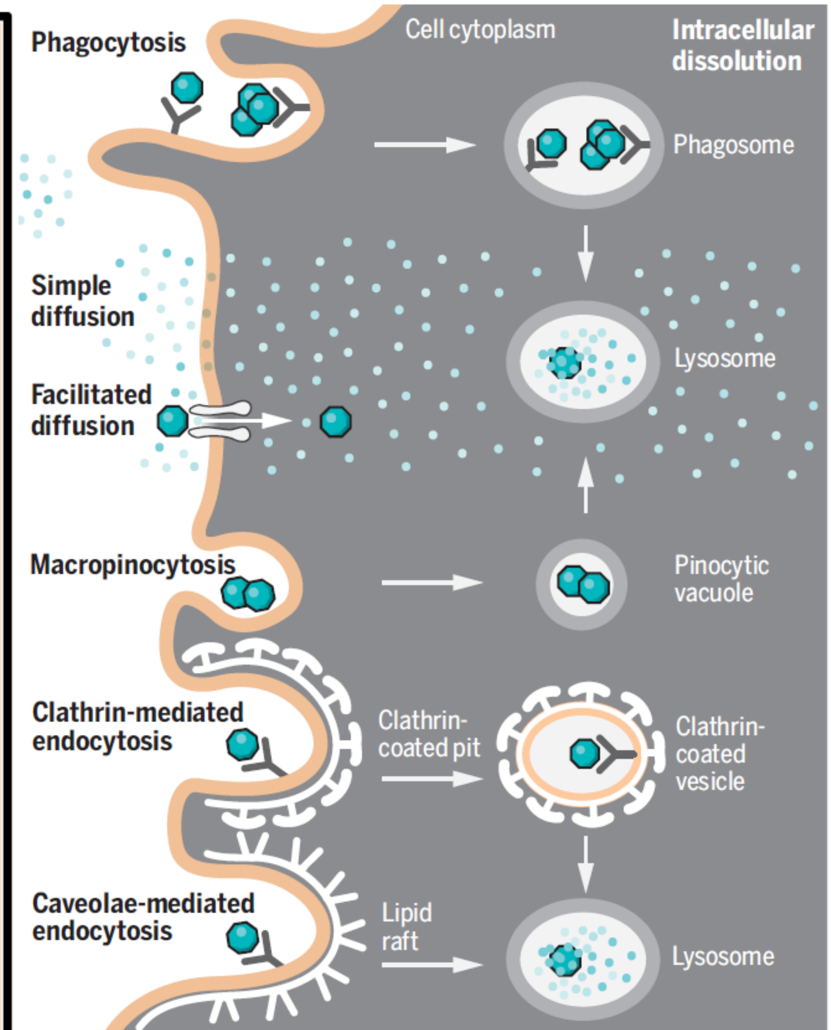
NanoFASE

Environmental reactors: Complex, but may they help?

Reactive nano materials in reactive environments => Transformations



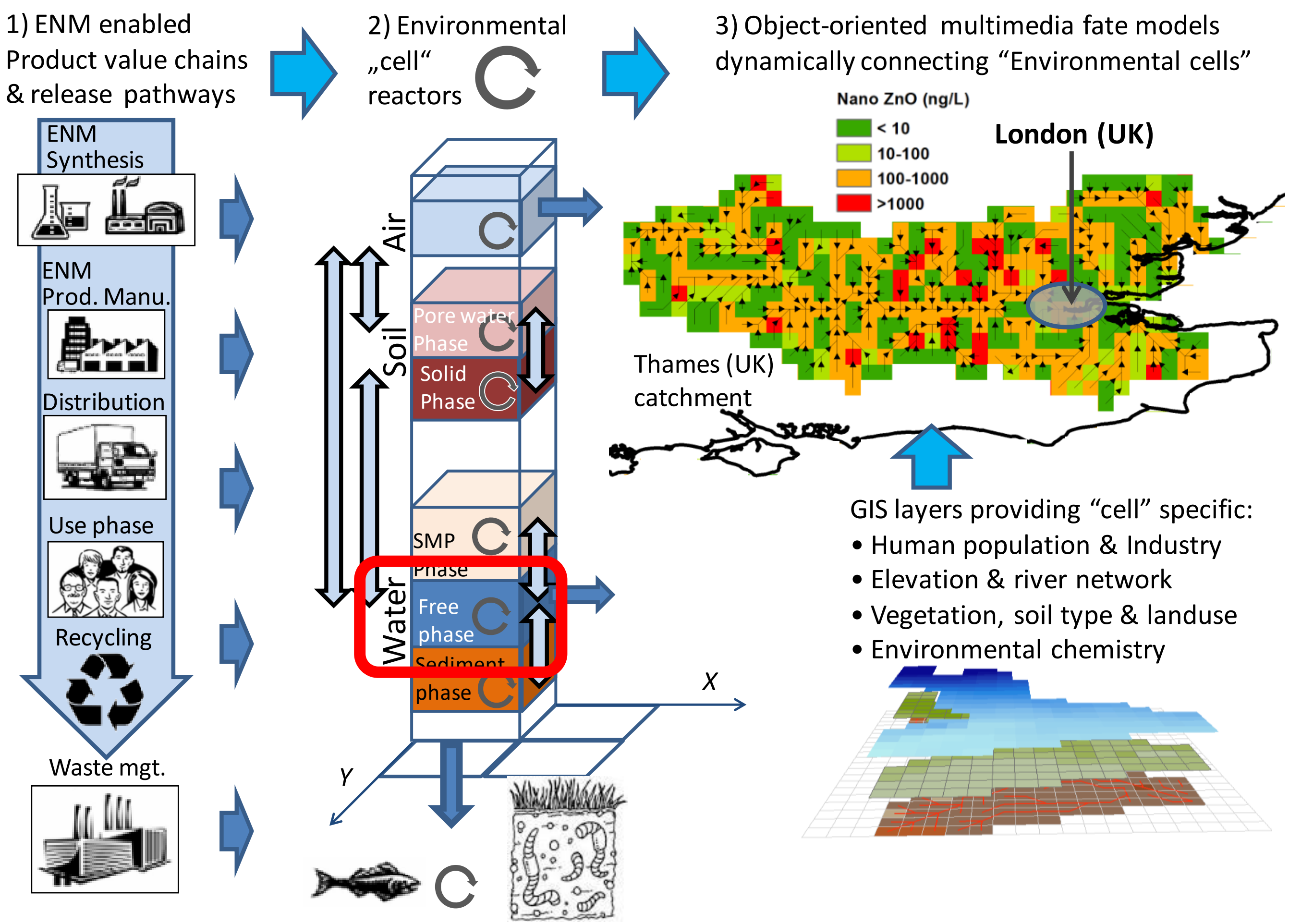
Modified from D Mitrano & B Nowack (EMPA)



ion and organismal uptake processes that occur for a nanomaterial in aquatic

Valsami-Jones and Lynch (2015) Science

What about a mild reactor – water?



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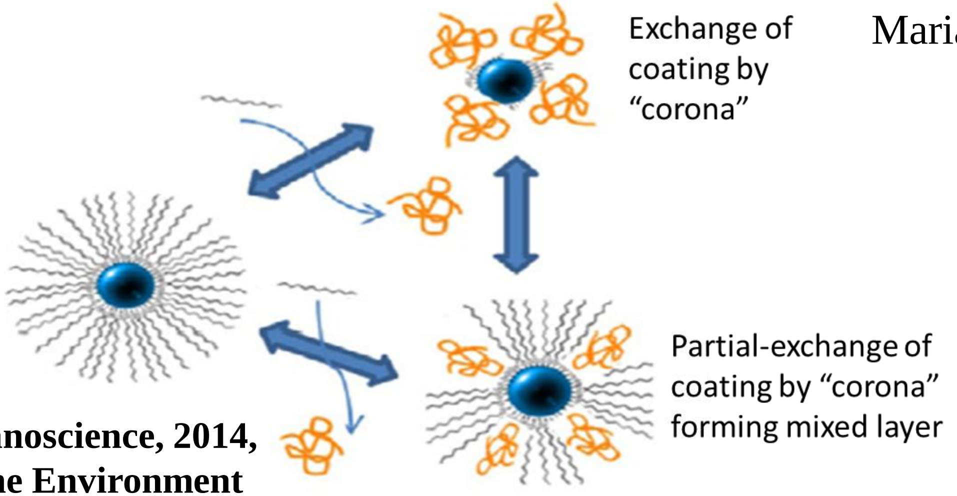
What about a mild reactor – water?

- The order of sensitivity to $AgNO_3$ and 2 x Ag NPs NPs has no simple correlation

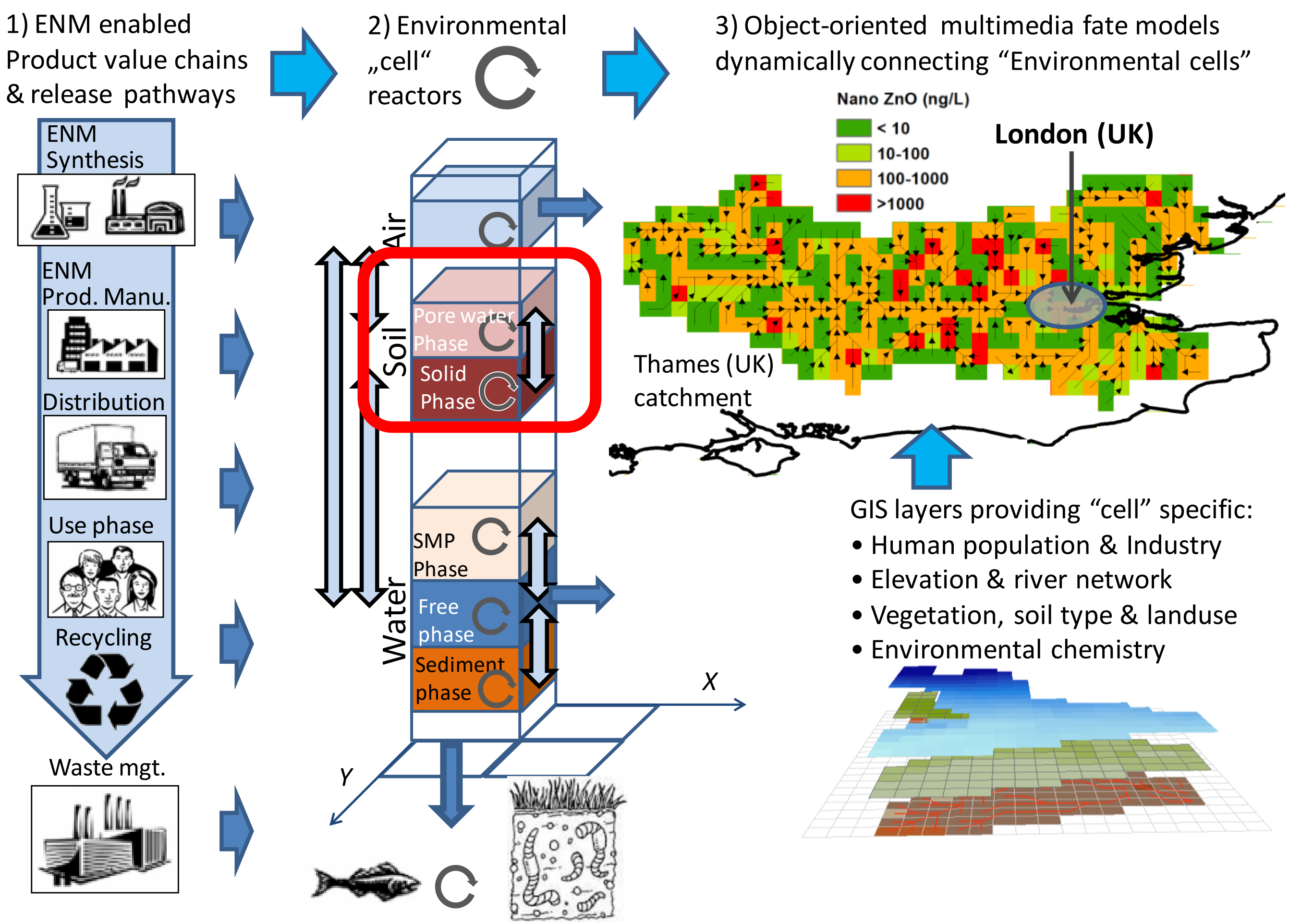
Bacteria IC50 (growth)	Type and habitat	$AgNO_3$ (µg/L)	5nm Ag uncoated (µg/L)	50 nm Ag PVP coated (µg/L)
B. Subtilis	*gram-positive, soil (reservoir) and human gut*	**0.7**	**8**	64
E. Coli	*gram-negative, intestines*	4	**9**	146
P. Fluorescence	*gram-negative, soil and water*	2	45	230
C. metallidurans	*gram-positive, belong to bacillus, **heavy metal contaminated environments***	10	66	**24**
P. Stutzeri	*gram-negative, first isolated from human spinal fluid*	**68**	76	**770**
B. Megaterium	*gram-positive, soil*	6	90	170
J. Lividium	*gram-negative, soil*	13	230	68
M. luteus	*gram-positive, soil/dust/water/air*	**0.01**	**1110**	62

Marianne Matzke, in prep



Lynch et al., in **Frontiers of Nanoscience, 2014, Volume 7: Nanoscience and the Environment**

What about a medium reactor – soil?



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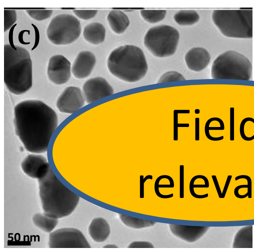
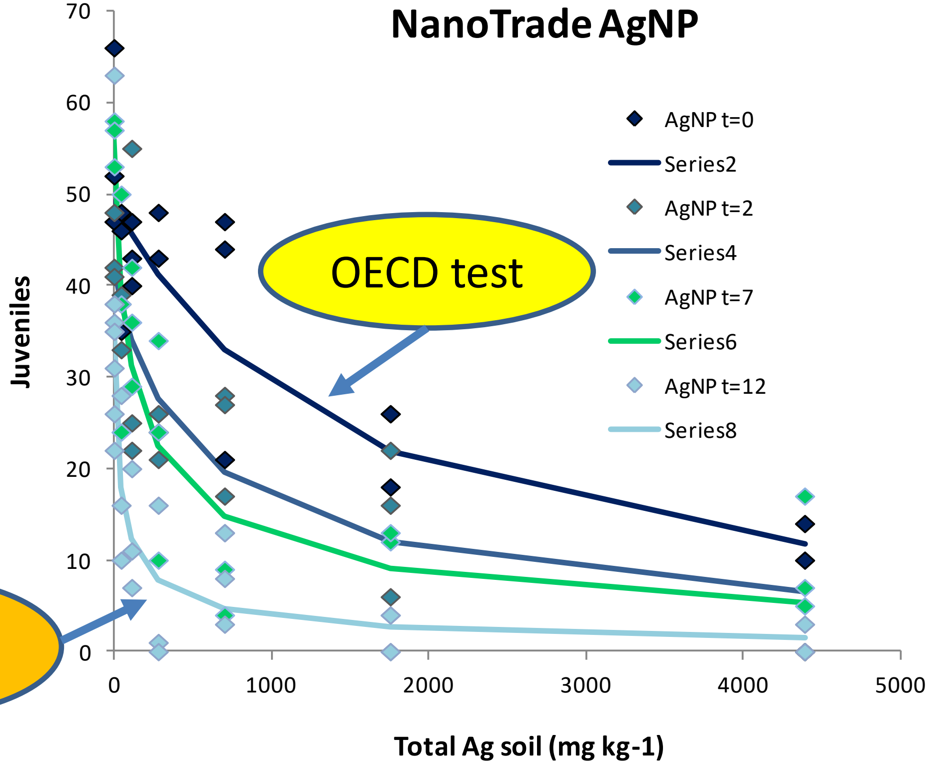
Dissolution time scales can be long

50nm AgNPs (uncoated)





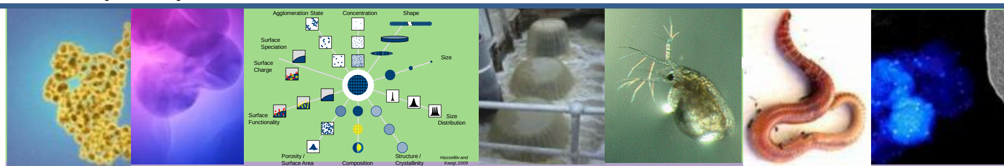
Ageing dosed soil for 0, 2, 7 & 12 months

- In dark at 20 ± 1°C
- Continuously aerated
- Moisture loss adjusted

Soil EC50 (mg/kg dry soil)	**T=0**	**T=2mth**	**T=7mth**	**T=12mth**
AgNP	1420 (407-2432)	588 (65-1110)	142 (5-278)	34 (-117)
$AgNO_3$	49 (46-51)	30 (16-43)	90 (29-151)	104 (63-144)

Diez-Ortiz, M *et. al.* Environmental Pollution, 203, 191–198 (2015)

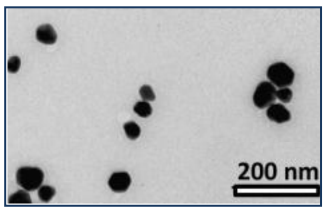
NanOFATE



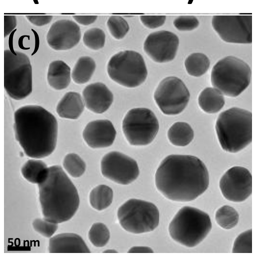
SEVENTH FRAMEWORK PROGRAMME

Coating, Uptake and Toxicity

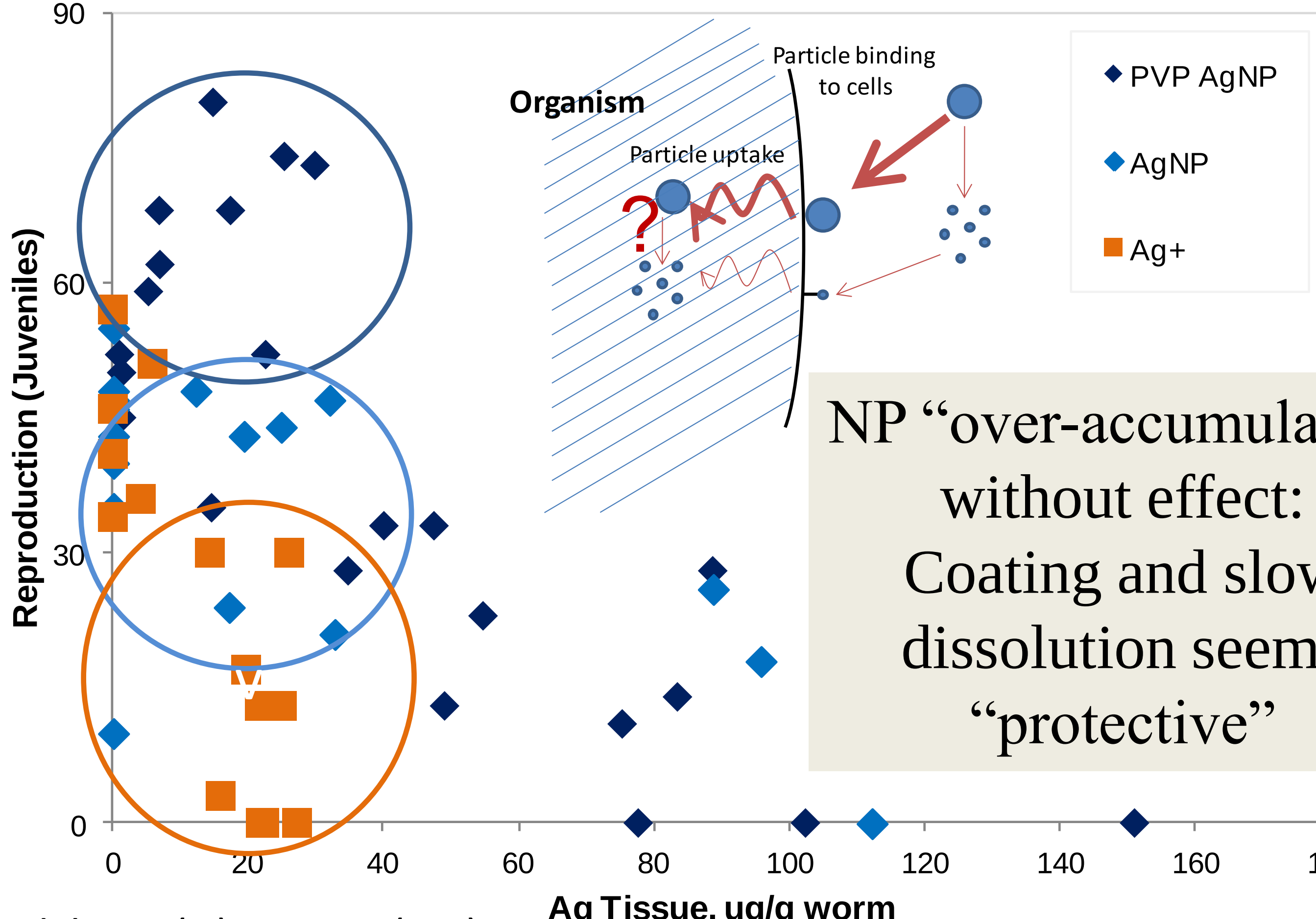
50nm AgNPs (PVP coated)



50nm AgNPs (uncoated)



SILVER UPTAKE AND TOXICITY IN EARTHWORMS EXPOSED 56DAYS (IN FRESHLY SPIKED SOILS)



NP "over-accumulates" without effect: Coating and slow dissolution seems "protective"

Diez-Ortiz, M *et. al.* Environ Tox and Chem 34 (10), 2263–2270 (2015)

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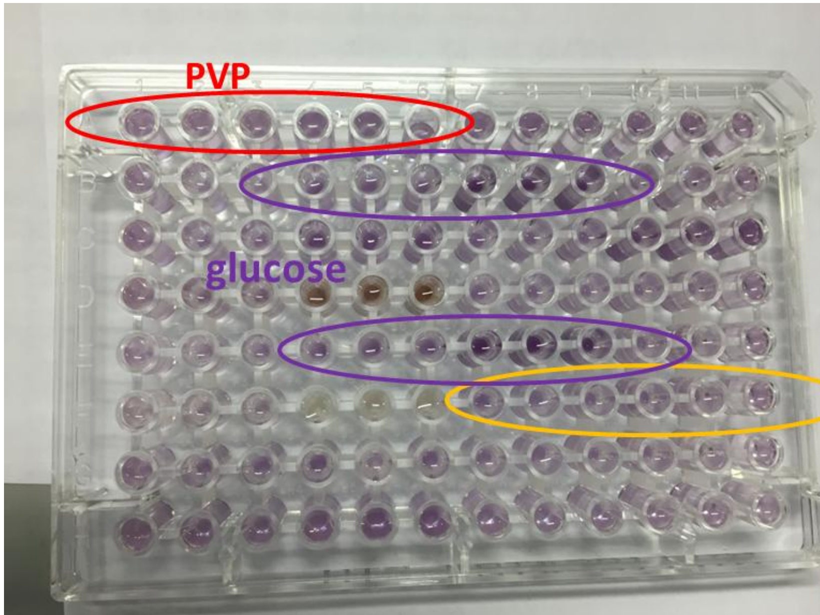
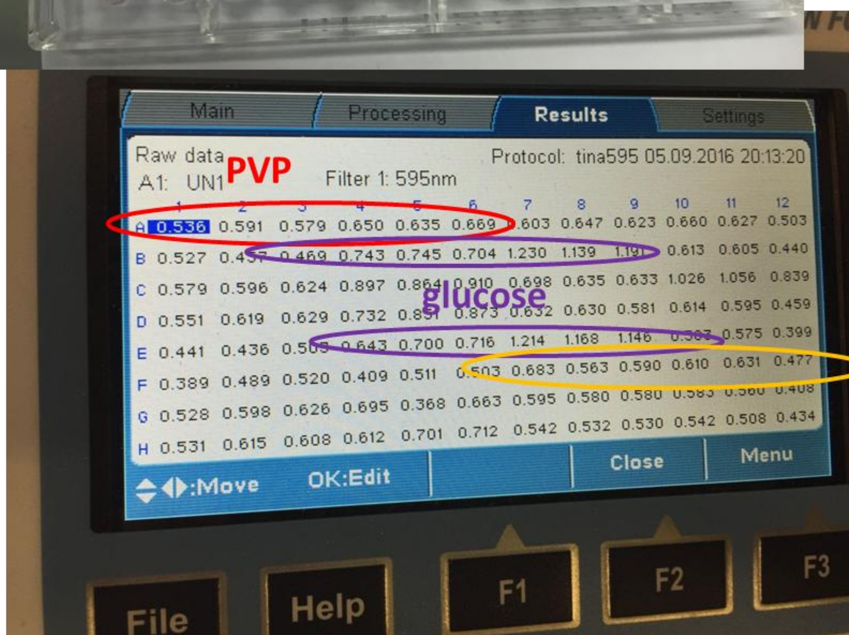
SEVENTH FRAMEWORK PROGRAMME

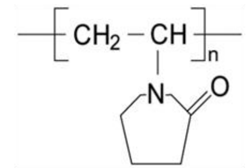
How to access coating stability in the environment ?



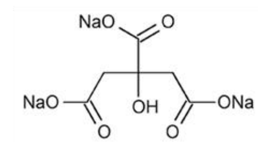


Sodium Citrate

Sodium Citrate



PVP relatively indigestible
E.g. compared to **glucose**



Sodium citrate – somewhat toxic, rather than being indigestible
- due to high pH.

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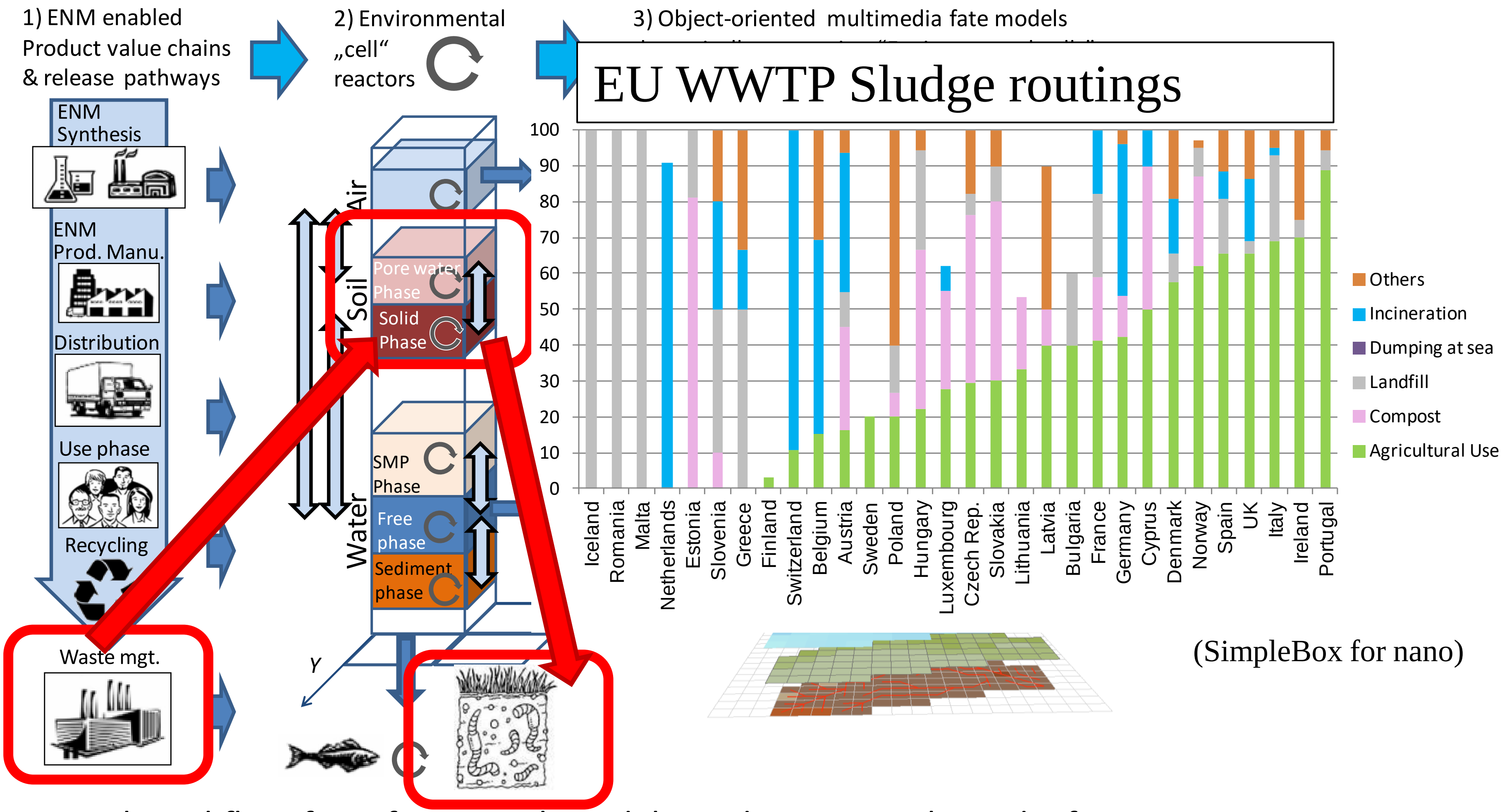
What about a chain of reactors – “real world”?



Conceptual workflow for a framework to deliver dynamic multimedia fate prediction both in a generalised model environment and GIS enabled mode.

Real world "Aged" sewage sludge NPs trials

Three sewage sludge streams

Control | **Ionic** | **NP**

Ionic: Zn + Ag

NP: Zn + Ag

Zn limit:

2800 mg/kg

Equivalent Ag:

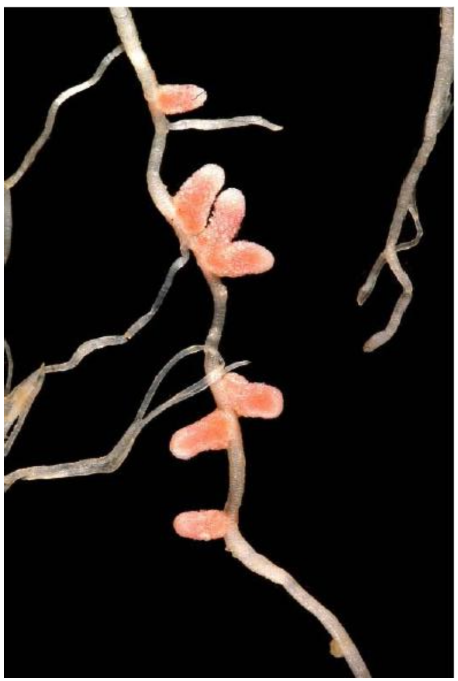
250 mg/kg

US EPA Guideline (CFR 40 part 503)

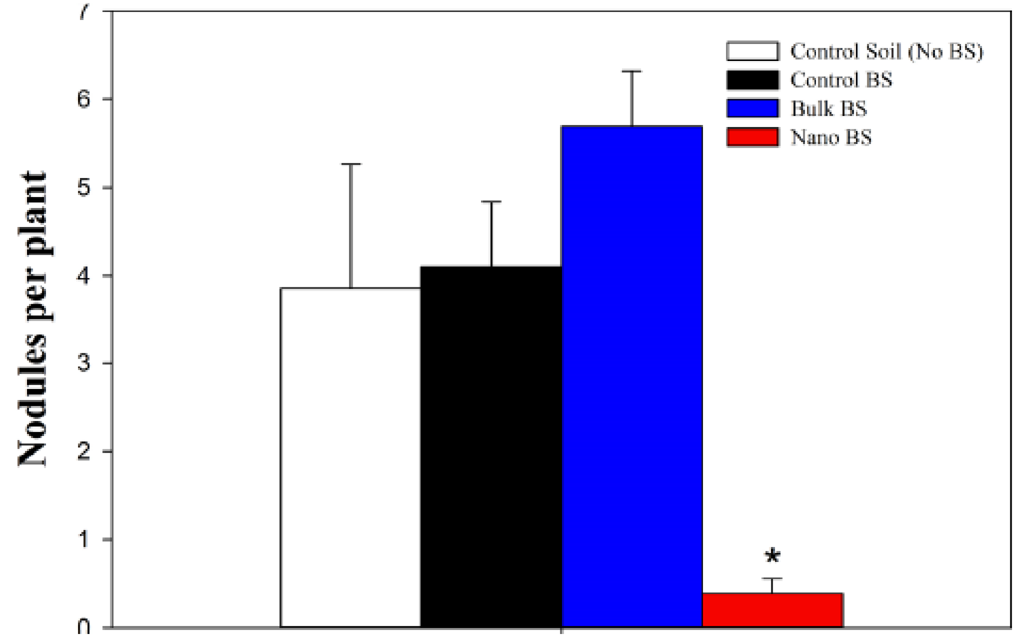
Control SS | Ionic SS | NP SS

- Mixed with soil to Max. Zn loading from sewage sludges in US soils = **1400 mg Zn/kg**
- **Aged 6months in outdoor mesocosms**

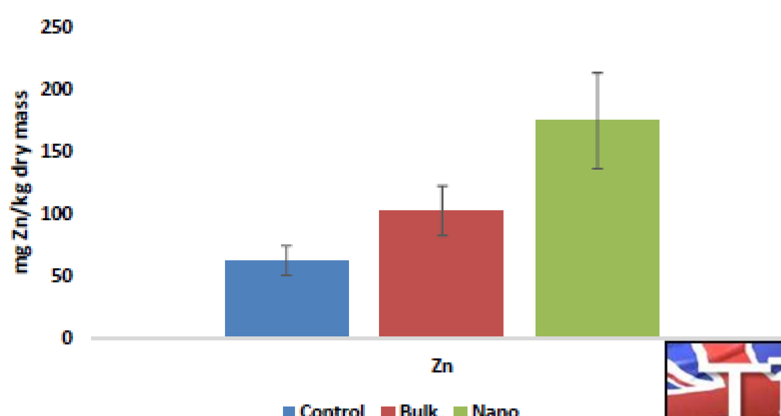
Effects on Clover nodulation



Medicago Nodulation (Legume N-acquisition)



45% Aged Biosolids

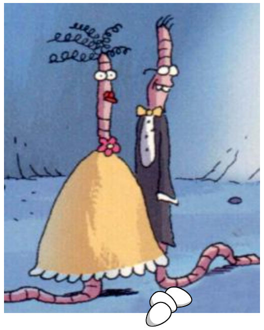


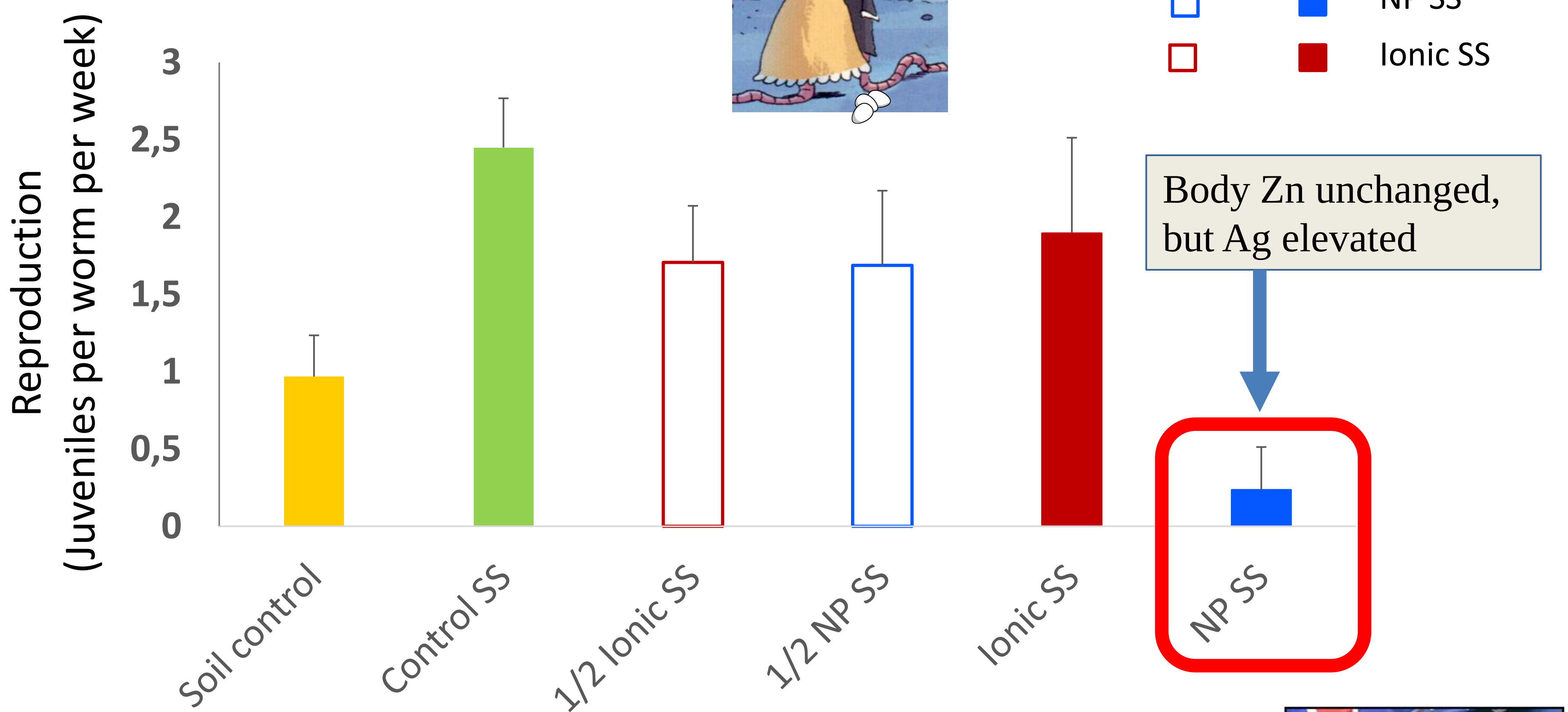
Judy, J. et. al. *Environ. Sci. Technol.*, **2015**, *49* (14), pp 8751–8758

Effects on earthworm reproduction

6-month aged SS

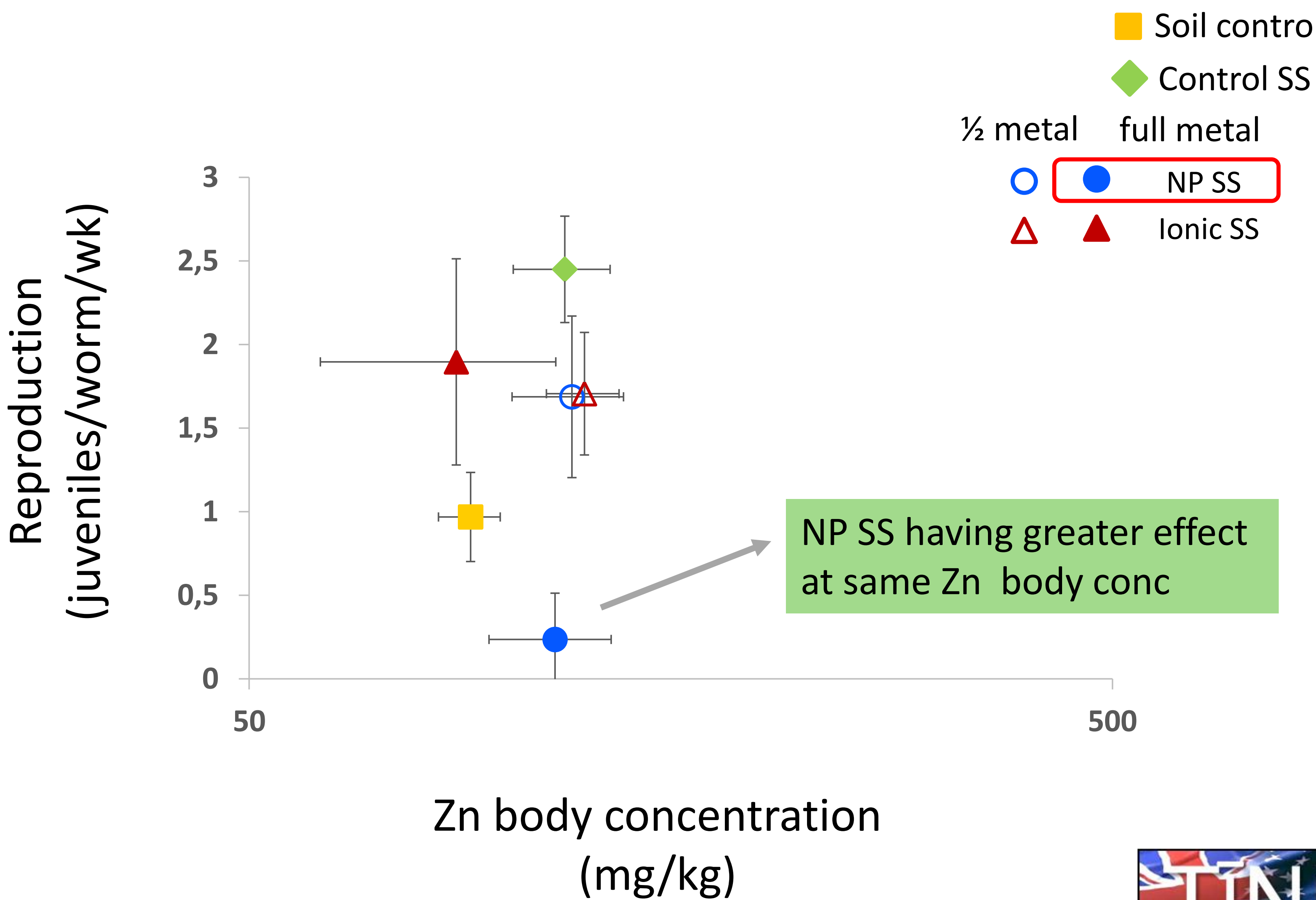
10 years of yearly SS application





Lahive, L. et. al. *Environ. Sci.: Nano,* ***2017****,4, 78-88*

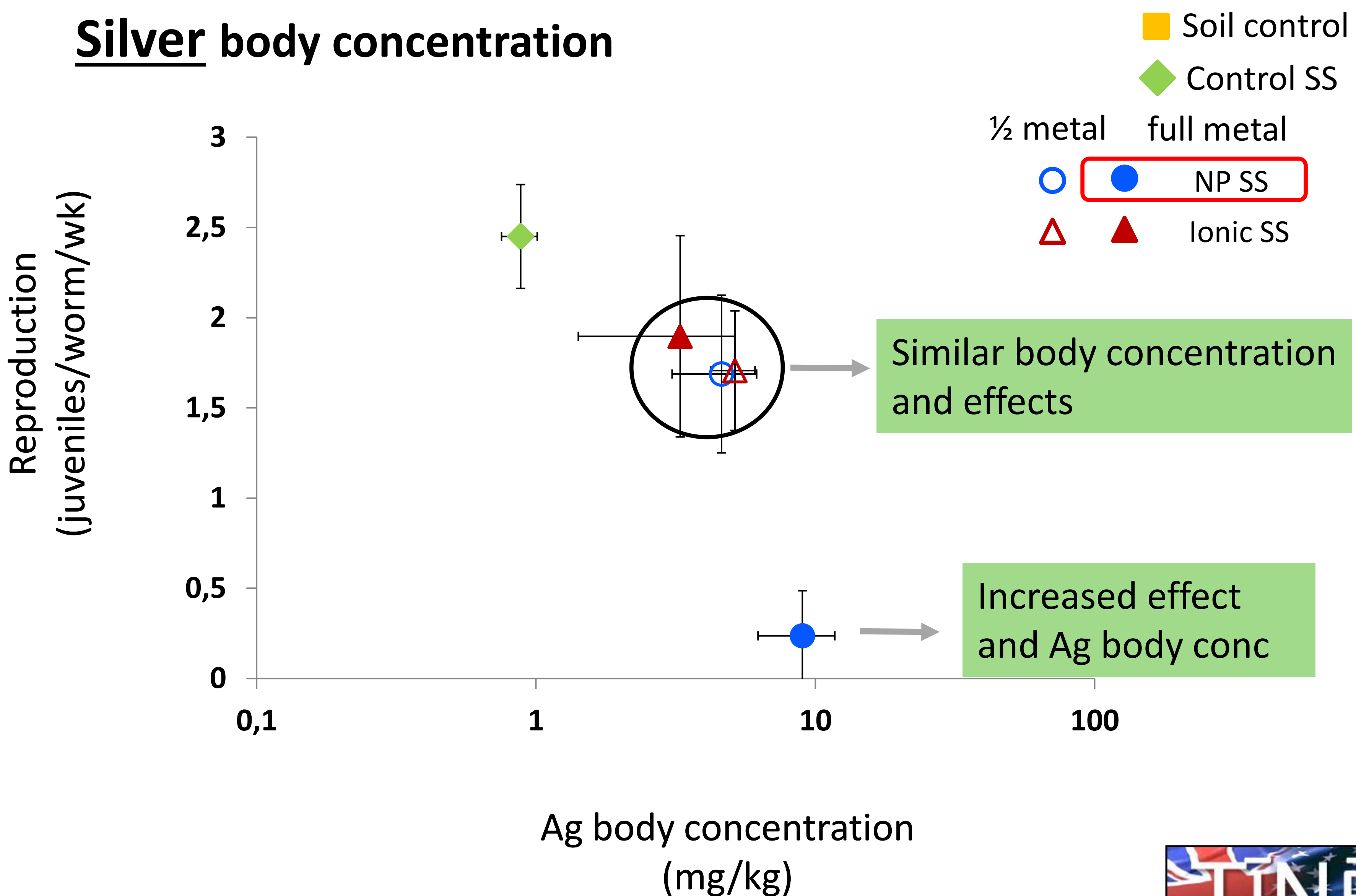
Reproduction + Earthworm body concentration



Lahive, L. et. al. *Environ. Sci.: Nano*, ***2017***,*4*, *78-88*

Reproduction + Earthworm body concentration

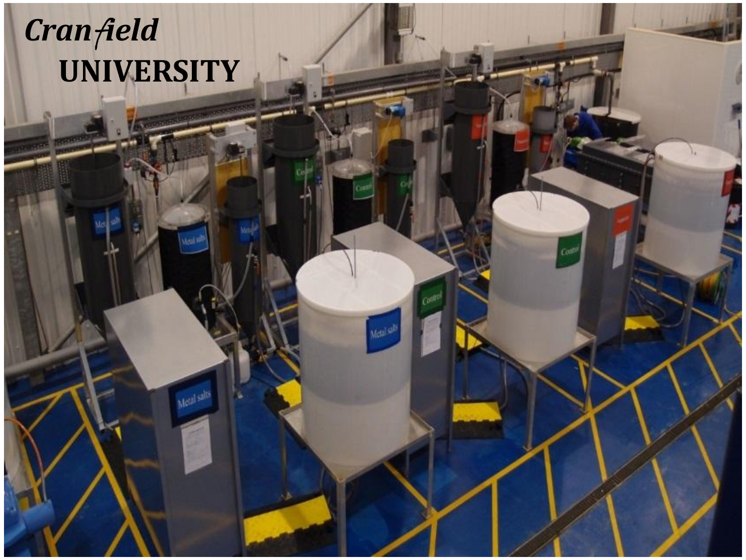
<u>Silver</u> body concentration

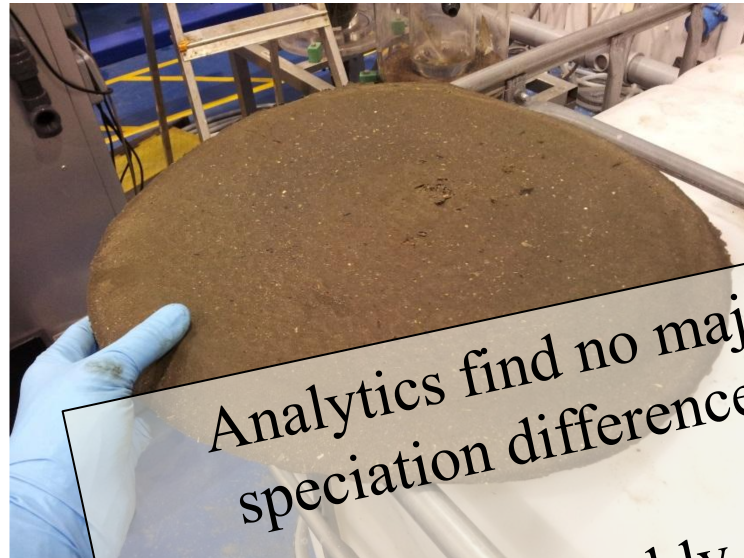


Lahive, L. et. al. *Environ. Sci.: Nano*, ***2017***,*4*, *78-88*

Real world "Aged" sewage sludge NPs trials

Question: What is different when metals arrive as NP vs. ions?

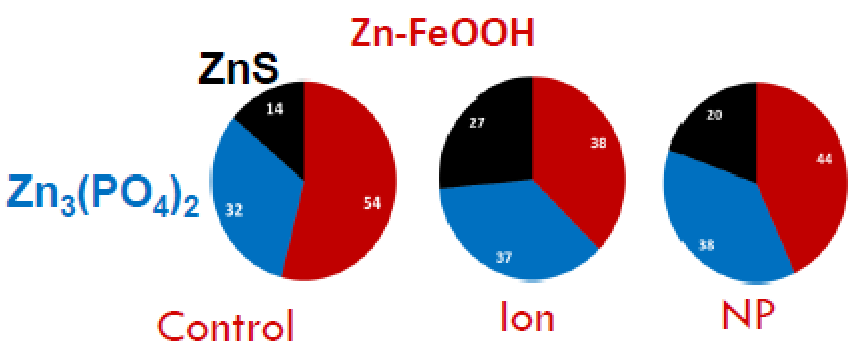


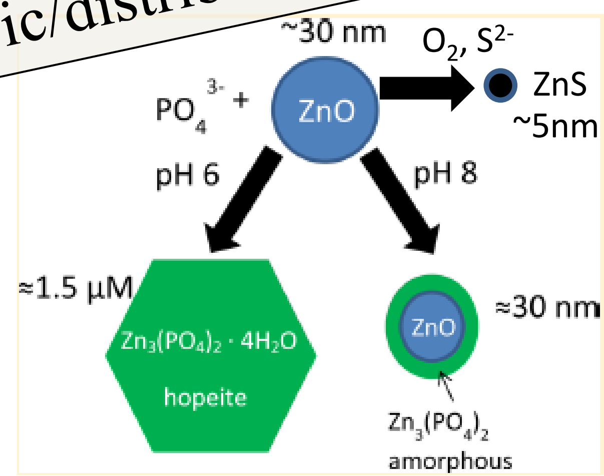


Analytics find no major speciation differences.

Differences probably due to geometric/distribution changes?

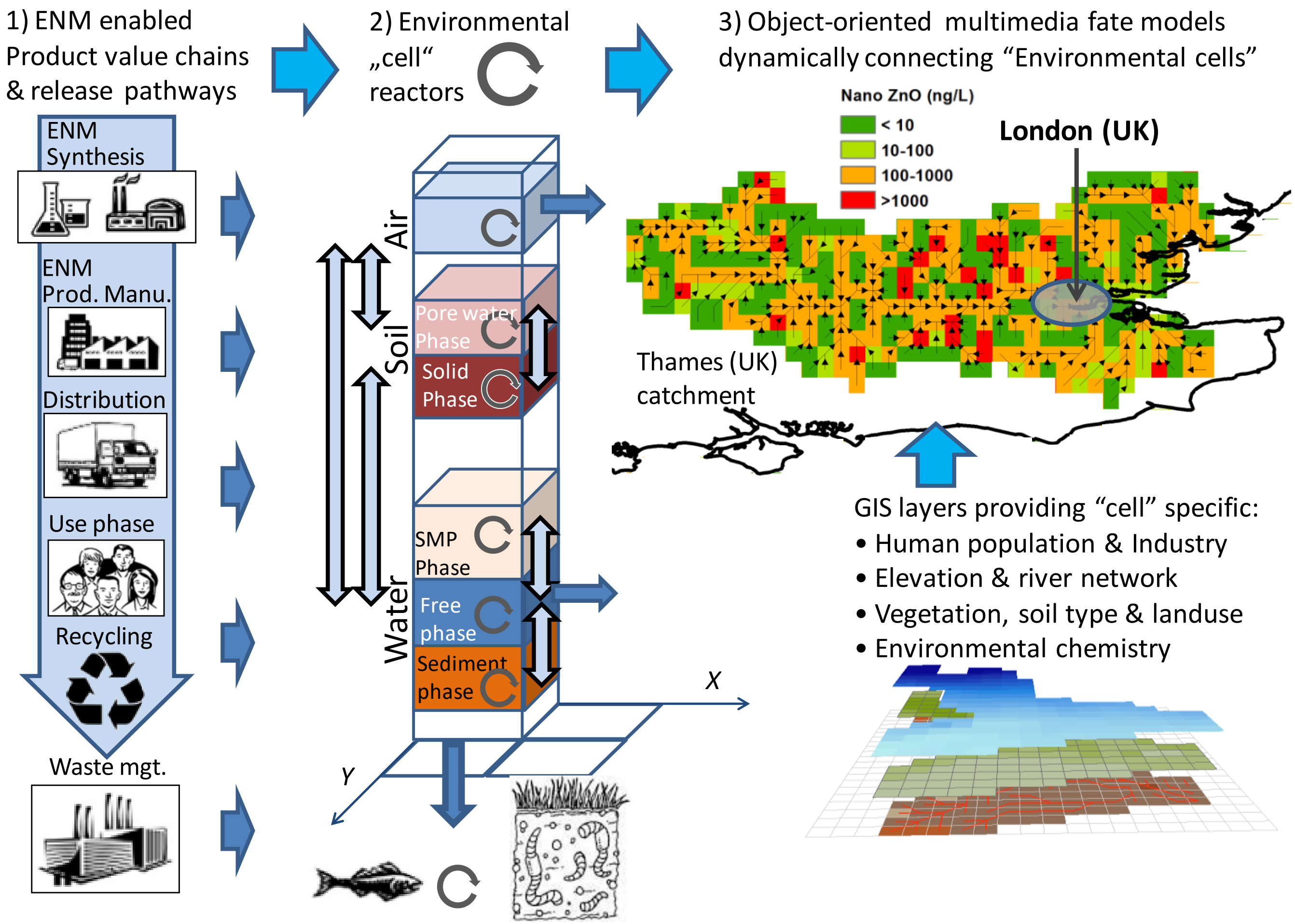
- **Three sewage sludge streams:** Control, Ionic and NP
- No Zn Speciation difference and no ZnO left
- (Ag too low concentration for speciation)





Exposure - Nanomaterial fate in the environment:

Where, what and for how long?



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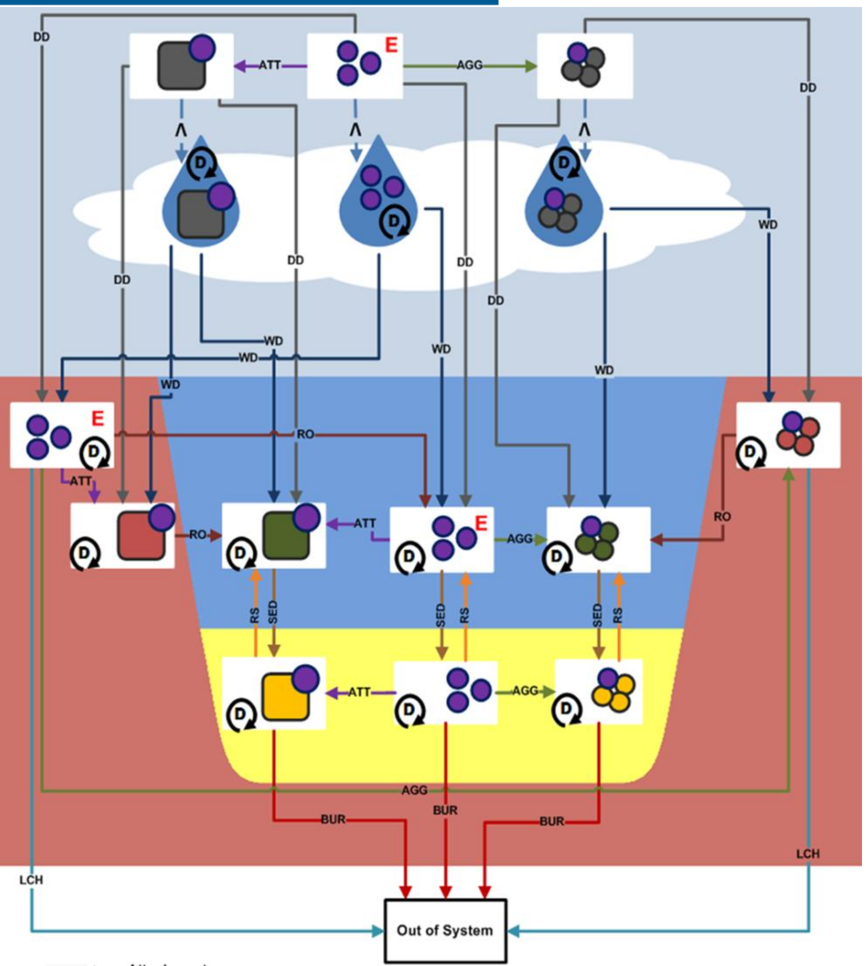
NanoFASE

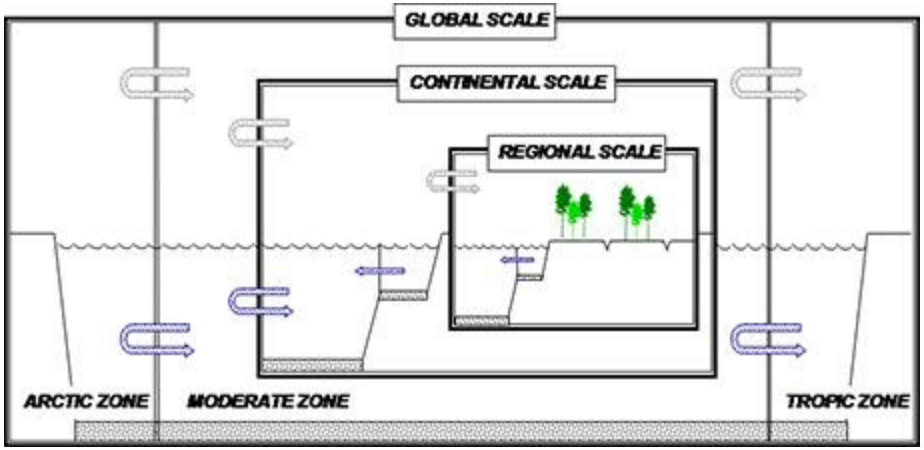
Exposure - Nanomaterial fate in the environment:

Where, what and for how long?

Incorporate modules into regulatory models e.g. EUSES Model

SimpleBox4.0-nano





Overall conclusions

- **Pristine nanoparticle info is meaningless – unless the patterns found are use in context of exposure relevant forms!**

- Fate determines if and where there may be possible Nano Exposures
  $\Rightarrow$ Including how potent the exposure relevant form is
  $\Rightarrow$ Long-term fate and hazard data is needed.

- Begin with good empirical relationships between properties, reactions (e.g. coating degradation, sulphurdation and dissolution) and consequent uptake/effects –
  - Identify key "undesirable" NM behaviours
  - Link these to properties to avoid or ensure are degradable

- Tune the properties of NM products so function is maintained in use phase, while ensuring fast environment degradation of ENMs or their Nano function.

Thank you

Acknowledgements: **UK (NERC)/US (EPA)** TINE

NanOFATE
www.NanoFATE.eu (EU CP-FP7 247739)

GUIDEnano
www.guideNANO.eu (EU CP-FP7 604387)

Centre for Ecology & Hydrology
NATURAL ENVIRONMENT RESEARCH COUNCIL

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