Probabilistic modelling of prospective environmental concentrations of gold nanoparticles from medical applications

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SUN-SNO-GUIDENANO Sustainable Nanotechnology Conference
9-11 March 2015, Venice

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Overall structure

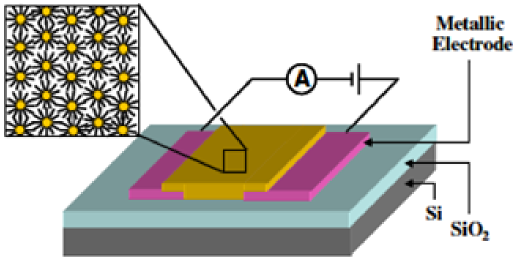
- Motivations
- Objectives
- Methodological approach
- Limitations
- Results
- Conclusions

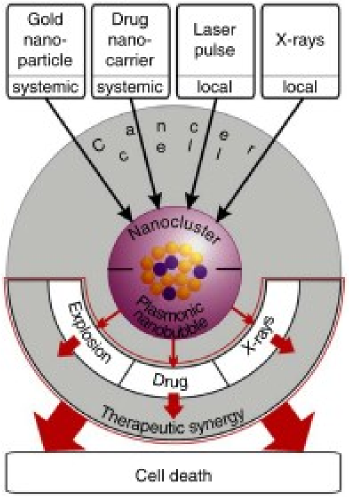
MOTIVATION

Motivation

- Increase in research with regard to gold nanoparticles (nano-Au) in the healthcare field due to
  - Unique properties at nanoscale
  - Ease of surface functionalisation
  - Easy synthesis
  - Relative biocompatibility

Tisch,U. and Haick, H. (2010) Reviews in Chemical Engineering. Volume 26, Pages 171–179





Lukianova-Hleb, E.Y., et al. (2014) Nature Medicine 20, 778–784

Motivation

- Some medical applications already in the market and some show high potential for translation for widespread diseases like cancer, diabetes
- No studies yet published to predict environmental concentrations of nano-Au from medical applications
- Increase in research with regard to nano-Au in other areas – catalysts for air and water purification, sensors for detecting harmful gases
- Nano-Au has been shown to be toxic to organisms in the environment

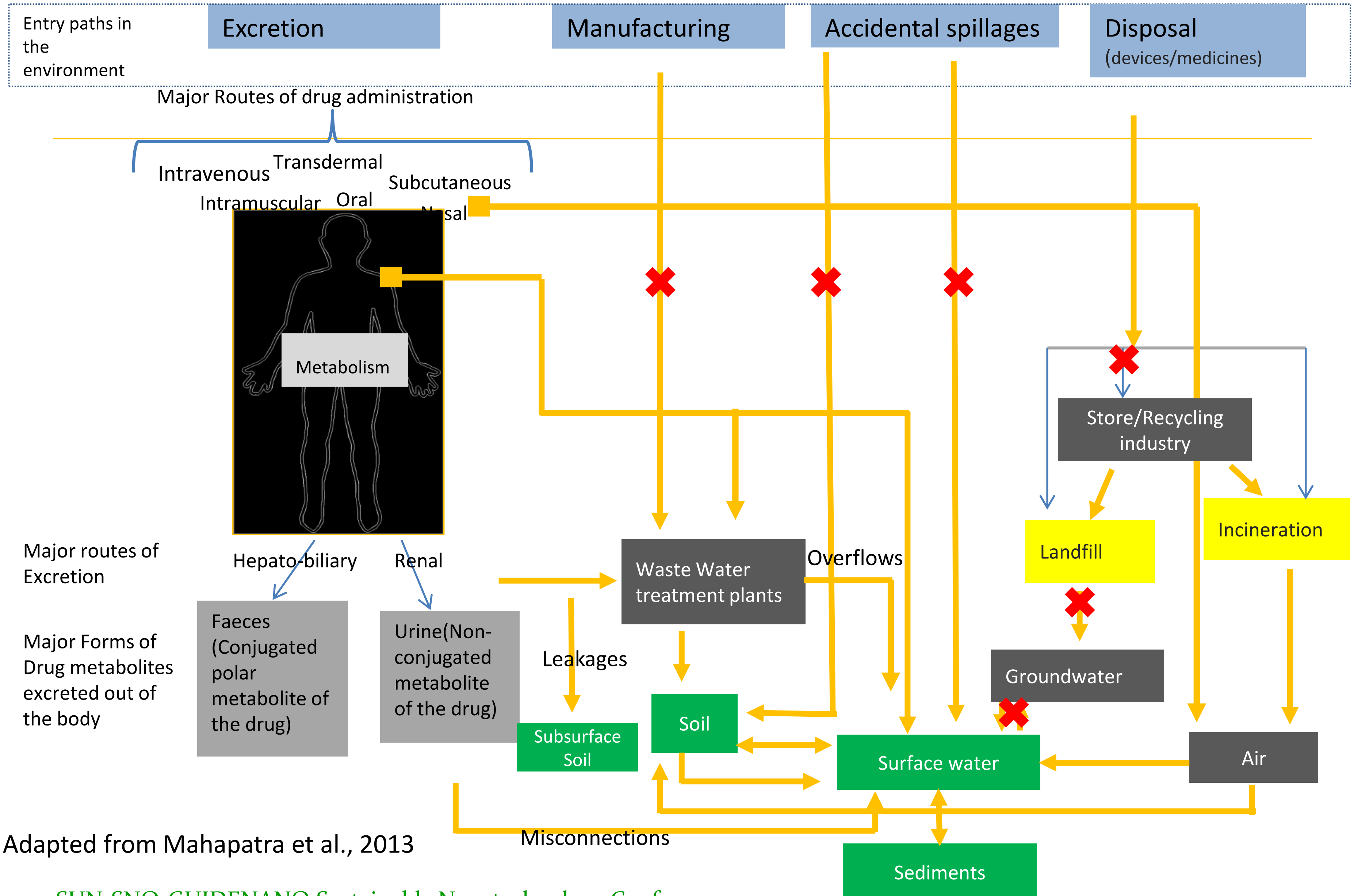
Objectives

- Estimate the yearly maximal possible consumption of nano-Au from current and prospective medical applications for the UK and US
- Model the concentrations in the transient compartments of Sewage Treatment Plants, Waste Incineration Plants and the environment compartments
- Perform environmental risk assessment

METHODOLOGICAL APPROACH

Methodological Approach

- **Model Type**: Probabilistic mass flow model developed by Gottschalk et al., 2009
- **Geographical regions**: UK and US
- **Consumption data**: 100% market penetration and all patients, irrespective of socio-economic status etc., have access
- **Risk assessment**: Probabilistic species sensitivity distribution (pSSDs) vs. Predicted environment concentration (PEC) method adopted from Gottschalk and Nowack, 2013



Adapted from Mahapatra et al., 2013

LIMITATIONS

Limitations: Model

- Static
  - Dynamic aspects not considered (time dependant particle release as well as kinetics)
  - Product use data of only one year

- Size, shape and surface chemistry cannot be considered: sphericity was assumed for all particles and the mass of nano-Au was calculated

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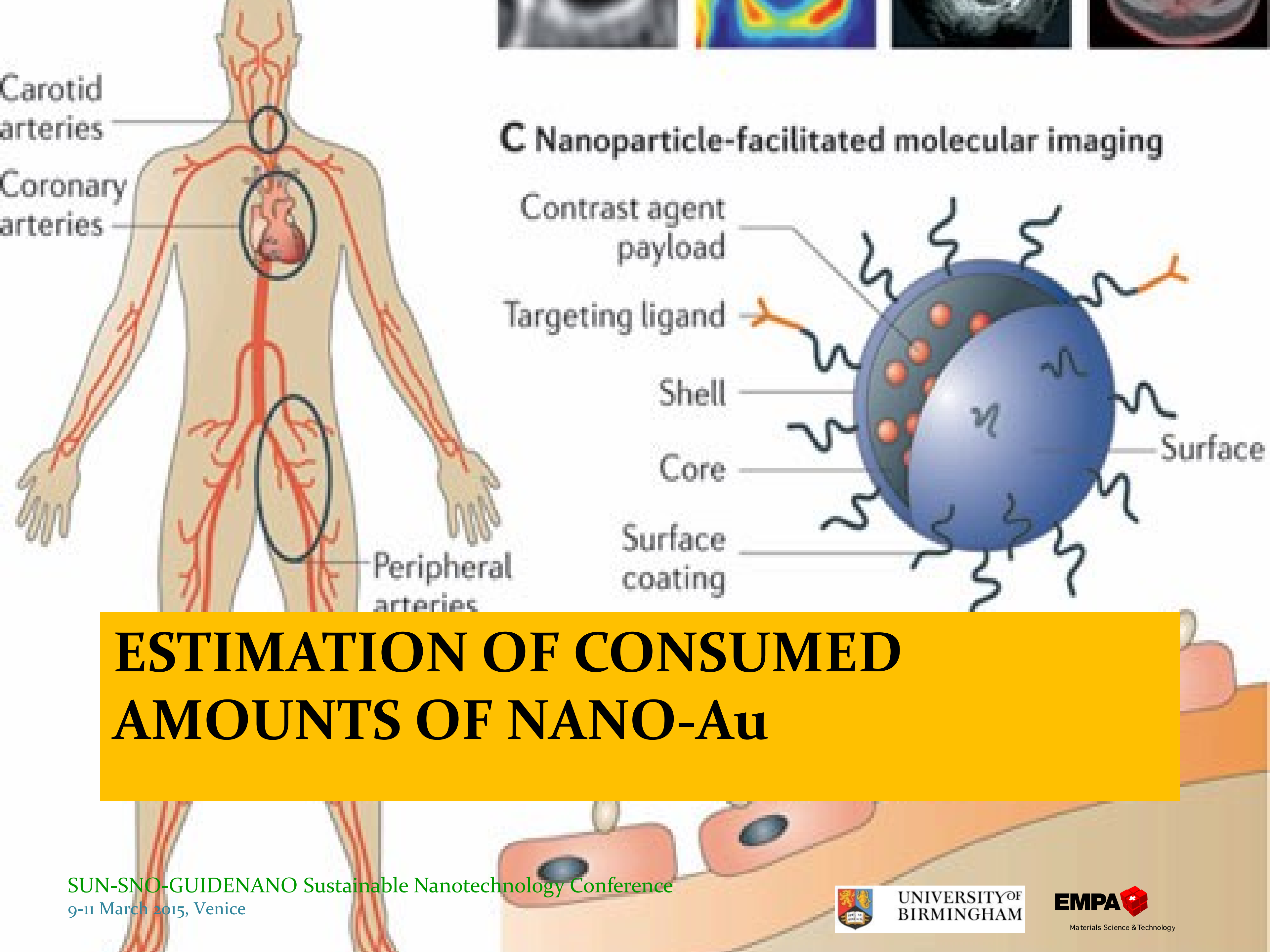
Limitations: Data

- Many extrapolations to estimate nano-Au amount in *in vitro* diagnostic devices
- Due to time lag in reporting and updating disease incidence and prevalence data in disease registries, not all data are for the same year
- No ADME (absorption, distribution, metabolism, excretion) studies in humans
- Very few studies on fate and behaviour of nano-Au in the environment
- No studies on transformation and fate of nano-Au in waste incineration plants
- Less toxicity data available with respect to soil organisms
- Limited chronic toxicity data for aquatic organisms

RESULTS

ESTIMATION OF CONSUMED AMOUNTS OF NANO-Au



Applications selected

- Pregnancy and ovulation test kits
- Test kits to diagnose HIV/AIDS
  - Home based
  - Lab based
- Removal of SA from nasal carriages to prevent nosocomial infection prevention
- Treatment of gum diseases
- Diagnosing septicaemia and respiratory virus
- Genetotyping diagnostic tests
- Diagnosis of different types of cancers and Chronic Kidney Disease via exhaled breath
- Treatment of cancers – thermal ablation
- Treatment of cancers – TNF delivery
- Diabetes management

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Method to arrive at nano-Au consumption estimates

Amount per device/application

✖

No. of application used per year

✖

Population

- Estimate the maximal possible nano-Au amount
  - mass of gold depending on particle size
  - amount required per test for *in vitro* diagnostic medical devices (IVD) or therapeutic dose
- Number of times a particular application likely to be used in a year or dose required for treatment
- Population estimate using disease incidence and prevalence data for the most recent year

Consumption of nano-Au

Application	UK	US	Unit	Waste compartment	Probability distribution function
Insulin delivery for diabetes management	128	842	kg	Sewage	Uniform
Treatment of Periodontitis	0.28 -107	1 - 365	kg	Sewage	Uniform
Removal of *Staphylococcus aureus* from the nasal passage of patients	0.03- 53	0.11 -165	kg	Sewage	Uniform
Diagnostic test kits for infectious diseases	74	356	g	Hazardous waste	Uniform
Home based *in vitro* HIV test kits	18	87	g	Municipal waste	Uniform
Pregnancy and ovulation test kits	3 -100	15-463	g	Municipal waste	Uniform

Consumption of nano-Au

Application	UK	US	Unit	Waste compartment	Probability distribution function
Solid tumors (colorectal, pancreas, breast)	0.07-(0.42)-1	0.31-(2)-5	kg	Sewage	Triangular
Solid tumors (colorectal, pancreas, breast) – Compassionate use	0.42	2	kg	Sewage	Uniform
Head & neck cancer and lung cancer	140 - 234	745 - 1241	kg	Sewage	Uniform
Head & neck cancer and lung cancer – compassionate use	105 - 175	468 -780	kg	Sewage	Uniform
Sensors for diagnosing cancer via breath	0.01 - 1589	0.03 - 4616	g	Hazardous waste	Uniform

CONCENTRATIONS IN ENVIRONMENT COMPARTMENTS AND RISK ASSESSMENT

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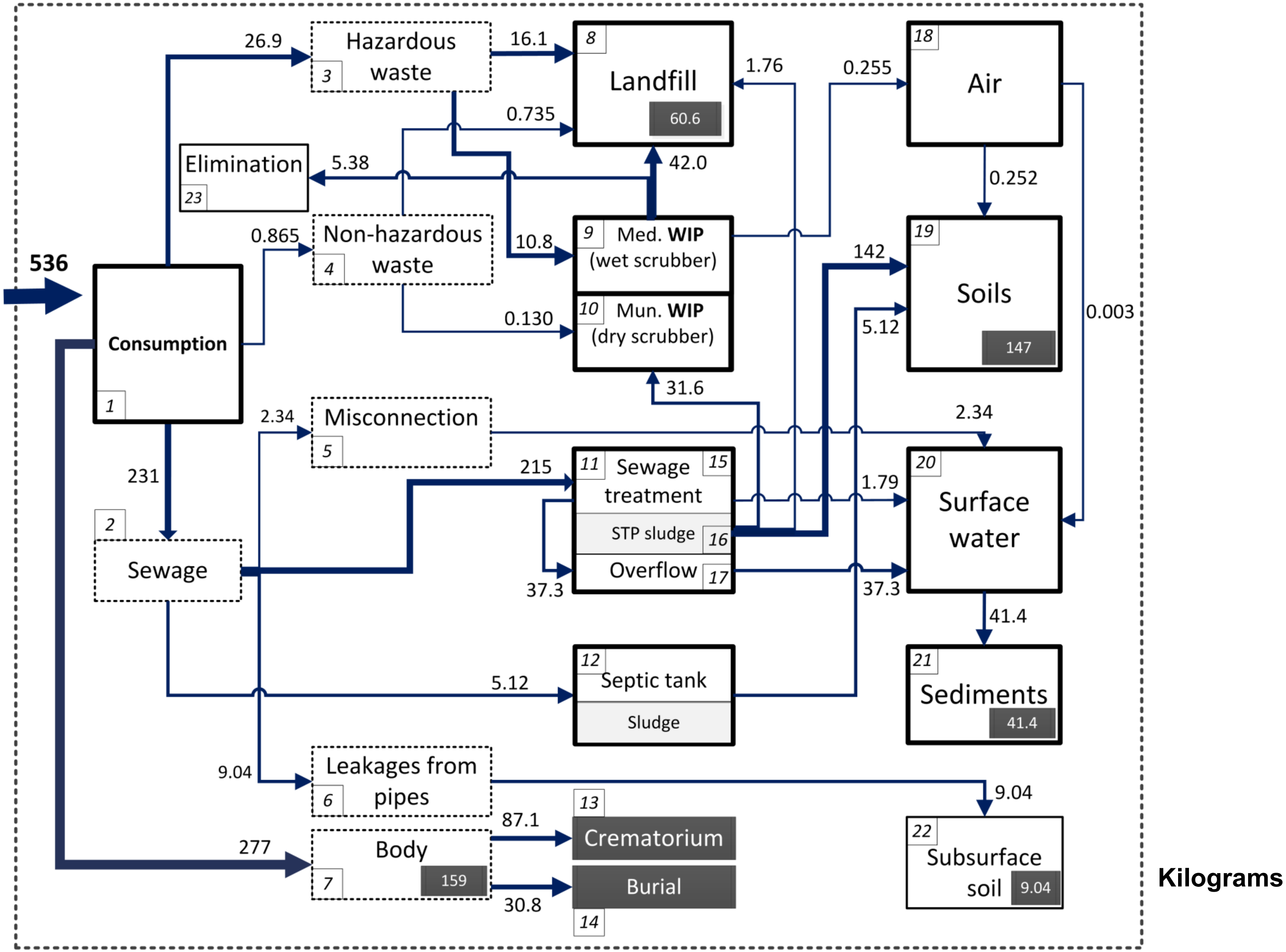
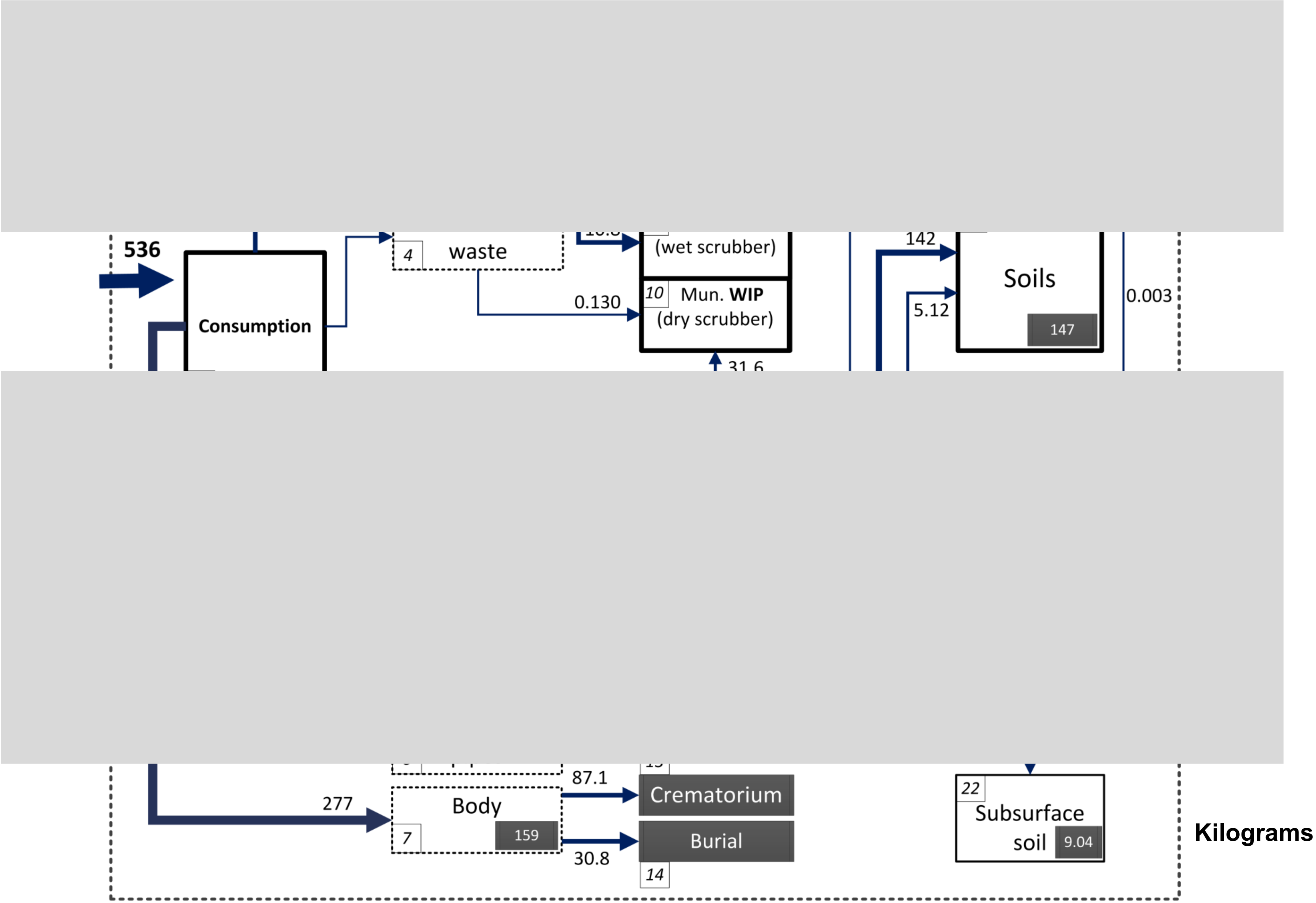
Flows of nano-Au in the environment (UK)



Flows of nano-Au in the environment (UK)



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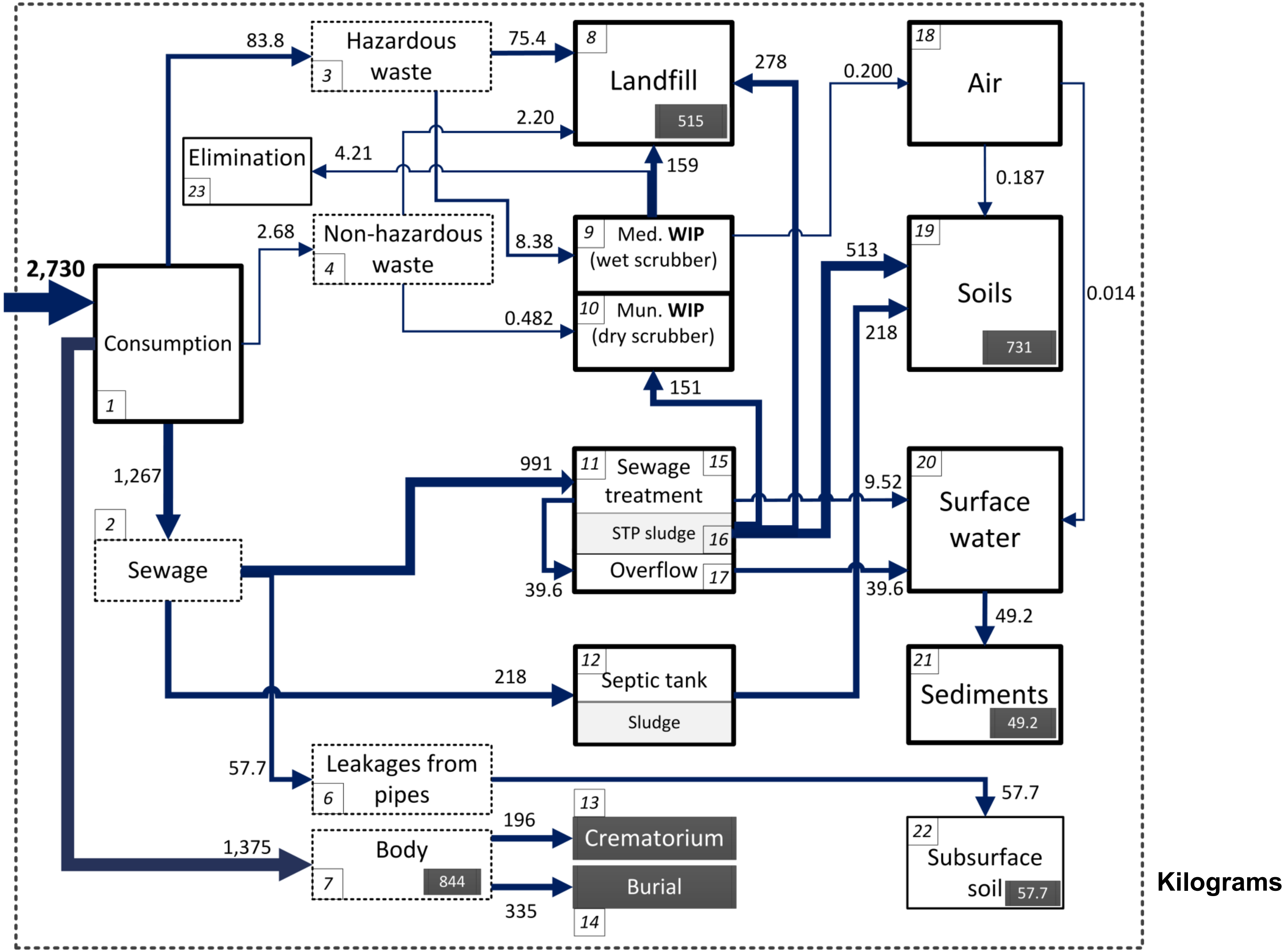
Flows of nano-Au in the environment (US)



Concentration of nano-Au in the technosphere

		Hazardous waste	Landfill	Medical Waste Incinerators		Municipal waste incinerators	
				Fly ash	Bottom ash	Fly ash	Bottom ash
		$\mu g\ kg^{-1}$	$\mu g\ kg^{-1}$	$\mu g\ kg^{-1}$	$\mu g\ kg^{-1}$	$\mu g\ kg^{-1}$	$\mu g\ kg^{-1}$
	Q15	23	3	36	27	39	28
UK	**Mode**	**34**	**4**	**28**	**23**	**51**	**28**
	Q85	130	5	518	393	67	52
	Q15	20	3	30	23	31	30
US	**Mode**	**16**	**4**	**27**	**20**	**38**	**30**
	Q85	110	5	431	330	48	38

Concentration in non-hazardous waste is less than $0.1 \mu g\ kg^{-1}$

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Concentration of nano-Au in the ecosphere

	Units	STP Effluent pg L^{-1}	Surface water pg L^{-1}	Sediment ng kg^{-1} y^{-1}	STP sludge µg kg^{-1}	Soil ng kg^{-1} y^{-1}
UK	Q15	217	214	132	94	227
	Mode	**359**	**268**	**165**	**126**	**301**
	Q85	665	725	447	154	368
US	Q15	95	3	3	119	121
	Mode	**168**	**4**	**5**	**145**	**147**
	Q85	271	7	8	171	174

Data rounded off to the nearest whole number

Environmental Risk Assessment

Exposure

Measure concentrations in the environment : field sampling and chemical analysis
Predict environmental concentrations via modelling

Probabilistic Mass Flow modelling (PEC)

Bioassay toxicity tests
Acute and chronic toxicity tests

Hazard

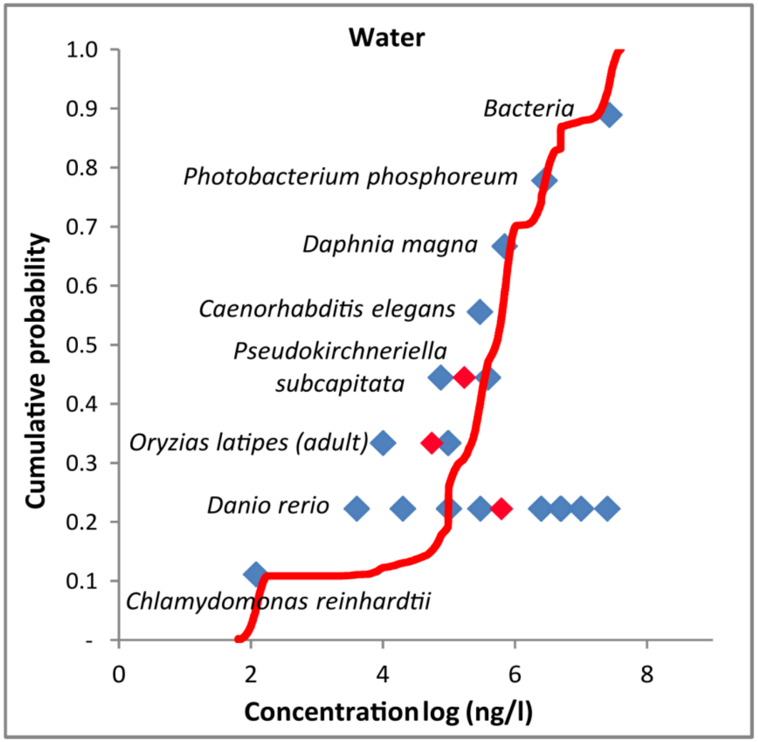
Probabilistic Species Sensitivity Distribution

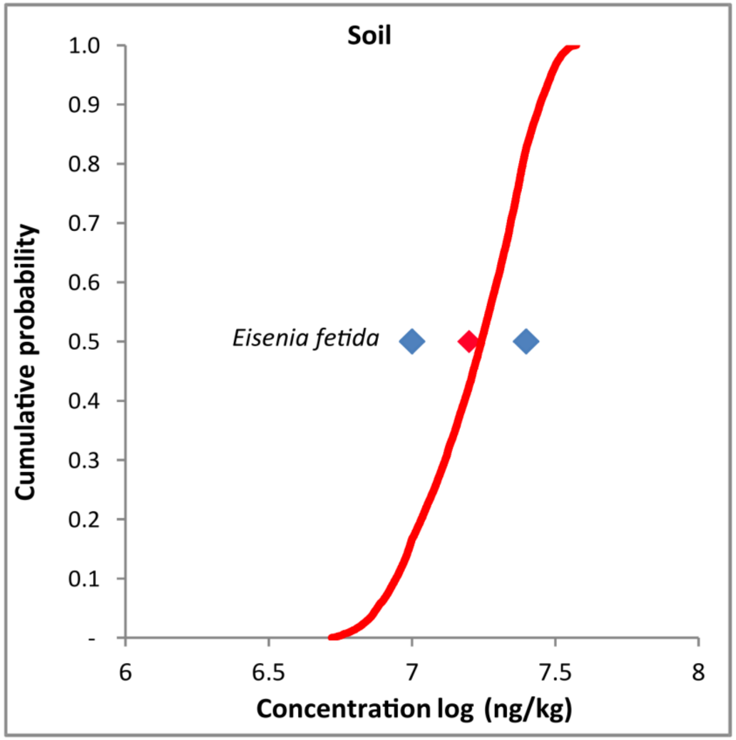
Risk

Details of data for creating the pSSD

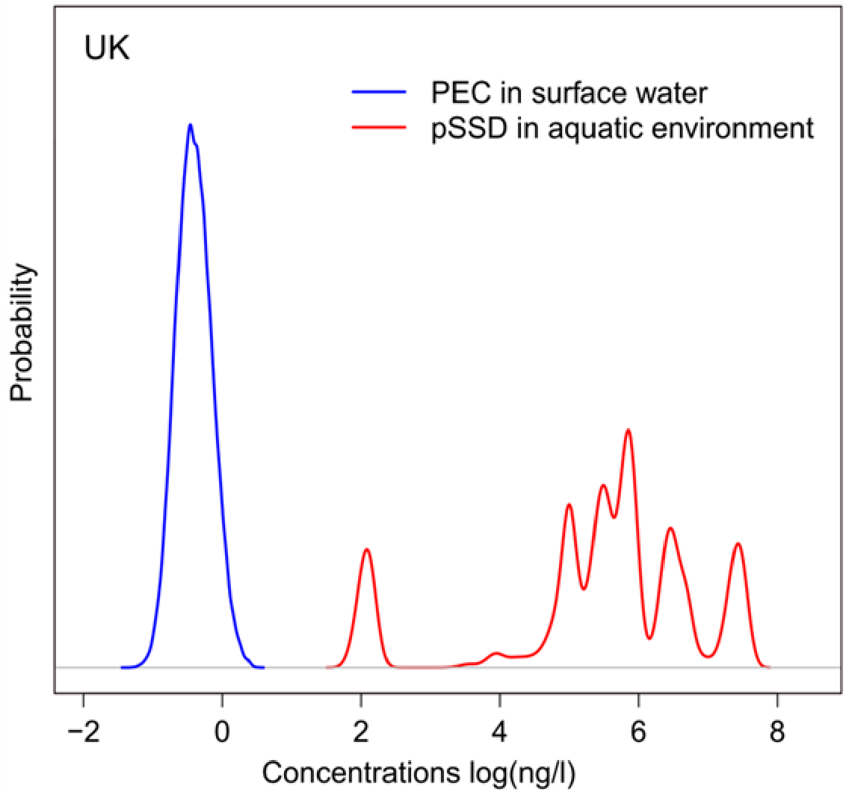
- 12 relevant studies
- 26 values
- Endpoints selected: mortality and malformation, growth inhibition, reproductive impairment and acute immobilisation
- Relevant assessment factors used to account for chronic toxicity and to arrive at No Observed Effect Concentration

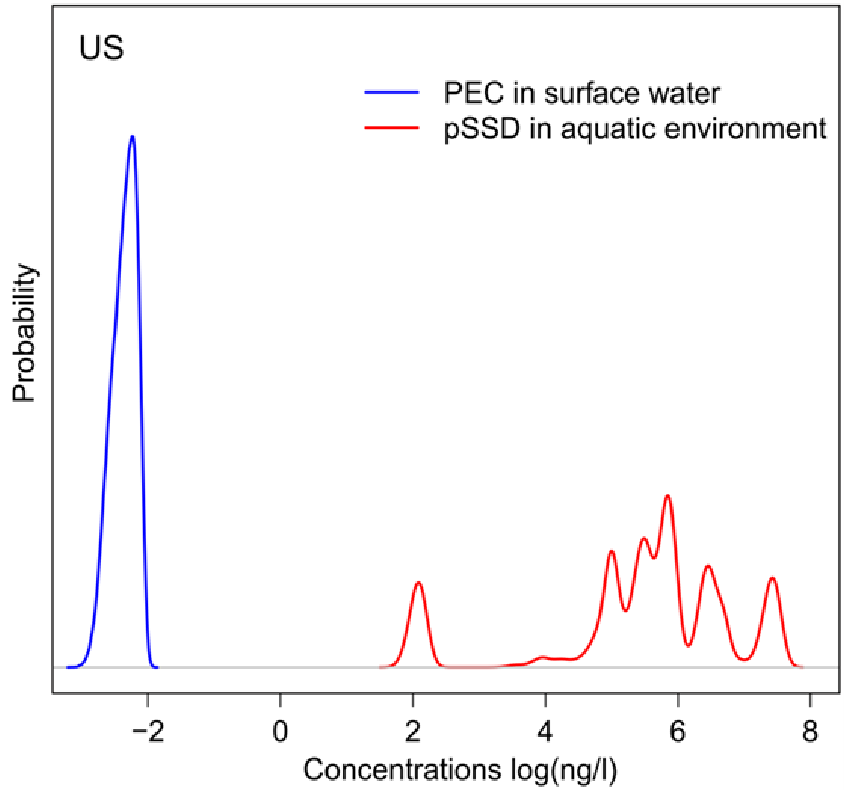
Probabilistic species sensitivity distribution (pSSD) for nano-Au in fresh water and soils



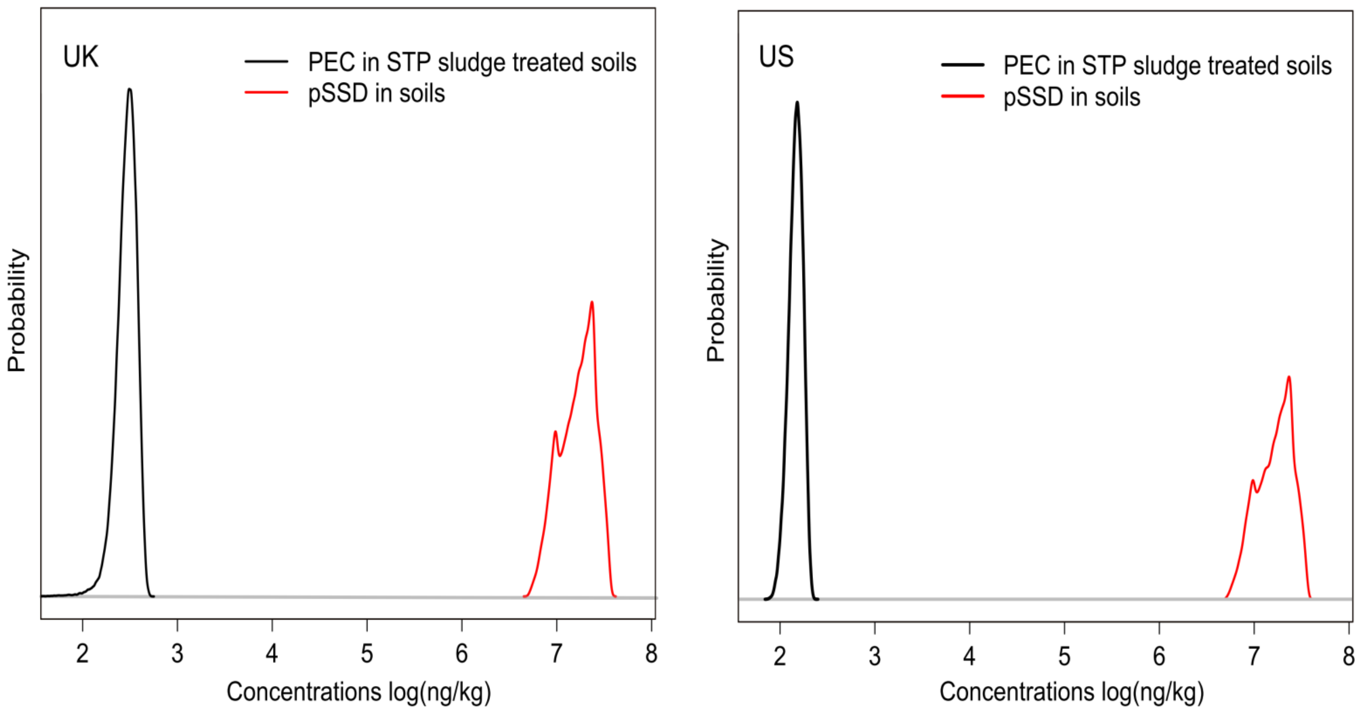


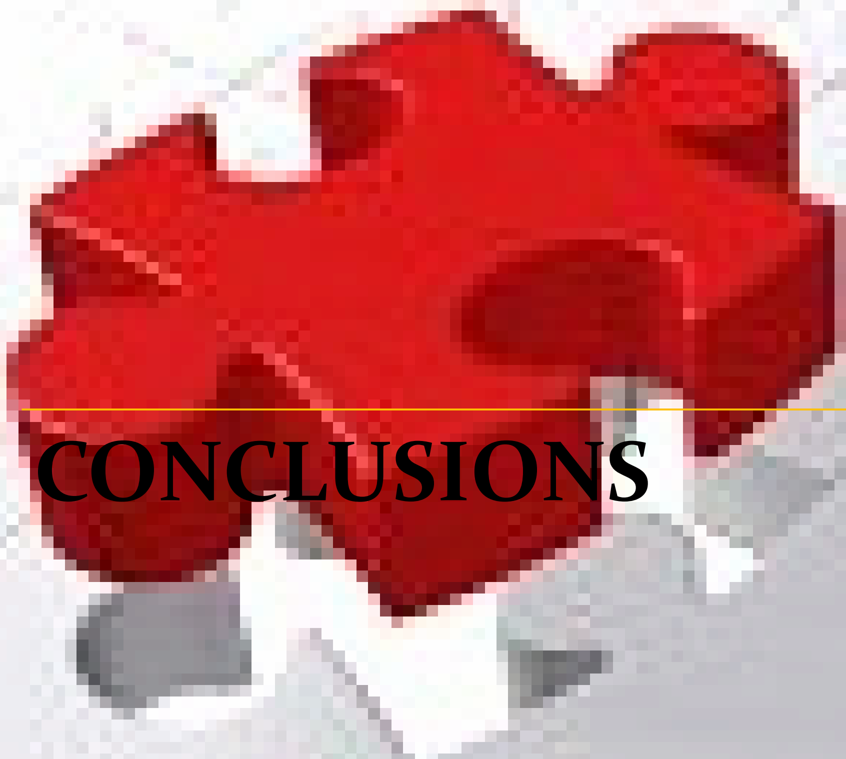
Probability distributions of the PECs and the pSSDs for nano-Au in surface water





Probability distributions of the PECs and the pSSDs for nano-Au in agricultural soils





CONCLUSIONS

Conclusions

- Total amount of nano-Au consumed in a year
  - UK: 540 kg
  - US: 2700 kg
- Significant release to the water compartment from therapeutics
- nano-Au concentration is surface water (0.0026 to 0.725 ng/L)is similar to background concentrations in freshwater (<1ng/L to 50 ng/L)
- nano-Au concentration in sludge (126 &145 µg/kg) is less than gold present in sludge (790 µg/kg - Sweden)
- No risk from nano-Au to aquatic and soil organisms, but more toxicity studies required

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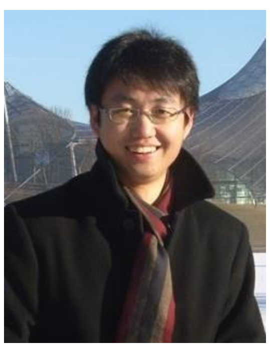

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Acknowledgement: NIHR Horizon Scanning Centre at University of Birmingham

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