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

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Overall structure

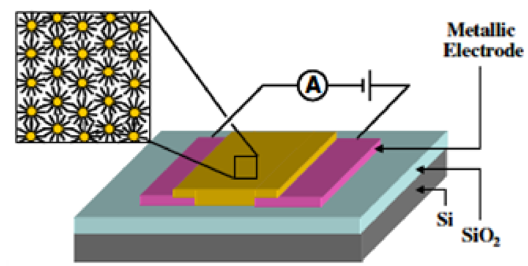
- Motivations
- Objectives
- Methodological approach
- Limitations
- Results
- Conclusions

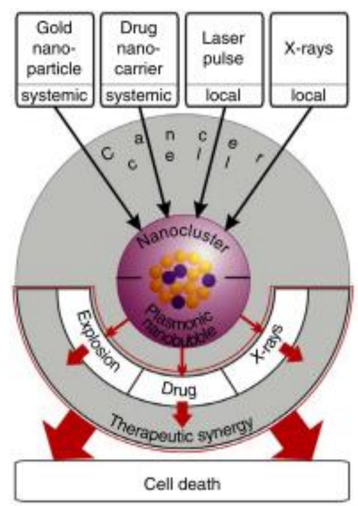
MOTIVATION

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

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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

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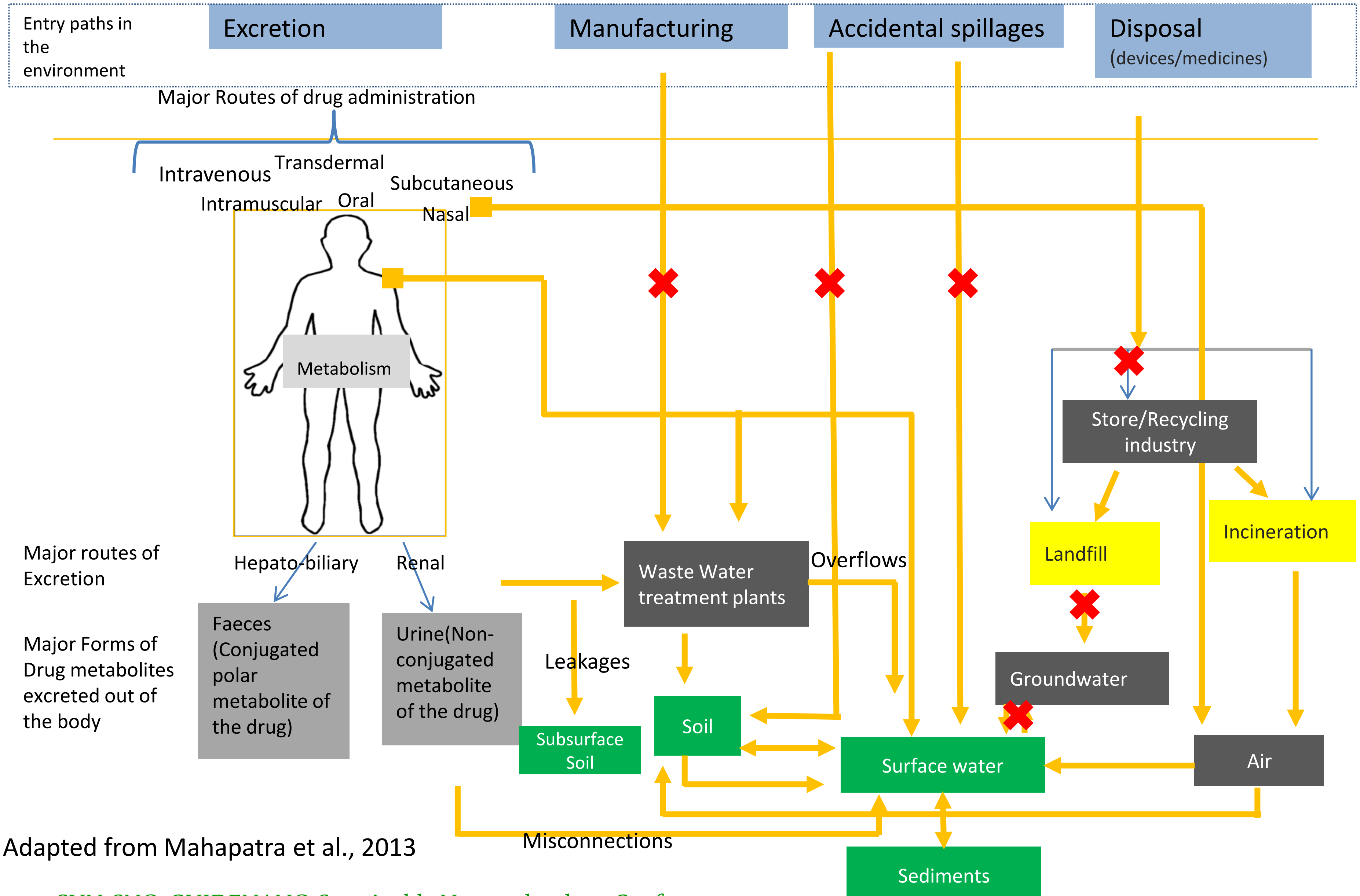
METHODOLOGICAL APPROACH

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

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

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CONCENTRATIONS IN ENVIRONMENT COMPARTMENTS AND RISK ASSESSMENT

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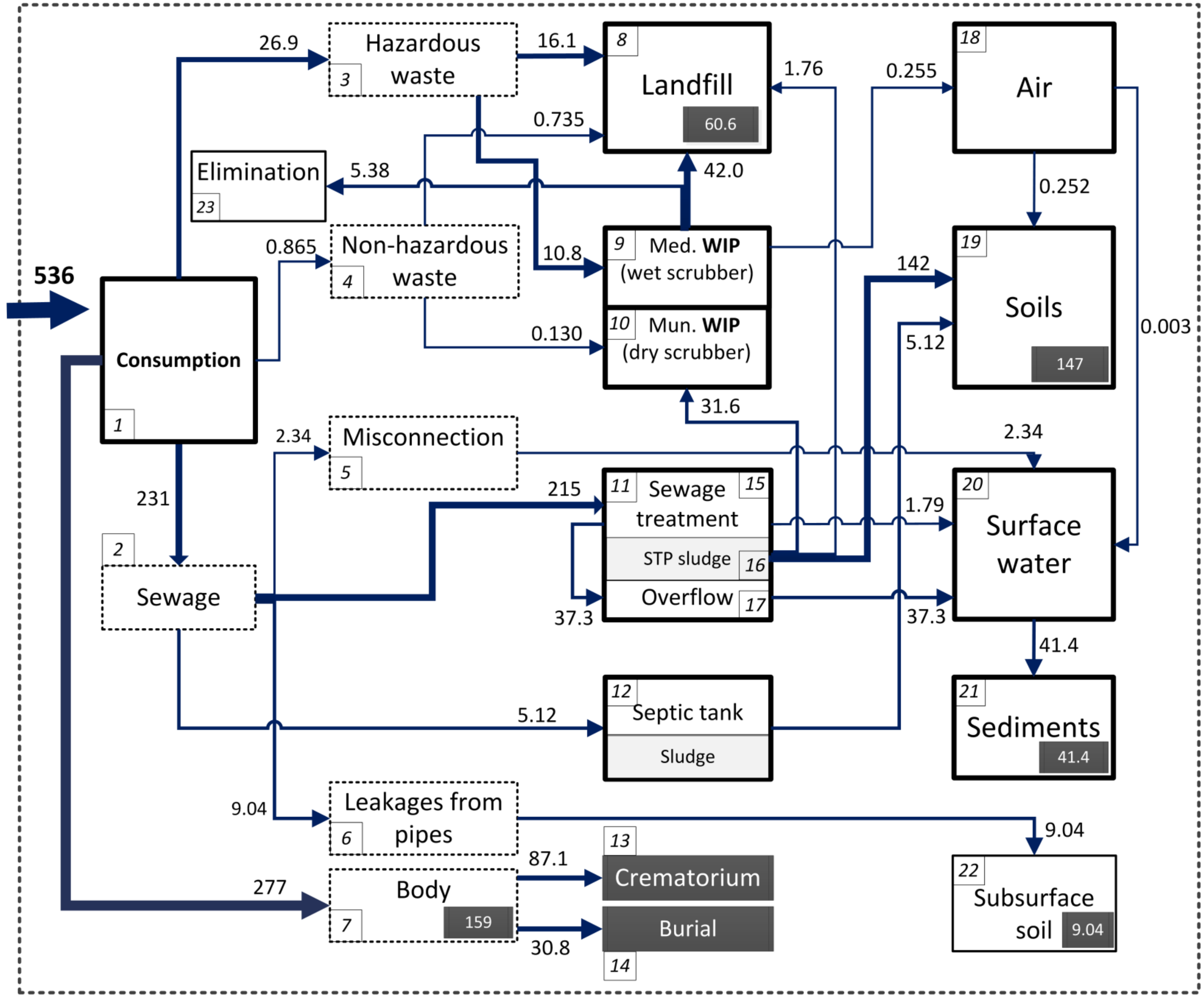
Flows of nano-Au in the environment (UK)



Kilograms

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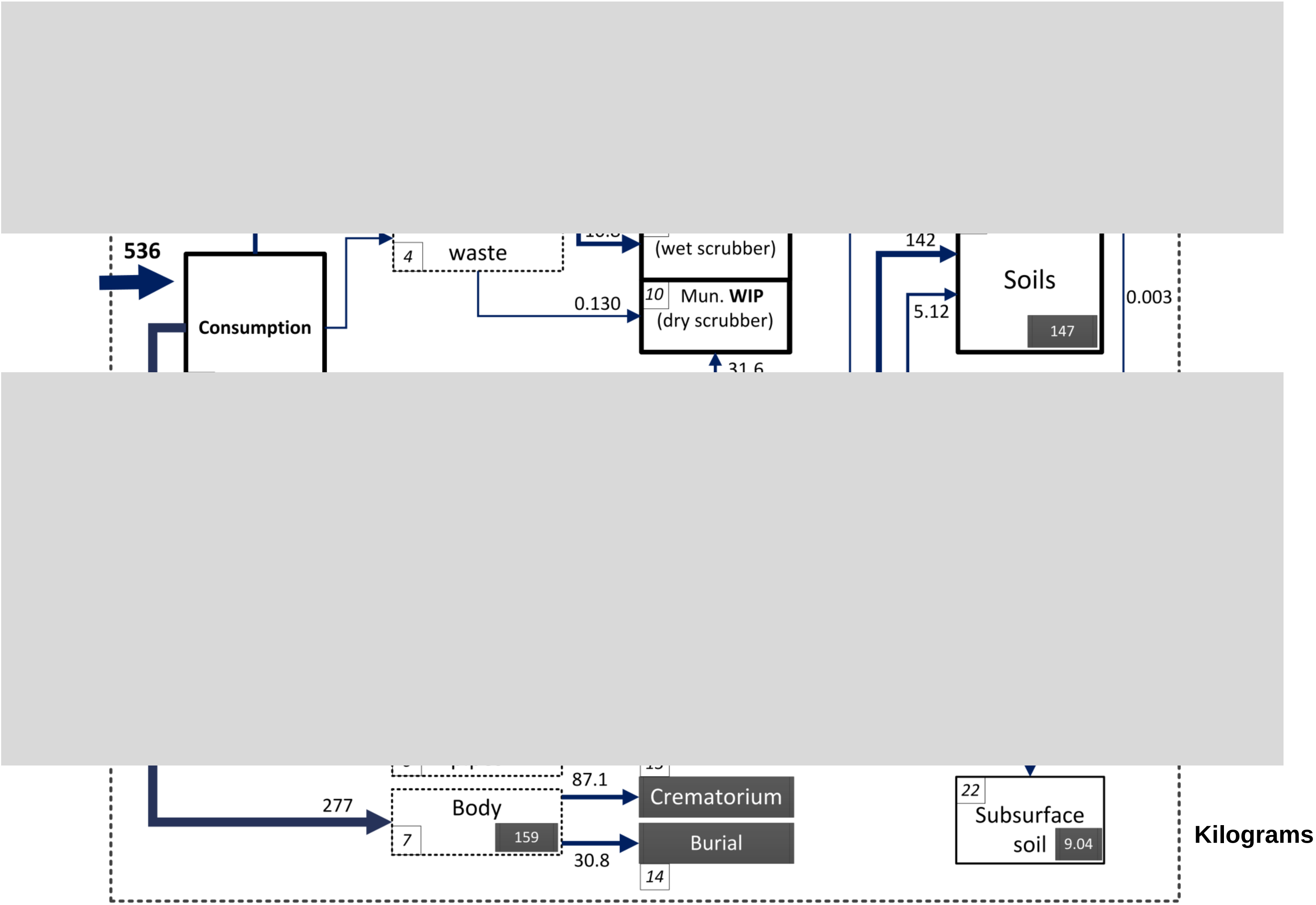
Flows of nano-Au in the environment (UK)



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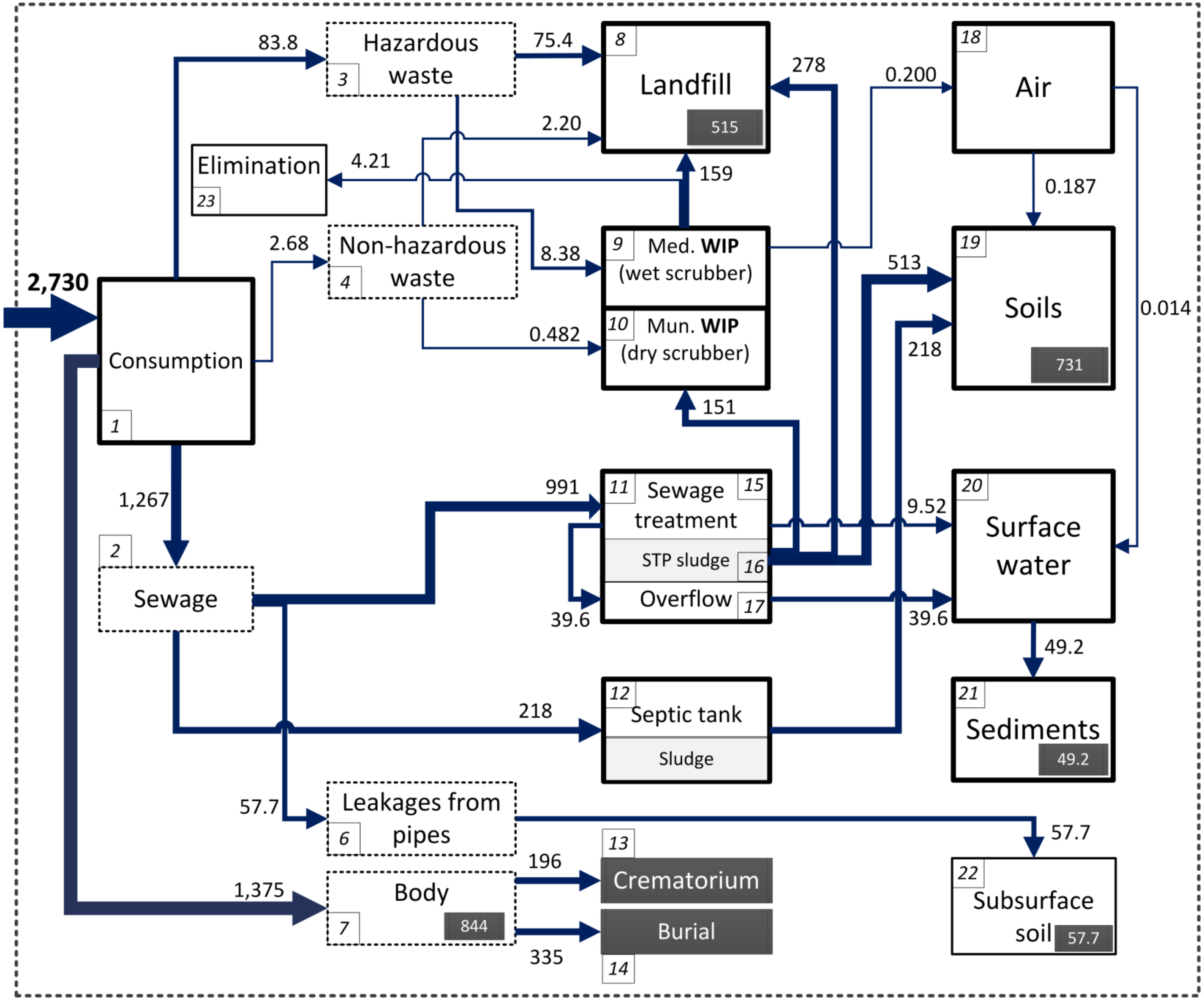
Flows of nano-Au in the environment (US)



Kilograms

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Concentration of nano-Au in the technosphere

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

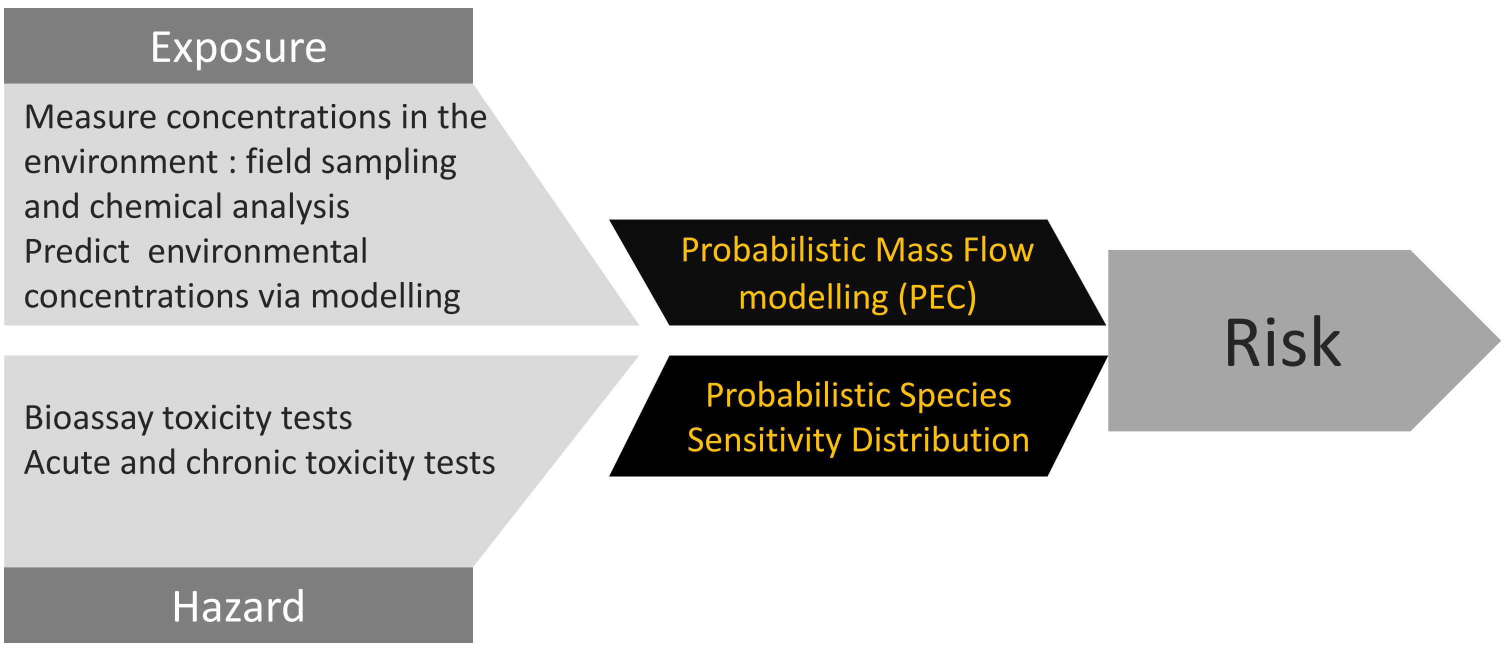
Concentration in non-hazardous waste is less than 0.1µg kg $^{-1}$

Concentration of nano-Au in the ecosphere

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

Data rounded off to the nearest whole number

Environmental Risk Assessment



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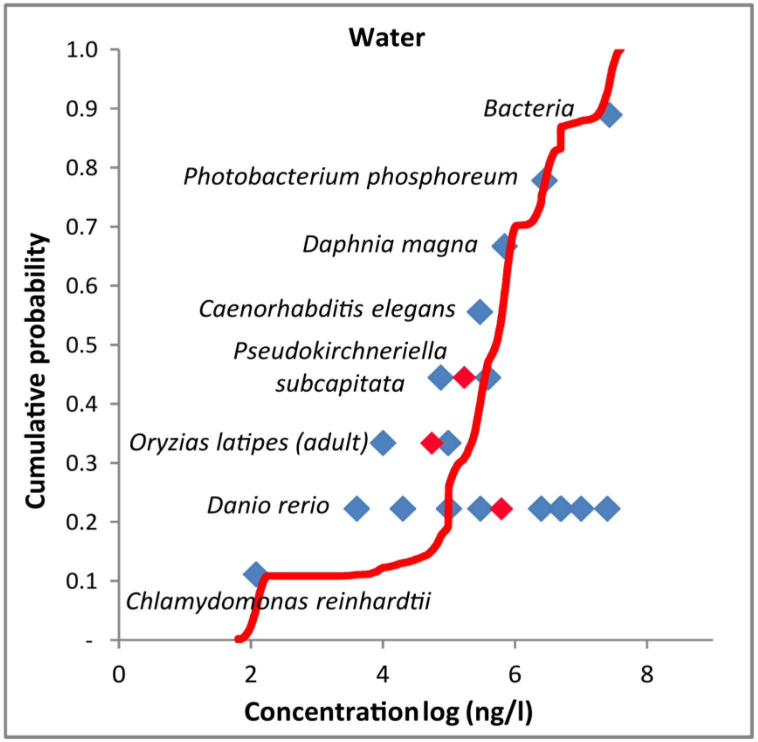
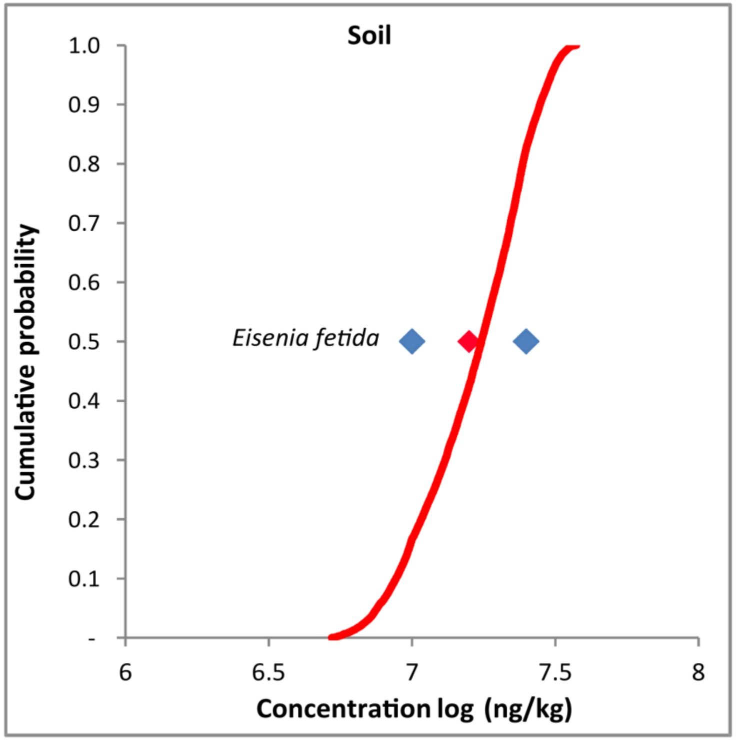
Details of data for creating the pSSD

- 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





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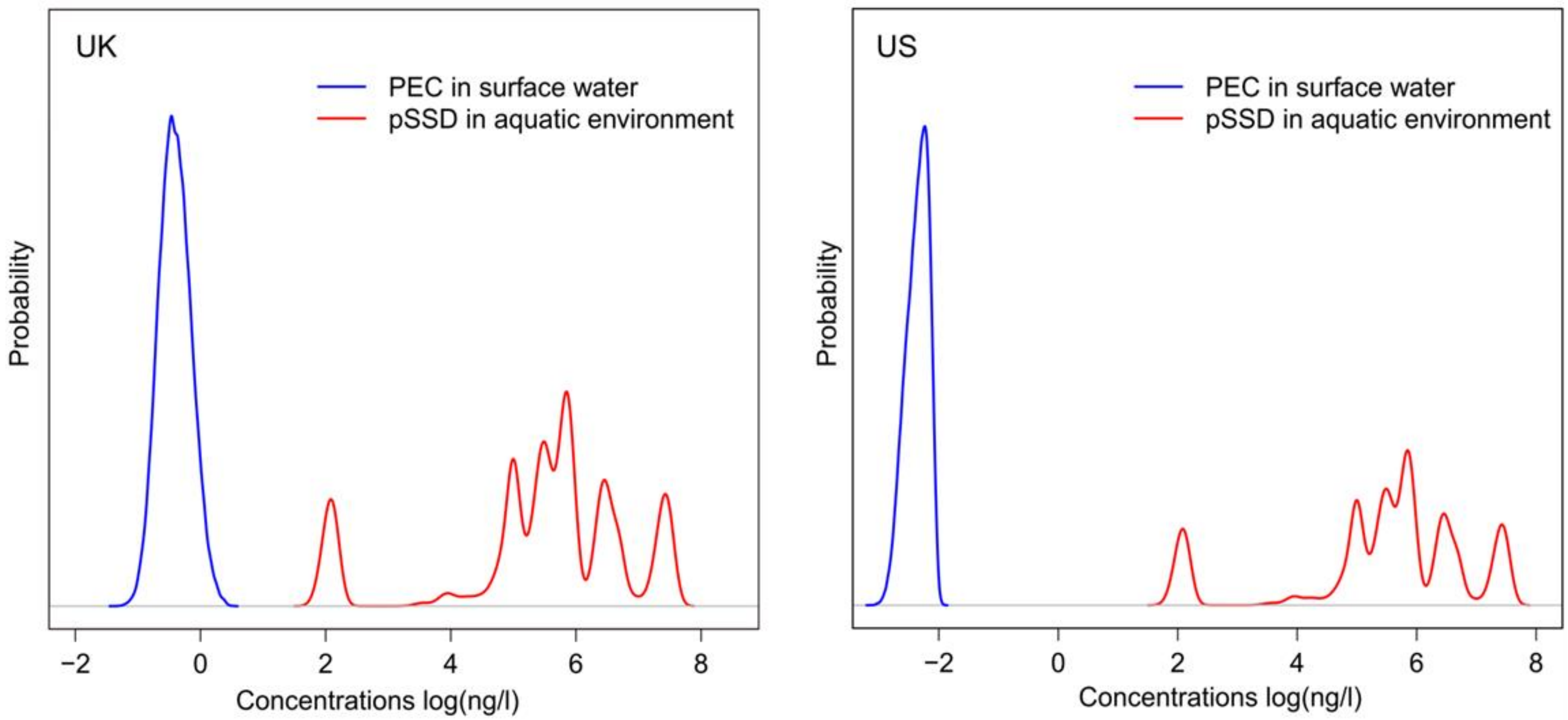
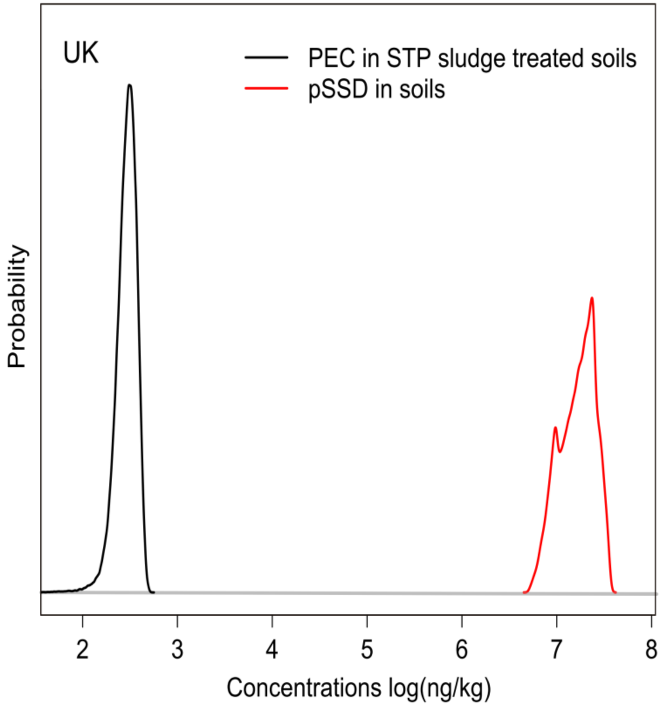
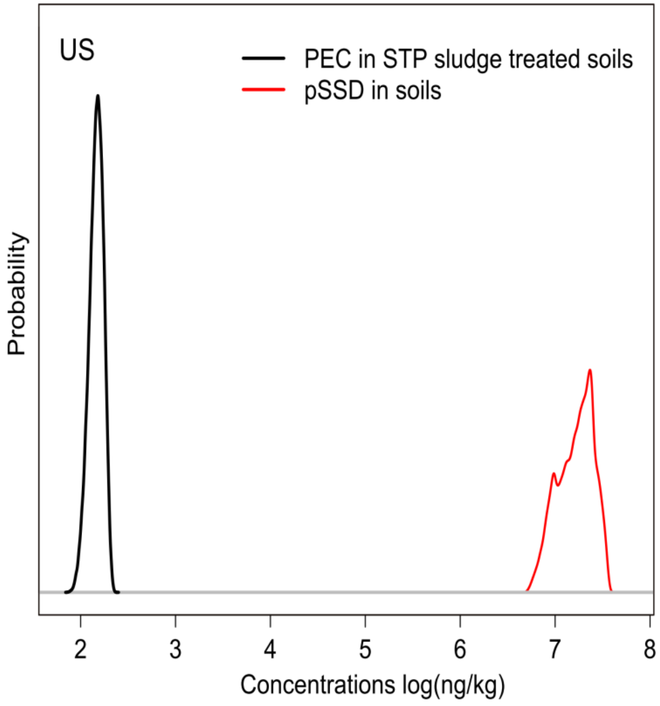
Probability distributions of the PECs and the pSSDs for nano-Au in surface water



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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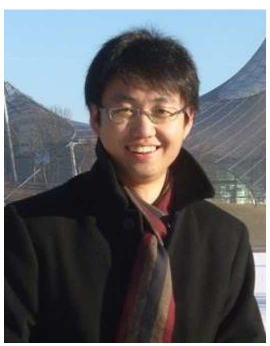
Tianyin Sun


Indrani Mahapatra

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