Toxicity assessment for Green Chemistry

Methods, insights, uncertainty and ignorance

2nd International Green and Sustainable Chemistry Meeting

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Universität Bremen

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Overview

- Technospheric vs. environmental chemistry

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- Elements of toxic effects

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- Examples

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- Examples
  - Antifouling biocides

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- Examples
  - Antifouling biocides
  - Ionic liquids

Technospheric vs. environmental chemistry

Technosphere

- High degree of control

Technosphere

- High degree of control
- High degree of knowledge on

Technosphere

- High degree of control
- High degree of knowledge on
  - temperatures, pressures

Technosphere

- High degree of control
- High degree of knowledge on
  - temperatures, pressures
  - chemical compositions

Technosphere

- High degree of control
- High degree of knowledge on
  - temperatures, pressures
  - chemical compositions
- Low combinatorial number of chemical interactions

Environment

- Low degree of control

Environment

- Low degree of control
- Low degree of knowledge on

Environment

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- Low degree of knowledge on
  - temperatures, pressures

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- Low degree of knowledge on
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  - temperatures, pressures
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Uncertainty and Ignorance

Chemistry dealing with biological and environmental systems has to deal with

- more complexity

Uncertainty and Ignorance

Chemistry dealing with biological and environmental systems has to deal with

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- more uncertainty

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Green and sustainable chemistry

includes both technospheric and environmental chemistry:

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⇒ High standards of deterministic knowledge in technospheric area

Green and sustainable chemistry

includes both technospheric and environmental chemistry:

⇒ High standards of deterministic knowledge in technospheric area

⇒ Great efforts to deal with uncertainty in environmental area

Where are the humans?

- Organized in social systems we control technical systems

Where are the humans?

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- As workers we are part of technical systems

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- As biological organisms we are are exposed to technical systems i.e. we belong to *their* environment
- As part of the global ecosphere we care for *our* environment

$\Rightarrow$ We belong to the technosphere *and* its environment

Elements of toxic effects

Ranke J (2001) PhD Dissertation

Five risk indicators

Technosphere

Environment

Five risk indicators

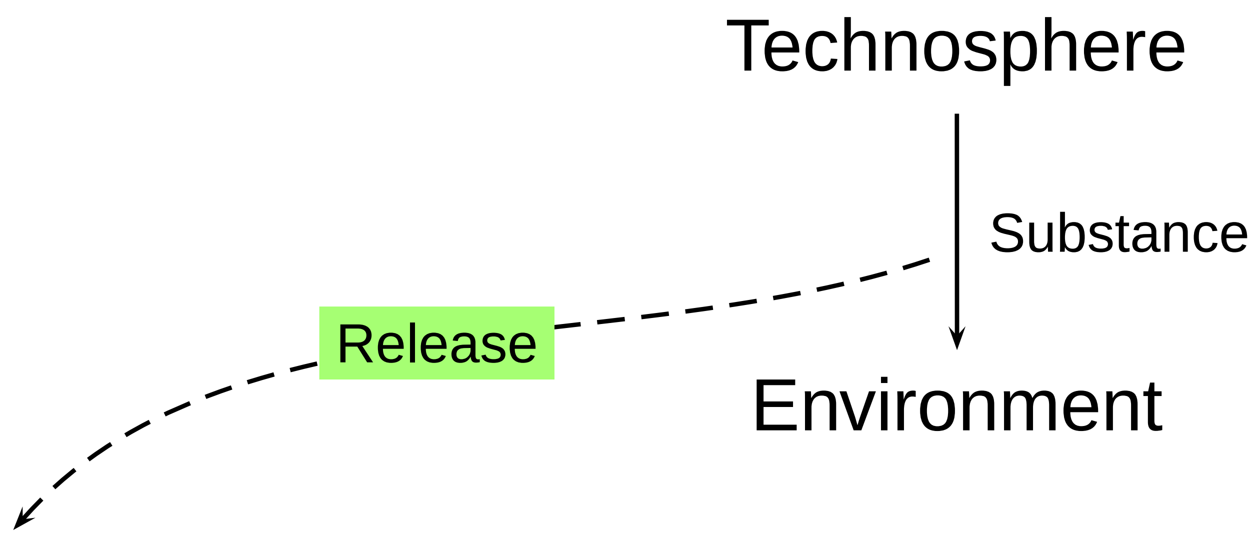
Technosphere

$\Big\downarrow$ Substance

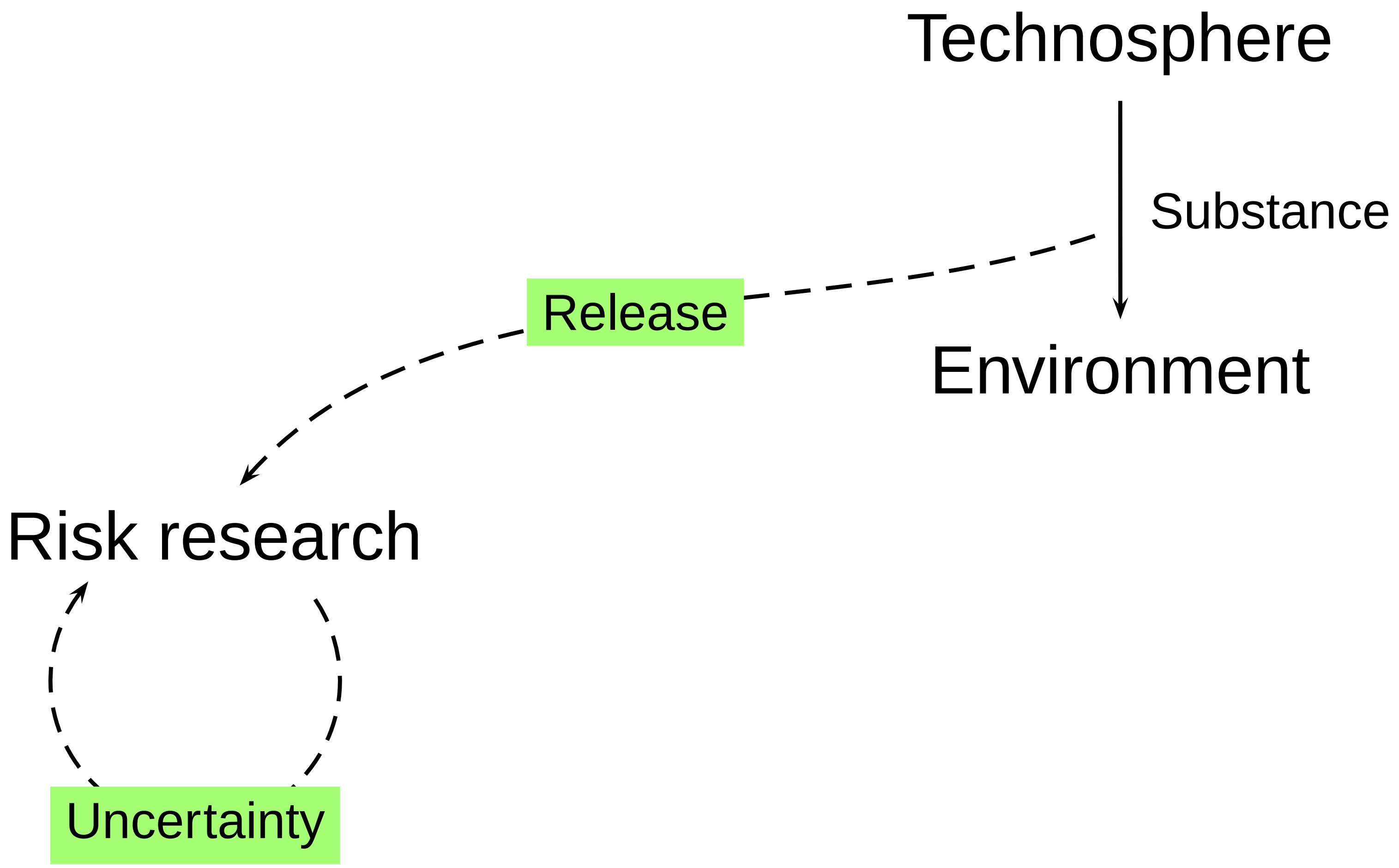
Environment

Ranke J (2001) PhD Dissertation

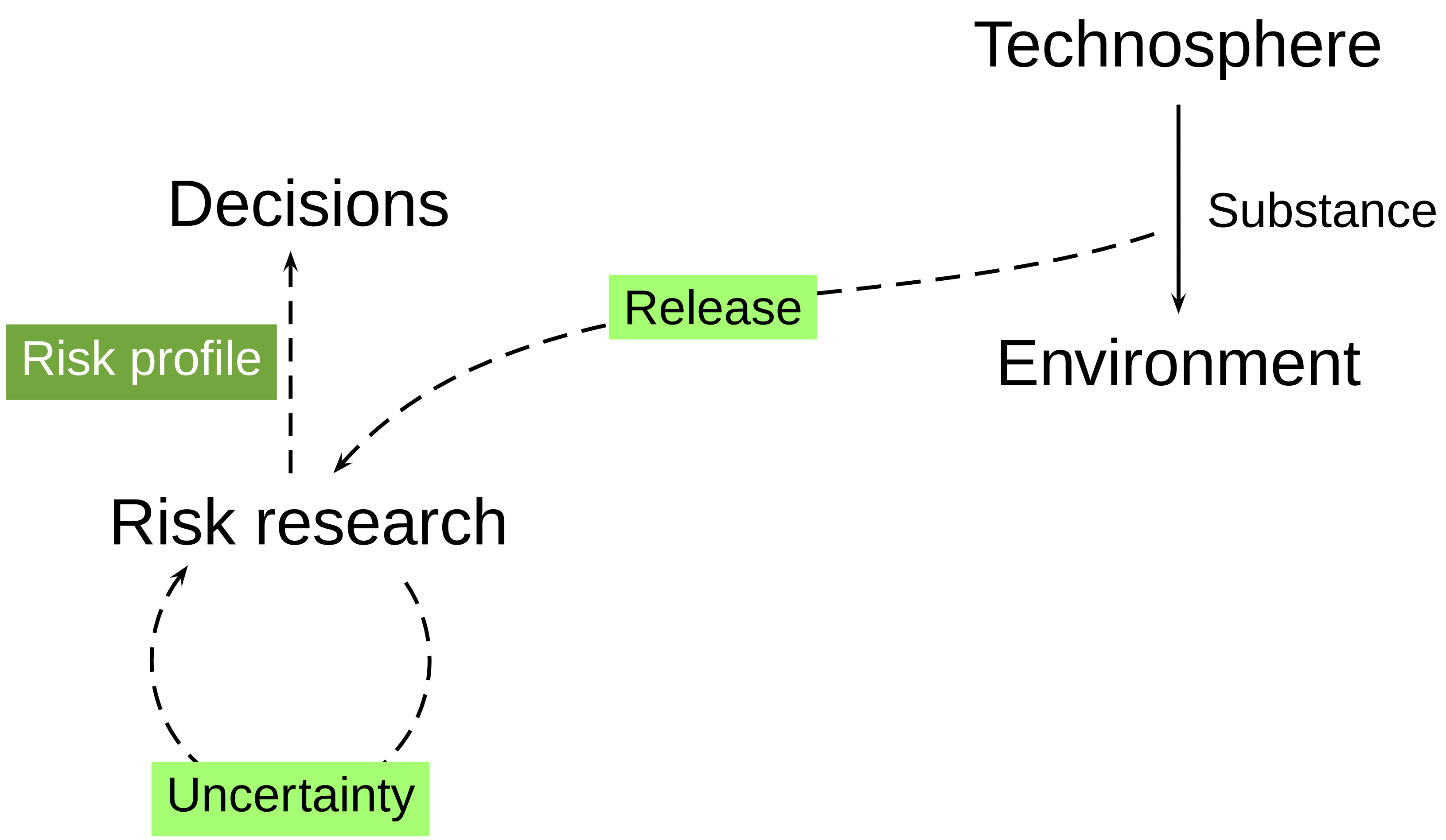
Five risk indicators



Five risk indicators



Five risk indicators



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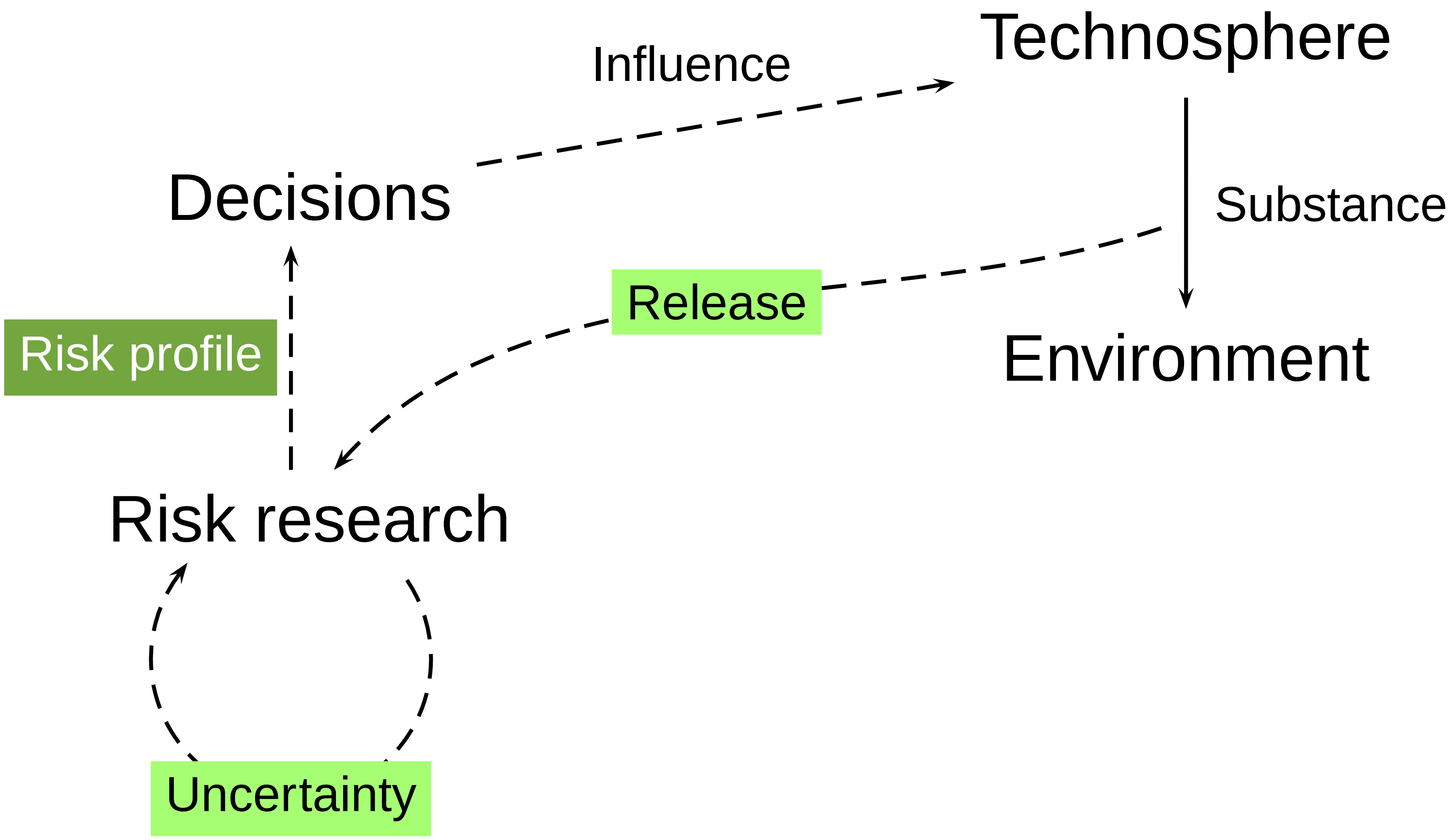
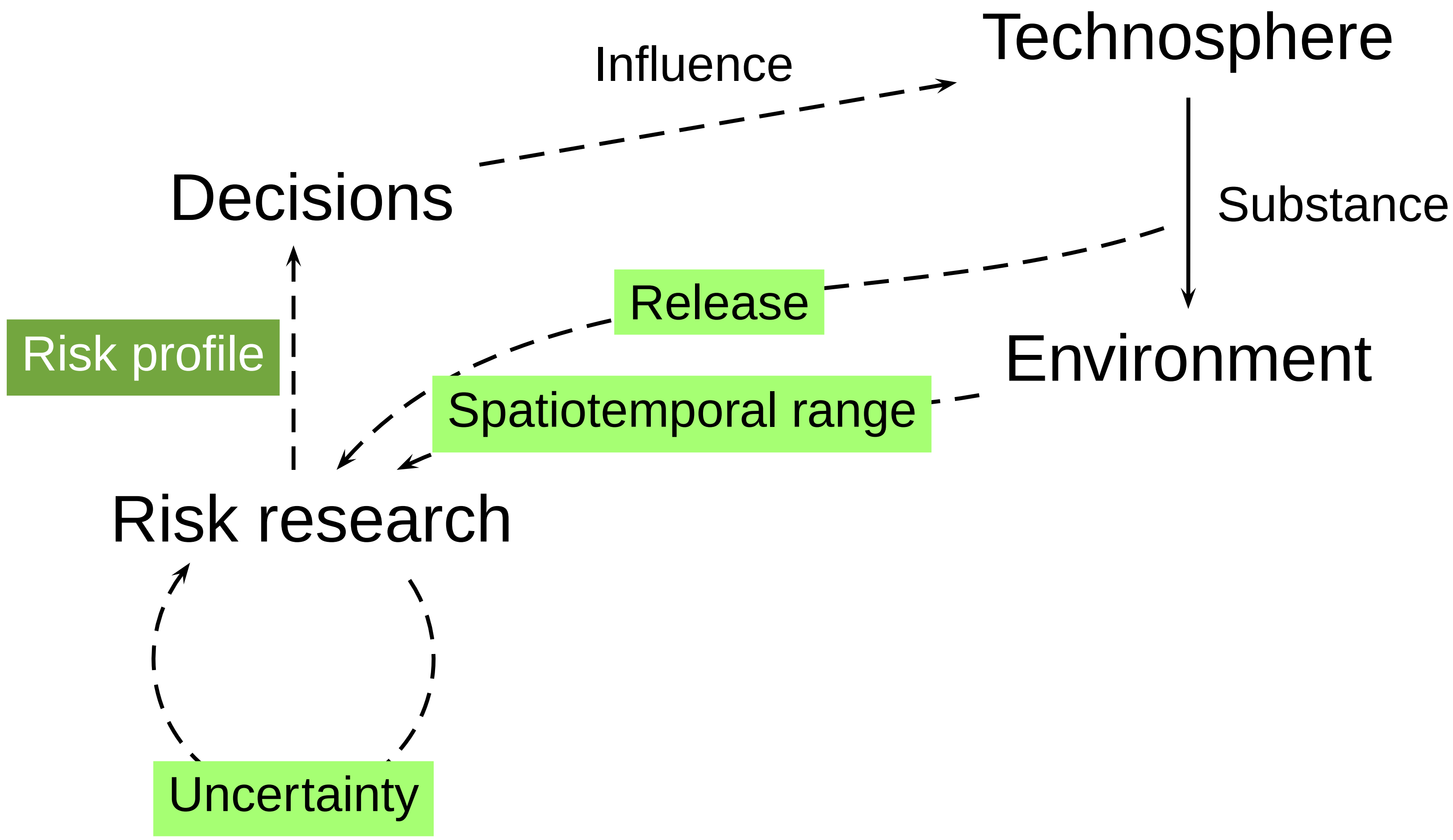
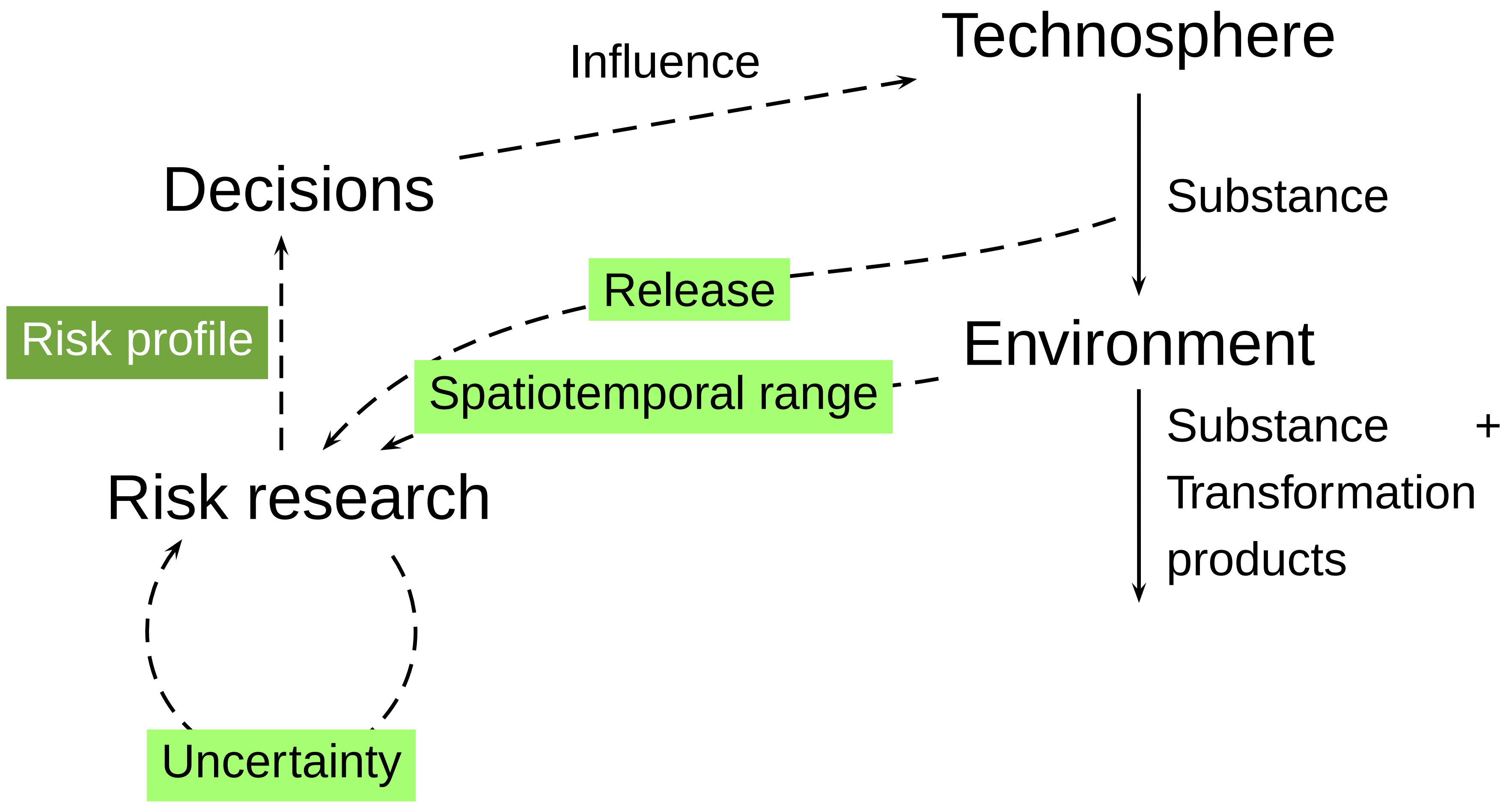


Five risk indicators



Five risk indicators



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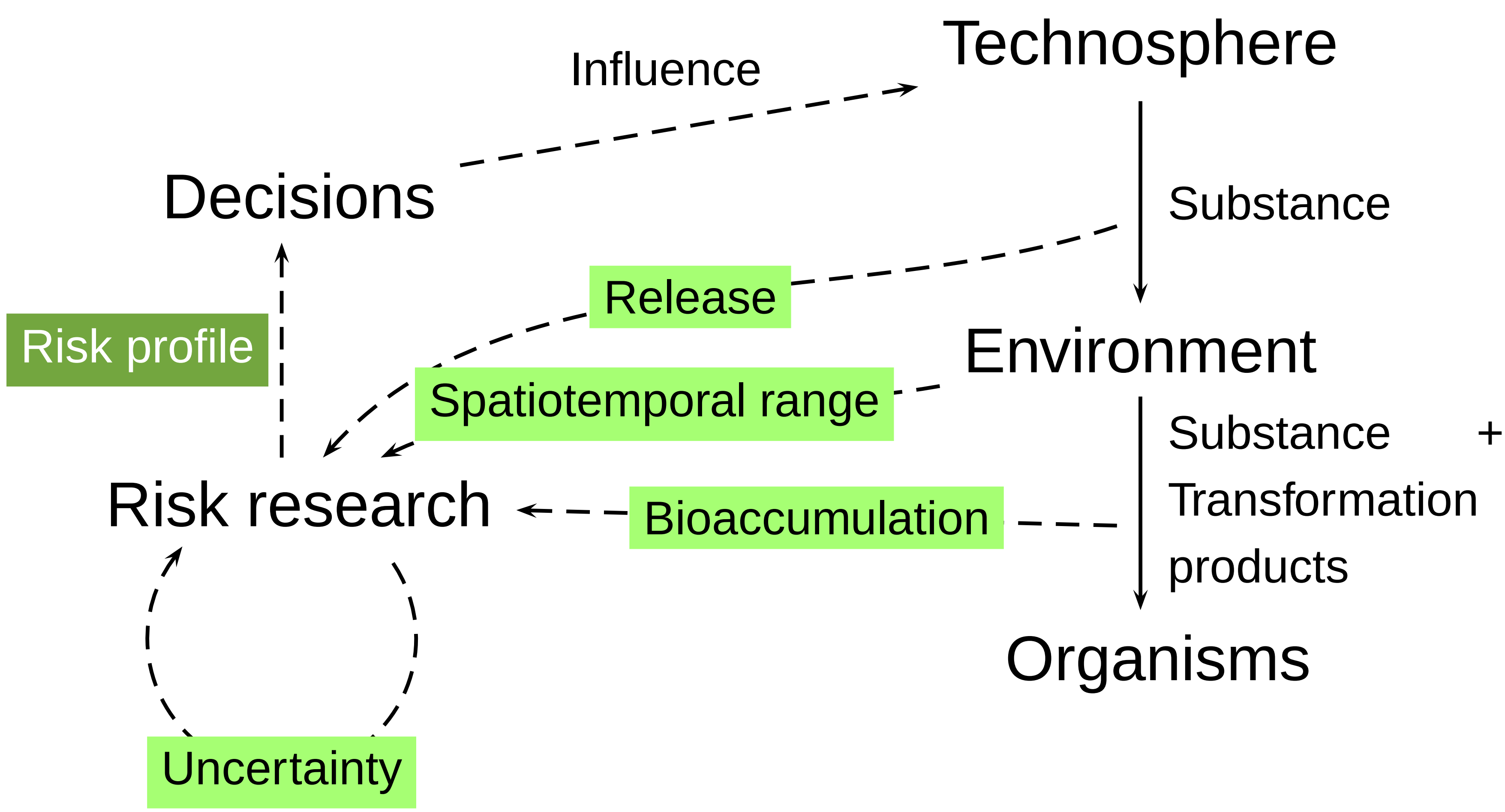
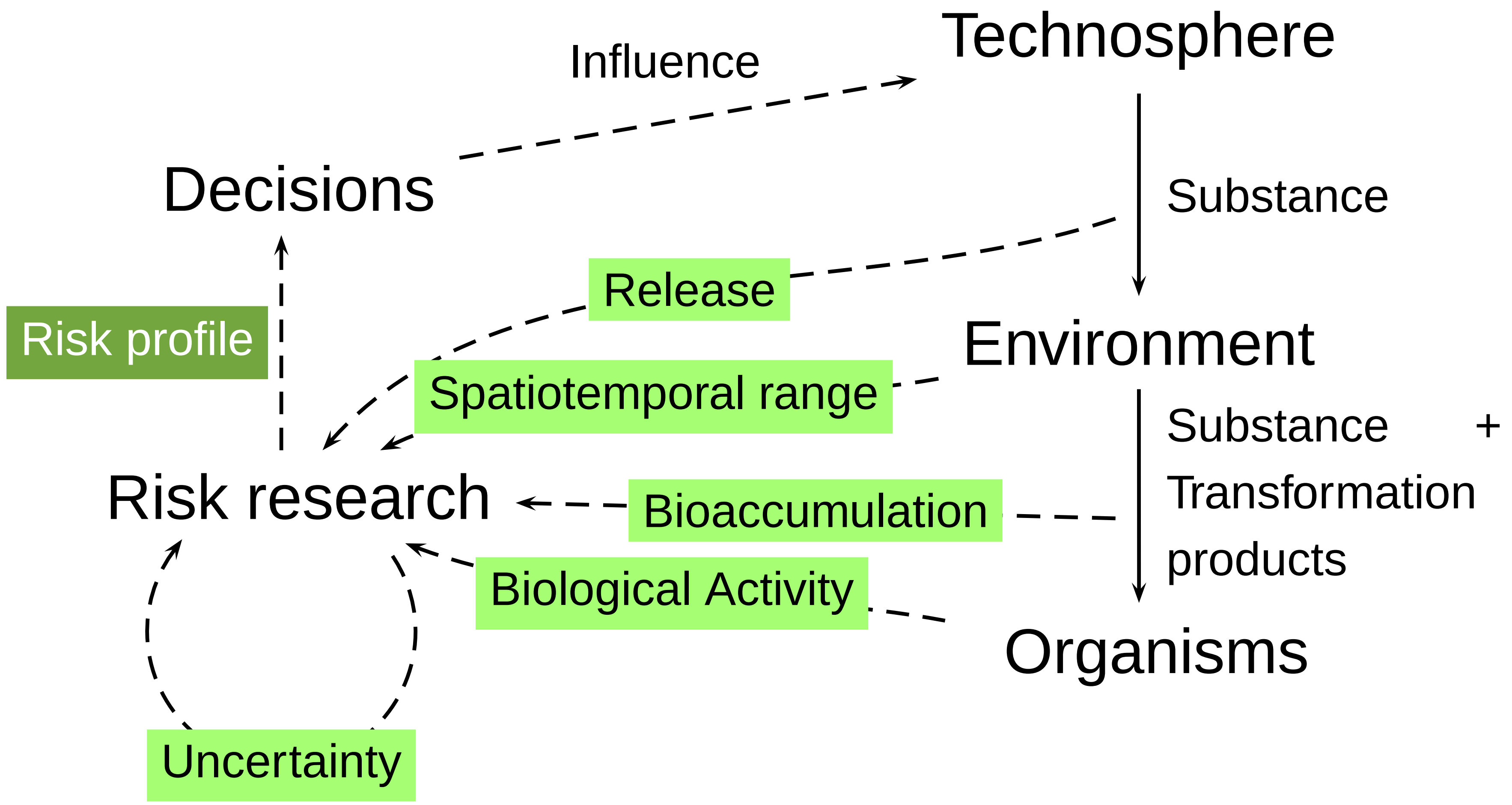


Five risk indicators



Antifouling biocides

Characteristics

Antifouling biocides used in commercial shipping

- Desired toxic effect

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- Global use pattern

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Antifouling biocides used in commercial shipping

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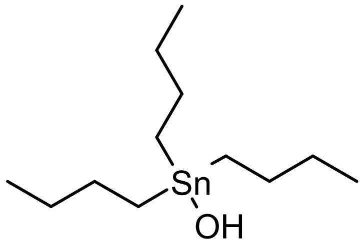
Which element of toxicity can be minimized?

Antifouling biocides

Release

Antifouling biocides

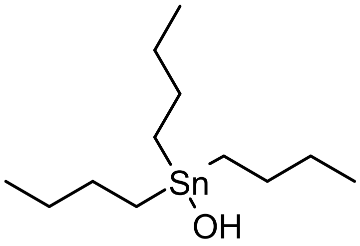
high risk examples



Release 1900 t/y

Antifouling biocides

high risk examples

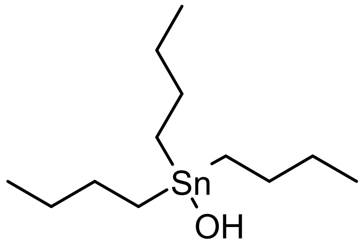


Release 1900 t/y

Spatiotemporal range

Antifouling biocides

high risk examples



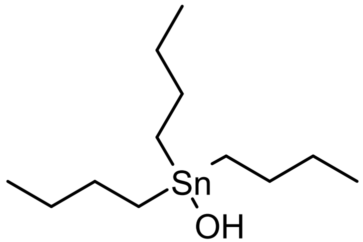
Release	1900 t/y
Spatiotemporal range	40 000 y

Cu^{2+}

Ranke J (2001) PhD Dissertation

Antifouling biocides

high risk examples



Release 1900 t/y

Spatiotemporal range 40 000 y

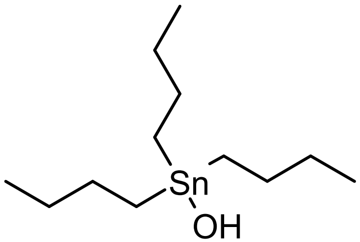
Cu^{2+}

Bioaccumulation

Ranke J (2001) PhD Dissertation

Antifouling biocides

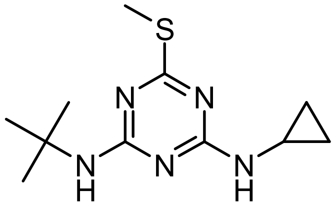
high risk examples



Release 1900 t/y

Cu^{2+}

Spatiotemporal range 40 000 y



Bioaccumulation 200 to 30 000 L/kg

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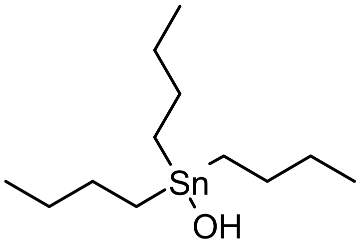
Ranke J (2001) PhD Dissertation

Antifouling biocides

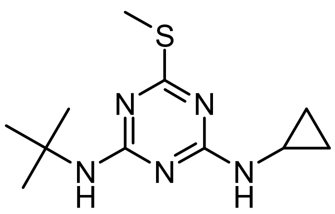
high risk examples



Release 1900 t/y

Spatiotemporal range 40 000 y

Cu^{2+}



Bioaccumulation 200 to 30 000 L/kg

Biological activity

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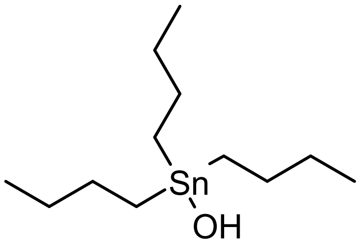
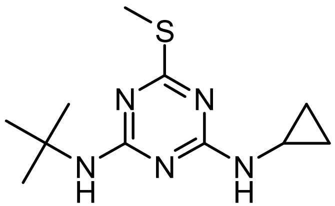
Antifouling biocides

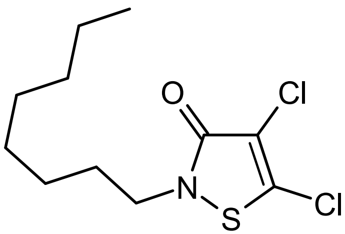
high risk examples



Release	1900 t/y
Spatiotemporal range	40 000 y
Bioaccumulation	200 to 30 000 L/kg
Biological activity	100 to 1 μg / L

Cu^{2+}

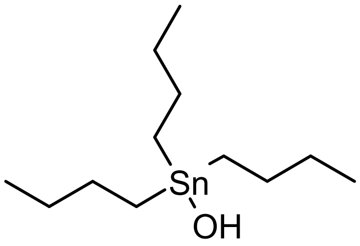




Ranke J (2001) PhD Dissertation

Antifouling biocides

high risk examples



Release 1900 t/y

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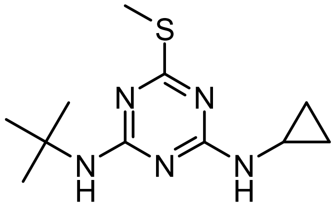
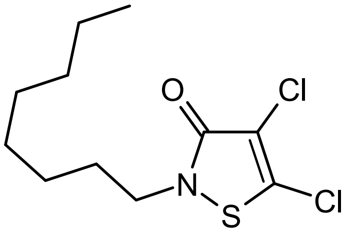
Cu^{2+}



Bioaccumulation 200 to 30 000 L/kg



Biological activity 100 to 1 μg / L

Uncertainty

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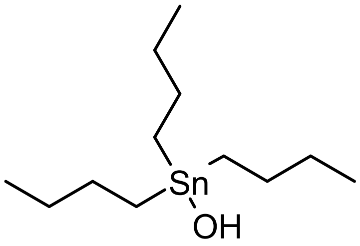
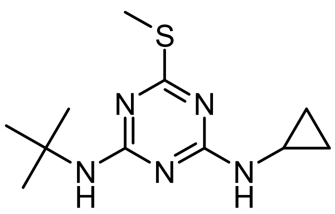
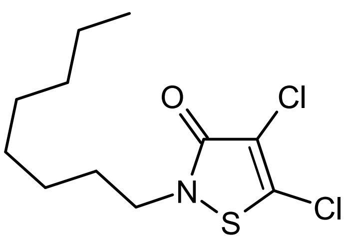
Antifouling biocides

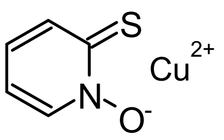
high risk examples



Release	1900 t/y	
Spatiotemporal range	40 000 y	Cu^{2+}
Bioaccumulation	200 to 30 000 L/kg	
Biological activity	100 to 1 μg / L	
Uncertainty	PT_2,$MePt^+$,...	







Release

- Copper is being used in most cases, so we compare "booster biocides"

Release

- Copper is being used in most cases, so we compare "booster biocides"
- Similar release rates

Spatiotemporal range

Build a fate model:

- Define environmental compartments

Spatiotemporal range

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- Collect substance data on

Spatiotemporal range

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- Collect substance data on
  - Degradation kinetics

Spatiotemporal range

Build a fate model:

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- Optional: estimate data distributions

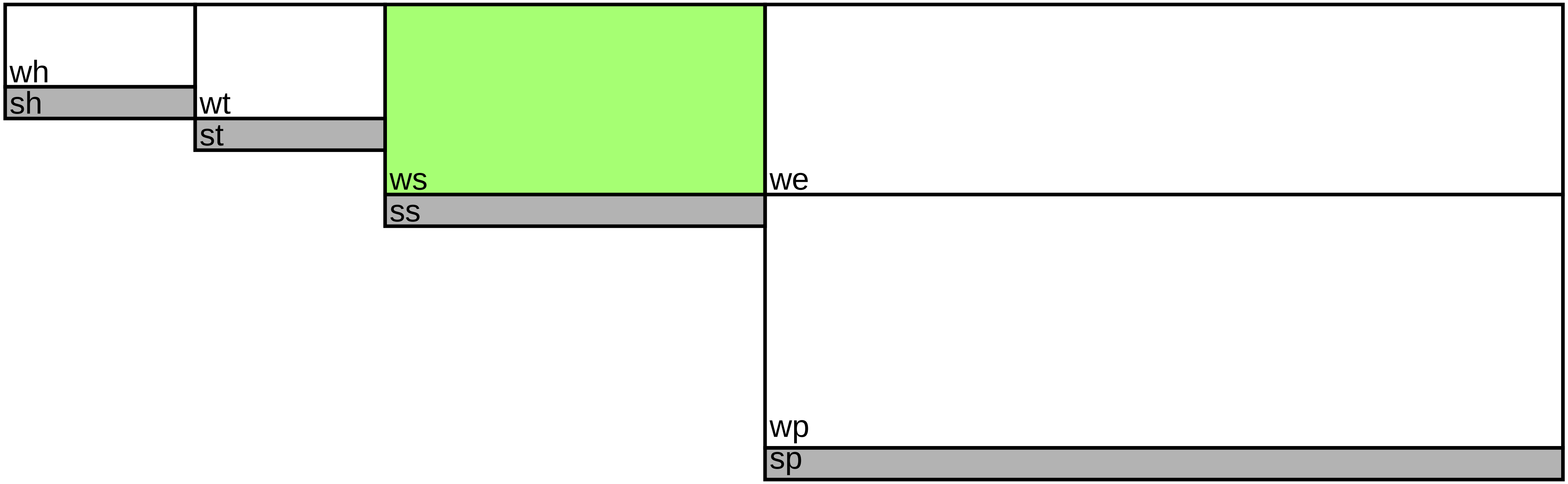
Spatiotemporal range

Build a fate model:

- Define environmental compartments
- Collect substance data on
  - Degradation kinetics
  - Particle water distribution
- Optional: estimate data distributions

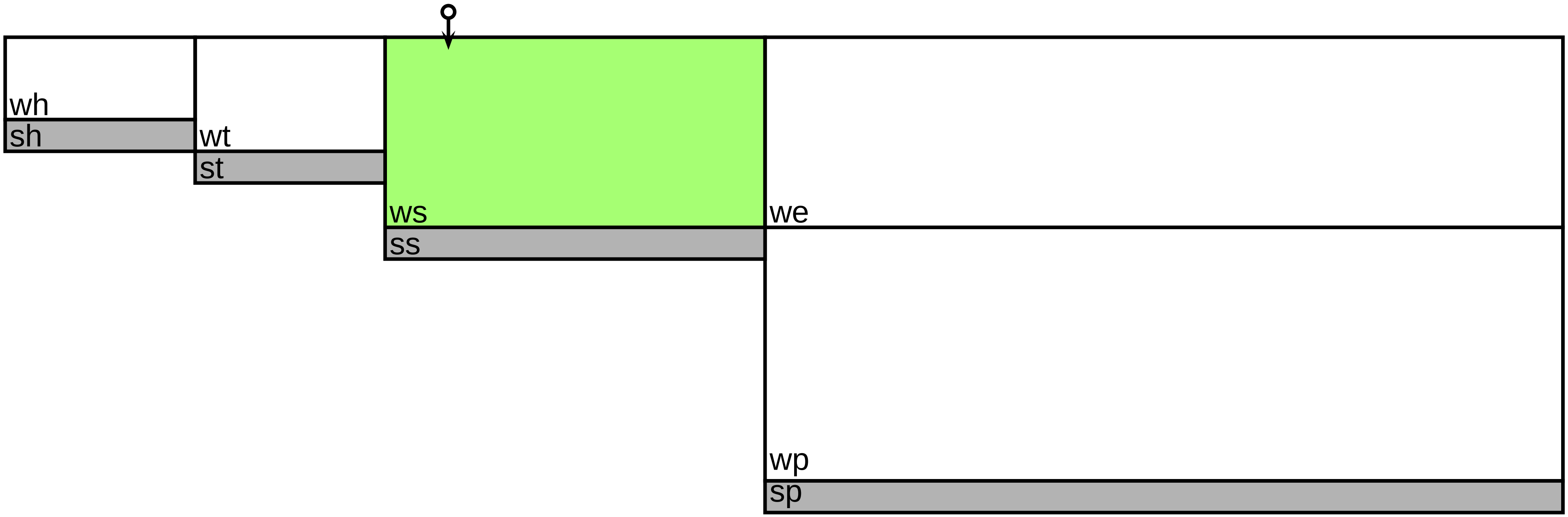
Estimate residence times in the environment

Fate model setup: water



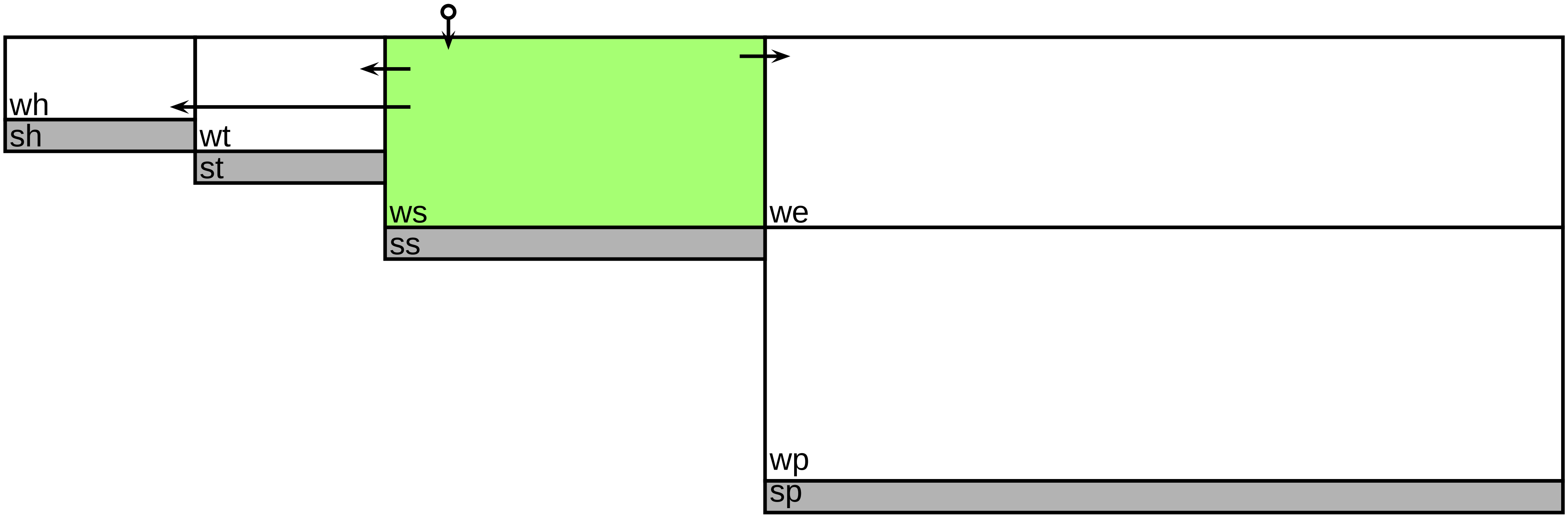
$$\dot{M}^{\mathrm{ws}} = \; 0$$

Fate model setup: water



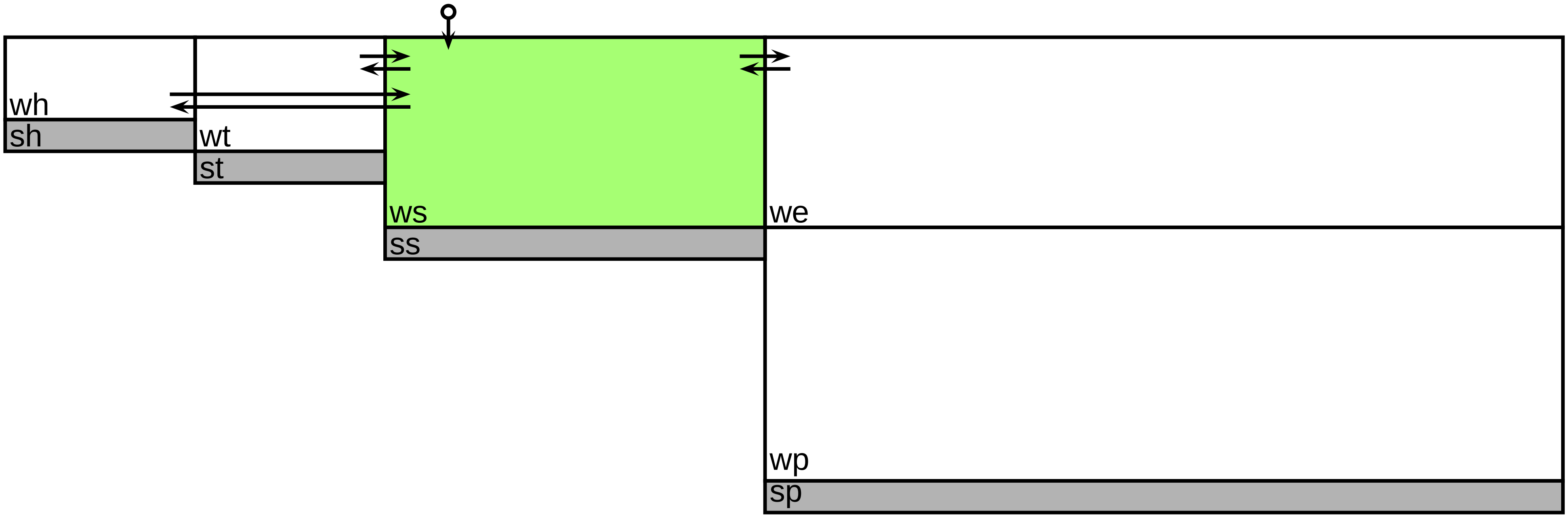
$$\dot{M}^{\mathrm{ws}} = \quad S^{\mathrm{ws}}$$

Fate model setup: water



$$\dot{M}^{\mathrm{ws}} = \quad S^{\mathrm{ws}} - \left(\frac{F_{\mathrm{w}}^{\mathrm{s}\rightarrow\mathrm{h}} + F_{\mathrm{w}}^{\mathrm{s}\rightarrow\mathrm{t}} + F_{\mathrm{w}}^{\mathrm{s}\rightarrow\mathrm{e}}}{V^{\mathrm{ws}}}\right) M^{\mathrm{ws}}$$

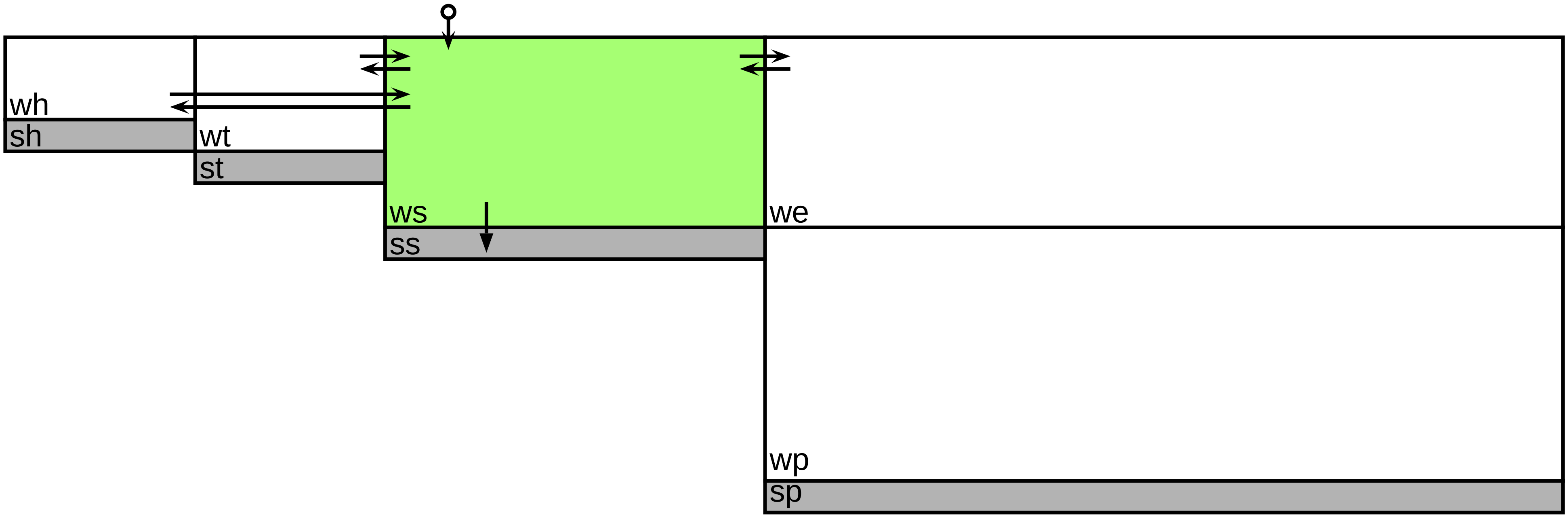
Fate model setup: water



$$\dot{M}^{ws} = S^{ws} - \left(\frac{F_w^{s\to h} + F_w^{s\to t} + F_w^{s\to e}}{V^{ws}}\right) M^{ws}$$

$$+ \frac{F_w^{h\to s}}{V^{wh}} M^{wh} + \frac{F_w^{t\to s}}{V^{wt}} M^{wt} + \frac{F_w^{e\to s}}{V^{we}} M^{we}$$

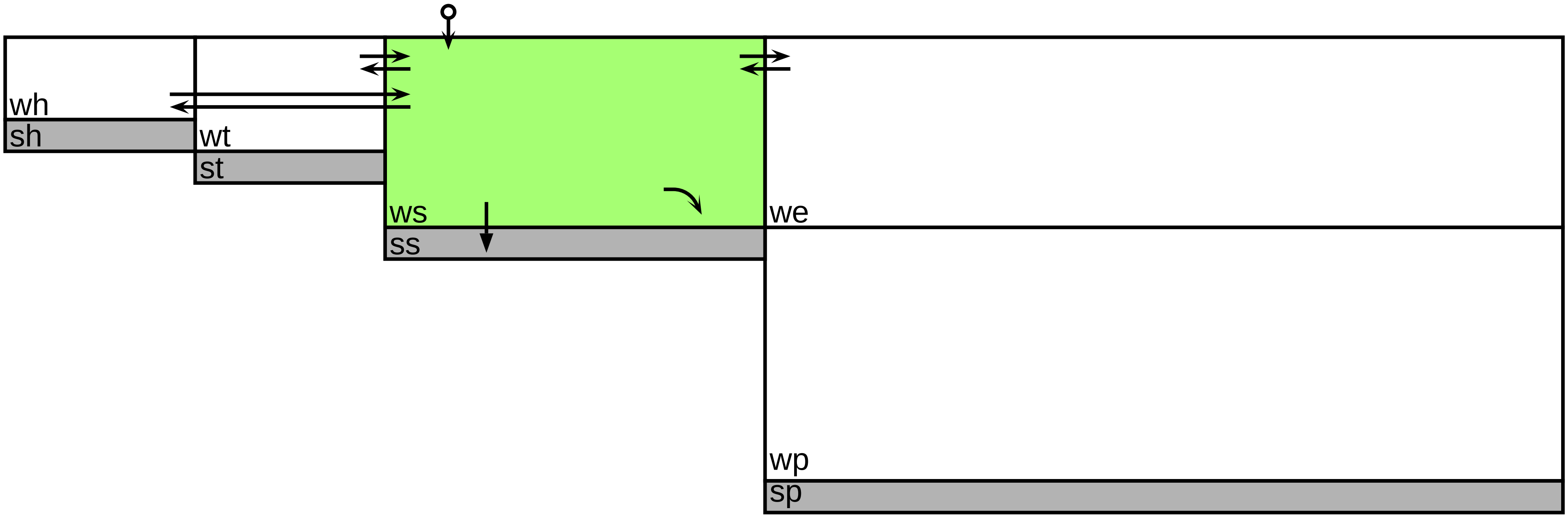
Fate model setup: water



$$\dot{M}^{\mathrm{ws}} = S^{\mathrm{ws}} - \left(\frac{F_{\mathrm{w}}^{\mathrm{s}\to\mathrm{h}} + F_{\mathrm{w}}^{\mathrm{s}\to\mathrm{t}} + F_{\mathrm{w}}^{\mathrm{s}\to\mathrm{e}} + f_{\mathrm{diss}} K_{\mathrm{pw}} F_{\mathrm{p}}^{\mathrm{ws}\to\mathrm{ss}}}{V^{\mathrm{ws}}}\right) M^{\mathrm{ws}}$$

$$+ \frac{F_{\mathrm{w}}^{\mathrm{h}\to\mathrm{s}}}{V^{\mathrm{wh}}} M^{\mathrm{wh}} + \frac{F_{\mathrm{w}}^{\mathrm{t}\to\mathrm{s}}}{V^{\mathrm{wt}}} M^{\mathrm{wt}} + \frac{F_{\mathrm{w}}^{\mathrm{e}\to\mathrm{s}}}{V^{\mathrm{we}}} M^{\mathrm{we}}$$

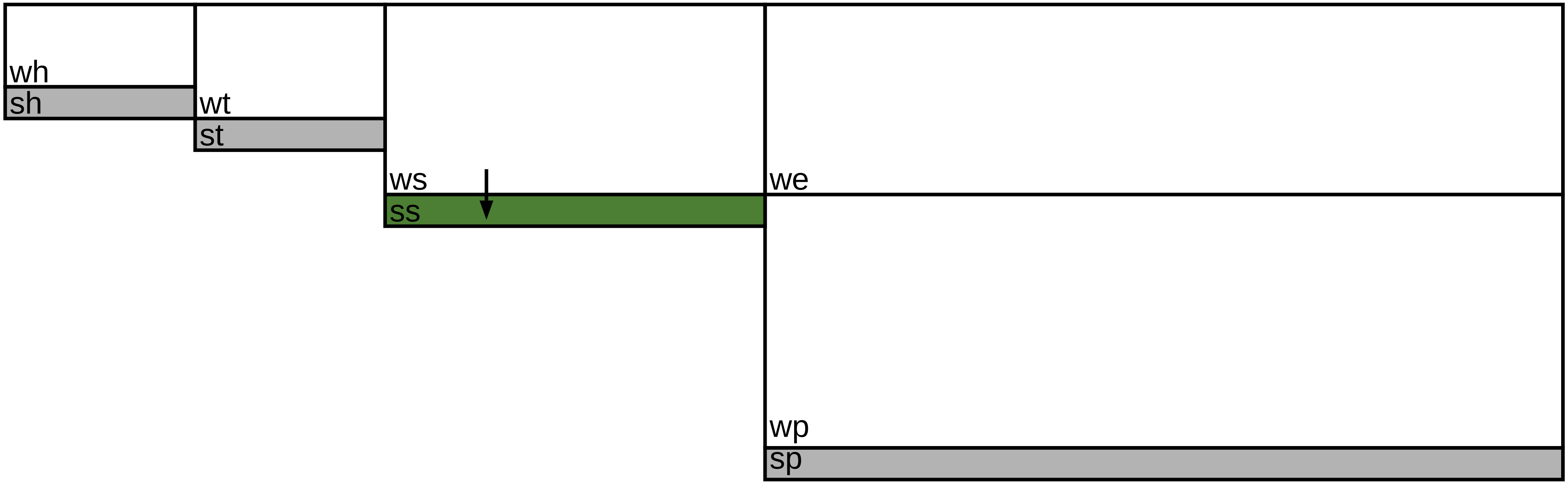
Fate model setup: water



$$\dot{M}^{\mathrm{ws}} = \quad S^{\mathrm{ws}} - \left(\frac{F_{\mathrm{w}}^{\mathrm{s}\rightarrow\mathrm{h}} + F_{\mathrm{w}}^{\mathrm{s}\rightarrow\mathrm{t}} + F_{\mathrm{w}}^{\mathrm{s}\rightarrow\mathrm{e}} + f_{\mathrm{diss}} K_{\mathrm{pw}} F_{\mathrm{p}}^{\mathrm{ws}\rightarrow\mathrm{ss}}}{V^{\mathrm{ws}}}\right) M^{\mathrm{ws}}$$

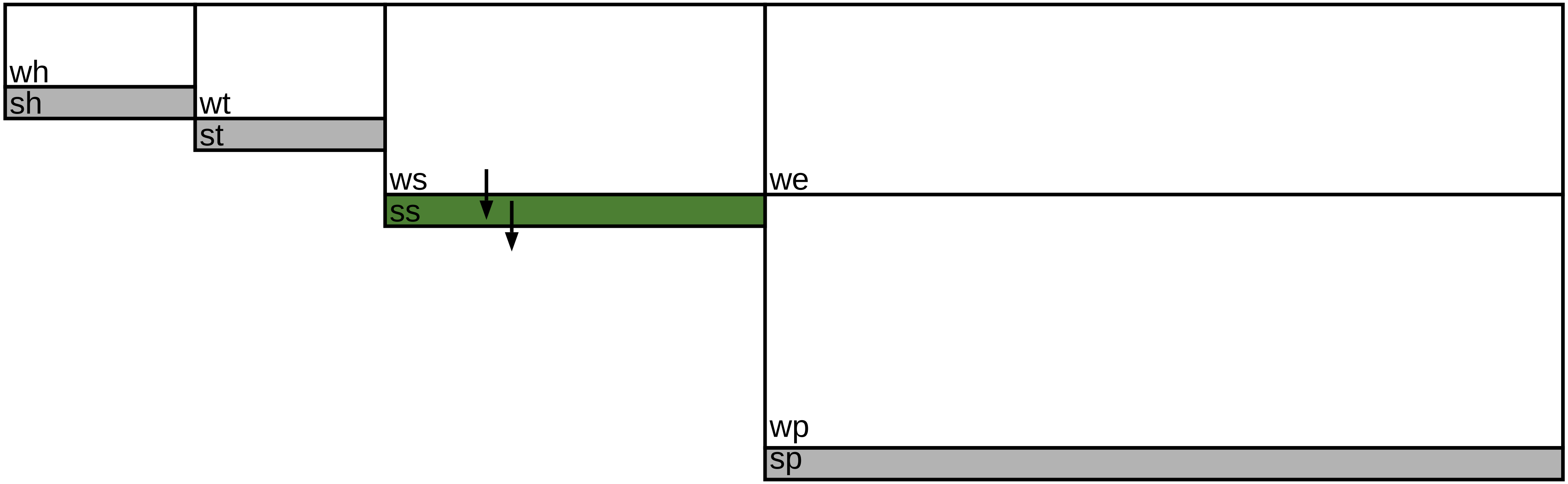
$$+ \frac{F_{\mathrm{w}}^{\mathrm{h}\rightarrow\mathrm{s}}}{V^{\mathrm{wh}}} M^{\mathrm{wh}} + \frac{F_{\mathrm{w}}^{\mathrm{t}\rightarrow\mathrm{s}}}{V^{\mathrm{wt}}} M^{\mathrm{wt}} + \frac{F_{\mathrm{w}}^{\mathrm{e}\rightarrow\mathrm{s}}}{V^{\mathrm{we}}} M^{\mathrm{we}} + k_{\mathrm{w}} M^{\mathrm{ws}}$$

Fate model setup: sediment



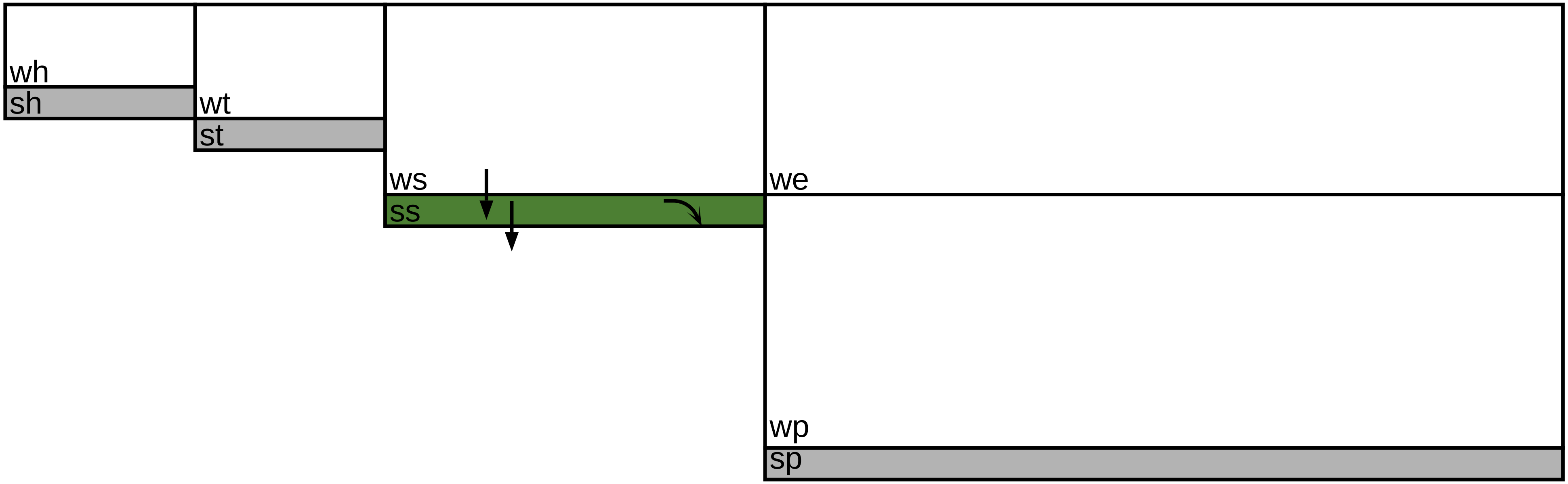
$$\dot{M}^{\mathrm{ss}} = f_{\mathrm{diss}} K_{\mathrm{pw}} F_{\mathrm{p}}^{ws \rightarrow ss} \frac{M^{\mathrm{ws}}}{V^{\mathrm{ws}}}$$

Fate model setup: sediment



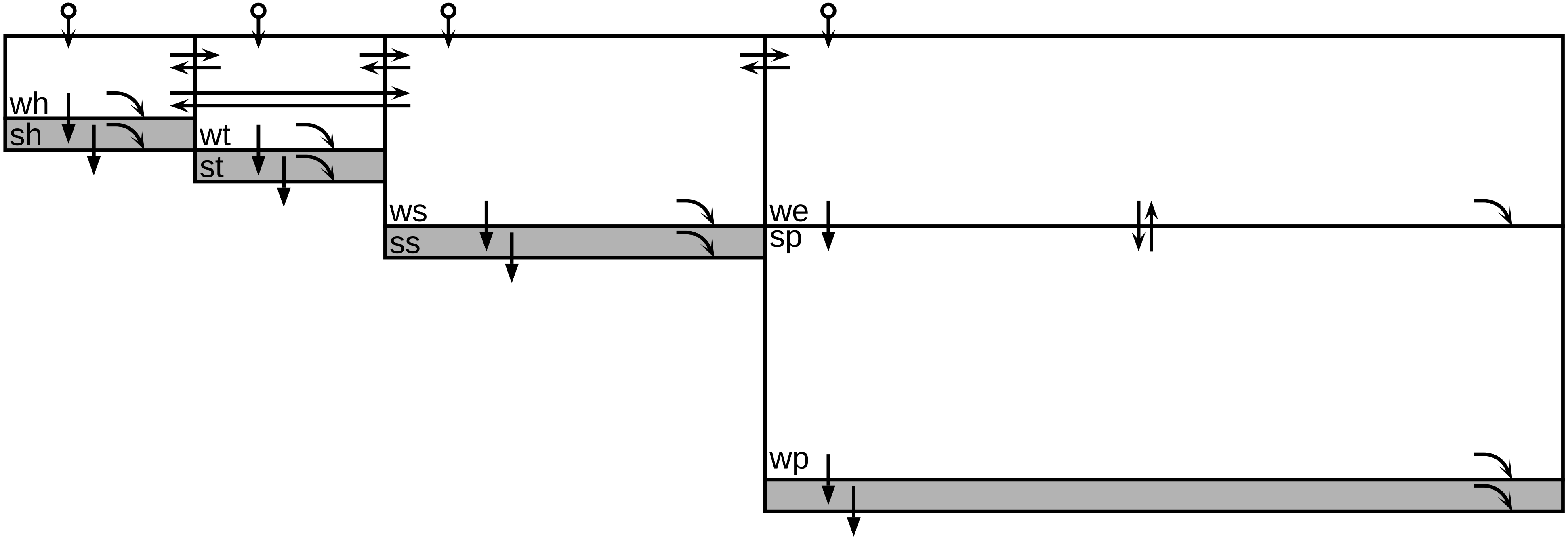
$$\dot{M}^{\mathrm{ss}} = f_{\mathrm{diss}} K_{\mathrm{pw}} F_{\mathrm{p}}^{ws \rightarrow ss} \frac{M^{\mathrm{ws}}}{V^{\mathrm{ws}}} - \frac{B^{\mathrm{sh}}}{z} M^{\mathrm{ss}}$$

Fate model setup: sediment

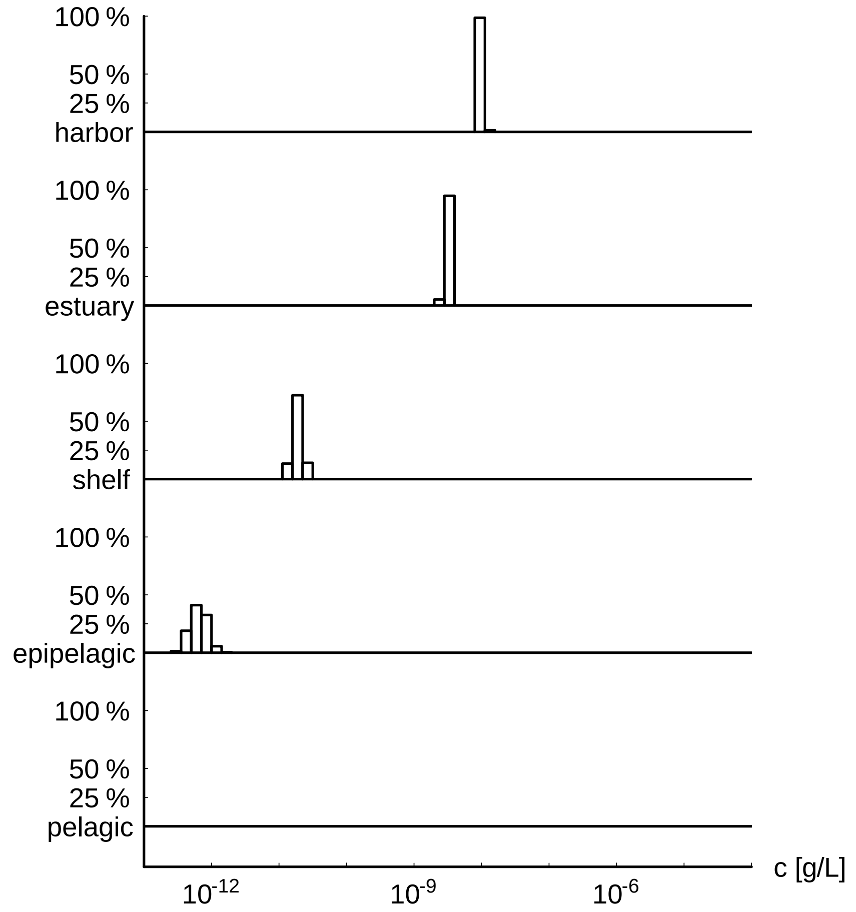


$$\dot{M}^{\mathrm{ss}} = f_{\mathrm{diss}} K_{\mathrm{pw}} F_{\mathrm{p}}^{ws \rightarrow ss} \frac{M^{\mathrm{ws}}}{V^{\mathrm{ws}}} - \left(\frac{B^{\mathrm{sh}}}{z} + k_{\mathrm{S}}\right) M^{\mathrm{ss}}$$

Model setup



TBT in water compartments



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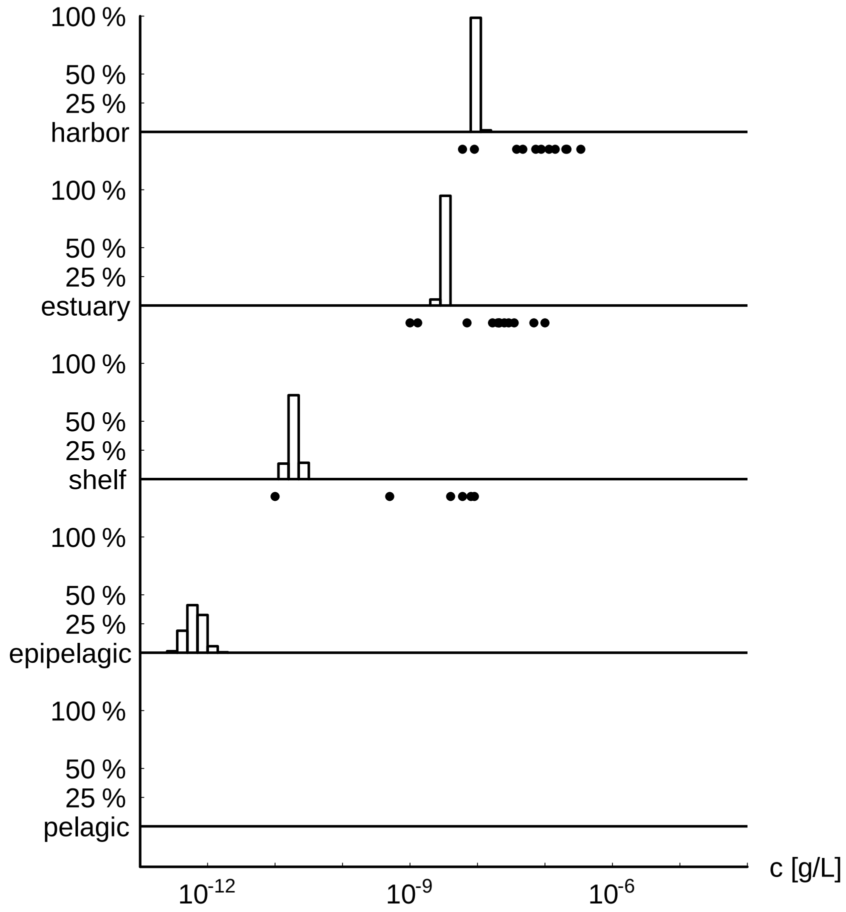
TBT in water compartments



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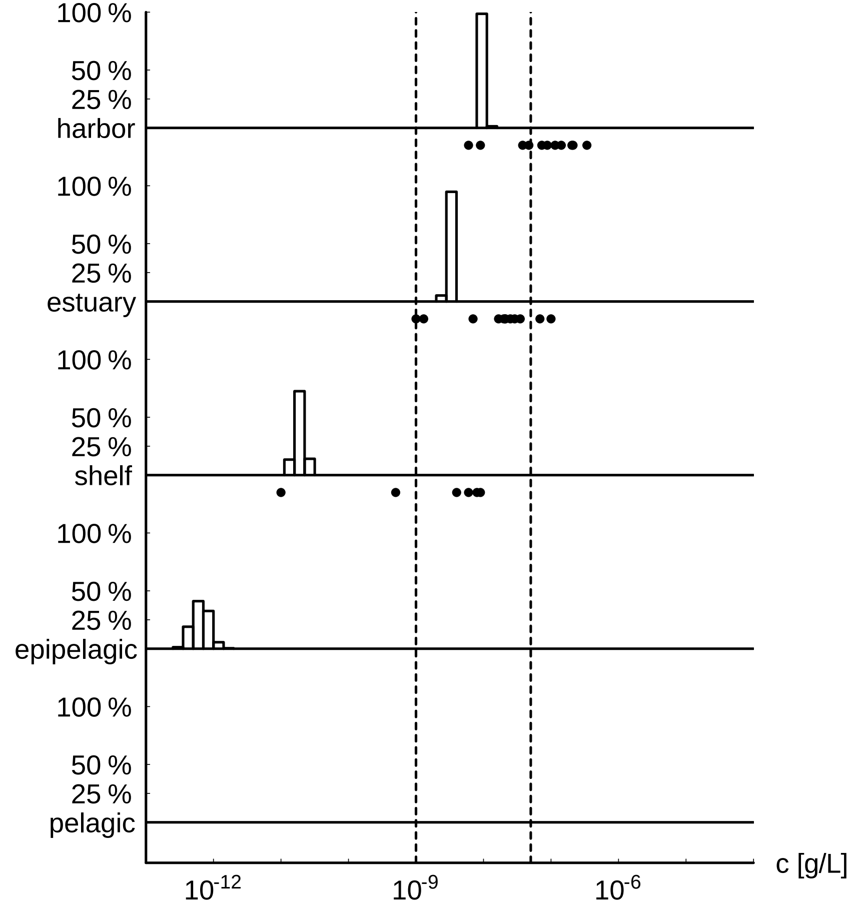
TBT in water compartments

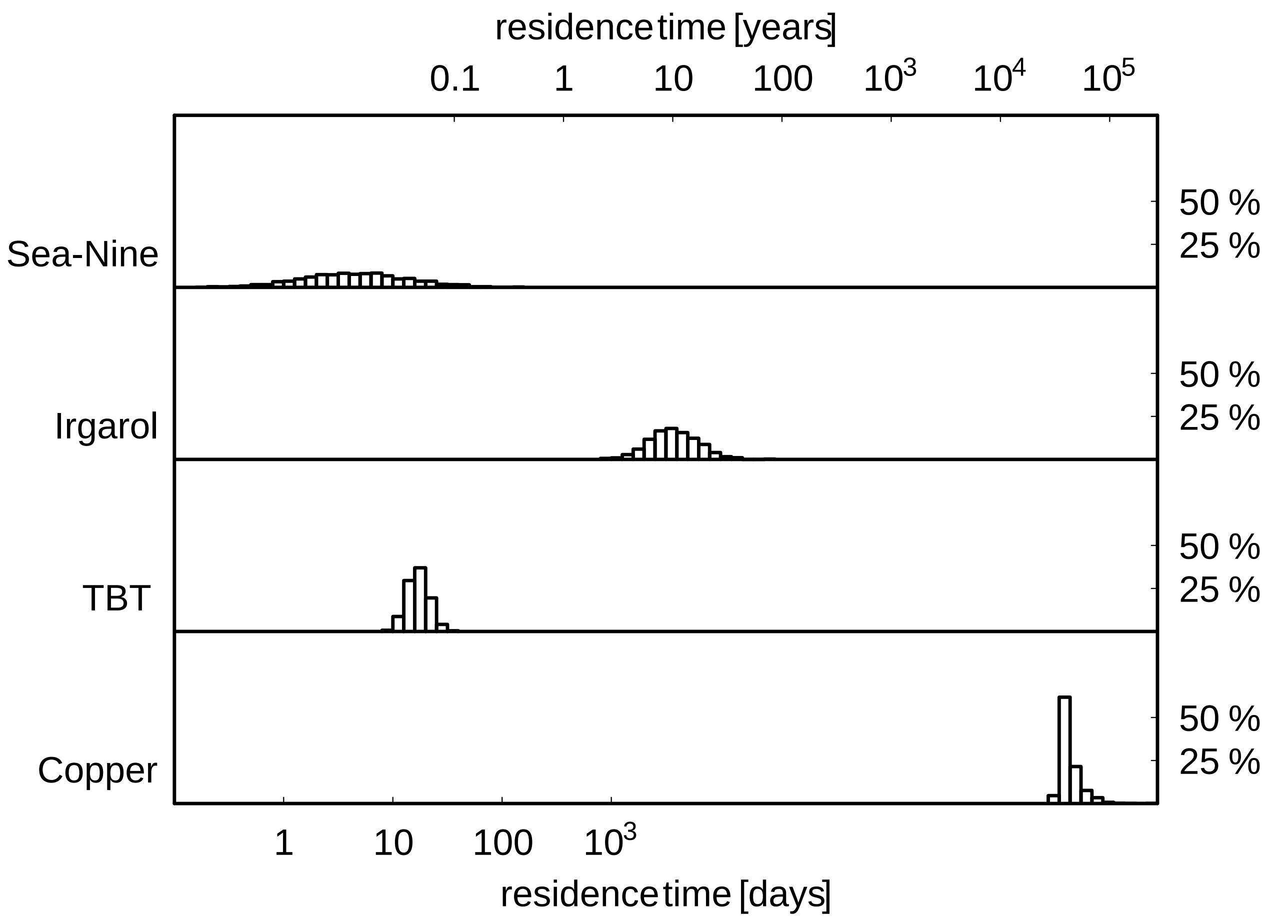


Ranke J (2002) *Environ Sci Technol* **36** 1539-1545

Estimated residence times

	τ^{w}	τ	
Sea-Nine	4.55	4.76	days
TBT	16.5	16.9	days
Irgarol	10.2	10.2	years
Cu^{2+}	8350	42700	years

Estimated residence times



Ionic liquids

Ionic liquids

- Salts with a melting point < 100 °C

Ionic liquids

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- Low vapor pressure, inflammable

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Ionic liquids = Green Chemistry?

Ionic liquid structures

P666-14 1SO3	Tributyl(tetradecyl)phosphonium methanesulfonate
Im14 PF6	1-Butyl-3-methyl-1H-imidazolium hexafluorophosphate
Pyr18 BF4	1-Methyl-1-octylpyrrolidinium tetrafluoroborate(1-)

Ionic liquid structures

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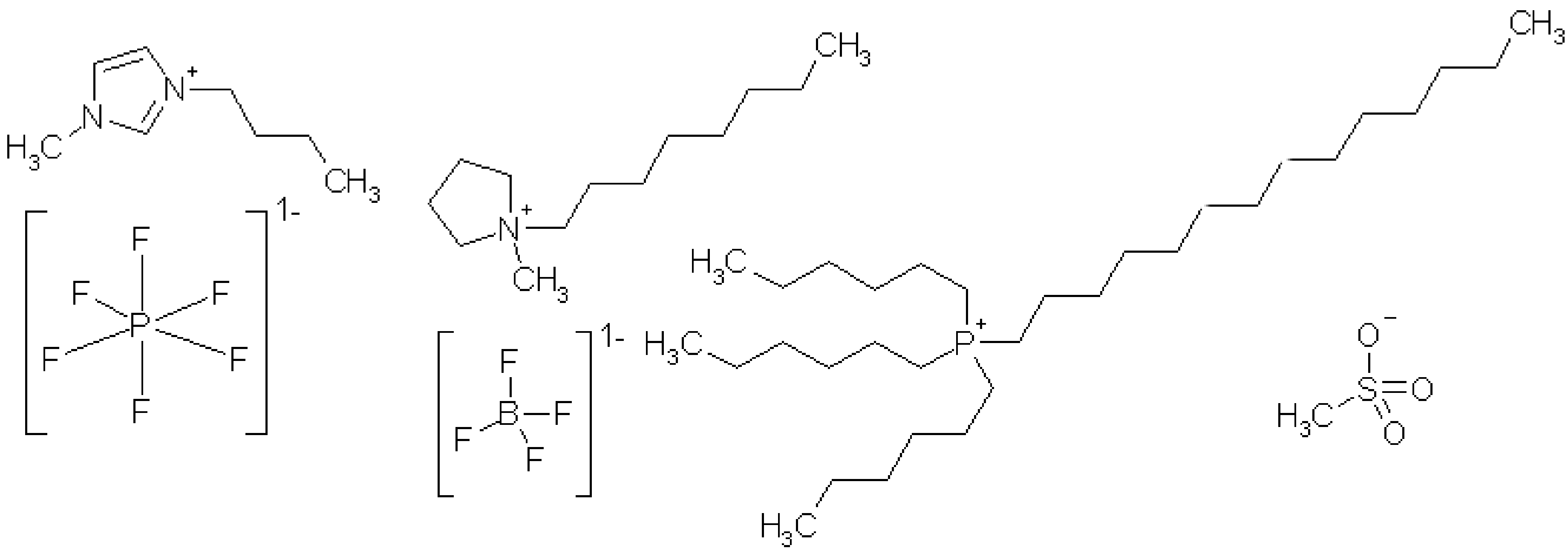


Ionic liquids

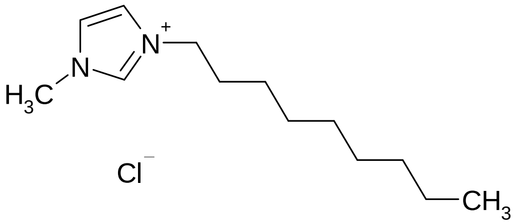
Release

Ionic liquids

low risk examples

Release

Research use only



Ionic liquids

low risk examples

Release

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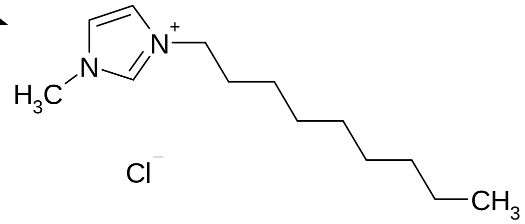


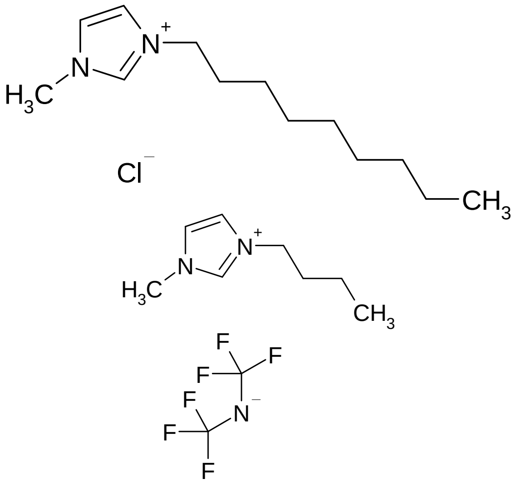
Spatiotemporal range

Ionic liquids

low risk examples

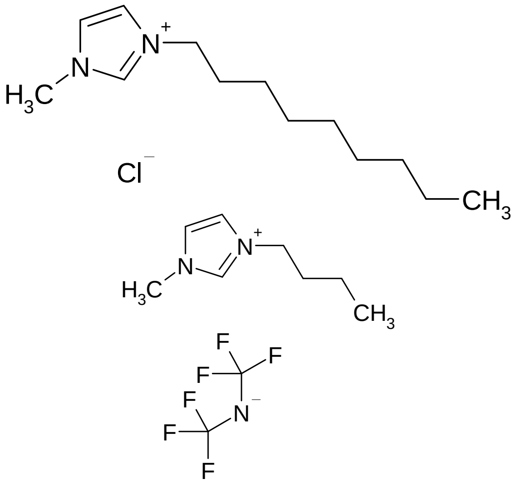
Release — Research use only

Spatiotemporal range — Fast hydrolysis (to?)



Ionic liquids

low risk examples



Release — Research use only

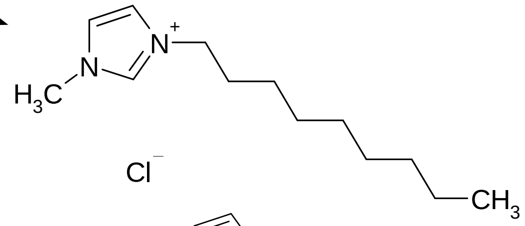
Spatiotemporal range — Fast hydrolysis (to?)

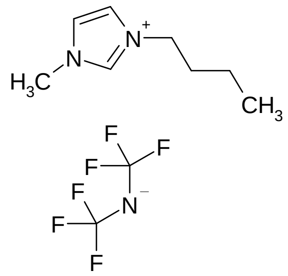
Bioaccumulation

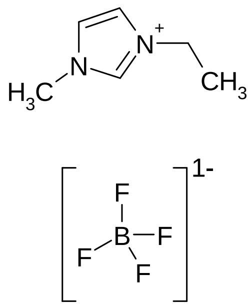
Ionic liquids

low risk examples

Release	Research use only
Spatiotemporal range	Fast hydrolysis (to?)
Bioaccumulation	Low lipophilicity

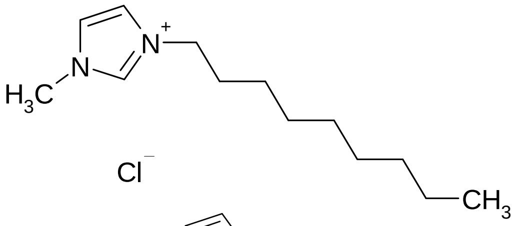


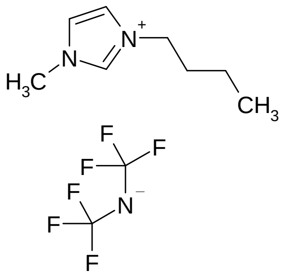


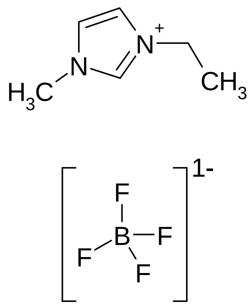


Ionic liquids

low risk examples



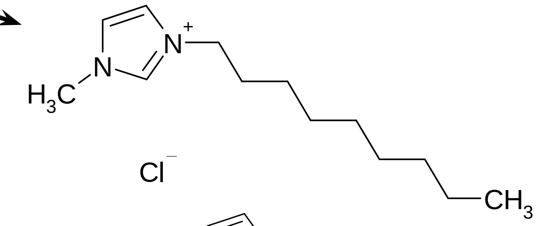




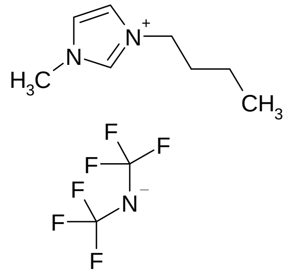
Release	Research use only
Spatiotemporal range	Fast hydrolysis (to?)
Bioaccumulation	Low lipophilicity
Biological activity	

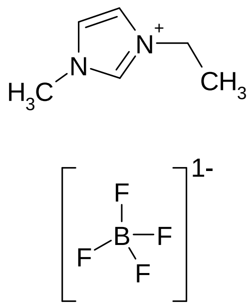
Ionic liquids

low risk examples



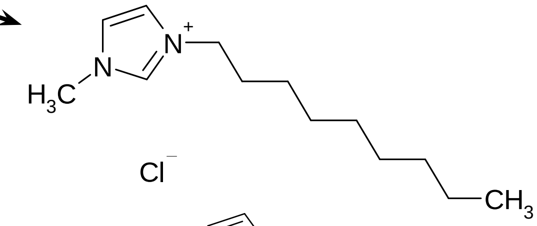
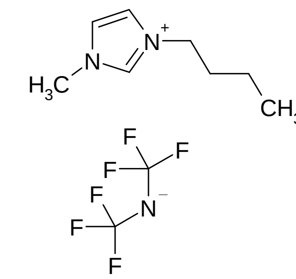
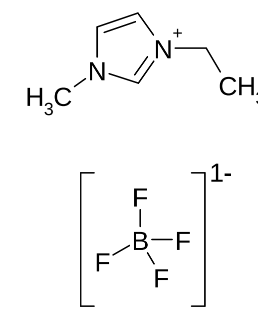
Release	Research use only
Spatiotemporal range	Fast hydrolysis (to?)
Bioaccumulation	Low lipophilicity
Biological activity	Low cytotoxicity





Ionic liquids

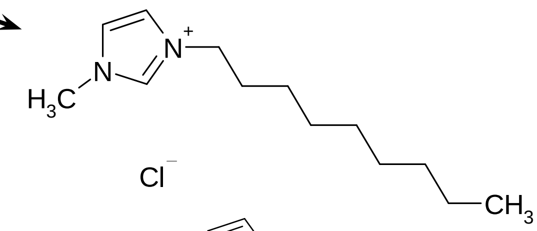
low risk examples

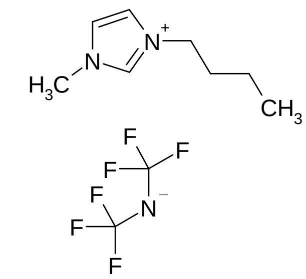
Release	Research use only	
Spatiotemporal range	Fast hydrolysis (to?)	
Bioaccumulation	Low lipophilicity	
Biological activity	Low cytotoxicity	
Uncertainty		

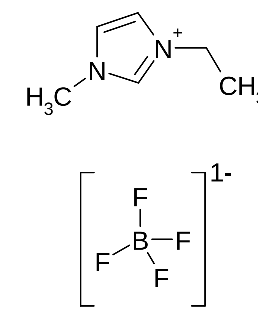
Ionic liquids

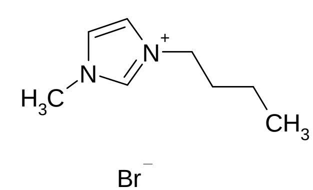
low risk examples

Release	Research use only
Spatiotemporal range	Fast hydrolysis (to?)
Bioaccumulation	Low lipophilicity
Biological activity	Low cytotoxicity
Uncertainty	Large amount of data



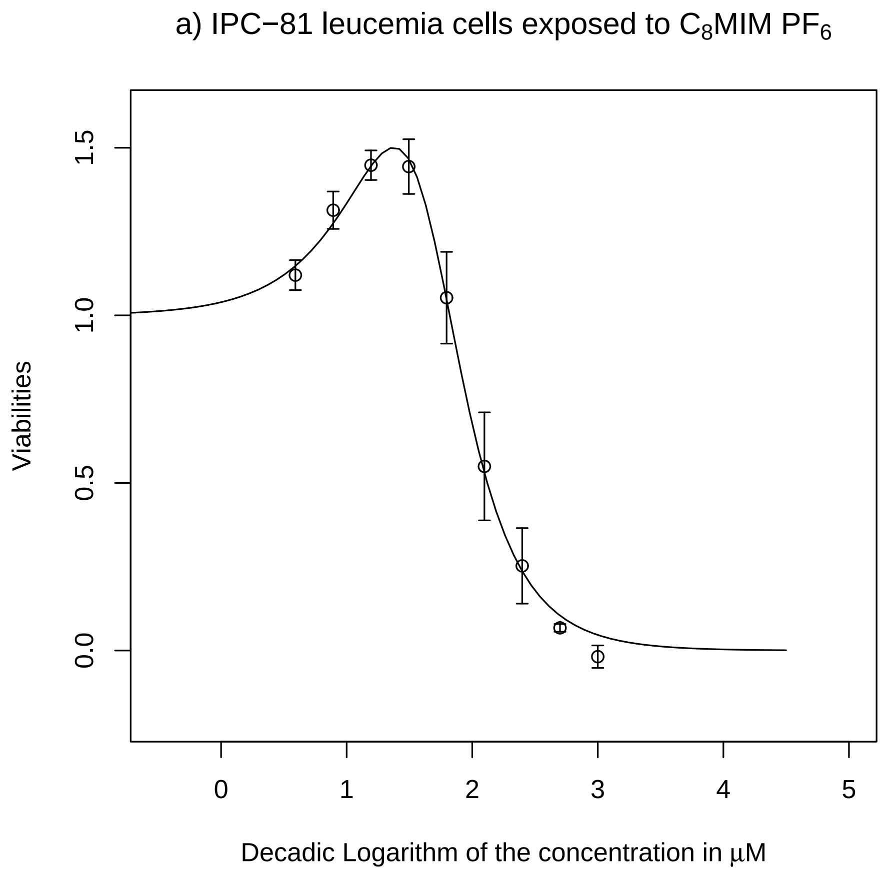






Rat lymphoma cell toxicity

Photometric measurement of the capability to reduce WST-1



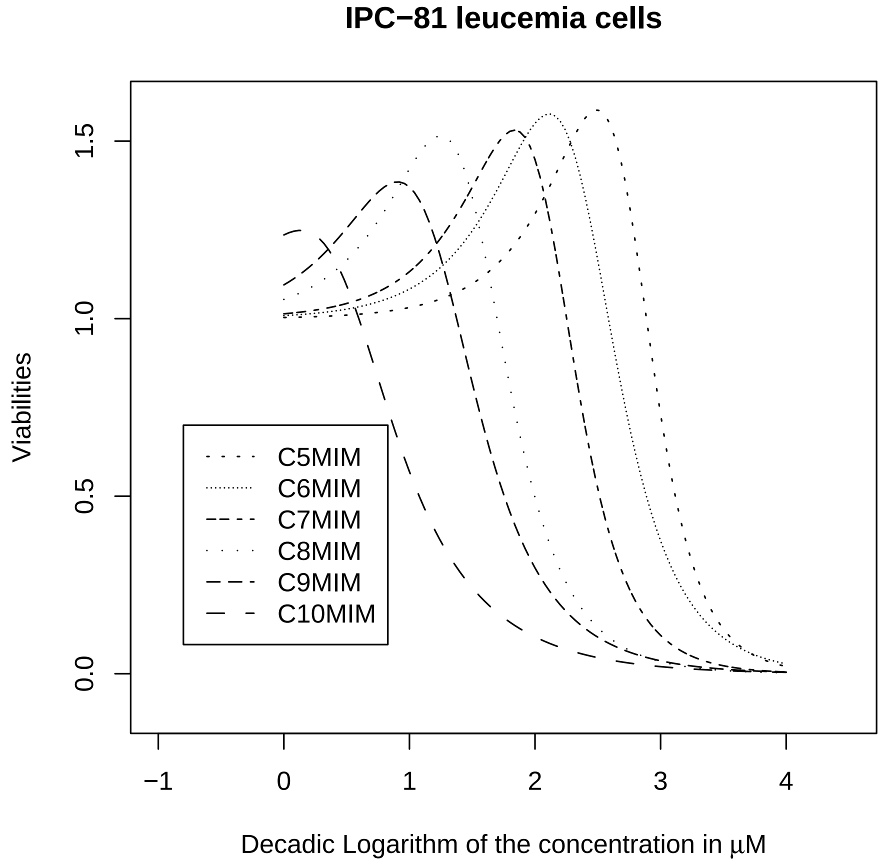
Ranke J, Mölter K, Stock F, Bottin-Weber U, Poczobutt J, Hoffmann J, Ondruschka B, Filser J, Jastorff B (2003) *Ecotoxicol Environ Safety* 58(3) 396-404

Universität Bremen

UFT

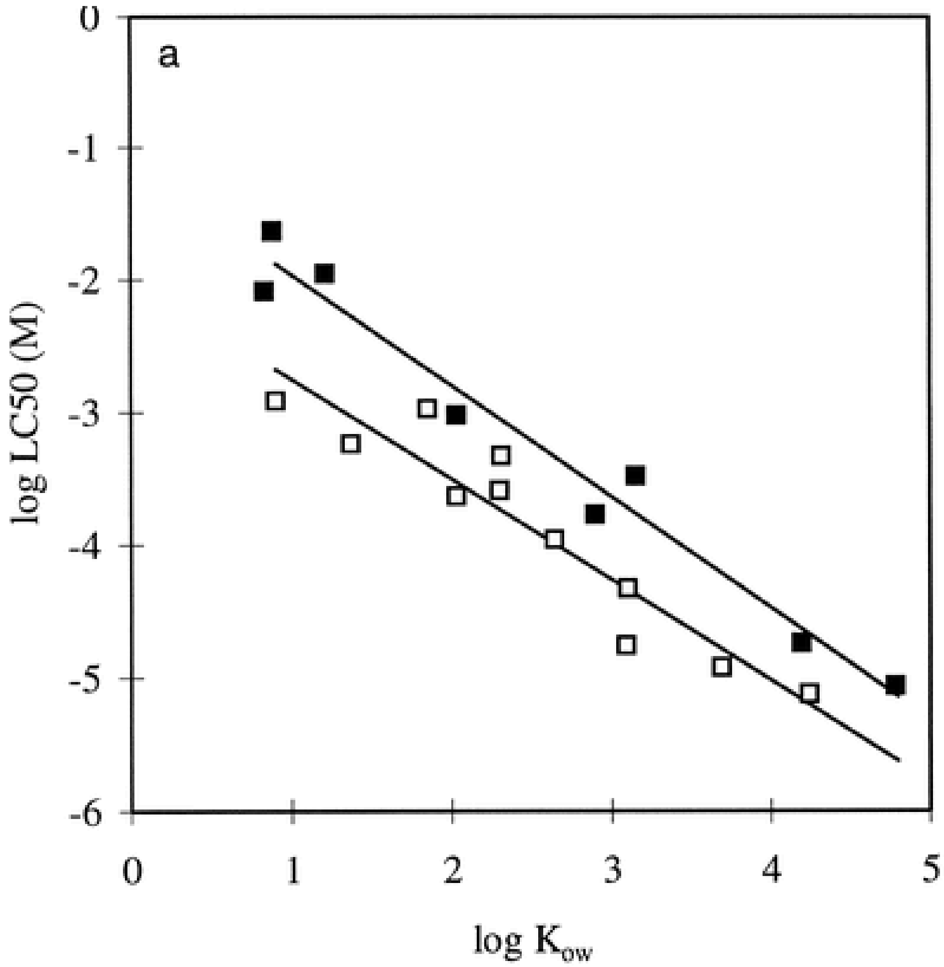
Alkyl chain length and cytotoxicity

$$\log_{10}(EC_{50}) = -0.69 \cdot n_{R1} - 0.31 \cdot n_{R2} + 5.24$$



Ranke J, Mölter K, Stock F, Bottin-Weber U, Poczobutt J, Hoffmann J, Ondruschka B, Filser J, Jastorff B (2003) *Ecotoxicol Environ Safety* 58(3) 396-404

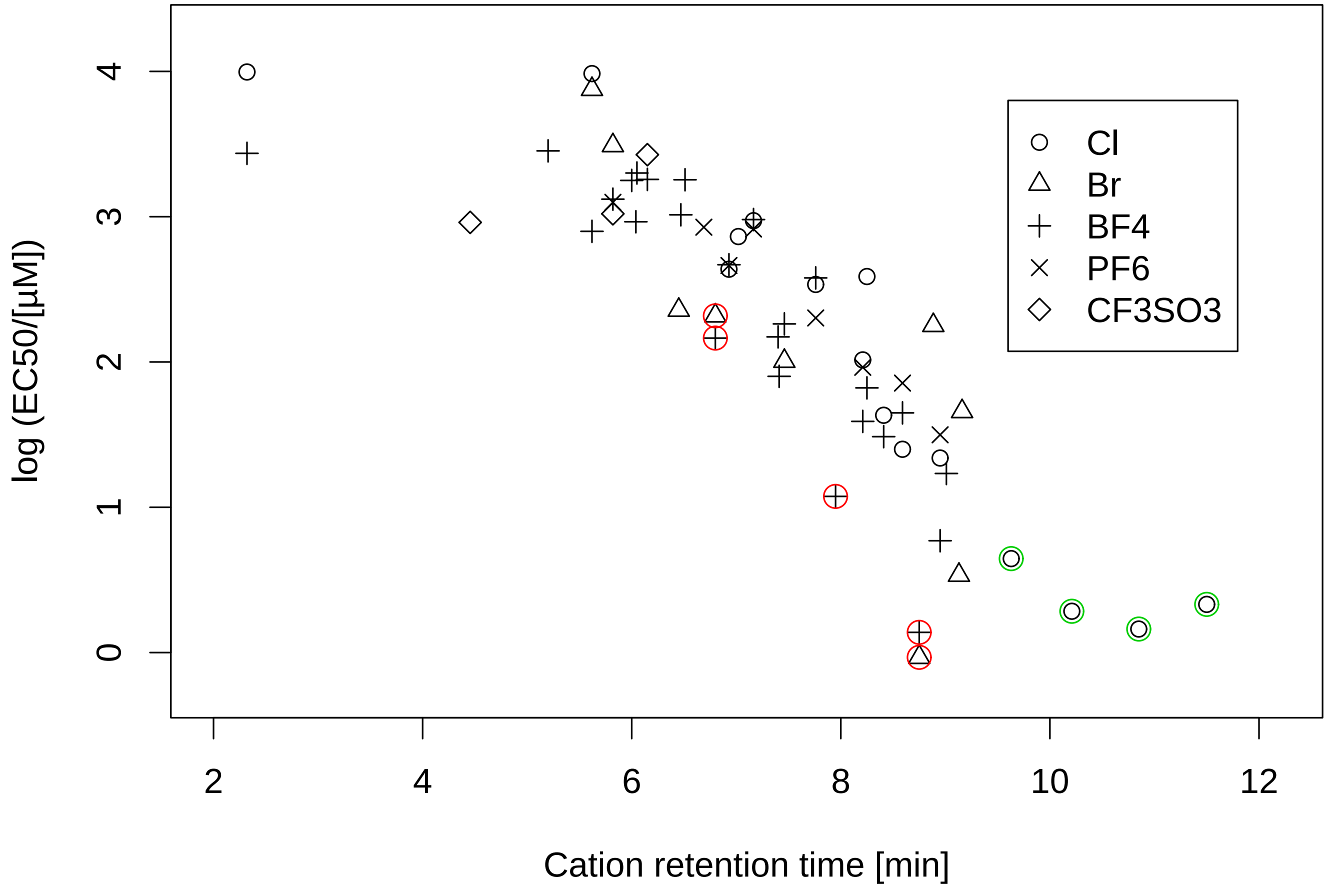
Baseline toxicity for fish



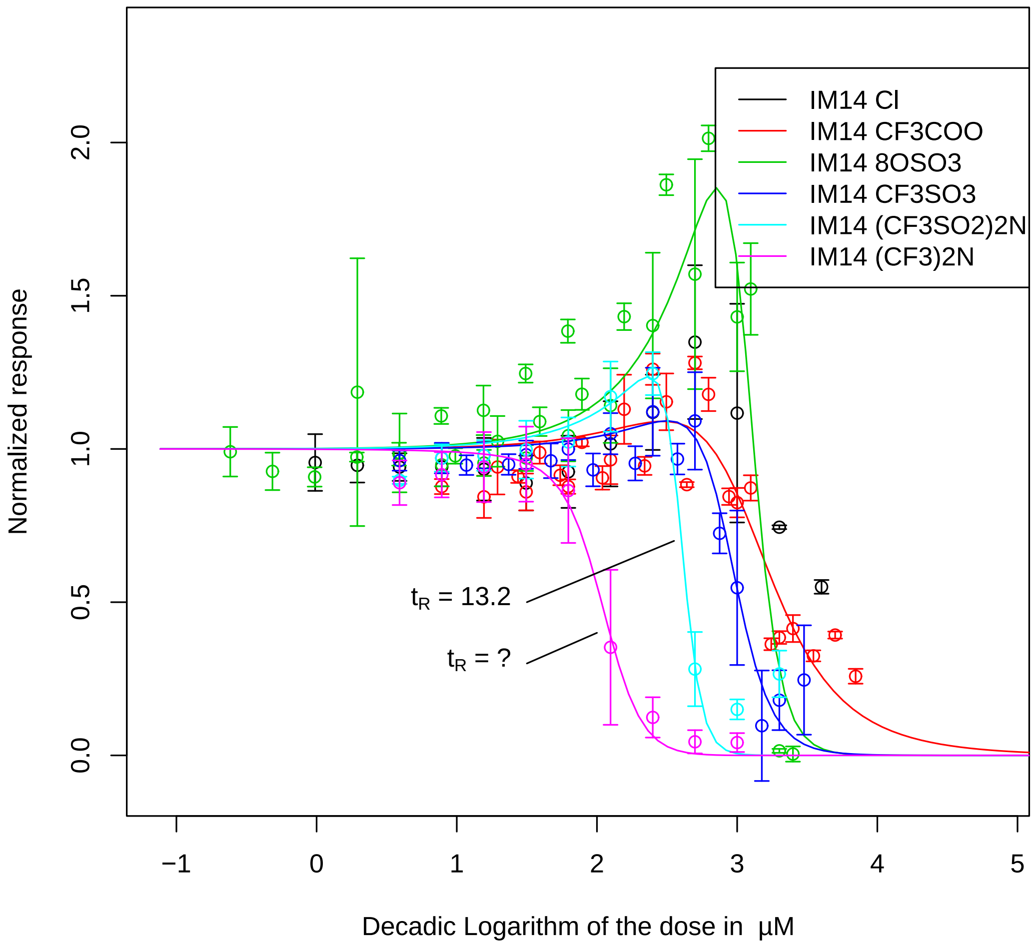
W. Vaes et al. *Environ Toxicol Chem* 17(7) 1380-1384.

Ranke J et al., in preparation

Baseline cytotoxicity

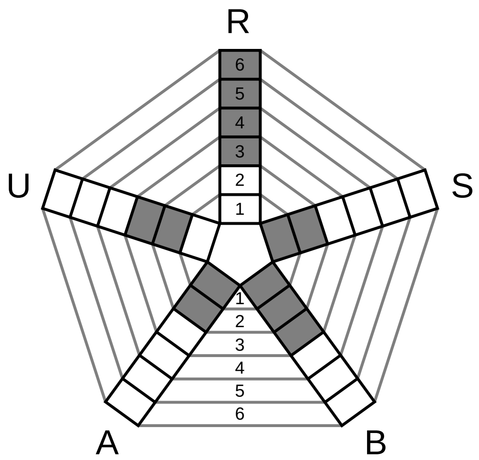


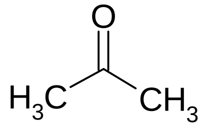
Anion impact



modified after Jastorff et al. (2003) *Green Chem* **5** 136-142

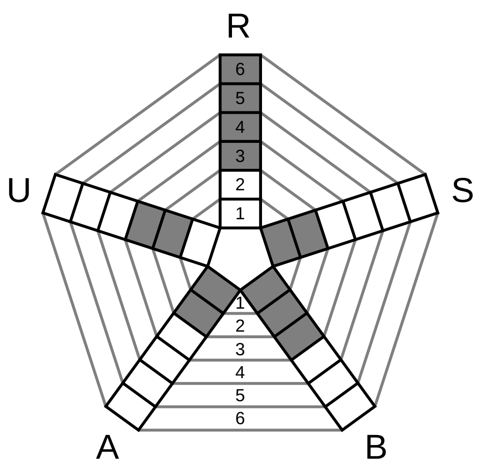
Preliminary risk profiles

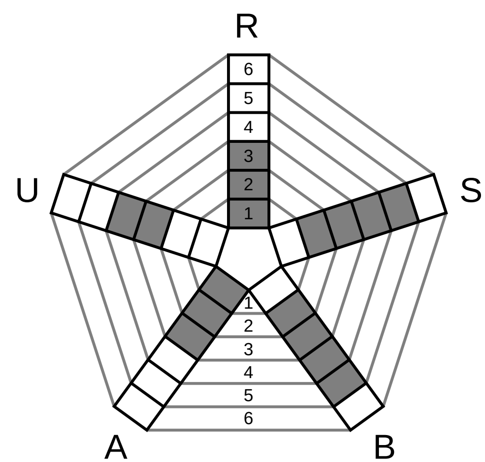


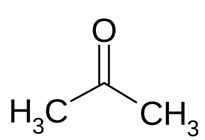


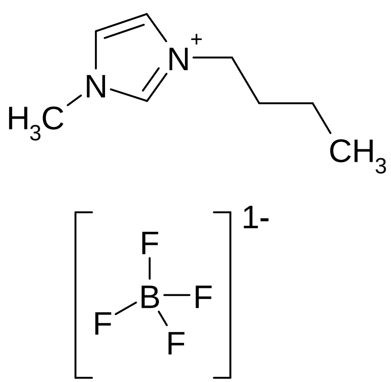
modified after Jastorff et al. (2003) *Green Chem* **5** 136-142

Preliminary risk profiles









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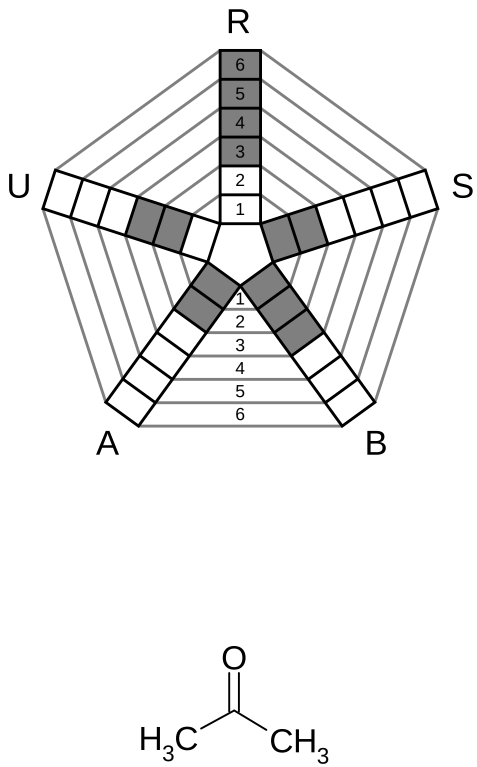
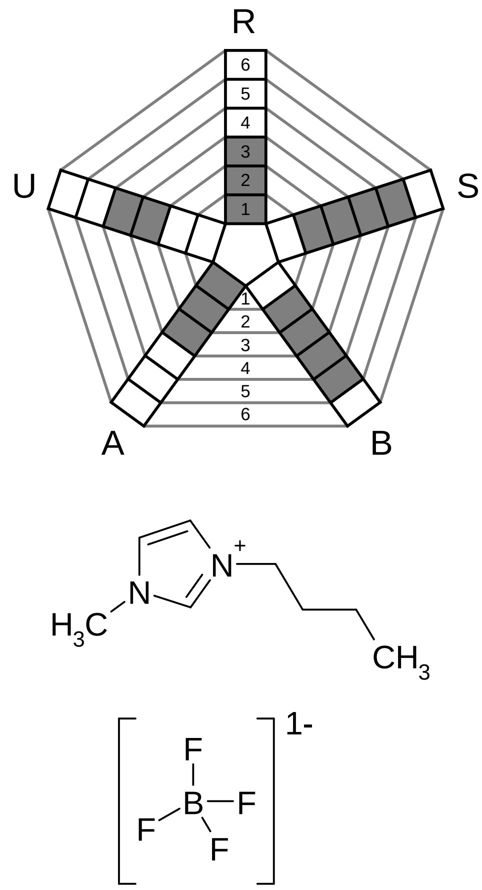
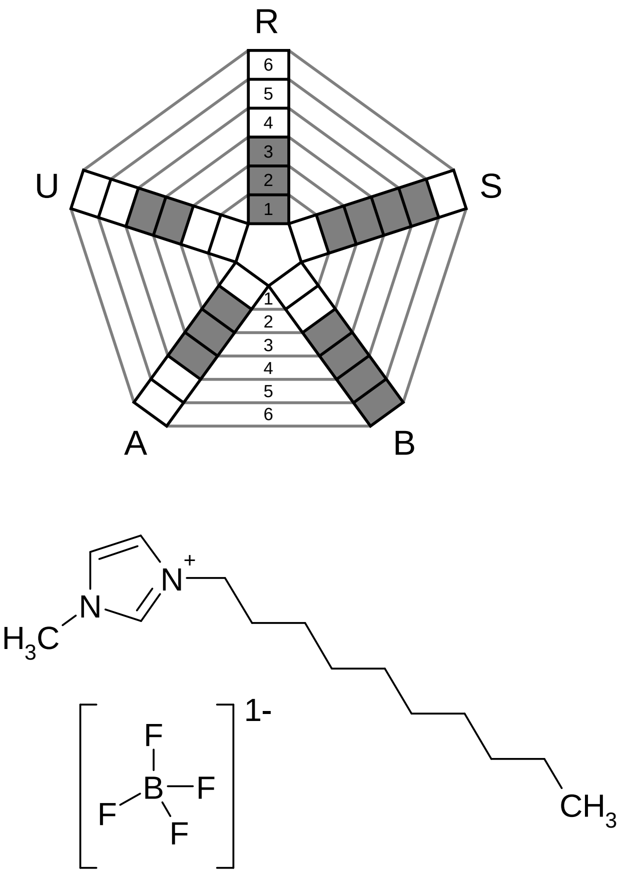
Preliminary risk profiles







Acknowledgments

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