Combined Modeling of Organic Chemical Fate and Human Exposure

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How are we exposed to chemicals indoors?

Indoor Chemical Fate

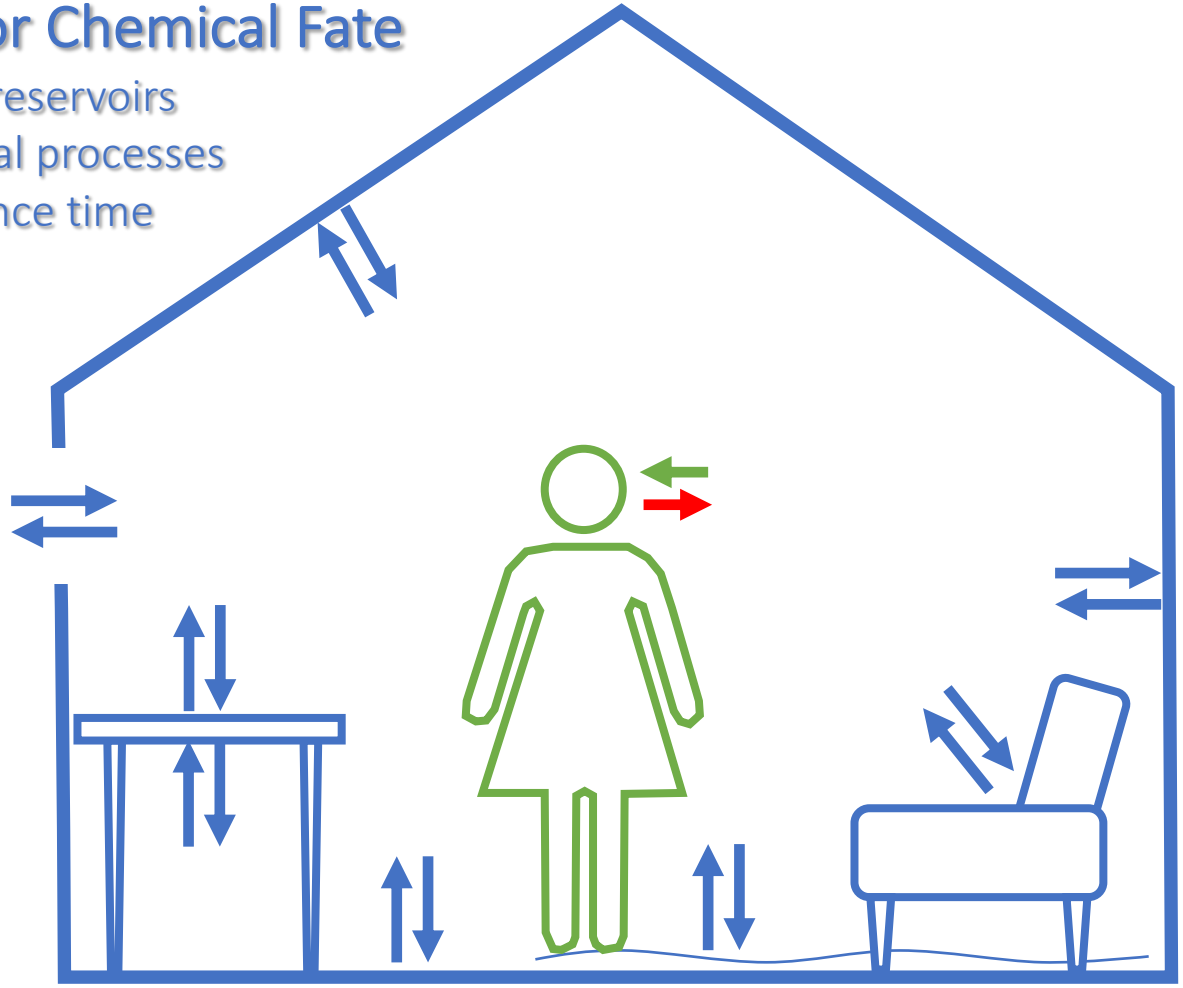
Major reservoirs
Removal processes
Residence time

Pathways of Exposure

Magnitude of exposure
Relative importance of different routes
Variability of exposure (age, behavior)

ADME within the Human

Uptake vs. intake
Internal concentrations
Elimination processes



The number of organic compounds indoors is very large

- Deliberately released (air fresheners, disinfectants, perfume, etc.)
- Inadvertently released from articles, products and building materials
- Inadvertently released during human activities (cleaning, cooking, smoking)
- Imported from outside
- Produced by reactions of other compounds

Could potentially be 10,000s of individual chemicals

Can we address this question comprehensively?

The central importance of phase distribution

Release

Product, Article, Material ←→ Gas phase

Indoor Fate

Surfaces/surface films (textiles, furniture, etc.) ←→ Gas phase

Human Exposure

Suspended particles ←→ Gas phase

Settled dust ←→ Gas phase

Surface films ←→ Settled dust

Skin ←→ Gas phase

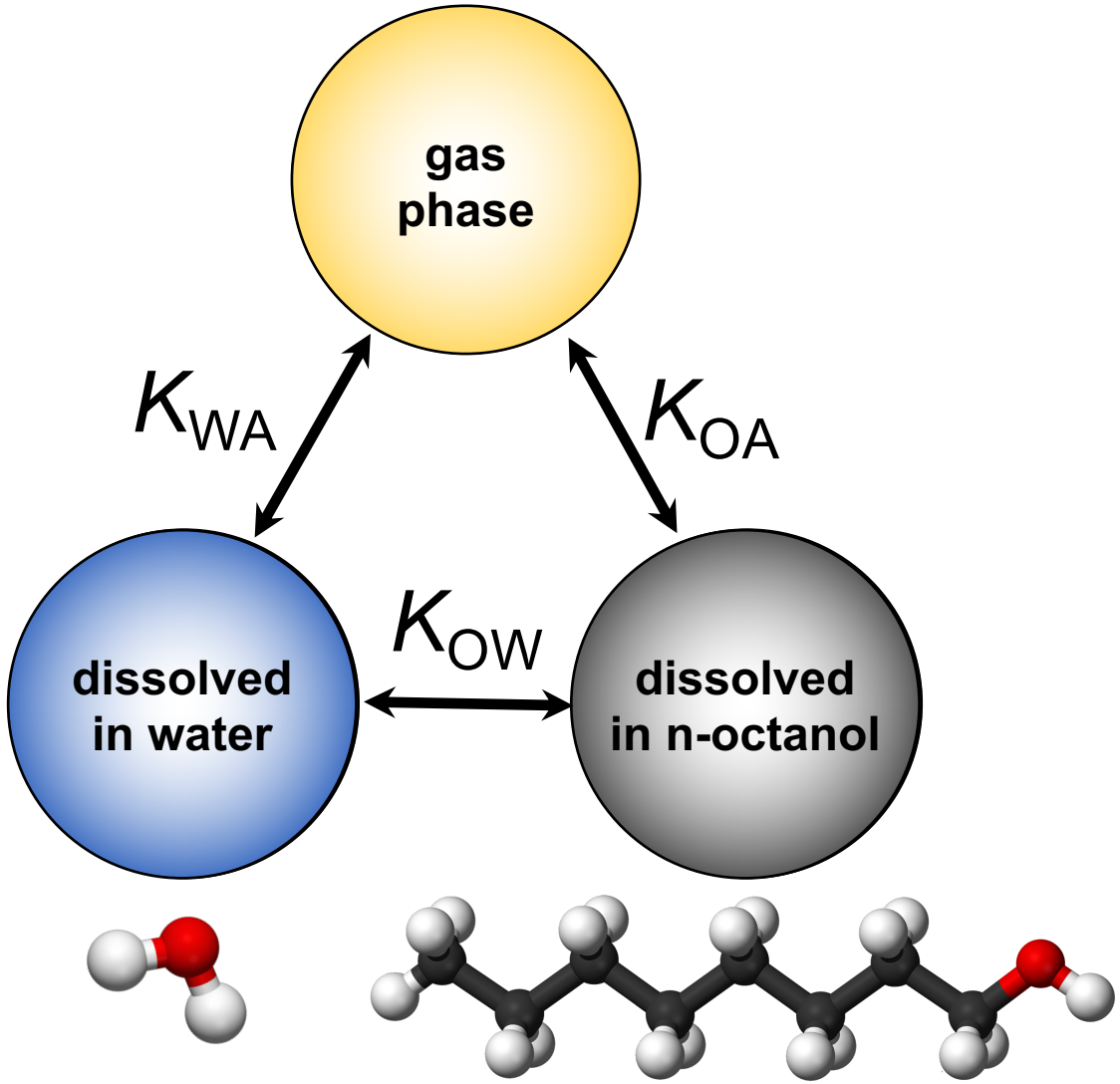
Fate within the Human

Blood ←→ Gas phase

Blood ←→ Urine

Blood ←→ Tissues (fat, liver, etc.)

Simplifying Phase Partitioning



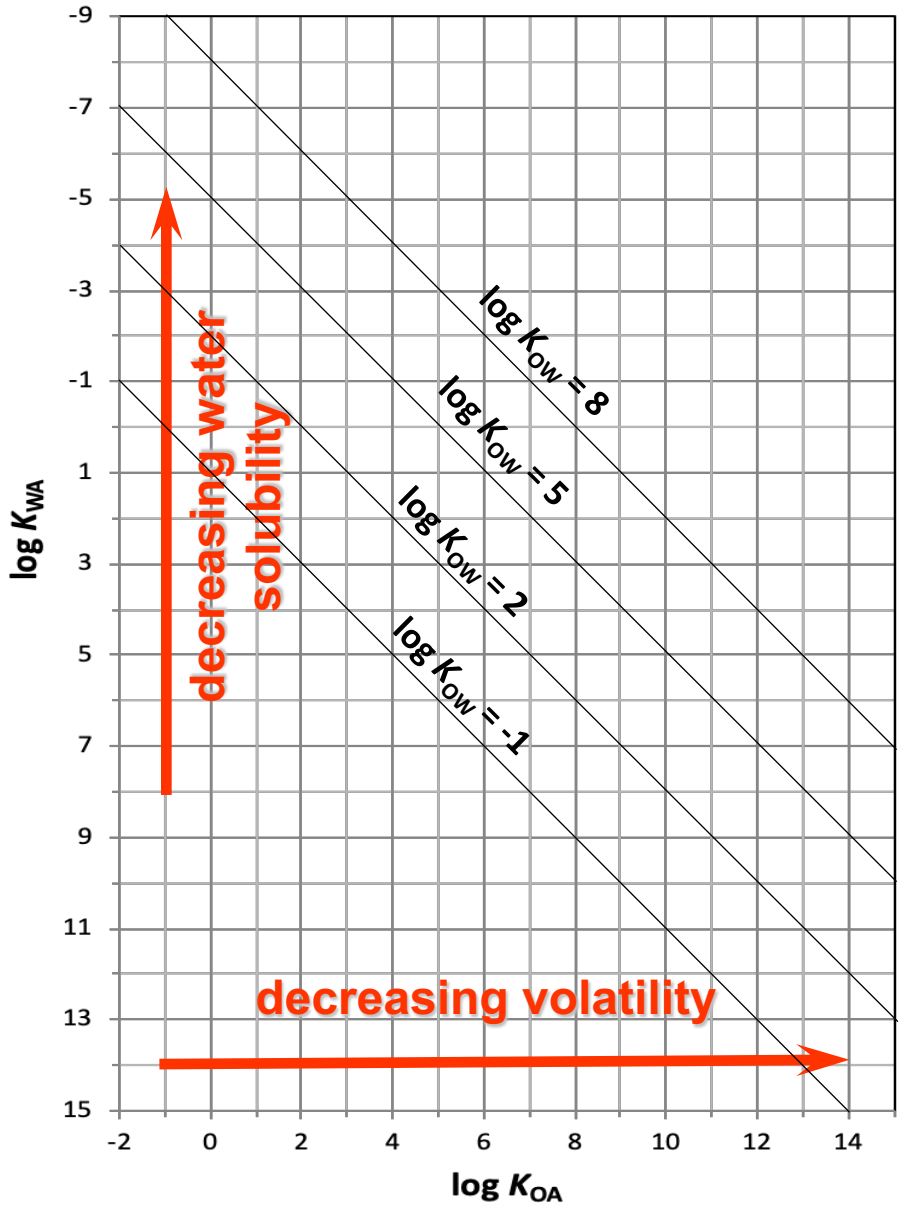
Linear free energy relationship relate partitioning coefficients with each other:

$\log K_{X\text{-}Gas} = m \cdot \log K_{OA} + b$

X = carpet, flooring, dust, suspended particles, surfaces, surface films, etc.

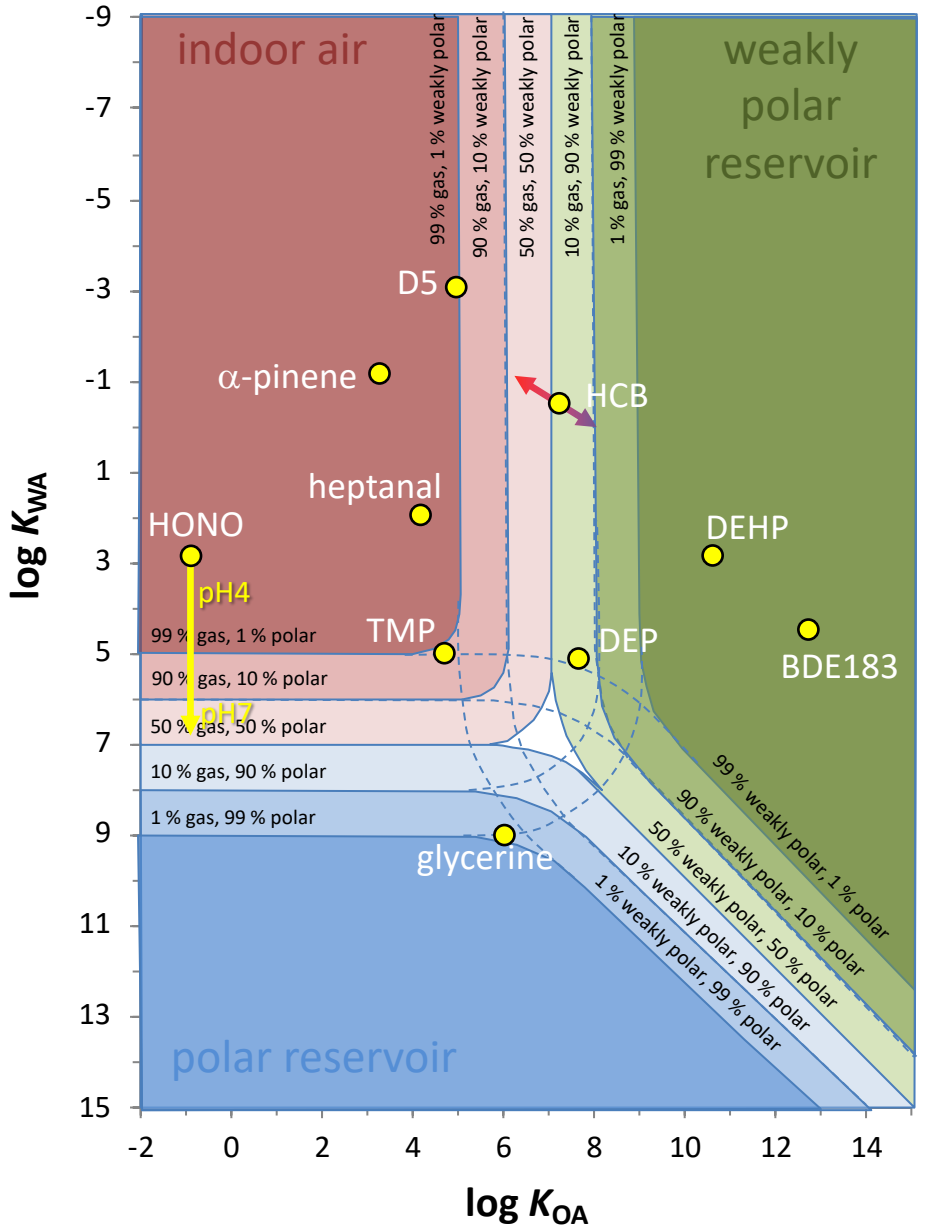
Every chemical's basic phase distribution preferences encoded with 2 of these 3 partitioning coefficients

The Chemical Partitioning Space



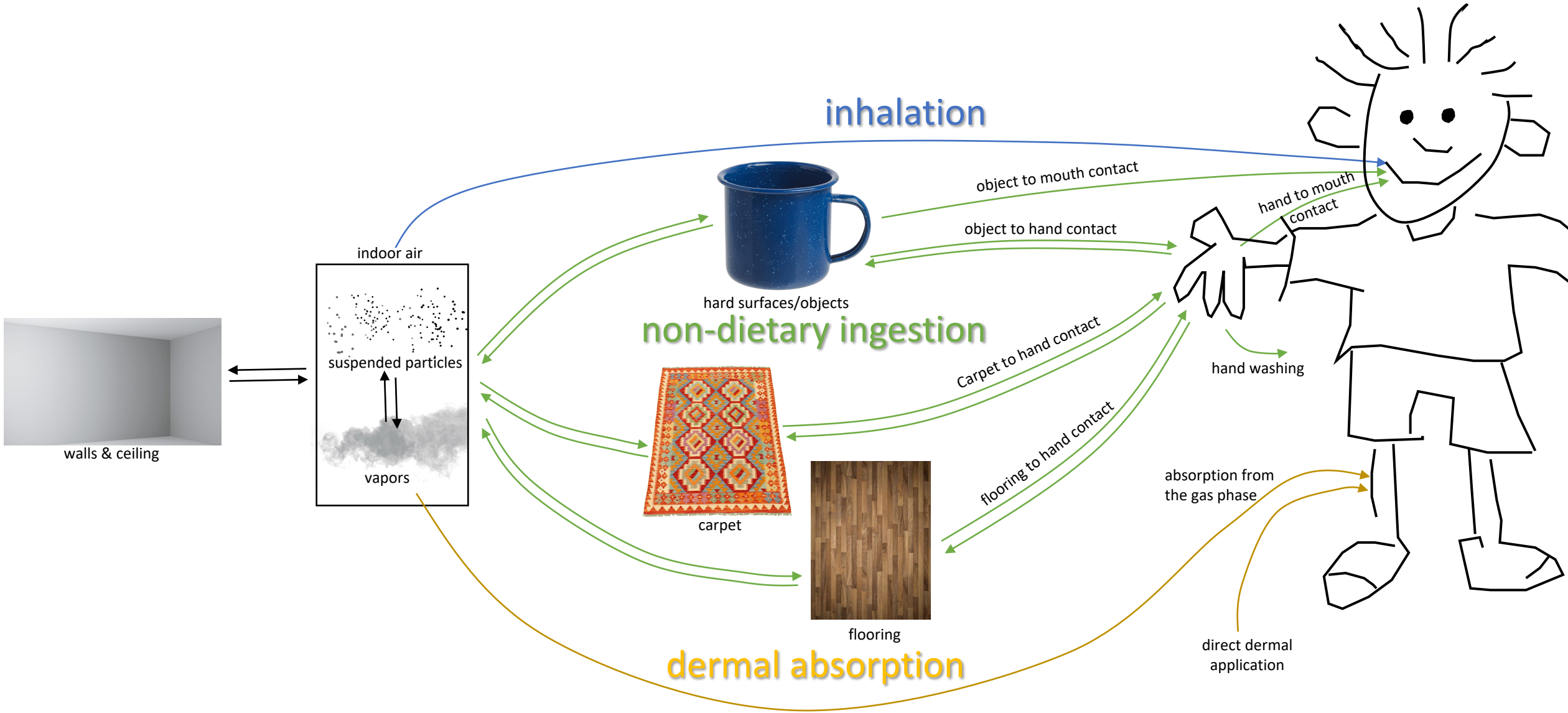
Indoor Fate

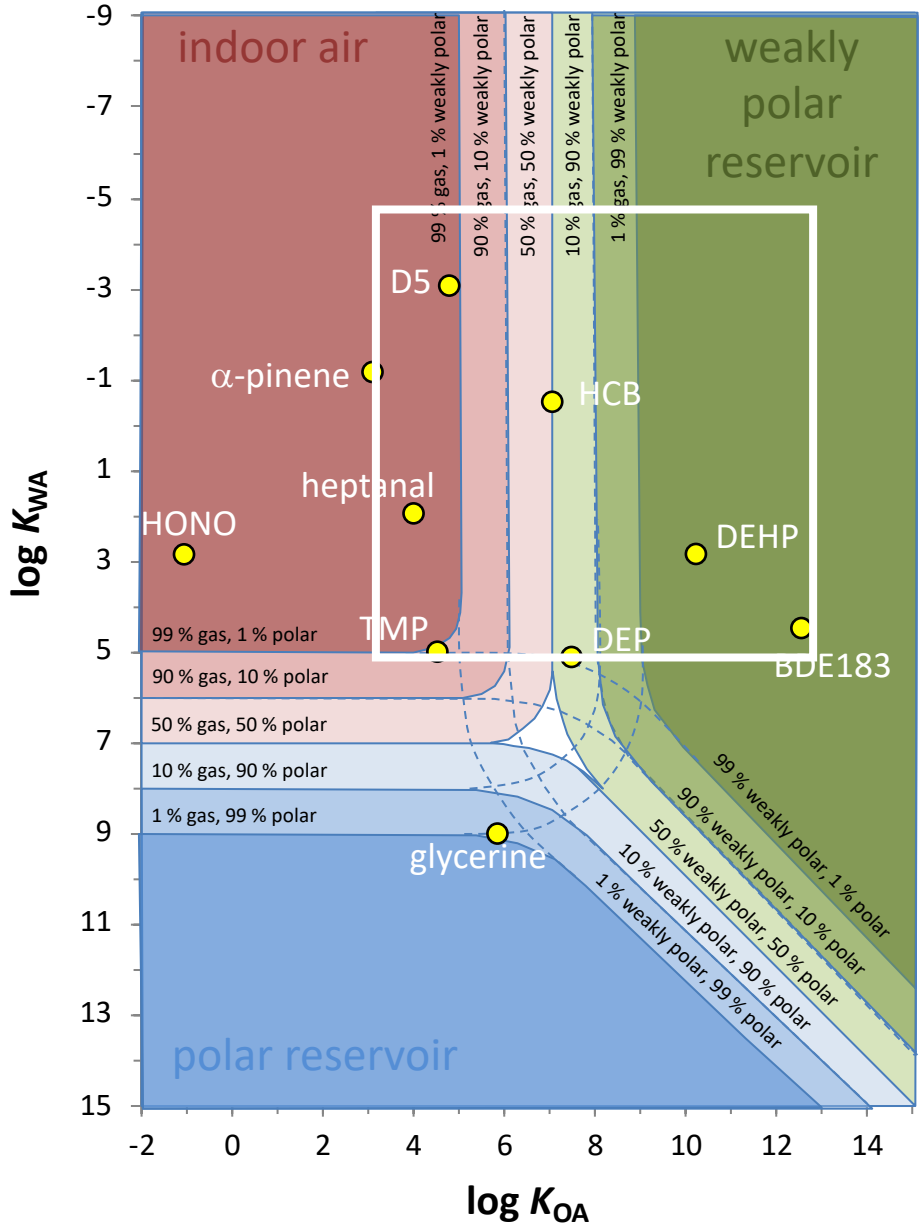
- Estimate size of the water- and octanol-like reservoirs within an indoor environment
- Assume equilibrium partitioning
- Predict phase distribution within the indoor environment by placing chemicals in the partitioning space based on their log K_{OA} and log K_{WA}
- Explore impact of temperature change, acid/base dissociation and pH of water-like reservoir



Wang, C. et al., *Sci. Adv.* **2020**, 6: eaay8973

Simulating Indoor Exposure




indoor air
weakly polar reservoir
polar reservoir
99 % gas, 1 % weakly polar
90 % gas, 10 % weakly polar
50 % gas, 50 % weakly polar
10 % gas, 90 % weakly polar
1 % gas, 99 % weakly polar
D5
α-pinene
HCB
heptanal
HONO
DEHP
TMP
DEP
BDE183
glycerine
99 % gas, 1 % polar
90 % gas, 10 % polar
50 % gas, 50 % polar
10 % gas, 90 % polar
1 % gas, 99 % polar
99 % weakly polar, 1 % polar
90 % weakly polar, 10 % polar
50 % weakly polar, 50 % polar
10 % weakly polar, 90 % polar
1 % weakly polar, 99 % polar
log K_{WA}
log K_{OA}
-9
-7
-5
-3
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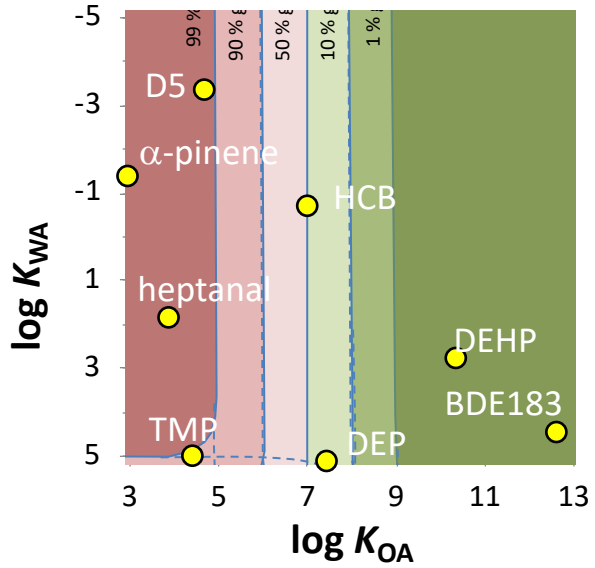
-2
0
2
4
6
8
10
12
14


-5
-3
-1
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3
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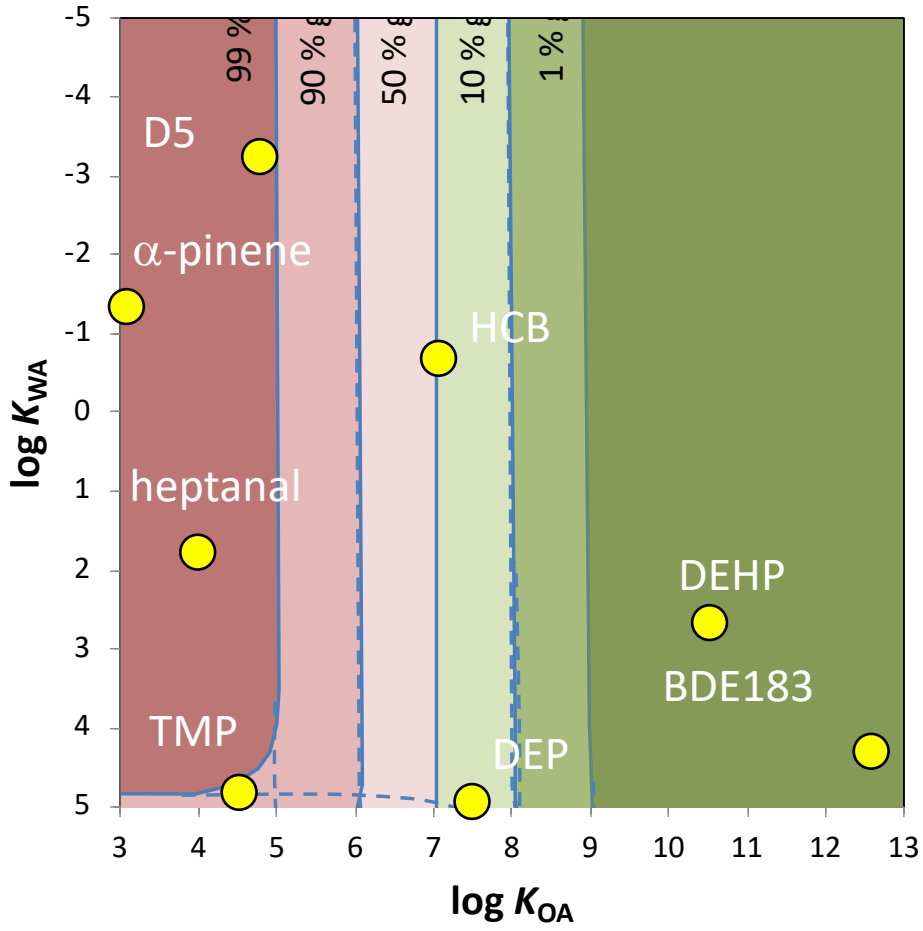
3
5
7
9
11
13
log K_{WA}
log K_{OA}
99 %
90 %
50 %
10 %
1 %
D5
α-pinene
HCB
heptanal
DEHP
BDE183
TMP
DEP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α-pinene
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heptanal
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log K_{WA}
log K_{OA}
-5
-4
-3
-2
-1
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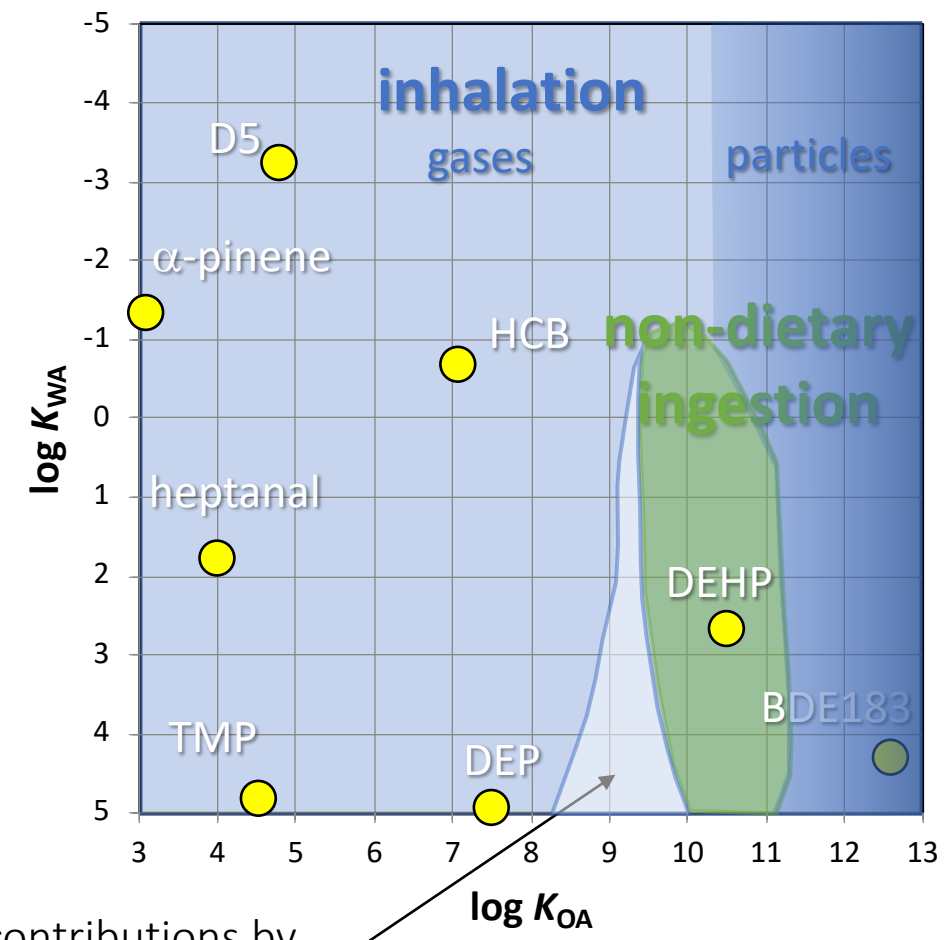
Dominant Indoor Exposure Pathway (> 50%)



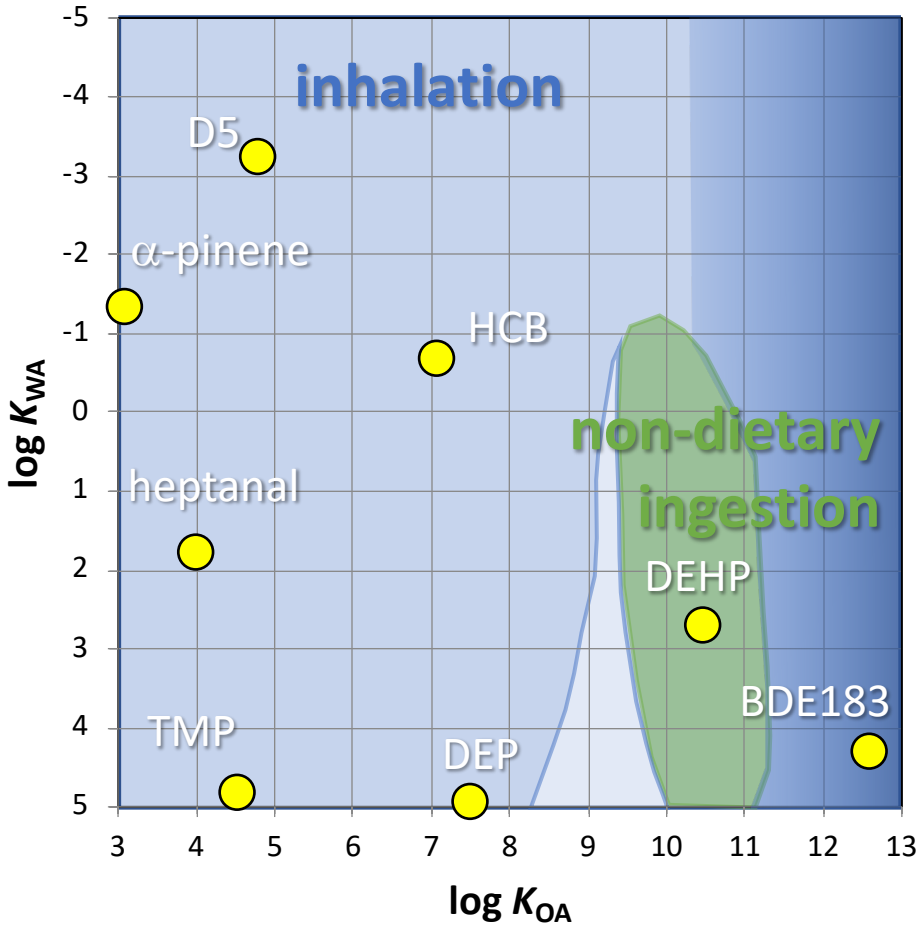
notable contributions by inhalation, non-dietary ingestion and dermal uptake

- Indoor exposure to most property combinations is by inhalation
- Dermal absorption is relevant for few property combinations
- While non-dietary ingestion is dominant for relatively few property combinations, this exposure route can be very efficient (dust and organic residue act as accumulation medium)

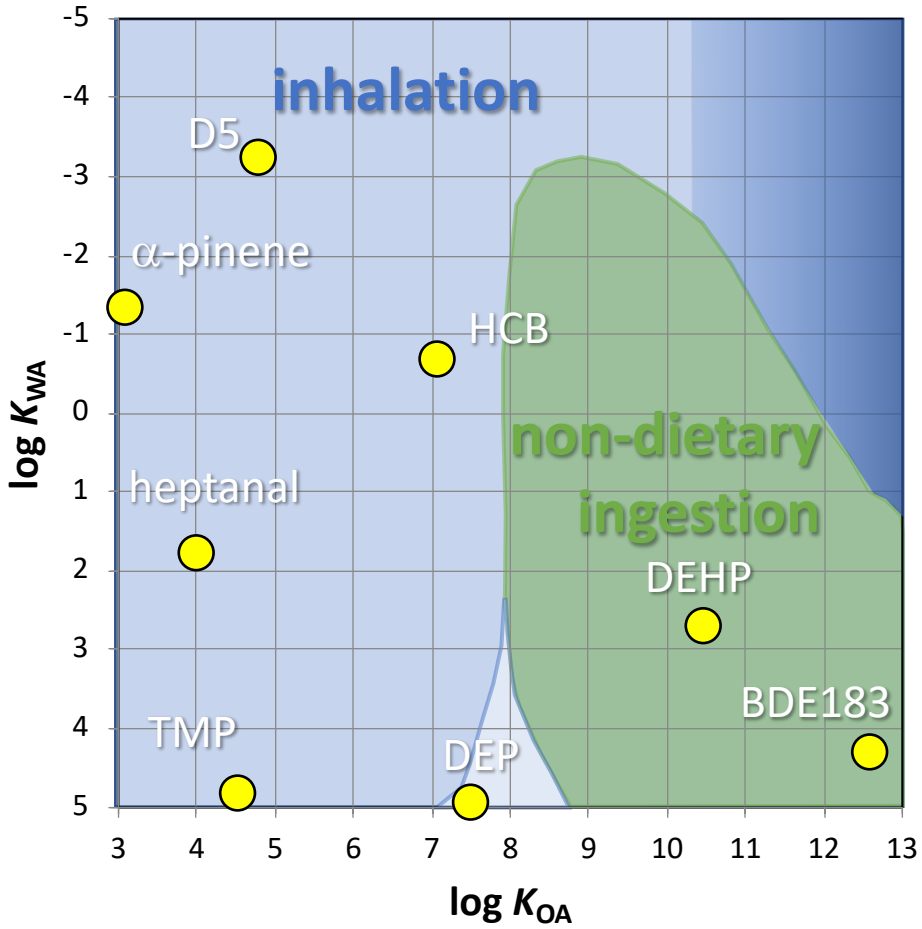
Li et al. *Environ. Sci. Technol.* **2019**, *53*, 11276−11284

Dominant Indoor Exposure Pathway (> 50%)

Adults

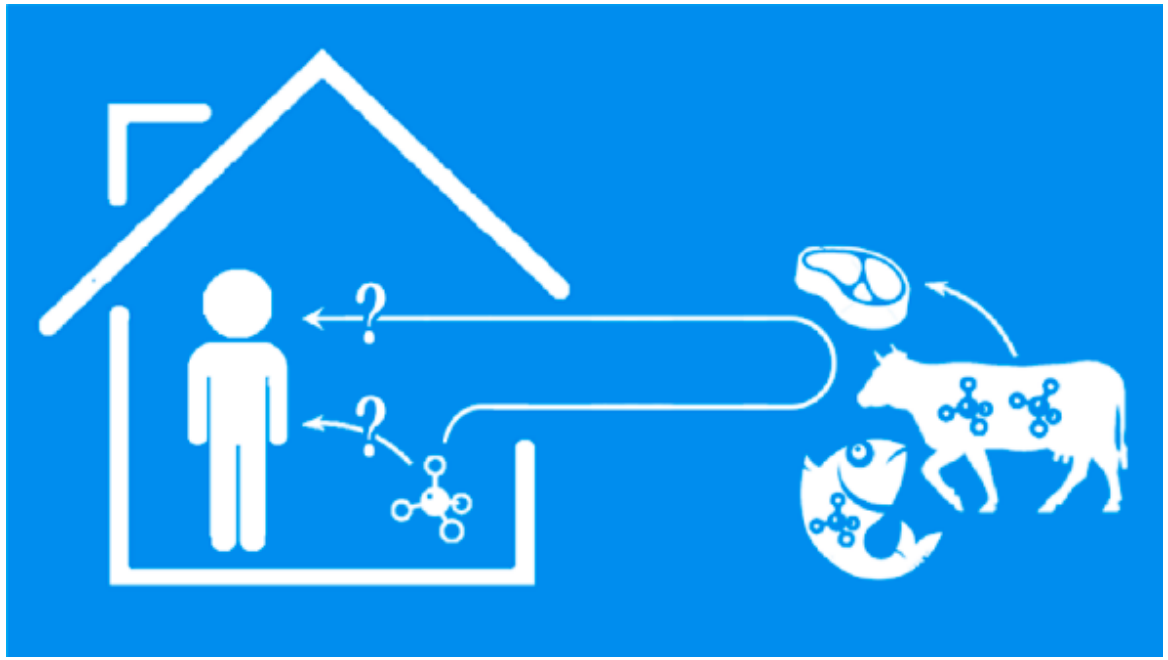


Children



Non-dietary ingestion dominates for a wider range of compounds in children

Chemicals released indoors may also accumulate in human food-chains



What contribution does dietary intake make to human exposure?

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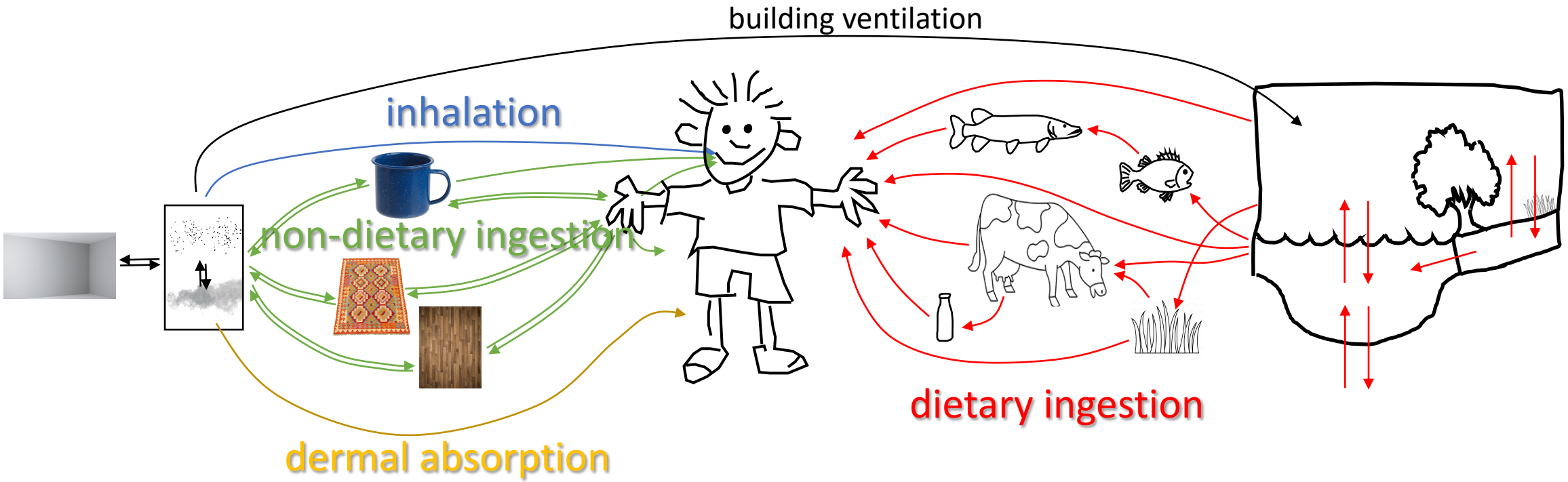
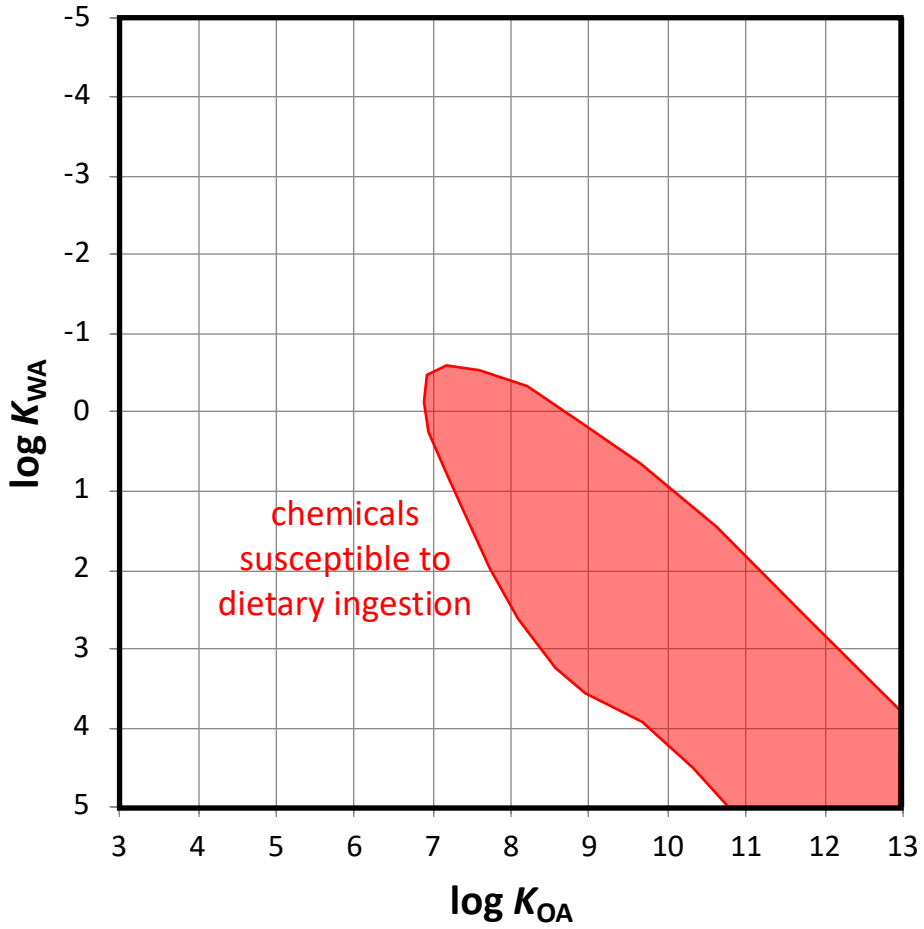
Simulating Indoor **and Dietary** Exposure



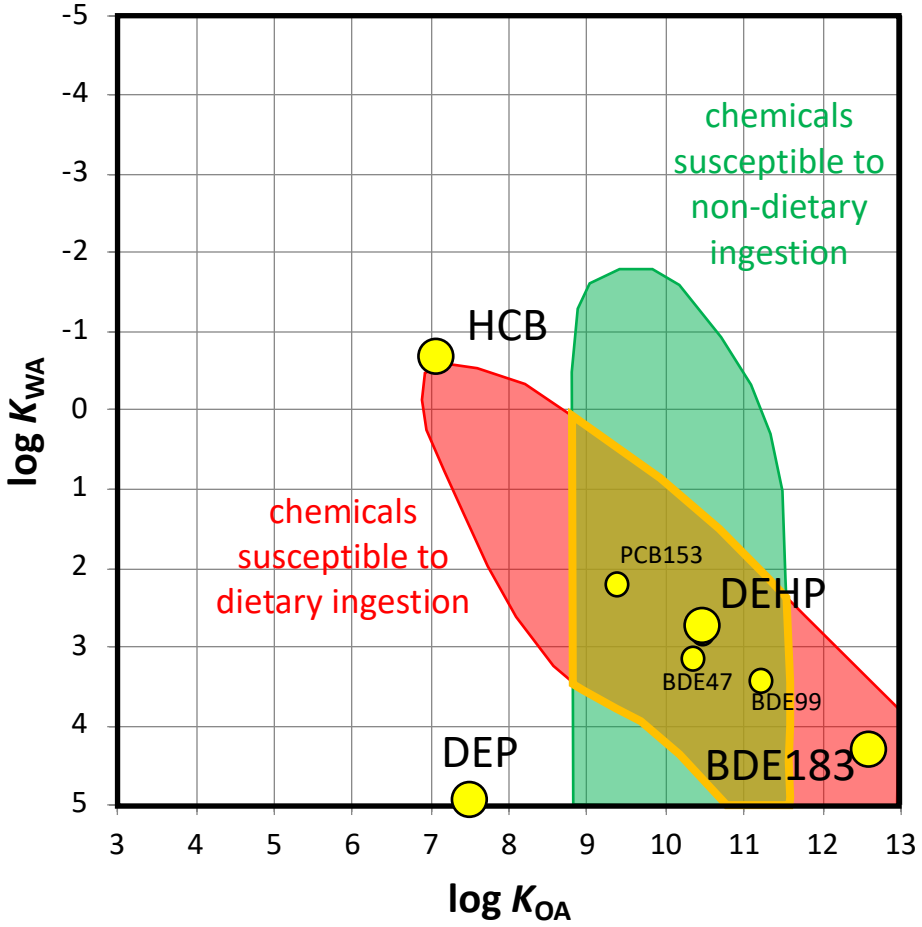
Combination of partitioning properties allowing for efficient human food chain bioaccumulation



Intermediate log K_{OW}
log K_{OA} > 6

Czub and McLachlan, *Environ. Sci. Technol*. **2004**, *38*, 2406−2412.

Combination of partitioning properties leading to dietary and non-dietary ingestion overlap



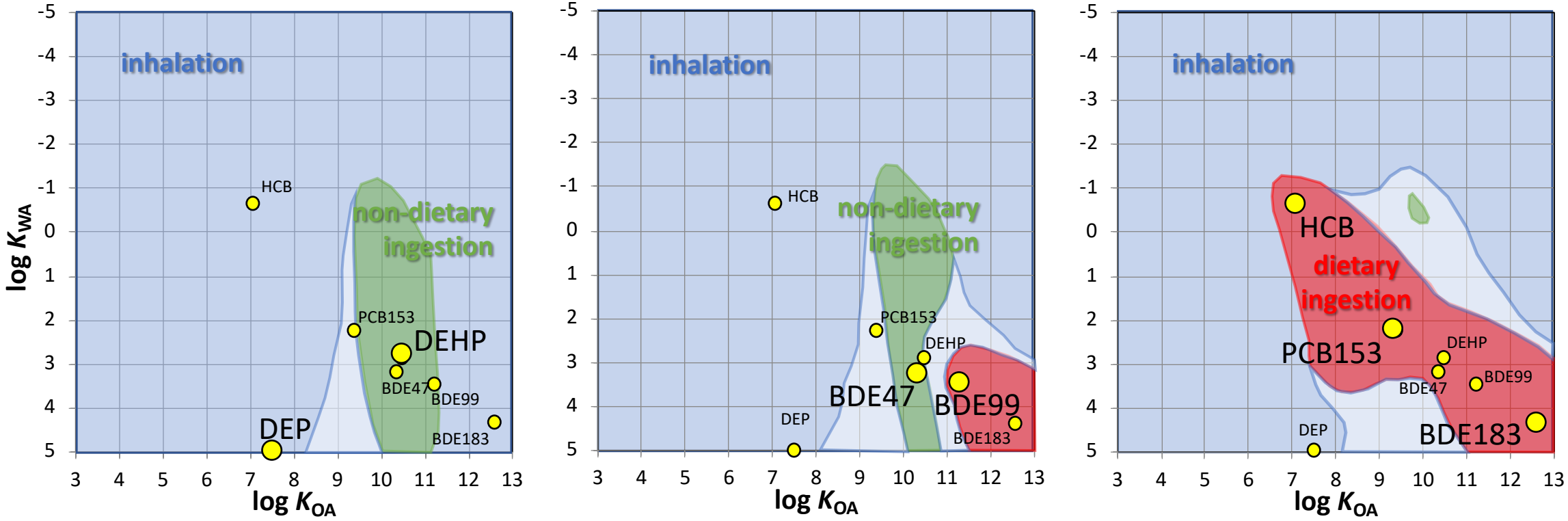
Which ingestion pathway dominates?

Dominant ingestion pathway depends on persistence

Degrades in air and outdoor surface media within a matter of days

Degrades in air within a matter of weeks, but is persistent in outdoor surface media

Persistent in air and outdoor surface media



Dietary ingestion of chemicals released indoors is only important if they are sufficiently persistent to reach, and accumulate in human food webs

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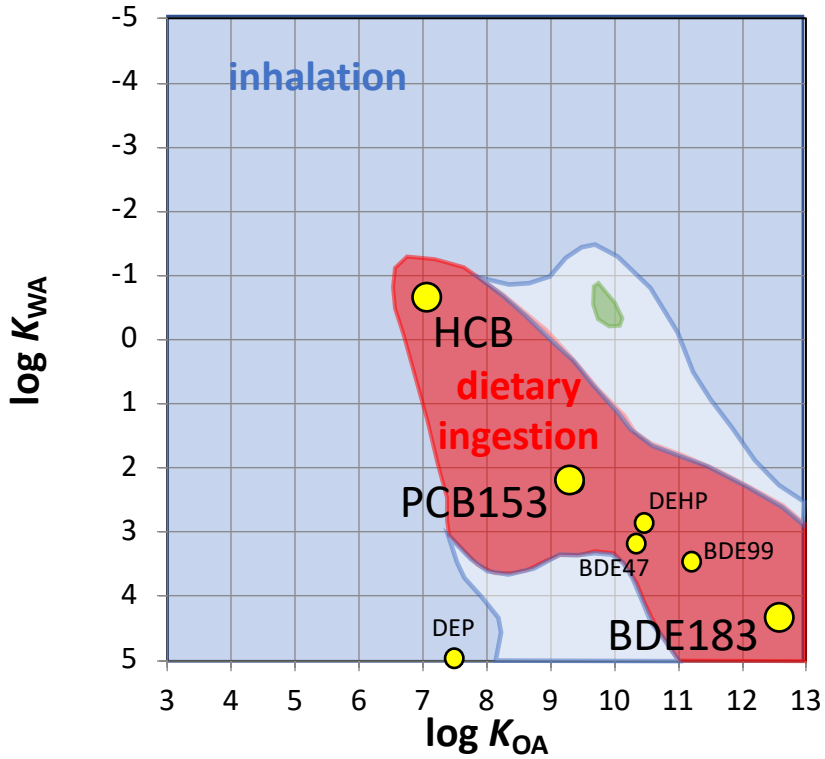
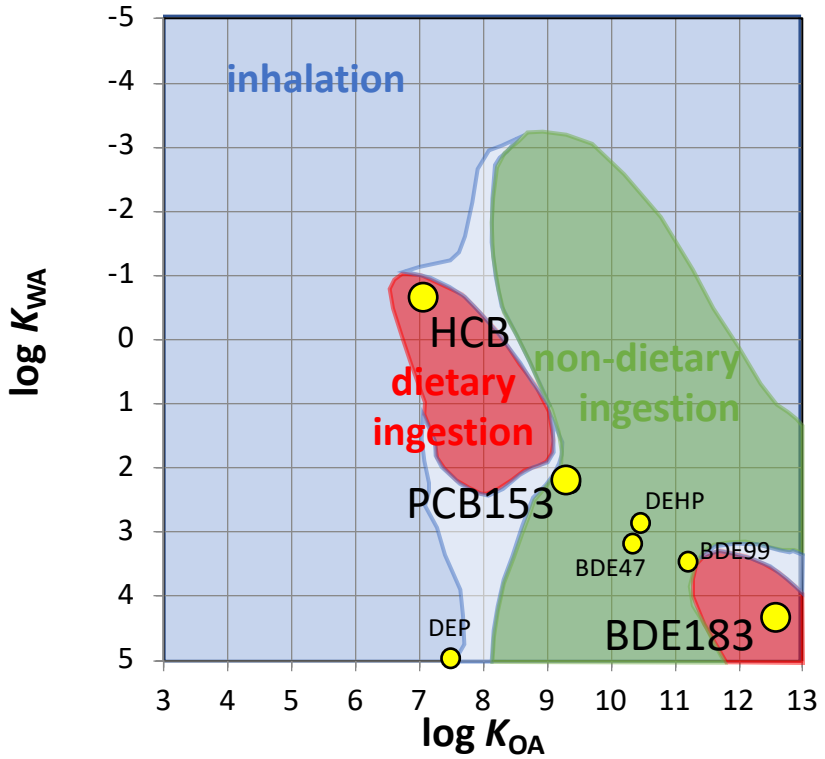
Dominant ingestion pathway of persistent chemicals depends on age

Adults



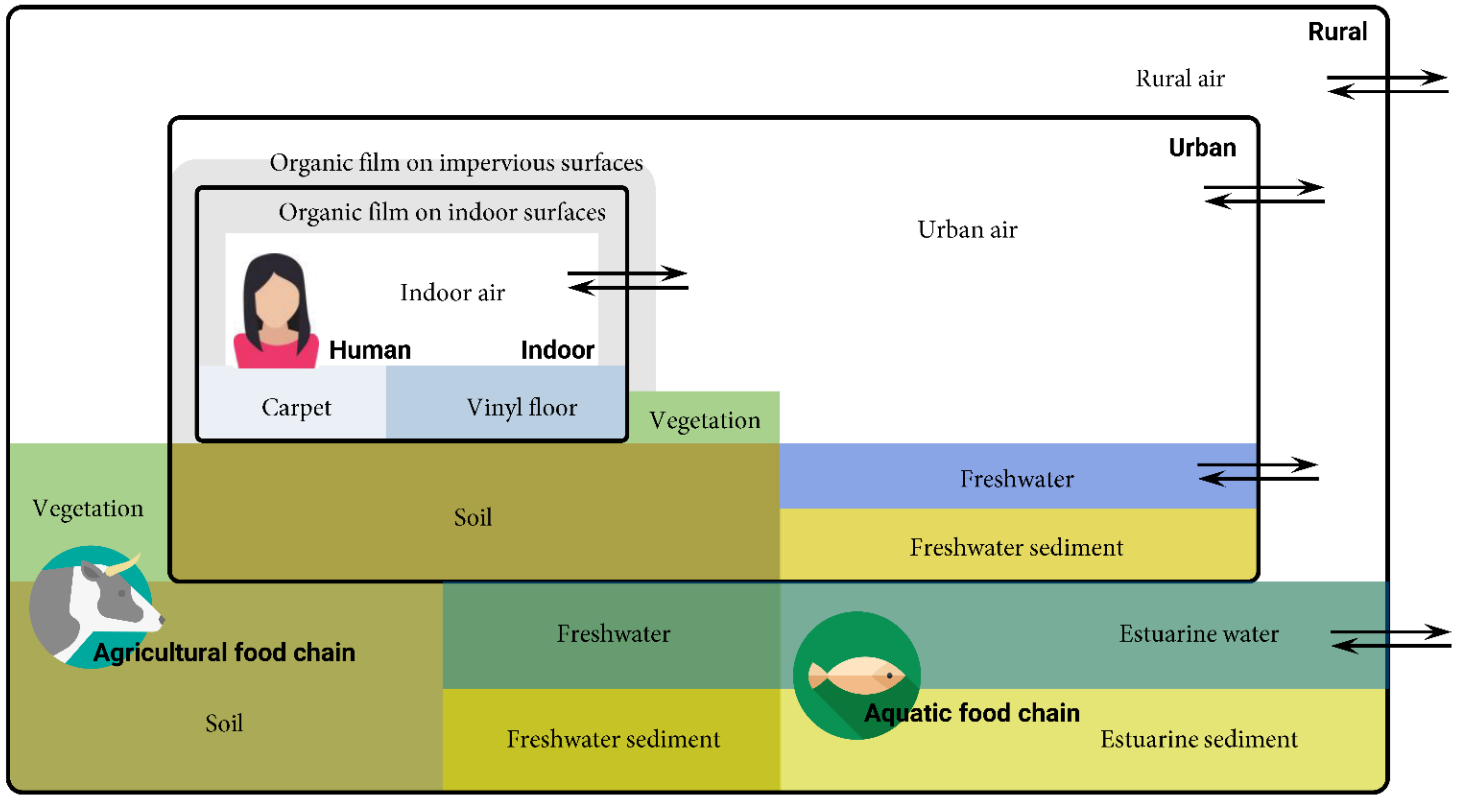
Children



Still Valid: Non-dietary ingestion dominates for a wider range of compounds in children

Li et al. *Environ. Sci. Technol.* **2019**, *53*, 11276−11284

PROduction To EXposure (PROTEX) Model



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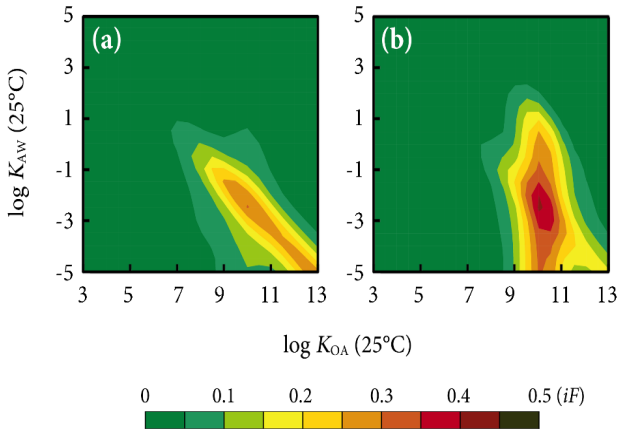
PROTEX can also calculate

- Absolute intake
- Internal exposure

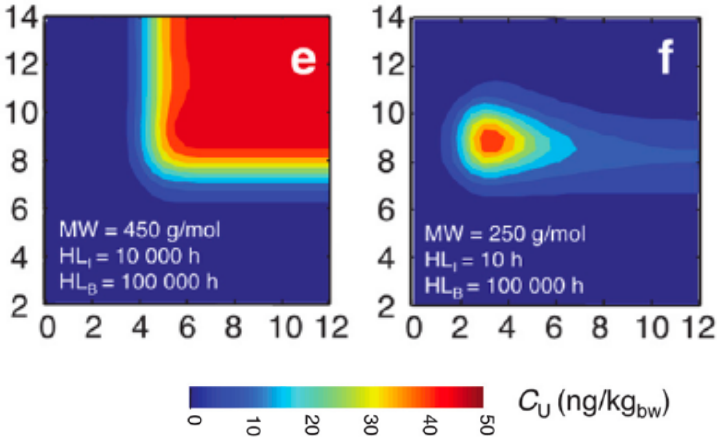
relative to rate of release

intake fractions



Li et al. *Environ. Sci. Technol.* **2019**, *53*, 11276−11284

concentrations within human



Zhang et al. *Environ. Sci. Technol.* **2014**, *48*, 12312−12319.

Time-variant simulations using actual chemical properties of a chemical

High-throughput simulations for large number of chemicals

Example Applications

Explain difference in time trends of PBDE concentrations in human biomonitoring studies

between different congeners

between different age classes

Li et al. *Environ. Sci. Technol.* **2020**, *54*, 166−175

Estimate health risk associated with the use of disinfectants

Li et al. Environ. Int. **2020,** *145*, art. 106108

High-throughput screening and prioritization of synthetic chemicals based on ecological or human exposure and resulting risks

Li et al. Development and evaluation of a holistic and mechanistic modeling framework for chemical emissions, fate, exposure, and risk. Submitted **2021**

Knowledge Gap

Mechanistic understanding of fate and exposure processes

- e.g., air-mediated transport of chemicals vs. direct migration from material to air
- indoor surface compartments as "sinks" vs. "sources" of chemicals indoors

Uncertainty in parameterizations

- Environment: Indoor settings
- Human: Human behavior and activities (diet, touching, cleanup, etc.)
- Chemical: Polar and ionizable organic chemicals; chemicals liable to ozonation, hydrolysis, photolysis, etc.

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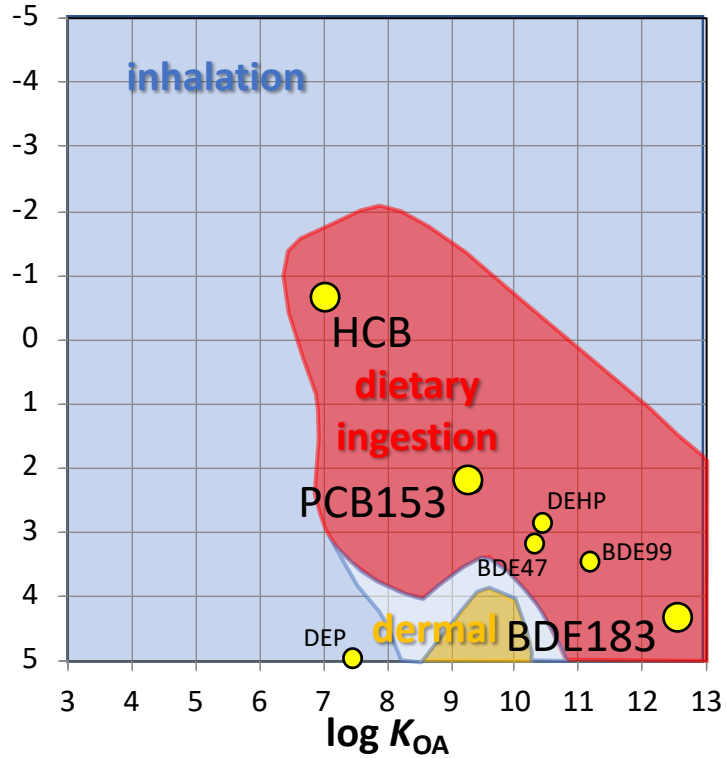
Dominant ingestion pathway of persistent chemicals depends on

cleanliness

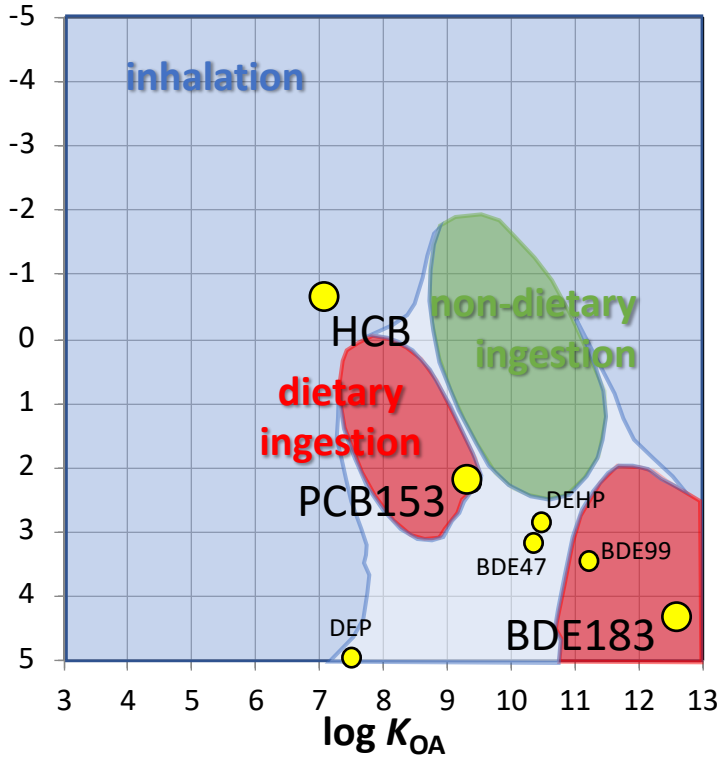
frequently cleaned house,
frequent hand-washing



House cleaning and personal hygiene can decrease rates of non-dietary ingestion

diet

vegetarian diet

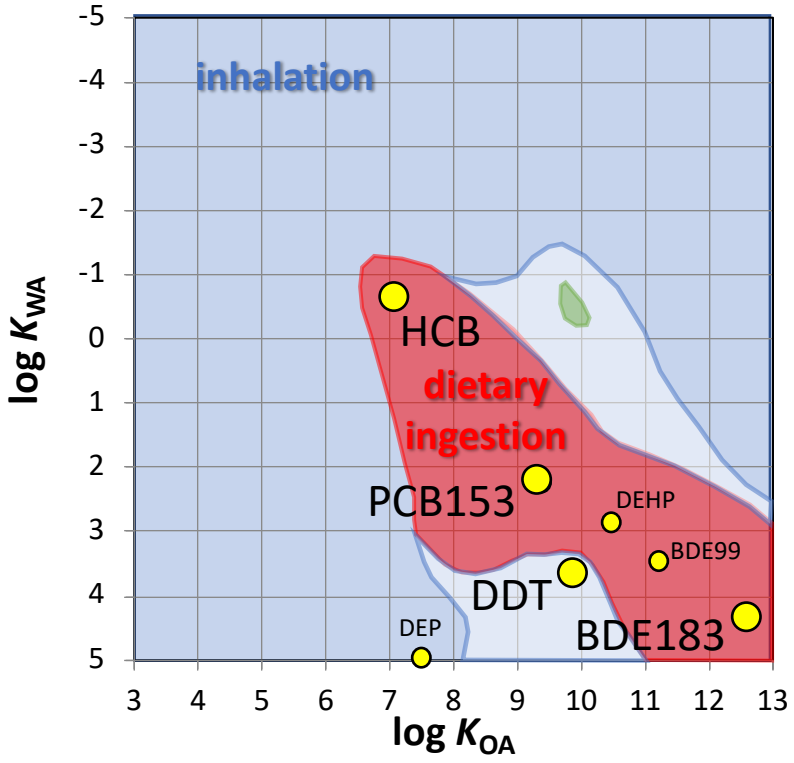


Vegetarian diet lowers dietary intake

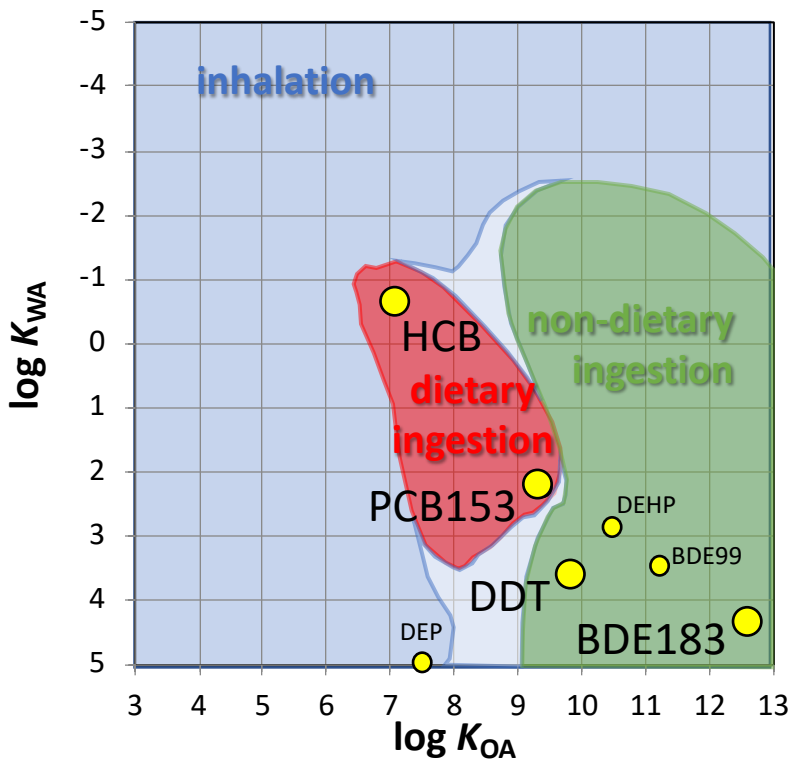
Li et al. *Environ. Sci. Technol.* **2019**, *53*, 11276−11284

Dominant ingestion pathway of persistent chemicals depends on mode of release

release to indoor air



release to indoor surface



Li et al. *Environ. Sci. Technol.* **2019**, *53*, 11276−11284