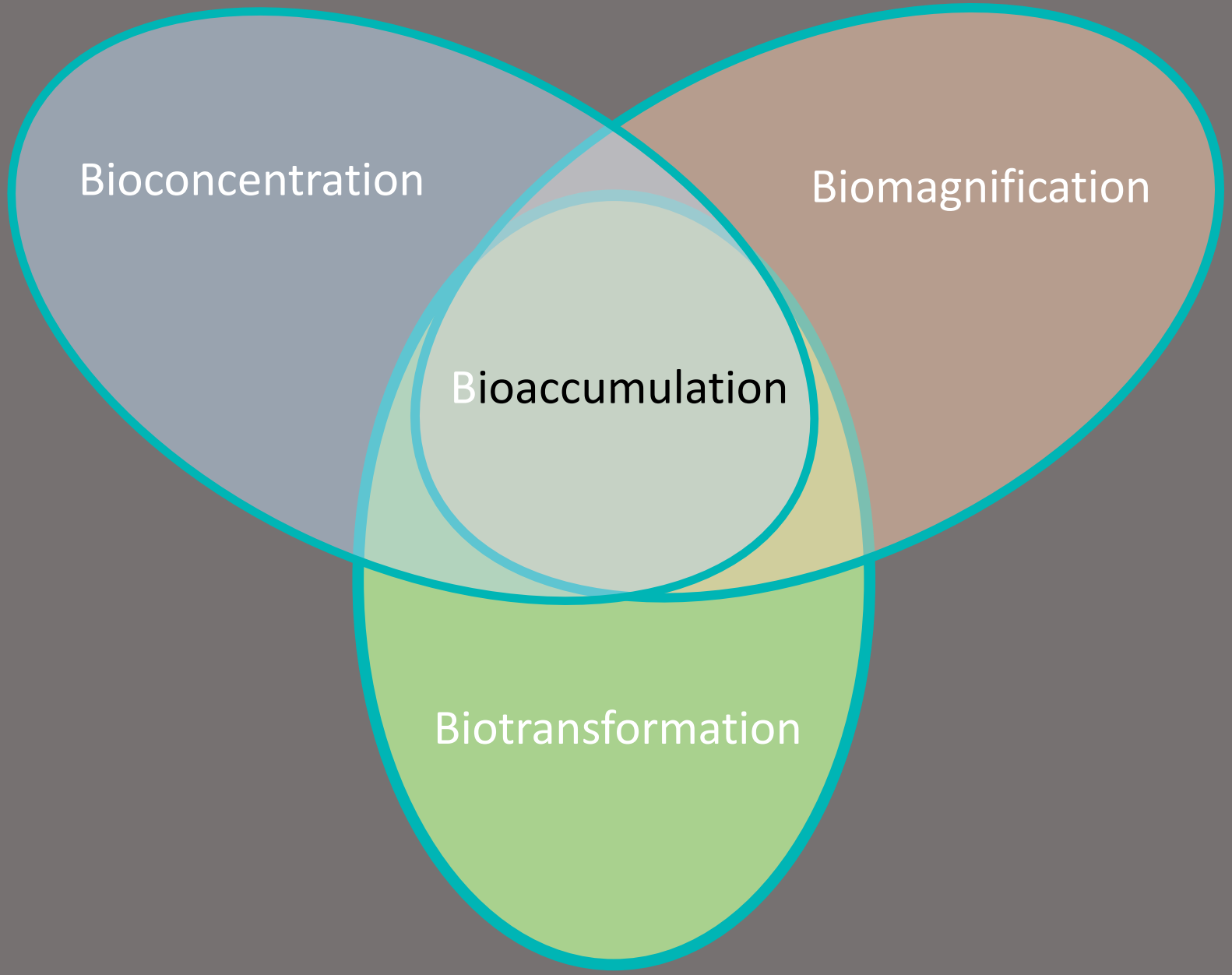
A Tiered Approach for Screening Chemicals for Biomagnification Potential in Humans

Alessandro Sangion, Jon Arnot, Paola Gramatica, Ester Papa


Bioconcentration
Biomagnification
Bioaccumulation
Biotransformation

Issues with the B assessment

Log K_{OW} > 5
BCF > 2000
BCF > 5000

Aquatic Organisms

Issues with the B assessment

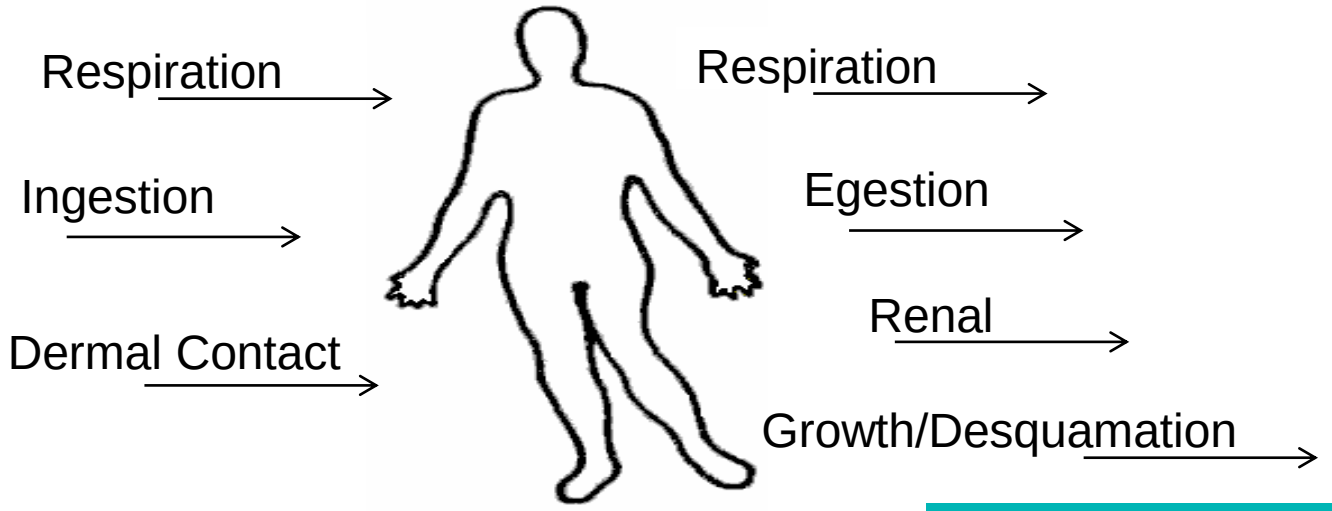
Log K_{OW} > 5
BCF > 2000
BCF > 5000

Air-Breathing Organisms ???

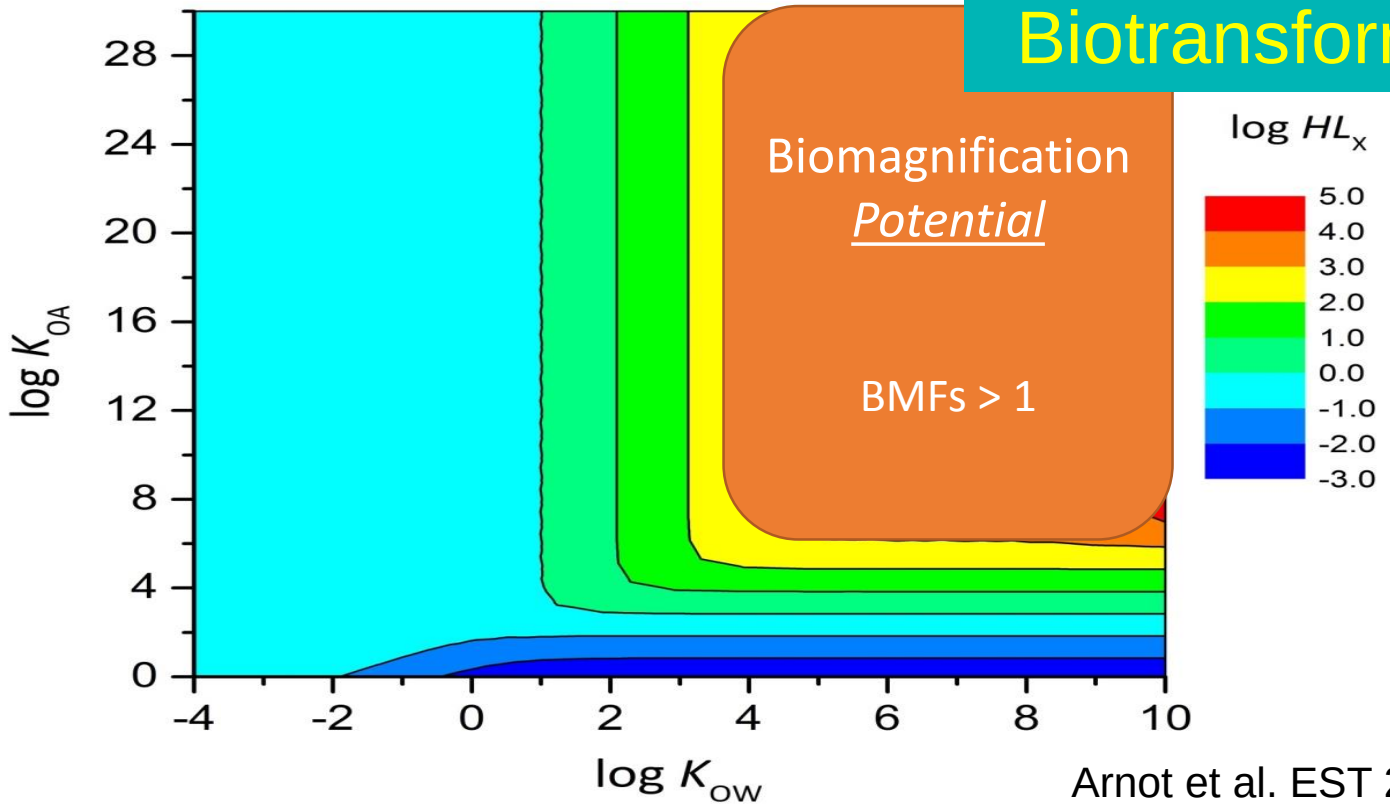
Issues with the B assessment

Air-Breathing organisms

Log K_{OW} > 2
Log K_{OA} > 5
BMF > 1



Exclude Biotransformation



Arnot et al. EST 2014

Issues with the B assessment

Elimination HL < 70 d

Goss et al. Environ Toxicol Chem 2013

Quantitative Structure Activity Relationships for Predicting the Bioaccumulation of POPs in Terrestrial Food-Webs

Frank A. P. C. Gobas, Barry C. Kelly and Jon A. Arnot

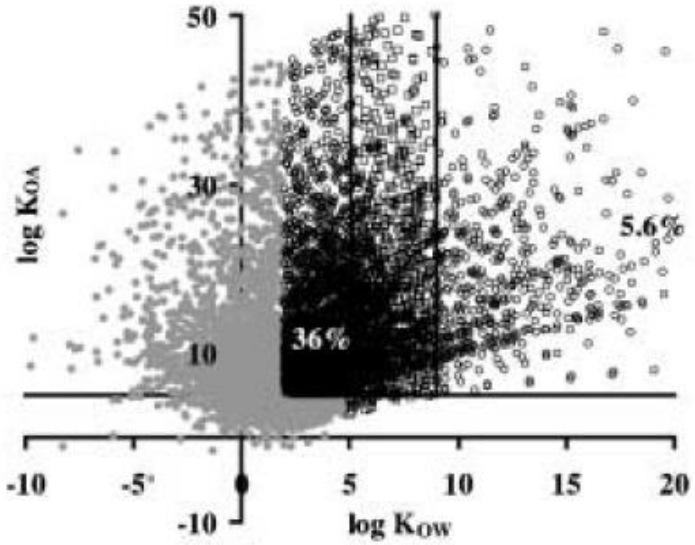


Figure 6. Relationship between K_{OW} and K_{OA} for approximately 12000 organic compounds on the Canadian Domestic Substances List. The graph identifies the percentage of low K_{OW} (i.e. log

Gobas et al. Mol. Info 2003

Biotransformation Matters

Screening organic chemicals for human biomagnification potential

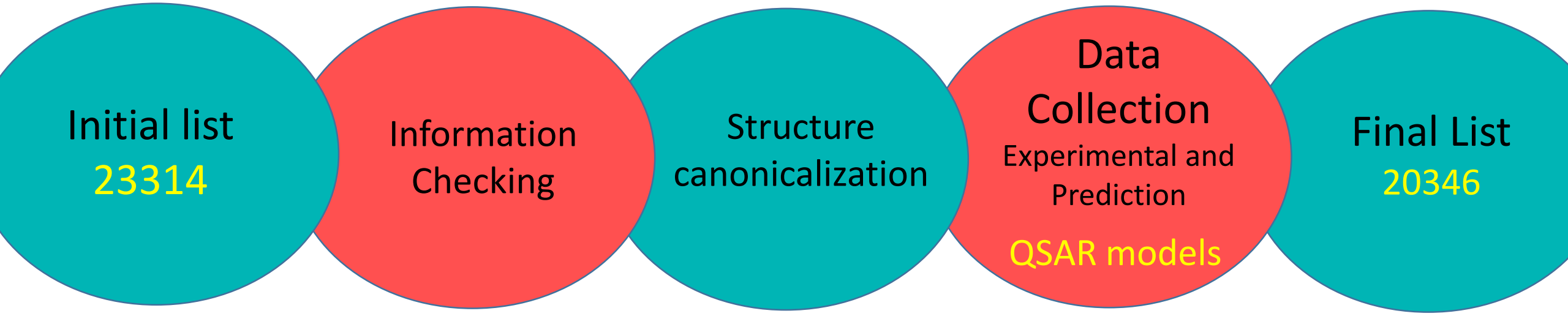
Data curation and analysis

RAIDAR MODEL -> Human BMFs

Tier 1	Kow-Koa	Biotic-partition	Neutral-ionic	Biotic-HLs	Env-HLs
Tier 2	Kow-Koa	Biotic-partition	Neutral-ionic	Biotic-HLs	Env-HLs
Tier 3	Kow-Koa	Biotic-partition	Neutral-ionic	Biotic-HLs	Env-HLs
Tier 4	Kow-Koa	Biotic-partition	Neutral-ionic	Biotic-HLs	Env-HLs

Realism

Data Curation

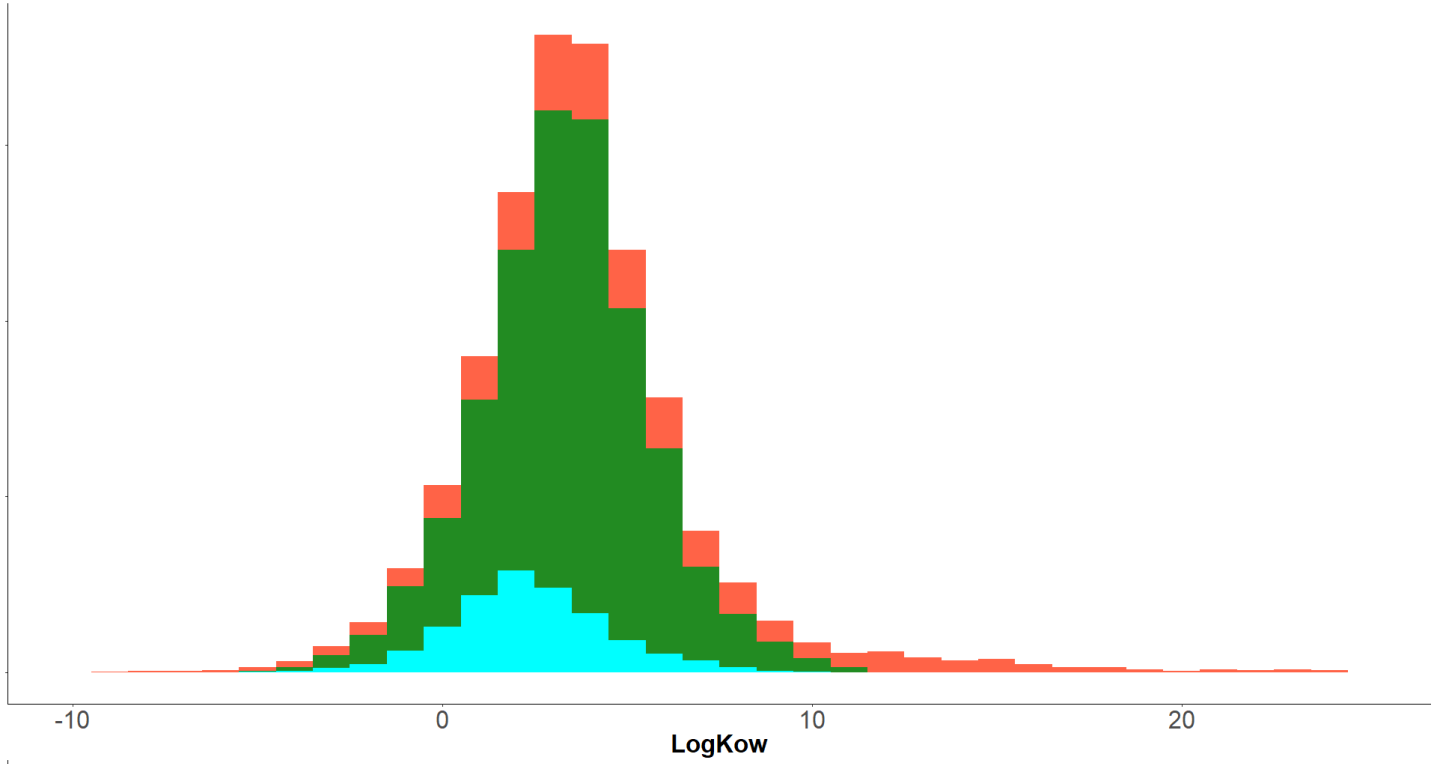


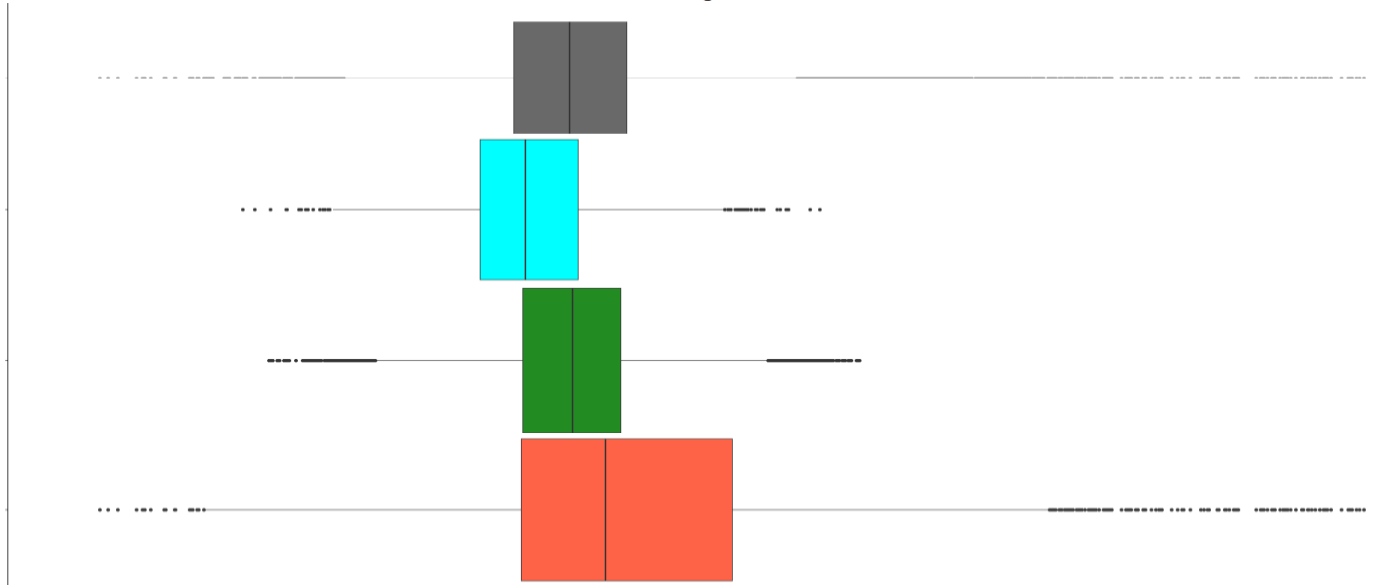
- SMILES
- CAS
- Name

- PubChem
- ChemSpider

- OpenBabel

- Kow
- Koa
- Biotic-partitioning
- pKa
- Bio-HLs





LogKow

Total 20346

13% Experimental data

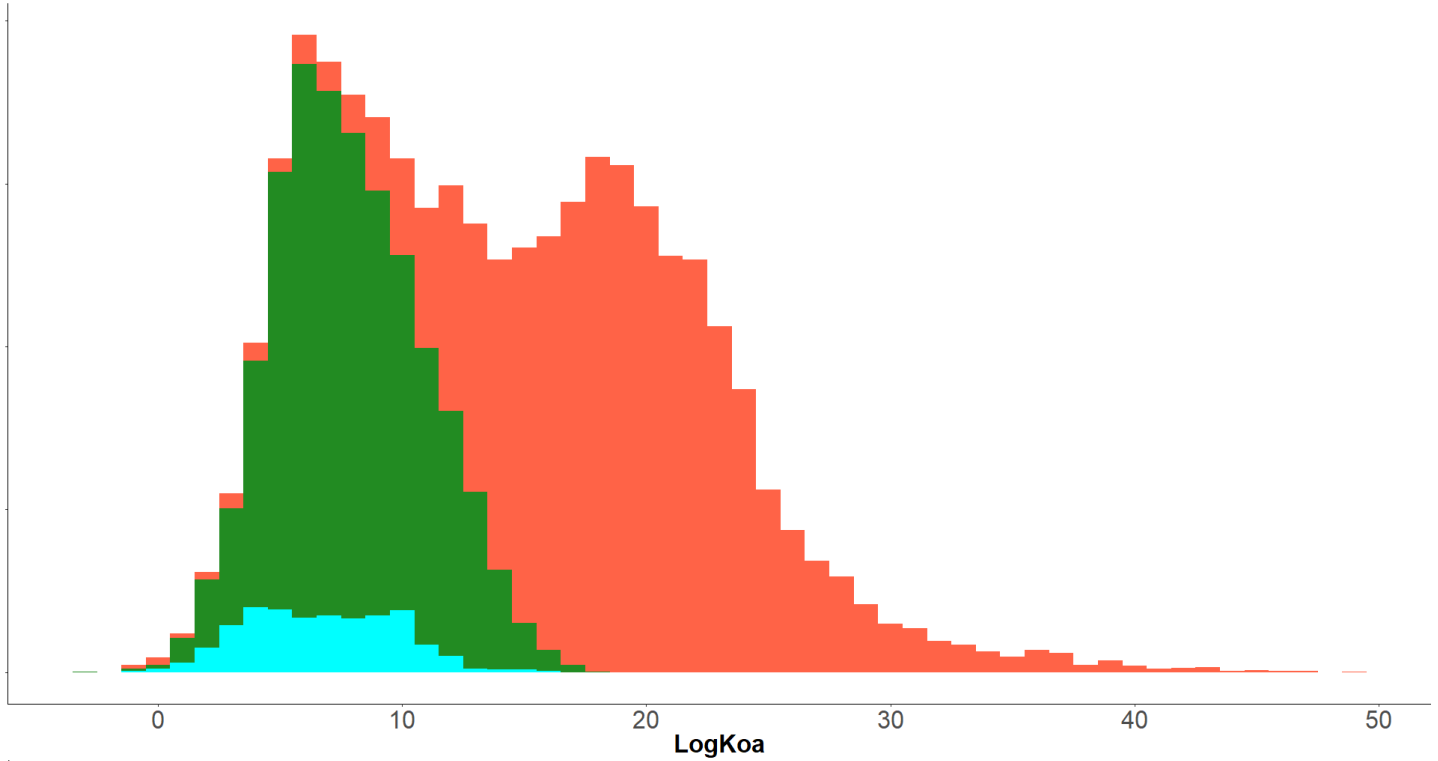
68% IN Applicability Domain

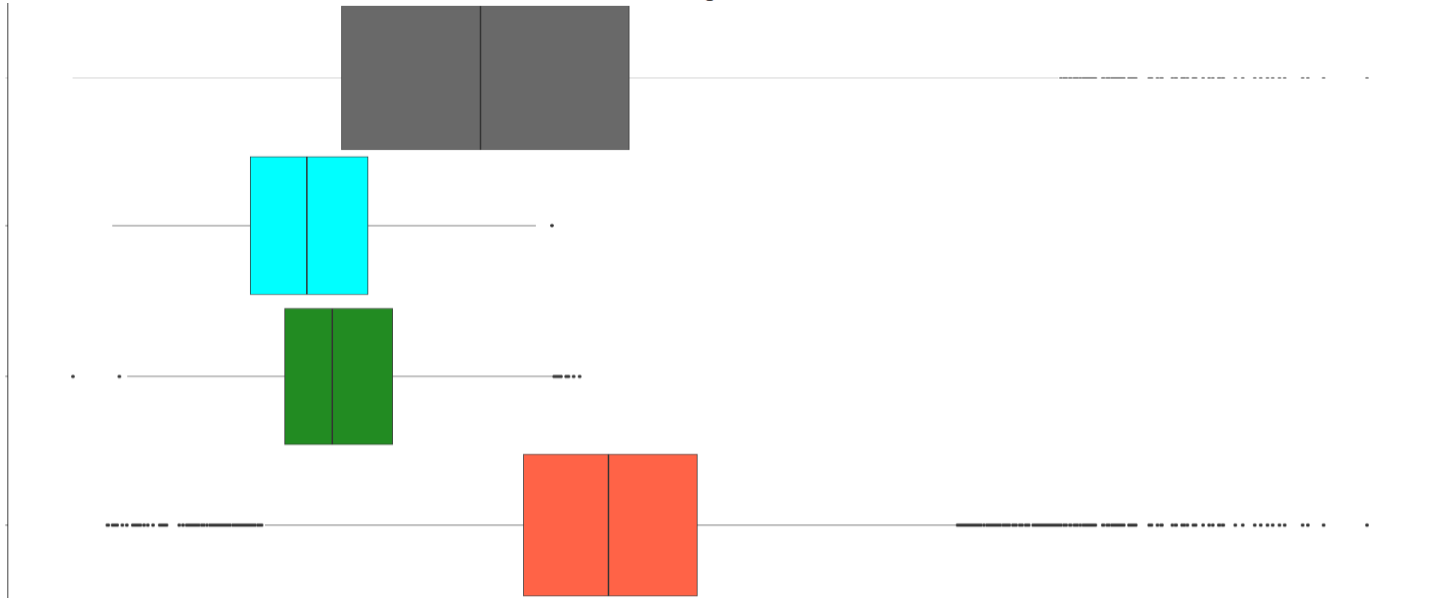
19% OUT Applicability Domain

Screening Criteria:

LogKow > 5 -> 25%

LogKow > 2 -> 74%





LogKoa

Total 20346

5% Experimental data

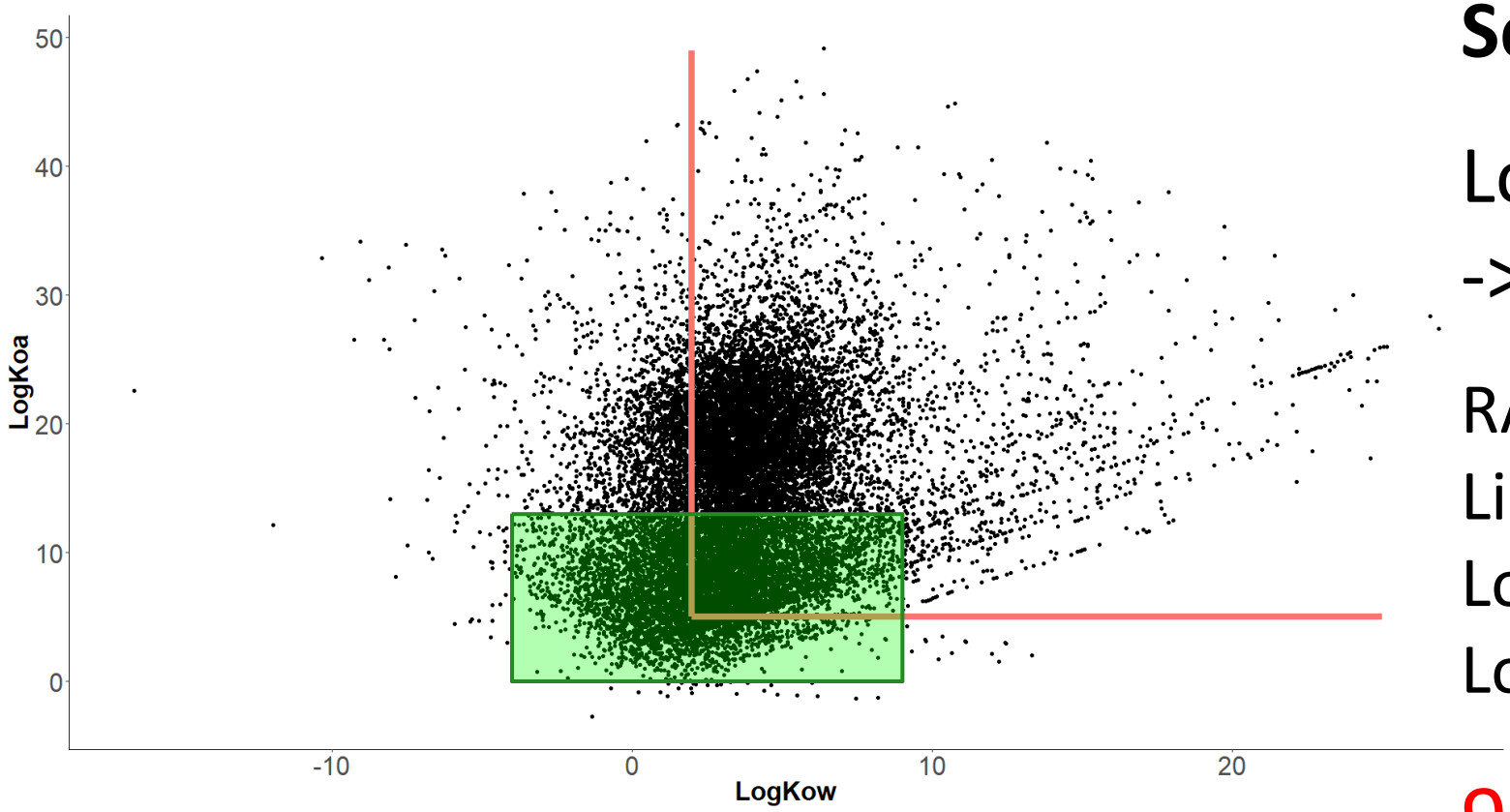
37% IN Applicability Domain

58% OUT Applicability Domain

Screening Criteria:

LogKoa >5 -> 92%

LogKow vs LogKoa



Screening Criteria:

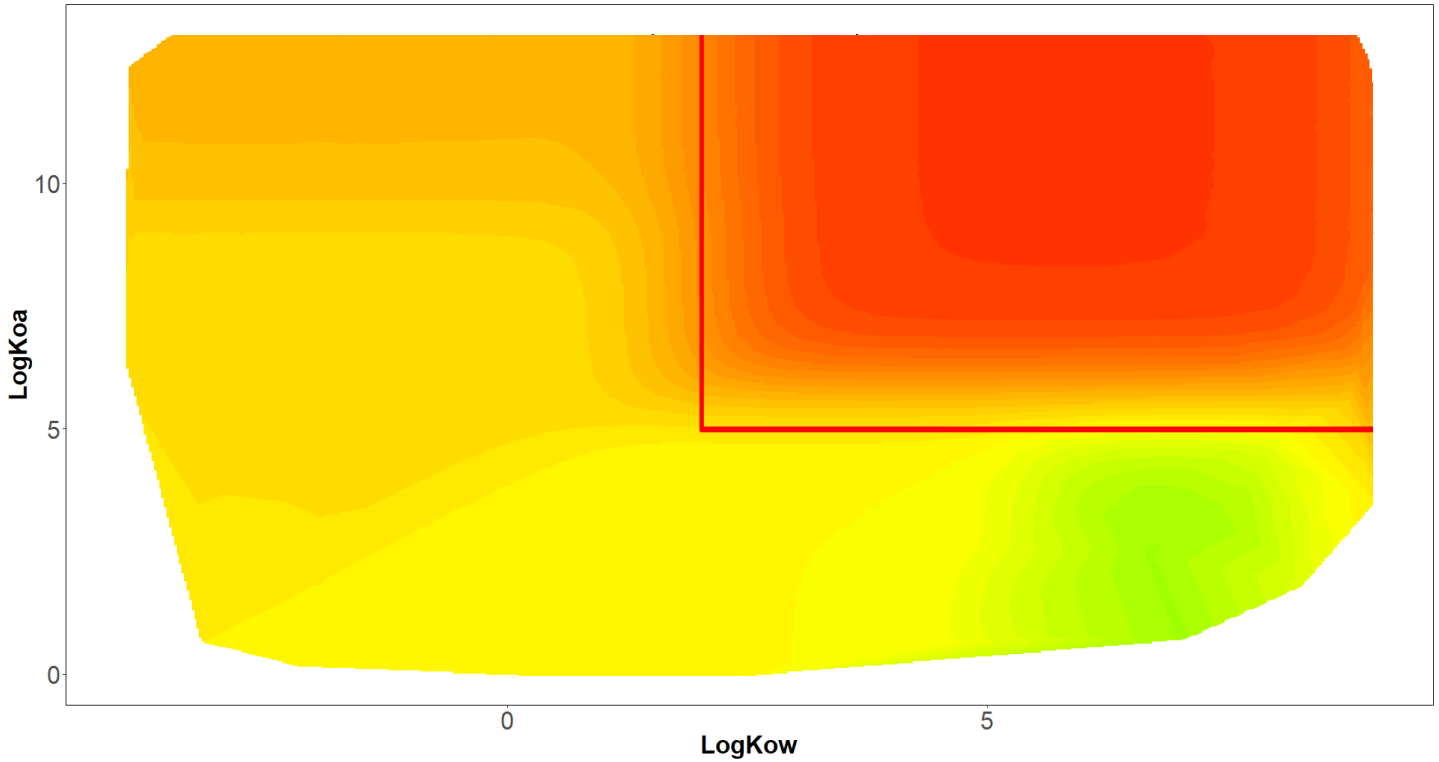
LogKow >2 & LogKoa >5
-> 74%

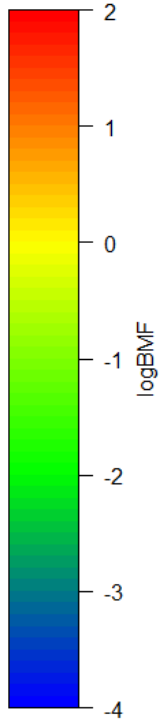
RAIDAR Domain of Applicability Limits:
LogKow -4 <> 9
LogKoa 0 <> 13

9344 Chemicals

Reliable BMF Estimations

Tier 1 BMF





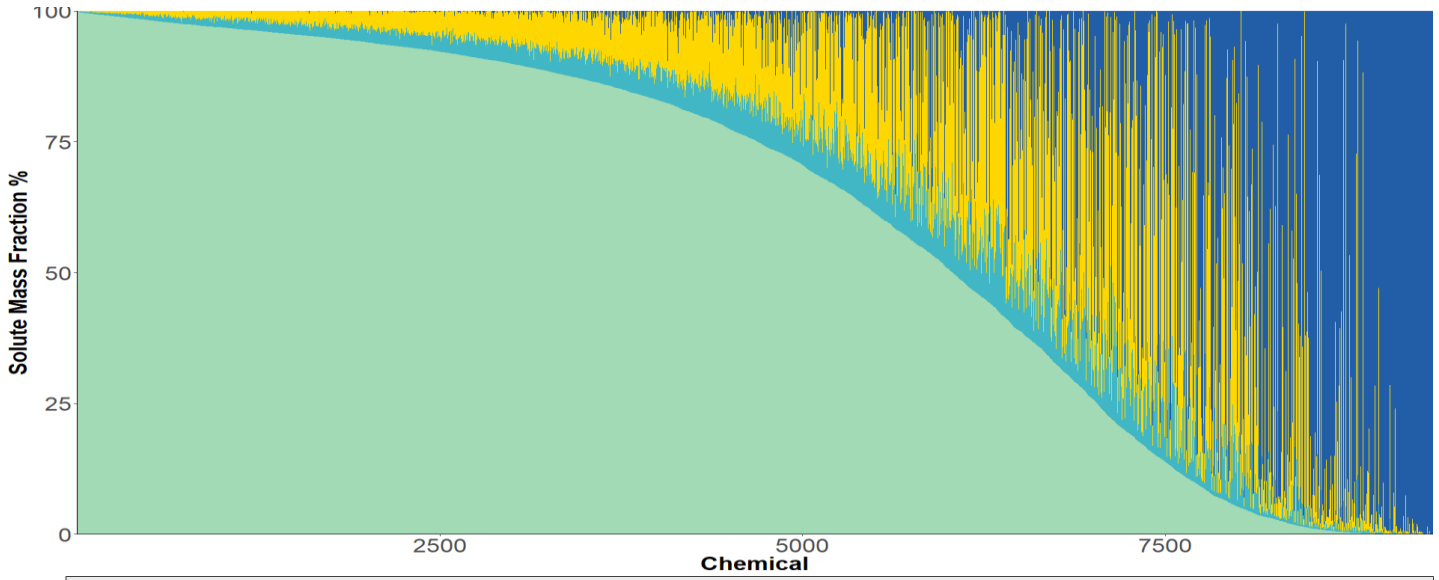
Total 9344

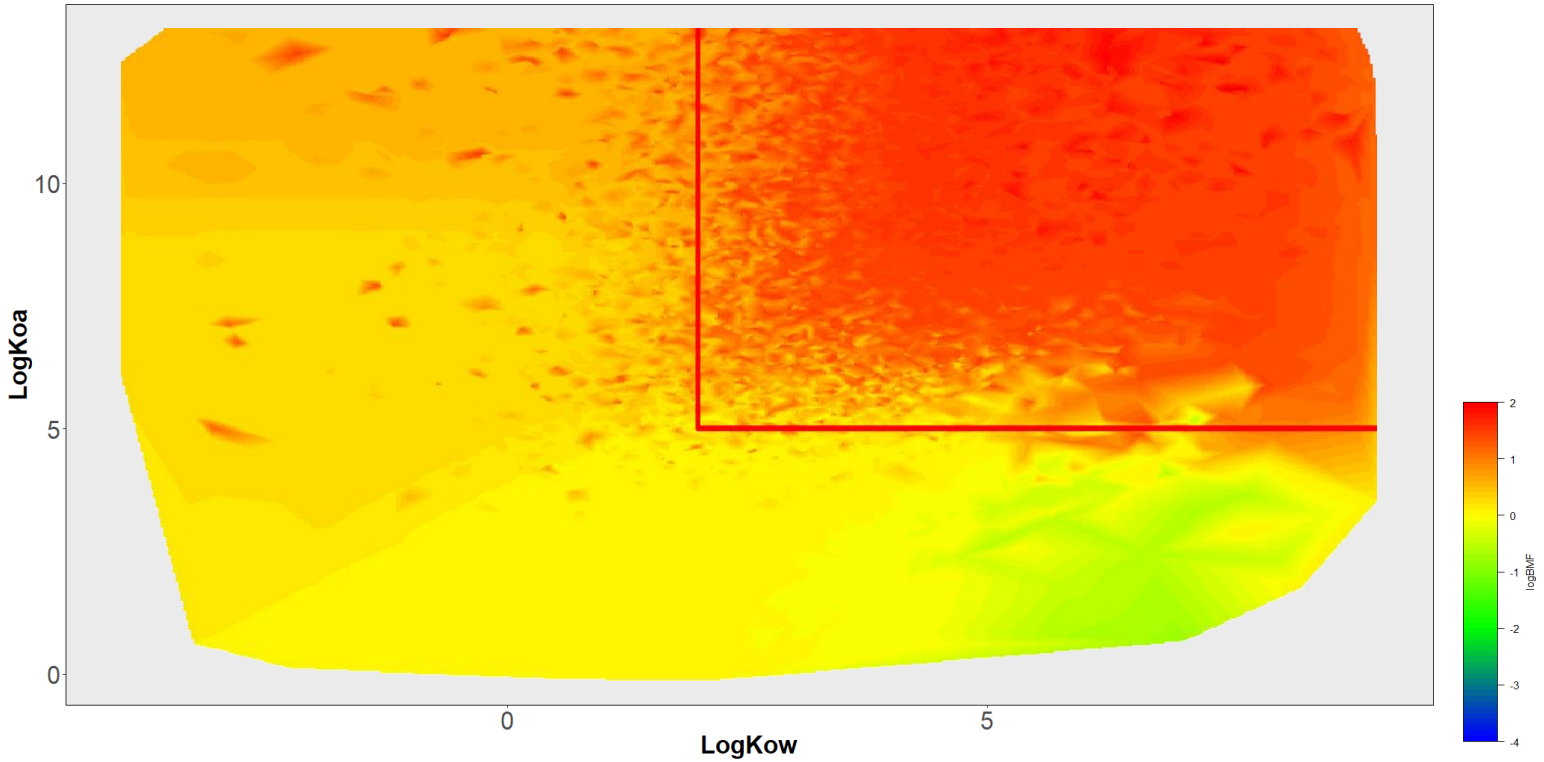
Screening Criteria:

LogKow >2 &
LogKoa >5
–> 64%

BMF >1 -> 94%

Smooth surface





Tier 2- Biopartitioning

Total 9344

69% Storage Lipid + Membrane Lipid

11% Protein

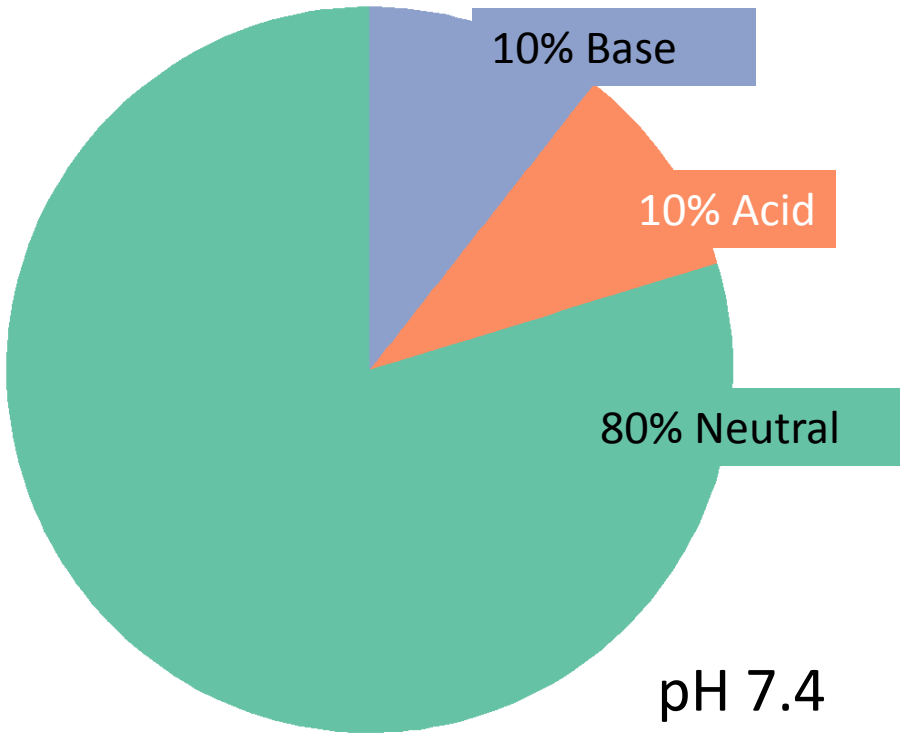
20% Water

BMF >1 -> 98%

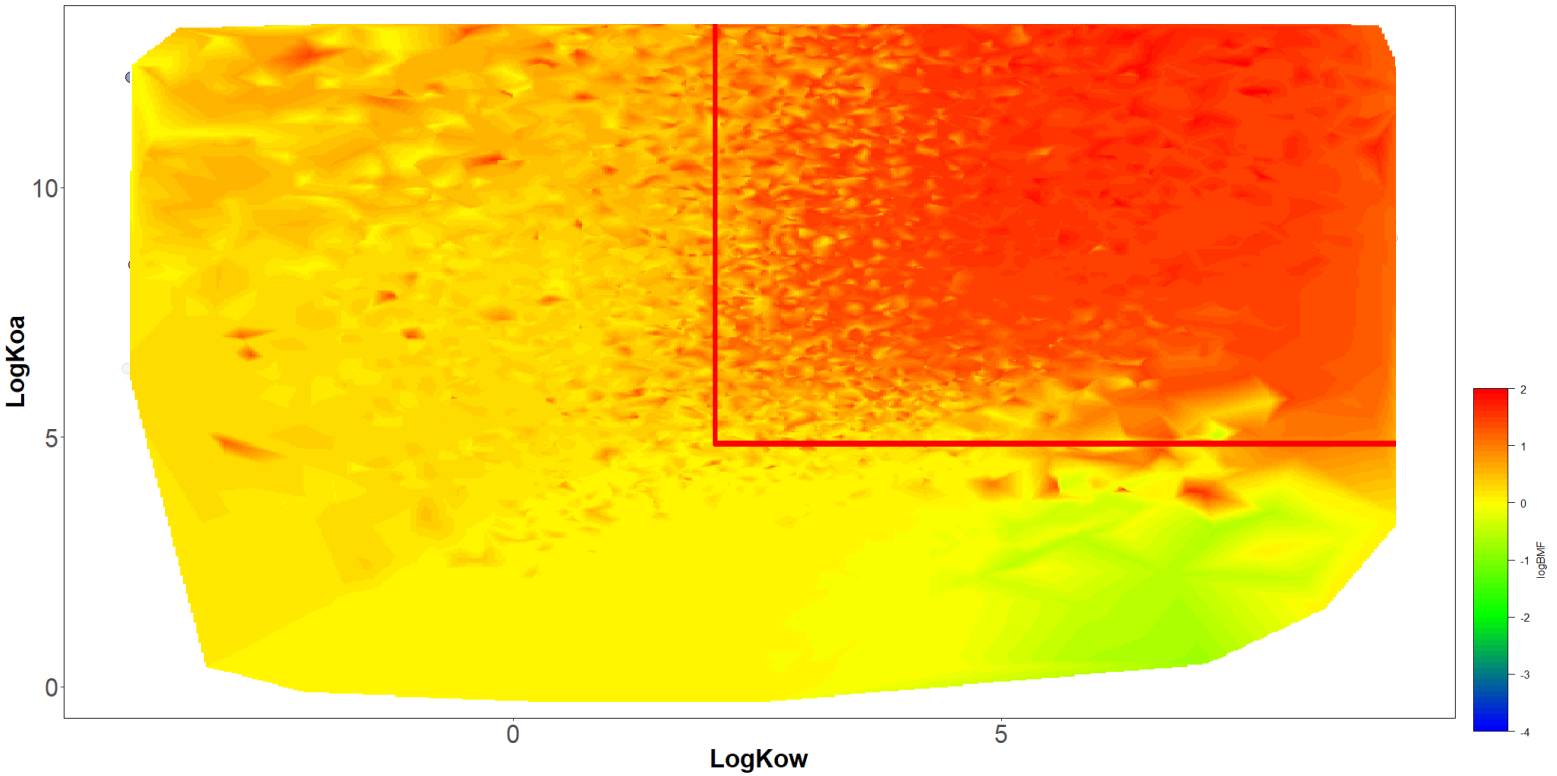
Protein accumulation

Tier 3

Total 9344

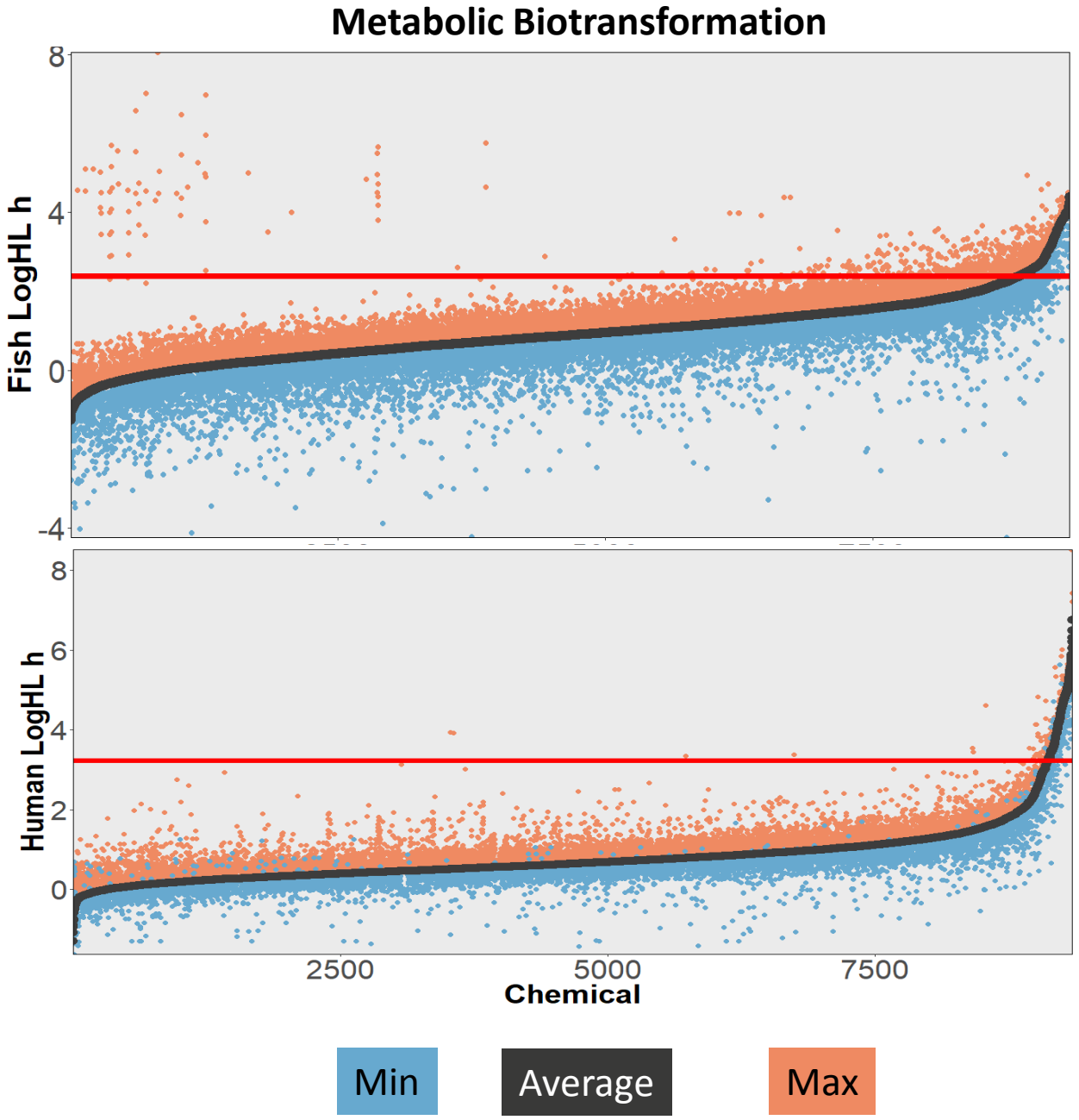


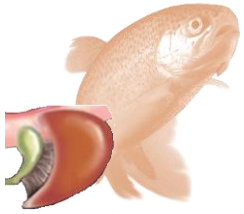
pH 7.4



Partitioning coefficient corrected according to pKa calculated by ACDLab

BMF >1 -> 98%





10 Days

70 Days

Tier 4

Total 9344

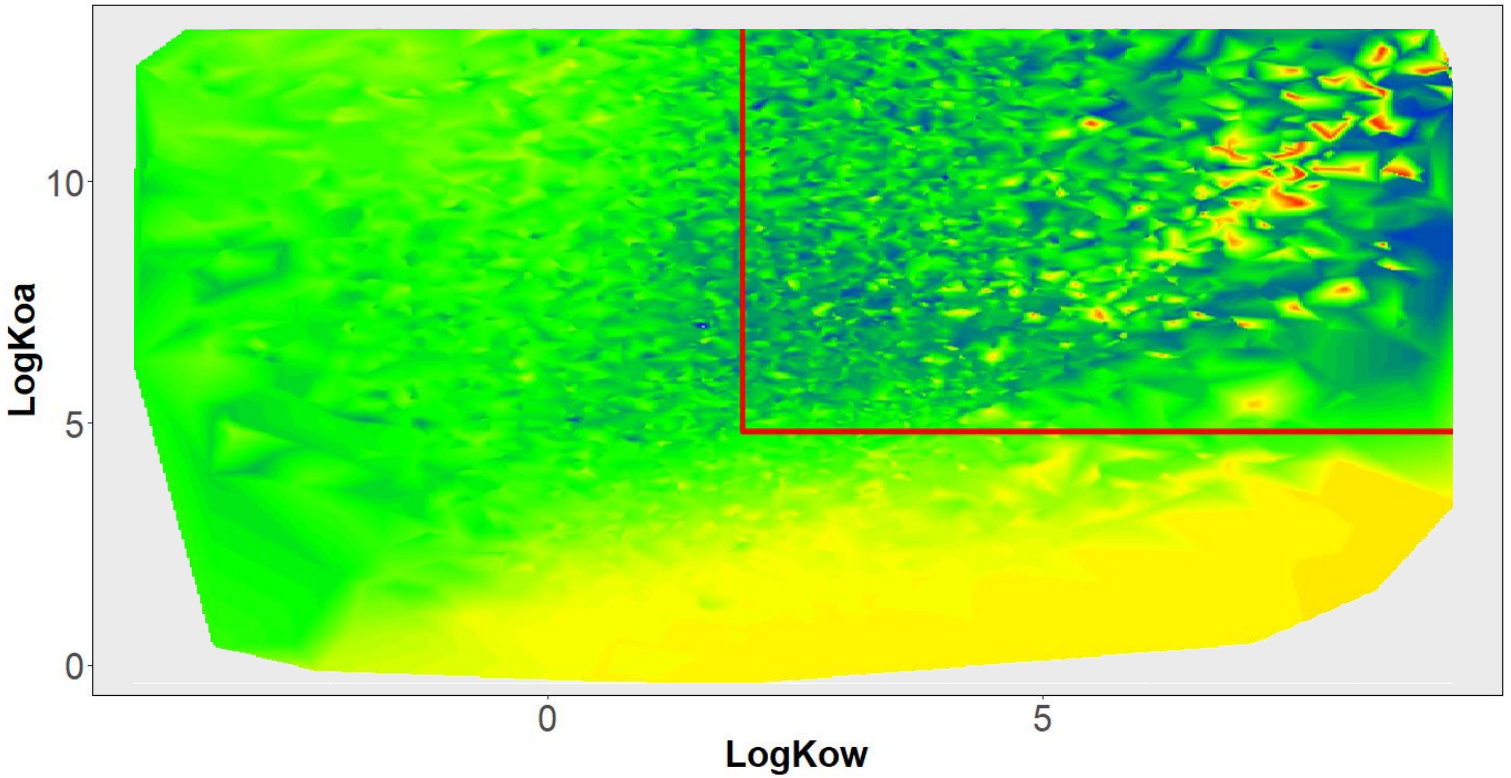
11% Experimental Data

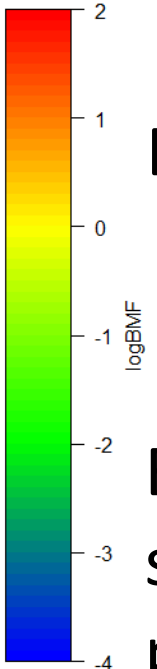
84% IN AD

5% OUT AD

94% Biotransformed Fast

Tier 4





BMF >1 -> 3%

Biotransformation seems the dominant process in the BMF estimation

Take home message

QSAR models can successfully be integrated in a broad framework as for example a food-web model

QSAR expertise is essential to provide reliable input parameters and get reliable outputs

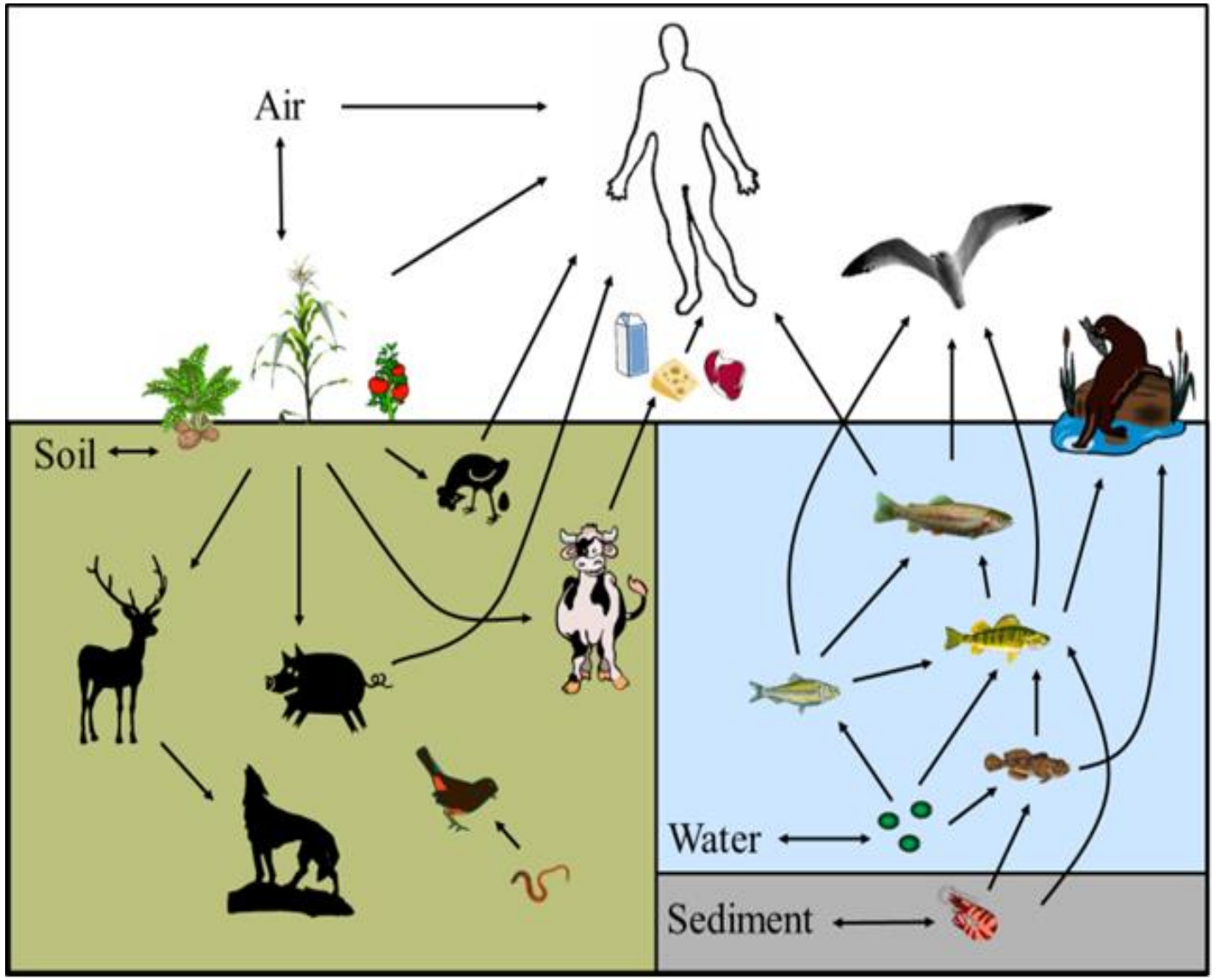
Biotransformation is an fundamental parameter in the bioaccumulation assessment with only ca. 3% of chemicals with a BMF>1 when Bio-HL are considered in the calculation

Thanks to:

Frank Wania
James Armitage
Liisa Toose
Karen Foster

Funding:
ACC-LRI

RAIDAR model (Arnot et al. 2006)



$$BMF = \frac{FugacityHuman}{FugacityDiet}$$