In Silico Modelling of Bioaccumulation of Per- and Polyfluoroalkyl Substances (PFAS)

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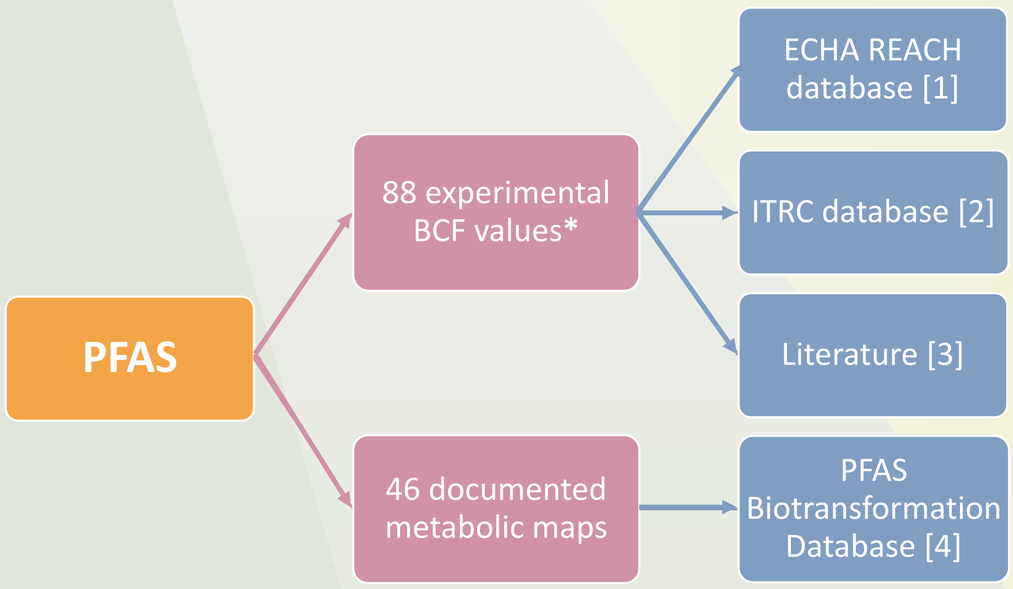
INTRODUCTION

Per- and polyfluoroalkyl substances (PFAS) are a large family of fluorinated chemicals that differ significantly in their chemical and physical properties. The persistence and mobility of some PFAS, combined with decades of widespread use in industrial processes and consumer products, have resulted in their presence in the environment worldwide. Toxicological studies have raised concerns regarding the bioaccumulative nature and potential health concerns of some PFAS. However, PFAS risk assessment is hampered by their unique physical and chemical properties that lead to not well understood biological and chemical transformation pathways and unique bioaccumulation mechanisms.

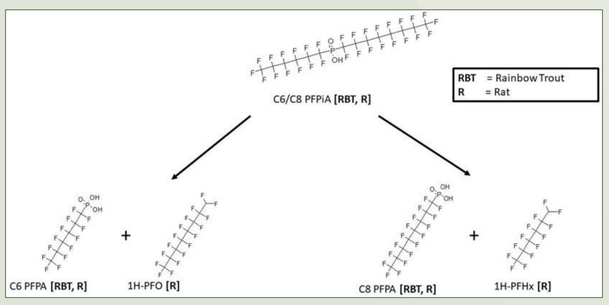
GOAL

Development of the mechanistic QSAR model to predict bioaccumulation of PFAS.

DATA AVAILABILITY



Example of documented metabolic map



* Data associated with OECD TG 305 were used only.

Example of experimental BCF data

	Log BCF Whole Body (L/kg) average ± sd (n)	Log BCF Muscle/Fillet (L/kg) average ± sd (n)
Carboxylic Acids - OECD Structure Category 102		
PFBA	1.18±0.08 (2)	-0.13±0.47 (4)
PFPA		-0.83±0.22 (2)
PFHxA	1.00±0.02 (2)	0.13±0.55 (4)
PFHpA		0.33±0.27 (2)
PFOA	1.45±0.83 (3)	1.20±0.76 (3)
PFNA	3.13±0.06 (2)	3.06±0.34 (2)
PFDA	3.88±0.13 (2)	3.51±0.76 (3)
PFUnDA	3.69±0.30 (4)	3.79±0.46 (3)
PFDoDA	4.08±0.18 (4)	4.16±0.46 (3)
PFTrDA	4.34±0.46 (2)	4.51±0.85 (2)
PFTeDA	4.60±0.56 (4)	4.76±0.55 (3)

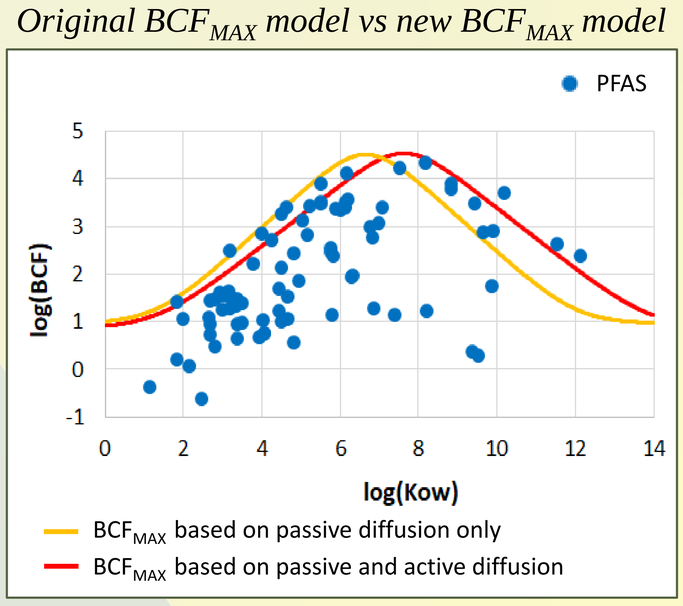
MODEL DEVELOPMENT

The concept of the original CATALOGIC BCF base-line model [6] is used to derive a new model that could predict the bioaccumulation of PFAS. Based on this concept, the new model consists of:

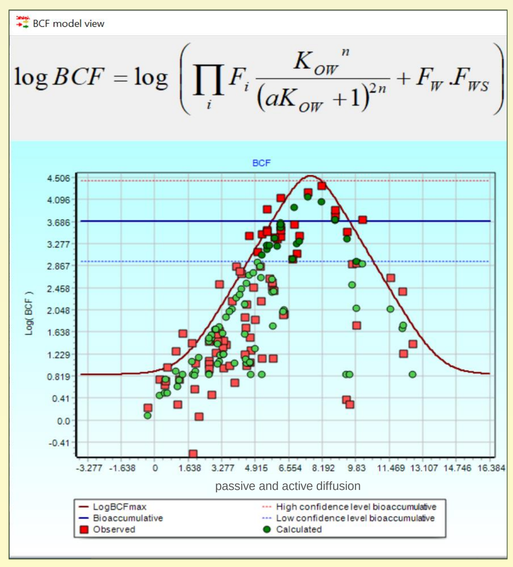
- ✓ Multi-compartment model describing the maximum bioconcentration potential (BCF_{MAX}) of PFAS based solely on chemicals' lipophilicity (passive diffusion) and binding to proteins (active diffusion).
- ✓ Mitigating factors that could reduce the BCF_{MAX}, such as metabolism, molecular size, ionization and water solubility.

Assumption for combined diffusions better explains distribution of PFAS in organism.

Original BCF_{MAX} model vs new BCF_{MAX} model

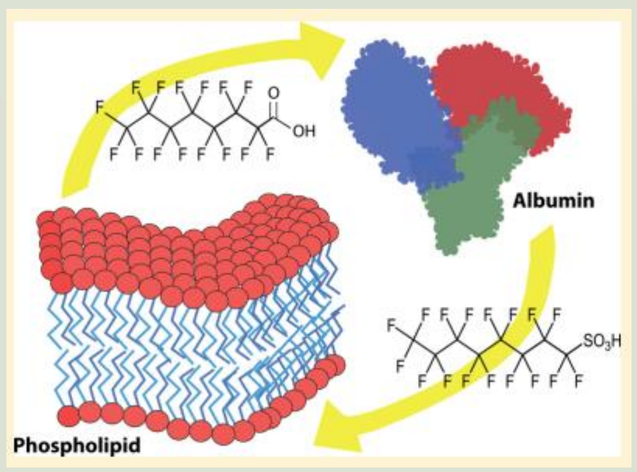


New model view



BIOACCUMULATION MECHANISMS

PFAS nature determines the types of interactions that occur within biota. PFAS are amphiphilic and thus are likely to interact with other organic molecules with both polar and nonpolar regions within living organisms. Many studies have found significantly different PFAS concentrations between body compartments, with the most accumulation occurring in the blood plasma, liver, and kidneys of many organisms [2]. Literature review shows that there are two hypotheses for the mechanisms that control the bioaccumulation of PFAS. The first one, known as passive diffusion, suggests that partitioning to membrane phospholipids can explain the high bioaccumulation potential of these compounds. The second, known as active diffusion, assumes that interactions with proteins determine the distribution of PFAS [5].



Screenshot from Ng et al., 2014 [5]

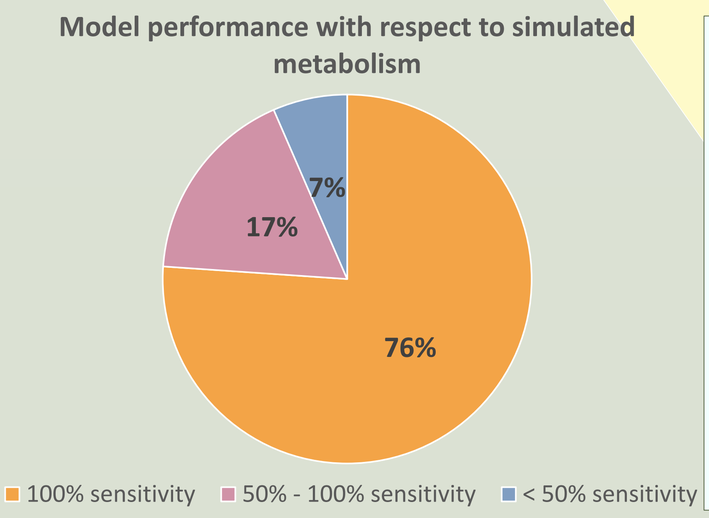
MODEL PERFORMANCE

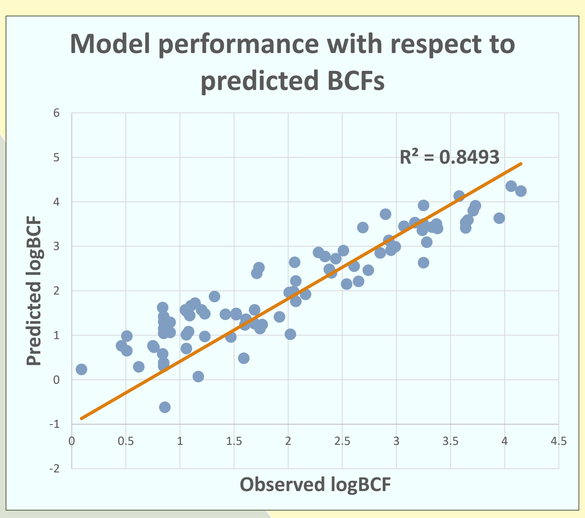
Performance of the model is investigated with respect to:

- ✓ Simulated fish liver metabolism
- ✓ Predicted BCF values

The model fully reproduces **76%** of the documented metabolic maps.

The accuracy of the predictions is **91%**. The goodness-of-fit of the model expressed by the correlation coefficient ($\mathbf{R^2}$) is **85%**.





REFERENCES

[1] ECHA REACH database available in OECD QSAR Toolbox 4.5SP1.

[2] ITRC. PFAS Technical and Regulatory Guidance Document, 2022.

[3] Burkhard, L. EPA-ECOS-ASTHO PFAS Science Call, 2020.

[4] Kolanczyk et al. *Toxics.* **2023**, 11, 74.

[5] Ng et al. *Environ. Sci. Technol.* **2014**, 48, 4637−4648.

[6] Dimitrov et al. *SAR QSAR Environ. Res*. **2011**, 23, 17–36.

CONCLUSIONS

1. A new QSAR model was developed for predicting BCF of PFAS.
2. It considers passive and active diffusion (interaction with proteins) of PFAS.
3. The model correctly predicts 91% of the training set chemicals within the range of experimental error.
4. The average sensitivity with respect to simulated metabolism is above 95%.
5. The results suggest that the QSAR model can be used to generate reliable predictions of fish BCFs.