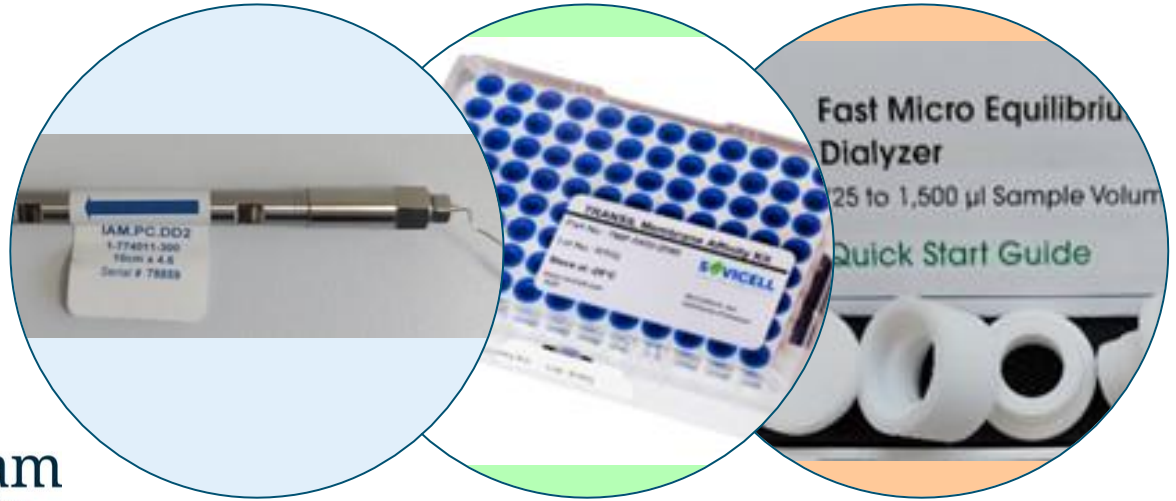
Assessment of methods for determining the membrane-water partition ratio for surfactants

Steven Droge, SETAC EU, Dublin 2023

N. Jansen, E. Barrett, A. Bejarano, J. Bietz, K. Connors, J. Dawick, M. Geurts, G. Hodges, E. Kearney, M.A. Miller, D. Schowanek, S. Wilhelm

Shell
Nouryon
Unilever
Clariant
ERASM
Procter & Gamble
Innospec
BASF

Durham University

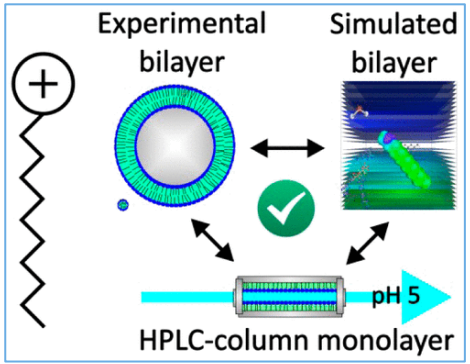


WAGENINGEN
UNIVERSITY & RESEARCH

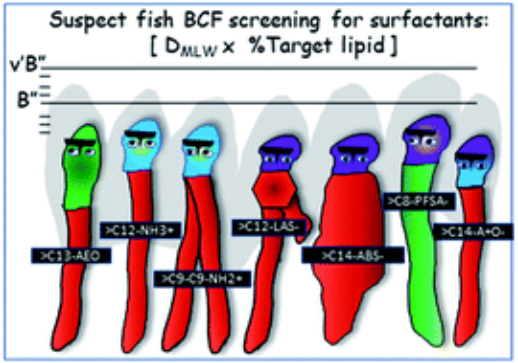
Outline

- Surfactant chemicals
- Issues on surfactant hydrophobicity assessment
- Methods/Tools available
- Project aim
- First results
- Method/tool comparison
- Comparison other data

Droge 2019, ES&T 53 (2),760–770



Timmer & Droge 2017, ES&T 51(5),2890



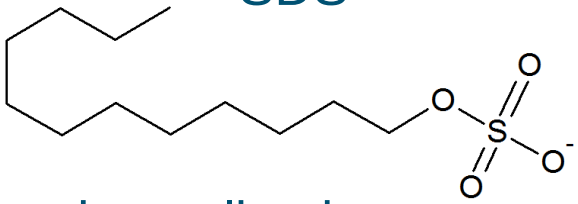
Droge et al. 2021, ESPI 23 (12),1930

WAGENINGEN UNIVERSITY & RESEARCH

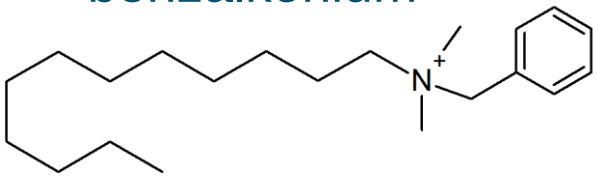
Surfactants: simple ionic/ionizable chemicals

1. Amphiphilic properties

SDS



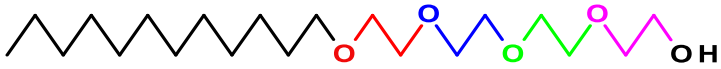
benzalkonium

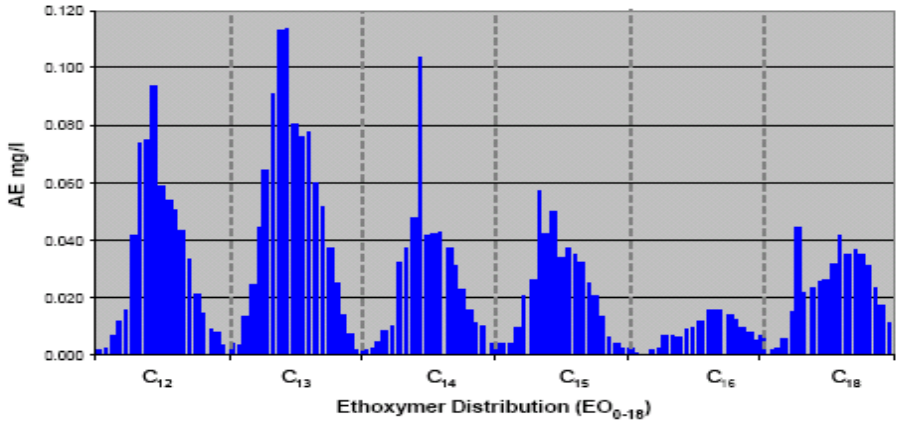


hydrophobic ← → hydrophilic

2. Technical mixtures/pure standards

Example (nonionic):
Alcohol ethoxylate: $C_{12}EO_4$





WAGENINGEN
UNIVERSITY & RESEARCH

Surfactants: chemical assessment

- Surfactants in consumer products designed to be safe

– e.g., readily biodegradable: branched -> linear alkyl chains, addition ester/amide bonds between alkyl - headgroup

But:

- Often high production volume chemicals, multiple >1000 t/y:
  - High disposal volumes
  - Extensive chemical dossiers
  - Assess risk of (low) % remaining in (treated) wastewater

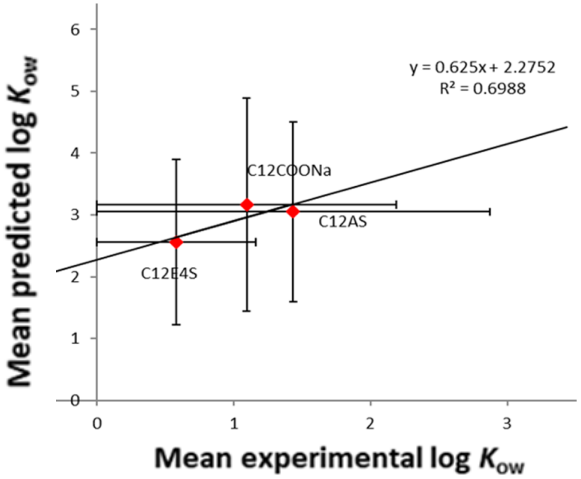
ECHA EUROPEAN CHEMICALS AGENCY

Surfactants: hydrophobicity issue

- Predict toxicity / bioaccumulation based on surfactant structure ?
- Difficulties in octanol/water (K_{OW}) testing:
  - OECD protocols exempt 'surface active agents'

  e.g., Surfactants can emulsify octanol into water

  - Octanol poorly reflects role ionic interactions



Hodges et al. (2019)*:

Highly variable experimental results for K_{OW} , also from computational tools

"*More biologically relevant and methodologically defensible alternative methods*"

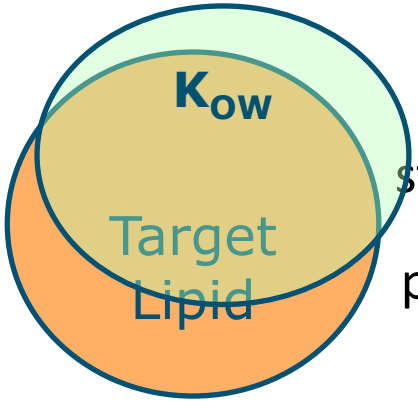
WAGENINGEN UNIVERSITY & RESEARCH

Environ. Sci. Eur., 31 (1), art. no. 1

Surfactants: “hydrophobic” = “lipophilic” ?

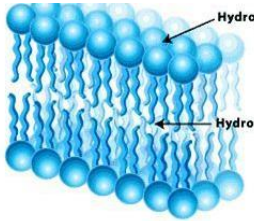
- Commission Regulation (EU) Amendment 2021/979 :

“experimental bioaccumulation study cannot be waived on the basis of low K_{OW} alone, if the substance is surface active or ionisable at environmental pH (4–9).”

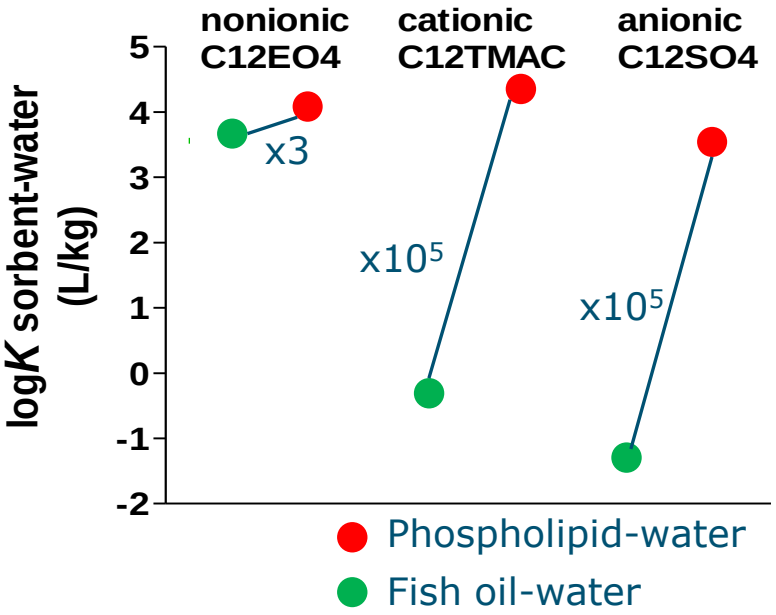


storage lipid (neutral)

phospholipid



(ionic headgroups)



WAGENINGEN UNIVERSITY & RESEARCH

Droge et al. 2021, ESPI 23 (12) p. 1930-1946

Aid surfactant risk assessment: phospholipid sorption data

Predict toxicity / bioaccumulation based on surfactant structure:

- BCF (excl. biotransf.) ~ $f_{\text{target lipid}}$ x $K_{\text{target lipid-water}}$
- Narcotic toxicity ~ *Critical membrane burden* x $K_{\text{membr-water}}$

No OECD guideline for $K_{\text{membr-water}}$: apply generic sorption assay?

Q: How to obtain accurate phospolipid sorption data for surfactants ?

Aid surfactant risk assessment with phospholipid sorption data

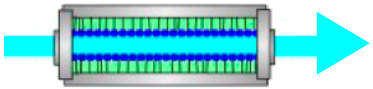
No OECD guideline available..., generic sorption assays?

Q: How to obtain accurate phospolipid sorption data for surfactants ?

Different experimental assays available

Liposome vesicles:
Golden standard

Bilayer cover on silica:
Easy to centrifuge

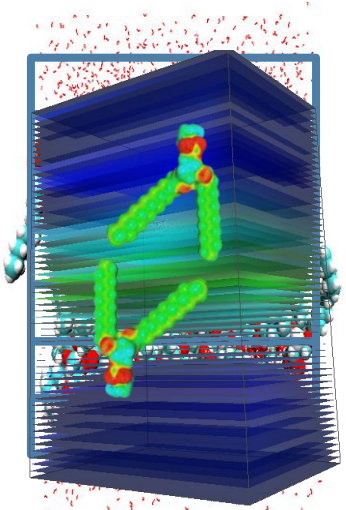


HPLC column:
(monolayer on silica)
High throughput

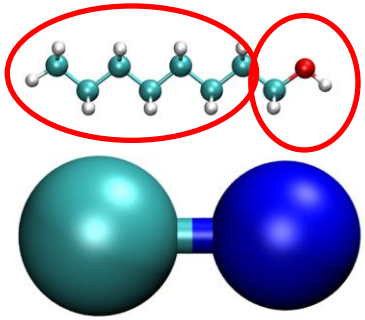
WAGENINGEN
UNIVERSITY & RESEARCH

Different computational tools available

Quantum-chemistry
(COSMOtherm)



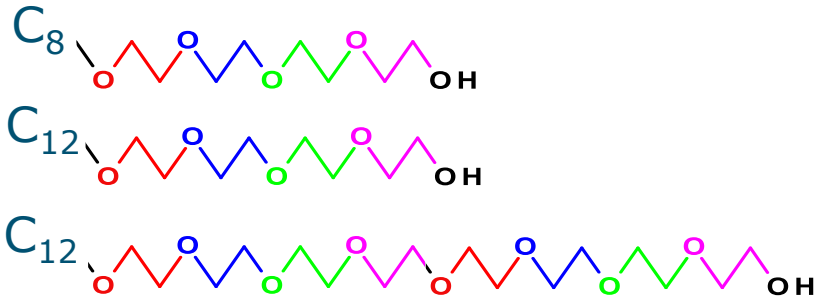
Coarse-grained
molecular dynamics



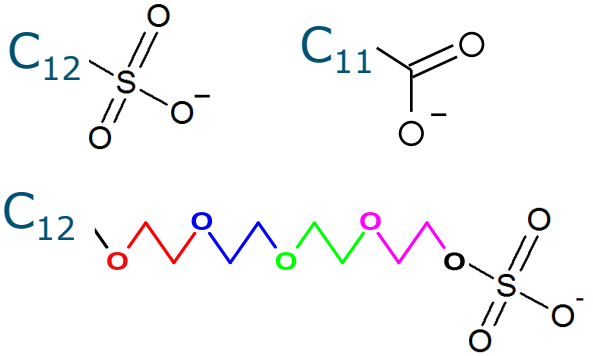
Polyparam.-LFER
(ion-extension)

Project aim: Phospholipid sorption data for 4 types of surfactants

3x nonionic

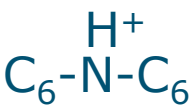


3x anionic



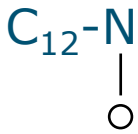
3x cationic

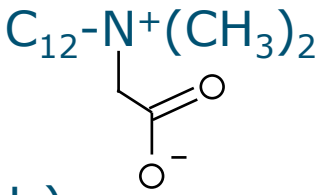
$C_{12}\text{-}NH_3^+$

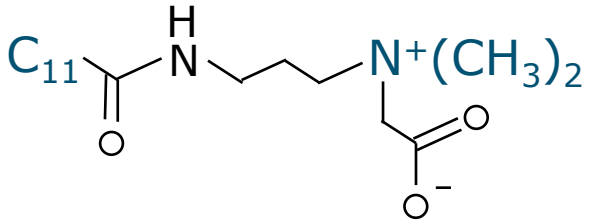


$C_{12}\text{-}N(CH_3)_3^+$

3x zwitterionic

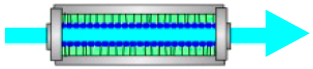






WAGENINGEN
UNIVERSITY & RESEARCH

Phospholipid sorption data (*prelim*.) for pure surfactant homologs



IAM-HPLC

Retention time

↓

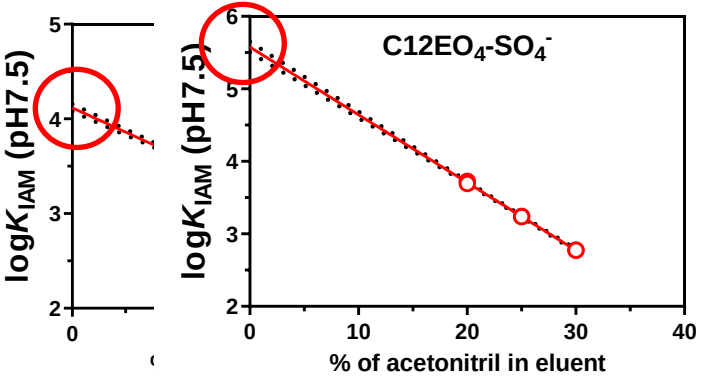
Retention capacity factor (k_{IAM})

↓

k_{IAM} 100% aqueous buffer

↓

Apparent sorption coefficient (K_{IAM})



SSLM

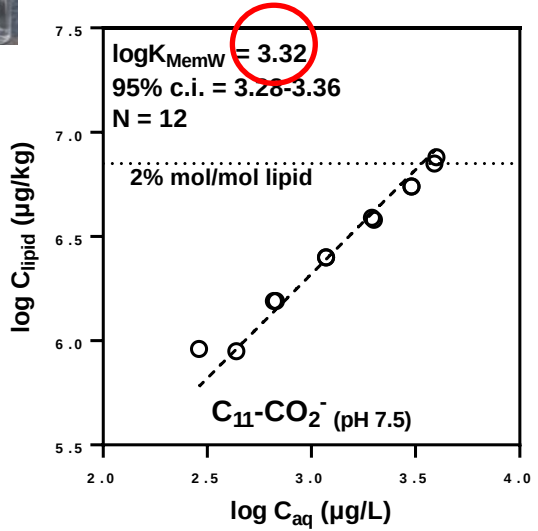
Batch sorbent dilution system

↓

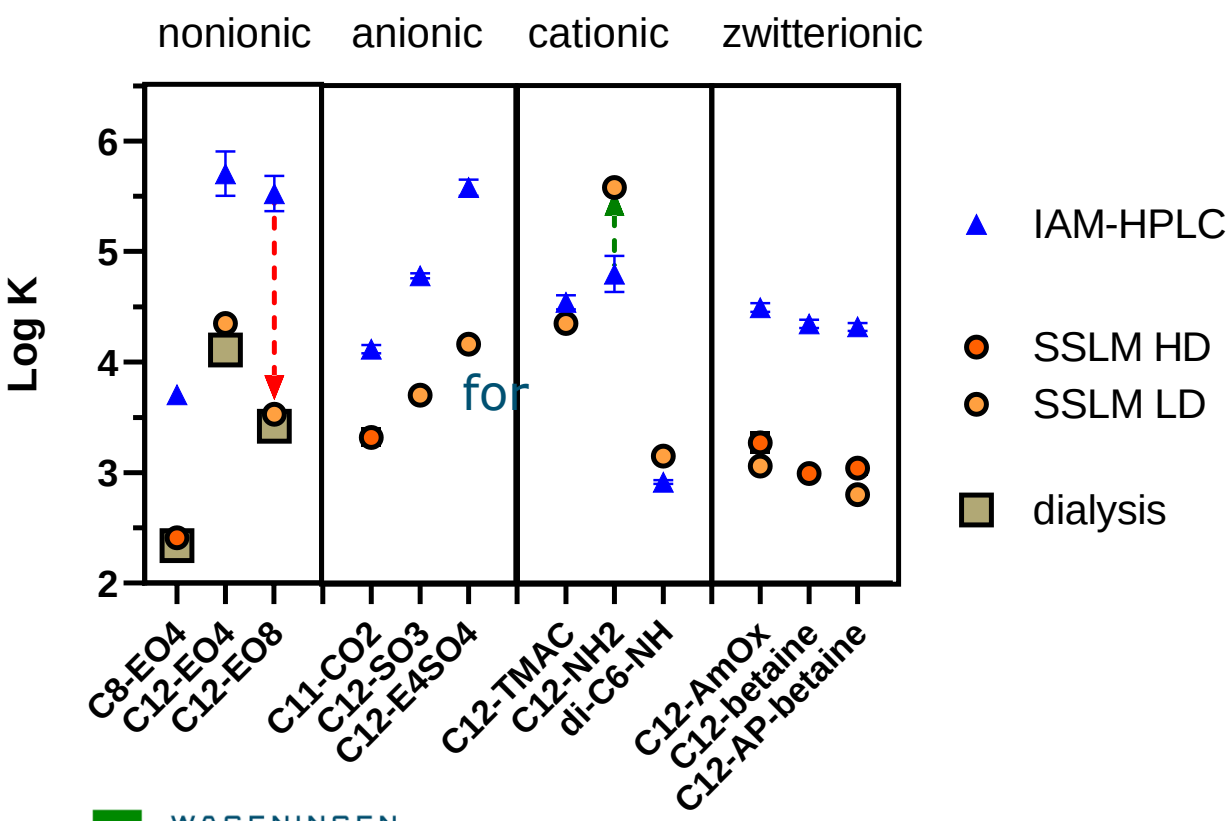
Analyse supernatant

↓

Only if 20-95% sorbed



Phospholipid sorption data for comparison of assays



IAM-HPLC - SSLM

IAM mostly overestimates K_{Mem-w}

Exception: some cations

Mostly as expected from previous studies

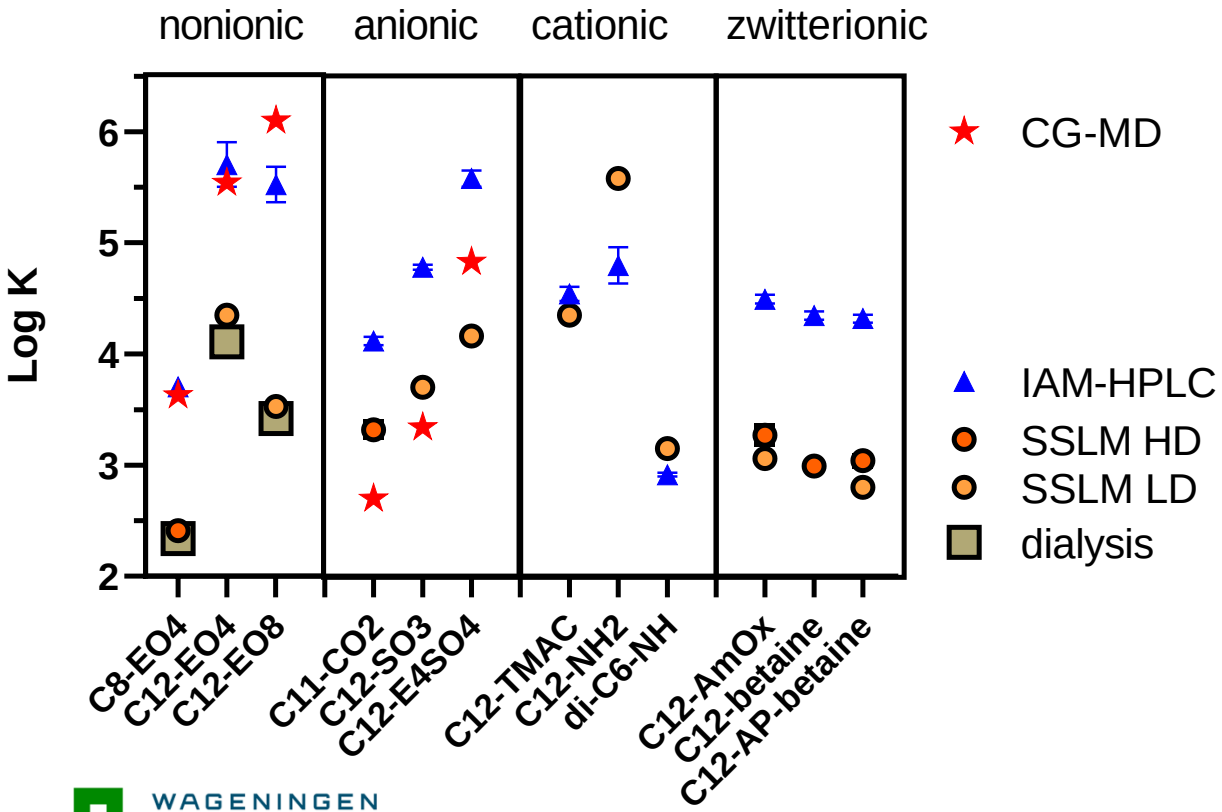
SSLM-dialysis

To be tested further... but close overlap between method and existing dialysis data non-ionics (1999)

Similar overlap SSLM & dialysis for PFAS (2021)

WAGENINGEN UNIVERSITY & RESEARCH

Phospholipid sorption computational tools: first results



Coarse Grain-Molecular Dynamics (CG-MD):

First trends:
Overestimate ethoxylates
Close for anionics

Still in progress...
(Durham University)

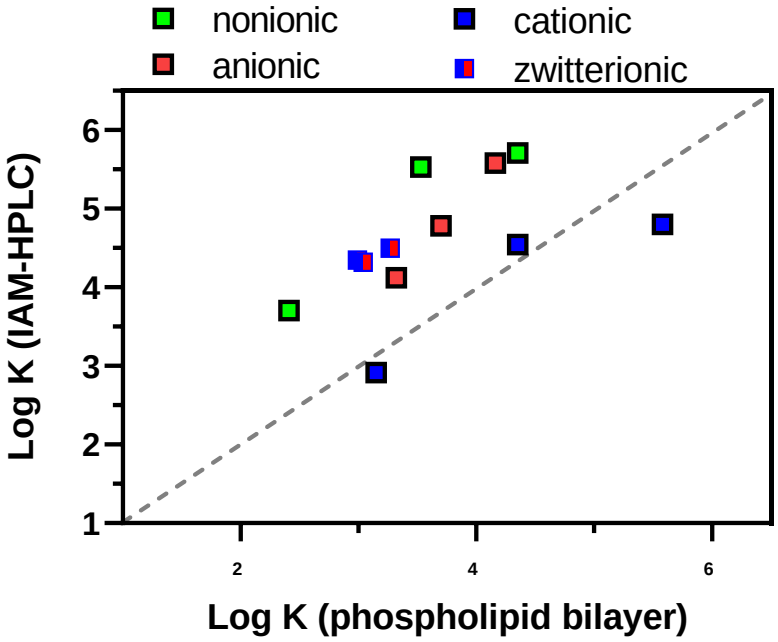
Cosmotherm:
In progress...

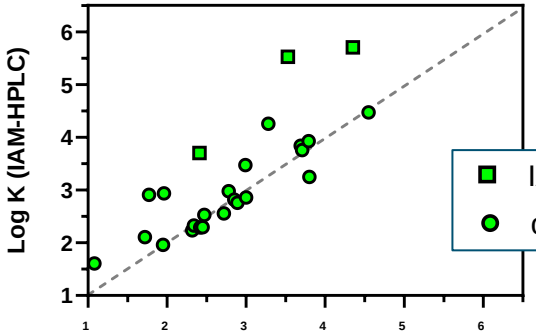
Pp-LFER for ions:
In progress...

WAGENINGEN
UNIVERSITY & RESEARCH

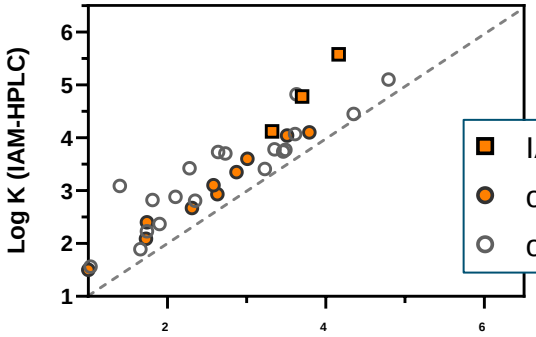
HPLC vs bilayer: published data*

Evaluation per surfactant type...

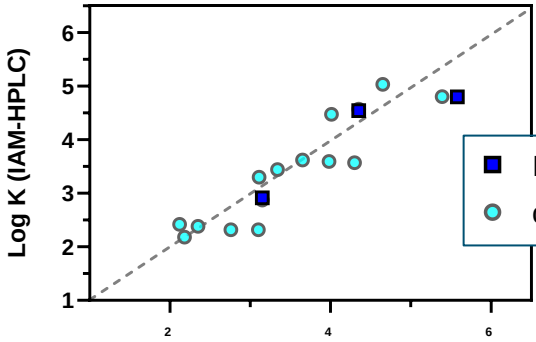




scatter...



~1-10x



~0.2-3x

WAGENINGEN UNIVERSITY & RESEARCH

*ES:P&I (2021), 23, p. 1930
ES:P&I (2023), 25, p. 621

Preliminary conclusions

Surfactants bind relatively strongly to phospholipid membranes

- Sorption coefficients can be made available for risk assessment
- Different tools are being evaluated for various surfactant types
- Assays with phospholipid bilayers align, give highest confidence
- Check applicability domains, experimental feasibility, ring testing

- Computational tools need to be validated for each surfactant type
- Computational tools can extend feasibility range

Thank you for your attention!

WAGENINGEN
UNIVERSITY & RESEARCH