Supplementary information

Predicting aquatic toxicity of anionic hydrocarbon and perfluorinated surfactants using membrane-water partition coefficients from coarse-grained simulations

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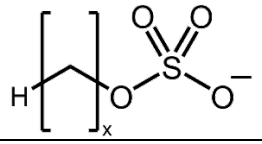
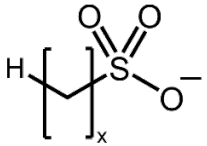
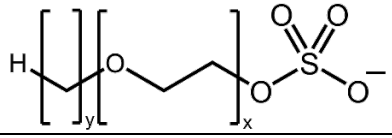
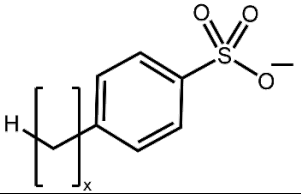
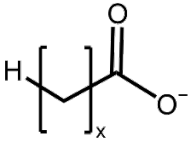
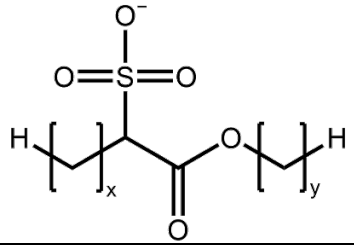
S1. Surfactant chemical space

Table S1. Naming and abbreviations of anionic surfactant groups

Groups of homologues	Abbreviation format/abbreviation	Structure
Alkyl sulfates (AS)	CXSO4, X = # of C-atoms	
Alkyl sulfonates	CXSO3, X = # of C-atoms	
Alkyl Ether Sulfates (AES)	CYEOXS, Y = # of C-atoms, X = # of ethoxylate (EO) groups	
Linear Alkylbenzene Sulfonate (LAS)	CX-LAS, X = # of C-atoms	
Salts of carboxylic acids (soaps)	CXCO2-, X = # of C-atoms	
Fatty Acids Ester Sulfonates (FAES)	CR(R')-FAES, X = # of C in the main chain, Y = # of C in the secondary chain	

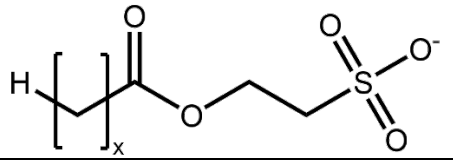
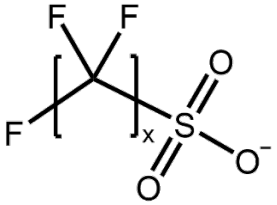
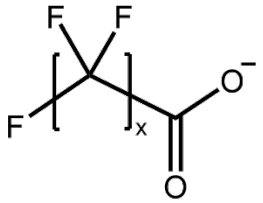
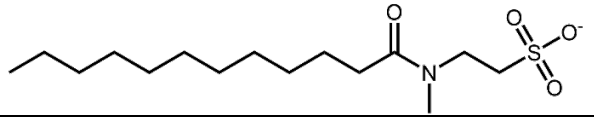
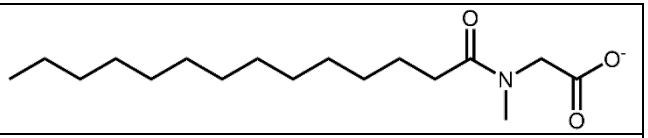
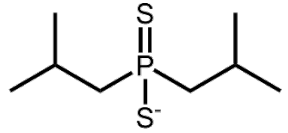
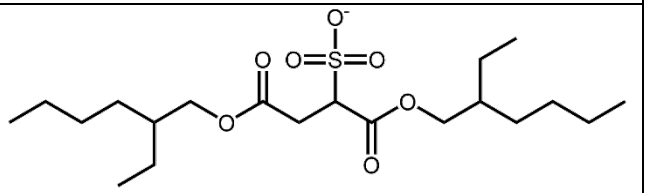
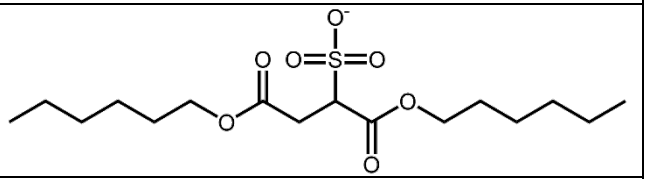
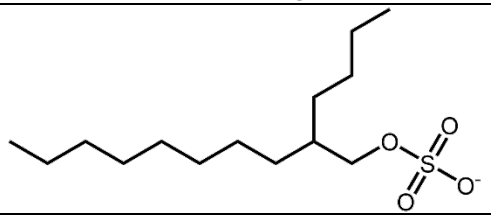
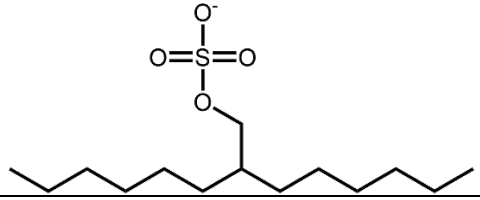
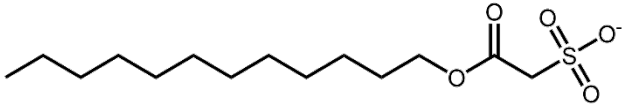
Alkyl Isethionates (AI)	CX-iseth, X = # of C-atoms in the main chain	
Perfluoroalkyl Sulfonic Acids (PFSA)	Abbreviation of a chemical name/xCF_y-SO3, x=number of perfluorinated carbons: x=4: Perfluorobutanesulfonic acid/PFBS x=6: Perfluorohexanesulfonic acid/PFHxS x=8: Perfluorooctanesulfonic acid/PFOS	
Perfluoroalkyl Carboxylic Acids (PFCA)	Abbreviation of a chemical name/nCFX-COOH, n=number of perfluorinated carbons: x=3: Perfluorobutanoic acid/PFBA x=4: Perfluoropentanoic acid/PFPeA x=5: Perfluorohexanoic acid/PFHxA x=6: Perfluoroheptanoic acid/PFHpA x=7: Perfluorooctanoic acid/PFOA x=8: Perfluorononanoic acid/PFNA x=9: Perfluorodecanoic acid/PFDA x=10: Perfluoroundecanoic acid/PFUnDA x=11: Perfluorododecanoic acid/PFDoDA	

Table S2. Naming and abbreviations of individual surfactant compounds

Individual compounds (surfactant group)	Individual compound abbreviation	SMILES	Structure
Taurates	C11SARSO3	CCCCCCCCCCCC(=O)N(C)CCS(=O)(=O)[O-]	

Sarcosinates	C14SAR	CCCCCCCCCCCCCC(=O)N(C)CC([O-])(=O)	
Dithiophosphate	PO4-2S-C4x2	CC(C)CP(=S)(CC(C)C)[S-]	
Sulfosuccinates	SO3-DOSS	CCCCC(CC)COC(=O)CC(C(=O)OCC(CC)CCCC)[S](=O)(=O)[O-]	
Sulfosuccinates	DiHexDiEsterSO3	CCCCCCOC(=O)CC(C(=O)OCCCCCC)[S](=O)(=O)[O-]	
AS-branched	C10(4)SO4	CCCCCCCCC(CCCC)CO[S]([O-])(=O)=O	
AS-branched	C8(6)SO4	CCCCCCC(CCCCCC)CO[S]([O-])(=O)=O	
Sulfoacetate	C12COOCSO3	CCCCCCCCCCCCOC(=O)CS(=O)(=O)[O-]	

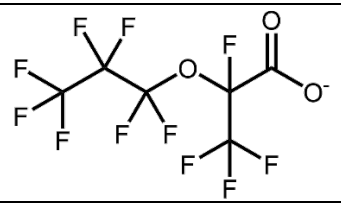
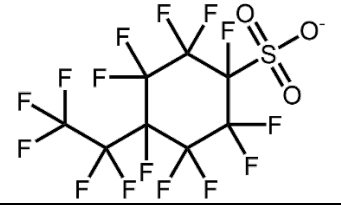
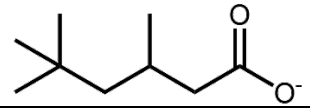
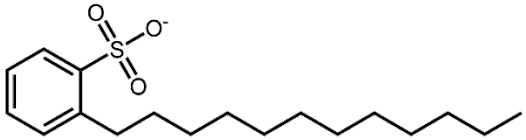
PFECA (perfluoroalkyl ether carboxylic acids)	GenX	C(=O)(C(C(F)(F)F)(OC(C(C(F)(F)F)(F)F)(F)F)(F)F)[O-]	
Cyclic PFSA	PFECHS	C1(C(C(C(C(C1(F)F)(F)F)(F)S(=O)(=O)[O-])(F)F)(F)F)(C(C(F)(F)F)(F)F)F	
Carboxylic acid salts (Soaps) - branched	BrC9CO2-	CC(CC(=O)[O-])CC(C)(C)C	
Linear Alkylbenzene Sulfonate	C12BzSO3	CCCCCCCCCCCCC1=CC=CC=C1S(=O)(=O)[O-]	

Table S3. List of all individual surfactants with SMILES, molecular weight and dissociation constants

Abbreviation	SMILES (unsalted, ionised)	Surfactant group/PFAS group[1]	Molecular Weight	pK_a
C12EO1S	CCCCCCCCCCCCOCCOS([O-])(=O)=O	AES	310.45	-3.55
C14EO1S	CCCCCCCCCCCCCCOCCOS([O-])(=O)=O	AES	338.503	-3.55
C15EO1S	CCCCCCCCCCCCCCCOCCOS([O-])(=O)=O	AES	352.53	-3.55
C12EO2S	CCCCCCCCCCCCOCCOCCOS([O-])(=O)=O	AES	354.503	-3.57
C13EO2S	CCCCCCCCCCCCCOCCOCCOS([O-])(=O)=O	AES	368.529	-3.57

C14EO2S	CCCCCCCCCCCCCCOCCOCCOS([O-])(=O)=O	AES	382.556	-3.57
C12EO3S	CCCCCCCCCCCCOCCOCCOCCOS([O-])(=O)=O	AES	398.555	-3.58
C12EO4S	CCCCCCCCCCCCOCCOCCOCCOCCOS([O-])(=O)=O	AES	442.608	-3.58
C14EO4S	CCCCCCCCCCCCCCOCCOCCOCCOCCOS([O-])(=O)=O	AES	470.661	-3.58
C13EO6S	CCCCCCCCCCCCCOCCOCCOCCOCCOCCOCCOS([O-])(=O)=O	AES	544.739	-3.58
C12EO8S	CCCCCCCCCCCCOCCOCCOCCOCCOCCOCCOCCOCCOS([O-])(=O)=O	AES	618.818	-3.58
C8SO3	CCCCCCCCS([O-])(=O)=O	Alkyl sulfonate	194.292	1.86
C10SO3	CCCCCCCCCCS([O-])(=O)=O	Alkyl sulfonate	222.345	1.85
C11SO3	CCCCCCCCCCCS([O-])(=O)=O	Alkyl sulfonate	236.371	1.84
C12SO3	CCCCCCCCCCCCS([O-])(=O)=O	Alkyl sulfonate	250.398	1.84
C8SO4	CCCCCCCCOS([O-])(=O)=O	AS	210.291	-3.26
C10SO4	CCCCCCCCCCOS([O-])(=O)=O	AS	238.344	-3.28
C11SO4	CCCCCCCCCCCOS([O-])(=O)=O	AS	252.371	-3.29
C12SO4	CCCCCCCCCCCCOS([O-])(=O)=O	AS	266.397	-3.29
C14SO4	CCCCCCCCCCCCCCO[S]([O-])(=O)=O	AS	294.451	-3.29
C14SO4	CCCCCCCCCCCCCCOS([O-])(=O)=O	AS	294.451	-3.29
C15SO4	CCCCCCCCCCCCCCCOS([O-])(=O)=O	AS	308.477	-3.29
C10(4)SO4	CCCCCCCCC(CCCC)CO[S]([O-])(=O)=O	AS-branched	294.451	-3.34
C8(6)SO4	CCCCCCC(CCCCCC)CO[S]([O-])(=O)=O	AS-branched	294.451	-3.31
PO4-2S-C4x2	CC(C)CP(=S)(CC(C)C)[S-]	Dithiophosphate	210.34	4.56
C12(1)-FAES	CCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	294.408	0.4
C10(4)-FAES	CCCCCCCCC(C(=O)OCCCC)S(=O)(=O)[O-]	FAES	308.434	0.61
C10(iso-4)-FAES	CCCCCCCCC(C(=O)OCC(C)C)S(=O)(=O)[O-]	FAES	308.434	0.59
C10(sec-4)-FAES	CCCCCCCCC(C(=O)OC(C)CC)S(=O)(=O)[O-]	FAES	308.434	0.59
C11(3)-FAES	CCCCCCCCCC(C(=O)OCCC)S(=O)(=O)[O-]	FAES	308.434	0.6
C12(2)-FAES	CCCCCCCCCCC(C(=O)OCC)S(=O)(=O)[O-]	FAES	308.434	0.67
C13(1)-FAES	CCCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	308.434	0.4
C7(7)-FAES	CCCCCC(C(=O)OCCCCCCC)S(=O)(=O)[O-]	FAES	308.434	0.75
C8(6)-FAES	CCCCCCC(C(=O)OCCCCCC)S(=O)(=O)[O-]	FAES	308.434	0.64

C8(sec-6)-FAES	CCCCCCC(C(=O)OC(C)CCCC)S(=O)(=O)[O-]	FAES	308.434	0.6
C9(5)-FAES	CCCCCCCC(C(=O)OCCCCC)S(=O)(=O)[O-]	FAES	308.434	0.61
C9(sec-5)-FAES	CCCCCCCC(C(=O)OC(C)CCC)S(=O)(=O)[O-]	FAES	308.434	0.58
C14(1)-FAES	CCCCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	322.461	0.4
C12(4)-FAES	CCCCCCCCCCC(C(=O)OCCCC)S(=O)(=O)[O-]	FAES	336.487	0.59
C12(sec-4)-FAES	CCCCCCCCCCC(C(=O)OC(C)CC)S(=O)(=O)[O-]	FAES	336.487	0.58
C14(2)-FAES	CCCCCCCCCCCCC(C(=O)OCC)S(=O)(=O)[O-]	FAES	336.487	0.67
C16(1)-FAES	CCCCCCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	350.514	0.4
C12(5)-FAES	CCCCCCCCCCC(C(=O)OCCCCC)S(=O)(=O)[O-]	FAES	350.514	0.6
C14(iso-3)-FAES	CCCCCCCCCCCCC(C(=O)OC(C)C)S(=O)(=O)[O-]	FAES	350.514	0.71
C14(4)-FAES	CCCCCCCCCCCCC(C(=O)OCCCC)S(=O)(=O)[O-]	FAES	364.54	0.59
C14(5)-FAES	CCCCCCCCCCCCC(C(=O)OCCCCC)S(=O)(=O)[O-]	FAES	378.567	0.6
C8-iseth	CCCCCCCC(=O)OCCS(=O)(=O)[O-]	Alkyl Isethionates	252.328	1.08
C10-iseth	CCCCCCCCCC(=O)OCCS(=O)(=O)[O-]	Alkyl Isethionates	280.381	1.08
C9-LAS	CCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	284.414	-0.45
C10-LAS	CCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	298.441	-0.45
C11-LAS	CCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	312.467	-0.45
C12BzSO3	CCCCCCCCCCCC1=CC=CC=C1S(=O)(=O)[O-]	LAS	326.494	-0.53
C12-LAS	CCCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	326.494	-0.45
C13-LAS	CCCCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	340.521	-0.45
C14-LAS	CCCCCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	354.547	-0.45
BrC9CO2-	CC(CC(=O)[O-])CC(C)(C)C	Salts of carboxylic acids (soaps)	158.238	4.8
C9CO2-	CCCCCCCCC([O-])=O	Salts of carboxylic acids (soaps)	158.238	4.78
C11CO2-	CCCCCCCCCCC([O-])=O	Salts of carboxylic acids (soaps)	200.318	4.78
C14SAR	CCCCCCCCCCCCCC(=O)N(C)CC([O-])(=O)	Sarcosinates	299.449	3.62 | -0.98
C12COOCSO3	CCCCCCCCCCCCOC(=O)CS(=O)(=O)[O-]	Sulfoacetate	308.434	0.5
DiHexDiEsterSO3	CCCCCCOC(=O)CC(C(=O)OCCCCCC)[S](=O)(=O)[O-]	Sulfosuccinates	366.47	0.11
SO3-DOSS	CCCCC(CC)COC(=O)CC(C(=O)OCC(CC)CCCC)[S](=O)(=O)[O-]	Sulfosuccinates	422.577	0.08

C11SARSO3	CCCCCCCCCCCC(=O)N(C)CCS(=O)(=O)[O-]	Taurates	321.476	1.42 | -0.70
GenX	C(=O)(C(C(F)(F)F)(OC(C(C(F)(F)F)(F)F)(F)F)(F)F)F)[O-]	PFECA (perfluoroalkyl ether carboxylic acids)	330.053	-1.36
PFBA	C(=O)(C(C(C(F)(F)F)(F)F)(F)F)[O-]	PFCA	214.038	0.37
PFBS	C(C(C(F)(F)S(=O)(=O)[O-])(F)F)(C(F)(F)F)(F)F	PFSA	300.1	-3.57
PFDA	C(=O)(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	514.083	0.52
PFDoDA	C(=O)(C(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	614.098	0.52
PFECHS	C1(C(C(C(C(C1(F)F)(F)F)(F)S(=O)(=O)[O-])(F)F)(F)F)(C(C(F)(F)F)(F)F)F	Cyclic PFSA	462.133	-3.56
PFHxA	C(=O)(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	314.053	0.42
PFNA	C(=O)(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	464.076	0.52
PFOA	C(=O)(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	414.068	0.5
PFOS	C(C(C(C(C(F)(F)S(=O)(=O)[O-])(F)F)(F)F)(F)F)(C(C(C(F)(F)F)(F)F)(F)F)(F)F	PFSA	500.13	-3.27
PFUnDA	C(=O)(C(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	564.091	0.52
10:2 FTCA	C(C(=O)[O-])C(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F	FTCA	578.117	3.42
10:2 FTUCA	C(=C(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)C(=O)[O-]	FTUCA	558.111	3.03
6:2 FTUCA	C(=C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)C(=O)[O-]	FTUCA	358.081	2.96
7:3 FTCA	C(CC(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)C(=O)[O-]	FTCA	442.122	4.22
8:2 FTCA	C(C(=O)[O-])C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F	FTCA	478.102	3.41
8:2 FTUCA	C(=C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)C(=O)[O-]	FTUCA	458.096	3.02

[1] Abbreviated as: AES = Alkyl Ether Sulfates, AS = Alkyl Sulfates, LAS = Linear Alkylbenzene Sulfonate, FAES = Fatty Acids Ester Sulfonates, PFCA = Perfluoroalkyl Carboxylic Acids, PFSA = Perfluoroalkyl Sulfonic Acids, FTCA = FluoroTelomer Carboxylic Acid, FTUCA = FluoroTelomer Unsaturated Carboxylic Acids

[2] pK_a values were calculated with ACD/Labs® software (2015, pack 2.5), Advanced Chemistry Development, Inc., 2015. Toronto, Canada. www.acdlabs.com.

S2. Experimental methods - additional information

Empirical membrane lipid-water partitioning coefficients (D_{mw}) were determined by one of two methods: liposome-water partitioning, based on the approach described by Ebert *et al.*[1] or SSLM (solid-supported lipid membrane) approach as described by Timmer *et al.*[2] For some substances, namely AES/AS and alkyl isethionates, D_{mw} values were newly generated for the purpose of this study. All other experimental D_{mw} values were obtained from existing literature (as presented in S4.1 Comparison of experimental data with simulation method

Table S12 compiles the experimental log *Dmw* values from the literature and newly generated values from this study (indicated as "New value"), with simulated log *Dmw* values for the same set of chemicals. The table is the basis of Figure 1 from the article.

Table S12, section S4). Details of the experimental methods are presented here.

Chemicals

The following chemicals were all obtained from Sigma-Aldrich (subsidiary of Merck KGaA, Burlington, USA) with purities >95%: Sodium Octyl Sulfate (C8SO4) and Sodium Dodecyl Sulfate (C12SO4), 2-oleoyl-1-palmitoyl-sn-glycero-3- phosphocholine (POPC) and phosphate buffer saline (PBS) tablets. C12EO3S and C14EO3S were obtained from TOCRIS (Bio-Techne Ltd. Abingdon UK). A commercial mixture of Alcohols, C12-C14, ethoxylated, sulfates, sodium salts (CAS 68891-38-3, EC 500-234-8) (SLES) were obtained from Unilever. Chloroform (99.8%) and formic acid (>99%) were from VWR Chemicals (Leuven, Belgium). LC-MS/MS grade water and acetonitrile were from Biosolve Chimie (Dieuze, France).

S2.1 Liposome method

Experimental D_{mw} values for selected AS/AES chain lengths were determined using liposome-water partitioning based on the experimental methodology described by Ebert et al.[1] Test materials included three single-chain standards obtained from Merck Life Sciences, Gillingham (C8SO4, C12SO4, C12EO3S, C14EO3S) and a commercial mixture of Alcohols, C12-C14, ethoxylated, sulfates, sodium salts (CAS 68891-38-3, EC 500-234-8) (SLES) and Alcohols, C12-C13, branched and linear, ethoxylated, sulfates, sodium salts (CAS 161074-79-9, EC 500-513-4) (SPES) obtained from Unilever.

Details of liposome preparation, as previously described in Potter *et al.*[3] are as follows: Solutions of POPC were prepared in chloroform in a round bottom flask. This flask was placed under a stream of nitrogen gas and gently agitated until a dry film was formed. This was re-suspended in pH 7.4 phosphate saline buffer, to a concentration of POPC of approximately 13.2 mM, forming a suspension of large multilamellar vesicles followed by 5 freeze-thawed cycles with liquid nitrogen and hot tap water immersion. This solution was then extruded 11 times through a 100 ηM polycarbonate membrane using a LiposoFast basic extruder (both Supplied by Avestin Europe GmbH, Mannheim, Germany) to form unilamellar liposome vesicles.

The liposome-water partitioning was determined in a 96-well plate Rapid Equilibrium Dialysis (RED) device (by Thermo Fisher Scientific). Each well in the RED device contains a donor cell (red cell) and a receptor (white cell) separated by a 12 kDa molecular weight cut-off cellulose membrane, through which the liposomes cannot permeate. The liposome solutions were diluted to approximately 4 mM with PBS solution (pH 7.4) and addition of the prepared mixture of test chemicals, thereby giving a final known donor concentration of POPC and Test chemical. Groups of test mixtures were chosen according to their suitability for analyses under

the same analytical method. Dose concentrations were chosen based on the total well load and expected concentration in the mixtures.

Prepared donor, controls and PBS blank solutions (400 µL) were added to the triplicate red cell of the rapid equilibrium dialysis (RED) plate, with PBS buffer (600 µL) added to the white cell. For each test chemical mixture control samples were also prepared where 400 µL solutions of spiked PBS at an equivalent concentration to the donor samples were added to the donor red cell and 600 µL of PBS added to the white receptor cell.

The plate was sealed and incubated at 37 ºC on an orbital shaker at ~80 rpm to allow equilibration through the membrane between the two wells. After removal from the incubator, and equilibration to room temperature, aliquots were taken to an autosampler vial. Acetonitrile was added, before a brief vortex prior to analysis.

Analysis was conducted on both red and white cells for control samples and blanks prepared in PBS and only the white cells for donor samples.

Analysis was carried out by Liquid Chromatography (Agilent 1290) with Electrospray triple quadrupole (6495) detection. Identification was done by using Multiple reaction monitoring (MRM), a highly sensitive method of targeted mass spectrometry (MS). Quantitation is carried out by mixed analyte external calibration curve. Analysis was carried out at both 24- and 48-hour incubation with stocks prepared at 50 and 100 µM concentration. The data reported are the mean of multiple analyses.

Analytical method for liposome analysis:

Liquid Chromatography conditions:

Mobile phase A: 0.1% formic acid in MQ (0.5ml Formic acid in 500ml Ultrapure water)

Mobile phase B: 0.1% formic acid in Acetonitrile (0.5 ml Formic acid in 500 ml Acetonitrile)

Injection volume: 5µL with Autosampler flush: 3 seconds using Mobile phase B after injection. A flow rate of 0.7 ml/min was used using a gradient analysis followed by a 2-minute re-equilibration prior to the next injection.

Column: Luna Omega 1.6 µM C18 100 Å 50 × 2.1 mm at 35 ºC

Minute	% Mobile phase A	% Mobile phase B
0	95	5
0.5	95	5
1.8	35	65
4.0	5	95
7.0	5	95

The first minute of each injection is diverted from the MS to waste, thus avoiding PBS buffer entering the source.

Mass detection conditions (negative polarity):

Sheath Gas temp 400 ºC, Sheath Gas flow 10 L/min

Drying Gas temp 230 ºC, Drying Gas flow 10 L/min

Capillary Voltage –2000 V, Nozzle voltage –2000 V, Nebuliser 30 psi

Cell accelerator: 7 V, Collision Energy: 20 V

Table S4. C12 AS/AES mass detection conditions

Analyte	C12SO4	C12EO1S	C12EO2S	C12EO3S	C12EO4S
Precursor ion *m/z*	265.1	309.2	353.2	397.2	441.3
Product ion *m/z*	97.1	97.1	97.1	97.1	97.1
Fragmentor (V)	135	135	135	135	135
Retention time (minutes)	~3.9	~4.1	~4.3	~4.4	~4.5

Table 5. C14 AS/AES mass detection conditions

Analyte	C14SO4	C14EO1S	C14EO2S	C14EO3S	C14EO4S
Precursor ion *m/z*	293.2	337.2	381.2	425.5	469.3
Product ion *m/z*	97.1	97.1	97.1	97.1	97.1
Fragmentor (V)	380	380	380	380	380
Retention time (minutes)	~3.9	~4.1	~4.3	~4.4	~4.5

Liposome calculation of log D_{mw}

The $\log_{10}$ of the membrane/water partition coefficient (log D_{mw}) was calculated as:

$$\log D_{\mathrm{MW}} = \log \frac{C_{\mathrm{lipid}}}{C_{\mathrm{aqueous}}}$$

Where C_{lipid} is the concentration of a chemical in the liposome phase and C_{aqueous} is the concentration of the chemical in the surrounding aqueous (PBS) phase, which are calculated from the RED experiment as follows:

$$C_{\mathrm{lipid}} = \frac{n_{\mathrm{lipid}}}{m_{\mathrm{lipid}}} = \frac{n_{\mathrm{total}} - n_{\mathrm{free}}}{n_{\mathrm{POPC}} \times \mathrm{MW}_{\mathrm{POPC}}}$$

Where n_{lipid} corresponds to the total amount of chemical in the liposomes phase (in mol), determined from the RED experiment as the difference between the total amount of chemical the liposome is exposed to (n_{total}) and the amount that remains free in solution (n_{free}). n_{total} is determined from the measured concentration in the control wells (without liposomes) and n_{free} is determined from the measured concentration in the white cell of the liposome-containing wells. m_{lipid} is calculated by multiplying the total mols of POPC used to make the liposomes (n_{POPC}) with the molecular weight of POPC (760.1 g/mol). C_{aqueous} is measured directly from the white cell of the liposome-containing wells.

Table S6. Summary of analytical results, D_{mw} values for SLES individual components and D_{mw} values of single component analytical standards

Abbreviation	SLES commercial mixture	Single component reference standard
C12SO4	4.44[1]	4.29[2]
C14SO4		5.13
C12EO1S	4.70[1]	
C12EO2S	4.60[1]	
C12EO3S	4.41[1]	4.47[3]
C12EO4S	4.06[1]	
C14EO1S	5.22	
C14EO2S	5.16	
C14EO3S	4.95	4.74
C14EO4S	5.15	

[1] Analysis was reported as a mean triplicate analysis, the remaining data reported a mean of duplicate analyses.
[2] n= 2, 50μM and 100μM after 48hrs 4.25 (n=3), 4.32 (n=3) respectively
[3] n= 4, 50μM and 100μM after 24hrs (4.85 (n=3), 4.27 (n=3), and 50μM and 100μM after 48hrs (4.43 (n=3), 4.32 (n=3))

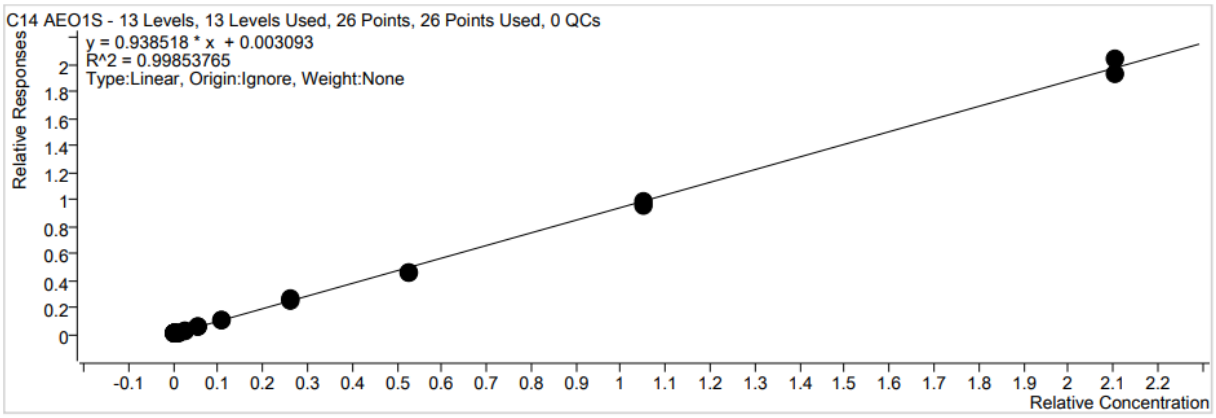


Figure S1. Example of the calibration line used for quantitation.

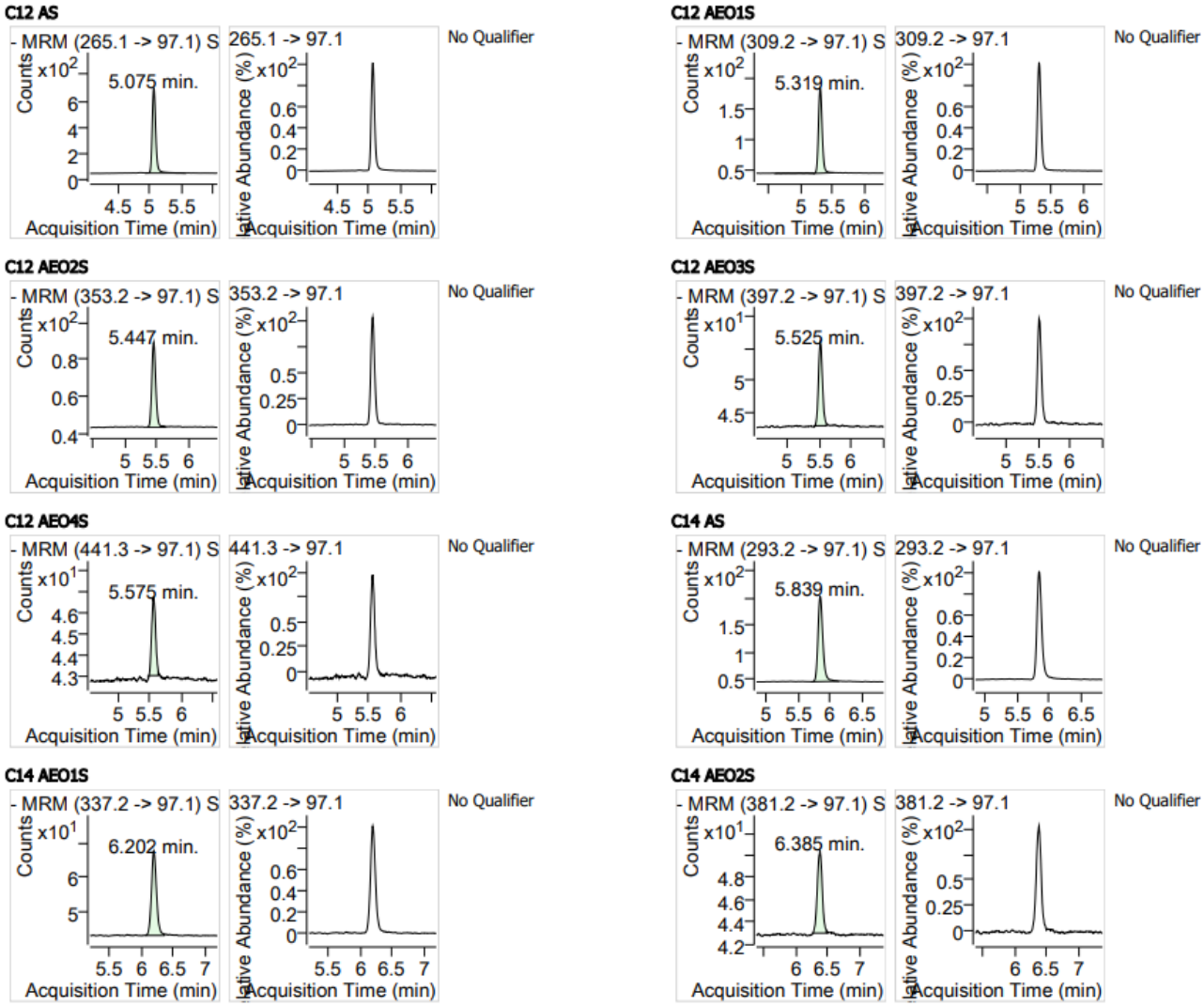


Figure S2. Typical chromatogram of EIC by LC/MS/MS

S2.2 Solid-supported lipid membranes (SSLM) method

The TRANSIL Intestinal Absorption Kit measures the affinity of a test item to immobilized phosphatidylcholine membranes with natural membrane fluidity. This membrane affinity is a partitioning coefficient of the drug (chemical) between the membrane and buffer[4]. TRANSIL Intestinal Absorption Kit – Sovicell (Leipzig, Germany) SSLM consists of supported bilayers which are created by the self-assembly of lipids onto solid supports, typically silica.

The membrane-water distribution coefficient (D_{mw}) of test substances sodium myristoyl isethionate, sodium octyl sulfate and sodium dodecyl sulfate were determined at pH 7.4, at 37 ± 1 ºC. Sodium decanoyl isethionate was determined at pH 7.4 at 20 ± 1 ºC, using solid-supported lipid membranes (SSLM).

Following the manufacturer's guidelines, the lipid density TRANSIL plate was defrosted overnight in a refrigerator and allowed to equilibrate to 20 ºC for at least 60 minutes. Excess buffer was removed and replaced with ammonium acetate buffer (pH 7.4) and the whole content including beads transferred to a glass vial. Another wash and centrifugation were carried out and the buffer was removed leaving the sorbent beads undisturbed. Fresh buffer was added to the vial and a stock solution of each test item was prepared in methanol and subsequently diluted to prepare individual dosing solutions. Each test vessel was dosed with a single aliquot of the corresponding dosing solution. The tests were performed in duplicate at six sorbent levels in HPLC vials with lipid beads from the standard density kit.

Once dosed, the vessels were agitated on an orbital shaker in an oven set to 20 ºC or 37 ºC (detailed below) for the required incubation time. The aqueous phase was separated by centrifugation and analysed by the appropriate LC-MS method. For each definitive test, at least one matrix blank sample was prepared and analysed concurrently with the samples, to determine possible interferences. T0 reference vessels (no sorbent) were used as fortified matrix samples to demonstrate recovery of the method.

SSLM Calculation of log D_{mw}

The concentration and total quantity of the test items in the lipid phase was calculated as follows:

$$c_{\mathrm{lipid}} = \frac{n_{\mathrm{total}} - n_{\mathrm{aqueous}}}{V_{\mathrm{lipid}}}$$

Where n_{total} is the total amount of a chemical and n_{aqueous} is the amount of a chemical in the aqueous phase, V_{lipid} is the volume of lipid on the SSLM beads, as specified by the manufacturers. We note that the concentration in the lipid phase is defined per unit *volume* of lipid in the SSLM method, but per unit *mass* of lipid in the liposome method (ESI Section 2.1) and simulations (ESI Section 3.7). However, since the density of the lipid phase is numerically close to unity in units of L kg^{-1}, the resulting definitions of D_{mw} are interchangeable in practice.

The $\log_{10}$ of the membrane/water partition coefficient ($\log D_{mw}$) was calculated as the intercept of the plot of the $\log_{10}$ of the lipid concentrations against the $\log_{10}$ of the aqueous concentrations using a forced slope of 1, calculated as follows:

$$\log D_{\mathrm{mw}} = \log c_{\mathrm{lipid}} - \log c_{\mathrm{aqueous}}$$

Where $\log c_{\mathrm{lipid}}$ is the mean $\log_{10}$ transformed concentration in lipid and $\log c_{\mathrm{aqueous}}$ is the mean $\log_{10}$-transformed concentration in aqueous phase.

Table S7. Method summary for SSLM standard and high plates

Test Item	T0 Mean aqueous recovery data %	mass balance (including vessel extraction)	Plate used for partitioning	Incubation temperature at pH 7.4	Overall dilution factor	Dosed concentration	Incubation time (hours)
C14-iseth	>85	>95%	Standard	37 ± 1 °C	2	50 µg/L	2
C10-iseth	>80	>85%	High [#1]	20 ± 1 °C	8	400 µg/L	144
C8SO4	112	nd	High [#1]	37 ± 1 °C	-	1 µM	0.5
C12SO4	>90	>85	Standard	37 ± 1 °C	4	0.69 µM	overnight

[#1]10x for low-affinity compounds

Analytical Conditions for SSLM analysis

The concentrations of the test items were measured using liquid chromatography mass spectrometry (LC-MS), as outlined below:

Instrument:	Thermo Vanquish UHPLC with Thermo Orbitrap Exploris 240 MS
Injection volume:	3 µL
Column:	Agilent, Poroshell-120 EC-C18, 50 x 2.1mm x 2.7 µM
Column temperature:	45 °C
Eluent flow rate:	700 µl/min
Eluent A:	0.1% formic Acid in LC-MS grade water
Eluent B:	0.1% formic Acid in LC-MS grade acetonitrile

Study samples were diluted as required and analysed against calibration standard solutions prepared in methanol: water 50:50.

Test Item preparation	Dilution	Dilution solvent
C14-iseth	2:5	Acetonitrile
C10-iseth	1:8	50:50 methanol/water
C8SO4	-	n/a
C12SO4	1:3	50:50 methanol/water

Mobile phase gradient timetable for C8SO4			Mobile phase gradient timetable for isethionates		
Time (mins)	A(%)	B(%)	Time (mins)	A(%)	B(%)
0.000	95	5	0.000	60	40
0.500	95	5	0.800	60	40
1.500	70	30	2.000	5	95
1.800	35	65	3.000	5	95
4.000	5	95	3.010	60	40
5.000	5	95	4.500	60	40
5.100	95	5			
7.0	95	5			

Sodium dodecyl sulfate was run isocratically at a ratio: 50:50 Eluent A: Eluent B

Source:	HESI		
Sheath gas pressure:	50 (Arb)	Spray Voltage:	positive: 3500 V; negative: 2500 V
Auxiliary gas pressure:	15 (Arb)	Vaporiser temperature:	350 °C
Ion sweep gas pressure:	1.0 (Arb)	Isolation width:	2 amu
Capillary temperature:	350 °C	Resolution:	45000

Table S8. Detection carried out using a single monitored ion for each component.

Analyte	Typical Retention Time (min)	Monitored Ion (Da)
C14-iseth	2.49	335.1898
C10-iseth	0.88	279.1270
C8SO4	2.1	209.0853
C12SO4	1.1	265.1479

Example Chromatograms, Calibration and log D_{mw} plots

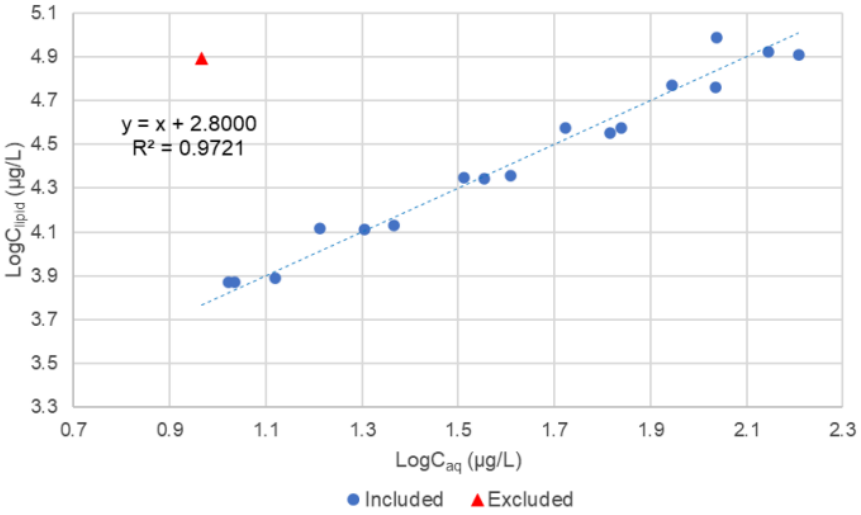


Figure S3. Example of the log D_{mw} (shown as intercept) calculation plot for sodium decanoyl isethionate

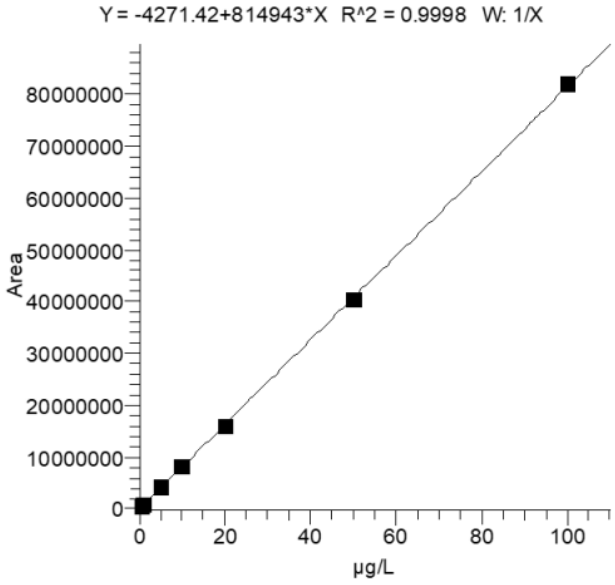


Figure S4. Typical LCMS calibration curve (Sodium myristoyl Isethionate) prepared in 50:50 water: methanol 1.0 – 100µg/L

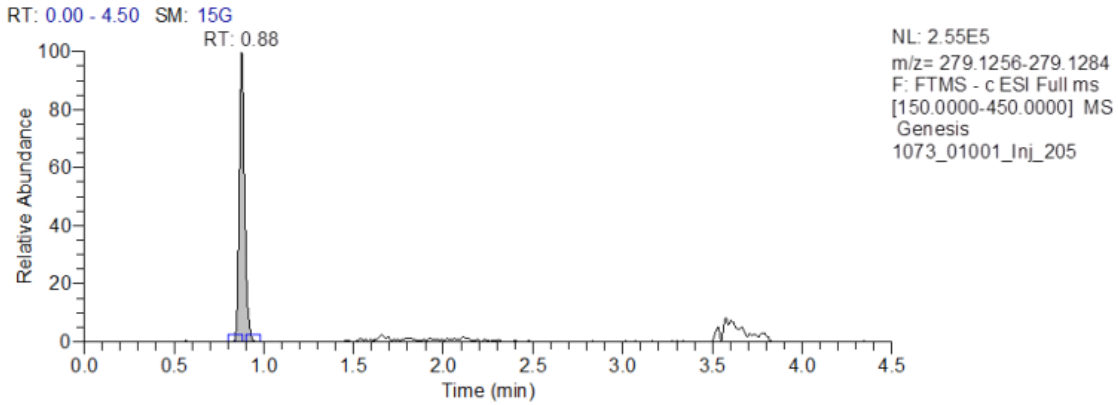


Figure S5. Example chromatogram of calibration standard (Sodium Decanoyl Isethionate)

Table S9. Summary of the log D_{mw} values for alkyl isethionates and alkyl sulfates determined by the SSLM method

Test Item	**log D_{mw}**
Sodium Myristoyl Isethionate (C14-iseth)	4.88
Sodium Decanoyl Isethionate (C10-iseth)	2.80
Sodium octyl sulfate (C8SO4)	2.19
Sodium dodecyl sulfate (C12SO4)	4.28

S3. Simulation methods – additional information

S3.1 Aliphatic Charged Bead Assignment

For expansion of the mapping and parametrisation algorithm to charged fragments, a manual parameterisation to literature and newly produced experimental D_{mw} data is required, as the K_{ow} data used to parameterise neutral fragments are unreliable for ionised species. Charged bead types in the Martini 3 force field[5] were assigned based on simple, linear-chain surfactants with each headgroup. The resulting headgroup assignment can then be applied to more complex species. This approach ensures the headgroup assignment is minimally biased by the chemical environment of the headgroup in the molecule. For instance, linear sulfonates can be used to assign the charged bead for the SO_3^- group, which can then be applied whenever that fragment arises, such as in benzyl sulfonates. The effectiveness of this transfer approach is shown in Figure 1 of the main article, where 20 of the 43 molecules were not used in the assignment of the charged bead, and still gave excellent predictions.

As the mapping and parametrisation algorithm has undergone development (e.g., centre-of-geometry mapping) since charged bead assignments were first made in this way,[3] pre-existing headgroup assignments were also reviewed to ensure that they remain optimal. The resulting bead assignments were SQ5n, Q2 and Q3 for carboxylates, sulfates and sulfonates, respectively. The sulfate and carboxylate assignments are unchanged from our previous work[3]. However, the sulfonate bead differs from previous publications, which assigned sulfonates as SQ4p. The change is due to the inclusion of additional chain lengths of linear sulfonates when assigning the charged bead in this work. The sulfonate group also appears in isethionates, and we use the Q3 bead there also. Figure S6 shows the change in D_{mw} for sulfonates and isethionates with the old (SQ4p) and new (Q3) assignments for the SO_3^- group.

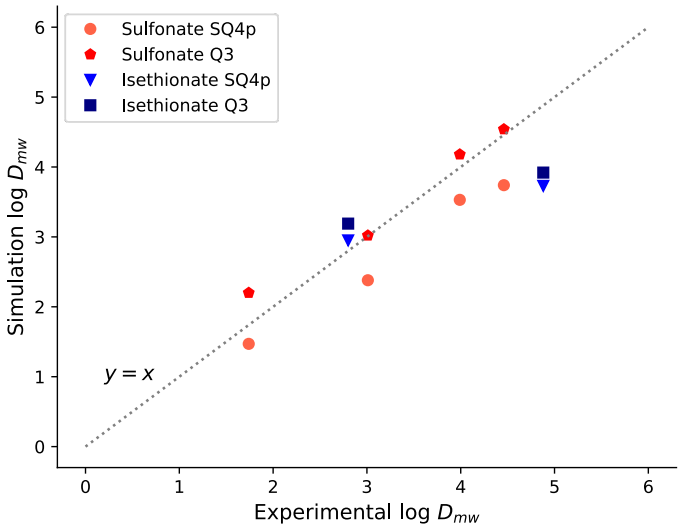


Figure S6. Simulated vs experimental log D_{mw} values for a series of chain lengths of alkyl sulfonates and alkyl isethionates with two bead assignments: the previous assignment[3], SQ4p, and the new assignment, Q3. Octyl-, dectyl-, dodectyl- and tridecyl-sulfonates are plotted. Two variants of decyl- and dodecyl- isethionates are plotted, two linear versions and two methylated versions with a methyl branch inserted between the sulfonate and ester group. These molecules are plotted due to the availability of experimental D_{mw} data, listed in S4.1.

S3.2 Perfluorinated surfactants

In the Martini model, the grouping of atoms into beads is based on heavy (i.e., non-hydrogen) atoms, with a regular bead typically containing four heavy atoms, along with any hydrogen atoms attached to them. Hence, C_4H_8 beads are common in alkyl chains. However, the corresponding perfluorinated fragment C_4F_8 formally contains 12 heavy atoms, which is far too many for a single Martini bead. Hence, perfluorinated molecules require different mappings from their aliphatic counterparts.

Due to its small size compared to other heavy atoms, the Martini developers advise treating fluorine as half a heavy atom when mapping a bead[5]. For instance, a bead of CF_2CF_2 would be treated as bearing four heavy atoms. The spectral mapping algorithm in our cg_param algorithm handles such cases well without special adjustments; in a perfluorinated molecule, alkyl carbons are paired first, with the remaining substituent fluorines forced into the carbon chains because they would otherwise be isolated as lone atoms. The resulting mappings are in line with the Martini developers' advice. Even though the mapping is not affected, cg_param has been modified to treat fluorine as half a heavy atom for compatibility with Martini 3 guidelines and further tests of our method in the future.

Having mapped perfluorinated surfactants into coarse-grained beads, the next step is to parametrise the beads. cg_param has been expanded to include the Martini halogenated 'X' beads, which are new in version 3 of the force field.[5] These beads differ from the rest of Martini's aliphatic beads in that their self-interaction increases, rather than decreases, in strength with increasing hydrophobicity. This feature allows the X beads to better capture the chemical nature of halogenated species. Figure S10 shows a comparison of log D_{mw} from simulation and experiment without (top panel) and with (middle panel) halogenated beads for the perfluorinated carboxylates and sulfonates sampled in this work. The inclusion of halogenated beads produces a systematic improvement. We caution that our algorithm does not yet deploy halogenated beads for aromatic moieties, due to a need for independent K_{ow} data for benchmarking such molecules.

Additionally, different charged-bead assignments were made for the perfluorinated carboxylates and sulfonates compared to alkyl carboxylates and sulfonates. Perfluorinated sulfonate beads were shifted from Q3 to Q1p. Perfluorinated carboxylates were shifted from SQ5n to SQ1p. Fluorination is widely reported to increase lipophilicity in neutral alkyl compounds[6]; for instance, octyl sulfonate shows a change from a log D_{mw} from 1.74[7] to 4.8[1,8] when perfluorinated. The bead assignments were based on the linear PFAS species with available log D_{mw} data.

Initial simulated values showed a major underestimation of these changes, as shown in **Figure S**7. A fit with most values around 2 log units under the experimental data is observed using the models generated with the default algorithm. Use of halogenated beads for the perfluorinated species brings the trend down to 0.8 log units of deviation when fitting the same charged beads as in the aliphatic cases. Shifting the charged beads down in hydrophobicity to the beads stated above most closely matches the experimental trend (bottom panel of **Figure S**7). Such changes can only be justified in highly specific cases like perfluorinated species which have reliable experimental data available. Insights gained in devising coarse-grained models for these groups can be used as a model for similarly perfluorinated species.

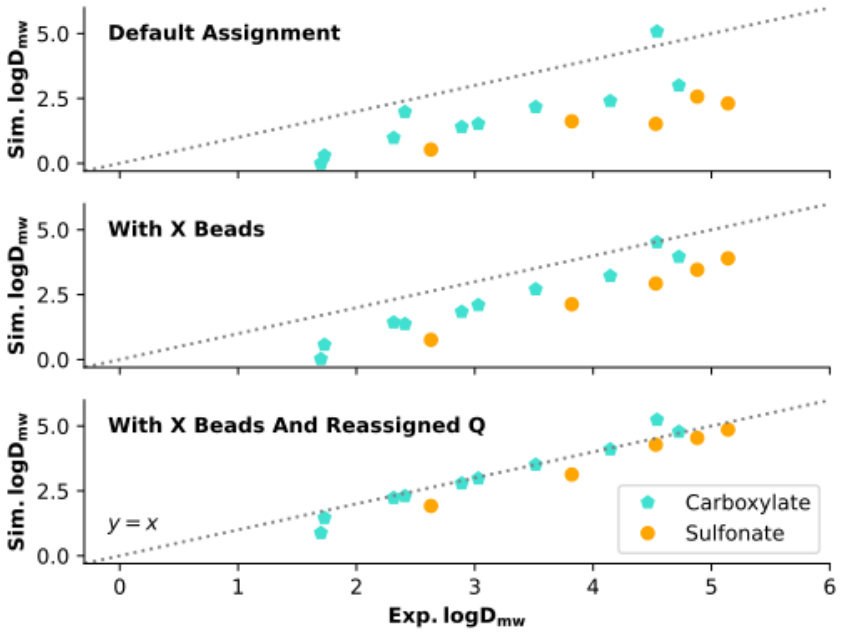


Figure S**7** Simulated vs experimental log D_{mw} values for a series of chain lengths of perfluorinated alkyl sulfonates and carboxylates. The top panel shows the results where Martini 3 halogenated 'X' beads are not used in the coarse-grained models, the middle panel shows the results with 'X' beads, and the bottom graph shows the results when 'X' beads are used and charged beads near fluorines are reassigned to account for the proximity of the fluorinated groups.

S3.3 Ester parameterisations

The mapping of diesters is challenging. It was noted that simulations of molecules with esters near other highly polar groups result in poor predications of experimental log D_{mw} values. This was determined to be due to limitations in the underlying building-block approach of Martini, where the properties of adjacent groups are treated as being independent. In practice, neighbouring polar groups can interact, requiring a parameterisation that depends not just on the log K_{ow} values of individual fragments, but also on those of neighbouring groups.

A systematic approach to the parameterisation of diesters is the subject of a separate publication (in preparation), as part of which manual ester assignments were determined. The issues with diesters appeared in the ISE and FAES classes of surfactants included in this paper, where neighbouring sulfate and ester groups appear. The manual ester assignments were therefore employed for all esters in the paper. These beads are C(=O)O,CC(=O)O, CCC(=O)O, COC(=O) and COC(C)=O, assigned as SP2, SN5, SN4, N6 and N4 respectively. Furthermore, the C(=O)O functional group is protected from being split across coarse-grained beads.

S3.4 Adaptive weighting in spectral mapping

Atomic mass is used as a "tiebreaker" when assessing the centrality of beads in the spectral mapping algorithm[7]. The inclusion of mass ensures that the process does not falsely detect molecular symmetry based on the topology of the bonding network alone. The masses, in atomic mass units, are placed on the diagonal of the molecular adjacency matrix. Off-diagonal elements are set to 1 when the corresponding two atoms are bonded and 0 otherwise. The centrality scores are the elements of the eigenvector with the largest eigenvalue for this matrix. However, when highly branched molecules with multiple heavy atoms are assessed, the centrality scores span many orders of magnitude. When the range of smallest to largest scores spans floating-point precision (typically 16 digits), matrix diagonalisation routines can fail. Typical signatures of this numerical problem are centrality scores with different signs (they

should all be the same) and incorrectly ordered fragments in topologically simple reference cases. Proceeding with faulty centrality scores then leads to spurious mappings that might not even be invariant with respect to equivalent SMILES codes of a given input molecule. In our work, the problem was most pronounced for long-chain sulfate species.

The onset of numerical difficulties with diagonalisation of the adjacency matrix is easy to diagnose from the ratio of the smallest to the largest centrality scores. The problem can be mitigated (or at least postponed to larger, more complex molecules) by reducing the size of the diagonal elements of the adjacency matrix. To resolve the problem while retaining some mass weighting and preserving consistency with previous results, we have made the weighting adaptive. We start by using masses in atomic mass units divided by 2 on the diagonals of the adjacency matrix. If diagonalisation then produces centrality scores that span more than 10 orders of magnitude or centrality scores with inconsistent signs, the diagonal elements of the adjacency matrix are divided by 2 again and the diagonalisation is repeated. This adaptive process dilutes the effect of mass-weighting only as far as needed to achieve a stable and reproducible result. Desirable mappings are produced for the molecules in this paper.

For even larger and more highly substituted molecules, it is in principle possible for mass-weighting to be reduced so far that it has no effect, resulting in mappings based purely on bonding topology. Such mappings will, nevertheless, be Martini-compatible and reproducible. In more extreme cases, it is possible that no reduction in mass-weighting will produce an adjacency matrix than can be reliably diagonalised. Although we have not encountered such a case so far, our script will now detect the problem and flag it to the user.

S3.5 Centre of geometry mapping

In line with Martini 3 advice, bead coordinates are now based on beads' centre of geometry (COG), as opposed to previous cg_param implementations which used the Martini 2 convention of the centre of mass (COM). The change results in better capture of fragment volume, but causes large shifts in inter-bead "bond" lengths for aromatic rings and substituted fragments. Figure S8 shows a comparison of D_{mw} calculations from COM and COG mappings for a range of neutral and substituted molecules in Martini 3 with published log D_{mw} values, showing only a minor difference between the two schemes. COG mapping is the standard for Martini models going forward and all coarse-grained models in this paper have been based on it.

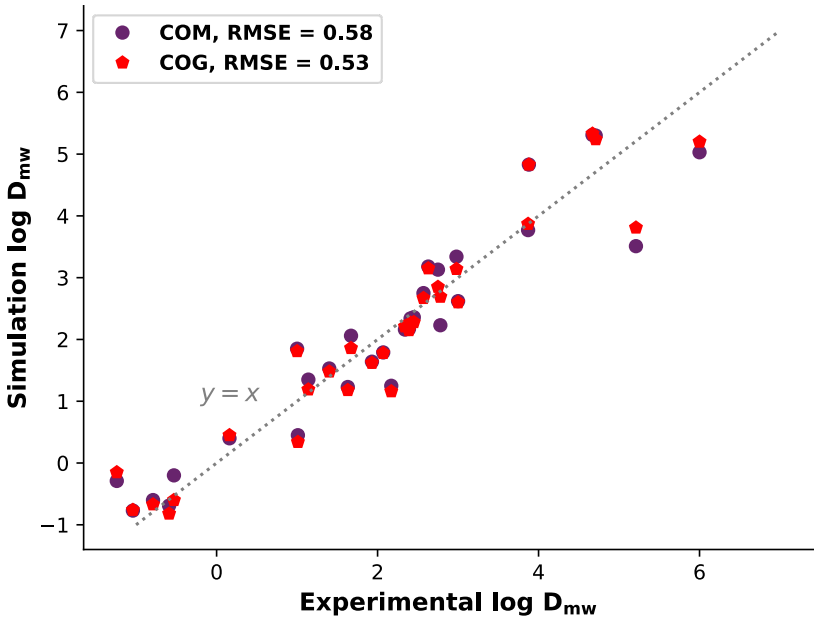


Figure S8. Simulated vs experimental log D_{mw} values for a series of neutral, simple molecules including alkyl, aryl and highly substituted compounds with both centre of mass (COM) and centre of geometry (COG) mappings. The full list of compounds is in Table S10.

Table S10. Details of molecules included in Figure S8.

Molecule	SMILES	Membrane	D_{mw} (Exp)	D_{mw} (Simulated COM)	D_{mw} (Simulated COG)	Reference
1,2,3-trichlorobenzene	c(c(c(cc1)Cl)Cl)(c1)Cl	DMPC	3.87	3.86	3.77	van der Heijden *et al.*, 2009[9]
1,3,5-tribromobenzene	c(cc(cc1Br)Br)(c1)Br	DMPC	5.21	3.70	3.51	Gobas *et al.*, 1988[10]
1-hexanol	OCCCCCC	DMPC	1.93	1.88	1.64	Janes *et al.*, 1992[11]
2,4,6-tribromobiphenyl	Brc2c(c(cc(c2)Br)Br)c1ccccc1	DMPC	6.00	5.20	5.03	Gobas *et al.*, 1988 [10]
2,4,6-trichlorobiphenyl	Clc1cc(Cl)c(c(Cl)c1)c2ccccc2	DMPC	4.71	5.26	5.30	Gobas *et al.*, 1988 [10]

2-nitrotoluene	N(=O)(=O)c(c(ccc1)C)c1	DMPC	2.41	2.28	2.34	Vaes *et al.*, 1997[12]
3-nitroaniline	N(=O)(=O)c(cccc1N)c1	DMPC	2.17	1.14	1.25	Vaes *et al.*, 1997[12]
3-pentanol	OC(CC)CC	DMPC	1.00	1.89	1.85	Vaes *et al.*, 1997[12]
4-bromophenol	Oc(ccc(c1)Br)c1	DMPC	2.39	1.99	2.17	Rogers *et al.*, 1980[13]
4-chlorophenol	Oc(ccc(c1)Cl)c1	DMPC	2.34	2.17	2.16	Rogers *et al.*, 1980[13]
4-ethylphenol	Oc(ccc(c1)CC)c1	DMPC	2.75	2.95	3.13	Rogers *et al.*, 1980[13]
4-fluorophenol	Fc(ccc(O)c1)c1	DMPC	2.07	1.81	1.79	Rogers *et al.*, 1980[13]
4-iodophenol	Oc(ccc(c1)I)c1	DMPC	2.57	1.77	2.75	Rogers *et al.*, 1980[13]
aniline	Nc(cccc1)c1	DMPC	1.63	1.04	1.23	Vaes *et al.*, 1997[12]
benzylalcohol	OCc(cccc1)c1	DMPC	1.14	1.20	1.35	Katz *et al.*, 1974[14]
chlorobenzene	c(cccc1)(c1)Cl	DMPC	3.00	2.55	2.62	Gobas *et al.*, 1988[10]
erythritol	OCC(O)C(O)CO	DMPC	-1.24	-0.58	-0.29	Katz *et al.*, 1974[14]

ethyleneglycol	OCCO	DMPC	-0.79	-0.61	-0.60	Katz *et al.*, 1974[14]
glycerol	OCC(O)CO	DMPC	-1.04	-0.15	-0.77	Katz *et al.*, 1974[14]
methanol	OC	DMPC	-0.53	-0.63	-0.20	Katz *et al.*, 1974[14]
n-hexane	C(CCCC)C	DMPC	3.88	4.83	0.80	De Young *et al.*, 1990[15]
N,N-dimethylaniline	N(c(cccc1)c1)(C)C	DMPC	2.45	2.26	2.36	Vaes *et al.*, 1997[12]
propylacetate	O=C(OCCC)C	DMPC	1.01	0.34	0.45	Vaes *et al.*, 1998[16]
p-xylene	c(ccc(c1)C)(c1)C	DMPC	2.98	3.08	3.34	Vaes *et al.*, 1997[12]
quinoline	n(c(c(ccc1)cc2)c1)c2	DMPC	1.67	1.85	2.06	Vaes *et al.*, 1997[12]
tert-butanol	OC(C)(C)C	DMPC	0.16	0.46	0.40	Katz *et al.*, 1974[14]
Tetrachlorocatechol	Oc1c(O)c(Cl)c(Cl)c(Cl)c1Cl	POPC	2.63	3.16	3.18	Schweiger t *et al*, 2001[17]
Urea	O=C(N)N	DMPC	-0.59	-0.82	-0.69	Katz *et al.*, 1974[14]
Warfarin	CC(CC(C1=C(c2c(OC1=O)cccc2)O)c3ccccc3)=O	POPC	1.40	4.07	4.21	Ottiger *et al.*, 1997[18]

S3.6 Simulation parameters

All simulations were performed using Gromacs 2021.4[19] and the Martini 3 force field[5] using a Linux Ubuntu 22.04.4 LTS operating system. Code development of the cg_param automatic parametrisation script utilised Python version 3.9.7 with the use of the open-source module RDkit 2020.09.1[20]. The Martini 3 default parameters for NaCl, water and the lipid POPC were used. Lipid bilayers were generated using the INSANE program[21]. Each leaflet contained 64 POPC lipids, with 3.5 nm of water on either side of the membrane surface. A NaCl concentration of 0.015 M was added to match the experiment and balance charge. A 20 fs time step was used with the leapfrog integrator. Electrostatics were calculated using the reaction field method with a relative permittivity of 15. Electrostatic interactions and van der Waals forces used a cutoff of 1.1 nm. Generated membrane structures were equilibrated for 1 μs through an *NPT* simulation with a Parrinello-Rahman barostat and a velocity rescale thermostat. The pressure was set to 1 bar and a coupling constant of 12 ps. The temperature was set to 310 K with a 1.0 ps coupling constant.

For each umbrella window, a solute molecule was inserted at a given *z* coordinate (i.e., a specified perpendicular distance from the centre of the membrane), and the configurations were minimised in energy and equilibrated. A simple harmonic restraint potential was applied to keep the solute within a target window on the *z* coordinate. For neutral molecules, the width of each window was 0.1 nm and the force constant for the restraint was 1000 kJ mol^{-1} nm^{-2}. For charged molecules, the window width was set to 0.05 nm and the force constant to 2000 kJ mol^{-1} nm^{-2}.

Both equilibration and umbrella sampling simulations maintained an *NVT* ensemble throughout, with the same settings otherwise. 100 simulations were run for 10 ns of equilibration and 50 ns of umbrella sampling, each using the *z-axis* as the reaction coordinate. The weighted histogram analysis method (WHAM)[22], which is integrated with Gromacs, was then used to combine data from the windows into a contiguous probability profile for the solute partitioning into the membrane.

S3.7 Calculation of D_{mw} from simulation data.

The umbrella sampling simulations and WHAM analysis lead to a probability profile of the solute as a function of perpendicular distance from the centre of the membrane at $z = 0$ into the aqueous phase. The partition coefficient was calculated from the probability profile using

$$D_{\mathrm{mw}} = \frac{V(z_n)}{M} \frac{\sum_{i=0}^{R} P_{\mathrm{Sol}}(z_i)}{P_{\mathrm{Sol}}(z_n)}$$

Where $V(z_n)$ is the volume of one umbrella sampling window in L and M is the mass of one bilayer leaflet in kg. The index i labels the umbrella-sampling windows, each centred at $z = z_i$, with $i = 0$ corresponding to the centre of the membrane, $i = R$ corresponding to the last window in which the solute interacts with the membrane[7], and *n* being the outermost window (furthest from the membrane, containing only solvent). $P_{\mathrm{Sol}}(z_i)$ is the probability of finding the solute molecule within umbrella window i.

S3.8 Statistical uncertainty in simulations

As spot-checks of statistical uncertainty in calculated D_{mw} values between simulations, five independent replica simulations were performed for each of the three representative molecules. The resulting log D_{mw} are reported in Table S11, alongside the standard deviation of these values to give an indication of the statistical uncertainty in our simulation results. For the short 14-carbon chain C14SAR and perfluorinated 10-carbon (CF_x) chain PFUnDA, the variation is less than 0.1 log units. Uncertainty generally increases with molecular length. For the longer-chain molecule C14EO4S it is 0.15 log units.

Table S11. Replica simulation results for three representative molecules. Standard deviations are reported to indicate the level of statistical uncertainty in individual simulations.

Molecules	Replica	log D_{mw}	Standard Deviation
C14SAR	1	3.34	0.09
	2	3.50	
	3	3.41	
	4	3.56	
	5	3.51	
PFUnDA	1	4.61	0.07
	2	4.44	
	3	4.55	
	4	4.47	
	5	4.53	
C14EO4S	1	5.32	0.15
	2	5.45	
	3	5.36	
	4	5.50	
	5	5.08	

S3.9 Other supporting files

In the zip folder attached to this paper:

- GROMACS topology files (.itp) for all surfactants in this paper.
- Example GROMACS input file (.mdp) for an umbrella sampling window.

Version 3.0 of the cg_param_m3 script was used for this work and is available at https://github.com/cgkmw-durham/cg_param_m3/tree/martini3_v3.

S4. Comparison of experimental data with simulation method and comparison of computational methods – additional information

S4.1 Comparison of experimental data with simulation method

Table S12 compiles the experimental log D_{mw} values from the literature and newly generated values from this study (indicated as "New value"), with simulated log D_{mw} values for the same set of chemicals. The table is the basis of Figure 1 from the article.

Table S12. Comparison of experimental log D_{mw} values with coarse - grained simulations

Chemical abbreviation	Experimental			Simulated
	log D_{mw}	Test method[a]	Reference	Martini 3 simulation value log D_{mw}
C10(1)-LAS	5.10	SSLM	Droge et al., 2021[23]	5.14
C10-LAS	4.79	SSLM	Droge et al., 2021[23]	5.14
C10SO3	3.01	SSLM	Droge, 2019[8]	3.02
C11-LAS	5.33	SSLM	Droge et al., 2021[23]	5.45
C12(6)-LAS	5.36	SSLM	Droge et al., 2021[23]	5.68
C12COOCSO3	4.26	SSLM	Droge et al., 2021[23]	4.29
C12EO1S	4.70	Liposome	New value (SLES)	4.42
C12EO2S	4.60	Liposome	New value (SLES)	4.22
C12EO3S	4.44	Liposome	New value, average of standard and SLES	4.36
C12-LAS	5.62	SSLM	Droge et al., 2021[23]	6.06
C12SO3	3.99	SSLM	Droge, 2019[8]	4.18
C13SO3	4.46	SSLM	Droge, 2019[8]	4.45
C13SO4	5.21	SSLM	Droge, 2019[8]	4.75
C14EO1S	5.22	Liposome	New value (SLES)	5.19
C14EO2S	5.16	Liposome	New value (SLES)	5.79
C14EO3S	4.85	Liposome	New value (SLES)	5.54
C14EO4S	5.15	Liposome	New value (SLES)	5.53
C14SO3	4.95	SSLM	Droge, 2019[8]	4.98
C14SO4	5.13	Liposome	New value (standard)	5.33
C8(1)-LAS	3.61	SSLM	Bittermann et al., 2014[24]	4.15
C8SO3	1.74	SSLM	Droge, 2019[8]	2.20
PFBS	2.75	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	1.84
PFHxS	3.98	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	3.17
PFOS	4.89	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	4.46
PFPeA	1.73	SSLM	Droge, 2019[8]	1.44
PFUnDA	4.54	liposome	Ebert et al., 2020[1]	5.24
SO3-DOSS	4.58	SSLM	Droge et al., 2021[23]	5.23
C10SO4	3.645	average liposome & SSLM	Potter et al., 2023, Droge, 2019[8]	3.32
C12EO4S	4.15	average liposome & SSLM	New value (SLES), Droge et al., 2021[23]	4.75
C12SO4	4.41	average liposome & SSLM	New value, average of standard and SLES, Potter et al., 2023[3], Droge, 2019[8], New value (SSLM)	4.38
C8SO4	2.32	average liposome & SSLM	Potter et al., 2023[3], Droge, 2019[8], New value (SSLM)	2.20

PFBA	1	SSLM	Droge, 2019[8]	0.86
PFDA	4.725	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	4.85
PFHpA	2.89	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	2.83
PFHxA	2.315	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	2.24
PFNA	4.145	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	4.15
PFOA	3.515	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	3.57
9Cl-PF3ONS (F-53B)	5.14	Liposome	Ebert et al., 2020[1]	4.86
C10-iseth	2.80	SSLM	New value (SSLM)	3.19
C14-iseth	4.88	SSLM	New value (SSLM)	4.89
HFPO-DA/GenX	2.41	Liposome	Ebert et al., 2020[1]	2.30
NaDONA	3.03	Liposome	Ebert et al., 2020[1]	2.98
PFECHS	4.53	Liposome	Ebert et al., 2020[1]	4.28

[a] SSLM = solid-supported lipid membrane, Liposome = liposome-water distribution coefficient

S4.2 Comparison of computational methods

To compare our coarse-grained simulation method against COSMO*mic* logK_{mw} values, experimental values of FC surfactants from Ebert et al., 2020[1] and Droge 2019[8] were plotted against COSMO*mic* from Ebert et al., 2020[1] and coarse-grained simulation values from this study (Figure S9). All plotted values are available in Table S13. Values from Ebert et al., 2020[1] correspond to the POPC phospholipid bilayers which were also used for coarse-grained simulations and experimental work in this study, hence they are appropriate for direct comparison. Droge, 2019[8] used 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) lipids and immobilized artificial membranes-based $K_{mw,IAM}$ method and hence, for his comparison of COSMO*mic* and experimental values for some anionic HC (alkyl sulf(on)ates and phenylalkylcarboxylates) and FC surfactants (PFCAs), reader is referred to the Supplementary Information of Droge, 2019, Figure S3B[8].

Table S13. Comparison of experimental log D_{mw}, COSMOmic and coarse-grained simulation values for the set of FC surfactants from Ebert et al., 2020[1]

Chemical abbreviation	Experimental			Simulated	COSMO*mic*
	log D_{mw}	Test method[a]	Reference	Martini 3 simulation value log D_{mw}	log K_{mw} COSMO (POPC), Ebert et al, 2020
PFBS	2.75	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	1.84	3.51
PFHxS	3.98	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	3.17	3.93
PFOS	4.89	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	4.46	4.69
PFUnDA	4.54	liposome	Ebert et al., 2020[1]	5.24	5.06

PFBA	1	SSLM	Droge, 2019[8]	0.86	3.17
PFDA	4.725	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	4.85	4.64
PFHpA	2.89	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	2.83	3.63
PFHxA	2.315	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	2.24	3.48
PFNA	4.145	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	4.15	4.3
PFOA	3.515	average liposome & SSLM	Droge, 2019[8], Ebert et al., 2020[1]	3.57	3.93
9Cl-PF3ONS (F-53B)	5.14	Liposome	Ebert et al., 2020[1]	4.86	5.15
GenX	2.41	Liposome	Ebert et al., 2020[1]	2.3	3.5
NaDONA	3.03	Liposome	Ebert et al., 2020[1]	2.98	3.77
PFECHS	4.53	Liposome	Ebert et al., 2020[1]	4.28	4.01

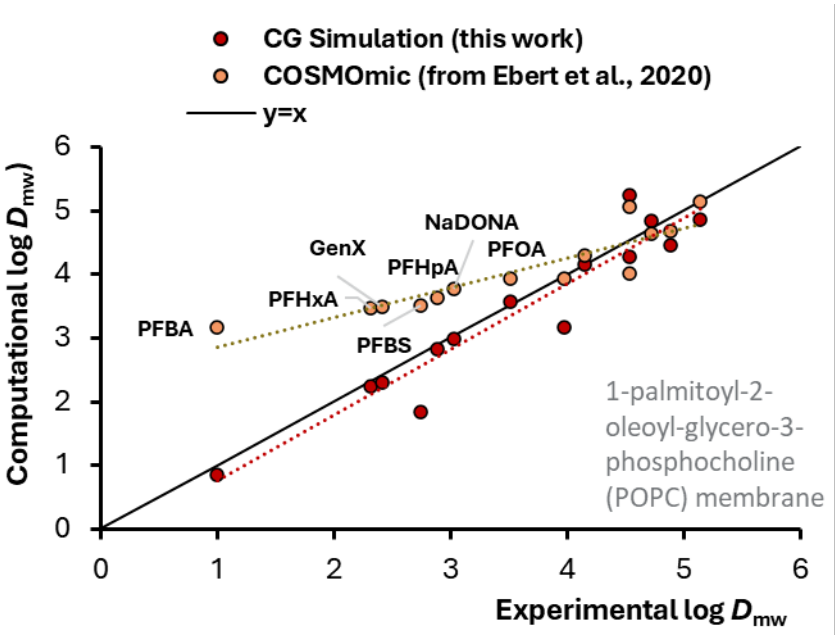


Figure S9. Comparison of COSMO*mic* generated log K_{mw} and coarse-grained simulation method-based log D_{mw} values against experimental log D_{mw} data (Table S13)

S5. Compilation of anionic surfactant identification database

An extensive database of anionic surfactants (with hydrocarbon backbone) was compiled, including chemical identifiers. Due to the highest availability, CAS number was chosen as the most appropriate identifier, but also to facilitate reliable searching of large ecotoxicological databases which commonly allow for a bulk export based on a string of CAS numbers. Frequently, the same surfactants are commonly referred to with different names (including tradenames) and are also commonly marketed (and tested) as mixtures. In addition, structural abbreviations can vary according to the source (e.g., regulatory databases, scientific literature, industry data).

To create the Surfactant Identification Database (SID), several approaches were taken:

Searching and merging existing surfactant lists with CAS numbers: Literature Survey of Surfactants in the Nordic Countries, 2012[25] and NORMAN network databases[26,27]. From NORMAN, Surfactant Suspect List from EI and UBA[28*] and TSCA Surfactants[29†] lists were used in the database compilation. However, the TSCA Surfactant list mostly contained only PEGs (polyethylene glycols, i.e. neutral surfactants) and was therefore not considered relevant for this analysis.

Using the "Explore" function in the USEPA ECOTOX database[30], based on the extensive list of surfactants from the Chemistry and Technology of Surfactants[31]. Keywords were extracted from Chapter 1 (containing all spheres of applications and surfactant groups) and inputted into the "Explore" function in USEPA ECOTOX and the resulting lists with CAS numbers and compounds were extracted. Lists were refined afterwards to eliminate any non-surfactants, assign the relevant charge, the specific surfactant class they belong to and identify if that exact CAS number was of a monoconstituent surfactant or not.

Extraction of the common names (by charge) from the Handbook of Industrial Surfactants and subsequent USEPA COMPTOX database search. Common names of surfactants by charge were extracted from the Handbook of Industrial Surfactants[32] and run through the COMPTOX USEPA database[33], in order to find matches with chemical identifiers (CAS, also SMILES, INChI etc.). The obtained list was cross-matched with the existing list and any duplicates were eliminated. Chemical structures of chemicals not already listed were checked to confirm if they could be classified as surfactants and sorted by the surfactant groups and subclasses.

CAS numbers from HERA assessments for groups of anionic surfactants. HERA assessments[34] for previously identified anionic surfactant groups were used for extraction of their CAS numbers to add to the list of surfactants and fill data gaps.

* A compiled list of eco-labelled surfactants from Environmental Institute (EI, SK) and the German Federal Environmental Agency (UBA, DE) assigning chemical structures to UVCB chemicals based on names and prior knowledge.
† Surfactant information compiled from TSCA by James Little while at Eastman Chemical. Contains an exhausting list of PEGs, with CAS numbers and other chemicals

S6. Ecotoxicity data and log D_{mw} values

Table S14. Anionic surfactants (hydrocarbon backbone) used in fish QSAR building, with log D_{mw} values from coarse-grained simulations and paired ecotoxicity data

Abbreviation	SMILES (unsalted, ionised)	Surfactant group	MW (g/mol)	Martini 3 simulation value log D_{mw}	Species Scientific Name	96h LC50 (mg/L)	96h pLC50 (mol/L)	Reference
BrC9CO2-	CC(CC(=O)[O-])CC(C)(C)C	Salts of carboxylic acids (soaps)	158.24	0.03	*Oncorhynchus mykiss*	122.00	3.11	ECHA Registration Dossier - 3,5,5-trimethylhexanoic acid[35]
C10-LAS	CCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	320.42	5.14	*Fathead minnow*	16.58	4.29	Belanger et al., 2016[36]
C10SO4	CCCCCCCCCCOS([O-])(=O)=O	AS	260.29	3.32	*Danio rerio*	177.00	3.17	SIDS for SIAM 25[37]
C11CO2-	CCCCCCCCCCCC([O-])=O	Salts of carboxylic acids (soaps)	222.30	2.44	*Danio rerio*	14.14	4.20	*EPA Office of Pesticides Program Database, 1992[38]
C11-LAS	CCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	335.46	5.45	*Fathead minnow*	7.08	4.68	Belanger et al., 2016[36]
C11SARSO3	CCCCCCCCCCC(=O)N(C)CCS(=O)(=O)[O-]	Taurates	345.47	4.00	*Danio rerio*	5.04	4.84	ECHA Registration Dossier - Sodium 2-[methyl(1-oxododecyl)amino]ethanesulfonate[39]
C11SO4	CCCCCCCCCCCOS([O-])(=O)=O	AS	269.37	3.57	*Lepomis macrochirus*	26.00	4.02	Little, 1991[40]
C12BzSO3	CCCCCCCCCCCCC1=CC=CC=C1S(=O)(=O)[O-]	LAS	326.49	6.05	*Oncorhynchus mykiss, Rita rita, Leuciscus idus, Lepomis macrochirus,*	4.96	4.82	ECHA Registration Dossier - Dodecylbenzenesulphonic acid[41], ECHA Registration Dossier - Ammonium dodecylbenzenesulfonate[42], *Lubinski et al., 1974[43], *Dolan, 1974[44]
C12EO1S	CCCCCCCCCCCCOCCOS([O-])(=O)=O	AES	332.39	4.42	*Oryzias latipes, Oncorhynchus mykiss*	10.04	4.52	BKH, 1994[45], Marshall, 1988 – Unilever internal study

C12EO3S	CCCCCCCCCCCCOCCOCCOCCOS([O-])(=O)=O	AES	420.48	4.36	*Oryzias latipes*	68.00	3.79	BKH, 1994[45]
C12-LAS	CCCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	348.48	6.06	*Morone saxatilis, Ameiurus melas, Micropterus dolomieu, Funduluciusousnus, Luxilus cornutus, Notropis atherinoides, Oreochromis mossambicus, Barbonymus gonionotus, Lepomis macrochirus, Esuciusius, Pimephales promelas, Cyprinus carpio, Carassius auratus, Catostomus commersoni, Oncorhynchus mykiss*	3.79	4.96	Belanger et al., 2016[36], *Thatcher, 1966[46], *McKim et al., 1975[46], *Patrick et al., 1968[47], *Calamari and Marchetti, 1973[48], *Solon et al., 1969[49], *Lewis and Suprenant, 1983[50], *Lemke and Mount, 1963 [51], *Jangchudjai et al, 1987[52], *Tsai and McKee, 1980[53], *Dolan III and Hendricks, 1976[54], *Pickering, 1966[55], *Rehwoldt et al., 1974[56], *Fairchild et al, 1993[57], *Hokanson and Smith, 1971[58], *Chattopadhyay and Konar, 1985[59], *Bishop and Perry, 1981[60]
C12SO4	CCCCCCCCCCCCOS([O-])(=O)=O	AS	260.32	4.38	*Cirrhinus mrigala, Cichlasoma nigrofasciatum, Gambusia holbrooki, Pimephales promelas, Lepomis macrochirus, Cyprinus carpio, Menidia menidia, Jordanella floridae, Oncorhynchus mykiss*	7.93	4.52	*Verma et al., 1984[61], *Newsome, 1982[62], *Nunes et al., 2005[63], *Braunbeck et al., 2005[64] , *Bishop and Perry, 1981 [60], *Verma et al., 1981[65], *Roberts et al., 1982[66], *Fogels and Sprague, 1977[67], *Jank et al., 1973[68], *Buhl and Hamilton, 2000[69]
C13EO6S	CCCCCCCCCCCCCOCCOCCOCCOCCOCCOS([O-])(=O)=O	AES	566.64	5.63	*Lepomis macrochirus*	1.10	5.71	BKH, 1994[45]

C13-LAS	CCCCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	363.51	6.61	*Fathead minnow*	0.63	5.76	Belanger et al., 2016[36]
C14-LAS	CCCCCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	377.54	6.91	*Fathead minnow*	0.26	6.16	Belanger et al., 2016[36]
C14SO4	CCCCCCCCCCCCCCOS([O-])(=O)=O	AS	316.43	5.33	*Danio rerio*	0.66	5.68	*Annunziato et al, 2020[70]
C15SO4	CCCCCCCCCCCCCCCOS([O-])(=O)=O	AS	325.48	5.59	*Lepomis macrochirus*	4.19	4.89	Little, 1991[40]
C16(1)-FAES	CCCCCCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	351.22	5.54	*Danio rerio*	1.10	5.50	Marshall, 1991 - Unilever internal study
C9CO2-	CCCCCCCCC([O-])=O	Salts of carboxylic acids (soaps)	158.24	2.44	*Pimephales promelas*	104.00	3.18	ECHA Registration Dossier - Nonanoic Acid[71]
PO4-2S-C4x2	CC(C)CP(=S)(CC(C)C)[S-]	Dithiophosphate	232.30	1.21	*Lepomis macrochirus*	375.00	2.79	ECHA Registration Dossier - Sodium diisobutyldithiophosphinate[72]
SO3-DOSS	CCCCC(CC)COC(=O)CC(C(=O)OCC(CC)CCCC)[S](=O)(=O)[O-]	Sulfosuccinates	444.56	5.23	*Danio rerio, Lepomis macrochirus*	41.94	4.03	ECHA Registration Dossier - Docusate Sodium[73]

* Values obtained from the USEPA ECOTOX database

Table S15. Anionic surfactants (hydrocarbon backbone) used in *Cerio(Daphnia)* QSAR building, with log D_{mw} values from coarse-grained simulations and Droge et al., 2021 log D_{mw} multiple regression equation for anionic surfactants (marked in green) and paired ecotoxicity data.

Abbreviation	SMILES (unsalted, ionised)	Surfactant group	MW (g/mol)	Coarse-grained simulation and Droge et al, 2021 $logD_{mw}$	Species Scientific name	48h LC50/EC50 (mg/L)	48h -log LC50 (mol/L)	Reference
C12EO1S	CCCCCCCCCCCCOCCOS([O-])(=O)=O	AES	310.45	4.42	*Ceriodaphnia dubia*	9.50	4.51	Dyer et al., 2000 [74]
C12EO2S	CCCCCCCCCCCCOCCOCCOS([O-])(=O)=O	AES	354.50	4.22	*Ceriodaphnia dubia*	55.98	3.80	Dyer et al., 2000 [74]
C12EO4S	CCCCCCCCCCCCOCCOCCOCCOC COS([O-])(=O)=O	AES	442.61	4.75	*Ceriodaphnia dubia*	118.26	3.57	Dyer et al., 2000 [74]
C12EO8S	CCCCCCCCCCCCOCCOCCOCCOC COCCOCCOCCOCCOS([O-])(=O)=O	AES	618.82	3.76	*Ceriodaphnia dubia*	43.46	4.15	Dyer et al., 2000 [74]
C14EO1S	CCCCCCCCCCCCCCOCCOS([O-])(=O)=O	AES	338.50	5.19	*Ceriodaphnia dubia*	4.08	4.92	Dyer et al., 2000 [74]
C14EO2S	CCCCCCCCCCCCCCOCCOCCOS([O-])(=O)=O	AES	382.55	5.79	*Ceriodaphnia dubia*	4.24	4.96	Dyer et al., 2000 [74]
C14EO4S	CCCCCCCCCCCCCCOCCOC COCCOCCOS([O-])(=O)=O	AES	470.66	5.53	*Ceriodaphnia dubia*	43.97	4.03	Dyer et al., 2000 [74]
C13EO2S	CCCCCCCCCCCCCOCCOCCOS([O-])(=O)=O	AES	368.53	5.20	*Ceriodaphnia dubia*	7.18	4.71	Dyer et al., 2000 [74]
C15EO1S	CCCCCCCCCCCCCCOCCOS([O-])(=O)=O	AES	352.53	5.52	*Ceriodaphnia dubia*	0.78	5.66	Dyer et al., 2000 [74]
C12SO4	CCCCCCCCCCCCOS([O-])(=O)=O	AS	266.40	4.38	*Daphnia magna*, *Daphnia pulex, Ceriodaphnia dubia, Daphnia ambigua*	10.13	4.42	Dyer et al., 2000 [74]; *Guilhermino et al, 2000[75]; *Cowgill., 1990[76]; *Martinez-Jeronimo and Munoz-Mejia, 2007[77]; *Harmon, 2003[78]; *Bishop, 1981[60]; *Mohammed,

								2007[79], *Martinez-Jeronimo and Garcia-Gonzalez, 1994[80]
C12SO3	CCCCCCCCCCCCS([O-])(=O)=O	Alkyl sulfonate	272.38	4.18	*Daphnia magna*	220.00	3.09	*Lundahl,P., and R. Cabridenc, 1978[81]
C14SO4	CCCCCCCCCCCCCCCOS([O-])(=O)=O	AS	294.45	5.33	*Daphnia m. and Ceriodaphnia d.*	8.15	4.56	*Lundahl,P., and R. Cabridenc, 1978[81] & Dyer et al., 2000 [74]
C8SO3	CCCCCCCCS([O-])(=O)=O	Alkyl sulfonate	216.27	2.20	*Daphnia magna*	3200.00	1.83	*Lundahl,P., and R. Cabridenc, 1978 [81]
C15SO4	CCCCCCCCCCCCCCCOS([O-])(=O)=O	AS	308.48	5.59	*Ceriodaphnia dubia*	0.59	5.72	Dyer et al., 2000 [74]
C12BzSO3	CCCCCCCCCCCCC1=CC=CC=C1S(=O)(=O)[O-]	LAS	325.49	6.05	*Daphnia magna* and *Ceriodaphnia dubia*	6.39	4.71	*Guilhermino et al, 2000[82], Kimerle and Swisher, 1977[83]
C9-LAS	CCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	284.41	4.77	*Daphnia magna*	53.00	3.73	Hodges et al., 2006 [84]
C10-LAS	CCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	298.44	5.14	*Daphnia m* and *Ceriodaphnia d*	21.01	4.15	Belanger et al., 2016[36], Hodges et al., 2006[84]
C11-LAS	CCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	313.47	5.45	*Daphnia m* and *Ceriodaphnia d*	10.83	4.46	Belanger et al., 2016[36], Hodges et al., 2006[84]
C12-LAS	CCCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	326.49	6.06	*Daphnia m* and *Ceriodaphnia d*	4.31	4.88	Belanger et al., 2016[36], Hodges et al., 2006[84]

C13-LAS	CCCCCCCCCCCC(C)c1ccc(S(=O)(=O)[O-])cc1	LAS	340.52	6.61	*Daphnia m* and *Ceriodaphnia d*	2.34	5.16	Belanger et al., 2016[36], Hodges et al., 2006 [84]
C14-LAS	CCCCCCCCCCCCC(C)c1ccc (S(=O)(=O)[O-])cc1	LAS	354.55	6.91	*Daphnia m* and *Ceriodaphnia d*	0.86	5.62	Belanger et al., 2016[36], Hodges et al., 2006[84]
DiHexDiEsterSO3	CCCCCCOC(=O)CC(C(=O) OCCCCCC)[S](=O)(=O)[O-]	Sulfosuccinates	366.47	3.89	*Daphnia magna*	715.00	2.71	Roberts 2006 - Unilever internal study,
SO3-DOSS	CCCCC(CC)COC(=O)CC(C(=O)OCC(CC) CCCC)[S](=O)(=O)[O-]	Sulfosuccinates	444.56	5.23	*Daphnia magna*	33.11	4.13	*Garcia et al., 2009[85]; Roberts, 2006 - Unilever internal study,
C10(4)SO4	CCCCCCCCC(CCCC)CO[S]([O-])(=O)=O	AS-branched	316.43	5.24	*Daphnia magna*	3.70	4.93	Marshall, 1991 - Unilever internal study
C8(6)SO4	CCCCCCC(CCCCCC)CO[S]([O-])(=O)=O	AS-branched	316.43	5.29	*Daphnia magna*	15.60	4.31	Marshall, 1991 - Unilever , internal study
C11SO3	CCCCCCCCCCCS([O-])(=O)=O	Alkyl sulfonate	258.35	3.43	*Daphnia magna*	115.00	3.35	Harding, 1998 - Unilever internal study
C10SO3	CCCCCCCCCCS([O-])(=O)=O	Alkyl sulfonate	244.32	3.02	*Daphnia magna*	415.00	2.77	Harding, 1998 - Unilever internal study
C12COOCSO3	CCCCCCCCCCCCOC(=O)CS(=O)(=O)[O-]	Sulfoacetate	330.41	4.29	*Daphnia magna*	10.49	4.50	Butler, 2015 Unilever - internal study
C10(4)-FAES	CCCCCCCCC(C(=O)OCCCC)S(=O)(=O)[O-]	FAES	330.41	3.87	*Daphnia magna*	170.00	3.29	Hodges et al., 2006 [84]
C10(iso-4)-FAES	CCCCCCCCC(C(=O)OCC(C)C)S(=O)(=O)[O-]	FAES	330.41	3.46	*Daphnia magna*	150.00	3.34	Hodges et al., 2006 [84]
C10(sec-4)-FAES	CCCCCCCCC(C(=O)OC(C)CC)S(=O)(=O)[O-]	FAES	330.41	3.73	*Daphnia magna*	220.00	3.18	Hodges et al., 2006 [84]
C11(3)-FAES	CCCCCCCCCC(C(=O)OCCC)S(=O)(=O)[O-]	FAES	330.41	3.53	*Daphnia magna*	120.00	3.44	Hodges et al., 2006 [84]
C12(1)-FAES	CCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	316.39	3.61	*Daphnia magna*	140.00	3.35	Hodges et al., 2006 [84]

C12(2)-FAES	CCCCCCCCCCC(C(=O)OCC)S(=O)(=O)[O-]	FAES	330.41	3.86	*Daphnia magna*	150.00	3.34	Hodges et al., 2006 [84]
C12(4)-FAES	CCCCCCCCCCC(C(=O)OCCCC)S(=O)(=O)[O-]	FAES	358.47	4.48	*Daphnia magna*	16.00	4.35	Hodges et al., 2006 [84]
C12(5)-FAES	CCCCCCCCCCC(C(=O)OCCCCC)S(=O)(=O)[O-]	FAES	372.49	5.23	*Daphnia magna*	7.20	4.71	Hodges et al., 2006 [84]
C12(sec-4)-FAES	CCCCCCCCCCC(C(=O)OC(C)CC)S(=O)(=O)[O-]	FAES	358.47	4.47	*Daphnia magna*	36.00	4.00	Hodges et al., 2006 [84]
C13(1)-FAES	CCCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	330.41	4.28	*Daphnia magna*	41.00	3.91	Hodges et al., 2006 [84]
C14(1)-FAES	CCCCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	344.44	4.55	*Daphnia magna*	8.50	4.61	Hodges et al., 2006 [84]
C14(2)-FAES	CCCCCCCCCCCCC(C(=O)OCC)S(=O)(=O)[O-]	FAES	358.47	4.86	*Daphnia magna*	8.00	4.65	Hodges et al., 2006 [84]
C14(4)-FAES	CCCCCCCCCCCCC(C(=O)OCCCC)S(=O)(=O)[O-]	FAES	386.52	5.50	*Daphnia magna*	3.70	5.02	Hodges et al., 2006 [84]
C14(5)-FAES	CCCCCCCCCCCCC(C(=O)OCCCCC)S(=O)(=O)[O-]	FAES	400.55	6.32	*Daphnia magna*	1.30	5.49	Hodges et al., 2006 [84]
C14(iso-3)-FAES	CCCCCCCCCCCCC(C(=O)OC(C)C)S(=O)(=O)[O-]	FAES	372.49	5.00	*Daphnia magna*	7.80	4.68	Hodges et al., 2006 [84]
C16(1)-FAES	CCCCCCCCCCCCCCC(C(=O)OC)S(=O)(=O)[O-]	FAES	372.49	5.54	*Daphnia magna*	2.80	5.12	Hodges et al., 2006 [84]
C7(7)-FAES	CCCCCC(C(=O)OCCCCCCC)S(=O)(=O)[O-]	FAES	330.41	3.73	*Daphnia magna*	140.00	3.37	Hodges et al., 2006 [84]
C8(6)-FAES	CCCCCCC(C(=O)OCCCCCC)S(=O)(=O)[O-]	FAES	330.41	3.76	*Daphnia magna*	180.00	3.26	Hodges et al., 2006 [84]
C8(sec-6)-FAES	CCCCCCC(C(=O)OC(C)CCCC)S(=O)(=O)[O-]	FAES	330.41	3.59	*Daphnia magna*	400.00	2.92	Hodges et al., 2006 [84]
C9(5)-FAES	CCCCCCCC(C(=O)OCCCCC)S(=O)(=O)[O-]	FAES	330.41	4.07	*Daphnia magna*	140.00	3.37	Hodges et al., 2006 [84]
C9(sec-5)-FAES	CCCCCCCC(C(=O)OC(C)CCC)S(=O)(=O)[O-]	FAES	330.41	3.94	*Daphnia magna*	270.00	3.09	Hodges et al., 2006 [84]
C10-iseth	CCCCCCCCCC(=O)OCCS(=O)(=O)[O-]	Isethionates	302.36	3.19	*Daphnia magna*	671.00	2.65	Roberts, 2013 - Unilever internal study
C8-iseth	CCCCCCCC(=O)OCCS(=O)(=O)[O-]	Isethionates	274.31	1.94	*Daphnia magna*	2340.00	2.07	Roberts, 2013 - Unilever internal study

[*] Obtained from export of the USEPA ECOTOX database

Table S16. Anionic surfactants (perfluorocarbon backbone) used in *Daphnia* QSAR building, with log D_{mw} values from coarse-grained simulations and paired ecotoxicity data. All ecotoxicity data were extracted from USEPA ECOTOX, sorted, averaged and reported with original references.

Abbreviation	SMILES (unsalted, ionised)	PFAS group	MW (g/mol)	Martini 3 simulation value log D_{mw}	Species Scientific Name	48h LC50/EC50 (mg/L)	-log L(E)C50 (mol/L)	Reference
GenX	C(=O)(C(C(F)(F)F)(OC(C(C(F)(F)F)(F)F)(F)F)F)[O-]	PFECA (perfluoroalkyl ether carboxylic acids)	329.05	2.30	*Daphnia magna*	215.69	3.18	Labine et al., 2022[86]
PFBA	C(=O)(C(C(C(F)(F)F)(F)F)(F)F)[O-]	PFCA	213.03	0.86	*Daphnia magna*	5251.00	1.61	Barmentlo et al., 2015[87]
PFBS	C(C(C(F)(F)S(=O)(=O)[O-])(F)F)(C(F)(F)F)(F)F	PFSA	299.09	1.84	*Daphnia magna*	2183.00	2.14	**Wildlife international., 2001
PFDA	C(=O)(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	513.08	4.85	*Daphnia pulicaria, Daphnia magna*	187.76	3.44	Boudreau, 2002[88], Ding et al., 2012 [89]
PFDoDA	C(=O)(C(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	613.09	6.02	*Daphnia magna*	79.22	3.89	Ding et al., 2012[89]
PFECHS	C1(C(C(C(C(C1(F)F)(F)F)(F)S(=O)(=O)[O-])(F)F)(F)F)(C(C(F)(F)F)(F)F)F	Cyclic PFSA	461.12	4.28	*Daphnia magna*	186.61	3.39	Houde et al., 2016[90]
PFHxA	C(=O)(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	313.05	2.24	*Daphnia magna*	1048.00	2.48	Barmentlo et al., 2015[87]
PFNA	C(=O)(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	463.07	4.15	*Daphnia magna*	89.90	3.71	Lu et al., 2015[91], Ding et al., 2012[89], Boudreau, 2002[88]

PFOA	C(=O)(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	413.06	3.57	*Daphnia carinata, Daphnia pulicaria, Daphnia magna*	254.47	3.21	Colombo, 2008[92], **3M, 2000 (a), Li, 2009[93], **3M, 2000 (b), **3M, 2000 (c), Logeshwaran et al., 2021[94], Boudreau, 2002[88], **3M, 2000 (d), Barmentlo et al., 2015[87], Lu et al., 2016[95], Ding et al., 2012[89], Yang et al., 2014[96]
PFOS	C(C(C(C(C(F)(F)S(=O)(=O)[O-])(F)(F)(F)(F)(F)(C(C(C(F)(F)(F)(F)(F)(F)(F)(F)F	PFSA	499.12	4.46	*Daphnia carinata, Daphnia pulicaria, Daphnia magna*	59.87	3.92	Logeshwan et al., 2021[94], Boudreau et al., 2003[97], Liang et al., 2017[98], **Drottar and Krueger, 2000, Li, 2009[93], Yang et al., 2019[99], Yang et al, 2014[96], Lu et al., 2015[91], Wang et al., 2020[100]
PFUnDA	C(=O)(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-]	PFCA	563.09	5.24	*Daphnia magna*	133.13	3.63	Ding et al., 2012[101]
***10:2 FTCA**	C(C(=O)[O-])C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F	FTCA (fluorotelomer carboxylic acid)	577.11	5.52	*Daphnia magna*	0.04	7.13	Phillips et al., 2007[101]
***10:2 FTUCA**	C(=C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)C(=O)[O-]	FTUCA (fluorotelomer unsaturated carboxylic acids)	557.11	5.56	*Daphnia magna*	0.48	6.06	Phillips et al., 2007[101]
***6:2 FTUCA**	C(=C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)C(=O)[O-]	FTUCA (fluorotelomer unsaturated carboxylic acids)	357.08	3.14	*Daphnia magna*	29.60	4.08	Hoke et al., 2012[102]

***7:3 FTCA**	C(CC(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)C(=O)[O-]	FTCA (fluorotelomer carboxylic acid)	441.12	4.05	*Daphnia magna*	0.96	5.66	Hoke et al., 2012[102]
***8:2 FTCA**	C(C(=O)[O-])C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F	FTCA (fluorotelomer carboxylic acid)	477.10	4.43	*Daphnia magna*	2.91	5.22	Hoke et al., 2012[102], Phillips et al., 2007[101]
***8:2 FTUCA**	C(=C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)C(=O)[O-]	FTUCA (fluorotelomer unsaturated carboxylic acids)	457.10	4.40	*Daphnia magna*	4.77	4.98	Hoke et al., 2012[102], Phillips et al., 2007[101]

* Fluorotelomer acids were not used in the QSAR building (see main text, section 3.2.2.).

** The original reference available to USEPA only, only available as ECOTOX database export

S7. Statistical analysis and QSAR validation

Text S1. Statistical criteria for QSAR evaluation

To ensure high-quality and reproducible QSARs, all QSARs were evaluated following the general requirements of the QMRF[103]

All parameters regarding the QSARs goodness-of-fit, robustness and predictive ability (i.e., coefficient of determination R^2, leave-one-out cross-validation Q^2, bootstrapping coefficient Q^2_{BOOT}, and the external validation coefficient) were determined using the methods detailed by Eriksson et al.[104] The latter article provides an overview of applicable and acceptable methods for the reliability of QSARs in the context of regulatory acceptance.

The performed statistical tests were as follows:

Goodness-of-fit

The least squares linear regression model was fitted to the data and residuals were calculated and checked for being normally distributed with a mean of 0. The R^2 was determined and assessed how close it is to a value of 1.

Robustness

To assess the robustness of QSARs, 1000 bootstrap datasets were created and models refitted. Parameters were checked for changes between samples. *Y* values ($-\log_{10}$ of toxicity) were randomly reassigned and models were refitted. The assessment was done if the R^2 and Q^2 values of the original dataset outperform the others (randomly assigned ones).

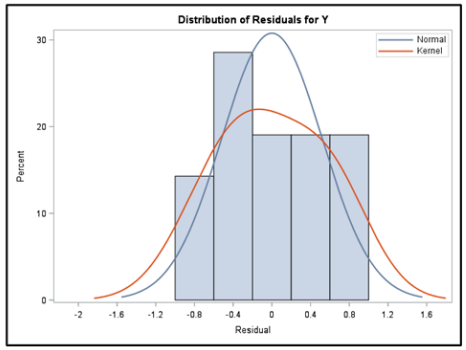
Predictivity

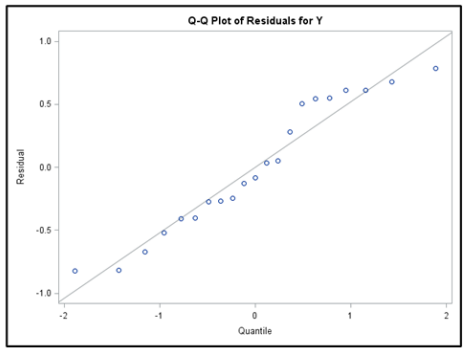
Cross-validation was performed to assess model predictivity. Data were randomly grouped into 7 groups and values were predicted from other 6 groups. Randomisation was repeated for 100 times. Two criteria were used for assessment:

a) Is median $Q^2 > 0.9$ (excellent) or > 0.5 (good)?
b) Is $R^2 - Q^2$ about 0.2 to 0.3?

Goodness of Fit

- $R^2 = 0.7058$

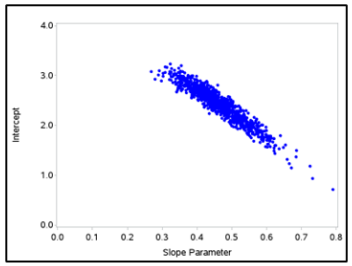




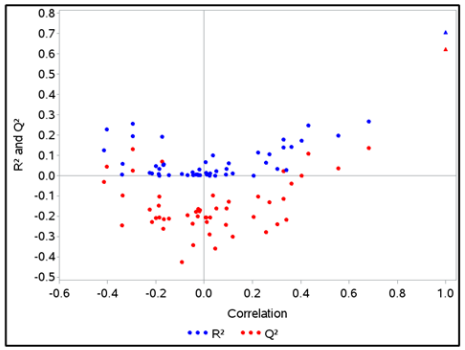
Robustness

Bootstrap results

- Intercept: 2.4954 (1.79, 2.96)
- Slope: 0.4522 (0.35, 0.59)

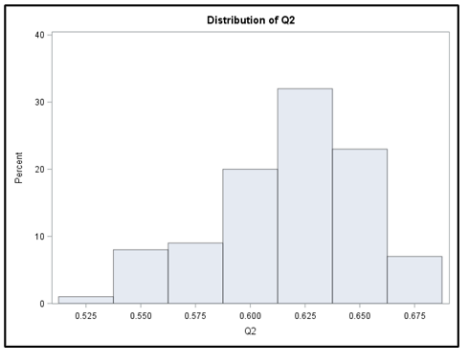


Permutation results



Predictivity

- $Q^2 = 0.6247$ (median)
- P05 = 0.5479
- P95 = 0.6671

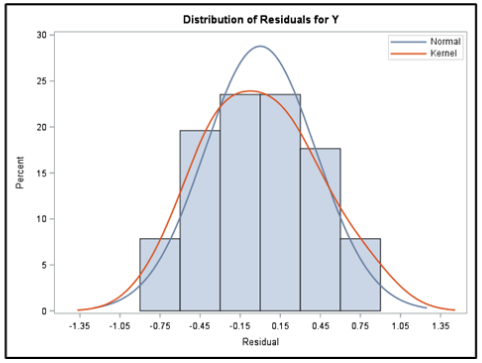


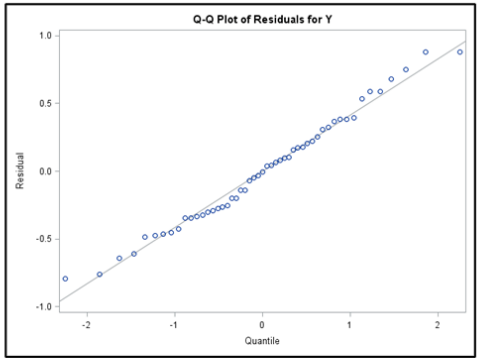
- Excellent: $Q^2 > 0.9$
- Good: $Q^2 > 0.5$
- $R^2 - Q^2$ about 0.25

Figure S10. Statistical evaluation of fish anionic (hydrocarbon, HC) surfactants QSAR

Goodness of Fit

- $R^2 = 0.7982$

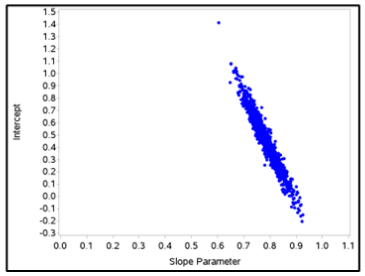




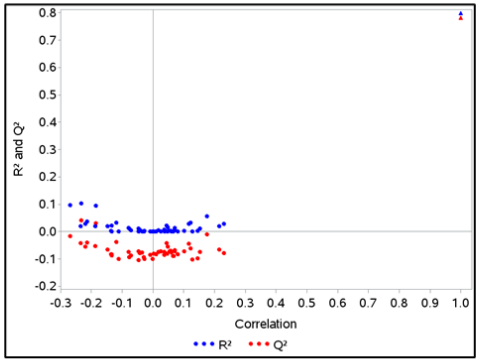
Robustness

Bootstrap results

- Intercept: 0.458 (0.082, 0.822)
- Slope: 0.782 (0.701, 0.869)

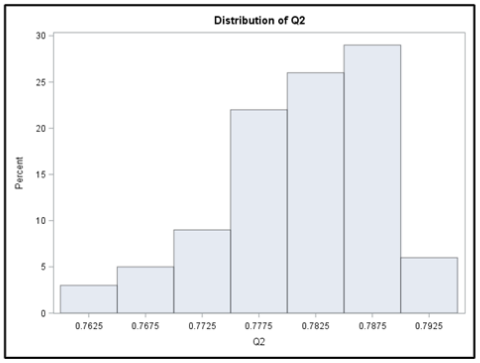


Permutation results



Predictivity

- $Q^2 = 0.7828$ (median)
- P05 = 0.7686
- P95 = 0.7902

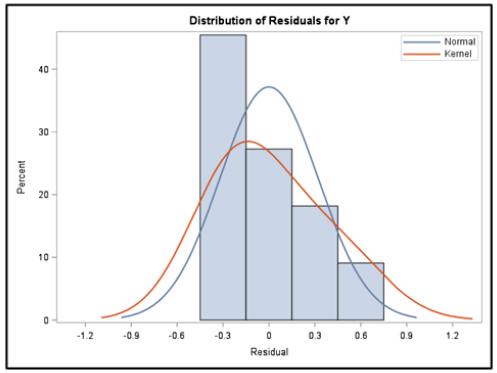


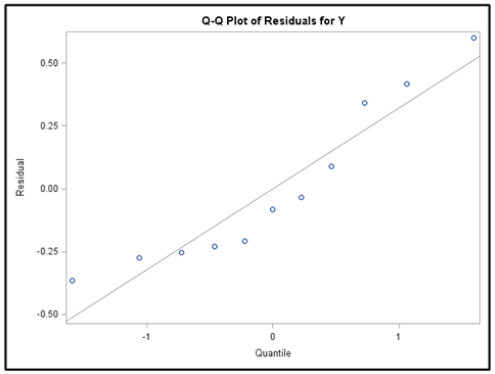
- Excellent: $Q^2 > 0.9$
- Good: $Q^2 > 0.5$
- $R^2 - Q^2$ about 0.25

Figure S11. Statistical evaluation of daphnids anionic (hydrocarbon, HC) surfactants QSAR

Goodness of Fit

- R^2 = 0.8178

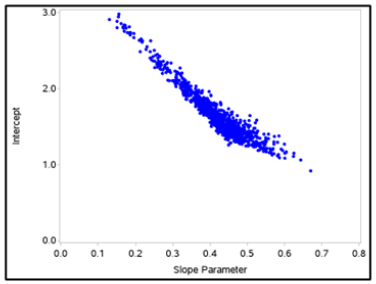




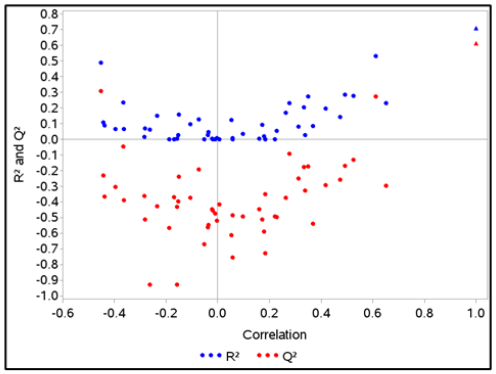
Robustness

Bootstrap results

- Intercept: 1.594 (1.266, 2.316)
- Slope: 0.425 (0.266, 0.538)

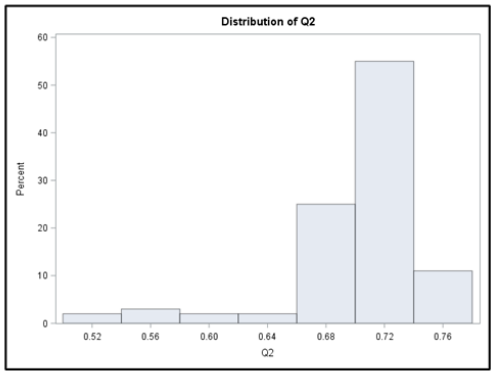


Permutation results



Predictivity

- Q^2 = 0.7112 (median)
- P05 = 0.5799
- P95 = 0.7577



- Excellent: $Q^2 > 0.9$
- Good: $Q^2 > 0.5$
- $R^2 - Q^2$ about 0.25

Figure S12. Statistical evaluation of daphnids anionic (perfluorocarbon, FC) surfactants QSAR

S8. References

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