Supporting Information for "Serum Albumin Binding of Structurally Diverse Neutral Organic Compounds: Data and Models"

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SI-1. Determination of PDMS-water partition coefficients.

PDMS-water partition coefficients ($K_{PDMS/w}$ [L/L]) of PAHs and endosulfan α were determined following the method described elsewhere.[1] Briefly, a 40 mm fiber was put into a glass flask with 100 mL buffer solution (for PAHs), or into a glass test tube with 5 mL buffer solution (for endosulfan α). The flasks and test tubes were spiked with 5 or 10 μL of methanol stock solution containing PAHs or endosulfan α, and were immediately closed with glass stoppers. Only one concentration level per compound was tested, and the equilibrium concentration in PDMS was 2–600 mg/L for each compound. The flasks and test tubes were shaken horizontally at 37 °C (GLS 400, Grant Instruments, UK). Twelve replicates were prepared for dibenzofuran, fluoranthene, benzo[*b*]fluoranthene, and benzo[*ghi*]perylene, and three replicates each time were sacrificed on days 2, 5, 10, and 20. The results of this time-series experiment (Figure S1) indicated that 2 d are sufficient for equilibrium of dibenzofuran and fluoranthene and 5–10 d for equilibrium of benzo[*b*]fluoranthene and benzo[*ghi*]perylene in our experimental setting. Based on the results here and in ref 1, an equilibration time of 2 d was given for endosulfan α, and 10 d for the rest of PAHs. After equilibration, fibers were retrieved, cleaned with tissue, and transferred to 1.5 mL vials. These fibers were extracted with 500 μL cyclohexane. The extracts were analyzed with GC/MS, as described in ref 1. $K_{PDMS/w}$ values were obtained from the mass balance calculation. To examine the conservation of compounds, an aliquot of the remaining test aqueous solution was liquid-liquid extracted using cyclohexane. High recovery (< 95 %) was obtained for all but pyrene (88 %) and benzo[*ghi*]perylene (87 %). For pyrene and benzo[*ghi*]perylene, a recovery correction was made to the mass balance calculation to derived $K_{PDMS/w}$. The results of the experiments are shown in Table S1. The $K_{PDMS/w}$ values obtained are in excellent agreement with the values from ref 2 (Table S1).

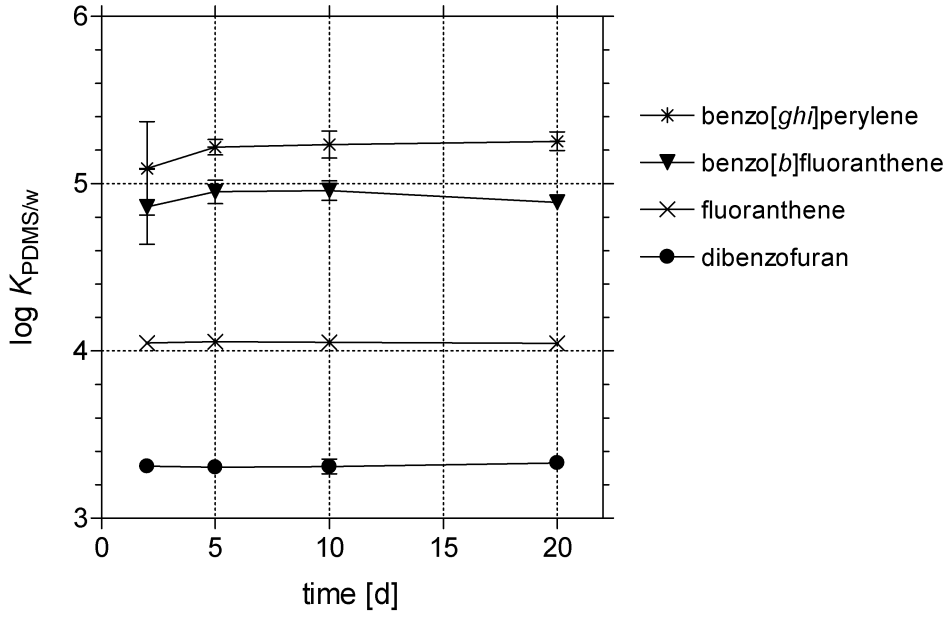

Figure S1. Time-series experiments for determination of $K_{PDMS/w}$ [L/L]. Error bars show standard deviations of triplicate measurements.

Table S1. Measured PDMS-water partition coefficients ($K_{PDMS/w}$ [L/L]) at 37 °C.

	log $K_{PDMS/w}$ (this study)	SD	*n*	recovery (± SD, %)	log $K_{PDMS/w}$ (ref 2)[d]
dibenzofuran	3.31[a]	0.03	12	97 ± 3	-
dibenzothiophene	3.63	0.01	5	100 ± 3	-
phenanthrene	3.66	0.02	5	102 ± 5	3.61
fluoranthene	4.05[a]	0.01	12	101 ± 1	4.01
pyrene	4.13[c]	0.01	5	88 ± 4	4.08
chrysene	4.55	0.02	5	117 ± 3	4.49
benzo[*b*]fluoranthene	4.92[b]	0.05	6	95 ± 11	4.93
benzo[*ghi*]perylene	5.24[b,c]	0.06	6	87 ± 14	5.33
endosulfan α	4.22	0.12	5	95 ± 7	-

[a] Data for days 2–20 in Figure S1. [b] Data for days 10 and 20 in Figure S1. [c] Values were recovery-corrected.
[d] Extrapolated from the data measured at 4, 12, 20, and 30 °C. There data were measured with a 0.01 M $CaCl_2$ and 50 mg/L NaN_3 solution.

SI-2. Extended table for $K_{BSA/w}$ data measured in this study.

Table S2. $K_{BSA/w}$ (L/kg) data measured in this study.

CAS-RN	compound	log $K_{BSA/w}$ (37 °C)	SD	*n*	recovery (± SD, %)	BSA concen--tration (w/v %)	method[a]
110-54-3	*n*-hexane	3.09	0.05	3		1	HS
142-82-5	*n*-heptane	3.59	0.03	3		1	HS
111-65-9	*n*-octane	4.01	0.02	3		1	HS
111-84-2	*n*-nonane	4.45	0.00	4	94 ± 1	0.5	HS
110-82-7	cyclohexane	2.01	0.06	3		1	HS
291-64-5	cycloheptane	2.52	0.01	4	96 ± 1	0.5	HS
292-64-8	cyclooctane	2.98	0.00	4	97 ± 1	0.5	HS
124-11-8	1-nonene	4.22	0.00	4	94 ± 2	0.5	HS
628-71-7	1-heptyne	2.49	0.01	4		0.5	HS
111-85-3	1-chlorooctane	3.85	0.02	4	85.4 ± 0.4	0.1	HS
56-23-5	tetrachloromethane	1.77	0.01	4		1	HS
79-01-6	trichloroethene	1.88	0.02	4	96 ± 15	0.5	HS
127-18-4	tetrachloroethene	2.40	0.01	4	97 ± 10	0.5	HS
75-25-2	tribromomethane	1.95	0.02	4		0.5	HS
58-89-9	γ-hexachlorocyclohexane	2.46	0.01	5	90 ± 2	0.5	PA fiber
26675-46-7	isoflurane	1.58	0.08	4		1	HS
13838-16-9	enflurane	1.59	0.05	4		1	HS
151-67-7	halothane	1.62	0.04	4		1	HS
76-38-0	methoxyflurane	1.77	0.01	4		1	HS
142-96-1	di-*n*-butyl ether	2.01	0.05	4	100 ± 2	0.5	HS
693-65-2	di-*n*-pentyl ether	3.00	0.02	6	101 ± 2	0.5	HS
111-13-7	2-octanone	2.09	0.04	4	102 ± 3	0.5	HS
821-55-6	2-nonanone	2.48	0.02	4	101 ± 6	0.5	HS
693-54-9	2-decanone	2.88	0.02	4	101 ± 6	0.5	HS
629-37-8	1-nitrooctane	3.38	0.04	4	90 ± 7	0.5	HS
126-73-8	tri-*n*-butyl phosphate	2.47	0.03	5	122 ± 3	0.5	PA fiber
71-43-2	benzene	1.58	0.01	4		1	HS
108-88-3	toluene	2.26	0.04	5	106 ± 3	0.5	HS
100-41-4	ethylbenzene	2.70	0.03	5	103 ± 1	0.5	HS
103-65-1	*n*-propylbenzene	2.95	0.03	4		0.1	HS
100-42-5	styrene	2.76	0.03	5	97 ± 1	0.5	HS
108-90-7	chlorobenzene	2.32	0.04	5	101 ± 1	0.5	HS
95-50-1	1,2-dichlorobenzene	3.03	0.02	4		0.1	HS
95-63-6	1,2,4-trimethylbenzene	3.35	0.02	4		0.1	HS
106-37-6	1,4-dibromobenzene	3.97	0.02	4		0.1	HS
120-82-1	1,2,4-trichlorobenzene	3.60	0.03	4	106 ± 5	0.1	HS
634-66-2	1,2,3,4-tetrachlorobenzene	4.21	0.02	4	99 ± 8	0.1	HS
392-56-3	hexafluorobenzene	1.55	0.04	4	107 ± 1	1	HS
771-56-2	methylpentafluorobenzene	2.32	0.02	4		0.7	HS
95-13-6	indene	2.92	0.02	5	97 ± 3	0.5	HS
91-20-3	naphthalene	3.56	0.01	6		0.1	HS
132-64-9	dibenzofuran	3.79	0.01	12	96 ± 1	0.1	PDMS fiber
132-65-0	dibenzothiophene	4.16	0.02	5	100 ± 3	0.1	PDMS fiber
85-01-8	phenanthrene	4.15	0.02	5	102 ± 5	0.1	PDMS fiber

206-44-0	fluoranthene	4.28	0.01	12	79 ± 1	0.1	PDMS fiber
129-00-0	pyrene	4.76	0.02	5	88 ± 4	0.1	PDMS fiber
218-01-9	chrysene	4.46	0.03	5	117 ± 3	0.1	PDMS fiber
205-99-2	benzo[*b*]fluoranthene	4.42	0.03	12	99 ± 3	0.1	PDMS fiber
191-24-2	benzo[*ghi*]perylene	4.76	0.03	11	80 ± 2	0.1	PDMS fiber
100-66-3	anisole	2.16	0.02	4	101 ± 2	0.7	HS
1009-14-9	valerophenone	2.70	0.01	12	96 ± 1	0.5	PA fiber
119-61-9	benzophenone	2.62	0.02	12	97 ± 1	0.5	PA fiber
131-16-8	di-*n*-propyl phthalate	2.84	0.02	12	96 ± 2	0.5	PA fiber
88-72-2	2-nitrotoluene	2.12	0.02	5	96 ± 1	0.5	PA fiber
121-14-2	2,4-dinitrotoluene	1.73	0.03	5	99 ± 1	0.5	PA fiber
86-57-7	1-nitronaphthalene	3.17	0.01	5	108 ± 1	0.5	PA fiber
100-17-4	4-nitroanisole	2.48	0.01	12	97 ± 1	0.5	PA fiber
91-66-7	*N*,*N*-diethylaniline	2.27	0.02	5	90 ± 1	0.5	PA fiber
111-27-3	1-hexanol	1.64	0.06	4	98 ± 2	1	PA fiber
111-70-6	1-heptanol	2.18	0.02	6	94 ± 5	1	PA fiber
111-87-5	1-octanol	2.74	0.02	5	95 ± 14	0.5	PA fiber
143-08-8	1-nonanol	3.10	0.01	5	106 ± 4	0.5	PA fiber
19780-44-0	4-ethyl-3-hexanol	1.48	0.07	4	98 ± 2	1	PA fiber
873-76-7	4-chlorobenzyl alcohol	2.10	0.02	6	98 ± 6	1	PA fiber
645-56-7	4-*n*-propylphenol	2.59	0.01	5	99 ± 1	0.5	PA fiber
90-43-7	2-phenylphenol	2.62	0.02	5	100 ± 1	0.5	PA fiber
371-41-5	4-fluorophenol	1.57	0.06	4	101 ± 1	1	PA fiber
108-43-0	3-chlorophenol	2.35	0.01	5	98 ± 2	0.5	PA fiber
106-48-9	4-chlorophenol	2.43	0.03	5	97 ± 2	0.5	PA fiber
106-41-2	4-bromophenol	2.81	0.02	5	98 ± 1	0.5	PA fiber
540-38-5	4-iodophenol	3.41	0.01	5	101 ± 3	0.5	PA fiber
80-05-7	bisphenol A	2.88	0.03	5	104 ± 8	0.5	PA fiber
100-01-6	4-nitroaniline	1.69	0.15	4	104 ± 2	1	PA fiber
95-51-2	2-chloroaniline	1.95	0.04	5	98 ± 2	0.5	PA fiber
540-37-4	4-iodoaniline	2.95	0.02	5	96.4 ± 0.4	0.5	PA fiber
92-67-1	4-aminobiphenyl	2.55	0.01	5	100 ± 2	0.5	PA fiber
120-72-9	indole	2.25	0.00	5	99 ± 1	0.5	PA fiber
86-74-8	carbazole	3.52	0.01	5	101 ± 1	0.5	PA fiber
51218-45-2	metolachlor	1.74	0.03	5	99 ± 2	0.5	PA fiber
1912-24-9	atrazine	1.77	0.08	5	97 ± 3	0.5	PA fiber
439-14-5	diazepam	2.68	0.02	5	107 ± 4	0.5	PA fiber
53-16-7	estrone	2.69	0.04	5	96 ± 8	0.5	PA fiber
115-29-7	endosulfan α	3.24	0.08	4	85 ± 8	0.1	PDMS fiber

[a] HS: headspace method; PA fiber: fiber extraction method using polyacrylate fiber; PDMS fiber: fiber extraction method using poly(dimethylsiloxane) fiber.

SI-3. Literature data for albumin-water partition coefficients.

Table S3. Literature data for albumin-water partition coefficients (L/kg).

CAS-RN	compound	log $K_{BSA/w}$	temp (C°)	method	albumin conc. (as stated in the cited reference)	pH	buffer composition	bound-to-total mole ratio of albumin (r)	ref
111-13-7	2-octanone	1.58	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
106-68-3	3-octanone	1.31	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
541-85-5	5-methyl-3-heptanone	1.38	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
821-55-6	2-nonanone	1.91	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
108-83-8	2,6-dimethyl-4-heptanone	1.66	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
693-54-9	2-decanone	2.20	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
628-63-7	amyl acetate	1.55	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
590-01-2	butyl propionate	1.53	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
106-70-7	methyl hexanoate	1.48	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
142-92-7	hexyl acetate	2.12	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
109-21-7	butyl butyrate	1.66	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
123-66-0	ethyl hexanoate	1.73	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
106-30-9	ethyl heptanoate	1.99	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
112-14-1	octyl acetate	2.56	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
66-25-1	hexanal	1.73	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
111-71-7	heptanal	2.29	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
124-13-0	octanal	2.41	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
112-31-2	decanal	3.39	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
112-44-7	undecanal	3.01	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
18829-56-6	trans-2-nonenal	2.34	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
3913-71-1	trans-2-decenal	2.69	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
71-36-3	butanol	0.89	37?	ultracentrifuge	4%	7.4	phosphate buffer	0.04	4
111-27-3	hexanol	1.58	37?	ultracentrifuge	4%	7.4	phosphate buffer	0.10	4
111-87-5	octanol	2.34	37?	ultracentrifuge, dialysis	4%	7.4	phosphate buffer	0.16	4
108-88-3	toluene	2.04	23	headspace SPME	4 mg/mL	7.0	100 mM phosphate	0.06	5
100-41-4	ethylbenzene	2.45	23	headspace SPME	4 mg/mL	7.0	100 mM phosphate	0.06	5

103-65-1	propylbenzene	2.77	23	headspace SPME	4 mg/mL	7.0	100 mM phosphate	0.06	5
104-51-8	butylbenzene	3.11	23	headspace SPME	4 mg/mL	7.0	100 mM phosphate	0.06	5
129-00-0	pyrene	5.10	20	depletion SPME	n.a.	n.a.	n.a.	n.a.	6
129-00-0	pyrene	3.77	25	depletion PDMS	0.1-12 g/L	n.a.	buffer	0.02-0.16	7
70362-49-1	3,3',4,5-tetrachlorobiphenyl (PCB 78)	5.19	25	depletion PDMS	2-10 mg/L	7.2	phosphate buffer	<0.03	8
60145-21-3	2,2',4,5',6-pentachlorobiphenyl (PCB 103)	5.02	25	depletion PDMS	2-10 mg/L	7.2	phosphate buffer	<0.03	8
38411-22-2	2,2',3,3',6,6'-hexachlorobiphenyl (PCB 136)	5.23	25	depletion PDMS	2-10 mg/L	7.2	phosphate buffer	<0.03	8
72-43-5	methoxychlor	4.20	25	depletion PDMS	0.1-12 g/L	n.a.	buffer	0.02-0.09	7
98-86-2	acetophenone	1.40	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
100-52-7	benzaldehyde	1.48	30	headspace SPME	1.4-14.4 mg/L	7.0	0.02 mM phosphate, 0.15 M NaCl	<0.01	3
98-95-3	nitrobenzene	1.72	24	immersion SPME	100 μM	7.4	100 mM phosphate	0.01-0.2	9
14938-35-3	4-n-pentylphenol	3.36	24	immersion SPME	20 μM	7.4	100 mM phosphate	0.05-0.7	9
59-50-7	4-chloro-3-methylphenol	2.66	24	immersion SPME	20 μM	7.4	100 mM phosphate	0.05-0.7	9
50-28-2	estradiol	2.93	22±2	negligible-depletion SPME	6.5×10^{-6}-6.1×10^{-3} M	7.4	50 mM Tris	<0.001	10
58-08-2	caffeine	1.19	25	dynamic dialysis	1.83 & 3.65%	7.0	40 mM phosphate	0-0.5	11
2921-88-2	chlorpyrifos	3.83	25	depletion PDMS	0.1-12 g/L	n.a.	buffer	0.02-0.11	7

CAS-RN	compound	log $K_{HSA/w}$	temp (C°)	method	albumin conc. (as stated in the cited reference)	pH	buffer composition	bound-to-total mole ratio of albumin (r)	ref
58-22-0	testosterone	2.48	25	equilibrium dialysis	6×10^{-5} M	7.4	phosphate (I = 0.1)	0-1.8	12
58-22-0	testosterone	2.64	20	equilibrium dialysis	0.2 or 0.3%	7.4	33 mM phosphate, 20 μg/mL gentamicin sulphate	0.02-0.2	13
439-14-5	diazepam	4.00	20	equilibrium dialysis	4%	7.0	33 mM phosphate	0.1-0.4	14
439-14-5	diazepam	3.52	25?	equilibrium dialysis	6×10^{-4} M	7.4	phosphate (I = 0.1)	<0.01	15
439-14-5	diazepam	4.09	23	immersion SPME	1 or 0.05 mg/mL	7.4	200 mM phosphate	0.20-1.03	16
50-28-2	estradiol	3.13	22±2	negligible-depletion SPME	2.2×10^{-6}-6.1×10^{-4} M	7.4	50 mM Tris	<0.001	17
57-83-0	progesterone	2.88	20	equilibrium dialysis	0.2 or 0.3%	7.4	33 mM phosphate, 20 μg/mL gentamicin sulphate	0.04-0.3	13
298-46-4	carbamazepine	1.33	22	ultrafiltration	30 g/L	7.4	67 mM phosphate	0.1-0.7	18
	carprofen methylester	3.18	25	equilibrium dialysis	50 μM	7.4	67 mM phosphate	0-7	19
91-64-5	coumarin	2.07	37	equilibrium dialysis	72.46 μM	7.4	67 mM phosphate	0.2-1.3	20
143-62-4	digitoxigenin	2.71	37	equilibrium dialysis	6.9 mg/mL	7.4	50 mM Tris, 100 mM NaCl	0.1-2	21

94-25-7	n-butyl-p-aminobenzoate	2.63	25	equilibrium dialysis	40 μM	7.4	67 mM phosphate	0.05-0.4	22
145-13-1	pregnenolone	2.81	25	equilibrium dialysis	6×10^{-5} M	7.4	phosphate (I = 0.1)	0-0.8	12

SI-4. Time-series experiments.

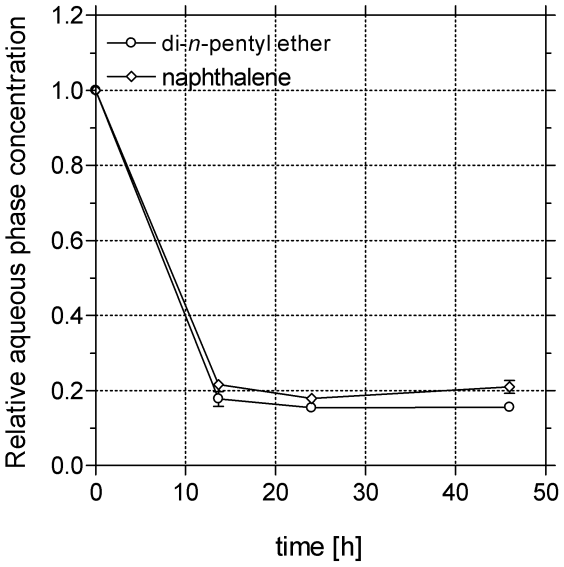

Figure S2. Time-series experiments for BSA binding using the headspace method. The vertical axis indicates the aqueous phase concentration measured by headspace method relative to the initial concentration. BSA concentrations were 0.5 w/v % for di-*n*-pentyl ether and 0.1 w/v % for naphthalene.

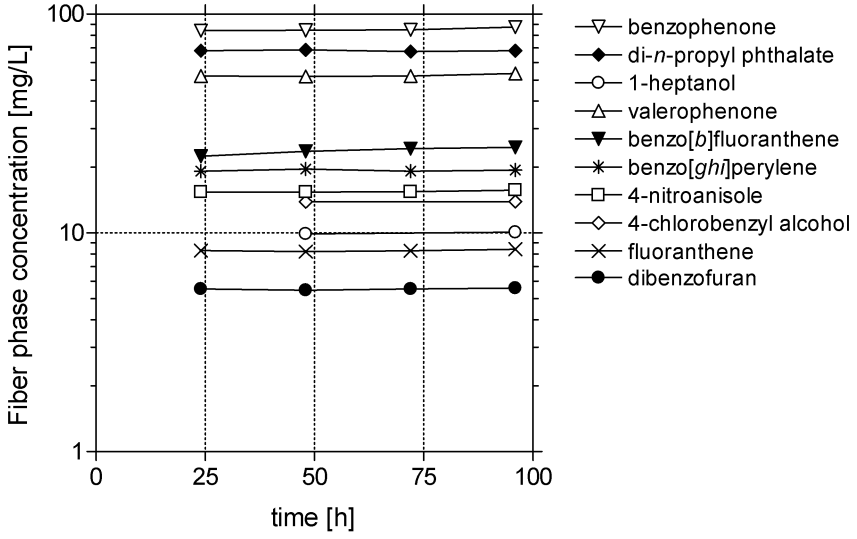

Figure S3. Time-series experiments for fiber-BSA-water three phase equilibrium. Standard deviations of triplicate measurements were smaller than the data symbols. BSA concentrations were 0.1 w/v % for PAHs (benzo[*b*]fluoranthene, benzo[*ghi*]perylene, fluoranthene, dibenzofuran), and 0.5 w/v % for the other compounds shown in the figure. PDMS fiber was used for PAHs, and PA for the other compounds.

SI-5. BSA binding isotherms.

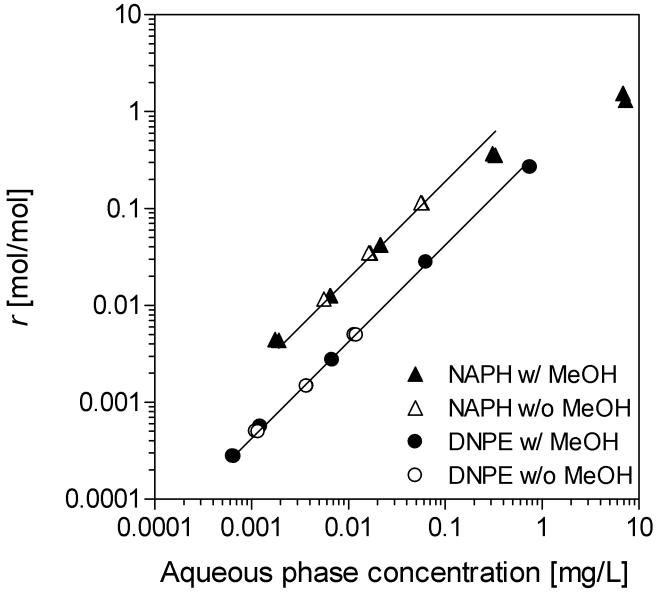

Figure S4. Binding isotherms of naphthalene (NAPH) and di-*n*-pentyl ether (DNPE) to BSA. Data obtained using a methanol stock solution ("w/ MeOH") and an aqueous stock solution ("w/o MeOH) are both presented. Lines indicate the linear model fitted to the data in the range $r < 0.3$.

SI-6. Dependence of measured values of $K_{BSA/water}$ on the BSA concentration.

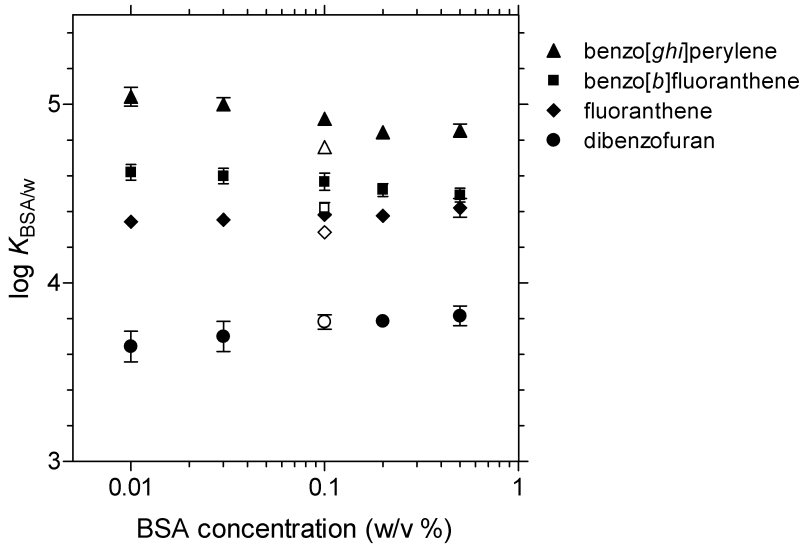

Figure S5. Dependence of measured values of log $K_{BSA/w}$ on the BSA concentration (solid symbols). Each data point represents the mean of four replicate measurements. Open symbols are the results from the kinetic experiment (Figure S3) and represent the mean of 11 replicates. Error bars indicate standard deviations, which are often smaller than the data symbols. Measurements were conducted with the PDMS-fiber extraction method.

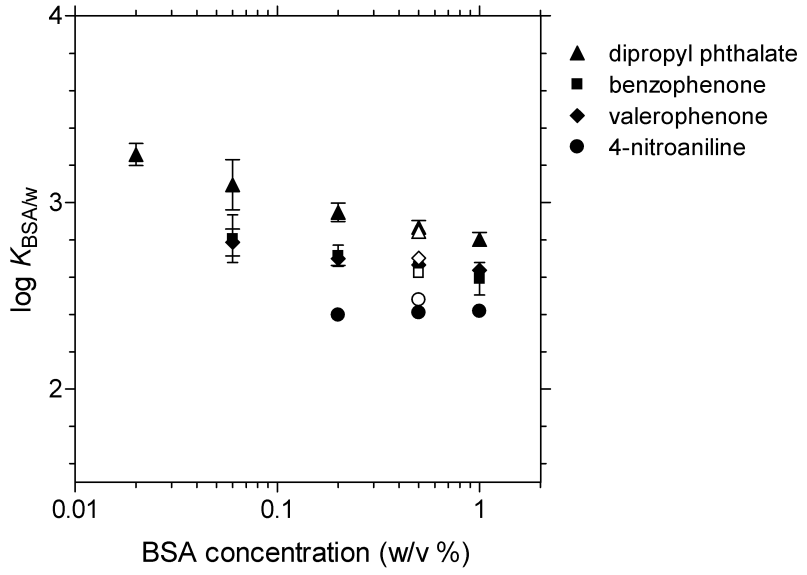

Figure S6. Dependence of measured values of log $K_{BSA/w}$ on the BSA concentration (solid symbols). Each data point represents the mean of four replicate measurements. Open symbols are the results from the kinetic experiment (Figure S3) and represent the mean of 12 replicates. Error bars indicate standard deviations, which are often smaller than the data symbols. Measurements were conducted with the PA-fiber extraction method.

SI-7. Values of log K_{ow} and PP-LFER descriptors used in this study.

Table S4. Values of log K_{ow} and PP-LFER descriptors used in this study.

	log K_{ow}	*E*	*S*	*A*	*B*	*V*	*L*
n-hexane	3.90	0.00	0.00	0.00	0.00	0.954	2.67
n-heptane	4.66	0.00	0.00	0.00	0.00	1.095	3.17
n-octane	5.18	0.00	0.00	0.00	0.00	1.236	3.68
n-nonane	5.65	0.00	0.00	0.00	0.00	1.377	4.18
cyclohexane	3.44	0.31	0.10	0.00	0.00	0.845	2.96
cycloheptane	4.00	0.35	0.10	0.00	0.00	0.986	3.70
cyclooctane	4.45	0.41	0.10	0.00	0.00	1.127	4.33
1-nonene	5.15	0.09	0.08	0.00	0.07	1.334	4.07
1-heptyne	n.a.	0.16	0.23	0.13	0.10	1.009	3.00
1-chlorooctane	n.a.	0.19	0.40	0.00	0.09	1.358	4.71
tetrachloromethane	2.83	0.46	0.38	0.00	0.00	0.739	2.82
trichloroethene	2.42	0.52	0.37	0.08	0.03	0.715	3.00
tetrachloroethene	3.40	0.64	0.44	0.00	0.00	0.837	3.58
tribromomethane	2.40	0.97	0.68	0.15	0.06	0.775	3.78
γ-hexachlorocyclohexane	3.72	1.45	1.28	0.00	0.50	1.580	7.57
isoflurane	2.06	-0.24	0.56	0.00	0.08	0.901	1.97
enflurane	2.10	-0.24	0.40	0.07	0.13	0.901	1.75
halothane	2.30	0.10	0.39	0.13	0.05	0.801	1.98
methoxyflurane	2.21	0.11	0.67	0.07	0.14	0.910	2.86
di-*n*-butyl ether	3.21	0.00	0.25	0.00	0.45	1.295	3.92
di-*n*-pentyl ether	n.a.	0.00	0.25	0.00	0.45	1.576	4.88
2-octanone	2.37	0.11	0.68	0.00	0.51	1.252	4.26
2-nonanone	3.14	0.12	0.68	0.00	0.51	1.392	4.74
2-decanone	3.73	0.11	0.68	0.00	0.51	1.533	5.25
1-nitrooctane*	n.a.	0.19	0.95	0.00	0.29	1.410	5.43
tri-*n*-butyl phosphate	4.00	-0.10	0.90	0.00	1.21	2.239	7.37
benzene	2.13	0.61	0.52	0.00	0.14	0.716	2.79
toluene	2.73	0.60	0.52	0.00	0.14	0.857	3.33
ethylbenzene	3.15	0.61	0.51	0.00	0.15	0.998	3.78
n-propylbenzene	3.69	0.60	0.50	0.00	0.15	1.139	4.23
styrene	2.95	0.85	0.65	0.00	0.16	0.955	3.86
chlorobenzene	2.84	0.72	0.65	0.00	0.07	0.839	3.66
1,2-dichlorobenzene	3.43	0.87	0.78	0.00	0.04	0.961	4.52
1,2,4-trimethylbenzene	3.63	0.68	0.56	0.00	0.19	1.139	4.44
1,4-dibromobenzene	3.79	1.15	0.86	0.00	0.04	1.066	5.32
1,2,4-trichlorobenzene	4.02	0.98	0.81	0.00	0.00	1.084	5.25
1,2,3,4-tetrachlorobenzene	4.60	1.18	0.92	0.00	0.00	1.206	6.17
hexafluorobenzene	2.55	0.09	0.56	0.00	0.01	0.943	2.35
methylpentafluorobenzene	n.a.	0.16	0.59	0.00	0.01	1.046	3.24
indene	2.92	1.00	0.77	0.00	0.20	0.988	4.56
naphthalene	3.30	1.34	0.92	0.00	0.20	1.085	5.16
dibenzofuran	4.12	1.41	1.02	0.00	0.17	1.274	6.65
dibenzothiophene	4.38	1.96	1.31	0.00	0.20	1.379	7.58
phenanthrene	4.46	2.06	1.29	0.00	0.29	1.454	7.63
fluoranthene	5.16	2.38	1.55	0.00	0.24	1.585	8.83
pyrene	4.88	2.81	1.71	0.00	0.28	1.585	8.83
chrysene	5.81	3.03	1.73	0.00	0.33	1.823	10.33

benzo[*b*]fluoranthene	5.78	3.19	1.82	0.00	0.40	1.954	11.63
benzo[*ghi*]perylene	6.63	4.07	1.90	0.00	0.45	2.084	13.26
anisole	2.11	0.71	0.75	0.00	0.29	0.916	3.89
valerophenone	n.a.	0.80	0.95	0.00	0.50	1.437	5.90
benzophenone	3.18	1.45	1.50	0.00	0.50	1.481	6.96
di-*n*-propyl phthalate*	3.27	0.71	1.40	0.00	0.88	1.992	7.70
2-nitrotoluene	2.30	0.87	1.11	0.00	0.28	1.032	4.88
2,4-dinitrotoluene	1.98	1.17	1.27	0.07	0.51	1.206	6.27
1-nitronaphthalene	3.19	1.60	1.59	0.00	0.29	1.260	7.06
4-nitroanisole	2.03	0.97	1.29	0.00	0.40	1.090	5.85
N,*N*-diethylaniline	3.31	0.95	0.80	0.00	0.50	1.380	5.29
1-hexanol	2.03	0.21	0.42	0.37	0.48	1.013	3.61
1-heptanol	2.62	0.21	0.42	0.37	0.48	1.154	4.12
1-octanol	3.00	0.20	0.42	0.37	0.48	1.295	4.62
1-nonanol	3.77	0.19	0.42	0.37	0.48	1.435	5.12
4-ethyl-3-hexanol	n.a.	0.17	0.36	0.33	0.57	1.295	4.18
4-chlorobenzyl alcohol	1.96	0.91	0.96	0.40	0.50	1.038	5.07
4-*n*-propylphenol	3.20	0.79	0.88	0.55	0.37	1.198	5.19
2-phenylphenol	3.09	1.55	1.40	0.56	0.49	1.383	7.23
4-fluorophenol	1.77	0.67	0.97	0.63	0.23	0.813	3.84
3-chlorophenol	2.50	0.91	1.06	0.69	0.15	0.898	4.77
4-chlorophenol	2.39	0.92	1.08	0.67	0.20	0.898	4.78
4-bromophenol	2.59	1.08	1.17	0.67	0.20	0.950	5.14
4-iodophenol	2.91	1.38	1.22	0.68	0.20	1.033	5.49
bisphenol A	3.32	1.61	1.56	0.99	0.91	1.864	9.60
4-nitroaniline	1.39	1.22	1.92	0.46	0.35	0.990	6.04
2-chloroaniline	1.90	1.03	0.92	0.25	0.31	0.939	4.67
4-iodoaniline	2.34	1.53	1.28	0.31	0.40	1.074	5.70
4-aminobiphenyl	2.86	1.57	1.48	0.26	0.48	1.424	7.33[b]
indole	2.14	1.20	1.12	0.44	0.22	0.946	5.51
carbazole	3.72	1.79	1.42	0.47	0.26	1.315	7.98
metolachlor	3.13	1.15	1.01	0.07	1.38	2.281	8.86
atrazine	2.61	1.22	1.29	0.17	1.01	1.620	7.78
diazepam	2.82	2.08	1.55	0.00	1.28	2.074	10.48
estrone	3.13	1.73	2.05	0.50	1.08	2.156	10.78
endosulfan α	3.83						
2-octanone	2.37	0.11	0.68	0.00	0.51	1.252	4.26
3-octanone*	2.46[a]	0.11	0.66	0.00	0.51	1.252	4.31
5-methyl-3-heptanone	2.49[a]	0.11	0.63	0.00	0.51	1.252	4.20
2-nonanone	3.14	0.12	0.68	0.00	0.51	1.392	4.74
2,6-dimethyl-4-heptanone	3.03[a]	0.05	0.60	0.00	0.51	1.392	4.24
2-decanone	3.73	0.11	0.68	0.00	0.51	1.533	5.25
amyl acetate	2.30	0.07	0.60	0.00	0.45	1.169	3.84
butyl propionate	2.36[a]	0.06	0.56	0.00	0.47	1.169	3.83
methyl hexanoate	2.40[a]	0.08	0.60	0.00	0.45	1.169	3.87
hexyl acetate	2.93[a]	0.06	0.60	0.00	0.45	1.310	4.29
butyl butyrate	2.96[a]	0.04	0.56	0.00	0.45	1.310	4.28
ethyl hexanoate	2.94[a]	0.04	0.58	0.00	0.45	1.310	4.25
ethyl heptanoate*	3.47[a]	0.03	0.58	0.00	0.45	1.451	4.73
octyl acetate	3.99[a]	0.03	0.60	0.00	0.45	1.592	5.27
hexanal	1.78	0.15	0.65	0.00	0.45	0.970	3.36
heptanal	2.16[a]	0.14	0.65	0.00	0.45	1.111	3.87
octanal	2.71[a]	0.16	0.65	0.00	0.45	1.252	4.36

decanal*	3.77[a]	0.13	0.65	0.00	0.45	1.533	5.38
undecanal*	4.30[a]	0.12	0.65	0.00	0.45	1.674	5.90
trans-2-nonenal*	3.06[a]	0.40	0.80	0.00	0.45	1.349	4.75
trans-2-decenal*	3.60[a]	0.40	0.80	0.00	0.45	1.490	5.19
butanol	0.88	0.22	0.42	0.37	0.48	0.731	2.60
hexanol	2.03	0.21	0.42	0.37	0.48	1.013	3.61
octanol	3.00	0.20	0.42	0.37	0.48	1.295	4.62
toluene	2.73	0.60	0.52	0.00	0.14	0.857	3.33
ethylbenzene	3.15	0.61	0.51	0.00	0.15	0.998	3.78
propylbenzene	3.69	0.60	0.50	0.00	0.15	1.139	4.23
butylbenzene	4.38	0.60	0.51	0.00	0.15	1.280	4.73
pyrene	4.88	2.81	1.71	0.00	0.28	1.585	8.83
3,3',4,5-tetrachlorobiphenyl (PCB 78)	6.26[a]	1.84	1.69	0.00	0.00	1.814	9.04
2,2',4,5',6-pentachlorobiphenyl (PCB 103)	6.06[a]	2.14	1.22	0.00	0.00	1.588	8.43
2,2',3,3',6,6'-hexachlorobiphenyl (PCB 136)	6.50[a]	2.30	1.33	0.00	0.00	1.711	9.12
methoxychlor	5.08						
acetophenone	1.58	0.82	1.01	0.00	0.48	1.01	4.50
benzaldehyde	1.48	0.82	1.00	0.00	0.39	0.87	4.01
nitrobenzene	1.85	0.87	1.11	0.00	0.28	0.89	4.56
4-*n*-pentylphenol*	4.06	0.79	0.88	0.55	0.36	1.48	6.08
4-chloro-3-methylphenol	3.10	0.92	1.02	0.67	0.22	1.04	5.29
estradiol	4.01	1.80	1.77	0.86	1.10	2.20	11.11
caffeine	-0.07	1.50	1.82	0.08	1.25	1.36	7.84
chlorpyrifos	4.96						
testosterone	3.32	1.54	2.59	0.32	1.19	2.38	11.27
diazepam	2.82	2.08	1.55	0.00	1.28	2.07	10.48
estradiol	4.01	1.80	1.77	0.86	1.10	2.20	11.11
progesterone	3.87	1.45	3.29	0.00	1.14	2.62	12.05
carbamazepine	2.45	2.15	2.18	0.76	0.88	1.81	9.40
coumarin	1.39	1.23	1.68	0.00	0.52	1.06	6.02
digitoxigenin	2.64						
n-butyl-*p*-aminobenzoate*	2.87	1.01	1.20	0.29	0.75	1.60	7.41
pregnenolone	4.22						

Log K_{ow} values are from the database for experimental log K_{ow} in ref 23. Values of the PP-LFER descriptors are from refs 24-33. Descriptors for the starred compounds include values extrapolated from their homologous compounds. [a] Estimated using the PP-LFER model[26]. [b] Estimated using the SPARC-online calculator (http://archemcalc.com/sparc).

SI-8. Comparison to the regressions for log $K_{BSA/w}$ on log K_{ow} from the literature.

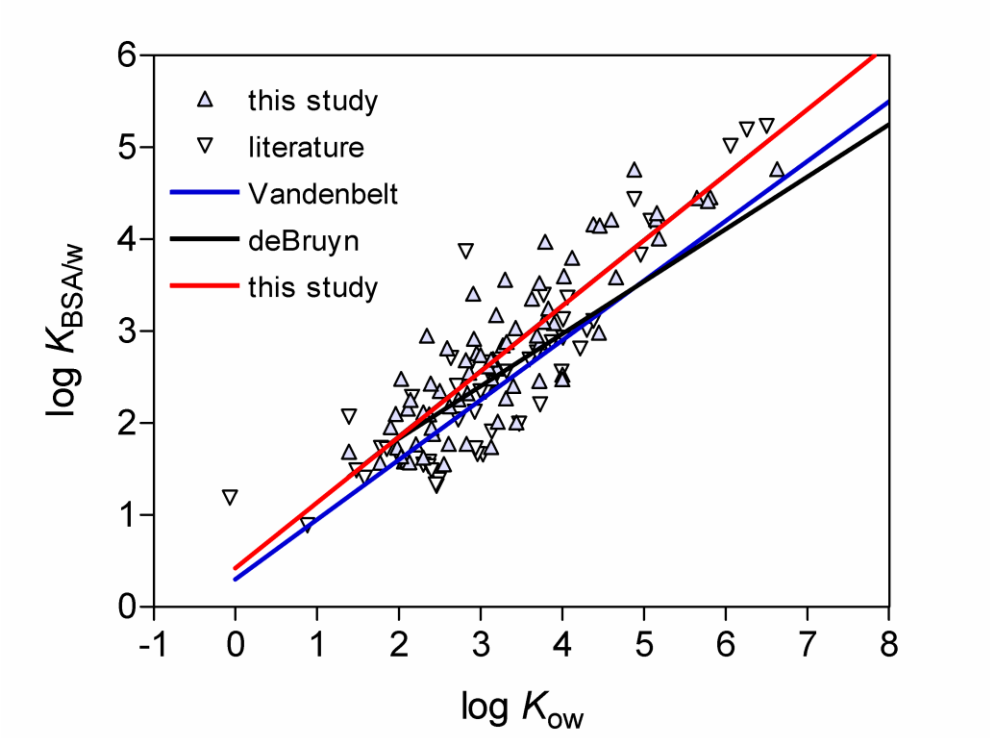

Figure S7. Comparison to the regressions for log $K_{BSA/w}$ on log K_{ow} from the literature. Regression lines from Vandenbelt et al.[34] and deBruyn and Gobas[35] are shown in the figure.

SI-9. Comparison between the measured data and the predictions from the PP-LFER equation from Valko et al. (2003).

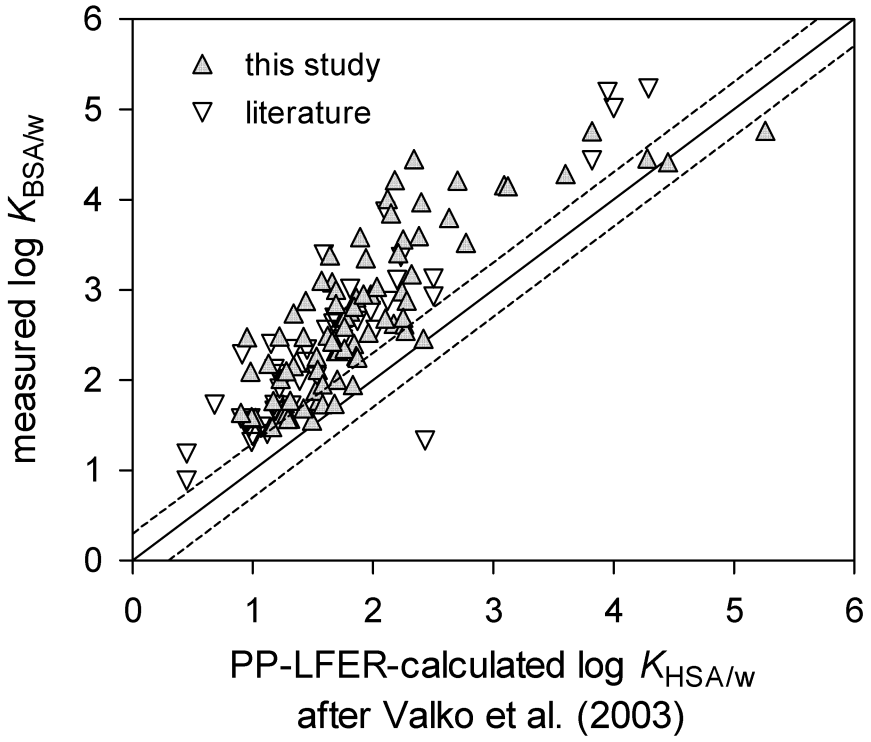

Figure S8. Comparison between the measured data and the predictions from the PP-LFER equation from Valko et al.[36] Note: The PP-LFER from ref 36 calculates a "log*K*" value that can be converted to log K_a through log K_a = log*K* + 3.22, according to ref 36. Here, log K_a was converted further to log $K_{HSA/w}$ as explained in the Appendix of the main manuscript.

SI-10. Fitting of a PP-LFER model to low-polarity compounds.

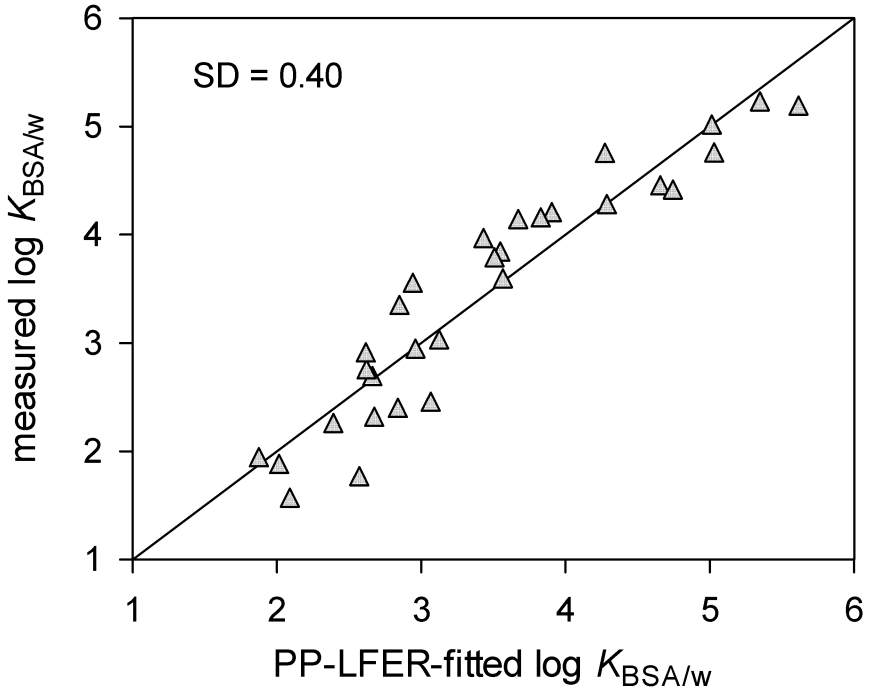

Figure S9. Comparison of measured and PP-LFER-fitted log $K_{BSA/w}$. For this figure, eq 4 was fitted to only the low polarity compounds shown in Figure 2 of the main manuscript.

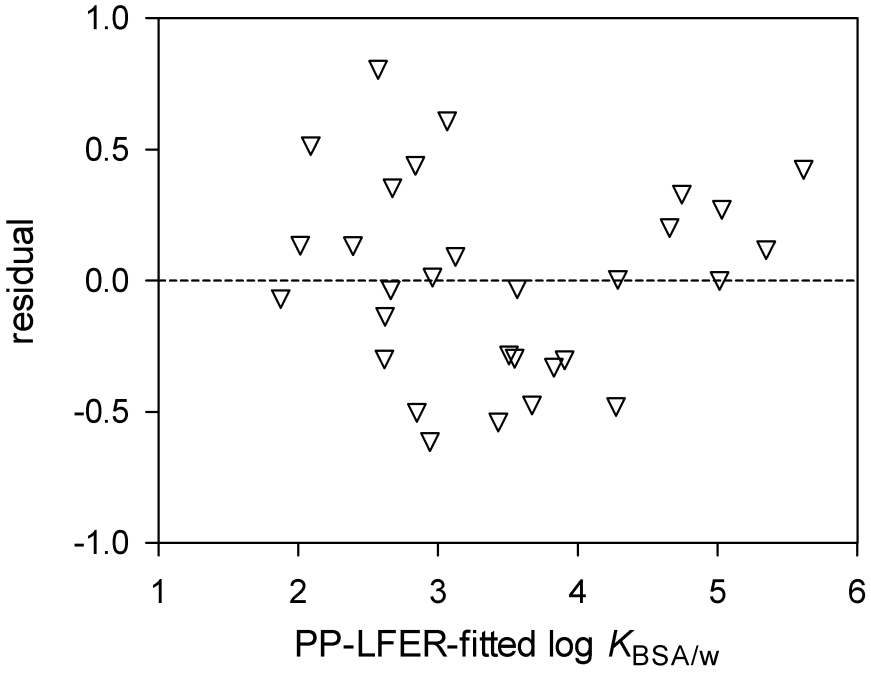

Figure S10. Residual plot for the fitting of eq 4 to the low-polarity compounds.

SI-11. Fitting coefficients and statistics of modified PP-LFER models (eqs 8–10).

Table S5. Fitting coefficients and statistics of modified PP-LFER models (eqs 8–10).

eq 8	*c*	*e*	*s*	*a*	*b*	*v*		*n*	SD	R^2	rmse, lit.[a]
	-3.50	0.39	-0.30	0.36	-3.11	6.46		82	0.39	0.81	0.51
	(0.50)	(0.11)	(0.19)	(0.22)	(0.27)	(0.51)					
eq 9	*c*	*e*	*s*	*a*	*b*	v_1	v_2	*n*	SD	R^2	rmse, lit.[a]
	-1.58	0.44	-0.36	0.31	-2.82	5.54	-1.05	82	0.39	0.82	0.55
	(0.51)	(0.12)	(0.19)	(0.22)	(0.30)	(0.75)	(0.27)				
eq 10	c_1	e_1	s_1	a_1	b_1	v_1		*n*	SD	R^2	rmse, lit.[a]
(V <1.2)	-1.25	1.15	-0.72	0.14	-2.25	3.91		44	0.28	0.83	0.33
	(0.37)	(0.16)	(0.20)	(0.23)	(0.41)	(0.40)					
	c_2	e_2	s_2	a_2	b_2	v_2					
(V > 1.2)	0.49	0.17	-0.10	0.19	-3.58	2.78		38	0.36	0.88	0.71
	(0.43)	(0.14)	(0.25)	(0.29)	(0.34)	(0.36)					
(overall)								82	0.32		0.61

[a] Root mean squared errors of predictions for the literature data. Values in parentheses are standard errors.

SI-12. Estimated mass distributions of neutral organic solutes in serum.

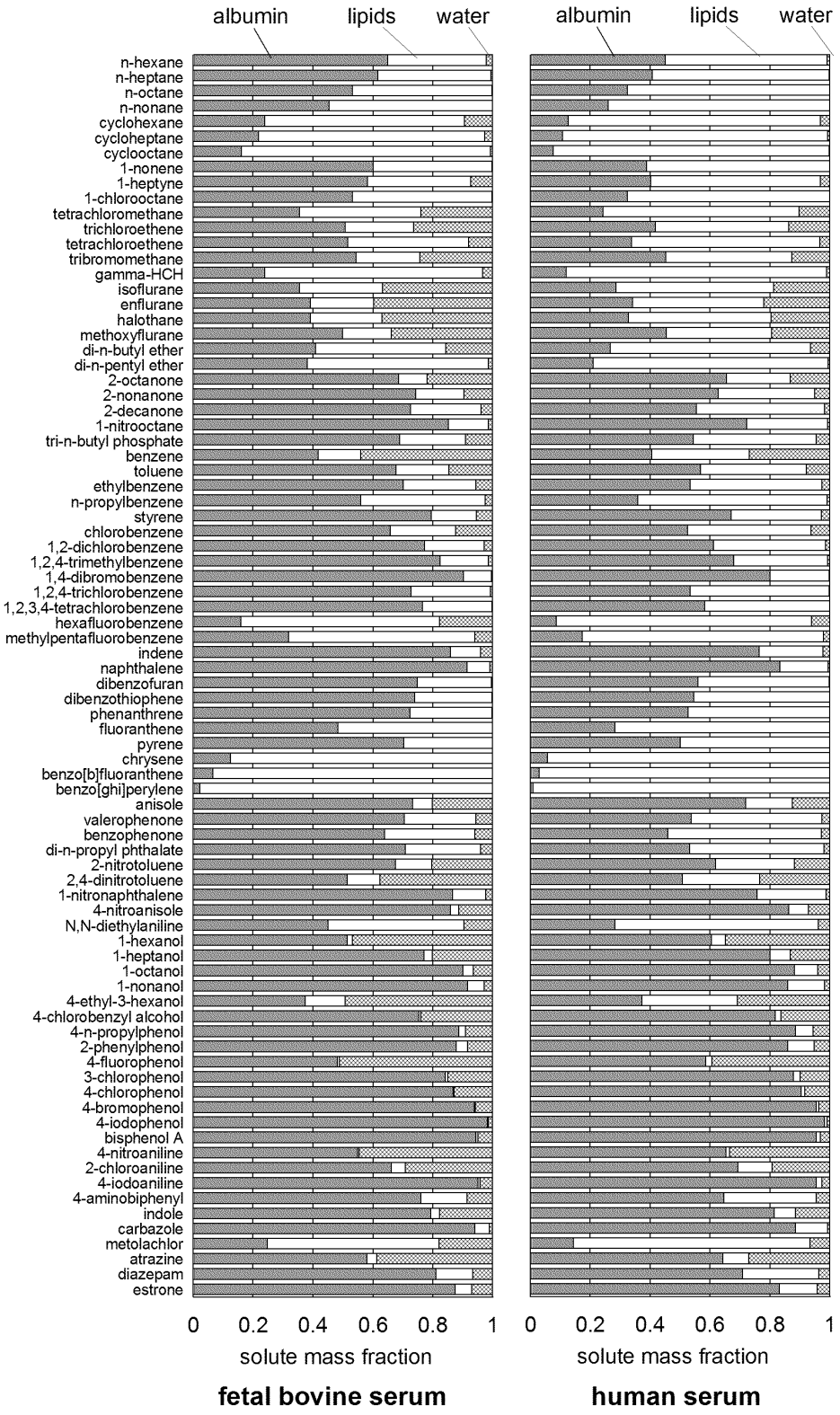

Figure S11. Estimated mass distributions of organic solutes in fetal bovine and human sera. The albumin and lipid concentrations were assumed to be 24 and 1.92 g/L, respectively, for fetal bovine serum, and 38 and 7.22 g/L, respectively, for human serum.

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