



Effect of dissolved organic matter on pre-equilibrium passive sampling: A predictive QSAR modeling study

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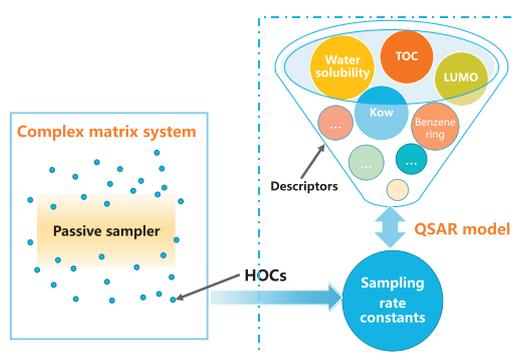
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HIGHLIGHTS

- A flow-through system was set up to obtain desorption rate constants in various complex matrices.
- Passive sampling rate constants significantly increased as the concentration of DOM increased.
- A QSAR model was proposed to predict passive sampling rate constants.

GRAPHICAL ABSTRACT



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ABSTRACT

Pre-equilibrium passive sampling is a simple and promising technique for studying sampling kinetics, which is crucial to determine the distribution, transfer and fate of hydrophobic organic compounds (HOCs) in environmental water and organisms. Environmental water samples contain complex matrices that complicate the traditional calibration process for obtaining the accurate rate constants. This study proposed a QSAR model to predict the sampling rate constants of HOCs (polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs) and pesticides) in aqueous systems containing complex matrices. A homemade flow-through system was established to simulate an actual aqueous environment containing dissolved organic matter (DOM) i.e. humic acid (HA) and (2-Hydroxypropyl)- β -cyclodextrin (β -HPCD)), and to obtain the experimental rate constants. Then, a quantitative structure-activity relationship (QSAR) model using Genetic Algorithm-Multiple Linear Regression (GA-MLR) was found to correlate the experimental rate constants to the system state including physicochemical parameters of the HOCs and DOM which were calculated and selected as descriptors by Density Functional Theory (DFT) and Chem 3D. The experimental results showed that the rate constants significantly increased as the concentration of DOM increased, and the enhancement factors of 70-fold and 34-fold were observed for the HOCs in HA and β -HPCD, respectively. The established QSAR model was validated as credible ($R_{Adj}^2 = 0.862$) and predictable ($Q^2 = 0.835$) in estimating the rate constants of HOCs for complex aqueous sampling, and a probable mechanism was developed by comparison to the reported theoretical study.

Main finding of the work: The present study established a QSAR model of passive sampling rate constants and calibrated the effect of DOM on the sampling kinetics.

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1. Introduction

Passive sampling, a relatively new approach in the analysis of hydrophobic organic compounds (HOCs), has been widely used in environmental monitoring for water and air (Baz-Lomba et al., 2017; Feng et al., 2016; Guo et al., 2017; O'Brien et al., 2011; Vrana et al., 2014; Xue et al., 2017). Although it can largely overcome obstacles in traditional sampling processes, a few technical shortcomings should not be ignored. There are two modes of passive sampling. One is equilibrium extraction, that has been validated to monitor free concentrations accurately but requires long sampling times, which greatly limits application to labile compounds (Zhang et al., 2011). Moreover, it is impractical to achieve real-time monitoring in highly dynamic systems, since analyte concentrations always change rapidly and the equilibrium state is fleeting. Therefore, for analysis of highly dynamic chemical changes in real environmental water and living systems, another mode, pre-equilibrium extraction that also known as kinetic passive sampling (Allan et al., 2006), is a better choice.

When applying pre-equilibrium extraction, sampling kinetics are of great importance because potential environmental factors such as temperature, salt, velocity, biofouling and dissolved organic matter (DOM) have a strong impact on the mass transfer kinetics of pollutants. All of these factors can be easily calibrated by considering parameters like diffusivity, viscosity, distribution coefficient in the system, except for the DOM. The effect of DOM can only be measured by semi-empirical equations because some related parameters remain unavailable (i.e. lability factor, diffusion coefficient of complex matrix, etc.). In recent years, although pre-equilibrium passive sampling has been reported for an extensive range of applications to measure organic compounds in complex matrix systems such as food (Lin et al., 2016; Ziólkowska et al., 2016), semisolid organization (Shiota et al., 2011; Xu et al., 2016) and environmental water (Mirasole et al., 2016), knowledge of the effect of complex matrices on the sampling kinetics is still very limited. Ter Laak et al. (2009b) first investigated the facilitation of the mass transfer of HOCs by DOM, and presented an expression to correct the mass transfer coefficient in complex matrices for passive samplers. Hereafter, a series of studies have given evidence to the influence of complex matrices on uptake kinetics of passive samplers, and new models have been proposed and demonstrated in the laboratory (Gilbert et al., 2014; Jiang et al., 2015a; Zielińska et al., 2012). In the existing reports, preloading passive samplers with performance reference compounds (PRC) was the only effective approach to calibrate the effect of complex matrices (Cui et al., 2013; Lin et al., 2017). This method was based on an isotropic process between the uptake of target compounds into the sampler and the desorption of PRC from the sampler. Despite the reliability and accuracy, application limitations were that not all PRC for the targeted compounds were available and that most PRC were very expensive. To overcome this limitation, Ouyang et al. (2009) proposed a one-calibrant kinetic calibration in which the desorption of a single PRC was used to calibrate all extracted analytes. However, this method could only be applied to water samples without any complex matrix.

Based on the above considerations, a relatively simple, fast empirical method based on essential parameters for HOCs and/or the exposure system, should be more applicable to environmental water. Therefore, we do a new attempt to construct a quantitative structure-activity relationship (QSAR) model to correlate the kinetic rate constants to the properties of analytes and the sample matrices. QSAR models are widely reported to be used in drug design (Ramsay and Di Giovanni, 2017; Tong et al., 2017), chemical engineering design (Fourches et al., 2015; Gonfa et al., 2016) and environmental studies (Shi et al., 2017; Tian et al., 2017). A QSAR model, which represents internal relationships between physical properties, environmental behavior, ecological toxicological parameters and the molecular structure of HOCs, is here investigated to study environmental indicators. It can incorporate the relevant environmental data for HOCs, sharply reduce experimental

costs and decrease the number of necessary experiments or even eliminate them altogether.

In the present study, the effect of complex matrices on the passive sampling kinetics was first investigated. Solid phase microextraction was selected as the passive sampler and a homemade flow-through system was established to model a real aqueous environment containing a complex matrix. The flow system effectively solves problems of traditional sampling methods, in which (a) HOCs might sorb to the wall stiffly due to high hydrophobicity, causing low concentration of HOCs in water; (b) the concentrations and states of the matrix are labile; or (c) long times are required to reach equilibrium. The rate constants of 19 HOCs in complex matrices containing humic acid (HA) and (2-Hydroxypropyl)- β -cyclodextrin (β -HPCD) were acquired. The relative structural and physicochemical parameters of the HOCs and complex matrix were calculated and selected as descriptors by Density Functional Theory (DFT) and Chem 3D. Genetic Algorithm-Multiple Linear Regression (GA-MLR) was used to establish a QSAR model which correlate the rate constants to the system state including the above-mentioned descriptors. Using the obtained QSAR model, the probable mechanism of the sampling kinetics can be further interpreted, and the relationship between rate constants and the system states can be clearly understood.

2. Materials and methods

2.1. Chemicals and instrument

Nineteen solid HOCs (Table S1) were divided into two groups. One was the polycyclic aromatic hydrocarbons (PAHs), which included naphthalene, acenaphthene, phenanthrene, fluorene, pyrene, chrysene, benzo[*k*]fluoranthene, benzo[*a*]pyrene and dibenz[*a,h*]anthracene. The other was the polychlorinated biphenyls (PCBs)/pesticides group, containing PCB-1, 3, 9, 11, 18, 77, pentachlorobenzene (penta-CB), hexachlorobenzene (hexa-CB), Aldrin-D and DDT. The PAHs and two complex matrices, humic acid (HA, fulvic acid $\geq 90\%$) and (2-Hydroxypropyl)- β -cyclodextrin (β -HPCD), were purchased from Sigma-Aldrich (Shanghai, China), while the PCBs/pesticides were purchased from J&K Scientific, Ltd. (Shanghai, China). The polydimethylsiloxane (PDMS) tubing (i.d. 310 μm , o.d. 640 μm) was purchased from PermSelect (Ann Arbor, MI, USA), and the stainless steel wire (diameter of 480 μm) was purchased from Vita Needle Co. (Needham, MA, USA).

An Agilent 7890 GC coupled to 5977A MS (Agilent technologies, CA, USA) was used for quantification purposes. The GC was equipped with a split/splitless injector and an HP-5MS (30 m \times 0.25 mm I.D. \times 0.25 μm thickness) fused-silica column. The injector temperature was set at 280 $^{\circ}\text{C}$, while the oven temperature was programmed from 80 $^{\circ}\text{C}$ to 280 $^{\circ}\text{C}$ at a rate of 20 $^{\circ}\text{C min}^{-1}$ and then held for 10 min at 280 $^{\circ}\text{C}$. Chromatographic separation was performed with helium as the carrier gas. A Selected Ion Mode (SIM) was used for all compounds, whose selected ion values are listed in Table S1. A GERSTEL Multi-Purpose System (MPS) was applied for the automation process (GERSTEL, Mülheim a der Ruhr, Germany). The correlation coefficients of calibration curves with GC-MS analysis were higher than 0.99 for all the HOCs. Internal standards were injected periodically to ensure the stability of the instrument.

2.2. Fiber preparation

Stainless steel wires with a core diameter of 480 μm were cut into pieces 4 cm long, sonicated in acetone and deionized water for 15 min each to remove impurities, and dried at room temperature. A piece of carefully cut PDMS tubing with an inner and outer diameter of 320 μm and 650 μm , respectively (1.0 cm), was used as the passive sampler. A swell-shrink method was applied since the inner diameter of PDMS tubing (320 μm) was smaller than the diameter of steel wire (480 μm). Briefly, the PDMS tubing was coated onto the end of the steel wire

after soaking in hexane for a few seconds for swelling, then the solvent (hexane) was evaporated in the air to shrink to the predetermined length (1.0 cm). Compared to the traditional method using epoxy glue (Xu et al., 2014), this improved swell-shrink method was more reproducible (RSD < 10%, $n = 10$); the extraction quantity of fibers did not differ due to uncertain amounts of epoxy glue.

2.3. Preparation of standard working solution and model complex sample

The HOC standard working solution was prepared by mixing a PAH stock solution and PCB/pesticides stock solution in a conical flask. The solvent was evaporated and the chemicals re-dissolved with methanol at a concentration of 1 mg L^{-1} . The HA solution was prepared by dissolving the solid sample in a 1 L volumetric flask and filtering the solution through $0.45 \mu\text{m}$ membrane filter. Then, 0.5 g sodium azide was added to each diluted solution as microbial inhibitor. The β -HPCD solutions were prepared in the same way for the following experiment. All solutions were prepared immediately before use to make sure their freshness.

Two sampling processes, loading and desorption, were studied using different experimental facilities; all experiments were performed at $25 \pm 1 \text{ }^\circ\text{C}$. In the loading process, probes coated with PDMS were first exposed to the HOC standard working solution with a pre-set concentration ($1\text{--}2 \text{ mg L}^{-1}$ for PAHs and $0.5\text{--}1 \text{ mg L}^{-1}$ for PCBs in the mixed solution, which contained acetone and water with a proportion of 2:8), with shaking at 200 rpm for 48 h to reach partition equilibrium. The loaded probes were removed and rinsed in ultrapure water for 5 s to remove residual HOCs solution on the surface. In the desorption process, a flow-through system that consisted of a digital pump, sampling chamber and sampling port (Fig. 1), was applied to study the complex matrix effect of the water sample on the rate constants. The loaded probes were exposed to the flow-through system for desorption, except for the blanks (desorption for 0 h). The water flowing through sampling chamber and sampling port was set at a rate of 1.5 mL min^{-1} . Ultrapure water was used throughout the experiment.

2.4. Rate constants from different sample matrices

According to the fundamentals of passive sampling (Birch et al., 2012), rate constants can be obtained from extraction/desorption time profiles, which follow a first-order association/dissociation equation (Fig. 2). The extraction and desorption processes are isotropic, thus by studying the effect of complex matrices on the desorption kinetics, one can understand the effect of complex matrices on the extraction process (Jiang et al., 2015a, 2015b; Ouyang and Pawliszyn, 2006; Site, 2001). Desorption of HOCs from the fiber can be described as (Cui et al., 2013)

$$q_f = q_0 e^{-kt} \quad (1)$$

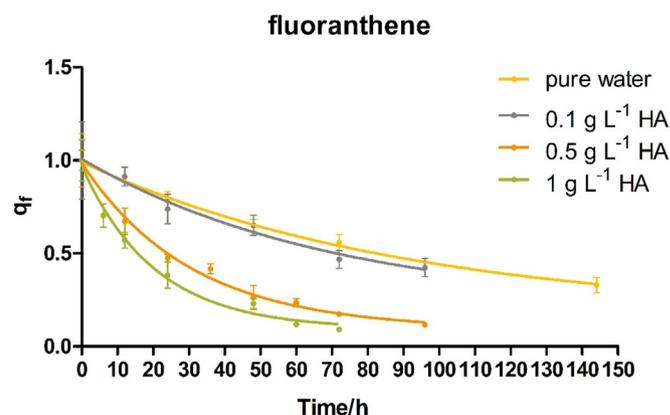


Fig. 2. Desorption time profiles for fluoranthene in pure water with various different concentrations of HA. Data are the mean \pm standard deviation ($n = 3$). Curves were fitted using the first-order disassociation equation: $q_f = q_0 e^{-kt}$. Both q_f and q_0 are the normalized values (dimensionless).

where q_0 is the preloaded amount of HOC on the fiber, q_f is the amount of HOC remaining at time t , and k is the desorption rate constant (dimensionless). Both q_f and q_0 are the normalized values (dimensionless).

In this study, desorption was studied to determine the rate constants of the HOCs using a flow-through system. The complex matrix effects on HOCs kinetics were investigated by comparing desorption rate constants in aqueous solutions containing complex matrices. A relatively high exposure dose of complex matrices was conducted under the laboratory conditions in order to observe significant effect of complex matrices on HOCs' kinetic process and for the following QSAR establishment. The concentrations of different substrates were set at 0, 0.1, 0.5, 1 g L^{-1} for HA; and 0, 0.5, 1, 2 g L^{-1} for β -HPCD, respectively. The solutions with complex matrices were added as flowing liquids (containing 0.5% NaN_3 to inhibit the growth of microorganisms), and probes were desorbed for various time periods (desorption of 0, 6, 12, 24, 36, 48, 60, 72, 96 h for complex matrices; and two more additional points, 120, 144 h, for pure water). Finally, the amount left on the fiber was completely extracted with hexane and quantified by GC-MS using an automated liquid sampler. Each experimental desorption point was conducted in triplicate.

2.5. Generation and validation of QSAR model

A QSAR model for the rate constants of the HOCs in a complex matrix was generated using a Multiple Linear Regression (MLR) method with the selected descriptors, based on the Abraham poly-parameter model (Abraham, 1992):

$$k = A + bB + cC + dD + eE \quad (2)$$

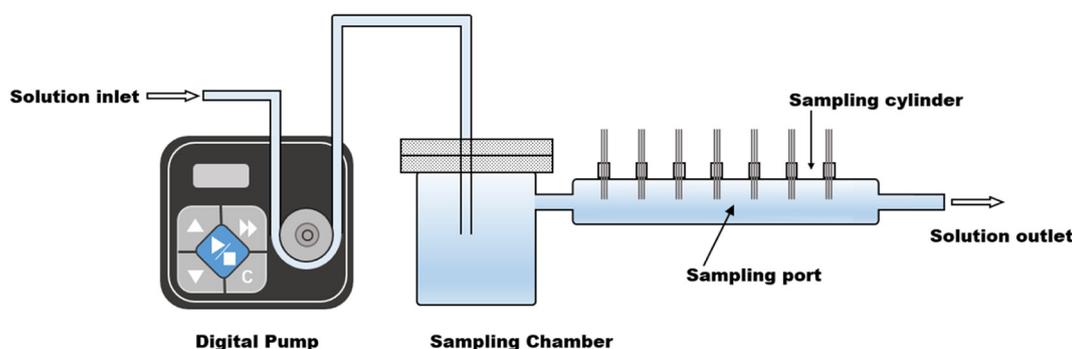


Fig. 1. Schematic diagram of flow-through system containing digital pump, sampling chamber and sampling port. The mobile phase contains a complex matrix in the pump, controlled at a rate of 1.5 mL min^{-1} and flowing through sampling chamber and sampling port. Loaded probes were inserted into the sampling cylinder for desorption.

where the right side of the equation includes parameters that account for the system properties. The uppercase letter in equation are descriptors, while the lowercase letters quantify the corresponding effects of the properties in the complex aqueous system.

DFT optimization at the B3LYP/6-31G* level was introduced to obtain structures for calculating the descriptors for the QSAR model. The DFT method at the level mentioned above was performed again to calculate the dipole moment, anisotropy and orbital energies as descriptors. Chem 3D was employed to obtain the other descriptors, such as molecular properties, surface area and volume, constitutional descriptors, and topological indices descriptors. Descriptor selection was performed via GA-MLR in Matlab using a homemade code (Wu et al., 2014). Complex matrices with different concentrations were quantitatively transformed into total organic carbon (TOC) and were considered a descriptor for model building.

Validation is essential for estimating the application of established models. For a traditional MLR model, its square of correlation coefficient (R^2), adjusted square of correlation coefficient ($R_{Adj.}^2$), variance ratio (F) and root-mean-square deviation (RMSD) were all given in the evaluation. Leave One Out–Cross Validation (LOO-CV) is commonly used in cross-validation. In LOO-CV, each compound was removed from the training set once and then was predicted by the model developed with the remained compounds. Its predictive coefficient (Q^2) was set as an evaluable value. When Q^2 is higher than 0.5, the model predictive ability is thought to be acceptable.

3. Results and discussion

3.1. Determination of rate constants

The rate constant describes how fast an absorption/desorption equilibrium can be reached in the sampling process. It is determined by the physical dimension of the sample matrix and passive sampling fiber, the distribution coefficient of the fiber, and the diffusion coefficient of the free dissolved compound and binding matrix (Jiang et al., 2015b). For the flow-through system with constant temperature, steady flow velocity and fiber and sample properties, the rate constant is only influenced by the complex matrix in the system. The desorption time constant in the matrix was determined by fitting the desorption time profile with a first-phase dissociation curve using data processing software such as Graphpad Prism (Fig. 2) for the following samples: (1) pure water with HA concentrations of 0, 0.1, 0.5 and 1 g L⁻¹, respectively; and (2) pure water with β -HPCD concentrations of 0, 0.5, 1 and 2 g L⁻¹, respectively. As shown in Fig. 3 and Table 1 (partial data shown in Fig. S1),

the rate constants significantly increased as the concentration of matrix increased. Compared to the sample without complex matrix, enhancement factors of up to 70-fold and 34-fold were observed for the HOCs in HA and β -HPCD, respectively.

Similar to the present study, several reports indicate that such a facilitation effect was caused by the addition of complex matrix, and it was verified that the mass transfer rates of HOCs were accelerated as the concentrations of complex matrix increased (Smith et al., 2011; Ter Laak et al., 2009a, 2009b). It was obvious that the complex matrix in the system played an important role in the sampling process of HOCs. The sampling process also greatly depended on the properties of HOCs, including hydrophobicity, polarity and topological structure (Yangali-quintanilla et al., 2010). Therefore, the traditional single-parameter QSAR (Patel et al., 2017) might be unable to meet the criteria for analysis of complex or actual samples and would fail to give a comprehensive understanding of kinetic transfer processes. According to the idea proposed by Ouyang et al. (2008), the rate constant of analyte 1, k_1 , could be used to deduce that of analyte 2, k_2 , based on the expression equation of rate constant. Likewise, our proposed QSAR model could be applied for obtaining the rate constants of analytes whose PRCs were not available when sampling in complex water.

3.2. QSAR model establishment and statistical model evaluation

Among the 20 chemical descriptors (Table S2) related to physico-chemical properties and the matrix concentration, which are critical for sampling, four were automatically selected as the descriptors with the most impact (detailed description and values in Table S3 and S4). The QSAR models of obtained rate constants were established, and Eqs. (3), (4) were the fitting equations for system containing HA and β -HPCD, respectively. For HA system:

$$k = 0.0184 + 0.0562 B + 0.0093 C + 0.0094 D - 0.0002 E \quad (3)$$

where B = TOC (g L⁻¹), C = Number of Benzene ring, D = Water solubility (mg L⁻¹), E = Connolly Molecular Area (Angstroms Squared). For this equation, $n = 73$; $R^2 = 0.958$; $Adj. R_{Adj.}^2 = 0.955$; $F = 384.57$; $RMSD = 0.013$; $Q^2 = 0.947$.

For β -HPCD system:

$$k = 0.1011 + 0.0514 B + 0.0114 C - 0.0099 D + 0.9589 E \quad (4)$$

where B = TOC (g L⁻¹), C = Water solubility (mg L⁻¹), D = K_{ow} (L kg⁻¹),

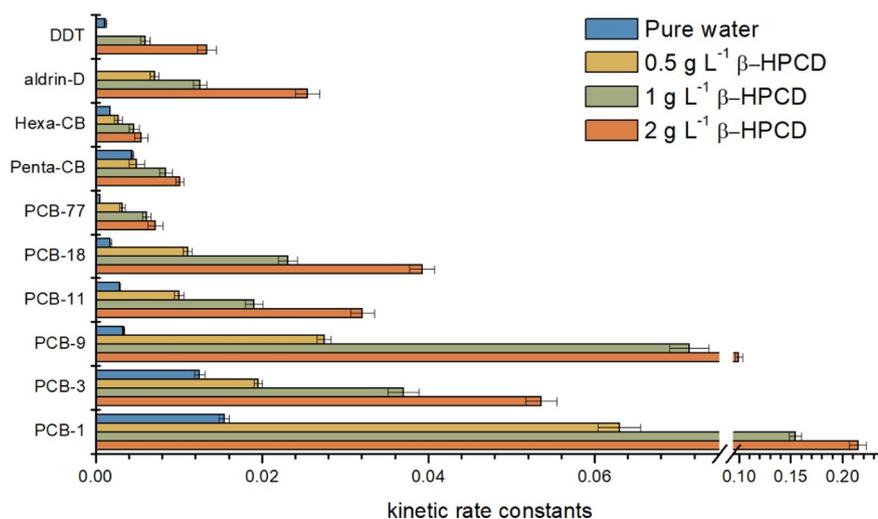


Fig. 3. Desorption rate constants (mean \pm standard deviation, $n = 3$) of PCBs in β -HPCD (partial data shown in Fig. S1); rate constants significantly increased as matrix concentration increased.

Table 1
Desorption rate constants (mean \pm standard deviation, $n = 3$) in different complex matrices.

Num	Name	Pure water	0.5 g L ⁻¹	1 g L ⁻¹	2 g L ⁻¹
(a) Desorption rate constants for 10 PCBs in β -HPCD					
1	PCB-1	0.0154 \pm 0.0006	0.0630 \pm 0.0025	0.1543 \pm 0.0060	0.2148 \pm 0.0082
2	PCB-3	0.0125 \pm 0.0006	0.0195 \pm 0.0005	0.0370 \pm 0.0018	0.0536 \pm 0.0019
3	PCB-9	0.0033 \pm 0.0001	0.0275 \pm 0.0008	0.0714 \pm 0.0023	0.0996 \pm 0.0036
4	PCB-11	0.0029 \pm 0.0001	0.0100 \pm 0.0005	0.0190 \pm 0.0011	0.0321 \pm 0.0014
5	Penta-CB	0.0044 \pm 0.0002	0.0049 \pm 0.0009	0.0084 \pm 0.0008	0.0101 \pm 0.0005
6	PCB-18	0.0018 \pm 0.0001	0.0111 \pm 0.0006	0.0231 \pm 0.0011	0.0392 \pm 0.0015
7	Hexa-CB	0.0018 \pm 0	0.0028 \pm 0.0005	0.0046 \pm 0.0006	0.0055 \pm 0.0008
8	PCB-77	0.0006 \pm 0	0.0032 \pm 0.0004	0.0061 \pm 0.0005	0.0072 \pm 0.0009
9	Aldrin-D	-0	0.0071 \pm 0.0005	0.0126 \pm 0.0008	0.0255 \pm 0.0015
10	DDT	0.0012 \pm 0.0002	-	0.0060 \pm 0.0006	0.0134 \pm 0.0011
(b) Desorption rate constants for 9 PAHs in β -HPCD					
1	Naphthalene	-	0.2696 \pm 0.0095	0.4652 \pm 0.0367	0.5353 \pm 0.0319
2	Acenaphthene	0.0429 \pm 0.0022	0.0437 \pm 0.0012	0.0746 \pm 0.0034	0.0774 \pm 0.0028
3	Phenanthrene	0.0340 \pm 0.0024	0.0499 \pm 0.0016	-	0.0857 \pm 0.0029
4	Fluoranthene	0.0080 \pm 0.0004	0.0106 \pm 0.0006	0.0171 \pm 0.0011	0.0226 \pm 0.0012
5	Pyrene	0.0075 \pm 0.0003	0.0081 \pm 0.0005	0.0129 \pm 0.0009	0.0155 \pm 0.0010
6	Chrysene	0.0005 \pm 0.0001	0.0073 \pm 0.0018	-	0.0191 \pm 0.0033
7	Benzo[k]fluoranthene	0.0010 \pm 0.0001	0.0046 \pm 0.0005	0.0088 \pm 0.0007	0.0149 \pm 0.0011
8	Benzo[a]pyrene	0.0012 \pm 0.0002	0.0059 \pm 0.0017	0.0089 \pm 0.0010	0.0166 \pm 0.0007
9	Dibenz[a,h]anthracene	~ 0	0.0168 \pm 0.0022	0.0192 \pm 0.0025	0.0260 \pm 0.0026
(c) Desorption rate constants for 9 PAHs in HA					
1	Naphthalene	-	0.3306 \pm 0.1384	0.3083 \pm 0.0366	0.3077 \pm 0.0130
2	Acenaphthene	0.0429 \pm 0.0022	0.0392 \pm 0.0025	0.0555 \pm 0.0012	0.0567 \pm 0.0029
3	Phenanthrene	0.0340 \pm 0.0024	-	0.0429 \pm 0.0020	0.1026 \pm 0.0097
4	Fluoranthene	0.0080 \pm 0.0004	0.0097 \pm 0.0008	0.0256 \pm 0.0008	0.0348 \pm 0.0018
5	Pyrene	0.0075 \pm 0.0003	0.0081 \pm 0.0005	0.0241 \pm 0.0008	0.0328 \pm 0.0017
6	Chrysene	0.0005 \pm 0.0005	0.0016 \pm 0.0004	0.0225 \pm 0.0014	0.0386 \pm 0.0022
7	Benzo[k]fluoranthene	0.0010 \pm 0.0001	0.0092 \pm 0.0007	0.0378 \pm 0.0014	0.0585 \pm 0.0027
8	Benzo[a]pyrene	0.0012 \pm 0.0002	0.0117 \pm 0.0008	0.0489 \pm 0.0017	0.0765 \pm 0.0032
9	Dibenz[a,h]anthracene	~ 0	0.0075 \pm 0.0010	0.0403 \pm 0.0029	0.0591 \pm 0.0064
(d) Desorption rate constants for 10 PCBs in HA					
1	PCB-1	0.0154 \pm 0.0006	0.0166 \pm 0.0008	0.0235 \pm 0.0010	0.0197 \pm 0.0015
2	PCB-3	0.0125 \pm 0.0006	0.0112 \pm 0.0006	0.0188 \pm 0.0008	0.0185 \pm 0.0014
3	PCB-9	0.0033 \pm 0.0001	0.0034 \pm 0.0003	0.0088 \pm 0.0007	0.0087 \pm 0.0010
4	PCB-11	0.0029 \pm 0.0001	0.0059 \pm 0.0004	0.0100 \pm 0.0007	0.0098 \pm 0.0011
5	Penta-CB	0.0044 \pm 0.0002	0.0044 \pm 0.0003	0.0092 \pm 0.0007	0.0086 \pm 0.0010
6	PCB-18	0.0018 \pm 0.0001	0.0018 \pm 0.0003	0.0058 \pm 0.0007	0.0063 \pm 0.0009
7	Hexa-CB	0.0018 \pm 0	0.0021 \pm 0.0003	0.0059 \pm 0.0007	0.0061 \pm 0.0008
8	PCB-77	0.0006 \pm 0	0.0023 \pm 0.0003	0.0091 \pm 0.0010	0.0076 \pm 0.0009
9	Aldrin-D	-0	0.0008 \pm 0.0003	0.0042 \pm 0.0009	0.0054 \pm 0.0010
10	DDT	0.0012 \pm 0.0002	-	-	0.0018 \pm 0.0011

in a logarithmic way), $E = LUMO$. For this equation, $n = 73$; $R^2 = 0.864$; $Adj. R^2_{Adj.} = 0.856$; $F = 107.65$; $RMSD = 0.033$; $Q^2 = 0.781$.

Both equations showed great linear correlations (R^2 equal to 0.958 and 0.864 in Eq. (3) and Eq. (4), respectively) and large predictive coefficients (Q^2 equal to 0.947 and 0.781 in Eq. (3) and Eq. (4), respectively). Considering the development of a general QSAR model for real water sampling, in which multiple types of complex matrices were present, a QSAR model fitted both the HA system and the β -HPCD system was developed as followed:

$$k = 0.0397 + 0.0526 B + 0.0104 C - 0.0163 D + 0.0121 E \quad (5)$$

where $B = TOC$ (g L⁻¹), $C = Water\ solubility$ (mg L⁻¹), $D = K_{ow}$ (L kg⁻¹, in a logarithmic way), $E = Radius$ (Atom(s)). For this equation, $n = 146$; $R^2 = 0.866$; $Adj. R^2_{Adj.} = 0.862$; $F = 226.84$; $RMSD = 0.028$; $Q^2 = 0.835$. The positive coefficient of the term in Eq. (5) indicated that the DOM did enhance the mass transport rate between water and passive sampler ($b = 0.0526 > 0$). The detailed mechanism is discussed in the next section.

Compared with Eqs. (3) and (4), Eq. (5) showed a reasonable linear correlation (R^2 equals to 0.866), with particularly small estimation errors ($RMSD = 0.028$) and a large predictive coefficient ($Q^2 = 0.835$). This means that the QSAR model had great credibility and predictability in the complex aqueous system, and TOC is an effective parameter to

represent different complex matrices. In the QSAR modeling, molecular structural descriptors and system state such as water solubility, polarity, concentration of complex matrix were considered, as they all represented a particular environmental index with a clear definition (Table S2). For the actual aqueous environment, a new QSAR model must be established by considering relative descriptors of the system state and several trial analytes, dispensing with tedious determination and calibration processes for the "k" values of all the analytes in the complex matrix. Using an empirical model, our study may be a shortcut to predicting the rate constants of HOCs and may be generalized to other compounds with similar structural properties (neutral, non-ionized and highly hydrophobic) in the homogenous complex matrix.

3.3. Probable mechanism interpretation

To further clarify the obtained QSAR model to predict the rate constants, the latest theoretical calibration equation developed for complex matrix system (Jiang et al., 2015a) was selected as a comparison to interpret the probable mechanism.

$$k = \frac{A(K_{fs}V_f + V_s)}{K_{fs}V_fV_s\delta_u} (F\% \cdot D_u + \xi B\% \cdot D_b)^{2/3} ((F\% + \xi B\%)D_u)^{1/3} \quad (6)$$

According to the equation, the sampling kinetics of passive sampling were correlated to the thickness of the boundary layer (δ_b), the percentages of freely dissolved ($F\%$) and binding ($B\%$) compounds in matrix, and the ratio of binding compounds that contribute to the free flux to the total binding compounds (also called “degree of lability”).

In Eq. (5), TOC described the concentration of the complex matrix, which had a significant impact on the mass transfer rate in the boundary layer and freely dissolved and bound compounds in the matrix. The positive coefficient in Eq. (5) indicated that the addition of a complex matrix did facilitate the mass transfer of HOCs during the desorption process ($b = 0.0526 > 0$). This result agreed with previous studies, which verified the enhancement effects of the matrix, including DOM and suspended particulate (SP) matter, for the transport of HOCs in the diffusion layer (Zielińska et al., 2012; Oomen et al., 2000; Smith et al., 2011; Ter Laak et al., 2009b). The water solubility of compounds largely depended on the sampling temperature and was closely related to the degree of lability. When the temperature increased, more binding compounds were desorbed from the matrix and the degree of lability would be closer to 1 (Jiang et al., 2015a). This was basically the same as increasing the water solubility for the HOCs ($c = 0.0104 > 0$). The partition coefficient between octanol and water (K_{ow}) describes the hydrophobicity of the chemicals and is a vital parameter in environmental studies. The desorption process by which HOCs desorbed from the PDMS fiber, passed through the diffusion layer and then reached aqueous phase was greatly influenced by the hydrophobicity of the compound. This QSAR model indicated that a more hydrophobic HOC led to a slower transfer rate ($d = -0.0163 < 0$). In many other reports (Doong and Chang, 2000; Droge et al., 2007; Hermens, 2005; Ter Laak et al., 2005, 2008), K_{ow} was proved be related to K_{fs} , the partition coefficient between fiber coating and the sample. Other physicochemical properties of the compounds, such as radius and topological diameter were certainly bound up with the mass transfer in the aqueous boundary layer, but had less impact on the mass transfer process than the above three parameters. As shown in Eq. (5), there was a positive correlation between radius and the rate constant (a) ($e = 0.0121 > 0$). However, more studies should be conducted at a molecular level to further understand the kinetic process in complex matrices.

3.4. Practical implications

As the passive sampling rate constants of HOCs in complex matrices are quite difficult to accurately determine by traditional methods and they are of vital importance for research on HOC migration, transformation and bioaccumulation in environmental water, our study tried to break through the wall of traditional theoretical derivation models by constructing an empirical model. We tested the hypothesis that the rate constant of HOCs can be estimated based on the system state, including descriptors of the HOCs and complex matrix. Based on pre-equilibrium passive sampling through a flow-through system, the rate constants of HOCs can be easily calculated, and an experimental QSAR model can be obtained by GA-MLR. The obtained QSAR model is verified as credible and predictable based on the correlation index and prediction weight, and can be applied to predict the sampling kinetics of compounds whose sampling rates are difficult to obtain. Compared with the PRC-preloaded method and the one-calibrant method, our model is much more direct, convenient and general for environmental sample analysis. This study expanded a new line of thought for preliminary prediction of the rate constants of HOCs using a QSAR model. However, as the DOM and HOC species used in this study were limited, more experiments should be conducted to further expand the QSAR model application in the actual environment.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2018.04.116>.

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