

3.4: Partitioning and Partitioning Constants

3.4. Partitioning and partitioning constants

3.4.1. Relevant chemical properties

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Learning Objectives

You should be able to:

- define the concept of hydrophobicity and to explain which chemical properties affect hydrophobicity.
- define which properties of a chemical affect its tendency to evaporate from water.
- calculate fractions ionized for acids and bases.

Keywords: Hydrophobicity, octanol-water partition coefficients, volatility, Henry's Law constant, ionized chemicals

Introduction

Different processes affect the fate of a chemical in the environment. In addition to the transfer and exchange between compartments (air-water-sediment/soil-biota), also degradation determines the concentration in each of these compartments (Figure 1).

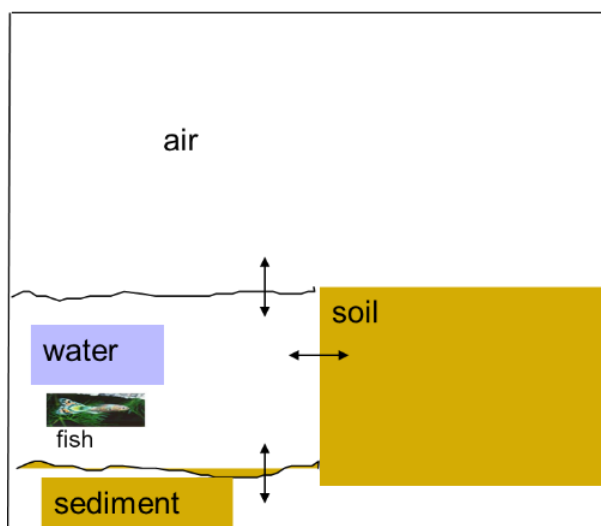


Figure 1. Environmental fate: exchange between compartments and degradation affect the concentration in each compartment.

Some of these processes are discussed in other sections (see sections on [Sorption](#) and [Environmental degradation of chemicals](#)). Some chemicals will easily evaporate from water to air, while others remain mainly in the aqueous phase or sorb to sediment and accumulate into biota.

These differences are related to only a few basic properties:

- Hydrophobicity (tendency of a substance to escape the aqueous phase)
- Volatility (tendency of a substance to vaporize)
- Degree of ionization

Hydrophobicity

Hydrophobicity means fear (phobic) of water (hydro). A hydrophobic chemical prefers to "escape from the aqueous phase" or in other words "it does not like to dissolve in water". Water molecules are tightly bound to each other via hydrogen bonds. For a chemical to dissolve in water, a cavity should be formed in the aqueous phase (Figure 2) and this will cost energy.

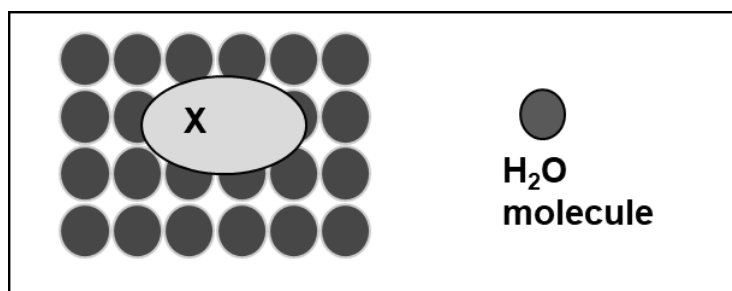


Figure 2. The formation of a cavity in water for chemical X.

Hydrophobicity mainly depends on two molecular properties:

- Molecular size
- Polarity / ability to interact with water molecules, for example via hydrogen bonding

It will take more energy for a chemical with a larger size to create the cavity making the chemical more hydrophobic, while interactions of the chemical with water will favour its dissolution making it less hydrophobic. Figure 3 shows chemicals with increasing hydrophobicity with increasing size and a decreasing hydrophobicity by the presence of polar groups (amino or hydroxy).

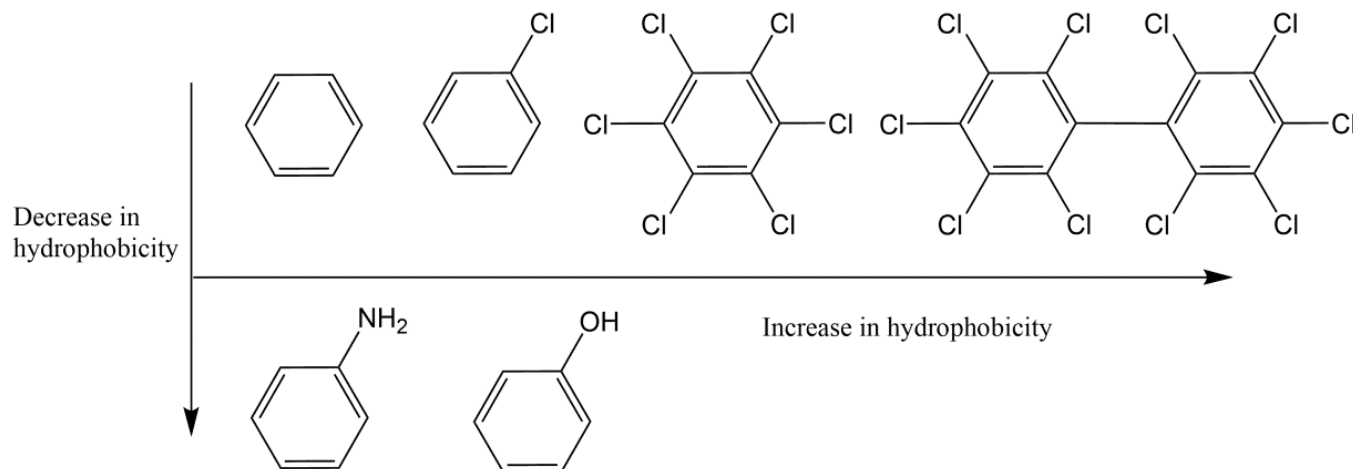


Figure 3. The effect of size and presence of polar groups on the hydrophobicity of chemicals. Increasing molecular size increases hydrophobicity; the introduction of polar groups leads to a decrease in hydrophobicity.

Most hydrophobic chemicals are non-polar organic micro pollutants. Well-known examples are the chlorinated hydrocarbons, such as polychlorinated biphenyls (PCBs) and polycyclic aromatic hydrocarbons (PAHs). Water solubility of these chemicals in general is rather low (in the order of a few ng/L up to a few mg/L).

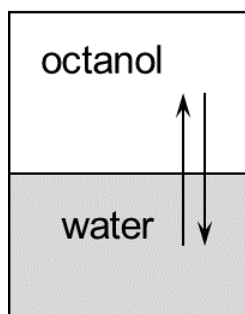
The hydrophobic nature mainly determines the distribution of these chemicals in water and sediment or soil and their uptake across cell membranes. Additional Cl- or Br-atoms in a chemical, as well as additional (CH)_x units, increase the molecular size, and thus a chemical's hydrophobicity. The increased molecular volume requires a larger cavity to dissolve the chemical in water, while they only interact with water molecules via VanderWaals interactions.

Polar groups, such as the -OH and -NH units on the aromatic chemicals in Figure 3, can form hydrogen-bonds with water, and therefore substantially reduce the hydrophobicity of organic chemicals. The hydrogen bonding of hydroxy-substituents works in two ways: The oxygen of -OH bridges to the H-atoms of water molecules, while the hydrogen of -OH can form bridges to the O-atoms of water molecules. Nearly all molecular units consisting of some kind of (carbon-oxygen) combination reduce the hydrophobicity of organic contaminants, because even though they increase the molecular volume they interact via hydrogen bonds (H-bonds) with surrounding water molecules. Additional polar groups in a chemical typically decrease a chemical's hydrophobicity.

Octanol-water partition coefficient:

A simple measure of the hydrophobicity of chemicals, originating from pharmacology, is the octanol-water partition coefficient, abbreviated as K_{ow} (and sometimes also called P_{ow} or P_{oct}): this is the ratio of concentrations of a chemical in n-octanol and in water, after establishment of an equilibrium between the two phases (Figure 4). The -OH group in n-octanol does allow for some

hydrogen bonding between octanol-molecules in solution, and between octanol and dissolved molecules. However, the relatively long alkyl chain only interacts through VanderWaals interactions, and therefore the interaction strength between octanol-molecules is much smaller than that between water-molecules, and it is energetically much less costly to create a cavity to dissolve any molecule.



$$K_{ow} = C(x)_{octanol} / C(x)_{water}$$

Example:

$$C(x)_{octanol} = 2.0 \cdot 10^5 \text{ ug/L}$$

$$C(x)_{water} = 2.0 \text{ ug/L}$$

$$K_{ow} = 10^5$$

$$\log K_{ow} = 5.0$$

Figure 4. Distribution of chemical X between octanol and water and an example of a chemical with log K_{ow} of 5.0.

Experimentally determined K_{ow} values were used in pharmacological research to predict the uptake and biological activity of pharmaceuticals. Octanol was selected because it appears to closely mimic the nonionic molecular properties of most tissue components, particularly phospholipids in membranes. Since the beginning of the 1970s, K_{ow} values have also been used in environmental toxicology to predict the hazard and environmental fate of organic micro pollutants. Octanol may partially also mimic the nonionic molecular properties of most organic matter phases that sorb neutral organic chemicals in the biotic and abiotic environment.

Not unexpectedly, water solubility is negatively correlated with octanol-water partition coefficients.

In practice, three methods can be used to determine or estimate the K_{ow} :

Equilibration methods

In the shake-flask method (Leo et al., 1971) and the 'slow-stirring' method (de Bruijn et al., 1989), the distribution of a chemical between octanol and water is determined experimentally. For highly lipophilic chemicals (log $K_{ow} > 5-6$), the extremely low water solubility, however, hampers a reliable analytical determination of concentrations in the water phase. For such chemicals, these experimental methods are not suitable. During the last two decades, the use of generator columns has allowed for quantification of higher K_{ow} values. Generator columns are columns packed with a sorbing material (e.g. Chromosorb®) onto which an appropriate hydrophobic solvent (e.g. octanol) is coated that contains the compound of interest. In this way, a large interface surface area between the lipophilic and water phases is created, which allows for a rapid establishment of equilibrium. When a large volume of (octanol-saturated) water (typically up to 10 litres) is passed slowly through the column, an equilibrium distribution of the compound is established between the octanol and the water. The water leaving the column is passed over a solid sorbent cartridge to concentrate the compound and allow for a quantification of the aqueous concentration. In this way, it is possible to more reliably determine log K_{ow} values up to 6-7.

Chromatography

K_{ow} values may also be derived from the retention time in a chromatographic system (Eadsforth, 1986). The use of reversed-phase High Performance Liquid Chromatography (HPLC), thin-layer chromatography or gas chromatography results in a capacity factor (relative retention time; retention of the compound relative to a non-retained chemical species), which may be used to predict the chemical distribution over octanol and water. HPLC systems have shown most successful, because they consist of stationary and mobile phases that are liquid. As a consequence, the nature of the phases can be most closely arranged to resemble the octanol-water system. Of course, this requires calibration of the capacity factors by applying the chromatographic method to a number of chemicals with well-known K_{ow} values. Chromatographic methods may reliably be applied for estimations of log K_{ow} values in the range of 2-8. For more lipophilic chemicals, also these methods will fail to reliably predict K_{ow} values (Schwarzenbach et al., 2003).

Calculation

K_{ow} values may also be calculated or predicted from parameters describing the chemical structure of a chemical. Several software programs are commercially available for this purpose, such as KOWWIN program of the US-EPA. These programs make use of the so-called fragment method (Leo, 1993; Rekker and Kort, 1979). This method takes into account the contribution to K_{ow} of different chemical groups or atoms in a molecule, and in addition corrects for special features such as steric hindrance or other intramolecular interactions (equation 1):

$$\log K_{ow} = \sum f_n + \sum F_p \text{ (eq.1)}$$

in which f_n quantifies the contributions of each fragment n in a particular chemical (see e.g. Table 1) and F_p accounts for any special intramolecular interaction p between the fragments.

This fragment approach has been improved during the last decades and is available in the [EPISUITE](#) program from the US Environmental Protection Agency. Other programs for the calculation of K_{ow} values are: [ChemProp](#), and [ChemAxon](#) from Chemspider.

Table 1. Fragment constants (K_{ow}) for a few fragments. (from the EPISUITE program)

Fragment	Fragment constant (f) ^a
-CH ₃ aliphatic carbon	0.5473
Aromatic Carbon	0.2940
-OH hydroxy, aromatic attach	-0.4802
-N aliphatic N, one aromatic attach	-0.9170

Note: the above calculations are given for non-ionized chemicals. The hydrophobicity of ionic chemicals is also highly affected by the degree of ionization (see below).

K_{ow} values can also be retrieved from databases like [echemportal](#) or [ECHA](#) and others.

Volatility

Volatility of a chemical from the aqueous phase to air (see Figure 5) is expressed via the Henry's law constant (K_H).

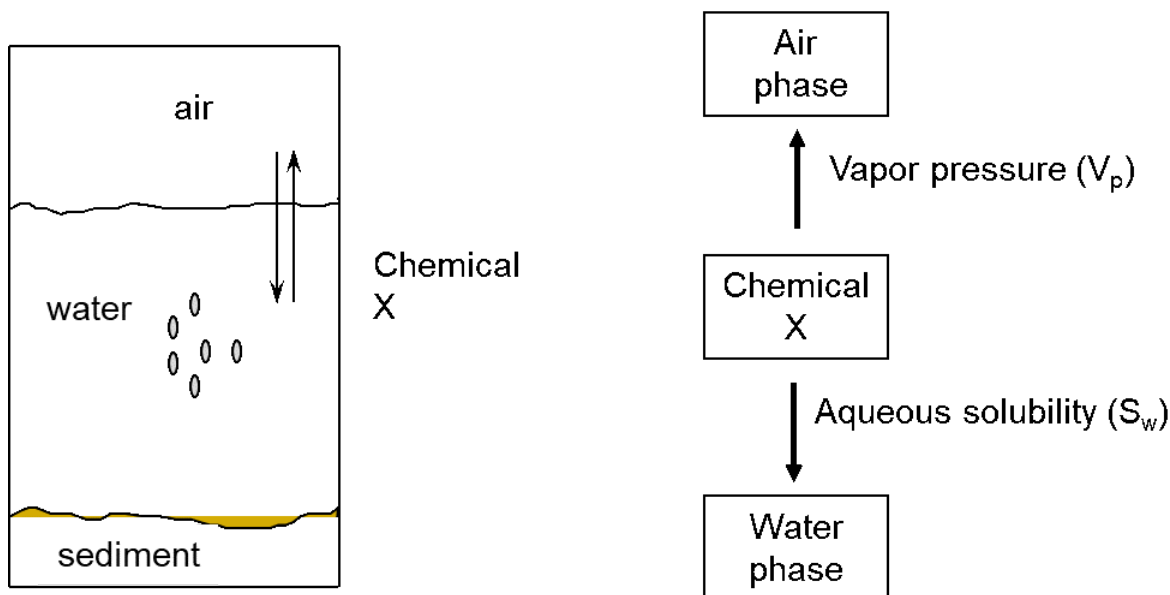


Figure 5. Evaporation of chemical X from water to air.

Henry's law constant (K_H , in $\text{Pa} \cdot \text{m}^3/\text{mol}$) is the chemical distribution between the gas phase and water, as

$$K_H = \frac{P_i}{C_{aq}} \text{ (eq.2)}$$

where in an equilibrated water-gas system:

C_{aq} is the aqueous concentration of the chemical (units in mol/m^3), and P_i is the partial pressure of the chemical in air (units in Pascal, Pa), which is the pressure exerted by the chemical in the total gas phase volume (occupied by the mixture of gases the gas-phase above the water solution of the chemical). Note that P_i is a measure of the concentration in the gas phase, but not yet in the same units as the dissolved concentration (discussed below)!

For compounds that are slightly soluble in water, K_H can be estimated from:

$$K_H = \frac{V_p}{S_w} \quad (\text{eq.3})$$

where:

K_H : Henry's law constant ($\text{Pa}\cdot\text{m}^3/\text{mol}$), V_p is the (saturated) vapor pressure (Pa), which is the pressure of the chemical above the pure condensed (liquid) form of the chemical, and S_w is the maximum solubility in water (mol/m^3).

The advantage of equation 3 is that both V_p and S_w can be experimentally derived or estimated. The rationale behind equation 3 is that two opposite forces will affect the evaporation of a chemical from water to air:

- (i) the vapor pressure (V_p) of the pure chemical - high vapor pressure means more volatile, and
- (ii) solubility in water (S_w) - high solubility means less volatile.

Benzene and ethanol (see Table 2) are good illustrations. Both chemicals have similar vapor pressure, but the Henry's law constant for benzene is much higher because of its much lower solubility in water compared to ethanol; benzene is much more volatile from an aqueous phase.

Table 2. Air-water partition coefficients ($K_{\text{air-water}}$) calculated for five chemicals (ranked by aqueous solubility) by equation 3.

Chemical	Vapor pressure (Pa)	Solubility (mol/m^3)	K_H ($\text{Pa}\cdot\text{m}^3/\text{mol}$)	$K_{\text{air-water}}$ (L/L, or m^3/m^3)
Ethanol	$7.50\cdot 10^3$	$1.20\cdot 10^4$	$6.25\cdot 10^{-1}$	$2.53\cdot 10^{-4}$
Phenol	$5.50\cdot 10^1$	$8.83\cdot 10^2$	$6.23\cdot 10^{-2}$	$2.52\cdot 10^{-5}$
Benzene	$1.27\cdot 10^4$	$2.28\cdot 10^1$	$5.57\cdot 10^2$	$2.25\cdot 10^{-1}$
Pyrene	$6.00\cdot 10^{-4}$	$6.53\cdot 10^{-4}$	$9.18\cdot 10^1$	$3.71\cdot 10^{-4}$
DDT	$2.00\cdot 10^{-5}$	$2.82\cdot 10^{-6}$	7.08	$2.86\cdot 10^{-3}$

Note: all chemicals at equilibrium have a higher concentration (in e.g. mol/L) in the aqueous phase than in the gas phase. Of these five, benzene is the chemical most prone to leave water, with an equilibrated air concentration about 4 times lower (22.5%) than the dissolved concentration.

Equations 2 and 3 are based on the pressure in the gas phase. Environmental fate is often based on partition coefficients, in this case the air-water partition coefficient ($K_{\text{air-water}}$). These partition coefficients are more or less 'dimensionless', because the concentrations are based on equal volumes (such as L/L), while K_H has the unit $\text{Pa}\cdot\text{m}^3/\text{mol}$ or something equivalent to the applied units (equation 4).

$$K_{\text{air-water}} = \frac{C_{\text{air}}}{C_{\text{aq}}} \quad (\text{eq.4})$$

where:

C_{air} is the concentration in air (in e.g. mol/m^3) and C_{aq} is the aqueous concentration (in e.g. mol/m^3).

$K_{\text{air-water}}$ can be calculated from K_H according to equation 5:

$$K_{\text{air-water}} = \frac{K_H}{RT} \quad (\text{eq.5})$$

where R is the gas constant ($8.314 \text{ m}^3\cdot\text{Pa}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$), and T is the temperature in Kelvin (Kelvin = $^{\circ}\text{Celsius} + 273$).

This use of "RT" converts this gas phase concentration to a volume based metric, and applies the ideal gas law which relates pressure (P , in Pa) to temperature (T , in K), volume (V , in m^3), and amount of gas molecules (n , in mol), according to the gas

constant ($R: 8.314 \text{ m}^3 \cdot \text{Pa} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$):

$P \cdot V = n \cdot R \cdot T$ (note that the units of both terms will cancel out) (eq.6)

At 25 °Celsius (298 K), the product RT equals $2477 \text{ m}^3 \cdot \text{Pa} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$.

Examples of calculated values for $K_{\text{air-water}}$ are presented in Table 2.

The influence of the chemical structure on volatility of a chemical from a solvent fully depends on the cost of creating a cavity in the solvent (interactions between solvent molecules) and the interactions between the chemical and the solvent molecules. For partitioning processes, the gas phase is mostly regarded as an inert compartment without chemical interactions (i.e. gas phase molecules hardly ever touch each other).

The molecules of a strongly dipolar solvent such as water that contain atoms that can interact as hydrogen acceptor (the O in an OH group) and hydrogen donor (the H in an OH group) strongly interact with each other, and it costs much energy to create a cavity. This cost increases strongly with molecular size, for nearly all molecules more than the energy regained by interactions with the surrounding solvent molecules. As a result, for most classes of organic chemicals, affinity with water decreases and volatility out of water into air slightly increases with molecular volume. For chemicals that are not able to re-interact via hydrogen bonding, e.g. alkanes, the overall volatility is much higher than for chemicals that do have specific interactions with water molecules besides van der Waals.

Degree of ionization

Acids and bases can be present in the neutral (HA and B) or ionized form (A^- and BH^+ , respectively). For acids, the neutral form (HA) is in equilibrium with the anionic form (A^-) and for bases the neutral form (B) is in equilibrium with the cationic form (BH^+). The degree of ionization depends on the pH and the acid dissociation constant (pK_a). Table 3 shows the equations to calculate the fraction ionized for acids and bases and examples of two acids (phenols) are presented in Table 4.

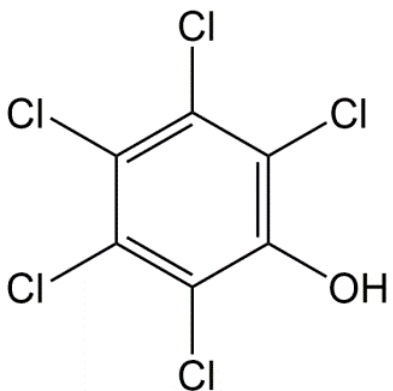
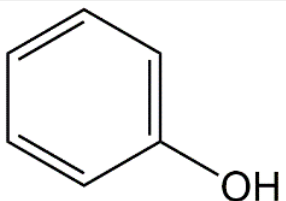
Table 3. Calculation of the fraction ionized for acids and bases.

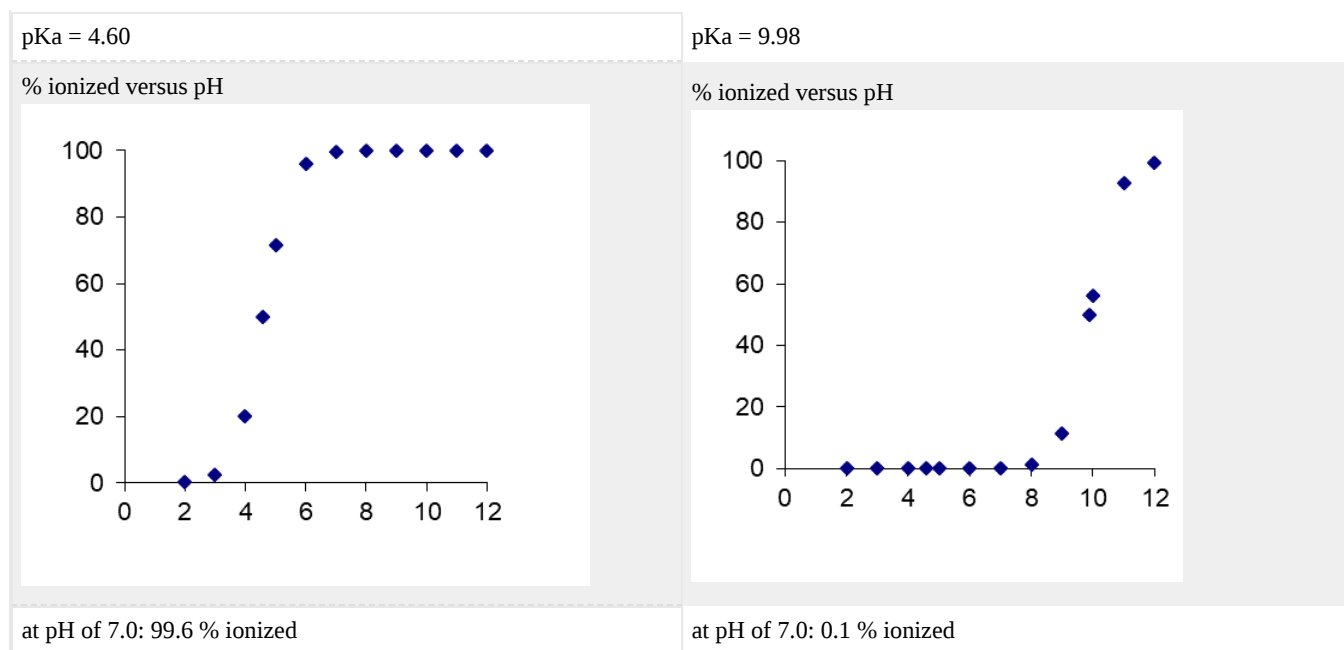
Acids	Bases
$HA \rightleftharpoons A^- + H^+$	$BH^+ \rightleftharpoons B + H^+$
$\text{fraction ionized} = \frac{1}{1 + 10^{(pK_a - pH)}}$	$\text{fraction ionized} = \frac{1}{1 + 10^{(pH - pK_a)}}$

$pK_a = -\log K_a$, where K_a is dissociation constant of the acidic form (HA or BH^+).

The degree of ionization is thus determined by the pH and the pK_a value and more examples for several organic chemicals are presented elsewhere (see Chapter Ionogenic organic compounds).

Table 4. The degree of ionization of two phenolic structures (acids).

Pentachlorophenol	Phenol
	



Examples for several organic chemicals are presented elsewhere (see section on [Ionogenic organic compounds](#)).

The fate of ionic chemicals is very different from that of non-ionic chemicals. The sediment-water sorption coefficient of the anionic species is substantially ($>100\times$) lower than that of the neutral species. If the percentage of ionization is less than $\sim 99\%$ (at a pH 2 units above the pKa), the sorption of the anion may be neglected (K_d is still dominated by the $>1\%$ neutral species) (Schwarzenbach et al., 2003). The reason for the low sorption affinity of the anionic acid form is twofold: anions are much better water soluble, but also most sediment particles (clay, organic matter, silicates) are negatively charged, and electrostatically repulse the similarly charged chemical. In that case the sorption coefficient K_d can be calculated from the sorption coefficient of the non-ionic form and the fraction of the non-ionized form (α):

$$K_d = \alpha K_d (\text{neutral form}) \quad (\text{eq. 7})$$

In environments where the pH is such that the neutral acid fraction $<1\%$ (when pH >2 units above the pKa), the sorption of the anionic species to soil/sediment may significantly contribute to the overall "distribution coefficient" of both acid species.

For basic environmental chemicals of concern, among which many illicit drugs (e.g. amphetamine, cocaine) and non-illicit drugs (e.g. most anti-depressants, beta-blockers), the protonated forms are positively charged. These organic cations are also much more soluble in water than the neutral form, but at the same time they are electrostatically attracted to the negatively charged sediment surfaces. As a result, the sorption affinity of organic cations to sediment should not be considered negligible relative to the neutral species. The sorption processes, however, may strongly differ for the neutral base species and the cationic base species. Several studies have shown that the sorption affinity of cationic base species to DOM or sediment is even stronger than that of the neutral species.

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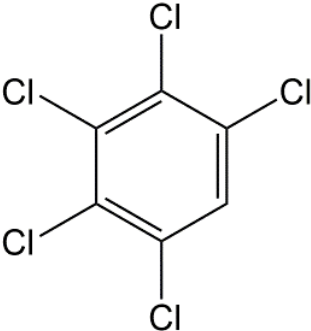
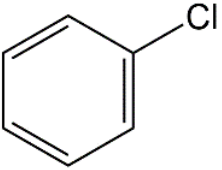
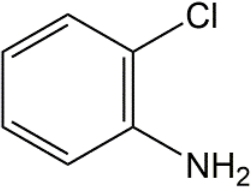
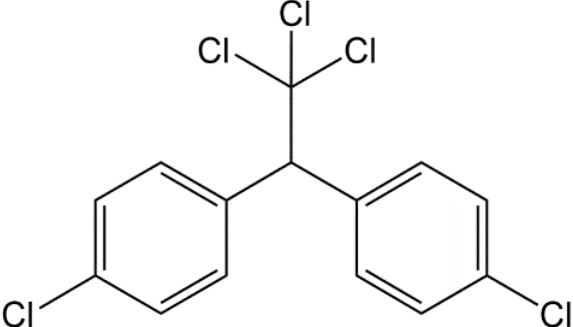
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3.4.1. Question 1

Explain the term hydrophobicity and mention two major properties that affect hydrophobicity of chemicals.

3.4.1. Question 2

What is the definition of K_{ow} . Rank the following chemicals from the Table below from low to high K_{ow} . 1. Pentachlorobenzene, 2. Monochlorobenzene, 3. Monochloroaniline, 4. DDT.

1. Pentachlorobenzene	
2. Monochlorobenzene	
3. Monochloroaniline	
4. DDT	

3.4.1. Question 3

Rank the chemicals in the Table according to their volatility as pure compounds and their solubility in water and volatility from water.

3.4.1. Question 4

Which two basic properties determine the volatility of a chemical from water to air.

3.4.1. Question 5

Calculate the percentage ionized for 2,3,4-trichlorophenol ($pK_a = 4.6$) at pH 3, 5, 7 and 9.

3.4.2. Sorption

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Learning objectives:

You should be able to:

- understand why information on sorption is important for risk assessment
- give examples that illustrate the importance of sorption for risk assessment
- understand the concept of sorption isotherms
- be familiar with different sorption isotherms (linear, Freundlich, Langmuir).

Keywords: Sorption isotherm, absorption and adsorption, organic matter, Freundlich model, Langmuir model, organic carbon content

Introduction

Sorption processes have a major influence on the fate of chemicals in the environment (Box 1). In general, sorption is defined as the binding of a dissolved or gaseous chemical (the sorbate) to a solid phase (the sorbent) and this may involve different processes, including:

(i) binding of dissolved chemicals from water to sediments and soils

and (ii) binding of gaseous phase chemicals from air to soils, plants, and trees.

Information about sorption is relevant because of a number of reasons:

- sorption controls the actual fate and thereby the risk of (many) organic and inorganic contaminants in the environment,
- sorbed chemicals cannot evaporate, are not available for (photo)chemical or microbial breakdown, are not as easily transported as dissolved/vapor phase chemicals, and are not available for uptake by organisms,
- sorption also plays an important role in toxicity tests, affecting exposure concentrations.

Box 1.

The Biesbosch is a wetland area in the Netherlands, an area in between the Rivers Rhine and Meuse and estuaries that are connected to the North Sea. The water flow is relatively low and as a consequence there is a strong sedimentation of particles from the water to the sediment. Chemicals present in the water strongly sorb to these particles, which in the past were polluted with hydrophobic organic contaminants such as dioxins and PCBs. The concentrations of these organic compounds in sediment are still relatively high because they are highly persistent. The reason for this persistence of these compounds is that these sorbed compounds are not easily available for degradation by bacteria. Also, the concentrations in organisms that live close to or in the sediment are high. These concentrations are so high that fishing on eel, for example, is not allowed in the area. This example shows the importance of sorption processes on fate, but also on effects in the environment.

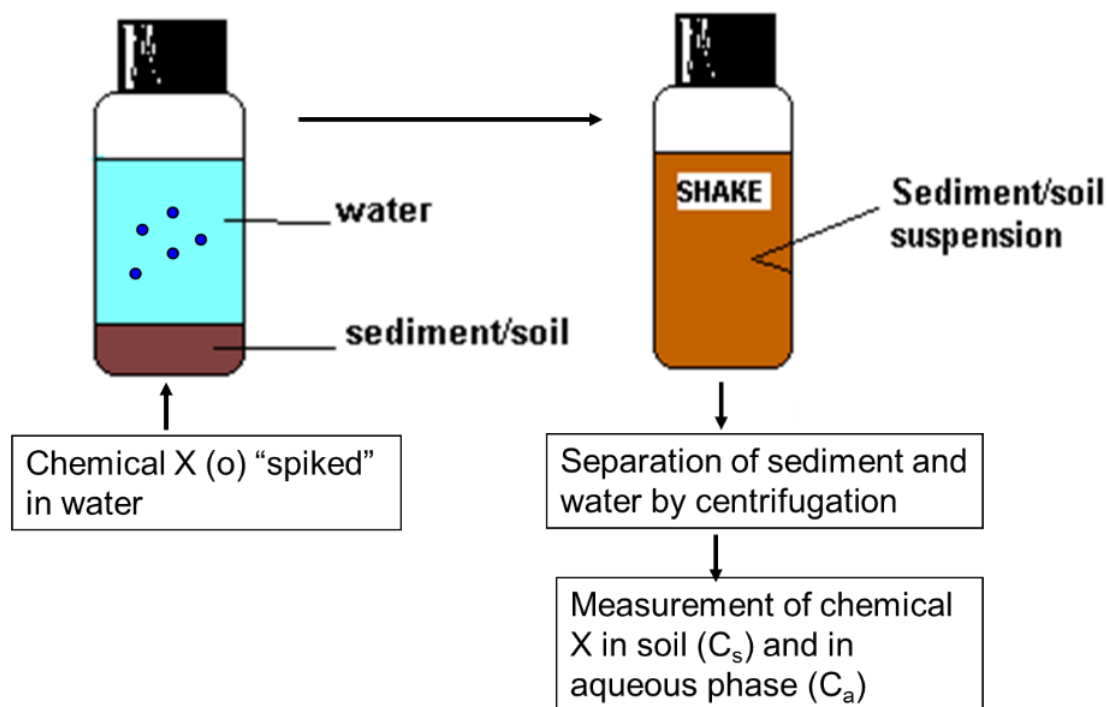


Figure 1. Measurement of sorption coefficients.

Measurement of sorption is a simple procedure. A chemical X is spiked (added) to the aqueous phase in the presence of a certain amount of the solid phase (sediment or soil). The chemical sorbs to the solid phase and when the system is in equilibrium, the concentrations in the sediment (C_s) and in the aqueous phase (C_a) are measured. The solid phase is collected via centrifugation or filtration.

The sorption coefficient K_p (equation 1 and box 2) gives information about the degree of sorption of a chemical to sediment and is defined as:

$$K_p = \frac{C_s}{C_a} \quad (1)$$

Box 2:

The concentration of a chemical X in sediment (C_s) is 30 mg/kg and the concentration in the aqueous phase (C_a) is 0.1 mg/L.

The sorption coefficient $K_p = C_s / C_a = 30 \text{ mg/kg} / 0.1 \text{ mg/L} = 300 \text{ L/kg}$

Note the units of a sorption coefficient: L/kg

In the environmental risk assessment of chemicals, it is very useful to understand the fraction of the total amount of chemical (A_{total}) in a system that is sorbed (f_{sorbed}) or dissolved ($f_{\text{dissolved}}$) (e.g. due to an accidental spill in a river):

$f_{\text{dissolved}} = A_{\text{dissolved}} / A_{\text{total}}$, and thus $f_{\text{sorbed}} = 1 - f_{\text{dissolved}}$

This is related to the sorption coefficients of X and the volume of the solvent and the volume of the sorbent material. The equation derived for calculating $f_{\text{dissolved}}$ is based on the mass balance of chemical A, which relates the concentration of X (C) to the amount of X (A) in each volume (V):

$C = A / V$, and thus $A = C \cdot V$

which for a system of water and sediment (air not included for simplification) relates to:

$A_{\text{total}} = A_{\text{dissolved}} + A_{\text{sorbed}} = C_{\text{water}} \cdot V_{\text{water}} + C_{\text{sediment}} \cdot V_{\text{sediment}} = C_{\text{water}} \cdot V_{\text{water}} + (K_p \cdot C_{\text{water}}) \cdot V_{\text{sediment}}$

$f_{\text{dissolved}} = A_{\text{dissolved}} / A_{\text{total}} = C_{\text{water}} \cdot V_{\text{water}} / (C_{\text{water}} \cdot V_{\text{water}} + K_p \cdot C_{\text{water}} \cdot V_{\text{sediment}})$

This way of separating out C_{sediment} from the equation using K_p can result, after rearranging (by dividing both parts of the ratio by $C_{\text{water}} \cdot V_{\text{water}}$) to the following simplified equation:

$f_{\text{dissolved}} = 1 / (1 + K_p \cdot (V_{\text{sediment}} / V_{\text{water}}))$

in this equation, 'sediment' can be replaced by any sorbent, as long as the appropriate sorption coefficient is used.

Let's try to calculate with chemical X from above, in a wet sediment, where 1L wet sediment contains ~80% water and 20% dry solids. The dissolved fraction of X with $K_p = 300 \text{ kg/L}$, is only 0.013 in this example. Thus, with 1.3% of X actually dissolved, this indicates that 98.7% of X is sorbed to the sediment.

Sorption processes

There are two major sorption processes (see Figure 2):

- Absorption - partitioning ("dissolution") of a chemical into a 3-D sorbent matrix. The concentration in the sorbing phase is homogeneous.
- Adsorption - binding of a chemical to a 2-D sorbent surface. Because the number of sorption sites on a surface is limited, sorption levels off at high concentrations in the aqueous phase.

A sorption isotherm gives the relation between the concentration in a sorbent (sediment) and the concentration in the aqueous phase and the isotherm is important in identifying a sorption process.

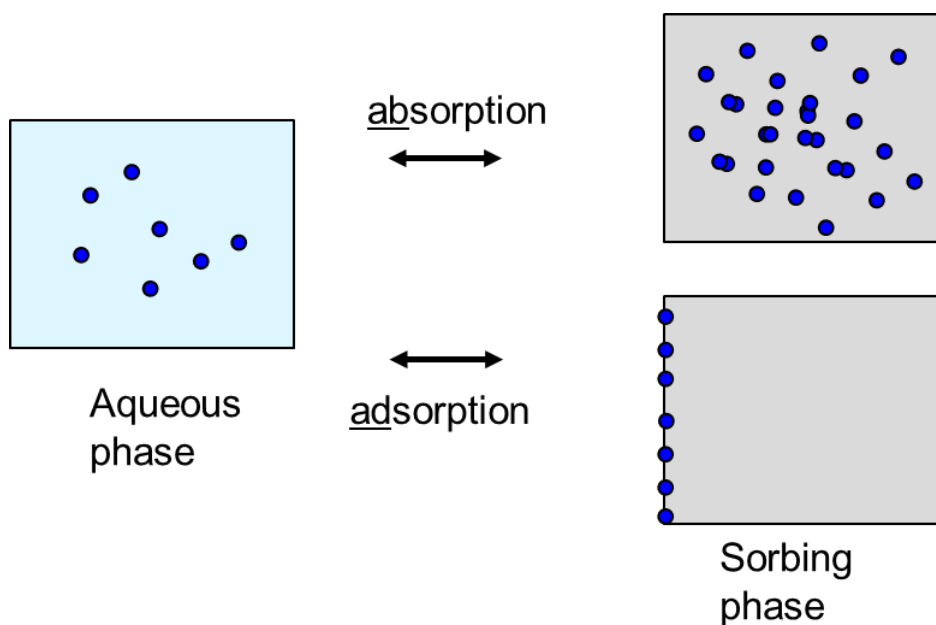


Figure 2. Two sorption processes: absorption and adsorption.

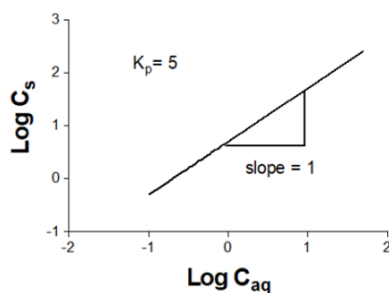
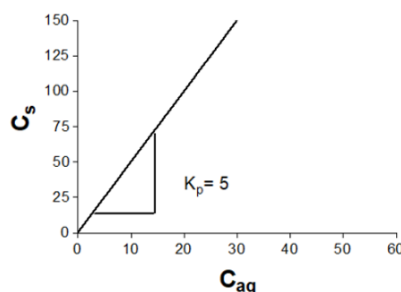
Absorption of a chemical is similar to its partitioning between two phases and comparable to its partitioning between two solvents. Distribution of a chemical between octanol and water is a well-known example of a partitioning process (see Section 3.4.1 on [Relevant chemical properties](#) for more detailed information on octanol-water partitioning). The isotherm for an absorption process is linear (Figure 3A) and the slope of the y-x plot is the sorption coefficient K_p .

A. Linear

K_p is the sorption coefficient

$$K_p = \frac{C_s}{C_{aq}}$$

$$\text{Log } C_s = \text{Log } (C_{aq}) + \text{Log } (K_p)$$

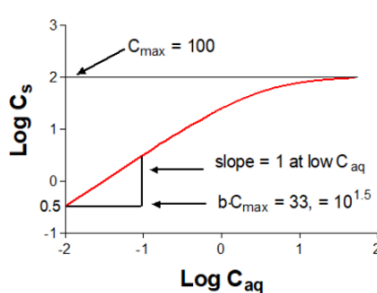
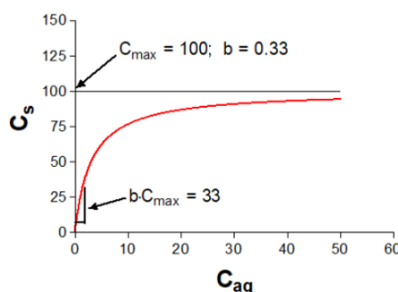


B. Langmuir

b is a constant related to the binding energy

C_{max} is the maximum sorption capacity

$$C_s = \frac{b \cdot C_{max} \cdot C_{aq}}{1 + b \cdot C_{max}}$$



C. Freundlich

K_F is the unit-dependent Freundlich coefficient

n is the Freundlich exponent

$$C_s = K_F \cdot C_{aq}^n$$

$$\text{Log } C_s = n \cdot \text{Log } (C_{aq}) + \text{Log } (K_F)$$

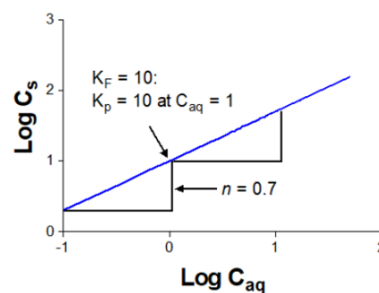
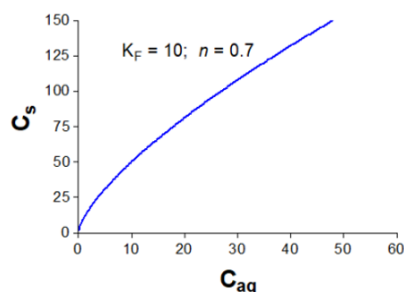


Figure 3. Sorption isotherms for absorption: linear model (3A), and for adsorption: Langmuir model (3B) or Freundlich model (3C).

In an adsorption process, where the sorbing phase is a surface with a limited number of sorption sites, the sorption isotherm is non-linear and may reach a maximum concentration that is adsorbed when all sites are occupied. A mechanistic model for adsorption is the Langmuir model. This model describes adsorption of molecules to homogeneous surfaces with equal adsorption energies, represented by the adsorption site energy term (b) and a limited number of sorption sites (C_{max}) that can become saturated (Figure 3B). The Langmuir adsorption coefficient (K_{ad}) is equal to the product ($b \cdot C_{max}$) at relatively low aqueous concentrations, where the product ($b \cdot C_{aq}$) $\ll 1$ (note that the denominator term will then be ~ 1). Indeed, the isotherm curve on a double log scale plot shows a slope of 1 at such low concentrations, indicating linearity.

Another mathematical approach to describe non-linear sorption is the Freundlich isotherm (Figure 3C), where K_F is the Freundlich sorption constant and n is the Freundlich exponent describing the sorption process non-linearity. Using logarithmic values for aqueous and sorbed concentrations, the Freundlich isotherm can be rewritten as:

$$\text{Log } C_s = n \cdot \text{log } C_{aq} + \text{log } K_F \text{ (eq. 2)}$$

This conveniently yields a linear relationship (just as $y = a \cdot x + b$) between $\text{log } C_s$ and $\text{log } C_{aq}$, with a slope equal to n and the abscissa (crossing point with the Y-axis) equal to $\text{log } K_F$. This allows for easy fitting of linear trend lines through experimental data sets. When $n = 1$, the isotherm is linear, and equals the one for absorption. In case of saturation of the sorption sites on the solid phase, $1/n$ will be smaller than 1. The Freundlich isotherm can, however, also yield a $1/n$ value > 1 ; this may occur for example if the chemical that is sorbed itself forms a layer that serves as a new sorbing phase and examples are described for surfactants.

Sorption phases

Soils and sediments may show large variations in composition and particle size distribution. The major components of soils and sediments are:

Sand	63 - 2 mm
Silt	2 - 63 μm
Clay	<2 μm
Organic matter	includes e.g. detritus, humic acids, especially associated with the clay and silt fractions
CaCO ₃	

Figure 4 gives a schematic picture of a sediment or soil particle. In addition to the presence of clay minerals and (soil or sediment) organic matter (SOM), sediment and soil may contain soot particles (a combustion residue).

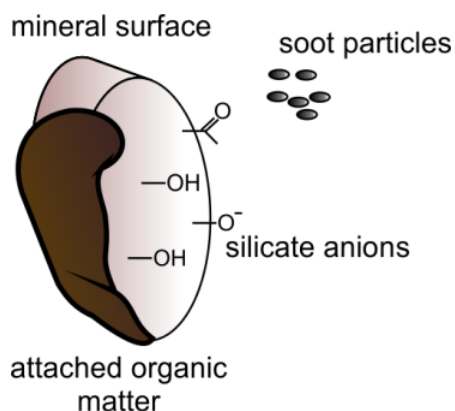


Figure 4. Structure of a soil or sediment particle showing the major components: organic matter and clay mineral and soot. Modified from Schwarzenbach et al. (2003) by Steven Droge.

Organic matter is formed upon decomposition of plant material and dead animal or microbial tissues. Upon decomposition of plant material, the first organic groups to be released are phenolic acids, some of which have a high affinity for complexation of metals. One example is salicylic acid (o-hydroxybenzoic acid), which occurs in high concentrations in leaves of willows, poplar and other deciduous trees. Further decomposition of plant material may result in the formation of humic acids, fulvic acids and humin. Humic and fulvic acids contain a series of functional groups, such as carboxyl- (COOH), carbonyl- (=C=O), phenolic hydroxyl- (-OH), methoxy- (-OCH₃), amino- (-NH₂), imino (=NH) and sulfhydryl (-SH) groups (see for more details the section on [Soil](#)).

Hydrophobic organic chemicals mainly sorb to organic matter. Because organic matter has the characteristics of a solvent, the sorption is clearly an absorption process and the sorption isotherm is linear. Because binding is mainly to organic matter, the sorption coefficient (K_p) depends on the fraction of organic matter (f_{om}) or the fraction of organic carbon (f_{oc}) present in the soil or sediment. Please note that as a rule of thumb, organic matter contains 58% organic carbon ($f_{oc} = 0.58 \cdot f_{om}$). Figure 5A shows the increase in sorption coefficient with increasing fraction organic carbon in soils and sediments. In order to arrive at a more intrinsic parameter, sorption coefficients are often normalized to the fraction organic matter (K_{om}) or organic carbon (K_{oc}). These K_{oc} or K_{om} values are less dependent of the sediment or soil type (Figure 5B).

$$K_{om} = \frac{K_p}{f_{om}} \quad (3)$$

$$K_{oc} = \frac{K_p}{f_{oc}} \quad (4)$$

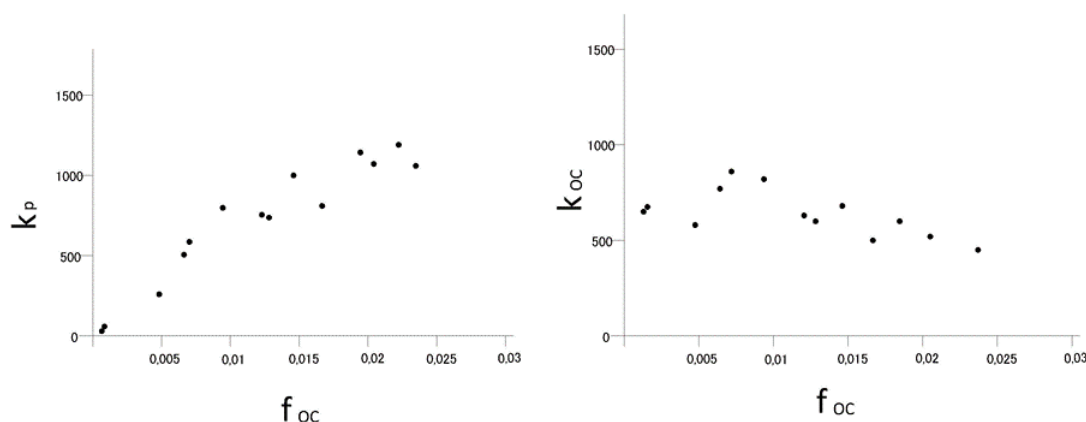


Figure 5. The relationship between the sorption coefficient (K_p) (left) and the organic carbon normalized sorption coefficient (K_{oc}) (right) and the fraction organic carbon (f_{oc}). Data from Means et al. (1980). Drawn by Wilma Ijzerman.

Hydrophobic chemicals can have a very high affinity to soot particles relative to the affinity to SOM. If a sediment contains soot, K_p values are often higher than predicted based on the fraction organic carbon in the organic matter (Jonker and Koelmans, 2002).

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- Jonker, M.T.O., Koelmans, A.A. (2002). Sorption of polycyclic aromatic hydrocarbons and polychlorinated biphenyls to soot and soot-like materials in the aqueous environment mechanistic considerations. Environmental Science and Technology 36, 3725-3734.

Suggested reading

- van Leeuwen, C.J., Vermeire, T.G. (Eds.) (2007). Risk Assessment of Chemicals: An Introduction. Springer, Dordrecht, The Netherlands. Chapter 3 and 9.
- Schwarzenbach, R.P., Gschwend, P.M., Imboden, D.M. (2003). Environmental Organic Chemistry. Wiley, New York, NY, USA. chapters 9, 11. Detailed information about sorption processes and sorption mechanisms.

3.4.2. Question 1

What is a sorption isotherm and what is the difference between absorption and adsorption?

3.4.2. Question 2

Why is the sorption isotherm to clay non-linear?

3.4.2. Question 3

What are the main sorption phases in sediment or soil?

3.4.3. QSPRs

Author: Joop Hermens

Reviewer: Steven Droge, Monika Nendza

Learning objectives:

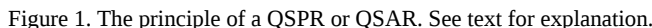
You should be able to:

- indicate which properties of chemicals are applied in a QSPR
- list different techniques to derive a QSPR
- indicate which interactions may occur between molecules.

Risk assessment needs input data for fate and effect parameters. These data are not available for many of the existing chemicals and predictions via estimation models will provide a good alternative to actual testing. Examples of estimation models are Quantitative Structure-Property Relationships (QSPRs) and Quantitative Structure-Activity Relationships (QSARs). The term "activity" is often used in relation to models for toxicity, while "property" usually refers to physical-chemical properties or fate parameters.

The elements in a QSPR or QSAR are shown in Figure 1 and include:

- the parameter for which the estimation model has been developed: the Y-variable (upper right),
- the properties of the chemical or chemical parameter: the X-variable (upper left),
- the model itself (center), and
- the prediction of a fate or effect parameter from the chemical properties (bottom).



Estimation models have been developed for many endpoints such as sorption to sediment, humic acids, lipids and proteins, chemical degradation, biodegradation, bioconcentration and ecotoxic effects.

An overview of the chemical parameters (the X-variable) used in estimation models is given in Table 1. Chemical properties are divided in three categories: (i) parameters related to hydrophobicity, (ii) parameters related to charge and charge distribution in a molecule and (iii) parameters related to the size or volume of a molecule. Hydrophobicity is discussed in more detail in the section on [Relevant chemical properties](#).

Other QSPR approaches use large number of parameters derived from chemical graphs. The [CODESSA](#) Pro software, for example, generates molecular (494) and fragment (944) descriptors, classified as (i) constitutional, (ii) topological, (iii) geometrical, (iv) charge related, and (v) quantum chemical (Katritzky et al. 2009). Some models are based on structural fragment in a molecule. The polyparameter linear free energy relationships (pp-LFER) use parameters that represent interactions between molecules (see under pp-LFER).

Table 1. Examples of parameters related to hydrophobicity and electronic and steric parameters (the X variable).

<i>Hydrophobic parameters</i>
Aqueous solubility
Octanol-water partition coefficient (K_{ow})
Hydrophobic fragment constant π
<i>Electronic parameters</i>
Atomic charges (q)
Dipole moment
Hydrogen bond acidity (H bond-donating)
Hydrogen bond basicity (H bond-accepting)
Hammett constant σ
<i>Steric parameters</i>
Total Surface Area (TSA)
Total Molecular Volume (TMV)
Taft constant for steric effects (E_s)

The model

Most models are based on correlations between Y and X. Such a relationship is derived for a "training set" that consists of a limited number of carefully selected chemicals. The validity of such a model should be tested by applying it to a "**validation set**", i.e. a set of compounds for which experimental data can be compared with the predictions. Different techniques can be used to develop an empirical model, such as:

- graphical presentations,
- linear or non-linear equations between Y and X,
- linear or non-linear equations based on different properties (Y versus X_1 , X_2 , etc.),
- multivariate techniques such as Principal Component Analysis (PCA) and Partial Least Square Analysis (PLS).

Linear equations take the form:

$$Y(i) = a_1X_1(i) + a_2X_2(i) + a_3X_3(i) + \dots + b \quad (1)$$

where $Y(i)$ is the value of the dependent parameter of chemical i (for example sorption coefficients); X_1 - $X_3(i)$ are values for the independent parameters (the chemical properties) of chemical i ; a_1 - a_3 are regression coefficients (usually 95% confidence limits are given); b is the intercept of the linear equation. The quality of the equation is presented via the correlation coefficient (r) and the standard error of estimate (s). The closer r is to 1.0, the better the fit of the relationship is. More information about the statistical quality of models can be found under "limitation of QSPR".

The classical approach in QSAR and QSPR studies is the Hansch approach that was developed in the 1960s. The Hansch equation (Hansch et al., 1963) describes the influence of substituents on the biological activity in a series of parent compounds with a certain substituent (equation 2). Substituents are for example a certain atom or chemical group (Cl, F, B, OH, NH₂) attached to a parent aromatic ring structure.

$$\log 1/C = c \pi + c' \sigma + c'' E_s + c''' \quad (2)$$

in which:

C is the molar concentration of a chemical with a particular effect,

π is a substituent constant for hydrophobic effects,

σ is a substituent constant for electronic effects, and

E_s is a substituent constant for steric effects.

c are constants that are obtained by fitting experimental data

For example, the hydrophobic substituent constant is based on K_{ow} and is defined as is defined as:

$$\pi(X) = \log K_{ow}(RX) - \log K_{ow}(RH) \quad (3)$$

where RX and RH are the substituted and unsubstituted parent compound, respectively.

The Hammett and Taft constants are derived in a similar way.

Multivariate techniques may be very useful to develop structure-activity relationships, in particular in cases where a large number of chemical parameters is involved. Principal Component Analysis (PCA) can be applied to reduce the number of variables into a few principal components. The next step is to find a relationship between Y and X via, for example, Partial Least Square (PLS) analysis. The advantage of PCA and PLS is that it can deal with a large number of chemical descriptors and that it can also cope with collinear (correlated) properties. More information on these multivariate techniques and examples in the field of environmental science are given by Eriksson et al. (1995).

Poly-parameter Linear Free Energy Relationship (pp-LFER)

The pp-LFER approach has a strong mechanistic basis because it includes the different types of interactions between molecules (Goss and Schwarzenbach, 2001). For example, the sorption coefficient of a chemical from an aqueous phase to soil or to phospholipids (the sorbent) depends on the interaction of a chemical with water and the interaction with the sorbent phase. One of the driving forces behind sorption is the hydrophobicity. Hydrophobicity means fear (phobia) for water (hydro). A hydrophobic chemical prefers to "escape from the aqueous phase" or in other words "it does not like to dissolve in water". Water molecules are tightly bound to each other via hydrogen bonds. For a chemical to dissolve, a cavity should be formed in the aqueous phase (Figure 2) and this will cost energy. More hydrophobic compounds will often have a stronger sorption (see more information in the section on [Relevant chemical properties](#)).

Hydrophobicity mainly depends on two molecular properties:

- Molecular size
- Polarity / ability to interact with water molecules, for example via hydrogen bonding

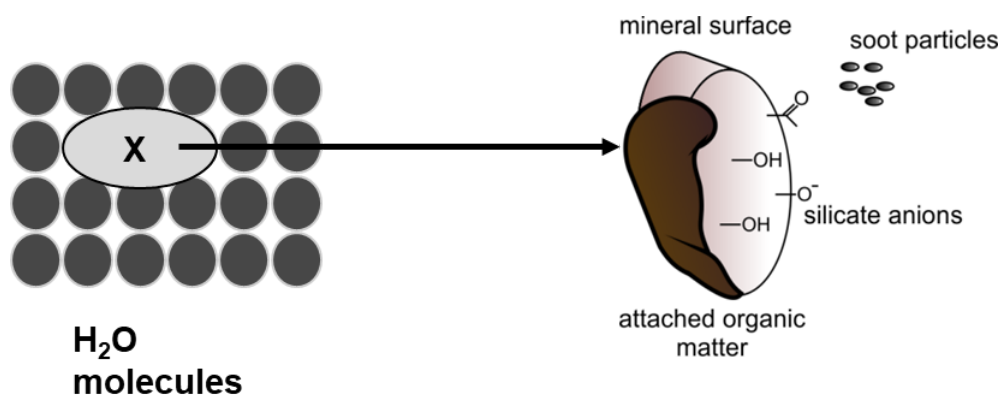


Figure 2. The formation of a cavity in water for chemical X and the interaction with another phase (here, a soil particle).

In the interaction with the sorbent (soil, membrane lipids, storage lipids, humic acids), major interactions are van der Waals interactions and hydrogen bonding (Table 2). Van der Waals interactions are attractive and occur between all kind of molecules and the strength depends on the contact area. Therefore, the strength of van der Waals interactions are related to the size of a molecule. A hydrogen bond is an electrostatic attraction between a hydrogen (H) and another electronegative atom bearing a lone pair of electrons. The hydrogen atom is usually covalently bound to a more electronegative atom (N, O, F). Table 2 lists the interactions with examples of chemical structures.

A pp-LFER is a linear equation developed to model partition or sorption coefficients (K) using parameters that represent the interactions (Abraham, 1993). The model equation is based on five descriptors:

$$\log K = c + e \cdot E + s \cdot S + a \cdot A + b \cdot B + v \cdot V \quad (2)$$

with:

E	excess molar refraction
S	dipolarity/polarizability parameter
A	solute H-bond acidity (H-bond donor)
B	solute H-bond basicity (H-bond acceptor)
V	molar volume

The partition or sorption coefficient K may be expressed as the sum of five interaction terms, with the uppercase parameters describing compound specific properties. E depends on the valence electronic structure, S represents polarity and polarizability, A is the hydrogen bond (HB) donor strength (HB acidity), B the HB acceptor strength (HB basicity), V is the so-called characteristic volume related to the molecule size, and c is a constant. The lower-case parameters express the corresponding properties of the respective two-phase system, and can thus be taken as the relative importance of the compound properties for the particular partitioning or sorption process. In this introductory section, we only focus on the volume factor (V) and the two hydrogen bond parameters (A and B).

Numerous pp-LFERs have been developed for all kinds of environmental processes and an overview is given by Endo and Goss (2014).

Table 2. Types of interactions between molecules and the phase to which they sorb with examples of chemicals (Goss and Schwarzenbach, 2003).

Compound ^{a)}	Interactions	Examples
Apolar	only van der Waals	alkanes, chlorobenzenes, PCBs
Monopolar	van der Waals + H-acceptor (e-donor)	alkenes, alkynes, alkylaromatic compounds ethers, ketones, esters, aldehydes
Monopolar	van der Waals + H-donor (e-acceptor)	CHCl ₃ , CH ₂ Cl ₂
Bipolar	van der Waals + H-donor + H-acceptor	R-NH ₂ , R ₂ -NH, R-COOH, R-OH

^{a)} Apolar: no polar group present; mono/dipolar: one or two polar groups present in a molecule

Examples of QSPR for bioconcentration to fish

K_{OW} based model

Predictive models for bioconcentration have a long history. The octanol-water partition coefficient (K_{OW}) is a good measure for hydrophobicity and bioconcentration factors (BCF's) are often correlated to K_{OW} (see more information in section on [Bioaccumulation](#)). The success of these K_{OW} based models was explained by the resemblance of partitioning in octanol and bulk lipid in the organisms, at least for neutral hydrophobic compounds. A well-known example of a linear QSAR model for the log BCF (Y variable) based on the log K_{OW} (X variable) (Veith et al., 1979):

$$\log \text{BCF} = 0.85 \log K_{OW} - 0.70 \quad (5)$$

Figure 3 gives a classical example of such a correlation for BCF to guppy of a series of chlorinated benzenes and polychlorinated biphenyls. When lipophilic chemicals are metabolised, the relation shown in Figure 3 is no longer valid and BCF will be lower than

predicted based on K_{OW} . Another deviation of this BCF- K_{OW} relation can be found for highly lipophilic chemicals with $\log K_{OW} > 7$. For such chemicals, BCF often decrease again with increasing K_{OW} (see Figure 3). The apparent BCF curve with K_{OW} as the X variable tends to follow a nonlinear curve with an optimum at $\log K_{OW}$ 7-8. This phenomenon may be explained from molecular size: molecules of chemicals like decachlorobiphenyl may be so large that they have difficulties in passing membranes. A more likely explanation, however, is that for highly lipophilic chemicals aqueous concentrations may be overestimated. It is not easy to separate chemicals bound to particles from the aqueous phase (see box 1 in the section on [Sorption](#)) and this may lead to measured concentrations that are higher than the bioavailable (freely dissolved) concentration (Jonker and van der Heijden 2007; Kraaij et al. 2003). For example, at a dissolved organic carbon (DOC) concentration of 1 mg-DOC/L, a chemical with a $\log K_{OC}$ of 7 will be 90% bound to particles, and this bound fraction is not part of the dissolved concentration that equilibrates with the (fish) tissue. This shows that these models are also interesting because they may show trends in the data that may lead to a better understanding of processes.

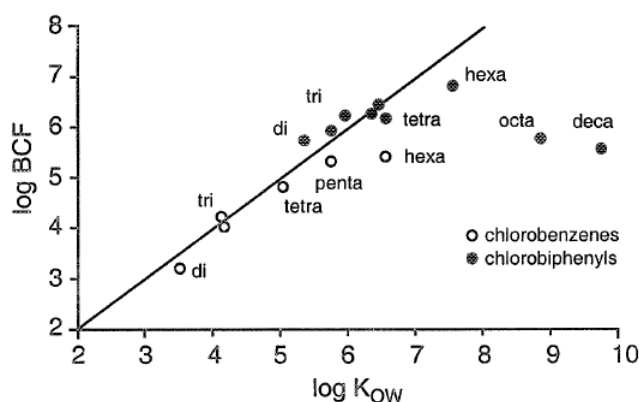
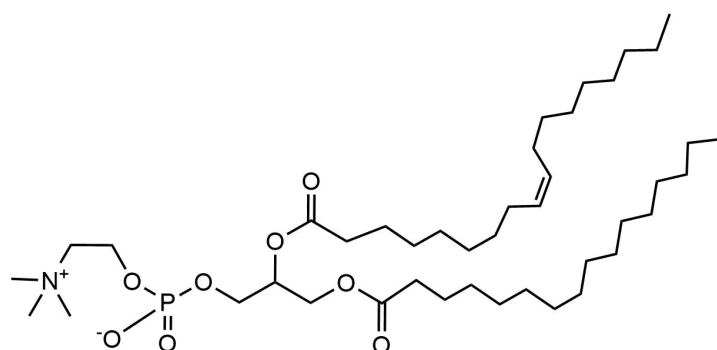


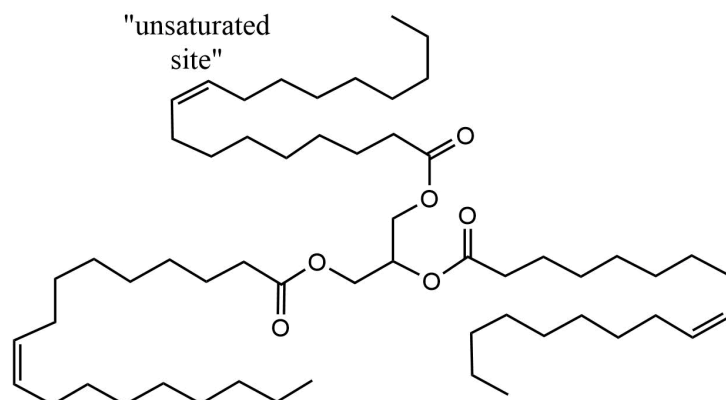
Figure 3. The relationship between bioconcentration factors in guppy and the octanol-water partition coefficients with data from (Bruggeman et al., 1984; Könemann and Leeuwen, 1980).

Examples of QSPR for sorption to lipids

K_{OW} based models are successful because octanol probably has similar properties than fish lipids. There are several types of lipids and membrane lipids have different properties and structure than for example storage lipids (see Figure 4, and more details in the section on [Biota](#)). More refined BCF models include separation of storage and membrane lipids and also proteins as separate sorptive phases (Armitage et al. 2013). pp-LFER is a very suitable approach to model these sorption or partitioning processes and results for two large data sets are presented in Table 3. The coefficients e , s , b and v are rather similar. The only parameter that is different in these two models is coefficient a , which represents the contribution of hydrogen bond (HB) donating properties (A) of chemicals in the data set. This effect makes sense because the phosphate group in the phospholipid structure has strong HB accepting properties. This example shows the strength of the pp-LFER approach because it closely represents the mechanism of interactions.



1-palmitoyl-2-oleoylphosphatidylcholine (POPC),
a key phospholipid in cell membranes



Triglyceride, storage fat

Figure 4. Structure of a phospholipid and a triglyceride. Note the similar glycerol part in both lipids.

Table 3. LFERs for storage lipid-water partition coefficients (K_{SL-W}) and membrane lipid-water partition coefficients (K_{ML-W} (liposome)). Listed are the parameters (and standard error), the number of compounds with which the LFER was calibrated (n), the correlation coefficient (r^2), and the standard error of estimate (SE). $\log K = c + eE + sS + aA + bB + vV$.

Parameter	c	e	s	a	b	v	n	r^2	SE
K_{SL-W}	-0.07 (0.07)	0.70 (0.06)	-1.08 (0.08)	-1.72 (0.13)	-4.14 (0.09)	4.11 (0.06)	247	0.997	0.29
From (Geisler et al. 2012)									
K_{ML-W} (liposome)	0.26 (0.08)	0.85 (0.05)	-0.75 (0.08)	0.29 (0.09)	-3.84 (0.10)	3.35 (0.09)	131	0.979	0.28
From (Endo et al. 2011)									

K_{SL-W} : storage lipid partition coefficients are mean values for different types of oil. Raw data and pp-LFER (for 37 °C) reported in (Geisler et al. 2012).

K_{ML-W} (liposome): data from liposomes made up of phosphatidylcholine (PC) or PC mixed with other membrane lipids. Raw data (20-40 °C) and pp-LFER reported in (Endo et al. 2011).

Examples of QSPR for sorption to soil

Numerous QSPRs are available for soil sorption (see section on [Sorption](#)). Also the organic carbon normalized sorption coefficient (K_{oc}) is linearly related to the octanol-water partition coefficient (see Figure 5).

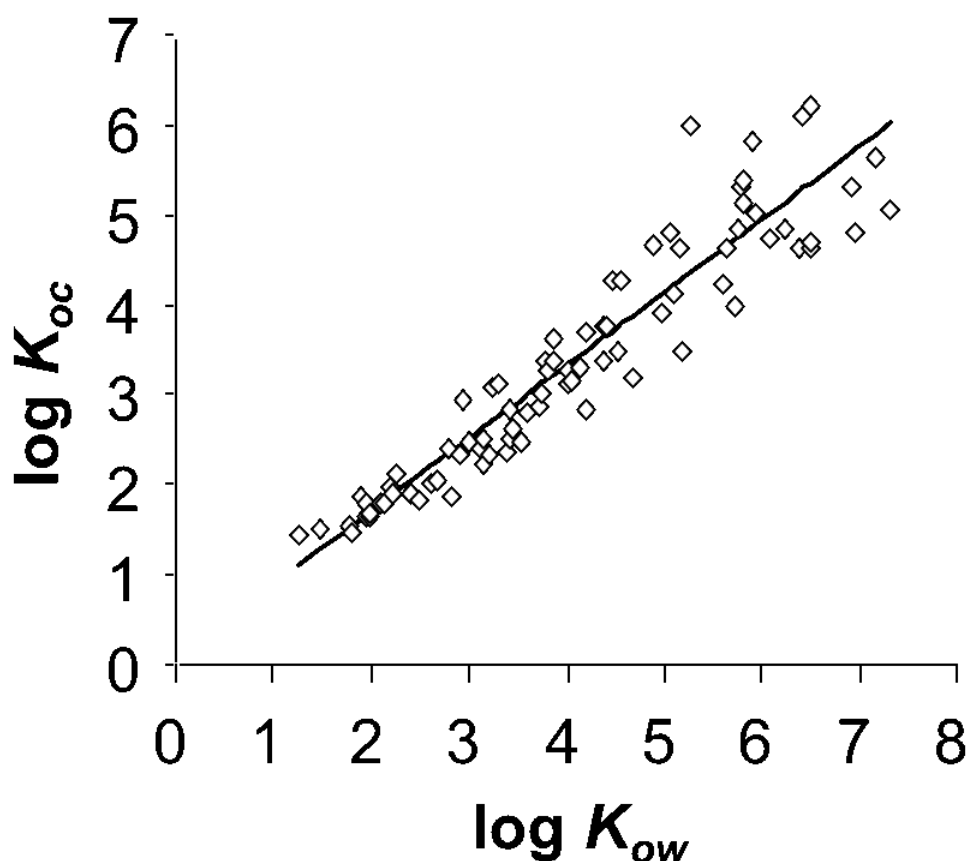


Figure 5. Correlation between the organic carbon normalized sorption coefficient to soil (K_{oc}) and the octanol-water partition coefficient (K_{ow}) for data from (Sabljić et al. 1995).

The model in Figure 5 is only valid for neutral, non-polar hydrophobic organic chemicals such as chlorinated aromatic compounds, polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyl (PCBs) and chlorinated insecticides or, in general, compounds that only contain carbon, hydrogen and halogen atoms. It does not apply to polar and ionized organic compounds nor to metals. For polar chemicals, also other interactions may influence sorption and a pp-LFER approach would also be useful.

The sorption of ionic chemicals is more complex. For the sorption of cationic organic compounds, clay minerals can be an equally important sorption phase as organic matter because of their negative surface charge and large surface area. The sorption of organic cations is mainly an adsorption process that reaches a maximum at the cation exchange capacity (CEC) of a particle (see section on [Soil](#)). Also models for the prediction of sorption of cationic compounds are more complicated and first attempts have been made recently (Droge and Goss, 2013). Major sorption mechanism for anionic chemicals is sorption into organic matter. The sorption coefficient of anionic chemicals is substantially lower than for the neutral form of the chemical, roughly a factor 10-100 for K_{OC} (Tülp et al. 2009). In case of weakly dissociating chemicals such as carboxylic acids, the sorption coefficient can often be estimated from the sorption coefficient of the non-ionic form and the fraction of the chemical that is present in the non-ionized form (see section on [Relevant chemical properties](#)).

Reliability and limitations of QSPR

Predictive models have limitations and it is important to know these limitations. There is not one single model that can predict a parameter for all chemicals. Each model will have a domain of applicability and it is important to apply a model only to a chemical within that domain. Therefore, guidance has to be defined on how to select a specific model. It is also important to realize that in many computer programs (such as fate modeling programs), estimates and predictions are implicitly incorporated in these programs.

Another aspect is the reliability of the prediction. The model itself can show a good fit (high r^2) for the training set (the chemicals used to develop the model), but the actual reliability should be tested with a separate set of chemicals (the validation set) and a number of statistical procedures can be applied to test the accuracy and predictive power of the model. The OECD has developed a set of rules that should be applied in the validation of QSPR and QSAR models.

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3.4.3. Question 1

What is a QSPR and why is it useful?

3.4.3. Question 2

Which techniques are applied to derive a QSPR.

3.4.3. Question 3

Which chemical parameters are applied in a QSPR?

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