

## Environmental Chemistry

# DYNAMICS OF HYDROPHOBIC ORGANIC CHEMICAL BIOCONCENTRATION IN FISH

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**Abstract**—A model is presented describing the kinetics of uptake and release of nonmetabolizing organic chemicals by fish from water. The model contains three parameters: a bioconcentration factor which is specific to the chemical (and can be characterized by the octanol/water partition coefficient and fish lipid content), a water-phase resistance term and a lipid-phase resistance term which are specific to the fish. These parameters can be estimated from uptake-clearance experiments. Part of the water-phase resistance term can be attributed to gill ventilation rate as estimated from gill uptake efficiencies and part is an "internal" resistance. Procedures are suggested for scaling these parameters to different fish sizes. The dependence of these resistances, and uptake and clearance rate constants, on chemical hydrophobicity is discussed and quantified.

**Keywords**—Bioconcentration Fish Model Hydrophobicity Gill ventilation Octanol/water partition coefficient

## INTRODUCTION

It is generally accepted that the bioconcentration process in which hydrophobic organic compounds are absorbed by fish from water and accumulated in fat tissue is basically one of physical-chemical partitioning controlled by the relative affinities of the compound for the water and fat tissue. If metabolic transformation of the absorbed compound is insignificant a simple two-compartment (water-fish) model with first-order rate constants usually gives a satisfactory description of the kinetics [1]. The ratio of the concentrations in the fish and the water under steady-state conditions (i.e., the bioconcentration factor  $K_B$ ) reflects these relative affinities [2], and can be related to the 1-octanol/water partition coefficient,  $K_{ow}$  [3-5]. Elimination rate constants ( $k_2$ ) generally decrease with increasing  $K_{ow}$  [3,6-11] and correlating equations have been proposed. Uptake rate constants ( $k_1$ ), however, show a less clear dependence on  $K_{ow}$ . It has been reported that  $k_1$  can either increase [3], remain constant [9], decrease, or show a parabolic relationship [6,8,12,13] with increasing  $K_{ow}$ .

To make reliable predictions about the kinetics of the bioconcentration process it is necessary to clarify how uptake and release kinetics are controlled and to elucidate which parameters are in-

volved. For this purpose we develop a model which is an extension of one presented earlier by Mackay and Hughes [14] and is based on principles described by Yalkowsky [15,16]. The Mackay-Hughes model was derived entirely from elimination-rate data and no uptake-rate data were considered or tested. It has therefore not been demonstrated if or how the principles applicable to elimination apply to the uptake process.

Independently, Gobas et al. [17] derived similar equations relating bioconcentration kinetics to the process of passive diffusion of chemicals through biological barriers as described by Flynn and Yalkowsky [18]. It was shown that the behavior of both uptake and elimination rate constants with respect to hydrophobicity can be explained by diffusion through membranes and aqueous diffusion layers. A similar mechanism was proposed by McKim et al. [19] for gill uptake in rainbow trout.

The objective of this article is to determine and quantify the transport resistances controlling uptake and elimination of organic chemicals by fish from water and thus improve methods of predicting bioconcentration parameters. We do not consider uptake from food, nor do we treat metabolizing chemicals. This limits the scope of the model, but we believe that it is best to model the simplest situations first and then to introduce these complexities in later models which will then be more soundly based.

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## MODEL DERIVATION

Accurate representation of chemical dynamics in a fish requires a pharmacokinetic model in which differential equations are written describing chemical uptake, release, reaction, and accumulation in all significant tissues. Since there are insufficient data to justify such models, only a simple model can be justified at present at which accumulation is primarily attributed to a lipid compartment which is accessed through a water compartment, the latter having a negligible capacity for the chemical.

Deriving such equations can be done in terms of fugacity [20] but the final equations can be written and even derived in conventional concentration form. We thus develop the equations using fugacity but use them in concentration form. We use the SI units of meters, moles, seconds and Pascals in the derivation, but the final equations can be used in more traditional units.

Briefly, fugacity  $f$  is the "escaping tendency" from a phase; it is linearly related to concentration  $C$  through a fugacity capacity term  $Z$  (i.e.  $C = Zf$ ). Since two phases at equilibrium have equal fugacities, the partition coefficient  $K_{\text{H}}$  is  $C_{\text{H}}/C_{\text{L}}$  or  $Z_{\text{H}}/Z_{\text{L}}$ . Transport is expressed by a transport parameter  $D$ , the rate of being  $D(f_{\text{L}} - f_{\text{H}})$ .  $D$  can reflect passive diffusion as expressed by diffusivities or mass transfer coefficients of fluid flow (e.g. in gill ventilation or blood flow) as  $GZ$  where  $G$  ( $\text{m}^3/\text{s}$ ) is the volumetric fluid flow rate.

The simplest expression of fish-water exchange is given by Equation 1:

$$\text{d}C_{\text{L}}/\text{dt} = k_{\text{L}} C_{\text{W}} - k_{\text{L}} C_{\text{L}}, \quad (4)$$

$$\begin{aligned} C_{\text{L}}(t) &= C_{\text{W}} k_{\text{L}} / k_{\text{L}} (1 - \exp(-k_{\text{L}} t)) \\ &= C_{\text{W}} K_{\text{B}} (1 - \exp(-k_{\text{L}} t)) \end{aligned} \quad (5)$$

Fish concentrations and bioconcentration factors can be expressed on a whole-fish wet-weight basis (i.e.,  $C_{\text{L}}$  and  $C_{\text{F}}/C_{\text{W}}$  or  $K_{\text{B}}$ ) or on a lipid basis (i.e.,  $C_{\text{L}}$  and  $C_{\text{L}}/C_{\text{W}}$  or  $K_{\text{L}}$ ). If all accumulation is assumed to be in the lipid and the volumes are  $V_{\text{L}}$  and  $V_{\text{F}}$  then the lipid volume fraction  $L$  is  $V_{\text{L}}/V_{\text{F}}$  and  $C_{\text{L}}$  is  $C_{\text{L}}/L$ ,  $K_{\text{B}}/L$  or  $Z_{\text{L}}/Z_{\text{W}}$ ,  $K_{\text{L}}$  is  $Z_{\text{L}}/Z_{\text{W}}$  and  $Z_{\text{L}}$  is  $Z_{\text{F}}/L$ . Comparison of Equations 3 and 5 shows that  $k_{\text{L}}/k_{\text{L}}$  is equivalent to  $K_{\text{B}}$  or  $Z_{\text{L}}/Z_{\text{W}}$  or  $LZ_{\text{L}}/Z_{\text{W}}$ . The elimination rate constant  $k_{\text{L}}$  is equivalent to  $D_{\text{L}}/V_{\text{F}}Z_{\text{L}}$  or  $D_{\text{L}}/V_{\text{L}}Z_{\text{L}}$ . Thus in summary

$$k_{\text{L}} = D_{\text{L}}/V_{\text{F}}Z_{\text{L}} = D_{\text{L}}/V_{\text{F}}Z_{\text{F}} \quad (6)$$

$$k_{\text{L}} = k_{\text{L}} Z_{\text{L}}/Z_{\text{W}} = D_{\text{L}}/V_{\text{F}}Z_{\text{W}} = D_{\text{L}} L/V_{\text{L}}Z_{\text{W}} \quad (7)$$

Equilibrium is thus controlled entirely by  $Z_{\text{W}}$ ,  $Z_{\text{L}}$ , or  $Z_{\text{F}}$  but the kinetics are also controlled by the relative volumes of lipid and water in the fish and  $D_{\text{L}}$ .

To gain insight into the processes controlling the exchange of solute chemical between the water and the fish it is assumed that solute transport to, and within the fish takes place in a series of aqueous and lipid phases. Therefore all  $D$  values applying to transport processes in aqueous phases are in water. Subscripts 'W' refer to water, 'F' to fish, and 'L' to lipid in which all the chemical is assumed to partition.

Integration of this equation with a constant  $f_{\text{W}}$  and an initial  $f_{\text{L}}$  of zero gives

$$f_{\text{L}} = f_{\text{W}} [1 - \exp(-D_{\text{L}}/V_{\text{F}}V_{\text{L}}Z_{\text{L}})] \quad (2)$$

Since  $f_{\text{L}}$  is  $C_{\text{L}}/Z_{\text{L}}$  and  $f_{\text{W}}$  is  $C_{\text{W}}/Z_{\text{W}}$ , Equation 2 can be rewritten as

$$C_{\text{L}} = C_{\text{W}} (Z_{\text{L}}/Z_{\text{W}}) (1 - \exp[-D_{\text{L}}/V_{\text{F}}V_{\text{L}}Z_{\text{L}}]) \quad (3)$$

Equation 3 is equivalent to the solution of the traditional differential equation describing the uptake and release in fish

$$\text{d}C_{\text{L}}/\text{dt} = k_{\text{L}} C_{\text{W}} - k_{\text{L}} C_{\text{L}}, \quad (4)$$

$$1/D_{\text{L}} = 1/Q_{\text{W}} + 1/D_{\text{L}} = 1/Q_{\text{W}} Z_{\text{W}} + 1/Q_{\text{L}} Z_{\text{L}} \quad (8)$$

This assumes that water and lipid transport processes apply in series and that transport resistances across lipid/water interfaces are negligible. Substituting Equation 8 into Equation 6 and Equation 7 results in the following equations expressing the elimination and uptake rate constants in terms of  $D_{\text{W}}$  and  $D_{\text{L}}$ :

$$1/k_{\text{L}} = V_{\text{L}} (Z_{\text{L}}/Q_{\text{W}} Z_{\text{W}} + 1/Q_{\text{L}}) \quad (9)$$

and

$$1/k_{\text{L}} = (V_{\text{L}}/L)(1/Q_{\text{W}} + Z_{\text{W}}/Q_{\text{L}} Z_{\text{L}}) \quad (10)$$

Since there are few data for lipid/water partitioning (i.e.,  $Z_{\text{L}}$  values) octanol is used as a surrogate organic phase for fish lipids. We can thus rewrite Equations 9 and 10 for correlating purposes in terms of octanol, replacing  $Z_{\text{L}}$  by  $Z_{\text{O}}$  in which  $K_{\text{H}}$  is  $Z_{\text{O}}/Z_{\text{W}}$  (and essentially redefine  $Q_{\text{L}}$  and  $Q_{\text{W}}$ ) to give

$$1/k_{\text{L}} = V_{\text{L}} (K_{\text{H}}/Q_{\text{W}} + 1/Q_{\text{L}}) \quad (11)$$

$$1/k_{\text{L}} = V_{\text{L}} (1/Q_{\text{W}} + 1/Q_{\text{L}} K_{\text{H}})/L \quad (12)$$

The significance of the terms in Equations 11 and 12 is worthy of emphasis. The ratios  $V_{\text{L}}/Q_{\text{W}}$  and  $V_{\text{L}}/Q_{\text{L}}$  have dimensions of time. They can be viewed as the times of chemical transport to or from  $V_{\text{L}}$  m<sup>3</sup> of water on lipid. Since the water and lipid transport processes occur in series, these times are additive and the longer time controls. But, if cleaning a given quantity of chemical requires clearance or transport of  $V_{\text{L}}$  m<sup>3</sup> of lipid, it will require the clearance or transport of a much larger volume,  $K_{\text{H}} V_{\text{L}}$  m<sup>3</sup> of water, because the chemical concentration in the water is a factor of  $K_{\text{H}}$  lower. The clearance time for water must thus be multiplied by  $K_{\text{H}}$ , prior to addition to that of the lipid clearance time. The times or "resistances" in the water phase and in the lipid phase are thus respectively  $V_{\text{L}}/Q_{\text{W}}$  and  $V_{\text{L}}/Q_{\text{L}}$ , or  $V_{\text{F}}/Q_{\text{W}}$  and  $V_{\text{F}}/Q_{\text{L}}$ .

As  $K_{\text{H}}$  increases, the water concentration drops relative to the lipid phase; thus the total resistance or clearance time increases and the overall process rate becomes dominated by water-

phase processes. We amplify this point later in the discussion.

In the conventional uptake Equation 4, the uptake constant  $k_{\text{L}}$  is often viewed as being related to the water flow rate being brought into contact with the fish. Indeed, in the absence of a lipid resistance  $k_{\text{L}}$  equals  $Q_{\text{W}}/V_{\text{F}}$  and can be viewed as a water flow rate  $Q_{\text{W}}$  divided by the fish volume. This occurs for large  $K_{\text{H}}$ , water-phase-resistant chemicals.

### Gill uptake efficiency

The rate at which a chemical is absorbed from the water depends on the water solution flow rate through the gill compartment and the efficiency with which the chemical is extracted. The efficiency for uptake of chemicals from water,  $E$ , can be defined as the ratio of the flux of chemical into the fish (i.e.,  $D_{\text{F}}(f_{\text{W}} - f_{\text{L}})$ ) to the flux of chemical into the gill compartment (i.e.,  $D_{\text{V}}/f_{\text{W}}$ ). Namely

$$E = (D_{\text{F}}/D_{\text{V}}) (f_{\text{W}} - f_{\text{L}})/f_{\text{W}} \quad (13)$$

where  $D_{\text{F}}$  is the net transport parameter into the fish and  $D_{\text{V}}$  is the transport parameter into the gill compartment and is  $G_{\text{V}}/Z_{\text{W}}$ , where  $G_{\text{V}}$  (m<sup>3</sup>/s) is the ventilation rate. Equation 13 suggests that at the beginning of the exposure period, when no compound is present in the fish and  $f_{\text{L}}$  is zero, the uptake efficiency is maximal and is  $D_{\text{F}}/D_{\text{V}}$ . Substitution of Equation 2 into Equation 13 shows that the efficiency should decrease with time and will eventually reach zero as the fish reaches equilibrium:

$$E = (D_{\text{F}}/D_{\text{V}}) \exp(-D_{\text{F}}/V_{\text{F}}f_{\text{L}}) \quad (14)$$

As a result we can write the following equation for the initial or maximum gill uptake efficiency  $E_0$  in fish:

$$1/E_0 = D_{\text{V}}/D_{\text{F}} = G_{\text{V}}(1/Q_{\text{W}} + 1/Q_{\text{L}} K_{\text{H}}) \quad (15)$$

Equation 15 shows that the gill uptake efficiency is related to  $Q_{\text{W}}$  and  $Q_{\text{L}}$  in a similar fashion to that of the uptake rate constants. Using Equation 10 it can be shown that  $k_{\text{L}}$  and  $E_0$  are related by

$$k_{\text{L}} = E_0 G_{\text{V}} L/V_{\text{F}} \quad (16)$$

Interestingly, when  $K_{\text{H}}$  is large, Equations 15 and 16 suggest that  $E_0$  and  $k_{\text{L}}$  become constant,  $E_0$  approaching  $Q_{\text{W}}/G_{\text{V}}$  and  $k_{\text{L}}$  approaching  $Q_{\text{W}} L/V_{\text{F}}$ .

of  $V_1$ ,  $K_{\text{m}}$ ,  $Q_w$  and  $Q_1$ . Generally  $V_1$  and  $K_{\text{m}}$  can be obtained from either simple measurements or calculations. However, no general procedures exist to predict the parameters  $Q_w$  and  $Q_1$  which are presumably specific to a particular fish species, its size, and its physiological condition.

Since relationships exist between the oxygen uptake capacity and body weight, similar relationships may exist between  $Q_w$  or  $Q_1$  and body weight ( $M$ ). In order to investigate how  $Q_w$  and  $Q_1$  are related to body weight, elimination rate constants for several fish species were gathered from the literature [8,10,11,19,22]. For illustrative purposes,  $1/k_1$  data for all fish species are plotted versus  $K_{\text{m}}$  in Figure 2, showing that  $1/k_1$  and thus  $V_1/K_{\text{m}}$  vary with size and species, and tend to increase with increasing fish size. Figure 3 demonstrates that  $1/V_1 k_1$  and hence  $Q_w$  varies from fish to fish. Apparently as fish weight  $M$  increases,  $Q_w$  increases but not in proportion. Examination of the data suggests that  $Q_w$  is proportional to  $M$  raised to a power of  $0.6 \pm 0.20$ , namely

$$Q_w = 1.4M^{0.6 \pm 0.2}$$

where the confidence interval has a 95% probability.

Unfortunately  $Q_1$  cannot be calculated accurately from these data because the elimination rate constants are primarily dependent on  $Q_w$  rather than on  $Q_1$ . It can be speculated from Figure 2 that for McKim's data set at low  $K_{\text{m}}$  values,  $k_1$  may approach a value of approximately  $10 \text{ d}^{-1}$  corresponding to a half-time of 10 min. If this is the case,  $Q_1$  would be approximately  $10 V_1 L \text{ d}$ . More experimental data for low  $K_{\text{m}}$  substances are needed before any reliable relationship between  $Q_1$  and fish body weight can be established.

Further justification for derived values of  $Q_w$  and information about the relationship between  $Q_w$  and body weight can be obtained by using a correlation for gill ventilation rate as it affects oxygen uptake. Norstrom et al. [21] and later Neely [3] and Bruggeman [8] expressed the ventilation volumetric rate as a function of the oxygen concentration in the water  $C_{\text{w}}$  (ml of  $O_2/\text{ml of water}$ ), the total energy metabolism of the fish  $T$  (ml  $O_2 \cdot h^{-1}$ ), and the efficiency of oxygen transfer across the gills  $E_{\text{m}}$  according to

$$C_{\text{v}} = T/(E_{\text{m}} C_{\text{w}}) \quad (22)$$

$T$  has been shown to be related to the fish's body weight,  $M$ , according to

$$C_{\text{v}} = T/(E_{\text{m}} C_{\text{w}}) \quad (22)$$

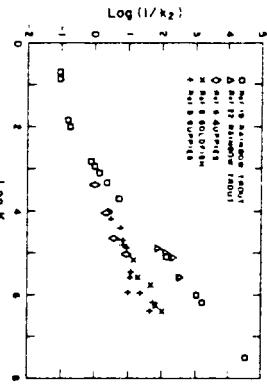


Fig. 2. Observed elimination rate constants in various fish species.

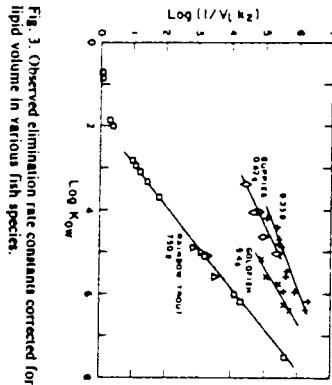


Fig. 3. Observed elimination rate constants corrected for lipid volume in various fish species.

where  $A$  is the metabolic rate coefficient (ml of  $O_2 \cdot h^{-1} \cdot g^{-0.7}$ ).  $G_v$  can be estimated by Equation 24, which is a combination of Equations 22 and 23:

$$T = AM^{0.6} \quad (23)$$

The model presented gives a good correlation of the experimental kinetic data and provides an insight into the parameters controlling the transfer of chemicals between the water and the fish. An increase in the lipid content of the fish leads to a proportional decrease in both  $k_1$  and  $k_2$ , which has been observed experimentally by Bruggeman et al. [8].

We believe that it is worthwhile discussing the significance of the model equations in some detail, especially to explain the relative roles of the various resistances.

Figure 4 is a schematic diagram of the biocompartmental system in which chemical is transported from water through the gills, through a second internal water resistance, and finally through a lipid resistance to a lipid storage. Each resistance is characterized by a  $Q$  or  $G$  term which could be an actual fluid flow ( $G$ ) or a diffusion process characterized by a mass transfer coefficient or a diffusivity. In reality these resistances may be in a different order and may be split into several components. The two water resistances (gill ventilation and internal) may be combined as shown in one resistance characterized by  $Q_w$ . In each case the resistance is proportional to  $1/Q$ ; thus  $Q$  is a

shown to be similar in magnitude to  $Q_w$ . In principle it is impossible for  $Q_w$  to exceed  $G_v$  since this would imply that the total resistance ( $1/Q_w$ ) is less than the gill ventilation resistance ( $1/G_v$ ). The large experimental error made in these calculations is believed to cause the somewhat higher values of  $Q_w$  compared to  $G_v$  for the puppy and goldfish. It seems that  $Q_w$  and  $G_v$  are similar for these species, thus demonstrating that gill ventilation has a major influence on uptake kinetics in small fish. For larger fish, however, like the rainbow trout, ventilation rate seems to have less effect on uptake and elimination kinetics. Other water-phase resistances thus become more important.

## DISCUSSION

The model presented gives a good correlation of the experimental kinetic data and provides an insight into the parameters controlling the transfer of chemicals between the water and the fish. An increase in the lipid content of the fish leads to a proportional decrease in both  $k_1$  and  $k_2$ , which has been observed experimentally by Bruggeman et al. [8].

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Table 2. Observed and calculated transport parameters for hydrophobic organic chemicals in different fish species showing relationship of  $Q_w$  and  $Q_1$  to body weight

Fish species	$\bar{M}$ (g)	$V_1$ (L)	$Q_w$ (l/d)	$Q_1$ (l/d)	$G_v$ (calc)
Rainbow trout [19]	750	$82 \times 10^{-3}$	94	1.2	143
Rainbow trout [22]	900	$98 \times 10^{-3}$	89	0.98	165
Goldfish [8]	4.5	$0.18 \times 10^{-3}$	5.4	2.4	0.49
Guppy [6]	0.62	$0.037 \times 10^{-3}$	0.51	0.49	0.11
Guppy [9]	0.35	$0.026 \times 10^{-3}$	1.0	0.1	0.01

shown to be similar in magnitude to  $Q_w$ . In principle it is impossible for  $Q_w$  to exceed  $G_v$  since this would imply that the total resistance ( $1/Q_w$ ) is less than the gill ventilation resistance ( $1/G_v$ ).

The large experimental error made in these calculations is believed to cause the somewhat higher values of  $Q_w$  compared to  $G_v$  for the puppy and goldfish. It seems that  $Q_w$  and  $G_v$  are similar for these species, thus demonstrating that gill ventilation has a major influence on uptake kinetics in small fish. For larger fish, however, like the rainbow trout, ventilation rate seems to have less effect on uptake and elimination kinetics. Other water-phase resistances thus become more important.

Numerical examples with  $K_{\text{m}}$  values of 100 and 1,000 illustrate the roles of the resistances. In the uptake cases transfer is from water to lipid and at the conditions described has reached 1% of the final equilibrium value, the lipid concentrations (in arbitrary units) being 100 in both cases. The water concentrations for  $K_{\text{m}}$  of 1,000 is thus 100, and for  $K_{\text{m}}$  of 1,000 is 10, the equilibrium lipid concentrations thus being 10,000 in both cases. The values of  $Q_w$ ,  $Q_1$ ,  $G_v$ ,  $V_1$  and  $I$ , which are common to both systems and independent of the chemical are given, as are the values of  $k_1$ ,  $k_2$ ,  $E$ , and  $Z$ , which are chemical-specific. Furthermore, if  $Z$  of 1,000 is arbitrarily assigned to both chemicals in the lipid phase, then  $Z$  in water is 10 for  $K_{\text{m}}$  of 100 and 1.0 for  $K_{\text{m}}$  of 1,000. The corresponding fugacities and  $D$  values can then be calculated as shown.

The fluxes and concentration and fugacity profiles through the system can be calculated using the equations presented earlier. At the interfaces between the resistances where equilibrium is assumed to be achieved, fugacities are equal, and the lipid/water concentration ratios are the  $K_{\text{m}}$  values.

In the case of  $K_{\text{m}}$  of 100, the fugacity drops from 10 in water to 7.525 at the gill surface  $A_1$  to 5.05 at the water/lipid interface  $B_1$  and to 0.1 in the lipid. Half of the total resistance thus lies in the water phases, the relative resistance values being  $K_{\text{m}}/G_v$  of 0.5,  $K_{\text{m}}/Q_1$  of 0.5, and  $1/Q_1$  of 1.0, totaling 2.0. The total water resistance  $K_{\text{m}}/Q_w$  is 1.0. The flux is 4,930 units/d.

When  $K_{\text{m}}$  is increased to 1,000, more resistance is added to the water phase because the water concentrations are lower and the water can only transport a smaller amount of chemical at these fixed flow rates. The flux is reduced to 900 units/d, the resistances being respectively 5, 5 and 1, totaling 11 (i.e., an increase by a factor of 5.5). The fugacities drop from 10 to 5.5 to 1.0 to 0.1. For  $K_{\text{m}}$  of 100,  $k_2$  is 5.0 and  $k_1$  is 50, whereas

A similar equation was proposed by Norstrom et al. [21] to describe uptake of chemicals from water in fish. However, in Norstrom's model  $E$  was considered to describe permeation across the gill membrane and thus to be independent of the ventilation rate of the fish. Equations 13 and 15 show that efficiency varies with  $G_V$ .

By experimental measurement of  $K_{ow}$ ,  $k_1$ ,  $k_2$  and  $E$  for a series of chemicals of varying  $K_{ow}$ , it is possible to "probe" the fish and determine fundamental kinetic terms,  $Q_w$ ,  $Q_i$ , and  $G_V$ . Assuming that the ventilation resistance  $1/G_V$  applies in series with another "internal" water resistance, which we designate as  $1/Q_i$ , we can quantify the contributions of each to the total water resistance  $1/Q_w$ , namely

$$1/Q_w = 1/G_V + 1/Q_i \quad (17)$$

For those who prefer to avoid using the fugacity approach, a conventional derivation can also be undertaken. Starting with the well-established Equation 5, one can postulate that  $k_1$  can be correlated by Equation 11 (following Flynn and Yalkowsky [18]), and since  $K_a$  is  $k_1/k_2$  or  $k_1 K_{ow}$ , Equation 12 can be derived. Finally, if Equation 17 is postulated the uptake efficiency can be expressed as Equations 15 and 16. Although SI units have been used in this derivation it is more convenient to use traditional units in the comparison with

experimental data. For example, all  $Q$  and  $G$  terms are expressed in L/d.

#### COMPARISON WITH EXPERIMENTAL DATA

Uptake efficiency ( $E$ ) data reported by McKim et al. [19] for a number of organic substances in rainbow trout (fish weight: 660–840 g) were fitted to Equation 15 as summarized in Table 1. Linear regression of the data (i.e.,  $1/E$  vs.  $1/K_{ow}$ ) is not desirable because  $1/K_{ow}$  varies over several orders of magnitude and would thus weigh heavily in favor of the data points with low  $K_{ow}$ . In addition, errors in  $K_{ow}$  generally involve similar factors rather than similar absolute amounts. The most appropriate regression is believed to be on a semilogarithmic basis of  $1/E$  versus  $\log K_{ow}$ , but

using the linear equation, a trial-and-error selection of the parameters  $Q_w$  and  $Q_i$ , using the reported  $G_V$  of 170 L/d with repeated plotting of  $1/E$  versus  $\log K_{ow}$ , was used to fit the data.

Assuming a fish density of 1.0 kg/L and a lipid density of 0.90 kg/L, values for  $Q_w$  of 94 L/d and  $Q_i$  of 1.2 L/d gave the best fit of the experimental data.  $Q_i$  is thus 210 L/d.

To test if the parameters  $Q_w$ ,  $Q_i$ , and  $Q_i$  also give a reasonable description of the elimination kinetics of rainbow trout, we used data on biotransformation half-lives of PCBs, reported by Niimi and Oliver [22] for rainbow trout of approximately the same weight and kept under similar conditions to

those used by McKim et al. [19]. Unfortunately, only 4 of 31 reported half-lives of the PCBs were considered to reflect accurately the elimination process. For the other PCBs decreasing lipid levels in the fish or metabolic transformation contributed more to the depuration of the chemicals than pure elimination itself. The biological half-lives of the four PCBs, summarized in Table 1, were corrected for decreasing lipid levels in the fishes as indicated by the authors and then converted to elimination rate constants by equating  $k_1$  to  $0.693/t_{1/2}$  (half-life). Values for  $Q_w$  and  $Q_i$  of 89.1 L/d and 0.98 L/d respectively resulted in the best fit of these elimination data. Since the  $Q_w$  and  $Q_i$  values are similar as deduced from both studies it appears that the same transport processes apply to uptake and elimination.

In summary, for rainbow trout investigated in these studies, the following parameters apply in units of L and days:

$$V_f = 0.750 \text{ (L)}$$

$$V_i = 0.082 \text{ (L)}$$

$$L = 0.109 \text{ (L/L)}$$

$$Q_w = 92 \pm 3 \text{ (L/d)}$$

$$Q_i = 200 \pm 10 \text{ (L/d)}$$

$$G_V = 170 \pm 40 \text{ (L/d)}$$

$$Q_t = 1.1 \pm 0.2 \text{ (L/d)}$$

The following equations thus describe the uptake and elimination kinetics, representing the substitution of these values into Equations 11, 12 and 15 and equating the bioconcentration factor  $K_a$  to  $k_1/k_2$ .

$$K_a = 0.082 K_{ow} \quad (18)$$

$$1/k_2 = 8.9 \times 10^{-4} K_{ow} + 7.5 \times 10^{-2} \text{ (d)} \quad (19)$$

$$1/k_1 = 8.2 \times 10^{-1} + 0.68/K_{ow} \text{ (d)} \quad (20)$$

$$1/E_0 = 1.85 \pm 15\% K_{ow} \quad (21)$$

The fraction of the total resistance in the water phase is  $8.9 \times 10^{-4} K_{ow}/(8.9 \times 10^{-4} K_{ow} + 7.5 \times 10^{-2})$ . Figure 1 and Table 1 present the experimental and correlated values of these quantities using these equations applied to the data from McKim et al. [19] and Niimi and Oliver [23]. The agreement is clearly satisfactory.

These plots illustrate the relative contributions of the water- and the lipid-phase transport to uptake by the fish. For compounds of low hydrophobicity (i.e.,  $K_{ow} \leq 10$ ) uptake is primarily controlled by transport processes in the lipid phases of the fish (i.e.,  $1/Q_i \gg K_{ow}/Q_w$ ). For these compounds uptake rate constants and gill uptake efficiencies increase with increasing hydrophobicity. For compounds of higher hydrophobicity (i.e.,  $K_{ow} \geq 1000$ ) uptake kinetics are primarily controlled by gill uptake processes in the aqueous phases of the fish (i.e.,  $K_{ow}/Q_w \gg 1/Q_i$ ) and uptake rate constants and gill uptake efficiencies are independent of the compound's hydrophobicity. Equal water and lipid resistances are encountered when  $K_{ow}$  is 84.

The ventilation volumetric rate contributes 55% of the total resistance to solute transfer in the water phase. The other 45% of the water-phase resistance phase is presumably due to other water-phase transport processes between the gill compartment and the final storage sites in the fish. These processes may involve diffusion through aqueous diffusion layers (in the gills or elsewhere in the fish) or flow-controlled transport, for example in blood.

#### TRANSPORT PARAMETERS AND FISH BODY WEIGHT

To predict the bioconcentration rate constants

<sup>a</sup> to 14 from ref. 19, 15 to 18 from ref. 22, 19 to 21 from ref. 22, 23 to 25 from ref. 22, 26 to 28 from ref. 22, 29 to 31 from ref. 22, 32 to 34 from ref. 22, 35 to 37 from ref. 22, 38 to 40 from ref. 22, 41 to 43 from ref. 22, 44 to 46 from ref. 22, 47 to 49 from ref. 22, 50 to 52 from ref. 22, 53 to 55 from ref. 22, 56 to 58 from ref. 22, 59 to 61 from ref. 22, 62 to 64 from ref. 22, 65 to 67 from ref. 22, 68 to 70 from ref. 22, 71 to 73 from ref. 22, 74 to 76 from ref. 22, 77 to 79 from ref. 22, 80 to 82 from ref. 22, 83 to 85 from ref. 22, 86 to 88 from ref. 22, 89 to 91 from ref. 22, 92 to 94 from ref. 22, 95 to 97 from ref. 22, 98 to 100 from ref. 22, 101 to 103 from ref. 22, 104 to 106 from ref. 22, 107 to 109 from ref. 22, 110 to 112 from ref. 22, 113 to 115 from ref. 22, 116 to 118 from ref. 22, 119 to 121 from ref. 22, 122 to 124 from ref. 22, 125 to 127 from ref. 22, 128 to 130 from ref. 22, 131 to 133 from ref. 22, 134 to 136 from ref. 22, 137 to 139 from ref. 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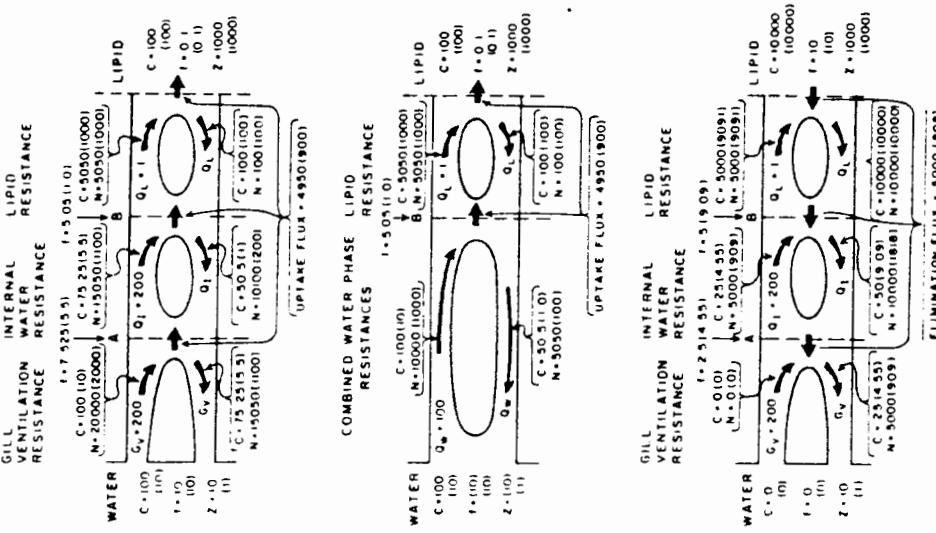


Fig. 4. Schematic diagram showing (top) uptake through two water resistances and a lipid resistance, (middle) identical uptake but with combined water resistance, and (bottom) elimination. The first values are for  $K_{ow}$  of 100 and the second in parentheses are for  $K_{ow}$  of 1,000.

increases to 90.9. The decrease in  $k_3$  is due to the increase in the water resistance, which slows transfer. The increase in  $k_3$  reflects the increase in gill uptake efficiency, resulting in a relative decrease in lipid-phase resistance. Also shown in Figure 4 is the condition for elimination of these chemicals from a fugacity of 10 into clean water. Again for the higher  $K_{ow}$  compounds most of the fugacity drop, and resistance, lies in the water phase. The changes in  $k_1$ ,  $k_2$ ,  $E_0$  and the percentage resistance in the water phase are shown in Figure 1. The most important feature is that at low  $K_{ow}$  values ( $\leq 10$ ) the lipid resistance controls;  $k_1$  increases with increasing  $K_{ow}$ , while  $k_2$  is constant. At intermediate  $K_{ow}$  ( $10\text{--}1,000$ ) both resistances are important,  $k_2$  falls and  $k_1$  rises. At high  $K_{ow}$  values the water resistance controls,  $k_1$  and  $E_0$  are constant, and  $k_2$  falls. The transfer from aqueous-lipid-controlled bioconcentration kinetics in rainbow trout occurs at a  $\log K_{ow}$  of approximately 2.

The model indicates that approximately half the resistance to solute transfer in the aqueous phase of the rainbow trout is due to gill ventilation and the other half is provided by other water-phase transport processes such as diffusion or flow. As a result, an increase in the ventilation rate of the fish leads to a less-than-proportional increase in uptake rate.

Only when the lipid-phase resistance ( $1/Q_1 K_{ow}$ ) is insignificant with respect to the water-phase resistance ( $1/Q_W$ ) and the ventilation volumetric rate controls the water-phase resistance (i.e.,  $G_V \ll Q_1$ ) does an increase in  $G_V$  lead to a proportional increase in  $k_1$  and  $k_2$ . This has been demonstrated for the brook trout [23], where the gill ventilation can be calculated to provide 80% of the total water-phase resistance and the endrin uptake rate constant increases by a factor of 2.2 as a result of 4.3-fold increase in gill ventilation rate.

The observed phenomenon [8,9,12,13,19] that uptake rates in fish decrease with respect to  $K_{ow}$  for superhydrophobic compounds ( $\log K_{ow} \geq 6$ ) shown by two data points in Figure 1 cannot be explained by this model. We are unable to identify the cause of this phenomenon, but the model does provide some insight into possible causes. The model shows that uptake and release of these compounds is almost fully controlled by solute transport in a water phase of the fish. If this effect is due to a resistance increase, it seems likely that it will be reduced solute transport in an aqueous phase rather than a lipid phase that causes the relatively low uptake rates.

To illustrate this point, we can explore the effect of variation in  $K_{ow}$  on the resistances for a situation in which  $Q_W = 100 \text{ L/d}$ ,  $Q_1 = 1.0 \text{ L/d}$ ,  $V_F = 1.0 \text{ L}$ ,  $V_L = 0.1 \text{ L}$ . In all cases  $K_b$  is  $L/K_{ow}$ .

The resistances for  $K_{ow}$  of  $10^4$  are respectively water ( $V_W K_{ow}/Q_W$ ) = 1,000 and lipid ( $V_L Q_1$ ) = 0.1, to give a total of  $10^4$  (i.e., by a factor of 10) instead of remaining constant at  $100 \text{ d}^{-1}$ , and this was due to a doubling of the total resistance, it could be caused by a decrease in  $Q_W$  by a factor of 2, or a decrease of  $Q_1$  by a factor of  $10^4$ , or a decrease in  $Z_w/Z_w$  by a factor of  $10^4$ , or to a combination of these changes.

It is difficult, but not impossible, to conceive a relatively small change in  $K_{ow}$ . It does not seem likely that  $Q_W$  changes, because it is a basic property of the fish. We suggest that the most likely explanation is sorption of the chemical on particulate matter, rather than on an increased resistance reflected by a decreased  $D_F$ . If this reduced uptake rate is viewed as being characterized by a reduced  $D_F/Z_w$  product in Equation 1, we suggest that the reason lies in a decreased  $f_w$  or bioavailability in the water.

Indeed, several studies have shown that reduced bioavailability causes both low uptake rates and bioconcentration factors [24,25]. Although a reduced membrane permeation of superhydrophobic compounds seems less likely to cause these low uptake rates—since it involves a transport process in a lipid phase—not a definite conclusion can be reached at present. For example, it has been suggested by Opperhuijsen et al. [9,26] that the observed lack of uptake of several superhydrophobic compounds in eelopes may be due to molecular dimensions interfering with diffusion through the membrane-water interface. Molecules with relatively large cross sections may therefore experience an unusually high resistance for membrane permeation, causing low uptake rates. Obviously this is a topic requiring further investigation before the factor or combination of factors causing this phenomenon can be identified.

## CONCLUSIONS

We have developed and discussed a model describing the uptake and clearance of conservative chemicals by fish from water. The key quantities are the fish weight and lipid content, the chemical's  $K_{ow}$ , and transport parameters  $Q_W$ ,  $Q_1$ ,

(which can be obtained from uptake/clearance experiments), and if desired  $G_V$ , the gill ventilation rate. From these data the bioconcentration factor, the uptake and clearance rate constants, and the uptake efficiency can be deduced. The model clearly shows the roles of water- and lipid-phase resistances in controlling exchange kinetics, lipid-phase resistance controlling at low  $K_{ow}$ , and water-phase resistance at high  $K_{ow}$ . It is suggested that  $Q_w$ ,  $Q_L$  and  $G_V$  are related to fish size and tentative relationships are proposed, but more experimental data are needed before a validated relationship can be established. We believe, however, that the general form of the relationships is correct.

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