Kinetic Models for Assessing Bioaccumulation

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Kinetic models for exposure of aquatic organisms were developed for water-only exposures to develop a method for shorter-term studies to estimate steady state (Branson et al., 1975; Neely, 1979). The toxicokinetics were assumed to be driven primarily by the thermodynamic differences in the chemical activities in the storage compartment (organism) and the source compartment (water). The driving force for the ultimate storage may be limited through a number of kinetically limiting steps representing a number of potential mechanisms. Some of these limits are external to the organism, some are external but driven by the interaction of the organism with its environment, and some represent internal physiological processes of the organism.

What are some of these physiological and environmental limitations? The rate of presentation of the contaminant to the uptake membrane may be limited by diffusion within the source compartment. The extreme example of a diffusion-restricted environment is sediment, where the diffusion path can be very tortuous. Such diffusion limitations can be reduced by organism behavior including increases in respiration, resulting in the active pumping of water across the gills and increased ingestion rates, which exposes the organism to a larger volume or mass of the source compartment and thus the contaminant. Environmental factors such as temperature may alter physiological processes and result in changes in physiological features such as respiration and metabolism. These in turn may alter the volume of the source compartment encountered and the resultant exposure. The balance may result in greater or lower concentrations over time. Limitations at the physiological level also include limitations of compound transport from the site of accumulation to the ultimate storage site within the organism. Such processes can limit or enhance the transport from the site of uptake. If the transport from the site of uptake is limited, then the apparent difference in chemical activity forcing the transport into the organism may be reduced and the rate process slowed. Likewise, if the internal distribution is rapid, a large chemical activity gradient can be maintained and the rate will be rapid. Changes in the metabolic rate within the organism can also alter the rate of biotransformation, and thus the ultimate rate and potential for the accumulation of the parent compound. However, in these cases the flux into the organism remains high, and if the metabolite is the toxic form, its flux and accumulation will be enhanced.

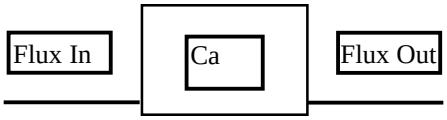
Using the simplest model of accumulation and loss, some of these various factors can be demonstrated, e.g., the effect of respiration rate on the uptake process. Assuming no biotransformation:

$$\frac{\Delta C_a}{\Delta t} = Flux_{in} - Flux_{out}$$

In this form, it is difficult to quantitate the changes in concentration in the organism or predict them, but by making additional restrictions, quantitation and prediction become possible. The formalisms available for this simple model can be represented in compartment, clearance volume, or fugacity forms. In this simple model, the various formalisms can be interconverted (Landrum et al., 1992a). However, each of the approaches has slightly different assumptions to yield mathematically equivalent results.

In addition to compartment-based kinetic models, both physiologically and bioenergetics-based models have been employed to describe the accumulation and distribution of contaminants in aquatic organisms (Landrum et al., 1992a). For instance, a bioenergetics model for the clam, *Macoma nasuta*, was studied with the contaminant hexachlorobiphenyl (Boese et al., 1990). In this case, the routes and rates of accumulation and loss could be well defined. The difficulty with these approaches is the need for a large amount of data to parameterize the model. These models are particularly useful for relating the exposure of organisms to fundamental processes such as respiration and feeding rates.

In the compartment-based formalism and the absence of biotransformation:



Back

$$\frac{dC_a}{dt} = k_u C_S - k_e C_a$$

Where:

k_u = uptake clearance (ml g^{-1} h^{-1})
C_s = concentration in the source (ng ml^{-1})
k_e = elimination constant (h^{-1})
C_a = concentration in the organism (mg g^{-1})

In this form, some restrictions that are not usually recognized come into play. First, the concentration in the source is the bioavailable concentration. If the total concentration is included as the source concentration, it will affect the estimate of k_u. This is useful for assessing differences in bioavailability assuming that the conditions of the experiment do not vary significantly. In water with little complexing capacity, it is generally the concentration in the water that is the source concentration. However, there are examples where water concentrations are modified by the presence of dissolved organic carbon (DOC) (Landrum et al., 1992a). In sediment, the fraction that is bioavailable is less clear and often the total sediment concentration or a concentration on some normalized basis, i.e., carbon, is employed. It is generally understood that C_s is not limiting and that the system is homogeneous. If this is not true, then the flux into the organism will vary considerably over time. Such variation would preclude exact integration of the differential equation and make it necessary to perform numerical integration, for which substantially more information is required.

In the compartment formalism, k_u is the clearance of the source compartment by the organism, usually expressed on a weight-specific basis for the organism and a volume- or mass-specific basis for the source compartment. It is assumed to remain constant over the course of a study or prediction. Whether it actually remains constant over longer predictions or measurements is questionable. This term includes the interaction between the source compartment and the organism and distribution rates for both the internal and external distribution of the compound. K_u is also conditional based on factors that affect the physiology of the organism, the chemistry of the source compartment, and the interaction between these two. Thus if k_u is to be used for comparison of differences in bioavailability, as it often is in many sediment contaminant evaluations, the conditions of the experiment need to be constant across a range of conditions, such as across a range of sediments, so that the comparisons will be valid. In addition, k_e is also assumed to remain constant and is subject to many of the physiological changes that occur in the organisms.

With aqueous exposures, there is an exact conversion between the compartment model and both the clearance volume model and a fugacity model. There are, however, some subtle differences in assumptions and definitions in these models. For the fugacity model, the system tracks the differences in chemical activity within the system. The concentrations are given in terms of moles per volume, and the relative capacities of the systems for the compound are expressed in terms of both partition coefficients and fugacity capacities. The model could work as well in sediment exposures as in aqueous exposures for it is really a compartment model in which the terms are redefined. In the case of the clearance volume model, there are some assumptions that are usually not readily recognized. In the aqueous case, the fluxes into and out of the organism are assumed to primarily occur across the same membrane or at least the membrane resistance is assumed to be equal. This leads to the description of the steady-state condition as the relative capacity of the organism compared to the source compartment. For sediments, it would be necessary to add additional routes of exposure to be accurate with this model. The volume of distribution would reflect the relative capacity of the aqueous phase of the system. Thus, it is not as easy to directly apply the clearance volume model to the sediment environment without modification of the mathematical formalism.

The simple compartment model approach to toxicokinetics in sediments has been employed to demonstrate differences in bioavailability among classes of contaminants, sediments, the effects of concentration, and the impact of normalization procedures. The toxicokinetics approach has shown that two major classes of contaminants, polychlorinated biphenyls (PCBs) and polycyclic aromatic hydrocarbons (PAHs) seem to have differential bioavailability when the log K_{ow} values are essentially the same (Landrum and Faust, 1991). This also seems to be the case for the relative bioavailability of other chlorinated hydrocarbons and PAHs as well (Harkey et al., 1994). This approach was also useful in attempting to evaluate the relative importance of exposure to interstitial water versus the exposure to whole sediment, suggesting that multiple routes can be important (Harkey et al., 1994). In this case, the relative k_u normalized for the organic carbon content in the media was much greater for exposure to whole sediment than for exposures to interstitial water, suggesting that the exposure in sediment employed additional sources (routes) of exposures compared to simple exposure to interstitial water. Exposures to varying concentrations of sediment-associated contaminants can cause accumulation of sufficient doses that the uptake is affected. When *Diporeia* spp. were exposed to pyrene, k_u increased to a maximum and then tended to decline at doses that produced mortality (Landrum et al., 1994). Finally, the relative bioavailability among sediments of individual contaminants has been estimated through exposures under essentially identical conditions but with differing amounts of DOC in water and among sediments. In one study, the variation in the bioavailability as measured using uptake clearance demonstrated that for sediments collected in Lake Michigan normalization to organic carbon removed essentially all the variability (Landrum and Faust, 1994). However, in the comparison to materials from another source, in this case a soil from Florissant, Missouri, the carbon normalization was not adequate to describe the difference in bioavailability and the differences increased with log K_{ow}. Additional work has shown that the range of variability among

sediments after carbon normalization is somewhat greater than a factor of 10 for selected organic contaminants.

The compartment approach has demonstrated some limitations to our ability to understand and measure the accumulation of contaminants from sediments. The first appearance of complications with this approach was demonstrated in the accumulation of a series of PAHs from a single sediment. The shapes of the kinetics curves varied with log K_{ow} of the compound. It was originally thought that this was an equilibrium problem between the sediment particles and the interstitial water (Landrum, 1989) similar to the observed chemical equilibrium and extraction problem with chemical analyses (Karickhoff, 1980). Experimental designs seemed to indicate that this disequilibrium was a valid issue (Landrum, 1989; Landrum et al., 1992b). However, exposures of organisms to field-collected sediments also seemed to show some of the same kinetic complications where organisms would in some cases rapidly accumulate a compound only to lose concentration over time. Since the sediments were field-collected, it was thought that they were less out of equilibrium than those dosed in the laboratory. Experimentally, it appears that the concentration of biologically available material is changing over time. If the desorption of a compound is inadequate to maintain the interstitial water concentration from the surface easily desorbed concentration, then the bioavailable component of the total contaminant load in the sediment will decline because diffusion within the sediment is limited. When the interstitial water is a greater source than sediment ingestion, as is probably the case early in the exposures, then the potential for depletion of the bioavailable fraction would seem more likely. This issue seems to be more problematic for compounds with log K_{ow} values less than about 5. When pyrene was studied with a laboratory-dosed sediment, the shape of the kinetic curve appeared to be a classic first-order curve with steady state. However, when the elimination estimated from such a curve was compared to directly measured elimination values, it appeared to be inordinately fast. This suggests that the depletion process is important from these sediments (Landrum, 1989; Landrum et al., 1992b). The issue becomes more pronounced with phenanthrene, a compound with a smaller log K_{ow} value. Compounds with larger log K_{ow} values do not generally show such depletion. However, in some work with oligochaetes, which have a faster initial uptake rate than *Diporeia*, an initial uptake with a subsequent plateau or decline was evident. Overall, it would appear that the rate of accumulation from the aqueous phase dictates some of this process and likely it is the relative rate of uptake versus the rate of desorption that is important since diffusion in sediment should be slow. In most of the work that has been performed to date, it is not possible to separate out the mechanisms that may be contributing to such observed variation in the kinetics. Some of the data that would be necessary to evaluate this include good estimates of the desorption rate constants from sediment and estimates of the feeding rate on sediment particles and the associated assimilation efficiencies.

Another feature of the kinetics with *Lumbriculus variegatus* that produced an apparent increase with a subsequent decline in contaminant concentration was found to result from loss of weight by the organisms. *Lumbriculus* from the culture are healthy and fat. When exposed in sediments, they sometimes lose weight and lipids with subsequent losses of contaminant, while in one study, the kinetics on a lipid basis formed a standard first-order uptake that approached steady state (Kukkonen and Landrum, 1994). In addition to the impact on the weight, when *Lumbriculus* were exposed in different ratios relative to the organic carbon content of the sediment, but at the same organic carbon-normalized concentrations, the kinetics changed, suggesting an interaction (Kukkonen and Landrum, 1994). At least by performing a kinetic study, the relationship to steady state for these organisms can be observed instead of assumed and variations in the conditions that impact the steady state determined.

Because of the limitations—in particular, the potential absence of homogeneity of sediment systems— moving from a concentration-based to a mass balance-based model that incorporates more of the physical-chemical processes can help demonstrate which processes are important in the accumulation process. A mass balance model was established to examine the accumulation of sediment-associated contaminants. The model attempted to parameterize the partitioning phenomena as well as the accumulation by several routes for *Diporeia* (Landrum and Robbins, 1990). This first pass at a mass balance model did demonstrate the importance of the role of desorption of contaminants from sediment, perhaps coupled with diffusion limits, on the accumulation process. Further, the desorption rate from particles seemed to be very slow compared to the uptake processes and may well dictate the bioavailability of sediment-associated contaminants along with the ingestion rate and assimilation efficiency. In the model as originally formulated, there was a general absence of data on desorption rates, assimilation efficiencies, and feeding rates.

Today, the ability to estimate the assimilation efficiency for ingested sediment remains extremely difficult. The difficulties are essentially twofold. First, it is nearly impossible to determine the concentration of contaminant in the ingested fraction of sediment for many invertebrates. For oligochaete worms that are general feeders, e.g., they do not strongly select particles, estimating the ingested contaminant concentration is easier. The second issue is to estimate the fraction of material that is retained by the organism. This is generally performed using a non-assimilated tracer. Polydimethylsiloxane and ^{51}Cr have been used, but in both cases the tracers do not sorb to the same particles or in the same proportion as the contaminants (Lydy and Landrum, 1993; Kukkonen and Landrum, 1995). Another approach has been to estimate the relative loss of carbon and subsequently estimate contaminant loss (Lee et al., 1990; Lydy and Landrum, 1993). However, there are not even good assimilation values for the carbon from sediments, so this approach is limited. Overall, development of good assimilation efficiencies is required to improve the estimation of contaminant

accumulation from sediments through kinetic models except with compounds with large log K_{ow} values, where desorption and uptake from interstitial water is of lesser importance.

Summary

Kinetic studies can demonstrate factors that affect the accumulation process and the relationship between the length of exposure and steady state.

Kinetic studies do not seem to be able to determine steady-state potential in all cases due to complications with changes in bioavailability or the length of time required to achieve steady state, which is coupled to changes in physiology.

Mass balance models or models incorporating more of the processes suggest that the desorption rate from sediment particles is an important kinetically limiting process.

Ingestion as the primary route of exposure compared with interstitial water is a less dominant route for chlorinated hydrocarbons compared to PAHs and a less dominant route for more hydrophilic compounds.

To improve kinetic models, data on ingestion rates, assimilation efficiency, desorption rates, feeding selectivity, and measure of contaminant concentrations on ingested particles need improved description and improved chemical measurement techniques. It will be important to move from bulk sediment measures to measures that reflect the exposure environment.

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Next