BIOAVAILABILITY
Physical, Chemical, and Biological Interactions

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Chapter 3

Synopsis of Discussion Session on the Kinetics Behind Environmental Bioavailability

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INTRODUCTION

Kinetics are involved in virtually all environmental processes. The time frame (frequency) can very from extremely brief, say, billionths of seconds, to very long, on the order of billions of years. However, only those rate processes which are within a few orders of magnitude of the examined biological rates are of practical importance. One of the most important determinants is the influence of body size on the different metabolic rates at which organisms live.[1,2] That is to say, internal processes and interactions with the external environment occur at a faster rate for small organisms than for larger organisms. Since this body-size effect can encompass several orders of magnitude, factors that influence environmental bioavailability may vary considerably between organisms of substantially different body sizes. Thus, the processes that are kinetically important for microbes will likely be different from those that are important for fish.

Rather than continuing to examine fundamental influencing factors, we propose to discuss kinetics within a toxicological framework, and on a process-orientated basis within that framework. Kinetics come into play in all three of the basic areas defined in classic toxicology/pharmacology:

1. Exposure—those factors external to the organism that control contact with the chemical;
2. Toxicokinetics—those physiological and behavioral factors controlling uptake, distribution, metabolic processing, elimination and, ultimately, delivery to the site(s) of toxic action; and
3. Toxicodynamics—those processes which constitute the biochemical and physiological sequelae resulting from the effects of the chemical at the site(s) of action.

For this report, discussion will be limited to the first two categories.

FUNDAMENTALS

Why Kinetics?

Many interesting and useful kinetic relations exist in the environment. Our objective is to describe those kinetic processes that alter exposure regimes and the toxicokinetic factors that result in toxicologically significant accumulation of chemicals on or in the body of exposed organisms. Once such factors are understood, it may then be possible to modify exposure regimes or avoid circumstances that create exposures so that adverse effects do not occur. This represents the essence of the current approach for the application of sound scientific principles to the development of exposure-based regulatory criteria for environmental protection. Within this scope, several areas of specific interest exist.

Description and Prediction of the Accumulation Process

Kinetic prediction of accumulation allows estimates not only of the steady-state condition, but also the time required to reach steady state and the shape of the accumulation-time curve.

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Current models use thermodynamic relations to empirically predict steady state, i.e., the relation between the bioconcentration factor (BCF) for nonpolar organic compounds and the octanol-water partition coefficient (K_{ow}).[3] Recent models for bioaccumulation include simple empirical mass-transfer models[4] and gill exchange models,[5,6] where accumulation of organics is controlled largely by hydrophobicity (usually approximated by log K_{ow}), as well as sophisticated physiologically based pharmacokinetic (PB-PK) models where not only body burden, but individual organ accumulation is determined.[7,8] These models are largely successful for nonpolar organic compounds where hydrophobicity dominates partitioning, somewhat successful for polar organic chemicals, and not currently viable for readily metabolized and/or reactive organics[9] and metals.

When organisms accumulate chemicals via multiple routes of exposure, such as occurs from a combination of water respiration and food ingestion, concentrations are often greater than for accumulation from water exposure alone (see Reference 10). This phenomenon is termed biomagnification, and forces the use of kinetic models in place of simple thermodynamic potential models. Similarly, chemical accumulation from mixtures requires an explicit consideration of the individual kinetics of the mixture components.[11]

Examination of the Mechanisms Affecting the Accumulation and Loss of Contaminants in Organisms

Mechanistic investigations focus on the rate-limiting barriers to accumulation and loss (see Session 6, Chapter 2). Several physiological measures for fish have been compared with the accumulation or loss processes (e.g., ventilation rate and accumulation from water).[12,13] Similar studies with invertebrates have been few[14,15] and were unable to establish predictive relationships. Furthermore, kinetic models facilitate study and interpretation of changes in physiology and environmental conditions that influence accumulation (e.g., growth, reproductive state, temperature, species). For example, the influence of seasonal changes on toxicant accumulation may be incorporated when the time to steady state is long enough to observe such environmental and physiological cycles.[16]

Prediction of Adverse Biological Responses using the Tissue Residue Approach

Toxicity assays, as actually reported, do not always ensure that the end points under consideration represent response at steady state, and rarely provide the kinetics so that the time-response curve can be interpreted, despite advice to the contrary.[17] Effects are generally measured for environmental contaminants; although, toxicity has been predicted for some classes of compounds using log K_{ow}.[18–23] Current efforts allow prediction of effects for nonpolar organics acting by a narcotic mechanism based on body-burden residue and should be predictable from accumulation models.[25,26] Such relations are not well established for metals or for organics with a specific mechanism of toxic action.

What Is Bioavailability?

The term bioavailability is used by a variety of investigators in various fields of research. The following series of definitions is proposed to help clarify the situation, especially since the well-established toxicological/pharmacological definition of bioavailability is not compatible with some other uses of this term.

Environmental availability can be defined as the portion of the total material in a compartment (or compartments) of the environment that is involved in a process or group of processes and is subject to physical, chemical, and biological modifying influences. This represents the total pool of material that is potentially available to organisms and represents the broadest sense of the concept.

Bioavailability can be viewed as a special case of environmental availability in which organisms are involved as a target rather than as part of a process. The exclusive use of the prefix "bio" indicates this. Thus bioavailability, by necessity, incorporates not only the characteristics of the chemical and its environmental speciation, but also the behavior and physiology of the organism. Incorporation of the biological component increases the complexity of the term. However, depending on the environment and specificity of the question of interest, groups of organisms with similar characteristics may be combined through the use of clear, up-front assumptions. Two definitions below reflect two related uses and are concerned with some portion of the material defined above as being environmentally available.

Toxicological bioavailability is the fraction of the total available dose absorbed by organisms which is distributed by the systemic circulation, and ultimately presented to the receptors or sites of toxic action. This description works well for systemic toxicants, but is of less value for topically active materials and is the classical toxicological definition of bioavailability. It is often estimated as the ratio of the absorbed dose, area under the blood concentration time curve of a drug under test conditions, compared with the absorbed dose under standard conditions were the administered doses are the same. Generally, the standard condition for reference is an intravenous dose.

The difficulty in applying this concept to the general bioavailability of contaminants in the environment is the definition of dose and the appropriate reference condition. Thus, to avoid confusion with the term bioavailability as employed in pharmacology and toxicology, the term environmental bioavailability should be employed. Environmental bioavailability (EBA) constitutes the fraction of the environmentally available compound which an organism accumulates when processing a given medium.

One approach to resolving the practical difficulties in estimation of environmental bioavailability is to employ the efficiency of accumulation from each matrix (e.g., water, sediment) as a representative measure of EBA. This would be formulated as the ratio of the uptake clearance divided by the rate at which as organism encounters a given contaminant for each matrix being processed.

$$\text{EBA} = \frac{\text{Uptake Clearance (Lkg}^{-1}\ h^{-1})}{\text{Encounter Rate (Volume/Mass)(Lkg}^{-1}\ h^{-1})}$$

EBA should be used for comparing the relative availability of a contaminant between systems and/or experimental conditions. However, as with any tool, it should not be used out of context. Thus, the exposure concentrations and the uptake clearance should always be provided, because under some special conditions the flux into an organism may increase even though the efficiency decreases. This will be found under conditions where the encounter volume increases faster than the uptake coefficient.

When sediment or food exposures are considered, it is likely that the encounter mass or volume may not always be well defined, particularly in the sediment case. Thus, the best comparison between exposure conditions that provides insight into the EBA may be comparison of the uptake coefficients of two exposures.[27] Hence, while the foregoing discussion attempts to describe the efficiency of accumulation, it will not describe the effective dose at the receptor. For that, toxicological bioavailability is suggested, and further discussion of this term is beyond the scope of this workshop.

When considering a framework for discussing the processes that may kinetically limit the EBA, it is useful to consider the following simple empirical kinetic model of accumulation by an organism.

$$\frac{dC_a}{dt} = k_1C_w + k_f\,C_f - (k_2 + k_e + k_m + k_g)\,C_a$$

where k_1 is the uptake clearance for accumulation from water (in milliliters per gram per hour); C_w is the contaminant concentration freely dissolved in the water (in micrograms per milliliter); k_f is the uptake clearance from diet (in grams per gram per hour); C_f is the contaminant concentration in the ingested food (in micrograms per gram); C_a is the contaminant concentration in the organism (in micrograms per gram); k_2 is the elimination rate constant (in hours) across diffusional membranes, e.g., the gill; k_e is the egestion (fecal, urinary, and biliary elimination) rate constant (in hours); k_m is the rate constant for metabolism (in hours); and k_g is the rate constant for growth dilution (in hours).

The uptake clearance from water incorporates the ventilation rate, the blood flow, and the membrane transfer efficiency for a contaminant flowing across the gill. Similarly, k_f incorporates the ingestion rate and assimilation efficiency for the selected food. It is not currently possible to identify all the factors that influence the assimilation efficiency for organisms ingesting sediment. Thus, while C_w represents the freely dissolved compound, which is presumably the biologically available portion of the compound in water, C_f represents the concentration in/on the ingested particles or food which is currently the best representation of the biologically available fraction that can be described. For organic contaminants in sediments, it is not sufficient to use whole-sediment concentration for C_f, as animals selectively, to varying degrees, ingest specific organic fractions of sediment,[28] nor will normalization to organic carbon completely solve the problem of EBA for organic contaminants.[29] Polar organics and metals have not been examined to date.

PHYSICAL FACTORS AFFECTING EXPOSURE

No clear distinctions can be made between the processes that control the mass transport of pollutants in an environment and those that directly affect bioavailability. If the pollutant is not transported to the environment where an organism lives, there can be no bioaccumulation or toxicity; in that sense, the transport processes are the rate-limiting steps. However, in this section, we will concentrate on the processes that affect the immediate environment of the organism and/or deviations from the exposure predicted from thermodynamic considerations. Based on physical factors, the potential or actual uptake of toxicants are affected by changes of either the concentration of the pollutant in the organism's immediate environment or the environmental bioavailability of the pollutant.

Temperature

All kinetic processes—physical, chemical, and biological—are influenced by the temperature of the system. Even homeotherms, with relatively constant body temperatures that reduce the effect of varying environmental temperatures on the kinetics of internal processes, are subject to the effects of temperature on the kinetics of external processes. Clearly, changes in environmental temperature will alter EBA under kinetically limited conditions.

Advection

Advection is the mass movement of a fluid past a point. The rate of advection can limit the rate of accumulation if it exceeds the rate of pollutant sorption/desorption so that equilibrium is not reached between, say, the water- and solid-phase compartments. In cases where the sediment is the source, the water concentration would be below that expected at equilibrium. Such disequilibria may be common in environments where relatively rapid currents of clean water flow over contaminated sediment, as in the case of the contaminated sediment surrounding the Los Angeles sewage discharge. A nonequilibrium distribution may also occur at a relatively low current speed if the sediment contamination is limited to a localized "hot" spot and substantial mixing occurs within the water body.

Another possible case where advection may drive a nonequilibrium condition is the advection of clean overlying water into the surface layer of contaminated sediments. Based on the advection of oxygen needed to maintain a 1-cm oxic layer, Lee[27] calculated that the interstitial water in the surface sediment layer would have to turn over about 80 times a day. Although this speculation needs to be tested, it raises the question of whether the exchange of interstitial water in some sediments exceeds the desorption rate of the more strongly sorbed compounds (i.e., highly hydrophobic compounds). In higher energy environments, turbulence with the bottom may be the advective mechanism that mixes the bottom waters and increases the volume of interstitial water to be equilibrated, creating an advective-limited system.

Sedimentation and Resuspension

Sedimentation is the major pathway for transport of many, if not most, hydrophobic organic pollutants from the pelagic to the benthic environment. Considerable progress has been made in predicting sedimentation in natural systems, and the near-field sedimentation around sewage discharges.[30,31] While whole-sediment pollutant concentrations appear relatively stable, at least over nonseasonal time frames, benthic organisms could experience substantially altered uptake because of short-term fluctuations in sedimentation if the deposited material was preferentially ingested. For example, *Diporeia* spp. shift their feeding from sediment detritus seasonally, and ingest the spring and fall diatom bloom as a major source of nutrition.[32] As discussed here, the kinetics of sedimentation are unlikely to be the rate-determining factor for the bioavailability of contaminants per se, although it will be one of the major transport processes controlling the ultimate sediment concentration of pollutants and organic matter in depositional environments.

Resuspension can have an immediate rate-enhancing effect on exposure concentrations and bioavailability. Resuspension and subsequent ingestion of contaminated sediment will greatly enhance the exposure of filter-feeding organisms, such as mussels or oysters, living above or surrounding a contaminated sediment. The flux of sediment into the water column may also increase the total concentration of aqueous-phase neutral organics, which would increase exposure to nonfilter-feeding organisms as well. Generally, this effect would be counterbalanced by simultaneous fluxes of dissolved organic matter (DOM) that could sorb the organic pollutants. For the metals, both the total concentrations and the bioavailability may increase in the water column with resuspension because reduced metals, such as those precipitated with acid volatile sulfide (AVS), could be oxidized and become bioavailable. Resuspension processes are generally short term and the additional exposure would need to be described through a kinetic model.

Transition Environments

Certain transition environments can undergo profound changes in key environmental factors in time frames faster than many of the corresponding physical/chemical processes. Bioaccumulative processes for organisms living in such environments may be subject to rapidly changing exposure conditions. Examples of such transitional environments include the zone of dilution surrounding sewage or industrial discharges and the turbidity maximum zone in estuaries. In a sewage discharge into marine waters, the freshwater effluent will be diluted by seawater on the order of 100 to 1 times or more within minutes. During this time, a host of changes take place including dilution of particles and dissolved materials, desorption, changes in pH and ionic strength, and flocculation of particles. Each of these processes occurs independently at its own rate. With so many factors occurring simultaneously, these environments are not at equilibrium and may be better thought of as zones of complex kinetics, at least in terms of bioavailability.

PHYSICOCHEMICAL FACTORS AFFECTING EXPOSURE

Dissolution

In general, chemicals must be dissolved in the exposure water before they can diffuse across absorbing membranes. When a chemical is present in the solid state, dissolution must occur prior to absorption, then dissolution is a potential rate-controlling process. The dissolution rate of chemicals is described by the Noyes-Whitney equation:[33]

$$DR = \left(\frac{DA}{h}\right)(C_s - C)$$

where D is the diffusion coefficient of the chemical in the aqueous stagnant boundary layer adjacent to the solid, A is the surface area of the solid, h is the thickness of the boundary layer, C_s is the solubility of the chemical in water, and C is the concentration of the chemical already dissolved in the water. The diffusion rate (DR) is increased by an increase in agitation intensity (via a decrease in *h*), and an increase in surface area (via a reduction in particle size). Also, DR is directly related to water solubility; among a series of chemicals, the slowest to dissolve will be those that are least soluble. Thus, dissolution rate-limited uptake will be more likely encountered with poorly water-soluble chemicals, some of which are relatively lipophilic. This process is particularly important for ingested materials.

Desorption (Complex Dissociation)

The role of sorbing phases is currently modeled as an equilibrium process in which the freely dissolved material is considered to be bioavailable. For nonpolar organics, organic carbon is considered to be the sorbing phase and the sorption is represented by the log-linear relation between K_{ow} and K_{oc}.[34] This simplification of sorption does not account for observed variability in the sorptive capacity of various molecular compositions of the organic matter. Similar relations remain elusive for metals and organic molecules with functional groups that interact with organic matter by other than a simple partitioning process.

Kinetics generally focus on the desorption rate of compounds from the sorbed phase. The desorption process for nonpolar organics is apparently sufficiently slow that it does not occur from dissolved organic matter during transition across the gill.[35] Therefore, for chemicals that accumulate from water the equilibrium representation appears to adequately describe the reduction in bioavailability. The kinetic data are not available for sorbed polar organics or for metals, so whether the desorption kinetics are fast enough to alter the EBA for uptake from water remains in question.

The kinetics for the sorption of nonpolar organic compounds to organic matter is of greatest importance in the sediment. The rate of desorption from particles will dictate the rate of accumulation from interstitial water because organisms rapidly accumulate freely dissolved compounds from interstitial water and diffusion is limited within sediments. The importance of the interstitial water accumulation route for infaunal benthos depends on the relative flux from all routes of accumulation. The influence of desorption on the encountered interstitial water concentration can be altered by the organism's movement to undisturbed interstitial water. However, this desorption process apparently limits the accumulation of poorly water-soluble polycyclic aromatic hydrocarbons by benthic organisms.[36,37] Thus, for these compounds, the uptake process from water is sufficiently fast that it is no longer the kinetically determinative step in the sediment environment. Rather, the uptake rate from interstitial water is determined by the desorption process from particles. The relative magnitudes of the particle desorption rates and the uptake rates from water are not known for polar organic molecules and metals. Therefore, whether desorption processes for these compounds are kinetically rate-limited is unknown.

A second phenomenon that significantly influences this desorption process is the contact time of the toxicant with the particle. For organic compounds that have low aqueous solubility, the sorption process can be described as a two-phase process. As contact time increases between the compounds and particles, the chemical extractability and EBA are both reduced.[38] Furthermore, the EBA declines faster than the chemical extractability.[36,39] The rates for these sorption processes are not well studied. Neither do we know whether this process occurs with polar organics or metals, or the extent of influence on EBA in the field.

A third issue involves sorption across a range of particles sizes. For example, hexachlorobiphenyl distribution does not always correlate with the organic carbon distribution among sediment particles.[70] Thus, sorption processes appear to be influenced by both particle size and composition and the influence on EBA remains in question.

The above discussion focused on sorption to an organic matrix. Sorption to the inorganic matrix of particles and sediment is well recognized for metals, but the importance of such phases for organic compounds needs study. We do not know how the kinetics of these sorption process will influence EBA. To summarize, we need to know more about both the time needed to reach equilibrium and desorption kinetics for sorption processes, so that significant kinetic limitations can be identified and properly modeled. Further, the sorption relations for polar organic compounds[40] and the complex sorption of metals are not fully defined, particularly in terms of the influence on EBA. Both the thermodynamics and kinetics of these processes relative to EBA should be investigated. Finally, the influence of the composition of the sorbing or complexing phase on the extent of sorption also needs study.

Diffusion

Some potential rate-controlling steps in bioaccumulation involve diffusion processes, i.e., chemical movement within sediments, movement across unstirred layers, and movement across membranes and epithelia. The process of diffusion involves random movements of the diffusant down an activity gradient which is usually described in terms of a concentration gradient. The rate of diffusion is described by Fick's Law:[41]

$$\text{Flux} = -D\left(\frac{dC}{dX}\right)$$

where D is the diffusion coefficient, and dC/dX is the concentration gradient across the diffusion barrier. The magnitude of the diffusion coefficient is influenced by the environmental variables in the Stokes-Einstein equation:[41]

$$D = \frac{kT}{6\pi\eta r}$$

where k is Boltzman's constant, T is absolute temperature, η is viscosity of the matrix in which the chemical is diffusing, and r is the radius of the diffusant. The diffusion coefficient will increase with an increase in temperature (due more to a decrease in η than an increase in T), a decrease in viscosity, and a decrease in molecular weight. For small molecules and metal species (< 1000 Da) molecular weight and temperature effects on D are small. In some matrices, there may be binding sites that can interact with the diffusant and reduce D, thereby creating an effective resistance to diffusion. For example, the presence of functional groups (e.g., hydroxyl and carboxyl) that can hydrogen bond to sites in a membrane will reduce the value of D. Similar interactions will be expected to occur with π bonding, including induced dipole interactions and charge-charge interactions.

Diffusion of a chemical in sediments occurs when an organism in a sediment has taken up chemical in its immediate vicinity, setting up a concentration gradient between the absorbing

surface of the organism and the sediment away from the absorbing surface. If the uptake of chemical by the absorbing surface is fast relative to diffusion of the chemical to the absorbing surface, the diffusion process can control the rate of uptake of the chemical. Such diffusion in sediments is also limited by the twisted path among sediment particles (tortuosity), as well as strict diffusion limits.

Similarly, at an absorbing membrane such as the gill epithelium, depletion of chemical from water immediately adjacent to the epithelium can set up a gradient in the water layer bounding the epithelium.[42] This layer is a "stagnant boundary layer"; it is stationary relative to the epithelium even though water farther from the surface is flowing. Diffusion across this boundary layer can be a rate-controlling step in the absorption of a chemical by the membrane, particularly when the permeability of the membrane is high relative to that of the boundary layer. Whether this boundary layer operates in the fish gill is not known with certainty. It may be that the close spacing of secondary lamellae precludes the development of an aqueous diffusion layer of sufficient resistance to control the rate of chemical uptake by the gill.

Where an aqueous diffusion layer offers significant resistance to chemical transfer (e.g., across the integument or to nonmobile particles), the resistance offered by the boundary layer can be influenced by its thickness which, in turn, is affected by the agitation intensity of the water or the rate at which water flows past the absorbing surface. When an aqueous diffusion layer controls the absorption rate, an increase in the ventilation rate should reduce the thickness of this layer and increase the rate of absorption. Thus, an increase in organism activity can reduce such diffusional resistance.

When an aqueous boundary layer controls the rate of exchange (uptake or elimination) at an adsorbing or absorbing surface (or a desorbing surface), binding or complexation of the chemical can reduce the resistance offered by the boundary layer in the absence of the binding or complexing agent.[43] The mechanism involves release of bound chemical from the complex to the membrane/water interface. This becomes another source of chemical entry into the stagnant layer, in addition to diffusion from the bulk-water phase. For this mechanism to operate, dissociation/desorption must be rapid relative to diffusion and uptake at the membrane/water interface. This mechanism was not observed in the fish gill for high the K_{ow} compounds, benzo(*a*)pyrene and tetrachlorobiphenyl, in the presence of the macromolecular binding agent, Aldrich humic acid.[35]

The diffusive flux of chemicals across a biological membrane is also described by Fick's Law, but in this case a term (K_m) is added to account for the difference in capacity between the membrane and the water:[44]

$$\text{Flux} = -DK_m \frac{dC}{dX}$$

The membrane is generally composed primarily of lipid, and the membrane/water distribution coefficient tends to correlate with distribution coefficients measured between water and other lipoidal phases, including common organic solvents. Because partition coefficients for solvents are much easier to measure than membrane/water coefficients, it is common to use K_{ow}, for example, to indicate the permeability of a membrane toward a chemical. The permeability of absorbing membranes generally increases for a series of chemicals as their K_{ow} values increase. As K_{ow} increases, membrane permeability increases and absorption is then limited mostly by blood flow through the absorbing surface and ventilation.[12,13] For relatively polar and charged chemicals (low K_{ow}; e.g., <1 for fish gill epithelium), diffusion across the absorbing membranes is the dominant rate-determining step.

Speciation

The rate at which the speciation of metals and reactive organics (weak acids and bases) can change forms may be fast enough to alter EBA or toxicity for externally acting materials. This

process is generally not an issue in the bulk environment, but it may play a significant role at the gill surface or other membrane surfaces, depending on transit time and the gill or gut chemistry. Under the conditions of transit, a metal (i.e., Al) may experience a microenvironment that results in a change in speciation. Such changes may be fast enough for precipitation to occur on the membrane surface, and it has been suggested as an important process for Al toxicity at the gill of fish.[45,56] Similarly, neutralization of an organic acid or base may occur in a micro-environment at a rate faster than the transit time. Such a change in speciation could make the compound more available for biological accumulation than would be predicted from the bulk environment. The importance of these processes has not been well studied.

Degradation

Processes that can compete kinetically for the biologically available compound can effectively reduce the EBA to the organism. Among the chemical processes, hydrolysis and photolysis can effectively reduce the available concentration before an organism can reach its thermodynamic limit. The mechanistic understanding of hydrolysis is good, and predictive models are under development.[3] For both direct and sensitized photolysis, predictive relations remain elusive. If sufficient sunlight is available, these processes are more than fast enough to alter the biologically available compound and reduce accumulation.

It is well recognized that redox processes control the speciation of metals. Often the rate-controlling factor is the diffusion of oxygen or production of sulfide. For organic compounds such as the polychlorinated biphenyls, reductive dechlorination alters the chemical composition and, thus, the particle sorption characteristics of compounds in sediments which, in turn, alter the bioavailability. However, this process is generally slower than other processes such as ingestion, which likely controls the EBA of highly sorbed sediment contaminants.

BIOLOGICAL FACTORS AFFECTING EXPOSURE

Diagenesis

As organic matter decays, the particle size decreases and total surface area per unit weight increases, at least until most of the carbon is decomposed. As DOM is released into the water, the chemical composition of the organic matter changes both in response to changes in the organic matrix and from colonization by microbes. The mass declines as carbon is respired by the microbes and multiple metabolic products are released by the colonizing bacteria and fungi. The rate of release of DOM from the carbon matrix and from the colonizing microbes will affect the percentage of "free" vs. bound organic contaminants in the overlying or interstitial water. This chain of physical and chemical alterations has major effects on the bioavailability of organics and metals, especially in sediments where most diagenesis occurs.

Sorption kinetics may change in response to the changes in the size distribution of the particles, whereas the equilibrium distribution between water and solids will change in response to changes both in the mass of particulate carbon and organic composition as well. As the particle size decreases and the surface area:volume ratio increases, the rate of sorption should increase. Presumably, the smaller the particles, the faster both the rapidly and slowly reversible contaminant pools should reach equilibrium.[38] This sorption appears to be multicompartmental, with the initial sorption rapidly reversible, and after extended contact between the contaminant and the particle the reversibility slows.[38]

Production of reducing end products by microbes during decomposition of organic matter[47] affects metal speciation and, hence, metal bioavailability. When the rate of production of these products exceeds the rate of oxygen transport into the sediment, the sediment becomes anaerobic

and many of the metals form insoluble metal precipitates. One end product of recent interest is acid volatile sulfide (AVS), which is hypothesized to be the primary regulator of the bioavailability of metals in sediments.[48]

The diagenesis of organic matter is largely controlled by bacteria and fungi, though marine and freshwater macroinvertebrates can play an important role in the initial physical breakdown of the organic matter. Because of the dominant biological control of diagenesis, the rates of diagenesis are sensitive to factors controlling microbial and macroinvertebrate activity. Temperature, especially, has a dominant influence. With the relatively high particulate and dissolved carbon contents of most sediments, short-term changes in the diagenesis rate are unlikely to have a major effect on bioavailability. However, changes over the course of a season can affect bioavailability from a sediment. For example, it is thought that the reduced production of AVS during the winter in certain sediments can result in substantial changes in metal bioavailability and toxicity.[48] With its lower concentrations of dissolved and particulate carbon, pelagic systems should be more sensitive to short-term changes in the rates of diagenesis.

Organic Matter Loading

The rate of organic matter input directly affects the particulate and dissolved organic content of both the water column and sediment, specifically, aqueous and solid-phase geochemistry and, hence, bioavailability. One end of the organic loading spectrum is oligotrophic lakes and low-productivity marine systems. Areas undergoing phytoplankton blooms and/or areas surrounding sewage discharges represent examples at the organic-rich end of the spectrum. In general, the lower the organic content the larger will be the fraction of aqueous-phase pollutants that are freely dissolved and bioavailable due to the reduced binding to DOM. Conversely, the high particle loads in organic-rich systems will tend to scavenge pollutants from the water column and transport a greater percentage to the near-field sediments.[49] During a phytoplankton bloom, the organic matter associated with phytoplankton and excreted DOM increases, thereby substantially altering the amount of freely dissolved chemical available for accumulation by biota that do not ingest the algae.

Bioturbation

Biological mixing of the sediment (bioturbation) results in significant alteration of the three-dimensional sediment structure. The extent and rate of bioturbation of the sediment matrix can profoundly affect the exposure environment, both of the species modifying the sediment and other species within and outside the benthic community.[50]

Bioturbation often results in the transport of deeper sediment to the surface. Such transport results in a mixing of the surface and subsurface materials.[38,51,52] This mixing prolongs the residence time of deposited materials and the exposure of benthic organisms in the bioactive zone to sediment-associated contaminants.[53] As sediment-associated contaminants are buried by the deposition of less contaminated sediments, a pollution maximum will move downward through the sediment column, as is observed for DDT off the Palos Verdes Peninsula.[54] As the contaminated sediment is buried, the exposure regime for organisms feeding at any particular depth varies over time. The rate of such burial and, hence, the rate of change in the exposure concentration depends on the rate of bioturbation, as well as the rate of net sediment deposition. In biologically active sediments, substantial changes in pollutant concentrations may occur within the life span of longer-lived benthic species.

Intense bioturbation can also increase the water content of muddy sediments and reduce their cohesion, such that they are easily resuspended. Once resuspended, as previously discussed, the contaminated sediments are potentially available to both infaunal filter-feeding organisms and epifaunal filter-feeding organisms above the sediment. Resuspension can also result in substantial

off-site transport of the sediment-associated pollutants. Such transport can result in increasing concentrations of particle-associated contaminants through sediment focusing into depositional basins.[49,53]

TOXICOKINETIC FACTORS AFFECTING EXPOSURE

Physiology and behavior control the volume or mass of the source compartment encountered by the organism over time. Further, the physiology also controls the internal compound distribution required to maintain concentration gradient for passive accumulation processes.

Encounter Volume

The maximum possible uptake rate of a chemical by an organism is controlled by the rate at which the chemical is presented to the absorption sites. For chemicals with high membrane permeability that are rapidly removed from the inside surface of the absorbing membrane (i.e., highly bound to blood), the rate of supply of a chemical can control its rate of uptake. Since both membrane permeability and blood binding increase with the lipophilicity, the probability of this happening increases with the lipophilicity of a compound. For fish, chemicals having a log $K_{ow}>3$ generally have encounter-volume rate-limited uptake.[55] In fish and other aquatic species with gills, the encounter volume is dominated by the volume of water that passes across the respiratory surfaces of the gill epithelium. This flow amounts to about 60 to 80% of the total flow of water across the gills. This concept also applies to organisms living in sediments, where the encounter volume is the volume of sediment-interstitial water adjacent to the organism and the volume transected while the organism moves through the sediment. Some sediment organisms (e.g., the clam, macoma) have very little contact with the interstitial water because they respire overlying water.

The encounter volume is strongly influenced by the activity of the organism, with an active fish able to encounter more than ten times the volume water of a fish at rest. For aquatic species with gills, the encounter volume is largely controlled by the ventilation rate and is sensitive to the concentrations of oxygen and carbon dioxide; low O_2 or high CO_2 in the water increases the encounter volume. The encounter volume also tends to increase with temperature, because dissolved oxygen decreases and metabolism increases.

The distribution of the chemicals to tissues in the organism by the blood or by diffusion will also be involved in the kinetics of accumulation for encounter-volume rate-limited uptake at the absorbing surface. This happens because encounter-volume rate-limited uptake is generally found for relatively lipophilic chemicals. Such chemicals also tend to have high affinity for poorly perfused tissues, like the adipose tissues. In such cases, the accumulation of chemicals by highly perfused tissues like muscle tissue may be controlled by the encounter volume, but the filling of the poorly perfused tissues may be controlled by blood flow to them. Further, the poorly perfused tissues tend to hold more lipophilic chemicals than the highly perfused tissues, often by a large amount. When this happens, accumulation of most of the chemical may not be controlled by the encounter volume, but by the smaller blood flow to the poorly perfused storage tissues, as observed with trifluralin accumulation by fish.[56]

Encounter Mass For Ingested Materials

Ingestion Rate

Gut uptake becomes increasingly important with higher K_{ow} compounds, and probably dominates for compounds with a log K_{ow} of about 6 and above.[10] This route will also likely dominate

other compounds strongly sorbed to particles. The ingested dose from food/sediment is a function of both the total mass of pollutant ingested, which is a function of the ingestion rate and the pollutant concentration in the food/sediment, and gut uptake efficiency for the pollutant. Any of these factors—ingestion rate, pollutant concentration, or assimilation efficiency—can become the rate-determining factor for bioaccumulation.

In fish, the ingestion rate of prey is related to the organism's energy or oxygen requirements. If the pollutant concentrations in the prey are known or can be predicted, the dose and resulting tissue residues can be predicted with a reasonable degree of accuracy from bioenergetic model equation (see Reference 57). The prediction of ingestion rates and ingested doses for sediment-ingesting invertebrates is complicated by the type of feeding mode (i.e., filter feeding or deposit feeding), the current speed, selective ingestion of particles based on size or composition, and the wide range of food "quality". As pointed out by Lopez and Levinton,[58] the range in food quality varies more widely among different particle types within a sediment than among prey items for herbivores or carnivores. Models predicting sediment ingestion have been developed based on a constant ingestion rate of carbon[59] and on optimal foraging strategy,[60] though none is as general or accurate as the fish ingestion model.

Assimilation Efficiency

A key factor in determining the kinetics of pollutant uptake from food or ingested sediment is the efficiency with which the pollutants are absorbed from the gut. Assimilation efficiencies in fish for neutral organics with relatively large K_{ow} values range from a few percent to about 90%.[61–63]

Assimilation efficiencies for compounds with large K_{ow} values have been reported in fish both as independent of, and varying with, the concentration of the pollutant in the food.[64,65] Some of this variation may be due to different study techniques, such as bolus doses vs. chronic exposures, and use of a lipid vehicle vs. dosing the food source. Nonetheless, it seems likely that assimilation efficiencies will vary, at least at extreme concentrations, though it is unclear whether this is an important source of uncertainty for the concentrations found in prey.

Determination of pollutant assimilation efficiencies is problematic for sediment-ingesting invertebrates. Most deposit feeders selectively ingest specific sizes or types of particles. Usually the finer, high TOC particles are ingested, so that the whole-sediment concentrations underestimate the actual pollutant concentration of the ingested particles. Furthermore, because of this selection, assimilation efficiencies cannot be calculated from the difference in the pollutant concentrations in the feces and the whole sediment. Various tracers are used to correct for the selection process,[28,66,67] although there are limits to all of these techniques. Even with these limitations, gut assimilation efficiencies for PCB congeners appear to decline in a marine clam, with the increase in K_{ow} from over 80% for a trichlorobiphenyl to only a few percent for decachlorobiphenyl.[71] The very low assimilation efficiencies for the high K_{ow} PCB congeners could limit the accumulation of these compounds by deposit feeders.

Metabolism

Metabolic breakdown or degradation can influence toxicity in two ways: (1) the biotransformation results in detoxication, and (2) the biotransformation results in a material of similar or greater toxicity. In the first case, the internal concentration of the absorbed chemical is reduced in proportion to the rate of degradation and any toxic effects are similarly reduced (e.g. diethylhexylphthalate[68]). Because metabolism is treated as an elimination constant in the simple model discussed earlier, the time to achieve steady state for the parent compound and the steady-state

concentration will decrease in proportion to the metabolic rate. For toxicity bioassays, the exposure concentration must be increased to compensate for the amount absorbed and metabolized before reaching the target sites. This makes the chemical appear less toxic than a compound of similar toxicity that is not metabolized. Typically, the rate must approach a significant portion of the uptake clearance to substantially influence the system. Conversely, in the second case, the rate of metabolism of the parent compound may determine the rate of appearance of the toxic agent in the organism and may well be the rate-determining step in production of adverse effects. Although considerable work has been carried out to estimate the metabolism of compounds as a function of chemical or physical properties, the rate of metabolic breakdown or transformation of chemicals cannot be reliably predicted for either terrestrial or aquatic organisms.

Growth

Organism growth can affect apparent accumulation of a chemical through growth dilution. As an organism grows, it increases in volume and, therefore, in capacity. If, for example, the rate of growth, which appears as a component of elimination in the simple model discussed earlier, is of the same magnitude as the uptake clearance rate, the body concentration will not change with time and will not achieve the thermodynamically predicted steady-state accumulation. For organic chemicals this effect has been noted to be seasonally significant in algae[69] and fish,[61] and can be estimated as a function of the size of the organism and the log K_{ow} of the chemical in question (see Section 6, Chapter 1). In addition to simple growth, as organisms grow they may also increase the proportion of lipid relative to other tissue types, which also increases the capacity of the animal to store nonpolar organics.

SUMMARY

The kinetics working group and workshop participants recognized that kinetics are involved as a part of all the topics of the workshop. Thus, this discussion paper reflects a more comprehensive discussion of kinetics and their potential effect than were covered under the two discussion initiation papers. The question was not whether the bioaccumulation processes had kinetic aspects, but whether the temporal scale was of a magnitude that they would alter bioaccumulation. The answer to this question depends on the size of the organism of interest and remains one of the most prominent for directing future research. In general, more insight and information on kinetic processes were available for nonpolar organic contaminants than for the polar-reactive organics and metals. Yet, despite the relatively large information base, kinetically limiting processes are not that well defined, and minimal information is available for the polar organic compounds and the metals.

Although there were many definitions of bioavailability presented at the workshop, the kinetics working group thought that the potential use of the environmental bioavailability concept, i.e., the efficiency of accumulation from a matrix of consideration, would provide a useful quantitative tool for comparisons between various experimental conditions and exposure scenarios. Other quantitative formulations will likely be developed with further research. Further, there may be situations where this concept would prove unworkable. However, research on the methodology and conceptual approach should be enhanced by having an initial definition against which to develop hypotheses. Finally, there are several recommendations within the manuscript for further research. Overall, improved recognition of the conditions that result in kinetic limitations and better predictive modeling could greatly improve our understanding of organism exposure and accumulation of contaminants.

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