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Developing and applying metamodels of high resolution process-based simulations for high throughput exposure assessment of organic chemicals in riverine ecosystems

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Abstract

As defined by Wikipedia (<https://en.wikipedia.org/wiki/Metamodeling>), “(a) metamodel or surrogate model is a model of a model, and metamodeling is the process of generating such metamodels.” The goals of metamodeling include, but are not limited to (1) developing functional or statistical relationships between a model’s input and output variables for model analysis, interpretation, or information consumption by users’ clients; (2) quantifying a model’s sensitivity to alternative or uncertain forcing functions, initial conditions, or parameters; and (3) characterizing the model’s response or state space. Using five models developed by the US Environmental Protection Agency, we generate a metamodeling database of the expected environmental and biological concentrations of 644 organic chemicals released into nine US rivers from wastewater treatment works (WTWs) assuming multiple loading rates and sizes of populations serviced. The chemicals of interest have log n-octanol/water partition coefficients ($\log K_{OW}$) ranging from 3 to 14, and the rivers of concern have mean annual discharges ranging from 1.09 to 3240 m³/s. Log-linear regression models are derived to predict mean annual dissolved and total water concentrations and total sediment concentrations of chemicals of concern based on their $\log K_{OW}$, Henry’s Law Constant, and WTW loading rate and on the mean annual discharges of the receiving rivers. Metamodels are also derived to predict mean annual chemical concentrations in fish, invertebrates, and periphyton. We corroborate a subset of these metamodels using field studies focused on brominated flame retardants and discuss their application for high throughput screening of exposures to human and ecological populations and for analysis and interpretation of field data

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1. Introduction

Under various federal laws [i.e., the Federal Food, Drug and Cosmetic Act (FFDCA); the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA); the Food Quality Protection Act (FQPA); the Toxic Substance Control Act (TSCA), etc.], the US Environmental Protection Agency (USEPA) assesses the safety of new and existing chemicals released into the environment using a risk assessment paradigm that couples the inherent toxicity (hazard) of chemicals to their expected environmental fate, transport, and bioaccumulation (exposure). Based on such assessments, the Agency may restrict a chemical's manufacture, use, or disposal (GAO, 2009). Conducting such assessments, however, is a daunting task due to the sheer number of chemicals that must be evaluated annually by the Agency. For example, under TSCA, the USEPA receives annually as many as 1200 Pre-manufacture Notifications (PMNs) for new industrial chemicals which must be reviewed within 90 days. Similarly, under FIFRA, the Agency must annually review both new pesticides and existing pesticides that have been registered for no more than 15 years. In fiscal year 2016 alone, almost 25,000 pesticide products were subject to reregistration review (<https://www.epa.gov/pesticide-reevaluation/reregistration-and-other-review-programs-predating-pesticide-registration>). Consequently, there is a real need to have tools (i.e., calculators and models) that can facilitate high throughput (HT) risk assessments.

Intuitively, the most likely tools for such assessments would be could be simple exposure and hazard models that require a limited number of input parameters. Such "screening" level models would include both empirical and simple process models. For example, chemicals that are currently or expected to be released from point sources into rivers or streams might be screened as follows. First, if the chemical's physicochemical (pchem) properties are unknown, they could be estimated using an existing pchem calculator, such as the EPI Suite™ software (USEPA, 2011). Using these properties and empirical Quantitative Structure Activity Relationships (QSARs), the chemical's expected transformation rates (e.g., biodegradation rates), accumulation factors (e.g., BAFs), and lethal exposure concentrations (e.g., LC₅₀s) could then be estimated to assess its expected environmental persistence, bioaccumulation, and toxicity, respectively. The chemical's steady-state water concentrations could then be forecasted using expected environmental release rates estimated by ChemSTEER (USEPA, 2013) and a simple dilution model like E-FAST (USEPA, 2007). Finally, predicted water concentrations could be compared to the estimated LC₅₀s to assess hazards to aquatic biota and combined with estimated BAFs to predict dietary exposures to humans and wildlife. Because such screening models would be expected to have simplified or limited representations for all but the major physical, chemical, and biological processes that determine the fate, transport, and bioaccumulation of chemicals in real world environments and ecosystems, such screening assessments would be

expected provide only a general picture of chemical risks to human and ecological populations whose uncertainty and variability would be difficult to quantify.

The USEPA has made the improvement of its chemical safety assessments a major priority (USEPA, 2015). Although many see increasing laboratory and field data to support such assessments as a major thrust (ICCA, 2011, NRC, 2012), improvements can also be achieved by using higher-tier models that add more process-based science to the exposure and risk assessments conducted by the Agency. Many such models have been developed and used by the Agency to obtain more robust representations of specific chemicals in targeted environments either as case studies or to support specific management decisions. Unfortunately, many of these models have not been widely used for risk assessments because they are considered too data-intensive or time-consuming to be used routinely.

In this paper, we demonstrate an approach for incorporating higher-tier process-based models into HT exposure assessments which circumvents the need to parameterize and execute the models of interest for every assessment. In this approach, technical experts in the use and the analysis of the process-based models of interest apply them to populations of chemicals and environments that span the range of chemical and environmental properties of concern to generate expandable databases of selected model outputs. These databases are then used to construct linear and nonlinear regression models which can evaluate the expected fate, transport, and bioaccumulation of non-database chemicals and environments for screening-level exposure assessments. Such metamodels not only capture the most salient features of the selected science models but also provide well-defined tools for conducting rapid exposure assessments. We demonstrate this approach for organic chemicals that are known to be released into rivers from point sources [e.g., treated discharges from publicly owned water treatment works (POTWs) or other wastewater treatment works (WTWs)]. For this demonstration, the chemicals of concern have log n-octanol/water partition coefficients ($\log K_{OW}$) ranging from 3 to 14, and the rivers of concern have mean annual discharges ranging from 1.09 to 3240 m³/s. We use five existing USEPA models to generate the required databases. To estimate the pchem properties and loading rates of the chemicals of interest, we used the Chemical Transformation Simulator (CTS) (Wolfe et al., 2016) and the High Throughput Stochastic Human Exposure and Dose Simulation Model (SHEDS-HT) (Isaacs et al., 2014), respectively. Using these data, we then simulate the dissolved and total water concentrations, and total sediment concentrations for each chemical-loading combination in the rivers of interest using the Exposure Analysis Modeling System (EXAMS) (Burns, 2004). Lastly, we use the K_{OW} -based Aquatic BioAccumulation Model (KABAM) (Garber, 2009) and the Bioaccumulation and Aquatic System Simulator (BASS) (Barber, 2012) to estimate expected BCFs of periphyton and phytoplankton and BAFs of benthic invertebrates, zooplankton, and fish in the rivers of interest. Using these BCFs and BAFs, expected whole-body concentrations of exposed fish and invertebrates are calculated for each chemical-loading-river combination. Each of the aforementioned models, which are described in Section 1 of our Supplemental information, has been peer reviewed and used routinely by the USEPA to assess the fate, transport, and bioaccumulation of chemicals in aquatic ecosystems (USEPA, 2003, USEPA, 2008, USEPA, 2014).

2. Materials and methods

The overall metamodeling approach described in this paper is illustrated in Fig. 1. Existing USEPA models that predict chemical properties, consumer product exposures, environmental fate and transport, and bioaccumulation are used to create a database of chemical concentrations in water, sediments, and biota for multiple rivers. Regression methods are then used to develop metamodels for predicting environmental concentrations in water and sediment as functions of river hydrology, chemical loading rates, and chemical properties. Metamodels are also developed to predict BAFs for exposed biota as functions of the chemical's K_{OW} and the biota's ecology and life history; chemical concentrations in exposed biota are then predicted using these metamodels coupled to those developed for simulated dissolved water concentrations. The methods used to develop these metamodels are described below.

2.1. Chemicals of interest

For this demonstration, we selected four categories of chemicals that have been and continue to be of concern to the Agency at large. These are household products (e.g., personal care products, residential insecticides, etc.) currently included in the SHEDS-HT database; chemicals identified as or suspected of being endocrine disruptors (EDCs) [e.g., List 1 and List 2 EDCs in the Federal Register (78 Fed. Reg. 35,922)]; brominated flame retardants (BFRs) and their proposed substitutes; and medium-chain chloroparaffins [MCCPs, also known as polychlorinated alkanes (PCAs)] which are used as secondary plasticizers in polyvinyl chloride, additives in metal working fluids, and flame-retardant plasticizers in rubbers and other polymeric materials (Campbell and McConnell, 1980, ECHA, 2005).

In aquatic environments, the partitioning of chemicals to suspended solids and benthic sediment is controlled by their K_{OW} s and S_{ws} , and their volatilization from surface waters is determined by their HLCs. If the chemicals of concern are ionizable, their partitioning and volatilization will also depend on their pK_a s and pK_b s and the pH of the ambient water. Supplemental information Table S1 summarizes the median pchem properties estimated by CTS for the 644 chemicals selected for this study.

Unlike the first three chemical classes, MCCPs (CAS No: 85535-85-9 and EINECS No: 287-477-0) are distributed commercially as complex mixtures of different carbon chain lengths with varying degrees of chlorination (ECHA, 2005). The most commonly available mixtures, however, have carbon chains ranging from C14 to C17 with chlorine contents of 40–50%, 50–60%, and 60–70%. An excellent overview of the occurrence of MCCPs and other chloroparaffins in air, water, sediments, aquatic biota, terrestrial wildlife, and human food is given by Feo et al. (2009). For this study, we considered MCCPs as consisting of 12 homologs having carbon chains ranging from C14 to C17 and chlorine contents approximately equal to 45%, 55%, and 65%; each homolog was then characterized using 15 randomly selected isomers.

Because the rates of chemical advection (i.e., river discharge) in the rivers of interest will dominate any of the abiotic or biotic transformation rates represented in EXAMS by

multiple orders of magnitude, for this study, we assumed that all EXAMS chemical transformations rates could be assumed to be zero without any loss of generality.

2.2. Rivers of interest

Nine rivers having US Geological Survey gauging stations were selected as representative of receiving waters for this demonstration; these were: the Caney River near Bartlesville, OK (USGS 07174400); the Hudson River near Waterford, NY (USGS 01335754); the Middle Oconee River near Athens, GA (USGS 02217500); the Ohio River near Warsaw, KY (USGS 03277200); the Saginaw River at Saginaw, MI (USGS 04157000); the River Raisin near Adrian, MI (USGS 04176000); the Sandusky River near Bucyrus, OH (USGS 04196000); the South Platte River near Littleton, CO (USGS 06710000); and the St Jones River near Dover, DE (USGS 01483700). Drainage areas of these rivers range from 82.6 to 215,000 km², and their mean annual discharges range from 1.09 to 3240 m³/s. Although more rivers could have been accommodated in this study to provide a broader regional or national picture, we chose only these nine for this demonstration.

EXAMS was parameterized for these rivers using prevailing climatic, hydrological, and limnological features. River characteristics included mean monthly discharges and water temperatures and the river's mean depth and width. All required hydrological data for these rivers were obtained from the USGS website (<http://waterdata.usgs.gov/nwis/inventory>). Climatic data required by EXAMS includes temperature, precipitation, cloud cover, relative humidity and wind speed. These data were obtained primarily from the NOAA National Climatic Data Center (<http://www.ncdc.noaa.gov/>) and supplemented as needed with meteorological data from USEPA's Exposure Assessment Models website (<http://www2.epa.gov/exposure-assessment-models/meteorological-data>). Supplemental information Tables S2 and S3 summarize the hydrological and climatic features of these rivers.

2.3. Fish communities of interest

Because fish community data were not available for the rivers of interest, we parameterized BASS generically to estimate expected fish BAFs in eastern and midwestern rivers. Recently, Barber et al. (2016) used BASS and data collected by the USEPA's Environmental Monitoring and Assessment Program (EMAP) to forecast mean annual biomasses and population densities, annual productions, and realized BAFs of fish in 352 randomly selected Mid-Atlantic wadeable streams and rivers in the eastern US. These authors showed that BASS-simulated total fish densities and relative biomasses of the dominant fish species in these waters were consistent with those observed by four other eastern US studies having similar species compositions (i.e., trout streams of the Catskill Mountains, NY and eastern Tennessee; smallmouth bass streams of the Boston Mountains in northern Arkansas and eastern Oklahoma; and impacted and referenced streams in the coal mining regions of Kentucky and West Virginia). Consequently, we updated and used these BASS project files for this demonstration. These updates included using KABAM-estimated BAFs and BCFs to calculate chemical concentrations in benthic invertebrates, periphyton, and zooplankton and using default fish parameter files generated by the most current version of the BASS parametrization software. This version of the software uses species-specific thermal niches,

as outlined by Zorn et al. (2008) and Lyons et al. (2009), and maximum species' body lengths from the PisCES [Piscine Community Estimation Software, see Cyterski et al. (2017)] database to calibrate fish growth rates and back-calculate associated feeding rates. The upper bounds of these thermal niches are defined to be the July mean water temperatures (JMT) of streams and rivers inhabited by the species of interest. Data sources used to construct and to assign these JMT-based niches included the WHATIF Hydrologytool (USEPA, 2016), Hinz et al. (2011), Lyons et al. (2009), and Zorn et al., 2012, Zorn et al., 2008.

2.4. Release scenarios

Screening-level down-the-drain per capita loadings for a case study of chemicals in consumer products were calculated using SHEDS-HT which merges estimates of chemical concentration (weight fraction) in different types of consumer products with corresponding "use pattern" or "habits and practices" data (population prevalence, frequency of use, mass per use, etc.) to estimate single-day exposures to chemicals via near-field (i.e., residential) product use for a simulated population (Isaacs et al., 2014). SHEDS-HT was also modified to estimate the mass of chemical going down the drain via use of a product. For each simulated person, for each product used, this was estimated as

$$m_{DD} = m_{\text{product}} \times WF \times f_{DD} \quad (1)$$

where m_{DD} is the mass of chemical going down the drain (g/d); m_{product} is the mass of product used per day; WF is the weight fraction of chemical in the product; and f_{DD} is the fraction of the product being disposed of down the residential drain (i.e. not including storm drains). The mass entering surface water, m_{loading} g/d, is then calculated as

$$m_{\text{loading}} = m_{DD} \times (1 - f_{WW}) \quad (2)$$

where f_{WW} is the fraction of chemical removed in wastewater/sewage treatment. Estimates of f_{WW} were obtained using the STPWIN module in EPI SuiteTM. Values of f_{WW} were assumed to be constant (point values) in this study.

Distributions of m_{DD} were estimated using SHEDS-HT, based on the simulated use of > 250 categories of consumer products including personal care, cleaning, home maintenance, pet, automotive, pesticide, and home office products. A population of 10,000 individuals was simulated. Product categories, use patterns (including m_{product} values for each type of product), and WF data have previously been described (Isaacs et al., 2014); WF values for each category were developed from two sets of publicly available data for consumer products (Goldsmith et al., 2014, USNLM, 2016). Conservative default distributions for f_{DD} were developed for all consumer product categories. Distributions were assumed to be uniform between the minimum and maximum values given in Table S4. In general, personal care products (e.g., toothpaste and shampoo) and other products to be applied to skin (e.g.,

body paint); interior cleaners designed to be applied and then removed (e.g., surface cleaners); laundry products; products for application to clothes (e.g., antistatic spray); and other products for washing/cleaning of humans or pets (e.g., adhesive remover for hands and pet shampoo) were assumed to have residential down-the-drain disposal fractions equal to 1.0. Products designed for permanent application to residential or other surfaces (e.g., paints and spray adhesives) were assigned f_{DD} values ranging from 0 to 0.1 to account for potential down-the-drain disposal of a portion of the mass used (e.g., via cleaning of containers or brushes). Other products (e.g., wood polishes and arts and crafts products) with larger uncertainties as to ultimate fate (i.e., retention on surfaces or disposal) were assigned f_{DD} ranging from 0 to 0.3. Products designed solely for complete application to outdoor surfaces with little potential for clean-up indoors (e.g., exterior cleaners or lawn products) or products that would only be disposed of via solid waste (e.g., cat litter) were assigned $f_{DD} = 0$. The conservative assumptions related to “product chemical prevalence” (the fraction of products used by the population that contain a given chemical) used in previous applications (Isaacs et al., 2014) were retained; if a chemical was found in any product category in the weight fraction dataset, it was assumed to be present in all products in that category used by the simulated population (e.g., a chemical reported as found in one toothpaste was assumed to occur in all toothpastes).

A total of 1502 individual substances (as labeled by CASRN) were identified in the consumer product *WF* dataset. Eliminating invalid CASRN (failed checksum) and CASRN for which f_{WW} could not be obtained resulted in 1321 chemicals for which SHEDS-HT could be run. A simulated population of 10,000 people and their consumer product use was generated; medians, means, standard deviations, and quantiles of m_{DD} and $m_{loading}$ were estimated for each chemical.

Loading rates for input to EXAMS were then estimated using the following procedure. First, all 1321 chemicals which could be run by SHEDS-HT were sorted into ascending order of their m_{DD} first quartiles. All chemicals having m_{DD} first quartiles equal to zero were then deleted from further consideration. This left 466 chemicals that had nonzero values for each of its m_{DD} quartiles. Table S5 summarizes the CASRNs, distributional statistics for m_{DD} , f_{WW} values, and the number of consumer product categories associated with each of these 466 chemicals. The minimum of the first m_{DD} quartile and the medians of each m_{DD} quartile were then calculated; these values were 0.00001, 0.00526, 0.0114, 0.0304, and $0.0560 \text{ g} \cdot \text{d}^{-1} \cdot \text{person}^{-1}$. Using these m_{DD} values, 20 total chemical loading rates (in units of kg/h) were calculated for each river of interest assuming that its discharging WTW serviced 5×10^3 , 25×10^3 , 125×10^3 , and 625×10^3 people. This procedure was used to estimate EXAMS loading rates for all chemicals with the exception of MCCPs; loading rates for these chemicals were estimated as the minimum and the first, second, third, and fourth quartiles of the local use-specific rates reported by European Chemicals Agency [see Table 3.5 in ECHA (2005)].

2.5. Special considerations for EXAMS, KABAM, and BASS metamodeling

Simulating expected environmental concentrations (EECs) of chemicals having low aqueous solubilities with EXAMS has potential limitations. In particular, EXAMS uses linear

isotherms to model the sorption of organic chemicals to sediment and suspended solids and assumes that such isotherms are valid only when the chemical's dissolved water concentration is less than half of its water solubility (Karickhoff et al., 1979). EXAMS, however, does not directly monitor violations of this condition; instead, it monitors whether its current loading rates and linearized derivatives can be expected to violate this condition during its next integration step. Unfortunately, this indirect monitoring can lead to false positives that result in aborted EXAMS simulations. These false positives were particularly prevalent at the start of our simulations with moderate to high loading rates into rivers with low January discharges [e.g., South Platte River near Littleton, CO (USGS 06710000)]. To circumvent these problems, we ran all EXAMS projects twice; whereas for the first set of runs, we used our CTS-estimated aqueous solubilities, for the second set, we assigned the aqueous solubility for all chemicals to be 100 mg/L. We then merged the two resulting output sets and excluded first all simulations whose predicted dissolved water concentrations exceeded EXAMS half solubility threshold and then all duplicate simulations.

In order to access KABAM's predicted BAFs efficiently, we created a new worksheet within the model's Microsoft® Excel workbook which constructs a two-variable data table. The first column of this data table specifies $\log K_{OWs}$ ranging from 0 to 14 in increments of 0.01, and the remaining columns specify the KABAM predicted log BAFs for phytoplankton, zooplankton, filter-feeding benthic invertebrates, nonfilter-feeding benthic invertebrates, and small, medium, and large fish which correspond to trophic levels 2, 3, and 4. This data table was used not only to calculate chemical concentrations in BASS's the nonfish compartments but also to calculate chemical concentrations in nonfish compartments directly from dissolved water concentrations predicted by EXAMS.

Although BASS could have been parameterized with all of the time varying exposure files generated by EXAMS for the 114,120 possible combinations of chemicals, loading rates, and rivers generated for this study, the time required to complete the resulting BASS simulations for each of the 352 target EMAP streams and rivers on a single desktop or laptop computer would easily exceed 1.11×10^6 h or 130 years. Consequently, we adopted a simpler approach to estimate fish BAFs for the fishes and chemicals of interest. This approach relies only on the assumption that regardless of a chemical's loading rate into a river of interest, its dissolved water concentration can be treated as a constant which equals its EXAMS estimated mean annual concentration. Under this assumption, BASS only needs to be executed once for each targeted EMAP stream or river to estimate the BAFs of all chemicals in all fish therein since BAFs are independent of dissolved water concentrations when those concentrations are constant [see for example Barber (2008) or Barber et al. (2016)]. To implement this approach, we simply selected a reasonable number (n_{chem}) of chemicals having $3 \leq \log K_{OW} \leq 14$ and assumed that the dissolved water concentration of each chemical is an arbitrary constant C_{wd} . For this study, we assumed that $n_{chem} = 26$ and that $C_{wd} = 1.0$ ng/L. Because the BAFs of fish appear to become independent of $\log K_{OW}$ when $\log K_{OW} > 7$ [e.g., see Arnot and Gobas (2006)], we assumed that the $\log K_{OWs}$ of these chemicals were equally spaced within three intervals. Whereas in the first and third intervals (i.e., $3 \leq \log K_{OW} \leq 6$ and $7.5 \leq \log K_{OW} \leq 14$), $\log K_{OWs}$ were distributed in increments of 0.5, in the second interval (i.e., $6.25 \leq \log K_{OW} \leq 7.25$), $\log K_{OWs}$ are

distributed in increments of 0.25 in order to characterize more accurately the transition between $\log K_{OW}$ dependent and independent BAFs.

2.6. Metamodels for EXAMS, KABAM, and BASS outputs

2.6.1. EXAMS metamodels—Two classes of metamodels for predicting EXAMS output concentrations were developed. The first class, which uses actual or estimated loading rates to predict these concentrations, is the log-linear regression model

$$\log C_y = \alpha_0 + \alpha_1 \log Q + \alpha_2 \log_{10} L + \alpha_3 \log K_{OW} + \alpha_4 \log HLC \quad (3)$$

where C_y denotes the chemical's mean annual dissolved water (mg/L), total water (mg/L), or total sediment (mg/kg dry wt) concentration; Q denotes the river's mean annual discharge (m^3/s); L denotes the chemical's mean annual or constant loading rate (kg/h) to the river; K_{OW} is the chemical's n-octanol/water partition coefficient, and HLC is the chemical's Henry Law constant ($atm \cdot m^3 \cdot mol^{-1}$). The second class of metamodels uses the mean annual concentration in medium x (e.g., sediment) to predict that in medium y (e.g., dissolved water); these metamodels are specified by

$$\log C_y = \beta_0 + \beta_1 \log Q + \beta_2 \log_{10} C_x + \beta_3 \log K_{OW} + \beta_4 \log HLC \quad (4)$$

We used Microsoft® Excel's standard multiple linear regression tools to calculate both classes of EXAMS metamodels.

2.6.2. KABAM and BASS metamodels—In this study, steady-state chemical concentrations in aquatic invertebrates and phytoplankton/periphyton and mean annual chemical concentrations in fish were calculated using BAFs predicted by KABAM and BASS, respectively, and dissolved water concentrations predicted by EXAMS. In particular,

$$BAF_b = \frac{C_b}{C_{wd}} \Rightarrow C_b = BAF_b C_{wd} \quad (5)$$

where BAF_b is the steady-state or the mean annual BAF (L/kg wet wt) of the biota of interest; C_b is the steady-state or the mean annual concentration (mg/kg wet wt) in that biota; and C_{wd} is the chemical's mean annual dissolved water concentration (mg/L). Readers should note, however, that while Equation (5) technically defines BCFs in the case of phytoplankton/periphyton, for the convenience of presentation, we will not draw that distinction. Because observed and predicted $\log BAF_b$ for aquatic invertebrates, fish, and phytoplankton/periphyton are generally linearly dependent on $\log K_{OW}$ for chemicals having $\log K_{OW} < 7$ and essentially independent of $\log K_{OW}$ otherwise [see for example Arnot and Gobas (2006)], we developed metamodels for $\log BAF$ s predicted by KABAM and BASS

using a two-step process. In the first step, we fitted predicted log BAFs to a non-rectangular hyperbola using the nonlinear optimization package NL2SOL (Dennis et al., 1981) in order to estimate the break point where BAFs transition from being K_{OW} dependent to being K_{OW} independent. To this end, we assumed that the desired hyperbola possesses the asymptotes

$$\log \text{BAF}_b = \gamma_1 + \gamma_2 \log K_{ow} = f_1 \quad (6)$$

$$\log \text{BAF}_b = \gamma_3 = f_2 \quad (7)$$

All hyperbolas having Equations (6) and (7) as asymptotes can then be expressed as

$$(\log \text{BAF}_b - f_1)(\log \text{BAF}_b - f_2) = h \quad (8)$$

where h is a constant to be determined (see Puckle, 1868). To describe the observed or simulated relationships between $\log \text{BAF}_b$ and $\log K_{OW}$, we assumed that $h > 0$ and used the minimum root of Equation (8), i.e.,

$$\log \text{BAF}_b = \frac{f_1 + f_2 - \sqrt{(f_1 - f_2)^2 + 4h}}{2} \quad (9)$$

as our metamodel for KABAM-predicted BAFs and as our preliminary metamodel for BASS-predicted BAFs. The break point ($\log \hat{K}_{OW}$) where BAFs transition from being K_{OW} dependent to being K_{OW} independent was then calculated as the intersection of Equations (6) and (7), i.e.,

$$\log \hat{K}_{ow} = (\gamma_3 - \gamma_1)/\gamma_2 \quad (10)$$

In the second step, we then used multiple linear regressions to construct separate metamodels for BASS-predicted BAFs for chemicals having $\log K_{OW} \leq \log \hat{K}_{OW}$ and $\log K_{OW} > \log \hat{K}_{OW}$. Whereas in the former case, BASS-predicted BAFs were fitted to the log linear model

$$\log \text{BAF}_f = \delta_1 + \delta_2 \log K_{ow} + \delta_3 \log W + \delta_4 \text{TP} \quad (11)$$

in the latter case, they were fitted to the log linear model

$$\log \text{BAF}_f = \varepsilon_1 + \varepsilon_2 \log W + \varepsilon_3 \text{TP} \quad (12)$$

In both cases, W denotes the fish's mean annual body weight (g wet wt), and TP denotes the fish's average trophic position which BASS calculates using a stable isotope model which is analogous to that of Hesslein et al. (1993) [see Barber (2012b Section 2.8. Modeling stable isotopes and trophic position)].

A simple inspection of Equation (5) reveals that metamodels for the log transformed chemical concentrations in aquatic invertebrates, phytoplankton, periphyton, and fish can be obtained by simply adding either of the EXAMS metamodels for $\log C_{dw}$ [i.e., Equations (3) or (4)] to the appropriate KABAM or BASS metamodel for $\log \text{BAF}_b$ [i.e., Equations (9), (11), or (12)].

2.7. Corroboration of EXAMS and BASS metamodels

To corroborate the ability of the aforementioned metamodels to forecast actual field concentrations, we compiled a test dataset of paired sediment and fish concentrations for BFRs [i.e., polybrominated diphenyl ethers (PBDE) and 1,2,5,6,9,10-hexabromocyclododecane (HBCD)] observed in European rivers having mean annual discharges within the range of those reported for the US rivers selected here. The only criteria used to include a study was that it provided all the information needed to parameterize these metamodels with the possible exceptions of river discharges and fish trophic positions that could be provided by alternative sources. The following studies were then selected for inclusion in this dataset: Sellström et al. (1998) for the Swedish River Viskan; Eljarrat et al., 2004, Eljarrat et al., 2005 for the Spanish River Cinca; Eljarrat et al. (2007) for the Spanish River Vero; Labandeira et al. (2007) for the Spanish River Cardener; Luigi et al. (2015) for the Italian River Po; and Fliedner et al. (2016) and Stiehl et al. (2008) for the German Rivers Elbe, Rhine, and Saar. The mean annual discharges of these rivers were assigned using data reported by https://es.wikipedia.org/wiki/R%C3%ADo_Cardenerfor_River_Cardener; Lacorte et al. (2006) for River Cinca; Luther and Schanze (2009) and Subedi et al. (2012) for Rivers Elbe, Rhine, and Saar; Luigi et al. (2015) for the River Po; Eljarrat et al. (2010) for River Vero; and HELCON (2011) for River Viskan. The principal PBDEs reported in these studies were PBDE-28, PBDE-47, PBDE-100, PBDE-118, PBDE-153, PBDE-154, PBDE-183, and PBDE-209. The estimated $\log K_{ow}$ s of these BFRs ranged from 5.82 to 11.02 which spans the break point where fish BAFs transition from being K_{OW} dependent to being K_{OW} independent. Fishes sampled by these studies were bream (*Abramis brama*), bleak (*Alburnus alburnus*), barbel (*Barbus haasi*), carp (*Cyprinus carpio*), pike (*Esox lucius*), zander (*Sander lucioperca*), and wels catfish (*Silurus glanis*). Except for Fliedner et al. (2016) and Luigi et al. (2015), each study reported individual or mean fish body weights (g wet wt); mean body weights for the former studies were estimated using reported fish ages and median von Bertalanffy growth models (VBGMs) reported by the FishBase database (version 10/2016, <http://www.fishbase.org/search.php>). The theoretical ages at zero body length for these VBGMs were assigned using the following sources: Treer et al. (2003), Alp et al. (2011), Pérez-Bote

and Roso (2012), and Saylar and Benzer (2014). Predicted body lengths (cm) were then converted to body weights (g wet wt) using the appropriate FishBase length-weight calculators. Lastly, the trophic position of each fish species was assigned using the FishBase database.

The reporting units of chemical concentrations in fish varied between studies, and only Eljarrat et al. (2005) reported whole-body concentrations that could be compared directly to EXAMS-BASS concentrations. Most fish concentrations were reported as ng/g wet wt muscle, and these were converted to whole-body concentrations assuming a whole-body/fillet ratio equal to 2 (see WADOH, 2004 Table C10). Lipid-normalized muscle concentrations were first untransformed using reported lipid fractions and then converted to whole-body concentrations. Luigi et al. (2015), however, reported chemical concentrations in fish livers which were both lipid-normalized and dry-weight based. To convert these concentrations, we first used data from Eljarrat et al. (2004) to calculate a log-linear regression between wet-weight liver and muscle concentrations (C_l ng/g wet wt liver and C_m ng/g wet wt, respectively); the resulting regression was

$$\log C_m = -0.106 + 0.996 \log C_l \quad (13)$$

($r^2 = 0.815$; SE = 0.509; $n = 40$). Liver concentrations reported by Luigi et al. were then untransformed using reported lipid fractions (g lipid/g dry wt liver) and converted to wet-weight liver concentrations (ng/g wet wt liver) using their suggested conversion factor of 0.25 g dry wt liver/g wet wt liver. Using Equation (13), these concentrations were then converted to muscle concentrations which, in turn, were converted into whole-fish concentrations as previously discussed.

In addition to the aforementioned studies, we also include DDT data reported by Lacorte et al. (2006) for the Spanish Ebro river basin in our corroboration dataset. Although these authors also reported PBDE concentrations in fish and sediment, those data were aggregated such that we could not use them for metamodel corroboration. However, we could use the authors' reported DDT data for this purpose. In addition to barbel, bleak, and carp, Lacorte et al. (2006) also sampled the minnows *Achondrostoma arcasii*, and *Parachondrostoma toxostoma*, the common rudd (*Scardinius erythrophthalmus*), and goldfish (*Carassius auratus*). Importantly, this study was one of the few studies that we found that reported river and tributary mean discharges and sampled multiple fish species of the same trophic position over a large size spectrum. We converted the authors' dry-weight whole-fish concentrations into wet-weight concentrations assuming a dry-weight/wet-weight ratio equal to 0.25.

Using this dataset, we predicted each study's unmeasured dissolved concentrations from its reported sediment concentrations using an EXAMS metamodel specified by Equation (4) and then used the appropriate BASS BAF metamodel [i.e., Equation (11) or (12)] to predict the study's observed fish concentrations. We assumed that a reasonable agreement between our predicted fish concentrations and the study's observed fish concentration could be claimed if these concentrations (1) demonstrated a significant positive Pearson correlation

coefficient, (2) their means were within one standard deviation of one another, and (3) could be described with a Reduced Major Axis [RMA] regression whose slope is close to unity [see for example Rayner (1985), McArdle (2003), or Smith (2009)].

3. Results

3.1. Metamodels for EXAMS, BASS, and KABAM Outputs

For this study, we generated 114,120 EXAMS projects, and 106,302 of these projects were successfully executed by EXAMS subject to the model's assumed linear isotherm constraint (i.e., $C_{wd} = S_w/2$ for all chemicals in all environments). The 7% failure rate of our generated EXAMS projects is easily attributed to the inevitable unrealistic pairings of high loading rates of low-solubility chemicals to rivers having low mean monthly discharges. For example, it is unrealistic to have a WTW serving a population of 625,000 people release high loadings of high log K_{OW} chemicals into a river with an average monthly discharge of less than 2 m³/s [e.g., St Jones River, DE (USGS 01483700)]. Table 1 summarizes the EXAMS metamodels calculated from these simulations.

Although we generated 497,250 BAFs using the scheme outlined in Section 2.6, we elected to use only a random sample of these BAF's in order to construct the metamodels defined by Equations (11) and (12). To select this sample, we first assigned each BAF a random number that was uniformly distributed within the interval [0,1]. We then selected all BAFs having their assigned random number less than 0.025 as our sample. Table 1 summarizes the resulting metamodels.

Table 2 summarizes the metamodels for the BAFs predicted by KABAM for phytoplankton / periphyton, zooplankton, filter-feeding benthic invertebrates, and nonfilter-feeding benthic invertebrates. Although each of these metamodels has a $r^2 > 0.9996$, this does not imply that they are virtually perfect fits to KABAM's predicted BAFs. Such results only imply that the sum-of-squares due to model error (i.e., SSE) are dwarfed by the total sum-of-squares of the data (SST). Nevertheless, the maximum and minimum of the residuals for these metamodels were: 0.0220 and -0.0242 for MM 7; 0.0385 and -0.0292 for MM 8; 0.0654 and -0.0493 for MM 9; and 0.0553 and -0.0394 for MM 10.

3.2. Corroboration of EXAMS and BASS Metamodels

In Section 2.7, we outlined an approach for corroborating our metamodels for EXAMS dissolved water concentrations (Table 1, MM 4) and for BASS BAFs (Table 1, MM 5 and MM 6) that relies on being able to predict PBDE, HBCD, and DDT fish concentrations in EU rivers having mean annual discharges comparable to the US rivers studied here. Fig. 2 displays a plot of those observed and predicted fish concentrations. We identified three criteria which could be used to conclude that the aforementioned metamodels were corroborated, i.e., (1) a significant positive correlation between observed and predicted fish concentrations; (2) the means of the observed and predicted fish concentrations being within one standard deviation of each other; and (3) observed and predicted fish concentrations being described by a RMA regression whose slope is close to unity. Each of these criteria were satisfied. In particular, the Pearson correlation coefficient between the log-transformed

observed and predicted fish concentrations was 0.416 and was significant at $P < 10^{-6}$ (t -score = 8.39, $df = 336$). Similarly, the means of the log-transformed observed and predicted fish concentrations were -1.98 ($SD = 1.01$, median = -1.99 ; $n = 338$) and -1.11 ($SD = 0.964$, median = -1.25 ; $n = 338$), respectively. Lastly, the calculated RMA regression between log-transformed observed and predicted fish concentrations was

$$\log C_{f, \text{obs}} = -0.814 + 1.05 \log C_{f, \text{model}} \quad (14)$$

($r^2_{\text{adjusted}} = 0.439$; $SE = 0.753$; $n = 338$). To understand this regression's sources of variability, we first note that the sums of metamodels MM4 and MM5 and of MM4 and MM6 are actually random variables, i.e.,

$$\log C_{f, \text{model}} + e_{Cf} = \log BAF_f + e_{BAF} + \log C_{wd} + e_{Cwd} \quad (15)$$

where e_{BAF} and e_{Cwd} denote the errors associated with a fish's estimated BAF and the dissolved water concentration to which it is exposed, respectively. Because these metamodels are independent of one another, it follows that the variance of e_{Cf} equals the sum of the variances of e_{BAF} and e_{Cwd} . Consequently, one component of Equation (14)'s standard error is

$$SE_{MM} = \sqrt{SE_{BAF}^2 + SE_{Cwd}^2} \quad (16)$$

For chemicals with $\log K_{OW} \geq 6.65$ (i.e., DDT, PBDE-28, and PBDE-47) $SE_{MM} = 0.381$; otherwise $SE_{MM} = 0.341$. This result implies that approximately half of Equation (14)'s standard error can be attributed to the metamodels MM4, MM5, or MM6 while the other half can be attributed to the variability in the "observed" data. The latter, in turn, can be attributed to a variety of sources which include but are not limited to: (1) the variability in the published data due to lipid normalization, sample pooling, etc., (2) the imperfect pairing of observed fish and sediment concentrations due to spatial or temporal sampling constraints, (3) the year-to-year variations of mean annual river discharges, (4) the factors used to convert observed muscle and liver concentrations into whole-body concentrations, and (5) the fact that our metamodels are constructed to predict mean annual values rather than the observations of discrete sampling dates.

Several important observations concerning Equation (14) can be made when its dependent and independent variables are both fitted stepwise to the log linear regression model

$$\log C_{f,*} = \phi_0 + \phi_1 \log Q + \phi_2 \log_{10} C_{st} + \phi_3 \log K_{OW} + \phi_4 \log HLC + \phi_5 \log W + \phi_6 TP$$

(17)

and the top six regressions for each dataset based on their Bayesian Information Criteria [BIC see Schwarz (1978)] are analyzed. The results of these regressions are summarized in Table 3. The first observation that can be made is that Equation (14) yields virtually the same r^2_{adjusted} and SE as does the top rated empirical regressions for $C_{f,\text{obs}}$. Despite this observation, however, the coefficients of $C_{f,\text{obs}}$ and $C_{f,\text{model}}$ regressions are dramatically different with exception of their HLC coefficients which are zero for all top rated regressions. The most important of these differences are observed for their $\log W$ and TP coefficients which are negative for the $C_{f,\text{obs}}$ regressions and positive for the $C_{f,\text{model}}$ regressions. Thus, the $C_{f,\text{obs}}$ regressions predict that the fish concentrations are decreasing functions of the body weights and trophic positions of fish whereas the $C_{f,\text{model}}$ regressions predict that these concentrations are increasing functions of body weight and trophic position. This difference, however, is an artifact of fish body weights being negatively correlated ($r = -0.179$; $df = 336$; $P < 0.001$) to sediment concentrations in our assembled corroboration dataset since Eljarrat et al. (2004; 2005) demonstrated that concentrations of individual BFRs in fish from the Cinca River are indeed increasing functions of body length and therefore of body weight. The trophic magnification factors (TMFs), which correspond to the antilogarithms of TP coefficients of these regressions [see for example Fisk et al. (2001)], are also dramatically different. In particular, whereas the $C_{f,\text{obs}}$ regressions predict TMFs that vary between 0.577 and 0.587, the $C_{f,\text{model}}$ regressions predict that 1.97 TMF 2.29. These latter TMFs agree well with the PBDE TMFs reported by Brandsma et al. (2015) for the total food web of the Western Scheldt estuary, the Netherlands which averaged 2.08 (SD = 0.492, $n = 5$) for the same range of congeners considered herein (i.e., BDE-28, BDE-47, BDE-99, BDE-100, BDE-153). Although these predicted TMFs are somewhat lower than those reported by Shao et al. (2016) for the marine food web of Bohi Bay, North China, which averaged 2.44 (SD = 0.605, $n = 9$), they are also somewhat higher than those reported by Kobayashi et al. (2015) for food web of the Omuta River estuary, Japan, which averaged 1.26 (SD = 0.396, $n = 7$). The average of all of these observed TMFs is 1.94 (SD = 0.717, $n = 22$).

3.3. Estimating Instream Loading Rates with an EXAMS Metamodel

An important management/research capability for understanding the downstream fate and transport of chemicals released from WTWs or other point dischargers is the ability of the manager/researcher to estimate the effective instream loading rates of chemicals of concern at different distances downstream of their release points using observed data at those locations. This capability is also useful for estimating upstream boundary conditions for fate and transport modeling of chemical discharges from cities, WTWs, etc. along large rivers. One approach to accomplish this task is to use a metamodel of the form

$$\log L = \lambda_0 + \lambda_1 \log Q + \lambda_2 \log_{10} C_{st} + \lambda_3 \log K_{OW} + \lambda_4 \log HLC \quad (18)$$

where L , Q , and C_{st} are the river's average instream loading rate (kg/h), mean annual discharge (m^3/s), and mean annual total sediment concentration (mg/kg dry wt) at the site of interest, respectively. When we fitted the outputs of our EXAMS simulations to this equation, the resulting metamodel was

$$\log L = -4.38 + 0.904 \log Q + 0.892 \log_{10} C_{st} - 0.181 \log K_{OW} + 0.00513 \log HLC \quad (19)$$

($r^2_{adjusted} = 0.889$; $SE = 0.499$; $n = 106,302$; $P < 10^{-6}$). To test the utility of this metamodel, we used it and penta-BDE sediment concentrations reported by Stiehl et al. (2008) to estimate daily instream loading rates (L kg/d) for the German Rivers Elba, Rhine, and Saar; we then compared these rates to those derived by European Commission (EC) Sub-Group on Review of the Priority Substances List (2011). Assuming that total penta-BDE in these rivers consists only of BDE-99 and BDE-100, we predicted an average instream loading rate equal to 0.0830 kg/d ($SD = 0.0799$, $min = 0.0125$; $max = 0.296$) which compares well to the local loading rate of 0.15 kg/d reported by the aforementioned EC subgroup.

3.4. Using EXAMS metamodels for Sensitivity Analysis

The ability to analyze the sensitivity of EXAMS's dissolved water concentrations (C_{wd} mg/L), total water concentrations (C_{wt} mg/L), and total sediment concentrations (C_{st} mg/kg dry wt) with respect to each river's mean annual discharge (Q m^3/h) and with respect to uncertain chemical loading rates (L kg/h), K_{OW} , and HLC is an important feature of metamodels MM1, MM2, and M3. To see how such analyses can be performed, one must first rewrite Equation (3) in its untransformed form, i.e.,

$$C_y = 10^{\alpha_0} Q^{\alpha_1} L^{\alpha_2} K_{OW}^{\alpha_3} HLC^{\alpha_4} \quad (20)$$

This equation, in turn, can be rewritten as

$$C_i = C_0 \prod_{j=1}^4 X_j^{\alpha_j} \quad (21)$$

where C_i is the EXAMS' concentration of interest; C_0 is a constant; and X_j denotes the EXAMS parameter of concern. In this form, one can verify that the proportional change in C_i due to a proportional change q in X_j is given by

$$\Delta_{ij}(q) = \frac{C_0 \left(\prod_{k \neq j}^4 X_k^{\alpha_k} \right) (qX_j)^{\alpha_j}}{C_0 \prod_{k=1}^4 X_k^{\alpha_k}} = \frac{\beta (qX_j)^{\alpha_j}}{\beta X_j^{\alpha_j}} = q^{\alpha_j} \quad (22)$$

Table 4 summarizes the proportional changes in EXAMS's water and sediment concentrations due to a 50% decrease and increase (i.e., $q = 0.5$ and $q = 1.5$, respectively) in a river's mean annual discharge (Q) and the chemical's assumed loading rate (L), K_{OW} , and HLC. These results show that EXAMS dissolved water, total water, and total sediment concentrations are insensitive to increases or decreases in HLC. EXAMS' total water concentrations are also insensitive to changes in $\log K_{OW}$. Dissolved water concentrations, however, increase with decreasing $\log K_{OW}$ and vice versa. Lastly, total sediment concentrations increase with increasing $\log K_{OW}$ and decrease with decreasing $\log K_{OW}$.

4. Discussion

4.1. Use of ecological metamodels in HT chemical prioritization and screening

The minimally-parameterized models developed here will help advance current efforts to prioritize chemicals for further study on the basis of risk to human and ecological systems. For example, under its Chemical Safety for Sustainability (CSS) Research Program, the USEPA is developing computational approaches to combine HT hazard information from the Toxicity Forecaster (ToxCast) program with HT exposure predictions from analogous Exposure Forecasting (ExpoCast) in an effort to support prioritization of chemicals in EPA's Endocrine Disruptor Screening Program (EDSP). To date, however, much of the EPA effort has focused on developing HT human exposure predictions. Under ExpoCast, EPA has developed a statistical approach – called the Systematic Empirical Evaluation of Models (SEEM) framework-for calibrating existing human exposure models against available biomonitoring data while simultaneously (1) inferring parent exposures from the monitoring data and (2) developing consensus exposure forecasts for thousands of additional chemicals (USEPA, 2014). This approach can be applied to ecological exposure models and data with minimal modification; development of water monitoring data for use in an ecological application of SEEM is an ongoing effort under ExpoCast. Integration of the metamodels developed here into SEEM could enable joint inference of chemical loading rates from ecological monitoring data and facilitate development of ecological exposure predictions for thousands of additional chemicals for comparison with HT hazard in prioritization schema.

4.2. Other applications

Although the primary goal of this work was to demonstrate how metamodels of higher-tier simulation models can be developed to assess the fate, transport and bioaccumulation of organic chemicals in rivers for screening-level exposure assessments with limited data (i.e., the chemical's K_{OW} , Henry's Law constant, and release rates and the mean annual discharge of the receiving river), these and similar metamodels can also be developed to analyze and interpret existing field data for other research or management needs. For example, questions that can be addressed by such metamodels include:

- Given a river with a mean annual discharge Q and an observed sediment concentration S of a chemical with $\log K_{OW} = x$, what is the river's estimated instream loading rate for that chemical?
- Given a river with a mean annual discharge Q and a drinking water standard D for human or wildlife consumption, what is the maximum allowable instream loading rate of a chemical with $\log K_{OW} = x$?
- Given a river with a mean annual discharge Q and an allowable/safe fish concentration for human or wildlife consumption, what is the maximum allowable/safe instream loading rate of a chemical with $\log K_{OW} = x$?
- Given a river with a mean annual discharge Q and observed sediment concentrations for a mixture of chemicals, what is the expected critical body residue [CBR see for example McCarty and Mackay (1993), McCarty et al. (2011); or Sappington et al. (2011)] of fish of a particular body weight and trophic position in that river?
- Given a river with a mean annual discharge Q and observed loadings L of a mixture of chemicals from a POTW/WTW, what are the expected CBRs of fish in that river?

4.3. Strengths and weaknesses of metamodels

A major strength of the metamodels presented here is their ability to forecast expected long-term patterns of chemical fate, transport, and bioaccumulation in river ecosystems under relatively stable environmental conditions (e.g., rivers whose climatic and hydrological features can be adequately characterized using long-term statistics) and constant or approximately constant chemical loading rates. In this regard, they can be likened to steady-state fate, transport, and bioaccumulation models which are obtained by setting the models' governing differential equations to zero and solving the resulting algebraic system for the concentrations of interest [see for example Arnot (2009) or Kim et al. (2017)]. Unlike such steady-state models, however, metamodels can also be used to analyze the sensitivity of those concentrations in a straightforward fashion without having to designate reference parameters or forcing functions.

The metamodels presented here, however, have significant weaknesses when the assumptions of relatively stable environmental conditions and constant chemical loading rates cannot be reasonably satisfied for the temporal and spatial scales of concern. Examples of such situations include: (1) episodic releases due to accidental discharges/spills, storm-water overflows, etc.; (2) changing meteorological features associated with local or regional climate change; and (3) changing hydrological features due to channel modifications for navigation or floor control, land use/cover, regional climate change, or changing water management needs.

4.4. Concluding remarks

The metamodels described here are not intended to replace the process-based models which generated the datasets used for their construction, but rather they are explicit examples of

how the proven and accepted science of such process-based models can be incorporated into screening-level exposure assessments. Although metamodels such as the ones described can never be as flexible or as accurate as their parent models, they do represent an important addition to the tools currently used for screening-level exposure assessments that have often assessed chemical fate, transport, and bioaccumulation based only on chemical properties. The metamodels developed here demonstrate how screening-level exposure assessments can almost seamlessly integrate not only the pchem properties of the chemicals of concern but also their expected loading rates, the hydrological features of their receiving waters, and the biological characteristics of the biota therein. If the uncertainties of such screening-level exposure assessments are unacceptably large, higher-tier modeling using the parent models could then be undertaken with the knowledge and confidence that both levels of the exposure assessments are logically consistent with each other.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Integrated fate, transport, and bioaccumulation modeling of chemicals in rivers.
- Developing metamodels for high throughput and screening exposure assessments.
- Metamodels corroborated with concentrations of flame retardants in EU rivers.
- Using metamodels for model sensitivity analysis and interpretation of field data.

Figure 1.
Diagram of a metamodeling system for rapid exposure assessments in riverine ecosystems.

Figure 2. Comparison of observed PBDE, HBCD, and DDT concentrations in fish to those predicted by metamodels MM4, MM5, and MM6. The line depicted in this graph represents the Reduce Major Axis regression calculated for these data [see Equation (14)].

Table 1

Summary of metamodels for environmental concentrations and BAFs predicted by the EXAMS and BASS, respectively. Dependent variables are denoted as follows: a chemical's dissolved water concentration (C_{wd} mg/L), total water concentration (C_{wt} mg/L), total sediment concentration (C_{st} mg/kg dry wt), and bioaccumulation factor (BAF_f L/kg wet wt) in fish. Independent variables are denoted as follows: the river's mean annual stream flow (Q m³/s); the chemical's loading rate (L kg/h), octanol-water partition coefficient (K_{ow}), and Henry's Law Constant (HLC atm·m³·mol⁻¹); and the fish's mean annual body weight (W g wet wt) and average trophic position (TP dimensionless). The average break point where BAFs transition from being K_{ow} dependent to being K_{ow} independent was $\log \hat{K}_{ow} = 6.65$ (SD = 0.00761; $n = 1000$). Due to the large size of the BASS-generated BAF dataset (i.e., $n = 497,250$), only a random sample of less than or equal to 2.5% of the available data were used for metamodels MM5 and MM 6.

Metamodel ID	Metamodel Equation	$r^2_{adjusted}$	SE	n
MM 1	$\log C_{wd} = 5.59 - 0.996 \log Q + 0.992 \log L - 0.584 \log K_{ow} + 1.20 \times 10^{-3} \log HLC$	0.937	0.588	106,302
MM 2	$\log C_{wt} = 3.12 - 1.00 \log Q + 1.00 \log L + 1.45 \times 10^{-3} \log K_{ow} - 1.94 \times 10^{-3} \log HLC$	0.998	0.070	106,302
MM 3	$\log C_{st} = 4.61 - 1.01 \log Q + 0.996 \log L + 0.200 \log K_{ow} - 4.67 \times 10^{-3} \log HLC$	0.923	0.528	106,302
MM 4	$\log C_{wd} = 0.984 + 0.0117 \log Q + 1.00 \log C_{st} - 0.784 \log K_{ow} + 3.44 \times 10^{-3} \log HLC$	0.991	0.220	106,302
MM 5	for $\log K_{ow}$ $6.65 : \log BAF_f = -2.24 + 1.27 \log K_{ow} + 0.0872 \log W + 0.0839 TP$	0.986	0.311	4,057
MM 6	for $\log K_{ow} > 6.65 : \log BAF_f = 5.54 + 0.100 \log W + 0.334 TP$	0.404	0.260	7,613

Table 2

Summary of metamodels for KABAM-predicted BAFs for phytoplankton/periphyton (BAF_p L/kg wet wt), zooplankton (BAF_z L/kg wet wt), nonfilter-feeding benthic invertebrates (BAF_{nb} L/kg wet wt); and filter-feeding benthic invertebrates (BAF_{fb} L/kg wet wt). The critical $\log K_{OWs}$ (i.e., $\log \hat{K}_{OW}$) where BAFs transition from being K_{OW} dependent to being K_{OW} independent are also reported. The sample size of all regressions is $n = 1101$.

Metamodel ID	Metamodel Equations	$\log \hat{K}_{OW}$	r^2	SE
MM 7	$\log BAF_p = \frac{1}{2} \left(0.999 \log K_{OW} + 3.96 - \sqrt{(0.999 \log K_{OW} - 6.54)^2 + 0.379} \right)$	6.54	1.00	0.0111
MM 8	$\log BAF_z = \frac{1}{2} \left(1.04 \log K_{OW} + 4.25 - \sqrt{(1.04 \log K_{OW} - 7.46)^2 + 0.350} \right)$	7.15	1.00	0.0157
MM 9	$\log BAF_{nb} = \frac{1}{2} \left(1.07 \log K_{OW} + 4.07 - \sqrt{(1.07 \log K_{OW} - 7.46)^2 + 0.0350} \right)$	6.96	1.00	0.0244
MM 10	$\log BAF_{fb} = \frac{1}{2} \left(1.05 \log K_{OW} + 3.73 - \sqrt{(1.05 \log K_{OW} - 7.35)^2 + 0.0446} \right)$	6.97	1.00	0.0203

Table 3

Summary of the top six regressions obtained by stepwise fitting the dependent and independent variables of Equation (14) to Equation (17) based on their Bayesian Information Criteria (BIC). See cited equations for variable names and units. Sample size for all regressions is $n = 338$, and parenthesis numbers signify the t-scores of the indicated coefficients being zero. All regressions and BICs were calculated using the USEPA Virtual Beach 3.0.6 software (Cyterski et al., 2013).

dataset	parameter	model 1	model 2	model 3	model 4	model 5	model 6
C_{tobs}	intercept	0.143 (1.010)	0.691 (2.558)	1.615 (3.117)	1.012 (2.200)	-0.337 (-0.933)	0.208 (0.489)
C_{tobs}	$\log C_s$	0.447 (11.817)	0.454 (12.043)	0.493 (11.783)	0.484 (11.532)	0.456 (11.913)	0.463 (12.142)
C_{tobs}	$\log Q$	--	--	--	--	0.080 (1.443)	0.081 (1.464)
C_{tobs}	$\log K_{ow}$	--	--	-0.101 (-2.086)	-0.097 (-1.985)	--	--
C_{tobs}	$\log HCL$	--	--	--	--	--	--
C_{tobs}	$\log W$	-0.368 (-8.136)	-0.284 (-4.969)	-0.296 (-5.179)	-0.382 (-8.380)	-0.358 (-7.838)	-0.274 (-4.762)
C_{tobs}	TP	--	-0.232 (-2.376)	-0.239 (-2.460)	--	--	-0.232 (-2.387)
C_{tobs}	$r^2_{adjusted}$	0.421	0.429	0.435	0.426	0.423	0.431
C_{tobs}	SE	0.765	0.760	0.756	0.762	0.764	0.759
C_{tobs}	BIC	-172.021	-171.845	-170.396	-170.149	-168.292	-168.185
C_{tmodel}	intercept	4.969 (39.742)	5.102 (34.810)	4.932 (38.438)	5.107 (33.976)	5.712 (42.786)	5.841 (35.805)
C_{tmodel}	$\log C_s$	0.926 (91.813)	0.923 (90.720)	0.921 (89.404)	0.917 (88.725)	0.937 (76.884)	0.934 (75.853)
C_{tmodel}	$\log Q$	--	-0.023 (-1.731)	--	-0.030 (-2.203)	--	-0.022 (-1.369)
C_{tmodel}	$\log K_{ow}$	-0.590 (-50.316)	-0.589 (-50.427)	-0.595 (-49.622)	-0.594 (-49.817)	-0.595 (-41.911)	-0.595 (-41.935)
C_{tmodel}	$\log HCL$	--	--	--	--	--	--
C_{tmodel}	$\log W$	0.062 (4.511)	0.059 (4.285)	--	--	0.168 (12.714)	0.166 (12.392)
C_{tmodel}	TP	0.295 (12.573)	0.295 (12.619)	0.359 (18.832)	0.356 (18.683)	--	--
C_{tmodel}	$r^2_{adjusted}$	0.964	0.964	0.962	0.962	0.947	0.947
C_{tmodel}	SE	0.183	0.182	0.188	0.187	0.221	0.221
C_{tmodel}	BIC	-1131.511	-1128.715	-1117.340	-1116.395	-1006.366	-1002.434

Table 4

Summary of the proportional changes (ϕ) in EXAMS' EECs due to a 50% decrease or increase (i.e., $q=0.5$ or $q=1.5$) in a river's mean annual stream flow (Q m³/s) or mean annual loading rate (L kg/h) or in a chemical's assumed octanol-water partition coefficient (K_{OW}) or Henry's Law Constant (HLC atm·m³·mol⁻¹). Concentrations are denoted as follows: dissolved water concentrations (C_{wd} mg/L), total water concentrations (C_{wt} mg/L), and total sediment concentrations (C_{st} mg/kg dry wt).

Concentration	q	Q	L	K_{OW}	HLC
C_{wd}	0.5	1.99	0.500	1.5	1.00
C_{wt}	0.5	2.01	0.500	1.00	1.00
C_{st}	0.5	2.01	0.500	0.87	1.00
C_{wd}	1.5	0.67	1.50	0.79	1.00
C_{wt}	1.5	0.67	1.50	1.00	1.00
C_{st}	1.5	0.66	1.50	1.08	1.00