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Trophic Magnification of Organic Chemicals: A Global Synthesis

D.M. Walters,*[,†] T.D. Jardine,[‡] B.S. Cade,[†] K.A. Kidd,[§] D.C.G. Muir,[∥] and P. Leipzig-Scott[†]

[†]U.S. Geological Survey, Fort Collins Science Center, 2150 Centre Avenue, Building C, Fort Collins, Colorado 80526, United States

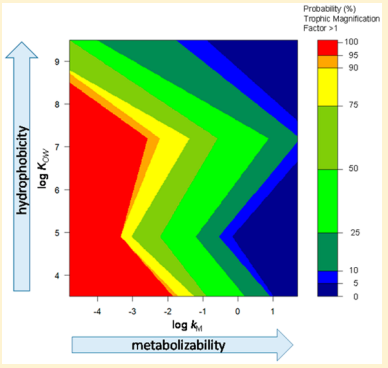
[‡]University of Saskatchewan, Toxicology Centre, 44 Campus Drive, Saskatoon, Saskatchewan S7N 5B3, Canada

[§]University of New Brunswick, Canadian Rivers Institute and Biology Department, 100 Tucker Park Road, Saint John, New Brunswick E2L 4L5, Canada

[∥]Environment and Climate Change Canada, Aquatic Contaminants Research Division, Burlington, Ontario L7S 1A1, Canada

Supporting Information

ABSTRACT: Production of organic chemicals (OCs) is increasing exponentially, and some OCs biomagnify through food webs to potentially toxic levels. Biomagnification under field conditions is best described by trophic magnification factors (TMFs; per trophic level change in log-concentration of a chemical) which have been measured for more than two decades. Syntheses of TMF behavior relative to chemical traits and ecosystem properties are lacking. We analyzed >1500 TMFs to identify OCs predisposed to biomagnify and to assess ecosystem vulnerability. The highest TMFs were for OCs that are slowly metabolized by animals (metabolic rate k_M < 0.01 day^{-1}) and are moderately hydrophobic (log K_{OW} 6−8). TMFs were more variable in marine than freshwaters, unrelated to latitude, and highest in food webs containing endotherms. We modeled the probability that any OC would biomagnify as a combined function of K_{OW} and k_M. Probability is greatest (~100%) for slowly metabolized compounds, regardless of K_{OW}, and lowest for chemicals with rapid transformation rates (k_M > 0.2 day^{-1}). This probabilistic model provides a new global tool for screening existing and new OCs for their biomagnification potential.



INTRODUCTION

Ubiquitous use of organic chemicals (OCs) threatens ecosystem health at regional and continental scales.[1] Chemical pollution is one of nine human-related activities threatening to push the earth beyond established "planetary boundaries" (the safe operating space for humanity with respect to Earth systems).[2] Quantitative thresholds are established for boundaries such as climate change and nutrient pollution (i.e., CO_2 concentration and phosphorus loading), but thresholds for chemical pollution (e.g., amount of OCs emitted or their accumulation in the environment) remain undefined.[2,3] Efforts to explore this boundary are stymied by large numbers of emitted chemicals and chemical mixtures, by complex interrelationships between emissions, environmental concentrations and exposures among ecosystems, and by their wide-ranging effects on biota.[4] A key challenge in this endeavor is to develop the knowledge base and techniques to screen chemicals that are predisposed to becoming global problems before they are emitted.[5,6]

The persistence (P), bioaccumulation potential (B) and toxicity (T) of synthetic chemicals dictate their risk to the environment and humans. Long-lived compounds that increase to potentially toxic concentrations along food webs (biomagnification) face scrutiny from regulators because of their likely adverse impacts at multiple levels of biological organization.[7] While many lines of evidence are used to classify substances as bioaccumulative, there has been a recent shift toward Trophic Magnification Factors (TMFs; per trophic level (TL) change in the log-concentration of a chemical) as the most conclusive evidence of biomagnification in food webs.[8−10] TMFs are calculated using stable isotope ratios of nitrogen ($^{15}N/^{14}N$; expressed as $\delta^{15}N$) as an indicator of TL because $\delta^{15}N$ increases predictably (approximately 3.4‰) with each trophic step.[11] OCs that have been in commerce for sufficient time can be measured in various food web components across diverse systems, allowing for calculation and broad-scale comparisons of TMFs. The many studies conducted over the past two decades show variable TMFs among and within OCs and offer an opportunity to synthesize these efforts to yield new insights into key drivers of contaminant biomagnification (such as was recently conducted for another priority pollutant, mercury)[12] and to contribute to screening techniques for PBT chemicals[5,6].

Various factors are proposed to govern the biomagnification of OCs. Chemical properties, notably hydrophobicity or fugacity capacity in different media,[13] as estimated by the octanol−water partition coefficient (K_{OW}), are key predictors of bioconcentration factors (BCFs, the ratio of the chemical in an organisms to that in water)[14] and TMFs,[15] typically with higher

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TMFs for higher K_{OW} chemicals. In contrast, chemicals with high metabolic biotransformation rates (k_M),[16] are less likely to biomagnify in higher-trophic-level organisms even if they have molecular structures (and K_{OW}) conducive to partitioning to lipids.[17] Biological factors believed to be important include growth rates linked to ambient temperatures (i.e., latitude)[18] and energetic requirements of organisms, with endothermic animals more likely to biomagnify chemicals than ectothermic species[19,20] because the latter have greater food consumption rates for a given body size.[21] It is unknown whether there are global patterns of TMFs that can be explained by both chemical properties and their receiving environments and food webs.

To assess the relative importance of chemical, ecological, biological, and environmental factors in determining TMFs, we assembled a database of published values from studies beginning in 1992. We first identified major gaps in the current understanding of OCs by highlighting where more TMF studies are needed and which compound classes are underrepresented. We then developed a global statistical model of TMFs for OCs as a function of their K_{OW} and k_M. Based on earlier synthetic analyses of BCFs and bioaccumulation factors (BAFs, accumulation of chemicals in organisms by all exposure pathways)[14], we predicted peaks in TMFs near log $K_{OW} \approx 7$. This is the approximate threshold above which large molecules can exhibit declining bioavailability and dietary uptake efficiency (ref 22 but see ref 23). Further, we predicted a negative relationship between TMF and k_M. Because k_M accounts for a large amount of residual variation in BAF vs log K_{OW} relationships,[24] we developed a global multivariate model of all TMFs using both log K_{OW} and log k_M. Next, we developed separate TMF models for different ecosystems (freshwater versus marine), climates (tropical, temperate, and Arctic), and food web types (food webs containing only ectotherms vs those that also had endotherms) to explore context-dependent patterns in biomagnification. We predicted, for example, that food webs containing endotherms, as are commonly studied in Arctic marine environments, would have higher TMFs. Finally, we used the empirical relationship between log K_{OW}, log k_M, and TMFs to develop a probabilistic model calculating the likelihood that any OC within the observed range of log K_{OW} and log k_M will biomagnify if released to the global environment.

MATERIALS AND METHODS

We tested whether compound K_{OW} and k_M, food web type (presence of endotherms and/or ectotherms), climate setting (tropical, temperate, Arctic), and ecosystem type (freshwater or marine) affect TMFs for OCs. TMFs are calculated as the antilog of the slope of the log or ln [contaminant] vs TL relationship, where TL is derived from $\delta^{15}N$ (ref 11 and Supporting Information (SI) Methods). We screened the literature for TMF studies published between 1992 and 2013 (see SI Methods for search criteria). A full description of criteria for inclusion or exclusion from the analysis is provided in the SI Methods. Our approach yielded 69 studies for 481 chemicals belonging to 10 broad classes of organic compounds (Table S1). Of these, we found $n = 1591$ TMF values for which we could obtain log K_{OW} values and $n = 1533$ values with both log K_{OW} and k_M values. Details for collecting K_{OW} and k_M values are provided in SI Methods. Briefly, in most cases we obtained K_{OW} values directly from the TMF studies. When K_{OW} was not reported, we retrieved it from either other published sources (e.g., ref 25), from online databases such as ChemSpider (http://www.chemspider.com/), or by using KOWWIN applications within the U.S. EPA's EPISuite 4.1 (Estimations Program Interface; http://www.epa.gov/oppt/exposure/pubs/episuite.htm). For compound-specific k_M, we used values standardized for a 10 g fish, obtaining median estimates from a summary database[16] when possible and the BCFBAF function in EPIsuite 4.1 to estimate the remainder, drawing structures as necessary. Here we used k_M values derived solely for one group of organisms (fish), but k_M values can vary widely across organisms included among the many TMF studies in this meta-analysis (e.g., endotherms have higher metabolic capabilities than fish). However, k_M has not been measured for the full range of organisms such as invertebrates and marine mammals. Thus, we use k_M within our modeling framework as a surrogate for the overall metabolizability of a compound by various types of organisms within and among food webs. These k_M values span a large gradient (>6 orders of magnitude) of metabolizability among chemicals included in the analysis.

We categorized TMF studies as occurring in either freshwater (rivers, wetlands, and lakes) or marine (marsh, estuarine, brackish, and offshore) ecosystems. Climate setting was categorized as Arctic (>60° latitude), temperate (30−60°) or tropical (<30°), and food web type as "cold" (those with ectotherms only), "warm" (those with endotherms only), or "whole" (those containing ectotherms and endotherms).[15]

Statistical Analyses. We used quantile regression[26,27] to assess relationships of $\log_{10}$ TMF with $\log_{10} K_{OW}$, $\log_{10} k_M$, and environmental and ecological factors (ecosystem type, climate, and food web type). Quantile regression is useful for data sets where the response variable (TMF in this case) demonstrates a high degree of variability, and we used this approach to determine if the response of TMF was similar across the full range of the TMF distribution (e.g., the median and upper and lower edges) and to determine if these trends were consistent among ecosystems, climates, and food webs. We developed models for the global data set, a two-group classification of marine and freshwater ecosystems, and a four-group classification of freshwater temperate cold, marine temperate cold, marine temperate whole, and marine Arctic whole food webs as they allowed estimation with sufficient observations in each group.

For each of these classifications, we estimated $\tau \in \{0.05, 0.10, 0.25, 0.50, 0.75, 0.90, \text{and } 0.95\}$ quantiles in the linear quantile regression package "quantreg" for the R statistical environment.[28] Our initial estimates of how $\log_{10}$TMF changed with $\log_{10} K_{OW}$ for the global data set suggested that piecewise linear relationships with different slopes changing around $\log_{10} K_{OW} = 5$ and 7 were reasonable approximations (SI Figure S1). Our estimates pooled all observations and used a linear quantile smoothing spline estimator that optimized the number and location (with the smoothing parameter $\lambda = 1$) of knots (e.g., break points or thresholds) in the splines independently for each quantile.

Based on these initial estimates, we determined that a simple linear b-spline function that had common knots for all seven quantiles could be estimated (SI Figure S1). We used b-splines in the conventional linear quantile regression model, trying various combinations of knots in a neighborhood of values around $\log_{10} K_{OW}$ common to all seven quantiles (model 1, SI Figure S2). We compared b-spline quantile estimates with Akaike Information Criterion (AIC) to select a model with common knot values across quantiles that provided estimates that were close to optimal (minimizing AIC) across all seven

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quantiles.[29] Next, we estimated linear quantile regression models for the global data set with $\log_{10} k_M$ as a predictor (model 2, SI Figure S3), and then by including both the linear $\log_{10} k_M$ predictor and the b-spline predictors for $\log_{10} K_{OW}$ (model 3, SI Figure S4). Though there is a general negative relationship between $\log_{10} k_M$ and $\log_{10} K_{OW}$,[16] the correlation of these two variables in our data set was low ($r = -0.23$), providing multiple regression estimates that were almost an orthogonal combination of the separate linear relationships for the two predictors. We compared these three models with AIC differences (ΔAIC scaled from the null model with just an intercept) by τ and computed coefficients of determination (R^1) for the quantile estimates to determine the proportion of variation explained by the modeled quantiles (SI Figure S5).

After establishing the model framework for the global data set, we estimated quantile regression models with the same choice of knots for b-splines of $\log_{10} K_{OW}$ across multiple groups classified by environmental factors (marine versus freshwater and for the four combinations of environment, climate and food web type as described above). This was done in a common model by including the groups, the linear b-spline functions of $\log_{10} K_{OW}$ and linear $\log_{10} k_M$ predictors, and their interactions. This allowed separate linear relationships between $\log_{10}$TMF and $\log_{10} K_{OW}$ and $\log_{10} k_M$ for each group, but with the constraint that the knots in the b-spline functions were held constant across groups to facilitate statistical comparisons. Improvements in model fit by grouping data according to environmental factors were assessed by comparing AIC values (ΔAIC) by quantile (SI Figure S5). Because quantiles are equivariant to monotonic transformations such as $\log_{10}$ (TMF), it is possible to back-transform estimates made in the transformed scale to the original scale (TMF) without bias or loss of information.

Because of the regulatory importance of TMF > 1,[10] we graphed contours of the probability of TMF > 1 for combinations of $\log_{10} k_M$ and $\log_{10} K_{OW}$ for the various compounds and quantiles using the global data set. These probabilities are based on the estimated proportion of the cumulative distribution with TMF > 1 ($\log_{10}$ TMF > 0) conditional on $\log_{10} k_M$ and $\log_{10} K_{OW}$ provided by the quantile estimates ($\tau \in \{0.05, 0.10, 0.25, 0.50, 0.75, 0.90, \text{and } 0.95\}$), where $1 - \tau$ is the proportion of the cumulative distribution exceeding the τth quantile estimate. These upper proportions of the cumulative distribution provide distribution-free, lower one-sided $(1 - \tau) \times 100\%$ prediction intervals of TMF for a single compound at a given combination of $\log_{10} k_M$ and $\log_{10} K_{OW}$ values based on the estimated quantile regression model. Our contour graphs show where the quantile estimates exceed TMF = 1 and thus, by definition, where the lower bounds of the $(1 - \tau) \times 100\%$ lower prediction intervals for TMF were >1. For example, the 95% probability contour includes the combinations of $\log_{10} k_M$ and $\log_{10} K_{OW}$ where $\tau = 0.05$ quantile estimates of TMF were >1. The interpretation of the empirical cumulative distribution function estimated by the quantiles as probabilities is predicated on the assumption that sampling frequencies approximate those that would be obtained under random sampling, a condition that is violated to an unknown degree in any meta-analysis.

RESULTS

Nearly all TMF studies were in the northern hemisphere (only two in the southern hemisphere), with studies concentrated in east Asia, northern and eastern Europe, and eastern North America (SI Figure S6). Most studies were in temperate climates (89%), followed by Arctic climates (9%), with only 2% in the tropics. The distribution of TMFs among compound classes was highly skewed (SI Figure S7). Approximately half were for polychlorinated biphenyls (PCBs, $n = 769$), with only a handful of measurements for other classes such as pharmaceuticals and personal care products or alkylphenols.

Relationships Among TMF, K_{OW}, and k_M. A piecewise linear b-spline model with knots at $\log_{10} K_{OW} = 4.9$ and 7.2 was the best model for estimating changes in $\log_{10}$ TMF with $\log_{10} K_{OW}$, with common breakpoints across all quantiles (Figure 1A and SI Figure S1). These estimates provided relatively homogeneous changes in $\log_{10}$TMF with $\log_{10} K_{OW}$ across the full range of observations, although with considerable variation in TMFs ($R^1 = 0.13$ at lower quantiles to $R^1 = 0.06$ at higher quantiles), increasing to a well-defined peak in TMF at $\log_{10} K_{OW} = 7.2$ (Figure 1A and SI Figure S1). There were negative rates of change in TMFs when log10 K_{OW} was <4.9 (Figure 1A, SI Figure S1). Lower quantiles showed a larger decline per unit K_{OW} than higher quantiles, but the quantiles were generally negative with confidence intervals well below zero except for the higher quantiles (SI Figure S2). These declines were subtle (10−30%, ΔTMF ≈ 0.1−0.3), and lower data density at the bottom range of K_{OW} values may limit the degree to which these relationships are generalizable compared to compounds with higher K_{OW}. A linear function of $\log_{10} k_M$ provided estimates that explained significant variation in TMF across quantiles, with negative changes in $\log_{10}$ TMF with increasing $\log_{10} k_M$ for all quantiles (Figure 1B). However, the TMF model that combined the negative linear relation of $\log_{10} k_M$ with the b-spline function of $\log_{10} K_{OW}$ (Figure 1C) explained a greater proportion of variation in quantiles (R^1 = 0.32 at lower quantiles to $R^1 = 0.11$ at higher quantiles) than either K_{OW} or k_M did individually, and this was a better supported model based on AIC (SI Figure S5). OCs with a combination of moderate hydrophobicity (log $K_{OW} \approx 6-8$) and slow biotransformation rates ($\log_{10} k_M < \approx -1$; $k_M < \approx 0.1$ day^{-1}) consistently biomagnified (Figure 1C and Figure 2). Uncertainty in estimates was lower for high TMFs, which had narrower prediction intervals (where mesh panels converge in Figure 1C) than lower TMFs (where mesh panels diverge in Figure 1C).

Estimates of TMF as a function of $\log_{10} K_{OW}$ and $\log_{10} k_M$ were improved by incorporating ecosystem type (marine and freshwater) and calculating separate relationships with the two predictors between the groups (SI Figure S8). TMFs in freshwaters were less variable and had fewer extreme values than marine systems, but the vast majority of freshwater TMFs were >1 (typically between 1 and 10, Figure 2 and SI Figure S8). Contour plots of the median $\log_{10}$ TMF estimates across combinations of $\log_{10} k_M$ and $\log_{10} K_{OW}$ indicated that TMFs for marine food webs had greater negative changes with $\log_{10} k_M$ and were more sensitive to changes in $\log_{10} K_{OW}$ than TMFs for freshwater food webs (Figure 2 and SI Figure S8).

A four-group classification of ecosystem type, climate setting, and food web type (marine temperate whole, marine temperate cold, marine Arctic whole, and freshwater temperate cold) further refined the model. The four-group model increased the proportion of variation in TMF quantiles explained across compounds to 41% ($R^1 = 0.41$) at lower quantiles and to 27% ($R^1 = 0.27$) at higher quantiles and was the best model according to AIC (SI Figure S5). A preponderance of high TMFs in marine systems were associated with whole food webs

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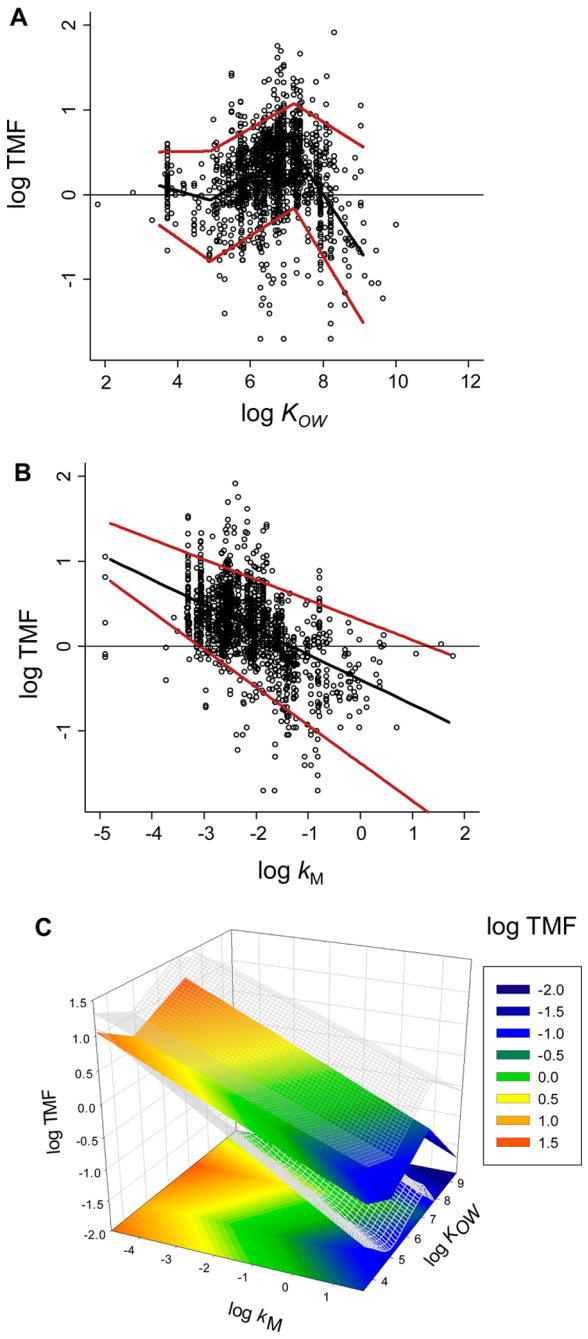

Figure 1. Estimated quantiles (0.95 = upper red, 0.50 = black, 0.05 = lower red lines) of $\log_{10}$ TMF as (A) a linear b-spline function of $\log_{10}$ K_{OW} with knots at $\log_{10}$ K_{OW} = 4.9 and 7.2, n = 1,591; (B) a linear function of $\log_{10}$ k_M, n = 1,533; and (C) a linear b-spline function of $\log_{10}$ K_{OW} (same knots) plus a linear function of $\log_{10}$ k_M for n = 1,533 for all studies combined. Black horizontal lines in A and B shows TMF = 1; values >1 indicate biomagnification. In C, the colored 3D surface shows the median (τ = 0.50) TMF; gray 3D grids are the 0.05 and 0.95 quantiles. Color shading on the bottom of C is a 2D contour plot of TMFs for the 0.50 quantile (z dimension represented as colored contours).

that include endotherms (marine Arctic whole and marine temperate whole food webs, Figure 2 and SI Figure S8). For example, Arctic whole food webs had the highest TMFs among food web types, and nearly all observations indicated biomagnification (Figure 2 and SI Figure S8). Though these food webs had the highest overall TMFs, we found no effect of latitude on TMFs, whether considering all food webs or freshwater food webs alone (SI Results and SI Figure S9, Table S2). Whole food webs typically had higher TMFs than cold food webs for a given compound regardless of latitude (SI Figures S9 and S10). This suggests that differences in TMFs we observed among climate groupings for the entire data set are likely driven by differential composition of the food webs (e.g., food webs that included endotherms) rather than any growth or physiological changes associated with temperature differences (e.g., slower growth rates at colder temperatures). Marine temperate cold food webs had fewer high TMF values than marine temperate whole food webs, and most of the very low TMFs were measured in this former category (Figure 2 and SI Figure S5). However, variability in TMFs for marine temperate cold food webs was quite high; for example extreme high and low TMFs were found where $\log_{10}$ K_{OW} ≈7 (SI Figure S8). In contrast, TMFs in freshwater temperate cold food webs were less variable (TMF typically between 1 and 10), and most observations indicated biomagnification (Figure 2 and SI Figure S8). Few freshwater studies were from tropical or Arctic climates or for whole food webs, and "freshwater" and "freshwater temperate cold" models were virtually indistinguishable (Figure 2).

Probability of OCs Biomagnifying in Food Webs. Based upon the estimated quantiles of the distribution of observations, we calculated the probability of an OC having TMF > 1 for all combinations of $\log_{10}$ K_{OW} and $\log_{10}$ k_M (Figure 3). Slowly biotransformed OCs with k_M < 0.01 d^{-1} ($\log_{10}$ k_M < −2) consistently biomagnified (probability 75−100%, red and yellow shading in Figure 3) except for the most hydrophobic compounds ($\log_{10}$ K_{OW} > 8). Examples of OCs with a high probability of biomagnifying include PCBs, particularly heavier molecular weight congeners with ≥6 chlorine atoms, and very heavy polybrominated diphenyl ethers (PBDEs, congeners 196, 197, 203, and 205−208) (SI Table S1). At the other end of the spectrum, rapidly biotransformed OCs with k_M > 3.2 d^{-1} ($\log_{10}$ k_M > 0.5), such as some of the phthalates, had a low probability of biomagnifying (probability ranging from ≈0−10%, blue and purple shading in Figure 3). Between these extremes is a large combination of chemical conditions with a substantial probability of TMFs > 1 (yellow and green shading in Figure 3). For midrange $\log_{10}$ k_M values, the increasing importance of $\log_{10}$ K_{OW} in predicting OCs with TMFs > 1 is apparent as the right-pointing chevron patterns corresponding with $\log_{10}$ K_{OW} at 7.2.

DISCUSSION

Gobas et al.[10] proposed that TMFs are the gold standard for B assessment. However, after more than two decades of research, integrating TMFs into regulatory and risk management decision-making remains a challenge.[9,15] A major hurdle is the lack of well-designed and consistent studies to assess changes in TMFs among different OCs, across large spatial scales, and among ecosystems.[8] We found that TMFs do vary predictably with K_{OW} and k_M, albeit with considerable variation, for a wide range of OCs and OC classes. This is similar to findings for BCFs and BAFs, which have a long history in B assessment supporting chemical regulation and risk assessments.[14] Beyond these effects of K_{OW} and k_M, major differences in TMFs related to ecosystem characteristics emerged. TMFs in freshwaters (dominated by cold food webs in temperate climates) were relatively invariant and largely conform to the median TMF response to K_{OW} and k_M at the global scale. In

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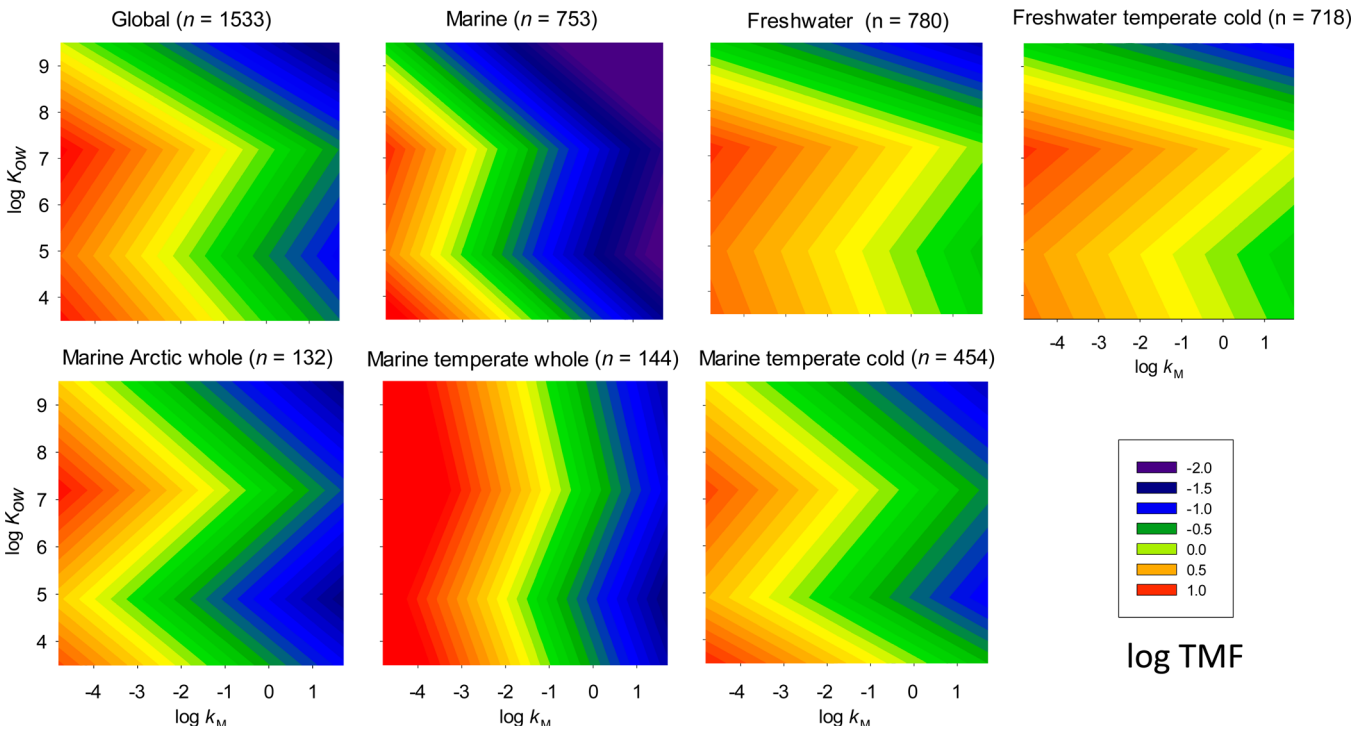

Figure 2. Contour plots illustrating the relationship between $\log_{10} k_M$ (x axis) and $\log_{10} K_{OW}$ (y axis) with TMFs (z dimension represented as colored contours). TMFs are mapped separately at the global scale, by ecosystem type (freshwater and marine), and for different food web types (e.g., marine Arctic whole). Data represent the median (τ = 0.50) TMF value as described in Figure 1.

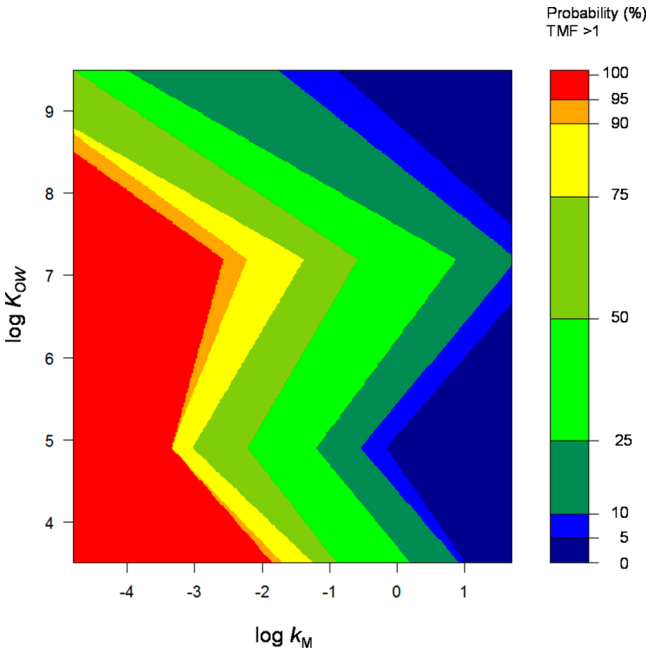

Figure 3. A 2D contour plot illustrating the probability (%) of TMF > 1 for any OC based upon its combination of $\log_{10} k_M$ and $\log_{10} K_{OW}$ values. Hot colors (red, orange, and yellow) indicate a high probability of TMFs > 1 and cool coolers (greens, blues) indicate a low probability of TMFs > 1 based on the upper, 1-sided $(1 - \tau) \times 100\%$ prediction intervals.

contrast, TMFs in marine systems were highly variable and account for the majority of "extreme" observations near the margins of the TMF distribution. Unusually high TMFs occur in marine food webs containing endotherms, regardless of climate, whereas unusually low TMFs occur primarily in marine temperate food webs containing only ectotherms.

As we predicted in our initial hypothesis, TMFs peaked around $\log_{10} K_{OW} \approx 7$ regardless of ecosystem attributes. For the 253 chemicals with $\log_{10} K_{OW}$ ranging from 6 to 8, 187 (74%) had TMFs > 1. OCs with $\log_{10} K_{OW} < 6$ or >8 were equally likely to demonstrate biodilution (TMFs < 1) or biomagnification in food webs. These patterns are consistent with prior findings that processes such as bioconcentration and respiration are critical for regulating uptake of less hydrophobic OCs.[14,30] Dietary uptake is the dominant process for compounds with midrange K_{OW}s, and these significant, positive increases in TMF or BAF to $\log_{10} K_{OW} \approx 7$ are observed across modeling studies, laboratory experiments, and field studies.[14,15,19,31−33] The importance of dietary uptake of these chemicals with $\log_{10} K_{OW}$ between 6 and 8 is manifest in much stronger relationships in the OC vs TL models used to calculate TMFs.[15] The declining TMF values at higher K_{OW}s that we observed are likely due to reduced intestinal absorption of very large molecules,[22] though much remains to be learned about uptake and elimination of these hydrophobic molecules.[23] As predicted, slowly metabolized OCs were prone to biomagnify across food webs, confirming that biotransformation is a key process regulating the bioaccumulation potential of OCs.[16]

Some variation in the TMF-$\log_{10} K_{OW}$ and $\log_{10} k_M$ relationship was related to ecological factors such as food web type. High TMFs in whole food webs can be explained in part by attributes of individual organisms, food web structure, and differences in chemical behavior in air or water. Food webs including endotherms tend to be longer (containing multiple predator trophic levels), thus increasing the likelihood of detecting a significant, positive slope in the OC versus TL relationship.[8,11] Organisms in Arctic food webs have more lipid-rich diets than those in warmer climates and are often longer-

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lived, both of which increase OC bioaccumulation and trophic transfer.[30] Adult birds and large mammals generally have a combination of efficient digestion[22] and negligible growth, and empirical data and models show that these types of organisms have biomagnification factors 1−2 orders of magnitude higher than aquatic animals (e.g., invertebrates and fish) with less efficient digestion and rapid growth.[21] Finally, chemicals with relatively low K_{OW}s but high octanol-air partition coefficients (K_{OA}) biomagnify to a higher degree in air-breathing organisms owing to low respiratory elimination rates.[33] Compounds with this combination of K_{OW} and K_{OA} in our data set include hexachlorobenzene and oxychlordane, and these demonstrated correspondingly high TMFs in whole food webs (TMF range hexachlorobenzene 0.5−12.3; oxychlordane 5.6−26.7).

TMFs in freshwater food webs generally described the median response for the global TMF data set, whereas TMFs for marine food webs were much more variable. It was difficult to assess the effect of ecological factors on TMFs in freshwaters, as the majority of TMFs were measured for a single category (freshwater temperate cold food webs). However, sufficient sample sizes were available to contrast marine and freshwater temperate cold food webs. Low TMFs in freshwater food webs were typically associated with cyclic methyl siloxanes, polychlorinated dibenz-(p)-dioxins and -dibenzofurans (PCDD/Fs), as well as PBDEs and other brominated flame retardants. High TMFs in freshwater food webs were dominated by a few PCBs (CBs 118, 138, and 153) and organochlorine pesticide breakdown products (DDE and oxychlordane). The largest TMFs in marine temperate food webs were measured for a broad suite of PCBs along with PBDEs (47 and 49), the latter of which had consistently low TMFs in freshwater systems. The very low TMFs in marine systems were dominated by PAHs, which are more easily metabolized than other chemical classes for a given range of K_{OW}s.[17]

Our findings suggest that metabolic biotransformation rate (k_M) may be even more important than hydrophobicity (K_{OW}) in driving biomagnification of OCs. For example, more rapidly metabolized compounds ($\log_{10} k_M > -2$) such as Octa- and Hepta-chlorinated PCDD/Fs[17] had TMFs < 1 despite having K_{OW}s in the range where TMFs peak. Both BCF and BAF are highly sensitive to k_M, leading to ranges of several orders of magnitude for a given K_{OW}, particularly for larger compounds ($\log_{10} K_{OW} > 5$)[14,24]). We observed the same effect for TMFs, with considerable scatter in the TMF vs log K_{OW} relationship that was related to differences in k_M. Of the 143 compounds with mean TMF > 1, only two had $k_M > 0.2$ d^{-1} ($\log_{10} k_M > -0.7$), consistent with earlier thresholds above which biomagnification does not occur in fish.[14] These results reinforce the importance of including k_M in bioaccumulation models,[24] and highlight the potential application of k_M in screening-level risk assessments for new chemicals.[6]

Several sources of uncertainty could have contributed to variation observed in our TMF models. Foremost is the uncertainty related to estimates of k_M and our application of k_M within our modeling framework. We used fish k_M values derived using kinetic mass balance models[16,34] and normalized to a 10 g fish at 15 °C (the approximate median values of data used to parametrize the model). Uncertainty in the estimates associated with method calculations vary by approximately 1−2 orders of magnitude, which is on par with variation observed among fish species and between routes of exposure (water vs diet).[16] Here, we extrapolated fish k_M values to entire food webs comprised of disparate organisms including endotherms, which have higher metabolic transformation rates than fish. An underlying assumption of our modeling framework is that these k_M values represent intrinsic properties of the chemicals themselves rather than properties of a particular food web or of the varied organisms comprising that food web. Our finding that k_M was a robust predictor of TMFs both at the global scale and among different food web categories suggests that k_M can be scaled from species to ecosystems, similar to the requirement of scaling k_M values for consistent application of mass balance bioaccumulation models.[16] As with k_M values, considerable uncertainty is associated with accurately estimating K_{OW}. Reported values for a given OC may differ by several log units,[35] and K_{OW} is particularly difficult to measure for very hydrophobic compounds.[23]

Other sources of uncertainty are related to the methods used to calculate the TMFs themselves. For example, disproportionate sampling of food webs affects the slope of the model used to calculate TMFs, and many TMF studies are heavily weighted to higher TLs (e.g., fish, birds, and mammals) compared to lower-TL taxa.[8] Another source of uncertainty involves the use of a constant trophic enrichment factor (TEF, usually 3.4‰) to calculate TL, a key determinant of TMF (Supporting Information eqs 2−5, ref 11). Actual TEFs can vary widely among consumers and food webs,[19,36,37] and violating the assumption of constant TEF can lead to over- or under-estimation of TMFs.[8,9,11,12,15] In addition, we focused on relatively few broad categories of environmental and ecological factors (marine vs freshwater, climate setting, and food web type), but other ecosystem characteristics such as primary productivity, physicochemical properties (e.g., dissolved organic carbon concentration), spatial heterogeneity of contamination, and animal movements potentially affect contaminant uptake and accumulation in food webs).[8,14,38−40] These variables were not systematically reported among studies, limiting our ability to assess their impact on TMFs. It is also possible that the analysis presented herein suffered due to inherent biases related to geography and the types of compounds studied. As an example, very few studies on freshwater food webs were from tropical or Arctic climates or on systems with endotherms, so our models for the "freshwater" and "freshwater temperate cold" groupings were virtually indistinguishable. Studies from the southern hemisphere, tropical systems, and warm food webs were also underrepresented. Finally, well-studied "legacy" OCs such as PCBs and organochlorine pesticides dominated the data set (accounting for a combined 1025 observations), and more research is clearly needed on emerging contaminants such as pharmaceuticals and personal care products. It is understandable that legacy chemicals have received more emphasis than other, newer OCs, and the numerical dominance of legacy OCs in the analysis could potentially bias our modeling results. However, it is important to note that the PCB and organochlorine pesticide classes include myriad different chemicals that span much of the observed range of $\log_{10} k_M$ (−3.58 to −0.37) and $\log_{10} K_{OW}$ (2.7−8.4) used to model TMF in our analysis. As a check on whether PCBs alone might be unduly influencing our modeled relationships, we estimated the global models for $\log_{10} k_M$, $\log_{10} K_{OW}$, and $\log_{10} k_M + \log_{10} K_{OW}$ eliminating all PCBs (new n = 822). Similar changes in TMF distributional patterns were observed as when all compounds were included, and estimated regression coefficients were similar (results not shown).

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Given the above limitations and the experience of handling >1500 TMF observations, we have some recommendations for future TMFs studies. Because of uncertainties in food web structure, the choice of a single organism to characterize the baseline $\delta^{15}N$ of ecosystems can lead to inaccurate TLs in complex food webs where multiple energy pathways (e.g., benthic vs pelagic carbon) exist. To account for this possibility, studies should include a benchmark chemical that consistently exhibits biomagnification[8,9] which would ensure that all organisms are deriving the majority of their energy and the contaminant of interest from a relatively linear food chain. PCB-153 is a strong candidate for this purpose,[22] as it had an average TMF of 6.0 (n = 50) that ranged from 1.5 to 34.0 in our database. These higher TMF values that were always >1 indicate that measured TMFs for other OCs should be viewed with caution if PCB-153 has an unusually low TMF in that particular food web. Other minor recommendations include providing CAS numbers or IUPAC names of OCs to facilitate searches of databases for chemical properties, providing more physical and chemical characteristics of the system, and lipid-normalizing data prior to TMF calculations. Most recent papers adhere to this latter guideline, but there remain examples where lipid normalization was deliberately avoided.[41,42] Although we did not exclude studies with a limited range in TLs, nor those studies where log[contaminant] vs TL regressions were nonsignificant, others have argued that, for a TMF to be valid, it must be derived from a significant regression that includes at least three TLs.[8,9,43] These strict criteria would have considerably reduced our database. Instead, we included all studies that contained multiple species, regardless of the range in TLs, and those studies with nonsignificant regressions. While this led to the inclusion of many values of TMF near (and not significantly different from 1), it allowed a fuller examination of key drivers of trophic magnification of OCs.

Despite the relatively strong predictive ability of the combination of K_{OW} and k_M, which holds promise for future modeling[31] and regulatory[6] efforts, there were important exceptions. For example, there were 210 OCs with $\log_{10}$ k_M <−2 (<0.01 day^{-1}), of which 33 unexpectedly had TMFs <1. While a handful of these were exceptionally large molecules (e.g., medium-chain chlorinated paraffins)[44] with extremely high log K_{OW} (>9) and were adequately predicted by our combined K_{OW} and k_M model, others, such as the brominated flame retardant BTBPE (better known as bis-tribromophenoxy ethane) seem to defy explanation. This OC has a predicted k_M of 0.0002 day^{-1} (EPIsuite 4.1) suggesting slow transformation, and a $\log_{10}$ K_{OW} = 7.88, near the range where TMFs peak. Yet TMFs measured for BTBPE were less than 1 in two independent studies (SI Table S1). Thus, this compound would be targeted for additional screening using our probabilistic model but would likely be deemed a "false positive" after further testing. Uncertainty in k_M and K_{OW} values used in our model likely contribute to the discrepancy between model prediction and field measurement of TMFs for BTBPE. First, the extremely slow metabolic rate of 0.0002 day^{-1} would be difficult to measure with precision using laboratory experiments. Second, K_{OW} for BTBPE has not been measured experimentally, and predicted values differ substantially. The published value (7.88[45]) we used in our analysis was estimated using ACD/Laboratories Software V9.04, but the BCFBAF function of EPIsuite estimates its $\log_{10}$ K_{OW} at 9.18. If this latter K_{OW} estimate is more accurate, it would explain the low TMFs for BTBPE observed in the two field studies (i.e., low bioavailability limits trophic magnification) and would be in much better agreement with our combined K_{OW} and k_M model.

The production and release of OCs is an ongoing issue of global concern.[4] Our findings indicate that the biomagnification potential of current and future OCs can be robustly assessed using the two widely available properties of chemical solubility (K_{OW}) and metabolic transformation rate (k_M). This probabilistic model can advance our ability to screen PBT chemicals and predict those chemicals that could play an outsized role in nudging the Earth beyond its boundary for chemical pollution.[3,5] However, it is important from a risk assessment perspective to consider that biomagnification is context dependent. That is, some ecosystems are more vulnerable than others to biomagnification of chemicals. These include freshwater ecosystems, where chemicals routinely biomagnify (vast majority of TMFs > 1), albeit at relatively lower levels, and marine ecosystems where endothermic predators such as birds and mammals are strongly reliant on aquatic prey, resulting in extraordinarily high TMFs.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.6b00201.

Methods for calculating TMFs and data acquisition. Chemical traits and TMFs for individual OCs (Table S1); summary of quantile estimates, AIC, and R^1 coefficients for models (Figures S1−S5); global distribution of TMF studies (Figure S6); TMF distribution by compound class (Figure S7); final TMF models for different ecosystems and food web types (Figure S8); effects of latitude on TMF (Table S2; Figures S9 and S10) (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*Phone: 970-226-9484; fax: 970-226-9230; e-mail: waltersd@usgs.gov.

Notes

The authors declare no competing financial interest.

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