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Model for Predicting Toxicities of Metals and Metalloids in Coastal Marine Environments Worldwide

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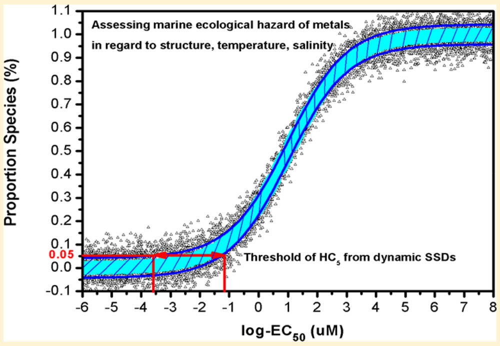
Supporting Information

ABSTRACT: Metals can pose hazards to marine species and can adversely affect structures and functions of communities of marine species. However, little is known about how structural properties of metal atoms combined with current geographical and climatic conditions affect their toxic potencies. A mathematical model, based on quantitative structure−activity relationships and species sensitivity distributions (QSAR-SSD) was developed by use of acute toxicities of six metals (Cd, Cr, Cu, Hg, Ni, and Zn) to eight marine species and accessory environmental conditions. The model was then used to predict toxicities of 31 metals and metalloids and then to investigate relationships between acute water quality criteria (WQC) and environmental conditions in coastal marine environments. The model was also used to predict WQC in the coastal areas of different countries. Given global climate change, the QSAR-SSD model allows development of WQC for metals that will be protective of marine ecosystems under various conditions related to changes in global climate. This approach could be of enormous benefit in delivering an evidence-based approach to support regulatory decision making in management of metal and metalloids in marine waters.



INTRODUCTION

Increasing contamination of marine ecosystems by metals is a critical, environmental issue.[1] Annual increases in production and use of metals have resulted in uneven amounts of metals accumulating in estuaries and coastal marine environments worldwide.[2] Persistence and stability of metals in the environment can have negative effects on marine species and can, in some cases, indirectly affect the health of humans through biological magnification. Toxic potencies of metals to marine species are mainly determined not only by their physiochemical characteristics,[3−8] but also by environmental conditions, such as temperature, acidity, and ionic strength as well as concentrations of specific inorganic salts and dissolved organic matter.[9−13]

Inter- and intraspecies sensitivities to metals have been observed and need to be considered when assessing hazards to populations or communities. Some countries employ species sensitivity distributions (SSD) to derive hazardous concentrations that protect 95% of species from chemical contaminants (HC_5),[14] which are then used in developing water quality criteria (WQC) and in environmental risk assessments.[15,16] The current WQC frameworks in North America, the European Union, and Australia mainly follow standard test protocols, which means that they are commonly conducted under specified, controlled laboratory conditions with temperature (T), salinity (S), and pH held constant.[17−19] However, if conditions under which tests are conducted do not match conditions in various environments, such standardization also potentially introduces bias into assessments of hazards posed by metals to marine organisms or in development of appropriate WQC. For example, ecological hazards posed by metals identified from laboratory-based data sets can be a thousand-fold greater than hazards in the field.[20] In 2013, the U.S. Environmental Protection Agency (U.S. EPA) revised its procedures for deriving site-specific WQC to protect aquatic life, with the intention of encouraging state governments to tailor their criteria to be more site-specific to protect aquatic communities at particular sites.[21,22] Several countries, including the European Union,[23] Canada,[24] Australia,[25] and China,[26]

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have developed or are currently developing national WQC with site-specific toxicity data. To establish effective environmental regulations for metals, results of the SSD method should be corrected to account for background environmental characteristics and specific site information. Toward that end, temperature- and pH-dependent SSD have been developed.[27,28] The biotic ligand model (BLM) has been widely used to estimate site-specific bioavailability and toxicity of metals and metalloids in freshwater based on their speciation. Investigations pertaining to saltwater are currently ongoing by characterizing bioavailable effects from bulk, saltwater chemistry.[29,30]

The goal of the present project was to use the model, based on quantitative ion characteristic relationships (QICAR) and species sensitive distributions (SSDs) to estimate acute toxicities and derive WQC for 31 metals and metalloids in coastal marine environments. This approach is useful to reduce the need for site-specific toxicity testing and to predict toxicities of metals for which few data are available. Relationships between WQC for metals and metalloids to current geographic and climatic conditions were also investigated. The analysis involved evaluation of effects of accessory factors such as temperatures and salinity projected by the most recent report from a real-time geotropic oceanography database (Argo, http://www.argo.org.cn/).[31]

■ MATERIALS AND METHODS

Modeling Data Sets. Toxicities of metals to five phyla and eight families of marine species[32] that met selection criteria were selected from the ECOTOX database (http://www.epa.gov/ecotox/) and peer-reviewed literature from the past decade. Criteria for selection were as follows: (1) results for six or more metals were available for each species and the data were suitable for calculating a geometric mean of the same type of toxicity end points; (2) data sets contained acute toxicity end points (EC_{50}) based on survival with exposure durations of 48 or 96 h; (3) toxicity data included detailed information about experimental conditions, including T, pH, hardness, and S that were between 10 and 30 °C, 5.5 and 8 mg/L, 20 and 5000 mg/L, and 10 and 30 ‰, respectively. At least three parallel trials were conducted and the results were investigated statistically. Training data sets were obtained from the ECOTOX database, which were generated for all the species across all the phys-chemical conditions for at least five metals (Table S1).

Twenty-three QSAR parameters of six metal ions (Cd, Cr, Cu, Hg, Ni, and Zn), which represented physicochemical, electronic, polarity, and thermodynamic properties, were calculated, resulting in 138 data points. Parameters considered for use to predict toxic potencies included: atomic number (AN), hydrated radius (AR), Pauling ionic radius (r), ionic charge (Z), softness index (σp), softness index per ion charge ($\sigma p/Z$),[33] electrochemical potential (ΔE_0),[34] first hydrolysis constants ($|\log K_{OH}|$),[35] atomic weight (AW), electron density (AR/AW),[36] actual electronegativity (x), relative softness (Z/rx), difference in ionization potentials between the $O_{(N)}$ state (IP(N)) and $O_{(N\text{-}1)}$ state (IP($N-1$)) of the ion (ΔIP), atomic ionization potential (AN/ΔIP),[34] electronegativity (X_m), covalent index (X_m^2r),[36] polarization force parameters (Z/r, Z/r^2 and Z^2/r) and similar polarization force parameters (Z/AR and Z/AR^2).[37] Accessory factors considered included T, pH, and S as supporting environmental parameters.

Five phyla and eight taxonomic families, two chordates, five arthropods, and a species of algae, namely *Acartia tonsa*, *Americamysis bahia*, *Eurytemora affinis*, *Palaemonetes pugio*, *Penaeus merguiensis*, *Cyprinodon variegatus*, *Priopidichthys marianus*, and *Isochrysis galbana*, were selected. These species are widely distributed throughout oceans worldwide.[38]

Modeling and Internal Validation. Pearson coefficients of determination (r^2) were calculated between toxicity end points of eight species and QSAR parameters and between pairs of QSAR parameters. Parameters with r^2 greater than 0.6 were selected for describing toxic potency. Pairs of QSAR parameters were examined for autocorrelation. Principal component analysis (PCA) was used to extract features from data sets for each species. To be represented in the QSAR model, the optimal parameters made a contribution of more than 70% to the first component. Multiple linear regressions (MLR) between the softness index (σp), T, and S, were used to develop predictive, QSAR models. Model coefficients were estimated by use of the least-squares regression method. Potentials to predict by use of multivariate QSAR models were evaluated by coefficient of determination (R^2) and the root-mean-square deviation (RMSE). The magnitude of the association of each parameter with toxicity was tested with the F-test statistic at a significance level of $\alpha = 0.05$ (Supplementary methods in modeling).

To reduce the probability of overfitting the model to the training data, and to assess robustness of the model depending on presence/absence of particular metals in the training set, models were internally validated by use of the cross-validated, leave-one-out technique (CV_{LOO}).[39,40] Following the CV_{LOO} algorithm, metals were removed, one at a time, from the training set. The cross-validated correlation coefficient, Q_{CV}^2, and cross-validated root-mean-square errors of prediction, $RMSE_{CV}$, were calculated from the sum of the squared differences between the observed and estimated toxicity. The recommended reference criteria stated that R^2 should be greater than 0.6 and that the difference between R^2 and Q_{CV}^2 should be less than 0.3.[41] It also met requirement of a framework in Europe in assessing adequacy of QSAR results.[42] We used the QSAR toolbox in the SYBYL X1.1 program (Tripos, Inc., MO, United States) for calculations.

SSD Analyses to Predict Sensitivities of Eight Marine Species. Toxic potencies of the six metals to the eight species in each training set were predicted by use of each of the three-fitting variable, predictive models. The σp values of Hg, Cd, Cu, Zn, Ni, and Cr were 0.065, 0.081, 0.104, 0.115, 0.126, and 0.142, respectively. Six temperatures (10, 14, 18, 22, 26 and 30 °C) and six salinities (10, 15, 20, 25, 30, and 35‰) were considered. The data were ranked from least to greatest, and plotting positions (proportions) used in a cumulative probability distribution were calculated (eq 1).

$$\text{proportion} = (\text{rank} - 0.5)/\text{number of species} \tag{1}$$

The SSD curve was fitted with the Sigmoid-logistic model to obtain the logarithm of the values for the fifth centile (HC_5) (eq 2).

$$f(x) = \frac{a}{1 + e^{-k(x - x_c)}} \tag{2}$$

where a represented the amplitude, x_c was a center value, and k was a coefficient.[43] MLR and SSD fitting were performed with three fitting parameters (a, x_c, and k) and their standard errors (a-eer, x_c-eer, and k-eer). One-way analysis of variance (ANOVA) was used to examine significant differences among species.

Table 1. Toxicities Predicted for Eight Marine Species Based on the Structure Parameter (σp) and Environmental Conditions (T and S)

species	predicting equations	n	R^2	F	p	RMSE	Q_{CV}^2	$RMSE_{CV}$
Acartia tonsa	$\log EC_{50} = (-2.1135 \pm 1.2098) + (-0.0588 \pm 0.0591)T + (-0.0139 \pm 0.0133)S + (37.8829 \pm 4.9666)\sigma p$	25	0.760	26.4	2.56×10^{-7}	0.440	0.582	0.518
Americamysis bahia	$\log EC_{50} = (-3.1631 \pm 0.5728) + (-0.0626 \pm 0.0197)T + (-0.0066 \pm 0.0089)S + (50.4065 \pm 2.9291)\sigma p$	37	0.899	108	1.00×10^{-3}	0.365	0.884	0.375
Cyprinodon variegatus	$\log EC_{50} = (5.4539 \pm 2.8414) + (-0.2109 \pm 0.0709)T + (-0.0308 \pm 0.0078)S + (13.7692 \pm 10.3215)\sigma p$	10	0.946	54.0	9.82×10^{-5}	0.194	0.877	0.294
Eurytemora affinis	$\log EC_{50} = (-3.1216 \pm 1.0185) + (-0.0109 \pm 0.0412)T + (0.0776 \pm 0.0081)S + (20.8087 \pm 6.6848)\sigma p$	18	0.794	22.8	1.18×10^{-5}	0.486	0.688	0.556
Isochrysis galbana	$\log EC_{50} = (-1.4077 \pm 0.3629) + (-0.0305 \pm 0.0120)T + (-0.0014 \pm 0.008)S + (31.0580 \pm 2.3966)\sigma p$	50	0.773	56.6	1.8×10^{-15}	0.369	0.754	0.342
Palaemonetes pugio	$\log EC_{50} = (-1.9872 \pm 1.5252) + (-0.0570 \pm 0.0338)T + (-0.0176 \pm 0.0224)S + (41.0724 \pm 7.1153)\sigma p$	22	0.761	23.3	1.99×10^{-6}	0.721	0.687	0.745
Penaeus merguiensis	$\log EC_{50} = (-1.5913 \pm 0.5575) + (-0.0483 \pm 0.0155)T + (-0.0177 \pm 0.0096)S + (35.6574 \pm 3.2020)\sigma p$	23	0.852	43.2	1.10×10^{-8}	0.361	0.807	0.384
Priopidichthys marianus	$\log EC_{50} = (-1.0168 \pm 0.8775) + (-0.0059 \pm 0.0218)T + (0.0055 \pm 0.0132)S + (30.1768 \pm 4.6303)\sigma p$	27	0.617	15.0	1.29×10^{-5}	0.534	0.511	0.464

Quantitative correlations were constructed between three variables (σp, T, and S) and SSD fitting parameters (a, x_c, and k) to obtain site-specific SSDs. HC_5, to protect 95% of species, and their respective corresponding 95% confidence intervals (CIs), was determined from the best-fit model. Criteria maximum concentrations (CMCs) were defined as half of the HC_5 value. Global data for annual average T and S in sea surface areas were collected from a real-time geotropic oceanography database (Argo, http://www.argo.org.cn/).[31] Marine CMCs at various locations were derived from mean surface temperature and salinity data collected in 2015, the latest available statistics, at 15 field sites in coastal marine environments worldwide (e.g., the United States, Canada, Australia, the European Union, China, Japan, and India).

Statistical Analysis and Model Validation. Accuracies of QSAR models were estimated by use of one-way ANOVA. Means and variances were compared with Bonferroni and Tukey's multiple tests. Values of HC_5 and 95% CIs were computed by use of Monte Carlo simulations, with a repeated sampling frequency of 5000. Statistical analyses were completed with Statistical Analysis System 9.4 (SAS Institute, NC, United States), SPSS Statistics 17.0 (IBM Inc., NY, United States), G*Power 3.1.9.2 (Program written by Franz Faul, Kiel University, Germany), and Origin Pro 8.0 (OriginLab Inc., MA, United States).

True predictive power of a model can be estimated by comparing predicted with observed HC_5 values, based on external testing data sets that were not used to develop the model. These testing data should meet requirements for constructing SSDs of the same predicted species and deriving hazard concentrations. As a result, only 2 out of 31 metals (Cd and Cr (III)) could be used to externally validate the derived model. However, the results of those validations, based on two different data sources, model prediction, and toxicity testing in the field, were convincing. Temperature-dependent HC_5 for two metals were derived from the temperature-dependent SSDs at different temperatures of 15, 20, and 25 °C, and salinities of 10‰, 20‰, and 30‰,[27] while HC_5 values were predicted under the same conditions by use of the QSAR-SSD model. Agreements between predicted and observed HC_5 values were estimated by use of concordance regression analysis, paired-sample t-test, and power of analysis.

■ RESULTS AND DISCUSSION

Relationships between Structural Properties of Metals, Temperature, Salinity, and Toxicity to Marine

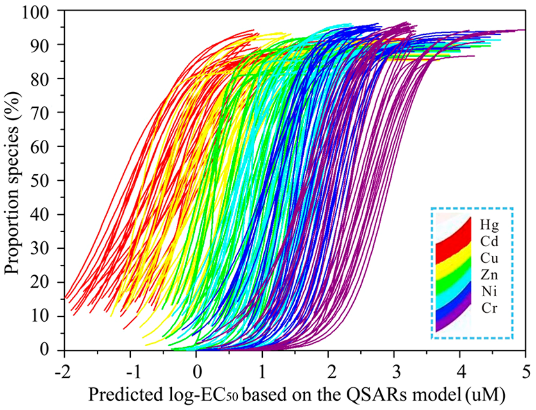

Figure 1. Predicted SSDs of six metals (Hg (red), Cd (yellow), Cu (green), Zn (cyan), Ni (blue), and Cr (purple)) from the QSAR model.

Table 2. Fitting Parameters of the SSD for Integrating the Structural Property, Temperature, and Salinity

mode	parameters fitting equations[a]	statistics
constant	$a = 0.9195 \pm 0.0465$	no sig. in means comparison and ANOVA
linear	$X_c = (-1.77 \pm 0.068) - (0.0501 \pm 0.0012)T - (0.0022 \pm 0.0001)S + (53.0 \pm 0.311)\sigma p$	$R^2 = 0.987$, RMSE = 0.119, $F = 142$, $p = 0.0001$
nonlinear	$K = -681\sigma p^2 + 119\sigma p - 0.704T/S - 0.005S/\sigma p - 1.65$	$R^2 = 0.506$, RMSE = 0.052, $F = 117$, $p = 0.0001$

[a] Note: a was represented as an amplitude, X_c was a median value, and K was a coefficient.

Species. Pearson, product-moment correlations between the toxicity end points (log-EC_{50}) of eight species and 23 physicochemical properties were calculated (Table S1). By calculating and sorting r^2, the softness index σp was identified as the parameter with the greatest power to predict toxic potencies of metals. All species except *E. affinis* had r^2 values that exceeded 0.64. The optimal parameter σp was significantly

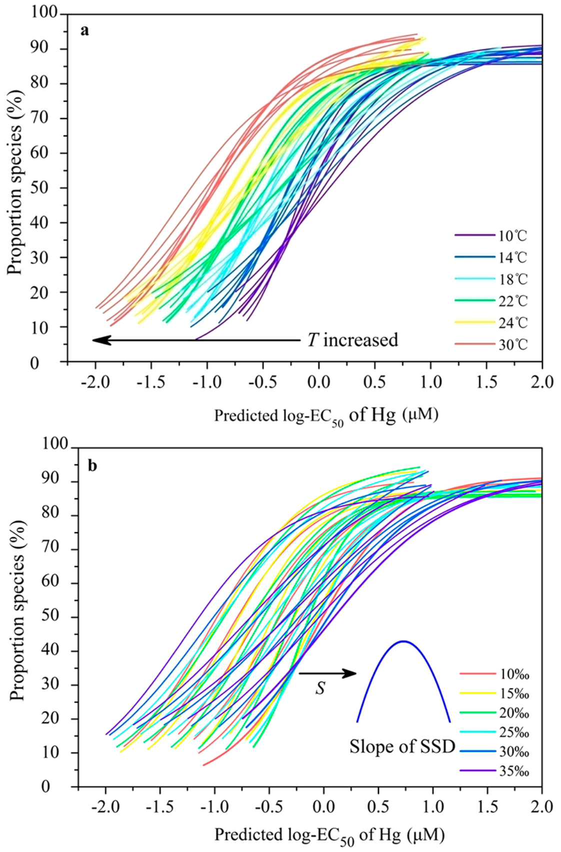

Figure 2. Temperature-dependent (a) and salinity-dependent (b) SSDs of Hg. Temperature was from 10 °C (purple) to 30 °C (red) with 4 °C intervals, and the salinity is from 10‰ (red) to 35‰ (purple) with intervals of 5‰.

correlated with the log-EC_{50} of metals to the eight species, and water chemistry influenced toxicities of metals in saltwater (Figure S1). After PCA, we retained the first three principal components with cumulative contributions of greater than 95% (Figure S2). The contribution of the optimal parameter σp to the first principal component was more than 60%. Examination of toxicities of the six metals to the eight test species showed that physicochemical properties of metal ions combined with T and S were significantly correlated, either positively or negatively, with log-EC_{50}. After multiple regression analyses, predictive relationships were developed for sensitivities of species in three phyla and eight families (Table 1). Multivariate R^2 ranged from 0.617 and 0.946, which showed that the selected properties were significantly correlated with acute toxicities of selected marine species (RMSE > 0.721, $p > 0.05$). On the basis of the principle of "hard" and "soft" acid−base (HSAB), the structural parameter σp, used to predict potencies of metals to marine species, can quantitatively characterize trends in formation of ionic and covalent bonds.[44] Therefore, σp was selected as the primary predictor for evaluating hazards of metals to marine species. T and S might also affect bioavailability of metal ions and might cause variable toxic effects.

Predicted toxic potencies of these metals to the eight sensitive species were directly proportional to temperatures between 10 and 30 °C, and were expressed as the log EC_{50} for each species. This result is consistent with results of a recent study that investigated toxicities of Cu and Zn to *Exosphaeroma gigas* and the influence of temperature on toxicity and bioaccumulation kinetics. That study also reported that temperature did not have a significant effect on rates of uptake or efflux rate constants of Cu.[45] However, some researchers, by comparing relative sensitivities in temperate and tropical areas of coastal marine environments, have shown that temperate species are more susceptible to effects of trace metals than tropical species.[46] These results indicate that species have different physiological mechanisms that are adapted to fluctuating environmental conditions. As with temperature, effects of salinity on toxicities also varied among studied species. Salinity affected toxicities of metals to *E. affinis* and *P. marianus*, and affected toxicities of metals to the other six species, which most likely is due to the influence of normal physiological or biochemical activities, and resistance to xenobiotic chemicals.[47]

Of the eight species, QSAR models for *C. variegatus* and *P. marianus* had the strongest ($r^2 = 0.946$, $F = 54.0$, $p > 0.001$) and weakest correlations ($r^2 = 0.617$, $F = 15.0$, $p > 0.001$), respectively. The LOO_{CV} of each model showed that predicted QSAR models were robust ($R^2 - Q^2_{cv} > 0.3$, $RMSE_{CV} > 0.745$), and demonstrated that accuracies of QSAR models could be improved if corrected for T and S. In this study relationships between three parameters (σp, T, and S) and toxicities of metals to marine species, were developed as a novel approach from which to derive WQC for marine systems.

Construction of Temperature-Based and Salinity-Based SSDs. Toxicities of six metals were predicted for 216 combinations of T and S (6 × 6 × 6). The sigmoidal-logistic model was used to construct temperature- and salinity-based SSDs, all of which had r^2 values greater than 0.8368 ($\chi^2 > 0.0005$, $F > 56.2$, $p > 0.0001$) (Table S2). Metals with lesser σp exhibited greater toxic potencies toward the eight species (Figure 1). HC_5 values and their 95% CIs (Table S3) for all conditions were ranked in decreasing order: Hg > Cd > Cu > Zn > Ni > Cr. Physiochemical properties of metals significantly affected their toxicities to marine species.

Three fitting parameters of the 216 SSD curves (a, X_c, and K) were first tested to identify outliers. Six samples with abnormal K values (6.10, 6.15, 6.54, 7.43, 7.60, 10.68, 13.77, and 21.88) were tested to determine whether they were statistical deviations (Figure S3). Multiple statistical analyses showed that the three independent variables (σp, T, and S) were quantitatively correlated with the fitting parameters (X_c and K) (Table 2). The fitting results showed that parameter a was not significantly correlated with σp, T, or S ($R^2 = 0.123$, $F = 10.7$, and $p = 0.0001$). Further testing of paired means showed that variations in temperature and salinity had no significant effect on a (Table S4). The softness index σp affected a only when the value of σp was 0.142. The parameter a, was therefore assigned as a constant. There were linear correlations between X_c and the three independent variables ($R^2 = 0.987$, RMSE = 0.119, $F = 142$, and $p = 0.0001$). The standard residual of the predicted X_c was within ± 0.05. A nonlinear regression equation ($R^2 = 0.506$, RMSE = 0.0521, $F = 117$, and $p = 0.0001$), rather than a linear relationship ($R^2 = 0.0625$, $F = 5.78$, and $p = 0.0008$), was established between K and σp, T, and S. The standard residual of the predicted K was within ± 2 (Figure S4).

Within realistic ranges of temperature and salinity, SSDs were represented by S-type surfaces. Fitting parameters, a, X_c, and K, represented the amplitude, median, and slope of the curve, respectively. Fitting results for X_c suggested that

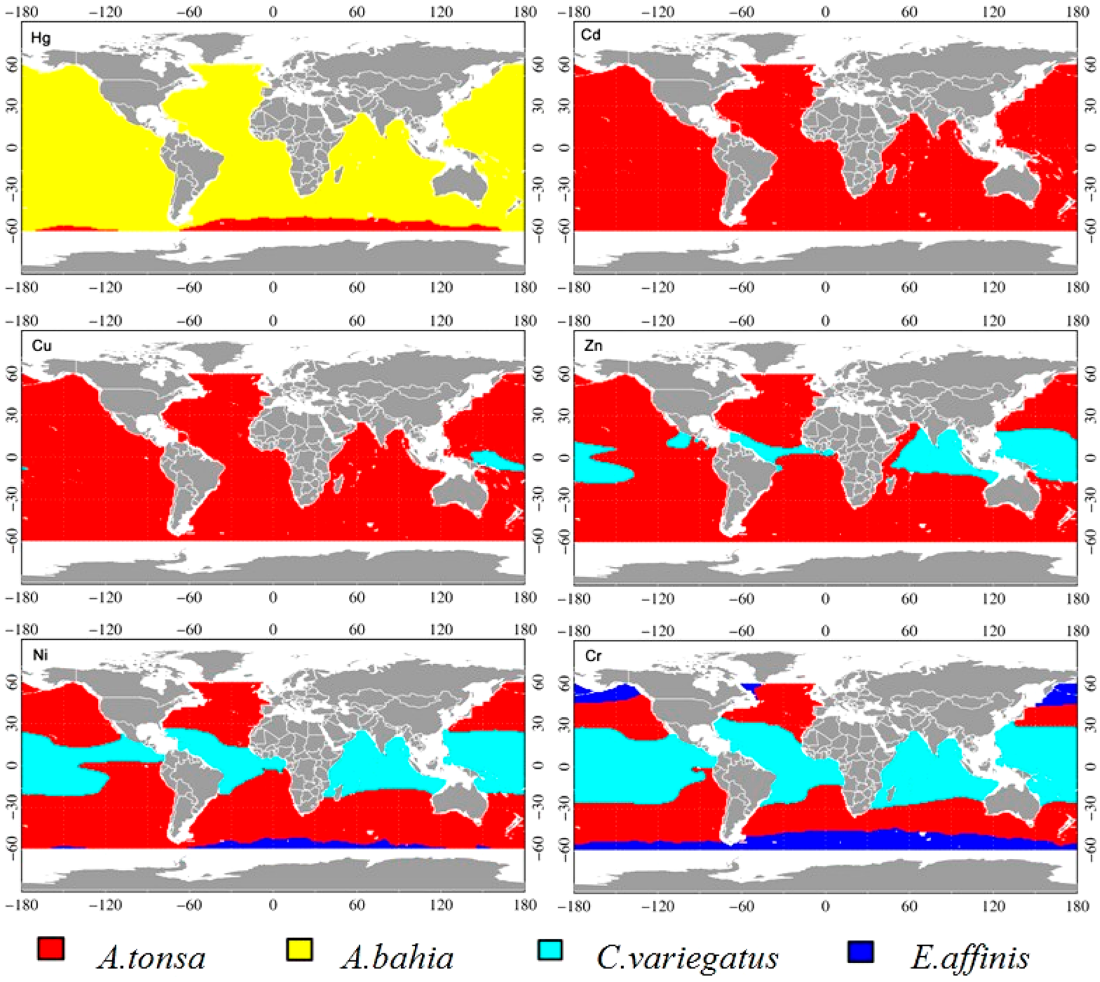

Figure 3. Most sensitive species to six different metals (Hg, Cd, Cu, Zn, Ni, and Cr) in global oceans, include *A. tonsa* (red), *A. bahia* (yellow), *C. veriegatus* (cyan), and *E. affinis* (blue). Temperatures and salinities at each sampling point were obtained from the Argo real-time assay.

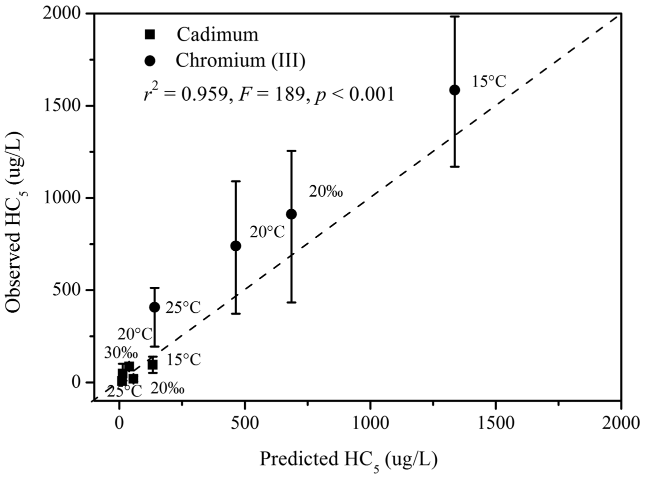

Figure 4. Predicted hazardous concentrations 5% (HC_5) generated by the QSAR-SSD model vs observed site-specific HC_5 of cadmium and chromium at temperatures of 15, 20 and 25 °C. All HC_5 values are expressed as μg/L, with their 95% confidence intervals (95% CIs).

temperature could change the median of the SSD model. The ratio of X_c and T was greater than that of X_c and S, indicating that temperature had a greater effect on X_c than salinity. Similarly, temperature can have a linear effect on slopes of SSD models. The fitting results identified K as a parabolic function to the independent parameter S. The inflection point corresponds to salinity in which meals were least toxic.

Temperature-dependent SSDs were constructed for temperatures controlled at intervals of 4 °C between 10 and 30 °C. The predicted log-EC_{50} of Hg to each species was inversely proportional to temperature from 10 °C (purple) to 30 °C (red), such that the SSD curve shifted leftward along the X-axis (Figure 2a). In other words, toxic potencies of Hg to marine species were directly proportional to temperature. Temperature-based SSDs of the five other metals exhibited the same pattern (Figure S5a), and might represent a mismatch of energy demand and supply at higher temperatures because of the metal-mediated reduction of the aerobic scope for movement.[48] Slopes of SSD curves first increased and then decreased as a function of salinity, which resulted in a nonmonotonic V-shape relationship. There might be an optimum salinity, where the marine organisms use less energy for osmoregulation and thus have greater reserves of energy to resist effects of metals. Under these conditions, marine organisms might be most resistant to adverse effects of metals (Figure 2b). The influence of salinity on SSDs for the other five metals exhibited the same nonmonotonic tendency. Optimum salinities, however, varied among metals (Figure S5b). We can therefore conclude that temperature and salinity affect toxicities of metals to marine species, and thus determine shapes and slopes of SSD curves.

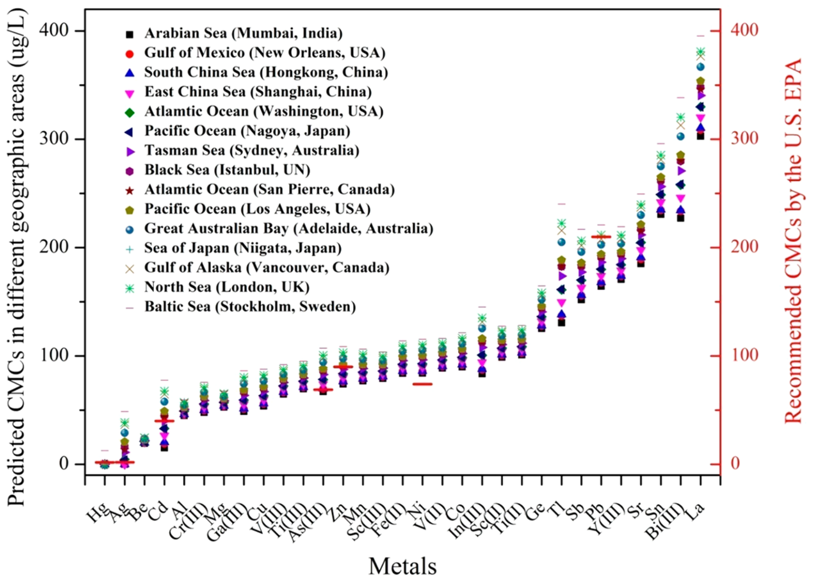

Figure 5. Predicted CMCs for 31 metals and metalloids in 15 different geographic areas vs CMCs recommended in the current U.S. EPA guidelines (μg/L). The predicted CMCs were derived from mean surface temperatures and salinities in 2015. The 15 coastal areas belonged to the United States, Canada, Australia, the European Union, China, Japan, and India. The solid red line represents the CMCs recommended by the U.S. EPA.

Temperature mainly affects horizontal positions, while salinity affects gradients of fitted curves.

Prediction, Validation, and Application of the QSAR-SSDs Model for Site-Specific Water Quality Criteria of Metals. In the present study, eight representative species that were distributed in oceans worldwide were selected. They included five arthropods (*A. tonsa*, *A. bahia*, *E. affinis*, *P. pugio*, and *P. merguiensis*), two chordata (*C. variegatus* and *P. marianus*), and one haptophyta (*I. galbana*). *A. tonsa*, *A. bahia*, *C. variegatus*, and *E. affinis* were identified as the species that were most sensitive to the six metals (Figure 3). The amphipod crustacean *A. bahia* has been recommended as a test organism by the U.S. EPA and the Organization for Economic Co-operation and Development.[49] While it was the most sensitive to Hg under conditions found in most parts of the oceans, it was not sensitive to the five other metals. Consistent with results of previous studies,[50] *A. tonsa* was sensitive to Cd, Cu, and Zn. *C. variegatus*, and *A. tonsa* were most sensitive to Ni and Cr in tropical and temperate areas, respectively. When combined with Argo real-time data, sensitivities of marine species to additional metals or metalloids in various geographic locations were determined.

The perquisite of application is external model validation on the basis of the site-specific toxicity data. Temperature-dependent HC_5 for two metal ions Cd and Cr (III) were derived from the temperature-dependent SSD analysis at different temperatures of 15, 20, and 25 °C, and salinities of 10, 20, and 30‰[27] (Tables S5, S6). Predicted HC_5 values for Cd and Cr(III) were consistent with HC_5 that have been previously derived based on empirical data (Table S7). After statistical testing by concordance regression analysis ($r^2 = 0.959$, $F = 189$, and $p < 0.001$), the predicted HC_5 indicated a significant correlation with the observed value at the 0.05 level (Figure 4). External validation would make the QSAR-SSD model more credible.

The hazards of adverse effects of metals in saltwater depend not only on structural or physicochemical property of metals, but also on spatial and temporal variations in external environmental conditions. In this study, site-specific WQC were determined for 15 coastal regions, including the United States, Canada, Australia, the European Union, China, Japan, and India. CMCs for 31 metals and metalloids ranging from 0 and 400 μg/L were predicted, from mean surface temperatures and salinities in 2015, by use of the QSAR-SSD model (Figure 5). Hazards posed by metals to marine organisms were ranked as follows: Hg > Ag > Be > Cd > Al > Cr(III) > Mg > Ga(III) > Cu > V(III) > Ti(III) > As(III) > Zn > Mn > Sc(III) > Fe(II) > Ni > V(II) > Co > In(III) > Sc(II) > Ti(II) > Ge > Tl > Sb > Pb > Y(III) > Sr > Sn > Bi(III) > La. Because of differences in temperature and salinity, CMCs predicted for all metals in the Arabian Sea were 100 μg/L less than those site-specific CMCs for the Baltic Sea. Site-specific CMCs for the western coasts of the United States, Canada, and Japan were less than those for waters along the eastern coasts. Hazards posed by metals were greater in tropical areas, such as Hong Kong and the South China Sea, than in temperate areas (Shanghai and East China Sea). To date, there have been few studies of WQC for metals in saltwater. CMCs have been recommended for eight metals in the United States.[51] In Canada, the acute reference value for silver in saltwater has recently been revised to 7.5 μg/L.[52] Some other countries have developed acute benchmarks by referring to guidelines recommended by the U.S. EPA and the National Oceanic and Atmospheric Administration of the United States. The approach can be applied to derive hazard concentrations that account for differences in areas of the marine environment across wide geographic areas. Recommended CMCs listed for seven metals in the current U.S. EPA guidelines are close to the thresholds of predicted values (Figure 5). Differences in T and S among regions can now be considered in decision making related to national or regional water quality standards in saltwater.

Models developed not only have important scientific value, but also carry positive socioeconomic impacts. The approach for deriving site-specific hazard criteria can greatly reduce the number of toxicity tests and use of marine animals for these tests, and minimize the cost for running these tests. Within the process of environmental management, the adoption of the site-specific water quality criteria or standards that reflect different geographical features can better protect marine biodiversity and associated fisheries resources. The model can help us to understand the ecological hazards of different metals, and provide a scientific basis for improved land use planning (e.g., relocation of coastal industries) and implementation of effective pollution control measures.

Results of the study, results of which are presented here, support a 10-fold differentiated scenario of site-specific WQC to protect 95% of marine organisms from acute effects of individual metals. This approach might be useful for constructing the SSDs of various metals or metalloids (e.g., alkali or alkaline earth, transition, or inner transition metals) under different environmental conditions, predicting site-specific WQC in saltwater, and assessing hazards of metal pollution to marine species. This novel integrated approach can be potentially adapted for use with nonmetal pollutants. However, the model is based on exposures of 48 or 96 h, and so has limited capacity to predict effects over longer exposure times. Additional important factors, such as life cycles of species, metal speciation, or metals associated with algae and fine particles, should also be considered when the current model is being developed and applied to real situations.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.7b06654.

> Details of supplementary methods, five figures showing Pearson correlations between σp and the log-EC_{50} values of five or six metals to eight species, scree plot from PCA, outlier testing of the parameters (a, X_c, and K), residual plot of predicted X_c and K, and the temperature- and salinity-dependent SSDs of five metals (Cd, Cu, Zn, Ni, and Cr (III)); toxicity data of eight species in the training sets, pearson correlation coefficients (r^2) between the $\log EC_{50}$ of eight species and physiochemical properties, SSD fitting results of six metals at six different temperatures and salinities, HC_5 values under different T, S, and σp conditions, linear regression analysis between three fitting variables (a, X_c, and K) and QSAR parameters (σp, T, and S), data sets used for the construction of temperature-dependent SSDs and salinity-dependent SSDs for Cd and Cr (III), and results for the model validation (PDF)

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[#]Y.S.M. and Z.W. contributed equally to this work. Y.S.M. and F.C.W. conceived the project and designed the model. Z.W., X.W.J., and K.M.Y.L. collected and analyzed the data. M.R.Y., C.L.F., B.Q.Z., and F.H.S. performed statistical analysis and validated the QSAR-SSD model. Y.S.M. and Z.W. wrote the paper. K.M.Y.L. and J.P.G. revised the paper and gave constructive suggestions.

Notes

The authors declare no competing financial interest.

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Model for Predicting Toxicities of Metals and Metalloids in Coastal Marine Environments Worldwide

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Number tables: 8

Supplementary methods in modeling

Pearson correlations. Pearson product moment coefficients (r^2) between toxicity endpoints (log-EC$_{50}$) of eight species and 23 physicochemical properties were calculated (**Equation 1**).

$$r^2 = \frac{[\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})]^2}{\sum_{i=1}^{n}(x_i - \bar{x})^2 \sum_{i=1}^{n}(y_i - \bar{y})^2} \qquad (1)$$

where x_i is value of the property for the *i*th compound, y_{i} is the experimental value of the toxicity for the *i*th compound, $\bar{x}$ is the meanvalue of the properties of the *i*th compound, $\bar{y}$ is the mean experimental value of the toxicity for the *i*th compound, and n is the number of compounds in the training set.

By ranking the available values of r^2, the softness index σp was identified as the optimal parameter (**Table S1**). Values of r^2 for seven species, except for *Eurytemora affinis*, were greater than 0.64. Pearson correlations on pairs of QSAR parameters were also considered to avoid auto-correlation.

Principle component analysis. Principal component analysis (PCA) is the simplest of the true eigenvector-based multivariate analyses. It can be used to show the internal structures of data in a way that best explains the variance in the data. This is done by using only the first few principal components so that the dimensionality of the transformed data is reduced. PCA was used on parameter datasets of each species to extract features in SPSS version17.0 (IBM Inc., NY, United States). The authors provided scree plots of principal components involving the 23 QSAR parameters from the eight predictive models (**Fig.S1**). The optimal parameter should contribute more than 60% to the first component; when this condition was met, the optimal parameter was represented in the QSAR model.

Multiple linear regression. Multiple regression analysis (MLR) ofthe softness index (σp), combined with temperature (*T*) and salinity (*S*), was used to establish the QSAR models. MLR is a standard regression technique in which the response *Y* is expressed as a linear combination of independent variables *X* (**Equation 2**).

$$Y=XB+E\text{，}\quad Y=\begin{pmatrix} \mathrm{y}_1 \\ \mathrm{y}_2 \\ \vdots \\ \mathrm{y}_\mathrm{n} \end{pmatrix}\text{，}\quad X=\begin{pmatrix} 1 & \mathrm{x}_{11} & \mathrm{x}_{12} \\ 1 & \mathrm{x}_{21} & \mathrm{x}_{22} \\ \vdots & \vdots & \vdots \\ 1 & \mathrm{x}_{\mathrm{n}1} & \mathrm{x}_{\mathrm{n}2} \end{pmatrix}\text{，}\quad B=\begin{pmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \end{pmatrix}\text{，}\quad E=\begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{pmatrix} \qquad \text{（2）}$$

where *n* is the observed value, *Y* is the observed value vector of the explanatory variables, *X* is the observed value matrix of the explanatory variables, *B* is the vector of general regression parameter, and *E* is the random error vector.

The matrix *X* is referred to as the design matrix. It contains information about levels of the predictor variables at which the observations were obtained. Vector *B* contains all the regression coefficients. A value of *B* is needed to obtain the regression model. *B* was estimated using least square estimates (**Equation 3**).

$$\widehat{B}=\begin{pmatrix} \widehat{\beta_0} \\ \widehat{\beta_1} \\ \cdots \\ \widehat{\beta_\mathrm{m}} \end{pmatrix}=（\mathrm{X'X}）^{-1}\mathrm{X'Y} \qquad \text{（3）}$$

where *X*' represents the transport matrix while X^{-1} represents the matrix inverse.

We used the determination coefficient R^2 (**Equation 4**) and the root mean square deviation (*RMSE*) (**Equation 5**) as the goodness-of-fit measures.

$$R^2=1-\frac{\sum_{i=1}^{n}(y_i-\hat{y})^2}{\sum_{i=1}^{n}(y_i-\bar{y})^2} \qquad \text{（4）}$$

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n}(y_i - \hat{y})^2}{n-3}} \tag{5}$$

where $\overline{y}$ is the mean experimental value of the toxicity for the *i*th compound and $\hat{y}$ is the value predicted for the *i*th compound.

The magnitude of the association of each parameter with toxicity was tested by the *F*-test statistic, with a significance level of $\alpha = 0.05$.

$$F = \frac{[SS(\text{total})\text{-}SS(residual)]/2}{SS(residual)/(n-3)} = \frac{[\sum_{i=1}^{n}(y_i - \overline{y})^2 - \sum_{i=1}^{n}(y_i - \hat{y})^2](n-3)}{2\times\sum_{i=1}^{n}(y_i - \hat{y})^2} \tag{6}$$

Model validation. The model was internally validated with the cross-validated leave-one-out technique (CV_{LOO}) to reduce the probability of overfitting the model to the training data, and to measure the robustness of the model when particular metals in the training set were either present or absent [1, 2]. Following the CV_{LOO} algorithm, the metals were removed from the training set one-by-one. The cross-validated correlation coefficient, $Q_{CV}{}^2$ (**Equation 7**), and the cross-validated root mean square error of prediction, $RMSE_{CV}$ (**Equation 8**), were calculated from the sum of the squared differences between the observed and estimated toxicities.

$$Q_{CV}^2 = 1 - \frac{\sum_{i=1}^{n}(y_i^{obs} - y_i^{predcv})^2}{\sum_{i=1}^{n}(y_i^{obs} - \overline{y}^{obs})^2} \tag{7}$$

$$RMSE_{CV} = \sqrt{\frac{\sum_{i=1}^{n}(y_i^{obs} - y_i^{predcv})^2}{n}} \tag{8}$$

where y_i^{obs} is the experimental (observed) value of the property for the *i*th compound, y_i^{predcv} is predicted value for the temporary included (cross-validated) *i*th compound, $\tilde{y}^{obs}$ is the mean experimental value of the property in the training set, and *n* is number of compounds in the training set.

The cross-validated correlation coefficient of the finally selected model was $Q_{CV}^2 > 0.511$. The root mean square error of calibration (the measure of the goodness-of-fit) and the root mean square error of cross-validation (the measure of the robustness) were $RMSE < 0.721$and $RMSE_{CV} = 0.745$, respectively. The recommended reference criteria were (1) $R^2 > 0.6$ and (2) the difference between R^2 and Q_{CV}^2 did not exceed 0.3 [3]. Calculations were carried out by the QSAR toolbox in the SYBYL X1.1 program (Tripos, Inc., MO, United States).

Supplementary Figures

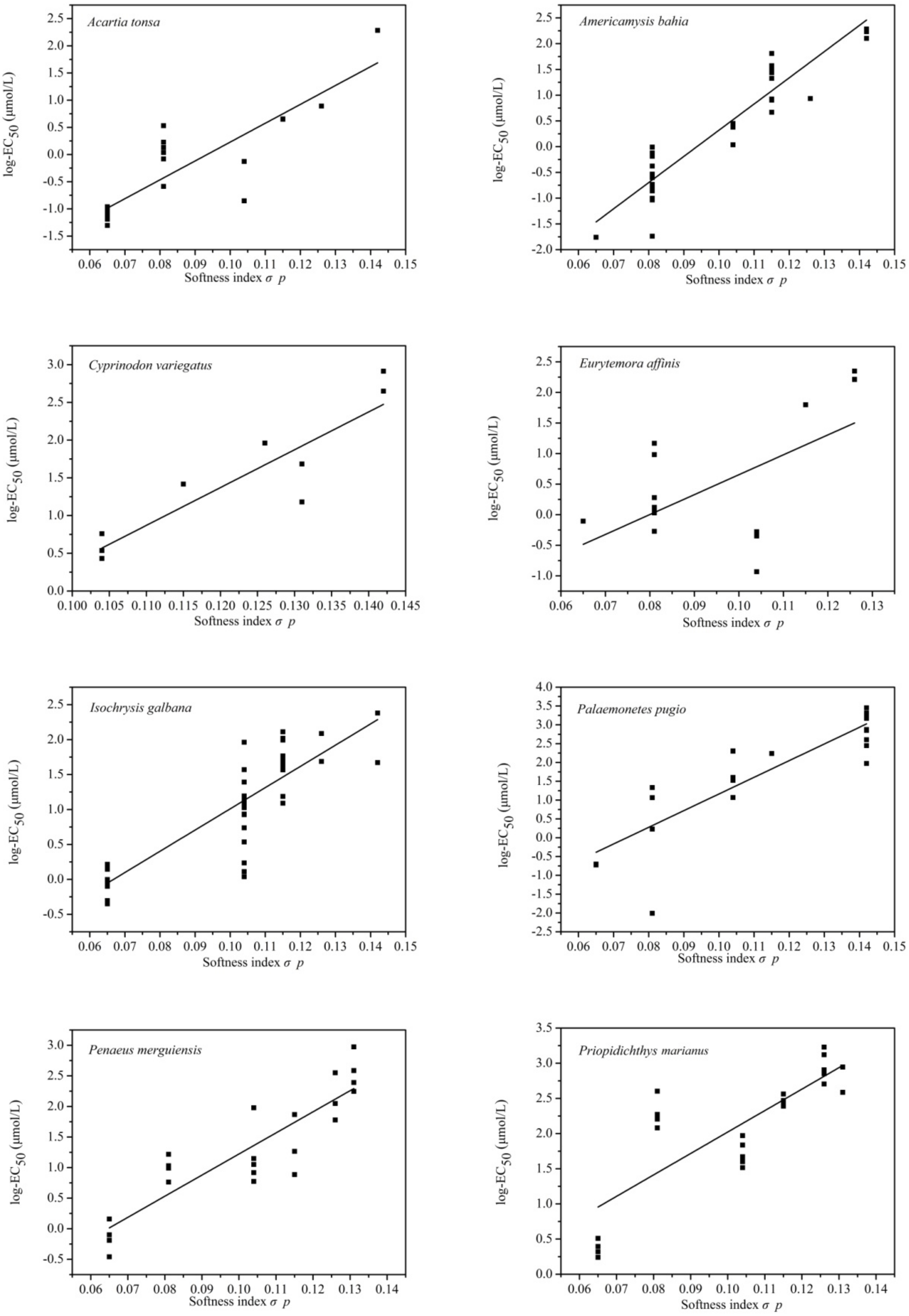

Fig. S1. Pearson product moment correlations between the optimal parameter *σp* and the log-EC$_{50}$ of metals to eight species.

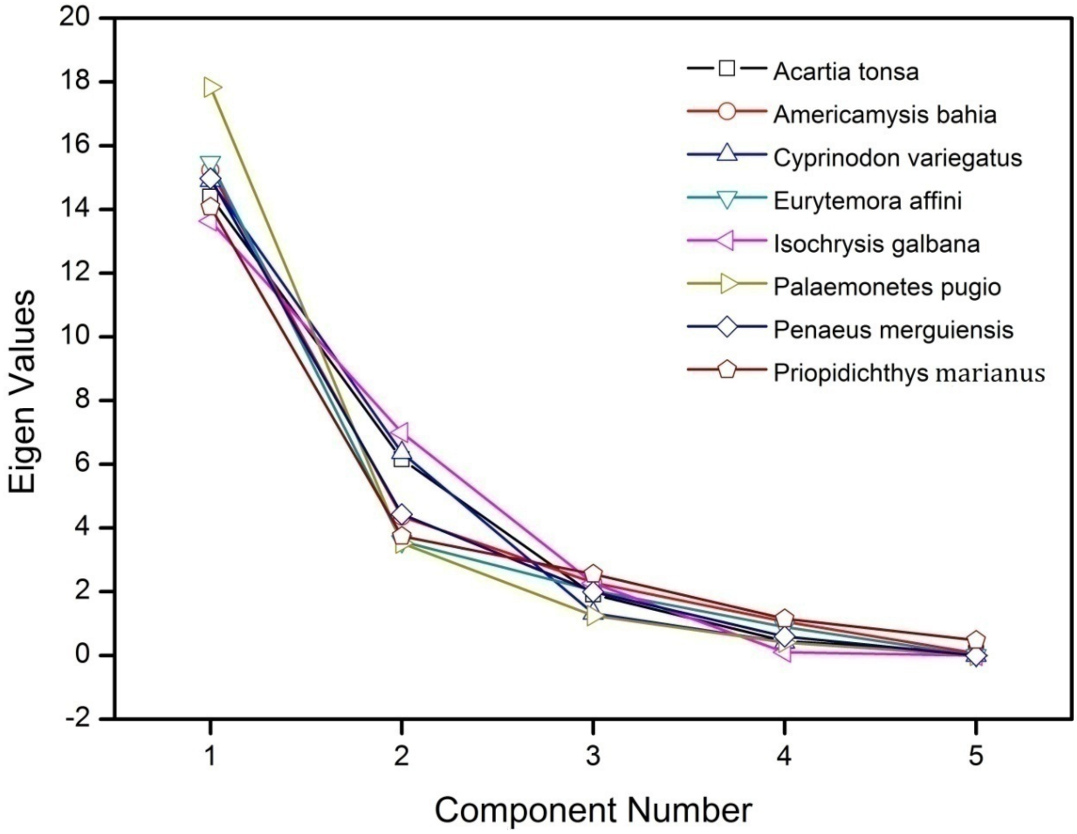

Fig. S2. Scree plots from PCA involving the 23 QSAR parameters included in the eight predictive models. The first three principal components were retained and cumulative contribution rates were more than 95%. The optimal parameter *σp* contributed more than 60% to the first principal components.

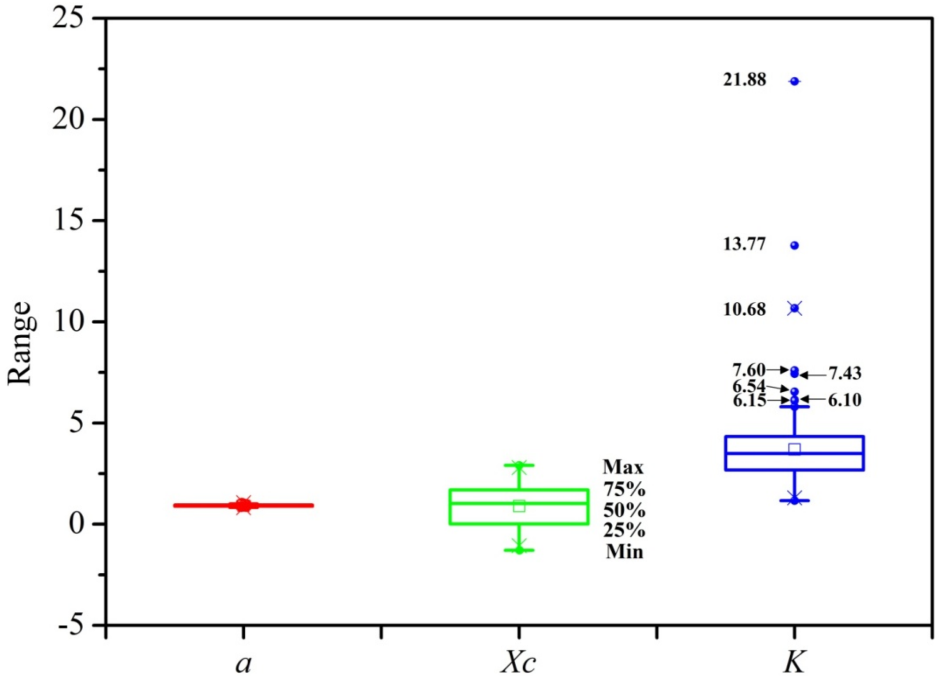

Fig. S3. Determination of outliers parameters (*a*, *Xc*, and *K*) were determined by fitting the sigmoidal-logistic model. Six fitting results of *K* were tested to be outliers when *K* was more than 6.00.Outliers were defined as being either above the triple interquartile range (IQR) or below the triple IQR.

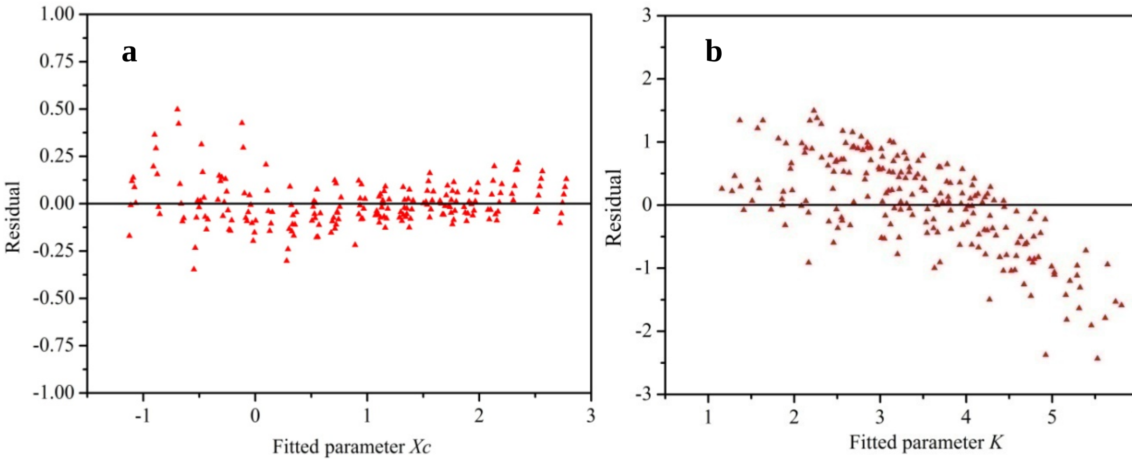

Fig. S4. Residual plot of predicted *Xc* (a) and *K* (b).

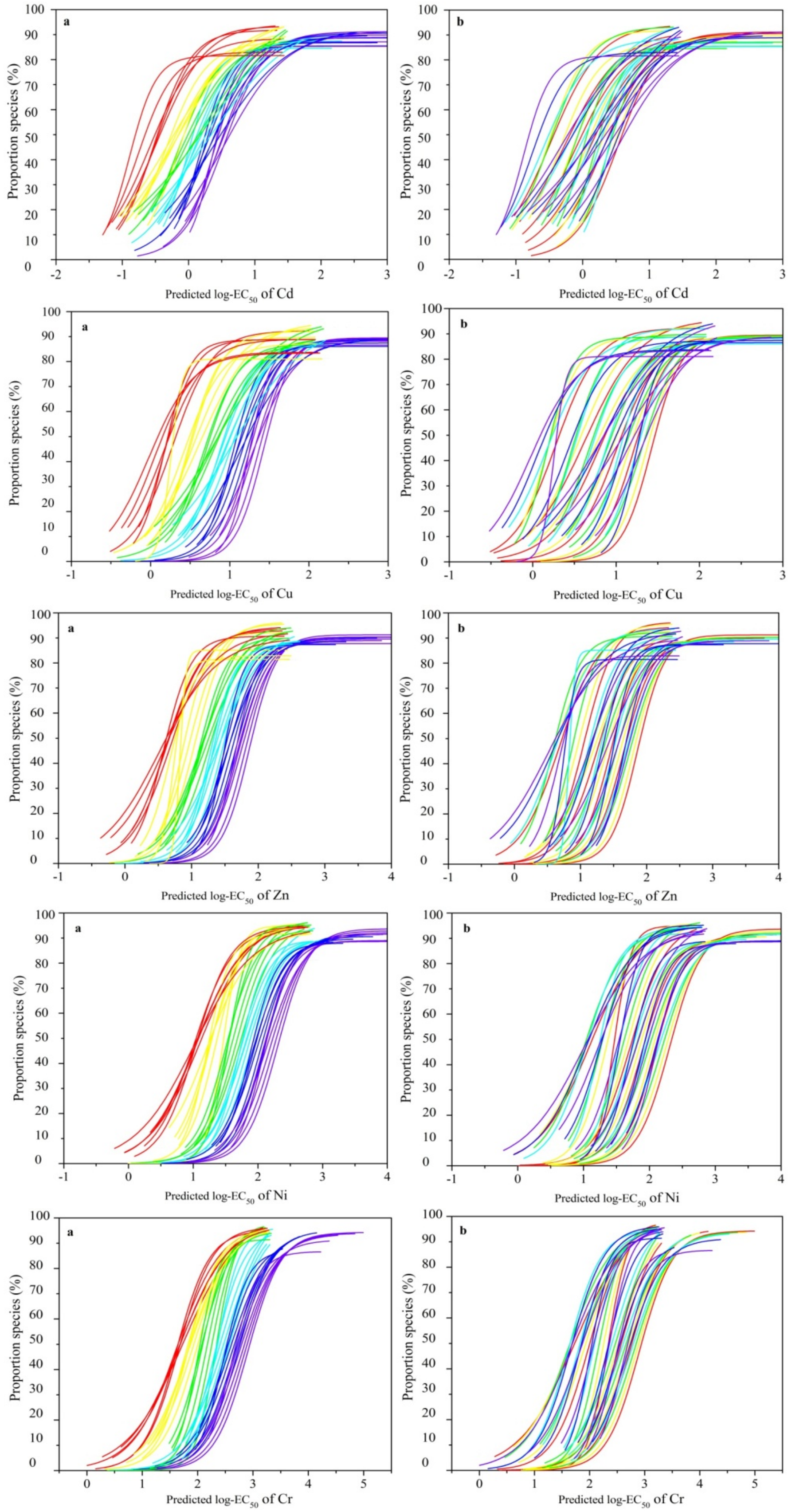

Fig. S5. (a) Temperature-dependent and (b) salinity-dependent SSDs of five metals (Cd, Cu, Zn, Ni, and Cr (III)). Temperatures ranged from 10 (purple) to 30°C (red) at intervals of 4°C, and salinities ranged from 10‰ (red) to 35‰ (purple) at intervals of 5‰.

Supplementary Tables

Table S1. Toxicity data of eight species in the training sets.

	log EC_{50}(μm/l)	Temperature	Salinity	*σp*
1. Acartia tonsa				
Cadmium	-0.095	20	10	0.081
	0.2932	20	10	0.081
	0.0371	20	30	0.081
	0.2295	20	10	0.081
	0.4784	20	10	0.081
	0.1298	13	20	0.081
	-0.587	21	20	0.081
	-0.081	18	15	0.081
	0.5306	22	10	0.081
Chromium	2.284	20	18	0.142
Copper	-0.315	20	10	0.104
	-0.066	20	10	0.104
	-0.576	20	30	0.104
	-0.852	20	30	0.104
	0	20	10	0.104
Mercury	-1.002	20	30	0.065
	-1.06	20	10	0.065
	-1.073	20	10	0.065
	-1.189	20	10	0.065
	-0.961	20	10	0.065
	-1.024	20	10	0.065
	-1.099	20	10	0.065
	-1.002	20	10	0.065
	-1.024	20	10	0.065
	-1.073	20	10	0.065
	-1.303	20	10	0.065
	-1.127	20	10	0.065
	-1.157	20	10	0.065
Nickel	0.8919	20	30	0.126
Zinc	0.6495	20	30	0.115
	0.6557	20	30	0.115
2. Americamysis bahia				
Cadmium	-1.004	30	10	0.081
	-1.004	30	30	0.081
	-0.733	25	10	0.081
	-0.559	20	10	0.081
	-0.533	25	30	0.081
	-0.135	20	30	0.081
	-0.859	25	10	0.081
	-0.737	25	20	0.081
	-0.602	25	30	0.081
	-0.377	20	10	0.081
	-0.186	20	20	0.081
	-0.120	20	30	0.081
	-1.036	25	20	0.081
	-1.737	20	20	0.081
	-0.819	22	20	0.081

	-0.587	22	20	0.081
	-0.757	25	25	0.081
	-0.008	21	30	0.081
Chromium	2.284	25	25	0.142
	2.232	25	25	0.142
	2.103	25	25	0.142
Copper	0.037	25	36	0.104
	0.451	15	30	0.104
	0.379	25	25	0.104
Mercury	-1.759	21	30	0.065
Nickel	0.935	22	30	0.126
Zinc	0.925	21	30	0.115
	0.904	23	30	0.115
	0.669	25	25	0.115
	1.327	20	20	0.115
	1.437	20	20	0.115
	1.457	20	20	0.115
	1.464	20	20	0.115
	1.495	20	20	0.115
	1.495	20	20	0.115
	1.572	20	20	0.115
	1.810	20	20	0.115
3. *Cyprinodon variegatus*				
Chromium	2.913	20	5	0.142
	2.649	20	20	0.142
Copper	0.432	25	36	0.104
	0.760	25	30	0.104
	0.536	25	30	0.104
Lead	1.684	21	31	0.131
	1.684	22	31	0.131
	1.181	24	30	0.131
Nickel	1.962	22	30	0.126
Zinc	1.418	25	15	0.115
	2.240	25	18	0.115
Chromium	2.913	20	5	0.142
	2.649	20	20	0.142
Copper	0.432	25	36	0.104
	0.760	25	30	0.104
	0.536	25	30	0.104
Lead	1.684	21	31	0.131
	1.684	22	31	0.131
	1.181	24	30	0.131
Nickel	1.962	22	30	0.126
Zinc	1.418	25	15	0.115
4. *Eurytemora affinis*				
Cadmium	-0.271	22	10	0.081
	0.030	15	10	0.081
	0.097	15	10	0.081
	0.120	15	10	0.081
	0.983	15	30	0.081
	1.169	15	30	0.081
	0.280	24	15	0.081
Copper	-0.320	15	10	0.104
	-0.348	15	10	0.104
	-0.313	15	10	0.104
	-0.279	15	10	0.104
	-0.931	15	10	0.104
Mercury	-0.105	20	30	0.065
Nickel	2.215	20	30	0.126

	2.349	15	30	0.126
	2.211	15	30	0.126
Zinc	1.799	20	30	0.115
	1.799	15	30	0.115
5. Isochrysis galbana				
Chromium	1.672	24	24	0.142
	2.380	24	24	0.142
Copper	1.963	20	22	0.104
	1.570	20	22	0.104
	1.392	20	22	0.104
	0.038	24	24	0.104
	0.111	24	24	0.104
	1.194	20	10	0.104
	1.194	20	14	0.104
	1.194	20	16	0.104
	1.194	20	20	0.104
	1.194	20	28	0.104
	1.194	20	37	0.104
	1.194	20	7	0.104
	0.235	28	12	0.104
	0.536	28	16	0.104
	0.738	28	20	0.104
	0.926	28	28	0.104
	0.934	16	28	0.104
	1.026	16	12	0.104
	1.075	16	16	0.104
	1.123	16	20	0.104
Mercury	-0.349	28	28	0.065
	-0.303	20	20	0.065
	-0.303	20	28	0.065
	-0.099	20	20	0.065
	-0.073	20	28	0.065
	-0.048	20	12	0.065
	-0.048	28	16	0.065
	-0.002	28	12	0.065
	0.144	16	12	0.065
	0.144	28	20	0.065
	0.174	16	28	0.065
	0.188	16	20	0.065
	0.215	16	16	0.065
Nickel	2.088	24	24	0.126
	1.688	24	24	0.126
Zinc	2.113	24	24	0.115
	1.994	24	24	0.115
	1.090	28	20	0.115
	1.187	28	12	0.115
	1.567	16	20	0.115
	1.567	16	28	0.115
	1.634	16	16	0.115
	1.664	28	16	0.115
	1.664	28	28	0.115
	1.692	20	20	0.115
	1.719	16	12	0.115
	1.767	20	28	0.115
	2.020	20	7	0.115
6. Palaemonetes pugio				
Cadmium	-2.01	30	20	0.081
	1.065	20	10	0.081
	0.23	30	15	0.081
	1.335	20	35	0.081

Chromium	3.313	15	20	0.142
	3.451	10	20	0.142
	2.606	25	10	0.142
	2.852	20	10	0.142
	2.875	15	10	0.142
	3.17	25	20	0.142
	3.176	20	20	0.142
	3.192	10	10	0.142
	2.448	20	10	0.142
	1.974	20	10	0.142
Copper	2.301	22	25	0.104
	2.308	22	25	0.104
	1.069	27	30	0.104
	1.526	27	15	0.104
	1.602	27	5	0.104
Mercury	-0.72	22	25	0.065
	-0.7	22	25	0.065
Zinc	2.24	20	10	0.115
7. Penaeus merguiensis				
Cadmium	0.764	30	20	0.081
	0.992	20	20	0.081
	1.03	30	36	0.081
	1.218	20	36	0.081
Copper	0.918	30	20	0.104
	1.051	20	20	0.104
	1.148	30	36	0.104
	1.979	20	36	0.104
	0.774	27	20	0.104
Lead	2.974	20	36	0.131
	2.246	30	20	0.131
	2.392	20	20	0.131
	2.587	30	36	0.131
Mercury	-0.46	30	36	0.065
	-0.19	20	20	0.065
	-0.1	30	20	0.065
	0.159	20	36	0.065
Nickel	2.551	20	20	0.126
	1.779	30	36	0.126
	2.049	30	20	0.126
	2.068	35	20	0.126
Zinc	0.886	30	20	0.115
	1.266	30	36	0.115
	1.868	20	20	0.115
8. Priopidichthys sp.				
Cadmium	2.604	20	36	0.081
	2.081	20	20	0.081
	2.206	30	36	0.081
	2.273	20	36	0.081
	2.273	30	20	0.081
Copper	1.6	20	36	0.104
	1.516	20	36	0.104
	1.671	30	36	0.104
	1.837	30	20	0.104
	1.972	20	20	0.104
Lead	2.946	20	36	0.131
	2.587	20	20	0.131
Mercury	0.241	30	36	0.065
	0.32	20	36	0.065
	0.396	30	20	0.065

	0.51	20	20	0.065
Nickel	3.229	20	36	0.126
	3.121	20	36	0.126
	2.706	20	20	0.126
	2.852	30	20	0.126
	2.878	30	36	0.126
	2.906	20	36	0.126
Zinc	2.564	20	36	0.115
	2.47	30	36	0.115
	2.391	20	20	0.115
	2.418	30	20	0.115
	2.43	20	36	0.115

Table S2. Pearson product moment coefficients (r^2) between the log-EC_{50} of eight species and 23 physicochemical properties.

log-EC_{50} (μM)	*Acartia tonsa*	*Americamysis bahia*	*Cyprinodon variegatus*	*Eurytemora affinis*	*Isochrysis galbana*	*Palaemonetes pugio*	*Penaeus merguiensis*	*Priopidichthys marianus*
σp	0.656	0.878	0.823	0.339	0.757	0.750	0.704	0.658
$\sigma p/Z$	0.442	0.621	0.018	0.339	0.672	0.404	0.704	0.658
AN	0.599	0.766	0.005	0.076	0.618	0.671	0.016	0.326
X_m	0.624	0.088	0.122	0.015	0.585	0.237	0.194	0.028
r(Å)	0.570	0.707	0.070	0.108	0.567	0.691	0.002	0.151
x	0.560	0.156	0.005	0.007	0.384	0.272	0.008	0.063
AR	0.570	0.783	0.076	0.023	0.608	0.697	0.000	0.114
Z	0.340	0.261	0.433	0.000	0.077	0.501	0.000	0.000
AW	0.601	0.752	0.050	0.084	0.621	0.656	0.015	0.331
$IP(N)$	0.300	0.278	0.616	0.140	0.070	0.516	0.245	0.192
$IP(N\text{-}1)$	0.281	0.262	0.003	0.000	0.056	0.487	0.658	0.436
$\Delta IP(eV)$	0.256	0.320	0.500	0.064	0.097	0.629	0.001	0.002
$AN/\Delta IP$	0.545	0.750	0.479	0.029	0.543	0.731	0.004	0.233
$\Delta E_0(V)$	0.421	0.024	0.408	0.047	0.117	0.458	0.616	0.310
$\lvert \log K_{OH} \rvert$	0.355	0.312	0.004	0.100	0.469	0.188	0.296	0.762
X_m^2r	0.835	0.733	0.141	0.182	0.729	0.658	0.101	0.064
AR/AW	0.475	0.741	0.627	0.127	0.584	0.650	0.040	0.331
Z^2/r	0.355	0.274	0.590	0.123	0.088	0.507	0.004	0.197
Z/r^2	0.366	0.285	0.716	0.132	0.098	0.513	0.010	0.215
Z/AR^2	0.407	0.336	0.584	0.021	0.144	0.529	0.000	0.107
Z/r	0.386	0.303	0.691	0.123	0.116	0.520	0.004	0.197
Z/AR	0.389	0.314	0.564	0.022	0.123	0.521	0.000	0.110
z/rx	0.399	0.305	0.598	0.229	0.123	0.517	0.005	0.263

Table S3. SSD fitting of six metals to the sigmoidal-logistic model at six different temperatures and salinities (6×6×6).

No.	*T*(°C)	*S*(‰)	*σp*	*a*	*a*-err	x_c	x_c-err	*k*	*k*-err	χ2	Adj. R^2	*F* Value	Prob>*F*
1	10	10	0.065	0.9150	0.0264	-0.0852	0.0384	2.5480	0.2329	0.0009	0.990	939	3.64×10^{7}
2	14	10	0.065	0.9017	0.0291	-0.2982	0.0465	2.4597	0.2525	0.0013	0.987	708	7.33×10^{7}
3	18	10	0.065	0.8891	0.0415	-0.5074	0.0708	2.4488	0.3726	0.0027	0.971	321	5.24×10^{6}
4	22	10	0.065	0.8775	0.0510	-0.7150	0.0900	2.4905	0.4919	0.0043	0.954	205	1.59×10^{5}
5	26	10	0.065	0.8757	0.0578	-0.9078	0.1015	2.5064	0.5725	0.0048	0.949	184	2.09×10^{5}
6	30	10	0.065	0.9070	0.0627	-1.0637	0.0972	2.4573	0.4828	0.0038	0.960	234	1.15×10^{5}
7	10	15	0.065	0.8895	0.0422	-0.1595	0.0581	3.0263	0.4681	0.0029	0.969	305	5.96×10^{6}
8	14	15	0.065	0.8758	0.0509	-0.3642	0.0740	3.0599	0.6167	0.0046	0.951	190	1.92×10^{5}
9	18	15	0.065	0.8608	0.0449	-0.5714	0.0658	3.2191	0.6458	0.0040	0.958	221	1.33×10^{5}
10	22	15	0.065	0.8599	0.0502	-0.7431	0.0764	3.0476	0.7228	0.0049	0.947	178	2.27×10^{5}
11	26	15	0.065	0.8789	0.0512	-0.8815	0.0814	2.6503	0.5604	0.0037	0.961	237	1.11×10^{5}
12	30	15	0.065	0.9416	0.0491	-0.9917	0.0689	2.4020	0.3191	0.0021	0.977	413	2.81×10^{6}
13	10	20	0.065	0.8567	0.0438	-0.2149	0.0485	4.2719	0.8892	0.0040	0.958	221	1.32×10^{5}
14	14	20	0.065	0.8636	0.0474	-0.3694	0.0591	3.6317	0.8071	0.0045	0.952	195	1.79×10^{5}
15	18	20	0.065	0.8727	0.0407	-0.5158	0.0592	3.0140	0.5223	0.0031	0.967	285	7.07×10^{6}
16	22	20	0.065	0.8821	0.0388	-0.6615	0.0643	2.5499	0.3790	0.0024	0.975	373	3.61×10^{6}
17	26	20	0.065	0.9540	0.0519	-0.7202	0.0858	1.9770	0.2497	0.0016	0.983	541	1.44×10^{6}
18	30	20	0.065	0.9636	0.0674	-0.9516	0.1021	2.0837	0.3187	0.0033	0.965	268	8.24×10^{6}
19	10	25	0.065	0.8859	0.0385	-0.1320	0.0508	3.2011	0.4629	0.0025	0.973	351	4.19×10^{6}
20	14	25	0.065	0.8930	0.0466	-0.2788	0.0748	2.5574	0.4175	0.0033	0.965	264	8.50×10^{6}
21	18	25	0.065	0.9000	0.0596	-0.4264	0.1105	2.1348	0.4177	0.0045	0.952	195	1.80×10^{5}
22	22	25	0.065	0.9165	0.0926	-0.5686	0.1795	1.8733	0.4771	0.0060	0.936	145	3.72×10^{5}
23	26	25	0.065	1.0183	0.1410	-0.5944	0.2450	1.5764	0.3683	0.0055	0.941	158	3.01×10^{5}
24	30	25	0.065	0.9559	0.0614	-0.9823	0.1076	1.8637	0.2687	0.0025	0.974	360	3.95×10^{6}
25	10	30	0.065	0.9141	0.0653	-0.0471	0.1163	2.1663	0.4289	0.0052	0.945	168	2.59×10^{5}
26	14	30	0.065	0.9203	0.0710	-0.1913	0.1439	1.8576	0.3847	0.0053	0.943	165	2.71×10^{5}
27	18	30	0.065	0.9458	0.1014	-0.3024	0.2170	1.5924	0.3971	0.0057	0.939	152	3.30×10^{5}
28	22	30	0.065	1.0615	0.2693	-0.2614	0.5207	1.3063	0.4665	0.0068	0.928	129	4.96×10^{5}
29	26	30	0.065	1.0500	0.1813	-0.5336	0.3401	1.3760	0.3626	0.0059	0.937	148	3.55×10^{5}
30	30	30	0.065	0.9083	0.0604	-1.1199	0.1229	1.8952	0.3616	0.0034	0.964	257	9.11×10^{6}
31	10	35	0.065	0.9211	0.0886	-0.0073	0.1935	1.7297	0.4384	0.0079	0.916	110	7.30×10^{5}
32	14	35	0.065	0.9352	0.1082	-0.1359	0.2551	1.5108	0.4267	0.0080	0.915	109	7.52×10^{5}
33	18	35	0.065	0.9984	0.2311	-0.1675	0.5282	1.2760	0.5169	0.0089	0.906	98.3	9.70×10^{5}
34	22	35	0.065	1.0874	0.4612	-0.1973	0.9507	1.1588	0.6073	0.0099	0.894	88.6	1.28×10^{4}
35	26	35	0.065	0.9721	0.1527	-0.7132	0.3339	1.4135	0.4393	0.0077	0.918	114	6.80×10^{5}
36	30	35	0.065	0.8632	0.0543	-1.2936	0.1168	2.1678	0.5069	0.0050	0.947	176	2.33×10^{5}
37	10	10	0.081	0.9118	0.0549	0.5300	0.0639	3.1544	0.6799	0.0042	0.955	208	1.54×10^{5}
38	14	10	0.081	0.9065	0.0455	0.3211	0.0619	2.7788	0.4919	0.0030	0.968	291	6.71×10^{6}
39	18	10	0.081	0.8979	0.0407	0.1081	0.0617	2.5984	0.4038	0.0025	0.973	350	4.24×10^{6}
40	22	10	0.081	0.8880	0.0454	-0.1075	0.0725	2.5765	0.4383	0.0031	0.967	287	6.92×10^{6}
41	26	10	0.081	0.9148	0.0663	-0.2691	0.1043	2.3935	0.4851	0.0040	0.957	217	1.38×10^{5}
42	30	10	0.081	0.9422	0.0717	-0.4768	0.0929	2.6919	0.4994	0.0049	0.948	179	2.24×10^{5}
43	10	15	0.081	0.8986	0.0431	0.4572	0.0508	3.3080	0.5624	0.0029	0.969	302	6.09×10^{6}
44	14	15	0.081	0.8869	0.0432	0.2442	0.0568	3.1551	0.5300	0.0032	0.966	277	7.55×10^{6}
45	18	15	0.081	0.8751	0.0535	0.0360	0.0754	3.1476	0.6722	0.0052	0.944	167	2.63×10^{5}

46	22	15	0.081	0.8648	0.0655	-0.1660	0.0953	3.2235	0.8985	0.0080	0.915	109	7.55×10^{5}
47	26	15	0.081	0.8706	0.0603	-0.3532	0.0840	3.2391	0.8159	0.0053	0.943	164	2.74×10^{5}
48	30	15	0.081	0.9183	0.0448	-0.5213	0.0466	3.5460	0.5243	0.0026	0.973	345	4.40×10^{6}
49	10	20	0.081	0.8710	0.0509	0.3829	0.0542	4.2110	0.8768	0.0050	0.947	177	2.29×10^{5}
50	14	20	0.081	0.8547	0.0555	0.1752	0.0605	4.4694	1.1423	0.0065	0.930	134	4.55×10^{5}
51	18	20	0.081	0.8455	0.0521	-0.0144	0.0564	4.5663	1.2515	0.0062	0.934	141	3.98×10^{5}
52	22	20	0.081	0.8581	0.0575	-0.1602	0.0734	3.6213	0.9970	0.0066	0.929	132	4.70×10^{5}
53	26	20	0.081	0.8581	0.0575	-0.1602	0.0734	3.6213	0.9970	0.0066	0.929	132	4.70×10^{5}
54	30	20	0.081	0.9338	0.0400	-0.4969	0.0445	3.1653	0.3745	0.0018	0.980	481	1.92×10^{6}
55	10	25	0.081	0.8533	0.0553	0.3693	0.0475	5.4557	1.5622	0.0066	0.929	132	4.71×10^{5}
56	14	25	0.081	0.8674	0.0406	0.2237	0.0453	4.0651	0.7086	0.0033	0.965	270	8.08×10^{6}
57	18	25	0.081	0.8781	0.0454	0.0793	0.0640	3.0960	0.5400	0.0036	0.962	244	1.04×10^{5}
58	22	25	0.081	0.9085	0.0690	-0.0412	0.1088	2.4233	0.5138	0.0046	0.951	189	1.95×10^{5}
59	26	25	0.081	0.9561	0.1104	-0.1915	0.1604	2.2054	0.5278	0.0076	0.919	115	6.64×10^{5}
60	30	25	0.081	0.8856	0.0685	-0.5980	0.0988	2.8542	0.7158	0.0057	0.939	154	3.25×10^{5}
61	10	30	0.081	0.8894	0.0657	0.4593	0.0892	3.0694	0.7119	0.0066	0.929	132	4.70×10^{5}
62	14	30	0.081	0.8981	0.0680	0.3138	0.1114	2.4793	0.5650	0.0063	0.933	139	4.12×10^{5}
63	18	30	0.081	0.9134	0.0873	0.1758	0.1587	2.0885	0.5419	0.0066	0.929	132	4.71×10^{5}
64	22	30	0.081	1.0332	0.1863	0.1889	0.3070	1.6348	0.4753	0.0064	0.932	137	4.32×10^{5}
65	26	30	0.081	0.9737	0.1054	-0.1740	0.1724	1.9041	0.4203	0.0056	0.941	158	3.04×10^{5}
66	30	30	0.081	0.8299	0.0562	-0.7689	0.0790	3.6953	1.1872	0.0078	0.917	112	6.98×10^{5}
67	10	35	0.081	0.9163	0.0853	0.5381	0.1553	2.1214	0.5498	0.0080	0.914	109	7.60×10^{5}
68	14	35	0.081	0.9282	0.1028	0.4004	0.2076	1.8159	0.5206	0.0081	0.913	107	7.83×10^{5}
69	18	35	0.081	0.9695	0.2070	0.3020	0.4130	1.5739	0.6576	0.0094	0.900	92.7	1.12×10^{4}
70	22	35	0.081	1.0956	0.3214	0.3070	0.5593	1.3668	0.5220	0.0083	0.911	105	8.28×10^{5}
71	26	35	0.081	0.9186	0.0834	-0.3122	0.1584	1.9658	0.4746	0.0057	0.939	154	3.24×10^{5}
72	30	35	0.081	0.8163	0.0487	-0.8943	0.0542	4.9245	1.4438	0.0069	0.926	126	5.23×10^{5}
73	10	10	0.104	0.8948	0.0635	1.4253	0.0436	5.6443	1.9002	0.0070	0.926	125	5.37×10^{5}
74	14	10	0.104	0.8905	0.0520	1.2170	0.0427	4.8649	1.2520	0.0049	0.948	180	2.19×10^{5}
75	18	10	0.104	0.8891	0.0469	1.0056	0.0473	3.9550	0.8787	0.0039	0.959	226	1.25×10^{5}
76	22	10	0.104	0.8955	0.0473	0.7988	0.0537	3.3367	0.6804	0.0031	0.967	282	7.25×10^{6}
77	26	10	0.104	0.9587	0.0448	0.6274	0.0471	2.9833	0.3627	0.0016	0.983	551	1.37×10^{6}
78	30	10	0.104	0.9232	0.0265	0.2764	0.0241	3.9260	0.3639	0.0009	0.991	1003	3.08×10^{7}
79	10	15	0.104	0.8925	0.0643	1.3679	0.0467	5.3922	1.8893	0.0074	0.921	118	6.23×10^{5}
80	14	15	0.104	0.8892	0.0501	1.1568	0.0436	4.5858	1.1664	0.0046	0.951	191	1.89×10^{5}
81	18	15	0.104	0.8877	0.0465	0.9425	0.0501	3.7001	0.8116	0.0038	0.959	231	1.19×10^{5}
82	22	15	0.104	0.8959	0.0460	0.7390	0.0540	3.2803	0.6023	0.0029	0.969	305	5.96×10^{6}
83	26	15	0.104	0.9371	0.0451	0.5439	0.0451	3.4357	0.4325	0.0020	0.979	438	2.42×10^{6}
84	30	15	0.104	0.8888	0.0502	0.1800	0.0404	5.1583	0.9644	0.0042	0.955	209	1.52×10^{5}
85	10	20	0.104	0.8930	0.0568	1.3071	0.0466	4.7478	1.3714	0.0058	0.939	152	3.31×10^{5}
86	14	20	0.104	0.8875	0.0539	1.0941	0.0529	4.0715	1.0046	0.0053	0.943	165	2.71×10^{5}
87	18	20	0.104	0.8744	0.0530	0.8783	0.0552	4.1044	0.9683	0.0055	0.942	161	2.91×10^{5}
88	22	20	0.104	0.8611	0.0533	0.6607	0.0546	4.4623	1.1295	0.0054	0.943	163	2.79×10^{5}
89	26	20	0.104	0.8979	0.0555	0.4747	0.0438	5.0257	1.0661	0.0041	0.957	216	1.40×10^{5}
90	30	20	0.104	0.8873	0.0420	0.1764	0.0279	6.1466	1.0354	0.0032	0.966	273	7.83×10^{6}
91	10	25	0.104	0.8816	0.0507	1.2494	0.0400	5.2915	1.1637	0.0050	0.947	175	2.34×10^{5}
92	14	25	0.104	0.8608	0.0547	1.0340	0.0425	5.8068	1.6076	0.0063	0.933	138	4.19×10^{5}
93	18	25	0.104	0.8644	0.0878	0.8646	0.0840	4.7050	2.3502	0.0153	0.837	56.2	3.74×10^{4}
94	22	25	0.104	0.8703	0.0657	0.6906	0.0631	4.5980	1.4998	0.0069	0.927	127	5.20×10^{5}
95	26	25	0.104	0.9210	0.0417	0.5022	0.0321	4.7374	0.6448	0.0021	0.977	415	2.78×10^{6}

96	30	25	0.104	0.8896	0.0556	0.1703	0.0615	3.7242	0.7793	0.0041	0.956	213	1.45×10^{5}
97	10	30	0.104	0.8660	0.0476	1.2422	0.0282	7.4307	1.8585	0.0047	0.950	187	2.01×10^{5}
98	14	30	0.104	0.8742	0.0453	1.0813	0.0396	4.9936	0.9772	0.0040	0.957	218	1.36×10^{5}
99	18	30	0.104	0.8828	0.0711	0.9262	0.0847	3.5105	0.9550	0.0079	0.916	110	7.35×10^{5}
100	22	30	0.104	0.9667	0.1201	0.8286	0.1407	2.6775	0.7164	0.0091	0.903	95.2	1.05×10^{4}
101	26	30	0.104	0.8718	0.0768	0.4172	0.0836	4.0151	1.4309	0.0079	0.916	110	7.28×10^{5}
102	30	30	0.104	0.8374	0.0617	0.0520	0.0780	3.9613	1.4000	0.0084	0.911	104	8.44×10^{5}
103	10	35	0.104	0.8871	0.0395	1.2978	0.0447	3.7017	0.5536	0.0025	0.973	348	4.31×10^{6}
104	14	35	0.104	0.8934	0.0603	1.1396	0.0859	2.8878	0.6251	0.0048	0.948	181	2.16×10^{5}
105	18	35	0.104	0.9509	0.1375	1.0457	0.2040	2.2285	0.7255	0.0074	0.922	119	6.11×10^{5}
106	22	35	0.104	0.9751	0.1254	0.8332	0.1710	2.2652	0.6113	0.0078	0.917	112	7.10×10^{5}
107	26	35	0.104	0.8105	0.0526	0.2527	0.0218	13.7748	5.5980	0.0083	0.911	105	8.31×10^{5}
108	30	35	0.104	0.8342	0.0616	-0.0207	0.0875	3.5492	1.3199	0.0090	0.904	96.2	1.02×10^{4}
109	10	10	0.115	0.9126	0.0688	1.8651	0.0498	4.9198	1.5721	0.0068	0.928	130	4.93×10^{5}
110	14	10	0.115	0.8999	0.0804	1.6552	0.0665	4.4424	1.9393	0.0104	0.889	83.7	1.43×10^{4}
111	18	10	0.115	0.8913	0.0671	1.4512	0.0569	4.6369	1.7565	0.0081	0.913	107	7.82×10^{5}
112	22	10	0.115	0.9104	0.0650	1.2534	0.0597	3.7964	1.1066	0.0052	0.945	170	2.53×10^{5}
113	26	10	0.115	0.9634	0.0696	1.0502	0.0496	4.3915	0.9708	0.0048	0.949	184	2.07×10^{5}
114	30	10	0.115	0.9451	0.0470	0.6861	0.0468	3.3409	0.4657	0.0023	0.976	383	3.38×10^{6}
115	10	15	0.115	0.9038	0.0696	1.8045	0.0532	4.7994	1.6542	0.0075	0.920	117	6.38×10^{5}
116	14	15	0.115	0.8950	0.0727	1.5967	0.0623	4.4351	1.7560	0.0090	0.904	96.5	1.01×10^{4}
117	18	15	0.115	0.8923	0.0640	1.3904	0.0598	4.1368	1.4104	0.0071	0.924	123	5.65×10^{5}
118	22	15	0.115	0.9428	0.0799	1.2168	0.0809	3.1132	0.8388	0.0051	0.945	171	2.48×10^{5}
119	26	15	0.115	0.9566	0.0780	0.9641	0.0569	4.3063	1.1521	0.0064	0.931	136	4.38×10^{5}
120	30	15	0.115	0.9301	0.0666	0.6118	0.0672	3.5217	0.6738	0.0053	0.944	167	2.64×10^{5}
121	10	20	0.115	0.9030	0.0651	1.7453	0.0561	4.2821	1.3205	0.0066	0.930	132	4.67×10^{5}
122	14	20	0.115	0.8942	0.0562	1.5383	0.0514	4.2483	1.1815	0.0055	0.941	158	3.02×10^{5}
123	18	20	0.115	0.8901	0.0555	1.3286	0.0555	3.9268	0.9991	0.0054	0.943	164	2.76×10^{5}
124	22	20	0.115	0.9327	0.0775	1.1567	0.0768	3.4446	0.8375	0.0059	0.937	149	3.50×10^{5}
125	26	20	0.115	0.9212	0.0923	0.8701	0.0607	5.2064	1.8450	0.0113	0.879	76.5	1.78×10^{4}
126	30	20	0.115	0.9068	0.0569	0.5793	0.0444	4.7772	1.0660	0.0050	0.947	177	2.28×10^{5}
127	10	25	0.115	0.8955	0.0486	1.6858	0.0439	4.3231	0.8656	0.0040	0.957	220	1.34×10^{5}
128	14	25	0.115	0.8850	0.0429	1.4846	0.0374	4.7858	0.8532	0.0035	0.963	250	9.77×10^{6}
129	18	25	0.115	0.8696	0.0367	1.2733	0.0306	5.2901	0.8779	0.0027	0.971	324	5.13×10^{6}
130	22	25	0.115	0.9004	0.0860	1.1082	0.0713	4.6840	1.6215	0.0085	0.909	102	8.78×10^{5}
131	26	25	0.115	0.8514	0.0558	0.8251	0.0120	21.8803	7.9646	0.0067	0.929	131	4.82×10^{5}
132	30	25	0.115	0.9378	0.0709	0.6252	0.0700	3.4059	0.7794	0.0057	0.939	154	3.22×10^{5}
133	10	30	0.115	0.8776	0.0476	1.6514	0.0354	5.7372	1.0983	0.0044	0.954	202	1.66×10^{5}
134	14	30	0.115	0.8735	0.0346	1.4768	0.0229	6.5428	1.0527	0.0024	0.974	364	3.85×10^{6}
135	18	30	0.115	0.8765	0.0322	1.3104	0.0259	5.3251	0.7600	0.0020	0.979	443	2.35×10^{6}
136	22	30	0.115	0.9450	0.0720	1.1672	0.0601	3.9954	0.7341	0.0048	0.949	182	2.13×10^{5}
137	26	30	0.115	0.8150	0.0529	0.7383	0.0270	10.6766	4.4680	0.0082	0.913	107	7.96×10^{5}
138	30	30	0.115	0.9243	0.0833	0.5955	0.1138	2.5633	0.6577	0.0065	0.931	134	4.53×10^{5}
139	10	35	0.115	0.8890	0.0457	1.7013	0.0401	4.6023	0.8390	0.0037	0.960	236	1.12×10^{5}
140	14	35	0.115	0.8879	0.0319	1.5293	0.0346	3.7905	0.4623	0.0017	0.982	523	1.56×10^{6}
141	18	35	0.115	0.9410	0.0597	1.4081	0.0710	2.8524	0.4498	0.0023	0.976	387	3.30×10^{6}
142	22	35	0.115	0.9379	0.0491	1.1438	0.0524	3.2419	0.4413	0.0022	0.976	397	3.11×10^{6}
143	26	35	0.115	0.8293	0.0529	0.6732	0.0516	5.3146	1.8318	0.0070	0.925	125	5.40×10^{5}
144	30	35	0.115	0.9010	0.0716	0.5244	0.1184	2.3143	0.6158	0.0055	0.941	158	3.01×10^{5}
145	10	10	0.126	0.9375	0.0427	2.3047	0.0356	4.0923	0.5763	0.0021	0.978	426	2.60×10^{6}

146	14	10	0.126	0.9145	0.0626	2.0955	0.0531	4.1880	1.1408	0.0054	0.943	163	2.81×10^{5}
147	18	10	0.126	0.9017	0.0815	1.8866	0.0712	4.0816	1.7267	0.0096	0.898	90.8	1.18×10^{4}
148	22	10	0.126	0.9602	0.1090	1.7199	0.0854	3.6636	1.3835	0.0083	0.912	105	8.24×10^{5}
149	26	10	0.126	0.9490	0.0900	1.4567	0.0381	7.5990	2.9902	0.0088	0.906	99	9.55×10^{5}
150	30	10	0.126	0.9739	0.0891	1.1110	0.1031	2.5740	0.5759	0.0062	0.934	142	3.97×10^{5}
151	10	15	0.126	0.9292	0.0444	2.2460	0.0390	3.9565	0.6329	0.0024	0.975	373	3.63×10^{6}
152	14	15	0.126	0.9063	0.0546	2.0356	0.0477	4.2187	1.0647	0.0045	0.952	196	1.78×10^{5}
153	18	15	0.126	0.8988	0.0737	1.8286	0.0664	4.0487	1.5016	0.0080	0.915	109	7.53×10^{5}
154	22	15	0.126	0.9657	0.0757	1.6658	0.0571	3.9402	0.9804	0.0048	0.949	184	2.08×10^{5}
155	26	15	0.126	0.9583	0.0687	1.3527	0.0475	4.5829	1.0310	0.0049	0.948	179	2.23×10^{5}
156	30	15	0.126	0.9611	0.0931	1.0451	0.1094	2.6760	0.6097	0.0076	0.919	115	6.65×10^{5}
157	10	20	0.126	0.9219	0.0371	2.1855	0.0348	3.7794	0.5358	0.0018	0.981	504	1.71×10^{6}
158	14	20	0.126	0.9080	0.0550	1.9769	0.0543	3.6812	0.8849	0.0044	0.954	202	1.65×10^{5}
159	18	20	0.126	0.9011	0.0647	1.7698	0.0622	3.7744	1.0636	0.0057	0.939	153	3.25×10^{5}
160	22	20	0.126	0.9706	0.0558	1.6040	0.0424	4.0216	0.6477	0.0028	0.970	316	5.44×10^{6}
161	26	20	0.126	0.9443	0.0444	1.2628	0.0346	4.3464	0.5484	0.0022	0.977	402	3.00×10^{6}
162	30	20	0.126	0.9437	0.0624	1.0075	0.0631	3.2946	0.5882	0.0042	0.956	211	1.49×10^{5}
163	10	25	0.126	0.9170	0.0395	2.1259	0.0409	3.4972	0.5015	0.0021	0.978	426	2.61×10^{6}
164	14	25	0.126	0.8983	0.0391	1.9168	0.0398	3.8162	0.5849	0.0024	0.974	361	3.91×10^{6}
165	18	25	0.126	0.8969	0.0523	1.7216	0.0500	4.0682	0.7880	0.0041	0.957	216	1.40×10^{5}
166	22	25	0.126	0.9487	0.0422	1.5342	0.0294	4.7928	0.5330	0.0018	0.981	493	1.81×10^{6}
167	26	25	0.126	0.9174	0.0384	1.2197	0.0249	5.6165	0.7735	0.0020	0.979	445	2.34×10^{6}
168	30	25	0.126	0.9469	0.0847	1.0393	0.0740	3.6421	1.1233	0.0079	0.916	110	7.34×10^{5}
169	10	30	0.126	0.8903	0.0396	2.0681	0.0381	4.2772	0.6267	0.0026	0.972	340	4.54×10^{6}
170	14	30	0.126	0.8800	0.0410	1.8803	0.0362	4.8398	0.7818	0.0031	0.967	281	7.28×10^{6}
171	18	30	0.126	0.8900	0.0484	1.7152	0.0387	5.0246	0.9800	0.0038	0.960	233	1.16×10^{5}
172	22	30	0.126	0.9521	0.0658	1.5399	0.0351	6.1038	1.1811	0.0046	0.951	190	1.93×10^{5}
173	26	30	0.126	0.9455	0.0411	1.2549	0.0365	3.8180	0.4264	0.0017	0.981	507	1.69×10^{6}
174	30	30	0.126	0.9519	0.0590	1.0464	0.0689	2.7420	0.4645	0.0031	0.967	281	7.31×10^{6}
175	10	35	0.126	0.8863	0.0351	2.0890	0.0286	5.0254	0.7523	0.0022	0.976	396	3.11×10^{6}
176	14	35	0.126	0.8887	0.0576	1.9284	0.0537	4.2439	0.9731	0.0056	0.940	157	3.09×10^{5}
177	18	35	0.126	0.9617	0.0426	1.8120	0.0384	3.4861	0.3819	0.0014	0.985	640	9.46×10^{7}
178	22	35	0.126	0.9324	0.0219	1.5043	0.0185	4.1477	0.2740	0.0005	0.995	1739	7.81×10^{8}
179	26	35	0.126	0.9260	0.0545	1.2144	0.0681	2.8893	0.4648	0.0029	0.969	301	6.18×10^{6}
180	30	35	0.126	0.9434	0.0529	1.0126	0.0796	2.1817	0.3409	0.0022	0.977	403	2.98×10^{6}
181	10	10	0.142	0.9431	0.0551	2.9075	0.0555	3.3406	0.5206	0.0031	0.968	289	6.83×10^{6}
182	14	10	0.142	0.9512	0.0435	2.7348	0.0437	3.2155	0.4080	0.0016	0.983	542	1.43×10^{6}
183	18	10	0.142	0.9822	0.1073	2.5644	0.0945	3.1365	0.8253	0.0034	0.964	261	8.78×10^{6}
184	22	10	0.142	0.9736	0.0832	2.3322	0.0454	5.5271	1.5005	0.0061	0.935	144	3.80×10^{5}
185	26	10	0.142	0.9821	0.1044	1.9924	0.0967	3.1190	0.7975	0.0074	0.921	118	6.22×10^{5}
186	30	10	0.142	1.0220	0.1431	1.7504	0.1859	1.9559	0.5774	0.0086	0.908	101	9.09×10^{5}
187	10	15	0.142	0.9393	0.0571	2.8544	0.0603	3.1999	0.5395	0.0033	0.965	271	8.00×10^{6}
188	14	15	0.142	0.9528	0.0510	2.6838	0.0533	3.0263	0.4595	0.0020	0.979	452	2.25×10^{6}
189	18	15	0.142	0.9953	0.1016	2.5176	0.0901	3.0298	0.7027	0.0025	0.973	353	4.14×10^{6}
190	22	15	0.142	0.9720	0.1029	2.2446	0.0650	4.6724	1.5828	0.0092	0.902	94.8	1.06×10^{4}
191	26	15	0.142	0.9852	0.0857	1.9200	0.0879	2.8218	0.5700	0.0049	0.948	178	2.25×10^{5}
192	30	15	0.142	1.009	0.1103	1.6828	0.1424	2.1351	0.5137	0.0070	0.926	126	5.32×10^{5}
193	10	20	0.142	0.9400	0.0519	2.8042	0.0578	3.0126	0.4755	0.0026	0.972	337	4.66×10^{6}
194	14	20	0.142	0.9559	0.0453	2.6321	0.0492	2.8485	0.3756	0.0013	0.987	695	7.69×10^{7}
195	18	20	0.142	1.0499	0.0950	2.5050	0.0866	2.6927	0.4557	0.0016	0.983	550	1.38×10^{6}

196	22	20	0.142	0.9668	0.0632	2.1608	0.0428	4.5234	0.9066	0.0037	0.961	237	1.11×10^5
197	26	20	0.142	0.9718	0.0705	1.8459	0.0767	2.8382	0.4527	0.0038	0.960	233	1.16×10^5
198	30	20	0.142	0.9758	0.0659	1.6250	0.0796	2.4920	0.3950	0.0033	0.965	268	8.18×10^6
199	10	25	0.142	0.9368	0.0376	2.7488	0.0444	2.8797	0.3296	0.0014	0.986	650	9.10×10^7
200	14	25	0.142	0.9497	0.0499	2.5726	0.0566	2.7968	0.3880	0.0015	0.985	607	1.08×10^6
201	18	25	0.142	1.0073	0.0589	2.4090	0.0539	2.9920	0.3591	0.0013	0.986	671	8.38×10^7
202	22	25	0.142	0.9524	0.0446	2.0686	0.0346	4.2247	0.5231	0.0020	0.979	452	2.25×10^6
203	26	25	0.142	0.9476	0.0507	1.7947	0.0514	3.3080	0.4218	0.0024	0.975	372	3.63×10^6
204	30	25	0.142	0.9510	0.0388	1.6157	0.0373	3.3757	0.3900	0.0015	0.985	607	1.08×10^6
205	10	30	0.142	0.9133	0.0448	2.6813	0.0542	3.1048	0.4436	0.0022	0.977	404	2.97×10^6
206	14	30	0.142	0.9036	0.0702	2.4889	0.0795	3.3733	0.7833	0.0048	0.949	183	2.09×10^5
207	18	30	0.142	0.9510	0.0555	2.3218	0.0476	3.8234	0.5189	0.0023	0.976	385	3.34×10^6
208	22	30	0.142	0.9151	0.0591	2.0073	0.0428	5.1686	1.0170	0.0040	0.958	222	1.31×10^5
209	26	30	0.142	0.9561	0.0605	1.8282	0.0545	3.5339	0.6039	0.0035	0.963	254	9.42×10^6
210	30	30	0.142	0.9643	0.0578	1.6619	0.0559	3.2381	0.5400	0.0031	0.967	284	7.13×10^6
211	10	35	0.142	0.8670	0.0610	2.6190	0.0664	4.1440	1.1245	0.0059	0.937	149	3.50×10^5
212	14	35	0.142	0.8719	0.0554	2.4633	0.0531	4.4328	1.0972	0.0045	0.952	194	1.82×10^5
213	18	35	0.142	0.9633	0.0395	2.3450	0.0262	4.7536	0.5140	0.0014	0.985	616	1.04×10^6
214	22	35	0.142	0.9478	0.0705	2.0462	0.0639	3.6672	0.6198	0.0044	0.954	201	1.67×10^5
215	26	35	0.142	0.9682	0.0706	1.8462	0.0816	2.6392	0.4447	0.0036	0.961	242	1.05×10^5
216	30	35	0.142	0.9743	0.0499	1.6645	0.0642	2.3190	0.2961	0.0017	0.982	513	1.64×10^6

Table S4. Hazardous concentrations 5% (HC_5) generated by the best-fit models and their 95% confidence intervals (95% CI) for different temperature, salinity, and *σp*. All HC_5 values were expressed as μmol/L.

No.	Metals	*T*(°C)	*S*(‰)	*σp*	*log-HC*$_5$	*LCL*$_5$	*UCL*$_5$
1	Hg	10	10	0.065	-2.646	-5.831	-1.289
2	Cd	10	10	0.081	-2.582	-6.099	-1.216
3	Cu	10	10	0.104	-2.480	-6.081	-1.192
4	Zn	10	10	0.115	-2.322	-5.279	-1.144
5	Ni	10	10	0.126	-2.196	-4.456	-1.166
6	Cr	10	10	0.142	-2.133	-3.818	-1.250
7	Hg	14	10	0.065	-1.879	-4.091	-0.776
8	Cd	14	10	0.081	-1.759	-4.428	-0.598
9	Cu	14	10	0.104	-1.704	-4.976	-0.513
10	Zn	14	10	0.115	-1.586	-4.560	-0.472
11	Ni	14	10	0.126	-1.423	-3.546	-0.474
12	Cr	14	10	0.142	-1.318	-2.939	-0.527
13	Hg	18	10	0.065	-0.850	-2.361	-0.024
14	Cd	18	10	0.081	-0.658	-2.136	0.167
15	Cu	18	10	0.104	-0.513	-2.382	0.386
16	Zn	18	10	0.115	-0.438	-2.802	0.484
17	Ni	18	10	0.126	-0.315	-2.307	0.528
18	Cr	18	10	0.142	-0.155	-1.445	0.516
19	Hg	22	10	0.065	-0.389	-1.613	0.315
20	Cd	22	10	0.081	-0.164	-1.331	0.528
21	Cu	22	10	0.104	0.019	-1.260	0.761
22	Zn	22	10	0.115	0.143	-1.405	0.913
23	Ni	22	10	0.126	0.236	-1.432	0.971
24	Cr	22	10	0.142	0.377	-0.769	0.962
25	Hg	26	10	0.065	0.054	-0.950	0.656
26	Cd	26	10	0.081	0.310	-0.558	0.856
27	Cu	26	10	0.104	0.529	-0.287	1.076
28	Zn	26	10	0.115	0.691	-0.301	1.292
29	Ni	26	10	0.126	0.790	-0.413	1.387
30	Cr	26	10	0.142	0.914	-0.007	1.423
31	Hg	30	10	0.065	0.628	-0.349	1.188
32	Cd	30	10	0.081	0.915	0.203	1.356
33	Cu	30	10	0.104	1.176	0.708	1.519
34	Zn	30	10	0.115	1.394	1.004	1.711
35	Ni	30	10	0.126	1.544	1.039	1.909
36	Cr	30	10	0.142	1.650	1.116	2.006
37	Hg	10	15	0.065	-2.403	-4.204	-1.432
38	Cd	10	15	0.081	-2.333	-4.505	-1.355
39	Cu	10	15	0.104	-2.208	-4.039	-1.307
40	Zn	10	15	0.115	-2.083	-3.476	-1.328

41	Ni	10	15	0.126	-2.018	-3.050	-1.356
42	Cr	10	15	0.142	-2.031	-2.971	-1.432
43	Hg	14	15	0.065	-1.632	-2.860	-0.839
44	Cd	14	15	0.081	-1.525	-3.051	-0.710
45	Cu	14	15	0.104	-1.461	-3.201	-0.632
46	Zn	14	15	0.115	-1.321	-2.765	-0.610
47	Ni	14	15	0.126	-1.224	-2.219	-0.648
48	Cr	14	15	0.142	-1.206	-1.963	-0.698
49	Hg	18	15	0.065	-0.623	-1.340	-0.106
50	Cd	18	15	0.081	-0.430	-1.185	0.077
51	Cu	18	15	0.104	-0.301	-1.214	0.257
52	Zn	18	15	0.115	-0.221	-1.269	0.357
53	Ni	18	15	0.126	-0.104	-0.889	0.371
54	Cr	18	15	0.142	-0.036	-0.533	0.309
55	Hg	22	15	0.065	-0.198	-0.905	0.255
56	Cd	22	15	0.081	0.034	-0.581	0.440
57	Cu	22	15	0.104	0.216	-0.385	0.618
58	Zn	22	15	0.115	0.317	-0.483	0.766
59	Ni	22	15	0.126	0.419	-0.248	0.832
60	Cr	22	15	0.142	0.501	0.114	0.790
61	Hg	26	15	0.065	0.212	-0.469	0.646
62	Cd	26	15	0.081	0.476	0.062	0.784
63	Cu	26	15	0.104	0.692	0.347	0.942
64	Zn	26	15	0.115	0.842	0.436	1.135
65	Ni	26	15	0.126	0.935	0.446	1.261
66	Cr	26	15	0.142	1.003	0.627	1.269
67	Hg	30	15	0.065	0.728	-0.341	1.221
68	Cd	30	15	0.081	1.026	0.428	1.351
69	Cu	30	15	0.104	1.289	1.051	1.459
70	Zn	30	15	0.115	1.494	1.373	1.590
71	Ni	30	15	0.126	1.607	1.281	1.861
72	Cr	30	15	0.142	1.688	1.350	1.928
73	Hg	10	20	0.065	-2.242	-3.327	-1.574
74	Cd	10	20	0.081	-2.146	-3.286	-1.513
75	Cu	10	20	0.104	-2.041	-2.911	-1.485
76	Zn	10	20	0.115	-1.982	-2.640	-1.509
77	Ni	10	20	0.126	-1.991	-2.597	-1.539
78	Cr	10	20	0.142	-2.091	-2.881	-1.560
79	Hg	14	20	0.065	-1.471	-2.089	-0.992
80	Cd	14	20	0.081	-1.391	-2.287	-0.835
81	Cu	14	20	0.104	-1.307	-2.229	-0.762
82	Zn	14	20	0.115	-1.210	-1.920	-0.765
83	Ni	14	20	0.126	-1.198	-1.786	-0.793
84	Cr	14	20	0.142	-1.280	-2.035	-0.826

85	Hg	18	20	0.065	-0.490	-0.880	-0.228
86	Cd	18	20	0.081	-0.314	-0.709	-0.042
87	Cu	18	20	0.104	-0.221	-0.823	0.173
88	Zn	18	20	0.115	-0.170	-0.996	0.269
89	Ni	18	20	0.126	-0.103	-0.716	0.275
90	Cr	18	20	0.142	-0.114	-0.544	0.172
91	Hg	22	20	0.065	-0.096	-0.572	0.214
92	Cd	22	20	0.081	0.124	-0.215	0.366
93	Cu	22	20	0.104	0.272	-0.140	0.579
94	Zn	22	20	0.115	0.350	-0.282	0.722
95	Ni	22	20	0.126	0.430	0.058	0.706
96	Cr	22	20	0.142	0.429	0.236	0.600
97	Hg	26	20	0.065	0.257	-0.487	0.638
98	Cd	26	20	0.081	0.512	0.073	0.772
99	Cu	26	20	0.104	0.708	0.349	0.969
100	Zn	26	20	0.115	0.836	0.469	1.106
101	Ni	26	20	0.126	0.917	0.644	1.123
102	Cr	26	20	0.142	0.917	0.765	1.064
103	Hg	30	20	0.065	0.693	-0.908	1.155
104	Cd	30	20	0.081	1.00	0.106	1.298
105	Cu	30	20	0.104	1.267	0.962	1.419
106	Zn	30	20	0.115	1.449	1.359	1.521
107	Ni	30	20	0.126	1.529	1.319	1.710
108	Cr	30	20	0.142	1.534	1.302	1.726
109	Hg	10	25	0.065	-2.181	-2.920	-1.673
110	Cd	10	25	0.081	-2.095	-2.827	-1.619
111	Cu	10	25	0.104	-2.035	-2.574	-1.586
112	Zn	10	25	0.115	-2.058	-2.689	-1.598
113	Ni	10	25	0.126	-2.121	-2.787	-1.676
114	Cr	10	25	0.142	-2.272	-3.194	-1.735
115	Hg	14	25	0.065	-1.441	-1.973	-1.056
116	Cd	14	25	0.081	-1.402	-2.323	-0.875
117	Cu	14	25	0.104	-1.312	-2.072	-0.847
118	Zn	14	25	0.115	-1.261	-1.719	-0.907
119	Ni	14	25	0.126	-1.315	-1.765	-0.975
120	Cr	14	25	0.142	-1.449	-2.063	-1.040
121	Hg	18	25	0.065	-0.489	-0.813	-0.223
122	Cd	18	25	0.081	-0.326	-0.605	-0.094
123	Cu	18	25	0.104	-0.254	-0.708	0.058
124	Zn	18	25	0.115	-0.211	-0.620	0.087
125	Ni	18	25	0.126	-0.247	-0.660	0.032
126	Cr	18	25	0.142	-0.350	-0.736	-0.078
127	Hg	22	25	0.065	-0.103	-0.497	0.145
128	Cd	22	25	0.081	0.099	-0.084	0.253

129	Cu	22	25	0.104	0.201	-0.159	0.458
130	Zn	22	25	0.115	0.232	-0.280	0.557
131	Ni	22	25	0.126	0.214	-0.250	0.535
132	Cr	22	25	0.142	0.135	-0.183	0.399
133	Hg	26	25	0.065	0.218	-0.452	0.544
134	Cd	26	25	0.081	0.460	0.198	0.653
135	Cu	26	25	0.104	0.606	0.344	0.818
136	Zn	26	25	0.115	0.646	0.096	0.993
137	Ni	26	25	0.126	0.618	-0.007	0.991
138	Cr	26	25	0.142	0.565	0.175	0.868
139	Hg	30	25	0.065	0.611	-0.617	1.047
140	Cd	30	25	0.081	0.886	0.318	1.180
141	Cu	30	25	0.104	1.094	0.842	1.270
142	Zn	30	25	0.115	1.174	0.783	1.457
143	Ni	30	25	0.126	1.166	0.612	1.503
144	Cr	30	25	0.142	1.113	0.679	1.408
145	Hg	10	30	0.065	-2.214	-2.805	-1.799
146	Cd	10	30	0.081	-2.140	-2.586	-1.809
147	Cu	10	30	0.104	-2.126	-2.415	-1.845
148	Zn	10	30	0.115	-2.207	-2.620	-1.880
149	Ni	10	30	0.126	-2.330	-2.810	-1.938
150	Cr	10	30	0.142	-2.514	-3.191	-2.019
151	Hg	14	30	0.065	-1.504	-1.926	-1.179
152	Cd	14	30	0.081	-1.451	-1.974	-1.076
153	Cu	14	30	0.104	-1.312	-2.064	-0.840
154	Zn	14	30	0.115	-1.489	-1.995	-1.126
155	Ni	14	30	0.126	-1.586	-2.023	-1.232
156	Cr	14	30	0.142	-1.759	-2.312	-1.358
157	Hg	18	30	0.065	-0.594	-0.833	-0.405
158	Cd	18	30	0.081	-0.520	-1.017	-0.167
159	Cu	18	30	0.104	-0.522	-1.347	-0.082
160	Zn	18	30	0.115	-0.543	-1.347	-0.091
161	Ni	18	30	0.126	-0.630	-1.250	-0.229
162	Cr	18	30	0.142	-0.799	-1.474	-0.391
163	Hg	22	30	0.065	-0.257	-0.650	-0.010
164	Cd	22	30	0.081	-0.143	-0.630	0.195
165	Cu	22	30	0.104	-0.149	-1.135	0.330
166	Zn	22	30	0.115	-0.187	-1.264	0.325
167	Ni	22	30	0.126	-0.225	-0.977	0.202
168	Cr	22	30	0.142	-0.352	-0.900	0.028
169	Hg	26	30	0.065	0.040	-0.482	0.356
170	Cd	26	30	0.081	0.205	-0.190	0.494
171	Cu	26	30	0.104	0.244	-0.487	0.669
172	Zn	26	30	0.115	0.222	-0.733	0.702

173	Ni	26	30	0.126	0.178	-0.540	0.604
174	Cr	26	30	0.142	0.064	-0.439	0.409
175	Hg	30	30	0.065	0.460	-0.117	0.784
176	Cd	30	30	0.081	0.648	0.353	0.832
177	Cu	30	30	0.104	0.726	0.339	1.012
178	Zn	30	30	0.115	0.737	0.278	1.074
179	Ni	30	30	0.126	0.695	0.278	1.007
180	Cr	30	30	0.142	0.599	0.286	0.838
181	Hg	10	35	0.065	-2.368	-2.839	-1.998
182	Cd	10	35	0.081	-2.360	-2.815	-1.976
183	Cu	10	35	0.104	-2.417	-2.887	-2.053
184	Zn	10	35	0.115	-2.518	-2.940	-2.166
185	Ni	10	35	0.126	-2.682	-3.186	-2.265
186	Cr	10	35	0.142	-2.914	-3.713	-2.340
187	Hg	14	35	0.065	-1.759	-2.562	-1.291
188	Cd	14	35	0.081	-1.744	-2.552	-1.256
189	Cu	14	35	0.104	-1.779	-2.550	-1.307
190	Zn	14	35	0.115	-1.878	-2.592	-1.408
191	Ni	14	35	0.126	-2.034	-2.770	-1.562
192	Cr	14	35	0.142	-2.260	-3.204	-1.671
193	Hg	18	35	0.065	-0.911	-1.446	-0.508
194	Cd	18	35	0.081	-0.950	-2.114	-0.402
195	Cu	18	35	0.104	-0.971	-2.150	-0.412
196	Zn	18	35	0.115	-1.008	-1.943	-0.503
197	Ni	18	35	0.126	-1.137	-1.899	-0.663
198	Cr	18	35	0.142	-1.313	-2.068	-0.839
199	Hg	22	35	0.065	-0.562	-1.002	-0.227
200	Cd	22	35	0.081	-0.563	-1.429	-0.089
201	Cu	22	35	0.104	-0.582	-1.613	-0.068
202	Zn	22	35	0.115	-0.616	-1.357	-0.138
203	Ni	22	35	0.126	-0.713	-1.247	-0.328
204	Cr	22	35	0.142	-0.865	-1.311	-0.524
205	Hg	26	35	0.065	-0.252	-0.616	0.012
206	Cd	26	35	0.081	-0.220	-0.813	0.178
207	Cu	26	35	0.104	-0.206	-0.821	0.218
208	Zn	26	35	0.115	-0.260	-0.843	0.140
209	Ni	26	35	0.126	-0.337	-0.742	-0.020
210	Cr	26	35	0.142	-0.471	-0.704	-0.260
211	Hg	30	35	0.065	0.126	-0.252	0.373
212	Cd	30	35	0.081	0.197	-0.283	0.501
213	Cu	30	35	0.104	0.246	-0.074	0.503
214	Zn	30	35	0.115	0.205	-0.172	0.479
215	Ni	30	35	0.126	0.112	-0.311	0.383
216	Cr	30	35	0.142	-0.002	-0.297	0.203

Table S5. Linear regression analysis between three fitting variables (*a*, *Xc* and *K*) and QSAR parameters (*σp*, *T* and *S*). One-way ANOVA was used to test the difference between the means of two variables.

Relationships	r^2	F	p	Means difference by Bonferroni & Tukey Test
a-T	0.0003	0.0110	0.999	0[a]
a-S	0.0164	0.673	0.644	0
a-σp	0.201	10.2	0	1
Xc-T	0.131	6.11	0	1
Xc-S	0.0012	0.0466	0.999	0
Xc-σp	0.861	250	0	1
K-T	0.0608	2.62	0.0257	1
K-S	0.0637	2.75	0.0200	1
K-σp	0.398	26.7	0	1

[a] Sig. equals 1 indicated the different between the means was significant at the 0.05 level. Sig. equals 0 indicated the difference between the means was not significant at the 0.05 level.

Table S6. Summary of data used for constructing temperature-based species sensitivity distribution (SSDs) for Cd and Cr (III) at the temperature of 15, 20, and 25°C [4]. The scientific name, taxonomic group, median lethal concentration (LC_{50}) and sources of data.

Cadmium

Temp.	Species Scientific Name	Taxonomic Group	Median Lethal Concentration (LC_{50}, μg/L)	Reference
15°C	*Ampelisca abdita*	Crustacea	1320	Kohn et al., 1994
	Balanus improvisus	Crustacea	160	Lang et al., 1981
	Cancer magister	Crustacea	247	Martin et al., 1981
	Crangon crangon	Crustacea	1000	Portmann and Wilson, 1971
	Emerita analoga	Crustacea	2110	Boese et al., 1997
	Eohaustorius estuarius	Crustacea	8559	DeWitt et al., 1992
	Eohaustorius estuarius	Crustacea	12510	Boese et al., 1997
	Eurytemora affinis	Crustacea	135	Sullivan et al., 1983
	Eurytemora affinis	Crustacea	1333	Lussier and Cardin, 1985
	Excirolana sp.	Crustacea	8000	Boese et al., 1997
	Gammarus locusta	Crustacea	590	Costa et al., 1996
	Grandidierella japonica	Crustacea	3140	Kohn et al., 1994
	Homarus americanus	Crustacea	28000	McLeese, 1976
	Lepidactylus dytiscus	Crustacea	6840	DeWitt et al., 1992
	Leptocheirus plumulosus	Crustacea	11447	DeWitt et al., 1992
	Monoculodes edwardsi	Crustacea	240	DeWitt et al., 1992
	Neomysis integer	Crustacea	9	Wildgust and Jones, 1998
	Pseudodiaptomus coronatus	Crustacea	1910	Lussier and Cardin, 1985
	Rhepoxynius abronius	Crustacea	1009	Kohn et al., 1994
	Rhepoxynius abronius	Crustacea	790	DeWitt et al., 1992
	Rhepoxynius abronius	Crustacea	10000	Werner and Nagel, 1997
	Rhepoxynius abronius	Crustacea	1510	Boese et al., 1997
	Talitrus saltator	Crustacea	27660	Ungherese and Ugolini, 2009
	Varuna litterata	Crustacea	47532	Kulkarni, 1983
	Agonus cataphractus	Actinopterygii	33000	Portmann and Wilson, 1971
	Limanda limanda	Actinopterygii	35000	Hutchinson and Manning, 1996
	Psetta maxima	Actinopterygii	6994	George et al., 1996
	Cerastoderma edule	Mollusca	3300	Portmann and Wilson, 1971
	Capitella capitata	Polychaeta	9889	Reish et al., 1977
	Ctenodrilus serratus	Polychaeta	3675	Reish et al., 1977
	Neanthes arenaceodentata	Polychaeta	5600	Reish and Gerlinger, 1984
	Neanthes arenaceodentata	Polychaeta	5600	Reish et al., 1977
	Neanthes arenaceodentata	Polychaeta	30300	Reish et al., 1977
	Ophryotrocha diadema	Polychaeta	9562	Reish et al., 1977
	Perinereis aibuhitensis	Polychaeta	3880	Zhang et al., 2008
20°C	*Acartia tonsa*	Crustacea	173	Sosnowski and Gentile, 1978
	Allorchestes compressa	Crustacea	780	Ahsanullah et al., 1988
	Americamysis bahia	Crustacea	59	Voyer and Modica, 1990

Americamysis bahia	Crustacea	2.1	Emson and Crane, 1994
Ampelisca abdita	Crustacea	2900	Scott et al., 1982
Ampelisca abdita	Crustacea	338	Redmond et al., 1994
Ampelisca abdita	Crustacea	2500	Werner and Nagel, 1997
Carcinus maenas	Crustacea	18951	Eisler, 1971
Chasmagnathus granulata	Crustacea	50000	Vitale et al., 1999
Chelura terebrans	Crustacea	630	Hong and Reish, 1987
Corophium insidiosum	Crustacea	1270	Hong and Reish, 1987
Corophium insidiosum	Crustacea	960	Boese et al., 1997
Crangon septemspinosa	Crustacea	727	Eisler, 1971
Elasmopus bampo	Crustacea	570	Hong and Reish, 1987
Grandidierella japonica	Crustacea	1170	Hong and Reish, 1987
Grandidierella japonica	Crustacea	340	Boese et al., 1997
Homarus americanus	Crustacea	78	Johnson and Gentile, 1979
Jaeropsis sp.	Crustacea	410	Hong and Reish, 1987
Leptocheirus plumulosus	Crustacea	2397	DeWitt et al., 1992
Limnoria tripunctata	Crustacea	7120	Hong and Reish, 1987
Neomysis integer	Crustacea	1.4	Emson and Crane, 1994
Neomysis integer	Crustacea	120	Verslycke et al., 2003
Nitocra spinipes	Crustacea	1800	Bengtsson, 1978
Pagurus longicarpus	Crustacea	12007	Eisler and Hennekey, 1977
Palaemonetes pugio	Crustacea	1774	Howard and Hacker, 1990
Palaemonetes vulgaris	Crustacea	4714	Eisler, 1971
Penaeus merguiensis	Crustacea	1427	Denton and Burdon-Jones, 1982
Rhepoxynius abronius	Crustacea	240	Hong and Reish, 1987
Tigriopus brevicornis	Crustacea	29	Forget et al., 1998
Tigriopus japonicus	Crustacea	25200	Lee et al., 2007
Uca pugilator	Crustacea	38149	O'Hara, 1973
Cyprinodon variegatus	Actinopterygii	62996	Eisler, 1971
Dicentrarchus labrax	Actinopterygii	4956	Gelli et al., 2004
Fundulus heteroclitus	Actinopterygii	69570	Eisler and Hennekey, 1977
Fundulus heteroclitus	Actinopterygii	44400	Burton and Actinopterygiier, 1990
Fundulus heteroclitus	Actinopterygii	35684	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	864	Voyer, 1975
Fundulus heteroclitus	Actinopterygii	20030	Middaugh and Dean, 1977
Fundulus heteroclitus	Actinopterygii	81932	Eisler, 1971
Fundulus majalis	Actinopterygii	53702	Eisler, 1971
Liza vaigiensis	Actinopterygii	6399	Denton and Burdon-Jones, 1986
Menidia menidia	Actinopterygii	4345	Middaugh and Dean, 1977
Priopidichthys sp.	Actinopterygii	23366	Denton and Burdon-Jones, 1986
Argopecten irradians	Mollusca	3036	Nelson et al., 1976
Crassostrea gigas	Mollusca	1517	Cardwell et al., 1979
Donax trunculus	Mollusca	5374	Neuberger-Cywiak et al., 2003
Monodonta lineata	Mollusca	2441	Cunha et al., 2007
Mya arenaria	Mollusca	8944	Eisler and Hennekey, 1977
Mya arenaria	Mollusca	28020	Eisler, 1971

	Mytilus edulis	Mollusca	93789	Eisler, 1971
	Mytilus edulis	Mollusca	960	Nelson et al., 1988
	Nassarius festivus	Mollusca	1520	Cheung et al., 2002
	Nassarius obsoletus	Mollusca	78262	Eisler and Hennekey, 1977
	Nassarius obsoletus	Mollusca	64029	Eisler, 1971
	Nucella lapillus	Mollusca	2644	Cunha et al., 2007
	Perna viridis	Mollusca	1570	Chan, 1988
	Urosalpinx cinerea	Mollusca	30793	Eisler, 1971
	Capitella capitata	Polychaeta	5085	Reish et al., 1977
	Capitella capitata	Polychaeta	5800	Reish, 1978
	Ctenodrilus serratus	Polychaeta	3168	Reish et al., 1977
	Ctenodrilus serratus	Polychaeta	20000	Reish, 1978
	Eurythoe complanata	Polychaeta	5000	Reish et al., 1988
	Eurythoe sp.	Polychaeta	18727	Kidwai and Ahmed, 1999
	Neanthes arenaceodentata	Polychaeta	11800	Reish and Gerlinger, 1984
	Neanthes arenaceodentata	Polychaeta	10189	Reish et al., 1977
	Neanthes arenaceodentata	Polychaeta	12100	Reish, 1978
	Nereis virens	Polychaeta	22821	Eisler and Hennekey, 1977
	Nereis virens	Polychaeta	25000	Eisler, 1971
	Nereis virens	Polychaeta	11000	Vranken et al., 1985
	Ophryotrocha diadema	Polychaeta	2168	Reish et al., 1977
	Ophryotrocha diadema	Polychaeta	4200	Reish, 1978
	Asterias forbesii	Asteroidea	22452	Eisler and Hennekey, 1977
	Asterias forbesii	Asteroidea	2143	Eisler, 1971
	Euplotes mutabilis	Spirotrichea	480	Al-Rasheid and Sleigh, 1994
	Nematostella vectinsis	Anthozoa	1184	Harter and Matthews, 2005
25°C	*Americamysis bahia*	Crustacea	23	Voyer and Modica, 1990
	Americamysis bahia	Crustacea	10	Emson and Crane, 1994
	Americamysis bahia	Crustacea	20	Cripe, 1994
	Artemia salina	Crustacea	78100	Crisinel et al., 1994
	Artemia sp.	Crustacea	260616	Espiritu et al., 1995
	Artemia sp.	Crustacea	21579	Xu et al., 1994
	Eurytemora affinis	Crustacea	65	Hall et al., 1995
	Leptocheirus plumulosus	Crustacea	265	DeWitt et al., 1992
	Leptocheirus plumulosus	Crustacea	1450	Boese et al., 1997
	Leptocheirus plumulosus	Crustacea	347	McGee et al., 1998
	Litopenaeus schmitti	Crustacea	418	Barbieri, 2007
	Litopenaeus vannamei	Crustacea	1422	Wu and Chen, 2004
	Metamysidopsis insularis	Crustacea	134	Garcia et al., 2008
	Moina mongolica	Crustacea	5036	An and He, 1991
	Neomysis integer	Crustacea	2.4	Emson and Crane, 1994
	Palaemonetes vulgaris	Crustacea	760	Nimmo et al., 1977
	Penaeus duorarum	Crustacea	4600	Bahner and Nimmo, 1975
	Penaeus duorarum	Crustacea	509	Cripe, 1994
	Penaeus japonicus	Crustacea	513	Bambang et al., 1995
	Varuna litterata	Crustacea	52380	Kulkarni, 1983
	Acanthopagrus schlegeli	Actinopterygii	26678	Koyama et al., 1992
	Chasmichthys dolichognathus	Actinopterygii	34742	Kuroshima and Kimura, 1990
	Chasmichthys	Actinopterygii	33434	Koyama et al., 1992

dolichognathus			
Cyprinodon dearborni	Actinopterygii	25981	Chung, 1983
Cyprinodon variegatus	Actinopterygii	1230	Hutchinson et al., 1994
Cyprinodon variegatus	Actinopterygii	303	Hall et al., 1995
Girella punctata	Actinopterygii	36998	Kuroshima and Kimura, 1990
Girella punctata	Actinopterygii	40453	Koyama et al., 1992
Mugil cephalus	Actinopterygii	10659	Koyama et al., 1992
Oreochromis mossambicus	Actinopterygii	80000	Chung, 1983
Pagrus major	Actinopterygii	4138	Kuroshima et al., 1993
Pagrus major	Actinopterygii	379	Koyama et al., 1992
Poecilia vivipara	Actinopterygii	37108	Chung, 1983
Rivulus marmoratus	Actinopterygii	7853	Park, et al., 1994
Ephemera japonica	Insecta	6527	Koyama et al., 1992
Ephemera japonica	Insecta	6000	Koyama et al., 1992
Brachionus plicatilis	Eurotatoria	47950	Snell and Persoone, 1989
Brachionus plicatilis	Eurotatoria	16435	Snell et al., 1991
Perna viridis	Mollusca	1500	Arasu and Reddy, 1994
Mytilus galloprovincialis	Mollusca	1700	Vlahogianni and Valavanidis, 2007
Monhystera microphthalma	Polychaeta	24000	Chapman et al., 1982

Chromium (III)

Temp	Species Scientific Name	Taxonomic Group	Median Lethal Concentration (LC_{50}, μg/L)	Reference
15°C	*Dunaliella bioculata*	Chlorophyceae	77000	Kusk and Nyholm, 1992
	Skeletonema costatum	Bacillariophyceae	5800	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	7700	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	3200	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	3500	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	3600	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	3600	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	3800	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	4400	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	5000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	500	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	60000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	60000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	25000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	25000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	54000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	54000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	63000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	12000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	15000	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	4200	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	4500	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	4500	Kusk and Nyholm, 1991
	Skeletonema costatum	Bacillariophyceae	7400	Kusk and Nyholm, 1991

Skeletonema costatum	Bacillariophyceae	7800	Kusk and Nyholm, 1991
Skeletonema costatum	Bacillariophyceae	4400	Kusk and Nyholm, 1992
Artemia salina	Crustacea	156000	Persoone et al., 1989
Artemia salina	Crustacea	160000	Persoone et al., 1989
Artemia salina	Crustacea	191300	Persoone et al., 1989
Artemia salina	Crustacea	206500	Persoone et al., 1989
Cancer magister	Crustacea	3440	Martin et al., 1981
Corophium volutator	Crustacea	180000	Bryant et al., 1984
Corophium volutator	Crustacea	32000	Bryant et al., 1984
Corophium volutator	Crustacea	90000	Bryant et al., 1984
Corophium volutator	Crustacea	12000	Bryant et al., 1984
Corophium volutator	Crustacea	30000	Bryant et al., 1984
Corophium volutator	Crustacea	38000	Bryant et al., 1984
Corophium volutator	Crustacea	44000	Bryant et al., 1984
Corophium volutator	Crustacea	52000	Bryant et al., 1984
Corophium volutator	Crustacea	6000	Bryant et al., 1984
Corophium volutator	Crustacea	65000	Bryant et al., 1984
Corophium volutator	Crustacea	75000	Bryant et al., 1984
Corophium volutator	Crustacea	11000	Bryant et al., 1984
Corophium volutator	Crustacea	15000	Bryant et al., 1984
Corophium volutator	Crustacea	17000	Bryant et al., 1984
Corophium volutator	Crustacea	17000	Bryant et al., 1984
Corophium volutator	Crustacea	2000	Bryant et al., 1984
Corophium volutator	Crustacea	26000	Bryant et al., 1984
Corophium volutator	Crustacea	4200	Bryant et al., 1984
Corophium volutator	Crustacea	9500	Bryant et al., 1984
Corophium volutator	Crustacea	2200	Bryant et al., 1984
Corophium volutator	Crustacea	4400	Bryant et al., 1984
Corophium volutator	Crustacea	4700	Bryant et al., 1984
Corophium volutator	Crustacea	5800	Bryant et al., 1984
Corophium volutator	Crustacea	6000	Bryant et al., 1984
Corophium volutator	Crustacea	9500	Bryant et al., 1984
Corophium volutator	Crustacea	17000	Bryant et al., 1984
Crangon crangon	Crustacea	100000	Portmann and Wilson, 1971
Crangon crangon	Crustacea	100000	Portmann, 1972
Palaemonetes pugio	Crustacea	107000	Fales, 1978
Palaemonetes pugio	Crustacea	39000	Fales, 1978
Praunus flexuosus	Crustacea	14000	McLusky and Hagerman, 1987
Praunus flexuosus	Crustacea	17000	McLusky and Hagerman, 1987
Praunus flexuosus	Crustacea	20000	McLusky and Hagerman, 1987
Praunus flexuosus	Crustacea	22000	McLusky and Hagerman, 1987
Praunus flexuosus	Crustacea	22000	McLusky and Hagerman, 1987
Praunus flexuosus	Crustacea	6000	McLusky and Hagerman, 1987

	Praunus flexuosus	Crustacea	10000	McLusky and Hagerman, 1987
	Praunus flexuosus	Crustacea	11000	McLusky and Hagerman, 1987
	Praunus flexuosus	Crustacea	13000	McLusky and Hagerman, 1987
	Praunus flexuosus	Crustacea	13000	McLusky and Hagerman, 1987
	Praunus flexuosus	Crustacea	8000	McLusky and Hagerman, 1987
	Praunus flexuosus	Crustacea	2500	McLusky and Hagerman, 1987
	Macoma balthica	Mollusca	29000	Bryant et al., 1984
	Macoma balthica	Molluscs	46000	Bryant et al., 1984
	Macoma balthica	Molluscs	64000	Bryant et al., 1984
	Macoma balthica	Molluscs	98000	Bryant et al., 1984
	Macoma balthica	Molluscs	110000	Bryant et al., 1984
	Nereis diversicolor	Polychaeta	12000	Bryant et al., 1984
	Nereis diversicolor	Polychaeta	16000	Bryant et al., 1984
	Nereis diversicolor	Polychaeta	22000	Bryant et al., 1984
	Nereis diversicolor	Polychaeta	7500	Bryant et al., 1984
	Nereis diversicolor	Polychaeta	7500	Bryant et al., 1984
	Nereis diversicolor	Polychaeta	8500	Bryant et al., 1984
	Nereis diversicolor	Polychaeta	9500	Bryant et al., 1984
	Nereis diversicolor	Polychaeta	12000	Bryant et al., 1984
20°C	*Chlorella protothecoides*	Chlorophyta	104	Stauber, 1995
	Dunaliella tertiolecta	Chlorophyceae	17004	Stauber, 1995
	Gymnodinium splendens	Dinophyceae	1000	Wilson and Freeburg, 1980
	Pseudokirchneriella subcapitata	Chlorophyceae	499.2	Stauber, 1995
	Thalassiosira pseudonana	Bacillariophyceae	1000	Wilson and Freeburg, 1980
	Thalassiosira pseudonana	Bacillariophyceae	350	Wilson and Freeburg, 1980
	Acartia tonsa	Crustacea	10000	Andersen et al., 2001
	Allorchestes compressa	Crustacea	6340	Ahsanullah, 1982
	Allorchestes compressa	Crustacea	5560	Ahsanullah, 1982
	Americamysis bahia	Crustacea	3600	Jop, 1989
	Americamysis bahia	Crustacea	4300	Jop, 1989
	Americamysis bahia	Crustacea	4900	Jop, 1989
	Americamysis bahia	Crustacea	2500	Jop, 1989
	Americamysis bahia	Crustacea	2700	Jop, 1989
	Artemia salina	Crustacea	113500	Persoone et al., 1989
	Artemia salina	Crustacea	128000	Persoone et al., 1989
	Artemia salina	Crustacea	48500	Persoone et al., 1989
	Artemia salina	Crustacea	52300	Persoone et al., 1989

Nitocra spinipes	Crustacea	80000	Dave et al., 1993
Nitocra spinipes	Crustacea	80000	Dave et al., 1993
Nitocra spinipes	Crustacea	51000	Dave et al., 1993
Nitocra spinipes	Crustacea	80000	Dave et al., 1993
Nitocra spinipes	Crustacea	21000	Dave et al., 1993
Nitocra spinipes	Crustacea	46000	Dave et al., 1993
Nitocra spinipes	Crustacea	80000	Dave et al., 1993
Nitocra spinipes	Crustacea	16000	Dave et al., 1993
Nitocra spinipes	Crustacea	37000	Dave et al., 1993
Nitocra spinipes	Crustacea	11500	Dave et al., 1993
Nitocra spinipes	Crustacea	14000	Dave et al., 1993
Nitocra spinipes	Crustacea	15000	Dave et al., 1993
Nitocra spinipes	Crustacea	15500	Dave et al., 1993
Nitocra spinipes	Crustacea	17000	Dave et al., 1993
Nitocra spinipes	Crustacea	20500	Dave et al., 1993
Nitocra spinipes	Crustacea	21000	Dave et al., 1993
Nitocra spinipes	Crustacea	22000	Dave et al., 1993
Nitocra spinipes	Crustacea	22700	Dave et al., 1993
Nitocra spinipes	Crustacea	24200	Dave et al., 1993
Nitocra spinipes	Crustacea	29000	Dave et al., 1993
Nitocra spinipes	Crustacea	34000	Dave et al., 1993
Nitocra spinipes	Crustacea	34800	Dave et al., 1993
Nitocra spinipes	Crustacea	34800	Dave et al., 1993
Nitocra spinipes	Crustacea	44600	Dave et al., 1993
Nitocra spinipes	Crustacea	50000	Dave et al., 1993
Nitocra spinipes	Crustacea	54600	Dave et al., 1993
Nitocra spinipes	Crustacea	7500	Dave et al., 1993
Nitocra spinipes	Crustacea	8700	Dave et al., 1993
Pagurus longicarpus	Crustacea	20000	Eisler and Hennekey, 1977
Pagurus longicarpus	Crustacea	5000	Eisler and Hennekey, 1977
Palaemonetes pugio	Crustacea	37000	Fales, 1978
Palaemonetes pugio	Crustacea	78000	Fales, 1978
Palaemonetes pugio	Crustacea	14600	Rao and Doughtie, 1984
Palaemonetes pugio	Crustacea	4900	Rao and Doughtie, 1984
Palaemonetes varians	Crustacea	32240	Van der Meer et al., 1988
Palaemonetes varians	Crustacea	32240	Van der Meer et al., 1988
Palaemonetes varians	Crustacea	57200	Van der Meer et al., 1988
Palaemonetes varians	Crustacea	83200	Van der Meer et al., 1988
Praunus flexuosus	Crustacea	5720	Van der Meer et al., 1988
Pseudodiaptomus coronatus	Crustacea	3650	Cardin, 1980
Pseudodiaptomus coronatus	Crustacea	3650	Lussier and Cardin, 1985
Tisbe longicornis	Crustacea	10000	Larrain et al., 1998
Aldrichetta forsteri	Actinopterygii	24000	Negilski, 1976
Aldrichetta forsteri	Actinopterygii	53000	Negilski, 1976
Cyprinodon variegatus	Actinopterygii	42600	Jop et al., 1986

Cyprinodon variegatus	Actinopterygii	23200	Jop et al., 1986
Fundulus heteroclitus	Actinopterygii	275000	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	315000	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	230000	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	275000	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	81000	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	81000	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	55000	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	81000	Dorfman, 1977
Fundulus heteroclitus	Actinopterygii	200000	Eisler and Hennekey, 1977
Fundulus heteroclitus	Actinopterygii	91000	Eisler and Hennekey, 1977
Menidia menidia	Actinopterygii	12423	Cardin, 1985
Menidia menidia	Actinopterygii	14271	Cardin, 1985
Mya arenaria	Mollusca	225000	Eisler and Hennekey, 1977
Mya arenaria	Molluscs	57000	Eisler and Hennekey, 1977
Nassarius obsoletus	Molluscs	390000	Eisler and Hennekey, 1977
Nassarius obsoletus	Molluscs	105000	Eisler and Hennekey, 1977
Asterias forbesii	Asteroidea	32000	Filenko and Samoylova, 2008
Asterias forbesii	Asteroidea	540000	Kidwai and Ahmed, 1999
Capitella capitata	Polychaeta	5000	Reish, 1978
Ctenodrilus serratus	Polychaeta	4300	Reish, 1978
Dinophilus gyrociliatus	Polychaeta	3300	Jop, 1989
Dinophilus gyrociliatus	Polychaeta	3000	Jop, 1989
Neanthes arenaceodentata	Polychaeta	3230	Mearns et al., 1976
Neanthes arenaceodentata	Polychaeta	2220	Mearns et al., 1976
Neanthes arenaceodentata	Polychaeta	3450	Mearns et al., 1976
Neanthes arenaceodentata	Polychaeta	3630	Mearns et al., 1976
Neanthes arenaceodentata	Polychaeta	3230	Oshida and Reish,1975
Neanthes arenaceodentata	Polychaeta	2000	Oshida and Reish,1975
Neanthes arenaceodentata	Polychaeta	2220	Oshida and Reish,1975
Neanthes arenaceodentata	Polychaeta	2800	Oshida and Reish,1975

	Neanthes arenaceodentata	Polychaeta	3450	Oshida and Reish,1975
	Neanthes arenaceodentata	Polychaeta	3630	Oshida and Reish,1975
	Neanthes arenaceodentata	Polychaeta	4300	Oshida and Reish,1975
	Neanthes arenaceodentata	Polychaeta	3200	Reish, 1978
	Nereis virens	Polychaeta	80000	Eisler and Hennekey, 1977
	Nereis virens	Polychaeta	2000	Eisler and Hennekey, 1977
	Ophryotrocha diadema	Polychaeta	5000	Reish, 1978
25°C	*Gracilaria tenuistipitata*	Florideophyceae	17000	Haglund et al., 1996
	Gracilaria tenuistipitata	Florideophyceae	2200	Haglund et al., 1996
	Gracilaria tenuistipitata	Florideophyceae	23000	Haglund et al., 1996
	Gracilaria tenuistipitata	Florideophyceae	600	Haglund et al., 1996
	Gracilaria tenuistipitata	Florideophyceae	950	Haglund et al., 1996
	Americamysis bahia	Crustacea	10000	Buikema et al., 1981
	Americamysis bahia	Crustacea	8880	Buikema et al., 1981
	Americamysis bahia	Crustacea	6590	Buikema et al., 1981
	Artemia franchiscana	Crustacea	4770	Kungolos et al., 2001
	Artemia salina	Crustacea	30900	Crisinel et al., 1994
	Artemia salina	Crustacea	22200	Persoone et al., 1989
	Artemia salina	Crustacea	27500	Persoone et al., 1989
	Artemia salina	Crustacea	30900	Persoone et al., 1989
	Artemia salina	Crustacea	31000	Persoone et al., 1989
	Artemia sp.	Crustacea	21800	Espiritu et al., 1995
	Artemia sp.	Crustacea	25400	Espiritu et al., 1995
	Artemia sp.	Crustacea	31200	Espiritu et al., 1995
	Artemia sp.	Crustacea	38600	Espiritu et al., 1995
	Artemia sp.	Crustacea	53200	Espiritu et al., 1995
	Artemia sp.	Crustacea	59500	Espiritu et al., 1995
	Artemia sp.	Crustacea	10500	Espiritu et al., 1995
	Artemia sp.	Crustacea	4600	Espiritu et al., 1995
	Artemia sp.	Crustacea	5000	Espiritu et al., 1995
	Artemia sp.	Crustacea	6300	Espiritu et al., 1995
	Artemia sp.	Crustacea	8300	Espiritu et al., 1995
	Artemia sp.	Crustacea	9900	Espiritu et al., 1995
	Artemia sp.	Crustacea	14000	Vanhaecke et al., 1980
	Artemia sp.	Crustacea	10000	Vanhaecke et al., 1980
	Artemia sp.	Crustacea	10000	Vanhaecke et al., 1980
	Artemia sp.	Crustacea	11000	Vanhaecke et al., 1980
	Artemia sp.	Crustacea	11500	Vanhaecke et al., 1980

Artemia sp.	Crustacea	12000	Vanhaecke et al., 1980
Artemia sp.	Crustacea	12000	Vanhaecke et al., 1980
Artemia sp.	Crustacea	12200	Vanhaecke et al., 1980
Artemia sp.	Crustacea	13000	Vanhaecke et al., 1980
Artemia sp.	Crustacea	13800	Vanhaecke et al., 1980
Artemia sp.	Crustacea	15000	Vanhaecke et al., 1980
Artemia sp.	Crustacea	16000	Vanhaecke et al., 1980
Artemia sp.	Crustacea	16000	Vanhaecke et al., 1980
Artemia sp.	Crustacea	17000	Vanhaecke et al., 1980
Artemia sp.	Crustacea	20500	Vanhaecke et al., 1980
Artemia sp.	Crustacea	23000	Vanhaecke et al., 1980
Artemia sp.	Crustacea	9880	Vanhaecke et al., 1980
Artemia sp.	Crustacea	9900	Vanhaecke et al., 1980
Artemia sp.	Crustacea	9900	Vanhaecke et al., 1980
Artemia sp.	Crustacea	9950	Vanhaecke et al., 1980
Callinectes sapidus	Crustacea	320	Bookhout et al., 1984
Callinectes sapidus	Crustacea	930	Bookhout et al., 1984
Metamysidopsis insularis	Crustacea	3530	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	4020	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	4050	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	4150	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	4290	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	2010	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	2080	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	2110	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	2150	Garcia et al., 2008
Metamysidopsis insularis	Crustacea	2300	Garcia et al., 2008
Moina mongolica	Crustacea	6620	An and He, 1991
Moina mongolica	Crustacea	4240	An and He, 1991
Palaemonetes pugio	Crustacea	21000	Fales, 1978
Palaemonetes pugio	Crustacea	77000	Fales, 1978
Rhithropanopeus harrisii	Crustacea	4400	Bookhout et al., 1984
Rhithropanopeus harrisii	Crustacea	5710	Bookhout et al., 1984
Chrysiptera cyanea	Actinopterygii	130000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	130000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	190000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	100000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	110000	Hori et al., 1996

Chrysiptera cyanea	Actinopterygii	75000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	105000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	60000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	85000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	42000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	50000	Hori et al., 1996
Chrysiptera cyanea	Actinopterygii	80000	Hori et al., 1996
Cyprinodon variegatus	Actinopterygii	31600	Hutchinson et al., 1994
Cyprinodon variegatus	Actinopterygii	22800	Jop, 1989
Cyprinodon variegatus	Actinopterygii	32100	Jop, 1989
Cyprinodon variegatus	Actinopterygii	31600	Jop, 1989
Menidia peninsulae	Actinopterygii	21800	D'Asaro, 1985
Menidia peninsulae	Actinopterygii	22000	Hansen, 1983
Oryzias latipes	Actinopterygii	320000	Hori et al., 1996
Oryzias latipes	Actinopterygii	350000	Hori et al., 1996
Oryzias latipes	Actinopterygii	400000	Hori et al., 1996
Oryzias latipes	Actinopterygii	160000	Hori et al., 1996
Oryzias latipes	Actinopterygii	240000	Hori et al., 1996
Oryzias latipes	Actinopterygii	340000	Hori et al., 1996
Oryzias latipes	Actinopterygii	155000	Hori et al., 1996
Oryzias latipes	Actinopterygii	220000	Hori et al., 1996
Oryzias latipes	Actinopterygii	290000	Hori et al., 1996
Oryzias latipes	Actinopterygii	120000	Hori et al., 1996
Oryzias latipes	Actinopterygii	155000	Hori et al., 1996
Oryzias latipes	Actinopterygii	210000	Hori et al., 1996
Brachionus plicatilis	Eurotatoria	100	Persoone et al., 1989
Brachionus plicatilis	Eurotatoria	250	Persoone et al., 1989

Table S7. Summary of data used for constructing temperature-based species sensitivity distribution (SSDs) for Cd and Cr (III) at the salinityof 20‰ and 30‰. The scientific name, taxonomic group, median lethal concentration (LC_{50}) and sources of data.

Cadmium

Sanility (‰)	Species Scientific Name	Taxonomic Group	Median Lethal Concentration (LC_{50}, μg/L)	Reference
10	*Acartia tonsa*	Crustacea	380	Roberts et al., 1982
10	*Acartia tonsa*	Crustacea	90	Sosnowski and Gentile, 1978
10	*Acartia tonsa*	Crustacea	220	Sosnowski and Gentile, 1978
10	*Acartia tonsa*	Crustacea	190	Sosnowski and Gentile, 1978
10	*Acartia tonsa*	Crustacea	337	Sosnowski and Gentile, 1978
15	*Acartia tonsa*	Crustacea	93	Toudal and Riisgård, 1987
10	*Eurytemora affinis*	Crustacea	60	Roberts et al., 1982
10	*Eurytemora affinis*	Crustacea	120	Sullivan et al., 1983
10	*Eurytemora affinis*	Crustacea	140	Sullivan et al., 1983
10	*Eurytemora affinis*	Crustacea	147.7	Sullivan et al., 1983
20	*Fundulus heteroclitus*	Actinopterygii	60000	Middaugh and Dean, 1977
20	*Fundulus heteroclitus*	Actinopterygii	100000	Eisler, 1971
20	*Fundulus heteroclitus*	Actinopterygii	128000	Voyer, 1975
20	*Fundulus heteroclitus*	Actinopterygii	134000	Voyer, 1975
20	*Fundulus heteroclitus*	Actinopterygii	144000	Voyer, 1975
20	*Fundulus heteroclitus*	Actinopterygii	200000	Voyer, 1975
20	*Leptocheirus plumulosus*	Crustacea	250	DeWitt et al., 1992
20	*Leptocheirus plumulosus*	Crustacea	280	DeWitt et al., 1992
20	*Leptocheirus plumulosus*	Crustacea	2060	DeWitt et al., 1992
20	*Leptocheirus plumulosus*	Crustacea	13370	DeWitt et al., 1992
25	*Mytilus edulis*	Molluscs	960	Nelson et al., 1988
25	*Mytilus edulis*	Molluscs	1550	Amiard-Triquet et al., 1986
20	*Neomysis integer*	Crustacea	2.43	Emson and Crane, 1994
20	*Neomysis integer*	Crustacea	1.38	Emson and Crane, 1994
15	*Palaemonetes pugio*	Crustacea	190	Howard and Hacker, 1990
20	*Palaemonetes pugio*	Crustacea	1830	Khan et al., 1988
20	*Palaemonetes pugio*	Crustacea	3890	Khan et al., 1988
20	*Palaemonetes pugio*	Crustacea	3280	Khan et al., 1988
20	*Palaemonetes pugio*	Crustacea	6810	Khan et al., 1988
20	*Penaeus merguiensis*	Crustacea	370	Denton and Burdon-Jones, 1982
20	*Penaeus merguiensis*	Crustacea	650	Denton and Burdon-Jones, 1982
20	*Penaeus merguiensis*	Crustacea	1100	Denton and Burdon-Jones, 1982
20	*Varuna litterata*	Crustacea	33300	Kulkarni, 1983

20	*Varuna litterata*	Crustacea	46000	Kulkarni, 1983
20	*Varuna litterata*	Crustacea	36100	Kulkarni, 1983
30	*Americamysis bahia*	Crustacea	11.1	Voyer and Modica, 1990
30	*Americamysis bahia*	Crustacea	32.8	Voyer and Modica, 1990
30	*Americamysis bahia*	Crustacea	28	Voyer and Modica, 1990
30	*Americamysis bahia*	Crustacea	82	Voyer and Modica, 1990
30	*Americamysis bahia*	Crustacea	85	Voyer and Modica, 1990
32	*Capitella capitata*	Polychaeta	5030	Reish et al., 1977
32	*Capitella capitata*	Polychaeta	5140	Reish et al., 1977
32	*Capitella capitata*	Polychaeta	6000	Reish et al., 1977
32	*Capitella capitata*	Polychaeta	5880	Reish et al., 1977
31.5	*Chasmichthys dolichognathus*	Actinopterygii	36400	Kuroshima and Kimura, 1990
33.5	*Chasmichthys dolichognathus*	Actinopterygii	17700	Kuroshima and Kimura, 1990
33.8	*Chasmichthys dolichognathus*	Actinopterygii	39500	Kuroshima and Kimura, 1990
34.1	*Chasmichthys dolichognathus*	Actinopterygii	31500	Kuroshima and Kimura, 1990
34.4	*Chasmichthys dolichognathus*	Actinopterygii	24500	Kuroshima and Kimura, 1990
28	*Corophium insidiosum*	Crustacea	960	Boese et al., 1997
35	*Corophium insidiosum*	Crustacea	1270	Hong and Reish, 1987
32	*Ctenodrilus serratus*	Polychaeta	3690	Reish et al., 1977
32	*Ctenodrilus serratus*	Polychaeta	2720	Reish et al., 1977
32	*Ctenodrilus serratus*	Polychaeta	2240	Reish et al., 1977
32	*Ctenodrilus serratus*	Polychaeta	6030	Reish et al., 1977
32	*Ctenodrilus serratus*	Polychaeta	2130	Reish et al., 1977
32	*Ctenodrilus serratus*	Polychaeta	3330	Reish et al., 1977
37.3	*Mugil cephalus*	Fish	34120	Hilmy et al., 1985
28.7	*Mytilus edulis*	Molluscs	3360	Dinnel et al., 1983
32	*Neanthes arenaceodentata*	Polychaeta	18540	Reish et al., 1977
32	*Neanthes arenaceodentata*	Polychaeta	5600	Reish et al., 1977
32	*Neanthes arenaceodentata*	Polychaeta	12100	Reish, 1978
32	*Neanthes arenaceodentata*	Polychaeta	5600	Reish et al., 1977
32	*Neanthes arenaceodentata*	Polychaeta	30300	Reish et al., 1977
32	*Ophryotrocha diadema*	Polychaeta	1370	Reish et al., 1977
32	*Ophryotrocha diadema*	Polychaeta	1770	Reish et al., 1977
32	*Ophryotrocha diadema*	Polychaeta	19090	Reish et al., 1977
32	*Ophryotrocha diadema*	Polychaeta	4790	Reish et al., 1977
33.5	*Pagrus major*	Actinopterygii	3900	Kuroshima et al., 1993
33.9	*Pagrus major*	Actinopterygii	6400	Kuroshima et al., 1993
34	*Pagrus major*	Actinopterygii	16300	Kuroshima et al., 1993
34.4	*Pagrus major*	Actinopterygii	22600	Kuroshima et al., 1993
35	*Palaemonetes pugio*	Crustacea	2420	Howard and Hacker, 1990
28	*Rhepoxynius abronius*	Crustacea	790	DeWitt et al., 1992
28	*Rhepoxynius abronius*	Crustacea	1510	Boese et al., 1997
35	*Rhepoxynius abronius*	Crustacea	240	Hong and Reish, 1987
30	*Uca pugilator*	Crustacea	23300	O'Hara, 1973
30	*Uca pugilator*	Crustacea	37000	O'Hara, 1973

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Sanility (‰)	Species Scientific Name	Taxonomic Group	Median Lethal Concentration (LC_{50}, μg/L)	Reference
20	*Artemia salina*	Crustaceans	8800	Persoone et al., 1989
20	*Artemia salina*	Crustaceans	413	Umarani,R., A.K.Kumaraguru, and N.Nagarani.,2012
20	*Artemia salina*	Crustaceans	519	Umarani,R., A.K.Kumaraguru, and N.Nagarani.,2012
20	*Artemia salina*	Crustaceans	748	Umarani,R., A.K.Kumaraguru, and N.Nagarani.,2012
20	*Artemia salina*	Crustaceans	887	Umarani,R., A.K.Kumaraguru, and N.Nagarani.,2012
20	*Artemia salina*	Crustaceans	1031	Umarani,R., A.K.Kumaraguru, and N.Nagarani.,2012
20	*Artemia salina*	Crustaceans	1192	Umarani,R., A.K.Kumaraguru, and N.Nagarani.,2012
20	*Artemia salina*	Crustaceans	3540	Govindarajan,S., C.P.Valsaraj, R.Mohan, V.Hariprasad, and R.Ramasubramanian.,1993
20	*Artemia salina*	Crustaceans	5300	Govindarajan,S., C.P.Valsaraj, R.Mohan, V.Hariprasad, and R.Ramasubramanian.,1993
20	*Pseudodiaptomus coronatus*	Crustaceans	3650	Cardin,J.A.,1980
20	*Pseudodiaptomus coronatus*	Crustaceans	3650	Lussier,S.M., and J.A.Cardin.,1985
20	*Corophium volutator*	Crustaceans	6000	Bryant et al., 1984
20	*Corophium volutator*	Crustaceans	20000	Bryant et al., 1984
20	*Corophium volutator*	Crustaceans	17000	Bryant et al., 1984
15	*Macoma balthica*	Molluscs	29000	Bryant et al., 1984
15	*Macoma balthica*	Molluscs	70000	Bryant et al., 1984
15	*Macoma balthica*	Molluscs	190000	Bryant et al., 1984
20	*Macoma balthica*	Molluscs	46000	Bryant et al., 1984
20	*Macoma balthica*	Molluscs	120000	Bryant et al., 1984
20	*Macoma balthica*	Molluscs	220000	Bryant et al., 1984
10	*Nereis diversicolor*	Worms	9500	Bryant et al., 1984
10	*Nereis diversicolor*	Worms	22000	Bryant et al., 1984
10	*Nereis diversicolor*	Worms	80000	Bryant et al., 1984
15	*Nereis diversicolor*	Worms	8500	Bryant et al., 1984
15	*Nereis diversicolor*	Worms	27000	Bryant et al., 1984
20	*Nereis diversicolor*	Worms	12000	Bryant et al., 1984
20	*Nereis diversicolor*	Worms	65000	Bryant et al., 1984
20	*Palaemonetes pugio*	Crustaceans	77000	Fales, 1978
20	*Palaemonetes pugio*	Crustaceans	78000	Fales, 1978
20	*Palaemonetes pugio*	Crustaceans	107000	Fales, 1978
20	*Palaemonetes pugio*	Crustaceans	147000	Fales, 1978
18	*Praunus flexuosus*	Crustaceans	13000	McLusky and Hagerman, 1987
18	*Praunus flexuosus*	Crustaceans	22000	McLusky and Hagerman, 1987
22.5	*Praunus flexuosus*	Crustaceans	13000	McLusky and Hagerman, 1987

22.5	*Praunus flexuosus*	Crustaceans	22000	McLusky and Hagerman, 1987
9	*Skeletonema costatum*	Algae	60000	Kusk and Nyholm, 1991
9	*Skeletonema costatum*	Algae	60000	Kusk and Nyholm, 1991
9	*Skeletonema costatum*	Algae	41000	Kusk and Nyholm, 1991
9	*Skeletonema costatum*	Algae	39000	Kusk and Nyholm, 1991
9	*Skeletonema costatum*	Algae	18000	Kusk and Nyholm, 1991
9	*Skeletonema costatum*	Algae	10000	Kusk and Nyholm, 1991
9.5	*Skeletonema costatum*	Algae	60000	Kusk and Nyholm, 1991
9.5	*Skeletonema costatum*	Algae	25000	Kusk and Nyholm, 1991
9.5	*Skeletonema costatum*	Algae	54000	Kusk and Nyholm, 1991
9.5	*Skeletonema costatum*	Algae	63000	Kusk and Nyholm, 1991
9.5	*Skeletonema costatum*	Algae	46000	Kusk and Nyholm, 1991
10	*Skeletonema costatum*	Algae	54000	Kusk and Nyholm, 1991
12	*Skeletonema costatum*	Algae	25000	Kusk and Nyholm, 1991

Table S8. Predicted hazardous concentrations 5% (HC_5) generated by the QSAR-SSD model *vs.* observed site-specific HC_5 of Cd and Cr (III). All HC_5 values were expressed as μg/L.

Metals	T(°C)	S(‰)	Predicted HC_5	Average predicted HC_5	Site-specific HC_5 (95% CI)	Average predicted HC_5	Site-specific HC_5 (95% CI)
Cadmium	15	10	158	133 (15°C)	96 (51, 139) (15°C)	62 (10‰)	/
	15	20	116				
	15	30	66				
	20	10	52	39 (20°C)	79 (66, 94) (20°C)	56 (20‰)	19 (6, 34) (20‰)
	20	20	41				
	20	30	23				
	25	10	14	11 (25°C)	7 (2, 14) (25°C)	13 (30‰)	48 (10, 101) (30‰)
	25	20	13				
	25	30	7				
Chromium (III)	15	10	1619	1336 (15°C)	1585 (1170, 1984) (15°C)	512 (10‰)	/
	15	20	1393				
	15	30	995				
	20	10	515	464 (20°C)	739 (373, 1090) (20°C)	686 (20‰)	912 (433, 1255) (20‰)
	20	20	504				
	20	30	373				
	25	10	133	141 (25°C)	407 (194, 513) (25°C)	300 (30‰)	/
	25	20	163				
	25	30	128				

/ notes that there is a lack of data to derive sanility-dependent SSDs

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