

# Estimating the Environmental Behavior of Inorganic and Organometal Contaminants: Solubilities, Bioaccumulation, and Acute Aquatic Toxicities<sup>1</sup>

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## ABSTRACT

The estimation of environmental properties of inorganic species has been difficult. In this presentation aqueous solubility, bioconcentration and acute aquatic toxicity are estimated for inorganic compounds using existing Linear Solvation Energy Relationship (LSER) equations. Many estimations fall within an order of magnitude of the measured property. For complex solution chemistry, the accuracy of the estimations improve with the more complete description of the solution species present. The toxicities also depend on an estimation of the bioactive amount and configuration. A number of anion/cation combinations (salts) still resist accurate property estimation, and the reasons currently are not understood. These new variable values will greatly extend the application and utility of LSER for the estimation of environmental properties.

## LSER ESTIMATES ENVIRONMENTAL PROPERTIES OF INORGANIC COMPOUNDS

Researchers, manufacturers, and regulating agencies must evaluate properties for chemicals that are either present in or could be released into the environment, many of these persistent and bioaccumulative. The routine use of more than 70,000 synthetic chemicals stresses the need for this information. However, minimal physical data and no toxicity data are available for about 80% of these compounds. The cost of testing these myriad present or potential chemicals is prohibitive, so researchers and managers increasingly rely on predictive models (i.e., quantitative structure-activity relationships (QSARs)) for chemical property estimation, hazard evaluation, and information to direct research and set priorities.

The Linear Solvation Energy Relationship (LSER) developed by Kamlet and others (1987, 1988) for neutral organic compounds can be a useful predictive tool, quite suitable for environmental property estimations (Hickey and others, 1990 and Hickey, 1996 compile most of the Kamlet and others LSER references). In LSER, the solution behavior of a substance (e.g., solubility, bioaccumulation, and toxicity) is directly related to several aspects of its chemical structure. The form of the equation used in this study is

$$\text{Log(Property)} = \underline{m}V_i/100 + \underline{s}B^* + \underline{b}\bar{\epsilon}_m + \underline{a}\bar{v}_m \quad (1)$$

where  $V_i$  is the intrinsic (van der Waals) molecular volume,  
 $B^*$  is the solute's ability to stabilize a neighboring charge or dipole by

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nonspecific dielectric interactions, and  $\Xi_m, \nabla_m$  are the solute's ability to accept or donate a hydrogen in a hydrogen bond, respectively.

The equation coefficients  $\underline{m}$ ,  $\underline{s}$ ,  $\underline{b}$ , and  $\underline{a}$  are coefficients for a particular set of conditions, determined by multiple linear regression of the LSER variable values for a series of organic chemicals against their measured values for a particular chemical property.

Estimation of environmental properties for both inorganics and organometals has presented a persistent challenge. Because LSER has proven to be a very useful QSAR for organics, LSER variable values were devised at the Great Lakes Science Center for inorganic species of the remaining periodic table elements (Hickey, in press). Proportional relationships were used for  $V_i/100$ , but the values for  $B^*$ ,  $\Xi_m$  and  $\nabla_m$  were deduced heuristically (*vide infra*) from literature values for the existing group of elements.

This presentation will examine the current utility of these unorthodox but useful inorganic LSER variable values with the estimation of 1) inorganic species aqueous solubilities, 2) inorganic species bioconcentration factors in freshwater fish, and 3) acute aquatic toxicities for several species, all estimations using published LSER equations.

## INORGANIC LSER VARIABLE VALUE ESTIMATION AND REFINEMENT

Values for the "steric" parameter  $V_i/100$  were calculated from atomic parachors (McGowan, 1956), through a characteristic molecular volume  $V_x$  (McGowan, 1978; McGowan and others, 1979) to a corresponding intrinsic molecular volume,  $V_i$  (Abraham and McGowan, 1987). For the other variables (dipolar  $\pi^*$  and hydrogen bonding  $\beta$  and  $\alpha$ ), reasonably complete sets of appropriate elemental property values (*vide infra*) were not available to serve as a proportional reference for value calculation for the remaining periodic table elements. A heuristic development process was followed that related trends from measured

physical property data with existing LSER parameter values in order to suggest parameter values for unassigned elements. Solution species and behavior were deduced from descriptive solution chemistry. The property data used were: 1) for  $\pi^*$ , dipole moments, polarizabilities and electronegativity and 2) for  $\beta$  and  $\alpha$ , ionization potentials (basicity), electron affinities (acidity) and pK values.

The LSER values for the neutral inorganic molecule or salt were the sums of contributions for the molecule components or salt anion and cation components. The resultant component values used are listed in Table 1. These suggested values were processed through a published LSER equation (Kamlet and others, 1987) for solubility estimation:

$$\text{Log}(S_w) = 0.05 - 5.85V_i/100 + 1.09\pi^* + 5.23\beta \quad (2)$$

where  $S_w$  is the aqueous molar solubility for the compound at 20°C.

Variable values for elements with the simplest solution chemistry (e.g., alkali and alkaline earth metals as halides), as well as for those elements with solution chemistry analogous to the eleven traditional LSER elements, were developed first. These parameter values were then used to develop values for more complex elements, in more complex salts or molecules. Overall agreement within an order of magnitude between observed and estimated solubilities for numerous compounds containing the element(s) in question was the criterion for parameter value "acceptance." The process was repeated until all elements were assigned LSER values. Since solubility is a fundamental factor involved in bioaccumulation and aquatic toxicity, the inorganic species LSER values generated by this process were then processed through pertinent published equations to determine general utility (*vide infra*).

The measured data used to test the accuracy of prediction using Equation 2 (aqueous solubility at 20 °C) consisted of solubility values compiled for a large list of inorganic compounds and salts from the 44th Edition of the CRC Handbook of Chemistry and Physics (Weast, 1961). For

Equation 3 (bioconcentration factors or BCF), a short set of “generic” BCFs (Bysshe, 1988) were used for metal ions for “generic” freshwater fish, mindful that BCFs are highly compound-, condition- and organism /species /gender-dependent. Hawker’s curvilinear equation (Hawker, 1990) accounted for the coordination energy difference between water and lipid molecules around the solute:

$$\text{Log}(K_b) = 1.125 - 0.477(V_i/100)^{4.3} + 0.58V_i/100 + 0.384(\pi^* - 0.4\delta) - 4.092\beta \quad (3)$$

Where  $K_b$  is the bioconcentration factor, and  $\delta$  is the polarizability correction factor to  $\pi^*$

No error limits were given for the data in either solubility or bioaccumulation data sets, and each set was assumed to have been compiled from more than one source. The solution structures of the compounds were for most-likely solution species.

For acute aquatic toxicity (EC50 or LC50), several aquatic organisms were examined, ranging from eukaryotes to vertebrates. These included Microtox (as *Vibrio fischeri* Beijerinck 1889), *Daphnia magna* (Hickey and others, 1990) and the Golden Orfe (*Leuciscus idus melanotus*) (Kamlet and others, 1988).

Microtox ( $\mu\text{M/L}$ , 15 min, 20 °C)

$$\log(\text{EC50}) = 7.49 - 7.39V_i/100 - 1.38\pi^* + 3.70\beta - 1.66\alpha \quad (4)$$

*Daphnia magna* (mM/L, 48hr, 20 °C)

$$\log(\text{EC50}) = 4.18 - 4.73V_i/100 - 1.67\pi^* + 1.48\beta - 0.93\alpha \quad (5)$$

Golden Orfe (M/L, 48hr, 20 °C)

$$\log(\text{LC50}) = 2.90 - 5.71V_i/100 - 0.92\pi^* + 4.36\beta - 1.27\alpha \quad (6)$$

where

EC50 is the effective concentration at which 50% of the test organisms demonstrate a particular biological endpoint, such as cessation of luminescence or movement, and  
LC50 is the lethal concentration at which 50% of the test organisms die.

Estimated toxicities were compared with composite sets of literature endpoint data to determine the prediction accuracy. LSER values for compounds examined in the Microtox test, *Daphnia magna*, and the Golden Orfe data were multiplied by a “bioavailable fraction” value adapted from Newman and McClosky (Newman and McClosky, 1996).

## RESULTS

From a comparison of predicted with observed aqueous solubilities for 233 inorganic and organometal compounds and salts, the estimated solubilities for most of the compounds were at or within an order of magnitude of the measured value. Solubilities for some salts and compounds (e.g., highly insoluble metal sulfides and chromates and other outlying species such as borates) were better estimated using multiple dominant solution species (e.g., 25%  $\text{CrO}_4^{2-}$  and 75%  $\text{Cr}_2\text{O}_7^{2-}$  for  $\text{Na}_2\text{Cr}_2\text{O}_7$ ) to reflect expected solution composition. The LSER values were calculated as a linear sum of the proportional contributions for each form. The difference between the the measured and the predicted values served as a non--statistical measure of prediction accuracy. Only 67 compounds had a prediction difference (Pred-Obs) greater than 1.3 log units, and 20 of these were highly insoluble salts. The outliers were primarily highly insoluble compounds including lead and barium compounds, silver halides and cyanides, aluminates, and metal acetates, oxalates and carbonates.

A short series of “generic” BCFs for metal ions was also estimated by LSER using the dominant solution species, generally the aquo ion. The inorganic ion or molecule was used without a counterion. Most estimations (Be, Cd, Cr, Co, Cu, Hg, Ni, Pb ) were at or within an order of

magnitude of the reported value. However, solution species for Sn, As, and Se could not be modeled well.

Acute aquatic toxicities of most nonreactive

**Table 1.** Metal LSER Parameter Values

Ion	V <sub>i</sub> /100	π*	β	α
Li <sup>+1</sup>	0.158	0.05	0.00	0.10
Na <sup>+1</sup>	0.229	0.00	0.05	0.00
K <sup>+1</sup>	0.360	0.10	0.06	0.00
Rb <sup>+1</sup>	0.417	0.07	0.06	0.03
Cs <sup>+1</sup>	0.533	0.10	0.10	0.03
Be <sup>+2</sup>	0.144	0.00	0.00	0.00
Mg <sup>+2</sup>	0.216	0.00	0.00	0.10
Ca <sup>+2</sup>	0.349	0.00	0.00	0.10
Sr <sup>+2</sup>	0.406	0.00	0.00	0.10
Ba <sup>+2</sup>	0.529	0.00	0.00	0.10
B <sup>+3</sup>	0.131	0.03	0.00	0.40
Al <sup>+3</sup>	0.202	0.06	0.00	0.20
V <sup>+5</sup>	0.316	0.05	0.10	0.10
Cr <sup>+3/+6</sup>	0.305	0.05	0.05	0.20
Mo <sup>+3/+6</sup>	0.362	0.10	0.05	0.10
Mn <sup>+2</sup>	0.294	0.10	0.10	0.00
Fe <sup>+2/+3</sup>	0.283	0.05	0.10	0.05
Co <sup>+2</sup>	0.272	0.10	0.05	0.35
Ni <sup>+2</sup>	0.261	0.10	0.05	0.30
Cu <sup>+2</sup>	0.251	0.10	0.05	0.35
Ag <sup>+1</sup>	0.307	0.15	0.05	0.25
Zn <sup>+2</sup>	0.240	0.15	0.00	0.25
Cd <sup>+2</sup>	0.296	0.20	0.00	0.25
Hg <sup>+2</sup>	0.319	0.19	0.00	0.55
Tl <sup>+1</sup>	0.311	0.03	0.00	0.15
Pt <sup>+2</sup>	0.337	0.15	0.05	0.25
As <sup>+3</sup>	0.207	0.23	0.13	0.05
Sb <sup>+3</sup>	0.263	0.35	0.09	0.07
Bi <sup>+3</sup>	0.294	0.18	0.10	0.08
Sn <sup>+2</sup>	0.274	0.05	0.03	0.00
Pb <sup>+2</sup>	0.302	0.00	0.00	0.00
Ce <sup>+3</sup>	0.507	0.00	0.00	0.20
Yb <sup>+3</sup>	0.405	0.04	0.03	0.00
Th <sup>+4</sup>	0.496	0.02	0.02	0.10
U <sup>+6</sup>	0.479	0.03	0.03	0.10
F <sup>-1</sup> covalent	0.077	0.08	0.19	0.06
F <sup>-1</sup> ionic	0.077	0.18	0.29	0.06
Cl <sup>-1</sup> covalent	0.149	0.35	0.15	0.06
Cl <sup>-1</sup> ionic	0.149	0.60	0.40	0.06
Br <sup>-1</sup> covalent	0.185	0.43	0.17	0.05
Br <sup>-1</sup> ionic	0.185	0.68	0.32	0.05
I <sup>-1</sup> covalent	0.242	0.45	0.18	0.04
I <sup>-1</sup> ionic	0.242	0.70	0.33	0.04
ClO <sub>3</sub> <sup>-1</sup>	0.269	0.50	0.40	0.30
ClO <sub>4</sub> <sup>-1</sup>	0.309	0.00	0.40	0.42
BrO <sub>3</sub> <sup>-1</sup>	0.458	0.60	0.30	0.41
BrO <sub>4</sub> <sup>-1</sup>	0.549	0.20	0.57	0.53

Ion	V <sub>i</sub> /100	π*	β	α
IO <sub>3</sub> <sup>-1</sup>	0.515	0.50	0.45	0.40
IO <sub>4</sub> <sup>-1</sup>	0.402	0.25	0.50	0.40
-OH ionic	0.105	0.45	0.50	0.00
-OH covalent	0.105	0.40	0.47	0.33
-SH ionic	0.176	0.25	0.20	0.00
-SH covalent	0.176	0.35	0.16	0.03
=O	0.091	0.34	0.10	0.12
=S	0.162	0.24	0.05	0.05
-O-	0.091	0.27	0.45	0.00
O <sup>-2</sup> ionic	0.091	0.10	0.15	0.00
S <sup>-2</sup> covalent	0.162	0.50	0.23	0.00
S <sup>-2</sup> ionic	0.162	0.10	0.00	0.00
Se <sup>-2</sup>	0.196	0.20	0.00	0.00
SO <sub>3</sub> <sup>-2</sup>	0.282	0.65	0.82	0.36
SO <sub>4</sub> <sup>-2</sup>	0.322	0.65	0.82	0.00
S <sub>2</sub> O <sub>3</sub> <sup>-2</sup>	0.433	0.89	0.87	0.41
-OS(=O) <sub>2</sub> OH	0.336	1.00	0.80	0.75
PO <sub>4</sub> <sup>-3</sup>	0.336	0.45	0.87	0.00
HPO <sub>4</sub> <sup>-2</sup>	0.350	0.95	0.80	0.75
H <sub>2</sub> PO <sub>4</sub> <sup>-1</sup>	0.364	0.95	0.75	0.75
(-O) <sub>2</sub> (H)P(=O)	0.310	0.75	0.75	0.00
(-O)(HO)(H)P(=O)	0.325	0.68	0.47	0.33
P <sub>2</sub> O <sub>7</sub> <sup>-4</sup>	0.581	0.90	1.74	0.00
VO <sub>3</sub> <sup>-1</sup>	0.436	1.07	0.40	0.46
CrO <sub>4</sub> <sup>-2</sup>	0.465	0.80	0.87	0.44
HCrO <sub>4</sub> <sup>-1</sup>	0.505	1.52	0.85	0.56
Cr <sub>2</sub> O <sub>7</sub> <sup>-2</sup>	0.839	1.49	1.15	0.64
MnO <sub>4</sub> <sup>-1</sup>	0.454	1.46	0.50	0.48
WO <sub>4</sub> <sup>-2</sup>	0.531	0.67	1.00	0.36
SeO <sub>4</sub> <sup>-2</sup>	0.356	1.14	0.84	0.24
SeO <sub>3</sub>	0.316	0.80	0.74	0.12
AsO <sub>3</sub>	0.327	1.25	0.43	0.41
AsO <sub>4</sub>	0.367	1.59	0.53	0.53
HAsO <sub>4</sub>	0.375	1.65	0.90	0.74
B <sub>4</sub> O <sub>7</sub> <sup>-2</sup>	0.498	1.04	1.54	1.60
NO <sub>2</sub> <sup>-1</sup>	0.184	0.53	0.49	0.00
NO <sub>3</sub> <sup>-1</sup>	0.224	0.50	0.49	0.00
[S=C=N] <sup>-1</sup>	0.282	0.63	0.22	0.00
[S=N=C] <sup>-1</sup>	0.282	0.85	0.42	0.00
-OC(=O)H	0.212	0.62	0.37	0.00
-OC(=O)CH <sub>3</sub>	0.308	0.65	0.80	0.06
CO <sub>3</sub> <sup>-2</sup>	0.230	0.44	0.55	0.00
-OC(=O)OH	0.252	0.55	0.48	0.55
[-O <sub>2</sub> CCO <sub>2</sub> -] <sup>-2</sup>	0.345	1.10	0.45	0.24
-C#N covalent	0.171	0.45	0.11	0.22
-C#N ionic	0.171	0.70	0.30	0.22
H <sub>2</sub> O	0.119	0.45	0.45	0.45
coordinated water	0.068	0.25	0.00	0.55
NH <sub>3</sub>	0.146	0.15	0.65	0.00
NH <sub>4</sub> <sup>+1</sup>	0.160	0.00	0.00	0.05

inorganic species were assumed to act by a baseline narcosis mechanism, and were estimated

at or within an order of magnitude of the observed value. Using an additional "bioavailable fraction" of the metal in solution greatly improved the prediction accuracy of many species. Outliers in common that were more toxic than estimated for their tested species included cyanides,  $\text{Pb}^{+2}$  and  $\text{Be}^{+2}$  salts,  $\text{AgNO}_3$ ,  $\text{CuSO}_4$ , and  $\text{HgCl}_2$ , with dominant specific toxicity mechanisms other than baseline narcosis.

## DISCUSSION

Reliable property estimation is rarely successful for inorganic species. While acknowledging that this present approach is highly irregular, it appears that LSER can provide a much-needed tool for estimating solubilities for inorganic and organometal compounds, when used in the equation developed for aliphatic compounds. Since the solubility equation was developed for nonionic organic compounds, the use of the whole salt as a neutral species indirectly addresses any question of valence. In view of the lack of error limits on the solubility data used as reference, an arbitrary outer difference limit of  $\pm 1.3$  log unit was used to define a "good fit". Use of the dominant solution species gave an accurate solubility estimation for a large number of salts.

The more difficult species to estimate accurately included the least soluble compounds, aluminates, borates, and some of the organometals. Improved solubility estimation for the difficult classes is likely as solution species are better defined. It is also likely that there is another variable needed to explain the activity of (and so estimate more accurately) the highly insoluble salts.

These inorganic LSER values must apply to all property-predictive LSER equations and to similar processes. Examination of a small series of generic BCFs using the curvilinear relationship (Equation 3) also demonstrated that proper solutionspecies were necessary to estimate bioconcentration. Most of the metal species were best modeled as the aquo ions. For two elements, Cr and Se, several structures were tested for each metal ion. No anionic chromate species was modeled well, but the observed reactivity of these species suggests that the ion would react

before it accumulated. A much better estimation was achieved with the  $\text{Cr}(\text{H}_2\text{O})_6^{+3}$  ion. The elements As, Se, and Sn eluded a satisfactory approximation for reasons not apparent.

Acute aquatic toxicity estimations also demonstrated the necessity for defining proper solution species by requiring a "bioavailable fraction" factor. The active toxic species may not be the predominant solution species, and will likely resemble the species successfully transported into the cell, so use of other probable solution species along with the bioavailability factor may give more accurate toxicity approximations.

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