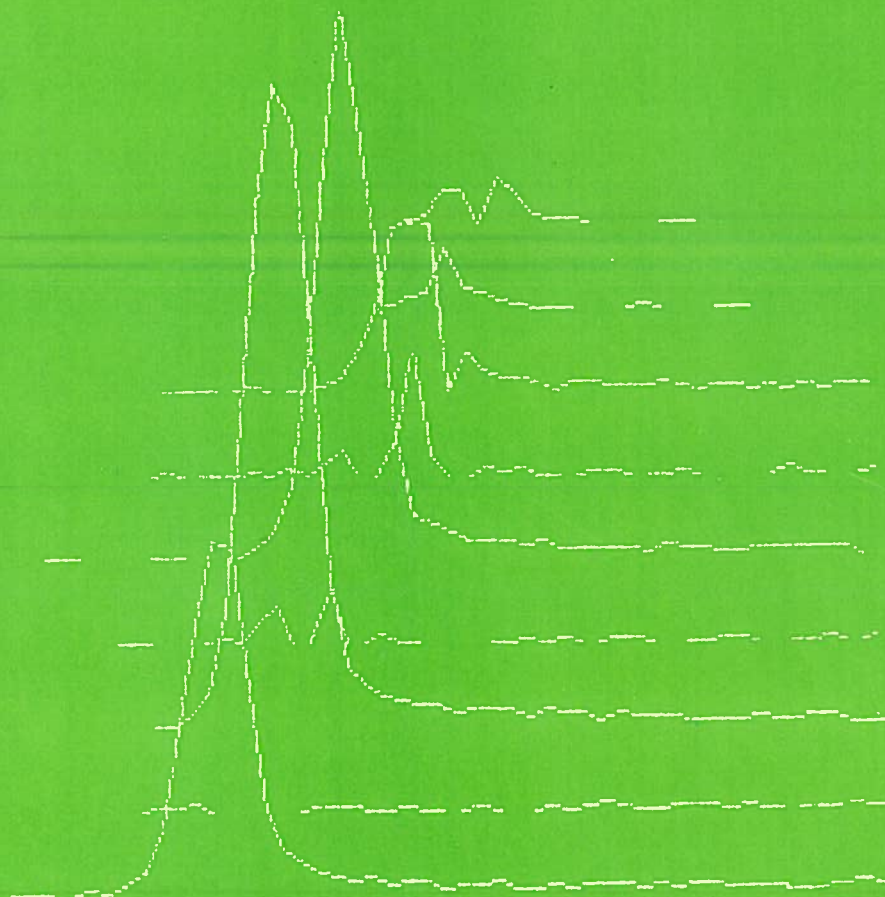# Research Notes from NERI No. 107

Miljøkemi

Title: **Linear Solvation Energy Relationships (LSER)**
Subtitle: A Method to Assess the Solubility of Inorganic Species

Tema: **Environmental Modelling**

Contents

Summary

The principles of Linear Solvation Energy Relationships (LSER) are summarized. The possible application of LSER to predict the solubility of inorganic compounds is evaluated with special focus on the work of Hickey. It is concluded that LSER, as applied by Hickey, does not lead to satisfactory modelling of experimental data.

Resumé

Principperne for Linear Solvation Energy Relationships (LSER) er præsenteret. Den mulige anvendelse af LSER til at forudsige opløseligeheder af uorganiske forbindelser (salte) er evalueret med særlig fokus på Hickey's arbejder. Det konkluderes at LSER i den af Hickey anvendte form ikke modellerer eksperimentelle data tilfredsstillende.

1 Introduction

Solubility is one of the fundamental parameters controlling fate and effects of chemical compounds in the environment.

The solubility of a chemical compound can in a very simplistic way be described as a reaction between the pure solute (S*) and water (W) leading to the dissolved solute (S_{aq})

$$S^* + W \rightarrow S_{aq}$$
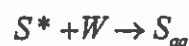
At saturation the an equilibrium between the pure and the dissolved solute prevails

$$S^* \leftrightarrow S_{aq}$$

Dissolution processes

Schematically the dissolution of the pure solute in water can be described as a sequence of processes (*Schwarzenbach et al., 1993, ch. 5*):

- breaking of S:S bonds in the pure solute
- breaking the W:W hydrogen bonds in the bulk water phase leading to a cavity formation
- Insertion of the solute in the cavity making S:W attractions
- Relaxation of the system and possible formation of hydrogen bonds between the water molecules and the solute

Whereas the first two reactions are energy demanding (endothermic, i.e. $\Delta G > 0$) the last two reactions are energy releasing (exothermic, i.e. $\Delta G < 0$) In Fig. 1 the reaction sequence is illustrated.

In the case of dissolution of inorganic salt a further reaction is brought into play, i.e., the rupture of the ionic bonds between the cations and anions in the solid salts giving rise the single ions in the aqueous solution (Fig. 2)
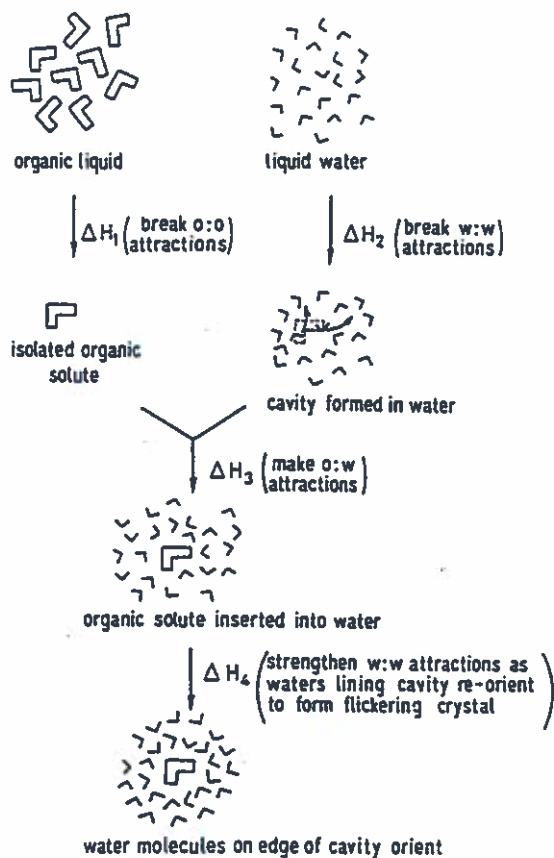
Figure 1. Schematic representation of the various enthlapies involved when dissolving a neutral organic molecule in water (Schwarzenbach et al., Environmental Organic Chemistry, Wiley, 1993. Reprinted with permission of John Wiley & Sons, Inc.)
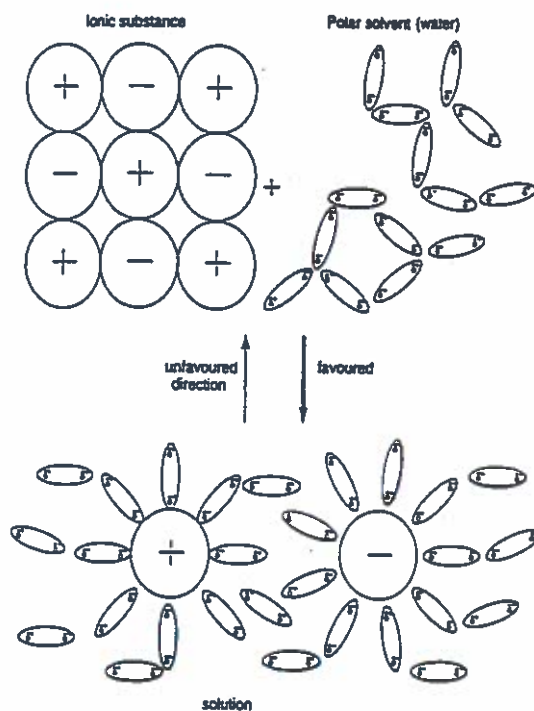
Figure 2. Solution of an ionic substance, such as sodium chloride, in a polar solvent, such as water (reprinted with permission from Connell, Basic Concept of Environmental Chemistry, 1997. Copyright CRC Press, Boca Raton, Florida,)

1.1 Quantitative Structure Activity Relationships

Obviously, experimental studies are both expensive and time consuming and as such in contradiction with the often required rapid evaluation of the possible environmental risk of a given chemical compound.

Thus, a wide variety of attempts to derive, e.g., solubilities of chemical compounds through quantitative structure-activity relationships (QSAR's) linking microscopic, i.e., molecular structure or structural and electronic characteristics of the compounds to macroscopic, i.e., empirical properties as the solubility, have been suggested.

Linear free energy relationships

One approach to elucidate physical, chemical or biological properties is Linear Free Energy Relationships (LFER), the approach having found wide-spread applications (*Shorter, 1973; Schwarzenbach, 1993; Cramer et al., 1993*). Originally the LFER approach was developed by Burkhardt (*1935*) and Hammett (*1935; 1937*).

Basically the LFER relationships provide the thermodynamical background for the assumption that equilibrium constants are functions of the structure of the molecule under investigation.

$$\Delta G^0 = -RT \ln K = \Delta H^0 - T\Delta S^0$$

The relationships have been use in a variety of cases to estimate e.g. solubilities, partitioning behaviour, sorption coefficients, acidity constants and reaction rates (*Schwarzenbach, 1993*), the most extensive developed LFER for octanol-water partitioning being developed by Hansch and Leo (*1979*). A wide variety of LFER's, or so-called LFER's, has been extensively reviewed by Jaffé (*1953*) and Exner (*1988; 1990*).

2 Linear Solvation Energy Relationships (LSER)

In the late seventies and in the eighties Kamlet and Taft and their coworkers extended the LFER's to solute/solvent interactions through their development of Linear Solvation Energy Relationships (LSER) (*Kamlet et al., 1977; 1981; 1983; 1986a; 1986b; 1988; Taft et al., 1985*).

LSER components

With basis in the above (cf. section 1) description of the solution process it is obvious that the parameters that measures solute-solvent interactions in step 3 and 4 comprise dipolar as well as hydrogen bonding interactions. Thus, solubility as well as a variety of other solvent-dependent properties, e.g., partitioning coefficients, sorption properties, toxicities, of various solutes, P, can be expresses in terms of linear combinations of energy contributions of three types reflecting a: cavity formation, b: dipolar interactions and c: hydrogen bonding interactions, respectively (*Abboud, 1977; Kamlet et al., 1977; 1981; 1983; 1986a; 1986b; 1988; Leahy, 1986; Taft et al., 1985*).

$$P = P_0 + cavity + dipolarity / polarizability + Hydrogen - bonding$$

The cavity term

The cavity term describes the energy required to break the hydrogen bonds in the bulk water to create the cavity and insert the solute. The cavity term, $V_i/100$, is typically computer-calculated, V_i being the 'intrinsic', i.e., van der Waal's molar volume. The calculated value, given in $Å^3$, is typically divided by 100 in order to obtain values for the cavity term in the same range as the other LSER parameters. The removal of the significant higher numerical level of the cavity data in respect to the other terms in the equation above, centers the data around the constant level, to make the importance of each term in the above expression equally important.

The dipolarity/ polarizability term

The dipolarity/polarizability term, π^* describes the energy associated with the interaction between the water molecules and the induced dipoles of the single solutes.

The H-bonding term

The H-bonding term describes the free energy associated with the formation of hydrogen bonds between the solute and the water molecules, the latter being a combination of a H-bond donor acidity , α, and H-bond acceptor basicity, ß, characteristics of the solute, respectively.

The LSER equation

If the solubilities, or other solute-solvent dependent properties of a set of different solutes in a single solvent, e.g. water is studied, LSER equation will have the following form

$$P = P_0 + aV_i/100 + b\pi^* + c\alpha + d\beta$$

Obviously the constants P_0, a, b, c, and d will vary from property to property. Thus in the case of solubity of a certain class of compounds in water, log S_w, the equation would be

$$\log S_w = \log S_{w,0} + a_{w,s} V_i /100 + b_{w,s}\pi * + c_{w,s}\alpha + d_{w,s}\beta$$

log $S_{w,0}$, $a_{w,s}$, $b_{w,s}$, $c_{w,s}$, and $d_{w,s}$ being specific constants related to the solubility in water.

Solvatochromic parameters

The single LSER parameters, often denoted the solvatochromic parameters are derived based on spectroscopy applying the so-called 'solvatochromic comparison method' (*Kamlet et al., 1981; 1983; 1986a; Taft et al., 1985*). The parameters for a wide variety of organic compounds, comprising non-polar as well as polar can be found tabulated in the literature (*e.g. Kamlet et al., 1981; 1983; 1986a*).

Group additivity principle

An alternative approach to the solvatochromic parameters was reported by Hickey (*1996*) suggesting a group additivity principle. Thus, Hickey (*1996*) provides a listing of a variety of organic moieties and heteroatom groups for which the LSER parameters are available. The group additivity principle allows a quick estimation of the four LSER parameters $V_i/100$, $\pi*$, ß, α for most of the organic molecules possibly being of environmental interest.

TLSER

A somewhat different approach has been introduced by Famini and coworkers (*Cramer et al., 1993; Cronce et al., 1998 Famini and Wilson, 1994; 1997*) using purely theoretically derived LSER parameters. The corresponding Theoretical Linear Solvation Energy Relationship (TLSER) equation appears as

$$S_w = S_{w,0} + a_{w,s} V_i /100 + b_{w,s}\pi * + c_{w,s}\varepsilon_\alpha + d_{w,s}q_+ + e_{w,s}\varepsilon_\beta + f_{w,s}q_-$$

TLSER parameters

The single parameters are calculated using semi-empirical molecular orbital calculations as MNDO or AM1, both being available, e.g., within the MOPAC software package (e.g. MOPAC, v. 7, QCPE 504).
In the present formalism the dipolarity/polarizability term, $\pi*$, is determined by dividing the polarization volume with the molecular volume, thus $\pi*$ being dimensionless. The normalization of the calculated polarity with respect to the molecular volume secures that the two descriptors, V_i and $\pi*$, are independent.

The hydrogen bonding acidity is in the TLSER formalism divided into two separate terms, the covalent acidity ε_α and the electrostatic acidity q_+, respectively. The covalent acidity ε_α is given by $0.30-0.01[E_{LUMO} - E_{HOMO,w}]$ and the electrostatic acidity q_+ by the charge, as absolute magnitude, of the most positive hydrogen in the molecule. Similarly the hydrogen bonding basicity is given by a covalent contribution, $\varepsilon_ß = 0.30-0.01[E_{HOMO} - E_{LUMO,w}]$ and an electrostatic contribution q_-, the latter being equal to absolute value of the most negatively charged atom in the molecule (*Famini and Wilson, 1997*). The unit of the covalent contributions is heV whereas the electrostatic contributions are given in acu.

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The constant 0.03 has been introduced to put the covalent contributions on the same order of magnitude as the other TLSER parameters.

3   LSER for inorganic compounds

Previously the LSER approach has been applied to organic compounds exclusively. However, the list of existing marketable chemicals in the EU (EINECS) contains more than 3500 inorganic compounds most of which have never been assessed for their possible toxic effects on the environment. However, the toxic effects of the individual cations and anions of these compounds are often well known, e.g., lead and chloride ions. Thus, assessing the environmental hazard can typically be approached by assessing the bioavailability, i.e., the water solubility. However, in many cases no information can be found on the relative water solubility of these compounds.

The "Hickey approach"

Recently Hickey introduced the LSER concept to inorganic compounds, i.e., the estimation of main group and heavy metals solution behaviour (*Hickey, subm-a; subm-b; subm-c*). It was claimed that estimates of water solubilities in error of less than ± 1.3 order of magnitude are obtainable, which for most cases for classification purposes would be acceptable.

LSER parameters for a wide variety of ions, including all metal ions and several of the environmentally more important anions, have been reported (*Hickey, subm-a; subm-b; subm-c*). In agreement with the above described group additivity principle the LSER parameters for the intact salt were calculated by simple addition of the single ion contributions (*Hickey, 1996*).

The LSER parameters for ions

The LSER parameters for the individual ions were deduced "heuristically" from the existing data. In the case of π^* electrical resistivity, electronegativity, dipolemoment and polarizabilities were taken into account whereas the H-bond donor acidity , α, and H-bond acceptor basicity, ß, characteristics were deduced using ionization potentials (basicity) and electron affinities (acidity) and pK values (*Hickey, subm-a; subm-b; subm-c*). It must be emphasized that the values for the dipolarity/polarizability and hydrogen bonding parameters are not derived by any formal equations (*Hickey, personal comm.*), and as such not necessarily scientifically founded. Values for LSER parameters for various compound classes, available in numerous published tables, of data were used to carefully intuiting values for new classes of compounds and subsequently to extrapolate/interpolate/intuit values for inorganic elements and anions/cations (*Hickey, personal comm.*)

The suggested LSER equation for inorganic compounds

Based on the derived LSER parameters Hickey (*subm-a; subm-b*) suggests an equation to calculate the solubility of inorganic compounds

$$\log S_w = 0.05 - 5.85 V_i/100 + 1.09\pi^* + 5.23\beta$$

The constants in the above equation are adopted from the equation for aliphatic compounds derived by Kamlet et al. (*1988*) based on multilinear regression including data for 115 compounds (r=0.9917). The basis for the application of the equation developed for aliphatic compounds to inorganic salts is the crucial assumption that the LSER-

derived solution behaviour of inorganic compounds can be addressed as solubility of the whole salt, e.g., the neutral species composed of x cations and y anions (*Hickey, personal comm.*).

In the following the above described approach to assess the solubility of inorganic species is critically reviewed.

3.1 A critical review of the "Hickey-approach"

In Table 1 the LSER parameters for cations and anions as derived by Hickey (*subm-a; subm-b; subm-c*) are given.

Table 1. LSER parameters for inorganic cations and anions. (The notation in the Table is adopted from Hickey (personal comm.) without corrections)

Compound	VxVi/100	π*	ß	α
H (Hydrogen)	0.065	0.00	0.50	0.00
Li^{+1}	0.158	0.05	0.00	0.10
Na^{+1}	0.229	0.00	0.05	0.00
K^{+1}	0.360	0.10	0.06	0.00
Rb^{+1} (Rubidium)	0.417	0.17	0.06	0.03
Cs^{+1} (Cesium)	0.533	0.20	0.10	0.03
Fr (Francium)	0.522	0.02	0.03	0.03
Be^{+2}	0.144	0.00	0.00	0.00
Mg^{+2}	0.216	0.00	0.00	0.10
Ca^{+2}	0.349	0.00	0.00	0.10
Sr^{+2}	0.406	0.00	0.00	0.10
Ba^{+2}	0.529	0.00	0.00	0.10
Ra (Radium)	0.513	0.00	0.00	0.03
Sc (Scandium)	0.338	0.02	0.02	0.00
Y (Yttrium)	0.395	0.02	0.03	0.00
Ti (Titanium)	0.327	0.10	0.02	0.05
TiF_6^{2-}	0.789	0.58	1.16	0.41
Zr (Zirconium)	0.384	0.08	0.08	0.10
ZrF_6^{2-}	0.846	0.56	1.22	0.46
Hf (Hafnium)	0.388	0.05	0.09	0.05
V^{+5}	0.316	0.05	0.10	0.10
VO_3^{-1}	0.436	1.07	0.40	0.46
Nb (Niobium)	0.373	0.15	0.15	0.05
Ta (Tantalum)	0.379	0.15	0.15	0.00
$Cr^{+3/+6}$	0.305	0.05	0.05	0.20
CrO_4^{-2}	0.465	0.80	0.87	0.44
CrO_4^{-2}	0.465	1.41	0.45	0.68
HCrO4-	0.505	1.52	0.85	0.56
$Cr_2O_7^{-2}$	0.839	1.49	1.15	0.64
$Cr_2O_7^{-2}$	0.839	2.41	1.15	1.12
Mo (Molybdenum)	0.362	0.10	0.05	0.10
W	0.371	0.10	0.05	0.10
WO_4^{-2}	0.531	0.67	1.00	0.36
Mn^{+2}	0.294	0.10	0.10	0.00
MnO_4^{-1}	0.454	1.46	0.50	0.48
Tc (Technetium)	0.351	0.10	0.10	0.00
Re (Rhenium)	0.362	0.10	0.10	0.05

ReO_4^{-1}	0.726	1.46	0.5	0.53
$Fe^{+2/+3}$	0.283	0.05	0.10	0.05
Ru (Ruthenium)	0.340	0.04	0.08	0.02
Os (Osmium)	0.354	0.04	0.04	0.00
Co^{+2}	0.272	0.10	0.05	0.35
Rh (Rhodium)	0.329	0.05	0.12	0.05
Ir (Iridium)	0.345	0.05	0.05	0.08
Ni^{+2}	0.261	0.10	0.05	0.30
Pd (Palladium)	0.318	0.05	0.10	0.10
Pt^{+2}	0.337	0.15	0.05	0.25
Cu^{+2}	0.251	0.10	0.05	0.35
Ag^{+1}	0.307	0.15	0.05	0.25
Au (Gold)	0.328	0.15	0.00	0.05
$AuCl_4^{-1}$	0.636	0.47	0.76	0.29
Zn^{+2}	0.240	0.15	0.00	0.25
Cd^{+2}	0.296	0.20	0.00	0.25
Hg^{+2}	0.319	0.19	0.00	0.55
B^{+3}	0.131	0.03	0.00	0.40
BH_4^{-1}	0.391	0.03	2.	0.4
BF_4^{-1}	0.439	0.35	0.76	0.64
$B_4O_7^{-2}$	0.498	1.04	1.54	1.60
BO_2^{-1}	0.313	0.57	0.9	0.4
BO_3^{-3}	0.404	1.05	0.3	0.76
Al^{+3} (Aluminum)	0.202	0.06	0.00	0.20
Ga (Gallium)	0.229	0.30	0.10	0.30
In (Indium)	0.285	0.03	0.00	0.18
Tl^{+1}	0.311	0.03	0.00	0.15
$[S=C=N]^{(-1)}$ thiocyanate	0.282	0.63	0.22	0.00
$[S=N=C]^{(-1)}$	0.282	0.85	0.42	0.00
-OC(=O)H	0.212	0.62	0.37	0.00
$-OC(=O)CH_3$	0.308	0.65	0.80	0.06
$CO_3^{(-2)}$	0.230	0.44	0.55	0.00
-OC(=O)OH	0.252	0.55	0.48	0.55
$[-O_2CCO_2-]^{(-2)}$	0.345	1.10	0.45	0.24
$C\equiv N$	0.171	0.45	0.11	0.22
$C\equiv N$ ionic	0.171	0.70	0.30	0.22
Si^{+4}	0.189	0.00	0.00	0.00
$-SiF_6^{-2}$	0.651	0.48	1.14	0.36
SiO_3^{-2}	0.462	0.88	0.5	0.12
SiO_4^{-2}	0.553	1.22	1.1	0.24
Ge (Germanium)	0.218	0.00	0.00	0.00
$GeF_6^{(-1)}$	0.68	0.48	1.14	0.36
Sn^{+2}	0.274	0.05	0.03	0.00
Pb^{+2}	0.302	0.00	0.00	0.00
-N<	0.104	0.15	0.65	0.00
-NH2	0.130	0.32	0.69	0.00
NH_3 (ammonia)	0.146	0.15	0.65	0.00
NH_3 (ammonia, coor.)	0.146	0.15	0.00	0.00
NH_4^+ (ammonium)	0.160	0.00	0.00	0.05
-N=N=N	0.210	0.30	0.10	0.05
$-N\equiv N+$	0.160	0.60	0.95	0.15
NO_2	0.184	0.53	0.49	0.00
NO_3	0.224	0.50	0.49	0.00
$PO_4^{(-3)}$ phosphate	0.336	0.45	0.87	0.00
HPO_4^{-2}	0.350	0.95	0.80	0.75
$H_2PO_4^{-1}$	0.364	0.95	0.75	0.75
$_2(-O)(H)P(=O)$	0.310	0.75	0.75	0.00

(-O)(HO)(H)P(=O)	0.325	0.68	0.47	0.33
$P_2O_7^{-4}$	0.581	0.90	1.74	0.00
As^{+3}	0.207	0.23	0.13	0.05
AsO_3	0.327	1.25	0.43	0.41
AsO_4	0.367	1.59	0.53	0.53
$HAsO_4$	0.375	1.44	0.86	0.05
$HAsO_4$	0.375	1.65	0.90	0.74
Sb^{+3}	0.263	0.35	0.09	0.07
Bi^{+3} (Bismuth)	0.294	0.18	0.10	0.08
-OH ionic	0.105	0.45	0.50	0.00
-OH	0.105	0.40	0.47	0.33
-OOH	0.150	0.41	0.36	0.40
=O	0.091	0.34	0.10	0.12
-O-	0.091	0.27	0.45	0.00
-OO-	0.130	0.28	0.34	0.00
O^{-2} ionic	0.091	0.10	0.15	0.00
H_2O	0.119	0.45	0.45	0.45
coordinated water	0.068	0.25	0.00	0.55
-SH ionic	0.176	0.25	0.20	0.00
-SH	0.176	0.35	0.16	0.03
=S	0.162	0.24	0.05	0.05
$SO_3^{(-2)}$ sulfite	0.282	0.65	0.82	0.36
SO_4^{-2}	0.322	0.65	0.82	0.00
$S_2O_3^{-2}$	0.433	0.89	0.87	0.41
-OS(=O)2OH	0.336	1.00	0.80	0.75
S^{-2}	0.162	0.50	0.23	0.00
S^{-2} ionic	0.162	0.10	0.00	0.00
Se^{-2}	0.196	0.20	0.00	0.00
SeO_3	0.316	0.80	0.74	0.12
SeO_4^{-2}	0.356	1.14	0.84	0.24
Te (Tellurium)	0.253	0.25	0.00	0.00
Po (Polonium)	0.285	0.45	0.35	0.00
F^{-1} covalent	0.077	0.08	0.19	0.06
F^{-1} ionic	0.077	0.18	0.29	0.06
Cl- covalent	0.149	0.35	0.15	0.06
Cl^{-1}	0.149	0.60	0.40	0.06
ClO_3^{-1}	0.269	0.50	0.40	0.30
ClO_4^{-1}	0.309	0.00	0.40	0.42
Br- covalent	0.185	0.43	0.17	0.05
Br^{-1}	0.185	0.68	0.32	0.05
$BrO_3^{(-1)}$ bromate	0.458	0.60	0.30	0.41
$BrO_4^{(-1)}$ perbromate	0.549	0.20	0.57	0.53
I- covalent	0.242	0.45	0.18	0.04
I^{-1}	0.242	0.70	0.33	0.04
$IO_3^{(-1)}$ iodate	0.515	0.50	0.45	0.40
$IO_4^{(-1)}$ periodate	0.402	0.25	0.50	0.40
At (Astatine)	0.277	0.48	0.18	0.00
He (Helium)	0.052	0.00	0.00	0.00
Ne (Neon)	0.064	0.00	0.00	0.00
Ar (Argon)	0.136	0.00	0.00	0.00
Kr (Krypton)	0.174	0.02	0.01	0.00
Xe (Xenon)	0.231	0.04	0.03	0.00
Rn (Radon)	0.268	0.06	0.03	0.00
La^{+3}	0.516	0.00	0.00	0.00
Ce^{+3} (Cerium)	0.507	0.00	0.00	0.20
Pr (Praesodymium)	0.499	0.02	0.02	0.00
Nd (Neodymium)	0.490	0.03	0.03	0.00

Pm (Promethium)	0.481	0.04	0.03	0.00
Sm (Samarium)	0.473	0.10	0.08	0.00
Eu (Europium)	0.465	0.03	0.03	0.00
Gd (Gadolinium)	0.456	0.03	0.03	0.00
Tb (Terbium)	0.448	0.04	0.03	0.00
Dy (Dysprosium)	0.439	0.04	0.03	0.00
Ho (Holmium)	0.431	0.04	0.03	0.00
Er (Erbium)	0.422	0.04	0.03	0.00
Tm (Thulium)	0.413	0.04	0.03	0.00
Yb $^{+3}$ (Ytterbium)	0.405	0.04	0.03	0.00
Lu (Lutetium)	0.396	0.05	0.03	0.00
Ac (Actinium)	0.505	0.03	0.05	0.00
Th $^{+4}$ (Thorium)	0.496	0.02	0.02	0.10
Pa (Proactinium)	0.488	0.02	0.02	0.00
U $^{+6}$ (Uranium)	0.479	0.03	0.03	0.10
Np (Neptunium)	0.470	0.04	0.03	0.00
Pu (Plutonium)	0.462	0.03	0.03	0.00
Am (Americium)	0.453	0.03	0.03	0.00
Cm (Curium)	0.445	0.03	0.03	0.00
Bk (Berkelium)	0.436	0.04	0.03	0.00
Cf (Californium)	0.428	0.04	0.03	0.00
Es (Einsteinium)	0.419	0.04	0.03	0.00
Fm (Fermium)	0.411	0.04	0.03	0.00
Md (Mendelevium)	0.402	0.04	0.03	0.00
No (Nobelium)	0.394	0.04	0.03	0.00
Lr (Lawrencium)	0.385	0.05	0.03	0.00

In Table 2 the LSER parameters for a series of intact salts are given, the parameters being derived using the group additivity principle (*Hickey, 1996*). The salts included are selected based on the availability of experimentally derived solubility data within the data set supplied by Hickey (*personal* comm).

Experimentally derived solubility data as well as the theoretically derived values based on the LSER parameters using the above mentioned equation for aliphatic compounds are included in Table 2 as are the difference between the experimental and predicted values.

Table 2. LSER parameters, experimentally and theretically derived solubility data and the difference between experimental and predicted values for selected salts. (The notation in the Table is adopted from Hickey (personal comm.))

Vi/100	π^*	ß	α	MFA	Est LogSw	P-O	Obs LogSw
					Solubility		

Vi/100	π^*	ß	α	MFA	Est LogSw	P-O	Obs LogSw
Group 1(IA)							
0.368	0.350	0.100	0.150	Li-N3	-1.20	-2.33	1.13
0.343	0.730	0.320	0.150	Br-Li	0.51	-0.80	1.31
0.427	0.550	0.400	0.400	ClO3 .Li	0.24	-1.50	1.74
0.467	0.050	0.400	0.520	ClO4 .Li	-0.54	-1.29	0.75
0.307	0.650	0.400	0.160	Cl-Li	1.05	-0.21	1.27
0.235	0.230	0.290	0.160	F-Li	0.44	1.43	-0.98
0.967	0.58	1.14	0.56	F6-Si .2 Li	0.99	0.32	0.67
0.263	0.500	0.500	0.100	LiOH	1.67	0.94	0.73
0.400	0.750	0.330	0.140	I-Li	0.25	-0.84	1.09
0.673	0.550	0.450	0.500	IO3 .Li	-0.93	-1.58	0.65
0.342	0.58	0.49	0.1	NO2 .Li	1.24	-0.13	1.37
0.382	0.55	0.49	0.1	NO3.Li	0.98	-0.14	1.11
0.81	0.6	0.87	0.3	Li3-PO4	0.52	2.99	-2.47
0.249	0.150	0.150	0.100	Li2-O	-0.46	-0.92	0.46
0.598	0.75	0.82	0.56	Li2.SO3	1.66	1.23	0.42
0.638	0.75	0.82	0.2	Li2.SO4	1.42	1.06	0.37
0.439	0.3	0.15	0.05	N3-Na	-1.41	-2.21	0.81
0.687	0.6	0.35	0.41	BrO3 .Na	-1.48	-1.84	0.36
0.414	0.68	0.37	0.05	NaBr	0.30	-0.75	1.05
0.538	0.	0.45	0.42	Na.ClO4	-0.74	-1.98	1.23
0.498	0.5	0.45	0.3	NaClO3	0.04	-0.94	0.98
0.378	0.6	0.45	0.06	Cl-Na	0.85	0.06	0.79
0.306	0.18	0.34	0.06	F-Na	0.23	0.23	0.00
0.334	0.45	0.55	0.	NaOH	1.46	0.03	1.44
0.744	0.5	0.5	0.4	NaIO3	-1.14	-0.80	-0.34
0.631	0.25	0.55	0.4	NaIO4	-0.49	-0.32	-0.17
0.471	0.7	0.38	0.04	I-Na	0.05	-1.03	1.08
0.413	0.53	0.54	0.	Na.NO2	1.04	0.21	0.82
0.453	0.5	0.54	0.	NaNO3	0.77	-0.25	1.02
0.62	0.1	0.1	0.	Na2-S	-2.95	-3.25	0.31
0.74	0.65	0.92	0.36	Na2SO3	1.24	0.91	0.33
0.78	0.65	0.92	0.	Na2SO4	1.01	0.87	0.14
1.18	0.48	1.14	0.46	Ba .F6-Si	-0.37	2.66	-3.03
0.811	0.65	0.82	0.46	BaSO3	0.30	3.34	-3.04
0.962	0.89	0.87	0.51	BaS2O3	-0.06	1.99	-2.05
0.851	0.65	0.82	0.1	BaSO4	0.07	5.06	-4.99
0.835	0.65	0.82	0.03	RaSO4	0.16	7.37	-7.21
0.961	1.	0.98	0.03	Ra(NO3)2	0.64	1.04	-0.40
1.543	1.	0.9	0.83	Ra(IO3)2	-3.18	0.34	-3.52
GROUP 13(IIIA)							
0.62	0.03	2.05	0.4	B-H4 .Na	7.18	6.01	1.16
0.751	0.13	2.06	0.4	B-H4 .K	6.57	6.02	0.55
0.599	0.35	0.76	0.69	B-F4 .H4-N	0.90	0.52	0.38

0.668	0.35	0.81	0.64	B-F4 .Na	0.76	-0.23	0.99
0.799	0.45	0.82	0.64	B-F4 .K	0.15	1.61	-1.46
0.856	0.52	0.82	0.67	B-F4 .Rb	-0.10	1.36	-1.46
0.535	0.87	1.35	0.8	B2-O3	4.93	5.43	-0.50
0.471	0.62	0.9	0.5	B-H-O2 .Li	2.68	2.96	-0.29
0.542	0.57	0.95	0.4	B-H-O2 .Na	2.47	1.87	0.60
0.673	0.67	0.96	0.4	B-H-O2 .K	1.86	0.93	0.94
0.601	0.78	0.51	0.92	NaOBOOH	0.05	0.56	-0.51
0.732	0.88	0.52	0.92	KOBOOH	-0.55	0.36	-0.91
0.446	1.23	1.41	1.39	B-H3-O3	6.16	6.14	0.01
0.446	1.38	1.5	0.4	B-H3-O3	6.79	6.90	-0.11
0.956	1.04	1.64	1.6	B4-Na2-O7	4.17	5.45	-1.28
0.956	1.04	1.64	1.6	B4-Na2-O7 .x H2-O	4.17	5.04	-0.87
1.218	1.24	1.66	1.6	B4-K2-O7	2.96	2.90	0.06
0.874	1.56	1.47	0.2	Al3NO3	4.33	3.85	0.48
0.433	0.3	0.57	0.38	Al-F3	0.83	2.00	-1.18
1.298	2.22	0.9	0.76	Al-Cl3 (as Al2Cl6)	-0.42	-0.83	0.42
0.524	0.71	0.82	0.2	"AlSO4"	2.05	1.64	0.41
1.37	2.07	2.46	0.4	Al2(SO4)3	7.16	7.27	-0.11
0.516	0.27	0.57	0.36	F3-In	0.31	0.61	-0.31
0.521	0.33	0.1	0.2	N3-Tl	-2.12	-0.20	-1.91
0.769	0.63	0.3	0.56	BrO3-Tl	-2.19	-0.22	-1.98
0.991	0.88	0.5	0.22	Ba SiO3	-2.17	-0.07	-2.10
0.902	0.58	1.19	0.71	CuSiF6	1.63	1.31	0.32
1.109	0.48	1.24	0.36	F6-Si .2 Na	0.57	3.03	-2.46
1.371	0.68	1.26	0.36	F6-Si .2 K	-0.64	-0.14	-0.50
1.485	0.82	1.26	0.42	F6-Si .2 Rb	-1.15	1.14	-2.29
1.4	0.68	1.26	0.36	F6-Ge .2 K	-0.81	0.88	-1.69
0.4	0.68	0.2	0.24	Ge-O2	-0.50	0.87	-1.37
1.267	1.13	1.15	0.12	(KO)2SnO	-0.12	-0.77	0.65
1.005	0.93	1.13	0.12	(NaO)SnO	1.09	0.63	0.46
				Transition metals			
				Group 3(IIIB)			
1.642	1.99	2.5	0.	Sc2(SO4)3	5.69	6.25	-0.56
1.769	1.82	0.93	1.23	YBrO3	-3.45	-4.00	0.55
0.842	1.07	0.48	0.18	Cl3-Y	-1.20	-1.80	0.60
1.067	1.52	1.5	0.	Y(NO3)3	3.31	2.62	0.69
1.756	1.99	2.52	0.	Y2(SO4)3	5.13	6.06	-0.94
1.509	0.78	1.28	0.41	F6-Ti .2 K	-1.23	0.04	-1.28
1.566	0.76	1.34	0.46	F6-Zr .2 K	-1.27	0.29	-1.56
0.692	0.4	0.84	0.34	F4-Zr	0.83	1.91	-1.08
0.804	1.68	1.96	1.42	H4-O4-Zr	7.43	10.33	-2.90
0.566	0.76	0.28	0.34	O2-Zr	-0.97	1.82	-2.79
				Group 6(VIB)			
1.251	0.87	1.12	0.36	K .1/2 O4-W	-0.46	-0.66	0.20
0.989	0.67	1.1	0.36	Na .1/2 O4-W	0.75	0.59	0.16
0.937	0.67	1.	0.46	O4-W .Sr	0.53	2.91	-2.38
0.742	1.1	1.08	0.	Mn(NO3)2	2.56	2.04	0.52
0.616	0.75	0.92	0.	MnSO4	2.08	1.44	0.63
1.437	2.920	1.000	1.060	Ba(MnO4)2	0.06	-0.17	0.22
1.257	2.92	1.	1.06	Ca(MnO4)2	1.11	0.03	1.08
0.814	1.56	0.56	0.48	KMnO4	-0.08	0.31	-0.39
0.761	1.61	0.55	0.73	AgMnO4	0.23	1.36	-1.13

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0.886	1.46	0.5	0.58	NH4ReO4	-0.93	-0.28	-0.64
0.955	1.46	0.55	0.53	K .O4-Re	-1.07	0.28	-1.35
0.511	0.45	0.25	0.11	F6-Re	-1.14	-0.10	-1.04
1.819	2.58	1.	0.94	O7-Re2. Na2	-2.55	1.57	-4.12
1.033	1.61	0.55	0.78	Ag ReO4	-1.36	0.69	-2.05
Group 8(VIII)							
0.605	0.7	0.92	0.05	FeSO4	2.09	1.84	0.24
1.532	2.05	2.66	0.1	Fe2(SO4)3	7.23	6.19	1.04
0.704	1.4	0.48	0.5	O4-Ru	-0.03	0.88	-0.91
Group 9(VIII)							
1.188	1.3	0.65	1.17	Co(BrO3=2	-2.08	-2.24	0.16
0.642	1.460	0.690	0.450	Br2-Co	1.49	1.01	0.48
0.890	0.100	0.850	1.190	Co(ClO4)2	-0.60	-1.19	0.59
0.570	1.300	0.850	0.470	Cl2-Co	2.58	2.17	0.41
0.426	0.460	0.630	0.470	Co-F2	1.35	2.16	-0.81
0.482	1.000	1.050	0.350	Co-H2-O2	3.81	8.27	-4.46
0.587	1.450	1.550	0.350	Co-H3-O3	6.30	10.84	-4.54
0.756	1.500	0.710	0.430	Co-I2	0.98	0.66	0.32
1.302	1.100	0.950	1.150	Co(IO3)2	-1.40	0.56	-1.96
0.923	0.58	1.19	0.71	Co .F6-Si	1.51	0.74	0.77
0.72	1.1	1.03	0.35	Co(NO3)2	2.42	1.99	0.44
0.817	0.5	0.55	0.7	Co2-O3	-1.31	3.41	-4.71
1.236	1.4	1.69	0.45	Co.2 H3-N.2 H2-O4-S	3.18	3.53	-0.34
1.636	1.6	1.81	0.35	Co .2 H2-O4-S .2 K	1.69	1.80	-0.11
1.75	1.74	1.81	0.41	Co .2 H2-O4-S .2 Rb	1.18	1.83	-0.66
0.594	0.75	0.87	0.35	CoSO4	1.94	1.57	0.37
0.434	0.600	0.280	0.350	Co-S	-0.37	4.01	-4.38
1.559	2.15	0.95	0.54	Cl6-Ir .2 H4-N	-1.76	0.05	-1.81
0.527	0.25	0.35	0.08	Ir-O2	-0.93	4.12	-5.05
1.177	1.3	0.65	1.12	Ni(BrO3)2	-2.02	-1.97	-0.05
0.631	1.46	0.69	0.4	Br2-Ni	1.56	0.85	0.71
0.799	1.1	0.85	0.9	Ni(ClO3)2	1.02	2.42	-1.40
0.879	0.1	0.85	1.14	Ni(ClO4)2	-0.54	-1.47	0.94
0.559	1.3	0.85	0.42	Cl2-Ni	2.64	1.95	0.69
0.415	0.46	0.63	0.42	F2-Ni	1.42	1.80	-0.38
0.471	0.9	0.99	0.96	H2-Ni-O2	3.45	6.31	-2.85
0.745	1.5	0.71	0.38	I2-Ni	1.04	0.44	0.60
0.709	1.1	1.03	0.3	Ni(NO3)2	2.49	2.06	0.43
0.709	1.1	1.03	0.3	H-N-O3 .1/2 Ni	2.49	2.06	0.43
1.625	1.6	1.81	0.3	H2-O4-S .K .1/2 Ni	1.75	2.43	-0.67
0.583	0.75	0.87	0.3	Ni(SO)4	2.01	1.32	0.69
0.908	1.05	0.4	0.22	Cl2-H6-N2-Pd	-2.03	-0.18	-1.84
1.767	2.73	1.07	0.65	(NH4)2PtBr6	-1.72	0.37	-2.08
2.167	2.93	1.19	0.55	Br6-Pt .2 K	-3.21	-1.64	-1.57
1.551	2.25	0.95	0.71	Cl6-Pt .2 H4-N	-1.60	0.20	-1.80
2.297	2.65	1.15	0.67	Cl6-Pt .2 Cs	-4.48	-1.04	-3.45
0.671	0.7	0.25	0.45	Cu(N3)2	-1.80	1.46	-3.27
0.461	0.4	0.15	0.4	Cu(N3)	-1.43	2.72	-4.15
0.771	0.7	0.5	1.	Cu(ClO3)2	-1.08	-2.07	0.99
0.902	0.58	1.19	0.71	Cu .F6-Si	1.63	1.31	0.32
0.699	1.1	1.03	0.35	Cu(NO3)2	2.55	2.07	0.47
0.573	0.75	0.87	0.35	CuSO4	2.07	1.95	0.11
1.729	1.74	1.81	0.41	Cu .2 Rb .2 H2-O4-S	1.30	1.92	-0.62

0.607	1.24	0.89	0.59	CuSeO4	2.51	2.41	0.10
1.157	1.35	0.87	0.35	Cu-H12-N4 .O4-S	-0.70	-0.60	-0.10
1.145	0.97	1.1	0.86	Ag2-O4-W	0.16	3.65	-3.49
0.775	1.95	1.2	0.23	Au-Cl3	3.92	3.57	0.35
1.428	1.97	0.74	0.25	Au-Br4 .K	-2.29	-1.83	-0.45
0.865	0.47	0.81	0.29	Au-Cl4 .Na	-0.26	-0.97	0.70
0.803	1.09	0.36	0.63	Hg-I2	-1.58	2.31	-3.89
1.89	1.8	0.9	1.23	Br-H-O3 .1/3 La	-4.34	-4.07	-0.26
2.061	1.5	1.35	1.2	H-I-O3 .1/3 La	-3.31	-1.72	-1.59
1.188	1.5	1.47	0.	H-N-O3 .1/3 La	2.42	1.76	0.67
1.998	1.95	2.46	0.	H2-O4-S .2/3 La	3.35	4.53	-1.17
0.954	1.8	1.2	0.38	Ce-Cl3	2.71	2.10	0.61
2.052	1.5	1.35	1.4	Ce .3 H-I-O3	-3.26	-0.64	-2.62
1.98	1.95	2.46	0.4	Ce2(SO4)3	3.46	4.27	-0.82
1.873	1.82	0.92	1.23	Pr(BrO3)3	-4.11	-4.68	0.57
0.946	1.07	0.47	0.18	Cl3-Pr	-1.86	-2.48	0.62
1.847	1.9	0.98	1.23	Sm(BrO3)3	-3.56	-3.89	0.33
0.92	1.9	1.28	0.18	Cl3-Sm	3.43	2.88	0.56
1.896	2.01	2.52	0.	Eu2(SO4)3	4.33	5.69	-1.36
1.678	0.7	1.28	0.46	K2F6-Th	-2.31	-1.50	-0.81
1.14	1.32	1.66	0.1	Th(SO4)2	3.50	4.92	-1.42

Based on the above given data it is possible graphically to evaluate the 'Hickey approach' to LSER-derived solubilities for inorganic compounds.

In Fig. 3 the predicted solubilities for all salts given in Table 2 are visualized as a function of the experimentally observed solubilities
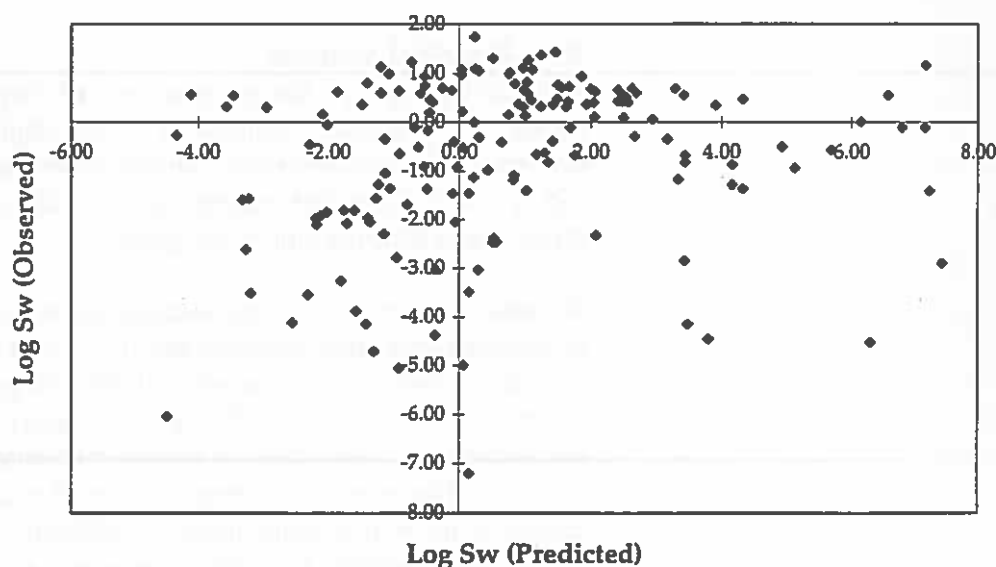
Figure 3. Predicted vs. experimentally observed solubilities for all salts.

It is immediately seen that no distinct correlation between observed and predicted values prevails. It has been stated (*Hickey, personal comm*) that in the case of salts with very low solubilities, the predicted values would differ significantly from the observed, i.e., with more than ±1.3 order of magnitude. However, even turning to the alkali metal salts, all of which are fairly easy soluble the same rather confusing picture, demonstrating the apparent lack of correlation develops (Fig. 4).
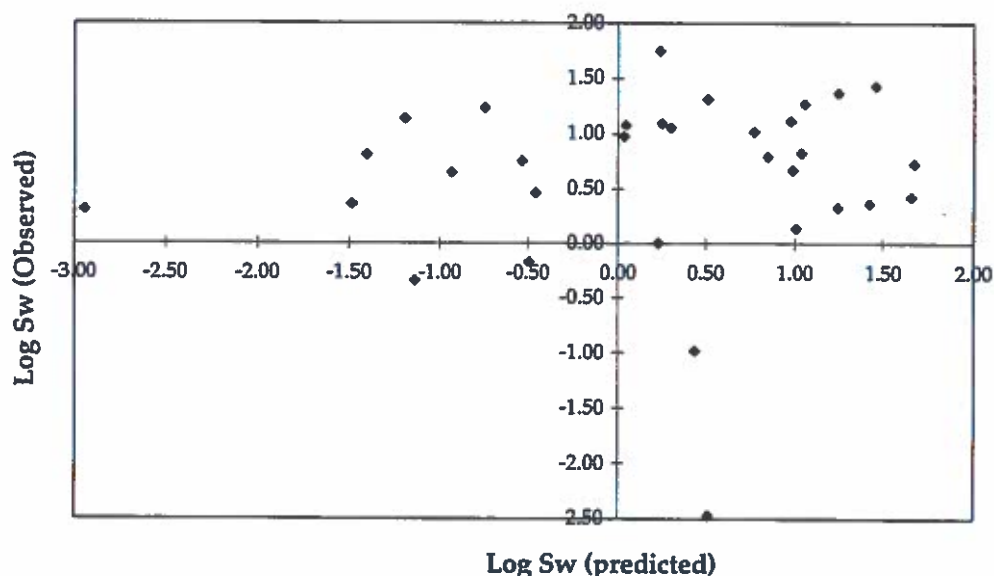

Figure 4. Predicted vs. experimentally observed solubilities for alkali metal salts.

Identical pictures develop for other subgroups of the salts given in Table 2.

3.1.1 Residual analysis

In order to look into the apparent lack of correlation in somewhat more detail the predicted solubilities were depicted as function of the difference between the predicted and experimentally observed values. In Fig.'s 5 and 6 the plot corresponding to all salts (cf. Fig. 3) and to the alkali metal salts (cf. Fig. 4) are given.

If a satisfying correlation between the experimentally observed and predicted solubilities prevailed the plots given in Fig.'s 5 and 6 should have developed with values of the difference between the predicted and observed values randomly distributed around 0 as an indication of a correct chosen model causing normal distributed residuals (*Funk et al.,1995*). However, it is immediate seen that the values are centered around a line with a slope distinctly different from zero. The linear trend is strongly indicative for either an incorrect approach or calculation error (*Funk, 1995*). In the present case it appears most likely that the adoption of the LSER equation developed for aliphatic compounds (*vide supra*) is not valid. In justice it should be emphasized that Hickey (*personal comm*) has not presented his LSER approach to solubilities of salt as a mechanistically founded model but simply as a statistical tool.
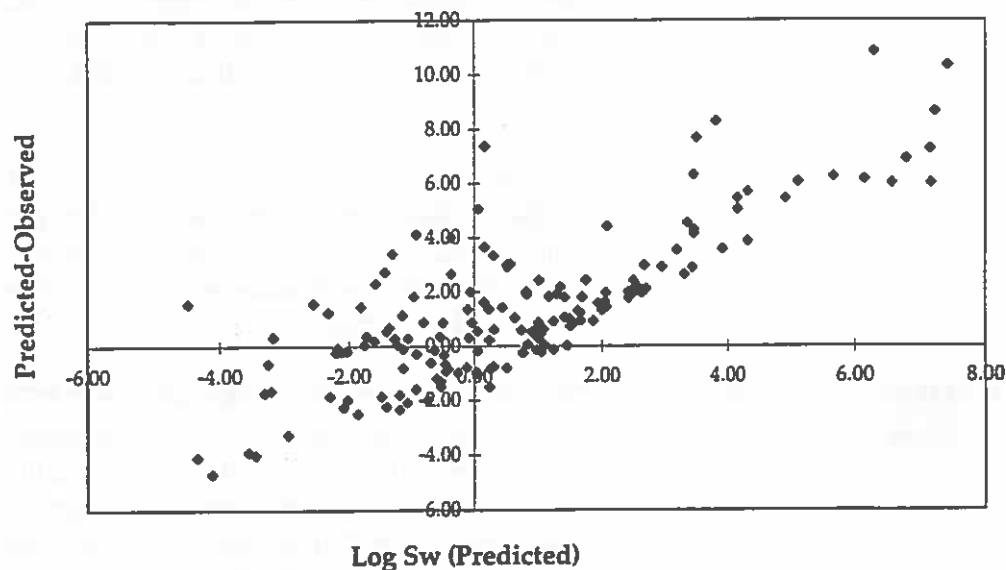
Figure 5. Predicted solubilities as function of the difference between predicted and experimentally observed values for all salts
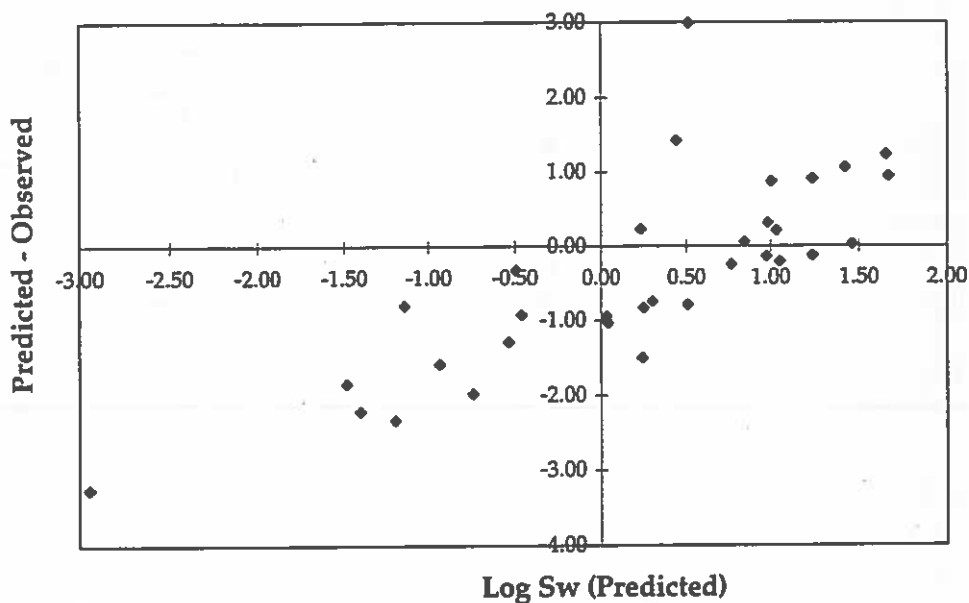

Figure 6. Predicted solubilities as function of the difference between predicted and experimentally observed values for alkali metal salts

Hickey (*subm-b*) reports a plot similar to the above visualized (Fig. 5), however, limiting the x- and y-axses to -7 to 7 and -3 to 5, respectively, obviously eliminating a significant part of the total picture as given in Fig. 5. Nevertheless, an identical trend in the data is likewise noted in the plot reported by Hickey (*subm-b*).

3.1.2 Multilinear regression analysis

Although the 'aliphatic approach' suggested by Hickey (*subm-a; subm-b; subm-c*) apparently does not seem to work, we are still left with the question whether the LSER parameters developed for inorganic compounds (cf. Tables 1 and 2) are applicable to set up a suitable LSER equation for salts.

In order to verify the possible applicability of Hickey's LSER parameters (Table 2), however, without adopting the 'aliphatic approach', we carried out a series of multilinear regression analyses using the LSER parameters given in Table 2 as descriptor with the aim to model the experimentally obtained solubilities.

MLR analysis using Hickey's LSER parameters

It became clear that the Hickey-derived LSER parameters (*Hickey, subm-a; subm-b; subm-c*) do not constitute a proper base for modelling the salt solubilities. It was noted that virtually no correlation between theoretically and experimentally obtained values could be obtained as visualized in Fig. 7 depicting the experimentally obtained solubilities as a function of their theoretically derived counterparts.
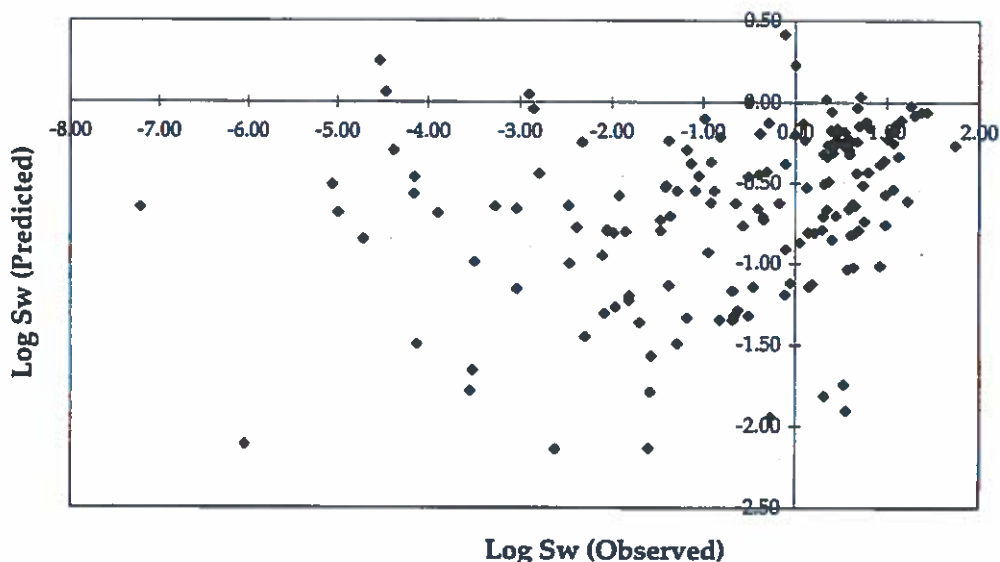
Figure 7. Experimentally observed vs. predicted solubilities based on multilinear regression using the LSER parameters given in Table 2 as descriptors

Intercorrelation of LSER parameters

As a part of the analysis the possible intercorrelation between the single LSER parameters was elucidated. If the parameters contains too much 'cross contamination' through intercorrelation, the statistical results will be virtually worthless.

The intercorrelation between the LSER parameters can be visualized in a scatterplot matrix (SPLOM). In the ideal case, i.e., totally independent parameters, plots with randomly distributed points expanding the single spaces would develop. On the other hand, if two parameters were fully intercorrelated the point would appear on a straight line within the appropriate space.

In Fig. 8 the SPLOM for the four LSER parameters for all salts (Table 2) is visualized, clearly demonstrating the not negligtible intercorrelation between the single parameters. Unambiguously this is a further disadvantage of the Hickey approach.
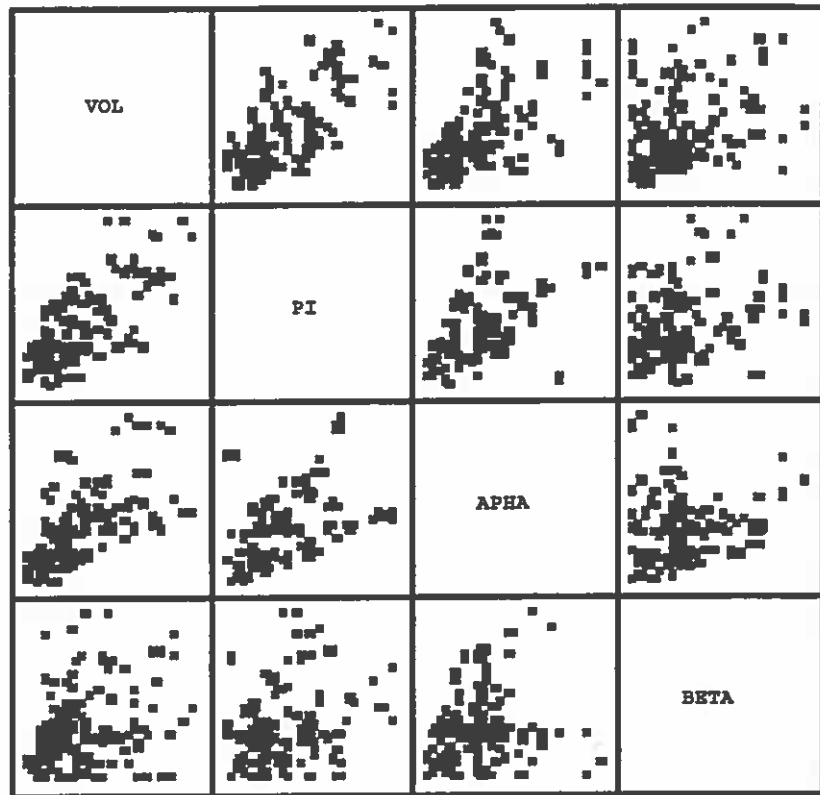

Figure 8. Scatterplot matrix visualizing the intercorrelation between the four LSER parameters

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4   Discussion

Linear Solvation Energy Relationships, experimentally (*Kamlet et al., 1977; 1981; 1983; 1986a; 1986b; 1988; Leahy, 1986; Taft et al., 1985*) or theoretically (*Cramer et al., 1993; Cronce et al., 1998 Famini and Wilson, 1994; 1997*) founded, have proved as a rather versatile tool in modelling various properties, including solubilities of a wide variety of organic compound classes.

The LSER concept, being based on the single elements in the in the general dissolution model (*Schwarzenbach et al., 1993*), should a priori be applicable to inorganic species as well. I appears, nevertheless, that the proposed LSER assessment of solubilities of salts (*Hickey, subm-a; subm-b; subm-c*) does not satisfactorily apply. Several reasons, or possible factors can be expected to be more or less responsible for the observed lack of correlation between the LSER-derived solubilities and the experimentally observed counterparts:

Why does the "Hickey approach" fail?

- the assumption that salts can be regarded as intact, i.e., neutral species
- the lack of inclusion of the dissociation of salts in cations and anions
- the assumption that the 'aliphatic approach' should apply to salts
- the LSER parameters derived for inorganic species are not appropriate descriptors for the modelling of solubilities

It appears without major problems to eliminate the first three possible problems and thus through appropriate statistical analyses, e.g., multilinear regression or partial least square analyses, to develop a proper model for predicting solubilities of inorganic species.

The last subject, i.e., the probable inadequacy of the used LSER parameters seems, on the other hand, more problematic. Obviously it is necessary to derive appropriate non-correlated descriptors for the single ions and salts. Descriptors may be experimentally derived values of possibly purely theoretically based.

Possible other LSER parameters

Possible parameters to be considered as suitable descriptors include:

- ionic volumes
- ionic charges
- electronegativities
- covalent bond characters
- ionic polarizabilities
- HSAB (Hard Soft Acid Base) characteristics
- coordination number
- frontier orbital energies (E_{HOMO}, E_{LUMO})

Presently, only the above discussed 'aliphatic approach' (*Hickey, subm-a; subm-b; subm-c*) has been applied to the study of the solubilities of inorganic species. Thus, the possible applicability of the above mentioned possible descriptors has not been elucidated.

5 Conclusion and Outlook

Linear Solvation Energy Relationships have been used successfully to model properties, e.g., solubilities of a wide variety of organic compounds.

An attempt to apply the LSER concept to inorganic species, salts, seems *a priori* unsuccessful. However, several obvious reasons for the apparent lack of correlation between experimentally observed solubilities and the corresponding LSER predicted values have been verified. These comprise

- the assumption that salts can be regarded as intact, i.e., neutral species
- the lack of inclusion of the dissociation of salts in cations and anions
- the assumption that the 'aliphatic approach' should apply to salts
- the LSER parameters derived for inorganic species are not appropriate descriptors for the modelling of solubilities

From a theoretical point of view, however, it appears reasonable to assume that a suitable LSER approach will allow satisfactorily to predicts salt solubilities.

It is suggested to further elaborate on the LSER concept to include inorganic species using scientifically sound descriptors, the latter possibly comprising

- ionic volumes
- ionic charges
- electronegativities
- covalent bond characters
- ionic polarizabilities
- HSAB (Hard Soft Acid Base) characteristics
- coordination number
- frontier orbital energies (E_{HOMO}, E_{LUMO})

in combination with appropriate statistics such as

- multilinear regression analysis
- principal component analysis
- partial least square analysis
- Hasse diagrams (partial order mathematics)

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