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Linear Free Energy Relationships. An Information Theoretic View

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With 3 Figures

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Summary

Linear free energy relationships are introduced by means of an information theoretic approach. In this view the well-known dilemma between the Hammond postulate and the assertion of an invariable transition state through linear free energy relationships does not appear.

The approach permits many parameter equations to be cast into physically interpretable forms, avoiding statistical coincidence. It is shown that in principle every multiparameter equation can be transformed into a definite single parameter linear free energy relationship.

Introduction

Linear free energy relationships (LFER's) are useful tools in predicting reaction rates and as indicators to mechanistic changes in chemical reactions.

However, quite often they seem to stand in considerable contrast to other principles, as for example to the Hammond postulate (HP) or to the reactivity-selectivity principle (RSP) [1, 2]. Both the HP as well as the RSP suggest more or less curved relationships. Nevertheless, LFER's generally show linear behaviour over considerable free energy changes. From a theoretical point of view this is unsatisfactory. In a review, JOHNSON [1] concluded: "The key problem facing theoreticians is the explanation of the efficiency of such simple and straight-forward laws in their government of the highly complex systems of organic chemistry".

The purpose of this paper is a theoretical deduction of LFER's by using variational theoretical arguments. The physical interpretation of the various parameters will be set forth and the opaque relationship to the HP will be discussed. Finally it will be shown that every multiparameter equation can be cast into a single parameter LFER.

Variational Methods and Information Theory

The use of variational principles in physics is well established. Typical examples are Hamilton's principle in mechanics, Fermat's principle in optics or Boltzmann's famous entropy law in equilibrium thermodynamics. In all these cases a given function is extremized with certain constraints.

In information theory, one is concerned with measuring the scarcity (i.e. the information) of events, quite independently of their nature. This can either be the occurence of the letter "e" in the English language or the appearance of a scattered electron within a given room angle dΩ. In analogy to statistical thermodynamics, SHANNON [3] defined the mean information content H as

$$H = -K \sum_i p_i \log (p_i) \tag{1}$$

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where p_i is the probability of the event i and K is a constant. Often, H is also called information entropy. Roughly spoken, H is a measure of the scarcity or diversity per event.

The problem we are confronted with is to make unbiased estimates leading to the p_i's which are in agreement with the available knowledge about our system. In principle, this is done in the way that all observable properties or characteristics act as constraints when the information entropy is maximized. It is assumed that in all systems, either physical or nonphysical, the information entropy will tend to its maximum, defining the system in its most probable state. Thus, the constraints lead the evolution of the system.

Information Theory and LFER's

To apply the concept to chemical reacting systems we want to identify the p_i's as the probability of getting a transition state (TS) (out of all collisions) of a definite (rate determining) elementary reaction i at a given temperature T. One of the central tasks is now to estimate the influence of substituents on p_i. It is assumed that the substituents are *not directly* involved in the reaction process, but only *perturb* the reaction centre. In other words, is it possible to estimate the extent of perturbation, i.e. its influence on the rate constant when the substituents are changed?

In this approach it is assumed that every substituent has a set of definite independent physical properties (as for example the size leading to steric effects, a charge leading to field effects etc.) which each influences the reaction centre.

Since we are only concerned with the substituent influence in a definite mechanism, we use "i" to index the various substituents bearing all the properties which will be indexed by α (Fig. 1).

To compare the reactivity of reaction centres bearing different substituents, consider an ensemble of identical reactions differing only in the substituents attached to the reaction centre (Fig. 2). It is possible to construct the ensemble expectation value for each substituent property indexed by α. This value f_α is given by

$$f_\alpha = \sum_i p_i f_{i\alpha} \qquad (2)$$

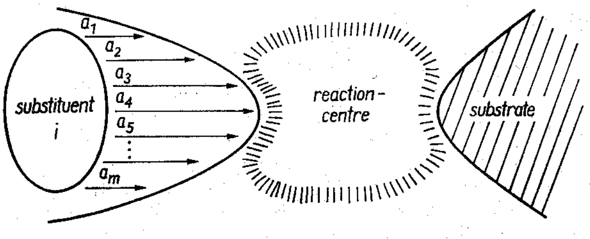

Fig. 1. Schematic representation of a reaction centre perturbed by the substituent i. It is assumed that every substituent i's contribution can be split into a set of independent properties α, each influencing the reaction centre independently. In principle, the total number of properties, m, is infinite

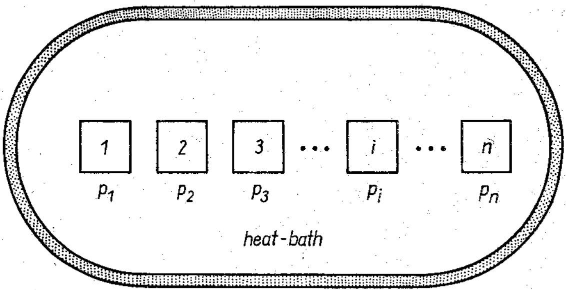

Fig. 2. Ensemble of similar reactions, differing only in the substituents attached to the reaction centres. Each box contains an elementary reaction with a particular substituent *i*. The p_i's refer to the probability of creating the TS out of a given number of collisions. The heat-bath ensures constant temperature

where $f_{i\alpha}$ simply is the property marked by α in the substituent *i*. We further add the usual constraint that the probability distribution is normalized, i.e.

$$\sum_i p_i = 1. \tag{3}$$

Our problem is now to find the maximum information entropy *H* under the constraints set up in eqs. (2) and (3). To solve this problem, the method of Lagrange multipliers is used, i.e. we have to vary the following sum

$$\delta\left[\frac{1}{K}H - (\lambda - 1)\sum_i p_i + \sum_\alpha \lambda_\alpha \sum_i p_i f_{i\alpha}\right] = 0 \tag{4}$$

where λ and λ_α are the constant Lagrange multipliers. After differentiating with respect to p_i and setting the resulting expression equal to zero, the following equation is obtained

$$\ln(p_i) = \sum_\alpha \lambda_\alpha f_{i\alpha} - \lambda. \tag{5}$$

However, the Lagrangian multipliers λ and λ_α are not universal constants, normally they will differ from one ensemble (mechanism) to the other.

It is not unreasonable to imagine ensembles where only one single property α dominates the influence to p_i. This may for example be the size of the substituents (let us call it β), as is the case in Taft's approach to quantify steric effects in the acid catalyzed hydrolysis of aliphatic carbolic esters [4]. In such a case only one λ_α dominates (namely $\lambda_\alpha = \lambda_\beta$) and eq. (5) becomes

$$\ln(p_i) = \lambda_\beta f_{i\beta} - \lambda. \tag{6}$$

To compare the reactivity of two different substituents *i* and *j*, a similar equation can be written for substituent *j*

$$\ln(p_j) = \lambda_\beta f_{j\beta} - \lambda. \tag{7}$$

When the two equations are substracted from each other, we get

$$\ln\left(\frac{p_i}{p_j}\right) = \lambda_\beta(f_{i\beta} - f_{j\beta}). \tag{8a}$$

Since our p_i's are directly proportional to the rate constant k_i, we can write

$$\ln\left(\frac{k_i}{k_j}\right) = \lambda_\beta(f_{i\beta} - f_{j\beta}). \tag{8b}$$

When j is a standard substituent (call it "o") to which all other substituents are compared, we finally get

$$\ln\left(\frac{k_i}{k_0}\right) = \lambda_\beta(f_{i\beta} - f_{0\beta}). \tag{8c}$$

The connection to various single parameter LFER's is now easily seen. In Taft's approach without electronic effects,

$$\log\left(\frac{k_i}{k_0}\right) = \delta E_i \tag{9}$$

λ_β plays the role of the susceptibility factor δ and $(f_{i\beta} - f_{0\beta})$ is identified with the substituent constant E_i.

In the Hammett equation [4] (10), β is mainly an electronic inductive property. The constant λ_β is related to the ϱ reaction constant, whereas $(f_{i\beta} - f_{0\beta})$ corresponds to the σ_i substitution constant.

$$\log\left(\frac{k_i}{k_0}\right) = \varrho\sigma_i. \tag{10}$$

Also in the Grunwald and Winstein [4] approach to describe solvent polarity the concept is easily applied. Here, $(f_{i\beta} - f_{0\beta})$ is related to the "solvent ionising power", whereas λ_β is a substrate parameter giving the sensibility of the effect.

It must be emphasized that normally more than one property $f_{i\alpha}$ is expected to contribute to the perturbation of the reaction centre. This depends to a great extent on *how* the contributing properties are defined. However, later we will see that under a suitable linear combination of the $f_{i\alpha}$'s every multiparameter equation [eq. (5)] can be cast into a single LFER [eq. (6)].

Physical Interpretation and Discussion

As we have seen in the previous section, the λ_α's can be identified with constants in several LFER approaches. Let us now consider their physical interpretation.

From eq. (5) we may write

$$p_i = e^{-\lambda} \exp\left(\sum_\alpha \lambda_\alpha f_{i\alpha}\right). \tag{11}$$

Applying the normalization condition [eq. (3)] we get

$$Z \sum_i \exp\Big(\sum_\alpha \lambda_\alpha f_{i\alpha}\Big) = 1 \tag{12}$$

with

$$Z = e^{-\lambda} = \Big(\sum_i \exp\Big(\sum_\alpha \lambda_\alpha f_{i\alpha}\Big)\Big)^{-1} \tag{13}$$

where Z is called the partition function. Thus, eq. (11) is rewritten:

$$p_i = Z \exp\Big(\sum_\alpha \lambda_\alpha f_{i\alpha}\Big). \tag{14}$$

To be in accordance with statistical thermodynamics and since p_i and k_i (the rate constant) are proportional we write

$$k_i = CZ \exp\left\{\frac{1}{k_\mathrm{B}T}\Big(\sum_\alpha \lambda'_\alpha f_{i\alpha}\Big)\right\} \tag{15}$$

where C is the proportional constant between p_i and k_i, k_B is the Boltzmann constant, and T is the temperature. The constant λ'_α is given by the relationship

$$\lambda'_\alpha = k_\mathrm{B}T\lambda_\alpha. \tag{16}$$

We want now compare eq. (15) with the Arrhenius equation (17)

$$k_i = A \exp\left(-\frac{E_i^{\ddagger}}{k_\mathrm{B}T}\right) \tag{17}$$

where $E_i^{\ddagger}$ is the activation energy of the reaction with the substituent i. Setting eq. (15) equal to eq. (17) and take the natural logarithm on each side, we obtain

$$\ln (CZ/A)^{k_\mathrm{B}T} + \sum_\alpha \lambda'_\alpha f_{i\alpha} = -E_i^{\ddagger}. \tag{18}$$

To get an explicit expression of λ'_α eq. (18) is differentiated with respect to the property $f_{i\alpha}$. We get

$$\lambda_\alpha = -\frac{1}{k_\mathrm{B}T}\left(\frac{\partial E_i^{\ddagger}}{\partial f_{i\alpha}}\right). \tag{19}$$

Since eq. (18) holds for every substituent, we have

$$\left(\frac{\partial E_i^{\ddagger}}{\partial f_{i\alpha}}\right) = \left(\frac{\partial E_j^{\ddagger}}{\partial f_{j\alpha}}\right) = -k_\mathrm{B}T\lambda_\alpha \tag{20}$$

for all i and j. From eq. (19), λ_α is interpreted as the sensitivity in the change of the activation energy when the property α of the substituents is varied. Note, that in principle $E_i^{\ddagger}$ and $E_j^{\ddagger}$ are different, i.e. a considerable change in the TS structure is possible *even when λ_α is constant* (conf. Fig. 3). Thus, the widely accepted view that the slopes of LFER's in some way measures TS *structures* is too vague. The apparent discrepancy, often quoted [1, 2, 4], does not appear.

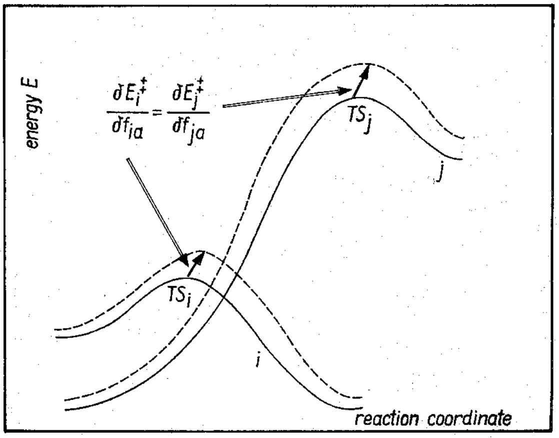

Fig. 3. Illustration of constant λ_α values at different TS structures. TS$_i$ and TS$_j$ are TS's with substituent *i* and *j*. Arrows in TS$_i$ and TS$_j$ indicate the change of the energy when the property α is changed by a unit step. Equation (19) relates it directly to the λ_α's

In addition, eq. (19) also indicate the temperature dependence of the λ_α's. When it is assumed that $(\partial E_i^{\ddagger}/\partial f_{i\alpha})$ is independent of the temperature, we get

$$\frac{\lambda_\alpha(T_1)}{\lambda_\alpha(T_2)} = \frac{T_2}{T_1}. \tag{21}$$

This is indeed the case for a few reaction series (for example ester hydrolysis) where eq. (21) is followed with high accuracy [5]. The thermodynamic aspects under which eq. (21) is valid are discussed by WELLS [5]. However, in general $(\partial E_i^{\ddagger}/\partial f_{i\alpha})$ will not be temperature invariant.

Multiparameter Equations

The connection to multiparameter equations as in the extended Hammett approach [4], in the Swain-Lupton dual parameter equation [4] or other approaches is also easily seen. In our view, the success of these methods is mainly due to the substituent constants describing properties which each perturb the reaction centre, while other factors are more or less constant. However, in multiparameter equations it is often difficult to give the substitution constants a proper physical interpretation. This leads us immediately to the question about the possibility to create a complete set of properties α, such that a general LFER can be defined

$$\log\left(\frac{k_i}{k_0}\right) = \sum_\alpha \lambda_i(f_{i\alpha} - f_{0\alpha}) \tag{22}$$

where α spans a complete set of properties defining *every* substituent *i*. This has the advantage that statistical ambiguities in the various σ scales can be easily avoided. The λ_α's directly give the sensitivity of the rate to the property α. In practice, the number of substituent properties is of course limited. In principle, all types of properties can be chosen (as long as they are independent). The only requirement given in eq. (2) is that the $f_{i\alpha}$ are summable properties such that f_{α} is a constant in every closed ensemble. Typical properties suitable for this purpose are the size/volume of the substituent, the electron affinity, the ionization energy, the polarizability, magnetic properties etc. It must be stressed, that even if one had a complete set of independent properties (which in principle is infinite), the set would not be unique. This is certainly true, since every independent property can act as a basis in a vector space. Therefore, every linear independent combination of property vectors will also define a suitable basis. However, by use of a suitable convention this ambiguity can be avoided.

From a mathematical point of view, it is interesting to note that every multiparameter equation of independent properties can be cast into a single parameter equation with unit slope. To see this, eq. (5) is interpreted as a linear transformation $\underset{\sim}{F}$ which maps every element of the property vector space $\underset{\sim}{V}^{m}$ into the probability vector space $\underset{\sim}{R}^{n}$

$$\underset{\sim}{F}(\underset{\sim}{x}) = \underset{\sim}{y}, \quad \underset{\sim}{x}\ \varepsilon\ \underset{\sim}{V}^{m},\ \underset{\sim}{y}\ \varepsilon\ \underset{\sim}{R}^{n}$$

It is now possible to cast the transformation F into its canonical form, i.e. the matrix representation of F is diagonal (for proof see ref. [6]). Thus, eq. (5) can be rewritten as

$$\ln(p_i) = f_{\alpha(i)}. \tag{23}$$

a single parameter equation with unit slope. However, the price to be paid is that $\alpha(i)$ now in general is a linear combination of all properties α *which is different for every substituent i.* In other words, the universality of the substituent constants $f_{i\alpha}$ is lost at the cost of a one parameter LFER, *valid only in the ensemble.* This means, going to another type of elementary reaction, the previous substituent constants do generally not create a LFER.

The main problem in applying the concept of generalized LFER to an experimental situation is to define properties of the substituent which independently influence the reaction centre. In most of the observed single parameter equations the universality of the substituent constants indicate that only one typical property (steric effects, inductive effects etc.) is responsible for the linearity. This seems also to be the case for σ^{+} and σ^{-} constants. In these cases, however, the substituent constant has to be redefined, since now also other electronic properties ("through conjugation“) contribute to the perturbation. According to the above mentioned theorem a single parameter LFER can be constructed. Note that the so-defined substituent constant σ^{+} and σ^{-} are not universal.

The use of once defined substituent constants (which reflect a definite property) would avoid the usage of different σ salces, and the parameters would have a reasonable physical interpretation.

To obtain the different $f_{i\alpha}$ substituent constants, either standard reactions which purely shows the influence of one property α have to be used, or quantum chemical calculations of properties have to be performed to define the substituent constants. Then, in this way unbiased multiparameter equations can be set up.

A limitation of our concept seems to be that only systems where the substituents perturb the reaction centre are considered. Thus, systems showing anchimeric assistance, steric acceleration and similar effects are not included in the derivation. However, in such situations often a new reaction centre can be defined, including the participating substituents. Nonreacting substituents attached to this new reaction centre will again result in single or multiparameter LFER's.

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