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Elementary Analysis of Chemical Electric Field Effects in Biological Macromolecules

I. Thermodynamic Foundations

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ABSTRACT: The analysis of bioelectric phenomena requires knowledge of the thermodynamics and kinetics of electric field effects on chemical reactions. Chemical relaxation kinetics in high electric fields is the method of choice in order to imitate the high electric fields operative in living entities like membranes or close to fixed charges like those in proteins and nucleic acids. The present account covers elementary aspects of chemical electric field effects. Part I deals with the thermodynamic foundations of the analytical formalism required for a rigorous treatment of chemical field effects. Part II utilizes this frame of concepts and provides kinetic information as to how to investigate chemical and orientational contributions to structural changes in macromolecules and membrane organizations. The basic formalism established so far for isolated macromolecular systems may be extended to treat more complex bioelectric phenomena on the level of membranes and of cells.

1. Introduction

Electric field effects play an important role in many biological cell processes. Phenomena as different as nerve excitation,(1-4) electrogenic ion transport, neurostimulated secretion of hormones and transmitter substances, or the photosynthesis of ATP(5,6) involve cell functions in which biochemical reactions are inseparably coupled to electric field forces.(7,8)

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It has been recognized that macromolecules and macromolecular organizations such as biological membranes are particularly effective media for the coupling of high electric fields with biochemical reactivity. Indeed, all biomembranes appear to be associated with electric membrane potentials.

Electrical chemical membrane processes are most evident in the rapid electric communication system of living entities. For example, the generation and rapid transmission of electric signals such as nerve impulses are based on interactions between electric fields and macromolecular membrane organizations. The acquisition and processing of external information, short-term storage, and retrieval of learned experience in the central nervous system are also believed to involve electric field changes coupled to structural transformations in the neuronal membranes.(9)

In order to understand the functional role of electric fields in the usually very complicated biological systems, basic knowledge of electric field effects on simple molecules and on (bio)chemical reactions is an essential prerequisite.

In experimental physics and physical chemistry, external electric fields have traditionally been applied in order to probe the electric–ionic properties of atoms and molecules and to study the electronic and optical details of matter. In particular, the combination of electrical and optical techniques represents a powerful tool for the investigation of overall shape and structure and of the dynamic properties of molecules and molecular interactions.

A particularly instructive example for the power of electro-optic analysis is the membrane-bound bacteriorhodopsin. In this macromolecular system electric fields cause major structural transitions which involve orientation changes of the chromophores retinal, tyrosine, and/or tryptophan residues and pK changes of at least two types of H^+-binding sites. The conformational changes are based on a saturable induced dipole mechanism associated with an extremely large anisotropic (electric) polarizability. On a molecular level the induced polarization appears to involve a restricted electric displacement of ionic groups (ion pairs) within the protein in a highly cooperative manner. The electric field effects observed in bacteriorhodopsin membrane fragments are of functional importance for this light-driven H^+-pumping system. The results are also suggestive of a possibly quite general polarization mechanism for a very effective interaction of macromolecular organizations with electric fields.(10,11)

Recent electro-optic data on linear polyelectrolytes like the K^+-salt of polyriboadenylate, poly(rA, K^+) demonstrate that the dissociation of counterions from the inner atmosphere and, coupled to it, the destacking of the adenine bases in high electric fields is highly anisotropic.(12) The anisotropy of the counterion movement along polyionic surfaces suggests that counterion exchange as well as influx and efflux of counterionic substrates or hormones occur preferably at the border lines of the ionic atmospheres which cover polyionic regions on macromolecular enzyme and receptor proteins and membranes. Once part of the ion cloud, such substrates and activator substances may reach the active sites via surface diffusion. In this model the border regions of the counterion atmosphere serve as a preferable cross section for trapping counterionic substrates.

Chemical thermodynamics and kinetics provide the formalism to describe the observed dependencies of chemical-conformational reactions on the external physical state variables: temperature, pressure, electric and magnetic fields. In the present account the theoretical foundations for the analysis of electrical–chemical processes are developed on an elementary level. It should be remarked that in most treatments of electric field effects on chemical processes the theoretical expressions are based on the "homogeneous-field approximation" of the continuum relationship between the total polarization and the electric field strength (Maxwell field). When, however, conversion factors that account for the molecular (inhomogeneous) nature of real systems are given, they are usually only applicable for nonpolar solvents and thus exclude aqueous solutions. Therefore, in the present study, particular emphasis is placed on expressions which relate experimentally observable system properties (such as optical or electrical quantities) with the applied (measured) electric field, and which include applications to aqueous solutions.

Since molecular-dynamical details of chemical-conformational transitions are derivable from relaxation kinetic measurements, kinetic analysis is therefore included in some theoretical and practical detail.

2. *Primary Aspects of Matter in Electric Fields*

An externally applied electric field is a vectorial perturbation for chemical or orientational distributions involving interacting molecules or molecular organizations. Unlike the isotropic temperature and pressure effects on chemical-conformational transformations, direct sensitivity to electric field forces is bound to certain electrical properties of the chemical structures involved. Major structural-chemical changes in electric fields require the presence of ions, or ionized groups, or permanent or induced dipolar charge configurations, preferably in macromolecular structures.

The primary molecular-mechanical effects of electric fields involve (a) the orientation of permanent dipoles or of dipolar parts in a more complex structure, in the direction of the applied field; (b) the deformation of polarizable systems (and also, but not necessarily, the subsequent orientation of the induced dipoles in electrically anisotropic particles) including changes in the distance between the charge centers of an ion pair in a macromolecular structure.

2.1. *Electrical–Chemical Coupling*

Chemically, molecular conformations with large electric moments increase in concentration at the expense of those configurations with smaller moments. Secondly, the presence of electric fields increases the dissociation of weak acids and bases and promotes the separation of ion pairs into the corresponding free ions (dissociation field effect, second Wien effect). The free ions or ionized structures then may move in the direction of the electric field (electrophoresis) and a field-dependent stationary state in the ion distribution may be established.

Thus, basically two types of electric–chemical coupling may be differentiated, (a) permanent or induced *dipolar equilibria*, and (b) *ionic* (dissociation and association) *processes* involving (macro-)ions and low molecular weight ions (of preferably opposite charge sign). Whereas dipolar equilibria in electric fields are accessible to thermodynamic analysis, ionic processes involving free ions require a kinetic approach.*(13–16)

2.2. *Elementary Chemical Processes*

Changes in the concentration of chemically interacting reaction partners may arise from two types of elementary chemical reactions: *intramolecular* (or monomolecular) and *bimolecular* elementary steps.

If the molecules B of a system equilibrate between two alternative structures or conformations, B_1 and B_2, according to

$$B_1(\uparrow) \rightleftharpoons B_2(\big\uparrow) \qquad (2.1)$$

where B_2 has the higher electric dipole moment (indicated by the longer arrow), an external electric field will shift this intramolecular equilibrium to the side of higher moments.

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* It should be mentioned that even in the absence of dipolar, polarizable, or ionic reaction partners, high electric fields may cause shifts in chemical distributions.(13–15) Such a field effect requires, however, that the solvent phase has a finite temperature coefficient of the dielectric permittivity or a finite coefficient of electrostriction; an additional condition is that the chemical reactions proceed with a finite reaction enthalpy (ΔH) or a finite partial volume change (ΔV). Electric field induced temperature and pressure effects of this type are usually very small; they may, however, gain importance for isochoric reactions in the membrane phase.

A bimolecular reaction step is involved in all dimerization processes like

$$B(\uparrow)\cdot B(\downarrow) \rightleftharpoons 2B(\uparrow) \tag{2.2}$$

When, for instance, the dipole moments compensate each other upon complex formation, the reaction is associated with a dipole moment change which is of the order of the monomer dipole moment. This is a particularly favorable condition for the electric field-induced shift to the right-hand side.

The bimolecular process in the reaction

$$(L^{+}\cdot B^{-}) \rightleftharpoons L^{+} + B^{-} \tag{2.3}$$

involves ion-pair formation to $(L^{+}\cdot B^{-})$ and may lead to neutralization via $(L^{+}\cdot B^{-}) \rightleftharpoons LB$. Such equilibria are always shifted by electric fields to the side of the freely mobile ions as far as the overall change is concerned; see, however, Ref. 12.

The exchange reaction according to

$$L + CB \rightleftharpoons LB + C \tag{2.4}$$

may proceed through an LBC intermediate or may involve the bimolecular elementary steps $BC \rightleftharpoons C + B$ and $LB \rightleftharpoons L + B$; in any case, on an elementary scale the reaction equation (2.4) only involves bimolecular steps.

In general, the equilibrium state of a chemical process between several interaction partners B_j,

$$0 \rightleftharpoons \sum_j \nu_j B_j$$

or

$$|\nu_1| B_1 + |\nu_2| B_2 + \cdots \rightleftharpoons \cdots \nu_n B_n \tag{2.5}$$

where the ν_j are the stoichiometric coefficients, may be characterized by an *apparent equilibrium constant* K (concentration ratio) according to

$$K = \prod \bar{c}_j^{\nu_j} \tag{2.6}$$

In this form, $\prod$ stands for product over species B_j; $\bar{c}_j$ is the equilibrium concentration (mol dm^{-3}) of B_j. The ν_j are negative for the reactants and positive for the products; the reaction equation (2.5) is read from left to right. [For Eq. (2.1) we have $K = \bar{c}_2/\bar{c}_1$ and for Eq. (2.3), $K = \bar{c}_L \cdot \bar{c}_B/\bar{c}_{LB}$.]

Whereas the K values are usually concentration dependent, the actual thermodynamic equilibrium constants, $K^{\ominus}$, defined as thermodynamic activity ratios $[K^{\ominus} = K \cdot \bar{Y} = \prod (\bar{c}_j \cdot \bar{y}_j)^{\nu_j}]$, are independent of concentration.

From a practical point of view it is frequently the concentration of a species which may be directly determined, for instance, by optical or electro-optic monitoring techniques. On the other hand the general theoretical analysis of electric field-induced concentration shifts or conformational shifts is, however, intrinsically bound to a formalism which describes the dependence of equilibrium and stationary-state distribution constants on the electric field intensity.

2.3. *Biological and Experimental Electric Fields*

In living organisms electric fields of sufficiently high intensity and of variations large enough to affect chemical processes are encountered not only within membrane phases, but also near the surfaces of membranes and protein organizations, for instance at the active sites of enzymes and receptors.(17)

The observed membrane potential differences, $\Delta\psi_m$, of up to 100 mV may correspond to average values of the electric field strength, $\bar{E} = \Delta\psi_m/d$, of about 100 kV cm^{-1} when the thickness, d, of the dielectric membrane part is about 10 nm.

2.3.1. *Polyionic Field Effects*

Besides the powerful field changes occurring within membranes, there are inhomogeneous electric fields originating from the surface of polyionic macromolecules and membranes. The electric potential $\psi(\mathbf{r})$ in the environment of these structures decays with increasing distance $\mathbf{r}$ from the surface of fixed ionized groups (or absorbed ions). The corresponding electric field forces $\mathbf{E} = -\mathrm{grad}\,\psi(\mathbf{r})$, however, are largely screened by counterion atmospheres at physiological ionic strengths (0.1–0.15 mol dm^{-3}). An effective direct interaction of these inhomogeneous fields with chemical reactions is limited to a short range of about 1 nm at 0.1 mol dm^{-3} ionic strength and can involve only low molecular weight species. The electric fields of polyionic surfaces may, however, indirectly affect chemical reactions by accumulating small ionic species in their immediate environment. In these regions of higher ionic strengths, rate and extent of chemical reactions between ionic reaction partners will be different from the behavior in the bulk solution. This catalytic effect will be very pronounced for polyelectrolyte structures. Theoretical approaches aimed at understanding polyionic electric field effects are being advanced; for instance, partial dehydration of ionic reaction partners in the high local electric field close to a polyionic surface appears to be one of the important factors.(18) A point not considered so far is that a kind of orientational "fixation" of a reactant in the locally high electric field of the polyion may either favour or disfavour a reaction. Practically, the ionic strength dependence of rate and equilibrium constants may be used in order to establish the mechanism of polyionic field effects.(17,19)

2.3.2. *Experimental Limitations*

The field intensities which are experimentally accessible are limited by dielectric breakdown. In aqueous solutions, fields up to 150 kV cm^{-1} may be controlled over distances in the millimeter and centimeter range. It is an additional limitation that in ionic solutions electric fields cannot be maintained for a long time. Owing to ionic currents the field will decrease and Joule heating may cause appreciable temperature increases. These problems can be minimized by applying field pulses of limited duration to ionic solutions and suspensions. In any case, the maximum homogeneous fields that can be experimentally achieved are comparable to the maximum values of electric fields encountered in biomembranes.

2.4. *Biopolymers*

Among the early examples of the successful use of electric fields to probe ionic structures and electrical and optical anisotropies are the linear polyelectrolytes. Basic information about macromolecular dimensions, size, and shape have been derived from the relaxation of field-induced changes in optical properties(20–22) and in electrical parameters of the electrically and optically anisotropic systems.(21,22) The analysis of electric conductivity measurements has demonstrated that linear polyelectrolytes are electrically anisotropic.(23–25) It was established that the extremely large dipole moments, which the electric field produces by displacement of the counterion atmosphere parallel to the long axis of the polyions, are responsible for their orientations in the direction of the external field.

Interest in electric field effects on macromolecules was appreciably revived when it was found that electric fields are capable of producing structural-conformational changes in biopolymers and membranes. Here, too, optical properties are a convenient indicator of field-induced processes. Initial hints of presumably chemical contributions to field-induced changes in birefringence were reported for DNA solutions of low ionic strength.(26) Dielectric measurements have shown that polypeptides in viscous organic solvents may undergo intramolecular helix-coil transitions in the presence of electric fields.(27) In the meantime there are many reports on field-induced conformation changes in multistranded as well as in single-stranded polyelectrolytes.(28-35)

Of particular interest in the discussion of electric field effects in biological structures is the observation of threshold phenomena. It has been found that electric impulses above a certain threshold intensity are capable of triggering conformational transitions in metastable polynucleotide structures. A similar threshold effect is associated with electric field-induced permeability changes in vesicle membranes(29,36) as well as in cellular systems.(37,38) Recently, nonlinear field dependencies of base stacking in single-stranded polynucleotides have been discussed as a threshold effect.(34) See also Part II, Chapter 5 of this volume.

3. General Thermodynamic Foundations

Electric field-induced chemical transformations in macromolecules and macromolecular organizations such as membranes cannot be analyzed satisfactorily in all cases because adequate theoretical approaches are lacking. The observed dependence of biopolymer reactions on the electric field intensity seems, however, to be very similar to that of small molecules. Therefore, it appears pertinent to introduce the analysis of field-induced macromolecular changes with relationships which are derived to describe field effects in reactions of small molecules.

3.1. General Reaction Parameters

It is well known that *chemical* processes are dependent on the intensive *physical* variables (z), e.g., temperature (T), pressure (P), or external electric field (**E**). This observation may be generally described by the z dependence of the thermodynamic and apparent equilibrium constants, $K^{\ominus}(z)$ and $K(z)$, and in terms of DeDonder's reaction variable, ξ(mol), or of a degree of transition, Θ. According to DeDonder, the differential change dn_j in the amount of substance n_j(mol) of the reaction partner j in a chemical process may be related to the stoichiometric coefficient ν_j (with the appropriate sign):

$$d\xi = dn_j/\nu_j = V dc_j/\nu_j \tag{3.1}$$

where V is the volume ($c_j = n_j/V$), or in integral form:

$$n_j = n_j(\text{ref}) + \nu_j\xi, \qquad c_j = c_j(\text{ref}) + \nu_j\xi/V \tag{3.2}$$

where n_j(ref) and c_j(ref) are the reference values (for instance, at given values of P, T, and **E**). As $K(z) = \prod \bar{c}_j^{\,\nu_j}$ is a function of z, ξ is also dependent on z. It is now important to realize that not only are the equilibrium values $\bar{c}_j$ and thus ξ a function of z but additionally the extent of a z-induced change, Δc_j or $\Delta\xi$, in c_j and thus in ξ depends on the actual "position" of the equilibrium. Indeed, there are optimum conditions of $\bar{c}_j$ (or ξ and $\bar{\Theta}$) for major z-induced chemical transformations. In order to describe this experimental experience, it is useful to express the z-induced changes in ξ or Θ, for instance by

$$d \ln \xi = (\partial \ln K/\partial \ln \xi)_z^{-1} d \ln K \tag{3.3}$$

$$d \ln \Theta = (\partial \ln K/\partial \ln \Theta)_z^{-1} d \ln K \tag{3.4}$$

where the subscript z refers to constant values of the z parameters.

For the intramolecular two-state transition represented by Eq. (2.1), we have $\Theta = \bar{c}_2/(\bar{c}_2 + \bar{c}_1)$ and $K = \bar{c}_2/\bar{c}_1 = \Theta/(1-\Theta)$. In this case the term $(\partial \ln K/\partial \ln \Theta)_z = \Theta(\partial \ln K/\partial\Theta)_z$ is equal to $1/(1-\Theta)$, and Eq. (3.4) takes the simple form

$$d \ln \Theta = (1-\Theta)\, d \ln K \tag{3.5}$$

The corresponding expressions for the bimolecular reaction in Eq. (2.3) are $\Theta = \bar{c}_B/c^0 = \bar{c}_L/c^0$ and $K/c^0 = \Theta^2/(1-\Theta)$, where the total concentration c^0 of a 1:1 component ratio is given by $c^0 = \bar{c}_L + \bar{c}_{LB} = \bar{c}_B + \bar{c}_{LB}$. Differentiation according to Eq. (3.4) yields

$$d \ln \Theta = [(1-\Theta)/(2-\Theta)]\, d \ln K \tag{3.6}$$

It is readily seen that in both these elementary cases of the intramolecular and bimolecular reactions, a z-induced *relative* shift in Θ and thus in ξ and c_j is maximal at $\beta \to 0$. The *absolute* displacements, however, have maximum values around $\Theta = 0.5$ as outlined below.

When the changes in K (and thus in Θ, ξ, or c_j) produced by the external perturbation steps δz_i are small, we may use linear approximations. For instance, Eq. (3.4) then reads

$$\delta\Theta/\Theta_{\text{ref}} = \{\Theta[\partial \ln K/\partial\Theta]_z\}^{-1}\, \delta K/K_{\text{ref}} \tag{3.7}$$

where

$$\delta K = K(z_i) - K_{\text{ref}} \ll K_{\text{ref}} \tag{3.7a}$$

and

$$\delta\Theta = \Theta(z_i) - \Theta_{\text{ref}} \ll \Theta_{\text{ref}} \tag{3.7b}$$

holds. The sign δ is used for small differences. K_{ref} and Θ_{ref} are appropriate reference values; for instance, these values may refer to $\mathbf{E}=0$. With the help of Eq. (3.7) estimates for the relative shifts of dipolar and ionic equilibria by external electric fields were calculated.(7,8)

3.2. General van't Hoff Relations

The dependence of the apparent equilibrium constant $K(z_i)$ on the intensive variable $z_i(P, T, \mathbf{E})$ may be expressed by a generalized van't Hoff relationship according to(13)

$$(\partial \ln K/\partial z_i)_{z \neq z_i} = \Delta Z_i/RT \tag{3.8}$$

where R is the gas constant, T the Kelvin temperature, and

$$\Delta Z_i = RT(\partial \ln K/\partial z_i)_{z \neq z_i} \tag{3.9}$$

is the extensive reaction quantity complementary to z_i. (The subscript $z \neq z_i$ means all z constant except z_i.)

It is recalled that when $z_i = T$, $\Delta Z_i = \Delta H/T$, where ΔH is the reaction enthalpy representing the enthalpy difference of *one* stoichiometric transition. When $z_i = P$, $\Delta Z_i = -\Delta \bar{V}$, where $\Delta \bar{V}$ is the molar partial volume change for one stoichiometric transformation. Finally, when $z_i = \mathbf{E}$, the measured electric field, then $\Delta Z_i = \Delta M$, where ΔM is the molar reaction dipole moment.(13-15) It will be shown below that ΔM of dipolar equilibria refers to the components parallel to $\mathbf{E}$, of the dipole moments of the interacting dipolar molecules or macromolecular substructures.

The Δ-sign used in the context of Eqs. (3.8) and (3.9) is defined by the partial differential $\partial/\partial\xi$. The extensive quantity Z_i is given by

$$Z_i = \sum n_j Z_{i,j} \tag{3.10}$$

where

$$Z_{i,j} = (\partial Z_i/\partial n_j)_{n \neq n_j} \tag{3.10a}$$

is the average value of the partial molar quantity Z_i of species j, By differentiation of Eq. (3.10) with respect to the reaction variable ξ and using Eq. (3.1) we obtain

$$\Delta Z_i \equiv (\partial Z/\partial \xi)_z = \sum \nu_j Z_{i,j} \tag{3.11}$$

The reaction quantity ΔZ_i may, in general, be dependent on the actual value of z_i and on ξ because of the dependence of the activity coefficient ratio Y on z_i and ξ; see below.

Formally we may introduce a van't Hoff relationship for the thermodynamic equilibrium constant $K^{\ominus}$:

$$(\partial \ln K^{\ominus}/\partial z_i)_{z \neq z_i} = \Delta Z_i^{\ominus}/RT \tag{3.12}$$

where at given values of $z \neq z_i$ the reaction parameter $\Delta Z_i^{\ominus}$ is a constant, independent of ξ and of Y.

3.3. Transition Curves

The z dependence of the general reaction variables, extent of reaction $\xi(z)$, degree of transition or degree of dissociation $\Theta(z)$, can be formulated in terms of thermodynamic quantities. By applying the chain rule of differentiation and using Eq. (3.8) the z_i-induced change in $\xi(z_i)$ is given by

$$\begin{aligned}(\partial \xi/\partial z_i)_{z \neq z_i} &= (\partial \xi/\partial \ln K)_z\ (\partial \ln K/\partial z_i)_{z \neq z_i}\\ &= (\partial \xi/\partial \ln K)_z\ \Delta Z_i/RT\end{aligned} \tag{3.13}$$

Since from Eq. (3.1), $dc_j = V^{-1} v_j\, d\xi$, the z dependence of the reaction can be expressed in terms of the concentration change of one of the reaction partners j by

$$dc_j = v_j \Gamma(\Delta Z_i/RT)\, dz_i \tag{3.14}$$

where the definition (3.15) is introduced$^{(13)}$:

$$\Gamma \equiv (\partial c_j/\partial \ln K)_z = 1\Big/\sum_j v_j^2/c_j \tag{3.15}$$

By analogy to Eq. (3.13) the z_i dependence of the fractional transformation variable Θ is given by

$$(\partial \Theta/\partial z_i)_{z \neq z_i} = (\partial \ln K/\partial \Theta)_z^{-1}\ \Delta Z_i/RT = \Gamma_\Theta\ \Delta Z_i/RT \tag{3.16}$$

As discussed in the context of Eq. (3.5), the quantity Γ_Θ of an intramolecular transition step according to Eq. (2.1) is given by

$$\Gamma_\Theta = (\partial \ln K/\partial \Theta)_z^{-1} = \Theta(1 - \Theta) \tag{3.17}$$

Hence, in this case, the maximum change in Θ can be achieved by a change in z_i at $\Theta = \Theta_m = 0.5$. For conditions where Eqs. (3.7) hold the maximum effect produced by a change δz_i is generally expressed as

$$(\delta\Theta/\Theta_m)_{z \neq z_i} = (1 - \Theta_m)(\delta K/K)_{z \neq z_i} \tag{3.18}$$

Similarly, the respective expressions for bimolecular steps like that in Eq. (2.3) with 1:1 component ratio, are

$$\Gamma_\Theta = \Theta(1-\Theta)/(2-\Theta) \tag{3.19}$$

$$(\delta\Theta/\Theta_m)_{z \neq z_i} = [(1-\Theta_m)/(2-\Theta_m)](\delta K/K)_{z \neq z_i} \tag{3.20}$$

In this case, Γ_Θ has a maximum at $\Theta_m = 2-\sqrt{2} = 0.586$, where δz_i produces a maximum concentration shift.

3.3.1. *Inflection Point*

Structural transitions in macromolecules and membranes are frequently cooperative, resulting in rather steep transition curves $\Theta(z_i)$, starting sigmoidal at low values of z_i, going through an inflection point, and finally reaching a saturation value. Very often the transition curves are symmetric having the maximum slope at $\Theta = 0.5$. The z_i value at $\Theta = 0.5$, $z_i(0.5)$, is commonly called the midpoint of transition.

In the vicinity of the inflection point the slope of the transition curve can be graphically determined with some reliability. In the case of a structural two-state transition step like that in Eq. (2.1), the Eqs. (3.16) and (3.17) can be used to derive an expression for the slope of the transition curve at $\Theta = 0.5$, where $z_i = z_i(0.5)$:

$$(\partial\Theta/\partial z_i)_{z \neq z_i, 0.5} = (\Delta Z_i)_{0.5}/4RT \tag{3.21}$$

Thus, the slope value $(\partial\Theta/\partial z_i)_{0.5}$ yields an estimate of the reaction quantity ΔZ_i at $\Theta = 0.5$.

3.3.2. *Integrated van't Hoff Relations*

When ΔZ_i is independent of z_i and ξ this van't Hoff reaction quantity is a constant describing the respective transition at constant $z \neq z_i$. If ΔZ_i is only a function of z_i, integration of Eq.(3.16) in the limits $\Theta(z_i)$ and $\Theta = \Theta^0$ at $z_i^{(0)}$ yields $\int \Gamma_\Theta^{-1}\, d\Theta = \int \Delta Z_i\, dz_i/RT$. From Eq. (3.17) we have $d \ln K = \Gamma_\Theta^{-1}\, d\Theta$, and in terms of the apparent equilibrium constant we obtain the integrated general van't Hoff relationship

$$\ln K(z_i) = \ln K(z_i^{(0)}) + \int \Delta Z_i\, dz_i/RT \tag{3.22}$$

For computational analysis it is useful to apply Eq. (3.22) in the form of

$$K(z_i) = K(z_i^{(0)}) \cdot e^x \tag{3.23}$$

where the x quantity is defined as

$$x \equiv \int \Delta Z_i \, dz_i / RT \tag{3.24}$$

3.4. Chemical Affinity

Before starting the thermodynamic analysis of electric–chemical field effects it is necessary to recall some relations familiar from processes in the absence of external electric fields. The most general equilibrium condition for processes where the temperature and the pressure are under experimental control is that the characteristic Gibbs free energy is at its minimum.$^{(39)}$ The Gibbs free energy is defined by

$$G \equiv U + PV - TS \tag{3.25}$$

where V is the volume, S is the entropy, and U is the inner energy of the system. The general Gibbs equation

$$dU = T\,dS - P\,dV + \sum_j \mu_j \, dn_j \tag{3.26}$$

combines the thermodynamic state functions with the reversible work term dW, which comprises all types of differential work dW.

The work term of chemical systems includes the chemical work $dW^{(\mathrm{ch})}$ of changing the amount of substance n_j at given chemical potentials μ_j of (neutral) molecules j. Thus, in addition to the volume work $dW^{(v)} = -P dV$, we have the (reversible) chemical work

$$dW^{(\mathrm{ch})} = \sum_j \mu_j \, dn_j \tag{3.27}$$

From Eq. (3.25) we obtain $dG = dU + P\,dV + V\,dP - T\,dS - S\,dT$. Substitution of equations (3.26) and (3.27) leads to the classical Gibbs equation:

$$dG = -S\,dT + V\,dP + \sum_j \mu_j \, dn_j \tag{3.28}$$

In the absence of an external electric field, the work function of an isobaric reaction is

$$dG_P(T) = -(H/T)\,dT + \sum_j \mu_j \, dn_j \leqslant 0 \tag{3.29}$$

where the identity $(H/T) = S$ was introduced. The corresponding expression of an isothermal reaction is

$$dG_T(P) = V\,dP + \sum_j \mu_j\,dn_j \tag{3.30}$$

At constant P and T, the work function characterizing chemical systems (in the absence of electric fields) is given by

$$(dG)_{P,T} = \sum_j \mu_j\,dn_j \leqslant 0 \tag{3.31}$$

Generally, for equilibrium processes $dG = 0$. For nonequilibrium states and irreversible processes we have $dG < 0$. Under isothermal–isobaric conditions, any dissipation of Gibbs free energy

$$(dG^{\mathrm{irr}})_{P,T} \equiv -T d_i S = -\sum \mu_j\,dn_j \tag{3.32}$$

where $d_i S$ is the internal entropy production, can only arise from irreversibly running chemical processes.(29)

From Eq. (3.29) we recall that the chemical potential of the (neutral) molecule j is defined by

$$\mu_j = (\partial G/\partial n_j)_{n \neq n_j} \tag{3.33}$$

where all n except n_j are held constant. For practical purposes a standard chemical potential $\mu_j^{\ominus}$ is introduced such that

$$\mu_j = \mu_j^{\ominus} + RT \ln a_j \tag{3.34}$$

where $a_j = c_j y_j$ is the thermodynamic activity and y_j the thermodynamic activity coefficient of species j. At unit activity ($a_j = 1$) we obtain $\mu_j = \mu_j^{\ominus}$.)

In a closed chemical system the n_j change when a chemical reaction is occurring. The chemical work term may then be rewritten as

$$dW^{(\mathrm{ch})} = \sum_j \nu_j \mu_j\,dn_j/\nu_j \tag{3.35}$$

DeDonder's chemical affinity A is defined by

$$A = -\sum_j \nu_j \mu_j \tag{3.36}$$

Recalling Eq. (3.1) and substituting Eq. (3.36) into Eq. (3.35) we obtain

$$dW^{(\mathrm{ch})} = \sum_j \mu_j\,dn_j = -A\,d\xi \tag{3.37}$$

Combination of Eqs. (3.27), (3.31), and (3.37) leads to a general expression for chemical processes in terms of the chemical affinity:

$$A = -(\partial G/\partial \xi)_{P,T} \geqslant 0 \tag{3.38}$$

In line with Eq. (3.30), the equilibrium condition is $A = 0$ and, corresponding to $dG < 0$, a nonequilibrium state is associated with $A > 0$.

Using Eqs. (3.34) and (3.36) we see that

$$A = -\sum_j \nu_j \mu_j^{\ominus} - RT \sum_j \nu_j \ln a_j \tag{3.39}$$

At equilibrium, $A = 0$ and all activities assume their equilibrium values $\bar{a}_j$. Since the thermodynamic equilibrium constant $K^{\ominus}$ is defined by

$$K^{\ominus} = \prod \bar{a}_j^{\nu_j} = \prod (\bar{c}_j \bar{y}_j)^{\nu_j} = K \cdot \bar{Y} \tag{3.40}$$

where

$$K = \prod \bar{c}_j^{\nu_j} \quad \text{and} \quad \bar{Y} = \prod \bar{y}_j^{\nu_j} \tag{3.40a}$$

we immediately see from Eq. (3.39) that (at $A = 0$)

$$\sum_j \nu_j \mu_j^{\ominus} = -RT \ln K^{\ominus} \tag{3.41}$$

Substitution of this expression into Eq. (3.39) yields

$$A = RT(\ln K^{\ominus} - \ln Q^{\ominus}) \tag{3.42}$$

where the notation of a nonequilibrium distribution is introduced according to

$$Q^{\ominus} = \prod a_j^{\nu_j} = \prod (c_j y_j)^{\nu_j} = Q \cdot Y \tag{3.43}$$

Clearly, analogous to Eq. (3.40), the definitions

$$Q = \prod c_j^{\nu_j} \quad \text{and} \quad Y = \prod y_j^{\nu_j} \tag{3.43a}$$

apply.

From Eq. (3.42) it may be seen that the chemical affinity represents a kind of "thermodynamic distance" of a nonequilibrium distribution from its equilibrium distribution. On the other hand Eq. (3.42) may be used to specify the conditions of applying the van't Hoff relations and their integrated forms to the analysis of experimental data, for instance, to relaxation kinetic amplitudes.

Step Perturbations. Suppose that an external parameter z_i (**P**, **T**, or **E**) can be "suddenly" changed in a practically rectangular fashion from an initial value $z_i^{(0)}$ to z_i. Immediately after this change, the previous activity ratio $K^{\ominus}(z_i^{(0)})$ at $z_i^{(0)}$ becomes a nonequilibrium ratio $Q^{\ominus}(z_i)$ at z_i. Thus, in systems with "inertia," initially we have $Q^{\ominus}(z_i)=K^{\ominus}(z_i^{(0)})$; then the nonequilibrium will relax until the new equilibrium characterized by $K^{\ominus}(z_i)$ is attained. Hence the sequence

$$K^{\ominus}(z_i^{(0)}) \rightarrow Q^{\ominus}(z_i) \rightarrow K^{\ominus}(z_i)$$

is a general thermodynamic representation of a chemical relaxation initiated by a "jump" in a physical state variable z_i.

3.5. *Application Limits*

There are some limitations for a straightforward application of the general van't Hoff relations in the form of Eq. (3.8) and all other equations based on it. Explicitly, the reaction quantity ΔZ_i may be dependent on z_i and on ξ.

We recall that the Gibbs Eq. (3.29) for the $z_i(=T, P)$ dependence of a closed chemically interacting system, to which Eq. (3.37) applies at constant $z \neq z_i$, may be expressed as

$$dG(z_i\xi)_{z\neq z_i}=Z_i\,dz_i-A\,d\xi \tag{3.44}$$

where $Z_i=-S, V$ and $z_i=T, P$, respectively. For $Z_i=M$ and $z_i=\mathbf{E}$, see below. Because dG is a total differential the second cross differentials are equal. Hence from Eq. (3.44) we derive

$$(\partial Z_i/\partial\xi)_z=(\partial A/\partial z_i)_{\xi,z\neq z_i} \tag{3.45}$$

With the definition of $\Delta Z_i \equiv (\partial Z_i/\partial\xi)_z$, Eq. (3.45) may be rewritten

$$(\partial[A/RT]/\partial z_i)_{\xi,z\neq z_i}=\Delta Z_i/RT \tag{3.46}$$

As seen in Eqs. (3.8) and (3.9), the reaction quantity ΔZ_i refers to the z_i dependence of the apparent equilibrium constant $K=K^{\ominus}/\bar{Y}$. Therefore

$$(\partial \ln K/\partial z_i)_{z\neq z_i}=(\partial \ln [K^{\ominus}/\bar{Y}]/\partial z_i)_{z\neq z_i} \tag{3.47}$$

Since $\bar{Y}$ is the value of Y at equilibrium, i.e., at $A=0$, we may use Eq. (3.42) in the form of

$$A/RT=\ln(K^{\ominus}/Y)-\ln Q \tag{3.48}$$

and specify Eq. (3.47) as

$$(\partial \ln K/\partial z_i) = (\partial \ln [K^{\ominus}/Y]/\partial z_i)_{z \neq z_i, A=0} \tag{3.49}$$

The z_i dependence of $K^{\ominus}/Y$ may now be expressed in terms of $\xi(z_i)$ at constant A by

$$\begin{aligned}(\partial \ln [K^{\ominus}/Y]/\partial z_i)_{z \neq z_i} &= (\partial \ln [K^{\ominus}/Y]/\partial z_i)_{\xi, z \neq z_i} \\ &\quad + (\partial \ln [K^{\ominus}/Y]/\partial \xi)_z \cdot (\partial \xi/\partial z_i)_{A, z \neq z_i}\end{aligned} \tag{3.50}$$

On the other hand Eq. (3.84) implies that the affinity $A(\xi, z_i)_z$ is a function of both ξ and z_i when all other z parameters are held constant. Hence

$$dA(\xi, z_i)_z = (\partial A/\partial \xi)_z \, d\xi + (\partial A/\partial z_i)_{\xi, z \neq z_i} \, dz_i \tag{3.51}$$

When A is constant, $dA = 0$; for $A = 0$, too. Equations (3.51) and (3.46) thus yield

$$(\partial \xi/\partial z_i)_{A, z \neq z_i} = -(\Delta Z_i/RT)[\partial(A/RT)/\partial \xi]_z^{-1} \tag{3.52}$$

The denominator of the right-hand side of Eq. (3.52) may be expressed in terms of Eq. (3.84) by

$$(\partial[A/RT]/\partial \xi)_z = (\partial \ln [K^{\ominus}/Y]/\partial \xi)_z + (\partial \ln Q/\partial \xi)_z \tag{3.53}$$

Since $K^{\ominus}$ only depends on the state variables z, we have at constant z

$$(\partial \ln K^{\ominus}/\partial \xi)_z = 0 \tag{3.54}$$

Furthermore, from Eqs. (3.1) and (3.43a) it is readily seen that

$$(\partial \ln Q/\partial \xi)_z = \sum (\nu_j/c_j)(\partial c_j/\partial \xi)_z$$

Using now Eq. (3.54) and the definition of $\Gamma = (\sum \nu_j^2/c_j)^{-1}$ in Eq. (3.15), we may rewrite Eq. (3.53) as

$$(\partial[A/RT]/\partial \xi)_z = -(\partial \ln Y/\partial \xi)_z - (V\Gamma)^{-1} = -(V\Gamma^*)^{-1} \tag{3.55}$$

where

$$(\Gamma^*)^{-1} \equiv \Gamma^{-1}[1 + V\Gamma(\partial \ln Y/\partial \xi)_z] \tag{3.56}$$

We now substitute Eq. (3.55) into Eq. (3.52):

$$(\partial \xi/\partial z_i)_{A, z \neq z_i} = V\Gamma^* \Delta Z_i/RT \tag{3.57}$$

Finally, the z_i dependence of $(K^{\ominus}/Y)_\xi$ is obtained by differentiation of Eq. (3.48) at constant ξ:

$$(\partial[A/RT]/\partial z_i)_{\xi,z\neq z_i} = (\partial \ln [K^{\ominus}/Y]/\partial z_i)_\xi + (\partial \ln Q/\partial z_i)_{\xi,z\neq z_i} \quad (3.58)$$

At constant ξ, $d\xi = 0$; hence, from Eq. (3.1), all dc_j are zero. Therefore, recalling Eq. (3.43a) we see that

$$(\partial \ln Q/\partial z_i)_{\xi,z\neq z_i} = 0 \quad (3.59)$$

Substitution of Eqs. (3.59) and (3.46) into Eq. (3.58) leads to

$$(\partial \ln[K^{\ominus}/Y]/\partial z_i)_{\xi,z\neq z_i} = \Delta Z_i/RT \quad (3.60)$$

We now introduce this expression together with Eqs. (3.57) and (3.54) into Eq. (3.50) and obtain

$$(\partial \ln [K^{\ominus}/Y]/\partial z_i)_{z\neq z_i} = (\Delta Z_i/RT)[1 - V\Gamma^*(\partial \ln Y/\partial\xi)_z] \quad (3.61)$$

At equilibrium, where $A = 0$, the quantities Γ^* (and Γ) and Y have their equilibrium values $\bar{\Gamma}^*$ (and $\bar{\Gamma}$) and $\bar{Y}$. Combining now the Eqs. (3.61) and (3.49) we obtain the final expression

$$(\partial \ln K/\partial z_i)_{z\neq z_i} = (\Delta Z_i/RT)[1 - V\bar{\Gamma}^*(\partial \ln \bar{Y}/\partial\xi)_z] \quad (3.62)$$

This relationship permits rigorous evaluation of the z_i dependence of equilibrium concentrations $\bar{c}_j(z_i)$ or $\Theta(z_i)$.

It is readily seen that Eq. (3.62) reduces to the commonly used Eq. (3.8) provided that the dependence of the activity coefficient ratio Y on ξ is negligibly small. This condition is usually fulfilled if (a) the change δz_i only produces a small shift in K and thus in Y, or (b) the value of Y is determined by an excess of components other than the reaction partners j, a condition commonly met when ionic reactions occur in the presence of an excess of inert electrolyte.

When $z_i = T$ or P the dependence of $\Delta Z_i = \Delta H/T$ or $-\Delta \bar{V}$, respectively, on T or P may be solely expressed in terms of Y.

Owing to Eq. (3.54) we have $(\partial \ln K^{\ominus}/\partial z_i) = (\partial \ln K^{\ominus}/\partial z_i)_\xi$. Using now Eq. (3.60) at $A = 0$, where $Y = \bar{Y}$, and Eq. (3.12) we obtain

$$\Delta Z_i/RT = (\partial \ln K^{\ominus}/\partial z_i)_{\xi,z\neq z_i} - (\partial \ln \bar{Y}/\partial z_i)_{\xi,z\neq z_i} \quad (3.63)$$

Therefore Eq. (3.64) holds$^{(13)}$

$$\Delta Z_i = \Delta Z_i^{\ominus} - (\partial \ln \bar{Y}/\partial z_i)_{\xi,z\neq z_i} \quad (3.64)$$

It is instructive to recall Eqs. (3.10) and (3.11) and compare with

Eq. (3.64). Obviously, $\Delta Z_i = \sum_j \nu_j Z_{i,j}$ refers to the general nonideal behavior. Ideal additivity refers to $Y = 1$; for this limiting case Eq. (3.11) reads

$$\Delta Z_i^{\ominus} = \sum_j \nu_j Z_{i,j}^{\ominus} \tag{3.65}$$

Thus, as usual, nonidealities are covered by the introduction of activity coefficients. Finally, it is shown below that in external electric fields ($z_i = \mathbf{E}$, $\Delta Z_i = \Delta M$) the specific expression for ΔM as a function of $\mathbf{E}$ depends on the mechanism of the field-dipole interactions.

3.6. *Electrochemical Potential*

The analytical treatment of electric field effects on chemical distributions may be started by recalling Guggenheim's original concept of the electrochemical potential $\tilde{\mu}_k$.(39) For a single (*isolated*) ion B_k, $\tilde{\mu}_k$ is written in the form

$$\tilde{\mu}_k = \mu_k + F\tilde{z}_k \psi_k^{\ominus} \tag{3.66}$$

where μ_k is the ordinary chemical potential, F the Faraday constant, $\tilde{z}_k$ the charge number (with sign), and $\psi_k^{\ominus}$ the ideal electrostatic Coulomb potential of the *isolated* ion B_k.

In the presence of other ions it is necessary to account for the screening effect of the ionic atmosphere. It is then useful to introduce a more general form of the electrostatic potential term of Eq. (3.66) by a charging integral

$$\tilde{\mu}_k = \mu_k + F \int \bar{\psi}\, d\tilde{z}_k \tag{3.67}$$

where $\bar{\psi}$ is the mean electric potential. Note that, at a given distance r from the charge center, usually $|\bar{\psi}(r)| < |\psi^{\ominus}(r)|$.

In a collection of species B_k the total electric work, $dW^{(\mathrm{el})}$, of charging B_k from $\tilde{z}_k = 0$ to $\tilde{z}_k$ is the sum over the charging integrals of all species:

$$dW^{(\mathrm{el})} = F \cdot \sum_k \left(\int \bar{\psi}\, d\tilde{z}_k \right) dn_k \tag{3.68}$$

Recalling the (neutral) chemical work term from Eq. (3.27):

$$dW^{(\mathrm{ch})} = \sum \mu_k\, dn_k \tag{3.69}$$

we may define an electrochemical work term by summation according to $dW^{(\mathrm{ch})} + dW^{(\mathrm{el})} = dW^{(\mathrm{ech})}$. Thus, with Eqs. (3.67)–(3.69) we obtain

$$\sum_k \tilde{\mu}_k \, dn_k = \sum_k \left(\mu_k + F \left[\int \bar{\psi} \, d\tilde{z}_k \right] \right) dn_k \tag{3.70}$$

The fundamental Gibbs Eq. (3.26) for ionic species may then be expressed as

$$dU = T\,dS - P\,dV + \sum_k \tilde{\mu}_k \, dn_k \tag{3.71}$$

and the Gibbs function dG for ionic systems is given by

$$dG = -S\,dT + V\,dP + \sum_k \tilde{\mu}_k \, dn_k \tag{3.72}$$

Analogous to Eq. (3.33) we have the familiar expression for the electrochemical potential:

$$\tilde{\mu}_k = (\partial \tilde{G} / \partial n_k)_{P,T,n \neq n_k} \tag{3.73}$$

3.6.1. Electrochemical Affinity

In line with Eq. (3.36), the electrochemical affinity of chemically reacting ions is defined by

$$\tilde{A} = -\sum_k \nu_k \tilde{\mu}_k \tag{3.74}$$

Introducing Eq. (3.70) into Eq. (3.74) we obtain

$$\tilde{A} = -\sum_k \nu_k \mu_k - F \sum_k \nu_k \int \bar{\psi} \, d\tilde{z}_k \tag{3.75}$$

Since in a chemical reaction in a closed system the total charge is conserved, i.e., $\sum \nu_k \tilde{z}_k = 0$, we see with Eq. (3.70) that

$$\tilde{A} = A \tag{3.76}$$

Recalling Eqs. (3.37) and (3.38) it is readily seen that

$$\tilde{A} = -(\partial G / \partial \xi)_{P,T} \geqslant 0 \tag{3.77}$$

Thus the electrochemical affinity is equal to the ordinary chemical affinity (in the absence of electric fields). Nevertheless, it is useful to introduce a standard value of the electrochemical potential according to

$$\tilde{\mu}_k^{\ominus} = \mu_k^{\ominus} + F \int \psi_k^{\ominus} \, d\tilde{z}_k \tag{3.78}$$

where $\mu_k^{\ominus}$ is the ordinary standard value for the case when B_k is neutral. Hence$^{(19)}$

$$\tilde{\mu}_k = \tilde{\mu}_k^{\ominus} + RT \ln a_k \tag{3.79}$$

3.6.2. *Electrochemical Activity Coefficient*

The formalism of the Eqs. (3.67), (3.78), and (3.79) is suited to explicitly showing that the (electric) activity coefficient of ionic species accounts for deviations from the ideal (unscreened) Coulomb behavior. It will be demonstrated below that an analogous formalism describes nonidealities in the interactions between dipolar species.

If the ionic species B_k is uncharged, the chemical potential is written in the familiar form of Eq. (3.34) as

$$\mu_k = \mu_k^{\ominus} + RT \ln a_k^{(0)} \tag{3.80}$$

where the superscript (0) is used to indicate the neutral form of the species B_k. Owing to the ionic character of B_k the activity, a_k, of the ion is different from the activity, $a_k^{(0)}$, in the neutral form.

By this formalism the quantity $\tilde{\mu}_k$ is once expressed in terms of $a_k^{(0)}$ and $\bar{\psi}$ and, alternatively, as a function of $\psi_k^{\ominus}$ and a_k:

$$\begin{aligned} \tilde{\mu}_k &= \mu_k^{\ominus} + RT \ln a_k^{(0)} + F \int \bar{\psi} \, d\tilde{z}_k \\ &= \mu_k^{\ominus} + F \int \psi_k^{\ominus} \, d\tilde{z}_k + RT \ln a_k \end{aligned} \tag{3.81}$$

Rearrangement leads to

$$F \int (\bar{\psi} - \psi_k^{\ominus}) \, d\tilde{z}_k = RT \ln(a_k/a_k^{(0)}) \tag{3.82}$$

Since we refer to the same amount of species B_k in the uncharged form and in the ionic form, the concentrations are equal, i.e., $c_k = c_k^{(0)}$. Hence

$$(a_k/a_k^{(0)}) = y_k/y_k^{(0)} \tag{3.83}$$

Remembering that solely electrostatic interactions are covered by the terms ψ and $\psi_k^\ominus$,

$$\psi_k^\ominus(\mathbf{r}) = \tilde{z}_k e_0/(4\pi\varepsilon_0\varepsilon\cdot r) \tag{3.84}$$

where $e_0 = 1.6\times10^{-19}\mathrm{C}$ is the (positive) elementary charge, $\varepsilon_0 = 8.854\times10^{-14}\,\mathrm{CV}^{-1}\,\mathrm{cm}^{-1}$ the permittivity of the vacuum, and ε the dielectric permittivity of the medium. Therefore, $y_k^{(0)} = 1$ and thus $y_k/y_k^{(0)} = y_k$. When we now rewrite Eq. (3.82) for this case as

$$F\cdot\int(\bar{\psi} - \psi_k^\ominus)\,d\tilde{z}_k = RT\ln y_k \tag{3.85}$$

it is readily seen that the (electrostatic) activity coefficient of ions indeed covers the difference between the actual and the ideal Coulomb potential of the formal charge $z_k e_0$.

Introducing Eq. (3.79) into Eq. (3.74), we obtain

$$\tilde{A} = -\sum_k \nu_k\tilde{\mu}_k = -\sum_k \nu_k\tilde{\mu}_k^\ominus - RT\sum_k \nu_k\ln(c_k\cdot y_k) \tag{3.86}$$

At equilibrium we have $\tilde{A} = 0$ and $c_k\cdot y_k = \bar{c}_k\cdot\bar{y}_k$. Since, by analogy to Eq. (3.41), the relation

$$\sum \nu_k\tilde{\mu}_k^\ominus = -RT\ln K^\ominus \tag{3.87}$$

holds, the application of Eq. (3.40a) leads to

$$K^\ominus = K\cdot\bar{Y}$$

and, by using Eq. (3.85), we obtain

$$RT\ln\bar{Y} = F\sum_k \nu_k\int(\bar{\psi} - \psi_k^\ominus)\,d\tilde{z}_k \tag{3.88}$$

As shown elsewhere,(17,19) relationship (3.88) may be used to estimate charge numbers of ionic binding sites on macromolecules in the framework of the Debye–Hückel approximations.

3.7. "Dielectrochemical" Potential*

For the description of interactions between ionic reaction partners which may associate to ion pairs, it is useful to extend Guggenheim's con-

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* The treatment of this section is formalistic, but the content is pictorial and instructive. The rigorous thermodynamic definition of the dielectrochemical potential is given in Section 4.

cept of an ***electrochemical potential*** of a single ion and to define a "*dielectrochemical* potential" of a dipolar ion pair.

Suppose that two ions B_q and B_k are in equilibrium with an ion pair $B_q^{(\tilde z_q)}\cdot B_k^{(\tilde z_k)}$ according to

$$B_q^{\tilde z_q}\cdot B_k^{\tilde z_k} \rightleftharpoons B_q^{\tilde z_q} + B_k^{\tilde z_k} \tag{3.89}$$

For simplicity we assume that B_q and B_k are equally but oppositely charged, i.e., $\tilde z_k = -\tilde z_q = \tilde z_j$. The position vectors of the charge centers in the pairing process are $\mathbf{r}_k$ and $\mathbf{r}_q$.

The pairing process may be quite formally viewed as a superposition of the "individual" electrochemical potentials $\tilde\mu_k(\mathbf{r}_k)$ and $\tilde\mu_q(\mathbf{r}_q)$. The sum is then a function of $\mathbf{r} = \mathbf{r}_k - \mathbf{r}_q$, which is the (average) vectorial distance between the charge centers. This distance dependence of the sum

$$\tilde\mu_{kq}(\mathbf{r}) = \tilde\mu_k(\mathbf{r}_k) + \tilde\mu_q(\mathbf{r}_q)$$

may be expressed in differential form as

$$d\tilde\mu_{kq}(\mathbf{r}_k) = d\tilde\mu_k(\mathbf{r}_k) + d\tilde\mu_q(\mathbf{r}_q) \tag{3.90}$$

At constant charge numbers $\tilde z_k$ and $\tilde z_q$, differentiation of Eq. (3.67) yields, respectively,

$$d\tilde\mu_k(\mathbf{r}_k) = d\mu_k(\mathbf{r}_k) + N_A e_0 \tilde z_k\, d\bar\psi(\mathbf{r}_k) \tag{3.91}$$

and

$$d\tilde\mu_q(\mathbf{r}_q) = d\mu_q(\mathbf{r}_k) + N_A e_0 \tilde z_q\, d\bar\psi(\mathbf{r}_q)$$

Substituting these expressions into Eq. (3.90) and using $\tilde z_k = -\tilde z_q = \tilde z_j$ and $d\mathbf{r} = d\mathbf{r}_k - d\mathbf{r}_q$, we may write

$$d\tilde\mu_{kq}(\mathbf{r}) = d\mu_{kq}(\mathbf{r}) + N_A e_0 \tilde z_j [d\bar\psi(\mathbf{r}_k) - d\bar\psi(\mathbf{r}_q)] \tag{3.92}$$

The electrostatic potential resulting from the superposition of the potentials of the individual charges defines an average potential $\bar\psi(\mathbf{r})$; thus $d\bar\psi(\mathbf{r}_k) - d\bar\psi(\mathbf{r}_q) = d\bar\psi(\mathbf{r})$. Introducing this definition into Eq. (3.85), and using the equation $d\bar\psi = (d\bar\psi/d\mathbf{r})\, d\mathbf{r}$, we obtain

$$d\tilde\mu_{kq}(\mathbf{r}) = d\mu_{kq}(\mathbf{r}) + N_A e_0 \tilde z_j (d\bar\psi/d\mathbf{r})\, d\mathbf{r} \tag{3.93}$$

The differential $(d\bar\psi/dr)$ defines the electric field $\mathbf{E}$ arising from the ion pair. According to Maxwell's definition

$$d\bar\psi/d\mathbf{r} = -\mathbf{E} \tag{3.94}$$

On the other hand the product $\tilde{z}_j \cdot e_0 \cdot d\mathbf{r}$ is the increment of the electric dipole moment

$$d\mathbf{m}_j = \tilde{z}_j e_0 \, d\mathbf{r} \tag{3.95}$$

Thus the ion pair $B_q \cdot B_k$ represents a dipole B_j which is associated with a dipole moment $\mathbf{m}_j$.

We now substitute Eqs. (3.94) and (3.95) into Eq. (3.93) and apply the definitions

$$\tilde{\mu}_{kq} = \tilde{\mu}_j, \qquad \mu_{kq} = \mu_j$$

In this way the "individual" electrochemical potentials of the ions of an ion pair are expressed in terms of the electric dipole work as

$$d\tilde{\mu}_j(\mathbf{r}) = d\mu_j(r) - N_A \mathbf{E} \, d\mathbf{m}_j(\mathbf{r}) \tag{3.96}$$

Since the electric moment of an *isolated* dipole is given by the product of charge $\tilde{z}_j e_0$ and distance, the integration of Eq. (3.96) in the limits $\mathbf{r} = 0$ and $\mathbf{r}$ yields

$$\tilde{\mu}_j = \mu_j - N_A \mathbf{m}_j^{\ominus} \mathbf{E}(\mathbf{r}) \tag{3.97}$$

In this form, $\tilde{\mu}_j$ may be called the *dielectrochemical potential* of one mole of *isolated* dipolar species B_j with the individual moment $\mathbf{m}_j^{\ominus}$.

For analytical purposes it is convenient to use a parallel-plate capacitor as a measuring cell. In this geometry only the component m_j (of $\mathbf{m}_j$) that is *parallel* to the electric field lines between the plates (or to an eventually applied external field creating the Maxwell field $\mathbf{E}$ in the dielectric) contributes to the measurable polarization. For capacitor geometry the scalar product of $\mathbf{m}_j \mathbf{E}(r)$ in Eq. (3.97) is given by the parallel component $(\mathbf{m}_j)_{\|} = \mathbf{m}_j \cos \vartheta_j$ and by $\mathbf{E}$, that is, the Maxwell field vector perpendicular to the capacitor plates; ϑ_j is the angle between $\mathbf{E}$ and $\mathbf{m}_j$. Therefore, Eq. (3.97) applies in the form

$$\tilde{\mu}_j = \mu_j - N_A (\mathbf{m}_j)_{\|} E \tag{3.98}$$

In a collection of many species B_j with different orientations of their dipole moments $\mathbf{m}_j$ relative to $\mathbf{E}$, an average contribution may be defined by

$$m_j = \langle \mathbf{m}_j \cos \vartheta_j \rangle = \mathbf{m}_j \langle \cos \vartheta_j \rangle \tag{3.99}$$

This average value will depend on the average field $\mathbf{E}$ resulting from the different orientations. Therefore Eq. (3.98) may be more generally written as

$$\tilde{\mu}_j = \mu_j - N_A \int m_j \, dE \tag{3.100}$$

When there is no preferential orientation like in a random distribution of dipoles, the contributions of all dipole moments parallel to **E** cancel each other, because $\langle \cos \vartheta_j \rangle$ in Eq. (3.99) for a random distribution of permanent dipoles is zero. In this case $\tilde{\mu}_j = \mu_j$ and no macroscopic polarization of the medium occurs.

Macroscopic organizations possessing a permanent electric dipole moment like electrets have a finite Maxwell field **E** which may be externally measured, for instance, as a plate capacitor field.

The measurable polarization of the dielectric electret within the capacitor plates is then given by

$$\begin{aligned} M = (\mathbf{M})_{\parallel} &= N_A \sum_j n_j \langle \mathbf{m}_j \cos \vartheta_j \rangle \\ &= N_A \sum_j n_j m_j = \sum_j n_j M_j \end{aligned} \tag{3.101}$$

where the parallel component, M_j, of the average partial *molar* dipole moment is defined by

$$M_j = (\partial M / \partial n_j)_{n \neq n_j} = N_A \mathbf{m}_j \langle \cos \vartheta_j \rangle \tag{3.102}$$

Hence, Eq. (3.100) may be used in the form

$$\tilde{\mu}_j = \mu_j - \int M_j \, dE \tag{3.103}$$

If on average there is no macroscopic electric field across the dielectric, we have $\tilde{\mu}_j = \mu_j$.

Recalling Eqs. (3.95), (3.96), and (3.101) and noting that $F = N_A e_0$, we may express Eq. (3.103) as

$$\tilde{\mu}_j(\mathbf{r}) = \mu_j - F\bar{z}_j \int \mathbf{r} \, d\mathbf{E} \tag{3.104}$$

In this form the dielectrochemical potential introduced here has a similar formal structure as Guggenheim's electrochemical potential as expressed in Eq. (3.67).

3.7.1. Polyionic Macromolecules

In macromolecular biological structures ion-pair formation frequently occurs. For instance, the inner counterions surrounding the polynucleotide macroanions as well as in all other linear polyelectrolytes appear to form ion pairs with the fixed polyionic matrix. Externally applied electric fields can compete with the inner fields and shift these counterions relative to the polyion, thus producing large dipole moments.(23–25) It is known that proteins may contain inner salt bridges, i.e., ion pairs between fixed ionized side chains of the amino acid residues of the polypeptide chains and/or other ionic groups. In particular membrane proteins like the bacteriorhodopsin of the purple membranes of halobacteria appear to contain an unusually large number of charged groups within the protein structure. In such a case we may group together oppositely charged groups into ion pairs. The total moment **M** of the macromolecule is then the vector sum over all individual contributions of the single ion pairs according to Eq. (3.101). When we now inspect Eq. (3.93) and rewrite as

$$d\tilde{\mu}_j(r) = d\mu_j(\mathbf{r}) - N_A \tilde{z}_j e_0 \mathbf{E}(d\mathbf{r}_k - d\mathbf{r}_q) \tag{3.105}$$

we see that changes in the distance between two charged groups with $\tilde{z}_k(\mathbf{r}_k)$ and $\tilde{z}_q(\mathbf{r}_q)$, respectively, will change the dielectrochemical potential and thus the contribution of this ion pair to the total polarization. On the other hand an externally applied electric field **E** of a sufficiently high field strength may change the distance between the charge centers of an ion pair. This type of distance variation by external fields appears to be responsible for the large induced dipole moments in bacteriorhodopsin of purple membranes.(10,41)

4. Thermodynamics in Electric Fields

4.1. The Characteristic Gibbs Function

The concept of a dielectrochemical potential introduced in the previous section is already implicit in Guggenheim's treatment of dielectrics in the presence of external fields. In order to apply the familiar criteria for reversible (equilibrium) processes and irreversible (nonequilibrium) processes in terms of an appropriate Gibbs function, Guggenheim introduced the characteristic Gibbs function in the presence of electric fields by a transformation.(39) We may express the transformed Gibbs free energy as

$$\tilde{G} = G - W^{(el)} \tag{4.1}$$

where G is the ordinary Gibbs free energy at **E** and $W^{(\mathrm{el})}$ is the (reversible) electric work.

The differential work term of the field-dipole interaction is

$$dW^{(\mathrm{el})} = \mathbf{E}d\langle \mathbf{M} \rangle = E\,dM \tag{4.2}$$

consistent with the work terms in Eq. (3.28). From Eq. (3.101) we recall that the total moment parallel to **E** is given by $M = \sum_j n_j M_j$, representing a specific case of the general expression (3.10). The partial molar dipole moment of species B_j is

$$M_j = (\partial M/\partial n_j)_{n \neq n_j, z} \tag{4.3}$$

By $M_j = N_A \mathbf{m}_j \langle \cos \vartheta_j \rangle$, M_j refers to the average of the field-parallel contributions of all individual moments $\mathbf{m}_j$.

Substitution of the integrated Eq. (4.2) into Eq. (4.1) yields

$$\tilde{G} = G - ME \tag{4.4}$$

In this context, Eigen and DeMaeyer$^{(13)}$ used the relationship $G^* = G - \mathbf{D}^* E$, with $\mathbf{D}^* = V \cdot \mathbf{P}$. where **P** is the polarization per unit volume and V is the volume.

It is now useful to denote the chemical potential of the (dipolar) species B_j in the presence of an electric field by a special symbol:

$$\mu(E) = \tilde{\mu} \tag{4.5}$$

The (reversible) chemical work term, analoguous to Eq. (3.27), is then of a dielectrochemical nature:

$$dW^{(\mathrm{ch})} = \sum_j \tilde{\mu}_j\, dn_j \tag{4.6}$$

The total differential work term of a chemically open system derives from an extension of Eq. (3.28). Using Eqs. (4.2) and (4.6) we find

$$\sum dW = -PdV + \sum_j \tilde{\mu}_j\, dn_j + EdM \tag{4.7}$$

The general Gibbs equation for the inner energy in the presence of **E** is obtained by substitution of Eq. (4.7) into (3.26):

$$dU = TdS - PdV + \sum_j \tilde{\mu}_j\, dn_j + EdM \tag{4.8}$$

From Eq. (3.25) we have

$$dG = dU + d(PV - TS) \tag{4.9}$$

Substitution of Eq. (4.8) into (4.9) results in

$$dG = -SdT + VdP + \sum_j \tilde{\mu}_j \, dn_j + EdM \tag{4.10}$$

We now clearly see that the ordinary Gibbs free energy increases in the electric field compared to $E = 0$.

In order to have the electric field as the independent variable instead of M, a Legendre transformation is required. By Eq. (4.4) the transformed Gibbs free energy is

$$d\tilde{G} = dG - d(EM) \tag{4.11}$$

Substituting Eq. (4.10) into (4.11) finally leads to the characteristic Gibbs function for chemically open systems in electric fields:

$$d\tilde{G} = -SdT + VdP + \sum_j \tilde{\mu}_j \, dn_j - MdE \tag{4.12}$$

The transformed Gibbs free energy clearly decreases in the presence of electric fields. This property is required for a consistent thermodynamic treatment of electric-chemical field effects.

For isobaric–isothermal conditions the characteristic Gibbs function reduces to

$$d\tilde{G}_{T,P} = \sum_j \tilde{\mu}_j \, dn_j - MdE \tag{4.13}$$

The fundamental relationship may now be used to rigorously derive an expression for the chemical potential of species B_j in the presence of field-dipole interactions. Consistent with general thermodynamic formalism we obtain from Eq. (4.13)

$$\tilde{\mu}_j = (\partial \tilde{G}/\partial n_j)_{T,P,E,n \neq n_j} \tag{4.14}$$

Following the rules of cross differentiation, Eq. (4.13) leads to

$$(\partial M/\partial n_j)_{T,P,E,n \neq n_j} = -(\partial \tilde{\mu}_j/\partial E)_{T,P,n} \tag{4.15}$$

Inspection of Eq. (4.3) results in

$$(\partial \tilde{\mu}_j/\partial E)_{T,P,n} = -M_j \tag{4.16}$$

According to Kirkwood and Oppenheim,$^{(40)}$ integration of Eq. (4.16) between E and $E = 0$ provides the relationship

$$\tilde{\mu}_j(E) = \tilde{\mu}_j(0) - \int M_j \, dE \tag{4.17}$$

Since $\tilde{\mu}_j(0)$ is the ordinary chemical potential μ_j at $\mathbf{E}=0$, Eq. (4.17) is rewritten as

$$\tilde{\mu}_j = \mu_j - \int M_j \, dE \tag{4.18}$$

and $\tilde{\mu}_j$ may be called the *dielectrochemical potential* of species B_j in external electric fields. By Eq. (3.100) it is evident that for completely random distributions of dipoles or at $\mathbf{E}=0$, the relation $\tilde{\mu}_j = \mu_j$ holds. In these cases the dielectrochemical potential equals the chemical potential.

4.2. Dielectrochemical Affinity

By analogy to Eq. (3.74), we may now define a "dielectrochemical affinity" for chemically interacting dipolar species B_j by

$$\tilde{A} = -\sum_j \nu_j \tilde{\mu}_j \tag{4.19}$$

Substitution of Eq. (4.18) into Eq. (4.19) yields

$$\tilde{A} = -\sum_j \nu_j \tilde{\mu}_j = -\sum_j \nu_j \mu_j + \sum_j \nu_j \int M_j \, dE \tag{4.20}$$

Introducing Eq. (4.19) with $dn_j = \nu_j \, d\xi$ into Eq. (4.13) we obtain the Gibbs function of chemically reacting systems in external electric fields:

$$(d\tilde{G})_{P,T} = -\tilde{A} d\xi - M dE \tag{4.21}$$

From this expression it is readily seen that the dielectrochemical affinity is consistently defined in terms of $\tilde{A}$ and ξ:

$$\tilde{A} = -(\partial \tilde{G}/\partial \xi)_{P,T,E} \tag{4.22}$$

It is remarked that reversible and irreversible processes in external electric fields are characterized by

$$d\tilde{G} \leqslant 0 \quad \text{and} \quad \tilde{A} \geqslant 0 \tag{4.23}$$

Thus the definitions of $\tilde{G}$ and $\tilde{A}$ permit the thermodynamic treatment of electric field effects in the framework of concepts which are familiar from ordinary chemical thermodynamics in the absence of electric fields.

4.3. Activity Coefficients

As in the case of ionic reactions it is also useful to define a standard value, $\tilde{\mu}_j^{\ominus}$, of the dielectrochemical potential for the dipolar species B_j:

$$\tilde{\mu}_j = \tilde{\mu}_j^{\ominus} + RT \ln \tilde{a}_j \tag{4.24}$$

where $\tilde{a}_j$ is the activity of B_j in the presence of **E**. Analogous to Eq. (4.18) the standard dielectrochemical potential is given by

$$\tilde{\mu}_j^{\ominus} = \mu_j^{\ominus} - \int M_j^{\ominus}\, dE \tag{4.25}$$

where $\mu_j^{\ominus}$ is the ordinary standard potential used in

$$\mu_j = \mu_j^{\ominus} + RT \ln a_j \tag{4.26}$$

Note that a_j is the activity of B_j at $\mathbf{E}=0$. $M_j^{\ominus}$ is the standard value of M_j of the isolated dipoles behaving ideally. There is a formal similarity between Eq. (4.25) for dipoles and Eq. (3.78) for ionic interaction partners. As in the case of the electrochemical potential, the dielectrochemical potential may also be expressed in two ways.

From Eqs. (4.18), (4.26) and (4.24), (4.25) we obtain

$$\begin{aligned}\tilde{\mu}_j &= \mu_j^{\ominus} + RT \ln a_j - \int M_j\, dE \\ &= \mu_j^{\ominus} + RT \ln \tilde{a}_j - \int M_j^{\ominus}\, dE\end{aligned} \tag{4.27}$$

Hence, analogous to Eq. (3.82) the relation

$$-\int (M_j - M_j^{\ominus})\, dE = RT \ln (\tilde{a}_j/a_j) \tag{4.28}$$

holds. Since we refer to the same mount of components, the concentrations are equal, i.e., $\tilde{c}_j = c_j$. Again, the activity ratio is thus given by the activity coefficients:

$$\tilde{a}_j/a_j = \tilde{y}_j/y_j \tag{4.29}$$

If only dipolar interactions are considered we set $y=1$. In this case Eq. (4.28) reads

$$-\int (M_j - M_j^{\ominus})\, dE = RT \ln \tilde{y}_j \tag{4.30}$$

In the form of this equation it is obvious that for dipolar species, too, the activity coefficient covers deviations from simple ideal additivities.

For the *ideal* case of pure additive superposition of the formal charge-distance products $z_j e_0 \mathbf{r}_j = m_j^{\leftrightarrow}$, where z_j is the integer charge number, the total (standard) polarization is given by

$$M^{\leftrightarrow} = \sum_j n_j M_j^{\leftrightarrow} = N_A \sum_j n_j m_j^{\ominus} \tag{4.31}$$

where

$$m_j^{\leftrightarrow} = \langle \mathbf{m}_j \cos \vartheta_j \rangle = m_j^{\ominus} \langle \cos \vartheta_j \rangle$$

and

$$M_j^{\ominus} = N_A m_j^{\ominus} \tag{4.32}$$

4.4. *Van't Hoff Relationship*

It is now pertinent to derive a rigorous expression for the dependence of the thermodynamic equilibrium constant $K^{\ominus}$ on the externally applied electric field. For this purpose we recall Eqs. (4.19) and (4.24):

$$\tilde{A} = -\sum_j \nu_j \tilde{\mu}_j^{\ominus} - RT \sum_j \nu_j \ln \tilde{a}_j \tag{4.33}$$

At equilibrium we have $\tilde{A} = 0$ and all activities are equilibrium values. For this case $K^{\ominus}(E) = \prod \tilde{a}_j^{\nu_j}$ and Eq. (4.33) yields

$$\mathrm{RT} \ln K^{\ominus}(E) = -\sum_j \nu_j \tilde{\mu}_j^{\ominus} \tag{4.34}$$

Further, from Eq. (4.26) we have

$$\sum_j \nu_j \tilde{\mu}_j^{\ominus} = \sum_j \nu_j \mu_j^{\ominus} - \sum_j \nu_j \int M_j^{\ominus}\, dE \tag{4.35}$$

When we now differentiate $M^{\ominus}$, defined by Eq. (4.31) as $M^{\ominus} = \sum_j n_j M_j^{\ominus}$, with respect to ξ and use Eq. (3.1) in the form $dn_j/d\xi = \nu_j$, we obtain

$$(\partial M^{\ominus}/\partial \xi)_{E,T,P} = \sum \nu_j M_j^{\ominus} = \Delta M^{\ominus} \tag{4.36}$$

The introduction of Eqs. (4.35) and (3.41) in the form of $RT \ln K^{\ominus}(0) = -\sum \nu_j \tilde{\mu}_j^{\ominus}$ at $\mathbf{E} = 0$, into Eq. (4.34) finally leads to

$$\ln K^{\ominus}(E) = \ln K^{\ominus}(0) + \int \Delta M^{\ominus}\, dE/(RT) \tag{4.37}$$

which is the integrated van't Hoff relationship for a dipolar equilibrium in an external electric field.

From Eq. (4.21) we obtain by cross differentiation

$$(\partial \tilde{A}/\partial E)_{\xi,T,P} = (\partial M/\partial \xi)_{E,T,P} = \Delta M = \sum_j \nu_j M_j \tag{4.38}$$

The relationship between the affinity and the M_j terms refers to constant ξ and thus to given values c_j. For chemically interacting species Eq. (4.30) is rewritten as

$$-\sum_j \nu_j \int (M_j - M_j^{\ominus})\, dE = RT \sum \nu_j \ln \tilde{y}_j \tag{4.39}$$

Substituting Eqs. (4.36) and (4.37) and recalling the definition $\tilde{Y} = \prod \tilde{y}^{\nu_j}$ yields the expression

$$\Delta M = \Delta M^{\ominus} - RT(\partial \ln \tilde{Y}/\partial E)_{\xi} \tag{4.40}$$

In this equation the quantities ΔM, $\Delta M^{\ominus}$, and $\tilde{Y}$ represent terms at a given field intensity E.

Since the thermodynamic and the apparent equilibrium constants are connected by $K^{\ominus} = K \cdot \tilde{Y}$, a comparison of the van't Hoff relations

$$(\partial \ln K^{\ominus}/\partial E)_{P,T} = \Delta M^{\ominus}/RT \tag{4.41}$$

and

$$(\partial \ln K/\partial E)_{P,T} = \Delta M/RT = (\Delta M^{\ominus}/RT) - (\partial \ln \tilde{Y}/\partial E)_{\xi,P,T} \tag{4.42}$$

with Eq. (4.30) shows that the activity coefficient product is given by

$$RT \ln [\tilde{Y}(E)/\tilde{Y}(0)]_{\xi} = -\int (\Delta M - \Delta M^{\ominus})\, dE \tag{4.43}$$

If $\tilde{Y}$ is independent of E, by $\Delta M = \Delta M^{\ominus}$ the reaction moment is independent of ξ (or of the concentrations of the reaction partners). In any case, the relationship (4.42) provides the basis for the analysis of electric field-induced concentration shift in dipolar equilibria. Whereas this part of the account dealt with thermodynamic foundations of the analysis of chemical electric field effects, the second part (Chapter 5) covers some kinetic and mechanistic aspects of macromolecular bioelectric processes.

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List of Symbols

A	Chemical affinity (DeDonder)
$\tilde{A}$	Dielectrochemical affinity in the presence of electric fields
A_λ	Absorbance (per centimeter) at wavelength λ
δA	Electric-field-induced absorbance change
δA_σ	Absorbance change at the light polarization angle σ
ΔA	Linear dichroism
A_q	Shape factor of the ellipsoid, q axis
a_j	Thermodynamic activity of species B_j; $\bar{a}_j$, equilibrium value; $a_j = c_j y_j$, dimensionless by division by $c^\ominus = 1$ mol dm^{-3}
$\tilde{a}_j$	Value of a_j in the presence of an electric field
c_j	Concentration of species B_j (mol dm^{-3}); $\bar{c}_j$, equilibrium value
e_0	Elementary charge (1.6×10^{-19} C)
$\mathbf{E}(E)$	Electric field strength vector (absolute value), Maxwell field
$\mathbf{E}_F(E_F)$	External electric field vector (absolute value), Fröhlich field
$\mathbf{E}_{\text{int}}$	Internal field vector
$\mathbf{E}_{\text{dir}}$	Directing field vector
f	Reaction field factor
F	Faraday constant (9.65×10^4 C mol^{-1})
G	Gibbs free energy (free enthalpy) (in J)
$\tilde{G}$	Guggenheim's characteristic free energy in electric fields, transformed Gibbs free energy
$g, \tilde{g}$	Conversion factors
g_K	Kirkwood correlation factor
I_c	Ionic strength (mol dm^{-3})
K	Apparent equilibrium constant (concentration ratio)
$K^\ominus$	Thermodynamic equilibrium constant (activity ratio)
$k, k^\ominus$	Rate constants corresponding to K, $K^\ominus$
k	Boltzmann constant (1.38×10^{-23} J K^{-1}), thermal energy kT (J)
$L[r]$	Langevin function of r
$\mathbf{M}$	Total polarization vector, macroscopic dipole moment, thermal average $\langle \mathbf{M} \rangle = \langle \mathbf{P} \rangle V$
M	Component of $\langle \mathbf{M} \rangle$ parallel to $\mathbf{E}$
M_j	Partial molar dipole moment (contribution to $\mathbf{M}$ of B_j)

ΔM	Reaction dipole moment, $\Delta M = (\partial M/\partial \xi)_z = \sum_j \nu_j M_j$
$\Delta M^{\ominus}$	Standard value of ΔM
$\mathbf{m}_j$	Individual dipole moment of species B_j, or charge configuration $\tilde{z}_j e_0 \mathbf{r}_j$
m_j	Average value of field-parallel component of $\mathbf{m}_j$
$\mathbf{m}_{(\alpha)}$	Induced dipole moment contribution to $\mathbf{m}$
$\mathbf{m}_{(p)}$	Permanent dipole moment contribution to $\mathbf{m}$
N_A	Avogadro constant $(6.02 \times 10^{23}\ \mathrm{mol}^{-1})$
n_j	Amount of substance of species B_j (mol)
N_j	Number of species B_j molecules
$\mathbf{P}$	Electric polarization per unit volume
P	Pressure
$\mathbf{p}$	Permanent dipole moment
q	Half-axis of ellipsoid polarization
$Q, Q^{\ominus}$	Concentration ratio, activity ratio
R	Gas constant $(R = kN_A = 8.31\ \mathrm{J\,K^{-1}\,mol^{-1}})$
$\mathbf{r}$	Radius vector (position vector)
T	Kelvin temperature (K)
t	Time
V	Volume
v	Reaction rate
v_p	Rate of product formation
v_r	Rate of reactant formation
W	Work (J)
x	Field-dependent exponent in $K(E) = K(0)e^x$
y_j	Thermodynamic activity coefficient of B_j
$\tilde{y}_j$	Activity coefficient in the present of $\mathbf{E}$
$Y, \tilde{Y}$	Activity coefficient ratio at $\mathbf{E} = 0$, at $\mathbf{E}$
Z_i	Extensive state variable (V, S, M,...) conjugate to the intensive property z_i
ΔZ_i	Reaction quantity conjugate to z_i
$\Delta Z_i^{\ominus}$	Standard value of ΔZ_i
z_i	Intensive property (P, T, E)
$\tilde{z}_k$	Formal charge number (with sign) of ion B_k
$\tilde{z}_j$	"Formal (positive) charge" of the dipole B_j with $\mathbf{m}_j = \lvert\tilde{z}_j\rvert e_0 \mathbf{r}_j$
α	Polarizability tensor
α_q	Polarizability component of the ellipsoidal axis q
Γ^*	Amplitude factor containing Γ and concentration dependence of Y
Γ	Amplitude factor $[\Gamma = (\sum_j \nu_j^2/c_j)^{-1}]$
γ	Field factor of the field dissociation effect
δ	Small change
$\vartheta(\delta)$	Angle between dipole axis of $\mathbf{m}_j$ and the electric field vector $\mathbf{E}$

Δ	Differential operator, $\Delta = \partial/\partial\xi$
ε	Permittivity tensor (dielectric constant)
ε_0	Vacuum permittivity (8.85×10^{-14} F Cm^{-1})
ε_{χ}	Permittivity characteristic for the induced polarization
ε_j	Extinction coefficient of species B_j; $\bar{\varepsilon}_j$ random average value of ε_j
$\boldsymbol{\theta}$	Degree of transition
κ	Electric conductance (S)
μ	Chemical potential (J mol^{-1})
$\tilde{\mu}_k$	Electrochemical potential of ion B_k
$\tilde{\mu}_k^{\ominus}$	Standard value of $\tilde{\mu}_k$
$\tilde{\mu}_j$	Dielectrochemical potential of dipolar species B_j in an electric field
$\tilde{\mu}_j^{\ominus}$	Standard value of $\tilde{\mu}_j$
ν_j	Stoichiometric coefficient (with sign)
ξ	Extent of reaction (mol)
σ	Light polarization angle between plane of polarization and electric field vector
τ	Relaxation time
ϕ	Orientation factor
$\phi^{(\mathrm{ch})}$	Chemical transformation factor
$\Psi_k^{\ominus}(\mathbf{r}_k)$	Electric potential of the isolated charge
$\Psi(\mathbf{r})$	Mean electric potential at position $\mathbf{r}$

References

1. K. S. Cole, *Membranes, Ions and Impulses*, University of California Press (1968).
2. I. Tasaki, *Physiology and Electrochemistry of Nerve Fibers*, Academic, New York (1982).
3. D. Nachmansohn and E. Neumann, *Chemical and Molecular Basis of Nerve Activity*, Rev., Academic, New York (1975).
4. P. L. Dorogi and E. Neumann, *Proc. Natl. Acad. Sci. USA* **77**, 6582–6586 (1980).
5. H. T. Witt, E. Schlodder, and P. Gräber, *FEBS Lett.* **69**, 272–276 (1976).
6. E. Schlodder, M. Rögner, and H. T. Witt, *FEBS Lett.* **138**, 13–18 (1982).
7. E. Neumann, in *Topics of Bioelectrochemistry and Bioenergetics* (G. Milazzo, ed.), Wiley, New York (1981), Vol. 4, pp. 113–160.
8. E. Neumann, in *Ions in Macromolecular and Biological Systems* (D. H. Everett and B. Vincent, eds.), Scientechnica, Bristol (1978), pp. 170–191.
9. A. Katchalsky and E. Neumann, *Int. J. Neurosci.* **3**, 175–182 (1972).
10. K. Tsuji and E. Neumann, *Int. J. Biol. Macromol.* **3**, 231–242 (1981).
11. K. Tsuji and E. Neumann, *FEBS Lett.* **128**, 265–268 (1981).
12. D. Schallreuter, Ph.D. thesis, Konstanz and Martinsried (1982); E. Neumann, K. Tsuji, and D. Schallreuter in *Biological Structures and Coupled Flows* (A. Oplatka and M. Balaban, eds.), Academic, New York (1983), pp. 135–138.
13. M. Eigen and L. C. M. DeMaeyer, *Tech. Org. Chem.* **8**(2), 895–1054 (1963).

14. K. Bergmann, M. Eigen, and L. C. M. DeMaeyer, *Ber. Bunsenges. Phys. Chem.*
819–826 (1963).
15. G. Schwarz, *J. Phys. Chem.* **71**, 4021–4030 (1967).
16. L. Onsager, *J. Chem. Phys.* **2**, 599–615 (1934).
17. H.-J. Nolte, T. L. Rosenberry, and E. Neumann, *Biochemistry* **19**, 3705–3711 (1980).
18. A. Enokida, T. Okubo, and N. Ise, *Macromolecules* **13**, 49–53 (1980).
19. E. Neumann and H. J. Nolte, *Bioelectrochem. Bioenerg.* **8**, 89–101 (1981).
20. C. T. O'Konski and A. J. Haltner, *J. Am. Chem. Soc.* **79**, 5634–5649 (1957).
21. M. Tricot and C. Houssier, in *Polyelectrolytes* (K. C. Frisch, D. Klempner, and A. V. Pa
sis, eds.), pp. 43–90, Technomic, Westport (1976).
22. E. Fredericq and C. Houssier, *Electric Dichroism and Electric Birefringence*, Clarendo
Oxford (1973).
23. M. Eigen and G. Schwarz, *Z. Phys. Chem. N.F.* **4**, 380–385 (1955).
24. M. Eigen and G. Schwarz, *J. Coll. Sci.* **12**, 181–194 (1957).
25. M. Eigen and G. Schwarz, in *Electrolytes* (B. Pesce, ed.), Pergamon, Oxford (1962)
pp. 309–335.
26. C. T. O'Konski and N. C. Stellwagen, *Biophys. J.* **5**, 607–613 (1965).
27. G. Schwarz and J. Seelig, *Biopolymers* **6**, 1263–1277 (1968).
28. E. Neumann and A. Katchalsky, *Proc. Natl. Acad. Sci. USA* **69**, 993–997 (1972).
29. E. Neumann, *Angew. Chem. Intern. Ed.* **12**, 356–369 (1973).
30. K. Kikuchi and K. Yoshioka, *Biopolymers* **12**, 2667–2679 (1973).
31. T. Yasunaga, T. Sano, K. Takahashi, H. Takenaka, and S. Ito, *Chem. Lett. (Japan)*,
405–408 (1973).
32. A. Revzin and E. Neumann, *Biophys. Chem.* **2**, 144–150 (1974).
33. D. Pörschke, *Nucl. Acid. Res.* **1**, 1601–1618 (1974).
34. D. Pörschke, *Biopolymers* **15**, 1917–1928 (1976).
35. K. Kikuchi and K. Yoshioka, *Biopolymers* **15**, 583–587 (1976).
36. E. Neumann and K. Rosenheck, *J. Membrane Biol.* **10**, 279–290 (1972).
37. U. Zimmermann, P. Scheurich, G. Pilwat, and R. Benz, *Angew. Chem.* **93**, 332–351 (1981).
38. J. Teissie and T. Y. Tsong, *Biochemistry* **20**, 1548–1554 (1981).
39. E. A. Guggenheim, *Thermodynamics*, 5th rev. ed., North-Holland, Amsterdam (1967); *J. Phys. Chem.* 33, 842 (1929).
40. J. G. Kirkwood and I. Oppenheim, *Chemical Thermodynamics*, McGraw-Hill, New York (1961).
41. K. Tsuji and E. Neumann, *Biophys. Chem.* **17**, 153–163 (1983).