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Editorial

Introduction: Electric Fields in Chemistry and Biology

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All molecular matter can be compactly described by electric fields that arise from electron density organizations due to intra- and intermolecular interactions such as polarization, charge transfer, Pauli repulsion, and dispersion. A balance among these basic electronic processes creates local electric fields that reach sufficient magnitudes to influence catalytic processes in enzymes and materials, surface affinities, binding thermodynamics, and chemical reactivity across chemical, geological, or biochemical systems.[1] The idea that inherent electric fields exist naturally leads to the creation and application of external electric fields to manipulate molecules and materials to create new synthetic catalysts and functional devices. This is familiar to everyone in a field effect transistor but applies also to electrode interfaces, gap junctions, and the transmembrane potential that drives much of bioenergetics and neuroscience. To illustrate the scales involved, the basic unit of electric field strengths ($1\ \mathrm{MV/cm} = 1.944 \times 10^{-4}$ atomic units) can span a large range of magnitudes depending on the phenomenon involved, and the energy units are associated with the spectroscopic method used to measure fields (e.g., cm^{-1} for IR and Raman spectroscopy).

This collection of review articles spans this divide between local electric fields and externally applied electric fields and their influence on a rich array of properties and functional outcomes for biological, chemical and materials systems. It is often challenging to separate local from external fields. For example, chemists first learn in inorganic chemistry about the splitting of the degeneracy of the d-orbitals in the presence of ligand ions depending on the geometry of the complex. Another example is hydrogen bonds, which can be described using an electrostatic framework. A parallel plate capacitor would seem to be a simple case, where both the applied voltage and distance between the plates are precisely known; however, the actual electric field felt locally is modified by the local field correction, in general a tensor that depends on the polarizability of the molecule and properties of the cavity it is located in, and this impacts many forms of spectroscopy. Irrespective of the origin of the field, it is important to measure its magnitude and direction on a length scale relevant to the interaction, and this is often challenging.

Fundamentally, electric fields inside versus between molecules are different and their experimental and theoretical interpretation requires an understanding of this distinction. The "electrochemical potential", which defines electric fields experienced between distinct molecular species, is different from the so-called "mean inner potential" that arises from averaging over all space including the interior regions of molecules.[2] This distinction is important, as it has given rise to confusion about electric field calculations using point-charge force fields that probe only the electrochemical potential versus electronic structure methods that primarily characterize the mean inner potential.[3−5] In turn this requires more careful consideration in what different experiments are actually measuring when they quantify electric fields. For example, vibrational Stark shifts primarily probe the relatively weak electrochemical effects of nonbonded interactions[6,7] while electron holography measurements pertain to the strong field mean inner potential.[8]

Understanding these fundamental differences in electric field origins in molecules and molecular assemblies is necessary as we scale up to the greater complexity of condensed phases, and water remains as life's most important bulk phase liquid. Traditionally, small length scale hydration physics refers to the appearance of empty cavities controlled by dipolar fluctuations that allow for aqueous solvation shells to form around small solutes without loss of hydrogen-bonding interactions.[9] The transition to large length scale hydration physics,[10] such as a collection of hydrophobic solutes or introduction of a symmetry breaking air or organic interface, leads to a complete reorganization of the interfacial hydrogen-bonded network to create broken hydrogen bonds that can create large electric field fluctuations.[11] More recently introduced spectroscopies indicate that free O−H groups can also form near small hydrophobic solutes,[12] and even atomic ions, and thus broken hydrogen bonds are now appreciated as a molecular feature shared with extended interfaces. This continuity between hydration of molecules to extended interfaces provides a useful interpretative picture offered by Dawlaty and co-workers of the local electric fields measured at charged monolayers formed over water. Using simple surfactants as an interfacial probe, they provide a comprehensive review of the theory and spectroscopy on the double layer organization of immobilized waters near the ionic head-groups, and diffuse layer of waters that are directly influenced by their local electric fields, to control the chemical equilibria of surface active species and

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ultimately greater complexity of proton transfer and redox chemistry at the interface.

The local electric fields at the active sites of natural enzymes[13] are central to the preorganized electrostatic interactions introduced by Warshel to explain, in part, their exceptional catalytic power.[14] The review by Eberhart and Alexandrova and their co-workers covers advances in theoretical models to quantify how the electric fields created by the organization of polar and polarizable groups at the active site of enzymes can lower the transition states of chemical reactions.[15] They also address the coupling of electric fields to statistical fluctuations that demonstrates the 21st century view of a structure-dynamics-function relationship.[16] Like protein-generated fields that are highly dynamic and heterogeneous, nonbiological polymers also exhibit nonuniform fields but lack the rational preorganization that enzymes have perfected over evolutionary time to control for functional outcomes. The review by Welborn et al. consider the optimization of local electric fields created by polymers through their building block constituents and supramolecular architecture, while also taking advantage of externally applied electric fields for the controlled fabrication of polymeric materials for electronic devices. Similarly, the active electrode under *operando* conditions in electrocatalysis creates external electric fields by design, but they are heterogeneous due to the relentless dynamical reorganization in electrolyte concentrations and composition and electron migration under applied bias occurring far from equilibrium. This makes a static thermodynamic model unrealistic for describing ions that diffuse to and from the electrodes as electrons are consumed or produced, affecting the electric field environment around the reacting species. Patel and Kastlunger review the importance of such non-Nernstian behavior in theoretical models while also suggesting how to couple to relevant experiments in order to unravel these nonequilibrium effects in electrocatalysis.

Almost certainly the local electric fields at the active sites of natural enzymes offer the most direct inspiration for the creation of external electric fields to create new synthetic devices and catalysts. The manipulation of external electric fields at the nanoscale is reviewed by Guo and co-workers and demonstrates their power for controlling electronic properties of molecules to create functional outcomes that may usher in a new future for information technology devices. They show the experimental challenges that have been overcome, aided by theoretical models, to create external electric fields that can lower the energy gap between the closed-shell singlet and open-shell triplet states to create logic gates, and the integration of molecules into electronic devices where molecules can be manipulated by these fields to improve performance such as reduction in both the physical device size and power consumption.

Similarly, designed external fields offer ground-breaking promise in manipulation of catalysis at the nanoscale, which must encompass the design and synthesis of new hybrid catalytic materials that preserve activity and selectivity of a molecular catalyst, but in a heterogeneous, high surface area, robust support system. The enclosing microstructure of the catalytic site within a supported catalyst generates both short-range and (often highly) anisotropic interactions, as well as long-range electrostatics (e.g., electric fields, field gradients, etc.); if well formulated, this environment not only provides selectivity for a given reactant but also stabilization of the transition state governing the kinetics of the underlying chemical reaction. Kubiak, Batista and Lian form a tight experimental-theory team that considers non-Faradaic electric fields to control the environment for supported molecular catalysts that will be more selective for the reagents, contribute to transition state stabilization, and increase formation of final products.

Finally, the molecular mechanism underlying the electrical stimuli in biological cells is reviewed by Malliaras and co-workers, in which applied fields can stimulate or regulate cell responses to treat neurological conditions such as epilepsy and Parkinson's disease, identifying tissue abnormalities such as tumors, or to control cargo transported into and out of cells.

All the reviews in this collection present a vision for how we can utilize electric fields in both fundamental and applied research. We hope that these reviews inspire students, postdoctoral researchers, and mature scientists to use their imagination on how electric fields can be harnessed at the intersection of chemistry and the environment, materials and technologies, and biology and medicine.

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Notes

Views expressed in this editorial are those of the authors and not necessarily the views of the ACS.

Biographies

Steven G. Boxer obtained his Ph.D. from the University of Chicago in 1976, after which he joined the Stanford Chemistry Department, where he is now Department Chair and the Camille Dreyfus Professor of Chemistry. His group has a long history of studying electrostatic interactions in proteins, initially by the introduction of charged amino acids inside myoglobin and measuring the impact of buried charges on redox potentials. The chance observation of a huge change in dipole moment associated with the nominally inversion symmetric carotenoid in the photosynthetic LH2 complex using electronic Stark spectroscopy led to the idea that protein organization can create large electric fields, in that case inducing a large difference dipole in a polarizable chromophore. His lab made the first measurements of the vibrational Stark effect, giving information on the sensitivity of vibrational frequencies to applied electric fields, and this was turned around to use vibrational frequency shifts as quantitative probes of electric fields. This is being applied at the active site of enzymes where the magnitude of these fields directly affects the activation free energy for catalysis. The vibrational Stark effect also provides a quantitative experimental test for MD force fields, and this approach is now being applied to diverse systems, both biological and nonbiological.

Teresa Head-Gordon obtained her Ph.D. from Carnegie Mellon University (1989) and was a Postdoctoral Member of technical Staff at AT&T Bell Laboratories (1990−1992). She joined Lawrence

Berkeley National Laboratory as a staff scientist in 1992. In 2001 she became an Asst. Professor, Assoc. Professor in 2004, and Full Professor in 2007, and subsequently the Chancellor's Professor chair at UC Berkeley. She is a leader in electrostatic and electric field theory, introducing analytical and semianalytical solutions to Poisson−Boltzmann, generalizing the 1934 solution of Kirkwood. She has made numerous contributions to advanced force fields using many-body theory and machine learned interaction potentials, resulting in highly accurate models of the potential energy surface for water, organics, and reactive systems. She has shown the necessity of including many-body interactions for conformational equilibria and spectroscopic observables, and for explaining how electric fields lead to chemical reactivity and catalysis for electrocatalytic surfaces and synthetic enzymes, natural enzyme turnover, and the emerging area of water and oil microdroplets.

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