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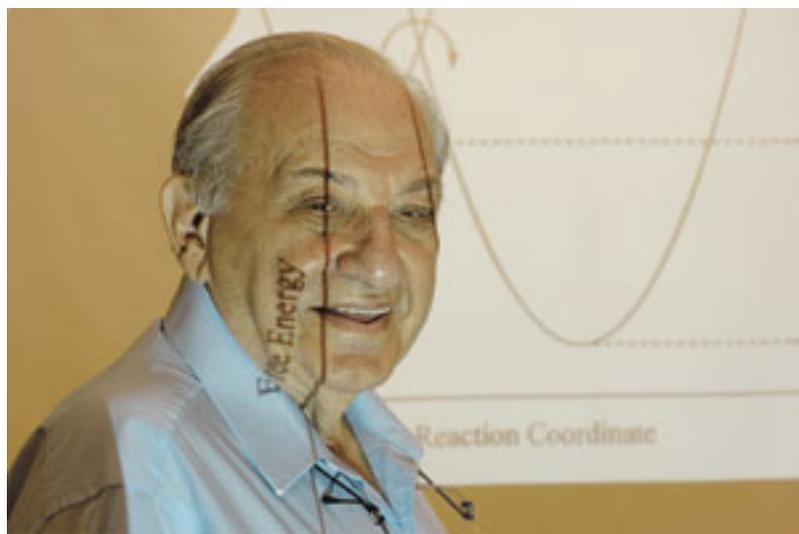
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## Five Decades Of Marcus Theories

### ACS Meeting News: Symposium celebrates golden anniversary of seminal electron-transfer and reaction-rate theories

Stephen K. Ritter

It's rare for a scientist to develop a new theory and then 50 years later have the opportunity to step back and view its impact—let alone make two such outstanding discoveries. But that's the story of chemistry professor Rudolph A. Marcus of California Institute of Technology, who was instrumental in developing electron-transfer theory and the RRKM unimolecular reaction-rate theory. Marcus and his two theories were the center of attention last month at a four-day symposium sponsored by the Division of Physical Chemistry during the American Chemical Society national meeting in San Francisco.



Robert Paz/CALTECH

Free Energy Marcus' theories have influenced the work of countless chemists in the past 50 years.

In 1956, Marcus published a pair of papers outlining the necessary thermodynamics and kinetics of electron-transfer reactions in chemical systems. The papers led to further research on electron transfer over the ensuing nine years, which allowed Marcus to generate a body of work that garnered him the

1992 Nobel Prize in Chemistry. It turns out that these electron-transfer reactions are commonplace in biological and physical systems, ranging from DNA repair and photosynthesis to conducting polymers.

Just a few years earlier, in 1952, Marcus had published a paper describing how to compute unimolecular reaction rates. The theory of chemical reactivity had been expounded by Oscar K. Rice and Herman C. Ramsperger in 1927 and by Louis S. Kassel in 1928. As a postdoctoral researcher in the early 1950s, Marcus generalized the RRK theory, as it had become known, by taking into account transition-state theory developed by Henry Eyring in 1935. The combined RRKM theory now provides a method to determine the rate of a reaction when only one molecule is involved in the transition state, such as an isomerization or rearrangement or a molecule shaking itself apart to form radicals or ions.

"A great scientist should make two outstanding discoveries, as a single discovery may be guided by luck or accidental circumstances," commented Joshua Jortner of Tel Aviv University, in Israel. "Rudolph Marcus admirably satisfies this criterion," he added. Jortner gives credit for the "two discoveries" statement to Physics Nobel Laureate Felix Bloch, who won the prize in 1952 for his work on nuclear magnetic resonance.

In San Francisco, Jortner and Alexander M. Kuznetsov of the Frumkin Institute of Physical Chemistry & Electrochemistry at the Russian Academy of Sciences, Moscow, each gave retrospective talks on the development and extensions of Marcus theory. They focused on electron transfer from its "romantic" early days, to its growing sophistication over the years, to its impact on current research, including their own.

Marcus' electron transfer theory "constitutes a central dogma in science, reflecting on the ubiquity, generality, universality, and conceptual unification of the phenomena of charge transfer and transport in chemistry, physics, biology, materials science, and nanoscience," Jortner said. And RRKM theory "laid the foundation for understanding of the central chemical phenomena of the acquisition, storage, and disposal of thermal energy in molecular systems," he said.

Overall, more than 40 talks were given during the Marcus symposium. "It was fantastic," commented Alexei A. Stuchebrukhov of the University of California, Davis, a former Marcus group member and a coorganizer of the event. "The talks were a terrific blend of history, personal reflections, cutting-edge science, and speculation about the future of physical chemistry," he told C&EN.

"Having been involved in this area almost since its inception, it was remarkable to watch the most recent results on electron transfer being presented while recalling the early days of the field," said Thomas J. Meyer of the University of North Carolina, Chapel Hill. "The symposium was poignant for me, since, as a graduate student with Henry Taube from 1963 to 1966, I carried out kinetic measurements on electron-transfer reactions involving ruthenium ammine complexes with the goal of testing 'Marcus theory.' My work must have been important, since both Taube and Marcus later won the Nobel Prize."

Marcus, now 83, delighted the audience with opening and closing talks outlining the history of the study of electron transfer and the contributions several researchers made to aid understanding of the

phenomenon. The theory depicts the thermodynamics and kinetics of reduction-oxidation, where the formal oxidation states of both reaction partners change, he explained. Marcus derived mathematical expressions for how the energy of such a system is affected by these changes and for the energy barrier an electron must overcome for transfer to occur. With a final quadratic equation, he was able to calculate and explain the greatly varying reaction rates measured for electron-transfer reactions.

"It was truly a eureka moment," Marcus told C&EN. "Although the key electron-transfer equation took just a month to derive, the intermediate equations were very complicated—as an examination of my two 1956 papers shows. But when the final result came out, I was astounded at its simplicity."

His additional work in the late 1950s and early 1960s "generalizing, extending, and applying" the equations allowed a depiction of a reaction in terms of parabola-shaped free-energy plots over the course of a reaction. One of the stunning findings was that, in some cases, when a reaction becomes more energetically favorable the process slows down instead of speeds up.

Early experiments in electron transfer were isotope-exchange reactions between radioactive isotopes of metals, which were widely available after World War II, Marcus said. Other early advances included the study of fast electron transfer at metal electrode surfaces. More recent experiments in biological systems include oxygen binding and transport, photosynthesis, cellular respiration, and detoxification of reactive species. One area of great current interest is long-range electron transfer in proteins and DNA, Marcus pointed out. Electron transfer is also important in chemiluminescence, corrosion, electron flow in conducting polymers, solar energy conversion, and more.

Stuchebrukhov's research is a good example of the advances that have been made in understanding biological systems using electron-transfer theory. In San Francisco, postdoctoral fellow Dragan M. Popović in Stuchebrukhov's group presented results on a computational model the group is developing to describe the proton-pumping mechanism of cytochrome c oxidase.

This membrane-bound enzyme is at the end of the respiratory electron-transport chain in mitochondria and catalyzes the four-electron reduction of O<sub>2</sub> to water using electrons and protons, Popović explained. In addition, it utilizes the free energy of the reduction to "pump" protons outside the mitochondrial membrane, which generates an electrochemical gradient. The energy stored by the gradient subsequently drives synthesis of adenosine triphosphate (ATP), the key molecule in intracellular energy transfer involved in converting food into energy. The mechanism of how electrons and protons are coupled in the enzyme is an ongoing unsolved problem, he noted.

In his presentation, Meyer focused on elementary pathways by which this type of proton-coupled electron transfer (PCET) occurs. He first encountered this phenomenon as a graduate student in Taube's lab, and it has continued to be integral to much of his group's work on mechanisms and catalysis, he said. Meyer and his coworkers coined the PCET term in a paper in 1981 to describe a pathway or elementary step in which both electrons and protons are transferred, but from and to different orbitals, Meyer explained. He now uses PCET to describe the net reaction and electron-proton transfer (EPT) to describe the elementary step for the coupled transfer.



with respect to how and where DNA can become damaged in the genome and how this damage may be sensed and repaired. "We are now building up a body of evidence that DNA base excision repair proteins may use DNA charge transport as a means to localize repair enzymes near sites of base damage," she told C&EN.

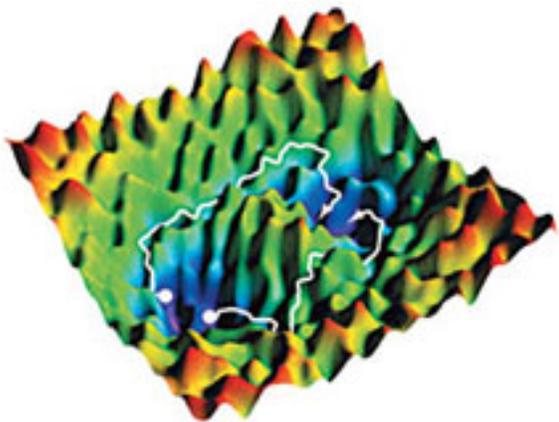
Maria E. Michel-Beyerle of the Technical University of Munich, in Germany, who has collaborated with Marcus in the past, commented that the symposium "turned out to be a fabulous compilation of basic concepts and recent directions in Marcus theories, showing that even after many decades, both theories have an undiminished effect."

She described her group's work on structure-based electron-transfer phenomena in proteins and DNA using temperature-dependent femtosecond absorption and emission experiments. With this technique, the researchers are able to determine the dependence of electron-transfer rate and mechanism on the energy of molecular bridges between the electron donor and acceptor in biological systems.

In one case, Michel-Beyerle laid out the mechanism of photoinduced electron transfer responsible for the unidirectional charge separation in the photosynthetic reaction center involved in light energy conversion to ATP in *Rhodobacter sphaeroides* bacteria. By using a bacteriochlorophyll pigment replacement in the active "A-branch" pathway of the reaction center, the rate of charge separation was significantly reduced to allow the inactive "B-branch" pathway to compete, which revealed the structural and energetic parameters responsible for the unidirectionality.

"This elementary scheme of photosynthetic energy conversion connects four discoveries that led to Nobel Prizes in Chemistry," Michel-Beyerle pointed out. One of them is Marcus' electron-transfer theory, and the others are chemiosmotic theory to understand biological energy transfer (prize in 1978); determination of the three-dimensional structure of a photosynthetic reaction center (1988); and the enzymatic mechanism underlying ATP synthesis and the discovery of the first ion-transporting enzyme, sodium/potassium-ATPase (1997).

John R. Miller of Brookhaven National Laboratory continued the discussion of the impact that Marcus' electron-transfer theory has had on the conversion of sunlight into useful energy, in his case using solar cells. Miller raised a question about what he called the "common conception" that if you want to split water, it should be done in water. "Marcus theory tells us if we want efficient energy storage, we should do it in 'chicken fat,' not water, meaning that a nonpolar medium would work best," Miller told C&EN. He showed how experimental data from his lab confirm Marcus' prediction about polarity effects on electron-transfer rates.



Courtesy of David Chandler

**Seeking Directions** Computed potential energy map is a useful tool to sample the many possible reaction pathways in a complex chemical system. Chandler's group at UC Berkeley devised this "transition path sampling method."

**Examples** of actual solar energy storage systems do, in fact, use nonpolar environments, he noted, giving support to the idea of using "chicken fat or its vegetarian equivalent" to facilitate solar energy storage. In plants, which are mostly water, the photosynthetic reaction center is imbedded in proteins that are nonpolar, and the proteins are in nonpolar lipid membranes, Miller said. And silicon, titanium dioxide used in dye-sensitized cells, and other inorganic solar cell materials are nonpolar, as are the next-generation organic-based "plastic" solar devices under development.

"If we want to create new, efficient chemical-based solar energy systems, we are missing information," Miller commented. "We need to know the energy levels for transfer of electrons to perform light-driven charge separation in nonpolar media. Electrochemistry provides that knowledge in the form of accurate thermodynamic potentials, but only in polar media with high concentrations of salt added. If we design and construct a molecular system to separate charge in a nonpolar medium, but we err in estimating where the energy levels will be, the system may fail to store energy or do so with low efficiency."

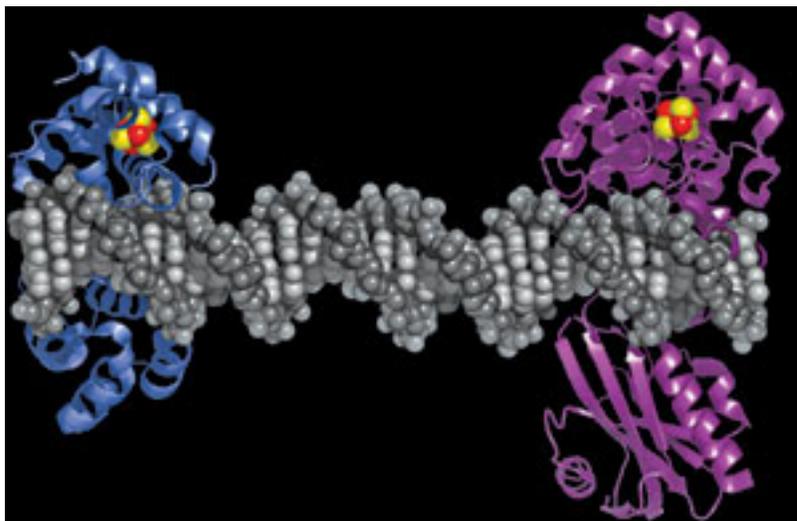
RRKM is a "lovely theory," though it is usually overshadowed by the "brilliance and generality" of Marcus' electron-transfer theory, noted [David Chandler](#) of the University of California, Berkeley.

RRKM's original focus on dynamics "was unusual for its time," Chandler said. As an illustration of the utility of modern dynamical theory, he described results of two studies by his group: the collapse of a hydrophobic chain in water, and the self-assembly of a virus capsid. "In both cases, we have uncovered pathways that explain how these processes occur, and the mechanisms thus revealed offer some interesting surprises," he said.

In the first case, it's the dynamics of the water solvent, not the chain, that drives the system through the transition states separating the extended chain from its more stable globular state, a process like protein folding, Chandler said. In the second case, thermodynamic stability is insufficient to guarantee successful formation of a completed capsid. Instead, kinetics plays the dominant role, and there are regimes where rates of assembly decrease with increasing thermodynamic stability.

"Our findings were made possible by a relatively new computational approach—the transition path sampling method," Chandler explained. "This is a general set of computational tools that allow us to discover reaction pathways in complex systems." He defined a complex system as one in which the potential energy surface, which can be viewed as a map, has an uncountable number of features, a few of which may correspond to transition states.

Computational studies of many processes of interest are often difficult because of this complexity, but transition path sampling provides the basis for finding possibly successful algorithms of a reaction pathway. The method is like "throwing ropes over rugged mountain passes (transition states) in the dark to connect two valleys (energy minima) of interest on the surface without any preconceived notions of a mechanism," he said. After a sequence of throws, physically pertinent pathways, some tortuous, can be determined.



Amie K. Boal/Caltech

Repair Shop Long-range electron transfer between distally bound proteins in a DNA-mediated reaction may play a role in damage detection by monitoring the integrity of DNA (gray). Illustrated are MutY (purple) and EndoIII (blue) base excision repair proteins that localize near base pair damage or mismatches; each protein contains a 4Fe-4S cluster cofactor (orange and yellow).

"**The breadth** of the applications of electron-transfer theory and RRKM theory is rather astounding," added Mark H. Thiemens of the University of California, San Diego. Thiemens spoke about his work on the theory of mass-independent isotopes, noting that Marcus' work "has been instrumental in providing a true quantum-based description of this effect we discovered some 20-plus years ago."

Thiemens documented an unexpected even ratio of the minor isotopes  $^{18}\text{O}$  to  $^{17}\text{O}$  in ozone ( $\text{O}_3$ ). The heavier masses of  $^{18}\text{O}$  and  $^{17}\text{O}$  lead to their being enriched in  $\text{O}_3$  relative to  $\text{O}_2$  in air, he explained. This enrichment would be expected to be greater for  $^{18}\text{O}$  than  $^{17}\text{O}$  because of the heavier mass, but it isn't. Marcus used RRKM theory to figure out that symmetry brought about by the location of isotopes in a molecule can override the mass effect, in the form of symmetry-enhanced non-RRKM effects, and give  $^{18}\text{O}$  and  $^{17}\text{O}$  equal access to a reaction path to form  $\text{O}_3$ , leading to the observed nearly even mass-independent ratio of  $^{18}\text{O}$  to  $^{17}\text{O}$ . Mass-dependence still plays a role in the rate at which  $\text{O}_3$  molecules

break apart.

Thiemens and his colleagues have developed methods to use this pronounced isotopic anomaly to monitor and understand natural processes. Some examples include studies from the South Pole to investigate changes in the ozone hole, studies on the origin and evolution of oxygen in Earth's early atmosphere, and studies on the origin and evolution of the solar system.

Reflecting on the past and the future of his science, Marcus added that "it's interesting to recall how experiments have stimulated new theoretical developments and how theory has led to new experiments." As for the next steps for electron transfer and RRKM, "I find it very difficult to predict what might be possible. In my experience, and I'm sure that of many others, the most exciting studies are those that haven't been predicted."