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Jack H. Freed

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A Personal Foreword

I am delighted to have this opportunity to write a foreword to this issue of *The Journal of Physical Chemistry* honoring Jack Freed on his 65th birthday. The many articles here relate in more than one way to Jack's pioneering contributions to theory, instrumentation, and practice of electron spin resonance (ESR) spectroscopy since the early 1960s when he first burst upon the ESR scene with a paper describing the discovery and his theoretical explanation of the anomalous alternating linewidths in the ESR spectra of dinitrobenzene anion radicals, as a graduate student with George Fraenkel at Columbia. This article led to what is now known as the Freed−Fraenkel theory of ESR linewidths and formed the basis of his subsequent comprehensive theory of ESR saturation and electron-nuclear double resonance (ENDOR) phenomena later in the 60s, and that is, fortunately, when our paths crossed.

I first met Jack in 1968 at the University of British Columbia in Vancouver, Canada, where I was a beginning graduate student. We were hosting an ISMAR conference, and Jack was one of the Plenary speakers. Jack's discussion of the theory and applications of ENDOR, and especially, the electron-nuclear triple resonance (TRIPLE) technique, was one of the conference highlights. ENDOR was developed in the late 1950s by George Feher for solids and extended to liquids in 1965 by Jim Hyde, and Jack provided the theoretical interpretation. He and his students later obtained extensive experimental verification of this theory. Around that time, it was clear that while ENDOR could provide orders of magnitude enhancement in resolution over standard ESR, it had the serious drawback of poor sensitivity. Based on his theoretical calculations and physical insight, Jack predicted in 1969 that this shortcoming could be surmounted if one induced both of the NMR transitions simultaneously, which is the TRIPLE technique alluded to above. Jack's predictions were soon supported by experimental evidence by at least two groups, the group of Charles McDowell at UBC (in which I was the main participant) and that of Klaus Möbius at Berlin (with R. Biehl and Peter Dinse as students). TRIPLE also enables one to determine the relative signs of the various hyperfine coupling constants, not generally possible with ENDOR. It is doubtful that ENDOR applications would have mushroomed as they have without the development of the TRIPLE capability.

Jack was also the first to apply his theory of ESR relaxation and electron-nuclear multiple resonance to the theoretical understanding of cross-relaxation effects in ESR spectroscopy. In a joint paper, Jim Hyde and he reported on a versatile spectrometer system to measure the electron−electron double resonance (ELDOR) response from a variety of nitroxide and other probes and provided the underlying theoretical interpretation. The data yield perhaps the most direct measure of the microscopic details of the molecular structure and dynamics of

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liquids, liquid crystals, membranes, and surfaces. He subsequently extended this CW ELDOR methodology to pulse techniques, which has opened up a whole new window on the local and global structure and dynamics of simple liquids as well as complex biological systems. It is remarkable that Jack had to develop not only the theory but also the microwave technology for pulse ELDOR. It is doubtful that this comprehensive advancement would have been possible without someone like Jack, who is so exceptionally gifted in both theory and experimental aspects of magnetic resonance techniques as well as microwave technology.

Simultaneous with these landmark developments, Jack carried out extensive investigations on the general theories of spin relaxation in liquids that ultimately led him to his now well-known solutions of the stochastic Liouville (SLE) equation, which is based on the synthesis of a classical Markov-type approach for the molecular dynamics in liquids with the quantum dynamics of the spins. The SLE approach has proved to be a powerful method for computing the complex ESR line shapes that one obtains when molecular motion is slow and perturbative techniques break down. This approach has now been applied by Jack and his collaborators to analyze their many experimental studies including molecular dynamics in isotropic liquids, liquid crystals, membranes, polymers, and proteins in liquids. This body of work represents the standard for such studies in most laboratories around the world. Equally impressive is the fact that despite the complexity of the theory, powerful new computational algorithms were developed in his laboratory, which have led to extremely efficient computer programs that are now utilized by many groups worldwide.

The past two decades have witnessed an explosive growth in new ESR methods. Two of the most significant advances have been in the development and applications of pulse techniques and high frequency, high-field methodologies. Jack and his group have been in the forefront of these developments. Jack was the first to introduce two-dimensional Fourier transform ESR (2D-FT-ESR), which is the analogue of 2D-NMR introduced by Richard Ernst. This development was a pioneering effort due in part to the substantial challenges in current microwave technology. Specifically, 2D-ESR needs spectral bandwidths of at least 200−250 MHz, nanosecond pulse widths, sub-nanosecond time resolution in the echo decays, and high sensitivity; the instrumentation meeting these requirements was not available and had to be developed in Jack's lab. With his characteristic focus and energy, Jack has succeeded in this pursuit, bringing ESR essentially parallel to NMR. He has demonstrated that SECSY-ESR provides an order-of-magnitude increase in the speed of data acquisition compared to the earlier field-swept pulse techniques, and in addition, for solids, it yields a detailed 2D pattern from nuclear modulation, which is more informative on molecular structure than conventional ESEEM. The three-pulse 2D-ELDOR experiment, also developed by him, is a uniquely powerful method for measuring cross-relaxation processes. It is the epitome of ELDOR methods. In studies of slow reorientational dynamics, it displays how the rotational motions spread the spins out from their initial orientations (and corresponding spectral positions) to new orientations as a function of the adjustable mixing time and provides a clear means of discriminating between many otherwise unanswerable questions that depend on the microscopic details of the motional process. This pioneering work has clearly demonstrated that 2D-ESR is the method of choice for ESR relaxation studies of fluids. Jack and his co-workers have more recently introduced pulse methods for generating multiple quantum coherences in ESR, matching in sophistication modern NMR methods. He has used this approach to develop the double-quantum coherence method to measure intramolecular distances ranging from about 12 to 70 Å in doubly spin-labeled organic and biomolecules with high sensitivity and accuracy. This will undoubtedly be a powerful methodology for structural and functional studies in large biosystems.

Over recent years, Jack has championed the development of very high frequency, far-infrared-ESR spectroscopy. He was the first to develop a resonator-based ESR spectrometer operating at 1.2 mm wavelength, 250 GHz. To accomplish this, Jack and his co-workers employed quasi-optical techniques, which have since been in use in many laboratories worldwide. He has shown how, by combining high and low frequency ESR into a multi-frequency approach, one can begin to unravel the even more complex molecular dynamics of complex fluids and biosystems. His studies on a glass forming fluid have enabled one to determine the dynamic role of the solvent cage on the rotational motion of solute probes of varying sizes as the solvent approaches the glass transition. The multifrequency approach has been particularly useful in studies of spin-labeled proteins, polymers, and DNA oligomers. He has shown that this approach enables one to distinguish between the internal (faster) modes affecting the local site that is labeled and the overall (slower) modes and to assign the respective rotational diffusion tensors and the local ordering potentials. This approach enables one to map out the complex protein dynamics as a function of the labeled site in the protein backbone using the site-directed spin-labeling method developed by Wayne Hubbell. The DNA study has shown sensitivity to its collective internal dynamics, which depends on the size of the oligomer. He has thus opened up a powerful new avenue for investigating protein folding and related problems that are difficult to study by other means. Also, in order to combine the virtues of high-frequency ESR and 2D-ELDOR, he and his co-workers have recently developed the technology for performing 2D-ELDOR with millimeter waves.

The above summary provides a glimpse of only a portion of Jack's accomplishments. He and his co-workers have also made major advances in the field of ESR imaging, via his 2D-FT-ESR and DID-ESR (dynamic imaging of diffusion) techniques, and he has recently developed an ESR microscope approaching micron resolution. He has also pioneered the subject of ESR studies of surfaces under ultrahigh vacuum conditions, wherein he developed a whole range of relevant spectroscopies including surface-suppressed electron resonance spectroscopy (SSERS) and CREMSEE (cyclotron resonance from microwave-induced secondary electron emission), which enables the study of free radicals adsorbed on clean metallic and oxide surfaces. Furthermore, Jack, in collaboration with his physics colleague David M. Lee, has carried out fundamentally important magnetic resonance research at very low (millikelvin) temperatures. These studies have led to the discovery of the novel phenomenon of nuclear spin waves in the quantum Bose gas of spin-polarized H atoms. This study may be thought of as a precursor to the later observation of Bose condensation in a gas of H atoms at even lower temperatures by Greytak and Kleppner at MIT.

Jack has thus been at the forefront of essentially every area of ESR spectroscopy. He has been recognized through numerous awards, including a Sloan Fellowship (1966−68), Senior Weizmann Fellow (1970), APS Fellow (1976), Buck-Whitney Award of the ACS (1981), Guggenheim Fellow (1984-85), Gold Medal of the International ESR Society (1993/94), Fellow of the American Academy of Arts and Sciences (1994), Irving Langmuir Prize of the American Physical Society (1997), International Zavoisky Prize, Russian Academy of Sciences (1998).

Finally, it is noteworthy that this present recognition comes at a time when the current level of Jack's contributions to magnetic resonance spectroscopy have perhaps never been greater, and it is abundantly clear that the best is yet to come. Hearty congratulations, and Happy Birthday, Jack!

Naresh Dalal