It seemed that everything was motivated by the pure excitement of ‘finding things out’. The intensity was wonderful; not the kind of intensity that produces stress, but an intrinsic one derived from McConnell's infectious dedication and knowing that the tools to solve important problems in biophysics were at hand in the laboratory, and time was the only limit (still is). Together with McConnell’s uncanny ability to sort out the scientific wheat from the chaff, this atmosphere produced daily discoveries.

My first encounter with this intensity came after I had been in the lab a few months. I had been assigned to explore a protein with the new technique of spin labeling, one of McConnell's many contributions to biophysics. I don’t remember the protein, but it was not going well, and I began to moonlight on another side project; the synthesis of a spin label that would bind to biological membranes (just for fun). Through the assistance of another graduate student (Richard Hoagland, who subsequently founded Molecular Probes, Inc.), I learned enough organic chemistry to synthesize a nitroxyl amide derivative of palmitic acid that bound to lipid vesicles and gave an unusual EPR spectrum that meant little to me at the time. One afternoon, McConnell walked by my desk and spotted the spectrum and demanded “What’s that? Bring it into my office.” I was certain that I was in trouble because it had nothing to do with the protein I was assigned to study. As it turned out, McConnell recognized that the lineshape showed evidence of anisotropic motion, and he soon outlined the framework for understanding this class of spectra in terms of an effective Hamiltonian. That gave rise to a tremendous flow of new ideas (mostly from McConnell), new molecules to make, new systems to explore, and a lot of excitement. When he would see me leaving the building he would yell down the hall “be careful on the way home!” When he was away at a meeting, there would be daily (or more frequent) calls to relay new ideas and receive new data. On weekends he would sometimes be off to plant trees at his ranch. On more than one occasion he asked that I come along. Not that he wanted help planting trees; in fact he refused to let me work. Rather, I was there to discuss science so time would not be wasted. At the end of such days, I was mentally exhausted trying to keep up with the train of thought.

At his 65th birthday party, attended by many past students and notable scientists (including Linus Pauling), McConnell gave a talk describing his recent thoughts on pattern formation in lipid systems; it seemed pretty esoteric. Norman Davidson, his mentor in graduate school at CalTech (McConnell was his first student), stood up and asked “Harden, why are you doing this?” The reply was “because it is interesting”. Davidson responded “I don’t believe it; there must be more, something of value.” Maybe Davidson didn’t believe it, but I did.

Early biophysical studies of membranes, with nitroxide spin labels, 1965–1985

Harden McConnell

It is a pleasure to hear from former graduate students and colleagues who have enjoyed their time in my laboratory. Their perspective on past events is often amusing, sometimes sobering, and always interesting. In respect to early spin label work here at Stanford, the history as I recall it is fairly clear. Nitroxide free radicals were known to be relatively stable. At CalTech graduate student Hayes Griffith had become interested in using these radicals as probes to study micelles, and when he came to Stanford with me he determined the nitrogen isotropic and anisotropic hyperfine interactions in an organic inclusion compound [J. Chem. Phys. 43, 2909–2910 (1965)]. The combination of a well-defined spin Hamiltonian and the potential for chemical synthetic versatility with nitroxides was an open invitation to use these free radicals as biophysical probes.

Early work involved both proteins and membranes, but for brevity I only discuss the membrane work. Examples include one of the first measurements of the lateral diffusion of phospholipids in lipid bilayers by postdoc Philippe Devaux [J. Am. Chem. Soc. 94, 4475–4481 (1972)], and the first...