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Editorial

A tribute to James H. Prestegard – 75 years young!

Many things in life are determined, at least partially, by chance. And sometimes chance events lead to results that are better than could possibly be achieved even after careful planning. An example of this is found in my choice of doctoral advisor, James H. Prestegard. After arriving at Yale University in the Fall of 1983 I was given a rotation project in Don Crother's laboratory calculating how DNA molecules would move in an electric field. This involved access to the single departmental computer and required, not surprisingly, large amounts of scrap paper for calculations. One day the calculations on the 'used' side of the scrap paper by someone else looked more interesting than the ones that I was doing. Recognizing that they involved density matrices for a spin-1 particle I quickly enquired as to what group was responsible for this research. And so I met Jim and quickly gravitated to his laboratory. Over the course of the next 4 years I received a wonderful education in Jim's laboratory in many different areas of NMR that has served me well over the three decades that have transpired since. I know that my experience in Jim's lab was not unique and that his trainees are extremely appreciative of the unique learning experience that was provided. With this in mind a small group of his students decided to submit a series of publications to the Journal as a mini-Festschrift in honor of Jim's 75th birthday in early 2019. A celebration was recently held in Georgia to commemorate this event.

Jim received a BS in Chemistry in 1966 from the University of Minnesota and a PhD in Chemistry under the direction of Sunny Chan at the California Institute of Technology in 1971. Like with me, I am told that the process Jim used to select a graduate supervisor was quite random, but likely did not involve density matrix calculations on scrap paper. After a very successful 4 years at Cal Tech Sunny advised Jim that the job market would be turning bad shortly and that if he wanted a faculty position he might wish to forgo postdoctoral training. So Jim immediately applied to a number of top places and decided upon Yale as this would require establishing an NMR facility from the ground up, unlike some of the other institutions that already had equipment running. Jim, at heart, was a builder, even in those early days.

Jim has always had a strong interest in both NMR methodology development and in applications to problems of biochemical importance. Initial studies focusing on membrane fusion and permeation of small molecules into vesicles naturally led to a long-time NMR exploration of lipid and glycolipid head group orientations using an array of different nuclei, including ^{1}H, ^{13}C and ^{2}H, and of course a large suite of different experiments – some of them newly minted – to extract maximum information content. It was probably from these early experiments that Jim began to think about orienting molecules in high magnetic fields based on magnetic anisotropy to extract dipolar couplings that could then be used as orientational constraints in structural studies. Certainly, many of his trainees spent at least some of their time generating such data. In those days we used carefully prepared organic liquid crystals that required just the 'right' amounts of each component. Since nobody had bothered to write down the recipe it required painstaking optimization by trial and error to get the ingredients right. Perhaps my most important contribution to the Prestegard laboratory was figuring out the recipe and writing it down!

In addition to work on glycolipids, Jim was also very interested in using NMR to extract dynamics information. Part of this interest may have resulted from a min-sabbatical in the late Dave Grant's laboratory at the University of Utah where Dave and his post-doctoral fellow Larry Werbelow had pioneered spin relaxation experiments in multi-spin spin systems to extract auto- and cross-correlated relaxation rates. Jim arrived with a fatty acid micelle sample where one of the methylene groups was CF_2 and proceeded to use ^{13}C NMR relaxation to study the dynamics of this methylene site. Notably, he observed the expected triplet structure, but one where the linewidth of the middle component was much smaller than the outer two lines, a tell-tale sign of cross-correlated spin relaxation in the limit where the methylene rotates rapidly around the acyl-chain long axis. This study had more than a passing interest for me since related cross-correlated spin relaxation studies in proteins formed the basis of my doctoral work in the Prestegard laboratory and because Jim's CF_2 study provided a hint as to how to exploit the multiplicity of spin interactions in the context of a methyl group that led to the development of methyl-TROSY NMR much later.

Jim also had a strong interest in protein structure and dynamics and carried out a series of important studies using acyl carrier protein (ACP) that merged his fascination with both lipids and proteins. These were the early days of structural studies by NMR and it was not clear what the best approach would be for solving structures on the basis of NMR constraints. The Prestegard laboratory contributed to addressing this important question through studies on ACP and later used this protein as a platform to develop new experiments for measuring coupling constants to extract information about local conformation. Perhaps the work that Jim is most famous for, leading to a shared Laukien Prize with Ad Bax and Aksel Bothner-By in 2002, was in connection with the development of orientational restraints such as residual dipolar couplings for structural and dynamics studies of proteins. As mentioned above, Jim had been working in this general area for decades but his famous PNAS paper coauthored with Joel Tolman really laid

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the foundations for the field. This study was based on magnetic alignment that exploited the high susceptibility anisotropy of myoglobin and required careful measurements because the resulting residual dipolar couplings were no more than 5 Hz in absolute value and mostly around −2 to 2 Hz at 750 MHz. Subsequent studies of myoglobin dynamics by the Prestegard group brought to light just how dynamic proteins could be and stimulated much discussion in the NMR community about the floppiness of these molecules. As is often the case in a nascent area of tremendous potential, new experiments had to be developed to measure these residual couplings and Jim's group played a leading role in this endeavor as well.

It was at about this time that Jim decided that a move to the Carbohydrate Research Center at the University of Georgia as an Eminent Scholar of NMR Spectroscopy would be appropriate. After 27 years in the Chemistry Department at Yale, and in mid-career, this transition – though certainly not forbidden – must have been one of high energy. Yet Jim quickly established himself in Georgia building up a famous center that remains to this day extremely well-equipped with high field NMR spectrometers for addressing a variety of important biophysical questions. Jim also played a major building role in the University community, serving on a large number of committees and offering his wise council to a large number of colleagues that continues unabated. Although Jim has become an Emeritus Professor he remains as scientifically active and as intellectually alert as ever. His work continues its strong focus on macromolecular structures involving carbohydrates, proteins, and lipids using novel methodologies that often his group develops. Jim continues to be an expert in magnetic resonance but is also at the leading edge in studies of cell-surface carbohydrates where his work has garnered much acclaim from carbohydrate scientists whose focus is distinct from NMR spectroscopy.

It is with great respect that Jim's trainees salute him for his widespread contributions to science and for the wonderful mentoring that each received during their stay in his laboratory. Jim's legacy is rich, both scientifically and personally, and we wish him much good health and happiness as he continues to set a wonderful example of how to be a great scientist and person.

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