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In Memoriam

Prof. Luis Diaz and the Early Days of Solid State NMR in Argentina – Recollections from his First Graduate Student

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It was with surprise and sorrow that I received Prof. Desimone's letter informing me of the compilation of this special issue, to be published *in memoriam* to the passing away of my Ph.D. advisor Prof. Luis Diaz. While we hadn't been in touch for several years, my recollections of the 10+ years that we spent together remain vivid in my mind.

I began studying towards my Ph.D. with him early in 1986, doing organic solid state nuclear magnetic resonance (NMR) at the School of Pharmacy and Biochemistry of the University of Buenos Aires. But in fact I had known Luis and his family –particularly his brother Francisco and wife Silvia- from much earlier; in fact, at a personal level. Indeed, sometime in the late 1970s, Luis began studying towards his Ph.D. in the Laboratory of Phytochemistry under the supervision of my father, the late Benjamin Frydman. At that time I was a teenager starting high-school, and Luis became quite close to my dad –he and his relatives were, to some extent, members of our "extended family". I therefore had numerous chances to meet him as a teenager, both in the lab as well as in our home. I vividly remember getting from him the impression of being "the coolest young scientist" one could aspire to be. Luis was handsome, skilled in the lab, an athletic, long-haired and bearded soccer player, he appeared full of enthusiasm, and he was engaged -later married- to a charming young lady. The image of him with a cigarette in his lips while doing some mysterious organic chemistry synthesis (although my dad didn't smoke, neither him nor anyone else saw anything unusual in smoking within a closed lab surrounded by flammable solvents), or of magically improving the field homogeneity of an NMR magnet with his right hand while his forehead reclined on his cigarette-holding left palm, are carved in my memory.

While coming from a biochemical sciences background, Luis did not hesitate in tackling during his Ph.D. the most physical, instrumentally-intensive challenges in the lab on those days. These clearly included keeping up and running new experiments on the FT80 Varian pulsed NMR spectrometer, which with its 4kbyte computer, bluish 4" monochrome display and ca. 1 ton magnet, exerted on Luis (and on my thirteen year-old eyes) an irresistible attraction as the *non-plus-ultra* instrument for probing the physical nature of matter. And so, while having joined Phytochemistry with the intention of carrying out organic synthesis and biochemical studies, Luis's research interests slowly but surely drifted into the challenging realms of NMR. Towards the end of his Ph.D. this attraction must have overpowered Luis's original training choices, as he decided to switch directions and further his training by delving into the emerging discipline of high resolution NMR of organic solids.

Solid state NMR had been reinvigorated in the late 1970s with the advent of cross-polarization and magic-angle-spinning (CPMAS), and Luis decided to explore the potential of this new and not-entirely-understood branch of science. Toward this end he received a fellowship that enabled him– accompanied by his wife and their recently born first daughter Cecilia– to join the laboratory of the late Prof. David M. Grant at the University of Utah. At that time David Grant was one of the most senior, renowned and distinguished specialists in this challenging field, deeply respected by his local colleagues (who eventually named the prominent chemistry facility housing his laboratory in his honor),as well as by peers worldwide. By the 1980s Grant had already made numerous seminal contributions to the field spanning outstandingly wide breadth and depth; from theoretical "Grant rules" on how to obtain chemical structures form ^{13}C chemical shift displacements, to insightful discoveries on the nature of ^{1}H-^{13}C heteronuclear cross-correlated relaxation (that have eventually enabled the application of NMR to very large proteins), to central hardware designs such as the Alderman-Grant resonator that is still used in contemporary NMR and MRI. Even more complex and less mature, both from theoretical and experimental perspectives, was the world of solid state NMR that Luis had decided to join. Surely a "culture shock" of sorts must have greeted the young father landing for the first time in the USA, which had to equip himself with tools in physics, electronics and mechanical design that surely a degree in biochemistry didn't supply. Like a boatman rowing against strong currents the beginnings in the

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1873-4316/16 $58.00+.00

Utah lab were far from easy, as I had a chance to confirm when in a personal trip my parents took me in a visit to Salt Lake, where we had dinner with Luis and Silvia.

Still, after a few years of very hard work Luis had found his way into the field, in a *modus vivendi* that allowed him to perform and use CPMAS NMR of solids, without having to go into the intricate spin physics that dominate these experiments, and explore its use in the still active field of biomolecules and pharmaceutical analysis of polymorphs and drug-excipient interactions [1-3]. Still, after a few years in America and while probably having a chance to stay there if they so wished, the Diaz's opted for returning to Buenos Aires. Luis applied and earned an assistant professorship position in Instrumental Analysis at the School of Pharmacy; still, it would have been a waste of his hard-earned Utah knowledge if this move would have meant departing from solid state NMR. There was, as mentioned, the FT80 NMR – yet there was little that this fully-booked and already obsolete platform could offer for performing the mechanically demanding and high-powered CPMAS experiment. To deal with this challenge Luis performed another act of ultimate ingenuity, when he and others persuaded David Grant to donate a 1960s XL100 spectrometer (Fig. **1**) to the School of Pharmacy. This machine, which had been modified by the Utah group form its original solution-state continuous-wave design to a pulsed CPMAS solids NMR operation, probably meant little for the well-equipped Grant lab, but provided a fundamental seed for NMR activities in Argentina over the coming decades. It was a win-win situation also for the Utah side, as it could enable to continue some of the studies that Luis had begun while in the US, while providing hardware that had already been decommissioned and which was already far from being state-of-the-art or even CPMAS-operational.

Still, the assimilation of this 3.5 tons "monster" was far from trivial, both in terms of its sitting, its powering up, and foremost its reliable, steady operation for scientific projects. The NMR lab in particular was rather "unconventional". It was located in a dark, strangely-odored second basement that the School of Pharmacy shared with the School of Medicine's morgue. This lead to unusual sights of all kind of body parts whose images have never left me, including well-fed cats and black rodents of impressive sizes. The lab itself was also far from conventional; as the School provided little or no infrastructure and procuring goods from Varian or other money-demanding vendors were out of the question in a perennially cash-strapped School, Luis had to make his operation entirely self-sufficient. This meant relying on large, cheap air extractors instead of on air conditioning, on an open flow water system for cooling the multi-kW magnet instead of a chiller, on an incredibly loud air pump to supply the air flows needed for CPMAS instead of a central air compressor, and entirely autonomous machining and electronic corners where all the mechanical and instrumental probe and console components needed for carrying out high-performance CPMAS were manufactured. To this effect Luis had recruited an outstanding partner, Eduardo Tessore, a most talented engineer that performed all kind of magic in-electronics, facilities and machining.

I arrived into the lab as Luis's first graduate student in the summer of 1985/1986, shortly after the magnet had been installed in an operation that –owing to an underpowered forklift that tipped over– almost cost Luis his life. With its unusual setting, noise, heat and odors, the lab impressed me as partly NASA / partly sweatshop. Still, in addition to the equipment, Luis had assembled another essential resource that was most valuable in those pre-internet days and third-world settings: books and Xeroxed monographs. These included wonderful texts that contained the secrets of how NMR worked –many of them donated by the British consulate before the Falklands War. Luis and Eduardo were aware that there was more in those texts than what their background allowed them to assimilate. Still, Luis put them all – including the wonderful classical treaties by A. Abragam, U. Haeberlen and H. Spiess, and the two-volume 1966 compendium from Emsley/Feeney/Sutcliffe- in my hands, and strongly encouraged me to read them all from beginning to end. Reading and re-deriving the contents of these books would became my daily activity, from well before dawn, over several years; explaining what I had learned upon arriving in the lab and while sipping the morning "mate" (a sort of herbal tea), and discussing their insightin terms of what we were trying or what we could do on the XL100, was also part of our daily morning routine.

Most of the rest of my initial Ph.D. days were invested into realizing and optimizing the CPMAS experiment, which for long months resisted to yield quality data in all but the simplest tuning compounds. For me this involved learning form Luis and Eduardo the secrets of machining "Andrew rotors" and Macor turbines for spinning the solids in the kHz regime, building "flip-flop" and phased-locked-loop circuits to perform the phase-shifts that the experiment needed but the spectrometer did not provide, designing and constructing low-noise preamplifiers, op-amp circuits and duplexers, and double-tuning the single-coil receiving NMR circuitry using those ever-arcing capacitors that our meager budget forced us to open and clean by sonication in detergent plus acetone on a weekly basis.

Challenging as it was, this environment–which was also devoid from travels to international conferences or access to journal except JACS and the Accounts of Chemical Research- did wonders in gaining my appreciation for the ingenuity and potential of all things related NMR?. It also allowed us to produce a string of basic studies on a variety of hardcore topics including analyses of valence and proton tautomerism in organic solids [4-6], NMR studies on drug/excipient interaction [7], on researches on the couplings between spin-1/2 and quadrupolar nuclei [8-10], and dynamic processes in solids [11].

Besides the scientific and technical educational exchanges between Luis, Eduardo and me over those long days, research in those seminal years also included a number of encounters with scientists that greatly contributed and enriched our activities. One was my dad, who would come down from his Phytochemistry lab around the early afternoon –when the building basement was impregnated with the smoke and delicious smell of the "asados" that the janitorial staff would grill every day. I can still hear his strong knocking:

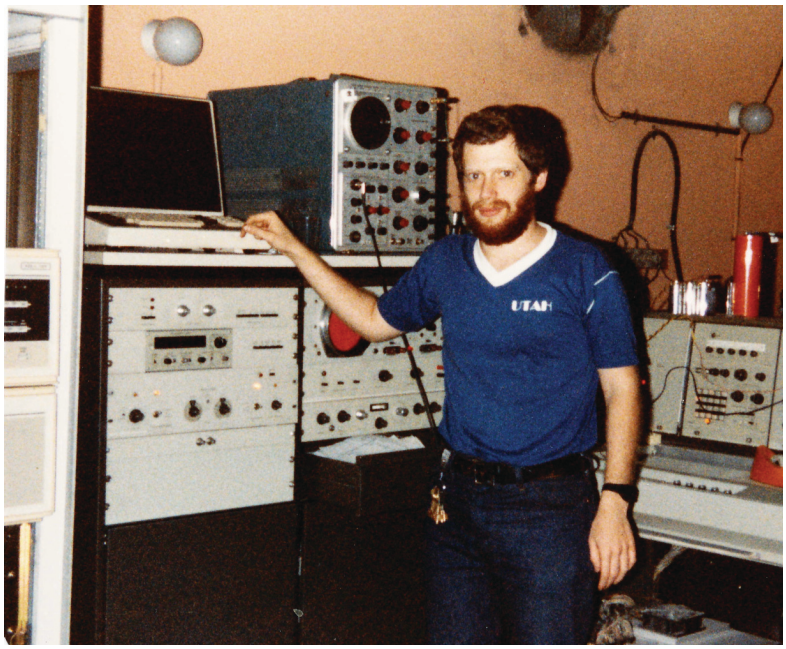

Fig. (1). The author operating the Varian XL100 NMR spectrometer brought by Luis Diaz from the University of Utah to the University of Buenos Aires.

clapping the door's heavy metal sliding lock onto the 10 cm thick wooden plates, requesting entrance into the lab in order to sit and discuss the new scientific developments of the last 24 hours. Another seminal contribution came from a young postdoc (now Professor) Alejandro Olivieri, who besides quantum mechanics taught me much about the importance of questioning common wisdoms regarding what can and cannot be achieved with limited research resources. A third team member to join was an even younger undergraduate (eventually graduate and now also Professor) Mariano Grasselli, who brought into the lab the art of simulating spectra using Pascal, together with the first 3.5" floppy disk I had seen. Last but not least was the joining of another brilliant engineer, Santiago Sobral, which though younger than Eduardo made up with skill and vision what his just-earned engineering studies had not yet taught him.

Eventually, by hook or by crook, experiments began to work and results to emerge. This gave both Luis and myself a chance to leave the "charming" atmosphere and noises of the lab and find refuge –at least for a few hours a day– in the more normal atmosphere of Luis's "Cátedra": office and lab space that he had been given in the main building's third floor. There we both had a chance to expand our activities – in his case by stepping into the realm of other analytical techniques, particularly mass spectrometry; in mine into the realm of numerical simulation of NMR phenomena in solids, using the DEC microVax computer that eventually showed up in Luis's lab. While exciting and adding a lot to our productivity and horizons, these developments also bifurcated Luis's interests from mine. We would still hold NMR discussions; we would still charge against the XL100 when he refused to deliver data; we would still keep up with each other's lives –but no longer in a regular basis. Eventually, new GC-MS and cyclic voltammetry instruments started catching Luis's inquisitive mind, and his interests in NMR decreased -while mine went into the opposite direction, expanding into the realm of nuclei other than ^{13}C and experiments involving liquids and liquid crystals. This divergence, coupled to both Luis's and mine strong single-mindedness, devotion to long days of work at the expense of other important things in life, and eventually my departure from Argentina to the US, weakened the personal links that among us had for years been particularly strong. Little can I do at this point, however, other than regretting that Luis's untimely departure did not give us a fairer chance to rekindle them.

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Received: November 22, 2015 Revised: December 02, 2015 Accepted: December 27, 2015