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Preface

António Xavier and his contribution to the development of Bioinorganic Chemistry

António V. Xavier was born in Oporto, on August 31, 1943. He began a degree in Chemical Engineering at the University of Oporto and in 1965 he moved to the Technical University of Lisbon, finishing the course in 1969. Bob Gillard, who gave a series of seminars in Lisbon in 1968/1969, sparked his interest in studying the role of metal ions in the Chemistry of Life, which would develop throughout his scientific career. After a brief stint at the Gulbenkian Science Institute in Oeiras, he applied for a scholarship from the Gulbenkian Foundation to fund a Ph.D. at Oxford in the laboratory of R.J.P. Williams. Not wanting to delay the start, he decided not to wait for the outcome of the application, asked for a bank loan and set off with his wife, Paquita. He worked day and night and produced a remarkably innovative thesis that included the development of NMR methods for studying the structure of flexible molecules in solution, using paramagnetic lanthanide ions as extrinsic probes. The boundless energy of António Xavier and his scientific insights were fundamental to enabling these pioneering efforts with the ultimate aim of obtaining structural information in proteins, just prior to the introduction of two-dimensional NMR techniques. Four years of work resulted in 12 scientific articles, one of which was in *Nature* [1]. Once his doctorate was completed in 1972, I think that I can detect the influence of J.J.R. Fraústo da Silva in his decision to return to Portugal, leaving behind extremely attractive invitations. In 1973/74 he was Assistant Professor at Instituto Superior Técnico (IST), joining the newly founded Universidade Nova de Lisboa shortly after, in 1974. In parallel, he began the Molecular Biophysics group at the Center for Structural Chemistry (CQE), Complex I in IST (Group V). Starting literally from scratch, he fought tirelessly with characteristic unwavering determination, not hesitating in the face of obstacles that seem insurmountable to others. The dynamism, enthusiasm and passion earned him the name of “enfant terrible” of Portuguese Science in the 1970’s. In 1975, he purchased the first NMR spectrometer, a JEOL 90 MHz installed at CQE. I well remember his joy at the arrival of this equipment. Of course a 90 MHz machine was not comparable with the 270 MHz spectrometer that he had worked with in the last years of his thesis at Oxford, but he was by no means discouraged by this, or gave up, or slowed his efforts, or fell into the trap of relying on his ex-supervisor, that would have given access to incomparably better conditions at the expense of much less effort. Quite the opposite, his main intent was to establish the infrastructures needed to develop science at a competitive level, in Portugal. The scientific work of António Xavier was greatly influenced by the collaboration initiated in 1974 with Jean LeGall, a great friend and excellent scientist with whom he collaborated almost until his death in 2003. Jean was an expert in sulfate reducing bacteria, from which a multitude of coloured proteins were isolated and characterized by spectroscopic techniques, including

NMR and EPR. The complementarity of skills and the deep friendship that they established were, in large part, the key to successful collaboration.

In 1979, in collaboration with H.A.O. Hill, he organized a NATO-ASI conference in Tomar, Portugal, on “Metal Ions in Biology” which would become a memorable milestone in the history of Bioinorganic Chemistry. According to Robert R. Crichton, this was probably the first Bioinorganic Chemistry meeting, and 3Fe/4S clusters were proposed then for the first time (ITQB Newsletter, 4, 2005). It was during this conference that an extraordinary episode occurred that is reported here to illustrate the somehow brave, rebellious, and lively, character of this young man of 36 years. The social program included a “Garraçada” (a kind of bullfight with young bulls), in a bullring near to Tomar. It was with fear and disbelief that we saw António Xavier, wearing white trousers and shirt, step onto a box placed in the arena. I learned later that the aim was to prove the implausible theory that bulls are blind to the colour white. After a few minutes of indifference, the animal charged the crate: the inevitable crash resulted in a severe leg fracture that necessitated an immediate transfer to hospital in Lisbon.

In 1985, António Xavier organized two other major meetings in Portugal (Praia da Falésia, Albufeira), the Second International Conference on Bioinorganic Chemistry, followed by a Special FEBS Meeting on Metals, Ions, Proteins and Membranes, which opened with a lecture by his PhD supervisor, R.J.P. Williams, on “The symbiosis of metals and protein functions”.

A born entrepreneur, he always wanted more, and in 1986 he founded the Instituto de Tecnologia Química e Biológica (ITQB), in Oeiras, pioneering a completely interdisciplinary format. He sacrificed much of his time and energy to boring tasks, precious time that he would have been able to devote to “his” science. He did this so that many researchers (us) could have competitive working conditions. It is not hard to imagine the difficulties and frustrations that he had to overcome, the energy that he had to mobilize. One wall of his office displayed an illustration with the expressive phrase from the book “Through the Looking Glass” by Lewis Carroll: “... here, you see, it takes all the running you can do, to keep in the same place. If you want to get somewhere else, you must run at least twice as fast as that!”

Despite using various spectroscopic techniques, NMR was his method of choice. The technique is expensive and highly dependent on advances in technology, and not suitable for those who have no resources to update equipment. In addition to the old 90 MHz spectrometer, he acquired a 300 in 1980, and in 1989 ITQB was able to install a second 300 and a 500 MHz spectrometer. In the plans of the new building, he carefully planned the room destined to receive a very high field spectrometer, an 800 MHz spectrometer which eventually was installed in 2007. Unfortunately

António did not live long enough to celebrate that exciting moment.

After so many years invested in building excellent working conditions, he wanted to be rid of administrative positions, red tape, corridors of Ministries, and finally devote himself full time to what gave him most pleasure: science. At the end of the ITQB installation period, in 1999 he did not accept the position of Director. In his view, the Institute he founded should stand on its own feet without the leadership of its author. Back in the lab, he made a sabbatical visit to Princeton University in 2001, finally having time to analyze results, imagine experiments, design models, test theories. Only a genuine love for science can explain this low profile, when he might well have opted for the fanfare of power and politics. His passion for science was the “oxygen” which gave him the energy to resist the disease that debilitated him for eighteen months. The certainty of the nearness of the end never led him to quit.

He came to ITQB every day, eagerly accepted invitations to lecture (the last was in December 2005); he never stopped working. He was disappointed because he could not finish an article in which he tried to refine the elegant model of molecular cooperativity that he conceived, and which he worked on obsessively during his last year [2,3].

António Xavier has a remarkable body of scientific work: he published about 250 scientific papers, mostly in the field of metalloproteins and mechanisms of energy transduction. An approach combining Chemistry, Structural and Molecular Biology resulted in the discovery and characterisation of several novel metal ions (clusters) in active sites of proteins (haem and non-haem Fe, Co, Ni, and Mo) mostly isolated from sulfate reducing bacteria. In the last years his interest focussed on the structural basis for cooperativity in electron/proton coupling mechanisms involved in vectorial energy transduction processes both in small soluble



António V. Xavier (foreground) at the Third International Conference on Bioinorganic Chemistry, Leiden, 1987. Background, left to right, Kenneth D. Karlin, Harry B. Gray, Ivano Bertini, Jan Reedijk, Helmut Siegel and Bo G. Malmström.



Instituto de Tecnologia Química e Biológica (ITQB), Oeiras, Portugal. António V. Xavier was the Founding President of ITQB from 1986 to 1998. Currently ITQB hosts 62 independent laboratories, with nearly 350 researchers.

mutiredox centre proteins, such as the tetrahaem cytochrome c_3 and, transmembrane enzymes, such as cytochrome c oxidase. He was visiting professor at universities of great reputation, gave lectures in the four corners of the world, played a central role at the international level in promoting research and teaching of the disciplines of Bioinorganic Chemistry and Biochemistry. He received important distinctions, the “Ferreira da Silva” Award of the Portuguese Society of Chemistry in 1985, was knighted as “Chevalier de l’Ordre des Palmes Academiques” in 1980, “Officier de l’Ordre des Palmes Academiques” in 1988 and as “Comendador da Ordem Militar de Santiago de Espada” in 1997. Unfortunately, he did not live long enough to receive the EUROBIC medal in July 2006, a distinction that should have been given years before. Soon after his death in May 7, 2006, Christian Brévard, President of Bruker BioSpin, announced the Prize António Xavier, which is awarded annually to distinguish scientific work carried out in Portugal in the area of Magnetic Resonance.

I knew António Xavier for thirty-three years, but it was during his last five years that I truly realized his deep love for science, his nobility of character, his generosity, boundless energy, the amazing courage with which he faced adversity, the ability of anticipation, of devotion to work, and especially his passion for the Institute he created, ITQB. I was deeply emotional and almost without words when he said that ITQB was much more important to him than life itself, and ITQB was even the subject of the few words I exchanged with him a few days before we parted for the last time. António Xavier was an educated man, affable, sensitive, gentle and courteous to all and especially to subordinates, a man

of the left, but without the shackles of party affiliation. He did not deal well with media attention, was shy of cameras, but had an invaluable wisdom, created over an intense life experience that was so much richer than could be expected for the 550 thousand hours that were granted to him.

Thanks António!

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References

- [1] Barry, C.D., North, A.C.T., Glasel, J.A., Williams, R.J.P. and Xavier, A.V. (1971) Quantitative determination of mononucleotide conformations in solution using lanthanide ion shift and broadening NMR probes. *Nature* 232, 236–245.
- [2] Xavier, A.V. (2002) A mechano-chemical model for energy transduction in cytochrome c oxidase: the work of a Maxwell's God. *FEBS Lett.* 532, 261–266.
- [3] Xavier, A.V. (2004) Thermodynamic and choreographic constraints for energy transduction by cytochrome c oxidase. *Biochim. Biophys. Acta – Bioenerg.* 1658, 23–30.

Helena Santos*

Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, Av. da República-EAN, 2780-157 Oeiras, Portugal

* Fax: +351214428766.

E-mail address: santos@itqb.unl.pt

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