

# A personal account of the history of X-ray crystallography at the University of La Plata, Argentina

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Prompted by visionary political leaders and a flowering economy, the University of La Plata was founded in 1905, the third Argentinian university after the Universities of Cordoba (1613) and Buenos Aires (1821). Differing from the older universities, more prone to professional formation, the new university was oriented towards teaching and scientific research following western European academic tradition. Along with the university was created the Institute of Physics, the first of its kind in Latin America. To pursue the foundational plan, the university recruited distinguished German physicists, some of whom became the first directors. From the start, the institute became acquainted with Röntgen rays, their generation and use, initially for radiographic images and later in occasional diffraction studies. The first dedicated crystallographic X-ray diffraction laboratory was set up in the early 1970s, when it solved the first molecular structures. Soon the fascination brought about by a methodology that afforded the visualization of atoms, molecules and crystals lured the local and national physical chemistry communities. In close partnership with an equally oriented laboratory at the University of Sao Paulo, Brazil, and in collaboration with several physical chemistry laboratories from Argentina and the Latin American region, and also from Europe, we undertook studies on the crystal structures and physicochemical and spectroscopic properties of a wide range of materials, including inorganic, organic, bioinorganic, metal-organic, organic-metal, supramolecular, pharmaceutical, organic minerals and liquid crystals. The present essay is a personal account of the origin and development of structural X-ray crystallography at the University of La Plata and its impact on the scientific research of Argentina and Latin America.

## 1. A new university for a new square lattice-shaped city

The National University of La Plata (UNLP) was created in 1905 by Joaquín V. González (Argentinian academic, educator, politician, 1863–1923) some years after the foundation of the city (by Gov. Dardo Rocha in 1882). La Plata city is located 55 km southeast of the Argentinian federal capital, Buenos Aires, and 12 km southwest of the La Plata River coast. It was designed and built from scratch by engineers, urbanists and architects in the prevailing western European style to serve as the seat of government of the Buenos Aires Province. The foundational core of the city has the unique layout of a square-bound lattice enclosing  $40 \times 40$  100 m squares blocks, featuring a park every six blocks in both directions and crossed by an arrangement of convenient diagonal streets (*The City of the Diagonals*).

Part of the foundational plan of the university was the creation of the Institute of Physics. It was the first centre for the research and teaching of physics in Latin America and, in fact, among the first in the southern hemisphere.



### 2. Beginnings of the Institute of Physics and its acquaintance with X-rays

The Institute of Physics (IF) was directed from 1906 until 1909 by Tebaldo J. Ricaldoni (Uruguayan–Argentinian civil engineer, inventor and teacher, 1861–1923). During his tenure, the university imported from Germany (Max Kohl Chemnitz) some 2761 pieces of fine equipment for demonstrations (Museo de Fisica, <http://museo.fisica.unlp.edu.ar>). Ricaldoni wrote comprehensive lectures on experimental physics, based on that instrumentation (Ricaldoni, 1908). The section on X-rays (then called ‘Röntgen rays’) covers experiences with cathodic beams of the sort that led to the discovery of the radiation by Röntgen in 1895 and describes its generation and some of its properties (absorption, fluorescence, *etc.*). In his course, he reproduced the first ever X-ray radiographs taken at La Plata, using as a source a Focus de Pouillet X-ray tube powered by a Ruhmkorff coil set to produce a 10 cm long spark and fitted with a mercury interrupter. One of the radiographs (taken *ca* 1907, after 4 s X-ray exposure) mimics the famous one taken by Röntgen in 1895 and shows a hand where can be observed an ankylosis developed in one finger.

Previously, news of Röntgen’s discovery had reached Argentina *via* a telegram from Vienna, published in the La Nacion newspaper on 30 January 1896. Dr Jaime Costa (Argentinian physician and professor, 1860–1909) was the first to employ the new technology to radiograph the elbow of a patient in 1898.

To pursue high-quality research and teaching in physics at the IF, the university recruited several distinguished German physicists, chemical physicists and engineers. Two of the most influential were Emil Hermann Bose (German physicist, 1874–1911) and Richard Martin Gans (German–Argentinian physicist, 1880–1954).

Emil H. Bose studied physics in Göttingen and obtained his PhD degree in 1898 under Walther Nernst. He researched electrochemistry, thermochemistry, fluid dynamics, the kinetic theory of matter and liquid crystals. Despite his youth, he excelled as an academic administrator in the organization of the Physics Institutes at Breslau and Danzig Universities, where he was professor. He was hired to succeed Ricaldoni in 1909 as Head of the La Plata Physics Institute. With the help of fellow scientists and qualified engineers, he adequately equipped a newly assigned building to pursue world-class research and teaching in physics and physical chemistry. Unfortunately, shortly after, he contracted typhus and died in 1911 aged 36.

Later in 1914, the Physics Institute chair was occupied by Dr Gans, who made important contributions to a wide range of topics in physics, including magnetism, the electrodynamics of moving bodies and thermodynamics. He is probably best known for his theoretical contribution to the scattering of electromagnetic waves (light) by colloidal particles (Tyndall effect) of any size and shape, sometimes quoted in the literature as Rayleigh–Gans–Debye (RGD) scattering.

Gans, besides his scientific achievements, was also an exceptional university educator, and science and teaching organizer and administrator. His two terms as head of the IF

(1914–1925 and 1947–1951) signalled truly golden periods for the institution.

### 3. The first laboratory of structural X-ray diffraction at La Plata

Besides sporadic use of X-ray diffraction in a pair of doctoral theses and a few articles, structural X-ray crystallography started in earnest at the IF in the 1960s. In 1965, Dr Alberto G. Álvarez, with the collaboration of his doctorand Eduardo E. Castellano and graduate student MSc Juan M. Andrieu, founded the Laboratory of X-rays. It was initially dedicated to the physics of X-ray generation by electron bombardment.

During the 1969–1970 period, Castellano realized a post-doctoral stay at the Chemical Crystallography Laboratory in Oxford, where he studied structural crystallography by X-ray diffraction under the supervision of Professor Keith Prout. This methodology is based on one of the most important discoveries in physics, namely the diffraction of X-rays by crystals. The phenomenon was conceived by Max von Laue in early 1912, inspired in Peter Ewald’s PhD work (under A. Sommerfeld), and demonstrated in a legendary experiment by Walter Friedrich and Paul Knipping (former doctorand of W. Röntgen) in Munich, Germany. An elated Albert Einstein would write in a 1912 letter: ‘*It is the most wonderful thing I have ever seen. Diffraction on individual molecules, whose arrangement is thus made visible.*’ Shortly after, in mid-1912, news of the discovery reached England and William Henry Bragg, who convened his son William Lawrence to work with him on the subject. The Braggs implemented the instrumentation (W. H. Bragg) and theoretical reinterpretation (W. L. Bragg) of the phenomenon to undertake the determination of simple crystal structures (Piro, 2016, and references therein).

Upon his return to La Plata, Castellano assembled in 1971 an elemental but complete laboratory to undertake structural work (X-ray generators, cameras for photographic data collection, crystallographic program packages, *etc.*). Thus, he founded what can reasonably be claimed to be the most important crystallographic laboratory of small- and medium-sized molecules in Argentina, and one of the most relevant in Latin America. There they had their initial training as graduate students who became distinguished macromolecular crystallographers, including D. A. Podjarny (Institute of Genetics and Molecular and Cellular Biology, CNRS, France), J. Navaza (Ecole Normale Supérieure de Cachan, France) and P. M. Alzari (Institut Pasteur in Paris).

Castellano thus endowed continuity and ‘aggiornamento’ to an old tradition of the country in structural X-ray diffraction (Ewald, 1962). It dates back to 1929, when H. Damianovich (a physicochemist, then at the University of Buenos Aires, UBA) travelled to Professor J. -J. Trillat’s laboratory in Paris to study by powder X-ray diffractometry the structure of platinum electrodes exposed to helium (Damianovich & Trillat, 1929), followed in 1933 by E. E. Galloni, who studied under Professor J. Palacios in Madrid the crystal structures of minerals (Palacios & Galloni, 1934). However, it was not until 1938, when using a powder X-ray Debye–Scherrer camera

installed at the Institute of Experimental Medicine of UBA, that the first structure to be wholly determined by X-ray diffraction (by trial and error on platinum oxide, Pt<sub>3</sub>O<sub>4</sub>) in Argentina was carried out (Galloni & Roffo, 1941).

The newly founded X-ray diffraction laboratory in La Plata, led by Castellano and in collaboration with local organic chemists, achieved in 1972 the first single-crystal structural determination of organic substances (Rivero, 1975), entirely measured, solved and refined in the laboratory. However, the greatest interest in the knowledge provided by the crystal and molecular structures of solids would come from the field of coordination chemistry, through Professor Pedro J. Aymonino. He was a former disciple of Hans Schumacher (German–Argentinian chemist, 1904–1985), considered to be one of the fathers of Argentinian physical chemistry, and himself a leading inorganic chemist in the country. Aymonino's laboratory would carry out the chemical synthesis and crystallization of coordination complexes and their spectroscopic characterization. This collaboration would result in the laboratory's first structural determination of coordination solids. The X-ray diffraction patterns were collected by oscillation and Weissenberg photographic methods, and the structures were solved by Patterson and Fourier methods and refined by least-squares methods. The strontium nitroprusside salt, Sr[Fe(CN)<sub>5</sub>NO]·4H<sub>2</sub>O (Castellano *et al.*, 1977), which followed the barium analog (published in 1973), required the visual estimation of the relative intensities of 1020 Bragg reflections, registered onto 5 films (!), and was part of my doctoral thesis (Piro, 1977).

Invited by Professor Yvonne Mascarenhas in 1977, Castellano emigrated to a position at the Institute of Physics of Sao Carlos (IFSC), University of Sao Paulo (USP), Brazil. There he would make a substantial contribution to the development of the structural crystal–physical chemistry of his adopted country and the Latin American region. At the same time, he would keep a close and fruitful collaboration with the La Plata laboratory which extends up to the present.

At the end of 1977, I moved to a two-year postdoctoral position at Dr Paul B. Sigler's laboratory of macromolecular crystallography of the Department of Biophysics and Theoretical Biology, University of Chicago. There, I developed ideas inspired by the thermodynamic fluctuations of statistic mechanics initiated in La Plata in a pioneer approach to the solution of the 'phase problem' of X-ray structural crystallography through information theory. The new approach was based on maximizing the structural entropy subjected to the experimental knowledge of X-ray diffraction intensities (Piro, 1983). Also, now in collaboration, I undertook preliminary studies on the molecular structure of an enzyme involved in the isomerism of a hormone steroid (Westbrook *et al.*, 1984) and determined the crystal structure of calcium oxalate monohydrate (Whewellite), a component of kidney stones (Deganello & Piro, 1981).

#### 4. The return

Upon my return to Argentina at the end of 1979, I resumed previous collaborations, now enhanced by access to data

obtained by Castellano in Brazil employing an automatic X-ray diffractometer.

The first structure determined in the context of this collaboration was the cobalt coordination complex K<sub>3</sub>[Co(CN)<sub>5</sub>N<sub>3</sub>]·2H<sub>2</sub>O (Castellano *et al.*, 1982). This compound and the previously solved barium and strontium nitroprussides constitute excellent examples of the structure–physical property relationship in solids. In fact, the crystallographic structure of the Sr and Ba nitroprusside salts revealed an antiparallel pile-up of neighbouring nitrosyl (NO) groups in the lattice. This gives rise to a strong transition dipole–dipole coupling which is seen in the IR absorption of this vibrational mode of the solid (González *et al.*, 1984). This finding was followed by a detailed quantitative study of the coupling through isotopic substitution methods (González *et al.*, 1986).

The crystal structure of the cobalt complex showed a similar arrangement of neighbouring azide groups in the lattice, again indicating a coupling between the strongly polar antisymmetric stretching vibrational modes of these groups in the crystal. This interaction was confirmed by combined IR and Raman spectroscopic analyses (Piro, 1985).

At that time (in 1986), we published the first of a series of articles on metastable states in the family of isomorphous crystals Na<sub>2</sub>[M(CN)<sub>5</sub>NO]·2H<sub>2</sub>O ( $M = \text{Fe}^{\text{II}}, \text{Ru}^{\text{II}}$  or  $\text{Os}^{\text{II}}$ ), a true tribute to the Mendeleev Periodic Table! Such metastable states are potentially useful in the optical storage of information and the interpretation of their IR spectra required knowledge of the optics of absorbent anisotropic crystals (Güida *et al.*, 1986, 1988, 1993, 1995, 1997).

#### 5. Crystal optics

Prompted by the need to interpret the spectroscopic behaviour of thin anisotropic and absorbent single-crystal plates, I realized the lack in the bibliography of a complete treatment on the interaction of electromagnetic waves (light) with those solid samples. I then undertook the derivation of new equations describing the phenomenon, which are of considerable theoretical interest in crystal optics and of practical relevance in the spectroscopy of solids (Piro, 1987). The equations were then applied to the interpretation of the vibrational structure of several solids (Piro *et al.*, 1987, 1988, 1989a, 1991; Güida *et al.*, 1989, 1992).

#### 6. High- $T_c$ superconductors

In 1986, J. G. Bednorz and K. A. Müller, then working at IBM, discovered the phenomenon of superconductivity at relatively high temperatures (boiling nitrogen temperature) in an improbable ceramic material (Bednorz & Müller, 1986). The finding triggered intense worldwide research activity never before seen in physics. As knowledge of the crystal and the molecular structures of these solids was key information in efforts to understand their workings, X-ray and neutron diffraction crystallography were from the beginning important tools for the study of these materials. Taking advantage of the synthesis facilities of the Materials Laboratory at the IFSC,

USP, we made with Castellano a brief excursion into this fashionable subject (Andreea *et al.*, 1987; Piro *et al.*, 1989*b*). Furthermore, employing a kit built at the IFSC, in July 1987 we demonstrated the phenomenon for the first time in La Plata to an audience of participants of the Latin American School of Physics (ELAF 1987) and other interested attendees.

### 7. Crystal physical chemistry of organic minerals

Shortly after my return to Argentina, I started an active collaboration with Enrique J. Baran, a former doctorand of Aymonino who became a world authority on the crystal-physical chemistry of bioinorganic and organic mineralogical materials. Among the around 60 published joint articles, I highlight a few of them originated in Baran's remarkable ability to identify relevant unsolved problems in coordination chemistry and mineralogy. One of them deals with the removal of long-standing structural uncertainties on an iconic complex of coordination chemistry, namely,  $\text{NaMg}[\text{Cr}(\text{oxalate})_3]\cdot 9\text{H}_2\text{O}$  (Piro *et al.*, 2015). The other is based on the synthesis of minerals, which afford high-purity single crystals (normally not attainable by natural means) adequate for detailed structural X-ray diffraction. Using this approach, and after respectively 60 and 50 years since their discovery in the basin of the Siberian Lena River, Russia, we revealed the structural beauty of stepanovite and zhemchuzhnikovite, and disclosed the fundamental role played by the crystallization water molecules and their hydrogen-bond network in the properties of these minerals (Piro *et al.*, 2016). We also undertook structural and spectroscopic work on the synthetic analog of novgorodovaite mineral,  $\text{Ca}(\text{C}_2\text{O}_4)\cdot\text{CaCl}_2\cdot 2\text{H}_2\text{O}$ , and the related synthetic  $\text{Ca}_2(\text{C}_2\text{O}_4)\text{Cl}_2\cdot 7\text{H}_2\text{O}$  salt, an interesting perfect triclinic twin featuring a layered structure that gives rise to its curious physical properties (Piro *et al.*, 2018*b*). As the heptahydrate crystal is obtained under the same preparative conditions as the novgorodovaite synthetic analog, we suggested that  $\text{Ca}_2(\text{C}_2\text{O}_4)\text{Cl}_2\cdot 7\text{H}_2\text{O}$  could be the synthetic analog of a mineral yet to be discovered. As a contribution to the crystal chemistry of organic minerals, we wrote a referential review on the subject (Piro & Baran, 2018).

### 8. Going back to the roots

Towards the end of the 1980s, I returned to the subject I pursued as a physics graduate student, namely, ligand field theory and electron paramagnetic resonance (EPR). In fact, I started a collaboration with a group led by Dr Rafael Calvo of the National University of the Littoral at Santa Fe, Argentina, to cover the structural aspects of studies dealing with the magnetic properties of  $\text{Cu}^{\text{II}}$  complexes with short chains of amino acids (two and three monomers). They are considered model systems of more complex metal-protein macromolecules. The collaboration extended until the early 2000s and produced about ten articles (Stere *et al.*, 1989; Levstein *et al.*, 1990; Calvo *et al.*, 1991, 1993; Martino *et al.*, 1991; Piro *et al.*, 1997; Castellano *et al.*, 1998; Dalosto *et al.*, 1999; Sartoris *et al.*, 1999; Rizzi *et al.*, 2000; Schweigkardt *et al.*, 2002).

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### 9. It was raining soup, and it surprised us with spoons in our hands

Concerning X-ray instrumentation, 1995 marked a milestone for the laboratory (since 1992 renamed the National Laboratory of Diffraction, LANADI). With the help of Castellano, we contacted a skillful Dutch engineer named Cees Bass, from Enraf-Nonius, to install a CAD-4 single-crystal X-ray diffractometer, equipped with a rotating-anode X-ray source and a scintillation detector. This equipment had been purchased with funding from CONICET during the late 1980s thanks to the efforts of two of my colleagues, Dr Blas E. Rivero (LANADI Director, untimely deceased shortly before the installation) and Dr Graciela Punte (who succeeded him as Director).

That year of 1995, Aymonino introduce me to Ángela F. Danil de Namor. Doctored in physical chemistry at the Southern University of Bahía Blanca and now full professor at the University of Surrey, Guildford, UK, she is renowned in the field of supramolecular physical chemistry, with an emphasis on thermochemistry, electrochemistry, UV-Vis and NMR spectroscopies, and solution conductometry. She proposed a collaboration to cover an essential aspect of the research in the field, namely, the supramolecular structure *versus* the physical chemical property relationship of those materials, particularly their chelating ability towards small organic molecules (solvent) and heavy metals. This is a subject just within the scope of structural crystallography and the proposal opened a new and stimulating line of research for which I immediately included Castellano. Surprisingly, at that time, it was raining soup, and we found ourselves with spoons in our hands! In fact, besides the old diffractometer at IFSC, USP, Brazil, now at La Plata, we had the recently installed diffractometer with an X-ray beam intensity nominally an order of magnitude higher. For sure, experimental and computational capacities have improved substantially since my first visual diffractometric measurements 20 years ago, a distinctive characteristic of the evolution of methodology, however, these supramolecules (mainly macrocyclics such as calixarenes and their complexes), of intermediate size between small molecules and biological macromolecules, could possess up to around 200 non-hydrogen independent atoms and require the measurement of between 20000 and 50000 Bragg reflections. It turns out, that due to the sequential character of the measurements with the above-mentioned diffractometers employing punctual scintillation detectors (one reflection at a time), the collection of a complete data set could take a week. These long X-ray exposition times conspired against the stability of single crystals and furthermore made it difficult (instrumentally and economically) to carry out measurements at low temperatures. This condition improves crystal stability and the data quality and the quantity of the diffraction data due to the low thermal agitation of atoms in those molecular solids. But, fortunately, instrumental

progress continued and in 2000 Castellano could have in Brazil an Enraf–Nonius diffractometer equipped with a CCD detector and facilities for low-temperature measurement. Again, Ing. Cees Bass installed the instrument and since then has carried out its periodic maintenance and always answered, from any place in the world where he happened to be, Castellano's phone calls to solve technical issues with the equipment. During a dinner at Castellano's home, in recognition to the skills of Cees Bass, I raised my glass to propose 'a toast to the man who keeps our toys running'.

The strategy of measurements with an area CCD detector (the same as the one used for radiographic recording) is the simultaneous collection of multiple reflections. This significantly shortened the time of measurements. In fact, the collection of a complete data set which could take one day with the old serial detector, now with a modern CCD detector, can be completed in an hour.

With these advanced tools, we pursued structural studies mainly on a series of new calix[4]arenes synthesized and crystallized by Danil de Namor's group, and also inclusion complexes of these macrocycles, both with solvent molecules within their hydrophobic calix and cations in their lower-rim hydrophilic cavities (Danil de Namor *et al.*, 1998*a,b*, 2002, 2005*a,b*). Calixarene molecules, because of their versatility, are of great interest in basic organic physical chemistry and in technology due to their applications as truly molecular reservoirs for the recognition and transport of smaller chemical moieties. This ability makes these macrocycles potentially useful in the extraction processes of precious metals (like silver) and of strategically and technologically relevant compounds (such as  $\text{UO}_2^{2+}$ ), and in environmental remediation removing aquifer contaminants, such as  $\text{Cd}^{2+}$ ,  $\text{Hg}^{2+}$  and  $\text{Pb}^{2+}$ , and herbicides. Part of the project, entitled *Development of viable technologies and monitoring systems for the remediation/detection of mercury in South American waters. Design of chelators with therapeutical properties (Mercury)*, during the 2002–2005 period was supported by the European Economic Community.

Related to the above pursuit, we ventured into molecular dynamics simulations of the systems. In fact, we determined new Lennard–Jones parameters for  $\text{Cd}^{2+}$  and  $\text{Pb}^{2+}$  ions, describing their interaction with water (De Araujo *et al.*, 2007). Based on those parameters and the crystallographic structures, we have successfully simulated the synergetic and equilibrium conformation in acetonitrile solution of  $\text{Cd}^{2+}$  and  $\text{Pb}^{2+}$  complexes with steric and ketonic derivatives of *p*-tert-butyl calix[4]arene. The macrocycles have the potential ability to sequester these environmentally dangerous ions (De Araujo *et al.*, 2008).

From the articles published in collaboration with Dr Danil de Namor, I would like to highlight two which can be considered our most relevant contributions to the molecular basis of extraction processes employing macrocycles, which furthermore emphasize the value of basic research in the development of technological systems for the remotion of aquifer contaminants. One of them reports the synthesis and structural X-ray diffraction studies in the solid and through diverse

physical chemistry methods in solution of two complexes of  $\text{Ag}^{\text{I}}$  and  $\text{Hg}^{\text{II}}$  ions with a partially sulfuretted derivative of *p*-tert-butyl calix[4]arene. There we suggested the potential application of these macrocycles in the removal of mercury from polluted waters, through its anchoring to a silica support, and demonstrated its practical performance as a recyclable molecular filter (Danil de Namor *et al.*, 2011). The other relevant article deals with similar studies on two molecular receptors, both amino derivatives of calix[4]arene, and their interaction with acid chlorophenolic herbicides. In this work, we assessed the recyclable ability of the receptors during the extraction of herbicides from contaminated waters, again through the anchoring of the receptors to a silica holder (Danil de Namor *et al.*, 2015).

## 10. La Plata River connection

Brokered by Baran, in 1997 we started a collaboration with the University of the Republic at Montevideo, Uruguay, initially with Eduardo Kremer and afterward with his doctorand Dinorah Gambino. Later in 2000, the La Plata River collaboration incorporated another highly active group, led by Mercedes González and Hugo Cerecetto. After a start on the structural studies of coordination compounds (of academic interest), the Uruguayan scientists changed their line of research, orienting it towards molecular pharmacology. To this purpose, they undertook the syntheses and structural and spectroscopic characterization of potential organic pharmaceuticals and, taking advantage of their background in coordination chemistry, of metal complexes with derivatives of semicarbazone ligands. This research was prompted by the belief that some pharmaceutical complexes with transition-metal ions could improve, modulate or modify drug bioactivity (Otero *et al.*, 2003, 2006; Noblía *et al.*, 2005; Rebollo *et al.*, 2005; Aguirre *et al.*, 2005; Gerpe *et al.*, 2006; Cabrera *et al.*, 2007; Rodríguez *et al.*, 2009; Fernández *et al.*, 2013; Álvarez *et al.*, 2014; Machado *et al.*, 2014; Soba *et al.*, 2023).

The above compounds are of interest in antitumour therapies and in the treatment of diseases caused by protozoa (*Chagas*, *Leishmania* and *T. vaginalis*). As a novelty for inorganic chemists, the Uruguayan group performs quantitative studies of the structure–biological activity relationship (QSAR) with the aim of recognizing the structural requirements for enhanced activity of the pharmaceuticals. A relevant quest as the *Chagas disease*, or *American trypanosomiasis*, which is a serious public health threat in Latin American countries, where it is endemic, due to the lack of effective methods of immune prophylaxis or chemotherapies. The disease is caused by the *Trypanosoma cruzi* protozoon and affects 16–18 million infected people and further constitutes a threat for a population estimated to be about 100 million people.

## 11. Winds of changes in the local inorganic field

The inorganic chemists at La Plata also felt the necessity of a change in the orientation of their research. Aymonino would

comment that in international scientific forums people referred to inorganic chemistry as the 'chemistry of death', while organic chemistry (and, of course, biochemistry) enjoyed the status of the 'chemistry of life'. This prompted his colleagues, led by Baran, and their co-workers to start working in the interface of this secular partition of chemistry, namely, in the field of bioinorganics, and in organic substances both natural and synthetic, with potential pharmacological interest. In this collaborative framework, we approached the structures of new synthetic substances potentially useful for the supplementation of the essential  $Mg^{II}$  ion, a relevant subject in human and veterinary medicine (Wagner *et al.*, 1999a), in complexes of the lithium ion as prospective pharmaceuticals for the treatment of depression and affective disorders (Tobón-Zapata *et al.*, 1998; Wagner *et al.*, 1999b), and also of the natural drug *diosgenone*, employed in the treatment of malaria (Piro *et al.*, 2002a). We also pursued structural studies of complexes of the  $Cu^{II}$  ion with possible antitumour (Williams *et al.*, 2008; Islas *et al.*, 2014), antibacterial (López Tévez *et al.*, 2011) and antimicrobial activity (López Tévez *et al.*, 2012), and the chlorozincate of *sertraline*. This latter compound exhibits in laboratory animals a remarkable antidepressive activity (Escudero *et al.*, 2017) and is currently the subject of a patent.

The active ingredient of many medicines derives from natural products. Taking advantage of the phytodiversity in the subtropical forest of the Argentinian northwest, researchers in the region (many trained in the rigours of La Plata inorganic physical chemistry) undertook the extraction, purification, crystallization, physicochemical and spectroscopic characterization, and assessment of the structure–pharmacological activity relationship of these natural products. Structural crystallography clearly plays a key role in this endeavour, hence prompting our contribution to the investigations. In particular, in collaboration with chemical researchers from the National University of Tucumán, we addressed the structural determination of natural pharmaceuticals, including (2*R*)-(–)-6-hydroxytremetone, a bioactive substance obtained from extracts of the *Xenophyllum poposum* (Phil) V. A. Funk plant and which is employed in the popular treatment of arterial hypertension, rheumatism and others conditions (Romano *et al.*, 2008), 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-6,8-dimethyl-4*H*-1-benzopyran-4-one, extracted from *Miconia iononeura* (M.i.) *Melastomataceae*, that grows in the Yungas region of the northwestern forest and which displays antimicrobial activity (Tracana *et al.*, 2010), and 4-hydroxy-3-(3-methyl-2-butenyl)acetophenone, an antifungicide extracted from *Senecio nutans* Sch. Bip. (*Asteraceae*) (Piro *et al.*, 2013). With researchers at the National University of Salta, we undertook similar studies for complexes of lapachol with transition-metal ions, such as  $Mn^{II}$ ,  $Co^{II}$ ,  $Ni^{II}$ ,  $Cu^{II}$ ,  $Zn^{II}$  and  $Cd^{II}$  (Martínez *et al.*, 2003, 2005; Farfán *et al.*, 2009, 2012, 2015). Lapachol (LapH) is a natural product extracted from the Lapacho tree (genus *Tabebuia ipe*) and its derivatives are employed as antitumour, antibiotic, antimalarial and antiulcer agents, and against the protozoa *Tripanosoma cruzi*, causative of the *Chagas* disease.

## 12. New collaborations

At the beginning of the 21st century, we began a brief but substantive collaboration with a group led by Dr Alejandro Arvia, a former disciple of H. Schumacher and a world authority in electrochemistry. The research focused on electroplating and the relationship between the crystal structure and corrosion of materials, a subject of great practical interest for the design of passivating agents to hamper this undesirable effect (Piro *et al.*, 2000, 2002b; Bolzán *et al.*, 2007; Pasquale *et al.*, 2007).

Also in the 2000s, and in collaboration with chemical physicists at UBA, we ventured into an investigation of the molecular structures of materials which present intermediate phases (mesophases) between the highly ordered one of crystals and the totally disordered one of liquids, called *liquid crystals*. Besides their interesting physical properties, these materials are of potential technological interest because of their application in screen displays and other electrooptical devices. The compounds are normally studied in their liquid crystal phase. However, the structural information at the molecular level that it is possible to extract from these partially disordered systems is limited. This is just within the reach of X-ray diffraction methods, which provide structural information at the atomic resolution of such compounds in their crystal phase, thus allowing the extrapolation of such knowledge to the partially ordered mesophase (Rusjan *et al.*, 2000; Zelcer *et al.*, 2002; Piro *et al.*, 2018a).

## 13. The later years

In 2006 I proposed to G. Punte (a true driving force behind the laboratory instrumentation) the presentation of a research project in the frame of the so-called Project for the Update of Research Laboratory Equipment (PME 2006) funded by the National Agency of Scientific and Technological Promotion (ANPCyT) to purchase a last-generation single-crystal X-ray diffractometer. Our project was approved and since 2009 we [obtained an Oxford (now Rigaku Oxford Diffraction Ltd) dual (Mo  $K\alpha$  and Cu  $K\alpha$  radiation) instrument, with an area CCD detector and a low-temperature accessory (down to about 90 K). What else can a crystallographer studying small and medium-sized molecules ask for? Due to the strong absorption of low-energy X-rays (long wavelength) by the heavy elements of inorganic crystals, which produce severely distorted diffraction data, it is necessary to employ the more energetic Mo  $K\alpha$  ( $\lambda = 0.71073 \text{ \AA}$ ) radiation of a molybdenum anode. On the other hand, for organic molecular solids, dominated by low-absorption elements on the second row of the Periodic Table, and frequently consisting of poorly diffracting crystals containing large molecules, it is convenient to employ the intrinsically more intense Cu  $K\alpha$  ( $\lambda = 1.54184 \text{ \AA}$ ) radiation from a copper anode. In addition, this radiation is essential to determine experimentally the chirality (based on anomalous X-ray scattering) of organic molecules, not a minor issue, which affects, among other properties, the biological activity of pharmaceuticals and inhibitors.

## 14. Epilogue

The remarkable interdisciplinary character of structural crystallography has taken us naturally to work in a wide diversity of subjects, including:

- solid-state physics, ligand field, magnetic properties;
- experimental and theoretical crystallography;
- crystal optics;
- experimental and theoretical spectroscopy;
- metastable states;
- high- $T_c$  ceramic superconductors;
- structural physical chemistry of a variety of materials, including inorganic, organic, bioinorganic, metal–organic, organic–metal, pharmaceutical and minerals;
- structural supramolecular physical chemistry, environment preservation and remediation;
- structure and properties of liquid crystals, *etc.*

This broad range of research has produced about 500 articles published in indexed journals, many in collaboration with tens of groups from Latin American countries, including Argentina, Brazil, Uruguay, Perú, Ecuador, Colombia and from Europe, including the United Kingdom, Spain and France. These collaborative works involve hundreds of researchers, doctorands and fellowship holders.

Besides scientific research, my colleagues and I have also led intense university teaching careers, including postgraduate courses on structural X-ray diffraction, solid-state vibrational spectroscopy and crystal optics, attended by hundreds of students. I believe that after about 50 years of trajectory, it is fair to claim for our laboratory a protagonist role in the development of the study of the structure–property relationship of materials in Argentina and the Latin American region, as well as in the diffusion of structural X-ray crystallography knowledge.

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