Special topic

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Science in my life

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Abstract: This paper presents an overview of my career from my first contact with chemistry in 1948, when I was in the second year of secondary school and realized, for the first time, the importance of this science. This discovery led me to focus my university studies toward a bachelor's degree in Chemistry. It was then that I had my first experience with the discipline of Crystallography, taught by Elisiário Távora, a young mineralogist who received his doctorate from MIT. Recognizing the importance of X-ray Crystallography for the elucidation of the molecular and crystal structure of all substances and for the understanding of their chemical and physical properties, I decided to dedicate myself to improving my knowledge of this subject with several visits to excellent international research groups working under the supervision of well-known crystallographers. Along with my scientific activities in Crystallography, another of my interests was to contribute to efforts to increase the number of crystallographers in Brazil and Latin-America, orienting several Master and PhD students. The support given by foreign visiting scientists and by those that became permanent members of our Institute and of other Brazilian research groups have been very important throughout my career.

Keywords: crystallography; Distinguished Women in Chemistry and Chemical Engineering; molecular structure; science diffusion; X-ray diffraction.

Introduction

The decision to start my undergraduate studies in Chemistry stems from my first contact with the subject in 1948, when I was in the second year of secondary school. At that time, students could choose between two course emphases: Scientific or Classical. My option for the Classical Course came from the fascination that languages, history, and literature exerted upon me at that time. Fortunately, however, we also had some math, physics, and chemistry in the curriculum. My attention was then drawn to chemistry by the influence of an excellent teacher, Albert Ebert, who uncovered the importance of chemistry to practically everything around us. He made me realize that the discoveries produced in research laboratories can unfold into numerous applications that range from the mineral world to that of living things.

My bachelor's degree in chemistry

In 1950, I passed the entrance examination for the bachelor's degree in Chemistry offered by the National College of Philosophy of the former University of Brazil, currently the Federal University of Rio de Janeiro. When the Physical Chemistry classes started, I engaged in an undergraduate research program on the electrical properties of natural insulating materials under the guidance of Professor Joaquim da Costa Ribeiro (1906–1980). The consequent need to study physics made me decide to do the Physics and Chemistry courses simultaneously, receiving my bachelor's degree in chemistry in 1954 and my bachelor's degree in physics in 1955.

The school year of 1953 brought me into contact with the disciplines of Crystallography and Mineralogy, including the topics of Optical Crystallography and X-ray Diffraction. The latter was taught by Elisiário

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Távora, a young mineralogist who had received his doctorate from MIT under the guidance of the renowned Professor Martin Julian Buerger (1903–1986). I went through this very inspiring course with much interest and pleasure.

In 1954, I married my university colleague Sergio Mascarenhas Oliveira, who had graduated in Chemistry 1 year ahead of me, and we both started to seek work in Rio de Janeiro. At that time, my main sources of income were the classes I taught in secondary schools and a scholarship granted by CNPq to initiate research on dielectrics under the guidance of J. Costa Ribeiro. My first son, Sergio Roberto, was born in 1955, and that same year my husband and I had an invitation to work at a new campus of the University of São Paulo, where an engineering school had recently been created. The campus was located in the small city of São Carlos, some 240 km away from the capital city of São Paulo state. After a brief visit that Sergio made to São Carlos, where he met Professor Theodoreto de Arruda Souto, Director of the new Engineering School, we decided to accept the invitation. That opportunity provided us with a full-time salary and the possibility of starting research in the same line as we had been doing at Professor Costa Ribeiro's laboratory in Rio de Janeiro.

We arrived at São Carlos in February 1956, and in July of the same year my second child, Yvonne Maria, was born. Her arrival was a great joy for the entire family! At the university, we started teaching General and Experimental Physics to first- and second-year students of the engineering school while working to set up our laboratory. Among the equipment we found in the lab was a brand-new radiological X-ray set, acquired by a French professor who had then returned to his home country. Sergio managed to convince the manufacturer's representative to exchange it for an X-ray generator for X-ray diffraction.

During this initial period in São Carlos, I conducted research on single crystalline dielectric solids in collaboration with Sergio. These studies evidenced the importance of the crystallographic direction along which the measurements were performed, as well as the presence of structural defects. However, research work developed very slowly during this period because of the attention I dedicated to my two very small children and the demands of preparing the physics classes that I had been assigned. On the other hand, I was concerned with improving my knowledge of crystallography in its applications for the characterization of defects in single crystals. For this I relied mainly on the book by C. S. Barret "Structure of metals: Crystallographic methods, principles, and data" (Metallurgy and metallurgical engineering series) – 1952.

Early in 1958, we learned of Roman Schmolukowski's visit to Brazil and, assuming that he was one of Albert Einstein's co-authors, I urged my husband to try to arrange a meeting with him. We did get to meet him but found out he was a professor of the Carnegie Institute of Technology in Pittsburgh, PA, USA, and the son of Einstein's co-author. Despite the mistake, the meeting had a very happy outcome: we became acquainted with Schmoluchowski's lines of research on solid-state physics and he, in turn, learned of the works developed by Sergio on dielectrics. This happy accident created an excellent condition for the immediate development of collaborative research and mutual friendship, and set us looking for funding to stay at least 1 year in Pittsburgh. The resources eventually came from the Fulbright Commission through the approval of two research fellowships, one for me and the other for my husband.

The beginning of my stay at Carnegie Tech was supposed to occur in the Department of Metallurgy, which, as I came to know, did not develop any research of interest to me at that time. Chance came to my rescue when I met Ernesto and Amélia Hamburger, two Brazilian scientists who were doing their PhD in Nuclear Physics at the University of Pittsburgh. When I told them of my dissatisfaction with the Carnegie Tech metallurgy group environment, they informed me that the University of Pittsburgh's Department of Crystallography was not only the best crystallography school in the United States, but also the best place to carry out research work on that subject. We then arranged an appointment with Prof. G. A. Jeffrey, director of the Department of Crystallography, who advised me to attend a night course on X-ray diffraction that was about to begin. A few weeks later, when I started attending the course, Jeffrey let me know that he already had a desk for me in the lab. This fact meant a complete change of my original plan: instead of devoting myself to the study of defects in crystals, I became fully involved in determining molecular and crystalline structures by using X-ray diffraction in single crystals. Although this area had been the most interesting to me since my early contact with crystallography in the course offered by Elisiário Távora during my undergraduate studies, I had always considered that the lack of specialists and laboratory infrastructure in Brazil made it too difficult to pursue.

My training in crystallography

My training was strongly influenced by the generous assistance of other laboratory students. As soon as I arrived at the Lab, Brian Craven, my advisor, showed me how to set a single crystal of violuric acid on a Weissenberg camera and try to orient it in one of its crystallographic directions. I must say that this task would have been much harder than itwas had I not received the help of Martin Sax, one of the PhD students. Martin introduced me to the practical use of reciprocal space concepts applied to the Weissenberg's chamber geometry and its use in orienting a crystal; to the recording of diffraction patterns on photographic films; to the development and interpretation of the many films obtained in the process of refining the orientation; and, finally, to obtaining symmetry and unit cell dimensions when the crystal was perfectly oriented. After this first step, I should start data collection.

Before starting data collection, I had to decide how to perform our measurements to obtain the best possible data for the calculation of electron density. After taking previous findings into account, Craven advised me that we should collect three-dimensional data. He considered chemical evidence for the following findings: that the violuric acid molecule is planar; that the volume of the unit cell and the calculated density of the crystal require the existence of four molecules per unit cell; and that the crystal belonged to the orthorhombic system, space group $Cmc2_1$, which reacquired eight molecules per unit cell if they were situated in a general position, but only four if the molecule was planar and located in the mirror plane of the space group. The option for three-dimensional data collection was not usual at that time due to the non-existence of good computing facilities and to the need for measuring a quite large number of reflection intensities by eye using an intensity scale. Nevertheless, Craven opted into it because it would allow the calculation of a three-dimensional molecular structure.

The intensities of 425 reflections were estimated by visual comparison with a standard scale. Afterwards, I had to manually punch the Hollerith-type cards – one card per reflection – that were used to feed data to the IBM 650 computer (a vacuum-tube computer with a rotating drum memory of 2000 words) at the University Data Processing Center. Then came the next step: producing models and testing them using the existing programs for the calculation of structure factors and electronic densities. Of course, I had never worked with computers before and I learned a lot from Professor Ryonoshuke Shiono, the computer specialist of the laboratory, as well as from Craven and other students like myself.

To solve the structure, I used the Method of Trial and Error, by which one must initially obtain several models of the structure. Thus, I drew a model of the molecule on a card using the known values of intramolecular distances and angles. I also drew on the same scale the size of face A, which is perpendicular to axis *a* of the unit cell and whose sides are the axes *b* and *c*. Then I tried to locate models of the molecule on the mirror plane m by considering the symmetry of the space group and avoiding overlapping parts of different molecules. This procedure generated several models that were tested using the atomic coordinates of the models in the calculation of the structure factors (values that are extracted from the measured intensities) of all the crystal diffracted beams. The model that generated the best agreement between the values of the calculated and experimentally measured structure factors was later refined and used in the calculation of the crystal electronic density maps. The crystal structure was considered solved when the molecular images on the map showed the expected molecular structure.

After all the steps above had been followed, the electron density maps revealed an unexpected result: the presence of a water molecule and a bifurcated hydrogen bond. Since this type of bond was already theoretically proposed but would be experimentally found for the first time in this structure, Craven wished to confirm it using neutron diffraction.

At that point, I had to return to Brazil and Craven spent still more time convincing himself of the occurrence of the bifurcated hydrogen bond using the neutron diffraction of a perdeuterated crystal of violuric acid. The results of this work were published only in 1964 in *Acta Crystallographica* in two separate papers, one with the results of X-ray diffraction where I appear as a co-author (*Acta Cryst*. (1964) **17**, 402), and the other with the neutron diffraction confirmation of the structure, by Brian and Takey (*Acta Cryst*. (1964) **17**, 415).

Activities after returning to São Carlos

In May 1961, my second daughter, my dear Helena, was born, and about 2 months later I proceeded with my research activities. I had samples of materials provided by Carnegie Tech researchers Marshal Merriam and Sergio De Benedetti, whom I had contacted during my stay in Pittsburgh, aiming to establish collaborations after my return to Brazil. Merriam worked with a superconducting HgIn alloy and Benedetti worked with magnetic salts, including manganous formate. As I had no equipment for X-ray diffraction by single crystals in São Carlos, I asked to use the laboratory facilities of the University of Pittsburgh to collect the diffraction data of the magnetic salt. Permission was promptly granted, and thus I began this determination after arriving at São Carlos. As we had a Debye-Scherrer camera suitable for polycrystalline samples, I started the study of the HgIn alloy. This was not so easy, because the alloy was liquid at room temperature and I had to adapt a cooling system to the camera.

After my arrival in Brazil I received a letter from the secretary of the International Union of Crystallography telling me that, although Brazil was a member of that Union, the Brazilian participation was null regarding both the payment of the Union dues and the participation of delegates in the General Assembly. I immediately contacted the president of the adhering body, the National Research Council (CNPq), and the problem was solved. For this reason, CNPq appointed me as a delegate for the upcoming Congress.

Soon in the first months after my arrival, I began to write a project to submit to CNPq requesting the purchase of a Weissenberg camera. As I anticipated that the response to such a request might take a year or more, I borrowed a camera that I knew existed in the Institute of Oil, Paints, and Varnishes of the Ministry of Agriculture in Rio de Janeiro. The director of this institution allowed me to keep it for a year. Simultaneously, I began the search for students interested in crystallography and tried to communicate with researchers in the fields of Chemistry and Physics who were interested in obtaining the structures of their compounds. Fortunately, the Chemistry Institute of USP, São Paulo Campus, invited me to give a seminar. From contacts that I made in this seminar, I started a collaboration with Ernesto Giesbrecht and Ivo Giolito, who worked with rare earth Selenium and Sulphur salts, and with Otto Gotlieb, a well-known chemist of natural products.

At the same time, I was trying to highlight the importance of Crystallography in scientific meetings and to obtain master and doctorate students. I was gradually forming a research group that would generate several works based on the samples brought from Pittsburgh and on substances of interest to the Brazilian community.

In 1968, my husband and I spent about 10 months in Princeton, NJ, USA. The purpose of this stay was to continue Sergio's research work in color centers initiated during his stay with Smoluchowski's group at Carnegie Tech. Schmoluchowski was invited to create the Materials Science Institute of Princeton University. While Sergio worked in Smoluchowski research group, I was set to work with Professor Neil Bartlett's group in the Chemistry Department of the same University. The group was supposed to synthesize compounds of fluorine with noble gases, and this innovative project interested me very much. However, when I got to Princeton, Professor Bartlett made me aware that unfortunately he had not, to that time, crystallized any of those compounds. In the face of this frustrating outcome, I looked for my friends from Pittsburgh and had my first experience with an automatic single crystal diffractometer. I had brought some samples of a copper complex of 11-amino-undecanoic acid synthesized by a friend from Rio de Janeiro, the chemist Lucia Tosi. The crystal had a relatively large unit cell and crystallized in the triclinic system. For this reason, I had to collect what was considered, at that time, a very large number of reflections. The data collection lasted a week, with Craven and I taking turns during the measurement, he from morning to evening and I during the night. The only drawback was that the result of the measurement of each reflection was registered to perforated cards, and the punching machine would insistently jam from time to time, causing the measurement to stop until one of us removed the crumpled card and resumed the data collection. Despite these minor hindrances, the data turned out to be good. The structure (of the room-temperature phase of chlorocuprate of bis- (11-amino-undecanoid acid)) was solved after my return to Brazil and presented during the 9th International Congress of the International Union of Crystallography, in Kyoto, 1972. During the congress, I had the pleasure of meeting Dorothy Hodgkin, who came to my oral presentation.

After my return from Princeton, in October 1969, my dear youngest son, Paulo Roberto, was born.

Activity in the 1970s

In December 1971, I received an unexpected invitation to participate in a congress of the Ibero-American Crystallography Group, to be held in January 1972 in Valdivia, Chile. My response was an immediate and enthusiastic yes, with the feeling of having received a wonderful gift from Santa: this would be an excellent opportunity to get to know the Latin American crystallographic community, which I believed should be a good source of future interactions and collaborations despite its small number of members. Moreover, I had always had a great deal of interest and admiration for that country and its democratic tradition, unique in Latin America. Nearly a year before, Chile had elected Allende, the first democratically elected socialist president.

During my participation in the event, I was impressed by the quality of the crystallographers I encountered there, including Argentina's, Aldo F. Craievich from the National University of Córdoba and Eduardo E. Castellano from the National University of La Plata, and Chile's, Mario Suwalski, Oscar Vitke, Hilda Cid, and Carmen Escobar.

I took the opportunity of the Congress to try to convince several Latin American participants to come to São Carlos as invited researchers. In the following year, after a brief visit, Aldo F. Craievich decided to accept our invitation and came to São Carlos to start a new area of research using Small Angle X-ray Scattering (SAXS). Soon after his arrival he had a grant approved by FAPESP (The Sao Paulo State Foundation for Research Support) for the acquisition of the necessary equipment to start working on the study of partially ordered glassy materials.

In August of 1972, I participated in the IX Congress of the International Union of Crystallography held in Kyoto, Japan, and then took an internship of about 6 months in the Crystallography Laboratory of the Department of Chemistry, Harvard University, whose director was Bill Lipscomb (1976 Chemistry Nobel Prize laureate). The subject of my work at Harvard was to try to find if some molecules provided by one of Lipscomb's collaborators from the University of Chicago would inhibit carboxypeptidase, an enzymatic protein whose structure he had solved a few years prior. To do this, I had to soak a carboxypeptidase enzyme single crystal in a solution containing the potential inhibitor and then set the crystal on the existing automatic diffractometer to collect the diffraction data, which I subsequently used for calculating the electron density map. Unfortunately, the maps had an empty active site for all tested molecules, therefore showing that those molecules were not carboxypeptidase inhibitors.

Although the work did not result in positive findings, I consider my attendance at the IUCr congress, together with that first experience in protein crystallography, a useful guide to decisions I would make in the future. From the observation of the enormous methodological advances in the crystallographic research brought by the automation of data collection and in the computational methods available, I became convinced that it would be impossible to conduct internationally competitive research in structural crystallography without the modern equipment available in the international laboratories of advanced countries.

By 1972 there was a small, yet significant community of physicists, chemists, and mineralogists in Brazil already involved in crystallographic projects. I decided to send a circular letter inviting them to attend an informal meeting in São Carlos to discuss the creation of a Brazilian Association of Crystallography. All the invited scientists accepted the idea and the Association was founded.

In 1973, I wrote a proposal to FAPESP with the purpose of acquiring a modern single crystal automatic diffractometer. After careful analysis of the instruments available on the market, I decided to buy the Enraf-Nonius Cad4 equipped with a PDP11 computer from Digital, which would allow data collection and the necessary calculations for the determination of molecular and crystalline structures by X-ray diffraction.

In 1974, I attended the International School of Crystallography held at the Ettore Majorana Foundation and Center for Scientific Culture, in Ericce, Sicily, Italy, under the direction of Professor Michael M. Woolfson. The International School of Crystallography (ISCoC) is a Scientific Session of the Ettore Majorana Foundation and Center for Scientific Culture (EMFCSC) devoted to promoting crystallographic knowledge in the scientific community. The idea of including Crystallography among the disciplines at the Majorana Center was suggested by Professor Michael M. Woolfson, (FRS, University of York, UK) to Lodovico Riva di Sanseverino

(Bologna University) in 1972. The School was officially started in 1974 (Prof. Michael Woolfson was also the Scientific Director of this very first Course on Direct Methods), under the scientific direction of Nobel Laureate Dorothy Hodgkin. I was very impressed with this event. In fact, after discussing with the director the possibility of sending Brazilian crystallographers to the next School, I came up with the idea of holding it, in due time, in Brazil.

Early in 1975, the Enraf Nonius diffractometer finally arrived and was installed in our Laboratory. Since it was the only machine of its kind in Latin America, I imagined that it might be used in collaboration with other crystallographers of this region. With this in mind, I contacted Michael Woolfson again to recall our idea of organizing a Latin American Course on Direct Methods for Resolution of Structures by X-ray Diffraction, similar to the one I attended in Ericce. I applied for and obtained financial support from several domestic and international agencies. The School relied on practically the same group of specialists as the Ericce School, namely M. Woolfson (Director) and Peter Main from England's York University; Isabella and Jerome Karle from the Naval Research Laboratory at Washington DC, USA; Herbert Hauptmann of the Medical Foundation of Buffalo, USA, who would receive, along with J. Karle, the 1988 Nobel Prize in Chemistry; and Paul Ewald, the creator of the concept of reciprocal space in Crystallography. About 20 Latin American crystallographers, most of which I had met in Valdivia, attended the School.

When Karle was elected president of the International Union of Crystallography (1981–1984) I was indicated as a member of the Teaching Committee of that Union, a position that I kept for several years.

During the course, we discussed the convenience of having at least one more senior researcher in our Group. Fortunately, Eduardo Ernesto Castellano from Argentina, who attended the School, accepted the invitation, thus initiating an intense collaboration between the Laboratory of Crystallography of the Institute of Physics of Sao Carlos and the Department of Physics of the National University of La Plata, Argentina.

During the 70s, as the infrastructure conditions gradually improved, and with the important contributions of the new laboratory members Aldo Craievich and Eduardo Castellano, it was possible to attract masters and doctoral candidates that contributed to many research projects in collaboration with chemistry and physics laboratories. Among the earliest doctorates, we can mention Regina H. de Almeida Santos, Cesar Cusatis, Servulo Folgueras Domingues, Julio Schpector, and Jean Rudiger Lechat.

The 1980–1990 decades

During the 1980s and 1990s, I became interested in two new areas of crystallography: the use of the powder method for the structural characterization of polycrystalline samples and the crystallography of proteins.

My first attempt to use powder patterns for the refinement of a crystal structure had the participation of my master student Carlos Alberto Simone. Initially, evaluated the integrated intensities of the reflections present in the powder diffractogram and used them for refining the structure. I must confess that we did not get good results, particularly when the diffractograms were more complex, with many overlapping reflections that we tried to decompose into component intensities admitting a Gaussian profile.

A breakthrough in my efforts came after I attended a wonderful lecture delivered by Ray Young, a Professor in the Physics Department of Georgia Tech, during a Meeting of the American Crystallography Association. In the lecture, "From ugly duck to beautiful swam", Young described his work on the crystal analysis of crystalline powder samples using an approach similar to the one applied by German crystallographer H. Rietveld for the refinement of structures using neutron diffraction data. Rietveld's idea was to refine the profile of the neutron diffractogram, proposing equations to describe the profile of all individual reflections and considering the total profile as the sum of the individual ones.

The successful application of this method by my doctoral student Carlos de Oliveira Paiva-Santos convinced me that this approach was the one to be used in our future works. Carlos's thesis, entitled "Study of piezoelectric ceramics by the Rietveld method with data of X-ray diffraction" (1990), was a success and his thesis is considered seminal in Brazil in the use of this methodology.

The application of the Rietveld Method was particularly important in the early 90s, when I received a letter from Silvia Cuffini, a young PhD from the Department of Chemistry of the National University of Córdoba, Argentina. Silvia was scheduled to come to Brazil accompanying her husband, who had already been hired by another research group of our Institute. This case made me see, once again, the traditional behavior of talented women who follow their husbands in their professional lives, while wanting very much to have an opportunity to build a career of their own. Silvia's CV described her previous experience in areas of our interest, and I readily invited her to come to work in our group. During her stay, she worked on the structural characterization of a series of polycrystalline ceramic compounds that she had synthesized for her doctoral thesis. This project perfectly suited our new research interests, so I immediately applied for a post-doctoral scholarship from FAPESP and, subsequently, a visiting scientist fellowship from CNPq, which supported her stay in São Carlos for about two and a half years. During these years, she worked intensely in collaboration with me, with other members of my Institute, and with members of the Department of Physics of the Federal University of São Carlos (UFSCar). These interactions resulted in five complete papers that were eventually published in specialized journals.

In 1994, as part of a bi-national collaboration I had with the University of Cuba, supported by CAPES (Coordination for the Improvement of Higher Education Personnel, Ministry of Education, Brazil) I received in my laboratory Juan Guevara Carrio, a doctoral student who had obtained his undergraduate and master's degrees from the University of Dresden, in the former East Germany. From 1994 to 1998, he carried out studies on the characterization of piezoelectric ceramics and published several papers that ultimately composed his doctoral thesis. This study was funded by a FAPESP thematic research grant that I coordinated. Juan was an excellent researcher and his interest led him to interact with other researchers from the Physics Institute, particularly with Silvia Cuffini and Jose Eiras, one of the principal investigators of our FAPESP Thematic Project and a professor at UFSCar.

I find it important to mention that Juan came to Brazil with his wife and first son. By the time they arrived, I knew that she had also attended the University of Dresden and had a degree in Engineering in the field of Metrology. To help her advance in her professional career, I immediately contacted the head of the Mechanical Engineering Department of the São Carlos School of Engineering (EESC) and he promptly accepted her as a PhD student. She also obtained her PhD and was hired by the Engineering School of the Lutheran University of Piracicaba, Piracicaba, São Paulo, Brazil.

A further outcome of our interaction with Silvia Cuffini happened in 1998, when she sent the doctoral student Carlos Meriles, also from the University of Córdoba, for a few months' stay in San Carlos. Carlos was approaching the end of his thesis work, and he studied phase transitions in various compounds containing biphenyl groups in their molecules, using both single crystal and low-temperature polycrystalline techniques. It was possible to achieve good results, which gave rise to two articles submitted and accepted for publication in specialized international journals.

My earlier projects in protein crystallography started with an interaction with Carlos Júlio Laure and R. Giglio of the Ribeirão Preto Medical School, USP, who dedicated themselves to the study of ophidian toxins. As the crystallization attempts of some of the purified samples of toxin components were negative, I decided to study, with my PhD student Jose Ramon Beltrán Abrego, from El Salvador, the conformation of these proteins using Small Angle X-ray Scattering technique (SAXS). To do this, I started a collaboration with Otto Glatter, a well-known molecular structure scientist and author of WHAT-IF, a computer program used for the interpretation of SAXS data. Otto was extremely collaborative, and with his generous support, Ramón determined the general shape and size of some protein venom components in solution, presented his thesis, and published several papers.

With another student, Johnny Olivieri, we investigated conformational variations of human serum albumin under different pH conditions. In his thesis, Johnny used the GNOM computer program, whose author is Dimitri Svergum. This allowed me to present some results at the meetings of the Brazilian Biochemistry and Molecular Biology Society and thus start an interaction with some of their members. I presented the results of the SAXS work on crotoxin, one of the components of the *Crotallus durissus terrificus* venom during the VII International Congress of the International Union of Crystallography (1966), held in Moscow.

On that occasion, I met two very important women working with protein crystallography: Jenny Glusker, from Philadelphia, with whom I shared a room, and Ada Yonath, from Weissmann University, who invited me to give a seminar at the Hamburg Synchrotron, were she worked on the structure of ribosomes. I accepted and visited her laboratory where, for the first time, I had the opportunity to see a group working in a very difficult and important project to determine the structure, not of an isolated molecule, but of a functional complex composed of many proteins.

Ramón and Johnny, the students involved in the SAXS researches on protein solutions, are currently faculty members of the Physics Department of IBILCE/Unesp, Campus of Rio Preto, where they established, with several young PhD and R. Arni, an active molecular biology and biophysics research group.

Otto Glatter and Dimitri Svergun visited Brazil to participate in Schools and train some students in the use of their programs for the interpretation of SAXS patterns.

Seeking to improve my experience in protein crystallography, I spent 10 months (1979–1980) at Birkbeck College, University of London, whose leader was Sir Thomas Blundell. During this period, I dedicated myself to the determination of the molecular structure of oxytocin, a hormonal polypeptide of great biological interest. Although I did not achieve the determination of the molecular structure, it was solved later and Tom Blundell generously included me as co-author in the published papers.

In 1986 I received a letter from Raghuvir Arni, a doctoral student in Protein Crystallography who was working with the renowned German crystallographer Wolfram Saenger at the Technische Universität Berlin, Germany, expressing a desire to join our laboratory as a post doctor. He remained in São Carlos from 1987 to 1988, and then returned to Germany, where he worked from 1989 to 1991 in the European Laboratory of Molecular Biology. He went over to Michigan State University, USA, from 1991 to 1992, and returned to Brazil in 1992 as full professor of IBILCE, UNESP, São José do Rio Preto, SP, where he established a productive group on Protein Crystallography.

The short period I spent at Birkbeck College was, in my view, decisive for the later establishment of Protein Crystallography in São Carlos by Glaucius Oliva, who obtained his master's degree with Castellano in 1984 and decided to do his doctorate in Tom Blundell's laboratory. Glaucius returned to Brazil in 1988 with excellent training and immediately began to set up a protein crystallography laboratory. He started to build its physical and human infrastructure with the participation of experienced researchers, such as Richard Garrett (PhD at Birckbeck College), Eduardo Horjales Reboredo (PhD in Molecular Biology, Sveriges Lantbruksuniversitet, Sweden (1985)) who participated in the Workshop I organized in 1989 on the subject of "Crystallography and Molecular Biology", Otávio Thieman (PhD Molecular Cell and Developmental Biology, University of California, Los Angeles (1998)) and many graduate students. Protein crystallography spread to other Brazilian centers as universities and research groups hired some of the students who had completed their PhD in São Carlos.

Activities since 2001

My compulsory retirement took place on July 21, 2001, when I turned 70. Since then I have a formal honorary link with my Institute, where I have access to office space and the use of its infrastructure. My projects remain eligible for funding from the research support agencies.

My activities are currently oriented in two directions: scientific diffusion in support of education and research in structural crystallography.

Scientific diffusion

Some of our activities are carried out directly in the schools, where we apply the pedagogy of "learning by projects" with sixth- and seventh-grade science teachers. This is not a new methodology. It emerged in the early twentieth century, influenced by the ideas of John Dewey, an American philosopher who defended the

idea of valuing, questioning, and contextualizing students' ability to think as an instrument for emotional and intellectual development. From this perspective, we seek out projects that enable students to experience situations related to daily life, promoting a reflection on social reality.

Working with a project requires a shift from the conception of teaching to the conception of learning. In this sense, teachers need to adopt a constructivist vision of teaching/learning in which their role will change from transmitters of knowledge to that of teachers actively engaged in the teaching-learning process. To do so, they must articulate the demands of the project with a new way of teaching, integrating the different media and contents, while students have a more active and collaborative role with their peers, all aiming at a common goal. The methodology also seeks to enable a more articulated way of learning across the contents of several areas of knowledge, which should lead to the perception of the integral and interdisciplinary character of knowledge as well as the importance of using various media (computer, smartphones, tablets, and books).

Although most teachers are aware of project pedagogy, its application is hampered in day-to-day activities due to the relatively high number of students per class and the fact that students attend the Brazilian public schools for only part of the day, either morning or afternoon. Our projects bring to the school material and human resources that help teachers apply this methodology. In general, the schoolteacher will receive the collaboration of a university professor who coordinates the project and of undergraduate students who support the activities of the students in the computer room and during the collection of data related to the theme of the project. Guidance is also given on the final presentation of the students' work, with the production of a magazine or a DVD.

Structural crystallography

The crystallography research I have been doing since 2001 is directed toward the study of conducting polymers, in association with a large project led by Roberto Faria, one of the full professors of our Institute. This project involves a network of laboratories spread throughout several Brazilian states. CNPq and FAPESP jointly support it. Its main objective is the study of conducting polymers and their application in microelectronic devices. My contribution is on the X-ray diffraction and Small Angle X-ray Scattering (SAXS) structural characterization of these materials with the involvement of my former doctoral student Edgar A. Sanches, MSc (2006) and PhD (2011). Edgar is currently a tenured professor at the Department of Physics of the Federal University of Amazonas (DF/UFAM) where he established a multidisciplinary research group aiming not only at the study of conductive polymers, but also the study and possible applications of various products of the Amazon Region. He coordinates the Graduate Program in Materials Science and Engineering of the same university. Currently, one of his students, André Ferreira, who obtained his master's degree under Edgar's guidance, is a PhD student under my own guidance.

Another line of research I have been working in is the characterization of synthetic and natural substances with schistosomicidal activity. Schistosomiasis is a serious endemic disease, in Brazil and in other countries, caused by several types of worms called Schistosoma. I am involved with this project because of my participation in another network of Brazilian laboratories that have been promoting the interest of graduate students in the solution of this and several others important endemic health problems. The initiative is funded by the Brazilian institution CAPES, mainly through the grant of graduate fellowships. The contribution of the Post Doctor Ana Carolina Mafud was very important to the success of this research project.

Events organization

Throughout my life I have organized, or helped to organize, several events to draw the interest of undergraduate and graduate university students to Structural Crystallography and its applications in Chemistry, Materials Science, Mineralogy, and Condensed Matter Physics.

Events on structural crystallography

1971	Foundation of the Brazilian Society of Crystallography with the participation of mineralogists, physicists and chemists
1974	André A. Guinier delivers a course in S. Carlos on X-Ray Diffusion by Imperfect Solids
1975	V Ibero-American Congress of Crystallography, held in Campinas under the coordination of Caticha Ellis. June 30 to July 6
1976	"Latin American School of Direct Methods for the Solution of Crystalline Structures", IFSC/USP/São Carlos
1982	Course on the determination of molecular structures in the Department of Chemistry of ICEx, UFMG, Belo Horizonte, MG (YP Mascarenhas Coordination, and participation of E. Castellano, J. Lechat, R. Santos)
1983	International Course on Crystallography Teaching for Materials Science, Campinas/SP. (Coordination of S. Caticha-Ellis) July
1986	Course Radio Crystallographic Techniques, Institute of Geosciences, University of Brasília/DF. (Coordination of Y. P. Mascarenhas and participation of E. Castellano, J. Lechat, R. Santos)
1987	Workshop on "The need for a rotating anode X-ray generator for the São Carlos region", São Carlos/SP
1988	XII Annual Symposium ACIESP on Protein Toxins, Campinas/SP, in which the Brazilian Soc. of Toxicology was founded
1988–1989	Courses during SBBq Annual Meeting, Campinas/SP
1989	Protein Crystallization Course, São Carlos/SP
1990	International Symposium on Crystallography and Molecular Biology, Guarujá/SP
1992	Course and Workshop on Structure Determination of Polycrystalline materials (Rietveld Method), during the Annual Meeting of ABCr, São Paulo/SP
1993	Course during SBBq Annual Meeting on "Results of Structural Crystallography of Proteins"
1994	Course and Workshop "Advanced Methods for Structural Analysis of Biomolecules", São Carlos/SP
1996	Workshop on Structural Characterization of polymers by X-rays Scattering
1997	Workshop on ceramic materials, São Carlos/SP
1998	Inauguration of the Brazilian Synchrotron at the National Laboratory for Synchrotron Light (LNLS) in Campinas, SP
2003	ABCr Meeting in São Carlos with the presence of Bill Duax, president of IUCr

Conclusion

While making this report and recalling the educational, cultural, scientific, and technological conditions that existed at the beginning of my career, I can see that much progress has been made by the effort of scientists of all areas and by the involvement of Brazil's federal and state funding agencies. It is true that our conditions are not yet comparable to those of developed countries, but in many Brazilian laboratories, our scientists work on research involving our regional needs and, in some others, our scientists act at the frontier of knowledge, often in collaboration with important international research centers. We hope that this will help to promote the bettering of the cultural, social and economic level of our people as well as the understanding and respect among the nations of all world.

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