The Challenges of Sciences. A Tribute to Carlos Chagas
Pontifical Academy of Sciences, *Scripta Varia* 103, Vatican City 2002
www.pas.va/content/dam/accademia/pdf/sv103/sv103-dealmeida.pdf

THE MAIN LINES OF MULTIDISCIPLINARY RESEARCH IMPLANTED AT THE INSTITUTE OF BIOPHYSICS BY CARLOS CHAGAS FILHO

DARCY F. DE ALMEIDA

To introduce the question of the implantation of science at the University of Rio de Janeiro I chose to offer you some not very well-known aspects of the routes followed by Chagas to face such challenge. For that purpose, I shall bring evidence from several sources, besides my own recollections from countless talks we had throughout the last fifty years of his life. I have arbitrarily established two phases to tell the story: (1) The starting point: a revolution from within; (2) A brief look at the first 25 years of the Institute of Biophysics.

1. *The starting point: a revolution from within*

A brief description of the academic and institutional life at the University of Rio de Janeiro in the 30s would seem quite fit as a background against which the initial actions take place. The characteristics of the XIX century and first two decades of the XX century still prevailed. The University existed exclusively as an assembly of professional charter-delivering schools. Internally, interchanges between the various chairs were not noticeable. Practically isolated from each other, every chair was regarded as personal property of its respective Professor, whose appointment depended on personal and/or political interests rather than on academic merits. Even though the title of University Professor carried with it a social prestige very useful for the private practice, the duties were strictly limited to magisterial classes, the only source of contact between the professor and his students. There was plenty of time left for the faculty to earn additional salaries, from alternative public and/or private activities,

to make up for their small wages from the University. In short, a thing such as a professional scientist was undreamed of (Schwartzman, 1979). Therefore the implantation of scientific investigation at the University of Rio Medical School was indeed a challenge, and not a trivial one.

Being trained at the Oswaldo Cruz Institute, Chagas had made up his mind rather early in his career. He was 21 years old in 1931, when he graduated in Medicine. Admitted as assistant professor to the Department of Pathology, he was seemingly oriented towards the study of tropical diseases. But a conference at the Oswaldo Cruz Institute made an extraordinary impression on him. It was given by Fauré-Frémiet, professor of Comparative Embriogenesis at the Collège de France from 1928 to 1954. The subject was the "kinetics of development", and the French professor showed that biological phenomena could not only be subjected to a mathematical treatment, but interpreted as well under the light of physical and chemical events. Chagas was, to use his own words, "*dazzled*" (Chagas Filho, 2000) by this approach and there and then decided to dedicate himself to it.

His father did not seem much disturbed when informed of that transmutation; only he recommended, before it was accomplished, that Chagas should spend a season at the hospital in Lassance, the small country town where the Chagas disease had been discovered. The intentions behind this paternal advice become clear when one hears from Chagas Filho that in Lassance he received the finishing touches of his medical education. There he acted not only as a physician, but also as pharmacist, confessor and, in general, a public authority. "*It was there that I learned really to know people* (…) *dealing with the patients, the simplicity and sincerity of those people feelings were of the utmost value to me*" (Chagas Filho, 2000). He was by then sure that the sciences were essential to help solving the problems posed by human diseases.

Back in Rio, events precipitated in rapid succession. While following complementary University courses on chemistry, physics and mathematics, in Manguinhos Chagas went through training in bacteriology and physiology; most importantly, he improved his physical chemistry knowledge under Carneiro Felipe. He was transferred in 1934 to the Department of Biological Physics, chaired by Prof. Rodrigues Pereira. Two years later, due to the untimely death of the department head, Chagas was appointed to the vacant chair, after the usual academic competition. Much earlier than he might have thought, since he was then 27 years old, the opportunity came for Chagas to start on the route to make his dream come

true. In the opening address to the Medical School class, not surprisingly dedicated to Carneiro Felipe, he insisted once more on the importance of the physical and physical-chemical interpretation of biological phenomena (Chagas Filho, 1938).

Aware of the importance of modern research techniques, and intent on extending his own scientific experience, in 1938 he worked in Paris, with René and Sabine Wurmser, at the laboratory of Physical-Chemical Biology and with Denise and Alfred Fessard, at the laboratory of electrophysiology of the Institut Marey. In England, he was received by A.V. Hill, at the University College Department of Biophysics, in London, and by lord Adrian, at the University of Cambridge Laboratory of Physiology.

Upon his return, in the address to the medical students, on August 8, 1938, he expressed his convictions: "*The introduction of new physical and physical-chemical techniques has propitiated the upsurge of a series of investigations that open new horizons for medicine and often modify generally accepted concepts*" (Chagas, 1940).

Meanwhile, a new Constitution had been proclaimed in 1937 by the Vargas government, which suppressed the often used double appointment in the public service. On account of the small salaries paid by the University, as mentioned before, the whole faculty of the Biological Physics chair left, with a single exception. Chagas looked at multiple quarters for help from idealistic people like himself. Tito E. Leme Lopes, his friend and colleague throughout the Medical School years, was the first to come. There followed two assistants, J. Moura Gonçalves and J.B. Veiga Salles, from the Department of Biochemistry in Minas Gerais, indicated by Baeta Viana, who had trained what was at the time perhaps the best group of biochemists in the country. Others, like M. Frota Moreira and H. Martins Ferreira, were locally recruited, from the University of Rio. This is a proper occasion to pay a tribute of praise to Guilherme Guinle, patron of the Institute of Biophysics, for the support that the Laboratory and later the Institute received from him. During the difficult initial years he was the main provider of funds for the experimental work and for the salaries of most of the staff.

A number of strategic innovations which might be called *patterns of development* were adopted by Chagas to achieve the implantation of scientific research in the University. An example of this kind is found as early as 1938, when he created the "Laboratory of Biophysics", defined as "*the research section of the Biological Physics chair* (…) *to make the experimental method accessible to the medical students and to make biologists and*

technicians acquainted with the new physical methods used in the study of vital processes" (Chagas Filho, 1942). Without any formality at all, Chagas institutes an activity which, in spite of being physically superposed on the traditional chair, possesses an identity of its own. That was a typical gambit played by Chagas, the first one in a series of creative innovations which strategically avoided conflicts with ingrained bureaucratic procedures. It is quite possible that the simple substitution of the designation of *laboratory* for *chair* would have faced, at that time, a strong opposition. Chagas had started what I chose to call *a revolution from within*.

In fact, to describe the Laboratory of Biophysics, Chagas cautiously states that *"its organization is dependent on the scientific activity there developed, and tries to answer the questions posed by problems arising in the course of experimental work"* (Chagas Filho, 1942). This rather vague declaration is quite in line with his usual saying, later on, that *"Biophysics is everything we do in the lab"*. Altogether they were about half a dozen local people, plus Sabine and René Wurmser, who had been taken in by Chagas as war refugees. Possibly there were no facilities for a more comfortable arrangement, such as independent individual laboratories.

However, it would appear as possible that, beyond the initial limitations, Chagas might also have found some inspiration in Bernal. Indeed, analysing the role of flexibility on the strategy of scientific advance, one reads from Bernal: *"Nothing could be more fatal to science than rigid adherence to a plan laid down beforehand* (…). *Perhaps a five- or ten-year scheme for the whole of science and shorter schemes for individual sciences would be workable* (…) *and provision would have to be made for changes, as at any moment* (…) *new integrating discoveries might* (…) *demand a complete recasting of pre-existing schemes"* (Bernal, 1939). I submit that these thoughts and propositions were not unknown to Chagas since in 1946, on the occasion of the First Joint Meeting of Biological Societies, in São Paulo (Chagas Filho, 1947), he chose to quote, from that same source: "(…) *the biophysicists' task is only just beginning. All the new methods of examination of the structure and changes of matter – electron microscopes, X-ray analysis, ultra violet and polarizing microscopes, thermal, electric, and acoustic detectors – require to be put in the service of biology and used by men who understand the significance of their finds both physically and biologically"* (Bernal, 1939). The profusion of quotes in documents produced during the few years antedating the creation of the Institute of Biophysics strongly indicates that Bernal's ideas on science planning were contemplated by Chagas at that time.

Two main research lines were soon established. First, the choice of the *Electrophorus electricus* as a research model organism was considered as quite appropriate for "*a multiplicity of research lines, besides* (offering) *the opportunity of a multidisciplinary investigation* (of bioelectrogenesis), *which is the surest way for scientific development*" (Chagas Filho, 2000). The choice of a common research model for the Institute had a predominant role, particularly in the early years, in propitiating the set up of a closely united group. Everybody had an interest in everybody else's work. That is probably the reason why the basic training of newly arrived students passed invariably through the study of bioelectrogenesis.

Second, in line with the familial scientific tradition, Chagas had planned to study the infection caused by the *Trypanosoma cruzi*. A laboratory was built for that purpose and acting upon his brother's advice Chagas invited Hertha Meyer, a German refugee, then working in the Rockefeller Foundation-sponsored Laboratory of Yellow Fever, in Manguinhos, to take the lead. She used the tissue culture technique to investigate "*the protozoan morphology, its evolution in the tissues and the cell changes it might cause*" (H. Meyer, 1943).

The 1942 publication classifies the activities of the Laboratory of Biophysics in groups of studies. No mention is yet made of specific laboratories, which indicates that the Laboratory of Biophysics remained a common space for research within the chair of Biological Physics.

The same organizational picture is portrayed in Chagas's "Comments on Biophysics", published the following year (Chagas Filho, 1943). While dealing with the extremely close relationship between the basic sciences, he provides an outline of Biophysics through a brief review of some of the main advances in the field, based on their respective experimental approaches. Once more he quotes Bernal: "*The great value of this approach as against that of either the older histologists or the biochemists is that with refinement of technique it is easier to approximate to the detailed study of the mechanism of an intact animal or plant*" (Bernal, 1939).

2. *A brief look at the first 25 years of the Institute of Biophysics*

Profound changes in the existing organization were brought by the creation of the Institute on December 17, 1945. The first article of its bylaws reads: "*the Institute aims at the investigation in Biophysics and the cooperation in the teaching of Biology, Chemical and Medical Physics, and in the development of cultural, scientific and technical activities of the University*

of Brazil". The scientific investigation comes explicitly to the forefront, and teaching is regarded as a research-derived activity. This was, with no doubt, a history-making pattern of development for the Brazilian University. It is furthermore possible to identify in the text a suggestion of multidisciplinary activities, through the integration with the university's multiple areas of study.

The *First Memory on the Institute of Biophysics*, published in 1948, is a most revealing document for the early history of the Institute. It shows that four Research Divisions, with their specific equipments and heads, had been created. They were the Divisions of Biological Physical Chemistry (J. Moura Gonçalves), Medical Physics and Radiobiology (M. Frota Moreira), Cell Biophysics (A.M. Couceiro and H. Meyer), and Electrobiology (A.A.P. Leão). These were then the main lines of research implanted by Chagas at the Institute of Biophysics. The study of the electric activity of the brain cortex had been quite recently added, under the direction of A.A.P. Leão, the discoverer of the cortical spreading depression, back in Rio after obtaining in 1944 his Ph.D. from Harvard University.

The faculty as a whole included ten graduate researchers – seven of which figured already in the 1942 document – and every Division contained undergraduate students (graduate courses did not exist until the early sixties).

Last, but most importantly, every one of the Divisions heads were under contract as a peculiarly named, unheard-of class, the "technical specialist".

Each one of these characteristics contains a pattern of development and deserves a comment. First, a University Institute primarily devoted to research is officially recognized.

The second is the strategy, successfully tried at the University of São Paulo, of regularly inviting foreign scientists to visit the Institute, which prevailed from the very beginning. Sometimes the visitors stayed for a few weeks or months, during which time they would work assisted by a chosen undergraduate student. The visits were reciprocated during each side respective summer, for several semesters. A most important result, not always duly stressed, derived from such strategy. Often it originated new laboratories which, in due time, developed into Departments of the Institute. Examples illustrating this point, together with the respective foreign visitor and the student associated to him, are: Radiobiology, with R. Latarjet and L.R. Caldas; Neurobiology, with Denise and Alfred Fessard and C.E. Rocha-Miranda and E. Oswaldo-Cruz; Radioisotopes, with J.D. Cooper and the graduate student E. Penna Franca; Heart

Electrophysiology, with B. Hoffman and A.P. de Carvalho; Electron Microscopy and Cell Ultrastructure, with H. Meyer (already a permanent member) and W. de Souza.

Third, as for the position of technical specialist, created by the public service authorities under Chagas inspiration, its real purpose was to provide a more becoming salary for recognizably competent people recruited for research work. At hindsight, this seems to have been an inventive temporary device to maintain the senior researcher while the full time regime did not come into practice.

Scholars studying the history of the Institute compared the initial group to a "family" (Mariani, 1978; Schwartzman, 1982). Outside observers and several members of the Institute of Biophysics associated this solidarity to the idea of a "*esprit de corps*" (Schwartzman, 1979).

At the Institute's 25th anniversary, its structure had taken a more conventional shape. There were four Departments, but it is still possible to trace their origin to the pre-1945 informal Divisions. The total count of laboratories went up to 26, in 1971. Today, scientific interests are considerably expanded: the Institute includes six Programs and a total of 39 laboratories.

Finally, I selected what I consider three landmarks of the work carried out at the Institute during its first 25 years. The first, in the early fifties, was the application of the modern microelectrode technique to the electroplate, which served to show the production of a sodium-dependent action potential on its innervated side (Keynes and Martins-Ferreira, 1953). Besides, Keynes visit in 1952 showed that this pattern of development could also function as a two-way road. According to Hogkin (1992), this work generated two by-products: one, the successful use of the electric organ as a source of material for the determination of the amino-acid sequence of the sodium channel and two, the development of Keynes's interest in South America, which led to his writings on the voyage of the Beagle and his discovery of the drawings by Darwin's artist Conrad Martens (Keynes, 1979; Hodgkin, 1992).

The second one has more to do with internal affairs of science administration, but it has been chosen because it was fundamental for the Institute survival, at the end of the sixties. E. Penna-Franca, then director of the Institute, obtained funding from a most unusual source – the Brazilian National Bank for Economic Development – thereby changing he face of biomedical sciences in the country. The contract provided the means of a thorough updating of the Institute's equipment,

there included, most notably, a modern Unit of Electron Microscopy and the introduction of the PDP-12 (LINC) computer into the research work.

To describe the third, I take the words of Rita Levi-Montalcini, guest of the Institute between September 1952 and January 1953, on the history of the nerve growth factor discovery. *"The finding that* (…) *extraembryonic transplants elicited the same effects as intraembryonic grafts gave definite evidence for the diffusible nature of the tumor nerve growth-promoting factor.* (…) *I then thought of resorting to the tissue culture technique* (…) *Lack of facilities in this field at* (…) *Washington University prompted me to ask hospitality from Professor Carlos Chagas, director of the Biophysics Institute* (…) *There, a friend of mine, Hertha Meyer, had built and was director of a most efficient tissue culture unit*. (…) *The tumor had given a first hint of its existence in St. Louis but it was in Rio de Janeiro that it revealed itself, and it did so in a theatrical and grand way, as if spurred by the bright atmosphere of that explosive and exuberant manifestation of life that is the Carnival in Rio*." (Levi-Montalcini, 1987).

It is difficult, perhaps impossible, to single out an efficient cause to explain why the implantation of research in the University was a successful project, but I would suggest that it took essentially a group of people who could individually repeat the saying many times uttered by Chagas: "*I have got the science under my skin*".