## Gregorio Weber's Roots in Argentina

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Abstract Professor Gregorio Weber was an outstanding, dedicated scientist, versed in a great variety of scientific subjects. But he was also an exceptional human being: of a reserved nature, he never placed himself above or before others, never put people down. He was a cultivated man with a brilliant intellect, amicable, generous, modest, and prone to listen. He had a real concern with the underlying social issues in all the countries where he lived. His childhood, youth, and university training up to his first doctoral degree took place in his home country, Argentina, and these periods of his life had a deep impact on the shaping of his persona, his cultural habits, and his scientific interests. His great mind and avid quest for knowledge in all spheres of life were undoubtedly nourished by the high standards of the educational system in Argentina at that time but were also fired by the crucial influence of his family and cultural environment, his circle of talented friends, and the informal training that he received in Buenos Aires.

**Keywords** Argentine science • G. Weber in Argentina • G. Weber medical studies • G. Weber ancestors

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#### 1 Introduction

Although the scientific community is well acquainted with Prof. Gregorio Weber's pioneer work and accomplishments in the fields of fluorescence, protein chemistry, and protein—ligand interactions, records of his formative years in Argentina are practically non-existent. When I first began trying to piece together Gregorio's early life in his home country, the task seemed intractable: his contemporaries in the scientific arena, also centennial, are no longer with us; trying to locate former colleagues who might have interacted with him in Argentina drew a blank; my literature search didn't come up with any written recollections associated with Gregorio's roots, and I realized that I was the only Argentine disciple who is still active in the field of fluorescence. However, talking to his daughters and some of his lifetime friends in the USA and the few contemporary family members still alive here in Argentina led me along a fascinating path of discovery and reconstruction as details of Gregorio's childhood, adolescence, and early scientific life began to unfold.

My search included visiting what remains of the old Faculty of Medical Sciences and the institute where Gregorio had read for his M.D. (the premises had been partly torn down decades ago and the remaining sections now form part of the Faculty of Economy of the University of Buenos Aires). Despite the frustration of not being able to find written records at the old building, I was pleased to discover a bronze plaque on an old classroom facing a restored patio with a central fountain (see illustration below) which reads: "These classrooms are the site of the Institute of Physiology of the Faculty of Medical Sciences of the University of Buenos Aires, which Prof. Bernardo A. Houssay directed between 1919 and 1946. Here were conducted the investigations in physiology that led to the award of the Nobel Prize in Medicine to Prof. Houssay in 1947. Dr. Luis F. Leloir, Nobel awardee in Chemistry 1971 also performed his biochemical investigations here. National Academy of Medicine. 1996." These were the laboratories where Gregorio Weber performed his experiments on fibrinogen for his first doctoral thesis at the University of Buenos Aires! Probably this was an inflexion point: I decided to leave aside the originally planned first part of this chapter on superresolution fluorescence microscopy and concentrate exclusively on Gregorio's personal and scientific life in Argentina.

I regret not ever overcoming my timidity and asking Gregorio more about this period of his life. My consolation, however, is that I have been able to embark on this most enjoyable historical research expedition which has renewed and enhanced my immense admiration for him, refueled by the warm memories transmitted by his nephews and nieces, his 100-year-old cousin, and the very few close acquaintances from his early years still alive. Reading the Ph.D. thesis he wrote after graduating as an M.D. and researching his origins, family, friends, tutors, and possible sources of inspiration has been a truly wonderful journey for me personally and one which, I hope, will fill a gap and supplement the excellent recollections of Prof. Weber's work and life in the northern hemisphere that Dave Jameson (e.g., [1] and [30]) has provided over the last decades.

### 2 Gregorio Weber's Family and Childhood in Buenos Aires

Prof. G. Weber was born in Buenos Aires on July 4th, 1916, son of Leon Weber and Rosa Gerchunoff, and named Gregorio after his maternal grandfather. Leon Weber was originally from Bessarabia, in more recent history a region under Russian rule up to World War I, united with Romania in 1918 and forming part of present-day Ukraine and Moldova. The Weber family lived for some time in Transylvania, the central part of Romania. When Leon Weber was about 18, he left Romania to escape from the 5-year military service ahead. He managed to stow away on a cargo ship belonging to the Dreyfus Armateurs Shipping Group, heading for the Caspian Sea. He was discovered on board before the ship reached port but was fortunately given the chance to work his way. Leon became a respected employee and the firm subsequently kept him in service, based in Hamburg. Thereafter Leon Weber accepted the company's offer to work in Argentina, where of course Gregorio was later born. He arrived on the ship "Santa María" on February 2nd 1908. Dreyfus currently accounts for about 10% of the world's agricultural commodity trade flows and one century ago the Buenos Aires branch was already a key outpost for grain commerce. It should be remembered that in the early twentieth century Argentina was ranked among the ten richest countries in the world. Once in Argentina, Leon became an expert in sampling grain for export, and was eventually head of the division for wheat quality control, a post he held until 1964.

Gregorio's mother, Rosa Gerchunoff, was the daughter of Rab Gershon Ben Abraham Gerchunoff and Anna Korenfeld. According to the 1895 last nominal census in Argentina, Rosa was 16 at that time, which puts her date of birth in 1879; her first name is written Rachila and the family surname appears as Herschenov. The family was originally from Proskurov, a town belonging to the Russian Empire (currently Jmelnítskiy, in the Ukraine). They later moved to Tulchyn, from where they emigrated in 1889 to Argentina together with another 135 families. When they arrived in Argentina they first of all settled in the Jewish colony Moisés Ville, in the



**Fig. 1** Gregorio Weber's maternal branch of the family in a typical group pose. Rosa Gerchunoff, Gregorio's mother, is the one standing on the *right*, aged 16. To her *left*, her famous brother Abraham (Alberto) Gerchunoff, Buenos Aires, 1901

province of Santa Fe and later moved to Rajil in the province of Entre Ríos, one of the colonies founded by Baron Maurice de Hirsch as havens for exiles from the Pogrom. The Gerchunoffs were intellectuals with no experience in work on the land. Adapting to farm life in the colony was hard, even more so when in 1891 Rosa Gerchunoff's father was murdered by a gaucho, an episode described in "The Crimes of Moisés Ville<sup>1</sup>" [2]. I was impressed to hear Gregorio's cousin Anita – currently aged 100 – narrate the story of her grandfather's murder by a drunk gaucho, a historical fact which was also an oral tradition received via her mother Cecilia Gerchunoff, and which motivated their moving to the province of Entre Ríos (Fig. 1).

Rosa's brother Abraham was born in 1881 according to the above census – the year of the Great Pogrom – although there are still discrepancies about the exact date of his birth, partly because in order to be able to work formally while he was an adolescent he may have declared himself to be older. He later became a journalist for the prestigious La Nación newspaper and a well-known writer under the name of

<sup>&</sup>lt;sup>1</sup> Moisés Ville, sometimes called "the Palestine of the Pampas," was the first Jewish agricultural colony in Argentina. The book by Javier Senay describes the circumstances surrounding the murder of 22 Ukrainian immigrants in this colony between 1889 and 1906. The gauchos felt that their livelihood and lifestyle were being threatened by the agricultural export model which involved the fencing off of land.

Alberto Gerchunoff. With his book "Los Gauchos Judíos," published in 1910 and translated into English in 1955 ("The Jewish Gauchos of the Pampas"), Alberto is widely considered to have successfully defended the ethnicity of the Jewish immigrants whilst at the same time assuring their "argentineness," showing the two to be compatible. It is reported that Jorge Luis Borges said Alberto Gerchunoff "was an indisputable writer, but his reputation transcends that of a man of letters. Unintentionally and perhaps unwittingly, he embodied an older type of writer ... who saw the written word as a mere stand-in for the oral, not as a sacred object."

Rosa met Leon through her elder sister Sofía's husband, Enrique Halperín, who also worked at Dreyfus. After their marriage Rosa and Leon Weber lived in San Juan Av. in the San Telmo district, the heart of the city's oldest colonial area. Their eldest child, Ana Sofía, was born on 31st May 1913, Frida arrived on December 7th 1914, and Gregorio was the youngest child, born on July 4th 1916. Rosa worked as a volunteer at the Israeli Hospital in Buenos Aires. She died in 1923 at the early age of 44 of tuberculosis, a common cause of death in the pre-antibiotic era, and it is presumed that she had contracted the disease while working at the hospital. Leon then moved with his family to 636 Hipólito Yrigoyen St., a 400-year-old street in the quarter of Montserrat, where the city of Buenos Aires was founded, and less than two blocks away from the presidential palace. Family members recall that when Gregorio was a very small child he always referred to himself as "yo, yo" (me, me), and soon Yoyo was adopted as his official nickname by the family at large, a substitute name which lasts to this day in the inner family circle and among his closest friends. Gregorio and his sisters were very close, especially after their mother's tragic death. Her sudden absence must have had quite a strong impact on Gregorio at his tender age. His aunt Sofía and her seven children were frequent visitors at the Weber family home after the death of Rosa and played an understandably crucial role in Gregorio's childhood and adolescence (Figs. 2 and 3).

Fig. 2 An already recognizable Prof. Weber, aged 1. Buenos Aires, 1917



**Fig. 3** Frida (12), Gregorio (10) and Ana (13) Weber. Buenos Aires, 1926



In the days when Gregorio attended primary school, calligraphy classes formed an important part of the curriculum during the first 2 years. Dip pens and ink-filled white porcelain pots were the tools of the time and children filled pages and pages of millimetrically equidistant cursive letters. Gregorio's tidy handwriting is definitely to be traced back to this early stage and stayed with him for his whole life.

Gregorio's eldest sister Ana studied chemistry at the Faculty of Exact Sciences, which in those days was a couple of blocks away from their Montserrat home. She worked for the National Roads System and later for the National Atomic Energy Commission (CNEA). Ana studied uranium compounds at the laboratory of Analytical Chemistry headed by Raquel Zukal. The CNEA had other laboratories working on radionucleids: the radiochemistry laboratory, headed by Walter Seelmann-Eggebert, a disciple of Otto Hahn, and the laboratory of general chemistry, under Arturo Cairo. Ana married Juan T. D'Alessio, a chemist who later undertook postgraduate studies in physics (the latter discipline did not exist as such in the Faculty of Exact Sciences when he was an undergraduate) and was a disciple of Teófilo Isnardi; as we'll see below, Juan had a great deal of influence on the shaping of Gregorio's scientific choices.

Frida, the second sister, studied philology and worked at the Institute of Spanish Literature. As a researcher she specialized in Spanish theater of the Golden (XVIth)

Century, drawing interesting and unsuspected links with Russian narrative when analyzing the structure of comedy [3]. She married a civil engineer, Alberto Kurlat. He was also the son of immigrants: Felix Kurlat was from a small town in the Ukraine, Krivoye Ozero, and his mother, Assa Liebeschütz, was from Odessa. Frida was a good friend of Aida Barenboim, mother of the famous pianist and conductor Daniel Barenboim. Frida's intellectual interests and her circle of friends may have been one of the influences on Gregorio's humanistic tastes and his permanent search for stylistic beauty and perfection in language.

One of Frida's daughters, Isabel, studied medicine, later specializing in neonatology. Before she had embarked on this specialization, while staying with his sister's family on one of his visits to Argentina in later years, Gregorio asked Isabel which branch of medicine she would like to follow. Isabel replied that she was thinking of specializing in pediatrics; with his characteristic wit and prescience Gregorio told her: "Don't worry, pediatrics is a malady that spontaneously gets resolved with time. . .". Before practicing her clinical specialization, Isabel worked for a few years at the chair of Biochemistry of the Faculty of Medicine with Prof. Andrés Stoppani, one of Gregorio's friends from university days.

Family life was very important for the extended Weber family. As mentioned, Gregorio's aunt Sofía Gerchunoff – married to Enrique Halperín – and her seven children often shared the family table with Leon Weber and his three offspring. Gregorio's mother's family played a decisive role in shaping his cultural tastes, if not his scientific inclinations. The Gerchunoff branch of the family was part of the rising intellectual middle-class in Buenos Aires, as were the Halperín cousins. By then Leon Weber had a well-paid job at Drevfus, and the family enjoyed a relatively comfortable economic position with access to the rich cultural offerings of Buenos Aires, the literary links cultivated by his cousin Alberto Gerchunoff and the more affluent branch of the Halperín cousins, particularly Gregorio Weber's eldest cousin, Gregorio Halperín, who was a professor of Latin, married to the Italian Renata Donghi, professor of Spanish and Italian literature. The son of Gregorio Halperín and Renata Donghi, Tulio Halperín-Donghi (1926–2014), later became a source of pride for the family: he was probably one of the country's most respected scholars of nineteenth and twentieth century Argentine history who later taught at Oxford and became a professor at Berkeley.

# 3 The City: Buenos Aires – and the Countryside – La Cumbre, Córdoba

When Gregorio Weber was born, Argentina had 7.5 million inhabitants. On the political front, during Gregorio's childhood and early adolescence Argentina lived a period of political stability: the year before his birth the first national elections under universal (but only male!) suffrage took place; after decades of conservative administrations, three successive democratically elected presidents from the more

liberal Radical Civic Union, one of the two major political forces in Argentina, succeeded one another in office. In tune with the political front, Argentina was living its economic and cultural Belle Époque: in the preceding 40 years the GDP had grown at an annual rate of 6%, the fastest recorded in the world at that time, attracting immigrants by the thousands: when Gregorio was born, half of the population of Buenos Aires was foreign-born. Argentina was among the ten richest countries in the world, ahead of Germany, France, and Italy. In contrast, Gregorio's adolescence was marked by the 1930 coup that installed the first of a series of de facto military rulers and signified the commencement of economic decline for Argentina as a consequence of the Great Depression and the collapse of commodity trade.

In 1929 Leon Weber bought a small property at the foot of the hills on the outskirts of La Cumbre, a resort in the Mediterranean province of Córdoba, where he and the family spent 3-month-long summer holidays together with their extended family, who also had a property there. Gregorio's cousin Ana ("Anita") – now aged 100 – told me several anecdotes about Gregorio's adolescence that are worth narrating here. They did not have a car, and the rides to and from town required taxis. They soon discovered that the taxi driver also hired horses, and horse-riding became Gregorio's passion and main activity when on holidays. Anita laughed heartily when recalling that as a young adult Gregorio had a very elegant jacket, which was probably meant for formal occasions. Instead, the dark jacket became his uniform when riding his horse, normally at full gallop. The inhabitants of the small town of La Cumbre must have wondered at this tall, elegant young man, flashing by on horseback dressed in what must have seemed like an Olympic equestrian uniform!

Back in Buenos Aires, whilst still an adolescent, Gregorio was very fond of music. According to his cousin Anita, she, Mauricio Goldenberg, Gregorio, and a "gorgeous" girlfriend of his at that time were regulars up in the Gods at the Buenos Aires opera house, the Colón Theater. Gregorio continued this tradition until his final years at medical school, with classmate and girlfriend Carola (see below).

# 4 Medical School Days and the Forging of Lifelong Friendships

If one rolls back Gregorio's scientific life, one inevitably wonders how it is that he chose to study medicine of all disciplines. Dave Jameson mentions that Gregorio's science teacher at secondary school advised him to study medicine in view of the difficulties involved in finding steady employment as a scientist in those days in Argentina [4]. The death of Gregorio's mother, Rosa, from an incurable disease, must have been a very painful experience for a 7-year-old child, and may also have played a role. The family story is that Ana, his eldest sister, was the one who wanted to be a physician, but in the early 1930s few women studied medicine

in Argentina and Leon Weber was not happy at all with the idea. The family's recollection is that Gregorio told Ana "I will study medicine for you."

Being a student at the School of Medical Sciences of the University of Buenos Aires, dating back to 1852, was not a light endeavor; but Gregorio had a very bright intellect and was a hard-working student. In those days, medical studies took a total of 6 years, and included a very tough entrance examination. He became part of a group of outstanding classmates and friends: Miguel Podolski, Leon Berlin, Mauricio Goldenberg, Carola Blitzman, Isabel MacDonald, Amalia Ingenieros, and Andrés Stoppani. After graduating Miguel Podolski and Leon Berlin practiced medicine for some years but subsequently left clinical practice and engaged in a highly successful endeavor, as owners of the Argentine branch of Odol, a pharmaceutical-cosmetic firm currently belonging to GlaxoSmithKline.

Mauricio Goldenberg was already friends with Gregorio from pre-university days. He trained as a phenomenological psychiatrist and later became a psychoanalyst famous for installing a communitarian "straitjacket-free" psychiatric approach in general hospitals and brought pioneer reforms in mental health treatment not only to Argentina but also to other Latin American countries. Isabel Fernández Vega, Mauricio's widow, recalls that the last time she and Mauricio, who she was dating at that time, saw Gregorio in Argentina was in 1943, when they visited him at his Yrigoyen St. apartment: he was packing his luggage to leave for England. Twenty five years later, the Goldenbergs were in exile in Venezuela, and Gregorio visited them in Caracas. They had a millionaire friend who sent his chauffeured limousine to drive Gregorio to visit the Catholic University Andrés Bello and later to dinner at an exorbitantly luxurious mansion. When asked about the experience, Gregorio replied "...too much for me..." The Goldenbergs settled later in the USA, where Isabel, now 96, still lives. "We remained friends with Yoyo for life"...she said with an emotive tone in a recent conversation (Fig. 4).

Like Gregorio, Andrés Stoppani also went to Malcolm Dixon's Department of Biochemistry in Cambridge with a British Council fellowship, partly overlapping with Gregorio's stay at that lab. Andrés Stoppani subsequently became professor of Biochemistry in Buenos Aires and Ph.D. supervisor of 1984 Argentine Nobel laureate in Medicine and Physiology César Milstein. Andrés was very close to Gregorio and was best man at Gregorio's wedding to Shirley Nixon in England. In fact, the Buenos Aires—Cambridge "connection" started in 1936, with Luis Federico Leloir conducting research under the supervision of Sir Frederick Gowland Hopkins. Ranwell Caputto, who would become a key figure in the research that led to Leloir's Nobel award in Chemistry in 1970, was another of the Argentine scientists working in Malcolm Dixon's lab at the time of Gregorio's stay in Cambridge. Ranwell traveled to the U.K. with a fellowship of the Argentine Association for the Progress of Science in 1943 (Fig. 5).

A special case among Gregorio's close companions during his student days was Carola Blitzman, currently Carola Eisenberg. She was born in 1917 (not 1923 as reported elsewhere) and formed part of the same "inner circle" of student friends. Carola told me that she had met Gregorio while queuing at the Faculty of Medicine: "I was 18 at that time. I fell in love with him. It was an adolescent, but serious love."



**Fig. 4** The "old" Faculty of Medical Sciences of the University of Buenos Aires (1935), where Gregorio Weber studied medicine. The tram rails running on Avenida Córdoba can be seen. The right wing of the building was partly torn down towards the end of the 1930s, while the new (current) building was being built, being completed in 1944

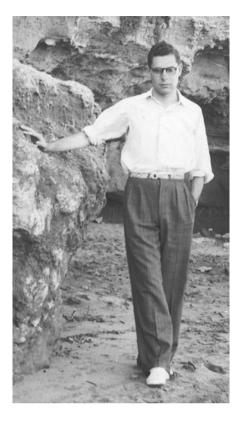
In "Tributes to Gregorio Weber (1916–1997)," a collection of homages collated by the University of Cardiff which appeared on the Internet, she wrote that "he was by far the brightest of us and by far the most interested in the basic science of medicine." She and Gregorio became inseparable and spent a great deal of leisure time together. She lived with her grandmother in the peripheral Buenos Aires quarter of Mataderos whereas Gregorio lived right in the downtown area, but Carola reminisces that Gregorio would gladly take the 1-hour bus journey, being a regular guest on weekends. Carola's grandmother regularly cooked Gregorio's favorite meal: filet steak. After some months, Carola's grandmother asked whether Gregorio was her "official" boyfriend: "he is so handsome and intelligent, I am sure he is in love with you, have you considered marrying him?" Carola, a bit annoyed, blushed, and responded: "have you considered the possibility that Yoyo is in love with you and your delicious steaks?" As mentioned earlier, they shared a common passion for classical music. On one of their walking expeditions, Gregorio gave her a recording of a Sibelius concert, a present which is dear to her even now. Carola's family had a house by the sea in Mar de Ajo, on the Atlantic coast, and one summer the inner group of medical students enjoyed an unforgettable holiday there. After graduating from Medical School in Buenos Aires in 1944, Carola obtained a fellowship to go to the USA where she specialized in child psychiatry with Leo

Fig. 5 The central patio on the ground floor of the "old" Faculty of Medical Sciences building (currently Faculty of Economy). Prof. Bernardo Houssay's laboratories and the Institute of Physiology where Gregorio Weber performed his Ph.D. thesis work faced the patio with the central fountain, 2016



Kanner at John Hopkins. Kanner was the first physician to be identified as a child psychiatrist in the USA and to introduce the term "autism." Carola married Manfred Guttmacher and subsequently Leon Eisenberg. She became Dean of Students of the Massachusetts Institute of Technology (the first woman to hold that position at MIT), Dean of Student Affairs at Harvard Medical School, and cofounder of Physicians for Human Rights. Carola, Gregorio, and their respective spouses renewed contact in the USA. At the age of 98 she reaffirmed her early love for Gregorio, and at the close of a recent conversation said: "...the one thing I regret at this stage of my life is not to have been able to visit Yoyo when he was terminally ill."

Fig. 6 Young medical student Gregorio Weber, aged 24, on holiday at the sea-side resort of Miramar, in the province of Buenos Aires. 1940



After Ana and Frida married and left the parental home and during Gregorio's time as a medical student, his cousin Nicolás Halperín moved into the family apartment for several years while studying law, sharing hours of study and leisure with Gregorio. Gregorio finished the 6-year medical career in time to graduate in 1942, completing his Ph.D. in medicine the following year. His father Leon had equipped a room for him at home with all the gadgets of the trade, from blood pressure monitor to stethoscope, but according to the family recollections the only time Gregorio ever practiced medicine was apparently when his nephew Enrique burnt his arm with boiling tea (Fig. 6).

### 5 Scientific Mentors and Influences During Early Research Days in Buenos Aires

Physiology, and in particular the way that Prof. Bernardo Houssay taught it at the Faculty of Medical Sciences, was Gregorio's favorite discipline during his studies at the University of Buenos Aires. Carola Blitzman reminisced that during the physiology lectures she would sit as far away as possible from Prof. Houssay to

avoid being questioned, whereas Gregorio would do the opposite and sit right at the front. When Gregorio felt the lure of basic research, it seems logical that he was attracted to Houssay, the first full-time professor of the university system in Argentina. In the 1930–1940s the Institute of Physiology was a world-class institution where physiologists from other countries were being trained, and one of the few places that cultivated state-of-the-art medically oriented research at the university, supported by the Rockefeller Foundation since 1929. It is also clear that Gregorio made the right choices – he was appointed teaching assistant at the best laboratory available and he had the best supervisor he could possibly find in the whole University of Buenos Aires. Houssay was to become the first Argentine Nobel awardee for Physiology and Medicine in 1947.

During his time at Houssay's Institute of Physiology Gregorio wanted to expand his horizons even further, particularly in physics. But the Faculty of Exact Sciences of the University of Buenos Aires did not have a critical mass of physicists; in fact, most of the Masters and Ph.D. thesis works were conducted in private or federal institutions outside the university, positioning the capital city's physical sciences behind those of La Plata (Province of Buenos Aires), where Emil H. Bose (1909–1911) and Richard Gans (1912–1925) headed the Institute of Physics with clear research aims, and Córdoba, where Gaviola set the pace from the Astronomy Observatory. Physics set off at the University of Buenos Aires with the hiring of Teófilo Isnardi, who had obtained his Ph.D. with Walter Nernst in Germany; the Institute of Physics was not founded until 1935, and the doctorate in Physics was launched in 1937 in marked contrast to Chemistry, for which a doctorate was implemented in 1897. Isnardi's chair was not only an isolated island; he was recognized as "an erudite who appeared to know everything" according to Juan J. Giambiagi, but research was clearly not a priority for him... perhaps not quite what Gregorio was looking for in a mentor.

Gregorio was well acquainted with the work of astrophysicist Ramón Enrique Gaviola in Córdoba, who had worked with Richard Gans at the University of La Plata at the time when Argentina was the only Latin American country whose scientific production in physics was quoted in the Citation Index; in fact Gaviola and Gans were the only two Argentine physicists who had "citation visibility" in Europe. In 1922 Gaviola was at the University of Berlin at the time of Max Planck, Max Born, and Albert Einstein, graduating from the University of Berlin in 1926. Gaviola constructed a phase fluorometer in 1927 [5] and had recorded not only spectra of stars but also, more closely to Gregorio's interests, was the first to measure excited state nanosecond lifetimes by phase fluorometry, with an instrument built in Pringsheim's laboratory [6]. Years later, while in Cambridge, Gregorio gave credit to Gaviola's seminal observations in one of his most famous publications on fluorescence polarization [7]. Gaviola had an immense impact on the development of science in Argentina. He was head of the Astronomy Observatory of Córdoba, founded in 1871, and introduced cosmic radiation research in Argentina. He hired scientists like the Austrian Guido Beck, who organized the so-called nucleus of theoretical physics, a group that led to the foundation of the Argentine Association of Physics in 1944. Gaviola was also a pioneer who

championed full-time research and teaching. He was succeeded by the astrophysicist Livio Gratton, Enrico Gratton's father.

Gregorio's wider interest in Science at large led him to informally train his mind in the subjects more akin to his future calling already during his medical school days. The person who played the key role in shaping Gregorio's choices was his brother-in-law Juan D'Alessio, the chemist and physicist married to his eldest sister, Ana. Juan D'Alessio was a teaching assistant at the Institute of Physics led by Isnardi and was Gregorio's coach in physics and chemistry, the two disciplines to which Gregorio was profoundly attracted and which became fundamental tools in his long research career.

### 6 Doctoral Thesis at the University of Buenos Aires

Gregorio wrote his first doctoral thesis work on "Viscosity anomalies of fibrinogen solutions" [8] under the formal supervision of Prof. Bernardo Houssay. The manuscript, written in impeccable Spanish, and with handwritten Greek characters in ink, is very short and concise, as was the custom for Ph.D. theses those days at the University of Buenos Aires, and focuses on a brief series of concatenated physicochemical experiments. It starts with theoretical considerations based on Newton's hypothesis on internal friction in liquids and the hydrodynamics of ideal liquids formulated one century later by Euler, Bernoulli, and others as a background for the experimental section on the thixotropy and other viscosity anomalies of fibrinogen solutions. Gregorio built an Ubbelohde-type viscometer and subsequently a Tsuda viscometer to be able to carry out his work. At the time Gregorio was reading for his thesis, the Faculty of Medical Sciences had appointed Dr. Venancio Deulofeu as professor of Biological Chemistry (1935) and Dr. Julio J. Rossignoli was in charge of Biological Physics at the Institute of Physiology. More interestingly, Dr. Dora Potick was studying the physicochemical alterations of blood serum by snake venoms. This is the closest thematic approximation to Gregorio's thesis subject. We do not know whether any of these scientists played a role in Gregorio's thesis, but they were likely to be knowledgeable in some aspects of the work. In my view Gregorio's first thesis is a cauldron in which the embryonic stages of his views on macroscopic and microscopic viscosities were concocted, and which he addressed years later after developing the appropriate fluorescence polarization tools (Figs. 6 and 7).



**Fig. 7** (a–b). Laboratories at the Institute of Physiology, Faculty of Medical Sciences, University of Buenos Aires, where Gregorio Weber performed his experimental work on fibrinogen reading for his Ph.D. Thesis. Photographs ca. 1936

# 7 Second Law of Thermodynamics: Irreversible Departure from Argentina

As a background to Gregorio's medical school days a democratically elected president brought back the Radical party and a period of stability (1938–1942) to Argentina. The Rector of the University of Buenos Aires was Carlos Saavedra Lamas, a professor in international and labor law who in 1936 had been the first Latin America Nobel Prize recipient (for Peace). However, by the time Gregorio left Argentina for England in 1943, the constitutional government was unpopular and weakened; the country was profoundly divided into the supporters of the Axis powers or the Allies in World War II, the army exerting enormous pressure on the government. An interim president and a new military coup followed in rapid succession. The universities were in turmoil, becoming strongholds of resistance against the de facto rulers, and some of the most outspoken professors, Houssay included, signed a manifesto against the government. By October 1943 they had been dismissed from the University. So Gregorio must have been able to participate in a democratic vote only once in his home country, and left Argentina at the climax of disturbances within the University, amidst a chaotic situation. Just like Gregorio's science teacher at school [4], Prof. Houssay did not encourage medical graduates to engage in full-time scientific research in Argentina unless they had the private means to support themselves (see, e.g., [9]): "You're not rich are you? Because I can't offer you anything.... the paid positions I have at the Institute are all occupied and they'll never increase the number of posts." Against this backdrop it is not surprising then, that Gregorio applied for and won a British Council Fellowship which would support his second Ph.D. studies at Cambridge University. According to his classmate and friend Carola Blitzman Eisenberg when he left for the UK "... Yoyo could hardly contain his enthusiasm and excitement with his new life ahead...". Apparently his father Leon was the major force behind Gregorio's decision to travel abroad. He passionately supported his son's choice of career and told Gregorio "all I have is at your disposal to follow your dream, anywhere in the world, even if it means never seeing you again."

I will not dwell on Gregorio's stay of several years in Cambridge and Sheffield (a subject covered copiously elsewhere; the reader is referred to a delightful short paper by Brian Hartley [10] and the most read homage articles on Gregorio, by Dave Jameson [1, 4] and Chapter 1 by Jameson in this monograph) except for a brief mention of an anecdote at the commencement of his stay. Upon arriving in England Gregorio stayed a few days in London before going on to Cambridge. As was customary, he was asked to leave his passport at the hotel reception desk. When he went to retrieve it upon leaving the hotel, it couldn't be found; it had mysteriously disappeared and he had to go through painstaking red tape to get a replacement. Apparently this was not an isolated incident and it was surmised at the time (1943) that Gregorio's passport joined the many others being used to help people attempting to escape from the Holocaust.

According to his friends, Gregorio was eager to leave Argentina in search of new horizons, but his almost 3 decades in Buenos Aires had already marked him forever. By the time he left he had command of other languages besides his native Spanish, having an innate ability to rapidly expand his vocabulary and read avidly in the original idiom.<sup>2</sup> He carried with him his distinct, unmistakable "porteño" accent in his native Spanish (not to be confused with the "Lunfardo" underworld slang) with a remarkable richness of terms and nuances; he also carried with him years of readings of his contemporary literary geniuses, like Borges, whose poems appeared first as pleasant surprises in a local newspaper. Gregorio's departure and personal background have a parallelism with César Milstein's, who left Argentina about a decade later: the two headed to Cambridge after finishing their first thesis work at the same Faculty of Medical Sciences, and both earned a second Ph.D. at Cambridge University. Both Gregorio and César were sons of immigrants, and the two had Ukrainian ancestors. The two were born, spent their youth, and were educated and professionally trained in Argentina, but found their success as scientists abroad.

### **8** Family Reencounters in the Northern Hemisphere

During Gregorio's stay in England his father Leon visited him several times, and back in Buenos Aires Leon and his married daughters eagerly awaited Gregorio's letters, concerned about the austerity of war and post-war conditions. Leon would personally make regular trips to the port of Buenos Aires to ship a box addressed to Gregorio's wife, Shirley Nixon Weber, containing Argentine goodies: tinned corned beef, *dulce de leche* and a special type of soft cheese, a ritual which involved endless red tape procedures. Years later, in January 1963, Gregorio's sister Frida, Mrs Kurlat by then, organized a trip to the UK with the whole family on the vessel "HMS Arlanza" with the idea of getting to know Shirley personally. Luck would have it that by the time the family arrived in England Gregorio and family had moved to Urbana-Champaign!

In the pre-laser era, a "short" light pulse was in the order of 20–50 ns. When Gregorio's brother-in-law Juan D'Alessio was at the Atomic Energy Commission in Argentina in 1961, he worked very hard trying to produce a lamp generating pulses of shorter duration and high energy to study second-order reactions in his flash photolysis experiments. In 1963 he was invited to work at Notre Dame University in Indiana where he spent 2 years continuing his research on flash photolysis, managing to lower the duration of the pulses to 10 ns. His stay at Indiana enabled

<sup>&</sup>lt;sup>2</sup> Dave Jameson described Gregorio's appreciation of the written language of Francis Perrin [4]: "...it was written in that transparent, terse style of XVIII century France, which I have tried, perhaps unsuccessfully, to imitate from then onwards." In my view, Gregorio definitely did achieve what he sought: elegance, precision and conciseness of expression in his written and oral language.

the D'Alessio family to resume the close relationship with Gregorio. Gregorio's nephew Enrique D'Alessio, a physicist, spent prolonged periods at Gregorio's apartment in Urbana. Back in Buenos Aires, Juan D'Alessio succeeded in further reducing the lamp pulses to less than 1 ns by using electrodes covered in liquid Hg which self-renewed themselves after each pulse. More than once I listened to Gregorio telling me about the splendid D'Alessio flash mercury lamp which obviously interested him as an excitation source for his polarization measurements. Pulsed lamps were subsequently superseded by high intensity laser sources with <0.1 ns pulses, but back in the D'Alessio lamp was one of the few instruments capable of delivering high intensity pulses with a decay time of 0.55 ns and which could be operated up to 50,000 pulses s<sup>-1</sup> in the 250–600 nm range (D'Alessio et al. 1964).

## 9 His Long Visit in 1970: A Brief Incursion into Argentine Neuroscience

In the membrane field, the series of polarity-sensitive fluorescent probes derived from (2-(dimethylamino)-6-(acyl)naphtalene introduced by Weber in the late 1970s [11] are among the best-known and most used fluorescent compounds. When solvent polarity increases, probes of this series (Laurdan, Prodan, Acrylodan, Patman) share the property of undergoing bathochromic shifts in their fluorescence emission spectra. The basis of this phenomenon is the increase in the dipole moment in the excited state, relative to that of the molecule in the ground state. From a chemical standpoint, the members of this family of environmentally sensitive fluorescent molecules share a naphthalene structure substituted with an electron acceptor (acyl substituted carbonyl group) and donor (alkylamino group) groups.

In 1970, well before the introduction of Prodan [11] and other dansyl polarity-sensitive fluorescent probes, which were to become so useful in membrane research, Gregorio visited his alma mater, the Faculty of Medicine at the University of Buenos Aires. This visit included the Institute of Cell Biology, where I was reading for my Ph.D. under the supervision of Eduardo De Robertis. The two knew each other from medical school days. After discussing the state of affairs in the lab, Gregorio suggested the synthesis of a dansyl-choline environmentally sensitive fluorescent ligand to study the aqueous-organic solvent partition properties of hydrophobic lipoproteins being studied in De Robertis' laboratory. The probe (1-dimethylaminonaphtalene-5-sulfonamidoethyl-trimethylammonium) was synthesized in Urbana-Champaign by one of Gregorio's students, David P. Borris, and was coined "DNETMA" or simply dansyl-choline. I performed the fluorimetric measurements under Gregorio's supervision (Fig. 8).

This was my first serious lesson in fluorescence spectroscopy – directly coached by the master in the field! The ingeniously simple experimental technique designed by Gregorio involved titration experiments in a two-phase solvent system [12].

$$\begin{array}{c} \text{H}_{3}\text{C} \\ \text{N} \\ \text{CH}_{3} \\ \\ \text{CIO}_{4}^{\ominus} \\ \\ \text{HN} \\ \text{-CH}_{2} \\ \text{-CH}_{2} \\ \\ \text{-N} \\ \\ \text{-CH}_{3} \\ \\ \text{CH}_{3} \\ \\ \text{CH}_{3} \\ \\ \text{CH}_{3} \\ \\ \text{-CH}_{3} \\ \\ \\ \text{-CH}_{3} \\ \\ \text{-C$$

Fig. 8 Dansyl-choline (1-dimethyl aminonaphtalene 5-sulphonamido ethyl-trimethylammonium perchlorate), an environmentally sensitive fluorescent probe with cholinergic pharmacological activity, designed by Gregorio Weber in Buenos Aires [12] during his 1970 working visit. The compound was subsequently used by Changeux's group at the Pasteur Institute [15] and addition of a longer spacer arm (C6) conferred the compound agonist activity [27–29]

The lower, organic phase contained the hydrophobic lipoprotein; dansyl-choline was initially present in the upper, aqueous phase. After equilibration, the fluorescence emission in the upper aqueous phase was measured and subsequently a series of non-fluorescent acetylcholine-mimicking compounds, i.e. cholinergic ligands like acetylcholine or decamethonium were added and fluorescence intensity recorded again. Professor Weber wrote down the readings by hand as his student Pancho performed the titrations in the Amino-Bowman fluorimeter; the time gaps in between additions were filled in by subtle comments and teachings on every possible subject – what a privilege! I still keep those records. Dansyl-choline shared the ethyl-trimethylammonium end with the natural neurotransmitter, acetylcholine, exhibited a high affinity for the lipoprotein binding acetylcholine in the organic phase [13] and for horse serum cholinesterase in aqueous media [14]. The compound thus became the first fluorescent probe for the study of cholinergic macromolecules, and the introduction of a propane spacer arm having an additional carbon was adopted in a subsequent version synthesized by Jean-Pierre Changeux's group at the Pasteur Institute. This series of experiments was performed on the membrane-bound nicotinic acetylcholine receptor from Torpedo marmorata electric tissue by Jonathan Cohen at the Pasteur Institute in Paris [15, 16].

During this visit to Argentina Gregorio was appointed honorary President of the Albert Einstein Center for Medical Research (CIMAE), a position which he held until 1997. He used this platform to deliver several courses on fluorescence spectroscopy and protein–ligand interactions which gathered essentially all young researchers interested in these topics and became a landmark in the field. Some of the formulae written on the blackboard and the notes that Gregorio scribbled down during that period were to become part of his classic book on Protein Interactions, dedicated to "those who put doubt above belief" [17]).

I feel very privileged to have been an active player during Gregorio Weber's first and only scientific incursion in the field of fluorescence in Argentina. I couldn't have wished for a more motivating teacher to prod my mind.

### 10 Gregorio Weber's Influence: A Personal Experience

Gregorio had a profound influence on my scientific career in several ways. The first resulted from the somewhat serendipitous choice made by my Ph.D. supervisor, Eduardo De Robertis, to put his student – me- under Gregorio's mentoring during his prolonged 1970s visit to Buenos Aires. This guru-shishya relationship was probably the best teacher-apprentice relationship I have ever had, involving a oneon-one crash course in fluorescence techniques! A few years later, when I was a fresh postdoc working with De Robertis and waiting for a position abroad to materialize, Gregorio was again to play a crucial role in my scientific career. I had applied to the Royal Society in London and was awarded a fellowship to go to Cambridge. Enthused with the success of my application, I wrote to Gregorio telling him the good news. My letter crossed with his, written during his sabbatical leave in Europe in 1973, where he told me he had met "a young scientist who had worked with Manfred Eigen and now heads the Department of Molecular Biology at the Max-Planck Institute for Biophysical Chemistry in Göttingen." The young scientist was Tom Jovin. In his letter, Gregorio suggested that I join Tom to start a group working on membranes and receptors. I followed Gregorio's advice and within 3 months I became a member of Tom's Department.

When I wrote my Ph.D. thesis in Buenos Aires, I consulted with my supervisor, Prof. De Robertis, about possible ways to defray the cost of printing the more than 10 copies needed (this may sound ludicrous now, but in those days it was done at expensive typesetting printing houses). Without further explanation, De Robertis told me to go and see a Dr. Podolski, president of a pharmaceutical firm. Dr. Podolski complied with my request and I happily received the funds to have my thesis printed. Many years later, after Gregorio sadly passed away I was contacted by friends in Urbana-Champaign in relation to raising funds to support the Gregorio Weber Memorial Fund at the University of Illinois. At that time I was back in Argentina, working at the University in Bahía Blanca. It occurred to me to phone Dr. Podolski again. When I explained the purpose of my call, without so much as a pause, he immediately replied "yes, of course, you can come and collect a check at your earliest convenience." It was a very generous sum for local standards. It is only now, through my research on Gregorio, that I learn Dr. Podolski was the very same Miguel Podolski who was one of Gregorio's "inner circle" during his medical school years in Buenos Aires!

During my stay in Göttingen, Gregorio's influence continued. Together with Hansjörg Eibl, and inspired by Gregorio's work on pyrene butyric acid, a very long lifetime fluorescent probe (e.g., [18, 19]), we synthesized 1-pyrene butyryl-choline (PBC). This pharmacologically active fluorescent probe which, tested by Bert Sakmann on the nicotinic acetylcholine receptor at the frog neuromuscular junction, turned out to be a blocker of cholinergic neurotransmission, a work presented to PNAS by Manfred Eigen [20]. We extended the use of PBC and related compounds to the study of the high-affinity choline uptake mechanism in synaptic endings [21]. We next resorted to another of Gregorio's favorites, tryptophan fluorescence; together with Tom Jovin and Bob Bonner we successfully used the

meager intrinsic fluorescence emission of the membrane-bound nicotinic receptor to measure agonist—receptor interactions using stopped-flow techniques [22, 23]. After joining forces with Bert Sakmann and Erwin Neher as a 5-year new research group at the Max-Planck Institute in Göttingen, I resorted to intrinsic fluorescence quenching and stopped-flow rapid kinetics experiments to study the ligand-induced desensitization phenomenon [24] and with Yusuf Tan we used the pyrene butyryl-choline derivatives and other extrinsic probes as pharmacological tools interrogated with T-jump fast kinetics to learn about antagonist ligand—receptor interactions [25, 26].

### 11 Exploring a Possible Return

At one point Gregorio had seriously considered the possibility of returning to Argentina and made his first short exploratory visit in 1947. He must have been quite amazed at that time to see the transformation of Buenos Aires after the installation of Peron's first presidency in 1946 and the process of internal migration with people from the countryside moving to the great city, coincident with the incipient industrialization of the country. However, the situation at the university under Peron's administration was hardly propitious for a possible reinsertion into the academic arena. His former supervisor, Bernardo Houssay, who was reincorporated to the University of Buenos Aires under the general amnesty in 1945, had been ousted from the university for a second time because of his liberal political ideas, and several other scientists had gone into exile. Gregorio's sister Frida was also thrown out of the University for political reasons. This scenario must have surely impinged on Gregorio's decision not to settle in Argentina at that time.

In 1951, the National Council of Technical and Scientific Investigations (CONITYC) was founded during Perón's second presidency. Physicists like José Balseiro, Enrique Gaviola, nuclear engineer Otto Gamba and astronomer Juan Bussolini were involved. This body was dissolved in 1955 by a military regime. By the time the current Argentine Scientific and Technical Research Council (CONICET) was created in 1958 with Gregorio's Ph.D. supervisor Bernardo Houssay as its first president, Gregorio was firmly settled abroad. The relationship with his home country would flow in the opposite direction, with the recruitment in Urbana of several Argentine students over the course of the subsequent decades: Roberto Morero, Alejandro Paladini, Leonardo Erijman and myself.

## 12 Subsequent Short Visits to Buenos Aires

More than a decade after his first prolonged visit to Buenos Aires in 1970, Gregorio decided to buy a pied-à-terre where he could stay from time to time and perhaps encourage his daughters to spend time with the Argentine branch of the family.

He bought an apartment in Vicente López on the northern outskirts of Buenos Aires and asked me to help him choose all that was needed to furnish the place. As with most other things in life, Gregorio had a developed sense of esthetics, and fortunately we found an adequate furniture shop that had a vast collection of mid-twentieth century modern classics. Before his corneal implant Gregorio's sight had deteriorated considerably, especially when looking downwards. During one of his visits to Argentina, leaving the apartment his sister called his attention to the fact that the shoes he was wearing didn't match; Gregorio looked at them and said with his customary humor: "Oh, yes, I must have another pair like this in the closet." During the 1970s and up to the mid 1990s Gregorio visited Argentina fairly regularly, spending December/January with the D'Alessio or Kurlat families, and living alternatively at his apartment or at the sea-side resort of Punta del Este, in Uruguay, with his friend Ruth Meerapfel. Ruth was a delightful, cultivated German lady from Karlsruhe who had escaped from the Nazi regime to the Netherlands during World War II, hiding above the same premises as Anne Frank at Prinsengracht 263 in Amsterdam. She and Gregorio had developed a very close friendship. Ruth's stepdaughter is a German-Argentine film director and screenwriter, and was a member of the 1984 jury for the Berlin Film Festival, the Berlinale, and currently president of the Berlin Akademie der Künste.

Thanks to Gregorio's generosity, my daughters Alexandra and Caroline lived in his apartment during term-time when they studied at university in Buenos Aires (we were living in Bahia Blanca at this time). The only proviso was that it be available for him during his summer visits. The arrangement worked admirably and Gregorio was delighted with two young ladies looking after his place. And I of course took every possible opportunity to engage in intellectual and gastronomical experiments with him in Buenos Aires.

In 1980 Gregorio's sister Frida was diagnosed with a metastatic melanoma in her brain. Faced with this family emergency, Gregorio set off from Urbana in a rush but upon completing the first leg of his flight in Miami, he realized that his documents were not in order. His family rapidly intervened to ensure he got the required papers in Miami so he could continue his journey on to Buenos Aires without further delay. His cousin Anita told me that on other more cheerful visits to Argentina, Gregorio used to wave goodbye saying "keep away from the doctor." At the healthy age of 100 she seems to have kept strictly to this rule.

In 1987 I organized a meeting in San Martin de los Andes, a small town within the beautiful Lanin National Park against the backdrop of the foothills of the Andes, in the Patagonian province of Neuquén. Gregorio was the guest of honor and his presence was an unforgettable experience, especially for the younger generations (Fig. 9). Although he continued visiting Argentina to see his family and friends, this was one of his last scientific interventions in Argentina. His very last visit was in 1997, when already physically weak with his terminal leukemia, he came to bid farewell to his closest relatives.

Fig. 9 From *left* to *right*: Gregorio Weber at the San Martin de los Andes meeting with the author of this chapter and Drs. George Hess (Cornell University) and Julio Azcurra (Univ. of Buenos Aires). 1987



Acknowledgement My sincere gratitude to Isabel Kurlat de Zitzer and Enrique D' Alessio, Gregorio's niece and nephew, for the very enjoyable time they generously shared with me, conversing about the family links and Gregorio's background, and for providing unique photographic material. I am particularly grateful to Gregorio's 100-year-old cousin Anita Wolovick, daughter of Cecilia Gerchunoff and Miguel Wolovik, to Dr. Carola Eisenberg, currently 98, and to Isabel Fernández Vega (Mauricio Goldenberg's widow), aged 96, for sharing their first-hand lifeenduring reminiscences and marvelous stories of Gregorio. I also thank Gregorio's daughter Juliet for contributing photographic material, and Dr. Antonia Stoppani, for telling me about her late husband's close contacts with Gregorio. Finally, I thank my wife, Phyllis, for critical reading of the manuscript and valuable suggestions.

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