Mexico, 1980: the construction of bacterial molecular genetics

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Abstract: At the beginning of the new millennium, in 2001 to be precise, a work began that at the time turned out to be a titanic task. The project of sequencing the genome of the bacterium *Rhizobium etli,* a nitrogen-fixing bacterium symbiotic with the bean plant- was the first to be carried out in Mexico, and the results were not published until a few years later. But how did molecular biology and genetic engineering arrive in Mexico? Among the many ways and paths that can lead to an answer, we chose the laboratory work of Dr. Fernando Bastarrachea Avilés (1933-2011) and his trajectory to answer this question but mainly how the practice of bacterial molecular genetics was constructed in Mexico during the last years of the Cold War (1970-1980). As a first step, we used the global history of science, where the units of historical analysis are the circulation of knowledge and collaborative networks. As a second step, we conducted in-depth qualitative interviews with former students of that laboratory in the 80's. Consequently, our aim is to account for the process of building socio-technical networks focused on the field of microbiology through the analysis of research topics, participation in academic networks, and the establishment of new research centers.
Keywords: Bacterial Molecular Genetics. Cold War. Fernando Bastarrachea. Global History of Science.

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México, 1980: a construção da genética molecular bacteriana

Resumo: No início do novo milênio, para sermos mais precisos, em 2001, começou um trabalho que na época acabou se revelando uma tarefa titânica. O projeto de sequenciamento do genoma da bactéria *Rhizobium etli* - uma bactéria fixadora de nitrogênio simbiótica com a planta do feijão - foi o primeiro a ser realizado no México e os resultados só foram publicados alguns anos mais tarde. Mas como a biologia molecular e a engenharia genética chegaram ao México? Entre as muitas maneiras e caminhos que podem levar a uma resposta, escolhemos o trabalho de laboratório do Dr. Fernando Bastarrachea Avilés (1933-2011) e sua trajetória para responder a esta pergunta, mas principalmente como a prática da genética molecular bacteriana foi construída no México durante os últimos anos da Guerra Fria (1970-1980). Como primeiro passo, usamos a história global da ciência, onde as unidades de análise histórica são a circulação do conhecimento e as redes de colaboração. Como segundo passo, realizamos entrevistas qualitativas profundas com ex-alunos daquele laboratório nos anos 80. Consequentemente, nosso objetivo é prestar contas do processo de construção de redes sociotécnicas, focalizadas no campo da microbiologia, através da análise de temas de pesquisa, da participação em redes acadêmicas e do estabelecimento de novos centros de pesquisa.
Palavras-chave: Genética molecular bacteriana. Guerra Fria. Fernando Bastarrachea. História Global da Ciência.

1 INTRODUCTION

At the beginning of the new millennium, in 2001 to be precise, a work began that at the time turned out to be a titanic task. The project of sequencing the genome of the bacterium *Rhizobium etli* a nitrogen-fixing bacterium symbiotic with the bean plant- was the first to be carried out in Mexico, and the results were not published until a few years later (González, *et al*., 2006). But how did this moment come about, and how did molecular biology and genetic engineering arrive in Mexico? Among the many ways and paths that can lead to an answer, we chose the laboratory work of Dr. Fernando Bastarrachea Avilés (1933-2011) and his trajectory to answer how the practice of bacterial molecular genetics was constructed in Mexico during the last years of the Cold War (1970-1980).

As a first step, we used the global history of science, where the units of historical analysis are the circulation of knowledge and collaborative

networks. This new look at the history of science focuses on the decentralization of specific geographical locations as centers of knowledge production. It emphasizes communication, exchange, interaction, and movement that transcend borders. The global turn in the history of science problematizes diffusionism. It shows the active role played by regions outside the United States and Europe -previously considered 'the peripheries'- in constructing scientific knowledge (Barahona, 2021).

To study laboratory work, it is necessary to "listen to the talk about what happens, the asides and the curses, the mutterings of exasperation, the questions they ask each other, the formal discussions and lunchtime chats," also "we must read the laboratory protocol books and rely on answers supplied by the scientists" (Knorr-Cetina, 1981, p. 21). However, knowing that there is no access to the original laboratory, there is still the question of how to carry out these activities. Thus, as a second step, we conducted in-depth qualitative interviews with those who were students at this laboratory in the 1980s to explain how a scientific practice, such as bacterial molecular genetics, was creating and guaranteeing scientific knowledge within different institutions of the National Autonomous University of Mexico (UNAM), such as the Institute of Biomedical Research (IIBm), the Center for Research on Genetic Engineering and Biotechnology (CIIGB, currently the Institute of Biotechnology - IBt) and the Center for Research on Nitrogen Fixation (CIFN, currently the Center for Genomic Sciences - CCG).

Consequently, our aim is to account for the process of building socio-technical networks, focused on the field of microbiology, through the analysis of research topics, participation in academic networks, the formation of research groups and the establishment of new research centers. We must mention, as justification, that the history of microbiology has been little addressed in the historiography of the life sciences compared to other topics such as evolutionary theory or human genetics (Meunier & Nickelsen, 2018, p.4).

2 THE GLOBAL TURN IN THE HISTORY OF SCIENCE

At the end of World War II, the world was transformed in such a way that an accelerated process of globalization took place, involving

factors that contributed to the dissolution of some empires, the independence of some colonies in the Middle East and the West, and, more importantly, to the conflicts between two political and social systems that sought to implement an economic model. Likewise, the events that arose in the period called Cold War (1945-1989/1991) were not only restricted to the local European geography but also reached the rest of the continents (Iggers, Wang & Mukherjee, 2013, pp. 250-251). In other words, during this period, the world began an unprecedented union, mainly because of the increasing communication between countries and the large circulation of information.

This global situation, under the influence of many authors we would like to call "context", is highly relevant to the global history of science. In this historiographical model, scientific activity occurs as a professional activity that can be national and transnational. Likewise, for science to be a successful practice, it must travel to other regions; that is, it must move. This global perspective of the history of science using the concepts of local and transnational represents one of the most viable ways to explain how scientific practices, ideas, teachings, materials, and even scientists themselves circulate across borders, thus departing from the diffusionist model and without considering a Eurocentric or Euro-American approach (Sivasundaram, 2010b, p. 157; Walker, 2012, pp. 359-360; Basalla, 1967, p. 612; Conrad, 2016, pp. 170, 180; Barahona & Raj, 2022).

In the same sense, the phenomenon of globalization was so great that it even reached the history of science, and one of its results during the Cold War period was Georges Basalla's diffusionist model, also known as the "diffusionist" or "centers and peripheries" model. In this proposal, scientific knowledge is "diffused" in three stages to "non-Western" places, i.e., to the peripheries; these are regions where no scientific knowledge apparently exists. Thus, science and the products of the centers (among which the United States and some European countries are considered) reach these peripheries, which will receive the knowledge in a passive way. The criticisms of this model of the history of science are widely known and have been quite discussed; however, one of the most important consequences derived from having made notice of the movement of science beyond its places of origin

allowed a new turn in the historical explanation of science at the beginning of the 21st century through the academic publications that began to devote themselves to this field: the "global turn" (Basalla, 1967; Raj, 2013, p. 339; Valera-Pacheco, 2017, p. 148).

This relatively recent look at the history of science focuses on the decentralization of specific geographical locations as centers of knowledge production. It highlights communication, exchange, interaction, and movement that transcend borders. The global turn problematizes the diffusionism of science. It shows the active role played by regions outside Europe and the United States, which were previously considered the peripheries, in the construction of scientific knowledge. This has allowed the development of the global history of science, which does not imply a total history; on the contrary, it seeks to situate science in each place and time for its subsequent movement throughout the world. In this new historiography, the circulation of knowledge has made it possible to question simplistic ideas of the discovery and diffusion of knowledge, practices, and technologies, as well as to identify the factors that contributed to the success or failure of such circulation in very specific situations (Gavrus, 2016, p. 363; McCook, 2013, p. 773; Sivasundaram, 2010a, p. 96).

Concerning this recent historiographical model of the global turn, it is worth asking which voices or which actors have been silenced or made invisible in the traditional narratives and, likewise, to ask what precisely is circulating to and from where (Nappi, 2013, p. 105; Raj, 2013, p. 344). For the time being, in the two subsequent sections, emphasis will be placed on the circulation of knowledge, on collaborative networks, and on the places where science is done to underpin the global history of science approach.

2.1 And yet (knowledge) moves

The first theme that guides this work is based on the proposal of the importance of circulation in the construction of knowledge, which suggests that science should be thought of as a form of communication and that the key to realizing this type of story is the understanding of scientific knowledge as a practice. Such circulation does not only occur abstractly but is also reflected in material forms of knowledge such as experimental instruments, natural specimens, models, pamphlets,

books, drawings, articles, notebooks, and even paintings (Secord, 2004, pp. 663-666).

One means by which these materials can move, and which has become another unit of historical analysis in addition to the circulation of knowledge, is through collaborative networks that, when studied, articulate appropriately with global history because they cross barriers of all kinds, such as empires, nations, and regions. If the notion of networks is used, in particular networks of knowledge and collaboration, then it promotes a global cut coverage that makes it necessary to look beyond "centers and peripheries" (Sivasundaram, 2010b, p. 158; Pestre, 2012, p.433). With this, it is evident that scientific activity is not isolated from its context, and the boundaries of science and the places where it is being built become blurred and almost imperceptible.

Likewise, it is recognized that science is an element that is contained in societies through discourses and practices that, in addition to being related to the world and its phenomena, is also related to aspects of social and political life. This capacity of knowledge to move shows that science can be understood as a "knowledge in transit" capable of crossing geographical, temporal and disciplinary borders due to its social nature. Under these premises, a country like Mexico, considered a periphery by the diffusionist model, turns out not to be a mere passive recipient of scientific knowledge (Secord, 2004, p. 654; González-Silva & Pohl-Valero, 2009, p. 7; Birn & Necochea-López, 2011, p. 523).

If so, then it is fulfilled that narratives involving the circulation of knowledge help to put non-European or non-US agents back into the story as active participants, these being mostly experts from different parts of the world who interact in the transit of knowledge, practices, and even people who are in scientific training as a constitutive part of knowledge construction (Safier, 2010, p. 143; Pestre, 2012, p. 523; Raj, 2017, p. 457). Thus, when aiming to write a certain global history of science and to construct broader narratives, it is necessary to incorporate other people and turn one's attention to the spaces in which science is constructed.

2.2 Places of science: the labs

Often, in the collective imagination, the first physical place that comes to mind when the word science is mentioned is the laboratory.

What an interesting place full of knowledge and full of people who often roam around inside in white coats, but how little emphasis is placed on the laboratory itself or on the other places of knowledge production that are sometimes taken for granted (Zabala & Rojas, 2020, p.140). These places are objects of Research that allow the explanation of the social and historically situated condition of science and, therefore, is the second axis that guides the present work.

The scientific activity takes place in very specific places ranging from museums or field stations to high-tech laboratories, as well as in cafeterias, cities, provinces, or countries (Livingstone, 2003, p. xi; Matharan, 2020, p. 170). These "science centers" in which botanical gardens, hospitals, and universities are also considered, have been studied since the 1970s with the constructivist perspective, which historically explores the constitution of these spaces (Golinski, 2005, p.79; Sivasundaram, 2010b, p.154).

These places of science are by far not empty or passive but have the capacity to shape the knowledge in construction. If knowledge is transformed according to the place or space to which it belongs, then it is not stable and varies from place to place. At the same time, it is important to emphasize that not only material places are inhabited but also a great variety of abstract spaces, such as social spaces. These have action and allow - and sometimes define - saying, doing, and understanding things. Therefore, scientific knowledge is acquired in specific places, circulates from place to place, and is made and reconstructed by how it is spoken (Livingstone, 2003, p. 6; Meusburger, Livingstone & Jöns, 2010, p. 5, 18; Raj, 2013, p. 345).

Therefore, the "geographical turn" is important for the global history of science as circulation happens within these spaces of science and whose geography changes historically. In other words, the space where scientific knowledge is constructed is important, whether physical, abstract, or metaphorical and is traversed by the networks and by the material that circulates in them, giving support to the units of analysis of the global history of science.

The growing formation of new generations of scientists, research groups, and their inhabited spaces have a great capacity to organize themselves around certain objectives in order to construct scientific knowledge, and their analysis allows us to understand how they operate

and what factors alter their functioning and/or productivity. Consequently, we would like to end this first part with a phrase from David Livingstone, which perfectly reflects the point underlying this work: "As it moves, it is modified; as it travels, it is transformed" (Livingstone, 2003, p. 4).

3 VISITING A LAB FROM THE PAST

Laboratory ethnographies have been carried out with a qualitative research method that collects information interactively when the person observing participates in the social life and day-to-day activities of other people who are part of a community, that is, in an *ad hoc* manner, the method of participant observation. In this way, it is possible to make an in-depth approach to the people and institutions to which they belong (Rodríguez-Gómez, Gil-Flores & García Jiménez, 1999, p.165).

However, access to the original laboratory was impossible due to the pandemic of the new SARS-CoV-2 coronavirus; access to any public facility, including historical archives, during all of 2020 and part of 2021 was null. An alternative was to conduct in-depth qualitative interviews that support oral history as a resource independent of historical archives. Interviews are the tool of choice for those seeking to gain knowledge about social life and are flexible and dynamic. In-depth qualitative interviews are:

> […] repeated face-to-face encounters between the researcher and the informants, encounters [...] aimed at understanding the informants' perspectives on their lives, experiences, or situations, as expressed in their own words. The interviews follow the model of a conversation among equals rather than a formal exchange of questions and answers. [...] The researcher himself is the instrument of the Research [...]. (Taylor & Bogdan, 1987, p.101)

For these purposes, it is pertinent to clarify that "informants" are understood to be all those with whom close relationships are established (the close relationships are called *rapport*), with whom interviews are conducted, and who are the primary sources of information. Among the interviews, three types can be distinguished: life history interviews, interviews aimed at learning about events and activities that

cannot be directly observed, and interviews that provide a broad picture of a range of scenarios, situations, or people (Taylor and Bogdan, 1987, p.61, 102-103).

Although all three types of interviews could well be explained, the one that was selected is the second one (learning about events and activities that cannot be directly observed). In these interviews, the informants are precisely the access that was denied because we did not coincide in the space and time of the event that occurred; that is, they are the eyes and ears of the past that come to the present moment of the interview, becoming a new written history and therefore a new primary source.

Regardless of the type of interview chosen, given the Research to be carried out, these latter three coincide in a series of basic techniques that involve (I) establishing a friendly and harmonious relationship with the informants, (II) establishing repeated contacts, (III) facilitating interviews with more informants, (IV) making explicit the purposes of the Research to be carried out and (V) allowing them to opt for anonymity, among others (Taylor and Bogdan, 1987, pp.104-110).

With the above methodology, it is possible to carry out a history capable of reconstructing socio-historical processes, converting oral testimony into a new primary written or audio-visual source, while at the same time allowing access to new data that are rarely found in the documents of historical archives. Likewise, a striking aspect of oral history is the ability to go beyond the classic spaces where historical Research is conducted, such as archives or libraries (Lara & Antúnez, 2014, p. 48).

Also, it is important to clarify that the notion of "oral history" is understood in two ways: first, as "information transmitted orally, in a personal exchange, of a kind likely to be of historical or long-term value", and second, "oral history" refers to the interview itself and to stories based on interviews (Chadarevian, 2012, pp. 52-58). Sometimes, the distrust for oral history lies in psychological aspects such as selective memory. However, the oral is not excluded from the written, but seeks in the latter its complementation, therefore, it is important to perform triangulation between interviews and with some other written primary sources (Lara & Antúnez, 2014, p. 53; Chadarevian, 2012, p.56).

Likewise, to establish coherence with the global history of science approach, the interviews conducted in this work are focused on informants who did not belong to a dominant power structure at the time of the standardization of molecular biology and genetic engineering techniques. On the contrary, they were students starting a scientific career and initiating their collaborative networks in a practice that was totally new for Mexico and for the institutions that were just beginning to build and structure themselves in the then-new field of bacterial molecular genetics.

4 THE CONSTRUCTION OF BACTERIAL MOLECULAR GENETICS

In the 21st century, at least in the year 2022, it is relatively easy for almost anyone who has read up on genetics and molecular biology to talk about biotechnology, genetic engineering, restriction enzymes, and recombinant DNA. However, and alluding to Lorraine Daston's article on the naturalization of objectivity and truth, rarely do scientists ask themselves why they use and replicate certain laboratory techniques and not others or why certain scientific practices exist (Daston, 2016, p. 10). This is precisely what this chapter tries to offer from the history of science: to answer these questions and to note the relevance of some people and institutions that were involved in the construction of bacterial molecular genetics in Mexico in the 1970-1980.

In Thomas Brock's book, *The emergence of bacterial genetics*, published in 1990, the last chapter is dedicated to what he calls the "biotechnological revolution", and he assures that this great change in experimental biology is due to the novel recombinant DNA techniques. He also states that without bacterial genetics, this new methodology in the biological sciences would never have been possible. In Brock's context, there were only two unique purposes of recombinant DNA research, and they still exist today. The first is to produce copies of DNA (or what in biology has been called molecular cloning) that can be used for biochemical and genetic Research. The second is to obtain the expression of cloned genes to produce large amounts of protein(s) (Brock, 1990, p. 325). The expectations of this new technology were directed toward seemingly unlimited Research to manipulate the famous "molecule of life" for multiple purposes and impacts.

4.1 Before genetic engineering in bacteria came to Mexico

Fernando Bastarrachea Avilés (1933-2011) obtained his degree as a bacteriological chemist and parasitologist from the National School of Biological Sciences of the National Polytechnic Institute (ENCB-IPN) with the thesis "Antibiotic of specific action for mycobacteria produced by a *Streptomyces* from the soil" in 1957. During the 1950s and 1960s, he published experimental research work with *Mycobacterium tuberculosis* in the *Revista Mexicana de Tuberculosis* (which after 1962 changed its name to *Pneumology and Thoracic Surgery*), in the *Revista Latinoamericana de Microbiología*, and in the *Acta Tuberculosea Scandinavi*ca. Much of his work with this bacillus was done in Dr. Luis Bojali's group in the Pathology Unit of the UNAM, which is currently the Research Unit in Experimental Medicine of the School of Medicine at UNAM and is located in the General Hospital of Mexico "Dr. Eduardo Liceaga" (Fernando Bastarrachea. Personal communication, 2008; Vázquez-García, 2017, p. 72; Camacho *et al.*, 2011).

During his studies at the University of Wisconsin (1957-1959) to obtain a Master of Science degree (Bacteriology), he continued working with *M. tuberculosis* and its enzymes under the direction of the American biochemist Dexter Stanley Goldman at the Tuberculosis Research Laboratory of the Veterans Administration Hospital (currently the William S. Middleton Veterans Hospital) and published his work in *Biochimica et Biophysica Acta*, and the *Journal of Bacteriology* (Fernando Bastarrachea, Personal communication, 2008; Bastarrachea & Goldman, 1961; Bastarrachea, Anderson & Goldman, 1961).

At that time, Dr. Goldman was an active member of the Veterans Administration Hospital, whose facilities since the 1950s focused on tuberculosis treatment and Research. This was because of the efforts of the United States government through the American physician Martin Cummings, who was the director of the Research Service, founded in 1953, and who worked to improve relations of the Veterans Administration Hospital with United States medical schools that lacked research laboratories (Hays, 2019, p. 183).

After completing his master's degree with his thesis "Aldolase and phosphofrutokinase from *Mycobacterium tuberculosis*", Bastarrachea returned to Mexico and studied for his doctorate (1960-1965) at the Cen-

ter for Research and Advanced Studies (CINVESTAV) under the direction of Mexican biochemist Manuel Valerio Ortega (Fernando Bastarrachea. Personal communication, 2008). Dr. Ortega was one of the founders of the Biochemistry Department at CINVESTAV in 1962, and during this same decade, he promoted microbial genetics and cell biology in Mexico (CINVESTAV Irapuato, 2021; CINVESTAV Departamento de Bioquímica, 2021; Barreda-Saldaña, 2021, El Universal, 2017). Bastarrachea began biochemical and genetic mapping research on *Escherichia coli* bacteria obtaining the Ph.D. degree with the dissertation "Studies on the phenomenon of conditional dependence to streptomycin in bacteria" (Bastarrachea & Ortega, 1967; David Romero. Personal communication, November 11, 2020).

Later he decided to do postdoctoral studies, from 1966 to 1967, in bacterial genetics with the American geneticist Alvin J. Clark in the Department of Molecular Biology at the University of California, Berkeley (Fernando Bastarrachea. Personal communication, 2008; Bastarrachea & Clark, 1968). In the same decade Dr. Clark was attached to the Department of Bacteriology and in collaboration with the American microbiologist Michael Doudoroff and the Canadian microbiologist Roger Stanier. They developed a close collaboration with the Department of Molecular Biology, which boosted work in the fields of knowledge of experimental pathology, animal virology and microbiology (University of California History Digital Archives, 2021). During his stay with Dr. Clark, Bastarrachea began to develop research on DNA recombination with the F plasmids of *E. coli* and:

> he designed a strain of *E. coli* that had three F factors introduced at different points on the chromosome [...] and what was easy to predict it happened. The surrounding sectors where each of those F factors were transferred very early in the conjugation. Nobody thought it was possible because they thought it was going to become a real mess in terms of conjugative transfer, but in practice it worked very well and earned him an article in PNAS [Proceedings of the National Academy of Sciences] with him [Fernando Bsatarrachea] and Alvin Clark as author. (David Romero. Personal communication, November 27, 2020).

During the same postdoctoral stay, Bastarrachea's work allowed him to become a John Simon Guggenheim Memorial Foundation Fellow in the field of Molecular and Cellular Biology in the category of

Natural Sciences for Latin America and the Caribbean. Upon his return to Mexico in 1967 as an expert in bacterial genetics, he joined CINVESTAV as a Full Professor with the research line of *E. coli* genes related to streptomycin resistance. Thus, he invited renowned international bacteriologists such as Françoise Jacob (Fernando Bastarrachea. Personal communication, 2008; Bastarrachea and Clark, 1968; Bastarrachea & Willetts, 1968; Bastarrachea, Tam & González, 1969; López-Revilla & Bastarrachea, 1971; Willetts & Bastarrachea, 1972; Sánchez-Anzaldo & Bastarrachea, 1974; Gómez-Eichelmann & Bastarrachea, 1974, pp. 47-58; Sánchez-Anzaldo, Gómez, & Bastarrachea, 1979; Ortega, 2004, p.10; Camacho *et al.*, 2011, p. 10).

In 1978 he left CINVESTAV and joined the academic staff of the UNAM within the IIBm as a Senior Researcher to start the project "Molecular Genetics of Nitrogen Metabolism", whose line of Research, besides being the most productive, opened the way to genetic engineering and in particular to bacterial molecular genetics (Fernando Bastarrachea. Personal communication, 2008; Camacho *et al.*, 2011, p. 10) that:

> [...] it was fundamental in Mexico because [...] we were [as a working group] at a very similar level to what was happening in the United States both in the issue of [...] gene isolation and its study and in the case of nitrogen metabolism. [...] We were playing against the strongest nitrogen metabolism group that was at MIT [Massachusetts Institute of Technology], and it was very stimulating [...]. In that sense, microbial genetics did have an impact in Mexico without a doubt. (Alejandra Covarrubias. Personal communication, January 8, 2021).

4.2 The dawn of scientific practice

In most books related to biotechnology, the history of genetic engineering begins with the experiments conducted in the laboratories of Herbert W. Boyer at the University of California, San Francisco, and Stanley N. Cohen at Stanford University. The former showed a very early interest in restriction enzymes in his studies as a biochemist, while the latter, schooled in genetics, studied bacterial plasmids and their role in antibiotic resistance (Hughes, 2011, pp. 2-7; Stevens, 2016, pp.41-43; Jasanoff, 2019, pp.48-49).

This conjunction of knowledge was made possible when, in November 1972 Boyer and Cohen coincided at a conference devoted to work on bacterial plasmids held in Honolulu, Hawaii. At this meeting -organized by Cohen, Tsutomu Watanabe and Donald Helinski- the attendees discussed the recently discovered *E. coli* plasmids capable of being transferred between bacterial strains. Unaware that they would be pioneers in genetic engineering, Boyer and Cohen met at Waikiki Beach for a walk to allow them a respite from the conference and a little refreshment. They were soon joined by microbiologists Stanley Falcon and Charles Brinton to enter a *deli* where they exchanged results from their respective labs. Boyer talked about the sequencing data obtained for the EcoRI cut site, and Cohen about the plasmid cut experiments, which at that time had not been published. Cohen states that "as Herb and I talked, I realized that EcoRI was the missing ingredient needed for molecular analysis of antibiotic resistance plasmids" (Cohen, 2013, p. 15524).

It was at that very informal time, so outside the academic environment and the classic laboratory full of people wearing white coats, that the group of microbiology specialists glimpsed the potential of combining their work on restriction enzymes and bacterial plasmids to give rise to modern biotechnology, *i.e.*, genetic engineering (Russo, 2003, p.456; Hughes, 2011, p.11; Cohen, 2013, p. 15524; Stevens, 2016, pp.43-45).

In a very general way, we can summarize the recombinant DNA technology developed by Boyer and Cohen as follows: first, the bacterial plasmid is isolated so that the EcoRI restriction enzyme then cuts the DNA. This leaves single strands of reduced size with protruding ends (sticky ends) to which the sticky ends of another DNA fragment that has also been cut by the restriction enzyme can be attached. Then, to join both fragments, the enzyme ligase -which promotes DNA binding- is used and allows the plasmid to incorporate the foreign DNA to later remake the plasmid with now an extra part of genetic material. Finally, the plasmid is reinserted into the bacterium and grown in culture medium so that, when it reproduces, it makes copies of the foreign DNA. Each copy can be amplified as much as the bacteria can divide (Cohen, 2013, p. 15525; Madigan *et al.*, 2015, p. 336; Stevens, 2016, p. 44).

4.3 A great convergence: genetic engineering in bacteria arrives in Mexico

By 1976, a young graduate student from the School of Chemistry at UNAM made a research stay in Boyer's laboratory and learned "the mysterious arts of molecular cloning" (David Romero. Personal communication, November 11, 2020). This young woman, named Alejandra Covarrubias, shared a worktable during her stay abroad with the then postdoc Francisco Bolívar Zapata, one of the creators of the most widely used plasmid in modern biotechnology, pBR322:

> [...] I had the opportunity to go to San Francisco just before starting my master's degree to Herb Boyer's laboratory, who was the person who started working with recombinant DNA together with others from Stanford University. So [...] I had just graduated from my bachelor's degree, and I had the opportunity [...] and there I learned a lot of things, which was a bit like applying my bachelor's thesis [...]. At that time the differences in technologies between a place like Mexico and the United States, at least where I was, were gigantic. My undergraduate thesis seemed like a joke because it was basically to purify a plasmid that, when I was there [in Boyer's laboratory], it was a daily routine [to purify plasmids]. I learned everything there. Basically, everything one wanted to learn about "modern" molecular biology -at that time, it was called that - which was to purify DNA, plasmids, [...]. Practically everything in bacteria because [...] molecular biology basically started thanks to, or in the framework of, microbial genetics [...]. (Alejandra Covarrubias. Personal communication, January 19, 2021).

Covarrubias finished her stay in 1978 and returned to Mexico to pursue her master's degree at the IIBm under the mentorship of Dr. Bastarrachea. By that time:

> [...] Dr. Bastarrachea's intention was to try to understand precisely the mechanism of regulation of this enzyme [glutamine synthetase] and, in general, how the bacteria used nitrogen and regulated nitrogen sources [...]. (Alejandra Covarrubias. Personal communication, January 8, 2021).

The enzyme glutamine synthetase is essential in the assimilation of nitrogenous compounds such as ammonia (NH_3) and in the synthesis of the amino acid glutamine. This enzyme acts as a nitrogen donor for protein and nucleic acid synthesis since it can incorporate NH_3 into

organic compounds (Madigan, 2015, p. 252; Vegara-Luque, 2018, pp. 43-45). During her master's studies, Alejandra Covarrubias wanted to:

> [...] show that it was possible to isolate a gene and that it was functional once *you* took it out of the bacterial genome. That was one reason. The other reason was that nitrogen metabolism is one of the metabolisms, along with carbon metabolism obviously, most important for any living organism, and at that time, bacteria were the model. And then, since glutamine synthetase is a central enzyme in this [nitrogen] metabolism, the challenge was, precisely, to learn more about the enzyme, knowing its sequence [...]. On the other hand, also knowing [...] the different genetic [...] data on the regulation of glutamine synthetase could be known in greater detail if we isolated the gene and other genes related to metabolism [...]. (Alejandra Covarrubias. Personal communication, January 8, 2021).

Covarrubias' opportunity to collaborate at another level with Dr. Bastarrachea materialized only in 1980 when she had barely finished her master's thesis and:

> [...] At that time, there were positions, and then I was given a research position [at UNAM]. I barely had my master's degree. So, it was great because Dr. Bastarrachea had his laboratory, where we always worked, and then, on the other side, in the laboratory that was next door, was the one they gave me. And then, we [Alejandra's new group] continued doing the molecular biology part, but we always had seminars together [with Dr. Bastarrachea]. To have a better relationship, what we did was to make a little door between the two laboratories [...] We had the door made and said, "No, we are like one [laboratory]," and we already had a direct pass. Dr. Bastarrachea's students - David Romero was Bastarrachea's student [...] - and my students, at that time, started to have a lot of complementation with molecular biology and genetics. So, it was super good for both of us. (Alejandra Covarrubias. Personal communication, January 8, 2021).

Alejandra Covarrubias and Dr. Bastarrachea established a collaborative relationship as if it were symbiosis because while she was learning bacterial genetics, he was learning molecular biology. This collaboration was not only academic but also spatial. They built a laboratory in the Department of Molecular Biology of the IIBm that gave them a work area where the two scientific practices converged: bacterial genetics and molecular biology. This was what David Romero, at the time

a student of the Basic Biomedical Research degree program, observed and experienced during his stay in Dr. Bastarrachea's laboratory:

> [...] From the beginning he [Bastarrachea] had a very close collaboration with Alejandra Covarrubias. At that time, [she] a young researcher who was still studying for her PhD. She was returning from a stay in the United States [...]. Both [Bastarrachea and Alejandra] were interested in [the] nitrogen metabolism in *Escherichia coli*. On the one hand, Fernando was working on the genetics part centered around the regulatory system for the glutamine synthetase gene in *Escherichia coli,* and Alejandra was interested in the molecular basis, she wanted to know the [glutamine synthetase] gene and link the information that was being obtained in Fernando's laboratory [...]. It was, I think, a very fruitful collaboration [...] There was no physical border between the two groups. The seminars were common; we spoke different languages [genetics and molecular biology], but the idea was to learn both languages. [...] It was two for the price of one. [...]. One particularity is that, for historical reasons, Fernando's lab and Alejandra's lab were joined. A wall was broken, and there was a communication between the two laboratories, then, one migrated from one laboratory to the other. They did part of the experiments in the other laboratory, part of the experiments in one and they reached a quite good agreement, a precursor of the one they would later meet at the Nitrogen Fixation Center [...] (David Romero. Personal communication, November 11, 2020).

The CIFN, from its inception, maintained an *ethos* of internal collaboration that:

> was moving things along quite well. [...] [and] it was part of the logistics of the Center itself. [...] The Center [CIFN] emanated from what was the Department of Molecular Biology of the Institute of Biomedical Research [IIBm]. The researchers who were there, some of them like Fernando [Bastarrachea or] Paco [Francisco] Bolívar, worked with bacteria such as *Escherichia coli* [and] collaborated [...]. (David Romero. Personal communication, November 27, 2020).

In this quest to understand nitrogen metabolism in *E. coli*, Alejandra Covarrubias and Dr. Bastarrachea were able to standardize the first bacterial molecular genetic techniques to understand the regulation of the *gnlA* gene for glutamine synthetase:

> [...] what Dr. Bastarrachea did, let's say, that the study strategy to try to elucidate the control mechanisms of glutamine synthesis was to generate mutants [...] that did not grow well in the presence of glutamine or the presence of some other nitrogen source, [...] map those mutants. Once those mutants were in the genome of *E. coli* genome, the idea was to clone [and] try to see whether or not those mutations corresponded to genes that were related to the control of glutamine synthetase. Then, he [Bastarrachea] did all this part of generating the mutants [and] characterizing the mutants, either by crosses to see that the mutations were in a particular gene, etc. [And to see] how this affected glutamine synthesis, *you* would measure glutamine levels, or ammonium levels in the bacteria, etc. [...] With the phenotypes of the bacteria, if the bacteria grew slower or slower on glutamine or some other nitrogen sources, *you* could deduce whether those mutations were in genes that regulated [glutamine synthetase]. So that's how it was determined that there were mutations that affected glutamine synthesis that were not in the gene for glutamine synthetase but were in other genes that were then deduced to be genes that regulated synthesis. And the genetic mappings then allowed us to define where the gene was [approximately]. Then, [...] in Dr. Bastarrachea's laboratory, they could say, "the gene is close or far away." That is the first part. [...] After cloning the glutamine synthetase gene, the idea was to try to look for those genes that corresponded to these other mutants, or mutated genes, that gave these other phenotypes. [...] To do that, what one initially proposes is *you* have [...] the genome of the bacterium, *you* cut it into pieces with restriction enzymes, *you* put those restriction enzymes into plasmids, and then *you* transform the bacterium that is mutated in those genes. Y*ou* see if there is a complementation of the phenotypes to a wild phenotype. And that's the way to look for the genes, which was what we [Alejandra's group] did, to look for the genes that complemented those mutations and determine if those genes really were [...] and where they were. And then that was how we and the other group we were competing with [at MIT] came to the same conclusion [...] at the same time, which was that at least two of the regulatory genes were [very close] to the glutamine synthetase gene and we determined that it was an operon [the glnALG operon]. (Alejandra Covarrubias. Personal communication, January 19, 2021).

Dr. Fernando Bastarrachea and his students worked for a little more than a decade, from 1980 until 1992, on the nitrogen metabolism of *E. coli* at both the CIFN and the then new CIIGB. Both centers were

built thanks to collaborations between scientists of the time who were dedicated to molecular biology and who belonged to the Department of Molecular Biology of the IIBm (Camacho *et al.*, 2011, p. 10).

> What that Department of Molecular Biology [of the IIBm] was gave rise to the molecular biology that currently exists in several of the university institutions. A lot of [molecular biology] ended up in Cuernavaca because of the movement of that Department of Molecular Biology [...] initially [...] as the Center for Nitrogen Fixation [CIFN]. The other part left three years later as the Center for [Research] on Genetic Engineering and Biotechnology [CIIGB], currently the Institute of Biotechnology [IBt]. From one day to the next, the molecular biology that was being done at UNAM ended up in Cuernavaca [...]. It was not the only place where molecular biology was done, of course, in the country. The other very important place was CINVESTAV, where Fernando [Bastarrachea] had left and where other researchers with whom he had collaborated had stayed [...] (David Romero. Personal communication, November 27, 2020).

Before his retirement, in 1993, Alicia González, Carmen Gómez, Guadalupe Espín, and Gloria Soberón organized in honor of Dr. Bastarrachea the International Symposium on "Molecular Genetics of Microorganisms" which lasted three days and was attended by just over 100 national and international participants (including his professor Alvin J. Clark). The following year, the journal *Critical Reviews in Microbiology* devoted issue number 2 of volume 20 with written reviews of those who participated in this Symposium (Camacho *et al.*, 2011, p. 10).

> When he [Fernando Bastarrachea] turned 60 in 1993, a commemorative symposium was held [...] a lot of researchers from abroad were invited. But also many nationals who had to do with him in different ways. That was in San José Vista Hermosa [Morelos, Mexico]. It was not that he was thinking of retiring; what he really wanted was, on the one hand, to stay in Brazil -another of the places that fascinated him- to learn more about the nitrogen-fixing bacteria that was attracting his attention: *Azospirillum* [spp.], and then what he wanted to do was to migrate to Yucatán [Mexico], his homeland, to work at the University of Yucatán doing Research there. He did that; he went to Yucatán [and] stayed there for several years [...], but unfortunately, the development was not what he needed [...], and so he sought to return to UNAM itself. It was an *apache dance* because he had already retired, so we had to reverse that retirement and hire him, and what was done

> was to hire him in a partial way [with] few facilities [since] he had already lost the laboratory. Rather, they gave him [a] small laboratory and a micro-aid in technical terms. But Fernando, at that time, was already getting into something that eventually turned out to be quite good. He had the notion that antibiotics did more than kill [...] what they could induce was a state of hypermutation in the cells [...] to that he dedicated his last years of work before dying in 2011 (David Romero. Personal communication, November 11, 2020).

With great honor, Rafael Camacho, Laura Camarena, Carmen Gómez, and Luis Servín (IIBm); Alicia González (Institute of Cell Physiology), and Alejandra Covarrubias (IBt) wrote in Dr. Bastarrachea's Obituary, published in the IIBm Newsletter, that:

> […] His students, colleagues, and friends will remember him, in recent years, reading articles and books with a magnifying glass in hand or talking with his students, critique in hand, with his genuine and generous desire to help and improve the work presented to him. We remember him self-absorbed in his pessimism, with his vision of reality, often in black and white, which provoked us to reflect, but also with his sonorous and radiant laughter, enthusiastic about promising results. We see him in memory, with his aversion to giving courses or lectures, but also with his bohemian taste for Yucatecan trova and *bossa nova*. El Maestro [as he was commonly known] is, without a doubt, a person that we will all miss but that we will keep alive in our memory and our work as researchers. (Camacho *et al.*, 2011, p.11)

5 CONCLUDING REMARKS

Historical reconstructions using the circulation of knowledge and collaborative networks lead to a global history of science that, although it does not have an exact methodology, provides a series of theoretical tools that show the decentralization of Western narratives, thus moving away from the Euro-American tradition. In this paper, we have found that bacterial molecular genetics emerges from the conjunction of two relatively new scientific practices in post-war Mexico: bacterial genetics and molecular biology.

In general, the global turn in the history of science allows us to go beyond historical explanations centered in Europe and the United States by addressing issues related to power and colonialism, taking up

key figures that had been erased from traditional narratives, as well as their practices. As it has been exposed, molecular biology is not only the product of the work of those doing science in the United States or Europe; high-quality molecular biology and genetic engineering was (and is) also done in Mexico. Much of what was developed with respect to genetic engineering in bacteria and what Thomas Brock calls the "biotechnological revolution" in *The emergence of bacterial genetics* -mainly in the United States- is still preserved in this 21st century and its first two decades.

Scientific knowledge, as a practice, and its materials circulate through the collaborative networks created by the interconnections of scientific endeavor. Thus, the global history of science highlights the interaction of experts of different nationalities. Although global history does not imply a total history, the overall picture is important, as it highlights mobility as a constitutive feature of scientific knowledge.

On the other hand, through the interviews, we have noted the social machinery that underlies the construction of scientific practice and makes the seemingly obvious -such as bacterial molecular genetics being the conjunction of two scientific practices- an object of enlightening Research to understand why we have some scientific practices and not others. Nevertheless, it is important to emphasize that these social dynamics mentioned above are rarely found or visible in the papers published by scientists. Consequently, and with the methodology of in-depth qualitative interviews, it is possible to construct a history capable of accounting for the multiple socio-historical processes and, at the same time, convert oral testimonies into new primary sources.

In the laboratory of Fernando Bastarrachea and Alejandra Covarrubias, initially, inside the IIBm, a door was built -literally and figuratively- that allowed the coming and going abroad of materials, concepts, and even young scientists in training. All these opened paths for new Research and built several scientific practices for the study of molecules and genetic mechanisms of nitrogen fixation in *E. coli*. And later for other microorganisms such as the fungus *Neurospora crassa* and the bacterium *Rhizobium etli*. Bacterial molecular genetics put Mexico at the cutting edge that the necessary investments were made by the institu-

tions capable of sponsoring such projects to be part of the first genomic sequencing projects in Mexico at the end of what Evelyn Fox Keller calls "the century of the gene".

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