ENCONTROS DISCIPLINARES

O caso da Física e da Biologia:
Perspectivas históricas e contemporâneas

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Dedico a tese de doutorado aos meus pais Joana Joaquim e Antonio Joaquim,
assim como dedico todo e qualquer êxito de minha vida, seja já alcançado ou
por vir, aos elos de amor que nos vinculam

Disciplinary Encounters
Where Physics meets Biology:
some historical and contemporary perspectives

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ABSTRACTS

ABSTRACT I: This paper aims at unfolding selected entwined aspects of two great scientific developments: quantum mechanics and molecular biology. As the entry point, we look at the contributions of three physicists that in the 1930s were protagonists of the quantum revolution and explorers of the field of biology, namely, Niels Bohr, Pascual Jordan, and Max Delbrück. Their common platform is the defence of the Copenhagen interpretation in physics and the adoption of the principle of complementarity as a way to look at biology. In 1927, Bohr formulated the complementarity principle and, subsequently, started to discuss wider applications of his arguments in quantum physics. In 1932, he gave the famous lecture entitled "Light and Life", addressing the problem of how far the results reached in the domain of physics might influence our views about living organisms. Jordan and Delbrück were followers of Bohr's ideas in the context of the debates on quantum mechanics interpretations and, also, of the expanded version towards biology. Jordan jumped into Bohr's hint, with even some extravagance. He wanted to combine the quantum revolution and biological phenomena. The understanding of his contributions demands an appreciation of the respective political context. In 1937, Max Delbrück migrated from Germany to the United States and, categorically, from physics to biology. He evolved from a former Bohr's disciple, to one of the greatest molecular biologists of the century. In the end, we provide a perspective on the actual impact of quantum mechanics on the advent of molecular biology, also making a comparison with contributions from other subfields of physics. We claim that the contributions of physics to biology can only be understood from a pluralist stance — in the sense that multiple approaches are required for the explanation and investigation of the natural phenomena — as well as that Bohr's biology pass through his epistemological proclivity, Jordan's biology pass through his political proclivity, and Delbrück, in turn, had a migratory proclivity.

KEY WORDS: Molecular biology, Quantum physics, complementarity principle, Bohr, Jordan and Delbrück

ABSTRACT II: This study is based on interviews conducted at several institutions in Brazil, Germany, Israel and the U.S. and engages with problems related to the circumstances under which physicists migrate to biology and approach biological problems. Biological research, particularly in the fields of systems biology and synthetic biology, has been increasingly dependent on computational methods, high-throughput technologies, and, consequently, on multidisciplinary skills. Collaborations between physicists and biologists are vigorous everywhere and interdisciplinary research in biology have increasingly been a subject of sociological research. The role of physicists in systems biology is precisely the concern of our study and we use oral history as a methodological tool to gather the empirical material presented here. We identify as topics with historical and epistemological significance the following ones, which guided our framing of the empirical results discussed here: why to move from physics to biology? To what extent? And, to which effects? We conclude that there are common reasons for this move, that the transition must be evaluated in terms of degrees and that contributions rooted in physics set major goals to systems biology. At the end, we state a general claim for a relation between physicists and biologists based on critical confidence instead of indoctrination.

KEY WORDS: Physicists, systems biology, interdisciplinarity, oral history interviews

ABSTRACT III: This study is based on interviews conducted at several institutions in Brazil, Germany, Israel and the U.S. and engages with challenges related to disciplinary cultures faced by physicists as system biologists. Physicists have been heavily required in biology for support, particularly quantitative support, and the collision of disciplinary worlds generates cultural issues, which can be the subject of sociological and epistemological investigations. Here, we focus on the challenges regarding the co-existence of many epistemological cultures in the scientific community, particularly on cultural impacts rooted in physics and issues of interdisciplinary communication at the lab. We used oral history as one of the methodological tools to gather the empirical material presented here, conducting interviews with physicists working in systems biology. We also based our results on labs observation, informal conversation with other research group members, occasional group meetings, and lectures. We present the results by illustrating cultural issues between biologists and physicists and their distinct ways of thinking. We also present examples of miscommunication and highlight the intense debate about modelling strategies. Many episodes of misunderstanding were reported in the interviews and, particularly, the judgments about what is supposed to be a model seems to be a matter of careful interdisciplinary debate. Finally, we discuss their local strategies to overcome such cultural issues. In our results, different views and attitudes towards the place of conceptual frameworks were clearly indicated. We conclude that systems biology is full of overlapping and competing meanings, ideas and approaches, and that cultural unconformities within the community bring up important consequences, particularly to the exchange of ideas and communication flow.

KEY WORDS: Physicists, systems biology, cultural challenges, interdisciplinary communication

INTRODUCTION

DISCIPLINARY ENCOUNTERS
WHERE PHYSICS MEETS BIOLOGY:
SOME HISTORICAL AND CONTEMPORARY PERSPECTIVES

The aim of the following pages is to present my doctoral research on the relation between physical and biological sciences: I investigate the circumstances under which physicists approached biological problems in the past and how these circumstances have changed at the present time. Therefore, I address the topic at two historical moments: First, I focus on three physicists that in the 1930s were protagonists of the quantum revolution and were also somewhat involved in the advent of molecular biology, namely, Niels Bohr (1885 – 1962), Pascual Jordan (1902 – 1980) and Max Delbrück (1906 – 1981). Then, I present a contemporary study of the current migration of physicists to the field of systems biology, using oral history as one of the methodological tools and focusing on the challenges regarding the co-existence of diverse epistemological cultures in that scientific community.

The very broad question that motivated this study was: How does physics help to understand the phenomena of life? This question has attracted substantial scientific attention throughout the centuries: One can find examples in the 17th century, in Borelli`s (1608-1609) biochemical investigations of muscle and skeleton or the contributions of Harvey (1578 – 1657) to the study of circulation mechanisms in animal bodies. In the 18th and 19th centuries, respectively, the works on bioelectricity by Galvani (1737-1798) and the research of Helmholtz (1821-1894) on ophthalmic optics and nerve physiology are other remarkable examples. In the 20th century, many physicists played crucial roles in the biological research, such as Niels Bohr, Max Delbrück, Francis Crick and George Gamow. The movement of physicists to biology has developed novel and new aspects in the 21st century, a period that, as it is frequently claimed, is the century of biology rather than physics, as biology seems to be outflanking physics as the queen of natural sciences (cf. e.g. Wise 2004, 2007, Keller 2005)[1]. Here, our approach is to tackle slices of the 20th and 21st centuries to discuss the role of physics in contemporary biology and in the past.

The historical study is a literature review essay. The bibliographical material was mainly gathered during two predoctoral research stays at Max Planck Institute for the History of Science (MPIWG – Berlin) at Department I and II in February 2010 and February to July 2012, respectively. Around the final stages, in April 2013 and March 2014, two visits to the Niels Bohr Library at the American Institute of Physics had significant impact on the literature review process.

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[1] Cf. e.g., Keller, E. F., (2002) *Making sense of life:* Explaining biological development with models, metaphors, and machines. Cambridge, MA: Harvard University Press; Keller, E. F., (2005) The century beyond the gene *J. Biosci*. Vol. 30, 3-10; Wise, M.N. (2004) *Growing Explanations: Historical Perspectives on Recent Science,* Durham: Duke University Press; Wise, M. N. (2007) Science as History. In: *Positioning the History of Science: Boston Studies in the Philosophy of Science.* V. 248, 177-183

For the contemporary study, we used oral history interviews as one of the methodological tools. The interviews were conducted with physicists belonging to the following institutions: Weizmann Institute of Science, Israel; Max Delbrück Centre for Molecular Medicine, Humboldt University and Max Planck Institute for Molecular Genetics, Germany; Rockefeller Foundation, Harvard University and Princeton University, United States, and; Federal University of Bahia, Brazil. I have met the interviewees in their respective countries during my research stays in 2012 and 2013.

Thereby, the present work consists of two interrelated parts. The very first concern is to integrate them harmoniously, namely, taking into proper account the challenges and aims of History of Science, Science Studies —along the lines suggested by Daston (2009)[2]— and contemporary historical research (see e.g. Doel & Söderqvist)[3]. The historical section is presented in chapter I and the contemporary one in chapters II and II. Each chapter will generate an independent paper. Below, I describe the historical and contemporary counterparts in further detail.

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[2] Daston, L., (2009) Science Studies and the History of Science. In*: Critical Inquiry*. 35. Vol. 4, pp. 798-813

[3] Doel, R. E. & Söderovist, T., (2006) *The historiography of Contemporary Science, Technology, and Medicine: Writing Recent Science* London; Routledge, 87-200

1. THE PHYSICISTS' INTERESTS IN BIOLOGICAL PROBLEMS: LESSONS FROM THE PAST

The idea of the historical study was inspired by and raised in Olival Freire's classes on "History of Physics of the 20th century", which I attended twice: during my master and early doctoral periods. During the classes, Olival frequently called me up —the only biologist among his students— in order to bring up that a particular physicist had turned to biology. The multiple cases progressively instigated my curiosity: Why has this particular quantum physicist gotten interested in biology? How could their perspective contribute to biological research at that moment? As quantum physics was already plagued with trouble and controversies, why would someone suddenly be attracted by living matter troubles? These questions and derived ones were the focus of my research at MPIWG and AIP's libraries. In the resulting chapter I, which is entitled *"Quantum explorers: Bohr, Jordan and Delbrück venturing into Biology"*, we approach our protagonists' views on the application of the complementarity principle to biology. Before getting into the details of the chapter I shall briefly outline the historical context and the scholarly literature the chapter is related to.

Throughout the 20th century, many scientists with distinguished careers in physics had been attracted to biology for several reasons, such as the prospect of using methods from physics to study biology, the expectation that living matter could be reduced to physics or the search for new laws of physics. In the middle of the century, many physicists were shocked by the military use of atomic energy during the Second World

War and biology shone as a science connected to life over a science connected to death. Overall, biology seemed to harbour a large number of unsolved interesting scientific problems. among the many remarkable historical characters who have attempted to understand the phenomena of life from the perspective of physics, one can name Niels Bohr, Pacsual Jordan, Max Delbrück, Erwin Schrödinger, Leó Szilárd, Maurice Wilkins, Nicolas Rashevsky, Walter Elsasser, Seymour Benzer, Francis Crick and George Gamow.

The literature about the actual influence of physics and physicists on biology in the 20th century took me to a vast range of issues. Such literature contains several approaches, focusing, for example, on a particular physicist and research group, on larger forces, such as political or institutional, or on experiments and findings. There are also plenty of controversies, for example, about the actual role of Schrödinger's book "What`s Life?"[4] or about the particular role that the Rockefeller Foundation programme played in the development of molecular biology.[5]

Although the scholarly literature has covered important aspects of the contributions of physics to biology in the 20th century, the actual comprehensiveness of this literature is a polemic topic. Some authors have the impression that there is not sufficient material about "the increasing contribution from physicists"[6], others claim that relevant aspects have been neglected and that "we still have not arrived at a fully adequate

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[4] Cf. e.g., Dronamraju, K. (1999) Erwin Schrödinger and the origins of molecular biology. *Genetics*,153, 1071–1076

[5] Cf. e.g., Abir-Am, P. (1982) The Discourse of Physical Power and Biological Knowledge in the 1930s: A Reappraisal of the Rockefeller Foundation's 'Policy' in Molecular Biology. *Social Studies of Science*, 12 (3) 341-382

[6] Salinas, S. R. A. (2010) A física do século XX . *Estudos Avançados*, *24* (68), 369-374, p. 373 (own translation)

answer" about what the contribution from physics was.[7] Still, some authors argue that there are aspects being neglected in previous approaches.[8] The opportunities for historical research in the variegated relation between physics and biology are often highlighted[9]. In accordance, we argue that perspectives focusing on the actual impact of quantum mechanics on the rise of molecular biology are still missing, particularly regarding conceptual and cultural trades between the fields.

In order to contribute to such gap, we add an account on how the Copenhagen interpretation of quantum mechanics, for a few of its upholders, turned out to be an ubiquitous perspective, and the complementarity principle, as its conceptual bedrock, embodied broader uses in biology. In a vein similar to Freire's paper[10], our strategy is to zoom in on particular protagonists in order to open a window on a complex historical moment and we call them "quantum explorers". The metaphorical use of the term "quantum explorer" is also explicitly analogous to Freire's term "quantum dissidents". The term "dissidents" gather a group of physicists who fought against a dominant attitude in physics, according to which foundational issues in quantum physics had already been solved. The term "explorers" involves quite the opposite spirit. We approach physicists that shared the conviction that foundational problems had been essentially cleared up in

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[7] Keller, E. F. (1990) Physics and the Emergence of Molecular Biology: A History of Cognitive and Political Synergy. *Journal of the History of Biology*. Vol. 23, no. 3, 389-490, p. 389

[8] Cf. e.g., Domondon, A. T. (2006) Bringing physics to bear on the phenomenon of life: the divergent positions of Bohr, Delbrück, and Schrödinger *Stud. Hist. Phil. Biol. & Biomed. Sci.* 37, 433–458

[9] Poon, W., (2011) Interdisciplinary Reflections: The Case of Physics and Biology, *Studies in History and Philosophy of Biological and Biomedical Sciences, 42* (2), 115-118

[10] Freire JR. (2009) O., Quantum dissidents: Research on the foundations of quantum theory circa 1970. Studies In History and Philosophy of Science Part B: *Studies In History and Philosophy of Modern Physics*, 40(4), pp. 280-289, p.281.

quantum mechanics, so that its powerful achievements were worth enough to be pursued in another field. They are all quantum explorers in the sense that they moved from quantum theory to an unknown field. Explorers also bring along values, culture, world views and, potentially, a will to persuade or convince the natives. As we shall see, our protagonists express their explorer's features in singular manners, differing on the form of the exploration and on which elements they wanted to export.

Accordingly, in Chapter I we present our protagonists' views on the application of the complementarity principle to biology: I discuss Bohr's original suggestions of a wider application of his arguments in quantum physics, Jordan's jump into Bohr's hint, with even some extravagance, and Delbrück's approach, who evolved from a former disciple of Bohr to one of the most important molecular biologists of the century. We characterise general proclivities in their respective contexts: Bohr's epistemological proclivity, Jordan's political proclivity and Delbrück's migratory proclivity. Finally, we provide a perspective on the actual impact of quantum mechanics on the advent of molecular biology.

Based on the historical study, we argue that there are similarities between what happened in biology in the past and the present transformations in this science and that the present interdisciplinary relation between the two disciplines can be better understood through a knowledge of the historical background.

2. THE CIRCUMSTANCES UNDER WHICH PHYSICISTS APPROACH BIOLOGICAL PROBLEMS NOWADAYS

The contemporary study is composed of two chapters entitled: *"From Physics to Biology: physicists in the search for systemic biological explanations"* and *"When disciplinary worlds collide: cultural issues about physicists working as systems biologists"*. As mentioned above, we used oral history as one of the methodological tools, so that I interviewed leading physicists in diverse institutions and countries. Chapter II is meant to extract the gist of the many hours of interviews and present general aspects of the migration from physics to biology. In chapter III, we discuss cultural differences in the interdisciplinary lab, focusing on communication gaps reported by the interviewees. In order to explain such structure, I would like to focus on the journey and the roads taken throughout the PhD research process.

A JOURNEY AS IMPORTANT AS ITS GOALS

When I first embarked on my PhD research project, I did not plan to do either interviews or even a contemporary study. The project started in 2010 at the MPIWG, exclusively as a historical study on the interface of physics and biology. The initial focus was on quantum physicists (i.e. Pascual Jordan, Niels Bohr, Max Delbrück, and Erwin Schrödinger) in the lines carried by Olival Freire's research group, which I had recently joined.[11] Only later, together with my supervisors, I developed the idea of a contemporary study on the migration as well. Whether or not this study would still be considered a historical account—such as contemporary history? or maybe Science Studies?—was not matter of hampering concern for me. I actually sensed some need to give a sheltering research field to my project in some particular occasions; such as when I submitted it to the International Congress of History of Science, Technology and Medicine and the committee placed me in the Science Studies section, or when I was awarded a grant for history of modern physics and allied fields. However, I opted not to worry too much about the label and just learn by doing. To be a doer was precisely my position towards the classification of our research in the context of the debate surrounding Science Studies vs. History of Science.

The contemporary study was mainly inspired by the fact that biology, and particularly systems biology, is experiencing very exciting times, in which the influx of quantitative scientists is an outstanding feature. Extraordinary advances have been made over the course of the past century in our understanding of living systems. In the post-genomic era, biological research has been increasingly dependent on computational modelling and high-throughput technologies, which, consequently, increase the need for interdisciplinary collaborations. In the wake of this transformation, new institutes, programmes, and departments jointly involving biologists, physicists, mathematicians, computational scientists, engineers and other professionals have proliferated. In fact,

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[11] Olival Freire and his group received the alien biologist at the lab in an open and kind way; helping me to grow as a person and nurturing my work. For Olival's teachings—notably in history, physics and politics—and interest, I am humbled and forevermore grateful.

physicists are, one more time in history, remarkably turning their attention to biological problems and their role on the search for biological systemic explanations is precisely the concern of our study.

The topic is often discussed in the literature through non peer-reviewed papers but rather as opinions, editorials, features, synopses and websites, which are useful as starting points for our research questions. I outline some of these questions in the next paragraphs. More generally, these sources highlight the collaborative success between physicists and biologists and point out some cultural challenges between the professionals and the disciplines, as stressed in the following quote:

> "(…) there is a cultural gap between the disciplines: biologists and physicists have different goals and traditions, they ask different kinds of questions, and perhaps even look for different kinds of answers. If the cross-fertilisation now being attempted is to be productive, that culture gap must be bridged, and for this to happen, some resolution of, or accommodation to, these differences is required."[12]

What is this cultural gap like? Which accommodations are required? Is there any communication problem between the disciplines? What are the circumstances under which physicists approach biological problems nowadays? What has motivated the influx of physicists? Does the claimed reversal of scientific prestige between biology and physics play a role among the circumstances that motivate the influx of physicists? What kind of contribution they provide? What does happen when biologists and physicists work together? What are the outputs of their interactions? Are there any cultural issues in this

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[12] Keller (2005), *loc. cit.*, note 1, p.6

particular interdisciplinary environment? Is there any disciplinarily rooted miscommunication?

UNTYING THE KNOT: ORAL HISTORY AS A METHODOLOGICAL TOOL

Thereby, I found my subject of concern and research questions. The next step could only be: how to investigate them? I spent quite some time stuck with the methodological choice for the contemporary study. I was used to first find my way through published material and peer-reviewed journals but then I faced a scarcity of sources, which is a typical problem of historical research on contemporary science. Interviews could breath life to this weak availability of material. With hindsight, oral history was somewhat a blind spot for me, even though other researchers in our lab have conducted interviews for their projects (see. e.g. Silva 2013).[13] For unknown reasons, I just could not easily sort out the puzzle and see the valuable tool lighting, so that if it were a chess match story I would have lost important chessmen on the way. It was Olival who pointed the way through oral history. In 2011, I presented a seminar to the group about the developing contemporary study when he declared in a trouble-free tone: "Just go and interview these physicists who turned to biology". Loaded with the physicist's traditional simplicity, the issue was set.

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[13] Silva, Indianara Lima (2013) Uma história do conceito de fóton na segunda metade do século XX: Para além de histórias do modelo bola de bilhar. Tese de Doutorado em Ensino, Filosofia e História das Ciências. Universidade Federal da Bahia e Universidade estadual de feira de Santana

Once the methodological question had been satisfactorily answered, it was time for a new bunch of doubts: how exactly to investigate? How to properly use this methodological tool? What kind of skills are required? and, importantly, how to choose the subjects for my interviews? The answers could be searched in the literature on oral history and systems biology, as well as through word of mouth information. I went after core members of the scientific community by searching on the internet, asking people and spreading the word. The physicists themselves were of great help in pointing out influential names inside the scientific community. Afterwards, I selected them considering geographical and financial restrictions of my project. Every first approach to each interviewee has been by an invitation email with a one-page project description attached, followed by the particular meeting arrangements in case of acceptance.

I started the interviews in Germany, since I was in the country for a research stay at MPIWG in 2012. There, I conducted five interviews with three research group leaders, i.e. Nikolaus Rajewsky, Hanspeter Herzel and Peter Arndt, and two postdoctoral researchers, i.e. Roman Brinzanik and Navodit Misra, at Max Delbrück Center for Molecular Medicine, Humboldt University and Max Planck Institute for Molecular Genetics. Next, I learned about outstanding research taking place at Weizmann Institute of Science, notably about Uri Alon and his influential book on systems biology.[14] In July 2012, I flew to Israel[15] to interview physicists who head systems biology research groups: Uri Alon, Joel Stavans and Eytan Domani. When I returned to Brazil later that year, I interviewed Suani Pinho,

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[14] Alon, Uri. *An introduction to systems biology: design principles of biological circuits*. Boca Raton: Chapman & Hall/CRC, 2007

[15] I thank Fapesb (Fundação de Amparo a Pesquisa do Estado da Bahia) for funding the travel.

one of the leading researchers in the FESC group (Física Estatística e Sistemas Complexos, in the Institute of Physics, Federal University of Bahia) and thus, she prevented my sample of being exclusively dominated by male interviewees.[16]

Trying to make sense of the data I had collected up to that point, I felt there was a missing piece. Because of the outstanding impact of research institutes and researchers in the United States, it became evident that interviews with American physicists would greatly complement and complete my international sample. So, I applied for a grant-in-aid for history of modern physics and allied fields which was eventually approved by the "Friends of the Centre for History of Physics at the American Institute of Physics" (AIP).[17] In the United States, I interviewed the following leading physicists: Erel Levine, Harvard University; Eric Siggia, Rockefeller Foundation, Ned Wingreen and Thomas Gregor, Princeton University[18]. Another relevant source of oral information was a conversation with Evelyn Fox Keller, in which we also explored her transition to biology as a physicist in the 1960s.

Although those professional physicists were my main interlocutors,[19] I also spoke to students, secretaries and other members of the labs. In fact, the interviewees often

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[16] For that and also for many conversations and insights, kind and special thanks go to Suani.

[17] I deeply thank AIP and MPIWG for financial and structural support, and, particularly, CAPES for funding the entire project.

[18] The AIP required me to deposit a digitally recorded copy of the interview in the Niels Bohr Library & Archives.

[19] This dissertation would not have been possible without the generous help of the physicists who welcomed me into their laboratories, gave me their time and taught me a lot about their scientific practices. My most sincere thanks go to all the interviewees and responsibility for any inadequate piece of information remains only mine.

introduced me to people who she/he thought to be helpful. We also drew our results on observations of the working places involving many scientists, including lab day-to-day routine, offices, group meetings, supervision sessions, lectures, and informal meetings in coffee rooms. I tried to be flexible - and a bit meddlesome - to attend the group activities according to the convenience of the interviewee.

As a side remark, this spontaneous field observation style brought around funny situations. For instance, the day I was at Princeton University to conduct two interviews. I got invited to attend a lecture about microRNA taking place that day. I used the free time to chat with students about their disciplinary commitments and interest in biology, so I did not discuss the details of the talk we were about to attend. In a twist of irony, once the talk started I figured out that the speaker was Erel Levine, whom I was going to interview in Harvard University a couple of days later. It felt coherent. I optimistically took coincidences like that as signs that I was on the right track.

The many informal conversations, field observations, e-mail exchanges, together with the scientific, philosophical and sociological literature on systems biology constitute alternative source, which are considered of great value to our analysis. A major concern of the present work was to evaluate if and how every information made available by the interviews agreed with other sources. Encouraged by my supervisors, I aimed at carefully comparing interviews and other sources.

Another significant matter of concern was how to approach the interviewees. The interviews were recorded and semi-structured. The protocols were constructed for each physicist, considering the particularity of their interests, research, working places, etc. The interviewees were encouraged to speak about, for instance, their careers, motivations to do research in biology, their background in physics, their research work and group, the culture of systems biology, and issues of interdisciplinary interactions. Each interview was preceded by an extensive preparation on my part, by reading their papers and researching about them.

Many topics turned out to be polemic during the interview and it was quite challenging to decide how to approach them. I encountered many stereotypes and labels to define physicists, biologists, physics and biology embedded in intellectual discrepancies. Very often it felt that I could be touching some personal feeling or attachment of the interviewees through some words. According to my emphasis, or even facial expression, I could easily please or offend them, so I struggled to develop non-biased questions and, also, an emotionless face. There were even occasions in which the scientific territoriality became ethically tricky, such as the time that a interviewee expressed disdain for biologists and even lumped me in the same category of *personae non gratae*. Overall, I aimed to reach some diplomatic approach, by providing guidelines for the discussion based on the protocol, but also keeping the interaction flexible enough for the physicists to talk freely about whatever they pleased. As Lilian Hoddeson elegantly put, “doing oral history requires historians to be at once confrontational and collaborative, objective and personal, and suspicious and trusting”.[20] In my experience, such combination calls for a very complex empathy system. I strongly hope to have succeeded in it during the interviews and, in the same empathetic spirit, to have made it clear in the

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[20] Hoddeson, L. The Conflict of Memories and Documents: Dilemmas and Pragmatics of Oral History. In Doel, Ronald Edmund, Söderqvist, Thomas. *The historiography of Contemporary Science, Technology, and Medicine: Writing recent science* (pp.187-200). London ; Routledge, 2006

ensuing chapters that our approach implies absolutely no intellectual subservience or subordination between disciplines. I personally meant to imply collaborative respect, or even love.

WRAPPING IT UP

Accordingly, the whole dissertation process has hinged on the following questions and answers: What to investigate? Physicists in contemporary biology. What are the research questions? There are many, regarding the circumstances under which the physicists approach biological problems. How to investigate? Oral history, alternative source and literature review. How exactly to investigate? How to properly use this methodological tool? What kind of skills does it require? The literature is the key to find it out. Who to investigate? Go after core members by researching and communicating. Finally, how to approach them? Be confrontational and collaborative, objective and personal, and suspicious and trusting. I can say that the PhD experience for me was just like the way, that is, *camino*, for Antonio Machado's poetic words: *"Caminante, son tus huellas, el camino y nada más; Caminante no hay camino, se hace camino al andar."* The way was subsequently carried on by asking how to analyse the empirical material and how to present the results. I describe the final structure in the next paragraphs.

Chapter II, entitled *"From Physics to Biology: physicists in the search for systemic biological explanations"*, is meant to explore general results from the interviews. Aiming at isolating topics with historical and epistemological significance, we frame our empirical results within the following questions: why to move from physics to biology? To what extent? And to which effects? We conclude that there are communal reasons for this move, that the transition must be evaluated in terms of degrees and that intellectual contributions rooted in physics set major goals to contemporary systems biology. At the end, we state a general claim for a more open-minded relation between physicists and biologists, instead of an indoctrinated one. For that task, physicists and biologists should overcome authoritarianism, combine respect with critical confidence, and set out with the idea of otherness.

In chapter III, which is entitled *"When disciplinary worlds collide: cultural issues about physicists working as systems biologists"*, we address cultural differences in the interdisciplinary environment of systems biology. The practitioners of the field come from different scientific cultures, they belong to different traditions, have different goals and, consequently, face multiple problems of intercultural communication. As the interviewee Uri Alon reported: *"It's almost like people from very different countries, like two continents. Conceptions about what is a good answer in science are different, about words like 'model' and a lot of technical knowledge"*. The focus lies on the scientific language[21] and we present episodes of miscommunication at the lab described by the interviewees. Many episodes of misunderstanding were reported in the interviews and, particularly, the judgments about

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[21] Attention to the scientific language is very crucial to the present work. Such important concern for me comes from a strong influence of both Charbel El-Hani (my co-supervisor) and Evelyn Fox Keller. The structure of scientific language and how it affects scientific practices are core themes in these authors' work. I would like to use the occasion to thank Charbel for the many years of support and genial scholarly insights. I also deeply thank Evelyn Fox Keller for kindly receiving me at her place in Cambridge for a coffee, in order to discuss my work.

what is supposed to be a model seems to be a matter of careful interdisciplinary debate. We also discuss their local strategies to overcome cultural issues. In our results, different views and attitudes towards the place of conceptual frameworks were clearly indicated. We conclude that systems biology is full of overlapping and competing meanings, ideas and approaches, and that cultural unconformities within the community bring up important consequences, particularly to the exchange of ideas and communication flow.

Up to now I described the structure of my dissertation. Yet, I would like to comment further on an important aspiration of the next pages: to be simple. Simplicity is a perspective that has been developed alongside with the dissertation, as I explain below.

3. THOUGHTS ON SIMPLICITY

> “ Beherrscht dich ein Gedanke, so findest du ihn überall ausgedrückt, du riechst ihn sogar im Winde”
> Thomas Mann, *Tonio Kröger* (1903)[22]

A new view on the idea of simplicity constituted the motif that—sometimes perhaps unconsciously—runs throughout this dissertation. During my journey through the physicists’ style of thinking, one of the most prominent feature I noticed was a quest for simplicity. It seems that physicists seek for the simplest way to uncover a system without losing contact with complex reality. This claim remains valid both for the historical and contemporary studies. When approaching biology, they naturally adapt the

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[22] If you are possessed by an idea, you find it expressed everywhere, you even smell it in the wind

quest for simplicity to biological complexity. The following interview excerpts from Uri Alon and Ned Wingreen illustrate the expectation for some underlying simplicity and the physicists' perspective:

> *"Biology is very very complex. There is no way one can doubt about that. But there are certain ways in which one can see simple principles that can explain some aspect of why it's built. That's what physicists are trained to do and works fantastically when we try to understand the simple stuff like metal, plastic, not living matter. The surprise is that it also works- at least the way I look at science and the results we get- it works remarkably really well if you know the model and you think about biology (…) The simpler, the better for me" (Interview with Alon, Weizmann Institute, July 2012)*

> *"(…) you realize that there are very simple biophysics in complex biological systems underlying that, there were something that was simple. I think it's very appealing to the physicists... that's what the physicist training was: finding underlying simplicity (…) If we are lucky and maybe have good partners, and someone has good taste we can dig in to that system and find some underlying simplicity. And then with more hard work and some more thoughts we can build backup from that simplicity to a real understanding of biology" (interview with Ned Wingreen, Princeton University, April 2013)*

When discussing modelling practices, the interviewees grip the search for the simple to describe the physicists' typical strategy. There was no exception to that. That was one of the most remarkable results: there are conceptual unconformities concerning the idea of model and the task of modelling in the interdisciplinary environment. The judgment of what is supposed to be considered a model seems to be a matter of interdisciplinary debate. Thus, the appropriate level of simplicity is a critical issue.

Briefly, they argue that physicists, in accordance with their training, try hard to consider only what is essentially important. The quotes below from Erel Levine and Nikolaus Rajewsky exemplify the sheer preoccupation with simplicity when modeling:

> *"(…) the real challenge is to go from very messy noisy complex data into a simple clear model. That's a huge challenge, it's a mental challenge (…) build a picture which is clear enough so you can write down a simple model" (interview with Erel Levine, Harvard University, May 2013)*

> *"(…) the physicists tend to try to simplify the problems with the hope of some unifying principles and try also to get a clearer understanding of the scales involved" (interview with Nikolaus Rajewsky, Max Delbrück Center for Molecular Medicine, June 2012)*

To simplify: physicists seem to ask why things are so complicated and find reasons why they are simple. A model is an attempt to represent some reality, so is a thesis. By investigating how the physicists approach biological problems, I turned some conclusions to my own issues as I found them comparable. The point I want to make regards the repercussion of it in my own PhD project: the job I had to do for my dissertation, as I saw it, was to organize my own complexity: bibliography, many hours of interviews and field annotations. It felt quite intimidating at some point, I must say. In a natural way, I felt inspired and driven to deal with it by handing simplicity as well. A simple approach towards a problem demands a tender sensitivity towards what is indispensable and what is disregardable. Accordingly, a delicate aspiration of the present work was to develop such a sense on myself. How to be concise but not meager? How to let things go? I attempted to use and broaden these reflections as substrate for growth as a PhD student.

My noteworthy goal here is to present a thesis which is simple. A work that lies successfully on Leminski's spot: não fosse isso/ e era menos / não fosse tanto / e era quase.

CHAPTER I

QUANTUM EXPLORERS:

BOHR, JORDAN AND DELBRÜCK VENTURING INTO BIOLOGY

ABSTRACT: This paper aims at unfolding selected entwined aspects of two great scientific developments: quantum mechanics and molecular biology. As the entry point, we look at the contributions of three physicists that in the 1930s were protagonists of the quantum revolution and explorers of the field of biology, namely, Niels Bohr, Pascual Jordan, and Max Delbrück. Their common platform is the defence of the Copenhagen interpretation in physics and the adoption of the principle of complementarity as a way to look at biology. In 1927, Bohr formulated the complementarity principle and, subsequently, started to discuss wider applications of his arguments in quantum physics. In 1932, he gave the famous lecture entitled "Light and Life", addressing the problem of how far the results reached in the domain of physics might influence our views about living organisms. Jordan and Delbrück were followers of Bohr's ideas in the context of the debates on quantum mechanics interpretations and, also, of the expanded version towards biology. Jordan jumped into Bohr's hint, with even some extravagance. He wanted to combine the quantum revolution and biological phenomena. The understanding of his contributions demands an appreciation of the respective political context. In 1937, Max Delbrück migrated from Germany to the United States and, categorically, from physics to biology. He evolved from a former Bohr's disciple, to one of the greatest molecular biologists of the century. In the end, we provide a perspective on the actual impact of quantum mechanics on the advent of molecular biology, also making a comparison with contributions from other subfields of physics. We claim that the contributions of physics to biology can only be understood from a pluralist stance — in the sense that multiple approaches are required for the explanation and investigation of the natural phenomena — as well as that Bohr's biology pass through his epistemological proclivity, Jordan's biology pass through his political proclivity, and Delbrück, in turn, had a migratory proclivity.

Science in the first half of the 20th century was dominated by theoretical physics, in particular quantum mechanics. In turn, biology, particularly molecular biology and genetics, has progressively gained prominence, especially after the DNA double helix proposal in 1953. Today, it is definitely a controversial task to elect the queen of the natural science[23]. In fact, what seems actually uncontroversial is that quantum mechanics has set a new epoch not only for physics, but for science in general and that historical relations between quantum mechanics and biology have been rich, prosperous and prolific.

This paper aims at unfolding a few entwined aspects of two great scientific developments: quantum mechanics and molecular biology. As an entry point, we look at the work of three physicists who were protagonists of the quantum revolution in the 1930s and were also somewhat involved in the advent of molecular biology, namely, Niels Bohr (1885 – 1962), Pascual Jordan (1902 – 1980) and Max Delbrück (1906 – 1981). Their common platform was the adoption of the principle of complementarity as an inspiration to look at life science.

In a vein similar to Freire's paper[24], our strategy is to zoom in on particular protagonists in order to open a window on a complex historical moment. The

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[23] See Evelyn F. Keller, Making sense of life: Explaining biological development with models, metaphors, and machines. (Cambridge: Harvard University Press, 2002); Evelyn F. Keller, "The century beyond the gene," Journal of Biosciences 30 (2005), 3-10, Norton M. Wise, Growing Explanations: Historical Perspectives on Recent Science (Durham: Duke University Press, 2004); Norton M. Wise, "Science as History", in Kostas Gavroglu and Jürgen Renn, eds., Positioning the History of Science. Boston Studies in the Philosophy and History of Science (Springer Publishers, 2007) pp. 177-183

[24] Olival Freire Jr. O. "Quantum dissidents: Research on the foundations of quantum theory circa 1970," Studies In History and Philosophy of Science Part B: Studies In History and Philosophy of Modern Physics, 40 (2009), 280-289

metaphorical use of the term "quantum explorer" is also explicitly analogous to the term "quantum dissidents". The term "dissidents" gather a group of physicists who fought against a dominant attitude in physics, according to which foundational issues in quantum physics had already been solved. The term "explorers" involves quite the opposite spirit. We approach physicists that shared the conviction that foundational problems had been essentially cleared up in quantum mechanics, so that its powerful achievements were worth enough to be pursued in another field. They are all quantum explorers in the sense that they moved from quantum theory to an unknown field. Explorers also bring along values, culture, world views and, potentially, a will to persuade or convince the natives. As we shall see, our protagonists expressed their explorer's features in singular manners, differing on the form of the exploration and on which elements they wanted to export. They were not alone. Exploring biology has been an appealing task to many physicists. In the 20th century, they have been often attracted to the mysteries of living matter for several reasons, such as the desire to apply methods and practices rooted in physics to tackle biological problems,[25] the expectation that living matter could be reduced to physics[26], or, especially after the military use of atomic energy, the appeal of a science attached to life over a science attached to death[27]. Among the many remarkable historical protagonists who have attempted to understand the phenomena of life from the

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[25] See e.g. Donald Fleming, "Emigre Physicists and the Biological Revolution", in Donald Fleming, & Bernard Bailyn, ed., The intellectual migration (Cambridge: Harvard University Press, 1968), pp. 152–189; Robert Olby, The Path to the Double Helix (Seattle: University of Washington Press, 1974; Lily E. Kay, Who Wrote the Book of Life? A History of the Genetic Code (Stanford: Stanford University Press, 2000)

[26] See e.g. John A. Fuerst, "The Role of Reductionism in the Development of Molecular Biology: Peripheral or Central?", Social Studies of Science 12 (1982), 241-278

[27] See e.g. Soraya de Chadarevian, Designs for Life. Molecular Biology after World War II (Cambridge: Cambridge University Press, 2002)

perspective of physics, we find minor and major figures, for example, Erwin Schrödinger, Robert Rompe, Leó Szilárd, Nicolas Rashevsky, Walter Elsasser, Seymour Benzer, Francis Crick, Edward Teller, Nicholas Metropolis, George Gamow, and Richard Feynman. Schrödinger's approach to biology is perhaps the most well known, since he published in 1944 the influential book "What's life?", which played an important role in molecular biology, particularly by attracting scientific attention from other areas to the field. There, he proposed to use quantum mechanics to explain molecular behaviour and stability, using Delbrück's model as the book's centrepiece. Just like our protagonists, Schrödinger was a great exponent of quantum mechanics, but, unlike them, he disagreed with Bohr on the principle of complementarity. Together with Planck and Einstein, he considered the idea of complementarity full of contradictions and, therefore, he also opposed to the use of the principle beyond physics[28]. Because of his dissonance and our intent to focus on the borrowing of the complementarity principle as a motivation to look at the new field, this quantum explorer is not approached in the present paper.

Although the scholar literature has covered important aspects of the contributions of physics to biology in the 20th century, the actual comprehensiveness of this literature is a polemic topic. Some authors claim that relevant aspects have been neglected and that "we still have not arrived at a fully adequate answer" about what the contribution from physics was[29]. The opportunities for historical research in the variegated relation between

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[28] John L. Heilbron. "The Earliest Missionaries of the Copenhagen Spirit," Revue d'Histoire des Sciences, 38 (1985), 195-230

[29] Evelyn F. Keller, "Physics and the Emergence of Molecular Biology: A History of Cognitive and Political Synergy, Journal of the History of Biology", Journal of the History of Biology, 23 (1990), 389 – 490, p. 389

physics and biology are often highlighted.[30] In accordance, we argue that despite the literature on this subject[31] perspectives focusing on the actual impact of quantum mechanics on the rise of molecular biology are still missing, particularly regarding conceptual and cultural trades between the fields. Here, we shall see how the Copenhagen interpretation[32] of quantum mechanics, for a few of its upholders, turned out to be an ubiquitous perspective, and the complementarity principle, as its conceptual bedrock, embodied broader uses in biology.

In the following sections, we present our protagonists' views on the application of the complementarity principle to biology. We discuss Bohr's original suggestions of a wider application of his arguments in quantum physics, Jordan's jump into Bohr's hint, with even some extravagance, and Delbrück's approach, who evolved from a former disciple of Bohr to one of the most important molecular biologists of the century. Finally, we provide a perspective on the actual impact of quantum mechanics on the advent of

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[30] Wilson C.K. Poon, "Interdisciplinary Reflections: The Case of Physics and Biology," Studies in History and Philosophy of Biological and Biomedical Sciences. 42 (2011), 115 – 118

[31] See Pninn Abir-Am, "Themes, Genres and Orders of Legitimation in the Consolidation of New Scientific Disciplines: Deconstructing the Historiography of Molecular Biology," History of Science 23 (1985), 73 – 117; Robert T. Blackburn, Interrelations: The Biological and Physical Sciences (Chicago: University of Chicago Press, 1966); John Cairns, Gunther S. Stent, James D. Watson, Phage and the Origins of Molecular Biology (CSHL Press, 2007); Krishna R. Dronamraju, "Erwin Schrödinger and the Origins of Molecular Biology," Genetics 153 (1999), 1071-1076; Fleming, Emigre Physicists (ref. 3); Fuerst, "The Role of Reductionism" (ref. 4); Francois Jacob, The Logic of Life (New York: Vintage Press, 1973); Lily E. Kay, Molecular Vision os Life (Oxford: Oxford University Press, 1993); Lily E. Kay, Book of Life (ref. 3); Evelyn F. Keller, Refiguring Life: Metaphors of Twientieth-Century Biology (New York: Columbia University Press, 1995); Michael Morange, A History of Molecular Biology (Cambridge: Cambridge University Press, 1998); Olby, Double Helix (ref. 3)

[32] We interchangeably use terms such as "interpretation of Copenhagen" and "principle of complementarity," which is current among scientists to designate the most influential, in its inception, interpretation of quantum mechanics. Scholar works, however, have shown that "interpretation of Copenhagen" is a term appearing only in the 1950s in the context of the controversy over the interpretation of this physical theory. See Olival Freire Junior, "Science and exile - David Bohm, the Cold War, and a New Interpretation of Quantum Mechanics", Historical Studies in the Physical and Biological Sciences, 36 (2005), 1-34; Don A. Howard, "Quantum Mechanics in Context: Pascual Jordan's 1936 Anschauliche Quantentheorie", in Massimiliano Badino and Jaume Navarro, eds., Research and Pedagogy: A History of Quantum Physics through Its Textbooks (Berlin: Editions Open Access, 2013), pp. 265-283; Kristian Camilleri, "Constructing the Myth of the Copenhagen Interpretation," Perspectives on Science 17 (2009), 30-32

molecular biology. We conclude that these scientists shared more than physics as primary standpoint and the Copenhagen perspective, they shared also the explorer spirit.

2. BOHR'S BIOLOGY AND EPISTEMOLOGICAL PROCLIVITY[33]

Bacon famously claimed that once the human understanding has adopted an opinion, it draws everything else to support and agree with it[34]. In the context of the ardent defence of Copenhagen interpretation of quantum mechanics, Bohr and Jordan clearly showed this human tendency. Bohr considered his puzzle solutions in quantum mechanics powerful enough to address broader problems. He was very much intrigued with paradox and, accordingly, was attracted by paradoxical kinds of problem, as shown by his main concerns in physics, which involved the duality between wave and particle aspects of matter, contradictions with classical physics, and counter-intuitive predictions.

In 1927, Bohr formulated the complementarity principle, which became an

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[33] The term proclivity is used here as a way to capture the interaction between actors and their context. It is intended as a tool to characterise the manner in which different actors responded to the potentialities intrinsic in their historically situated context. This manner is essentially rooted in the historical situation, but it also depends importantly on the specific trajectory of the actor (his education, personal experience, social commitments, research agenda). Concerning how actors relate to the situation in which their are embedded, our view is in accordance with Wise's alternative model, in which the emphasis goes upon resources and participation instead of influences and capitalisation. Proclivity, in our sense, encompass the tendency to draw on cultural resources, rather than being influenced by a local culture that would act on the individual. Those forms of proclivity are directed to cultural resources—epistemological, political, migratory—on which the actors drew on to pursue their own research. Our protagonists are understood as participants with individual motivations and choices within a given context (Cf. Norton M. Wise,, "Forman Reformed, Again," in Cathryn Carson; Alexei Kojevnikov; Helmuth Trischler, Org., Weimar Culture and Quantum Mechanics: Selected Papers by Paul Forman and Contemporary Perspectives on the Forman Thesis. (London: Imperial College Press & World Scientific 2011), pp. 415-431

[34] Francis Bacon, Novum organum (19620), in Edwin A. Burtt, The English philosophers from Bacon to Mill (New York: Ramdom House, 1939), pp. 24-123

essential part of the Copenhagen interpretation of quantum mechanics[35]. Regarding the distinction between waves and particles, Bohr proposed that there are complementary ways of understanding reality, and that it is not a matter of crucial concern whether one way is more real than the other. The properties of wave and particles must be considered as complementary aspects of reality, inasmuch as each express an important feature of the phenomena of light and atoms. Complementarity depends on the way in which the experimenter asks questions and the chosen method determines whether one will observe particle-like or wave-like behaviour. Earlier, Heisenberg formulated his uncertainty relations, providing what would become the physical counterpart for Bohr's epistemological complementarity. The uncertainty principle also became an essential element of the Copenhagen interpretation. Bohr was convinced that the new physics, in the way he interpreted it—which is to say, in accordance with the complementarity principle and uncertainty relations — not only made possible, but even demanded new approaches to a wider range of knowledge domains.

Complementarity became such a central theme of his thinking that, circa 1929, he suggested that a general notion of complementarity could be applicable in other fields than physics, particularly in psychology and biology. Progressively, Bohr began to express his expanded argument to new audiences. In 1932, Bohr gave the famous lecture entitled "Light and Life", addressing the opening meeting of the International Congress of Light Therapy in Copenhagen. His proposal was to draw attention to the problem of how far the

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[35] The history of the Copenhagen interpretation is plentifully supplied with narratives. See e.g., Mara Beller, Quantum Dialogue: The Making of a Revolution (Chicago: Chicago University Press, 1999); Don Howard, Who Invented the 'Copenhagen Interpretation'? A Study in Mythology, Philosophy of Science 71 (2004), 669-682; Camilleri, Perspectives on Science (ref. 10)

results reached in the domain of physics might influence our views about living organisms, since for him "the efforts of physicists to master this situation [the description of light] resemble in some way the attitude towards the aspects of life always taken more or less intuitively by biologists"[36]. Along the lecture, Bohr attempted to make it clear what he meant and what he did not mean. As perhaps expected, his window to look into biology was not a consideration of life as a chemical phenomenon, upon which quantum mechanics could be applicable to understand the chemical behaviour of all atoms. Even though there could be no doubts concerning the Newtonian teaching that "the real basis of science is the conviction that nature under the same conditions will always exhibit the same regularities,[37] his question was not whether quantum physics could explain the basis of life, but "whether some fundamental traits are still missing in the analysis of natural phenomena, before we can reach an understanding of life on the basis of physical experience"[38]. The analysis of living and non-living phenomena were not directly comparable, since that — because of the need of keeping the object of investigation alive— biological investigation permits the organism to "hide its ultimate secret from us"[39]. Therefore, life must be accepted as an elementary fact, as he put: "the existence of life must be considered as an elementary fact that cannot be explained, but must be taken as a starting point in biology, in a similar way as the quantum of action, which appears as an irrational element from the point of view of classical mechanical physics, taken together

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[36] Niels Bohr, "Light and Life," Nature 133 (1933), 457-459, p. 457

[37] Ibid., p. 458

[38] Ibid., p. 457

[39] Ibid., p. 458

with the existence of the elementary particles, forms the foundation of atomic physics"[40]. The insufficiency of mechanical analysis regarding the understanding of the stability of atoms that was encountered in physics would be analogous to the impossibility of a physical and chemical explanation of life. Therefore, the acceptance of the quantum postulates in physics could be seen as analogous to the acceptance of life as an elementary fact in biology. In this way, Bohr was not interested in connecting quantum and living phenomena at a microscopic level; rather, he proposed analogies between the corresponding sciences. As Delbrück[41] later noted, Bohr had a dialectical approach that had been encountered in the field of quantum physics, but could be pursued in many paradoxical problems. His biological complementarity was mainly, and unsurprisingly, an epistemological proposal.

Bohr's lecture was not transcribed, but in 1933 he published a version in *Nature*[42]. "Light and Life" was the main spark to motivate Jordan and Delbrück to look at the phenomena of life, as we shall see. However, what prompted Bohr was more than a speculative question. Probably, the Rockefeller Foundation policy change on scientific funding in the 1930s, which favoured experimental biology, played also a role[43] Besides, there was also a long-dated sensitivity to the subject, since his father Christian Bohr was a prominent physiologist, and the influence from John Scott Haldane (father of J. B. S.

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[40] Ibid., p. 458

[41] Max Delbrück, Interview by Carolyn Harding. Oral History Project (California Institute of Technology Archives Oral Histories, 1979)

[42] See also Bohr, "Light and Life" (ref. 12), Niels Bohr, "Licht und Leben-noch einmal," Naturwissenschaften 50 (1963) 725-727, Gunther S. Stent, "Light and Life: Niels Bohr's Legacy to Contemporary Biology" Genome 31 (1989), 11-15

[43] Finn Aaserud, Redirecting Science: Niels Bohr, Philanthropy and the Rise of Nuclear Physics (Cambridge: Cambridge University Press, 1990)

Haldane) is also to be taken into account.[44] Bohr's commitment to the Copenhagen interpretation seems undoubtedly a genuine determining factor, such that his approach in biology reflects his position as a philosophically-minded theoretical physicist. As Bohr's interest in biological questions was mainly philosophical, he performed no concerted research, but carried it on through unrestrained discussions and debates. Markedly, different approaches were taken by his followers Jordan and Delbrück.

3. JORDAN'S BIOLOGY AND POLITICAL PROCLIVITY

Among the founding fathers of quantum mechanics, Jordan is the less known among audiences which are not experts in the field of physics or history of physics. His contributions were, however, various, the most prominent being his contribution to the creation of matrix mechanics. Indeed the celebrated work known as the "three-man paper", which has fundamental importance for the history of Quantum Mechanics,[45] had Jordan as one of the authors, together with his doctoral advisor Max Born and Werner Heisenberg.

Jordan was an enthusiastic supporter of Bohr's ideas in the context of the debates on quantum mechanics interpretations and, also, of the expanded version towards new fields. On Jordan's reading, the complementarity principle not only made sense of the new

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[44] David Favrholdt, Niels Bohr Collected Works Volume 10, Complementarity beyond Physics (1928-1962) (Amsterdam: Elsevier, 1999)

[45] See e.g. Bartel L. van der Waerden, Sources of Quantum Mechanics (New York: Dover, 1967), p. 42

physics, but could also revolutionise the entire scientific thought.[46] Jordan approached a huge array of topics in biology, advocating complementary relations in a more committed way than Bohr himself, as he pursued bolder connections between the atomic and the macroscopic level. Indeed, Jordan argued for an extension of the quantum revolution to the life sciences, as well as to other domains of knowledge.

Pascual Jordan was an "unusual and complicated working physicist in an unusual and complicated setting"[47], presenting many disparate idiosyncrasies, especially when combining science and politics. For instance, he was a member of the Nazi Party, but simultaneously performed a practice of science independent of races, supporting Jewish physicists[48], as well as Jews in different intellectual circles, such as Freud.[49] On the one hand, Jordan attempted to ensure a place for the new quantum mechanics in the Third Reich, where it was rejected as many Jews were among its founders. On the other hand, Jordan's plan for a quantum biology institute would encompass race research.[50] The quantum biology institute was organised at the end of 1930 and was to be built after the supposed victory of Germany. Still expressing his disparate idiosyncrasies, he ardently supported the prevalently left-wing Vienna Circle. His biological speculations were even

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[46] Pascual Jordan, Anschauliche Quantentheorie: Eine Einführung in die moderne Auffassung der Quantenerscheinungen (Berlin: Julius Springer, 1936)

[47] Howard, "Quantum Mechanics in Context" (ref.10) p. 265

[48] See e.g., Richard E. Beyler, From Positivism to Organism: Pascual Jordan's Interpretations of Modern Physics in Cultural Context. PhD thesis. (Havard University, 1994); Norton M. Wise, "Pascual Jordan: Quantum Mechanics, Psychology, National Socialism", in Monika Renneberg and Mark Walker, eds., Science, Technology, and National Socialism, (Cambridge: Cambridge University Press, 1994), pp. 224-254; Dieter Hoffmann, Pascual Jordan im Dritten Reich: Schlaglichter (Berlin: Max-Planck-Institut für Wissenschaftsgeschichte, Preprint 248, 2003)

[49] Heilbron. "The Earliest Missionaries" (ref. 6)

[50] Richard E. Beyler, "Targeting the Organism: The Scientific and Cultural Context of Pascual Jordan's Quantum Biology, 1932-1947," Isis 87 (1996), 248-273

published in *Erkenntnis*, the Circle's official journal.[51] And, if we consider the scientific domain in itself, he was also involved in considerable dissimilar trends, such as organicism—which was antimechanistic and antiphysicalistic — and target theory — which was a methodology for analyzing the effects of radiation based on the hypothesis that submicroscopic targets were reached by radiation.[52] Overall, his contradictions reflect the character trait of someone not especially committed to intellectual coherence. Due to his peculiar way of combining politics, morality and sciences, Jordan's suggestions concerning biology were neither supported nor criticised by many groups, including the Nazis,[53] the positivists,[54] and the scientific community (e.g. Bohr himself or Delbrück)[55]. Considering also his usual involvement with controversies over the epistemological status of quantum mechanics (e.g. Einstein, Schrödinger, and Planck presented opposite views on such status), one can state that Jordan's contributions both to physics and to biology have been plagued with exciting controversies. The criticisms and disputes must not overshadow his granted values. Jordan was one of the founders of quantum mechanics, as he was author and co-author of several papers that constituted the foundation of the new physics and actively participated in the debates. Even though he did not obtain a Nobel Prize, his work is considered as fundamental to the development of quantum theory, as

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[51] Pascual Jordan, "Quantenmechanische Bemerkungen zur Biologie und Psychologie", Erkenntnis 4 (1934), 215-252

[52] Beyler, "Targeting the Organism" (ref. 26)

[53] Dieter Hoffmann and Mark Walker, eds., The German Physical Society in the Third Reich. Physicists between Autonomy and Accommodation, (Berlin:Max-Planck-Institut für Wissenschaftsgeschichte, 2012)

[54] Moritz Schlick, "Ergänzende Bemerkungen über P. Jordan Versuch einer Quantentheoretischen Deutung der Lebenserscheinungen," Erkenntnis 5 (1935), 181-183; Beyler, "From positivism" (ref. 24)

[55] Heilbron, "The Earliest Missionaries" (ref. 6), Beyler, "Targeting the Organism" (ref. 26)

much as many of those whose contributions were recognised with the prize.[56]

Jordan firstly published his biological investigations in 1932,[57] the same year Bohr delivered his "Light and Life" lecture. Previous discussions motivated them to sharp their own speculations. Although Jordan had been strongly influenced by Bohr and they were both convinced that the new physics demanded a novel approach to biology, they strongly differed in their particular views. In fact, Bohr tried to avoid being identified with Jordan's biological claims[58]. As we have seen, Bohr's suggestions were mainly epistemological. In turn, Jordan looked at biology with a more audacious perspective, willing to combine the quantum revolution and biological phenomena.

For that task, Jordan proposed more than complementary relations in biology. He hoped to unify quantum physics and biology by investigating possible connections between the microscopic and macroscopic scales. Jordan proposed the hypothesis of an "amplifier theory" (*Verstärkertheorie*) to account for the way in which living systems may be able to amplify signals, so that quantum events in the cell would trigger macroscopic events.[59] According to his theory, living cells presented two zones: a zone of causal determinism and a zone containing centres of life. The centres of life had directing and stabilising functions, as well as were able to control the former zone and express

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[56] Howard, "Quantum Mechanics in Context" (ref.10)

[57] Pascual Jordan, "Die Quantenmechanik und die Grundprobleme der Biologie und Psychologie," Naturwissenschaften 20 (1932), 815-821; see also Jordan, "Quantenmechanische Bemerkunge" (ref. 27)

[58] Heilbron. "The Earliest Missionaries" (ref. 6)

[59] Pascual Jordan, "Die Verstärkertheorie der Organismen in ihrem gegenwärtigen Stand," Naturwissenschaften 26 (1938), 537-545

themselves through amplifier structures.[60] Therefore, he suggested a speculative model to approach how events from the atomic level could be amplified to the macroscopic level. Jordan's look at biology was filled with the hope of linking quantum and macro dimensions, and thus the hope of leading biology to follow the big changes in physics.

When it comes to understand Jordan's thinking and its repercussions, it is important to appreciate the political context. It is his political opinion that tied his idiosyncrasies together,[61] including, unsurprisingly, his vision of biology. For instance, as Wise and Beyler[62] interestingly noted, Jordan's view of cellular leadership was analogous to the political *Führer*, in which the extension of the power of the Germans reflected the extension of quantum mechanics to other fields of knowledge. Besides, his organismic view in biology is considered as an attempt to reject scientific materialism, which reflects a rejection of left-liberalism materialism.[63] For Jordan, science, either physics or biology, properly understood — namely in accordance with Bohr's principle of complementarity — undermined Marxist materialism and would go along with Nazi ideas.

Accordingly, as much as Bohr's biology passed through his epistemological proclivity, Jordan's biology passed through his political proclivity. Delbrück, in turn, can be conceived in terms of a migratory proclivity.

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[60] Richard E. Beyler, "Exporting the quantum revolution: Pascual Jordan's biophysical initiatives", in Dieter Hoffmann, Jürgen Ehlers and Jürgen Renn, eds., Pascual Jordan 1902–1980 (Berlin: Max-Planck-Institut für Wissenschaftsgeschichte, Preprint 329, 2007), pp. 69-81

[61] See Howard, "Quantum Mechanics in Context" (ref.a); Beyler, "Targeting the Organism" (ref. 26); Hoffmann, Pascual Jordan (ref. 24)

[62] Beyler, "Targeting the Organism" (ref. 26); Wise, "Pascual Jordan" (ref. 24)

[63] Beyler, "Targeting the Organism" (ref. 26)

In 1937, Max Delbrück migrated geographically and scientifically: from Germany to the United States and from physics to biology. By scientific migration, we mean a deeper degree of involvement with biological research, since he built a whole career in molecular biology and genetics. In that year, Delbrück benefited from a Rockefeller fellowship to leave Nazi Germany for Caltech, in California, where he decided to definitively pursue his interest in biology, which had been strongly signalised before (as shown, for instance, by Timofeev-Ressovsky, Zimmer & Delbrück[64]). There, he started working in *Drosophila* genetics but became especially prominent by his bacteriophage research and, thus, his participation in the so-called phage group, raising to leadership in molecular biology. His contributions were eventually awarded a Nobel Prize in physiology in 1969, and he became a Board of Trustees Professor of Biology emeritus at the California Institute of Technology in 1977.

Previously in physics, Delbrück studied astrophysics, shifting towards theoretical physics to complete his studies in Göttingen in the late twenties, just after the breakthrough of quantum mechanics. Such shift was natural as Göttingen was a spawning ground for quantum mechanics. Afterwards, he worked abroad, in England and also in Switzerland and Denmark, where he collaborated with Bohr and Wolfgang Pauli. His

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[64] Nikolay Timofeev-Ressovsky, Karl G. Zimmer and Max Delbrück, "Über die Natur der Genmutation und der Genstruktur," Nachrichten von der Gesellschaft der Wissenschaften zu Göttingen: Mathematische-Physikalische Klasse, Fachgruppe VI, Biologie 13 (1935) 189-245, see also Philip R. Sloan and Brandon Fogel, Creating a Physical Biology: The Three-Man Paper and Early Molecular Biology (Chicago and London: The University of Chicago Press, 2011)

achievements in physics are regarded with great respect. In 1932, in Berlin, as an assistant to Lise Meitner, he met regularly a group of physicists and biologists who shared an interest in molecular biology.

Overall, Delbrück was a person interested in working abroad and cross-cultural learning, to the extent that he migrated considerably between countries and scientific fields. It is important to make it clear that, by raising the term migratory proclivity, we do not mean any kind of determinism or psychological essentialism. We do not imply that one type of migration lead to another. Needless to mention, the social-political conditions in Nazi Germany doubtlessly led Delbrück and many German scientists (particularly jews) to migrate. Intending no psychological inference, we wish to suggest that adapting and immersing into a new culture, being it scientific or local, was something that Delbrück was familiar with along his trajectory.

Delbrück was neither one more physicist that attempted to contribute to biology from his/her ivory tower, nor one more German scientist who stayed in Germany although unhappy with political abuses. Delbrück actually migrated. With regard to the political migration, Delbrück defended the decision of other scientists, particularly Heisenberg, to remain in Germany. He even admired the position of those who stayed and showed gumption as much as it was possible. Concerning the scientific migration, he rejected the attitude of those who thought they could simply apply a specific technique rooted in physics without being involved in the raising of questions, which is a common way to physicists to look at biology even nowadays[65]. He thought that asking someone

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[65] For a present-day study of physicists that, like Delbrück actually changed fields, see the next chapters of the present dissertation

else to name a problem in biology is "an unprofitable thing to do" and that, once one is interested in the field, one should become a biologist and find the problems.[66]

As we have pointed out, Delbrück's interest in biology was first inspired by Bohr. They had a mentor-disciple relationship and Bohr knew he was in the position of intriguing Delbrück. To ensure his presence, Bohr asked his collaborator Léon Rosenfeld to pick up Delbrück at the train station in Copenhagen, in August 1932, so as to take him directly to the "Light and Life" lecture.[67] Bohr successfully made an impression and Delbrück himself declared on numerous occasions that the lecture was a starting point for his interest in biology.[68]

Bohr's complementarity principle was a very intriguing physical idea for Delbrück, which he thought could be effectively taken as an inspiration for analogies to be used in biology.[69] The following quote illustrates how Delbrück interpreted Bohr's suggestion:

> […] here you have the hydrogen atom, and you have a proton and an electron running around, and you can do classical physics until your dying day and you'll never get a hydrogen atom out of it. In order to get the hydrogen atom out of it you

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[66] Max Delbrück, Interview (ref. 17)

[67] Gino Segrè, Ordinary geniuses : Max Delbrück, George Gamow, and the origins of genomics and big bang cosmology (New York: Viking-Penguin, 2011)

[68] See Max Delbrück, "A Physicist Looks at Biology," Transactions of the Connecticut Academy of Arts and Sciences 38 (1949), 173-190; Max Delbrück, "Light and Life III," Carlsberg Research Communications, 41 (1976), 299-309; Lily E. Kay, "The secret of life: Niels Bohr's influence on the biology program of Delbrück," Rivista di Storia della Scienza 2 (1985), 207-246; Andrew T. Domondon, "Bringing physics to bear on the phenomenon of life: the divergent positions of Bohr, Delbrück, and Schrödinger," Studies in History and Philosophy of Biological and Biomedical Sciences, 37 (2006), 433–458

[69] Nils Roll-Hansen, "The application of complementarity to biology: From Niels Bohr to Max Delbrück," Historical Studies in the Physical and Biological Sciences 30 (2000), 417–442

> have to use this complementary approach. His analogy was that maybe, if you look at even the simplest kind of cell, you know it consists of the usual elements of organic chemistry, and obeys otherwise the laws of physics; you can analyse any number of compounds in it but you'll never get a living bacterium out of it, unless you introduce a totally new and complementary point of view. That, together with the very recent success that happened in quantum mechanics, the uncertainty principle, showing in a hopeless situation a great simplicity, was an intriguing idea[70]

Accordingly, Delbrück took complementarity as an idea discovered in quantum mechanics that could have an analogous counterpart in living systems. However, in the course of his deep involvement with biology, he pursued independent questions with full force. He distinctively approached avid experimental work and teamed up with very proficient collaborators, notably Salvador Luria and Alfred Hershey.[71] Far beyond the search for complementary relations in biology, Delbrück's road to success was his bacteriophage research. The philosophical machinery borrowed from quantum mechanics, notwithstanding, played little role in Delbrück's experimental biology. Because of his migration and deeper contact with biological phenomena, Delbrück believed he had reached a special status among the physicists-turned-to-biologists, as he wrote to Bohr: "It was you who inspired me 30 years ago to go into biology and I believe I am the only one

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[70] Max Delbrück, Interview (ref. 17), p. 94

[71] For further details on Delbrück's scientific views, trajectory and contribution, see Sloan and Fogel, "Creating a Physical Biology" (ref. 40) and Lily E. Kay, "Conceptual and analytical tools: The biology of physicist Max Delbrück. Journal of History of Biology," Journal of History of Biology 18 (1985), 207-246

of your disciples who has made his way in this direction".[72]

5. QUANTUM REVOLUTION AND THE ADVENT OF MOLECULAR BIOLOGY IN THE 1930S

The quantum explorers Bohr, Jordan and Delbrück expected the quantum revolution to have a striking impact on biology. They had different views and attitudes towards how it would happen, as there was a progression of levels of involvement with the new field, being Delbrück the most committed one. Despite the distinct styles, they all advocated their philosophical credo, namely, the Copenhagen interpretation of quantum mechanics. They originally believed that its essential part, the complementarity principle, would be the way through which a revolution would happen to molecular biology.

The philosophical implications of quantum mechanics certainly played an important role at the emergence of molecular biology.[73] However, it happened mainly by means of far-sighted suggestions and inspirational power, rather than as a theoretical or conceptual revolution. Outstanding contributions from the field of physics were experimental technologies and analytical procedures, such as centrifuging, electrophoresis, X-ray diffraction, and optical methods such as spectroscopy. These physics-based approaches have often been used by physicists with applicable technical training. For instance, a branch of physics that turned out to be indispensable to the development of

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[72] Delbrück's letter to Bohr from 1962, reproduced in Favrholdt, "Niels Bohr Collected" (ref. 20) p. 488

[73] Marco Bischof, "Introduction to integrative biophysics", in Fritz-Albert Popp and Lev Beloussov, eds., Integrative biophysics: biophotonics (New York: Springer, 2003)

molecular biology and genetics was crystallography. None of these techniques were directly derived from quantum mechanics. In the 20th century, several crystallographers became interested in investigating the internal structure of biological molecules. Notably, the X-ray images provided by Rosalind Franklin were crucial for Watson and Crick's proposal of the DNA double helix model. Therefore, one can say that revolutionary contributions to the life sciences were not only stimulated by the philosophical machinery of quantum mechanics, but striking contributions came into biology from other fields of physics. Crystallography turned out to set a watershed in the history of molecular biology.

In a twist of irony, most of those physics-based experimental technologies and analytical procedures, such as diffraction and crystallography, demanded a wave formalism to be approached, that is considering radiation such as X rays was waves, which is closer to the classical physics formalism than to the quantum one. For a diffraction experiment, only the wave nature of X-ray really matters. The long debates surrounding complementarity relations, as well as the classical incompatibility between waves and particles are irrelevant to run a diffraction experiment. For crystallographers, the relevant aspect was simply: X-ray is a wave that provides images of the biological object under investigation.

We are far from suggesting a battlefield between quantum and classical physics, or between realistic and epistemological approaches to the core of biology, and we do not wish to evaluate whether one way to look is more impactful than another. Our point is that the set of contributions of physics to biology can only be understood from a pluralistic stance,[74] in the sense that multiple approaches are required for the explanation and investigation of the living phenomena. Such phenomena cannot be fully investigated using a single approach and our historical episode illustrates precisely this aspect. Besides, we also wish to suggest that the conceptual trading—namely, the exchange of scientific concepts in zones of interdisciplinary negotiation—such as the extension of complementarity to other fields, is a very complex and delicate type of trade across disciplinary boundaries[75]. The borrowing of language is a serious issue for anyone concerned with the practice of science, no matter if from a scientific or philosophical point of view. A problematic underestimation of cultural miscommunication between physicists and biologists, however, will be exploited elsewhere.[76]

6. CONCLUDING REMARKS

At first, a clarification here is in order: By conceiving Bohr, Jordan and Delbück in terms of specific proclivities, we do not undermine, deny or downplay the important intersections between epistemological commitments, political views, and

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[74] See Stephen H. Kellert, Helen E. Longino, and C. Kenneth Waters, Introduction: The Pluralist Stance, in Stephen H. Kellert, Helen E. Longino, and C. Kenneth Waters, eds., Minnesota Studies in the Philosophy of Science. Scientific pluralism; volume XIX (Minneapolis: The University of Minnesota Press, 2006) vii-xxix

[75] The term is used in the sense of Galison's metaphor of trading zone. See Peter Galison, Image and Logic: A Material Culture of Microphysics (Chicago: Chicago University Press, 1997)

[76] In the chapter III of this dissertation, we address, through an empirical study, cultural differences in an interdisciplinary environment composed by physicists and biologists

cosmopolitanism. Rather, it means to stress that these intersections can coalesce differently in different actors and give rise to unequal tendencies toward one of the other axes of the three-pronged configuration of proclivities we have suggested here. The richness of such historical episode, namely the influence of quantum physics in the emergence of molecular biology, and the extensive literature about it, compelled us to propose patterns, in order to organize our narrative. Those proclivities are non-reductionist organisational instances, rather than a stiff interpretative frame.

Accordingly, Bohr pursued his philosophical interests in biology and sowed his inspirational seed. Jordan followed it up through his political vein. Delbrück went along and migrated. The common reason for their movement towards biology was the powerful inspiration raised by the quantum revolution and, in the case of the last two, raised by Bohr. The quantum revolution fuelled a feeling of trust, namely the faith or conviction that great scientific issues were reachable and solvable. These physicists shared more than the Copenhagen spirit, they shared also the explorer spirit.

The extents to which they were involved with biology were dissimilar. Bohr displayed his interest mainly through freewheeling discussions. Jordan carried on a more committed approach, although he never stopped publishing in physics and, towards the end of his life, turned his attention to cosmology. Delbrück was an explorer who moved to a new field, uncovering its riddles and mastering its language and culture. Consequently, their contributions to biology were also unlike. Regarding profitability, the spotlight shines upon Delbrück. His success in biology had to do with the abandonment of the original idea, that is, the influential but preliminary expectation to export complementary relations, together with a full migration to the new field and the grasping of its particular problems.

In fact, the famous complementary relation in biology turned out to be the base pairing between a synthesised DNA and a messenger RNA (RNAm), and between a RNAm and a transfer RNA (RNAt), in the transcription process, as part of the gene expression machinery. Base-paring complementarity shares, however, only verbal similarity with quantum complementarity.

The decision making process behind the movement from physics to biology seemed to present the psychological propensity of confirmation bias, understood as a tendency to favor, search for, interpret and focus on information in a way that confirms one's entrenched belief,[77] as the Copenhagen interpretation was for them. However, we firmly prefer to avoid psychological hypotheses and present these historical episodes from the exploration point of view. Perhaps the precise word would be 'coloniser', in the sense of an explorer that is certainly also a carrier of values, beliefs and procedures. In any case, Bohr, Jordan and Delbrück were quantum explorers, in the sense of someone who "need the tonic of wildness", who is "earnest to explore and learn all things", who requires "things to be mysterious and unexplorable" and, above all, who "can never have enough of nature"[78], either animate or inanimate.

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[77] See e.g., Margit e. Oswald and Stefan Grosjean, "Confirmation Bias", in Pohl, Rüdiger F. Pohl, ed., Cognitive Illusions: A Handbook on Fallacies and Biases in Thinking, Judgement and Memory (Hove: Psychology Press (2004) pp.79–96

[78] Henry Thoreau, "Walden, or Life in the Woods"

CHAPTER II

FROM PHYSICS TO BIOLOGY:

PHYSICISTS IN THE SEARCH FOR SYSTEMIC BIOLOGICAL EXPLANATIONS

ABSTRACT: This study is based on interviews conducted at several institutions in Brazil, Germany, Israel and the U.S. and engages with problems related to the circumstances under which physicists migrate to biology and approach biological problems. Biological research, particularly in the fields of systems biology and synthetic biology, has been increasingly dependent on computational methods, high-throughput technologies, and, consequently, on multidisciplinary skills. Collaborations between physicists and biologists are vigorous everywhere and interdisciplinary research in biology have increasingly been a subject of sociological research. The role of physicists in systems biology is precisely the concern of our study and we use oral history as a methodological tool to gather the empirical material presented here. We identify as topics with historical and epistemological significance the following ones, which guided our framing of the empirical results discussed here: why to move from physics to biology? To what extent? And, to which effects? We conclude that there are common reasons for this move, that the transition must be evaluated in terms of degrees and that contributions rooted in physics set major goals to systems biology. At the end, we state a general claim for a relation between physicists and biologists based on critical confidence instead of indoctrination.

KEY WORDS: Physicists, systems biology, interdisciplinarity, oral history interviews

1. INTRODUCTION: PHYSICISTS GOING INTO SYSTEMS BIOLOGY

How may physics help to understand the phenomena of life? This question has raised substantial scientific, historical, and philosophical attention throughout the history of science, particularly in the 20th and 21st centuries. Physicists have been often attracted to the mysteries of living matter and migrated to biology for several reasons, such as the application of methods and practices rooted in physics to tackle biological problems (see, e.g., Fleming 1968, Olby 1974, Kay 2000), the expectation that living matter could be reduced to physics (see, e.g., Fuerst 1982), or, especially after the military use of atomic energy, the appeal of a science attached to life over a science attached to death (see, e.g., de Chadarevian 2002). Among the many physicists who have attempted to understand the phenomena of life from the perspective of physics, we can name important figures such as Niels Bohr, Pascual Jordan, Max Delbrück, Erwin Schrödinger, Leó Szilárd, Nicolas Rashevsky, Walter Elsasser, George Gamow, Seymour Benzer, and Francis Crick.

In the post-genomic era, the great scientific challenge of converting an unprecedented amount of data into knowledge depends on interdisciplinary skills. Particularly the fields of systems biology and synthetic biology draw on theoretical and methodological approaches that strongly involve interdisciplinary research. Physical scientists, among other experts, are being heavily required in biology for support, particularly quantitative support. Collaborations between physicists and biologists are vigorous as never before. The migration of physicists and their role in biological research, particularly in the search for systemic biological explanations are precisely the concern of our study. Among those fields, we approach in our empirical study the field of systems biology, as it is currently more established than synthetic biology, with a longer history of physicists' migration.

Before getting into the details of our empirical study, let us provide a brief historical context. Throughout the final part of the 20th century, our understanding of biological systems has changed substantially, videlicet: less than 50 years after the proposal of the double helix model for DNA structure, we witnessed the publication of complete genomic sequences; first for a nonhuman living organism (1995) and then for a human being (2001). The development of molecular analysis techniques and tools have originated a huge amount of data at the molecular level of living systems. It has increasingly become clear that a restricted focus on sequencing is not enough to provide a full understanding of the system and, therefore, systemic approaches came to the fore (see, e.g., Ideker et al., Galitski & Hood, 2001; Kitano 2002a, Hood 2003). Sidney Brenner (2010 p. 207) summed up the situation metaphorically: "Sequencing the human genome was once likened to sending a man to the moon. The comparison turns out to be literally correct because sending a man to the moon is easy; its [sic] getting him back that is difficult and expensive". The research on protein folding developed by the physicist Eytan Domany — who was an interviewee in our empirical study — and his group exemplify the shift in focus from sequences to dynamics. Their theoretical approaches aim at predicting the structure of a protein from its sequence by using methods from statistical physics and computational tools. Sequencing turned out to be a step to tackle the crucial problem: the ways a protein chain folds into complex shapes, according to physiological conditions and evolutionary factors, in order to perform a specific function. (Cf. Vendruscolo, Najmanovich & Domany, 1999)

Overall, the scientific challenge for those concerned with living systems has become to deal with more dynamical and systemic problems, and, also, with big data. For that task, biological research has increasingly relied on computational methods and high-throughput technologies and, consequently, on the skills of those trained to deal with complexity in other disciplines (see e.g. Auffray, Imbeaud, Roux-Rouquié & Hood 2003, Ideker et al. 2001). In this context, new institutes, programs, departments, conferences, chairs and journals dedicated to systems biology have proliferated (Agrawal 1999, Powell, O'Malley, Müller-Wille, Calvert & Dupré 2007), clearly showing the institutionalisation of the new discipline (Lenoir 2004)

Now we would like to take a stock and clarify what we mean by systems biology. The term is a flexible one, since it involves different kinds of analytical approaches (Cf. Keller 2005a, 2007a). Previous attempts to apply systems theory to biology in the past, notably from von Bertalanffy in the 1930s and Weiss in the 1950s, have established a new systemic approach that strongly influenced many scientific subjects since then. However, these approaches have not generated an institutionalised scientific field at that time. We relate our definition of systems biology to the present day scientific field. For the sake of clarity, we define systems biology as the study of how molecules and cellular components interact and come together to give rise to sub-cellular machineries that are capable of operations required for physiological functions, dynamics and processes. Additionally, it encompasses both top-down and bottom-up approaches, i.e., starting both from a description of whole systems and going down to the components, and from cellular components to the higher-level system (on these approaches, see, e.g., Bruggeman & Westerhoff 2007).

Systems biology investigates biological systems by combining experimental practices with theoretical work, aiming at predictions and model building using a mathematical language. Quantitative techniques are applied to analyse large database sets collected from wet-lab experiments (e.g., clustering, data visualisation techniques, network construction, and gene-set enrichment analyses) and subsequent to model phenomena, systems, and processes of interest. To perform such combination of demands, the field of systems biology gather biologists, physicists, mathematicians, computational scientists, and engineers with the goal of extracting knowledge from biological data (Calvert 2010). Due to its distinctive interdisciplinary character, systems biology has become the subject of sociological investigation (Cf. e.g., Calvert & Fujimura 2011, Rowbotton 2011). Among the scientists working on systems biology, our focus here lies exclusively upon the physicists.

Physicists are, one more time in history, playing a central role in biological research and physics is claimed to be an important candidate to offer a theoretical framework to systems biology (Keller 2005a). They are joining biological departments with the conviction that their mindset may provoke an impact in mainstream biology.[79] This state of affairs raises a number of questions, such as the following: What are the circumstances under which physicists approach biological problems in systems biology? From the

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[79] For instance, Keller (2005a) argues that physicists can be helpful in forging an appropriate theoretical framework to systems biology; Knight (2002) emphasizes the positive aspects of the interaction between physicists and biologists and claims that the background of physicists in dealing with complexity can boost the study of biological systems, Ouellette (2003) selects and presents some suggestions from physicists that have moved to biology, Wolgemuth (2011) discusses to which extent the perspectives of physicists are helpful to analyze cellular mechanisms and argues that the way in which physicists simplify models is crucial to understand living systems.

perspective of the physicists, what kind of interdisciplinary challenges must be tackled? There seems to be a scarcity of written sources about this issue, at least in terms of peer-reviewed papers, something not uncommon in historical research on contemporary science. The topic is more often discussed through sources like opinions, editorials, features, and synopses.

In order to engage with this problem, we use oral history as one of the methodological tools to gather the empirical material presented here: we conducted interviews with physicists working in systems biology. We also based our results on laboratory observation, informal conversation with research group members, occasional group meetings, lectures, and so on. We will explain the approach in further details in the next section. Subsequently, we will organize and discuss our empirical results into the following frames: Why to move from physics to biology? To what extent? And to which effects? We conclude that there are communal motivations for this move, that the transition must be evaluated in terms of degrees, and that intellectual contributions rooted in physics set major goals to contemporary systems biology. We finally state a general claim for a relation between physicists and biologists based on critical confidence instead of indoctrination.

We conducted recorded semi-structured interviews with thirteen physicists working in systems biology problems in four different countries. A number of pertinent informal conversations with other members of the groups, students and secretaries were also performed and, sometimes, recorded.

In Germany, we conducted five interviews with three research group leaders, i.e. Nikolaus Rajewsky, Hanspeter Herzel and Peter Arndt, and two postdoctoral researchers, i.e. Roman Brinzanik and Navodit Misra, at Max Delbrück Center for Molecular Medicine, Humboldt University and Max Planck Institute for Molecular Genetics. In Israel we interviewed physicists who head systems biology research groups: Uri Alon, Joel Stavans and Eytan Domani. Then, we interviewed Suani Pinho, a research group leader in Brazil[80]. In the United States, we interviewed the following leading physicists: Erel Levine, Harvard University; Eric Siggia, Rockefeller Foundation, Ned Wingreen and Thomas Gregor, Princeton University. Another relevant source of oral information was a conversation with Evelyn Fox Keller, in which we also explored her transition to biology as a physicist in the 1960s.[81]

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[80] Systems biology is one of the funding priorities in the United States, Germany, and Israel. In turn, Brazil does not have a systems biology network developed to the same extent. In this country systems biology is currently still trying to establish itself as a new field. The interviewed Brazilian physicist, Prof. Dr. Pinho, identified herself as a systems biologist based on her research interests.

[81] This conversation is considered apart from the interviews because the subject matters addressed went far beyond the semi-structured interviews, conferring to it a particular status.

Each interaction happened in person, since one of the authors has met the interviewees in their respective countries. We argue that the oral history approach can be largely enriched by a personal contact between the interviewed and interviewee, and impaired by exclusively virtual interaction. The main consequent advantage of the physical presence of the interviewer in the research environments is that our results also benefitted from observations of the working places involving scientists, including lab everyday routine, offices, group meetings, supervision sessions, lectures, and informal meetings in coffee rooms. The interviewer attended group activities as often as possible, according to the convenience of the interviewees. An online interaction would reduce the complex interactional perception to a mere collecting of reports through a computer.

Both time limits and places where the interviews were conducted were set by the physicists. The average time granted for an interview was around one hour. The longest one took around 85 minutes and the shortest, 42 minutes.

The physicists themselves were of great help in pointing out the main characters within the scientific community working on systems biology. We selected the scientists to be interviewed considering geographical and financial restrictions. We argue that the geographic dimension and the qualitative approach — which was chosen in order to provide a maximum focus on the details — justify the relatively small sample. Further studies both in other countries and through quantitative approaches are, however, worth pursuing.

The interviews were constructed for each physicist, considering the particularity of their interests, careers, working places, etc. Thus, each interview was preceded by an extensive preparation by reading their papers and researching about the interviewees.

They were encouraged to speak about, for instance, their careers, motivations to do research in biology, their background in physics, their research work and group, the culture of systems biology, and issues of interdisciplinary interactions. While the interviewer attempted to provide guidelines for the discussion based on the protocol, she also kept the interaction flexible enough for the physicists to talk freely.

Regarding the analysis of the raw data obtained through the interviews, the aim was to isolate recurrent topics with historical and epistemological significance. The results must be seen as trends concerning the contemporary movement from physics to biology. In the following sections, a discussion of the main general findings is presented.

All the physicists gave informed consent for the interviews and for the use of the information derived from them. In order to respect the interviwees's privacy, we do not refer to them by their names when mentioning their reports.

3. WHY TO MOVE?
MOTIVATIONS BEHIND THE MOVEMENT FROM PHYSICS TO BIOLOGY

The interviewees are motivated by a perception that there is something fresh to be pursued in the field of biology. They pointed out several personal reasons for being attracted to biological research, such as a particular book, a particular person, or the awareness that they could apply their knowledge and methods to innovatively solve problems in the new field. Nonetheless, one reason has been often enthusiastically highlighted: the perception that biology has a “smell of breakthrough in the air”, as the interviewee Eytan Domany elegantly put it. This comes together with a sense that the field of physics has reached a satisfactory maturity for the time being.

In physics, they claim, there is higher likelihood of getting involved with well-known problems, in the sense that they have been established and thoroughly analysed by the great pioneers of the past. Physicist 12 reported that previously, in the field of condensed matter physics, much of his work was to find what scientists like Philip Warren Anderson and Lars Onsager have not done: “You have to look at the little corner which has been relevant back then when they have done the theory”. Nevertheless, the fascination for the field of physics remained strong among the interviewees and was often combined with some initial aversion to biology, as we can see, for example, in the following comment: “Why would any physicists want to waste his or her time with something that is so soft and unreproducible?” (Physicist 12). In turn, biological research, and in particular systems biology and the even younger field of synthetic biology, offers room for an abundance of questions that are still wild in a unique way.[82] To the extent that these questions are related to the theory and modelling of complex systems, physicists are in the position to find them welcome.

We want to illustrate this process of tackling new and stimulating questions by commenting upon the prominent research topic of RNA-based regulation, which is investigated by many of our interviewed physicists (Erel Levine, Eric Siggia, Eytan Domany, Hanspeter Herzel, Joel Stavans, Thomas Gregor, and Uri Alon). Noncoding RNA has been put aside and neglected in the sequencing-oriented phase of molecular biology for having apparently no biological function. In the 1960s and 1970s, the DNA sequences responsible for the coding of these molecules were even dubbed “junk DNA”. By contrast, biological research over the past years revealed that noncoding RNA molecules are involved in significant regulatory control mechanisms of gene expression. As findings regarding gene regulation have transformed our views about noncoding RNA, new exciting research questions of great relevance started to pour in and attracted many researchers, including physicists.

The approaches towards these questions are inevitably rooted in the disciplines the scientists come from; when studying regulatory machineries in different organisms, such as bacteria, worms, drosophila and alike, biologists are often concerned with the evolutionary link between the species, since their mindset is commonly embedded into evolutionary thinking. Physicists, in turn, tend to look for unifying principles that dictate regulation, since their thinking style relies on the assumption that organisms share the

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[82] Physicist 12 reported that half or more of the prospective graduate students that looked for his supervision have been motivated by synthetic biology and its novel, fresh questions

same physics. Keller (2005a) conjectured that physicists and biologists ask different kinds of questions and look for different kinds of answers. In our empirical study, her assumption is supported. As it was reported, biologists and physicists are "(…) almost like people from very different countries, like two continents. Conceptions about what is a good answer in science are different, about words like 'model' and a lot of technical knowledge" (Physicist 6, see section 5 for further comments on the physicists' perspectives).

The general point we want to make is that the contribution of physicists to biology goes far beyond technical application of knowledge, methods, and problem-solving approaches. It reaches the process of question-making in a field perceived as being less established and more in flux than physics. This state of affairs is extremely attractive for the physicists. Physics is undoubtedly a field of big questions, but sometimes, as in any field, physicists may feel unmotivated. Physicist 11 reported "I got a little bored with physics and drifted to biophysics and biology". In the new field, physicists seem seduced again by the possibility of being the first ones to know a novel bit of the furniture of nature.

It is evident that the awareness of possible upcoming breakthroughs and the consequent motivational feeling are embedded in perceptions concerning the history of physics and the history of biology. In particular, as mentioned above, there is the distinctive impression that the field of physics has reached a state of maturity, whereas the field of biology seems to be the place where the action is (Wise 2004, 2007). A popular historical account among the interviewees was that, although biology has been enormously successful in the past by asking questions that do not necessarily require mathematics, at some point it turned out that without quantitative approaches the distance between what molecular biologists were doing "and the understanding of the phenomena that they were really interested in was growing" (Physicist 6). Therefore, the physicists place themselves in this moment in history and claim that the field of systems biology experiences a great creative phase that partly explains the transition. However, it is worth emphasising that many other factors are involved in their moving from one field to the other, particularly more pragmatic ones, such as the proportion of funding and positions, which seems to be currently larger in biology than in physics.

That a perception of distinctive creative phases turns into a reason for changing fields is not unprecedented in history. For instance, Max Delbrück related his transition to biology to the perception that quantum mechanics has become "the final word" on the "behaviour of atoms", while biology was a field that "was not yet at the point", where they were "presented with clear paradoxes" (Delbrück 1949). Even though Delbrück was referring to his earlier transition, there seems to be a strong similarity between his perception and those reported in our interviews. Many interviewees consider themselves as lucky to be "in the right place at the right time" (Physicist 6). Some physicists explicitly expressed a comparative view that "biology is today what physics was in the first half of twentieth century with the advent of all the big revolutions" (Physicist 7), as "the things are moving in an extremely fast pace" (Physicist 8). To sum up, the feeling that in comparative terms biological research is considered to be in earlier stages than physical research (Cf. Keller 2002) is an important and recurrent factor underlying physicists' move from one field to the other.

4. TO WHAT EXTENT?
DIFFERENT DEGREES OF COMMITMENT TO BIOLOGY

To move, or not to move: that is not the only question a physicist faces. We claim that the transition to biology must be understood in terms of degrees. Therefore, the crucial question for physicists is: to what extent do I get involved with the new field?

One can find many historical examples of great physicists who worked on biological topics in different degrees. On the one hand, Werner Heisenberg briefly speculated on the relation between quantum theory and biological phenomena, and George Gamow worked on the specific problem of protein synthesis, after becoming enthusiastic about the double helix model. On the other hand, we can mention Seymour Benzer and Francis Crick as physicists who have built a whole career in genetics and molecular biology.

Nowadays, along with the rise of more quantitative approaches to biology and, consequently, the increasing ways through which a physicist can apply technical and intellectual knowledge to the new field, the range of degrees of involvement has expanded. Physicists can, for example, apply their mathematical skills, or she/he may go to the wet laboratory and engage herself/himself with experiments involving organisms. There are many degrees of proximity between the physicists and the biological realm, and, accordingly, different ways and degrees of moving, as a interviewee expressed according to his own experience:

> “I will define a move myself: you can stay in physics, you use your tools, your models to analyse some data and some biological problems. This I wouldn’t call a move. It’s more an application of a certain concept to other types of data. (…) Until ‘96 I was a physicist applying techniques to biological problems. In ‘96, I got the chair here in theoretical biology and this was a real move (…) not only in terms of institute (…) but also in spirit. Until ‘96 I had a lot of methods and some applications. After 2000, I had a lot of biological problems that I asked myself critically ‘can I contribute to these topics?’ (…) then I learned biology over the years, started collaborations, get to know experimental data. Then I had a new topic. (…) It was not a move, it was a graduated transition (…) from thinking like a physicist to now. In the last 10 years, I feel a bit like a biologist“(Physicist 2).

Prima facie, the fact that there are many degrees of involvement may seem an obvious fact, but it has important implications, particularly for the laboratory structure and organisation, as well as for institutional policies. In the next paragraphs, we discuss these implications from the interviewees’ perspective as well as from our own field observations. The interviewees were encouraged to talk about their research environments and communities, and, due to the fact that the interviewer visited their institutions, she could visit a number of labs, offices, departments, and institutes. Hereby we describe some observations alongside with oral information provided by the physicists. For those acquainted with the work in a systems biology laboratory, the present account will look very familiar.

Each research group we visited is strongly interdisciplinary and gathers biologists, physicists, computer scientists, among others. The division of labor varies from lab to lab.

There are people doing pure experiment, people doing pure theory, and people doing both. The organisation of the workspace also varies remarkably in terms of the disciplinary setting and the source of the biological data. For example, in the Weizmann Institute of Science, in Israel, the interviewer has visited two independent research groups, both presenting wet and dry labs side by side. Nonetheless, one of them is located in the department of physics and the other in the department of biology. In Harvard, in the United States, the office and laboratory buildings are separated by a walking distance. At Humboldt University, in Germany, the visit was restricted to the office, since the biological data comes from collaborations outside the campus. At the Federal University of Bahia, in Brazil, the biologists usually go to the Institute of Physics for the official meetings and the biological material upon which mathematics is applied comes from another university in the same state, from sources located in another Brazilian state, and from international databases.

Three main research approaches were identified, which are not isolated but often combined: experiment-oriented, theory-oriented, and tool-oriented. The groups that perform wet experiments, such as the group of Rajewsky, at the Max Delbrück Center for Molecular Medicine, in Germany, deal with biological matter by applying techniques from molecular biology and biochemistry in order to generate data. The theory-oriented groups with no wet lab must either work in close liaisons with experimental labs or find database sets collected from wet lab. For instance, Brinzanik and Misra—from the Max Planck Institute for Molecular Genetics, in Germany—and Suani Pinho—from the Federal University of Bahia, in Brazil—do not go to the wet lab to perform high-throughput analysis of cancer material. All the groups had a theory-oriented section. Finally, some groups may also present a major concern with the development of the instruments and artifacts they apply, like Gregor's group in Princeton University, in the U.S., which builds custom microscopes for live imaging.

Based on the description above, we can conclude that, in addition to the question we posed previously — i.e., to what extent does a physicist involve herself/himself with the new field?—, there are still two crucial derived questions for the physicist-turned-into-biologists: Do I go to a wet lab and handle biological matter? Should I work at the biology building?

The first question is to be tackled by taking into account the research circumstances and the scientists' personal career interests. According to our observations, the research group leader has a crucial role in this decision. Physicist 6 defended that the need to stimulate interactions between scientists, so that the biologists more often invite the physicists to plan the experiment together and the physicists, in turn, invite the biologists to plan the analysis together. At his lab, the physicists are encouraged to understand the wet experiment in further details. Some other groups were less concerned with these interactions. For instances, there was no biologists in one of the groups visited, as physicist 11 does not defend the need for a close interaction between physicists and biologists. Physicist 11 explains in his interview that people he hires are exclusively physicists, mathematicians, and computer scientists, due to their stronger quantitative approaches, and the biological material comes from other labs.

Regarding the second question, we would like to present some reflections on what we perceived as a historical innovation in institutional terms. Today, cutting-edge research environments often present exclusively theoretical labs placed in biology departments, and labs of experimental biology located in physics departments. Therefore, very alike workplaces, in which similar scientific questions are asked and similar aims are pursued, may be placed in distinct buildings under the banners of physics or biology. Physicist 8 even reported: “I’m seating in physics but I could seat in biology, anyway.” Still, not necessarily a lab located in a department of physics is mainly theory-oriented. Joel Stavan’s lab is an elegant example: in interview, he emphasised the strong experimental point of view of his group, which is based in the Department of Physics of Complex Systems, at the Weizmann Institute of Science, in Israel, and includes a wet lab. Another possible format is a lab that belongs to the environments of both biology and physics, such as Levine’s lab, at Harvard University, which is part of both the Department of Physics and the Center for Systems Biology.

We argue that the diversity of institutional formats provides a new intertwined picture of the interfaces between physics and biology. Thus, the current scenario may harbour a unique episode in the long historical relation between the disciplines. Such a scenario has many implications to research policies, funding structures, and university teaching. Thus, it is worth pursuing further historical and sociological investigation on this institutional interface and its new configurations.

Physicists have a rationale for searching for general principles and for simplifying the systems under study: that is the gist of their thinking and the way they provide satisfactory explanations, and, consequently, the style of their look at biological systems, the questions they ask, and how they search for answers. In our study, this is particularly visible when it comes to comparing modelling styles. The following quote illustrate a popular claim among the interviewees:

> "I think there are some differences when you discuss a certain problem with a biologist and a physicist... let's say there is an idea of how to dissect the problem or how to solve the problem... and the biologists will all the time and in many cases they will tend to bring in 'yeah but this you haven't really considered in your model' (...) they have been used to easily add the missing layers of complexity in the model right away (...) the physicists tend to try to simplify the problems with the hope of some unifying principles and try also to get a clearer understanding of the scales involved..... 'maybe there is the complex level A and B but maybe the A is only important for complex data regarding certain scales which is different from complexity B.. maybe you shouldn't be so concerned about the complexity type B because you are only interested for now maybe in the world living on the scale A" (Physicist 1).

As the quote emphasizes, physicists ask different questions from biologists: they usually favor global accounts over detailed descriptions and search systemic explanations by looking to general principles. The expression of such style is evidently stronger or weaker according to the physical sub-cultures the physicists are trained in. On the whole, for a long time the physics community has been using conceptual tools that are very powerful in explaining many aspects of reality, such as the principle of conservation of energy or the principle of least action.

Still according to the quote, a crucial problem is: how to tell what exactly must be considered into a model? Overall, it was often reported that biologists tend to consider more factors, given their presumed descriptive tradition, the fact that they are mainly concerned with the biological reality behind a phenomena, and their supposed focus on its complexity, and physicists tend to consider less factors, since they see themselves as simplicity-oriented and mainly concerned with the equations behind a phenomena. The obvious risk for the former is to include irrelevant complexity, and for the latter is to omit something relevant. In the case of modelling, the big challenge is to find the "sweet spot, where the balance is just right" (Rowbotton 2011, p. 149).

A fine example of successful resonance between physics and biology cultures is the research on network motifs developed by Uri Alon and his group. In large networks, including biological networks (e.g., gene regulatory networks, protein interaction networks, metabolic networks), there is a plethora of possible interaction patterns. Surprisingly, a few types of recurring and statistically significant interaction patterns called motifs have been identified as local properties of many biological networks. The group found out that the network motifs appear to function as simple building blocks of transcription networks from bacteria to mammals (Cf., e.g., Alon 2007, Milo, Shen-Orr, Itzkovitz, Kashtan, Chklovskii & Alon 2002). Accordingly, Alon's research provides a fundamental understanding of a huge class of systems. The research indicates that one level of simplicity can be generalised to a large set of biological networks (see also Bruggeman & Westerhoff 2007).

Finding general principles is a major goal for contemporary systems biology. It may be a winning choice, but it is crucial to devote critical attention to evaluate in which situations it is useful to simplify, looking for maximising generality, and in which situations to pay attention to the complexity, historicity, variation of living systems is a better choice. Moreover, it is important to understand the kinds of analytical tools suitable to inquiring styles maximising generality or not (see also Keller 2007b).

Another typical result of the physicists' mindset is the search for new physics in biology. Historically, this is a recurrent topic: Niels Bohr, Max Delbrück, and Erwin Schrödinger, for instance, have investigated the idea that new physics could emerge from the study of life (Cf. Bohr 1933, Schrödinger 1944, Delbrück 1949), though they differed in their assessment of what kind of new physics it was likely to be (see also Stent 1998). Today, along with the advances in our understanding of living systems, there are reshaped hopes of finding new physics in the unique properties of living matter. The question is the same: is there something that has been hidden and cannot be easily revealed in the inanimate world? In the face of what the scientists currently know about biological complexity, the search for a new physics turned out to be more a hope or a maturing goal than an acknowledged research aim. For instance, physicist 13 considered the hope of finding some new physics in the living world as a long-term goal, and physicists 10 gracefully calls the quest for fundamental principles in biological systems as his "holy grail."

The inquiring styles traditionally based on physics that we described above must be taken carefully, particularly due to the conspicuous differences between biological and physical complexities. Complexity in biology is fundamentally different from the homologous concept in physics: it has its own specificities concerning, for instance, constraining factors, hierarchy, nonlinearity, and non-generality, which come into existence by the evolutionary processes (see e.g. Keller 2005b). Although complex living systems obey the laws of physics, these basic laws do not explain their behaviour: the multiple interactions generate unforeseeable emergent properties (El-Hani & Emmeche, 2000; Cohen & Harel, 2007). Physics is indeed all over the place, but so is evolution. Physicist 2 put in interview: "if you cannot isolate a subsystem, then you have to address the whole cell as a whole body, and then physics is very limited. (…) Biology is a kind of history. The history of evolution dictates what kind of solution is found".

Finally, we would like to comment some other assumptions grounded on physics reported by our interviewees. Their discourse vary from complex to simple narratives regarding philosophical debates about their work. They often engaged themselves in self-reflection during the course of the interview, raising philosophical issues such as what counts as theory and as experiment in physics and biology; the distinction between theorising and modelling; conceptual differences between the disciplines (e.g., laws, complexity, emergence); the status of constraining factors in physical and biological systems; what is the experimental status of computer simulations - Are computer simulations in biology considered experiments as in physics? Or running a computer program is just part of the theorising process performed once the experimental approach is over? These are concerns of both scientists and philosophers of science (e.g., Winsberg 1999, Galison 1996, Keller 2000, 2003)

The interviewees proposed both similar and dissenting answers for the many philosophical doubts and showed both appreciation and dislike for comparisons between the fields, as well as for alternative views of the philosophical topics they raised. A interviwee, for instance, raised a few honest wonders: "I think phenomenology is an obscene world in biology. You are not allowed to say this word so instead you say modelling, or… but from the theoretical perspective, it is not even clear. So we have our personal belief, and we do believe that there are fundamental principles to biology... but can we prove that they are there?" (Physicist 10)

Our findings support the claim that systems biology is a field in search of a philosophical foundation (Boogerd et al. 2007) and that systems biologists are developing their own philosophy of science (Calvert and Fujimura 2011). Given the increasing popularity of systems biology, or more broadly speaking, interdisciplinary research into biological systems, we need to face philosophical issues head on, increasing the thorough concern and conscious debate about epistemological aspects of this new field. They are crucial to forging productive research strategies in it.

6. SUMMARY AND CONCLUSIONS

In order to present the circumstances under which physicists currently approach systems biology, we focused upon the questions 'why', 'to what extent' and to 'which effects'. Thus, we have seen that there are common reasons to move, that the transition must be understood in terms of degrees, and, finally, that there are typical effects on systems biology research that are rooted in physics, such as the search for general principles.

In each section, we have mentioned recurrent trajectories in the long history of physicists moving into biology. Ironically, von Bertalanffy himself, one of the founders of general systems theory, has argued someway along these lines when he applied his systemic thinking to historical analysis. For him, "the historian of science always finds that the number of germinal ideas is limited, that they tend to reappear spiral-wise at increasingly higher level of sophistication" (von Bertalanffy, 1967, p. 60). We suggest that the history of how physicists approach biology, in both present and past science, presents many "germinal ideas" of this kind. History of science can be crucial to understand the origin of some recurrent approaches, for instance, the confidence in the explanatory role of general principles (see Morange 2007).

Concerning the empirical study, it is worth mentioning that there are relevant aspects we deliberately did not address in the present work, particularly regarding the cultural and epistemological challenges in the interdisciplinary environment (Keller 2002, Galison 1997), and the relations between research practices, interdisciplinary interactions, and joint knowledge construction inside the lab (Latour & Woolgar 1979, Knorr Cetina 1981, Pickering 1984). We will turn to these subjects in earnest elsewhere, when we will focus on the epistemological cultures in the interdisciplinary community of systems biology.

In the present work, the role played by the physics tradition was precisely our subject of concern, mainly because physics is probably the best candidate for a theoretical framework to systems biology (Keller 2005a) and physicists proliferate in the field. These were the reasons why we pursued this issue. We have often encountered during the interviews a pool of stereotypes and labels to characterise people and fields, such as: physicists are traditionally arrogant, biologists are traditionally loathed to face mathematics, physics is the queen of natural sciences, biology is the new queen of natural sciences. There were even cases in the fieldwork in which the conflict became ethically challenging for the interviewer to deal with. For example, when an interviewee expressed scorn for a group of scientists and said things like "I found biologists impossible to communicate with" or "there are some people who go into biology because they read some review or something (…) and don't ask themselves for a sec if this (their work) is anyway relevant or interesting".

We hope, however, to have made it clear that our approach implies absolutely no intellectual subservience or subordination between the disciplines. Those who misunderstands it may evoke taking sides and proud feelings. After all, scientists are inevitably rooted in their disciplines and, consequently, tend to identify themselves with specific scientific communities and display sets of common values and, perhaps, stereotypes. In our fieldwork, we have witnessed manifestations of disciplinary territoriality in the scientific community, which may come together with intolerance, lack of interest, and even irritation. In conducting the present work we kept a constant concern with a view of neutrality and non-subservience. There are no enemies in this arena, except in the minds of those that are in the habit of making enemies. The very general claim we would like to make is for a less indoctrinated position and for a more open-minded one. For that task, physicists and biologists should overcome authoritarianism, combine respect with critical confidence, set out with the idea of otherness/alterity, and thus, favor collaborationism over competitiveness.

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CHAPTER III

WHEN DISCIPLINARY WORLDS COLLIDE:

CULTURAL ISSUES ABOUT PHYSICISTS WORKING AS SYSTEMS BIOLOGISTS

ABSTRACT: This study is based on interviews conducted at several institutions in Brazil, Germany, Israel and the U.S. and engages with challenges related to disciplinary cultures faced by physicists as system biologists. Physicists have been heavily required in biology for support, particularly quantitative support, and the collision of disciplinary worlds generates cultural issues, which can be the subject of sociological and epistemological investigations. Here, we focus on the challenges regarding the co-existence of many epistemological cultures in the scientific community, particularly on cultural impacts rooted in physics and issues of interdisciplinary communication at the lab. We used oral history as one of the methodological tools to gather the empirical material presented here, conducting interviews with physicists working in systems biology. We also based our results on labs observation, informal conversation with other research group members, occasional group meetings, and lectures. We present the results by illustrating cultural issues between biologists and physicists and their distinct ways of thinking. We also present examples of miscommunication and highlight the intense debate about modelling strategies. Many episodes of misunderstanding were reported in the interviews and, particularly, the judgments about what is supposed to be a model seems to be a matter of careful interdisciplinary debate. Finally, we discuss their local strategies to overcome such cultural issues. In our results, different views and attitudes towards the place of conceptual frameworks were clearly indicated. We conclude that systems biology is full of overlapping and competing meanings, ideas and approaches, and that cultural unconformities within the community bring up important consequences, particularly to the exchange of ideas and communication flow.

KEY WORDS: Physicists, systems biology, cultural challenges, interdisciplinary communication

1. INTRODUCTION

This study is based on interviews conducted at several institutions in Brazil, Germany, Israel and the U.S. and engages with problems related to the circumstances under which physicists approach biological problems. Nowadays, the collaborations between physicists and biologists are vigorous everywhere, and even 'flourish today as never before' (Keller 2007 p.113). Physicists are being heavily required in biology for support, particularly in the field of systems biology and synthetic biology, which draws on theoretical and methodological approaches that strongly involve interdisciplinary research. In our empirical study, we approach the field of systems biology, which is currently more established and has a longer history of physicists' migration. Synthetic biology is a novel research program, strongly related to the bridging of biology and engineering. We focus on the challenges regarding the coexistence of many epistemological cultures in the scientific community.

Systems biology investigates biological systems by combining experimental practices with theoretical work, aiming at predictions and model building by using a mathematical language. Quantitative techniques are applied to analyse large database sets collected from wet lab experiments. Such a set of activities is very suitable for physicists. They are, thus, one more time in history playing a central role in biological research and physics is claimed to be an important candidate to offer a theoretical framework to systems biology (Cf. Keller 2005). However, as in any interdisciplinary scenario, there are several challenges to be tackled. Referring to the field of systems biology, Keller claims for an attentive concern to interdisciplinary issues:

> “As many have observed, there is a cultural gap between the disciplines: biologists and physicists have different goals and traditions, they ask different kinds of questions, and perhaps even look for different kinds of answers. If the cross-fertilisation now being attempted is to be productive, that culture gap must be bridged, and for this to happen, some resolution of, or accommodation to, these differences is required”. (Keller 2005 p.6)

The general questions that inspired this study were: What does such cultural gap look like? Which accommodations are required? What are the circumstances under which physicists approach biological problems in systems biology? What kind of interdisciplinary challenges must be tackled? And, particularly, how is communication and cultural exchange taking place in the trading zone of systems biology? In order to engage with these problems, we used oral history as one of the methodological tools to gather the empirical material presented here, conducting interviews with physicists working in systems biology. We also based our results on labs observation, informal conversation with other research group members, occasional group meetings, and lectures. We will explain the methodological approach in further details in the next section.

Due to its distinctive interdisciplinary character and demands for broader collaboration between scientists from different backgrounds, systems biology has become a subject of sociological and epistemological investigations (Cf., e.g., Calvert 2010). Calvert and Fujimura (2011) investigated the epistemic aspirations of the field of systems biology and explored its epistemic tensions, reflecting on their sociological dimensions. Rowbottom (2011) explored issues arising from the interaction between condensed matter physicists and molecular biologists, particularly related to modelling practices. He reflected on the modelling strategies used in the field of systems biology. Kastenhofer (2013) investigated prevalent 'epistemic cultures' (Cf. Knorr-Cetina 1999) and 'communities of vision' of systems biology and synthetic biology.

Concerning the broader literature on social arrangements within science, we will briefly point out a few pioneering studies that were crucially influential to the present work, although we cannot do proper justice here to this literature. Most classical laboratory studies adopted an ethno-anthropological point of view. They tackled epistemological questions by assuming lab dynamics as belonging to an autonomous culture: how certain entities become objects of research, how scientific knowledge is constructed, what is adequate knowledge, and other notorious conundrums. We do not intend to bring a contribution here to a central question that has divided science studies since Kuhn's book "The Structure of Scientific Revolutions", namely whether science is fundamentally contingent on the scientific practices. The debate regarding the social construction of scientific facts will remain only implicit here (Hacking 1999). In the present study, we are concerned with the communication issues within a particular field of science and with the sources of miscommunications, particularly, whether they lie in an epistemological or linguistic sphere.

Perhaps the most influential work among laboratory studies is the study of Jonas Salk's laboratory at the University of California at San Diego conducted by Bruno Latour and Steven Woolgar (1979). They provided a close inspection of the life inside the lab and portrayed it as seen through the eyes of a newcomer. The basic methodology involved what they called "anthropological strangeness", which is aimed "to depict the activities of the laboratory as those of a remote culture and to thus explore the way in which an ordered account of the laboratory life can be generated without recourse to the explanatory concepts of the inhabitants themselves", being provided by "an observer" (p. 41). Although the main target of our methodological approach are the oral sources (Cf. section 2), laboratory observations were also performed, in which we attempted to consider Latour and Woolgar's influential teachings.

Andrew Pickering famously considered the relationship between groups of theorists and experimentalists to develop his constructive view of scientific facts (Pickering 1984). He claims that there is a symbiosis between experiment and theory, which is "a far cry from the antagonistic idea of experiment as an independent and absolute arbiter of theory" (p.14). Scientific facts not solely emanate from experiments, as human (inter) subjectivity imposes itself on those facts and, consequently, a process of social construction plays a major role. Again, we do not intend to provide here an account of social constructionism. However, what is essential for the present study is the view that the process of pursuing scientific facts is dependent on many sociological factors, among them and importantly, the flow of communication inside a scientific community.

Also from the perspective of social constructionism, Karin Knorr-Cetina provided an anthropological description of the knowledge cultures of science. She proposed the term "epistemic culture", which she defined as "an amalgam of arrangements and mechanisms—bonded through affinity, necessity and historical coincidence—which in a given field, make up *how we know what we know.* Epistemic cultures are cultures that create and warrant knowledge, and the premier knowledge institution throughout the world is, still, science" (Knorr-Cetina 1999, p.1). Her main tenet is that different laboratories do not share the same way of producing scientific knowledge, as they are endowed with distinct epistemic cultures. She is concerned about the machine deployed in knowledge production and she looks upon scientists as enfolded in construction machineries that are organised dynamically and thought about, but not governed by single actors. The notion of epistemic cultures represents an important guiding hypothesis of the present research: epistemic cultures constitute specific ways of producing knowledge, which determines different ways of inquiring and interpreting science.

While Knorr-Cetina aims at an essential sociological/anthropological description of the cultures of scientific knowledge, Evelyn Fox Keller aims at a description of the epistemological assumptions of these cultures. In her *Making Sense of Life*, Keller discussed the differences between cultures of scientists in terms of epistemological cultures, regarding a community of physicists and biologists. By epistemological cultures, she means "the norms and mores of a particular group of scientists that underlie the particular meanings they give to words like theory, knowledge, explanation, and understanding, and even to the concept of practice itself". (Keller 2002, Cf. also 2005, 2007). She notes that her usage of epistemological culture invokes a kinship with what Ian Hacking calls "style of reasoning", a widely debated device to understand scientific practice (for a critical perspective, see Hacking 1992). Through a sophisticated analysis of the cultures of physics and biology, by focusing on the problems that arise in developmental biology, Keller pleads for a proper attention to the meanings of the words scientists use and the way in which they use them. She pleads also for a more serious approach to linguistic and narrative dimensions of explanations. In full accordance, the usage of the notion of epistemological culture and the appreciation of linguistic clarity in science played a guiding role in the present research.

A last important guiding theoretical reference to our empirical study is Peter Galison's study on the collaboration of instrumentalists, experimentalists, and theoreticians in high-energy physics. (Galison 1997, Cf. also Galison 1996). He developed the metaphor of *"trading zones"* to explain how physicists and engineers from different cultures worked together to develop particle detectors and radar. To explain their successful communication, Galison treats the movement of ideas, objects and practices in the context of the establishment of pidgin and creole languages, and claims that two different groups are able to find a common ground to communicate by means of such languages.

What is the case for the community of biologists and physicists in systems biology? Is contemporary systems biology a case of successful trading zone? What elements do we need to analyse a contemporary case, namely a scientific practice whose actual successful outcome is to be evaluated in the future? In the following section, we present how we engaged with these nested questions and, also, with other derived issues that appeared along research.

2. METHODOLOGY: PHENOMENOLOGY OF THE LAB

We conducted recorded semi-structured interviews with thirteen physicists working in systems biology problems in four different countries. A number of pertinent informal conversations with other members of the groups, students and secretaries were also performed and, sometimes, recorded.

In Germany, we conducted five interviews with three research group leaders, i.e. Nikolaus Rajewsky, Hanspeter Herzel and Peter Arndt, and two postdoctoral researchers, i.e. Roman Brinzanik and Navodit Misra, at Max Delbrück Center for Molecular Medicine, Humboldt University and Max Planck Institute for Molecular Genetics. In Israel we interviewed physicists who head systems biology research groups: Uri Alon, Joel Stavans and Eytan Domani. Then, we interviewed Suani Pinho, a research group leader in Brazil[83].

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[83] Systems biology is one of the funding priorities in the United States, Germany, and Israel. In turn, Brazil does not have a systems biology network developed to the same extent. In this country systems biology is currently still trying to establish itself as a new field. The interviewed Brazilian physicist, Prof. Dr. Pinho, identified herself as a systems biologist based on her research interests.

In the United States, we interviewed the following leading physicists: Erel Levine, Harvard University; Eric Siggia, Rockefeller Foundation, Ned Wingreen and Thomas Gregor, Princeton University. Another relevant source of oral information was a conversation with Evelyn Fox Keller, in which we also explored her transition to biology as a physicist in the 1960s.[84]

Each interaction happened in person, since one of the authors has met the interviewees in their respective countries. We argue that the oral history approach can be largely enriched by a personal contact between the interviewed and interviewee, and impaired by exclusively virtual interaction. The main consequent advantage of the physical presence of the interviewer in the research environments is that our results also benefitted from observations of the working places involving scientists, including lab everyday routine, offices, group meetings, supervision sessions, lectures, and informal meetings in coffee rooms. The interviewer attended group activities as often as possible, according to the convenience of the interviewees. An online interaction would reduce the complex interactional perception to a mere collecting of reports through a computer.

Both time limits and places where the interviews were conducted were set by the physicists. The average time granted for an interview was around one hour. The longest one took around 85 minutes and the shortest, 42 minutes.

The physicists themselves were of great help in pointing out the main characters within the scientific community working on systems biology. We selected the scientists to

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[84] This conversation is considered apart from the interviews because the subject matters addressed went far beyond the semi-structured interviews, conferring to it a particular status.

be interviewed considering geographical and financial restrictions. We argue that the geographic dimension and the qualitative approach — which was chosen in order to provide a maximum focus on the details — justify the relatively small sample. Further studies both in other countries and through quantitative approaches are, however, worth pursuing.

The interviews were constructed for each physicist, considering the particularity of their interests, careers, working places, etc. Thus, each interview was preceded by an extensive preparation by reading their papers and researching about the interviewees. They were encouraged to speak about, for instance, their careers, motivations to do research in biology, their background in physics, their research work and group, the culture of systems biology, and issues of interdisciplinary interactions. While the interviewer attempted to provide guidelines for the discussion based on the protocol, she also kept the interaction flexible enough for the physicists to talk freely.

Regarding the analysis of the raw data obtained through the interviews, the aim was to isolate recurrent topics with historical and epistemological significance. The results must be seen as trends concerning the contemporary movement from physics to biology. In the following sections, a discussion of the main general findings is presented.

All the physicists gave informed consent for the interviews and for the use of the information derived from them. In order to respect the interviwees's privacy, we do not refer to them by their names when mentioning their reports, with few exceptions. For instance, when the report is related to the interviewee's particular research topic or personal experience, we mention their names in order to cite them properly.

3. RESULTS AND DISCUSSION:

TACKLING CHALLENGES OF THE INTERDISCIPLINARY ENVIRONMENT OF SYSTEMS BIOLOGY

In this section we present the outcomes from the interviews, field observation and other interactions with the scientists. The results must be seen as trends concerning the cultural challenges between physicists in biology in contemporary systems biology. Firstly, we state cultural issues between biologists and physicists, then we discuss what is considered as good questions for them, and we bring examples to illustrate their distinct ways of thinking. We present examples of miscommunication as well, and highlight the intense debate about modelling strategies. Then we discuss local strategies to overcome cultural challenges, such as the process of learning a scientific language and the role of the mentor as a mediator.

3.1. CULTURAL ISSUES BETWEEN BIOLOGISTS AND PHYSICISTS

Physicists and biologists come from two clearly distinct epistemological cultures. They have different traditions, goals, and ways of dealing with the unknown. As an researcher, who leads an interdisciplinary research group, reported in interview, they face problems like those of an intercultural communication:

> "This is a major topic that I struggle with over the years and I discovered ways to work but it's something that really needs a lot of work: biologists and physicists, and computer scientists they all come from different cultures. It's almost like people from very different countries, like two continents. Conceptions about what is a good answer in science is different, about words like models, what it means, and a lot of technical knowledge etc…" (Physicist 6)

Another interviewee, who heads an interdisciplinary group at Harvard University, also used a similar analogy to address the cultural difference:

> "Every newcomer to the lab or to the field has the same language problem that any immigrant moving to a new country. Even if you did learn the language in the school in your own country, when you come to this new country you very quickly discover that you don't know what people is talking about, that they are using slangs that you don't understand, that they are using words in a way that does not make any sense to you. All you need is to overcome this language barrier. The worst thing you can do is to try to hide from it". (Physicist 10)

The learning of a new language is claimed to be a very crucial step of the cultural adaptation process. It was emphasised the need of a full cultural involvement by the physicists, instead of a distant application of their techniques and equations. As the following interviewee's report illustrates:

> "As physicists we have to come across to learn the language of the biologists to come with an equation and say 'listen this is what we need solved' you are gonna wait a long time. You have to be able to go and say 'we understand the terminology (…) what you mean when you talked about activators, repression, transcription factors'. All these things. We don't have to be experts in all the details the way biologists are but we have to be the ones who turn that kind of mental picture of what is going on into a real quantitative mathematical description. You cannot just say 'you package it for me, and then I will do the math that I'm so good at', you have to go through how do they do experiments? What should I be careful about in interpreting the data? (…) You have to be aware of all these kinds of considerations and try to formulate what is going on and not be misled by all the complexity of these biological systems". (Physist 12)

The efforts for cultural learning are certainly not only unidirectional, but bidirectional: physicists must adapt to biology and biologists to physics. However, it demands more from the physicists, as they are the ones changing fields and dealing with a new type of system. A researcher declared in interview: "I have found in my experience with biologists that I had interacted with, that it's we, the physicists, that have to make the much more significant effort to adapt to their language and way of thinking than they to us" (Physicist 7). At his lab the interviewer was kindly invited to talk with other scientists and the hunch that the main effort to adapt to the language comes from the physicists was confirmed by a biologist who stated the following:

> “[…] I should understand their (the physicists’) terms but I cannot learn all those years of education. I just have to understand the main, or crucial terms. But actually Joel knows how to deal with people like me, so he would talk to me in a different way or explain me something in a basic way. When I explain the biological system —you can see my diagrams here—I give them not too many details. We communicate in a way that everyone knows how to explain to the other with his/her own terms. That’s the idea. So it’s not only that I adjust, he also adjusts to me”. (informar conversation with a biologist, member of a visited research group)

Through learning and teaching strategies like those, the scientists develop ways to understand each other. The interviewees reported many episodes in which scientists found a common ground to communicate, overcoming language barriers. Physicist 13 told us a case of successful exchange in his lab:

> “[…] There are biologists and physicists, these are the two main groups that I have in the lab. They need to learn each others’ language, they need to learn each others’ way of thinking, and it takes a while for them to be able to communicate. One of the most successful work that has been going on in my lab over the last three years was the connection between a developmental biologist — a postdoc who used to work with zebrafish and now works with drosophila — and a physicist — grad student who came in a string theorist. So think about that, take a string theorist and a developmental biologist, put them in a box and shake it really hard and something

> nice emerges. That's the fun part of this job. It took a while at the beginning to make them communicate in the right way 'cause one was essentially getting the data and the other was analysing the data". (Physicist 13)

However, the flowing of communication is not always trouble-free. In fact, the overall situation seems to be the opposite. For instance, an interviewee reported a case of a research associate from biology he had been working together for a year and still could not understand the context of the problems or why they are interesting. A number of interviewees commented about the stress between different world-views expressed by referees and some mentioned that sometimes there are even aggressions in interdisciplinary meetings. In the next sections, we analyse cases in which the communication flow is taken as difficult and some reported reasons for that. First we analyse the biologists and physicists' ways of thinking and making questions, which reflect their respective background. Then we present episodes of miscommunications, with either successful or unsuccessful ends.

3.2. MULTIPLE THINKING STYLES

Physicists and biologists have traditionally different ways of thinking. Keller (2002, 2005a) conjectured that physicists and biologists ask different kinds of questions and look for different kinds of answers. In our interviews, her conjecture was supported. An essential difference, she summarised in interview, is that while biologists want to know how systems work, the primary question for the physicists is how they could work. An interviewee declared: “It was very interesting to me how biologists were asking very different questions from the questions I would ask”, and connected his migration to biology to this difference in question-making: “there are enough people out there that do fantastic biology (…) the only way to justify (the coming of a physicist) is that I perhaps ask different questions and come with different approaches”. Following up on it, he described an episode in which he was working in a collaborative project and naturally raised the question “how many?” to his co-workers, more precisely, “how many proteasomes?”, which his colleagues considered as a queer question. According to a interviwee, his colleagues “never bother to ask these ‘how many’ questions because it was never relevant for the questions they were already asking”. As a physicist, asking about quantities is both natural and a priority: “coming from physics, the first thing you wanna know is the numbers of what we are talking about”. (Physicist 10). Along with their sensitivity for numbers, physicists claim they have a particular concern with the bigger picture of a system, that is, general principles, constraining factors, equilibrium and linear laws.

A fine example of searching for general principles is the research on network motifs developed by Uri Alon and his group. In large networks, including biological networks (e.g., gene regulatory networks, protein networks, metabolic networks), there is a plethora of possible interaction patterns. Surprisingly, a few types of recurring and statistically significant interaction patterns called motifs have been identified as local properties of many biological networks. They found out that the network motifs appear to function as simple building blocks of transcription networks from bacteria to mammals (Cf. e.g. Alon 2007, Milo et al. 2002). Accordingly, Alon's research provides a fundamental understanding of a huge class of systems. This research indicates that one level of simplicity can be generalised to a large set of biological networks (see also Bruggeman & Westerhoff 2007). In interview, he pointed at examples of typical inquiries for generalities: "Are there general principles for how this biological matter is made? Why do you see all these particular molecules interacting the way they do? (…) How precision can work despite the randomness?" (Interview with Alon, Weizmann Institute of Science, July 2012)

Both Herzel, at the Humboldt University, and Stavans, at the Weizmann Institute of Science, drew attention to the notion of equilibrium as a distinguishing feature. Physicists have been educated to use the notion of equilibrium in most of their systems of study. In Biology there are mainly non-linear dynamics and, thus, an overall tendency to non-equilibrium. Therefore, it is impossible to understand many aspects of biology by regarding living systems in terms of equilibrium schemes, that is, the way physicists are used to. There are fundamental features of biological systems that physicists are not familiar with. Stavans illustrated that with the example of preservation of biological information through generations: "It's impossible to understand the accuracy of replication using equilibrium ideas, you need to involve non-equilibrium schemes. (…) At least for me it has been very shocking: that some of the frameworks that were very well established in our minds to treat certain systems, cannot be applied to biology" (Interview with Stavans, Weizmann Institute of Science, July 2012)

The search for simplicity was emphasised by most of the interviewees as a typical rationale rooted in physics. The following interview reports illustrate the expectation for some underlying simplicity from the physicists' perspective:

> "Biology is very very complex. There is no way one can doubt about that. But there are certain ways in which one can see simple principles that can explain some aspect of why it's built. That's what physicists are trained to do and works fantastically when we try to understand the simple stuff like metal, plastic, not living matter. The surprise is that it also works- at least the way I look at science and the results we get – it works remarkably really well if you know the model and you think about biology (…) The simpler, the better for me". (Physicist 6)

> "(…) you realize that there are very simple biophysics in complex biological systems, underlying that there were something that was simple. I think it's very appealing to the physicists... that's what the physicist's training was: finding underlying simplicity (…) If we are lucky and maybe have good partners, and someone has good taste we can dig in to that system and find some underlying simplicity. And then with more hard work and some more thoughts we can build backup from that simplicity to a real understanding of biology". (Physicist 12)

Another thinking style mentioned was the traditional disavowal of mathematics by the biologists. A interviewee mentioned that there is “the fear of math, when the biologists feel that, by being a biologist, he or she has the license not to know mathematics”. He shared an episode in which a student came to him to ask for help with the theorising part of her work. She had the experiment and even the differential equation, but she could not solve it by herself. She approached him under the excuse she was allowed to not to know it as a biologist. Instead of solving the equation, the professor used the opportunity to explain two different approaches: she indeed could simply plug her experiment into mathematics, but it would be much better if she understood what the solution actually meant: “solving a differential equation that you already have is not physics, and this we definitely work hard to change”. (Physicist 10)

Physicists often commented on the descriptive tradition of biology. It is pointed out that biologists are trained to describe phenomena and complexity in details, which may potentially compromise the search for what is essential. Many interviewed criticised an apparent confusion between factual description and understanding, for instance: “when I listen to a biologist and they say ‘this gene does it’, ‘we found the function’, ‘this gene regulates that gene’, or ‘this transcription factor bonds to that’, these are facts. It does not teach me anything”. (Physicist 5).

Finally, an important key difference in ways of thinking is related to the biologist’s evolutionary point of view. Physicist 2 reported that “Physicists are looking for data-related simple principles, simple models, toy models. Mathematicians also use the same equations but they are not close to experimental data. They want to make it per se (…)

they want to prove something and so on. So even if they study the same equations, physicists want to explain some effects and mathematicians want to prove something and the biologists are asking how is the functioning and how it evolved”. Eytan Domani put emphasis on the process of evolution and the need to consider it carefully. He explains that physicists are trained to identify causes and to understand time as moving forward: “There is one thing that happened now, and another thing that happened a minute from now, and what happened now could cause what happened a minute from now, and not the other way around (…) We feel that we understand something if we understand how A cause B”. Evolution, in turn, requires a backward looking. He argued through an example that a lack of understanding of that jump of perspective may lead to the wrong direction. The example concerned one of his group’s project, on leukaemia in children affected by Down syndrome. The aim was to understand why children with Down syndrome have much higher probability of showing leukaemia. Along the study, they faced two important findings: that a big fraction of the cells under study have an amplification of a particular receptor, and that a sizeable fraction of the cells that have this particular amplification also have a mutation of in a gene coding for a kinase that interacts with that receptor. These two elements together give the cell a boost of cell division, which means cancer, and so, this would be a way of triggering leukaemia. The main evidence was that all those cells that have the mutation also have the amplification. Accordingly, the natural question for them was: what is the relation between the receptor amplification and the mutation in the kinase gene? “As a physicist”, he reported, “it is obvious that the amplification somehow causes the mutation because in order to have the mutation you must have the amplification (…) So there must be a causative connection between the amplification and the mutation". However, in the course of the study, it became clear that the gene which is amplified is in one chromosome and the mutated kinase gene is in an absolutely different chromosome. Therefore, the causal relation was not obvious and the question for Domany turned out to be "what could be the causal path going from the amplification to the mutation?", and the physicist then "spent sleepless nights trying to figure this out". The denouement of the story happened through an intervention of a collaborator who was a medical doctor and biologist. This collaborator pointed out that there was no causal relation between the events, as a physicist would expect, and that what might explain the concomitance of the two events would be a selective process. The two events together, which happened by chance long time ago, conferred the cell an advantage, that is, fast proliferation rates. Thus, the events were selected together, having no causal relation with one another. In these situations, the physicist has to learn how to look backwards in time and to be careful with inferences of simple causality, such as: A and B are correlated, so A causes B. Perhaps A and B are correlated because of C, and C may be a process of selection taking place in the past. According to Domany, "this is something that a physicist who works in biology should be aware" (Interview with Domany, Weizmann Institute of Science, July 2012).

The distinct thinking styles we presented illustrate that the agreeing on the research questions and the ways of looking for answers are issues that demand mutual adaptations and careful work. It is fruitless to underestimate the fact that "there are different cultures, and it's very clear that this is a big issue in such interdisciplinary collaborations. In order to bridge the gap in terminologies and approaches, even in research questions, we have to agree in the questions that you want to study together" (Physicist 4).

3.3. MISCOMMUNICATION ACROSS DISCIPLINES

Several interviewees reported episodes of miscommunication or misunderstanding within the scientific community. There are stories that are easily manageable, such as uncommitted conversations during lunch time/coffee break. A physicist told a story in which it took many months for him to explain a few research interests to a biologist colleague. When finally understanding was reached, he said: "I could hear the click and then he got it (…) and now we even have a student that we are co-advising. It just took some time" (Physicist 10). The fact that understanding takes time to happen can be more or less of a problem depending on the particular situation. Another report illustrates a more consequential case, since the misunderstanding affected the development of a paper. The members of the collaborative group meant different things by the word 'active' and had to clarify the issue. He stated that these kinds of misunderstanding often happen:

> “We just had this experience very recently with one of our collaborations, we were writing a paper together and we meant different things by the word active. One may think: ‘it’s a simple world’. As physicists we meant the probability to be in a particular state that we were calling active and the biologists were talking about biochemical activity which depends on the presence of substrates, as well as the state, and so on. As a result, obviously it was not a long term problem but these things do come up. I think this is an opportunity to physicists to force their biology colleagues to be very precise in their languages, this is something that physicists can bring...” (Physicist 12)

In a similar way, physicist 3 commented that the word ‘isochore '— which in general refers to patterns of large-scale variation of base composition in the genome — may be understood in different ways by different scientists.

Naturally, the lack of specific knowledge may lead to a wrong question. Physicist 10 gave a fine example, which is related to *quorum sensing*. It happens that a lack of understanding of a specific fact — namely, that when bacterial cells move from the exponential phase to the stationary phase, they stop growing and accumulate proteins — has resulted in misleading research questions. Physicists that don’t know that fact, which “any microbiologist would tell”, may think that the concentration of protein has something to do with the circuit of functionality of the system, instead of concluding from that fact that there was a phase transition, therefore, raising the wrong hypothesis (Physicist 10).

3.3.1. MODELLING STRATEGIES IN INTERDISCIPLINARY SYSTEMS BIOLOGY

The most recurrent issue raised by the physicists concerned the notions of model and modelling. The growth of biological understanding has been strongly dependent on the formulation of models and, accordingly, modelling is a crucial task in systems biology. However, modelling in biology has been a subject of critical debate. Keller (2002) argues that not even traditional attempts of mathematical biology have been successful from a standpoint of the great triumphs of the field, such as Stéphane Leduc's efforts in artificial life, D'Arcy Thompson's classical attempts on mathematical biology and Alan Turing's mathematical model of embryogenesis. Presently, new roles for mathematical and computational modelling raise unlimited ways of giving voice to biological data. What models are and what they intend to serve divide the epistemological cultures in systems biology, as the scientists have distinct ways of grasp and approach modelling. In this interdisciplinary community, in the words of one of our interviewees, "we end up with total different meanings for the world model" and even though scientists are aware of that, "it still creates some difficulties" (Physicist 12) Our findings indicate that the difficulties lie in two main unconformities: models mean traditionally different things in physics and biology, and physicists and biologists have distinct and typical approaches in model construction. The search for simplicity by physicists and the higher compromise in grasping the biological context by biologists are key factors.

Traditionally, for biologists models can be qualitative or quantitative, and, accordingly, they are very different from the models employed in theoretical physics. They often expressed dissatisfaction with such difference, for instance: "A lot of biological models are not mathematical (…) they are like this does that, it's a very qualitative thing (…) I don't trust that, because there is no number". (Physicist 5). They urge for a rejection of any qualitative notion of model. As Arndt puts: "In physics a model is always somewhat quantitative, while in biology it could be a qualitative model. Of course I don't interact with all biologists, but with those with whom I do, I guess we have more or less the same concept of a model and that is a quantitative one" (Physicist 3). A interviewee explained the difference by associating the model for a biologist with a scheme, which is not necessarily quantitative:

> "Words like model mean a completely different thing for biologists and for the physicists. A biologist would call a model something which is more a kind of picture or scheme for a physicist. When you take a paper in biology, written by biologists, and they refer to a model (…) they say well we have this model and they put you a picture and the picture is of course very descriptive, it's capturing thousands of words in one image. But you could substitute the word picture for model and nothing would change. For a physicist a model is completely different. It's the ability to distill the important quantities of the problem, be able to link them

> mathematically in one formalism, let's say a set of differential equations and analysing these equations in order to make predictions. So conceptually it is very different". (Physicist 7)

The differences in the conceptions of models have problematic consequences for question making and data interpretation, as it was stressed in the following report:

> "For physicists a model means: 'I have mathematical understanding of what I am looking at, I can describe my phenomena in the language of math, which gives a very strong predictive power.' (…) I think the biologist sees a model more in terms of a pathway, 'well I know protein A attracts protein B and now I look at protein C and how it links to these two proteins', so it's a kind of a ball and stick model. The questions you can ask with this type of model are more yes and no questions. (…) In mathematical models that are phrased in mathematical language you get a number in the end and this number can be closer to one scenario or another". (Physicist 13).

Along with the traditional conceptual differences about models, there are also disciplinarily rooted modelling strategies. As a interviewee expressed it: "Typically, physicists look for toy models, (…) minimal models, and they try to reduce the system as much as possible but not any further. Biologists, engineers and mathematicians try to keep complexity" (Physicist 2). A source of uniformity is the evaluation of what exactly must be considered as belonging to a model. Overall, it was often reported that biologists tend to consider more factors, given their descriptive tradition, the fact that they are mainly concerned with the biological reality behind a phenomenon, and their focus on its complexity, and physicists tend to consider less factors, since they are simplicity-oriented and concerned with the equations behind a phenomena. Such divergence of perspectives was explained as follows:

> "I think there are some differences when you discuss a certain problem with a biologist and a physicist... let's say there is an idea of how to dissect the problem or how to solve the problem... and the biologists will all the time and in many cases they will tend to bring in 'yeah but this you haven't really considered in your model' (...) they have been used to easily add the missing layers of complexity in the model right a way (...) the physicists tend to try to simplify the problems with the hope of some unifying principles and try also to get a clearer understanding of the scales involved; 'maybe there is the complex level A and B but maybe A is only important for complex data regarding certain scales which is different from complexity B' (…) maybe you shouldn't be so concerned about the complexity type B because you are only interested for now maybe in the world living on the scale A". (Physicist 1).

The obvious risk for the biologists is to include irrelevant complexity, and for the physicists, to omit something relevant. Joel Stavans explained the situation bringing up his study on iron homeostasis. He and his colleagues proposed a mathematical model to capture the main features of an observed behaviour related to the role of iron in the damped oscillation of gene expression. Iron homeostasis network in bacteria employs feedback loops to regulate iron usage and uptake (Amir et al. 2010). Along with the model building, it was possible to come up with many variables that, a priori, would be important to describe the process under study. However, they wanted to build it as minimal and simple as possible:

> “So we showed, in trying to think of a model, for a physicist what is important is to be able to make a minimal model. A model that will reproduce what you see but without spurious variables. To distill what is important. So we came up with a model of three variables and we could reproduce essentially everything we saw. (…) To arrive to what is essential we tried many things, but we were guided by biologists”. (Interview with Stavans, Weizmann Institute of Science, July 2012)

With the help of a biologist, the process consisted in knocking down the components in order to get insights on what the components do and when they are important. They knocked down many different genes and, at some point, they discovered that one particular gene destroys the very oscillation under investigation. It was a gene involved in iron transport through the membrane. So, it became clear that those genes involved in iron transport would be important to describe the oscillation. The investigation encompasses an effort to figure out spurious components and is “a process that builds up in trying to see what are the important variables. A physicist would really try to minimize that to get a minimal description”. (Interview with Stavans, Weizmann Institute of Science, July 2012)

The interviewees, naturally, advocate the physicists’ style. They claim that by including many things, a model can end up too big to be understandable: “one probably cannot understand, they have no parameters. You can fit any data with it and it does not end up satisfactory. The reason, I think, is basically lack of modelling skills, which is a whole discipline that physics has hundreds of years of experience." (Physicist 6). Independently of which style is right, the big challenge is to find the "sweet spot, where the balance is just right" (Rowbotton 2011, p. 149)

Accordingly, the adequate level of simplicity when modelling is a critical issue in the interdisciplinary communication and sometimes it may be a challenge to find a common ground in the discussion, as a physicist puts it: "As a physicist you try somehow to reduce things to simple models, and biologists, for example, they are very often full of knowledge, all kinda of knowledge about the details and it's very hard to find a common ground in the discussion, because biologists talk about many many different things (…) And a physicist would like to identify which of those are really important. (…) this is a very difficult thing" (Physicist 4).

3.4. LOCAL STRATEGIES TO OVERCOME CULTURAL ISSUES

Physicists don't perceive the cultural issues as stumbling blocks. Overall, when recognising disciplinary gaps, they are confident that they manage to communicate well enough to work together. In words reported in interview: "Good communication solve all this. Once you start to talk with someone, you spend time with him or her, then it's easy to clarify. It’s a matter of will”. The researchers just have to “identify that they have common interests and that they can help each other. Then the rest is just about trying to be very clear and just communicate” (Physicist 10)

For the task of communicating well, they point out several strategies, such as getting familiar with the language through books, papers, reading material, seminars, collaborations, etc. Interacting with other scientists was also mentioned as a tool for learning by most of them. They highlighted the need to talk to people coming from different fields in order to improve the communication:

> “You can still find when you come here people that speak your native language, they might help you. But the more you rely on them, the less you are gonna fit in, and the less you will understand what is really going on (…) it’s true that if you are talking to someone who is similar to you, that speaks your language, the communication is just faster and easier. But when you talk to someone who has different concepts, different ideas, that might require more energy (…) It’s a lot of fun to talk to someone who agrees with you but it’s much more fruitful to talk to someone who does not.” (Physicist 10)

They spoke about distinct amounts of time spent to learn biology or solve communication issues. Gregor mentioned a collaborative project between a physicist and a biologist in his lab that took more than a year to get on the flow. Alon mentioned that a physicist can understand a lot in three months and in one year they can give a talk with words they wouldn't understand one year before. Herzel, who moved to biology much earlier, in 1996, said that students learn quickly what is needed to satisfy practical purposes, but “still there are communication problems from group to group”. He stated that it took two to three years to solve communication problems. Concerning a collaboration with a biologist, he hypothesises: “So I have to know what are the pleas in his systems, what are the important diseases (…) this might take a year or two. And the biologists has to learn what I mean by model, why do I care about sample size”, the meaning of several terms such as “clustering, or cooperativity, or biostability, biomodelity, oscillation”. About his own experience, he said that “It took me about 5 years to arrive in biology, to know what my colleagues are interested in, and to get a feeling on how are the topics in the journals. Now I know both languages very well” (Interview with Herzel, Humboldt University, May 2012)

Besides learning the language, a way of talking also needs to be developed. They overall claimed that adaptation is the key, as one illustrates: “Of course I had to adapt to communicate with biologists. You just would focus on different aspects of your model”(Physicist 3). They claim that the adaptation implies flexibility: “even the same project you would tell differently to a condensed matter physicists or to an evolutionary biologist” (Physicist 10).

Collaborations between physicists and biologists that are mediated by a mentor were observed in many labs and are considered by a few interviewees as an important strategy: “We try to make the biologist invite the physicists to plan the experiment together and the physicist invite the biologists to plan the analysis together. And they present to me together” (Interview with Alon, Weizmann Institute of Science, July 2012). Alon explained that context orientation is a recurrent task as a mentor, in order to provide understanding for the whole interdisciplinary group. In a group meeting about mathematical models and how modularity evolved in biology, some of the members did not understand the difference between two models, because they could not understand the reason for some mathematical equations: “We had to stop the group meeting and make a table saying ‘old model’ and ‘new model’ and the differences. So people could go back and get the context. Why these mathematical equations are interesting at all? Again, we need to get them to context orientation. It happens again and again”. (Interview with Alon, Weizmann Institute of Science, July 2012). The role of the mentor was very often emphasised:

> “I try to give physicists the minimum they need in biology to be able to operate, obviously I cannot bridge the gap of many years of experience in biology. (…) In the same way as I’m not trying to make from the biologist students physicists, I am not trying to make the physicists biologists. Because we would be very poor biologists, in the same way that biologists would be very poor physicists. But there is a minimum of ability to be able to swim between the two. And for me it is very important, as a teacher.”f (Physicist 7)

Although many of them interpret their roles as mentors in connection with an attention to language, others do not see this as a high priority, for instance, a interviewee defended that “they don’t need to be pushed towards the language. I can help them to do some more efficiently by pointing out the right papers, but they don’t particularly need” (Physicist 11). Therefore, several strategies and priorities concerning cultural issues were reported. However, what is common to all of the interviewees, and perhaps, to the whole community, is the trust in their ability to overcome cultural issues and communicate well enough.

4. CONCLUDING REMARKS

This paper has explored physicists' discourses on the routine and challenges of interdisciplinary systems biology. These discourses show that quantitative scientists bring to systems biology not only analytical tools but also traditions and values, so an important barrier to overcome is essentially cultural. The cultural barrier comes along with consequences, particularly to the exchange of ideas in the community. Many episodes of misunderstanding were reported in the interviews and, particularly, the judgment of what is supposed to be a model seems to be a matter of careful interdisciplinary debate. The interviews illustrate several misunderstandings between scientists which are more epistemological than merely linguistic and, consequently, indicate that some accommodations are necessary.

According to the interviewees, the miscommunications are always fixable. In order to tackle cultural barriers, the physicists defend (1) a deeper understanding of biological explanations on their part (together with adjustments on the part of the biologists) and (2) more extensive debates among scientists coming from different disciplinary cultures. Concerning the claim for deeper understanding, they argue that the research cannot be overly compartmentalised. The research must not happen in a way that the biologists pack the problem and the physicists do the math. The physicists are supposed to learn the nitty-gritty of biology and be careful about interpreting data. It is not enough to come with equations and quantitative approaches. Although the physicists themselves claim for that, during the lab visits, the interviewer observed many different styles of distribution of labor and degrees of involvement with the biological topics. Secondly, the physicists argue that the misunderstandings are clarified by more extensive debate, in which the scientists involved express their points of views and what they mean or how they interpret the particular cases. This seems to be a feasible solution for specific cases in interdisciplinary research groups, but it cannot avoid that such misunderstandings come up in the whole scientific community. Therefore, the questions that remained unanswered in this study are: In fact, how urgent is it to reach precision of language and research aims? And what kind of strategy will satisfy the need for linguistic and epistemological clarity in such community?

Such situation is not unprecedented in science (cf. Kuhn 1962 and Galison 1997 on theoretical physics), and not even in biology. Our finding that physicists, as systems biologists, are confident in their communication skills comes along with Keller's claim that scientists are rarely troubled by the coexistence of several terms they rely upon, that despite the lack of precision in their conceptual language, they have no trouble in considering that they know what they mean (Interview with Evelyn Fox Keller, May 2013, cf. also Keller 2012b and Keller's talk at University of King's College, entitled "Kuhnian Revolutions and Contemporary Biology: Lexicons, Kinds, and World Changes"[85]).

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[85] Available online at: http://vimeo.com/63426966

According to her, the lexicons of genetics, developmental biology, evolution and ecology are filled with overlapping terms that researchers do not precisely bother themselves about (Cf. e.g. Keller 2000, 2012a).

As the scientists are confident that they manage to communicate well enough, the field of systems biology presents similarities to what Galison characterises as *trading zone*. Systems biologists coming from different backgrounds are able to exchange goods, despite differences in language and culture. Their discourse show that they find local solutions towards good communication, namely, “the trading partners can hammer out a local coordination, despite vast global differences” (Galison 1997, p.783). Further studies and probably even time for the field to develop are necessary to label systems biology as a successful trading zone. If systems biologists succeed, there will be another example of how exchanges across disciplinary boundaries can reach systems of discourse stablished and rich enough to support scientific development.

However, it may well be the case of a less successful status, such as a rupture, as ambiguity and polysemy are sources of division of a scientific community (Cf. Kuhn 1962, Keller’s talk at University of King's College, entitled “Kuhnian Revolutions and Contemporary Biology: Lexicons, Kinds, and World Changes) has taught us that ambiguity and polysemy are sources of rupture. There is a chance that this community splits in two, but, also, that the overlap of meanings may persist for a long period of time without exerting an actual pressure on the community to divide. The following comment made by one of our interviewees about modelling diversity might be interpreted as a sign of division: “we already have a kind of physicists’ school, I would say, in systems biology and there of course I don’t face this problem because we agree that models should be explaining, they should be simple” (Physicist 4). Another example would be: “In my group of 10 people or so, we have no serious communication problems” (Physicist 2). Or still: “I found biologists impossible to communicate with” (Physicist 11). What would be the way to establish a successful trading zone, instead of such unhappy ending as a rupture?

We believe that a focus on mini-crisis solving is a venturesome strategy, it is, solving local issues may not access global stumbling blocks. As we believe that language shapes the questions scientists ask and the way of answering them, language have, therefore, a significant effect on scientific practices. We argue that linguistic clarity and integration of epistemological aims deserve higher priority, if unreservedly flowing communication and productivity are to be established. However, a claim for a proper handling of conceptual precision may easily become a cry in the wilderness, as it is not obvious what is a sufficient level of precision and the scientist, overall, trust in their natural precision skills. Besides, imprecision may perhaps play a certain role in a communication flow, which is not necessarily negative. Thus, we are ready to propose a simpler suggestion. In accordance with Calvert and Fujimura (2011), we defend that awareness and appreciation are much more feasible goals. Interdisciplinary communication in systems biology could strongly benefit from a greater awareness and appreciation of the epistemological differences between scientists coming from distinct fields and, also, of their consequences.

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