Scientific Protocols as Recipes: A New Way to Look at Experimental Practice in the Life Sciences and the Hidden Philosophy Within

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ABSTRACT

The experimental practice in contemporary molecular biology oscillates between the creativity of the researcher in tinkering with the experimental system, and the necessity of standardization of methods of inquiry. Experimental procedures, when standardized in lab protocols, might definitely be seen as actual recipes. Considering these protocols as recipes can help us understand some epistemological characteristics of current practice in molecular biology. On the one hand, protocols represent a common ground, i.e. the possibility of reproducibility, which constitutes one of the essential properties for contemporary science to define an actual discovery. At the same time, however, protocols are flexible enough to be adapted by the individual researcher (within a space of maneuver given by the experimental system and by the practices that each individual discipline gives to itself) to his/her specific needs. These variations, just like the recipes, remind us that the legitimacy of an experimental practice, involves both objective and subjective constraints and it is articulated on a fuzzy background rather than a rigid and clear context. Moreover, looking at experiments according to this perspective can provide a key to understanding how different forms of science (which adopt different methodologies but which investigate the same phenomena), such as computational biology, are precisely different in the use of a different "cookbook". Indeed, given the procedural/operational realism of biologists towards phenomena, the clash of different procedures has opened a discussion also about the nature and the meaning of the obtained results. Thus, according to the recipe-perspective that, we propose a constructivist account arguing that the methodological struggle over the nature of biological phenomena (and their ways of discovery) among scientists, might be seen as a not always explicit, philosophical debate, however coming from the practice of science itself.

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1. Introduction

Experimenting is definitely a crucial component of contemporary science.

Nevertheless, philosophy of science, previously focused almost exclusively on the role of theories, began to devote attention to experimental practice, of peculiar sciences such as biology, only a few decades ago (see, among the others, Burian 1997; Schaffner 1993; Bechtel and Richardson 1993; Rheinberger 1997). In biology, experiments have been viewed as procedures to establish causal links (see Woodward 2004), or to provide the empirical basis for the mechanisms that biologists use to study phenomena of interest to them, such as protein synthesis or cell division (Machamer , Darden, & Craver 2000).

However, the way scientists perform experiments is far from being univocal. Indeed, experimenting requires a methodological frame in which to take place but it cannot be fully reduced to the automatic and uncritical application of a methodology. The life sciences might offer a good example to highlight this point.

As also remarked by François Jacob:

> [i]n biology, any study [...] begins with the choice of a 'system'. Everything depends on this choice: the range within which the experimenter can move, the character of the questions he is able to ask, and often also the answers he can give (Jacob 1988, p234).

Rheinberger (1997) famously developed the notion of experimental system as the privileged level of inquiry to better understand the scientific practice of making experiments. The experimental system can thus be seen as the *space of possible manipulations* structured not to answer to specific questions but rather to "poke and prode nature" and observe the outcome of these interventions. Accordingly, in biology, it is the adoption of the system that guides the research (e.g the type of questions to be answered) rather than the theory.

Thus, experimental systems delimit the purpose, the boundaries and constraints of scientists' research efforts. These systems are constituted by the range of techniques adopted, the types of material instruments and resources, and, of course, the models (such as the model organism on which the research will be conducted but also the formal models which will provide a meaningful interpretation of data produced) and granularity of these models (e.g. a murine model may be instantiated by the entire organism or just specific cells of it). In other words, experimental systems are those portions of reality, epistemically and practically individuated, in which molecular biologists try to "make discoveries" (such as the genetic code). In this sense, by following Hacking (1983), experimental systems are those things that allow phenomena to emerge from the chaos of experience, and to let them be isolable, detectable and, measurable. According to Rheinberger (1997) discoveries made within experimental systems do not "exhaust" them. This means that once a particular phenomenon has been discovered, the experimental system can be still serve (being also modified or adapted to) for the discovery of other phenomena, even beyond the previous knowledge of experimenters.

In this discovery process, the experimental practice in contemporary molecular biology oscillates between the creativity of the researcher in tinkering with the experimental system, and the necessity of standardization of methods of inquiry (e.g the way certain cells must be cultured or the order of certain experimental passages or even the temperature to which certain samples must be stored in order to obtain stable/robust results). Roughly speaking, this is due to the fact that science requires reproducible results (in which methodological standardization plays an important role) but also the capacity to evaluate, assess and adapt methodologies to specific questions or problems, thus demanding ways of thinking "out of the scheme". Indeed, a good experimenter is not someone who just knows how to apply a given method, but also the one who can consistently (e.g. not taking random outcomes as wanted or producing evidence through ways that cannot be controlled or replicated) work on the experimental system.

Experimental procedures, when standardized in lab protocols, might definitely be seen as actual recipes. At first glance, in fact, a cooking recipe is, in its way, a codified procedure. Nevertheless, within certain limits (established by the reference community and disciplinary practice), it presents the possibility of being interpreted, updated, modified, even violated.

Nevertheless in the kitchen, as well as in scientific practice, not all violations are acceptable, meaning that not all alterations in the procedure will be compatible with a result that fulfills the criteria of a good experimental practice (or a good dish). In other words, tinkering with the experimental systems (as well while preparing food) cannot be equated to random modification. Rather, it involves the development of a peculiar expertise, both practical and theoretical (see Rheinberger 1997). This kind of expertise should not be intended just as a formal adhesion to certain epistemic principles or methodologies but as the result of a training within a given "epistemic culture" (see Hacking 1983, Rheinberger 1997 and Cetina 1999).

Indeed, those who do not know how to cook make alterations that can, not only produce poor results or not produce results at all, but also violate the recipe to such an extent that it no longer makes it so. Similarly, it may be thought that those who have not been educated in science do not have sufficient knowledge and skills to know within what limits to alter a protocol.

However, it is also worth remembering that the real experimental innovations arise precisely when someone completes a new and totally unforeseen procedure which, however, is able to ″explain″ how much the previous procedures, but through an innovative technical (and conceptual) apparatus (see Feyerabend 1975, Hacking 1983).

Considering scientific protocols as recipes can help us understand some epistemological characteristics of current practice in molecular biology.

As briefly mentioned, on the one hand, protocols represent a common ground, *i.e.* the possibility of reproducibility, which constitutes one of the essential properties for contemporary science to define an actual discovery. At the same time, however, protocols are flexible enough to be adapted by the individual researcher (within a space of maneuver given by the experimental system and by the practices that each individual discipline gives to itself) to his/her specific needs. These variations, just like recipes, remind us that the legitimacy of an experimental practice, involves both objective and subjective constraints and it is articulated on a fuzzy background rather than a rigid and clear context (see also Hacking 1983).

Moreover, looking at experiments according to this perspective can provide a key to understanding how different forms of science (which adopt different methodologies but which investigate the same phenomena), such as computational biology, are precisely different in the use of a different "cookbook".

Indeed, given the procedural/operational realism of biologists towards phenomena, the clash of different procedures has opened a discussion also about the nature and the meaning of the obtained results. Thus, according to the recipe-perspective, the methodological struggle over the nature of biological phenomena (and their ways of discovery) among scientists, might be seen as a not always explicit, epistemological debate, however coming from the practice of science itself.

In this paper, I will argue that experimental protocols and cooking recipes share some remarkable features. The paper is structured as follows. Initially, I will describe what a culinary recipe is and I will highlight some aspects, of a constructive nature, which will be important for the discussion on experiments. Next I will focus on scientific practice and make some examples of experimental protocols to show the similarities with recipes. Specifically, I will argue that both science and cooking, in their practice, are guided by the choice of ″manipulative systems″.

Next, I will show how such analogies allow us to hold a constructivist position about the experimental founding of a scientific claim. Finally, I will argue that such a perspective is also useful for analyzing the current debate between classical manipulative approaches and computational studies in molecular biology. I will then hypothesize that this clash, in addition to more well-known epistemic-methodological problems, also hides deeper and purely philosophical questions.

2. What is a recipe?

At first sight, recipes, as the etymology suggests, are prescriptions. In other words, it is something related to establishing, ordering, or giving a direction, on the basis of previously settled rules or norms. A recipe can be seen as a "what must be done", (e.g. the behavior to be kept) to obtain a certain result. Also according to the etymological dictionary, the term "recipe" later came to designate the instructions for preparing food[1].

According to Borghini:

> In a nutshell, a dish is the *stuff*, a recipe is the *idea*. More precisely, a dish is a specific concoction of (typically perishable) edible stuff, such as *those* specific actions that led to *this* slice of pizza sitting on my kitchen counter. On the other hand, a recipe—in first approximation—comprises the array of repeatable aspects of a dish whose replication would deliver a dish of the same sort. (Borghini, 2015, pp. 721-722)

In his analysis, Borghini observes how, in culinary recipes, there are aspects that usually should be maintained (to obtain a certain dish) and which are normally actions that must be replicable under certain conditions. Modifying certain actions in an arbitrary way (throwing the pasta into the pot before the water is boiling) or not taking into account the context (cooking pasta at high altitude) can result in the *failure* of the recipe and therefore in the non-production of the desired outcome (the dish you wanted to eat).

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[1] https://www.etymonline.com/word/recipe

However it is true that in some situations the recipe takes place as "for the first time", without there being a specific expected outcome. In this case it is as if the chef is *exploring* the possibilities of her/his ingredients, her/his tools, her/his technical skills and her/his knowledge. In other words, she/he is working on an analog of an experimental system: call it the *culinary system*. What she/he can do is not guided solely or mainly by a defined theoretical framework (e.g. ″the rules of Mediterranean cuisine″, if there are any) but by the conditions of the ″culinary system". Indeed, think of the famous "fusion cuisine", where elements and rules of various ″theories″ are amalgamated according to the needs and directions made possible by the culinary system.

Borghini then adopts an approach that we could label as *constructivist* concerning the existence of a recipe.

Accordingly, a recipe is not univocally determined by specific procedures in themselves but by the recognition of the activities that produce the recipe as a legitimate one (by the reference community).

Interestingly, Borghini argues that the recipe exhibits 3 key characteristics.

The first is *expertise*. A cook is not simply someone who knows how to mechanically apply the procedures of the recipes but she/he is someone who knows how to work with these procedures even in a creative but still recognizable way (i.e. she/he tinkers with the culinary system). The cook′s ability to follow recipes and elaborate new ones therefore also lies in her/his training, in her/his immersion in a specific ″epistemic culture" (precisely as an experimenter, see Knorr Cetina 1999 on this aspect).

The second characteristic is the *authenticity* of the dish (as the result of a recipe). According to Borghini, authenticity is based on two distinct values: *fit* and the *approval rating*. The fit of a dish is determined by the ability to resemble what it has been declared to serve and by the context conditions. The cook′s ability to modify the recipe without the final dish not being perceived as too different (that is, it respects certain standards or conventions) falls within the possibilities of operating on the culinary system. In other cases the recipe is modified by circumstances of *force majeure* (think of unleavened bread). In that case the recognition of the dish as such requires a new check of standards and conventions (in the example, at the end the product is still defined as a kind of "bread″). Finally, the recipe is accepted as such by a reference community. Obviously the standards can change over time. There can be more conservative or more progressive attitudes that make membership to the reference class a fuzzy property, at least.

Finally, recipes are *open-ended* processes. This means that they should not conceived into an essentialist frame. As Borghini writes himself:

> The evolution of a recipe rests on a complex historical process driven by multiple variables, including the creativity of the cooks, the opinions of the diners, and the conditions under which the recipe will be prepared. For each recipe, the possible trajectories of evolution are countless. (Borghini 2015 p. 736)

Following this perspective, I will now try to show, in the next sessions, the strong similarities between experimental practices and culinary recipes.

3. Experiments as procedures: an example

In many research areas, such as molecular biology (but not only), for instance, it is possible to discriminate between *experiments to learn* and *experiments to prove (*Franklin 2005, Waters 2007, Boem and Ratti 2016).

The first type refers to a set of new experiments on a given (new) topic fulfilling an exploratory role. Experiments to learn have a less regimented space of maneuver in epistemic terms. This means that scientists pose less constraints because they are exploring either new phenomena or new experimental scenarios. Accordingly, the results of this kind of experiments display a higher degree of uncertainty, but also a proportional higher acceptance, and are less capable of leading scientists to suddenly modify the most accepted theoretical framework. New areas of investigation are more epistemically fluid and a plurality of diverse results (also when contrasting each other) are tolerable.

On the contrary, experiments to prove are usually thought to test the robustness of widely accepted hypotheses. This means that these procedures are that kind of experiments whose results are somehow expected. Thus these experiments serve to check the "current beliefs" (within the epistemic frame in which the specific scientific practice is conducted) of the tester. These types of experiments are usually more standardized, often guided by shared experimental protocols, in order to obtain a clear expected outcome (as in cook′s recipes). Indeed, these experiments have a confirmatory role, in checking the solidity of the experimental system. Therefore, unforeseen results in this situation are perceived as more dubious, they are more rigorously scrutinized, and they often are regarded as methodological mistakes rather than being considered evidence for a change in theoretical framework (see Boem and Ratti 2016, Waters 2007, Franklin 2005).

To provide a simple example of experiments to prove, in molecular biology, it is quite common to check whether a particular protein is present in a given sample. This is relevant for different reasons.

First, the presence of a protein may reveal that a particular molecular pathway is active (or, in other conditions, that it not active). Indeed proteins are so crucial because they constitute many causal actors in biological phenomena (from the vast majority of enzymes to transcription factors).

Second, proteins display several functions. Detecting a protein in a specific cell line, in a given context, may lead scientists to elaborate more precise hypotheses on their phenomena of interest.

Third, the knowledge about proteins is crucial since, for instance, genomic and transcriptional analysis are not sufficient, as such, to claim that a particular protein is actually produced and it is performing a certain function. Molecular biology has developed several techniques to verify the presence of proteins.

One of the most famous is the so called "Western blot" (from now on WB).

It consists of a biochemical technique (indeed a procedure)[2] that allows to identify a specific protein in a biological sample, through the recognition by specific antibodies. Usually, in order to foster recognition, proteins are separated according to their size (or molecular weight) using, generally, a polyacrylamide gel. Next, proteins are transferred onto a support, which is commonly a nitrocellulose membrane. Last, the protein is actually recognized by using a specific antibody.

WB analysis is a particularly useful tool for the confirmation of expected results, *i.e.* checking whether a protein which is expected to be present in the sample is actually there. Thus, if the experiment goes well (meaning it shows what it has been pursued for), normally scientists will conclude that additional evidence has been produced in support of a particular claim. Usually poor (i.e. not easy to understand or "dirty") results can depend on different factors, most commonly due to methodological mistakes. However, sometimes a weird or counter-intuitive result, if confirmed as such, can reveal something different.

Despite the scientific meaning of the WB, if one looks at lab webpages on WB or those of biotech companies advertising for new WB kits, it could be surprised by considering how much many details resemble a recipe.

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[2] In this sense, I use the term "technique" as a collection of activities, codified within a community of skilled practitioners.

First, most of them start by presenting the common/shared ground. A WB is indeed a procedure that can be described through different, codified, steps that can be roughly summarized in this way:

1. Sample preparation;
2. Gel electrophoresis;
3. Transfer on the membrane;
4. Blockade of non-specific membrane sites (meaning to reduce the "noise");
5. Identification of the protein of interest by hybridization with antibodies (a primary that recognizes the antigen followed by a secondary, conjugated to a detection system, which recognizes the primary);
6. Detection of antibody-antigen binding (usually by colorimetric reaction or in chemiluminescence).

However, a list like that is not yet a recipe. This is because it is not "interactive". As a matter of fact a recipe definitely presents a toolbox made of resources and actions but cannot be reduced to that. A recipe should furnish indications (flexible enough) to inform the performer on how to deal with "ingredients" and "techniques". In this perspective a scientific protocol such as the WB is not different.

For instance, let us take the protocol provided by a famous biotech company such as Abcam (https://www.abcam.com/protocols/general-western-blot-protocol). After a brief recap of what a WB is, the page displays some "ingredients" of this scientific recipe, in order to produce lysis, running, transfer, and blocking buffers. The webpage provides a variety of indications suggesting several ways to obtain good/adequate performances or results as recommendations on how properly store the buffers, *e.g.* "these buffers may be stored at 4 °C for several weeks or aliquoted and stored at -20 °C for up to a year", or suggesting possible alternatives *e.g.* "1.0% NP-40 (possible to substitute with 0.1% Triton X-100)".

The protocol continues by indicating how samples for lysate could be prepared. In this case chemical components (i.e. "ingredients") are not just mentioned but concrete actions and modes of interactions are explicitly displayed such as "[p]lace the cell culture dish on ice and wash the cells with ice-cold PBS". Also in this case, sub-procedures are described quite in detail, and epistemically robust alternatives are reported, such as "[s]crape adherent cells off the dish using a cold plastic cell scraper, then gently transfer the cell suspension into a pre-cooled microcentrifuge tube. Alternatively cells can be trypsinized and washed with PBS prior to resuspension in lysis buffer in a microcentrifuge tube". As in cook recipes, qualitative suggestions are also present, such as "[g]ently remove the tubes from the centrifuge and place on ice", thus pointing more at skills resulting from scientific practice rather than forms of propositional knowledge.

This aspect reflects the fact that becoming a working scientific researcher does not imply the simple adherence to a theoretical framework and the application of a set of methodologies. These factors are surely necessary but not sufficient. To become a scientist one should be embedded into a specific "culture", both epistemic and practical (on this aspect see for instance Knorr Cetina 1999). In other words, as Ian Hacking nicely points out:

> In schools and colleges experiments are repeated ad nauseam. The point of those classroom exercises is never to test or elaborate the theory. The point is to teach people how to become experimenters. (Hacking 1983, p.231).

These recommendations, which are directed to the scientist itself (so the subject who is pursuing the experiment), are perfectly understood by someone who is in control of a theoretical and methodological apparatus but yet they go beyond, calling for his/her personal judgement to come into play. As already mentioned, making experiments requires a subjective capability involving a balance between the adherence to the common framework and the possibility to violate it. This requests inventing ingenious ways that need to preserve reproducibility and consistency (in order to face the burden of proof of the scientific community and not to fabricate results) but also to go beyond them. On this fact, coming back to the WB Abcam protocol, it is worth noticing how the webpage displays also a tutorial video (analogous to those appearing on recipe websites or tv cooking channels) showing a scientist performing the experiment in its all steps.

If we take a WB protocol from another bio-tech company, the situation is obviously similar but also with peculiar differences. Let us briefly examine, for instance, te protocol of Cusabio (https://www.cusabio.com/m-244.html). In this case, when the protocol describes the preparation for lysate (which represents a shared-required passage), we find more information: "[a]fter the cell confluence reaches 80%, place the cell culture dish on ice and wash the cells with ice-cold PBS for 3 times". Indeed, while the types of action are almost the same, their instantiation differs a lot in terms of qualitative components and in additional recommendations. As a matter of fact, we can see that here there are more indications on how interacting with the experimental system. For instance, the protocol recalls some parametric threshold (*i.e.* confluence) and also suggests to repeat the washing 3 times, at least.

More precision in this details might also affect the perception of the experimenter in the light of his/her expertise. Beginners will be more confident if their space of maneuver will be restricted, while senior scientists might find certain specification too strict since they might be too general and less flexible to be adapted to the particular given samples. This also means that differences in protocols may reflect differences in their capacity of being modified according to specific needs, thus displaying distinct appeals to scientists.

Next, there can be other discrepancies. In the case of Cusabio, for instance, there is no video showing the procedure, however at the end of the protocol some tables are displayed, filled with more frequently asked questions. Some of those concern bad (e.g. the result is not clearly legible or it presents such a poor outcome that contradictory conclusions might be derived) or unexpected results. This could be extremely instructive since they can guide the scientists in his/her choices. Moreover these questions can also suggest possible explanations that could help the researcher in the evaluation of the protocol and of the ways to modify it in a successful manner.

4. Recipes as modes of knowledge

From these simple cases we can derive some important lessons.

The triumph of molecular biology as a discipline (compared to natural history) that "makes discoveries" goes along with other experimental sciences (see Morange 2000 among the others). Accordingly, understanding nature requires manipulation and it cannot just be observed, untouched. In other words, the natural world must be also directly questioned. Thus, the practice of experimenting is somehow "questioning nature" and depending on the types of questions and the modes of asking, different kinds of answers can be obtained. Scientific questions appear to be more robust and conclusive that normal ones. This is because they are methodologically structured and controlled. However, as already mentioned, scientific methodology does not consist of merely applying a set of procedures. The application of procedures is always sensitive to the experimental system.

Thus, like recipes, experiments are a *constructive* enterprise between the experimenter and natural world. However, this should not be intended, naively, in a strong sense. “Construction” does not mean “creation”. Phenomena of course are neither “fabricated” nor “solipsistically generated”.

Nevertheless, scientists do not simply observe the phenomena. They need to let them “emerge” from the chaos of perceptible world. Thus, again following Hacking’s suggestions, the procedural aspect of scientific efforts, with its balance between tinkering and standardization, allows scientists to highlight the phenomena, otherwise hidden within (and immersed in) the complexity of the real world.

As Hacking puts it:

> In nature there is just complexity, which we are remarkably able to analyse. We do so [...] by presenting, in the laboratory, pure, isolated phenomena (Hacking 1983, p 226).

Experimental protocols, like recipes, have their power also constrained by the “obstinacy of data”, meaning that the empirical world offers a resistance, as a sort of friction, limiting the space of experimental possibilities and because of that enhancing the creative capacities of the experimenter. As in formal disciplines, where constraints are an essential ingredient for the development of techniques and results, so in the experimental context, material constraints and patterned and regulated procedures constitute the basis for making the scientific enterprise innovative and successful.

Particularly in molecular biology the practice of experimentation - the making of science - often precedes the theoretical specification at the epistemic level. Following Hacking’s idea (1983), experiments have their own life. This is not to say that theory does not play any role in the development of molecular research. However, those epistemological reconstruction that rely just on theoretical justification fail to entirely grasp the efforts of contemporary biology. Accordingly, it is the *manipulation* of scientific entities (such as genes) at the experimental level, that grounds the possibility of a more adequate epistemic understanding of what molecular biology is in its practice[3].

As in a recipe, we do not judge the outcome of an experiment only on the basis of its adherence to the standardized result. If so, it would be like, selecting cooking utensils before examining the ingredients and then believing in the

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[3] The debate on this issues is extremely vast. Concerning, more in general, the role of theory in science, see among the others Duhem 1906, Hanson 1958, Popper 1959, Van Fraassen 1980, 2008, Bechtel and Richardson Galison and Daston 2007

goodness of our results based on the fact that we managed to cook something edible. In the same way, experimental techniques and protocols are not created a *priori*, by virtue of the postulation of the entities (*e.g*: a gene) involved in our experiment. Rather, scientists ″cook″ the recipes of science, building procedures that are necessarily shaped, modified and updated in comparison with the object of study. However, this object is not simply "given" to the experimenter. Rather, it is formed precisely by virtue of its possible capacity to be manipulated. Different approaches to manipulation will guarantee interventions of different depths and therefore the creation of new conditions, which will make new phenomena ″emerge″, by presenting them in "isolation". It is not possible in this sense, not to mention Woodward′s *theory of manipulability* (Woodward 2004). In brief, this theory provides an account of the necessary and sufficient conditions for any factor to be a cause of a phenomenon, in the light of a set of considered variables. Accordingly, experimental manipulations should be understood as the possibility of changing the factor being investigated, preserving the other variables. In this way it is possible to ″measure″ the causal contribution of a factor on the result.

In this sense, controlled experimentation, that is the application of a protocol, (or a recipe), offers a constrained context in which verifying causal relationships. Indeed, the procedure, by virtue of its manipulability, allows scientists to directly control the factors involved in the investigation, giving the possibility "to scroll" the protocol also back and forth, to review certain passages etc. By breaking down and articulating the causal path in a manipulative protocol, scientists can control their activity, make assumptions to improve some steps or identify errors and shortcomings, even trying to understand "where″ (i.e. at which stage of the procedure) the procedure has not been effective in obtaining the result.

Finally, again following Woodward (2004), the manipulative protocol facilitates the description of the causal links in counter-factual terms. Obviously in this case the interest is not abstractly epistemological: the ″possible worlds″ with which to evaluate the different causal patterns are not the result of similarity criteria of a purely theoretical-metaphysical nature but rather determined by material conditions of manipulation and intervention.

By adopting the characteristics developed by Borghini about the recipes, let us now try to see what are the analogies with the experimental practice.

First of all the *expertise*.

As already analysed, being a scientist does not simply mean applying procedures (mechanically) or adhering to a method in an uncritical way. Experimenting is an activity that requires a specific training within a given epistemic culture. This training is not aimed only at the acquisition of technical-practical skills (however necessary to become experimenters). The specific expertise grants the possibility of operating on the experimental system in a consistent way. Like the expert cook who alters recipes by hypothesizing which changes might be promising (but also recognizing those alterations that have led him/her astray), so the experienced experimenter is able to modify the experimental protocol by evaluating where the result will be robust. Similarly she/he will be retracing her/his steps if the outcome is not sufficiently controllable/replicable (it is assumed that there is an ethics of the research and that obviously the experimenter does not aim to falsify the results).

Second, *authenticity*.

The "fit" of an experimental outcome is also determined by its resemblance with certain types of results (e.g. it is possible to claim that a given protein is present in the sample). The experimenter's ability to modify the protocol without outcome being perceived as too different falls within the possibilities of operating on the experimental system. Finally, a protocol is accepted as such by a reference community. Also in this case there can be more conservative or more progressive attitudes within the community. For instance (as presented more in depth in the next section) the debate over biological claims made due to computational approaches were firstly questioned precisely because the community did not recognize them as experimentally grounded.

Finally, *open-endedness*.

By paraphrasing Borghini (2015), the evolution of a protocol rests on a complex historical process driven by multiple variables, including the creativity of the experimenter, the opinions of the peers and colleagues, and the conditions under which the protocol will be constructed. Again, the case of in silico exploratory experiments is intriguing, given that there is a fierce debate, within scientific community (see for instance Ratti 2015 and Boem and Ratti 2016) as to whether such approaches can be considered legitimate (i.e. comparable to experimental ones) ways of producing scientific results.

Last, this picture also offers us an indication of the type of knowledge produced in this way. Summing up, biological phenomena are studied through procedures, within experimental systems, which allow to circumscribe and put in evidence the "objects" or the "processes" of interest. The resulting knowledge is shaped and developed by inducing the experimental system to react. These reactions through material modifications that conform to excitatory and inhibitory strategies.

The similarities between experimental protocols and recipes allow us to formulate a further argument in favor of constructivist-interactionist approaches about establishing scientific facts. Through this interpretative lens, among other things, it is possible to better justify the ongoing clash, within molecular biology, about the supremacy of experimental approaches over computational ones (see the next section).

Thus, according to this perspective, the natural world is investigated by "cooking with it", altering, adapting and modifying the experimental system, which represents the constraints shaping the space of maneuver of the experimenter. Following the analogy with cooking, these results of scientists' activity on the natural world produce the material part of the "dish" we "feed" our mind with: knowledge.

5. Another type of knowledge?

As already mentioned, experiments in molecular research are not usually performed in order to test theories (see Burian 1997, 2007; Rheinberger 1997, O'Malley 2007; Waters 2007). Most likely, experiments pursued through roughly standardized protocols are crucial tools in order to select and formulate hypotheses regarding working models.

However, this is not the only way to do biology nowadays.

Starting with the Human Genome Project (HGP), a different style of doing molecular biology has come into play. As matter of fact, some people do not consider these approaches as truly molecular: it is a "different book of recipes". It is *computational biology*. A new method to "generate" (à la Hacking) biological phenomena, by applying *in silico* tools and often relying on the so called Big Data science (see Boem and Ratti 2016).

Even if we do not have a clear definition, computational biology is not just "biology plus the computers". Some crucial features, such as the capacity to process a vast amount data in a short time and order and cluster them to provide general representations, definitely characterize and distinguish this new scientific enterprise from more traditional ones (Kitchin 2013, 2014, Boem and Ratti 2016).

These kind of science is now becoming ubiquitous in several areas of biological studies. Moreover, this has impacted the way science is organized at the institutional level. The shift towards computational approaches has prompted the creation of big consortia, such as the Encode Project Consortium, Roadmap Epigenomics Mapping Consortium, and The Cancer Genome Atlas.

These institutions have started to generate unprecedented, vast databases. The most striking feature is that these database are not just repositories. They can be used, explored. Even more, their data can be ordered and reordered in order to produce new and different biological knowledge (Boem and Ratti 2016).

In other words, this "new biology", is mainly pursued just *in silico.* Thus, the practice of data-mining, is not only a way to recover the information stored within databases. Rather, it is a way to pursue a new kind of experiments, which lack the material component and yet are extremely "real". By that it is meant that computational/in silico experiments can produce knowledge (complementary to experimental one) which can be directly used to make predictions and guide other interventions (also material ones). For instance, Ratti (2015) has highlighted how some computational approaches may provide so-called ″eliminative inferential procedures″. Such research strategies constitute a new tool in prioritizing certain mechanistic hypotheses and may even contribute to developing new ones. In addition, computational biology can also serve as an *in silico* version of exploratory experiments. These explorations will obviously be ″large-scale″ ones, aimed at more generalized claims (compared to more fine grained ones of material explorations) and oriented towards the integration of the hypothesis prioritization procedure.

Moreover, Boem and Ratti (2016) have also shown how, in computational biology, scientists still perform experiments, *i.e.* they put in place forms of interventions, even in absence of material manipulation. Indeed, data can be ordered and reordered within datasets, thus highlighting hidden information (pattern-dependent) that can be used to produce new discoveries.

However, these experiments are different. They follow different standards, they display different techniques, producing different kind of outcomes with different explanatory features and powers. Even more, the rise of computational biology has generated a heated debate concerning the nature of its discoveries, its scientificity and reliability (Boem and Ratti 2016). These differences are not affecting just the methodology. Rather, they touch the implicit ontological aspect of scientific research.

It would be like saying that the scientists here are not only cooking different recipes, but adopting a recipe book and new practices, such as cooks who generate dishes with tastes and flavors never tried. These new dishes not only reveal properties of the ingredients that were previously "invisible", but also show associations and combinations that were impossible to achieve with traditional forms of cuisine.

The difference could be such as to make someone asks if it really is food or rather something else. The results are certainly edible, but the flavors and textures are so strange or unusual that one may think that, in fact, we are faced with something profoundly different. The way people taste are deeply rooted (culturally) and traditions play a fundamental role in the judgment given on the dishes. These aspects often discriminate what we consider food (implicitly ontologically) from what it would be not (think about bats in Wuhan!).

In the same way experimental traditions, arisen and flourished within certain epistemic cultures, shape scientists' ontological dictionary (not always explicit or aware). Thus, following Hacking's famous motto ("if you can spray them, they exist", 1983), it is easy to show that molecular biologists adopt a sort of procedural/operational realism of biologists towards phenomena they can observe through their manipulatory protocols. Accordingly, the struggle between molecular and computational biology can be seen as the clash of different procedures. Such a controversy has definitely opened a discussion about the nature of the results obtained. This because the underlying *operational realism* is different and differently founded.

Paying attention on the different "recipes" scientists use to "cook" the natural world, could offer a new perspective to analyze the struggle, among scientists, over the nature of biological phenomena (and their ways of discovery). Such a struggle is not only a the epistemic level. It is also a struggle over realism of scientific objects, differently produced. Indeed, another hidden, philosophical debate, from the practice of science itself.

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