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The Limits of Reductionism in the Life Sciences

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Abstract

In the contemporary life sciences more and more researchers emphasize the “limits of reductionism” (e.g. Ahn et al. 2006a, 709; Mazzocchi 2008, 10) or they call for a move “beyond reductionism” (Gallagher/Appenzeller 1999, 79). However, it is far from being clear what exactly they argue for and what the envisioned limits of reductionism are. In this paper I claim that the current discussions about reductionism in the life sciences, which focus on *methodological* and *explanatory* issues, leave the concepts of a reductive method and a reductive explanation too unspecified. In order to fill this gap and to clarify what the limits of reductionism are I identify three reductive methods that are crucial in the current practice of the life sciences: decomposition, focusing on internal factors, and studying parts in isolation (i.e. not *in vivo*). Furthermore, I argue that reductive explanations in the life sciences exhibit three characteristics: they refer only to factors at a lower level than the phenomenon at issue, they focus on internal factors and thus ignore or simplify the environment of a system, and they cite only the parts of a system in isolation.

Keywords:

reductionism, reductive explanation, decomposition, part-whole, simplification

1. Introduction

The issue of reductionism has a long history in the philosophy of science. It also is a controversial topic in the life sciences themselves, and scientific publications referring to reductionism have increased in the last decade. However, in the majority of cases the reference to reductionism is negative: life scientists highlight the “limits of reductionism” by investigating the behaviour of complex system (e.g. Ahn et al. 2006a, 709; Mazzocchi 2008, 10); they offer substantial evidence “against reductionism” in biomedical research (Levenstein 2009, 709); and they call for a move “beyond” or “away from reductionism and toward a new kind of biology for the 21st century” (Gallagher and Appenzeller 1999, 79; Elser and Hamilton 2007, 1403). Richard Dawkins has claimed that reductionism is “one of those things, like sin, that is only mentioned by people who are against it” (1996, 13). Although this may be an overstatement, it does capture something about the current situation in the life sciences, where the topic is usually only brought up in order to criticize reductionism or to point out its limits.

What is the reason for this current skeptical or even hostile stance on reductionism? The story that is commonly being told goes as follows: With the rise of molecular biology in the 1950s and 60s research in the life sciences became mostly reductionist. In order to explain a certain behaviour of a biological system (e.g. protein synthesis) the system was dissected into its parts (mostly, into molecular parts) and the parts were studied in isolation. In the 1970s and 80s molecular biology (and with it many other disciplines) “went genomic” (Darden and Tabery 2009). The attention shifted towards discovering the DNA-sequence of the genome of various organisms, including humans (Venter et al. 2001). Information about genetic structure

and about the molecular processes that are involved in the expression of genes was expected to explain the occurrence of phenotypic traits. With respect to human diseases like cancer, diabetes, and schizophrenia the idea was that a limited number of genetic variants would be discovered that explain why these diseases occur and provide the required information to cure them. In short, the optimistic idea was: “A gene is broken, fix the broken gene and cure disease” (Joyner and Pedersen forthcoming, 1018).

It turned out that things were much more complicated than originally anticipated. Nowadays, in the so-called “post-genomic era”, most researchers are skeptical about reductionist studies that claim to have discovered one or a few genes responsible for complex diseases like depression, cancer or Alzheimer’s disease. In the “century beyond the gene” (Keller 2005, 3) it has been realized that the relation between genes and phenotypic traits is much more complex than the reductionist picture suggests. A single gene can influence multiple phenotypic traits (pleiotropy), the expression of a gene can alter the expression of another gene (epistasis), and many different genes may be involved in the formation of a single trait (polygenic inheritance). Most complex diseases, for instance, are caused by various risk factors, each of which often has only a relatively weak effect (Buchanan et al. 2006). In addition, more and more life scientists emphasize that the behaviour of complex systems cannot be fruitfully investigated and explained merely on the level of isolated parts of the system (e.g. Kitano 2002; Service 1999). They argue that a non-reductionist approach is needed which takes into account the “system as a whole”, studies the dynamical interactions between parts of the system, and also attends to environmental influences on the system’s behaviour (Chong and Ray 2002, 1661).

In sum, the prevalent opinion in the life sciences seems to be that, if the complexity, dynamics and context-sensitivity of biological systems is to be taken seriously, then this requires abandoning reductionism or, at least, to recognize its limits and supplement it with a more holistic, systems-oriented approach – as it is, for example, aspired by systems biology.¹ At first sight, this seems to be very plausible. But what makes research in the life sciences an implementation of reductionism? What does it mean to investigate and explain biological systems in a reductionist manner? How does a researcher move beyond reductionism? My thesis is that without a definite answer to these kinds of questions it remains obscure what the message of the above cited scientific papers is and where exactly the limits of reductionism lie. Although the biological literature provides many fruitful insights to answering these questions, it lacks an explicit and coherent account of what exactly reductionism is and what it is that constitutes the reductive character of explanations. Philosophy can and needs to provide remedy here. In this paper, I will provide answers to the above questions by offering such an account of reduction.

However, it is not the case that only science can profit from philosophy. I think, the other way round, philosophy also needs to pay special attention to science. The new developments in the life sciences with their special focus on complex behaviours of systems provide new resources as well as new challenges for philosophy. At this point I agree with Sandra Mitchell who has recently argued that we need a broadened philosophical perspective and new analytical tools in order to account for the contemporary practice of the sciences of complex systems (Mitchell 2009, 1-5 and 11-19). Contrary to her (Mitchell 2009, 21-25 and 105-107), however, I emphasize that this also holds for the practice of reduction. Although much water

has flown down the river since Ernest Nagel (1961) developed his classical model of theory reduction, I think the current philosophical debate about epistemic reductionism and reduction in the life sciences is not satisfactory. There are some philosophers who cannot let Nagel's model go (e.g. Dizadji-Bahmani et al. 2010; Schaffner 1993, 2006; and Bickle 1998, 2003), at least not his focus on formal issues and on theories as the key units of reduction (Kaiser forthcoming). Others abandon the concept of reduction altogether (e.g. Bechtel and Richardson 2010; Craver 2005, 2007; Darden 2005; Darden and Maull 1977). But the majority of philosophers agrees that we need a revised and elaborated philosophical account of what reduction in the life sciences is. And although there are some promising approaches (e.g. Wimsatt 2007; Sarkar 1998, 2005a; Hüttemann and Love 2011), an established and in-depth account of reduction that takes the contemporary developments in the biomedical sciences seriously is far from accomplished. The goal in this paper is to fill this gap and to provide a scientifically informed account of what life scientists mean when they talk about reductionism, about the limits of reductionistic research strategies and about the inadequacy of explaining the behavior of complex systems or complex diseases in a reductive manner.

In the first part of my analysis (Section 2) I reveal which kinds of questions about reductionism life scientists are primarily interested in. It turns out that their discussions are centered on methodological and explanatory issues but that from the discussions alone it is not clear what exactly reductive methods are, which characteristics make explanations reductive, and what their limits are in investigating and explaining complex systems. I provide an answer to these questions in the second part of the paper where I develop my own account of what reductive methods and explanations are (Section 3, 4, and 5). I start with the

most well-known reductive method of decomposition, which often leads to the construction of part-whole explanations (Section 3). I identify the lower-level character of part-whole explanations as the first characteristic that all reductive explanations in the life sciences exhibit. Furthermore, I argue that there is a subset of lower-level reductive explanations, that is, fundamental-level reductive explanations (i.e. molecular or genetic explanations), and that discussions about explanatory reductionism should not be restricted to this second, narrower understanding of reductive explanations. In Section 4 I discuss a second reductive strategy that is used in scientific practice, namely the method of focusing on internal factors and ignoring or simplifying the environment. Correspondingly, I reconstruct a second feature many reductive explanations in the biomedical sciences possess, namely that they focus on internal factors and include environmental factors only in form of background or input conditions. Finally, I identify the strategy of investigating the parts of a system in isolation as a third important reductive method in the research practice of the life sciences (Section 5). This strategy corresponds to a third characteristic of reductive explanations, that is, that they refer only to parts in isolation. I propose that this should be understood in the sense that reductive explanations include only those relational properties and interactions between the parts of a system that can be studied *in vitro* (and not *in situ*).

2. What Is the Subject of Debate?

A look into the current biomedical literature reveals that almost all discussions about reductionism and its limits are focused on methodological and explanatory issues. The central

question life scientists are concerned with is not whether, for instance, cells “really” are composed of proteins, DNA, and other macromolecules only, interacting in certain ways with each other to produce higher-level effects. It is also not whether the theories, laws, and concepts from one field can be reduced to those of another field. Rather, they are interested in how to carry out fruitful research and how to develop adequate explanations. Their question is whether applying reductive methods is a permissible and profitable research strategy, and whether the resultant reductive explanations of the system’s behavior can be considered adequate explanations or not.

How does this diagnosis relate to the philosophical debate about reductionism? Philosophers have early recognized that the issue of reduction comprises different kinds of questions. Francisco J. Ayala (1974) first introduced such a distinction of different types of reductionism. He distinguished ontological, methodological, and epistemic reductionism. Since then, his classification has been taken up and revised by many authors.ⁱⁱ This distinction has even made its way into the life sciences itself, although relatively few scientists have picked it up (e.g. Fang and Casadevall 2011, 1401; Mazzocchi 2008, 11). Before I specify what kind of reductionism the debates in the life sciences are about, let me briefly characterize these different types of reductionism.

Ontological reductionism is a claim about what kinds of entities exist in the world. It is assumed that there exists nothing over and above physical objects, properties, events, facts, etc. – for example, no vital forces. Every particular biological object (e.g. an ecosystem, organism, organ or cell) is composed of nothing but physical or physicochemical objects (e.g. molecules, atoms, quanta) and can in this sense be reduced to them.ⁱⁱⁱ This thesis is also called

token-physicalism. It is important not to confuse token-physicalism with the claim that biological types of objects or properties can be reduced to physical types. This would also be an ontological-reductionist thesis but contrary to the reducibility of particular biological objects (tokens), which is nowadays widely accepted in the debate, the reducibility of types of biological objects or properties (e.g. the type 'wing' or 'being a Mendelian gene') is considered as highly problematic, due to the multiple realizability of such types. In philosophy of the life sciences, ontological reductionism in the weak version of token-physicalism is an assumption shared by everybody, and discussed by almost nobody. "We're all physicalists now," as Alexander Rosenberg (2006, 4) once put it.

Methodological reductionism is a thesis about the most successful way of conducting biological research. It is claimed that biological systems are most fruitfully investigated when reductive methods (or strategies or "heuristics;" Wimsatt 2007, 76) are applied, for instance "decomposition and localization" (Bechtel and Richardson 2010, xxviii), simplifying or ignoring the environment, and simplifying the organization of the system's parts. Proponents of methodological reductionism make the normative claim that systems should be investigated in a reductionist manner and that researchers should seek reductive explanations even for the behaviour of complex systems.

Epistemic reductionism is neither a normative thesis nor a claim about the actual practice of biological research. It is rather a thesis about the *result* of this process, i.e. biomedical knowledge, or elements of it like theories, laws, explanations, etc. For a long time the debate about epistemic reductionism was centered on theories (which Nagel conceived as sets of law statements; 1961, 80) as the relevant epistemic units of reduction, and the relation of

reduction was characterized in a formal manner, that is, as a relation of logical derivation (*theory reductionism*). In addition, the debate focused on quite global cases of reduction like the reduction of biology to physics and chemistry or at least to molecular biology (Rosenberg 2006), and the reduction of classical genetics to molecular genetics (Kitcher 1984). Hence Francis Crick's famous claim, that the "ultimate aim of the modern movement in biology is to explain all biology in terms of physics and chemistry" (Crick 1966, 10). Thus, the central question was whether the knowledge of one scientific domain (consisting primarily of theories and laws) could be reduced to the body of knowledge in another domain. Some biologists have this kind of global theory reductionism in mind when they reject epistemic reductionism (Mayr 1988, 475) or when they stress that this is *not* what they are talking about (Fang and Casadevall 2011, 1401).

However, to focus on theories, formal issues, and global cases of epistemic reduction is not the only option and, as I have argued elsewhere (Kaiser forthcoming), it does not capture the cases of epistemic reductions that in fact are most important in the research practice of contemporary life sciences. A more promising way to specify epistemic reduction is to turn towards individual reductive explanations. This is how philosophers like Sahotra Sarkar (1998, 2005a) or Andreas Hüttemann and Alan Love (2011) proceed, and it is also the strategy I will adopt. The disputes about *explanatory reductionism* that correspond to this kind of analysis do not center on global questions such as whether all biological explanations can be reduced to molecular and in the end physical explanations. They also do not correspond to the kind of explanatory reduction Rosenberg defends as "Darwinian Reductionism" (2006). Rosenberg characterizes explanatory reduction as the "transformation" (53) of a higher-level

explanation to a lower-level (i.e. molecular) explanation of the same phenomenon. This kind of explanatory reduction is different from the kind that is involved in reductive explanations. As I will elaborate in the subsequent sections, in reductive explanations the relation of reduction holds not between *two different* explanations of the same phenomenon but between the *explanandum* (i.e. phenomenon to be explained) and the *explanans* (i.e. explanatorily relevant factors) of *one particular* explanation. More specifically, the relation of reduction in reductive explanations holds between a representation (or description or model) of the phenomenon (or behaviour of a system) to be explained (*explanandum*) and the representation of the causal factors referred to in the explanation (*explanans*), which I will call explanatory relevant factors. Hence, discussions about reductive explanations concern their frequency and especially their adequacy with respect to a limited class of phenomena investigated in a specific field. Explanatory reductionists argue that the behaviours of systems studied in a certain field (or at least part of it) can be reductively explained and that these reductive explanations are adequate. Opponents of explanatory reductionism, in contrast, underline the limits of reductionism by arguing that all, most or some reductive explanations of the behaviour of the systems in question are inadequate.

It is these kind of explanatory issues, alongside questions about methodological reductionism, that life scientists at present are concerned with. Consider the example of virulence (i.e. degree of pathogenicity) of microorganisms like bacteria and fungi. Some microbiologists, who study this phenomenon, also reflect about the issue of reductionism (e.g. McClelland et al. 2005; Casadevall et al. 2011). They primarily ask whether it is appropriate or not to pursue a reductionist research strategy that identifies a set of microbial characteristics associated with

virulence independently of each other and independently of the conditions that are present in a susceptible host. A closely related question is whether the resulting reductive explanation of the virulence of a certain microbe adequately accounts for observed variation of virulence in relation to other factors and to host dependence.

These microbiologists do not question whether a microbe is composed of a variety of different macromolecules interacting with each other (ontological reductionism).^{iv} They are also not interested in disputing epistemic questions in the spirit of theory reductionism, nor do they wonder, in the spirit of Rosenberg, whether all microbiological explanations can be reduced to biochemical or physical explanation. Microbiologists are not engaged in discovering laws of nature or developing global theories. Instead, the discussions of microbiologists center on methodological and explanatory reductionism: Is the application of reductive methods the most fruitful strategy to study the virulence of microbes? And are reductive explanations (which are frequently the result of applying reductive methods) the most adequate modes of explaining the virulence of a certain kind of microbe?

As I have pointed out in the introduction, the overall tone of the current discussions about methodological and explanatory reductionism in the life sciences is negative. The argument is that, especially when it comes to the behaviour of complex systems and to complex diseases, reductive research strategies are either of limited value (e.g. Gallagher and Appenzeller 1999; Ahn et al. 2006a) or completely misleading or “ineffective” (Soto et al. 2009, 5) because they provide deficient results and, if applied exclusively, they result in inadequate reductive explanations. Hence, many contemporary life scientists challenge the normative thesis of methodological reductionism that research should always be pursued in a reductionist manner.

Likewise, they question the correctness of explanatory reductionism by pointing out that many phenomena cannot be adequately explained in a reductive manner. However, it is important to note that, despite their overall negative attitude, most scientists concede that reductionist research strategies have been and still are of value and that the behavior of many systems can adequately be explained reductively. One can read statements like “Reductionism has served [...] biologists well in the past decades” (Powell 2004, 299), or “Over the past century, significant advances in medical practice and healthcare have been achieved based on traditional reductionist biomedical research” (Roukos 2011, 695). In general, criticisms of reductionism in the life sciences tend to point out only that the value of reductive methods and the adequacy of reductive explanations is *limited* (Fang and Casadevall 2011, 1402). For instance, reductive explanations are only adequate with regard to a limited class of phenomena like acute, simple diseases (e.g. urinary tract infection, appendicitis, etc.; Ahn et al. 2006b, 2). Or reductive strategies provide only limited insights into a complex system, that is, insights into the behaviour of the isolated parts but not into the “dynamics of a system as a whole” (Sorger 2005, 9).

In this section it should have become clear what kinds of questions about reductionism life scientists nowadays are concerned with. However, in order to understand what exactly the envisioned limits of methodological and explanatory reductionism are we need to understand what methodological and explanatory reduction is. For instance, one cannot understand why reductive explanations of a certain class of phenomena are inadequate without understanding what constitutes the reductive character of an explanation. Likewise one cannot assess the limitations of investigating complex systems by applying reductive methods without knowing

what characterizes a reductive research strategy. In the remaining sections of this paper I will provide this understanding, that is, I will base the scientific debates on methodological and explanatory reductionism and their limits on an explicit and coherent philosophical account of what reductive methods and reductive explanations are.

3. Decomposition and Part-Whole Explanations

When life scientists discuss reductionism they frequently mention the strategy of “dissecting... systems into their constituent parts” (Van Regenmortel 2004, 1016) for which Bechtel and Richardson (2010, 23) have proposed the term “decomposition”. The strategy of decomposing a system into its parts, components or constituents (I will use these terms interchangeably) can be regarded as the reductive method *par excellence*. It is also named “analysis” (Mayr 1988, 475; cf. Mazzocchi 2008, 10) and, since the system is considered to be located on a higher level of organization than its components, decomposition is characterized as involving “downward looking” (Lidicker 1988, 278; Bechtel 2009, 543). Into which parts a system is decomposed depends on technical constraints, on the explanatory interests and “perspectives” that are accepted in a given field (Wimsatt 2007, 227), and on how the behaviour of the system to be explained is characterized (Glennan 2002, 344; cf. Kauffman 1970, 258, 260-263).

Applying the reductive method of decomposition successfully usually leads to the development of a certain kind of explanation which is called part-whole explanation. It is conceived as being *the* paradigmatic case of a reductive explanation in the life sciences.

However, two things should be noticed: First, the application of reductive methods like decomposition does *not always* give rise to the construction of *reductive* part-whole explanations. On the one hand, the attempt to develop an adequate reductive explanation by applying reductive methods can *fail*. For instance, sometimes a complex system can be dissected into parts but it turns out that studying the parts in isolation does not shed light on how the parts behave *in situ* (i.e. in the system). On the other hand, the fact that *some* of the applied methods are reductive does not guarantee that the resulting explanation is reductive, too. For example, a complex system is decomposed into its parts but it turns out that not only the parts but also higher level or environmental factors are important for explaining the behaviour of the system. In such cases utilizing *reductive* methods (together with non-reductive methods) can lead to the development of *non-reductive* explanations. Second, although part-whole explanations are paradigmatic cases of reductive explanations not *all* part-whole explanations are reductive explanations. This will be an important result of my subsequent analysis: For an explanation to be reductive it needs to satisfy more conditions than just being a part-whole explanation. What these additional restrictions are will become clear in the next sections.

But first things first. Before we move on to these additional characteristics of reductive explanations let us dwell a bit on the thesis that reductive explanations are part-whole explanations developed by decomposition. An example of a reductive part-whole explanation is the explanation of sickle-cell anemia. This disease is explained by decomposing the organism (the “whole”) into certain parts and describing interactions between these parts. Of primary interest are the mutations that occur in genes coding for hemoglobin, how modified

hemoglobin molecules affect the shape and elasticity of red blood cells, and through which physiological processes this, in the end, brings about a specific disease pattern (e.g. vaso-occlusive crisis, aplastic crisis, etc.). Characteristic for reductive part-whole explanations is that they bridge (at least) two levels of organization: the higher level of the phenomenon to be explained (e.g. sickle-cell disease) and the lower level(s), on which the explanatory relevant factors cited in the *explanans* are located (e.g. mutated genes, hemoglobin, blood cells, etc.). In other words, part-whole explanations are reductive because they explain a certain phenomenon *exclusively* in terms of entities (and interactions among those entities) located on a *lower level* than the phenomenon. Since the direction of a part-whole explanation runs from the lower level to the higher level life scientists also refer to them as “bottom-up” explanations (Sorger 2005, 9; Soto et al. 2009, 5) or “upward explanation[s]” (Mikkelsen 2004, 120).

It is important to note that many discussions about reductionism in the biomedical sciences are based on a far narrower picture of what a reductive part-whole explanation is. In particular researchers, who adopt a critical attitude towards reductionism, identify reductive explanations with molecular or genetic explanations. This is evident, for instance, in the following statements:

[B]iological research became largely reductionist (i.e. increasingly involved in the analysis of *molecular* details). (Grizzi and Chiriva-Internati 2005, 29; my emphasis)

[A] great number of biologists insist that explanations should always be sought for at the *gene* and/or *gene product level* [...]. This stance [is called] genetic reductionism [...]. (Soto and Sonnenschein 2005, 104; my emphasis)

As these citations reveal, exploring the behaviour of a system in a reductive manner is often equated with decomposing the system into molecular parts or trying to identify the genes and the (molecular) gene products that give rise to the behaviour of the system. Accordingly, the concept of a reductive (part-whole) explanation is narrowed down to a molecular and/or genetic explanation. I call this narrower understanding of reductive explanations *fundamental-level reduction* since in many fields the molecular level (including genes) is conceived as being the “fundamental level” on which, not all explanations, but all *reductive* explanations “bottom out” (Machamer et al. 2000). Some philosophers use the term ‘*fundamental*’ in a broader sense. That is, they call any level on which explanations of a certain biological field bottom out “relatively fundamental” (Machamer et al. 2000, 13). In this sense “more fundamental” means the same as “being located on a lower level” (e.g. Hüttemann and Love 2011, 527-530). As a consequence, almost each biological level can count as (relatively or locally) fundamental, i.e. as fundamental with respect to a phenomenon or a certain field. By contrast, I use the concept in a more restricted sense as referring to a level which is designated to be *the one level* on which all biological explanations bottom out.

Such a narrow concept of a reductive explanation is, for example, presupposed in the dispute about reductionism in cancer research (e.g. Malaterre 2007, Soto and Sonnenschein 2005, 2006). In this debate the controversial issue is whether the reductionist approach (i.e. the somatic mutation theory, in short ‘SMT’; cf. Weinberg 1998) provides an adequate

explanation of carcinogenesis. Researchers in the tradition of SMT explain cancer by identifying the genes in a cell, whose mutations cause the tumor progression, and the intracellular molecular process that are involved. Opponents of SMT deny the adequacy of this reductive explanation. They argue that carcinogenesis needs to be explained in a non-reductive manner, that is, on the tissue level by referring to the disruption of tissue organization (Soto and Sonnenschein 2005).

My main thesis in this section is that, although it is correct that some reductive explanations in the life sciences are molecular and/or genetic, and thus fundamental-level part-whole explanations, it would be misleading to restrict the concept of a reductive explanation to them. In many research areas the studied systems are decomposed into parts, but not into molecular parts. The corresponding part-whole explanations exclusively refer to lower level factors (i.e. parts of the system and their interactions), but do not go further down until the fundamental, molecular or genetic level. I see no reason why these non-fundamental part-whole explanations cannot be characterized as being reductive explanations too. What is crucial for the reductive character of an explanation is that it includes *only* lower-level factors, not that it refers only to fundamental-level factors (i.e. molecules and genes). Especially when it comes to life sciences such as ecology and evolutionary biology it seems erroneous to limit the notion of a reductive explanation to fundamental-level reductions. Consider, for instance, the explanation of the behaviour of a population (e.g. changes in its density; Schoener 1986) in population ecology. So-called “individual-based models” (Huston et al. 1988, 682) explain the behaviour of a population exclusively in terms of its parts, namely individual organisms, their properties (i.e. size, growth rate, biomass, etc.) and the interactions between them (cf.

Sarkar 2005b). These ecological explanations are reductive because they only refer to entities (i.e. individual organisms) that are located on a *lower level* than the system whose behaviour is to be explained (i.e. the population), and does not include higher-level factors such as other populations or food-web details.

In sum, I propose to characterize reductive explanations as part-whole explanations that refer exclusively to entities located on a *lower-level* than the level of the explanandum phenomenon (lower-level reductions). Hence, reductive explanations do not mention higher-level factors, that is, factors located on the level or above the level of the system whose behaviour is to be explained. Fundamental-level reductions constitute a special case of lower-level reductions, namely reductive explanations that bottom out at the fundamental level of molecules and/or genes. Let us now turn to the additional features of reductive explanations that I mentioned at the beginning of this section. Contrary to the part-whole (or lower-level) character of reductive explanations these additional features have not received much philosophical attention so far.

4. Focusing on Internal Factors

In the biomedical literature another reductive research strategy is mentioned – far from being cited as frequent as decomposition, but nevertheless referred to frequently enough to be important for my analysis. When specifying the reductionist methodology, life scientists speak about an embracement not only of a “search... downward in the hierarchy of organic organization” but also of a “search *inward* [i.e., into the system]” (Lidicker 1988, 278; my

emphasis). In other words, “advocacy of a reductionist approach coincides with emphasizing *internal*, rather than external, factors” (Schoener 1986, 102; my emphasis). By contrast, non-reductionist research (also called ‘systemic’ or ‘holistic’ research) is characterized as involving “putting things in a context” (Grizzi and Chiriva-Internati 2005, 28) and “look[ing] outwardly from the boundaries of the phenomenon under study” (Lidicker 1988, 280).

The picture that is portrayed in these statements is the following: When biologists investigate the behaviour of a certain system in a reductionist manner they focus on factors that are *internal* (or intrinsic) to the system and ignore or simplify factors that belong to the environment or context of the system, i.e. external (or extrinsic) factors. Usually, the distinction between internal entities (which belong to the system) and external entities (which belong to the environment of that system) is spelled out in a *spatial* manner. The idea is that the system is surrounded by a spatial boundary, ideally a continuous, constant line, like the cell membrane and that every entity (with its properties and associated interactions or operations) located inside this boundary is referred to as ‘internal’ and everything located outside is called ‘external’. For instance, in studying the contraction of muscle fibers biologists mostly focus on the processes that take place *inside* the muscle fiber, that is, on how the sliding of the thick and thin filaments past each other is caused by the various interactions between different molecules (e.g. actin, myosin, tropomyosin, calcium ions, ATP, etc.; cf. Campbell/Reece 2011, chapter 49). External factors are either completely ignored or simplified. Attention is paid neither to the process that generates the signal leading to the contraction of a muscle fiber, nor to how this signal is transmitted to a certain motor neuron, how the action potential causes the release of neurotransmitters into the synaptic cleft and

how this, in turn, triggers an action potential inside the muscle fiber. When investigating muscle contraction this entire process is simplified by using the formula of an ‘incoming neuronal signal’.

This reductionist research strategy can also be characterized as shielding the system from its environment and treating biological systems as if they were closed or semi-closed systems. If the environment cannot be ignored altogether, it is at least simplified. This reductionist procedure is beneficial because it makes the investigation, especially that of complex systems, more manageable and, thus, the construction of explanations of the system’s behaviour easier (cf. Bechtel and Richardson 2010, 234-236). But since biological systems are generally open systems as well as systems that evolved under the influence of specific environmental conditions, in most cases the environment is crucial for the functioning of these systems and cannot be ignored and simplified as easily as the reductionist might wish.^v The more important the environment is for the behaviour of a system the more the adequacy of applying this reductive method is called into question. A non-reductionist procedure that also takes into account the context of the system seems to become inevitable. Applying such a non-reductive method would, for instance, involve to explore how changes in the environmental conditions affect changes in the interactions between the system’s parts and how this in turn influences whether the system displays the behaviour in question or not.

What follows from these methodological considerations for the character of reductive explanations in the life sciences? I claim that the reductive method of focusing on internal factors and ignoring or simplifying the environment of the system discloses a second feature that many reductive explanations in the life sciences exhibit: They refer only to entities (their

properties and interactions) that are *internal* to the system, that is, located *inside* the spatial boundary of the system whose behaviour is to be explained. In the philosophical literature this characteristic of reductive explanations has been either overlooked or lumped together with its lower-level character for a long time. Only recently Hüttemann and Love (2011) have taken on this issue and pointed out that the internal character and the lower level character – they call them “intrinsicity” and “fundamentality” (527) – are two distinct “aspects” (523) of reductive explanations.

I agree with this view, It is clearly not necessary that each explanatorily relevant factor that is located on a lower level than the system whose behaviour is to be explained also has to be located inside the system. For instance, in the case of signal transduction the environmental factors that are included into the explanation are in many cases extracellular signal molecules that bind to specific cell-surface receptor proteins and in this way cause certain intracellular changes. Since these external factors are molecules they can be said to be located on a lower level than cells. Thus, extracellular signal molecules are an example of entities that are external to a certain system but, nevertheless, located on a lower level than the system.^{vi} To sum up: In my view the lower-level character is a *necessary condition* for an explanation to possess a reductive character, whereas the internal character is just a feature *many* (but not all) reductive explanations in the biomedical sciences exhibit. Furthermore, I claim (contrary to Hüttemann and Love 2011) that both of these conditions are not sufficient (neither on their own nor together) since reductive explanations exhibit a third characteristic that I will elaborate in the next section.

But before I close this section, let me further specify what the internal character of reductive explanations in the life sciences means. I claim that many reductive explanations do not only focus on factors that are internal to the system in question, but also ignore or simplify its environment. The second part of this thesis is new in the debate and shall thus be further clarified. Reductive explanations typically either completely ignore environmental factors, that is, they exclude them from the explanation or they include a few of them but simplify them in a significant manner. To include but to simplify selected environmental factors can mean two things: Either they are conceptualized as being mere *background conditions*, which remain constant over time, and are thus only *implicitly* included into the explanation. An example is the reductive explanation of protein folding which does not explicitly mention external factors as a certain temperature, pH-value, and salt-concentration but which, nevertheless, implicitly includes these factors as background conditions necessary for the folding to occur. Or contextual factors are simplified as being pure *input conditions*, which need to be satisfied at the beginning of the process that brings about the *explanandum* “automatically” (i.e. without further help of other environmental factors). Consider again the explanation of muscle contraction. In a reductive explanation of this phenomenon only a single environmental factor, namely the incoming neuronal signal, is mentioned. In addition, this factor is simplified since the only thing that matters is that it is present and that it induces the entire process of muscle contraction. The exact nature of this signal, how and where it originates and how it is transmitted to the muscle fiber is irrelevant to the explanation, as we saw above. Another example that illustrates this point is the PI 3-kinase/Akt pathway that explains how cell survival is promoted and how apoptosis is inhibited (Alberts et al. 2008, 934). The details of this signal transduction process are complex and it involves interactions

between many different molecules (e.g. RTK, PI 3-kinase, PI(3,4,5)P3, Akt, PDK1, Bad; etc.). The only external, or more precisely, extracellular entities that are referred to in the reductive explanation are the so-called survival factors that bind to the transmembrane receptor RTK and induce the signal transduction process. Again, the only thing of interest is that this survival factor is present. The specific features of this external factor (e.g. that it is a member of the insulin-like growth factor family) as well as its origin are treated as explanatory irrelevant in reductive explanations.

5. Parts in Isolation

In the scientific papers on the limits of reductionism cited above a third characteristic of reductive explanations and a third reductive method is implicitly mentioned. Philosophers have not paid much attention to them yet but the current vivid discussions about reductionism in the life sciences demonstrate that they should. A common argument put forward in the context of systems biology in particular goes as follows: Reductionism is deficient because the behaviour of complex systems cannot be understood (and explained) by investigating the parts of the system in isolation. For instance, Lisa Chong and Bryan Ray claim in their introduction to a special issue on systems biology in *Science* that “‘systems’ of various orders [are] not understandable by investigation of their respective parts *in isolation*” (2002, 1661; my emphasis). In cancer research similar statements can be found. For instance:

The behaviour of complex physiological processes cannot be understood simply by knowing how the parts work *in isolation*. (Bizzarri et al. 2008, 173; my emphasis)

And even in ecology this way of characterizing reductionist procedures is at hand:

The reductionist myth of simplicity leads its advocates to *isolate* parts as completely as possible and study these *isolated* parts. (Levins and Lewontin 1980, 76; my emphasis)

What underlies these quotations is the assumption that methodological reductionism does not only recommend to decompose the system under study into its parts, but also to investigate the identified parts of the system in isolation. The reductive method to investigate the parts of a system in isolation can be conceptually distinguished from the reductive method of decomposition. However, in practice the application of these two methods are frequently entangled. With respect to reductive explanations the above statements suggest that reductive explanations exhibit a third characteristic, namely, that they refer only to lower-level, and often internal, parts in isolation.

But what exactly does this add-on “in isolation” mean? Does it imply that in a reductive explanation only non-relational properties of the parts are cited as *explanantia* and that the organization of the parts and the interactions between them are ignored altogether? Does it mean that each part of a system is studied *completely on its own*, isolated from all other entities? I do not think so. Investigating the parts in complete isolation from other entities is problematic because one cannot get information (or, at least, very limited information) about the relational properties of the parts and their interaction with other entities. Since this is exactly the kind of information that is crucial for understanding the behaviour of many systems, in actual experimental settings the parts of a system rarely studied in complete

isolation.^{vii} Understanding the reductive method of studying the parts in isolation in this way builds up a straw man that is never realized in practice but easy to attack. The same holds for reductive explanations. Hardly any explanation of the behaviour of a system in the life sciences excludes all relational properties and interactions between the parts. Thus, it would be weird to demand this from reductive explanations.

In this paper I propose that to investigate the parts of a system in isolation stands for investigating them not *in situ*, that is, in the context of the system they are part of, but *in vitro*, that is, detached from the system. Thus, to study the parts of a system in isolation should be understood as investigating the parts isolated from the system they are part of but not isolated from everything else. Consequently, a reductive explanation that refers exclusively to parts in isolation can both refer to relational properties of the parts and include information about how the parts interact with other kinds of entities. But reductive explanations only include information that is discovered by exploring the parts *in vitro*, not *in situ*.

6. The Limits of Reductionism

Now that I have clarified what the reductive method of studying parts in isolation is, and what the third characteristic of reductive explanations is, namely that they refer only to the properties of parts that can be explored *in vitro*, we can turn towards the limits of applying this method and explaining the behaviour of systems in a reductive manner. What are the envisioned “shortfalls in reductionism [that] are increasingly apparent” (Gallagher and

Appenzeller 1999, 79) and how do they come about? Again, we get fruitful insights from the scientific literature itself. A common line of argumentation is that applying reductive methods like decomposition and studying parts in isolation leads only to a very limited understanding of a complex system since they fail to “put together” (Grizzi/Chiriva-Internati 2005, 28) the parts again. They claim that decomposing a system into its parts and investigating the parts of a system in isolation does not reveal “how these parts are assembled” and “how the individual components dynamically interact” (Kitano 2002, 1662), that is, “how all these things are integrated” (Service 1999, 81) into the system as a whole. In other words, the thesis is that studying the parts outside of the system does provide only limited insights into the properties the parts exhibit *in situ*, how they are organized in the system and which interactions take place between the parts when the system displays the behaviour in question.

This is particularly the case when scientists are concerned with so-called “integrated systems” (Bechtel and Richardson 2010, 149), whose parts are organized in such a complex way that the properties of the parts and their interactions are co-determined by the systemic organization.^{viii} This high degree of integration of the parts of complex systems makes it impossible to reach a complete understanding of the behaviour of a system merely by studying the system in a reductive manner, that is, by decomposing the system and investigating the parts in isolation. The reason is that the parts may exhibit different properties when they are integrated into the system and when they are taken out of it and studied in isolation (Chong and Ray 2002, 1661; Keller 2005, 9). What is needed in addition to the reductionist approach is an “integrative agenda” (Gallagher and Appenzeller 1999, 79) that explores the “dynamics of the system as a whole” (Sorger 2005, 9), that is, which properties

the parts of a system possess *in situ*, how they are organized into the whole system, and through which interactions the parts *in situ* bring about the behaviour of the system in question.

To sum up, it can be said that the more complex the organization of a system is and the more its parts are integrated and interdependent on each other the more *limited* are the insights into the system one can achieve by utilizing the two reductive methods decomposition and investigation of parts in isolation. With respect to reductive explanations the consequence is even more radical: The more complex and integrated a system is, the less adequate appear reductive explanations that refer exclusively to lower-level, internal entities (the parts of the system), and only to those properties and interactions between these entities that can be studied *in vitro*.

7. Conclusion

The issue of reduction is far away from being an obsolete topic about which everything crucial has already been said. This paper points out that in the post-genomic era questions about reductionism and particularly about the limits of reductionism are pressing issues that many contemporary scientists vividly discuss. However, this paper also reveals that the current disputes about the limits of reductionism in the life sciences require more conceptual clarification. In the considered scientific papers it remains too vague what exactly it means to investigate a complex system or a complex disease like cancer, depression, or diabetes in a reductive manner and why these reductive research strategies are only of limited value.

Likewise, it is not specified what constitutes the reductive character of an explanation and why reductive explanations, especially of the behaviour of complex systems, are frequently assessed to be inadequate. This paper has tried to remove these obscurities by offering an elaborate and scientifically informed account of what reductive methods and explanations are and where their limits lie.

My analysis yields three major results. First, I identify three reductive methods that are crucial in the current research practice of the life sciences: decomposing a system into its parts (Section 3), focusing on factors internal to the system while ignoring or simplifying the system's environment (Section 4), and studying the parts of a system in isolation, that is, not completely isolated but taken out of the system (Section 5). These reductive research strategies are important, but they are only of limited value for investigating the behaviour of complex, integrated systems since they do not account for higher level factors, for the environment of a system, for the whole range of interactions between the parts, and for their complex organization.

Second, I argue that most reductive explanations in the life sciences exhibit (at least) three characteristics: they refer only to lower-level factors (Section 3), they focus on internal factors and include environmental factors only as background- or input-conditions (Section 4), and they cite only the parts of a system in isolation, that is, they include only those relational properties and interactions between the parts that can be investigated *in vitro* and not *in situ* (Section 5). The first and the last of these three features are necessary conditions, whereas the second feature is only exhibited by most reductive explanations. Explaining the behaviour of a complex system or a complex disease in a reductive manner often proves to be problematic

because higher-level or environmental factors cannot be adequately ignored or simplified and because the interactions that are known by studying the parts in isolation do not suffice to illuminate how the system's parts give rise to the behaviour of the system to be explained.

Third, the first characteristic of reductive explanations (i.e. their lower-level character) implies that explanations need not refer exclusively to molecules and/or genes (i.e. to fundamental-level factors) in order to be reductive. That is, molecular and genetic explanations are important cases of reductive explanations but they are by far not the only cases. Hence, discussions about explanatory reductionism should not be confined to this subset of reductive explanations – contrary to what is sometimes the case (e.g. Grizzi and Chiriva-Internati 2005, Soto and Sonnenschein 2005). My analysis of important reductive methods in the life sciences, of the characteristics of reductive explanations and of the limits of utilizing reductive strategies and explaining phenomena reductively aims to provide a novel, scientifically informed contribution to the philosophical debate about reduction. In addition, the conceptual clarifications it entails are meant to further discussions about the limits of reductionism in the life sciences itself.

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Endnotes

ⁱ For an introduction to this relatively young discipline see for instance Joyner/Pedersen 2011 and Kitano 2002.

ⁱⁱ For example, some authors added subcategories (e.g. theory and explanatory reductionism as subtypes of epistemic reductionism; Sarkar 1992; Brigandt/Love 2008) and thereby sometimes ignored other categories (e.g. methodological reductionism; Mayr 1988; Sarkar 1992). Others introduced new names (e.g. ‘constitutive reductionism’ instead of ‘ontological reductionism’; Mayr 1988, 2004; Sarkar 1992), and still others employed a strongly modified classification (e.g. ontological and explanatory reductionism were subsumed under the same category ‘ontological reductionism’; Brandon 1996).

^{iv} Life scientists are in general very reserved with respect to questions about ontological reductionism. For instance, Ferric Fang and Arturo Casadevall (2011) think that questions about ontological reductionism belong into the realm of philosophy and not into biology. They admit that they were “feeling increasingly uncomfortable” as they “tiptoe[d] gingerly through metaphysics” (1401) in their paper.

^v Exceptions are for instance *homeostatic systems*, which possess the capacity of self-regulation, i.e. of sustaining the internal conditions under a certain range of variations in the environmental conditions (cf. Campbell/Reece 2011, 906-914).

^{vi} This is only one example that clearly shows that the internal character of an explanation should be distinguished from its lower-level character. Another example is the development of the heart during embryogenesis in vertebrates (Hüttemann and Love 2011, 528-530).

^{vii} Other philosophers like C. D. Broad agree with me on this point: “It is clear that in *no* case could the behaviour of a whole composed of certain constituents be predicted *merely* from a knowledge of the properties of these constituents, taken separately” (1925, 63).

^{viii} Since the mode of organization of integrated systems is far away from being additive they are clearly “more than the sum of its parts” – to consult this old slogan. For further details about different modes of integration and complexity of systems see Bechtel and Richardson 2010, Chapter 2, 7, and 9.