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Bridging the Lab-field Divide? The “eco” in Ecological Genomics

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ABSTRACT - The emerging field of ecological genomics promises to bring about a marriage between ecological and laboratory-based, genomic investigations. In this paper, I will reflect on this promise by exploring how ecology and genomics are integrated in the two approaches that currently dominate this field: the *organism-centred approach*, focusing on individual (model) organisms, and the *metagenomic approach*, concentrating on (the metagenome of) entire microbial communities composed of a variety of species. I will show that both approaches have already taken some important steps in bridging the gap between genomics and ecology. Since the introduction of next-generation sequencing methodology in 2007, the organism-centred approach does not need to stick to classical model organisms like *Arabidopsis* anymore. Instead, it is now able to apply genomic tools to ecologically interesting species (e.g. amphibians, reptiles, birds) as well. The metagenomic approach has been able to give ecology a more prominent place in its investigations, in another way. Contrary to classical microbiology (the field from which it originates), it does not study microbial communities under controlled laboratory settings, but under nature’s own conditions. However, in the marriage between genomics and ecology, genomics still appears to be the dominant partner, especially in the case of the organism-centred approach that continues to study the new ecological models in artificial lab environments. Moreover, the organism-centred and metagenomic approaches employ a gene-centred perspective in understanding critical ecological interactions, thus strengthening a reductionist rather than a holistic (systems-oriented) approach.

KEYWORDS - Ecological genomics, ecology, genomics, metagenomics, model organisms, holism, reductionism

All particulars become meaningless if we lose sight of the pattern which they jointly constitute.

Michael Polanyi, 1962

Introduction

Since the beginning of the twentieth century, our understanding of the role of genes in living systems has developed rapidly. The “century of the gene” (Keller 2000) started in 1900 with the rediscovery of Gregor Mendel’s work on plant hybridization by Hugo DeVries, Carl Correns, and Erich von Tschermak, and ended with the Human Genome Project (HGP), devoted to the identification of all the genes on the human genome. After the completion of the HGP in 2003, the “genomics revolution” expanded beyond genetics, and started to influence many other areas of the life sciences, including ecology (Van Straalen and Roelofs 2006).

In this paper, I will focus on ecological genomics, an area of research that seeks to incorporate techniques and approaches originating from genomics in the context of ecology. As ecological and laboratory-based, molecular investigations traditionally occupied different areas within the biological sciences, this merging of ecology and genomics promises to “revolutionize our understanding of a broad range of biological phenomena” (Ungerer et al. 2008, 178). The focal point of this paper will be to explore how ecology and genomics are integrated in the two different approaches that currently dominate ecological genomics: the *organism-centred* and *metagenomic approaches*. Whereas the first approach aims to improve our understanding of ecosystem functioning by focusing on the level of the individual (model) organism, the second concentrates on (the metagenome of) entire microbial communities composed of a variety of species.¹ I will argue that the organism-centred and metagenomic approaches have already taken some important steps in bridging the gap between ecology and genomics. Thanks to the introduction of next-generation sequencing methodology, which became widely available in 2007 (Evanko and Rusk 2008), the organism-centred approach does not need to stick to classical model organisms like *Arabidopsis* and *Drosophila* anymore. Instead, it now proves to be able to apply genomic tools to ecologically interesting species, i.e. species that provide insight in critical ecological interactions, for instance reptiles, amphibians, and birds. The metagenomic approach has succeeded in giving ecology a more prominent place in its investigations, in another way. It has revo-

¹ In principle, the metagenomic approach could also be applied to identify eukaryote species assemblages (cf. Chariton et al. 2010). This type of research, however, is not (yet) dominant in ecological genomics.

lutionised the field of microbiology (the field from which it originates) by enabling the study of microbial populations in their native habitats. Thus, instead of studying communities of microorganisms under controlled laboratory settings, metagenomics allows us to explore them under nature’s own conditions. The organism-centred and metagenomic approaches, however, still seem to be “orientated more towards ‘genomics’ than towards ‘eco’” (Ouborg and Vriezen 2007, 14). This applies especially to the organism-centred approach, which continues to study the new ecological models in the artificial environment of the laboratory. Moreover, in understanding ecosystem processes, the organism-centred and metagenomic approaches employ a gene-centred perspective. DNA is regarded as the main determining factor, and not as “just one of the many functioning components of a larger interacting molecular system” (Barnes and Dupré 2008, 73).

By exploring the latest developments within ecological genomics, this paper seeks to contribute to a better understanding of this intriguing field of emerging research, as well as to clarify its methodological and epistemological challenges. As the field is still in its infancy, such an endeavour will be relevant not only for involved researchers, but also for policy makers and other users of the kind of knowledge ecological genomics is producing. I will start with a section that describes how the most important pillars of the field were formalised by Feder and Mitchell-Olds in their paper “Ecological and Evolutionary Functional Genomics” (2003). Next, I will explore how ecological genomics seeks to bridge the gap between ecological and genomic investigations, as its very name suggests it will. Thirdly, I will analyse how ecology and genomics are integrated in the organism-centred approach on the one hand, and the metagenomic approach on the other.

The inception of ecological genomics

In August 2003, Martin Feder and Thomas Mitchell-Olds published the article “Evolutionary and Ecological Functional Genomics” [EEFG] in *Nature Reviews Genetics*. This publication laid the foundation of a new field of research. The authors claimed that “a unique combination of disciplines is emerging – evolutionary and ecological functional genomics – which focuses on the genes that affect ecological success and evolutionary fitness in natural environments and populations.” The goal of EEFG is to understand how wild-type organisms can flourish in nature in spite of severe challenges from their biotic and abiotic environments. This can be accomplished by a detailed study of “the biological mechanisms that

influence or underlie ecologically important traits.” Feder and Mitchell-Olds maintain that such a study requires a multidisciplinary approach: “Understanding a given trait usually requires the simultaneous use of molecular, cellular, organismal, population and ecological approaches” (Feder and Mitchell-Olds 2003, 649).

Key scientists have labelled the paper by Feder and Mitchell-Olds as the birth of a new research area, generally referred to as “ecological genomics” – sometimes abbreviated as “eco-genomics” or “ecogenomics” (Ouborg and Vriezen 2007, 9; Maphosa et al. 2010, 308; Gobler et al. 2011, 4352).² For instance, in “An Introduction to Ecological Genomics” (2006), the first textbook entirely dedicated to this field, Van Straalen and Roelofs claim that in the ecological arena, “the interaction between genomics and ecology has led to a new field of research, *evolutionary and ecological functional genomics*” (Van Straalen and Roelofs 2006, 1 – authors’ emphasis).³ Renn and Siemens also refer to Feder and Mitchell-Olds’s paper as the birth of ecological genomics: “Inception of the field [i.e., ecological genomics] was formalized in a publication by Feder and Mitchell-Olds (2003) with the descriptive title ‘Evolutionary and Ecological Functional Genomics’” (Renn and Siemens 2010, 3025).

Why was the publication by Feder and Mitchell-Olds considered such a crucial moment for the history of ecological genomics? In an interview, Van Straalen explained that genomics was directly linked to ecology in this paper for the first time.⁴ Strictly speaking, this singling out of Feder and Mitchell-Olds as the founding fathers of the new field may be questioned, as there are some earlier examples. Notably, the Israeli biology professor Eviatar Nevo had already published a plea for an integrated ecological genomics discipline in 1998. Nevo explicitly called the synthesis he proposed “ecological genomics.” He introduced the concept in an article entitled “Molecular evolution and ecological stress at global, regional and local scales: The Israeli perspective” (1998), which appeared in the *Journal of Experimental Zoology*. Three years later, he further elaborated his views in an article that was published in *Proceedings of the National Academy of Sciences of the United States of America* (PNAS). Nevo presents ecological genomics as a new approach, building on eco-

² Sometimes, the field is also referred to as “environmental genomics” (e.g. Van Straalen and Feder 2011, 3). The latter term, however, is more frequently used as a synonym for “metagenomics” (e.g. Venter et al. 2004, 1; Quince et al. 2011, 1).

³ As since 2006 ecological genomics has moved forward very fast, in 2012, the second edition of Van Straalen and Roelofs’s textbook appeared, describing the latest developments in the field. For chronological purposes, I will refer to the first edition.

⁴ Interview between the author and Van Straalen (Amsterdam, 12 May 2010). With the term “interview,” I refer to semi-structured philosophical conversations that I had with several of the key players in the (Dutch) ecological genomics field.

logical genetics. In the 1960s, the school of ecological genetics founded by the English biologist Edmund Brisco Ford had aimed to elucidate the reciprocal relationships between organism and environment. Ford and colleagues tried to accomplish this by studying phenotypic evolution in wild populations. Nevo argues that thanks to the genomic revolution, evolutionary processes can now be studied in much greater detail: “Ecological genetics advanced by Ford [...] could now develop into the new science of ecological genomics, interacting with comparative structural and functional genomics” (Nevo 2001, 6239).

So actually, Nevo was the first to use the term ecological genomics in an academic publication, preceding Feder and Mitchell-Olds’s paper by five years. He explained his motivation for introducing this term as follows: “I did not see it elsewhere and used it because I very much believe in the interdisciplinarity of science and all my work has shown that the evolutionary process is dependent on the linkage between ecology and genetics or now between ecology and genomics.”⁵ Although Nevo’s interpretation is very similar to the view elaborated by Feder and Mitchell-Olds, the real breakthrough in ecological genomics only came after the publication by the latter two authors. One of the reasons for Feder and Mitchell-Olds’s success might be that they were able to gather a large research network around them. This network was formalised by the 2003 Gordon Research Conference on Evolutionary and Ecological Functional Genomics, which was intended to be the “conference of record” for the EEFG community.⁶ The importance of Feder and Mitchell-Olds’s publication is also reflected in the following statements. Loretta Johnson, co-director of the Ecological Genomics Institute (EcoGen) at Kansas State University, explained to me that “everyone was very much influenced by the seminar paper by Feder and Mitchell-Olds (2003) in *Nature Reviews Genetics*.”⁷ Ouborg and Vriezen even go a step further by implicating that Feder and Mitchell-Olds use the exact term eco-genomics: “This approach, which has been named ‘eco-genomics’ (Feder and Mitchell-Olds 2003), integrates the disciplines of ecology and molecular biology” (Ouborg and Vriezen 2007, 9).⁸

⁵ E-mail correspondence between the author and Nevo (11 November 2010).

⁶ Gordon Research Conferences [<http://www.grc.org/programs.aspx?year=2003andprogram=evolecol>] – last accessed 25 September 2013.

⁷ E-mail correspondence between the author and Johnson (21 January 2011).

⁸ The term “ecogenomics” was in fact introduced by the marine biologist Robert Chapman in the article “EcoGenomics – a consilience of comparative immunology” (2001), which appeared in *Developmental and Comparative Immunology*. Chapman characterises ecogenomics as “a convenient descriptor for the application of the tools of genomics [...] to ecology. Its purpose is to provide insight into the physiological status of organisms and to translate this into an understanding of the responses and interactions of organisms to the environment and to one another” (Chapman 2001, 549).

Feder and Mitchell-Olds themselves, however, neither used the terms ecogenomics nor ecological genomics in their 2003 paper, but only the more extended version EEFG. What is more, their main motivation for writing “Evolutionary and Ecological Functional Genomics” was not in the first place to introduce a new research area, but to emphasise the role of evolution in ecological processes. In an interview, Feder argued that in his experience, “ecologists are sometimes not strongly evolutionary. [...] the notion of time is not extremely important to some of them. There is time in the sense of community succession, but the idea that the species themselves change over time in the process of evolution is not one that they worry about a great deal.”⁹ Feder and Mitchell-Olds stress that, in order to understand wild type organisms and their evolution, interdisciplinary approaches are required: “The molecular tools and functional understanding that are required to accomplish the goals of the field are beyond the capacity of any single investigator, which necessitates sustained interactions among research communities” (Feder and Mitchell-Olds 2003, 649). A similar message can be found in Feder’s proposal to the National Science Foundation, in which he explains how each of the four components of EEFG are needed to achieve the goals of the field. As EEFG seeks “to understand the interaction of genes, function, environment and time in a rigorous, comprehensive sense, corresponding investigations will need to include genetics/genomics, function, ecology, and evolutionary biology.”¹⁰

Crossing the lab-field border

It is interesting to note that, from the beginning, readers of Feder and Mitchell-Olds’s paper paid particular attention to two of the four components that shape EEFG: ecology and genomics. This becomes apparent in their definitions of the field. Van Straalen and Roelofs define ecological genomics as “a scientific discipline that studies the structure and functioning of a genome with the aim of understanding the relationship between the organism and its biotic and abiotic environments” (Van Straalen and Roelofs 2006, 1). Ungerer, Johnson and Herman give a similar definition: “We define ecological genomics as an integrative field of study that seeks to understand the genetic mechanisms underlying responses of organisms to their natural environment” (Ungerer et al. 2008, 178). Based on these

⁹ Skype interview between the author and Feder (5 May 2010).

¹⁰ Feder M.E., 2000, “Evolutionary and Ecological Functional Genomics: Jumpstarting a Multidisciplinary Field,” Proposal to the National Science Foundation. (Available upon request from the author for this paper.)

definitions, it might appear that ecological genomics merely applies a new tool – i.e. genomics – for the purpose of analysing fundamental ecological questions. Van Straalen and Roelofs nevertheless emphasise that “the merging of genomics with ecology includes more than the incorporation of a toolbox, because with the new technology new scientific questions emerge and existing questions [in ecology] can be answered in a way that was not considered before” (Van Straalen and Roelofs 2006, 1). Ungerer and colleagues have great expectations of the field as well: “Such an integration of fields [...] will revolutionize our understanding of a broad range of biological phenomena” (Ungerer et al. 2008, 178).

Why are the authors mentioned so convinced that the merging of genomics and ecology will be such a great leap forward? Ungerer and colleagues answer this question as follows:

Ecological and laboratory-based genetic/genomic investigations traditionally have occupied different areas of the biological sciences [...]. With a few notable exceptions, research programs are generally positioned in one domain or the other, but do not regularly cross the boundary that separates these disciplines by utilizing the tools and approaches of both. (Ungerer et al. 2008, 178)

EEFG, and consequently ecological genomics, seek to integrate these investigations by incorporating techniques and approaches originating from genomic research in an ecological context. Ouborg and Vriezen have a similar view of the revolutionary potential of ecological genomics. Ecology and molecular biology are rooted in different research traditions:

Molecular biologists prefer to work in controlled environments and with homogeneous well-defined genetic material, aiming to remove as much variation as possible. For ecologists, environmental and genotypic variation is their core business, which they try to incorporate in experimental designs rather than controlling for it. (Ouborg and Vriezen 2007, 13)

Although Ouborg and Vriezen present ecological genomics as a field with great promise, they emphasise that achieving a true synthesis between ecological and molecular approaches will prove to be a difficult challenge: “The challenge to ecogenomics is to fine-tune experimental designs of ecology and molecular biology in order to accomplish true integration of the data that originate from these two fields” (Ouborg and Vriezen 2007, 13).

The gap between ecological and molecular investigations can be elucidated by the book *Landscapes and Labscales* (2002) by the historian and sociologist of science Robert Kohler. He explores the cultural differences between laboratory and field science from the 1890s to the 1950s by concentrating on the subset of field disciplines that back then were

most strongly influenced by lab culture: ecology and evolution. Kohler's exploration helps us to understand the cultural gap between the two approaches that are at the core of ecological genomics. According to Kohler, laboratory and field work are marked by various differences. Firstly, the notion of "place" figures differently in lab and field practices. Laboratory workers try to eliminate the element of place from their experiments: "It is precisely the stripped-down simplicity and invariability of labs – their *placelessness* – that gives them their credibility." By contrast, field biologists consider "places [...] as much the object of their work as the creatures that live in them. [...] Plants and animals are elements of natural environments, along with topography, habitat, and weather: they are not mere passive guests as they are in labs, but actively *alter* their environments." A second difference between lab and field is that the former are pre-eminently *controlled* environments. On the contrary, natural places are *particular* and *variable* places, "each the result of a unique local history, never the same from one moment to the next, unpredictable, unrepeatable, beyond human control" (Kohler 2002, 6-7; my emphases). In the next section, I will apply Kohler's insights to the case of ecological genomics.

Overcoming reductionism

The difference between laboratory (molecular) and field (ecological) research is sometimes described as a difference between *reductionist* and *holistic* approaches (Bergandi and Blandin 1998; Gierer 2002; Zwart 2007). Zwart draws a distinction between a strong and weak version of reductionism. According to the strong version (also referred to as "ontological reductionism"), "all phenomena in nature can ultimately be reduced to a limited number of causal units [...]. These primal causal units are regarded as determinants of everything else" (Zwart 2007, 192). Representatives of the weak version of reductionism do not actually believe that the system as a whole can be explained on the basis of a limited set of mono-causal relationships. They see reductionism as a *methodological requirement*. In the context of laboratory research, it is impossible to do justice to the complexity of the real world. The number of factors that can be meaningfully studied is limited. "Once the relationships between these factors have been established, researchers will try to extrapolate their research findings to the real world, in the expectation that, out there, things will prove to be much more complicated" (Zwart 2007, 193).

Holists maintain that "breaking nature down into its atomistic parts cannot result in a true understanding of the whole" (Worster 1994, 22).

The whole of nature is more than or different from the sum of its parts. As ecologists frequently argue that "special qualities emerge out of interactions and collectives" (Worster 1994, 22), ecology is often seen as one of the exemplary approaches to holism. This applies especially to ecosystem ecology, as this field emphasises "the interconnections among things and events sometimes distant in space and time" (Burns 1990, 193).¹¹

In the preceding section, I explained that ecological genomics aims to reconcile the experimental languages of ecologists and molecular biologists. Using the concepts set out in the above, it could be argued that the holistic and reductionist research cultures of ecology and molecular biology must learn to speak a common language. Van Straalen and Roelofs, however, seem to suggest that in the research field of ecological genomics, this confusion of tongues has already been overcome; not only ecology, but also genomics undermines the deterministic, reductionist approach of laboratory culture. Van Straalen and Roelofs explain that genomics allows us to study the genome and its products as a *unitary whole*; it is based on the observation that "the impact of one gene on the phenotype can only be understood in the context of the expression of several other genes or, in fact, of all other genes in the genome, plus their products, metabolites, cell structures, and all the interactions between them" (Van Straalen and Roelofs 2006, 3). The authors argue that, by integrating ecological and genomic approaches, it has become possible to conduct a detailed study of ecosystem functioning both on the *macro-* and *micro-*level. Thus, ecological genomics enables us to explore phenotypic biodiversity as well as genome diversity: "With this new discipline, ecology is enriched by genomics technology and genomics is enriched by ecological questioning and evolutionary views" (Van Straalen and Roelofs 2006, 3). In a focus issue on ecological genomics of the journal *Environmental Science and Technology*, Van Straalen and Feder explicitly call the genomic approach *holistic*. "The typical approach of genomics," they claim, "is to look upon the organism as a unitary whole, that is, to try and analyse as many genes as possible [...]. Such a holistic view of organism function has been made possible by technological and computational advances" (Van Straalen and Feder 2012, 4).

How can we interpret these claims? Should we conclude that ecological genomics has already succeeded in bridging the gap between ecological and molecular approaches? All in all, it appears to be too early for such a statement. It is true that, compared to traditional genetics,

¹¹ Some scientists and philosophers of science qualify this view by pointing out the role idealisations and simplifications play in ecological modeling. For instance, Colyvan and colleagues maintain that one of the factors determining model choice in ecology is tractability: "We obviously do not want models as complicated and as cumbersome as the systems they model" (Colyvan et al. 2009).

genomics is much more aware of “any effects elsewhere in the genome, outside the system under study” (Van Straalen and Roelofs 2006, 3). As Zwart argues, whereas classical genetics focused on a limited number of genes, “genomics allows us to simultaneously study the function of *all* the genes on the genome of an organism” (Zwart 2007, 193 – author’s emphasis). Genomics, however, does not entirely escape reductionism. Firstly, it is important to keep in mind that the study and analysis of complex relationships still takes place *within* a laboratory setting. Genomicists assume that, thanks to the availability of new research tools (high throughput analysis, bioinformatics, computational biology, micro-array research), laboratory experiments are consistent with actual ecological processes. Secondly, in understanding the system as a whole, DNA is still considered the main determining factor, instead of being “reconceptualized as just one of the many functioning components of a larger interacting molecular system” (Barnes and Dupré 2008, 73).¹²

Two approaches in ecological genomics

Earlier, I explained that different research communities are active in ecological genomics. As Ungerer and colleagues argue, a deeper understanding of the genetic mechanisms underlying responses of organisms to their natural environments, requires a multidisciplinary approach, “combining organismal analyses with molecular genetics and genomics, laboratory experiments with field studies and all within an ecologically relevant framework” (Ungerer et al. 2008, 187). Currently, the field is dominated by two different approaches, one focusing on the level of the individual organism, the other on entire ecosystems (Feder and Mitchell-Olds 2003; Ungerer et al. 2008; Mitchell-Olds et al. 2008). Ungerer and colleagues describe the difference between both approaches as follows:

One goal of ecological genomic studies is to understand the genetic mechanisms underlying responses of organisms to their natural environments. This question typically is focused at the level of the *organism*. Another goal of ecological genomic research is to understand how genomes interact at *higher levels of organization*, for example, is there a “community genome” and if so, can we understand how it functions. (Ungerer et al. 2008, 181 – my emphasis)

¹² Barnes and Dupré do not make explicit whether or not they share this view of genomics as a (partly) reductionist approach. Their aim is rather to reflect on the implications of different interpretations of genomics.

The “organism-centred approach” (Marco 2010, preface)¹³ seeks to improve our understanding of critical ecological interactions by focusing on the level of individual organisms, for instance by exploring how organisms respond to environmental change and how populations can adapt to environmental toxicants (Van Straalen and Feder 2012). As a rule, the organism-centred approach is organised around classical laboratory-based model organisms, i.e. organisms with well-characterised gene expression patterns and large research networks organised around them. Examples of such model species are the plant *Arabidopsis thaliana*, the fruit fly *Drosophila melanogaster*, and the nematode *Caenorhabditis elegans* (Jackson et al. 2002, 409; Van Straalen and Roelofs 2006, 4; Maher 2009, 695; Ankeny and Leonelli 2011, 316). By exposing the model to different environmental conditions (humidity, drought, etc.), the genes and gene functions that matter most in a given ecological interaction are identified (Ungerer et al. 2008). According to Feder, model organism studies are based on the assumption that such studies “can provide insight into the biology of some or many (if not most or even all) other organisms” (Feder 2006, 163). Recent advances in genomics have validated this assumption: “[...] large amounts of the genomes sequenced to date are clearly homologous among organisms” (Feder 2006, 163). Thanks to these homologies, the data and theories obtained from the models are expected also to be applicable to ecologically interesting species (Aparicio et al. 2002).

The “metagenomic approach” does not concentrate on the level of the individual organism, but aims to study ecosystems *as a whole*; the starting material is not derived from a single species, but from many different organisms (Dale et al. 2012). This approach is also referred to as environmental genomics (Venter et al. 2004; Mitchell-Olds et al. 2008), community genomics (Dupré and O’Malley 2007; Xu 2010), and environmental community genomics (Van Straalen and Feder 2012). Sometimes, ecogenomics and ecological genomics are used as synonyms for metagenomics as well (Béjà 2004; DeLong 2005; Dupré and O’Malley 2007; Xu 2010).¹⁴ Metagenomics enables “the culture-independent genomic analysis of microbial communities” (Schloss and Handelsman 2003, 303). It started as a method to study the chemical diversity of soil life. In the nineties, most microbiologists still assumed that the majority

¹³ Kloet et al. (2011) refer to the organism-centred approach as “model organism ecogenomics.” In the last few years, genomic tools have increasingly been applied to non-model species, and the expression “model organism genomics” thus appears to be too narrow to cover all research conducted under this label. That is why I prefer the term “organism-centred approach.”

¹⁴ Researchers who use ecological genomics and/or ecogenomics as synonyms for metagenomics thus have a more narrow interpretation of these terms than Feder and Mitchell-Olds’s readers.

of soil microbes could be recovered by culturing them in the laboratory. An increasing amount of evidence has nevertheless shown that “fewer than 0.1% of the microorganisms in soil are readily cultured using current techniques. [...] the other 99.9% of soil microflora is emerging as a world of stunning, novel genetic diversity” (Handelsman et al. 1998, 245). By providing access to the previously unknown world of microorganisms, metagenomics has revolutionised our understanding of the earth’s microbial diversity.¹⁵

Mitchell-Olds, Feder and Wray argue that, taken together, the two above-discussed approaches “offer great potential for uncovering the molecular mechanisms responsible for adaptation” (Mitchell-Olds et al. 2008, 100). In other words: the organism-centred and metagenomic approaches help us to understand the mechanistic causes of fitness variation (Ouborg and Vriezen 2007). In the next four sections, I will discuss both approaches in more detail. In particular, I will focus on the question how and to what extent ecology is integrated in both approaches.

The organism-centred approach: To model or not to model?

In the preceding, I explained that the organism-centred approach is usually organised around classical model organisms with fully sequenced genomes. As the genomes of organisms share a significant degree of homology with related species, research on model organisms is expected also to provide insight into the biology of ecologically interesting species. The general applicability of standard model organisms in ecological genomics studies, however, needs to be critically assessed. According to Feder, the question of whether or not to use these species depends very much on the issue we want to address: “[...] if the underlying research question is general (e.g., Does susceptibility to environmental stress increase during development?), then standard model systems are often [...] readily applicable” (Feder 2006, 164). By contrast,

[i]f the underlying research question is specific and species-driven (e.g., How does the fairy shrimp tolerate extreme temperatures or [high salt] concentrations early in development?), then application of standard model systems is likely to be as problematic as the phylogenetic and ecological distance between the nearest standard model and the species under investigation. (Feder 2006, 164)

¹⁵ Van Straalen and Roelofs (2006) also distinguish a third approach, to which they refer as “comparative genomics.” This approach studies the relationship between genome structure and function among different species. As comparative genomics is generally based on model organism studies, I will not treat this as a separate approach, but as part of the organism-centred approach.

The physiologist August Krogh warned against uncritical generalisations from model systems to solve physiological problems as early as 1929. In an article entitled “The progress of Physiology”, he argued that “a general physiology which can describe the essential characteristics of matter in the living state is an ideal to which we may hope that our successors may attain after many generations” (Krogh 1929, 4). He claimed that “the route by which we can strive toward the ideal is by a study of the vital functions in all their aspects throughout the *myriads* of organisms” (Krogh 1929, 4 – my emphasis). In 1975, Krogh’s considerations inspired the physician and biochemist Hans Krebs to formulate the *August Krogh principle*, which assumes that for every physiological problem, there is an animal in which this problem can be most conveniently studied. Applied to ecological genomics, the principle urges us to critically reflect on the extent to which model organisms can represent ecologically important pathways, processes and structures. Jackson and colleagues are very critical in this respect. They argue that species such as *Arabidopsis* and *Drosophila* have not become models in genomics because of their ecological or evolutionary importance or their applicability to ecological questions, “but were selected on the basis of particular genetic and developmental features (e.g. clonal propagation, self-fertilization and short generation times) and for ease of growth in the laboratory” (Jackson et al. 2002, 409). Ouborg and Vriezen express the same criticism: “These species have become model species of genomics because of their suitable properties: small genomes, short generation times and easy maintenance in the glasshouse. They are not chosen because of their specific ecology, and they certainly do not cover all life-history strategies and habitats” (Ouborg and Vriezen 2007, 12; cf. Van Straalen and Feder 2011, 3).

What makes a species a suitable model for ecological genomics? Van Straalen and Roelofs come up with three criteria. Firstly,

the new range of models should embrace diverse phylogenetic lineages, varying in their physiology and life-history strategy. [...] Considering the diversity of life histories, species differing in their mode of reproduction and dispersal capacity should be chosen; for example, hermaphroditism versus gonochorism, parthenogenesis versus bisexual reproduction, etc. (Van Straalen and Roelofs 2006, 8)

Secondly, species have to take part in critical ecological interactions, for instance “mycorrhizae, nitrogen-fixing symbionts, pollinators, natural enemies of pests, parasites, etc.” Finally, the new “ecogenomic” models should be suitable for field research, since “[n]ot all species lend themselves to studies of behaviour, foraging strategy, habitat choice, population size, age structure, dispersal, or migration in the field.” Examples of species that fit these criteria are reptiles, amphibians, molluscs, an-

nelids, birds and non-insect arthropods. For these organisms, however, adequate genomics resources (funding, research programmes, research consortia) are not always available. As Van Straalen and Roelofs argue, “many popular ecological models have a poorly characterized genome and lack a large community of investigators” (Van Straalen and Roelofs 2006, 8-9; cf. Jackson et al. 2002).

Ecological genomicists are thus faced with a dilemma: “Should the ecology of selected organisms that may not be very representative be studied, or should the genomic capabilities of more ecologically interesting taxa be developed?” (Ungerer et al. 2008, 181). Feder and Mitchell-Olds describe this *model versus non-model* question as a

near-philosophical debate, the extremes of which are whether to make the customary biomedical model organisms do “double duty” as model wild organisms, for which they are often not well suited, or to forego the advantages of massive community support to optimize the insights that are emerging from the study of non-classical model organisms. (Feder and Mitchell-Olds 2003, 654)

New models for the organism-centred approach

In the editorial *Evolutionary and ecological functional genomics* (2008), building on the 2003 article with the same title, Mitchell-Olds and colleagues argue that thanks to “changing technology and decreasing costs, the time is approaching when genomic tools can be applied to diverse non-model species, characterizing new levels of complexity in natural systems and enabling tests of fundamental hypotheses in ecology and evolution” (Mitchell-Olds et al. 2008, 101). Ungerer and colleagues have similar expectations for the future: “Genomic resources are now also being developed for several species with rich histories of ecological investigation; these species will likely emerge as the new ‘models’ for ecological genomics research” (Ungerer et al. 2008, 182). According to Van Straalen, the shift from traditional model organisms to ecologically interesting species implies a *qualitative change* for the ecological genomics field.

Which technological advances have facilitated this shift towards new model species? A first step was the development of DNA microarrays, first described by Schena and colleagues in 1995. By attaching a collection of microscopic DNA spots on a coated glass plate, the expression levels of large numbers of genes could be studied simultaneously. This now classical technology has later been joined by technologies such as quantitative RNA sequencing (RNAseq) and high-throughput quantitative polymerase chain reaction (qPCR). The real breakthrough for the organism-centred approach, however, only became possible after the in-

roduction of next-generation sequencing methodology (NGS), which became widely available in 2007 (Evanko and Rusk 2008). According to Van Straalen and Feder, this technology has brought about a new revolution, “as the nonmodel genomes of environmental science have become as tractable as genomes of classical genetic models” (Van Straalen and Feder 2012, 3). Although Feder and Mitchell-Olds already discussed the possibility to study non-classical model organisms in 2003, it took until 2011 before the entire genome of the first real “ecological species” was sequenced, namely that of the water flea *Daphnia pulex* (Van Straalen and Feder 2012). This crustacean arthropod is a keystone species of freshwater ecosystems; it is not only a principal grazer of algae, but also a primary forage for fish, and a protector of lentic inland ecosystems. As water fleas are sensitive to modern toxicants in the environment, they can be used to assess the ecological impact of environmental change (Colbourne et al. 2011).

The above shows that the organism-centred approach has recently taken some important steps in crossing the boundary between ecological and genomic investigations. However, a real merging of these disciplines has not yet taken place. Rather than bringing about a marriage between ecology and genomics, the organism-centred approach still seems to contribute more to a *genomicalisation* of ecology than to an *ecologisation* of genomics (cf. Ouborg and Vriezen 2007). Firstly, the rise of non-classical model species does not necessarily imply the end of gene-centredness. Although the organism-centred approach promises to go “beyond making claims on gene functions in cells or individual organisms” and “to generate insight in the *relationship* between organisms [...] and their environment” (Kloet et al. 2011, 24 – authors’ emphasis), it is mainly interested in understanding the *genetic* mechanisms underlying this relationship. Secondly, the new ecological models are still studied under laboratory rather than field conditions. Earlier, I explained that genomicists assume that, thanks to the availability of new research tools, complex organism-environment relationships can now be thoroughly studied in the lab; ecological research is thus no longer field-bound. The introduction of next-generation sequencing methodology has only supported this assumption. However, a profound understanding of critical ecological interactions seems to require more than the replacement of classical model organisms by ecologically relevant species. The artificial environments created in labs lack the unpredictability and variability of natural ecosystems, even if they are studied with the “right” model (cf. Kohler 2002). In the next sections, I will explore the extent to which metagenomics has succeeded in bridging the gap between ecology and genomics.

The metagenomic approach: the era of ecosystems biology

Earlier, I explained that in the nineties, most microbiologists still assumed that the majority of microorganisms in a sample could be recovered by culturing them. As a result, most knowledge about microorganisms was laboratory knowledge, “attained in the unusual and unnatural circumstances of growing them optimally in artificial media in pure culture without ecological context” (Committee on Metagenomics 2007, 13). By enabling the culture-independent analysis of microbial populations, metagenomics has revolutionised the field of microbiology in two ways. Firstly, “it offers a window on an enormous and previously unknown world of microorganisms” (Handelsman 2007, 8). Secondly, as I will elaborate later on, it allows the study of microbial communities in their *native* habitats. Xu therefore argues that metagenomics announces a new era in biology, “that of *ecosystems biology*” (Xu 2010, 1 – my emphasis).

Although microbiologists started to apply culture-independent methods already in the nineties, Schloss and Handelsman introduced the term “metagenomics” as late as 2003. The term “metagenome” – referring to the object of research – was launched by Handelsman and colleagues five years earlier in an article that appeared in *Chemistry and Biology*. The prefix “meta” is derived from the ancient Greek μετά, meaning *to transcend*, or *to go beyond*. In the context of metagenomics, ‘meta’ can be interpreted as follows. Firstly, in its approaches and methods, metagenomics “circumvents the unculturability and genomic diversity of most microbes” (Committee on Metagenomics 2007, 13). In other words, the field *transcends* technical limitations to understanding microbial diversity (O’Malley and Dupré 2010). Secondly, ‘meta’ means that “this new science seeks to understand biology at the *aggregate* level, transcending the individual organism to focus on the genes in the community and how genes might influence each other’s activities in serving collective functions” (Committee on Metagenomics 2007, 13). Metagenomics thus exceeds “the limitations of a focus on individual genes and particular species, as well as the separation of organisms from environments” (O’Malley and Dupré 2010, 185).

I have presented metagenomics as one of the two approaches that currently dominate ecological genomics research. As explained earlier, the organism-centred and metagenomic approaches both seek to improve our understanding of critical ecological interactions. The difference between both approaches is that, whereas the first focuses on the level of the individual (model) organism, the second explores the genome of (terrestrial and aquatic) ecosystems as a whole (Ungerer et al. 2008). However, not all research conducted under the label “metagenomics” is ecologically-oriented. Even though metagenomics started as a method to study the col-

lective genomes of the soil, the term presently covers the investigation of *any* microbial community: it not only refers to the exploration of terrestrial or aquatic ecosystems, but for instance also to the genomic analysis of the human microbiome – the community of microorganisms living in the human body (cf. Handelsman 2007; Liebert 2008).¹⁶ As Xu argues:

The broad-sense metagenomics now encompasses any investigation involving the application of modern genomics techniques to the study of biological communities directly in their natural environments, bypassing the need for the isolation, the laboratory cultivation and observation of individual organisms. (Xu 2010, 1)

In the context of ecological genomics, metagenomics should be understood in a more narrow sense. Here, the term refers to the exploration of microbial communities living in natural ecological niches, for instance soil, water, or air. Such ecologically-oriented investigations are at the core of one of the basic experimental approaches applied by metagenomicists: the *sequence-driven approach*. This approach concentrates on the screening of microbial communities to reveal the overwhelming diversity of its members:

DNA from the environment of interest is sequenced and subjected to computational analysis. The metagenomic sequences are compared to sequences deposited in publicly available databases [...]. The genes are then collected into groups of similar predicted function, and the distribution of various functions and types of proteins that conduct those functions can be assessed. (Handelsman 2007, 4)

Metagenomics, however, was not only a method to learn about the contributions to the biosphere made by its uncultivable community members; “it was also designed for practical gains, such as the discovery of new genes and gene products that would lead to new medical chemistry, agricultural innovations and industrial processes” (Handelsman 2007, 3-4). This more practical focus is central to the *function-driven approach*. Here, the DNA extracted from the environment is not sequenced, but screened for potential applications and products, such as antibiotics, vitamins and enzymes. Handelsman claims that the potentials of metagenomics are endless: “It [...] promises to provide a more complete understanding of the global cycles that keep the biosphere in balance, offer clues to the basis for many diseases, lead to development of new antimicrobial therapies and present solutions to environmental and biotechnological challenges” (Handelsman 2007, 8).

¹⁶ In his contribution to the book *New Visions of Nature* (Drenthen et al. 2009), Eric Juengst argues that metagenomics encourages us to think of *human beings* as ecosystems.

The “eco” in metagenomics

In this final section, I will explore how ecology is integrated in, as I will call it, *narrow-sense* metagenomics, i.e. in ecologically-oriented metagenomic investigations. Van Straalen explains the contribution of ecology to narrow-sense metagenomics as follows: microbial DNA is not studied under controlled laboratory settings, but under *nature's own* conditions.¹⁷ Xu, moreover, argues that metagenomicists are aware of the fact that the artificial environments created in labs are very different from natural environments. In order to obtain critical and realistic understanding of microbes in nature, it is essential to investigate microbial populations in their native habitats (Xu 2010, 2). Because of this move out of the laboratory, metagenomics is often referred to as a *holistic* approach (Leveau 2007; Cubillos-Ruiz et al. 2010; Kemperman et al. 2010). Guazzaroni and colleagues, for instance, claim that the ultimate goal of metagenomics is to get “a holistic view of the functioning of [the] microbial world” (Guazzaroni et al. 2010, 56).

If we consider how metagenomics enabled the shift from laboratory-based research to the *in situ* exploration of microbial communities, this approach can indeed be described as holistic. Thanks to the move from lab to field, metagenomics has provided “access to environmental communities in their whole complexity” (George et al. 2010, 121). Thus, compared to classical microbiology (the field from which metagenomics originates), ecology is given a much more prominent place. Moreover, as O'Malley and Dupré point out, metagenomics urges us to reconsider the “one organism, one genome” conception of organisms: “Life is traditionally conceived to be organized around the pivotal unit of the individual organism” (O'Malley and Dupré 2010, 189). Metagenomics invites us to replace this ‘monogenomic’ conception by an organism- and species-free context:

Despite the tendency to think of humans and other traditionally conceived organisms as monogenomic possessors of a unique genome, a metagenomic examination of any such organism reveals that biological success depends on multilined and multigenomic cooperations. Rather than conceiving of monogenomic organisms as autonomous individuals, we suggest that the basis of any attribution of autonomy has to be functional wholeness, which is a product of cooperative interaction. (O'Malley and Dupré 2010, 187)

From a different angle, however, the presentation of metagenomics as a holistic approach can be challenged: as was the case for the organism-centred approach, metagenomics employs a gene-centred perspective.

¹⁷ Interview between the author and Van Straalen (Amsterdam, 16 March 2009).

In exploring environmental samples, it concentrates on the genetic elements available to microbial communities. Genes are seen as *the* functioning components of the microbial system (cf. Barnes and Dupré 2008, 73). This focus on genes is clearly expressed by Handelsman:

Metagenomics presents a system-level view of microbial communities. Instead of studying single organisms or single functions, metagenomics examines the entire complement of genes in a community, enabling construction of a scaffold of genes and functions on which to build principles about community structure and function. (Handelsman 2007, 5)

Conclusion

The initial promise of ecological genomics was to bring about a marriage between ecology and genomics. In this paper, I have argued that this promise has only been partly fulfilled: in the marriage between ecology and genomics, genomics is still the dominant partner. It is not self-evident that we should strive for a more equal marriage between genomics and ecology. After all, a successful marriage does not necessarily need to be an equal marriage. In my view, however, it is important to keep in mind that the ‘genomic language’ at the core of ecological genomics tends to overshadow other narratives that seek to describe nature in general, and complex ecological processes in particular. Both the organism and metagenomic approaches within ecological genomics have their own histories that have little in common with the ecological tradition as shaped by Aldo Leopold, Stephen Forbes, William Ritter, Charles Adams, and Edward O. Wilson, among others. The question of whether ecological genomics could try to do more justice to this powerful tradition within ecology, is beyond the scope of this paper.

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