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**SIZE DOESN'T MATTER:
TOWARDS A MORE INCLUSIVE PHILOSOPHY OF BIOLOGY**

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Abstract

Philosophers of biology, along with everyone else, generally perceive life to fall into two broad categories, the microbes and macrobes, and then pay most of their attention to the latter. 'Macrobe' is the word we propose for larger life forms, and we use it as part of an argument for microbial equality. We suggest that taking more notice of microbes – the dominant life form on the planet, both now and throughout evolutionary history – will transform some of the philosophy of biology's standard ideas on ontology, evolution, taxonomy and biodiversity. We set out a number of recent developments in microbiology – including biofilm formation, chemotaxis, quorum sensing and gene transfer – that highlight microbial capacities for cooperation and communication and break down conventional thinking that microbes are solely or primarily single-celled organisms. These insights also bring new perspectives to the levels of selection debate, as well as to discussions of the evolution and nature of multicellularity, and to neo-Darwinian understandings of evolutionary mechanisms. We show how these revisions lead to further complications for microbial classification and the philosophies of systematics and biodiversity. Incorporating microbial insights into the philosophy of biology will challenge many of its assumptions, but also give greater scope and depth to its investigations.

Keywords

Microbes, macrobes, microbiology, multicellularity, ontology, evolution, taxonomy, biodiversity

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Introduction: Microbes and Macrobes

The distinction between micro- and macro-organisms is one of the most widely assumed in thinking about life forms. While we have two words for the first group – microorganisms or microbes – there is none in common use for macroorganisms. We propose to fill this gap with the word 'macrobe'. The contrast between microbes and macrobes is very close to that between multi-celled and single-celled organisms. Microbes are also defined by features such as invisibility and a perceived lack of morphological and cellular sophistication; macrobes by a positive account of those features. But regardless of choice of defining features, neither of these categories would normally be attributed much biological coherence.

In general, any organism too small to be seen without a microscope is called a microbe or microorganism, even though many of them are visible when clustered together (e.g.: mould and algae filaments). Microbes comprise two of the three superkingdoms, Bacteria and Archaea, as well as single-celled eukaryotes (protists and yeasts) and viruses. Viruses, because they have no cells or metabolic function and require other organisms to replicate, tend to be placed in a grey zone between living and non-living things (or organisms and chemicals), but their evolutionary history, involvement with prokaryotes and eukaryotes, and some surprising biological capacities (Villarreal 2004a; Raoult et al. 2004; Luria et al. 1978) make it difficult to dismiss them as non-living. We will focus on bacteria and archaea in this paper, though many fascinating stories and philosophical complications could also be drawn from viruses and protists (e.g.: Villarreal 2004b; Nanney 1999; Corliss 1999; Sapp 1987). Bacteria and archaea

– until the 1970s considered under the single classification of bacteria – are now distinguished from each other by important differences in cell wall chemistry, metabolic pathways, and transcriptional and translational machinery (Allers and Meverech 2005; Woese and Fox 1977; Bell and Jackson 1998).

Macrobes comprise the remainder of the Eukarya, the kingdoms Animalia (including the Metazoa), the Fungi and the Plantae. The distinction between macrobes and microbes is not entirely sharp: various social single-celled organisms, both prokaryotic and eukaryotic, such as the myxobacteria and cellular slime moulds, have long-recognized claims to multicellularity. We frame our argument round this distinction for two reasons, however. First, the macrobes are no more diverse a group than the microbes, so it is worth reflecting on why the latter seems so much more natural a concept than the former. But second, and this is the main thesis of this paper, we believe that an indefensible focus on macrobes has distorted several basic aspects of our philosophical view of the biological world.

Microorganisms dominate life on this planet, whether they are considered from an evolutionary or an ahistorical perspective. Evolutionarily, the first three billion years of life on the planet was primarily microbial, with the Cambrian explosion of modern multicellular metazoan body forms beginning only about 545 million years ago (Conway Morris 2003; Carroll 2001). Microbes have far greater metabolic diversity than macrobes and can utilize a vast range of organic and inorganic energy sources via numerous metabolic pathways (Amend and Shock 2001). They are deeply implicated in the geochemical development of the planet, from the formation of ore deposits to the creation and maintenance of the oxic atmosphere on which macrobes depend (Kasting and Siefert 2002; Newman and Banfield 2002). They can thrive in conditions that are intolerable for most plants and animals. Prokaryotes flourish in temperatures over 100C and at least as low as -20C. They colonize extremely acidic, alkaline, salty, metal-rich, radioactive, low-nutrient and high-pressure environments. They can be found in high-altitude

clouds and on human artefacts in space, several kilometres deep in the earth's crust, as well as on and in every eukaryote organism alive or dead (Horikoshi and Grant 1998; Price 2000; Nee 2004; Newman and Banfield 2002). Just one gram of ordinary uncontaminated soil contains 10^{10} prokaryote cells which consist of as many as 8.3×10^6 species (Gans, Wolinsky and Dunbar 2005). Microbial species diversity in all of earth's environments is only estimated but it exceeds all other life forms, as do estimates of their global cell numbers. The natural history of life on earth was and always will be 'the age of bacteria' (Gould 1994).

Even an exclusive interest in mammalian or human biology cannot justify ignoring microbes. There are estimated to be at least 10 times as many microbial cells in our bodies as there are human somatic and germ cells (Savage 1977; Berg 1996), as well as perhaps 100 times more genes (Xu and Gordon 2003). A full picture of the human organism sees it as a 'composite of many species and our genetic landscapes as an amalgam of genes embedded in our *Homo sapiens* genome and in the genomes of our affiliated microbial partners (the microbiome)' (Bäckhed et al. 2005; Lederberg, in Hooper and Gordon 2001). Our microbiome functions as an additional 'multifunctional organ', carrying out essential metabolic processes that we, in the narrow single-organism or single-genome sense, have never evolved for ourselves (Xu and Gordon 2003). Every eukaryote can, in fact, be seen as a superorganism, composed of chromosomal and organellar genes and a multitude of prokaryote and viral symbionts (Lederberg, 2000, in Sapp 2003). This multispecific interactionist perspective, apart from fostering a far richer understanding of the biodiversity existing in the ecological niches provided by human bodies, should also lead to a better understanding of how human health, disease resistance, development and evolution have depended and continue to depend on interactions with microbes.

Despite the biological significance of microbes and the centrality of their study to some of the most exciting biology of recent decades (see below), the philosophy

of biology has focused almost exclusively on multicellular life. Decades of heated philosophical discussion about systematics and concepts of species have either not noticed the microbial world or found it convenient to dismiss it. It is rare, even in classification and species discussions, for philosophers to invoke microbial phenomena. Philosophical discussions of biodiversity produce only apologies for ignoring microbial biodiversity (e.g.: Lee 2004). Even in philosophical debates about evolutionary processes, little notice is taken of microbes except when they are placed as backdrops to what is in truth merely 'the sideshow of metazoan evolution' (Sterelny and Griffiths 1999: 307).

In our conclusion we speculate briefly on why this has happened. Our main aim in this paper, however, is to argue for an end to this myopia. We aim to show the radical revisions new understandings of microbes force upon some long-established ways of thinking in the philosophy of biology, specifically with respect to ontology, evolution, and taxonomy (including biodiversity). We will start with outlines of some recent developments in microbiological understandings of sensory capacities, communication processes and gene transfer, and show how these present fundamental challenges to traditional ways of thinking about microbes as primitive individual cells.

Microbiology: a brief history

Early microbiology and the pure culture approach

The history of microbiology begins with the invention and development of the microscope in the late sixteenth and early seventeenth century, but it took a considerable time for any deep understanding of microbes to develop. Their long-hypothesized association with illness, fermentation and food spoilage became an important topic of investigation in the late 1700s. In the early 1800s the stage was set for the first 'golden age' of microbiology with experimental tests of the spontaneous generation hypothesis, followed some decades later by the

rejection of bacterial pleiomorphism (the thesis that all microbes could shift from their present form to any other and thus did not have constant effects or species characteristics) and the development of methods for the identification of numerous pathogens involved in disease and putrefaction (Drews 2000). The key method for such rapid success was formalized by Robert Koch, whose 'postulates' of removing organisms from their complex communities and experimentally isolating the disease-causing process dominated microbiology for more than a century (despite the fact alternative 'mixed culture' and ecological approaches were available).

Koch's postulates emphasized two things: microbes as static individuals of single-cell types from which pure cultures could be developed, and tightly controlled uniform environments that were laboratory creations (Bull and Slater 1982a; Penn and Dworkin 1976; Caldwell et al. 1997; Shapiro and Dworkin 1997). Both these emphases have skewed microbiology, and only in very recent decades has alternative work on bacteria as dynamically interacting components of multicellular systems in a diverse range of non-laboratory environments taken hold.

Microbial biochemistry, genetics and molecular microbiology

As bacteriology matured from medical and industrial applications into a biological discipline at the end of the nineteenth century, it increasingly used biochemical tools and analyses to understand the biological processes of bacteria and other microbes (Brown 1932; Summers 1991). The origins of modern biochemistry are, in fact, attributed to the isolation of fermentation enzymes from the microbe yeast in the late 1890s (Kohler 1973; Manchester 2000). Biochemical investigation generated rapid growth of understanding of intracellular processes in bacteria and other microbes, but these insights were retained within the specialized domain of bacteriology and were of little interest to mainstream biology and genetics.

The transition from microbial biochemistry to molecular microbiology and microbial genetics took microbiology right into the centre of modern biology (Magasanik 1999). It was not until the 1940s that bacterial genetics was founded on the basis of the realization that bacteria have genetic material and that their study would enhance investigations of genotype-phenotype relations. This merger of biochemistry and genetics to study bacteria, viruses and unicellular eukaryotes was responsible for the greatest triumphs of molecular genetics in the second half of the twentieth century and had a profound impact on a range of other disciplines from evolutionary biology to epidemiology (Brock 1990; Luria 1947). Major breakthroughs gained via microbial analysis included many of the most famous insights into DNA, RNA and protein synthesis (e.g.: Beadle and Tatum 1941; Luria and Delbrück 1943; Avery et al. 1944; Lederberg and Tatum 1946). In addition, the subsequent (1970s) development of recombinant DNA technology on the basis of knowledge of bacterial genetic systems generated a huge body of biological insight and biotechnological applications (Brock 1990).

Microbial sequencing and genomics

The experimental focus of molecular microbiology achieved enormous advances in microbiology and genetics, but it was painstaking work that continued to revolve around lab-cultured microbes. These approaches were still unable to produce data sufficient for a 'natural' classification system that would surpass the purely pragmatic one often considered unsatisfactory for a true microbial science (Stanier and Van Niel, 1941; Stanier et al., 1957).

The advent of sequencing technology transformed microbiology's datasets and breadth of knowledge. The early sequencing revolution in microbiology was initiated by Carl Woese and his colleagues as an implementation of Zuckerkandl and Pauling's methodological outline of how to use molecules as fossils or documents of the evolutionary history of organisms. Zuckerkandl and Pauling had proposed that the evolutionary trees inferred from the comparison of genetic or protein sequence data from different organisms would map onto those inferred

from traditional phenotypic characters and thus converge upon real macroevolutionary patterns (Zuckerlandl and Pauling, 1965; Pauling & Zuckerlandl, 1963). They posited that a molecular clock was ticking in these sequences in the form of accumulated mutations, and because of its regularity, the time of evolutionary divergence in sequences could be calculated (within a margin of error) and ancestral relationships much more firmly established. Early molecular work on the phylogenetic relationships between microbes used a variety of amino acid and nucleotide sequences, but Woese settled on small subunit ribosomal RNA (SSU rRNA) and rDNA sequences, particularly the 16S gene, as the best 'molecular chronometers' because of their ubiquity, highly conserved structure, functional constancy, predictable rates of variation in different regions, and practical ease of sequencing (Woese and Fox 1977; Fox et al. 1980).

Woese's discovery of the archaea dramatically transformed biology's basic classificatory framework of life from two fundamental domains or superkingdoms (prokaryotes and eukaryotes) to three, and cast new light on the origins and subsequent differentiation of biological lineages. Although disputed by many taxonomists, especially those outside microbiology (e.g.: Mayr, 1998), Woese's work made more sense of molecular data and appeared finally to enable a 'natural' phylogenetic classification of bacteria instead of the prevailing phenetic approaches used – however reluctantly – as defaults (Olsen et al. 1986; Woese 1987; Woese et al. 1990).

The cumbersome methods and limited data of early microbial sequencing were rapidly overwhelmed by high-throughput whole-genome sequencing methods. The first microbial genome sequenced was that of *Haemophilus influenzae* in 1995 (Fleischmann et al. 1995), followed quickly by the smallest bacterial genome then known – *Mycoplasma genitalium* (Fraser et al. 1995) – and then the archaeal genome of *Methanococcus jannaschii* (Bult et al. 1996). There are now more than 230 whole prokaryote genomes sequenced (with 370 in the

pipeline, and over 1500 virus genome sequences) – more than 12 times the number of eukaryote genomes available (www.ncbi.nlm.nih.gov/genomes). The comparative work done with these sequences has been enormous and has enabled an increasingly complex understanding of gene function and evolution (Ward and Fraser 2005; Brown 2001). Genomic insights have illuminated inquiries into the transition from prokaryotes to eukaryotes, indicated the minimal genome required to support cellular life, and tracked pathogenic diversity over the course of a disease and virulence mechanisms across a range of species (Ward and Fraser 2005; Schoolnik 2001). Simultaneously, however, genomic data pointed to phylogenetic contradictions between the 16S and other genes used as markers of evolutionary history. The inconsistent stories such markers tell challenge the practice of equating the evolutionary history of organisms with the history of molecules – a challenge we will outline and explore in the section below on lateral gene transfer.

Microbial ecology and environmental microbiology

Ecological studies of microbes (historically not part of general ecology, but a subfield of microbiology) have been marginalized throughout most of the history of microbiology by the pure culture paradigm and the lack of effective alternative methods (Brock 1966; Atlas and Bartha 1998; Costerton 2004). Early articulations of microbial ecology are attributed to Russian soil microbiologist, Sergei Winogradsky, and the founder of the famous Delft school of microbiology, M. W. Beijerinck, at the end of the nineteenth century. It was not until the late 1960s, however, with the availability of a range of new molecular methods and a revived ecological sensibility that microbial ecology began to flourish as a subfield that proclaimed the limitations of studying bacteria as isolated individuals in artificial environments (Brock 1987; Caldwell and Costerton 1996). These limitations were highlighted by the ‘great plate count anomaly’, which drew attention to the several orders of magnitude of discrepancy between microscopic cell counts of environmental samples and plate counts of bacteria cultured from those samples (Staley and Konopka 1985; Jannasch and Jones 1959; Cutler and

Crump 1935). Once these discrepancies were no longer attributed to observed cells being 'non-viable', they led to estimates that as many as 99% of prokaryotes could not be observed or studied further because their culture evaded all available techniques (Amann et al. 1995). Molecular microbial ecology is increasingly integrated with biogeochemical approaches that study microbial interactions with the chemistry and geology of ecosystems (Doney et al. 2004; Croal et al. 2004; Newman and Banfield 2002) and has been further enhanced by the development of imaging technologies that enable *in situ* observation at the cellular and subcellular level (Daims et al. 2006; Brehm-Stecher and Johnson 2004).

This environmental turn has also occurred within microbial genomics itself, which has extended its approach beyond laboratory cultures of microorganisms to DNA extracted directly from natural environments (Stahl et al. 1984; Olsen et al. 1986; Amann et al. 1995). While this move out of the laboratory vastly expanded the scope of the data collected as well as understandings of biodiversity and evolution (Pace 1997), the continued focus on particular genes as phylogenetic markers still gave limited assessments of diversity (Dykhuizen 1998; Schloss and Handelsman 2004) and did not provide much information about the physiological or ecological characteristics of the organisms (Brune and Riedrich 2000; Rodríguez-Valera 2002; DeLong and Pace 2001; Staley and Gosink 1999).

A potential remedy to these shortfalls lies in the development of metagenomics, an approach in which the DNA of entire microbial communities in their natural environments (the metagenome) is sequenced and screened and then further analysed in attempts to understand functional interactions and evolutionary relationships (Handelsman et al. 1998; Handelsman 2004; Rodríguez-Valera 2004; DeLong 2002; Riesenfeld et al. 2004). These studies are not only discovering new genes and strains of prokaryotes and viruses, but are also revealing wholly unanticipated functions and mechanisms such as photobiology in oceanic bacteria (DeLong 2005; Béja et al. 2000) and the molecular

complexities of symbiotic relationships (Kitano and Oda 2006). Metagenomics is still at a very early stage of constructing inventories of microbial diversity, however, and it will need to integrate many other approaches in order to understand the complexity of microbial interactions in their diverse environments.

Prokaryotes as multicellular organisms

The tendency for other disciplines to ignore or marginalize microbes and microbiology may be because of assumptions that prokaryotes are simple separate cells that are behaviourally limited and the equivalent of evolutionary fossils of life's primitive beginnings. A great deal of recent and older evidence can be marshalled in support of the very opposite conclusion: that bacteria are complexly organized multicellular entities with sophisticated and efficient behavioural repertoires (many elements of which are not available to multicellular eukaryotes) and that microbes are, in fact, the evolutionary sophisticates who exhibit far more capacity to adapt to dramatic environmental change than does multicellular eukaryotic life.

A growing group of microbiologists now argue that to study prokaryotes exclusively as unicellular organisms is highly misleading (Slater and Bull 1978; Caldwell and Costerton 1996; Shapiro 1998; Kolenbrander 2000; Davey and O'Toole 2000). Prokaryotes rarely live in isolation but in a variety of communal organizations that often include macrobes. Microbes engage in a range of associations with other organisms, some of which are competitive or parasitic, and others of which are commensalisms (benefiting one partner) or mutualisms that benefit all involved (Wimpenny 2000; Bull and Slater 1982b). Many of these may be loose or temporary, whereas others are more stable and obligate (e.g.: endosymbiont or intracellular symbiotic relationships).

Everyone may agree that there are intercellular relationships and loose communities, but the argument is about whether such interactions justify the

postulation of multicellularity (e.g.: Jefferson 2004). Traditional definitions of multicellularity emphasize task sharing by tissue differentiation and the permanent alteration of gene expression patterns, thereby excluding non-microbial forms of cellular organization. However, a more encompassing definition is suggested by the molecular and cellular study of microbial communities. These communities exhibit well-defined cell organization that includes specialized cell-to-cell interactions, the suppression of cellular autonomy and competition, and cooperative behaviour that encompasses reproduction (Keim et al. 2004; Kaiser 2001; Carlile 1980).

By working together as functional units, microbes can effect a coordinated division of labour into zones of differentiated cell types that enable them access to a greater variety of energy sources, habitats, protection and other collective survival strategies (Webb et al. 2003; Crespi 2001; Shapiro and Dworkin 1997; Gray 1997). Many of these are activities that individual microbes are unable to accomplish and which are, in fact, often achieved at the expense of 'altruistic' individual microorganisms. In the most common community structure of biofilms, individual cells usually show lower growth rates than do free-living individuals (Kreft 2004). The 'suicidal' programmed cell death or autolysis (self-disintegration) of individual cells appears to directly benefit the group (Rice and Bayles 2003; Ameisen 2002; Lewis 2000; Velicer 2003; Dworkin 1996). A great variety of communal strategies have been observed and experimented on in single-taxon populations, but the most common forms of complex cooperation are found in mixed (multi-taxa) consortia of prokaryotes and other microbes. Their communal activities range from carrying out coordinated cascades of metabolic processes to the regulation of host-parasite interaction and environmental modification (Shapiro 1998; Crespi 2001; Kolenbrander 2000; Hooper et al. 1998; 2001; Dworkin 1997). Recent decades of studies of the collective behaviours involved in biofilm formation, chemotaxis, quorum sensing and genetic transfer give a great deal of support to the multicellular description of microbial communities.

Biofilms

Biofilms are the favoured lifestyle of most prokaryotes and are found in all microbial environments with surfaces, nutrients and water, from fast-flowing hot springs to catheters. They are often visible and may contain many millions of cells. Biofilms are constructed by microorganisms exuding and surrounding themselves with slimy biosynthetic polymers. Formation occurs in clear stages of adhesion, attachment, maturation and detachment (Stoodley et al. 2002; Costerton et al. 1995). Different environmental conditions influence a variety of biofilm architectures, and other materials and new species are incorporated into (or break away from) the biofilm as it develops. The prokaryotes in biofilms express genes in patterns that are very different from free-floating (planktonic) microbes, and gene expression in a biofilm changes at each stage of its development (Stoodley et al. 2002).

Living in a biofilm prevents the annihilation of bacterial communities in adverse conditions, even those of heavy and repeated antibiotic therapy (Stewart and Costerton 2001; Wimpenny, 2000; Davey and O'Toole 2000). Biofilms enable close intercellular contact that involves the exchange of many different molecules and allows greater metabolic diversity, as in the multistage digestive processes carried out by prokaryotes in the bovine rumen, as well as genetic transmission between cells and the rapid acquisition of antibiotic-resistance or virulence genes (Watnick and Kolter 2000). Although biofilms have been studied intensively since the late 1970s, it is only in recent years that researchers have emphasized their biological aspects (over their physico-chemical) and begun to conceptualize biofilm formation as a multicellular developmental process (Davies 2000; Stewart and Costerton 2001; O'Toole et al. 2000). It is a more flexible form of development than metazoan development because although biofilm formation is directional, it is strongly influenced by environmental conditions, and is reversible and not locked into a rigid sequential process as is metazoan development (Parsek and Fuqua 2004; see Note 36).

Chemotaxis

Chemotaxis is the directed movement of cells to or away from chemical stimuli. First studied in the late nineteenth century, its molecular mechanisms were not understood until the late 1960s (Adler 1969; Eisenbach 2005). 'Bacterial' (including archaeal) chemotaxis is achieved by a two-component signal transduction system that involves transmembrane receptors on the prokaryote cell. These respond to subtle changes in environmental chemicals and regulate the motor activity and type of movement, thereby altering the cell's direction (Falke et al. 1997). Moreover, chemotaxis is a social process in which prokaryotes are attracted by the chemicals secreted by neighbours. The assemblies they then form enable and enhance further social interactions associated with biofilm formation, communication and genetic exchange (Park et al. 2003).

A feedback methylation system (in which the methylation states of the receptors are modulated by enzymes affected by stimulus response) allows the cells to adapt to the initial stimulus. This process is frequently analogized to memory because it allows cells to compare their present situation with the past and respond accordingly (Grebe and Stock 1998; Falke et al. 1997; Koshland 1979). The sophistication of these chemotaxis receptor systems has led some researchers to argue that they are 'nanobrain' – tiny organs with enormous computational power that use sensory information to control motor activity (Webre et al. 2003; Baker et al. 2005).

Quorum sensing

Quorum sensing is a form of communication-based cooperation that is often called 'chemical language' and analogized to hormonal communication between metazoan cells (Bassler 2002; Shiner et al. 2005). Quorum sensing can only be carried out in communities because it is population-density dependent. It involves the release of small signalling molecules (called 'autoinducers'), through which

cells are able to assess population density. When it is high and the molecules reach a threshold of concentration, they interact with proteins that regulate gene expression thereby activating collective behaviours from biofilm formation to the production of virulence or bioluminescence (Dunny and Winans 1999; Miller and Bassler 2001; Henke and Bassler 2004). The behaviour of individual cells thus reflects regulation at a multicellular level (Gray 1997) and indicates 'primordial social intelligence' (Ben Jacob et al. 2005). The communities in which quorum sensing operates include not only prokaryote species but also eukaryote hosts, where interactions may involve the bi-directional modulation of gene expression in host and commensals (Shiner et al. 2005; Federle and Bassler 2003; Brown and Johnstone 2001; Visick and Fuqua 2005).

Lateral gene transfer

The genome itself participates in the multicellular life of prokaryote communities through processes of genetic transfer between cells – perhaps the 'ultimate interaction' between organisms in communities (Dworkin, 1997: 10; Shapiro, 1997). Lateral or horizontal gene transfer (LGT or HGT) involves the transfer of diversely packaged genetic material from one organism to another most commonly by conjugation, transduction, or transformation. Conjugation is the transfer of DNA that involves cell-to-cell contact between organisms and the transfer of a mobile genetic element (a conjugative plasmid or transposon); transduction is the transport of DNA from one organism to another by bacteriophages; transformation is the direct uptake of free environmental DNA by a 'competent' organism into its genome (Ehlers 2000; Bushman, 2002; Thomas and Nielsen 2005). Competence is an induced state of ability to bind, import and recombine free DNA (Solomon and Grossman 1996) – an ability that is at least partly regulated by extracellular chemical signals between organisms in communities (Dunny and Leonard 1997; Lee and Morrison 1999; Peterson et al. 2004).

The transfer of genetic material enables communities to adapt rapidly to

changing environments (Reanney et al. 1982). Laterally acquired advantages include novel capacities with which to take over new environments, new metabolic functions, resistance to antibiotics, and increased pathogenic virulence (Ochman et al., 2000; Sonea and Mathieu, 2001; Levin and Bergstrom, 2000; Feil and Spratt, 2001). The genes for the entire chemotaxis system, for example, were probably transferred as one unit between bacteria and archaea (Faguy and Jarrell 1999; Aravind et al. 2003). Current research indicates that genetic transfer by conjugation and transformation is much more frequent and efficient in biofilms than amongst planktonic bacteria (Hausner and Wuertz 2003; Molin and Tolker-Nielsen 2003; see Ehlers 2000 for methodological limitations of these studies). Genetic transfer and its mechanisms also appear to have positive effects on the development and stability of biofilms, meaning it is a communal activity that has both short-term lifestyle benefits as well as longer-term evolutionary benefits (Molin and Tolker-Nielsen 2003).

The capacity for lateral gene transfer in communities has many implications for evolutionary theory and taxonomic practice (discussed below), but the main point we are making here is that the 'one-organism one-genome' equation is insufficient to describe the genetic constitution of microbial communities. The concept of the metagenome is based on this extended understanding of a community genome as a resource that can be drawn on by the community organism – the metaorganism or superorganism. This genomic perspective backs up the notion of microbial communities as multicellular organisms.

The body of evidence above not only challenges the unicellular perspective in microbiology itself but also raises important issues for the philosophy of biology, especially in relation to how philosophers understand biological individuality, evolutionary transitions and processes, and the concept of species. We will examine each of these areas from the microbiological platform we built above, and outline some issues of major relevance to philosophers of biology.

1. Ontology

The central ontological categories for traditional philosophy of biology have been the individual organism and the lineage, the latter sometimes extended to include the more controversial notion of species as individuals (Hull 1987b). Populations, whether sexually or asexually reproducing, have been conceived of as constructed out of individuals. Individual microbes have an unproblematic status in microbiology as well but, as explained above, the notion of community in its various forms has also deeply informed the discipline's theory and research.

If communities are self-organizing entities that operate as functional units and are more than simple aggregations of individuals (Kolenbrander 2000; Ben-Jacob et al. 2000; Andrews 1998), they can only be excluded from multicellular status if the definition of multicellularity is closely based on knowledge of multicellular eukaryotes. Broader definitions (mentioned above) are able to include groups of interacting microbes, of one or many taxa, including sometimes eukaryote hosts (Dworkin 1997). This, in turn, suggests that rather than see macrobes as a 'higher' level of biological organization, we should view macrobes and microbial communities as constituting alternative strategies for coordinating the activities of multiple differentiated cells.

Philosophers may want to ask some basic questions about the ontological status of microbial communities, particularly whether the community organism is more fundamental than the individual organism. Microbial ecologists have tended to shy away from any notion of communities having functional properties analogous to organisms because clear spatial and temporal boundaries appear to exist only at the level of the individual organism (Parker 2004; Looijen 1998). Communities of plants, for example, do not typically appear to have firm boundaries or discreet forms due to the continuous nature of the environmental conditions that shape them. Consequently, communities are defined very loosely, usually as groups of

populations in a place the ecologist happens to be studying rather than as biological individuals (Underwood 1996; Collins 2003). The notion that communities might have emergent properties that individuals do not is explicitly rejected by many ecologists (e.g.: Underwood 1996). This 'boundary problem' for communities of plants and animals is presumed to be even worse for microbes, which are generally considered to be globally distributed and environmental will-o'-the-wisps (Finlay and Clarke 1999).

A first response to these doubts might be that clear boundaries are not necessarily connected to ontological fundamentality. Philosophers of biology willing to accept the thesis of species as individuals in conjunction with even limited hybridity should have no difficulty acknowledging this point. Second, the biofilms that are the preferred lifestyle of prokaryotes make possible their study as bounded multicellular entities as well as contradicting common conceptions of bacteria as free-floating individuals in occasional and highly impermanent contact. Finally, there is a large body of empirical work which challenges standard views of boundaries because it reverses expectations about organismal integrity and microbial ubiquity. In regard to the former, the omnipresence of genetic exchange in microbial communities shows organism boundaries to be much more permeable than might have been thought. For the latter, although it has long been presumed that 'everything is everywhere' in relation to microbial distribution, meaning that microbes have *no* biogeography (Finlay and Clarke 1999), recent studies taking a more extensive and finely resolved genomic perspective have found that communities of bacteria and archaea in hot springs and soils, for example, do actually have geographic limits at the strain level (Papke and Ward 2004; Whitaker et al. 2003; Cho and Tiedje 2000).

Communities may not possess the level of physiological integrity that individual (monogenomic) organisms do, but the recent research that we have outlined clearly indicates that they are much more than just individuals who happen to have blundered together. It seems more promising to conceptualize microbial

communities as individuals with somewhat indeterminate boundaries that have some 'un-organism-like properties' (McShea 2004) while still possessing many organismal (or proto-organismal) characteristics. If the community system is posited as more ontologically fundamental than the individual components, then its causal properties will have detectable and important influences on the constituents. The avenues of research mentioned above concerned with understanding the multicellularity of bacterial communities appear to demonstrate such 'downward' causation, and at the least provide strong reasons for pursuing this issue further.

2. Evolution

Evolution has, for the most part, been about microbes, and many of the most fundamental evolutionary questions revolve around unicellular life: how life began, how prokaryotes evolved to eukaryotes, and how transitions from unicellular to multicellular life were accomplished. The philosophy of biology is, of course, interested in these issues but primarily as a background to its evolutionary focus on multicellular organisms. The neglect of microbes can be particularly striking in one of the most exciting topics in philosophy of evolution, evolutionary developmental biology or 'evo-devo'. For example, Robert (2004: 34), in a pioneering philosophical treatment of ontogeny, writes: 'Development is what distinguishes biological systems from other sorts of systems, and it is the material source of evolutionary change'. Since microbes, though they go through cycles of internal reorganization do not, in the macrobial sense, develop at all, it would appear that on this view they are not biological systems and apparently could not have evolved. Of course, as we have been arguing, it might turn out that individual microbes are not the best way to understand microbial organization and development, and it may be that only as communities could they have evolved. But it is doubtful whether communities have exactly the kind of developmental properties that the eukaryotic multicellular vision requires, and

it is certain that Robert did not intend to describe the development of prokaryote communities. Surely it reflects an oversight, but one we think is very telling of the tendency for philosophy of biology to focus exclusively on macrobes and also nicely illustrates how evolutionary microbiology can enrich and challenge standard evolutionary theory.

Units of selection and evolutionary transitions

A long-standing debate in the philosophy of biology has been about the units and levels of biological organization on which selection acts. A key divide has been whether selection operates in a privileged way on genes and organisms, or whether it also operates at group and other levels (Brandon and Burian 1984; Sober and Wilson 1994; Wilson, 1997). Although considerable conceptual progress has been made over the last two decades (Lloyd 2000; Brandon 1999; Okasha 2003), prokaryote communities have hardly ever been used as illustrations or objects of analysis in the debate. One of the obvious questions the discussion of community function raises is whether these apparently coevolved relationships and community-level properties are selected for, or whether their existence can be fully accounted for by selection at the individual gene/organism level (Collins 2003; Whitham et al. 2003). Can such entities as prokaryote communities be conceived of as units of selection? There is experimental evidence that supports group selection in prokaryote communities (e.g.: Queller 2004). Is there competing selection of individual cells and genes that threatens the cooperation achieved at the community level? If we accept the arguments for microbial communities as biological individuals, then it is a plausible speculation that systems involving commensal microbes and sometimes macrobes could be considered to be *the* standard unit of selection. Community-level accounts of selection may even provide the key to identifying the mechanisms that allowed a hierarchy of biological organization to evolve in the first place (Okasha 2004; 2003).

One of the great benefits of attention to microbes is that it draws attention to the

problem, easily overlooked when the transition to multicellularity is interpreted as self-evident progress, of *why* multicellularity evolved at all. Explanations of the evolution of multicellularity tend to take it for granted that eukaryotic multicellularity is obviously superior, so the discussion tends to be about *how* it evolved. For the multicellular organism to have become an individual in its own right (as opposed to an aggregation of cells), selfish tendencies of single cells would have had to have been regulated and cooperative interactions promoted (Michod 1997a, b; Buss 1987; Okasha, 2004). Maynard Smith and Szathmáry's (1995) account of major evolutionary transitions specifies that entities that replicated independently before the transition can replicate only as part of the larger whole (or next level of organization) afterwards. Okasha (2003) and Michod (1997a, b) make this point more subtly and argue that the transition to multicellularity would begin on the basis of group fitness equalling average (lower-level) individual fitness, but that higher-level fitness would eventually decouple from component fitness as the transition proceeded.

It may be that while this point is basically correct, its formulation still suffers from a residually microbial perspective. The components of an integrated community would not be capable of independent replication, not because replication had become a specialized function but because the various components could only function cooperatively. Sequestered reproduction or the specialization of reproductive cells grounds one very interesting form of cellular cooperation, but perhaps we should avoid thinking of it as the only possible form. If there is something incoherent about the idea of an organism reproducing through the independent reproduction and subsequent reintegration of its parts, it is an incoherence that needs to be demonstrated.

The preceding point can be seen as part of the broader project of rethinking much more generally the possibility for aggregation of cells into more complex structures. We are inclined to speculate that microbial multicellularity (like organelles in eukaryote microbes) is just a frozen, less flexible, obligate analogue

of bacterial multicellularity. Prokaryote cell differentiations can dedifferentiate whereas metazoan multicellularity is irreversible. In eukaryote multicellularity, for example, aerobic metabolism is essential because this form of multicellularity has high energy demands that cannot be met by anaerobic means (Fenchel 1996). Prokaryote multicellularity, however, is an energy-efficient form and metabolic diversity is not sacrificed. The eukaryote multicellularity we commonly think about had to be selected for, to be sure, but in the long run of evolution it is likely to be much less well able to adapt to major changes in environmental conditions, such as atmosphere. Or, if it does adapt, this may be very much dependent on the more diverse capacities of microbial commensals. Microbes have a proven track record of living in a world devoid of eukaryotes, but multicellular eukaryotes are unlikely to be able to manage in a microbeless ecosphere.

In many ways, microbial communities have experienced a great deal more evolutionary and ecological success than macrobes. No doubt the key to understanding how macrobes evolved at all is to locate more clearly what it is that they do better than microbial communities (unless, indeed, we should see macrobes in a neo-Dawkinsian way, as primarily vehicles for the billions of microbes that live in the many niches macrobes provide, designed to transport them to especially large and attractive energy resources).

At any rate, we need to resist the temptation to see microbes as primitive precursors of macrobes and the transition to multicellularity as representing unambiguous progress. Rather, we must face the fact that much of our evolutionary theory is grounded in features peculiar to macrobes and has questionable relevance to microbial evolution — which is to say, by far the largest part of all evolution. It is also, in a real sense, the most important part of evolutionary history. For it is clear that the basic machinery of life evolved in microbes prior to what might, in relative terms, be seen as no more than a severe narrowing and slight diversification of the applications of that chemistry in macrobes. And, of course, it is only due to ancient prokaryotic mergers that there

are eukaryotes at all (Margulis 1970).

Evolutionary process and pattern

As important as these questions about major evolutionary transitions is the need to reflect on the mechanisms by which microbial communities adapt and evolve. The philosophy of evolutionary biology must take account of the rapidly growing body of work in microbial phylogeny on horizontal or lateral gene transfer. The capacity for resource exchange that LGT allows has been described as a distributed genome or a genetic free market (Sonea and Mathieu 2001) – a global resource too big for single cells but accessible when populations find ecological reasons to acquire DNA for new functions. A strong interpretation of gene transfer means that individual genomes are ephemeral entities fleetingly maintained ‘by the vagaries of selection and chance’, and taxa are only an ‘epiphenomenon of differential barriers’ (environmental, geographical and biological) to lateral gene transfer (Charlebois et al. 2003).

The findings of comparative evolutionary genomics have raised enormous problems for the dominant eukaryo-centric paradigm of vertical inheritance and mutation-driven species divisions that give rise to a single tree of life (Doolittle 2002; 1999; Stahl and Tiedje 2002; Gogarten and Townsend 2005; O’Malley and Boucher 2005). While comparative genomic studies confirmed the distinctiveness of the archaea, they also complicated the simpler stories told by popular single-gene phylogenetic markers (such as the 16S ribosomal gene) by revealing huge amounts of atypical DNA in the genome. Many genomic sequences do not match organismal or species patterns due to the complex histories of gene exchange. Frequent transfers result in mosaic genomes which consist of genetic contributions from many sources, even phylogenetically distant ones (Doolittle et al. 2003; Koonin et al. 2001; Lawrence and Hendrickson 2003). This lack of a unilinear history to genomes has inspired a number of methods that attempt to capture not only vertical lines of descent (as bifurcating tree branches) but also the web-like complexity of lateral movement between lineages (e.g.: Huson 1998;

Bryant and Moulton 2004).

Microbial populations exhibit much more rapid rates of evolutionary change than do their macrobial equivalents, the variety of dynamics and mechanisms of evolution is more diverse, and extinction means something quite different if indeed it has any relevance at all to microbes (Stahl and Tiedje 2002; Myers, Paulson and Fraser 2006; Lawrence 2002; Weinbauer and Rassoulzadegan 2004; Staley 1997). It seems likely that the biologically significant loss in a microbial context would be something like a metabolic capacity rather than a particular microbial strain. But given the possibility of a wide distribution of genomic resources underlying these capacities, such extinction may be an improbable event. If so, then extinction, which plays a major role in standard models of macroevolution, is irrelevant for theorizing the evolution of microbes.

Most importantly, the genetically isolated lineage, often conceived of as the fundamental unit of evolutionary theory, may have no real analogue in the microbial world. It might be possible in principle to construct evolutionary models in which microbial clones play a similar role to the familiar macrobial lineages. But even apart from the great diversity of clonal structure exhibited by different microbial taxa, there are some serious difficulties with such models. The most obvious is time scale. Microbial clones have lifespans of hours or days rather than the thousands of years typical of macrobial lineages. This suggests a need for higher level models if any sense is to be made of long term evolutionary change. It further needs to be decided how the beginning and end of a clone are to be defined for this purpose, especially in light of a large body of evidence that shows little true or enduring clonality in most bacterial populations (Maynard Smith et al. 1993; Maynard Smith et al. 2000). The prevalence of mobile genetic elements moving between microbial units again points to a focus on larger units within which these movements take place.

This point suggests a slightly different formulation of the question raised earlier

about the boundaries of communities. If it turns out that the lateral circulation of genetic material takes place within reasonably clearly delineated microbial communities, it may be useful to consider these as units of selection. Surely such relative isolation will apply to communities defined by their residence in, for example, a particular human gut. Whether the same applies to aquatic bacteria, say, is another matter. If not, either microbial evolution is limited to more peripheral, isolated environments or, more likely, we will need to expand on traditional macrobial models in search of an adequate understanding of microbial evolution.

Microbial genomics and metagenomics have evolutionary implications that reach into the most basic representations of evolution since they make clear that most of life and its history cannot be simply configured as a tree-like pattern of evolutionary outcomes (Doolittle 2005). This realization makes yet further deep inroads into the philosophy of biology because of its extensive implications for microbial taxonomy, the units of taxonomy, and the philosophical appreciation of biodiversity.

3. Taxonomy and biodiversity

Taxonomy

Identifying categories of organisms is central to the task of understanding the diversity of past and present forms of life and the evolutionary relationships between them. While the philosophy of biology has often recognized prokaryote classification as a special case (e.g.: Sterelny 1999; Hull 1987a; Wilkins 2003), it has paid the issues involved hardly any attention and continues to believe that evolutionarily defined categories of organisms can be represented as bifurcating lineages that compose a tree of life. A variety of concepts have been proposed to define the species that make up this tree, but all of them prove unsatisfactory when gene exchange and genomic heterogeneity are brought into the picture.

Prokaryote taxa simply refuse to show the clear, consistently definable characteristics often associated with eukaryotic species and classification schemes (Roselló-Mora and Amann 2001). There is, of course, controversy over how sharp the species boundary is even in eukaryotes but to whatever extent it is a problem there, it is considerably worse in prokaryotes (Dupré 2002).

The early history of microbial classification is a struggle for the specificity of bacteria and the recognition that groups have inherent characteristics that distinguish them from other putative species groups (Cohn 1875, in Drews 2000). The key issue from a microbial genomics perspective is whether to think of prokaryote taxa as continua or as discrete clusters of species-specific genetic diversity (Konstantinidis and Tiedje 2004; Doolittle 2002; Lan and Reeves 2000). Although the biological species concept (BSC) has never found much purchase in microbial systematics because of its exclusion of asexual reproduction and difficulties in coping with gene transfer between evolutionarily distant lineages (Maynard Smith 1995; Cohan 2002; Dupré 2002), there is an active debate between microbiologists about what constitutes an appropriate evolutionary or phylogenetic definition (Roselló-Mora and Amann 2001). In its simplest form, this simply means species are defined by common ancestry. Usually, however, this basic concept is accompanied by assumptions about which molecules are more reliable bases of such phylogenetic inference, and ribosomal DNA sequence is generally considered to be the prime candidate for divulging 'natural relatedness groups, the phylogenetic divisions' (Hugenholtz et al. 1998; Ward 2002).

As we outlined above, the role of 16S rRNA gene sequence as the ideal phylogenetic marker has been undermined by conflicting genomic evidence, which has also damaged more generally the idea of a single true marker for microorganismal evolutionary history. Other microbiologists emphasize the importance of ecological forces on populations, with 'ecotypes' (equivalent to strains) being the product of ecological (but not reproductive) divergence (Cohan 2002; Palys et al. 1997; Gevers et al. 2005). Pragmatists, generally more

convinced of the extent and implications of gene exchange, use the word 'species' as a purely practical term that means 'assemblages of related organisms for which microbiologists have attached specific names rather than natural kinds' (Gogarten et al. 2002). These are 'species-like' entities (Rodríguez-Valera 2002) whose classifications are created by classifiers, not nature, and these must be constantly revised in light of new evidence and emerging inconsistencies.

Popular operational measures reflect the mixture of concepts and conceptual problems at work in microbial systematics. The currently predominant measure of where the boundary falls between prokaryote species is below a 70% rate of DNA-DNA reassociation in hybridization tests of the total genomic DNA of two organisms (Roselló-Mora and Amann 2001; Dijkshoorn et al. 2000). This crude measure of genomic distance is commonly considered equivalent to 97% rRNA identity. The first value was chosen because it appeared to map onto phenotypic clusters for no known evolutionary reasons; the second because it conveniently mapped onto the 70% measure (Cohan 2002; Lan and Reeves 2000). Apart from the fact that both measures ignore apparently important genomic differences, there is no evolutionary reason why 70% DNA-DNA similarity values should be a species boundary, nor for 16S genes to be considered adequate representatives of a species history (Boucher et al. 2001; Lan and Reeves 2001; Palys et al. 1997). Moreover, the correlation between DNA-DNA reassociation and 16S sequence varies in different genera, and it is well known that the 16S gene lumps together physiologically diverse strains (Staley and Gosink 1999; Kämpfer and Roselló-Mora 2004).

An influential proposal designed to overcome these problems is the quasi-official (American Society of Microbiology) species definition (Vandamme et al. 1996; Stackebrandt et al. 2002). It combines genomic, phylogenetic and phenotypic approaches into a pragmatic and 'phylophenetic' (or 'polyphasic') taxonomic framework in which a species is 'a monophyletic and genomically coherent

cluster of individual organisms that show a high degree of overall similarity with respect to many independent characteristics, and is diagnosable by a discriminating phenotypic property' (Roselló-Mora and Amann 2001: 59). In practice, however, any such practical species measure is still anchored phylogenetically by the 16S rRNA gene (Young 2001; Dijkshoorn et al. 2000) which is seen as a proxy for natural units and their boundaries, and helps overcome the discomfort of many microbial systematists with 'non-natural' classification concepts and methods (e.g.: Ward 1998; Coenye et al. 2005).

Another operational measure with the aim of natural classification uses the concept of a 'core' genome. Although there were earlier hopes of finding a phylogenetically definitive universal core of genes common to all prokaryotes, current measures focus on pools of genes that determine 'properties characteristic of all members of a species' (metabolic, regulatory and cell-division genes) and are seldom transferred (Lan and Reeves 2000). Because there is presumed to be a barrier to the interspecific recombination of core genes, they reveal the evolutionary history of the species (Wertz et al. 2003). Core genes are contrasted to more variable 'auxiliary' genes which often enable niche adaptation but are unreliable as species indicators. There is still, however, great difficulty in finding genes that provide core conserved functions but are not transferred (Saunders et al. 2005; Doolittle 2005; Boucher et al. 2001) and different patterns of variability and stability in genomes of different species may require a range of species-genomes concepts. The idea of a core genome may be capable of providing a definition of species, but is unlikely to ground a fully phylogenetic taxonomy given the prevalence of lateral gene transfer over deep time.

If, as is strongly suggested by the several lines of research outlined above, the individual microbe is not the fundamental ontological unit in microbiology, then it should be no surprise that attempts to find a division of individual microbes into natural kinds are doomed to failure. Microbiologists should be well prepared for the discovery that species genomes or phylotypes (a taxon defined by a

particular gene marker) fail to capture the way microbial life has organized itself or, indeed, that microbial life and evolution does not lend itself to a monistic, consistently applicable species concept that allows evolutionary history to be represented as one true tree of life.

Many further questions remain in this area. Is there potential for a taxonomy of communities or community lineages, or do these entities have limited taxonomic significance because of their weak boundaries and evolutionary lability? Should genomic identity or functional role guide the classification of participants in community systems? Finally, if we let the idea of the communal genome as a dynamic community resource further undermine the notion of stable species boundaries, what are the implications for how we understand biodiversity?

Biodiversity

Microbial diversity is generally given short shrift by biodiversity studies and philosophers of biodiversity (Ehrlich and Wilson 1991; Loreau et al. 2001; Sarkar 2002; Oksanen and Pietarinen 2004; Nee, 2005), mostly because of methodological and technical limitations. Microbiologists have long known that their understanding of microbial diversity has been restricted both by technology and by a health- or agriculture-based bias towards pathogens. Microbes' enormous diversity of habitats, metabolic versatility and physiological adaptability are still only beginning to be understood. Genomics-driven estimates have risen to as many as 10^7 - 10^{12} prokaryote 'species' (Dykhuizen 1998), of which fewer than 36,000 are indicated by rRNA sequence analysis (Schloss and Handelsman 2004) and only 7,800 of those are named and described (Kämpfer and Rosselló-Moro 2004).

Simple numerical comparisons of eukaryotic and prokaryotic diversity by species counts or estimates are inadequate for several reasons. As we have just seen, there are deep conceptual problems in defining the microbial species. If eukaryote species were designated by the same broad genomic hybridization

criteria that prokaryote species are, then groups such as humans, chimpanzees, orangutans, gibbons, baboons and lemurs and would all belong to the same species (Staley 1997). Environmental genomics is centrally concerned with escaping these limitations, although it still relies heavily on ribosomal gene sequence to do so. One of the early benefits anticipated for metagenomics is the contribution to a broader and deeper understanding of microbial diversity.

At present, broad studies of microbial diversity are largely occupied by cataloguing exercises, but as the research deepens to include multilevel interactions and processes rather than things, the object of study could become biodiversity in the extended functional sense of how microorganisms are involved in ecosystem processes such as resource use, decomposition and nutrient cycling (Finlay et al. 1997; Loreau et al. 2001). Appropriate ecological assessments of biodiversity need to be able to take into account the variability of microbial populations as well as the relationship between community structure, biogeochemistry and ecosystem function (O'Donnell et al. 1994; Stahl and Tiedje, 2002; Ward 2002; Buckley 2004). They also need to incorporate explanations of 'the tempo, mode and mechanisms of genome evolution and diversification' in relation to higher-order biological and ecological processes (DeLong 2004; Falkowski and de Vargas 2004) and obviously the findings of biogeographic patterns in the distribution of prokaryotes and other microbes (Martiny et al. 2006; see above) will be part of this analysis.

Clearly, these are not straightforward research programmes that will give simple answers about biodiversity, but they are aspirations towards understanding complex phenomena for which technology and tools of analysis are beginning to develop. As understanding of the role of microbial communities in ecosystem function grows, and microecological studies are integrated with macroecological, it is likely that philosophical and practical arguments for microbial conservation – not recognized at all in the philosophy of conservation – will also develop (Colwell 1997; Staley 1997). It remains to be seen whether we *should* be much

concerned about microbial conservation. Our remarks above about extinction raise the question of whether there is any serious risk to be evaluated. However, given the fundamental role of microbes in all life, it would be good to know how microbial diversity is affected by environmental changes already profoundly affecting macrobial biodiversity. Philosophical analysis could make important contributions to framing the questions that need to be asked.

Towards a more inclusive philosophy of biology

Even prior to recent developments stemming from the growth of genomic technology, philosophy of biology has been culpable in its failure to take serious account of the microbiological realm. Today this omission is inexcusable. The range of diverse and interconnected microbiological perspectives that we have outlined above have fundamental importance for how we understand life. These reconceptualizations are not just a background development but a major transformation in understanding that needs to be reflected in the philosophy of biology.

Finally, it might be worthwhile hazarding a guess as to why the philosophy of biology has been so willing to ignore microbes and microbiology. Candidate reasons could be the intractability of microbial analysis, ignorance, authority, invisibility, and a progressive view of evolutionary history. Intractability of analysis (difficulties in coming up with a natural classification system and measures of diversity) is an implausible answer, as it might just as easily have stimulated philosophical scrutiny. It is not a simple matter of ignorance either, because many philosophers of biology are at least aware enough to sweep microbes aside. Does philosophy of biology focus on metazoans simply because of some old and still unchallenged attributions of status to zoology and animals (over botany and plants as well)? An even more basic explanation could be a cognitive bias towards larger, more visible phenomena – the same reason Sean Nee

(2004) gives for the public indifference to microbes. But philosophers have shown no reluctance to get involved in debates about the molecular minutiae of other biological findings, so this explanation is not compelling either. Similarly one might point to the rapid development of techniques and theoretical frameworks in microbiology as inhibiting factors, but this rapidity would not distinguish it from various other biological subfields, especially in molecular biology, with which philosophers have been quite willing to keep up to date.

Some scientists perceive 'an unspoken philosophy of "genomic supremacy"' (Relman and Falkow 2001: 206) that is accorded to more complex animals because of genome size and number of predicted genes. If this were strictly true, then cereals, amphibians and some amoeba – whose genomes are up to 200 times larger than those of humans (Gregory 2001) – would be ranked higher and receive more philosophical attention than mammals, which is patently not the case. Any unspoken philosophical ranking of life forms and their study would need to propose a broader view of human supremacy (Paabo 2001) and comparative genomics is more likely to challenge such a notion than to support it.

Taking this explanation in terms of human supremacy further, Stephen Jay Gould (1994) sees general indifference to microbes as part of the 'conventional desire to view history as progressive, and to see humans as predictably dominant' thus leading to overattention to 'complexifying creatures'. This view places at the centre of life a 'relatively minor phenomenon' instead of the most salient and enduring mode of life known to this planet. Is it possible that philosophers, usually amongst the first to condemn notions of progressive evolution, are under the influence of this view of the history of life when they ignore microbes? Perhaps a more charitable interpretation is that the discontinuity of life forms implied by the prokaryote-eukaryote division (Stanier and Van Niel 1961; Olsen et al. 1994; Sapp 2005; Woese 2005) and the emphasis of negative characteristics of prokaryotes (no nucleus, no internal membranes, small size) gave rise decades ago to a generally unchallenged notion amongst philosophers

that microbes were less interesting than their (assumed-to-be) categorically different multicellular descendants. That this notion is maintained despite the growth of knowledge and theory in microbiology means that adherence to a bad habit is the only reasonable explanation for the reluctance of philosophers of biology to deal with microbes. In that case, delving even briefly into the recent microbiological literature might provide just enough of a conceptual kick to initiate a wider range of thinking in the philosophy of biology and perhaps even stimulate a philosophy of microbiology.

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