Studies in History and Philosophy of Biological and Biomedical Sciences xxx (2016) 1–8

Contents lists available at ScienceDirect

Studies in History and Philosophy of Biological and Biomedical Sciences

journal homepage: www.elsevier.com/locate/shpsc

The metaphor that viruses are living is alive and well, but it is no more than a metaphor

M.H.V. van Regenmortel

UMR 7242 Biotechnologie et Signalisation Cellulaire, Université de Strasbourg-CNRS, 300, Boulevard Sébastien Brant, CS 10413 67412 Illkirch cedex, France

ARTICLE INFO

Article history:
Received 22 January 2016
Accepted 27 February 2016
Available online xxx

Keywords:
Concepts of life
Human immunodeficiency virus
Metaphors in virology
Nature of viruses
Tree of life
Viral factories

ABSTRACT

Virologists often use anthropomorphic metaphors to vividly describe the properties of viruses and this has led some virologists to claim that viruses are living microorganisms. The discovery of giant viruses that are larger and have a more complex genome than small bacteria has fostered the interpretation that viral factories, which are the compartments in virus-infected cells where the virus is being replicated, are able to transform themselves into a new type of living viral organism called a virocell. However, because of the widespread occurrence of horizontal gene transfer, endosymbiosis and hybridization in the evolution of viral genomes, it has not been possible to include metaphorical virocells in the so-called Tree of Life which itself is a metaphor. In the case of viruses that cause human diseases, the infection process is usually presented metaphorically as a war between host and virus and it is assumed that a virus such as the human immunodeficiency virus (HIV) is able to develop new strategies and mechanisms for escaping protective host immune responses. However, the ability of the virus to defeat the immune system is solely due to stochastic mutations arising from the error-prone activity of the viral enzyme reverse transcriptase. The following two types of metaphors will be distinguished: an intentionality metaphor commonly used for attributing goals and intentions to organisms and the living virus metaphor that considers viruses to be actually living organisms.

1. Introduction

By the end of the 19th century, filtration experiments had clearly established that several infectious diseases were caused by agents smaller than bacteria and therefore invisible by light microscopy, which could not be cultured on conventional bacteriological media. Dimitri Ivanovsky in St Petersburg, Russia was the first to show in 1892 that the agent causing the tobacco mosaic disease was able to pass through a Chamberland sterilizing filter although he did not grasp the significance of his observation (Van Regenmortel, 2010a; 2010b). He remained convinced that he was dealing with a small bacterium rather than with a new type of infectious agent and thought that the filter he used might have had fine cracks allowing small spores of a microbe to pass through it (Witz, 1998). However, Ivanovsky's misinterpretation did not prevent Russian and other virologists to claim many years later that he was the father of virology (Lvov, 1993; Stanley, 1944). In 1898, Martinus Beijerinck in Holland repeated Ivanovsky's experiments but in addition he showed that the infectious agent in filtered tobacco sap was able to diffuse through several millimeters of an agar gel. This led him to conclude that the agent was not a microbe but was a contagious living fluid which he glorified with the Latin label *contagium vivum fluidum*. However, he also demonstrated that the agent could reproduce itself in a tobacco plant and he called the agent a virus. This led Dutch virologists a century later to claim that Beijerinck was obviously the father of virology (Bos, 1995, 1999).

In 1898, Friedrich Loeffler and Paul Frosch in Germany reported that the causative agent of foot-and-mouth disease in cattle also passed through a Chamberland-type filter but not through a finer grain Kitasato filter, from which they correctly concluded that the causative virus which multiplied within the host was a corpuscular particle and not an ill-defined living fluid. Beijerinck, however, did not agree with their interpretation that the virus was a small particle (Witz, 1998). This led German virologists to claim that Loeffler

E-mail address: vanregen@unistra.fr.

http://dx.doi.org/10.1016/j.shpsc.2016.02.017
1369-8486/

and Frosch should actually be considered the fathers of virology (Horzinek, 1995).

The discovery that viruses were a new type of infectious agent was thus attributed by virologists from three countries to scientific compatriots, which apart from nationalistic preferences illustrates the difficulty of agreeing on what constitutes a scientific discovery. A discovery is not simply making a novel observation such as the filterability of an infectious agent but requires in addition a correct interpretation of what is being observed since this is essential for grasping the significance of a new experimental finding. The controversy about who should be considered the father of virology reminds us that scientific facts are never obvious but need to be correctly interpreted.

The current debate on whether viruses are living is another case of disagreements that are fuelled not necessarily by new observations but by different ways of interpreting them. The present review will argue that such disagreements often arise from the tendency of many virologists to use anthropomorphic metaphors for describing more vividly the properties and behaviors of viruses.

In the third edition of their book *Principles of Virology*: *Pathogenesis and Control*, Flint, Enquist, and Racaniello (2009) pointed out that viruses do not actually "do" anything although many virologists succumb to the temptation of ascribing various actions and motives to viruses. They warned that while remarkably effective in enlivening a lecture or an article, anthropomorphic characterizations are inaccurate and often misleading. According to them, a multitude of anthropomorphic expressions should be banned because "Viruses cannot think, employ, ensure, synthesize, exhibit, display, destroy, deploy, depend, reprogram, avoid, retain, evade, exploit, generate etc". They also claimed that "infected cells and hosts do many things in the presence of viruses, but that viruses themselves are passive agents totally at the mercy of their environments" and they further admitted that because "it is extremely difficult to purge anthropomorphic terms from virology communications", they had to spend many hours removing such terms when preparing their textbook (Flint et al. 2009). It will be argued here that the claim that viruses are alive is only a metaphor based on several anthropocentric interpretations that are no doubt responsible for much of its appeal but which also makes it difficult for a scientific consensus to emerge. Metaphors are frequently used in scientific discourse and the role they play in shaping scientific concepts has become a major theme in the philosophy of science. However, this falls outside the scope of the present review and interested readers may want to consult Black (1962), Bradie (1999), Keller (2002) and Bailer-Jones (2002). Lily Kay (2000) in her history of the genetic code entitled *Who Wrote the Book of Life* described the many metaphors used by molecular biologists such as the language of life, DNA and protein codes, messengers, recipients as well as genetic information, which implied that genetic and verbal information systems were analogous. She pointed out that the Book of Life metaphor produced information without meaning, codes with no language, messages with no sender and writing devoid of authorship (Kay, 2000, p. 296). Since a human language is impossible without consciousness, a Book of Life without consciousness yielded numerous inadequate metaphors that are still widely used in biology. Metaphors may sometimes be useful as epistemic and theory-construction devices, but it is must be emphasized that they do not tell us how the world actually is (De Donato & Arroyo-Santos 2011; Hoffman, 1980).

The present review will first describe the orthodox view held by most virologists that viruses are subcellular, genetic parasites that do not self-replicate but are being replicated by the cells they have infected. The properties of living organisms as members of a reproductive lineage will then be analyzed. This will make clear why organisms are different from organs and other living tissues that are not functionally autonomous. Some biologists have suggested that a viral factory, which is the compartment in infected cells where virus replication takes place, is able to transform a virus into a living organism called a virocell. It will be argued that this putative ability of viruses to generate new types of living cells finds its origin in metaphors that attribute to viruses human-like capacities of intentional, goal-directed behavior. The Tree of Life (TOL) will then be described and it will be shown that viruses cannot be included in a universal TOL. Other metaphors will be discussed, for instance the interpretation that viruses are involved in battles and wars with their hosts and that the human immunodeficiency virus (HIV) is able to develop new strategies to escape the host immune system. Finally, it will be argued that design terminology is not appropriate for describing neither the behavior of HIV battling with host cells nor the attempts of scientists who try to develop an HIV vaccine by so-called rational design.

2. The nature of viruses: the orthodox view

At the present time, the majority of virologists still adhere to the view that viruses are subcellular, genetic parasites (Lwoff, 1957) that do not self-replicate or reproduce themselves but are being replicated, passively rather than actively, by the metabolic activities of the cells they have infected. The replication of viruses occurs through a process of copying carried out by parts of the cellular machinery of their host cells and this replication process is totally different from the process of fission that occurs when living cells reproduce themselves. When a virus infects a cell and the viral genome becomes integrated in the infected host, it may seem that the virus has become part of a living system although it is actually no more alive than other constituents of the host cell such as its genes, macromolecules or organelles. Most biologists accept that the simplest biological system that can be said to be alive is a cell and that cells always originate from other cells but that the individual components of a cell are not themselves alive. Virus particles, like genes, are inert outside cells but when the viral genome is integrated in an infected cell, it is able to instruct the cell to produce viral proteins and virions although it is still the cell that synthesizes them.

Many authors have discussed the nature and origin of life in terms of a series of hypothetical steps that could possibly explain the transition from non-life to cellular life in a prebiotic Earth through the spontaneous emergence of biomolecules, primitive membranes, metabolic networks and self-replicating systems (for a review, see Luisi, 2006). Once life had appeared, it spread over our entire planet without the need for periodical spontaneous generation events. However, even if one considers that something that evolves by natural selection is already alive, this still does not provide a clear-cut frontier between a non-living state of matter and a living system (Bruylants, Bartik, & Reisse, 2010), and the search for such a boundary has until now remained a futile exercise (see section 3). It is as difficult to ascertain at which moment life emerges as it is to decide at which moment it disappears upon the death of an organism.

Stanley in 1935 had suggested that tobacco mosaic virus (TMV) was a crystallizable molecule that lied at the borderline between chemistry and biology (Norrby, 2008; 2010). This raised the possibility that viruses could be alive and it was believed by some that if a protein could be a living infectious agent, viruses might hold the key to the origin of life. However, it was later shown that TMV was not a pure protein but a RNA-containing nucleoprotein (Bawden & Pirie, 1937) and it subsequently became clear that it was the RNA in the virus that was the infectious entity.

Viruses are considered to be biological entities because they possess a genome and give the impression to human observers of being able to adapt to particular hosts and biotic habitats. However, viruses do no not possess the functional autonomy that would allow them to actively evolve by themselves since they are passively evolved *by* the cells they have infected. Moreira and López-Garcia (2009) have suggested that this is somewhat analogous to human

Please cite this article in press as: van Regenmortel, M. H. V., The metaphor that viruses are living is alive and well, but it is no more than a metaphor, Studies in History and Philosophy of Biological and Biomedical Sciences (2016), http://dx.doi.org/10.1016/j.shpsc.2016.02.017