Virus Ontology: Thing, Being, Process, or Information?

Nicolae Sfetcu

24.10.2020

Sfetcu, Nicolae, "*Virus Ontology: Thing, Being, Process, or Information?*", SetThings (October 24, 2020), DOI: 10.13140/RG.2.2.35874.66241, URL = https://www.setthings.com/en/virus-ontology-thing-being-process-or-information/

Email: nicolae@sfetcu.com

Translation of:
Sfetcu, Nicolae, "*Pandemia COVID-19 – Abordări filosofice*", SetThings (14 octombrie 2020), MultiMedia Publishing (2020), ISBN: 978-606-033-416-3, DOI: 10.13140/RG.2.2.27611.39205, URL = https://www.setthings.com/ro/e-books/pandemia-covid-19-abordari-filosofice/

Abstract

The study of viruses raises pressing conceptual and philosophical questions about their nature, their classification, and their place in the biological world. A major set of problems concerns the individuality and diachronic identity of a virus: what is the virus, the viral particle (virion) or the entire viral cycle? The correct identification of the virus has significant ontological consequences, also related to the place and time when biological entities begin and end.

Virus Ontology: Thing, Being, Process, or Information?

The study of viruses raises pressing conceptual and philosophical questions about their nature, their classification, (O'Malley 2014, 45–94) (Mayr 1953) and their place within the biological world.

A major set of problems concerns the individuality and diachronic identity of a virus: what is the virus, the viral particle (virion) or the entire viral cycle? The correct identification of the virus has significant ontological consequences, also related to the place and time when biological entities begin and end. (Bouchard and Huneman 2013)

The main metaphysical thesis considers that the world is composed of things or substances, with things identified by their properties. But Dupre and Guttinger believe that widespread symbiosis threatens the clarity of the boundaries between organisms and even the uniqueness of these boundaries. (Dupré and Guttinger 2016) The integrated nature and blurred boundaries between organisms have led to claims that "traditional (substance-based) metaphysical accounts of individuality should be replaced with a process ontology, as the only 'philosophy of organism' that can make sense of the biological phenomena as we now know them." (J. Dupré and Guttinger 2016) (Henning and Scarfe 2013))

Dupre and Guttinger make an ontological statement that biological systems are processes. In this context, they challenge the view that viruses are distinct entities that follow their own intrinsic (and pathogenic) agenda, based on two arguments: symbiotic systems can include viruses, and viruses must be seen as processes. They argue that viruses are vital and ubiquitous elements of the larger flow of interconnected processes that make up biological systems. (Dupré and Guttinger 2016)

Microbial symbionts involved in the modulation of development and playing a central role in the development and homeostasis of the immune system, (Spasova and Surh 2014) with connection to the central nervous system, (Bravo et al. 2012) have contributed to a major philosophical reconsideration of the concept of biological individual. The human microbiome would consist not of passengers, but of parts of an integrated individual, the organism itself in its stable state proving to be a product of countless interactions between the host and microbes. Thus, viruses provide services to biological systems, some even vital. Viruses are an integral part of the system, rather than parasites, kept under control enough to allow the system to function. (Wylie, Weinstock, and Storch 2012) Basically, the virus responds gradually and systematically to dietary changes. (Minot et al. 2011) suggesting a positive functional response to environmental changes.

Viruses kill the cells in which they reproduce and maintain their own life cycles, but it is considered possible that this killing of cells is functional for the larger system of which the virus is also a part. The result is a stable ecological relationship between viruses and their hosts, beneficial for the system as a whole, including in regulating the morphology and function of the intestine and in shaping the immune system.

Retroviruses have a single-stranded RNA genome that is reverse transcribed after infection in double-stranded DNA and inserted into the host genome. After insertion, the viral DNA is treated by the host as its own DNA, which means that it is transcribed and reproduced together with the rest of the host genome. (J. Dupré and Guttinger 2016) In some cases, retroviruses reach the host genome and can transform into what is known as endogenous retroviruses. It is estimated that up to 8% of the human genome actually consists of endogenous retroviruses, (Griffiths 2001) resulting in significant proportions of DNA from eukaryotic organisms initially entering the cell line via a virus.

The virus may function as a vast repository of genetic resources. (Minot et al. 2011) Thus, the human genome itself can be thought of as a database or library of resources that can be used in many ways by the cell. (Noble 2006) It can be speculated here that “the ability of microbes, specifically our symbiotic microbiome, to recruit genetic resources from the biotic environment may be a much more efficient way of responding to environmental contingencies than evolution by random genetic variation and selection." (Dupré and Guttinger 2016)

Given this close interconnection between viruses and their hosts, it seems plausible that viruses in complex multi-organic systems are vital functional parts of the whole, and can play essential roles in eliminating harmful cells, mediating the transfer of genetic resources, developing their hosts, and their survival in difficult conditions. (Dupré and Guttinger 2016)

The question of whether viruses are alive has been asked repeatedly throughout the history of virological research. The answer is difficult, and it has changed over time. (Smith and Szathmáry 2000) A related issue is the extent to which viruses could be considered as organisms (in the idea that all organisms are living beings, but not all living beings are organisms). Many biologists believe that viruses are not organisms, which involve a very high degree of functional organization and cooperation, with strong interactions between the parties. (Huneman 2006)

Other biologists believe that discrimination between living things and things does not suit the specific case of viruses: the answer would depend on pre-existing conceptions of "life". In addition, the question of what viruses do is at least as important as the question of what they are (i.e., their living or non-living state). (Pradeu, Kostyrka, and Dupré 2016)

Koonin and Starokadomsky define the status of viruses among biological entities in the replicator paradigm. All biological replicators form a continuum along the selfishness-cooperativity axis, from completely selfish forms to fully cooperative ones. In this context, all organisms are communities of replicators that interact, co-evolving, from different classes. (Koonin and Starokadomskyy 2016)

According to Lewis et al., there is a third state, characteristic of latent cells (with reduced metabolic activity and able to resume growth and division according to external conditions), which is neither truly living nor non-living. (Lewis 2010)

In general, a dead organism still falls into the category of life. However, when it comes to viruses, these different aspects of life are tangled and are usually discussed together. Indeed, viruses can be seen as not belonging to the category of living beings, because they are incapable of autonomous reproduction, and extracellular virions are in a latent (inert) state.

Koonin and Starokadomsky argue that it is always possible to say whether a particular entity belongs to the realm of biology, within the fundamental concept called of the "replicator paradigm." (Koonin and Starokadomskyy 2016) Replicators form a continuum along the axis of autonomy. The only universal feature shared by all replicators is the presence of a signal that allows replicative autonomy. (Kristensen et al. 2013) An orthogonal dimension of the replicating universe involves reproductive strategies (or lifestyles), from complete selfishness (associated with parasitism) to full cooperation. (Joh and Weitz 2011)

Transitions from one type of replicator to another have occurred on numerous occasions during evolution, but there is no evidence of evolutionary transitions between cells and viruses. (Koonin and Starokadomskyy 2016) Nor about the origin of the selfish elements in the “escaped genes” (which become autonomous, selfish replicators) of cellular life forms. Most essential viral genes (viral marker genes) do not have close counterparts between the genes of cellular life forms, being probably originated in a primordial, pre-cellular gene pool. (Koonin and Dolja 2013)

Virion stability and inactivity provide intuitive support for the common claim that viruses are not living things. The only thing that is constant throughout the viral cycle is the viral genome. Dupre and Guttinger believe that, therefore, the virus should simply be identified with its genetic material. But identifying the virus with something less than a cycle will lead to failure. The episode or virion is just part of what the virus does. " What matters is not the DNA molecule itself but what it does (or can do) in a particular context," (J. Dupré and Guttinger 2016) such as cell invasion and replication, rather than having a certain intrinsic property. Thus, an endogenous retrovirus is a virus only as long as it maintains the ability to contribute to a viral process. If it lives in a host genome it is immaterial. And in the case of viral latency as episome, it should be considered viral.

Lopez-Garcia and others believe that viruses cannot be considered alive because of their inability to reproduce without a cellular host. (Lopez-Garcia 2012)

The common perception is that disinfectants kill most types of viruses. The logic here is simple: you can't kill something that isn't alive. Likewise, if something can get sick and eventually die, it is certainly alive. (Pearson 2008) Raoult and Forterre classify viruses as one of two fundamental categories. of organisms (encoding capsids, as opposed to organisms encoding ribosomes, i.e. cellular life forms), with the obvious implication that viruses are living things. (Raoult and Forterre 2008)

Living systems consist of complex interactions between elements that form lines of several different types. These elements include viruses. Dupré and O'Malley argued that the standard reasons for denying that viruses are alive are wrong: most of the criteria involved, such as the criterion of autonomy (that viruses require essential resources from the host cell for reproduction) would exclude them from the category of living entities. (J. O. Dupré 2009) But, going by these considerations, we ourselves depend vitally on a multitude of symbiotic organisms, so that on this criterion we would not be alive either. (J. Dupré and Guttinger 2016)

Rather than considering a set of features that qualify something as a virus, we should consider the activities that make up the viral life cycle. So, we should see viruses as processes rather than things. J. Dupré and Guttinger 2016) But the perspective of the process involves conceptual difficulties.

If we adopt the perspective of a process ontology, we can understand the constant fusion and separation, because the processes can unite in a single process and even maintain their identity.

Collaboration between virus and host is not a simple interaction, but a collaborative interaction between processes. The virus itself can only be understood if it is described as a cycle.

This process-centered perspective provides a very different understanding of activity and function in biological systems than just the interaction of discrete, evolutionary individual things. According to Guttinger, at least the virions are certainly not living, but are stages of living processes. (J. Dupré and Guttinger 2016)

Nicholas Rescher introduces a vision of processes as defined by a functional unit; there is a "programmatic structure" that characterizes and unifies a process. (Rescher 1996) The interconnected activities that form a functional unit are the key to understanding processes: "A process is made into the item it is not through its continuing ("essential") properties, as with a classically conceived substance, but by its history, by the temporal structure of its descriptive unfolding across time. The identity of a process is constituted through a sequential pattern of action.". (Rescher 1996, 41)

Who is a fundamental feature of the world, becoming or being? In a substantial perspective, the being is usually seen as fundamental, the activity deriving from the being. For a process ontologist, becoming is seen as the fundamental feature of the world, according to which a stable "thing" is actually a (slow) process. (Guttinger 2020b, 3) According to Dan Nicholson and John Dupré in the introduction to the Everything Flows essay collection:

> "As processes, and unlike things or substances, organisms have to undergo constant change to continue to be the entities that they are." (Nicholson and Dupré 2018)

What would contradict a vision of the process is that stability is a fundamental feature of the world. Thus, a process ontology should explain how these stable patterns occur. (Guttinger 2020, 3)

Stephan Guttinger considers the viral population in an organism to be an extremely diverse and, importantly, dynamic system, forming what researchers call a "mutant cloud" or "swarm". Through the interactions between cloud members and between the cloud and its wider context, the virus acquires new behavioral characteristics, responding quickly to environmental changes, including the avoidance of antiviral drugs or cellular defense mechanisms. Thus, the diversity of the virus is, at least in part, defined by the larger systems in which the cloud develops and moves. (Guttinger 2020a, 1)

This concept leads researchers to new approaches in antiviral treatments, looking for ways to interfere with the dynamics of the mutant cloud. The result is the need to move from a vision of things to a process-based understanding of viruses, with a more relational and dynamic vision.

During a viral cycle, the original virus is completely destroyed and only the associated information is passed on to the next generation. This is different for cellular organisms, which have to pass on a physical part of them from generation to generation. The viral information hypothesis states that genetic information is reproduced to the detriment of the system's energy efficiency. According to this hypothesis, viruses are the only biological entities that simply reproduce as information. When a virus enters its host, the virion completely disassembles and the nucleic acid is copied into new genomes, which are then packaged and released as new virions. Physically, there is nothing left of the original form of the virion. "Not one single molecule, atom, or quark must be transferred between the old and new. The only thing that must be moved between viral generations is the information to build the next set of viruses." (Rohwer and Barott 2013)

According to Forest Rohwer and Katie Barott, in *Viral information*, the viral information hypothesis states that:

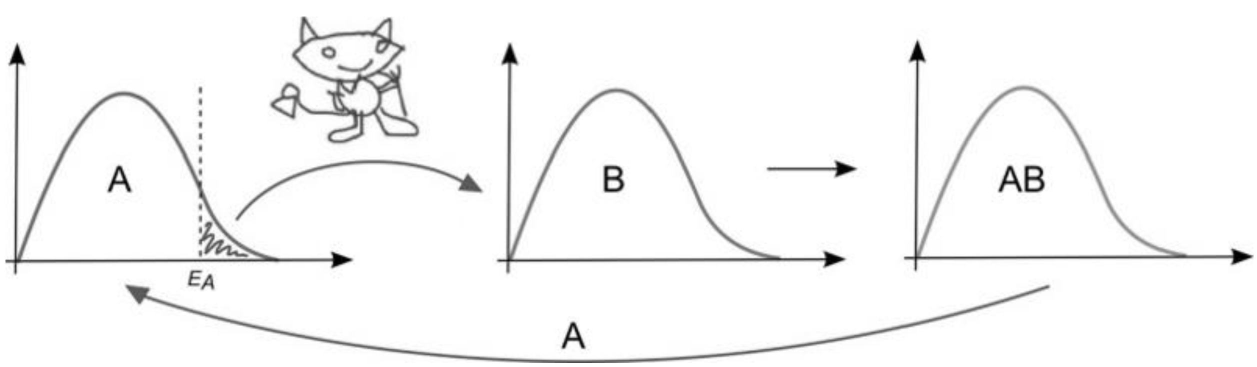
1. Physical information refers to the position in the Universe.

2. Biology creates physical information by changing the position of matter, effectively functioning as Maxwell's Demon.

3. Viral information converts different types of physical information in itself to the detriment of overall energy efficiency.

4. The destruction of physical information has a thermodynamic cost, which is quantified by Landauer's principle. Extremely large populations, such as viruses, experience selection at the Landauer limit and this is observable. (Rohwer and Barott 2013)

The dynamics of viruses are incredible. (Weinbauer 2004) Every week 10^{31} viruses disintegrate and 10^{31} new viruses appear. Practically 1.7×10^{25} new viruses are produced every second, and for each new virus approximately 50,000 base pairs of DNA must be synthesized. (Steward, Montiel, and Azam 2000) It turns out that every second more than 10^{30} pairs of viral DNA bases are performed, involving the death of approximately 10^{24} microbial cells every second.



Maxwell's Demon Illustration and Landauer's Principle. The demon / enzyme selectively selects "A" molecules with enough energy to react with "B" reactant, leading to the "AB" product. This process slightly cools the "A" population. This heat loss is brought back into the system by the surrounding universe. During degradation / erasure of "AB", "A" returns to its population and this heat can be measured using methods such as isothermal calorimetry. Source: (Rohwer and Barott 2013

In the sense of communication, information is a measure of "surprisal". (Tribus 1961) (Rohwer and Barott 2013) The bigger the surprise, the more information we find out. The thermodynamic consequence of physical information was defined mathematically by Rolf Landauer. (Landauer 1996) The heat released by erasing physical information can best be imagined by invoking Maxwell's Demon. The demon is a hypothetical creature that can collect "hot" molecules from one container and move them to another. This creates a temperature difference that could be turned into mechanical work. The daemon actually gains information about the relative position of the molecules. (Szilard 1929)

Rohwer and Barott propose that biology behave like Maxwell's Demon. Genetic information is the set of instructions for building Maxwell's Demon. This new information has a thermodynamic cost when it is erased, and the amount of heat released by destroying the information is also described by the Landauer Principle. (Toyabe et al. 2010) It should thus be possible to observe the link between physical information and thermodynamics and use it to better understand biology and, in particular, the success of viruses. (Rohwer and Barott 2013)

To prove that the viral information is real, Djamali and colleagues used isothermal calorimetry to study the heat released by marine microbial and viral communities. (Djamali et al. 2012) The decrease in the number of cells, together with the increase in diversity, is very similar to viral information. (Rohwer and Barott 2013)

The additional energy costs of the physical information associated with a mutation could explain why identical viral sequences are observed on a global scale. Rohwer and Barott conclude that imagining the biosphere as a massive system that ultimately feeds viruses, thus explaining why biological diversity is dominated by viruses. The viral information hypothesis has the potential to synthesize ecology and the theory of evolution by incorporating viruses with the rest of biology in a thermodynamic framework.

The boundaries between viruses and related entities are not easy to define. A very important class of related entity, plasmids, are generally considered to be differentiated from viruses by their lack of a capsid, consisting of empty DNA. But viruses do not have capsid at all stages of their life cycles, and can attach to a host eukaryotic genome in the form of an episome, the difference between a viral and a plasmid episome being quite unclear. Dupre and Guttinger conclude from this that they are parts of processes that differ at different stages of their life cycles. (J. Dupré and Guttinger 2016)

To find out what a virus really is, an ontology of the substance has little to offer. The point of view of substance assumes its essentialism and / or individualism, but none of them fits well with the interconnected image of the biological world that the natural sciences paint. (J. Dupré and Guttinger 2016)

Koonin and Starokadomsky state that the status of viruses in the field of biology is naturally defined within the replicator paradigm. (Koonin and Starokadomskyy 2016) The whole history of life is a story of parasite-host coevolution that includes the struggle between them and various forms of cooperation. Thus, the replicator paradigm provides the conceptual framework for the theoretical and experimental study of interactions in the replicator community. The complementarity of replication and metabolism (broadly defined to include energy production) is the biological manifestation of the dualism of information (entropy) and energy, as Schroedinger explains. (Schrodinger, Schrödinger, and Dinger 1992) But here, too, a dilemma arises: replication or metabolism first? Different approaches are possible. In conclusion, the replicator paradigm is considered central in biology, helping to establish the status of viruses in the biological world.

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