DO WE EVEN KNOW WHAT A VIRUS IS?

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There is often a gap between what we think we know and what we really know, and the bias or conviction of knowledge may blind us to other possibilities, preventing us from exploring alternative interpretations. Faraday noticed that "the inclination we exhibit in respect of any report or opinion that harmonizes with our preconceived notions, can only be compared in degree with the incredulity we entertain towards everything that opposes them" (in a lecture to the Royal Institution in 1854). For his part, Sherlock Holmes was forever admonishing Watson for not keeping an open mind until all the facts had been collected, "you see but you do not observe" (*A Scandal in Bohemia*).

Take for example the humble virus.

There seems to be a medical consensus that it is a minute organism; a bit of genetic material, keen on causing misery and suffering, but when we take a closer look, things are not nearly so simple and many questions arise.

In *The Selfish Gene,* biologist Richard Dawkins has cleverly inverted our thinking by convincing us to consider genes as cognitive entities that use organisms only for their own replication. Unfortunately, this has developed into a self-fulfilling prophecy of genetic dominance that even its author seems to have started to take seriously.

The later sequencing of the genome has led to the wildest of speculations about genetic treatment possibilities, from cures for cancer to immortality (or 'cures' for mortality). This distracts us from the essential findings that DNA is merely a reference molecule, though admittedly a very stable one (unstable molecules would be worthless as reference), yet a simple molecule non-the-less. It is the cell that uses this molecule as reference for its functions and interprets it on the basis of a constant stream of information received from the internal and sometimes external environment. Without the cell the genetic material is meaningless.

When we consider the virus, simplest among known organisms, a number of questions show up:

Is a virus even an organism, and if it is, would its likely purpose in life be to cause us suffering? Can it even be considered to be alive?

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By most definitions of life and living organisms (defined as any continuous living system), the virus does not really qualify. It neither has a metabolism nor does it multiply (I will come back to this seemingly surprising statement later). The most we can say is that a virus is a collection of inert genetic material with a protein covering. This genetic material may contain information, though information depends on a message being interpreted, and only for certain cells does the viral material seem to make any sense. Only very specific cells are able to interpret the information contained in a particular viral genetic code, and in essence a virus is (for those cells) almost pure information in an envelope. For all other cells it might as well not exist, for they are incapable of interacting with it or interpreting its message, so for all other organisms the virus is little more organic 'noise'.

A virus is generally species-specific. It needs a very *specific* receptor mechanism that *actively* transports the genetic material into the cell and actively transports the genetic material (DNA or RNA) to *specific* locations within that cell. For those unusual situations where a virus crosses over to other species; where it must encounter a suitable receptor, it is generally more virulent and unpredictable than the common species-specific viruses. At least that is what we tend to think, but since we generally only study viruses that cause illness, that may be a selective observational bias—more of that later. Nonetheless, the virus must encounter a specific receptor, and it is curious that many of our most virulent virus infections have been shown to have originated in other species: yellow fever, Ebola, HIV, and so forth—examples abound and are exhaustively studied. However, the single most important finding is that all these viruses must find specific receptors to be actively admitted.

A very elegant example of a multispecies virus is the rabies virus (the Lyssavirus genus of the Rhabdoviridae family of RNA viruses) this has the unusual characteristic of using the acetylcholine receptors to get into the cell (or rather the unsuspecting nerve cell uses its acetylcholine receptors to welcome this dangerous genetic sequence and bring it into its protoplasm). The virus reaches these receptors via a bite or a wound that exposes the acetylcholine receptors of muscles plates and nerve endings. Once actively transported into the cell its RNA molecules can induce that cell to manufacture damaging proteins and new virus particles, transported via the neural fibers to the central nervous system where they will cause irreparable damage, before migrating out along the nerve fibers to the salivary glands from where they can be transmitted to a new organism.

It is a conceptual error to think that a virus multiplies itself. A virus cannot in fact do so since it does not contains any of the metabolic mechanisms required for multiplication. Its genetic material merely induces the cell to producing new viral particles based on the genetic

templates incorporated into the cell metabolic systems. The new virus particles are purely the product of the incubating cell. There is no physical continuity from one virus generation to the next (an essential aspect of the definition of 'life'). The original generation is entirely incorporated into the cell and remains there for the life of that cell and its direct descendants. The new generation is formed entirely by that cell from cellular content and by cellular mechanisms, and exported. *It is essentially a cell product!* Only the information is transmitted, and information always requires both a sender and a receiver. Information cannot, as far as we now understand it, exist on its own as an independent entity, for without interpretation it would be indistinguishable from (environmental) noise, and it is debatable if information in itself can have an 'intention' as promoted by the selfish gene concept. To summarize thus far: a virus is a cell product, it is not alive, and it contains information for a specific receiver cell generally of a specific species.

In essence, then, a virus may be seen as a message. Transmitting information from one specific cell to another specific cell that has the correct receptors and capability of interpreting that message. The new cell may also produce new messages to transmit to other cells, for it is a highly efficient method of transmitting information, often requiring only a single initial virus particle. The information may be transmitted within the organism to some or most of its other cells or via subtle transmission mechanisms spread outside to other organisms (think of a sneeze that can project virus particles over a large area). With rare exceptions, some examples of which have already been mentioned, it is usually restricted to the same species, since is rare for viruses to cross to other species. While it is entirely possible that the entire message consists of information for generating or manufacturing new virus particles, there may well be other information included that modifies cellular function in subtle ways. We would unlikely be able to detect or even notice these altered functions unless they translated to alterations of cell-membrane proteins or other cell products that would cause an immune response within the organism. Another possible reason we do not detect the more subtle modifications is simply that we are not looking for them, for we have convinced ourselves that viruses are parasitic organisms, intent only on causing damage. Louis Pasteur was confident that chance favors the prepared mind and, conversely, it may be true that the unprepared mind will not recognize chance observations.

For a moment, let us change our perspective for the sake of argument and invert the usual sequence of a virus infecting a cell, producing damage and multiplying to produce more virus particles to infect more cells and so on, for some obscure motivation somehow embedded in its meagre genetic sequences. If we were to consider the virus as a cell product;

perhaps a small envelope of genetic material containing relevant information and transmitted from one cell to another and one organism to others.

This leaves us free to speculate on the possible content of this message. What would be useful for one cell to transmit via this highly efficient mechanism to other cells? Would we be able to detect this message within the viral sequences (alongside the replication information every virus carries)?

So far we have studied only where things go wrong; where the message is potentially damaging, as a letter to a lover accidentally read by a spouse or an insulting tweet sent by mistake to the boss as well as the colleagues it was intended for. Such communication metaphor allows for endless and possibly fruitful speculation.

Would cells and organisms have use for such an information system?

What information might be transmitted?

We may need to delve deeper into the subtleties of cellular mechanisms and cast off the genetic blinkers that consider only the DNA molecules as relevant within the cell.

I will leave you to speculate further and end this essay where it began, with Arthur Conan Doyle. He gave Sherlock Holmes the immortal quotation: "Life is infinitely stranger than anything which the mind of man could invent"—later partly plagiarized by J.B.S. Haldane (who incidentally also combined the concepts of Darwinian evolution and Mendelian inheritance that led to the somewhat conceptually limiting neoDarwinian theories of random mutations as the underlying cause) as: "my own suspicion is that the Universe is not only queerer than we suppose, but queerer than we can suppose." So it is entirely possible (though not scientifically provable), that Richard Dawkins is correct and that DNA is a mysterious self-aware molecule using us as a means of multiplying itself, and viruses may be evil little parasites intent on causing bodily harm to unsuspecting organisms.

Would it not be delightful if we could discover an entirely new system of genetic modification rather than the boring old random mutations and the equally boring intelligent design? Both essentially amount to much the same thing—if you examine it closely these two opposing camps are not so very different as they would like to think—both remove the problem outside the scientific sphere... and both insist there can be no alternative option, and perhaps more importantly, neither is falsifiable.

And while that may be desirable in religion, science must always remain open to alternative explanations. Absence of proof does not imply proof of absence.