CONTRIBUTIONS to SCIENCE, 2 (1): 105-110 (2001)
Institut d'Estudis Catalans, Barcelona

focus

Can Nietzschean power relations be experimentally investigated using theoretical and viral quasispecies?

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Nietzsche was the first major philosopher contesting Darwin's principle of «struggle for existence» as the motor for evolution. Nietzsche opposed to this principle that of «struggle for power». Nietzsche did not deny natural selection, but thought that selection acted essentially on those transformations produced by the struggle for power. The testable hypothesis proposed by Nietzsche is that the victory in the struggle for power does not belong to the strongest, most fortunately constituted individual but rather to the more abundant, meanest individuals (Table 1). However, science has not provided a mechanistic formulation of the Nietzschean concept of power relationships capable of undertaking the challenge of some experimental exploration. In this essay we propose that there has been a theoretical formulation, amenable to experimental analysis, which provides a test of power relationships among components of a population of individuals. We refer to the self-replication model of M. Eigen formulated to describe early replicons at the origin of life, and which has found an application in the understanding of RNA viruses. We describe experimental observations on competition among RNA genomes, and we relate the findings to Nietzschean power relationships.

Introduction

This article was inspired by experimental work carried out with the RNA virus, vesicular stomatitis, by J.C. de la Torre and colleagues [1]. The main conclusion of this study was that a highly fit virus variant, displaying considerable reproducing capability, was unable to outnumber the other variants forming the parental viral population from which the fit variant originated. Here, we wish to draw attention to the fact that the experimental result of the silencing of the fittest vesicular stomatitis virus (VSV) variant agrees with Nietzsche's prediction about the non-triumph of the strongest, in his formulation of power relationships[2,3]. Although this coincidence begs an explanation, science lacks descriptions of the possible genetic or evolutionary mechanisms involved in the Nietzschean relations of power.

The first difficulty associated with this task is the non-scientific form of Nietzschean formulations of power. These power relations do not constitute a system of scientific propositions characterised by a definite set of properties and laws, but rather they form a cosmology that can only be approached through metaphors. In order to articulate their meaning in a language compatible with science, here we adopt an analytical approach of an ontological nature, which in this case is more specifically a narrative interpretation of the entities and relationships that constitute the forms of life, and therefore more in keeping with Eigen's error-prone replication model[4, 5].

Eigen's model of error-prone self-reproduction: genetic connections and the units of selection

In 1971, Professor Manfred Eigen formulated the replication mechanism of RNA elements, characterised by a low copying fidelity (error-prone replication) as a possible phase in the early development of life [5]. In this theory, he defined the concept of quasispecies as a set of non-identical self-replicating molecules, closely related to each other, which evolve as a single unit in response to changes in the environment. Figure 1 shows a schematic representation of a quasispecies. The theory rejects the classical dichotomy between mutants and wild type as being a match between two separate categories in the evolution of RNA replicons. Instead, all the related variants, regardless of their frequency in the ensemble have to be considered as a population of replicons connected by their progenies [4].

Variant sequences are connected by mutational pathways, and they occupy interconnected points of what has been called «sequence space». Each sequence (each point in the «sequence space» represented by p, x, y... and o, a, b...; see Fig. 2) replicates to yield either identical copies of itself or erroneous copies containing one or more mutations. In Figs. 2B and 2C the circular arrows represent replication yielding exact copies of each sequence, while the linear arrows indicate error prone-replication producing either one-error copies (solid arrows) or multiple-error copies (dotted arrows). Multiple-error copies connect points which are distant in sequence space. Thus, together with the environ-

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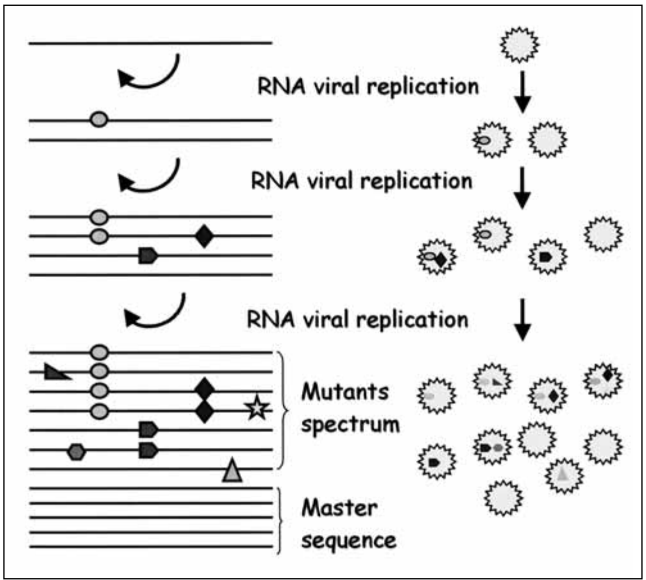

Figure 1. Schematic representation of a molecular (left) and viral (right) quasispecies. From an original genomic sequence (top), each round of replication leads to the appearance of variant genomes. At any point in time the population is composed of a commonly represented sequence (master) and a spectrum of closely related sequences (the mutant spectrum). Symbolic viral particles are drawn on the right. Each line represents a viral genomic sequence and the symbols on the lines depict point mutations (discrete modifications of the genetic material). In viruses, each infectious particle (right) contains one genomic sequence which constitutes the genetic programme of the virus.

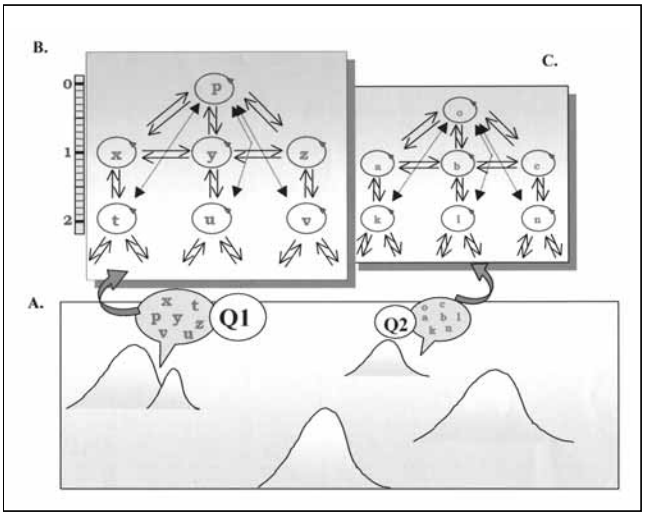

Figure 2. A represents a hypothetical space of biological replication efficiencies with valleys and peaks within it. Two different groups of genetic sequences are indicated, one comprising the sequences represented by the letters p, x, y, z, t, u, v (left), and the other by the letters o, a, b, c, r, l, n, (right). They constitute two quasispecies termed Q1 and Q2 which act as units of selection.
B-C. Diagrammatic representation of the relationship between the genetic sequences that constitute the viral quasispecies Q1 and Q2. Each sequence is represented by a letter (as in Fig. A), and each has a correct replication rate assigned (circular arrows around each genome) that characterises the continuous increase in number of identical sequences, and an erroneous replication rate (linear arrows) that represents the production of certain sequences through other neighbour sequences, for instance, of p from x, y, z, or in a lower degree of the neighbours further away (dotted arrows) for instance, the production of p from t and v, as it decreases with genetic distance (quantifiable if associated to a metrical distance –indicated to the left of Fig. B, and if represented correctly in a multidimensional space– not indicated in the figure.

ment, the replicative capacity of each variant sequence depends on its genetic neighbourhood (Figs. 2B and 2C other variant replicons, similar yet different) through the reception of the mutated progenies of others [4].

Eigen proposed that a variant in a population environment –genetic neighbourhood– of high replication values is much more likely to appear than a corresponding mutant in an environment of low replication values. It is thus not possible to derive selection values for a single variant in a population from its replicative capacity, rather the contribution of a whole set of similar replicons needs to be considered – this new replicative unit is the quasispecies (Fig.2 A: Q1 and Q2). The quasispecies selected is the one with the highest replication potential, quite independently of specific, individual components [4, 6]. In this frame, the individual replicon may be viewed as the donor, the beneficiary, and the vehicle of the replicative force through Eigen's sequence space.

Studies with RNA phages and animal and plant RNA viruses have revealed that these genetic elements fulfil most of the predictions of Eigen's quasispecies theory, including the impossibility of defining a viral genome as a single defined sequence, «but rather as a weighted average of different individual sequences» [7].

The earliest evidence indicating the quasispecies nature of an RNA virus was obtained through the quasispecies clonal analysis of a bacterial virus, the bacteriophage QB [7]. Subsequently, work with animal viruses, namely vesicular stomatitis virus and foot-and-mouth disease virus, was instrumental in the understanding and testing of the quasispecies concept [8, 9]. In the case of the human immunodeficiency [10, 11] and hepatitis C viruses [12], their quasispecies dynamics has been used to explain, at least in part, the capacity of the viruses to provoke persistent infections and, because of their high rates of evolution, to escape antiviral treatment.

Nietzsche and Darwinism

Nietzsche, although no Darwinist, disputed neither the importance nor the partial validity of Darwin's theory of natural selection. However, he did attack the metaphysical foundations of the theory. In Darwin's conception of evolution, individuals struggle with each other to guarantee their self-preservation. Nietzsche treated this view of the essence of life as being ontologically equivalent to Spinoza's concept of *conatus* – the striving for self-preservation exhibited by all natural things [2, 3, 13]. Nietzsche criticised the interpretation of life based on self-preservation and «struggle for existence» as perspectival and an anthropocentric construct [2, 3], supporting his arguments by reference to the industrial revolution with its fierce competition, misery and poverty. According to Heidegger, self-preservation would be so preoccupied with what it has at hand that it would become blind to its essence [14].

Table 1. Nietzsche's proposals in relation to classic evolutionary thought

Character	*Nietzsche*	*Darwin*	*Relation*
Ontologic	Self-improvement	Self-preservation	Generative
Metaphoric	Struggle for power	Struggle for existence	Generative
Mechanistic	Discipline - Selection	Variation - Selection	Ambiguous
Experimentally testable	Triumph of the meanest	Triumph of the best	Opposite

In contrast to Spinoza's theory, Nietzsche claimed that the real, or at least, the most frequent «struggle of life» is not to conserve one's life, but rather to improve oneself. Instead of adapting, Nietzsche believed that the organism attempts to assimilate or to force its environment and others to adapt to it, thereby providing life with a somewhat more creative attitude. Adaptation to an external environment is not, however, totally neglected, but rather is viewed as a secondary activity [2, 3, 15, 16, 17]. The fundamental drive in life, according to Nietzsche, is to expand and increase one's power, what he metaphorically typifies as the «struggle for power» [2, 3, 15] (Table 1).

«the struggle for existence is only an exception, a temporary restriction of the will to life. The great and small struggle always revolves around superiority, around growth and expansion, around power -in accordance with the will to power which is the will to life» [3].

Nietzschean power relations in biology

Until the second half of the 19th century, the meaning of power, or power relations, had been largely confined to the realms of politics and economics [18, 19]. Following Darwin's rupture with tradition [20], Nietzsche argued that power relations took on a biological course, and as the relation between conflicting forces (reproductive, instinctive, cultural, etc.) [21] they constitute the origin of life and its ultimate explanation.

Nietzschean power relations have been extensively reviewed in the philosophical literature and a detailed discussion of their meaning lies beyond the scope of this article. Here we only wish to summarise certain ideas that might help clarify their meaning while refering to replicons.

According to the interpretation, which in line with Nietzsche, M.Foucault [18, 22] and G.Deleuze [15, 23] make of power relations, a relation of power coincides with those relations between forces: forces (social, psychological, biological, etc.) acting upon other forces *as opposed to* forces acting upon objects, i.e. forces of violence and repression. A biological example of this distinction was provided by E.Canetti [24] who visualised a power relation between the cat and the mouse: a mouse held in the mouth of the cat is reduced to a mere object controlled by the force of the cat's jaw; however, once liberated from the cat's mouth but still under the cat's visual control and that of its claws, the mouse is no longer an object but an active creature (a force) subjected to the cat's forces and in this sense, within the cat's power domain.

More specifically, in terms of the Leibnizian distinction between external relations of comparison (resemblance, equality, disequality) and internal relations of connection (which include some kind of attaching: cause-effect, relations of the whole to part, part to part, etc.) [25], power relations, as force to force relations, have been identified with the latter [18, 19].

For Nietzsche, the idea that the struggle of life can be explained as a competition (a war of all against all) ignores the immense amount of co-operation in the struggle (simultaneous co-operation and competition), because this struggle is not to preserve one's life, but rather in the main to achieve power:

«My idea is that every specific body strives to become master over all space and to extend its force (its will to power) and to thrust back all that resists its extension. But it continually encounters similar efforts on the part of other bodies and ends by coming to an arrangement ('union') with those of them that are sufficiently related to it: thus they conspire together for power. And the process goes on» [26].

In order to remain coherent with this premise, Nietzsche could not agree that the result of the struggle of life is the triumph of the fortunate individual endowed with the strongest constitution. Rather, the result is that average individuals will finally beat the exceptional ones, and this is so because average individuals, being greater in number than their exceptional counterparts, in their urge for self-improvement, will interact to confront the strongest [15, 2, 3].

To date, science has not produced a mechanistic description of how power relationships operate that would allow us to investigate Nietzsche's criticisms of Darwin experimentally. Moreover, as pointed out by J. Gayon in a recent systematic evaluation of Nietzsche's work with regard to Darwinism [20], such studies have been rare in philosophy since the middle of the last century.

Objective

Here we suggest that Eigen's formulation of error-prone genome replication provides a unique opportunity to distinguish, epistemologically and mechanistically, those relationships that Nietzsche refers to in his «struggle for power», on the one hand, from those which operate in the «struggle for existence» and which are described in the theory of natural selection, on the other.

This distinction may allow us to examine the paradoxical Nietzchean proposal concerning the triumph of the meanest types in mechanistic and experimental terms and to speculate on its consequences for biology.

Methods

Interpreting the nature of the relations in Eigen's error-prone replication in Leibnizian terms of interaction and comparison

Among the entities participating in Eigen's formulation, i.e. the individual replicon and the quasispecies [6], we can distinguish two different kinds of relations: those based on internal relations and those based on external relations. In making this distinction we used that which the philosopher Leibniz drew between internal relations –of interaction– and external relations -of comparison, based on the criterion of the reducibility of relations to one predicate for one *relata* [19, 25]. We followed Kusch's deduction scheme [19]. In our case, «Quasispecies 1 reproduces more rapidly than Quasispecies 2» can be reduced to «Quasispecies 2 reproduces somewhat rapidly» and «Quasispecies 1 reproduces very rapidly» where «very» represents a degree superior to «somewhat». Because of the possibility of this reduction, «Quasispecies 1 reproduces more rapidly than Quasispecies 2» qualifies as an external relation of comparison. However, we can not construct a proposition of the same type with individual replicons because as explained in the introduction «replicon *p* reproduction benefits from the replicon *y* error-prone reproduction». This last proposition cannot be reduced in the same way as above; there is a connection between *p* and *y* that cannot be split, and this is because *p* has the feature of being benefited *in virtue of y* error-prone reproduction and its genetic similarity (proximity in Eigen's sequence space) to *y*. This relation is categorised as an internal relation of interaction, and as replicative force acting over other replicative force, a power relation.

Results and discussion

Distinguishing Nietzschean power relations from Darwinian selection. Concept, mechanism and experiment

In the preceding paragraph we undertook the interpretation of replicons and quasispecies relations entirely in Leibnizian terms of comparison and connection. For Leibniz these relations were pure mental categories of understanding. Therefore, before passing to the experimental judgement based on Leibniz epistemological differentiation (iii), we have mapped these Leibnizian relations in our knowledge of natural selection theory and of Nietzsche's power relations alternative project (i). Second, in order to make Nietzsche's proposal helpful to scientific research, we provide a narrative description of the power relations' operating mechanism which may lead to the triumph of the meanest types in «the struggle for power» (ii).

(i) Concept: Variation and selection are the two steps through which natural selection acts [27]. The first step is the production of variation that will serve as the material for the second step, the actual process of selection or elimination. Comparison relations allow us to understand variations or differences between entities, and thus, the second step of the selection theory is established – according to the Leibnizian system – on the basis of previous relations of comparison (in our case comparison between quasispecies). Nietzschean co-operation-selection [28, 29], unlike Darwinian variation-selection, poses the question within the first step of the selection procedure, that is, on the structure or the organisation of the substrate being selected; as if a different kind of variation could be reached by means of co-operation (discipline, education, in Nietzschean terms). Leibnizian relations of interaction are those which we draw on in order to understand the alliances between variant replicons as the action of replicative forces over other replicative forces.

Our interpretation establishes a clear split between fitness (from comparison) and power (from interaction). This distinction is one of ontic perspective that illegitimatises correlations between fitness and power: a survival-oriented perspective gives us a kind of rationale (natural selection) through which it is acceptable to compare singular entities (the units of selection) [30]; by restoring the interdependence and interconnectedness together with the competition, we gain the power perspective that has so far been missing. By redefining the replicon as relational rather than as self-contained, we bring Nietzschean power relationships to biology as constitutive of the substrate of the selection process (Fig. 3).

Changes due to those internal relations of interactions remain confined within the sphere of power, and cannot cross by themselves the process of evolution without previously passing a process of comparison and selection.

(ii) Mechanism: The mechanism is based on error-prone reproduction and the genetic resemblance between replicons. It may be proposed that, inasmuch as the mutual redistribution of replicative force irradiated by erroneous self-reproduction is not symmetric (this depends on the particular environment the replicons occupy), some replicons would acquire more replicative force than others. The most frequent replicons would be expected to have more opportunities to benefit from their mutual erroneous replicative forces than those with an exceptionally large replication rate, which is expected to be somewhat more different (located in a bend within the occupied sequence space) to the rest of the possible genetic neighbours than the difference between these neighbours.

(iii) Experiment: The distinction between internal interaction and external comparison relations may help to focus the analysis, and to interpret the challenging Nietzschean proposal in quantitative terms. For instance, the experimental result of *de la Torre et al.* expressed in the title «RNA virus quasispecies can suppress a vastly superior mutant progeny» [1] is confusing in the sense that a comparison between «a mutant» and a «quasispecies» cannot be established: the in-

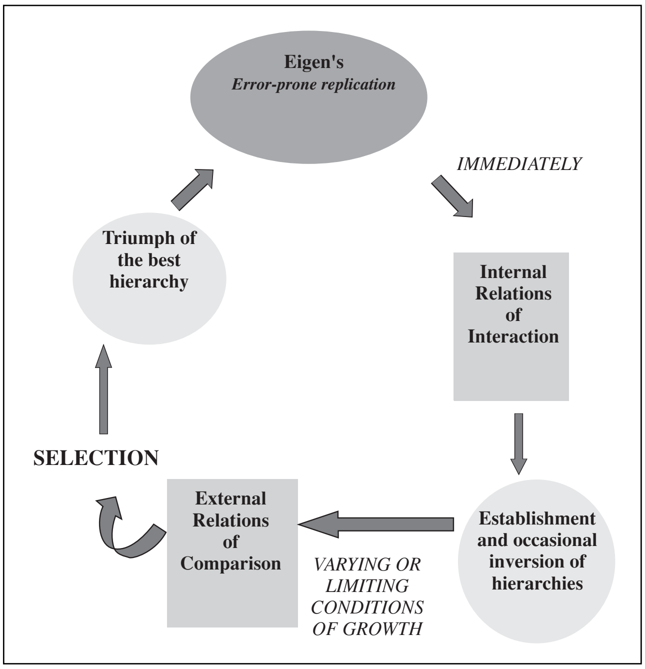

Figure 3. Diagram showing connection from replication, replicons interaction and selection. Even in an ideally rich, buffered or unlimited environment, internal relations of interaction happen immediately as a consequence of error-prone replication of short RNA replicons, generating an organised (mastered) structure of replication. When restrictions occur, subgroups of structured replicons are subjected to rating for the external limiting factor according to a selection process (comparison-selection).

dividual mutant does not exist for comparison relations in the way that a quasispecies does. Thus, our interpretation is that those mutants distinguished by a lower replication component may outnumber those distinguished by the highest component, but the main point is that this happens within the structure of internal interaction relationships, and in particular within the structure of Nietzschean power relationships, and not as a result of a comparison-selection process.

This narrative description of de la Torre's result (i.e. the non-triumph of the best), coincides with Nietszchean predictions about the result of the struggle for power [2, 3, 15] (inversion of the hierarchy according to the original replicative force of replicons). Were it not referring to a different type of relation, as explained earlier, it would represent an anti-Darwinian result [2].

Conclusions

Our theoretical investigation reveals that: (i) Eigen's mechanistic formulation allows the relationships participating in natural selection to be distinguished from those that Nietzsche calls power relationships; (ii) the result reported for the VSV of the non-triumph of the most reproductive fall within the scope of Nietzschean power relationships. Therefore, it becomes neither an evolutionary result, nor an anti-Darwinian result, and yet neither does it require the dissolution of the concept of quasispecies to understand the experimental result of J. C. de la Torre *et al.* (iii) RNA viruses and Eigen's theoretical model are adequate in order to explore Nietzschean power relationships in biology; and, by extension, (iv) Nietzschean power relationships and RNA viruses as a model of error-prone replication in current life suppose a new «metaphysical program of investigation» for testing scientific theories, as is the case of the theory of evolution through natural selection according to Popper [31].

Acknowledgements

We would like to thank all our colleagues who have made comments on this and all earlier versions of the manuscript, in particular E.Domingo, C.Escarmis, P.Casacuberta, L.Ruiz, M.Montserrat, A.Martí, T.Otero, B.Cabot, M.Piron, A.J.Lyons, H.D.Robertson and P.Puigdomenech. We dedicate this essay to our friend and molecular biologist Virginia Stiefel.

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