To Define Life and Species as to Demarcate the International Date Line

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Abstract

"What is life?" and "What is a species?" are the two of the most fundamental questions and the hottest topics in many disciplines of the life sciences. Since Darwin's time, various definitions of life and species have been proposed at the different evolutionary levels, from the molecular level to the macro-organism level; however, none of them is universal or can satisfy all features of life or a species, which should be attributed to the dynamic, continuous, and gradational progress of evolution. Therefore, up to now, diverse definitions of 'life' and 'species' reflects our comprehension to the gradation of evolutionary entities. In the author's opinion, the definition of life or a species should divulge its biological, ecological and evolutiological connotation.

Key words: life; prelife; species; Velasco's paradox; Universal tree of life; science; life science; biology

Introduction

Although our understanding of 'life' was much earlier than that of 'evolution', we did not seriously consider a scientific definition for 'life' until the 19th century, after our beginning of forming evolution thoughts. During the past two centuries, the puzzling difference found between extant macro- and micro-organisms and those left in fossils on Earth have been attributed to evolution, which was elucidated scientifically by different theories.[1-21]

From the fimpological perspective, no matter whether evolution is looked from its intension or extension, it is really a dynamic, continuous, and gradational progress or course,[22, 23] which results in an interesting phenomenon: on the one hand, we study, classify and discuss extant living things and/or extinct macro organisms and microorganisms from the biological, ecological and evolutiological perspective; on the other hand, despite of our gargantuan effort we still have not been able to create a universal definition for 'life'.

The early study on macroorganism evolution uncovered its gradational characteristic; and Darwin's Tree of Life (TOL) was the exemplar that followed the order from the lowest level to the highest level and from the simplest entities to the smartest mammals. However, the lowest starting point of evolution was unclear in the 19th century,[24] which was then dug into the cellular level after entering the 20th century when cells were believed to be the simplest life form. 'Age of Bacteria' was set up as the oldest life form on Earth, and followed by 'Age of Invertebrates', 'Age of Fishes', 'Age of Reptiles', 'Age of Mammals', and 'Age of Man'; [25] and this evolutionary order has also been supported by a series of fossils. For example, the oldest prokaryotic cell fossils indicated that bacteria appeared on Earth sometime between 3.5 and 3.8 billion years ago and have been the dominant life forms since then;[26, 27] unequivocal fossil evidences further showed that the emergence of eukaryotic unicellular algae occurred at least 1.9 billion years ago;[28] and the first well documented eukaryotic multi-cellular animals appeared less than 600 million years ago.[25, 29]

However, since the discovery of viruses, an evolutionary entity smaller and simpler in structure and function than a bacterium, evolutiologists have confronted several knotty questions, for example, "Are viruses and phages of life?" "Are they living organisms? Or do they have life?" Indeed, on the one hand, according to the traditional definition of life, virus and phage are not living organisms, mainly because they cannot replicate themselves independently; on the other hand, according to the continuous feature of evolution, sub-cellular entities should appear earlier than prokaryotic cells, such as cyanobacteria. There is certainly an evolutionary relation between sub-cellular entities and cellular entities. Therefore, how to connect these sub-cellular entities with TOL from the evolutiological perspective is challenging our existing theoretical systems. If we try to answer these questions, we first have to answer two critical questions: "what is life?" and "what is a species?" In this paper, the author briefly reviews the existing understanding of life and species, and proposes the fimpological opinions.

What is Life?

This question is not only the concern of philosophy, politics, sociology, and religions, but also one of the hottest topics in many disciplines of the life sciences.[30-35] Recently, many interesting controversies emerged around the concept of life.[33, 34, 36-41] Some scholars argue that it is impossible, unnecessary and meaningless to define 'life' because of its dynamic, relativity and infinity.[32, 33, 37, 42-44] Some others believe that 'life' is the evolutionary transition between the non-living and the living.[43, 45] Jortner even alleges that "The question 'what is life?' is not only an extremely difficult question, but also perhaps not the right question." and "One does not require a definition, but requires a scientific theory."[31]

Since the 19th century, the question "what is life?" has been connected with evolution theories, especially Charles Darwin's *On the Origin of Species*. Although we are still in confusion to define life from an evolutionary entity perspective or from the perspective of biological, ecological and evolutiological mechanisms, it is a generally accepted scientific recognition that extant living organisms are the products of evolution which is not only a progress occurred at the macro- and micro-biological level, but also a chemical reaction arose at the molecular level,[14, 46-57] and even a physical procedure happened at the cellular level.[14, 58-60]

Different definitions for life at different evolutionary levels

Indeed, from different evolutionary levels, the definition of life may be dissimilar as what Benner pointed out "Any definition is intricately connected to a theory that gives it meaning." [36]

At the macro-biology level

In the Oxford Dictionary, 'life' is defined as '*the condition that distinguishes animals and plants from inorganic matter, including the capacity for growth, reproduction, functional activity and continual change preceding death'*.[61] Clearly, this definition of life focused on those unique features and functions including 'growth', 'reproduction' and 'death' of the entities, such as plants and animals at the macro-organism individual level; and it was made by traditional macro-biologists. However, if we observe macro-organisms from the cellular perspective, this definition is inaccurate because there are still many living cells (eukaryotic and/or prokaryotic cells) within a corpse or a dead plant; and these cells maintain their capabilities in growth and reproduction (duplication).

At the cellular level

In 1847, Theodor Schwann and M.J. Schleyden first proposed the Cell Theory, which hypothesized all living entities are built from cells;[36] and thereafter, our understanding of life has been extended into the cellular level where life is defined as that an organism entity has its independent metabolic and reproductive capabilities.[62] Under this definition, mineral crystals and viruses are nonliving things and cells are the simplest life form.[62] Life's evolution was believed to begin at the cellular level. Woese imagined "The cell is a complex dynamic system. As its connectedness increases such a system can reach a critical point, where a phase change occurs, where a new, higher level organization of the whole emerges." [63, 64] and LUCA (the Last Universal Cellular Ancestor) was proposed to be the initial point for life's evolution.[65-67]

At the sub-cellular level

Since the existence of viruses, a subcellular entity of the micro-world was proved morphologically in the 1930s; today, the viral role in evolution has attracted much attention and initiated lots of controversies. Unlike cellular organisms, viruses cannot replicate on their own, and are totally dependent on their host cells' machinery to make copies for themselves; and therefore, viruses are usually considered to have no place in Darwinians' universal tree of life.[68-71] Recently, Forterre proposed a definition of life at the sub-cellular level in order to encompass viruses: life is the mode of existence of an integrated system with interdependent structures and functions.[72]

At the molecular level

More interestingly, at the molecular level, DNA was also defined as life by Crick, a co-finder of DNA.[72] Nowak and Ohtsuki proposed a much more general definition for life: "Life is that which replicates and evolves. The origin of life is also the origin of evolution." [56] Martin said that "Life is a chemical reaction." [17] NASA in 1994 proposed that life is a 'self-sustaining chemical system capable of Darwinian evolution'. [14, 36] Wilson pointed out that molecular and cellular biology occupy the two lowest levels of biological organization; and all living phenomena are obedient to the laws of physics and chemistry.[73]

To define life in much the same way as to define the International Date Line

Such confusing status in the definition of life is extremely similar to the realistic problem encountered by imagined extraterrestrial ‘aliens’: how to define ‘the beginning of a new day’ for Earth while confronting the global and spinning planet. In fact, the solution created by modern humans on Earth was to arbitrarily set up an imaginary line, called ‘The International Date Line (IDL)’, as the demarcation for the end of the last calendar day and the beginning of the following calendar day.

In my opinion, life is only a special status within the evolutionary process of universe where the distributions of evolutionary entities are between negative infinity and positive infinity. We cannot rule out the possibility of extraterrestrial polymer pre-life and/or life in universe.[74-77] According to the evolutionary path which built up along the orders from the simple to the complex, the low to the high, the inorganic to the organic, and sub-life to living organisms,[45, 56, 78] we have to choose a point, or a milestone as the beginning of life in the time scale of evolution; and then those evolutionary entities emerged before the point could be called ‘prelife’ (or prebiotic) entities. In fact, our understanding on cellular entities, multi-cellular macro-entities and social systems is historically matured and territorial fossil-supported from the perspective of life on Earth; and therefore, I prefer to keep the traditional concept of life and to set up ‘cells’ as the earliest form of life although there may be no any evolutionary breaks between prelife entities and living organisms. Recently, Nowak and colleagues also proposed the term ‘prelife’,[56, 79, 80] which refers to ‘a system’ where activated monomers ‘can undergo spontaneous polymerization’.[79] In contrast, my ‘prelife’ refers to the period before the beginning of life in the time scale of evolution, during which, inorganic, organic and sub-cellular entities evolved.

However, the solution of defining “what is life?” on Earth does not mean the elucidation of “what are the *origins* of life?” and “what’s the definition for life in the Cosmos?” Tessera pointed out “The question of the primordial ancestor must be approached through the search for the origin of evolution, not through the search for the origin of life.” [42] Recently, a newly emerged discipline named ‘astrobiology’ has indicated that some scientists already sense that the evolution on the Earth cannot be separated from that of the Universe.[31, 55, 81-92] Therefore, I feel that evolution on Earth should be part of evolution of the Universe, and must comply with the universal laws of evolution. In addition, there has been a huge disagreement on the issue whether evolutionary process is an unbroken course or a discontinuous history in the time scale of evolution;[93-95] and the two different opinions have their own supporting evidences respectively. In my opinion, there are no evolutionary chasms between the inorganic and the organic, between microorganisms and macroorganisms, between prokaryotes and eukaryotes, between animals and human beings, and between biological individuals and social population; and there only are temporary knowledge gaps in our understanding.

What is a Species?

To define species has lots of practical applications in industry, agriculture, and medicine [96] besides its critical position in biology, ecology and evolutiology. Unfortunately, the definition of a ‘species’, like that of ‘life’, is also varied and controversial.[96-102] It was estimated that more than twenty conceptions were proposed for defining species of eukaryotic macro-organisms.[103-105] Traditionally, 'species' is an essential concept in macro-biology, and was initially defined by naturalists from the macrobiological perspective. Since the emergence of evolutionary theories and ecology in the 19th century, 'species' has been branded with ecological and evolutiological markers,[99, 103, 106-110] such as 'the unit of diversity',[107] or 'the fundamental units of ecology and evolution'.[108] Moreover, at the cellular level and the sub-cellular level, 'species' may be replaced by 'lineage' and 'strain' respectively.

A universal concept of a species in Cohan's paper said: "A species is a group of organisms whose divergence is capped by a force of cohesion; divergence between different species is irreversible; and different species are ecologically distinct." [108] George Simpson, the paleontologist, defined species as the following: "species is a lineage (an ancestral-descendant sequence of populations) evolving separately from others and with its own evolutionary role and tendencies." [99, 103, 106] A.E. Emerson's definition was "a species is an evolved or evolving genetically distinctive, reproductively isolated, natural population." [103] An ecological definition of a species was given as the following: 'a set of individuals that can be considered to be identical in all relevant ecological properties', [111] or "a species consists of the organisms occupying the same niche." [107] Ian Tattersall and Jeffrey Schwartz proposed their own definition of species: "species are historically differentiated entities that, osteologically, may be differentiated to inconveniently varying extents." [112]

Mayr's definition of species for macro-biological organisms

Ernst Mayr (1904-2005) defined the macro-biological species at the population level in 1942: "Species are groups of actually or potentially interbreeding natural populations that are reproductively isolated from other such groups." or "Species are groups of interbreeding natural populations that are reproductively isolated from other such groups." [103, 113-115]; and such reproductive isolation was believed to be the consequence of 'differences between closely related species in ecologically selected characters such as habitat preference, reproductive timing, courtship behavior, or pollinator attraction'.[110]

Clearly, Mayr's species definition at the macro-biological population level is based on that "the actual demarcation of species taxa uses morphological, geographical, ecological, behavioral, and molecular information to infer the rank of isolated populations." [103] Mayr's definition was used in some ecological studies on aquatic macroorganisms and plants.[109, 116-119] Thompson argued that "species in pure isolation simply do not make sense… Many, possibly most, species are collections of genetically differentiated populations." [120] For example, inter-specific hybrids frequently occurred in plants, for which "botanists have often expressed doubt that plant species even exist." [109]

Defining species for micro-biological organisms

Since our understanding advances deep into the micro-world, it has been found that Mayr's species definition failed to define species for those evolutionary entities at the cellular, sub-cellular and molecular levels.[121] Morganand and Pitts argued that "Mayr's biological species concept fails because there is no useful viral analog to sexual reproduction." [122] For example, to define species for those asexually reproductive microorganisms, such as bacteria, Mayr's biological species concept is utterly incompatible, with which Mayr himself agreed.[103]

Although the first description of bacteria was made in the 1670s, when Antoni van Leeuwenhoek watched them under his single-lens microscope, the concept of defining bacterial species hadn't been proposed until 1991 when Dykhuizen and Green published their paper discussing the definition of biological species;[123] and then such concept was refined further by Lan and Reeves.[124-126] Rossello-Mora and Amann made their species concept for prokaryotes: "a monophyletic and genomically coherent cluster of individual organisms that show a high degree of overall similarity in many independent characteristics, and is diagnosable by a discriminative phenotypic property." [104].

Bacterial species have typically been defined by using the sequence of a single locus (16S rRNA for example), multiple house-keeping loci, or whole genome similarity.[29, 99, 127, 128] For example, at the cellular level, a prokaryotic microorganism species was defined as a collection of cellular strains sharing 70% or more DNA homology.[107]

However, Fraser and colleagues pointed out that horizontal gene transfer and variable rates of recombination occurred in bacterial DNA made it difficult to define a bacterial species naturally.[96, 129]

Velasco's paradox and the fimpological view

Recently, Joel D. Velasco asked a paradoxical question, which should be considered to be a knotty problem while defining species: "We could ask whether or not a human organism includes its gut flora (the trillions of microorganisms that live in our digestive tracts)… If organisms are defined in terms of some type of functional or causal dependency, then surely gut flora are part of the human organism. We could not live without them. But if this is the case, an organism does not have a single genealogy, but rather, has many parts, which may have different genealogies." [101]. From the fimpological perspective, similarity is relative and variation is absolute. Therefore, species is a relative conception for a set of similar individual entities from a population perspective because no two individual entities of an evolutionary level are entirely same. The definition of species is subject to the given evolutionary level of entities at the population level, and should reflect the biological, ecological and evolutiological significance; to define species may be also in much the same way as to demarcate the International Date Line; and therefore, the best way to solve Velasco's Paradox may be to arbitrarily choose the unique criteria for the evolutionary entities at a corresponding population level. According to this strategy, the unique criteria are to be chosen from morphological, geographical, ecological, and behavioral characteristics at the macro-organisms' population level, not from molecular markers at the molecular level. For example, anatomic features, sexual reproduction, diseases patterns, cultures, languages and the geographic and ecological distribution are the examples of the functions and behaviors of human beings at the individual or population level.

However, when such strategy is applied to defining species of microorganisms, the biggest challenge is that we know little of the unique criteria at the micro-organisms' individual or population level. Although DNA or RNA sequencing approaches have been used in defining species of fungi, bacteria and viruses, what they reflect is the difference or similarity at the *molecular* level, not their morphological, geographical, ecological, and behavioral differences at the microorganisms' individual or population level.

Moreover, the morphological, geographical, ecological, and behavioral characteristics at the microorganisms' individual level are not only determined by DNA and/or RNA, but also controlled by non-nucleotide molecules and sub-cellular systems which are dynamic under interior and exterior influences. The recent empirical and theoretical advantages indicated that modern genetics is not enough to reflect the whole content of biological heredity at the macro-organism individual level,[22, 130-136] which suggests that DNA and/or RNA-centered approaches may not play an all-round role in defining species at the cellular or individual level.

Speciation, species boundary and species-barriers

The diversity of species on the Earth is realistic despite of diverse definitions, from which, the question "how did species form?" arose. In fact, there had not been any scientific answers to it until the emergence of evolution thought in the 19th century when Lamarck and Darwin proposed their theories for accounting for biological evolution at the macro-organism level. Therefore, speciation actually reflects the mechanism of evolution.

According to our modern prevailing comprehension of evolution—the Modern Synthesis that unified Darwinian natural selection and Mendelian genetics in the mid-20th century—two mechanisms of speciation: (i) ecological speciation and (ii) mutation-order speciation [117, 119, 137, 138] have been developed.

Ecological speciation was defined as 'the evolution of reproductive isolation between populations, or subsets of a single population, as a result of ecologically-based divergent natural selection'.[119] Clearly, the incarnate consequence of this mechanism is the reproductive isolation at the macro-organism individual and population levels. In fact, the above two mechanisms of speciation stand on merely two piers: one is at the molecular level and the other is at the macroorganism level, which is also the characteristic of the Modern Synthesis. During the past decades, rapidly growing evidences and facts have indicated that the tremendous evolutionary gap between the molecular world and macro-organism world had been underestimated or ignored in the Modern Synthesis [22]; and therefore, the Modern Synthesis-based understanding on the mechanism of speciation has similar deficiencies. From the fimpological perspective, speciation at different evolutionary levels involves different mechanisms, which will be discussed deeply later in other papers.

Because of various definitions for species and the insufficiency of our understanding on speciation, the explanation for "what and where the species boundary or species-barrier is?" is also diverse. Ernst Mayr defined that the species-barrier was at the individual level, and reflected whether or not the individuals of a species had the capability to interbreed.[113] If we say that species boundary, or 'species-barriers' at the macro-organism level is clear, as we enter the cellular, sub-cellular and molecular levels, the boundary of species among different evolutionary entities gradually become indistinguishable.[139-143]

Speciation of bacterial microorganisms was believed to have resulted in genetic barriers among intra-species organisms.[144] For example, the species pan-genome of a given bacterial species was thought to be consisted of both core and accessory genomes; and only the core genomes exist in all isolates of that species. This notion was first used by Lan and Reeves to define bacterial species.[111,124-126, 145, 146] As the consequence, the species boundary or 'species-barriers' at the molecular level is actually replaced by genetic barriers including recombination barriers and mismatch repair, which have been studied widely in prokaryotic cells.[147-155] However, Matic, Taddei and Radman pointed out that the barriers of bacterial species should include both the variety of microhabitats and hosts, and the divergence of genomic sequence and restriction-modification systems [156].

An experimental study on the populations of the filamentous fungus Neurospora showed that matings between lineages that were adapted to the same environment had greater sexual reproductive success than matings between lineages that were adapted to different environments,[157] which suggested that reproductive isolation at the microorganism individual level may associate with some unknown environmental entities. Cohan argued that demarcating species of bacterial microorganisms should have been guided by 'a theory-based concept of species'.[158]

Indeed, the species boundary has been proved to be rather fragile and indistinct in inter-species of sub-cellular evolutionary entities, such as viral entities and membrane-enclosed microentities.[10, 22, 159] For instance, prions, newly recognized protein-based genetic elements, have been recognized as pathogenic molecular entities,[160] which also faces a species problem, a challenge in 'phylogenetic taxonomy' or 'phylogenetic nomenclature',[102, 161-163] especially while confronting their environment-driven phenotypic alterations which are the consequence of protein folding variations rather than polyribonucleotide-associated changes.[164-171] Therefore, while we are unable to make a perfect universal definition for species of all natural pre-life entities and mono- or multi-cellular organism entities, the reality and accuracy of 'species-barriers' is also truly doubtable.

Summary

It has been shown that defining 'life' and 'species' may be one of the most critical, imperative, and thorny challenges in the life sciences. Despite various definitions of 'life' and 'species', we failed to find a universal one for both respectively, which should be attributed to the dynamic, continuous, and gradational progress of evolution. In the author's opinion, life is only a special status of relevant evolutionary entities within the evolutionary process of universe where the distribution of evolutionary entities are between negative perpetuity and positive infinity; 'species' as a descriptive concept for evolutionary entities at the population level should reflect its biological, ecological and evolutiological connotation; and therefore, to define life and a species could be as to demarcate the International Date Line, which is the consequence of compromise between the reality and the ideality.

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