

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

**Shu-dong Yin**

Cory H. E. R. & C. Inc. Burnaby, British Columbia, Canada

Email: sdyin@fimpology.com

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## Abstract

“What is life?” and “What is a species?” are 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 different evolutionary levels, from the molecular level to the macro-organism level; however, none of them is universal or can satisfy all the features of life or a species, which should be attributed to the dynamic, continuous, and gradational progress of evolution. Therefore, to date, diverse definitions of “life” and “species” reflect our understanding of the gradation of evolutionary entities. In my opinion, the definition of life or a species should reveal its biological, ecological and evolutiological connotation.

Key words: Life; Prolife; Species; Velasco’s paradox; Universal tree of life;

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## Introduction

Although our understanding of “life” predates our consideration of “evolution”, we did not seriously consider a scientific definition for “life” until the 19<sup>th</sup> century, after the beginning of our formation of evolution thoughts. During the past two centuries, the puzzling differences 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<sup>[1-21]</sup>.

From the fimpological perspective, no matter whether evolution is viewed from its intension, or extension, it is really a dynamic, continuous, and gradational progress or course,<sup>[22, 23]</sup> which results in an interesting phenomenon: on the one hand, we study, classify and discuss extant living things and/or extinct macroorganisms and microorganisms from the biological, ecological and evolutiological perspective; on the other hand, despite 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 19<sup>th</sup> century, [24] which was then dug into the cellular level after entering the 20<sup>th</sup> 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, phages, and viroid or previroid forms of life?” “Are they living organisms? Or do they have life?” Indeed, on the one hand, according to the traditional definition of life, viruses and phages are not living organisms, mainly because they cannot replicate themselves independently; on the other hand, according to the continuous feature of evolution, subcellular entities should appear earlier than prokaryotic cells, such as cyanobacteria. There is certainly an evolutionary relation between subcellular entity and cellular entity. Therefore, how to connect these subcellular entities with TOL from an 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, I briefly review the existing understanding of life and species and propose the fimpological opinions.

## What is Life?

This question is not only a 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 have emerged around the concept of life. [33, 34, 36-41] Some scholars argued that it is impossible, unnecessary, and meaningless to define “life” because of its dynamic, relative, and infinite. [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 argues 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 19<sup>th</sup> century, the question “what is life?” has been connected with evolution theories, especially Charles Darwin’s *Origin of Species*. Although we are still confused about how 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 that occurs at the macro- and micro-biological level, but also a chemical reaction that arises at the molecular level, [14, 46-57] and even a physical

procedure that happens 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 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 the unique features and functions, including “growth”, “reproduction”, and “death”, of 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 remain their capabilities for growth and reproduction (duplication).

### At the cellular level

In 1847, Theodor Schwann and M.J. Schleyden first proposed the Cell Theory, which hypothesized that all living entities are built from cells; [36] and thereafter, our understanding of life has been extended to the cellular level, where life is defined as an organism entity having its own independent metabolic and reproductive capabilities. [62] Under this definition, mineral crystals and viruses are non-living 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 starting point for life’s evolution. [65-67]

### At the sub-cellular level

Since the discovery of viruses, a subcellular entity of the micro-world, in the 1930s, the viral role in evolution has attracted much attention and initiated many controversies. Unlike cellular organisms, viruses cannot replicate on their own and are totally dependent on their host cells’ machinery to make copies for themselves. 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-discover 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 obey the laws of physics and chemistry. [73]

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

This confusing status in the definition of life is extremely similar to the real problem encountered by imaged 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 distribution of evolutionary entities is 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 that has been built up along the orders from simple to complex, low to high, inorganic to organic, and sub-life to living organisms, [45, 56, 78] we have to choose a point or milestone as the beginning of life on the time scale of evolution; and then those evolutionary entities that emerged before that point can be called “prelife” (or prebiotic) entities. In fact, our understanding of cellular entities, multi-cellular macro-entities, and social systems is historically matured and supported by fossil evidence from the perspective of life on the Earth; and therefore, I prefer to keep the traditional concept of life and to set up “cells” as the earliest form of life, even though there may be no 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 definition of “prelife” refers to the period before the beginning of life on the time scale of evolution, during which inorganic, organic, and sub-cellular entities evolved.

However, defining “what is life?” on Earth dose not mean the elucidation of “what are the origins of life?” and “what is 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 believed that evolution on Earth should be part of evolution of the Universe, and must comply with universal laws of evolution. In addition,

there has been a huge disagreement on whether evolutionary process is a continuous course or a discontinuous history on the time scale of evolution; <sup>[93-95]</sup> and both opinions have their own supporting evidence. In my opinion, there are no evolutionary chasms between the inorganic and organic, between microorganisms and macroorganisms, between prokaryotes and eukaryotes, between animals and human beings, and between biological individuals and social populations; there are only temporary knowledge gaps in our understanding.

## What is a Species?

Defining a species has many practical applications in industry, agriculture and medicine <sup>[96]</sup> in addition to its critical position in biology, ecology and evolution. Unfortunately, the definition of a “species”, like that of “life”, is also various and controversial. <sup>[96-102]</sup> It was estimated that more than twenty conceptions have been proposed for defining species of eukaryotic macro-organisms. <sup>[103-105]</sup> Traditionally, “species” is an essential concept in macrobiology, and was initially defined by naturalists from a macrobiological perspective. Since the emergence of evolutionary theories and ecology in the 19<sup>th</sup> century, “species” has been branded with ecological and evolutionary markers, <sup>[99, 103, 106-110]</sup> such as “the unit of diversity”, <sup>[107]</sup> or “the fundamental units of ecology and evolution”. <sup>[108]</sup> Moreover, at the cellular level and the subcellular 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.” <sup>[108]</sup> George Simpson, the paleontologist defined species as follows: “Species is a lineage (an ancestral-descendant sequence of populations) evolving separately from others and with its own evolutionary role and tendencies.” <sup>[99, 103, 106]</sup> A.E. Emerson’s definition was “a species is an evolved or evolving genetically distinctive, reproductively isolated, natural population.” <sup>[103]</sup> An ecological definition of a species was given as follows: “A set of individuals that can be considered to be identical in all relevant ecological properties”, <sup>[111]</sup> or “a species consists of the organisms occupying the same niche.” <sup>[107]</sup> Ian Tattersall and Jeffrey Schwartz proposed their own definition of a species: “Species are historically differentiated entities that, osteologically, may be differentiated to inconveniently varying extents.” <sup>[112]</sup>

## 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.” <sup>[103, 113-115]</sup> 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”.<sup>[110]</sup>

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.”<sup>[103]</sup> Mayr’s definition has been used in some ecological studies on aquatic macroorganisms and plants.<sup>[109, 116-119]</sup> Thompson argued that “species in pure isolation simply do not make sense... Many, possibly most, species are collections of genetically differentiated populations.”<sup>[120]</sup> For example, inter-specific hybrids frequently occurred in plants, for which “botanists have often expressed doubt that plant species even exist.”<sup>[109]</sup>

## Defining species for micro-biological organisms

As our understanding has deepened into the micro-world, it has been found that Mayr’s species definition fails to define species for evolutionary entities at the cellular, subcellular, and molecular levels.<sup>[121]</sup> Morganand and Pitts argued that “Mayr’s biological species concept fails because there is no useful viral analog to sexual reproduction.”<sup>[122]</sup> For example, Mayr’s biological species concept is utterly incompatible with defining species for asexually reproductive microorganisms, such as bacteria, which Mayr himself agreed with.<sup>[103]</sup>

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 wasn’t proposed until 1991 when Dykhuizen and Green published their paper discussing the definition of biological species;<sup>[123]</sup> and then the concept was further refined by Lan and Reeves.<sup>[124-126]</sup> 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.”<sup>[104]</sup>

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.<sup>[29, 99, 127, 128]</sup> For example, at the cellular level, a prokaryotic microorganism species is defined as a collection of cellular strains sharing 70% or more DNA homology.<sup>[107]</sup> However, Fraser and colleagues pointed out that horizontal gene transfer and variable rates of recombination in bacterial DNA made it difficult to define a bacterial species naturally.<sup>[96, 129]</sup>

## Velasco’s paradox and the fimpological view

Recently, Joel D. Velasco asked a paradoxical question that should be considered 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.”<sup>[101]</sup> 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 the same. The definition of species is subject to the given evolutionary level of entities at the population level and should reflect their biological, ecological and evolutiological significance. To define species may be done in much the same way as demarcating the International Date Line, and the best way to solve Velasco’s Paradox may be to arbitrarily choose unique criteria for the evolutionary entities at a corresponding population level. According to this strategy, unique criteria are to be chosen from morphological, geographical, ecological, and behavioral characteristics at the macroorganism population level, not molecular markers at the molecular level for defining macroorganisms’ species. For example, anatomic features, sexual reproduction, diseases patterns, cultures, languages, and the geographic and ecological distribution are examples of the functions and behaviors of human beings at the individual or population level.

However, when such a strategy is applied to defining species of microorganisms, the biggest challenge is that we know little of the unique criteria at the micro-organism 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 difference or similarity at the microorganism individual or population level. Moreover, the morphological, geographical, ecological, and behavioral characteristics at the microorganism individual level are not only determined by DNA and/or RNA, but also controlled by non-nucleotide molecules and subcellular systems, which are dynamic under interior and exterior influences. Recent empirical and theoretical advantages indicate that modern genetics is not enough to reflect the whole content of biological heredity at the macroorganism individual level,<sup>[22, 130-136]</sup> which suggests that DNA and/or RNA-centered approaches may not play an all-round role in defining species at the cellular level or individual level.

## Speciation, species boundary, and species-barriers

The diversity of species on Earth is realistic despite diverse definitions, leading to the question “how did species form?” In fact, there were no scientific answers until the emergence of evolutionary thought in the 19th century, when Lamarck and Darwin proposed their theories for accounting for biological evolution at the macroorganism level. Therefore, speciation reflects the mechanism of evolution.

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

Ecological speciation is defined as “the evolution of reproductive isolation between populations, or subsets of a single population, as a result of ecologically-based divergent

natural selection”.<sup>[119]</sup> Clearly, the consequence of this mechanism is reproductive isolation at the macroorganism individual and population levels. In fact, the above two mechanisms of speciation stand on two piers: one at the molecular level and the other at the macroorganism level, which is also a characteristic of the Modern Synthesis. During the past decades, rapidly growing evidence and facts have indicated that the tremendous evolutionary gap between the molecular world and macroorganism world has been underestimated or ignored in the Modern Synthesis,<sup>[22]</sup> and therefore, the Modern Synthesis-based understanding of the mechanism of speciation has similar deficiencies. From the fimpological perspective, speciation at different evolutionary levels involves different mechanisms, which will be discussed further in other papers.

Due to various definitions for species and the insufficiency of our understanding of speciation, the explanation for “what and where the species boundary or species-barrier is?” is also diverse. Ernst Mayr defined that the species-barrier as being at the individual level and reflecting whether or not the individuals of a species are capable of interbreeding.<sup>[113]</sup> If we say that the species boundary, or “species-barriers,” at the macroorganism level is clear, as we enter the cellular, subcellular, and molecular levels, the boundary of species among different evolutionary entities gradually become indistinguishable.<sup>[139-143]</sup>

Speciation of bacterial microorganisms was believed to result in genetic barriers among intra-species organisms.<sup>[144]</sup> For example, the pan-genome of a given bacterial species was thought to consist of both a core and accessory genomes, with only the core genome present in all isolates of that species. This notion was first used by Lan and Reeves to define bacterial species.<sup>[111,124-126, 145, 146]</sup> As a result, 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.<sup>[147-155]</sup> However, Matic, Taddei and Radman pointed out that the barriers of bacterial species should also include both the variety of microhabitats and hosts and the divergence of genomic sequences and restriction-modification systems.<sup>[156]</sup>

An experimental study on the populations of the filamentous fungus *Neurospora* showed that matings between lineages adapted to the same environment had greater reproductive success than matings between lineages adapted to different environments,<sup>[157]</sup> suggesting that reproductive isolation at the microorganism individual level may be associated with some unknown environmental entities. Cohan argued that demarcating species of bacterial microorganisms should be guided by “a theory-based concept of species.”<sup>[158]</sup>

Indeed, the species boundary has been proved to be rather fragile and indistinct in inter-species of subcellular evolutionary entities, such as viral entities and membrane-enclosed microentities or extracellular vesicles.<sup>[10, 22, 159]</sup> In addition, prions, newly recognized protein-based genetic elements, have been recognized as pathogenic molecular entities,<sup>[160]</sup> which also face a species problem, a challenge in “phylogenetic taxonomy” or “phylogenetic nomenclature”,<sup>[102, 161-163]</sup> especially when confronted with their environment-driven phenotypic alterations, which are the result of protein folding variations rather than polyribonucleotide-associated changes.<sup>[164-171]</sup> 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 doubtful.

## Concluding Remarks

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 have failed to find a universal one for both, which should be attributed to the dynamic, continuous and gradational progress of evolution. In my opinion, life is only a special status of relevant evolutionary entities within the evolutionary process of the universe where the distribution of evolutionary entities is 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, defining life and a species could be like demarcating the International Date Line, which is a compromise between reality and ideality.

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