

Paradigm shifts in biology of the 19th century

- "Theory of natural selection" by Darwin and "Negation of spontaneous generation theory" by Pasteur

Here I will briefly describe the history of the theory on the origin of species. Until recently, the majority of naturalists believed that all species were invariable and created separately. This view has been maintained eloquently by many writers. However, only a small number of naturalists believed that species were subject to transformation, and the existing life forms are the true descendants of preceding generations of preceding forms of life.

(Charles Darwin "The Origin of Species" p. 1)

As you go down the chain of animals from the most complete to the most incomplete, we are faced with the singular situation of the gradual degradation in the configuration of the system - it is natural that I should think that the various life forms produced by life are born in sequence, developing from the simplest form to the most structured form.

(Jean Baptiste Lamarck, "Animal Philosophy", p. 8)

How could a material transform to a living organism by itself. In other words, could a living form come into existence without parent and without ancestors? That is the problem that requires a solution. Actually it must be said that the belief in spontaneous generation has been the belief of many eras. It was believed in ancient times and it is debated more and more in modern times. What I am rebutting is this belief.

(Louis Pasteur, "Consideration of Spontaneous Generation Theory")

This chapter will describe the outline of the paradigm shift experienced by 20th century physics and 19th century biology. The intention is to reach the understanding that 20th century biology also faces the need for a new paradigm shift. Next we shall give an overview of the achievements of molecular biology soon after its birth, and discuss about the “theory of natural selection” proposed by Darwin and the negation of “spontaneous generation” proved by Pasteur. Then, after pointing out the issue of origin of life as the limit of applicability of the natural laws that they discovered, I will describe the state of research on the origin of life and my views on its issues.

Paradigm shift in physics and biology – creative development of science

Physics in the 20th century, faced with a succession of unexpected experimental results, was confronted with the need to try to entirely re-examine theoretical foundations that had been believed for more than 200 years. Relativity theory denied the concepts of absolute space and absolute time that classical theory had considered obvious. Quantum mechanics required that the two concepts of “wave” and “particle”, which had been inconsistent concepts in classical theory, be recognized as different attributes of the same object. However, when one tries to unify these two new theories of relativity and quantum mechanics, one faces a logical contradiction that does not have a mathematical solution. It was not possible to avoid this contradiction just by mathematical generalization. New conceptual changes due to Shinichiro Tomonaga’s “kurikomi” (renormalization) theory were necessary.

Through repeated paradigm changes, we have learnt valuable lessons.

Firstly, the construction of a new theory is not just a problem of mathematical formulation. It must be accompanied by a fundamental conceptual change. Needless to say, in order to fundamentally change a concept, inspiration is more important than computational power.

Secondly, it is not possible to take a theory obtained by observing one aspect of nature and apply it to other phenomena in the same form. Different theories obtained by observing different phenomena may appear to be mutually contradictory. However, by making clear the limits of applicability of theories, it is possible for theories that appear to contradict to coexist.

Hence, whatever the theory, the validity, at every opportunity, should be checked against the most recent experimental results, and the range of applicability should be clearly limited *.

* According to Godel's "incompleteness theorem", it can be said that "Any powerful formal theory, by itself cannot guarantee the determinability of its theorems or the absence of self-contradiction". Such limits, although they may decrease with the development of the theory, will continue to exist. Thus, we can only approach subjects approximately. For just this reason, we must forever repeat the constructive process and continue to endeavor to get closer to the subject, one step after another.

Thirdly, when we learn a theory, we must correctly understand the assumptions upon which the theory was obtained. When a theory becomes widely accepted, often the very assumptions upon which it is based are forgotten*. Then the form of nature will be more and more distorted to fit the theory. However, if we correctly understand the underlying assumptions, it should be possible, to some extent, for us to prevent the theory from "running away".

It must be remembered that, in the development of a theory, in addition to the accumulated history of human thought over many generations, in other words, in addition to the phylogenetic history, there is the additive history of thought of each single person, in other words the ontogenetic history of the theory. It is not possible to correctly understand the limits of applicability of a theory without unraveling this historical context of the establishment of a theory.

As did physics, 19th century biology also experienced paradigm shifts. The "Creation theory", according to which man and other higher beasts were created separately by God and are immutable throughout life, and the "Spontaneous generation theory", according to which microorganisms and other lower life forms were generated spontaneously from septic waste, that were believed up to that time, were each negated, by Darwin and Pasteur.

It was a time when the concept of genes was not yet established, and the significance of the discovery of natural laws that are still valid today was unmeasurable. However, speaking in analogy with physics, it was just "classical" theory. Just like 20th century physics, biology faces the need to continue to shift its paradigms.

In the words of Ukichiro Nakaya in “Methods of Science”, “The truth of science is the joint product of man and nature, and science forever evolves and changes” (Iwanami Shinsho, p. 197). In other words, science is not the digging up of something that already has a shape, as in treasure hunting.

The scholars Hadamard (“The psychology of invention in the mathematical field”) and Piaget (“Genetic epistemology”) cite the historical fact of the discovery of America by Columbus in the context of “treasure hunting” in the sense of Ukichiro Nakaya.

Ukichiro Nakaya, *Methods of Science* (“Kagaku no hoohoo”, Iwanami Shinsho, p. 197)
Jacques Hadamard, *The psychology of invention in the mathematical field* (“Sugaku ni okeru hatsumei no shinri”, Misuzu Shobo, p. 7)

Jean Piaget, *Genetic epistemology* (“Hasseiteki ninshikiron,” Hakusuisha, p. 104)

With regard to the complex subject of nature, the choice of what and how to study, and how to describe the results, always deeply involves human factors. Moreover, against the background that science forever evolves and transfigures, and is tied with “creativity” and “historicity”, we cannot ignore the “internal observation” problem that we are not thinking about nature from outside of nature - our thinking selves are also part of nature. It can be said that this has a commonality with the ontogenetic issue of the development of our body and mind through repeated divisions starting from a single fertilized egg, and the phylogenetic issue of our evolution from a single original species. Cognition is forever in parallel with genesis and evolution. Hence, science, like life, forever evolves in a creative way.

Here, I think there is a reason why the “conflictual coexistence of self and non-self” that is the essence of life, as described in the previous chapter, is essentially the same as the essence of science, which is the product of human cognition. Hence, we cannot expect the healthy advancement of science if we do not allow the coexistence of conflicting concepts, and emphasize only phenomena that can be treated with a single concept.

It is just as, so long as you do not consider abnormal developments such as disease and cancer, you cannot understand the normal development of an organism, and you cannot expect to understand the whole process of life if you ignore regularity and only

emphasize irregularity.

In regard to the problem of cognition too, I think that studying not just the brains and neural systems of higher organisms, but also apparently unrelated living phenomena, such as the agents of infection - germs, virus, prions, and studying not just animals, but also plants and fungi, will give a more essential understanding of cognition.

Now, the number of wonders of life that confront us, or the number of mysteries of life that we must solve, are extremely numerous.

For example, there is no shortage of topics, the origin of life made possible by changes of material states, the origin of mind brought about through the long evolution of living organisms, the allergies known as modern diseases, the AIDS virus which causes immunodeficiency, the infectious agent prion which does not have genes, the E. coli bacteria O-157 with Shigella verotoxin gene, the environmental “hormones” that are attracting attention as endocrine disruptors, and so on.

And, for example, even manipulating advanced mathematics such as accessible only to mathematicians, or, conversely, introduce an easily solvable “toy model”, a method often used by physicists, as long as researchers are obsessed with “classical theory”, it is not possible to understand living phenomena *.

The expression “toy model” is used, for example, by Dyson (“Origins of life”) and Shin-ichiro Tomonaga (“Quantum mechanics and I”). What it means is a model that does not exist but is mathematically easy to solve. Just like a child’s toy, it might not be useful, but it is suitable for children to play with and might even be educational.

Freeman Dyson, “Seimei no kigen”, Kyoritsu Shuppan, p. 55

Shin-ichiro Tomonaga, “Ryoshi rikigaku to watashi”, Iwnami Bunko, p. 218

Just as Darwin and Pasteur were not constrained by the preceding old paradigms, now, we have to seek a road to liberation from the spells of Darwin and Pasteur. For this purpose, it is necessary to correctly understand the assumptions and achievements of the “classical” theories, and their limits, and perhaps doubt the assumptions themselves, and even re-lay the fundamental concepts of genes, evolution, origins and essence of life. I

would like to give an overview of the achievements of molecular biology soon after its birth, within the context of this chapter.

The achievement of molecular biology in describing the single origin of life – the rise of reductionism

The spectacular advancement of molecular biology from the 1950s through the 1960s, saw many new discoveries, one after the other, with such momentum that one could think that the mystery of life would be completely solved. It was also the success of thorough reductionism, which sought essence in “simplicity”, rather than “complexity”, of living phenomena.

* Piaget says “The opposition to reductionism had to appeal to structuralism. Between two structures at different levels, there does not exist reduction in one direction, rather there exists mutual assimilation” (“Genetic epistemology,” Hakusuisha, p. 145)

Be that as it may, let us list here some of the glorious successes of molecular biology at that time.

- All living things have genes consisting basically of a nucleic acid DNA, and that substance has a splendid spiral structure.
 - The genetic code of DNA, consisting of three nucleotide sequences that specify amino acids, is basically common in all forms of life
 - Even though there are hundreds of amino acids that have been artificially synthesized, there are only 20 types of amino acid in the protein actually used in living organisms.
 - The same amino acids are common, regardless of the form of life.
- And so on.

Let us synthesize these facts. It can be very clearly seen that the various forms of life living and breathing on the earth – from the fish living in the deepest seas, to the birds flying high in the sky, towering trees and microorganisms that can only be seen with a microscope – have common ancestry.

However, long before these results of molecular biology became apparent, even before the “laws of inheritance” were discovered by Mendel, there was a person who theoretically argued that the various living forms transformed progressively from a single original species. He was Charles Darwin *.

* Alfred Wallace (“The Malay Archipelago”) also independently arrived at the same conclusion as Darwin. That Darwin even considered withholding from publication after reading an essay sent to him from Wallace is well-known as an episode that calls to mind his character.

Darwin’s “Law of Natural Selection” – thinking from “models” of domestic animals and cultivated plants

Darwin synthesized the theories of the time, collected as many observational facts as possible, and published “The Origin of Species” in the form of a compilation. It was 1859. That Darwin was able to have sharp insights about the origin of the variety of life forms at a time when “Divine creation” was widely believed, is encouraging for us in our research, as we run this way and that way observing complex living phenomena. Here I wish to touch a little on the history of Darwin’s reasoning.

Darwin was interested in the fact that organisms placed in an artificial environment, such as cultivated plants and domestic animals, are full of a lot of variants that cannot be seen in the field. He focused on traits that human mutations appear by chance in individuals, and considered that it was the result of repeating "artificial selection" using a genetic predisposition for similar things to produce similar things.

Namely, it was realized that it is not that humans directly did something to suddenly create a new variant, but rather that by simply accumulating “genetic mutations” through generations, they indirectly selected a variant. Hence, it was thought that mutations that are not inherited are not important even if they are large, and mutations that are inherited, even if they are small, can have large cumulative effect due to “human selection”. Thus, Darwin, by first considering the origin of domesticated species, discovered “the law of variation of species” that comes from “genetic mutation” and “human selection”.

Next, Darwin considered that this law, which was discovered in an artificial environment, could hold similarly also in natural environments. It just so happens, Darwin, who was reading Malthus’ “An Essay on the Principle of Population”, was deeply sympathetic with claims such as “Conflict is selection, and also creation”.

For this reason, if we assume that all living creatures in the natural world were to leave more offspring than is necessary, we can imagine that a tough “struggle for existence” would unfold. Actually, the fact that imported animals spread quickly because they have few natural competitors, vividly speaks of the “struggle for existence” that is always going in every place.

And Darwin thought that in the “struggle for existence”, if an individual happens to be born with a feature that is even a little advantageous in the struggle, then that individual would be naturally selected. This is “natural selection”. Further, if such an advantageous feature were passed to the next generation, then the offspring of the individuals who survived due to natural selection would increase in number more and more. During this proliferation process, “genetic mutation”, “struggle for existence”, and “natural selection” continues relentlessly, and eventually no doubt a new species could appear. In this case, the origin of a new species in the natural world can be explained by the law of transformation consisting of genetic mutation, struggle for existence, and natural selection.

So then, with this law in hand, let us look back at the history of the variety of species that exist today. Then, the many species can be aggregated into a few ancestral species. This small number of ancestral species can be reduced to an even smaller number of primitive species. Finally, we reach a single primitive species. In this way, it was shown that the variety of species that exist today can be derived progressively through the accumulation of random mutations starting from a single primitive species. At the same time it meant a negation of the “divine creation theory”. This is the logical process of Darwin.

In Darwin’s research method, it is possible to point out two aspects that are useful for pursuing our research. The first aspect is that he used a “model” to probe living phenomena, and checked the validity of the insights obtained the model by observing the living phenomena in the natural world. The specific “model” in his case was breeding animals and cultivated plants. The second aspect is that, by the most naïve method, observation, he explored simple laws from complex living phenomena.

Of course, the two aspects pointed out here were indispensable for the discovery of the “law of natural selection”. But at the same time we must not forget that it also demonstrates the limit of applicability of the “law of natural selection”. First, we should

be careful of the point that the “model” of breeding animals and plants has an implicit hidden assumption that breeding animals and plants essentially do not differ from wild animals and plants. Incidentally, this assumption is not necessarily obvious. That is because living organisms in high stress states of breeding environments exhibit higher mutation, and cooperative rather than competitive relations are often observed in wild animals. Hence, that there are differences between the conclusions of the “segregation theory” of Kinji Imanishi who focused on the social behavior of wild life, and “the natural selection theory” of Darwin who considered breeding animals, does not mean that we should think one is correct and the other is incorrect.

The issue here is not which theory is right and which theory is wrong. Rather, the problem is that it has not been made clear which theory is applicable to which domain, and not applicable to which domain. For Kenji Imanishi’s “segregation theory” see “Seibutsu shakai no ronri” (Heibonsha). And comparison with Darwin’s “natural selection” is described in “Dauin ron” (ChukoShinsho). The sprouts of Imanishi-style natural science can be seen in “Seibustu no sekai” (Kodansha).

Kinji Imanishi, “The world of living things” (Translation Pamela J. Asquith, Routledge 2002)

However, the “natural selection theory” of Darwin should not be regarded as a principle of “from unity to diversity”. Certainly, there is no doubt that a single original species was transformed into a variety of species. However, for this, there is a premise that before the single original species began to speciate the individuals belonging to the species already had variety. Each individual, each in its own way, adapts to various environments. This is how new species are formed. In other words, the origin of the variety of the species is the variety of the environment and the variety intrinsic in living organisms that could respond and realize transformation. This is what I would like to treat as a principle of “diversity from diversity”.

Once Darwin’s “natural selection” theory was accepted, it soon came to be called “Darwin’s evolution theory”, and spread to more and more people. However, here there is a puzzle. Actually, in “The Origin of Species” the word “evolution” cannot be found. Instead, the words “genetic transformation” and “change” are frequently used. Why is that? We can point to one possible reason that in the biological science of the time the concept of “evolution” was not established.

This may be just the reason why “The Origin of Species” caused such a great reaction. However, the concept of “evolution” was well-known in social science and philosophy, politics and natural science, and we shouldn’t forget that before the publication of “The Origin of Species”, it was already introduced to biology by Herbert Spencer (for example, recorded in “Sekai no meicho 36”, Chuokoronsha), who is also known for proposing using the term “survival of the fittest” in place of “natural selection”,

* Daisetz Suzuki (D.T. Suzuki), says that "Evolution is development toward the outside. ... We are destined to involution, i.e., proceeding toward the inside" (“Toyo no kokoro”, Shunjusha, p. 144). These words resonate with the observation of Hideki Yukawa, cited in the introduction, “observation from the inner side”.

It seems simply because there was such a foreshadowing, that the concept of evolution rapidly became established as popular knowledge in the 10 years after the publication of "The Origin of Species". This can also be perceived from the fact that in the preface of "Origin of human race" that Darwin published in 1871 (for example, “Sekai no meicho 39”, Chuokoronsha) he uses the word “evolution” without hesitation when citing "The Origin of Species". However, even in the sixth edition of the "The Origin of Species" published the following year, the word “evolution” is still not used. There must be an important reason. The reason will become apparent by consideration of the "Origin of life" in the following.

Darwin in the conclusions of “The Origin of Species” writes “life was imbued with breath by the creator”. From this expression it should not be simply concluded that “in regard to the origin of life, there is a divine domain where the scientific scalpel cannot enter, even for Darwin”. In a letter to friend Hooker in 1871, there is mention of “there exists ammonia, phosphate, light, heat, electricity, ...”, intimating that the origin of life was “evolution” of living phenomena from chemical phenomena.

Here we finally solve the mystery of why Darwin did not use the word 'evolution' in the "The Origin of Species". As we know from the observation by Thomas Huxley, Darwin grasped his own theory in this way. “It is a theory which assumes that living things first existed, and clarifies the mechanism for their changing”. Since it assumes that life existed, it is clear that it cannot be used to explain the origin of life.

* The achievement of Darwin is that he revealed the law of transformation exhibited by species that already exist. From this “law of transformation” it is impossible to fundamentally argue about “What is life?” - in other words “What does it mean for life to exist?” In order to have a fundamental debate, I think it is necessary to mention about “How is life born?” and “How is consciousness born?” However, if the origin of life is considered as the evolution from chemical phenomena to living phenomena, the law of evolution must be a law that also explains the origin of life. Perhaps it was because Darwin was aware of the limitations of his theory, that he did not use the word evolution.

Here, I want to consider a little bit about the context of the scientific revolution leading to the paradigm shift of the negation of the Creation Theory. While for better or for worse Darwin’s “The Origin of Species” was causing a stir, the “Law of inheritance” discovered by Mendel (1866) had been forgotten for 30 years. I think that this fact teaches us a valuable lesson.

First, it can be said that for a scientific revolution to take place, it is important that a number of scientists independently acquire awareness of the same issue as the discoverer. In the case of Darwin, Wallace’s existence was valuable. Also, it was certain that there was a mutual effect from Spencer bringing the idea of “evolution” to biology. Moreover, we shouldn’t overlook the fact that Huxley, as “Darwin’s bulldog”, not only advocated the claims of Darwin, but he also made speeches and obtained the understanding of the masses. However, unfortunately in the case of Mendel, he was not blessed with (the support of) such intellectuals*.

Hideki Yukawa in “My reason for living” (Kagaku bunmei to sōzōsei, Yukawa Hideki Chosakushū 4, Iwanami Shoten, p. 265), makes the following point. “In the beginning when I have a new idea, it is absolutely a minority view. It is creative because I think of it by myself. This original idea might later become recognized by others. Then it is truth. However, it might not be recognized by others. In some cases, it is possible that the idea might never be recognized in one’s lifetime. I realized that even then it is very important to keep trying.” There are many things that make us think about how original was the “Laws of inheritance” discovered by Mendel (see Chapter 5, pp. 123-137).

However, more important than anything, we should remember, as Huxley said, “the work of Darwin is the greatest compilation of biological knowledge that could be made

by one man". It is full of the vigor of Darwin as a pioneer. Taking the opposite view, already many intellectuals were becoming aware of the "transformation of species". However, the reason why we have the impression that Darwin's achievements stand out, is because he doesn't just emphasize the conclusion of "transformation of species", but he collected and presented encyclopedic evidence, and showed the derivation of the conclusion, "transformation of species", in "The Origin of Species". For this reason, readers of "The Origin of Species", as they read, can reconstruct the logical process of Darwin, each in his own way. This process of constructing from separate elements is essential for understanding new concepts.

Now, here a dilemma occurs. The reason for the success of Darwin in changing the paradigm was his work exhibited a high degree of completion for the time. However, because it was so complete, 20th century biology faces the dilemma that it cannot take a step toward a new paradigm change. The only way to overcome this difficulty is to take more time than Darwin took, take an original voyage into a "new world" that he did not know, and make a compilation of it.

Lamarck's "Use and disuse theory" – fluid motion theory with the model of simple lifeform amoeba

Exactly a half century before Darwin's "The Origin of Species", in 1809, French naturalist Lamarck published "Animal Philosophy". In it, he proposed the "use and disuse theory" (organs that are used develop, and organs that are not used degenerate) based on the assumption that the individual adapts to the environment. And he claimed that the adaptive changes of the individual to the environment were inherited – in other words, there was inheritance of acquired characteristics, and so any individual could uniformly achieve adaptive transformations. In regard to explaining the variety of species, while Darwin considered the variety of individuals as important, Lamarck considered that the variety of the environment was more important than the variety of the individuals.

* A complete translation of "Animal Philosophy" was published in 1988 from Asahi Press series Phase II "Great Books of Science", Series II, Volume 5. The subtitle of this chapter only mentions Pasteur and Darwin. Actually, when I started to write this book a few years ago now, I myself was within the flow of modern biology, and I was unable to incorporate a conflicting concept in my "concept construction". Hence I had a

negative view of Lamarck. What gave me the motivation to read “Animal Philosophy” and an opportunity to have an interest in Lamarck was one book that I found by chance in the English books section of a bookstore, (E. Jablonka, and M. J. Lamb, “Epigenetic Inheritance and Evolution-The Lamarkian Dimension”, Oxford University Press, 1995).

** Lamarck theory stands on the assumption that “individuals are homogenous” and claims that the whole species transforms simultaneously together, as if the individuals are the species and the species is the individuals”. I wish to point out the point that this claim is consistent with what Kinji Imanishi claimed (“Dauin ron”, Chukoshinsho, p. 43) based on the “truth” obtained from observations of living creatures in the wild, that “the species and the individuals are one and the same, when a species changes the each individual must change in the same way”. In contrast, Darwin, since he was assuming the variety of the individual, he was for the first time able to explain the “truth” obtained from observations of breeding animals and plants. My intention is not to emphasize the conflict between incompatible theories, but to re-emphasize that the conflict occurs because the observation subjects differ – in other words, “conflicting coexistence” is the true essence.

The word “evolution” is not in Lamarck’s “Animal Philosophy” either of course, Instead, “progression” is used *. This is because, as motivation for writing this book, while observing various animals, he realized that there was no absolute constancy in the concept of “species” – it is always relative with even an artificial ambiguity. Then there arose the irresistible question of why the concept of “species” is such a relative one. As a question to that question, he thought that the variety of animal and plant structures could be always “progressing” in the direction of increasing complexity. Moreover, he claimed that the origin of the advanced complexity of body and sophisticated intelligence exhibited by humans, can both be found in the “fluid motion” of life forms with extremely simple structures, such as amoeba. Although the “fluid motion theory” of Lamarck would be discarded, this approach, that is a constructive approach based on phylogenetic history, would be useful for understanding not only the bodies and intelligence of we humans, but various living phenomena, including health and disease phenomena such as immune systems and cancer.

* In order to distinguish between animals and plants that continue to “progress” with ever increasing variety, and substances that do not exhibit such “progress”, Lamarck invented the word “biology”.

As Lamarck himself emphasized, the reason for writing "Animal Philosophy" was not just to present a conclusion, but to rely on the descriptions there to re-construct conclusions that the readers would judge to be reasonable. Actually, in the preface of "Animal Philosophy", he writes "As is well known, one inference can always be met by another inference... So, the truth that can be clearly trusted is in practice only the facts of observation. Not the conclusion that is drawn from them." (Asahi Shuppansha, p. 15).

Despite the care to add annotations to caution against over-emphasizing the conclusions that he derived, ironically, his conclusions have continued to be misunderstood to this day. One of the possible reasons, is that in the English translation which was published in 1814, five years after the publication of "Animal Philosophy", the word "besoin" was translated as "will" or "wish" instead of "need", giving the wrong impression to many intellectuals, including Darwin.

In regard to Lamarck's annotations, I completely agree. However, in regard to whether or not Lamarck's theory is logically and scientifically constructed, or whether it requires modification in the light of the new facts known today, some discussion is necessary. So next I will point out problems in Lamarck's theory.

The first problem, is the point that in the "use-disuse theory", he assumes from the beginning that "an individual adapts to its environment throughout its life". Thus, for example, the claim that the adaptive changes of an individual are accumulated in later generations through the inheritance of acquired characteristics, leading consequently to adaptive transformation, falls into circular reasoning. In order to avoid this circular reasoning, it is necessary to clarify the mechanisms and laws underlying the initial assumption that "individuals adapt to the environment", without relying on the concept of "adaptation". Actually, the concept of "adaptation" can be explained by the law of transformation involving genetic mutation, survival struggle, and natural selection, as discovered by Darwin.

The second problem is that he invokes two assumptions that cannot be accepted today. One is the assumption that spontaneous generation of simple living species occurs continually, in the past and today. (As we show in the next section, this spontaneous generation theory was brilliantly negated by the experiments of Pasteur). The other is

the assumption that in nature, species do not become extinct. These assumptions induce complete inconsistency with the facts.

The third problem is, in regard to inheritance of “acquired characteristics”, Lamarck does not make clear a concrete mechanism. Incidentally, the concept of “inheritance of acquired attributes” was widely accepted as “common knowledge” at the time. Therefore, Darwin also had accepted this concept. In his publication “The Variation of Animals and Plants under Domestication” (1868) he endeavored to explain how acquired characteristics were inherited by the next generation. This is the “pangenesis” hypothesis. However, today Lamarck’s theory of “inheritance of acquired characteristics” and is often used as if synonymous with “adaptive evolution” (or “directed evolution”). Just as genetic information changes as it gets successively copied, concepts and theories become completely transformed when they leave their original text and get copied from book to book. For this reason, it is important as much as possible to return to the original text and understand it correctly.

Anyway, while Darwin’s theory of natural selection spread widely, Lamarckism was hidden in the shadows. However, as will be discussed in Chapters 5 and 6, the facts prompt the rise not only of neo-Darwinism but also of neo-Lamarckism.

Pasteur’s “negation of spontaneous generation” - Consequences from the ideal “model” of fermentation phenomenon

In England, Darwin wrote the "The Origin of Species", and negated "creation theory". Then just two years later, in France now, Louis Pasteur authored "Study of the Theory of Spontaneous Generation” and negated the "theory of spontaneous generation".

The theory of spontaneous generation, supported also by philosopher Aristotle of ancient Greece, was widely believed until the late Middle Ages. According to it, for example, "a frog may occur from the mud of the swamp, and an eel is generated from the water of the river". Of course, needless to say, such “beliefs” were destroyed one by one by facts. Finally, spontaneous generation was negated and the issue was settled with the proof that maggots, which were believed to generate from rotting flesh, actually came from the eggs of flies. It looked like spontaneous generation theory was gone and forgotten. However, from around the beginning of the 18th century, observation with microscopes became widespread, and the world of microorganisms could not only be

seen with marvel, but also exaggerated and dramatized by imagination, and the spontaneous generation theory reappeared. Doubtless such circumstances of this age were also behind Lamarck's assumption of spontaneous generation of life forms with simple structures.

In such an era, Pasteur, without heeding the warnings of his friends, headed toward "An examination of the doctrine of spontaneous generation". It is perhaps more correct to view that it was due to the fact that the fermentation that Pasteur had studied to then was a suitable model for examination of spontaneous generation, rather than due to the fact that examination of spontaneous generation was the subject of a prize sponsored by the Paris Scientific Academy.

In the fermentation theory of the time, one could not deny the possibility that "when two substances are mixed together, a change occurs and as a result the organic substance yeast is spontaneously generated". The two substances are a fermentable substance such as sugar and a proteinaceous substance that acts on it. It was thought that when the proteinaceous substance comes into contact with air, the characteristic of yeast – namely the tendency to act on the fermentable substance - was acquired.

Pasteur was particularly interested in the origin of yeast. It had already been established in 1836 that beer yeast was organic. The issue was "Was an organic substance generated from a non-organic substance, or was it already mixed in with the non-organic substances?" As a result of investigating various fermentation phenomena, including lactic acid fermentation, butyric acid fermentation, and malic acid fermentation, Pasteur arrived at the conclusion that in all cases "organic material already existed with the non-organic substances".

In this way, because Pasteur was able to use the "model" of fermentation as his basis, it was possible for him to scientifically advance the study of spontaneous generation, which till then was considered the touchstone of wisdom of naturalists. He decided to use an even simpler experimental system to study the crux of the problem of the origin of yeast in fermentation. It was an experiment that would see if life was spontaneously generated by sealing a substance like milk that changes easily in a glass container and bringing it into contact with air. The experimental results were very clear. They showed that if the air was treated with strong heating, no change was observed in the milk, and if the milk is placed in an atmosphere that is not heat-treated then mold and bacteria

breed quickly. Obviously, the origin of the mold and bacteria was in the air. Thus the law that “only life begets life” was established.

By careful observation, Pasteur was able to show that when the growth of mold was rapid, the growth of bacteria was very small. He explains the reason as “the things that first multiply inhibit others” (L. Pasteur, in “Consideration of Spontaneous Generation Theory” (“Shizenhassei setsu no kento”, Iwanamibunko, p. 72)). It can be said that this observation by Pasteur graphically shows that the “struggle for survival” also occurs in the world of microorganisms. In other words, the pattern that Darwin was observing in the world of animals, Pasteur was also observing in the world of microorganisms.

Thus, it became definite that all species, from lower organisms to higher organisms, have been transformed from a single original species, in accordance with "natural selection theory" of Darwin. Of course, needless to say, the law discovered by Pasteur at this time, that “only life begets life” became the basis for the subsequent development of medical and biological sciences. Actually, the first application of this law can be seen in the success of rabies vaccine by Pasteur himself. He saved the life of a boy called Meister who had been bitten by a rabid dog, by using an inactive vaccine in which the pathogen had been killed and the ability to infect had been lost. The reason he was able to use the vaccine was because he was confident that once the pathogen was killed it would not reappear. The simple method for long term preservation of foods in cans and bottles is possible because once germs are killed, they do not re-generate. The law discovered by Pasteur saw one application after enough. However, even this law, which is now common knowledge, has a counter-example. That is the “origin of life”, when life appeared from non-living substances for the first time.

In the 18th century, Jenner developed attenuated live vaccine using cow pox instead of human pox. However, in live vaccine, the pathogen is not dead, and in this respect is more dangerous. The name vaccine came from “vacca” meaning cow.

It may be thought that after the important discoveries in biology, of “natural selection” by Darwin and “negation of spontaneous generation” by Pasteur, that the discovery of a natural law concerning the origin of life would be achieved in just a few more steps. However, to this day, 140 years since the publication of “The Origin of Species”, the law of the origin of life has not been found.

So next, we will give an overview of what modern molecular biology has made clear about the problem of the origin of life.

The achievements and limits of molecular biology in regard to the origin of life – the outlook for reduction to elemental “processes”

In 1983, an RNA nucleic acid called “ribozyme” that had genetic information and catalytic function was independently discovered by Cech and Altman (Cech, 1990). The reason why this discovery aroused interest was because it was thought that the “chicken and egg” paradox that had continued for many years would be immediately resolved. The “chicken and egg” paradox refers to the ongoing debate about whether the first molecule to appear is the nucleic acid (the egg) or the functional protein (the chicken), since nucleic acid (the egg) cannot be copied without protein (the chicken), but protein (the chicken) cannot be synthesized without the corresponding nucleic acid (the egg). However, so far, RNA that can catalyze its own self-replication or catalyze the replication of other RNA has not been found in the natural world. The discovered ribozyme function just catalyzes the splicing and linking of RNA. Nevertheless, it is clear that the discovery that one type of molecule RNA can have both information and function overturned the common sense that “there is an absolute distinction between information molecules and functional molecules and there is no cross-over between them”. Thus it came to be thought that the first domain of life is RNA – as named by Gilbert, “the RNA world” (W. Gilbert, 1986)

However, here we face the next paradox. Let us try to imagine the origin of the single species of RNA molecule. Certainly, if we adopt the assumption that self-replicating RNA modules exist, natural selection will lead to the selection of an optimal RNA molecule species. However, the situation is not promising. If RNA was “spontaneously generated”, such a species would not have self-replicating ability. Then we would have to consider how the process of evolution could be driven. We can think of two possibilities. One is the viewpoint focusing on the “self-organizing function” within RNA itself. The other possibility is the viewpoint that considers an evolutionary process different from RNA.

The situation became confused again with multiple claims about the “domain for the origin of life” - crystals of clay by the English chemist Cairns-Smith (Cairns-Smith, 1985, 1987), metallic-surface of pyrite by the German lawyer and amateur researcher,

Wachtershauser (Wachtershauser, 1988, 1990), and sulfur compound called thioester by the Belgian biochemist De Duve (De Duve, 1991). It is still not yet clear what laws govern the evolution from materials to life. In other words, the original living species has been just replaced by the molecular species of RNA, and the problem of the origin of the “RNA world” has not been fundamentally solved.

In 1993, the book “The RNA World” (eds. R. F. Gesteland and J. F. Atkins, 1993) was published from Cold Spring Harbor Research Laboratories. Crick and Watson each separately wrote prefaces, and many famous researchers contributed papers. In the beginning is a paper by Joyce and Orgel. The conclusion of their paper commences with the following sober phrase. "After dreaming of self-replicating ribozymes..., and having nightmares about the difficulties ..., we awaken to the cold light of day ...” (Joyce and Orgel, 1993, p.22) *.

Following after the well-received first edition, a second edition with recent findings was published in 1999 (eds. R. F. Gesteland, T. R. Cech, and J. F. Atkins, 1999). However, the conclusion of Joyce and Orgel, that a fundamental solution to the problem was a long way off, was the same as in the first edition.

Moreover, Stanley Miller, who in 1953 shocked scientists throughout the world by succeeding in synthesizing amino acid in a primitive atmosphere experiment, severely assessed the situation with the comment “At this time, no-one has said anything conclusive” (Hogan, 1991).

Thus, so far, research about the origin of life has run aground. What is the reason for this? Perhaps it is because the strong adherence to the reductionist research method has resulted in too much focus on searching for the molecules that are directly linked to the origin. Reduced to molecules, the essence of life will be lost. I do not think that molecules that are missing the essence of life can be used to grasp the origin of life. It is necessary to not adhere to old paradigms, and take up new viewpoints. I think that in order to discover the law of the origin of life, it is necessary to clarify the origin of the “process” of “evolution”. This is where “process” reduction theory can be used.

Here I wish to raise a problem. In the experimental research concerning the origin of life, as in the research of artificial life, moral discussions are necessary *.

* Moral issues are described for example in the postscript of theoretical biologist Maturana 's "Biology of Cognition" ("Autopoiesis", Kokubunsha, pp. 161-241)

H. R. Maturana, "Biology of Cognition" in "Autopoiesis and Cognition: The Realization of the Living", Dordrecht: D. Reidel Publishing Co., 1980, pp. 5-58.

<http://www.enolagaia.com/M70-80BoC.html>

In each case, assuming the experiment is successful, in Pasteur's law that "only life begets life", another exception will be added in addition to the origin of life. That is not the only problem. It is conceivable that at that time we will lose the basis for medical and biological sciences that we have built up starting with the rabies vaccine. That will bring on a very serious situation. I think of "life" as a system that can exchange all of structure, function, information, and energy. Hence, undoubtedly, such "life" after being created would immediately negate our own existence.

Finally, I would like to finish the chapter by summarizing my views about the essence of paradigm change, comparing "development of cognition" and "advancement of biology".

The essence of paradigm change – development process of cognition and development process of biology

Just as in embryology, there was a paradigm shift from "preformation theory", in which the structure of the individual exists before development, to "postformation theory", in which the structure is composed, in the field of natural history there was a paradigm shift from "divine creation theory", in which animal species forever remain the way that they were created by God, to "species transformation theory", in which animal species forever transform. Thus, a "Copernican revolution", so to speak, from 'static' existence to 'dynamic' existence is a common criterion for realizing scientific revolution, in any field of study.

For example, consider we thoroughly analyze the embryo and adult organism of an animal. Most likely, we would discover a set of properties of the subject. However, since such 'intra-subject' analysis only grasps the 'static' existence, the description is no more than local. As the next stage of cognition, we shift our focus from the embryo to the adult, and from the embryo and adult of one species to the embryo and adult of

another species. From this 'inter-subject' comparative analysis it is possible to see the mutual relations between subjects. By linking up the inter-subject relations it is possible to see the embryonic process and evolutionary process as 'dynamic' processes. This is what was referred to earlier as the Copernican revolution in the history of biology.

Of course, cognition proceeds to the next stage. Once the mutual relations between objects are seen by 'inter-subject' analysis, then 'inter-relation' analysis is possible. In the example described above, this corresponds to the 'embryonic process' from embryo to adult derived through 'inter-subject' analysis, and then the 'evolutionary process' from one animal species to another animal species. At this time, our interest is not in the animal embryo and adult which were the original subject of analysis, but in aiming for a larger unification that allows us to grasp the whole of life while exploring the dynamic processes common to genesis and development. In that case, through the changing processes, it will become possible to construct new concepts with which we can explain the existence of life. As an example, we can give the comparative study of 'antigen recognition by the immune system' and 'the onset of cancer in a healthy cell' as unfolded in the next chapter. These two seemingly completely different processes were perceived by Barnett as 'natural selection' processes at the molecular level *. Thus 20th century biology transcended the Copernican revolution of the 19th century, and headed toward an even larger unification.

* As we describe in the next chapter, according to Burnett, the concept of 'evolution' and Darwin's concept of 'natural selection' have almost the same meaning. However, as will become clear as we proceed through Chapters 5 and 6, it is necessary to reconsider the concept of 'evolution'. The reason is that 'evolution' has aspects that can be reduced to the transformation process based on Darwin's 'natural selection', but there are aspects that cannot be understood in this way – for example, aspects linked with the 'origins' of new structures with leaps. In other words, it is necessary to redefine 'evolution' as a wider concept that can incorporate continuous transformation processes and 'origins' with non-continuous leaps

In this way, our interest transcends the original subjects (in this case, the subjects embryo and adult organism introduced at the beginning), and aims for a larger integration of genesis, evolution, immune system, and cancer – which can be expressed as 'super subject'. By continuing this operation further, from the phase of change that is 'process' it becomes possible provide an explanation about the 'reality' that is life. Here,

another revolution (opposite to a Copernican-like revolution) occurs, from ‘dynamic’ process to ‘static’ existence (here we aim for a systematic explanation of life).

We note that the terms ‘intra-’, ‘inter-’ and ‘trans-’ used here are due to the work of Piaget and Garcia (“Psychogenesis and the History of Science”). I think that one of the greatest achievements left by Piaget is, comparing children and scientists from the point of view of development of cognition, and found the general process of development of cognition from ‘intra-’ to ‘inter-’ and then to ‘trans-’ as a characteristic of the development of cognition. However, in the case of Piaget, the scientists that he compared with children were mainly mathematicians and physicists. I constructed the history of biology introduced here by including biologists in the comparison, and in regard to biological phenomena, I considered not only normal processes but also abnormal processes.

I wish to add one additional explanation. In Chapter 1, I pointed out that, whether it was nucleic acid or protein, new diseases evolve with historical development from intra-species propagation to inter-species propagation. Such transition from “intra” to “inter” has been taking place commonly not only in the development of our cognition, but also in the world of living organisms.

Summary of this chapter

With the theme that it is essential that, like living organisms, the study of living organisms that is biology, changes continually, we gave an overview of 19th century biology, focusing on Darwin’s “theory of natural selection” and Pasteur’s “negation of spontaneous generation”. As history shows, these theories caused a paradigm shift in 19th century biology. However, there remain many problems that are not solved by these theories. One is the problem of the “origin of life”. Despite the spectacular advancements of the molecular biology that was born in the mid-20th century, it is the truth that we are still troubled by the fact that there is not even an outlook toward solving the problem.

In the second part, the reason that I propose “Self-non-self circulation theory” is, by focusing on the elemental process, we throw a light on such unsolved problems.

In the next chapter, I wish to discourse about how we came to be able re-grasp both antigen cognition by immune system, which is representative of “health”, and cancer, which is representative of “disease”, in the context of “theory of natural selection at the cell level”.