What is life? Despite the advanced studies of Western science and the progress of modern technology, we have not yet answered this problem satisfactorily. What is worse, it is a double problem that we cannot realize how we are deeply influenced by the traditional way of Western thinking in attacking the above problem. Owing to the dichotomy of subject (or endo) and object (or exo), together with its corresponding reductionism, we have specified more and more the detailed components of a living system and have also required the reproducibility principle that the living system shows the same responses to the same stimuli under the same conditions. A dichotomy perspective of this kind, which has been central to modern science, stands on the assumption that opposites are mutually exclusive and even contradictory.

Contrary to this dichotomy perspective, there is an alternative complementarity perspective typical of Eastern philosophy, which is surprisingly similar to Niels Bohr’s complementarity principle in modern physics. It actually suggests that opposites are not mutually exclusive, but merely complementary to one another, because opposites are thought to be only different aspects of the same wholeness. This means that there is no clear distinction between subject (endo) and object (exo). As there is no definitely isolated object, the reproducibility principle is mostly violated. We must therefore pay much attention to the transients—or processes—during the past history of life.

On the basis of this complementarity idea, we are encouraged to have a holistic view by integrating fragments of knowledge at various component levels and time scales when investigating the history of life. In this sense, we need a new synthesis of Western science and Eastern philosophy,
instead of considering either of them separately. Only then, it is possible to attack the long-standing question: what is life?

Along these lines, in the present paper, a process of endo-exo circulation is introduced as an essential paradigm of life. As a living organism is engaged in challenges from both its internal and external environments, it contains unlimited conflicts and oppositions, which in turn must be the driving force for its evolution and development. It is such reconstructive dynamics that can give rise to an identity of the living organism. The resultant identity of life is represented by the Eastern image of the Mandala as an emergent symbol generated by the process of endo-exo circulation.

1. Introduction

Logic starts from the division of subject and object, and belief distinguishes between what is seen and what is not seen. The Western mode of thinking can never do away with this eternal dilemma, this or that, reason or faith, man or God, etc. With Zen all these are swept aside as something veiling our insight into the nature of life and reality.

_Daisetz T. Suzuki_ 1938, p360-361

...our science – Greek science – is based on objectification...But I do believe that this is precisely the point where our present way of thinking does need to be amended, perhaps by a bit of blood-transfusion from Eastern thought.

_Erwin Schrödinger_ 1958, p130

We have eternally been faced with the fundamental question: what is life? Not only is this the exact title of Erwin Schrödinger's book (1) published in 1944; it is even the very question that we have often asked, but not yet answered satisfactorily. This is probably not because we lack complete knowledge of components such as molecules, organelles, cells or organs at different hierarchical levels of a living system, but because we lack a holistic view integrating the fragments of knowledge at different levels during our investigations of the history of life (2).
Indeed, global features of the living system cannot be understood by analyzing the component parts separately. This is true even for non-living systems (3). Remember the revolutionary concept of Niels Bohr’s complementarity principle in modern physics (4). In classical theory, particle phenomena and wave phenomena are considered to be mutually exclusive and even contradictory. From quantum theory, however, they can be viewed as merely different aspects of the same phenomena, known as complementarity. We need paradigm shifts from one view of considering opposites as contradictory to another view of considering opposites as complementary towards a synthesis (5).

This reminds us of the famous story about six blind men and the elephant, where there were quite different impressions of the same animal as being a wall, a snake, a spear, a tree, a fan and a rope. All these answers are right, and also wrong. It is not a question of which one is correct and which is not. All these answers only describe small parts of the same animal. Lessons learned from this famous story suggest that the real question is, “By taking different kinds of complementary approaches, how do we acquire an improved understanding within given constraints?” (7, 8)

Under the influence of the traditional way of Western thinking, we are again apt to ignore the important role of the external environment, especially an environment that is polluted, on life’s processes (9). It is no longer possible and even a mistake to investigate life itself without considering its surrounding environment under various conditions of time and space during its past history from the beginning (9, 10). The dichotomy of nature and nurture, reflecting the dichotomy of subject and object, is only one of many similar dichotomies, which has inevitably shaped our way of thinking and our understanding of life and environment (10, 11). The present paper proposes a new paradigm of life by means of endo-exo circulation (9, 12).

2. Beyond the limits of traditional Western thinking

In traditional Western thinking, it is assumed that there is a very clear distinction between subject and object. Based on this assumption, it is
believed that we can obtain our knowledge about a given object as it is strictly isolated. A lot of knowledge has been accumulated, and hence our scientific world picture has been made from this gathered knowledge, where there is only a causal linkage (cf. Fig.4a). We have been, however, mistaken within the framework of our world picture. Ironically, it is impossible to ask a question about the reliability of this scientific framework within the framework itself.

Revolutionary breakthroughs in particle physics can give insights into better understanding of how we make great progress (13). Remember Heisenberg’s uncertainty principle in modern physics. It suggests that observing a particle is also perturbing it, and that we cannot avoid an essential uncertainty in regard to the state of the particle. It appears to be a problem that there is no clear distinction between subject and object; we are both spectators and actors. The only way to make progress in our understanding is to predict the outcome of experiments statistically.

Surprisingly, the everyday questions of life typical of Eastern philosophy resemble the scientific questions revealed by Heisenberg’s uncertainty principle as well as Bohr’s complementarity principle (5). When we are observing a thing, we are also acting on our past knowledge to choose unconsciously a particular thing. From a psychological point of view, therefore, it is the case that we are both spectators and actors in the world. There seems to be a serious dilemma: without right knowledge, we cannot rightly observe what is there; but without right observation, we cannot get right knowledge (9, 14). It is a developing and dynamical process that would operate in the interpretation of knowledge itself through the interaction between thinking subject and observed objects. This dialectical process not only proceeds during an evolutionary history of science, but also occurs during a developmental history of an individual human life, as both are undoubtedly conducted by continuous actions of human minds within the real world and simultaneously unavoidable reactions from it (9).

In fact, the developing process of knowledge arising from the relationship between perceiving subject and perceived objects during a history of science would be similar to the evolutionary process of their structure and function arising from the interaction of organisms with
their environment during a history of life (15). The parallel relationship between the development of knowledge and adaptation of life occurs because both the perceiving subject and the perceived object share the same kind of reality through evolution (16). In other words, organisms, including humans, are at once experiencing subjective entities and objective physiological entities: this dual capacity leads to the blurring of boundaries between subject and object.

This kind of mysterious relationship between subject and object can be well illustrated by “Drawing Hands” by M. C. Escher, as shown in Figure 1. Since hands are drawing each other, it is very difficult to predict the complete picture. Of course, the beginning and ending of this process are unclear, but instead, the process of drawing exists definitely; this suggests that the identity of life, in general, can be ascribed not only to the ‘object’ itself but also to some dynamical process. To understand life itself, therefore, we must identify not only the elements but also the elementary processes within and around the organism. Only then, normal states, disease states, senescent states, and even non-living (or dead) states can be interpreted in terms of dynamic changes in the elementary processes as well as plastic changes in the elements (2).

![Figure 1: Drawing Hands by M. C. Escher. Hands are drawing each other, so the origin of the process is unknown. Reprinted from Figure 5 by Maturana and Varela (17).](image-url)
3. The Constitution Principle: from an open chain to a closed loop

Let us consider complex networks in the brain. This seems to obey the Constitution Principle (18): if a region A connects to B, then B connects reciprocally back to A. Generally, this principle holds not only within subsystems of the brain but also at the level of connections among those subsystems. The resulting dense interconnections among various components in the brain thus ensure cooperativeness both locally and globally. The brain becomes the entirely coherent system: what a local component within some subsystem is doing coherently depends on what all the other components of all the subsystems are doing. There appears the intrinsic (or autonomic) nature of dynamics leading to self-organization and context-dependent behavior. It is the emergent properties that arise from such an intrinsic nature of dynamics in the brain.

Now note that the Constitution Principle — if A connects to B, then B connects reciprocally back to A — is almost the same as the Complementarity Principle in modern physics and even in Eastern philosophy.

Let us consider the life of a Zen-master (8). As Daisetz T. Suzuki (1960) explained, there are five steps (or go-i in Japanese) in Zen training (19). These five steps are divided into two groups: noetic and conative (or affective). The first three are noetic and the last two are conative (or affective). The third step, the middle one, is the turning point at which the noetic becomes conative: knowledge turns into life. At this point, the noetic comprehension of Zen life becomes dynamic. In the forth step, the Zen-master strives to realize his insight to the utmost of his abilities. In the last step, he finally reaches his destination, though it is really no destination.

![Figure 2](image_url)

Figure 2: The first three of the five steps in the Zen training are represented in a, b and c.
The first three steps are described in some detail as follows: The first step indicates that the one is in many. This is symbolically represented by Figure 2a. The second step indicates that the many are in the one, as the many is what makes the one possible. This stage is represented by Figure 2b, which corresponds to the reciprocal connection in the case of the Constitution Principle in the brain. The third step, as described above, is the most critical point at which static knowledge becomes dynamic life. This critical stage is shown by four different kinds of symbols in Figure 2c, though each of them represents the same meaning. Most of us are very familiar with the Chinese symbol of yin and yang philosophy. Here, dynamic motion is indicated by curved arrows (Note that this stage resembles “Drawing Hands” by Escher as shown in Figure 1).

Of course, the details are completely different between the emergence of coherent behavior in the brain and the emergence of dynamic motion in the life of a Zen-master at the third step. But the essential point must be the same, as the critical transition always occurs from a sequential linear chain to a circular looped relationship, from which dynamic motion can arise. In other words, the ‘phase transition’ from open-ness to closed-ness must be the essential feature towards an autonomic nature of life (20).

4 Endo-exo circulation as a paradigm of life

Reviewing the continuous challenges to the traditional nature-nurture questions, Murase (12) proposed the Endo-Exo Circulation Theory of Life. This theory not only describes the membrane processes known as endocytosis and exocytosis through the growth, budding and fusion of plasma membranes (21), but also accounts for the origin of life.

Figure 3 illustrates how a closed endo-system not only shows identity in contrast with the open environment (or exo-world), but also undergoes evolution through variation and ‘weak selection’ in the context of a combination of elements involved. A closed endo-system can keep its identity as it has boundaries which isolate the internal materials from the exo-world. Suppose that such a closed endo-system is subject to
formation-deformation cycles as shown in the lower panel — that is, the boundaries are broken, allowing entry of new elements from the exo-world, and resealed. At each cycle, the closed endo-system could not retain the same composition as it was before, but instead evolve in a spiral fashion as shown in the upper panel. This interactive process between the endo-system and the exo-world is referred to as endo-exo circulation.

![Endo-exo circulation](image)

**Figure 3** Evolution of a closed endo-system by means of endo-exo circulation.

Traditionally, identity and evolution have been ascribed to the same self-replicating genetic systems, because such genetic systems maintain identity by self-replication and yet undergo Darwinian evolution through variation and natural selection. Recent studies on present-day cells, however, suggest that the membrane processes — such as the growth, budding and fusion of plasma membranes and vesicles, together with membrane transport and membrane transduction — are not directly controlled by genetic systems, and still they are essential for the adaptive behavior of cells, the biogenesis of intracellular organelles and many other functions (21).

Interestingly, each endo-exo circulation can create new combinations of elements involved which might be subject to weak selection through inter-elementary interactions, and therefore, it can reach beyond the
boundaries of its identity. Furthermore, the enclosed internal-environment can provide a basis for open evolution, because an almost infinite number of elements are supplied by the exo-world at every cycle. Note that the endo-exo circulation can link different levels of the hierarchy such as opened linear fragments, and closed membranous boundaries. As a result, the endo-system can undergo continuous complexification with the emergence of new levels of the hierarchy.

Based on this paradigm of endo-exo circulation, we have to consider both nature and nurture, but not just one of them. They are tied together from the beginning and inseparable through a dynamic process such as circulation. Such endless circulation between nature and nurture — or between self (or endo) and nonself (or exo) in the terminology of Murase’s theory — gives rise to the emergence of new orders. It is the new orders that account for both creative and destructive features of life. Here the proposed paradigm of endo-exo circulation is turned to be the same as the thinking of the Zen-master mentioned above.

5 How to approach the long-standing questions: what is life?

It is well known that there are two kinds of thinking patterns (22, 23, 24). It is typically Western to think in terms of cause and effect (Fig.4a), whereas thinking in simultaneities is said to be typically Eastern (Fig.4b). To the Westerner, it is an important question to ask ‘what came first, the chicken or the egg’, and it is very natural to think in the form of a time lapse, where cause precedes effect. When a current state of affairs is derived from a preceding cause, it is considered that an explanation is now obtained satisfactorily. In contrast, Eastern thinking is based on a comprehensive or a field-like view rather than a cause-and-effect or an arrow-like view.

As Nisbett (23) emphasized, both Western thinking and Eastern thinking are equally important in our life. The same is true in our science. It is not a good question of which approach is correct and which is not. Different kinds of complementary approach should be required for an improved understanding. The real question is thus how
to approach reality under the given constraints. The best way to consider both Western thinking and Eastern thinking is to create a circular relationship between the two modes of this thinking. As the development of our knowledge and the adaptation of living organisms obey the same principle of endo-exo circulation, the best way to thinking should be the same.

\[ a \]
\[ \rightarrow \ A \rightarrow B \rightarrow C \rightarrow D \rightarrow \text{Western thinking} \]

\[ b \]

\[ \text{Eastern thinking} \]

Figure 4: Western thinking and Eastern thinking.

6 The Mandala as a symbol of life

Life as thinking subject and observed object should be understood by the way of thinking of endo-exo circulation. Life must be therefore characterized by unlimited conflicts and oppositions. Indeed, the Japanese Philosopher, Kitaro Nishida (25), emphasized the important roles of conflicts and oppositions in experiencing and thinking. Likewise, life in general seems to always contain conflicts and oppositions such as struggle between evolving cancer cells and defending host immune systems (2), regulation between on and off states (9), and so on.

How do we describe this situation? To answer this question, I propose
my original Mandala, as illustrated in Figure 5. Historically, Mandalas have been tools for the religious to see reality behind complex features through training. Despite its almost infinite variations, most Mandalas have a very universal meaning and structure: it is a symbol of wholeness that represents a synthesis of endless conflicts. Carl G. Jung realized that Mandalas can be good tools for mental patients to recover from mental illness (26).

![Figure 5: Mandala. The emergence of complex dynamics occurs as a result of intra-, inter- and trans-subsystem conflicts.](image)

As shown in Figure 5, an undivided unit, ○, placed in the center starts to divide into opposing units, ○⇔○, which in turn build up a higher unit as a synthesis of opposition, ○⇔○, and the same process continues to build up a whole system. This is just like the circulation between the exo-world and the endo-system. The targeting whole system is the same as the beginning unit, though there is a difference in size and complexity. So, the Mandala shows historical processes of both division and synthesis. At the same time, the Mandala is also a picture representing
special arrangements of different kinds of subsystems, in which there are intra-, inter- and trans-subsystems’ conflicts. Each unit is indicated by a closed line. The Mandala is therefore the nested hierarchical structure, as there are no edges like an open line. Note that we can get this Mandala by projecting the three-dimensional diagram (see Fig.4) onto the two-dimensional plane.

Mandalas are good tools for us to acquire improved understanding, because we can speculate missing opposites behind complex features. Under the given constraints, it is rather difficult to understand the ‘outside’ world beyond the constraints. However, it is relatively easy to get rid of them by taking their negation. Figure 6 illustrates this situation. Since the Mandala is based on intra-, inter- and trans-subsystems’ conflicts, we have to expect that conflicts also appear beyond the whole system. This may reflect the idea of an inverse relationship given by Kitaro Nishida. A set of two opposing whole systems, represented by clockwise and anti-clockwise rotational arrows would play an important role in predicting the emergent phenomena. Interestingly, there are parallel similars at any level of this symbol.

Figure 6: A set of two whole systems. Note that there is self-similarity at any level of the symbol.
In conclusion, the endo-exo circulation can not only cover both Western thinking and Eastern thinking, but also provide a symbol of life like the Mandala, because it can be an universal principle behind complex life phenomena. The resulting complex pictures exhibit opposed phenomena, sometimes observed as conflicting results. But such opposed phenomena are merely the two sides of a double-edged sword. In other words, the endo-exo circulation can be considered as a new paradigm of life. An interdisciplinary perspective would be welcomed to advance this idea.

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