A Systems Biological Interpretation of the Concept of No-Self (anātman)

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Abstract

Systems Biology is the study of the interactions between the elements (genes, proteins and other molecules) of living systems. Genes do not act in isolation either from each other or from the environment, and so I replace the metaphor of the selfish gene with metaphors that emphasize the *processes* involved rather than the molecular biological components. This may seem a simple shift of viewpoint. In fact it is revolutionary. Nothing remains the same. There is no 'book of life', nor are there 'genetic programs'. The consequences for the study of the brain and the nature of the self are profound. They lead naturally to the concept of *anātman*, no-self, and to a better understanding of the relation between the microscopic and macroscopic views of the world. Organisms are viewed as variable open systems, rather than as determinate closed systems.

Introduction

First, I will explain what I mean by Buddhism in the context of this paper. And what is Systems Biology?

Buddhism

Historically, and also today, Buddhism refers to many things, and some of these are even antithetic to science. Those who defend the tradition in a scientific context would say that this is because Buddhism, as it transformed itself in the various cultures to which it was transmitted from its origins, acquired many of the superstitious forms of folklore of those cultures – hence the wide variety of beliefs found in different Buddhist cultures. So much so that the early Western missionaries did not recognise them as all having the same origin, and even mistook some of what they found to be a modified form of western religion (Batchelor, 1994 : 167).

This history is the basis of the story (Jupitereans) in the last chapter of my book, *The Music of Life* (Noble, 2006). I imagine that some space travelers have found a form of religion in a civilization on one of the moons of Jupiter, but in fact the story represents the mistakes made by Western missionaries when they first encountered Buddhism and tried to make it conform to the structure of Christianity.

The reason for which that fails is that there is a central set of ideas that are not only far from superstitious; they themselves are incompatible with virtually all forms of what we, in the West, would call religious practice. Thus, one of the Korean Zen Masters writes: “The teaching of the Buddha is not really a religion at all. Buddhism is a path.” (Sahn_Master_Seung_Sahn, 1997 : 17). He also writes, just before this quotation, "Buddhism is a subject religion" to distinguish it from what he calls 'object religions', like Christianity, i.e. there is no revelation; practice resides in examining oneself. This is also true of many modern Western forms of Buddhism, as expressed in, for example, *Buddhism without Beliefs* (Batchelor, 1997) — see also (Batchelor, 1994; 2010).[1] These writers and practitioners follow the tradition that the Buddha himself encouraged people not to ask metaphysical questions that couldn't be answered (Gombrich, 2009).

I suspect that this is at least part of the origin of the Buddhist form of debate, the *kōan*, a kind of challenge that, like "what is the sound of one hand clapping?", has no straightforward answer. Its function is not to be answered, but rather to provoke reflection. In a debate in Oxford with HH the Dalai Lama seven years ago I was thrown such a challenge in the form of asking how far down the animal kingdom would I go in showing respect. My reply was to look around the audience and appear clueless, much to their amusement. But I think it was the correct reply — until, unfortunately, I opened my mouth and tried to say something![2]

Another way to express this view of Buddhism is to say that it is itself a form of science, open to test in the form of personal experience in examining oneself and one's relationship to others and to the world. It is a key aspect of that experience to find that there is no such thing as the self, an idea of no-self (*anātman* in Sanskrit) that resembles David Hume's view that

[1] A dialogue between the author and Stephen Batchelor is on http://www.voicesfromoxford.org/video/buddhism-and-science-12-discussion-with-stephen-batchelor/110

[2] A more recent debate with HH The Dalai Lama can be found on https://www.youtube.com/watch?v=cpWNm81aews

the self is just a set of interconnected perceptions (see also (Parfit, 1986).

In this paper I will argue that modern systems biology leads, by a rather different route, to a similar conclusion.

Systems Biology

Twentieth century biology was characterized by the identification and characterization of the molecular components of living systems: their proteins, genes and other molecules, such as lipids and metabolites. Almost as an extension of this approach it was assumed by many that the higher functions, such as consciousness, the will, the self, would also eventually be identified as objects, in particular as parts of the brain, or the workings of those parts. I believe that this was a profound mistake and that the biology of the 21st century, which is a systems approach, is set to correct this mistake.

For this to be true, though, it is important to note that systems biology is not just a 'next step' development of molecular biology, as many of my scientific colleagues may think. It represents a profound revolution. The philosophy of systems biology is completely different from that of molecular biology (Kohl et al., 2010; Noble, 2010). To use a musical analogy, if molecular biology is the identification of the notes in a score, then systems biology is the music itself. If the molecular components are compared to the instruments of an orchestra, or the pipes of a cathedral organ, then systems biology is the performance. Whichever musical metaphor one might prefer (and I use several in my book, *The Music of Life* (Noble, 2006), each highlighting a different aspect of the difference between molecular and systems biology) the microscopic alone, i.e. the identification of the smallest components, is not sufficient to characterize its function. Even the concept of a gene as a DNA sequence is in serious difficulty (Beurton et al., 2008) as a consequence of recent discoveries in the field of epigenetics. We need a systems approach even to assess what a gene is (Noble, 2008b). Beurton et al. go so far as to say that a gene "begins to look like hardly definable temporary products of a cell's physiology".

Systems Biology is revolutionary

So, my first question is: why do we need a revolution in biology?

The turn of the century saw the ultimate achievement of the molecular biological revolution that can be dated as having its beginning in the discovery of the double helix by Watson and Crick in 1957. The announcement in the year 2000 of the first drafts of the sequencing of the human genome was, appropriately, accompanied by governmental fanfares on both sides of the Atlantic Ocean. For it was a Herculean achievement. As DNA sequencing now becomes so common as to be used even in law courts, it will become progressively more difficult to remember how audacious and technically challenging the human genome project was when it was first proposed. Nevertheless, the acclaim was misplaced in a very important respect.

What was wrong with the acclaim was not any misjudgment of the scientific and technical achievement. That achievement was fundamental. It was rather the promises that were made as we were told that, at last, we could read the 'book of life'. Cures for diseases would come tumbling out of the reading of that book. At last, molecular biology would deliver on its promise to reveal the secrets of life. Francis Crick was even bold enough to claim that it would solve the great riddles of consciousness and the nature of the self. "You, your joys and your sorrows, your memories and your ambitions, your sense of personal identity and free will, are in fact no more than the behavior of a vast assembly of nerve cells and their associated molecules" (Crick, 1994). Two decades earlier, another prophet of the molecular genetic revolution, Richard Dawkins, had also claimed that "They [genes] created us body and mind" (Dawkins, 1976, 2006). All these claims are false.

First, the genome is not a book (Noble, 2010). It is not even a program, despite the colorful metaphor of "le programme génétique" introduced by Jacob and Monod (1961). It is a quite simply a database, used by the organism as a whole. It needs the highly-complex eukaryotic egg cell to read it and to even begin to make sense of it. Focusing on it as containing the secret of life is almost as misguided as focusing on the bar code of a product in a supermarket. It is to mistake the, possibly contingent, coding for the system itself.

Second, the level of the "nerve cells and associated molecules" is simply too low for attributes like personal identity, intentions and similar attributes of a person even to be comprehensible. The astonishing thing about the title of Francis Crick's book, *The Astonishing Hypothesis*, is that it could ever have been seriously formulated by a highly intelligent scientist.

Third, as Dawkins himself acknowledges elsewhere in his later books "genes" simply "aren't us" (Dawkins, 2003).

It is therefore re-assuring to find that the architects of the human genome sequencing project are vastly more cautious. In his fascinating biography, Craig Venter writes, "One of the most profound discoveries I have made in all my research is that you cannot define a human life or any life based on DNA alone......". Why? Because "An organism's environment is ultimately as unique as its genetic code" (Venter, 2007). Precisely so and, one should add, the environment is an open system.

Sir John Sulston, who led the UK sequencing team, is also cautious: "The complexity of control, overlaid by the unique experience of each individual, means that we must continue to treat every human as unique and special, and not imagine that we can predict the course of a human life other than in broad terms" (Sulston and Ferry, 2002). Sulston also emphasized the immensity of the combinatorial explosion that occurs when one considers the number of possible interactions between 25,000 genes. As he says, "just a few dozen genes...... can provide an immense amount of additional complexity". Even more mind-boggling, "there wouldn't be enough material in the whole universe for nature to have tried out all the possible interactions, even over the long period of billions of years of the evolutionary process" (Noble, 2006).

Sequencing the human genome has therefore brought us right up against the problem of complexity in biological systems. This is the challenge that 21st century biology faces. Its foundations must therefore be built on how to integrate our knowledge, rather than simply follow a reductive mode. Having broken life down into its molecular components, the greater problem is going to be how to put those components back together again and to understand the logic of life at all the various biological levels. This raises difficult questions. Could there be a general theory of biology at a systems level? (Capra and Luisi, 2014; Longo and Montevil, 2014) Or are living systems so 'history-dependent' as evolution has careered through its billions of years on earth that there will always be a contingent, unpredictable aspect to life? (Gould, 2002) This is one of the reasons I referred earlier to DNA as a kind of 'bar code'. I admit though that we do not yet know how necessary or contingent the development of that code might have been.[3] There are indications though that evolutionary changes in the genome are not random and that the process might be predictable (Shapiro, 2011; Stern and Orgogozo, 2009).

To address these questions, we cannot rely on 'next step' science. We need some bold re-assessments of where we are going. I suggest that these re-assessments will be of at least two kinds. The first kind will be philosophical and linguistic. We need to identify and neutralize the misuse of metaphorical language that has for too long paraded as the truth in biological science. I have attempted to do this in several recent articles (Noble, 2011b; Noble, 2015). The second kind will be heuristic. Integrative approaches will be needed, and they must be at least as rigorous as the successful reductive approaches that characterized the second half of the 20th century. My belief is that this means that the integrative approaches must necessarily be mathematical (Noble, 2010; Noble, 2012).

[3] I thought a lot about the use of the word 'code' here. Of course, there is no code as usually understood as a system of communicating between a sender and a receiver. But the word is so deeply embedded in modern molecular biology that, as with the word 'program', it is longwinded to try to eliminate it. In the context of this discussion it simply means that the DNA acts as a template for the production of proteins and RNAs and that we now know the relationship between the DNA sequences and the amino acid sequences.

Biological functionality is multi-level

In order to characterize the philosophy necessary for such research we need to clarify the principles of systems biology (Noble, 2008a). The first principle is that "Biological functionality is multi-level".

It is impossible to conceive biology without making reference to the concept of level. Between the molecular level of genes and proteins, and the level of the whole organism, we can distinguish between at least eight levels. From the reductionist viewpoint, the causal chain looks like this:

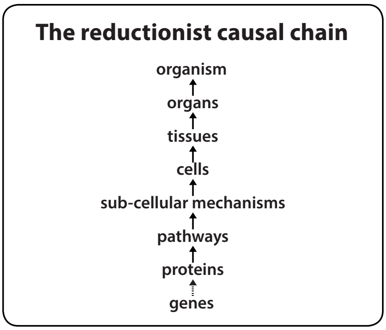

Figure 1. The reductionist causal chain

The chain runs upwards. It is a 'one-way' system, from the genes to the organism. The idea is that, if we knew all about the lowest level elements, genes and proteins, then everything about the organism would be clear to us. We could work out what happens at the higher levels, and explain it completely, in terms of our low-level knowledge. We could reconstruct the whole organism from the bottom up. The DNA sequences would be much more than bar codes. They would form a meaningful map of the entire organism — a 'book of life' indeed.

But this project is impossible (Noble, 2011a). The molecular biologist and Nobel laureate, Sydney Brenner, has beautifully expressed this impossibility. “I know one approach that will fail, which is to start with genes, make proteins from them and to try to build things bottom-up” (in Novartis_Foundation, 2001 page 51)

Downward causation

The second principle is the existence of downward causation. Downward causation exists between all the levels between which there are feedbacks. Events at higher levels can trigger cell signaling, all the levels are involved in the control of gene expression, it is protein machinery that reads genes to ensure their expression, and all levels can determine epigenetic marking. This marking is very important. It consists of another level of information and control superimposed on the DNA: a kind of chemical pattern carried by the DNA and which differs according to the cell type. It is this marking that ensures the correct gene expression patterns are transmitted from generation to generation in the tissues of the body in multicellular organisms. There are many forms of downward causation.

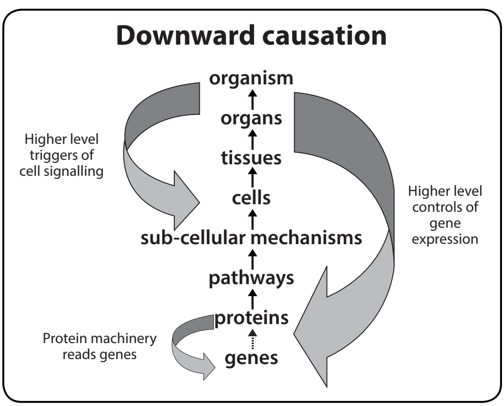

Figure 2.
Downward causation

Inheritance is not determined by DNA alone

The third principle is that DNA is not the sole transmitter of inheritance.

DNA does not come to us in a 'pure', unalloyed form. It must necessarily be inherited together with a complete egg cell. From the viewpoint of systems biology, the genome is incomprehensible as a 'book of life' unless it is read and translated into physiological functions by cellular mechanisms, beginning with the egg cell. I maintain that this functionality is not to be found at the level of genes. It is impossible because genes are 'blind' to what they do, just as are the proteins and higher-level structures such as cells, tissues and organs.

To these I want now to add two more important points. Proteins are not the only molecules in biological systems that determine function. Function is also dependent on the properties of water, lipids and many other molecules that are not coded for by genes. The lipids are essential for the construction of membranes and intracellular structures like mitochondria, ribosomes, the nucleus, the reticulum.

Moreover, a lot of what their products, the proteins, do is not dependent on instructions from the genes. It is dependent on the poorly understood chemistry of self-assembling complex systems (Capra and Luisi, 2014; Longo and Montevil, 2014). It is as though the genes specify the components of a computer, but not how they should be put together. They just do this by doing what is chemically natural to them.

No privileged level of causality

The fourth principle is that there is no privileged level of causality. This is necessarily true in systems with multiple levels and feedbacks downward and upward between the levels.

The fundamental point is that, to the extent that all the levels can be the point of departure for a causal chain, any level can be used as the starting point for a simulation. In biological systems there is no privileged level that dictates the behaviour of the rest of the system. I sometimes call this principle a theory of biological relativity: a relativity of causation (Noble, 2008c; Noble, 2012). I find that there are interesting parallels of this idea in some Buddhist commentaries (e.g. Sahn_Master_Seung_Sahn, 1997 page 91). Some relativity theorists have also pointed this out (Nottale, 2000 page 111). In this context, it is worth acknowledging the ideas developed by Auffray and Nottale (Auffray and Nottale, 2008; Nottale and Auffray, 2008) on the relation between a particular form of relativity theory (scale relativity) and a possible theoretical basis for systems biology.

Gene ontology requires higher-level insight

The fifth principle is that gene ontology will fail without higher-level insight.

The majority of genes (and the modules of DNA that form them) are very ancient. Genes are a little like linguistic metaphors. Evolution repeatedly re-uses them for new functions. The genetic codes also share another aspect in common with languages. Even if, originally, the modules had simple functions (what we call meaning in languages), the system as a whole is far from simple. In fact, when one tries to unravel it, the first impression is that of a form of chaos. Evolution: that is the problem. As the genomes (or languages) have evolved, the functions (meanings) have changed. And they have often changed along routes that have little connection with their original functions (meanings). Half the genes found in a simple sea squirt correspond to ones that we humans have. But we have functions served by those genes that the sea squirt does not know about. 500 million years of evolution are responsible for these differences.

The genome is not a program of life

The sixth principle is that the genome is not a program that determines life.

It must be admitted that the idea of a genetic program, introduced by Monod and Jacob in the 1960s, has been very powerful. At that time computers were machines that could not keep all the programs in their memory. One had to write the programs on paper tape, or later on punched cards that were inserted into the reader of the machine each time one wished to do a calculation. So, the programs were a series of instructions completely separate from the machine itself.

But there is no reason at all why nature should have developed separate programs if this wasn't necessary. As Enrico Coen, the distinguished plant geneticist, put it in his lovely book, *The Art of Genes*, "Organisms are not simply manufactured according to a set of instructions. There is no easy way to separate instructions from the process of carrying them out, to distinguish plan from execution" (Coen, 1999).

There are no programs of life

The seventh principle is that there are no programs at any other level. Living systems are not Turing machines, they are interaction systems (Neuman, 2008; Noble, 2008b). Even the word 'machine' is inappropriate.

My book, *The Music of Life*, was written a little like a detective novel. If the genome itself is not a program, where then is the program of life? Is there really a program, or are there programs, located somewhere in organisms? I lead the reader through all the levels. I hesitate a little at the level of the cell. Sydney Brenner said at a Conference in Columbia University in 2003, "I believe very strongly that the fundamental unit, the correct level of abstraction, is the cell and not the genome." But even at this level, so important, particularly in evolution, the reason for its importance is that many functions are integrated at the cellular level, and this is the level at which transmission occurs between the generations. But, the concept of a programw is superfluous. The cellular networks of interactions are themselves the biological functions necessary for life. Effectively, the 'music of life' functions without a conductor. Everything emerges by itself. The grand composer, evolution, was even more blind than Beethoven was deaf!

No programs in the brain

The eighth principle is that there are no programs (or representations), even in the brain, and with this principle I begin, at last, to approach the central question of this paper: how does Systems Biology help us with questions of the self and free will?

I hesitated a little at the level of the cell. But some of my readers will already have concluded that there is an obvious answer to the question 'what controls the processes of the body?' Yes, the nervous system is certainly a central integrator and controller of some kind. The question is what kind. Must we go along with Crick, and many other biologists, in looking for a place in the brain where it all, as it were, comes together in a central consciousness? Could a bit of the brain, or any other part, do this? For example, the claustrum, as Francis Crick proposed (see later).

And, if so, how does this conscious centre see what it sees, hear what it hears, feel what it feels? Does the nervous system serve up our sensations to it in a special form, converting the light, sound and pressure waves into special qualitative phenomena (some philosophers and scientists call them sense data or qualia) that exist inside our heads? This is an area where biology and philosophy strongly interact and, some would say, overlap. So how do biologists and philosophers think that we perceive the world?

My arguments against these ideas are difficult to explain briefly in an article like this. They depend on philosophical ideas developed during the 20th century, particularly by philosophers like Wittgenstein. In chapter 9 of my book (Noble, 2006) I try to explain these ideas in relatively simple language by using dialogues and little stories. The essence of the argument is that biological interpretations that suppose the existence of a part of the brain responsible for central control resemble the mistake to which I have already referred, i.e. of imagining that there must be programs that determine functions in the body. There are no such programs, because the only networks that could correspond to such programs *are* *themselves the biological function*. If I play a piece of guitar, for example, neural networks are activated, of course, but these are not programs that *determine* how I play the music. These networks, and the movements of my fingers, are *me* (well, *part* of me)[4] playing the guitar.

The self is not a neural object

This insight leads to the ninth principle which is that the self is not a neural object. If it is anything at all, it is an integrative process (Noble et al., 2014). It is the highest *process* of the body. The all-singing, all-dancing, ninth symphony of systems biology!

The mind is not a separate object. It seems to me that the idea that it is was based on an error that greatly resembles Descartes' error. Bennett and Hacker, in their book *The Philosophical Foundations of Neuroscience* (2003), use the term "mereological fallacy" to describe this kind of problem, which consists in attributing to a part of an object a property which cannot be ascribed other than to the whole of the object. At the level of the brain, the self is more a process than an object. And the brain contains only part of the processes involved.

Despite these philosophical problems, many biologists look in the brain to find the self, or consciousness. Thus, Ramachandran refers to a conversation with Francis Crick: "I think the secret of consciousness lies in the claustrum — don't you? Why else would this one tiny structure be connected

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[4] And that is, partly, the point being made here.

to so many areas in the brain?" And as I have already noted, Crick himself wrote, "You, your joys and your sorrows, your memories and your ambitions, your sense of personal identity and free will, are in fact no more than the behavior of a vast assembly of nerve cells and their associated molecules" (Crick, 1994).

The activities of the self, such as intentional actions, cannot be understood on the basis of neural activity alone without taking into account the social context in which intentionality can have any meaning. I tell a story to illustrate this problem in chapter 9 of *The Music of Life*.

Comparisons with the Buddhist tradition

While it is important to recognize and acknowledge the resemblances between my conclusions as a systems biologist and the conclusions of the Buddhist tradition, from its very beginning, it is important to note a very important difference in the way in which the conclusions have been derived. My route to these insights has come from long reflection on the nature of biological science. I started my biological research as a rather naïve reductionist as I analyzed some of the lowest-level components of biological systems, the proteins that form ion channels in the heart (Noble, 2004a). I developed my view of a systems approach through many years of interactions with philosophers and other scientists. I have been constrained in my thinking to abandon the reductionist approach as the only means by which we can analyze living systems by the very nature of biological science as I think it is developing.

The Buddhist tradition has used a completely different route: that of direct personal experience through meditation. As

I understand it, *anātman*, the idea of no-self, is seen by many Buddhists as an *experiential* fact, though it is also a conceptual insight as I explain later. Ultimately, however, our understanding of science and our direct experiences of ourselves must coincide. Whether we have reached that point of coincidence with the development of systems biology is a fascinating question.

Moreover, the difference is not complete. Buddhist insights through personal experience have, time and again, been complemented by philosophical enquiry into the nature of the world, the person and of experience itself.

When I wrote chapter 9 of *The Music of Life*, on the brain, I was reflecting on how to apply the systems approach to neuroscience. Some of my previous articles (Noble, 1989a; Noble, 1989b; Noble, 1990; Noble, 2004b; Noble and Vincent, 1997) had already developed the idea that the self is a construct, a useful one of course, but not one to be identified either with an immaterial substance or simply with the brain. The way I express this in chapter 9 is to say that it is better regarded as a process than as an object. Just as it doesn't make sense to talk about heart rhythm at the level of genes and proteins, it doesn't make sense to talk of the self at the level of neurons or hormones. At those levels, it is as though there is no self at all. The idea of no-self (*anātman* in Sanskrit, an = no, *ātman* = self) is, of course, precisely that of Buddhism.

Or is it? It has taken me several years to try to answer that question. The original insight 2500 years ago may have been part of the general non-metaphysical stance of the historical Buddha, Siddhartha Gautama (Batchelor, 2010), but it is hard to decide precisely what this insight was. We live in such a different world from that of Gautama and it is all too easy, as Gombrich (2009) has warned, to take his words out of context. I started out thinking that it was an empirical discovery. Perhaps, during meditation, he looked for the self, the I, the soul, and simply didn't find it, rather as David Hume famously examined his thoughts and perceptions two millennia later and came to the conclusion that none of them could be identified as 'the self', that in that sense such a thing did not exist.

But, to say that something doesn't exist, we do at least need to know what it would mean for it to exist, how we would recognize it if we tried to find it. And, of course, we don't know how to recognize it. I recognize you, the reader, as a person, as having a sense of self, and we know what words like 'yourself', 'myself', 'himself', mean. To indicate these, we would point at you, me or him as the case may be. You can also point at yourself to indicate yourself. But, if we had your brain out on a dish, as it were, how could we possibly say that this is you? The brain is necessary to you, but it is not sufficient. That is the basis of my story of 'the frozen brain' in chapter 9 of *The Music of Life*.

Looking at the question this way, we are forced to say that the concept of no-self is, just that, a conceptual truth not an empirical one. No scientific, or meditative, experiment is necessary to establish such a truth. To return to the quotation from Crick earlier in this paper, looking for such things at the level of neurons and molecules is a conceptual mistake. These ideas have been explored further in Noble et al. (2014)

In chapter 10 of *The Music of Life* I used the famous Oxherder parable (Wada, 2002) from the Chinese Buddhist tradition as a way of explaining the object of meditation to, as it were, subdue the self. One of the ten pictures is just of an empty circle, as though the self (the ox in the story) has disappeared. I no longer think of it this way. I now think of it rather as a parable about how to subdue *selfishness*, not the self. Buddhist meditation has, as one of its aims, to remove selfish, greedy and angry attitudes — the causes of suffering, and one of the central aims of any ethical practice.

So, there are two kinds of 'discovery' here. The first is the conceptual truth that it doesn't make sense to talk of the self as an object in the sense in which our brains are objects. The second is that, through meditative techniques we can subdue selfishness. But doing that is not equivalent to some conjuring trick of 'making the self disappear'. I am reinforced in that conviction by the idea that what the Buddha was arguing against was not so much the self, as usually conceived when we refer to 'himself', 'myself', but rather against the idea that it was an unchanging thing (Gombrich, 2009). That idea fits well with the concept of the self as a process, as Gombrich also argues.

Does that mean that our experience, e.g. of meditation, is irrelevant? I don't think so. Experience can lead us to a conceptual truth even when it is not itself necessary to that truth. It was seeing the images of gravitational lensing produced by the Hubble telescope that led me to take the idea of the bending of space by huge gravitational fields seriously. Yet the theory of general relativity does not require me to have that experience in order for it to be a valid theory of the structure of the universe.

I hesitated about writing chapters 9 and 10 of *The Music of Life*. They were the most difficult to write. The book could have finished on evolution in chapter 8. But that would have cut its head off. You can’t ask a question as audacious as ‘what is life’ and not deal with questions of the brain and the self.[5]

Reflections on the Buddhist Philosophy of Won Hyo.

In a previous article on Buddhism and science (Noble, 2008d) I drew attention to a remarkable discovery that I made in the work of the Korean monk, Won Hyo 元晓 (원효) (617-686). The text below comes from the Kŭmgang sammaegyŏng ron 金刚三昧经论 (quoted in Kim, 2004 : 119) where he uses a seed and the fruit to illustrate the application of four-cornered logic (derived I believe from Nāgārjuna) to illuminate the concept of being/non-being.

> “The fruit and the seed are not the same,
> for they have different shape.
> However, they are not different.
> Besides the seed and the fruit are not annihilable,
> for the fruit is produced from the seed.
> However, they are not eternal,
> for there is no seed when it is in the state of the fruit.
> The seed did not enter into the fruit,
> for the seed does not exist when it is in the state of the fruit.
> The fruit does not extinguish the seed,
> for the fruit does not exist when it is in the state of the seed.
> Since it neither enters nor is extinguished,
> there is no arising.
> Since it is neither eternal nor annihilable,
> there is no ceasing.

[5] Relevant videos on this part of my article are on https://www.youtube.com/watch?v=hS6PDOcJwY8&list=PLnqQJI0EhuwwdoH18CnKcOC6j4qaU_yXI&index=7 andhttps://www.youtube.com/watch?v=mj3_J19rqTw&feature=youtu.be

Since there is no ceasing, non-being cannot be proclaimed.
Since there is no arising, being cannot be proclaimed.
Since it is free from the two extremes [being and non-being],
it cannot be stated as both being and non-being.
Since it does not correspond to the middle,
it cannot be stated as neither being nor non-being.
Therefore it is stated that it is free from the four perspectives
and cut off from verbal expression.
As such the *amala* fruit transcends language."[6]

This can be seen as a version of the main point made in this paper on the interaction between genotype and phenotype. To illustrate this, in the second version below I have replaced 'seed' with 'genotype' and 'fruit' with 'phenotype'.

"The phenotype and the genotype are not the same,
for they have different shape.
However, they are not different.
Besides the genotype and the phenotype are not annihilable,
for the phenotype is produced from the genotype.
However, they are not eternal,
for there is no genotype when it is in the state of the phenotype.
The genotype did not enter into the phenotype,
for the genotype does not exist when it is in the state of

[6] Won Hyo actually represents this text as 8-cornered, a clear sequence 次明 of 8 negations 八不. The original is much tighter than any English translation can be. 'Same" could also be 'one', 'shape' could be 'form' – translation inevitably destroys some of the clarity. Here is the original text in Chinese characters:
"次明八不. 非直法尔 唯前四不 亦乃具绝一异等八.
所以然者 果种不一 其相不同故.
而亦不异 离种无果故. 又种果不断 果续种生故.
而亦不常 果生种灭故. 种不入果 果时无种故.
果不出种 种时无果故.
不入不出故不生. 不常不断故不灭. 不灭故不可说无. 不生故不可说有.
远离二边故 可说为亦有亦无. 不当一中故 不可说非有非无.
故言离诸四傍 言语道断. 阿摩勒果 如是绝言.
法忍之心 亦不异此. 故言无生心性 亦如是等也."

> the phenotype.
> The phenotype does not extinguish the genotype,
> for the phenotype does not exist when it is in the state of the genotype.
> Since it neither enters nor is extinguished,........"

In this form, his text could appear almost as a modern text of systems biology. Anyone who understands this text will see that a strict distinction between the replicator (the genome) and the vehicle (the phenotype), which is the fundamental basis of the Selfish Gene idea, disappears since they are totally interdependent (Noble, 2011b).

It is important not to misunderstand this historical comparison. Of course, I am not saying that Won Hyo and people who thought like him over a millennium ago were systems biologists before their time, even less that the Buddha was such a biologist. I am simply saying that the Buddhist stance uses ideas that resemble those of systems biology, just as we can also identify ideas in the Buddhist tradition that resemble relativity theory. The word 'stance' captures the idea here. What is common is a thought system that distances itself from what are perceived to be misunderstandings in the way in which language is used. I think that this is the sense of the reference to the fruit 'transcending language'. The four-cornered logic approach encapsulates this stance, which can then be seen as a form of philosophical ground-clearing. I don't think this last line should be interpreted as a form of mysticism, still less as obscurantist. I would translate the last line 言语道断 simply as 'can't say in words', meaning that our words, 'seed' and 'fruit', lead us to think we are talking of completely separate objects, which is not the case.

The same kind of idea (but not exactly the same of course) applies to 'mind' and 'body'. The mistake is to see the mind as an object in the same sense as the body or, even worse, to think it is to be found or identified as part of the body.

Conclusions

In conclusion, systems biology is very different, both from a philosophical and from a heuristic point of view, from molecular biology, even though it greatly profits from the results of molecular biology. Reduction and integration are both necessary (Kohl and Noble, 2009) as tools to develop a good biological reply to the question "what is life?" Systems Biology requires a revolution in the way in which we study life. One of the important results of this revolution is that we cannot understand living beings on the basis of DNA alone, or the proteins for which it forms a template. It is necessary to understand more than the molecular components. We must understand also how these components act in processes at the higher levels. The highest such process is the self, which should be analysed as a process that depends, like all other functions in living beings, on the environment, including particularly the social environment in this case.

But, finally, I want to express an important hesitation. In the last chapter of *The Music of Life* I advise readers to throw my metaphors away. They are simply ladders to a better form of understanding. Describing the self as a process is better than describing it as a thing, but processes can also be reified in ways that confuse. We should avoid even that. I believe that the concept of *anātman* requires nothing less if we are to succeed in distancing ourselves from the misuse of language.

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REFERENCES

Auffray, C., and L. Nottale. 2008. Scale relativity theory and integrative systems biology 1. Founding principles and scale laws *Progress in Biophysics and Molecular Biology* 97:79-114.

Batchelor, S. 1994. The awakening of the West. Parallax Press, Berkeley.

Batchelor, S. 1997. Buddhism without Beliefs. Bloomsbury Publishing, London.

Batchelor, S. 2010. Confession of a Buddhist Atheist. Spiegel and Grau, New York.

Bennett, M.R., and P.M.S. Hacker. 2003. Philosophical Foundations of Neuroscience. Blackwell Publishing, Oxford.

Beurton, P.J., R. Falk, and H.-J. Rheinberger. 2008. The Concept of the Gene in Development and Evolution: Historical and Epistemological Perspectives. Cambridge University Press, Cambridge.

Capra, F., and P.L. Luisi. 2014. The systems view of life. Cambridge University Press, Cambridge.

Coen, E. 1999. The Art of Genes. Oxford University Press, Oxford.

Crick, F.H.C. 1994. The Astonishing Hypothesis: The Scientific Search for the Soul. Simon and Schuster, London.

Dawkins, R. 1976, 2006. The Selfish Gene. OUP, Oxford.

Dawkins, R. 2003. A Devil's Chaplain. Weidenfeld and Nicolson, London.

Gombrich, R. 2009. What the Buddha Thought. Equinox, London.

Gould, S.J. 2002. The Structure of Evolutionary Theory. Harvard, Cambridge, Mass.

Jacob, F., and J. Monod. 1961. Genetic regulatory mechanisms in the synthesis of proteins *Journal of Molecular Biology* 3:318-356

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[7] See http://www.voicesfromoxford.org/news/buddhism-and-science-video-list/337

Kim, J.-i. 2004. Philosophical contexts for Wŏnhyo's interpretation of Buddhism. Jimoondang International, Seoul.

Kohl, P., E. Crampin, T.A. Quinn, and D. Noble. 2010. Systems Biology: an approach. *Clinical Pharmacology and Therapeutics* 88:25-33.

Kohl, P., and D. Noble. 2009. Systems Biology and the Virtual Physiological Human. *Molecular Systems Biology* 5:292, 291-296.

Longo, G., and M. Montevil. 2014. Perspectives on Organisms: Biological Time, Symmetries and Singularities. Springer,

Neuman, Y. 2008. Reviving the living: meaning making in living systems. Elsevier, Amsterdam and Oxford.

Noble, D. 1989a. Intentional action and physiology. In Goals, No Goals and Own Goals. A.C.R.G. Montefiore, and D. Noble, editors. Unwin-Hyman, London. 81-100.

Noble, D. 1989b. What do intentions do? In Goals, No Goals and Own Goals. A.C.R.G. Montefiore, and D. Noble, editors. Unwin-Hyman, London. 262-279.

Noble, D. 1990. Biological Explanation and Intentional Behaviour. In Modelling the Mind. K.A.M. Said, W.H. Newton-Smith, R. Viale, and K. Wilkes, editors. OUP, Oxford. 97-112.

Noble, D. 2004a. Modeling the Heart. *Physiology* 19:191-197.

Noble, D. 2004b. Qualia and Private Languages. *Physiology News* 55:32-33.

Noble, D. 2006. The Music of Life OUP, Oxford.

Noble, D. 2008a. Claude Bernard, the first Systems Biologist, and the future of Physiology. *Experimental Physiology* 93:16-26.

Noble, D. 2008b. Genes and Causation. *Philosophical Transactions of the Royal Society* A 366:3001-3015.

Noble, D. 2008c. Mind over Molecule: activating biological demons. *Annals of the New York Academy of Sciences* 1123:xi-xix.

Noble, D. 2008d. The Music of Life: a systems biology view of Buddhist concepts of the self/no self. *Journal of the International Association of Buddhist Universities* 1:89-108.

Noble, D. 2010. Biophysics and Systems Biology. *Philosophical Transactions of the Royal Society A* 368:1125-1139.

Noble, D. 2011a. Differential and integral views of genetics in computational systems biology. *Interface Focus* 1:7-15.

Noble, D. 2011b. Neo-Darwinism, the Modern Synthesis, and Selfish Genes: are they of use in physiology? *Journal of Physiology* 589:1007-1015.

Noble, D. 2012. A Theory of Biological Relativity: no privileged level of causation. *Interface Focus* 2:55-64.

Noble, D. 2015. Evolution beyond neo-darwinism. *Journal of Experimental Biology* **:

Noble, D., R. Noble, and J. Schwaber. 2014. What is it to be conscious? In The Claustrum. J. Smythies, V.S. Ramachandran, and L. Edelstein, editors. Academic Press, 353-364.

Noble, D., and J.-D. Vincent. 1997. The Ethics of Life. UNESCO, Paris. 238 pp.

Nottale, L. 2000. La relativité dans tous ses états. Du mouvements aux changements d'échelle Hachette, Paris.

Nottale, L., and C. Auffray. 2008. Scale relativity and integrative systems biology 2. Macroscopic quantum-type mechanics. *Progress in Biophysics and Molecular Biology* 97:115-157.

Novartis_Foundation. 2001. Complexity in Biological Information Processing. Wiley, Chichester.

Parfit, D. 1986. Reasons and Persons. Oxford University Press, Oxford.

Sahn_Master_Seung_Sahn. 1997. The Compass of Zen. Shambhala, Boston and London.

Shapiro, J.A. 2011. Evolution: a view from the 21st century. Pearson Education Inc, Upper Saddle River, NJ.

Stern, D., and V. Orgogozo. 2009. Is Genetic Evolution Predictable? *Science* 323:746-751.

Sulston, J., and G. Ferry. 2002. The Common Thread. Bantam Press, London.

Venter, C. 2007. A life decoded. Allen Lane. Penguin books, London.

Wada, S. 2002. The Oxherder. George Braziller, New York.

CONCLUSION