Contextual Models and the Non-Newtonian Paradigm

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Abstract

Biological systems exhibit a wide range of contextual effects, and this often makes it difficult to construct valid mathematical models of their behaviour. In particular, mathematical paradigms built upon the successes of Newtonian physics make assumptions about the nature of biological systems that are unlikely to hold true. After discussing two of the key assumptions underlying the Newtonian paradigm, we discuss two key aspects of the formalism that extended it, Quantum Theory (QT). We draw attention to the similarities between biological and quantum systems, motivating the development of a similar formalism that can be applied to the modelling of biological processes.

Keywords: contextuality, non-separability, biological models

1. Contextuality in Biology and the Failing Newtonian Paradigm

Biological systems are inherently contextual. Genes, species, and even ecosystems can all exhibit profoundly different responses to the same stimulus if it occurs within a different context. Despite this extreme complexity, it is often assumed that a basic Newtonian modelling paradigm will prove sufficient when it comes to the mathematical description of these systems. Thus, it is common to assume that those techniques successful in the modelling of simple physical systems will prove adequate to the description of biological ones. However, the very assumptions of separability that are built into this paradigm make such a straightforward application problematic, and indeed has led to claims that a profoundly new *bio-mathematics* will be required for the description of biological systems (Simeonov, 2010).

However, the question of what form such a new bio-mathematics needs to take is not an easy one to answer. Many of our mathematical frameworks

are implicitly built upon the very same Newtonian paradigm, as they were initially developed in an attempt to understand phenomena that arose in the physical world. Thus, geometry arose from attempts to model the size, shape and relative positions of objects; calculus was developed in order to model motion; and even probability theory came from attempts to predict the likelyhood of discrete, classical events. An immediate challenge just to conceptualise the likely form of a truly novel mathematics arises, but this "Newtonian bias" also suggests a way forwards; perhaps the historical developments of physics can themselves provide an intuitive way in which to conceptualise the form that a future bio-mathematics will take. Indeed, Kitto (2008) argued that the move from Newtonian to a quantum paradigm in physics arose with the recognition that a set of fundamental and quite implicit assumptions were incorrect for a certain class of complex system.

It is the purpose of this paper to show that the same set of Newtonian assumptions break down for biological processes. This will lead to the claim that a bio-mathematics will require a sophisticated treatment of context, right at its core. While this might at first seem like a difficult objective to achieve, the historical developments of physics themselves suggest a way forwards. There is already a class of mathematics capable of modelling contextuality, Quantum Theory (QT), which arose to replace certain Newtonian models as they were shown to be incapable of modelling the contextuality of physical systems. Two aspects of this formalism will be introduced in section 4, and their potential application to certain biological processes will be discussed in section 5.

We begin with a brief consideration of contextual behaviour as it arises in a range of biological systems and processes. This will lead to a general understanding of this behaviour, which is all too frequently assumed to be specific to the system under description. We will draw attention to the manner in which contextuality underlies much of the complexity of biological systems, which itself suggests that these effects can be coherently modelled with a mathematical apparatus that can treat context in a non-naive manner.

2. Genes, species and fitness

Biology is rife with complex contextual dependencies, and this serves to complicate our attempts to mathematically formalise it. It is clear that biological systems display contextual behaviour, more so in obviously complex

scenarios concerning behaviour, cognition and ecological interactions, but also in relatively simple systems involving only limited numbers of genes.

For example, what is the unit of selection in biology? Context appears to pervade all attempts to identify such a factor, and certainly affects the specification of those units which have been put forward. Thus, one of the earliest definitions of a gene, which borrowed heavily from the Newtonian paradigm to specify that it was "the smallest segment of the gene-string that can be shown to be consistently associated with the occurrence of a specific genetic effect" (Stadler, 1954) has been demonstrated to be largely incorrect, and today we find the notion of a gene becoming increasingly complex.

A likely example of genetic contextuality is discussed by Dibbens et al. (2008), who have found an X-linked mental retardation syndrome, named Epilepsy and Mental Retardation Limited to Females (EFMR), that does not follow the canonical X-linked recessive or partial dominance mode of inheritance. Instead this syndrome affects only carrier females who bear one normal and one mutant copy of the *PCDH19* gene; males who carry only a single copy of the gene, normal or mutant, are unaffected. Dibbens et al. (2008) propose that while "hemizygous transmitting males will have a homogeneous population of PCDH19-negative cells, ... affected females are likely to be mosaics comprising PCDH19-negative and PCDH19–*wild type* cells. Such tissue mosaicism may scramble cell-cell communication, which manifests clinically as EFMR." Here we see the contextual effect of interaction between discordant neural domains resulting in pathological neural behaviour. Thus, it is impossible to consider one gene (normal or mutant) as causing the resulting phenotype; both are necessary for the effect to occur, with signals transmitted by one cell type being scrambled by the other, which takes on the role of a contextual factor, not directly influencing signaling, but notheless affecting it.

A second interesting example arises in a recent finding regarding the importance of epigenetic factors in primate evolution. Zeng et al. (2012) examined the distribution of gene methylation in chimpanzee and human brains, finding that hundreds of genes exhibit significantly lower levels of promoter methylation in the human brain than in the chimpanzee brain. Such a finding is highly significant as it can start to explain why these two species, which have highly similar genomes (the genomes show 96% sequence identity), exhibit a number of key differences at the phenotypic level. For example, the two species have very obviously different cognitive abilities, and humans are far more likely to develop both cancer and autism. DNA methylation sup-

presses gene expression without changing a cell's genetic information, and plays a role in controlling developmental gene expression. Thus, it inhibits oncogenesis and suppresses the activity of viruses and mobile repetitive elements. Keeping genes off that should be off reduces the likelihood of having a gene that drives cellular proliferation from starting an oncogenic cascade, and similarly repressing gene expression by transposable elements and viruses reduces their capacity to proliferate. Thus, it appears that chimpanzees have more stable (or less dynamic) genomes due to their higher level of DNA methylation. However, while this leaves them less prone to disorders such as cancer and autism, it also makes them less fluid in their neural development, diminishing the development of their cognitive abilities. That DNA methylation may be implicated in explaining the differences between human and chimpanzee cognitive abilities suggests that a simple change in phenotypic context leads to the general suppression of gene activity, and so alters the qualitative behaviour of the resulting system (Zeng et al., 2012).

Thus, these two examples serve to illustrate the complexity, and in particular the contextuality, that can be exhibited, even at the genetic level which was originally proposed as fundamental. Such behaviour forces us to significantly expand our notion of a gene. Indeed, Jorgensen (2010) points out that while the term 'gene' is still frequently taken as referring to protein coding sequences, a more modern understanding suggests that genes are comprised of many interdependent elements, and that this makes it very difficult to delimit even the boundaries of a gene. In a more recent work he refers to a gene as a "field of possibilities" (Jorgensen, 2011), taking his inspiration from the quantum paradigm, which arose when a concerted effort to create a Newtonian model of the particle met a similar set of problems.

Modern day Epigenetics has most certainly opened up the notion of inheritance as dependent upon far more than a set of particulate genes (as the second example discussed above illustrated). It has shown how heritable changes in gene expression can arise due to mechanisms other than changes in a DNA sequence, and so further added to the complexity of early biological systems. Indeed, at the end of this spectrum of increasing complexity, the Hologenome Hypothesis first described in detail by Jefferson (1994) suggests that the holobiont (an animal or plant with all of its associated microorganisms) should be considered as a unit of selection in evolution (Zilber-Rosenberg and Rosenberg, 2008; Rosenberg et al., 2009). According to the hologenome theory of evolution, genetic variation can arise from changes in either the host or the symbiotic microbiota genomes, and the fitness of an

organism might change quite profoundly, even in the same environment, if it develops a different microbiota.

Even when classically conceived, it is not clear where the boundary between selective units and their environments lie; a gene is subject to its environment, but this includes not only its cellular and extracellular environment, but other genes and regulatory elements that it shares a nucleus with, including in the case of diploid organisms, its homologue. Increasingly in molecular biological research, the notion of functional units is expanding to include network modules, rather than just genes (Barabási and Oltvar, 2004). In a biological sense, the functional unit should be considered as the unit of selection, but the complexities raised above show that this move does not help as much as might have been expected.

Indeed, even if a single unit of selection can be defined, we must still acknowledge further environmental complexities. Thus, organisms with the same genotype may, if placed in a different environment, reveal significantly different phenotypes, to the extent that they may even be identified as different species. Such phenotypic plasticity may be realised as alternative morphologies, physiological states, and even behaviour, in response to differing environmental conditions (West-Eberhard, 1989). Evolutionarily important characters do not have to be 'genetic' (immune to environmental effects) reinforcing an often cited (but perhaps not truly recognised) fact that the phenotype is a product of *interaction* between the genotype *and* the environment. Phenotypic plasticity forces us to accept that the phenotype depends in a very strong way upon the environment that surrounds an organism; a different environment can result in a vastly different organism. As West-Eberhard (1989) states: "There is no one-to-one relation between phenotypes and genes, yet a gene mutation is often visualized as the originator of a new phenotypic trait", a mistake that invariably results in the attribution of a diminished importance to the context in which an organism develops. Furthermore, selection generally operates at the level of an organism, and so the importance of development cannot be ignored.

Even fitness is not a characteristic that can be ascribed simply to an organism. It is well accepted that fitness landscapes can change quite dramatically depending upon the environment in which an organism is found (Brandon, 1990; Maynard Smith, 1993). For example, while it is beneficial that a person's skin colour be darker in colour in regions of high UV exposure, and consequent risk of melanoma, it may be less beneficial to have the same skin tone in less sun-exposed regions where skin pigmentation reduces the

efficiency of vitamin D production (which is light-dependent). Also, fitness is not just affected by abiotic factors; the fitness of a species of bird that lays its eggs in a cliff can be quite profoundly changed if there is a species of lizard in the same vicinity that is capable of climbing to the nest.

Thus, even after this brief discussion we see that the basic units of a biological system can be very difficult to define, with the context in which those units are defined frequently being just as important to the characteristics of the system as the units themselves (Canny, 1981). A bio-mathematics must be able to treat such contextual effects in a sophisticated manner, but as the bulk of our mathematical techniques are derived from an attempt to model physical reality, we are frequently limited within an implicit Newtonian paradigm. This presupposes a set of characteristics that seem unlikely to be apparent in the biological realm (and indeed many other realms where complex behaviour is the norm rather than an exception (Kitto, 2008)). We shall now attempt to define two key Newtonian assumptions, drawing attention to their origins, as well as to their inaccuracy for the case of many biological systems.

3. The Failing Newtonian Paradigm

The discussion above leaves us with the recognition that biological systems are more complex than those of physics, at least in its initial formulation of the Newtonian paradigm. However, this obvious point has not suppressed the creation of a wide range of highly Newtonian models. For example, classical genetics and biochemistry are the epitome of Newtonian thinking, considering their fundamental units (genes and proteins) as functionally atomic entities. Similarly, the more modern molecular approaches (i.e. molecular genetics and molecular biology), which are essentially the children of these two older approaches, still understand genes and protein complexes as discrete objects undergoing well specified interactions which can be understood with reference only to the relevant genetic factors. While it must be admitted that a certain amount of success has been achieved with these overly simplistic approaches, we might ask ourselves at what cost. Kitto (2008) suggests that our standard reductive approach to mathematical modelling, which is inherited from the Newtonian paradigm, appears to fail when it is applied to systems exhibiting *high end complexity*, due to two closely related barriers, one of objects, and the other of objectivity. These serve to trap our thinking about systems and their modelling, and a genuine bio-mathematics

will require a move beyond both of the naive assumptions that underlie them. In this section we shall consider each of these assumptions at some length, calling attention to both their origins in the original formulation of the Newtonian paradigm, as well as to the manner in which they quickly break down for many biological systems.

3.1. Objects

As a species, we have evolved to recognise objects, and to classify the world according to their behaviour. Furthermore, we have a predilection across many different cultures and language groups to recognise *the same* objects as fundamental, and this is reflected in vocabularies that are largely translatable (Phelps and Duman, 2012). This tendency continues in our mathematical structures, with sets frequently forming the basis of our mathematical approaches to modelling *per se* (French and Krause, 1999), and when it came to modelling physical reality, this tendency resulted in the attribution of an elevated status to objects. Indeed, as discussed in the comprehensive account by Pullman (1998), the use of the object construct can be traced back to at least as early as the fifth century BC, when Democritus and Leucippus designated "atoms" as the indivisible basic elements of matter, almost as the first step in our development of a modern theory of matter. This particulate assumption has tended to form the basis of more modern approaches, right up until the dawn of the quantum age. Thus, Dalton proposed an atomic model to explain the chemical behaviour of materials, which was refined as our physical understanding of atomic structure matured through to a planetry model, proposed by Rutherford, where the atom was considered as in turn made up of smaller objects (electrons, protons and neutrons). It is interesting to note that at each point through this general development process, at least up until the advent of quantum mechanics, the behaviour of matter was explained in terms of more primitive objects, and at no point was a fundamentally different model accepted into the mainstream model of matter.[1]

This physical model profoundly affected the construction of biological models. Indeed, as we saw above in section 2, the earliest models of the

[1]Some notable exceptions to this basic object driven mentality include both the wave model of matter (Pullman, 1998), and Leibniz' monadic theory (Leibniz, 1992). Note however, that in each case description was still reduced to a set of primitive elements; waves in the first case, and relations in the second.

gene were very much derived from the same ontological viewpoint, with genes being taken as indivisible and smallest progenitors of some phenotypic effect. It is no accident that a well respected physicist (Schrödinger, 1965), provided a very early account of the kind of structure (eventually discovered as DNA) that would be required to explain the accruing biological inheritance effects that experiments were finding.

However, even at the time that Schrödinger (1965) proposed an early model of DNA (his book was originally published in 1944), he was simultaneously working upon the new Quantum Theory (QT). This model saw a shift away from objects as fundamental, posing fundamental constraints upon our ability to completely describe a system, which in turn suggests that the concept of an object with a predefined set of properties is inadequate, even at the level of physics. This model was even further developed with the move to Quantum Field Theory (QFT), where the notion of a vacuum was considerably extended, and now forms a considerable part of the very definition of a particle (Auyang, 1995). In this setting, the fundamental particle arises from a constant and seething interaction with a vacuum that is itself made up of a similar set of "virtual particles" which have a very similar status to the original particles. The notion of a fundamental object becomes very difficult to define in this setting.

Thus, even in physics, we see that the basic Newtonian hypothesis that reality has smallest building blocks relevant to the description of higher order phenomena is no longer considered correct, and yet a very similar set of assumptions appear to have pervaded the early biological discussions of genetics. While much of modern biology suggests that an object driven ontology is incorrect, the field is riddled with references to objects; just as physicists still refer to particles in a very classical sense, which could be seen to result in many of the "paradoxes" of modern physics, biology is also rife with implicit references to genes, that few practicing biologists would actually support if pressed. And yet the assumption is a hard one to break.

However, there are many reasons to suppose that a set oriented approach to the modelling of all systems is inappropriate (Davies, 1984; Rohrlich, 1999; Auyang, 1995). While more recent frameworks such as Category Theory attempt to bypass this heavy dependency upon objects described by sets, they do this at the expense of attributing a very similar status to relations; we are heavily biased towards describing the world in terms of objects and their interactions.

This natural predilection is perhaps not the most appropriate when it

comes to the description of complex biological systems. For example, as we saw above, the very notion of a gene is becoming increasingly difficult to pin down to a specific object that undergoes a set of well defined interactions. Indeed, the transformation of our understanding of a gene, from the physically inspired classical particle, to the far more complex "field of possibilities" described by Jorgensen (2011) is highly reminiscent of the very similar transformation that occurred with the physical understanding of a particle, as it transformed from a classical smallest unit of matter, to a quantum wave, and finally to the highly complex quantum field that is undergoing a constant interaction with the vacuum. This very fact suggests a way forwards, as physics evolved a sophisticated toolkit to model this extended understanding of the particle, all based upon the formalism of quantum theory. Indeed, the context-driven actualization of potential (CAP) model suggested by Gabora and Aerts (2005, 2008), discusses the difficulty of finding natural units of selection in biology, and proposes a quantum inspired model will be necessary for the description of the early appearance of life.

Additionally, it is important to recognise the openness of biological systems, which is in great contrast with the standard approximations of Newtonian physics. Living systems must engage in a constant interaction with their environment, drawing in nutrients and excreting waste products in a far from equilibrium setting (Prigogine, 1996) just to maintain their integrity as living objects. Thus, living objects seem to belong to a profoundly different category of object from those that arise in the early physical models, which are by construction considered to be closed and are frequently only discussed in an equilibrium scenario. Even when an interaction is defined between a physical system and its surrounding environment (as is the case in, for example, the grand cannonical ensemble of statistical mechanics), this interaction is tightly controlled, allowing for little of the emergent novelty that arises in many natural systems (Kitto, 2006). The objects of the Newtonian paradigm are indivisible and fundamental, and biological systems do not intuitively appear to fall into this category. This fundamental problem relates to a closely related second core assumption of the Newtonian paradigm, that of objectivity.

3.2. Objectivity

The assumption that the subject of our experiments passively yields information about its state is an old one, and of profound importance to science. We assume that our systems possess a certain level of objectivity; there is

a reality 'out there' which our experiments reveal, but is this assumption correct?

It is common to assume that systems can be consistently described through a reductive approach that separates them, into those components in which we are interested, and those that are extraneous. However, as our understanding of natural systems progresses we are finding more and more examples where this is not necessarily the case. Many systems that we seek to understand cannot be cleanly separated from their surroundings, and this is frequently due to a dependence on context. Relevant contexts might include the experimental arrangement itself, factors external to the apparatus (*e.g.* the environment surrounding the system and experimental apparatus), the history of other experiments performed upon the system, *etc.*. Such contextuality is often perceived as negative, leading to the loss of realism, but this is a far stronger claim than is justified. Admittedly, there is a very real problem when it comes to analysing such systems; if a contextual system is examined under two different contexts then a very different set of results may be obtained. This implies that experiments and observations are not merely discovering reality. There is a very real sense in which they might be interacting with that reality, and we must be very careful to track the impact of experimental design in such scenarios.

For example, it is reasonable to assume that a football has a well defined separation from its surroundings, occurring at the boundary of the ball itself. This assumption allows us to measure the position of the ball without directly interfering with it (indeed the notion of scoring a goal is based upon this very principle). We can also measure the position of the ball via a direct interaction, when for example we kick it, but this interaction does not change the position of the ball before the kick itself occurs, only after the interaction takes place is the ball's dynamics affected. The ball can be assumed to satisfy a basic principle of objectivity; our measurements merely reveal information about its current state. As physics progressed, this assumption was adopted at its core, and yet many systems do not behave in such a well defined manner. Thus, although the particle analogy is very much adopted from the classical picture of the ball described above, modern physics tells us that particles do not exhibit an equivalent objectivity. Indeed, properties such as particle spin yield contradictory results if they are assumed to be properties that exist 'out there' independent of the process of measurement, as for example, repeating a Stern-Gerlach experiment will not always result in spin measurements that are compatible with previous outcomes (Sakurai, 1985). Such behaviour

belies the fiction that our measurements simply reveal information about a system; some systems can only be considered with a proper reference to their context.

Similarly, biological systems tend towards an active interaction with measurements and interactions. Indeed, the discussion of section 2 drew attention to a number of scenarios where the context in which an interaction was occurring resulted in a very different phenotype. Such behaviour violates the assumption of objectivity, as the basic units of explanation (e.g. the genes) will engage in different behaviour depending upon the context in which they are found. Thus, the notion of objectivity is a very hard one to take as fundamental within the modelling of biological processes.

Returning to the conception of openness introduced above, we can immediately recognise that an open system will exhibit a contextual dependence upon its environment; a changed environment can quite easily lead to different phenotypes, adjusted fitness characteristics, and other emergent phenomena, all of which suggest that reality is not something 'out there' to be measured, but is rather created 'on the fly', within a given context. While openness can result in contextual behaviour, it is important to recognise that contextuality is a more general concept. Thus, phenomena such as EFMR cannot be attributed to openness, although they can be attributed to contextuality.

3.3. A New Paradigm?

Having considered two underlying assumptions of the Newtonian paradigm, we start to see a way forwards. Physics itself has developed a new set of models to describe the behaviour of systems that did not satisfy such assumptions, and the quantum formalism was born as a result. We shall now start to develop the hypothesis that the quantum formalism can form the basis of a new class of contextual mathematics that will assist with the development of both a future bio-mathematics and more generally, of contextuality as it occurs in a wide class of complex systems. The promise of a quantum inspired formalism arises from its (admittedly often implicit) recognition that the Newtonian paradigm, as is exemplified by the assumptions of objects behaving objectively, cannot adequately describe the behaviour of all phenomena that we might choose to model. We do not claim that an exact naive application of quantum mechanics to the problem of modelling biological phenomena will prove sufficient. Rather, we propose that the quantum formalism offers a

number of highly promising formal avenues and techniques, some of which we shall now introduce in section 4.

4. Contextual Mathematics

In this section we shall consider two key concepts as they arise in the quantum formalism, and show that there is every reason to suppose they can be adapted as a first step in the creation of a non-Newtonian biological mathematics. We start with a set of probabilistic tests that can be used to determine if a Newtonian approach to the modelling of a system is appropriate.

4.1. Tests for contextuality

A simple toy example will serve to illustrate the much about the assumptions of objects and objectivity, and how a mathematical model of contextuality differs from a simple Newtonian model.

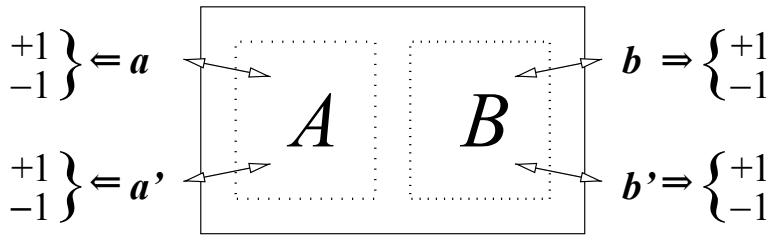

Figure 1: A potentially compositional system S, consisting of two assumed sub-components A and B. S can perhaps be understood in terms of a mutually exclusive choice of experiments upon those sub-components. Two alternative experimental settings probe either proposed sub-component, represented by a or a' for sub-component A, and b, b' for sub-component B. Each of these experiments can return a value, which we shall denote as $+1$ or -1 for generality, but could be considered as 'yes' or 'no' responses to the questions represented by a, a', b, b'.

Figure 1 depicts a hypothetical system S, in an environment E, which we might seek to understand through the very standard trick of separating S into two proposed components (or objects), A and B, that influence each other only via direct interaction. There are many questions that can be asked about the validity of performing such a separation: can A and B truly be regarded as separate or do they somehow indirectly influence one another?; Would a consideration of the combined system $A \oplus B \oplus E$ give the

same specification of behaviour as $S \oplus E$? What components of this system exhibit causal interdependencies? Rather than resorting to philosophical discussions however, many of these questions can be answered through the use of probabilistic techniques, and a number of quite counter-intuitive results have emerged when systems displaying contextual interdependencies have been examined.

For example, while it is generally assumed that a system is by definition separable in a well defined manner from its environment, whether a similar separation can be performed between A and B is not a question that can be so easily answered, even when there is no causal connection between the two components. Breaking the system down further, many different fields assume scenarios of experimental separability. For example, suppose that two different experiments can be carried out upon each of the presumed subsystems, which will answer a set of 'questions' with binary outcomes. We shall represent these questions using four possible measurement settings, consisting of two alternative questions asked of either sub-component. Thus, a choice of two experimental settings a or a' can be applied to sub-component A, and similarly b or b' can be applied to sub-component B. Each of these experimental questions lead to a binary outcome (traditionally in QT a detector clicks or it does not) which represents either a 'yes' or a 'no' answer to the question asked of the system. For the sake of generality we shall denote these responses as $+1$ or -1 respectively, they form a set of random variables that we shall label as $\mathbf{A}, \mathbf{A}', \mathbf{B}$, and $\mathbf{B}'$. It is now possible to consider the notion of the probability distribution over these outcomes; what characteristics will be possessed by the random variables describing this system?

As with many systems, the outcomes of our experiments will have a statistical distribution over all available outcomes, and this can be used to determine whether the sub-components can be considered as isolated, influencing one another, or in some sense irreducible. Frequently, joint probability distributions such as $\Pr(\mathbf{A}, \mathbf{A}', \mathbf{B}, \mathbf{B}')$ are used to model the behaviour of systems like that represented in figure 1, however, it has been shown that this joint probability does not exist for certain quantum (Fine, 1982) and psychological systems (Dzhafarov and Kujala, 2012; Busemeyer and Bruza, 2012; Bruza et al., 2012), which raises the possibility that a similar result might be found in contextually dependent biological systems. When such behaviour is evident, we have clear reason to suppose that the system under examination is contextual; experiments performed upon sub-system B affect the results of experiments performed upon sub-system A, even though the two sub-systems

were presumed independent. Thus, the context of sub-system A, as represented by sub-system B, can have a well defined *non-causal* influence upon its behaviour.

More generally, an entire class of tests have been developed which can be used to determine the validity of the assumption that a system is non-contextual. Results such as Bell's theorem, the Clauser–Horne–Shimony–Holt theorem, Greenberger–Horne–Zeilinger and Hardy's results, as well as the Kochen–Specker theorem[2], all generate strong restrictions on the possible form that a separable system can have, and their violation frequently entails contextual behaviour.

Many of these tests are based upon a variation of the triangle inequality, which allows for the simultaneous comparison of a set of expectation values describing the outcomes of experiments performed upon systems such as that depicted in figure 1. We shall use an even simpler proof, which depends instead upon recognising that the random variables contribute to average values (represented by here by $|\bar{.}|$) which must be less than or equal to 1:

$$|\bar{\mathbf{A}}| \leq 1, \qquad |\bar{\mathbf{A}}'| \leq 1, \qquad |\bar{\mathbf{B}}| \leq 1, \qquad |\bar{\mathbf{B}}'| \leq 1. \tag{1}$$

We can then derive a restriction on the probability distribution that must be satisfied by a *separable system*, which in this case is defined as a system for which experiments performed at A will not affect those performed at B and vice versa. More specifically, the result of running experiments a or a' do not depend upon the experimental settings at B (i.e. b or b'), and a ± 1 result at B does not depend upon the experimental settings at A (i.e. a or a').

Now, it is possible to construct a joint probability, describing the distribution of outcomes in the two experimental regions, and how it might depend upon a set of hidden parameters, or latent variables, denoted λ, which is assumed to have a normalised probability distribution $\rho : \int d\lambda \rho(\lambda) = 1$. The joint probability for experimental arrangement a, b becomes

$$P(a,b) = \int d\lambda \rho(\lambda) \mathbf{A}(a,\lambda) \mathbf{B}(b,\lambda) \tag{2}$$

[2]The interested reader could consult any of Bell (1987); Laloë (2001); Greenberger et al. (1990); Shimony (1984); Mermin (1993) for a broad introduction to many of these results as they arise in quantum physics.

and a similar set of relationships can be constructed for all experimental arrangements. Thus, for example, it becomes possible to make claims about how the probability distributions for different experimental arrangements should be related:

$$P(a,b) - P(a,b') \tag{3}$$

$$= \int d\lambda \rho(\lambda) \mathbf{A}(a,\lambda)\mathbf{B}(b,\lambda) - \int d\lambda \rho(\lambda) \mathbf{A}(a,\lambda)\mathbf{B}'(b',\lambda) \tag{4}$$

$$= \int d\lambda \rho(\lambda) \left[\mathbf{A}(a,\lambda)\mathbf{B}(b,\lambda)\right] \left(1 \pm \mathbf{A}'(a',\lambda)\mathbf{B}'(b',\lambda)\right)\right]$$

$$- \int d\lambda \rho(\lambda) \left[\mathbf{A}(a,\lambda)\mathbf{B}'(b',\lambda) \left(1 \pm \mathbf{A}'(a',\lambda)\mathbf{B}(b,\lambda)\right)\right]. \tag{5}$$

Then, making use of assumption (1), we can construct an inequality

$$|P(a,b) - P(a,b')| \leq \int d\lambda \rho(\lambda) \left(1 \pm \mathbf{A}'(a',\lambda)\mathbf{B}'(b',\lambda)\right)$$

$$+ \int d\lambda \rho(\lambda) \left(1 \pm \mathbf{A}'(a',\lambda)\mathbf{B}(b,\lambda)\right) \tag{6}$$

$$= 2 \pm \left(P(a',b') + P(a',b)\right), \tag{7}$$

and a little rearrangement results an inequality that has become somewhat notorious in the field of quantum physics:

$$|P(a,b) - P(a,b')| + |P(a',b') + P(a',b)| \leq 2. \tag{8}$$

This is the Clauser–Horne–Shimony–Holt (CHSH) inequality (Clauser et al., 1969), and it must be satisfied by any probabilistic system that satisfies the basic conditions introduced to obtain it. Thus, it is a very general statement about the possibility of separating a system into objective components which interact only via the proposed variable λ. If this inequality is violated, then this separation is impossible, and the Newtonian paradigm does not apply.

It is worth emphasising the generality of this result. While it was originally obtained in the field of quantum theory, the derivation repeated here for the scenario represented in figure 1 makes no assumptions as to the nature of the system that is modelled by the probabilistic framework that it proposes, merely as to its potential separability. Biological systems (such as those discussed in section 1) are highly likely to exhibit similar forms of non-separability due to their inherently contextual nature, and tests such as

the CHSH inequality can provide a clear dividing line between those systems that can be described by a Newtonian approach, and those that should not be.

In section 5 we shall make use of a more specific modification of the CHSH inequality that has been proposed in a recent work by Bruza et al. (2012).[3] This test takes the framework discussed above, and rather than considering a proposed latent variable, directly models the manner in which two random variables can contextually influence one another. Thus, adding the joint probabilities $p_1, p_2, ...p_{16}$ to the model, we can consider their interdependent effects in a very concise matrix form:

$$
\begin{array}{ccc}
 & & B \\
 & & \begin{array}{cc|cc} \multicolumn{2}{c}{\mathbf{B}} & \multicolumn{2}{c}{\mathbf{B}'} \\ +1 & -1 & +1 & -1 \end{array} \\
\begin{array}{c} \\ \mathbf{A} \\ \\ \\ \mathbf{A}' \\ \\ \end{array} & \begin{array}{c} +1 \\ -1 \\ \\ +1 \\ -1 \end{array} & \left(\begin{array}{cc|cc} p_1 & p_2 & p_5 & p_6 \\ p_3 & p_4 & p_7 & p_8 \\ \hline p_9 & p_{10} & p_{13} & p_{14} \\ p_{11} & p_{12} & p_{15} & p_{16} \end{array} \right) = P_{AB} \\
A & & &
\end{array}
\tag{9}
$$

where, for example, $p_1 = P(\mathbf{A} = +1, \mathbf{B} = +1)$, and $p_{14} = P(\mathbf{A}' = +1, \mathbf{B}' = -1)$. This matrix exhibits some highly interesting structural properties that arise from a violation of equations like (8). In particular, when

$$\Delta = |2(p_1 + p_4 + p_5 + p_8 + p_9 + p_{12} + p_{14} + p_{15} - 2)| > 2 \tag{10}$$

then a similar CHSH style non-separability result has been obtained.[4]

The quite curious form of (10) calls for some explanation. With reference to P_{AB} in (9) we can see that (10) results from summing the diagonal probabilities of the first three quadrants, but with the fourth quadrant of (9) contributing via its reverse diagonal $(p_{14} + p_{15})$. As each quadrant in (9) is a joint probability distribution, it must sum to one, and so we find Δ taking its theoretically maximal value $|2(4-2)| = 4$, when all of its probability mass is

[3] Based upon work originally performed by Cereceda (2000) for the case of quantum systems.

[4] Note that a set of these equations can be obtained through permutation of the associated variables.

centred on the appropriate diagonals.[5] This allows us to understand how a general violation of the inequality in (10) can take place. Probabilities on the diagonals correspond to cases where a set of responses to a given experimental context is either purely correlating, or anti-correlating with that context. A little algebra shows that if the senses are perfectly correlated in all four experimental contexts, (i.e., if $p_1 + p_4 = 1,\ p_5 + p_8 = 1,\ p_9 + p_{12} = 1$, and $p_{13} + p_{16} = 1$) then (10) has the value 2. Maximal correlation is not sufficient for a violation of (10), which requires sufficient anti-correlated probability mass on a reverse diagonal (i.e. $p_{14} + p_{15}$). Thus, a positive non-separability result in this framework requires a complex set of interdependent responses to a set of contexts.

In section 5 we shall consider a number of scenarios where this analytical framework might be applied to the analysis of biological systems, but for now we shall introduce a second aspect of the quantum formalism.

4.2. Emergence and Novelty

The very potentiality of the quantum formalism makes it a prime candidate for modelling the emergence of new structures and objects. Indeed, a number of different researchers have drawn attention to useful features of the quantum formalism in the description of behaviour frequently identified as biological, including Primas (1983) who noted that it is possible to perform a perturbation expansion over multiple time scales, Fröhlich (1988) who proposed that coherent phase correlations will play "a decisive role in the description of biological materials and their activity", and Davydov (1991) who considers a biological soliton that is resistant to thermal fluctuations (see also Aerts et al. (2006) for a more recent treatment). These specific proposals all rely upon a shift to Quantum Field Theory (QFT), which entails an added mathematical complexity, but allows for more than one stable ground (i.e. lowest energy) state (Umezawa, 1993; Vitiello, 2001) in a mechanism that makes use of the notion of *spontaneous symmetry breaking*. In short, if a system falls into a situation where its ground state does not have the same continuous symmetry as its dynamics (as represented by its Lagrangian) then it is considered to be exhibiting spontaneous symmetry breaking. Goldstone's theorem then implies that a number of massless bosons will be generated, the number which will equal the number of broken symmetries in the system

[5] That is, $p_1, p_4, p_5, p_8, p_9, p_{12}, p_{14}, p_{15}$.

(Marshak, 1993). These bosons are termed Nambu–Goldstone modes (NG-modes), and due to their massless nature they are long-range, and can move through an entire system without losing energy which provides long range coherence between different extended parts of that system (Vitiello, 2001). Because of their boson status many NG-modes may occupy the same ground state without changing the energy of the system, which means that it can be found in many structurally different ground states. This means that the system can be found in a number of lowest energy configurations, all of which are stable. It can evolve between these states and so change its configuration, without the input of energy that would be required if only one ground state was available.

Biologically, the innovation provided by a mathematical description of multiple ground states is essential. Stability is ubiquitous and common in biological systems, rather than a special case. A mathematical approach to the description of such systems, which allows for multiple lowest energy states, bypasses the need to explain how biological systems can maintain their stability while obviously changing their current state. The different configurations of these modes represent alternative stable arrangements of the system, i.e. each is physically different and yet stable. This scenario is not possible in a classical or even a standard quantum system; there is only one lowest energy state in these theories. QFT is the only quantum formalism (of which we are currently aware) that is capable of generating emergent novelty in a system, rather than the more standard modelling of a set of pre-existing components and their interactions (Umezawa, 1993; Vitiello, 2001; Kitto, 2006). This is to be expected since its basis could be argued to lie in the necessity of modelling the creation and annihilation of particles in modern high energy experiments; QFT was invented to model the emergence of new particles.

In what follows, we shall describe the specific mathematical mechanism underlying this effect, which we shall term *NG-emergence*, after its key developers in physics (Nambu (1960b,a) and Goldstone (1961)). First proposed in a model for superconductivity (Nambu, 1960b), NG-emergence is a mechanism essential to the modern formulation of particle physics (Weinberg, 1996). It is also widely utilised in modern formulations of condensed matter physics (Umezawa, 1993; Altland and Simons, 2010). Less standard uses have also arisen, in models of memory (Vitiello, 2001), fiscal dynamics (Sornette, 2003) and sympatric speciation (Kitto, 2008). This raises the possibility that a generalisation of the mechanism beyond physical systems might be possi-

ble, and this section will briefly discuss the manner in which this mechanism arises with the aim to facilitate its generalisation. We caution the reader that it would be a mistake to assume that this discussion is sufficient as a full introduction to the topic, it should merely be taken as a non-technical introduction to a field that can be very difficult to approach. The interested reader is encouraged to consult any of (Weinberg, 1996; Peskin and Schroeder, 1995) for a more thorough treatment of these concepts as they arise in particle physics, or (Altland and Simons, 2010; Umezawa, 1993) for an introduction more oriented towards condensed matter physics. An excellent general review of Goldstone bosons in nuclear, particle and condensed matter physics is provided by Burgess (2000), and an overview of conceptual foundations and issues in the field is provided by either Cao (1999) or Marshak (1993).

The first step in making the switch to a QFT requires the introduction of a field, which is an effect generally distributed over a spatial extent (rather than the more traditional localised particle, which is very much in keeping with the Newtonian paradigm). When describing the dynamics of a system of fields $\phi(t)$, physics tends to make use of the *action* $S[\phi]$, which is a time integral over the difference between the kinetic (T), and potential (U) energies of that system at a point in time t:

$$S = \int_{t_1}^{t_2} (T(t) - U(t))\, dt. \tag{11}$$

This is the time integral of the *Lagrangian* $L[\phi(t)]$, which can in turn be described by taking the spatial integral of the Lagrangian density $\mathcal{L}$:

$$S[\phi(x)] = \int L[\phi] dt = \int dt \int dx\ \mathcal{L}[\phi, \partial_x \phi, \partial_t \phi]. \tag{12}$$

Thus, the action describes the spatiotemporal configuration of a system and its relationship to its energy. Physical systems satisfy the *Principle of Least Action* (Feynman et al., 2005): $\delta S[x] = 0$, meaning that any physical system will have a dynamics that minimises its action and so gives it a tendency towards manifesting in a configuration that is energetically least costly. This result in turn implies the Euler–Lagrange equations of motion, i.e. the dynamics of the system must take the following form:

$$\partial_\mu \left(\frac{\partial \mathcal{L}}{\partial(\partial_\mu \phi)} \right) - \frac{\partial \mathcal{L}}{\partial \phi} = 0, \tag{13}$$

where ∂_μ indicates a differentiation with respect to either time or the relevant space upon which the field is defined and ϕ might refer to a system of fields ϕ_i. Equation (13) corresponds to a system of equations that must be satisfied by any physical system.

Such systems often exhibit symmetries, which are simply configurations of some property of the system which remain invariant under some sort of transformation (e.g. a translation, reflection, or a rotation of the system). We shall consider only continuous symmetries here, as these are the ones that are important for the concept of NG-emergence. Mathematically, a continuous symmetry can be approached by considering our field $\phi(x)$ to be varying over some space x that will for our purposes remain unspecified. We can discover much about this field by considering an infinitesimal transformation of it:

$$\phi(x) \to \phi'(x) = \phi(x) + \sum_a \omega^a \xi_a(\phi), \tag{14}$$

where the ω^a are a collection of independent symmetry parameters and $\xi_a(\phi)$ are the relevant deformations of the field. We take the opportunity here to discuss some notational simplifications commonly utilised in physics. Firstly, note that the field ϕ represented in (14) makes no reference to dependencies upon time, multi-dimensional space, etc. and appears to be relatively simple. However, (14) can in fact represent the transformation of a high dimensional field: $\phi(x) = \phi(t, x_1, x_2, \dots)$, and should be treated carefully. For the sake of simplicity, what follows will utilise the simplified notation $\phi(x)$. Secondly, the summation symbol in (14) is generally dropped in the physics literature, with the double index $x^a y_a \equiv \sum_a x^a y_a$ used to denote summation.

The transformation (14) is called a symmetry if it leaves the equations of motion invariant, which is in itself ensured if the action is unchanged, or that the Lagrangian density must be invariant up to a 4-divergence (Peskin and Schroeder, 1995; Burgess, 2000).

$$\delta\mathcal{L} \equiv \partial_\mu(\omega^a V_a^\mu), \tag{15}$$

for some quantities $V_a^\mu(\phi)$. This requirement is related to *Noether's theorem*, which states that for every transformation that leaves the equations of motion (13) invariant (i.e. for every symmetry), there is a conserved physical quantity, often termed a *charge* Q, which has the form

$$Q = \int_{space} j^0 dx, \tag{16}$$

where the current[6], j can be defined

$$j_a^\mu \equiv -\frac{\partial \mathcal{L}}{\partial(\partial_\mu \phi)}\xi_a + V_a^\mu \tag{17}$$

such that it satisfies the set of equations $\partial_\mu j_a^\mu = 0$ (i.e. it is conserved). Looking at equation (13) we can intuitively explain this result. The second term in this equation describes the change of the Lagrangian with a change in the field. A symmetry in the Lagrangian with respect to the field (i.e. $\partial\mathcal{L}/\partial\phi = 0$) implies that the change in the first quantity with respect to x should be zero. This means that the first quantity in (17) will be conserved under differentiation.

We now come to the main point. When a continuous symmetry of the underlying theory (i.e. the dynamics represented by the Lagrangian) does not match the symmetry of the ground state, $|\Omega\rangle$ (i.e. there is a degeneracy of the ground state, meaning that there are multiple lowest energy states) then a massless Goldstone boson arises, ϕ_{NG}, one for every independent broken symmetry. The new emergent state, $|\phi_{NG}\rangle$, is defined by the fact that the matrix element specified by taking the inner product between it and the charge applied to the ground state must be non zero:

$$\langle \phi_{NG}|j^0(x)|\Omega\rangle \neq 0. \tag{18}$$

Thus, (18) gives a relationship that must be satisfied by the new emergent dynamics in the system, and so restricts the behaviour of the new objects that arise within its mathematical description.

What causes a symmetry to break? A good overview is provided by Castellani (2003), who discusses the manner in which physicists break symmetry both explicitly (through the specific addition of terms) and spontaneously (where solutions exist to the dynamical equations of a system which break the symmetry of those equations). Both mechanisms could prove relevant to the description of biological systems, but it is highly likely that the symmetries of biology are going to be much more complex than those of physics. A strong case for the a description of biological processes that made use of NG-emergence would require the establishing of a relevant symmetry group, and then finding a mechanism whereby it could be spontaneously

[6]While this nomenclature (charge and current) is originally derived from electrodynamics, it can be extended to any other symmetry and conserved quantity in physics (e.g. conservation of energy from invariance of physical laws under shifts in time).

broken, perhaps through an environmental interaction. Thus, an underlying mechanism that would creates a divergence between the symmetry of the dynamics of the system and its solutions. We expect that this mechanism will prove very important in biological modelling, although it has a less well understood status in fundamental physics due to the lack of understanding as to what can drive the dynamical influence. However, a proof of principle toy model was proposed by Kitto (2006, 2008), which presented a model of sympatric speciation based upon this mechanism, and so there is reason to hope that such a model can be applied in the field of biology. In section 5.4 we shall propose a second possible application of this mechanism in the field of developmental biology.

5. Contextual Models of Biological Processes

This section will point to four examples from biology, drawing attention to their specifically contextual features, and the manner in which the formalism introduced above can be brought to bear upon their analysis.

5.1. Non-separability of the G matrix?

Evolutionary biology frequently seeks to predict the future response of a species to selection, and conversely, to estimate the selection pressure that was responsible for the production of a phenotype that is currently under consideration. Quantitative genetics has made significant contributions to the mathematical understanding these responses, in both natural and domestic populations, and one mathematical approach focusses upon the *G matrix* (Phillips and McGuigan, 2006; Roff, 2000), which provides a prime candidate for the application of the formalism that was discussed in section 4.1.

The G matrix arises from an extension of the breeders' equation, which models a proportional relationship between Response, R, heritability h and the selection differential S as $R = h^2S$. Thus, with a stronger selection pressure, or a more heritable trait, a bigger response can be generated in a population that one is trying to shift in a desired direction. In its more complex form, each of these terms are elevated to a multivariate form, thus, the vector Δz is used to describe the mean response of a population to selection, which changes with a dependency upon: a matrix of Phenotypic variances and covariances P; a vector of selection differentials S; and G, the matrix of genetic variances and covariances

$$\Delta z = GP^{-1}S. \tag{19}$$

This relationship gives a system of interdependent, and potentially quite complex equations. While it is common to consider only two traits, and so to obtain a 2×2 G matrix, this formalism can be used to consider the effects that arise when far more genes are covaried. However, even in its simplest form, the tests for contextuality that were introduced in section 4.1 provide a new way in which to analyse the behaviour of systems that can be formalised in this setting.

Returning to the matrix P_{AB} that was introduced in (9) and its relationship to the G matrix in equation (19), we can consider the influence that two genes might have upon the eventual development of a phenotype. Making use of the idea that a gene can be either 'on' or 'off', in response to a set of contexts, we can almost directly map the formalism above into this scenario. Thus, for two genes A and B, each being considered within two different contextual scenarios a, a' and b, b', we denote a gene that switches 'on' with $+1$, and 'off' with -1. This now allows for a consideration of the non-separability of the response of the two genes that are considered within a G matrix construct — can they be considered independently (in which case $\Delta \leq 2$ for a given set of data), or are their responses contextually non-separable? Furthermore, if their responses are non-separable, how will this affect the evolution of the phenotype as is represented in (19)?

We anticipate that (9) could be used to discover contextual interdependencies between genes for which no mechanism has yet been discovered. This would allow for the identification of scenarios where new biological processes are yet to be understood, and so would help to suggest fertile areas for future biological work and empirical investigation.

Future work will seek data that can be analysed within this framework, and search for scenarios where a genetic response must be designated as contextually non-separable.

5.2. Ecosystem analysis

What are the fundamental units of an ecosystem? This question is frequently answered too quickly, without reference to the context in which the question is asked, which can lead to the assumption that an ecosystem is equivalent to the species within it. However, the scale at which an ecosystem is examined can profoundly affect even the designation of its basic units:

> *Depending on the spatiotemporal scale or window through which one is viewing the world, a forest stand may appear (1) as a dynamic entity in its own right, (2) as a constant (i.e., nondynamic)*

> *background within which an organism operates, or (3) as inconsequential noise in major geomorphological processes. Thus, it becomes impossible to designate* the *components of* the *ecosystem. The designations will change as the spatiotemporal scale changes.*
>
> O'Neill et al. (1986, p83)

Thus, the notion of a fundamental object is rather difficult to maintain in an ecosystem, as it is inherently affected by the level of analysis. A similar problem arises within QFT, where even non-composite (i.e. fundamental) particles (such as photons and muons) can decay into other particles, making the notion of a fundamental unit very difficult to justify, and highly contingent upon the level of analysis. Mathematical approaches such as the Renormalisation Group can be used in QFT to investigate the changes that arise in a system as it is viewed at different scales, and such an approach has already been suggested in the field of ecology (Milne, 1998). Furthermore, the manner in which new species evolve in a particular ecosystem can be modelled using a QFT framework, and Kitto (2008) introduces a simple toy model of sympatric speciation that is built upon this very foundation.

An alternative approach which could be utilised in the modelling of ecosystems was presented in section 4.1, where we proposed a class of tests that could be used to determine whether the elements in a system could be considered as separable or not. We anticipate that tests such as these can be used to determine whether changing the interactions that one species in a system undergoes can have an effect upon the interactions that another is participating within. Thus, this class of tests could prove essential to the anticipatory probabilistic modelling of ecosystem dynamics, and we are currently searching for appropriate scenarios in which to apply them.

5.3. Non-monotonicity in equine repeat groups

Another potential scenario where the quantum formalism might be applied concerns the apparent contextuality that arises in the modern analysis of repeat groups in the equine genome (Adelson et al., 2010). This study concerned the evolution and function of parasitic genomic elements known as retrotransposable elements (RTEs). RTEs are able to duplicate their sequence of nucleic acid bases into genomic sites that are distant from the original element. As is the case with most biological systems, RTEs interact both with their host, where there is a tension due to potential genomic damage that they can cause, and with other similar elements in the host;

some classes of RTE are unable to autonomously replicate, but are able to make use of the replication systems of other classes, making them essentially parasitic on those autonomously capable classes. These interactions give rise to a dynamic environmental landscape in which the elements evolve, similar to the situation in macro-scale ecosystems. In their analysis of the horse genomic repeat organisation, Adelson et al. (2010) examined the effect that bin size (essentially the scale of locality) has upon the correlation analysis of the repeat groups in the genome, and somewhat surprisingly found that 34% of the pairs had a bin size dependent response of correlation to bin size. This indicated that some associations appeared to be specific for certain scales, or genomic distances. Such an effect is generally assumed not to exist in biological systems; an increasing bin size should include more relevant information and so lead to strengthened correlations, indeed, 61% of pairs did precisely this. More intriguingly, almost 10% of pairs had correlations that changed sign as a function of bin size. The assumption that strengthened correlations will result from increasing bin size springs from a false assumption that the groups under consideration can always be separated into components A and B which exhibit a stable response irrespective of the amount of genetic material that is considered within one bin. A dependence upon bin size indicates that material considered extraneous to the subsystem $A \oplus B$ is not in fact so.

This effect is a prime candidate for a contextual model of the form introduced in sections 4.1, however, the development of this model will require more data than is available in the considered paper, and will be left for future work.

5.4. The development of an embryo

A final potential domain in which to build a quantum inspired model concerns the process of embryonic development. Here, it seems possible to approximate an unfertilised egg as a sphere satisfying a $SO(3)$ symmetry group. This means that the egg can be rotated in any direction, by any amount, and still look essentially the same. However, environmental cues (such as sperm penetration, the point of attachment during implantation, etc.) frequently act to break this symmetry. Thus, when fertilised, the point at which sperm enters an egg acts to dynamically break this symmetry, and the system can no longer be arbitrarily rotated. This then offers a situation in which the mechanism of NG-emergence can conceivably be applied, with the emergent modes then acting as the basis of the tissue differentiation that

starts to develop. Furthermore, if the influence of the sperm upon the egg is treated as a signal, then it is possible to develop a picture of a wave of influence that sweeps through the egg, further breaking the symmetry, and potentially generating a further set of new NG modes. Future work will seek to formalise this proposed model.

6. Conclusions

This paper has drawn attention to the highly contextual nature of biological systems, at all levels of analysis. We have proposed that this contextuality makes the Newtonian paradigm of modelling, which assumes set-like objects that can be objectively probed in our experiments without interacting with them, inappropriate as an underlying formalism. However, a way forward beckons, and it can be approached through reference to Quantum Theory, the formalism that extended the Newtonian paradigm in physics itself. We have discussed two aspects of this formalism that seem particularly appropriate to the modelling of biological systems and processes, and discussed some possible scenarios where they might be fruitfully applied.

Although we have made direct reference to the quantum formalism in presenting this paper, we do not anticipate that a contextual mathematics aimed at the modelling of biological processes would share all of its aspects with the one that was developed to model the contextuality of physical processes. Thus, while the formalism that we have introduced here owes many of its characteristics to physics, it is likely that this formalism will become far more complex as it is extended to biology. Indeed, we hold with the idea advocated by Rosen (1991), that a formalism aimed at the modelling of biological processes will prove more general than that aimed at their physical counterparts, and thus anticipate that the quantum inspired approaches that we have introduced here will require significant extension as they are applied to biological modelling (Kitto et al., 2009). Meeting this challenge is likely to expand upon our understanding of both fields, providing us with significant new insights about the modelling of a reality that is far more complex than we ever imagined.

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