INTRODUCTION

It has been a half-century since Canadian neuropsychologist Donald Hebb authored *Alice in Wonderland or Psychology among the Biological Sciences* (Hebb, 1958) in which he argued that psychology needed to reassess its position with respect to the increasing contributions of the biological sciences. Now biology stands at a similar crossroads and is forced to consider its place under the growing impact of the computational sciences. There is no doubt that the modern post-genomic era has irreversibly changed the landscape of biology. However, it is essential to examine this trend in the context of its ability to contribute and further the bounds of our understanding of life and its processes, versus its ability to ostrify and potentially alienate vital knowledge from mainstream biology and science in general.

Perhaps as a response to this change in scientific climate, more traditional fields of biology have recently begun to embrace the need for an integrative approach to the biological sciences. Thus, integrative biology and systems biology strive to reconcile various levels of biological complexity by developing theories that answer a particular biological question in terms of simultaneously supported genomic, molecular, physiological, and ecological models. Moreover, these approaches to biology are receptive to the kinds of modeling that occur in the physical sciences and engineering (Conti et al., 2007). Although this intuitively seems to offer a more comprehensive exploration of a given phenomenon, it begs the question of whether this truly represents a revolutionary way of thinking about biology, or whether it simply forces once traditional biologists to operate in multiple niches. Consequently, we are left to ponder a variety of problems that range in scale from defining the scope of biology to considering the very limitations of our own biology, with respect to the constraints it imposes on us to arrest and understand the very world before us.

Indeed our elementary ability to conduct science, let alone biology, is fundamentally limited by our ability to interpret the world and then ask questions about these interpretations, thereby invoking an iterative reconsideration of both our immediate phenomenology and our abstract representations about what we believe that we know. Therefore, we must concede that some...
facets of biology, science, and knowledge in general will lie forever outside of the grasp of even our most convoluted abstractions. While first appearing to be only a philosophical musing, assenting to this fact has an immensely real impact on our realization that a comprehensive and wholly integrative model of science may not be fully achievable for humankind.

The limitations of human hardware

The practice of biology is often fundamentally disadvantaged because its practitioners fail or refuse to recognize that biology is itself carried out by biological entities and, therefore, can never be explored from a truly external perspective. In other words, our uniquely human hardware predisposes our methodology and our efficacy in attempting to unravel ourselves and the world around us (Nagel, 1974). As a result, we should feel compelled to examine at least some of the most salient aspects of our own neurobiology and how these translate into the phenomenology of being human, before cascading into our limited perception and subsequent representation of natural phenomena.

The course of our own hominid evolution has imposed upon us a collection of biological artifacts that give rise to our immediate ability to tackle the environment in which we operate (Suddendorf, 2008). For example, our rendering of reality is dominantly facilitated by our visual perception (Posner et al., 1976). If we considered the vast amounts of knowledge that science has amassed it is more than mere coincidence that virtually every human effort to summarize data exists as tabular representation, or its close cousin, the two-dimensional graph with x and y axes. Moreover, our visual dominance is compounded by our limited capacity to process information (Miller, 1956). Thus, it is conceptually impossible for us to imagine a world beyond three dimensions, even when so much of what we believe about science is derived from a vastly multidimensional search space. In fact, a primary motivation for applying transformations such as principal component analysis is to extract the main factors from highly dimensional data, or in other words, to transform something too complex for humans into something more arrestandable.

Another powerful aspect of our visually biased perspective is driven by the existence of cortical structures such as the fusiform gyrus which has been implicated in human facial recognition (Chaminade et al., 2007) and the medial frontal cortex which is believed to support representations that facilitate reflection on values and outcomes (Amadio et al., 2006). Facial recognition and reflective thought are indispensable skills for cooperative and social animals like humans. However, our ability to extrapolate faces from shapes comes with the artifact of anthropomorphism (Chaminade et al., 2007). Similarly, our capacity for reflective thought produces an affinity for the assignment of motivations and teleological interpretations to virtually all objects and events (Kelemen, 1999). DNA has been characterized as selfish, parasitic, non-essential, and a host of other descriptors. While these terms offer a type of cognitive economy through novel semantic synthesis, they do so at a cost of conceptual stigmatization. Even the most benign of terms, such as natural selection, cannot escape a modicum teleological contamination: nature is an entity and it makes selections. Our most earnest efforts at objectivity will forever be shackled by the anthropomorphic and teleological predilections that imbue our every abstraction, particularly language.

Perhaps our most definitively human quality is the ability to use complex language and to be able to represent it symbolically (Hauser et al., 2002). Although adequately exploring the scope of language as a constraint on human conceptual abilities is not possible here, nevertheless, in passing it is paramount to wonder how knowledge can be obtained, conveyed, or otherwise exist, with respect to language. Certainly every human initially does exist as a non-verbal being that is capable of recruiting new knowledge. In fact, complex behaviours like primitive tool construction have been documented in apes in the complete absence of language (Donald, 1999). Nevertheless, the acquisition of language likely causes an indelible change to the types of knowledge that can be gained, and the manner in which they are acquired and represented. As a result, we are confined to the realm of speculation when we ask whether or not we can conceive of a question or a concept for which we have no vocabulary and hence no ontology or operational definitions.

The limitations of our human hardware have a direct bearing on the epistemological underpinnings of how we define and pursue science. Empirical observation, the very cornerstone of science, is directly contingent upon observation by way of one of the five senses, thereby linking the foundation of science directly to our frontline phenomenology. From such rudimentary observations, we strive to synthesize prediction-oriented schemas about natural phenomena. Moreover, it is of critical importance that any hypotheses be able to be subjected to a mechanism of potential falsifiability in order to qualify as scientific (Popper, 1959). It is here that science distinguishes itself from other explanatory systems, such as religion and magic. Nevertheless, these constraints still permit science to accept a collection of ad hoc models on a rather speculative basis. Theories are required to integrate with one another only at their boundary points, so as to preserve and promote the notion of a greater and unified whole. This seems an acceptable necessity as Egler (1977) and others have pointed out that a complete phathoming of intricate and interactive
systems is simply beyond our means. While this notion coincides with the previous explanation of our limited phenomenological and perceptual capacities, it does not extinguish the question of whether a piecemeal approach to science can ever hope to generate a truly broad understanding of anything.

**Reductionism: A double-edged sword**

We have now arrived at a central conflict in science and scientific thinking: reductionism versus holism. In many ways reductionism assests to our previously described conceptual limitations. It strives to understand greater systems by examining their constituent parts (Van Regenmortel, 2004). In contrast, some scientists feel that reductionism fails to capture synergistic relationships and emergent processes (Van Regenmortel, 2004). While much of science has historically employed a reductionist approach, rising fields like integrative biology assert that this strategy has reached its limits and that advancing the understanding of biological complexity requires a paradigm that can adequately address nonlinear and non-additive effects (Van Regenmortel, 2004). However, as we have already seen, the ability to conceive, never mind implement, the bigger picture in science may lie outside of our perceptual faculties. If that is indeed the case, then we must deliberate on how we can reconcile this disparity between what we need to represent and what we are able to represent.

Ironically, the solution to this fundamental crux may rest on the realization that reductionism itself may be integratable with holism. Woese (2004) argued that there is an inherent dichotomy within reductionism between empirical reductionism and fundamentalist reductionism. The former is described as an approach to analysis, a type of methodological structure (Woese, 2004). In contrast, the latter is a metaphysical perspective that asserts that any conceptual construct is the aggregate product of smaller constructs, and simultaneously the constituent of some greater construct (Woese, 2004). Woese (2004) goes on to criticize the present state of biology which acknowledges the need to address emergent processes that do not obey the bounds of fundamentalist reductionism, yet at the same time it clings to its fundamentalist apron strings. Thus, the previous question more precisely becomes can we adequately foster a broad view of natural phenomena that is free of fundamentalist reductionism, but still render it amenable to our modest conceptual capacities by way of empirical reductionism.

**Reconciling conceptual needs with conceptual limitations**

More than six decades ago, Novikoff (1945) noted the potential for representing biology as a layered system where the complexity of each layer is made possible by the components of the conceptual layer beneath it. Furthermore, Novikoff (1945) recognized that such a design would permit the simultaneous consideration of constituent components, as well as their aggregate impact as an integrated whole. Likewise, Hebb (1958) advocated that the reconciliation of our modest conceptual faculties versus the infinite complexity of the natural world rested in our ability to encapsulate objects and events at different levels of hierarchical complexity. These remarkably foresighted notions bear a striking resemblance to modern software engineering paradigms and network protocols like the Open Systems Interconnection (OSI) model (Zimmerman, 1980). So perhaps the resolution between metaphysics versus methodology can be found in the very computational models that have shaken the foundations of biology in the first place.

A core pursuit of software engineering is the abstraction of real world objects into some type of structural representation and the abstraction of existing processes into behaviors for the corresponding structures. Moreover, such representations are not confined to the realm of physical objects and real events; they can emulate any conceivable abstract object or imagined event. Better still, a structure can be composed of one or more member structures, hence, offering an immediate circumvention of our meager conceptual power through the technique of encapsulation. Therefore, software engineering strategies demonstrate how we might be able to decompose biology, both conceptually and in terms of manpower for its implementation.

Having determined the need to use empirical reductionism and having seen the benefits offered by a layered model of abstractions, we can now consider the logistics of a radical proposition for a wholly integratable biology. Team development strategies have been employed by software engineers for decades to allow for the conception, completion, and maintenance of projects vastly beyond the grasp of an individual, or even a small group of specialists (Schach, 2005). While modern software engineering is a precise practice built around standardized conventions like the Unified Modeling Language (UML) (Schach, 2005), the general spirit of modular designs that can be assembled into larger components coincides with our requisites of empirical reductionism and layered abstraction. Although this may seem superficially similar to the status quo of scientific practice, it does, however, have a crucial difference in that current practice is under no constraint to develop models that integrate with one another in a specified manner, according to a previously devised design and enforced by a mutually understood ontology. As stated earlier, scientific theories typically interface only at their respective boundaries, if at all, and biology risks a situation
Biology among the computational sciences

comparable to the binding problem (Revonsuo et al., 1999) in cognitive neuroscience that prevents the explanation of how lower level constructs unify to form a larger whole. This can be avoided by decoupling the functionality of biological systems from their implementation as abstract structures.

Just as we needn’t understand how an internal combustion engine operates in order to drive a car, we need only be aware of what functionality existing structures can provide us, not how such functionality was accomplished. For example, to model a network of functional interactions, we might make use of an existing abstraction for an individual functional interaction. Our network becomes an implementation that is based on the properties and actions of its member components, without regard to how these were implemented or what member components that they may subsequently contain. This general technique can be iteratively applied so that at any level of our layered model we are aware of what services are provided by lower level constructs and what services we need to provide to higher levels of abstraction. Fig. 1 shows a simple layered model for biology that was inspired by the OSI model.

However, so far this has only amounted to suggesting that biologists should each model their own areas of interest while keeping in mind some hope of integration with a larger conceptual body. Even worse, there cannot be a definitive completion point for modeling biological systems. Therefore, it seems that software development is not sufficient for comparison to the creation of an ever growing and constantly refining model for biology. Yet, remarkably the two ventures are more similar than different. Software is often highly dynamic and must be able to undergo revision, adaptation, and expansion throughout the course of its lifecycle (Schach, 2005). The fact that maintenance of ‘completed’ software is such a central issue to software engineering is another major aspect of why it makes such a suitable paradigm for modeling biological systems.

Biology: An object-oriented approach

If we entertain the possibility of a large-scale team effort to model biology into a unified construct, then we must consider the implementation of such a venture. A layered model approach allows developers to build abstractions at their particular level of interest with consideration of available services from the immediately lower level and knowing what services are required by the immediately higher level, but without needing an understanding of the entire model. Thus ecologists can become the beneficiaries of molecular biology in a transitive manner, without the burden of knowing how these molecular constructs were represented. Next, we must explore how the actual representations might be abstracted by interested developers working within a particular layer.

Further pursuing the avenue of software engineering, we can see that the use of object design and modeling combined with ontologies exemplify how component-based models can exist within a framework of rules that is often driven by non-additive or emergent forces. In fact, the field of synthetic biology has already adopted a similar perspective but one that is inspired by real world hardware and components (Andrianantoandro et al., 2006). From our software perspective, object-oriented design can be used to represent both real world objects and abstract objects as unique classes of data types that have discrete properties and behaviours (Siricharoen 2007). Furthermore, object modeling is dedicated to the interaction and behaviour between a set of objects, rather than the relationship between the

Figure 1: A simple layered model for biology inspired by the OSI model. A keyword that denotes a core conceptual unit from conventional biology is associated with each layer. Also, some traditional fields that are encapsulated by the model are listed with respect to layer.
information that they encapsulate (Siricharoen, 2007). Therefore, this approach offers a means to represent the stochastic models of empirical reductionism as objects, while permitting these entities to exert their potentially non-linear effects on one another through their behaviours, as enforced by an object model.

Although seemingly unconventional, an object-oriented approach to biology offers several compelling benefits, especially in the context of developing a unified domain of knowledge. First, a hierarchy of objects allows for a corresponding hierarchy of conceptual complexities, ranging from molecular to ecosystemic in scope. Within each level, entities and processes can be subsequently decomposed until they reach manageable proportions and can be adequately abstracted into discrete objects. Second, because object design is decoupled from object modeling, the behaviour of individual components can implemented and adjusted without affecting the conceptual design of the component itself. Similarly, the representation of the component can be updated without necessarily altering its available repertoire of behaviours and services. Third, composite objects are highly amenable to conversion into formats such as the Extensible Markup Language (XML) or the Resource Description Framework (RDF) (World Wide Web Consortium, 2009). This would make biological models more readily interpretable to computer applications and relational databases, thereby enhancing the potential for novel research. Fourth, the event-driven interaction of objects with one another can accommodate emergent processes that more accurately capture the dynamics of biological relationships.

Any exhaustive model of a wholly integratable biology is likely to require a prior specification in the form of an ontology. Any system of organized knowledge, such as biology, is an instance of conceptualization aimed at abstracting and simplifying some facet of the world before us, either implicitly or explicitly (Gruber, 1993). An ontology is specifically an explicit declaration of a conceptualization (Gruber, 1993). An important aspect of a common ontology is its portability. If the specification of terms is shared at the knowledge level, rather than the implementation level, then it is possible for a common ontology to be utilized by multiple systems and representations (Gruber, 1993). This is crucial because a primary goal of our unified model is to allow experts to represent biological subsystems independently of one another in their respective areas of interest, at the appropriate layer of the model. Therefore, panning the way for a fully integrated biology is ultimately contingent upon how we choose to define what biology is versus what biology should be, with respect to a truly objective vantage point that is not constrained by traditional views or practices.

Challenges in specifying a unified ontology

There have been previous efforts to bring ontology to biology, most notably the creation of the Gene Ontology (GO) (Ashburner et al., 2000). However, even an effort as ambitious as the GO is still confined to addressing only a portion of what we define as the biological sciences. Genuinely broad thinking is likely to require re-thinking that might meet with immense impedance from the scientific community. Nevertheless, such re-thinking may ultimately become a necessity. For example, Conti et al. (2007) refer to the mythology of nonhierarchical genes as a major stigma that persists in current biological thought. Yet at the same time, genomics provides ongoing evidence of modular organization within genomes and the cascading effect of networked interactions. In fact, works such as that presented by Janga et al. (2008) have offered evidence for the higher-order organization of genes in eukaryotic chromosomes.

The accepted relationship between gene and protein has always mandated a one-to-one cardinality. However, this may be an artifact of conceptual convenience that has propagated to every corner of biological thought, rather than a rigidly understood stochastic rule. There is a growing body of evidence in functional genomics, proteomics, and epigenetics that points to organization greater than an encapsulated unit of inheritance resting at a fixed chromosomal locus. Genomes are not flat files; they exhibit robust topologies that defy the simplicity of a one-to-one cardinality. Perhaps our entire perspective on genomes has been skewed by the tremendous impact of the one-gene-one-protein model. In the broadest sense, a genome is a spatial pattern. Its means of implementation and execution are somewhat secondary to its function. As a result, the life of an organism can be considered in terms of a spatial-temporal pattern of genomic expression with genes being invoked differentially with respect to time. Moreover, we are left to consider whether genomes facilitate organisms or if the reverse is actually more parsimonious. Further still, perhaps the organism should not be the basic unit of taxonomy; maybe groups of genes, such as operons in Prokaryotes or other functional modules more accurately portray the perpetuation of genomes.

CONCLUSION

Biology has before it the opportunity to redefine itself, both in terms of addressing its current limitations and harnessing the vast utility that the computational sciences can bestow upon it. The challenge in building a unified biological science is in reconciling our human conceptual limitations with the need for a broad and
dynamic whole. We can employ empirical reductionism to derive composite entities that can participate in a layered model, thereby offering integration without the burden of understanding the entire implementation of the model. Object design and modeling combined with a single mutual ontology have demonstrated how this might be humanly achievable, if we should chose to organize ourselves toward such a goal. However, the most challenging problem in developing a comprehensive ontology to regulate such a venture rests in the task of interpreting what biology and biological problems should strive to portray, and to consider this from the broadest vantage point, without the influence of the established and the conventional. Otherwise, biology risks becoming supplanted by its own progeny, fields such as genomics and proteomics. Thus, Hebb’s urgings should echo now in the ears of modern biological theorists as a reminder that science is ceaselessly dynamic and demands constant reevaluation and vigilance against conceptual stagnancy.

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References