mental reality of a mutational path that proteins follow in evolving new properties.

This lack of quantitative thinking underlies a second, fatal blunder resulting from the mistaken assumptions Behe makes about protein interactions. The author has long been concerned about protein complexes and how they could or, rather, could not evolve. He argues that the generation of a single new protein-protein binding site is extremely improbable and that complexes of just three different proteins "are beyond the edge of evolution." But Behe bases his arguments on unfounded requirements for protein interactions. He insists, based on consideration of just one type of protein structure (the combining sites of antibodies), that five or six positions must change at once in order to make a good fit between proteins—and, therefore, good fits are impossible to evolve. An immense body of experimental data directly refutes this claim. There are dozens of well-studied families of cellular proteins (kinases, phosphatases, proteases, adaptor proteins, sumoylation enzymes, etc.) that recognize short linear peptide motifs in which only two or three amino acid residues are critical for functional activity [reviewed in (*7–9*)]. Thousands of such reversible interactions establish the protein networks that govern cellular physiology.

Very simple calculations indicate how easily such motifs evolve at random. If one assumes an average length of 400 amino acids for proteins and equal abundance of all amino acids, any given two–amino acid motif is likely to occur at random in every protein in a cell. (There are 399 dipeptide motifs in a 400–amino acid protein and $20 \times 20 = 400$ possible dipeptide motifs.) Any specific three–amino acid motif will occur once at random in every 20 proteins and any four–amino acid motif will occur once in every 400 proteins. That means that, without any new mutations or natural selection, many sequences that are identical or close matches to many interaction motifs already exist. New motifs can arise readily at random, and any weak interaction can easily evolve, via random mutation and natural selection, to become a strong interaction (*9*). Furthermore, any pair of interacting proteins can readily recruit a third protein, and so forth, to form larger complexes. Indeed, it has been demonstrated that new protein interactions (*10*) and protein networks (*11*) can evolve fairly rapidly and are thus well within the limits of evolution.

Is it possible that Behe does not know this body of data? Or does he just choose to ignore it? Behe has quite a record of declaring what is impossible and of disregarding the scientific literature, and he has clearly not learned any lessons from some earlier gaffes. He has again gone "public" with assertions without the benefit (or wisdom) of first testing their strength before qualified experts.

For instance, Behe once wrote, "if random evolution is true, there must have been a large number of transitional forms between the *Mesonychid* [a whale ancestor] and the ancient whale. Where are they?" (*12*). He assumed such forms would not or could not be found, but three transitional species were identified by paleontologists within a year of that statement. In *Darwin's Black Box*, he posited that genes for modern complex biochemical systems, such as blood clotting, might have been "designed billions of years ago and have been passed down to the present ... but not 'turned on'." This is known to be genetically impossible because genes that aren't used will degenerate, but there it was in print. And Behe's argument against the evolution of flagella and the immune system have been dismantled in detail (*13*, *14*) and new evidence continues to emerge (*15*), yet the same old assertions for design reappear here as if they were uncontested.

The continuing futile attacks by evolution's opponents reminds me of another legendary confrontation, that between Arthur and the Black Knight in the movie *Monty Python and the Holy Grail*. The Black Knight, like evolution's challengers, continues to fight even as each of his limbs is hacked off, one by one. The "no transitional fossils" argument and the "designed genes" model have been cut clean off, the courts have debunked the "ID is science" claim, and the nonsense here about the edge of evolution is quickly sliced to pieces by well-established biochemistry. The knights of ID may profess these blows are "but a scratch" or "just a flesh wound," but the argument for design has no scientific leg to stand on.

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EVOLUTION

A Multilevel Exploration

David Jablonski

In the natural world, as in human societies, complexity is almost always organized hierarchically. From the nested structures of armies and corporations to the classical biological progression from molecule to cell to tissue to body to species, the "particles" at each level tend to be grouped into ever more inclusive units. However, despite the ubiquity of natural hierarchies, their evolutionary implications have been anything but clear.

Evolution and the Levels of Selection is a major contribution toward putting this controversial area on a coherent conceptual and philosophical footing. Samir Okasha's argument hinges on two components, neither of them new but here powerfully and creatively integrated and extended. First is the fundamental distinction between two disparate kinds of multilevel selection (MLS), often conflated despite their formal introduction 20 years ago (*1*), with even earlier precedents. The failure to appreciate this distinction has generated an enormous amount of confusion, at times bordering on fury, and Okasha's use of this conceptual framework brings exceptional clarity and precision to a wide range of issues. In essence, for MLS1 the sole focal level is the individual (at any level), but its fitness depends partly on the group to which it belongs. The classic example is the seeming paradox of altruism: how can selection drive behavior that aids others at the

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> *by Samir Okasha*
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actor's expense? Under MLS1, altruists have lower fitnesses within their groups than selfish individuals, but groups containing a higher proportion of more altruists contribute more individuals to the global population. Okasha (a philosopher of science at the University of Bristol) greatly clarifies this process and shows how its logic can apply to many evolutionary problems, from the operation of selfish intracellular elements to the origin of complex cells.

In contrast, MLS2 involves multiple focal levels, with selection operating on units at each of those levels simultaneously and with effects cascading both upward and downward. The classic example is species selection, where

From unicell to multicell. Evolutionary transitions to multicellular animals required two kinds of multilevel selection, as formerly independent units were subordinated into a large whole.

both organisms within populations and species within lineages are subject to differential survival and reproduction according to heritable variation. Variations in speciation rates, extinction rates, or both can thus drive large-scale evolutionary changes independent of the fitnesses of the organisms within those species and can indirectly shift the mean phenotypes of lineages. Okasha notes that such indirect effects, often termed "upward and downward causation," are the essence of multilevel selection. When is the differential proliferation of a given biological property on some level the result of direct selection at that level, and when is it a by-product of processes at a lower or higher level? (As Okasha makes clear for the first time, these cross-level processes are fundamentally different under MLS1 and MLS2.)

To address this problem, Okasha applies the second major element of his argument: the Price equation, a general statistical statement of the covariance between a character and fitness that can provide a formal separation of levels of selection. One of the real pleasures of this book is watching Okasha view a succession of problems in multilevel selection through the lens of the Price equation in its different forms. It proves a powerful conceptual tool, although it does not always perform ideally. For example, Okasha finds the Price equation to be theoretically inferior to an alternative called contextual analysis as an approach to detecting MLS1.

Okasha is not quite as precise on the notion of emergent properties, another highly contentious area in the multilevel selection debates. Okasha recognizes the existence of such properties, irreducible to characters at lower hierarchical levels, but does not see them as required for the operation of multilevel selection. For him, the essence of the problem is the emergent relation between a character and fitness at a given level. This is a reasonable stance, although not the only one possible. In fact, in several places Okasha skates very close to treating emergent species properties as integral to the operation of species selection, as did Stephen Jay Gould in his magnum opus (*2*). For example, Okasha accepts that the increased frequency over time of gastropod species having larvae that do not feed in the plankton should be classified as species selection because "[d]ifferences in species' fitness were not caused by differences in the fitnesses of their constituent organisms, but by differences in the extent of within-species gene flow." [Such gene flow, with the associated genetic population structure, is arguably a species-level property; for a lucid analysis of opposing concepts of emergence, see (*3*).]

The final chapter derives fresh insights from Okasha's integrative framework for some of the most profound evolutionary events in the history of life. The evolutionary transitions to new kinds of individuals—from prokaryote to eukaryote, unicell to multicellular organism—must have entailed the subordination of lower-level units into a larger whole. Okasha makes a strong argument that such transitions involve both types of multilevel selection, operating in succession. His deep understanding of the evolutionary models and his integration of the philosophical issues really pay off here. This chapter alone is worth the price of the book.
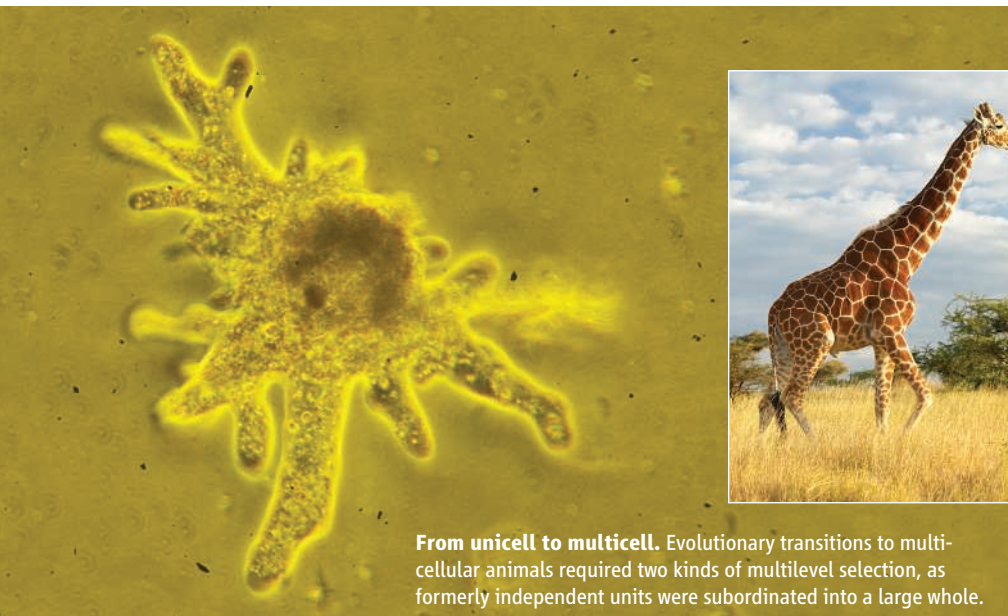
Elsewhere in the book, however, MLS2 seems to get short shrift. This is a shame, because that is another growth area that could benefit from closer philosophical attention. As Okasha notes, most workers concede the plausibility of MLS2; the uncertainty lies in the efficacy of processes above and below the traditional dynamics of bodies within populations. But species selection receives the shortest chapter in the book, and the burgeoning macroecological literature on the size, position, phylogenetic distribution, and organismic correlates of geographic range (accepted by Okasha as a potential factor in strict-sense species selection) is not mentioned. Nor is the even larger paleontological and neontological literature on comparative analyses of clades, where organismic and species properties are tested for their statistical associations with differential diversification rates. I was eager to see Okasha bring his conceptual arsenal more fully to bear on these and other nearly unexplored potential sources of data and theory. [(*4*) offers an entry into these aspects of the debate.]

A hierarchical view of the evolutionary process, with potentially opposing, reinforcing, or orthogonal forces in play at multiple levels, may be harder to grapple with than the more traditional view, but Okasha has greatly clarified many of the central issues. I can't imagine anyone working on multilevel selection—or attempting to dismiss it—without reading this book.

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