Sahotra Sarkar
Molecular Models of Life:
Philosophical Papers on Molecular Biology.
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The philosophy of biology community has long been guided by Dobzhanky's famous saying that nothing in biology makes sense except in the light of evolution. Now however, one of our intellectually rigorous members of that community, Sahotra Sarkar, only out of concern about any creationists' abuse, restrains from insisting that 'much of the received framework of evolution makes no sense in light of molecular biology' (5).

Sarkar's book comprises thirteen papers written in the fifteen-year period from 1988 to 2004 plus a new introduction designed to relate these papers to one another and embed them into a wider context. Sarkar defends a model of 'strong reduction' in which properties of wholes are explained entirely through properties of their parts, a model laid down in detail in the first three chapters. Arguably the most important and compelling view presented in these chapters is that a substantive reductionism in biology does not need to, and in fact should help to refute, a simplistic genetic reductionism or determinism.

The second section of the book explores the major challenge to reductionism presented by functional explanations that are ubiquitous in biology, including molecular biology. Unfortunately the three chapters that comprise this section all take a narrowly evolutionary perspective on the concept of function, something that would not be surprising in a philosopher guided by Dobzhansky's maxim, but which seems strangely at odds with the book's declared objective of providing a new and unifying molecular perspective on life complementary to the received evolutionary view. Only Chapter 7 goes some way to fulfill this promise, highlighting the Human Genome Project as a research program not guided by functional questions, although this argument is surely weakened by the extensive criticism of that research project elsewhere in the book. It would have added substantively to the book if Sarkar had extended on the alternative, much broader sense of function outlined in the introduction, a sense which comes closer to how function is understood in molecular biology and by critics of the evolutionary concept of function from developmental biology and complexity theory.

Other topics touched on in the introduction and the final chapter remain tantalizingly explored in the body of the book, such as the extension of evolutionary theory by developmental biology, bridging the gap between proximate and ultimate explanations in biology, and reconciling molecular reality with many received assumptions of evolutionary theory. Sarkar is one of the philosophers most competent to offer substantial insights into these issues, but he does not do so here.

Arguably the most exciting, if somewhat mutually redundant, chapters come in the third section of the book and give a detailed analysis of the concept of information in molecular genetics. Whilst Chapters 8 and 9 conclude that the terms 'biological' or 'genetic' information are mostly used incoherently and arguably only masquerade as a substantive technical concept, Chapter 10 develops a rather specific notion of semiotic information based on the twin criteria of specificity and arbitrariness. Its usefulness, however, remains unclear since its rigorous conditions can — if at all — only been met by prokaryotic genetics but, at least theoretically, also by certain environmental factors. By detailing the complexities of eukaryotic genome expression these chapters show that eukaryotic DNA alone does not specify the primary sequence of amino acids of a protein, let alone their tertiary structure or a phenotypic trait. A point not driven home sufficiently (though hinted at in the introduction at p. 25), which is hard to square with Sarkar's reductionist stance, is what constitutes a 'gene' in the first place — where it begins and ends, and which sequences it comprises — is determined by the cellular and extracellular phenotype at each point in an organism's developmental trajectory. The whole determines what counts as a part.

The introduction takes the discussion of bioinformation further by embedding the concept of genetic information in a broader analysis of the use of language metaphors in molecular genetics, their shortcomings and their effect of 'obfuscating the physical complexity and developmental contingency of gene expression' (25) and thereby promoting an unwarranted genetic reductionism. Picking up on this theme, Sarkar's last chapter argues that biological agency is distributed over different kinds of molecules and different levels of biological organization.

The last section of the book contains three chapters on the problem posed by directed mutations in bacteria for Darwin's model of evolution by natural selection by violating some of its central assumptions. Again the introductions proves extremely useful, this time through the integration of these chapters in a wider discussion of how developments in molecular biology have challenged many of the assumptions of the received view of evolution.

It is worth asking how the defense of strong reductionism in this book is likely to hold up in the light of twenty-first-century molecular biology. Although twentieth-century molecular biology had many spectacular successes, it also made clear that a mere inventory of genes, proteins, and metabolites is not sufficient to understand the cell's complexity. There is remarkable integration of the various layers, both regulatory and structural, and most biological characteristics arise from interactions between numerous cellular constituents. Viewing the cell as a *network* of genes, RNAs, proteins and metabolites offers a viable strategy for addressing the complexity of living systems. Therefore, a key challenge for postgenomic biology is to understand how interactions between the molecules of a living cell determine the function of its enormously complex machinery, both in isolation and when surrounded by other cells. The future lies with 'systems biology' rather than

with proteomics, as Sarkar in several places suggests, or any other 'omic' inventory of cellular contents.

Thus, for example, biologists are increasingly turning to three-dimensional cell cultures. In mammalian tissues, cells are embedded into a structure called the extracellular matrix (ECM) of proteins that give tissues their mechanical properties and help to organize communication between cells. Receptors on the surface of the cells anchor their bearers to the ECM, and also determine how the cells interpret biochemical cues from their immediate surroundings. This complex mechanical and biochemical interplay leads to distinctive patterns of gene expression and other biological activities and renders the whole of a cell tissue more than the sum of its parts.

While Sarkar acknowledges the universality of molecular structures and mechanisms at the cellular level, results from the new field of network and systems biology suggest that the universality increases enormously with every higher level of organization from gene-regulatory motifs and metabolic pathways over functional modules to the organization of the system's large-scale architecture, a universality not mirrored at the level of its molecular constituents. No matter if the system is approached from the bottom up or from the top down, the acknowledgement that functions are deeply interlinked forces us to complement the 'local' molecule-based research with integrated approaches that address the properties of the system as a whole.

The introduction is ample evidence for how much more Sarkar has to offer for a unifying molecular perspective on life than the selection of papers suggests, and it is to be hoped that he will soon publish a monograph laying out his current perspective. This aside, the book comprises an impressive body of work that combines conceptual, historical, and technical considerations into philosophy of (molecular) bioscience of the highest quality. *Molecular Models of Life* appears at a time of an unexpected transformation of molecular biology from genetic to (post) genomics and systems biology and offers the interested philosopher of science a scientifically informed window into this new exciting field of study.

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