Is the cell more than molecules?

The Way of the Cell: Molecules, Organisms and the Order of Life

By Franklin M. Harold

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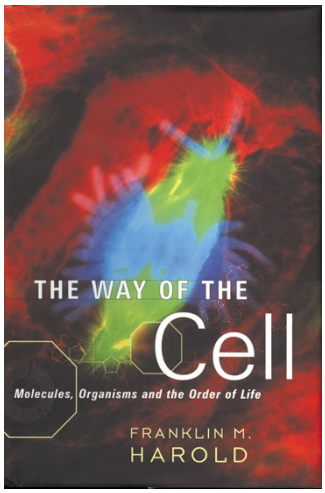
The cell is the true 'miracle' of evolution. The rest was relatively easy, as little had to be invented for the transition to multicellularity. In *The Way of the Cell*, Franklin Harold's aim is to assess how far we have come towards an understanding of life, and so he rightly focuses on the life of the cell. Particular emphasis—he calls it a celebration—is placed on microorganisms, which he feels have not received the attention they deserve, even though they ruled the living world for billions of years and it is from them that the eukaryotic cell evolved. The other emphasis is on organization, which he regards as the basis of life, and which remains too often neglected.



The author thinks that the book may be suitable for a general reader, and tries to make cell metabolism, protein synthesis and cell division comprehensible to such readers. But the description is quite standard, and some sections are very technical, like those dealing with Mitchell's chemiosmotic ideas, the behavior of cells when shifted to an environment that does not contain amino acids, and bacterial chemotaxis.

Harold questions what he regards as a seductive idea, namely that biological organization is fully determined by molecular structures—he thinks it fundamentally wrong, as it disregards that the cell as a whole is necessary to create the proper environment for assembly to proceed. But we know that many key processes can occur in the test tube, like microtubule formation, actin polymerization and much of metabolism. The treatment of cell movement is quite dated. His discussion of cell division, which might reasonably be thought to be fundamental to life, focuses almost entirely on the mechanism of division itself in bacteria, and the processes involved in the eukaryotic cell cycle are not even mentioned. After all, the most recent Nobel Prize in medicine was given for progress in just this area. Yet he favors a view that suggests that the cell serves as a templet (not a template), which he describes as a source of configurational information on which the daughter cell organizes itself. But what exactly does this concept mean and how does it help us understand the cell? I cannot see this as a helpful idea. The essence of cell multiplication is that the cell grows so as to make itself twice as large, everything is doubled, and then this is divided into two daughters. Only the DNA replicates; the rest is essentially protein synthesis and interactions.

He repeatedly points out that the genes do not provide a blueprint for the cell, but that is well known. It is the activity of the proteins they encode that determines the properties of the cell. But he is right in pointing out that we still have some way to go in explaining apical growth of the hyphae of fungi or the form of ciliates. He favors a dynamical systems approach to morphogenesis along the lines suggested so brilliantly by Alan Turing. I know of no case in all of biology, however, where a reaction-diffusion system like that proposed by Turing has been convincingly shown to generate a pattern.

Have all organisms descended from a single ancestor in the distant past? How did that life begin? This remains the central problem—even mystery—in relation to understanding life. Harold would like whatever mechanism is proposed to involve compartmentation of some kind, lipid membranes perhaps. He is also sympathetic to the idea of an early 'RNA world' and also to the possible key role of thermophilic bacteria. The origin of the eukaryotic cell is claimed to be the most significant event in the evolution of life and he embraces Lynn Margulis's suggestion that endosymbiotic bacteria had a central role. But he is uneasy with the idea that evolution is the result only of changes in genes. In his view, for example, spatial order does not emerge from the genetic program but from the dynamics that generate morphogenetic fields. Those so-called fields, however, are no more than the result of protein interactions, which in turn are determined by the pattern and timing of gene expression.

Harold claims that there are no detailed accounts of Darwinian evolution explaining any biochemical or cellular system. I take the opposite view and argue that he has not appreciated sufficiently the difference and relation between genotype and phenotype—only DNA replicates and thereby determines the phenotype of future generations. His suggestion that membranes can effectively be inherited ignores that some of their components are proteins and hence are determined by genes. More importantly, he does not consider the evidence from genetic algorithms. These use the computer to generate, randomly, a number of solutions to a particular problem. Selection of those that show some of the required properties, followed by mating and mutation repeated again and again, can yield surprisingly novel solutions. Signal transduction clearly reflects such a process. Evolution by random variation and selection is an astonishingly powerful process for generating complex functioning systems like the cell.

All told, though the book contains some interesting comments and highlights cells that perhaps do not get the attention they deserve, it does not really help us understand how cells function. In the end, cell biologists may indeed have to turn to more complex models, but better arguments will be required to persuade them that conventional molecular biology will not give them the answers they seek, or that Darwinian evolution cannot account for cellular evolution. □