



In Search of Cell History: The Evolution of Life's Building Blocks

By Franklin M. Harold

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The origin of cells remains one of the most fundamental problems in biology, one that over the past two decades has spawned a large body of research and debate. With *In Search of Cell History*, Franklin M. Harold offers a comprehensive, impartial take on that research and the controversies that keep the field in turmoil.

Written in accessible language and complemented by a glossary for easy reference, this book investigates the full scope of cellular history. Assuming only a basic knowledge of cell biology, Harold examines such pivotal subjects as the relationship between cells and genes; the central role of bioenergetics in the origin of life; the status of the universal tree of life with its three stems and viral outliers; and the controversies surrounding the last universal common ancestor. He also delves deeply into the evolution of cellular organization, the origin of complex cells, and the incorporation of symbiotic organelles, and considers the fossil evidence for the earliest life on earth. *In Search of Cell History* shows us just how far we have come in understanding cell evolution—and the evolution of life in general—and how far we still have to go.

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Editorial Review

Review

“A must-have. . . . *In Search of Cell History* is a wise and useful summary of the issues facing origins research. Importantly, it refocuses the origin problem onto the cell in toto, as a unit of living matter; it represents a solid foundation for origins research where chemists have begun only very recently to make significant advances in understand the crowding and structuring of biomacromolecules in living cells. There is no need to throw in the towel yet.”

(Jan Spitzer, Mallard Creek Polymers, Inc. *Microbe*)

“Harold manages to cover a lot of ground, offers a piece of writing that is highly instructive and broad in its treatment of cellular evolution, and includes a helpful glossary at the end. He also provides a wonderful historical summary and perspective. . . . We can thank Harold for his fine work, so broad and sweeping, on leading us to nature’s ultimate mystery—the link of the LUCA to the cosmos.”

(Paul Schimmel, Scripps Research Institute *FASEB Journal*)

“Wonderful. . . . A loving distillation of connections within the incredible diversity of life in the biosphere, framing one of biology’s most important remaining questions: how did life begin? . . . Using [a] deceptively casual approach, Harold cleans up the vast untidy mess of biology and stacks the fundamental concepts in an orderly and creative way for readers to enjoy. . . . Harold’s book is like a balloon that will let [young scientists] rise above the trees for a while and look down to better understand the scope and shape of the forest—and perhaps then descend to pluck some low-hanging fruit. Senior scientists like myself will take pleasure in comparing perspectives with Harold’s. This is, after all, a story to conjure with—that of how life began and evolved into eukaryotic cells, a hundred trillion of which compose the human body. No one can yet tell this story in its entirety, but Harold’s book is a good place to start.”

(David Deamer, University of California, Santa Cruz *Nature*)

“The big questions in evolution are the ones that grab our imagination: How did life begin? Where do cells come from? How did eukaryotes come to be? How does life become organized? How does it become complex, and what is biological complexity in the first place? How does energy figure into cell evolution? Where did the genetic code come from? Those are the kinds of questions that Franklin Harold, a grand master of cellular workings and bioenergetics, has packed into his latest book. . . . Sound interesting? It is. The book is a must for those interested in microbial evolution, life’s origin, or both. . . . Coming into the final chapter, the reader gets a strong sense that judgment day and the unabated Wrath of God are lurking just around the corner, to be delivered ablaze with lightning bolts from above. There is chilling suspense that Harold is finally going to part the waters and thunder forth what he really thinks about all these ideas on early evolution, namely that individually and in sum they cut neither ice nor mustard, and that we are best advised to repentantly seek our drawing board, eraser firm in hand, with renewed resolve to do better in our next sixty years of attempt. I will not divulge here how much hellfire and damnation the final verdicts hold.”

(William F. Martin, University of Düsseldorf, Germany *BioEssays*)

“Within *In Search of Cell History* Harold deftly discusses the definition of life, successes and problems of classification of cells, how cells get and use energy, the great divergence of cell types into three loose families, cell symbionts, and even tackles the ultimate riddle of where cells first came from. His approach is a classic scientific one, starting with what is known and provable then moving into theories of what is not

known. He is clear to separate fact from speculation, not hesitating to state his own opinions as such and contrasting them point by point with others in the field. It is very refreshing to read about the forward edge of cell research without polemics of any kind. The talent of his writing is twofold, first; I felt a part of a conversation among the leading lights of cell research, and second; Harold has no problem stating what is not known. . . . This is a book that illustrates what scientific writing should be; precise, exciting, and presenting the unknown in such a way as to inspire us to want to learn more.”

(*San Francisco Book Review*)

“A fine addition to the many books on how cells originated and evolved. It is well written, accessible, thorough, and illustrated with helpful figures, focusing on cellular organization and how that organization diversified as various life-forms evolved. Harold comprehensively discusses the important process of fusion between cells (symbiosis) in cell evolution as well as information on cellular structure and organization that can be gleaned from the fossil record. . . . Highly recommended.”

(B. K. Hall, Dalhousie University *Choice*)

“*In Search of Cell History* offers an ambitious, one-stop overview of early cell evolution that covers all major theories related to the origin of life, the early evolution and diversification of cells, and the emergence of eukaryotic cells with their structural novelties, such as nuclei, mitochondria, and plastids. . . . The bottom line: I really admire this book and expect to refer to it frequently in the future. . . . Harold does a marvelous job of reviewing and summarizing an unwieldy mass of literature on the origin and early diversification of life and providing some opinions about which theories and lines of research seem promising.”

(David Baum, University of Wisconsin-Madison *Reports of the National Center for Science Education*)

“This book is a rare pleasure: a beautiful, rational, wise, and eloquent framing of life’s greatest mysteries, what remains to be known, and how we might get there. It should be read by anyone who wonders, seriously, how we came to be. If it does not provide all the answers, that is because we honestly do not know.”

(Nick Lane *University College London* and author of *Life Ascending: The Ten Great Inventions of Evolution*)

“When dealing with difficult questions such as the origin of life, one yearns for writing that is both sagacious and readable, two qualities that don’t always go together. Fortunately, we can forego the need for making a choice. Harold’s book provides an account that is both masterful in the pursuit of the very question and in the clarity with which he unravels relevant phenomena. I daresay that few more helpful guides to a complex terrain have come forth since Dante’s Beatrice.”

(Moselio Schaechter, Distinguished Professor, emeritus *Tufts University*)

“The origin of life is one of the great enigmas yet to yield to modern science. While there are other books that attempt to place their own spin on how life came about, *In Search of Cell History* stands alone in that it is written not by one of those advocating a particular viewpoint but instead by one who tries to remain a detached, albeit extremely well informed, observer of events. An excellent piece of scholarly work by a suitably unbiased and appropriately skeptical researcher.”

(Mark A. Farmer *University of Georgia*)

About the Author

Franklin M. Harold was born in Germany, grew up in the Middle East, and became a scientist at the City College of New York and the University of California, Berkeley. His professional career spans forty years of research and teaching, mostly in Colorado. He is professor emeritus of biochemistry at Colorado State University and affiliate professor of microbiology at the University of Washington. Harold’s interests include the physiology, energetics, and morphogenesis of microorganisms, with a continuing interest in

evolution. He is a member of the American Academy of Microbiology. Harold is also the author of The Vital Force: A Study of Bioenergetics and The Way of the Cell: Molecules, Organisms, and the Order of Life.

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Jane Nelsen:

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