Preface

"The story of a theory's failure often strikes readers as sad and unsatisfying. Since science thrives on self-correction, we who practice this most challenging of human arts do not share such a feeling. We may be unhappy if a favored hypothesis loses or chagrined if theories that we proposed prove inadequate. But refutation almost always contains positive lessons that overwhelm disappointment, even when no new and comprehensive theory has yet filled the void."

Stephen Jay Gould

There can have been very few occasions on which an unresolved issue in science such as *The Origin of Chirality in the Molecules of Life* has been the subject of such a large number of approaches, nor that the theories intended to explain it have arisen from such widely different perspectives. Ranging from sophisticated theories in quantum physics and the complexity of evolutionary biochemistry, to the simple trivialization of the problem, this topic leaves hardly anybody impassive. Even after more than 150 years of discussion the issue remains a provocative open question.

Attempting to forecast the future in science can be fun, but more often than not it is a hopeless cause. Very occasionally a scientist of outstanding intelligence appears, and Louis Pasteur was one of these. He arrived at the conclusion that a *dissymmetric force* in Nature was in some way responsible for biomolecular handedness. From this theory he initiated the search for *deterministic theories* which might explain the contemporary observation of homogeneous chirality in biomolecules—but he never saw the fruits of his search. Pasteur's original concept of a dissymmetric force in the Universe was in essence correct, however. Although he could hardly have imagined its fundamental nature and extent, it was in some respects a premonition of the discovery of the weak force a century later. The weak force is a permanent chiral bias acting everywhere

The Origin of Chirality in the Molecules of Life
Albert Guijarro and Miguel Yus

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and at all times in the Universe. It is thought—although this has not so far been established quantitatively—to be responsible for what is probably the largest asymmetry occurring in the Universe, the overabundance of matter rather than antimatter, or charge asymmetry. It also determines the arrow of time, signifying the direction of the time–flow in particle physics, and it allows a preference for an absolute chirality, establishing an energy difference between enantiomers.

At our current level of knowledge and our ability to interpret the facts, the origin of these asymmetries is tied in with the forces existing immediately after the Big Bang, and specifically with the weak force. Being left-handed in character, the weak force imprinted its sign on the evolving Universe. However, when extrapolated to the molecular level—of particular relevance to us here—the weak force is unable to provide a complete answer to the origins of biomolecular homochirality. It has still to be unequivocally established whether the connection between the preference of the weak force for one enantiomer, and the homochirality displayed by living organisms, exists or not, and if the one is the cause of the other.

"One never notices what has been done; one can only see what remains to be done."

Marie Curie

Dozens of alternative deterministic theories have been postulated in the past, many of them resting on solid ground but in every case unsupported by clear experimental evidence. Theories that rely on long or even evolutionary timescales, mainly due to the smallness of the suggested chiral bias, have little chance of ever being tested experimentally. In other cases, rather like fashionwear, some of the better older theories have drifted out of favor and acceptance and have become unfashionable, overshadowed by theories which although more recent are not necessarily better. Re-examination of these ideas, faded with time but still good in shape, has been felt worthwhile and has been one of the goals of this work.

"A philosopher once said, 'It is necessary for the very existence of science that the same conditions always produce the same results.' Well, they don't!"

Richard P. Feynman

This quote could be taken as an introduction to an alternative group of theories considered in this book, those based on *chance mechanisms*. In chance theories there is no requirement for Pasteur's dissymmetric force or chiral influence. Chance mechanisms inherently produce a random outcome to ultimate macroscopic chirality. In any event, an amplification of an initial random chiral fluctuation at the molecular level seems to be the underlying mechanism, the robustness of this amplification determining the feasibility of the process.

The replication of a polynucleotide of randomly generated chirality is one obvious choice for such an autocatalytic growth mechanism. On the other hand, a similar role could be provided by certain polypeptides, or other as yet undetermined macromolecules of prebiotic relevance. Within these theories, the ultimate sign displayed by molecules in the biosphere has developed by chance—and it is certainly untestable. But some mechanisms should still explain the randomness of the outcome and possibly reproduce this effect.

> *"It seems plain and self-evident, yet it needs to be said: the isolated knowledge obtained by a group of specialists of a narrow field has in itself no value whatsoever, but only in its synthesis with all the rest of knowledge and only inasmuch as it really contributes in this synthesis towards answering the demand, 'who are we?'"*
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> Erwing Schrödinger

Some of the theories discussed in this book could be discarded if we were capable of addressing another old but still unanswered question: is life a common feature of the Universe? Would it be reasonable to expect life to have emerged in other planets under conditions similar to those on Earth? Research efforts on the origin of chirality in the molecules of life run parallel to those involved in the search for the origins of life, and they could retrieve important information from the same sources. Exobiology is one of these. Undoubtedly the search for molecular life or its vestiges in other planets is of the upmost importance. More accessible, although still a difficult task, is the search for traces of fossil life in Archean sediments; of special significance (and difficulty) would be to rescue any traces of organic matter, possibly prebiotic, that may somehow have escaped destruction during geological processes. Replication of plausible prebiotic reactions in the laboratory and developing them to the point of giving them self-replicative and evolutionary functions akin to living matter is another of these fronts, at the moment perhaps the most accessible.

If life at any molecular level is in fact such a highly exceptional occurrence, every theory has a chance of being correct, including those which seem at first sight most improbable. On the other hand, if life is indeed a common feature—and this is perhaps the more widely accepted view—theories based on a remote combination of factors become less convincing. Clues to this puzzle are likely to emerge from studies in widely different fields, including geology, biology, chemistry, physics and astronomy, and will involve the expertise of a broad interdisciplinary array of scientists. Important pieces of information will arise from observations at the extremes of two of the frontiers of science, outer space and the subatomic world. Observations on distant planets and galaxies, and even the actual sampling of celestial objects outside the solar system, are projects currently in hand. At the opposite end of the spectrum experiments are planned which will reveal the elemental properties of matter beyond the framework of current physics, such as symmetry and interactions between the fundamental forces of Nature. We are at present only beginning to appreciate the levels at which fundamental forces might operate, and we can be confident that these efforts are about to bear fruit.

Finally, we wish to pay tribute to the protagonists of this work: those scientists from all fields of science who have contributed in one way or another to its shaping. Arising from their stimulating teaching and the heated discussion which have often been generated, we have made an attempt to collect the essentials of the theme as it has evolved over a period of many years. We apologize for any omissions which may come to light. Unfortunately these are almost inevitable in compiling such a vast and interdisciplinary review and condensing it to a concise format. Finally, we extend our special thanks to those with whom we have shared stimulating discussions, and who have enlightened our thinking. We are also grateful to all those who have played a part in the editing and production process.