Short Note

Preface for the Updated Chinese Translation of Gilbert N. Ling's *Life at the Cell and Below-Cell Level*

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TO THOSE familiar with modern cell biology but unfamiliar with the work of Gilbert Ling, the message in this book will come as a surprise. Ling's view of cell biology will appear to have come from another planet. It is entirely different from the textbook view. On the other hand, we have come to know that the view from outer space can reveal insights that are not easily discernible from vantage points on the planet itself. And, that is what is brought by the monumental contribution of Gilbert Ling's extraordinary and unique insights.

I first met Gilbert Ling at a small meeting in Hungary in the mid 1980s, although I'd known of his alternative views for many years. For me, this meeting was a turning moment. The strength of his evidence, the logic of his arguments, and the sheer sense of resonance created by his paradigm convinced me that he was onto something of fundamental significance. And, others at the meeting shared my views.

New to this field, I not only read his books and papers avidly, but also dispersed them to the best of my students and fellows, who devoured them. Not one of them thought the message was any less than very close to ground truth, and I soon realized that my initial response may have been correct after all. Ling had apparently identified the most foundational features of the living cell, and our laboratory began turning its attention in that direction. Although my own book, *Cells, Gels and the Engines of Life* (Ebner and Sons, 2001) moves in a slightly different direction, it nevertheless builds on the central concepts identified by Gilbert Ling.

This book is Ling's attempt to summarize his views for the non-expert. Please don't expect an easy read. Because the book is built on orthodox physical chemistry, any attempt to circumvent the basics will have resulted in a piece that could easily come across as superficial. This book is anything but superficial. Hence, non-experts will need to spend some time dwelling on the many conceptual gems in this crown of a book. And, the reward will be great because Ling provides a fresh foundation on which to build.

To me, Ling's message contains two striking departures from convention. The first is that the cellular machinery considered by cell biologists to lie mainly in the cell membrane actually lies in the cytoplasm. Ling disputes, for example, the existence of cell-membrane pumps. One needs to take his arguments seriously because they are based on

evidence that has yet to be seriously challenged, though biologists continue to "discover" more and more membrane pumps. The story is fascinating—so much so that more than a few students to whom I've shown his arguments have been compelled enough to change their research directions.

A second departure from convention is long-range water ordering. Ling disputes the widely held view that most cellular water is ordinary bulk water, and argues instead for long-range ordering. If cellular water is ordered, then the milieu inside the cell is qualitatively different from convention, which holds that solutes readily diffuse through the cell. Ordered water excludes solutes, which would evidently have difficulty diffusing through such a milieu. I'm pleased to say that our own experiments have confirmed Ling's prediction even more powerfully than perhaps even he might expect: next to hydrophilic surfaces, ordering out to even millions of molecular layers can occur in some circumstances. Hence, Ling's assertion appears to be valid. It fits his construct very well, while modern cell biology has no easy way to deal with this feature, which in itself implies that the textbook view must be fundamentally erroneous.

So, please do read this book. It will open your eyes to fresh views of how biology may really work.

I cannot close without making reference to the emerging system of doing science. In this system, Gilbert Ling is an anomaly. While modern science has become incremental in nature, Ling fits more naturally with the older system of doing science in which kudos were given to approaches that tackled big questions. Gilbert's questions are indeed big. If he is right, then the way the cell really operates is grossly out of accord with the way textbooks would have it. For many, such an upending of the prevailing view borders on the impossible, for the entire—or almost entire—scientific world has come to a single foundational view, and looks upon those who are audacious enough to challenge that view with considerable skepticism. It has become virtually impossible to challenge a foundational construct without risking one's career.

In that sense Gilbert Ling is a scientific hero. He has bucked the establishment for more than a half century and has continued, year after year, to strengthen his basic position and to further open up new avenues of exploration. On this point, I believe that the substantially updated content of this volume will be a more eloquent persuader than I, regardless of how many words of praise I can add to this preface.

So, I urge the reader to immerse himself/herself with an open mind. Ling's book may appear to have been written by a scientist from another planet; but, after all, can one be certain that life on another distant planet might not be more advanced than life on earth?

Erratum

An article entitled "*Nano-protoplasm: the Ultimate Unit of Life"* was published in 2006 in this journal in Volume 39 from page 111 to page 234. In this article, an Equation 10 is presented on page 149 as follows:

$$n = \exp (- \gamma / 2). \qquad (10)$$

In this equation, n stands for the *Hill coefficient*. The symbol exp stands for natural exponential function to the base e. $- \gamma / 2$ stands for the *nearest neighbor interaction energy.* Unfortunately, as such this equation is incorrect because something has been left out. The corrected equation reads:

$$n = \exp (- \gamma / 2 RT). \qquad (10)$$

Here R represents the gas constant equal to 0.987×10^{-3} kcal/mole and T is the absolute temperature. At room temperature of 25°C, or absolute temperature of 298 °K, RT equals 0.593 kcal/mole. For a $- \gamma / 2$ equal to +0.67 kcal/mole, the corrected equation yields a Hill coefficient n of 3.1. This value agrees with other n-value equivalents of different $- \gamma / 2$ values given in Table 3, which appears on the same page where Equation 10 appears.