mological challenges provided by new technologies, such as molecular imaging, computer simulations of regulatory networks, and artificial life.

I have mentioned before that Keller is not a typical historian of biology and by her own admission she does not write comprehensive historical treatments. Yet, in the case of *Making Sense of Life,* the particular arrangement of chapters and themes and the implicit linear time frame does suggest a certain developmental perspective on its own. Therefore, the selection of topics is more of an issue in this work than it has been in Keller's other writings. Keller carefully selected her examples as illustrations for her main themes; the role and meaning of models, metaphors, and machines in explanations of development and the changing standards for explanation and "understanding" in the recent history of developmental biology. Following a standard practice of developmental biologists, Keller chose several "outliers," hoping that the unusual cases reveal more about the epistemological conditions than the mainstream or "normal" cases. While I am sympathetic to this approach—I do think that we can learn as much if not more about science from its failures than from its successes—I also believe that such an approach only makes sense when it is embedded within a reasonably detailed account of the historical development of the discipline at large, much the same way as gene knockouts or tissue transplantations need to be interpreted within the framework of a theory of "normal" development.

Therefore, I find the many omissions of the (successful) history of attempts to understand the development of the embryo in *Making Sense of Life* rather problematic. Keller provides us with insights into the work of Leduc, D'Arcy Thompson, Rashevsky, and Turing; discusses the theoretical work related to genetic information, regulation, and positional information; and introduces recent developments in visualization, computer simulation, and artificial life. However, without any or very little reference to the work of Roux, Driesch, Wilson, Loeb, Goldschmidt, Spemann, Needham, Przibram, Kühn, and Waddington as well as the more recent contributions of Gierer, Gehring, Hadorn, Lewis, Wieschaus, and Nüsslein Volhard, etc., Keller's analysis suggests a rather one-sided picture of what "understanding" meant in 20th century developmental biology.

Another point of critique is Keller's implicit equation of theoretical biology with mathematical biology. With the exception of Leduc's osmotic models and his vision of a synthetic biology, Keller introduces only specifically mathematical approaches to development and investigates their epistemological status and historical fate. This bias owes a lot to Keller's own acculturation within mathematical biology; however, it also leaves out a whole discourse of theoretical biology that was not specifically mathematical and that contributed a lot to explanations of development. Conceptual questions of the kind that Keller addresses in her book have been part of a more inclusive discourse of theoretical biology during the first decades of the 20th century. Interestingly enough, this discourse of theoretical biology was also closely linked with empirical studies. One of the centers of this earlier version of theoretical biology was the *Prater Vivarium*, Vienna's privately owned Institute for Experimental Biology, devoted to the experimental study of development, evolution, and regeneration in a variety of animal and plant species. The declared goal of its founder Hans Przibram was to arrive at "generalizations" that would unite several detailed empirical studies (Przibram, *Experimentalzoologie* vol. 1–7, Wien: Deuticke, 1907–1929). Przibram also contributed to mathematical biology (Przibram, *Aufbau mathematischer Biologie*, Berlin: Borntraeger, 1923) and, as the mentor of both Paul Weiss and Ludwig von Bertalanffy, his influence continued well into the second half of the 20th century. Examples such as the *Prater Vivarium* make Keller's experience of the total separation between the cultures of experimental and mathematical biologists less of an inevitable epistemological divide. Such examples might also lead to a different answer with regard to Keller's question whether "Life" is a natural or a human kind. The continuity of the experimental tradition in developmental biology, especially when compared to the more contingent history of mathematical models, certainly represents a challenge to philosophical interpretations that concentrate largely on linguistic systems (see Rheinberger, *Towards a History of Epistemic Things: Synthesizing Proteins in the Test Tube*, Stanford, CA: Stanford University Press, 1997). It does not, however, diminish the importance of detailed historical analysis of these developments.

In conclusion, *Making Sense of Life* is a stimulating and irritating book. It is stimulating with regard to the questions it raises about what constitutes an adequate explanation in developmental biology and how we can reconcile different explanatory paradigms. It is irritating with regard to what it leaves out (much of the important work in developmental biology of the 20th century) and what it suggests (a very narrow and restrictive definition of theoretical biology as mathematical biology and a rather unconvincing challenge to the possibility of us reaching an understanding of development due to the enormous complexities of life). Yet Keller's essays are an important and much needed and appreciated contribution to our current discourse in developmental biology. Reading *Making Sense of Life* and arguing with Keller (in effigy or in person) is indeed thought provoking, inspiring, and rewarding.

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About the Description and the Origin of Biological Differences

Biochemical Adaptation: Mechanism and Process in Physiological Evolution
By Peter W. Hochachka and George N. Somero
Oxford: Oxford University Press (2002).
544 pp. $40.00

About 3.8 billion years ago, the primitive earth was composed of unusual environments from which cell prototypes, somewhat similar to certain modern prokaryotic and eukaryotic cells, were born. In relation to this point, three fundamental questions can be addressed. (1) What were the physico-chemical properties of the protobiotopes from which life eventually emerged? (2) Was early life characterized by a certain biodiversity? (3) How have these primeval cells evolved? In other words, what are the processes that have fashioned, century after century, the actual biodiversity we now observe?

The answers will not be found in the book by P. Hochachka and G. Somero, but the complexity of the problem and of the challenging tasks and unresolved questions that await intrepid scientists is underlined.

When I started to read this book, a few days after receiving it, terrible news was brought to me by Janet Storey. Peter Hochachka passed away on September 16th, victim of an aggressive lymphoma; he was in his 65th year. A farewell letter written by Peter just a week before his death was sent to me and to his other friends and colleagues. This letter was full of dignity, without any anger, bitterness, or sadness; it was rather a message of hope underlining how his scientific life had been a wonderful experience. I will certainly remember forever the last sentence: "I now have my next assignments: to check out the concept of parallel universes and the implications of entanglements."

Peter Hochachka and George Somero are two names that have been associated with the production of some of the best papers related to the adaptation of organisms to various environmental conditions. Two scientists who have really marked the field of fundamental comparative biochemistry and physiology through their perspicacity and ability to accurately predict adaptation mechanisms based only on scarce experimental evidence. Two visionaries who, through their enthusiasm and capacity to present complex matters simply, have inspired many young scientists to join the challenging field of biological adaptation processes. Two people so different in character but undoubtedly so complementary: Peter Hochachka being highly extroverted, boiling with ideas, having as he often said "a noisy brain," and George Somero, much more reserved, thoughtful, rather favoring the systematic approach. They are back, with the third and probably now the last edition of their book. The twelve chapters of the previous edition, published in 1984, have been regrouped and synthesized into only seven in the new one. The topics covered are, however, quite similar to those of the 1984 book and correspond in fact to matters that have been investigated by the authors in their respective laboratories.

Generally speaking, the book appears to cover two different aspects related to adaptation: the first describes the biodiversity in certain environments without focusing on the mechanism sustaining the adaptation to local or transitional changes. The second is clearly an attempt to elucidate the processes, as in the chapter on temperature, that have led to biochemical and physiological adaptation to a specific physical or chemical parameter. This is clearly indicated in the first chapter, "The goals and scope of this volume," which defines the vocabulary used. For example, by "adaptation" they connote either the process through which a biochemical trait arose and its history or the current utility of the trait. They also underline the importance of time when speaking about adaptation, signifying the time available to fabricate the response. This varies principally according the underlying source of the adaptive mechanism: genotypic adaptation requires numerous generations of selection, while phenotypic adaptation is more rapid and generally entails modulating the activities of biochemical systems through changes in gene expression. Another important fact is underlined: that the biological world is both unified, by conserved processes such as glycolysis, and divided, by diverse strategies in other arenas.

The second and third chapters provide background on cellular metabolism and homeostasis, and on oxygen availability, respectively. There are minor mistakes and omissions in the equations related to ATP production here and some confused classification of certain anaerobic respiration processes, like the reduction of CO_2 into methane and SO_4^{2-} into S^{2-}, as fermentation. (Regeneration of NAD^+ is not required in these contexts; however, in true fermentation processes, oxidation should be compensated by a reduction step, such as in glycolysis where pyruvate is reduced to lactate in order to regenerate the needed NAD^+.) These chapters nevertheless provide a valuable comparison of ectotherms and endotherms in extreme situations such as oxygen depletion during prolonged or abrupt physical activity, and a very interesting in-depth treatment of high-altitude adaptation and hypoxia tolerance studies in fish and invertebrates.

Chapter 4 is devoted to the analysis of the biochemical and physiological parameters involved in the adaptation to diving, focusing mainly on data obtained from seals. In relation with what was mentioned earlier, the authors illustrate the fact that some characteristics required for diving are in fact conserved in all vertebrates (unity) even in those that are not usually diving animals, but there are other characteristics that are more variable and possibly species specific (diversity). One will learn, for example, that during diving, the heart rate in Weddell seals goes down dramatically from 65 beats per minute to about 5 beats per minute after 20 minutes of diving and that similar observations were made in human beings, with one individual displaying a heart rate as low as 6 beats per minute on diving. A comparison with the hibernation process shows that both adaptations have common characteristics, including cardiac output and hypometabolism. Variable characters directly related to diving capacity or performance are spleen and blood volume as well as red blood cell mass in relation, of course, with blood viscosity and O_2 carrying capacity.

The chapter on diving is followed by a chapter discussing human hypoxia tolerance. This is mainly treated by comparing the physiological and biochemical status of lowlanders, suddenly or progressively exposed to high altitude, to that of native highlanders such as the Quechuas from the Andes or the Sherpas from the Himalayas. One of the apparent paradoxes resulting from the acclimatization of lowlanders to high altitude is that the postexercise blood lactate concentration decreases as a function of the altitude; the higher the altitude, the lower the lactate peak. This is apparently due to the coupling of lactate and ATP production, thereby shifting the equilibrium of the reaction catalyzed by creatine phosphokinase towards the production of ATP. Although a high proportion of the physiological characters related to the adaptation to altitude of lowlanders and highlanders are conserved, adaptable characteristics are also observed. It is not surprising to record that heart metabolism in lowlanders utilizes fatty acids, glucose, or lactate depending on the availability. In highlanders, however, the use of glucose is significantly preferred because the ATP yield per O_2 consumed is significantly higher than for the fatty acids. Another striking characteristic of highlanders is the higher proportion of slow twitch fibres in their skeletal muscles, consistent with their ability to reduce the lactate accumulation during exercise. The phylogenetic origin of human hypoxia tolerance is also discussed, first under the form of a convergence hypothesis resulting from the selective pressure exerted by high altitude, and second by a common descent hypothesis based on the possible fact that the human species originates from cold and dry environments characterized by medium altitudes.

Chapter six is, in my opinion, the most interesting chapter of the book. It deals with the roles played by water in living organisms and therefore is of general interest. It addresses some fundamental questions regarding the types of solutes, organic and inorganic, that have been selected and how they are taken up or synthesized. Other questions treated are why intracellular K^+ has been preferred to the more commonly encountered Na^+ and how macromolecular structures such as proteins can be stabilized, through the exclusion principle, by compatible solutes such as polyols, other sugar derivatives, and amino acids. The importance of water as a bad solvent for amino acid side chains in the folding of proteins is also stressed. In this context, the role of hydrophobic interactions may be overestimated. Indeed, the authors write, "In hydrophobic interactions, the entropy change plays the dominant role in the overall free energy change (ΔG) of the process." If this is true at low and moderate temperatures, at higher temperatures the hydration process does not play a significant role and the entropy change tends to zero. Therefore, the hydrophobic interactions do not occur with a positive modification of the enthalpy anymore but a negative modification due to the fact that the only residual force is due to Van der Waals interactions. The authors are certainly aware of this, since at the end of the chapter, the hydrophobic effect is more generally discussed in the context of thermophilic organisms. I cannot, however, accept the idea that hydrophobic stabilization is lost at elevated temperatures even if it is reduced to Van der Waals interaction that are almost independent of the temperature (Makhatadze and Privalov, Adv. Prot. Chem. *47*, 307–425, 1995). An interesting paragraph is also devoted to the performance of intracellular enzymes, both at the fundamental level of the interrelation of substrate concentrations, k_{cat} and K_M values, as well as at the cellular level of the organization of proteins in the cytoplasm. The problem of halophilicity is also analyzed as well as that of the adaptation to desiccation, with a thorough analysis of the role played by trehalose and sucrose in the survival of desiccated cells.

The final chapter is also the longest (160 pages) and is an exhaustive analysis of the effects of temperature on living organisms. To my knowledge, it is the only publication that covers the numerous temperature adaptation processes known to exist in living organisms. This has obviously forced the authors to an extraordinary effort of synthesis, which was in any case worthwhile and extremely helpful for the reader. The chapter classically starts with the reductionist approach describing the effect of low and high temperatures on macromolecular structures such as proteins and supramolecular structures such as membranes. Several incursions in the extremophile world of prokaryotes, both psychrophiles and thermophiles, are made, underlining the importance of flexibility for preserving enzyme activities at low and high temperatures in a way similar to the homeoviscosity concept in membranes. Again there are, in my opinion, some thermodynamic concepts that are oversimplified, such as the activation entropy compensation phenomenon encountered in cold-adapted enzymes. Indeed, the ΔS^* for cold-adapted enzymes is not always negative; it can also be positive as hydration processes play an important role in entropy changes, depending on the enzyme concerned. What is important is that the difference between the activation entropy change of a cold-adapted enzyme and its mesophilic counterpart Δ (ΔS^*)p-m is always negative (Lonhienne et al., Biochim. Biophys. Acta *1543*, 1–10, 2000), and this explains to a certain extent why the adaptation cannot be fully achieved. Furthermore, on p. 341, in relation to hydrophobic interactions, it is questionable whether the term [$-T\Delta S$] takes on a smaller absolute value as temperature is reduced since the entropy changes largely increase concomitantly. These points are of course minor and do no affect the overall quality of the writing, which continues well, with an analysis of the differences between endothermy (homeothermy) and ectothermy, and the role played by the brown adipose tissue as a heat producer. In the same context, mechanisms of heat generation through shivering and nonshivering thermogenesis are also analyzed. The chapter ends with freeze avoidance mechanisms through the production of antifreeze compounds, which allows some insects to survive exposure to temperatures as low as -55°C, as well as freeze tolerance with a thorough description of the chemicals involved.

In summary, this is an extremely valuable and well-written book, a remarkable synthesis of the extremely diverse studies devoted to the physiological and biochemical adaptations in various living organisms, in particular multicellular organisms. The different chapters are rendered more readable thanks to the clear interpretation and careful analysis of the data by these two prominent scientists.

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