sors. Unfortunately, the cytokine appears not to influence B lymphopoiesis in humans and no factor with comparable function has been found. There are also dramatic species differences in expression of the enzyme TdT during human, but not murine fetal life. This has important consequences for the diversity of lymphocyte antigen receptors at birth, and we should be reminded that our experimental models have limitations.

One of the attractive aspects of immunology is the fact that strongly held opinions are frequently demolished by new data. While this is a good thing for the experimentalist, it creates a challenge for textbook authors. Schemes for early stages of lymphocyte differentiation shown in this book are already being questioned and other "likely" scenarios will fall with further study. Fortunately, tables from the book will be available and frequently updated on a web site. It would have been even better if this terrific idea were extended to many of the 156 figures in this volume.

Throughout the text, the author treats us to many amusing metaphors. For example, we learn about lymphocyte precursors that are not "truly committed in an irreversible Calvinistic sense." Immature self-reactive B cells are "given an opportunity to reform themselves" via receptor editing "and become useful citizens." In contrast to apoptotic cells, "necrotic cells erupt in explosive incandescence, singeing their neighbors and generally trashing the neighborhood." This lightens the mood and reminds us that lymphocytes are more than lists of molecules.

In summary, Pillai casts a wide net—generating a very dense textbook of immunology. Not intended for beginning students, it is nevertheless a very useful reference with nice capsule summaries of such diverse topics as apoptosis, immunodeficiency, and NK cells. While comprehensive, we are left with the certainty that there is much yet to learn about lymphocyte development. That is good news for students looking for a hot field.

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Come Together

Protein-Protein Recognition
Edited by Colin Kleanthous
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The ability of proteins to recognize each other in a specific manner and to form stable complexes is a hallmark of most cellular processes, including signal transduction, cytoskeletal remodeling, and vesicle transport. With such a large number of disparate functions to be carried out in the life of the cell, it is not surprising that the factors that govern these interactions are exceedingly complex and incompletely understood. Many fundamental chemical factors, such as van der Waals attraction, hydrogen bonding, hydrophobic packing, and shape and charge complemetarity, have been known to be important in protein-protein interactions for decades. Other, less ubiquitous and more evasive, factors, such as allostery, cooperativity, and plasticity, have also been identified as important influences on protein-protein recognition. While the advent of recombinant protein production, site-directed mutagenesis, and sophisticated techniques for determining the energetics of protein binding have made it possible to begin to dissect each of these influences individually in model protein interaction systems, the facile extension of these findings to the entire spectrum of protein-protein interactions has commonly been wrought with pitfalls. The reasons for this conundrum are likely to be as numerous and complex as the factors that influence these interactions, perhaps not the least of which is what appears to be the inherent messiness of biology which, relative to fields such as physics, presents a paucity of general theories and overarching laws. Further confounding the issue is that we seem to be expanding the list of rules that govern these interactions at least as quickly as we are understanding those that have been on the list for so long. Realizing, for example, that two interface hydrogen bonds that appear structurally equivalent can diverge so radically from an energetic standpoint (that is, while one of the bonds is an energetic "hot spot" the other is energetically insignificant) goes a long way in preventing the simple classification of hydrogen bonds according to their importance in protein interactions. Some factors that influence protein recognition, such as protein plasticity, have been deemed important in this regard so recently that it is not even clear whether they have generally negative or positive impacts on binding affinity. Still other, as yet undetermined, factors that influence these reactions are certain to be lurking around the next bend. In the evolution of elucidating the mechanisms that govern protein-protein interactions, we are hardly walking upright.

Understanding protein-protein recognition, though, is only becoming more critical if we hope to harness the power of nature for those uses that are deemed most worthy. As an example, the rapidly growing availability of crystal structures of therapeutically relevant protein-protein complexes has created opportunities to design small molecule inhibitors of protein-protein association that bind their targets with high affinity and specificity. However, this task has proven exceedingly difficult, with the affinities of designed compounds for their target proteins rarely exceeding the micromolar range. In contrast, there are numerous examples of high-affinity, rationally designed small molecule inhibitors of enzymes which, unlike the large and relatively flat interfaces characteristic of protein-protein complexes, generally have deep pockets on their surface in which ligands can bind. As we pass into the post-genomic era, our attention naturally shifts to the products of the genomes that have been unravelled—proteins. While the initial focus of this new age will be the description of the three-dimensional structures of all of these gene products, not far behind must be the determination of how they all fit together. If a gene is considered only as good as the protein for which it codes, it follows that a protein is only as good as the interaction(s) in which it is involved; that is to say,

the process by which it carries out its function. In a world in which the sequencing of entire genomes, the structural elucidation of massive, multicomponent complexes such as the ribosome, and the identification of the proteins involved in every protein-protein interaction in an entire organism have become feasible, utilization of all of this information will increasingly depend on the succint definition of the biochemical requirements for protein complex formation.

Colin Kleanthous certainly understands the increasing importance of protein-protein interactions and has assembled an excellent and timely book on the subject. The book begins with two introductory chapters that deal, in turn, with the thermodynamics and kinetics of protein interactions and the structural basis for protein recognition. Kinetics and thermodynamics are presented here from a truly biological viewpoint. This is not the formal language of the physical chemistry textbook collecting dust on your bookshelf, but instead is a more practical treatment of the subject and highly reflective of the reality of collecting and making sense of the kinetic and thermodynamic data pertinent to biological systems. The first chapter by Janin is exceptional as an introduction to anyone interested in the energetic quantification of biological interactions and would lend itself well to graduate courses dealing with macromolecular association. The second chapter by Jones and Thornton concerns itself with the generalities of protein interfaces, including their size, shape, complementarity, hydrophobicity, and polarity. Description of these interface attributes for a variety of protein complexes is followed by a brief review of current work in predicting the surfaces of proteins that are involved in protein-protein interfaces, which serves to tie them together nicely.

The remainder of the book is devoted to a series of chapters concerning different classes of proteins. Each of these chapters serves as a concise and illuminating review of the proteins and protein-protein interactions inherent to electron transfer (Mathews, Mauk, and Moore), integrin (Humphries and Liddington), antibody-antigen (Braden and Poljak), MHC-T cell receptor (Daffron and Lesk), signal transduction (Hyvonen, Begun, and Blundell), and protease (Laskowski, Qasim and Lu) and nuclease (Kleanthous and Pommer) inhibitor complexes. By themselves, the review chapters are not so different than detailed reviews found in any number of journals. The collective power of these reviews, however, comes not only from their assembly together in one text, but also from their clever arrangement according to the affinities of the protein complexes they describe, from millimolar to femtomolar. Thus, the book describes protein-protein interactions along the entire affinity spectrum relevant to biological systems. Just as proteins come together to form complexes that carry out the necessary functions of the cell, the collection of review chapters in *Protein-Protein Recognition* come together to paint a tableau of recurring themes that are imperative to the understanding of complex formation by proteins. While at first glance the review chapters may appear to lack a certain coherency, a complete reading of them creates a synergistic effect. Not only will the reader better understand the interplay between the different types of chemical interactions in protein interfaces with the kinetics and thermodynamics of binding, but will also further his or her appreciation of some of the more complicated influences on protein interactions such as allostery, avidity, cooperativity, and plasticity throughout the affinity spectrum and their involvement in the mechanistic roles of these proteins.

The introductory chapters are indispensable as guides to common factors observed in protein-protein interactions, and each review chapter is well written and well referenced, representing excellent platforms for further investigation to each of their respective classes of proteins. It is the collection of the parts, however, that produces a book more valuable than their sum, one that will prove helpful to many a protein biochemist. While *Protein-Protein Recognition* will serve as an exceptional sourcebook for its subject for some time to come, we hope, and expect, that our understanding of the rules that govern protein-protein interactions will progress to the point that shifts the balance of chapters toward those defining the common characteristics of these reactions and away from those that serve as reviews of particular classes of proteins.

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An All Too Visible Adversary

The Invisible Enemy: A Natural History of Viruses
By Dorothy H. Crawford
Oxford: Oxford University Press (2000). 275 pp. $25.00

By the time this review appears, the pyres currently burning across the UK will, hopefully, be declining and Britain will be emerging from the latest of its bouts of livestock infection and health scares. The recent epidemic of foot and mouth disease virus (FMDV) infection of cattle, sheep, and pigs, which by mid-April saw more than 1 million animals slaughtered, paralyzed regions of the British countryside, destroyed agricultural and rural businesses, and cost the taxpayer untold millions. It also served to again emphasize our fragile relationship with viral pathogens and the huge economic and emotional burden these agents impose on our societies. The view has been expressed that this particular incident is further evidence of declining standards in British agriculture driven by the persistent demand for cheap food. While the rapid dissemination of the virus may well have been encouraged by the way we choose to traffic and kill our domestic farm animals, it is undoubtedly the case that these sorts of epidemics are likely to occur, and with increasing frequency, when large populations of susceptible hosts are available for infection. Indeed epidemics and pandemics of one virus or another in humans, or our crops and livestock, seem to be on the increase. Perhaps this is not too surprising given the nature of the social existence we have developed for