classed correctly as helix, strand, turn, or irregular. It now seems clear that the secondary structure is determined to a significant degree by interactions in the threedimensional structure between residues distant in the primary structure. The most striking demonstration of this is that 80% of pentapeptides with the same sequences have different conformations in unrelated proteins (although the relevance of this observation is disputed by the editor on p. 220). The more adventurous now attempt to incorporate tertiary structure into their predictions by using concepts such as amphipathicity (discussed here by Finer-Moore et al.) and hydrophobic moments (Rose and Dworkin; Eisenberg et al.) and distinguishing between different classes of tertiary structure.

Most attempts to predict protein tertiary structure concentrate upon finding patterns in sequences that are compatible with a single conformation that is already known, and there have been some noteworthy successes of this approach. In 1979, Ptitsyn, Finkelstein, and Murzin predicted the unknown protein uteroglobin to have four αhelices and proposed that it had a four-helix bundle structure, like that found in several known proteins. When the crystal structure was subsequently determined, the four helices were confirmed, but the dimeric molecule had them packed together somewhat differently. This structure also contained two unnatural disulfide bonds, however, and the natural protein demonstrates considerable flexibility, so the verdict on this prediction needs to be reserved. More recently, in 1987, Crawford, Miermann, and Kirschner analyzed the sequences of ten tryptophan synthase α-subunits and noticed that eight repeated β-strand/turn/α-helix/ turn motifs were predicted. This suggested that the tertiary structure is an eightfold α/β barrel of the type observed first in triosephosphate isomerase and subsequently in at least 15 additional proteins with apparently unrelated sequences. The crystal structure of the α-subunit entirely confirmed this prediction. Interestingly, another prediction was misguided by experimental evidence that the protein contained two independent domains. In the same year, Pearl and Taylor were able to match the sequence of an HIV protease with the acid protease structure and to propose a model for the HIV protease that was largely confirmed. Regan and De-Grado reported the successful preparation of a four-helix protein that had been designed entirely de novo. Although the exact structure has not yet been determined experimentally, all the evidence is consistent with its being the intended conformation. The folded conformation is remarkably stable, which

is perhaps the most impressive demonstration of the advances that have been made. Unfortunately, none of these accomplishments are mentioned in this volume.

Other shortcomings of the volume are common to multiauthor works: the unevenness of presentation (one chapter, Fasman's account of the development of the subject, is 124 pages long, whereas six are no more than 16 pages), that half of the chapters were apparently completed three years before publication, others one year, and that some authors fail to address the topic of the volume, concentrating instead on their usual interests. For readers in quest of the Holy Grail of protein prediction, however, this will hardly be noticed, for they will be engrossed in the large amount of detailed information available.

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