

The time-average structure [of a protein] observed by X-ray diffraction is something of an abstraction, since it is not itself widely—or even sparsely—represented at any given time in the population of molecules. I mean by this that if we were to take an instantaneous picture of the molecular population showing us all the coordinates of the atoms for each individual molecule we would have difficulty in finding one that will match the average in *all* respects, although *most* of the molecules will have *most* of the features in common with it. Indeed, the protein molecule model resulting from the X-ray crystallographic observations is a “platonic” protein, well removed in its perfection from the kicking and screaming “stochastic” molecule that we infer must exist in solution. The great importance of the former lies in that it has permitted us to see the origin of the “bulk properties” of the protein, which result from averaging over the whole population. However, when it comes to the conversion of one structure into another, and to render account of any dynamic function of the protein, consideration of the “stochastic” species is indispensable.

Gregorio Weber. (1975). “Energetics of ligand binding to proteins.” *Advances in Protein Chemistry* 29:64-65