Protein Crystal Structures at Atomic Resolution*

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The structural chemistry of the last 50 or more years was underpinned by small-molecule crystallography which provided a complete description of the molecule at atomic (roughly 1 Å) resolution. Crystallography could reveal the positions of all atoms in the unit cell and provide a detailed 3-D geometry of the whole molecule. No other technique gives comparable information. Protein crystallography is now playing a comparable role for biological chemistry and a full description of a protein is no longer complete without a 3-D structure. This is made even more important by advances in molecular genetics which mean that most proteins are potentially available in quantities suitable for crystallisation. X-ray analyses of crystals of macromolecules pose special problems are to the nature of the molecules themselves and of the way they pack into crystals. That they have large molecular weights means that the unit cells are large, resulting in large numbers of reflections, all of which are weak relative to the small-molecule case, with a low signal-to-noise ratio. This in recent years has been alleviated by the advent of efficient detectors, and most importantly, high-intensity synchrotron radiation (SR). However, this is not enough. In addition, the crystals contain on average about 50% disordered aqueous solvent and the molecules themselves betray substantial disorder especially at the solvent interface. Hence the intensities of the high-resolution data are even more weak or indeed absent. Furthermore, the crystals at room temperature are subject to substantial radiation damage. The latter problem has been greatly alleviated by the use of cryogenic freezing in the last decade which is now used for the majority of SR experiments. Taken together, the use of SR, 2-D detectors, and cryogenics have meant that for an increasing number of protein atomic resolution data (to 1.2 Å or better), can be recorded. This allows much more accurate models to be analysed with a full anisotropic model. Results on a representative set of examples will be described and implications for the future discussed. Most of the results have come from work carried out at EMBL Hamburg.

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