Effects of hydration and temperature on side-chain conformational heterogeneity in protein crystals

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Protein crystals contain large amounts of solvent, typically 30-70% by volume, that fills intermolecular spaces within the unit cell as well as internal protein cavities. Crystal solvent content depends on relative humidity (r.h.). Monoclinic lysozyme provides a remarkable model for studying structural changes induced by dehydration, as it maintains excellent order for relative humidities down to 5%. In this study, the modulation of main-chain and side-chain conformational heterogeneity and solvent structure in monoclinic lysozyme crystals by dehydration and temperature is examined.

Decreasing the relative humidity (from 99% to 11%) and decreasing the temperature both lead to contraction of the unit cell, to an increased area of crystal contacts and to remodeling of primarily contact and solvent-exposed residues. Both lead to the depopulation of some minor side-chain conformers and to the generation of new conformations. Dehydration from 99% to 93% r.h. and cooling from 300 to 100 K result in a comparable number of remodeled residues, with dehydration-induced remodeling somewhat more likely to arise from contact interactions. When scaled to equivalent temperatures based on unit-cell contraction, the evolution of side-chain order parameters with dehydration shows generally similar features to those observed on cooling to T = 100 K.

These results illuminate the qualitative and quantitative similarities between structural perturbations induced by modest dehydration, which routinely occurs in samples prepared for 298 and 100 K data collection, and cryocooling. Differences between these perturbations in terms of energy landscapes and occupancies, and implications for variable-temperature crystallography between 180 and 300 K, are discussed.