Protein Crystallization: Can Spherical Cows Help?

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X-ray crystallography is the gold standard for determining protein structures. Yet obtaining high-quality protein crystals usually relies on experimental trial and error. Understanding the physical drive for proteins to crystallize would help improve the experimental approach. Here, we consider a soft matter approach to study the crystallization mechanism of a family of proteins. By performing atomistic simulations, we characterize the surface contribution to protein pair interactions. The results indicate that the interaction varies significantly from one crystal contact to the other. Comparisons with homologs and mutants identifies high entropy residues as destabilizing factors in the formation of crystal contacts. We also analyze how salt concentration affects the pairwise interaction, both for hydrophilic and hydrophobic interfaces. This information is used to parametrize a "patchy" interaction model; the patch geometry, the range of interaction and the width of the patches is determined obtained this way. The phase diagram and crystallization pathway of the different proteins under study is then traced with advanced Monte Carlo techniques. The results show that the difference in the strength of the interaction between patches can drastically impact the position of the solubility curve, suggesting new strategies to achieve protein crystallization.