A Soft-Matter Perspective on Protein Crystallization

Crystallography may be the gold standard of protein structure determination, but obtaining the necessary high-quality crystals is more akin to prospecting for the precious mineral. Although the fields of structural biology and soft matter have independently sought out fundamental principles to rationalize the process, conceptual differences and limited crosstalk between the two disciplines have prevented a comprehensive understanding of the phenomenon to emerge. I present a computational study of proteins from the rubredoxin family that bridges the two fields. Using atomistic simulations, we characterize the crystal contacts, which we then use to parameterize soft matter models. Comparing the models’ phase diagrams with experimental results enables us to critically examine the assumptions behind the two approaches. We notably find that protein pair interactions vary widely from one patch to the other. We thus explore how interaction anisotropy affects protein crystallization. In order to better understand the chemical physics behind crystallization, we also perform a cheminformatics study of a large protein crystallization database. The Gaussian process approach we used is especially well suited to account for non-linearity among the system’s variables. This aspect is crucial for protein crystallization, which requires specific trade-offs between the effects. Preliminary results show that the model has high predictive power and identifies the key physico-chemical processes that control crystallization.

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