How a new Chemical Compatibility Test Facilitates Protein's Crystallization

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In early stages of a macromolecule's crystallization, when little information is known about a protein's solubility versus various chemicals, the selected strategy is to setup usual initial screens at protein concentration selected from past experience. Factors such as availability of protein or intrinsic protein physical properties can be used as guidelines, but again, they provide little help in selection of initial screens conditions.

During development of new optimization procedures and initial screens, we needed to find a new startegy which would address this question, and enable us to orient crystallization appropriately. Presented here is a new method to test a macromolecule's solubility against many chemicals which can be applied straightforwardly at experimental setup. Using this method, not only did we obtain a reasonable and necessary high level of precipitation in any selected initial screens, but results from this test can also be applied directly to optimization strategies like "Pro-Active" or "The Optimizer Series" presented earlier.

This strategy was applied to a series of 10 proteins, where solubility was tested against a series of salts, polymers, organics and buffers. From results obtained, initial screens and optimization methods were selected. This preliminary solubility evaluation, performed prior to crystallization setup, benefited not only initial screening results but also accelerated optimization process, using less protein compare to the classical optimization method.

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