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Protein Crystallization in the Year Twenty-two AM: What Have We Learned from High Throughput Crystallization and Structural Genomics We Did Not Know Before? Bernhard Rupp, Univ. of California, LLNL, Livermore, CA.

Twenty two years ago the first edition of Alex McPherson's seminal hardcopy "Preparation and Analysis of Protein Crystals" was published, followed by later refined editions. Since then, the NIH sponsored (PSI) structural genomics centers and similar efforts world wide have produced a wealth of crystallization data. One would assume that the analysis of massive amounts of proteomics and crystallization trial data engendered by the PSI centers should enable deployment of statistical methods and machine learning to gain new knowledge and to develop predictive algorithms for effective protein crystallization with confidence. However, there are already some indications that this process may not be as straightforward as it appears. The sources for the difficulties lie fundamentally in the complex physico-chemical nature of protein crystallization, resulting in non-trivial experimental design issues, which significantly limit the power of the data mining algorithms that can be deployed to tackle the problem. Although some new knowledge has emerged, one of the surprising results is that a great deal of what was initially based on empirical experience and chemical intuition has indeed been validated. The largest impact on improved crystallization so far seems to be the increasing availability of affordable robotics, which greatly reduce the tedium of protein crystallization. It would be interesting to speculate what the state of our knowledge of crystallization would be, had the 2004 Fankuchen awardee had access to such machinery in the BM age.