Letter to the Editor

COMMENT ON ‘PROTEIN ISOELECTRIC POINT AS A PREDICTOR FOR INCREASED CRYSTALLIZATION SCREENING EFFICIENCY’

A recent article in this journal (Kantardjieff and Rupp, 2004) describes a statistical predictor to increase the efficiency of protein crystallization screens. The approach is based on the observation that a correlation exists between the calculated isoelectric point of a protein, pI, and the difference between the pI and pH of the solution in which the protein was crystallized. Kantardjieff and Rupp specifically comment on the lack of any statistically significant correlation between a protein’s pI and pH of crystallization conditions. This has been well documented in the literature (Page et al., 2003; Wooh et al., 2003) and is also well understood in condensed matter science, where polymer model systems have been studied theoretically as well as experimentally for a long time (Belloni, 2000; Frenkel, 2002).

The purpose of this comment is to point out that while there is always a correlation between pI and pH–pI, it is of no significance when no correlation between pI and pH exists. Ignoring this fact has lead to a serious misinterpretation of the data. Ignoring this fact has lead to a serious misinterpretation of the data. This is visually illustrated using 10 000 pI and pH data distributed randomly and uniformly over the full pH range (Fig. 1A and B). Figure 1C and D was produced using the same analysis that Kantardjieff and Rupp used to produce Figure 3 in their paper, and which lead them to the conclusion ‘It is clear that basic proteins have a tendency to crystallize 0.5–3 pH units below their pI, whereas acidic proteins prefer to crystallize 0–2.5 pH units above their pI.’ Here, we demonstrated, that this conclusion is based on misinterpretation of the data and should not be used to guide crystallization experiments until a correlation between pH and pI is demonstrated.

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REFERENCES


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Fig. 1. A total of 10,000 uniformly, randomly distributed pI, pH data. (A) pH versus pI. (B) pH–pI versus pI. Because pI and pH are uniformly random over the same range, $\sigma_{pI} \approx \sigma_{pH}$ and $r_{pI,pH} \approx 2^{-1/2}$. (C) Frequency distribution of pH–pI for data with pI > 7. (D) Frequency distribution of pH–pI for data with pI < 7.