Computational Studies of Thioredoxin Superfamily

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Electrostatic interactions play important roles in diverse biological phenomena, controlling the function of many proteins. Their alterations are reflected in pKa values of ionisable, functional groups and in redox potential. Polar molecules can be studied with the FDPB method solving the Poisson-Boltzmann equation on a Finite Difference grid [1]. We present a method for the prediction of pK_a and redox potentials in the thioredoxin superfamily. The results are compared with experimental pK_a data where available and predictions are made for members lacking experimental pK_a data. The CXXC motif of this superfamily is essential for the catalysis of redox reactions and exhibits extensive variation of redox equilibria. A noteworthy example is the difference between *E. coli* thioredoxin E_0'=-270mV and *E. coli* DsbA E_0'=-122mV [2]. We show how our model, which includes sidechain rotamer variation for the CXXC motif, can be an effective predictive tool for pK_as and redox potential in the superfamily. A qualitative, rather than quantitative, correlation between cysteine pK_a and redox potential indicates that a pH-independent factor also plays a role in determining redox potentials across the superfamily [3]. A possible molecular basis for this feature is proposed. A clustering method that uses matrices of distances improves the speed of our calculations without loosing any accuracy. A pK_a spectrum across members of the superfamily is presented.

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