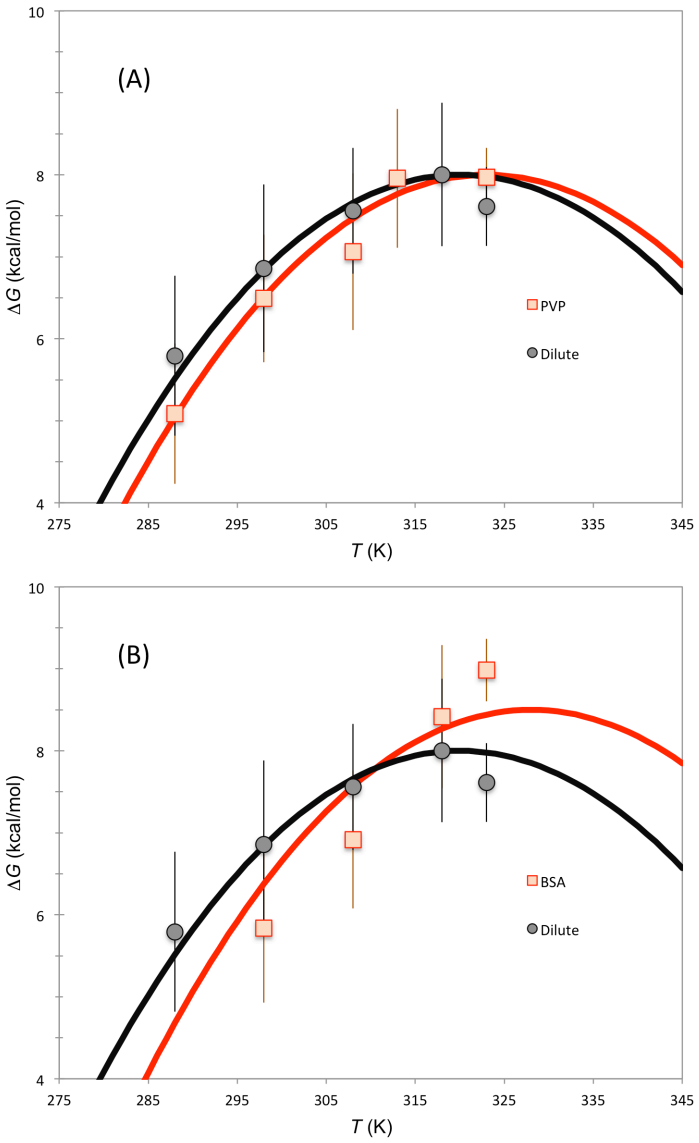

Supplementary Figure S1. Re-analysis of the Wang et al. data for temperature-dependent crowding effects of (A) PVP and (B) BSA on the folding stability of ubiquitin. The curve for the dilute solution has T_s = 320 K and ΔH_s = 8 kcal/mol (same as shown in Fig. 3); for PVP and BSA, δT_s = 3 and 8 K and $\delta\Delta H$ = -4.5 and -11.5 kcal/mol, respectively. The data shown here and in Fig. 3 are averages of the opening free energies of 9 residues that were thought to be exposed only by global unfolding; a 10th residue, K29, is excluded because of the erratic dependence of its opening free energy on temperature (e.g., changing from 2.58 to 10.90 kcal/mol upon a temperature change from 288 to 298 K in 100 g/l lysozyme). Also excluded are opening free energies that are lower by 3 kcal/mol than the highest opening free energy among the 9 residues in a given experimental condition. The error bars are variations among the opening free energies in a given experimental condition.

The data in Fig. 4 for CI2 in the dilute solution and in the presence of 100 g/l Ficoll are collected from Benton et al. in a similar way. Averages are among 6 putatively global opening residues (I20, L21, I30, L49, F50, and V51); the variations in this case are much smaller. The data in the presence of 200 g/l sucrose are not re-analyzed in the present study.