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Supplemental Information

**Conformational Dynamics and Cooperativity Drive the Specificity of a
Protein-Ligand Interaction**

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SUPPORTING MATERIAL

Conformational Dynamics and Cooperativity Drive the Specificity of a Protein-ligand Interaction

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INVENTORY OF SUPPLEMENTAL INFORMATION:

Figure S1. Methyl-bearing ¹³C-HSQC spectra of Tiam2 WT and QM PDZ domains.

Figure S2. SDC1 and Caspr4 binding to Tiam2 WT and QM PDZ domains monitored by solution NMR.

Figure S3. Relaxation dispersion curves for the Tiam2 WT PDZ domain.

Figure S4. Relaxation dispersion curves for the Tiam2 QM PDZ domain.

Figure S5. Guanidine hydrochloride denaturation unfolding curves for Tiam2 WT and QM PDZ domains.

Supporting Figures

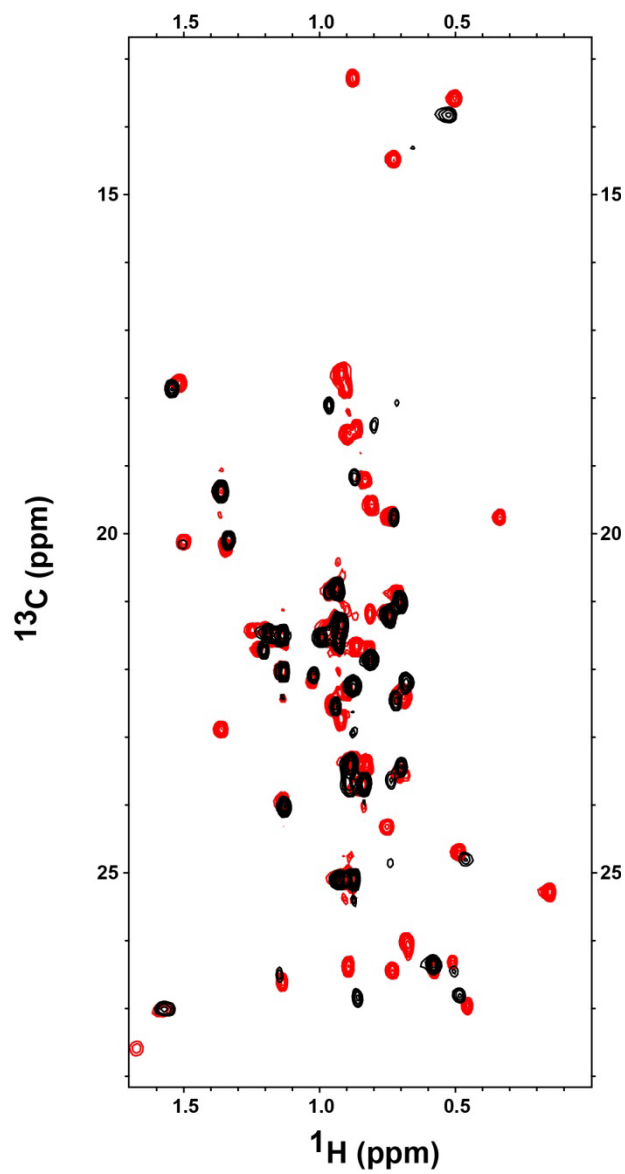


Figure S1. Methyl-bearing ^{13}C -HSQC spectra of Tiam2 WT and QM PDZ domains.
Overlay of ^1H - ^{13}C HSQC spectrum of Tiam2 PDZ WT (red) Tiam2 PDZ QM (black).

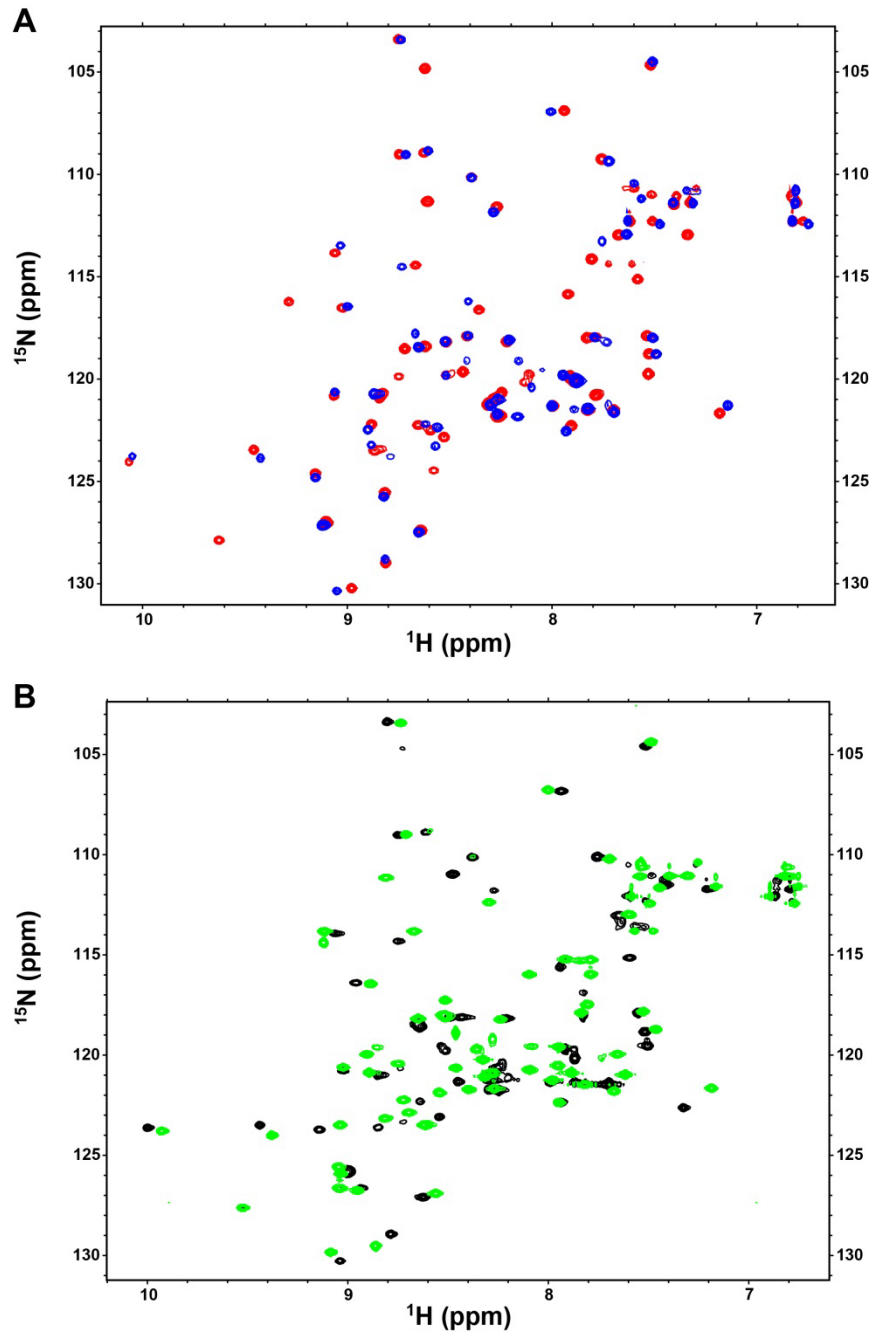


Figure S2. SDC1 and Caspr4 binding to Tiam2 WT and QM PDZ domains monitored by solution NMR. (A) Overlay of ^1H - ^{15}N HSQC spectrum of Tiam2 PDZ WT in apo (red) and SDC1-bound (blue) state. (B) Overlay of ^1H - ^{15}N HSQC spectrum of Tiam2 PDZ QM in apo (black) and Caspr4-bound (green) state.

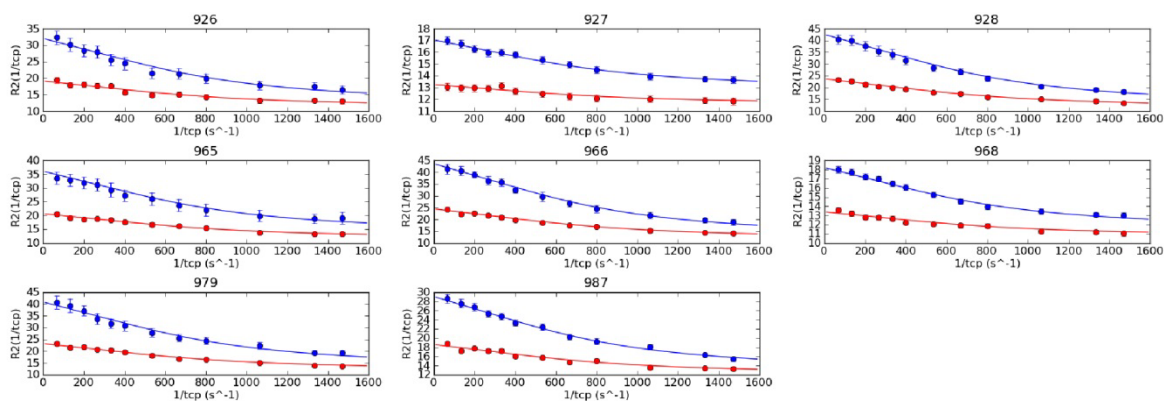


Figure S3. Relaxation dispersion curves for the Tiam2 WT PDZ domain. Data for the 8 residues having R_{ex} were collected at 500 and 800 MHz and plotted in red and blue, respectively. The curves are plotted using parameters from global fitting.

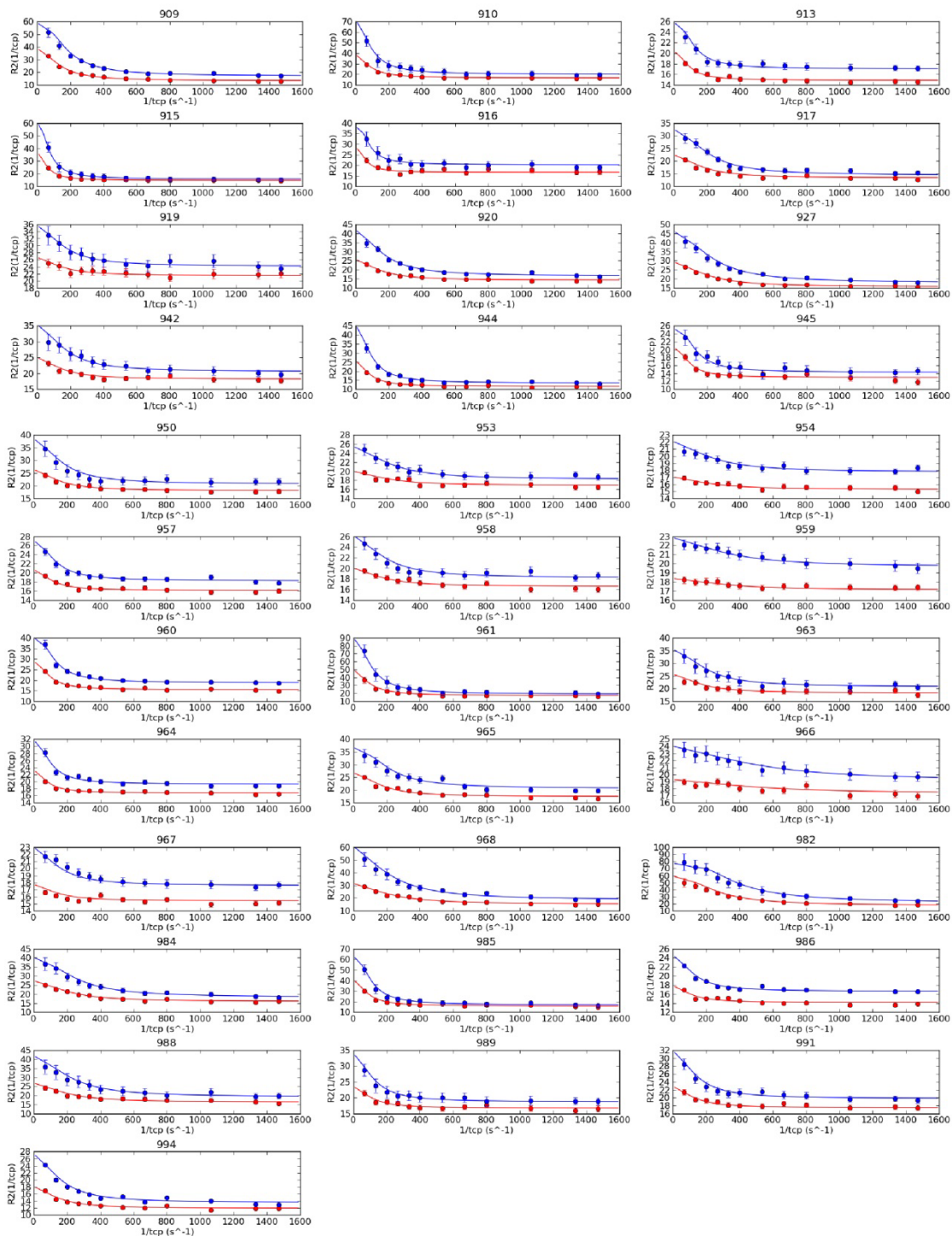


Figure S4. Relaxation dispersion curves for the Tiam2 QM PDZ domain. Data for the 34 residues having R_{ex} were collected at 500 and 800 MHz and plotted in red and blue, respectively. The curves are plotted using parameters from local fitting.

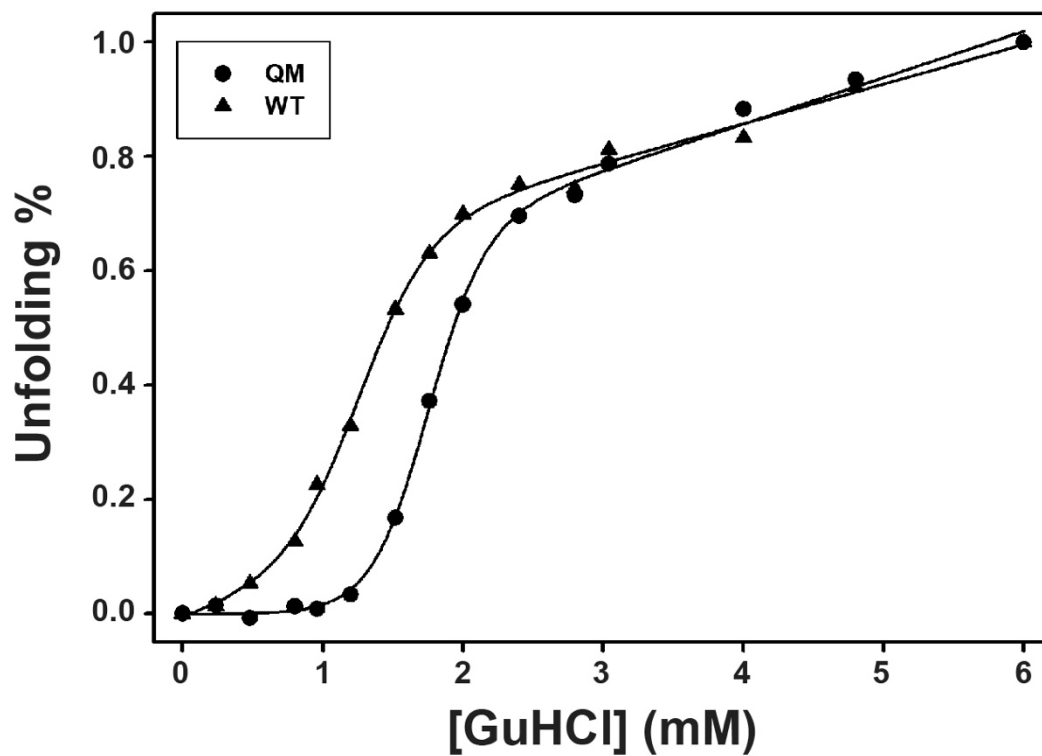


Figure S5. Guanidine hydrochloride denaturation unfolding curves for Tiam2 WT and QM PDZ domains. The CD signal at 220 nm of Tiam2 PDZ WT (\blacktriangle) and QM (\bullet) was monitored as a function of guanidine hydrochloride concentration and fit to a two-state unfolding model, respectively. The experiments were carried out in triplicate.