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| **Figure 6–figure supplement 3. Representative Conformations of PSG Supramodule from PSD-95. A)** Representative conformations and their population occupancy in the highly sampled α-basin with PDZ3 interacting with the SH3 domain. PDZ3 is colored cyan, SH3 colored orange, and GuK colored purple. A multiplicity of states is sampled within the fuzzy α-basin. The top centroid cluster in the α-basin shows PDZ3 to reorient away from the HOOK helix and sample the β1-β2 loop (RT loop in canonical SH3 domain). The pairwise contact maps from DMD show that interactions within the α-basin involved degenerate electrostatic interactions engaged by all conformations with occasional hydrophobic interactions leading an occluded PDZ3 binding pocket. **B)** Representative conformations and their population in the β-basin with PDZ3 interacting with the GuK domain of PSG. The β-basin was comparatively well defined due to involvement of exposed hydrophobic residues in β3-α1 of PDZ3 and a relatively hydrophobic surface in GuK formed by α7, α5, and β10-11 (e.g., L349-F684, L342-L608), which support a limited range of conformations. Both basins infrequently engaged the canonical GLGF motif, which would prevent peptide binding to PDZ3. An RMSD cutoff of 8.0 Å was used to select the centroid clusters of α- and β-basins. |