Figure 2. Experimentally determined states of flexible proteins are captured by evolutionary couplings.

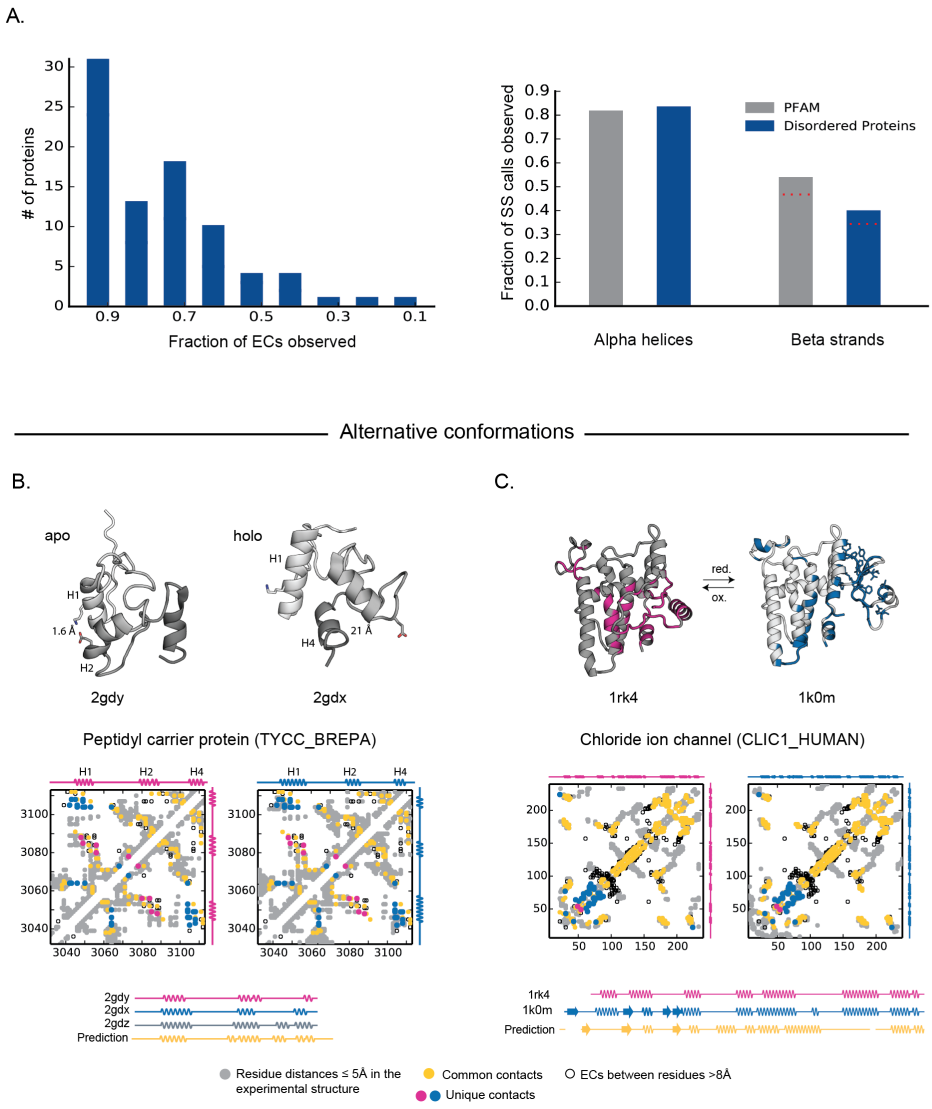

Figure 2. Experimentally determined states of flexible proteins are captured by evolutionary couplings. **(A)** Overall performance predicting experimental contacts for a set of 83 flexible and disordered proteins with known structures for significant long-range ECs (left panel) and precision of the secondary structure propensity scores on a per residue basis for a set of over 3800 PFAM families and our validation set of 83 flexible and disordered proteins with known structures (right panel). For residues with a propensity score suggesting both α-helix and β-strand we took these residues to be α-helical given stronger evolutionary constraint; red-dashed lines show the decreased precision including these calls in β-strand as well. **(B)** Peptidyl carrier protein (PCP) undergoes large conformational changes, including the repacking of its helices, upon cofactor binding (left: apo form, 2gdy; right: holo form, 2gdx). ECs reflect interactions between helix1 and helix2 (magenta circle, only in apo 3D structure) as well as helix1 and helix4 (blue circle, only in holo 3D structure). Many residue-residue distances change substantially between the two conformations. For example, there is strong coupling between residues K18 and E58, which form a salt bridge in the apo form, while they are >20 Å apart in the holo form. Our secondary structure propensity score predicts all 4 helices of PCP, the third being present only in the intermediate state between the apo and holo form (2gdw). **(C)** ECs agree with a known conformational switch in the chloride ion channel protein (CLIC1) undergoes redox condition dependent conformational switch, including α-helix to β-strand transitions.