The Vps4 Dimer Interface

We reasoned that recurring crystal packing interactions might recapitulate aspects of Vps4 dimerization in solution, and therefore examined all of the intermolecular lattice contacts in the different known $Vps4_{\Delta MIT}$ crystal forms. The different interfaces are summarized in Table 2 and Supplemental Figure 1, and subsets of the interfaces are shown in Fig. 5a. The various yeast Vps4 crystal lattices show six different classes of dimer interfaces, five of which exhibit two-fold rotational symmetry (Interfaces 1-5) and one of which lacks symmetry (Interface 6). Interface 1, the largest of the two-fold symmetric interfaces, involves contacts between residues in helix 3 and strand 2 in adjacent large domains. This interface is seen in three different crystal forms, and buries an average of 620±130Å^2/subunit. Variants of Interface 1 were seen in our $Vps4_{\Delta MIT}$-SO_4 crystals (480Å^2) and also in two other $Vps4_{\Delta MIT}$ crystal forms, one with a bound sulfate (2QP9) and one without a bound ligand (2RKO) (740Å^2 and 640Å^2, respectively). We note that although similar contact surfaces are used to create Interface 1 in these three crystal forms, the interactions differ significantly in detail (see Supplemental Figure 1).

Hartmann et al. have argued that the crystallographic Vps4 Interface 1 also forms in solution based upon their report that the Q216A interface mutation blocks $Vps4_{\Delta MIT}$ dimerization in solution[27]. In our hands, however, the Q216A mutation did not alter the gel filtration mobility of $Vps4_{\Delta MIT}$, indicating that this mutation did not inhibit dimer formation in solution (Fig. 5b, panel 1, compare red and black chromatograms). This conclusion was confirmed in analytical ultracentrifugation experiments, which showed