Our cryo-EM model for the Vps4 dodecamer indicates instead that the two hexameric rings adopt very different conformations, the more constricted of which resembles the p97 D1 homology model. In this model, the Vps4 subunits interact through a surface that is similar, but not identical to the crystallographically defined Interface 6, which can explain why only a subset of mutations within Interface 6 inhibit Vps4 assembly. Vps4 residues that make up the intersubunit interaction surface in the p97 homology model are shown in detail in Supplemental Fig. 4. The conservation of many of these interface residues between the Vps4, p97 D1, and spastin proteins, further supports the homology model. This model can also explain why Vps4 becomes an active ATPase upon assembly because hexamerization would position each ^{288}RR^{289} dipeptide into the active site of an adjacent subunit, in close proximity with the γ-phosphate of the ATP. The use of such “arginine fingers” (sometimes also termed the second region of homology (SRH)) is a recurring feature in AAA ATPase active sites[18], and serves an important catalytic role because the arginine(s) interacts with the γ-phosphate, making it a better leaving group. However, in the spiraling hexamers seen in crystal form 2 and related Vps4 crystal forms, the SRH residues of the adjacent subunit are located at least 12Å away from the γ-sulfate and therefore do not make interactions that would promote ATP hydrolysis. In our p97-based Vps4 hexamer homology model, these residues move much closer to the γ-sulfate, with the Arg288 residue brought to within 3.5Å of a γ-sulfate oxygen, where it could contact the terminal phosphate/sulfate and perform its expected role in catalysis.