Understanding conformational changes in MCM-family helicases through experimental structures and SVD-based metadata analysis´

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Amid the global coronavirus outbreak, the academic research in progress has been greatly curtailed or redirected to COVID-19. As we navigate through this pandemic, one of the ways to strategize and protect research in progress is to shift efforts from data acquisition to analysis. In characterizing structural and dynamical features of macromolecular structures, there are not many structural analysis tools available besides those applied to molecular dynamics simulations. Hence, we are often computationally limited and rely on correlating structure-dynamics-functions relationships based on conformational comparisons of superimposed structures such as wild-type verses variants proteins or homologous proteins. Here we focus on MCM-family helicases. These hexameric AAA+ enzymes are usually associated with the archaeal and eukaryotic replication fork, but are also encoded by some bacterial mobile genetic elements. We present crystallographic and cryo-EM structures of a bacterial MCM-like helicase (both in ~3.2 Å resolution) in the apo and ssDNA-bound states and analyze the conformational changes between the two using distance and R.M.S.D. matrices. The analysis is then expanded into metadata analysis of all 28 MCM-family helicase structures currently available in the PDB using singular value decomposition (SVD). The SVD analysis highlights correlations among the relative positions of the DNA-binding loops, the DNA, the nucleotide cofactor (di- vs. triphosphate) bound at each inter-subunit interface within the hexameric ring, and the tightness of that interface. Our immediate goal is to use this meta-analysis to determine the conserved "core" architectural features of these enzymes that allow them to convert the free energy of ATP hydrolysis into mechanical translocation along ssDNA. Our work shows that these methods can be adapted toward any structural analysis or start-from-scratch project at home. For metadata, this may be an effective tool in identifying and presenting subtle yet concerted conformational changes that are otherwise difficult to relate among multiple structures and various experimental conditions.