Binding and Channelling of Alternative Substrates in the Enzyme DmpFG: A Molecular Dynamics Study

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Supplementary Material

Additional figure to show an example of a dual topology hydrid molecule:

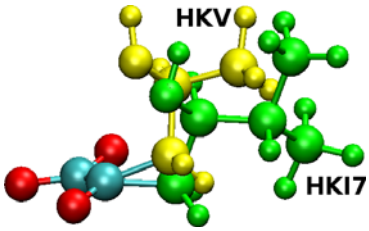

Fig. S1: Dual topology hybrid of HKV (yellow side chain) and HKI7 (green side chain) utilised in the FEP calculations.

Additional figure to demonstrate the convergence of free energy values obtained from Free Energy Perturbation simulations:

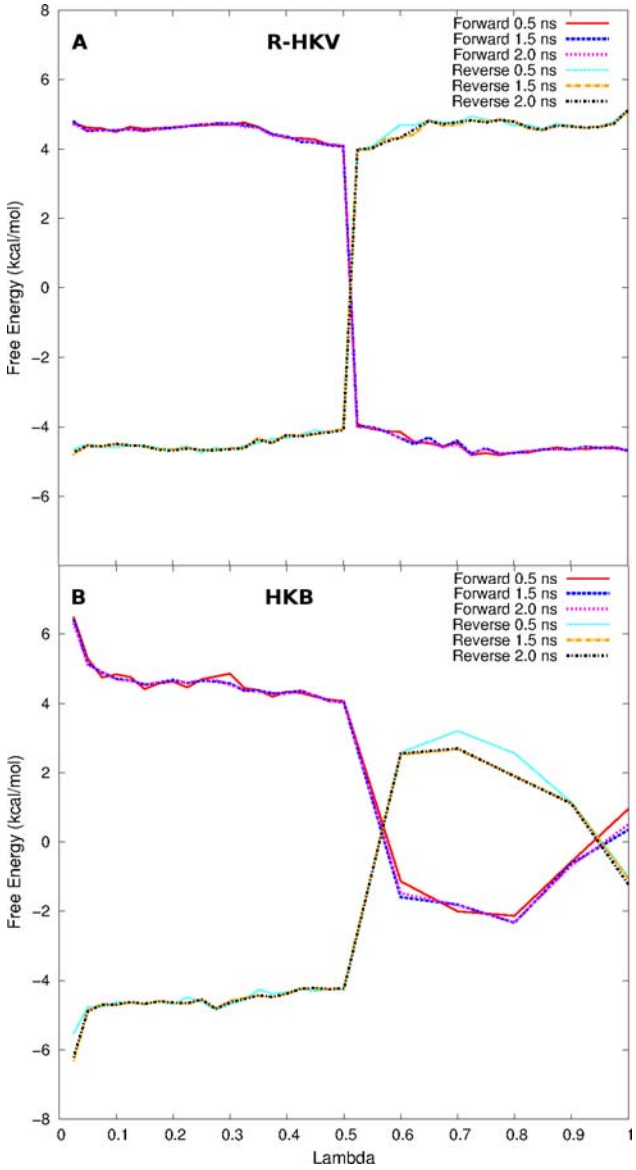

Fig. S2: The convergence of the free energy values obtained in each lambda window from the free energy perturbation simulations for both R-HKV relative to S-HKV (A), and HKB relative to S-HKV (B), in protein with time. Both the forward and reverse simulations are shown.

Additional figure to demonstrate the convergence of the free energy profiles obtained in this study:

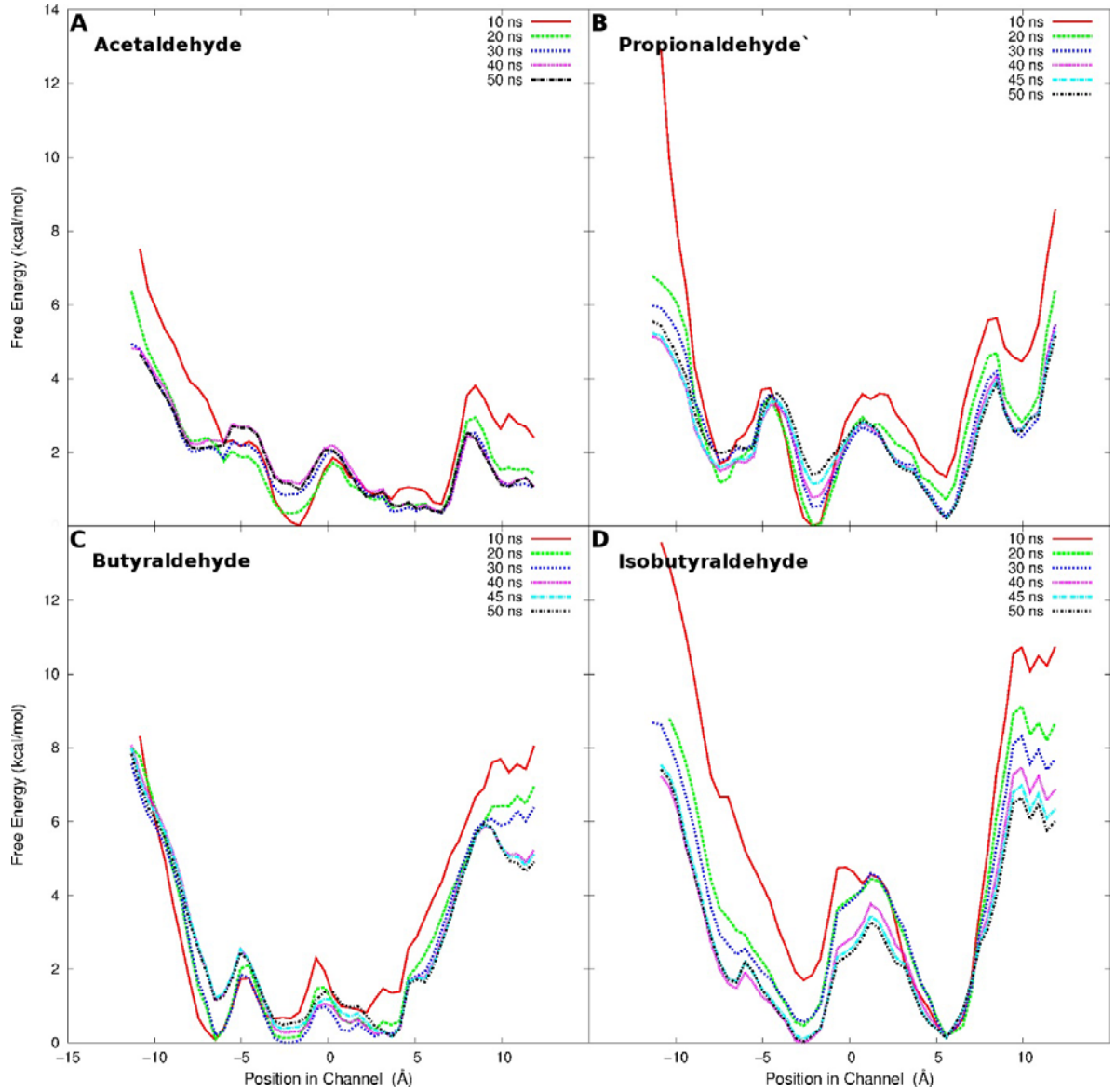

Fig. S3: Convergence of each free energy profile with time for acetaldehyde (A), propionaldehyde (B), butyraldehyde (C) and isobutyraldehyde (D).

Additional figure to demonstrate the convergence of the free energy profiles for benzaldehyde obtained in this study:

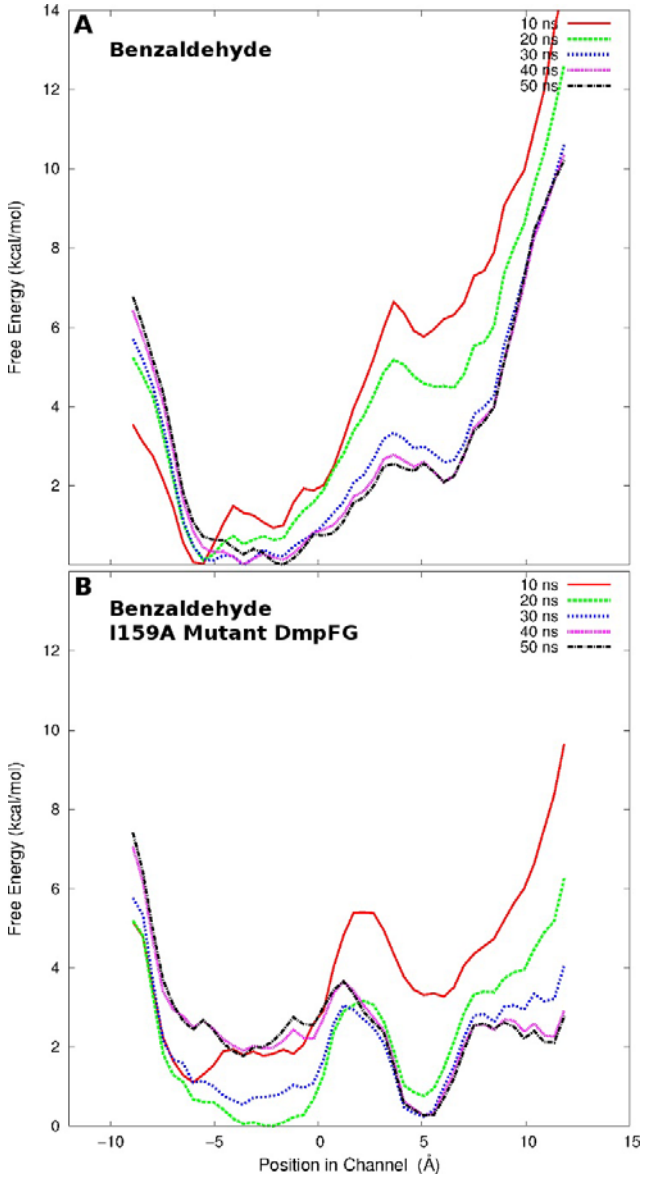

Fig. S4: Convergence of the free energy profile of benzaldehyde in WT (A) and I159A mutant (B) DmpFG with time.

Additional figure to determine the statistical error in each data set:

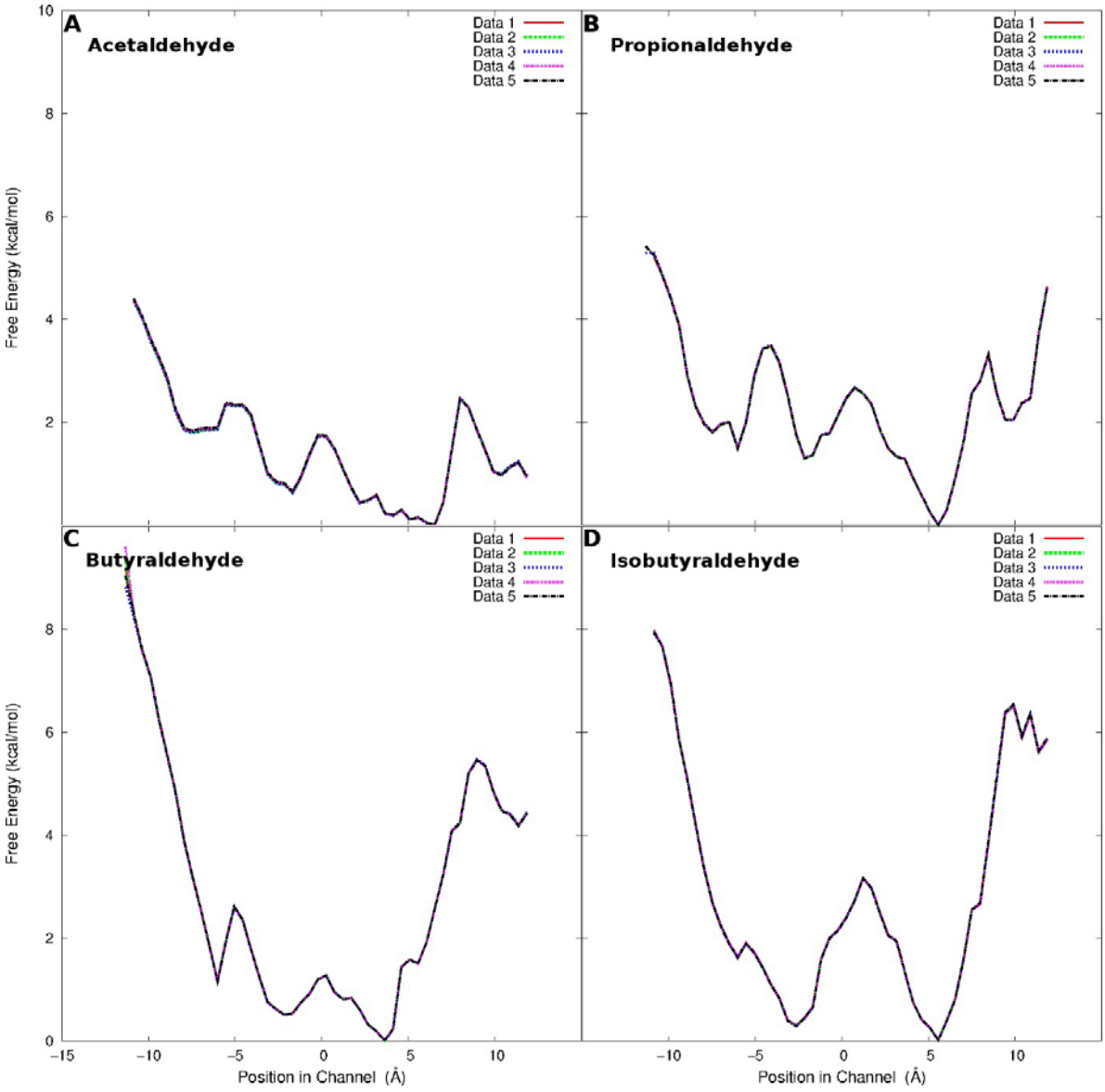

Fig. S5: The free energy profiles obtained when each complete data set (50 ns) was randomly shuffled and split into 5 separate data sets. A free energy profile was obtained for each data set allowing a standard error to be determined for each aldehyde.

Additional figure to determine the statistical error in each data set:

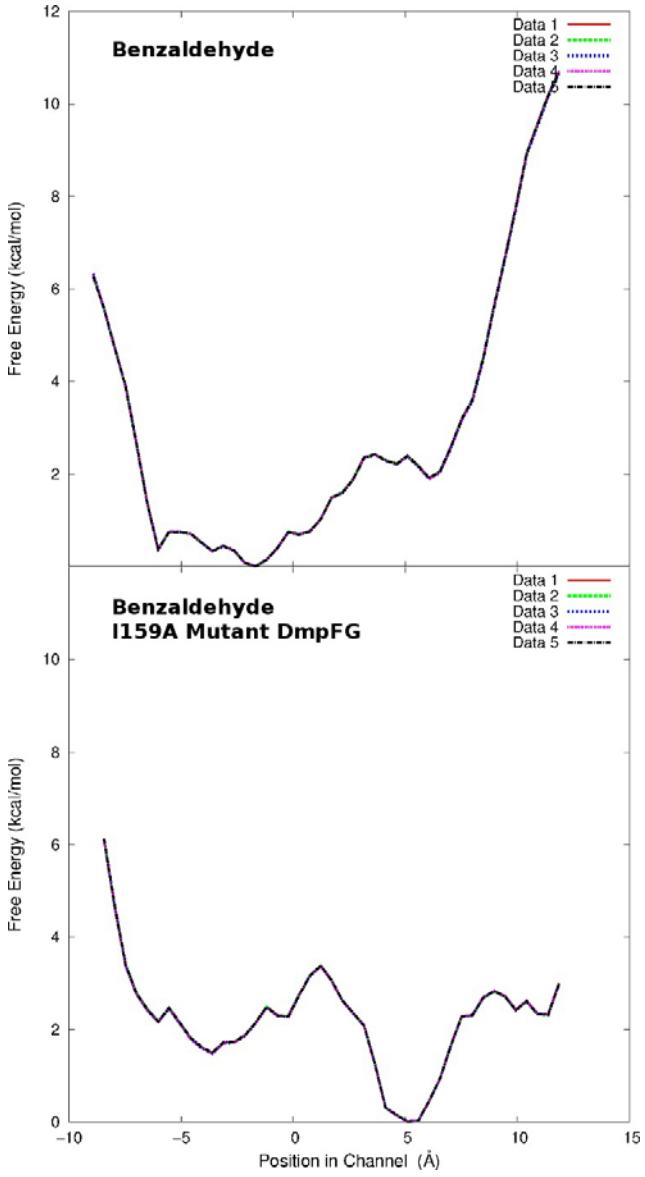

Fig. S6: The free energy profiles obtained when each complete benzaldehyde data set (50 ns) was randomly shuffled and split into 5 separate data sets. A free energy profile was obtained for each data set allowing a standard error to be determined.

Additional figure to show the sequence alignments obtained for the aldolase DmpG and its orthologues:

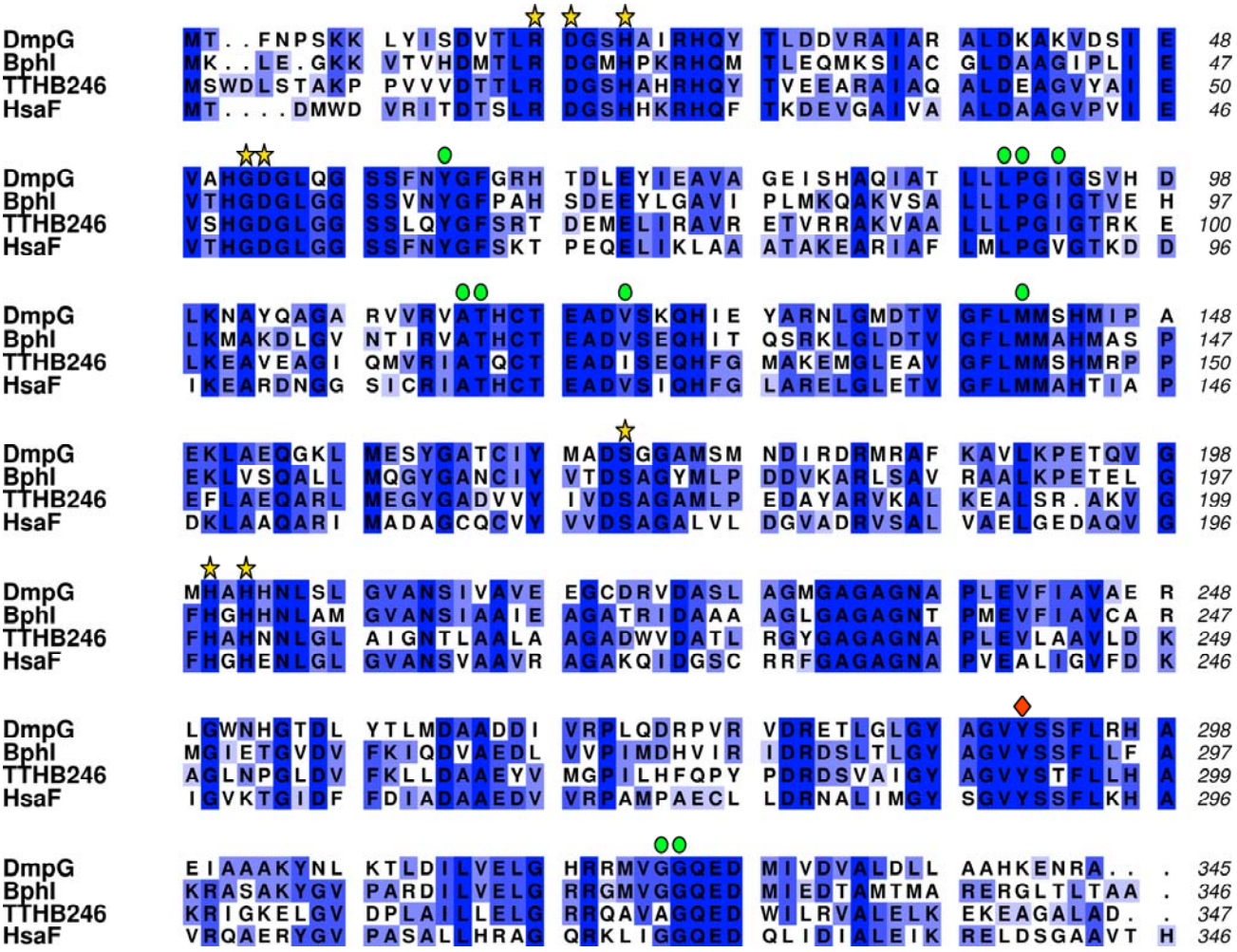

Fig. S7: Sequence alignments of DmpG with three of its orthologues: BphI, TTHB246 and HsaF. Levels of conservation between the orthologues are indicated by shades of blue. For clarity, a blank space has been inserted after every 10 residues of DmpG. Yellow stars indicate residues thought to have a role in either the reaction mechanism or substrate positioning, green ovals indicate channel lining residues and red diamonds indicate proposed channel gating residues.

Additional figure to show the sequence alignments obtained for the dehydrogenase DmpF and its orthologues:

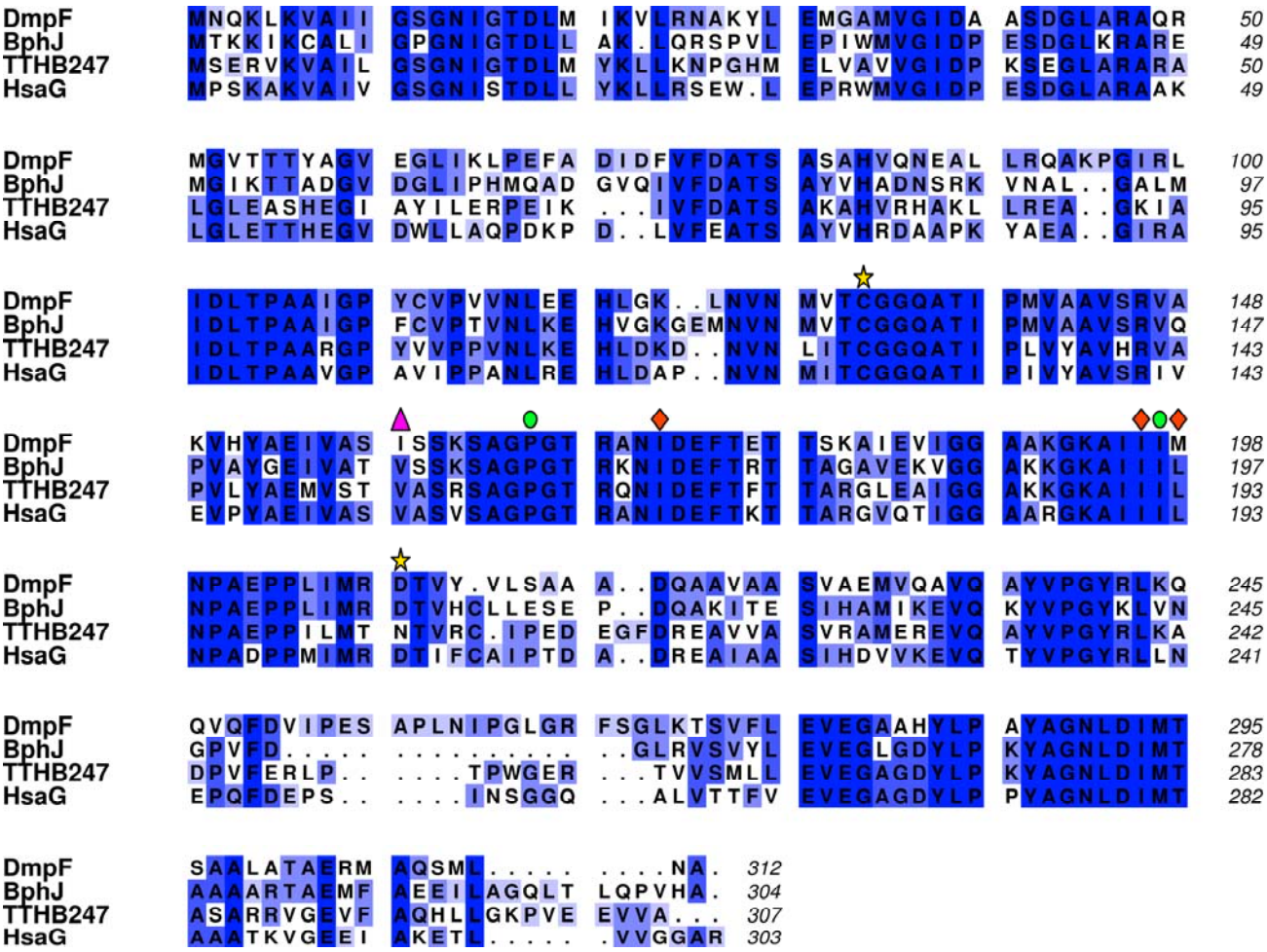

Fig. S8: Sequence alignments of DmpF with three of its orthologues: BphJ, TTHB247 and HsaG. Levels of conservation between the orthologues are indicated by shades of blue. For clarity, a blank space has been inserted after every 10 residues of DmpF. Yellow stars indicate residues thought to have a role in either the reaction mechanism or substrate positioning, green ovals indicate channel lining residues and red diamonds indicate proposed channel gating residues. The pink triangle indicates Ile159 which was mutated in this MD study.