Supporting Information for:

New crystallographic snapshots of large domain movements in bacterial HMG-CoA reductase

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Figure S1. DaHMGR steady-state kinetic data with respect to (A) the cofactors NADH (circles, with Michaelis-Menten fit) and NADPH (squares, with linear fit), and (B) the substrate HMG-CoA (circles, with Michaelis-Menten fit). (C) Competitive citrate inhibition with respect to HMG-CoA (double-reciprocal plots with linear fits). Assays were performed in triplicate, and the data points represent mean values, with error bars depicting standard error of the mean (SEM).



Figure S2. Absence of electron density for NADH in the cofactor-binding site of the mevalonate-bound DaHMGR structure. Protein shown in pink cartoon, with bound mevalonate in sticks (at right, C in pink and O in red). A modeled NADH molecule from an alignment of the structure of DaHMGR with NADH bound is shown in semi-transparent sticks (C in gray, N in blue, O in red, and P in orange). Electron density is shown as a $2mF_o - DF_c$ map in blue mesh contoured at 1.0 σ , which indicated the presence of a bound sulfate molecule, shown in sticks (S in pink, O in red).



Figure S3. Crystal packing in the C-terminal domain (CTD) regions of the NADH-bound DaHMGR structure (gray). (A) Nearby symmetry-related monomers (chains C' and C" in green and magenta, respectively) pack against the CTD of chain B (black). (B) Nearby symmetryrelated monomers (chains B' and C' in green and blue, respectively) pack against the CTD of chain C (black).



Figure S4. Steric clash (violet star) between the "flipped" CTD conformation (blue cartoon) and the CoA moiety of bound HMG-CoA (sticks). One monomer of the DaHMGR homodimer is shown in gray surface, and the other monomer is shown as orange cartoon, with "flipped" CTD in blue and NADH in sticks (C colored pink). HMG-CoA is shown in sticks from the aligned structures of substrate-bound SpHMGR (PDB entry 5WPJ) with C colored green, and substrate-and NAD⁺-bound PmHMGR (PDB entry 1QAX) with C colored cyan. N colored blue, O colored red, P colored orange, and S colored yellow.