

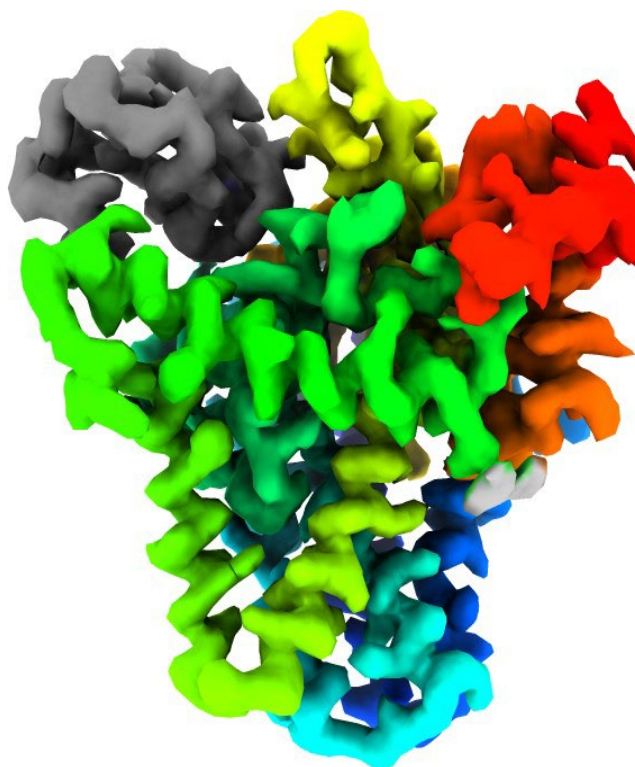
# Structural Basis for Enzymatic Terminal C–H Bond Functionalization of Alkanes

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Alkane monooxygenase AlkB is a widely occurring integral membrane metalloenzyme that catalyzes the initial step in the functionalization of recalcitrant alkanes with high terminal selectivity. AlkB enables diverse microorganisms to use alkanes as their sole carbon and energy source. Here we present the 48.6 kDa cryo-EM structure of a natural fusion from *Fontimonas thermophila* between AlkB and its electron donor AlkG at 2.76 Å resolution. The AlkB portion contains six transmembrane helices with an alkane entry tunnel within its transmembrane domain. A dodecane substrate is oriented by hydrophobic tunnel-lining residues to present a terminal C-H bond towards a diiron active site. AlkG, a Fe-4S rubredoxin, docks via electrostatic interactions and sequentially transfers electrons to the diiron center. The archetypal structural complex presented reveals the basis for terminal C-H selectivity and functionalization within this broadly distributed evolutionary class of enzymes.



**Figure 1**