

15 + 5 = 20

10-22-01

Howitt

Aconitate Hydratase

Aconitate hydratase is a globular, three-domain molecule that consists of 754 amino acid residues. It binds two ligands: an iron sulfur complex (Fe_4S_4) and citrate, which it isomerizes to isocitrate. Aconitase is a mixed structure of 23 helices and 34 β -strands, which comprise 10 β -sheets (figure 1). The overall architecture of the N-terminal domain (residues 1-315) is four β -sheets (2 antiparallel, 1 mixed, and 1 parallel) flanked by α -helices on three sides (figure 2). A random coil connects this region to another where three α -helices flank two triple-stranded parallel β -sheets (residues 170-315). The second domain (residues 320-482) consists of two double-stranded antiparallel β -sheets and one triple-stranded β -sheet sandwiched between three α -helices on top and one on each side. A random coil with a single β -strand connects the second and third domains (figure 3). The third domain (residues 580-754) has a topology of alternating α -helices and β -strands, with an antiparallel β -sheet of three strands stacked next to a parallel β -sheet of three strands. The α -helices are concentrated near the center of the molecule where the ligands bind.

The cube-shaped iron-sulfur cluster, with Fe at four vertices, and S at the other four, is bound to the enzyme via three cysteine residues (Cys 358, 421, 424). Aconitase is activated when the vacant corner of the cluster binds a Fe^{2+} atom. This Fe can then coordinate the C-3 carboxyl and hydroxyl groups of citrate. Isocitrate is surrounded by alpha helices with four positively charged arginines (Arg 447, 452, 580, 644) interacting with isocitrate's negatively charged carboxylate groups. The polar residues of a beta turn (Asp 165, Ser 166) provide hydrogen bonding contacts for the isocitrate molecule. Aconitase has an asymmetric binding site for citrate, which allows the substrate to bind to the enzyme in only one orientation and the subsequent transfer of the hydroxyl group occurs only according to this orientation.

Very nice job

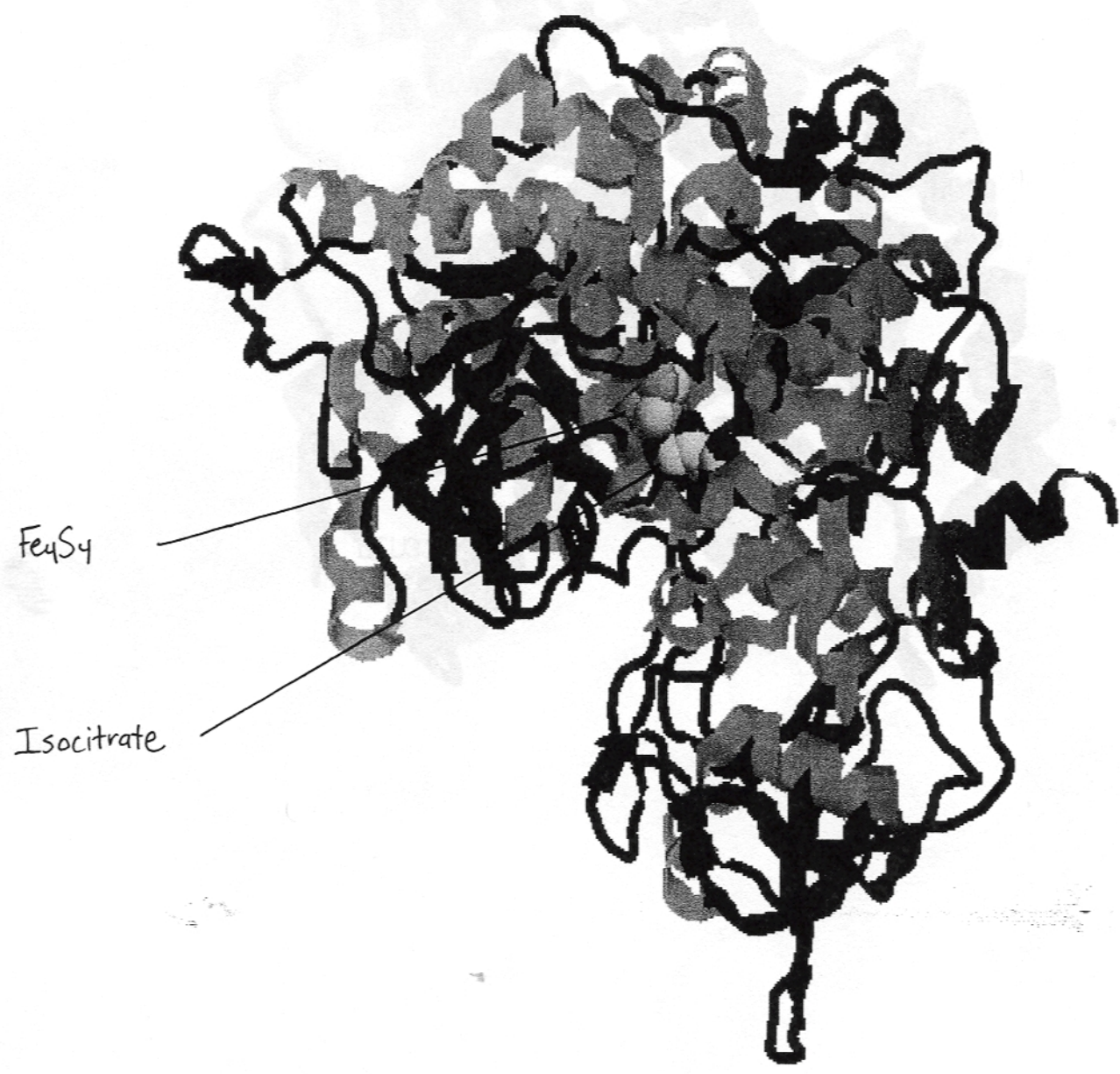
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FIGURE 1: Domain 1 (residues 1-315)

FIGURE 1: ACONITATE HYDRATASE

4PDA.CA N-terminus



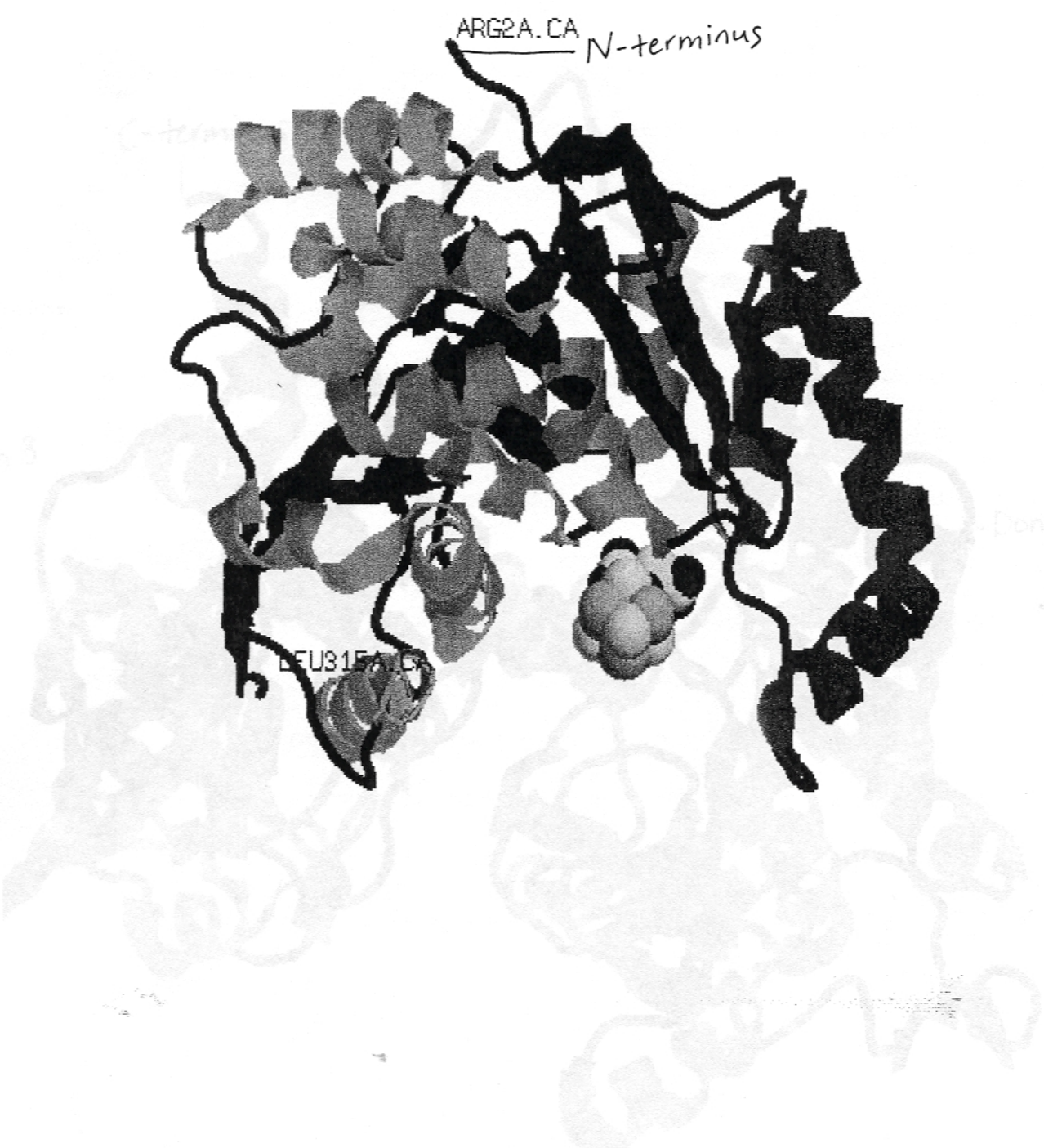
Fe₄S₄

Isocitrate

5,814 atoms selected.

MDL

FIGURE 2: Domain 1 (residues 1-315)



21 atoms selected.

MDL