# Supporting information for "Dynamics of the streptavidin-biotin complex in solution and in its crystal lattice: Distinct behavior revealed by molecular simulations"

David S. Cerutti [†], Isolde Le Trong [▽,◇], Ronald E. Stenkamp [▽,‡,◇], and Terry P. Lybrand [†,*]

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† Center for Structural Biology and Department of Chemistry, Vanderbilt University; 5142 Medical Research Building III, 465 21st Avenue South, Nashville, TN 37232-8725

▽ Department of Biological Structure, University of Washington, Seattle; Box 357420, Seattle, WA 98195-7420

‡ Department of Biochemistry, University of Washington, Seattle; Box 357350, Seattle, WA 98195-7350

◇ Biomolecular Structure Center, Univ. of Washington, Seattle; Seattle, WA 98195-7742

∗ To whom correspondence should be addressed. Phone: (615) 343-1247. Fax: (615) 936-2211. Email: terry.p.lybrand@vanderbilt.edu

# 1 Maps of the biotin-streptavidin complex

Several images of the streptavidin proteins' backbone traces were prepared to provide a clear description of the loops and other regions described in the text. The relationship of the two monomers within the tight streptavidin dimer is shown in Figure 1; the arrangement of two dimers to form the biologically active tetramer is shown in Figure 2; a detailed view of the loops that become more active upon transition from the crystal lattice to the solution phase is given in Figures 3. A view of the biotin ligand itself is provided in Figure 4.

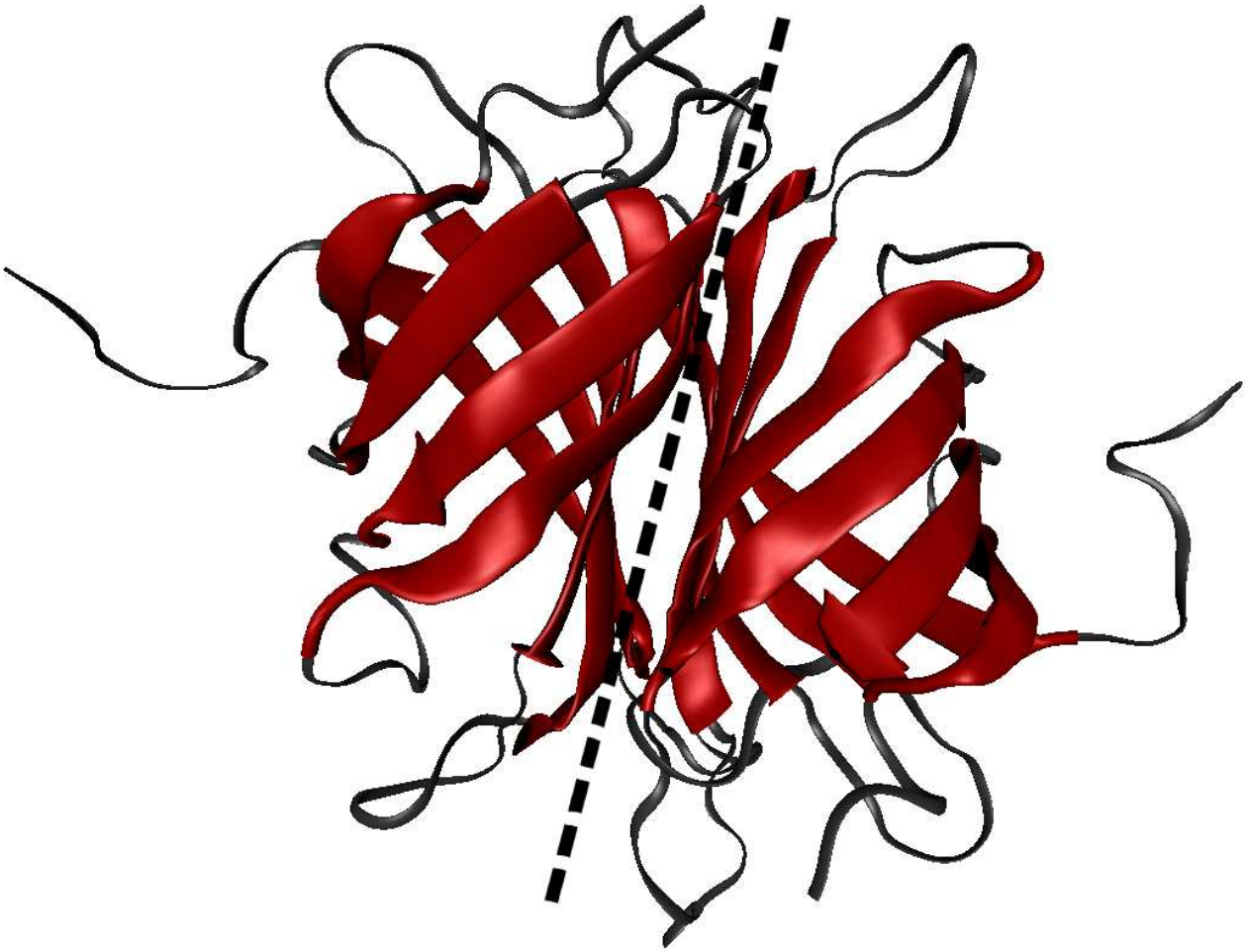

Figure 1: **A pair of $\beta$-barrel cores in the streptavidin dimer.** Each of the streptavidin monomers is a $\beta$-barrel protein (core residues colored as red cartoon, other residues colored as black ribbons). The dimer possesses $C_2$ symmetry; the extensive, rigid interface between the two monomers is located roughly along the dashed line.

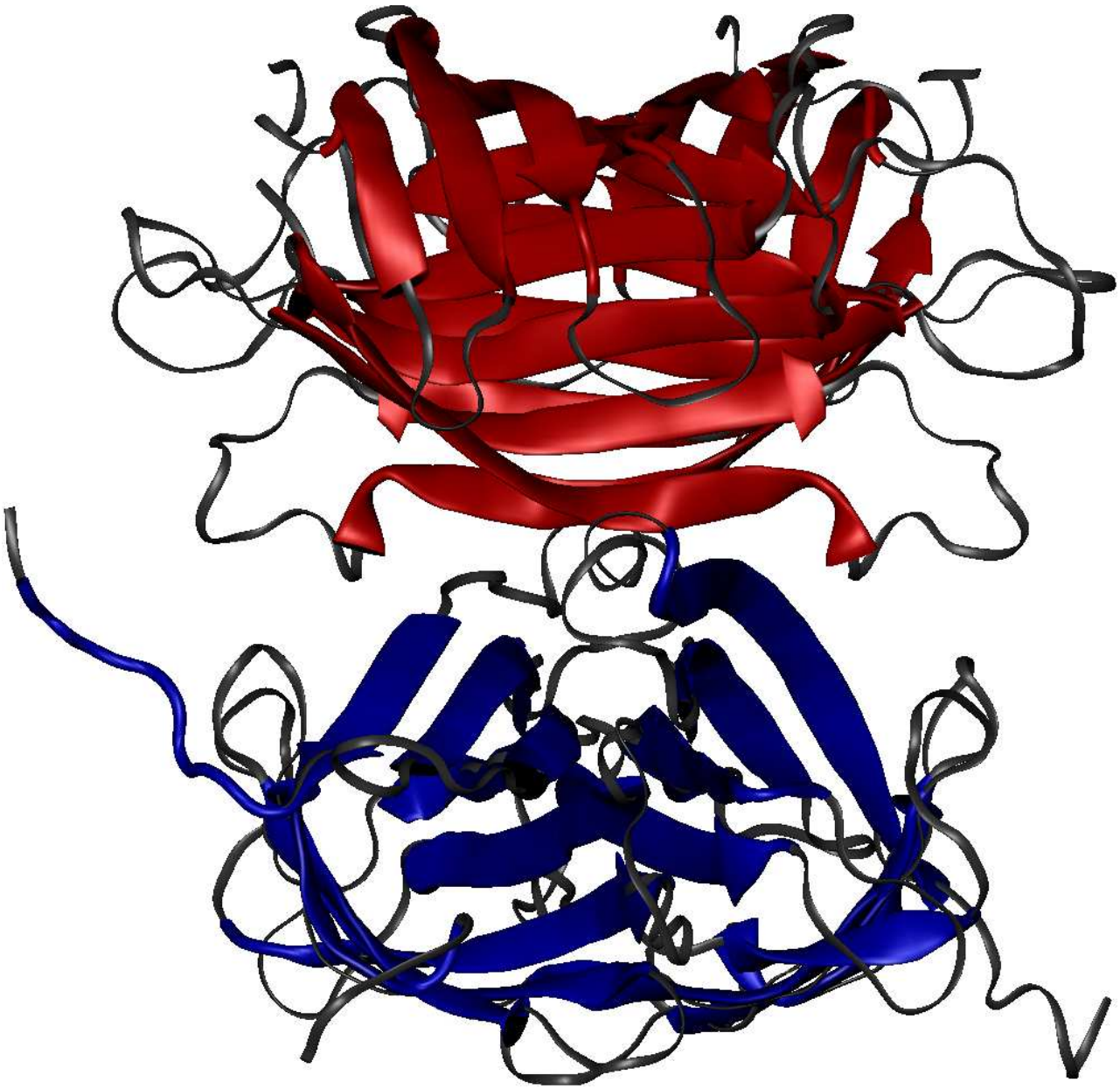

Figure 2: **A dimer of dimers in the streptavidin tetramer.** Two tightly coupled streptavidin dimers (colored blue and red) come together across a weaker interface to form the biologically active tetramer, which displays $D_2$ symmetry.

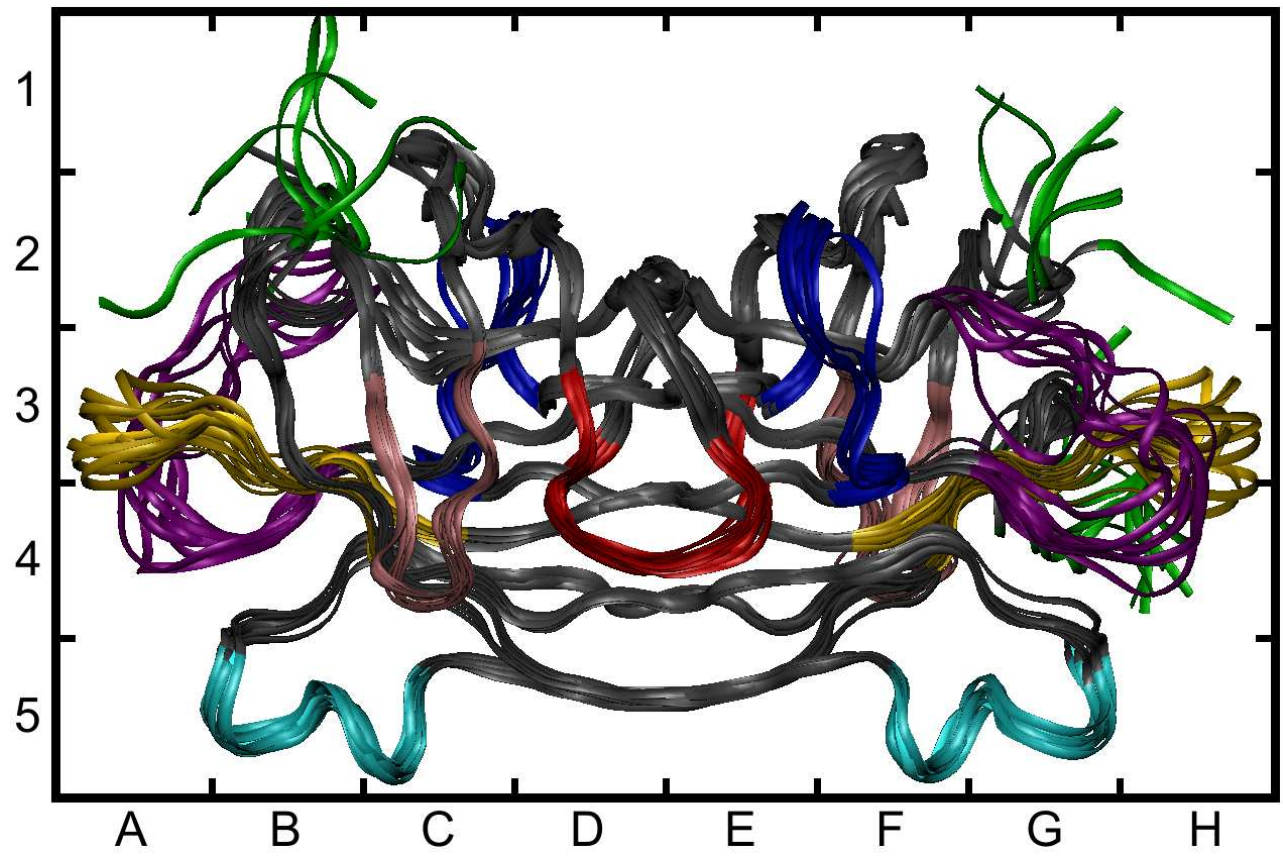


Figure 3: **Loops showing increased activity in the solution-phase simulation.** The streptavidin dimer is shown in ribbons, highlighting a number of loop regions in both monomers which become more active (in simulations) upon transition from the crystal lattice to the solution phase. To depict the relative magnitudes of fluctuations in different regions of the protein, nine snapshots of the first dimer from the solution-phase simulation are superimposed on one another, aligned by $\beta$-barrel core residues (see Figure 1). Reconstructed terminal residues are colored green in sectors A-B,G-H/1-2; residues 63 to 71, the most active loop of the protein, are colored purple in sectors A-B,G-H/3-4; residues 95 to 105, the next most active loop of the protein, are colored gold in sectors A-C,F-H/3-4; residues 117 to 122, a loop bearing residue Trp120 which mediates dimer:dimer interactions and contributes to biotin binding in adjacent subunits, are colored sky blue in sectors B-C,F-G/5; residues 22 to 29 are colored pink in sectors C,F/3-4; residues 80 to 88 are colored navy blue in sectors C-F/2-3; residues 45 to 50 (the biotin binding loop, which is very stable when biotin is bound, regardless of the environment) are colored red in sectors D-E/3-4.

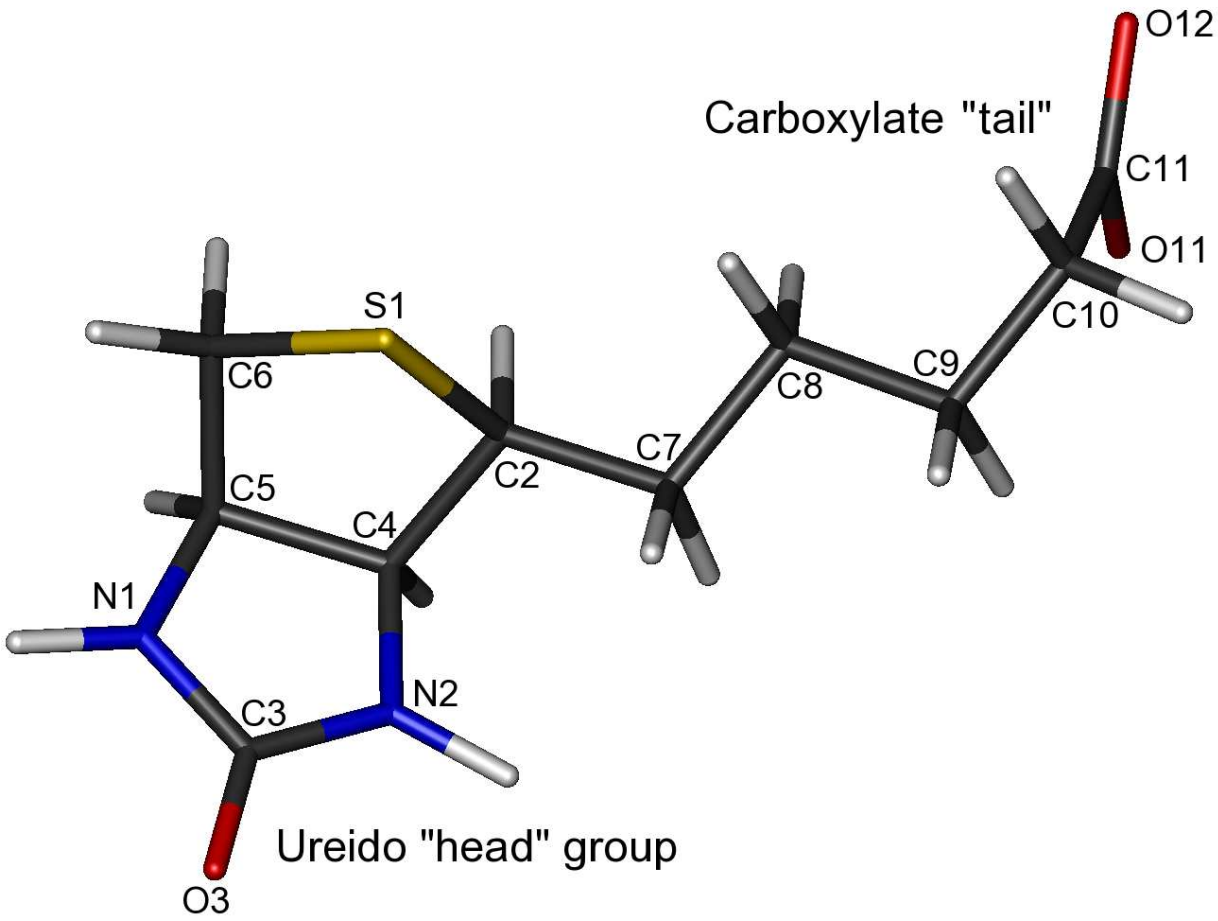


Figure 4: **The biotin ligand in all-atom detail.** Biotin consists of a heterocyclic double ring system and a carboxylate group connected by a long hydrocarbon chain. On the five-membered ring, the ureido group (the nitrogens, plus oxygen O3 and carbon C3) is a hub for as many as five hydrogen bonds to the streptavidin protein. Ser27, Tyr43, and possibly Asn23 all make hydrogen bonds to the ureido O3 atom (in the 1MK5 structure, one of the streptavidin monomers has Asn23 oriented to make a hydrogen bond with the biotin O3 atom, but the other does not). Ser45 and Asp128 form strong hydrogen bonds with ureido nitrogens N2 and N1, respectively. Additional hydrogen bonds are formed between the carboxylate tail and residues Asn49 and Ser88 on the streptavidin surface.