Supporting Information

Interactions of Multimodal Ligands with Proteins: Insights into Selectivity using Molecular Dynamics Simulations

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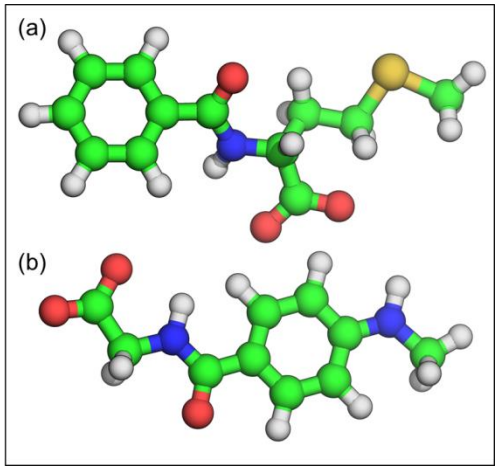

Figure S1. Multimodal ligands studied for interactions with proteins: (a) Capto MMC, and (b) Nuvia cPrime. (Color code for atoms: green=carbon, white=hydrogen, red=oxygen, blue=nitrogen, yellow=sulfur). Figure 2a is reprinted (adapted) with permission from [31].

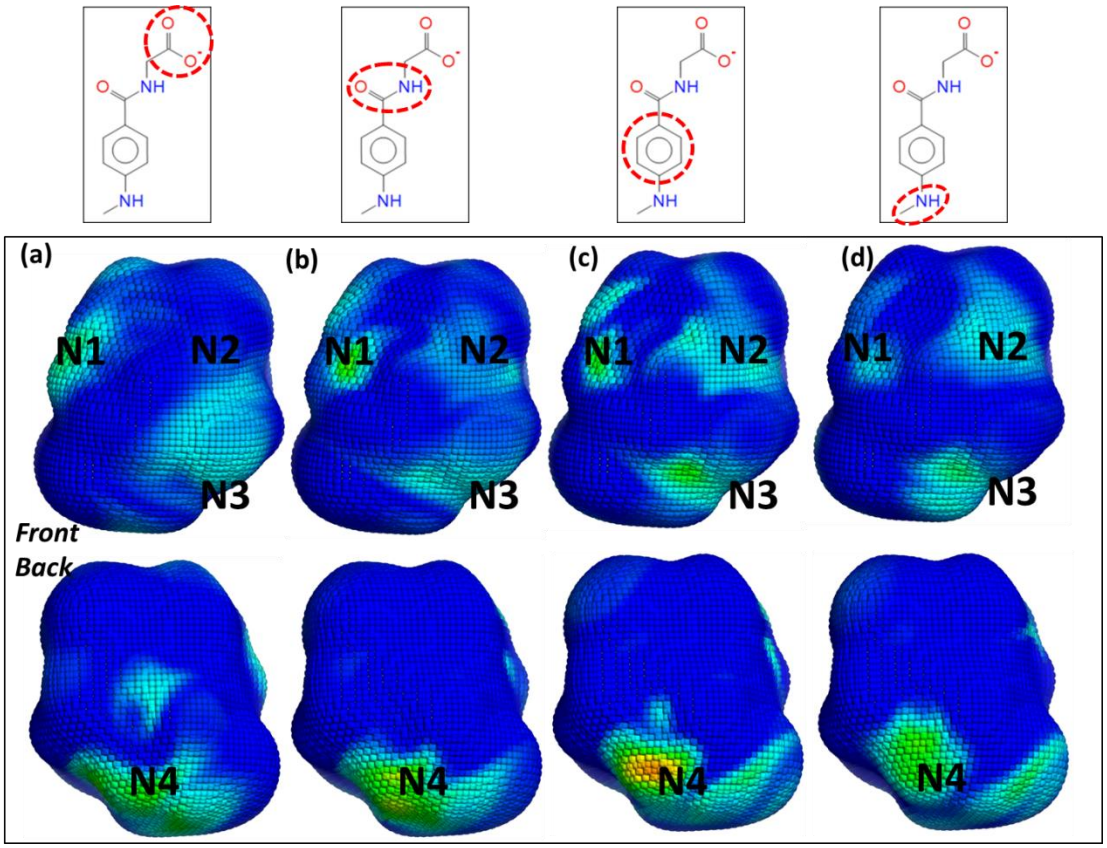

Figure S2. ρ/ρ_0 values plotted for different subgroups of the Nuvia cPrime ligand in the local domain of cytochrome C (top: front face, and bottom: back face): (a) carboxylate group, (b) amide group, (c) benzene group, and (d) amine group. Red indicates regions of high ligand density (ρ/ρ_0~130) while blue indicates regions of low ligand density (ρ/ρ_0~1). Values are plotted at the protein density interface with $\rho' = 0.2$.

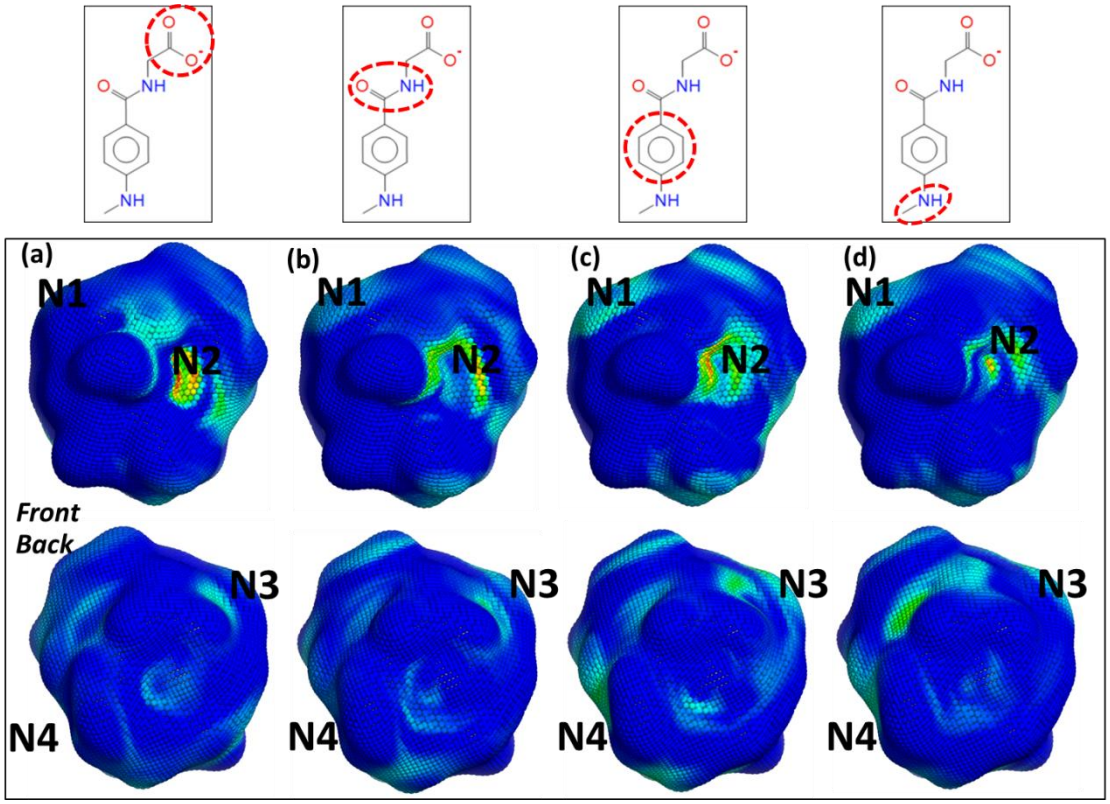

Figure S3. ρ/ρ_0 values plotted for different subgroups of the Nuvia cPrime ligand in the local domain of α-chymotrypsinogen A (top: front face, and bottom: back face): (a) carboxylate group, (b) amide group, (c) benzene group, and (d) amine group. Red indicates regions of high ligand density (ρ/ρ_0~130) while blue indicates regions of low ligand density (ρ/ρ_0~1). Values are plotted at the protein density interface with $\rho' = 0.2$.

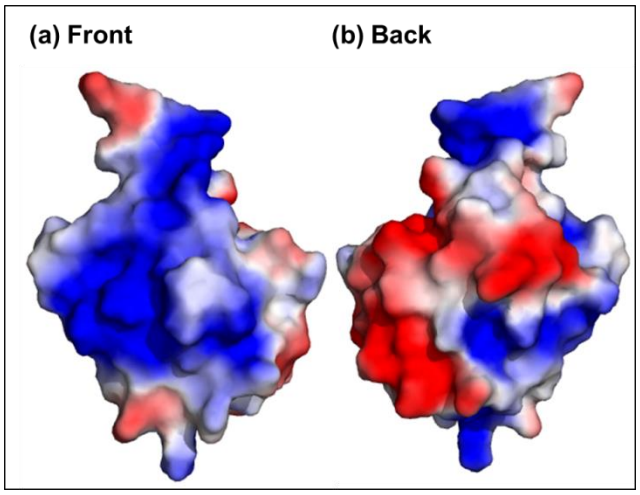

Figure S4. Electrostatic potential map of ubiquitin: (a) front, and (b) back. Blue indicates a value of 2kT/*e* and red indicates a value of -2kT/*e*.

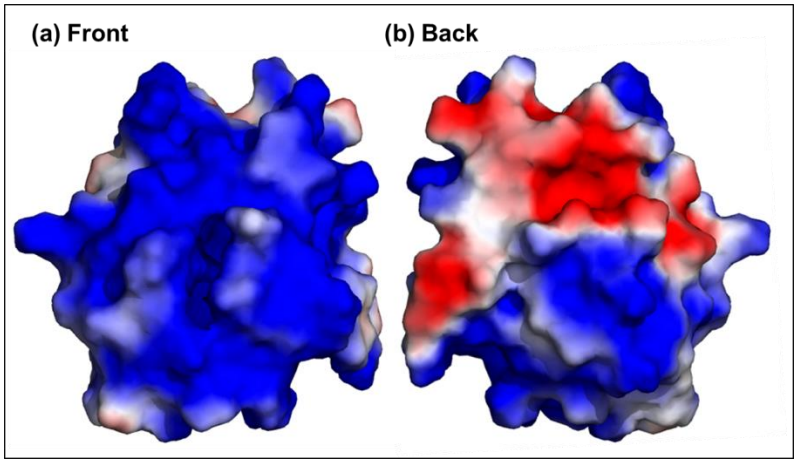

Figure S5. Electrostatic potential map of cytochrome C: (a) front, and (b) back. Blue indicates a value of 2kT/*e* and red indicates a value of -2kT/*e*.

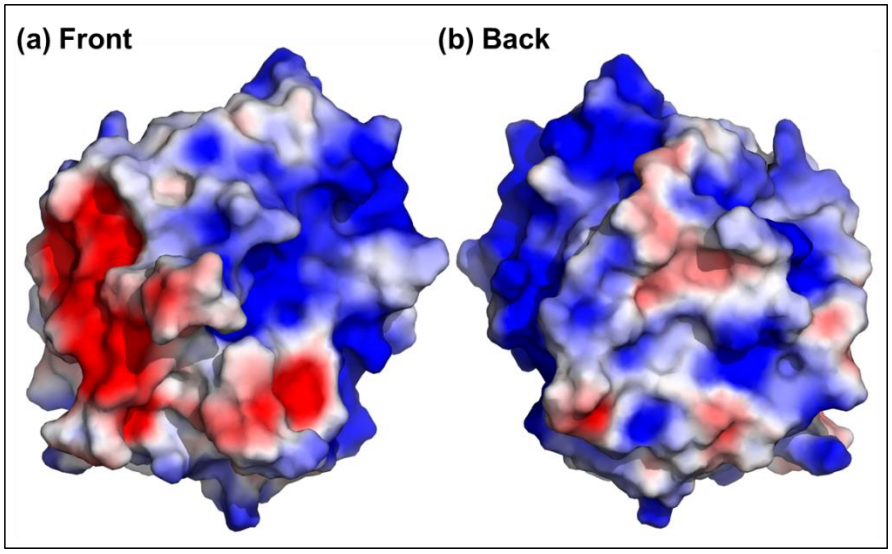

Figure S6. Electrostatic potential map of α-chymotrypsinogen A: (a) front, and (b) back. Blue indicates a value of 2kT/*e* and red indicates a value of -2kT/*e*.

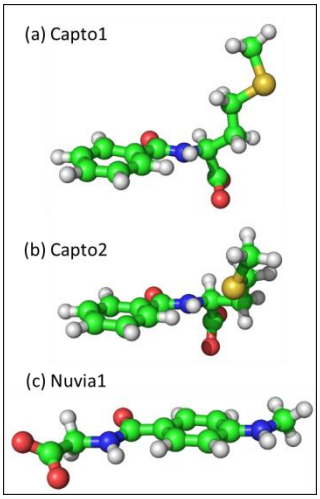

Figure S7. Dominant ligand conformations identified for the two multimodal ligands: (a-b) Capto MMC, and (c) Nuvia cPrime in bulk water.