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Distribution and solvent-exposure of Hsp70 chaperone binding sites across the E. coli proteome

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Abstract

Many proteins must interact with molecular chaperones to achieve their native folded state in the cell. Yet, how chaperone binding and binding-site characteristics affect the folding process is poorly understood. The ubiquitous Hsp70 chaperone system prevents client-protein aggregation by holding unfolded conformations or by unfolding misfolded states. Hsp70 binding sites of client proteins comprise a nonpolar core surrounded by positively charged residues. However, a detailed analysis of Hsp70 binding sites on a proteome-wide scale is still lacking. Further, it is not known whether proteins undergo some degree of folding while chaperone bound. Here, we begin to address the above questions by identifying Hsp70 binding sites in 2,258 *E. coli* proteins. We find that most proteins bear at least one Hsp70 binding site and that the number of Hsp70 binding sites is directly proportional to protein size. Aggregation propensity upon release from the ribosome correlates with number of Hsp70 binding sites only in the case of large proteins. Interestingly, Hsp70 binding sites are more solvent-exposed than other nonpolar sites, in protein native states. Our findings show that the majority of *E. coli* proteins are systematically enabled to interact with Hsp70 even if this interaction only takes place during a fraction of the protein lifetime. In addition, our data suggest that some conformational sampling may take place within Hsp70-bound states, due to the solvent exposure of some chaperone binding sites in native proteins. In all, we propose that Hsp70-chaperone-binding traits have evolved to favor Hsp70-assisted protein folding devoid of aggregation.

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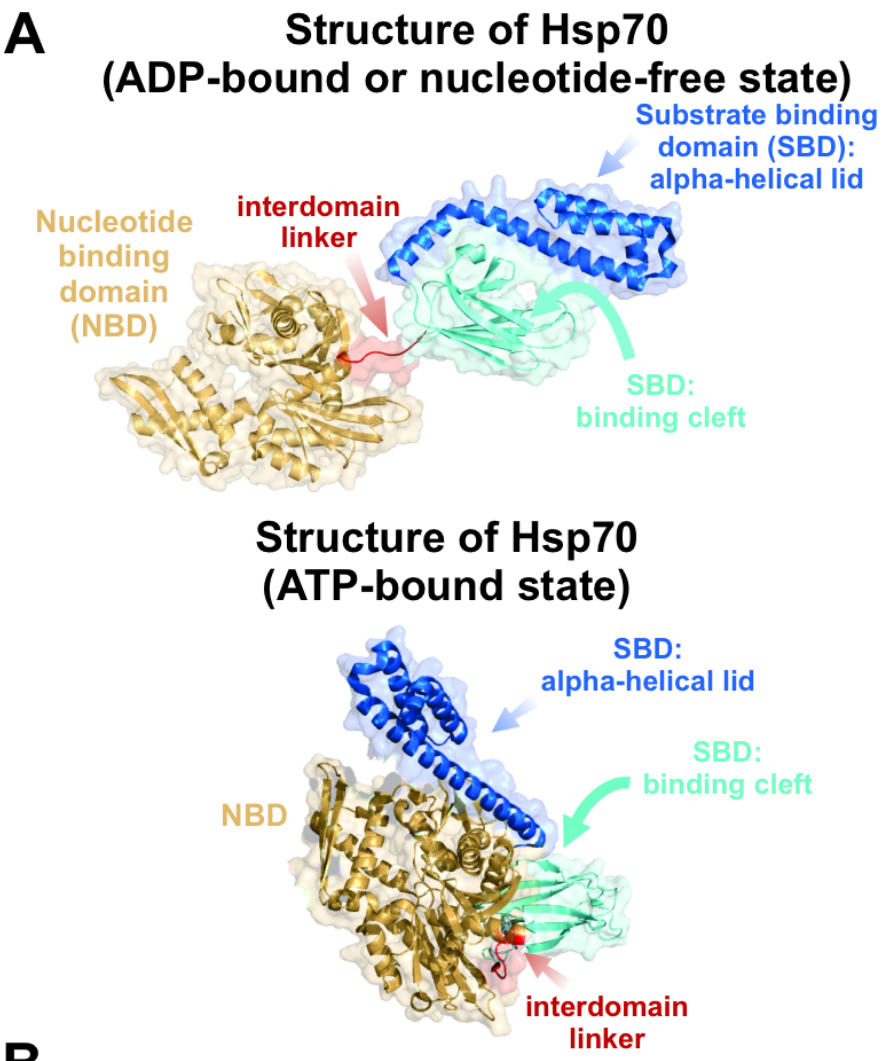

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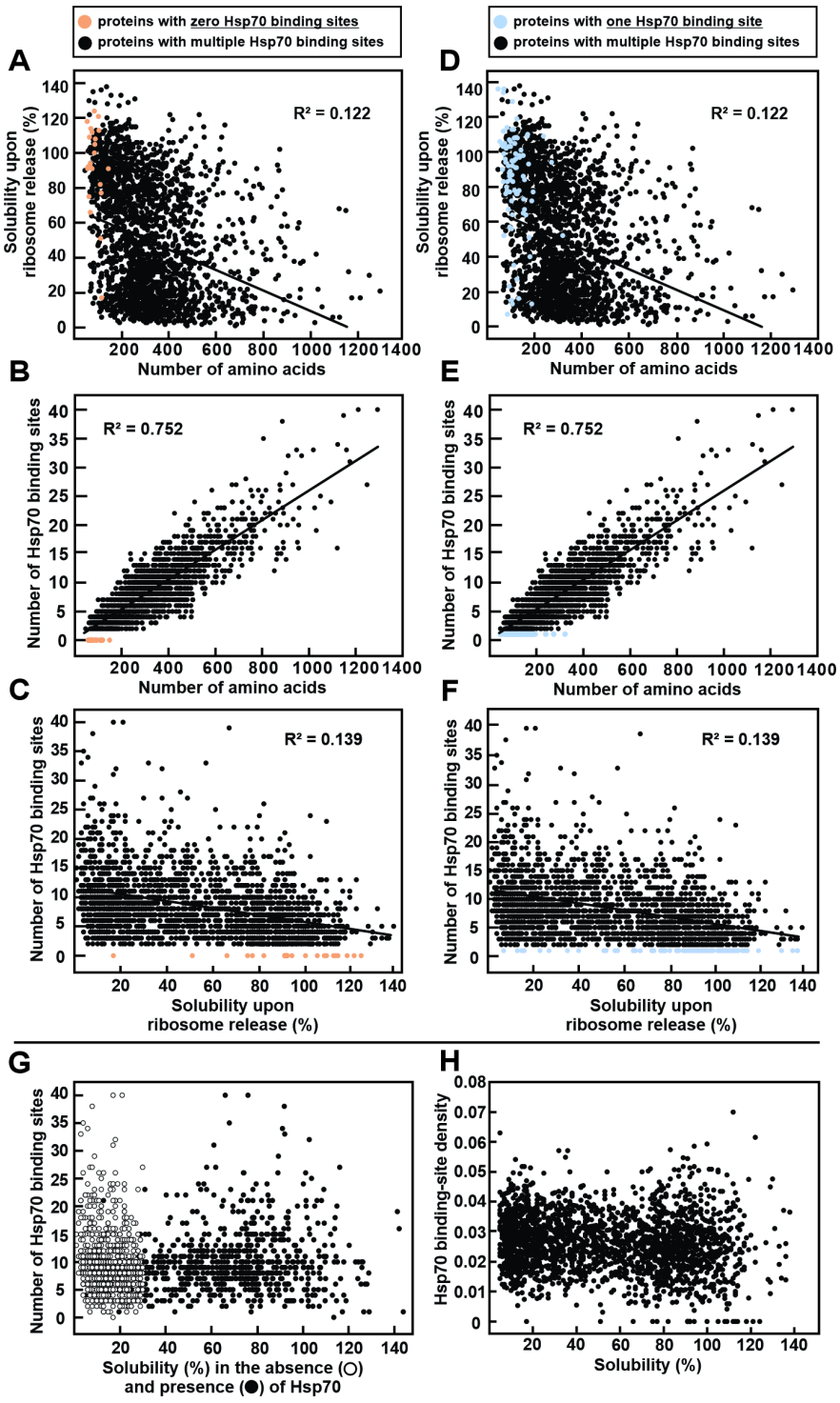

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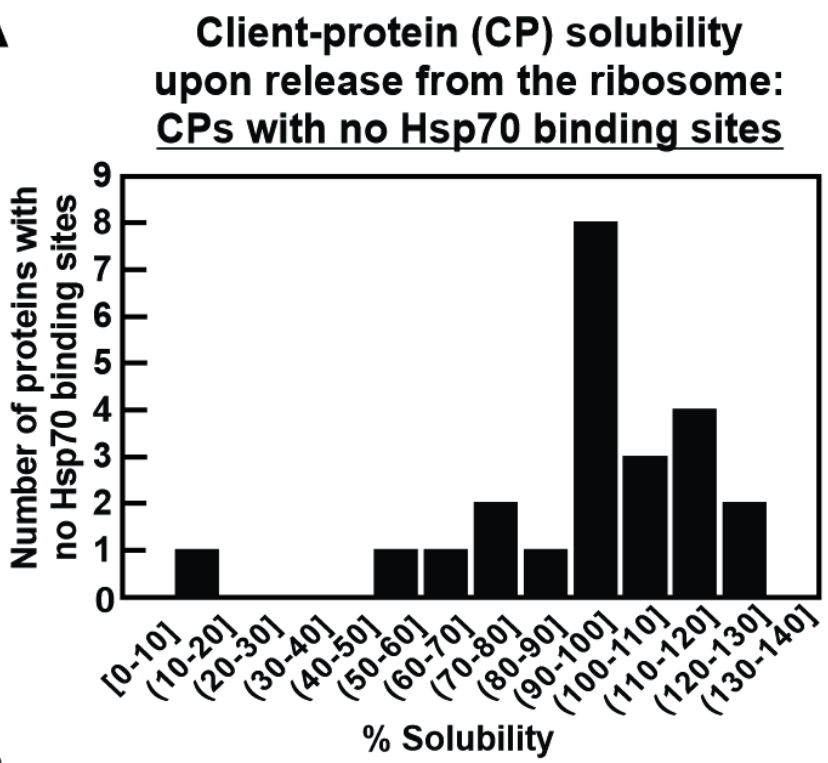

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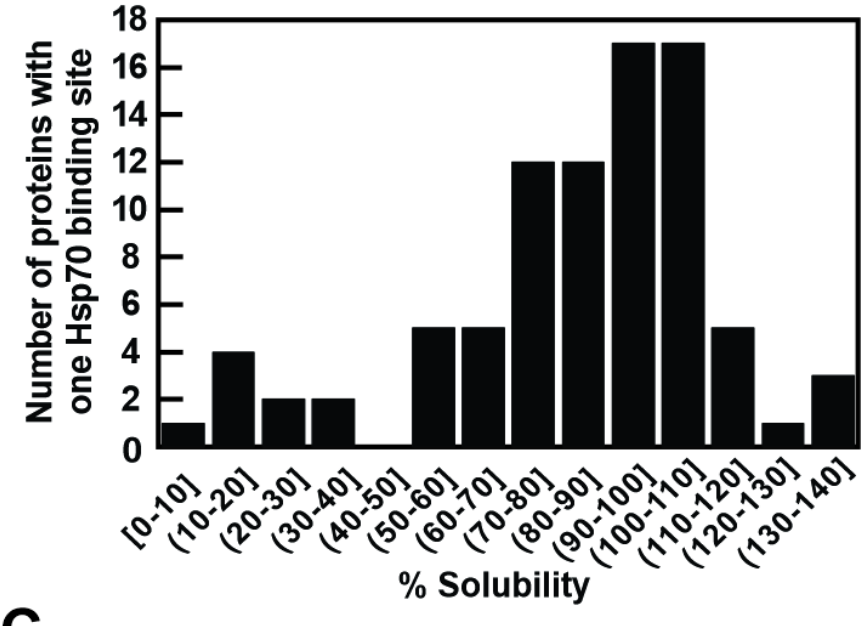

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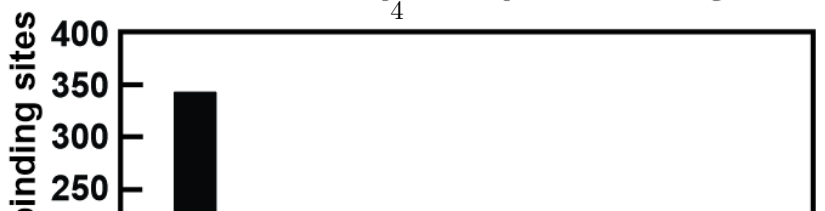

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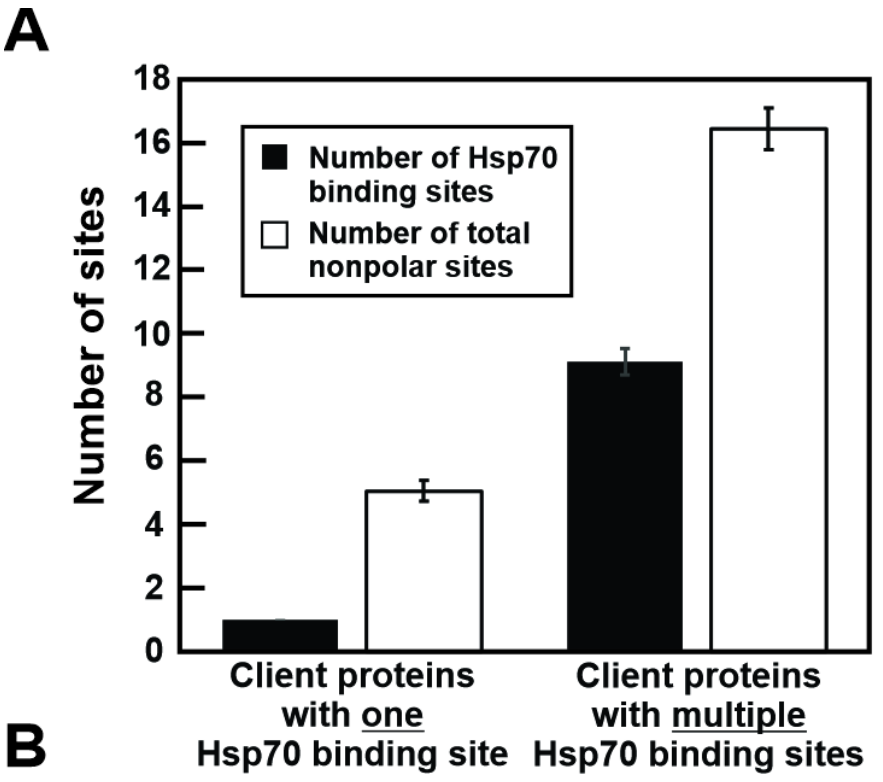

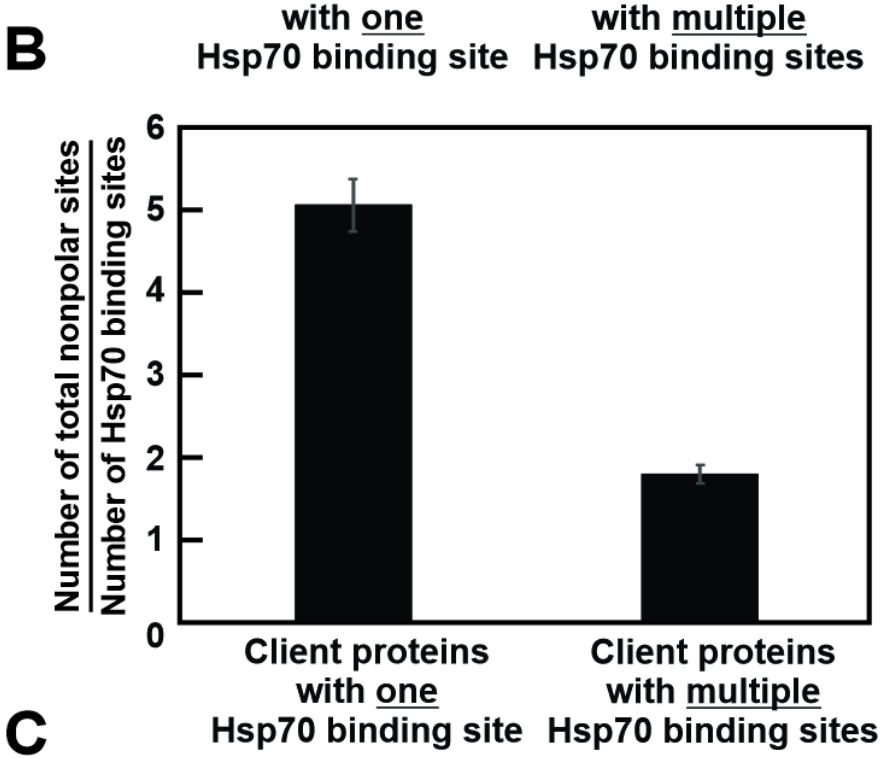

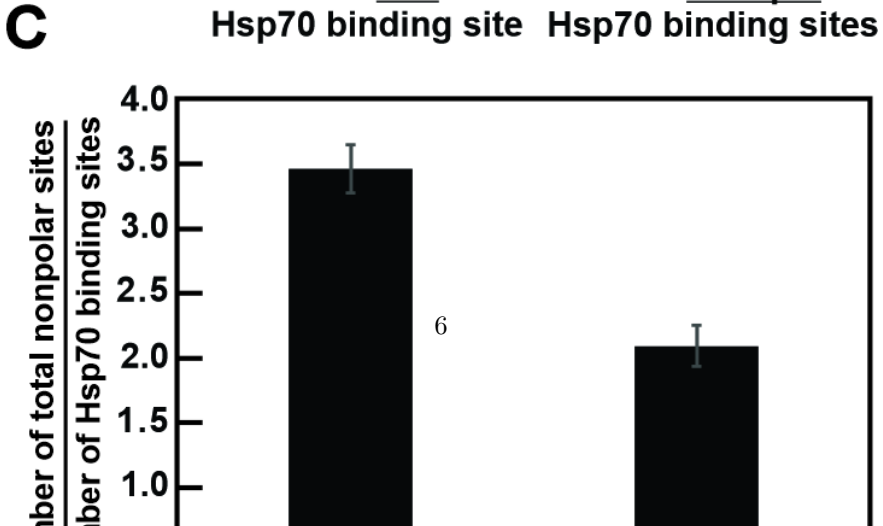

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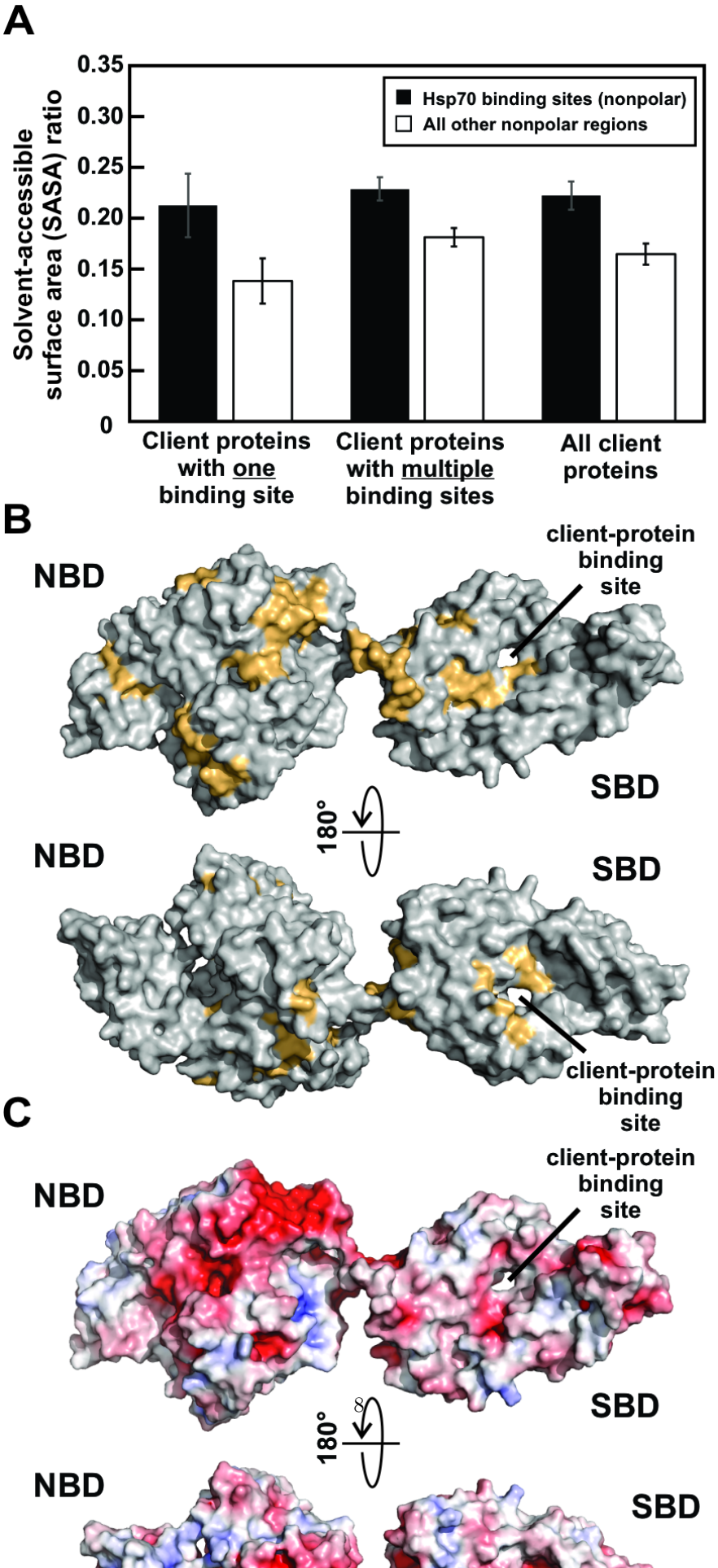

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