Allosteric Effects of Gold Nanoparticle on Human Serum Albumin

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Table S1. Force field parameters for protein-nanoparticle sphere-sphere interactions. The parameter *r* is the distance between Cα atom (Gly and Pro)/sidechain center of mass (other protein beads) and the center of mass of the nanoparticle. The interaction energy unit: kJ/ml

r (nm)	Gly	Ala	Val	Pro	Thr	Ser	Asn	Asp	Arg	Lys
2.08	-4.737	5.247	34.503	39.546	34.861	14.108	10.754	-6.645	-28.727	31.962
2.09	-13.281	-0.305	29.904	30.22	33.022	9.46	8.097	-10.117	-32.651	31.701
2.1	-21.387	-4.673	24.407	20.135	30.785	5.205	5.128	-12.682	-35.533	30.896
2.11	-28.895	-7.779	18.234	9.675	28.213	1.468	1.973	-14.362	-37.436	29.35
2.12	-35.75	-9.628	11.709	-0.701	25.405	-1.646	-1.224	-15.243	-38.503	26.952
2.13	-41.987	-10.294	5.217	-10.518	22.45	-4.064	-4.336	-15.466	-38.87	23.69
2.14	-47.693	-9.922	-0.841	-19.34	19.439	-5.749	-7.245	-15.194	-38.679	19.696
2.15	-52.951	-8.725	-6.126	-26.829	16.441	-6.711	-9.874	-14.602	-38.038	15.214
2.16	-57.81	-6.972	-10.382	-32.796	13.532	-6.991	-12.168	-13.843	-37.027	10.591
2.17	-62.242	-4.959	-13.494	-37.221	10.777	-6.69	-14.098	-13.054	-35.732	6.213
2.18	-66.156	-2.97	-15.466	-40.248	8.23	-5.938	-15.661	-12.332	-34.225	2.435
2.19	-69.407	-1.245	-16.417	-42.154	5.967	-4.9	-16.859	-11.746	-32.593	-0.486
2.2	-71.844	0.06	-16.533	-43.279	4.038	-3.744	-17.696	-11.318	-30.942	-2.436
2.21	-73.351	0.885	-16.04	-43.971	2.49	-2.632	-18.176	-11.056	-29.346	-3.462
2.22	-73.885	1.266	-15.157	-44.497	1.342	-1.702	-18.3	-10.921	-27.873	-3.754
2.23	-73.49	1.318	-14.051	-45.024	0.583	-1.034	-18.066	-10.866	-26.536	-3.578
2.24	-72.295	1.193	-12.841	-45.59	0.164	-0.669	-17.485	-10.821	-25.306	-3.236
2.25	-70.49	1.04	-11.59	-46.128	0.021	-0.572	-16.581	-10.718	-24.129	-2.985
2.26	-68.292	0.959	-10.318	-46.502	0.076	-0.684	-15.394	-10.514	-22.949	-2.997
2.27	-65.898	1	-9.017	-46.551	0.252	-0.908	-13.992	-10.167	-21.672	-3.333
2.28	-63.469	1.171	-7.672	-46.142	0.49	-1.146	-12.458	-9.653	-20.259	-3.961
2.29	-61.101	1.423	-6.272	-45.2	0.75	-1.312	-10.896	-8.979	-18.694	-4.774
2.3	-58.82	1.679	-4.822	-43.731	1.014	-1.326	-9.391	-8.168	-16.952	-5.638
2.31	-56.599	1.866	-3.354	-41.82	1.266	-1.156	-8.018	-7.272	-15.06	-6.402
2.32	-54.381	1.916	-1.902	-39.579	1.507	-0.829	-6.838	-6.347	-13.087	-6.955
2.33	-52.103	1.817	-0.508	-37.151	1.738	-0.393	-5.872	-5.449	-11.104	-7.233
2.34	-49.715	1.586	0.787	-34.689	1.964	0.075	-5.115	-4.611	-9.202	-7.223
2.35	-47.192	1.287	1.946	-32.304	2.185	0.49	-4.531	-3.865	-7.491	-6.946
2.36	-44.551	0.982	2.941	-30.067	2.403	0.793	-4.086	-3.235	-6.048	-6.462
2.37	-41.843	0.737	3.769	-28.01	2.622	0.943	-3.728	-2.72	-4.9	-5.848
2.38	-39.137	0.586	4.427	-26.121	2.83	0.931	-3.409	-2.292	-4.057	-5.171

2.39	-36.494	0.536	4.922	-24.358	3.03	0.771	-3.103	-1.922	-3.494	-4.507
2.4	-33.984	0.57	5.26	-22.671	3.209	0.514	-2.783	-1.585	-3.156	-3.897
2.41	-31.68	0.647	5.454	-21.021	3.349	0.211	-2.437	-1.274	-2.975	-3.383
2.42	-29.622	0.718	5.519	-19.391	3.432	-0.071	-2.072	-0.97	-2.882	-2.978
2.43	-27.824	0.749	5.466	-17.779	3.436	-0.292	-1.706	-0.678	-2.819	-2.691
2.44	-26.278	0.729	5.315	-16.232	3.345	-0.423	-1.357	-0.409	-2.755	-2.522
2.45	-24.949	0.65	5.082	-14.781	3.157	-0.462	-1.052	-0.17	-2.66	-2.454
2.46	-23.784	0.53	4.785	-13.471	2.881	-0.427	-0.816	0.022	-2.534	-2.46
2.47	-22.72	0.398	4.438	-12.329	2.545	-0.351	-0.657	0.164	-2.377	-2.527
2.48	-21.712	0.269	4.061	-11.38	2.183	-0.265	-0.585	0.251	-2.205	-2.62
2.49	-20.706	0.171	3.662	-10.631	1.831	-0.202	-0.599	0.297	-2.016	-2.719
2.5	-19.686	0.113	3.26	-10.071	1.525	-0.186	-0.672	0.307	-1.831	-2.808
2.51	-18.633	0.1	2.871	-9.662	1.284	-0.215	-0.782	0.297	-1.655	-2.869
2.52	-17.559	0.13	2.51	-9.359	1.115	-0.271	-0.886	0.261	-1.498	-2.89
2.53	-16.463	0.197	2.186	-9.115	1.008	-0.334	-0.958	0.222	-1.369	-2.866
2.54	-15.372	0.289	1.909	-8.891	0.944	-0.372	-0.977	0.183	-1.276	-2.787
2.55	-14.286	0.389	1.691	-8.651	0.908	-0.368	-0.937	0.151	-1.229	-2.666
2.56	-13.231	0.49	1.528	-8.375	0.877	-0.31	-0.844	0.142	-1.226	-2.499
2.57	-12.213	0.579	1.414	-8.057	0.85	-0.211	-0.722	0.162	-1.261	-2.312
2.58	-11.245	0.658	1.348	-7.703	0.825	-0.078	-0.594	0.225	-1.323	-2.118
2.59	-10.34	0.719	1.317	-7.345	0.808	0.067	-0.485	0.331	-1.397	-1.929
2.6	-9.514	0.77	1.323	-6.99	0.806	0.195	-0.401	0.479	-1.469	-1.757
2.61	-8.776	0.812	1.348	-6.663	0.819	0.302	-0.345	0.655	-1.528	-1.604
2.62	-8.125	0.851	1.39	-6.373	0.857	0.37	-0.309	0.842	-1.568	-1.468
2.63	-7.553	0.886	1.441	-6.124	0.908	0.411	-0.279	1.021	-1.593	-1.343
2.64	-7.054	0.922	1.498	-5.918	0.966	0.428	-0.239	1.168	-1.603	-1.221
2.65	-6.595	0.951	1.56	-5.739	1.02	0.43	-0.186	1.272	-1.608	-1.096
2.66	-6.158	0.971	1.62	-5.576	1.062	0.431	-0.117	1.334	-1.605	-0.97
2.67	-5.721	0.968	1.687	-5.409	1.09	0.428	-0.03	1.355	-1.596	-0.847
2.68	-5.266	0.938	1.751	-5.231	1.1	0.425	0.063	1.35	-1.577	-0.737
2.69	-4.802	0.878	1.814	-5.039	1.088	0.418	0.156	1.336	-1.538	-0.645

Table S2 Force field parameters for protein-nanoparticle sphere-sphere interactions. Please refer to caption of Table S1 for definition.

r(nm)	Glu	Gln	Leu	Ile	Phe	Tyr	Trp	Met	Cys	His
2.08	22.974	11.221	19.437	34.945	11.183	13.105	20.447	31.855	10.349	20.064
2.09	19.757	6.825	14.66	33.49	7.415	8.345	14.803	28.867	3.125	15.879
2.1	15.998	2.73	10.127	31.336	3.07	3.064	8.637	24.557	-3.309	10.799
2.11	11.981	-0.918	6.022	28.413	-1.637	-2.332	2.244	19.053	-8.614	4.971
2.12	7.978	-4.077	2.456	24.723	-6.423	-7.441	-4.073	12.677	-12.642	-1.347
2.13	4.244	-6.808	-0.556	20.327	-10.955	-11.927	-10.064	5.88	-15.407	-7.78
2.14	0.94	-9.222	-3.059	15.392	-14.924	-15.595	-15.566	-0.822	-17.085	-13.93
2.15	-1.867	-11.457	-5.116	10.158	-18.09	-18.392	-20.511	-6.925	-17.936	-19.411
2.16	-4.193	-13.595	-6.777	4.931	-20.32	-20.4	-24.89	-12.028	-18.233	-23.939
2.17	-6.112	-15.67	-8.05	0.032	-21.599	-21.792	-28.74	-15.895	-18.215	-27.354
2.18	-7.728	-17.622	-8.917	-4.229	-22.028	-22.787	-32.094	-18.472	-18.018	-29.657
2.19	-9.133	-19.337	-9.316	-7.603	-21.782	-23.561	-34.958	-19.873	-17.687	-30.99
2.2	-10.397	-20.679	-9.214	-9.949	-21.075	-24.241	-37.29	-20.324	-17.199	-31.584
2.21	-11.56	-21.534	-8.619	-11.246	-20.102	-24.862	-39.023	-20.104	-16.506	-31.701
2.22	-12.62	-21.831	-7.599	-11.594	-19.019	-25.414	-40.084	-19.48	-15.563	-31.575
2.23	-13.562	-21.59	-6.271	-11.2	-17.918	-25.835	-40.436	-18.659	-14.376	-31.372

2.24	-14.351	-20.883	-4.797	-10.308	-16.829	-26.06	-40.089	-17.766	-12.996	-31.16
2.25	-14.954	-19.834	-3.347	-9.18	-15.739	-26.044	-39.121	-16.847	-11.522	-30.915
2.26	-15.348	-18.579	-2.068	-8.032	-14.614	-25.767	-37.658	-15.902	-10.065	-30.555
2.27	-15.52	-17.24	-1.044	-7.013	-13.425	-25.24	-35.858	-14.9	-8.713	-29.98
2.28	-15.478	-15.907	-0.302	-6.192	-12.165	-24.492	-33.875	-13.826	-7.537	-29.1
2.29	-15.234	-14.643	0.181	-5.552	-10.846	-23.554	-31.84	-12.674	-6.553	-27.877
2.3	-14.816	-13.431	0.471	-5.038	-9.509	-22.453	-29.852	-11.476	-5.75	-26.325
2.31	-14.284	-12.254	0.662	-4.571	-8.196	-21.218	-27.954	-10.268	-5.075	-24.511
2.32	-13.683	-11.083	0.834	-4.088	-6.952	-19.879	-26.172	-9.083	-4.468	-22.527
2.33	-13.031	-9.906	1.058	-3.541	-5.812	-18.471	-24.491	-7.952	-3.883	-20.495
2.34	-12.344	-8.716	1.368	-2.926	-4.781	-17.02	-22.903	-6.897	-3.3	-18.519
2.35	-11.629	-7.54	1.762	-2.268	-3.847	-15.567	-21.386	-5.908	-2.718	-16.667
2.36	-10.895	-6.413	2.205	-1.607	-2.986	-14.168	-19.939	-4.973	-2.158	-15.001
2.37	-10.146	-5.383	2.644	-0.988	-2.174	-12.882	-18.559	-4.068	-1.656	-13.533
2.38	-9.391	-4.502	3.037	-0.446	-1.381	-11.753	-17.238	-3.19	-1.238	-12.255
2.39	-8.662	-3.771	3.309	-0.016	-0.596	-10.794	-15.972	-2.36	-0.93	-11.144
2.4	-7.965	-3.2	3.431	0.285	0.182	-10.012	-14.758	-1.611	-0.729	-10.157
2.41	-7.322	-2.763	3.366	0.476	0.926	-9.377	-13.584	-0.983	-0.63	-9.262
2.42	-6.731	-2.41	3.12	0.572	1.608	-8.842	-12.441	-0.516	-0.607	-8.416
2.43	-6.19	-2.094	2.73	0.606	2.2	-8.358	-11.324	-0.244	-0.649	-7.597
2.44	-5.691	-1.783	2.252	0.599	2.666	-7.904	-10.224	-0.169	-0.716	-6.783
2.45	-5.221	-1.462	1.744	0.572	2.974	-7.452	-9.149	-0.286	-0.788	-5.974
2.46	-4.77	-1.127	1.264	0.542	3.108	-6.992	-8.105	-0.554	-0.853	-5.182
2.47	-4.344	-0.794	0.867	0.506	3.062	-6.53	-7.121	-0.919	-0.898	-4.441
2.48	-3.942	-0.494	0.57	0.454	2.86	-6.072	-6.215	-1.317	-0.928	-3.77
2.49	-3.578	-0.252	0.382	0.381	2.54	-5.635	-5.403	-1.683	-0.938	-3.2
2.5	-3.26	-0.084	0.282	0.28	2.154	-5.223	-4.703	-1.972	-0.939	-2.758
2.51	-3.004	0.01	0.249	0.14	1.757	-4.838	-4.111	-2.155	-0.932	-2.445
2.52	-2.802	0.037	0.252	-0.029	1.396	-4.465	-3.618	-2.228	-0.919	-2.265
2.53	-2.658	0.017	0.26	-0.21	1.107	-4.094	-3.214	-2.221	-0.898	-2.197
2.54	-2.558	-0.032	0.257	-0.382	0.891	-3.705	-2.881	-2.16	-0.857	-2.212
2.55	-2.487	-0.088	0.237	-0.531	0.748	-3.286	-2.597	-2.08	-0.793	-2.282
2.56	-2.446	-0.14	0.202	-0.634	0.653	-2.841	-2.351	-2.02	-0.695	-2.364
2.57	-2.414	-0.185	0.155	-0.676	0.567	-2.389	-2.142	-1.991	-0.556	-2.434
2.58	-2.39	-0.218	0.125	-0.659	0.47	-1.95	-1.962	-1.993	-0.386	-2.466
2.59	-2.36	-0.243	0.123	-0.59	0.348	-1.537	-1.819	-2.006	-0.189	-2.446
2.6	-2.319	-0.253	0.148	-0.479	0.193	-1.164	-1.716	-2.005	0.022	-2.374
2.61	-2.264	-0.253	0.205	-0.353	0.023	-0.836	-1.664	-1.97	0.226	-2.259
2.62	-2.187	-0.235	0.291	-0.223	-0.146	-0.541	-1.656	-1.883	0.403	-2.12
2.63	-2.095	-0.207	0.394	-0.097	-0.29	-0.259	-1.698	-1.741	0.544	-1.974
2.64	-1.989	-0.164	0.501	0.002	-0.383	0.025	-1.775	-1.558	0.635	-1.835
2.65	-1.869	-0.126	0.604	0.081	-0.418	0.324	-1.877	-1.354	0.684	-1.706
2.66	-1.751	-0.105	0.693	0.134	-0.396	0.626	-1.984	-1.162	0.704	-1.577
2.67	-1.63	-0.108	0.758	0.181	-0.326	0.933	-2.076	-0.993	0.699	-1.444
2.68	-1.515	-0.132	0.796	0.225	-0.222	1.2	-2.143	-0.866	0.682	-1.297
2.69	-1.417	-0.18	0.808	0.286	-0.103	1.426	-2.177	-0.79	0.661	-1.127

Table S3. The number of water molecules and ions in the simulation systems for the four protein-nanoparticle complexes. All systems contain an albumin protein (5873 atoms) and a 4.0 nm gold nanoparticle (1985 atoms).

Complex	Water molecules	Na+	Cl-	Total number of atoms
A	28711	93	78	94162
B	28211	93	78	92662
C	28253	93	78	92788
D	29172	93	78	93560

Table S4. The IDs of amino acid residues that have $\Delta Sec^i > 0.5$ and $d_i > 5.0$ nm in four complexes

A	57,116,300,503,504,506,507,508,510,511,512,513,514,515,540,541,542,543,544,545, 546,547,560,561,563,564,565,566,567,568,579
B	32,33,57,61,77,78,79,84,106,109,147,248,250,297,298,300,304,305,311,312, 314,511,512,513,514,515,568,569
C	300,305,306,307,314,338,451,495
D	81,205,206,305,306,312,313,314,341,353,375,376,416,417,418,435,450,457,460,461, 481,482,483,497,503,504,505,507,511,512,513,514,515,540,542,543,544,545,546,547, 559,561,562,564,568

Table S5 The IDs of amino acid residues in binding sites of HSA proteins[1]

Binding Site	Residues
Fatty acid binding sites	
FA1	Tyr138, Tyr161
FA2	Tyr150, Arg257, Ser287
FA3	Ser342, Arg348, Arg485
FA4	Arg410 Tyr411, Ser489
FA5	Tyr401, Lys525
FA6	Arg209, Asp324, Ser480, Lys351, Glu354
FA7 (Suldow's site I)	Tyr150, Lys199, Arg218, Arg222, His242, Arg257, Leu328, Ala291
FA8	Lys195, Lys199, Arg218, Asp451, Ser454
FA9	Glu187, Lys432
Heme binding	Arg114, His146, Lys190
Thyroxin binding sites	
Tr1	Tyr150, Lys199, Trp214, Arg218, Arg222, Arg257
Tr2	Glu390, Asn391, Leu394, Ala406, Arg410, Tyr411, Ser489
Tr3/Tr4	Asp301, Residues 502-514, Ala528, Leu532
Bacteria protein (BacP)	Phe228, Ala229, Asn318, Glu321, Ala322, Val325, Phe326, Met329
Metal Binding sites (Metal)	Asp1, Ala2, His3, Cys34, His67, Asn99, His247, Asp249

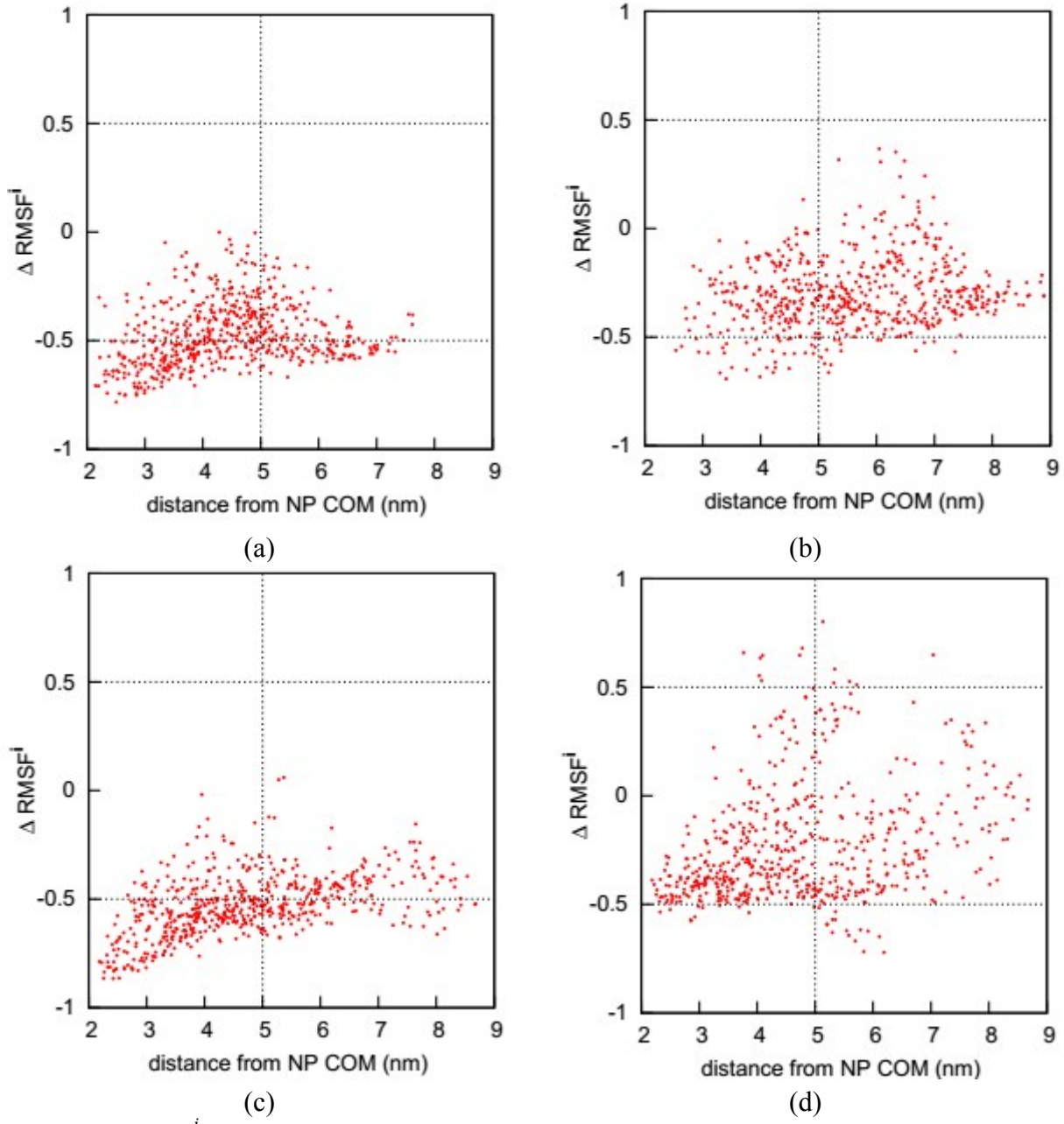

Figure S1. $\Delta RMSF^i$ of Cα atoms on the HSA protein vs. their distance from the center of mass of the gold NP in (a) Complex A, (b) Complex B, (c) Complex C, and (d) Complex D. A negative value indicates that the residue decreases its flexibility and a positive value indicates that the residue increases its flexibility compared to its flexibility in the bulk solution.

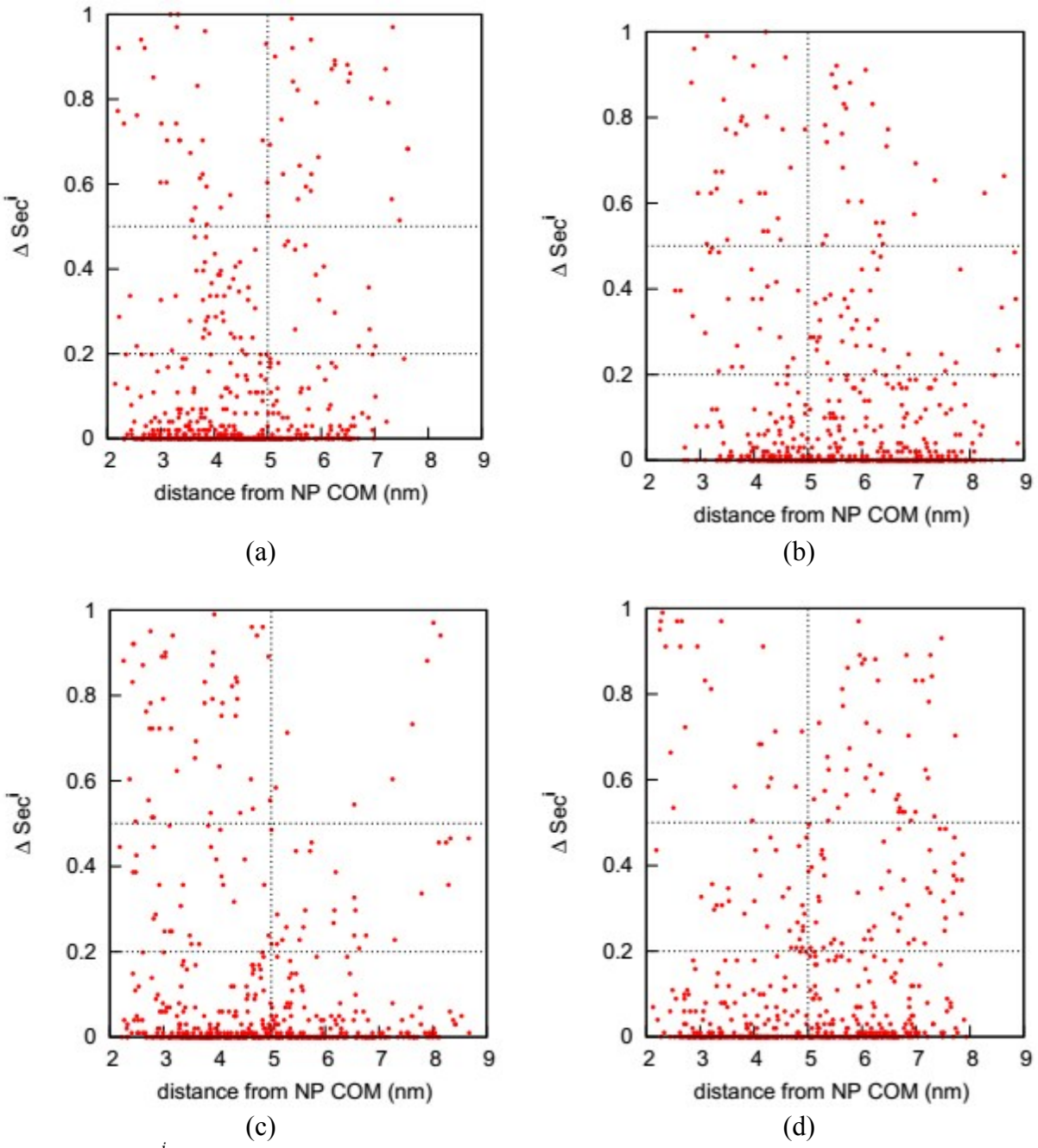

Figure S2. ΔSec^i of individual residues i vs. distance between their Cα atoms and the center of mass of the gold NP. (a) Complex A, (d) Complex B, (c) Complex C and (d) Complex D. Many residues have $\Delta Sec^i > 0.5$; the binding of the gold NP changes the secondary structure of these residues significantly. These residues are distributed on regions close to and distant from the NP.

Reference:

[1]G. Fanali, A. di Masi, V. Trezza, M. Marino, M. Fasano and P. Ascenzi, *Molecular Aspects of Medicine*, 2012, **33**, 209-290.