Electronic Supplementary Material (ESI) for Nanoscale.
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Can small hydrophobic gold nanoparticles inhibit β_2-microglobulin fibrillation?

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Table S1: Orientations of β2-microglobulin protein on the single NP surface obtained following a standard MD protocol. A series of four simulations were performed on the first and second most representative complexes from docking, each with different initial velocities. The final global orientation of the systems after the simulation, is reported. In the last column, the time evolution of the protein contact residues along the entire 50 ns dynamics are plotted and differentiated by colour.

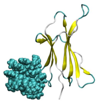
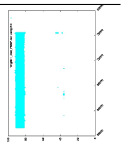
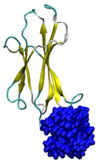
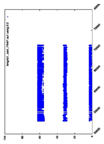
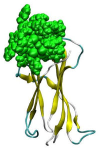
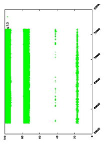
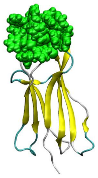
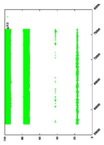
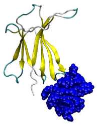
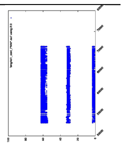
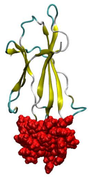
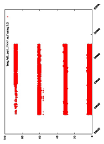
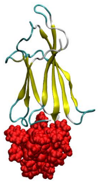
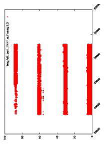
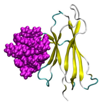
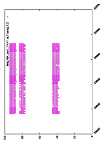
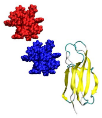
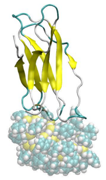
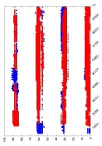
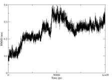
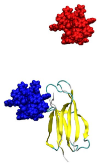
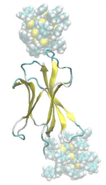
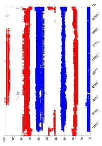
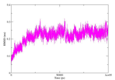
Complex Num	Init. Vel.	Global orientation		
Complex A	d1	converted to E		
Complex A	d2	converted to B		
Complex A	d3	converted to C		
Complex A	d4	converted to C		
Complex B	d1	stable		
Complex B	d2	stable		
Complex B	d3	stable		
Complex B	d4	converted to A		

Table S2: Orientations of $\beta 2$-microglobulin protein interacting with two identical nanoclusters. A series of four simulations with different initial velocities were repeated in two cases. A: the two NPs starting at the same vertex of the box and B: the two NPs at two opposite vertexes of the box. For initial orientations C and D only one different initial velocities was used. In columns: (a),(d) we report the final global orientation of the systems after the simulation, (b),(e) we plot the time evolution of the protein contact residues along the entire 100 ns dynamics. In columns (c),(f) RMSD plots of 100 ns MD clearly show that the simulation time is effective in sampling stable patches.

(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)
							
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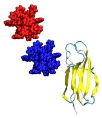	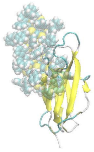	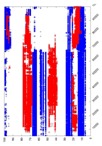	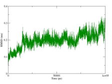	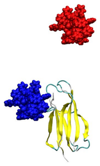	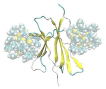	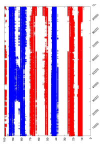	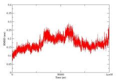
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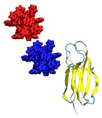	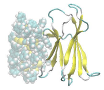	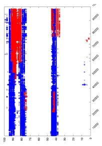	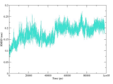	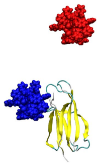	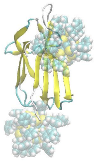	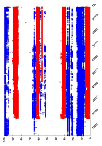	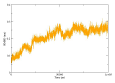
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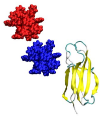	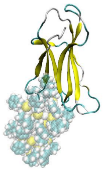	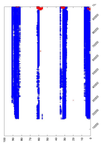	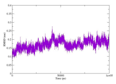	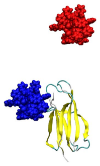	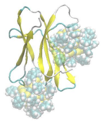	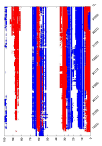	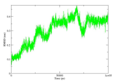
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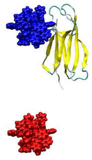	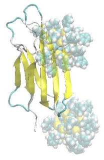	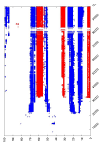	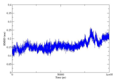	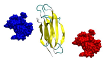	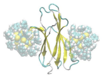	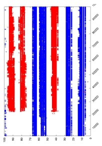	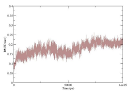
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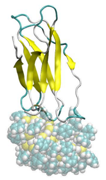
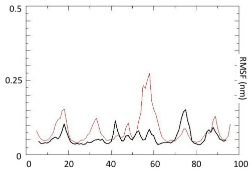
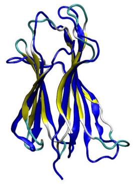
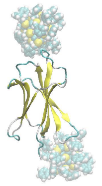
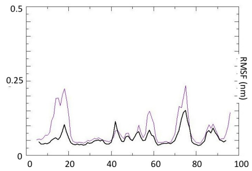
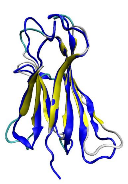
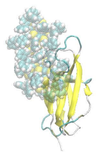
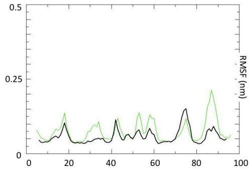
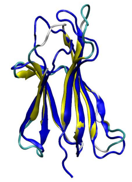
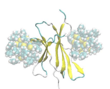
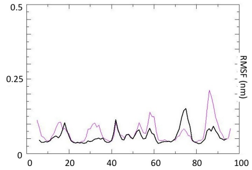
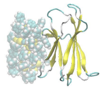
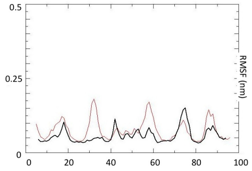
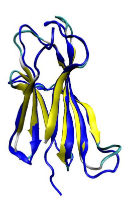
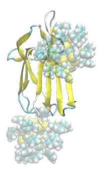
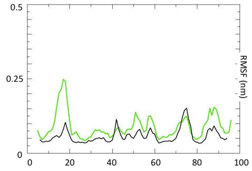
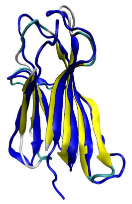
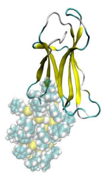
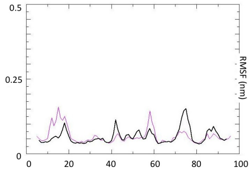
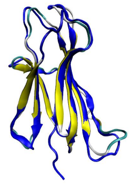
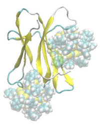
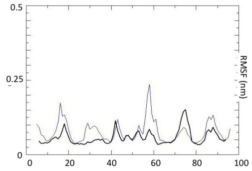
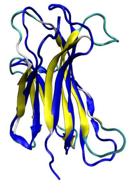
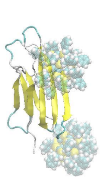
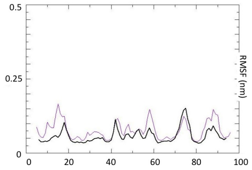
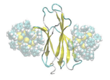
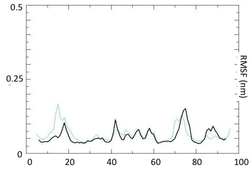
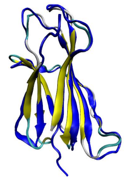
Table S3: Orientations of β2-microglobulin protein interacting with two identical nanoclusters. (a),(d) Most stable orientations of the couple of NPs after 100 ns MD at T=300 K (b),(e) the avergae root mean square fluctuation (RMSF) of backbone residues along the entire 100 ns dynamics. (c),(f) the divergence of each protein refined structure (excluding the N-terminal and C-terminal tails) with respect to the starting NMR structure (native state)

(a)	(b)	(c)	(d)	(e)	(f)
 EB			 BC		
 A'C			 A'D		
 A'E			 BC		
 EB			 BC		
 BC			 A'D		

Tab. S4: Total Energies are taken from the last 20 ns of the four indipendent MD runs for each complex. The values refers to systems having the same number of water molecules within an equal number of NPs.

Average Energy (kJ/mol)	Patch
-374598	E
-374568	B
-373697	C
-374558	C
-380051	B
-379991	B
-380047	B
-380016	A’
-809040	EB
-808697	A’C
-808946	A’E
-807613	EB
-807035	BC
-807134	A’D
-807244	BC
-807347	BD
-807083	BC
-807168	A’D

Table S5:Development of force field parameters for the gold nanoparticle: the organic ligand part of the system has been parametrized by the standard OPLS/AA method, while the gold core and the covering RS-Au-SR motifs are developed consistently with the GolP parameters. The parametrization involved the following steps: a) electronic structure calculations of the crystal structure of the GNP to be used as a reference to test the suitability of the force field parameters to reproduce ab-initio results, b) parameterization of the bonded interactions between the atoms of the GNP, c) charge derivation, d) parameterization of the van der Waals terms by fitting to MP2 calculations on model systems. The bond stretching and angle bending force constants were parameterized through a linear least-square fitting approach. Such fittings were performed for the Au-Au bond and the Au-Au-Au angle of the internal gold core and for the Au-S, S-C, S-Au-S and Au-S-Au angle parameters. In addition bonding parameters were created for the Au-S-Au (labelled AU-SB-AUC in panel D) and for C1-SB-AUC which is the angle defined by the first carbon atom of the ethyl group attached to the sulphur atom which is bonded directly to the gold atom forming the icosahedron. Parameters were obtained by using the Minpack nonlinear optimization package. In order to allow the rigidity of the inner gold structure, parameters for the angle defined by the sulphur atom, the gold forming the icosahedron and the gold core atom (labelled SB-AUC-AUC) were developed. Panels A,B,C show the results of the regression coefficients of these bonds and angles. The force constants of the bond length and the angle strength were calculated using the above model. Van der Waals terms, accounted for by 12-6 Lennard Jones potentials, were parametrized by fitting the MP2 interaction energies between the model compound shown in panel A and a methane molecule placed at different relative orientations and distances on a regular grid. The LANL2DZ basis set with an additional d shell on S (exponent=0.55 a.u.) was used.