

Supplementary information: How does the Water Solvent and Glutathione Ligands Affect the Structure and the Electronic Properties of Au₂₅(SR)₁₈⁻?

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DFT calculations

AIMD simulations were performed within the Car-Parrinello¹ approach, which is based on DFT, and using the CPMD package.² A fictitious electron mass of 600 a.u. and an integration time step of 0.12 fs guaranteed a good control of the adiabaticity for ionic and electronic equations of motion in all the systems where QM or QM/MM molecular dynamics simulations were performed. The simulation temperature was set to 300 K by coupling it to a Nosé-Hoover chain thermostat for the ionic degrees of freedom.³⁻⁵ The Kohn-Sham orbitals were expanded in a plane wave (PW) basis set with a kinetic energy cutoff of 90 Ry. The exchange-correlation functional employed the parametrization by Perdew-Burke-Ernzerhoff (PBE)⁶, which has been widely used to describe AuMPCs. Furthermore, a hybrid functional (PBE0⁷) was used to compute

HOMO-LUMO gaps for the optimized structures in order to evaluate the effect of including a portion of the exact exchange interaction on the electronic properties. The gold atoms were represented by a Goedecker⁸⁻⁹ type pseudopotential ($5d^{10}6s^1$ valence), carbon and sulfur by a Troullier-Martins¹⁰ type, and hydrogen by a Car-von Barth type, as in references ¹¹ and ¹². For geometry optimization, an annealing factor was introduced for MD and its value has been gradually incremented from 0.9 to 0.999 to remove kinetic energy from the ionic degrees of freedom. We have considered that the structure is optimized when the largest nuclear gradient is lower than $5.0 \cdot 10^{-4}$ atomic units.

Hybrid QM/MM simulations

Prior to the QM/MM molecular dynamics, MM simulations with classical potentials were performed using the NAMD¹³ software. Ligands were modelled with the FF99SB force field,¹⁴ and water molecules were described with the TIP3P force field.¹⁵ Snapshots of the MM equilibrated systems in Figure 1 were taken from the subsequent QM/MM simulations. The QM/MM interface is modelled by the use of monovalent carbon pseudopotentials which saturates the valence of the QM atoms of the border (linking atoms).¹⁶ The electrostatic interactions in the interface of the two regions are described in reference ¹⁷. The average structure over 7.5 ps of QM/MM MD simulation at room temperature was considered for analysis. The solvated structure of $\text{Au}_{25}(\text{GSH})_{18}^-$ was compared with those of isolated and solvated $\text{Au}_{25}(\text{SCH}_3)_{18}^-$ to investigate the effect of the bulky biological ligand (GSH) with respect to the small inorganic alkanethiolates used in the synthetic methods.

Structures and trajectories were analyzed using the standard tools of VMD.¹⁸ VMD is used also to compute other important parameters that provide structural

information such as the radius of gyration, the solvent accessible surface area (SASA) and radial distribution functions.

Systems analyzed

Three different systems were prepared:

- i) **Isolated $\text{Au}_{25}(\text{SCH}_3)_{18}^-$** : The AuMPC is placed in a $20.3\text{\AA} \times 21.0\text{\AA} \times 21.3\text{\AA}$ box. A full QM description is used.
- ii) **Solvated $\text{Au}_{25}(\text{SCH}_3)_{18}^-$** : The AuMPC is surrounded by 1465 water molecules. A sodium cation is also added to neutralize the negative charge of the AuMPC. The size of the full box is $36.9\text{\AA} \times 34.9\text{\AA} \times 35.7\text{\AA}$. A classical molecular mechanics simulation (MM) of 2 ns is performed to equilibrate the solvent and the alkane chains of the methanethiolate ligands. For the subsequent QM/MM study, only the AuMPC is considered in the QM region, with the water molecules and the cation being part of the MM region.
- iii) **Solvated $\text{Au}_{25}(\text{GSH})_{18}^-$** : The AuMPC is surrounded by 3576 water molecules , and 19 sodium cations are added, 18 to neutralize the negative charge of the GSH peptides and 1 to neutralize the global charge of the AuMPC. The size of the full box is $53.0\text{\AA} \times 55.5\text{\AA} \times 53.7\text{\AA}$. A classical MM simulation of 8 ns is performed to equilibrate the solvent and the peptides. Solvent is equilibrated in less than 2 ns, but the peptides need more than 3 ns. We have considered an *S* configuration for the asymmetric carbons (it is known that there is no influence in considering *S* or *R* configuration).¹⁹ For the subsequent QM/MM study, the 25 gold atoms and the 18 cysteines (only the $\text{S-CH}_2\text{-C-}$ part of cysteine) of each GSH form the QM region (115 atoms). The rest of the cysteine, glutamate, glycine, 19 sodium cations and 3576 water molecules are taken into account in the MM part.

The optimized coordinates of solvated Au_{25} clusters (SCH_3 and GSH ligands) are given as separate xyz-files. The files include also solvent molecules/cations within a 4.0 Å cut-off from any nanocluster atom.

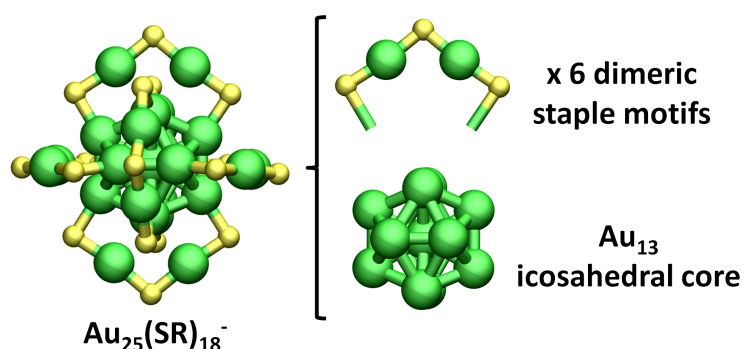


Figure S1. Description of the pieces that form the structure of $\text{Au}_{25}(\text{SR})_{18}^-$. The organic ligands attached to the sulphur atoms are not shown for clarity. Six dimeric staple motifs are the protecting units that are bonded to the Au_{13} icosahedral core. Gold and sulphur are shown green and yellow, respectively.

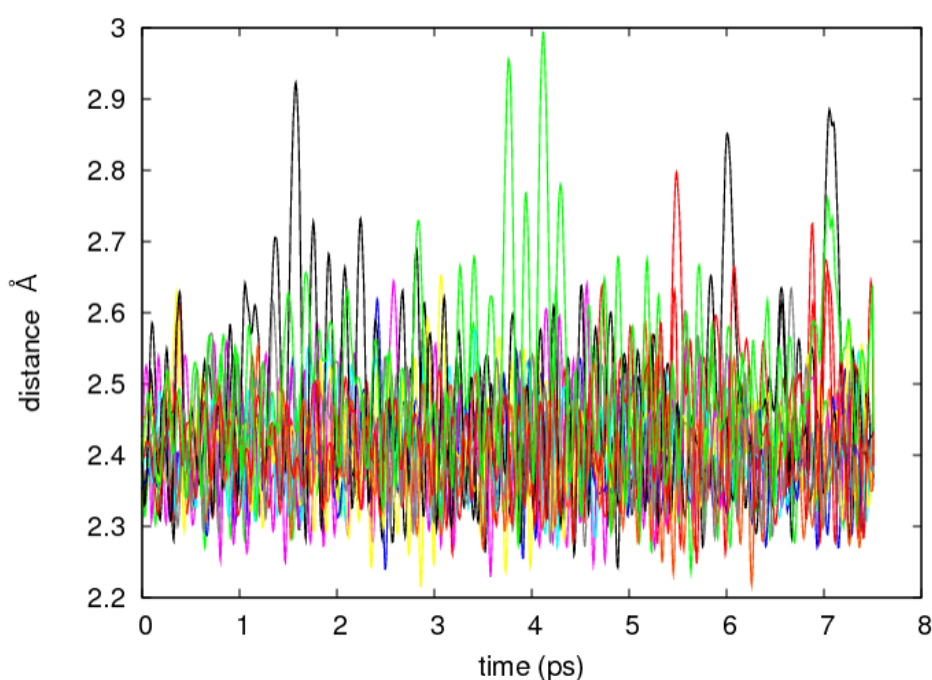


Figure S2. Variation of the twelve S-Au(a') bonds of the six dimeric staple motifs with the icosahedral Au_{13} core along the 7.5 ps of QM/MM simulations at 300 K. The fluctuations cause asymmetric S-Au(a') distributions, see Figure S3.

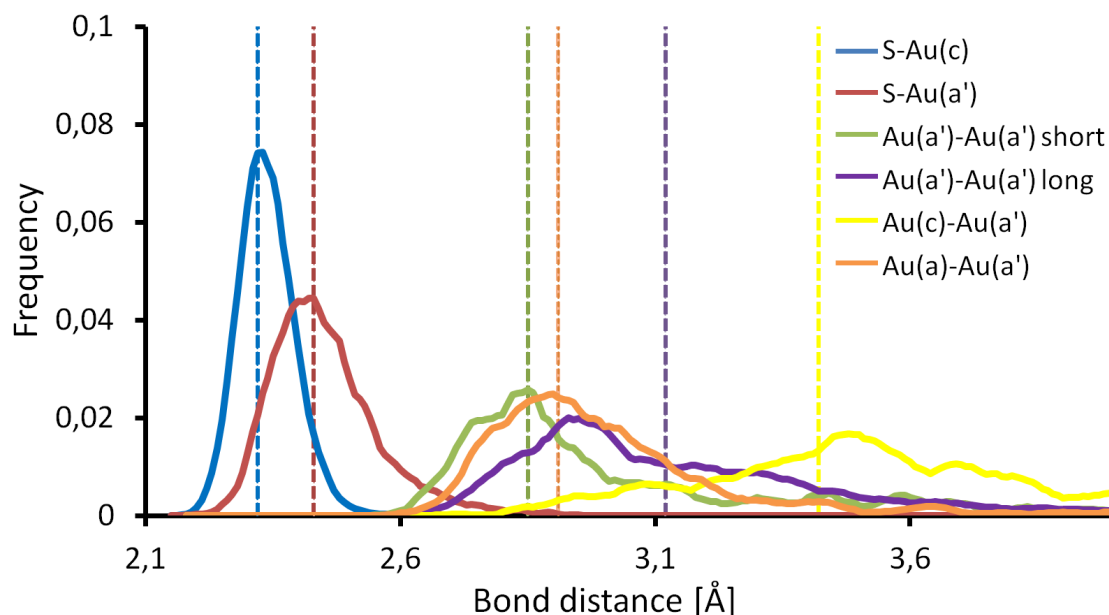


Figure S3. Histogram of the six main distances that define the structure of $\text{Au}_{25}(\text{GSH})_{18}^-$ during the 7.5 ps QM/MM simulation at 300 K. The dashed lines show the optimized values for each distance. Note that the $\text{Au}(\text{c})\text{-Au}(\text{a}')$ bonds are weak (“aurophilic”). The calculated radii of gyration are 4.12 and 4.10 Å for the full Au_{25} cluster or 1.49 and 1.44 Å for only the Au_{13} gold core, for ligands being GSH and SCH_3 , respectively.

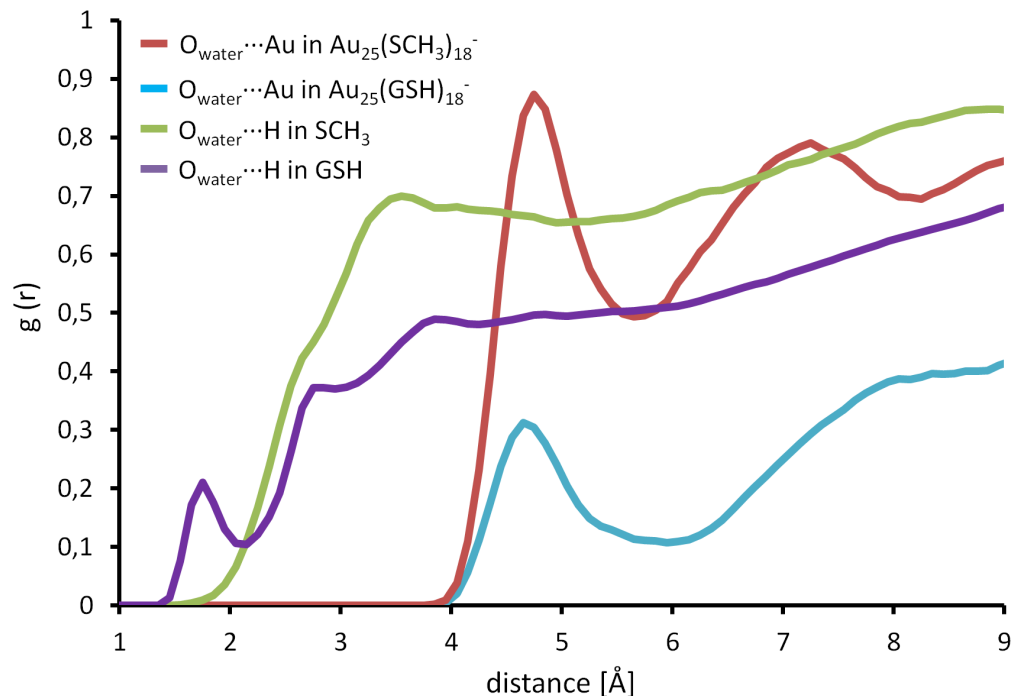


Figure S4. Radial distribution functions of the oxygen atoms of water molecules with respect to gold ($\text{O}_{\text{wat}} \cdots \text{Au}$ in $\text{Au}_{25}(\text{SR})_{18}^-$; red and blue curves) and with respect to the corresponding ligands ($\text{O}_{\text{wat}} \cdots \text{H}$ in SR; green and purple curves). Unlike GSH peptides, methyl groups do not form hydrogen bonds with water (missing first peak).

System	a	a'	c	S	S _{ap}
Au₂₅(SCH₃)₁₈⁻ in vacuum	-0.673	-0.176	0.455	-0.263	-0.423
Solvated Au₂₅(SCH₃)₁₈⁻	-0.649	-0.182	0.445	-0.307	-0.436
Solvated Au₂₅(GSH)₁₈⁻	-0.591	-0.176	0.400	-0.294	-0.481

Table S1. Hirshfeld charges of the five key atoms of Au₂₅(SR)₁₈⁻. The labelling of the atoms is the same as in Figure 1.

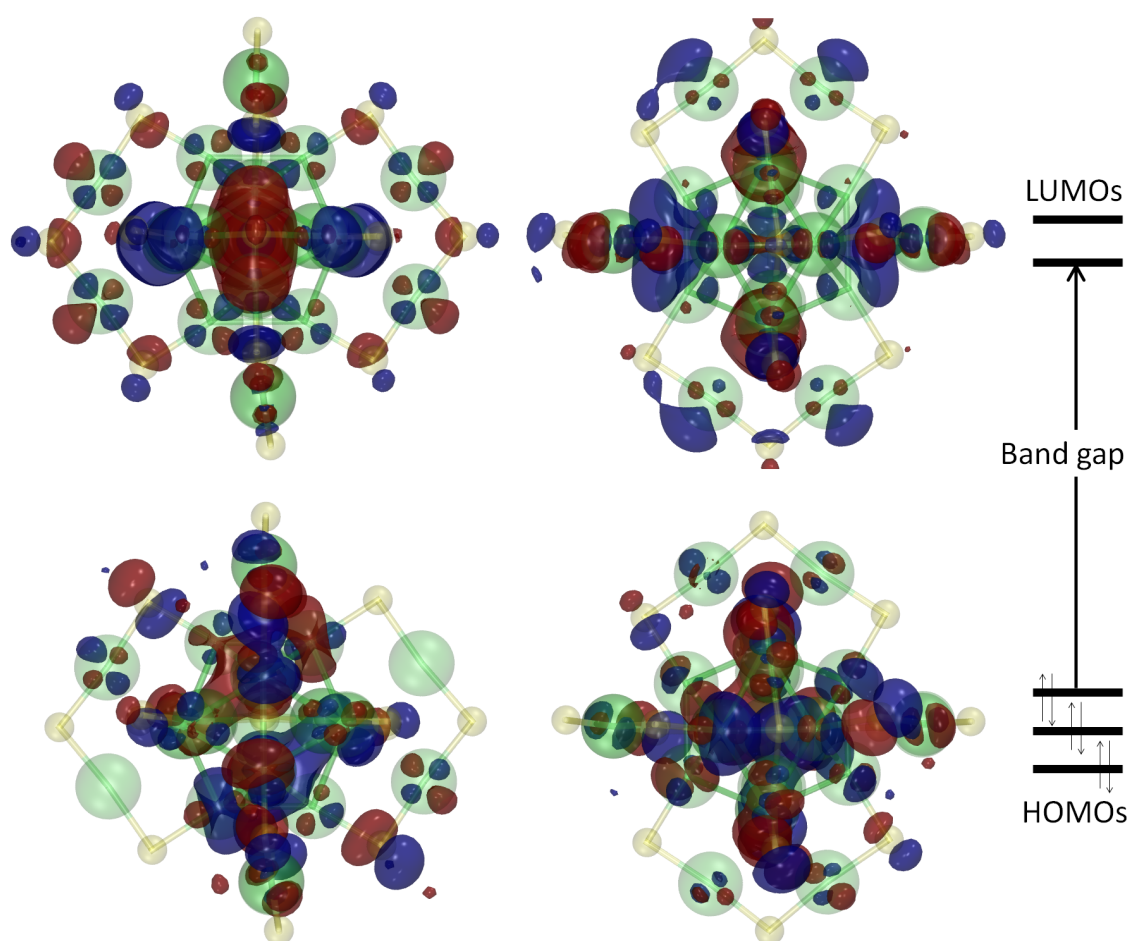


Figure S5. Shapes of the Kohn-Sham orbitals for Au₂₅(SR)₁₈⁻. HOMO (1P symmetry) and LUMO (1D symmetry) wavefunctions are displayed from two perspectives to better visualize their shapes. The wavefunctions are depicted in blue and red to highlight different signs. The AuMPC is shown transparent for clarity.

Framework	Au ₂₅ (SCH ₃) ₁₈ ⁻	Au ₂₅ (GSH) ₁₈ ⁻
Au ₂₅	0.23	0.67
Au ₂₅ S ₁₈	0.42	1.57
Au ₂₅ S ₁₈ C ₁₈	2.43	-

Table S2. Tolerance (in Å) necessary to yield the C_i point group symmetry with respect to the given framework.

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