Computational modelling of the interface between metallic nanoparticles and cysteine

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INTRODUCTION

- Metallic nanoparticles (NPs), including silver (AgNPs) and gold (AuNPs), are extensively researched for biomedical uses.
- Their interaction with biomolecules in the human body may result in transformations of NPs and changes in functionality of biomolecules.
- Evaluation of nano-bio interactions is a key part of their quality, safety and efficacy assessment.
- AgNPs and AuNPs react with thiols due to high affinity of sulfur for metals.
- Binding and oxidative dimerization of cysteine during formation of AgNPs and AuNPs in cysteine-rich environment was first observed experimentally, and now modelled theoretically.

RESULTS

- Cysteine and cystine interact with Ag and Au through thiol and carboxyl groups.
- Ag and Au lower the energy barriers for cysteine dimerization.
- The mechanism of cysteine dimerization with Ag and Au clusters as catalysts is proposed.
- Both cysteine and cystine spontaneously adsorb to Ag and Au surfaces.
- Explanation is provided for experimentally observed dimerization of cysteine during AgNP and AuNP preparation.

METHODS

- Optimization of cysteine and cystine complexes with Ag_n and Au_n (n=2,4), transition states, energy calculations
  → Gaussian 16, TPSS-D3/LANL2DZ//SMD-B3LYP/LANL2DZ
- Molecular dynamics simulations of Ag(111) and Au(111) plates with cysteine or cystine and 2000 waters
  → Amber17, Interface FF, 70 ns
- Binding energies
  → MM-GBSA

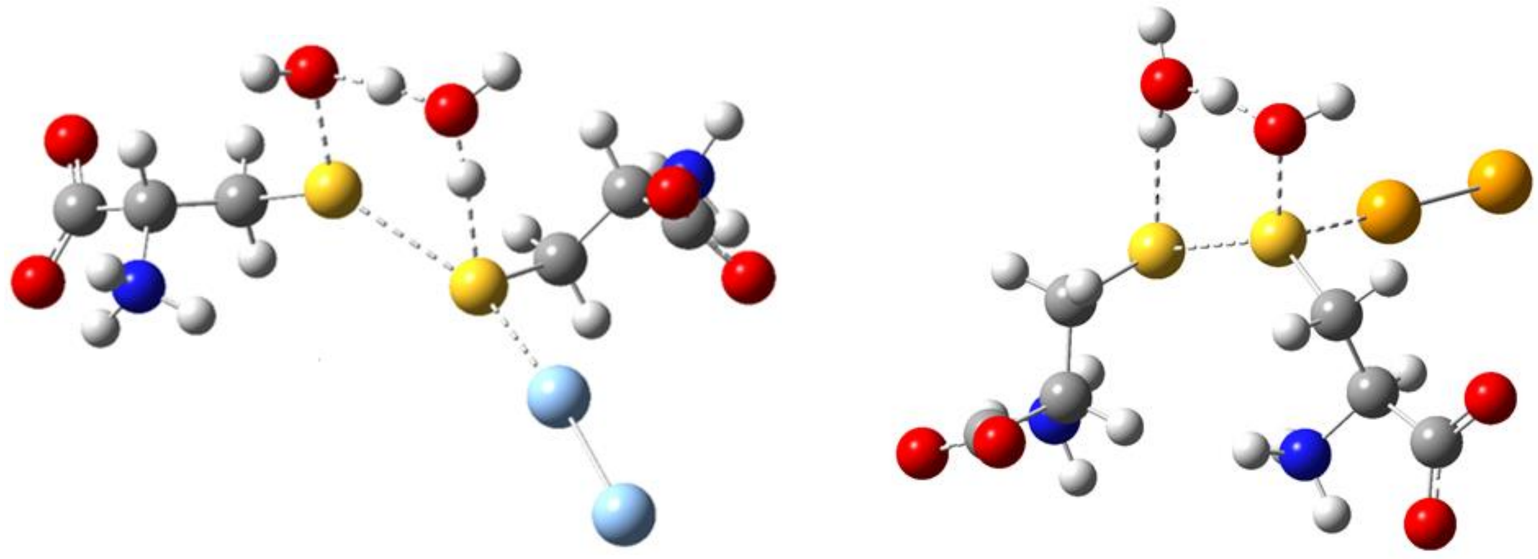
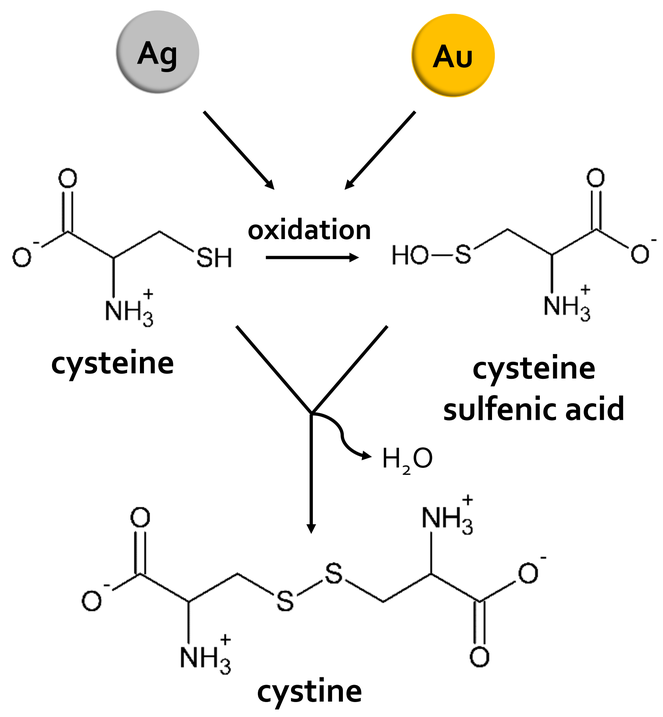
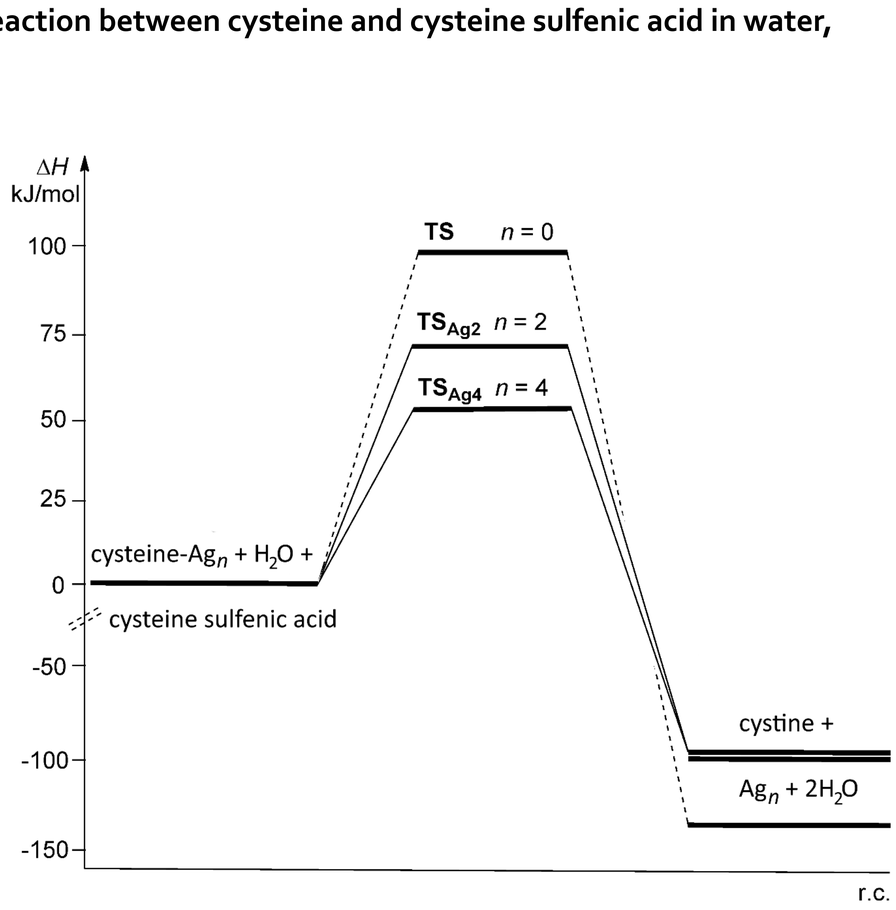


Figure 1. Transition state (TS) structures for the reaction between cysteine and cysteine sulfenic acid in water, catalysed by Ag2 (left), and Au2 (right) clusters.



Scheme 1. Proposed mechanism for the formation of cystine in the reaction of cysteine and cysteine sulfenic acid (created during the formation of Ag and Au).



Scheme 2. Energy diagram for the reaction between cysteine and cysteine sulfenic acid in water catalyzed by Ag_n clusters, where *n* = 2 or 4. The formation of cystine without the assistance of Ag cluster (*n* = 0) is depicted by a dashed line.

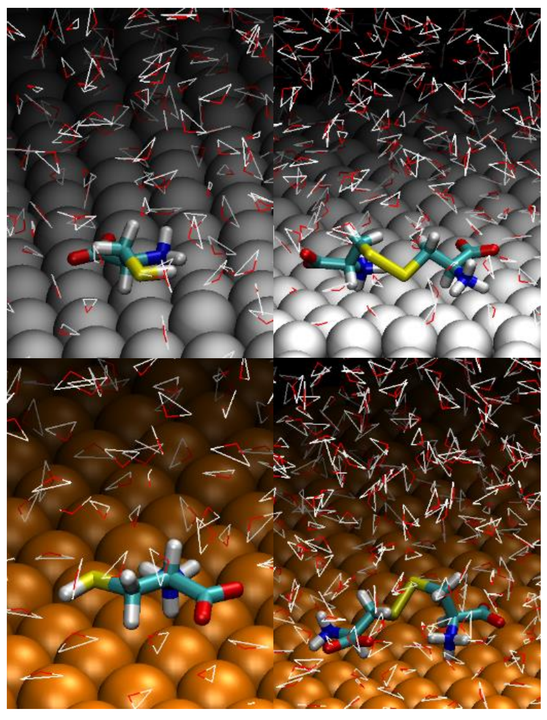


Table 1. Calculated adsorption energies for different MD systems containing either cysteine or cystine as ligands on the Ag or Au nanosurface as receptors.

System	ΔG_{ads} (kJ/mol)	$\Delta\Delta G_{ads}$ (kJ/mol) (Ag – Au)	$\Delta\Delta G_{ads}$ (kJ/mol) (cysteine – cystine)
Cysteine – Ag	-82.0763	+8.525	+61.588
Cysteine – Au	-90.6008	0.0	+89.487
Cystine – Ag	-143.6652	+36.421	0.0
Cystine – Au	-180.0865	0.0	0.0

Figure 2. The close-up snapshots of the last frames of the production runs from classical MD simulations. Top row: cysteine (left) and cystine (right) on Ag nanosurface. Bottom row: cysteine (left) and cystine (right) on Au nanosurface.

FULL PAPER
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