Thiol vs. disulphide: a DFT study of the nano-bio interface

Barbara Pem,[a] Valerije Vrček,[b] Ivana Vinković Vrček[a]

[a]Institute for Medical Research and Occupational Health, Ksaverska cesta 2, Zagreb, Croatia
[b]Faculty of Pharmacy and Biochemistry, University of Zagreb, Ante Kovačića 1, Zagreb, Croatia

bpem@imi.hr

INTRODUCTION

The increasing number of potential applications of silver and gold nanoparticles in medicine brings about the need to elucidate their interactions with the biological system. Adsorption of proteins to the nanoparticle surface is particularly important as it changes their identity and impacts their behaviour and fate in biological matrices.[1] Considering high affinity of sulphur for metals, special emphasis should be given to the role of thiol residues in nano-bio interactions,[2] although cysteine residues in proteins and peptides often form disulphide bonds.[3] This study aims to explore the difference in the reactions of free thiols and disulphides with silver and gold by computational approach. Cysteine and cystine are used as representatives of thiol and disulphide-containing molecules. Both molecules were placed in the vicinity of neutral and cationic silver and gold clusters in several orientations, to explore the potential energy surface and to identify most stable structures.

Stable cysteine complexes with Ag and Au atoms or clusters
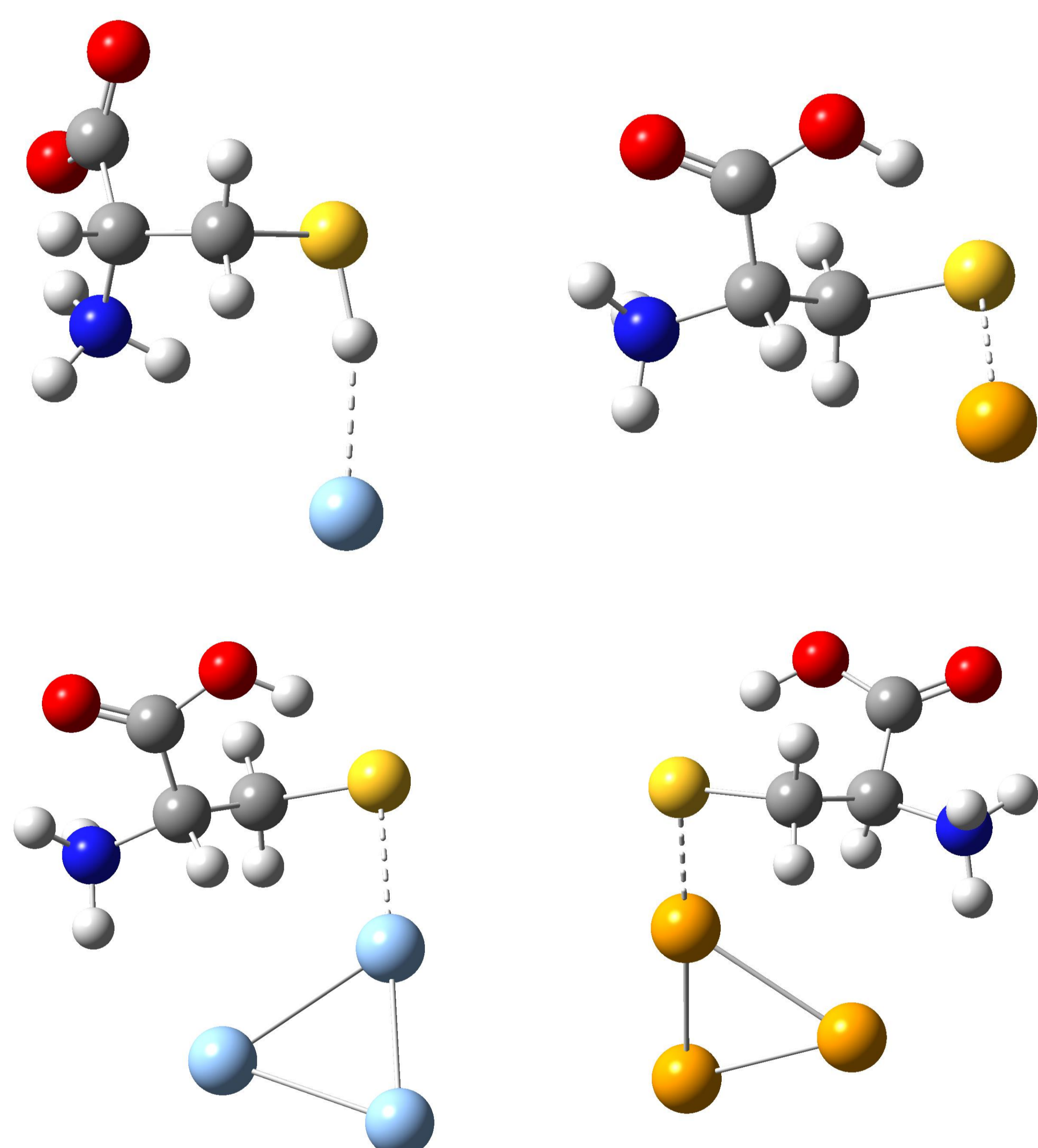
Structure	Thiol group protonation state	S – Ag/Au distance (Å)
Ag-cysteine	Protonated	N/A
Au-cysteine	Deprotonated	2.667
Ag$_3$-cysteine	Deprotonated	2.614
Au$_3$-cysteine	Deprotonated	2.479

Disulphide bond cleavage after cystine interactions with Ag and Au atoms/clusters
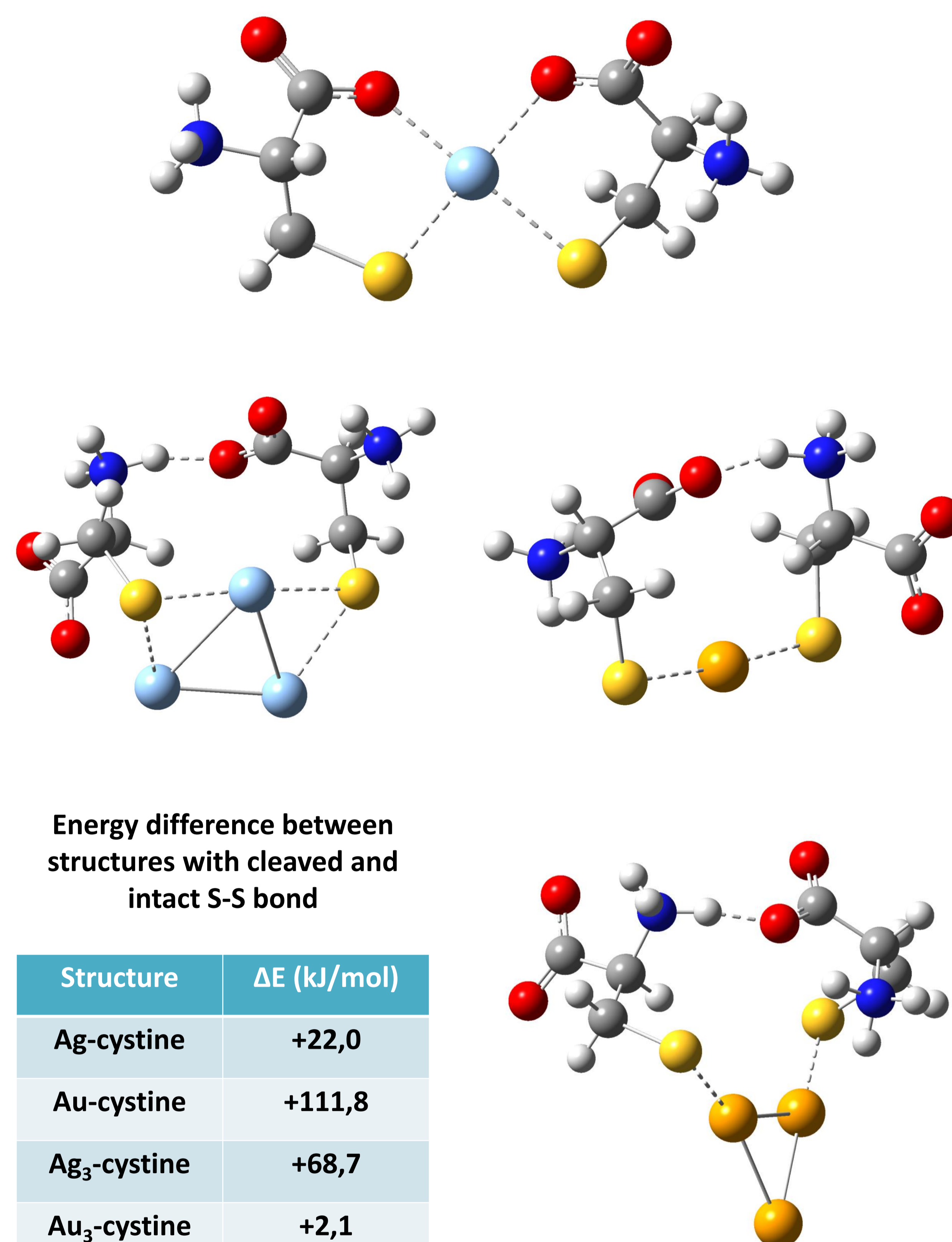
Energy difference between structures with cleaved and intact S-S bond

Structure	ΔE (kJ/mol)
Ag-cystine	+22,0
Au-cystine	+111,8
Ag$_3$-cystine	+68,7
Au$_3$-cystine	+2,1

METHODS

All calculations were performed in Gaussian 16 software, on the B3LYP level of theory with LANL2DZ basis set. Structures were optimized in implicit solvent (water) using the PCM method. Metals were manually placed in the vicinity of the thiol group and the full conformational search was conducted.

RESULTS

Computations demonstrated the interactions of neutral silver and gold to with sulphur in thiol or disulphide form. The thiol group of cysteine is deprotonated and it binds Ag and Au clusters as a thiolate. Cystine, on the other hand, can form complexes through both sulphur and carboxyllic oxygen. The most significant finding is the metal-induced disulphide bond cleavage, highlighting further mechanistic research on interaction between nanoparticles and proteins. These findings, combined with experimental work, will provide important contributions towards understanding of the nano-bio interface.

REFERENCES

1. Saptarshi et al. *J Nanobiotechnol* 2013, *11*, 26
2. Cheng et al. *Nanoscale* 2013, *5*, 3547
3. Gustarini et al. *J Gerontol* 2006, *61*, 1030