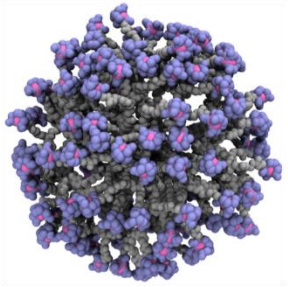

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NANO2CLINIC

CANCER NANOMEDICINE - FROM THE BENCH TO THE BEDSIDE

Computational approach to the study of nano-bio interface

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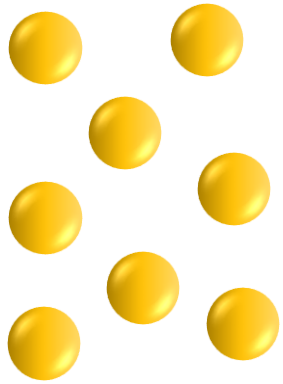
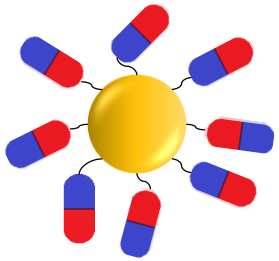
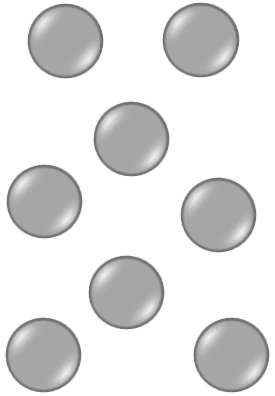
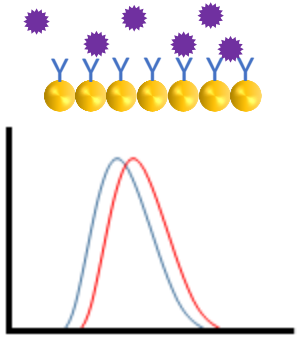
Gold (AuNP) and silver nanoparticles (AgNP)





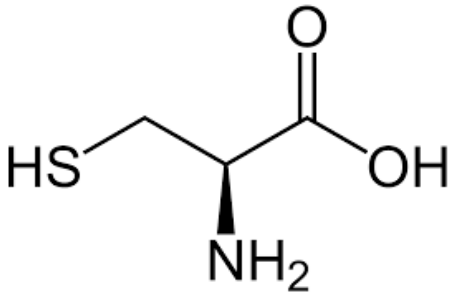
potential diagnostic and therapeutic agents in anticancer therapy



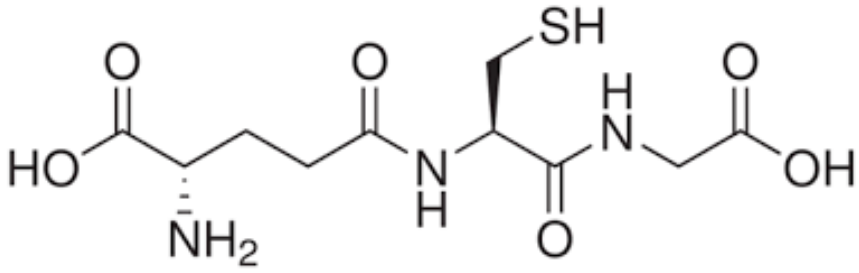


Successful therapy is dependent on detailed knowledge of the interaction of nano-systems with biological media

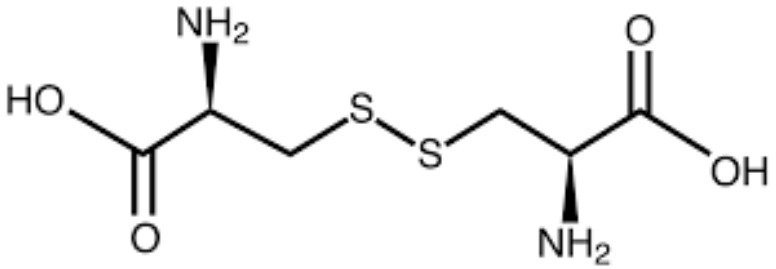
Model small sulfur-containing biomolecules



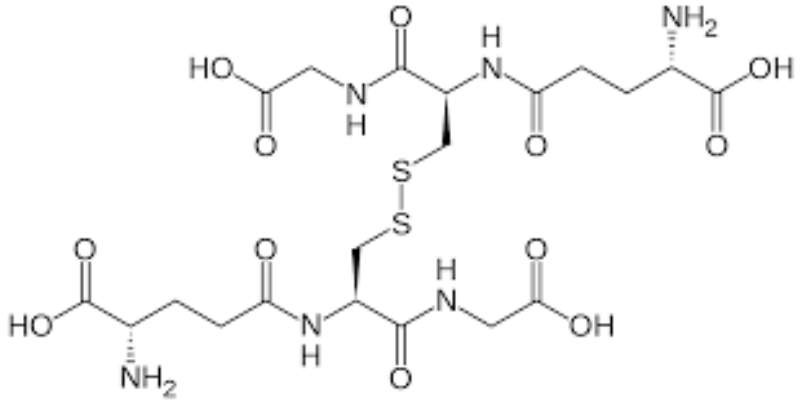
cysteine (CYS)



glutathione (GSH)



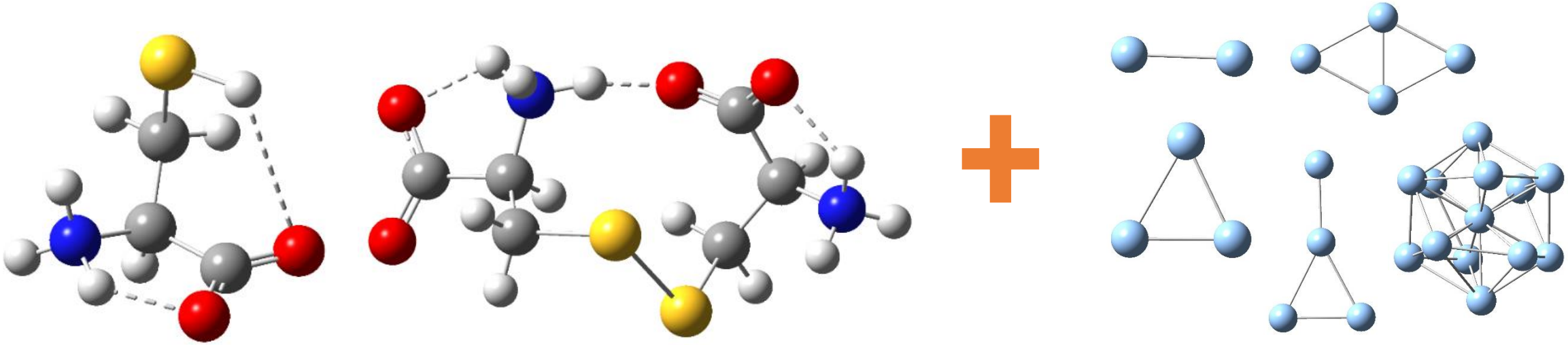
cystine



oxidized glutathione (GSSG)

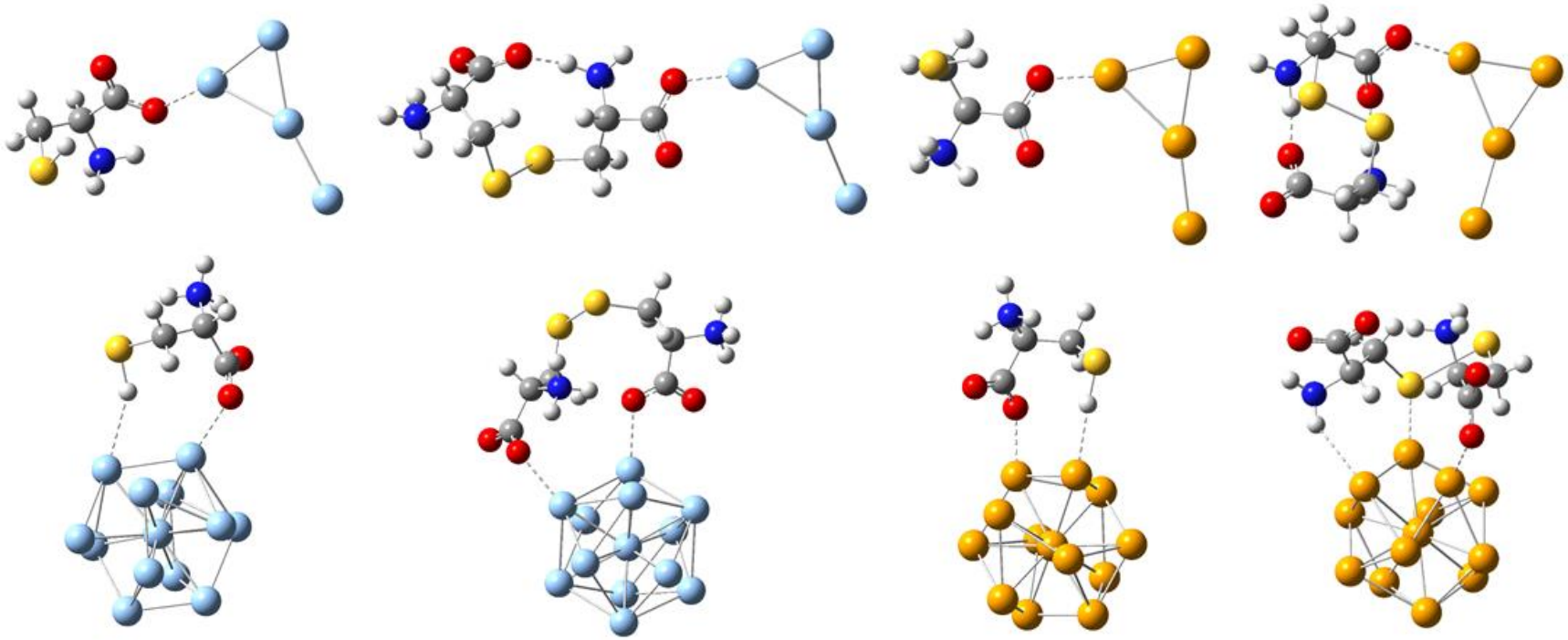
Interaction of biomolecules with metallic clusters

- Gaussian 16
- Density Functional Theory
- conformation analysis of CYS and cystine→ SMD-B3LYP/LANL2DZ
- complexes of CYS and cystine with Ag_n and Au_n (n= 1, 2, 3, 4, 13)
- geometric optimization, frequency calculation, NBO



Interaction of biomolecules with metallic clusters

- interaction occurs primarily through the carboxylate, less frequently through other functional groups
- non-covalent interactions (dipole-induced dipole)

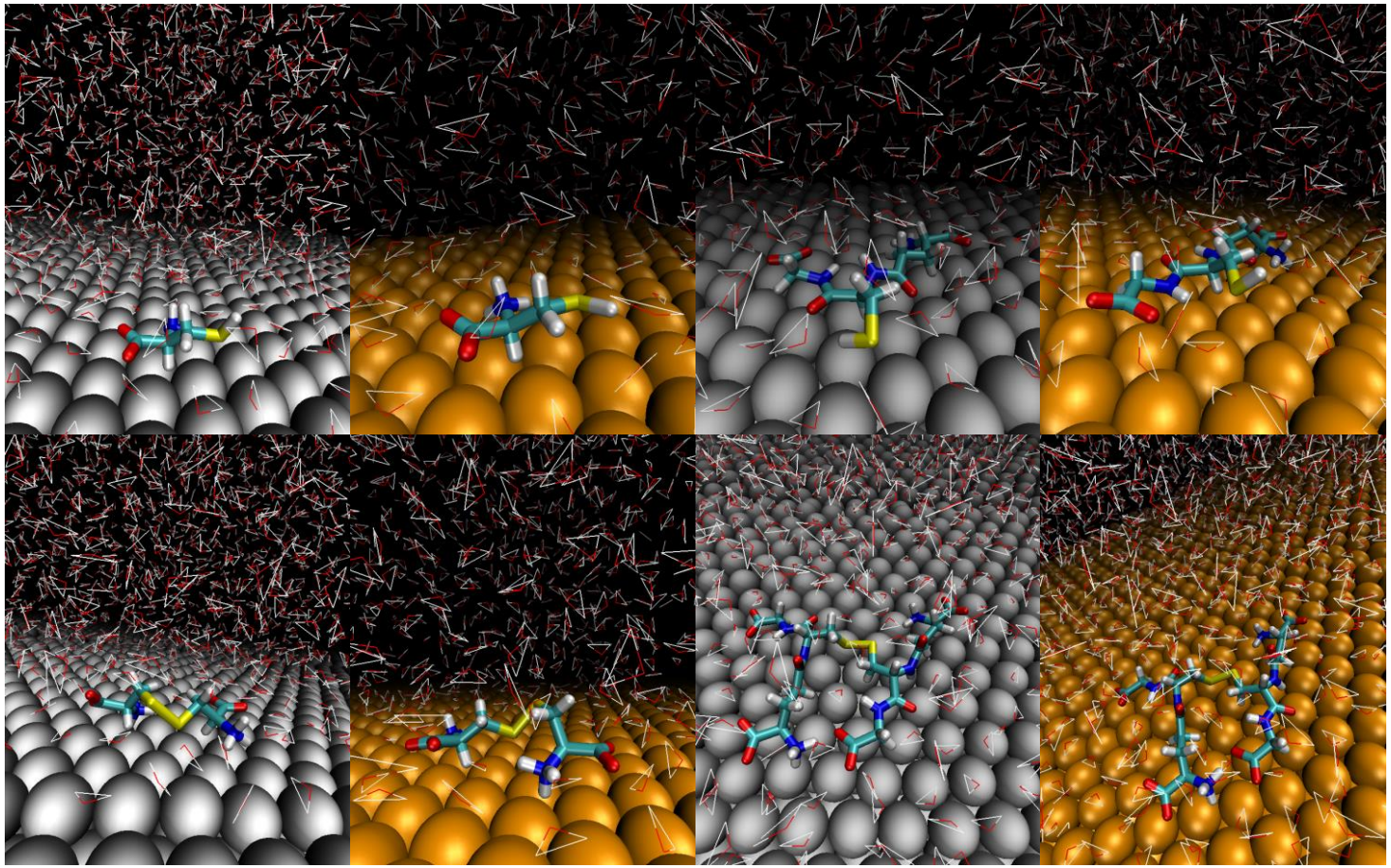


Adsorption of biomolecules to nanosurfaces

- Amber 17
- simulation box 32*43*55 Å
- metallic plate (748 atoms), ligand (biothiol or disulfide at 15 Å distance from the surface), 2000 water molecules
- periodic boundary conditions
- force fields: Interface (metal), GAFF (ligand) + TIP3P model for water
- total time: 70 ns
- MM-GBSA for the calculation of binding free energies

Adsorption of biomolecules to nanosurfaces

- spontaneous adsorption of molecules to the metallic surface
- all functional groups participate in the interaction



Adsorption of biomolecules to nanosurfaces

- higher affinity of ligands for Au than for Ag
- disulfides possess higher affinity towards metals compared to thiols

System	ΔG_{ads} (kJ/mol)	$\Delta\Delta G_{ads}$ (kJ/mol) (Ag – Au)	$\Delta\Delta G_{ads}$ (kJ/mol) (thiol – disulfide)
CYS – Ag	-82.1	+8.5	+61.6
CYS – Au	-90.6	0.0	+89.5
cystine – Ag	-143.7	+36.4	0.0
cystine – Au	-180.1	0.0	0.0
GSH – Ag	-90.8	+2.1	+287.9
GSH – Au	-92.9	0.0	+339.3
GSSG – Ag	-378.7	+53.5	0.0
GSSG – Au	-432.3	0.0	0.0

Conclusion

- interaction of sulfur-containing molecules with silver and gold is achieved through non-covalent interactions
- all functional groups participate in the binding
- adsorption is spontaneous and exergonic in all cases

Acknowledgements

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Cancer Nanomedicine – From the Bench to the Bedside

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