Interactions of gold(I) complexes with models of Thioredoxin reductase; DFT & QM/MM studies

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One of the treatment options for oncological diseases is programmed cell death (PCD) induced by increased oxidative stress. One of the main PCD types is so-called apoptosis, which is regulated by thioredoxin systems. [1] The thioredoxin reductase enzyme, one of the key thioredoxin system components, can be blocked by gold(I) complexes and hence cause therapeutic oxidative stress. [2]

First, we investigated the interactions of a selected gold(I) complex with the active site of the enzyme using the density functional method. For this purpose, structures of reactants, transition states, and products for different redox states and (de)protonations of the active site were explored. From these calculations, Gibbs activation energies and standard reaction energies of the reaction profiles were determined.

Recently we performed QM/MM MD calculations with Umbrella sampling technique on the more extended systems where the quantum core comprised tetrapeptide sequence on the C-end of the enzyme together with the gold(I) complex. This active site was completed by the rest of the enzyme and explicit solvent water treated by classical MD force field.

All the computational models predict spontaneous gold coordination to both S- and Se-sites especially in neutral and basic environments.

***Keywords**: thioredoxin reductase, gold(I) complexes, DFT, QM/MM*

References:

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