The Gold Ampicilin Interface At the Nanoscale : A Numerical Simulation Study

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The accelerating emergence of multi-drug-resistant (MDR) pathogenic microbia has become a significant global public health threat [1]. The World Health Organization estimates 10 millions death a year due to these MDR [2]. Since the discovery of new antibiotic family stopped in the 90's, new methods to fight this increasing threat have to be found. Very recently, it has been shown that gold nanoparticles (AuNPs) conjugated with antibiotics are potential bactericidal agents with unique properties that subverted antibiotic resistance mechanisms of MDR bacteria. Furthermore, resistance to antibiotics-conjugated gold nanoparticles develops significantly more slowly than to the last commercial molecules generation [3].

The ampicillin molecule (C\textsubscript{16}H\textsubscript{19}N\textsubscript{3}O\textsubscript{4}S), belonging to the β-lactam family, is a broad spectrum antibiotic used to treat a lot of different diseases. It acts by inhibiting the creation of the bacterial cell wall, thus leading to lysis. However, its overuse as a prevention agent in fields like livestock battery led to a huge decrease in its efficiency. Bhattacharya and al. [4] have conjugated AuNPs with several antibiotics including ampicillin. The results showed that the AuNP-ampicillin complex exhibits outstanding properties. It is stable (UV, heat and prolonged storage), allowing for transportation and industrialization. It is also more efficient than the free antibiotic in the fight against bacteria. A. N. Brown and al [5] also shown that such complex is able to kill MDR while the free ampicillin molecule is inefficient.

To rationalize and control the stability of such promising hybrid systems, a deep understanding of these complexes at the atomic scale is essential. Using numerical simulations (DFT and ab initio Molecular Dynamics), we have investigated the structure of the interface between the ampicillin antibiotics and three flat gold facets Au(111), Au(110) and Au(100) for different antibiotics coverage (from single molecule to auto-organization). These calculations indicate that the adsorption of a single ampicillin on these facets goes through multiple partially covalent bonding, the corresponding large adsorption energies explaining the stability of the AuNP/ampicillin nanoconjugates [6]. Moreover, these calculations have shown that the grafted antibiotic has a constrained spatial orientation which could be very favorable towards the antibacterial activity of these hybrid systems. When increasing the coverage, hydrogen bonds and van der Waals dispersion forces play an important role in the stabilization of the whole system. At high coverage, a possible auto-organization of the ampicillin molecules on the AuNP surfaces can be found, without loss of the favorable orientation of the antibiotics active site.

![Figure 1. Auto-organization of ampicillin molecules on Au(111)](image)

References
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