Dissertation topic:

Quantum chemical calculations of structural and electrical properties and reactivity of the A-cluster, the active center of acetyl-CoA synthase

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Summary:

Nickel is an element which plays an important role in the biology of plants and anaerobic bacteria and archaea. It is present in the centers of the reactivity of enzymes which catalyze biochemical reactions many of these organisms. Seven of the eight nickel metalloenzymes catalyzes reactions in which they are produced or processed following gases: CO, CO_2, CH_4, H_2, NH_3 and O_2. Their knowledge is important for understanding the emergence of life on Earth, ecological sustainability and because of the potential applications in industry.

The object of research in theoretical chemistry methods within the scope of the presented dissertation is a dinickel complex of $[Fe_4S_4]$-Ni_pNi_d, called A-cluster. It is the active center of the acetyl-CoA (ACS), an enzyme that catalyzes synthesis of acetyl-CoA from CO, CH_3 and CoA (CoASH) in the bacteria: *Moorella thermoacetica* and *Carboxydothermus hydrogenoformans*. Crystallography and Mössbauer spectroscopy and EPR have provided many experimental structural data and reactivity of the cluster, but there is little computational work associated with. In addition, they present different approaches to the issue in question.

The fundamental objectives of the work include: (i) To develop a model and methodology of calculation, which correctly reproduces experimental structural data, redox potentials and the pK_a values for the A-cluster. (ii) To propose a mechanism to reduce the oxidized form of the A-cluster (A_{ox}). (iii) To indicate the mechanism of the methylation reaction of the A-cluster, which is one of stages of acetyl-CoA formation.

The calculations were carried out with the use of Gaussian09 program. The DFT method was employed with BP86 functional and TZVP basis set. The effect of protein environment was taken into account by the PCM solvent model with the dielectric constant ε=4, 12, 20 and 80. The camputations were performed for several structural models of the A-cluster. Geometry optimization was carried out for the oxidized A_{ox}, one- and two-electron reduced A-cluster (A_{red1} and A_{red2}, respectively) as well as for A-cluster with ligands important in the catalytic cycle. This allowed to assess the impact of the model size and the protein environment on redox properties of the A-cluster.

The main conclusions of the work can be formulated as follows: (a) Geometry and the redox properties of the A-cluster (reduction potentials and pK_a values) are strongly dependent on the structural model size and the dielectric constant of the solvent in the calculation of PCM. (b) The calculations have clearly shown that the protonation takes place at the Ni_p atom in reduced species of the A-cluster (c) Since redox potenetals of the A-cluster are strongly dependent on the solvent dielectric constant, the enzymatic reaction is strongly influenced by the reaction medium. In less polar solvents, it can proceed via radical mechanism, whereas in polar solvents it may involve a S_N2 mechanism.