Iron-sulfur (Fe-S) compounds were probably the first catalysts that enabled hydrogenation of the carbon dioxide, thus paved the way to organic molecules and assemblies. First organisms used catalytic properties of the Fe-S clusters and incorporated them into protein scaffold. Obtained metalloproteins were highly sensitive to the presence of oxygen and the evolution gradually led to the exchange of iron with other transition metals, e.g. zinc. However, some important proteins resembled the ancient active site. They play crucial role in the citric acid cycle (aconitase) or in the DNA repair (DNA primase). Some bacteria employ Fe-S clusters to transport electrons. In the case of hydrogenases, such electron transfer chain ends in the vicinity of the active site responsible for hydrogen oxygenation and reduction (break and formation of H-H bond, respectively). The production of H_2 represents a process of a fundamental economical interest. In contrary to industrial-scale production methods, enzymatic catalysis avoids unwanted by-products like CO_2 and high energy consumption. Industrial applications of the organisms that feature such enzymes is hampered by high oxygen sensitivity, a prerequisite of any practical application. Thus, it seems very attractive to mimic the protein scaffold in, possibly more effective, synthetic systems where oxygen sensitivity might be controlled. However, our current understanding of factors that control enzymatic catalysis is still limited what results in molecular catalysts that are neither as effective nor as flexible as natural machinery.

The major aim of the project is to provide insides into the influence of a protein matrix on the properties of $[Fe_4S_4]$ cubane clusters at a most basic, molecular level. Such properties include electron transfer abilities and reactivity. Usually the cluster is bound to the protein by four cysteine amino acids. **Figure 1** shows that some of the iron-sulfur entities does not follow this pattern and feature in place of one cysteine other ligand, for example histidine. Cysteine binds to the iron via sulfur atom while nitrogen forms this bond in case of a histidine. Other ligands include aspartic acid (binding via oxygen atom) or some small molecules, like water in the case of the aconitase. There exist also a large group of enzymes that possess $[Fe_4S_4]$ cluster of an unknown first coordination sphere (some ferredoxins or hydrogenase assembly protein HydF).

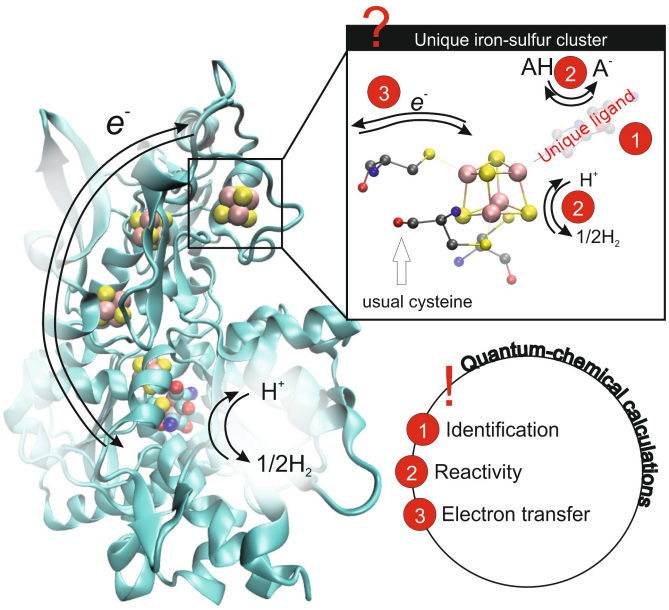

***Figure 1**. Graphical presentation of the project aims. A typical hydrogenase has three [Fe_4S_4] clusters that form an electron transfer chain to/from the active site. The outermost iron-sulfur cluster that features unique ligand was highlighted. Using state of the art quantum chemical methods we will (1) provide data for experimental ligand identification, (2) determine the impact of such unique ligand on the cluster reactivity and examine its potential applicability in the hydrogen production as well as (3) look at the role of the unique ligand in the modulation of the electron transfer properties in proteins.*

The goal of the project is to identify biological role of such a ligand exchange. The central idea is that cysteine to histidine/aspartate mutations in the first coordination sphere of the iron-sulfur cubane provide the protein with an additional flexibility in the electron transfer parameters modulation and influences the reactivity. Using state of the art quantum chemical methods we will check the influence of the unique ligand on the properties of $[Fe_4S_4]$ cluster. Moreover, we will look at the changes of these properties upon hydrogen cation (H^+) attachment/detachment. Such a change in the acidity (change in pH) might have a crucial role in the direction of electron transfer, thus can be viewed as a natural switch between oxygenation and reduction reactions (hydrogen consumption and production, respectively). We also aim to simulate X-ray absorption and emission spectra for a series of synthetic and protein-based models with biologically relevant ligands to support experimental determination of the ligating agent. Finally, through quantum chemical investigation of the reactivity of such clusters towards H_2 production, we aim to check if they can be used as a part of a working photocatalytical setup.

All research carried out within this project are basic research. The development of highly accurate quantum chemical methods allowed us, for the first time at the atomic level, to look at the properties of the $[Fe_4S_4]$ clusters. In this work we will examine the influence of unique ligands on the cluster properties such as electron transfer parameters or ligand affinity. Using only first principles we aim to uncover secrets of the natural regulation processes, that will undoubtedly pave the way to new and efficient bio-inspired catalytical systems even beyond hydrogen production.