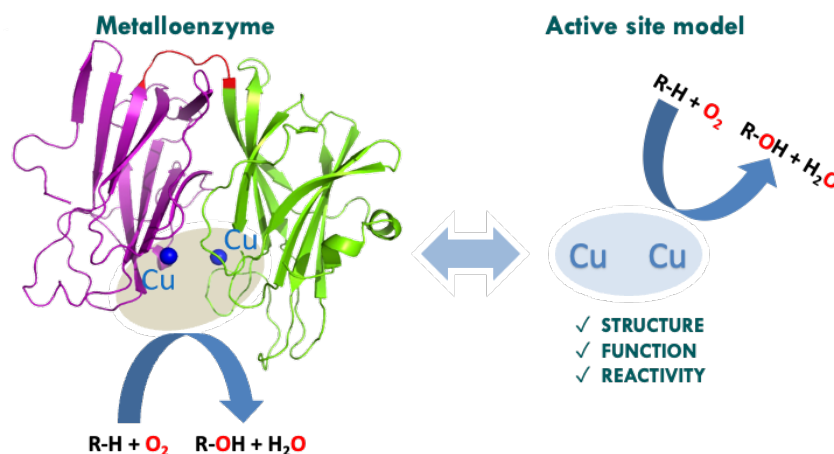


## RESEARCH TOPIC

My research combines both experimental and theoretical approaches in bio-inorganic chemistry, focusing on the structure, properties, and reactivity of molecular architectures. This work has significant implications in fields like biology and catalysis, including the study of organic radicals and transition metal complexes, as well as the active sites of metalloproteins.



Central to my work is the computational modelling of these molecular architectures. Using quantum chemistry tools, I investigate various aspects such as magnetic properties, reaction mechanisms, and catalytic performance, with an emphasis on developing new synthetic targets. This aspect of my research significantly depends on computational chemistry to accomplish various objectives:

1. Computing reaction mechanisms.
2. Improving the catalytic efficiency.
3. Predicting magneto-structural correlations.
4. Developing innovative synthetic targets.

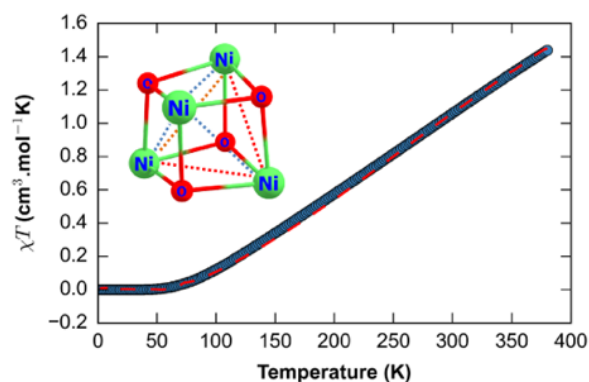
Through this integrated approach, my research aims to advance the field of bio-inorganic chemistry by bridging theoretical models with practical applications.

### 1) POLYNUCLEAR MAGNETICALLY COUPLED SYSTEMS

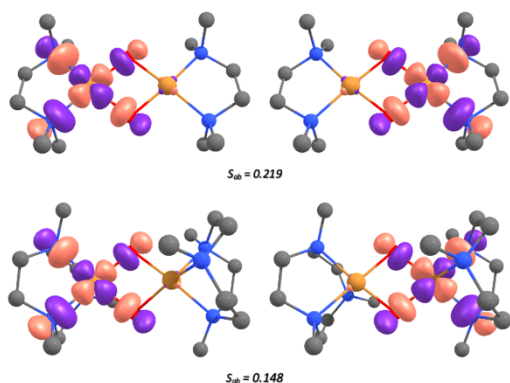
Polynuclear transition metal complexes containing paramagnetic cations have been thoroughly studied since they represent the crossroad to important research fields, *e.g.*, magnetic, electronic, and optical materials and biomimetic and catalytic systems. Unique electronic and chemical properties arise when the unpaired electrons of two or more open-shell centres interact. Understanding the electronic configuration of these magnetically coupled systems has been crucial in investigating essential areas such as the oxygen-evolving complex, bioinspired synthetic metal complexes, and single-molecule magnets.

Due to the presence of paramagnetic centres, polynuclear metal complexes present characteristic magnetic properties and can exhibit different ground spin states depending on the metal centres, the oxidation state, the coordination number, and the nature and positioning of the ligands. As a result, their magnetic behaviour can be tuned, which is crucial for designing new catalysts with improved activity.

Unfortunately, as the number of paramagnetic centres increases, so does the complexity of the magnetic properties, and the extraction of the observables becomes challenging using experimental methods alone. Therefore, theoretical approaches are of prime importance in studying polynuclear systems, as they allow a detailed and in-depth analysis of the magnetic properties, thereby complementing experimental observations. My expertise in handling such systems spans various theoretical approaches and computational methodologies, including Broken-Symmetry DFT (BS-DFT) and Complete Active Space Self-Consistent Field (CASSCF) coupled with n-Electron Valence State second-order Perturbation Theory (NEVPT2).



## Theoretical Magnetic Properties Calculation



Accurately predicting the spectroscopic and magnetic properties using computational methods is challenging due to the intrinsic multi-determinantal character of electronic states and the associated static and dynamic correlations. Clearly, one must consider the multideterminant character of the system to be able to describe the ground spin state accurately. Within the post-HF multireference methods (MR), Complete Active

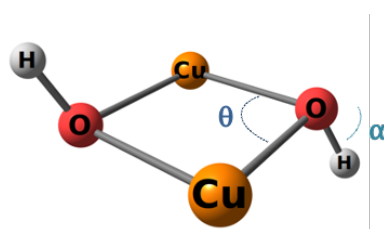
Space Self-Consistent Field (CASSCF) and Complete Active Space Configuration Interaction (CASCI) are the most commonly used. However, the primary concern of MR methods is the high computational cost due to the complexity of the wave function. On the other hand, because the low spin states are intrinsically multiconfigurational, they cannot be treated with a single-determinant. Instead of using a multideterminal wave function, the broken-symmetry (BS) approach within the DFT framework relies on a single determinant to extract the energy of the antiferromagnetically coupled state. In collaboration with the Max Planck Institute and Bochum University, I explored various theoretical methods for calculating magnetic parameters in transition metal complexes, crucial for interpreting experimental data and understanding inorganic and bioinorganic catalysts. Methods included BS-DFT, CASSCF with NEVPT2, Density Matrix Renormalization Group (DMRG), Difference-Dedicated Configuration

Interaction (DDCI), and Coupled-Cluster Broken Symmetry (CC-BS). However, limitations such as accuracy issues and computational costs were evident. For instance, while BS-DFT is moderately accurate, it depends heavily on the chosen functional and system, and DDCI, despite its precision, is impractical for larger systems due to its computational intensity. These findings emphasize the importance of carefully evaluating computational tools to accurately describe magnetic properties beforehand.

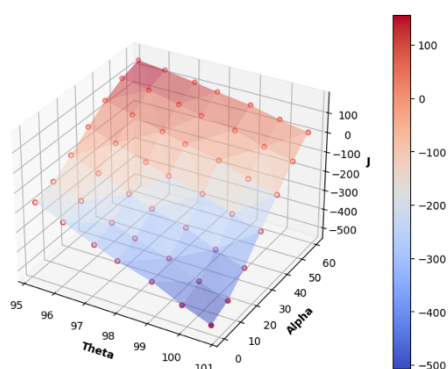
**Publication:** a) Gurjot Singh, **Stefani Gamboa**, Maylis Orio, Dimitrios A. Pantazis and Michael Roemelt. *Theoretical Chemistry Accounts*, **2021**, 140:139

## Magneto-Structural Correlation in Dinuclear Copper Complexes

Understanding the underlying mechanism that governs the magnetic interaction in paramagnetic complexes is tightly connected with their intrinsic geometrical parameters. Many factors tune the magnetic interaction of two or more paramagnetic centers in close vicinity. However, the structural parameters and the exchange interaction are



strongly correlated. Specifically, we found that the out-of-plane angle ( $\alpha$ ) of the hydroxo bridging ligand in a family of dinuclear copper complexes is as crucial as the Cu-O-Cu angle ( $\theta$ ) in determining the magnetic coupling. This, in turn, is tightly correlated to the ability of the counterion to form hydrogen bonding. We found that accurately describing the magnetic properties of copper complexes with  $\mu$ -hydroxo bridging ligands requires accounting for the out-of-plane angle ( $\alpha$ ) and the counterion. We developed a protocol to position the hydroxo hydrogen more reliably and used spin projection methods to model the magnetic properties of different crystal structures with diverse counterions. We successfully modified the experimental  $J$  values by tuning the counterion, highlighting its role in influencing the magnetic coupling. Furthermore, by combining experimental and computational inputs, we constructed



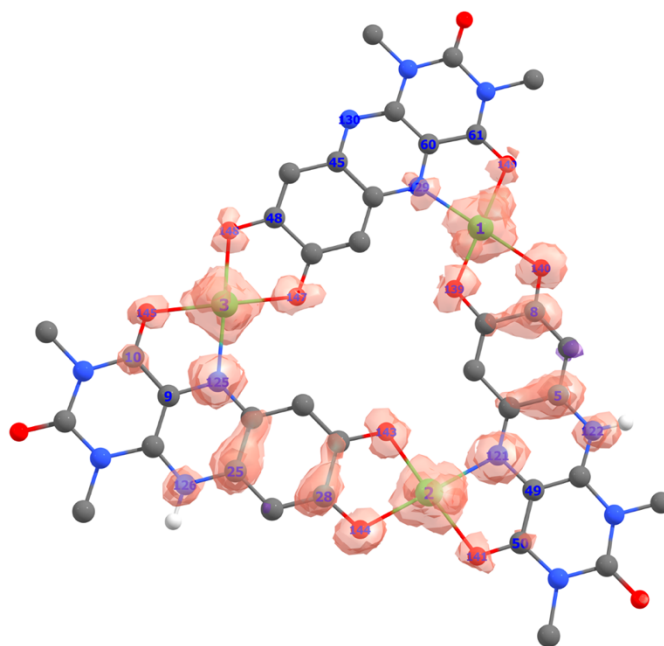
a three-dimensional correlation between  $\alpha$ ,  $\theta$ , and  $J$ , which improved the prediction of  $J$  values for the 20 copper complexes I synthesized and measured the magnetic properties when  $\alpha$  was corrected in the crystal structure. This emphasises the importance of considering geometrical parameters for accurately predicting magnetic properties in paramagnetic systems, providing insights for designing and optimising magnetic materials.

**Publication:** **Stefani Gamboa-Ramirez**, Michel Giorgi, Sylvain Bertaina, A. Jalila Simaan, and Maylis Orio. Manuscript in preparation.

## 2) BIO-INSPIRED POLYNUCLEAR METAL COMPLEXES

### Hybrid Catechol-Alloxazine Trinuclear Nickel: Electronic and Magnetic Analysis

A unique Ni(II) complex with the ability to store metal and organic radicals within its ligand was studied in a combined experimental and theoretical approach in order to elucidate its correct electronic and magnetic structure. This complex features a promising model to study systems with potential applications as energy storage.



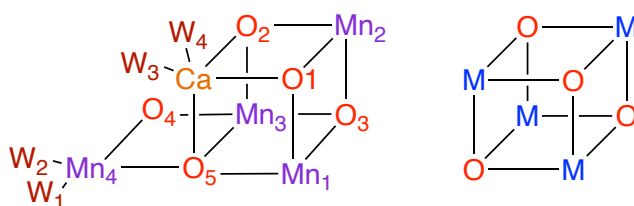
Extensively analyzed for its electronic structure and magnetic properties using quantum chemical methods, the complex's ability to stabilize radicals when bound to metal, and the potential for protonation at specific sites, were key factors in understanding its properties. We identified that certain high-energy configurations were less favourable compared to a more stable model featuring three protons and three organic radicals. However, a fully protonated state was inconsistent with experimental findings from X-ray crystallography and High-Resolution Mass Spectroscopy, leading us to a partially protonated state as the optimal configuration. This state results in three high-spin (HS) Ni(II) centres and two delocalized organic radicals within the ligand. Through spin density distribution and Mulliken spin population analysis, we gained further insights, notably the localization of spin density at the Ni centres and certain ligand atoms, forming the semiquinone radicals. This led to the proposal of three distinct magnetic interactions within the complex. Theoretical calculations and SQUID measurements on two model systems, A and B, were crucial in understanding these interactions and predicting the magnetic properties of the complex. The magnetic interactions were modelled within the BS-DF<sup>T</sup> framework, and the calculated exchange coupling constants indicated strong and weak ferromagnetic interactions for different pairs within the complex. These theoretical predictions closely matched experimental SQUID measurements. The study successfully combines theoretical and experimental approaches to reveal the electronic structure and magnetic interactions in this unique trinuclear nickel complex. Its special

structure, featuring two protons on the ligand and three high-spin Ni(II) ions coupled to two ligand-based radicals, offers valuable insights into bioinorganic systems and their potential in energy storage applications.

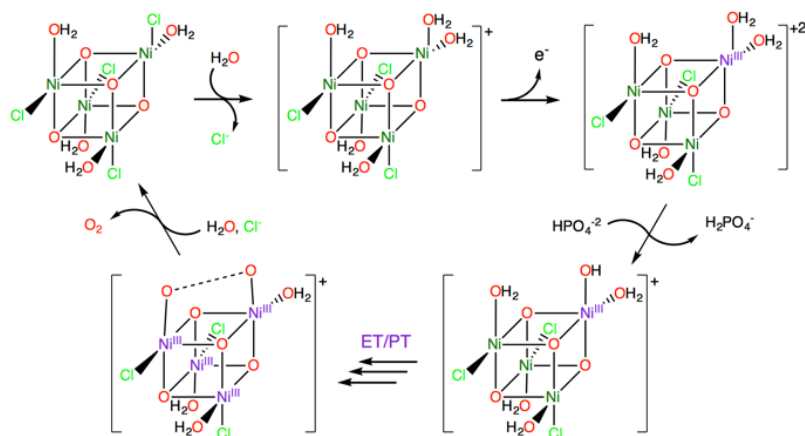
**Publication:** Das, A.; Jobelius, H.; Schleinitz, J.; Gamboa-Ramirez, S.; Creste, G.; Kervern, G.; Raya, J.; Le Breton, N.; Guénet, A.; Boubegtiten-Fezoua, Z.; Grimaud, L.; Orio, M.; Rogez, G.; Hellwig, P.; Choua, S.; Ferlay, S.; Desage-El Murr, M., *Inorg. Chem. Front.* **2021**, 8 (24), 5286–5298.

## Oxygen evolution catalyst design

Transforming solar energy into chemical energy is one of the most critical processes sustaining life on Earth. In the case of photosynthesis, it involves the four-electron oxidation of dioxygen



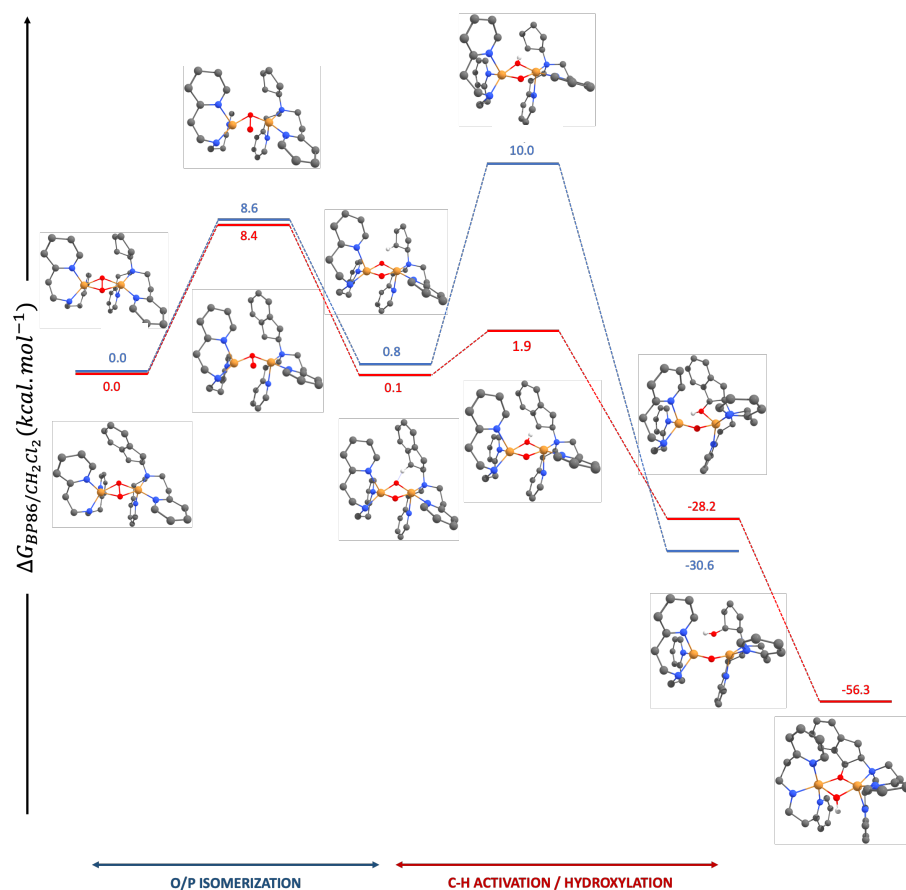
into water driven by solar light. Organisms that are able to convert light into fuel rely on a membrane protein called Photosystem II (PSII). The active site of PSII, where the water oxidation occurs, is known as the oxygen-evolution complex (OEC), comprised of a Mn<sub>4</sub>O<sub>5</sub>Ca cluster. Hence, catalytic water oxidation, as part of water splitting strategies, could provide abundant fuels from renewable sources, which is much needed judging from the current energetic crisis. Unfortunately, catalytic water oxidation is a global challenge representing the bottleneck for water splitting, and much remains to be done. Taking inspiration from the OEC topology where PSII can accumulate four electrons within a tetrametallic-oxo cluster, one can imagine a bioinspired model featuring metal-oxo subunits, leading to “cubane”-type M<sub>4</sub>O<sub>4</sub> complexes. Two robust nickel cubanes were prepared in good yields from readily available starting materials under ambient conditions. These tetranuclear complexes are active for electrocatalytic water oxidation at neutral pH, as proven by combining experimental and theoretical approaches. The BS-DFT approach was successfully employed in the study of the magnetic properties of the Ni-cubanes, as well as to elucidate their ground-state electronic structure. Using the HDvV Hamiltonian within the BS-DFT framework, we provided the computed magnetic sublevels that allow the assignment of both ground and first excited states. Furthermore, theoretical reactivity studies confirmed the feasibility of the oxygen evolution carried out by both Ni-cubanes. Extension of this self-assembly strategy for preparing other water oxidation catalysts with benzimidazole-based ligands and earth-abundant metals (Co and Fe) is currently underway using both experimental and theoretical tools.



**Publication:** Ana C. García-Álvarez, **Stefani Gamboa-Ramírez**, Diego Martínez-Otero, Maylis Orio and Ivan Castillo. *Chem. Commun.*, **2021**, 57, 8608.

## Oxygen activation: Structure-function studies of copper monooxygenases

Molecular magnetism is closely related to the study of magnetic and electron transport in bioinspired model compounds. Understanding the electronic and magnetic properties of these compounds can lead to a better understanding of their reactivity. Copper-containing enzymes are involved in many essential biological processes and play a key role in oxidation reactions. In particular, monooxygenases that catalyze the activation and hydroxylation of C-H bonds under mild conditions are of great interest for potential applications in alternative energy sources. In this study, we aimed to reinvestigate the stereoselective Cu-mediated hydroxylation of intramolecular C-H bonds from tridentate ligands using DFT calculations. However, computational investigation of dinuclear copper species presents a major challenge due to the nature of the  $\text{Cu}_2/\text{O}_2$  adducts. The **O** intermediate is a closed-shell system, while the **P** isomer is in an open-shell arrangement. Therefore, the isomerization equilibrium between **P** and **O** presents a bottleneck for computational methods, as single determinant methods cannot properly describe the singlet ground spin state, while multiconfigurational approaches remain rather costly for medium-to-big sized systems. To overcome this, we developed a computational protocol based on DFT methods to provide the correct electronic structure of the reaction intermediates before proceeding with mechanistic studies. Our analysis provides insights into the C-H hydroxylation's mechanism, regio-, and stereoselectivity using ligands with activated or non-activated C-H bonds. Computational tools such as Nudge Elastic Band (NEB), time-dependent DFT (TD-DFT) and spin-projection methods were utilised to calculate the reaction mechanism pathway, spectroscopic and optical properties such as g-tensor ( $g$ ), isotropic hyperfine coupling constant ( $A_{\text{iso}}$ ) and UV/Vis spectra.



**Publication:** Stefani Gamboa-Ramirez, Bruno Faure, Marius Réglér, A. Jalila Simaan, and Maylis Orio. *Chem. Eur. J.* **2022**, e202202206.