

To,

*Prof. Dr. Gerard Roelfes
Stratingh Institute for Chemistry,
University of Groningen*

I am writing to express my keen interest in conducting a short research stay of 4–6 weeks in your esteemed laboratory at the University of Groningen. Your work on artificial metalloenzymes has intrigued me, and I believe it will allow me to gain hands-on experience in experimental enzyme engineering. Your lab's pioneering work in artificial metalloenzymes and noncanonical amino acid incorporation aligns with my research interests, and I have been particularly engaged by your publications on these topics.

I am a PhD candidate at the Computational Biochemistry and Biophysics Lab ([CBBL](#)), led by my supervisor Prof. Dr. Jordi Villà-Freixa at the University of Vic - Central University of Catalunya. My thesis focuses on investigating epistatic interactions arising from amino acid variations that influence the presence or absence of peroxidase activity in mouse and human glutathione peroxidase (GPX) systems. To explore this, we developed an empirical valence bond (EVB) model on the stepwise reaction mechanism, incorporating structural data from the mouse GPX6 protein and the human GPX6 structure. EVB/FEP calculations are employed to analyze energetic and mechanistic differences across protein variants. Additionally, we investigate the conformational flexibility of GPX6 in both species, providing insight into how structural dynamics influence enzymatic function. Furthermore, we examine the hypothetical linking in going from human to mouse and mouse to human GPX6 proteins. Using a greedy algorithm, we systematically identify key residues in both systems that may have contributed to functional divergence and enhanced enzyme activity. We expect this protocol to be of general applicability to guide directed evolution strategies for the rational design of protein variants with improved catalytic properties.

While my primary work lies in computational chemistry, I have basic knowledge of molecular biology techniques, including microscopy, plasmid isolation, blotting, tissue culture, PCR, and electrophoresis, which I acquired during my BSc studies. This foundational experience has provided me with an understanding of experimental workflows, and I am eager to build upon this knowledge during my stay in your lab. I am particularly keen to gain hands-on experience in protein expression and purification of artificial metalloenzymes with noncanonical amino acids, as well as enzyme kinetics and activity assays for experimental validation of computational predictions.

I would be grateful for the opportunity to discuss how we can tailor this research, which will mostly be funded as an Erasmus exchange to best complement your ongoing projects. Thank you for your time and consideration. I look forward to the possibility of contributing to and learning from you and your research team.

Sincerely,

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