**University of Leicester**

**Future 50 PhD Scholarship**

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| **Project Reference** | CHEM Pickering |

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| **Additional Supervisor** |  |

**Section 2 – *Project Information***

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| **Project Title** | How do dynamics direct reactivity in heme proteins? | |
| **Project Highlights:** | 1. | Ultrafast spectroscopy, including transient absorption and stimulated Raman spectroscopies |
| 2. | Determining fundamentals governing reactivity in heme proteins through combination of biophysics and molecular biology |
| 3. | Likely collaborations with national/international facilities |
| **Project Summary** | | |
| Heme-containing proteins are ubiquitous in biological oxygen metabolism, playing a variety of roles including oxygen transport, detoxification of reactive oxygen species, catalysis of monooxygenation reactions, and the complete four-electron reduction of oxygen to water. Despite this wide-ranging reactivity, proteins with very different biological functions often house the heme group in environments that are almost identical from a structural perspective. In these cases, the differences in reactivity toward oxygen remain largely unexplained, but are likely to be controlled by subtle factors involving protein dynamics at timescales much shorter than the typical nanosecond to millisecond processes in which chemical bonds are broken and formed. In fact, intramolecular processes such as changes in charge (electron transfers and redox chemistry), and instantaneous fluctuations in hydrogen bonds, occur on timescales of picosenconds or faster. Protein dynamics on such fast timescales are inaccessible to conventional kinetic methods, but can be accessed by using ultrafast lasers and spectroscopic techniques.  In this project you will build a microscope for ultrafast stimulated Raman spectroscopy and related methods using state-of-the-art femtosecond laser systems at the University of Leicester. This microscope will allow you to expand our understanding of heme protein reactivity beyond insights available through standard ‘static’ spectroscopic and structural biology methods. Crucially, the microscope will also allow heme proteins to be interrogated in their ‘natural’ environment (including in vivo), and on their natural timescales, in solution and at room temperature. The ability to probe heme proteins under physiologically-relevant conditions is critical: conflicting electronic structures for the heme-oxygen adduct have been proposed depending upon whether protein is in solution or in the crystalline state. Electronic structure is critical to reactivity, hence it is vital to use methods capable of probing structure and dynamics under realistic conditions.  This multidisciplinary project will involve experimental design, ultrafast laser spectroscopy, bioinorganic chemistry, computational chemistry, and programming. The project will be suited to a candidate with a background in any of these areas, and who is keen to gain experience of a highly multidisciplinary research environment. There are likely to be opportunities to undertake research at national and international facilities throughout the project. | | |