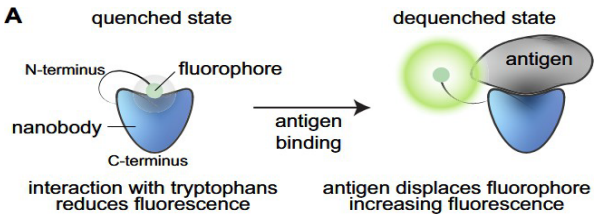
QUBIC
The Australian Research Council Centre of Excellence in Quantum Biotechnology

Understanding Tryptophan-Mediated Fluorescence Quenching in Nanobodies for Sensitive Disease Detection

Institution	University of Wollongong
Project details	The detection of disease biomarkers is a cornerstone of modern medicine. Immunoassays are a widely used method for detecting the presence or concentration of disease-specific antigens [1], relying on the observation of their specific interactions with antibodies.  One such strategy involves fluorescence quenching, where a normally bright fluorophore interacts with quenching residues in antibody, resulting in reduced fluorescence that depends on antigen concentrations. We recently developed optimized nanobody based quenchbodies for protein detection[2]. Upon binding of disease-specific antigen targets to the nanobody, fluorescence increases as the tryptophan residues become unavailable for quenching, enabling sensitive detection[2]. A large body of work has been dedicated to understanding this reaction[3] and this process is typically understood as tryptophan donating an electron to the fluorophore in a process called photoinduced electron transfer, thereby quenching fluorescence. However, many mechanistic questions remain to be addressed including the relative contribution of each specific tryptophan residue and strategies to optimise quenchbody design for improved sensitivity. In this project, we will investigate the quenching processes by examining the electronic structure of tryptophan induced quenching in detail. We aim to identify the key tryptophan residue(s) that are important in the quenching process, setting the state for important publishable scientific works. In this role, you will be trained in multiscale modelling techniques, the basics of electronic structure theory, and gain valuable experience in data analysis and coding. 1. Hage; Analytical Chemistry; **1999**; 71, 12, 294-304. 2. Cater, El Salamouni, Mansour, Hutchinson, Mc Guinness, Mueller, Spinks, Shanmugam, Pichard-Kostuch, Zahoransky, Ghodke, Ribezzi-Crivellari, Yu, van Oijen, Griffiths, & Spenkelink; Communications Biology; **2025**; 8, 937. 3. El Salamouni, Cater, Spenkelink, & Yu; Febs Open Bio, **2024**; 15, 2, 236-253.
Who can apply	We are seeking a student with a background in physics or chemistry. Computer literacy is important, as the project involves using supercomputers to perform calculations. Most importantly, we require that the student is excited by this work; interest/motivation is vital.
Contatct / Project supervisors	Dr. Anjay Manian – amanian@uow.edu.au Dr. Nehad El Salamouni – nehade@uow.edu.au Prof. Haibo Yu – hyu@uow.edu.au