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Designing a more efficient CO_2-fixing enzyme by interpreting Molecular dynamics simulation data
Master degree project / Research training / Internship

We are looking for an ambitious student with an interest in data analysis, protein structure-function, carbon fixation or molecular dynamics for a project to identify amino acid residues that contribute to increased binding affinities in nature's notoriously inefficient CO_2-fixing enzyme.

The CO_2-fixing enzyme ribulose-1,5-bisphosphate carboxylase/oxygenase (Rubisco) has a slow catalytic rate and exhibits poor substrate specificity (CO_2/O_2 selectivity) such that its catalysis often limits the growth rate of photosynthetic organisms, including crop plants and cyanobacteria used for biofuel production. Attempts to engineer a more efficient Rubisco have been underwhelming, at best, and single point mutations distant from the catalytic site often dramatically impair enzyme function without any obvious explanation.

We used Molecular Dynamics (MD) simulations to investigate how CO_2 and O_2 diffuse from the surface of Rubisco into the active site, because we want to identify amino acids that may contribute to enhanced CO_2/O_2 selectivity. We calculated how much every single amino acid in the protein contributes to the binding affinities of the Rubisco subunits, and now we want to identify the residues whose contribution to binding affinity changes the most in the presence of different gases, because these amino acids may be important for enhancing CO_2/O_2 selectivity.

In this project you will (i) identify amino acid residues that contribute to a higher binding affinity in the presence of different gases, (ii) identify the level of conservation of these amino acids in Rubisco variants from different species, and (iii) suggest point mutations that could be introduced into the protein subunits to test the importance of specific residues for enzyme performance. This information will be used to physiologically confirm our MD results and to engineer more efficient CO_2-fixing enzymes.

Mandatory skills: good experience with spreadsheets (Excel) and statistical data; some basic biochemistry i.e. protein structure and structural motifs.
Desirable (but not mandatory): previous experience analysing large datasets; some experience with visualization programs as PyMol or VMD; willing to learn a little bit of molecular dynamics (e.g. how to get missing data, visualize molecular systems).

If you find this project interesting, please contact Laura Gunn:

Laura Gunn, laura.gunn@icm.uu.se Institute for Cell and Molecular Biology. BMC, Uppsala University
Group website: https://www.icm.uu.se/molecular-biophysics