Contribution ID: **22** Type: **Poster**

Prediction of more thermostable ApPDC variants by Constraint Network Analysis and ProteinMPNN to enable an industrial application

Tuesday 20 February 2024 10:45 (1 hour)

Carbon-carbon bond-forming reactions are essential for organic synthesis. In conventional petrochemical-driven approaches, these reactions rely on organic solvents and hazardous starting materials. In contrast, biocatalysts offer an alternative pathway based on second-generation feedstocks. In particular, pyruvate decarboxylase from Acetobacter pasteurianus (*Ap*PDC) offers a sustainable alternative in the synthesis of chiral aromatic derivatives, facilitating the C-C bond formation between, e.g., benzaldehyde and pyruvate in aqueous solution. However, *Ap*PDC exhibits insufficient thermostability for widespread industrial application.
Using molecular dynamics simulations, we generated a diverse conformational ensemble upon which we applied our in-house software, Constraint Network Analysis (CNA), to perform thermal unfolding simulations. These simulations unveiled weak spots within the protein structure. To validate our approach, we compare these identified weak spots with a previously described variant with a remarkable 12 ℃ enhancement in the melting point, which differs in 14 amino acid positions from the wild type. Our analysis successfully identifies 8 out of 14 specific weak spots within the ApPDC variant, underscoring the predictive capabilities of CNA in pinpointing thermal weak spots.
The predicted weak spots are substituted by mutations derived from ProteinMPNN that enhance the stability of *Ap*PDC. Overall 5000 sequences with enhanced thermostability were generated. This research paves the way for accelerated progress in enzyme engineering for enhanced industrial applications.

Consent

Yes

Authors

Becker, Daniel[1]; Schott-Verdugo, Stephan[2]; Gohlke, Holger[1, 2]

Affiliation

[1] Mathematisch-Naturwissenschaftliche Fakultät, Institut für Pharmazeutische und Medizinische Chemie, Heinrich-Heine-Universität Düsseldorf, 40225 Düsseldorf, Germany; [2] Institute of Bio- and Geosciences (IBG-4: Bioinformatics), Forschungszentrum Jülich GmbH, 52425 Jülich, Germany

Primary authors: BECKER, Daniel Fritz Walter (Heinrich-Heine-Universität); GOHLKE, Holger (IBG-4, Forschungszentrum Jülich GmbH); SCHOTT-VERDUGO, Stephan (IBG4)

Presenter: BECKER, Daniel Fritz Walter (Heinrich-Heine-Universität)

Session Classification: Poster session