AI/ML-ASSISTED REDESIGN OF NATIVE PROTEINS

Nanobody Thermostability Prediction Using Structural And Sequence Features

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Single-domain antibodies (sdAbs) have recently received prevalent attention due to their small size (~15 kDa), robust thermostability, and diverse applications in biotechnology and therapeutics. As modern biotechnology makes a breakthrough in protein sequence generation through generative deep learning methods, the prominent interest in antibody engineering, particularly their melting temperature (Tm), is crucial for their successful utilization. In this study, we present a predictive modeling approach for estimating the Tm of sdAbs using computational methods. Our methodology integrates structural features from NetSurfP3 and outputs from AlphaFold2, with predictive machine learning techniques to develop accurate Tm prediction models. This approach is validated experimentally determined Tm values for a diverse set of sdAbs from an in-house dataset and a recently published database, NbThermo, which contains more than 500 unique sequences. Our results demonstrate the efficacy of the proposed method in reliably predicting the Tm of sdAbs, thus offering a valuable tool for the optimization of sdAbs for various biomedical and therapeutic applications. This predictive model not only enhances our understanding of sdAb thermostability but also streamlines the development process, ultimately facilitating the broader applicability of both naturally-occurring and synthetic sdAbs in biomedicine and beyond.

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