

Peer Review

Review of: "AlignAb: Pareto-Optimal Energy Alignment for Designing Nature-Like Antibodies"

Truong Son Hy^{1,2}

1. Department of Computer Science, University of Chicago, United States; 2. Department of Computer Science, UAB The University of Alabama at Birmingham, Birmingham, United States

The paper "AlignAb: Pareto-Optimal Energy Alignment for Designing Nature-Like Antibodies" presents a novel three-stage deep learning framework for antibody sequence-structure co-design. The approach integrates pre-training on large-scale antibody sequence data, diffusion-based model training for joint sequence-structure optimization, and energy-based alignment to improve antigen binding. A key innovation is the extension of Antibody Direct Preference Optimization (AbDPO) to achieve Pareto-optimal energy alignment, balancing repulsion and attraction forces at the antigen-binding site. The method incorporates iterative learning and temperature scaling to enhance generalization and efficiency. Extensive experiments demonstrate that AlignAb generates more nature-like antibodies with higher binding affinity and stability compared to existing baselines, improving rationality and functionality in antibody design.

Declarations

Potential competing interests: No potential competing interests to declare.