3D Antibody Modeling with Orion Cloud Modeling Platform

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Summary:

- Select diverse sequences with high epitope affinity using the AbXtract™ engine from Specifica
- Predict 3D structure from sequence at scale and compute predictors of developability
- Sample conformational space based on physically meaningful shape and chemical feature description

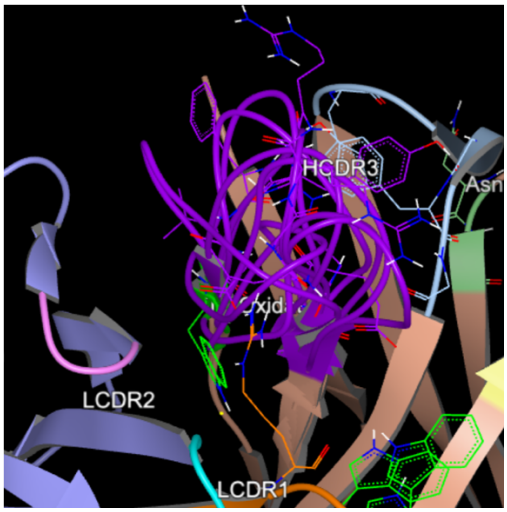
Product Keywords: Orion®, AbXtract™, Antibody Modeling, Enhanced Sampling MD

Abstract:

OpenEye's suite of antibody modeling tools on the Orion® cloud modeling platform includes Specifica's state-of-the-art antibody sequence analysis tool, AbXtract™, and open-source tools such as ImmuneBuilder for antibody structure prediction.

The process of modeling antibody structure on Orion begins by extracting sequences from a selection campaign, which are then analyzed using AbXtract. 3D structures are subsequently generated using the AI-driven structure predictor ImmuneBuilder, which requires only around 100 ms per structure when predicting at a multi-thousand scale. From these structures, a wide range of physico-chemical properties is calculated to facilitate the selection of antibodies with the highest likelihood of successful development into human therapies.

Structural diversity in the complementarity determining region (CDR) can be further explored using knowledge-based loop modeling, while enhanced sampling molecular dynamics (ESMD) is used to explore global conformational diversity. Clustering is then applied to identify structural families within computed ensembles, utilizing similarity based on a physically rigorous shape and chemical feature distribution of the CDRs. Individual sequences can be optimized through single or multi-point mutations and/or loop replacement. These new hypotheses can be submitted for physico-chemical property profiling and conformational exploration.



CDR loop ensemble generation followed by enhanced sampling molecular dynamics using Orion cloud modeling platform

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