

In silico VHH Aggregation Prediction

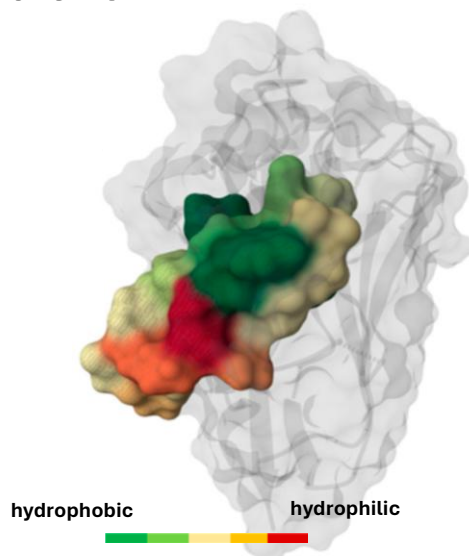
Nanobodies are single-domain antibody fragments with strong therapeutic potential but are often limited by aggregation-prone framework residues. Addressing these hotspots is essential to improve stability, solubility, and overall developability in the context of rational nanobody engineering strategies.

The **xyna.bio Nanobody Aggregation Pipeline** implements the sequence-based scoring framework of Geyer et al. 2025, with a particular focus on FR2 region hotspots.

The pipeline integrates residue-level analyses of:

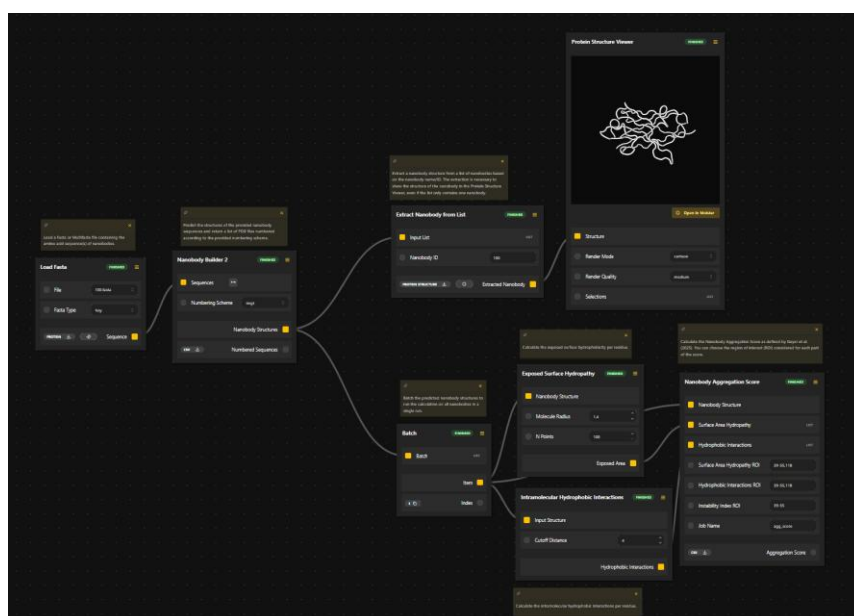
- Exposed surface hydropathy
- Intramolecular hydrophobic interactions
- Instability index from FR2 composition

This scoring system employs a hybrid approach, integrating sequence- and structure-derived parameters for a more holistic prediction of aggregation risk. These descriptors are merged into a unified aggregation score, enabling early candidate prioritization and design directly from sequence data, presenting only the initial step toward an AI-driven *in silico* VHH optimization platform on xyna.bio.



3D structure prediction of a VHH sequence with the key FR2 region highlighted. Residues here are prone to drive aggregation behavior, with a major characteristic being residue hydropathy.

Adapted from Geyer et al. 2025.



Explore the xyna.bio Nanobody Aggregation Score pipeline at www.xyna.bio.