A190 · An ILP Framework for Repertoire-Scale Antibody Lineage Tracking

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Tracking how antibody clonal families evolve across immunisation timepoints is central to understanding affinity maturation, yet existing tools cluster sequences within a single timepoint and offer little support for matching families across timepoints at repertoire scale. We present a method for cross-timepoint lineage tracking that treats lineage reconstruction as a global optimisation over candidate progenitor-descendant pairs and solves it with an integer linear program. We analyse nanobody sequences from a five-timepoint phage display panning experiment against SARS-CoV-2 and hACE2. Our framework works first by clustering the data into clonal families to reduce the assignment problem from millions of individual sequences to tens of thousands of families using NanoMap, our nanobody clonal clustering framework. The ILP then minimises total dissimilarity across all assignments subject to constraints on clonal expansion, with explicit penalties for families that acquire no progenitor or spawn no descendants, yielding a globally optimal assignment rather than a greedy one. We evaluate assignments by panning target concordance, CDR k-mer Jaccard similarity, and the Adjusted Rand Index. We further use a parameter sweep characterises the trade-off between assignment coverage and precision. This approach offers a tractable route to repertoire-scale lineage reconstruction where phylogenetic methods are computationally infeasible, and yields paired progenitor-descendant assignments suitable as training data for repertoire evolution.