Dynamic molecular fingerprints for therapeutic interfaces: From drug-protein recognition to nanocarrier design

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The development of molecular therapeutics, drug delivery platforms, and theranostic systems increasingly requires descriptors that go beyond static structural characterization or endpoint affinity measurements. Therapeutic performance often emerges from dynamic and heterogeneous interfaces, including drug-protein complexes, protein-nanocarrier contacts, and cargo-loaded supramolecular assemblies. In these systems, binding, remodeling, stability, and functional response are not determined only by average structures, but by the persistence, redistribution, and evolution of molecular interactions over time.

Here, we present a modeling-oriented dynamic molecular fingerprinting strategy in which biophysical measurements and molecular simulations are converted into quantitative descriptors for the engineering analysis of therapeutic interfaces. The approach integrates biophysical observables and molecular modeling to describe how drugs, ligands, cargos, proteins, and nanocarriers mutually reorganize each other. Experimental information from fluorescence spectroscopy, circular dichroism, UV-vis spectroscopy, calorimetry, and nanoscale characterization can be combined with simulation-derived descriptors such as contact persistence, native and non-native interaction patterns, binding-site flexibility, solvent exposure, compactness, conformational clustering, and free-energy landscape reshaping.

The key aim is to translate complex molecular behavior into engineering-relevant descriptors. For drug-protein systems, dynamic fingerprints can identify whether a ligand simply occupies a binding pocket or actively remodels its interaction network and conformational ensemble. For nanocarrier-based systems, the same logic can reveal whether a cargo behaves as a passive payload or as an active structural modulator of the carrier. In both cases, the molecular interface is treated as a dynamic process rather than as a fixed structural endpoint.

Representative examples from our ongoing work include protein-ligand recognition and binding, receptor-ligand interaction landscapes, and self-assembling nanocarrier/cargo systems. These case studies illustrate how experimentally anchored molecular descriptors can support a more rational comparison between compounds, payloads, and formulation conditions. Rather than replacing experimental characterization, molecular modeling acts as a mechanistic layer that helps interpret why apparently similar systems may differ in binding persistence, local remodeling, dynamic stability, or delivery-relevant behavior.

This framework proposes a shift from descriptive characterization toward molecular process engineering of therapeutic interfaces. By converting dynamic molecular information into comparable fingerprints, the approach may support the design of more effective drug delivery systems, ligand-based therapeutics, and nanotechnological platforms for biomedical applications.