



**A Modern Approach to Protein
Higher Order Structure (HOS) Analysis**

Critical Use Cases of
Fox[®] Protein Footprinting
Technology in BioPharma



Fox® Systems from GenNext® Technologies revolutionize HOS analysis with advanced Hydroxyl Radical Protein Footprinting (HRPF) technology—delivering high resolution, rapid turnaround, and cost-effective structural analysis of proteins and their interactions.

By exposing proteins to hydroxyl radicals, HRPF selectively modifies solvent-accessible amino acids, enabling precise mapping of binding sites and conformational changes, all critical insights for drug design and biotherapeutic development.

With HRPF performed using GenNext's Fox Technology, structural biologists gain a powerful, next-generation tool to accelerate drug discovery, development, and optimization, providing actionable results in hours or days.

Biotherapeutics & Monoclonal Antibodies (mAbs)

First-in-Class Drugs & Biosimilars

Epitope & Paratope Mapping

Fox Systems deliver unparalleled precision in mapping epitope and paratope regions in monoclonal antibodies. By selectively modifying solvent-accessible residues, HRPF provides high resolution insights into protein-protein interactions—ensuring a deeper understanding of molecular recognition—critical for optimizing mAb therapeutics.

Aggregation Analysis

Aggregation compromises mAb stability, efficacy, and immunogenicity. Fox Footprinting enables high resolution assessment of aggregation-prone regions by tracking changes in solvent accessibility, offering actionable insights into formulation optimization to mitigate aggregation risks.

Biosimilarity Assessment

Regulatory agencies demand rigorous protein HOS characterization for biosimilars. Fox Footprinting provides a relative comparison of reference biologics and biosimilar candidates, detecting structural differences due to manufacturing or formulation variances to ensure comparability and regulatory compliance.

Stability & Storage Optimization

Fox Footprinting assesses how formulation conditions, temperature, and storage impact mAb structural integrity over time. By monitoring solvent-accessible regions, researchers can predict degradation pathways, optimize storage conditions, and enhance shelf-life stability.

Formulation Development

Manufacturing processes introduce conformational variations in mAbs. Fox Footprinting enables a direct comparison of structural changes due to pH shifts, excipients, stabilizers, or process modifications, ensuring batch-to-batch consistency and product quality.

Drug Delivery Considerations

Optimizing delivery formulations requires precise protein structure insights. Fox Systems evaluate mAb stability under different delivery conditions, supporting the development of effective IV, subcutaneous, and novel administration strategies without compromising therapeutic integrity.

Fox Systems are a game-changing tool for mAb design, production, and biosimilar development, offering high-resolution, residue-level insights into antigen-antibody interactions in days, not months—outpacing traditional techniques like NMR, X-ray crystallography, and cryo-EM. Unlike lower-resolution screening techniques (e.g., SPR, BLI, ITC), Fox Footprinting delivers actionable data critical for therapeutic refinement, accelerating the entire drug development pipeline from discovery to regulatory submission.

Small Molecule Drug Discovery

Allosteric & Orthosteric Therapeutics

Target Engagement & Response

In the pursuit of allosteric and orthosteric small-molecule therapeutics, high-throughput (HT) primary screening rapidly identifies initial hits from chemical libraries, often through fragment-based drug discovery. However, distinguishing specific, high-affinity binders from non-productive interactions remains a major challenge.

The Fox[®] Protein Footprinting platform transforms secondary screening by unambiguously identifying therapeutic binding sites and characterizing target response upon drug engagement. This capability ensures that only promising leads advance while eliminating compounds that fail to bind appropriately or induce the desired allosteric effect.

Lead Optimization & Structure-Activity Relationships

During lead optimization, chemical modifications are introduced to enhance specificity and binding affinity. Fox Footprinting provides residue-level precision, confirming whether optimized leads retain productive target engagement and response. Compared to ultra high-resolution techniques like cryo-EM, NMR and crystallography—all of which are time- and resource-intensive — Fox Footprinting delivers actionable structural insights within days, empowering medicinal chemistry, SAR studies, and rational drug design with unprecedented efficiency.

Only Fox Footprinting rapidly enables the identification of the therapeutic binding site as well as target response at the amino acid level, enabling researchers to promote promising leads while killing those that inappropriately bind or elicit no or an undesired target response.

Artificial Intelligence & Computational Biology Validation


Bridging the Gap Between AI Models & Experimental Validation

While AI-driven drug discovery generates structural predictions at an unprecedented scale, these models often fail to accurately predict binding sites, target response, allosteric regulation, and protein flexibility—necessitating real-world validation. Traditional structural biology methods, such as cryo-EM and X-ray crystallography, require months or even years to confirm AI-generated hypotheses, creating a bottleneck in drug development.

Only the Fox Footprinting platform is capable of rapidly adjudicating and informing AI-generated drug discovery models in just days, solving a critical gap in computational biology. Fox Systems enable high-resolution, real-time validation of protein-drug interactions by mapping solvent accessibility and conformational changes, reducing workflow complexity and costs while ensuring scalable validation of AI models.

In a recent study, Fox Technology confirmed AI-predicted drug binding and target response within a single week, while traditional methods required 6 to 8 months for validation. Subsequent results from cryo-EM and X-ray crystallography ultimately confirmed Fox's rapid footprinting data, proving its reliability and speed.

By integrating high-speed, empirical validation into AI-driven workflows, Fox Footprinting accelerates the drug discovery process, reduces costs, and actualizes the true potential of computational biology—delivering actionable results within days.



Advantages of Fox[®] Technology

- **Flexible Access** – Available through instrument purchase or contract research services to fit your workflow and budget.
- **Rapid Turnaround** – Delivers high-resolution structural insights in days, compared to months or years with traditional methods.
- **Excellent Structural Resolution** – Provides amino acid-level resolution, ensuring precise mapping of protein interactions and conformational changes.
- **Highly Reproducible** – Generates consistent, reliable data for confident decision-making in drug discovery and development.
- **Minimal Sample Requirements** – Requires only microgram quantities of protein, preserving valuable samples.
- **Cost-Effective** – Reduces expenses on capital equipment, reagents, and staffing, making advanced structural analysis more affordable.
- **Streamlined & Automated Workflow** – Features an easy-to-use, automation-assisted protocol, enabling efficient, high-throughput analysis.



Fox[®] Technology empowers researchers to optimize drug efficacy and specificity while minimizing off-target effects. The ability to assess protein stability under different conditions ensures the development of more effective and safer therapeutics.

Purchase a System or Service Contract

Harness the power of fully automated, chip-based HRPf with the new AutoFox[®] System. Save time and money, enjoy a simplified and faster workflow, and produce robust and reproducible HOS data.

Contact us to learn how our technology can easily fit into your lab's workflow or test-drive the AutoFox System on an outsourced project basis.