BIOVIA

3DEXPERIENCE®

ACCELERATING DRUG DESIGN
CATALYZING INNOVATION IN LIFE SCIENCES R&D

Datasheet

DASSAULT SYSTEMES

The pharmaceutical industry has experienced a boom of innovation over the past two decades. New techniques (and even entire fields) such as cryo-EM, genomics and systems biology have opened the door to thousands of potential therapeutic targets. Yet in spite of this boom, R&D productivity has remained nontrivially difficult: most drug discovery projects take in excess of 5 years and require testing thousands of compounds to find a single viable candidate. This struggle to get drugs out of the lab and to the market is compounded by growing demands for demonstrable efficacy and improved safety by regulatory organizations. To move forward, organizations need to increasingly target their work at the bench on candidates that are more likely to succeed. *In silico* methods such as molecular modeling and machine learning (ML) can provide needed insight into the intermolecular mechanisms that researchers need to identify and optimize lead candidates faster and at lower cost.

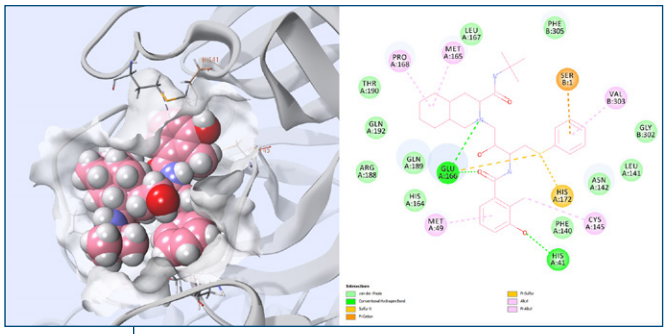


Figure 1. (left) A candidate drug docked in a protein's binding pocket; (right) a map of the intermolecular interactions between the protein and ligand.

EXPANDING THE SCOPE OF INNOVATION

The Accelerating Drug Design initiative spurred by the BIOVIA brand from Dassault Systèmes brings together an industry-leading suite of methods to characterize protein-ligand interactions and to generate and screen candidate compounds for targeted, more efficient drug discovery and development.

Lead Identification

The foundation for any successful drug discovery project is a thorough characterization of the intended drug target. Even minor changes in protein sequence can have drastic impacts on its overall structure and function. Additionally, many proteins do not have high quality crystal structures, making identification of active sites and describing the interactions that affect ligand binding difficult. Molecular modeling and simulation techniques can help researchers foster a better understanding of their target proteins and how they interact with ligands. Characterizing this interplay between target and candidate can provide key insights to improve drug design.

- Create homology models to predict and refine target protein structure based off of existing crystallography data of related proteins
- Identify and explore the key interactions that impact ligand binding by docking compounds in known or user-defined binding sites
- Test and score candidate drugs by calculating their binding energies with target proteins via established MM-PBSA or MM-GBSA CHARMm-based methods
- Characterize key intermolecular interactions that impact ligand binding in 3D space to generate pharmacophores for high-throughput screening of candidates

Lead Optimization

Increasing regulatory pressure to create demonstrably efficacious and safe drug candidates has placed strain on traditional models for small molecule R&D. These added design requirements has created s system of tradeoffs that teams must account for when moving candidates further down the pipeline. This multiobjective optimization problem is a perfect fit for ML-driven approaches. Additionally, organizations can utilize existing data – extending the value of their historical knowledge base – to better inform this optimization process. Utilizing ML-based methods can expand the scope of innovation for an R&D organization, allowing them to vet thousands of compounds quickly in a low-resource environment. Armed with this knowledge, they can then pass only the most promising compounds on for further testing in the lab.

- Accelerate lead optimization efforts with ML-driven generative methods to create and suggest new candidates for lab testing
- Improve R&D productivity with user-defined traits to optimize compounds for or against, such as target/off-target affinity, toxicity, solubility, etc.
- Facilitate active learning within predictive models with simplified methods to retrain models in light of new experimental data and expert input
- Further characterize and refine lead activity with high fidelity physics-based methods such as Multi-site Lambda Dynamics and Free-Energy Perturbation

Figure 2. Generative ML methods can iteratively create and screen successive generations of candidates to meet multiple design requirements (EC/IC50, solubility, toxicity, etc.).

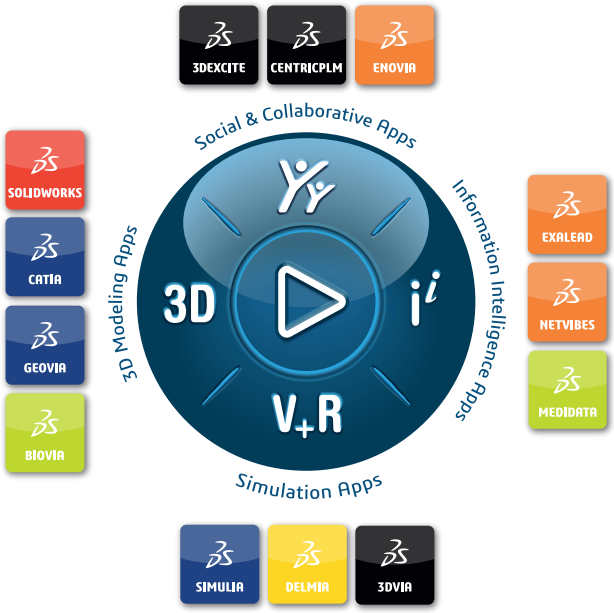
PRODUCING SAFER, MORE EFFICACIOUS THERAPEUTICS FASTER

Drug discovery and development is quickly modernizing. As a result, organizations need to utilize every tool at their disposal to better guide their teams in the lab. *In silico* methods can help researchers better characterize their targets and identify potential candidates faster and at lower cost than ever before. The resulting synergy between virtual methods and physical experimentation at the bench can drastically improve R&D productivity, helping teams push safer, more efficacious treatments to the patients that need them faster and more efficiently than ever before.

Our **3D**EXPERIENCE® Platform powers our brand applications, serving 11 industries, and provides a rich portfolio of industry solution experiences.

Dassault Systèmes, the **3DEXPERIENCE** Company, is a catalyst for human progress. We provide business and people with collaborative virtual environments to imagine sustainable innovations. By creating 'virtual experience twins' of the real world with our **3DEXPERIENCE** platform and applications, our customers push the boundaries of innovation, learning and production.

Dassault Systèmes' 20,000 employees are bringing value to more than 270,000 customers of all sizes, in all industries, in more than 140 countries. For more information, visit **www.3ds.com**.



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