Standigm
AI for new drug R&D

STELLA

Revolutionizing Drug Discovery with Standigm AI-Powered Multi-Objective Optimization

Introduction

The landscape of drug discovery is evolving rapidly, driven by advancements in artificial intelligence (AI) and computational methods. STELLA, a cutting-edge platform developed by Standigm, revolutionizes the complex, costly, and time-consuming traditional drug discovery process by leveraging advanced genetic algorithms and AI to accelerate and optimize drug design. From concept to market-ready molecular design, STELLA facilitates hit-to-lead optimization by rapidly creating and refining drug candidates, ensuring swift progression through the drug discovery pipeline. This whitepaper explores the capabilities, features, and benefits of STELLA, highlighting its transformative potential in modern drug discovery.

Overview of STELLA

Advanced Molecular Design

STELLA integrates powerful genetic and AI algorithms to facilitate advanced molecular design. This platform can generate over 10,000 unique molecules tailored to specific research goals within days, maintaining momentum in drug discovery projects and ensuring timely progression from initial concept to market-ready molecular designs. Figure 1 illustrates the complete drug design cycle using STELLA.

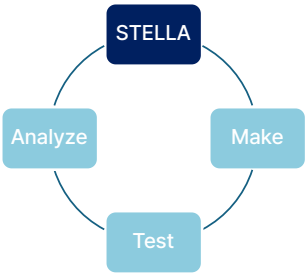

Figure 1. The complete DMTA (Design, Make, Test and Analyze) cycle with STELLA.

Multi-Objective Optimization

STELLA excels in multi-objective optimization (MPO), aligning molecular design with specific research goals and constraints. By incorporating various parameters such as molecular properties, druggability, selectivity, ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) properties, and synthesizability, STELLA ensures that the generated compounds efficiently meet the desired pharmaceutical properties. Figure 2 illustrates how STELLA generates molecules and identifies drug candidates. Starting from the reference ligand with the target protein, STELLA uses crossover, mutation, and trimming to generate molecules based on selections from the previous episode. These selections follow the base properties set by the user, allowing STELLA to satisfy any specific project scope and generation scenario.

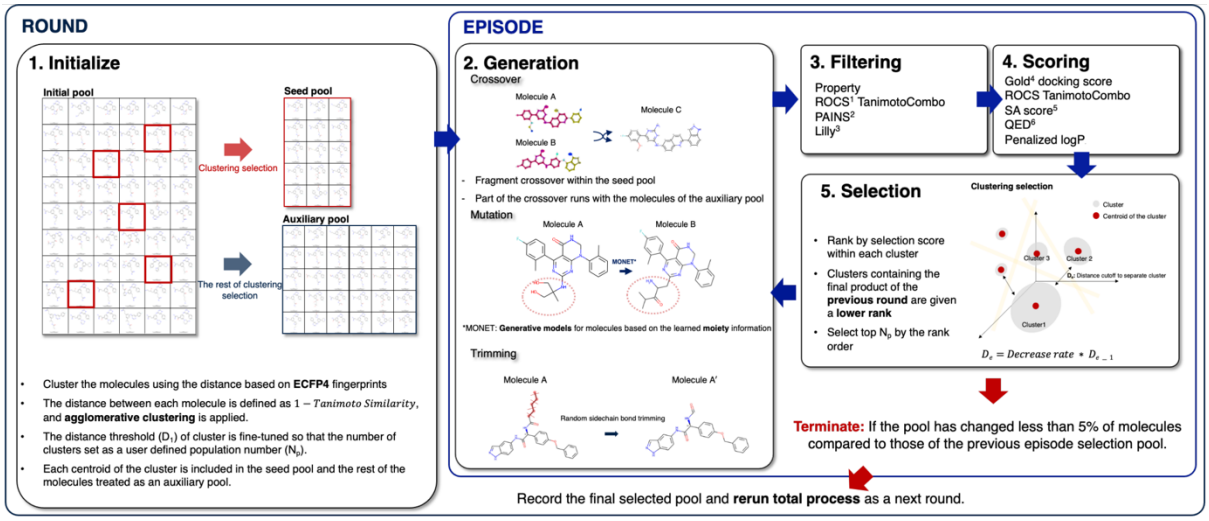

Figure 2. Multi-objective optimization workflow in STELLA.

Integrated ADMET Prediction

The platform is equipped with Standigm's QIP-ADMET, an AI-driven solution for rapid and reliable ADMET prediction. QIP-ADMET enhances the drug discovery process by providing swift insights into the pharmacokinetic and toxicological properties of potential drug candidates, thus accelerating their journey towards clinical success.

Project-Based Management

STELLA offers a comprehensive project management interface that facilitates cross-functional team collaborations. Users can create and manage projects, monitor and view results, set design scenarios, and configure molecular generation processes, all through an intuitive web-based interface, as shown in Figure 3.

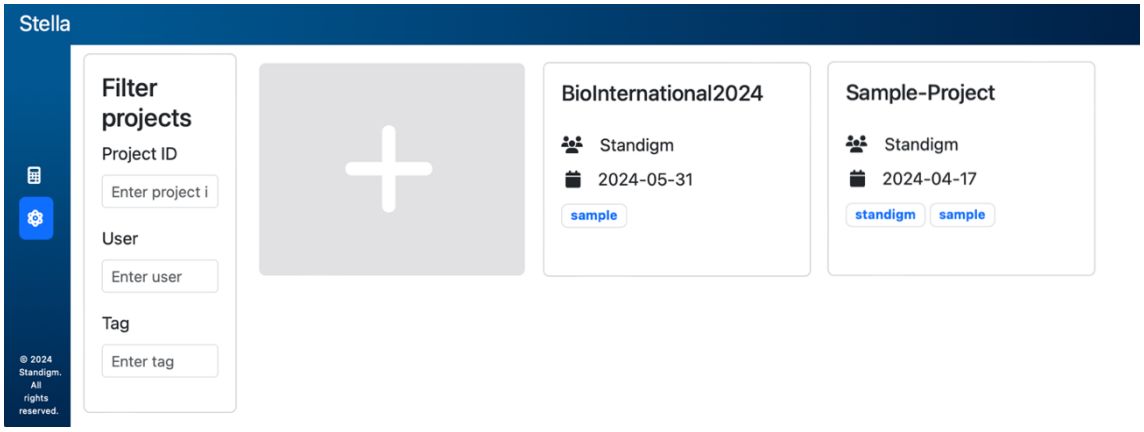

Figure 3. STELLA's project management interface.

Customizable Design Platform

The platform is highly customizable and easily scalable to fit any organizational need. This ensures that STELLA can be seamlessly integrated into existing workflows, enhancing its utility across various stages of drug discovery. Figure 4 illustrates the customizable generation configuration, which can be modified to meet any user requirements. Following the user-defined generation scenario, every configuration can be freely modified or deleted.

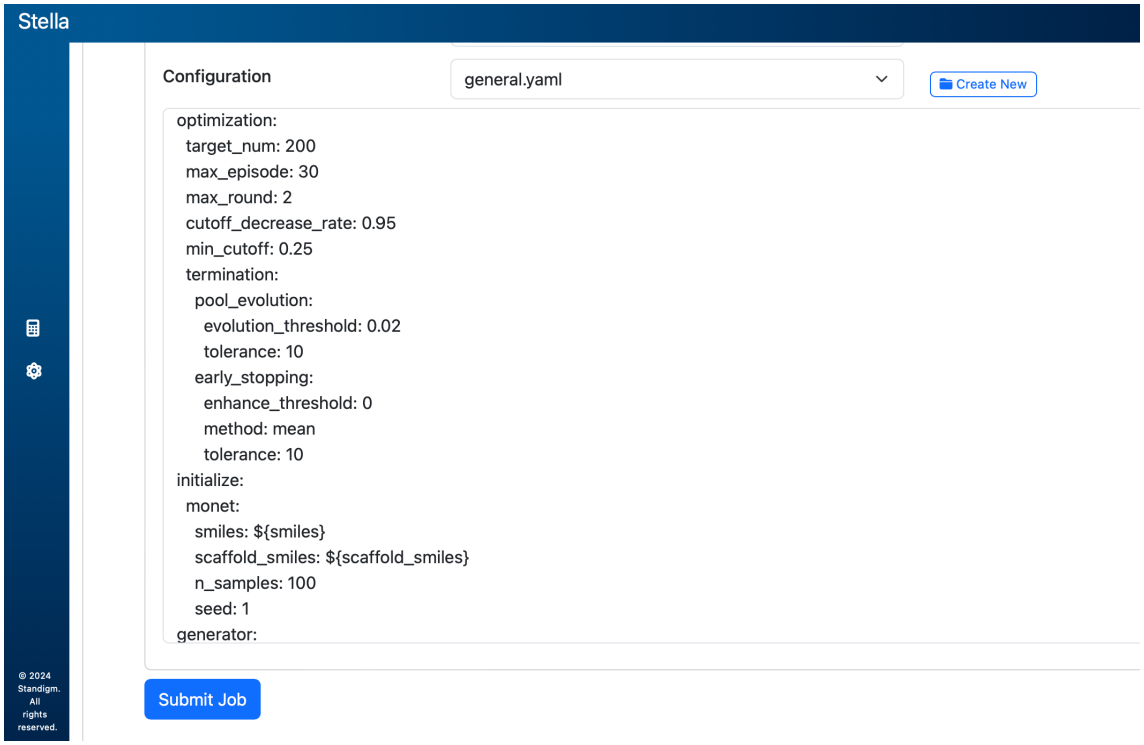

Figure 4. Customizable generation configuration of STELLA.

STELLA's Design Strategies

STELLA offers four comprehensive design strategies that cover a wide range of molecular design possibilities: de novo design, scaffold-based design, linker-based design, and lead optimization. De novo design involves crafting new molecules analogous to reference compounds. Scaffold-based design, illustrated in this section, generates molecules with similar or better properties than a reference ligand and target protein using fixed scaffolds, making it a practical strategy frequently employed by medicinal chemists in the pharmaceutical industry. Linker-based design bridges fragments with innovative or new scaffolds, while lead optimization focuses on enhancing a lead compound to meet drug development objectives.

Example: Scaffold-based Design

Scaffold-Based Design

STELLA's scaffold-based design approach enables researchers to innovate upon reference molecules by incorporating diverse functional groups. By selecting a scaffold to maintain throughout the design process, users can intuitively set configurations and generate new molecular variants. This method optimizes lead evolution to better meet drug development objectives.

Genetic Algorithms and Filtering

STELLA employs a combination of genetic algorithms, filtering, and multi-objective optimization (MPO) to iteratively generate and refine molecular designs, as shown in Figure 2. This iterative process ensures that the generated compounds are optimized across multiple objectives, providing a robust solution for hit-to-lead optimization. Molecules are generated based on the specific requirements of the generation scenario, with optimization guided by user-defined objectives.

Scaffold-based Design Example

Figure 5 illustrates the scaffold-based design process using STELLA. The initial step involves preparing the target protein and reference ligand. Users can upload the protein's PDB file and the ligand's SDF file or enter the SMILES directly into the STELLA web interface, as shown in Figure 5(a).

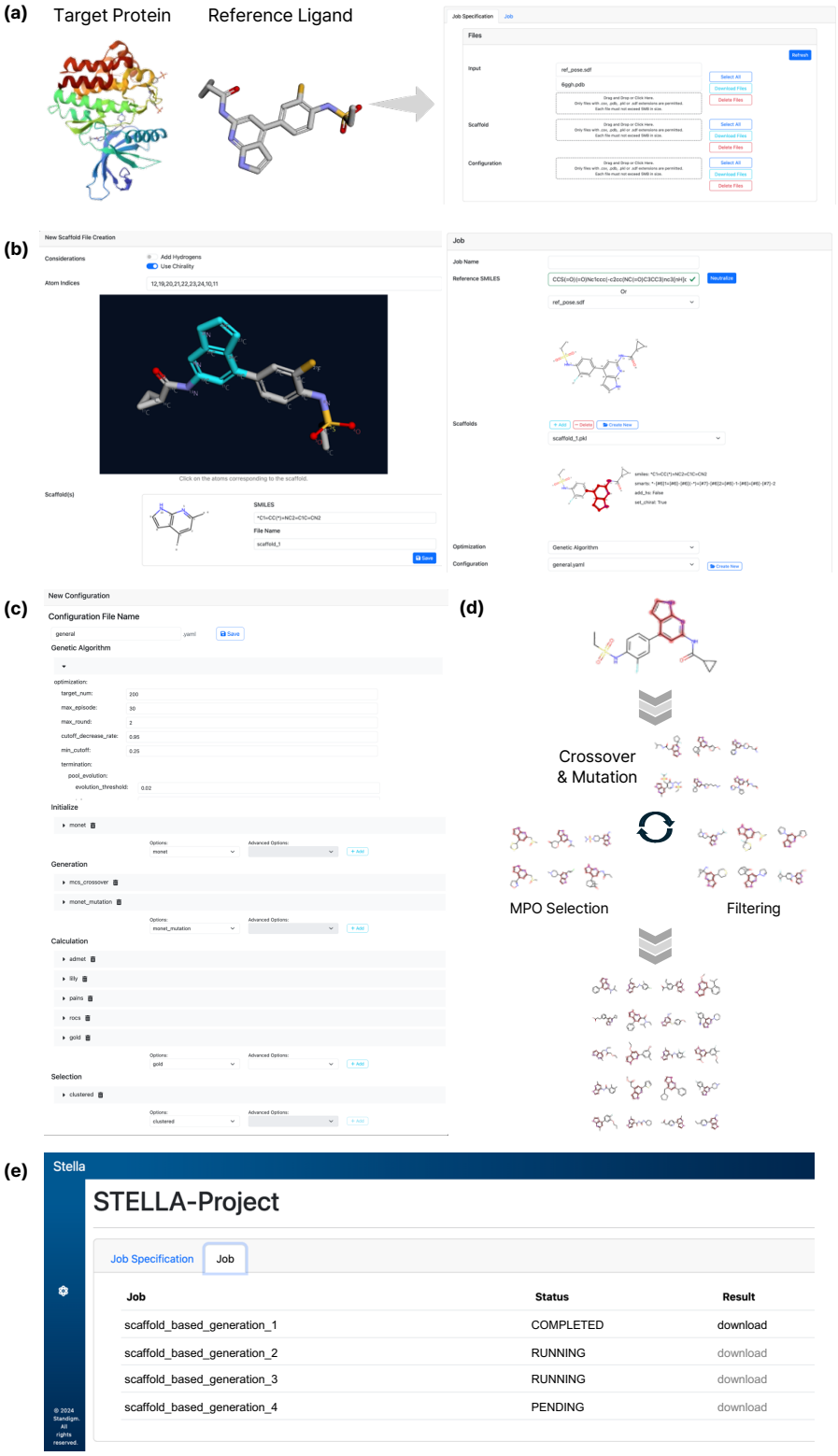

Figure 5. Scaffold-based design example in STELLA. (a) Preparation of the protein and reference ligand. (b) Selection of the scaffold to maintain throughout the design process. (c) Configuration settings to align with design scenario and objectives. (d) An illustrative view of the generation process, showcasing steps such as crossover, mutation, filtering, and selection. (e) Interface for reviewing the generation process and downloading results.

For scaffold-based generation, which focuses on fixing a scaffold throughout the design process while varying functional groups, users must provide scaffold information. This can be done by uploading SMILES and SMARTS of the scaffold, or interactively selecting atoms on the displayed reference ligand in the web interface, as depicted in Figure 5(b). It's possible to set multiple scaffolds to remain fixed during the generation process.

Users can then intuitively customize configurations through the web interface. These configurations are highly flexible, allowing adjustments to genetic algorithm parameters, such as crossover and mutation, and desired molecule properties, including ADMET, Lilly, PAINS, ROCS, and docking criteria. Figure 5(c) displays the configuration web interface.

Figure 5(d) provides an illustrative view of the generation process, showcasing steps such as crossover, mutation, filtering, and selection. This begins with the reference molecule and progresses through several cycles to generate variants aimed at multi-objective optimization.

Finally, users can check the generation status, review, and download results through the web interface, ensuring efficient monitoring and iteration on the design process.

Supporting Technologies

GT-AutoML

GT-AutoML, a part of STELLA's suite of tools, enables the creation of tailored Structure-Activity Relationship (SAR) models. These models, both ligand-based and structure-based, are simplified through automated machine learning, making it easier to derive meaningful insights from complex data.

QIP-ADMET

QIP-ADMET is Standigm's AI-driven solution designed for rapid and reliable ADMET prediction. The QIP-ADMET model leverages extensive datasets that include experimental data, in silico quantum mechanical data, and molecular descriptors to ensure reliable performance and provide comprehensive ADMET insights.

SPICA

SPICA is Standigm's AI-based novelty prediction model, which swiftly evaluates the novelty of new molecular structures. This tool ensures that the innovative compounds generated by STELLA can be effectively patented, providing a strategic advantage in the competitive pharmaceutical landscape.

Conclusion

STELLA stands out as a revolutionary platform in the field of drug discovery, combining the power of AI and genetic algorithms to optimize the hit-to-lead process. Its advanced molecular design capabilities, rapid compound generation, multi-objective optimization, and integrated ADMET prediction make it an invaluable tool for researchers aiming to accelerate the journey from concept to clinic. With its project-based management, customizable design platform, and robust supporting technologies, STELLA is poised to transform the future of pharmaceutical research and development.

For more information and to explore how STELLA can enhance your drug discovery efforts, visit Standigm's STELLA page and Standigm's website.

Contact Us

STELLA: http://stella.standigm.com
Standigm: http://www.standigm.com

Reference

- H. Jeon, H.S Lee, and I. Joung, GALAPAGOS: Fragment-based Evolutionary Algorithm for Simultaneous Optimization of Drug-likeness and Affinity**,** *ACS Fall 2022*.