BIOVIA CONNECT | Molecular Modeling & Simulation

Wednesday April 2 AGENDA

Drug Discovery

VIRTUAL ONLY

9:00 AM EST	Designing Novel Molecules Against Pathogenic Bacteria with Machine Learning and Molecular Modelling **Rupesh Chikhale, PhD**, Cambridge Crystallographic Data Centre
9:20 AM EST	Retrosynthesis for the Medicinal Chemist **Alexandre Cabaye, PhD** and **Laurent Naudin, PhD**, BIOVIA
9:40 AM EST	*In Silico* Design of Multi-Specific Protein Therapeutics **Mahiuddin Ahmed, PhD**, VITRUVIAE
10:00 AM EST	OpenFold Consortium: The Development of OpenFold3 **Lucas Nivon, PhD**, Cyrus Biotechnology & OpenFold Consortium
10:20 AM EST	Biophysics Inverted: From Function to Structure **Abhishek Singharoy, PhD**, Arizona State University
10:40 AM EST	AI-driven approaches in Nanobody Epitope Prediction: Are We There Yet? **Floriane Eshak, PhD**, University of Paris Cité
11:00 AM EST	Designing Protein Binders with BIOVIA **Reed Harrison, PhD**, BIOVIA

ABSTRACTS

9:00 AM - 9:20 AM

Designing Novel Molecules Against Pathogenic Bacteria with Machine Learning and Molecular Modelling

Rupesh Chikhale, PhD, **BIOVIA**

The CCDC and Dassault systems are working together to fight against the global challenges of anti-microbial resistance. In this presentation, we will talk about how we have combined forces to tackle this challenge by improving how we can design novel molecules against some of the most pathogenic bacteria. We leverage CSD-GOLD for virtual screening, BIOVIA Generative Therapeutics Design (GTD) for AI-driven lead optimization, and BIOVIA Discovery Studio Simulation to improve the outputs of GTD with Molecular Dynamics simulations and free energy calculations. This work showcases how combining machine learning with classical molecular modelling methods can help build and optimize workflows, accelerating therapeutics discovery with higher precision.

9:20 AM – 9:40 AM

Retrosynthesis for the Medicinal Chemist

Alexandre Cabaye, PhD, **BIOVIA**

AI/ML based methods for drug discovery and optimization can generate dozens, even hundreds of new or modified compounds. However, having virtually found good compounds is not the end of the story, the goal is to get to the next design steps and be able to synthesize them. With our Reaction Planner app we aim to help chemists to find the best synthetic pathways, while providing a user-friendly interface completely integrated within the 3DEXPERIENCE platform.

ABSTRACTS

9:40 AM – 10:00 AM

In Silico Design of Multi-Specific Protein Therapeutics

Mahiuddin Ahmed, PhD, **VITRUVIAE**

Multi-specific protein therapeutics, such a bispecific antibodies, present unique challenges that can be addressed using in silico methods. Case examples will be presented where Discovery Studio tools have been utilized to optimize the properties of these molecules for therapeutic efficacy and manufacturability.

10:00 AM – 10:20 AM

OpenFold Consortium: The Development of OpenFold3

Lucas Nivon, PhD, **Cyrus Biotechnology** & **OpenFold Consortium**

OpenFold is an open-source, industry-driven initiative focused on developing state-of-the-art machine learning models for protein modeling and design. Its key projects include OpenFold3, inspired by AlphaFold3, antibody-antigen complex modeling, and advancements in experimental protein thermostability data collection. The consortium aims to provide customizable and trainable open-source bio AI tools for life sciences that surpass existing tools in performance, and establish an industry-led foundation for bio AI innovation.

ABSTRACTS

10:20 AM – 10:40 AM

Biophysics Inverted: From Function to Structure

Abhishek Singharoy, PhD, **Arizona State University**

Most of computational biology, including the powerful integrative models we know, are predicated upon the sequence → structure → function → phenotype paradigm. Thanks to AI and the availability of data at various scales, researchers have been trying to bridge gaps between the different tiers of this process, starting from the age-old genotype–phenotype modeling to CASP and Alphafold's sequence-structure up to recent attempts to go from sequence to ensemble. However, physical causality is often missing in the traditional bioinformatic models, thus far sidelining the AI-driven advances only to predictions of the forward direction. The talk will introduce physical ideas to conceive generative models that backmap phenotypes down to an ensemble of structures and sequences. While on one hand, such an inverted approach allows to associate biophysics with biodiversity, on the other hand, it finds applications in catch bonding and molecular immunology.

10:40 AM – 11:00 AM

AI-driven approaches in Nanobody Epitope Prediction: Are We There Yet?

Floriane Eshak, PhD, **University of Paris Cité**

Nanobodies have emerged as a versatile class of biologics with promising therapeutic applications, driving the need for robust tools to predict their epitopes, a critical step for *in silico* affinity maturation and epitope-targeted design. While molecular docking has long been employed for epitope identification, it requires substantial expertise. With the advent of AI-driven tools, epitope identification has become more accessible to a broader community increasing the risk of models' misinterpretation. In this talk, we will discuss the nanobody epitope prediction performance of two leading models: AlphaFold3 and AlphaFold2-Multimer (v.2.3.2), highlighting their strengths and limitations. Our analysis can be extended to assess the accuracy of emerging deep learning models adopting a similar approach to AlphaFold3.

ABSTRACTS

11:00 AM – 11:20 AM

Designing Protein Binders with BIOVIA

Reed Harrison, PhD, **BIOVIA**

With the recent development in computational protein design and protein structure and with the 2024 Nobel prize in Chemistry being awarded to David Baker, Demis Hassabis, and John Jumper, methods to design proteins are becoming increasingly popular and useful. In this talk, we explore how users can use tooling in BIOVIA Discovery Studio Simulation to design protein binders for protein targets.