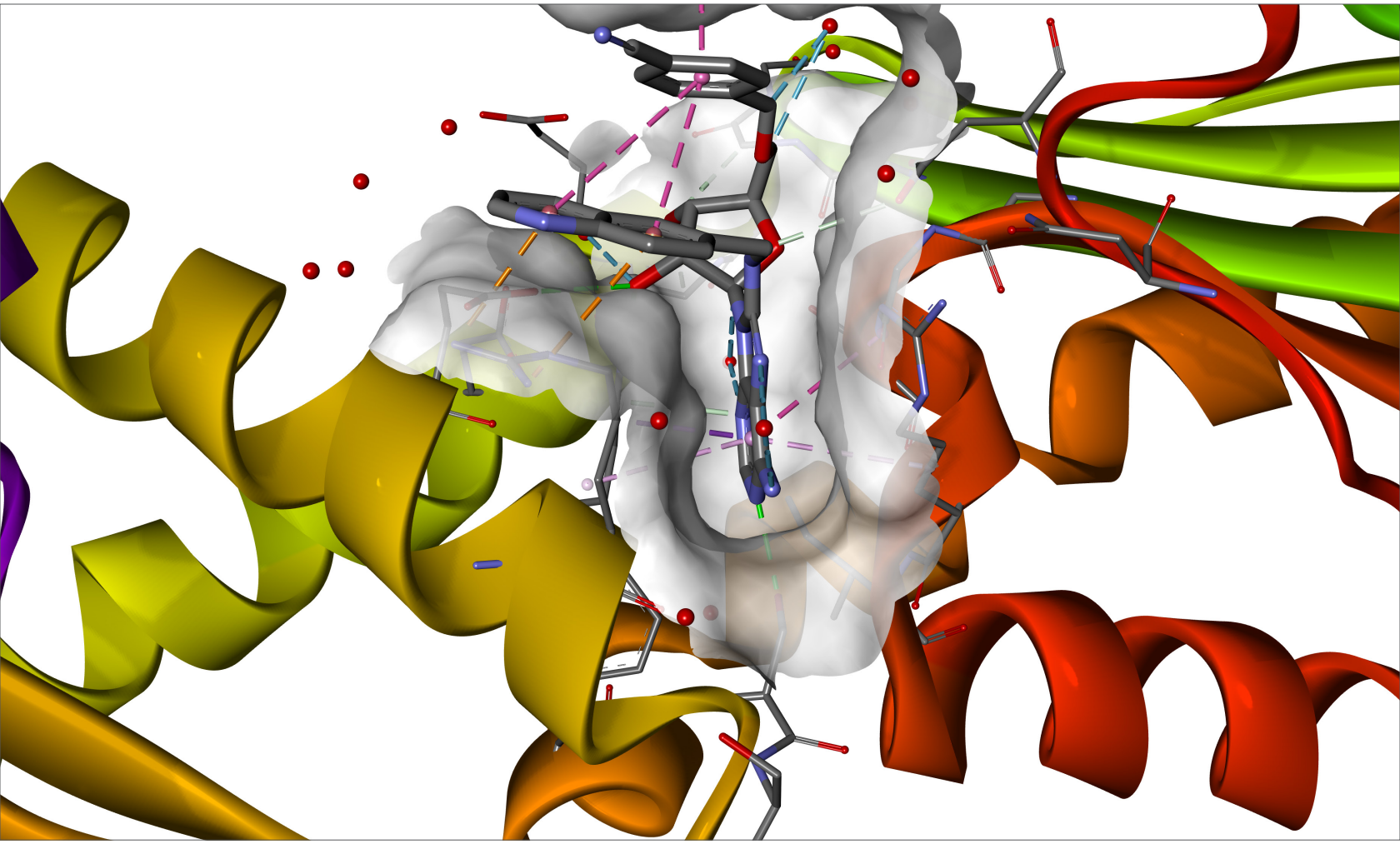
DASSAULT SYSTEMES

BIOVIA

STRUCTURE-BASED DESIGN WITH BIOVIA DISCOVERY STUDIO®

DATASHEET



OPTIMIZING RATIONAL DRUG DESIGN

Structure-Based Design (SBD) and the related Fragment-Based Design (FBD) are now well established strategies in the rational development of small molecule drugs. Knowledge of how a small molecule binds into a protein offers considerable advantages, both in terms of prioritizing compounds for early stage screening, through to optimizing potency and selectivity. BIOVIA Discovery Studio delivers a comprehensive, scalable portfolio of scientific tools, tailored to support and assist SBD and FBD strategies from hit discovery through to late-stage lead optimization.

PROTEIN MODELLING

- Build high-quality homology models automatically with **MODELER**
- Refine structural models using minimization or molecular dynamics with **CHARMm**

PROTEIN PREPARATION

- Generate protein reports to identify potential problems
- Automatically fix and prepare protein structures
- Build missing loops, optimize side-chains of missing residues, and manage alternate conformations
- Calculate pK and ionize at a required pH

BINDING SITE ANALYSIS

- Find binding sites using a bound ligand or protein cavity
- Align and superimpose protein structures to compare binding sites
- Visualize and color properties of binding site

LIGAND PREPARATION

- 2D to 3D conversion
- Enumerate ionization states, tautomers and isomers
- Multiple rapid and exhaustive conformational generation methods
- Molecular properties and fingerprints for filtering
- Filter poor candidates with undesirable functional groups and Lipinski and Veber rules
- Enumerate libraries for screening using reactions or core and R-groups

DOCKING AND VIRTUAL SCREENING

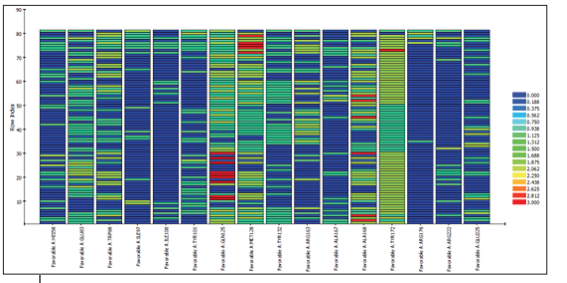
- High throughput screening with **LIBDOCK**
- Perform virtual screening using structure-based **CATALYST** pharmacophores
- Interface to **GOLD** from the CCDC*
- Accurate docking optimization with molecular dynamics-based **CDOCKER**
- Docking with flexible protein using **ChiFlex** and **ChiRotor** with **LIBDOCK** and **CDOCKER**

FRAGMENT-BASED LIGAND DESIGN AND LEAD OPTIMIZATION

- Probe binding sites with fragments using **MCSS** (Multiple Copy Simultaneous Search)
- **Grow** optimized leads ***in situ*** using reaction-based enumeration of reagents and scaffold
- **Replace** fragments to identify new and improved chemical scaffolds
- Create fragment pharmacophores to find new scaffolds
- Generate novel hybrid ligands with BREED
- Screen and link fragments ***de novo***, using LUDI

SCORING, POST-PROCESSING AND ANALYSIS

- Refine docking poses with ***in situ*** ligand minimization
- Rank poses with empirical literature scoring functions
- Score binding interactions with explicit solvent ***in situ*** MM-PBSA or MM-GBSA CHARMm-based methods
- Accurately predict relative ligand binding energy using CHARMm-based free energy perturbation (FEP) simulations
- Analyze and filter poses using a comprehensive perception of favorable, unfavorable and unsatisfied non-bond interactions between the protein and ligand
- Filter poses based on pharmacophore features
- Generate ROC curves, hit-rate plots and heat maps
- Visualize 2D protein-ligand interactions diagrams with non-bond interactions



Ligand interaction heat map generated from a LIBDOCK docking study of kinase inhibitors against thymidine kinase [PDB: 1KIM]

* GOLD is available from the Cambridge Crystallographic Data Centre:
http://www.ccdc.cam.ac.uk/products/life_sciences/gold/
A valid GOLD license is required to run GOLD and GOLDscore

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Dassault Systèmes Corporate
Dassault Systèmes
175 Wyman Street
Waltham, Massachusetts
02451-1223
USA

BIOVIA Corporate Americas
BIOVIA
5005 Wateridge Vista Drive,
San Diego, CA
92121
USA

BIOVIA Corporate Europe
BIOVIA
334 Cambridge Science Park,
Cambridge CB4 0WN
England