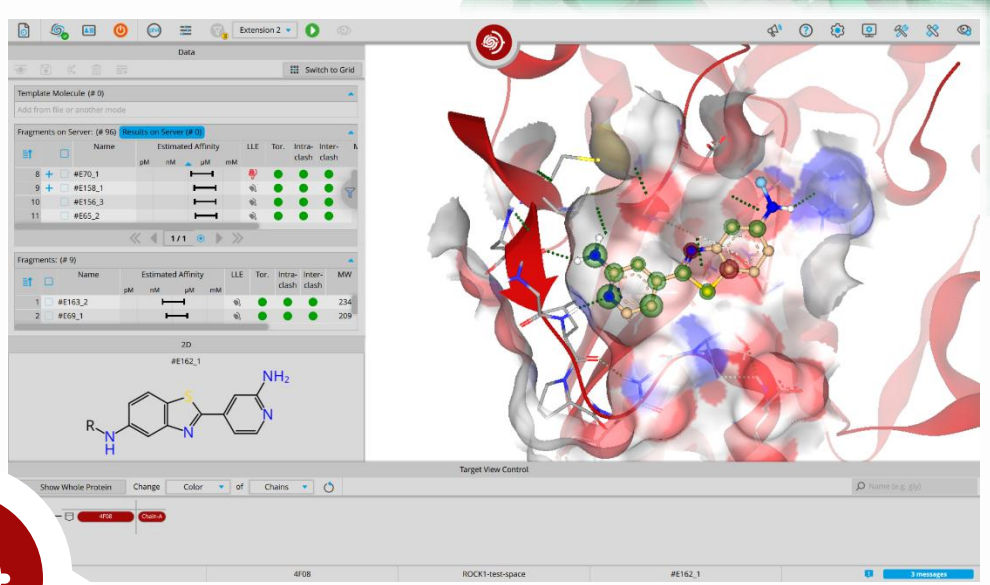
BioSolveIT
expect actives!

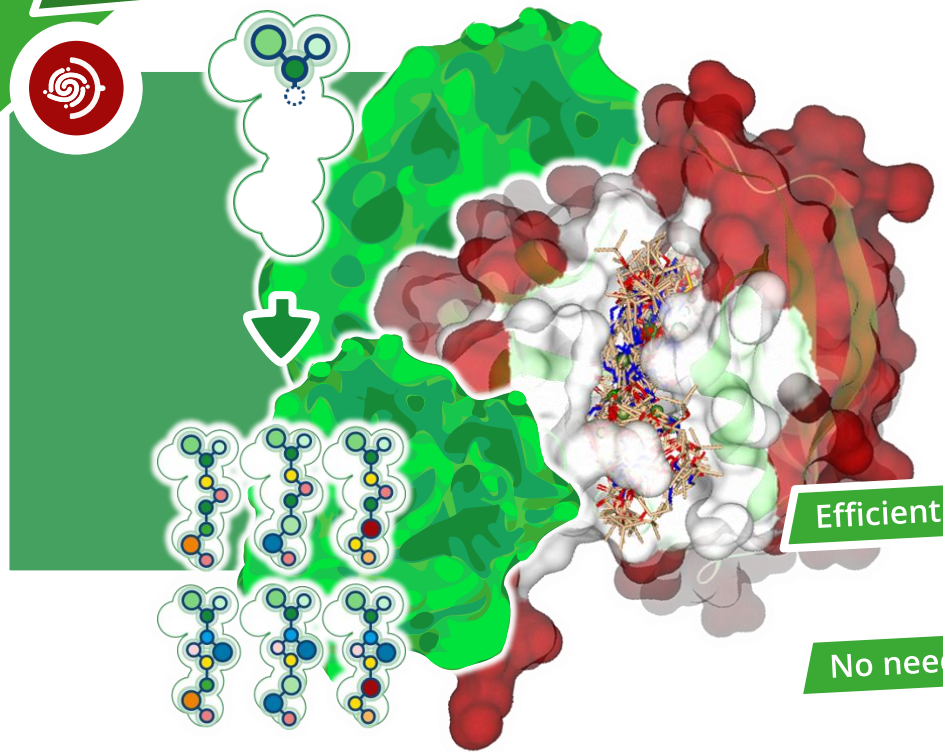


Chemical Space Docking™

Unlocking the molecular universe

Browse through unprecedented numbers of drug-like compounds with only a fraction of the associated computational effort for the most promising candidates.

What Is Chemical Space Docking™



C-S-D™ is BioSolveIT's response to structure-based exploration of billions or even trillions of compounds and the next level of virtual screening.

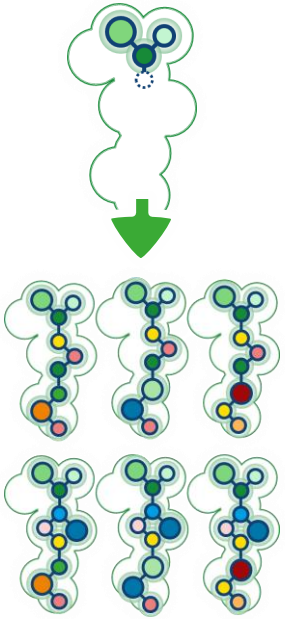
In an interactive dialog between the drug design dashboard SeeSAR and the workflow manager HPSee, users can conveniently set up their screening campaign in a visual user interface and efficiently perform the calculations in a scalable environment.

- Efficient mining from a trillion-sized compound collection
- Runs on your hardware
- No need for server farms or expensive cloud computing

Chemical Space Docking™

Unlocking the Molecular Universe

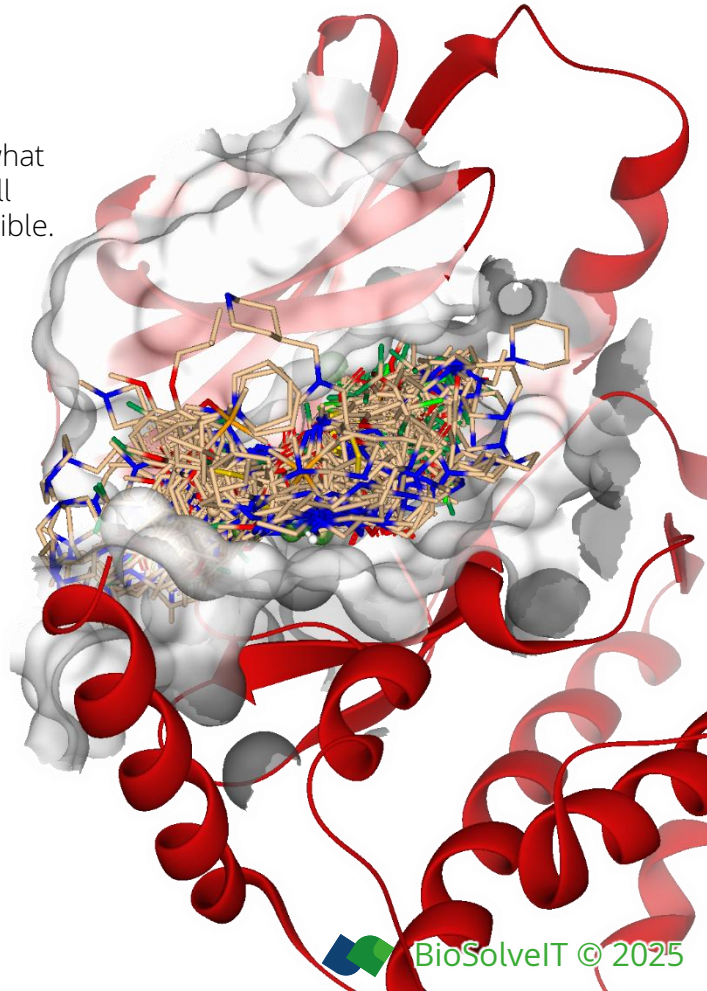
Access to the most relevant AND tangible compounds is what truly accelerates the drug discovery process. Per design, all compounds retrieved with C-S-D™ are synthetically accessible.



C-S-D™ provides you with the best **accessible** and synthesizable results out of trillions of molecule, requiring **only a fraction** of the typical computational resources

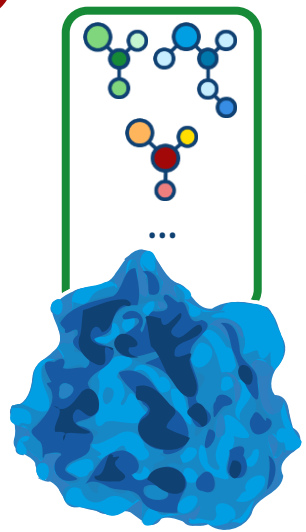
We collaborate with globally known compound suppliers in the creation of Chemical Spaces featuring commercially available, **make-on-demand** entries.

- Ambinter (**AMBrosia**)
- eMolecules (**eXplore**)
- Enamine (**REAL Space**)
- Freedom Space (**Chemspace**)
- OTAVA (**CHEMriya**)
- WuXi Labnetwork (**GalaXi**)

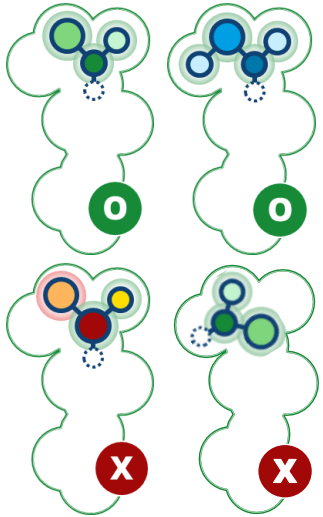


C-S-D™ Workflow

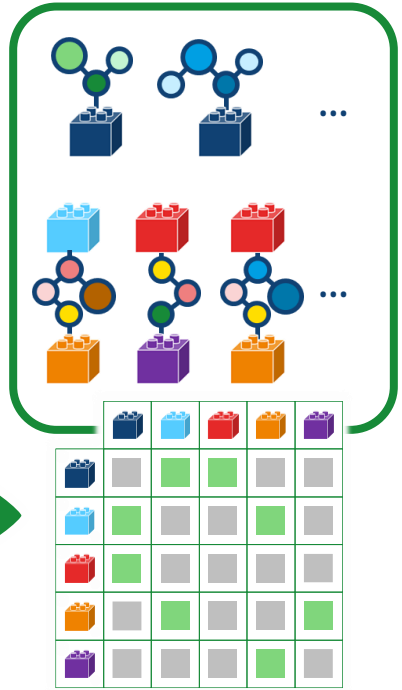
Browsing X-illions



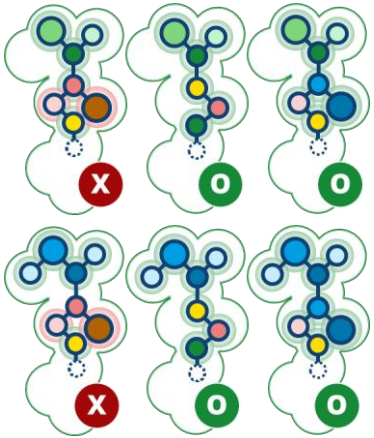
Chemical Space
(containing building blocks)



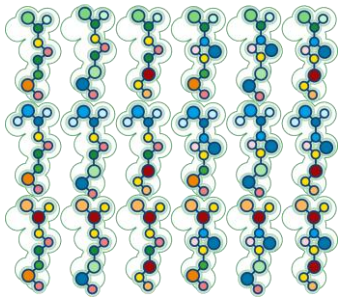
Docking of synthons into
target's binding site
(smallest % of 10^{12})



Chemical compatibility
of building blocks



1st extension

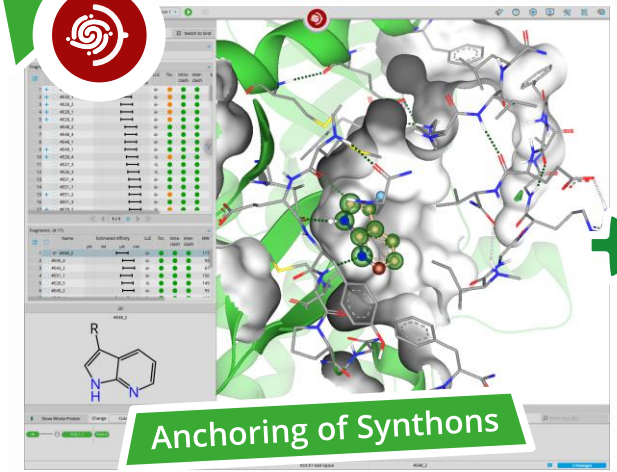


2nd extension

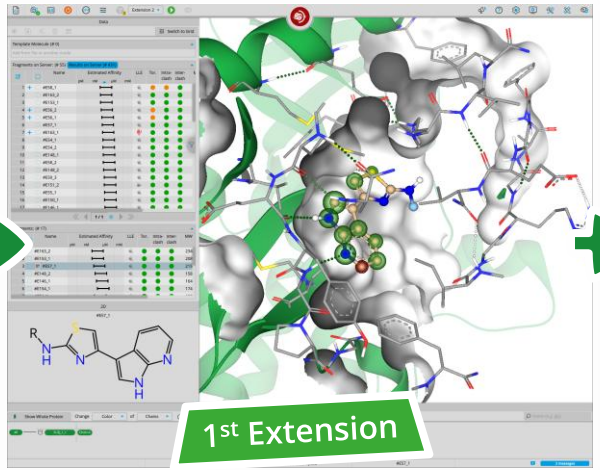
Interactive Workflow

Extracting the Most Relevant Chemistry

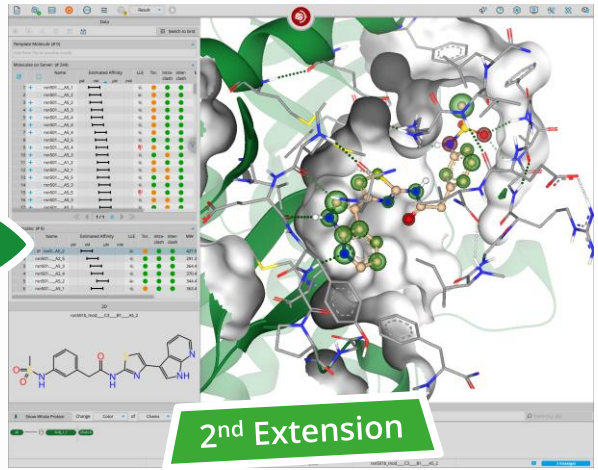
Assessing trillions of molecules using just a small portion of the typical computational resources, thanks to a novel approach.



Docking and scoring of the building blocks containing an **extension vector** (“synthons”) to spot the best candidates forming high-quality interactions with the target.



All possible, chemically accessible compounds originating from the selected synthons are created and docked. Since synthons with bad scores were discarded, only a fraction of resources is required to efficiently screen the whole Chemical Space.

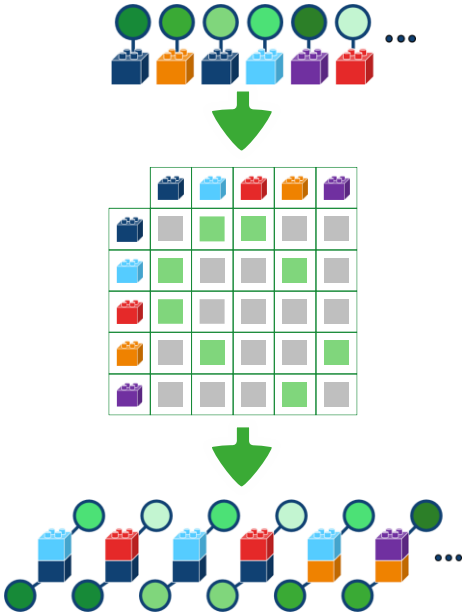


Some compounds are already complete after the first extension. In some cases, a second extension is possible leading to the final molecule. Given the nature of the approach, all results are **synthetically accessible**.

Combinatorial Chemical Spaces

Handling Trillions of Tangible Compounds

The defined combination of commercially available building blocks results in trillion-sized compound catalogs featuring chemically diverse molecules.

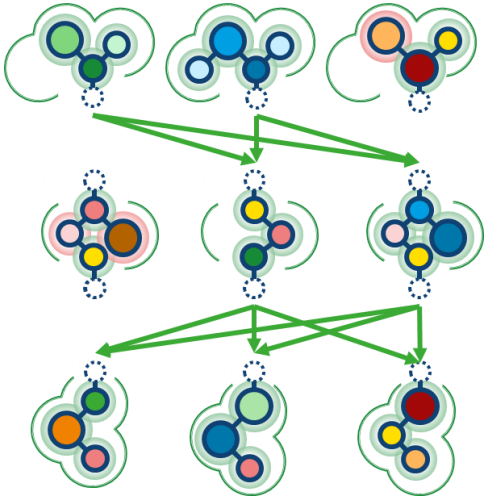


Combinatorial built-up

The combinatorial Chemical Spaces feature reactions that determine which compounds can be created, ensuring that every entry is synthetically accessible. Results from one of our partners' Chemical Spaces can be ordered and delivered to you within a few weeks.

Mining for gems

Only synthons displaying high-quality interactions are considered during the extension steps. Scoring, visual support and other parameters help you to identify the best candidates for follow-up.
It was proven that C-S-D™ outperforms brute-force docking in **enriching high-scoring candidates**.



Success Stories

Proof of Speed and Efficiency

Magnet for the Needle in Haystack: "Crystal Structure First" Fragment Hits Unlock Active Chemical Matter Using Targeted Exploration of Vast Chemical Spaces

Janis Müller,[▽] Raphael Klein,[▽] Olga Tarkhanova, Anastasiia Gryniukova, Petro Borysko, Stefan Merkl, Moritz Ruf, Alexander Neumann, Marcus Gastreich, Yurii S. Moroz, Gerhard Klebe, and Serghei Glinca*

Cite This: https://doi.org/10.1021/acs.jmedchem.2c00813 Read Online

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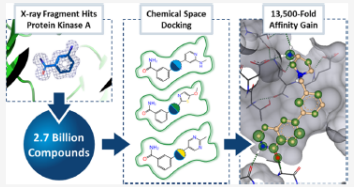
ABSTRACT: Fragment-based drug discovery (FBDD) has successfully led to approved therapeutics for challenging and "undruggable" targets. In the context of FBDD, we introduce a novel [illegible]ary method to identify active molecules from [illegible]l space. Starting from four small-molecule [illegible]f protein kinase A (PKA), a template-based [illegible] Enamine's multibillion REAL Space was [illegible]3 molecules out of 106 selected compounds [illegible]sized. Forty compounds were active in at [illegible]lidation assay with the most active follow-up having a [illegible] gain in affinity. Crystal structures for six of the most [illegible] binders were rapidly obtained, verifying the binding [illegible] overall success rate for this novel fragment-to-hit [illegible]as 40%, accomplished in only 9 weeks. The results [illegible]nt prescreening paradigm since the [illegible]dustrial filters for fragm[illegible] [illegible]sed the initial fragments.



Study featured on the cover of J.Med.Chem

Link to publication

Starting from four small molecule fragment complexes of Protein Kinase A (PKA), CSD was performed in collaboration with Crystals First to screen for novel inhibitor chemotypes. Out of the 93 synthesized molecules, 40 (43%) were active. The best follow up of the fragments displayed a 13,500-fold gain in affinity and six X-ray crystal structures were obtained. The whole process took only nine weeks.

Article https://doi.org/10.1038/s41467-022-33981-8

Chemical space docking enables large-scale structure-based virtual screening to discover ROCK1 kinase inhibitors

Received: 16 September 2021

Accepted: 5 October 2022

Published online: 28 October 2022

Check for updates

Paul Beroza[1], James J. Crawford[1], Oleg Ganichkin[2], Leo Gendelev[1], Seth F. Harris[3], Raphael Klein[4], Anh Miu[5], Stefan Steinbacher[2], Franca-Maria Klingler[4,6] & Christian Lemmen[4]

With the ever-increasing number of synthesis-on-demand compounds for drug lead discovery, there is a great need for efficient search technologies. We present the successful application of a virtual screening method that combines two advances: (1) it avoids full library enumeration (2) products are evaluated by molecular docking, leveraging protein structural information. Crucially, these advances enable a structure-based technique that can efficiently explore libraries with billions of molecules and beyond. We apply this method to identify inhibitors of ROCK1 from almost one billion commercially available compounds. Out of 69 purchased compounds, 27 (39%) have K_i values < 10 μM. X-ray structures of two leads confirm their docked poses. This approach to [illegible]ents that span a chemical space [illegible]aster than traditional docking.

Link to publication

In collaboration with Genentech, the C-S-D™ approach was applied to identify inhibitors of ROCK1 kinase. From 69 purchased compounds, 27 (39%) had Ki values <10 μM. Two leads were crystallized with the ROCK1 protein, and the structures showed excellent agreement with the docked poses.

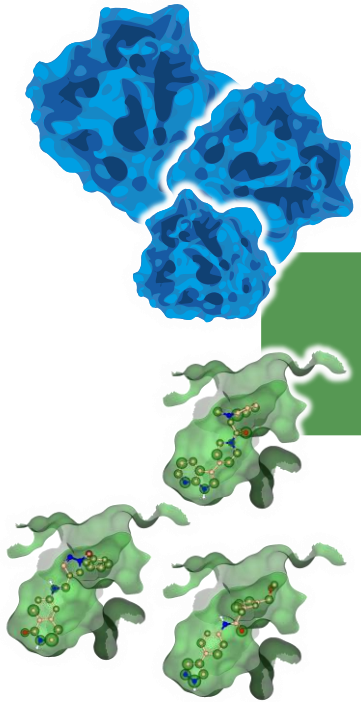
More Than Virtual Screening

Special Traits of Chemical Space Docking™

Our Approach represents the next generation of augmented hit finding.
Several advantages set this method apart from standard procedures.

Chemical Space Docking™ runs **on your own hardware**. No need to share your data with third parties and to rely on a service provider.

Furthermore, slim hardware is enough. Although more is always better, you can achieve high computational efficiency without the need for expensive, high-performance machines, allowing for **cost-effective and secure in-house operations**.



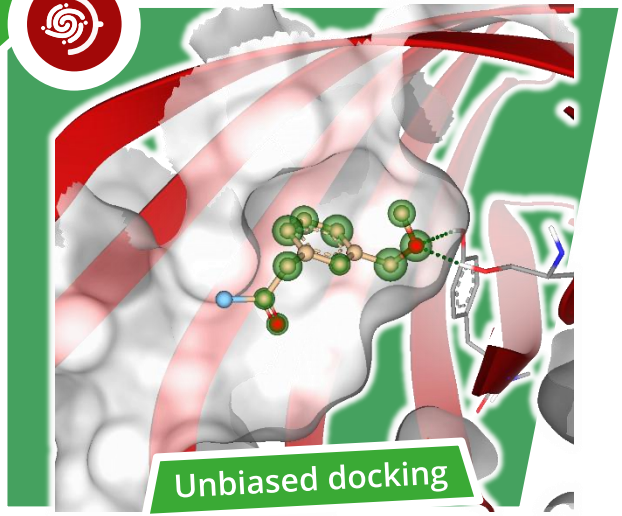
Several commercial Chemical Spaces are available, each coming with their own building blocks and reactions.

SeeSAR was developed to cater towards beginners and experts alike. Every stage of the workflow is **easy to understand and to operate**.

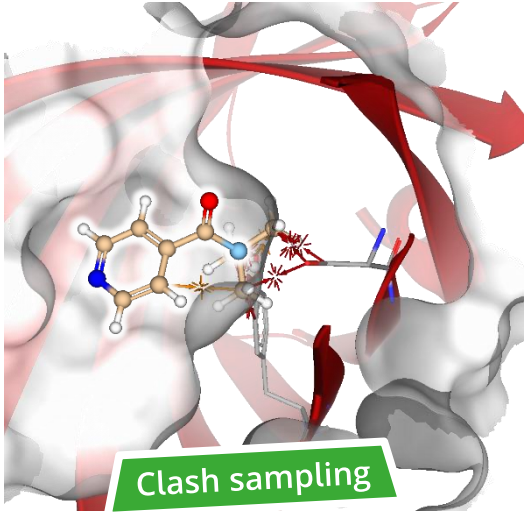
The method retrieves **diverse chemistry** complementing different subpockets of the target, fueling your pipeline with a variety of scaffolds.

Fine-Tuned Approach

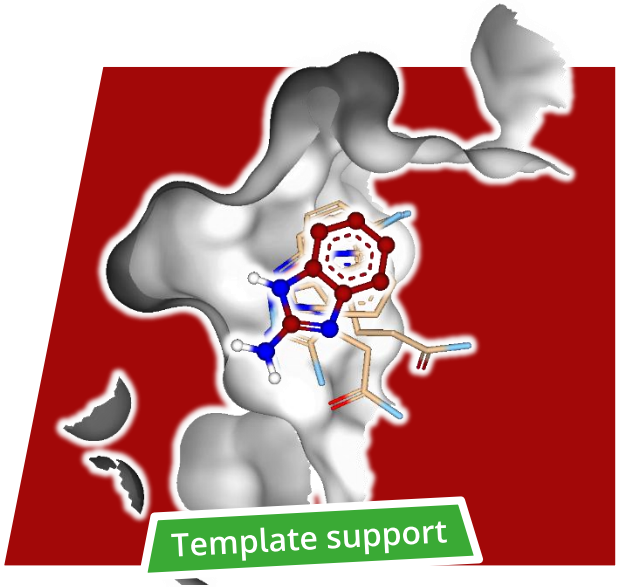
Meticulous Attention to Details



C-S-D™ docks real synthons. Instead of relying on the smallest product for each building block, we introduce an unbiased extension vector (a ‘dummy atom’) into the ligands for the binding mode prediction.



The dummy atom of the synthon scans its environment for potential clashes with the target surface during the extension step. This reduces generation of synthon poses that would lead to a clash during extension



Support your anchoring step with a template molecule from the co-crystallized complex or docking predictions to speed up and guide the pose generation.

Technical Summary

Overview on the Next Level of Structure-Based Virtual Screening

Developed by	BioSolveIT
Docking and scoring	FlexX, Hyde
Synthon docking	chemically unbiased synthon (dummy atom)
Number of available commercial Chemical Spaces	6 (Enamine, Ambinter, WuXi, OTAVA, Chemspace, eMolecules)
Template-based support on ligands	yes (MCS based)
Reported hit rates	ROCK1: 40% PKA: 27%
Development stage	software product