CERTARA

SYBYL-X: Molecular Modeling from Sequence through Lead Optimization

For more than 30 years, Certara has helped the world's largest research and discovery organizations save valuable time, optimize processes and organize workflows, in the search for the next big life sciences solutions. SYBYL-X epitomizes this commitment to excellence, ease-of-use, and bullet-proof science. Using SYBYL-X, life science researchers can streamline tasks, rapidly navigate discovery mazes, and lower the total cost of implementing the most powerful set of molecular discovery tools available. SYBYL-X's science offers unique, competitive advantages in a number of key areas vital for today's successful discovery research, which are summarized below:

3D QSAR: Use the power of industry leading comparative molecular field analysis (CoMFA) in a new way to generate novel ideas for R-groups—predict the level of biological activity or potency based on structure-activity data, not just yes/no activity predictions.

Ligand-based virtual screening: Search millions of compounds overnight—don't miss hits because you only screened subsetted portions of your database.

Cheminformatics: Produce highly focused queries that avoid false positives using rich set of 3D queries; on-the-fly conformational searching means you only store a single conformation of your molecules, keeping database size small and very transportable.

Docking: Custom tailor and fine-tune docking to a particular receptor site using information like structure-activity relationships (SAR) or known poses to improve rank ordering of ligands.

SYBYL-X provides new ways to approach life science molecular discovery projects, while extending the unrivaled, worldwide acceptance of the original SYBYL technology, known for its robust, well-validated science.

SYBYL-X and unique 3D QSAR

With SYBYL-X, you aren't limited to taking chemists' ideas and ranking them or making a prediction; you can go a step further, generating novel ideas for R-groups that will optimize a biological property or biological activity. Using the latest QSAR technologies in SYBYL-X, it's practical to automate the processing of large datasets. Imagine being able to develop models, not just for a single kinase of interest, but across a range of kinases to aid in predicting selectivity, and being able to create local absorption, distribution, metabolism, and excretion (ADME) models where you have the SAR. 3D quantitative structure–activity relationship (QSAR) in SYBYL-X allows you to make multiple models quickly and easily, to think in terms of multiple biological outcomes, and to analyze and optimize all of the various properties required to satisfy the many competing criteria necessary in a lead optimization project.

SYBYL-X Suite includes the following for one low price:

Core Technologies
- SYBYL-X Base
- Concord Sketch
- MOLCAD
- Advanced Computation

Pharmacophore Perception
- GALAHAD
- Tuplets
- GASP
- DISCOtech
- Distill

QSAR Technologies
- QSAR and CoMFA
- Advanced CoMFA
- HQSAR
- cLogP/CMR

Protein Modeling and Structure Prediction
- Biopolymer
- Advanced Protein Modeling

Virtual Screening/Docking
- Surflex-Dock
- CScore

Virtual Screening/R-Groups
- Topomer CoFMA
- Topomer Search

Combinatorial Chemistry
- CombiLibMaker/Legion*
- DiverseSolutions*
- Selector

Cheminformatics
- UNITY Base and 3D
- Concord Standalone**
- StereoPlex**

Value-added Tools
- Confort
- ProtoPlex**
- Surflex-Sim

* Not available on Windows®

** Only available at command line or from within SYBYL-X workflows on Windows

SYBYL-X and unique ligand-based virtual screening with shape and pharmacophore-based searching

SYBYL-X has a demonstrated track record for both lead and scaffold hopping—prospectively as well as retrospectively. With SYBYL-X, you can search databases of over 10 million compounds overnight! Since it's practical to search your entire database, there's no need to subset your database before screening, so you don't have to worry about missing hits because you failed to screen them. Additionally, with SYBYL-X, ligand-based virtual screening is very easy to use; you don't have to provide any information, know the biologically relevant conformation, or do any kind of conformational expansion on the database. No feature mapping, input, or guidance is needed—just give it your active molecules and let it run.

SYBYL-X and unique cheminformatics

SYBYL-X's UNITY databases are efficient and transportable. SYBYL-X handles conformational flexibility on the fly during 3D database searching, so you only have to store a single conformation of your molecules, keeping database size small and very transportable. UNITY provides a very rich 3D query set with the kind of pharmacophore features, extension features, and receptor site features you have at your fingertips. You can even use receptor site cavity information and create queries using receptor surfaces to constrain searches. With UNITY, you can easily produce highly focused queries that avoid producing false positives, which is a competitive advantage. For 2D searching, UNITY is extremely fast and reliable. Finally, SYBYL Line Notation is superior for chemical representation, powerful and flexible but still very compact.

SYBYL-X is unique for docking

Comparative studies show that Surflex-Dock is recognized as a top-tier docker, second to none. A particularly unique aspect of Surflex-Dock is the ability to custom tailor and fine tune the scoring function to a particular binding site. Many dockers can reproduce poses quite well but the ability to rank order ligands with docking scores is still very much a challenge. Surflex-Dock is really unique in being the only docker that allows you to fine-tune the docking scoring function to the particulars of your binding site using information like SAR data or known poses. This offers a unique and valuable approach for CADD scientists to employ.

Whether you're looking for the next new breakthrough drug, the next generation in pesticides, the most exciting new flavor or fragrance, or any other molecular discovery project, you can use SYBYL-X to address questions around lead discovery and optimization using ligand-based or structure-based design strategies, cheminformatics, and much more.

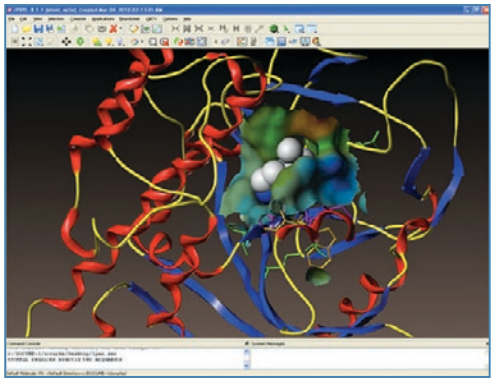
SYBYL-X is the most complete drug and molecular design environment available, with comprehensive tools for molecular modeling—including small molecule and macromolecular modeling and simulation, cheminformatics, lead identification and lead optimization—all in a user interface recently redesigned to save time and simplify workflows for molecular modelers.

Small molecule modeling and simulation

SYBYL-X provides industry proven tools for small molecule modeling and simulation, allowing researchers to perform critical tasks such as hit or lead expansion and lead or scaffold hopping, and to understand and consider critical molecular and physical properties early in the discovery process. Key supporting capabilities include SAR modeling, pharmacophore hypothesis generation, and molecular alignment.

Macromolecular modeling and simulation

SYBYL-X includes the most up-to-date, modern homology modeling science and workflows available today. Homolog recognition, structure and function prediction from sequence, ligand binding site analysis, and 3D modeling techniques to address critical structural biology design tasks are included in the SYBYL-X Suite.



Cheminformatics

SYBYL-X empowers users to extract usable information from the volumes of data generated by modern research methods. With core science and integrated applications to address critical tasks such as data mining and analysis, structure representation and optimization, SYBYL-X users can easily explore the chemical and biological data that is key to the success of drug discovery programs.

Lead identification

SYBYL-X allows researchers to perform critical lead discovery tasks such as hit or lead expansion, lead or scaffold hopping, and virtual screening, and to consider critical molecular properties or predicted ADME and physical properties early in the discovery process. Key ligand-based design tasks, like SAR modeling, pharmacophore hypothesis generation, and molecular alignment, are included in SYBYL-X, as well as structure-based virtual screening to identify promising lead candidates that interact with a receptor of interest.

Lead optimization

Researchers can develop ligand-and/or structure-based models that address the multiple criteria that must be considered in lead optimization. Going beyond categorizing structures as active or inactive, SYBYL-X enables prediction of the level of biological activity or potency based on structure-activity data. Users can easily model multiple biological endpoints, understand and rationalize a drug's interactions with its receptor to identify potential new binding interactions that will provide "step jumps" in potency, identify options for improving ADME or physical properties without disrupting key receptor interactions, use SAR information to improve scoring and customize scoring for the target of interest. When the structure of the drug's target isn't known, pharmacophore hypothesis generation and molecular alignment can be used to deduce spatial requirements for drug binding and test new ideas to see how they match to a set of lead drug candidates.

Unique strengths in 3D QSAR, ligand-based virtual screening, cheminformatics and docking, coupled with comprehensive molecular modeling technologies, empower molecular modelers to find and optimize new leads. From small molecule and macromolecular modeling and simulation, to cheminformatics, to lead identification and optimization; with SYBYL-X you get both structure-based and ligand-based approaches that can address any key molecular discovery question, making SYBYL-X the molecular modeling program of choice for life science researchers. From a business perspective, the comprehensive science in SYBYL-X, coupled with availability on the Windows® as well as Linux® platforms, combined with Certara's new simplified licensing programs, make SYBYL-X the most affordable molecular modeling available on the market today.

With SYBYL-X, routine tasks are fast and easy, and discovery workflows have been enhanced from obtaining data all the way through to delivering findings. All of this is coupled with the highest quality science for molecular discovery.

About Certara

Certara is a leading provider of decision support technology and consulting services for optimizing drug development and improving health outcomes. Certara's solutions, which span the drug development and patient care lifecycle, help increase the probability of regulatory and commercial success by using the most scientifically advanced modeling and simulation technologies and regulatory strategies. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions and key regulatory agencies.

For more information visit www.certara.com or email sales@certara.com.

BR May 2016 v2 082916