- Identify more effective compounds
- Speed-up compound selection
- Make decisions with confidence
- Get the most from your research

StarDrop™ 5

Software that guides you
to successful drug discovery

Introducing an extended suite of plug-in modules

StarDrop is a suite of software
for guiding decisions in drug discovery, helping project teams
identify high-quality compounds, fast.

optibrium

Complex, often conflicting, requirements combined with uncertain data, make it difficult to decide with confidence which lines of enquiry to pursue and which compounds to prioritise. Add to the mix, poorly balanced chemistries and lengthy, wasteful testing, and it's no surprise that most research in drug discovery results in expensive failure.

But there is an answer to these problems...

StarDrop™

StarDrop is a suite of software that helps you to deliver optimally balanced, effective drugs - fast.

By quickly highlighting diverse, high-quality compounds, StarDrop dramatically reduces the time it takes to find effective leads and then transform them into candidate drugs which will have a high probability of success downstream.

StarDrop works by evaluating complex data, which is often uncertain because of experimental variability or predictive error. In scoring this data, it brings confidence and intuitive simplicity to decision-making: guiding and validating the direction you take and which compounds you prioritise. Its instantly interactive tools then enable you to efficiently explore ways to further improve your chosen chemistries.

Highly visual and easy-to-use, StarDrop also works with your existing IT infrastructure to integrate a multiplicity of data sources. Recently updated, it now comes with enhanced features that help you to explore and manage your data. The addition of the BIOSTER database within StarDrop's Nova plug-in module expands its capabilities to generate new compound ideas, while the new Derek Nexus module provides knowledge based toxicity prediction from the industry-leading platform. Other modules include predictive ADME models, P450 metabolism prediction, automatic model building and Cresset's torch3D module, using their unique field technology, that helps to understand and apply 3D SAR.

Optibrium software solutions are designed to intuitively guide decision-making through complex and uncertain data.

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Create more effective drugs

Designing and selecting compounds with an optimal balance of potency, ADME and other properties is a challenge and is where so much drug discovery research fails. By highlighting high-quality chemistries StarDrop guides your research to achieve 'multi-parameter optimisation' and targets areas of investigation with the best potential for success.

Speed-up compound selection

StarDrop dramatically reduces the time it takes to identify high-quality leads and candidates by guiding you through the maze of possibilities. Faster findings mean you can more quickly identify where balance will not be possible, confidently eliminating lines of enquiry early-on and significantly reducing wasted time. 'Virtual design' with instant, interactive feedback significantly reduces the number of compounds you need to synthesise. On top of all this, StarDrop's visual representation of data and easy-to-use interface all help you explore, evaluate and optimise your chemistries with maximum speed and efficiency.

Make decisions with confidence

StarDrop works by helping you to make objective decisions, so you can be confident that you're making the right choices. StarDrop helps you to manage the uncertainty inherent in drug discovery data as a result of experimental variability or predictive error. Integrating data from many sources, such as predictive models and experimental assays, it scores this information, based upon specific project goals, allowing for the variability in the underlying data. This highlights any statistically significant differences, creating a solid foundation and consistent benchmark for compound analysis and selection.

Get the most from your research

StarDrop adds real value to your project by helping you to get the most from all of your resources. Seamlessly integrated into your informatics set-up, StarDrop's flexibility makes project management easier: project scientists and decision-makers can be provided with direct access to in-house models and databases. And, because the StarDrop system is modular, you only purchase the parts you need.

StarDrop – bringing confidence and intuitive simplicity to your decision-making...

- Faster hit-to-lead and lead optimisation
- Design high-quality chemistries
- Dramatically reduce wasted time and effort
- Used by top 10 pharma companies and small research groups alike
- Easy-to-use, instantly interactive
- Integrates easily into your current IT set-up

Fully updated with enhanced features

StarDrop 5: Features

Probabilistic Scoring

Start by rigorously assessing your compounds' potential for success against your project objectives

Define the profile of properties your project needs

Weight the importance of each property

Score all compounds to assess their likelihood of success

Chemical Space

Visualise chemical diversity, identify high-quality compounds, create diverse and balanced selections

Map compound scores onto your project's chemical space

Analyse the underlying property data

Select high-quality chemistries

SAR Analysis

Instantly analyse and explore the structure-activity relationships in your chemical series

Generate Interactive SAR tables for your series

Understand the relationships between functional groups and properties

Explore the potential of all R-group combinations

Glowing Molecule™

Explore the relationship between properties and structure, then re-design and optimise with instant feedback

Re-design your molecules to improve their properties

Compare compounds across your data set

Visualise the impact of functional groups on a property

From selection…

… to design

A modular suite of software with a range of plug-ins...

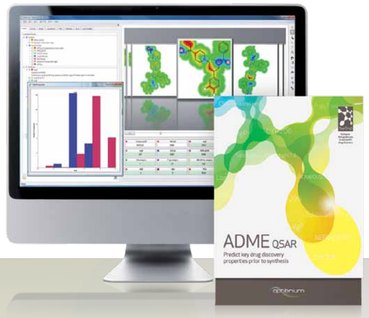
ADME QSAR

Predict key properties prior to synthesis

This module enables you to predict a broad range of ADME and physicochemical properties using a suite of high-quality QSAR models including;

- logP (Octanol/Water)
- $logD_{7.4}$ (Octanol/Buffer at pH 7.4)
- Solubility
  - Aqueous Solubility
  - Solubility in PBS at pH 7.4
- Human Intestinal Absorption
- CNS (blood-brain barrier) Penetration
- Cytochrome P450 Affinities
  - CYP2C9
  - CYP2D6
- P-gp Transport
- hERG pIC50

All ADME QSAR models provide Glowing Molecule results.



Auto-Modeller™

Analyse data and produce predictive models

This module gives novice and expert users alike access to the tools needed to produce validated, predictive models. Output from the Auto-Modeller includes Glowing Molecule results.

Even if you are not an expert in modelling you can:

- Automatically generate predictive models
- Use multiple advanced modelling techniques, including Gaussian Processes, Radial Basis Functions, random forest, PLS and Decision Trees
- Train, test and validate: automatically split your data into sub-sets to rigorously choose and validate the best model
- Use a suite of built-in descriptors; MWt, logP, polar surface area and many other 2D structural descriptors are included with the Auto-Modeller

As an expert user you can also manually tune modelling methods, data sets and descriptors.

INTRODUCING...

NEW

Derek Nexus

Knowledge based toxicity prediction

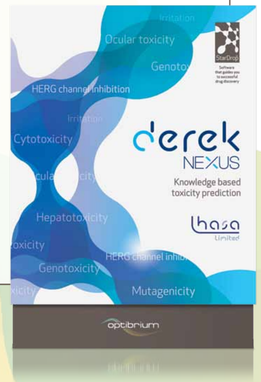
Toxicity of drug candidates is a major cause of expensive, late-stage failure in pre-clinical and clinical development. The Derek Nexus module for StarDrop provides Lhasa's world-leading technology for knowledge-based prediction of key toxicities. Using data from published and donated (unpublished) sources, Derek identifies structure-toxicity relationships that alert you to the potential for your compounds to cause toxicity. The Derek Nexus module provides predictions of the likelihood of a compound causing toxicity in over 40 endpoints, including mutagenicity, hepatotoxicity and cardiotoxicity.

Redesign to overcome liabilities

Seamlessly integrated with StarDrop's Glowing Molecule visualisation, regions of compounds that trigger alerts are highlighted, helping to guide the redesign of your compounds to overcome liabilities. Derek Nexus models are dynamically linked to StarDrop's interactive designer, generating instant feedback as you explore strategies to reduce the risk of toxicity.

Collaborate to guide decisions

Easy-to-use reporting makes it simple for chemists and expert toxicologists to collaborate in order to interpret and understand the relevance of a potential liability. Toxicity predictions can be given an appropriate weight in StarDrop's Probabilistic Scoring to intuitively balance the reduction of toxicity risk with the other requirements for a successful, safe and efficacious drug in hit-to-lead and lead optimisation. The result? Effective, early decision-making regarding the prioritisation of chemistries in the drug discovery process.



P450

Quantum mechanical simulation of drug metabolism

Using StarDrop's P450 metabolism models you can quickly identify the regions of your molecules that are most vulnerable to metabolism by the major drug metabolising isoforms of cytochrome P450. StarDrop's P450 metabolism models predict the regioselectivity of metabolism. However, while valuable, predicting the relative proportion of metabolite formation at different sites on a molecule is only a partial solution to designing more stable molecules. Therefore, StarDrop's quantum mechanical approach goes beyond other methods that predict only the sites of metabolism, to provide valuable additional information on the vulnerability of each site to metabolism by CYP3A4 on an absolute scale.

StarDrop 5: Plug-in modules

Integration

Seamless integration with your infrastructure

Access your models and data from within StarDrop

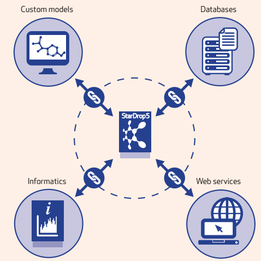
Interact with other informatics platforms to complement StarDrop's features, e.g.:

- Retrieve data directly from your own database
- Make predictions with in-house or 3rd party models
- Run custom scripts or protocols from platforms such as Pipeline Pilot®

Interact with StarDrop from other platforms

Many of StarDrop's capabilities can also be accessed from your own informatics platform via web services, e.g.:

- Make predictions using StarDrop's models, including those provided by the ADME QSAR and P450 modules
- Run models built from your own data in the Auto-Modeller module
- Calculate probabilistic scores against property profiles developed in StarDrop



torch3D™

Understand and apply 3D SAR

cresset

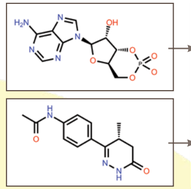
StarDrop's torch3D module, using Cresset's molecular Field technology, provides a unique, 3-dimensional (3D) insight into the biological activity, properties and interactions of your compounds, helping to guide the design of novel, potent compounds with a high chance of success.

Understand the interactions of your compounds

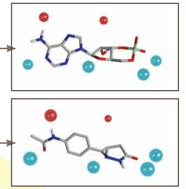
torch3D is a powerful molecular design and 3D Structure Activity Relationship (SAR) tool that allows you to compare the molecular Fields of multiple compounds in their bioactive conformations. By highlighting both similarities and differences between molecules, torch3D shows you where and how lead molecules bind to their protein target. This enables you to quickly identify regions of active molecules that can be replaced to perfect the design of a new lead compound.

Compare compounds' Fields to find novel actives

Given the 3D structure of an active molecule and a series of 2D compound structures, torch3D will generate the best 3D alignment for your compounds. Every alignment is scored and ranked according to its Field similarity with the known active, so you can prioritise the compounds with the most similar activity. With this information, you can screen small compound libraries to look for novel series with greater structural diversity, or optimise the design of focused libraries for synthesis or initial screening.



Above left: 2D structures of structurally diverse bioisosteres both active at PDE3, cAMP (the natural substrate) and SKF93741, a PDE3 inhibitor



Above right: The Field patterns of the compounds reveal that they are biologically similar and share a similar activity

Nova™

A new generation of possibilities

New ideas, broader horizons

Nova helps you to expand your searches, develop new chemistry strategies and find ways around patents by opening a world of opportunities in the hunt for those elusive, high-quality compounds. Nova offers both virtual library enumeration and an engine for 'idea generation' to help you to find new approaches you may have overlooked or simply not thought of.

Variations on a theme

Nova can generate new ideas to exponentially broaden your search by taking a 'parent' molecule and creating new generations of related compounds. Using a built-in collection of over 200 typical 'medicinal chemistry' transformations, Nova explores generations of potential 'children'. This library may be extended with your own transformations or the optional BIOSTER database, providing over 20,000 precedented bioisosteric replacements.

Generating more choice isn't good in itself if the additional choice isn't realistic. Nova creates compounds that 'make sense' from a medicinal chemistry perspective because its transformation rules are derived from practical experience.

Virtual library enumeration

Nova also enables you to design virtual libraries, providing flexible and easy scaffold-based enumeration to rapidly explore new chemistry ideas. After drawing the scaffold on which your library will be based, you can select multiple functional groups, atoms or fragments to vary at each point of modification.

A step-change in your thinking

Nova works like a team of experts, taking full advantage of your in-house expertise by allowing you to include your own substitutions and transformations on an individual basis or in a centrally managed library. By using these to generate more ideas than a single chemist, it boosts your potential to find an optimal compound. You can then quickly determine which ideas to focus on using StarDrop's Probabilistic Scoring, chemical space, Glowing Molecule and other data visualisation.

INTRODUCING... NEW

BIOSTER™

A world of chemistry experience

A comprehensive bioisostere collection

Bioster brings the collective experience of the chemistry community to help you to discover new active analogues of your compounds based on the tried and tested principle of isosterism. The BIOSTER module contains a unique compilation of over 20,000 precedented bioisosteric transformations, manually curated from the literature by Dr István Ujváry, complete with references to the original publications in which they are described.

Transform your chemistry

BIOSTER is developed and updated in collaboration with Digital Chemistry and is available as an optional extension to StarDrop's Nova module. This combination enables you to quickly and easily search the comprehensive BIOSTER database to identify transformations that are relevant to your compounds. These can be automatically applied to generate novel structures with a high likelihood of biological activity and synthetic accessibility, prioritised against the property profile you require for your project.

digital chemistry

COLLABORATION

Community

- Interact with StarDrop users in the forums
- Download and share free add-ons for StarDrop
- Read the latest publications by Optibrium and other StarDrop users
- Everything you need to know about StarDrop is right here! (Videos, tutorials, FAQs...)

www.optibrium.com/community

Our partners

At Optibrium we are committed to providing access to the best computational methods through our user-friendly StarDrop environment. Through ongoing collaborations with Cresset, Digital Chemistry and Lhasa Ltd we are able to offer our users integrated access to tools to understand and apply 3D SAR, explore new chemistry using a library of over 20,000 bioisosteric transformations and to predict the likelihood of toxicity for more than 40 endpoints.

cresset™ lhasa limited digital chemistry

For online demos, case studies and detailed information call: +44 1223 815900, email: info@optibrium or visit

www.optibrium.com

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