

Legion™

CONSTRUCT VIRTUAL COMBINATORIAL LIBRARIES

Triplos™
Go. Discover

Legion™ creates virtual combinatorial libraries that can be used to design diverse or focused libraries for screening or lead optimization. Complex reactions of any type can be specified, including cyclization, cycloaddition, or rearrangements. Legion builds libraries while maintaining user specifications of chirality, regioselectivity, and stereospecificity. In cases where the regio- or stereoselectivity of a reaction is not absolute, all or some of the product permutations can be included in the library. Variation sites can range from simple R-group replacement to complex, multivalent substitutions.

Applications

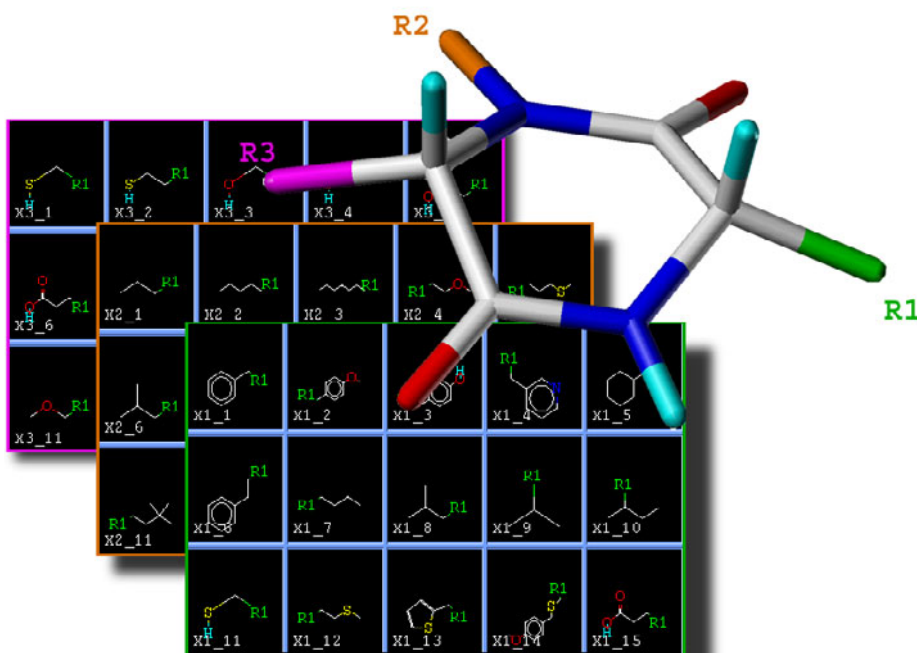
- Build combinatorial libraries for virtual screening
- Enumerate and name libraries, subsets, and sublibraries for registration in a corporate database
- Facilitate design of diverse libraries for screening or focused libraries for lead optimization
- Create and store candidate libraries for later enumeration

Advantages

- Legion works efficiently with Selector™ and DiverseSolutions® for the design of diverse libraries for screening,² or focused libraries to optimize a lead compound.^{3,4}
- Legion uses cSLN for compact storage and efficient transfer of virtual combinatorial libraries to other applications. Large libraries can be generated without full enumeration to minimize storage requirements, and can be enumerated in full or in part when needed.
- Legion readily constructs complex libraries, including product cores with multiple attachment points and variations nested within variation sites, and creates branch points or rings as required.
- Legion allows complete user control of chirality, stereoselectivity and regioselectivity, and correctly maintains these attributes during library creation.

Legion allows reaction-based or product-based specification of libraries, and can easily move between the two modes for construction of a combinatorial library. Product-based library specifications make systematic variations at sites on a core structure. Legion provides lists of common substituents that can be readily expanded or tailored to meet specific needs. In reaction-based mode, virtual libraries are constructed by providing lists of reagents and the reaction they undergo.

In either approach, Legion can create massive virtual libraries and store them in a concise combinatorial SLN¹ format (cSLN). Full libraries, subsets, or sublibraries can be enumerated when needed for registration, virtual screening, or library design.



The core structure and some of its variants in a virtual library of metalloproteinase inhibitors built using Legion.

Features

- SLN viewer for visual inspection of substituents and products during library specification
- Reagent input via Molecular Spreadsheet™, UNITY® Hitlist, or SD file
- Creates libraries as 2D cSLN for direct use by CombiFlexX® for virtual screening
- Select site variations from Legion's substituent spreadsheets or a UNITY hitlist, draw in SYBYL's sketcher, or enter as SLNs
- Store reagent relational data with library
- Variety of naming strategies to support compound registration

Hardware and Software Requirements

Legion requires a separate license and is accessible through the SYBYL® expert molecular modeling environment. SYBYL and Legion run on workstations operating under IRIX® (SGI®) or Linux® (x86).

Complementary Software

- **Selector™** for characterizing and sampling compound libraries.
- **DiverseSolutions®** for designing, comparing, or selecting compound libraries.
- **UNITY®** for locating compounds in databases that match a pharmacophore or fit a receptor site.
- **CombiFlexX** for rapidly docking combinatorial libraries into a receptor site.

- **FlexS™** for performing shape-based screening of ligands in the absence of receptor structure.
- **ClogP/CMR** for including molar refractivity and logP in QSAR and ADME models.
- **Concord®** for generating accurate 3D coordinates.
- **StereoPlex®** for expanding the stereochemical diversity of a database.
- **CombiLibMaker™** for building virtual combinatorial libraries in cSLN format.
- **VolSurf™** for predicting ADME properties.

References

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2. Thorpe, D.S.; Chan, A.W.E.; Binnie, A.; et al. "Efficient Discovery of Inhibitory Ligands for Diverse Targets from a Small Combinatorial Chemical Library of Chimeric Molecules." *Biochem. Biophys. Res. Commun.* **1999**, *266*, 62-65.
3. Matter H.; Lassen, D. "Compound Libraries for Lead Discovery." *CHIMICA OGGI/Chemistry Today* **June 1996**, pgs. 9-15.
4. Molecular Diversity Manager Generates Lead Followup Synthesis Candidates. *Tripos Technical Notes* **1995**, *1*, 1-6.



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