LIGANDSCOUT 2.0

INTUITIVE STRUCTURE-BASED 3D PHARMACOPHORE PERCEPTION AND ADVANCED PHARMACOPHORE MODELING

LIGANDSCOUT creates pharmacophores from structure-based complex data, and allows sophisticated pharmacophore analysis and fine-tuning to create selective pharmacophoric screening filters for a specific target. Using pharmacophore perception rules that are based on several years of experience in pharmacophore modeling, LIGANDSCOUT offers a large range of chemical feature definitions including hydrogen bonding vectors, chargeable groups, aromatic plane interactions and aromatic-positive ionizable interactions. An advanced alignment algorithm allows to overlay pharmacophores and molecules such that common binding modes may be detected and shared chemical features can be interpolated. LIGANDSCOUT is designed as an open platform, supporting various file formats and also exports to Catalyst/DiscoveryStudio^{tm}, MOE^{tm} and Phase^{tm}.

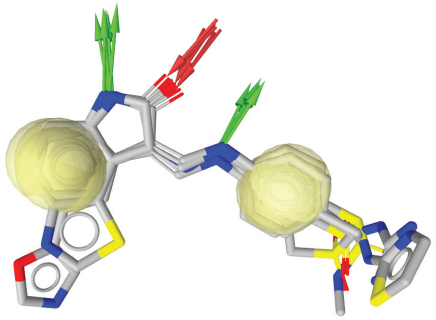
Advantages:

- Automatic interpretation of PDB ligands using geometry, dictionaries and rules
- State-of-the-art user interface with advanced 3D graphics and undo-function
- 2D view and hierarchical view directly linked to 3D interface
- Comprehensive 2D depiction of protein-ligand interaction
- Fast alignment of molecules in their bio-active conformation to other molecules and 3D pharmacophores
- From several ligands and/or pharmacophores, shared feature pharmacophores can be derived to understand and model the relevant mode of action
- Advanced handling of co-factors, ions, water molecules, and metal binding locations (Fe, Mg, Zn)
- Advanced docking result view, easy creation of pharmacophores from docking poses
- Pharmacophore export to Catalyst^{tm,} MOE^{tm} and Phase^{tm} for virtual screening

LIGANDSCOUT starts with a macromolecule/ligand complex and automatically detects bound ligands creating a standard residue hull around the non-standard residues. The advanced ligand bond interpretation is based on geometric interpretation as well as a matching algorithm to optimally distribute double bonds among sp^2 atoms [1].
The position of the ligand within the macromolecule is visualized using an animated protein-ligand handling that allows the user to zoom back into the protein without modifying the macromolecule at any time. From the protein-ligand interaction pocket a pharmacophore is derived by identifying complementary interactions following extensive heuristics consisting of chemically and geometrically elaborated rules. Hydrogen bonds are represented as vectors optionally including projected points, aromatic PI-interactions are represented by planes, and lipophilic areas are represented as a set of spheres. Steric constraints in the form of inclusion volume spheres are added to make sure that lipophilic molecule parts are kept rigid in a virtual screening run.
Once a pharmacophore is created, it can be aligned to imported or extracted molecules. Unlike other programs, the alignment is based on pharmacophoric points rather than on atomic contributions and thus better reflects the way the small molecule presents itself to the active site of the macromolecule. From several molecules or pharmacophores, a shared feature pharmacophore can be derived to determine common features, which then can be exported to several virtual screening platforms.
LigandScout runs on all common operating systems.

References

[1] G. Wolber and T. Langer. *LigandScout: 3-D Pharmacophores Derived from Protein-Bound Ligands and Their Use as Virtual Screening Filters* J. Chem. Inf. Model; 2005; 45(1); 160-169.



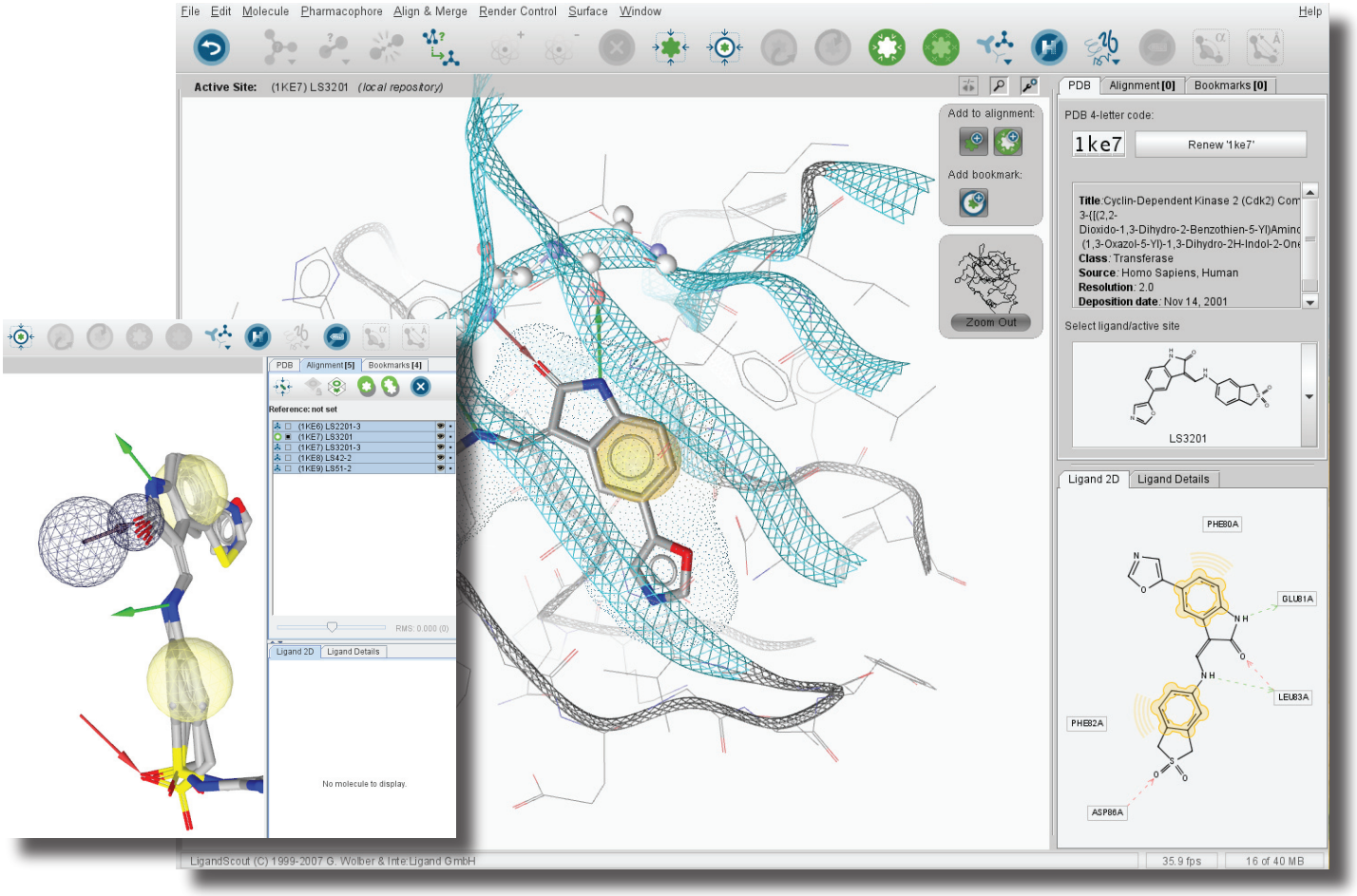
Ligand-based pharmacophoric alignment of four cyclin-dependent kinase inhibitors within their LigandScout pharmacophore

Inte:Ligand has specialized in the development of algorithms and software that support scientists in in-silico bio-activity prediction. Besides contract research services, we offer direct access to our highly specialized and user-friendly software.

inte:ligand

Your partner for in-silico drug discovery.

STRUCTURE-BASED DRUG DESIGN WITH LIGANDSCOUT



Features:

- Easy-to-use, intuitive and straight-forward user interface
- Extensive parameter control for more experienced users
- Unlimited undo-levels
- Generic high-quality 2D depiction linked to 3D editor
- Advanced PDB ligand perception and easy manual correction while modeling in the active site
- Ability to treat co-factors and waters as part of the ligand or part of the macromolecule
- Intuitive pharmacophore-based alignment of molecules
- Generation of shared feature pharmacophores
- Support for most common molecule and graphics file formats
- Pharmacophore export to Catalyst/DiscoveryStudio™, MOE™ and Phase™
- Sophisticated file and repository management of edited and stored binding sites, molecules and pharmacophores

System requirements:

- 512 MB RAM (2 GB recommended)
- OpenGL-capable graphics card (common graphics cards fulfill this requirement)
- Microsoft Windows™, Apple MacOS X (Tiger or Leopard), support for various Linux distributions available
- Support for different operating systems may be available upon request

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