News about LigandScout

and the Inte:Ligand KNIME Extensions

What's New in LigandScout 4.4

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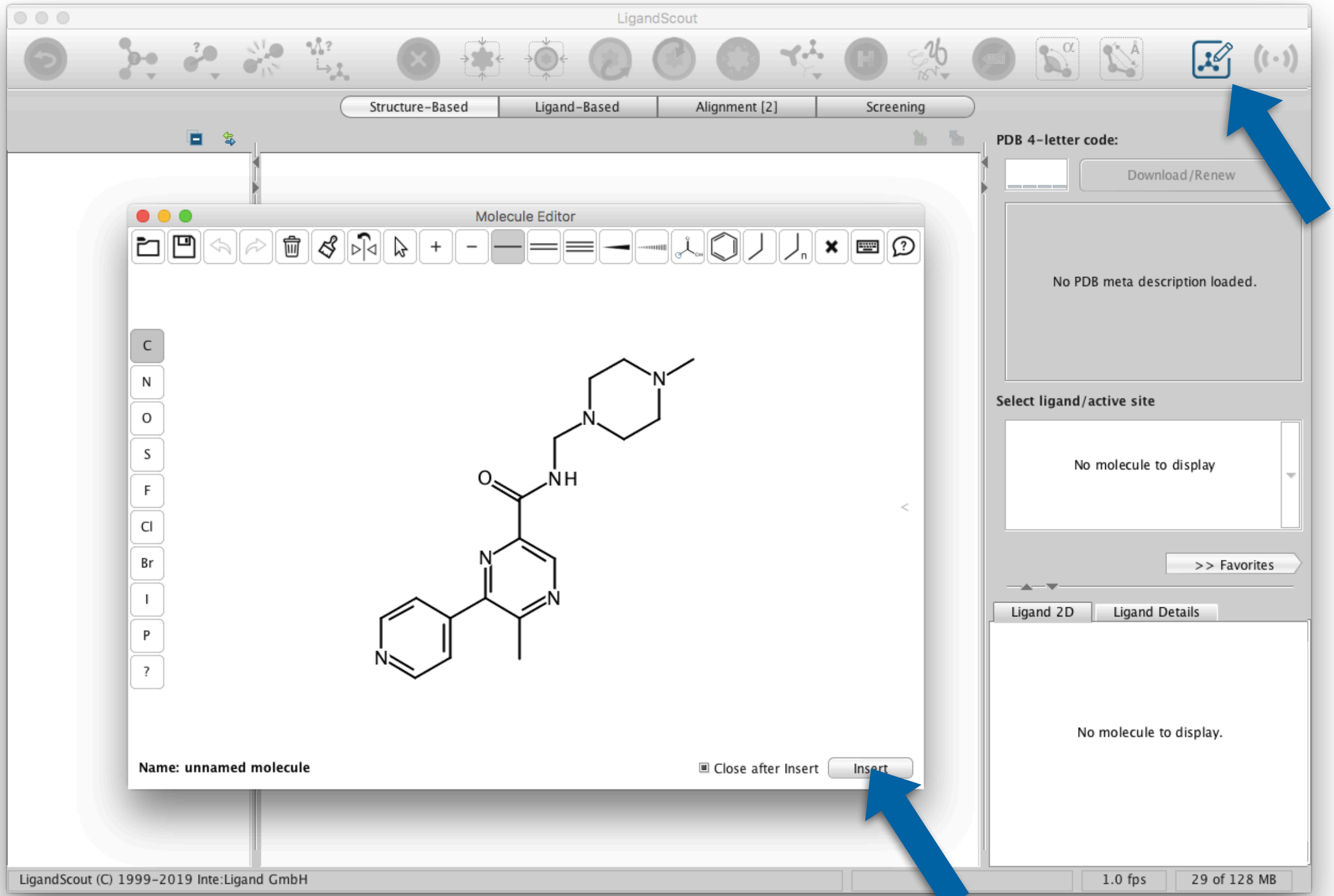
New 2D Molecule Editor



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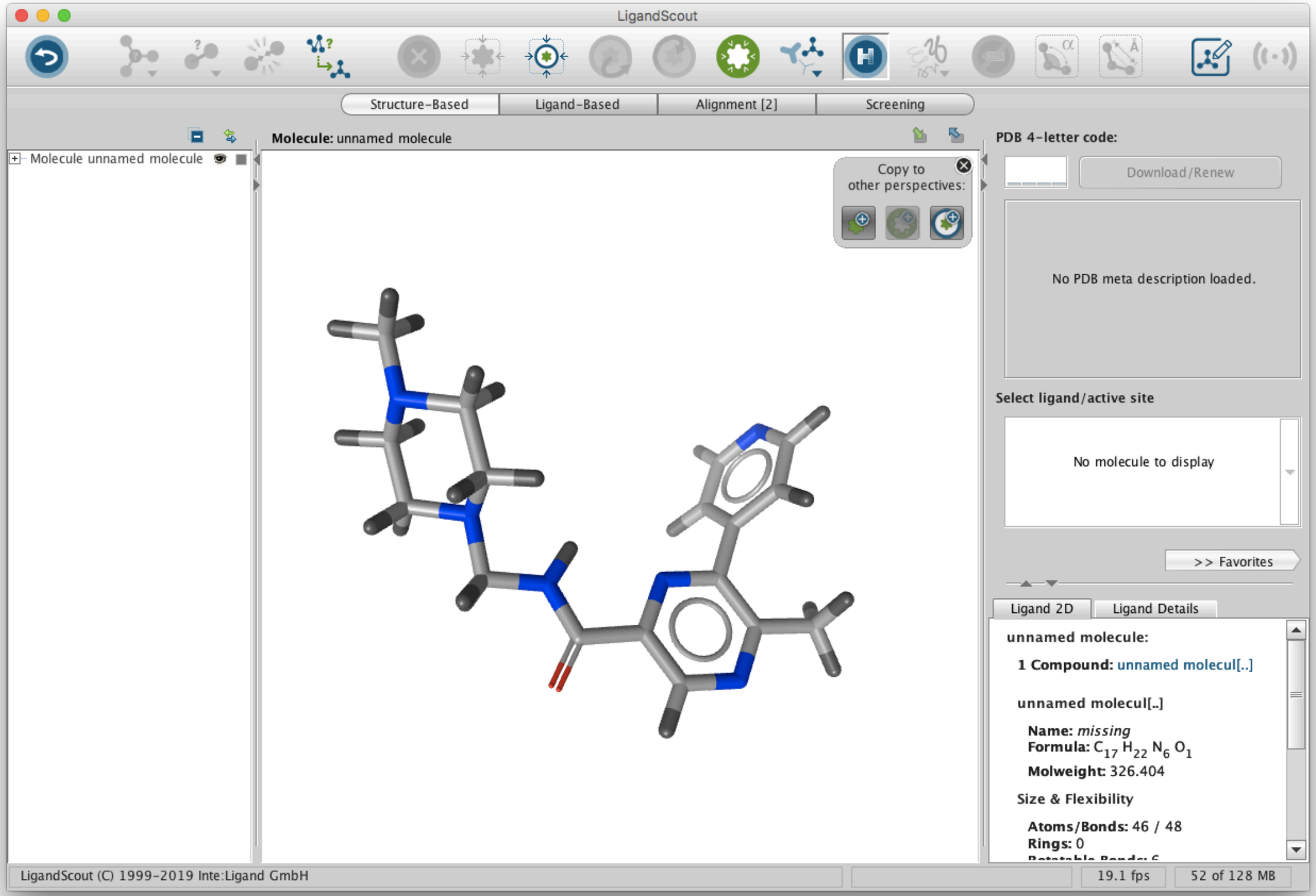
New 2D Molecule Editor



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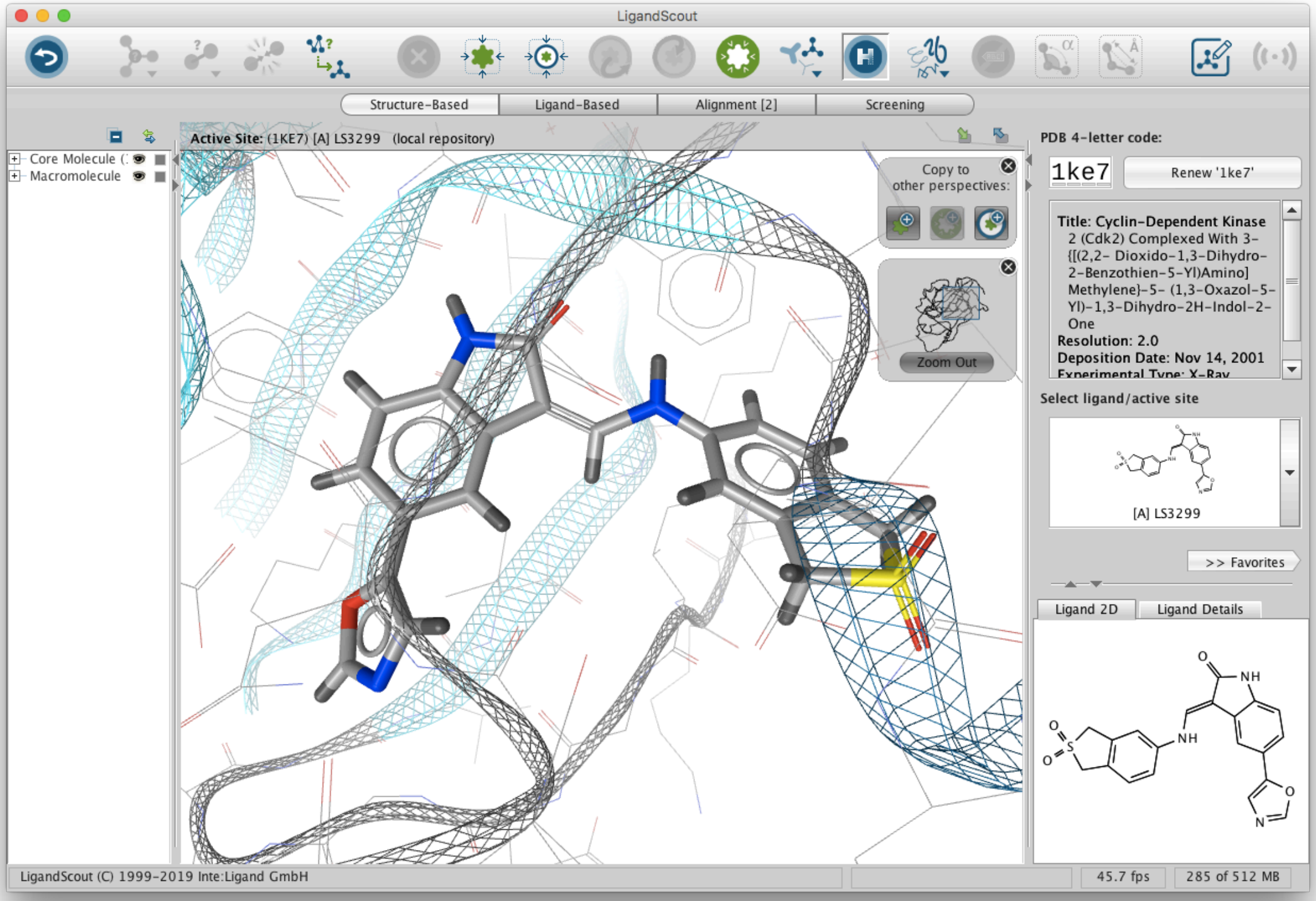
New: Interactive Binding Affinity Estimation



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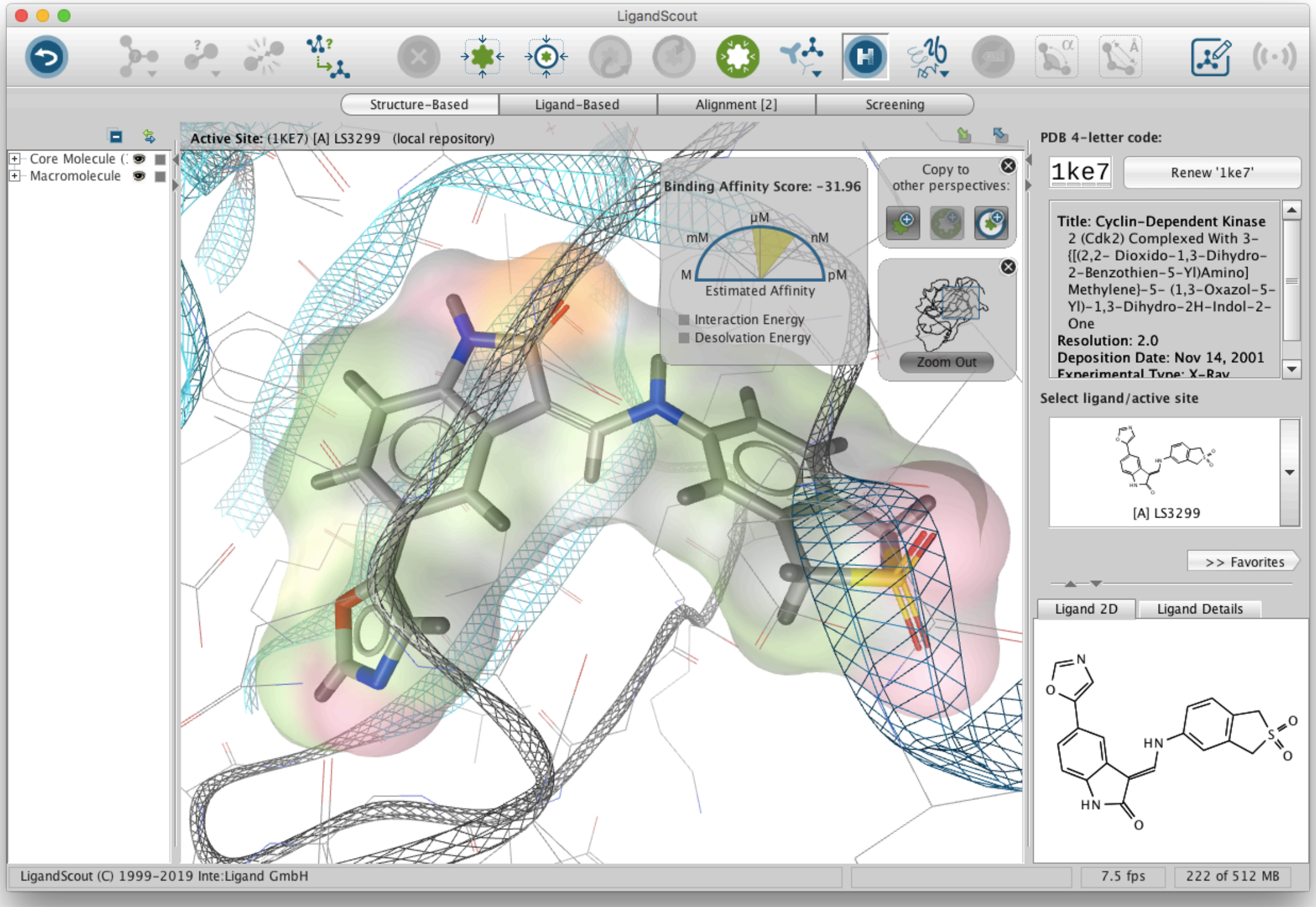
Interactive Binding Affinity Estimation



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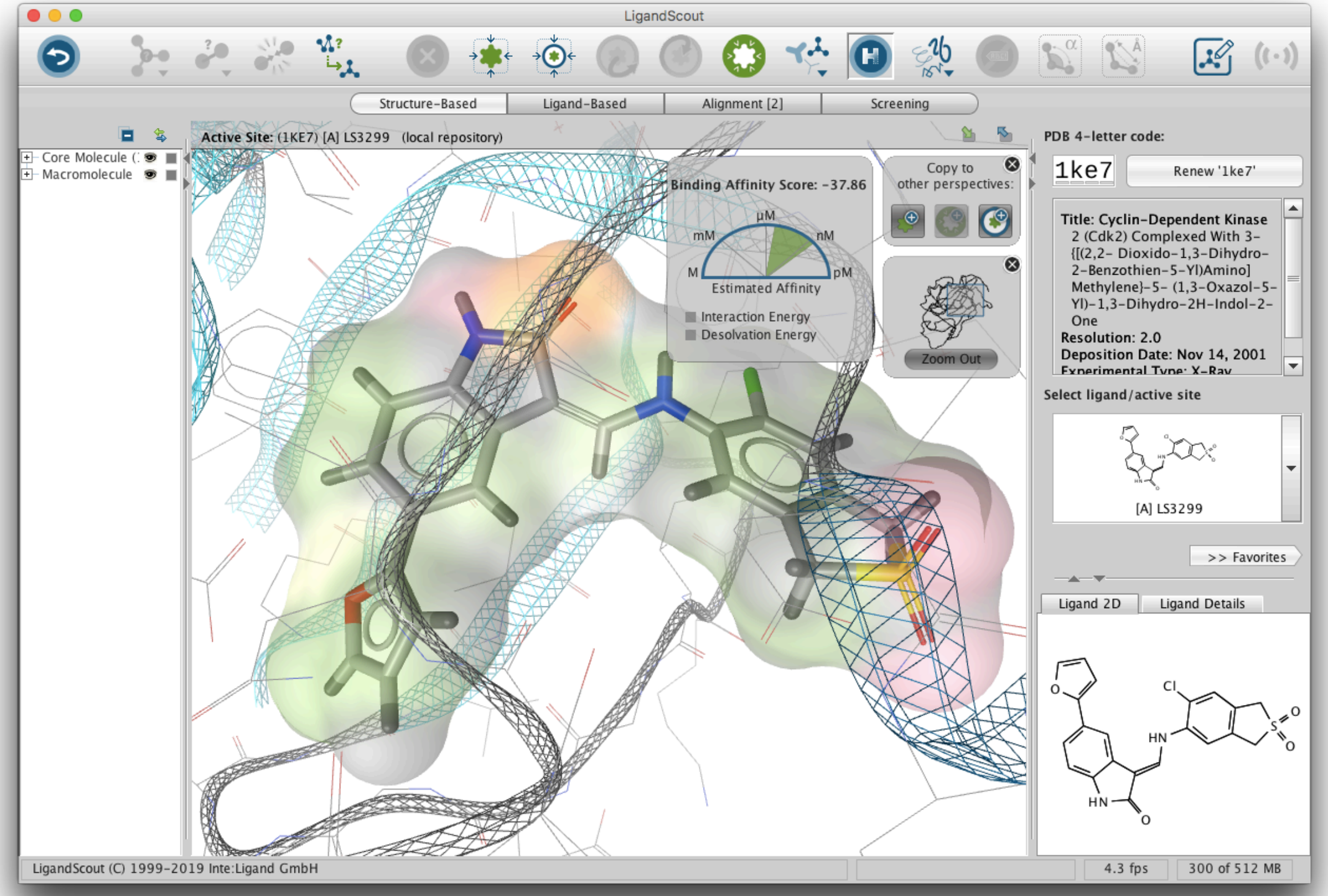
Interactive Binding Affinity Estimation



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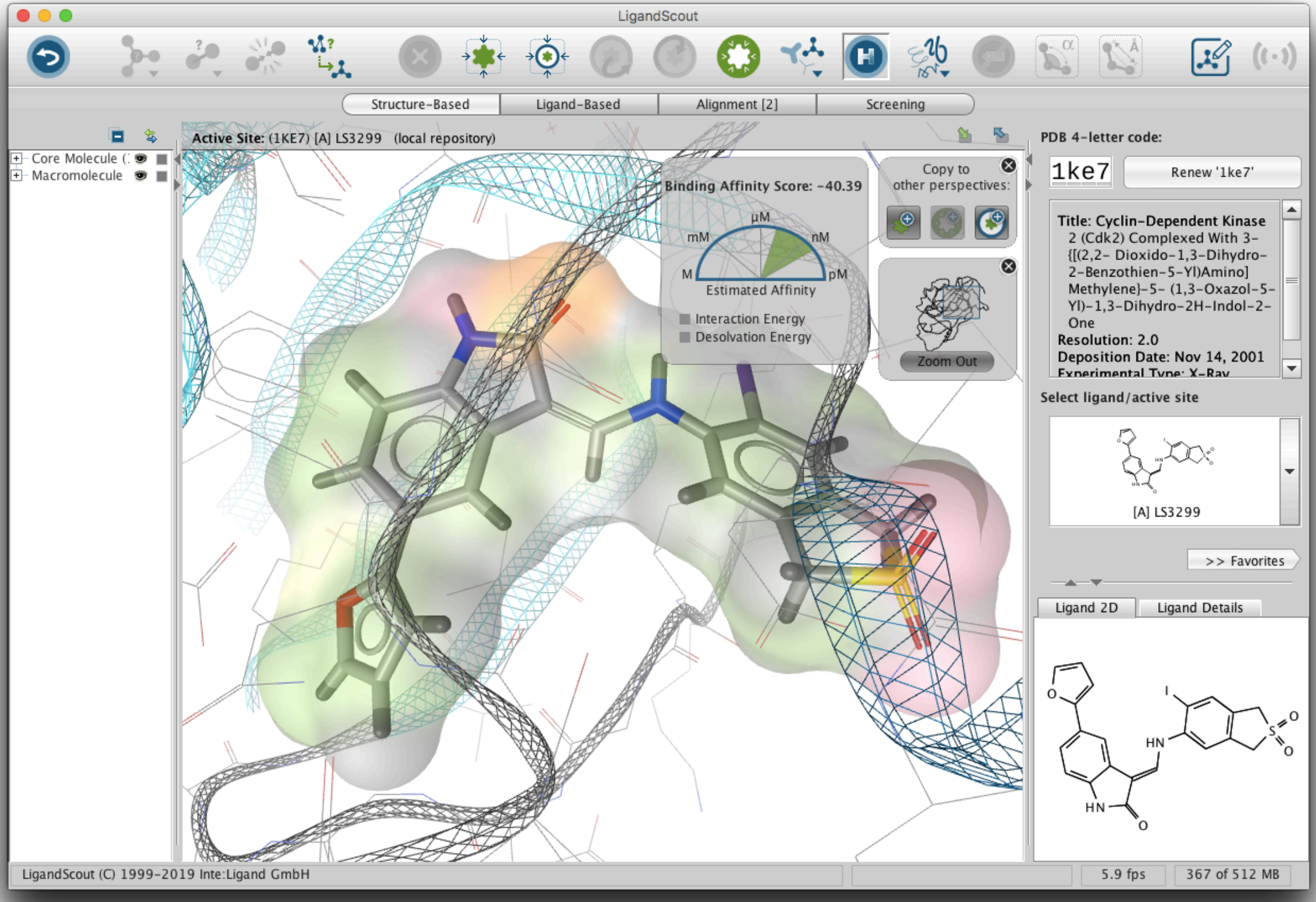
Interactive Binding Affinity Estimation



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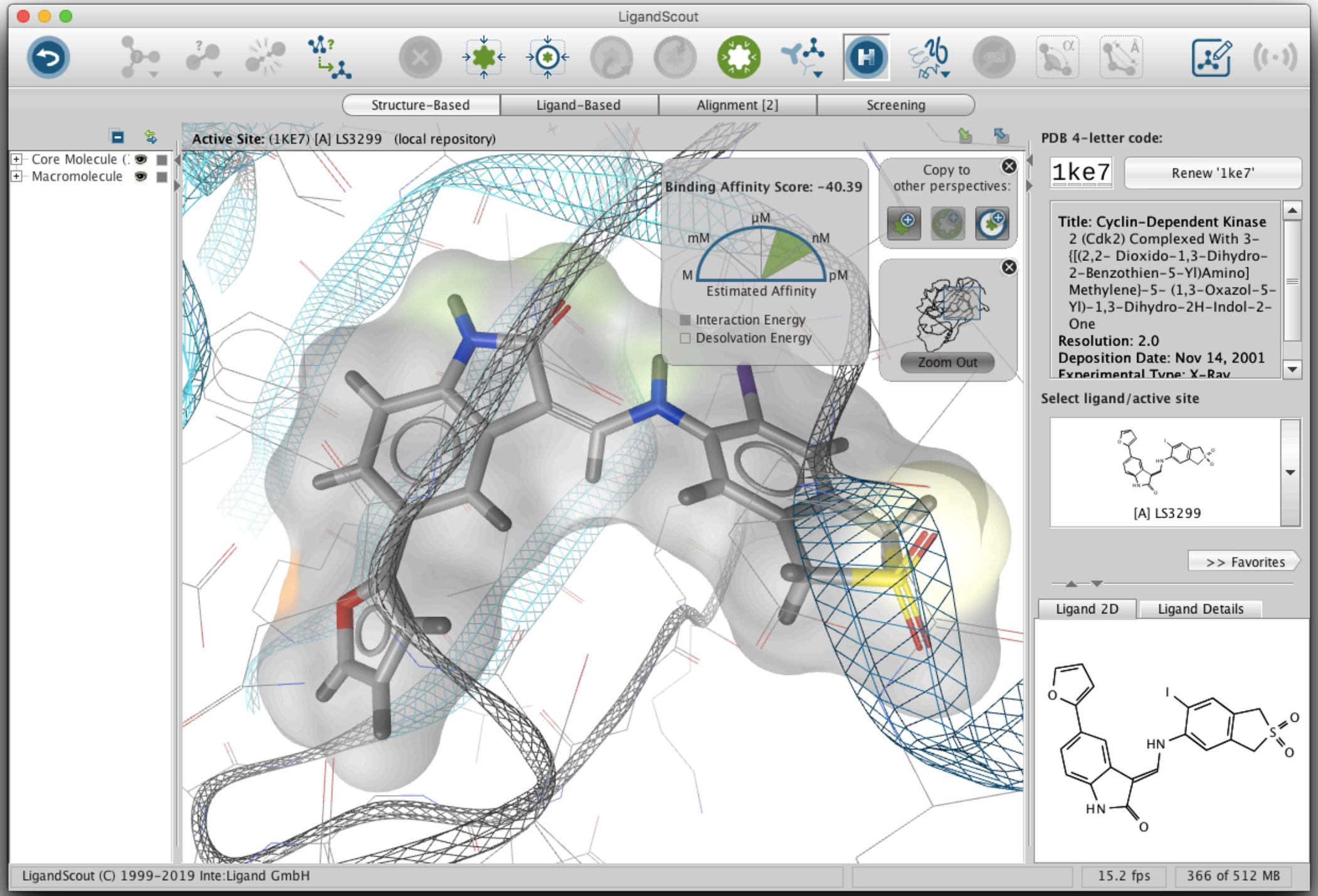

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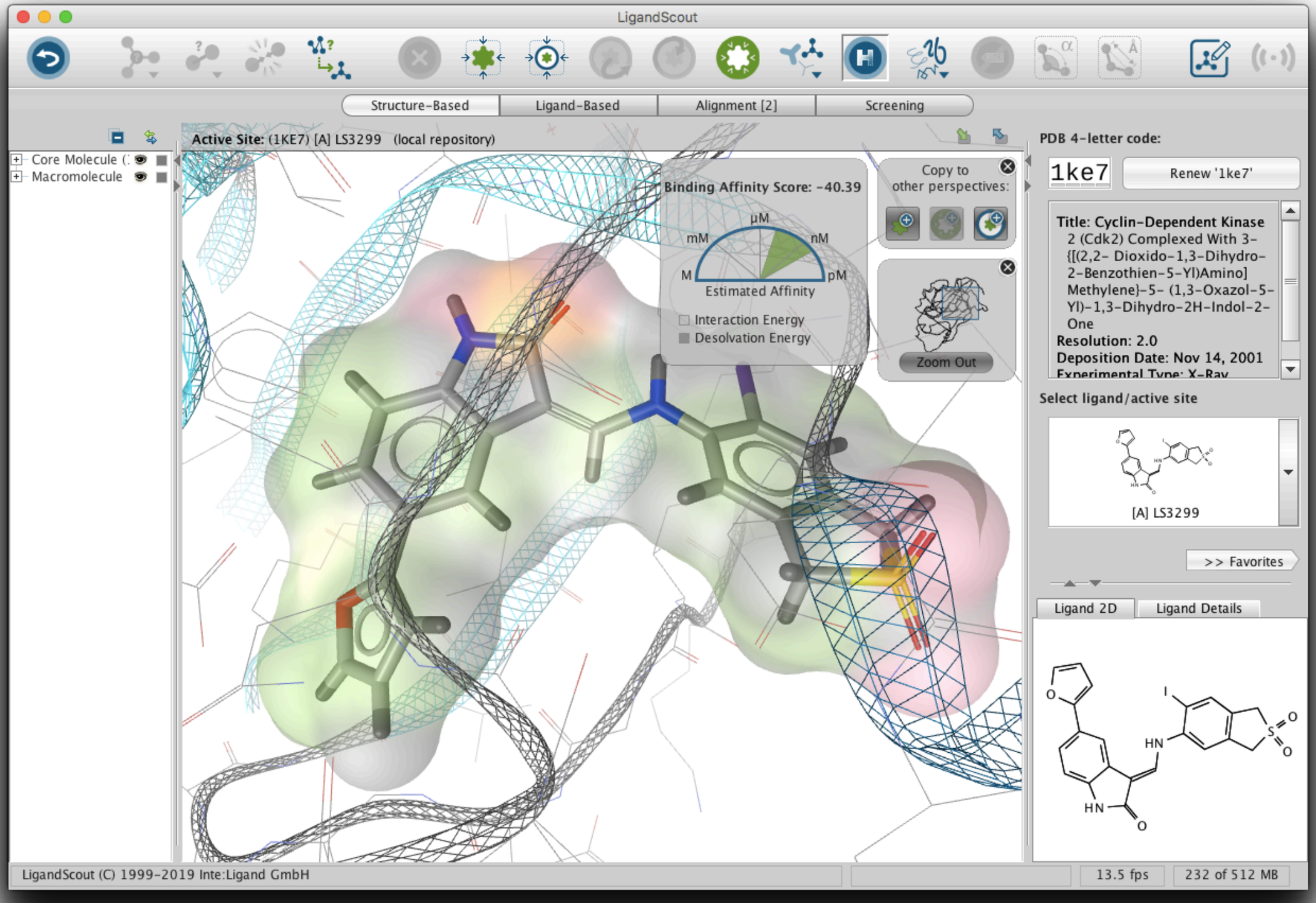
Interactive Binding Affinity Estimation



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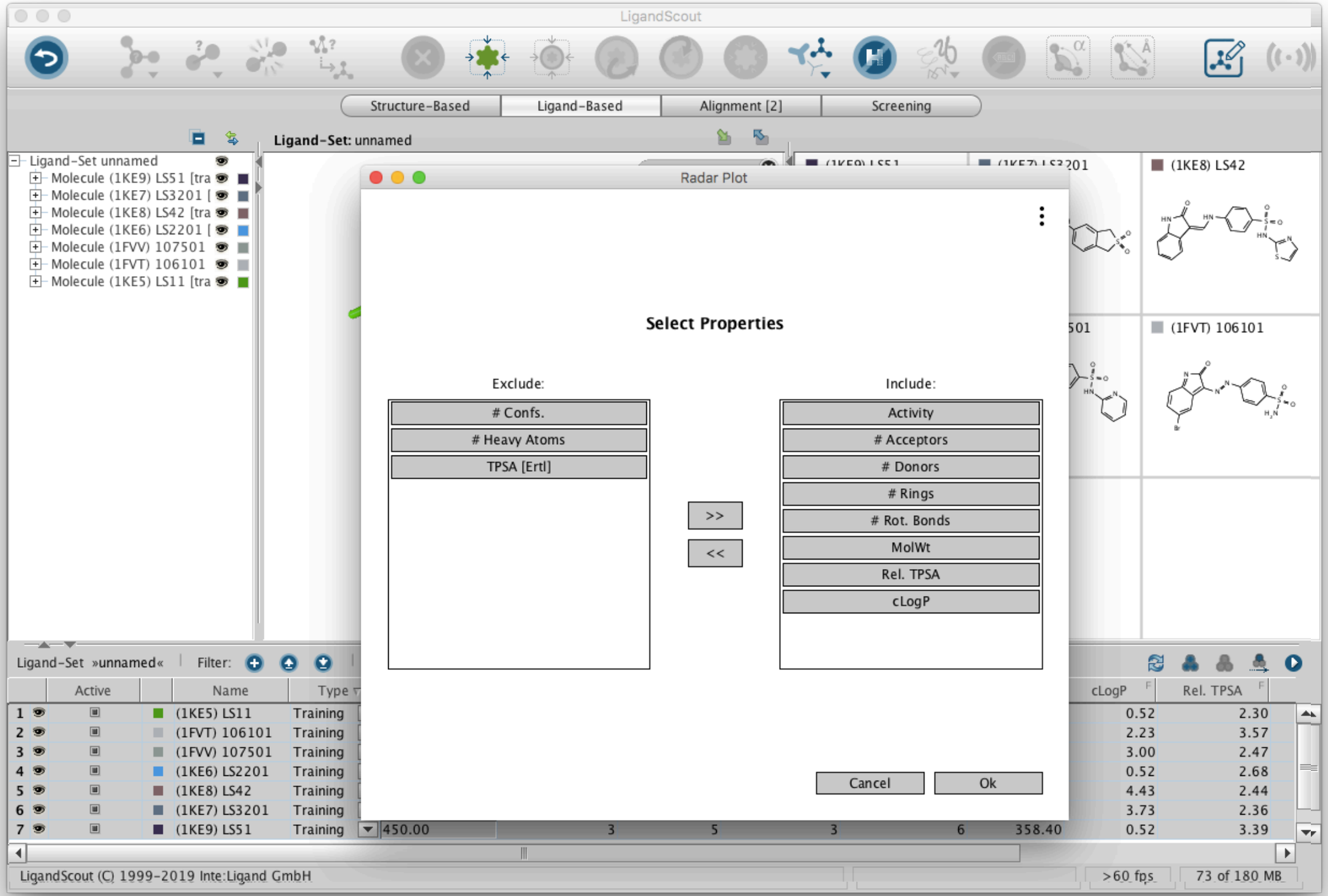
Interactive Data Analysis: Radar Plot



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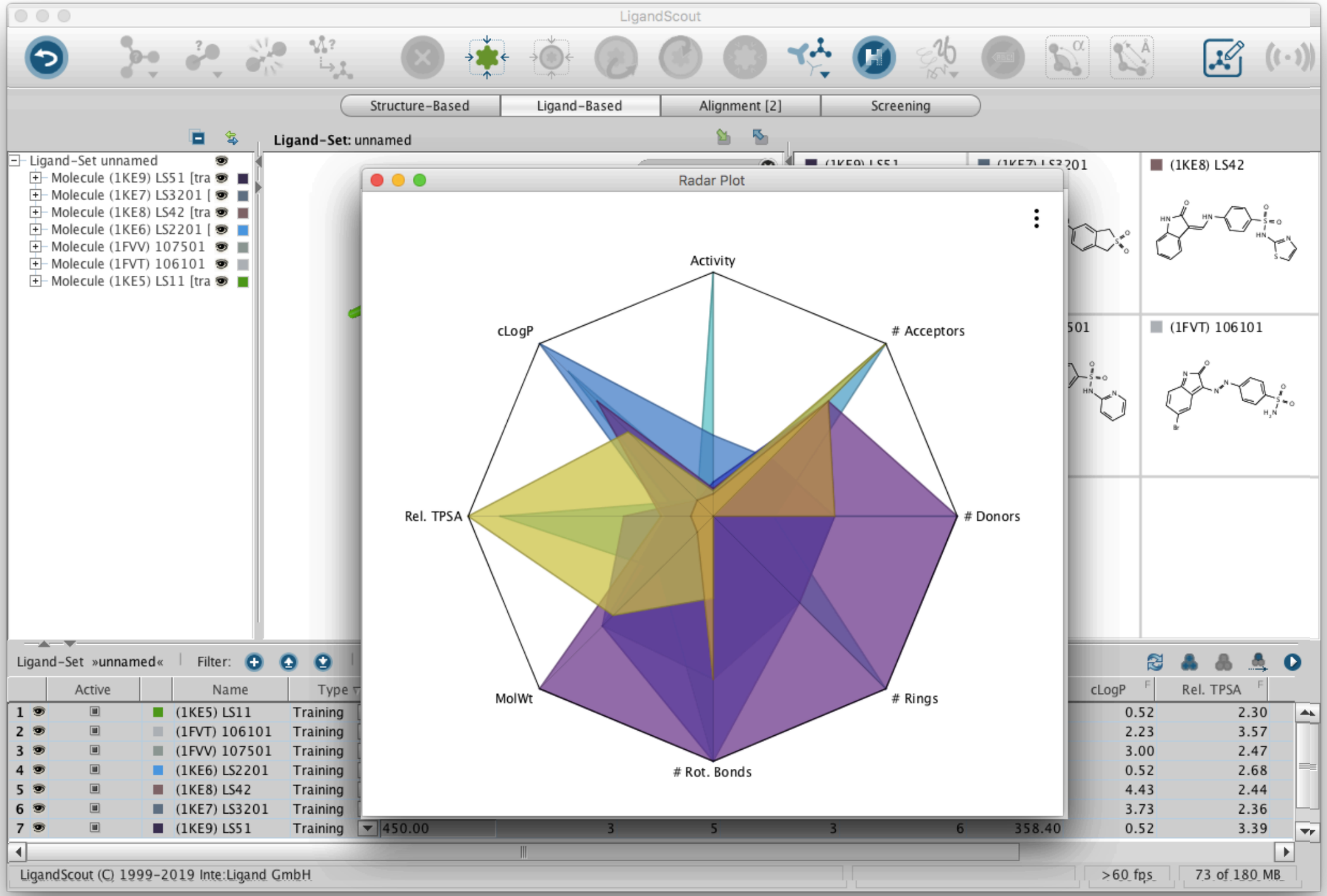

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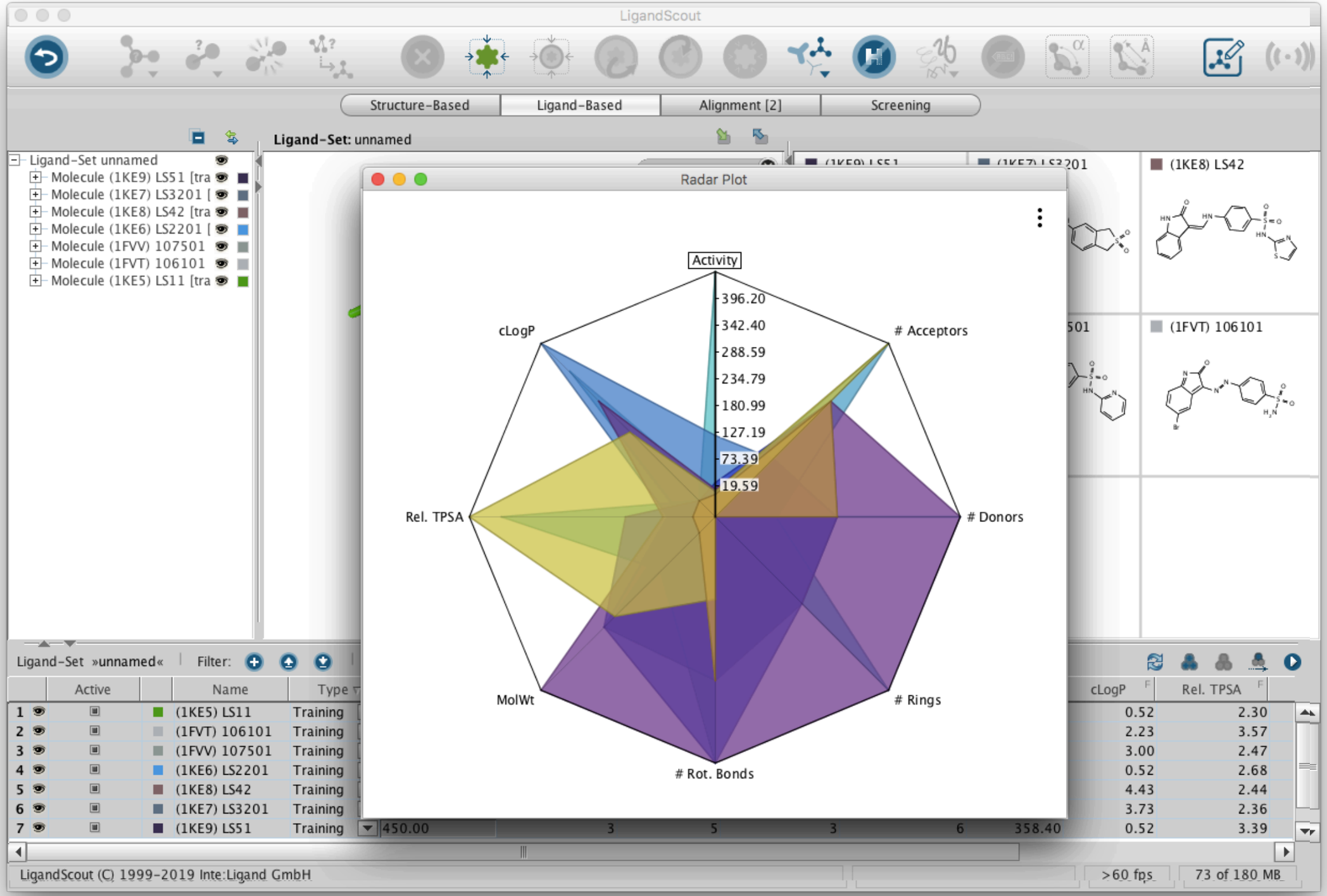

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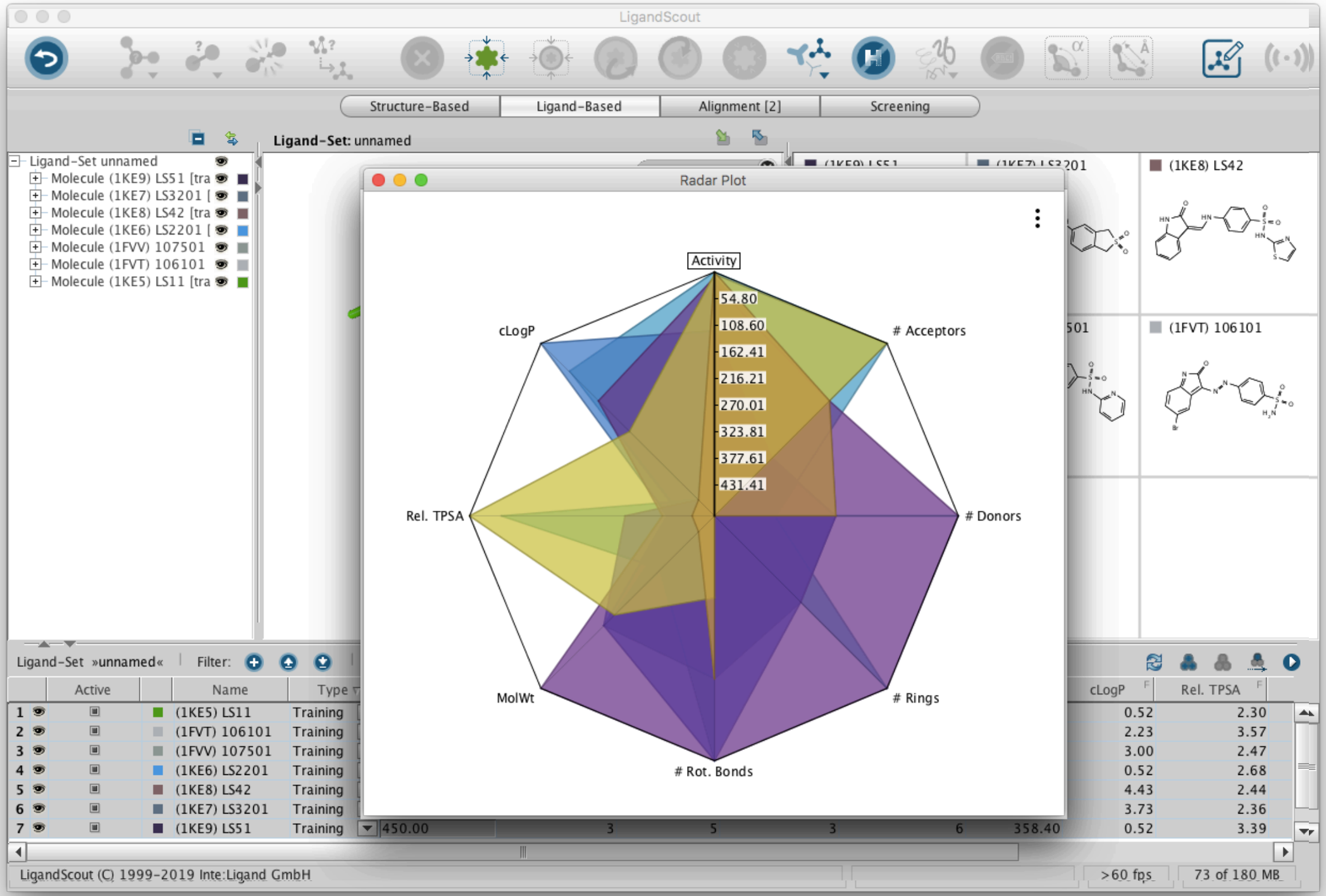
Interactive Data Analysis: Radar Plot



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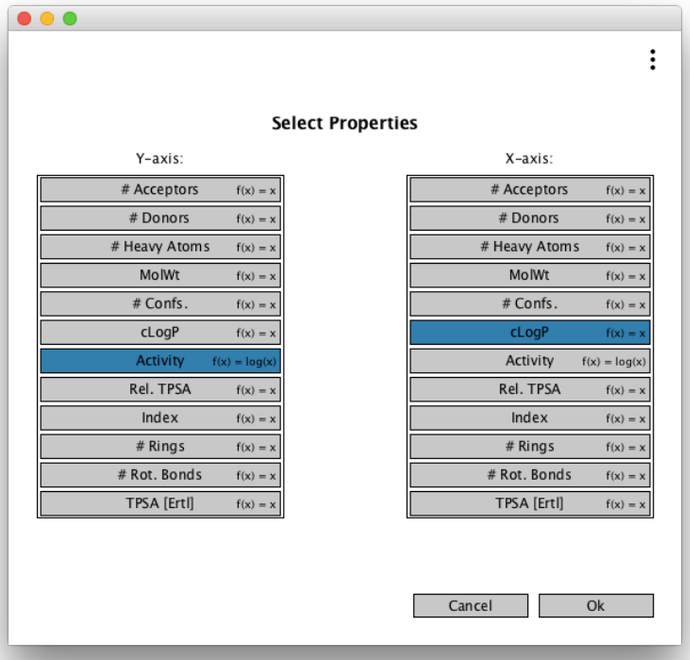
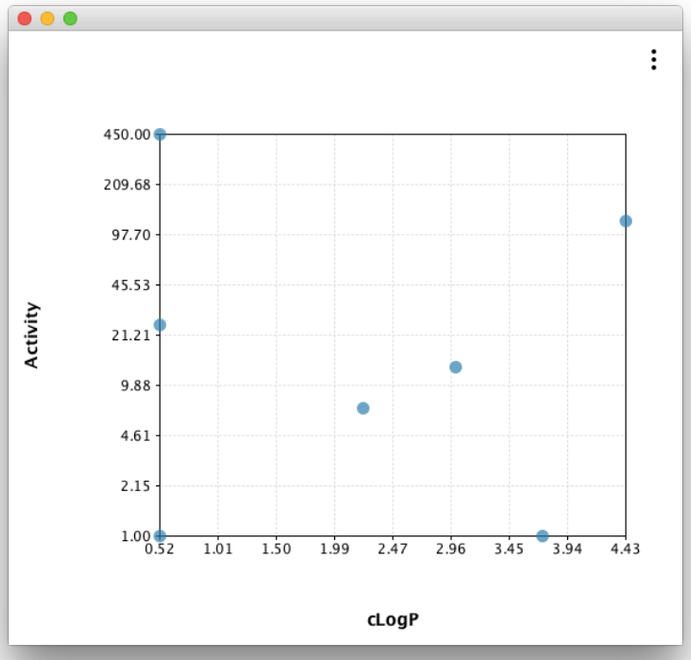
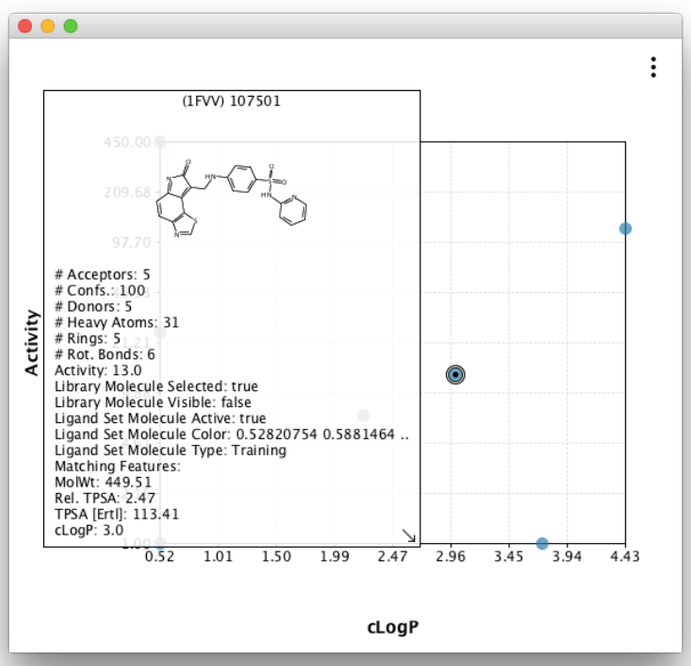
Interactive Data Analysis

- New features in scatter & parallel coordinate plots
  - Invert axes
  - Scale axes with pre-defined math functions and define ranges
  - Obtain molecular information interactively







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What's New in LigandScout 4.3 ?

- Remote execution from the GUI:
  - iScreen on local HP clusters or on the Amazon Cloud*
  - idbgen on local HP clusters or on the Amazon Cloud*
- Halogen bond acceptor feature
- New fully searchable online help system

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Remote Execution from the GUI

LigandScout Remote: A New User-Friendly Interface for HPC and Cloud Resources

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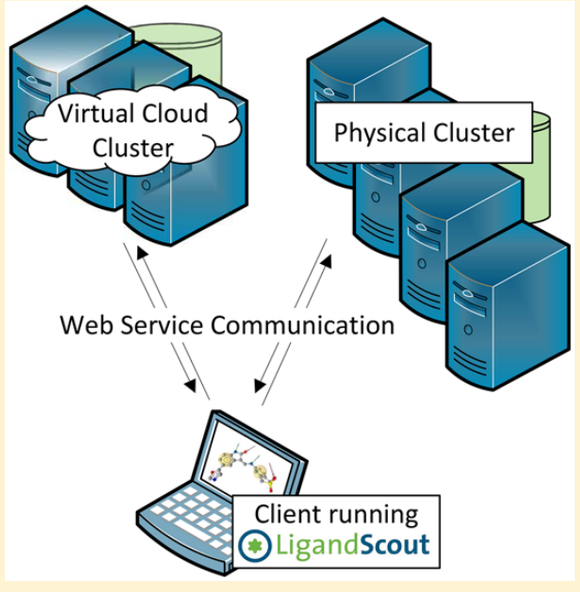
[‡]Inte:Ligand Software Development and Consulting GmbH, A-1070 Vienna, Austria

[§]Department of Pharmaceutical Chemistry, University of Vienna, A-1090 Vienna, Austria

JCIM JOURNAL OF CHEMICAL INFORMATION AND MODELING

ABSTRACT: High-performance computing (HPC) clusters play a major role in scientific research. However, working with these clusters is often cumbersome, especially for researchers without a formal background in computer science. It requires preparation and transfer of the input data, manual gathering of results, and command-line expertise. Current approaches for improving accessibility to remote HPC clusters are focused on providing web-based graphical front-ends that allow jobs to be submitted to the distributed resource management system running on the cluster. This comes with significant usability benefits over command-line usage but does not circumvent the need for manual handling of the input and output files. With `LigandScout Remote`, we propose a different solution. Our software enables the seamless integration of HPC resources into the `LigandScout` desktop application that scientists use also in their day-to-day work. By handling necessary data conversion and network communication transparently to the user, this approach completely evades any HPC usability barriers. We show that the developed software combines the usability of local graphical desktop applications with the performance of HPC clusters.



https://doi.org/10.1021/acs.jcim.8b00716

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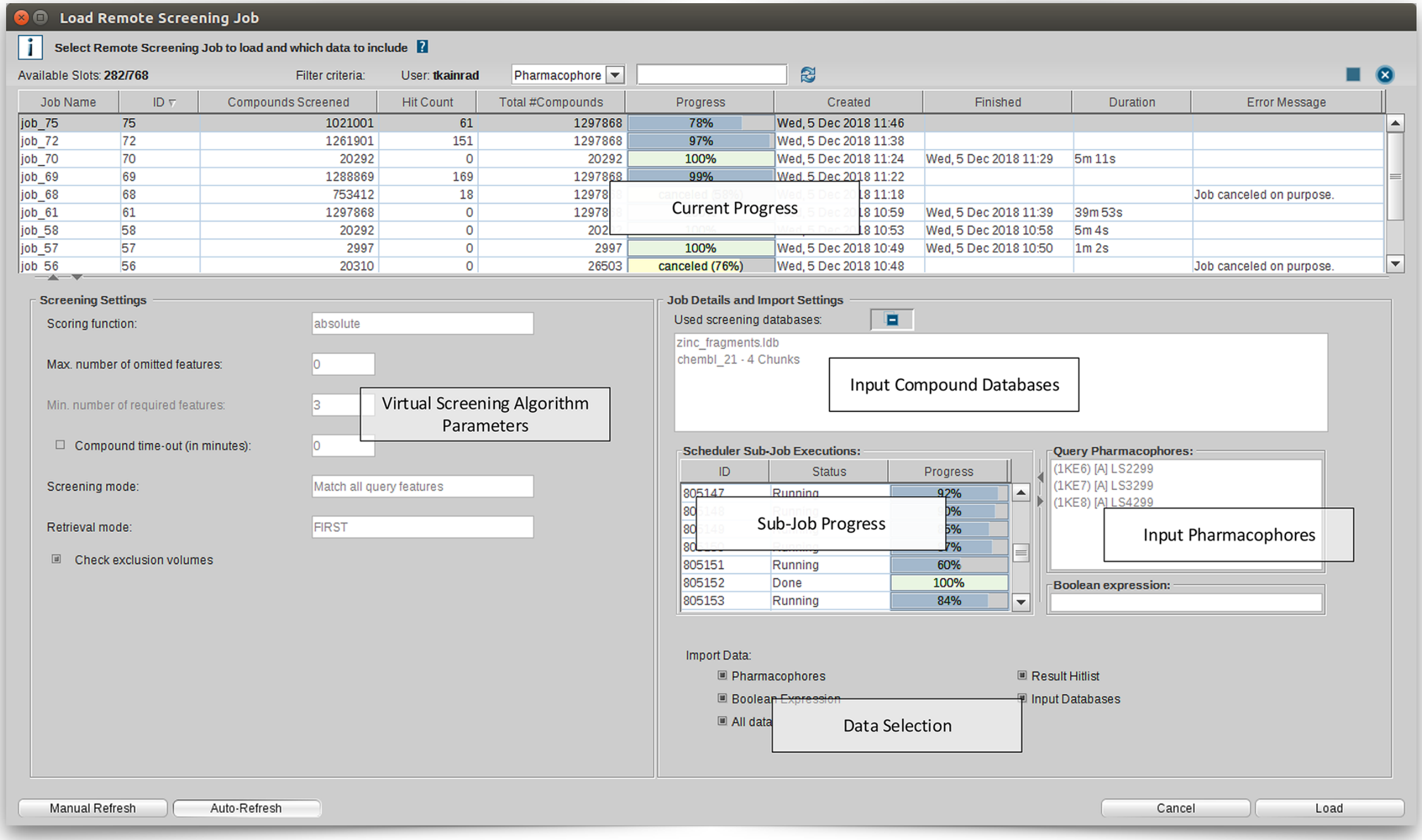
Remote Execution from the GUI



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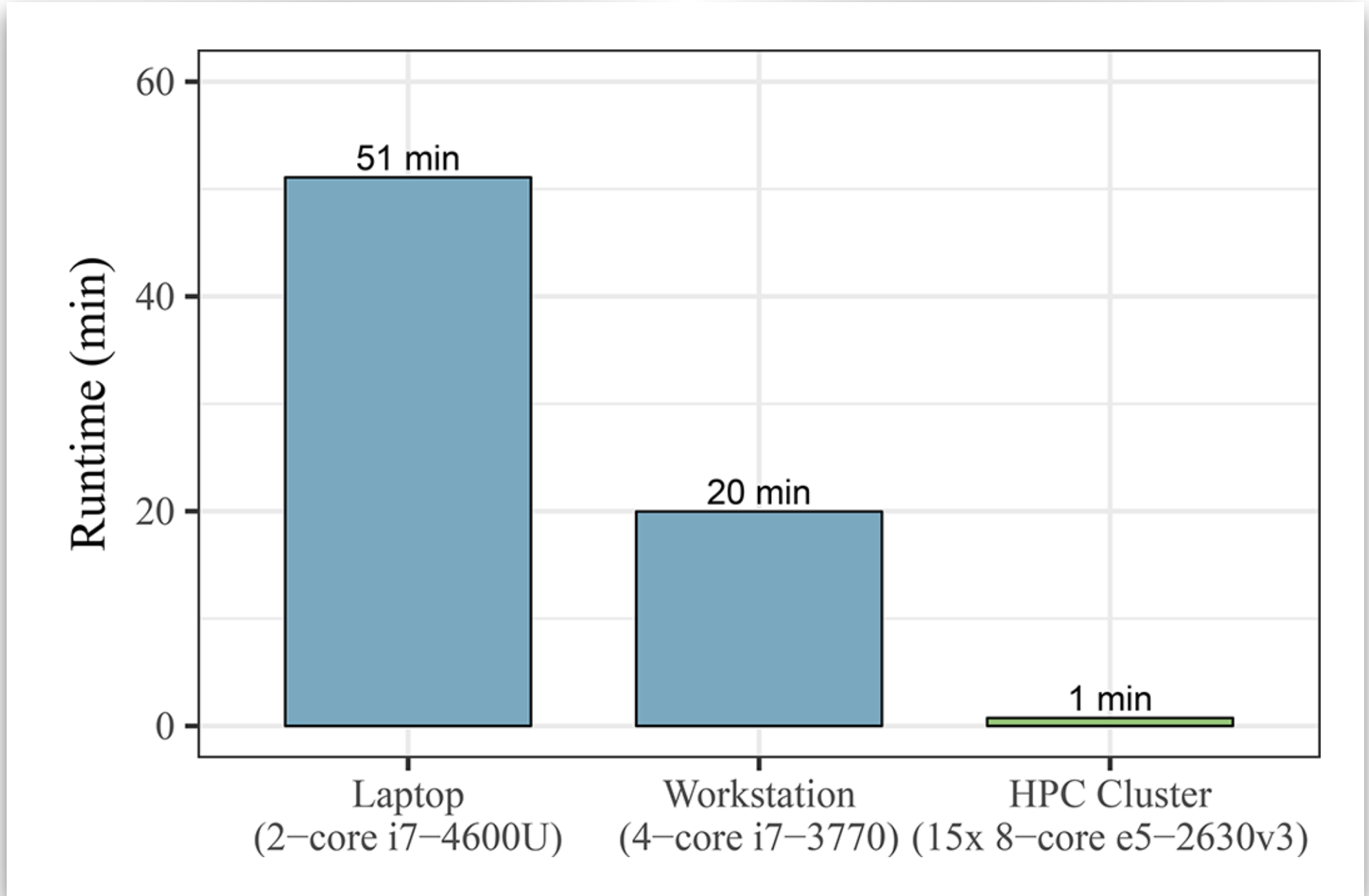
Screening Performance Comparison



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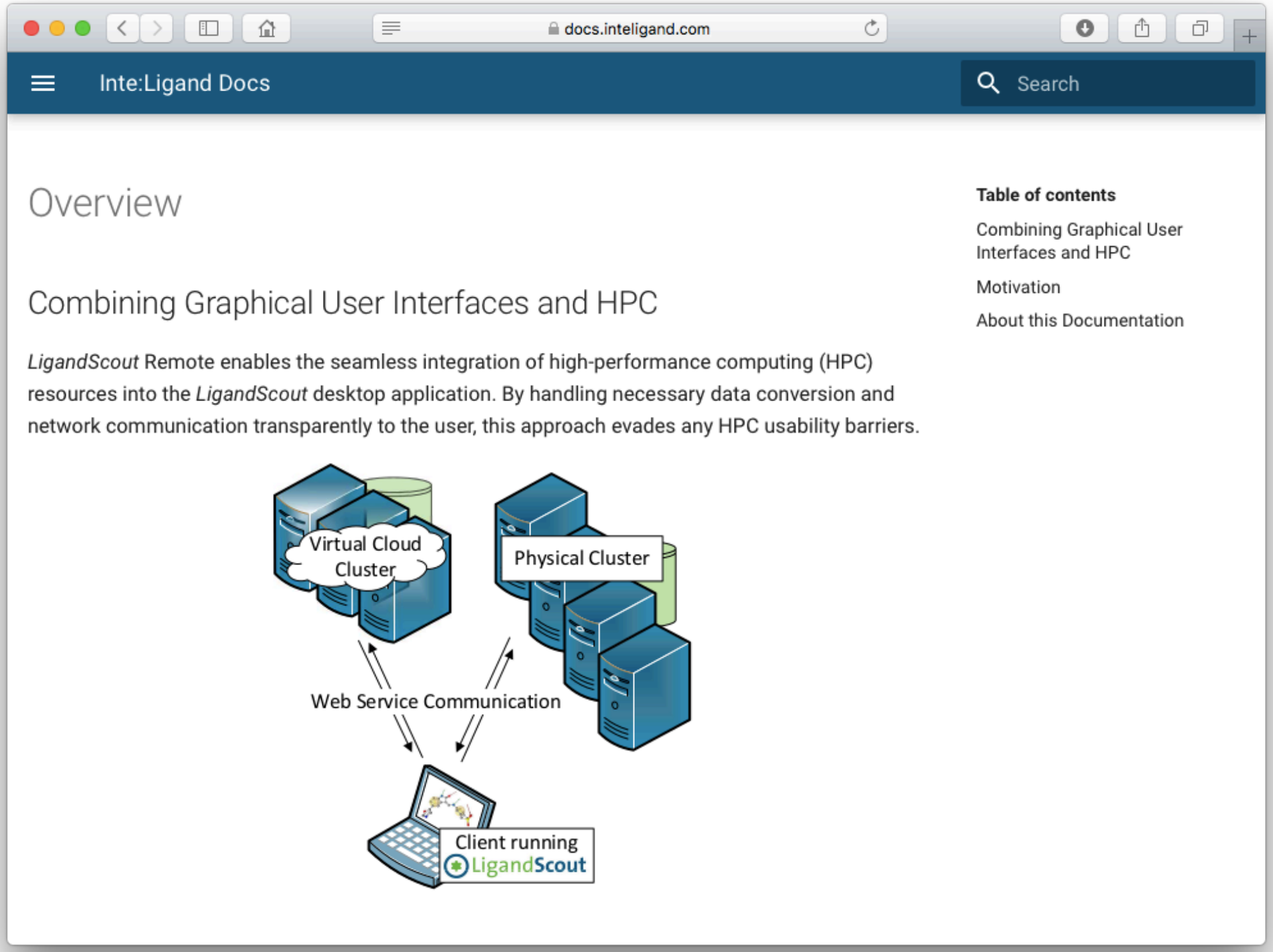
https://docs.inteligand.com/ls-remote



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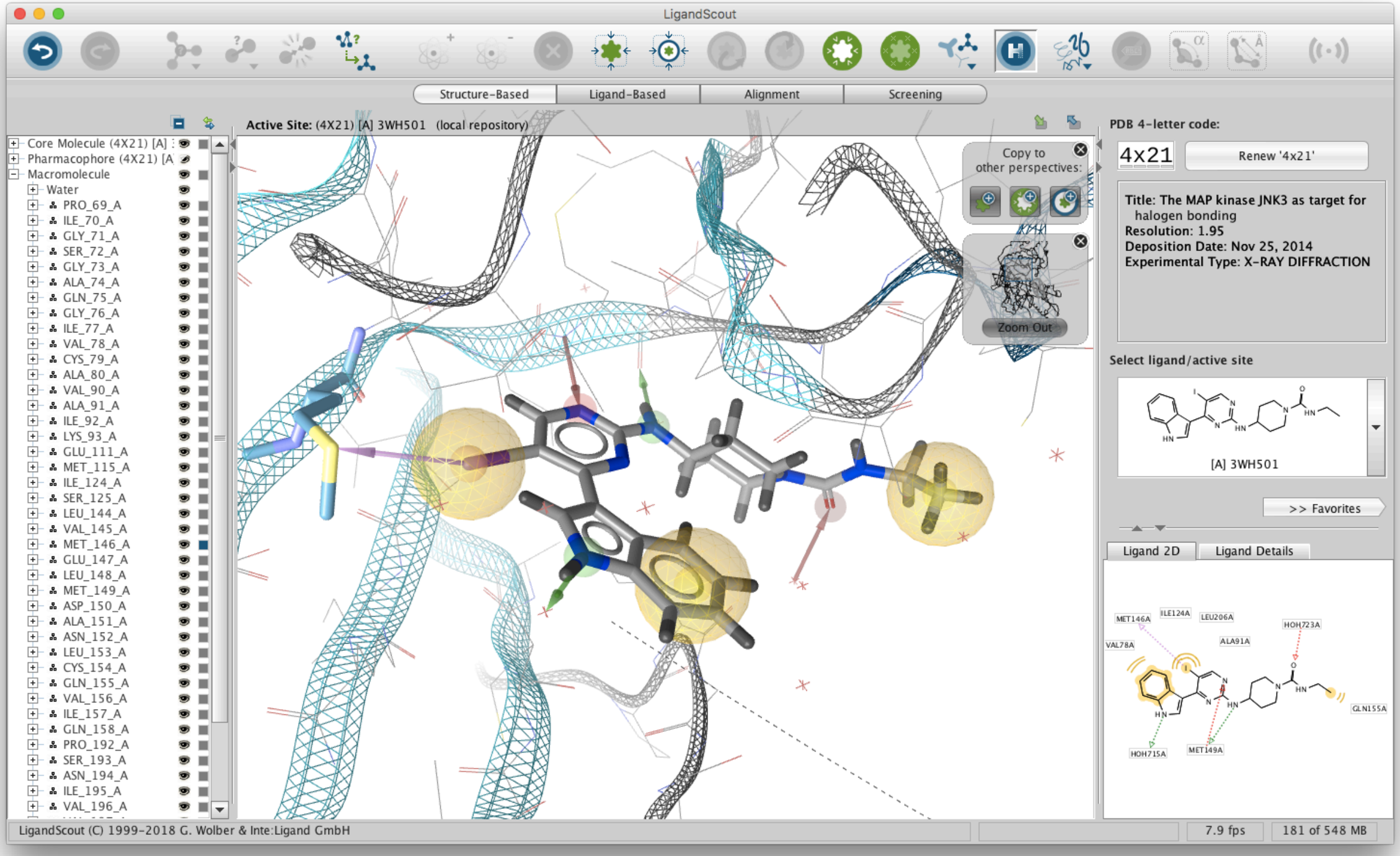
New: Halogen Bond Acceptor Feature



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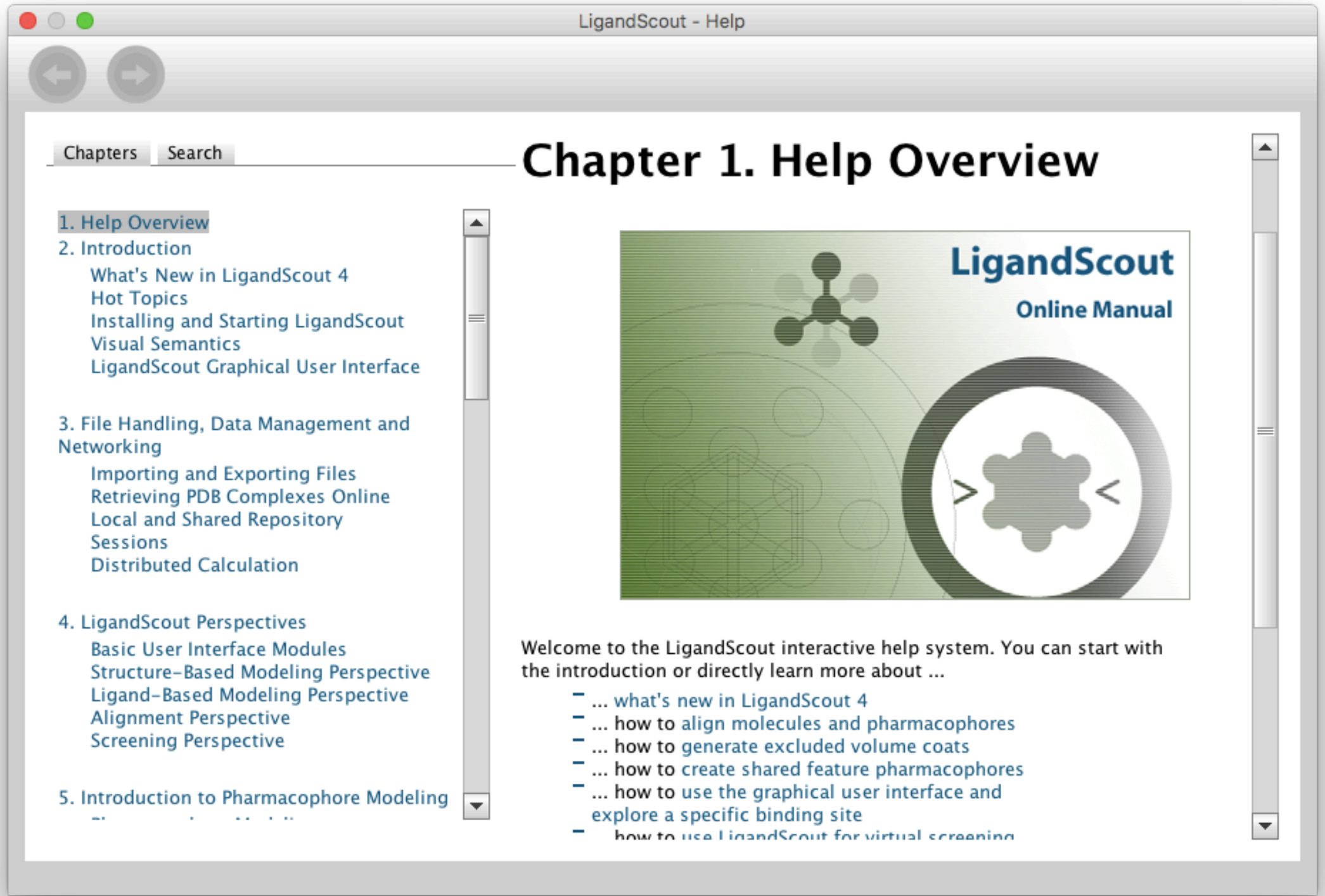
Fully Indexed Online Help Manual



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What was new in LigandScout 4.2 ?

- User interactive charts for analyzing and filtering tables
- Fully editable tables, import & export from and to Excel
- Fully editable parameter sets for library filtering
- Find ligands present in the PDB database in any table
- Remodelled workflow for ligand-based pharmacophore generation
- Visualization of multiple superimposed binding sites
- MD trajectory import from Amber & Gromacs, in addition to Charmm
- Automated creation of pharmacophores from MD trajectories
- Tools for analysis of pharmacophores derived from MD

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Some Unique Features of LigandScout

Structure-based pharmacophore modeling

- Automated recognition of ligand-protein interactions
- User-friendly analysis of tautomers & side chain rotamers

Ligand-based pharmacophore modeling

- Pharmacophore-based ligand clustering
- Automated creation of exclusion volume for ligand-based pharmacophores
- Unlimited number of features per pharmacophore

Virtual screening

- Speed & accuracy increases with the number of features

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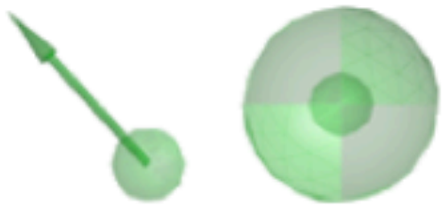
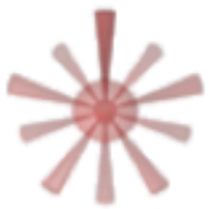
LigandScout Pharmacophore Features



Hydrogen Bond Donor

Hydrogen Bond Acceptor

Positive Ionizable Area



Negative Ionizable Area

Hydrophobic Interactions

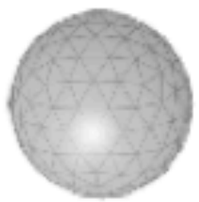
Aromatic Ring

Iron Binding Location

Zinc Binding Location

Magnesium Binding Location

Manganese Binding Location



Excluded Volume

Covalent Bond Feature

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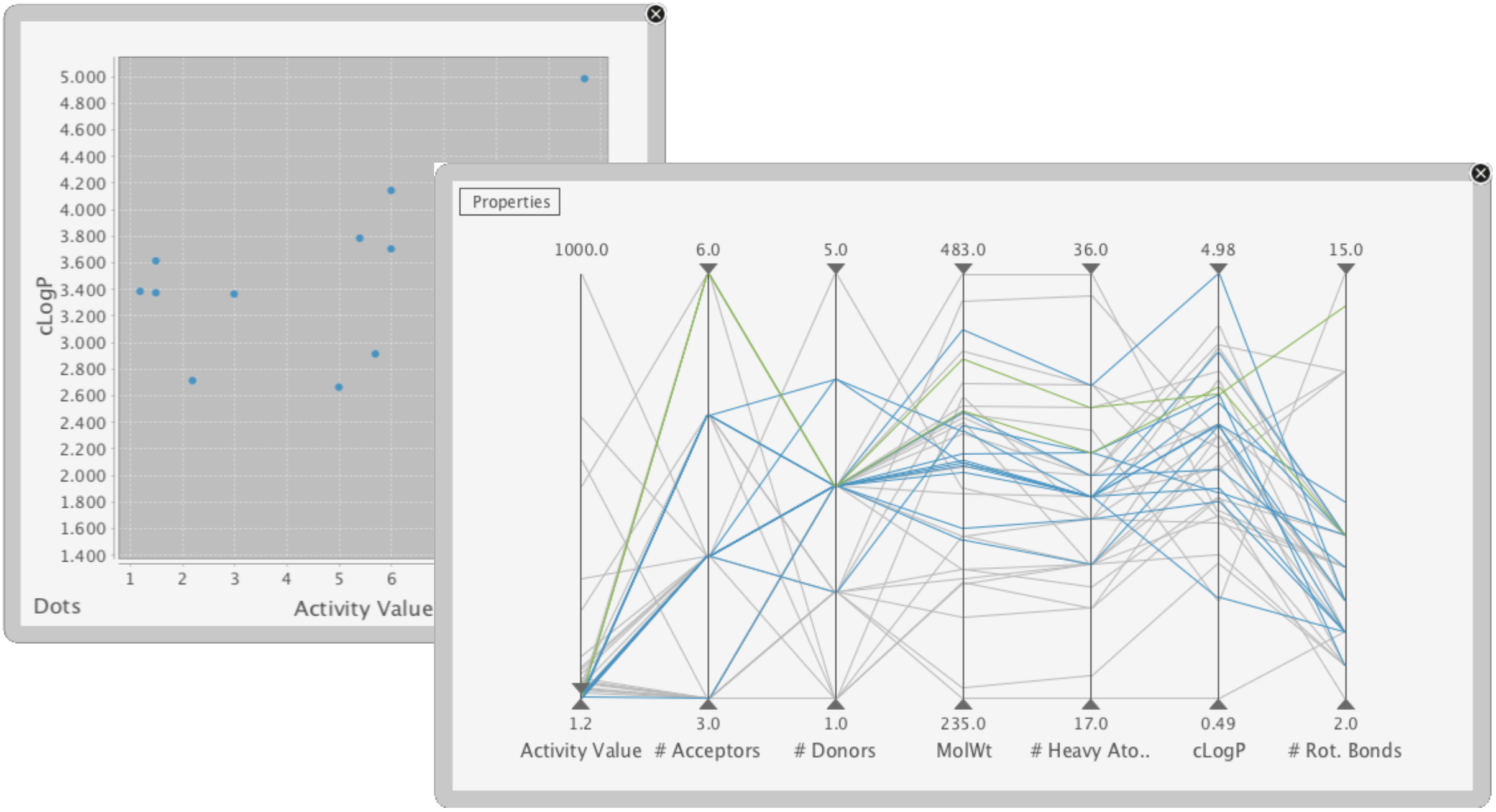
Interactive Charts

- Use interactive charts for analyzing and filtering your tables



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Tables: Now Fully Editable

- Add and remove information, import & export from and to Excel

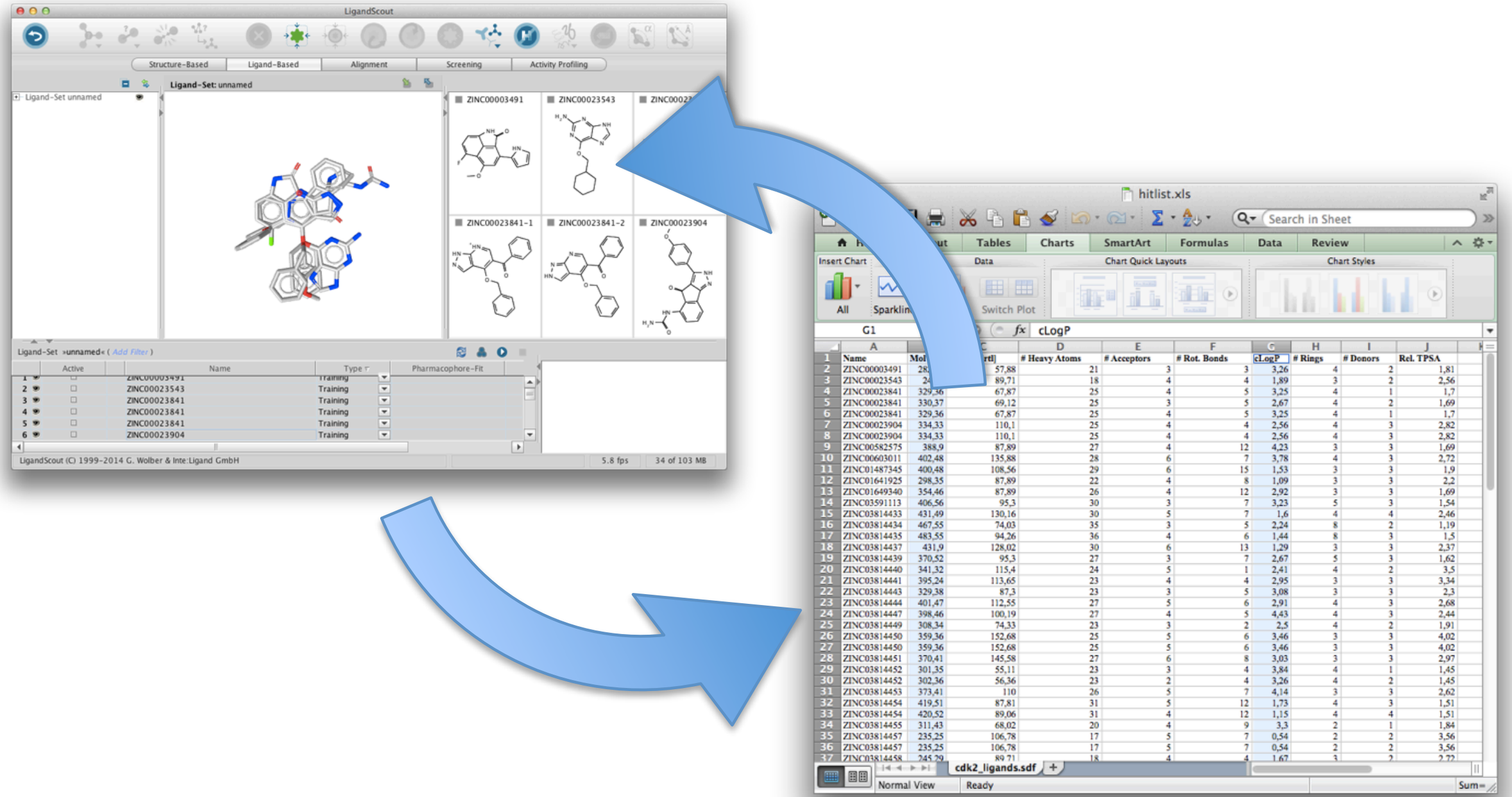

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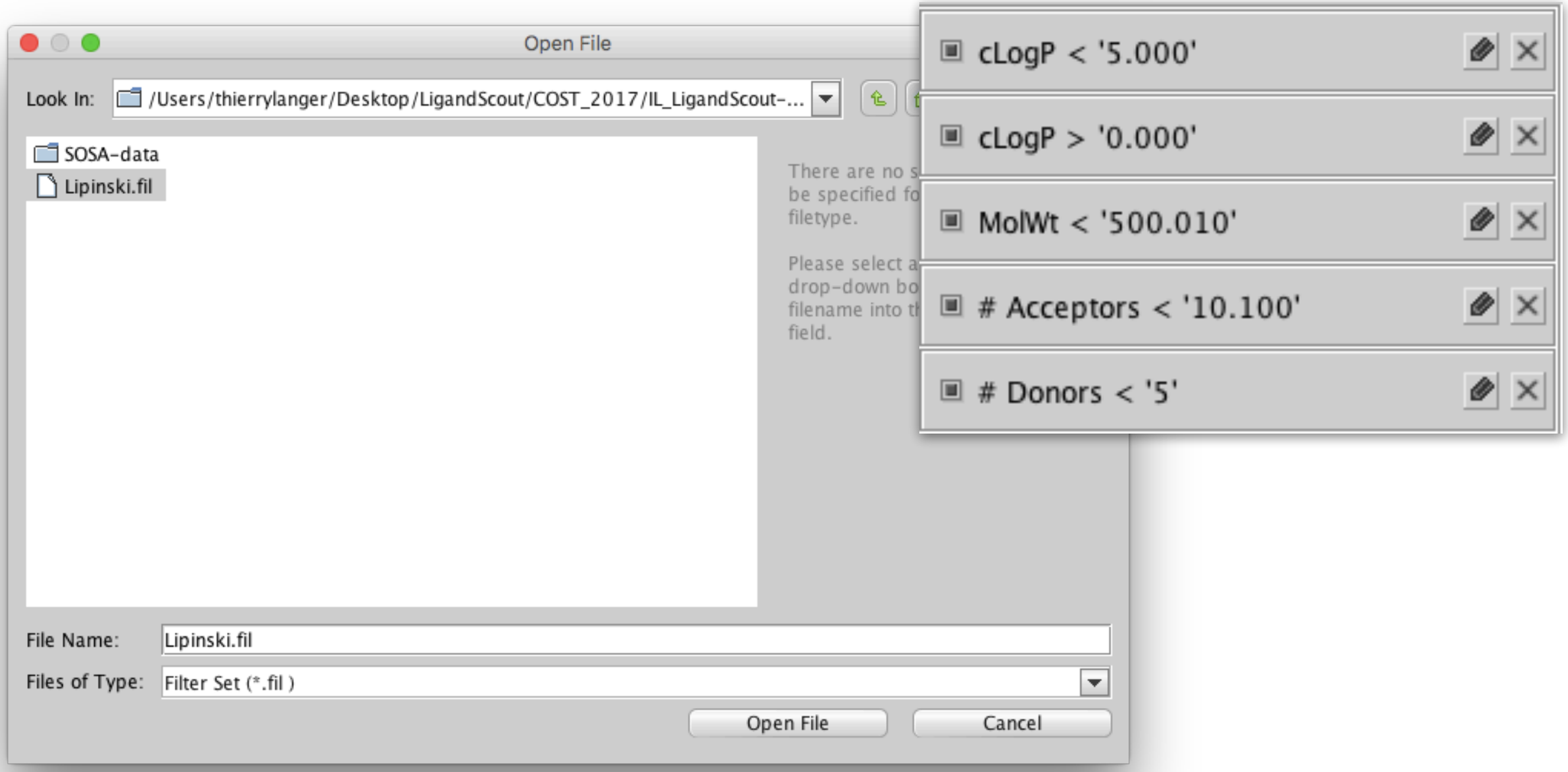
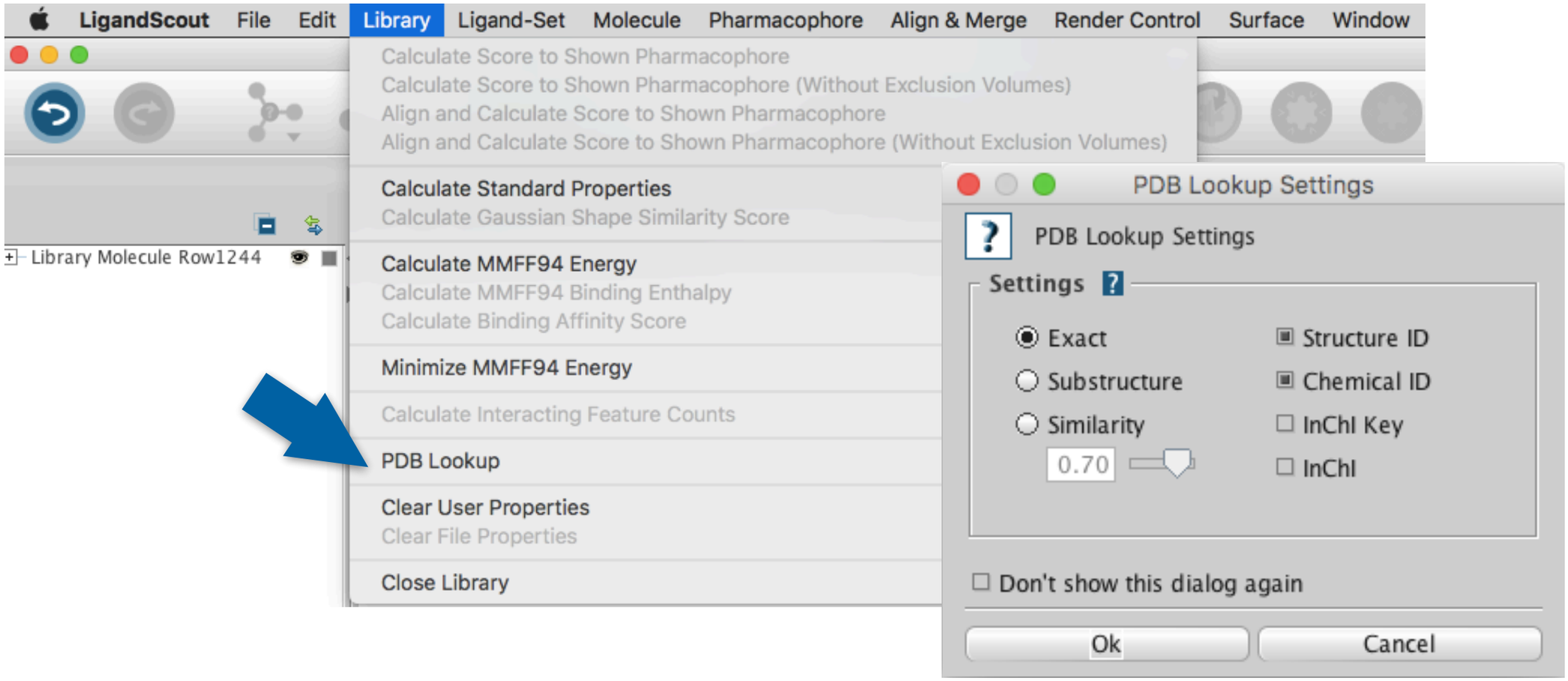
Table Filtering

- Save and import your parameter sets for table and library filtering



PDB Online LookUp

- Find out if a molecule from your table is present in the PDB database
- Check also for similar structures or search for substructures



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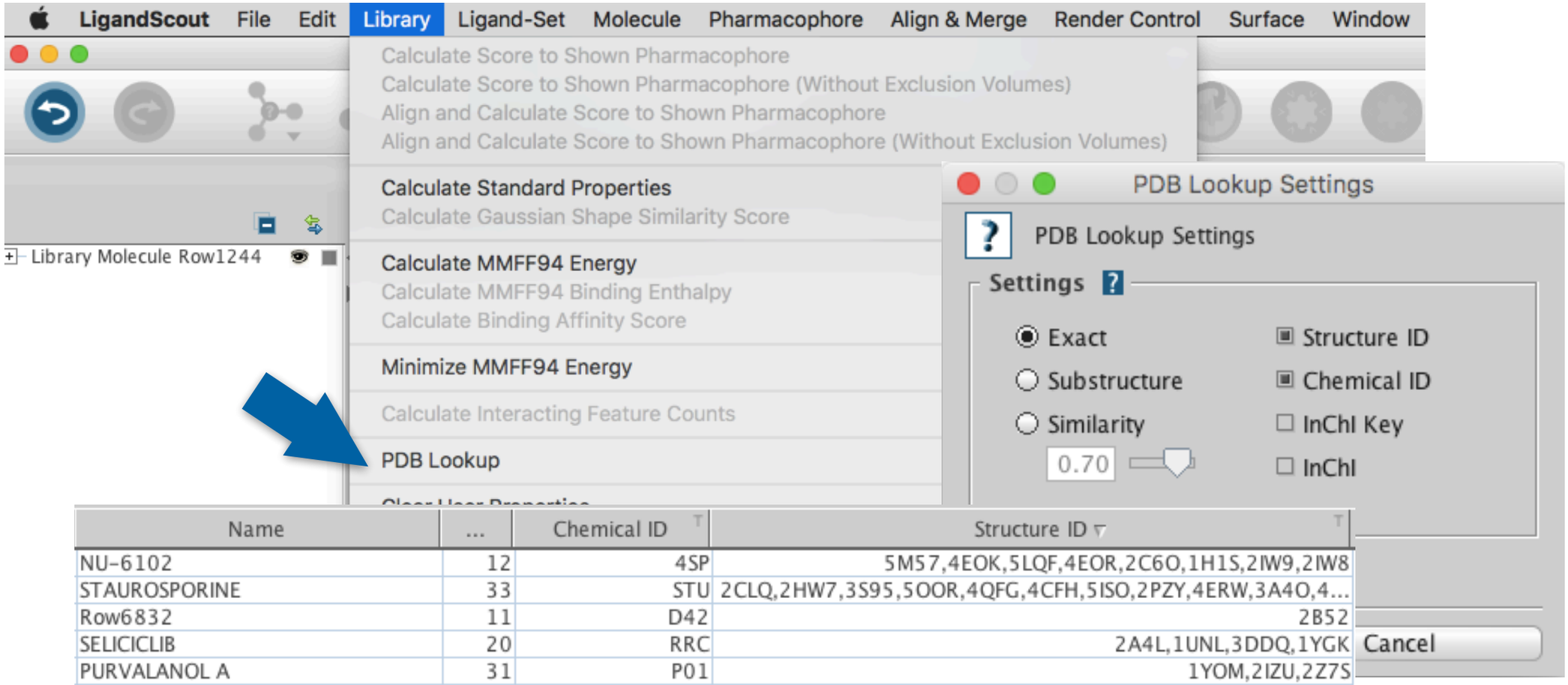

Name	...	Chemical ID	Structure ID
NU-6102	12	4SP	5M57,4EOK,5LQF,4EOR,2C6O,1H1S,2IW9,2IW8
STAUROSPORINE	33	STU	2CLQ,2HW7,3S95,5OOR,4QFG,4CFH,5ISO,2PZY,4ERW,3A4O,4...
Row6832	11	D42	2B52
SELICICLIB	20	RRC	2A4L,1UNL,3DDQ,1YGK
PURVALANOL A	31	P01	1YOM,2IZU,2Z7S
INDIRUBIN SULFATE	30	SU9	1PF8,3PY0,3PY1
(7S)-HYDROXYL-STAUROSPORINE	5	UCN	1OKZ,1NVQ,1PKD
Row653	28	HDY	1OIR
Row3341	22	LS5	1KE9,4FKP
Row2862	23	LS4	1KE8
Row2674	24	LS3	1KE7
Row1763	25	LS2	1KE6
Row202	26	LS1	1KE5
Row8112	18	I17	1G5S

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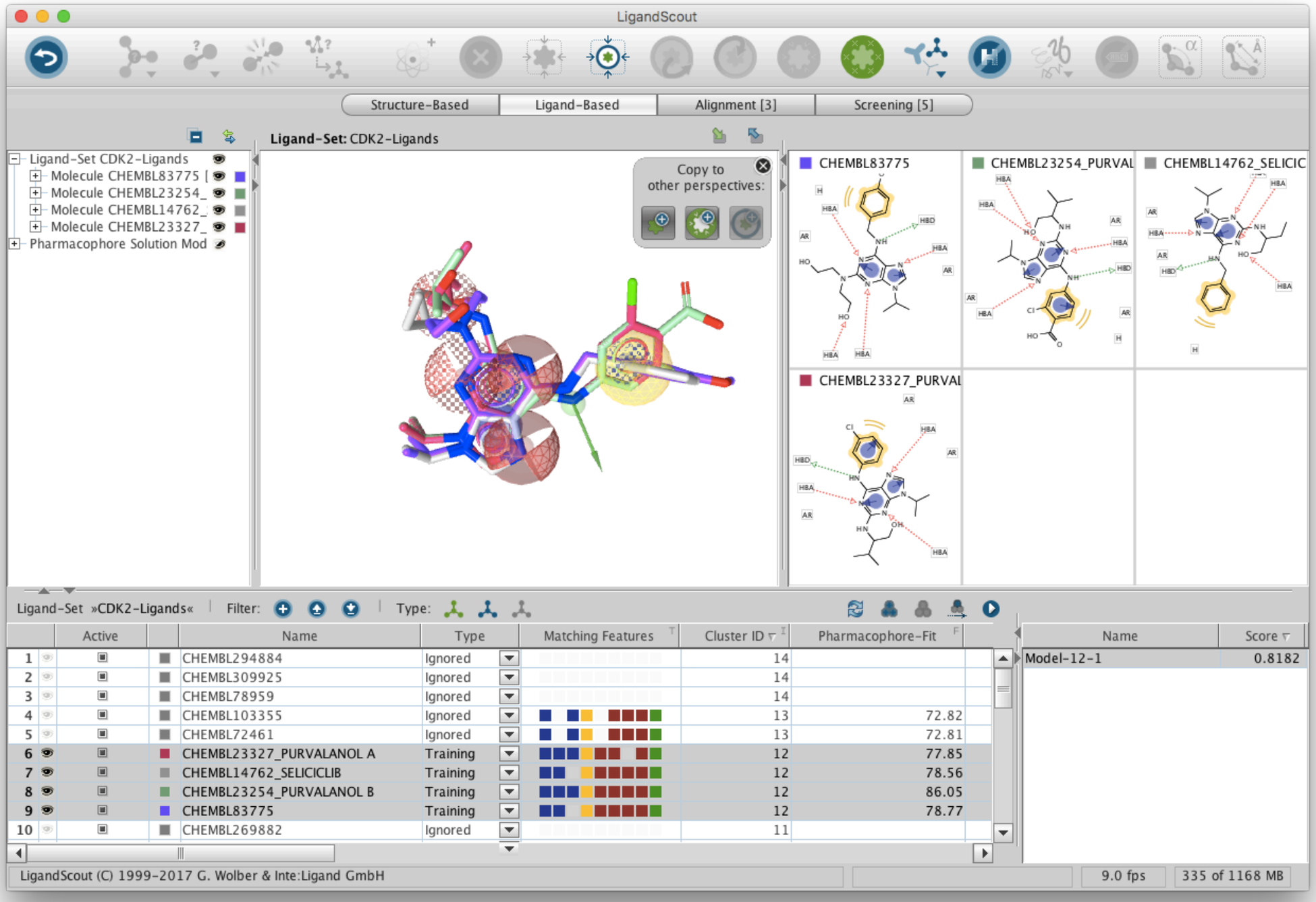
Single Click Ligand-based Model Generation

- Use new single click generation workflow



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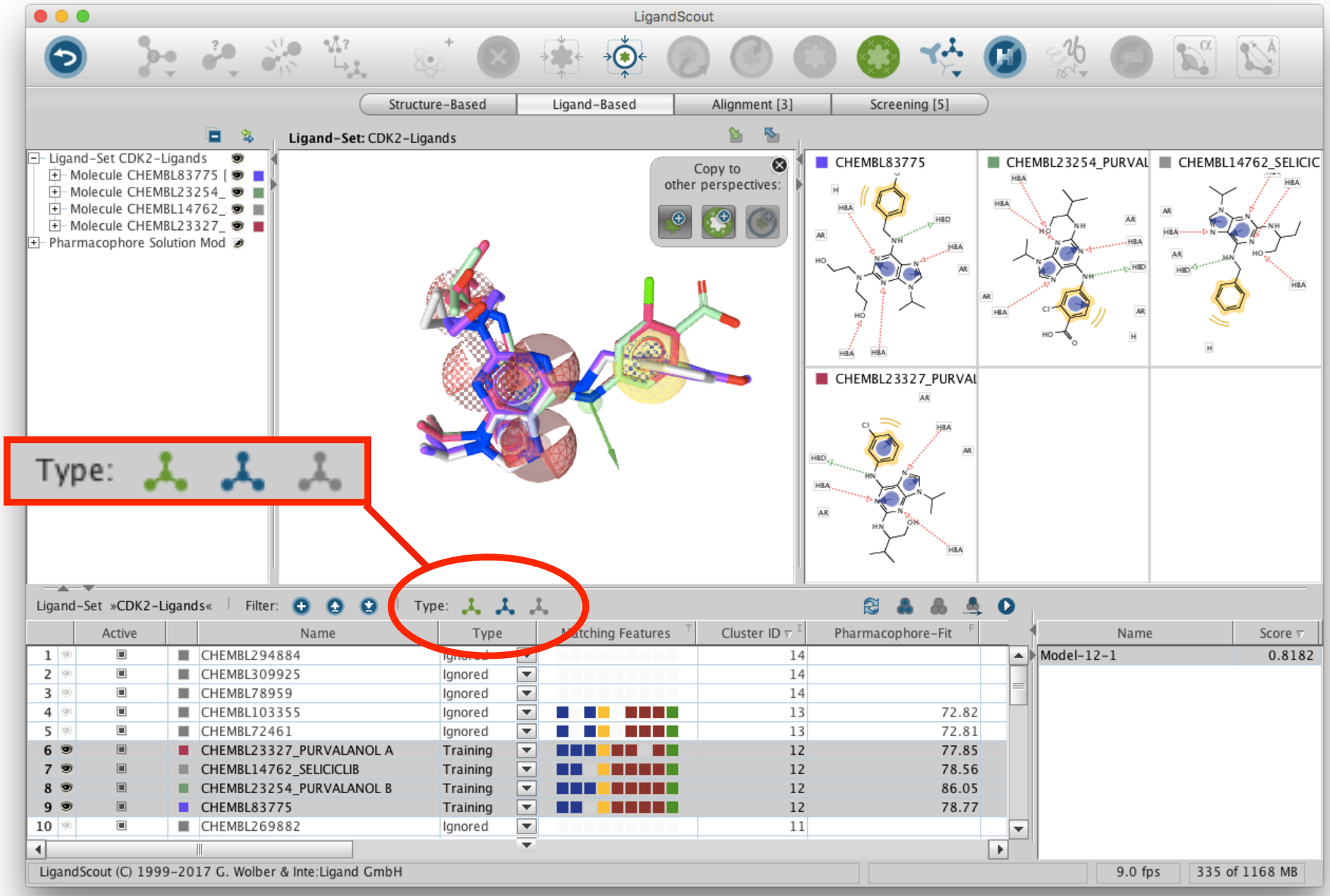

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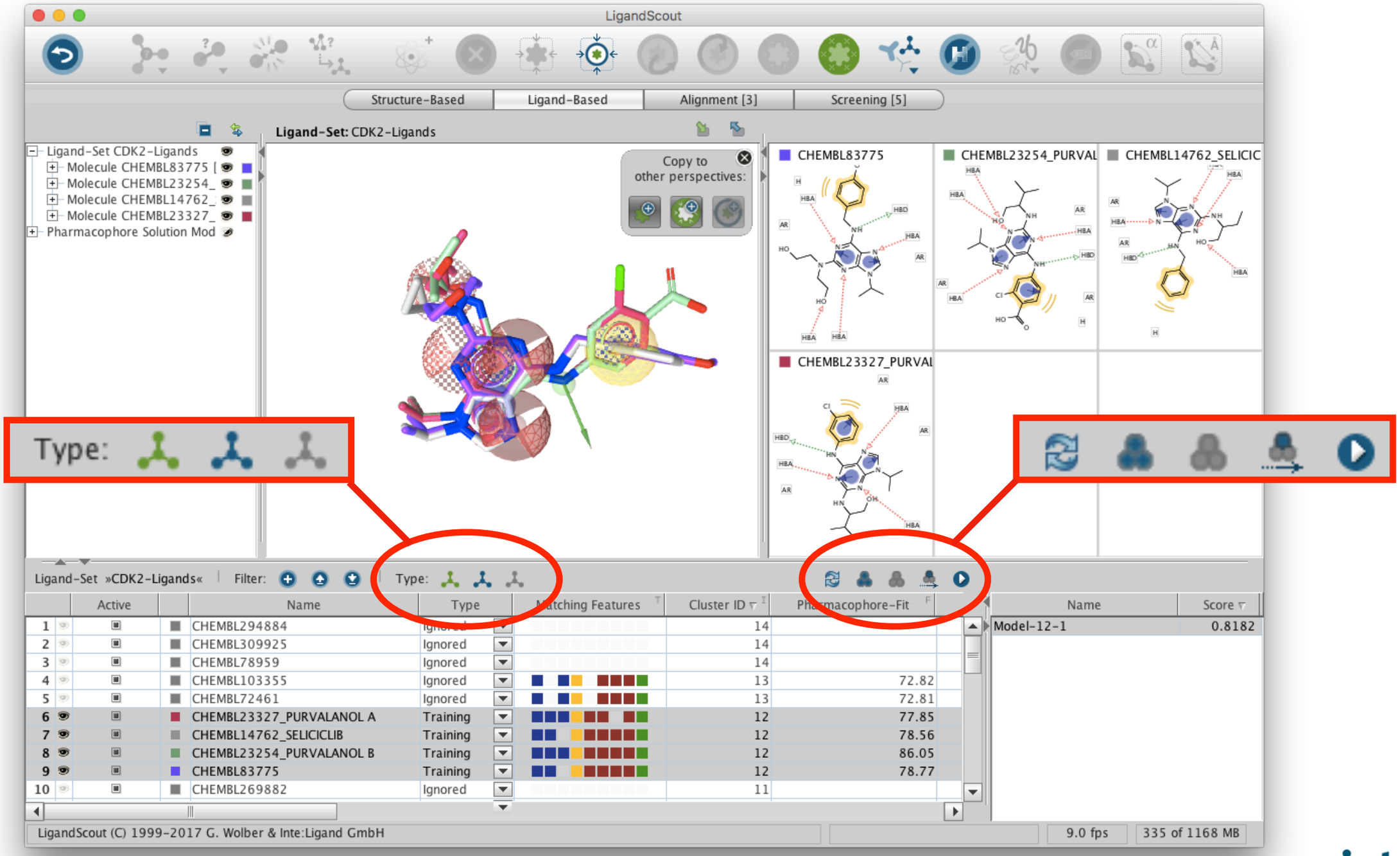

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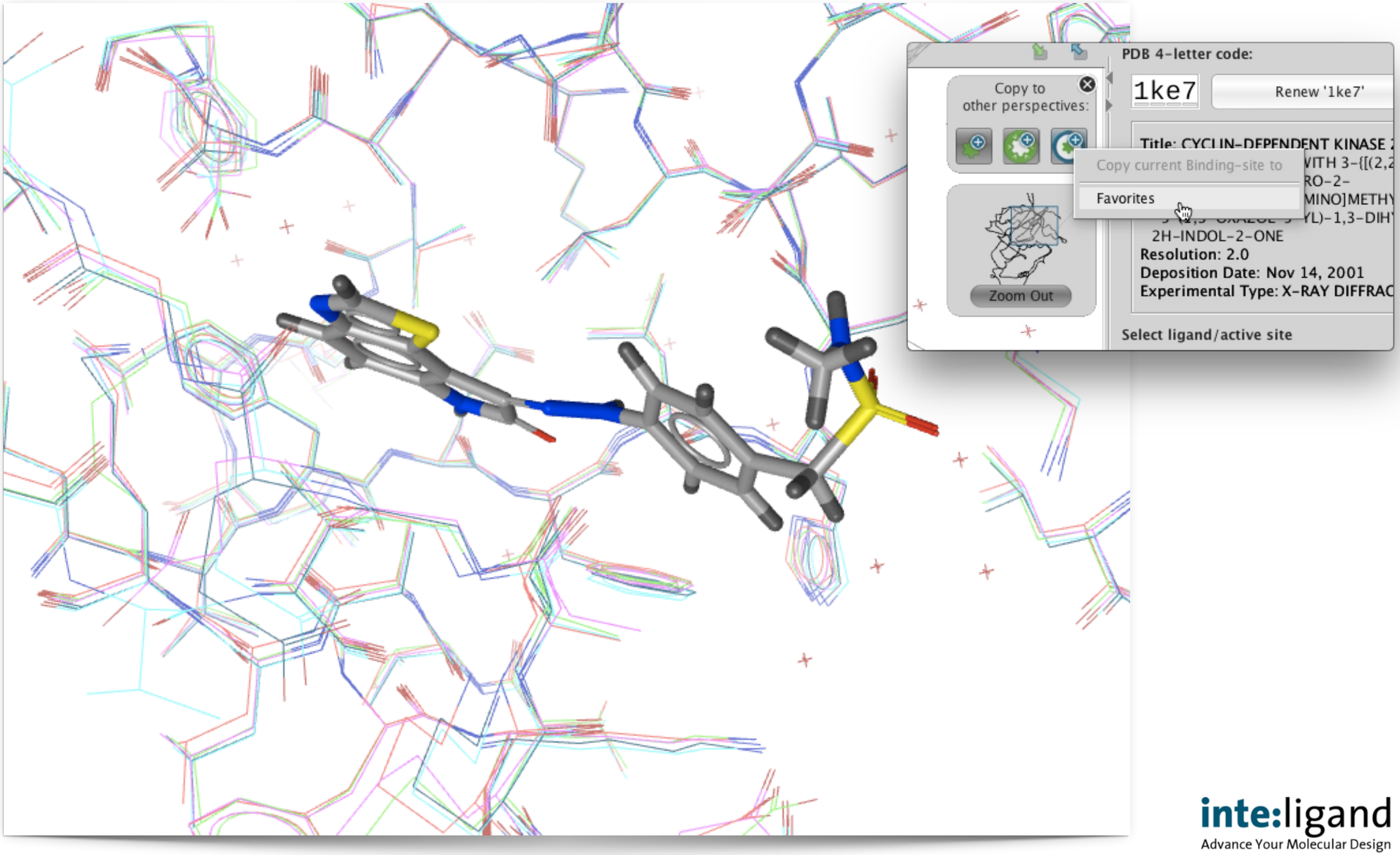
Protein Binding Site Analysis

- Visualize multiple superimposed binding sites in the favorites view



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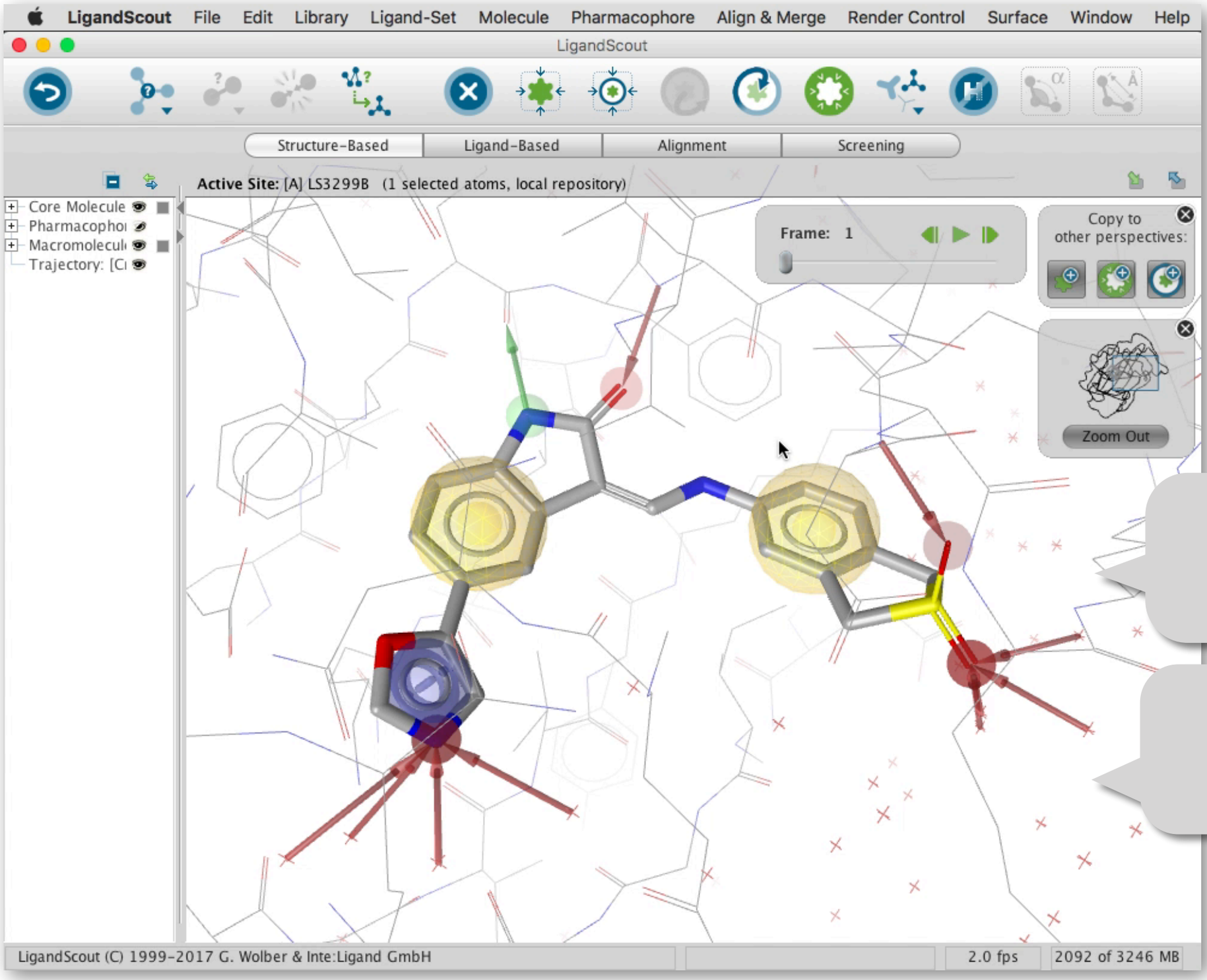
MD Trajectory Analysis

- Create automatically pharmacophores from your MD trajectories



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Windows & Linux

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macOS

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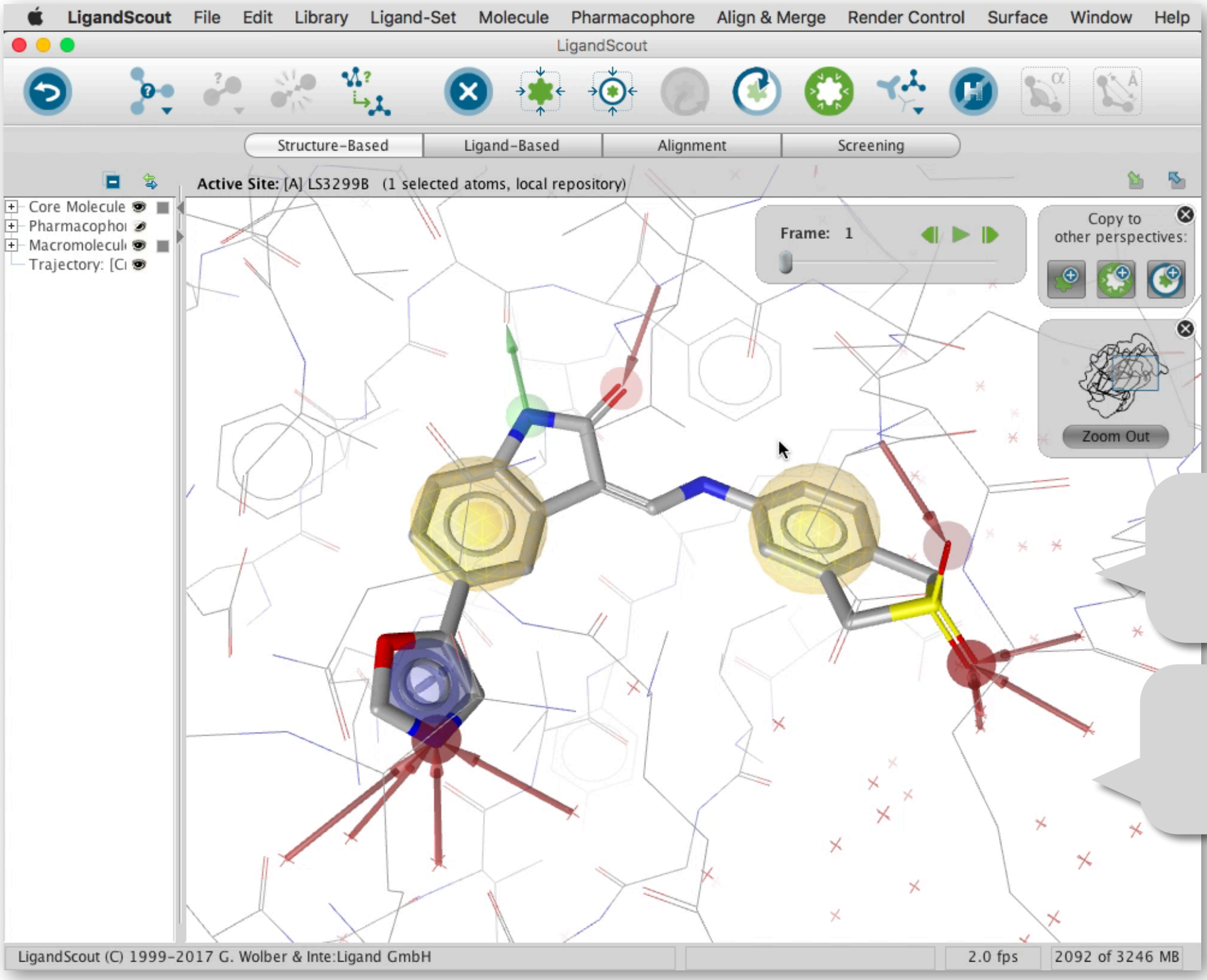

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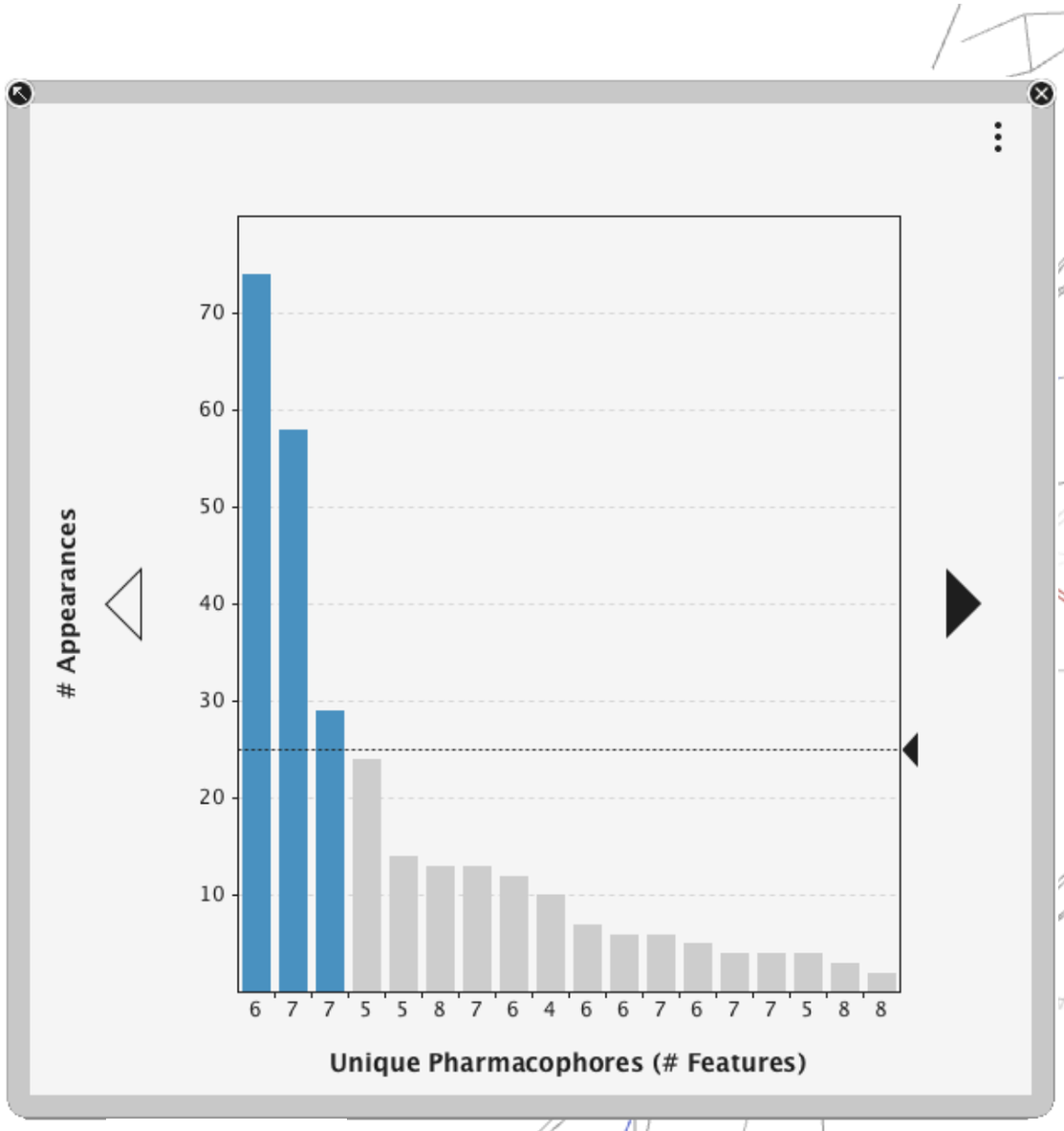
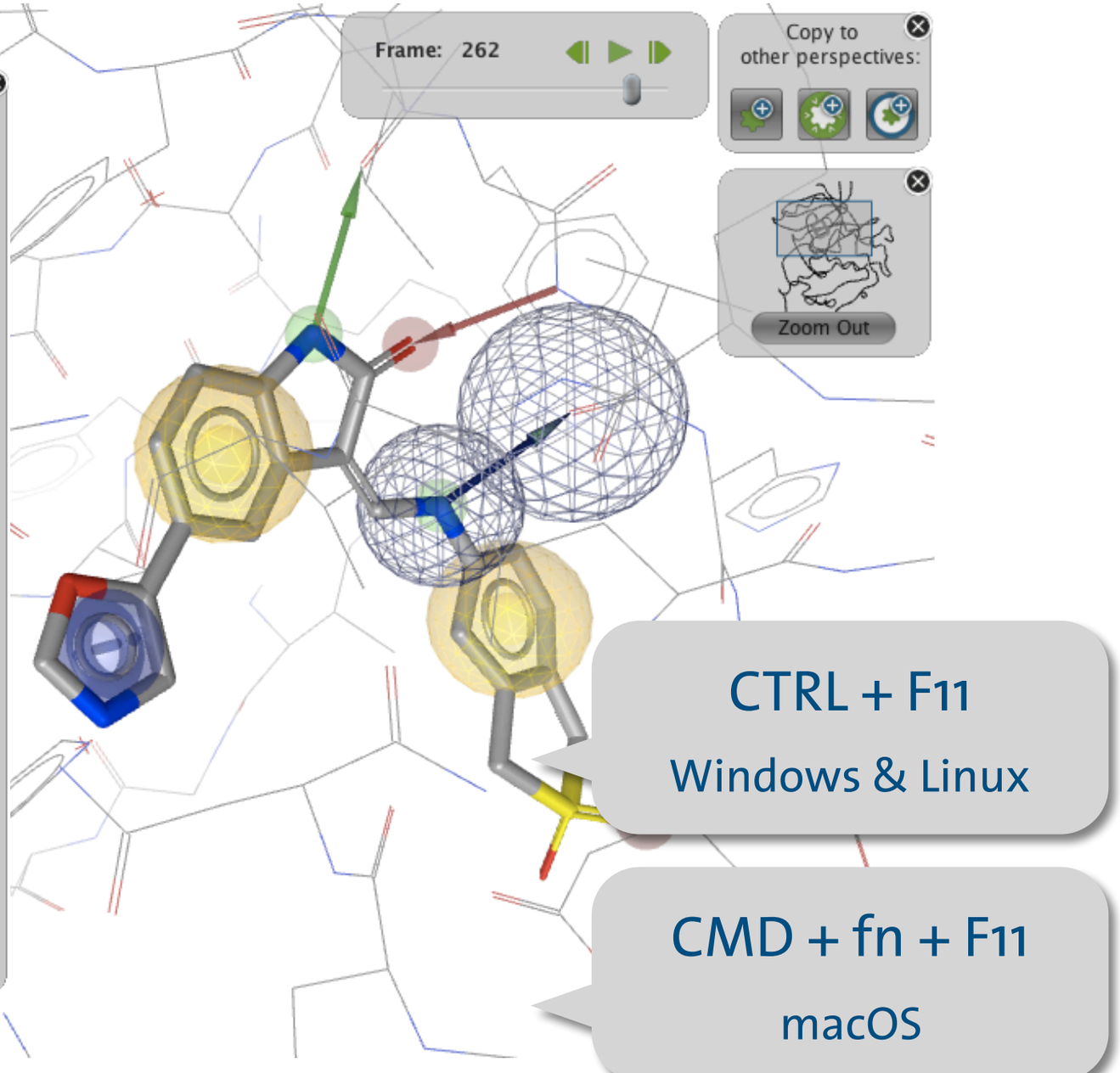
Tools for Pharmacophore-based MD Analysis

- Find all different unique pharmacophore models





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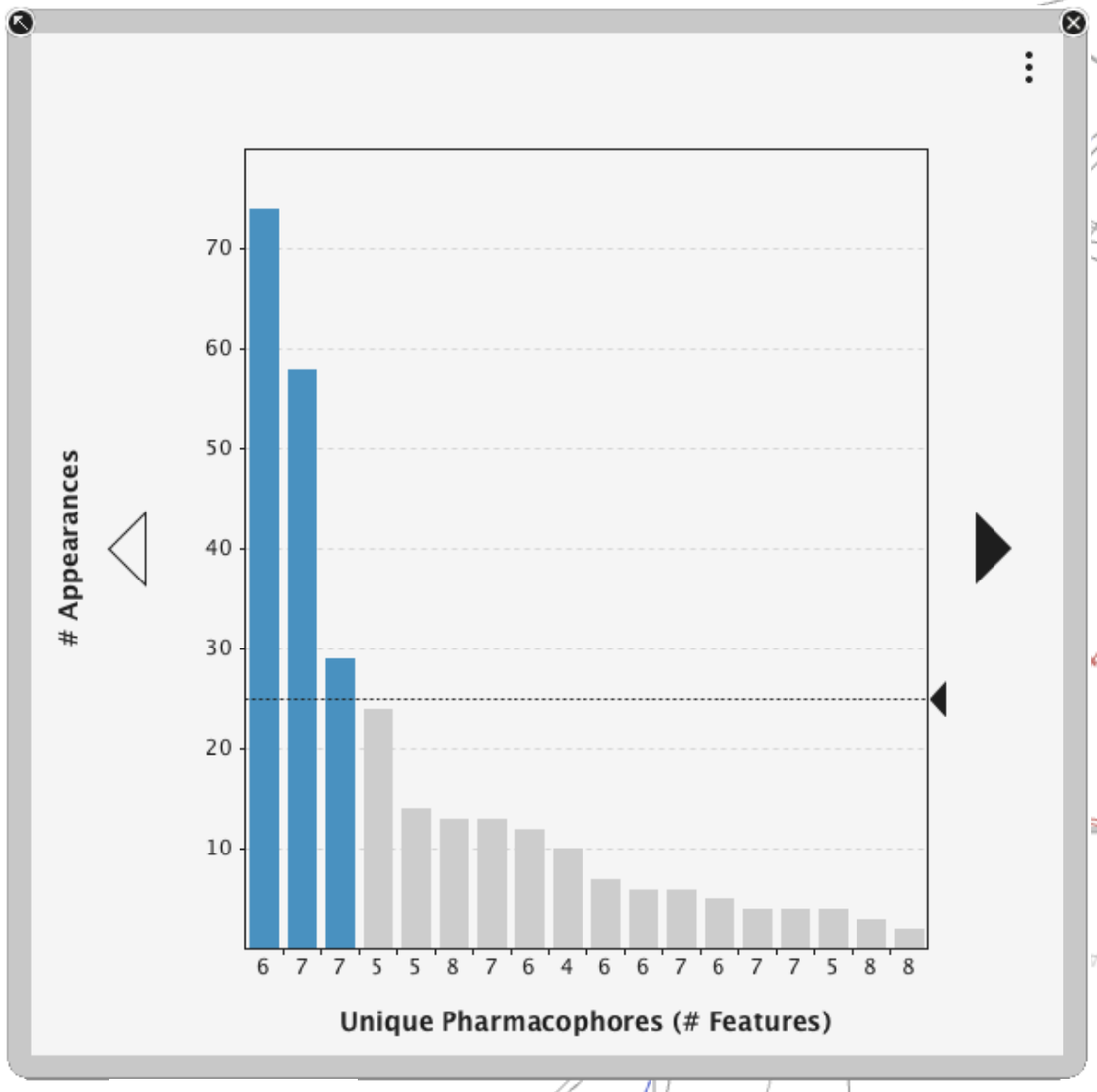

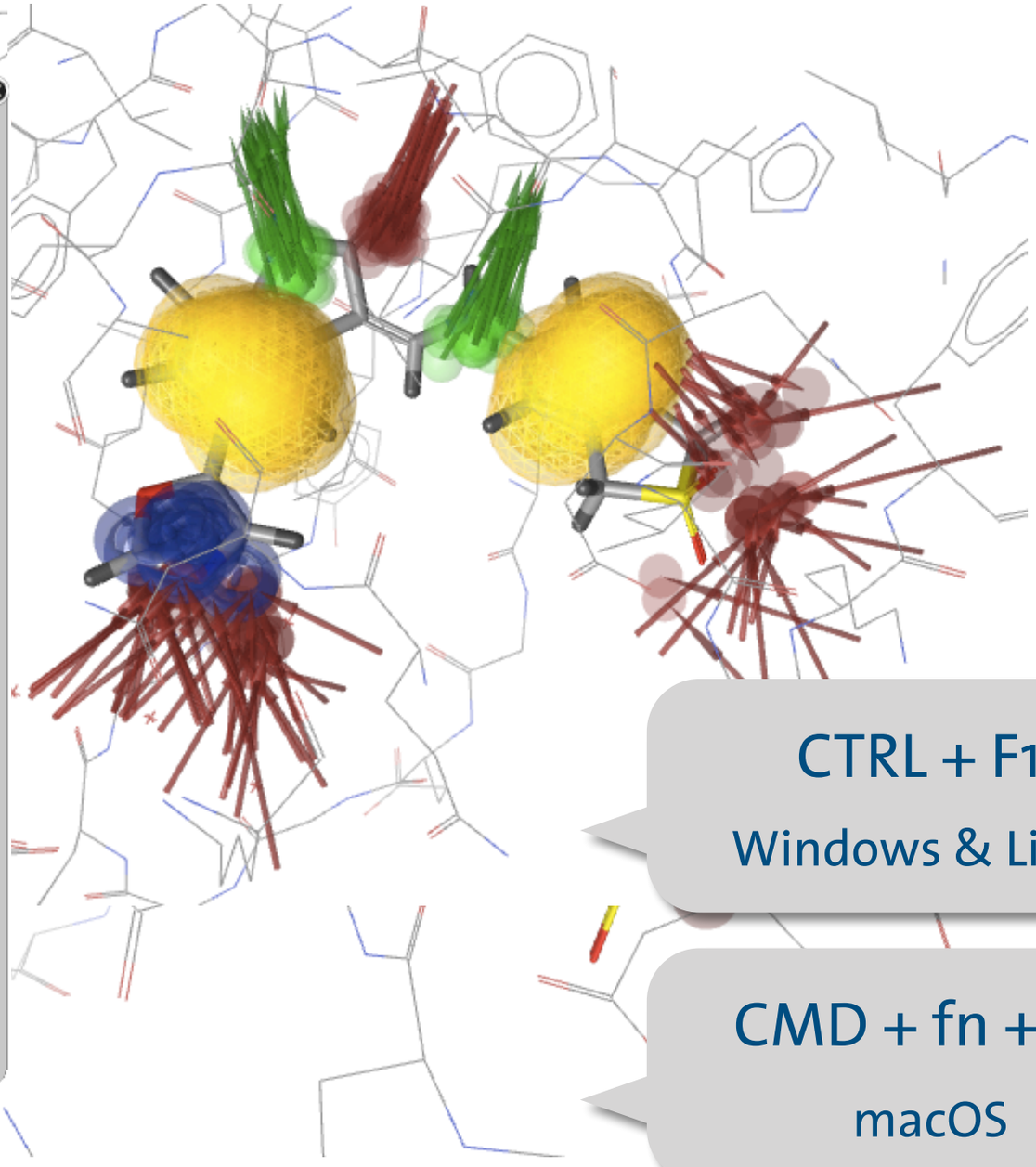

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macOS

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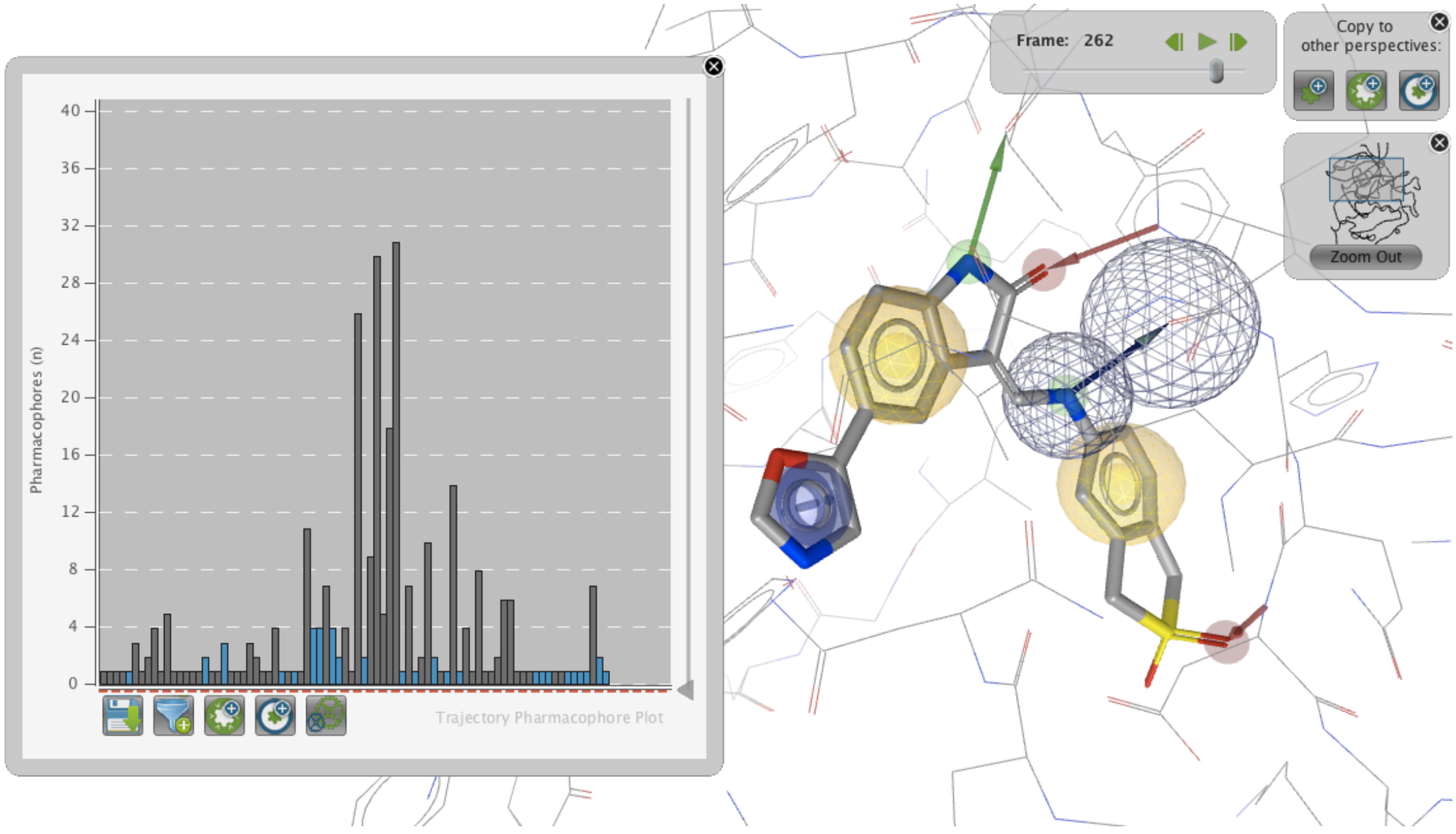
Tools for Pharmacophore-based MD Analysis

- Find all frames containing a selected pharmacophore feature



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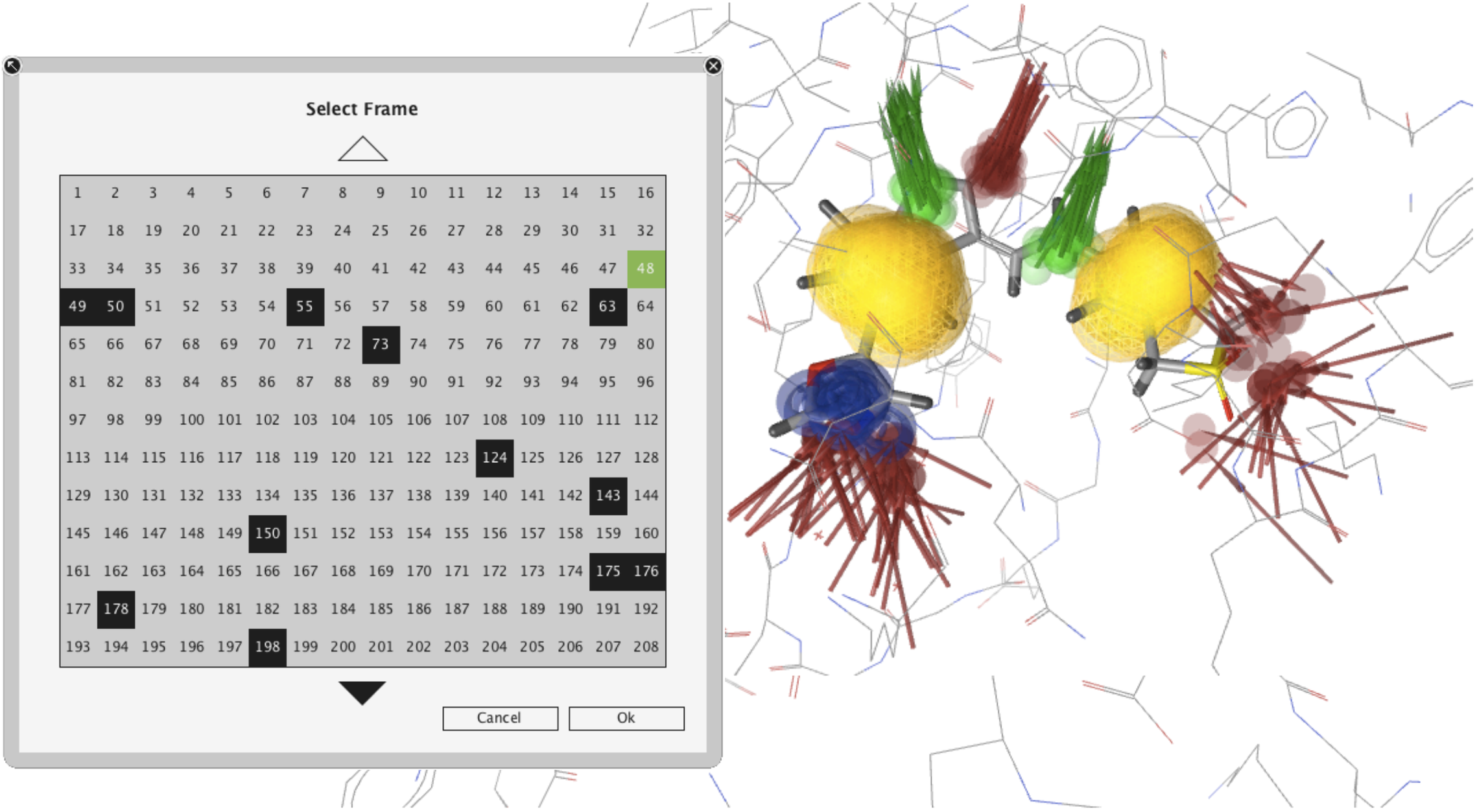

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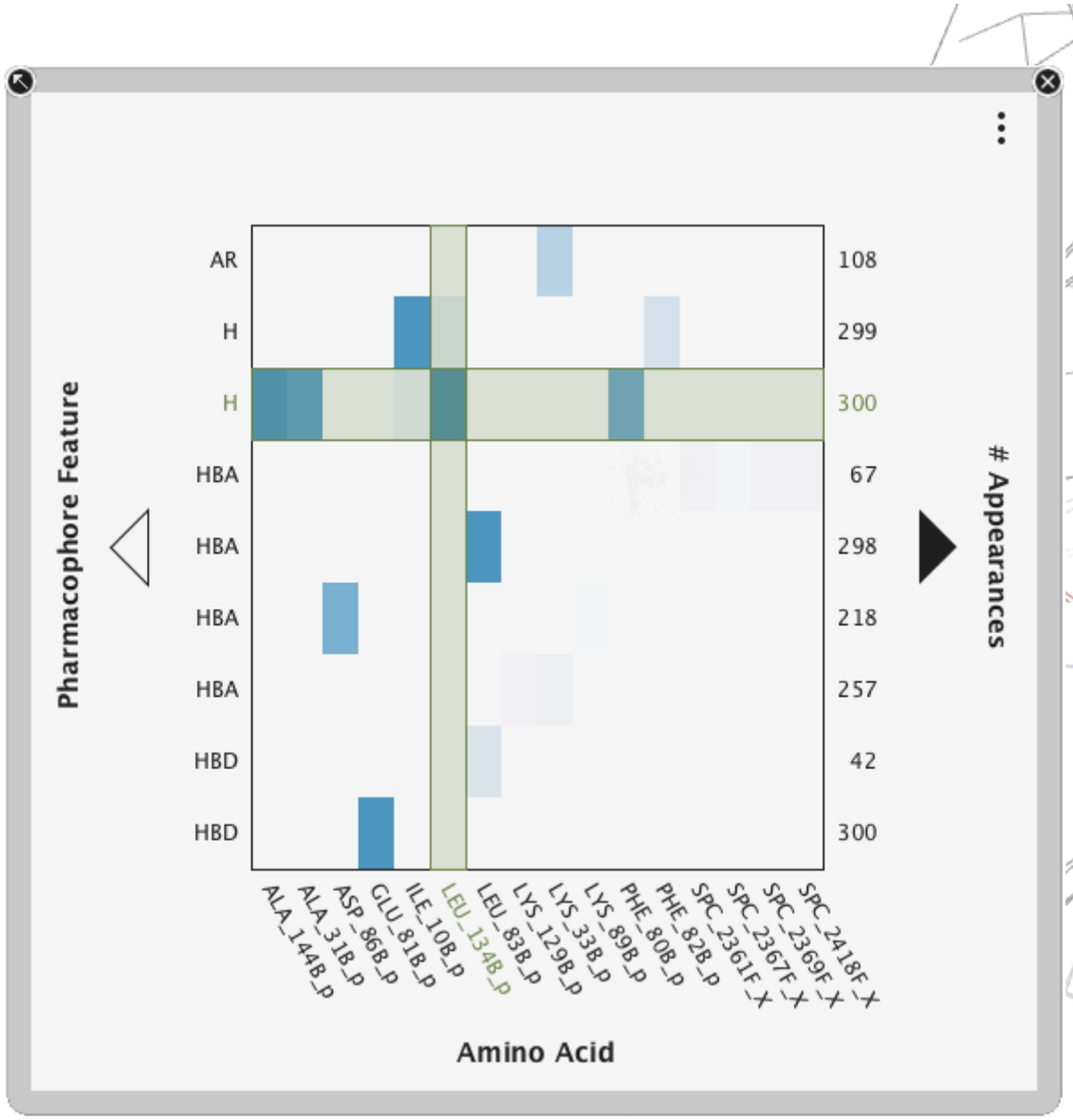
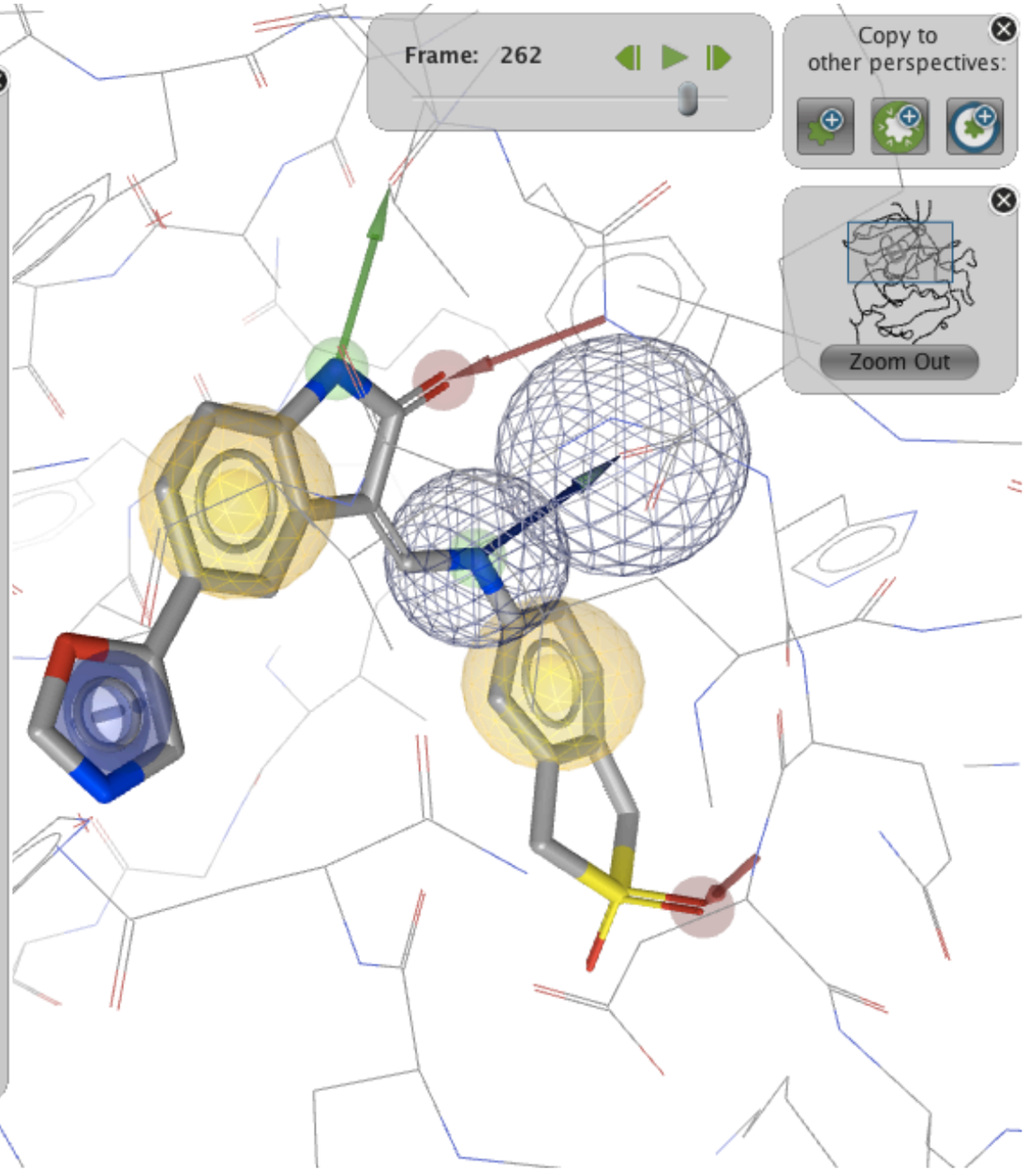
Tools for Pharmacophore-based MD Analysis

- Display pharmacophore interaction map





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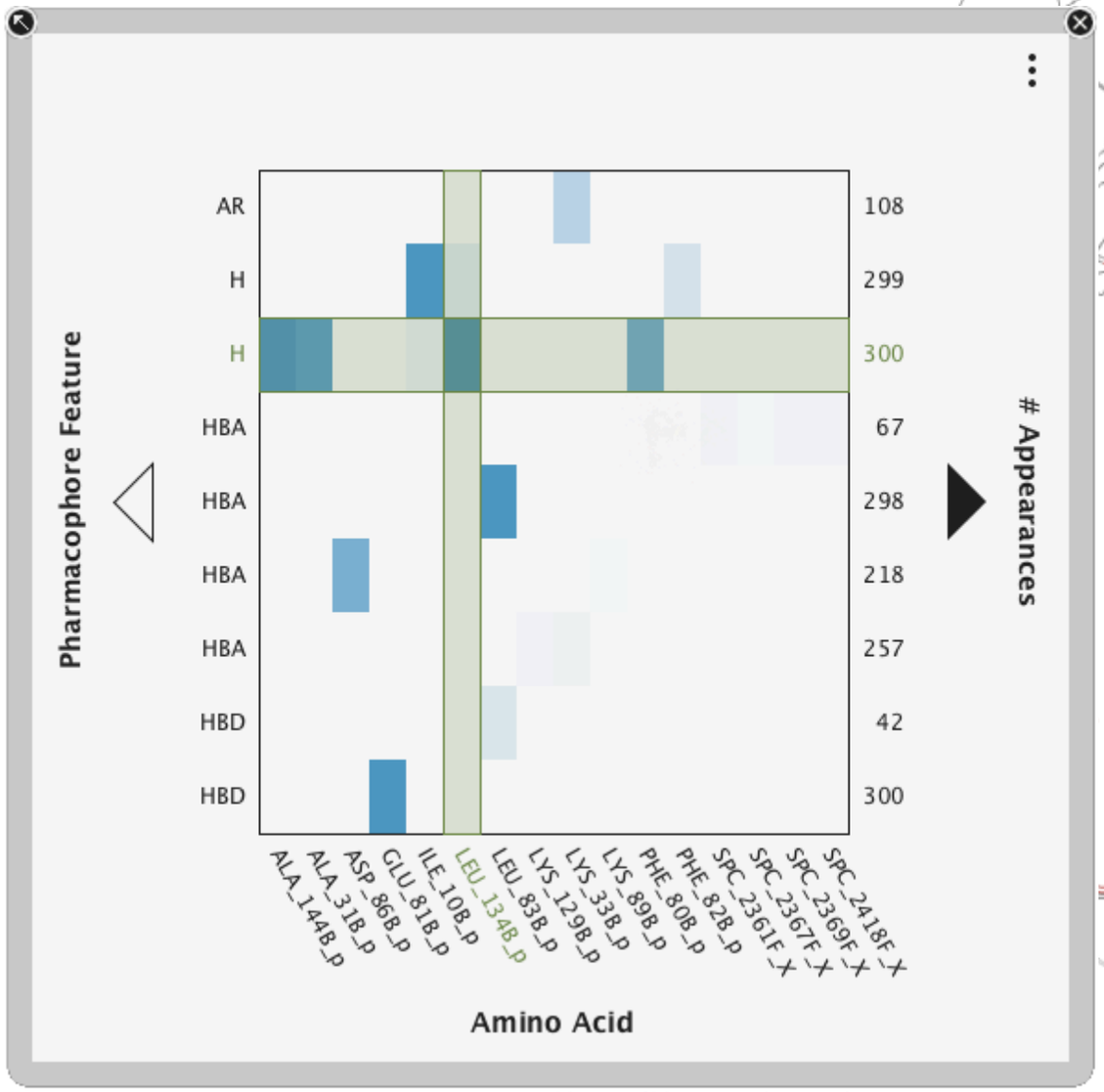
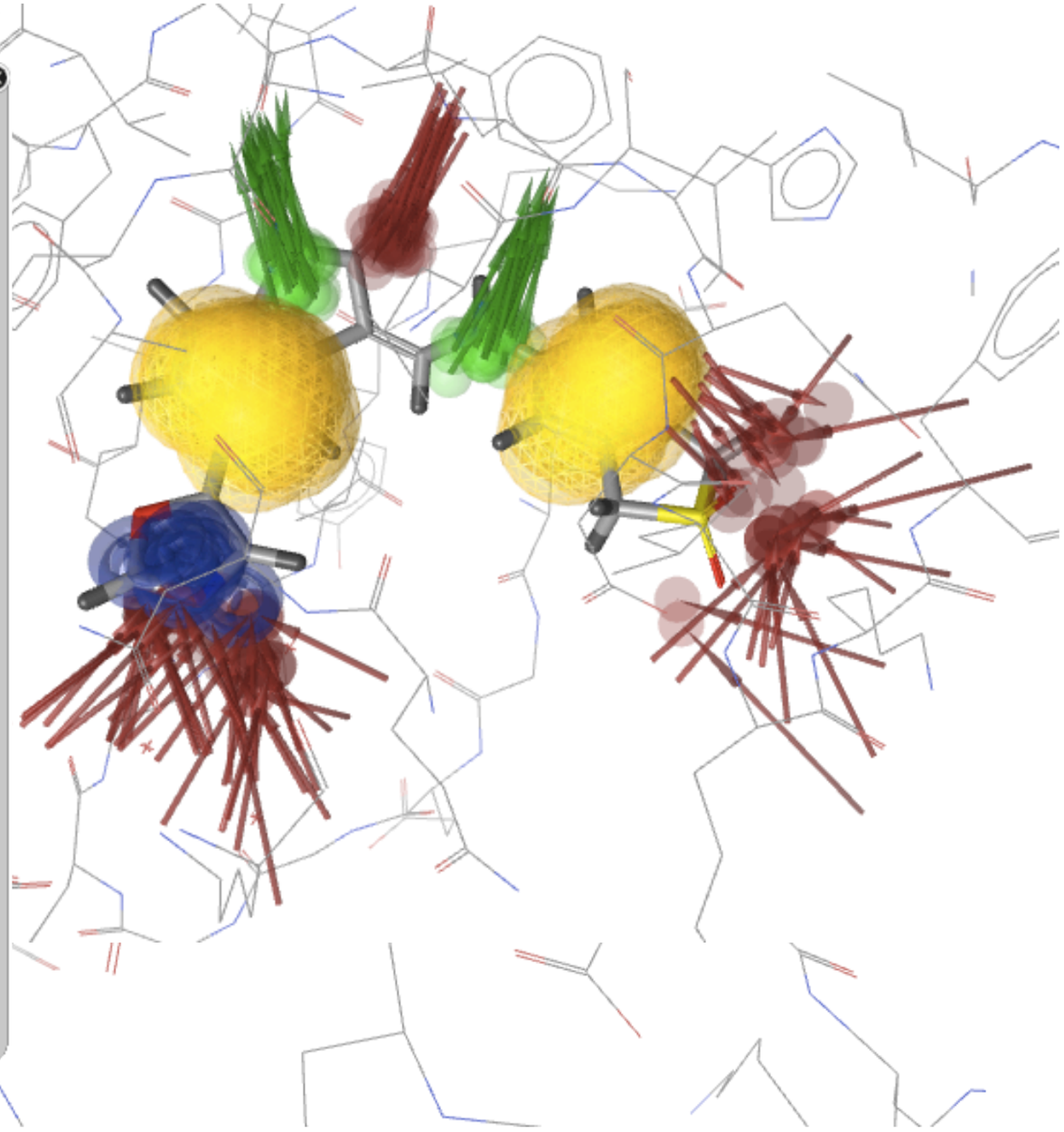
- Display pharmacophore interaction map





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New Features in LigandScout 4.1

Usability Enhancement

- Drag & Drop
- Extended pharmacophore editing
- Extended table functionality & export
- Automatic background job queuing system

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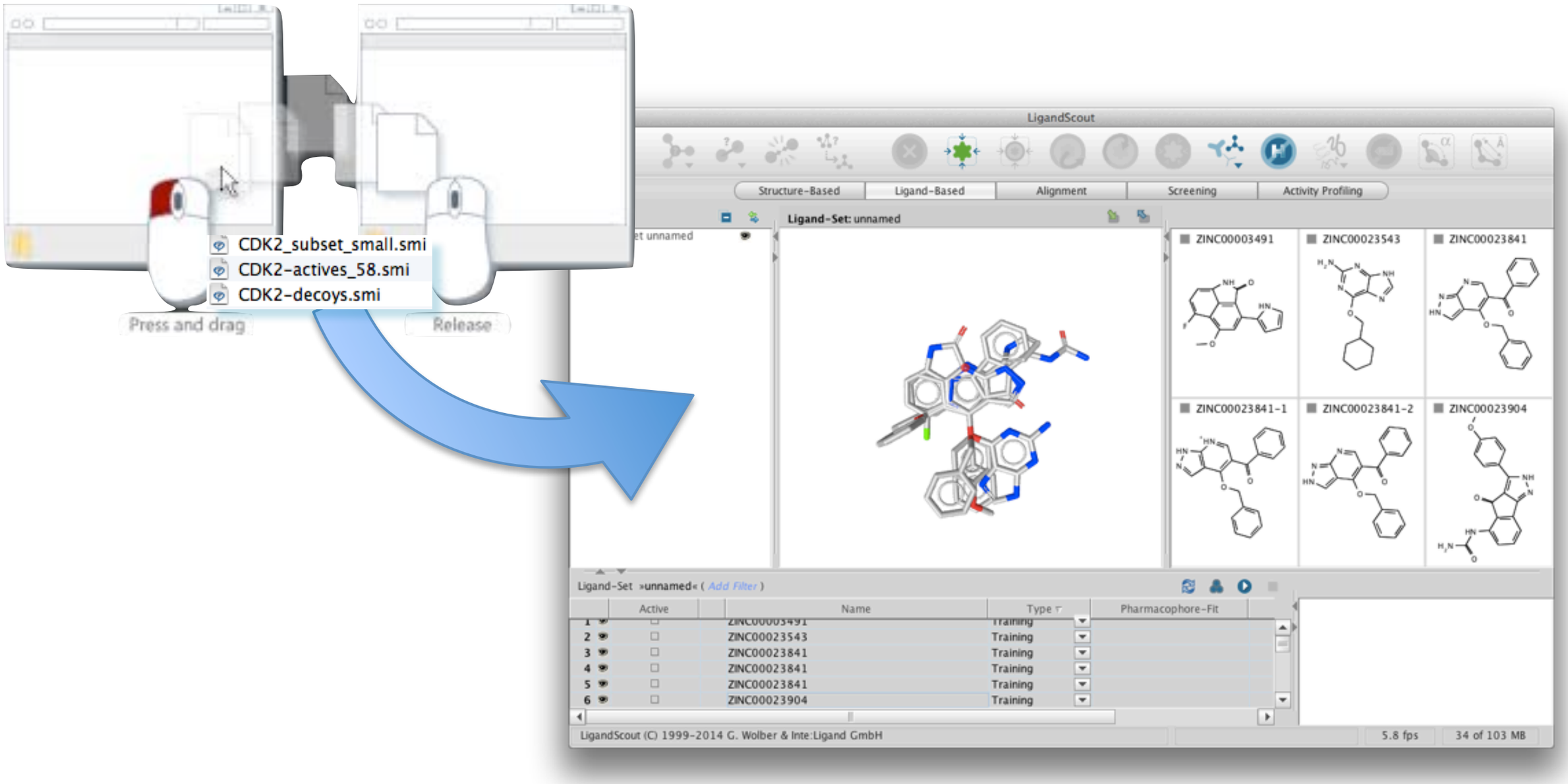
Drag & Drop Molecule Files into GUI



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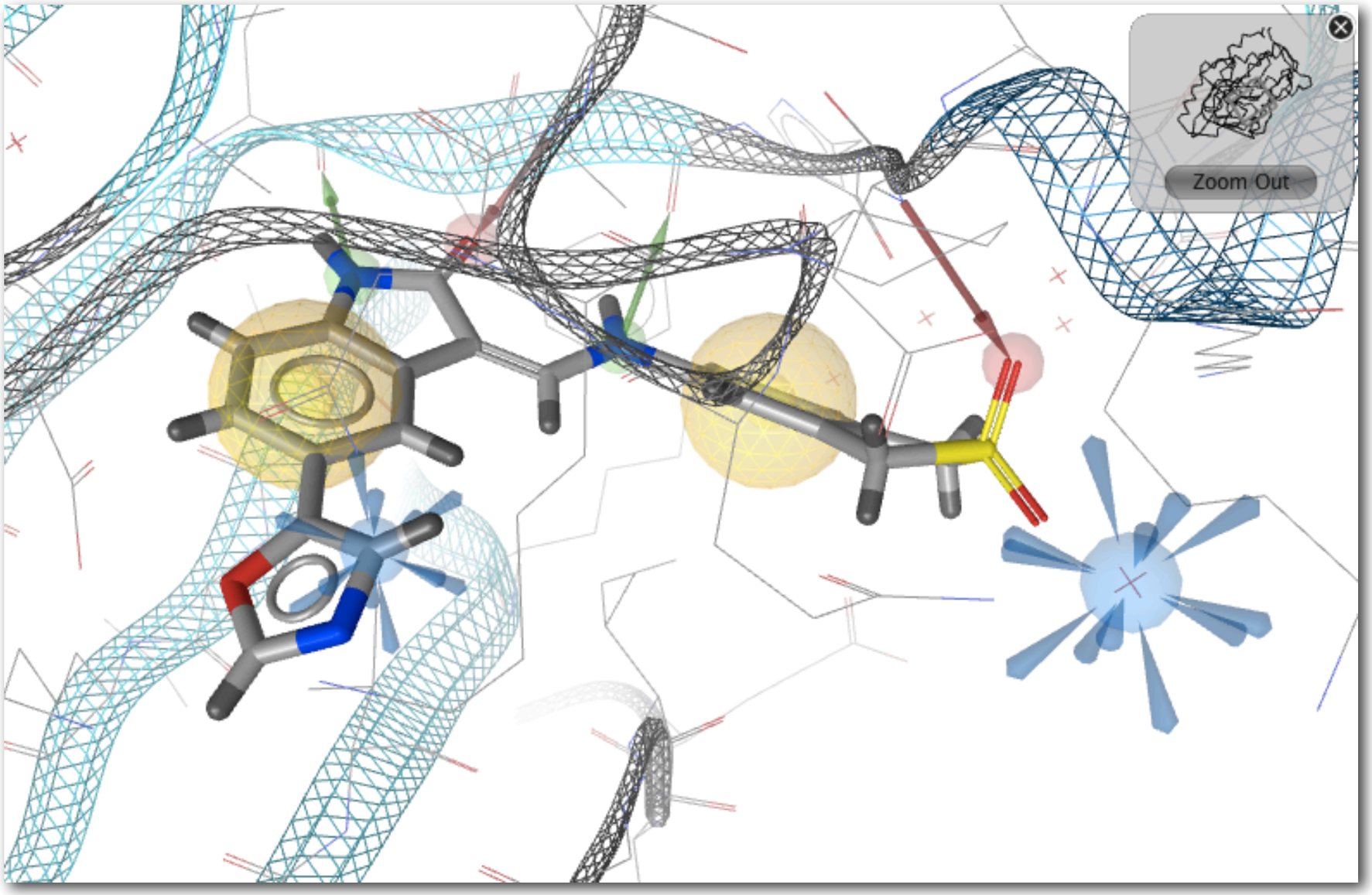
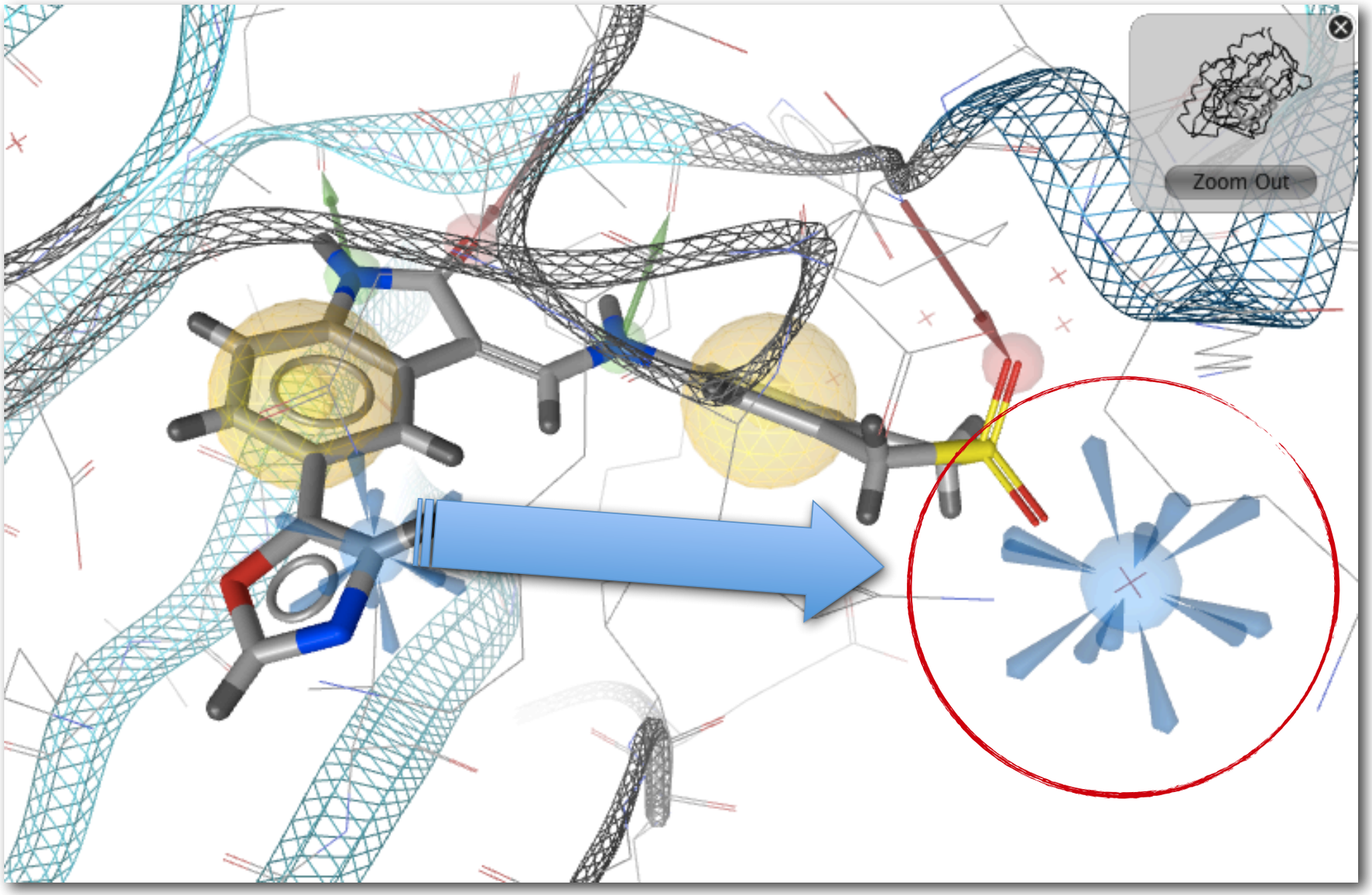
Extended Pharmacophore Editing

- Move pharmacophore features in 3D space



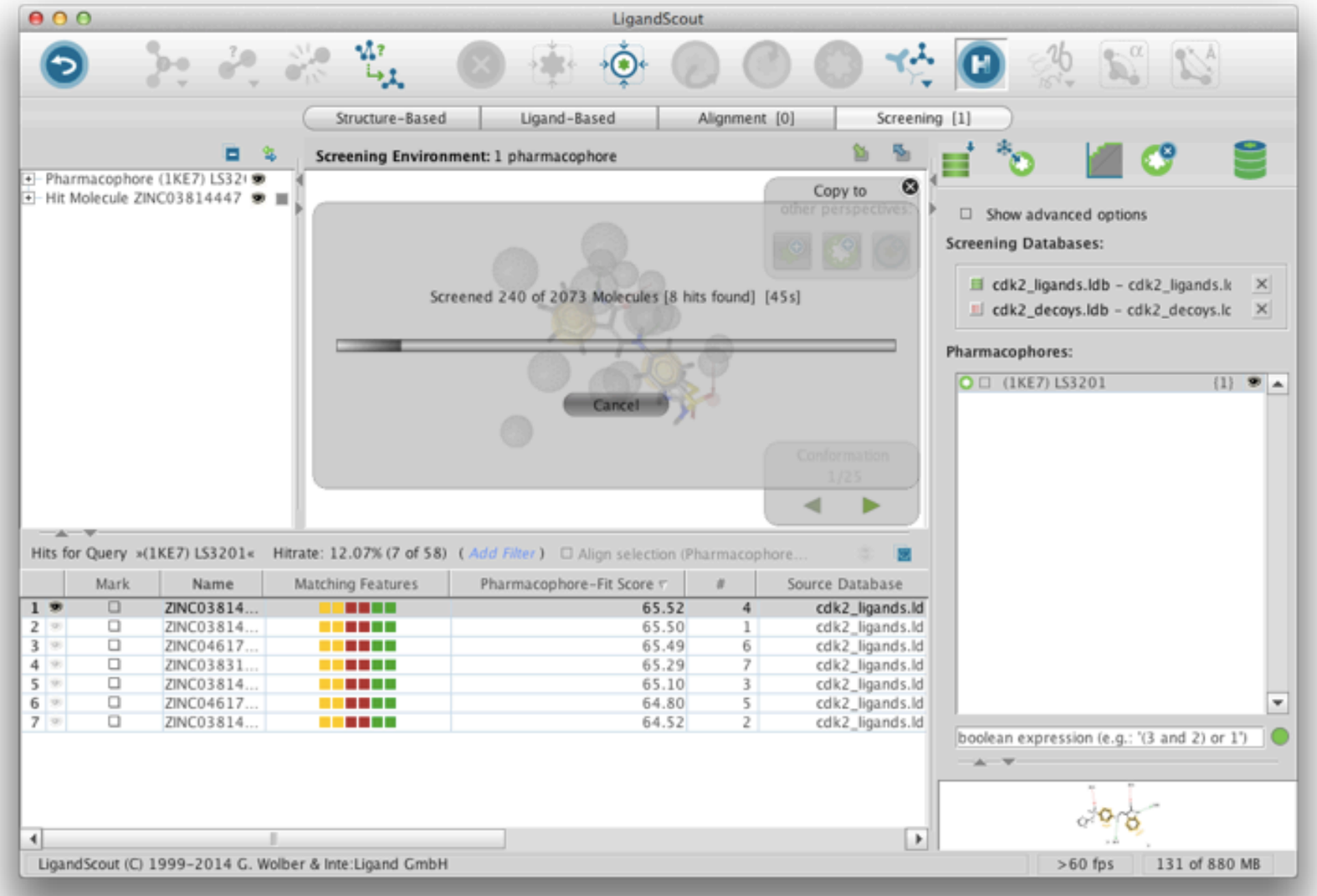
Extended Pharmacophore Editing

- Move pharmacophore features in 3D space



Background Job Queuing System

e.g. while screening in the GUI, continue modeling ...



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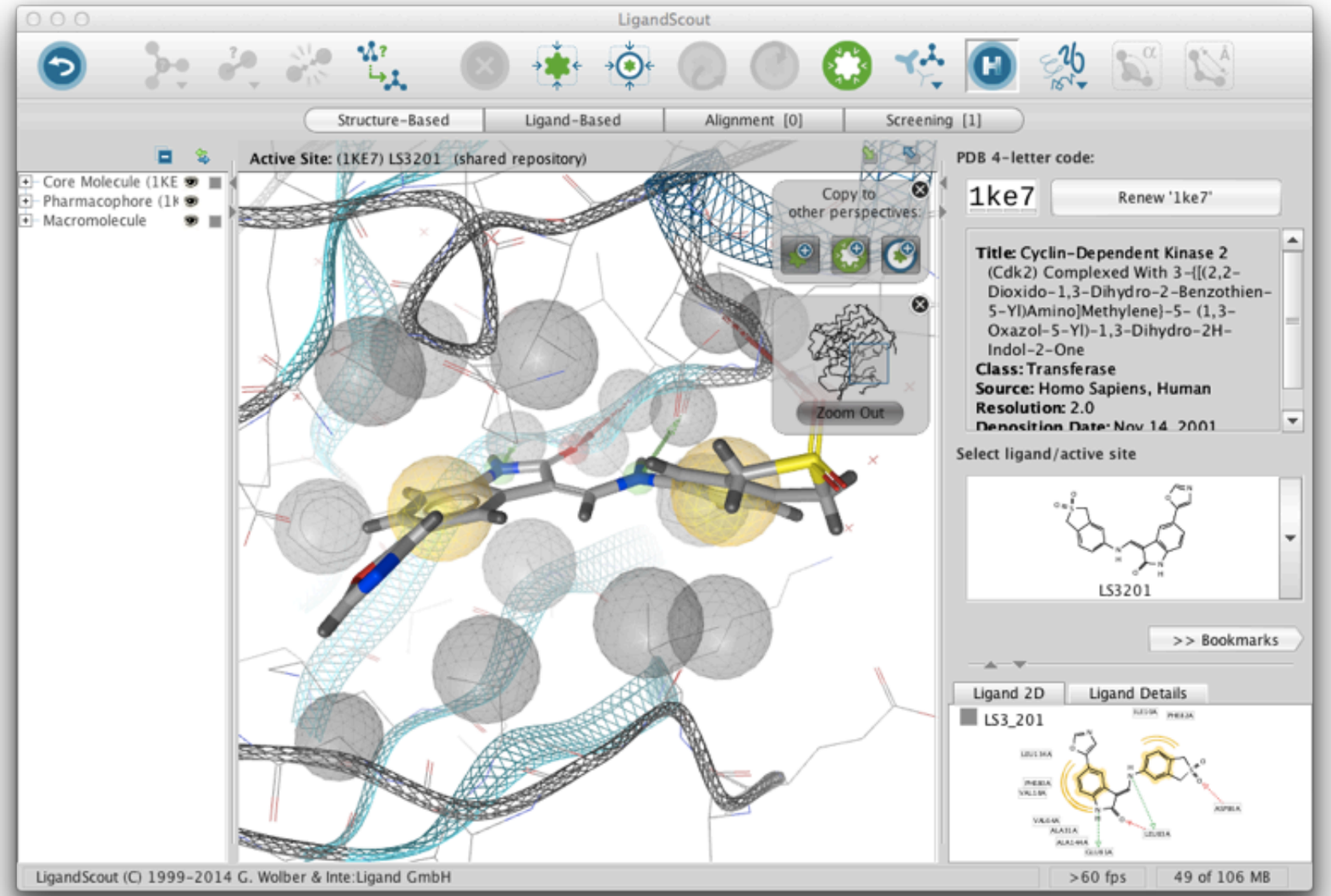

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New Features in LigandScout 4.1

Usability Enhancement

- Drag & Drop
- Extended pharmacophore editing
- Extended table functionality & export
- Automatic background job queuing system

New Functionality

- New conformer generator in addition to OMEGA
- Apo protein binding site pharmacophore generation
- Integration into KNIME workflow environment
- Molecular dynamics trajectory pharmacophore analysis
- Docking with AutoDock 4.2 / AutoDock Vina

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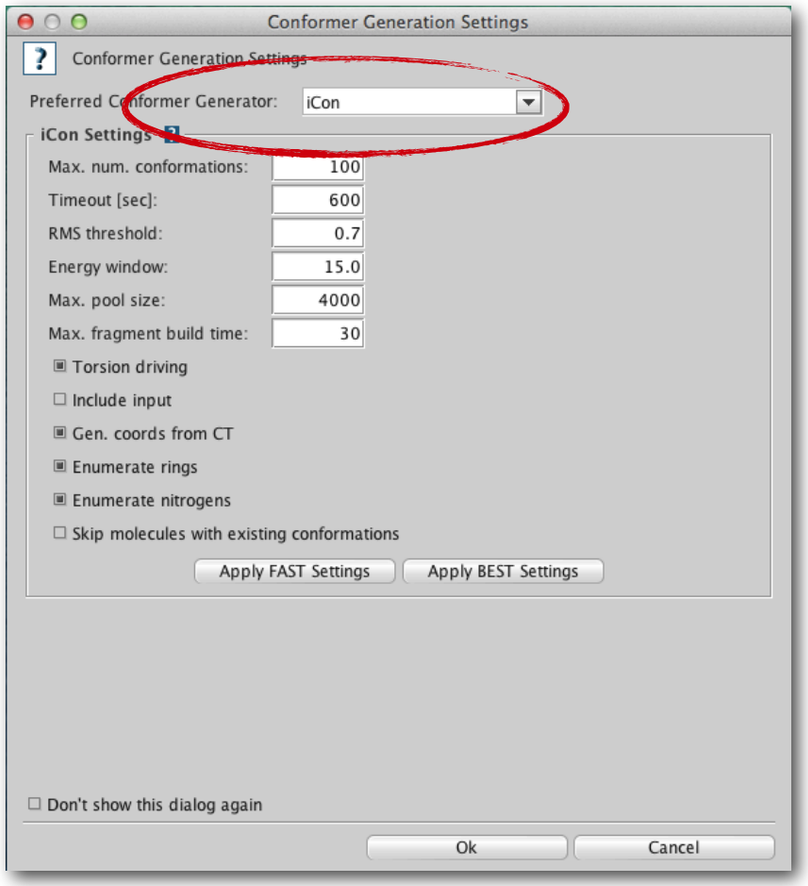
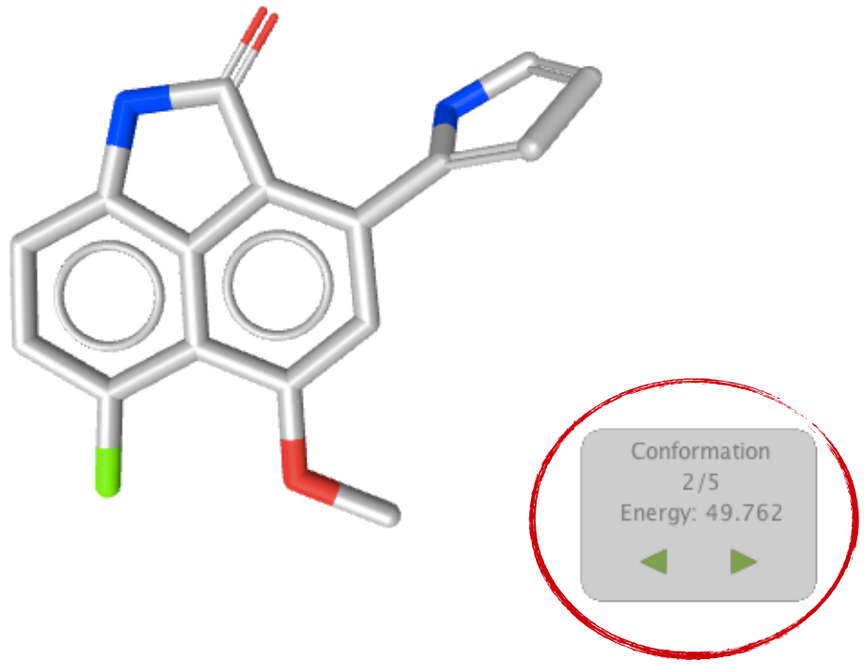
New Features in LigandScout 4.1

New conformer generator “iCon”

- Higher accuracy, better conversion rate
- Visualization of conformational energy values





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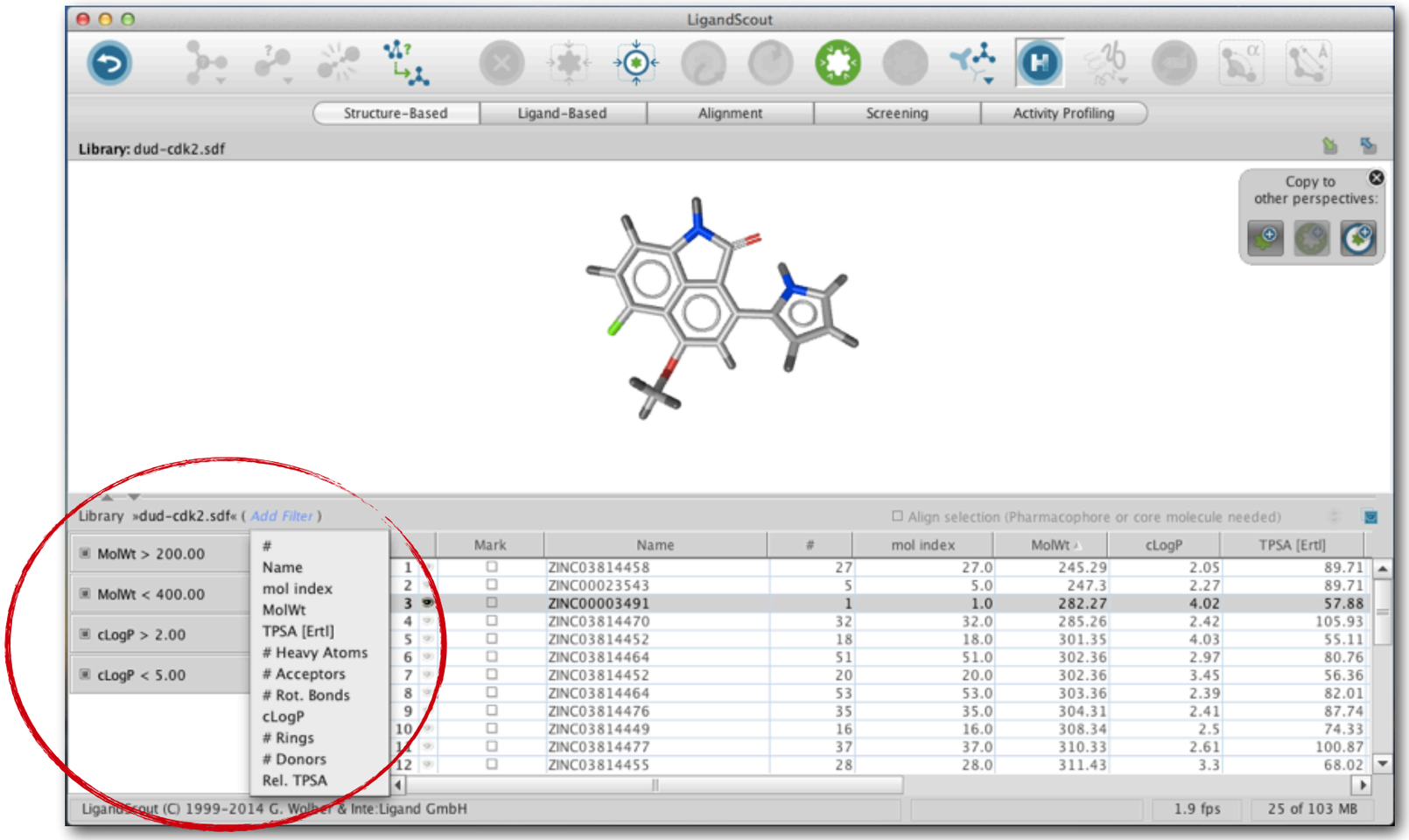
Extensive Table Management

New: Relational database behind each table

- allows rapid filtering and selecting of data subsets



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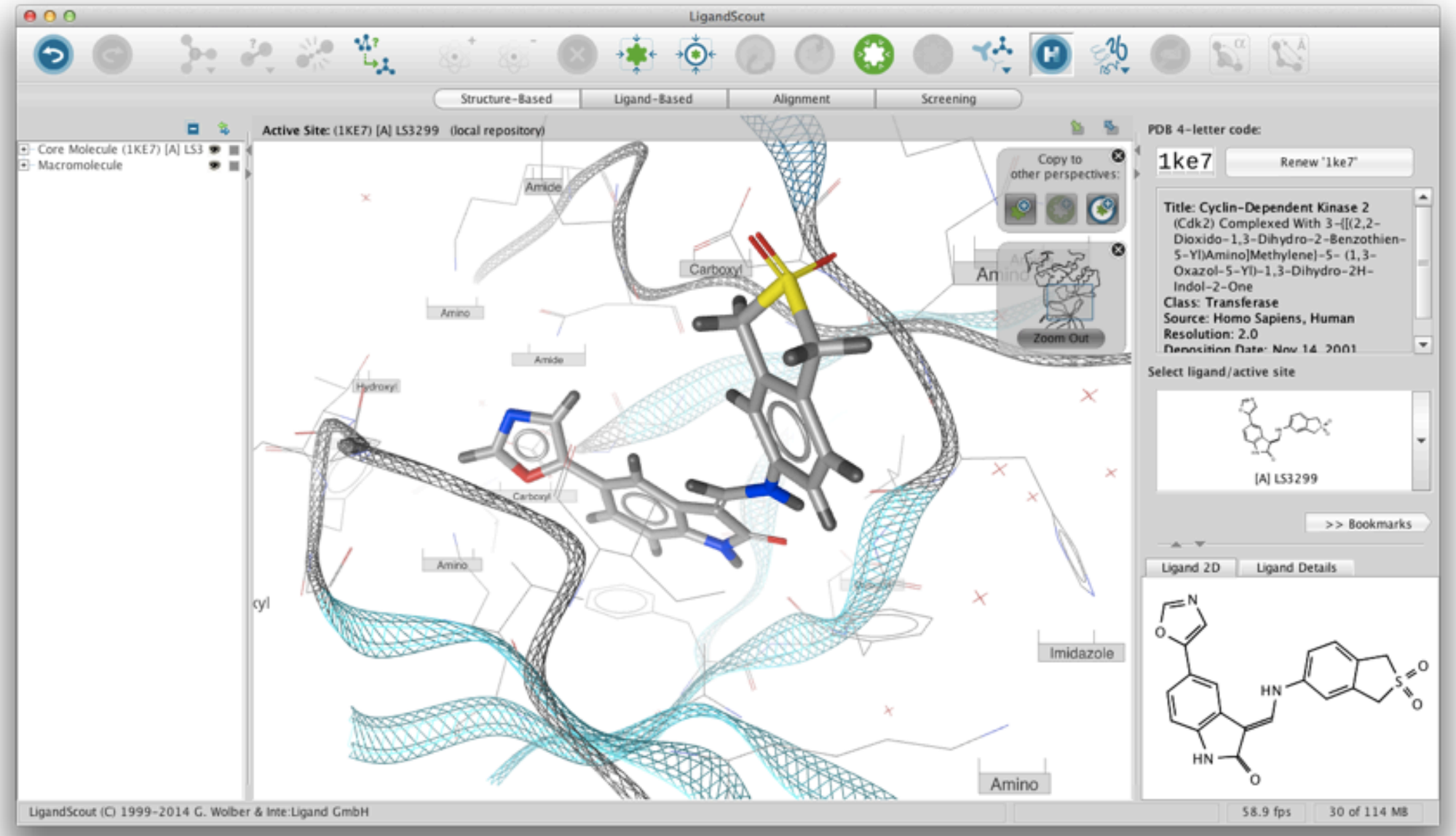
Binding Site Amino Acid Analysis & Editing



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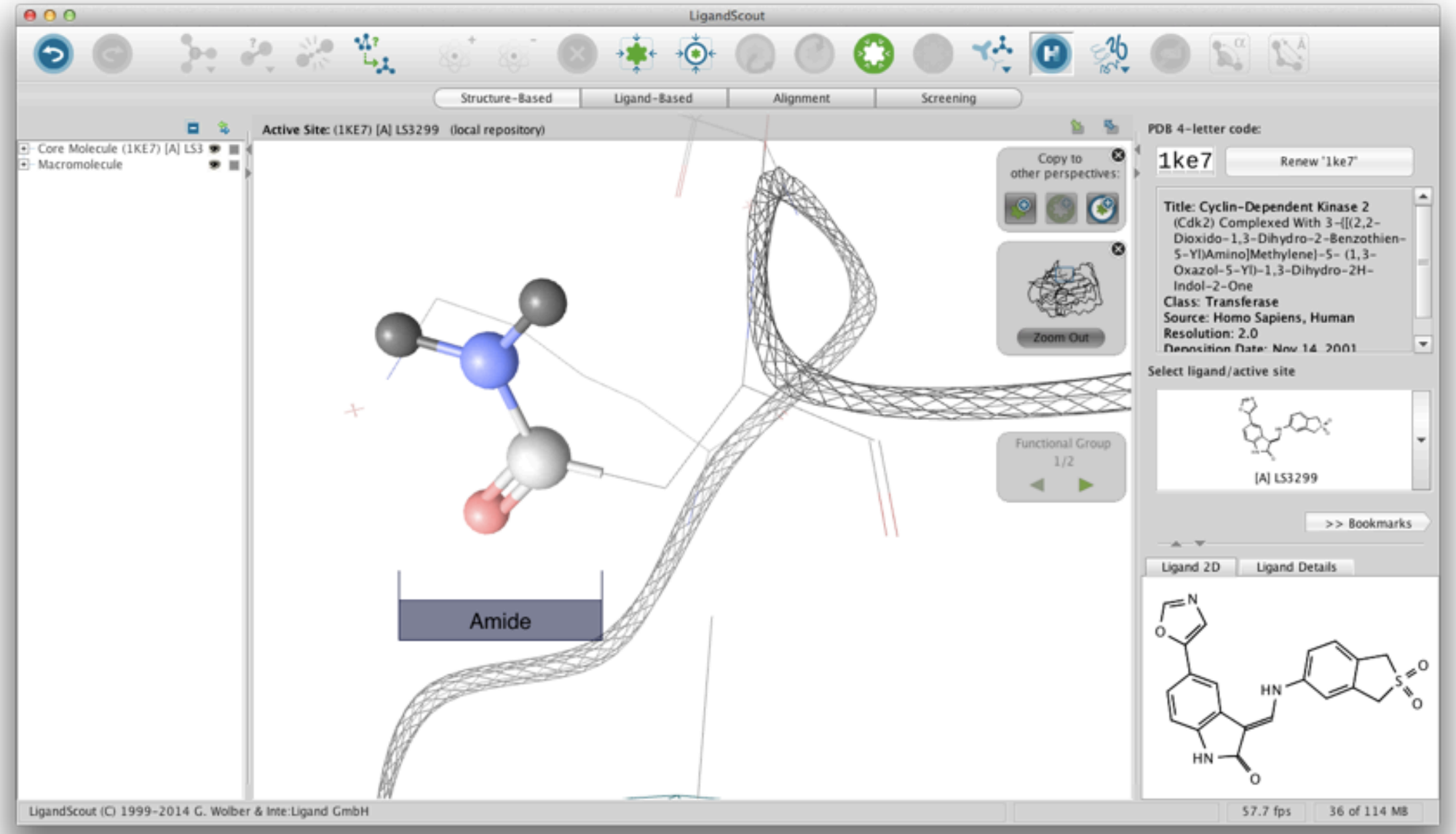
Binding Site Amino Acid Analysis & Editing



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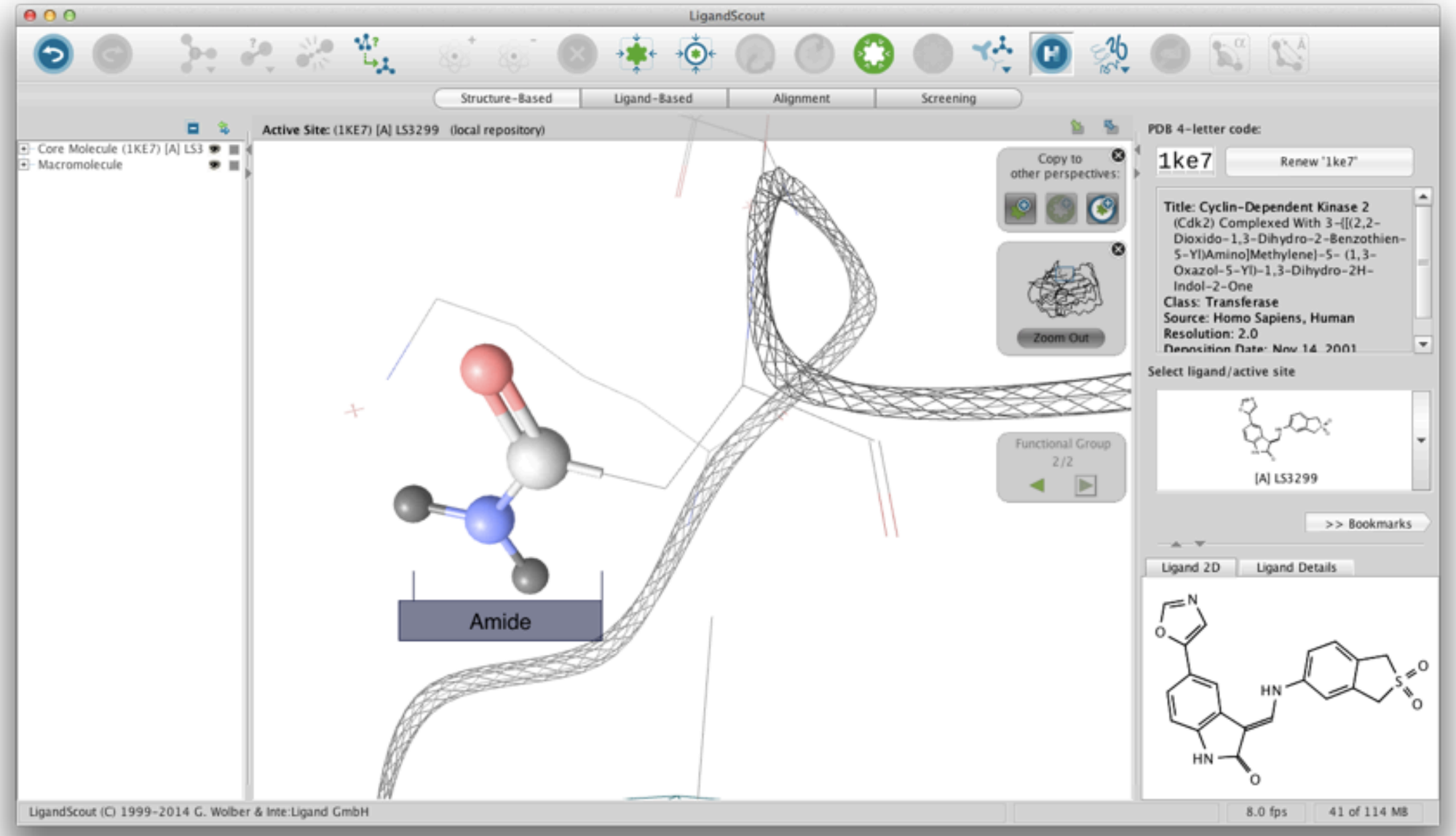
Binding Site Amino Acid Analysis & Editing



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Create Pharmacophores from Apo Protein Site

Intuitive modeling of pharmacophores in empty binding sites (e.g in apo protein / allosteric sites)

- Detect protein pockets using the Pocket Finder
- Calculate a grid-based ligand accessible surface
- Calculate interaction feature probabilities
- Create automatically customized apo-site model
- User can add pharmacophore features on surface points

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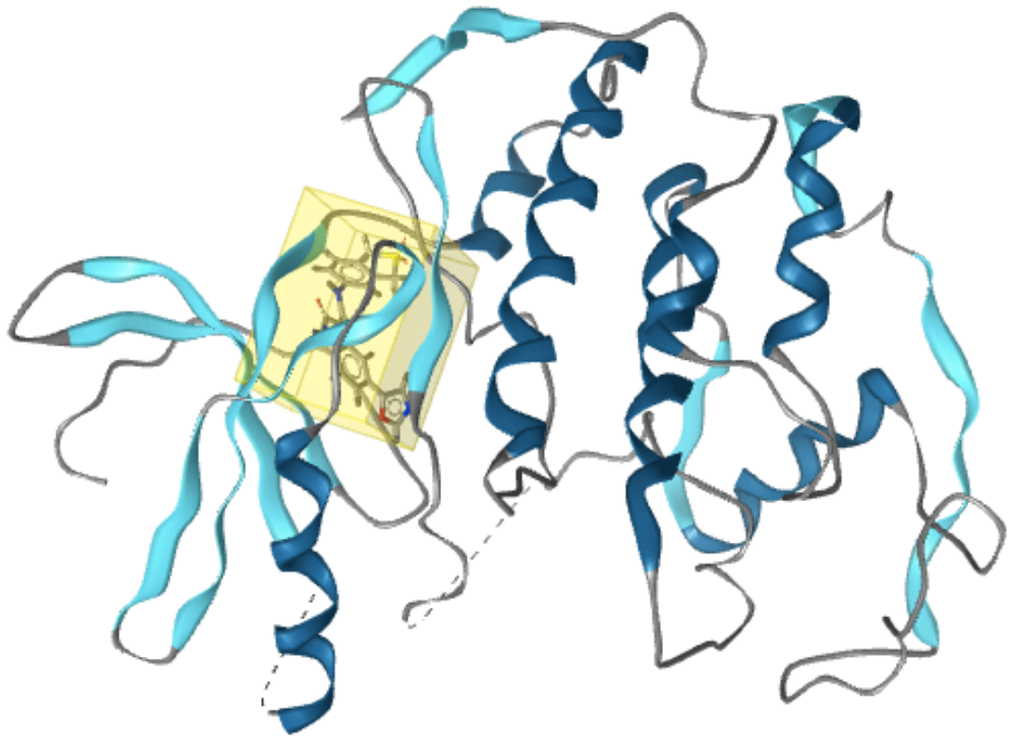
Explore Empty Protein Sites

- Create binding sites wherever you want or use the new pocket finder



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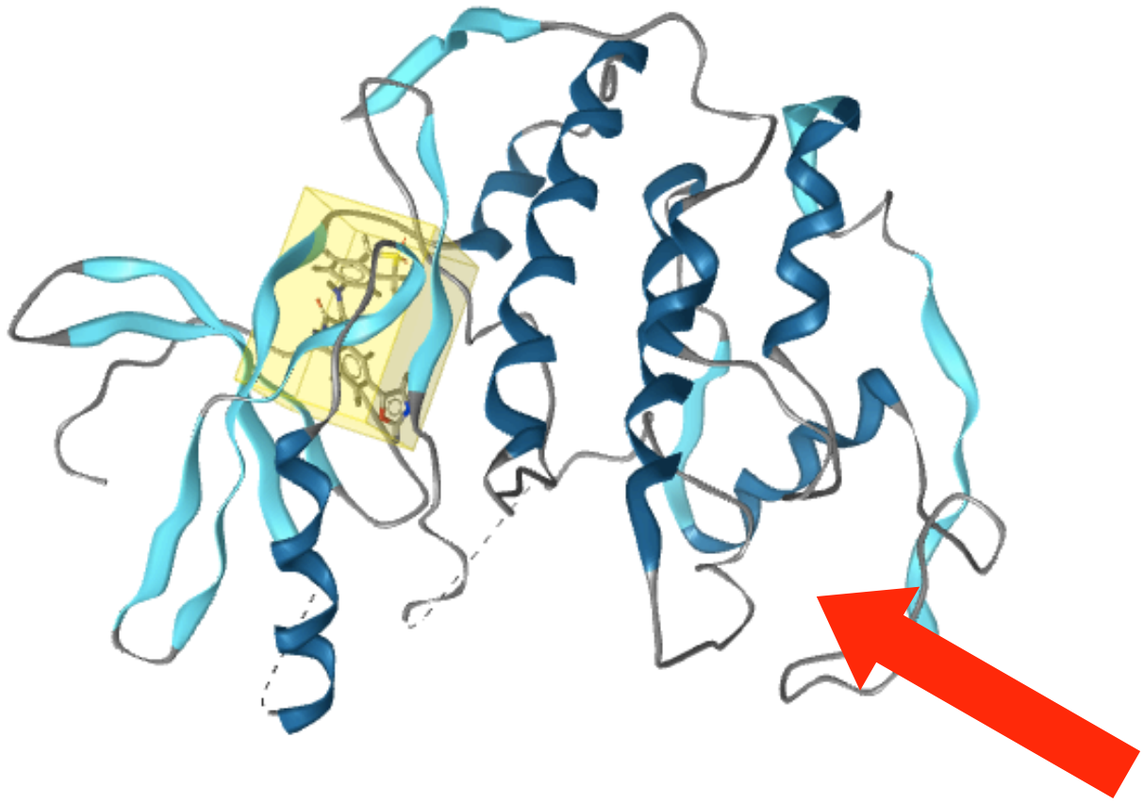

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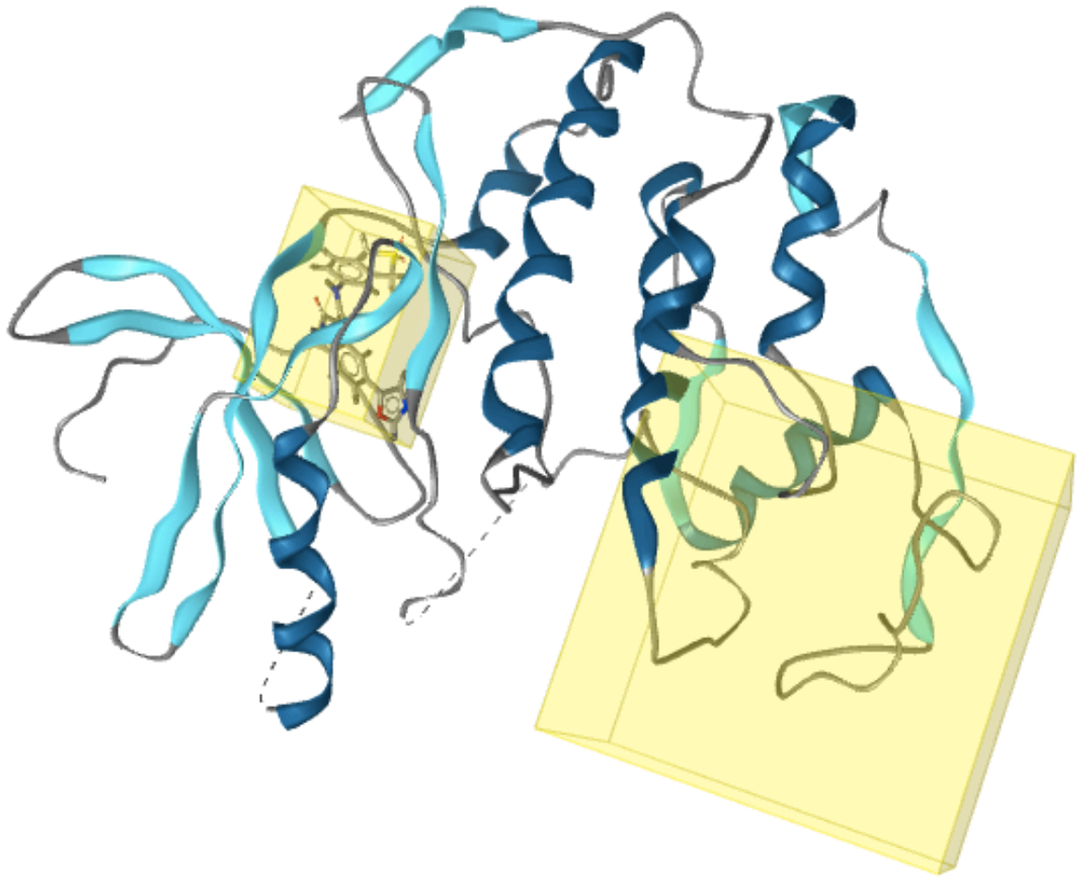
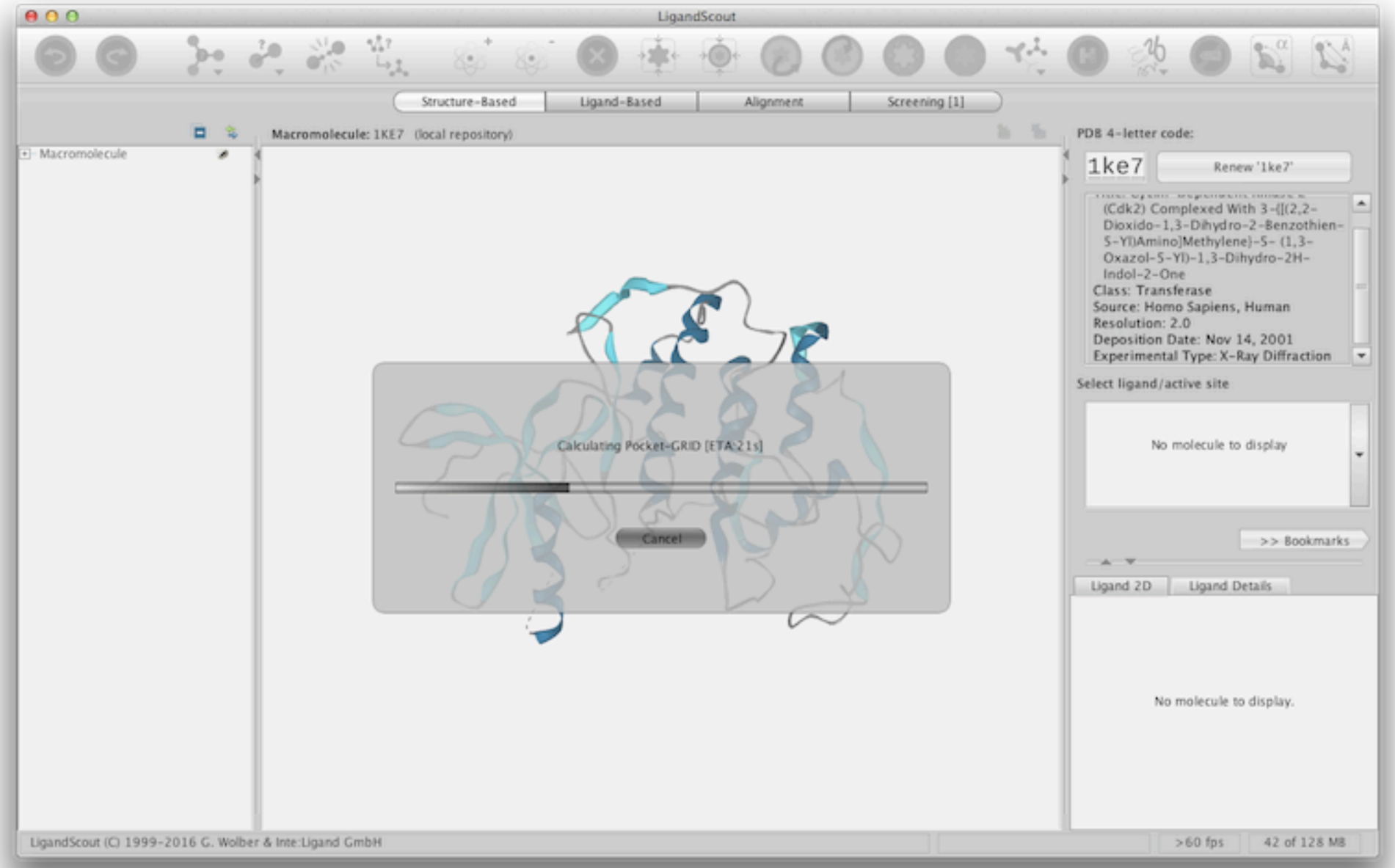


Pocket Finder



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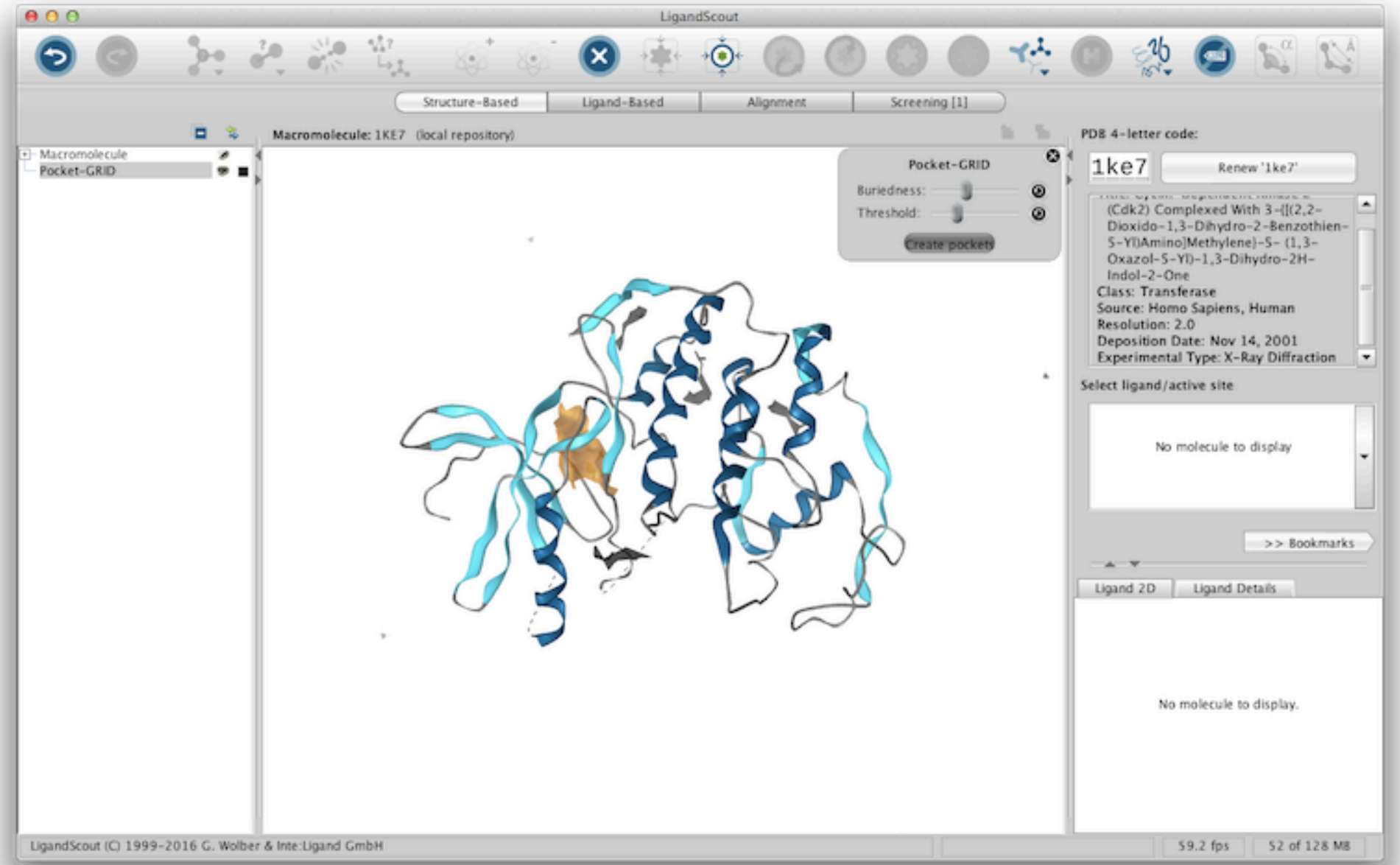
Pocket Finder



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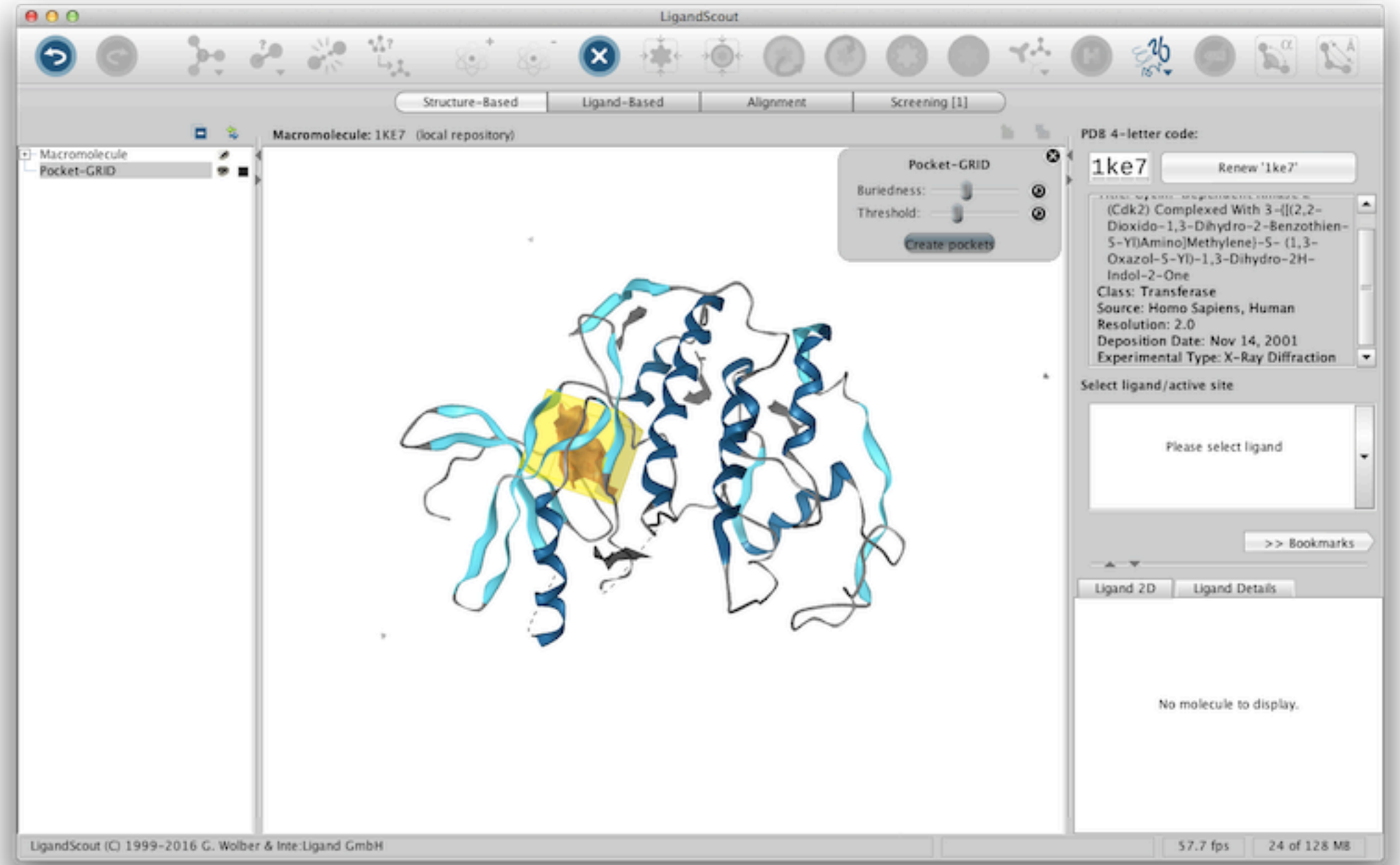
Pocket Finder



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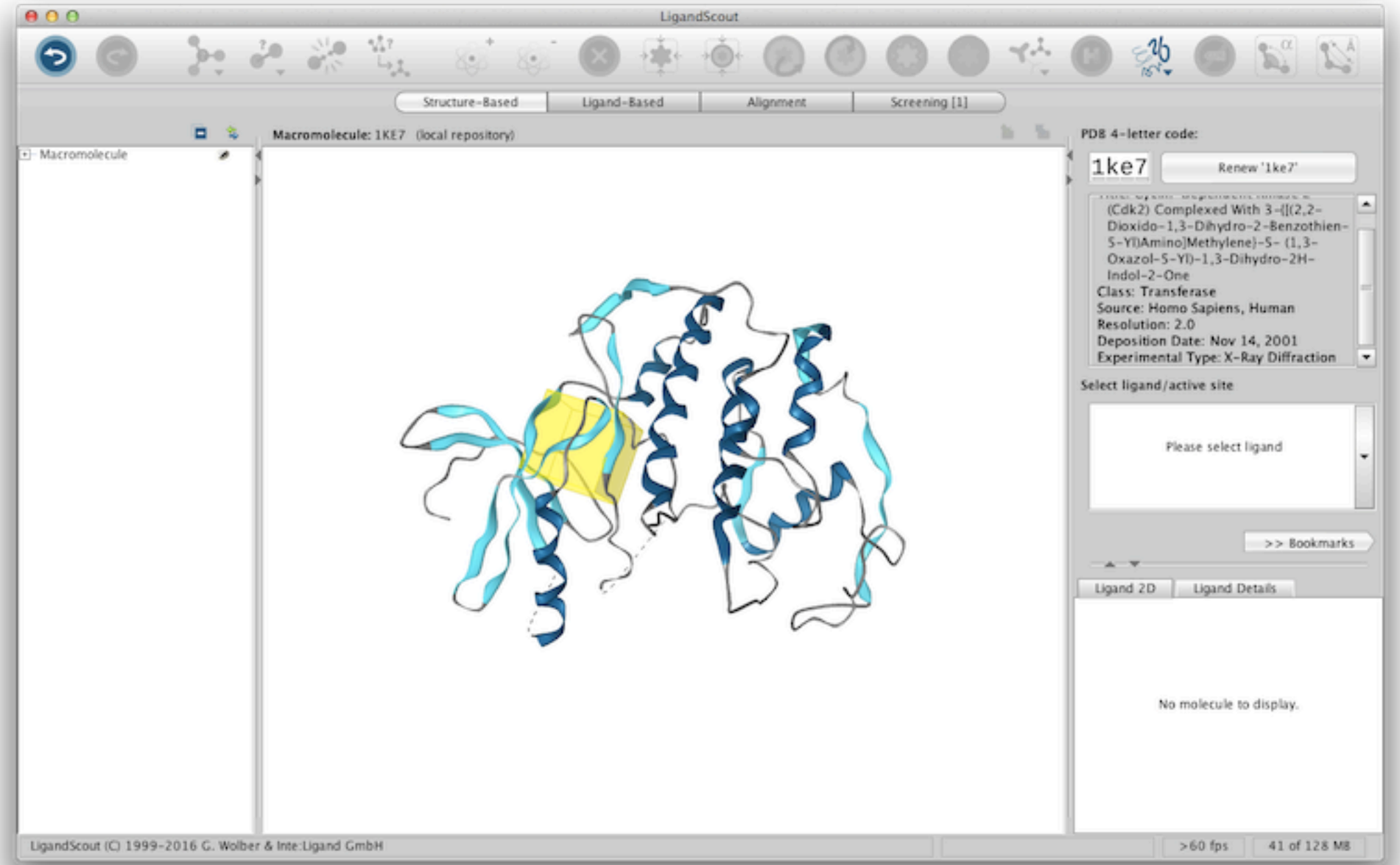
Pocket Finder



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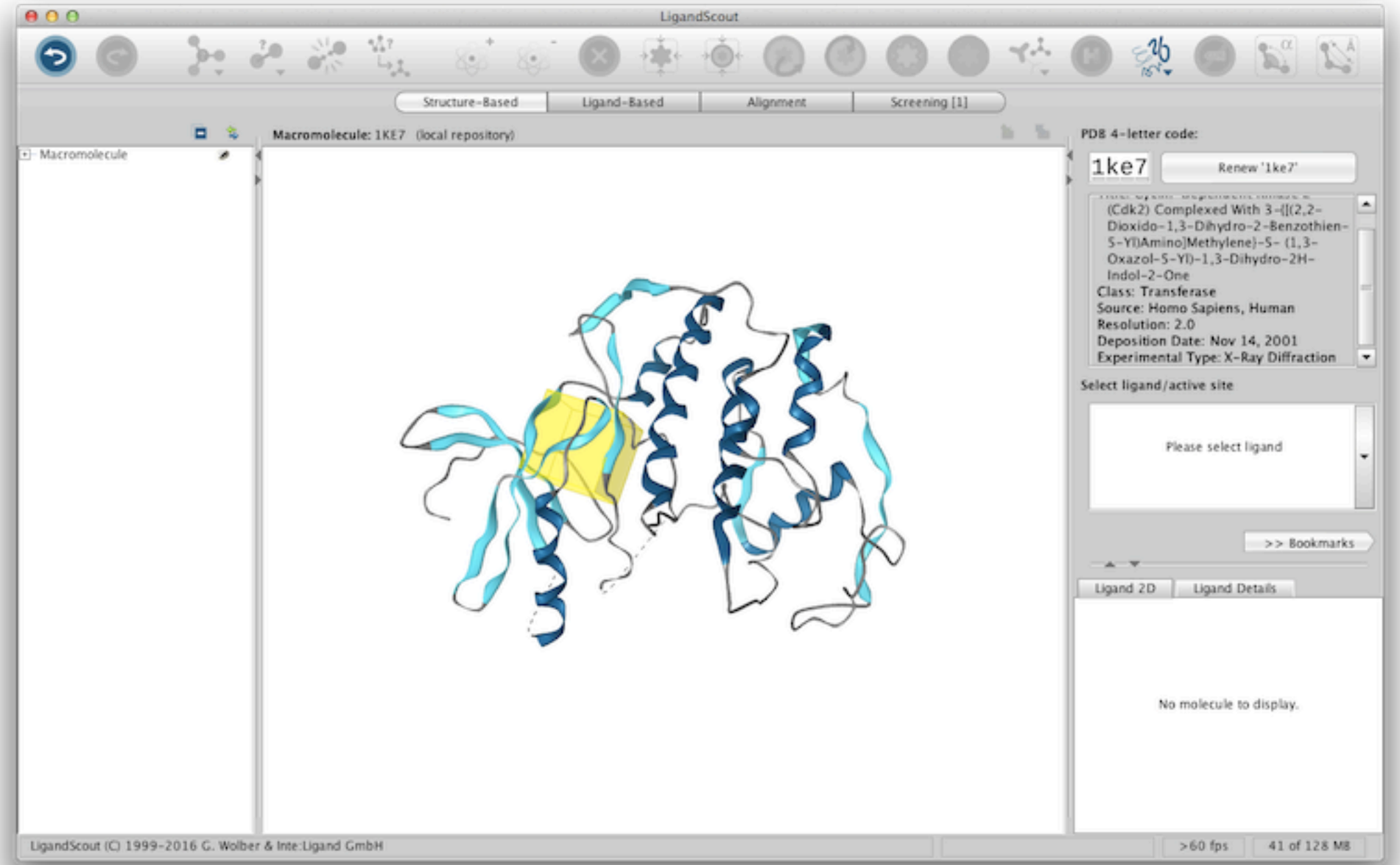
Comparison with Original Ligand Position



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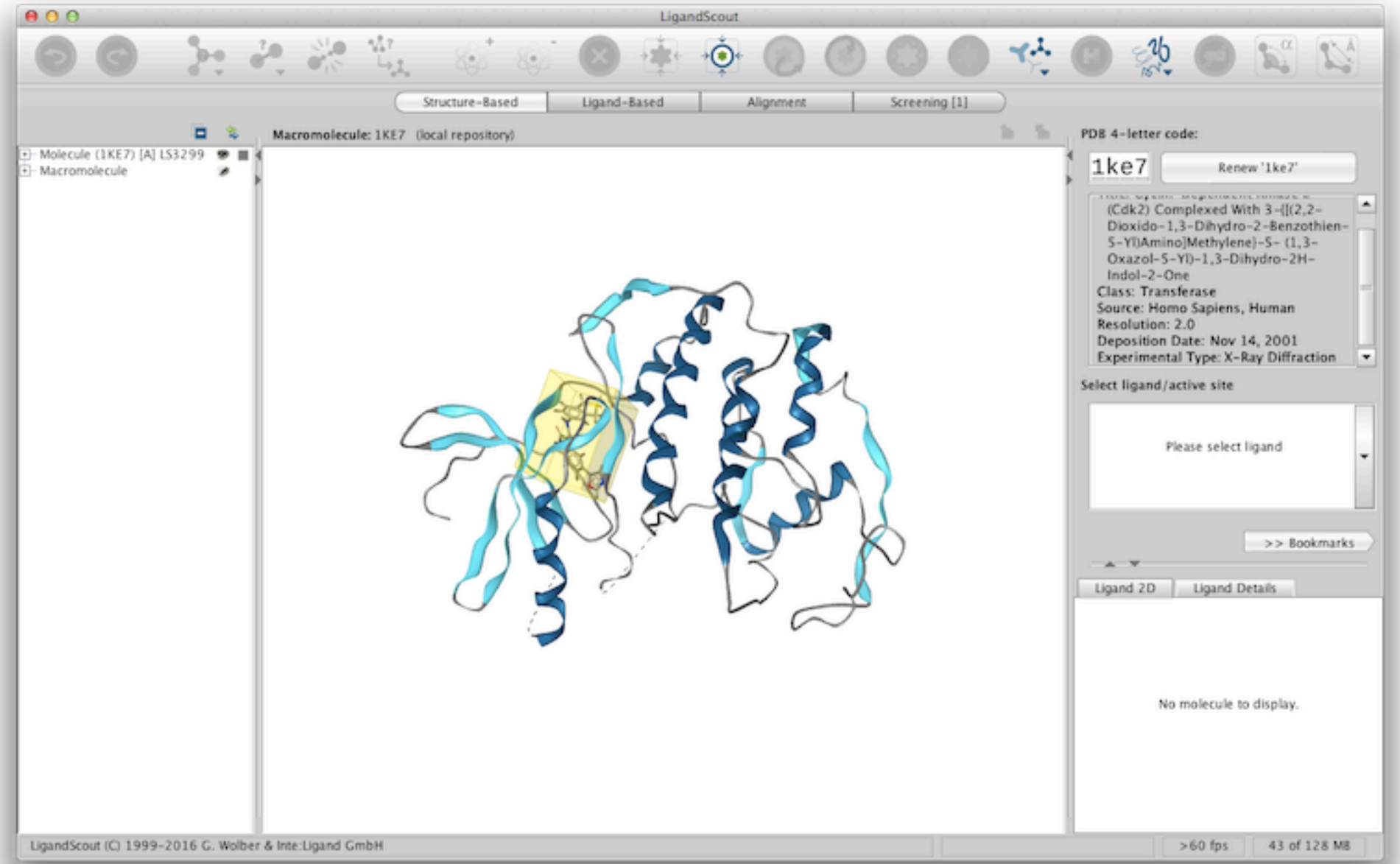

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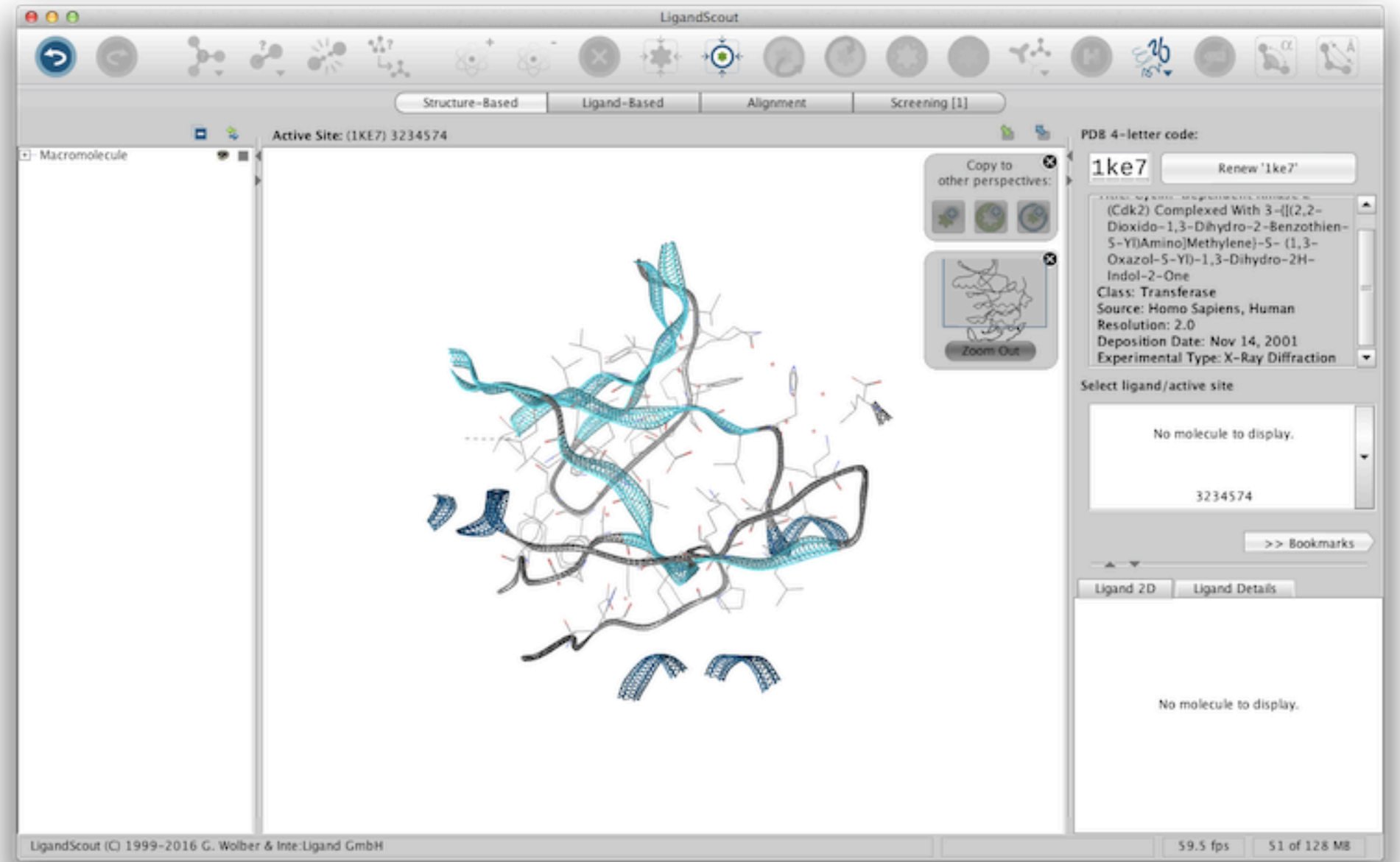
Apo Binding Site Pharmacophore Generation



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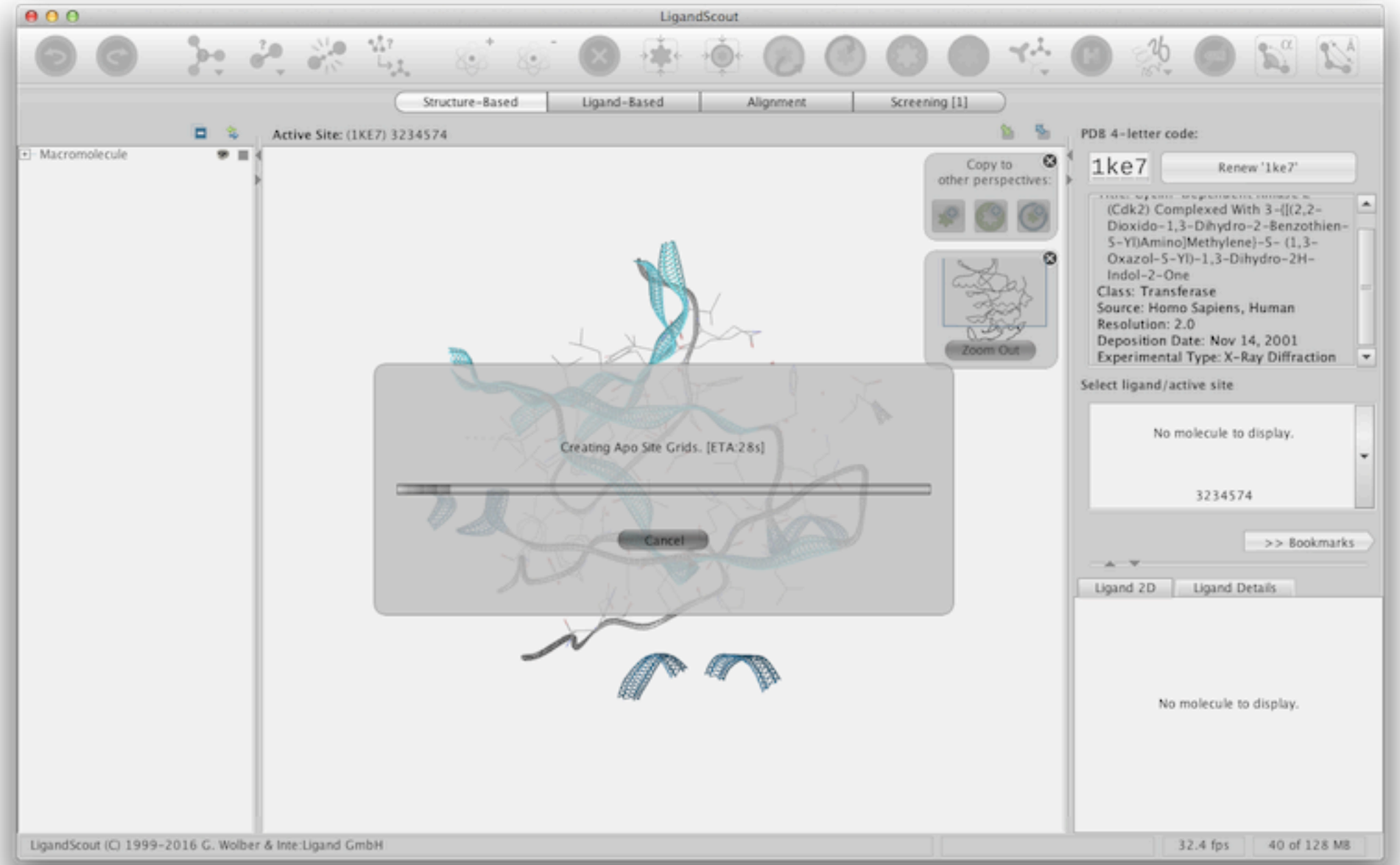

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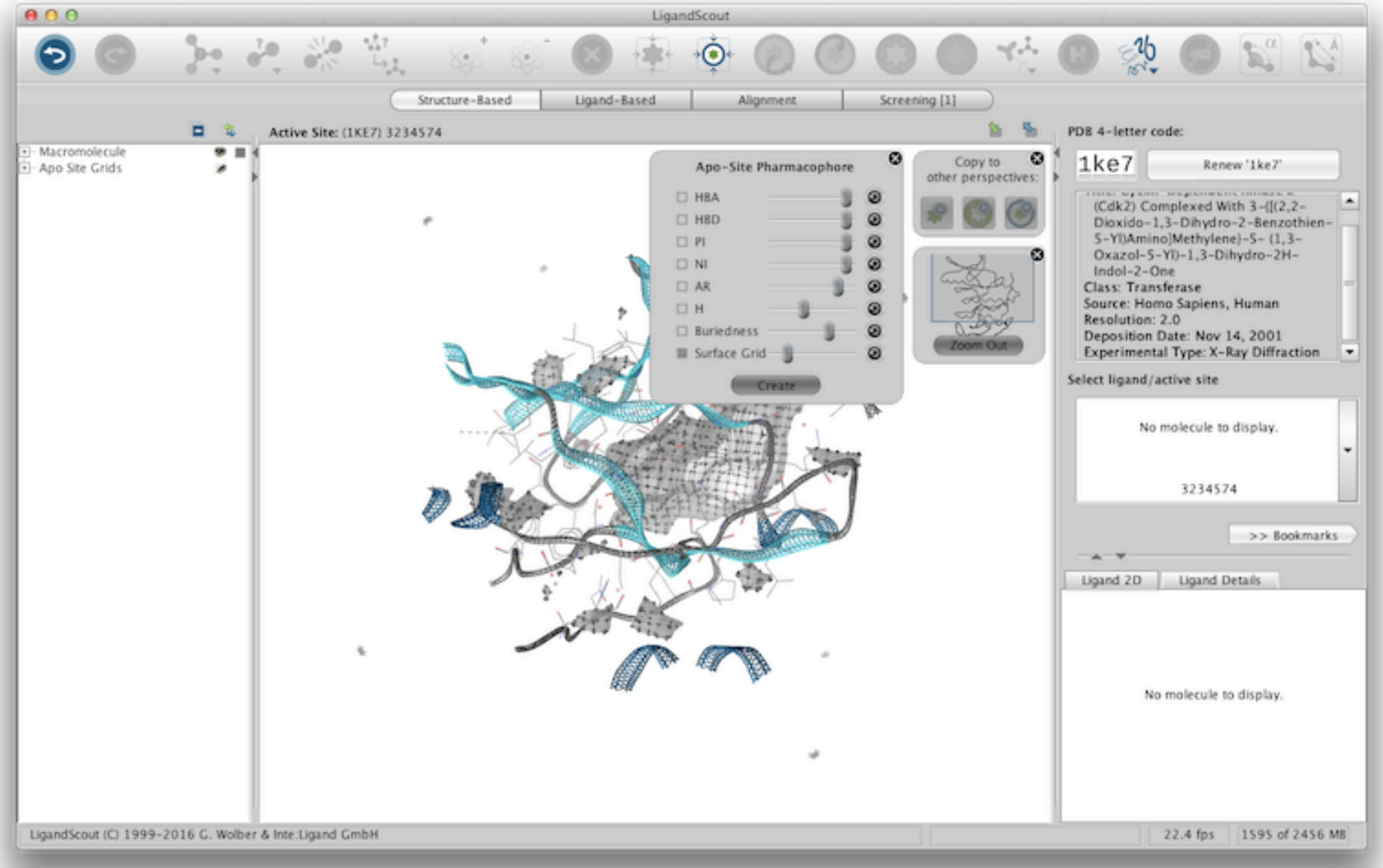

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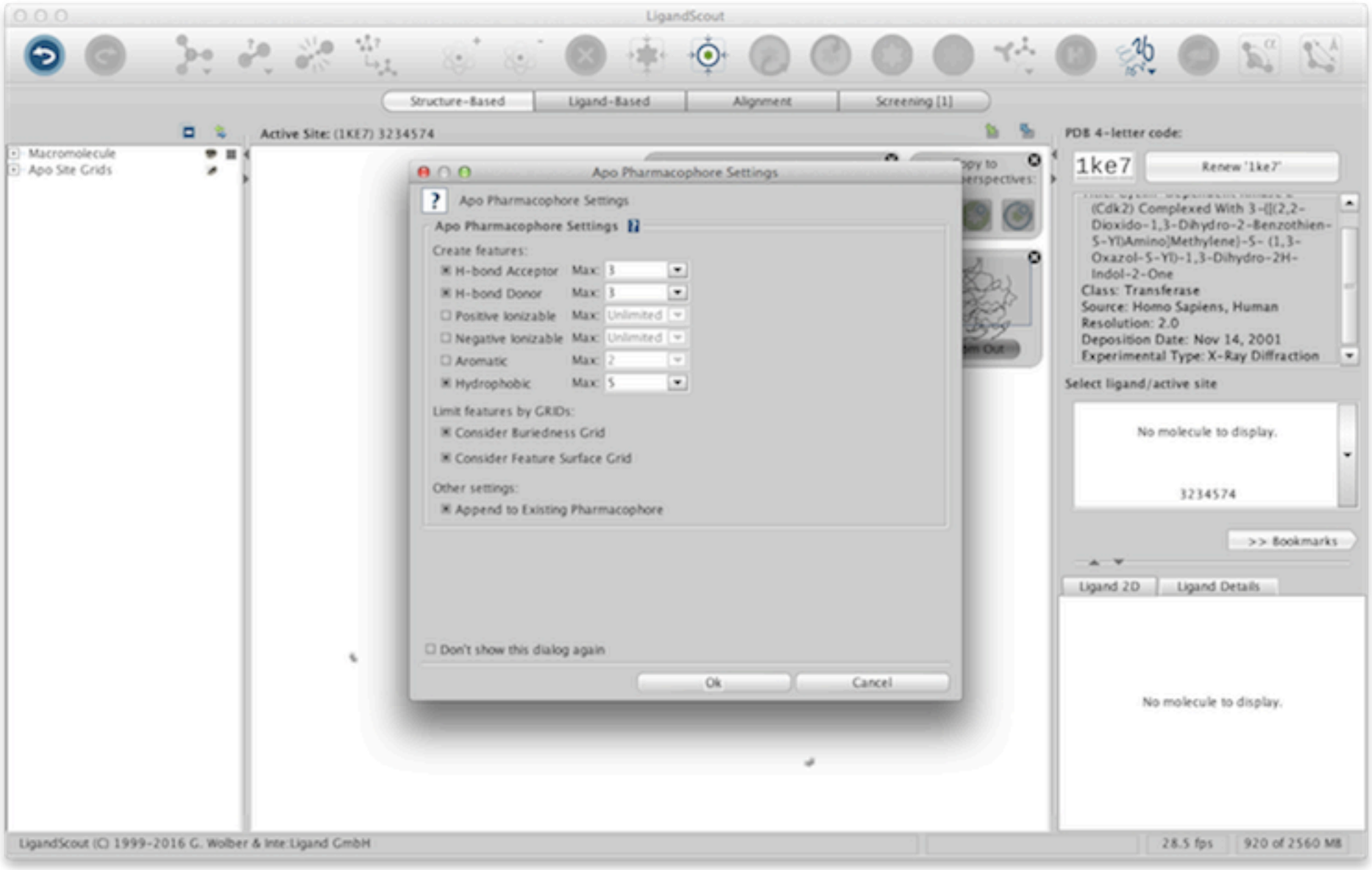

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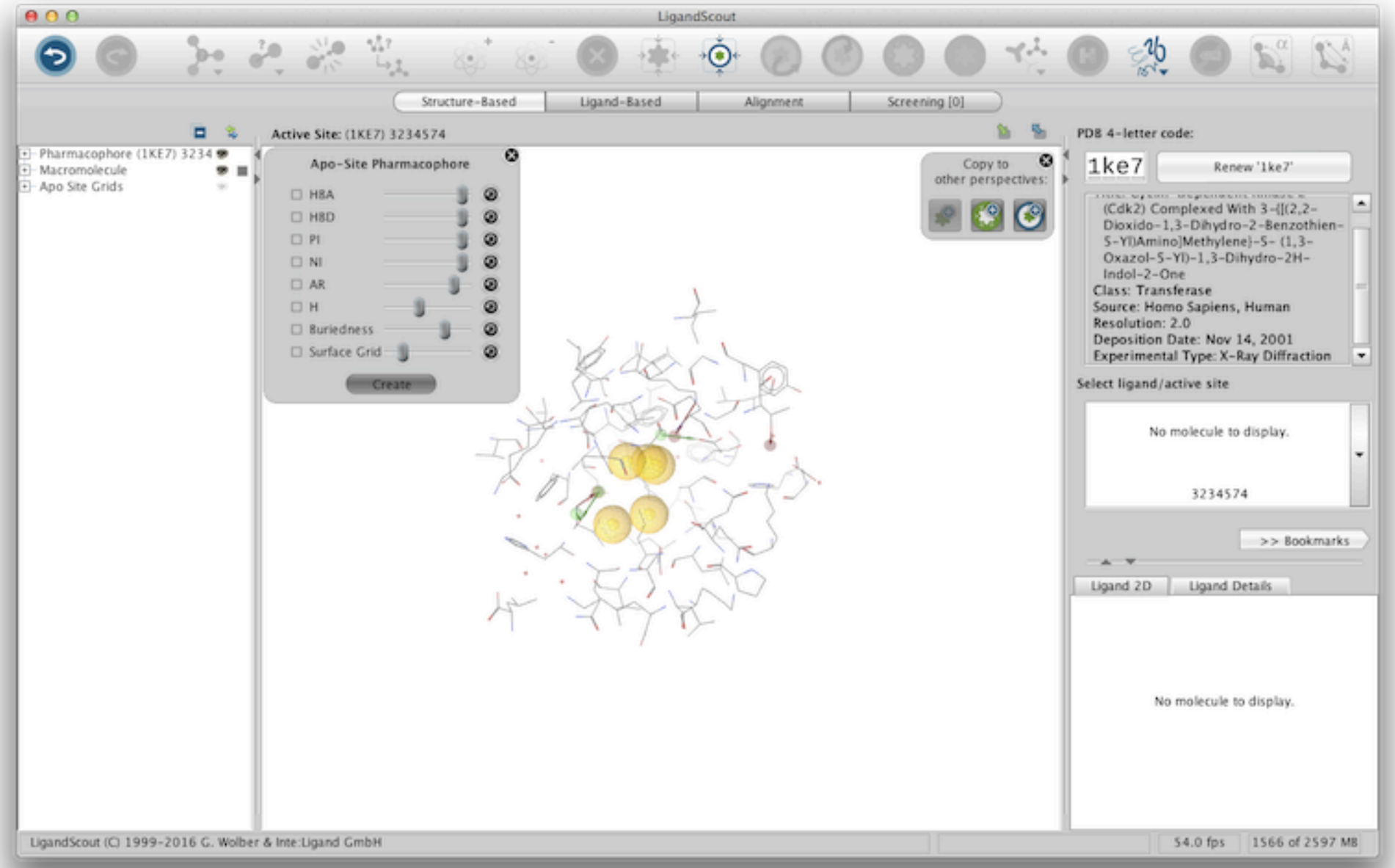

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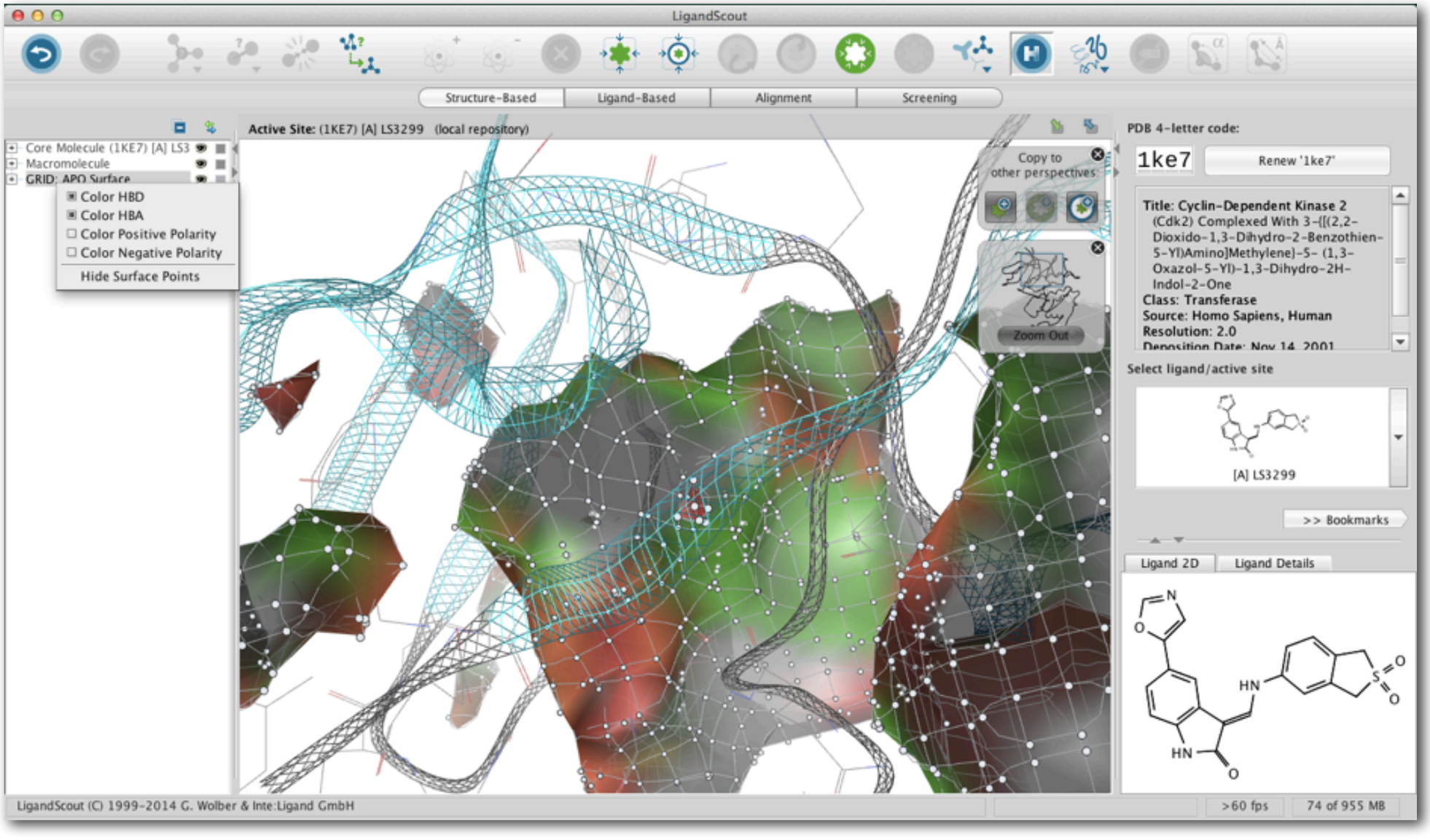
Manual Apo Site Pharmacophore Building



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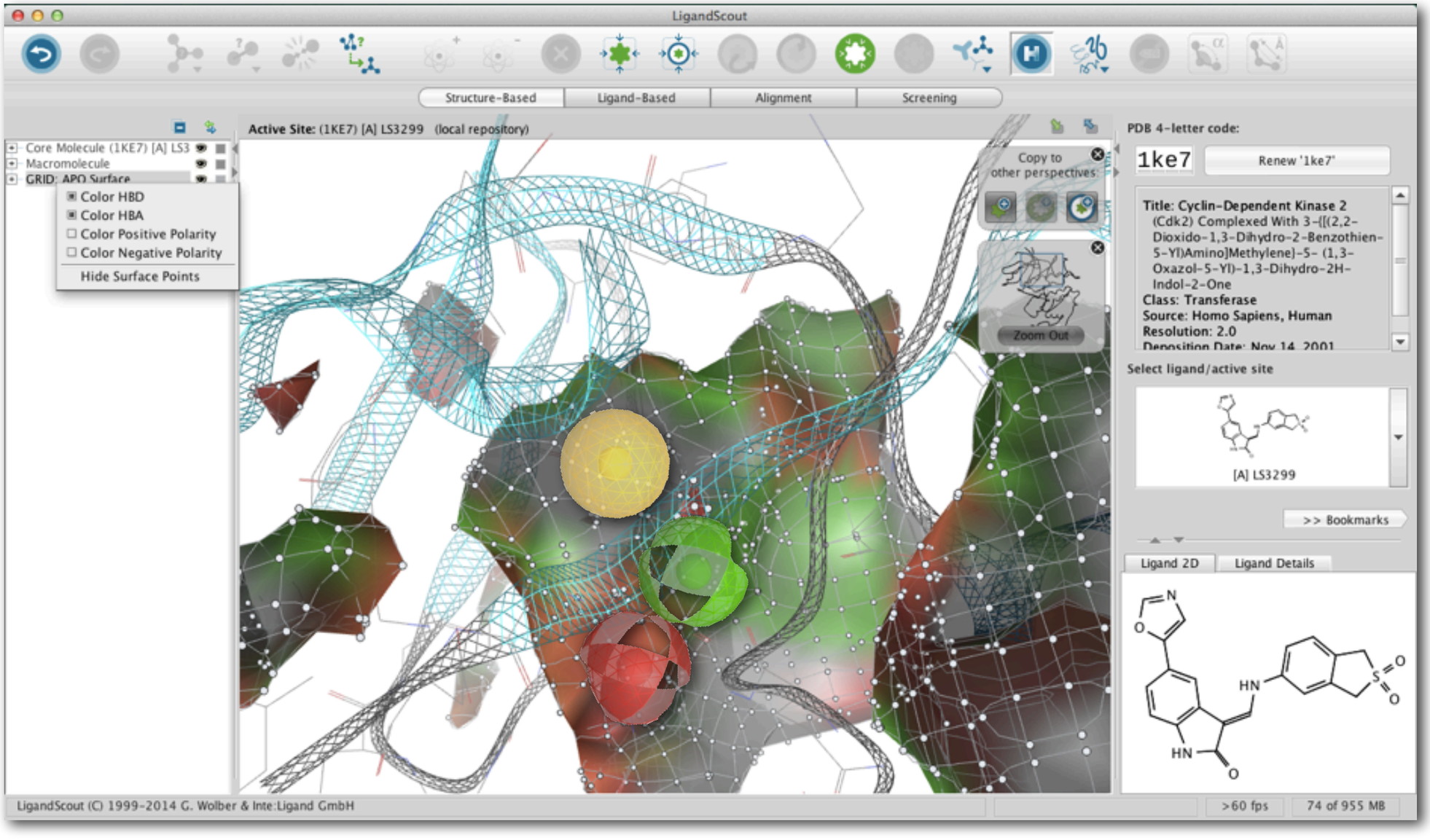

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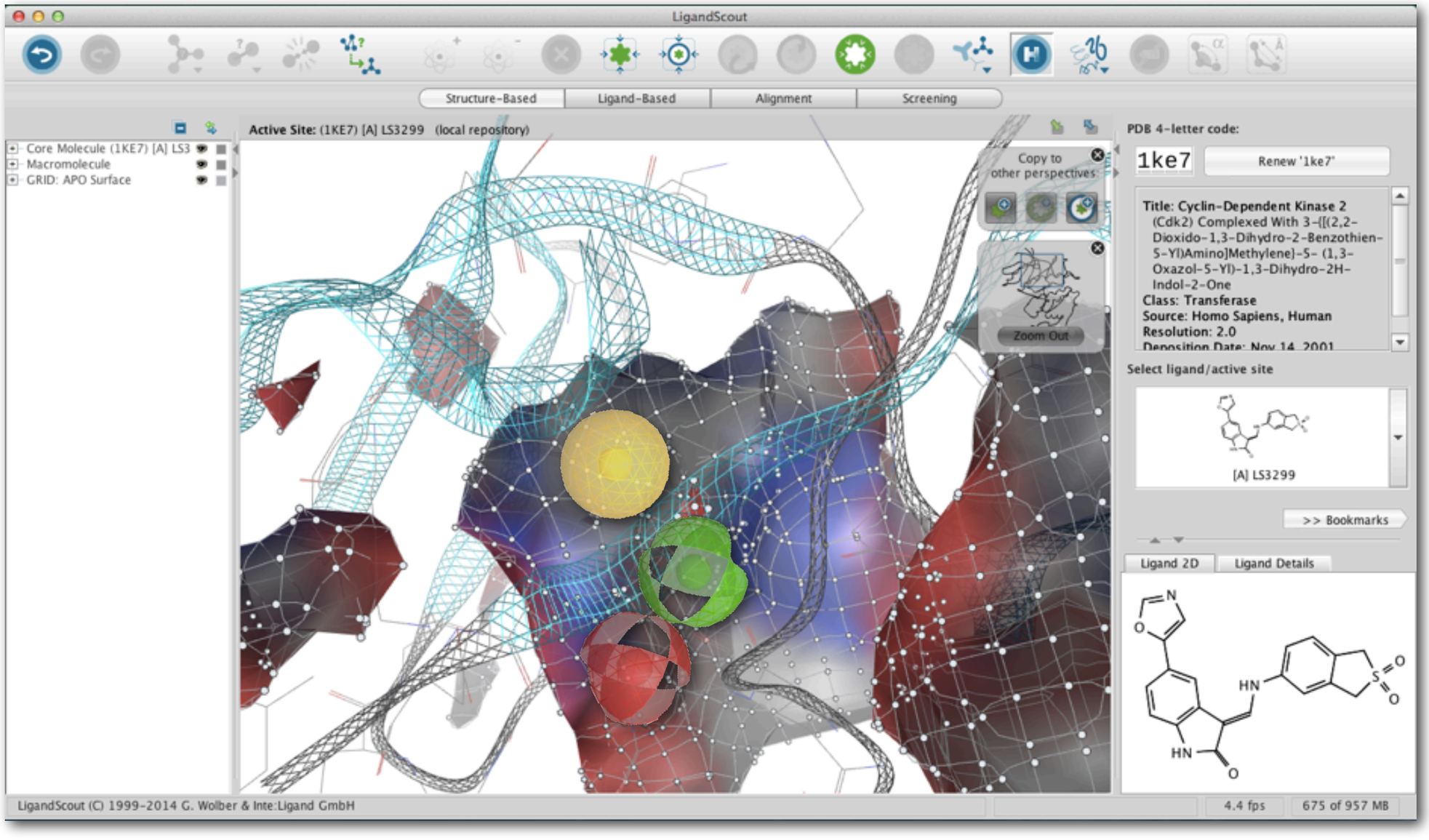

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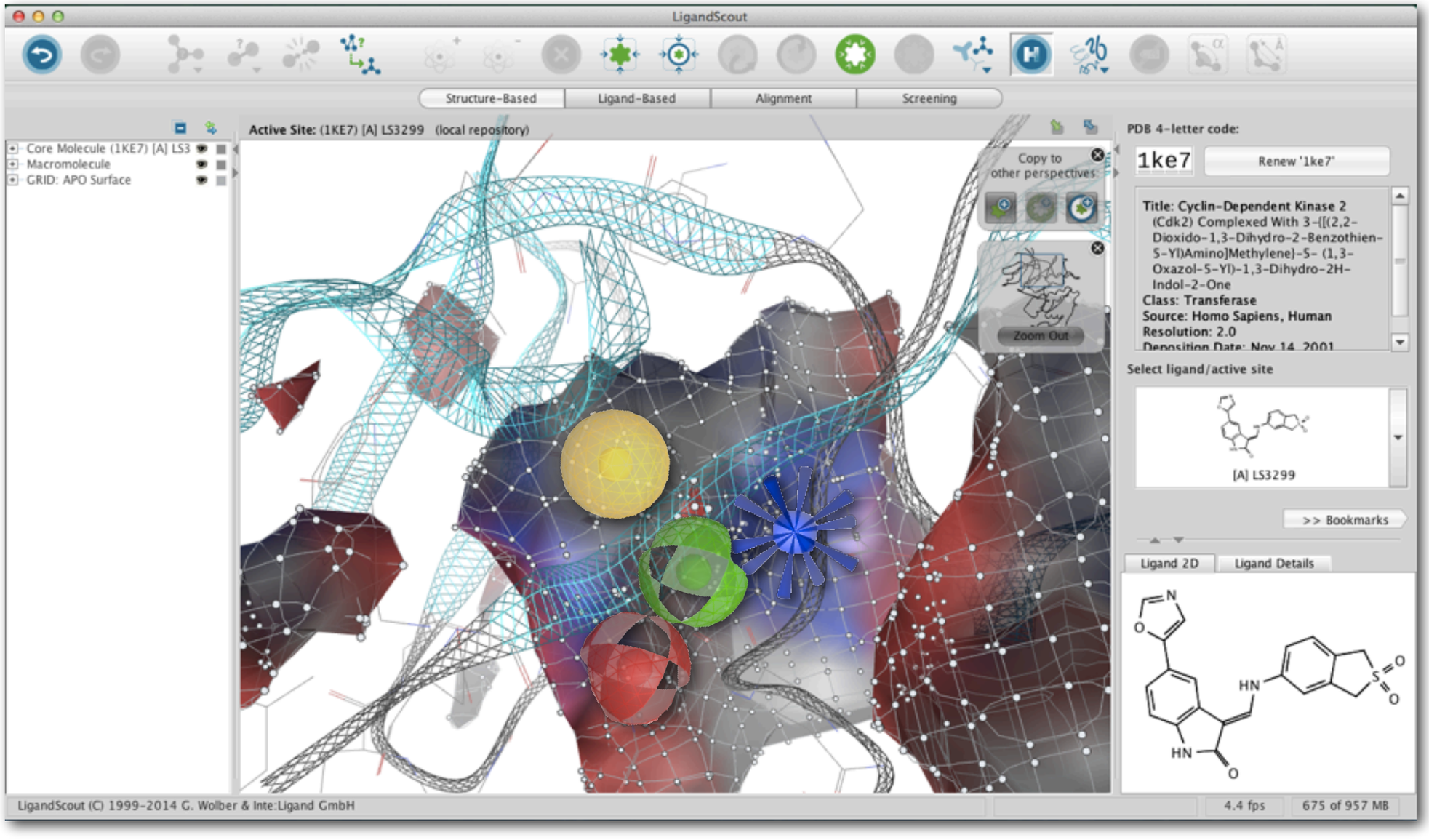

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Docking With AutoDock 4.2 / AutoDock Vina

Integration: High Quality Docking & Pharmacophores

- Interactive docking in active site viewer
- Analyze and filter the results in flexible table view
- Re-score interactively using pharmacophores
- Estimate binding enthalpies using MMFF94s
- Estimate free energy of binding using new scoring function

Makes docking user friendly and understandable

- Seamless workflows in most user friendly interface

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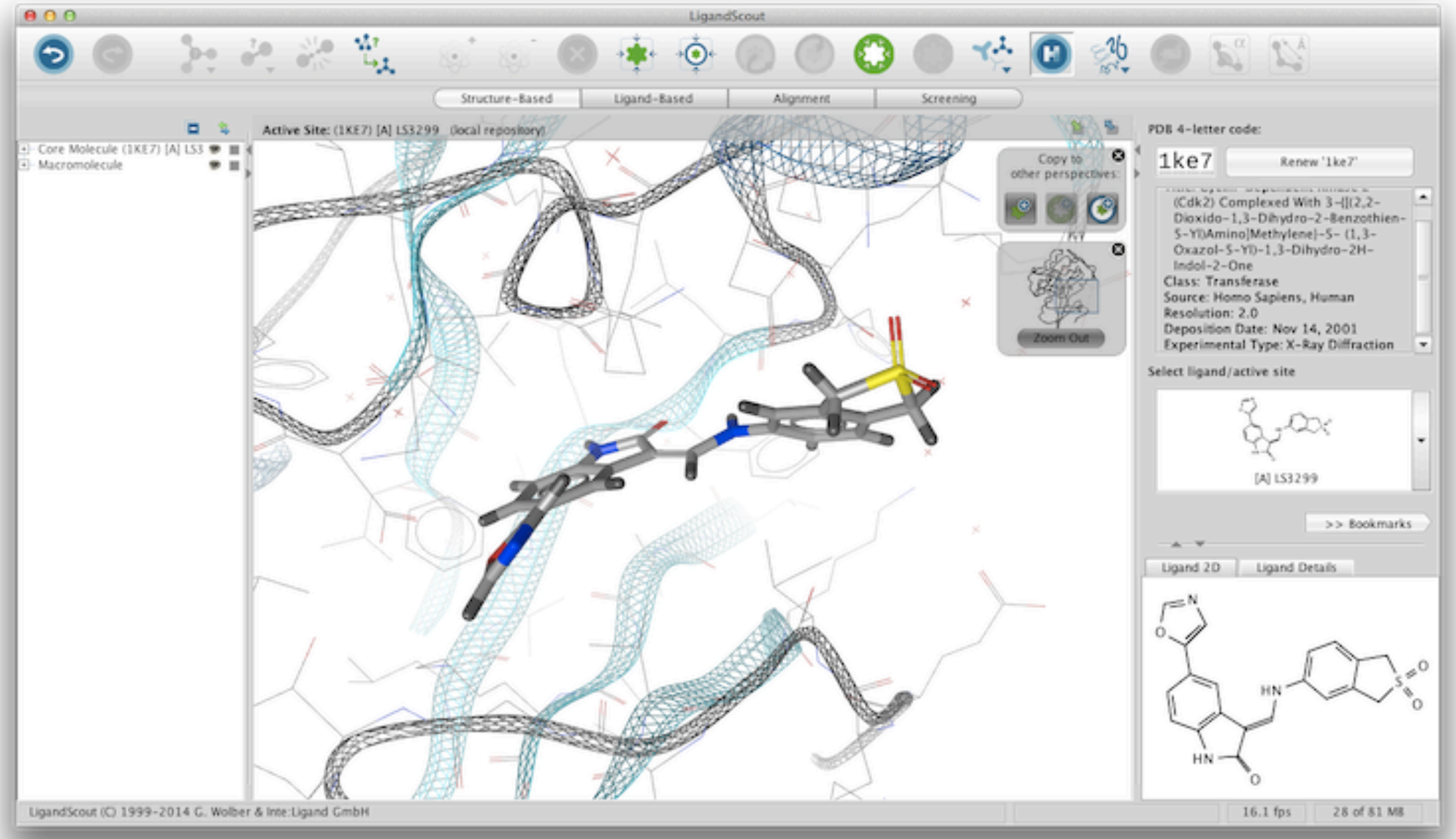
Docking With AutoDock 4.2 / AutoDock Vina



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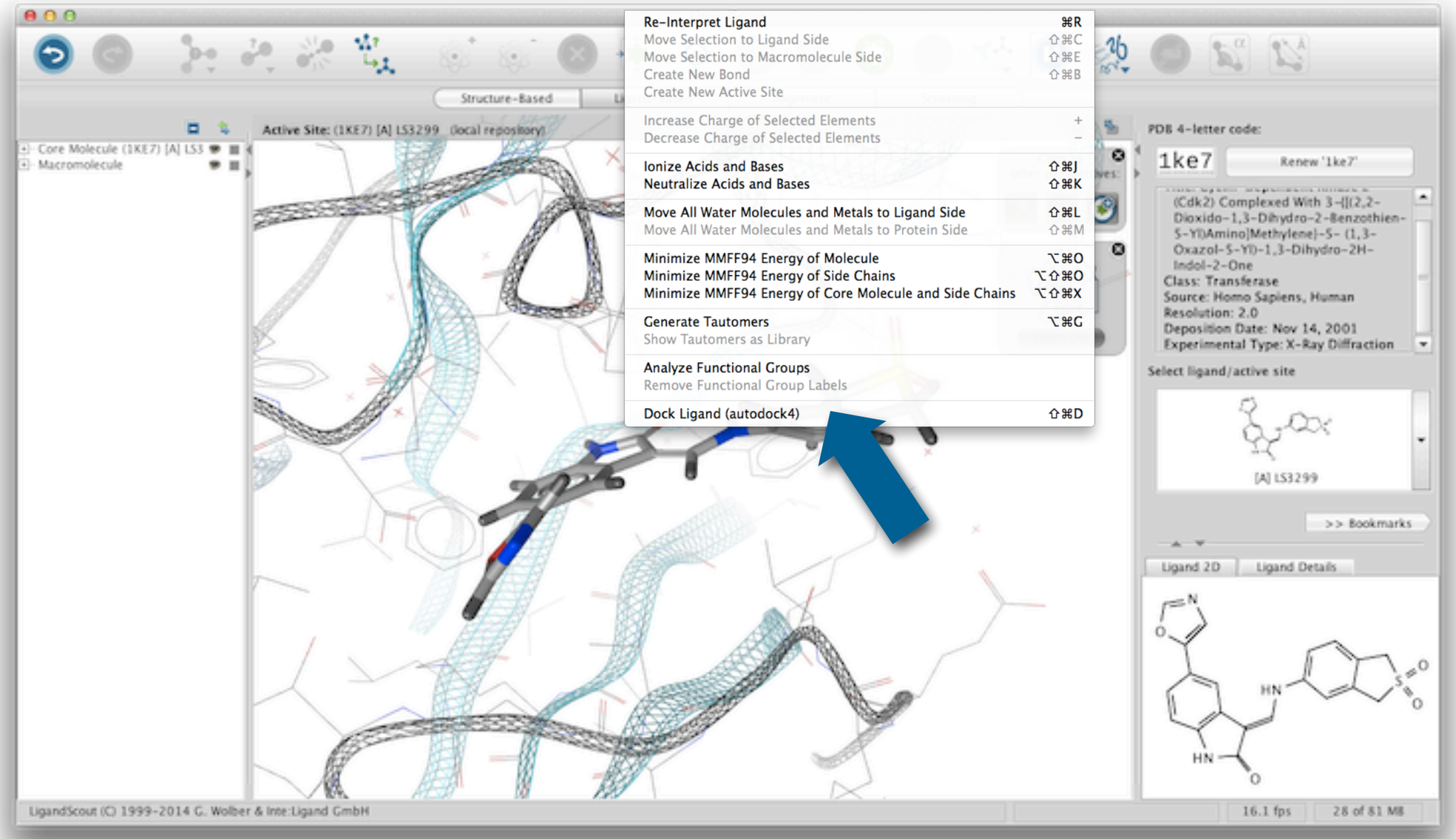

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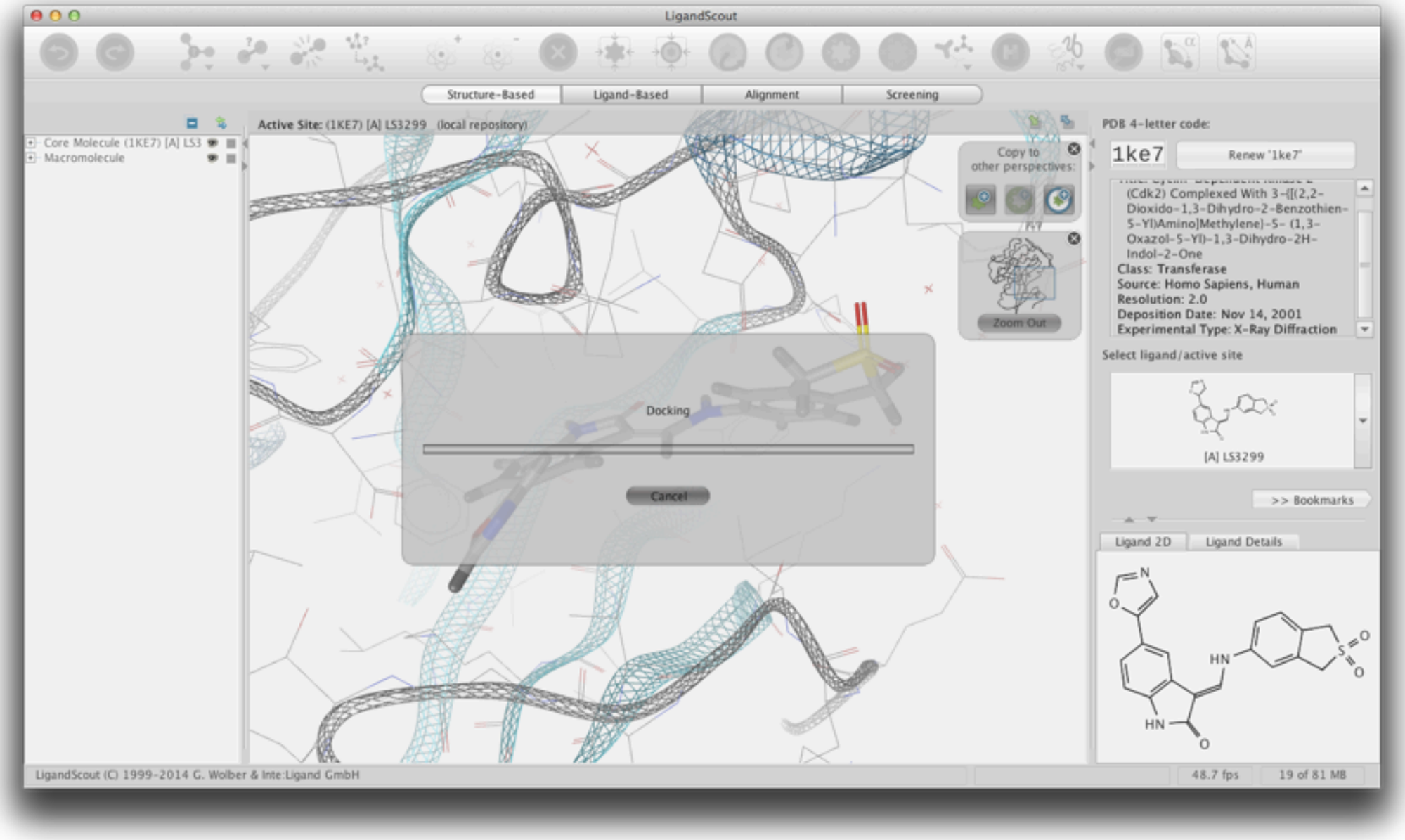

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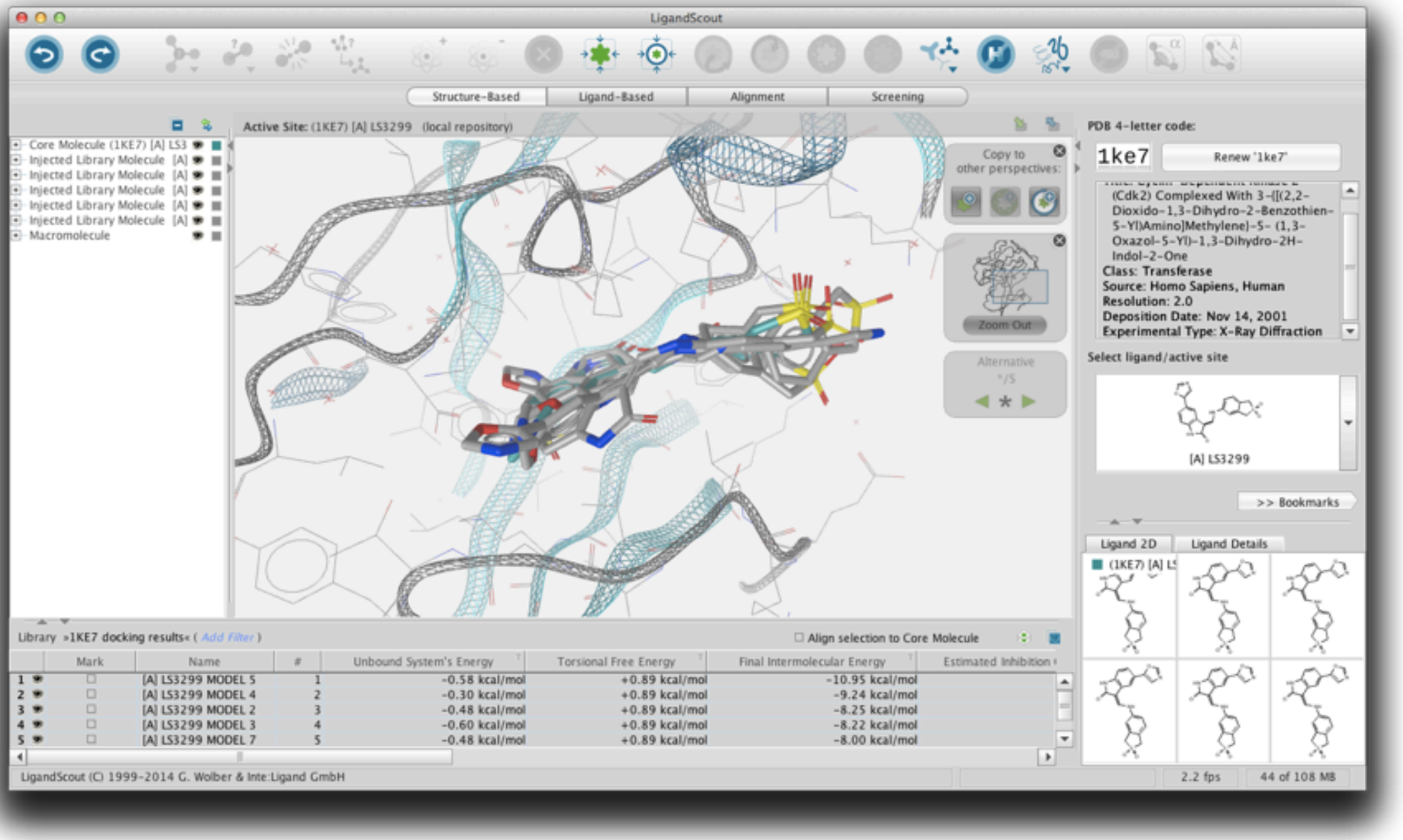

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Reading Molecular Dynamics Trajectories

Integration of MD into the Pharmacophore World

- Create multiple pharmacophore models directly from MD Analyze conformational behaviour of ligand/protein complex
- Analyze the formation of transient binding pockets
- Dock ligands into transient pockets

Makes MD trajectory analysis rapid and transparent

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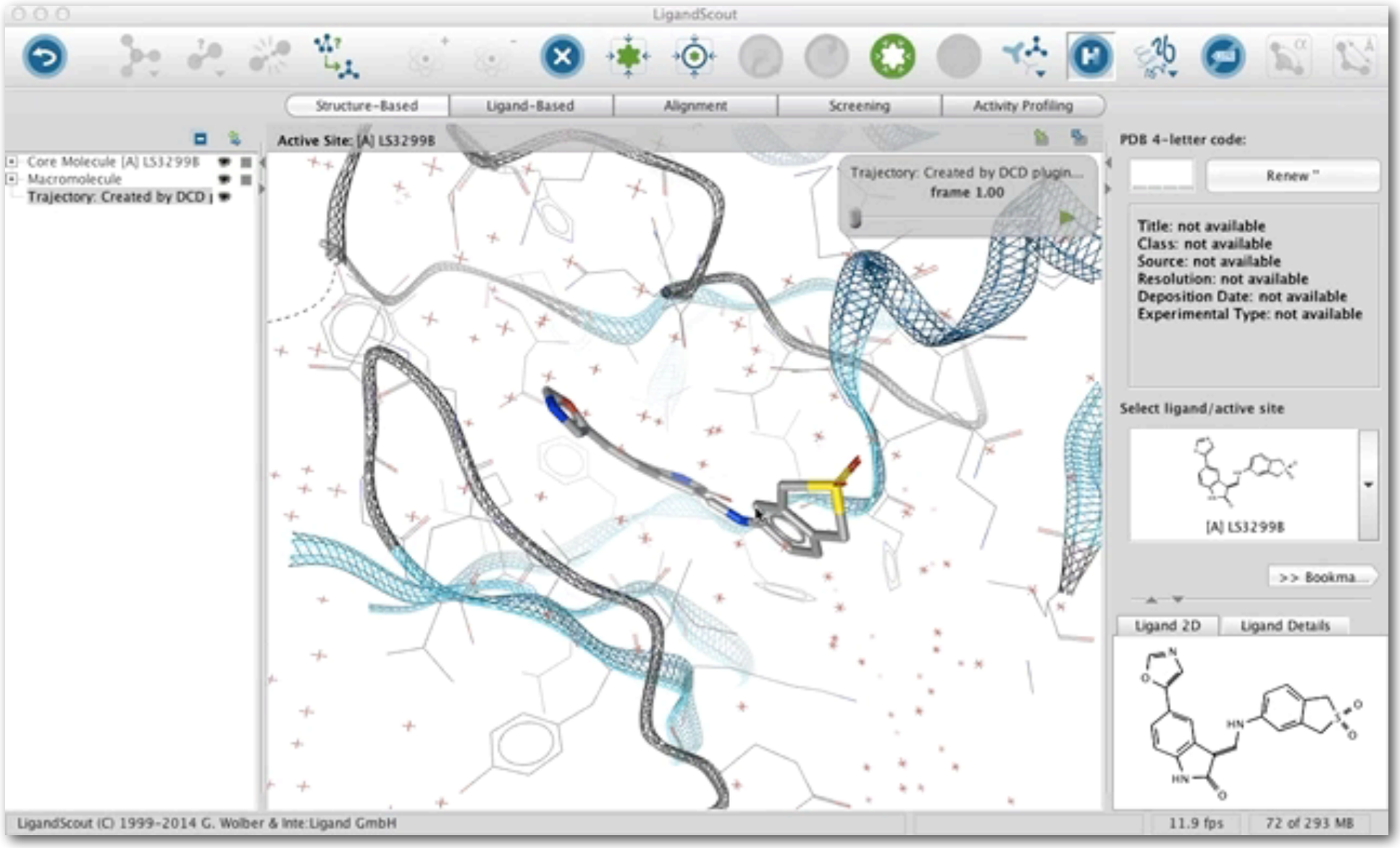
Analyzing MD within LigandScout



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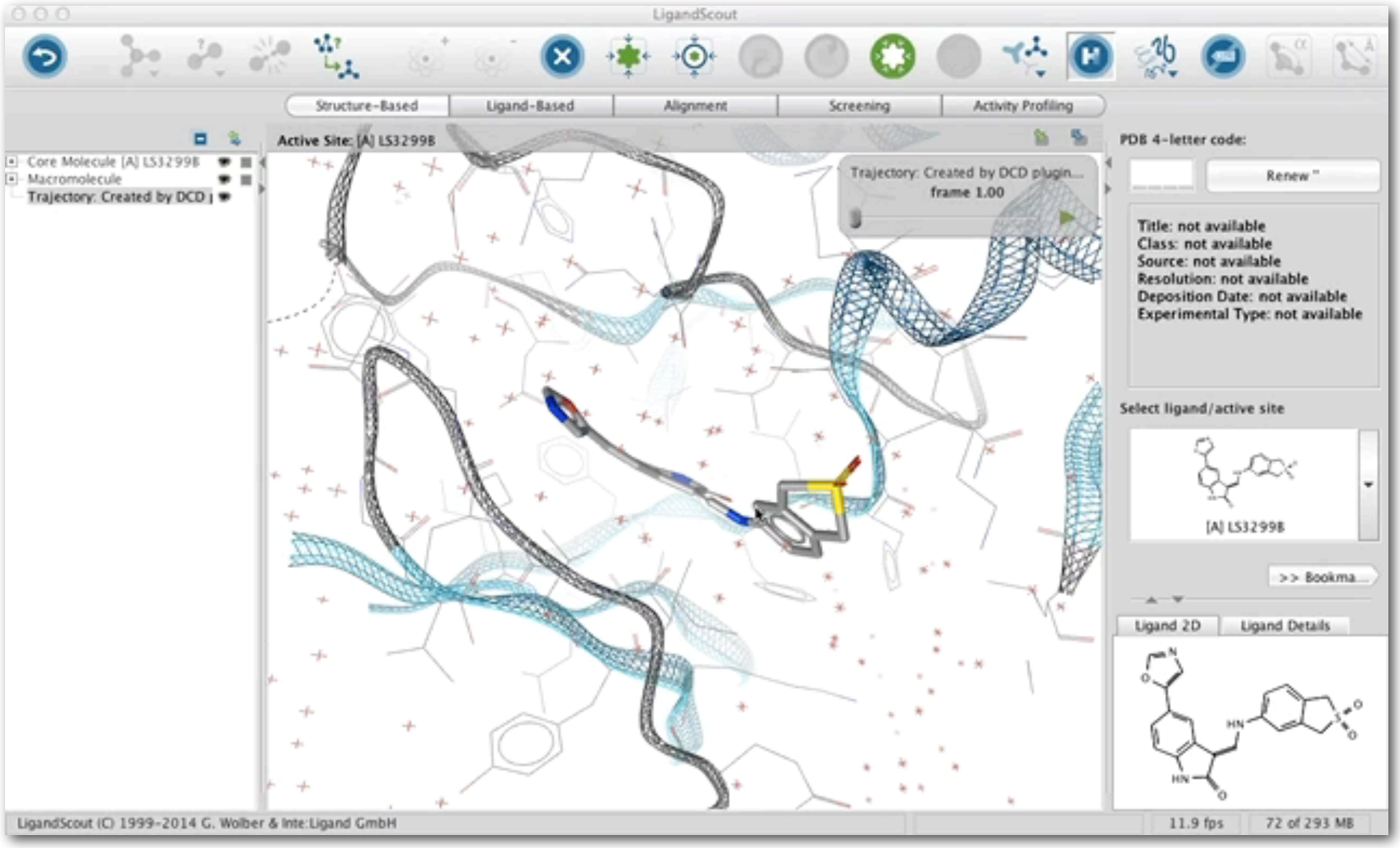
Analyzing MD within LigandScout



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LigandScout KNIME Integration

LigandScout functionality available in KNIME workflow

- Molecular structure data input and output
- Data set manipulation
- Conformational analysis
- LigandScout 3D database generation
- Query builder for ChEMBL online databank
- Patent searching in SureChEMBL
- Virtual screening & Activity profiling
- MD trajectory analysis using pharmacophores
- Access to Inte:Ligand's Pharmacophore Databases (license necessary)

Deploy easy-to-use workflows to co-workers

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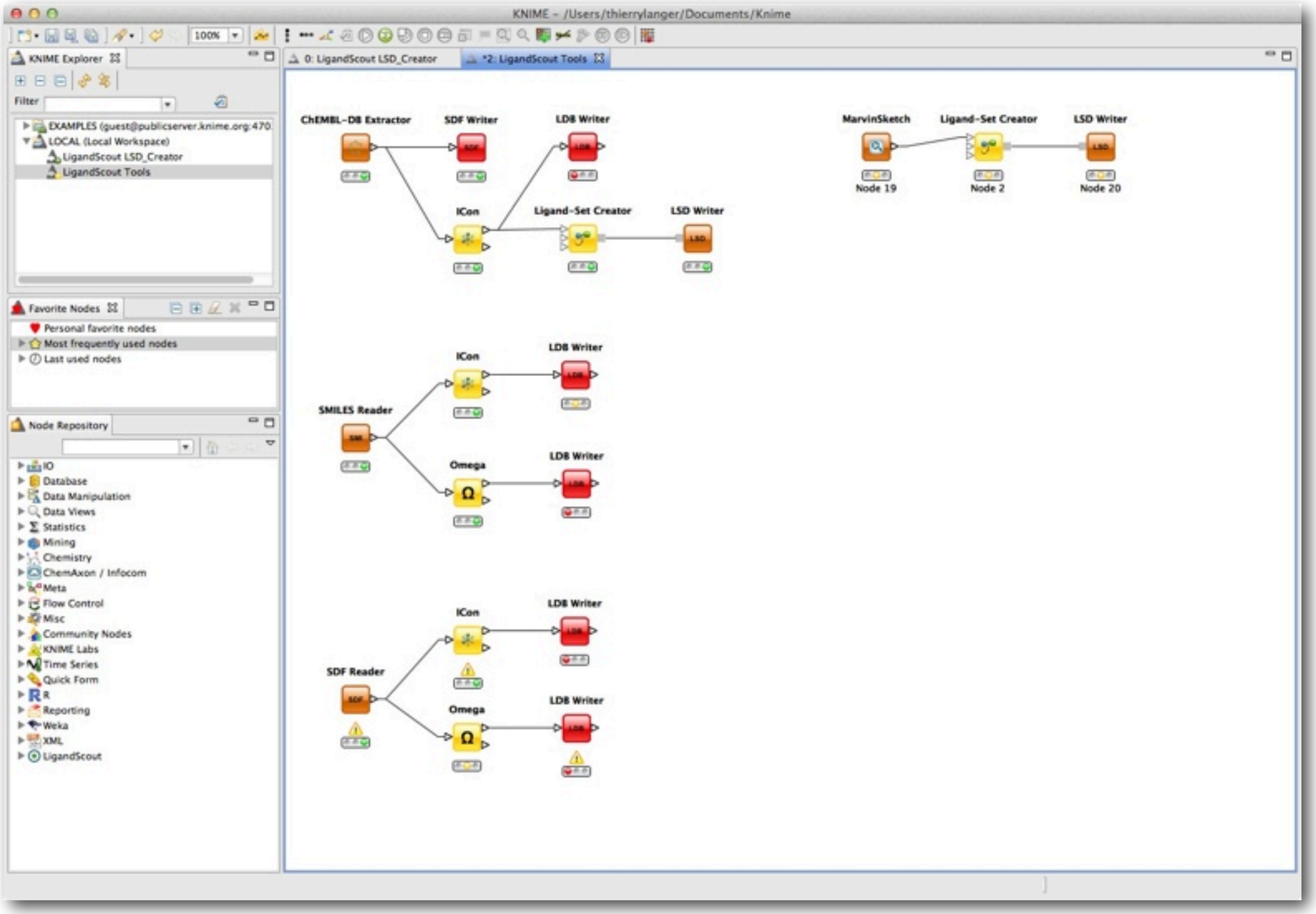
KNIME Workflows



Open for Innovation ® KNIME

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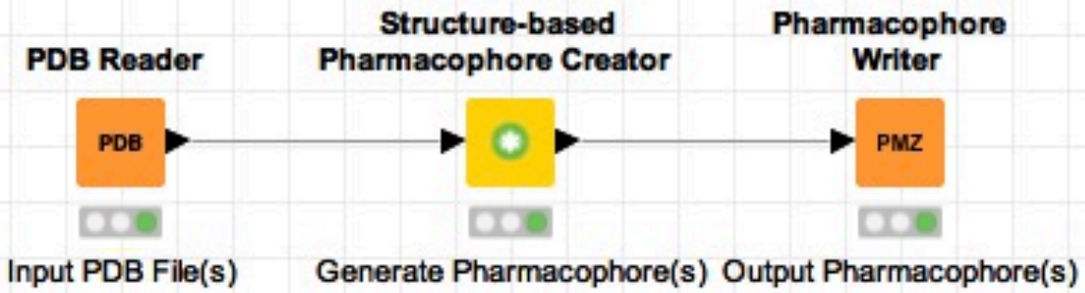
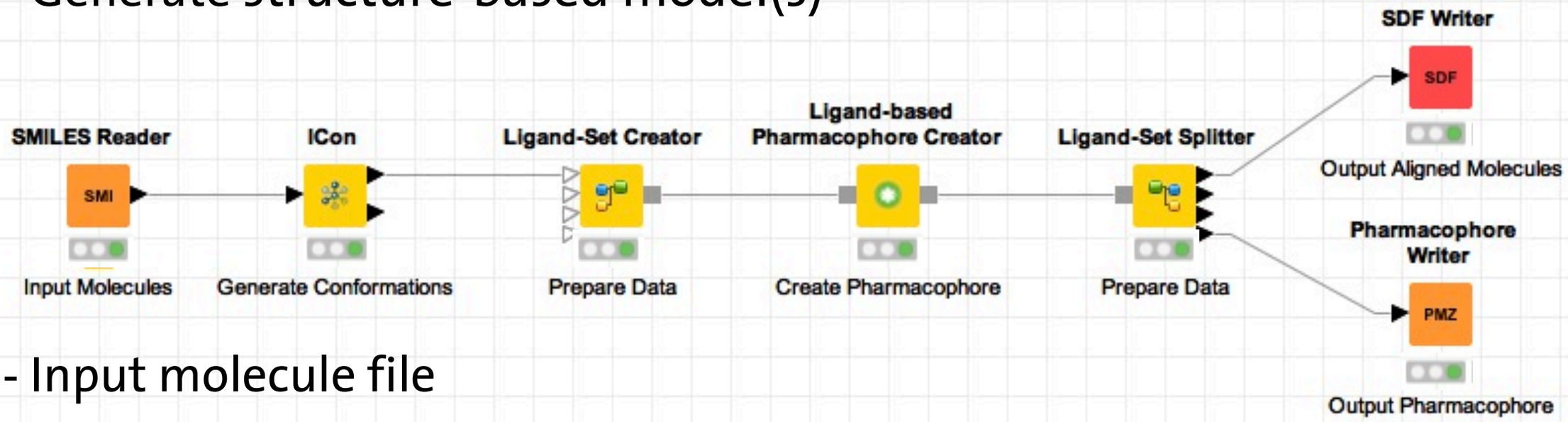
Batch Mode Pharmacophore Generation



- Input pdb protein-ligand complex file(s)
- Generate structure-based model(s)



- Input molecule file
- Generate ligand-based model(s)

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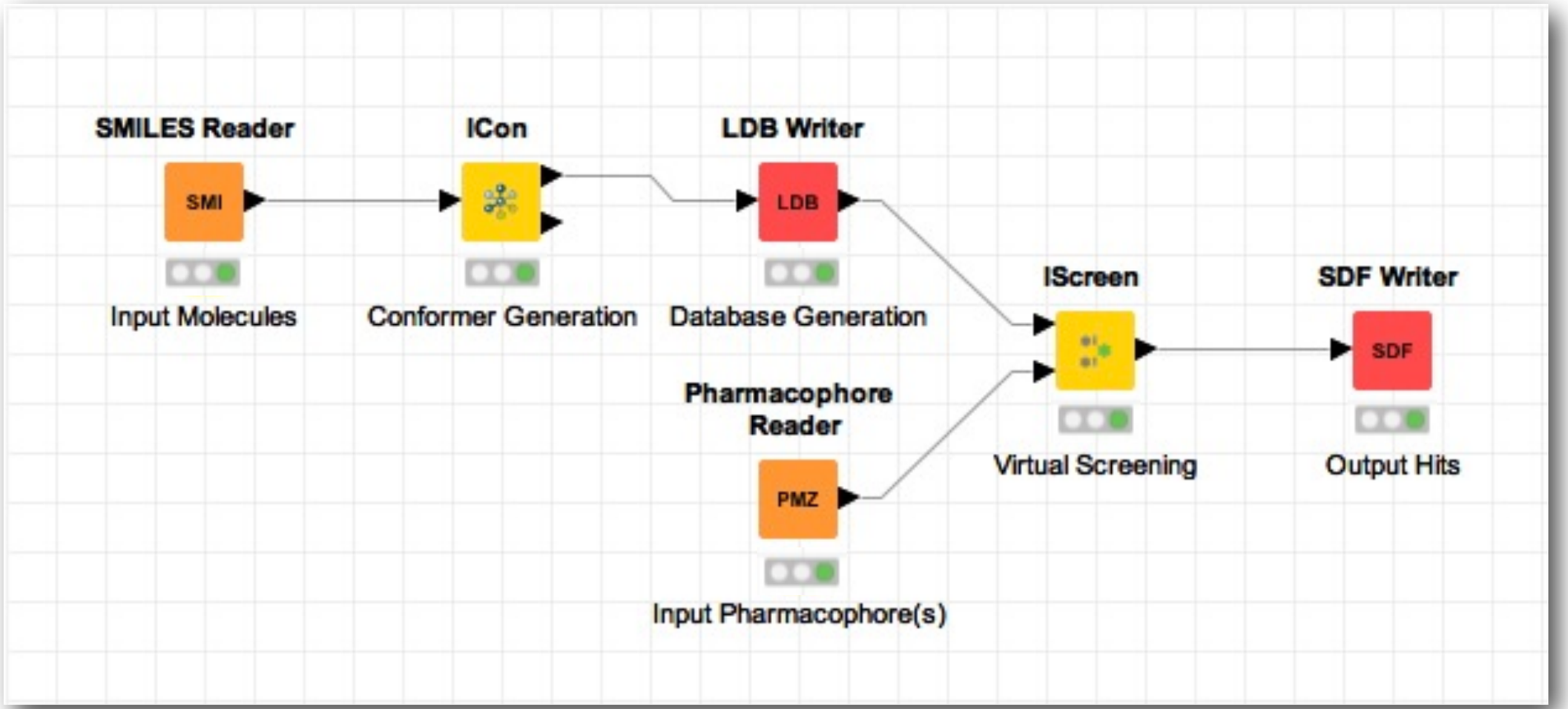
LigandScout KNIME Extensions



- Input molecule files (smiles/sdf/mol2)
- Screen with your favorite pharmacophore model(s)
- Retrieve ranked hits

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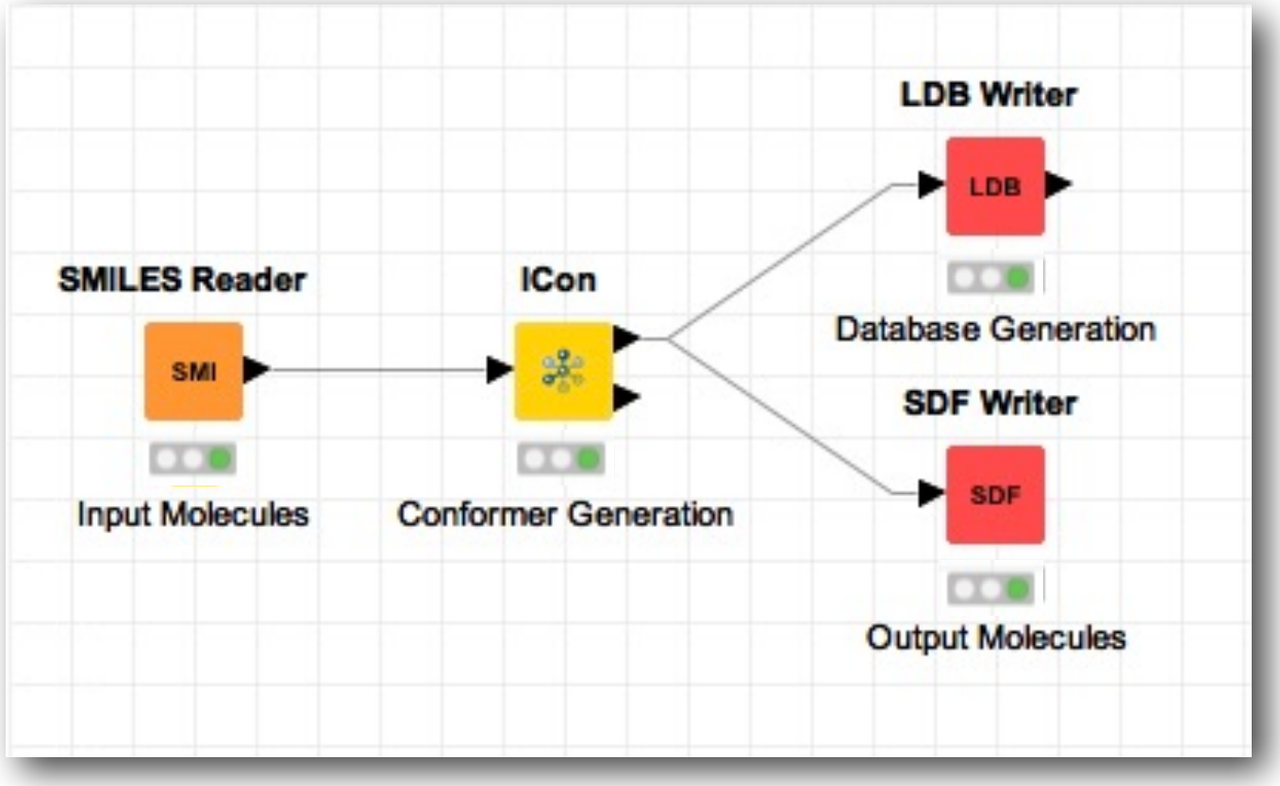
Automated Conformational Analysis

Building of a 3D multiconformational database for VS



- Input molecule files (smiles/sdf/mol2)
- Retrieve LigandScout compound database or multiconf SDF

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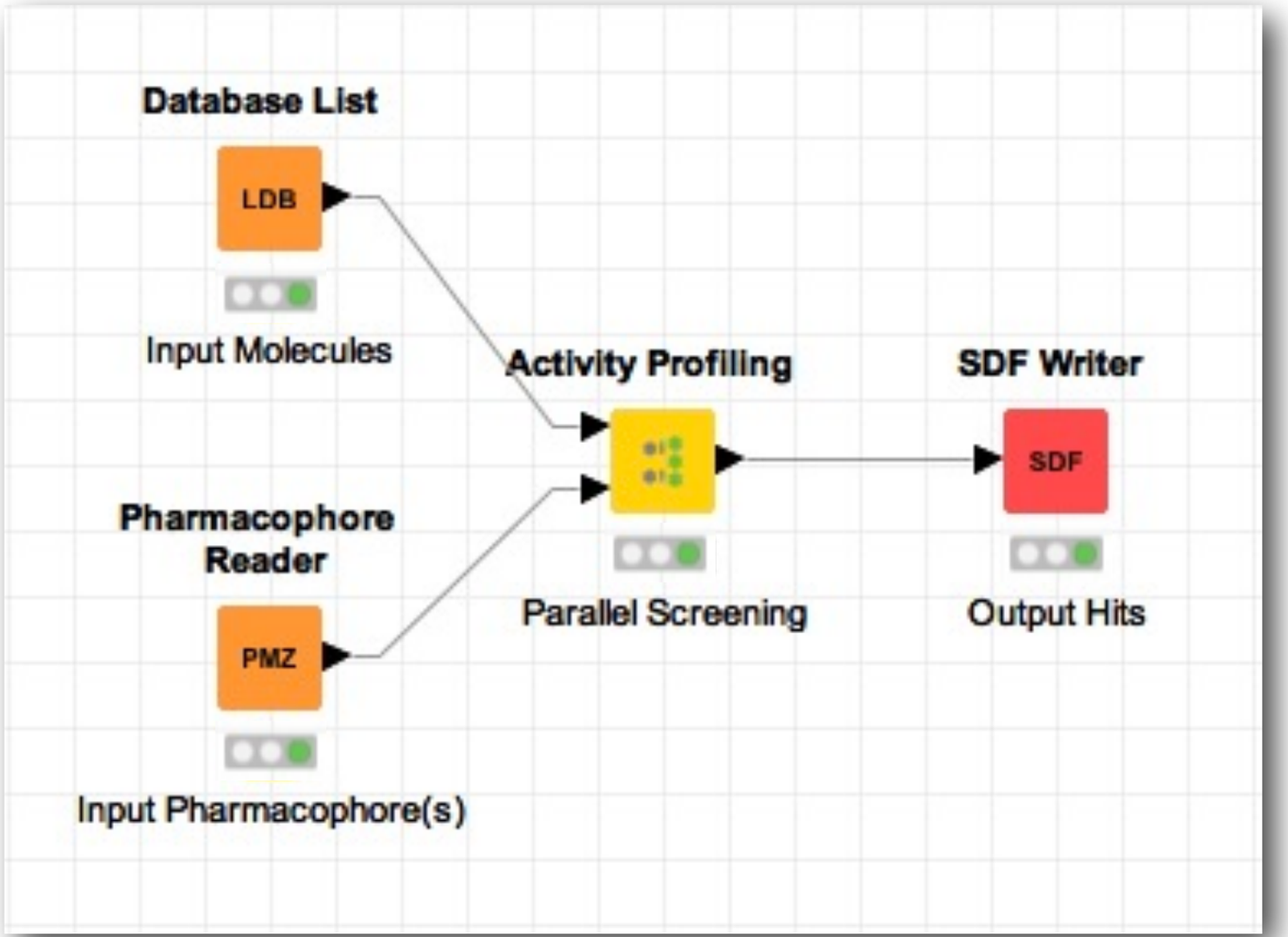
LigandScout KNIME Extensions

e. g. Automated Compound Activity Profiling



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LigandScout KNIME Extensions

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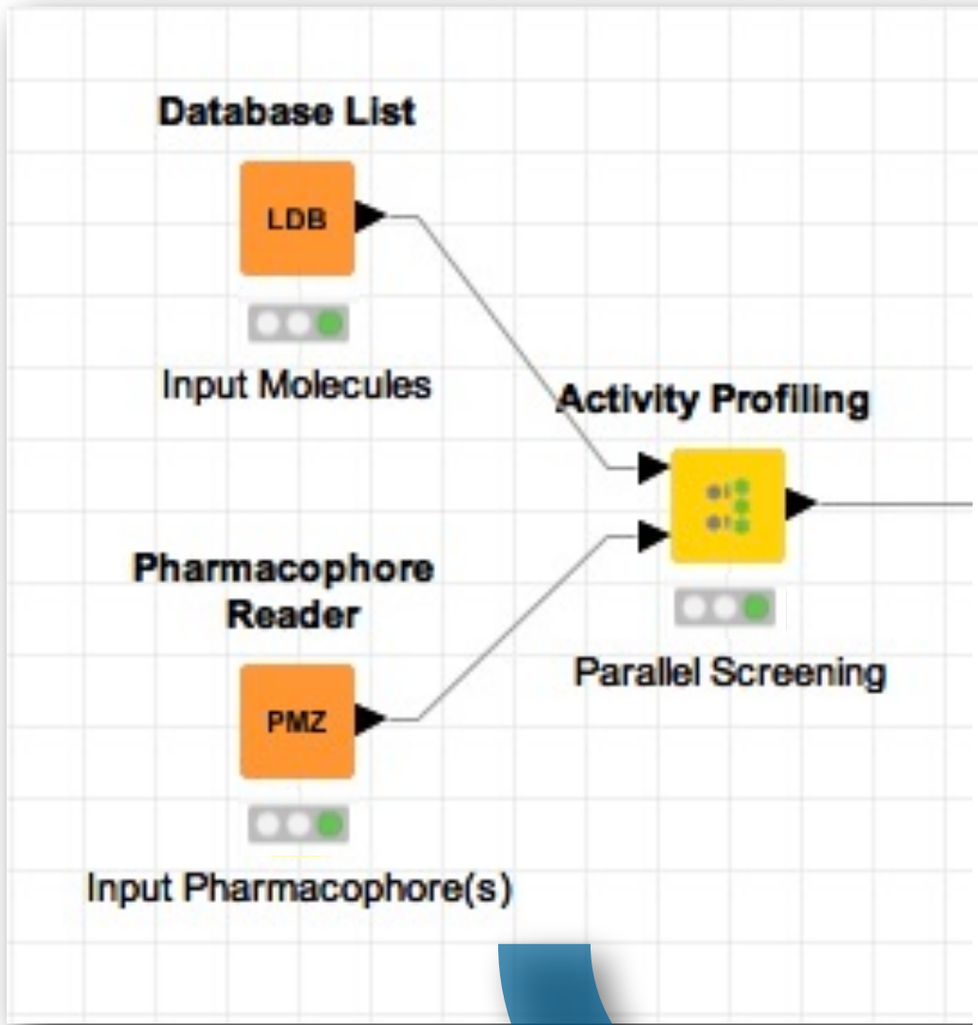

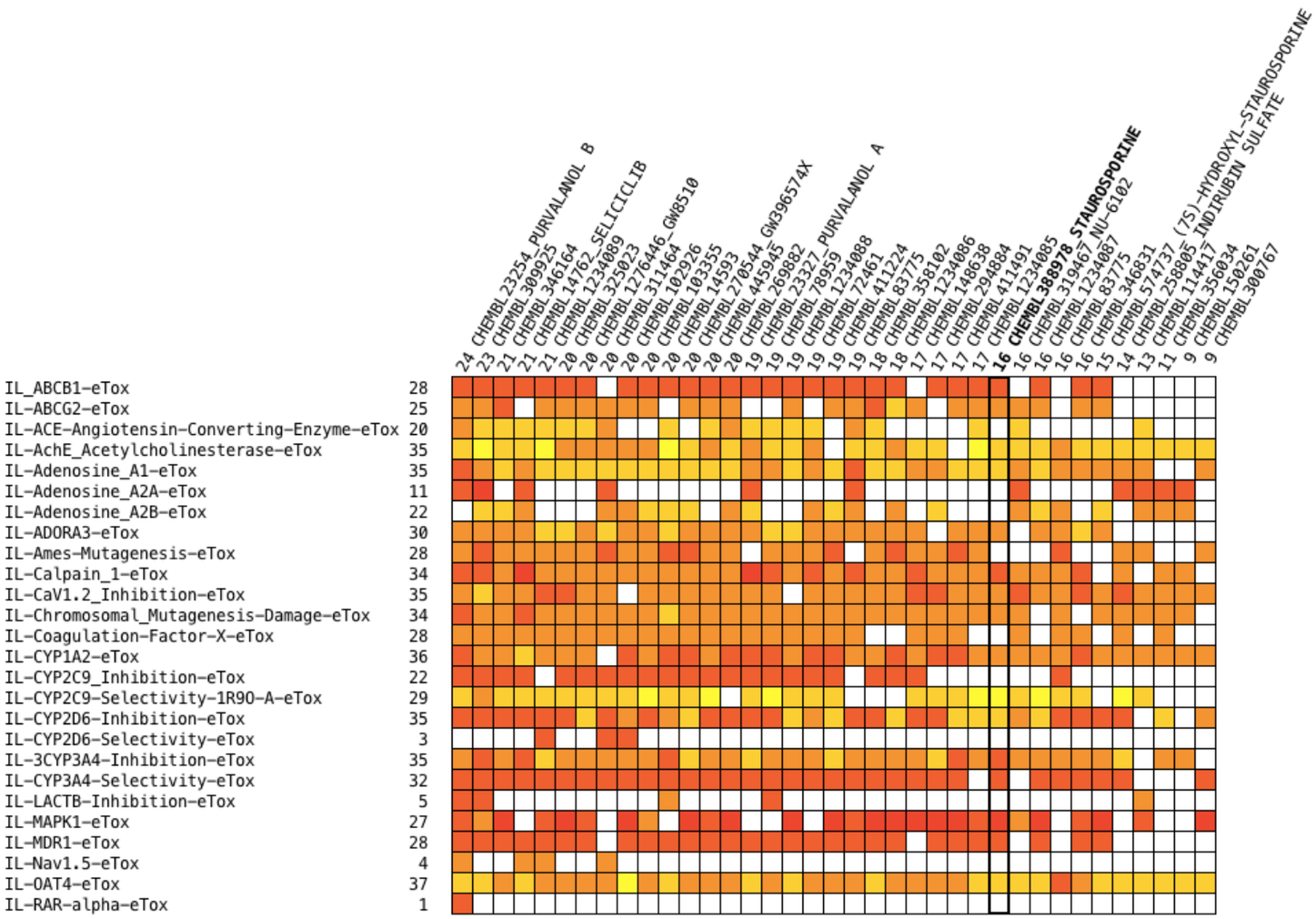

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Inte:Ligand's Toxicity Assessment Models

7 year collaborative EC Project on Toxicity Prediction

Executive Committee

NOVARTIS · Bayer HealthCare Pharmaceuticals · Fundació IMIM · SYNAPSE RESEARCH MANAGEMENT PARTNERS

EFPIA

AstraZeneca · Boehringer Ingelheim · ESTEVE · gsk GlaxoSmithKline · janssen · Lundbeck · Pfizer · Roche · SANOFI · SERVIER · ucb

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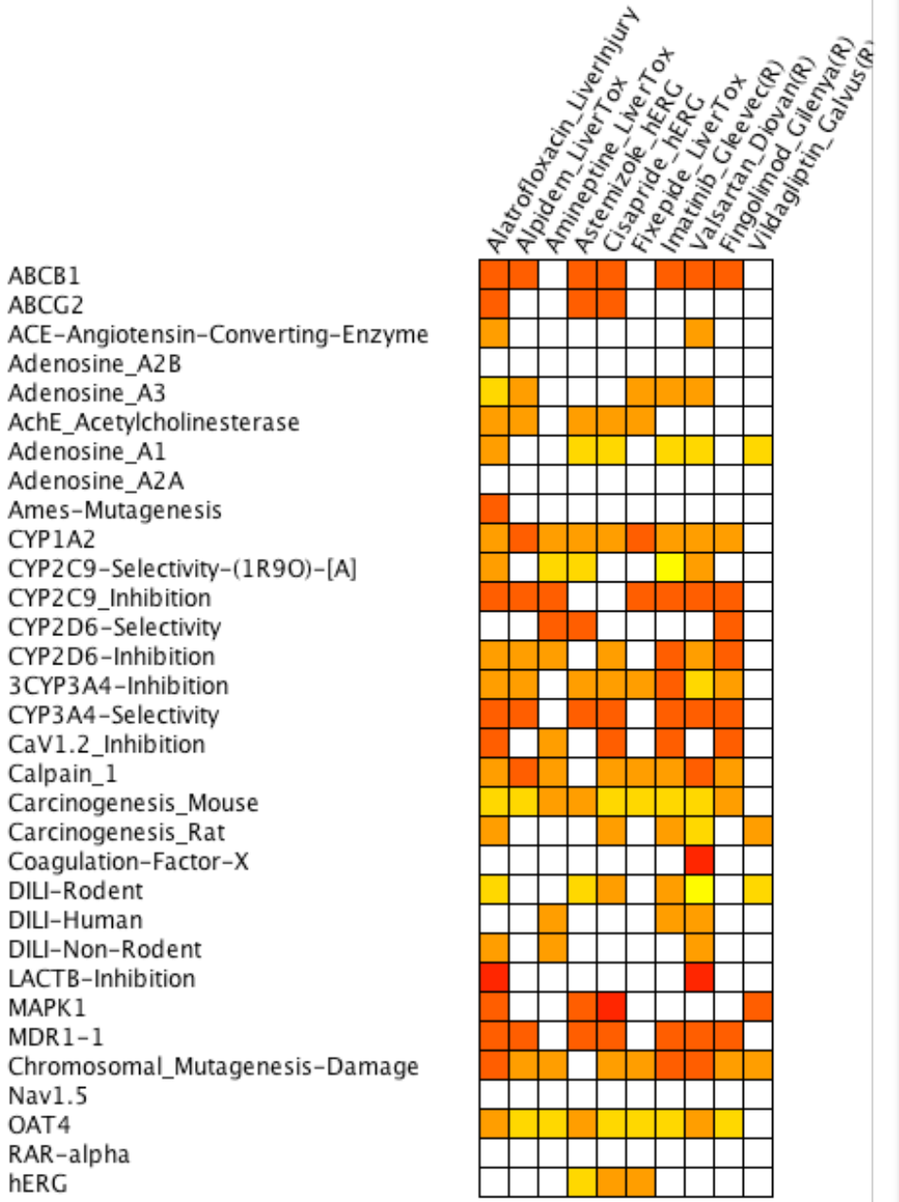
SMEs

Chemotargets · inte:ligand · LMD Lead Molecular Design s.l. · Lhasa Limited · Molecular Networks Inspiring Chemical Discovery



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KNIME Nodes Available for …

- LigandScout
  - Alignment
    - Pharmacophore/Molecule Alignment
  - Clustering
    - Diversity Picker
    - Fingerprint Clustering
    - Pharmacophore/Molecule Clustering
  - Conformer Generation
    - ICon
  - Data Manipulation
    - Ligand-Set Creator
    - Ligand-Set Splitter
  - Database
    - ChEMBL-DB Extractor
    - Database List
    - Database Merger
    - Patent
  - Docking
    - AutoDock 4
    - AutoDock Vina
  - Filtering
    - Duplicate Remover
    - Library Filter

- I/O
  - Database List
  - GRO Reader
  - LDB Reader
  - LDB Writer
  - LSD Reader
  - LSD Writer
  - Mol Reader
  - Mol Writer
  - Mol2 Reader
  - Mol2 Writer
  - PDB Reader
  - PDB Writer
  - Pharmacophore Reader
  - Pharmacophore Writer
  - SDF Reader
  - SDF Writer
  - SMILES Reader
  - SMILES Writer

- Minimization
  - MMFF94 Library Minimizer
  - MMFF94 Minimizer
- Models
  - IL-Carcinogenesis-Models
  - IL-DILI-Models
  - IL-MAO-Models
  - IL-Tox-Models
  - IL-hERG-Models
- Molecular dynamics
  - AMBER Trajectory Reader
  - CHA Filter
  - CHA Re-Score
  - DCD Trajectory Reader
  - MD Pharmacophore Creato
  - TRR Trajectory Reader
  - XTC Trajectory Reader

- Molecule Property
  - Chiralator
  - Fingerprint Calculator
  - Fingerprint Similarity Calculator
  - InChI Generator
  - Property Appender
  - Standard Properties
- Pharmacophore
  - Ligand-based Pharmacophore Creator
  - Merged Pharmacophore Creator
  - Shared Pharmacophore Creator
  - Structure-based Pharmacophore Creator
- Screening
  - Activity Profiling
  - IScreen
- Tautomerization
  - Tautomer Generation
- Tools
  - 3D Viewer
  - ChartView
  - Table Merger

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KNIME Tutorial Workflows

Inte:Ligand KNIME EXTENSION TUTORIAL CARD 2

Create Ligand Based Pharmacophore Models

Experience level: intermediate
Time needed: 15 minutes

Node Repository	Sequence
○ I/O - PDB Reader ○ Pharmacophore - Ligand-based Pharmacophore Creator	○ Read a SMILES file by using "SM ○ Connect the output of "SMILES Conformer Generator" node ○ Configure "Icon Conformer Gen ○ Connect the first port of "Icon C with the second input port of " Clustering" node and execute it ○ Connect the second output po "Pharmacophore/Molecule Clus port of "Ligand-based Pharmac ○ Configure "Ligand-based Pharm selecting the "Treat cluster ind ○ Connect "Ligand-based Pharma "Pharmacophore Writer" node "Export all pharmacophores t ○ Choose the folder in which sa execute the node

Description

In the Node Repository panel, open the "I/O" drop do the "SMILES Reader"[1] node and drag and drop it into F6.[2] A pop-up window for configuration will appear the traffic light underneath the node, which was red right click on it and press "Execute" from the pop-up visit the Node Repository panel again and open the " Look for the "Icon Conformer Generator" node and dr node (black triangle) with the input port of the "Icon node and configure it. In the pop-up window, click o (F7). In the "Clustering" drop down menu select the ' connect the first output of the "Icon Conformer Gene "Pharmacophore" drop down menu, drag and drop ' second output port of "Pharmacophore/Molecule Clu configure it selecting the "Treat cluster individually" the first output port of the "Ligand-based Pharmacop pharmacophores to a single file" and choose a nam Press OK and execute the node (F7). [4] The progran the pharmacophore model(s) you have generated.

Where to go from here:

- Screening database(s) against pharmacophore
- Use generated pharmacophores for Activity Pr

Inte:Ligand KNIME EXTENSION TUTORIAL CARD 1

Create Structure Based Pharmacophore Models

Experience level: basic
Time needed: 10 minutes

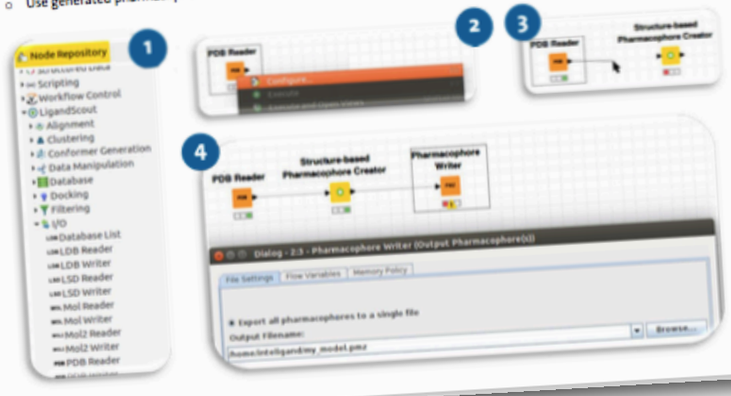
Node Repository	Sequence	Advanced controls (opt.)
○ I/O - PDB Reader - Pharmacophore Writer ○ Pharmacophore - Structure-based Pharmacophore Creator	○ Read a PDB file by using "PDB Reader" node ○ Connect the output of "PDB Reader" node with "Structure-based Pharmacophore Creator" node ○ Configure "Structure-based Pharmacophore Creator" node and execute it ○ Connect "Structure-based Pharmacophore Creator" node with "Pharmacophore Writer" node ○ Configure "Pharmacophore Writer" node selecting "Export all pharmacophores to a single file" ○ Choose the folder in which save my_model.pmz, then execute the node	○ Prepare batch mode processing: - Configure "PDB Reader" node to read multiple PDB files at the same time ○ Modify pharmacophore creation parameters - Configure "Structure-based Pharmacophore Creator" node to add the exclusion volume coat to the model ○ Explore the options of the "Pharmacophore Writer" node (e.g. pharmacophore models saved as separate files)

Description

In the Node Repository panel, open the "I/O" drop down menu in the LigandScout section to see all the Input/Output nodes. Look for the "PDB Reader" [1] node and drag and drop it into the workspace. Configure the "PDB Reader" node by using a left double click or by pressing F6. [2] A pop-up window for configuration will appear and you enter the path to the PDB file you want to load. Press the "Add" button. You can add multiple PDB files. After pressing OK, the traffic light underneath the node, which was red before, will turn to yellow. Press F7 to execute the node (alternatively, you can right click on it and press "Execute" from the pop-up menu). The traffic light will turn green once the node has finished the task. Now, visit the Node Repository panel again and open the "Pharmacophore" drop down menu in the LigandScout drop down menu. Look for the "Structure-based Pharmacophore Creator" node and drag and drop it into the workspace. Connect the output port of the "PDB Reader" node (black triangle) with the input port of the "Structure-based Pharmacophore Creator" node (black triangle) [3]. Select the "Structure-based Pharmacophore Creator" node and configure it. In the pop-up window, select the minimum number of features necessary or creating the model (3) and the set the flag for adding an exclusion volume coat. After pressing OK, execute the node as before (F7). Once the task is finished the traffic light underneath the "Structure-based Pharmacophore Creator" node will turn green. In the "I/O" drop down menu select the "Pharmacophore Writer" node and drag and drop it in the workspace, connect the output of the "Structure-based Pharmacophore Creator" node with it and start the configuration as before. In the pop-up windows select "Export all pharmacophores to a single file" and choose a name for the output (you can also browse for the folder). [4] Press OK and execute the node (F7). The program will save a file in the specified directory containing the pharmacophore model(s) you have generated.

Where to go from here:

- Screening database(s) against pharmacophore model(s)
- Cluster pharmacophores
- Use generated pharmacophores for Activity profiling



Inte:Ligand KNIME EXTENSION TUTORIAL CARD 3

Calculate Physicochemical Properties and Filter a Database

Experience level: basic
Time needed: 5 minutes

	Advanced controls (opt.)
by using "SDF Reader" node tput of "SDF Reader" node with "Standard dard Properties" node and execute it d Properties" node with "Library Filter" node y Filter" node and execute it output port of "Library Filter" node with d output port of "Library Filter" node with	○ Calculate physicochemical properties: - Configure "Standard Properties" node to compute different sets of properties ○ Modify filtering parameters: - Add other text and/or numeric filters in "Library Filter" node - Configure the "Library Filter" node adding multiple properties to your filter - Explore all the filtering operators (equal, different, smaller than, greater than)

drop down menu in the LigandScout section to see all the Input/Output nodes. Look for
nto the workspace. Configure the node as showed in previous tutorial cards (by pressing
e Repository panel again and open the "Molecule properties" drop down menu in the
tandard Properties" node and drag and drop it into the workspace. Connect the output
ort of the "Standard Properties" node. Select the "Standard Properties" node and configure
chemical properties you want to compute (these properties will be used in the next
ll at once by pressing the corresponding "Select all" button. After pressing OK, execute
u select the "Library Filter" node and drag and drop it in the workspace, connect the
and continue with its configuration. In the pop-up windows, the "Library Filter" node
s by string (pressing the "+abc" button)[1 red circle] or numeric property (pressing the
utton and a filtering row will appear. Configure the row by choosing "MolWt" in the
tton[2] until "<" symbol appears. Write then in the editable text box a value to use for
, the node will filter out molecules with molecular weight smaller than 400. Explore
Writer" node and drag and drop two of them in the workspace. Connect them with
respectively. The "SDF Writer" node connected to the first output port of the
olecular weight smaller than 400, while the one connected to the second output
greater than 400. Configure the "SDF Writer" nodes choosing the name for the
failed_molecules.sdf for the second). Execute them with F7.[4]

Inte:Ligand KNIME EXTENSION TUTORIAL CARD 4

Perform Virtual Screening

Experience level: intermediate
Time needed: 15 minutes

controls (opt.)
gand parameters: re "SDF Reader" node to extract name ifferent column "Icon Conformer Generator" settings (e.g. ST settings) meters for "iScreen" node: he scoring function agment screening mode fferent retrieval modes the node in order to not check the olumes mode processing: Pharmacophore Reader" node to read s at the same time ean expression with "iScreen" node not 3. Numbers are referred to the res ranking in the "Pharmacophore

into the workspace. Configure the
op the "Icon Conformer Generator"
port of the "SDF Reader" node
" node. In the pop-up window,
/O" drop down menu ,select the
on Conformer Generator" node
DB file.[3] Execute and then
drop down menu. Add the
rmacophore model you want to
second input port of the
e name for the output file.
lecules as a sdf file.

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