



Integrated Cheminformatics to Guide Drug Discovery

Matthew Segall, Ed Champness, Peter Hunt, Tamsin Mansley

CINF Drug Discovery Cheminformatics Approaches

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Overview

- The impact of fragmentation of cheminformatics tools
- Challenges of integration
 - Examples: Data access and docking/alignment
- Illustrative application
- Conclusions

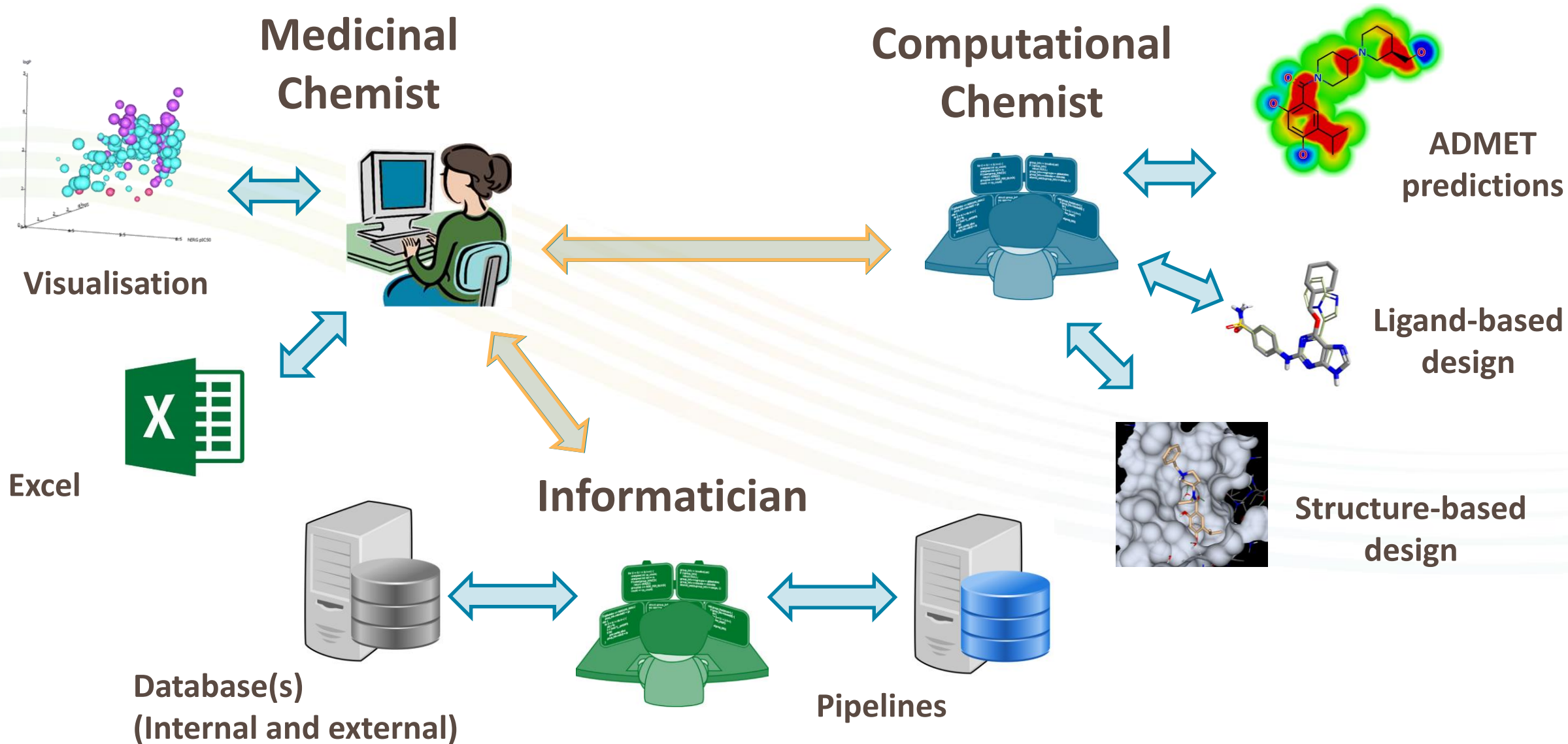
Fragmentation



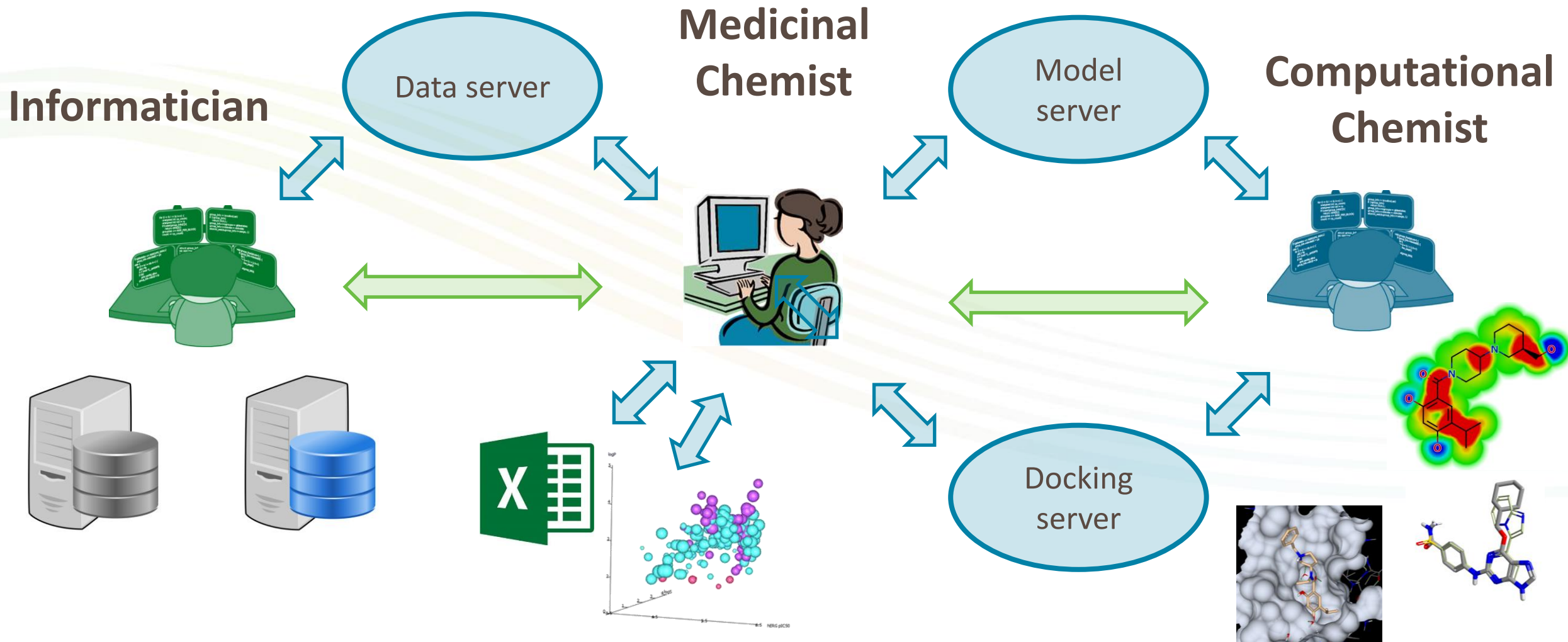
Fragmentation of Cheminformatics Tools

- Many capabilities are required to drive drug discovery projects
 - Database access
 - Visualisation and analysis of data
 - 2D predictive modelling (QSAR)
 - 3D structure-based design
 - ...
- Disparate tools for these features create bottlenecks and inefficiencies
 - Reformatting of data to move between applications
 - o Time consuming and lost information
 - Different user interfaces
 - o Training burden
 - ‘Expert’ tools can be impenetrable to non-computational chemists
 - o Support from experts even for mundane tasks
 - o Delay and distraction of experts from adding scientific value

Common Situation



Better Situation



Advantages

- Project leader can have all information available in one place
 - (Ideally) single, common interface
 - Can get instant feedback on new design ideas
- Computational and data experts do not waste time on routine, mundane calculations
 - Focus on scientifically interesting and valuable activities
- Encourages closer collaboration
 - Uninteresting ideas are quickly eliminated
 - Collaborations can focus on high-value ideas for more detailed investigation

Integration



The Challenges of Integration

- Different software preferences for many tasks
 - Database/ELN providers
 - ‘Favourite’ docking or alignment platforms
 - Must be agnostic to the source of data and predictions
- Different architectures
 - Web, web services, desktop, command line...
- Interaction is key
 - Stimulates new ideas and strategies
 - Black boxes are not trusted
- Must be user-friendly and intuitive
 - Low barrier to use
 - ‘Gluing’ lots of different software together leads to a poor user experience

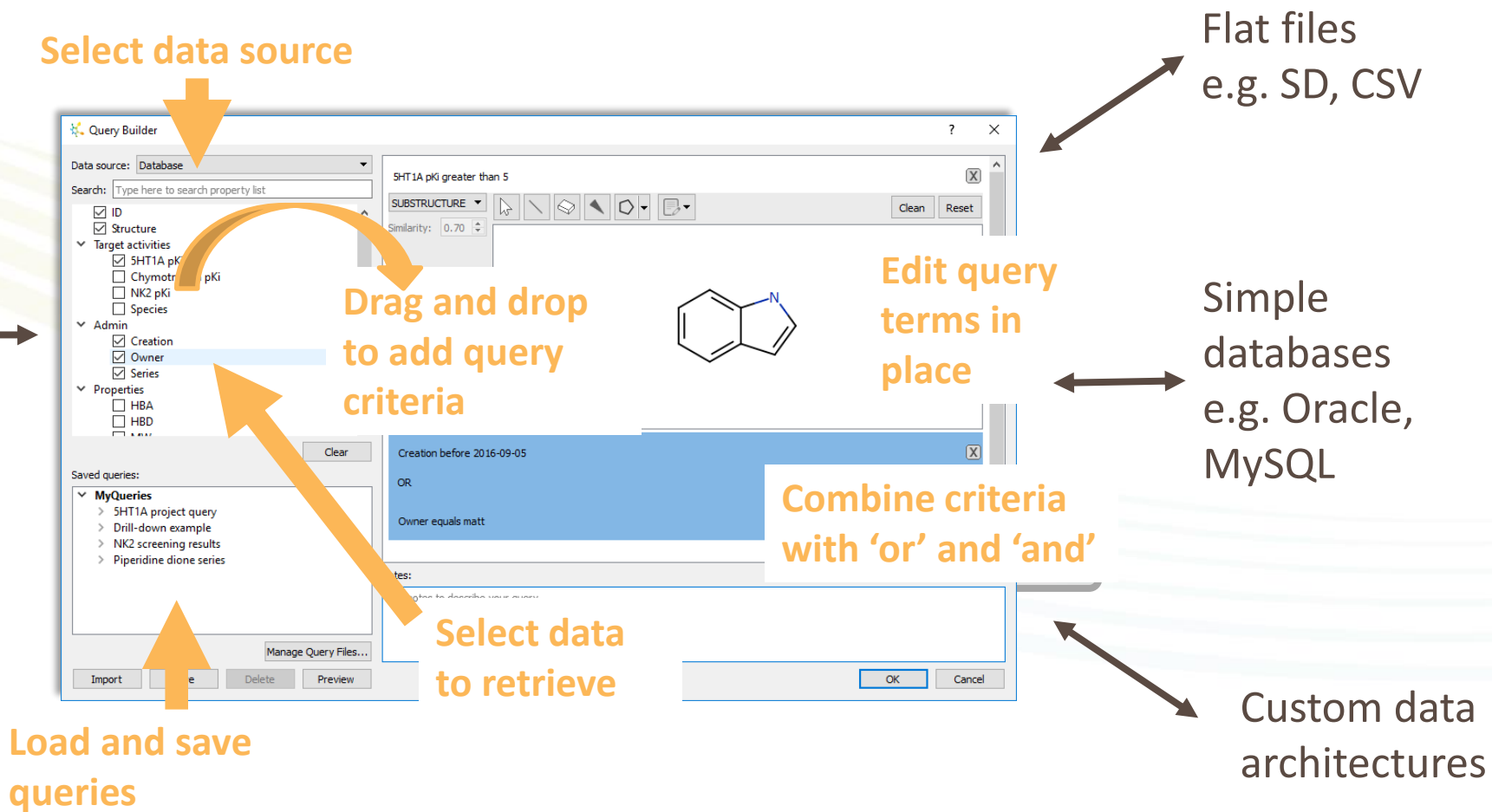
Example: Database access

Challenge

- Provide access to multiple data sources, e.g.
 - SQL via ODBC
 - Flat files
 - Web services...
- User-friendly definition of search criteria and fields
 - Support for criteria based on chemical structure, numerical, date, textual and categorical fields
- Save, share, edit and execute pre-defined queries
 - Stored individually or by project
- Support for multiple data aggregation levels
 - Drill-down to underlying data

Example: Database access

Solution



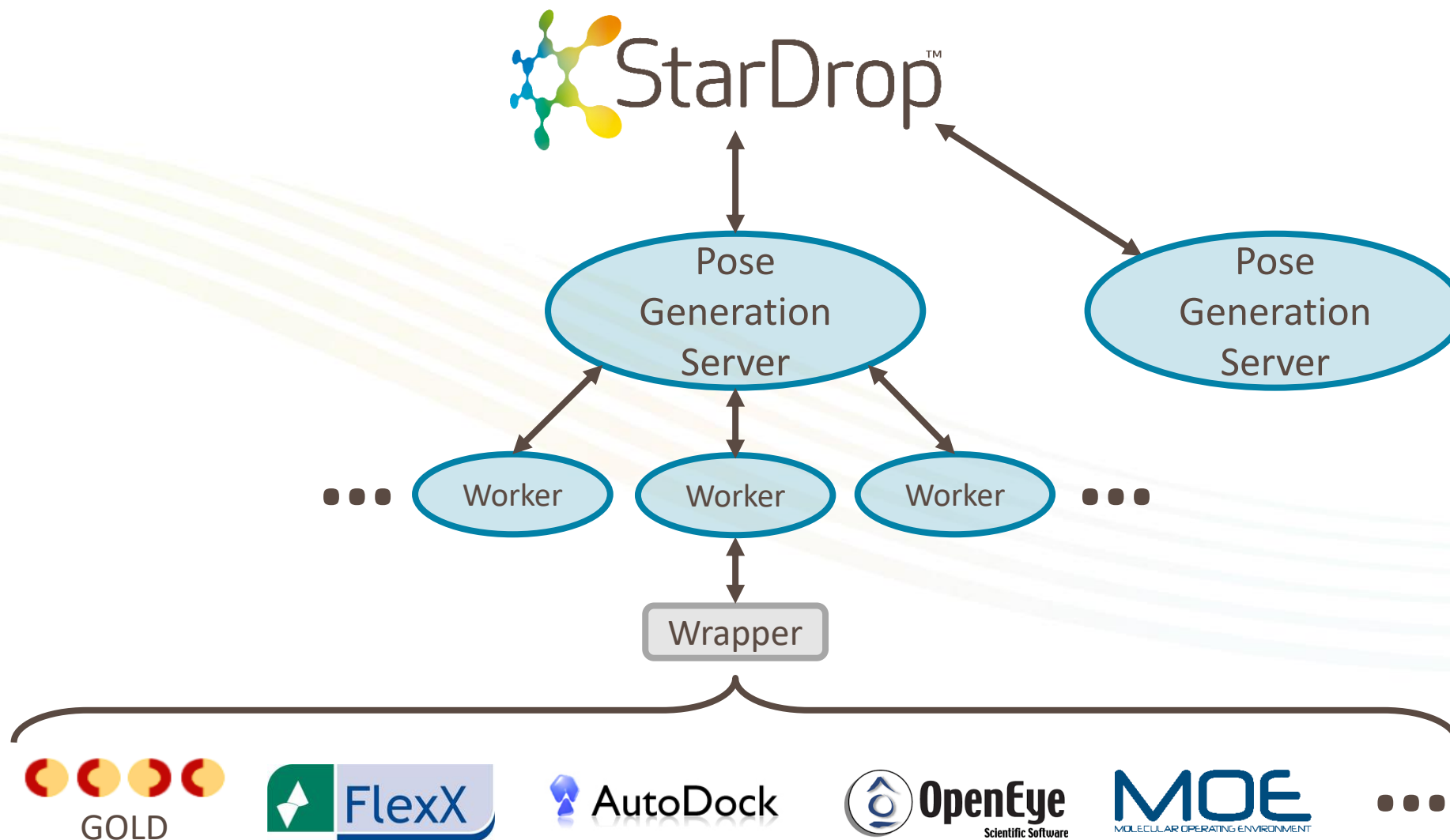
Example: Docking and Alignment

Challenge

- Enable non-expert users to run docking, pharmacophore or conformation generation calculations
 - Quick feedback on new compound designs
 - Link information from 3D models with other analyses and data
- Support for all major 3D modelling platforms
 - Flexibility to run models using preferred methods
- Expert computational chemists can easily publish new 3D models
 - Configuration files for new targets 'drop in' on server
- Server to enable queuing and batch processing of long calculations

Example: Docking and Alignment

Solution

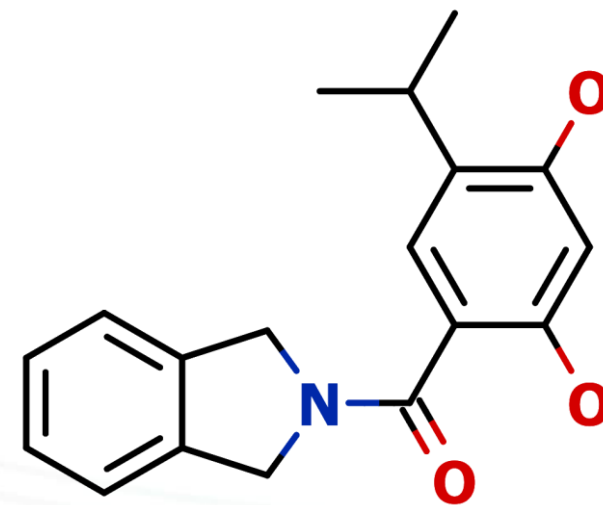


Example Application



Background

- Target: Heat-shock protein 90 (HSP90)
- Initial hits based on fragment based drug discovery
 - PDB: 2XAB
 - SAR explored around resorcinol in isoindoline resorcinol series
- Objectives
 - Explore substitutions and replacements for isoindoline
 - Identify high quality compounds for oncology target
 - Decide on synthetic strategy
- Based on initial SAR from Woodhead *et al.* J. Med. Chem. 53 p. 5956 (2010)
 - N.B. This is not the process used in this project; structures and data used for illustrative purposes only



Retrieve Data for Latest Hits

Unsubstituted isoindolines

The screenshot displays the 'Query Builder' application window. The 'Data source' is set to 'Project Data'. The search criteria are defined in the left-hand pane:

- Biological Data:**
 - HCT116 IC50
 - HSP90 Kd
 - hERG inhibition @ 3 uM
 - hERG inhibition @ 30 uM
- Compound Information:**
 - Identifier
 - Structure
- Physchem Properties:**
 - logD @ pH 7.4
 - pKa

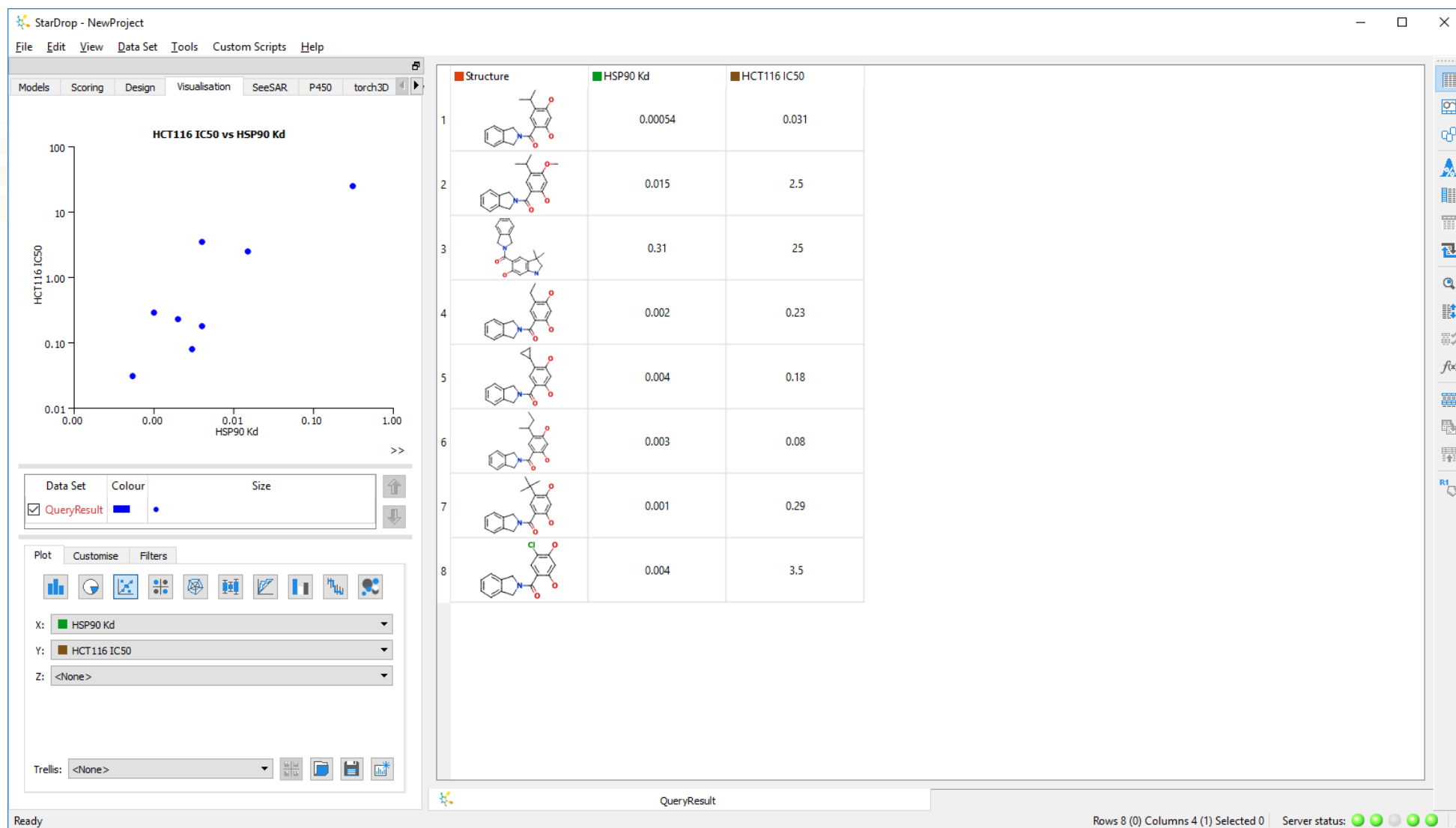
The 'Saved queries' section on the left includes:

- MyQueries:**
 - > 5HT1A project query
 - > Piperidine dione series
- ABase queries:**
 - > Chymotrypsan series
- ProjectQueries:**
 - > NK2 Project

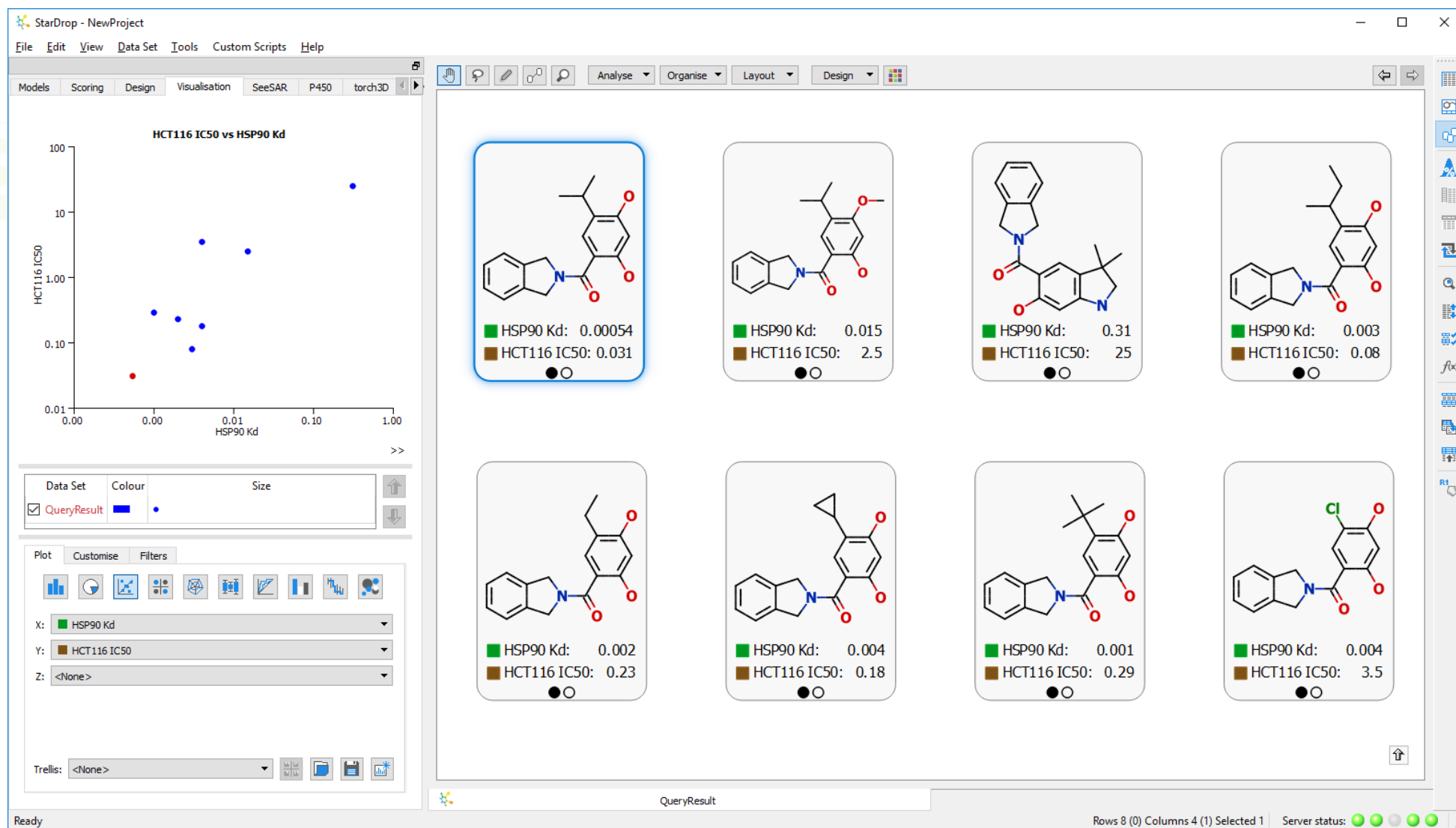
The main workspace shows a 'SUBSTRUCTURE' view with a similarity filter of 0.70. A chemical structure of unsubstituted isoindoline is displayed, with the SMILES string C1=CC=C2C(=C1)NCC2. Below the structure, the query is defined as 'HSP90 Kd less than 1'. The 'Notes' field is currently empty.

Buttons at the bottom of the window include 'Import', 'Save', 'Delete', 'Preview', 'OK', and 'Cancel'. A 'Manage Query Files...' button is also present.

Initial SAR



Initial SAR



Crystal Structure

PDB 2XAB

The screenshot displays the StarDrop software interface. On the left, a 3D molecular model shows a protein (grey) with a ligand (orange) bound in its pocket. The interface includes a menu bar (File, Edit, View, Data Set, Tools, Custom Scripts, Help) and a toolbar with various icons. Below the 3D model is a table with columns for Structure and ID. The main area on the right shows a grid of eight ligand structures, each with its HSP90 Kd and HCT116 IC50 values. The first structure in the top-left is highlighted with a blue border.

| Structure | ID | HSP90 Kd | HCT116 IC50 |
|-----------|----|----------|-------------|
| | | 0.00054 | 0.031 |
| | | 0.015 | 2.5 |
| | | 0.31 | 25 |
| | | 0.003 | 0.08 |
| | | 0.002 | 0.23 |
| | | 0.004 | 0.18 |
| | | 0.001 | 0.29 |
| | | 0.004 | 3.5 |

Dock with HSP90 Model

StarDrop - NewProject

File Edit View Data Set Tools Custom Scripts Help

Models Scoring Design Visualisation SeeSAR P450 torch3D

Protein Display Show Binding SeeSAR Powered by

Structure ID

Ready

Rows 8 (0) Columns 4 (1) Selected 1 Server status: ●●●●●●●●

Select Pose Generation Target

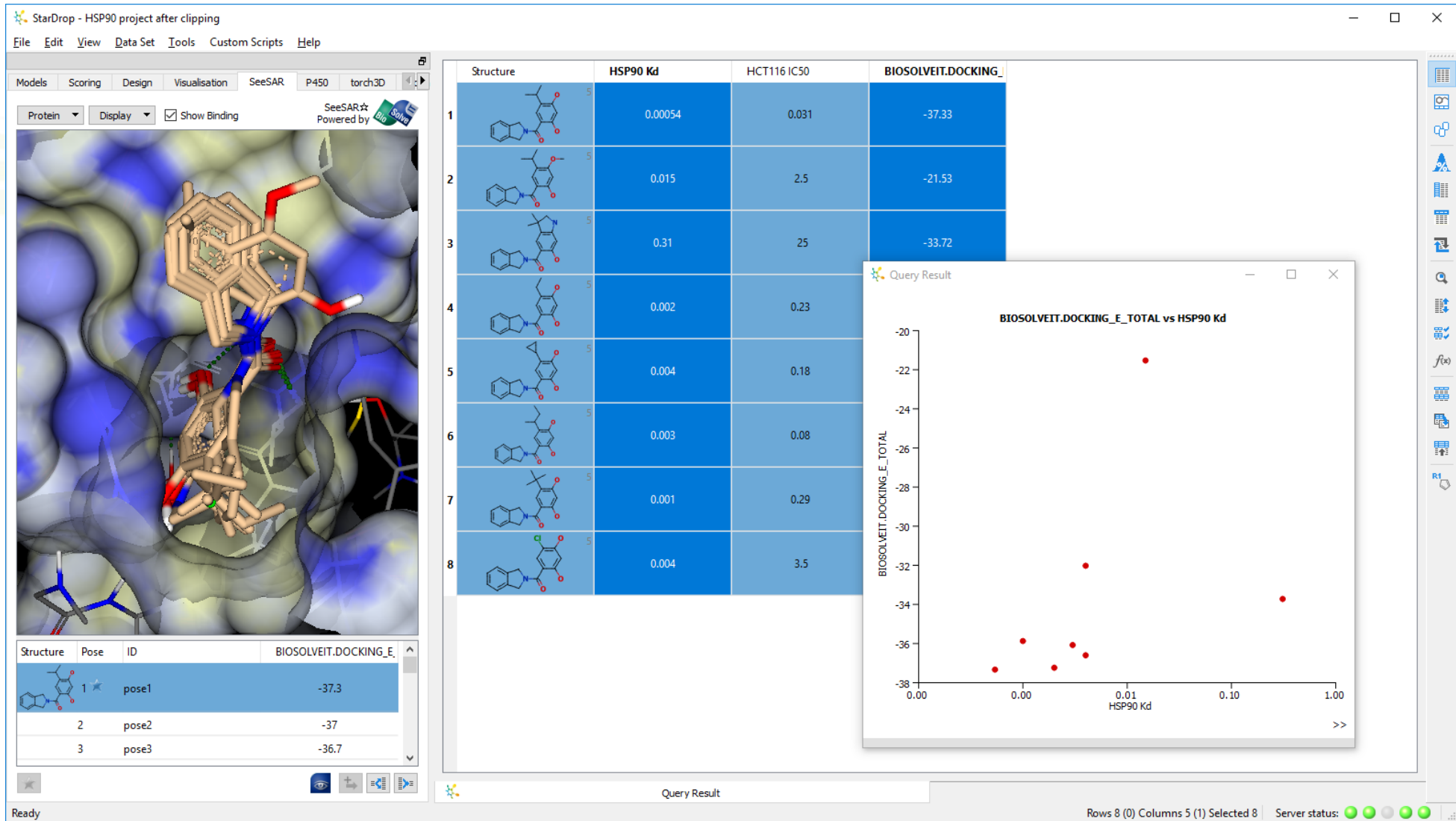
Filter targets: Type to filter the list of targets

| Target | Engine | Description |
|------------------|-----------------|--|
| ▼ Pose Genera... | Pending Jobs: 0 | |
| HSP90 | AutoDock | Heat shock protein 90 |
| HSP90 | FlexX | Heat shock protein 90 |
| HSP90 | GOLD | Heat shock protein 90 |
| HSP90 | MOE | Heat shock protein 90 |
| HIV Prot... | AutoDock | HIV Protease |
| Confor... | MOE | Free movement without QM - allows rotation of a... |
| Confor... | MOE | Restricted movement with QM |
| Confor... | MOE | Restricted movement without QM |
| CYP2D6 | GOLD | CytochromeP450 CYP2D6 - Human |
| CYP2D6 | MOE | Cytochrome P450 Isoform 2D6 - taken from PDB e... |
| CDK2 | GOLD | Cyclin-dependent kinase 2 - from pdb code 1OIT - ... |
| CDK2 | MOE | Cyclin-dependent kinase 2 - Human - A PH4 requir... |
| 7HVP | GOLD | HIV Protease |
| 7HVP | MOE | HIV Protease |
| 3RZE | AutoDock | Human histamine H1 receptor |
| 3RZE | FlexX | Human histamine H1 receptor |

Use 3D coordinates if available

OK Cancel

HSP90 Docking Results



Search eMolecules

Substituted isoindolines and potential replacements

The screenshot displays the StarDrop software interface. The main window shows a 3D molecular model of a protein-ligand complex. The protein is shown as a blue and grey surface, and the ligand is shown as a stick model. The interface includes a menu bar (File, Edit, View, Data Set, Tools, Custom Scripts, Help) and a toolbar with various icons. The 'Structure Query' window is open, showing a list of molecules with their chemical structures and associated data. The data includes HSP90 Kd and HCT116 IC50 values. The molecules are displayed in a grid, and the user can interact with them using the 'Structure Query' window.

| Structure | ID | HSP90 Kd | HCT116 IC50 |
|-----------|-----|----------|-------------|
| | 001 | 0.31 | 25 |
| | 002 | 0.003 | 0.08 |
| | 003 | 0.004 | 3.5 |
| | 004 | 0.29 | |

Search eMolecules Results

The screenshot displays the StarDrop software interface. On the left, a 3D molecular model shows a protein surface with a ligand bound in a pocket. The interface includes a menu bar (File, Edit, View, Data Set, Tools, Custom Scripts, Help) and a toolbar with options like Models, Scoring, Design, Visualisation, SeeSAR, P450, and torch3D. A 'Show Binding' checkbox is checked. Below the model is a 'Structure ID' panel with a small chemical structure and a search bar.

On the right, a table displays search results for 'Secondary amines'. The table has the following columns: VID, SMILES, eMolecules URL, Price, Currency, Quantity, and Units. The results are as follows:

| VID | SMILES | eMolecules URL | Price | Currency | Quantity | Units |
|--------------|--------|---|-------|----------|----------|-------|
| 126 70097331 | | https://www.emolecules.com | 463 | USD | 250 | mg |
| 127 11488411 | | https://www.emolecules.com | ? | | ? | |
| 128 711743 | | https://www.emolecules.com | ? | | ? | |
| 129 50763605 | | https://www.emolecules.com | ? | | ? | |
| 130 81847119 | | https://www.emolecules.com | ? | | ? | |
| 131 716504 | | https://www.emolecules.com | ? | | ? | |
| 132 529586 | | https://www.emolecules.com | ? | | ? | |
| 133 2793805 | | https://www.emolecules.com | 255 | USD | 1 | g |
| 134 530212 | | https://www.emolecules.com | 30 | USD | 25 | g |
| 135 44230272 | | https://www.emolecules.com | ? | | ? | |
| 136 01071307 | | https://www.emolecules.com | ? | | ? | |

The bottom status bar shows 'Ready', 'QueryResult', 'Secondary amines', 'Rows 209 (0) Columns 18 (2) Selected 0', and 'Server status: [green circles]'.

Clip Reagents

The screenshot displays the StarDrop software interface for a project named "StarDrop - HSP90 project after clipping". The interface includes a menu bar (File, Edit, View, Data Set, Tools, Custom Scripts, Help) and a toolbar with various icons. Below the menu bar, there are tabs for "Models", "Scoring", "Design", "Visualisation", "SeeSAR", "P450", and "torch3D". A "Protein" dropdown menu and a "Display" dropdown menu are visible, along with a checked "Show Binding" option. The main workspace is divided into two sections. On the left, a 3D molecular model shows a protein surface (blue and grey) with a ligand (orange and red) bound in a pocket. On the right, a grid of six chemical structures is displayed, each with its ID and an "R-group" label. The structures are: 1) ID 53992956, a benzimidazole derivative; 2) ID 208145379, a benzimidazole derivative with a methyl group; 3) ID 40958902, a benzimidazole derivative with a vinyl group; 4) ID 40958884, a benzimidazole derivative with a cyclopropyl group; 5) ID 49802918, a benzimidazole derivative with a methyl group; 6) ID 48663805, a benzimidazole derivative with a fluorine atom. Each structure is shown in its original form and as an R-group variation (indicated by a green square and a plus sign). The bottom status bar shows "Ready", "QueryResult", "Secondary amines", "Clipped", "Rows 209 (0) Columns 20 (0) Selected 0", and "Server status: [green circles]".

StarDrop - HSP90 project after clipping

File Edit View Data Set Tools Custom Scripts Help

Models Scoring Design Visualisation SeeSAR P450 torch3D

Protein Display Show Binding SeeSAR Powered by

53992956

R-group:

208145379

R-group:

40958902

R-group:

40958884

R-group:

49802918

R-group:

48663805

R-group:

Ready

QueryResult Secondary amines Clipped

Rows 209 (0) Columns 20 (0) Selected 0 Server status: [green circles]

Enumerate Library

StarDrop - HSP90 project after clipping

File Edit View Data Set Tools Custom Scripts Help

Models Scoring Design Visualisation SeeSAR P450 torch3D

Protein Display Show Binding SeeSAR Powered by Solera

Nova Wizard

Select Task

- Nova Ideas Ge
- Library Enume
- Matched Serie

Library Enumeration

Define R-Groups

R1 =

Estimated library size = 169 compounds

Fragment Library... < Back Next > Finish Cancel

40958902

R-group:

48663805

R-group:

(0) Columns 20 (0) Selected 0 Server status: ●●●●●

Enumerated Library

The screenshot displays the StarDrop software interface for a project named "StarDrop - HSP90 project after clipping". The interface is divided into several sections:

- Parents:** An empty box for defining parent structures.
- Current:** A box containing a single chemical structure, which is a complex molecule with a benzimidazole core and a substituted benzene ring.
- Children:** An empty box for defining child structures.
- Structure and Analysis2 R1 Grid:** A 11x2 grid of chemical structures. The left column is labeled "Structure" (green icon) and the right column is labeled "Analysis2 R1" (red icon). Each cell contains a chemical structure with a small number (1-11) to its left, representing the enumeration of the library.
- Bottom Panel:** Includes buttons for "Transformations...", "Fragments...", and "Show Details...". Below these are tabs for "QueryResult", "Secondary amines", "Clipped", and "Library". The status bar at the bottom right shows "Rows 207 (0) Columns 2 (0) Selected 0" and "Server status: [green circles]".

Dock Library

StarDrop - HSP90 project after clipping

File Edit View Data Set Tools Custom Scripts Help

Design Visualisation SeeSAR P450 torch3D Nova Auto-Modeller

Parents:

Current:

Children:

Transformations... Fragments... Show Details...

Ready

QueryResu

Structure Analysis2 R1

1 2 3 4 5 6 7 8 9 10 11

Select Pose Generation Target

Filter targets: Type to filter the list of targets

| Target | Engine | Description |
|------------------|-----------------|--|
| ▼ Pose Genera... | Pending Jobs: 0 | |
| HSP90 | AutoDock | Heat shock protein 90 |
| HSP90 | FlexX | Heat shock protein 90 |
| HSP90 | GOLD | Heat shock protein 90 |
| HSP90 | MOE | Heat shock protein 90 |
| HIV Prot... | AutoDock | HIV Protease |
| Confor... | MOE | Free movement without QM - allows rotation of a... |
| Confor... | MOE | Restricted movement with QM |
| Confor... | MOE | Restricted movement without QM |
| CYP2D6 | GOLD | CytochromeP450 CYP2D6 - Human |
| CYP2D6 | MOE | Cytochrome P450 Isoform 2D6 - taken from PDB e... |
| CDK2 | GOLD | Cyclin-dependent kinase 2 - from pdb code 1OIT - ... |
| CDK2 | MOE | Cyclin-dependent kinase 2 - Human - A PH4 requir... |
| 7HVP | GOLD | HIV Protease |
| 7HVP | MOE | HIV Protease |
| 3RZE | AutoDock | Human histamine H1 receptor |
| 3RZE | FlexX | Human histamine H1 receptor |

Use 3D coordinates if available

OK Cancel

Rows 207 (0) Columns 2 (0) Selected 0 Server status: ●●●●●

Dock Library

The screenshot displays the StarDrop software interface for a project named "StarDrop - HSP90 project after clipping". The interface is divided into several sections:

- 3D Visualization:** A central window shows a protein structure (grey) with a docked ligand (orange sticks) inside a semi-transparent surface representation of the protein's binding pocket. The protein is labeled "SeeSAR" and "Powered by Biosolveit".
- Results Table:** A table on the right lists docking results for various ligands. The table has three columns: "Structure" (with a green icon), "Analysis2 R1" (with a red icon), and "BIOSOLVEIT.DOCKING_" (with a purple icon). The rows are numbered 82 to 92. Row 85 is highlighted in blue, indicating the best result.
- Table Data:**

| Structure | Analysis2 R1 | BIOSOLVEIT.DOCKING_ |
|-----------|--------------|---------------------|
| 82 | 5 | -33.89 |
| 83 | 5 | -35 |
| 84 | 5 | -33.68 |
| 85 | 5 | -34.72 |
| 86 | 5 | -34.33 |
| 87 | 5 | -34.02 |
| 88 | 5 | -32.69 |
| 89 | 5 | -31.78 |
| 90 | 5 | -33.85 |
| 91 | 5 | -33.62 |
| 92 | 5 | -30.56 |
- Bottom Panel:** A small table shows the top three poses for the selected structure (ID: BIOSOLVEIT.DOCKING_E):

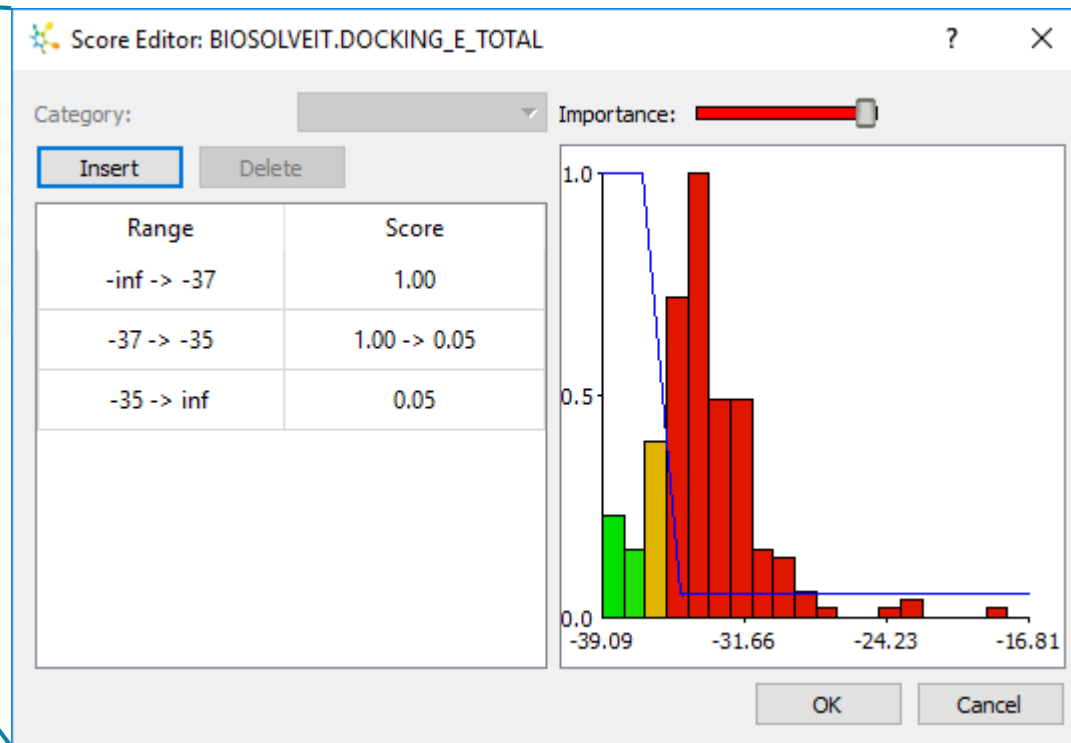
| Structure | Pose | ID | BIOSOLVEIT.DOCKING_E |
|-----------|------|-------|----------------------|
| | 1 | pose1 | -34.7 |
| | 2 | pose2 | -34.5 |
| | 3 | pose3 | -34.3 |
- Bottom Bar:** Shows the current selection: "QueryResult", "Secondary amines", "Clipped", and "Library". It also displays "Rows 207 (0) Columns 3 (0) Selected 1" and "Server status: [green circles]".

Good Docking Score is Not Enough

Multi-parameter optimisation

- Also require good Absorption, Distribution, Metabolism, Excretion and Toxicity (ADMET) properties

| Property | Desired Value | Importance |
|--------------------------|---------------------------|------------|
| BIOSOLVEIT.DOCKING_E... | $-\infty \rightarrow -37$ | 1.00 |
| logS | > 1 | 1.00 |
| HIA category | + | 1.00 |
| logP | $0 \rightarrow 3.5$ | 0.05 |
| hERG pIC50 | ≤ 5 | 0.05 |
| 2D6 affinity category | low medium | 0.05 |
| 2C9 pKi | ≤ 6 | 0.05 |
| P-gp category | no | 0.05 |
| PPB90 category | low | 0.05 |
| BBB category | - | 0.05 |
| BBB log([brain]:[blood]) | ≤ -0.5 | 0.05 |



MPO Scores

StarDrop - HSP90 project after clipping

File Edit View Data Set Tools Custom Scripts Help

Models Scoring Design Visualisation SeeSAR P450 torch3D

Profile: Docking + Oral Non CNS Scoring Profile

| Property | Desired Value | Importance |
|--------------------------|---------------|------------|
| BIOSOLVEIT.DOCKING_E... | -inf -> -37 | |
| logS | > 1 | |
| HIA category | + | |
| logP | 0 -> 3.5 | |
| hERG pIC50 | ≤ 5 | |
| 2D6 affinity category | low medium | |
| 2C9 pKi | ≤ 6 | |
| P-gp category | no | |
| PPB90 category | low | |
| BBB category | - | |
| BBB log([brain]:[blood]) | ≤ -0.5 | |

Available Properties Criteria Importance

- Carcinogeni...
- Photocarcin...
- Chromosom...
- Photo-induc...
- Mutagenicity
- Photomutag...
- Non-specific...
- Photo-induc...

Scoring Profiles Location

- Oral Non CNS Scoring Profile File
- Oral CNS Scoring Profile File
- NK2 Project File
- Matsy Oral CNS Scoring Profile File
- Lipinski Rule of Five File
- Intravenous Non CNS Scoring Profile File
- Intravenous CNS Scoring Profile File
- Hvde pKi + Oral Non CNS Scoring Profile File

MPO Explorer:

Build profile... Analyse... Sensitivity...

| | Docking + Oral Non CNS | Structure | Analysis2 R1 | BIOSOLVEIT.DOCKING_E... | logS | logP | 2C9 pKi |
|----|------------------------|-----------|--------------|-------------------------|-------|-------|---------|
| 1 | 0.4346 | | | -37.25 | 1.902 | 1.826 | 5.495 |
| 2 | 0.4118 | | | -38.56 | 2.334 | 2.3 | 5.188 |
| 3 | 0.3953 | | | -38.4 | 2.156 | 2.822 | 5.284 |
| 4 | 0.3899 | | | -38.71 | 1.624 | 2.609 | 5.371 |
| 5 | 0.3762 | | | -37.48 | 2.169 | 2.672 | 5.464 |
| 6 | 0.3468 | | | -38.91 | 1.718 | 2.814 | 5.317 |
| 7 | 0.3282 | | | -37.17 | 1.925 | 3.2 | 5.567 |
| 8 | 0.3199 | | | -37.56 | 1.925 | 3.2 | 5.561 |
| 9 | 0.2954 | | | -38.24 | 1.791 | 2.935 | 5.418 |
| 10 | 0.2894 | | | -38.62 | 1.791 | 2.935 | 5.413 |
| 11 | 0.2827 | | | 20.00 | 1.020 | 2.27 | 5.425 |

QueryResult Secondary amines Clipped Library

Rows 207 (0) Columns 14 (0) Selected 0 Server status: ●●●●●

Compound Overview

StarDrop - HSP90 project after clipping

File Edit View Data Set Tools Custom Scripts Help

Models Scoring Design Visualisation SeeSAR P450 torch3D

Analyse Organise Layout Design

Profile: Docking + Oral Non CNS Scoring Profile

| Property | Desired Value | Importance |
|--------------------------|---------------|------------|
| BIOSOLVEIT.DOCKING_E... | -inf -> -37 | |
| logS | > 1 | |
| HIA category | + | |
| logP | 0 -> 3.5 | |
| hERG pIC50 | ≤ 5 | |
| 2D6 affinity category | low medium | |
| 2C9 pKi | ≤ 6 | |
| P-gp category | no | |
| PPB90 category | low | |
| BBB category | - | |
| BBB log([brain]:[blood]) | ≤ -0.5 | |

Add rule Delete Sort Edit Save

| Available Properties | Criteria | Importance |
|----------------------|----------|------------|
| Carcinogeni... | | |
| Photocarcin... | | |
| Chromosom... | | |
| Photo-induc... | | |
| Mutagenicity | | |
| Photomutag... | | |
| Non-specifi... | | |
| Photo-induc... | | |

| Scoring Profiles | Location |
|---|----------|
| Oral Non CNS Scoring Profile | File |
| Oral CNS Scoring Profile | File |
| NK2 Project | File |
| Matsy Oral CNS Scoring Profile | File |
| Lipinski Rule of Five | File |
| Intravenous Non CNS Scoring Profile | File |
| Intravenous CNS Scoring Profile | File |
| Hvde pKi + Oral Non CNS Scoring Profile | File |

MPO Explorer:

Build profile... Analyse... Sensitivity...

QueryResult Secondary amines Clipped Library

Rows 207 (0) Columns 14 (0) Selected 0 Server status: ●●●●●●●●●●●●●●

Identify Chemotypes

The screenshot displays the StarDrop software interface for a project named "StarDrop - HSP90 project after clipping". The main window is divided into several sections:

- Left Panel:** Contains a "Profile: Docking + Oral Non CNS Scoring Profile" with various properties and their desired values and importance levels. Below this is a list of "Available Properties" and "Scoring Profiles".
- Top Panel:** Includes navigation and analysis tools like "Analyse", "Organise", "Layout", and "Design".
- Main Grid:** A 4x4 grid of chemical structures, each accompanied by a bar chart and a "Docking + Oral Non..." score. The scores range from 0.2817 to 0.4346.
- Find Rows Dialog:** A central dialog box with "Text Search" and "Substructure Search" tabs. It shows a chemical structure of a bicyclic amine and buttons for "Find Next" and "Find All".
- Bottom Panel:** Shows a status bar with "Rows 207 (0) Columns 14 (0) Selected 40" and "Server status" indicators.

| Property | Desired Value | Importance |
|--------------------------|---------------|------------|
| BIOSOLVEIT.DOCKING_E... | -inf -> -37 | High |
| logS | > 1 | High |
| HIA category | + | High |
| logP | 0 -> 3.5 | High |
| hERG pIC50 | ≤ 5 | High |
| 2D6 affinity category | low medium | High |
| 2C9 pKi | ≤ 6 | High |
| P-gp category | no | High |
| PPB90 category | low | High |
| BBB category | - | High |
| BBB log([brain]:[blood]) | ≤ -0.5 | High |

| Chemotype | Score |
|--------------|--------|
| Structure 1 | 0.4346 |
| Structure 2 | 0.4118 |
| Structure 3 | 0.3953 |
| Structure 4 | 0.3899 |
| Structure 5 | 0.3884 |
| Structure 6 | 0.3871 |
| Structure 7 | 0.3282 |
| Structure 8 | 0.3199 |
| Structure 9 | 0.2954 |
| Structure 10 | 0.2894 |
| Structure 11 | 0.2827 |
| Structure 12 | 0.2817 |

Stack Chemotypes

The screenshot displays the StarDrop software interface for a project named "HSP90 project after clipping". The main window shows a docking profile and a search window for "Isoindoline".

Profile: Docking + Oral Non CNS Scoring Profile

| Property | Desired Value | Importance |
|--------------------------|---------------|------------|
| BIOSOLVEIT.DOCKING_E... | -inf -> -37 | High |
| logS | > 1 | High |
| HIA category | + | High |
| logP | 0 -> 3.5 | High |
| hERG pIC50 | ≤ 5 | High |
| 2D6 affinity category | low medium | High |
| 2C9 pKi | ≤ 6 | High |
| P-gp category | no | High |
| PPB90 category | low | High |
| BBB category | - | High |
| BBB log([brain]:[blood]) | ≤ -0.5 | High |

Available Properties

| Criteria | Importance |
|----------------|------------|
| Carcinogeni... | High |
| Photocarcin... | High |
| Chromosom... | High |
| Photo-induc... | High |
| Mutagenicity | High |
| Photomutag... | High |
| Non-specifi... | High |
| Photo-induc... | High |

Scoring Profiles

| Scoring Profiles | Location |
|---|----------|
| Oral Non CNS Scoring Profile | File |
| Oral CNS Scoring Profile | File |
| NK2 Project | File |
| Matsy Oral CNS Scoring Profile | File |
| Lipinski Rule of Five | File |
| Intravenous Non CNS Scoring Profile | File |
| Intravenous CNS Scoring Profile | File |
| Hvde pKi + Oral Non CNS Scoring Profile | File |

Find Rows

Text Search | Substructure Search

Chemical structure: Isoindoline

40 of 207 (19.3%)

Docking + Oral Non CNS S...

BIOS...: [Bar Chart]

Library

Docking + Oral Non...: 0.2817

Rows 207 (0) Columns 14 (0) Selected 40 Server status: [Green Circles]

StarDrop - HSP90 project after clipping

File Edit View Data Set Tools Custom Scripts Help

Models Scoring Design Visualisation SeeSAR P450 torch3D

Profile: Docking + Oral Non CNS Scoring Profile

| Property | Desired Value | Importance |
|--------------------------|---------------|------------|
| BIOSOLVEIT.DOCKING_E... | -inf -> -37 | |
| logS | > 1 | |
| HIA category | + | |
| logP | 0 -> 3.5 | |
| hERG pIC50 | ≤ 5 | |
| 2D6 affinity category | low medium | |
| 2C9 pKi | ≤ 6 | |
| P-gp category | no | |
| PPB90 category | low | |
| BBB category | - | |
| BBB log([brain]:[blood]) | ≤ -0.5 | |

Add rule Delete Sort Edit Save

| Available Properties | Criteria | Importance |
|----------------------|----------|------------|
| Carcinogeni... | | |
| Photocarcin... | | |
| Chromosom... | | |
| Photo-induc... | | |
| Mutagenicity | | |
| Photomutag... | | |
| Non-specifi... | | |
| Photo-induc... | | |

| Scoring Profiles | Location |
|---|----------|
| Oral Non CNS Scoring Profile | File |
| Oral CNS Scoring Profile | File |
| NK2 Project | File |
| Matsy Oral CNS Scoring Profile | File |
| Lipinski Rule of Five | File |
| Intravenous Non CNS Scoring Profile | File |
| Intravenous CNS Scoring Profile | File |
| Hvde pKi + Oral Non CNS Scoring Profile | File |

MPO Explorer:

Build profile... Analyse... Sensitivity...

38 of 207 (18.4%)

38 of 207 (18.4%)

50 of 207 (24.2%)

Docking + Oral Non C...

Isoindoline

3-amino indoline

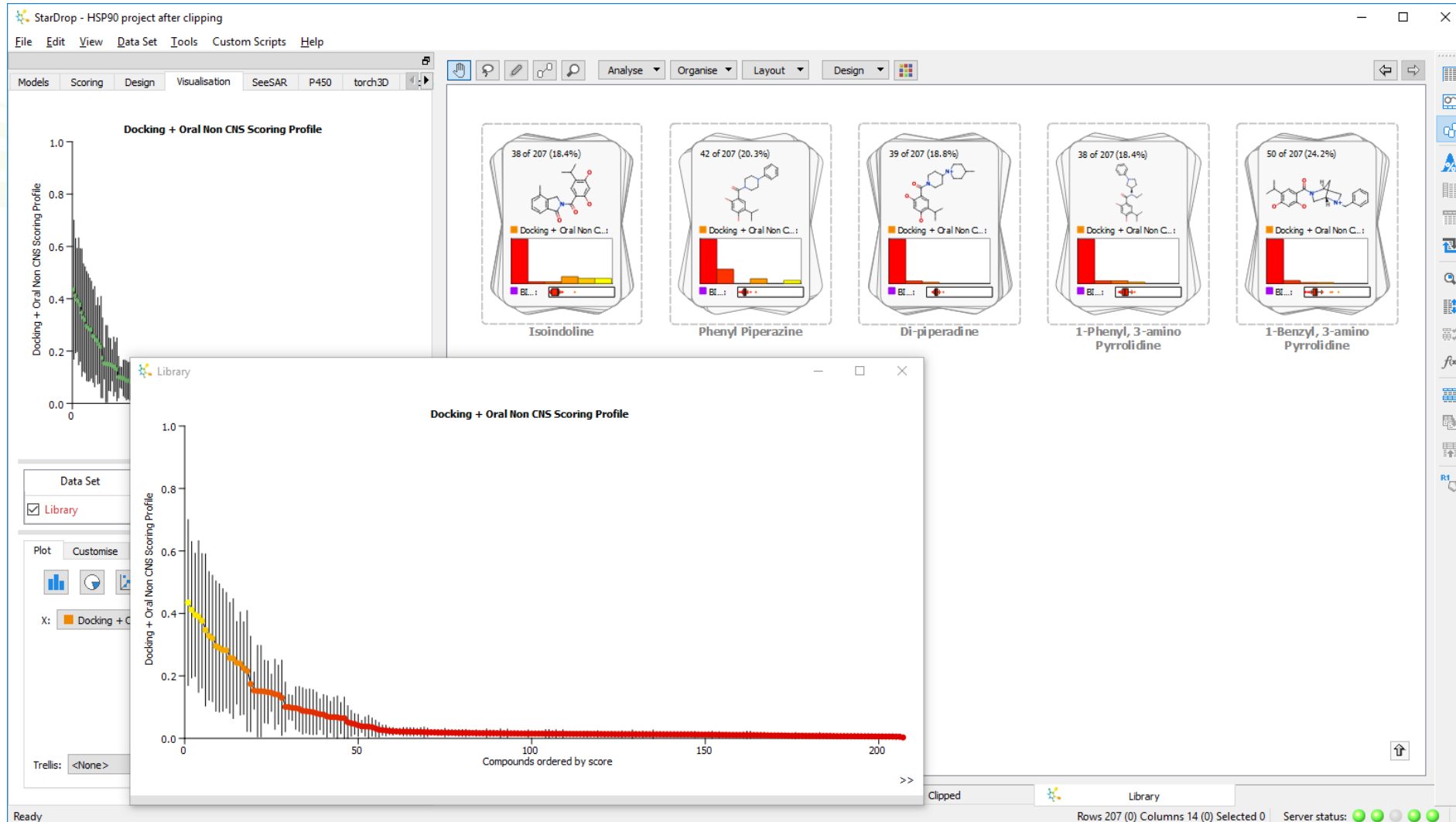
1-Benzyl, 3-amino Pyrroldine

Isoindoline

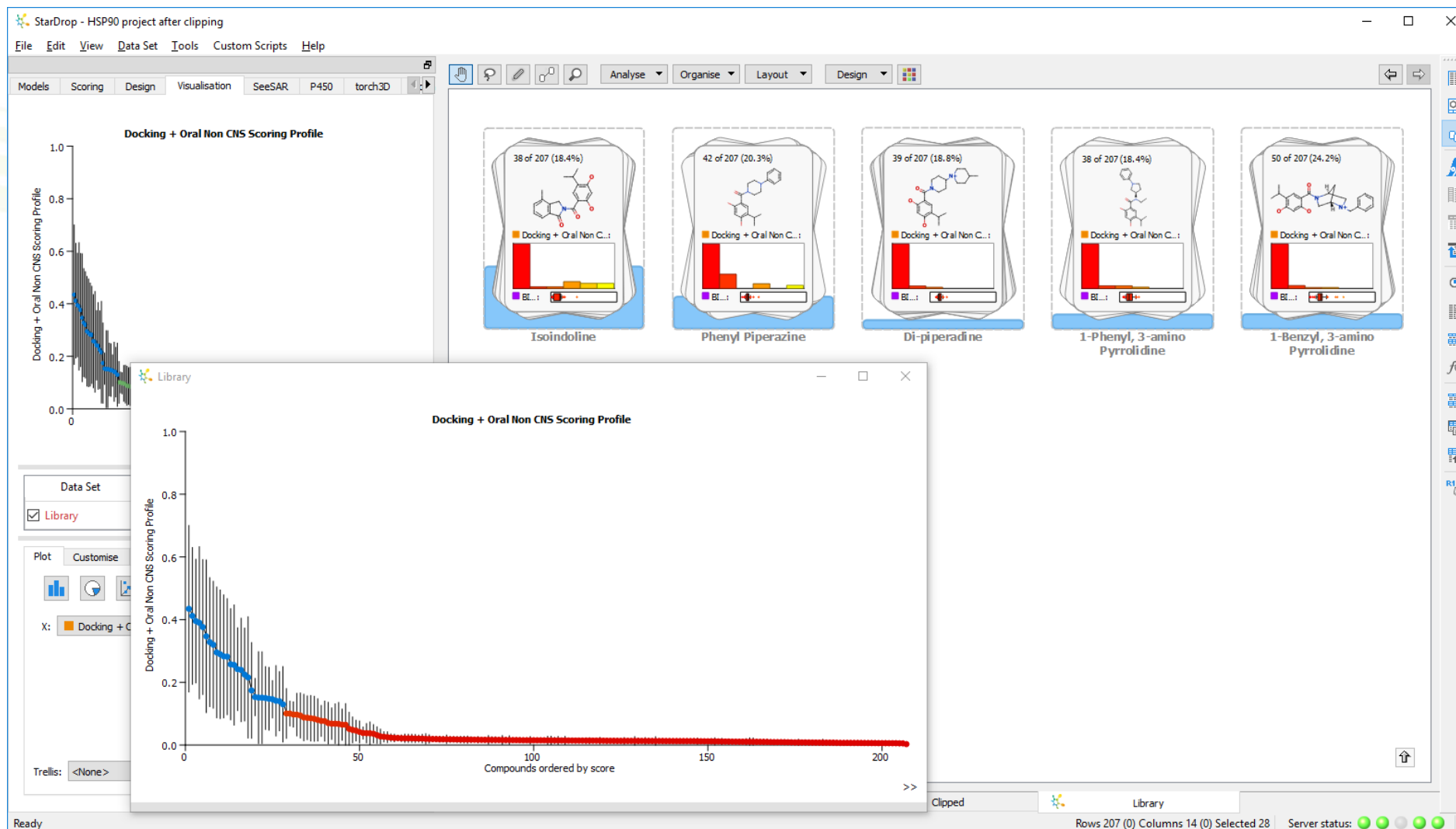
QueryResult Secondary amines Clipped Library

Rows 207 (0) Columns 14 (0) Selected 0 Server status: ●●●●●

Score Distribution



Compound Selection



Conclusion

- Integration of cheminformatics and computational chemistry tools is essential for efficient drug discovery
 - Quick and good decisions on compound selection and design
- Ease-of-use and interactivity critical
 - All users should be able to intuitively access data and predictions
 - Bring together all data to target high-quality compounds
- Big challenges
 - Compatibility with wide range of vendors and in-house platforms
 - Support for variety of architectures
- For more information: www.optibrium.com

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