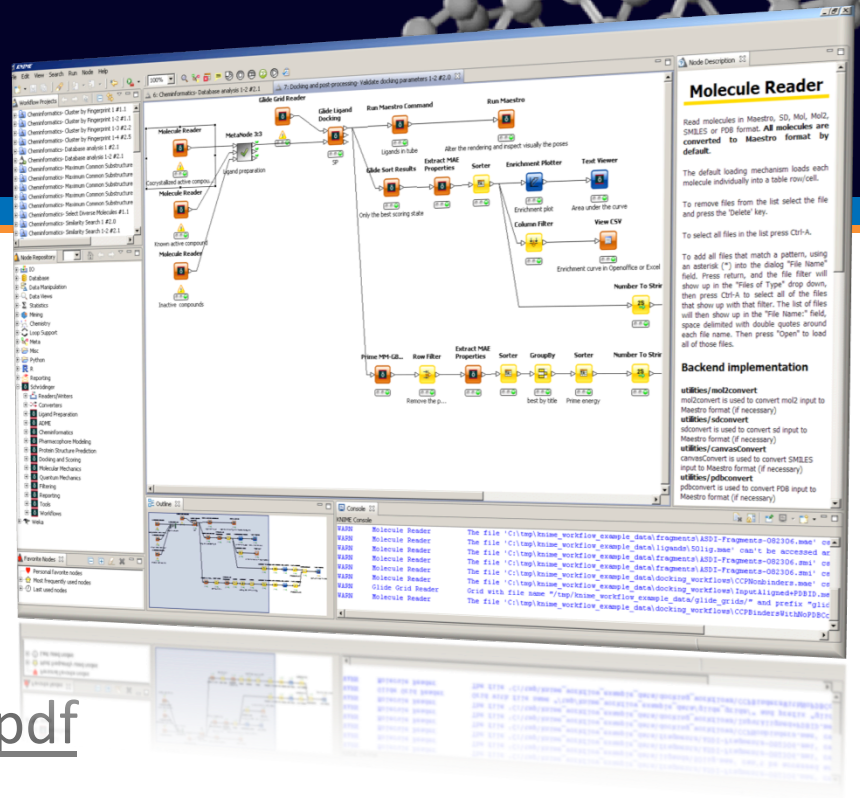
KNIME desktop and Schrödinger extensions overview



Jean-Christophe Mozziconacci and Volker Eyrich

http://www.schrodinger.com/upload/KNIME_Overview.pdf

Schrödinger extensions

- 150+ nodes:
  - Covering most of the Schrödinger tools
    - Most recent additions: Residue scanning, Prime Energy, SiteMap, PyMOL, Glide grid writer
    - Many take in and output sdf and pdb or mol2 on top of Maestro format
    - Newest nodes use the same configuration panel as Maestro (see the Residue scanning node)
  - Structure and data manipulation nodes (eg Split by structure, delete atoms)
  - GUI nodes (eg Run Maestro, Run PyMOL)
  - Scripting nodes: Run Maestro command, Chemistry external tool, Python nodes
  - Utility nodes: Setup diagnosis and workflow list
- 50+ workflow examples
  - Workflow page: descriptions and download the ones of interest
  - Whole set can be downloaded with the Suite
  - Many other workflow drafts available on demand

Schrödinger extensions

- Tested with latest KNIME version and include the version available at the time of the release
- Parameter flow variable capability
  - Use the options not exposed in the configuration panels (eg command line only)
  - Implemented for the main nodes eg Glide, MMod (eg OPLS 2.1), Jaguar
- 2D renderer
  - 2D coordinate generation and rendering

    The default renderer can be set for Maestro columns
  - Can be used in the Report designer

Schrödinger extensions

- More and simplified start-up options and stand-alone installation configuration in the Preferences
  - In $SCHRODINGER/knime start-up script
  - eg use a stand-alone KNIME installation, set temporary directories, the memory limit…
- KNIME menu in Maestro
  - Connect to KNIME mode to exchange structures with a KNIME session

    KNIME-Maestro connector node (Improved in 2015-1: automatic connection/close, more modes)
  - Build, import, edit and run workflows from Maestro on project table data

    Dynamically generated GUI to alter some parameters.
- Simplified batch execution: KNIME_batch.py
  - Batch command generation based on workflow annotations

    Stand-alone dynamically generated GUI
  - Useful options eg -stderr/out
- Easier installation creation and update
  - Using Eclipse machinery in KNIME_install.py
  - eg list of extensions to install, from several (zipped) update sites

Schrödinger extensions

See details in:

http://www.schrodinger.com/upload/KNIME_Overview.pdf

- The new features slides:
  - Parameter flow variables (2014-1)
  - Simplified batch execution (2013, 2014-1)
  - Chemistry external tool node improvements
  - KNIME menu in Maestro (2012)
  - Start-up script (2012)
- Workflow examples:
  - Labs > Parameter flow variable usage
  - General > Installation (KNIME_install.py scenarios)
  - General > Workflow list
  - General > Chemistry external tool node usage
  - Phase > Shape screening, docking (batch execution)
  - 2D renderer in the report designer

Why use KNIME

Automation
- Automate repetitive tasks (especially complex / error prone tasks)
  - e.g. PDB set preparation, Ligand database preparation

Collaboration
- Share workflows with colleagues (also in Maestro and Seurat)
- Not a black box
  - e.g. Ensemble docking, HTS analysis

Prototyping
- Test parameters
  - e.g. Validate docking parameters

Documentation
- Easy debugging, interruptions, data included, inspect each step (2D, in Maestro/PyMOL)

Combine various Tools
- Schrodinger and third party tools (vendor agnostic), scripts (Python, Java, shell),
  - e.g. QM workflows

Reporting
- Nodes for reporting results
  - e.g. Enrichment plotter node, pdf, tables, etc.
- KNIME report designer (free), web portal (KNIME.com)

Inexpensive

Overview

- Organized by level:
  - Get started
  - Intermediate
  - Advanced functionalities
- And by topics:
  - KNIME desktop: GUI, specificities, nodes
  - Schrödinger extensions: specificities, nodes
- You can jump between the sections using links (marked with ► or◄). See the overview slides.
- There are also links to use-case examples (marked with ♦).

Get started

KNIME desktop

- GUI ▶
- Specificities ▶
- Nodes ▶

Schrödinger extensions

- Specificities ▶
- Schrödinger nodes ▶

▶ Intermediate

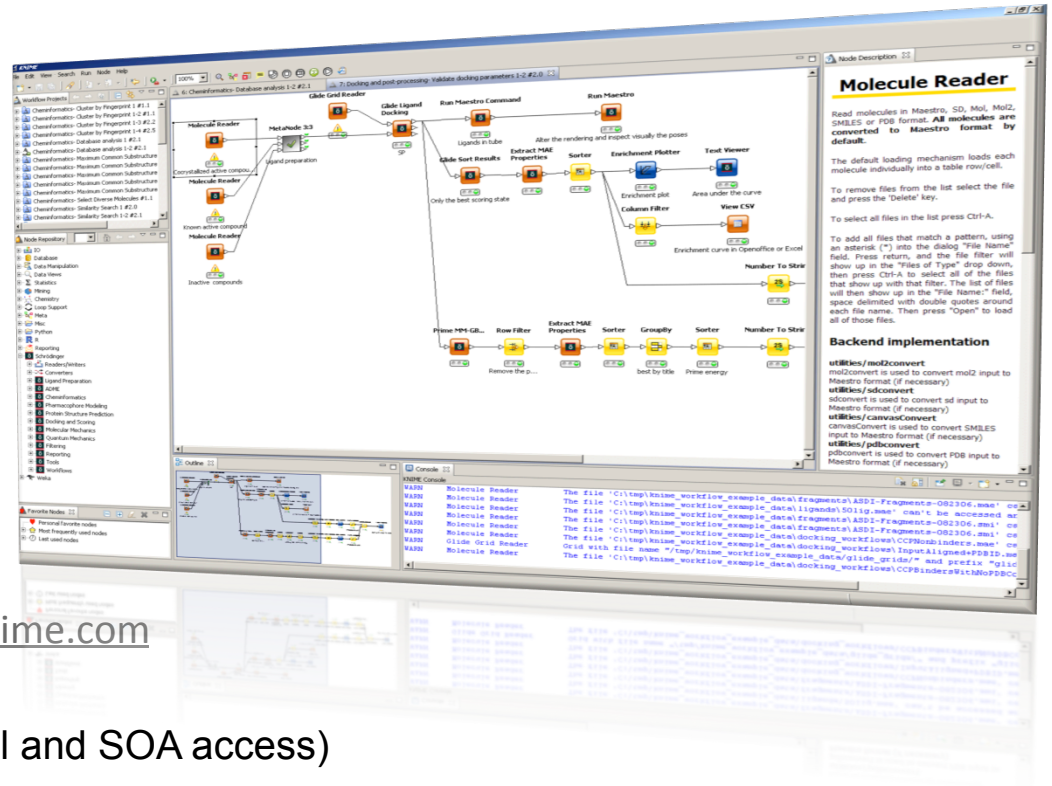
KNIME desktop GUI

- Knime.org and Knime.com
- KNIME desktop
- Start Knime
- Create a new workflow and organize a workspace
- Run a node
- Import and export workflows
- Tips and tricks
- Documentation

Konstanz Information Miner and Ecosystem

KNIME.org

- Leading open-source ‘pipelining/workflow’ tool
- Freely available to **academic** and **industrial** researchers
- KNIME Desktop, based on Eclipse http://www.knime.org
- Community contributions:
  - Modeling tools
  - Marvin sketcher
  - RDKit
  - Indigo
  - CDK
  - R Scripting
  - Erlwood
  - Image Processing
  - HCS Tools
  - Next Generation Sequencing
  - Palladian (mainly GPL3)



KNIME.com Enterprise products and Services http://www.knime.com

- Report designer (free)
- KNIME team space (share workflows) and KNIME server (web portal and SOA access)
- Cluster execution (scalability)
- KNIME professional (support, maintenance and training)
- Commercial development

KNIME Extensions

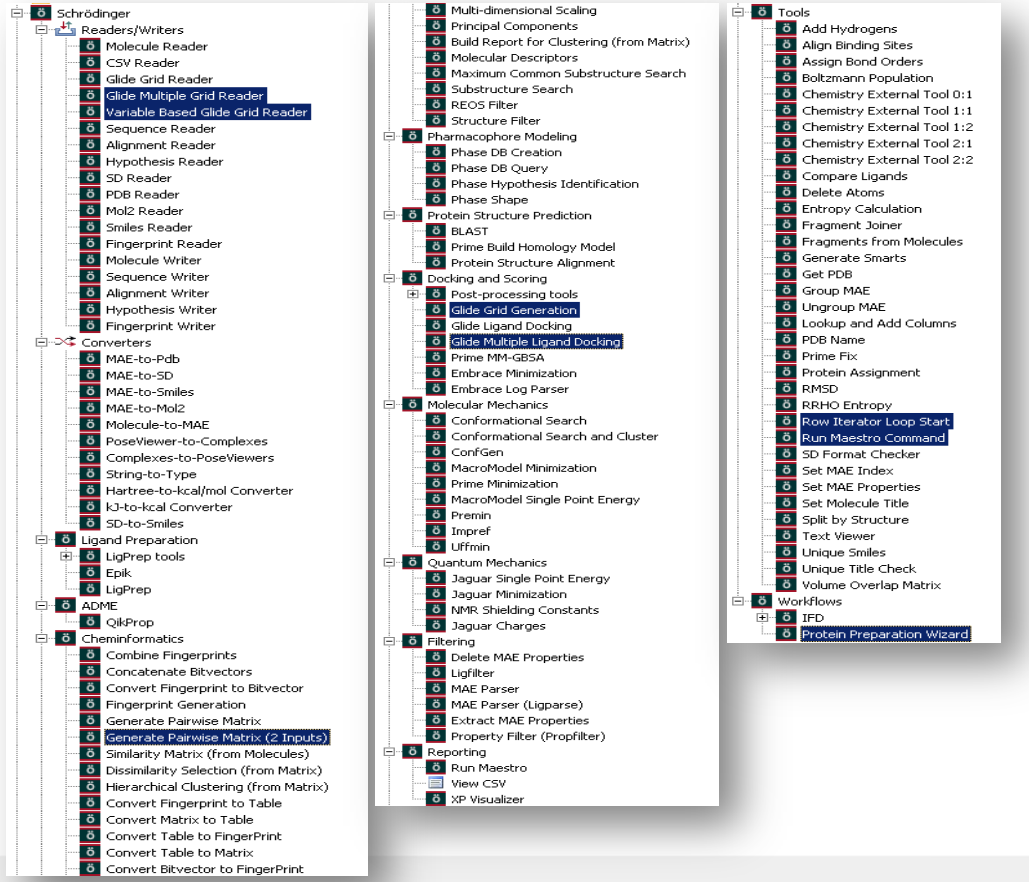
15+ Extension Providers

Extensible, cross-platform, vendor neutral:

Schrödinger, CCG, Tripos, ChemAxon/Infocom, BioSolveIT, Cresset, Dotmatics, Molecular Discovery, Molegro…

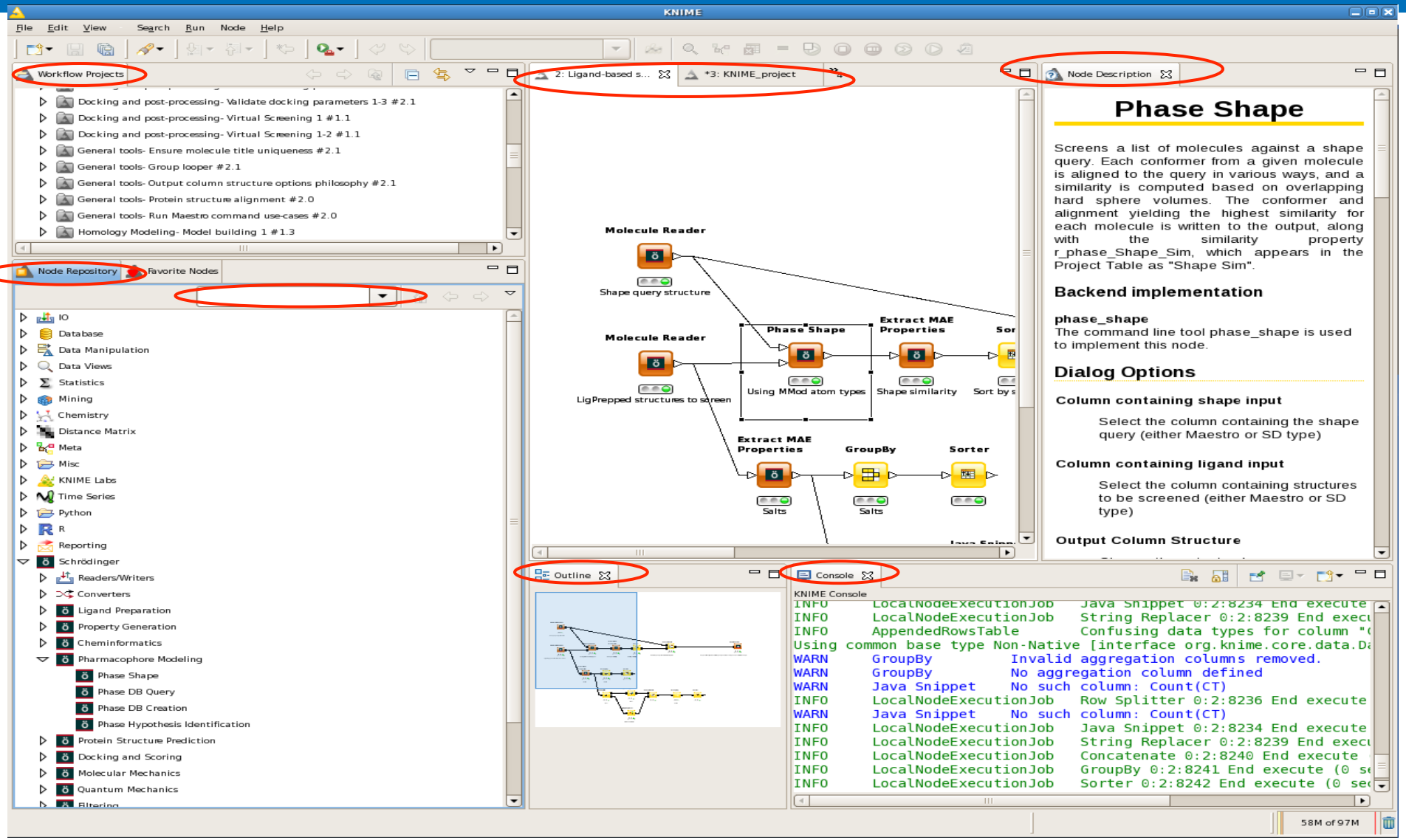
Schrödinger Extensions

- First released in 2007
- 150+ nodes
  - Molecular mechanics
  - Molecular dynamics
  - Quantum mechanics
  - Cheminformatics
  - Pharmacophore modeling
  - Combinatorial libraries
  - Docking
  - Protein structure prediction
  - Structure and data manipulation
- Maestro integration
  - Workflow execution
  - Structure exchange



SCHRÖDINGER.

KNIME Desktop GUI



- Full screen mode
- Forget about Eclipse specific menu items

More about:

- The console ▶

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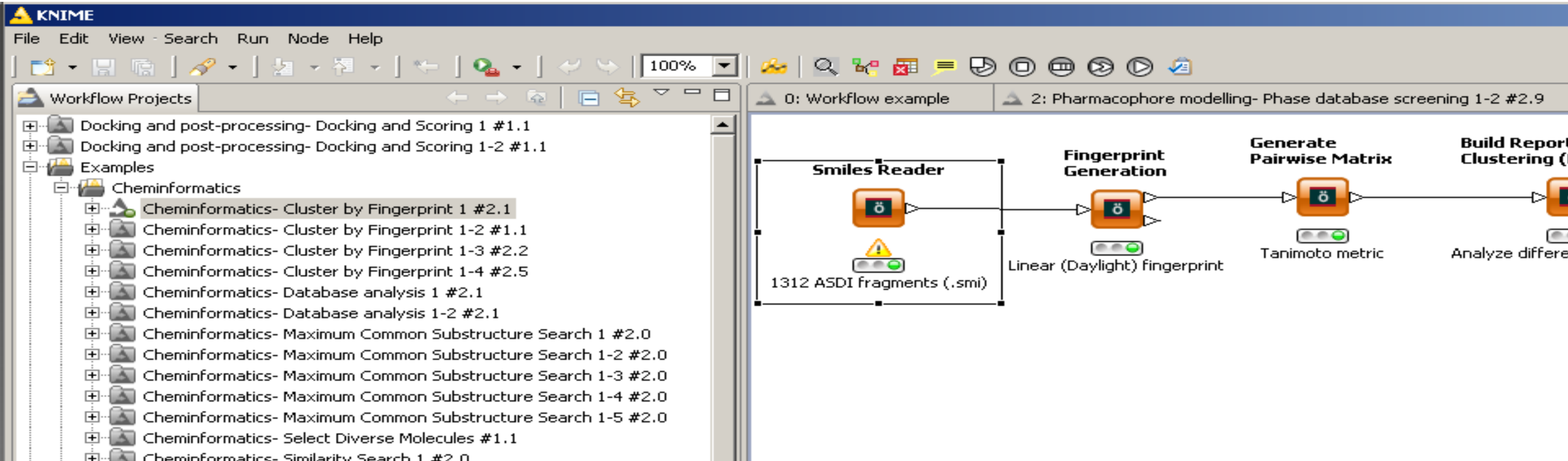
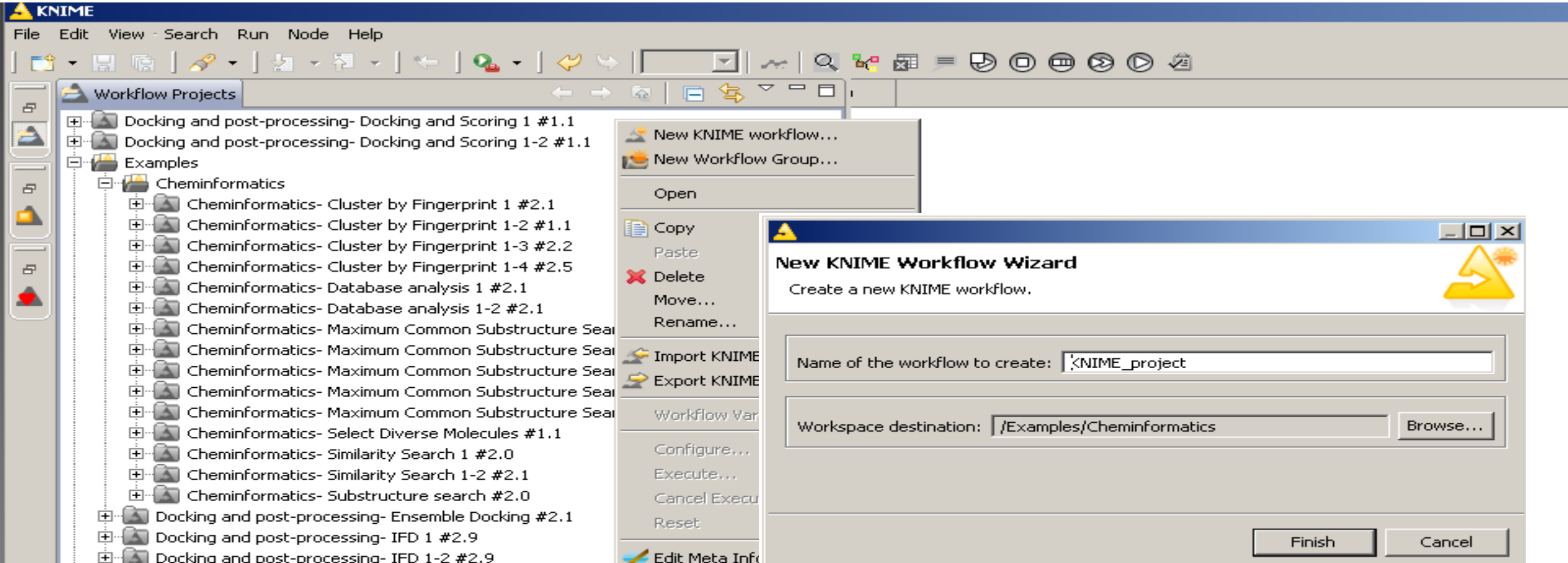
Start KNIME

- Start up KNIME:
  - On Linux: run $SCHRODINGER/knime
  - On Windows: click on the icon
  - Use -data MyWorkspace to open a specific workspace
  - File > Switch workspace, but KNIME takes time to start up again
- Workspace, workflows and workflow groups:



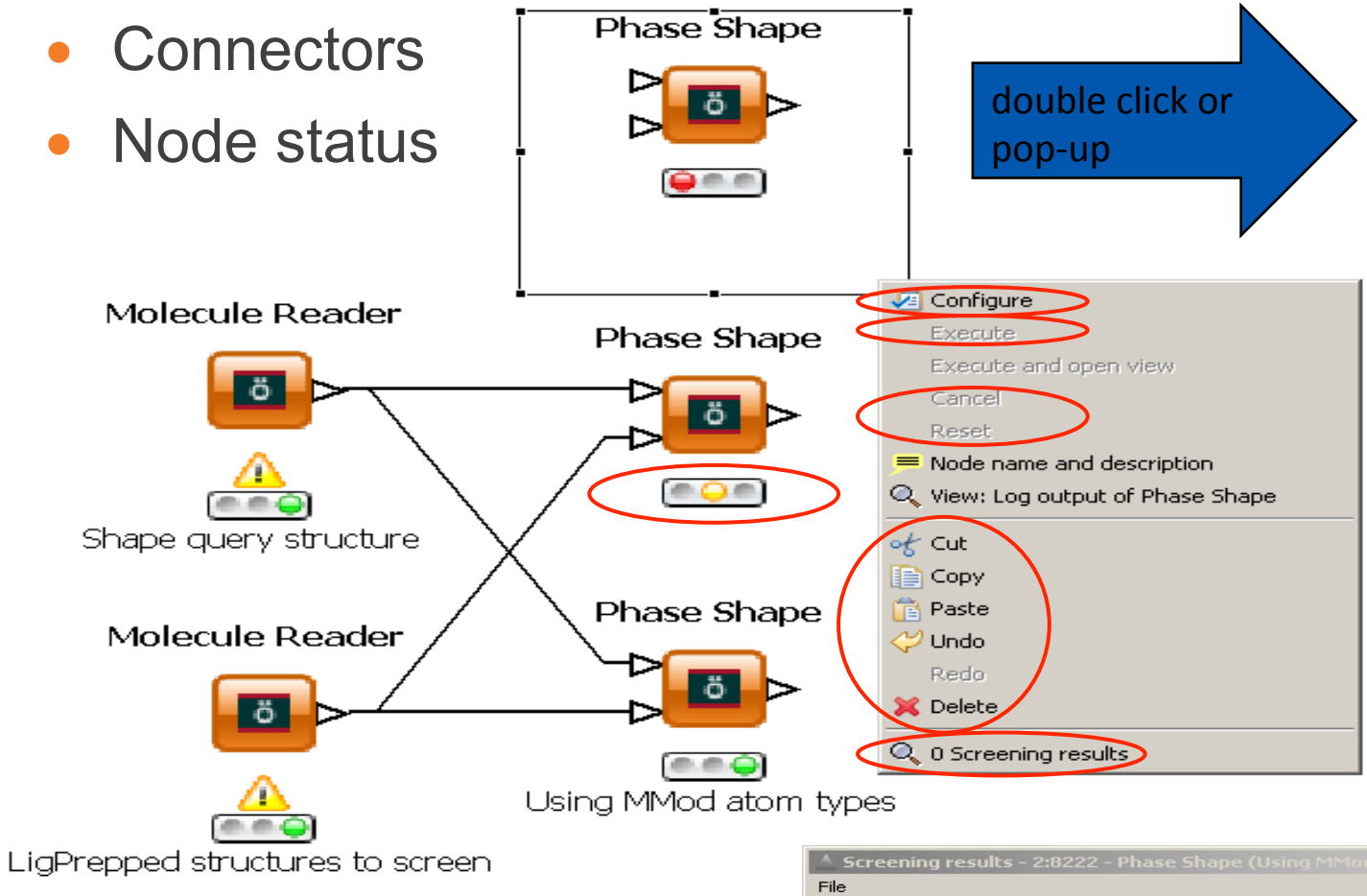
Create a new workflow and organize a workspace

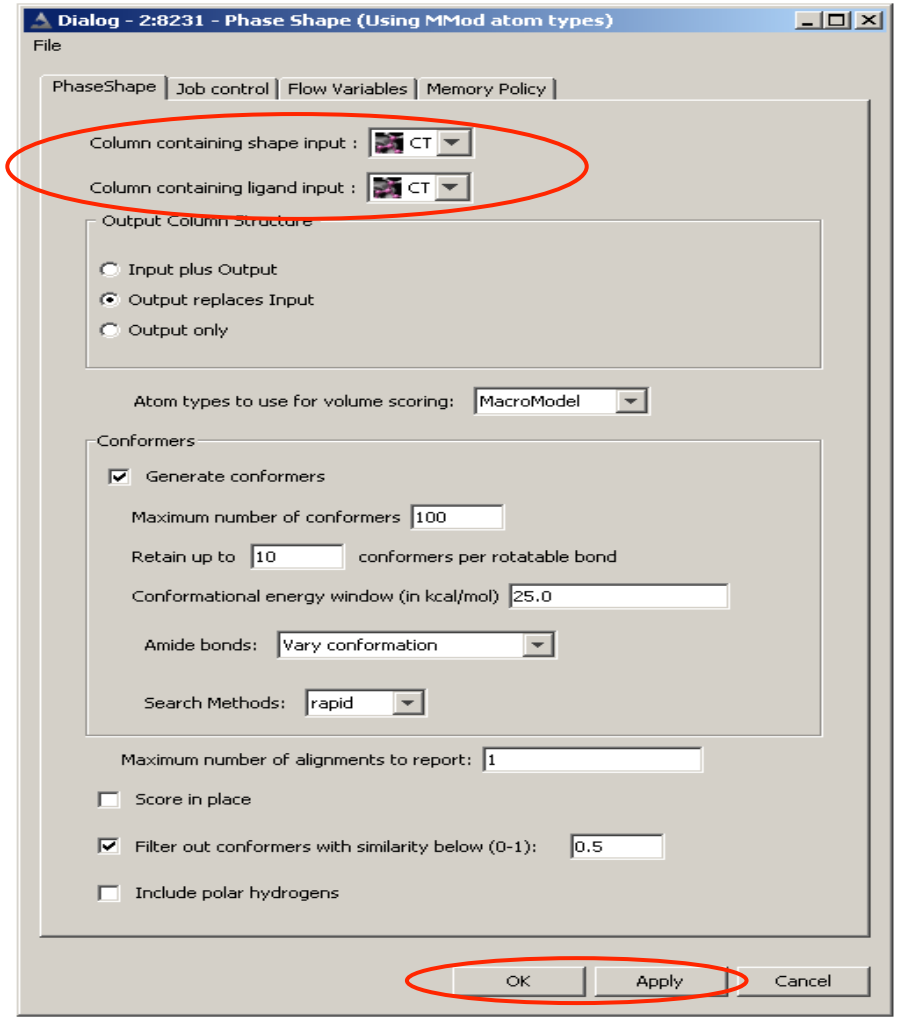
- Under the pop-up menu of Workflow Project repository:
  - New KNIME workflow and New Workflow group
  - Copy, Paste, Delete, Move, Rename
- Drag and drop the workflows in the Workflow project repository



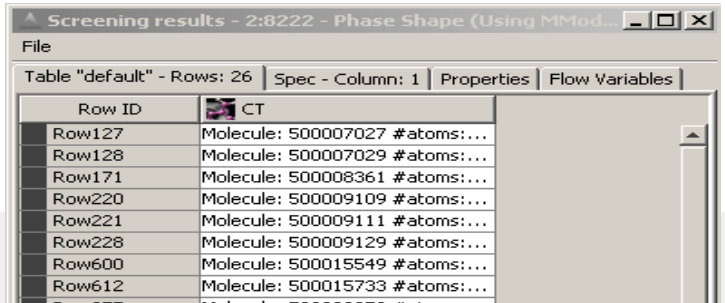
Run a node

- Connectors
- Node status





- Input and output data tables



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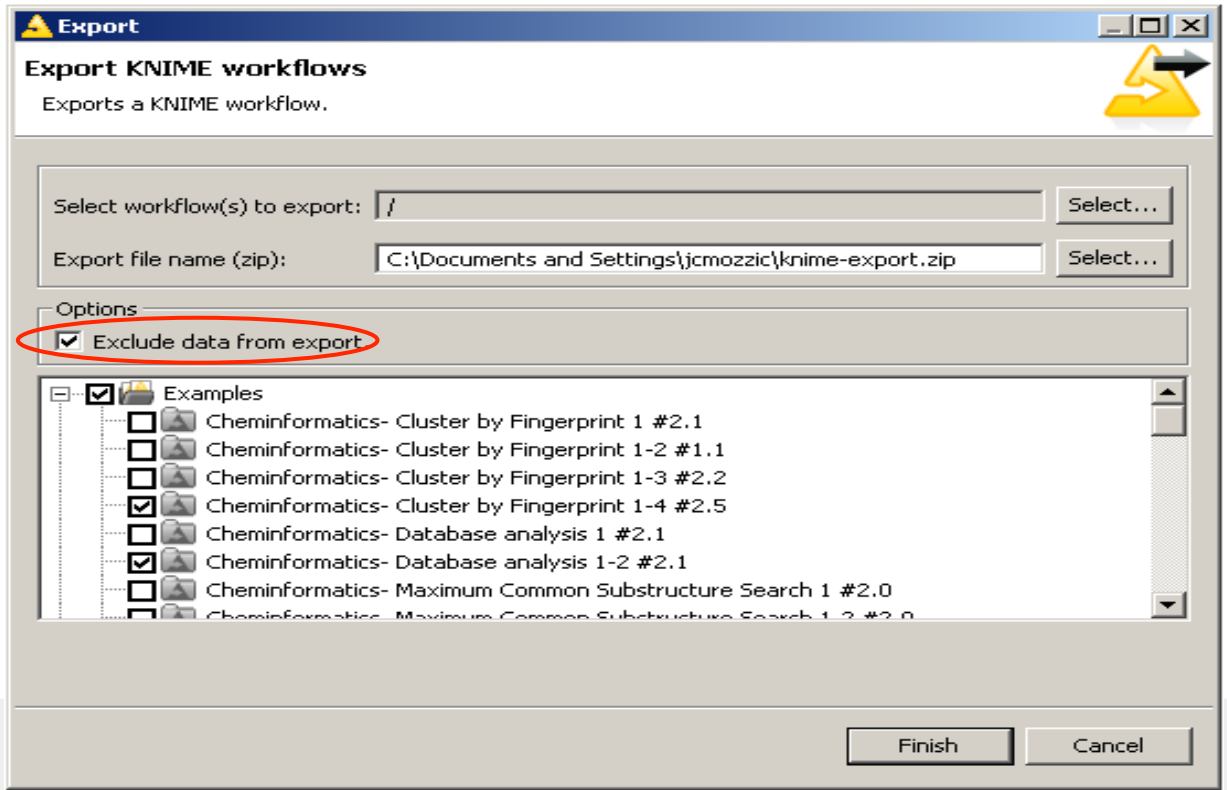
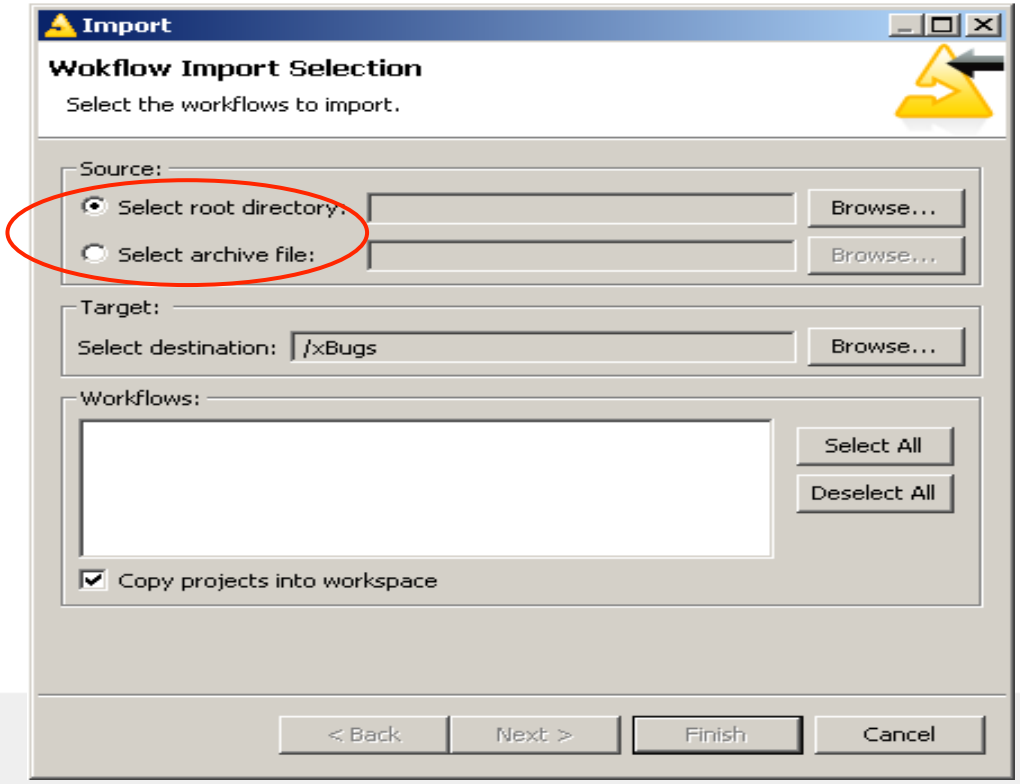
Import and export workflows

- File > Import KNIME workflow / Export KNIME workflow
  or under the pop-up menu of a Workflow Project group
- Import from another workspace or an archive file (zip)
- Select 1 or several workflows > export as a zip file
  Exclude or not the cached data from the exported file





Tips and tricks

- Save regularly the changes. Since KNIME 2.10 there is an auto save functionality but it isn't on by default.

  Save while running calculations (see Preferences ▶)
- Multiple undo and redo apply on workflow edition (execution data lost though)
- The KNIME desktop isn't based on a client-server architecture. If you close the KNIME instance while a calculation is running it won't kill it nor you will be able to recover the results when opening the workflow again.

Documentation

- Node descriptions. Also accessible from Help > Help content > Knime > Node descriptions

  Type in search field and inspect the configuration panel
- Product page http://www.schrodinger.com/KNIME-Extensions

  New Features, New Features Slides, KNIME Overview
- Schrödinger KNIME manual $SCHRODINGER/docs/knime/user_manual/kni13_user_manual.pdf
- Schrödinger FAQs http://www.schrodinger.com/kb
- Workflow page (examples) http://www.schrodinger.com/knimeworkflows/
- Schrödinger's extensions webex http://www.schrodinger.com/seminarprior/19/24/
- KNIME.org
  - Workflow examples (preconfigured server access in KNIME explorer)
  - Screencast http://www.knime.com/introduction/screencasts
  - Forum http://www.knime.org/forum/

KNIME desktop GUI ▶

- Preferences
- Advanced node functionalities
- Errors, warnings and Console information
- Flow variables and workflow variables
- Metanodes
- Memory limit
- Tips and tricks

KNIME desktop specificities

- Stepwise execution
- Data table column types and conversion

Stepwise execution

- Only stepwise execution

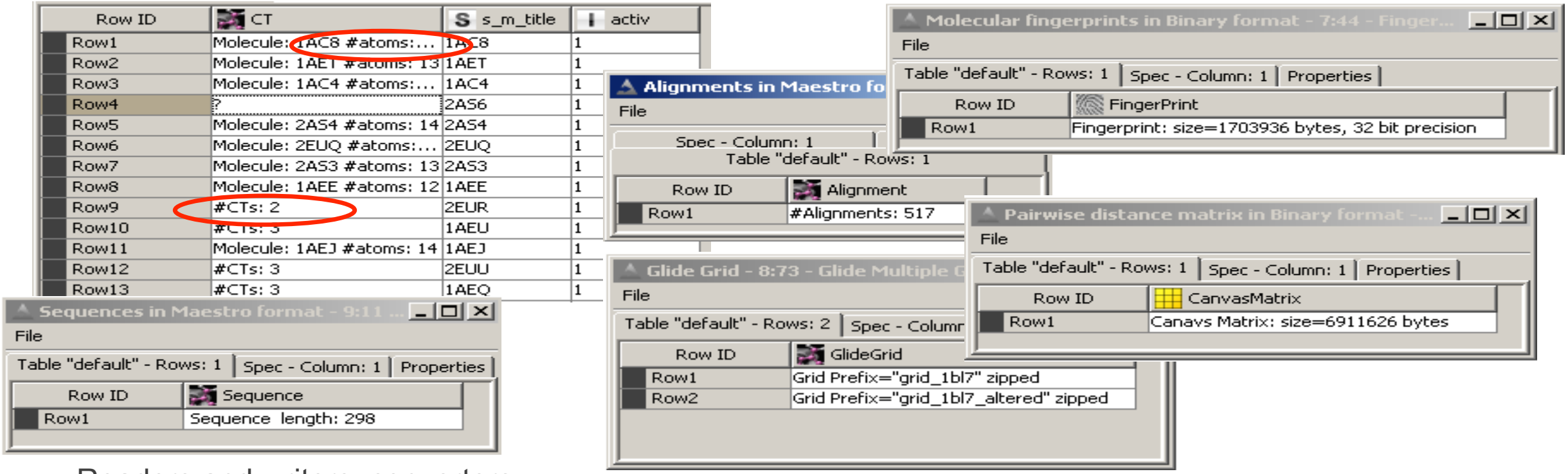
  Ideal to take advantage of Schrödinger's jobcontrol infrastructure
- No predefined execution order for non connected branches. Use the flow variable ports [KNIME 2.3]
- Data cached at each step
- Preferences > KNIME > Maximum working threads far all nodes
- 1:1 connection between nodes (use the concatenate node to combine input flows)

Data table column types and conversion

- KNIME relies on strict data table column typing
- Converter nodes:
  - Double to Int (integer), String to number, Number to string
  - Molecule type cast (but no Maestro conversion)
  - Openbabel, CDK to molecule, Molecule to CDK
- In the Schrödinger extensions:
  - String-to-type
  - Molecule-to-MAE, MAE-to-Pdb, MAE-to-SD, MAE-to-Smiles, MAE-to-mol2, SD-to-smiles
  - Canvas object converters

Schrödinger specific cell types

- Structures: Maestro, Sequence, Alignment
- Several files: Glide grid, Phase Hypothesis
- Desmond trajectory
- Binary formats: Canvas fingerprint and matrix



Readers and writers, converters

KNIME workbench nodes

- KNIME workbench nodes
- Data manipulation nodes
- Data exchange

KNIME workbench nodes

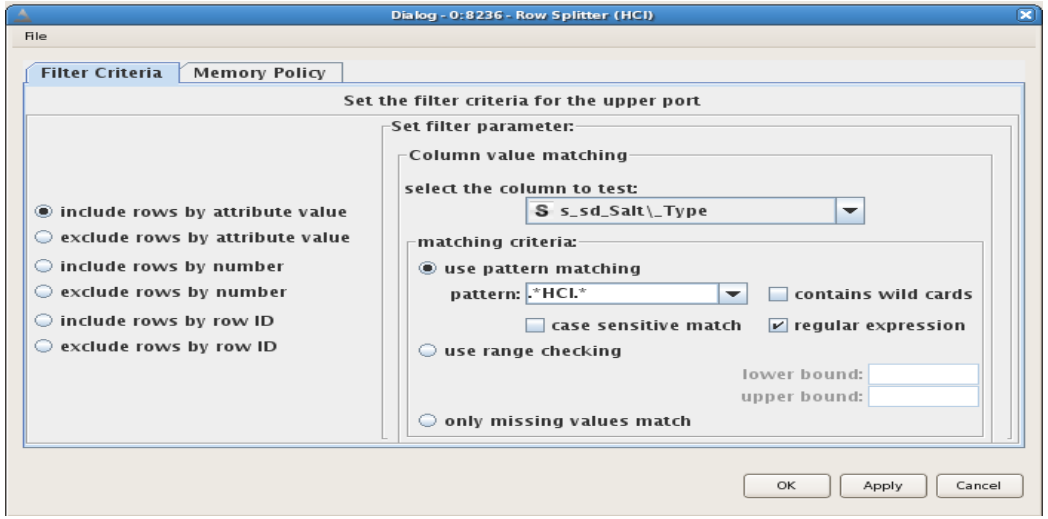
- I/O nodes for reading and writing data from files and databases
- Data manipulation nodes for managing the internal data tables that are used to pass information between nodes
- Charting and plotting tools
- Loop support, time Series, Distance matrix
- Statistics and data mining nodes (Mining, Weka) such as clustering, neural networks, decision trees, Lib SVM

  R statistical computation
- Basic chemistry-aware nodes (CDK)

  very limited, see Schrödinger extension nodes ▶

The most often used nodes for data manipulation

- Row filter, Row splitter and Sorter
- Column filter, Column resorter, Column combiner and Rename
- Joiner (see also Schrödinger Look up and add column node ▶) and Concatenate (only 2 inputs)



And also:

- Java snippet, RowID and GroupBy node ▶
- Schrödinger nodes for data manipulation ▶

Data exchange

- As text files: File reader and csv writer nodes
- In Excel format: xls reader and xls writer nodes
- Between workflows: table reader and table writer nodes

- See also among the Schrödinger nodes:
  - Schrödinger reader and writer nodes
  - CSV reader (read several files)
  - View CSV ▶

KNIME workbench nodes

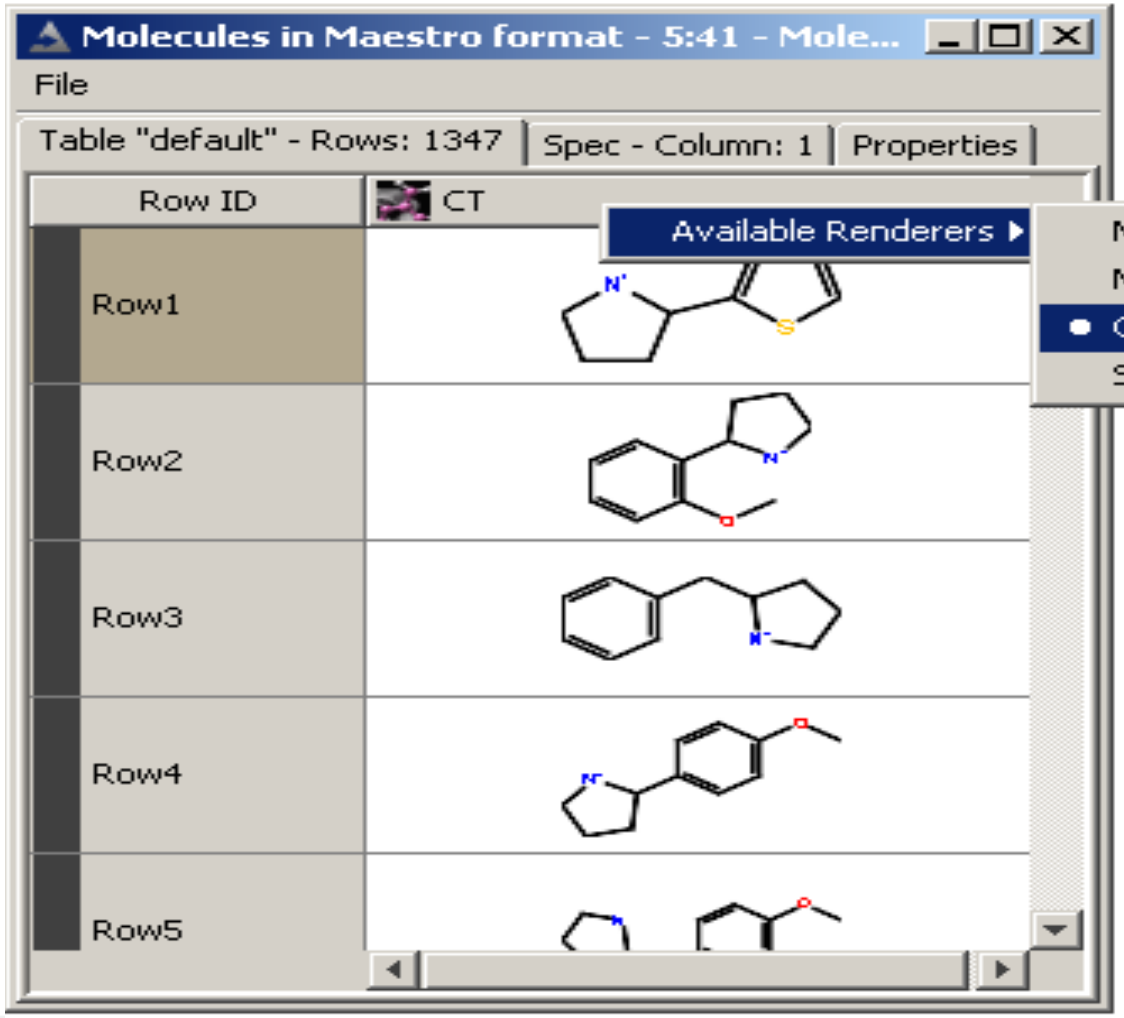
- KNIME.com Labs nodes
- Scripting and run a third party tool
- Java snippet
- RowID
- Group by
- Miscellaneous nodes: Interactive table, Math formula, CDK Sketcher
- Plotting facilities
- Looping functionalities - Basics
- Model building nodes

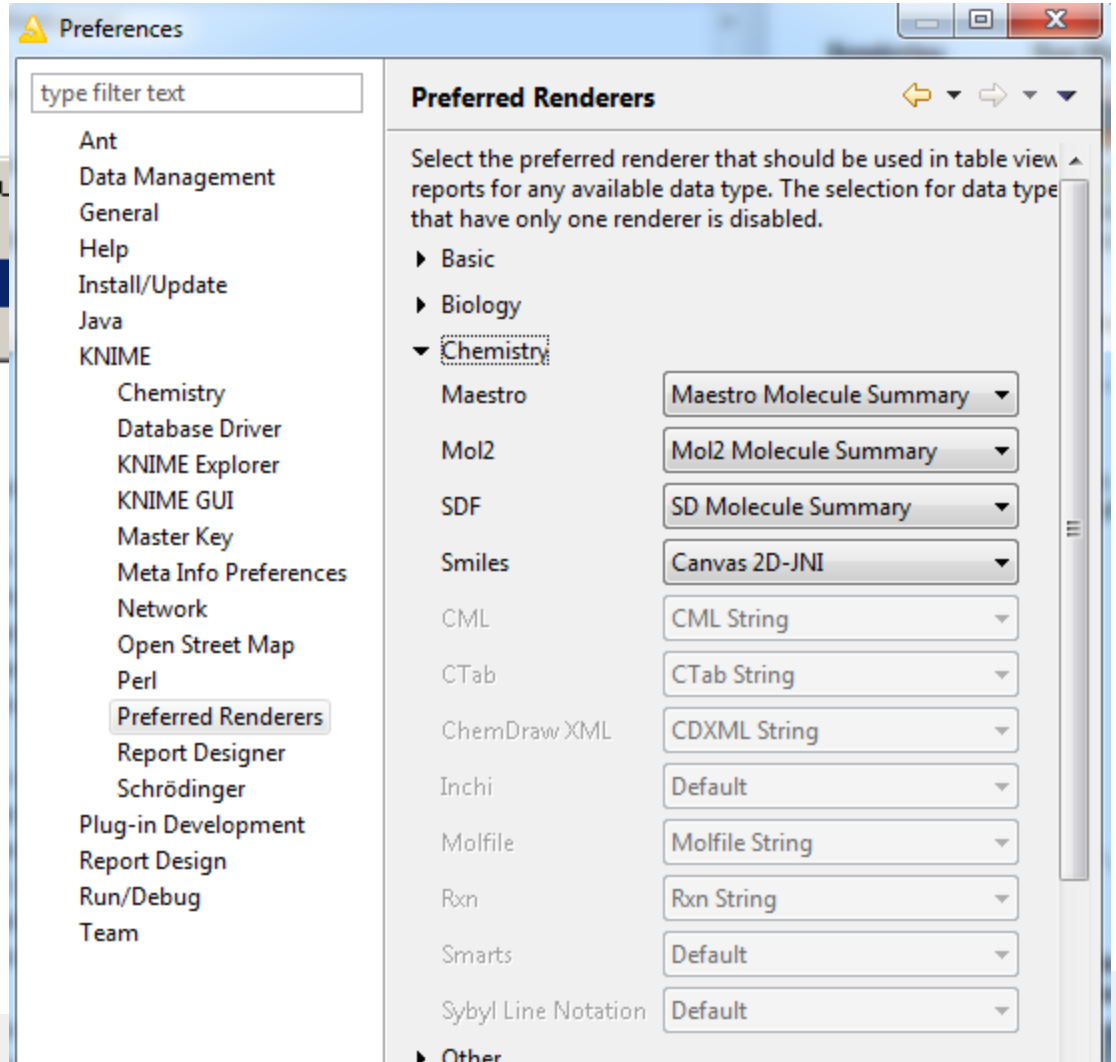
Schrödinger extensions specificities

- Canvas 2D renderer
- Grouped structures in a cell
- Output column structure options
- Jobcontrol tab

Canvas 2D renderer

- Preferences > KNIME > Preferred renderer

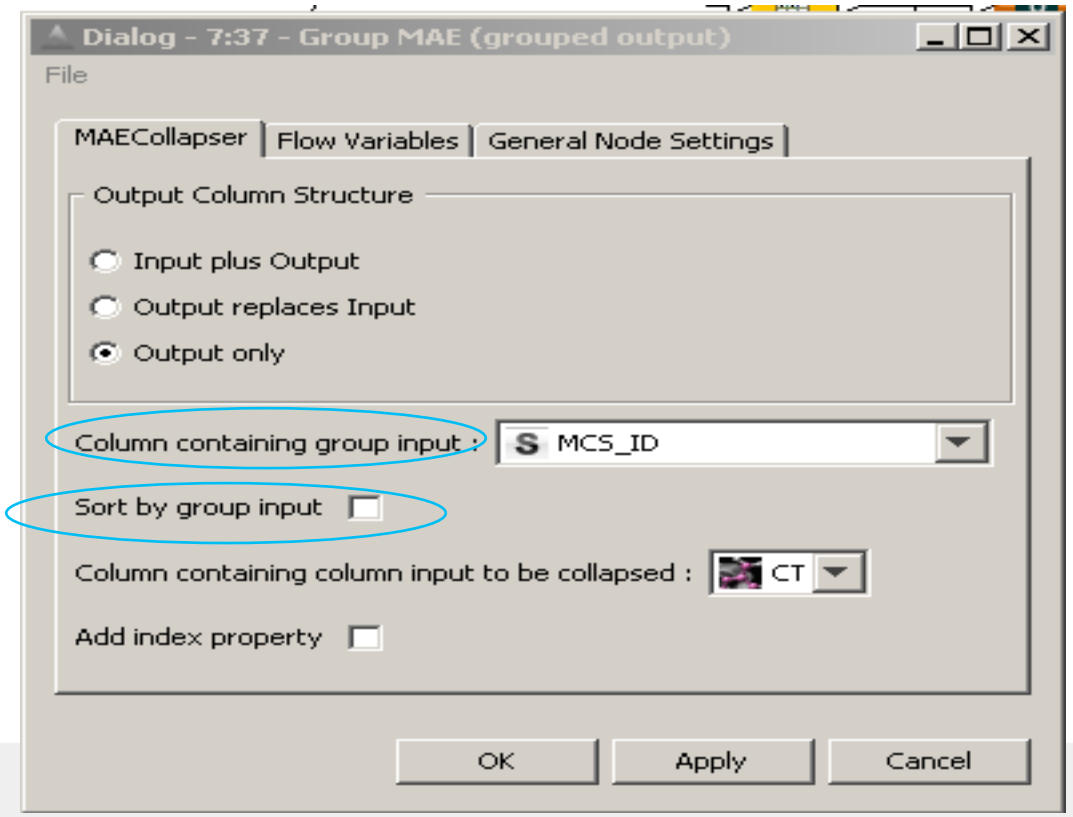




Grouped structures in a cell

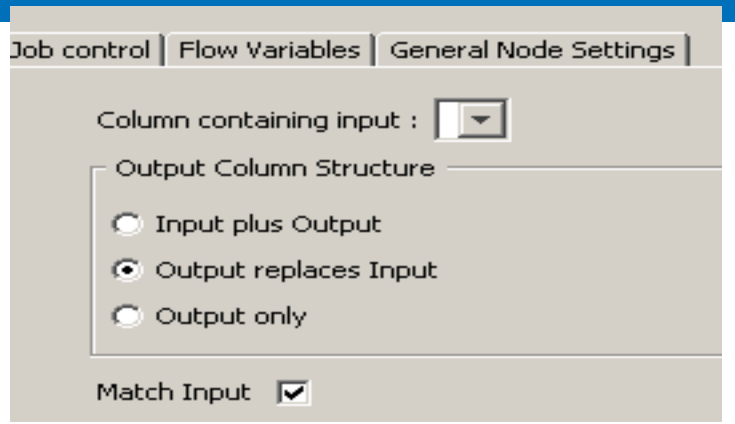
- #CTs: number of structures
- Set of conformations, Glide poses, Ligprep forms…
- Group and ungroup nodes, match option
- Also grouped SD, mol2

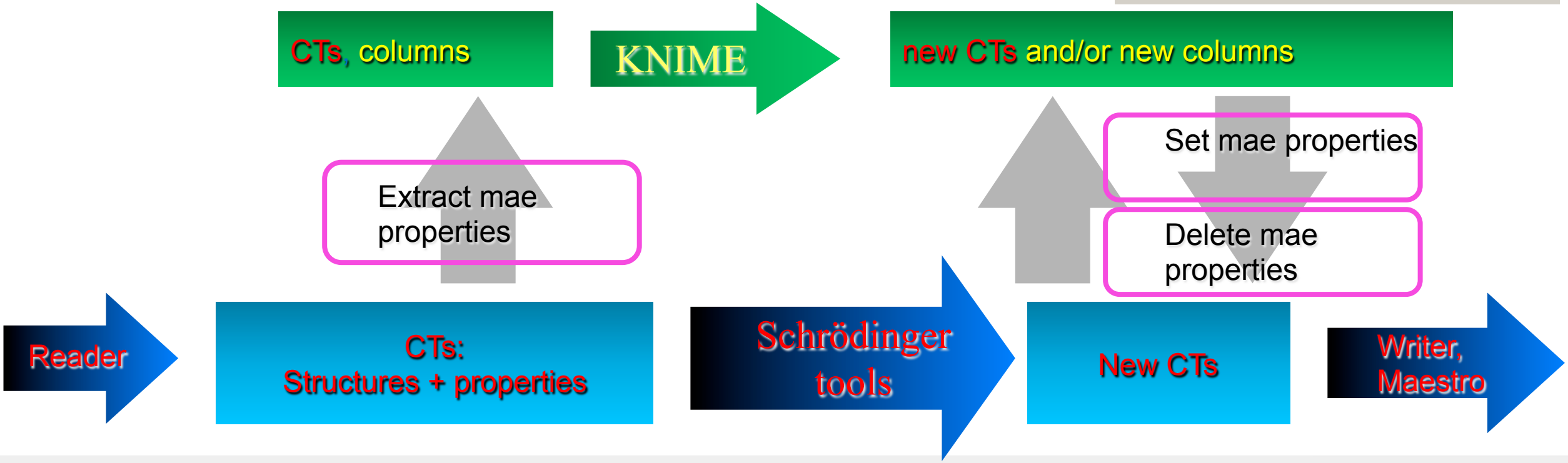
Row ID	CT	s_m_title	activ
Row1	Molecule: 1AC8 #atoms:...	1AC8	1
Row2	Molecule: 1AET #atoms: 13	1AET	1
Row3	Molecule: 1AC4 #atoms:...	1AC4	1
Row4	?	2AS6	1
Row5	Molecule: 2AS4 #atoms: 14	2AS4	1
Row6	Molecule: 2EUQ #atoms:...	2EUQ	1
Row7	Molecule: 2AS3 #atoms: 13	2AS3	1
Row8	Molecule: 1AEE #atoms: 12	1AEE	1
Row9	#CTs: 2	2EUR	1
Row10	#CTs: 3	1AEU	1
Row11	Molecule: 1AEJ #atoms: 14	1AEJ	1
Row12	#CTs: 3	2EUU	1
Row13	#CTs: 3	1AEQ	1



Output column structure options

- Input plus Output, Output replaces Input, Output only
- Extract MAE properties, Set MAE properties and delete MAE properties nodes





Output column structure options

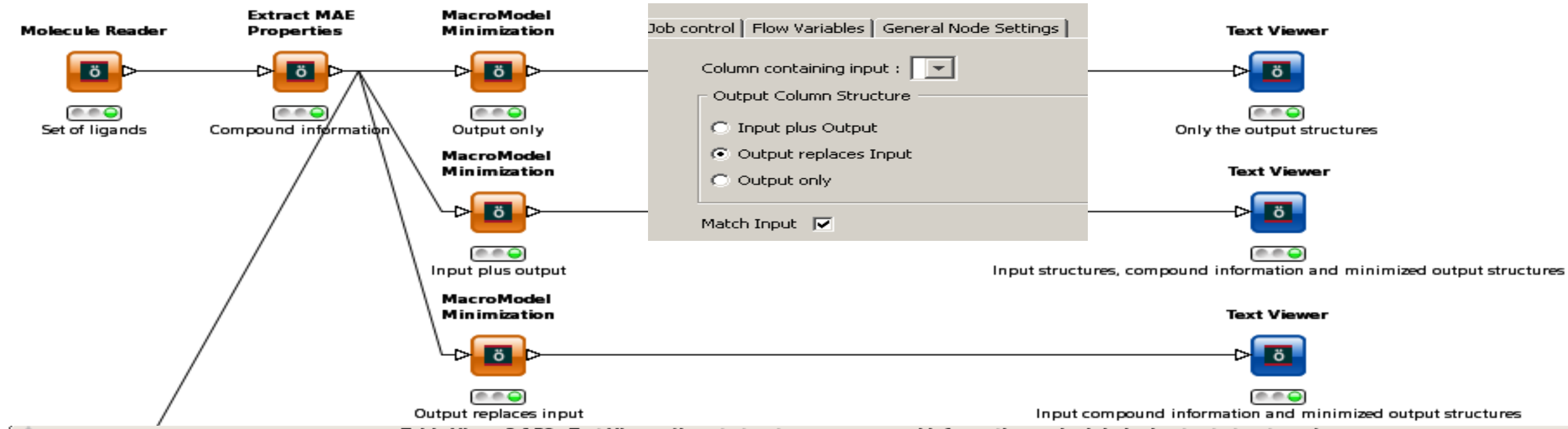
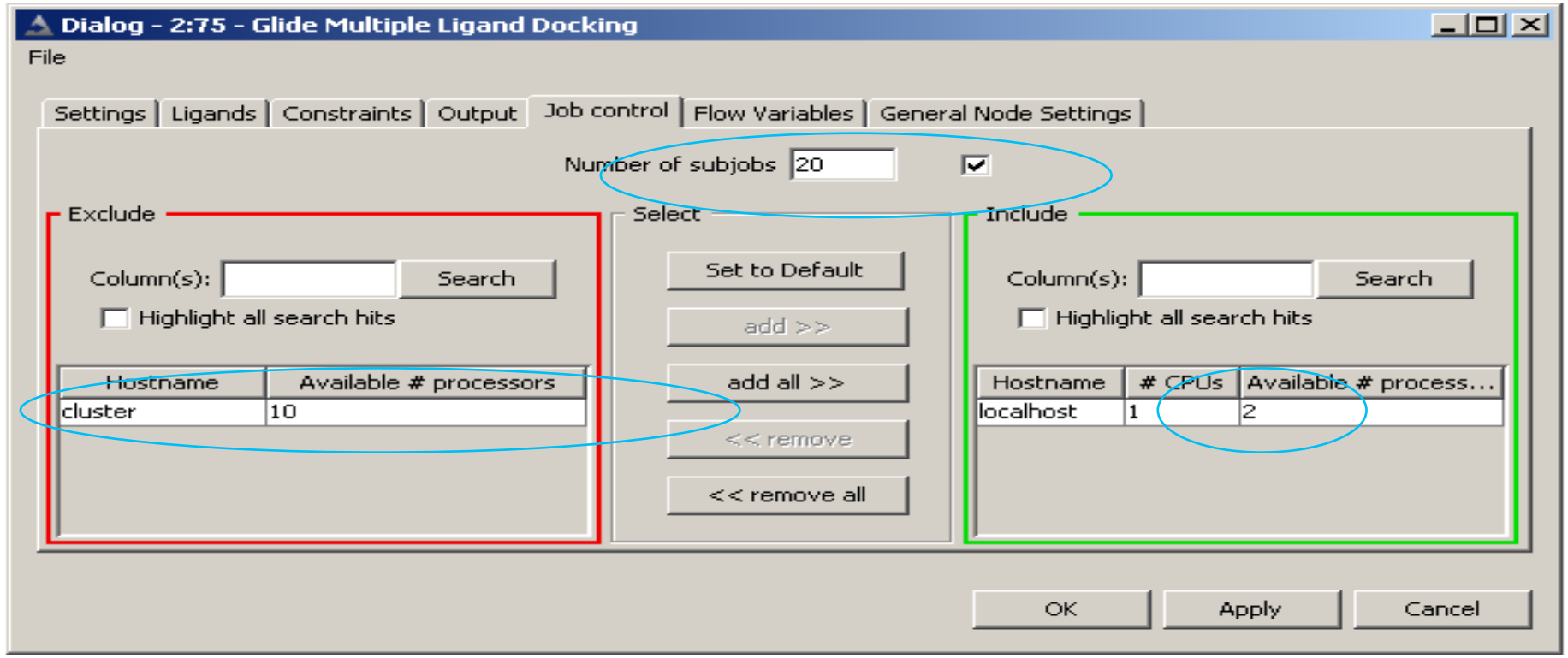


Table View - 2:158 - Text Viewer (Input structures, compound information and minimized output structures)

File Hilite Navigation View Output

Row ID	CT_input	s_knime_origin_directory	s_knim...	s_knim...	s_m_entry_...	s_m_title	CT
Row0	Molecule: 35 #atoms: ...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	35	Molecule: 35 #atoms: ...
Row1	Molecule: 141500 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	141500	Molecule: 141500 #at...
Row2	Molecule: 151943 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	151943	Molecule: 151943 #at...
Row3	Molecule: 165006 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	165006	Molecule: 165006 #at...
Row4	Molecule: 177616 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	177616	Molecule: 177616 #at...
Row5	Molecule: 184284 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	184284	Molecule: 184284 #at...
Row6	Molecule: 193459 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	193459	Molecule: 193459 #at...
Row7	Molecule: 290782 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	290782	Molecule: 290782 #at...
Row8	Molecule: 334669 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	334669	Molecule: 334669 #at...
Row9	Molecule: 399636 #at...	/tmp/knime_workflow_example_data/ligan...	50lig.mae	workstatio...	dl-400mw-cul...	399636	Molecule: 399636 #at...

Jobcontrol


Dialog - 2:75 - Glide Multiple Ligand Docking
File
Settings
Ligands
Constraints
Output
Job control
Flow Variables
General Node Settings
Number of subjobs
20
Exclude
Column(s):
Search
Highlight all search hits
Hostname
Available # processors
cluster
10
Select
Set to Default
add >>
add all >>
<< remove
<< remove all
Include
Column(s):
Search
Highlight all search hits
Hostname
CPUs
Available # process...
localhost
1
2
OK
Apply
Cancel

Schrödinger extensions specificities

- Schrödinger preferences
- Start-up script options
- Access to flow variables

Schrödinger nodes

- Schrödinger node repository
- Configuration panel visual coherence
- Nodes of general use:
  - Readers and converters
  - Run Maestro and Run Maestro command
  - Structure manipulation
  - Data manipulation and viewers
  - Scripting
- KNIME workflow webpage

Access to Schrödinger tools via KNIME

- Run on Linux, Mac and Windows 32 and 64 bit
- Add our extensions to an existing KNIME installation using the update site
- 150+ nodes covering the whole Schrödinger Suite

Molecular Mechanics
- MacroModel Single Point Energy
- MacroModel Minimization
- MacroModel Coordinate Scan
- ConfGen Standard
- ConfGen
- Conformational Search
- Conformational Search and Cluster
- Premin
- Impref
- Uffmin

Quantum Mechanics
- Jaguar Single Point Energy
- Jaguar Minimization
- NMR Shielding Constants
- Jaguar Charges

Cheminformatics

Fingerprint Based Tools
- Fingerprint Generation
- Generate Pairwise Matrix
- Generate Pairwise Matrix (2 Inputs)
- Similarity Matrix (from Molecules)
- Dissimilarity Selection (from Matrix)
- Build Report for Clustering (from Matrix)
- Hierarchical Clustering (from Matrix)

Filters and Mining Tools
- Maximum Common Substructure Search
- Substructure Search
- REOS Filter
- Structure Filter

Utilities and Converters
- Principal Components
- Multi-dimensional Scaling
- Combine Fingerprints
- Concatenate Bitvectors
- Convert Fingerprint to Bitvector
- Convert Fingerprint to Table
- Convert Matrix to Table
- Convert Table to FingerPrint
- Convert Table to Matrix
- Convert Bitvector to FingerPrint

Modeling
- Bayes Classification Model Building

Pharmacophore Modeling
- Phase Shape
- Phase DB Query
- Phase File Query
- Phase DB Creation
- Phase Hypothesis Identification

Docking and Scoring
- Glide Grid Generation
- Glide Ligand Docking
- Glide Multiple Ligand Docking
- XP Visualizer

Post-processing
- Prime MM-GBSA
- Embrace Minimization
- Strain Rescore
- Pose Entropy
- Pose Filter
- Glide Ensemble Merge
- Glide Merge

Protein Structure Prediction
- BLAST
- Prime Build Homology Model
- Prime Side Chain Sampling
- Prime Minimization

Schrödinger nodes

Workflows

Protein Preparation

- Protein Preparation Wizard
- Protein Assignment

Induced-fit docking

- IFD and individual steps

Ligand Preparation

- LigPrep
- Ligprep individual tools (Ionizer, Desalter, Neutralizer…)
- Epik

Property Generation

- QikProp
- Molecular Descriptors
- Calculate properties

Filtering

- Ligfilter
- Ligparse
- Property Filter (Propfilter)

Scripting

- **Run Maestro Command**
- **Chemistry External Tool** 0:1, 1:0, 1:1, 1:2, 2:1 and 2:2 nodes
- **Python Script** 0:1, 1:0, 1:1, 1:2, 2:1 and 2:2 nodes

Desmond

- System builder
- Molecular Dynamics
- Trajectory extract frames and manipulation
- Trajectory reader, CMS reader

Reporting

- Run Maestro
- Run Canvas
- View CSV (open xls/ooffice)
- Text Viewer

Tools

Combinatorial Libraries

- CombiGlide Library Enumeration
- CombiGlide Reagent Preparation

Fragments

- Fragment Joiner
- Fragments from Molecules

Data Manipulation

Compare Ligands

Lookup and Add Columns

Group MAE

Ungroup MAE

Structure Manipulation

- Add Hydrogens
- **Delete Atoms**
- **Split by Structure**
- **MAE Parser**
- Extract MAE Properties
- Delete MAE Properties
- Set MAE Properties
- Set Molecule Title
- Set MAE Index

Utilities

- Get PDB
- Align Binding Sites
- Protein Structure Alignment
- Prime Fix
- **RMSD**
- Assign Bond Orders
- Unique Title Check
- PDB Name
- SD Format Checker
- Generate Smarts
- Unique Smiles
- Entropy Calculation
- RRHO Entropy
- Boltzmann Population
- Volume Overlap Matrix

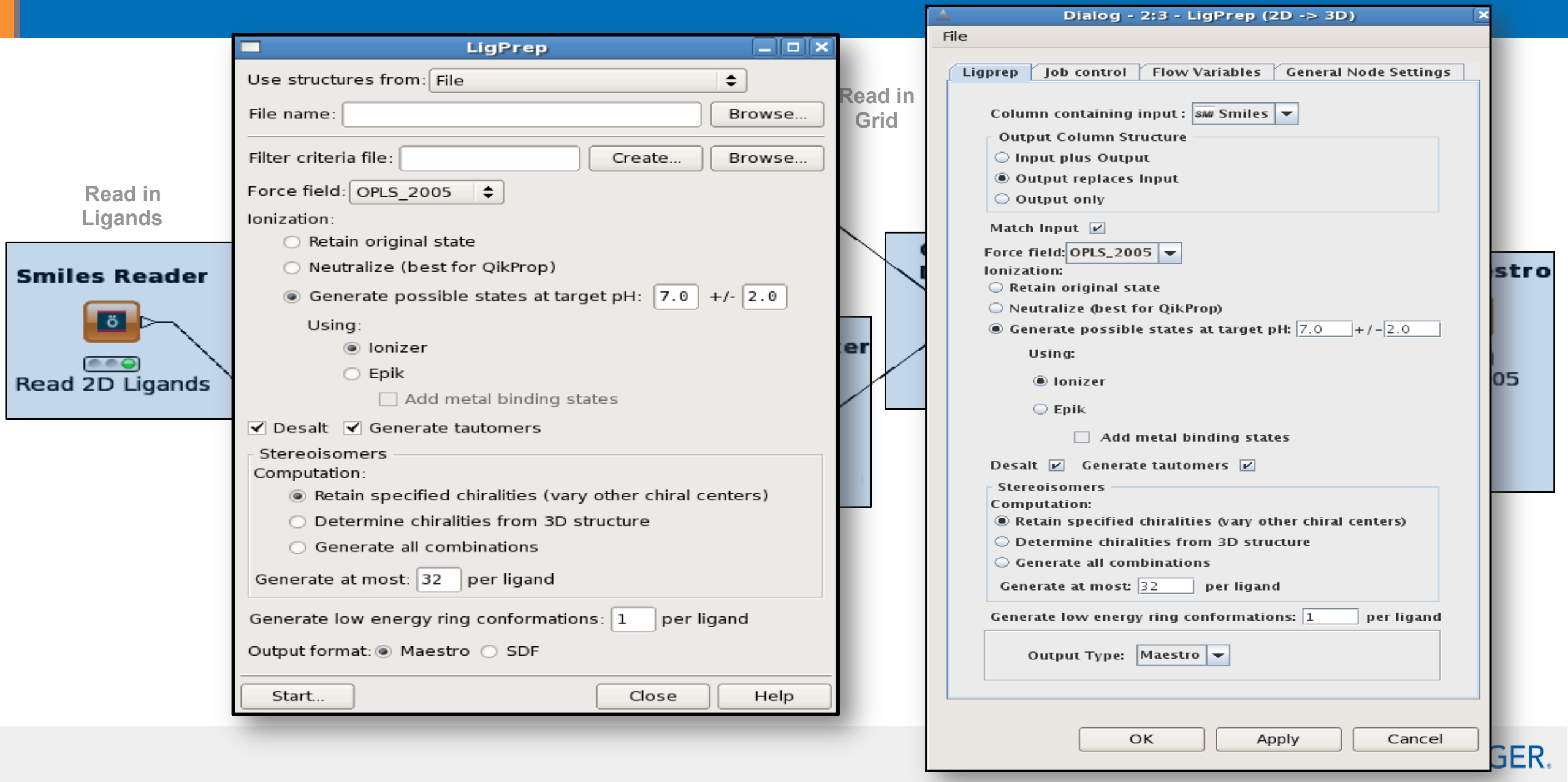
Readers/Writers

- CSV Reader
- Molecule Reader
- SD, PDB, Mol2 Reader nodes
- Sequence Reader
- Alignment Reader
- Fingerprint Reader
- Hypothesis Reader
- Glide Grid Reader
- Glide Multiple Grid Reader
- Variable Based Glide Grid Reader
- Molecule Writer
- Sequence Writer
- Alignment Writer
- Hypothesis Writer
- Fingerprint Writer

Converters

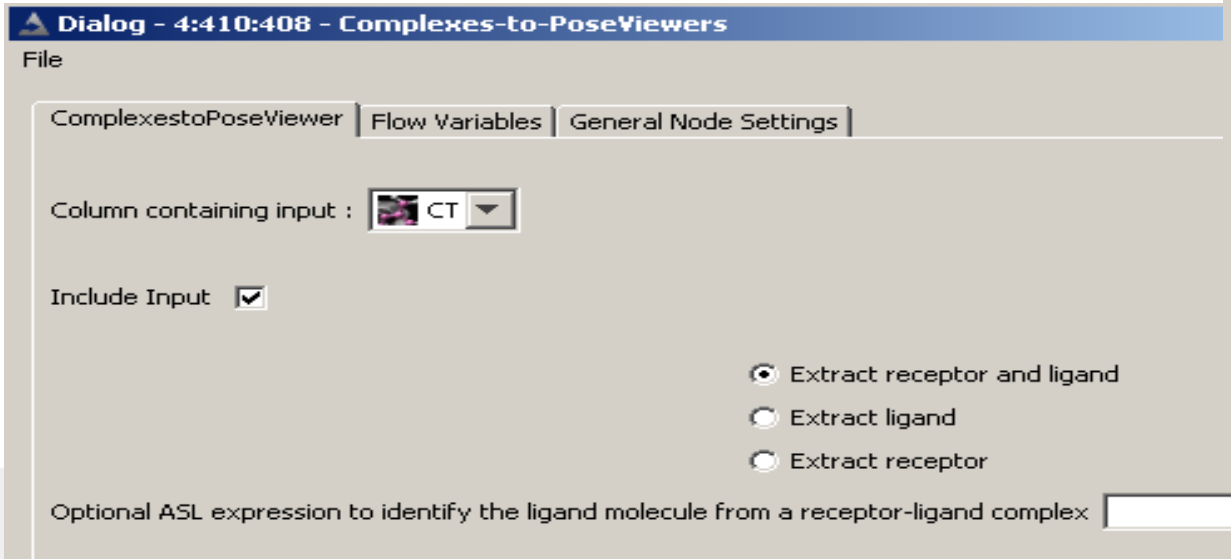
- Molecule-to-MAE
- MAE-to-Pdb, to-SD, to-Smiles and to-Mol2
- SD-to-Smiles
- PoseViewer-to-Complexes
- Complexes-to-PoseViewers
- String-to-Type
- Hartree-to-kcal/mol Converter
- kJ-to-kcal Converter

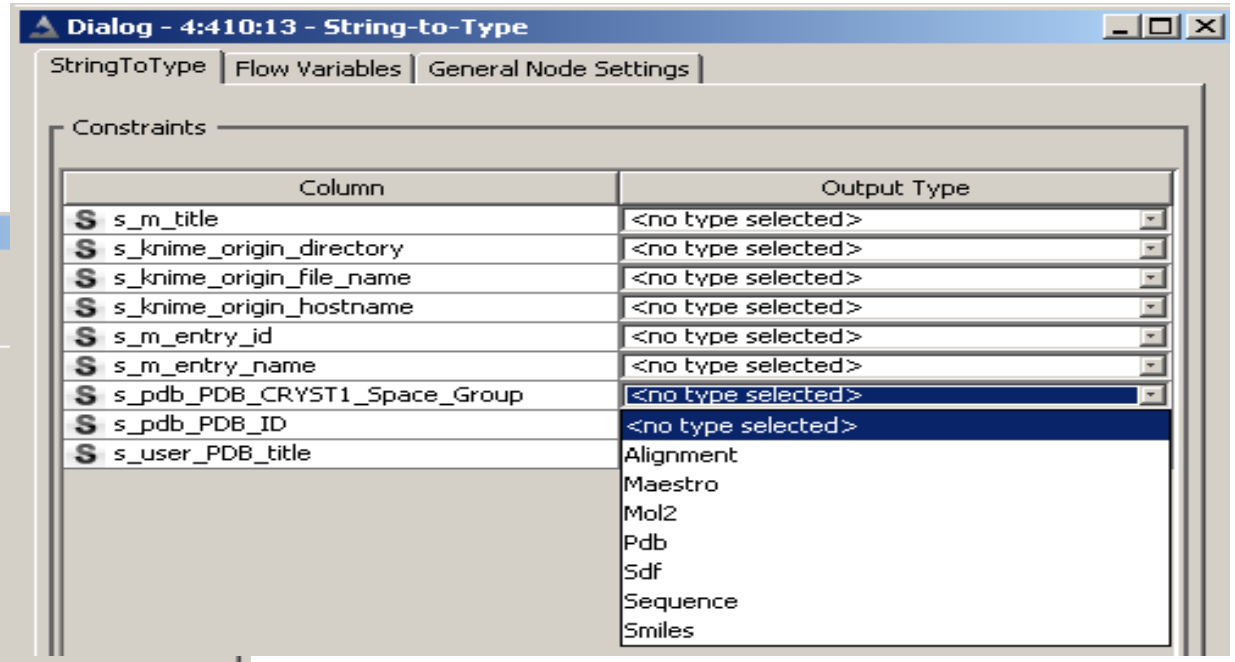
Visual Coherence – Maestro vs. KNIME



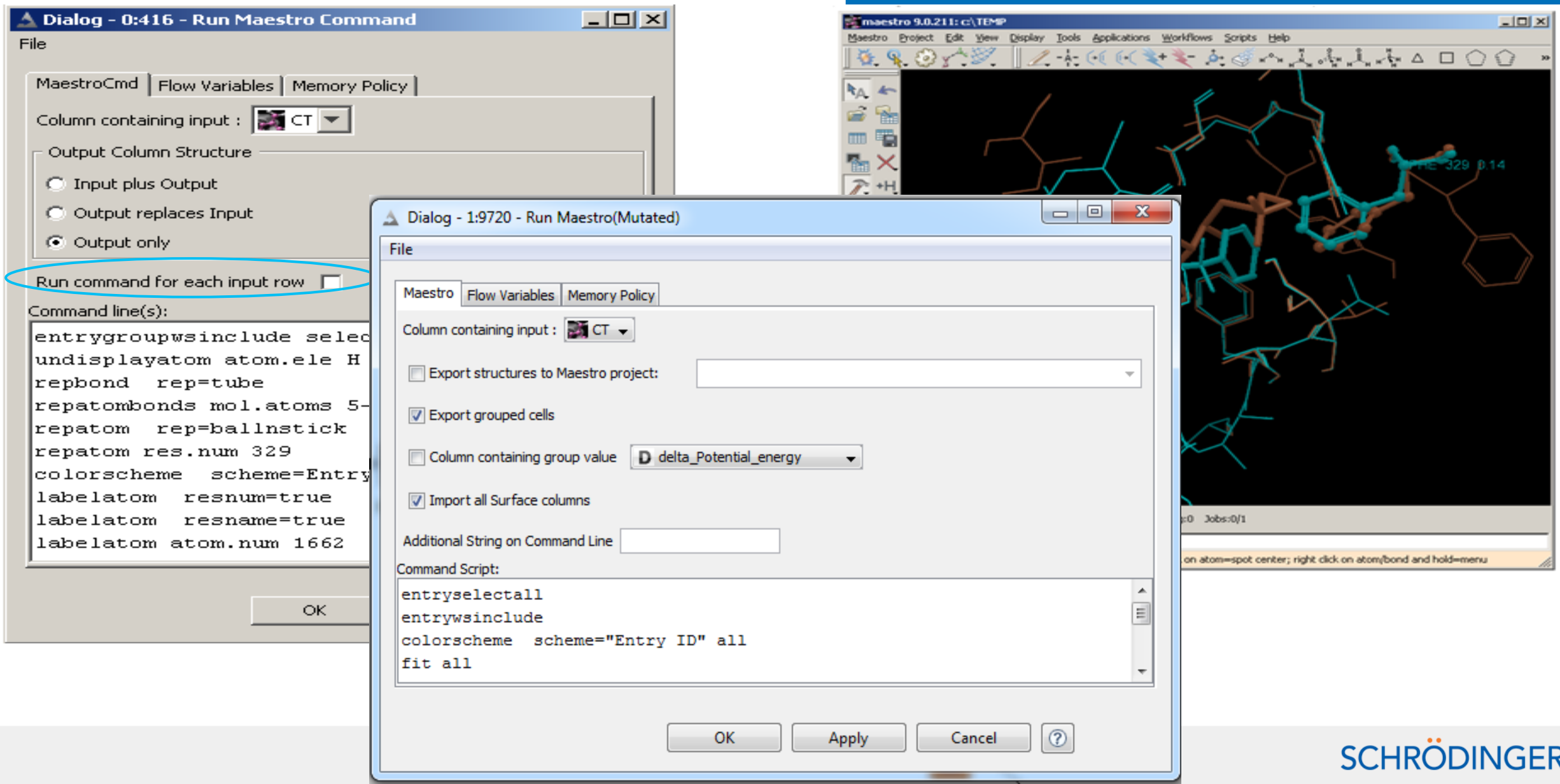
Nodes of general use - Readers and converters

- Molecule reader, SD reader... Glide grid reader...
- Converters (Maestro, mae.gz, SD, sd.gz, mol2, PDB, smiles) including Molecule to MAE, string to type. Canvas converters (Matrix, Fingerprint, Bitvector from and to table). SD format checker
- Pose viewer to complexes and Complexes to PoseViewer





Run maestro command and Run Maestro



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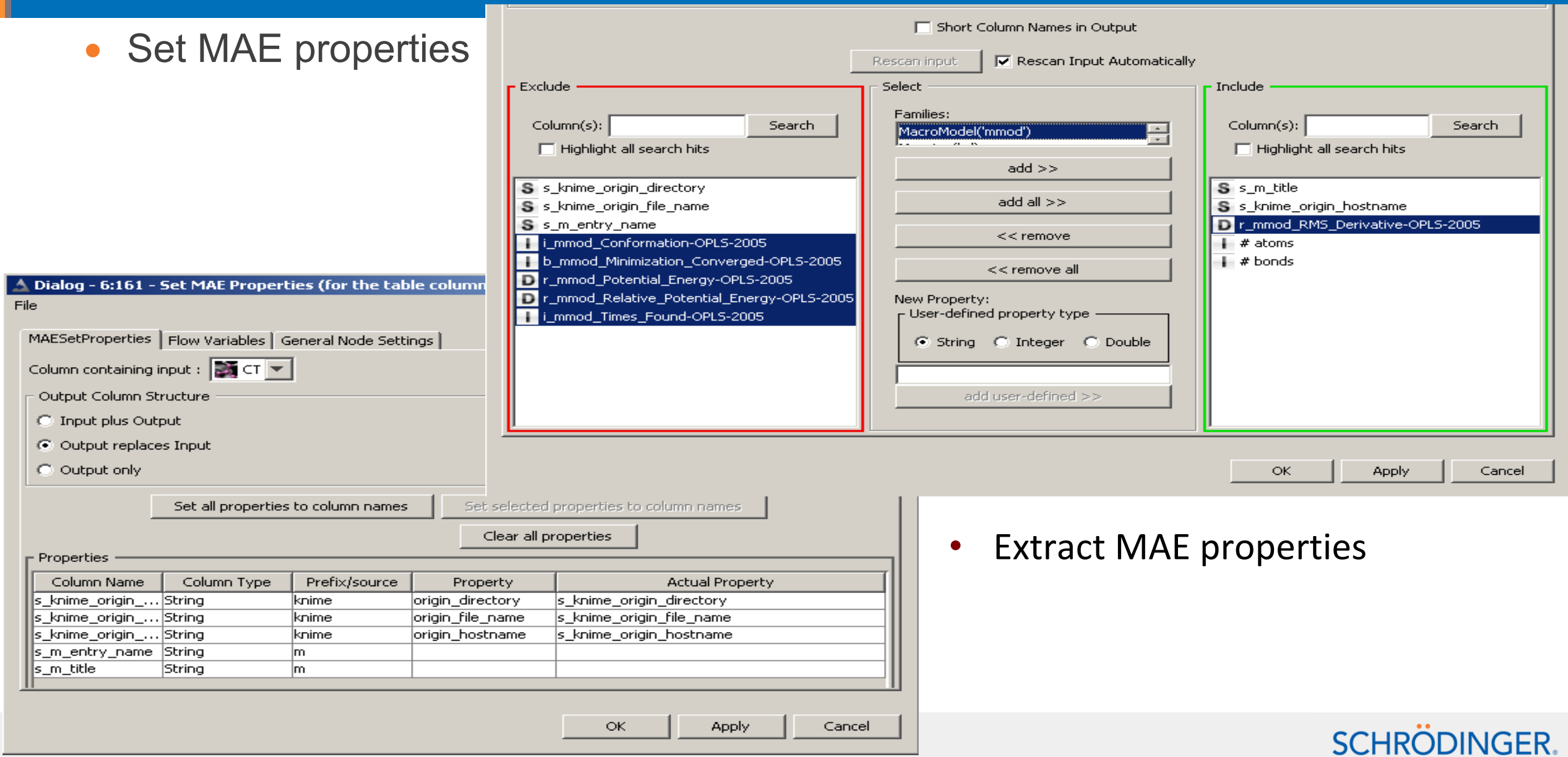
Nodes of general use - Structure manipulation

- Set MAE properties



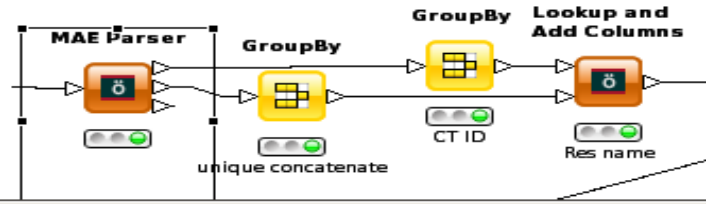
- Extract MAE properties

Nodes of general use - Structure manipulation

- Extract and Set MAE properties
- Group and Ungroup, Set MAE index
- MAE parser
- Split by structure, Delete atoms
- Compare ligands
- Unique smiles, Unique title check, Ligfilter,

Align binding sites, RMSD,

Volume overlap matrix...

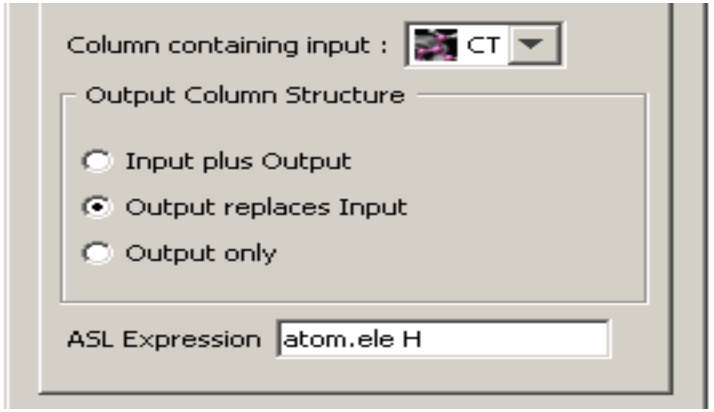


Atom properties - 2:1451:1100 - MAE Parser

File

Table "default" – Rows: 887 | Spec – Columns: 35 | Properties

Row ID	ct-id	atom-id	i_m_m...	r_m_x_...	r_m_y_...	r_m_z_...	i_m_re...	s_m_in...	s_r
Row 1	1	1	2	41.858	7.688	24.757	100		X
Row 2	1	2	15	41.794	8.906	24.854	100		X
Row 3	1	3	3	41.806	6.775	25.963	100		X
Row 4	1	4	25	42.111	7.042	23.642	101		X
Row 5	1	5	3	42.191	7.68	22.362	101		X
Row 6	1	6	2	41.047	7.296	21.464	101		X
Row 7	1	7	15	40.64	6.12	21.387	101		X
Row 8	1	8	3	43.446	7.282	21.676	101		X
Row 9	1	9	2	44.659	7.788	22.399	101		X
Row 10	1	10	2	45.301	6.953	23.288	101		X



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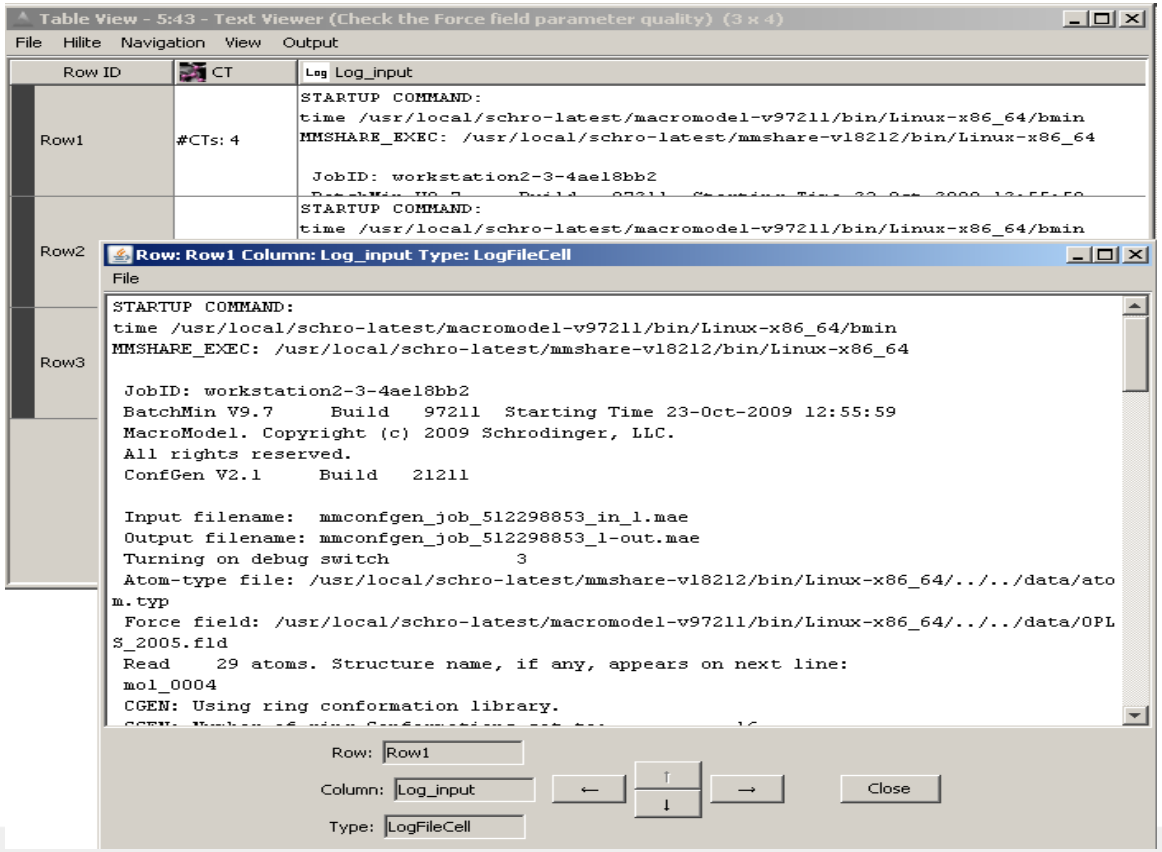
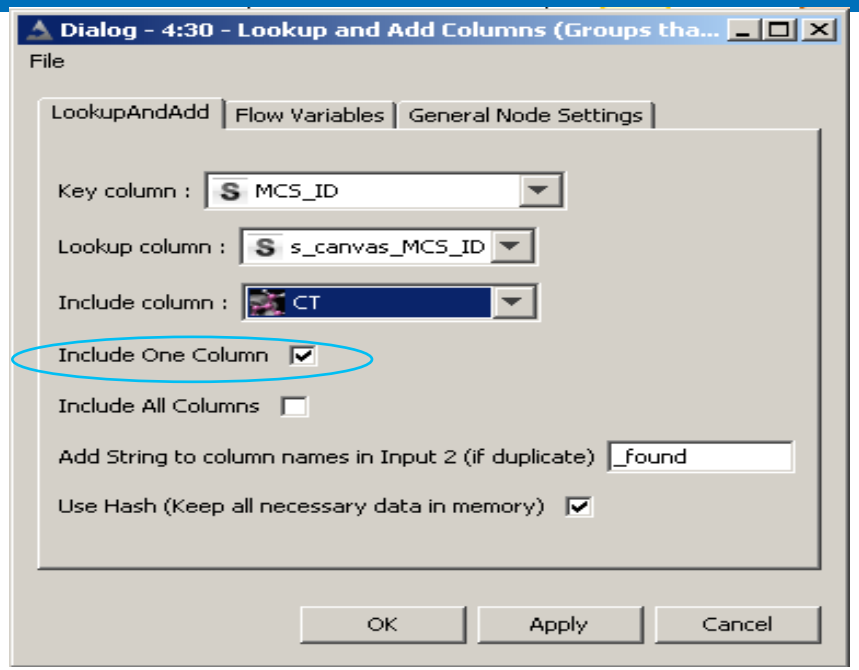
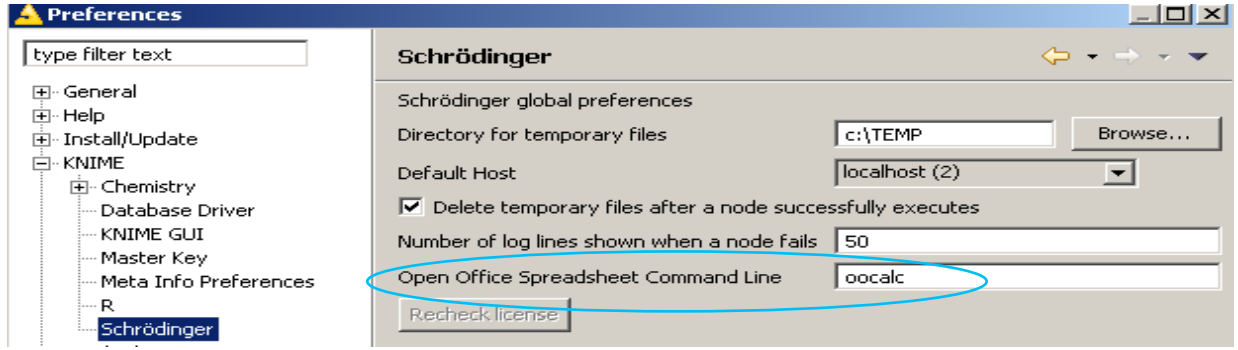
Nodes of general use - Data manipulation and viewers

- Look up and add columns
- Run Spreadsheet viewer(OpenOffice/Excel)
- Table viewer







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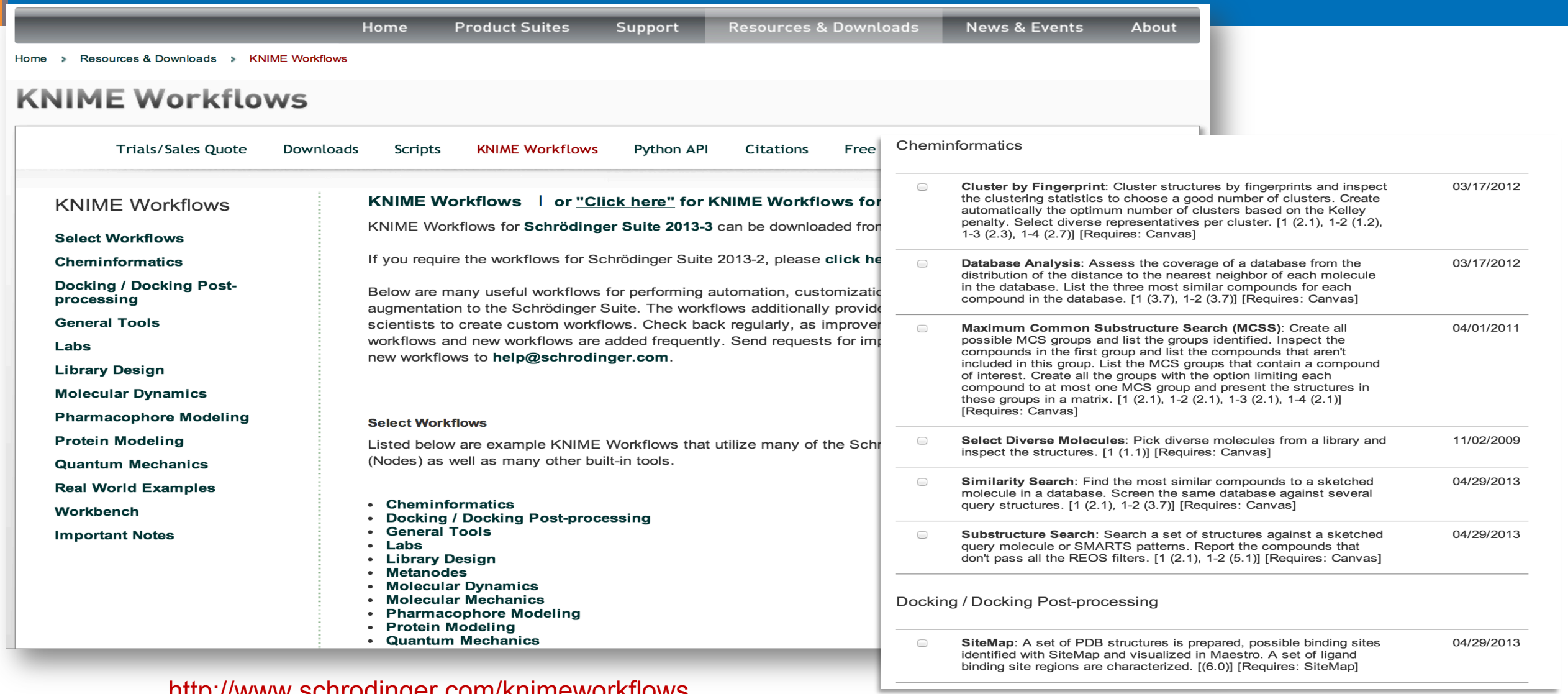
KNIME Workflows Available for Download



http://www.schrodinger.com/knimeworkflows

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Other KNIME Workflows

Cheminformatics
- Cluster by Fingerprint
- Database Analysis
- Maximum Common Substructure Search (MCS)
- Select Diverse Molecules
- Similarity Search
- Substructure Search

Docking and Post-Processing
- Docking and Scoring
- Ensemble Docking
- Loop Over Docking Parameters
- Protein Preparation and Glide Grid Generation
- Validate Docking Parameters
- Virtual Screening
- SiteMap

Pharmacophore Modeling
- Phase Hypothesis Identification
- Phase Screening
- Shape Screening

Molecular Dynamics:
- Desmond Simulation

Molecular Mechanics
- Compare Conformational Search Methods
- Conformational Search and Post-Processing

Quantum mechanics
- Conformational Search and QM Refinement
- ESP Charges
- Jaguar pKa
- Quantum Mechanical Properties
- Semi-empirical Optimization

Library Design
- Library Enumeration

Protein Modeling
- Induced Fit Docking Protocol
- Model Building

Workbench
- Group By Use-cases
- Group Looper
- Unpivot

Real World Examples
- Binding Site Shape Clustering
- Sitemap and Glide Grid Generation
- Vendor Database Preparation

Labs
- Glide Grid Writer
- Parameter Flow Variable Use-cases
- Run Maestro 1:1 Use-cases

General tools
- Chemistry External Tool Use-cases
- Ensure Molecule Title Uniqueness
- Output Column Structure Option Philosophy
- Protein Structure Alignment
- Python Script Node Use-cases
- Run Maestro Command Node Use-cases
- Run PyMOL
- Split and Align Multimers
- Webservice
- Workflows in the Current Workspace

http://www.schrodinger.com/knimeworkflows/

Schrödinger nodes

- Chemistry tool nodes
- Python nodes
- Row iterator loop start
- Look up and add vs. Joiner node
- Miscellaneous nodes: Compare ligands, Set molecule title

Intermediate

KNIME workbench

- GUI
- Nodes

Schrödinger extensions

- Specificities
- Schrödinger nodes

◀ Get started

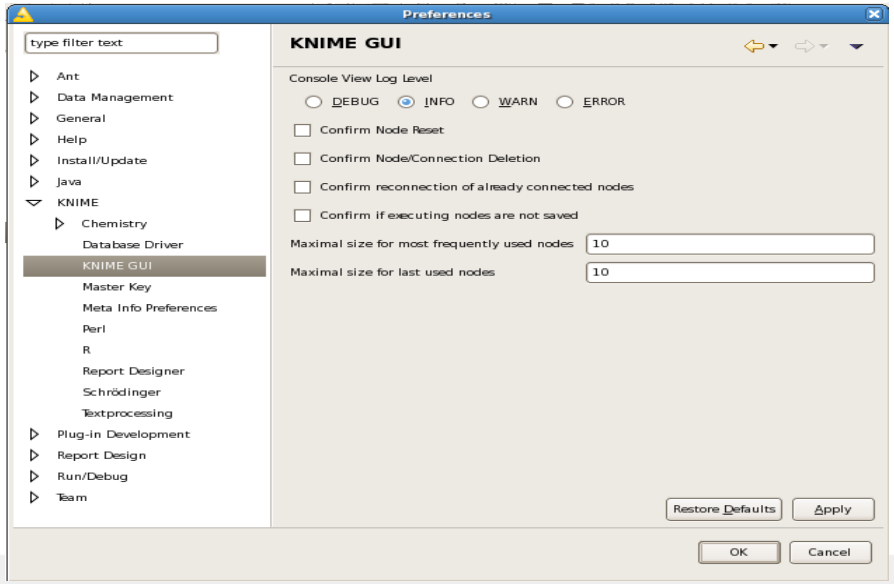
▶ Advanced functionalities

KNIME workbench GUI

- Preferences
- Advanced node functionalities
- Errors, warnings and Console information
- Flow variables and workflow variables
- Metanodes
- Memory limit
- Tips and tricks

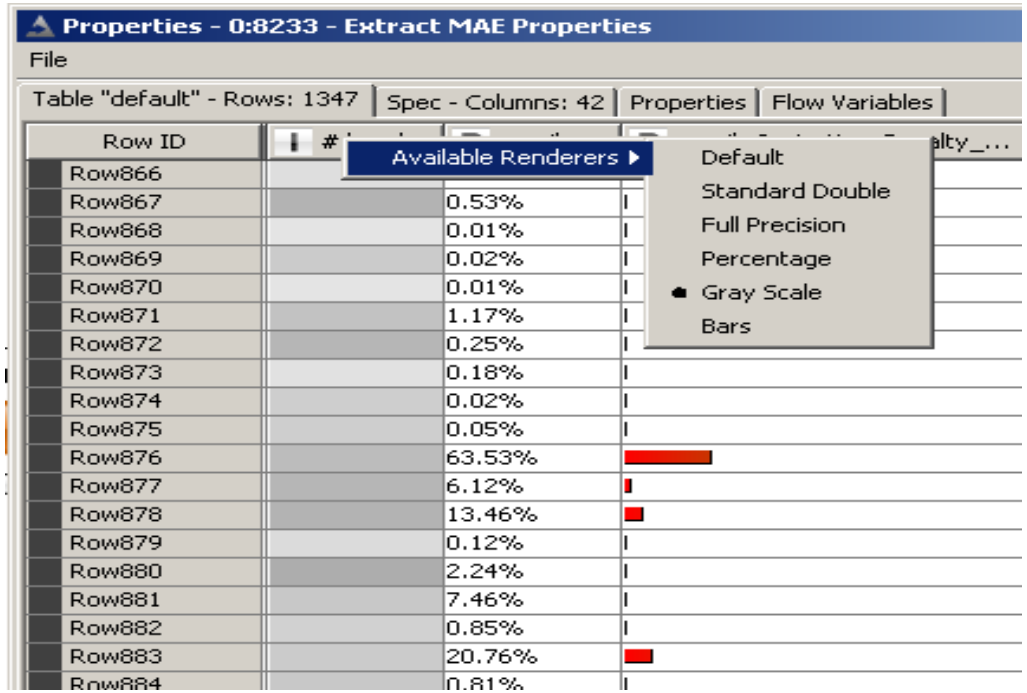
Preferences > KNIME

- Directory for temporary files (See also Schrödinger preferences ▶)
- KNIME GUI- disable the node reset, deletion and reconnection confirmation
- KNIME GUI- Console view log level: recommended to change to INFO. Example of information provided by Schrödinger nodes ▶



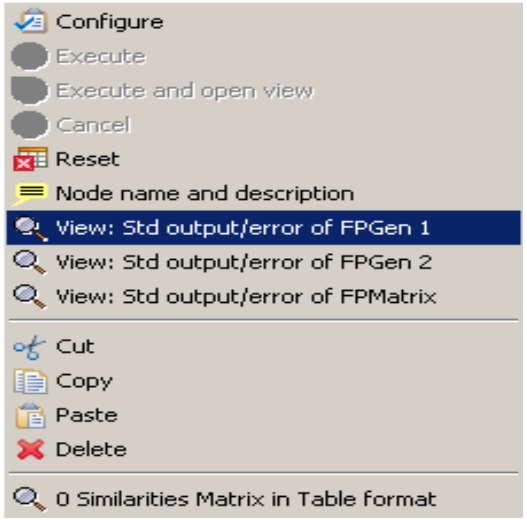
Advanced node functionalities

- Hovering over an input connector tells you what the node takes as input (eg Molecules in Maestro, SMILES or SD format)
- Hovering over an output connector reports the number of rows and columns in the output table
- Comment a workflow: Node pop-up menu > Node name and description
- Data table > change the renderer



Errors, warnings and Console information

- Popup-menu > View Std output/error
- Warning sign above the node status when the node completed with potential errors
- Console information:



INFO HierarchicalClusteringNodeModel Preparing input file '/tmp/HierarchicalClustering_in_423741.mat'

INFO HierarchicalClusteringNodeModel Finished preparing file time 0.35 seconds

INFO HierarchicalClusteringNodeModel 10:42:45 11.17.2009:

Running cmdline[0]='=/**usr/local/schro-latest/utilities/canvasHC -im HierarchicalClustering_in_4116794508031023741.mat -ot HierarchicalClustering_in_4116794508031023741.tree -og HierarchicalClustering_in_4116794508031023741.csv -linkage schrodinger -n 123'**

INFO HierarchicalClusteringNodeModel Completed time 1.626 seconds

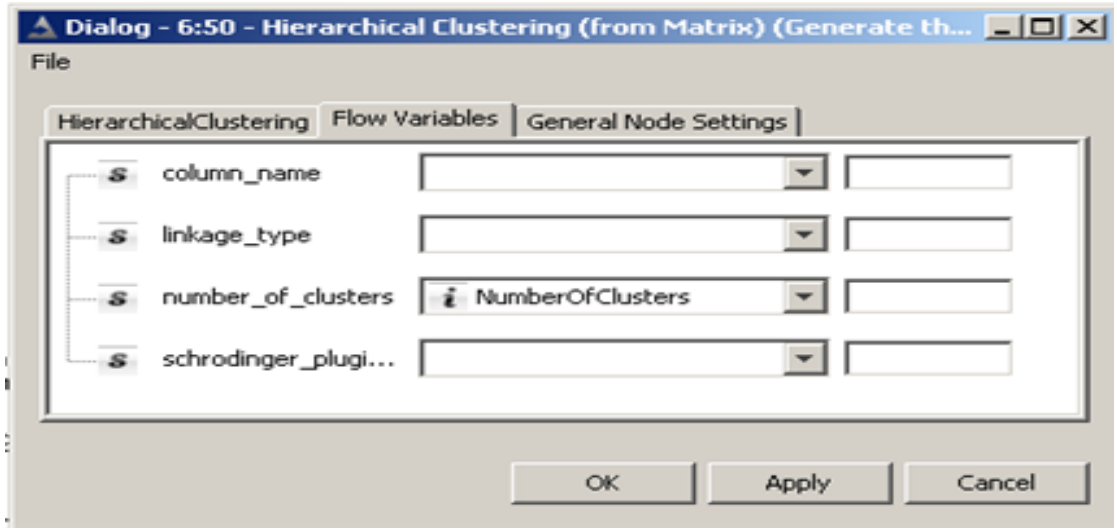
INFO HierarchicalClusteringNodeModel Preparing output

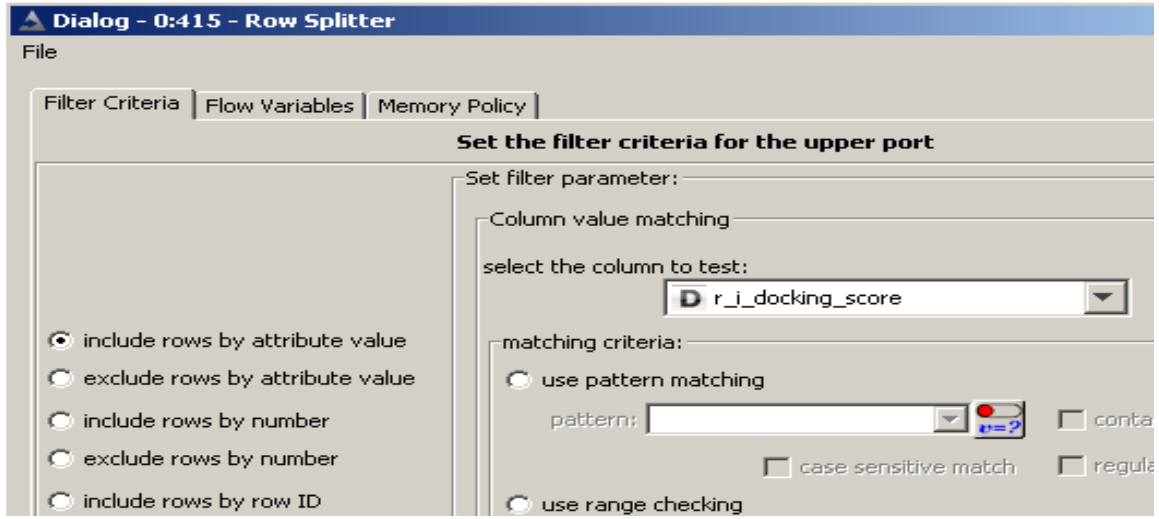
INFO HierarchicalClusteringNodeModel Finished preparing output: time 0.06 seconds

INFO LocalNodeExecutionJob Hierarchical Clustering (from Matrix) 0:2:50 End execute (2 secs)

Flow variables and workflow variables

- The Flow variables are used pass data between nodes on top of the connections.
- In the flow variable tab or the configuration panel for a couple of nodes:





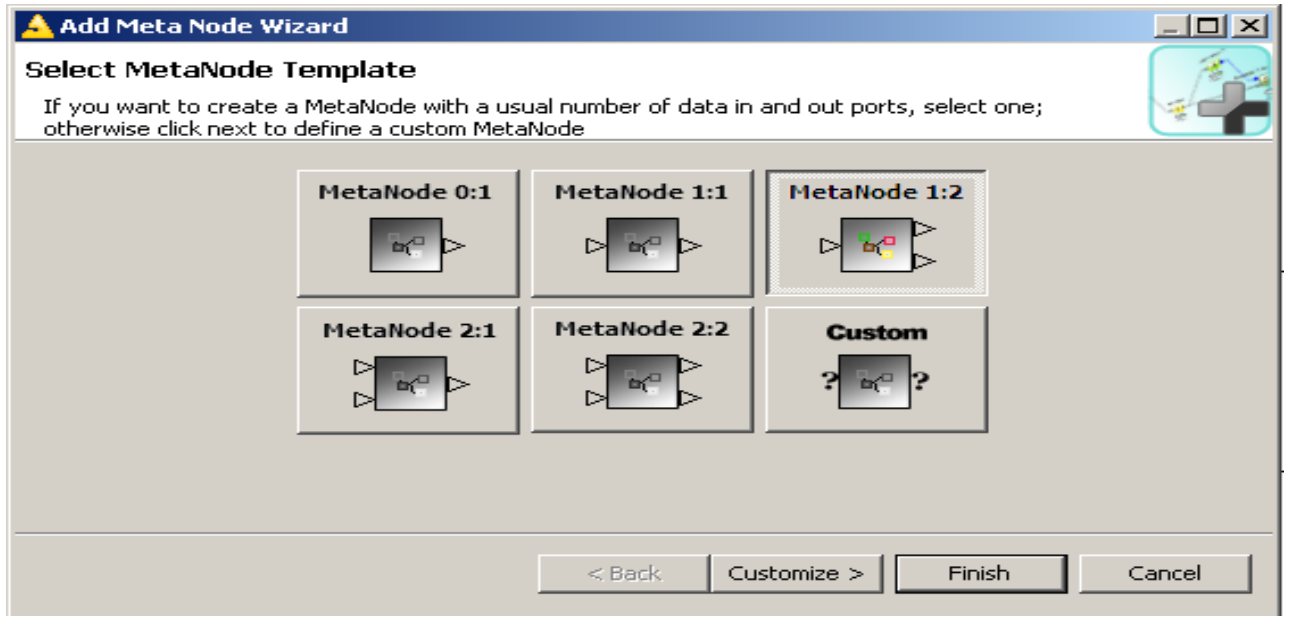
- Global variables can also be set: with the Java snippet node ▶

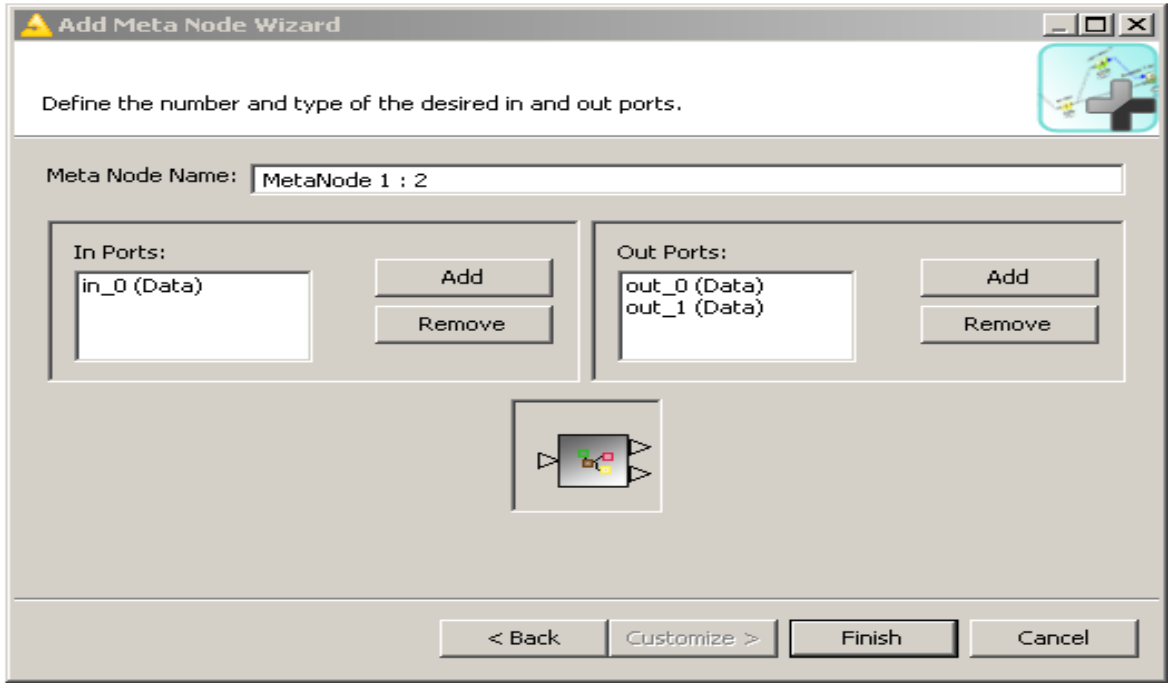
Or in the Workflow project repository select the workflow and Workflow variables in the pop-up menu.

See also Schrödinger specificities ▶ and nodes to edit variables ▶

Metanodes

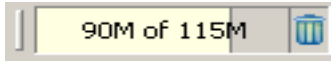
- To hide the complexity and organize a workflow
- Chose the number and type of input/output
- The metanodes open up in new tabs





Memory limit

- Check the memory limit: Help > About Knime > Installation details > Configuration and search for a line starting with "eclipse.vmargs=-Xmx" (close to the top).
- Increase the memory allocated to KNIME:
  - $SCHRODINGER\knime -maxHeap 4096m
  - knime –Xmx4096m (as last option in the command line)
  - in $SCHRODINGER\knime-v*\bin*\knime.ini: change -Xmx1024M into 2048M (or higher on 64 bit)
- The error message usually contain "Java heap space“ when there is a KNIME is running out of memory.
- Preferences > General > Show heap status and use the garbage collector.
- Knime and Schrödinger tools (eg Canvas) don't compete for memory.



Tips and tricks

- Copy and paste some nodes to a specific place:

  Select, copy the nodes (Ctrl+C), right click where you want to paste the nodes and select Paste in the pop-up menu.

  Using Ctrl+V instead the nodes will be pasted a little below the original ones.
- The keyboard shortcuts for items on the menus are listed as usual with the menu item. In File > Preferences > General > Keys you can view all the key bindings to commands, modify the bindings, and create your own shortcuts.
- All the branches can be run at the same time using the GUI toolbar Execute all executable nodes button. See also Cancel all running nodes.

Known issues

- If you can´t save the workflow with a Java heap space error try to disconnect the last node or run the garbage collector.

KNIME workbench GUI

- Report designer
- Global variables
- Batch execution
- Tips and tricks

KNIME workbench node

- KNIME.com Labs nodes
- Scripting and run a third party tool
- Java snippet use-cases
- Manipulate the table row IDs using the RowID node
- Aggregation using the GroupBy node
- Miscellaneous nodes: Interactive table, Math formula, CDK Sketcher
- Plotting facilities
- Looping functionalities- Basics
- Model building nodes

KNIME.com Labs nodes

- Pipeline Pilot Connector (other way around?)
- Web Service client, etc

Specific update site: http://labs.knime.org/

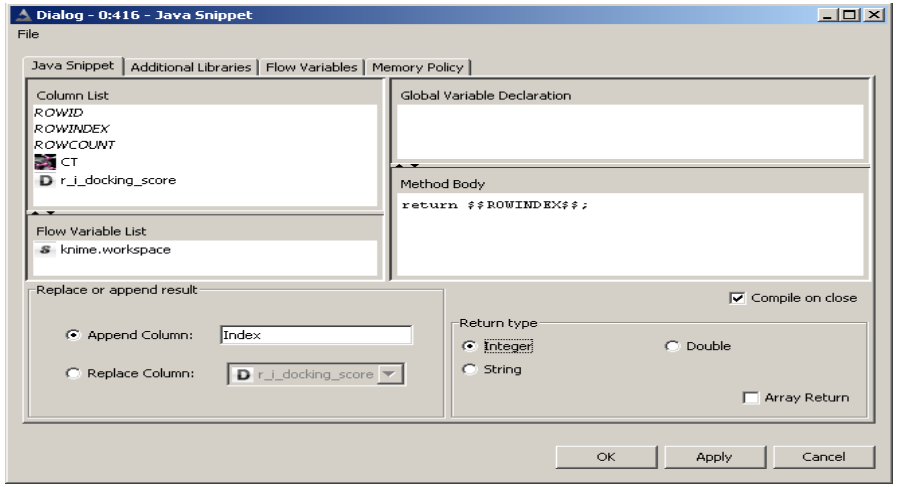
Scripting and run a third party tool

- Java snippet ▶
- Jython and Schrödinger Python nodes ▶
- Perl scripting
- External tool and Schrödinger Chemistry external tool nodes ▶
- Run Maestro commands ▶

Java snippet use-cases

- Duplicate numeric or string columns
- Create a new column from scratch (eg a tag)
- Combine columns (and flow variables) but use the Combiner node for simple tasks

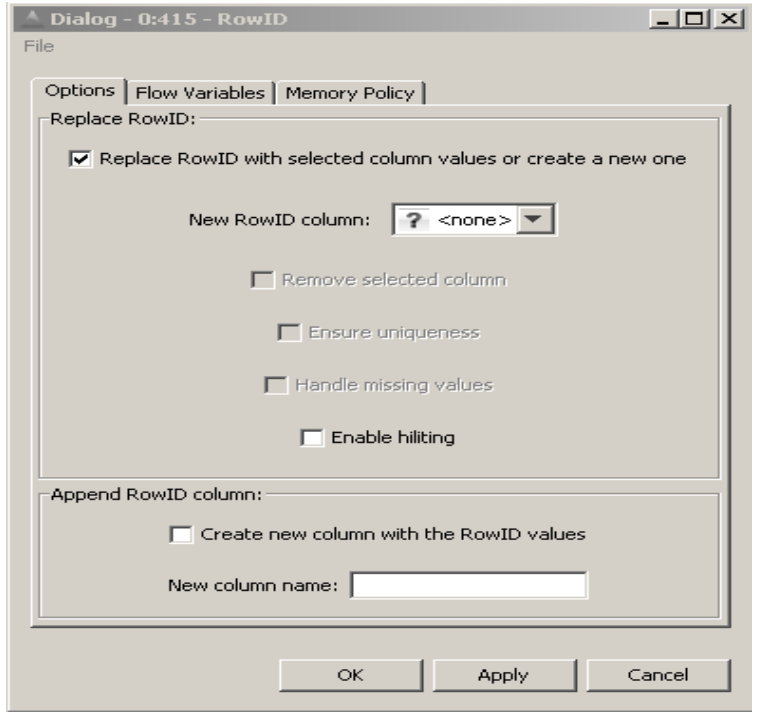
  eg return "prefix-"+$$FlowVar$$+"_ref_"+$Col1$;
- Add a row index (see also Set MAE index)



See the corresponding workflow example.

Manipulate the table row IDs using the RowID node

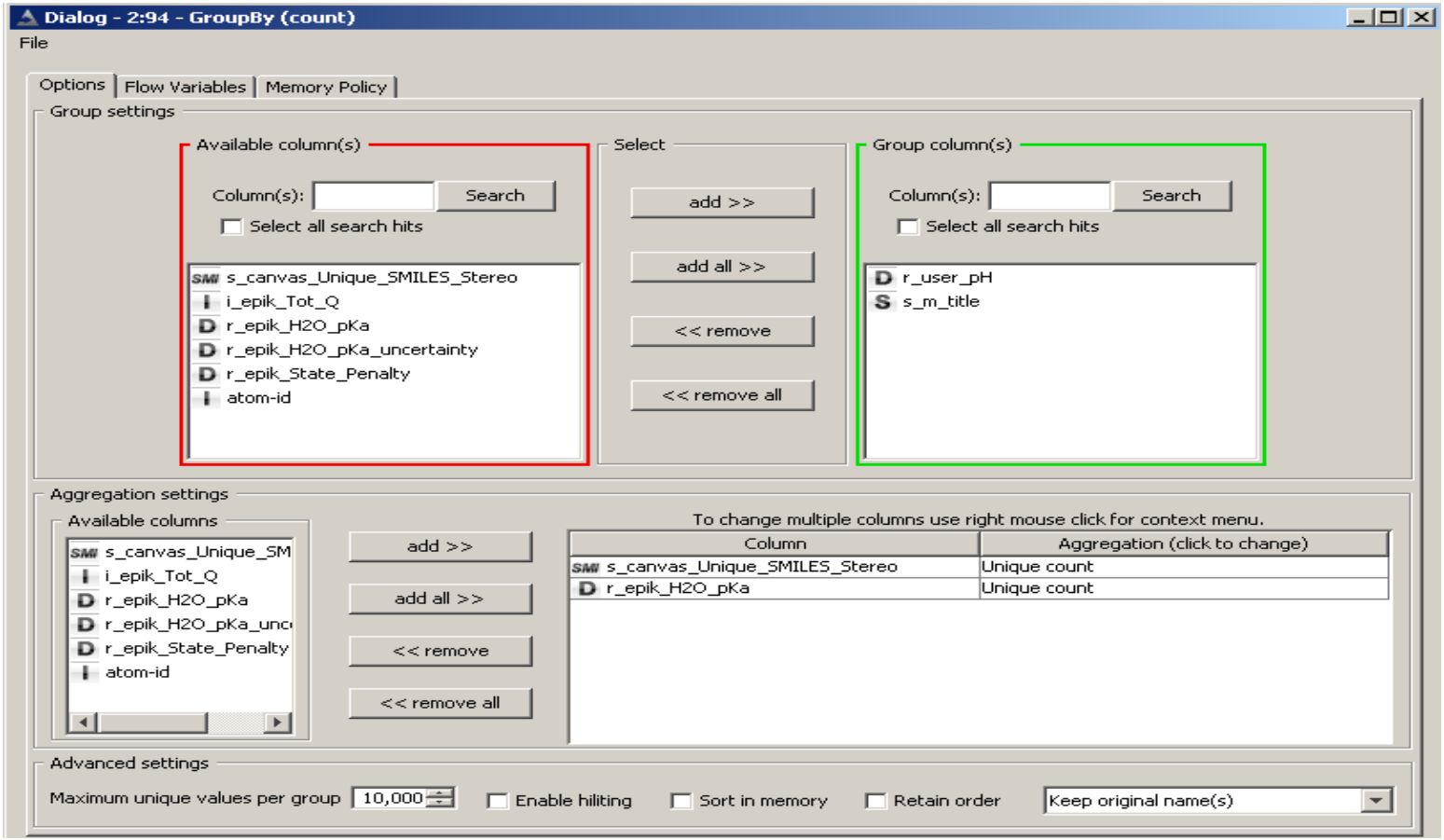
- Use data table column values as row IDs and store Row IDs in a column. Use-cases:
  - before transposing a data table
  - Set the labels to be used by the Plotter node
- Ensure row ID uniqueness
  - eg for Canvas tools before creating a matrix)



Aggregation using the GroupBy node

Some of the aggregation methods:

- first, last
- max, min
- Mean
- Sum
- Concatenate
- (unique) count
- List
- Set



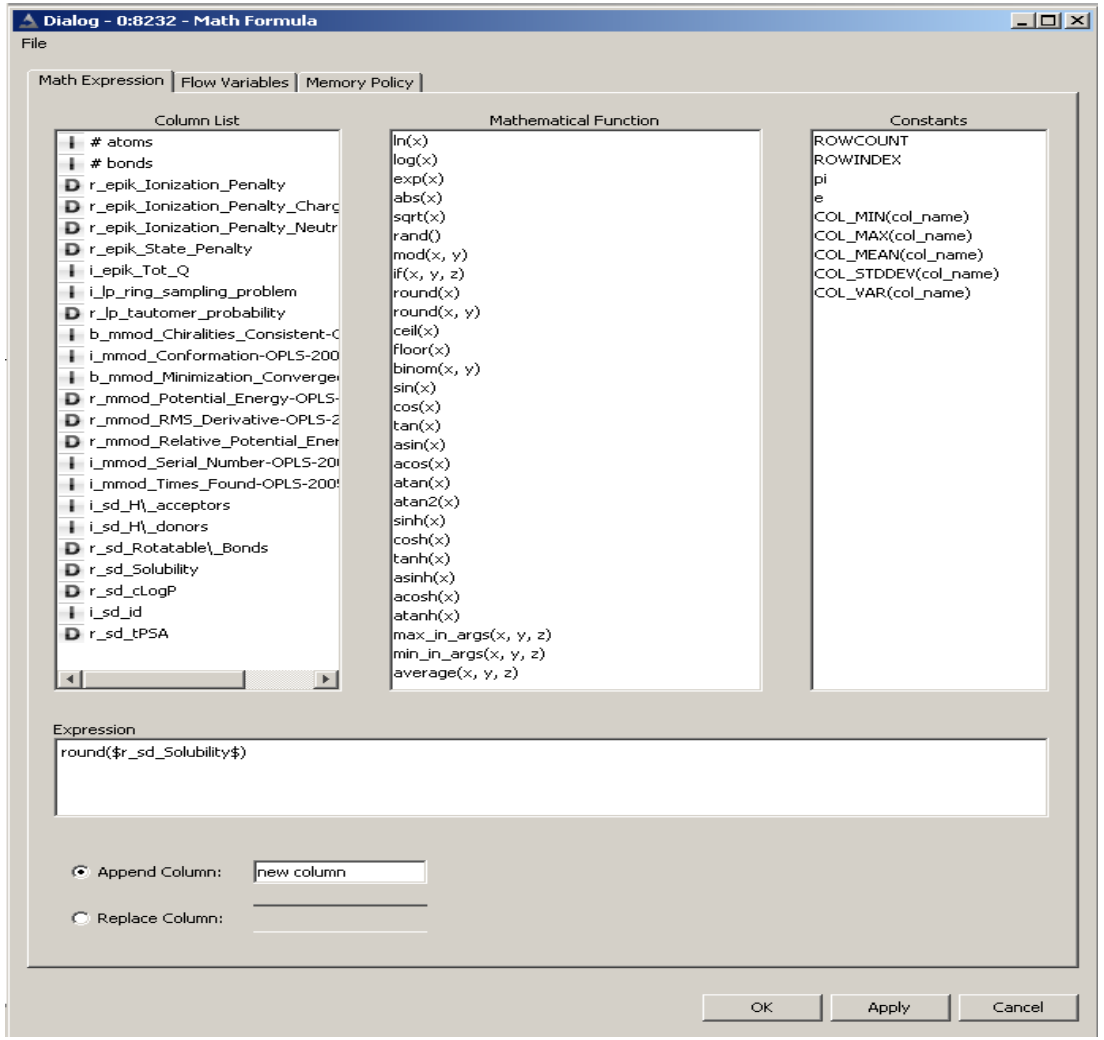
Miscellaneous nodes

- Interactive table: Find & Find Next

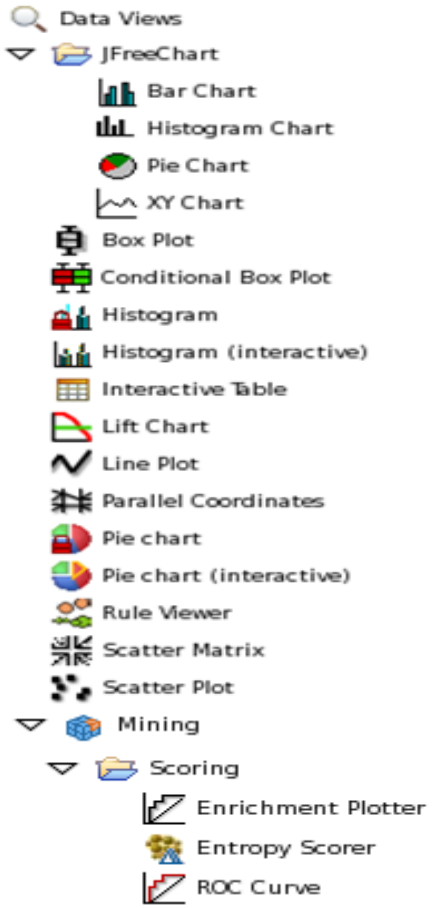
equivalent to the Schrödinger Text viewer node that have more functionalities

- Math formula
- CDK Structure sketcher or Marvin sketch

  (free of charge from Infocom)



Plotting facilities

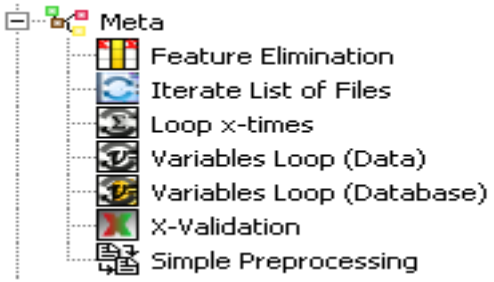


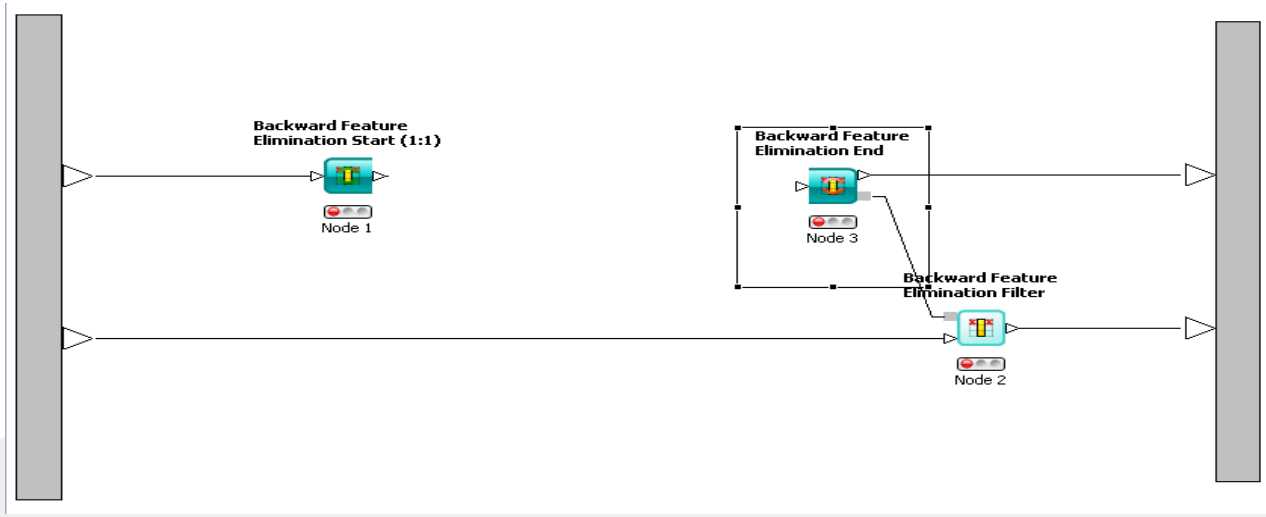
- Data Views: Plotter, Histogram…
- Mining > Scoring: Enrichment plotter, ROC curve
- Advanced capabilities available in KNIME Report designer ▶

Looping facilities- Basics

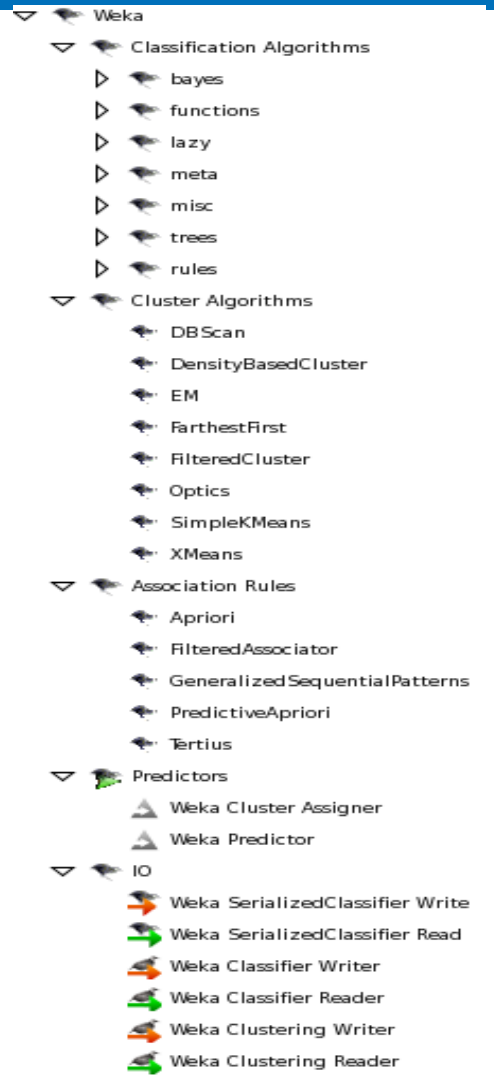
- Loop start … Loop end
- Inject and extract variables
- TableRow/Column to and from variables
- Prebuilt protocols

- Schrödinger node: Row iterator loop start ▶



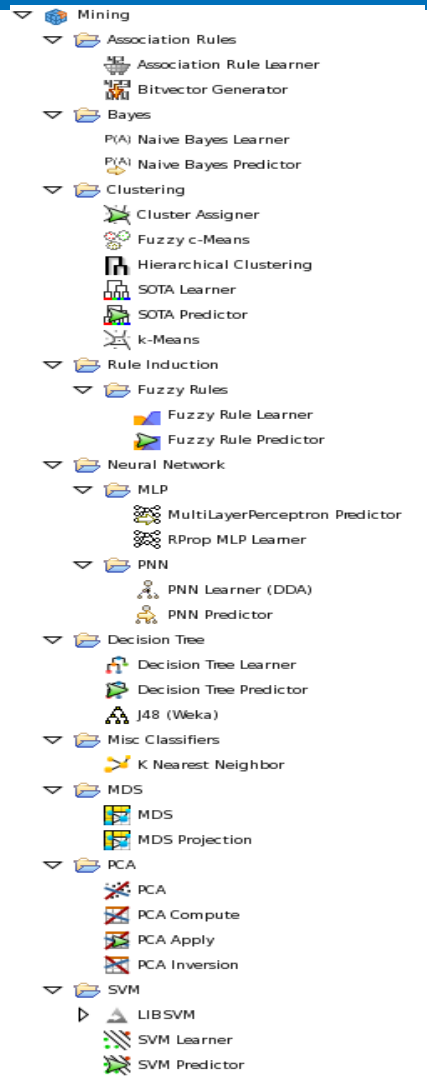


Model building nodes



+ Future Canvas nodes

(already some prototypes)



KNIME workbench nodes

- Edit variables and advanced looping functionalities
- Hilite functionalities
- Database nodes
- Miscellaneous useful nodes

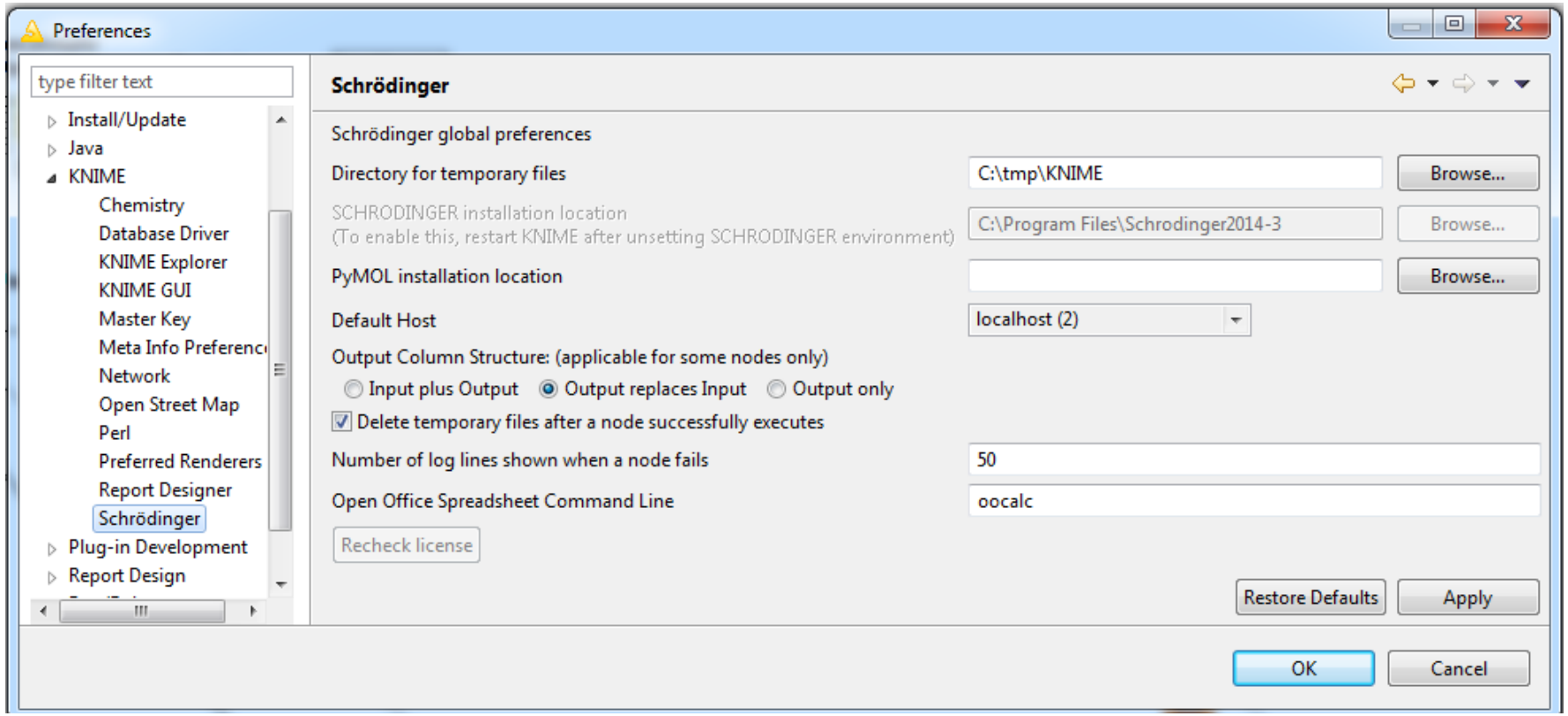
Schrödinger extensions specificities

- Schrödinger preferences
- Start-up script options
- Access to the flow variables

Schrödinger Preferences

- A specific scratch directory can be specified for Schrödinger nodes
- Delete temporary files after a node successfully executes

  Toggled off to run the calculation through the command line again



Start-up script options

To pass user/machine/OS-specific parameters

-maxHeap	Maximum heap size	eg 2048 for 2G
-maxThreads	Maximum working threads	
-tempDir	Schrödinger extensions temporary directory	
-defaultHost	Default host	
-deleteTempFiles true/false	Delete temporary files on or off.	
-ooCmd <value>	Excel / Open Office Spreadsheet command	

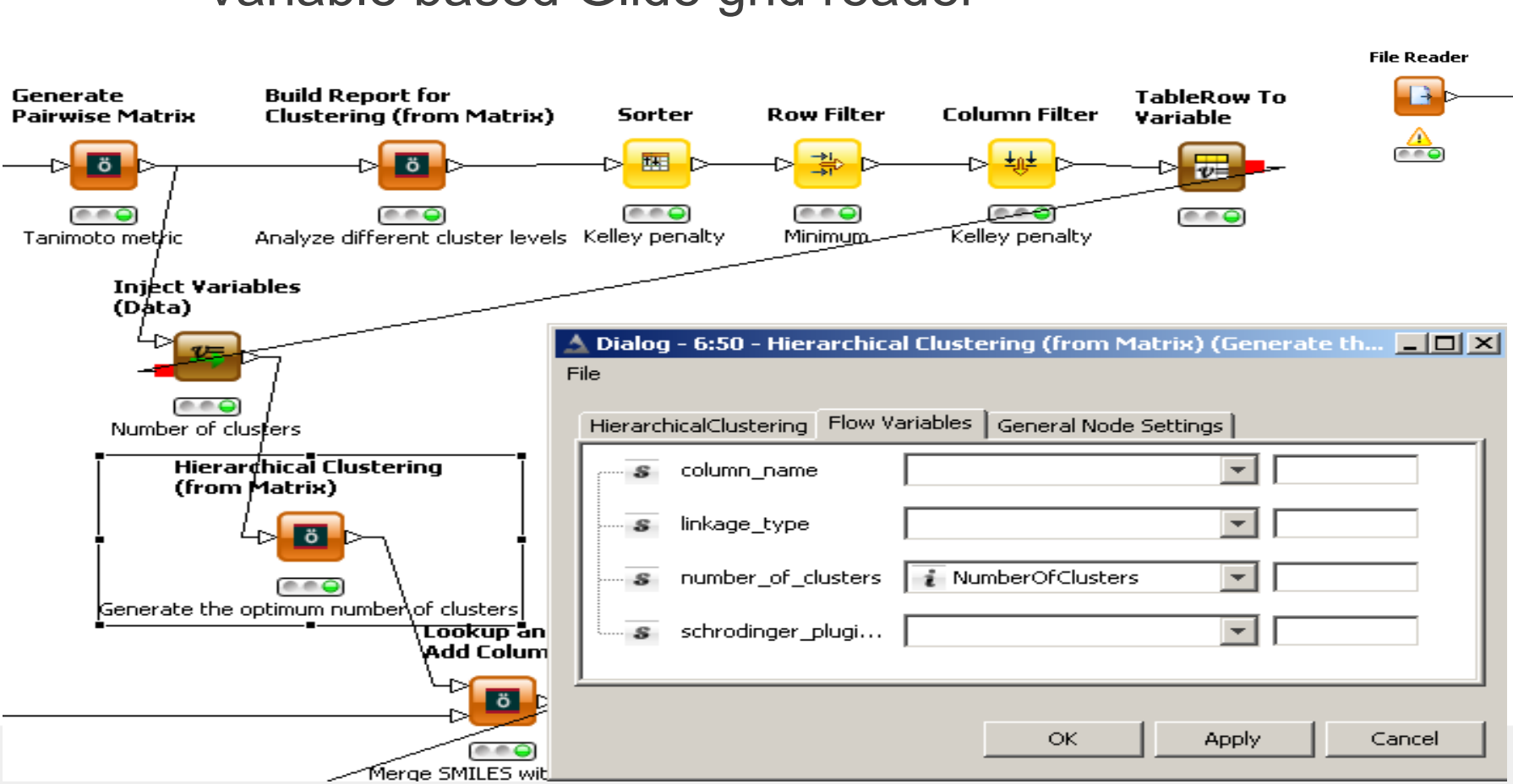
eg oocalc

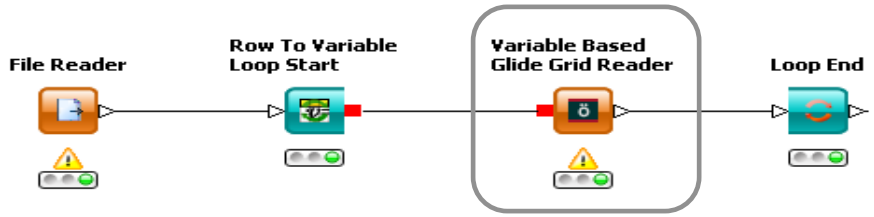
or C:\Program Files (x86)\Microsoft Office\Office12\EXCEL.EXE

And more (see knime –h message)

Access to the flow variables

- Access to the flow variables in the Flow variable tab including the Chemistry external tools nodes (using %flow_n%)
- Variable based Glide grid reader





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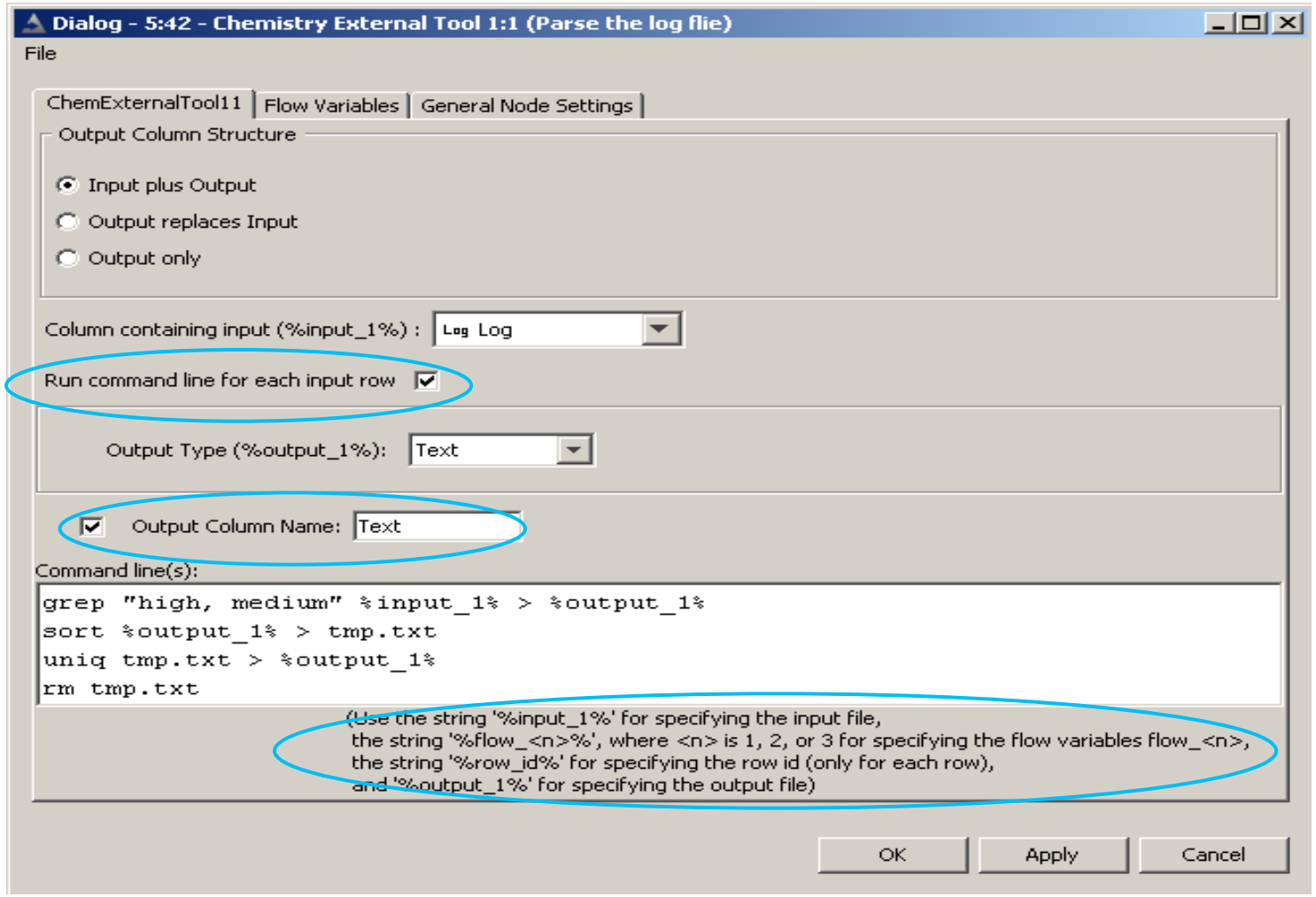
Schrödinger nodes

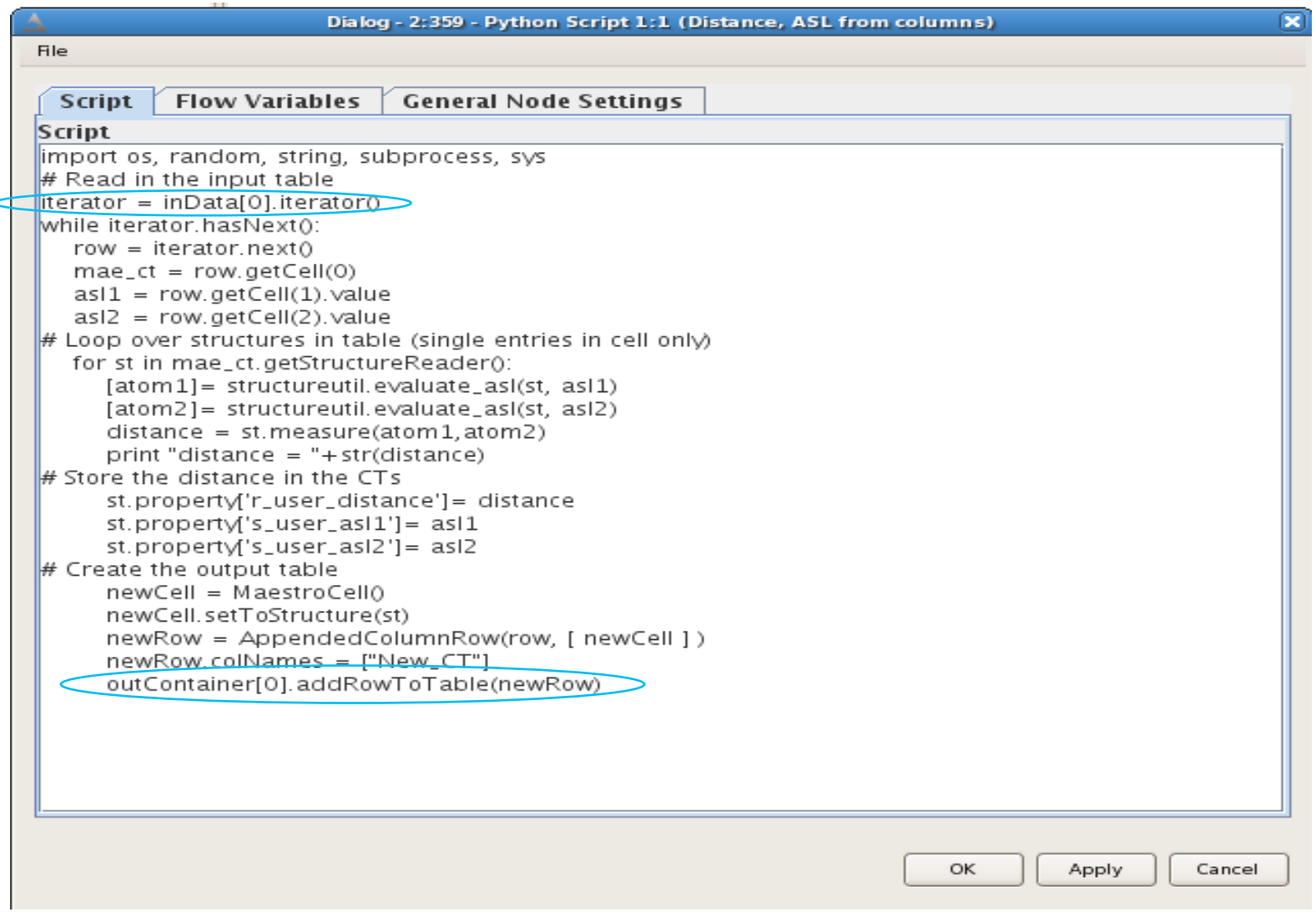
- Chemistry tool nodes
- Python nodes
- Row iterator loop start
- Look up and add vs. Joiner node
- Miscellaneous nodes: Compare ligands, Set molecule title, Get PDB

Chemistry external tool nodes



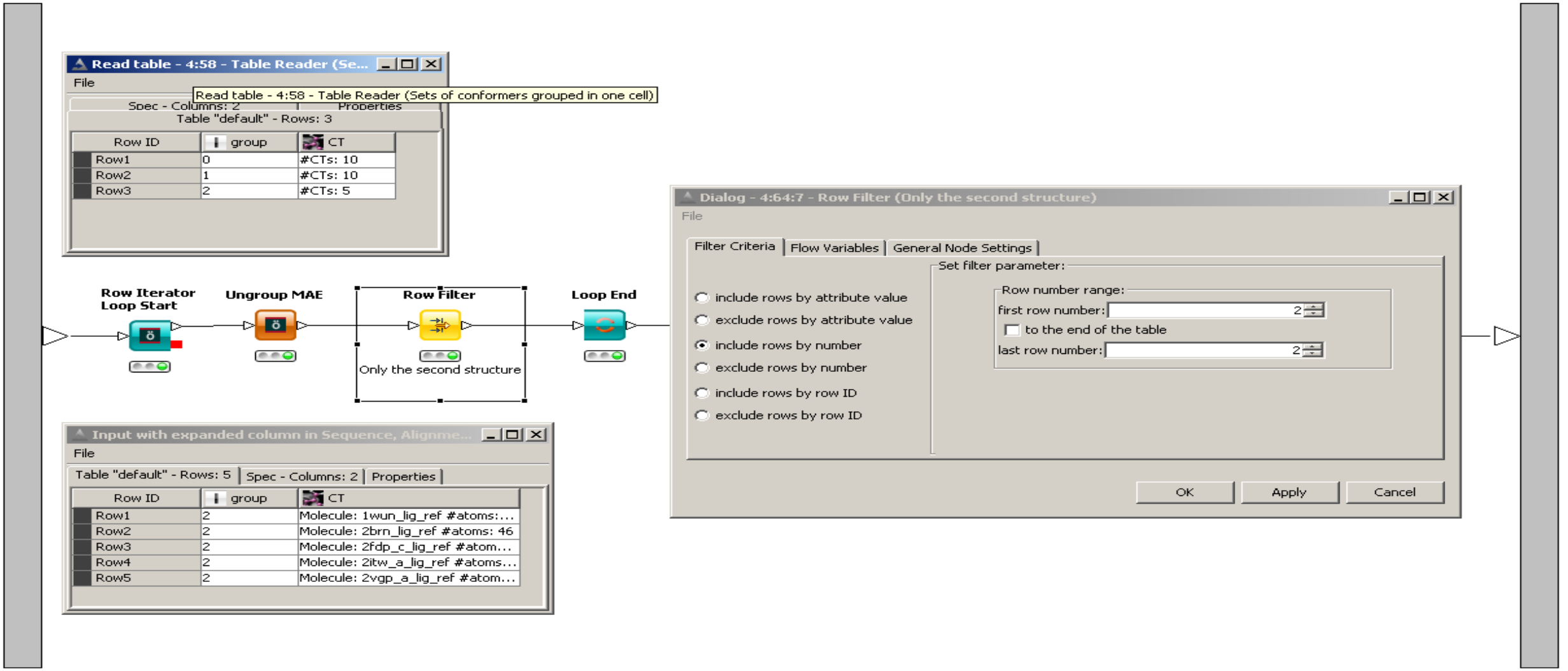
- Input/output types:
  - Maestro, SD, mol2, Smiles
  - Double, Integer
  - String, Text
  - Sequence, alignment
  - FingerPrint, Canvas Matrix
  - Phase Hypothesis, Glide Grid

Python nodes



- Input/output connectors: 0:1, 1:1, 1:2, 2:2
- Schrödinger's APIs
- Possibility to include third party APIs

Row iterator loop start



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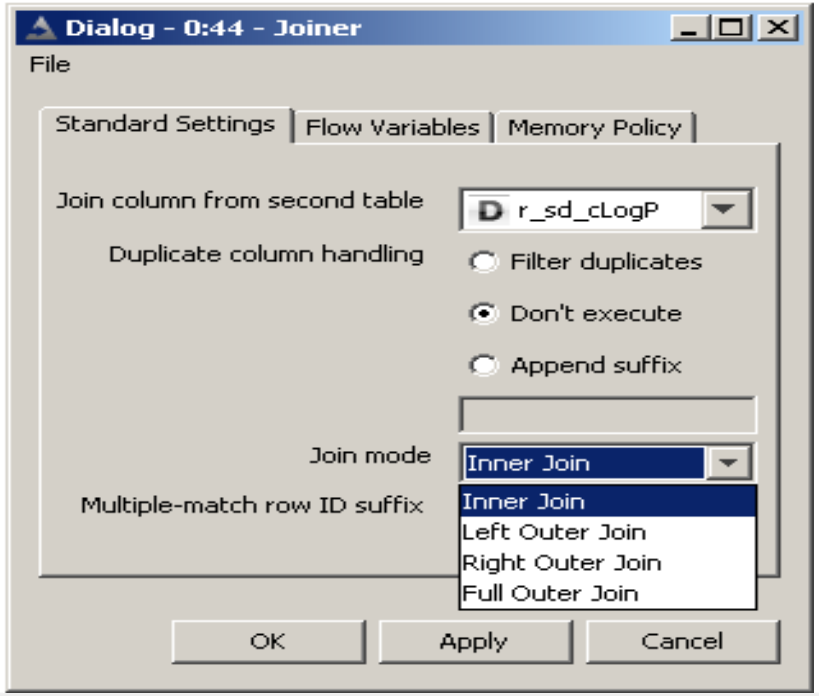
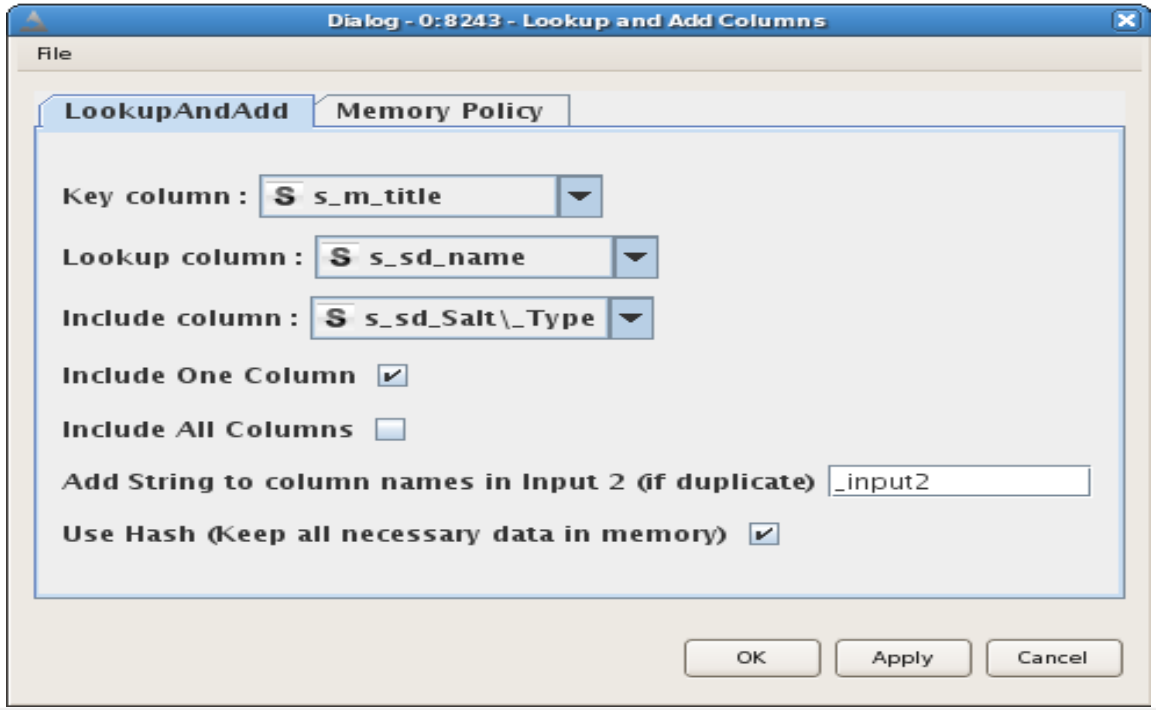
Look up and add vs. Joiner node

- Take advantage only 1 column, concatenate columns

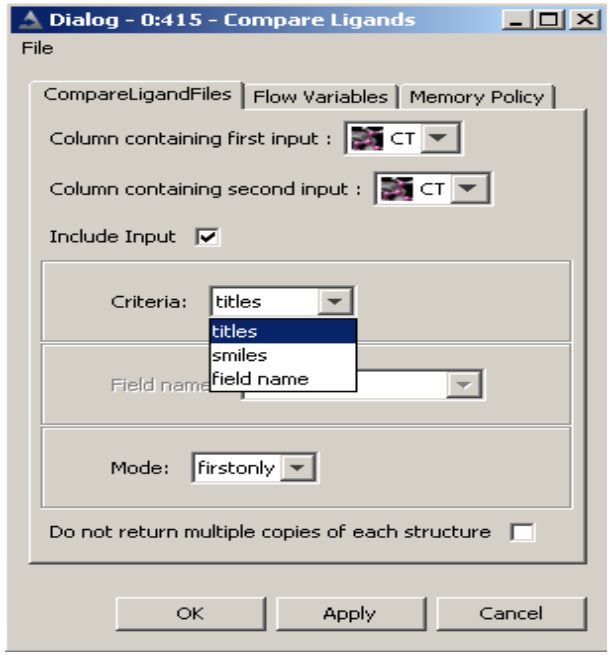
The Joiner node is the easiest way to concatenate columns when the table have the same number of rows and same rowIDs.





Miscellaneous nodes

- Get PDB: easy way to get one or several structures
  use the | symbol as a delimiter for the list of codes
- Set molecule title
- Compare ligands: the modes are First only, both, either



Schrödinger nodes

- Simple workflow examples
- Workflow development support for customers
- Automatic protein preparation
- Scientifically relevant application of the workflow examples
- Interactive work with Knime using the HiLite functionalities
- Use a workflow again

Advanced functionalities

KNIME workbench

- GUI
- Nodes

Schrödinger extensions

- Advanced workflow examples

◀ Intermediate

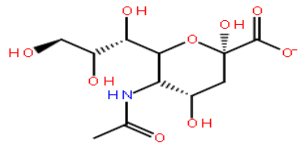
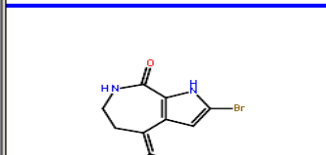
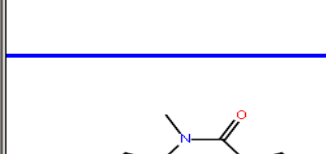
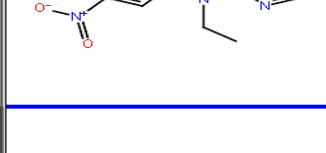
KNIME workbench GUI

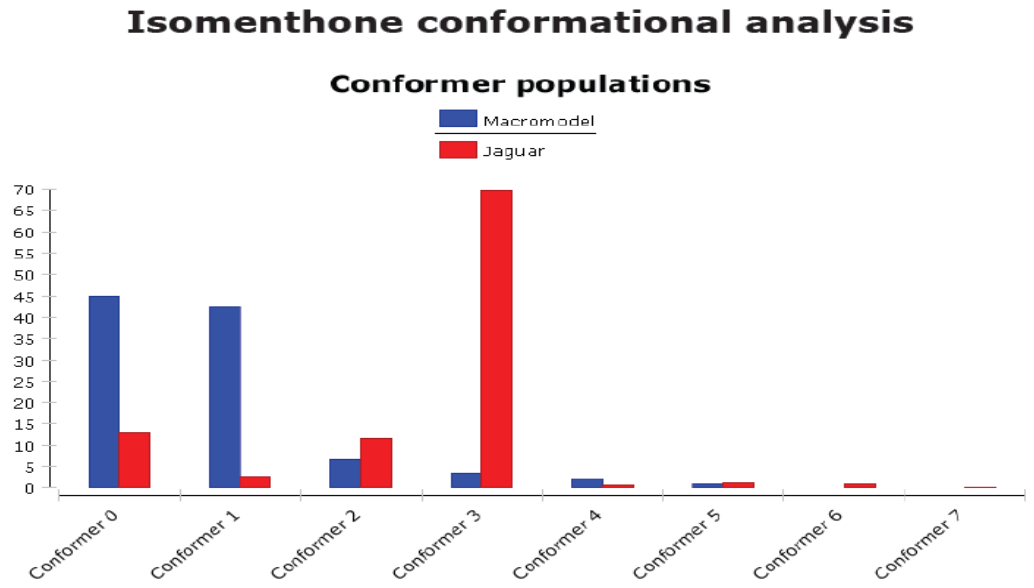
- Report designer
- Global variables
- Batch execution
- Tips and tricks

Report designer

- From knime.com but free of charge. Included in our distribution
- Include To report node(s) in the workflow (can't be in metanodes) and switch to the Report designer mode

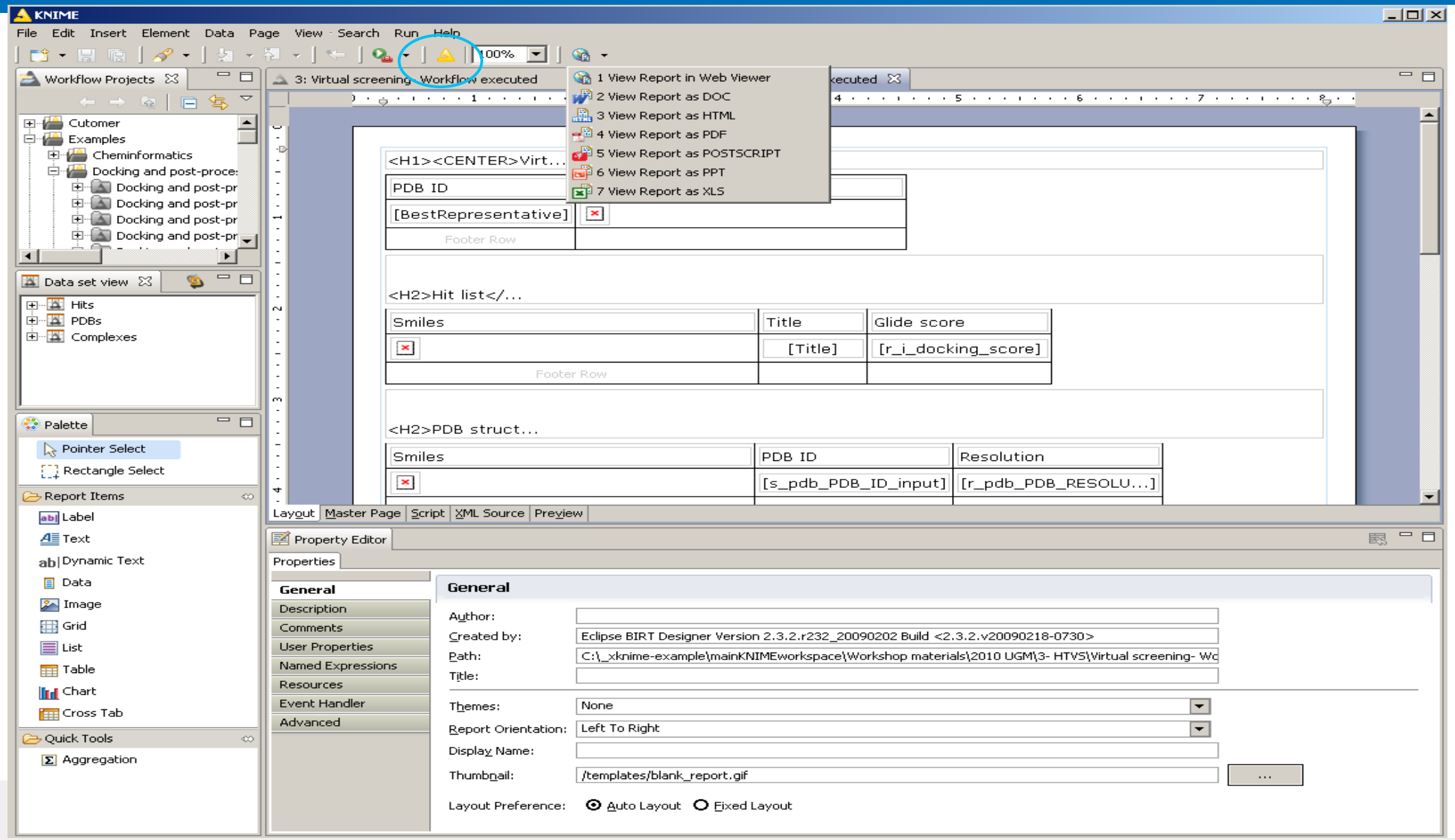
BIRT Report Viewer

Ligand	Complex	Ligand origin	Binding site	Mutations
	1a4q	1nsc	ligand A:DPC2	No
	1buh	1dm2	residues A:18,A:80,A:314	No
	1c1c	1rth	ligand Z:UNK999	A:102,A:227,A:234,B:102,B:234
	1dba	1dbb	ligand _:STR1	H:104



	Jaguar			MacroModel		
Row ID	Relative Energy	Ring conformation	Boltzmann population	Relative Energy	Ring conformation	Boltzmann population
Conformer 3	**0.0**	**-104.2**	**69.9**	6.32	-104.3	3.6
Conformer 4	11.65	-80.0	0.7	7.67	-85.9	2.1
Conformer 5	10.29	-68.9	1.1	9.9	-82.7	0.8
Conformer 7	15.96	-18.4	0.1	18.55	-20.4	0.0
Conformer 6	10.55	-18.3	1.0	17.95	-21.3	0.0
Conformer 0	4.17	-1.1	13.1	**0.0**	**-5.3**	**44.8**
Conformer 1	8.09	1.3	2.7	**0.15**	**-3.1**	**42.2**
Conformer 2	4.52	6.5	11.4	4.82	1.3	6.5

Report designer- template mode



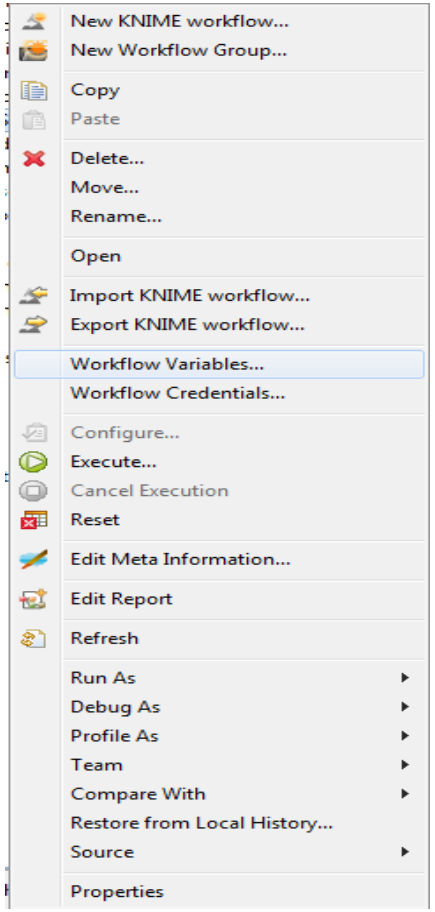
Report designer- Canvas 2D renderer

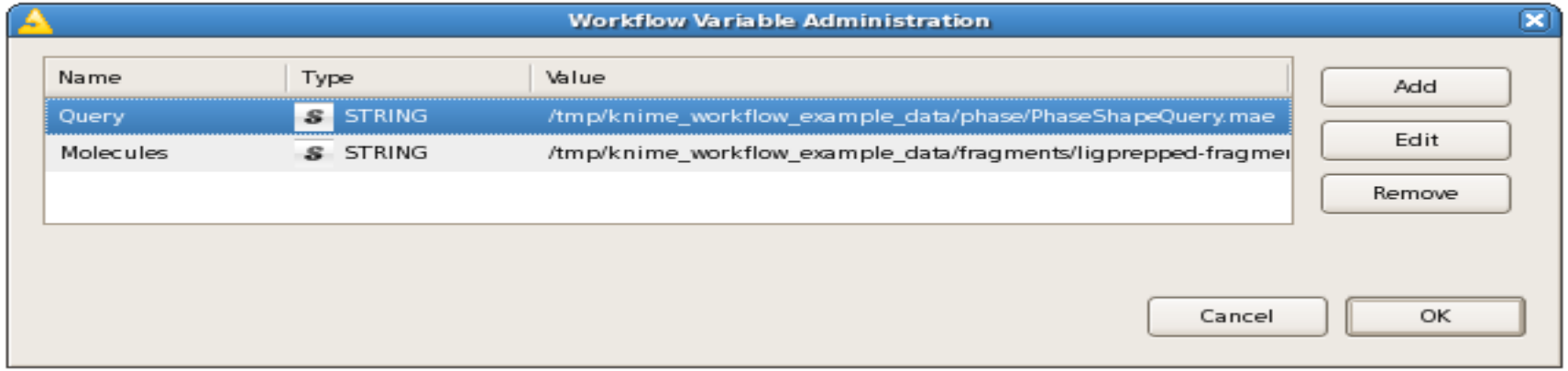
The structures can be shown in a report using Canvas 2D renderer using the following procedure:

- 1. In the workflow, add a MAE-to-smiles node and a To report node.
- 2. In Reporting mode, in the Layout tab, add a table to the report (drag and drop from the Data set view).
- 3. Insert in the "[smiles]" cell (Table- detail row) an Image widget from the Report Items list.
- 4. Configure the widget (using "Edit" on the widget), select "Dynamic image", and press "Select Image Data..." to select the source column (which should be the Smiles column). Delete "[smiles]" if you want just the image and no SMILES. You may want to alter the size of the cell by dragging the border vertically and horizontally if necessary.
- 5. Change the size of the image to something like 300x300, which is done by editing the Data set view (right click -> Edit -> Parameters), and changing (or creating new Parameters typed as integer if they don't exist yet) the knime-image-height and knime-image-width parameters.
- 6. Check the view in the Preview tab

Global variables

- In the Workflow project list, right-click on the workflow, under Workflow variables





Batch execution

- $SCHRODINGER/knime **-batch –reset –nosplash -nosave**
  -workflowFile=<path>/<wkf>.zip or **-workflowDir**=<path>/<workspace>/<wkf>
- Alter some settings **-option=nodeNumber,valueName,value,type**
  -option=7,filename,"/tmp/new-molprops.csv",String (int, double or String)

Find the node number in the configuration panel header (add the metanode numbers)

eg 123/456/78 for the node 78 in the metanode 456 in the metanode 123

Find the option name in the workspace directory: <workflow>/node_name(#7)/node.xml eg:

<config key="DataURL">

<entry key="array-size" type="xint" value="1" />

<entry key="0" type="xstring" value="/C:/serotonin_unique.sdf" />

-option=2,DataURL\0,"file:/tmp/new-input.mae",String

When the input is an array

- Pass some variables: **-workflow.variable=name,value,type** (int, double or String)
- Workflows can be run from Maestro using a simple Python script wrapper

Tips and tricks

- Rearrange the panels
- Workflow Meta-Infos
- Try to open a workflow modified with a newer version of KNIME alter the 2 following lines of the file

<workspace>/<workflow>/workflow.knime:

<entry key="created_by" type="xstring" value="2.0.3.0021120"/>

<entry key="version" type="xstring" value="2.0.0"/>

KNIME workbench nodes

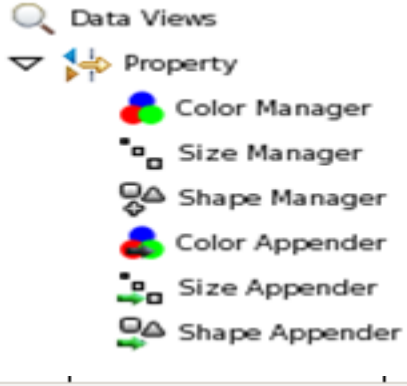
- Edit variables and advanced looping functionalities
- HiLite functionalities
- Database nodes
- Miscellaneous useful nodes

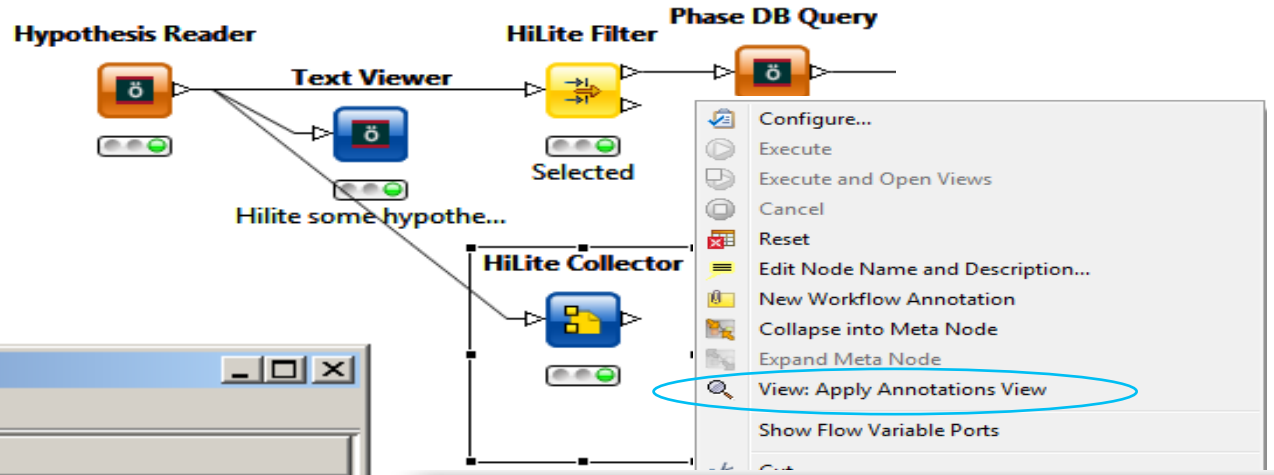
Edit variables and advanced looping functionalities

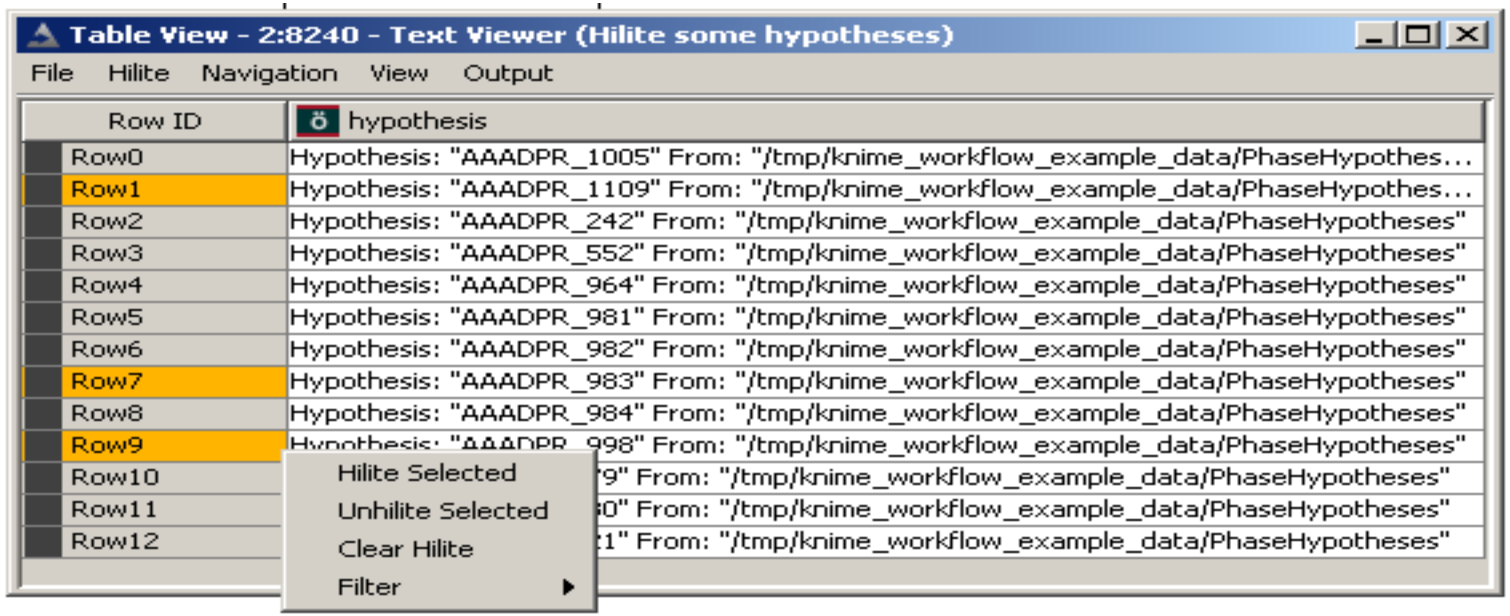
- Extract variable (data) and Inject variable (data)
- TableRow to Variable (use the first row), Variable to TableRow and Variable to TableColumn

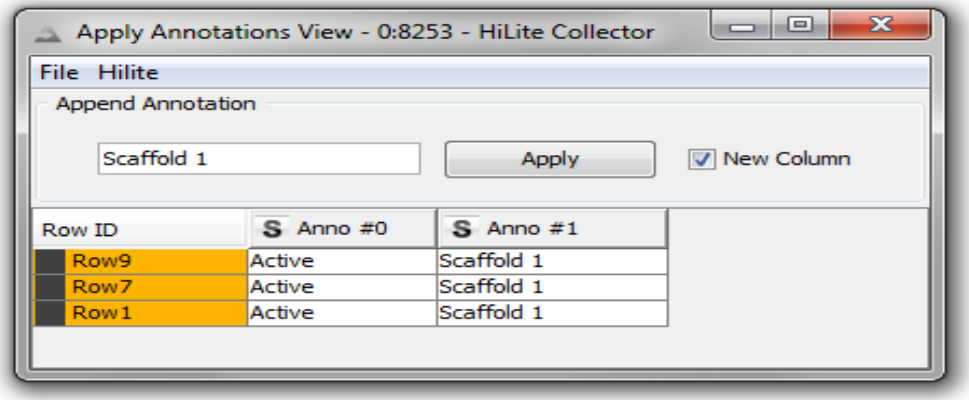
Hilite functionalities

- HiLite filter and HiLite collector nodes
- Color, Size and Shape Manager/Appender nodes









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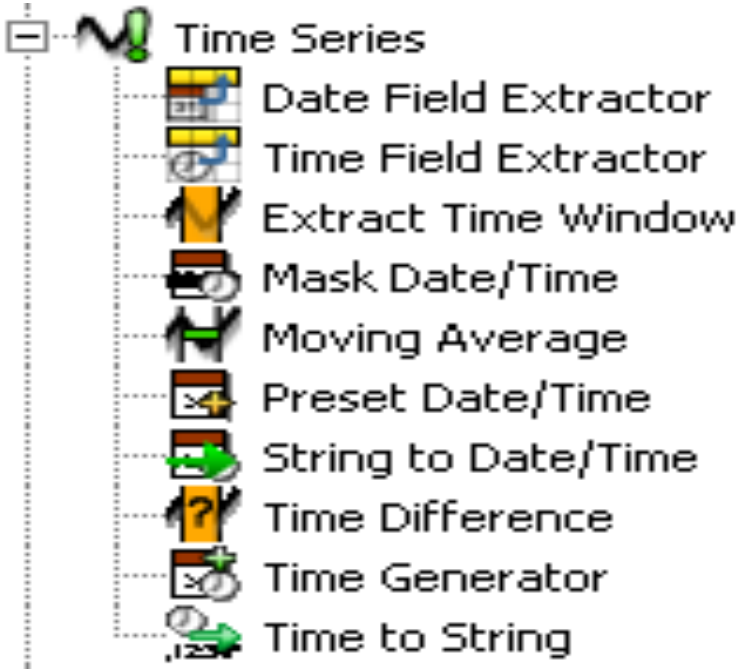
Database nodes

See simple examples (not on the Workflow page yet)

Time series support



- See simple examples (not on the Workflow page yet)

Miscellaneous nodes: Cell splitter, Numeric binner

- Reference row filter, Reference column filter, Nominal value row filter
- Missing values
- Create collection column and Split collection
- Text manipulation: String replacer, Case converter, Cell splitter
- Row sampling, Partitioning, Shuffle
- Numeric binner

KNIME workflow examples

- KNIME workflow page
- Workflow development support for customers
- Workflow example presentation

KNIME workflow page - http:/www.schrodinger.com/knimeworkflows/

Cheminformatics

- Substructure Search
- Clustering, diversity selection, similarity search
- Database analysis
- Maximum Common Substructure

Docking and post-processing

- Protein preparation and Glide grid generation
- Docking and scoring, Virtual screening, Ensemble docking, Induced Fit Docking
- Loop over docking parameters
- Validate docking parameters

Pharmacophore modeling

- Phase Shape screening
- Phase hypothesis identification
- Phase database screening

Molecular Mechanics

- Compare conformational search methods

Quantum mechanics

- Conformational search and QM optimization
  Using the Report designer

Homology modeling

- Model building and refinement

Library design

- Library enumeration
  including a Run Maestro 1:1 prototype

Real World Examples

- Vendor database preparation

General tools

- Python script node use-cases
  including a Run PyMOL prototype
- Chemistry external tool node use-cases
- Run maestro command node use-cases
- Output column structure option philosophy

KNIME workbench

- Workflows in the current workspace

KNIME workbench- looper

- Group Looper

Simplest, **most exciting**, **new** and improved workflows

Workflow development support for customers

Combine or expand the workflow examples

- Hierarchical clustering and diverse compounds from each cluster

Waiting for new nodes to be developed

- CombiGlide library enumeration, MacroModel coordinate scan (now available)
- PCA on per residue interactions (Chemistry external tool node)
- Distance measurement in protein and run script in Maestro, descriptor calculation, create protein mutants (Python script node)

Specific workflows

- Various MacroModel protocols using the Python node for accessing advanced functionalities (eg contraints)
- Prime MM-GB/SA on a set of complexes (ligand detection, flexible residues)
- Simplifying compound docking with KNIME, Dr. Robert Happel, Boehringer Ingelheim, Vienna
  http://www.schrodinger.com/seminarprior/19/26/
- Cris Guimaraes MM-GB/SA paper reproduction and improvements

  http://www.schrodinger.com/Download.php?type=seminarentry&type2=slides&ident=105
- Protein preparation protocol

Real World Case Study: Binding Site Clustering and Ensemble Docking

Chem Biol Drug Des 2012; **80:** 182–193
Research Article

doi: 10.1111/j.1747-0285.2012.01396.x

Generation of Receptor Structural Ensembles for Virtual Screening Using Binding Site Shape Analysis and Clustering

David J. Osguthorpe[1], Woody Sherman[2] and Arnold T. Hagler[1,3,*]

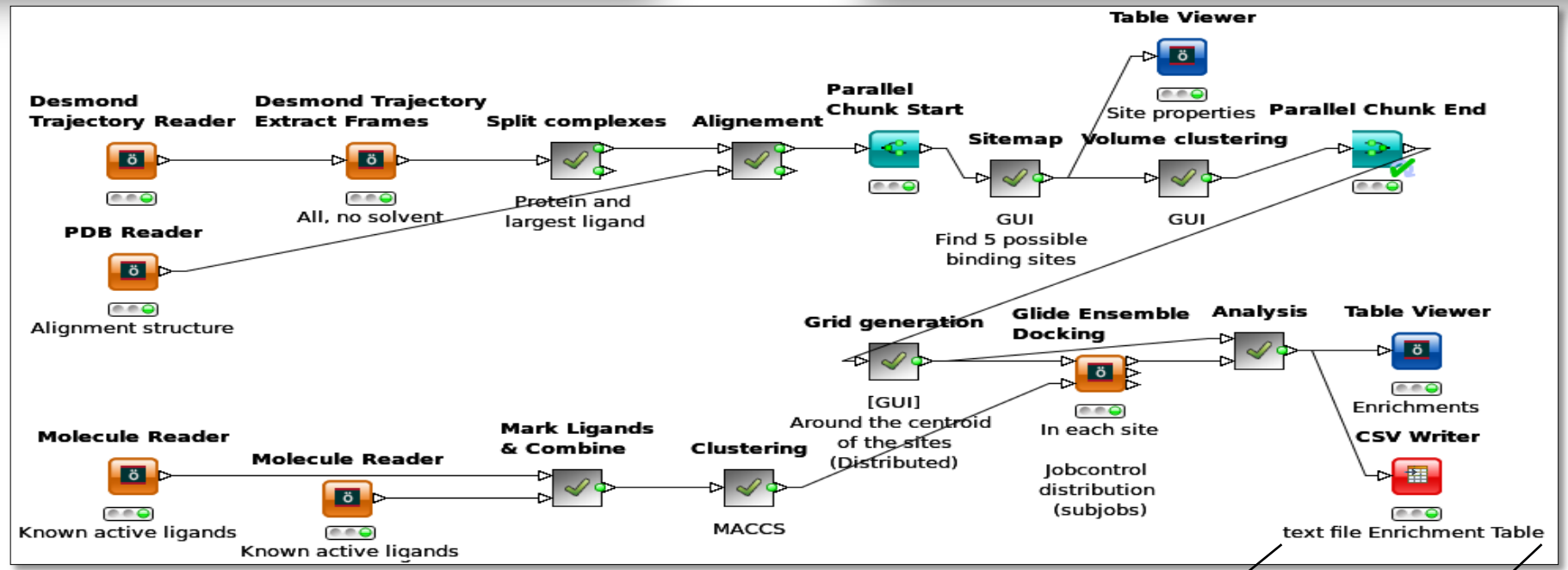
Virtual screening is an important part of computer-aided drug design, with many reviews (1–3) and successful applications reported (4–7) in the literature. Although ligand-based methods have been shown to

THE JOURNAL OF PHYSICAL CHEMISTRY B
Article
pubs.acs.org/JPCB

Exploring Protein Flexibility: Incorporating Structural Ensembles From Crystal Structures and Simulation into Virtual Screening Protocols

David J. Osguthorpe,[†] Woody Sherman,[‡] and Arnold T. Hagler*[,†,§]

[†]Shifa Biomedical, 1 Great Valley Parkway, Suite 8, Malvern, Pennsylvania 19355, United States
[‡]Schrödinger, Inc., 120 West 45th Street, 17th Floor, New York, New York 10036, United States
[§]Department of Chemistry, University of Massachusetts, 701 Lederle Graduate Research Tower, 710 North Pleasant Street, Amherst, Massachusetts 01003-9336, United States



File Hilite Navigation View Output

Row ID	Sitemap	AUC	ef 1%	1%	ef 4%	4%	Sitescore
activ#6	Frame 120_site_1		23.72		8.372		1.175
activ#0	Frame 0_site_1		22.875		9.65		1.244
activ#3	Frame 40_site_1		15.547		9.893		1.219
activ#8	Frame 160_site_5		6.949		3.786		0.636
activ#2	Frame 0_site_4		2.94		0.715		0.878
activ#4	Frame 80_site_3		2.819		1.047		0.66
activ#1	"activ#2" (5/9)		0		0		0.686
activ#5	Frame 80_site_5		0		0.687		0.559
activ#7	Frame 160_site_3		0		1.737		0.794

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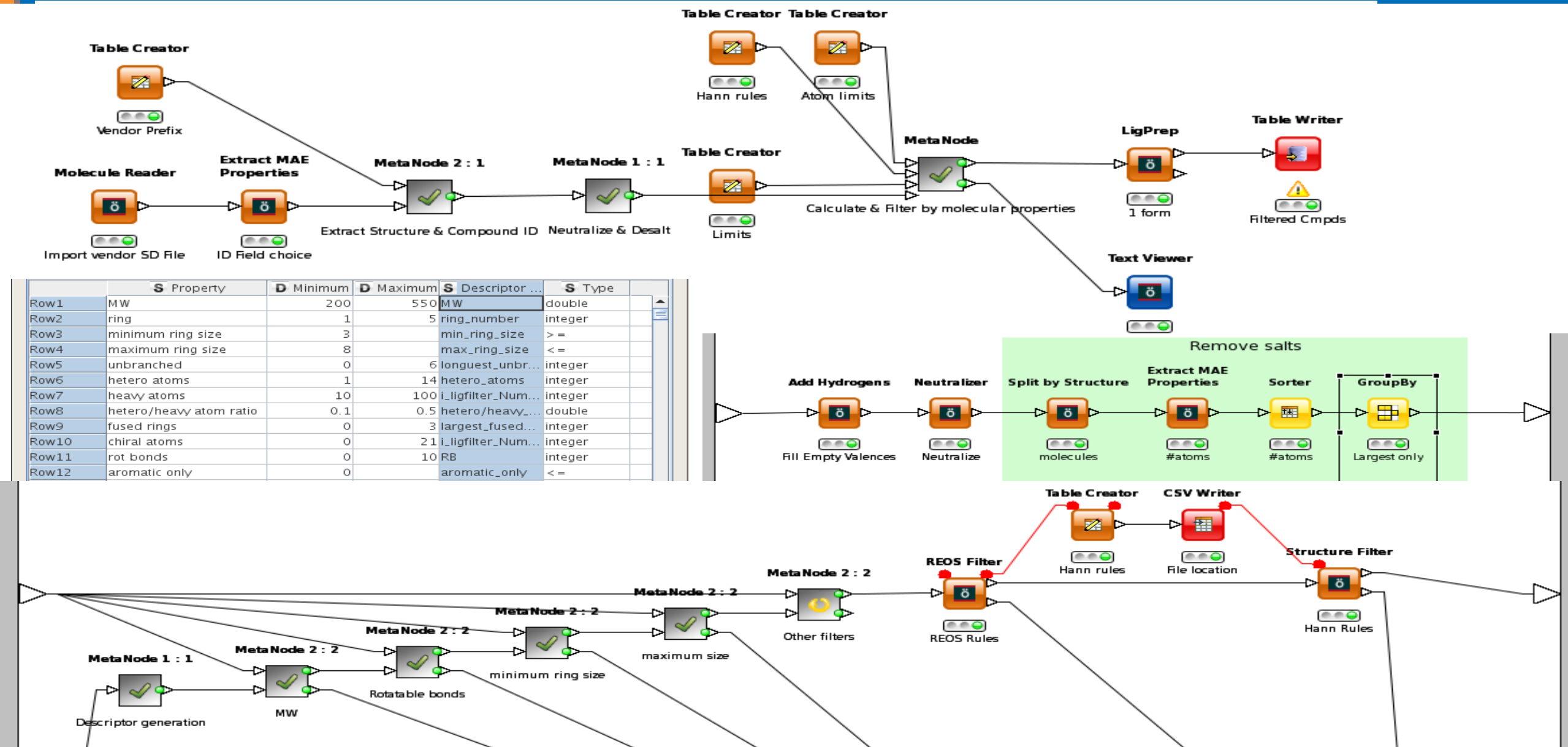
Real life applications...



	S Property	D Minimum	D Maximum	S Descriptor ...	S Type
Row1	MW	200	550	MW	double
Row2	ring	1	5	ring_number	integer
Row3	minimum ring size	3		min_ring_size	>=
Row4	maximum ring size	8		max_ring_size	<=
Row5	unbranched	0	6	longuest_unbr...	integer
Row6	hetero atoms	1	14	hetero_atoms	integer
Row7	heavy atoms	10	100	i_ligfilter_Num...	integer
Row8	hetero/heavy atom ratio	0.1	0.5	hetero/heavy_...	double
Row9	fused rings	0	3	largest_fused...	integer
Row10	chiral atoms	0	21	i_ligfilter_Num...	integer
Row11	rot bonds	0	10	RB	integer
Row12	aromatic only	0		aromatic_only	<=

Workflow example presentation

Feel free to request this other presentation including:

- Simple examples
- More advanced examples from the Workflow page
- Scientifically relevant applications

Schrödinger KNIME Extensions

KNIME Extensions Product Manager: Jean-Christophe Mozziconacci (jcmozzic@schrodinger.com)

Vice President of Technology: Volker Eyrich

Main Developer: Ravikiran Kuppuraj and the PyDev development team

QA: Simon Foucher

Workflow examples: Tanvi Bhola

Technical Support: Katalin Phimister, Pavel Golubkov

Marketing: Jarred Yacob