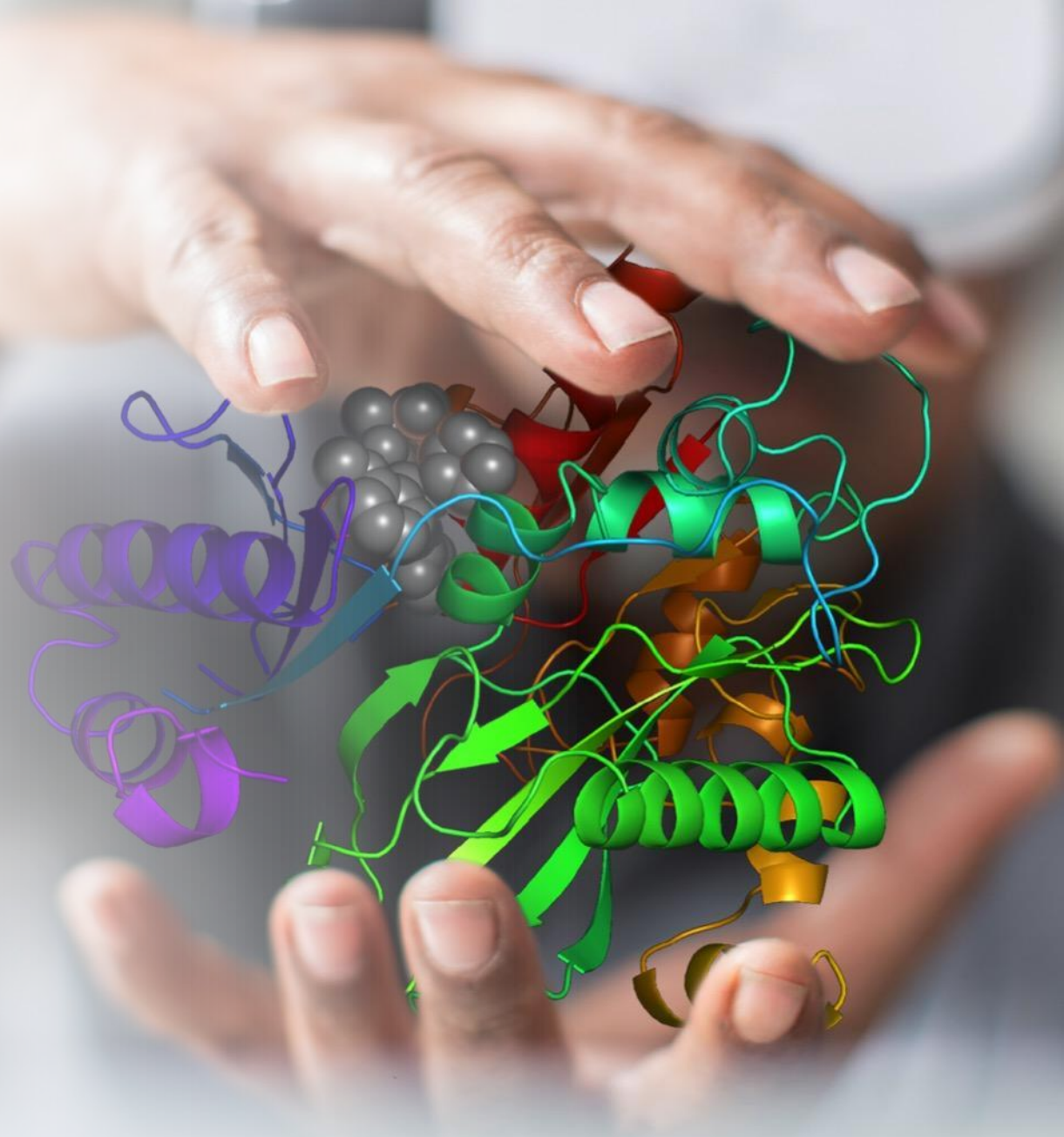
SCHRÖDINGER®

KNIME workflows in LiveDesign

Validated models



Jean-Christophe Mozziconacci

Validated KNIME LiveDesign computational models

A variety of KNIME LiveDesign computational models are available on the KNIME hub and easy to upload to any LiveDesign instance thanks to the Upload as LiveDesign model node. These models will be added to the KNIME folder under the Computational Models section of the Data & Columns tree.

https://hub.knime.com/schroedinger/spaces/LiveDesign_models/latest

- ADME and molecular properties
- Docking
- Ligand preparation and library design
- Miscellaneous
- Plotting
- Protein preparation and refinement
- QSAR
- Run on a KNIME Server
- Structure alignment

Validated KNIME LiveDesign computational models

- **ADME**
  - **ADME:** Calculates some ADME properties with QikProp.
  - **Atropisomerism:** ADME properties are calculated with QikProp.
  - **ESP surface:** Runs a semiempirical calculation to optimize the ligand geometry and generates the ESP surface.
- **Ligand preparation and library design**
  - **Bioisosteres:** Replaces functional groups of each input ligand with bioisosteres, generating all the single replacements.
  - **Low energy conformation:** Reports the lowest energy conformation from a MacroModel conformational search.
  - **Protonation forms:** Generates protonation forms with Epik and adds a new column with the structure of the most probable form.
- **Miscellaneous**
  - **Basic example:** Adds 2 simple columns to the LiveReport.
  - **FEP analysis:** Extracts simulation quality analysis information from a FEP map column.
  - Installation test

Validated KNIME LiveDesign computational models

- **Docking**
  - **Binding pose strain:** Minimizes the binding pose conformation to a local minimum and runs a conformational search to find the global minimum. Calculates the conformation energy difference between the local and the global minima
  - **Docking and ligand strain:** Docks the compounds with Glide, minimizes the binding pose conformation to a local minimum and runs a conformational search to find the global minimum. Calculates the conformation energy difference between the local and the global minima. Aligns the global minimum conformation on the initial binding pose.
  - **Docking and protein surface:** Docks the compounds with Glide. Also generates the protein surface and changes the rendering of the binding site (atoms displayed, residues labelled and the atom representation) to highlight important residues.
  - **Docking and rendering:** Docks the compounds with Glide and changes the rendering of the binding site (atoms displayed, residues labelled and the atom representation) to highlight important residues
  - **Ensemble docking:** Docks the compounds with Glide in 2 binding site conformations and reports the binding site conformation where it scores the best and the corresponding docking pose.

Validated KNIME LiveDesign computational models

- **Plotting**
  - **Ligand CNS desirability plot:** Generates radar plots for the CNS desirability MPO properties.
  - **Ligand CNS desirability range plot:** Generates radar plots of the CNS desirability MPO properties and the number of rotatable bonds with the optimal property range.
  - **Ligand property radar plot:** Plots a set of molecular properties and reports the radar plot generated for each ligand as image in the LiveReport.
- **QSAR**
  - **Random forest:** Runs a pregenerated random forest QSAR model using physicochemical properties generated with QikProp and reports the predictions.
- **Run on a KNIME Server**
  - **Workflow running on a KNIME server:** Runs another workflow remotely on a KNIME server.

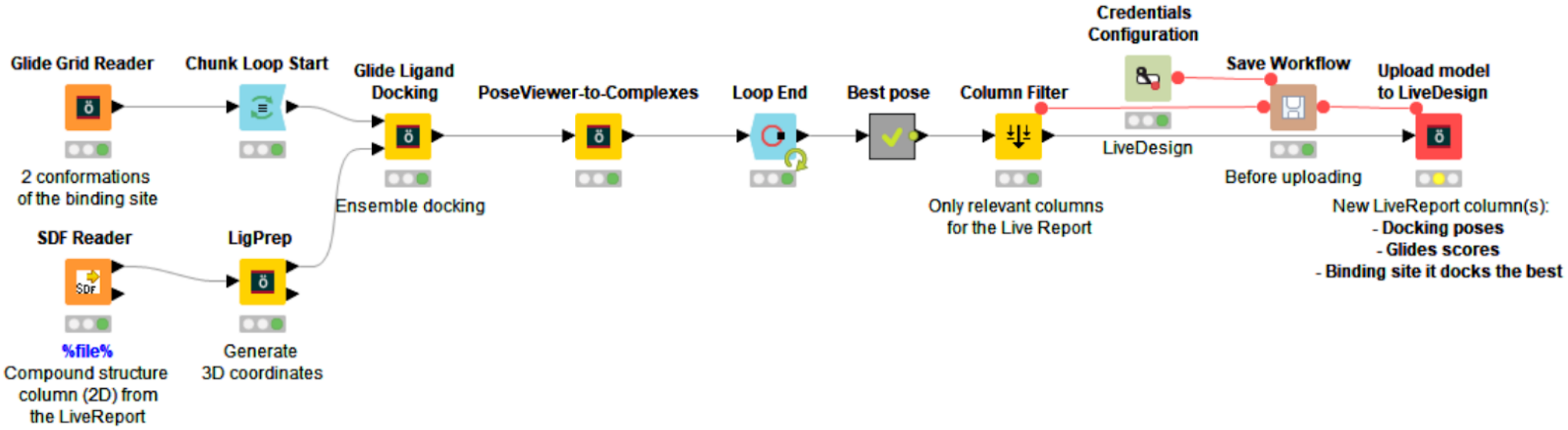
Validated KNIME LiveDesign computational models

- **Protein preparation and refinement**
  - **Cocrystallized ligands:** Prepares the protein-ligand complexes in the selected column from the LiveReport and extracts the ligand structures and list.
  - **Get PDB:** Download the structure for the PDB IDs listed in the selected column from the LiveReport, extract and create new columns with the structures and corresponding structural information.
  - **Get PDB from FFC:** Downloads the structure for the PDB IDs listed in the selected Free Form Column from the LiveReport, extracts and creates new columns with the structures and corresponding structural information.
  - **Get PDB from FFC and preparation:** Downloads the structure for the PDB IDs listed in the selected Free Form Column from the LiveReport, optinoally prepare the structures, extracts and creates new columns with the structures and corresponding structural information.
  - **Related PDB structures:** PDB structures containing ligands similar to each LiveReport structures are listed. The PDB structure with the most similar ligand is prepared and added to a new column in the LiveReport. New columns are also populated with the Ligprepped ligand and its Epik protonation and tautomeric forms.

Validated KNIME LiveDesign computational models

- **Structure alignment**
  - **Alignment on a cocrystallized ligand:** Aligns ligands on a rigid template structure using Shape screening. The template structure file can be changed on the model admin panel. The workflow is uploaded as Computational model in LiveDesign.
  - **Ligand alignment:** Aligns ligands on a template structure using Shape screening.
  - Pharmacophore screening
  - **Installation test:** Runs basic test and installation checking.

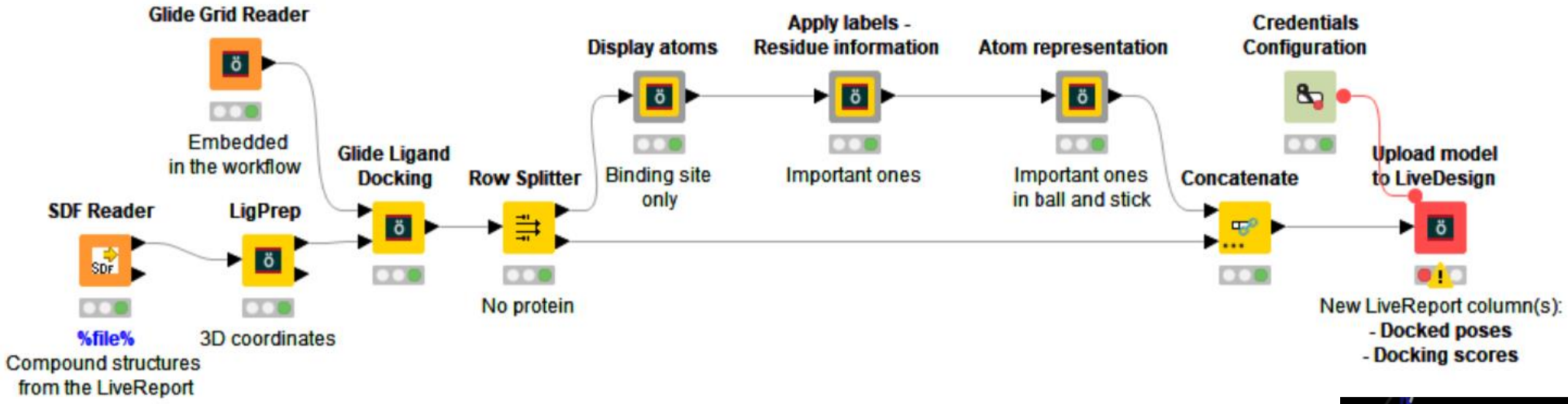
Docking – Ensemble docking

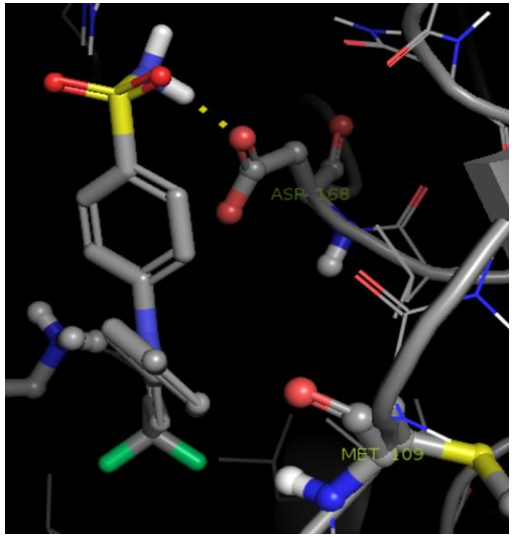


Docks the compounds with Glide in 2 binding site conformations and reports the binding site conformation where it scores the best and the corresponding docking pose.

- Uses “KNIME workflow” generic protocol
- Replace the Glide grid file located in “_Files” folder in the workflow with your grid file or in the Glide grid reader node in KNIME
- Takes Compound structure column as input

Docking – Docking and rendering

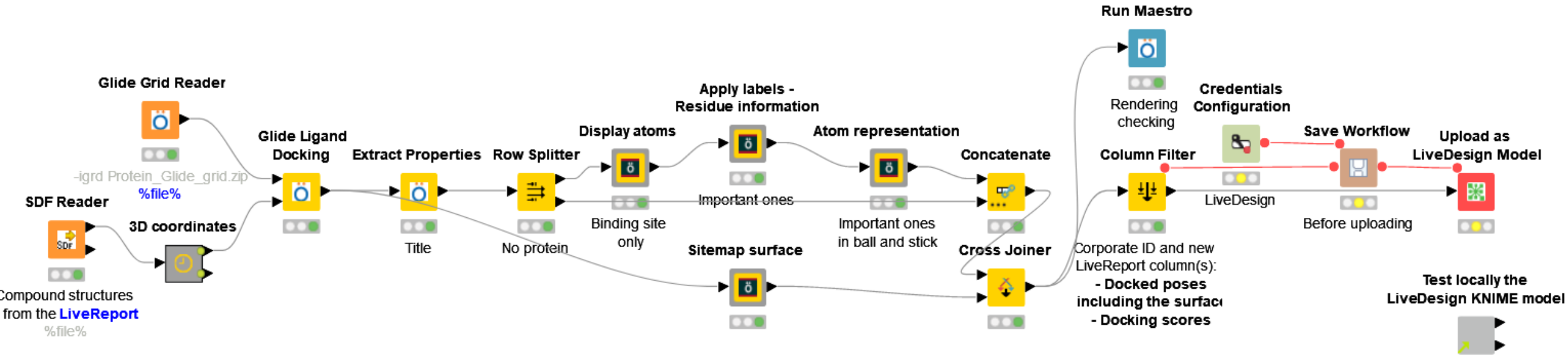




Docks the compounds with Glide and changes the rendering of the binding site (atoms displayed, residues labelled and the atom representation) to highlight important residues.

- Uses “KNIME workflow” generic protocol
- Takes Compound structure column as input
- New LiveReport column(s):
  - Docked poses
  - Glide scores
- Replace the Glide grid file located in “_Files” folder in the workflow with your grid file.

Docking – Docking and protein surface

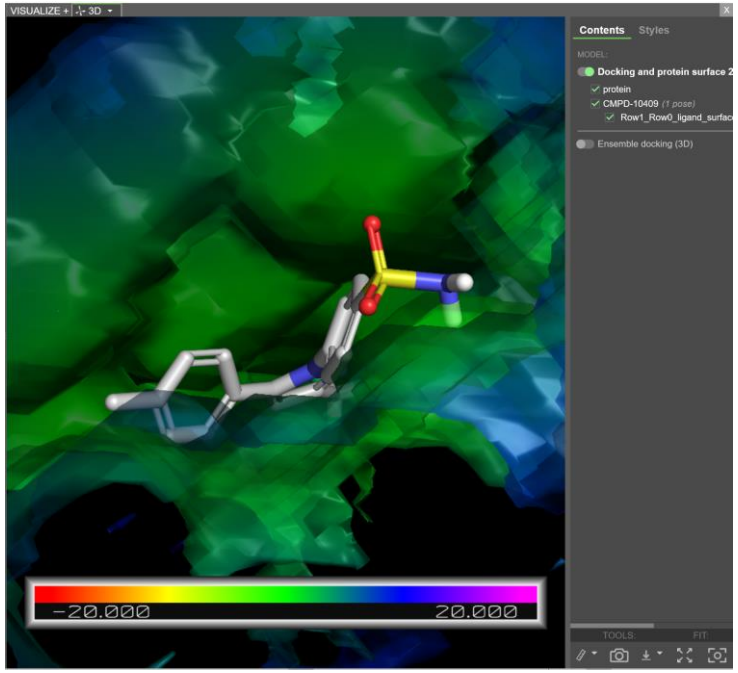


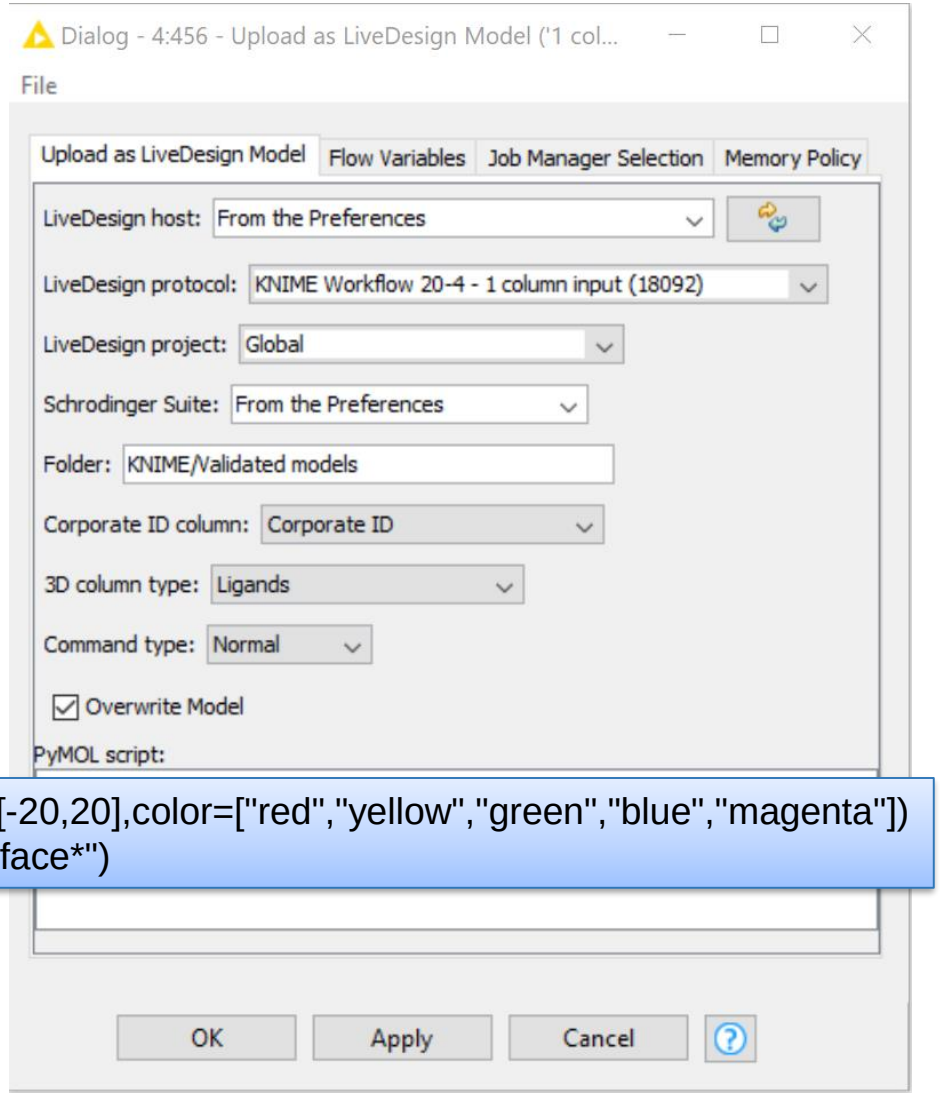
Docks the compounds with Glide and generates the protein surface.

- Uses “KNIME workflow” generic protocol
- The Glide grid can be changed from the Admin page
- Takes Compound structure column as input and creates the following new LiveReport column(s):
  - Docked poses including the surface
  - Docking scores

Docking – Docking and protein surface

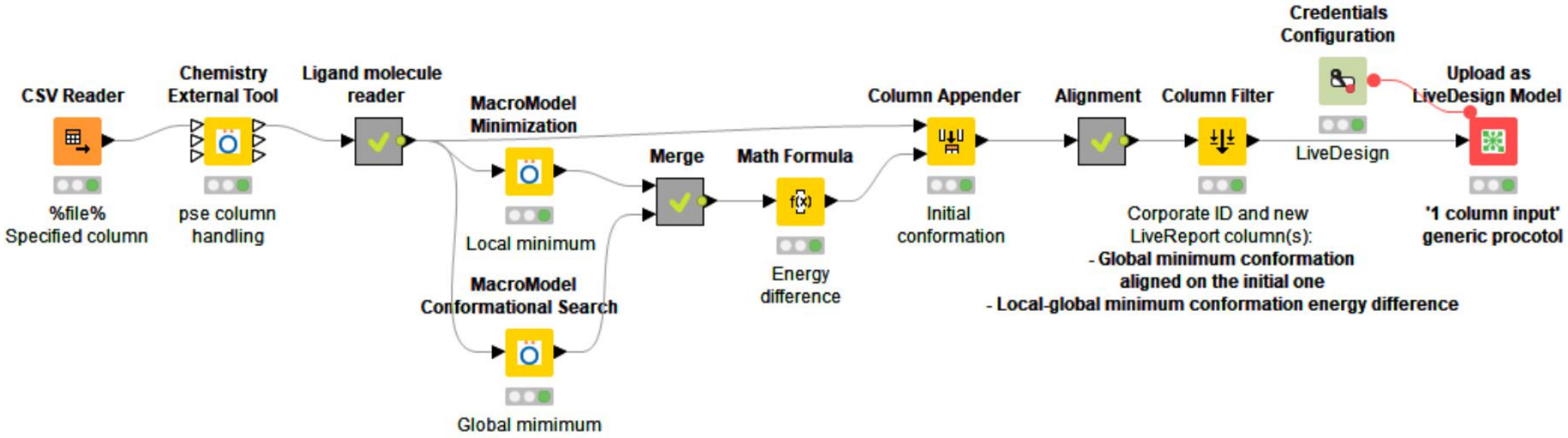
- PyMOL script section to control the surface rendering





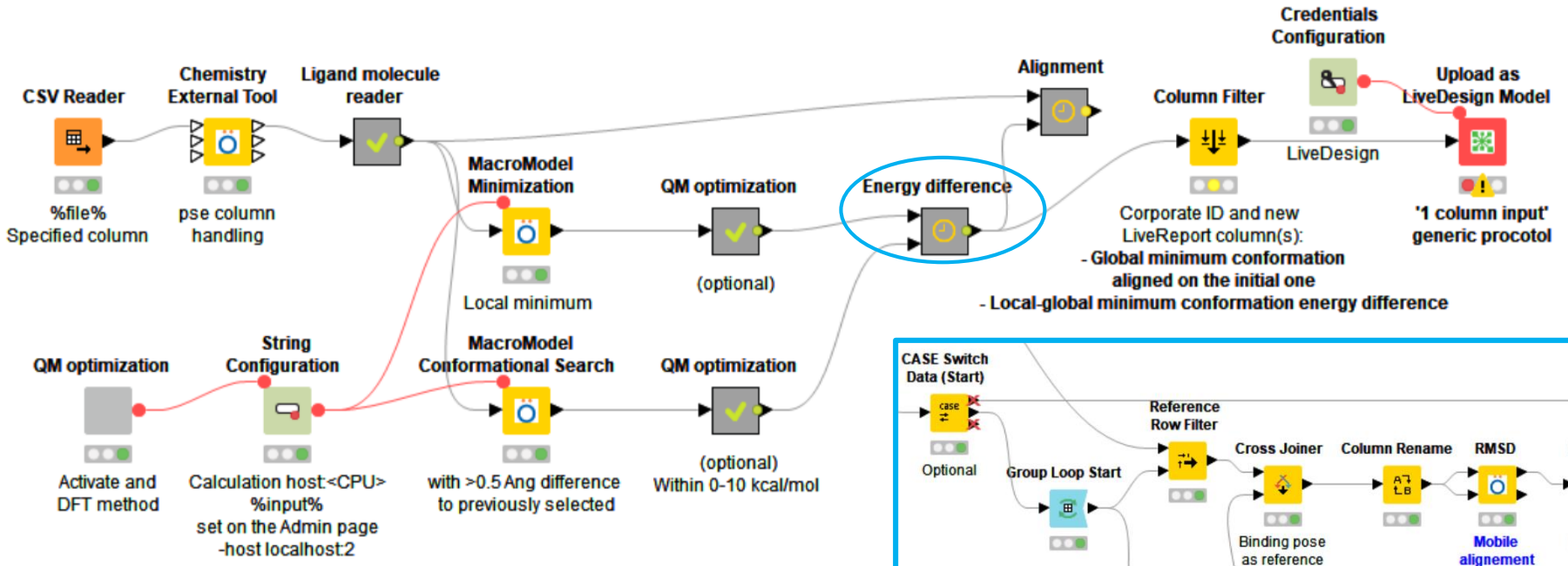

```
cmd.ramp_new("surf","CT",range=[-20,20],color=["red","yellow","green","blue","magenta"])
cmd.set("surface_color","surf","Surface*")
```

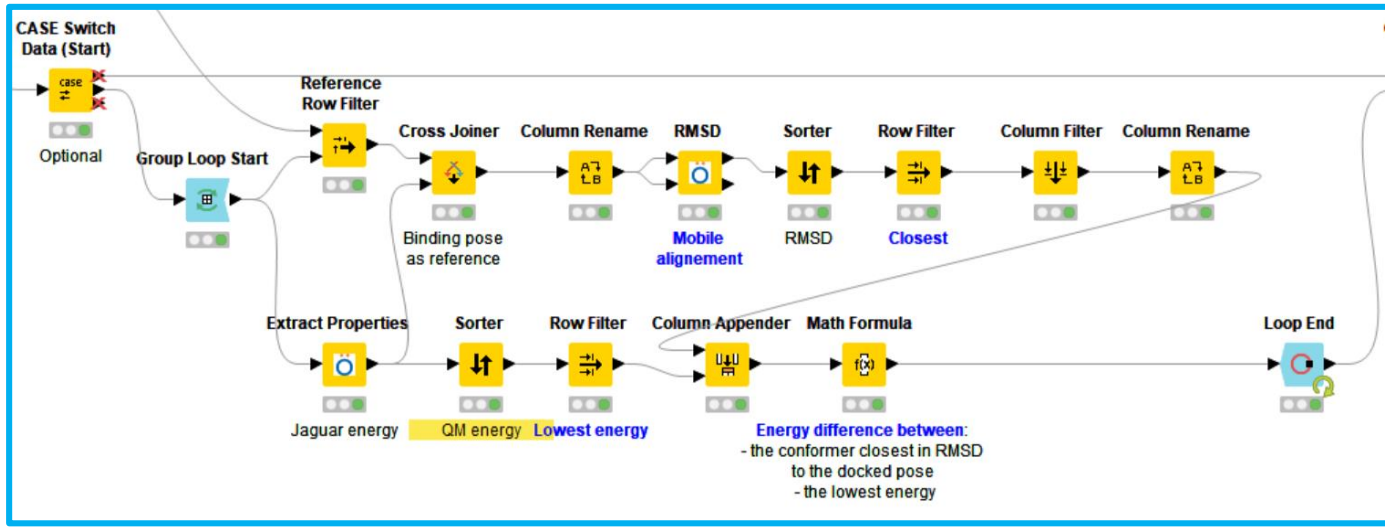
Docking – Binding pose strain



- Minimizes the binding pose conformation to a local minimum and runs a conformational search to find the global minimum. Calculates the conformation energy difference between the local and the global minima
- Takes a Pose Viewer 3D column as input
- New LiveReport column(s):
  - Global minimum conformation aligned on the initial one
  - Local-global minimum conformation energy difference

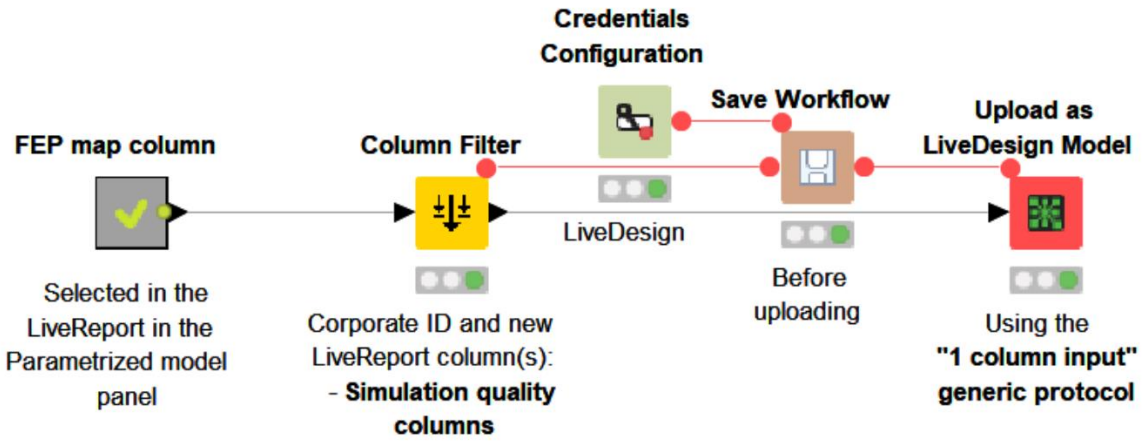
Docking – Binding pose QM strain





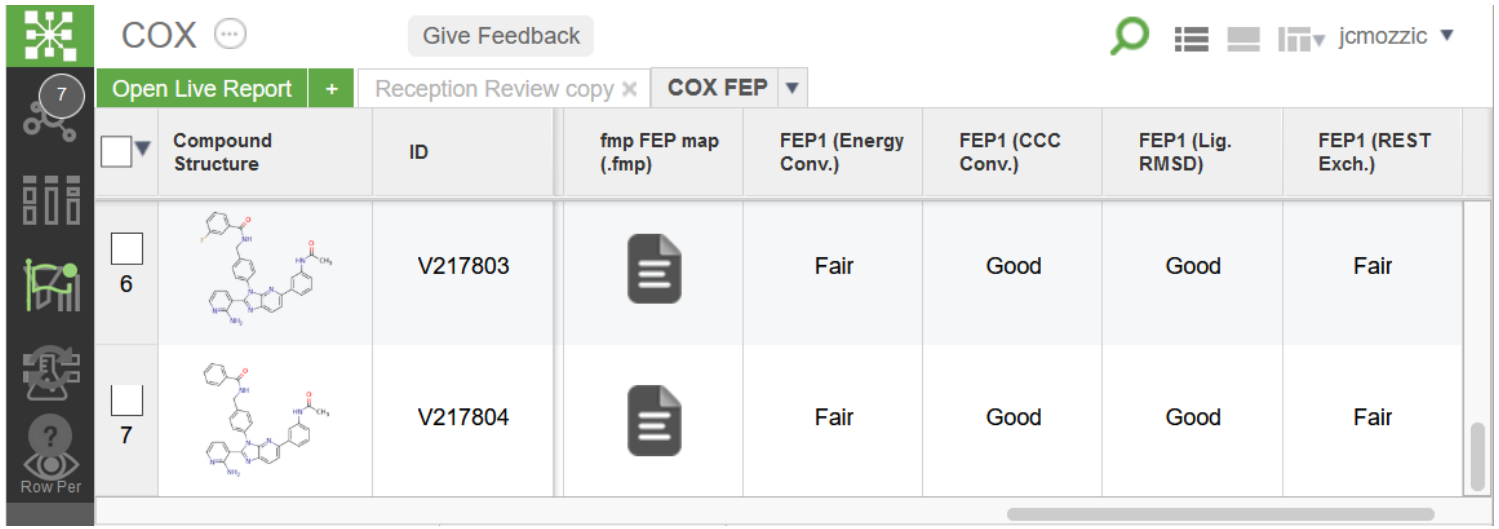
- Takes a Pose Viewer 3D column as input
- New LiveReport column(s):
  - Global minimum conformation aligned on the binding pose
  - Conformation energy difference between
    - the conformer closest in RMSD to the docked pose
    - the lowest energy

Miscellaneous – FEP analysis

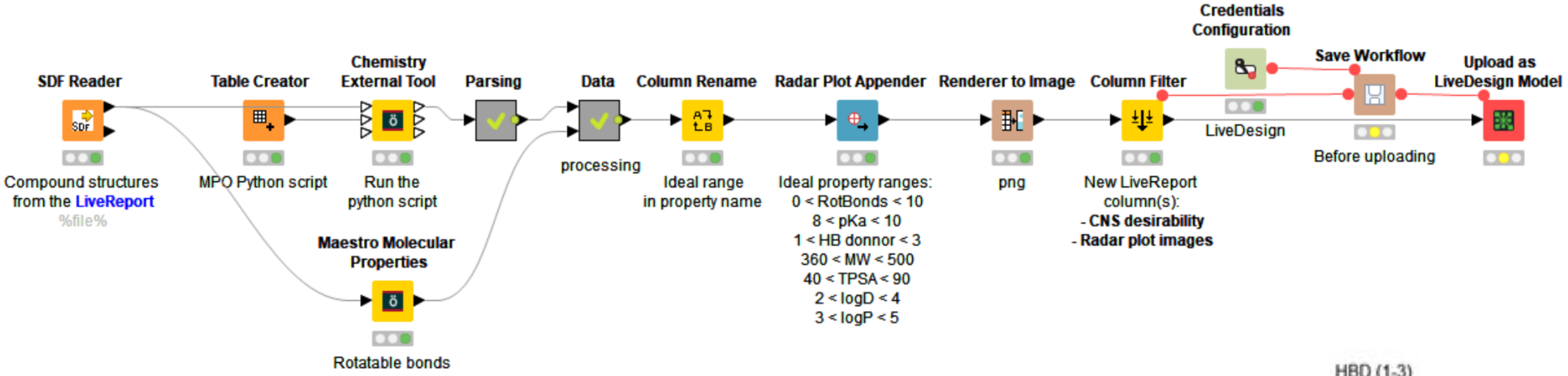


Extracts simulation quality analysis information from a FEP map column.

- Uses “KNIME workflow – 1 input column” generic protocol
- Takes a FEP+ map column as input
- New LiveReport column(s):
  - Energy convergence
  - CCC convergence
  - Ligand RMSD
  - REST exchange

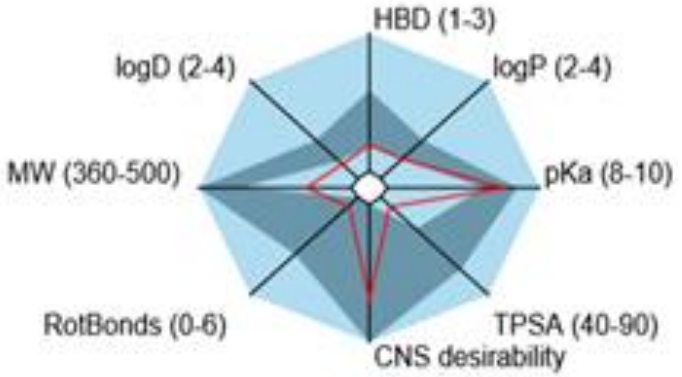


Plotting – CNS desirability radar range plot

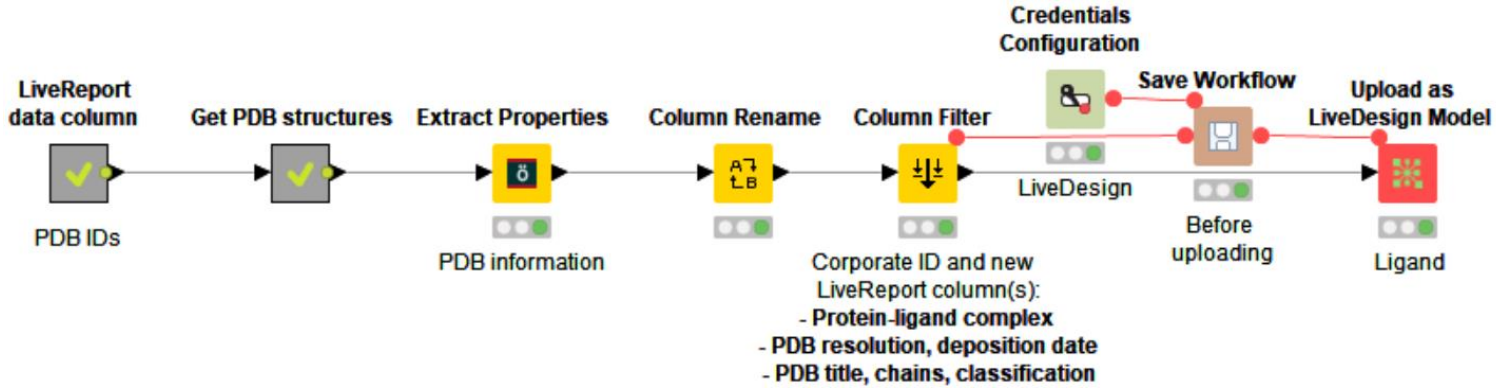


Generates radar plots of the CNS desirability MPO properties and the number of rotatable bonds along with the optimal property ranges.

- Takes the Compound structure column as input
- New LiveReport column(s):
  - Radar plot image
- Uses “KNIME workflow” generic protocol
- The mode and overview are available here on the KNIME hub



Protein preparation and refinement – Get PDB



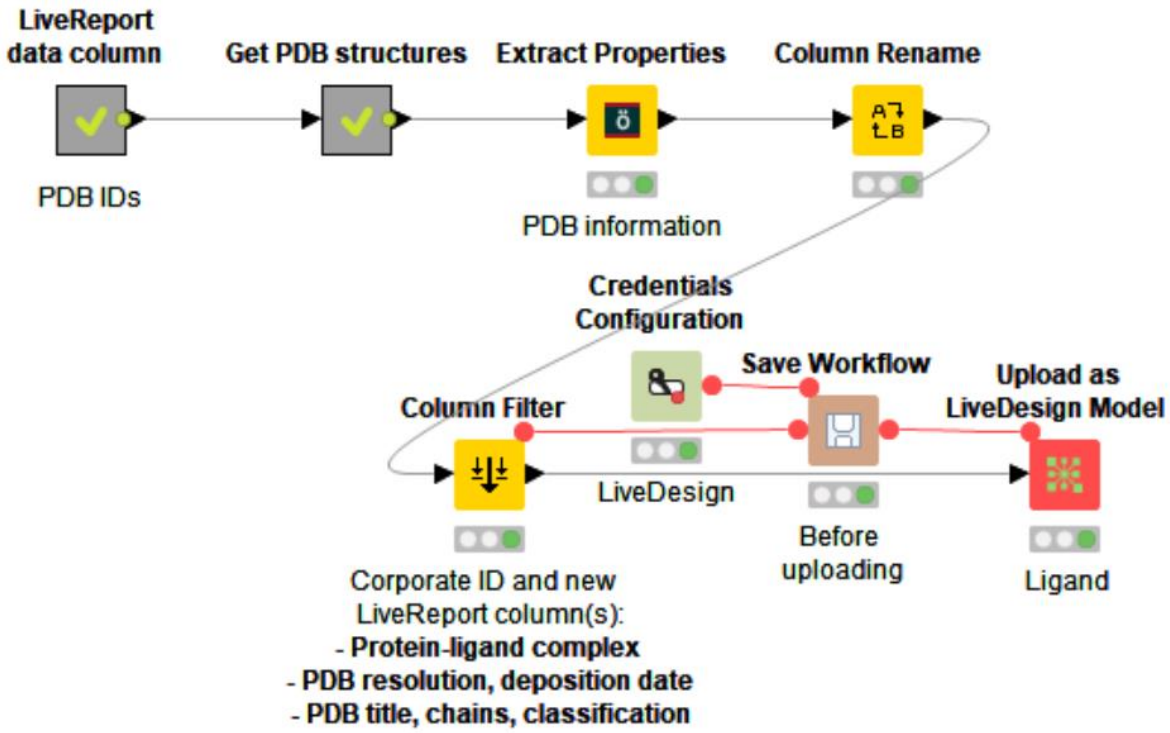
Downloads the structure for the PDB IDs listed in the selected column from the LiveReport, extracts and creates new columns with the structures and corresponding structural information.

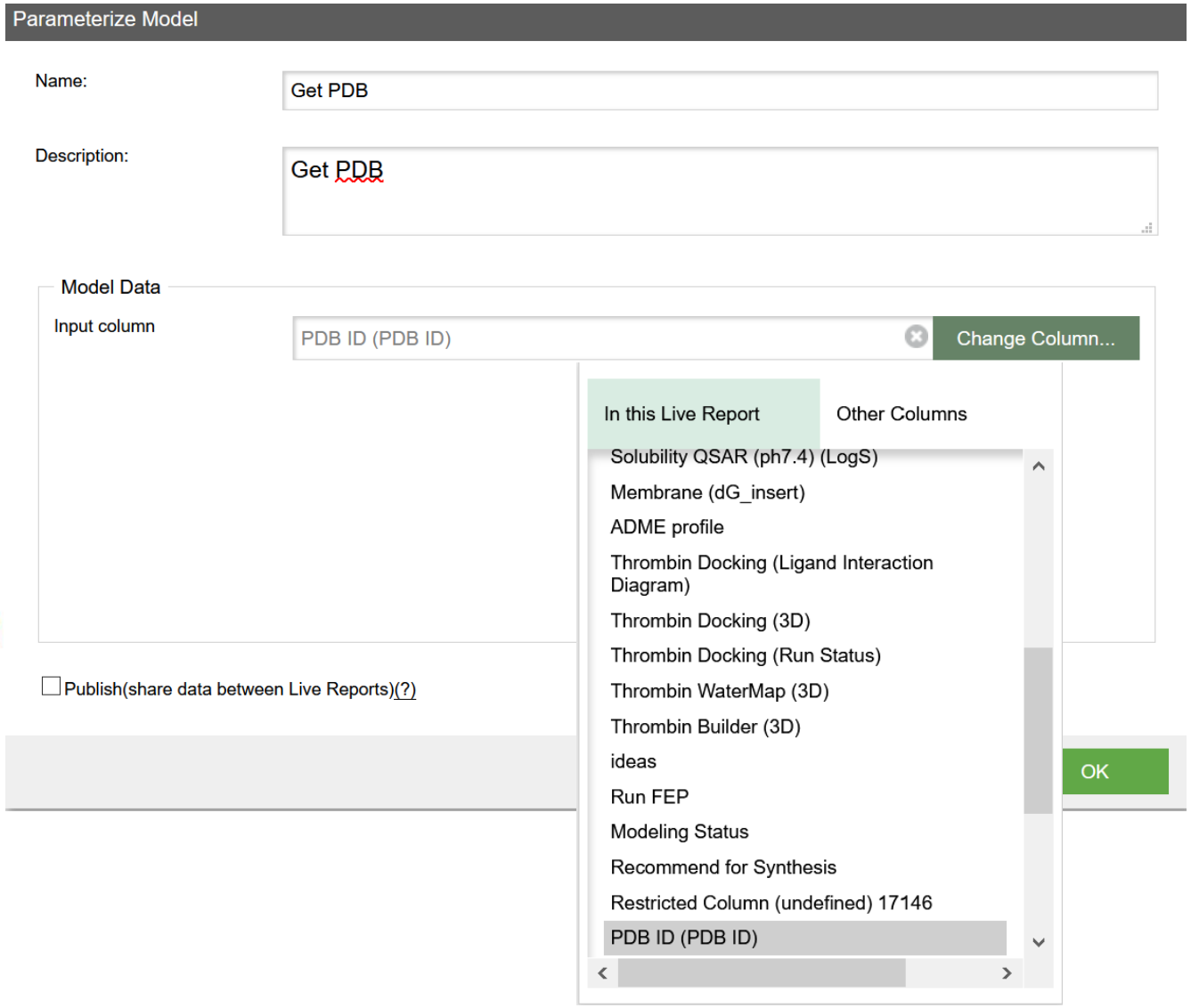
- Uses “KNIME workflow – 1 input column” generic protocol
- Takes a text column with PDB IDs as input
- New LiveReport column(s):
  - Protein-ligand complexes
  - PDB resolution, deposition date
  - PDB title, chains, classification

PDB ID (PDB ID)	FFC	Get PDB (PDB classification)	Get PDB (3D)	Get PDB (Deposition date)	Get PDB (PDB title)	Get PDB (Chain list)	Get PDB (Resolution)
1TBF 1TBF	1ETR	HYDROLASE		20-MAY-04	CATALYTIC DOMAIN OF HUMAN PHOSPHODIESTERASE 5A IN COMPLEX WITH SILDENAFIL	A	1.3

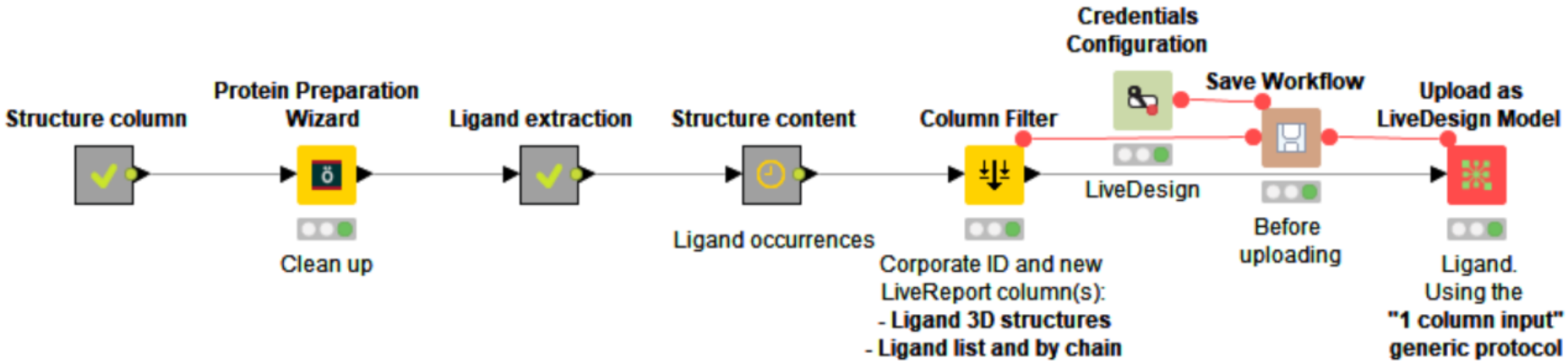
Protein preparation and refinement – Get PDB

- Select the PDB ID column from the LiveReport





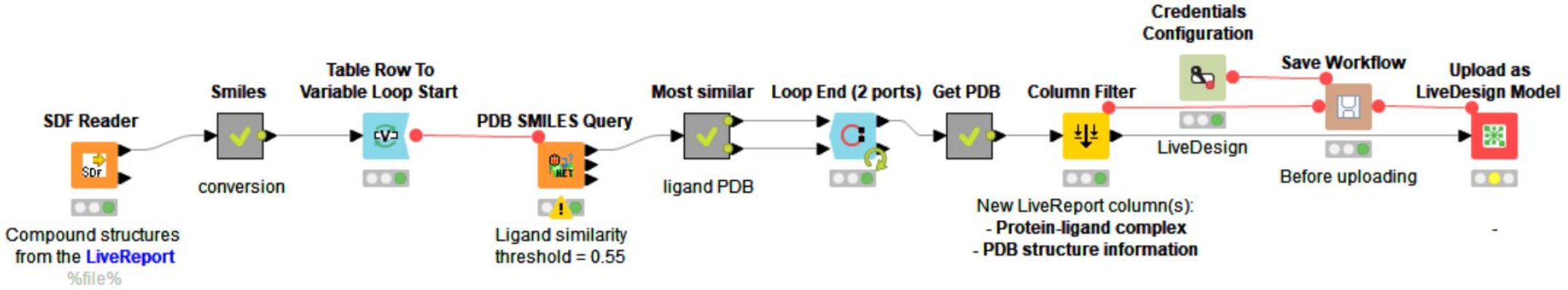
Protein preparation and refinement – Cocrystallized ligands



Prepares the protein-ligand complexes in the selected column from the LiveReport and extracts the ligand structures and list.

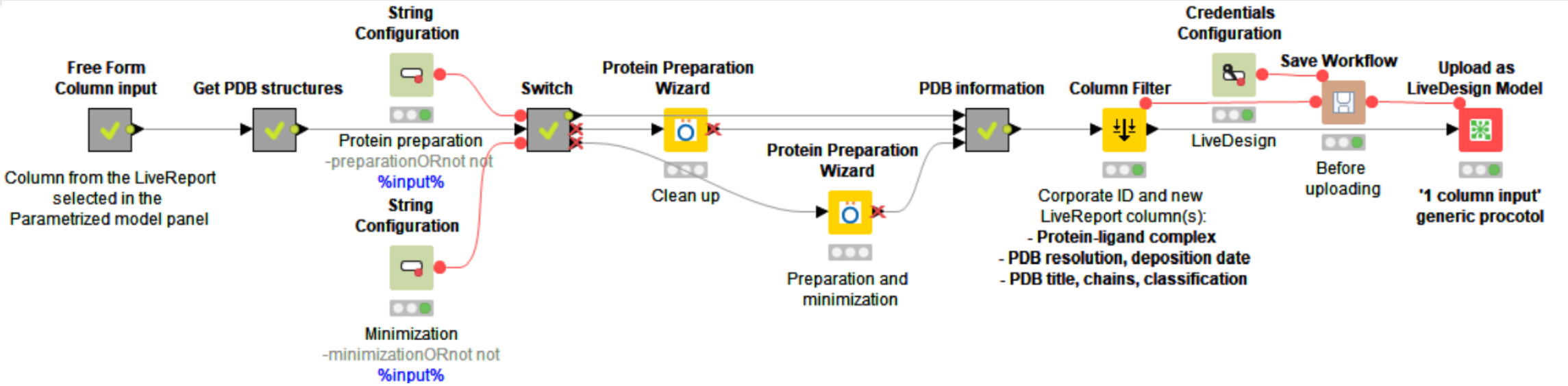
- Uses “KNIME workflow – 1 input column” generic protocol
- Takes a 3D structure column with protein-ligand complexes as input and add the New LiveReport columns:
  - Ligand 3D structures
  - Ligand list and list by chain

Protein preparation and refinement – Related PDB structures



- Requires a Vernalis node

Protein preparation and refinement – Get PDB from FFC and preparation

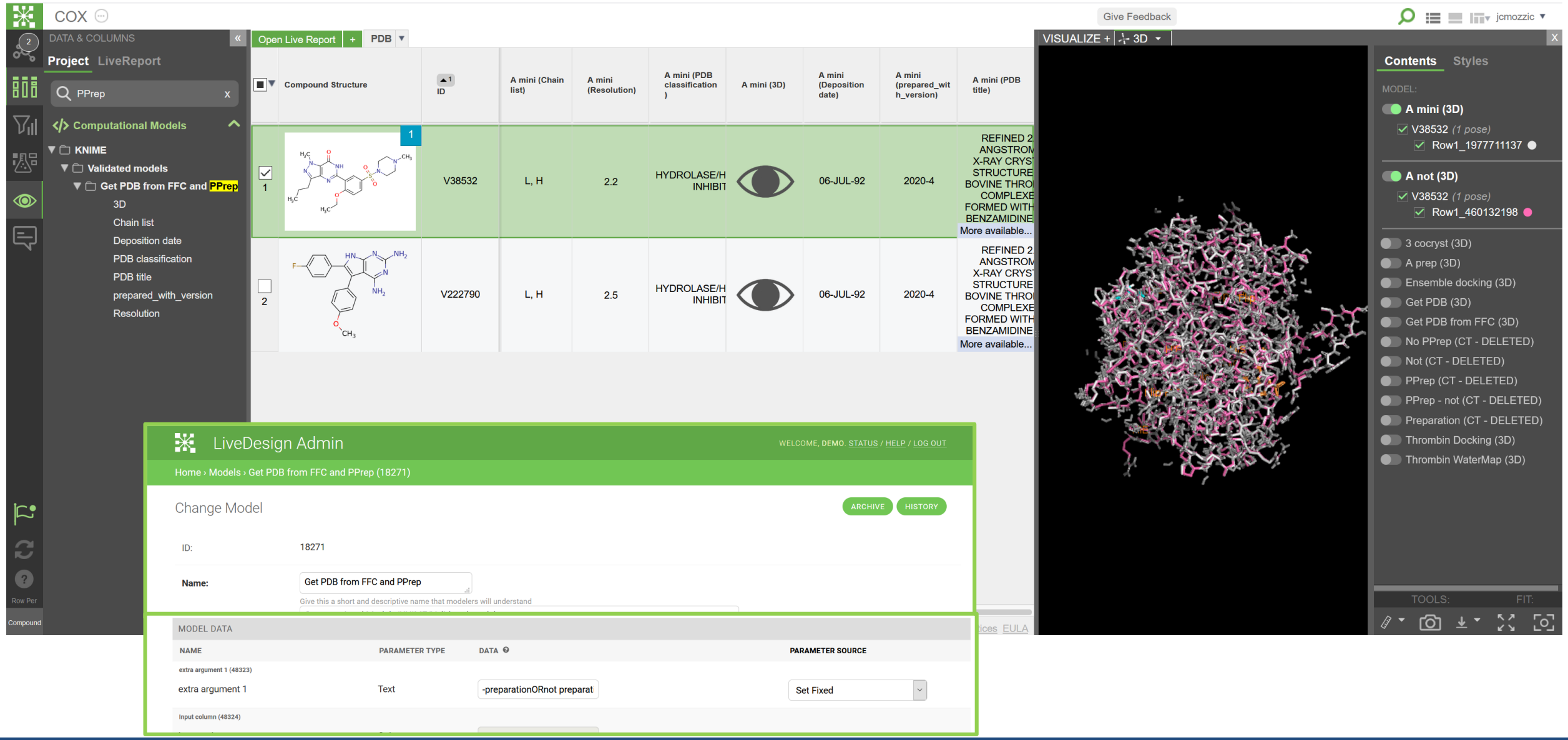


- Uses “KNIME workflow – 1 input column” generic protocol
- The Preparation and minimization can be un/disabled from the Admin page

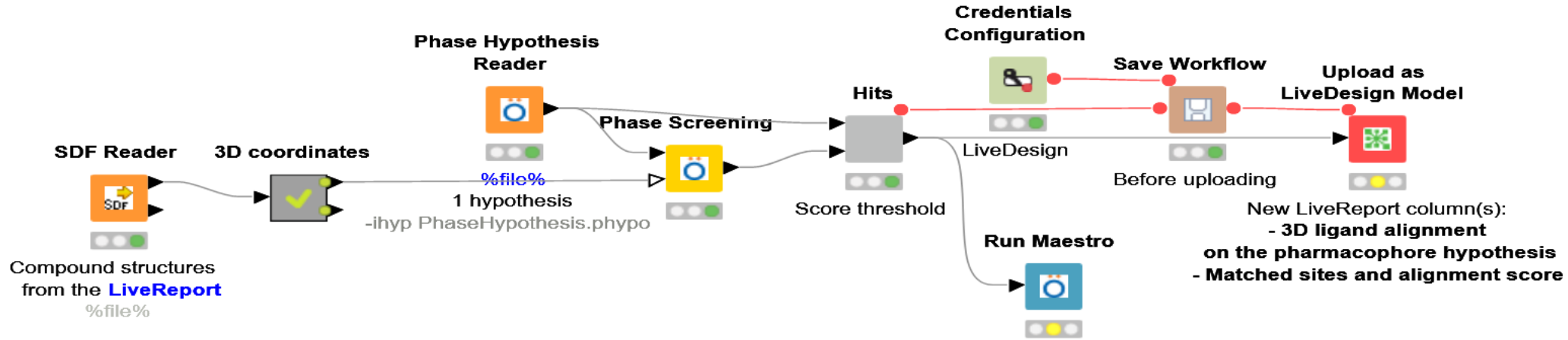
MODEL DATA

NAME	PARAMETER TYPE	DATA
extra argument 1 (48323)		
extra argument 1	Text	-preparationORnot preparati

Protein preparation and refinement – Get PDB from FFC and preparation



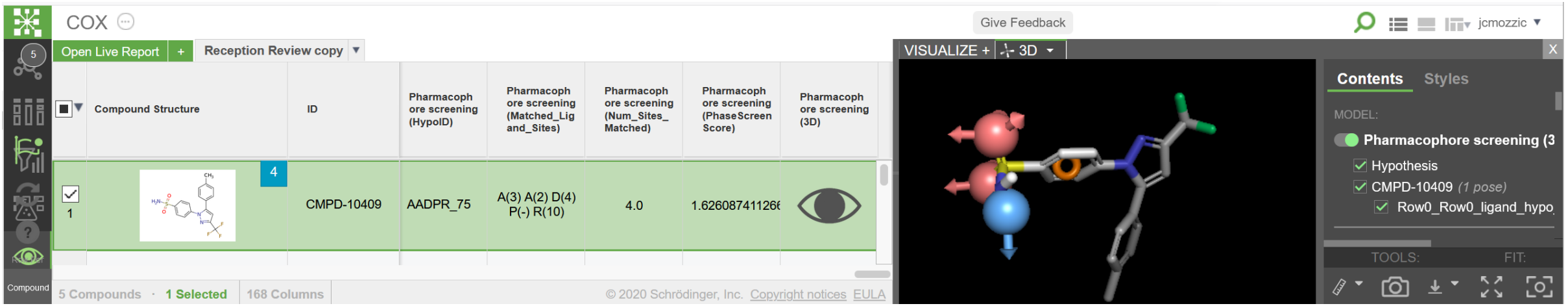
Alignment – Pharmacophore screening



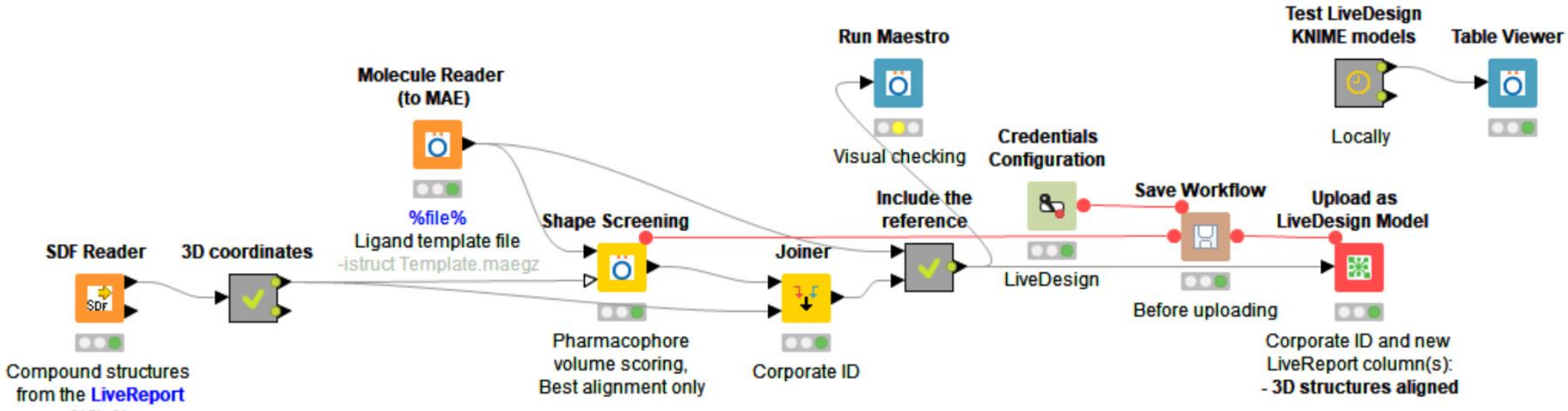
- Screens the LiveReport ligands against a pharmacophore hypothesis.
- It takes the Compound structures as input and adds as new LiveReport columns:
  - The structures aligned on the pharmacophore features
  - The matched site list
  - The alignment score
- The Pharmacophore query file can be changed from the Admin page

Alignment – Pharmacophore screening

- Uses “KNIME workflow” generic protocol



Alignment - Alignment on a cocrystallized ligand



- Aligns ligands on a rigid template structure using Shape screening. The template structure file can be changed on the model admin panel. The workflow is uploaded as Computational model in LiveDesign.
- Takes the Compound structure column as input and creates the following new LiveReport column(s):
  - 3D structures aligned
- Uses “KNIME workflow” generic protocol
- The template file can be changed on the Admin page