



KNIME in LiveDesign

Deploy easily computational methods to the medicinal chemists

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KNIME LiveDesign models

- Address needs for LiveDesign computational models
 - Validated models based on KNIME workflows
 - Available for download and may be easy to adapt to similar needs
 - Growing set of workflows and developed on request
 - Possibly simpler/faster than a python script
- Deployment to LiveDesign
 - From KNIME
 - With a python script
 - No KNIME installation required. No need to open the admin page
 - Simple for modelers and Solution Architects
- Computational model execution
 - Same look and feel (KNIME run behind the scene on the LiveDesign host)
- Customization
 - On LiveDesign Admin page (eg replace system specific files, parametrize model)
- Model change and improvements
 - 1 click to update the model from KNIME

The screenshot displays the KNIME Hub interface for the 'Random forest - to be run in LiveDesign' workflow. The top navigation bar includes the KNIME logo and the Schrodinger logo. The breadcrumb trail reads: KNIME Hub > schrodinger > Spaces > Public > LiveDesign_models. Below this, a table lists the workflow details:

Type	Name
Workflow	Random forest - to be run in LiveDesign

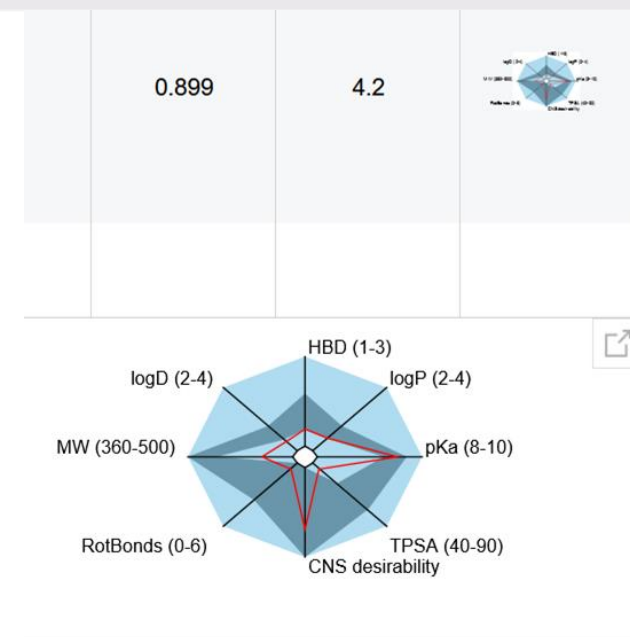
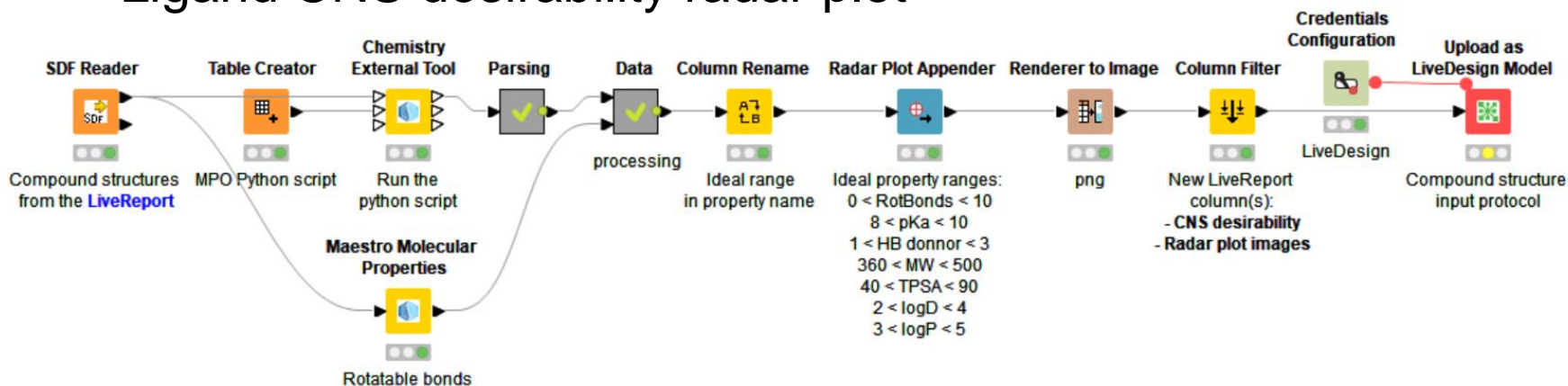
The main content area shows a detailed view of the workflow. The workflow diagram includes nodes such as SDF Reader, LigProp, QikProp, Extract Properties, Random Forest Predictor (Regression), Column Filter, LiveDesign testing, and Upload model to LiveDesign. A description below the diagram states: 'Random forest : Runs a pregenerated random forest QSAR model using physicochemical properties generated with QikProp and reports the predictions. The workflow is uploaded as Computational model in LiveDesign.'

On the right side, there is a list of related workflows, each with a download icon:

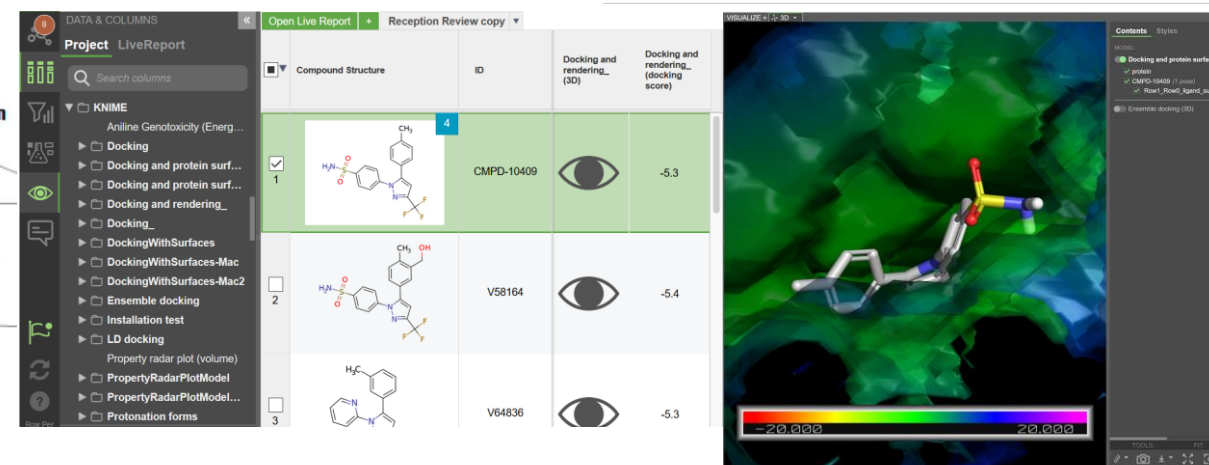
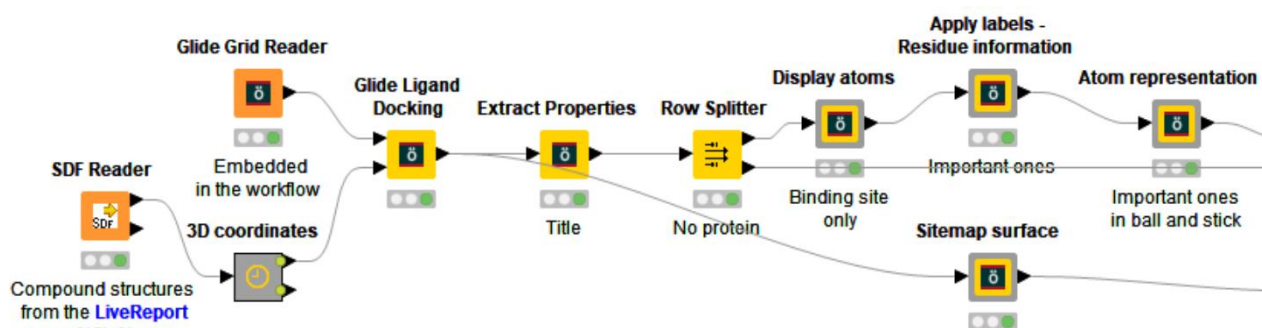
- Installation test
- Ligand alignment
- Ligand property radar plot
- Low energy conformation
- My workflow running on a KNIME server
- Protonation forms
- Random forest

KNIME LiveDesign model examples

- Ligand CNS desirability radar plot



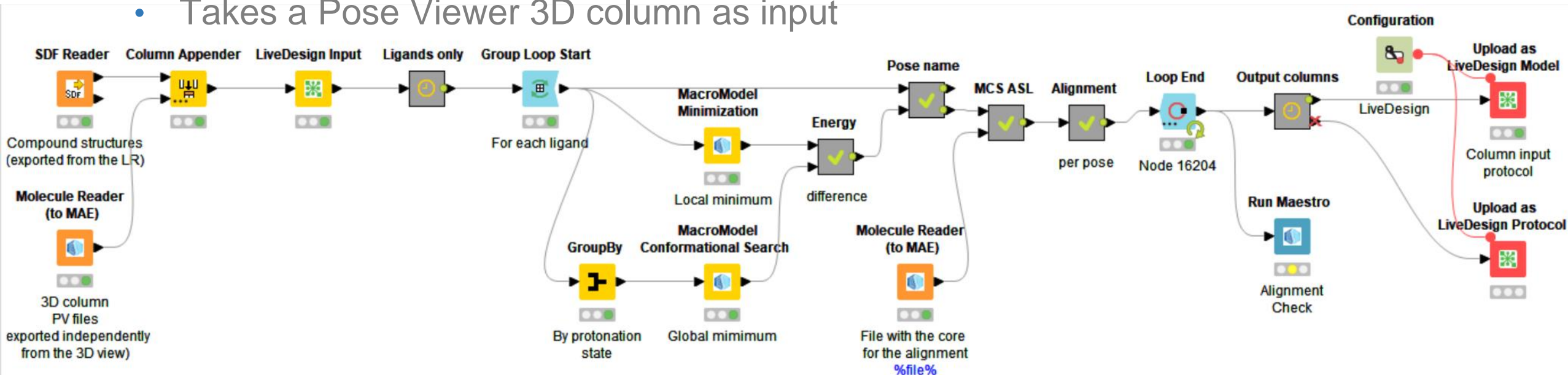
- Docking and protein surface

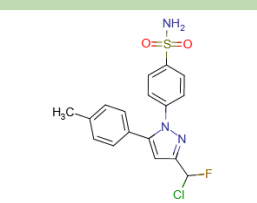
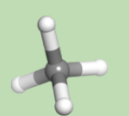


- Find more on: https://hub.knime.com/schroedinger/spaces/LiveDesign_models/latest/

KNIME LiveDesign model examples

- Binding pose strain
 - Takes a Pose Viewer 3D column as input



Compound Structure	ID	npl	Binding pose strain - dedicated protocol (3D)	Binding pose strain - dedicated protocol (Energy difference)
	V181360			2.4

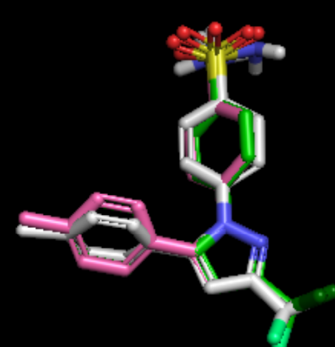
Contents **Styles**

MODEL:

- ☒ Binding pose strain - de
- ☒ V181360 (3 poses)
- ☒ binding_pose_1
- ☒ local_minimum_1
- ☒ global_minimum_1

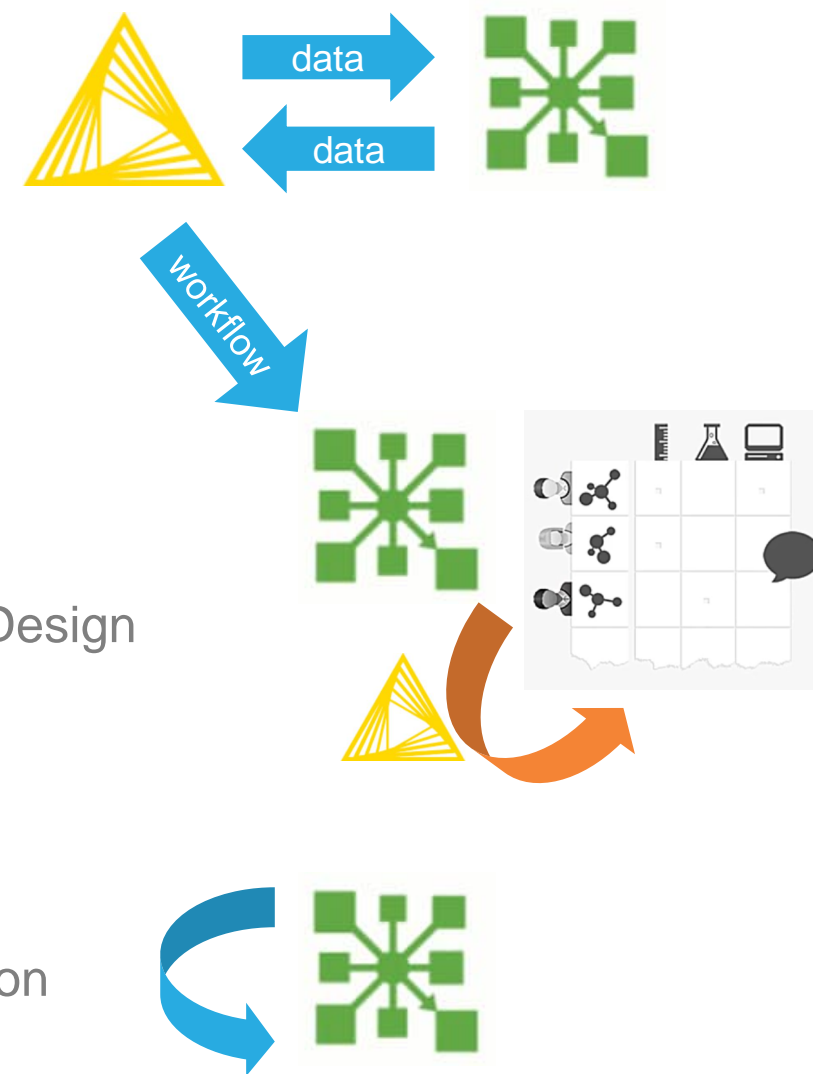
1 (3D)

1 (3D)



LiveDesign Nodes in KNIME

- Import from LiveDesign
 - Populates a KNIME table with data from a LiveReport
 - Same configuration panel as Maestro
- Export to LiveDesign
 - Sends data from a KNIME table to a LiveReport
- Export images to LiveDesign
 - PNG or SVG images stored in Free Form Columns
- Upload a workflow as LiveDesign model or protocol
 - **Creates a model** which executes the KNIME workflow in LiveDesign (no need to open the LiveDesign administration panel)
 - The model is now ready to be **run in any LiveReport** and the output will be added as new columns
- Administrate LiveDesign models and protocols
 - eg backup copies, testing copies, copy from testing to production instance, new version deployment, version comparison
- List LiveDesign models and protocols



KNIME workflow uploaded as models in LiveDesign

DATA & COLUMNS

Project LiveReport

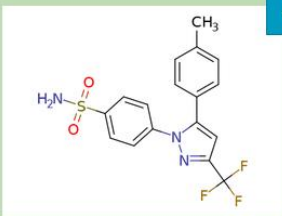

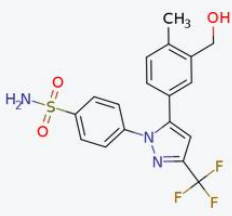

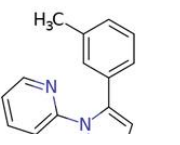

Search columns

KNIME

Aniline Genotoxicity (Energy...)

- ▶ Docking
- ▶ Docking and protein surf...
- ▶ Docking and protein surf...
- ▶ Docking and rendering_
- ▶ Docking_
- ▶ DockingWithSurfaces
- ▶ DockingWithSurfaces-Mac
- ▶ DockingWithSurfaces-Mac2
- ▶ Ensemble docking
- ▶ Installation test
- ▶ LD docking
- Property radar plot (volume)
- ▶ PropertyRadarPlotModel
- ▶ PropertyRadarPlotModel...
- ▶ Protonation forms

Open Live Report + Reception Review copy

	Compound Structure	ID	Docking and rendering_ (3D)	Docking and rendering_ (docking score)
1		CMPD-10409		-5.3
2		V58164		-5.4
3		V64836		-5.3

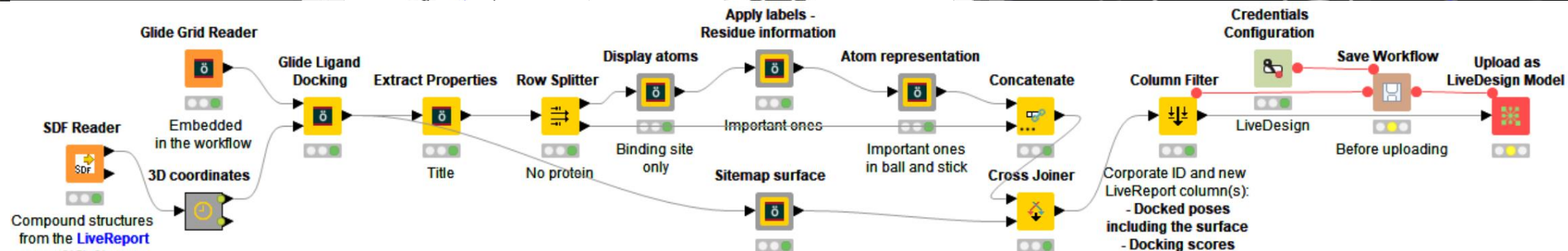
Visualize + 3D

Contents

- ☐ COX1 (3D)
- ☐ COX2 (3D)
- ☐ Docking (3D)
- ☐ Docking and protein ...
- ☐ Docking and protein ...
- ☒ Docking and renderin...
- ☒ protein
- ☒ CMPD-10409
- + 1 pose
- ☐ DockingWithSurface...
- ☐ Docking_ (3D)
- ☐ Ensemble docking (3D)

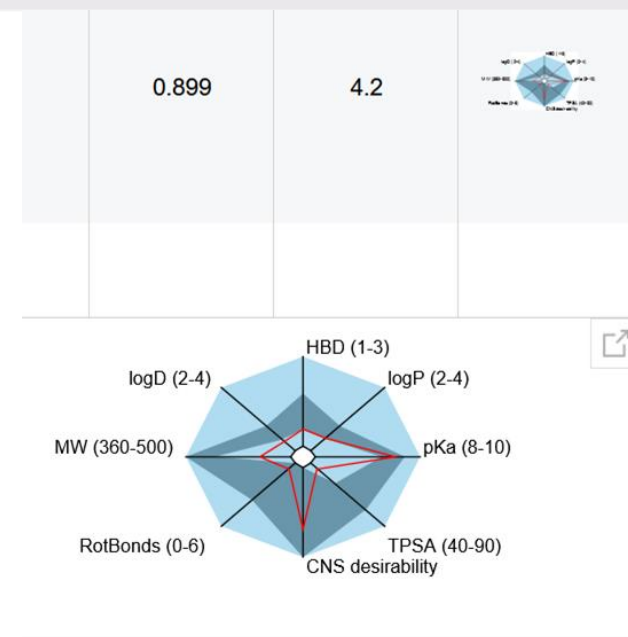
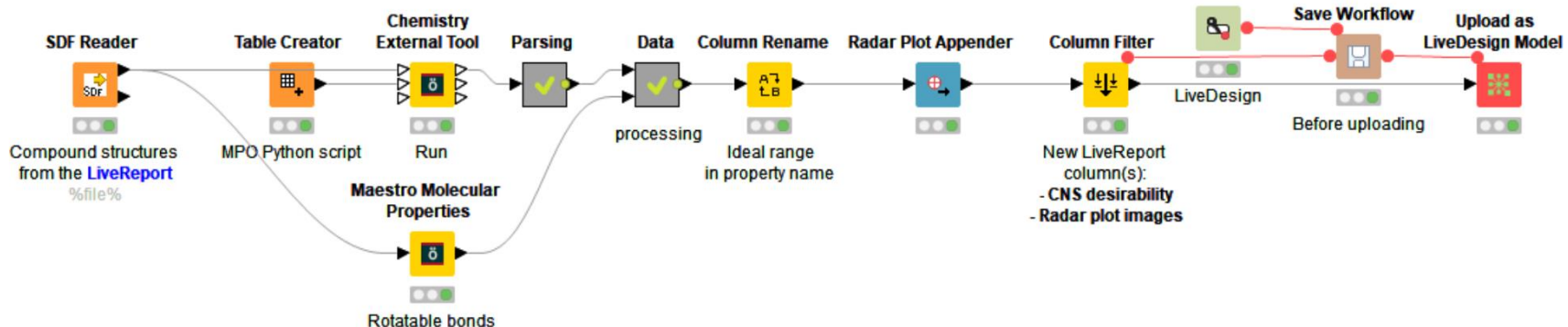
+

Add 3D models to visualize selected compounds: Click here, then browse or search for any models containing the word '(3D)' in the list that appears on the left.

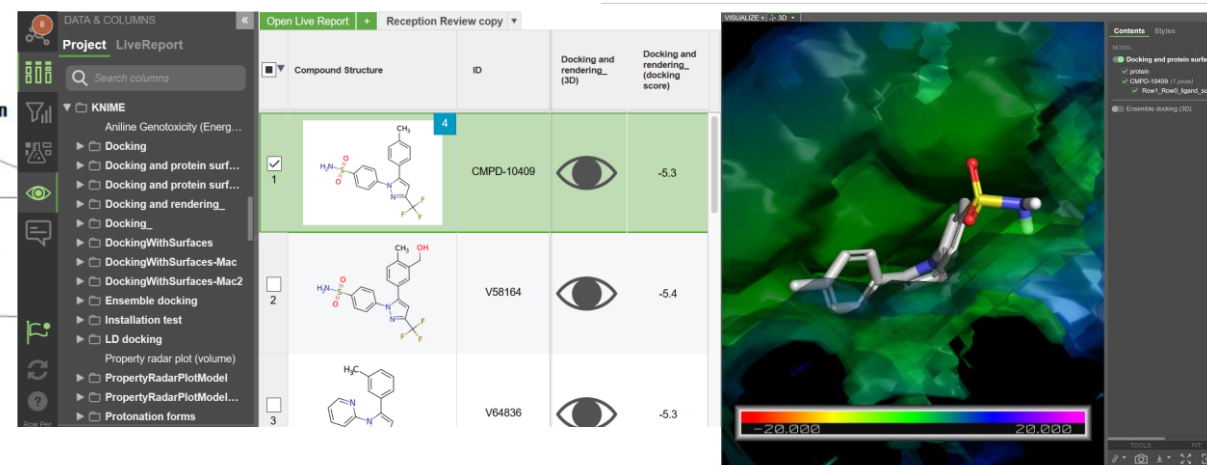
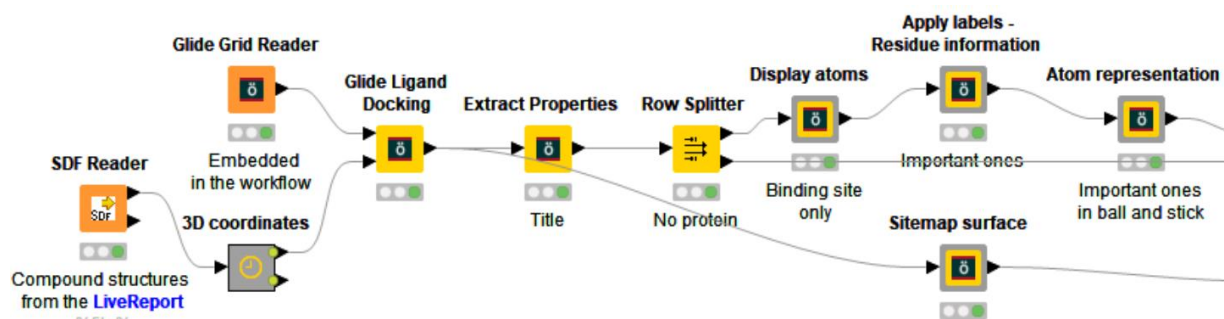


KNIME LiveDesign model examples

- Ligand CNS desirability radar plot

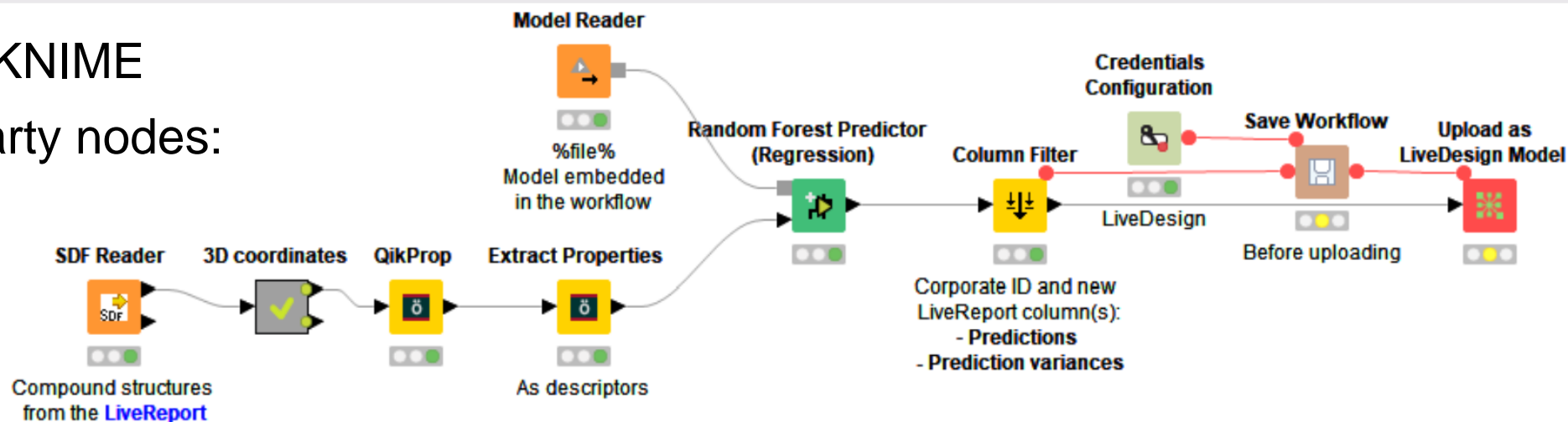


- Docking and protein surface

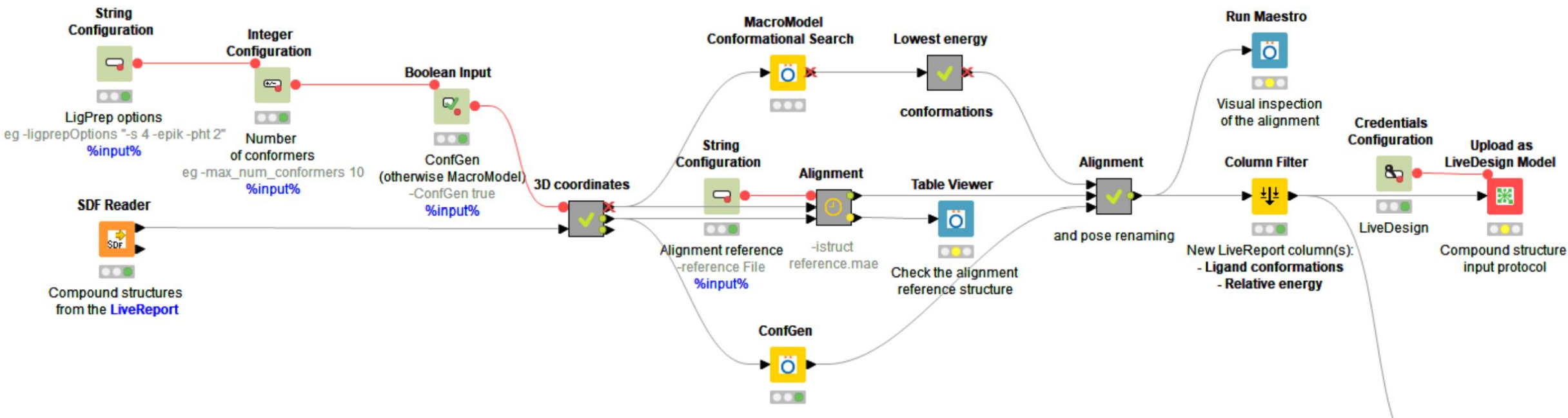


KNIME computational models – examples

- Using KNIME or third party nodes:



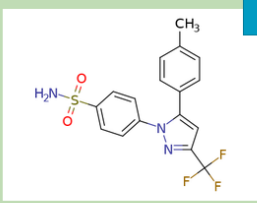

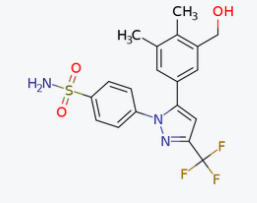

- Workflow control:



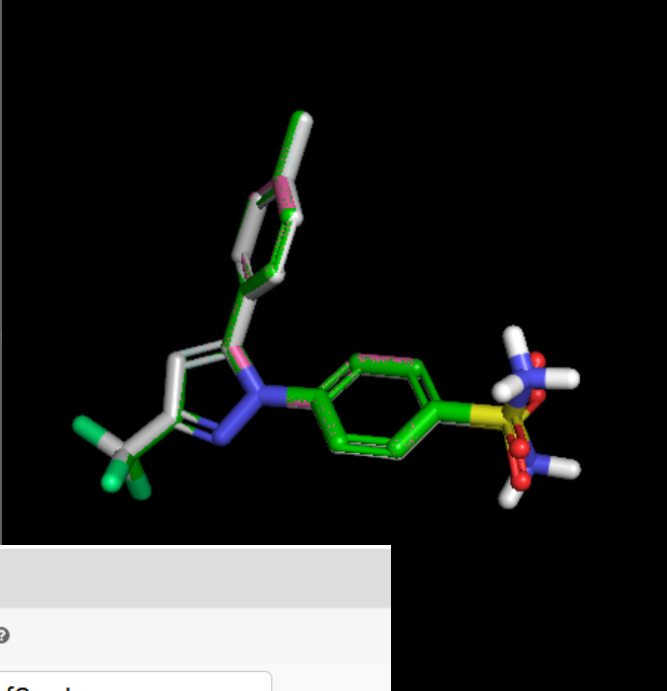
Workflow control

```
$SCHRODINGER/run KNIME_batch.py ${workflow:FILE-INPUT} -run -destFile=$PWD/executed.knwf -isdf ${SDF-FILE}  
${extra argument 1:TEXT-INPUT} ${extra argument 2:TEXT-INPUT} ${extra argument 3:TEXT-INPUT} -data workspace -configuration  
$PWD/ExtraExtensions/configuration
```

Open Live Report + 21-1 testing ▾

<input type="checkbox"/>	Compound Structure	ID	Low energy conformation (3D)	Low energy conformation (Relative)
<input checked="" type="checkbox"/>		CMPD-10409		0.0 0.006 0.007 0.007 0.126 0.282 0.313 0.571 More available...
<input type="checkbox"/>		V64860		0.0 0.14 0.449 0.483 0.769 0.995 1.031 1.082 More available...

VISUALIZE + 3D ▾



Contents Styles

MODEL:

☒ Low energy conformation (3D)

☒ CMPD-10409 (10 poses) ▾

☒ 0_0.0_1743076806 ●

☒ 1_0.006_615768295 ●

☒ 2_0.007_1174613324 ●

☒ 3_0.007_1756598433 ●

☐ 4_0.126_855777056 ●

☐ 5_0.282_1894630593 ●

☐ 6_0.313_443848968 ●

☐ 7_0.571_1660388703 ●

☐ 8_1.153_1356054653 ●


☐ 9_1.169_1812412864 ●

☐ 1 (3D)

☐ 1 (3D)

☐ 1 (3D)

TOOLS: FIT:



MODEL DATA

NAME	PARAMETER TYPE	DATA ⓘ
extra argument 3	Text	<input type="text" value="-ConfGen true"/>
extra argument 1 (60370)		
extra argument 1	Text	<input type="text" value="-istruct reference.mae"/>
extra file 1	File	Parent File: <i>mockup.txt</i> Currently: <i>reference.mae</i> <input type="checkbox"/> Clear Change: <input type="button" value="Browse..."/> No file selected.

The workflow parameters and reference file can be controlled either from the model Admin page or from the Parametrize model panel.

Validated models – workflows ready to be deployed

Available on: https://hub.knime.com/schroedinger/spaces/Public/latest/LiveDesign_models

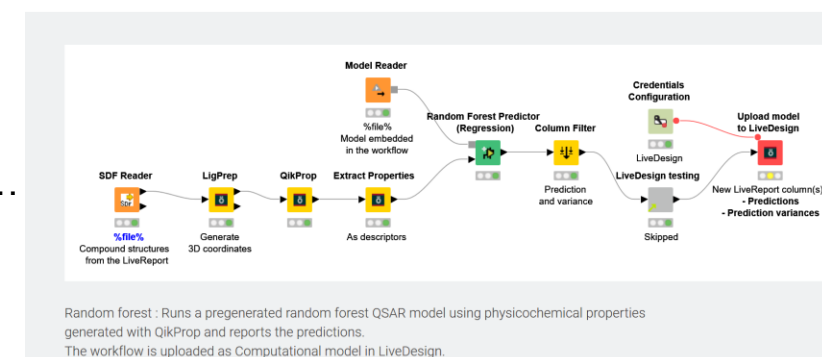
The workflow list and overview screenshots: .../LiveDesign_models/Validated_KNIME_models.pdf

- ADME and molecular properties
 - ADME
 - Atropisomerism
 - ESP surface
- Cheminformatics
 - AutoQSAR and DeepAutoQSAR
 - QSAR - random forest
 - Biased diversity selection
- Docking
 - Docking and binding site rendering
 - Docking and protein surface
 - Ensemble docking
- Docking post-processing
 - Binding pose strain
 - Interaction surface
 - Low energy conformations
- Ligand preparation and library design
 - Bioisostere replacement
 - Protonation forms

- Plotting
 - Ligand property radar plot
 - Ligand CNS desirability radar plot
 - Torsion profiles
- Structure alignment
 - Ligand alignment by shape with a cocrystallized reference
 - Ligand alignment by shape with a flexible reference
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- Protein preparation and refinement
 - Get PDB and preparation
 - Cocrystallized ligands
 - Sequence descriptors
- Workflow running on a KNIME server
- Structure alignment
 - By shape, with cocrystallized reference...
- Miscellaneous
 - FEP convergence
 - Highlight substructure

Spaces > Public > LiveDesign_models		
Type	Name	
	..	
	ADME	
	Bioisosteres	
	Docking	
	Docking and protein surface	
	ESP surface	
	Ensemble docking	
	Installation test	
	Ligand alignment	

Random forest - to be run in LiveDesign



Upload as LiveDesign model node – create and update

To update an existing model. eg:

- QSAR model building
 - Local KNIME workflow
- QSAR prediction in LiveDesign

1. Prototyping

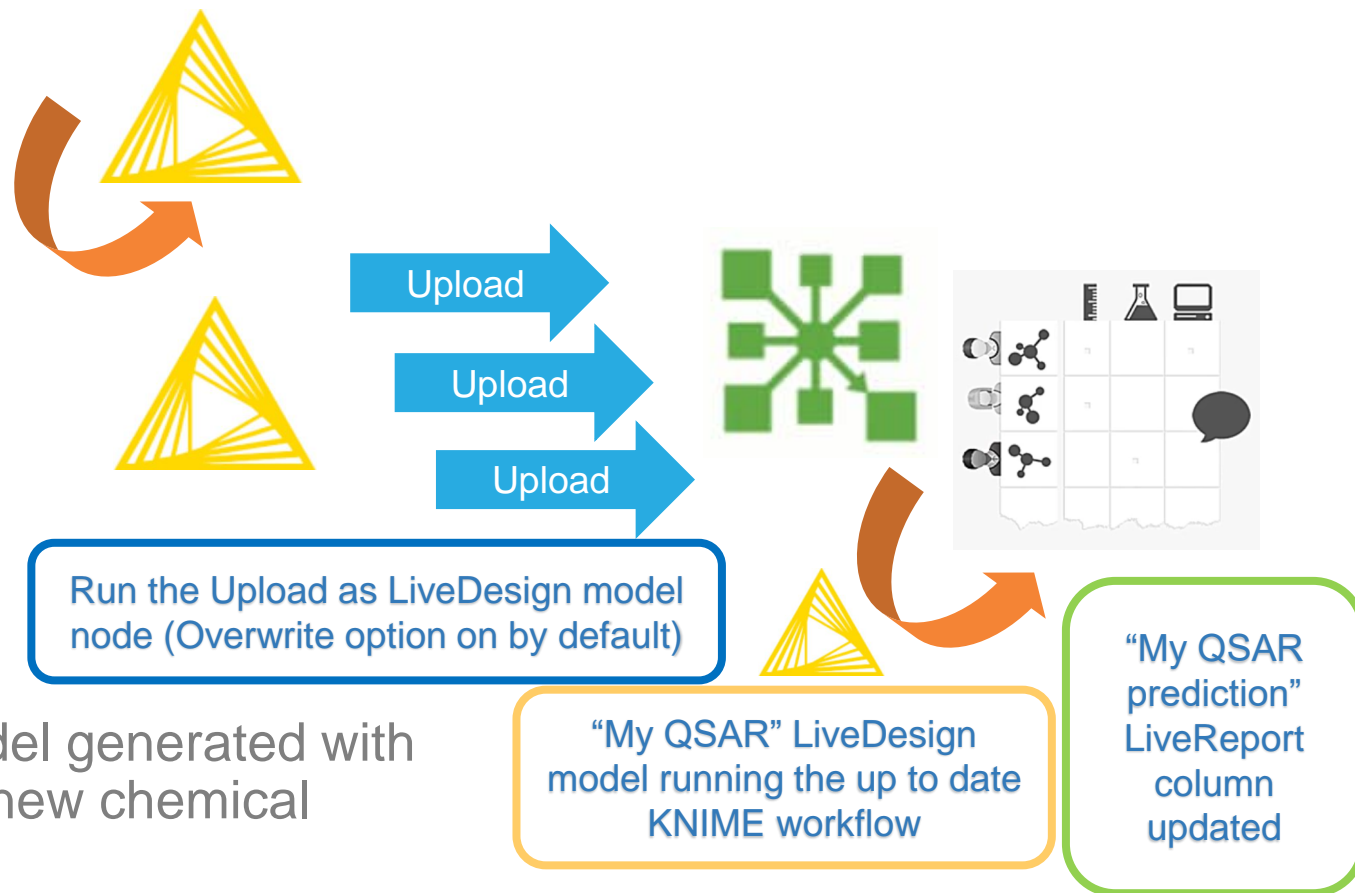
- Workflow fixes tested locally
- Then tested in LiveDesign

2. Improvements

- Uploaded and tested in LiveDesign

3. Updates

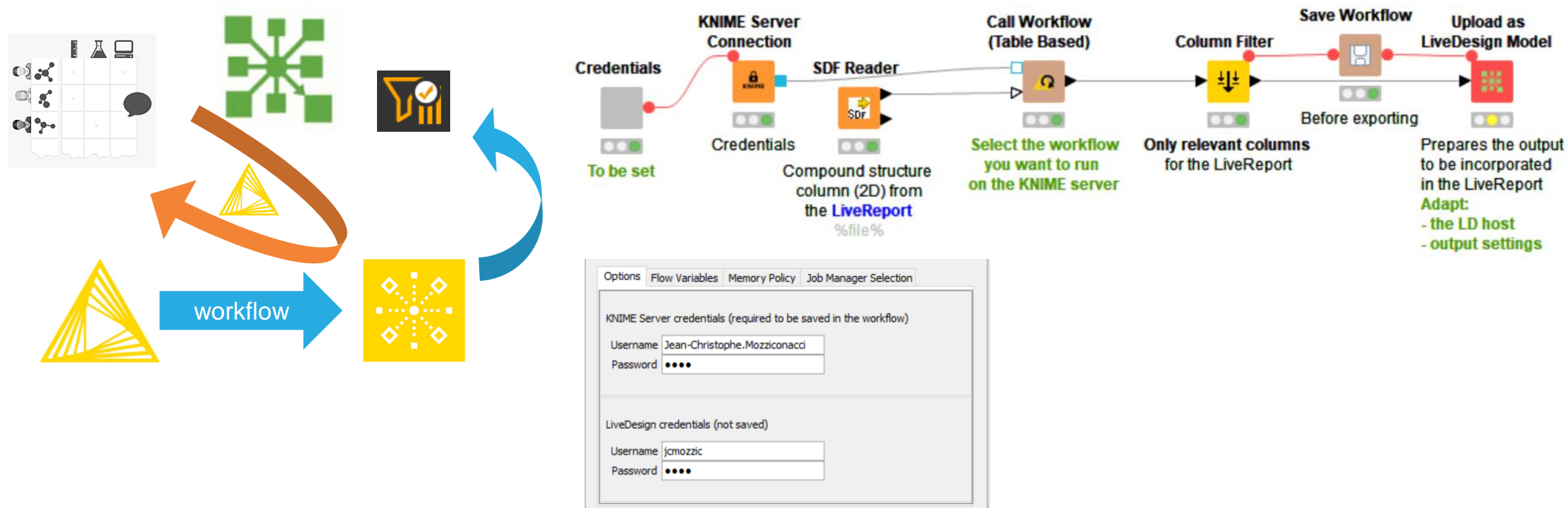
- With new versions of the QSAR model generated with the QSAR building workflow run on new chemical structures



Run a workflow on a KNIME Server from LiveDesign

- Using the Upload as LiveDesign model node:
 - Configured to use the generic KNIME Workflow protocol
 - See example the follow validated model running a workflow on a KNIME server:

https://hub.knime.com/schroedinger/spaces/LiveDesign_models/latest/Run%20on%20a%20KNIME%20Server/My%20workflow%200running%20on%20a%20KNIME%20server



Run a workflow on a KNIME Server from LiveDesign – advantages

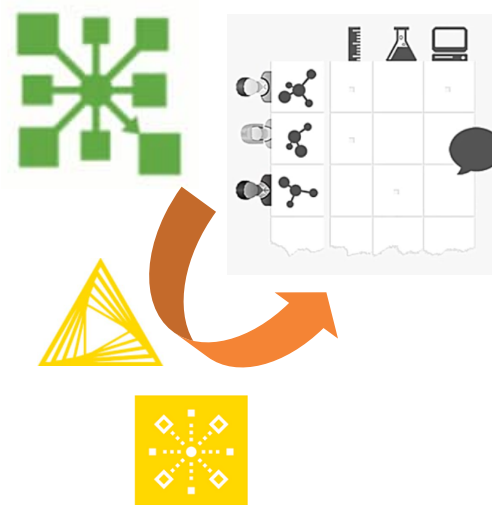
- **Workflows**
 - Stored, shared and modified centrally
 - Use existing workflows
- **Use existing infrastructure:**
 - Extra extensions
 - Installed and maintained from the KNIME Server
 - Otherwise Schrodinger installation change required at each release
 - Access to corporate data, databases, tools and license servers
 - Set up and maintained from the KNIME Server
 - Computational expensive calculations
 - Limited resources on the LiveDesign instance
 - No need to setup access to external computational resources
- **More suitable when used in LiveDesign Gadgets**

Summary

- KNIME computational models
 - Some ready to be installed and used
 - Growing set of models derived from the KNIME workflow examples available on <https://hub.knime.com>
- Model deployment or improvement
 - 1 click to create or update the model from KNIME
 - No need to use LiveDesign admin page
- Computational model execution
 - Same look and feel
 - KNIME run behind the scene on the LiveDesign host
 - Or run on a KNIME Server

The modelers can more easily deploy their methods to LiveDesign to the medicinal chemists

Complementarity between LiveDesign and KNIME Analytics Platform or KNIME Server



KNIME Hub > schroedinger > Spaces > Public > LiveDesign_models

	ADME	
	Atropisomerism	
	Bioisosteres	
	Docking	
	Docking and protein surface	
	ESP surface	
	Ensemble docking	
	Installation test	
	Ligand CNS desirability plot	
	Ligand CNS desirability range plot	
	Ligand alignment	
	Ligand property radar plot	
	Low energy conformation	
	My workflow running on a KNIME server	
	Protonation forms	
	Random forest	

Development Team

KNIME Extension Product Manager:

Jean-Christophe Mozziconacci

KNIME Extension Developer:

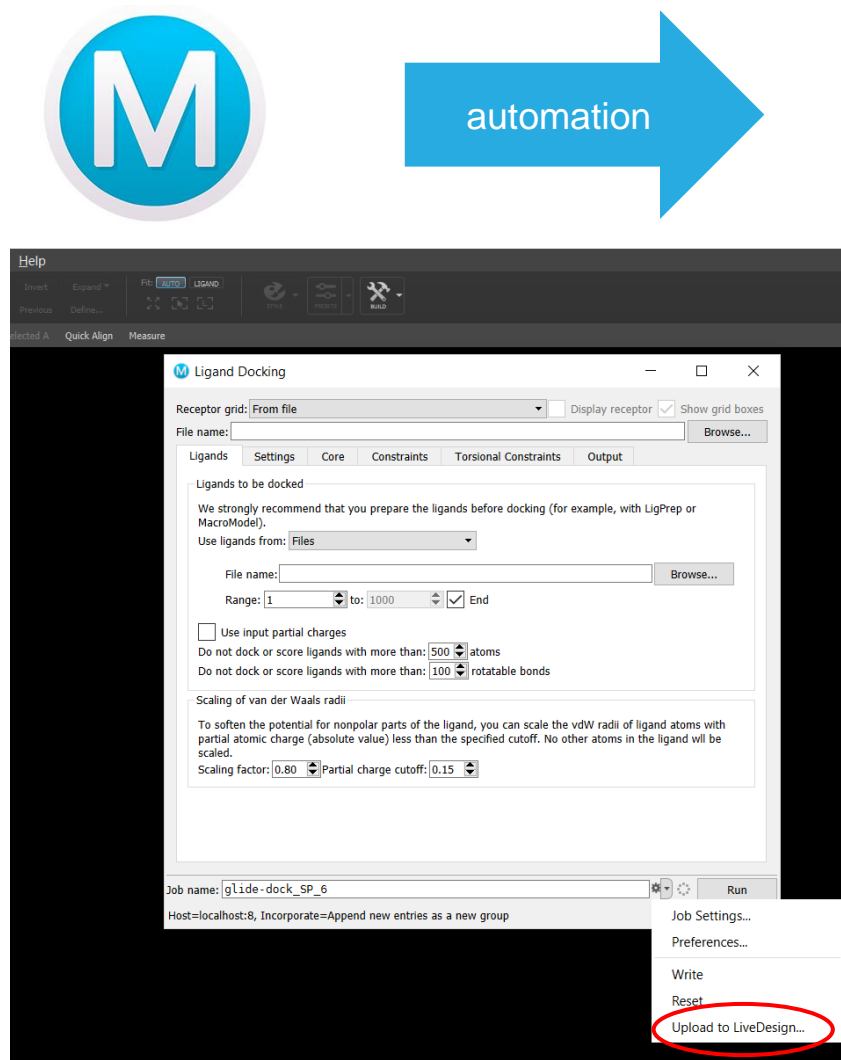
Ravikiran Kuppuraj

Vice President:

Matt Repasky

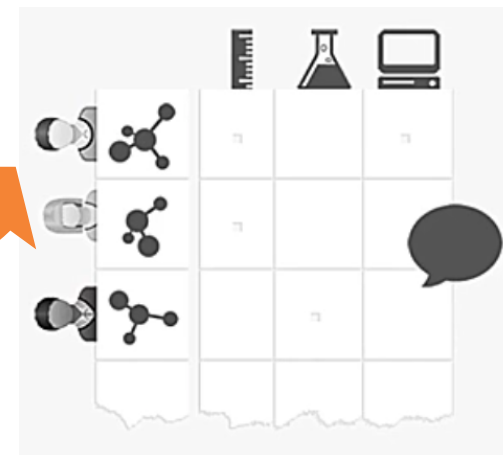
With the help of the LiveDesign team led by Erin Davis

Glide docking from Maestro to LiveDesign



- Glide python script

Computational model



- Other specialized python scripts are available in LiveDesign
- But what about a more complex docking workflow?
eg Docking in several protein conformations

LiveDesign Admin pages to create Protocols and Computational models



automation

```
Schrodinger Command Prompt
C:\>

import simpleknn
from bigfile import BigFile

if __name__ == "__main__": PYTHON API
    trainCollection = 'toydata'
    nimages = 2
    feature = 'f1'
```

Computational model



LiveDesign Admin

Site administration

MODEL AND PROTOCOL CONFIGURATION

Drivers

Protocols

Models

Parameterized Models

Tasks

COMMAND

ID 3960

```
export SCHRODINGER=/mnt/suites/suite2019-2 && $SCHRODINGER/run ${pythonfile:FILE-INPUT} ${SDF-FILE} --maxconf
${MaxNumOfConformers:NUMERIC-INPUT} --smarts ${matching smarts:TEXT-INPUT} --force_field ${forcefield:TEXT-INPUT}
```

DRIVER

1

ID 3961

cat results.csv

+ Add Another Command

MODEL DATA

NAME

PARAMETER TYPE

DATA

PARAMETER SOURCE

pml_script (21224)

pml_script

File

-

From Parent

Glide Runner Script (21226)

Glide Runner Script

File

-

From Parent

Grid File (.zip) (21225)

Grid File (.zip)

File

-

From Parent

Input File (.in) (21227)

Input File (.in)

File

-

From Parent

PREDICTIONS

NAME (IN MODEL)

DISPLAY NAME

TYPE

DECIMAL PLACES

ID 12826

diagram

Ligand Interaction Diagram

Image (e.g. .png, .jpg)

0

ID 12827

score

Score

Real

2

ID 12828

ligand

Ligand

3D Structure Ligand

0

ID 12829

protein

Protein

3D Structure Target

0

ID 12830

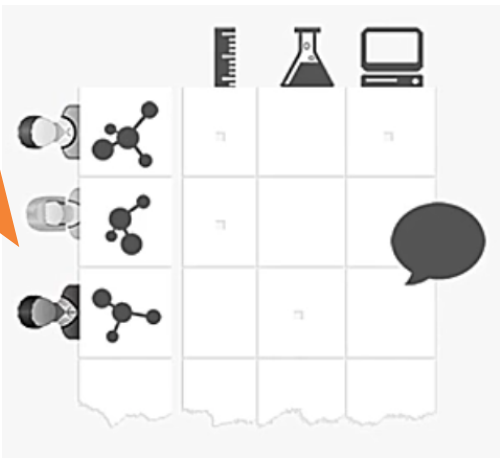
status

Run Status

String

0

+ Add Another Prediction



KNIME models for more complex workflows



automation

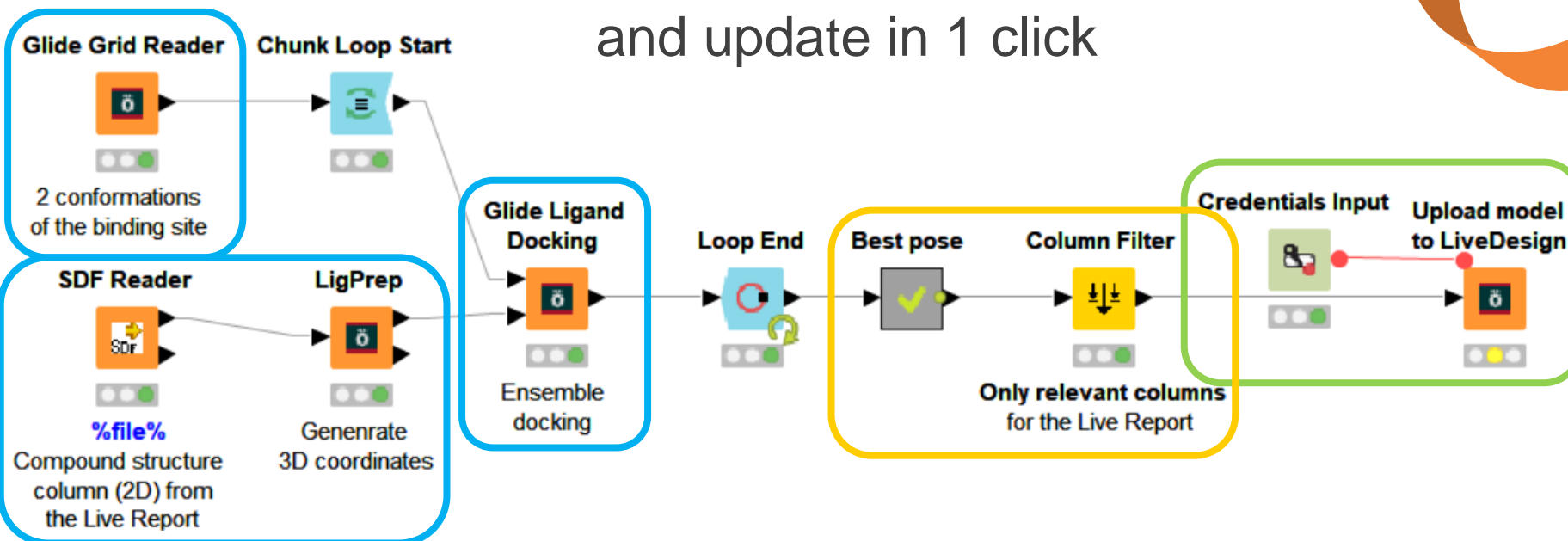
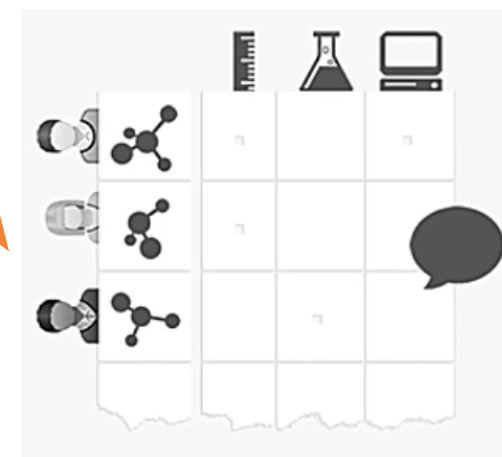
**KNIME
workflow**



Computational
model



- More complex/different workflows
- Computational model creation and update in 1 click



KNIME LiveDesign models

- Models running KNIME workflows
 - Standard LiveDesign models
 - Same look and feel
 - KNIME run behind the scene on the LiveDesign host
- Model deployment
 - The model are created automatically
 - No need to open LiveDesign admin page
 - From KNIME GUI
 - Iterative improvement and test
 - From the command line using a Python script
 - usually by the Solution Architects
- KNIME workflows
 - Visual (programming, communication)
 - Set of validated models
 - Growing set of workflows addressing modelling needs
 - Available from the KNIME hub website
 - Easy to adapt to similar needs



KNIME Hub > schroedinger > Spaces > Public > LiveDesign_models



Spaces > Public > LiveDesign_models

Type	Name	
	..	
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	Bioisosteres	
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KNIME in LiveDesign

Validated models

Validated models – workflows ready to be deployed

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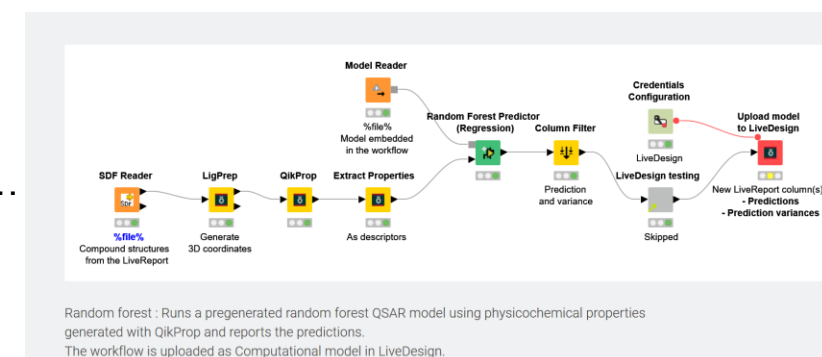
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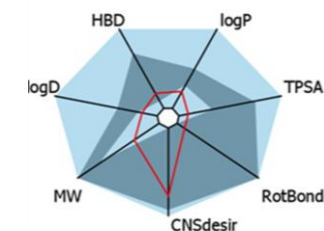
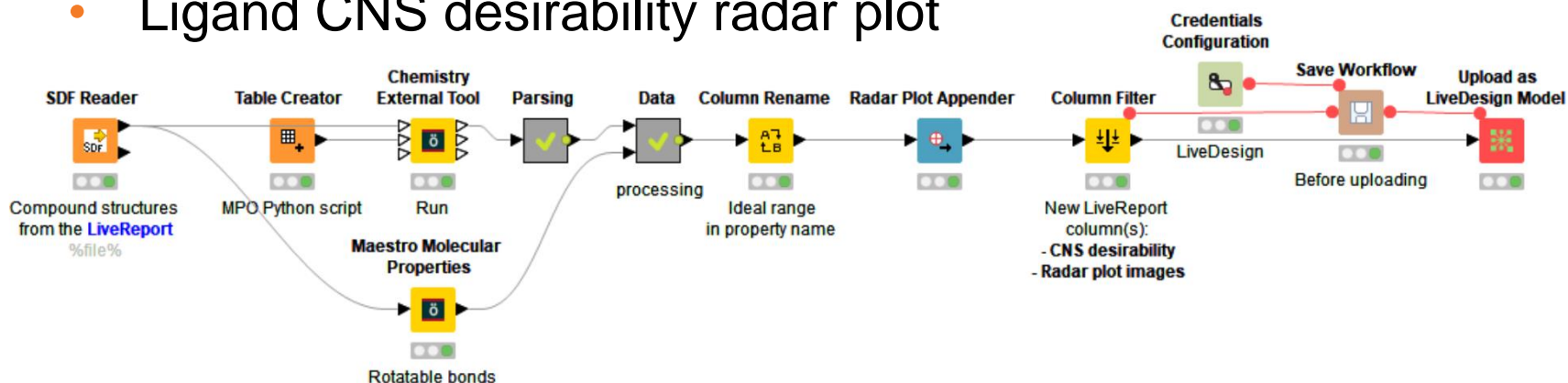
Spaces > Public > LiveDesign_models		
Type	Name	
Folder	..	
Workflow	ADME	Download
Workflow	Bioisosteres	Download
Workflow	Docking	Download
Workflow	Docking and protein surface	Download
Workflow	ESP surface	Download
Workflow	Ensemble docking	Download
Workflow	Installation test	Download
Workflow	Ligand alignment	Download

Random forest - to be run in LiveDesign

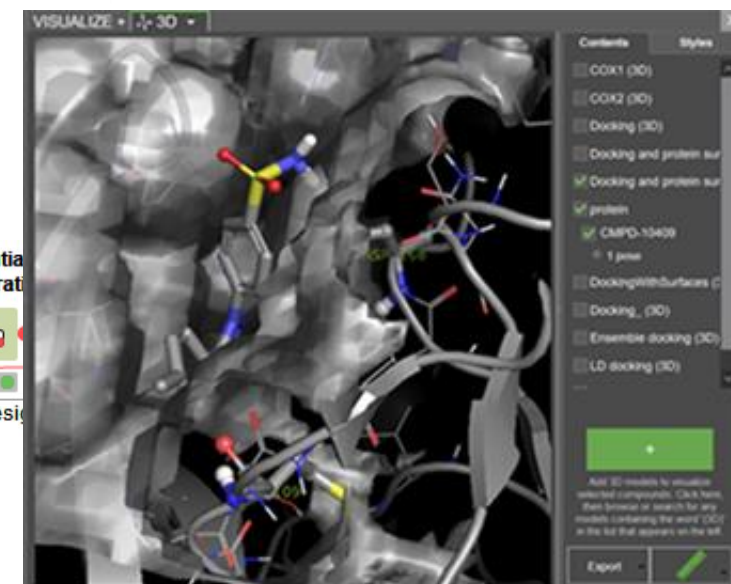
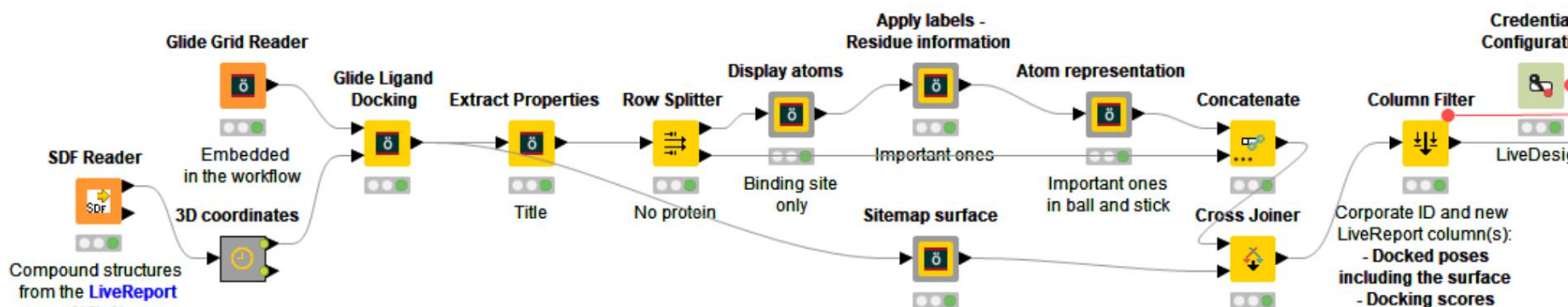


KNIME computational models – examples

- Ligand CNS desirability radar plot



- Docking and protein surface

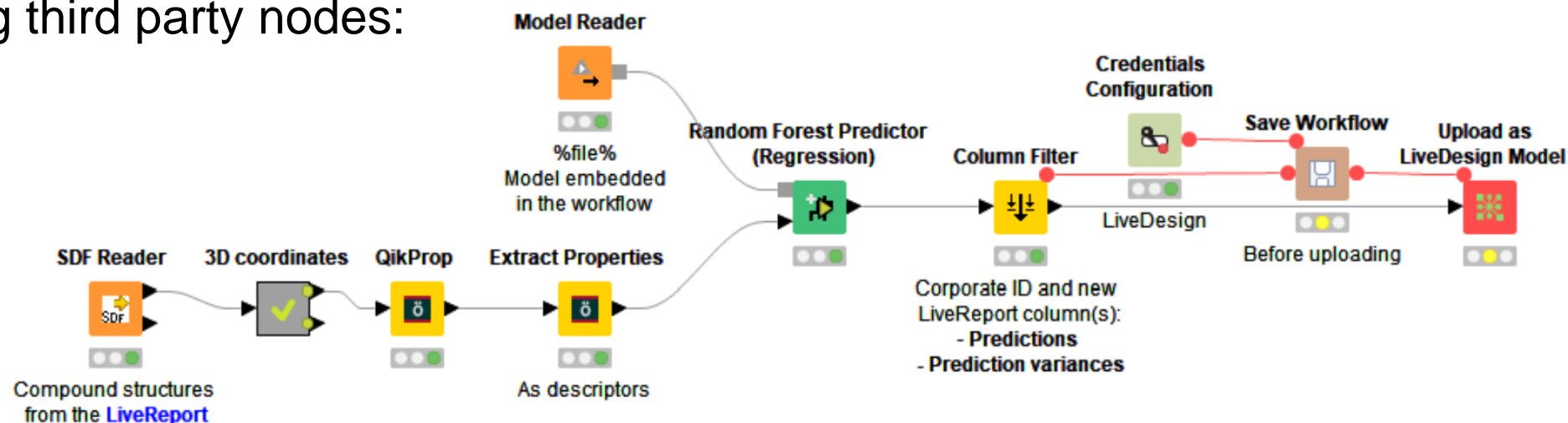


- Many more can be derived from the hundred of KNIME workflow examples:

https://hub.knime.com/schroedinger/spaces/Public/latest/Schrodinger_workflow_examples

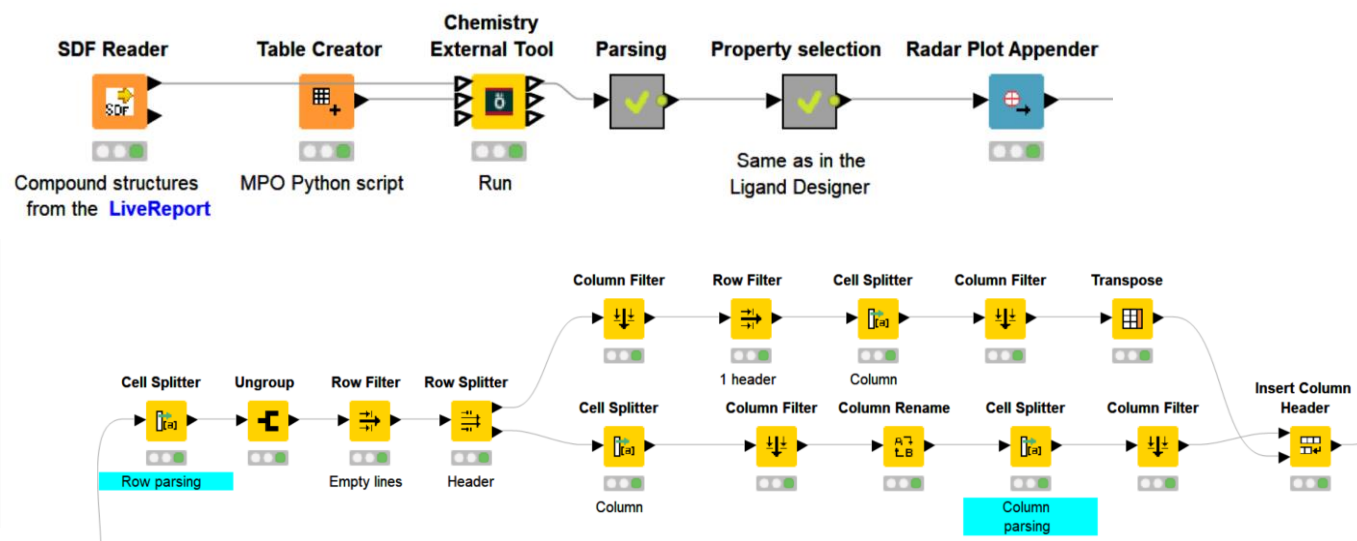
KNIME computational models – examples

- Using third party nodes:



- Running a python script:

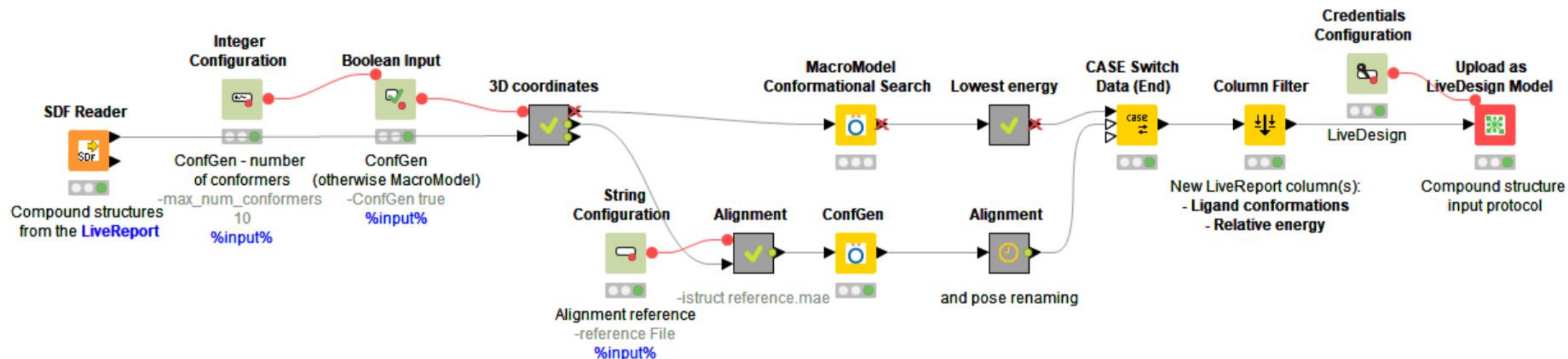
```
Script
Row 135 hbd_desir = _mono_decr_desirability(hbd, 0.5, 3.5)
Row 136 pka_desir = _mono_decr_desirability(pka, 8, 10)
Row 137
Row 138 cns_desir = alogp_desir + alogd_desir + mw_desir + tpsa_desir + hbd_desir + pka_desir
Row 139
Row 140 writer.writerow([corp_id, alogp_desir, alogd_desir, mw_desir, tpsa_desir, hbd_desir, pka_desir, .
Row 141
Row 142
Row 143 def main():
Row 144     parser = argparse.ArgumentParser(
Row 145         'Calculate Pfizer CNS MPO')
Row 146     parser.add_argument('ligands', help='name of sd file')
Row 147
```



KNIME computational models – examples

- Low energy conformations

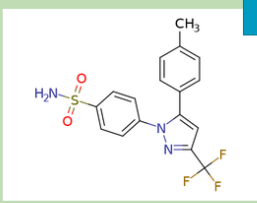

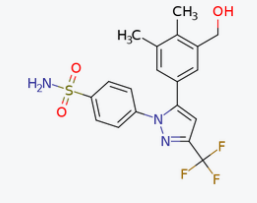

- Runs a MacroModel or ConfGen conformational search on the Compound structure column structures from the LiveReport, prepared with LigPrep.
- The lowest energy conformations are reported back in the LiveReport as poses as well as a column with the corresponding relative energies. These are also included in the pose name.
- The conformational search method and number of conformers can be controlled from LiveDesign admin panel or from the Parameterize model panel.



KNIME computational models – low energy conformations

- The conformations and the ligands are aligned
- Pose name: conformer ID, relative energy

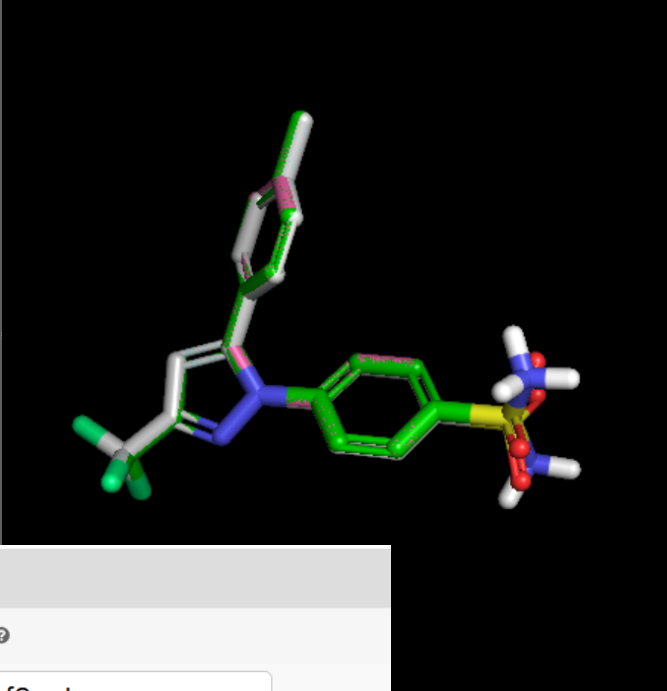
Open Live Report + 21-1 testing ▾

Compound Structure	ID	Low energy conformation (3D)	Low energy conformation (Relative)
<input checked="" type="checkbox"/> 1 	CMPD-10409		0.0 0.006 0.007 0.007 0.126 0.282 0.313 0.571 More available...
<input type="checkbox"/> 2 	V64860		0.0 0.14 0.449 0.483 0.769 0.995 1.031 1.082 More available...

MODEL DATA

NAME	PARAMETER TYPE	DATA
extra argument 3	Text	-ConfGen true
extra argument 1 (60370)		
extra argument 1	Text	-istruct reference.mae
extra file 1	File	Parent File: <i>mockup.txt</i> Currently: <i>reference.mae</i> <input type="checkbox"/> Clear Change: <input type="button" value="Browse..."/> No file selected.

VISUALIZE + 3D ▾



Contents Styles

MODEL:

☒ Low energy conformation (3D)

☒ CMPD-10409 (10 poses) ▾

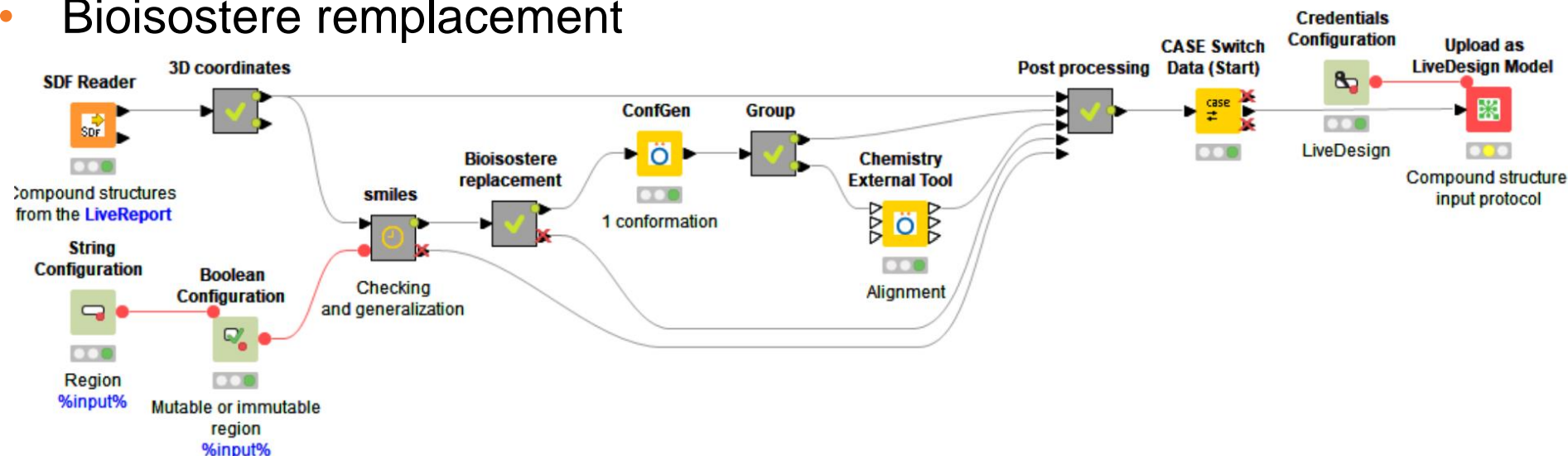
- ☒ 0_0.0_1743076806
- ☒ 1_0.006_615768295
- ☒ 2_0.007_1174613324
- ☒ 3_0.007_1756598433
- ☐ 4_0.126_855777056
- ☐ 5_0.282_1894630593
- ☐ 6_0.313_443848968
- ☐ 7_0.571_1660388703
- ☐ 8_1.153_1356054653
- ☐ 9_1.169_1812412864

TOOLS: FIT:

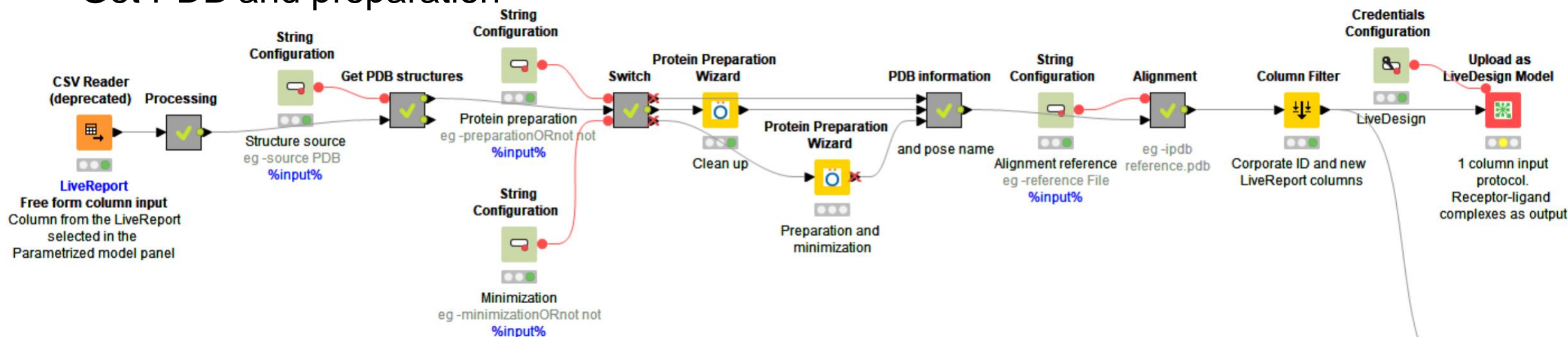
The workflow parameters and reference file can be controlled either from the model Admin page or from the Parametrize model panel.

KNIME computational models – examples

- Bioisostere replacement



- Get PDB and preparation



Get PDB from a FFColumn and Protein preparation

COX

DATA & COLUMNS

Project LiveReport

PPrep

Computational Models

KNIME

Validated models

Get PDB from FFC and PPrep

3D

Chain list

Deposition date

PDB classification

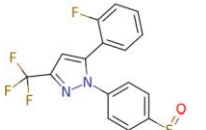
PDB title

prepared_with_version

Resolution

Row Per

Compound

Compound Structure	ID	All IDs	PDB ID
	CHEMBL418574	V64710 CHEMBL418574	6Y3C
	V58218	V58218	3KK6

Get PDB from FFC and preparation

Modified January 20, 2021 by jcmozzic

2021/01/18 15:37:09

--- Get PDB from a FFColumn and Protein preparation :

Input column: PDB IDs in a Free Form Column

Downloads the structure for the PDB IDs listed in the selected Free Form Column from the LiveReport, optionally prepare the structures, extracts and creates new columns with the structures and corresponding structural information. The sgstructure source, preparation and alignment steps can be controlled from LiveDesign admin panel.

[LiveDesign,PPrep]

Schrodinger 20.4.1

Add to LiveReport

Parameterize Model

Name: Test

Description: 2021/01/18 15:37:09
--- Get PDB from a FFColumn and Protein preparation :

Model Data

Input column PDB IDs Change Column...

extra argument 1 -preparationORnot preparation

extra file 3 1CX2 with V49629 docked with constraints.pdb Upload File...

☐ Publish(share data between Live Reports)(?)

Cancel OK

Get PDB from a FFColumn and Protein preparation

COX

DATA & COLUMNS

Project LiveReport

PPrep

Computational Models

KNIME

Validated models

Get PDB from FFC and PPrep

3D

Chain list

Deposition date

PDB classification

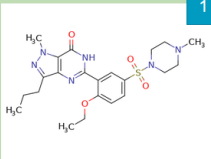

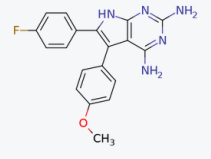

PDB title

prepared_with_version

Resolution

Open Live Report

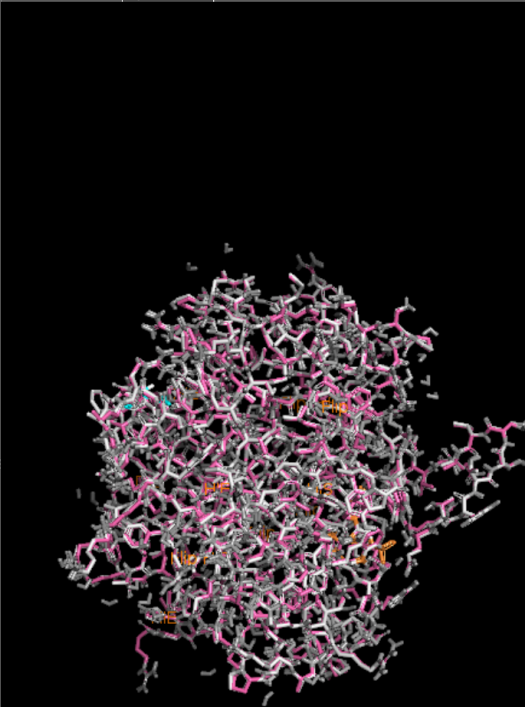
PDB

	Compound Structure	ID	A mini (Chain list)	A mini (Resolution)	A mini (PDB classification)	A mini (3D)	A mini (Deposition date)	A mini (prepared_with_version)	A mini (PDB title)
1		V38532	L, H	2.2	HYDROLASE/H INHIBIT		06-JUL-92	2020-4	REFINED 2 ANGSTROM X-RAY CRYSTAL STRUCTURE BOVINE THROMBIN COMPLEX FORMED WITH BENZAMIDINE More available...
2		V222790	L, H	2.5	HYDROLASE/H INHIBIT		06-JUL-92	2020-4	REFINED 2 ANGSTROM X-RAY CRYSTAL STRUCTURE BOVINE THROMBIN COMPLEX FORMED WITH BENZAMIDINE More available...

2 Compounds · 1 Selected 100 Columns (6 Hidden)

Give Feedback

Visualize + 3D



Contents

Styles

MODEL:

A mini (3D)

V38532 (1 pose)

Row1_197771137

A not (3D)

V38532 (1 pose)

Row1_460132198

3 cocryst (3D)

A prep (3D)

Ensemble docking (3D)

Get PDB (3D)

Get PDB from FFC (3D)

No PPrep (CT - DELETED)

Not (CT - DELETED)

PPrep (CT - DELETED)

PPrep - not (CT - DELETED)

Preparation (CT - DELETED)

Thrombin Docking (3D)

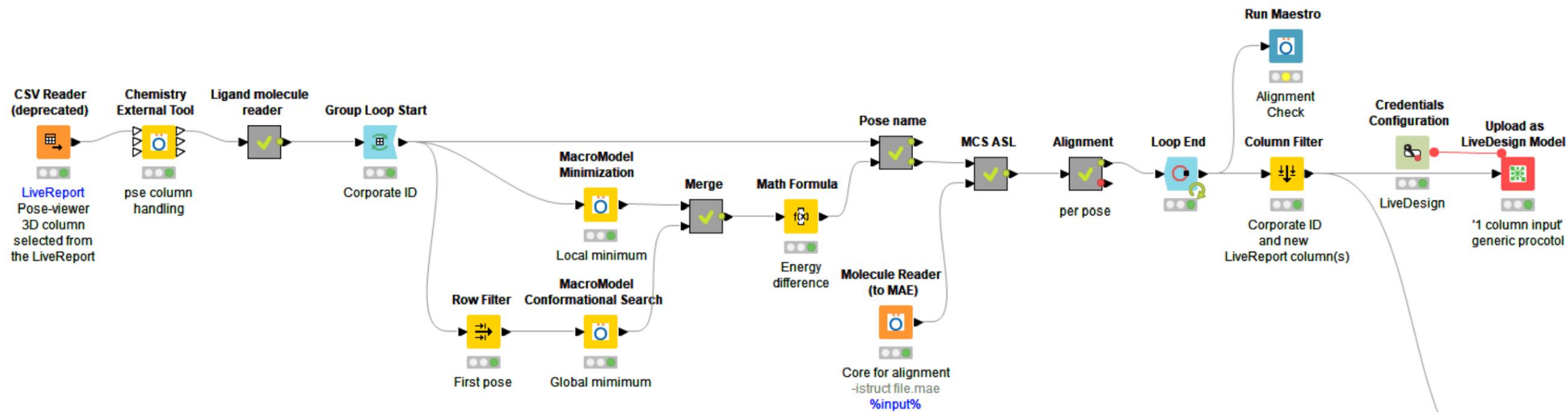
Thrombin WaterMap (3D)

TOOLS:

FIT:

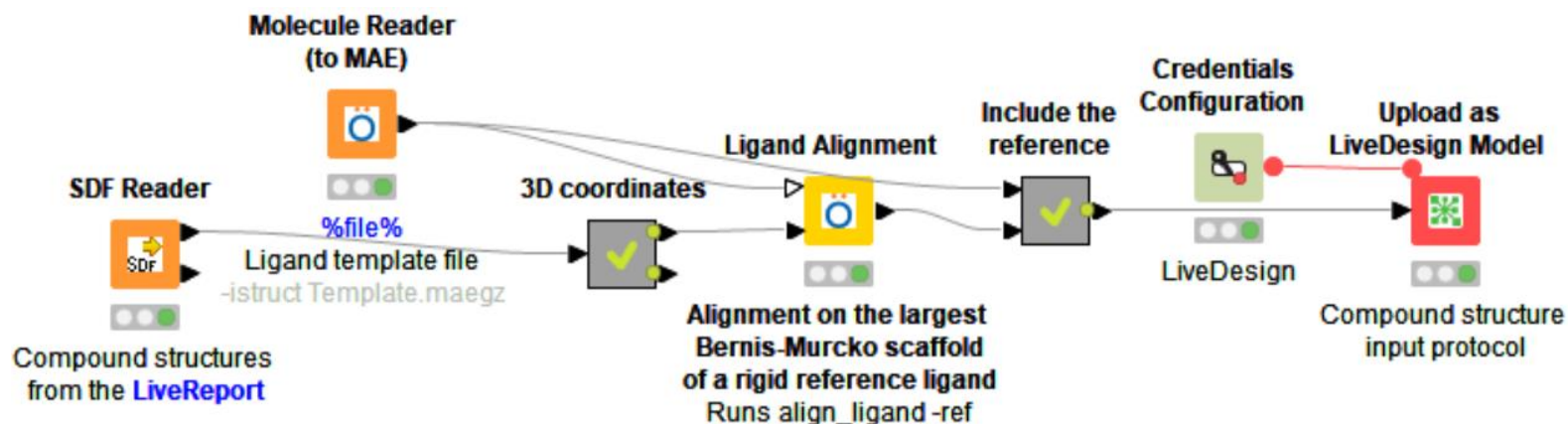
KNIME computational models – examples

- Binding pose strain



KNIME computational models – examples

- Structure alignment – Ligand alignment with a cocrystallized reference





KNIME in LiveDesign

Add a KNIME computational model to LiveDesign

- KNIME computational models
 - Workflow saved as 1 zip file with model data included
 - A set of workflow examples is available to download, ready to be uploaded
- Upload to LiveDesign
 - For the SAs and sysadmin
 - 1 command line to run
 - For the normal users
 - From KNIME: 1 node to run

KNIME Computational model.knwf

Upload

KNIME Hub

KNIME Hub > schrodinger > Spaces > LiveDesign_models

```
$$SCHRODINGER/run  
-FROM knime  
LiveDesign_admin.py  
-host <LiveDesign  
host> -username  
<username> ...
```

Home

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

DATA & COLUMNS

Project LiveReport

Search columns

KNIME

- Aniline Genotoxicity (Energ...
- Docking
- Docking and protein surf...
- Docking and protein surf...
- Docking and rendering_
- Docking_
- DockingWithSurfaces
- DockingWithSurfaces-Mac
- DockingWithSurfaces-Mac2
- Ensemble docking
- Installation test
- LD docking
- Property radar plot (volume)
- PropertyRadarPlotModel
- Property
- Protonat

Row Per

Compound

Open Live Report

Compound Str

1

2

H₃C

Atropisomerism (Found)

Modified May 28, 2020 by jcmozzic

Atropisomerism

Add to LiveReport

KNIME workflow uploaded as models in LiveDesign

DATA & COLUMNS

Project LiveReport

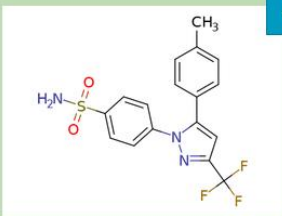

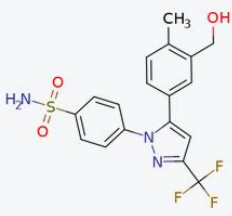

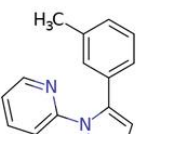

Search columns

KNIME

Aniline Genotoxicity (Energy...)

- Docking
- Docking and protein surf...
- Docking and protein surf...
- Docking and rendering_
- Docking_
- DockingWithSurfaces
- DockingWithSurfaces-Mac
- DockingWithSurfaces-Mac2
- Ensemble docking
- Installation test
- LD docking
- Property radar plot (volume)
- PropertyRadarPlotModel
- PropertyRadarPlotModel...
- Protonation forms

Open Live Report + Reception Review copy

	Compound Structure	ID	Docking and rendering_ (3D)	Docking and rendering_ (docking score)
1		CMPD-10409		-5.3
2		V58164		-5.4
3		V64836		-5.3

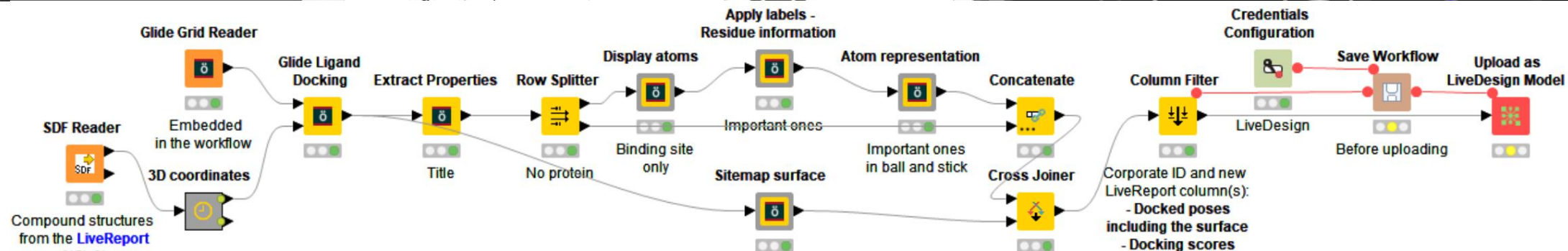
Visualize + 3D

Contents

- COX1 (3D)
- COX2 (3D)
- Docking (3D)
- Docking and protein ...
- Docking and protein ...
- ☒ Docking and renderin...
- ☒ protein
- ☒ CMPD-10409
- + 1 pose
- DockingWithSurface...
- Docking_ (3D)
- Ensemble docking (3D)

+

Add 3D models to visualize selected compounds: Click here, then browse or search for any models containing the word '(3D)' in the list that appears on the left.

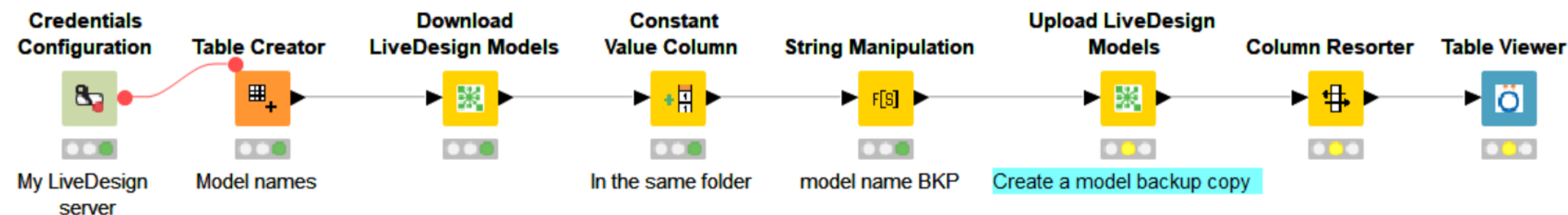


LiveDesign model and protocol administration nodes

- Nodes to upload, download and verify
 - Operate on a list of model or protocol names or files
- Application examples:
 - Create backup copies of some models before they are updated
 - Create a model or protocol copy for testing changes and only visible from a specific project
 - Copy from a testing to a production LiveDesign instance
 - Deploy the latest version of the validated models available from the KNIME hub
 - Deploy the latest version of the generic KNIME protocols
 - Compare 2 versions of a protocol or a model
- Run LiveDesign_admin.py script
 - The command lines are reported in the node output table.
So they can be run in a shell if the LiveDesign host isn't accessible from the KNIME session
 - **The script can also be used on non-KNIME models and protocols**

LiveDesign administration nodes – application example

- Create backup copies of some models



S Model name	S model path	Txt model download logs	S mo
Alignment on a cocrystallized ligand	C:\Users\jcmozzic\AppData\Local\Temp\Alignment_on_a_cocrystallized_ligand.knwf	Matched items: Computational Models/KNIME/Validated models/Alignment on a cocrystallized ligand (10196) https://qa-demo-8-9.dev.bb.schrodinger.com/admin/extprops/ldmodel/10196/change/ Temporary directory created at 'C:\Users\jcmozzic\AppData\Local\Temp\Model_agitlp6v' Deleting temporary directory: C:\Users\jcmozzic\AppData\Local\Temp\Model_agitlp6v KNIME Model successfully downloaded	\$SCHRO
Ligand alignment	C:\Users\jcmozzic\AppData\Local\Temp\Ligand_alignment.knwf	Matched items: Computational Models/KNIME/Validated models/Ligand alignment (14014) https://qa-demo-8-9.dev.bb.schrodinger.com/admin/extprops/ldmodel/14014/change/ Temporary directory created at 'C:\Users\jcmozzic\AppData\Local\Temp\Model_mz7q24a7'	\$SCHRO
S model download command	S model download additional args		
\$SCHRODINGER/run -FROM knime LiveDesign_admin.py -host https://qa-demo-8-9.dev.bb.schrodinger.com -username jcmozzic	-type model -mode download -name "Alignment on a cocrystallized ligand" -folder "KNIME/Validated models"		
\$SCHRODINGER/run -FROM knime LiveDesign_admin.py -host https://qa-demo-8-9.dev.bb.schrodinger.com -username jcmozzic	-type model -mode download -name "Ligand alignment" -folder "KNIME/Validated models"		

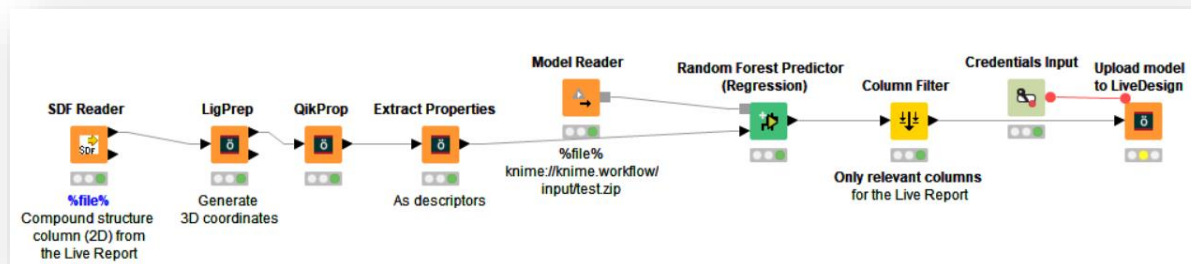
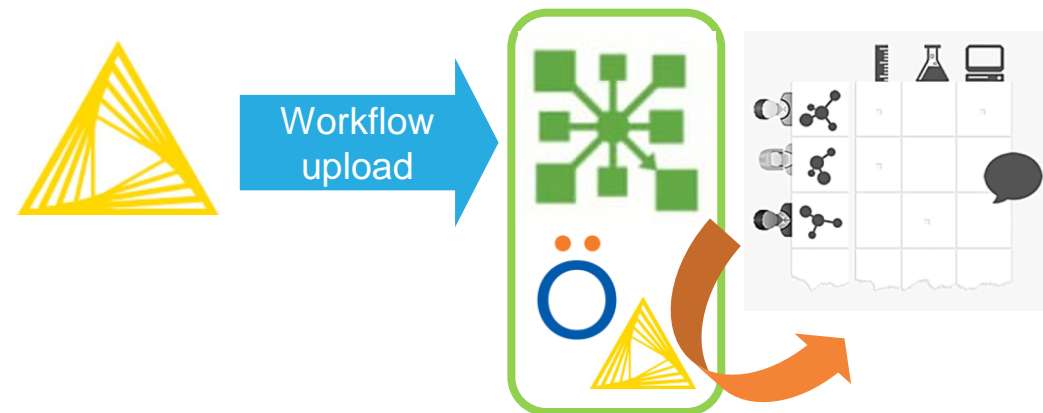
Model execution


The workflow is run by the KNIME installation embedded in the Schrodinger installation on the LiveDesign host

The progress can be tracked from the Task page on LiveDesign Admin panel

<https://LiveDesignServer.com/admin/tetasks/task/>

- Workflow overview image
- The workflow execution log
- The executed workflow along with the other temporary files



 LiveDesign Admin

Home > Tasks > 5e1b7ea0757a47fe04f8575d

Task Details

ID:	5e1b7ea0757a47fe04f8575d
Status:	Finished
Submitter:	jean-christophe.mozziconacci

Input files:

- [LiveDesign - KNIME_server_execution.knwf \(download\)](#)
- [workflow.svg \(download\)](#)
- [params.json \(download\)](#)
- [input.sdf \(download\)](#)

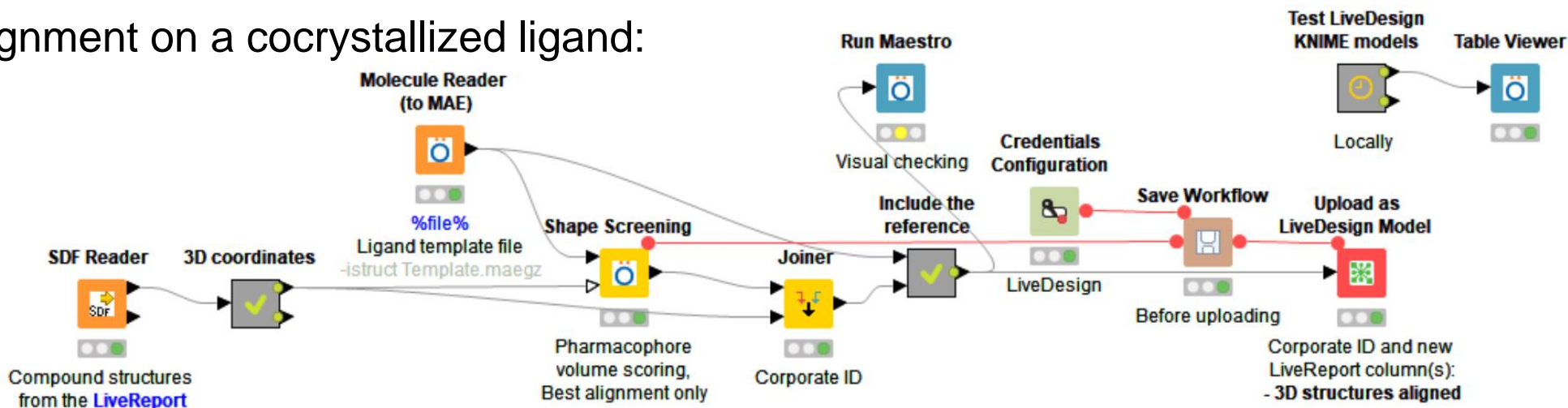
Customize a KNIME computational model

System specific files can be changed from LiveDesign admin page

- No need to open KNIME, nor a the Parameterize model configuration panel each time
- eg ligand alignment template, Glide grid, QSAR model file
- The corresponding KNIME_batch.py arguments have to be added to the page too
 - See Batch test node output

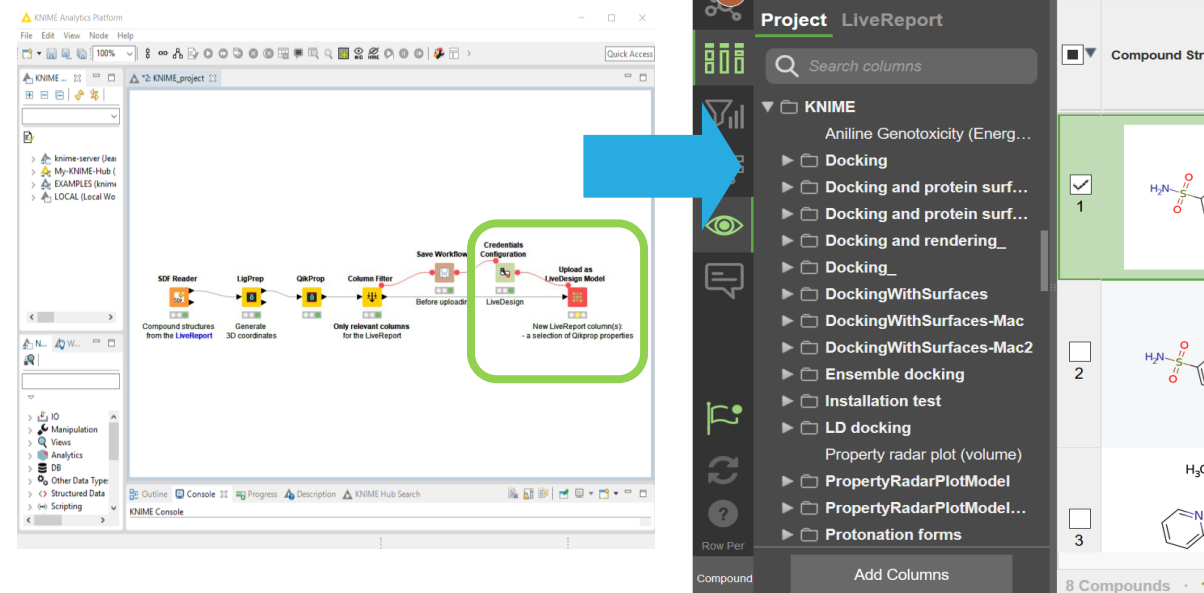
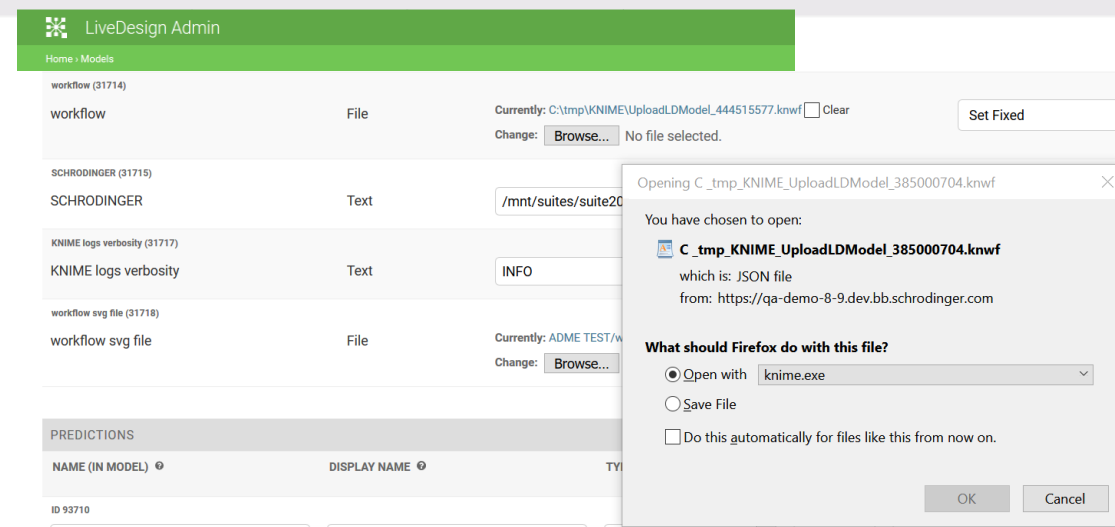
MODEL DATA			
NAME	PARAMETER TYPE	DATA	PARAMETER SOURCE
extra file 1	File	Parent File: <i>mockup.txt</i> Currently: <i>Template.maegz</i> <input type="checkbox"/> Clear Change: <input type="button" value="Browse..."/> No file selected	<input type="text" value="Set Fixed"/>
extra argument 1	Text	<input type="text" value="-istruct Template.maegz"/>	<input type="text" value="Set Fixed"/>

Alignment on a cocrystallized ligand:



Modify a KNIME Computational model

- Download the workflow from LiveDesign admin page
 - .knwf file from the Models or Tasks pages
 - Or from <https://hub.knime.com>
- Edit the workflow in KNIME
 - and run the Upload node again
- Run the Upload as LiveDesign model node
- The new model version is deployed
 - Ready to be tested
 - To be used by your colleagues to add the output columns to their LiveReport



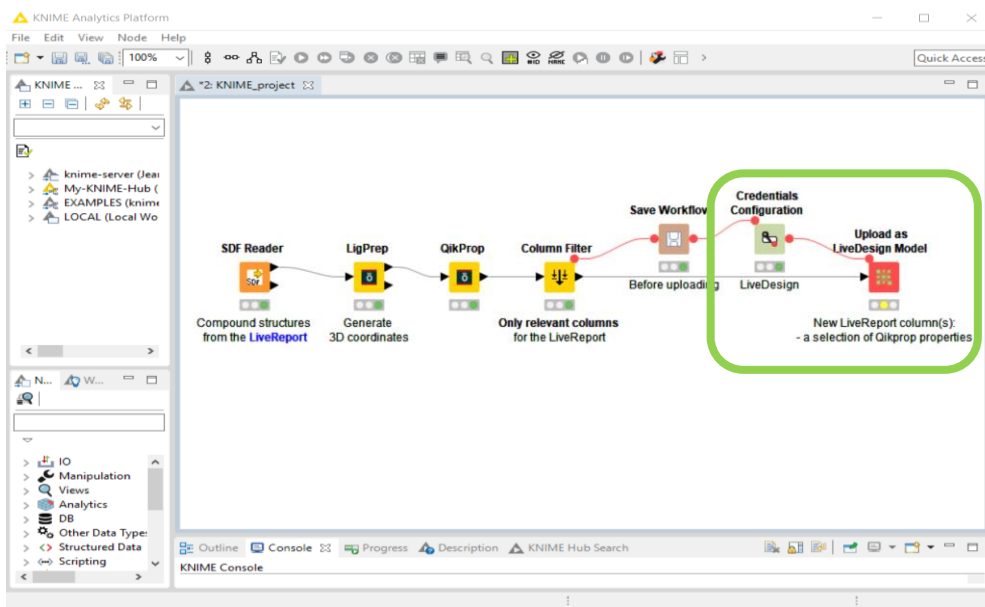
Turn a KNIME workflow into a LiveDesign Computational model

- In the workflow in KNIME
 - Add the **LiveReport** label to the input SDF reader node
 - Configure and execute the Upload as LiveDesign model node

The workflow is uploaded to LiveDesign and available under Computational models >

KNIME section

- In the LiveReport
 - The KNIME model is run on the LiveReport compound structures and new column(s) added.



The LiveDesign interface shows a table of compound structures with columns: Compound Structure, ID, All IDs, 3D (3D), Upload to Live Design (Extensions), and 19-3 KNIME QSAR (Prediction). The 'KNIME' section is highlighted in the left sidebar, and the 'Upload to Live Design - Random forest' model is selected. The table contains four rows of data, each with a chemical structure, ID, and prediction results.

Compound Structure	ID	All IDs	3D (3D)	Upload to Live Design (Extensions)	19-3 KNIME QSAR (Prediction)
	V35000	V35000			23
	V35002	V35002			27
	V35006	V35006			5
	V35010	V35010			19

Upload as LiveDesign model node – Example

- Tagged input SDF reader node and Upload as LiveDesign model node as output

SDF Reader
Compound structures from the LiveReport %file%

LigPrep
Generate 3D coordinates

QikProp

Column Filter
Only relevant columns for the LiveReport

Save Workflow
Before uploading

Credentials Configuration
LiveDesign

Upload as LiveDesign Model
New LiveReport column(s): - a selection of Qikprop properties

Read molecules - 0:2...

Row ID	sdf Molecule	Molecule name
Row0	Molecule: V64...	V64713
Row1	Molecule: V64...	V64719
Row2	Molecule: V64...	V64721

Filtered table - 0:38 - Column Filter (Only relev...

Row ID	CT	Molecule name	QPropBB
Row0	Molecule: V64713 #atoms:...	V64713	-0.694
Row1	Molecule: V64719 #atoms:...	V64719	-1.377
Row2	Molecule: V64721 #atoms:...	V64721	-0.201

Dialog - 2:181 - Credentials Input (Live Design)

Control Flow Variables Job Manager Selection Memory Policy

Label: LD credentials

Description: Enter Description

Variable Name: ld_credentials

Parameter Name: ld_credentials

Username: Jean-christophe.mozziconacci

Password:

☒ Prompt user name in wrapped metanode dialog/wizard

☐ Save password in configuration (weakly encrypted)

☐ Use KNIME Server Login (when run on server)

Dialog - 4:456 - Upload as LiveDesign Model ('1 col...

File Upload as LiveDesign Model Flow Variables Job Manager Selection Memory Policy

LiveDesign host: From the Preferences

LiveDesign protocol: KNIME Workflow 20-4 - 1 column input (18092)

LiveDesign project: Global

Schrodinger Suite: From the Preferences

Folder: KNIME/Validated models

Corporate ID column: Corporate ID

3D column type: Ligands

Command type: Normal

☒ Overwrite Model

PyMOL script:

OK Apply Cancel ?

Upload as LiveDesign model – configuration

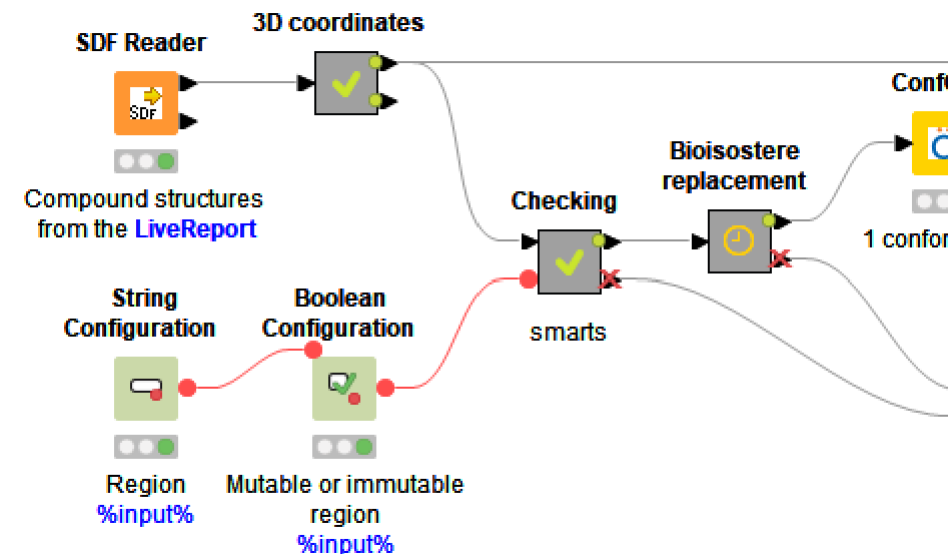
- **Machine specific** - LiveDesign host and Schrodinger suite
 - Mandatory, but ideally from the workspace preferences
 - Ideally running the same KNIME version as used to create the workflow
- **Model location** - Project and Folder
 - Can keep the defaults
- **Workflow input** - Protocol and Corporate ID
 - Mandatory, but set by the workflow creator
 - LiveDesign **protocol**
 - The 2 generic protocols
 - Modified protocols for specific scenarios
 - **Corporate ID** column
 - To be used to match the workflow results with the LiveReport entries
- Workflow execution and output - 3D column, Command type, Overwrite and PyMOL
 - Optional, workflow specific and set by the workflow creator

The screenshot shows a configuration window for uploading a model to LiveDesign. It contains several dropdown menus and checkboxes. A green oval highlights the 'LiveDesign host' and 'Schrodinger Suite' dropdowns, both set to 'From the Preferences'. A blue oval highlights the 'LiveDesign project' dropdown set to 'Global' and the 'Folder' dropdown. A yellow oval highlights the 'LiveDesign protocol' dropdown set to 'Choose a protocol' and the 'Corporate ID column' dropdown set to 'Molecule name'. Other visible options include '3D column type' set to 'Ligands', 'Command type' set to 'Normal', and a checked 'Overwrite Model' checkbox. At the bottom, there is a text area for the 'PyMOL script'.

- 3D output column type
 - Ligands, Docked poses, Protein-ligand complexes
- Command type
 - Click to run or automatically

Upload as LiveDesign model – extra argument and extra file fields

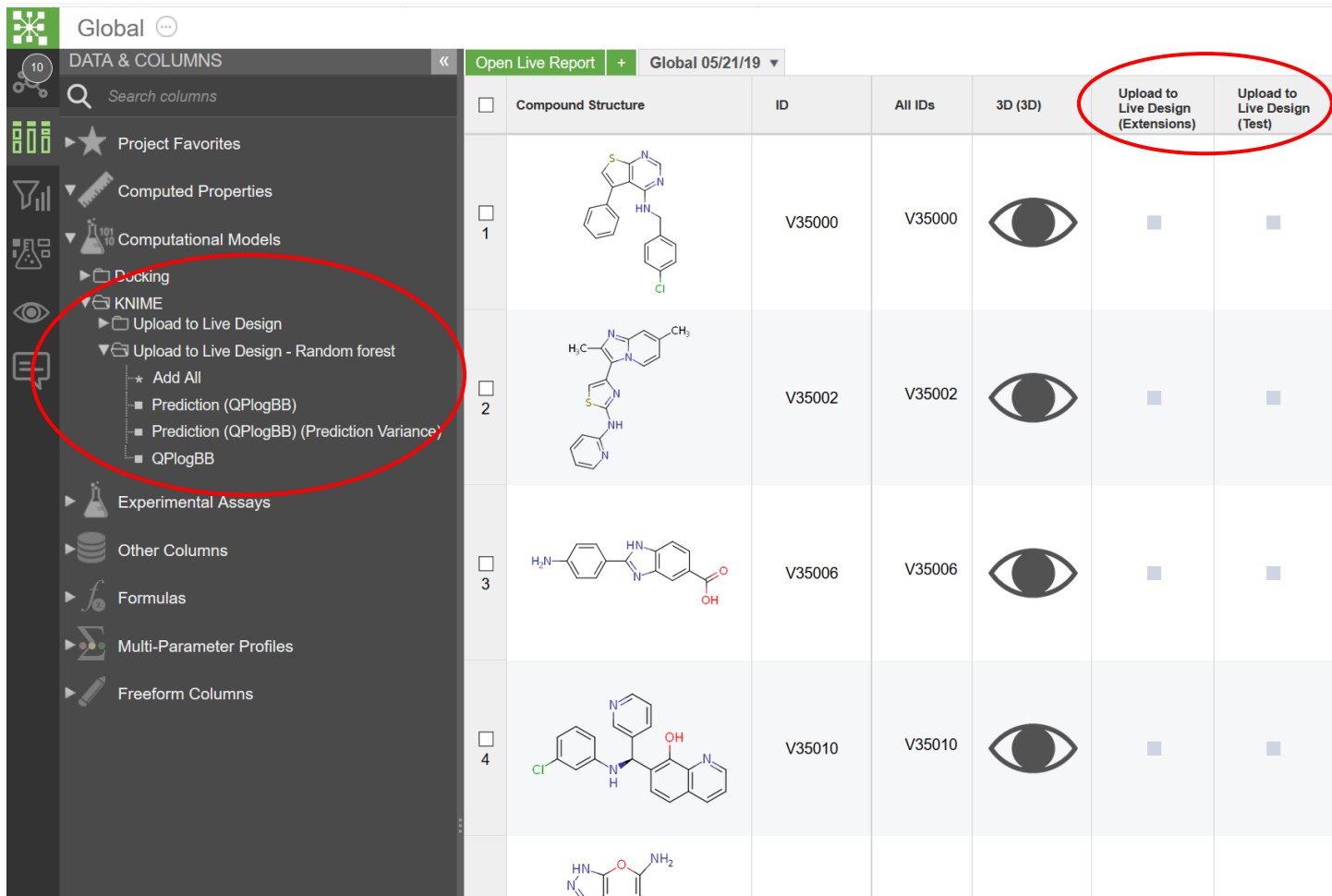
- The extra argument and extra file fields are populated automatically
 - For the nodes tagged with *%input%*
 - Find the list of supported nodes in the output of the Get help node with `$SCHRODINGER/run KNIME_batch.py` and `-print_allowed`
 - In a Parametrized model the CSV reader node taking the data from the LiveReport must be tagged with *LiveReport*
- These fields can be exposed in the Parametrize model panel
 - Changing the Parameter source on the model Admin page



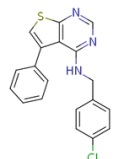

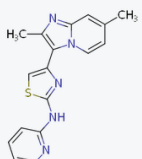

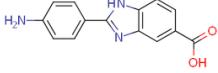

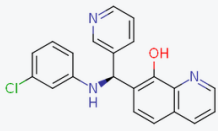

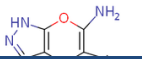
MODEL DATA			
NAME	PARAMETER TYPE	DATA ⓘ	PARAMETER SOURCE
extra argument 1 (20927)			
extra argument 1	Text	Parent Data: -dummy -region 'c1cccc1'	Set Default ▾
extra argument 2 (20942)			
extra argument 2	Text	Parent Data: -dummy -mutable false	Set Fixed ▾
extra argument 3 (20924)			
extra argument 3	Text	Parent Data: -dummy -dummy	Set Fixed ▾

Upload as LiveDesign model node – Example

- The workflow is uploaded as Model to LiveDesign
 - Using a dedicated KNIME protocol
 - Add or ask your Solution Architect to add the generic Protocols to your LiveDesign host
 - The workflow is run on the LiveReport structures and new columns are added



The screenshot displays the Schrodinger LiveDesign interface. On the left, a sidebar titled 'Global' contains a 'DATA & COLUMNS' section. Within this section, the 'KNIME' folder is expanded, showing a workflow 'Upload to Live Design - Random forest' which is circled in red. The main panel on the right shows a table of compound structures with columns for 'Compound Structure', 'ID', 'All IDs', '3D (3D)', and two 'Upload to Live Design' buttons (one for 'Extensions' and one for 'Test'), both of which are also circled in red.

	Compound Structure	ID	All IDs	3D (3D)	Upload to Live Design (Extensions)	Upload to Live Design (Test)
<input type="checkbox"/>		V35000	V35000		<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>		V35002	V35002		<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>		V35006	V35006		<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>		V35010	V35010		<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>						

KNIME computational models and protocols

- **Protocols**

- Generic protocols
 - KNIME Workflow
 - Takes the 'Compound Structure' column (ligands in 2D) as input
 - KNIME Workflow - 1 column input
 - Takes 1 column from the LiveReport as input (3D structure, FEP map, string...)
 - Selected when executing the corresponding Parametrized model
 - Use as template to create customized protocols for specific scenarios
- Run KNIME_batch.py from the Schrodinger Suite
- Available under: \$SCHRODINGER/knime-v*/data/
- LiveDesign_admin.py -type protocol -mode upload -file KNIME_Workflow_20-3.json ...

- **Outputs**

- String, number, image columns
- 1 structure column (ligand, pose viewer or complexes), with possibly several poses, a surface or pharmacophore hypothesis

Upload as LiveDesign model node – Overwrite option

To update an existing model. eg:

- QSAR model building
 - Local KNIME workflow
- QSAR prediction in LiveDesign

1. Prototyping

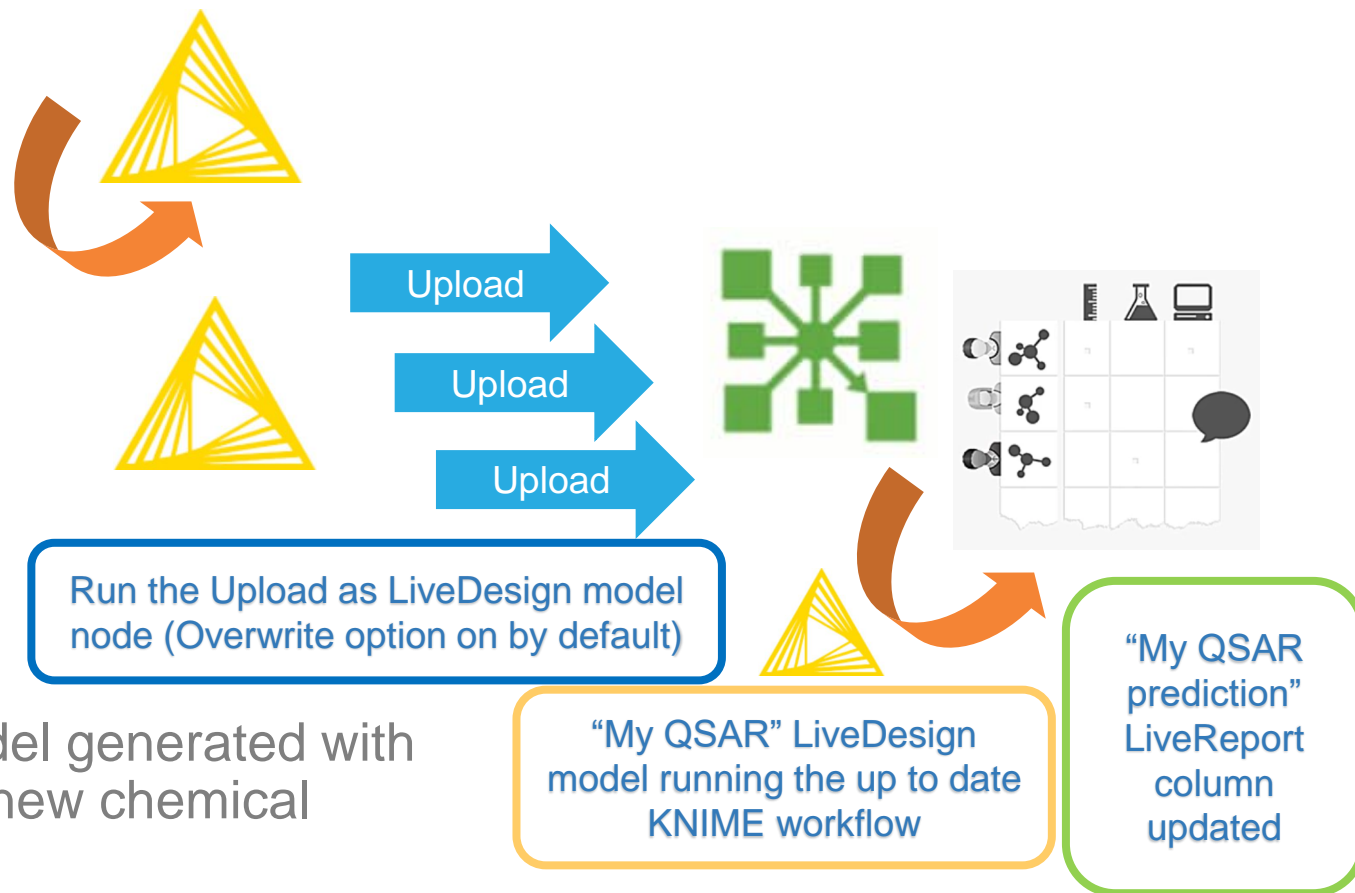
- Workflow fixes tested locally
- Then tested in LiveDesign

2. Improvements

- Uploaded and tested in LiveDesign

3. Updates

- With new versions of the QSAR model generated with the QSAR building workflow run on new chemical structures



Summary

- KNIME computational models
 - Some ready to be installed and used
 - Growing set of models derived from the KNIME workflow examples available on <https://hub.knime.com>
- Deploy to LiveDesign
 - Through a python script (no KNIME installation required)
- Customization
 - Replace system specific files (outside of KNIME)
- Model creation or improvement
 - 1 click to create or update the model from KNIME
 - No need to use LiveDesign admin page
- Computational model execution
 - Same look and feel
 - KNIME run behind the scene on the LiveDesign host

The modelers can more easily deploy their methods to LiveDesign to the medicinal chemists



KNIME Hub > schroedinger > Spaces > Public > LiveDesign_models

	ADME	
	Atropisomerism	
	Bioisosteres	
	Docking	
	Docking and protein surface	
	ESP surface	
	Ensemble docking	
	Installation test	
	Ligand CNS desirability plot	
	Ligand CNS desirability range plot	
	Ligand alignment	
	Ligand property radar plot	
	Low energy conformation	
	My workflow running on a KNIME server	
	Protonation forms	
	Random forest	

Deploy your computational methods in LiveDesign

Upload and run KNIME workflows

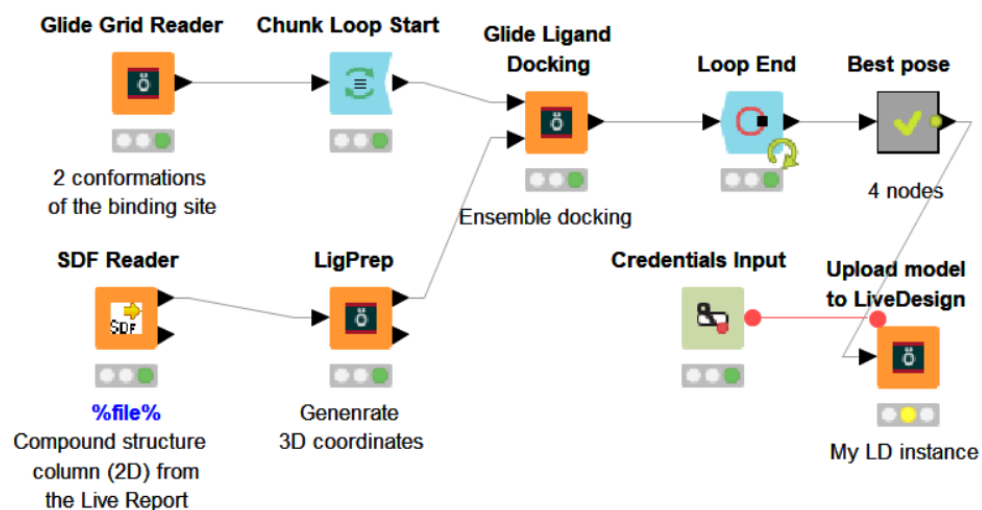
- **Flexible**
 - Especially suitable for more complex or specific workflows
 - Visual programming and overview of the workflows
- **Simple and quick**
 - Create workflows yourself or edit the parameters of some provided by Schrodinger
 - Upload and update the Computational models in 1 click
- **Open to third party tools**
 - Community nodes: RDkit, Lilly, Vernalis, R scripting nodes...
 - Other provider nodes: Chemaxon/Infocom, MOE, BioSolveIT, Cresset...
 - Any command line tool
- All Computational models have the same look and feel in LiveDesign



KNIME vs. Python

KNIME workflow

- Visual programming



- Upload or update the computational model in LiveDesign in 1 click

Python script

- Scripting
 - 300+ lines of code
- LiveDesign Administration panel
 - Set up the command, inputs and outputs



LiveDesign Admin

Site administration

MODEL AND PROTOCOL CONFIGURATION

Drivers

Protocols

Models

Parameterized Models

Change

Change

Change

Change

DATA

PARAMETER SOURCE

-

From Parent

TYPE

Image (e.g. .png, .jpg)

Real

3D Structure Ligand

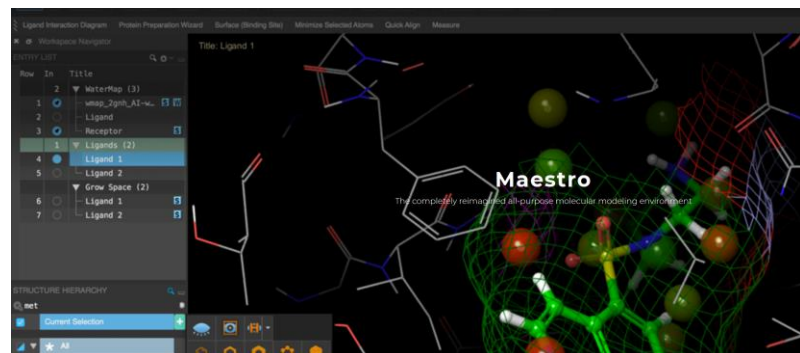
3D Structure Target

String

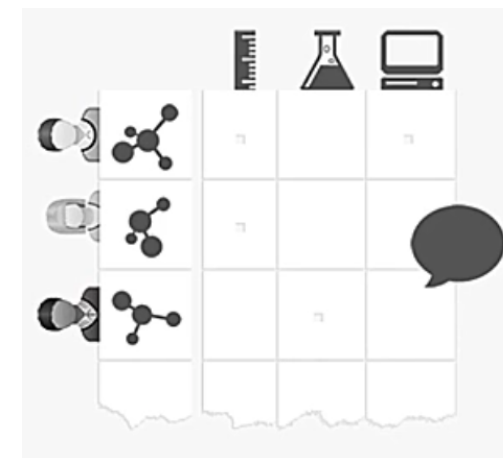
Deploy computational methods in LiveDesign



- Maestro tasks



- In LiveDesign



Deploy computational methods in LiveDesign



automation

Automation tool

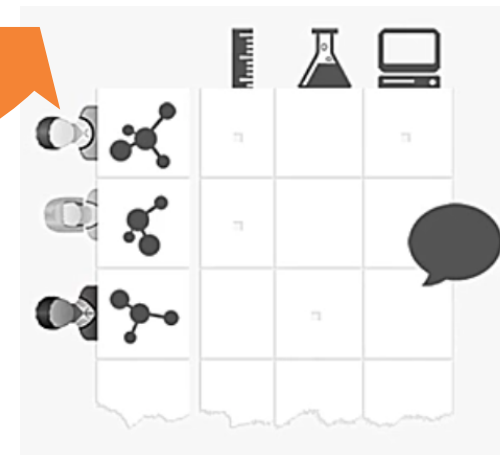
Computational
model



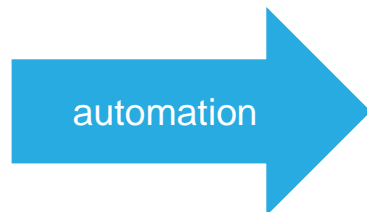
Maestro tasks:

- 1 command or tool
eg Glide docking in 1 grid
- Several tools
including pre and post
processing steps
- Third party tools

...



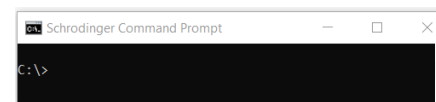
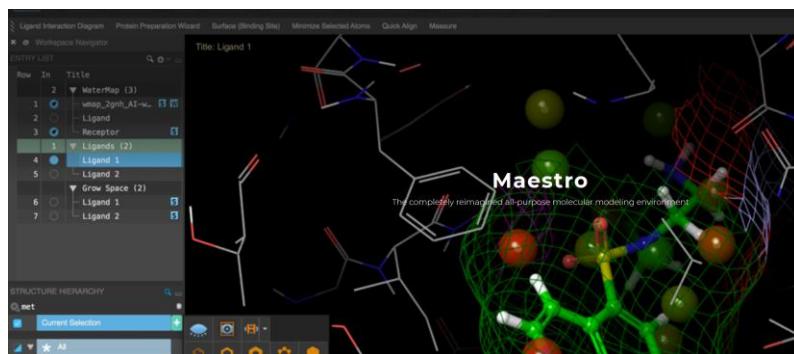
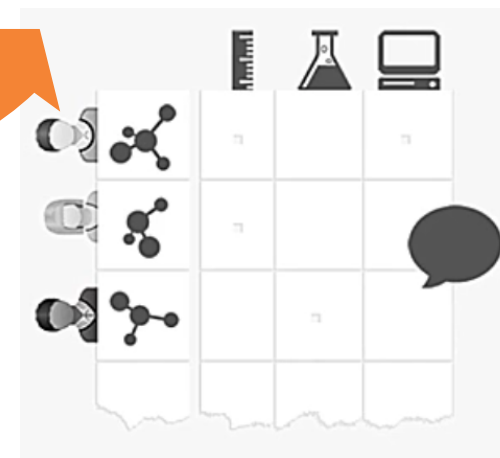
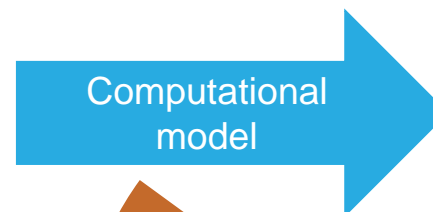
Automation tools



Automation tools:

- Command lines or VSW
- Python script
- Visual programming: KNIME, Pipeline Pilot

...

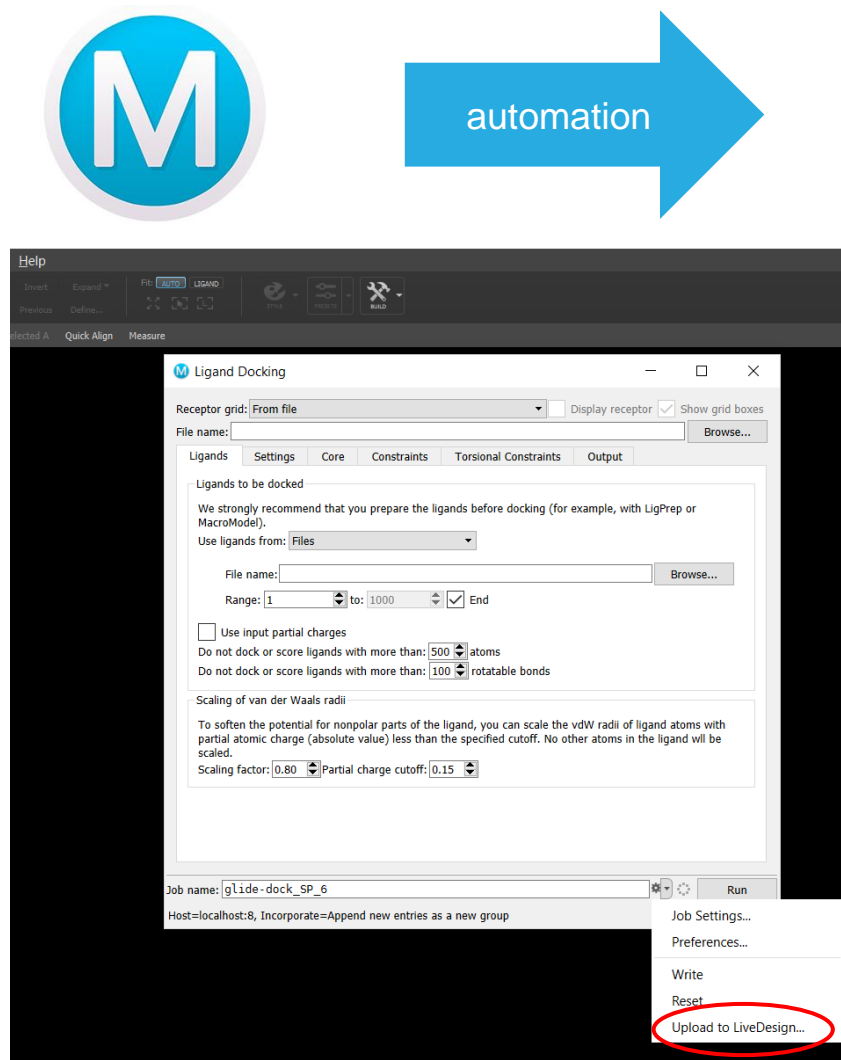


```
import simpleknn
from bigfile import BigFile

if __name__ == "__main__": PYTHON API
    trainCollection = 'toydata'
    nimages = 2
    feature = 'f1'
```

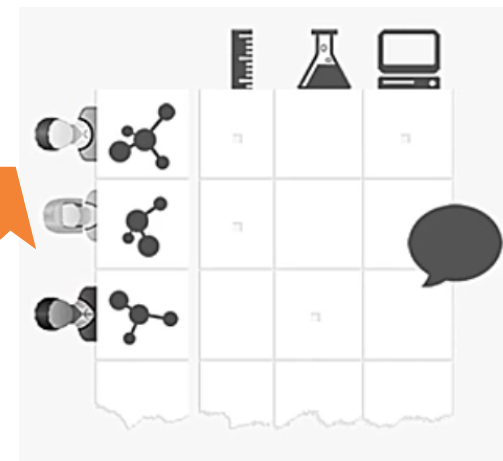


Glide docking from Maestro to LiveDesign



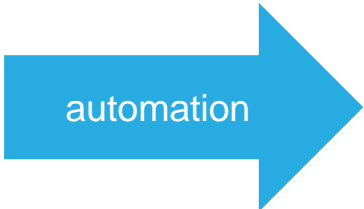
- Glide python script

Computational
model



- Other specialized python scripts
are available in LiveDesign
- But what about a more complex docking workflow?
eg Docking in several protein
conformations

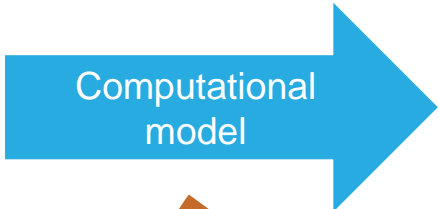
Create Protocols and Models manually



```
Schrodinger Command Prompt
C:\>

import simpleknn
from bigfile import BigFile

if __name__ == "__main__": PYTHON API
    trainCollection = 'toydata'
    nimages = 2
    feature = 'f1'
```



COMMAND	DRIVER
ID 3960 export SCHRODINGER=/mnt/suites/suite2019-2 && \$SCHRODINGER/run \${pythonfile:FILE-INPUT} \${SDF-FILE} --maxconf \${MaxNumOfConformers:NUMERIC-INPUT} --smarts \${matching smarts:TEXT-INPUT} --force_field \${forcefield:TEXT-INPUT}	1

ID 3961
cat results.csv
[+ Add Another Command](#)

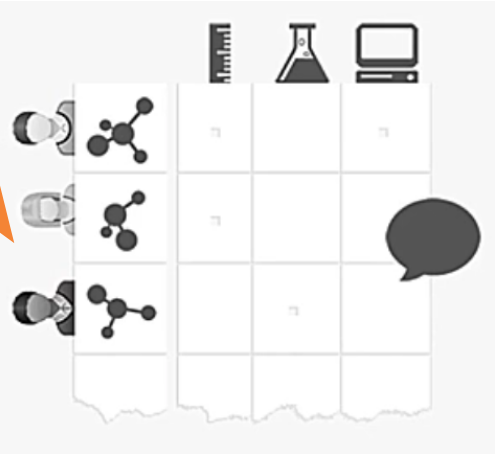
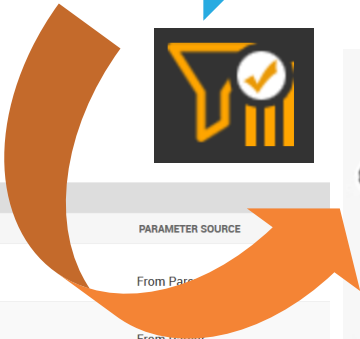
MODEL DATA			
NAME	PARAMETER TYPE	DATA	PARAMETER SOURCE
pml_script (21224)			
pml_script	File	-	From Parent
Glide Runner Script (21226)			
Glide Runner Script	File	-	From Parent
Grid File (.zip) (21225)			
Grid File (.zip)	File	-	From Parent
Input File (.in) (21227)			
Input File (.in)	File	-	From Parent

PREDICTIONS			
NAME (IN MODEL)	DISPLAY NAME	TYPE	DECIMAL PLACES
ID 12826			
diagram	Ligand Interaction Diagram	Image (e.g. .png, .jpg)	0
ID 12827			
score	Score	Real	2
ID 12828			
ligand	Ligand	3D Structure Ligand	0
ID 12829			
protein	Protein	3D Structure Target	0
ID 12830			
status	Run Status	String	0
+ Add Another Prediction			

Site administration

MODEL AND PROTOCOL CONFIGURATION

- Drivers
- Protocols**
- Models
- Parameterized Models
- Tasks



Upload KNIME workflows to LiveDesign



automation

KNIME
workflow



Computational
model



- Several tools/steps in Maestro
- Third party tools
 - RDkit
 - Vernalis' PDB query tools
 - MOE
 - Cresset
 - Spotfire
 - ...
- Any command line tool
eg Tripos Unity

- **Visual programming**
And a generalization of the
Glide Upload mechanism:
- **Flexible**
- **Easier** and less error
prone than in LiveDesign
Administration page
configuration



Docking in several receptor conformations



automation

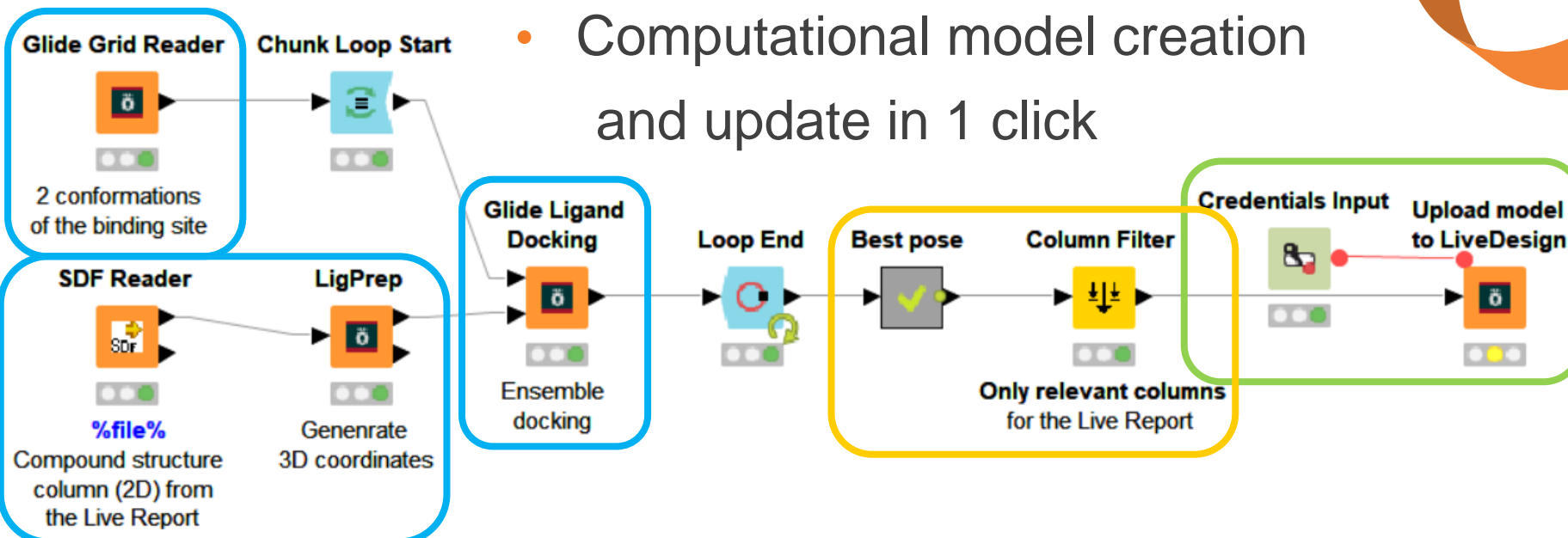
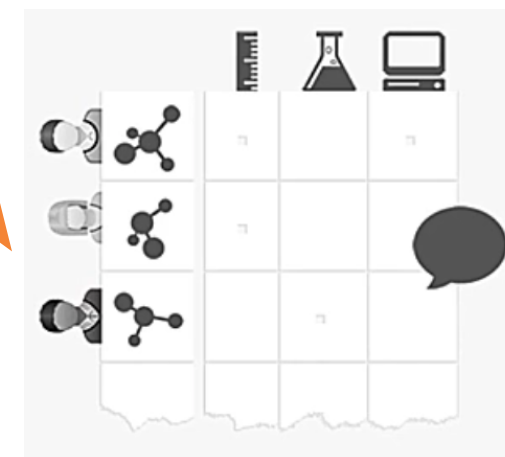
KNIME
workflow



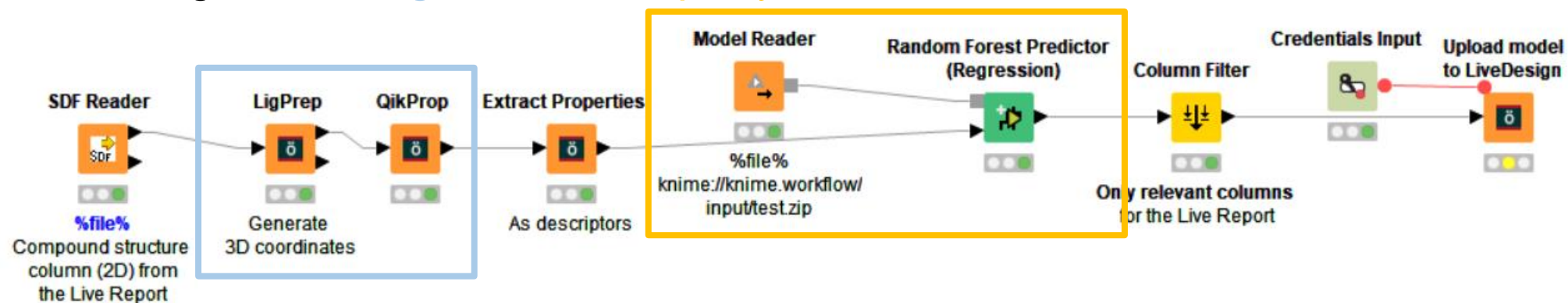
Computational
model



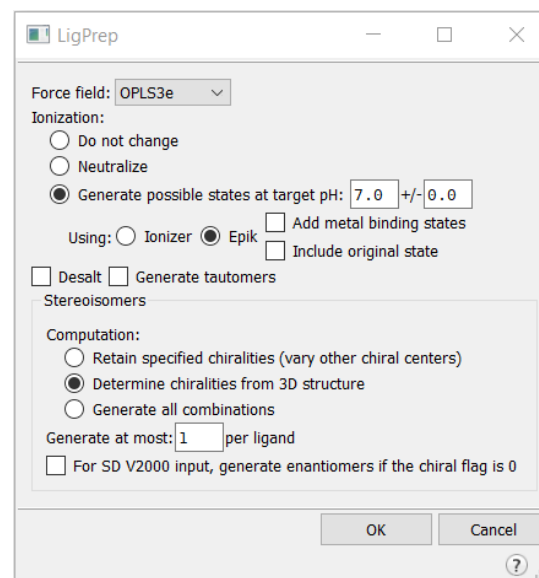
- More complex/different workflow
- Other output columns
- Computational model creation and update in 1 click



- Combining Schrodinger and third party nodes



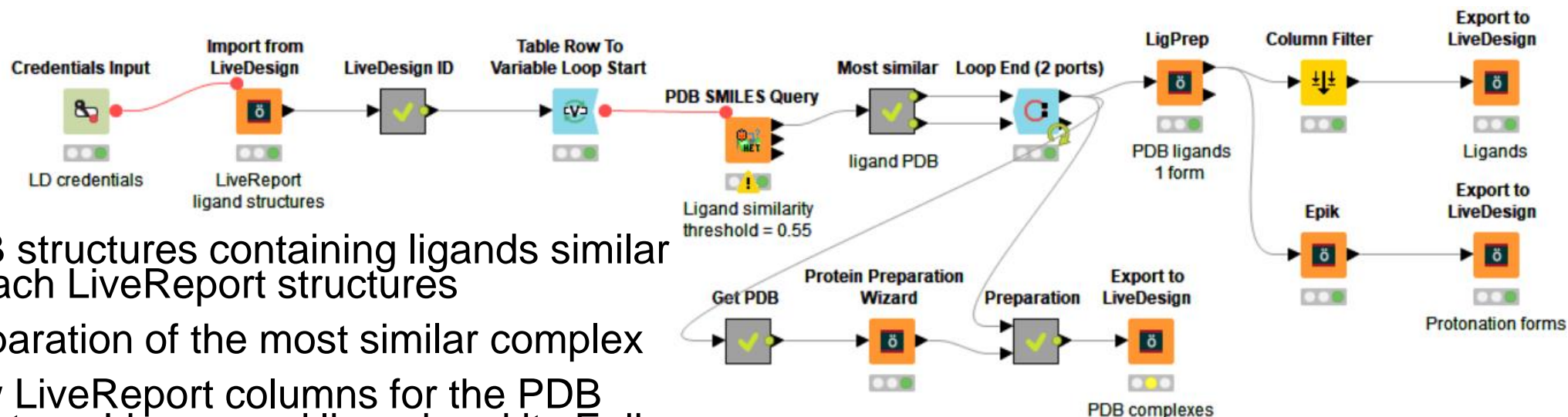
- Visual coherence
between the KNIME
nodes and Maestro
panels



- Run any command line tool
in the Chemistry external tool node

Export to LiveDesign – structure columns

- PDB structures containing ligands similar to each LiveReport structures
- Preparation of the most similar complex
- New LiveReport columns for the PDB structure, Ligprepped ligand and its Epik protonation forms.



	Compound Structure	ID	Docking complexes (3D)	Docking poses (3D)	2D view	PDB ligand (3D)	Epik (3D)	PDB (prepared with version)	PDB (PDB ID)	PDB (3D)
1		CHEMBL192						2020-1 2020-1	1TBF 1TBF	
2		CMPD-10182						2020-1 2020-1	1TBF 1TBF	

10 Compounds • 1 Selected 32 Columns (4 Hidden)

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Contents Styles

- ☐ A2A Watermap (3D)
- ☐ COX1 (3D)
- ☐ Docking complexes (...)
- ☐ Docking poses (3D)
- ☐ Epik (3D)
- ☐ Ligprep (3D)
- ☒ PDB (3D)
- ☒ Protein/Other
- ☒ CMPD-10182

Export

