Deployment of ADMET Predictor®
as a Solution for
In-Silico Modeling of ADMET Properties

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Webinar Outline

- ADMET Predictor modules
- License and deployment options
  - Standalone license versus network license
  - Deployment options
- License checkout in graphical user interface (GUI)
  - FULL versus VIEWER mode
- Chemistry module

…

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- Analysis/visualization tools
- MedChem Designer license
- Command line options
- Wokflow Tools: KNIME
  - Configuring nodes
  - Example workflow

ADMET Predictor® Modules

PCB
pKa, Lipophilicity
Permeability, Solubility,
Transporters

HTPK
Simulation-Based
Estimates of PK
Parameters and
Optimal Dose (Human
or Rat)

Toxicity
Cardiac, Liver, Acute,
Carcinogenicity,
Sensitization,
Environmental

Metabolism
CYP, UGT, AOX
Substrate/nonsubstrate,
Sites of Metabolism,
Kinetics, Inhibition,
Total HLM/RLM Clearance

"Core" & Chemistry
Free

MedChem Studio™
Clustering, R Tables, Design, SAR

ADMET Modeler™
QSPR Model Building

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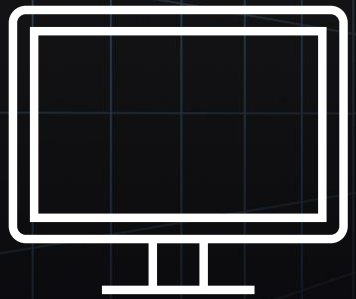
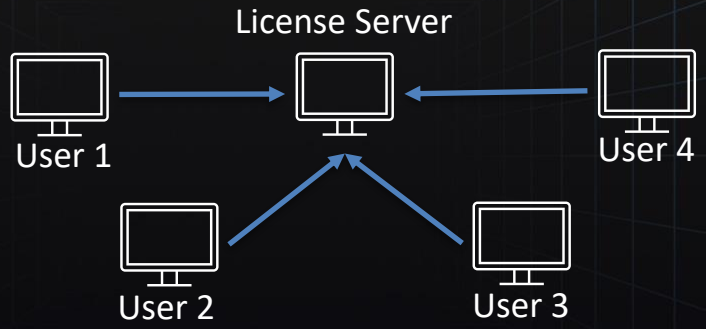
Deployment Options



Standalone license options:

- Licensed issued for running on a single computer
- Used by a single person or shared (eg, not a named user/seat)
- Remote Desktop Protocol



Network license options:

- AP is installed on individual computers
- License server is contacted when AP is started
- Allows users to have customized settings

Cloud Options:

We offer Cloud computing hosted by AWS

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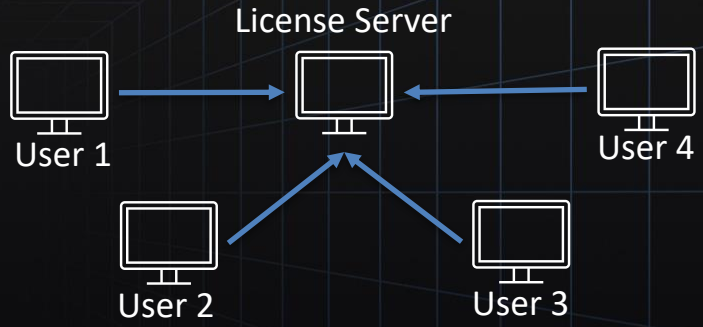
License Options

Standalone license

- Software can only be used on single computer
- Can run multiple sessions

Upgrade is Free !



Network license

- License server – hosts Flexera
- Software can be used on any computer that can communicate with server
- If all licenses are checked out then program opens in VIEWER mode

Standalone and network licenses are the same price!

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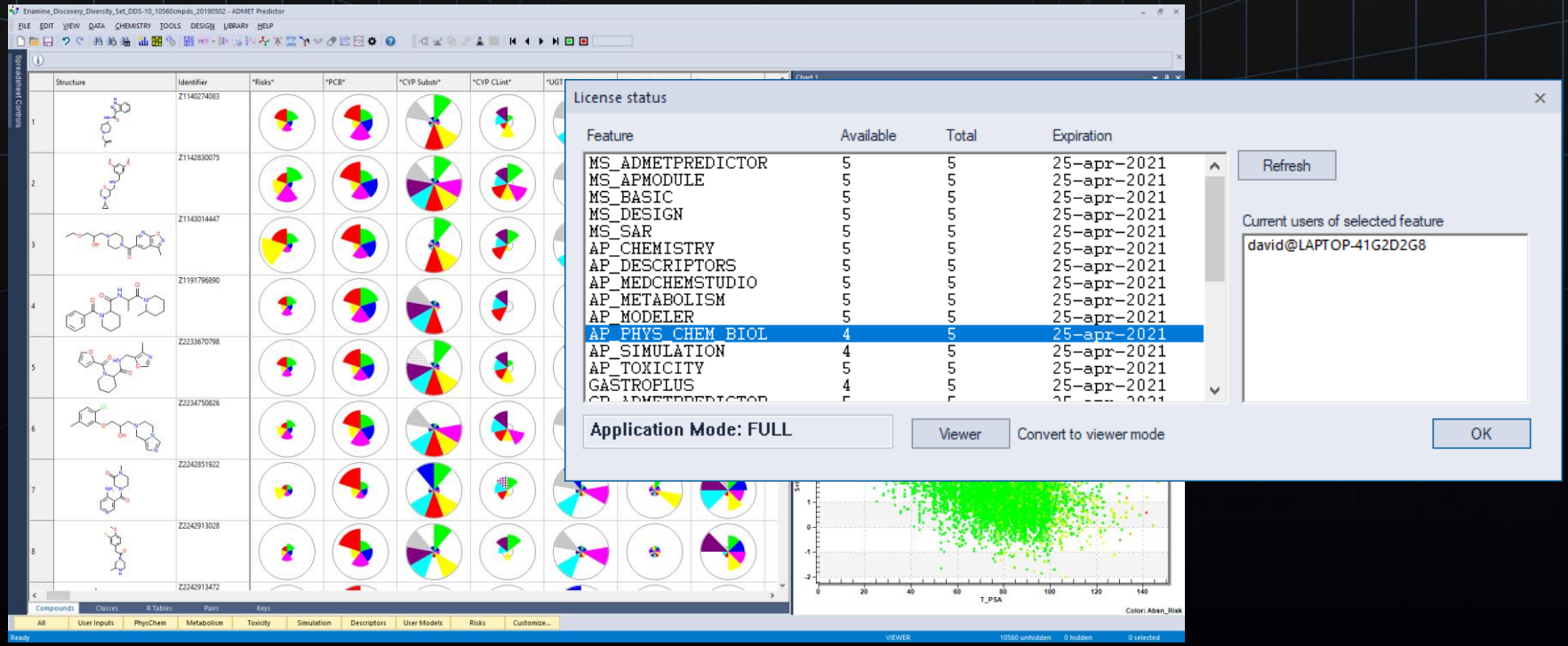
Deploying Native ADMET Predictor®



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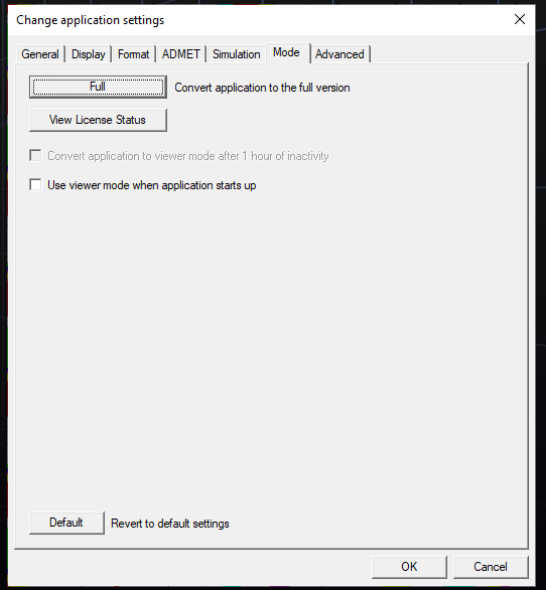
Native AP Licensing

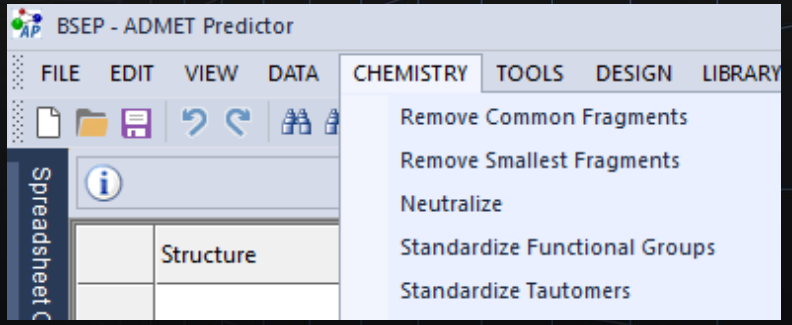
- No licenses consumed in visualization
- Can start in Viewer Mode
- Licenses consumed only in active calculations
  - Used and retained
  - Used and returned to the pool
- Can revert to Viewer Mode if unused
  - Manually
  - Automatically after a set time (set in preferences)

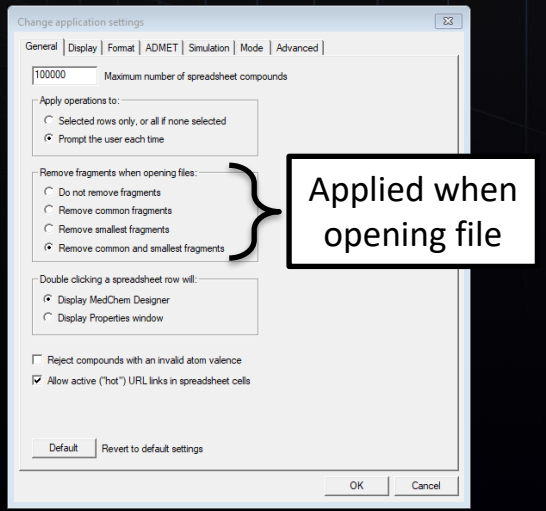


Chemistry Module

The commands in the Chemistry module standardize molecules

- Remove common and smallest fragments are applied when a structure file is opened
- Neutralize adds or removes hydrogens from charged atoms
- Standardize functional groups converts groups to a standard form
  - N(=O)(=O) converted to [N+]([O-])=O
- Standardize tautomers converts tautomers to the same representation





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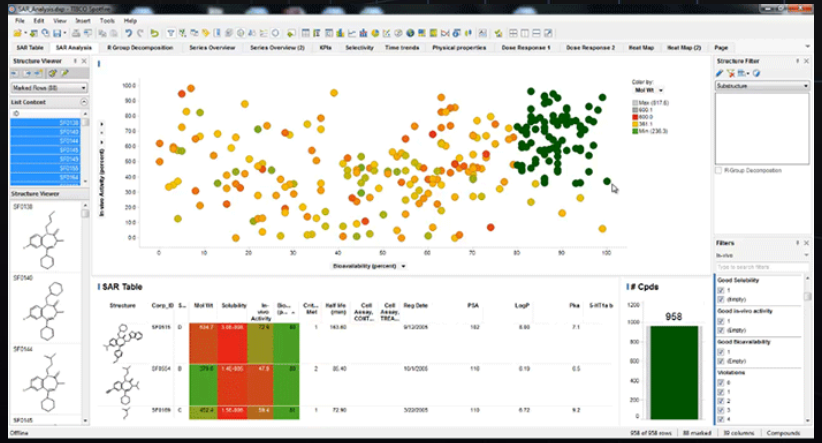
ADMET Predictor Deployment Options

Command Line

```
Options :
   -t <filetype>     type of input data [SDF, RDF, MOL, QMD, or SMI]
                     This option is required.
   -d <dimension>    dimension of input data [2D (default) or 3D]
                     WARNING: 3D is not allowed for QMD or SMI files.
   -u <filetype>     type of the output file [DAT (default), SDF, or RDF]. Results are saved in
                     *.dat, *_ADMET_2D.sdf, or *_ADMET_2D.rdf files, respectively.
                     Descriptors are not output in SDF/RDF formats.
   -m <module, ...>  limit output to the specified combination of one or more modules
                     separated by comma: PCB = Physico-chemical and Biopharmaceutical,
                     MET = Metabolism, TOX = Toxicity, SIMFaFb = Simulated percents absorbed
                     and bioavailable, SIMDose = Simulated optimal dose, GLB = Global,
                     USR = User models, DSC = Descriptors.
   -l                activate leave-one-out in all associative models
   -g                Write GastroPlus Drug Table (in *_DrugTable.txt) and GastroPlus Acid/Base Table
                     (in *_AcidBaseTable.txt) using default settings.
                     Note: this option invalidates all other output formats (DAT, SDF, RDF)!
   -p <pH>           pH for pH-sensitive ADME models [ default 7.4 ]
   -i                also calculate ionization descriptors at indicated pH. Warning: use of this
                     option invalidates ADMET predictions other than S+pKa!
                     Note: -i must be used with -p, ignored otherwise.
   -a <upper_limit>  exclude acidic pKa above the <upper_limit>
   -b <lower_limit>  exclude basic pKa below the <lower_limit>
   -o                include aliphatic -OH groups
   -n                include aliphatic amides
   -c                include carbon protonation
   -k <num_igroups>  skip molecules with more than <num_igroups> ionizable groups
   -h                write version + usage information and quit
   -x                exclude predictions outside models' applicability domains. In these
                     cases, predicted values are replaced by the '~' (tilde) character.
   -y                report predictions outside the chemical scope of models in a separate tab-delimited file *.ots.
                     report regression uncertainty estimates of models in a separate tab-delimited file *.unc.
                     May be invalidated by options -z and -w; see below.
   -w <workflow>     save pKa microstates in an SDF file *_ADMET_2D.sdf formatted in accordance with the given
                     <workflow> argument: MC = Medicinal Chemist, PC = Physical Chemist, CI = Cheminformatician,
                     CC = Computational Chemist. See User Manual. If option -u is SDF, then all ADMET predictions
                     are also included in *_ADMET_2D.sdf. Other -u settings are nullified and cause option -y to
                     be ignored. This option supersedes option -z.
   -s <threshold>    skip from the SDF output pKa microstates whose contributions are smaller than the given
                     numeric <threshold>. Threshold must be given in %; it's default value is 1. This option works
                     only in connection with option -w.
   -z                save all predictions including pKa microstates in a separate RDF file (*_ADMET_2D.rdf)
                     suitable for constructing the hierarchical tables in ISIS/Base(TM) databases.
                     If option -u is RDF then all ADMET predictions are also included in *_ADMET_2D.rdf.
                     Other -u settings are nullified and cause option -y to be ignored.
   -path <path>      optional path to non-default folder containing model files.  If specified,
                     this folder must exist.
   -license <path>   optional path to Flexera license.  Typical values are @localhost or port_num@xx.xx.xx.xx
Demos >
```

Alternate Front End



- TIBCO Spotfire®
- Command-line access (Windows + Linux)
- Workflow platforms
  - Pipeline Pilot
  - KNIME

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Parallelization and Productivity

- Multi-threaded calculations available for all descriptors and models (including HTPK)
- Calculation benchmark with all ADMET properties

10,560 diverse compounds from Enamine Diversity Set

  - AP 9.5: 3min. 30 sec (50 cmpds/sec)
  - AP X with multi-threading: 58 sec (182 cmpds/sec)

- No special licenses necessary to activate multi-threaded mode
- Only 1 license of the feature is consumed while multi-threading

4x to 6x performance improvement, depending on hardware

- Hardware: DELL Vostro Laptop with Intel® Core™ i7-8550U CPU 1.8 GHz, 16 GB RAM, 64-bit, running Windows 10.

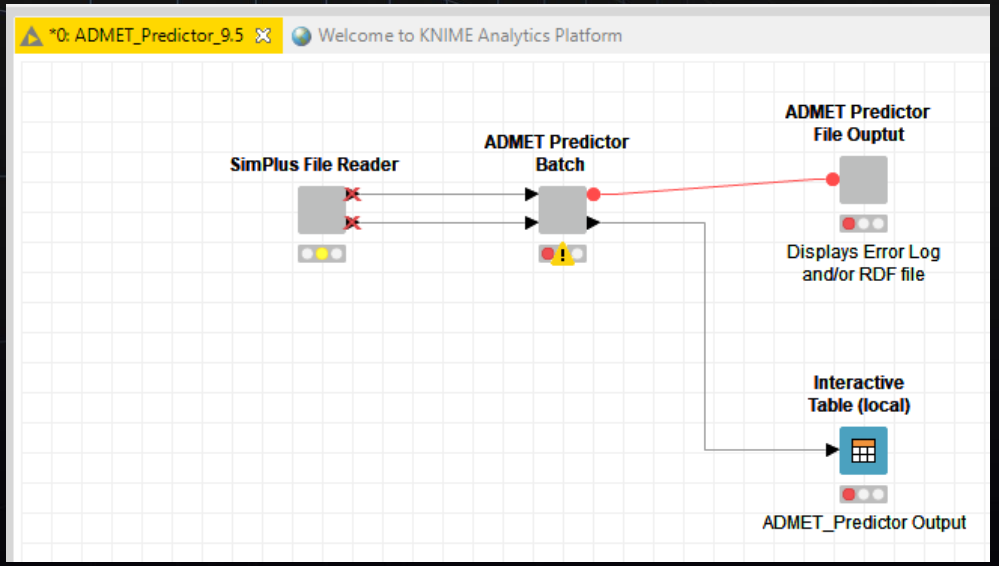
MedChem Designer License

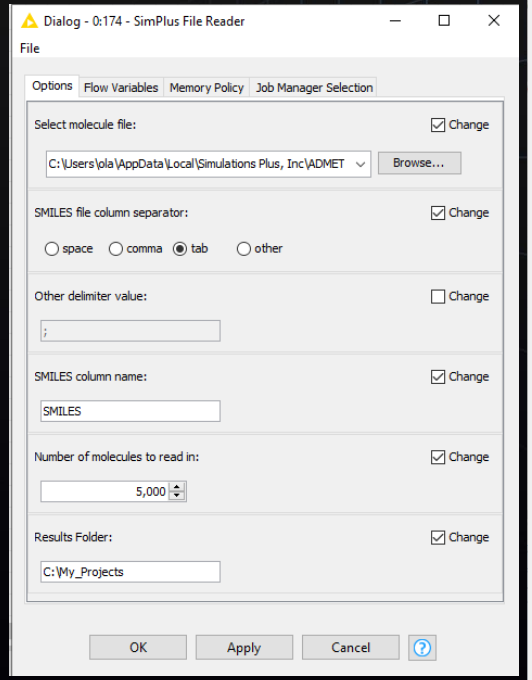
- Exists as standalone free-for-all application with thousands of users around the world. Also exists in ADMET Predictor®.
- A MD_ADMETPREDICTOR feature is issued for each ADMET Predictor module that is licensed (except HTPK Simulation and Descriptors)
- MedChem Designer can display up to 100 compounds
- ADMET Properties can be computed depending on the licensed modules
- Now includes several prediction and display features from ADMET Predictor, including pKa microstate display, Atomic Properties windows, logD and solubility versus pH curves, and HPTK features such as %Fa/%Fb prediction.

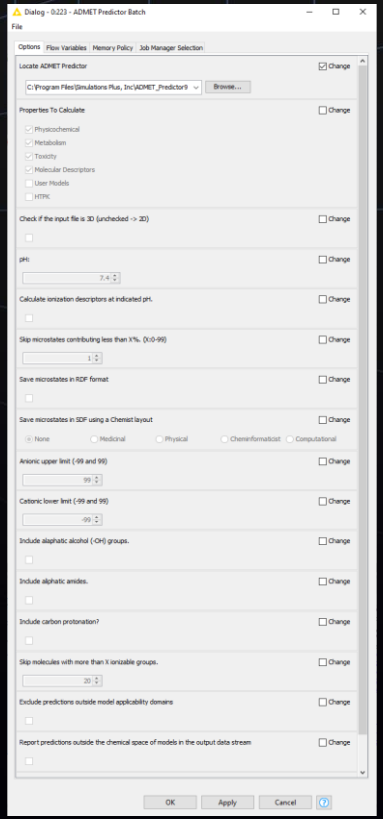
Command line Options

- Output from running ADMET Predictor can be read into other programs
- Options include ADMET property output, HTPK results, descriptors, control of pH, output for specific workflows (medicinal chemistry), out of scope predictions…etc

Example of KNIME Workflow







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Thank You

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