

Open Systems Pharmacology

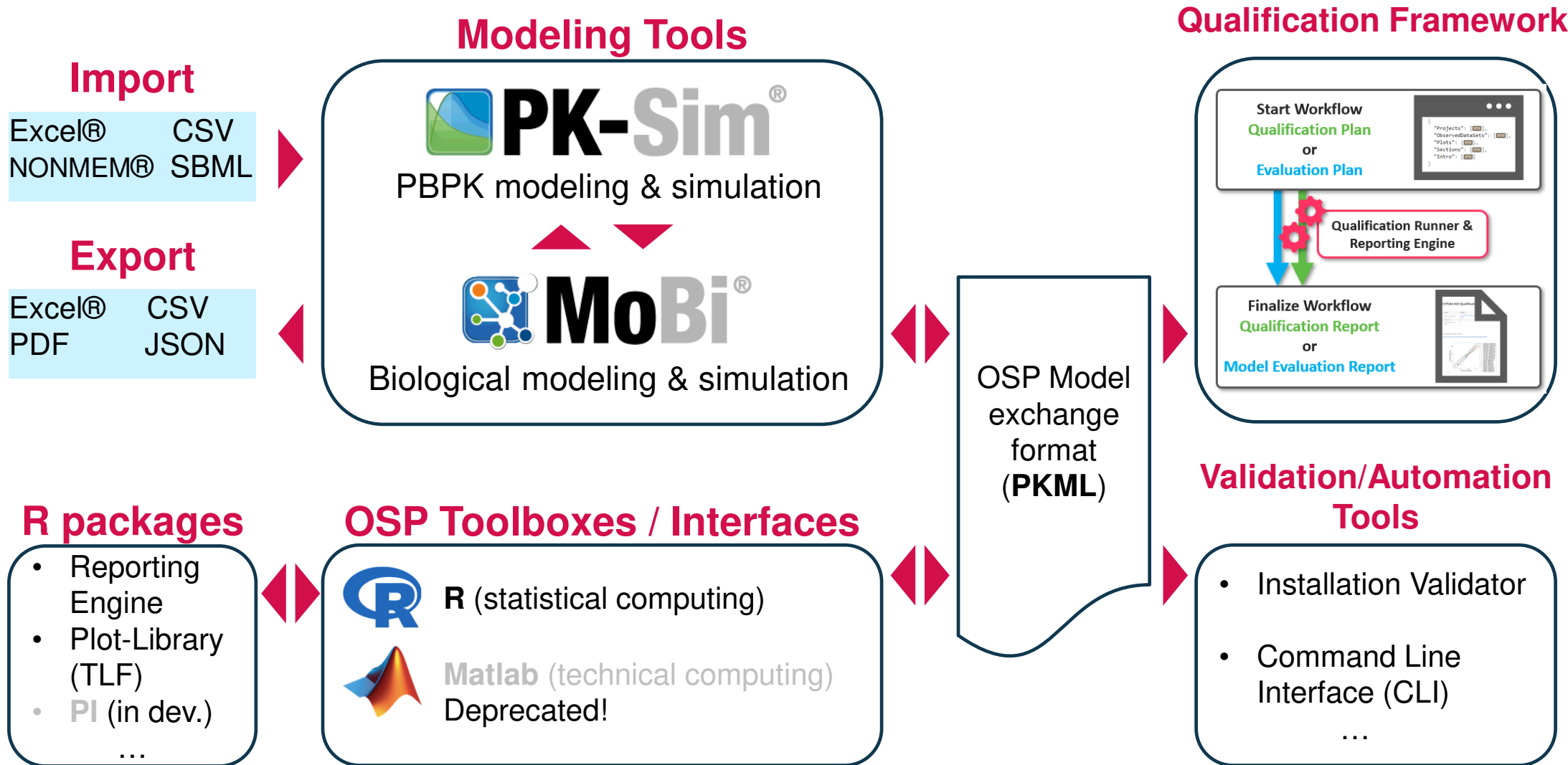
MoBi and R-Toolbox

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April 2021

- OSP software landscape
- PK-Sim vs. MoBi: when to use
- MoBi: Overview
- MoBi: modeling concepts
 - Building blocks
 - „Generic“ modeling
- R-Toolbox

OSP software landscape

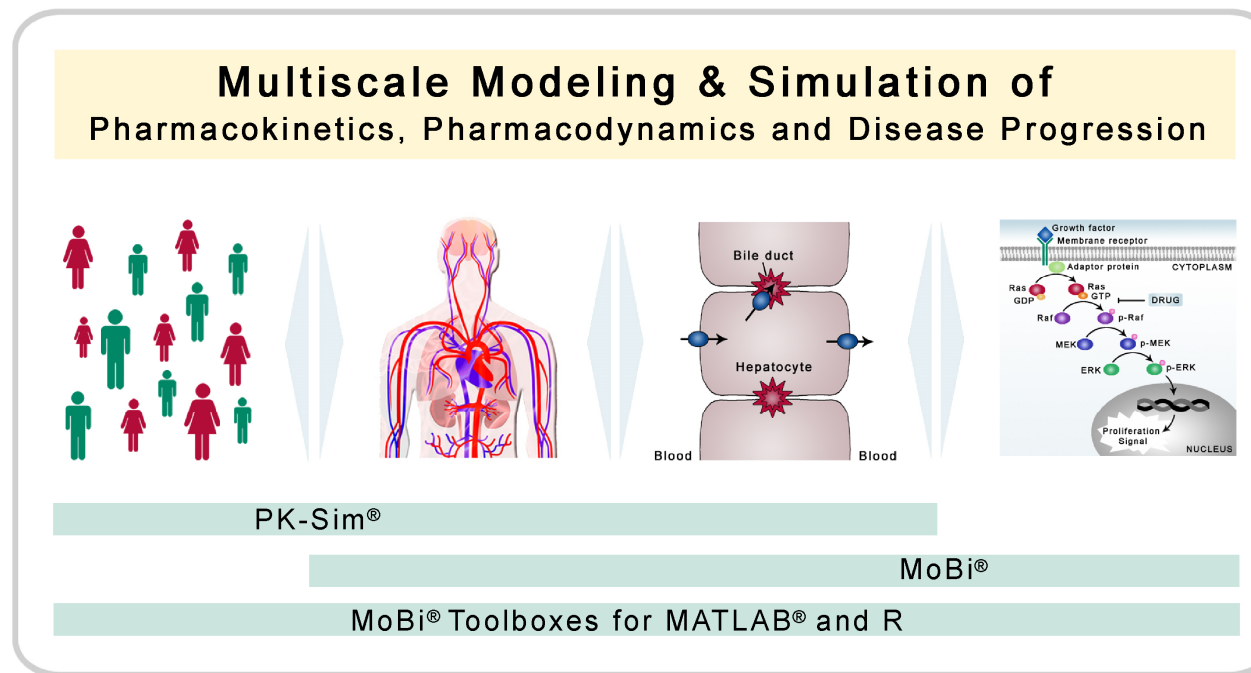


OSP Modeling Tools: PK-Sim and MoBi

- PK-Sim® is a comprehensive software tool for **whole-body physiologically based pharmacokinetic (PBPK) modeling**.
- Like most PBPK modeling tools, **PK-Sim® is designed for use by non-modeling experts and only allows for minor structural model modifications**.
- It enables rapid access to all relevant anatomical and physiological parameters for humans and common laboratory animals contained in the integrated database.
- Users can access different PBPK calculation methods, which enables fast and efficient model building and parameterization.
- PK-Sim® offers different model structures to choose from, e.g., to account for important differences between small and large molecules.
- More importantly, PK-Sim® is fully compatible with the expert modeling software tool MoBi®, thereby allowing full access to all model details including the option for extensive model modifications and extensions.

OSP Modeling Tools: PK-Sim and MoBi

- MoBi® is a systems biology software tool for multiscale physiological modeling and simulation.
 - Within the restrictions of ordinary differential equations, almost any kind of (biological) model can be imported or set up from scratch.
 - Examples include biochemical reaction networks, compartmental disease progression models, or PBPK/PD models.
 - However, de novo development of a PBPK model, for example, is very cumbersome such that the preferred procedure is to import them from PK-Sim®.



PK-Sim vs. MoBi: main features

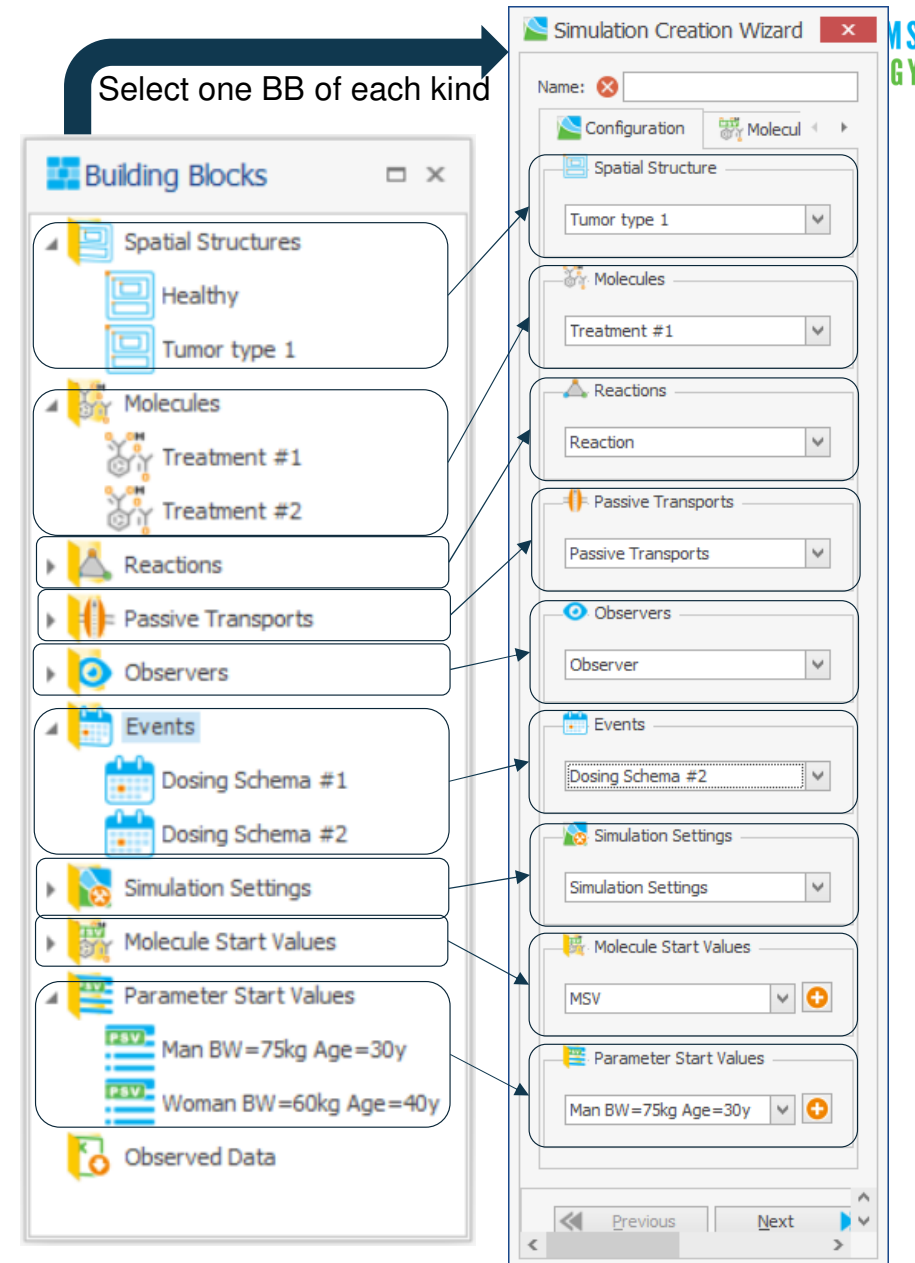
| | PK-Sim | MoBi |
|---|--------|----------|
| Integrated databases with: <ul style="list-style-type: none"> - anatomical and physiological properties of humans and laboratory animals - protein expressions - whole-body model structures for small molecules and biologics - prediction models for tissue partition coeff. / cellular and intestinal permeabilities^(*) | X | (*)X |
| Template library for: <ul style="list-style-type: none"> - optional processes (DDI / metabolizing pathways / active transporter / protein binding) - food effects / administration protocols / formulations | X | |
| Creating of individuals and populations | X | |
| Building Block (BB) Concept: Simulation creation by simple combining of previously defined BBs | X | X |
| Visualization: plotting of all calculated time courses | X | X |
| Visualization: population plots (Box-Whisker, Range, Scatter, ..) | X | |
| Fully integrated Parameter Identification (PI) Toolbox | X | X |
| Sensitivity Analysis (SA) of PK-Parameters (AUC, Cmax, ...) vs. simulation parameters. | X | X |
| Built-in working journal for manual annotation of models and simulations | X | X |
| „No limits“ modeling: modify formulas, change structure beyond templates, ... | | X |

When will we use MoBi® ?

- Changes in parameters that are not accessible in PK-Sim® .
- Structural physiological changes (e.g., adding an organ).
- PK-PD modeling (e.g., tumor growth and growth inhibition).
- Modeling of metabolic or signaling networks (non-PK models), in vivo and in vitro scenarios.
- ... (and many more)

MoBi: Building Block Concept

- MoBi® uses **building blocks (BB)** that are grouped into:
 - Spatial Structures
 - Molecules
 - Reactions
 - Passive Transports
 - Observers
 - Events
 - Molecule Start Values
 - Parameter Start Values
 - Observed Data
- Building blocks out of the above-mentioned groups can be combined to generate models.
- The advantage of building blocks is that they can be reused.
- For example, a different set of parameter start values may define a new scenario, situation, or individual.



Export from PK-Sim® to MoBi®: Where to find what

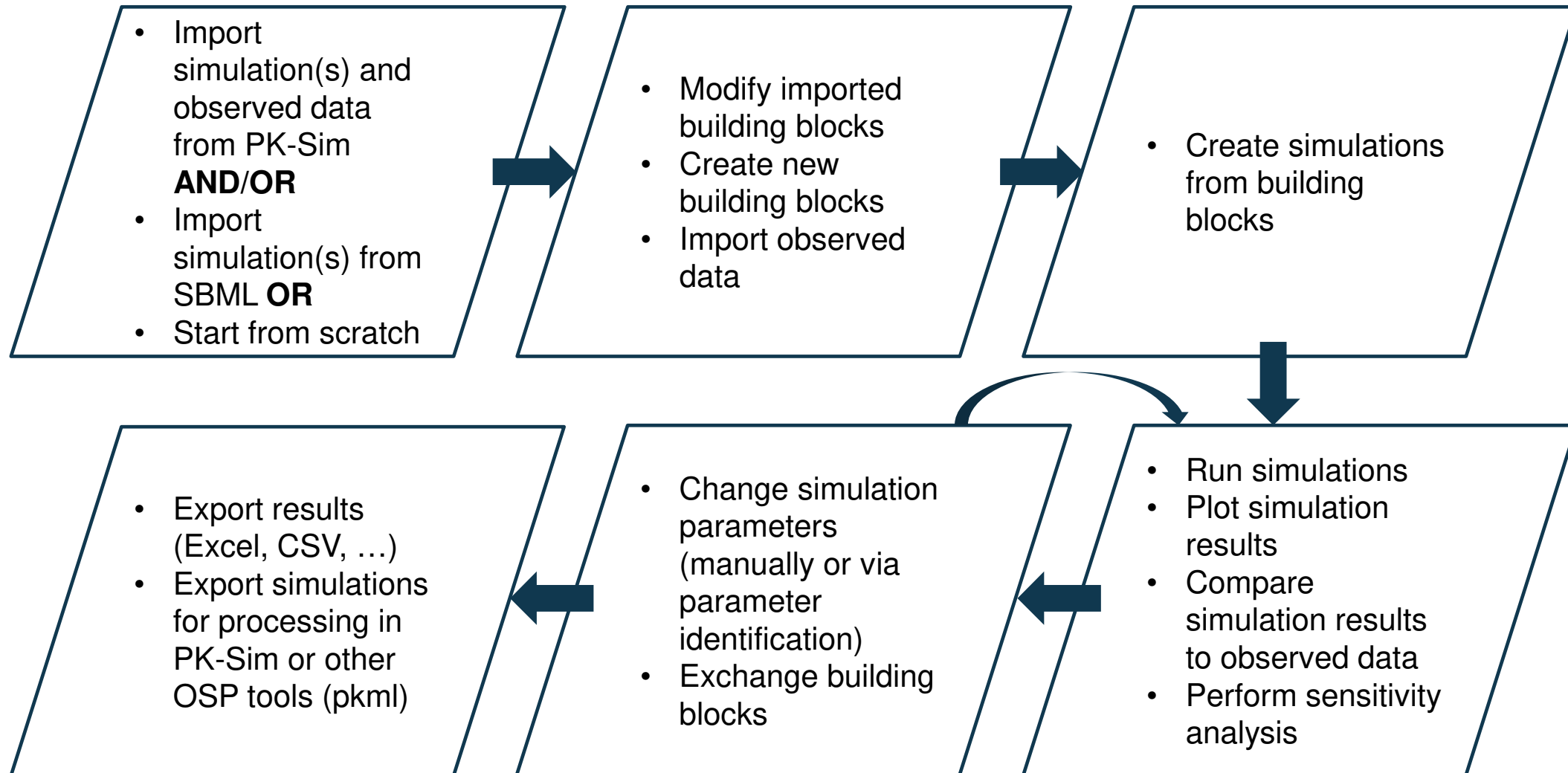
Building blocks in PK-Sim®

- Individuals
- Populations
- Compounds
- Formulations
- Administration Protocols
- Events
- Observed Data
- Observers

Building blocks in MoBi®

- Spatial structure
- Molecules
- Reactions
- Passive Transports
- Observers
- Events
- Simulation Settings
- Molecule Start Values
- Parameter Start Values
- Observed Data

MoBi: Workflow



MoBi: Quick Tour

File Modeling Parameter Identification & Sensitivity Working Journal Import/Export Utilities Views **Edit Reaction**

New Load Load From Template Insert Molecule Zoom In Zoom Out Fit to Page Add Edit

Tabs and Ribbon bar

Building Block Explorer

- Spatial Structures
- Molecules
- Reactions
 - Reaction
- Passive Transports
- Observers
- Events
- Simulation Settings
- Molecule Start Values
- Reaction Check Values

Building Block Editor

Reactions: Reaction x

Reactions Formulas

Chart List Favorites User Defined

Diagram Area

Properties Editor

Properties Stoichiometry Modifiers Parameters Container Criteria

Name: R1

☐ Create process rate parameter ☐ Plot process rate parameter

Kinetic

Formula type: Formula (an explicit formula)

Formula name: R1

Alias Path Dimension

Description:

History Manager

History

Undo Add Label Edit Comment

Rollback 90

| State After Action | Command Type | Object Type | Description | User | Time |
|--------------------|--------------|-------------|-----------------------------------|-------|------------------|
| 90 | Delete | Molecule | Remove Molecule 'B' from '_Mol... | admin | 2018-11-04 13:57 |
| 89 | Delete | Molecule | Remove Molecule 'C' from '_Mol... | admin | 2018-11-04 13:57 |

Search Area

Search

Scope Project

☐ Match whole word

☐ Use regular expression

☐ Match case

Search results

Project Item

Type Path

Working Journal

Journal

Title Crea... Tags

.....

Simulation Explorer

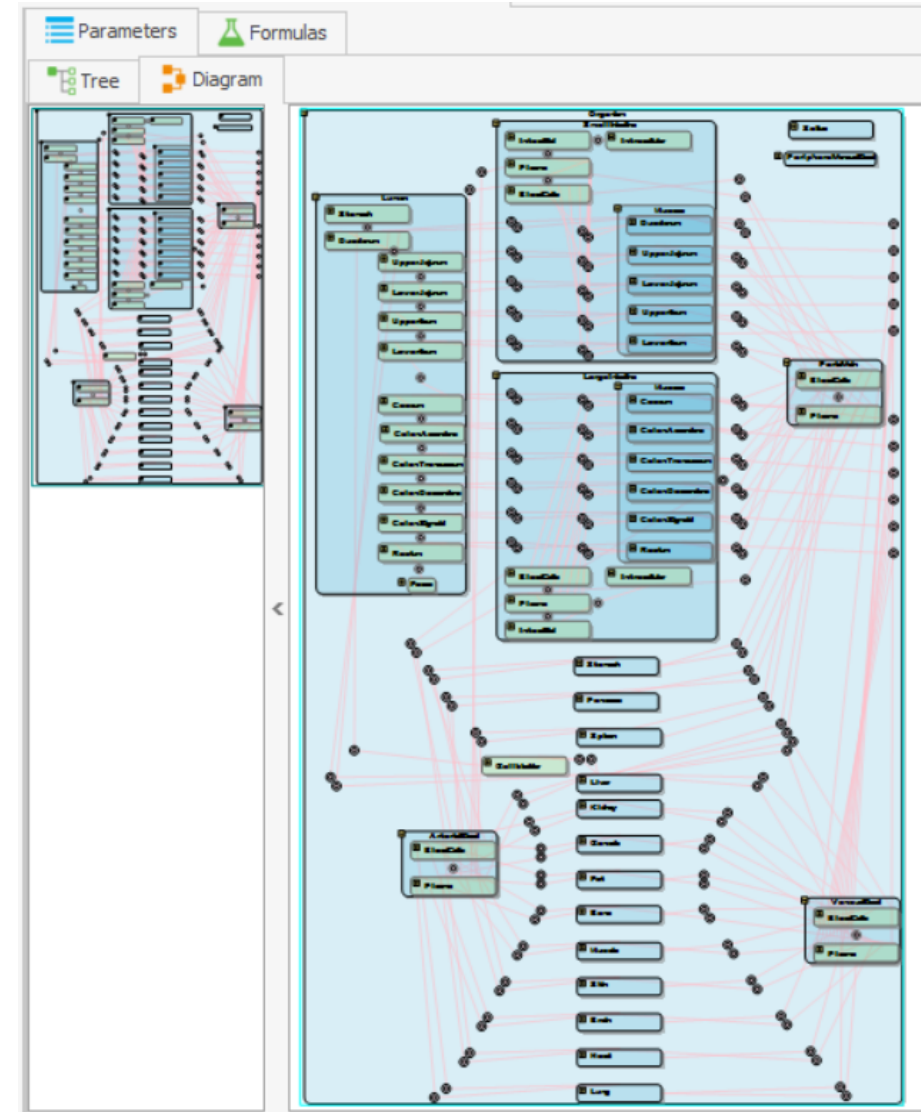
Simulations

- Simulations
- Parameter Identificati...
- Sensitivity Analyses

MoBi: Modeling concepts

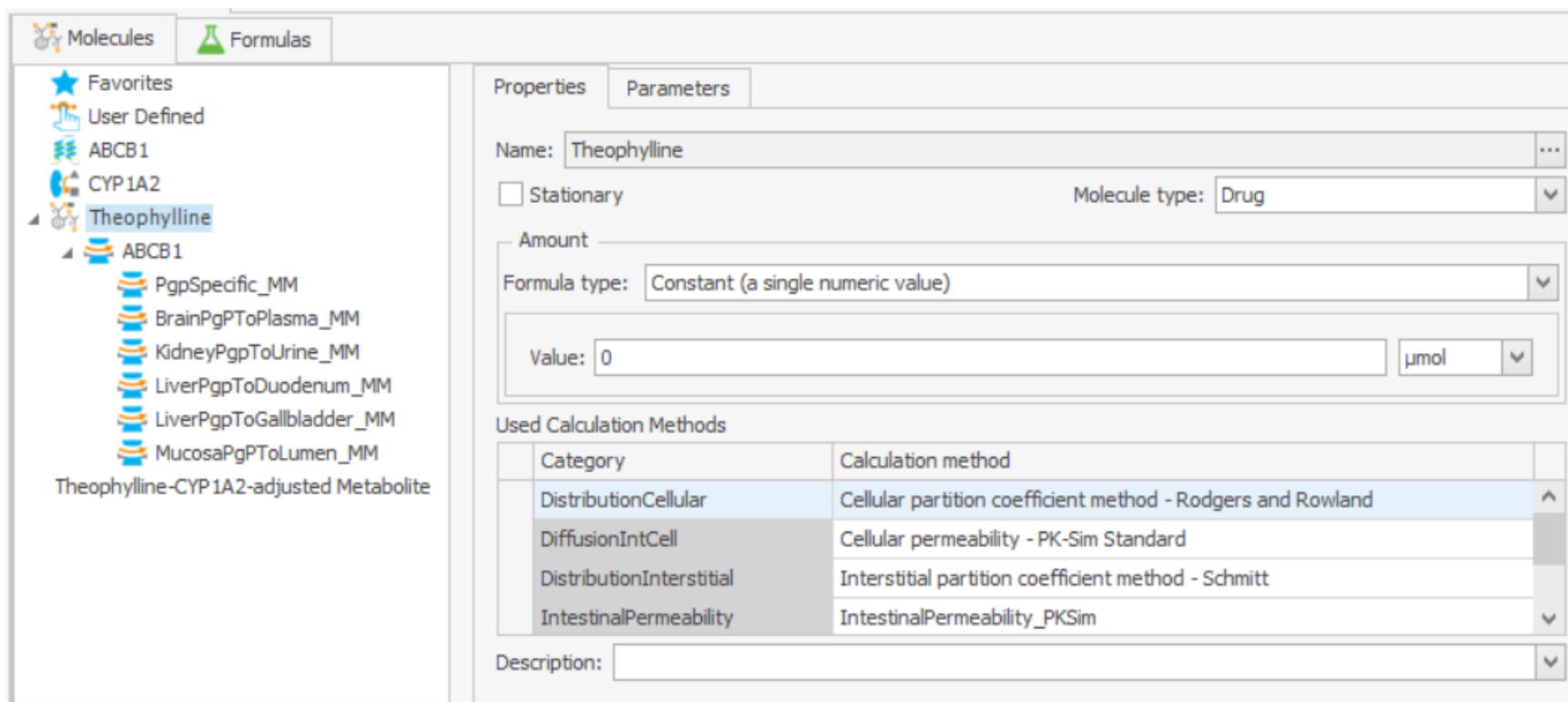
Spatial Structure: define and connect model compartments

- A spatial structure can be an organism consisting of organs, cells and other substructures. Alternatively, it can be a laboratory setup, like a test tube.
- Containers of a spatial structure can be defined as **Physical**, which may contain molecules in the simulation. They can also be defined as Logical, meaning they do not represent a real container with molecules but instead just representing a grouping of sub-containers.
- Any container may have parameters associated with it. They can describe physical or biological properties of the container that are required for processes like transports or reactions (e.g., *Volume*, *pH*, ...)
- Containers are connected via **Neighborhoods**
- Containers and neighborhoods may be labelled with **tags**. These tags, together with the name given to a container or neighborhood, may be used for selectively enabling observers, active or passive transports, or events.



Molecules:

- Mostly, molecules will be chemical or biological compounds and can either be quantified by amount or by concentration.
- It is important to specify whether a molecule may move freely through all containers of a model, which is the default setting, or if it is stationary, i.e., it is immobilized in the current container. In the latter case, for example, the molecule may represent a membrane-bound receptor protein.



The screenshot shows the 'Molecules' tab in the software interface. On the left, a tree view lists 'Favorites', 'User Defined', 'ABCB1', 'CYP1A2', and 'Theophylline'. Under 'Theophylline', there is a sub-entry 'ABCB1' with several associated models: 'PgpSpecific_MM', 'BrainPgPToPlasma_MM', 'KidneyPgpToUrine_MM', 'LiverPgpToDuodenum_MM', 'LiverPgpToGallbladder_MM', and 'MucosaPgPToLumen_MM'. Below these is 'Theophylline-CYP1A2-adjusted Metabolite'.

The right panel shows the 'Parameters' sub-tab for 'Theophylline'. It includes a 'Name' field with 'Theophylline', a 'Stationary' checkbox (unchecked), and a 'Molecule type' dropdown set to 'Drug'. Under the 'Amount' section, the 'Formula type' is 'Constant (a single numeric value)', and the 'Value' is '0' with a unit dropdown set to 'μmol'. Below this is a table titled 'Used Calculation Methods'.

| Category | Calculation method |
|--------------------------|---|
| DistributionCellular | Cellular partition coefficient method - Rodgers and Rowland |
| DiffusionIntCell | Cellular permeability - PK-Sim Standard |
| DistributionInterstitial | Interstitial partition coefficient method - Schmitt |
| IntestinalPermeability | IntestinalPermeability_PKSim |

At the bottom, there is a 'Description' field.

Molecule Start Values

- This building block defines the initial amounts or concentration of all molecules in the model.
- If you want to exclude a specific molecule from a specific container, de-select the "is present" checkbox.

Molecule Start Values
Formulas

☐ Show only changed values
☐ Show only new values

Source of start value not defined

Newly added values

Start value is modified

Delete values:

Delete Selected
Apply

Is present:

Mark all as present
Apply

Start values:

Refresh all from source
Apply

Neg. values:

Mark all as allowing neg. v...
Apply

Drag a column header here to group by that column

| Molecule Name | Path Element 1 | Path Element 2 | Start Value | Scale Divisor | Is Present | Neg. Values Allowed | Formula | | |
|-------------------------|----------------|----------------|-----------------|---------------|-------------------------------------|--------------------------|------------------------|---|---|
| UGT1A4 | Brain | BloodCells | <Not Available> | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | ^ |
| GABRG2 | Brain | BloodCells | <Not Available> | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | |
| Efavirenz | Brain | BloodCells | 0 µmol | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP1A2-War... | Brain | BloodCells | 0 µmol | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP2B6-War... | Brain | BloodCells | 0 µmol | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP3A4-War... | Brain | BloodCells | 0 µmol | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP3A5-War... | Brain | BloodCells | 0 µmol | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP2A6-Ogb... | Brain | BloodCells | 0 µmol | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| CYP1A2 | Brain | Interstitial | <Not Available> | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | |
| CYP2B6 | Brain | Interstitial | <Not Available> | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | |
| CYP3A4 | Brain | Interstitial | <Not Available> | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | |
| CYP3A5 | Brain | Interstitial | <Not Available> | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | |
| CYP2A6 | Brain | Interstitial | <Not Available> | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | |
| UGT1A4 | Brain | Interstitial | <Not Available> | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | |
| GABRG2 | Brain | Interstitial | <Not Available> | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | STARTAMOUNT_Protein... | X | |
| Efavirenz | Brain | Interstitial | 0 µmol | 1.0000 | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP1A2-War... | Brain | Interstitial | 0 µmol | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP2B6-War... | Brain | Interstitial | 0 µmol | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP3A4-War... | Brain | Interstitial | 0 µmol | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |
| Efavirenz-CYP3A5-War... | Brain | Interstitial | 0 µmol | 1.0000 | <input type="checkbox"/> | <input type="checkbox"/> | <Not Available> | X | |

Parameter Start Values

- This building block defines the start values of the parameters in the model.
- This allows for the setting of specific physiological parameters if different individuals, species or patient subgroups are to be considered.

Parameter Start Values

Formulas

☐ Show only changed values
 ☐ Show only new values

Source of start value not defined

Newly added values

Delete values:

Delete Selected

Apply

Start values:

Refresh all from source

Apply

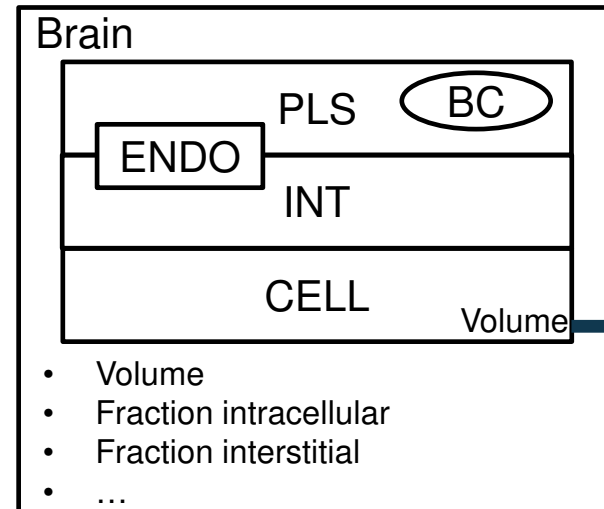
Start value is modified

Drag a column header here to group by that column

| Parameter Name | Path Element 0 | Path Element 1 | Path Element 2 | Path Element 3 | Start Value | Formula | Dimension | | |
|------------------------------|----------------|----------------|----------------|----------------|-----------------|--------------------------------|-----------------------|---|---|
| Ontogeny factor | CYP1A2 | | | | 1.0000 | <Not Available> | Dimensionless | X | ^ |
| Ontogeny factor GI | CYP1A2 | | | | 1.0000 | <Not Available> | Dimensionless | X | |
| Reference concentration | CYP1A2 | | | | 1.8000 µmol/l | <Not Available> | Concentration (molar) | X | |
| Rel. exp. variability factor | CYP1A2 | | | | 1.0000 | <Not Available> | Dimensionless | X | |
| Relative expression | Organism | Gallbladder | CYP1A2 | | 0 | <Not Available> | Fraction | X | |
| Relative expression | Organism | VenousBlood | Plasma | CYP1A2 | <Not Available> | RelExpPlasmaGlobal (rel_e... | Fraction | X | |
| Relative expression | Organism | VenousBlood | BloodCells | CYP1A2 | <Not Available> | RelExpBloodCellsGlobal (rel... | Fraction | X | |
| Relative expression | Organism | ArterialBlood | Plasma | CYP1A2 | <Not Available> | RelExpPlasmaGlobal (rel_e... | Fraction | X | |
| Relative expression | Organism | ArterialBlood | BloodCells | CYP1A2 | <Not Available> | RelExpBloodCellsGlobal (rel... | Fraction | X | |
| Relative expression | Organism | Bone | Plasma | CYP1A2 | <Not Available> | RelExpPlasmaGlobal (rel_e... | Fraction | X | |
| Relative expression | Organism | Bone | BloodCells | CYP1A2 | <Not Available> | RelExpBloodCellsGlobal (rel... | Fraction | X | |
| Relative expression | Organism | Bone | Interstitial | CYP1A2 | 0 | <Not Available> | Fraction | X | |
| Relative expression | Organism | Bone | Intracellular | CYP1A2 | 0 | <Not Available> | Fraction | X | |
| Relative expression | Organism | Brain | Plasma | CYP1A2 | <Not Available> | RelExpPlasmaGlobal (rel_e... | Fraction | X | |
| Relative expression | Organism | Brain | BloodCells | CYP1A2 | <Not Available> | RelExpBloodCellsGlobal (rel... | Fraction | X | |
| Relative expression | Organism | Brain | Interstitial | CYP1A2 | 0 | <Not Available> | Fraction | X | |
| Relative expression | Organism | Brain | Intracellular | CYP1A2 | 0 | <Not Available> | Fraction | X | |
| Relative expression | Organism | Fat | Plasma | CYP1A2 | <Not Available> | RelExpPlasmaGlobal (rel_e... | Fraction | X | |
| Relative expression | Organism | Fat | BloodCells | CYP1A2 | <Not Available> | RelExpBloodCellsGlobal (rel... | Fraction | X | |
| Relative expression | Organism | Fat | Interstitial | CYP1A2 | 0 | <Not Available> | Fraction | X | |

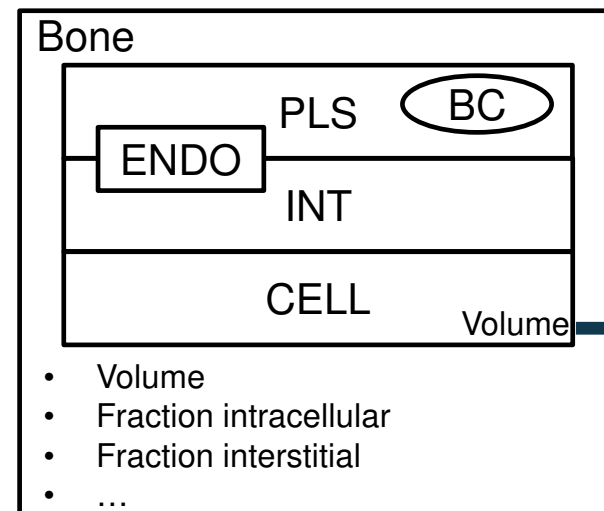
„Generic“ modeling: Formulas in building blocks

- Example 1: compartment volume of the intracellular space in a tissue organ is defined by the product of the **organ volume** and the **fraction of intracellular space** of the organ



$\text{Volume_Brain} * \text{Fraction_intracellular_Brain}$

- This could be defined by a separate formula in each tissue organ



$\text{Volume_Bone} * \text{Fraction_intracellular_Bone}$

...

- Disadvantages
 - N formulas need to be defined (one per tissue organ)
 - If a modification of intracellular volume definition is required: N formulas need to be adjusted

„Generic“ modeling: Formulas in building blocks

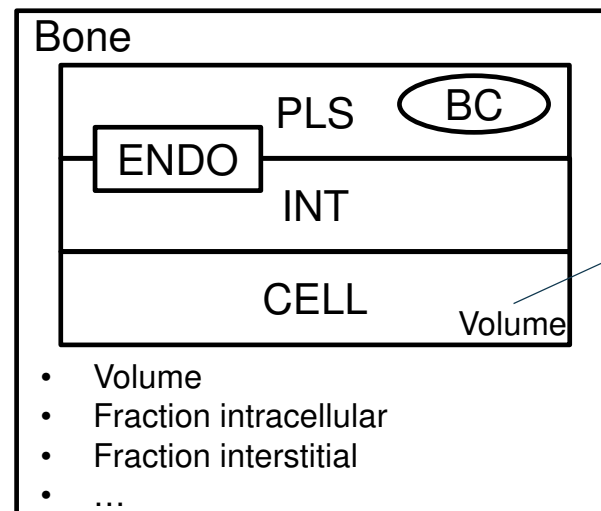
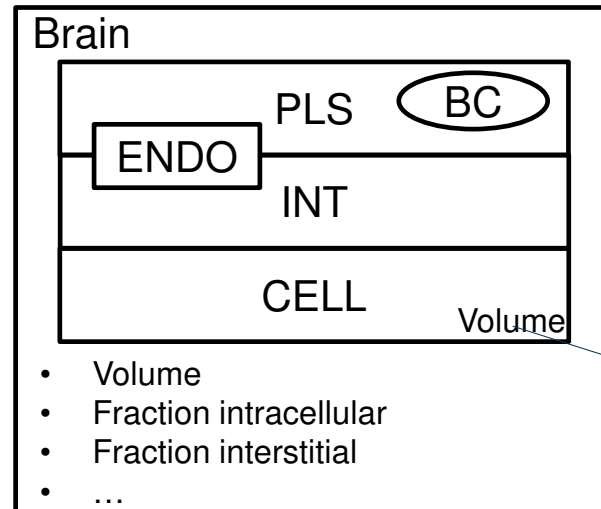
- Better solution: ONE formula shared between all tissue organs – possible due to the usage of “**generic**” **references** to the formula items

Formula type: Formula (an explicit formula)

Formula name: VOLUME_cell_4Comp

| Alias | Path | Dimension |
|--------|------------------------------|---------------|
| f_cell | Fraction intracellular | Dimensionless |
| V | Volume | Volume |

f_cell*V



Volume_**PARENT_ORGAN** *
Fraction_intracellular_**PARENT_ORGAN**

„Generic“ modeling: Formulas

- Example 2: Blood flow transports from arterial blood plasma to (tissue) organs plasma:

$$\text{Rate} \sim \text{Concentration_arterial} * \text{BloodFlow_organ}$$

- N tissue organs
- M transported molecules
- But just one formula for the transport rate!

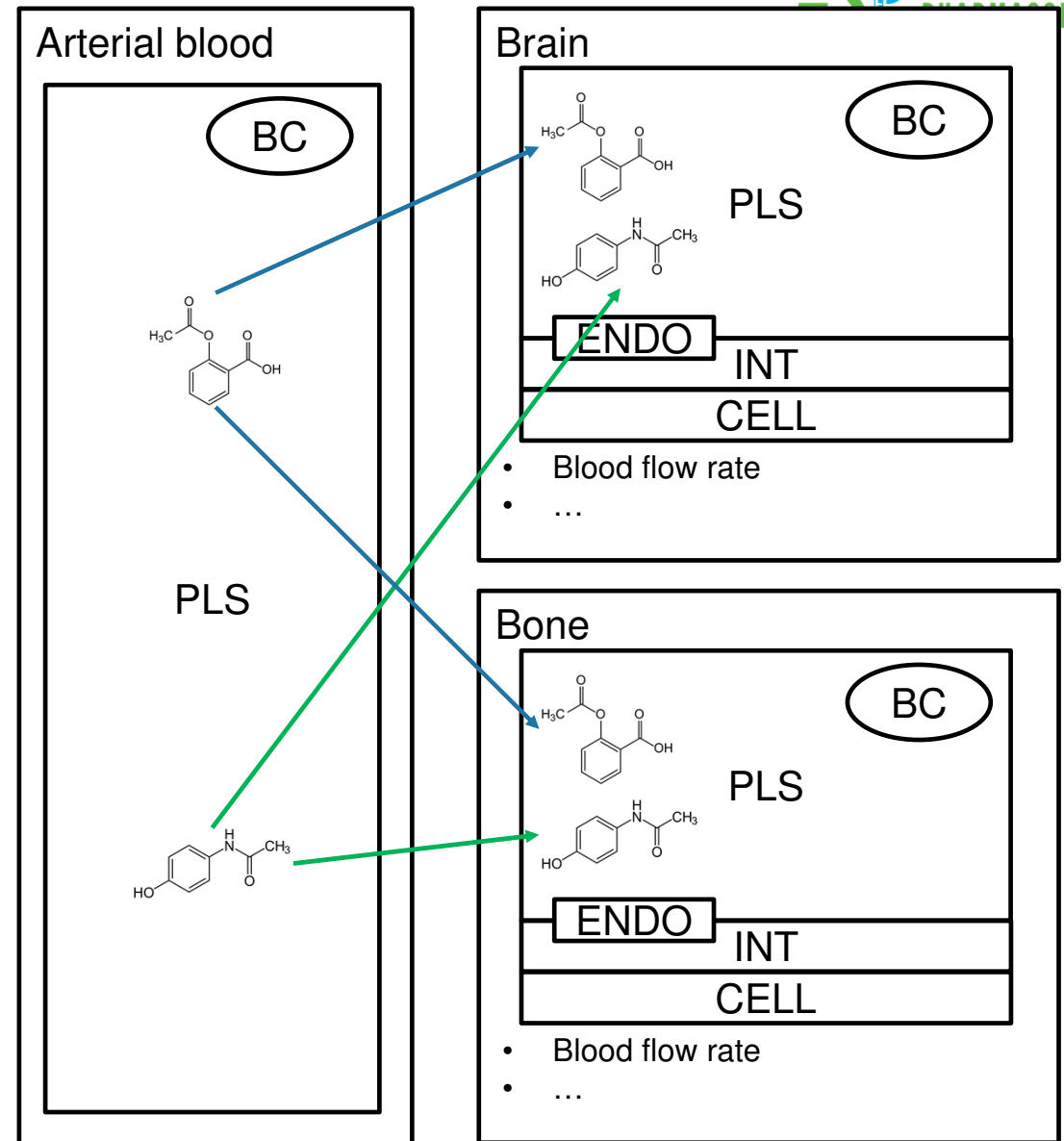
Blood_Flow_rate_**TARGET_ORGAN** *
Concentration_**SOURCE_MOLECULE** *
...

Formula type: Formula (an explicit formula)

Formula name: MassTransferBloodPool2OrgPl

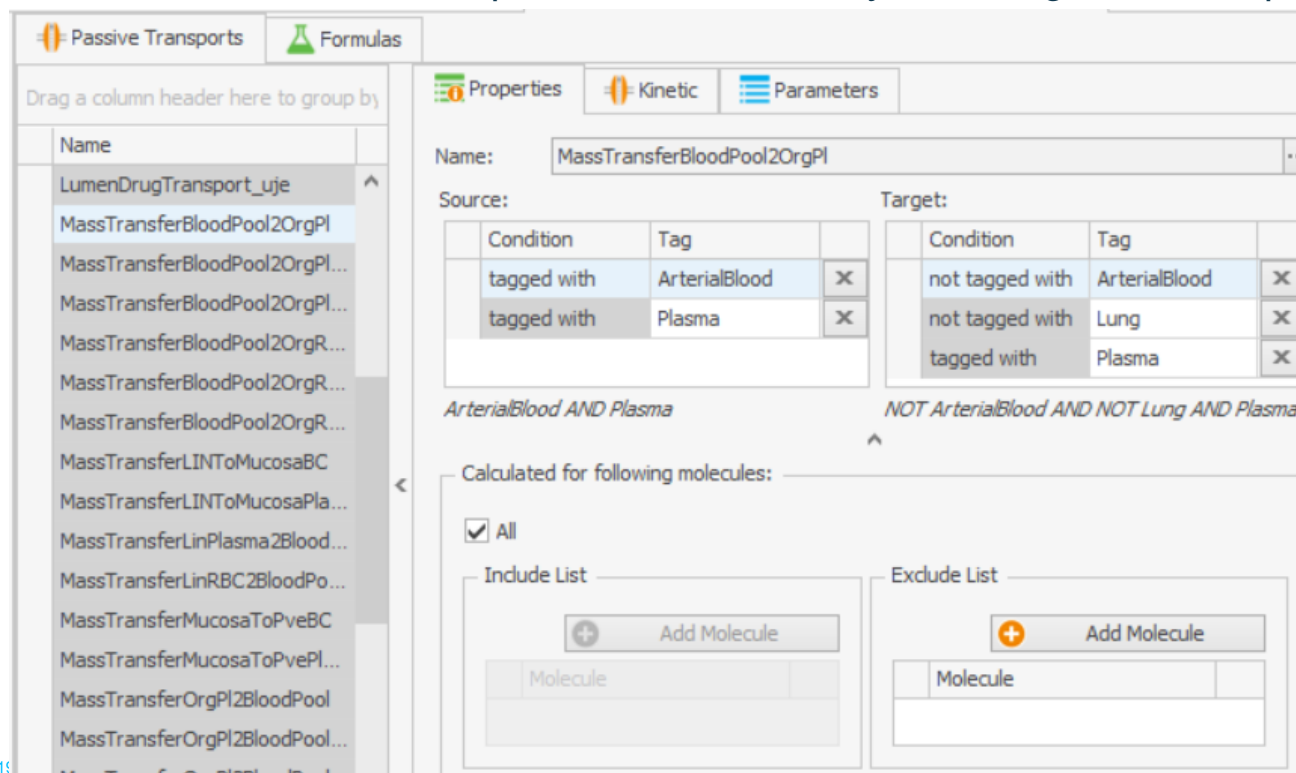
| Alias | Path | Dimension |
|-------|--|-----------------------|
| Q | TARGET .. Blood flow rate | Flow |
| C_pls | SOURCE MOLECULE Concentration | Concentration (molar) |
| HCT | Organism Hematocrit | Dimensionless |

dN/dt = Q*C_pls*(1-HCT)

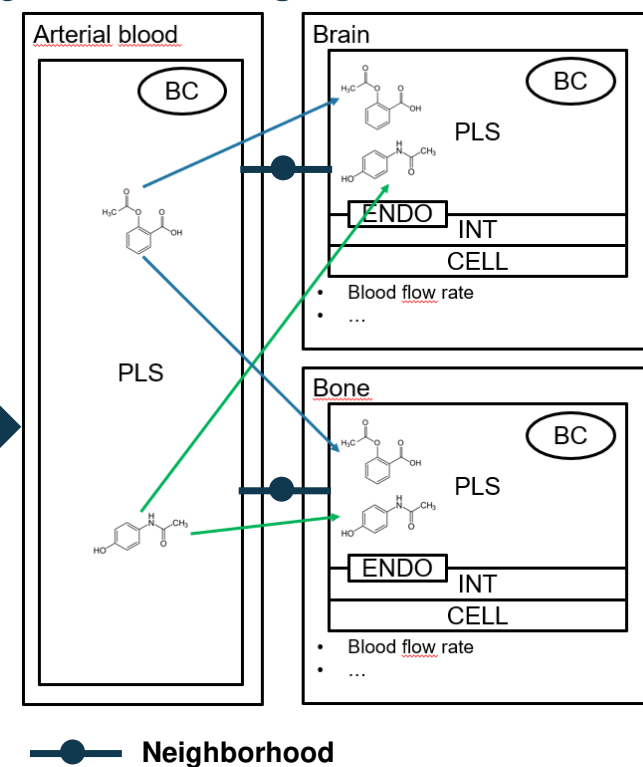


Passive Transports

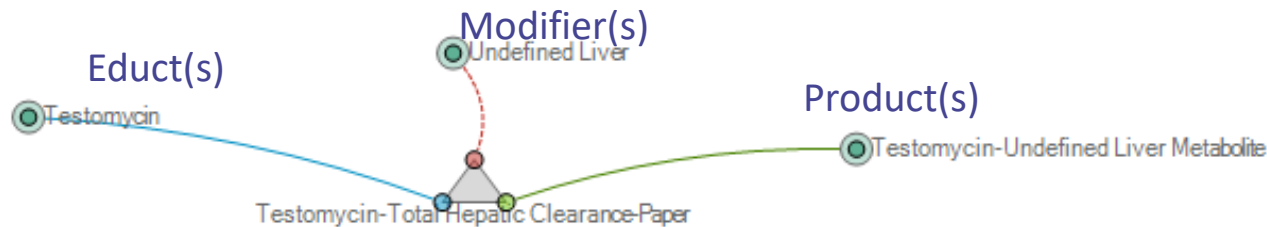
- Passive transports will affect non-stationary molecules. Examples are passive diffusion, the flow of body fluids like blood, or perfusion processes.
- A passive transport is defined by source and target, while the transport rate is defined by a kinetic formula.
- Often, it is desired to define transport processes by a generic type of equation, e.g., in all organs from blood to interstitial space. This is done by selecting the corresponding **container tag conditions**.



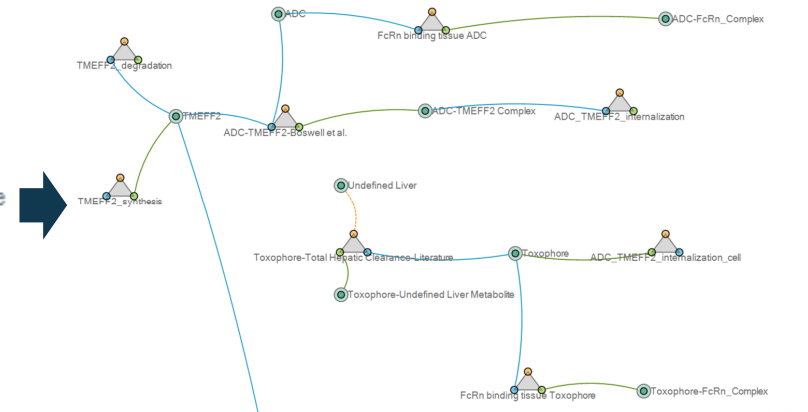
The screenshot shows the 'Passive Transports' tab in the software. The 'Name' field is set to 'MassTransferBloodPool2OrgPl'. The 'Source' is defined by two conditions: 'tagged with ArterialBlood' and 'tagged with Plasma'. The 'Target' is defined by three conditions: 'not tagged with ArterialBlood', 'not tagged with Lung', and 'tagged with Plasma'. The summary text below the conditions reads 'ArterialBlood AND Plasma' and 'NOT ArterialBlood AND NOT Lung AND Plasma'. The 'Calculated for following molecules:' section is set to 'All'.



Reactions and reaction networks



- In a Reactions building block, all (bio-)chemical reactions which are of interest for the current project are defined.
- A reaction is defined by lists of reaction partners (educts, products and modifiers), stoichiometry and reaction rate
- Reactions are defined **independent of the location** and take place wherever all reaction partners are present in non-zero amounts.
 - Can be restricted by **container criteria**



| Properties | Stoichiometry | Modifiers | Parameters | Container Criteria |
|--|-------------------------|-----------------------|------------|--------------------|
| Name: <input type="text" value="Efavirenz-CYP1A2-Ward2003"/> | | | | |
| <input type="checkbox"/> Create process rate parameter | | | | |
| Kinetic | | | | |
| Formula type: <input type="text" value="Formula (an explicit formula)"/> | | | | |
| Formula name: <input type="text" value="Efavirenz-CYP1A2-Ward2003-MetabolizationSpecific_MM"/> | | | | |
| Alias | Path | Dimension | | |
| V | .. Volume | Volume | X | + |
| CP | .. CYP1A2 Concentration | Concentration (molar) | X | + |
| dN/dt = <input type="text" value="CP * kcat * V * K_water * C / (Km + K_water * C)"/> | | | | |

Further Building Blocks

- **Observers:** An observer which can be displayed in a chart is an output derived from one or several molecules or parameters by a defined formula.
- **Events** (and Applications):
 - An **event** is used to change an entity, like the amount of molecules or a reaction rate, when a given condition is met. Examples: food intake, sports activities, ...
 - An application will be (in almost all cases) will be created within PK-Sim® and then transferred to MoBi®
- **Simulation Settings** include some additional setting like
 - *output time intervals* for which results should be generated
 - Numerical settings of the (ODE) solver
 - output selections (quantities which will be shown in charts)
 - (Default) chart templates
- **Observed data:** experimental data can be imported and used in VPC-plots, for (automated) parameter identification etc.

OSP R-Toolbox

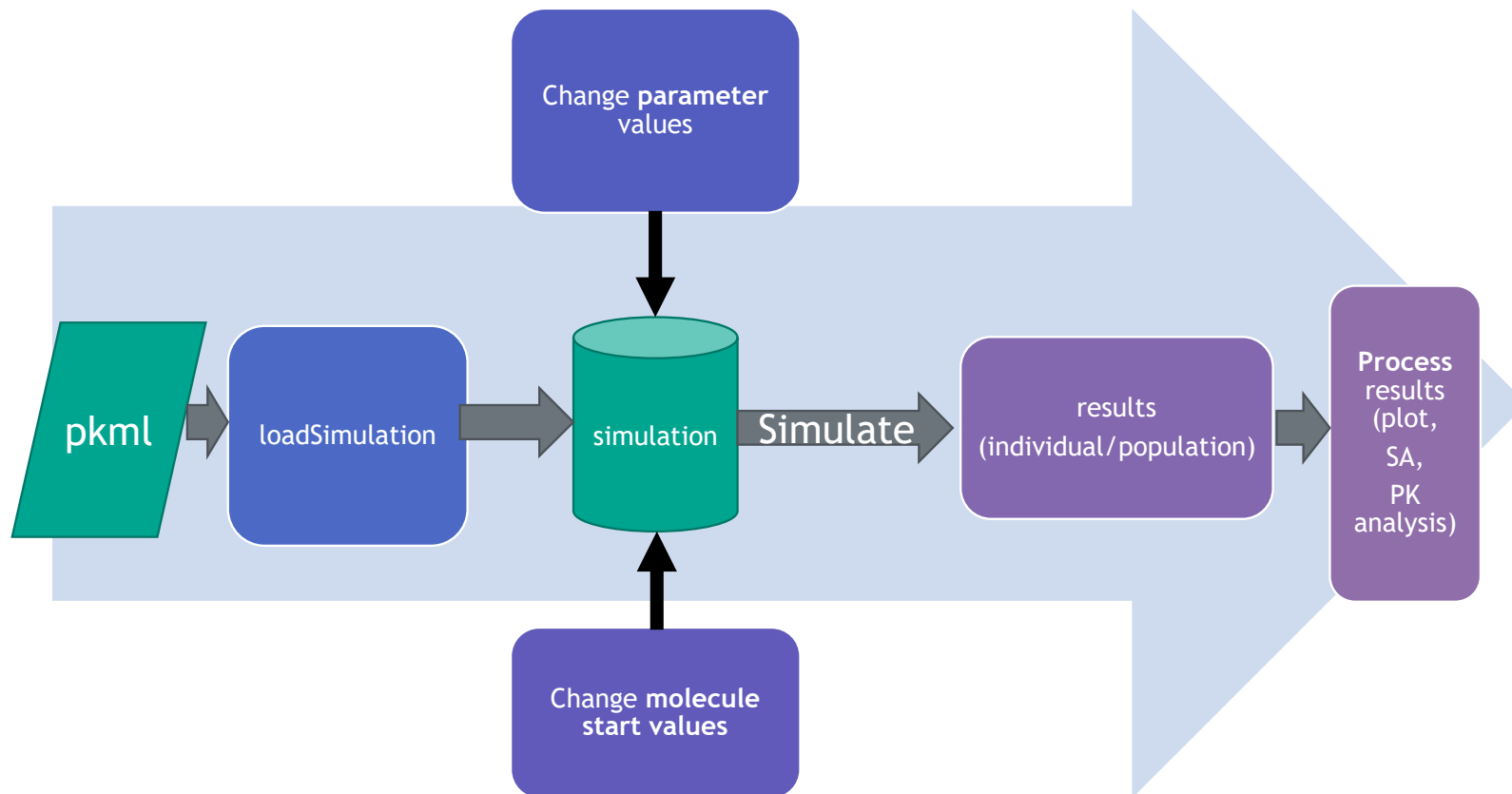
R-Toolbox: main features

- R-Toolbox provides methods to read, manipulate, and simulate (and write) pkml models
 - Change *values* of *parameters* and *start values* of *molecules*
 - Get simulated results as vector of values
 - But: You CANNOT change the structure or equations of the model!
- Creation of individuals and populations
- Individual and Population simulations
- PK-analysis (**user-defined** PK-parameters can be easily created)
- Sensitivity analysis
- Supports Windows and Linux (runs **standalone** - OSP Suite Installation not required)

R-Toolbox: motivation

- Why use R with OSPS?
 - Flexibility and reproducibility – create figures that are fit for your objective
 - Automation – create your own workflows
 - Advanced parameter identification – use advanced algorithms, objective functions...
 - Save time! - parallel simulations (incl. ready to use **Docker container**, allowing simple plug&play into HPC/Cloud environments (e.g., Amazon Web Services (**AWS**)) via the **Docker** technology)

General Workflow



Example 1: run individual simulation, change parameters

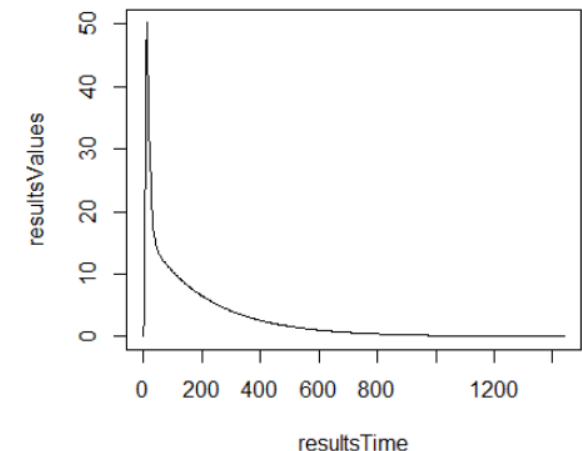
```
library(ospsuite)

# Load simulation
sim <- loadSimulation("Aciclovir.pkml")

# Change parameter value (liver volume)
liverVolume <- getParameter("Organism|Liver|Volume", sim)
print(liverVolume)
#> Parameter:
#> Path: Organism|Liver|Volume
#> Value: 2.1675 [1]
#> isDistributed: TRUE
#> isStateVariable: FALSE
setParameterValues(liverVolume, 1)
print(liverVolume)
#> Parameter:
#> Path: Organism|Liver|Volume
#> Value: 1.00 [1]
#> isDistributed: TRUE
#> isStateVariable: FALSE

# Run simulation
simulationResults <- runSimulation(simulation = sim)

# Get the first simulated output and plot it
resultsPath <- simulationResults$allQuantityPaths[[1]]
print(resultsPath)
#> [1] "Organism|PeripheralVenousBlood|Aciclovir|Plasma (Peripheral Venous Blood)"
resultsData <- getOutputValues(simulationResults, quantitiesOrPaths = resultsPath)
resultsTime <- resultsData$data$Time
resultsValues <- resultsData$data$`Organism|PeripheralVenousBlood|Aciclovir|Plasma (Peripheral Venous Blood)`
plot(resultsTime, resultsValues, type = "l")
```



Example 2: create population, run population simulation

```
library(ospsuite)

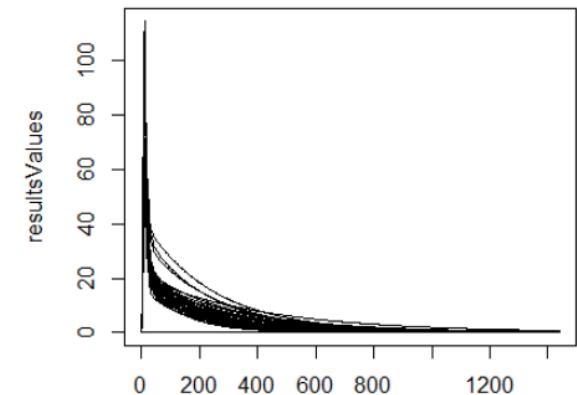
# Create population from population characteristics
populationCharacteristics <- createPopulationCharacteristics(
  species = Species$Human,
  population = HumanPopulation$Asian_Tanaka_1996,
  numberOfIndividuals = 50,
  proportionOfFemales = 50,
  weightMin = 30, weightMax = 98, weightUnit = "kg",
  heightMin = NULL, heightMax = NULL,
  ageMin = 0, ageMax = 80, ageUnit = "year(s)")

myPopulation <- createPopulation(populationCharacteristics = populationCharacteristics)

# Load simulation
sim <- loadSimulation("Aciclovir.pkml")

# Run population simulation
populationResults <- runSimulation(simulation = sim, population = myPopulation)
print(populationResults)
#> SimulationResults:
#>   Number of individuals: 50

# Get the first simulated output and plot it
resultsPath <- populationResults$allQuantityPaths[[1]]
print(resultsPath)
#> [1] "Organism|PeripheralVenousBlood|Aciclovir|Plasma (Peripheral Venous Blood)"
resultsData <- getOutputValues(populationResults, quantitiesOrPaths = resultsPath)
resultsTime <- resultsData$data$Time
resultsValues <- resultsData$data$`Organism|PeripheralVenousBlood|Aciclovir|Plasma (Peripheral Venous Blood)`
plot(resultsTime, resultsValues, type = "l")
```



resultsTime

Example 3: Calculate pk values in a population simulation

```
library(ospsuite)

# Create population from population characteristics
populationCharacteristics <- createPopulationCharacteristics(
  species = Species$Human,
  population = HumanPopulation$Asian_Tanaka_1996,
  numberOfIndividuals = 50,
  proportionOfFemales = 50,
  weightMin = 30, weightMax = 98, weightUnit = "kg",
  heightMin = NULL, heightMax = NULL,
  ageMin = 0, ageMax = 80, ageUnit = "year(s)")

myPopulation <- createPopulation(populationCharacteristics = populationCharacteristics)

# Load simulation
sim <- loadSimulation("Aciclovir.pkml")

# Run population simulation
populationResults <- runSimulation(simulation = sim, population = myPopulation)

# Calculate PK-analyses
pkAnalysis <- calculatePKAnalyses(results = populationResults)

# print available PK parameter names
pkAnalysis$allPKParameterNames
#> [1] "C_max"      "C_max_norm"  "t_max"      "C_tEnd"      "AUC_tEnd"      "AUC_tEnd_norm"
#> [7] "AUC_inf"    "AUC_inf_norm" "MRT"        "Thalf"       "FractionAucLastToInf" "CL"
#> [13] "Vss"       "Vd"

# Get C_max parameter
c_max <- pkAnalysis$pkParameterFor(quantityPath = resultsPath, pkParameter = "C_max")
print(c_max)
#> Organism|PeripheralVenousBlood|Aciclovir|Plasma (Peripheral Venous Blood): C_max
#> Dimension: Concentration (molar)
#> Unit: µmol/l
c_max$values
#> [1] 56.58231 53.85415 55.56487 53.30254 54.23650 59.40544 96.93449 54.66903 59.37316 60.1951
#> [15] 52.09306 106.74448 80.44911 66.90536 102.34718 58.16575 58.75869 66.63985 83.09749 53.540
#> [29] 66.23164 65.73529 72.27832 63.65108 60.89072 69.34486 61.48062 74.38184 71.07183 63.598
#> [43] 66.29802 61.69744 57.31629 60.77491 78.32831 61.15554 78.40282 81.85518
```

Documentation

<https://docs.open-systems-pharmacology.org/working-with-r/r-introduction>

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R: R package to manipulate OSPSuite Models

R package to manipulate OSPSuite Models

Documentation for package 'ospsuite' version 10.0.20

DESCRIPTION file

User guides, package vignettes and other documentation

Help Pages

A C D E F G H I L M O P Q R S T U V misc

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[addOutputInterval](#)

[addOutputs](#)

[addUserDefinedPKParameter](#)

[AgingData](#)

[allAvailableDimensions](#)

[AllMatchingMethod](#)

[AllPathsInMethod](#)

[allPKParameterNames](#)

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Adds an interval to the output schema of the simulation

Adds the quantities as output into the 'simulation'. The quantities can either be specified using exp

Adds and returns a User-Defined PK-Parameter to the managed list of PK-Parameters

AgingData

Returns the name of all available dimensions defined in the OSPSuite platform

Names of the .NET container tasks of the type "AllXXXMatching"

Names of the .NET container tasks of the type "AllXXXPathsIn"

Returns the name of all pk parameters defined in the system

ApiConfig

Application

-- C --

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[calculatePKAnalyses](#)

[clearOutputIntervals](#)

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[CompareBy](#)

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[createIndividual](#)

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[createPopulation](#)

[createPopulationCharacteristics](#)

[createSimulationBatch](#)

Cache

Calculates the pkAnalyses for all output values available in 'results'.

Removes all intervals as well as all single time points from the output schema defined in 'simulat

Removes all selected output from the given 'simulation'

How should comparison of entities be performed

Container

Creates the parameter distributions based on the given individual 'individualCharacteristics'

Creates an individual using the PKSim Database

Creates an individual using the PKSim Database

Creates an population using the PKSim Database

Creates the population characteristics used to create a population

Creates and returns an instance of a 'SimulationBatch' that can be used to efficiently vary parame

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DataColumn

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R: Vignettes and other documentation

Vignettes and other documentation

Vignettes from package 'ospsuite'

[ospsuite::create-individual](#)

[ospsuite::create-run-population](#)

[ospsuite::introduction-ospsuite](#)

[ospsuite::load-get](#)

[ospsuite::pk-analysis](#)

[ospsuite::run-simulation](#)

[ospsuite::sensitivity-analysis](#)

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Creating individuals

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Running a simulation

Sensitivity analysis

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Table parameters

Dimensions and Units

Questions?