

Open Systems Pharmacology

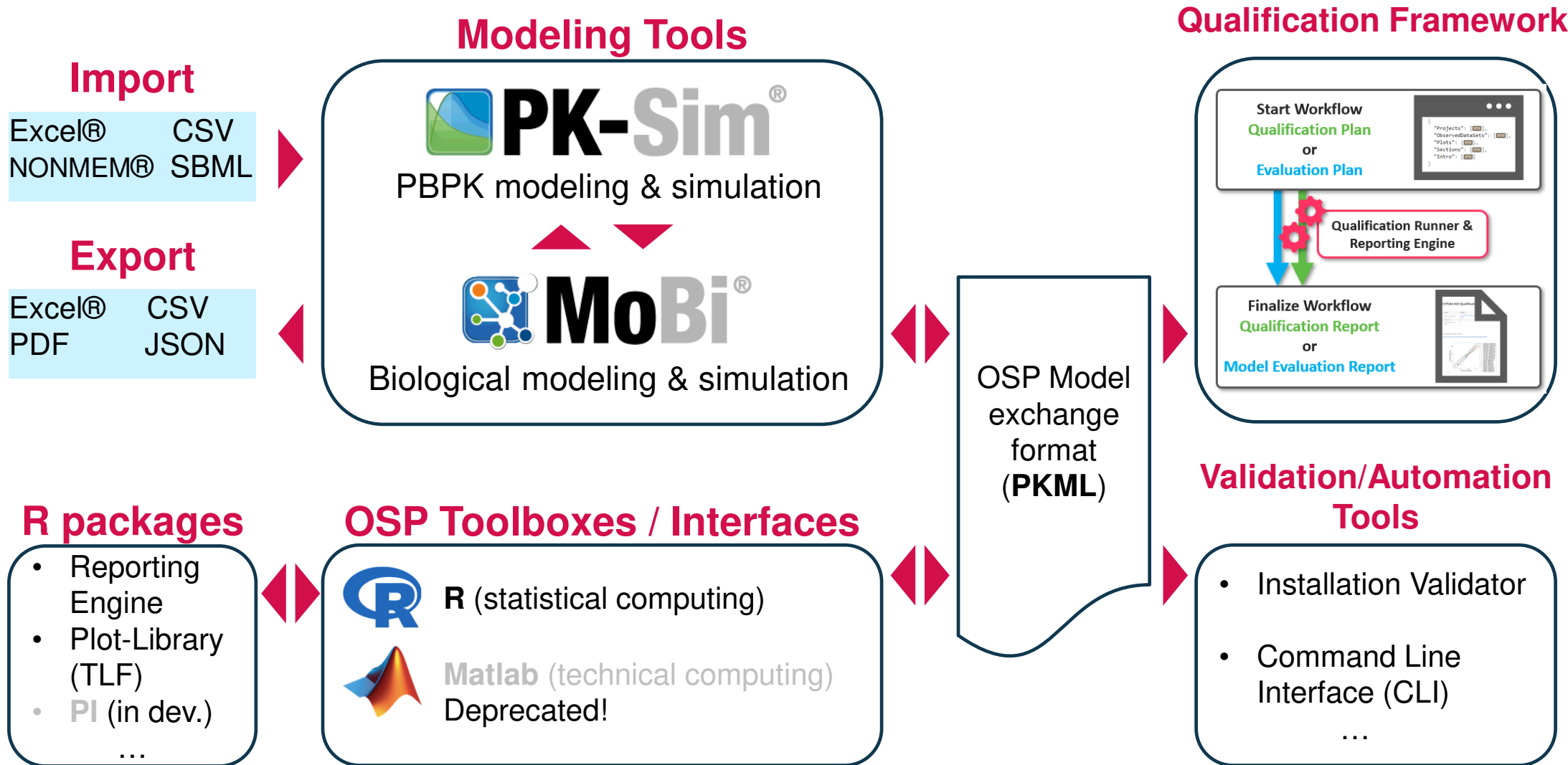
## *MoBi and R-Toolbox*

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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

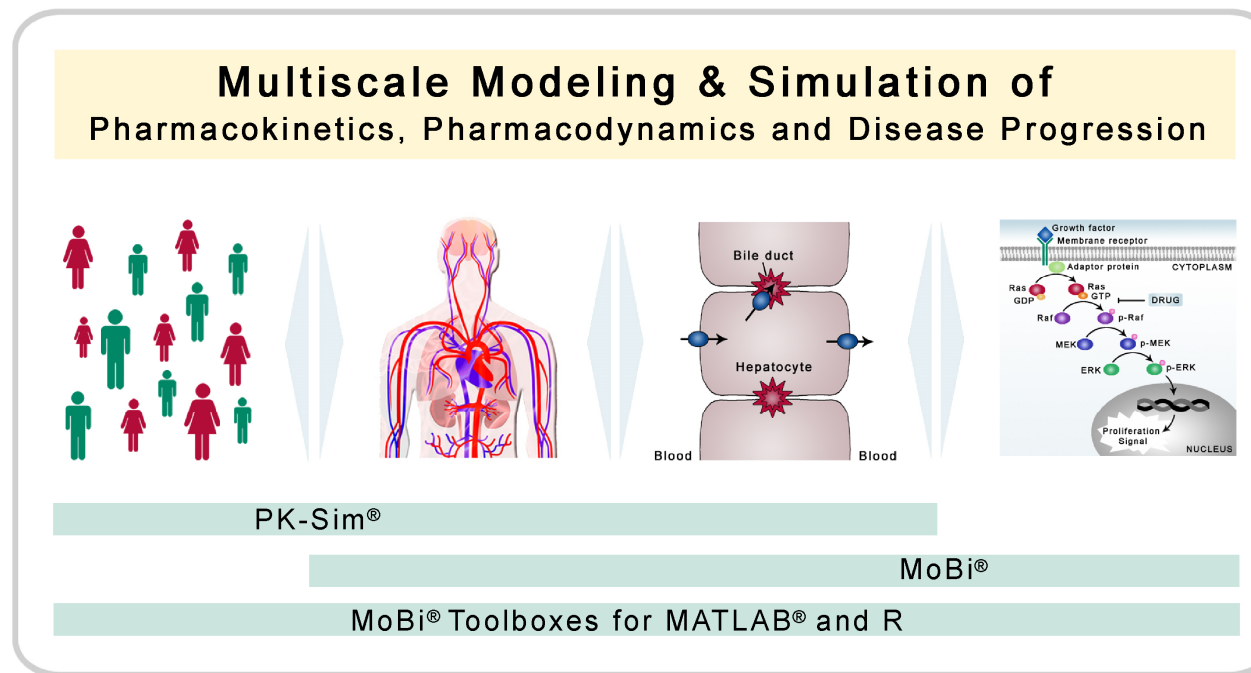


# OSP Modeling Tools: PK-Sim and MoBi

- 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

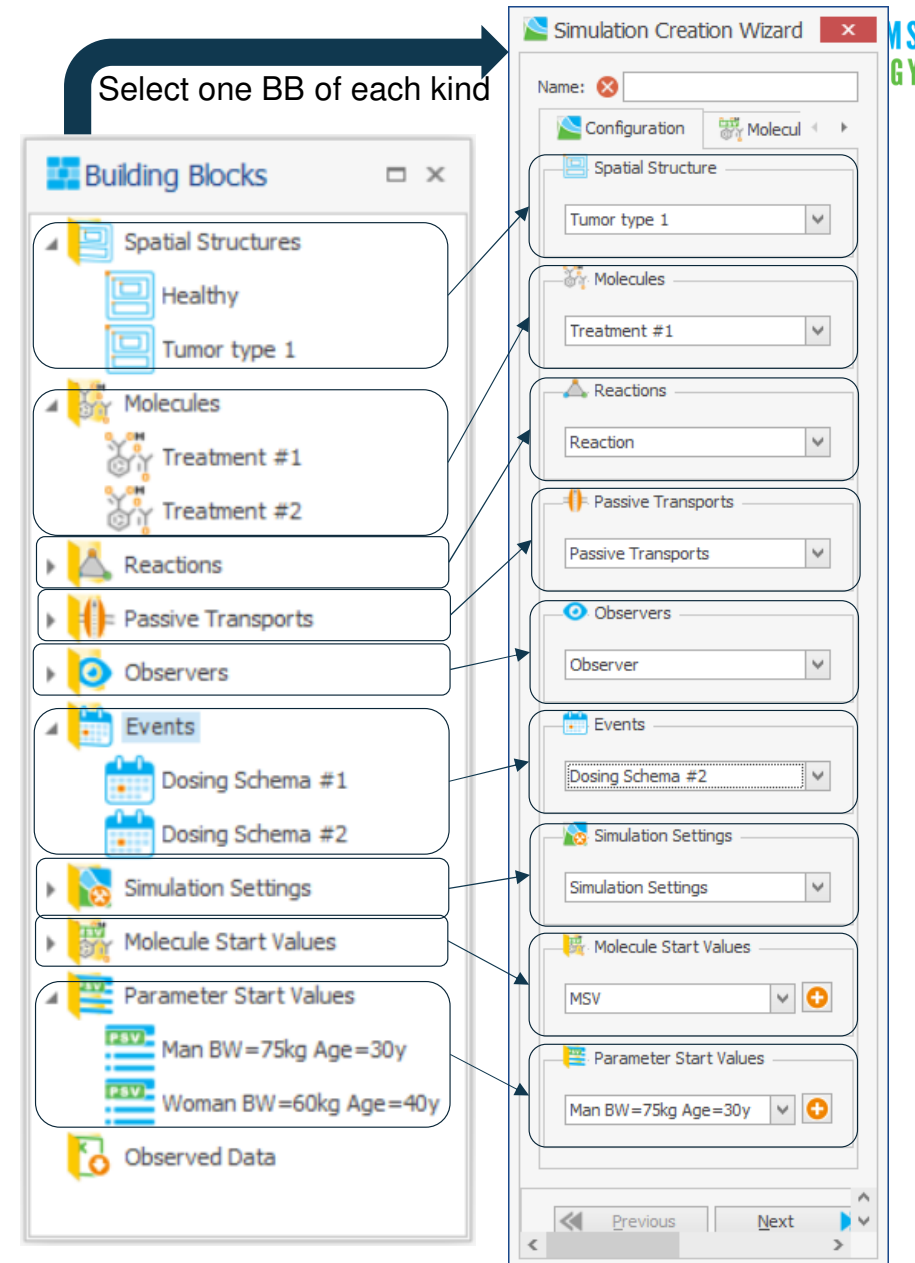
	PK-Sim	MoBi
Integrated databases with: <ul style="list-style-type: none"> <li>- anatomical and physiological properties of humans and laboratory animals</li> <li>- protein expressions</li> <li>- whole-body model structures for small molecules and biologics</li> <li>- prediction models for tissue partition coeff. / cellular and intestinal permeabilities<sup>(*)</sup></li> </ul>	X	(*)X
Template library for: <ul style="list-style-type: none"> <li>- optional processes (DDI / metabolizing pathways / active transporter / protein binding)</li> <li>- food effects / administration protocols / formulations</li> </ul>	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
<b>„No limits“ modeling: modify formulas, change structure beyond templates, ...</b>		<b>X</b>

# 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®

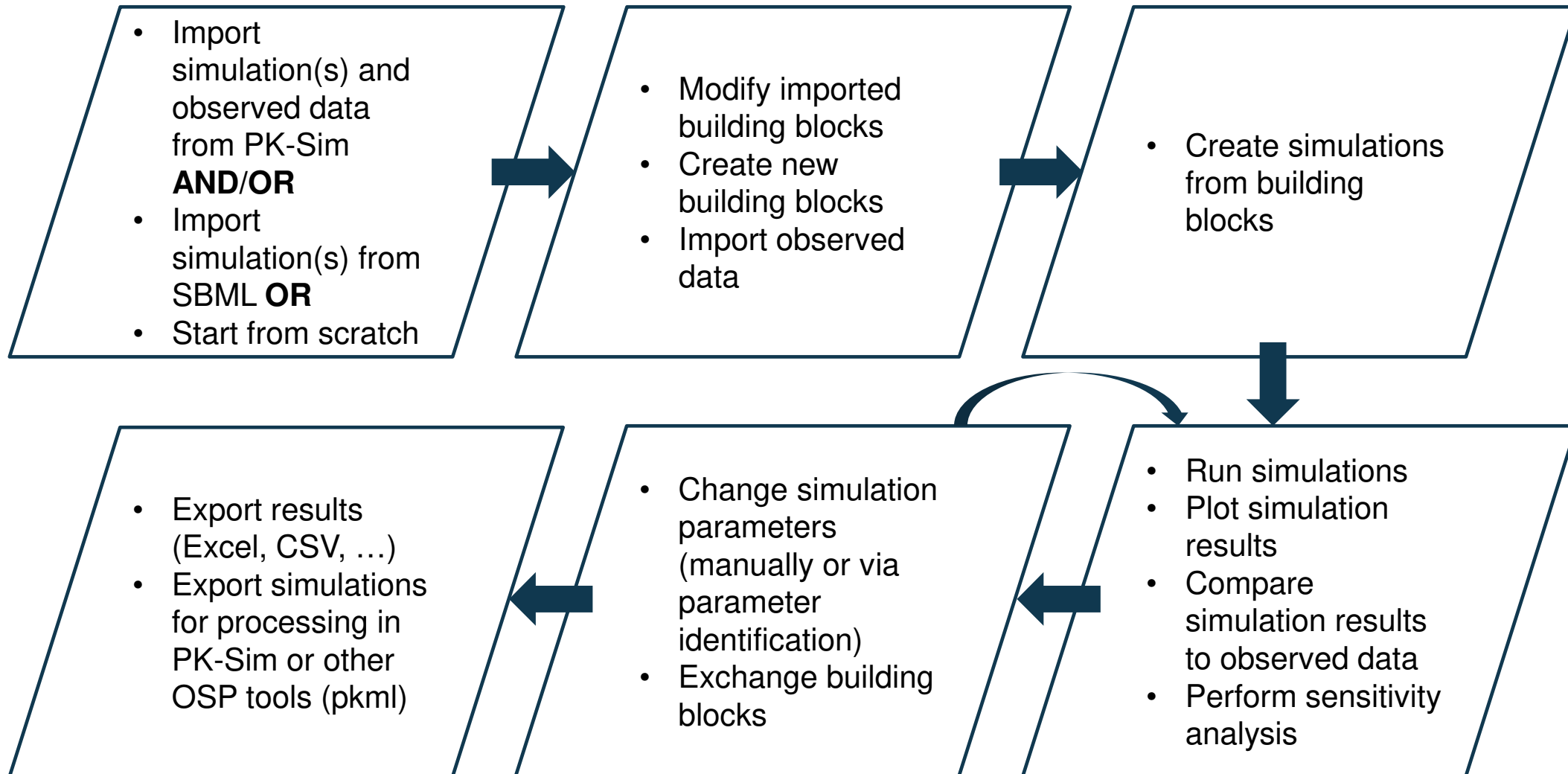
- Individuals
- Populations
- Compounds
- Formulations
- Administration Protocols
- Events
- Observed Data
- Observers

## 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

**Simulation Explorer**

- Simulations
- Parameter Identificati...
- Sensitivity Analyses

**Reactions: Reaction**

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**

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**

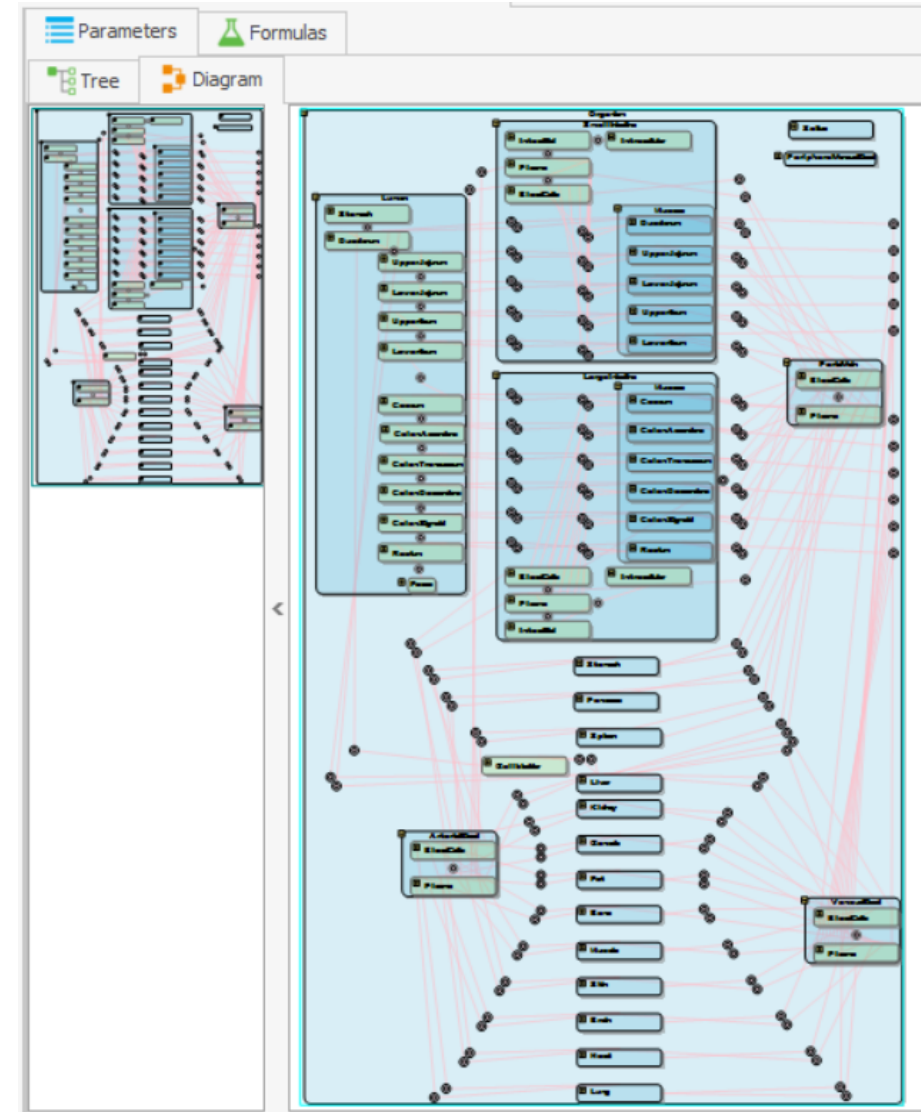
Title Crea... Tags

.....

# *MoBi: Modeling concepts*

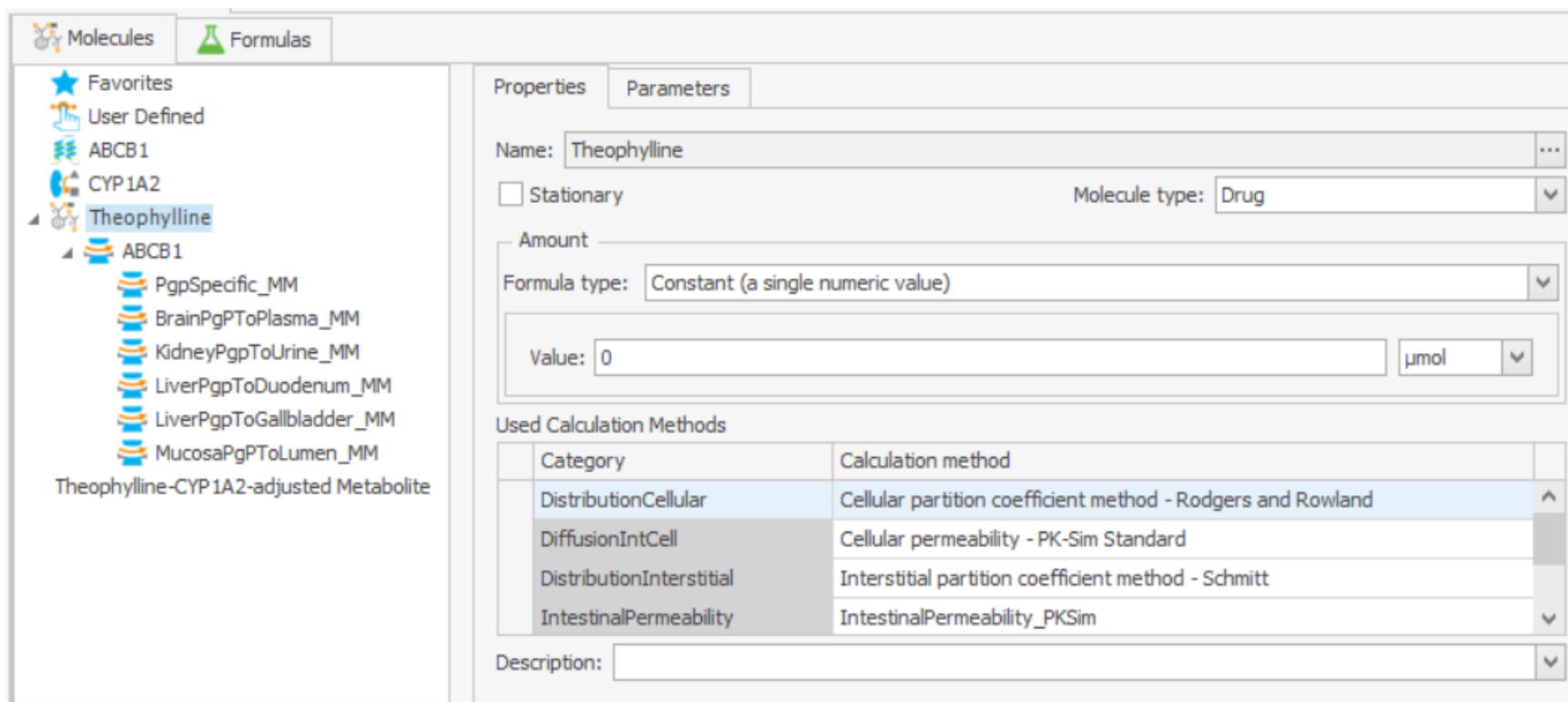
# Spatial Structure: define and connect model compartments

- 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.



**Molecules** | **Formulas**

**Properties** | **Parameters**

Name: Theophylline

☐ Stationary

Molecule type: Drug

Amount

Formula type: Constant (a single numeric value)

Value: 0 μmol

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

Description:

# 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

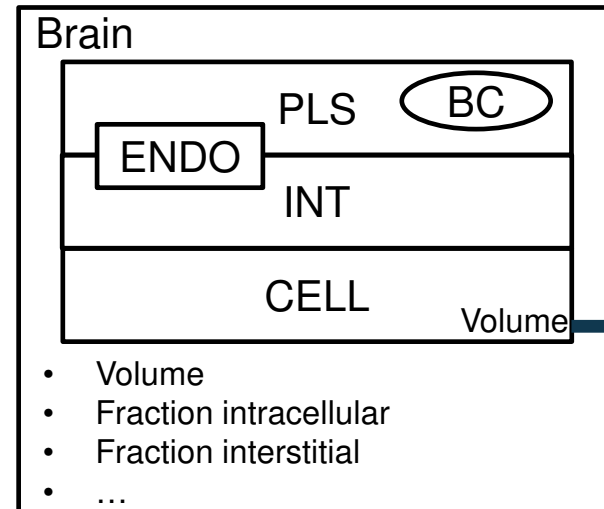
Start value is modified

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	

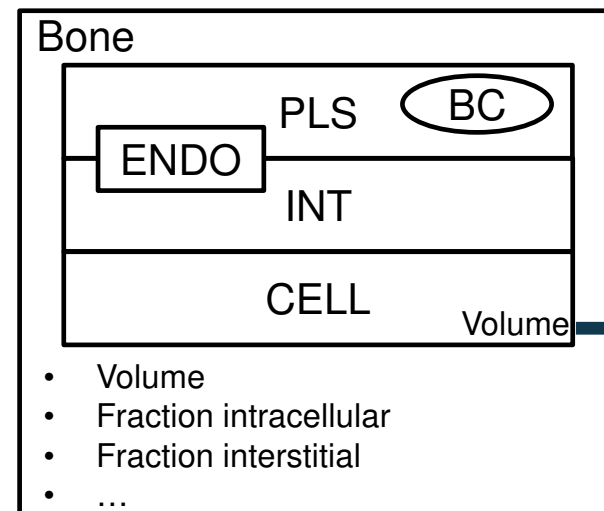
# „Generic“ modeling: Formulas in building blocks

- 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

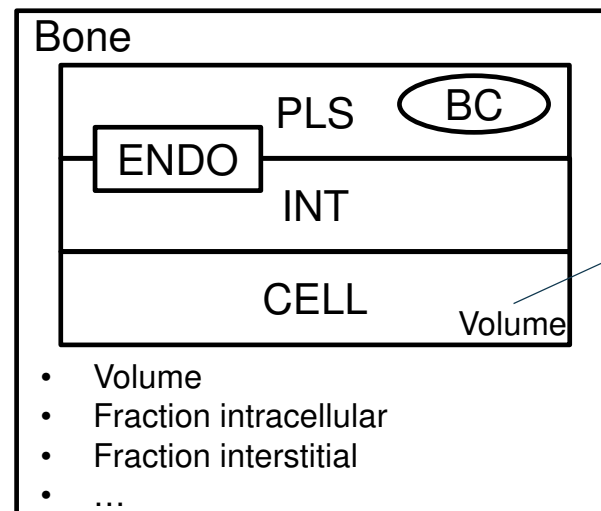
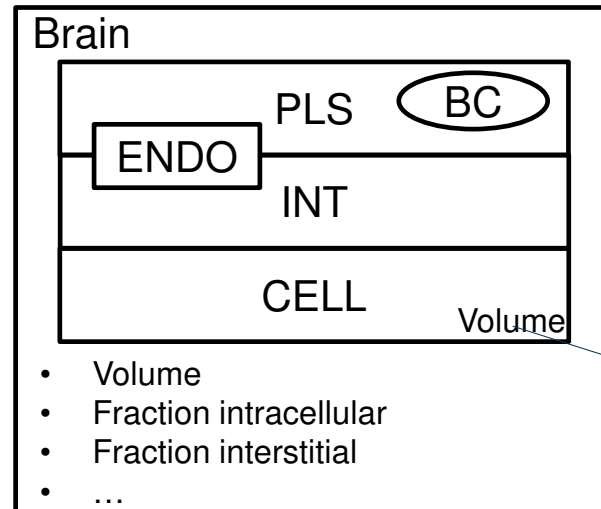
- Better solution: ONE formula shared between all tissue organs – possible due to the usage of “**generic**” **references** to the formula items

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!

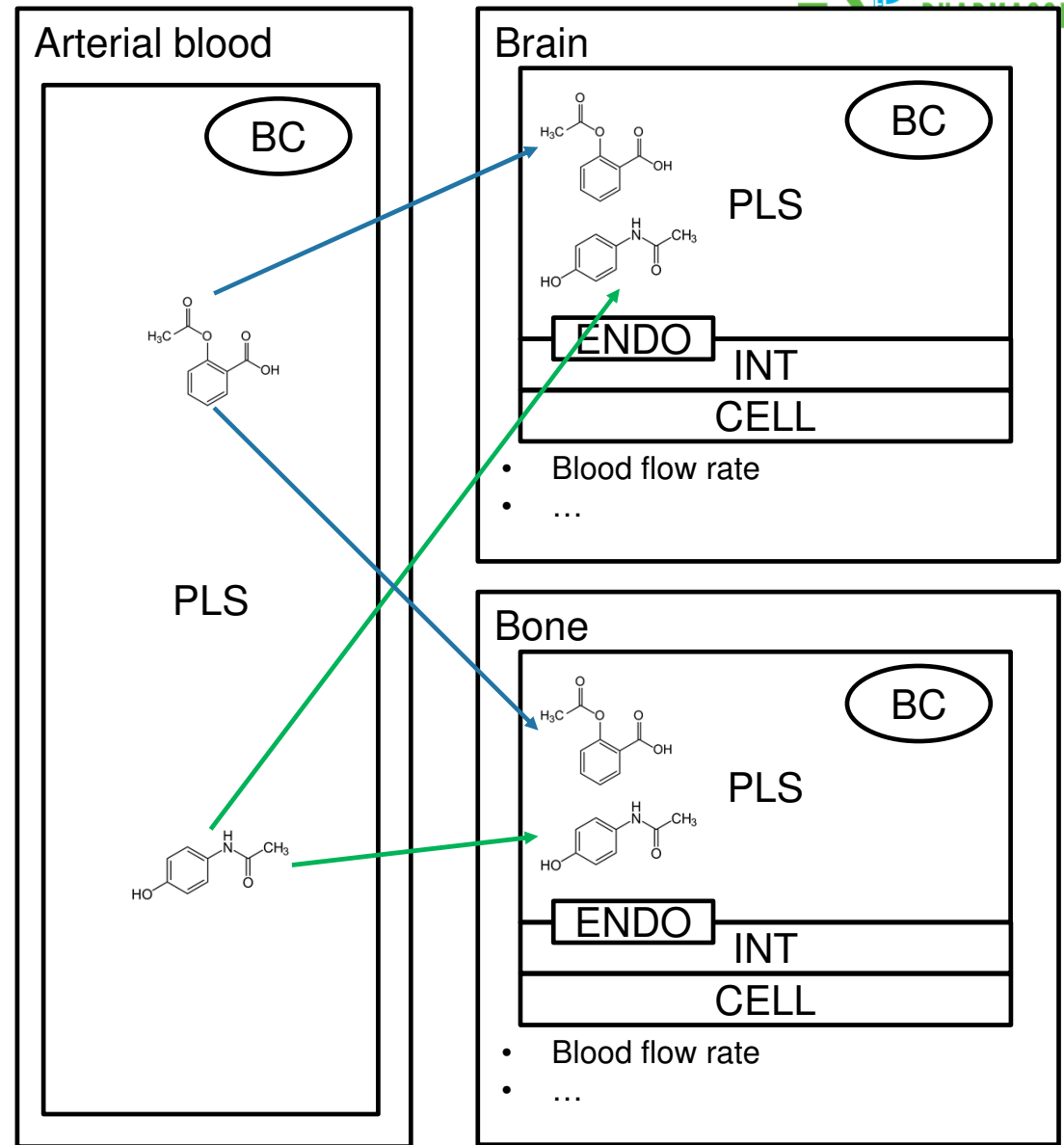
Blood\_Flow\_rate\_**TARGET\_ORGAN** \*  
 Concentration\_**SOURCE\_MOLECULE** \*  
 ...

Formula type:

Formula name:

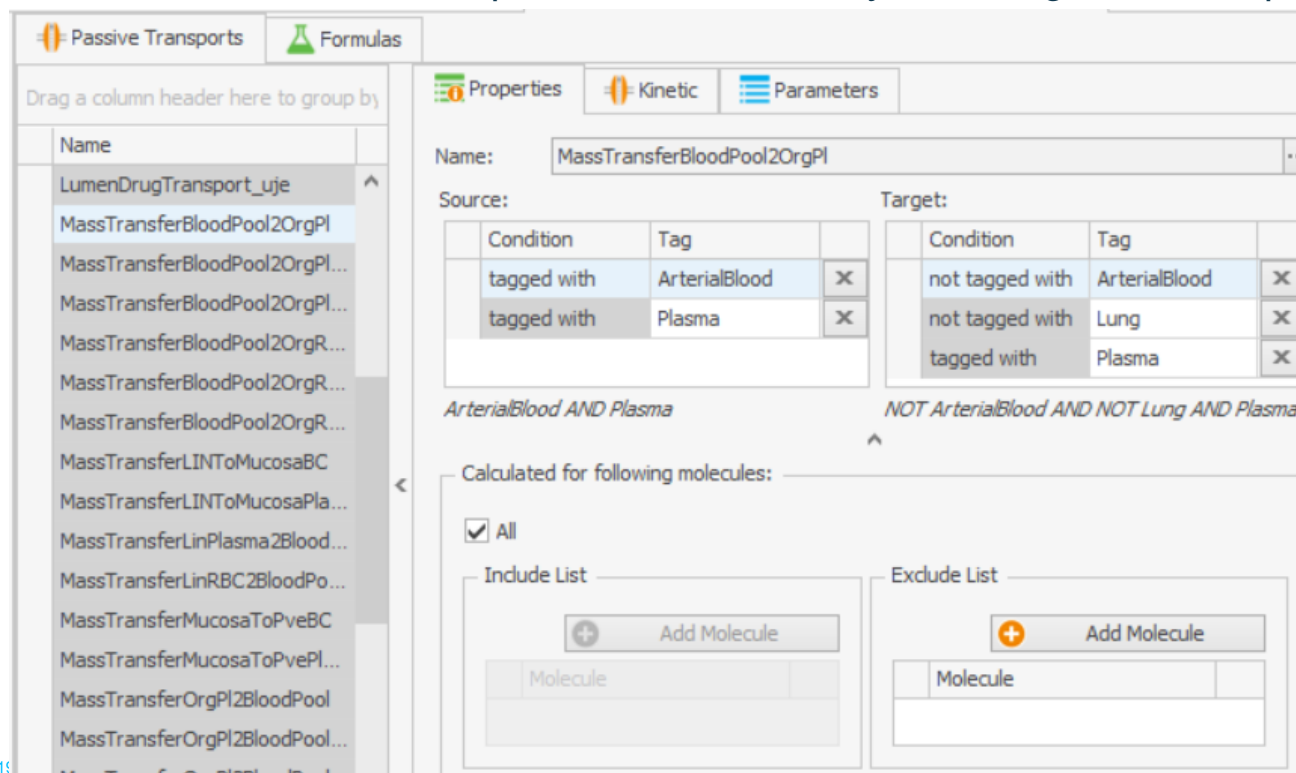
Alias	Path	Dimension
Q	<b>TARGET</b>   ..   Blood flow rate	Flow
C_pls	<b>SOURCE</b>   <b>MOLECULE</b>   Concentration	Concentration (molar)
HCT	Organism   Hematocrit	Dimensionless

dN/dt =



# Passive Transports

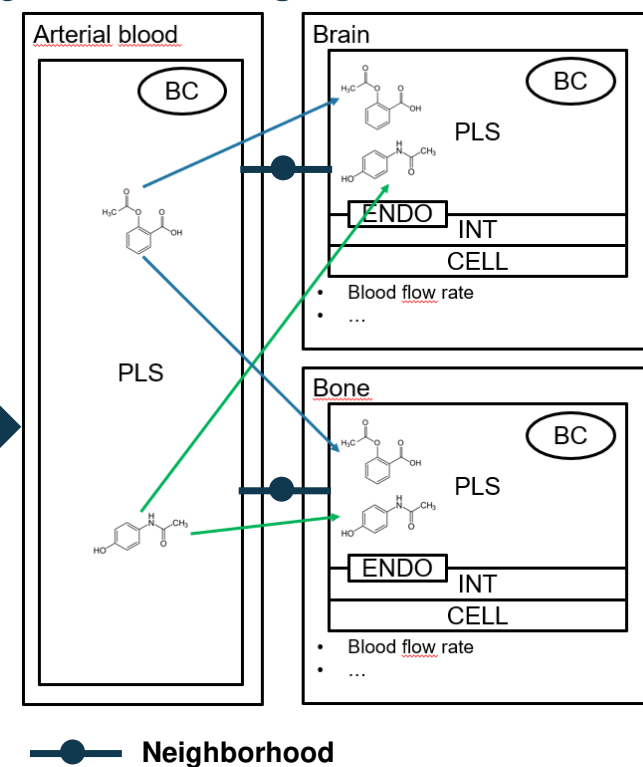
- Passive transports will affect non-stationary molecules. Examples are passive diffusion, the flow of body fluids like blood, or perfusion processes.
- A passive transport is defined by source and target, while the transport rate is defined by a kinetic formula.
- Often, it is desired to define transport 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**.



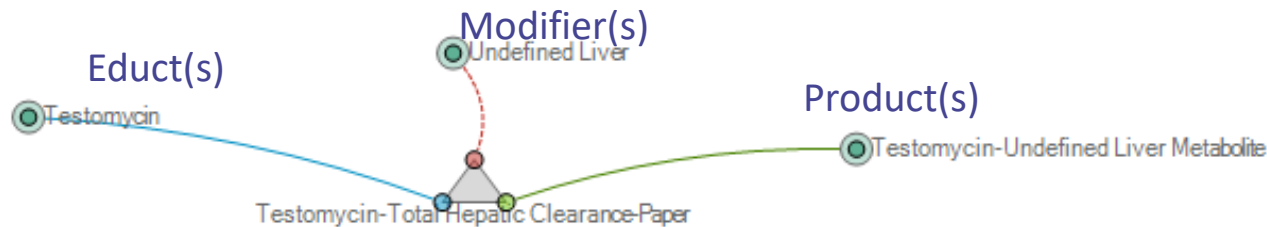
The screenshot shows the 'Passive Transports' tab in the software. The 'Name' field is set to 'MassTransferBloodPool2OrgPl'. The 'Source' and 'Target' tables define the transport conditions:

Condition	Tag		Condition	Tag	
tagged with	ArterialBlood	X	not tagged with	ArterialBlood	X
tagged with	Plasma	X	not tagged with	Lung	X
			tagged with	Plasma	X

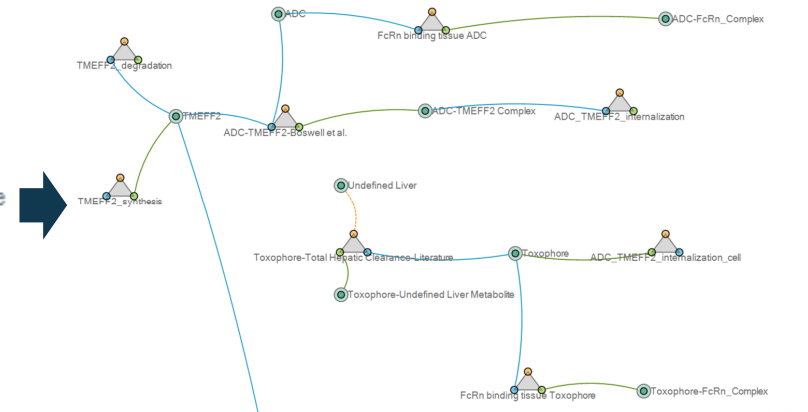
The 'Calculated for following molecules:' section is checked for 'All' molecules. The 'Include List' and 'Exclude List' are empty.



# 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	+ v
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

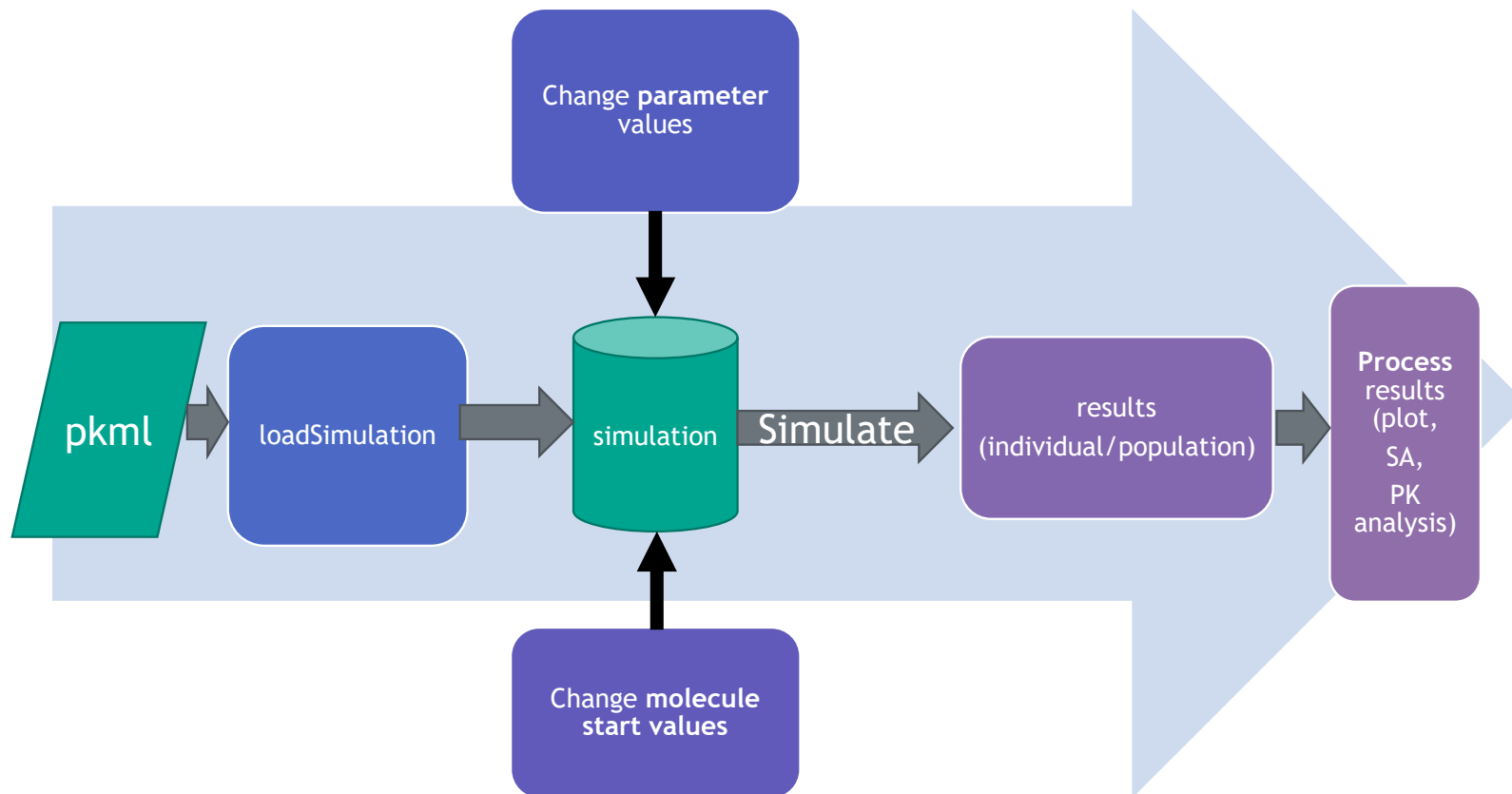
- R-Toolbox provides methods to read, manipulate, and simulate (and write) pkml models
  - Change *values* of *parameters* and *start values* of *molecules*
  - Get simulated results as vector of values
  - But: You CANNOT change the structure or equations of the model!
- Creation of individuals and 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

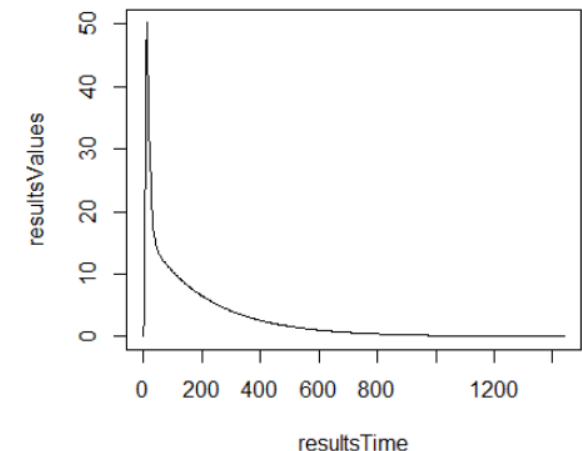
```
library(ospsuite)

# 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)

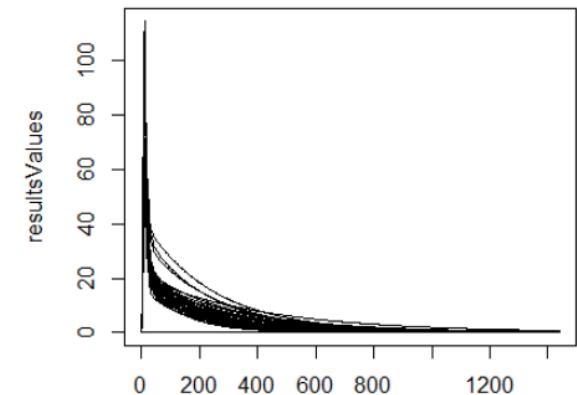
# Create population from population characteristics
populationCharacteristics <- createPopulationCharacteristics(
  species = Species$Human,
  population = HumanPopulation$Asian_Tanaka_1996,
  numberOfIndividuals = 50,
  proportionOfFemales = 50,
  weightMin = 30, weightMax = 98, weightUnit = "kg",
  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 Find in Topic

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

-- A --

[addOutputInterval](#)  
[addOutputs](#)  
[addUserDefinedPKParameter](#)  
[AgingData](#)  
[allAvailableDimensions](#)  
[AllMatchingMethod](#)  
[AllPathsInMethod](#)  
[allPKParameterNames](#)  
[ApiConfig](#)  
[Application](#)

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 --

[Cache](#)  
[calculatePKAnalyses](#)  
[clearOutputIntervals](#)  
[clearOutputs](#)  
[CompareBy](#)  
[Container](#)  
[createDistributions](#)  
[createIndividual](#)  
[createIndividualCharacteristics](#)  
[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 'simulation'  
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 a 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 param

-- D --

[DataColumn](#)  
[DataRepository](#)

DataColumn  
DataRepository

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R: Vignettes and other documentation Find in Topic

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](#)  
[ospsuite::set-values](#)  
[ospsuite::table-parameters](#)  
[ospsuite::unit-conversion](#)

Creating individuals  
Population simulations  
Introduction to ospsuite  
Loading a simulation and accessing entities  
Calculating PK parameters of simulation outputs  
Running a simulation  
Sensitivity analysis  
Changing parameter and molecule start values  
Table parameters  
Dimensions and Units

*Questions?*