Open Systems Pharmacology Suite - 12 Installation Validation

User1

February 7, 2025

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Chapter 1

Installation Validation Results

Overall Validation Result

Valid

1.1 Validation Summary

Run Duration

Start time: 2025-02-07 02:35 End time: 2025-02-07 03:27

Validation performed in 52m:31s:285ms

Input Configuration Folder

 $C: \label{lem:condition} C: \label{lem:condition} Pharmacology \label{lem:condition} In tallation \label{lem:condition} Validator \label{lem:condition} 12.0 \label{lem:condition} In puts \label{lem:condition} Batch Files$

Local Outputs Location

Application Versions

PK-Sim Version 12.0.440 MoBi Version 12.0.434

Language Settings

Chinese (Traditional, Taiwan) (zh-TW)

Computer Name

DESKTOP-DBSLF5P

Operating System

Windows 10 Pro

Architecture

x64

Running on Virtual Machine

Yes

Running on Terminal Session

No

1.2 Comparison Results

Overall Comparison Result

Valid

Installation Folder

 $C: \ \ Program Data \ \ Open \ Systems \ Pharmacology \ \ Installation \ \ Validator \ \ \ \ \ Batch Files$

Computed Folder

1.2.1 Valid Simulations (155/155)

 $Simulation: Beagle_SingleORAL_Dissolved-Beagle_SingleORAL_Dissolved$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|drug|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 0

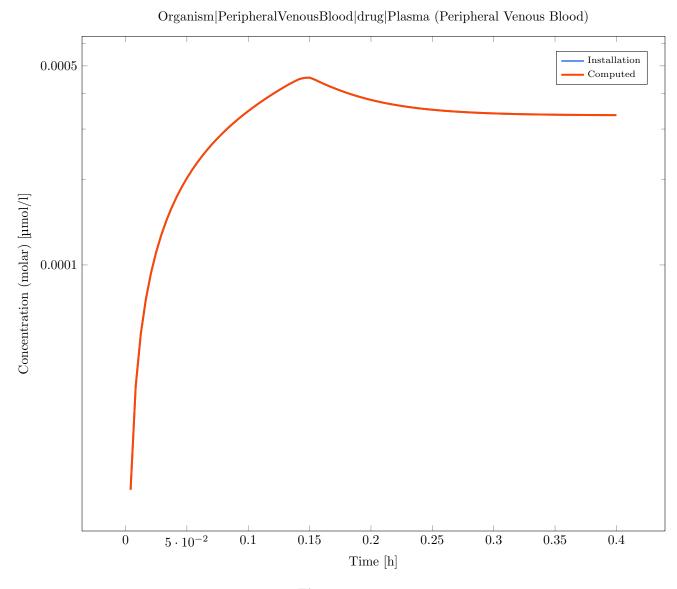


Figure 1.1

 $\label{lem:simpleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5\\ Result of the validation: Valid$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: $\mathbf 0$

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

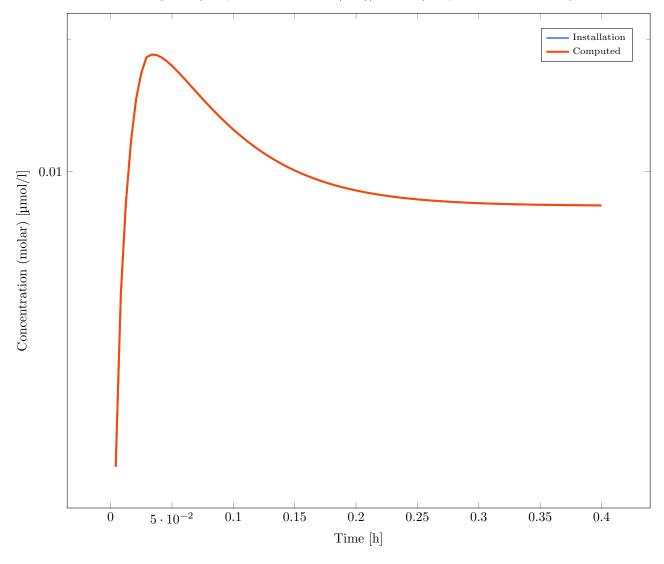


Figure 1.2

 $\label{lem:simulation:beagle_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_--5 \\ Result of the validation: Valid$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: $\mathbf 0$

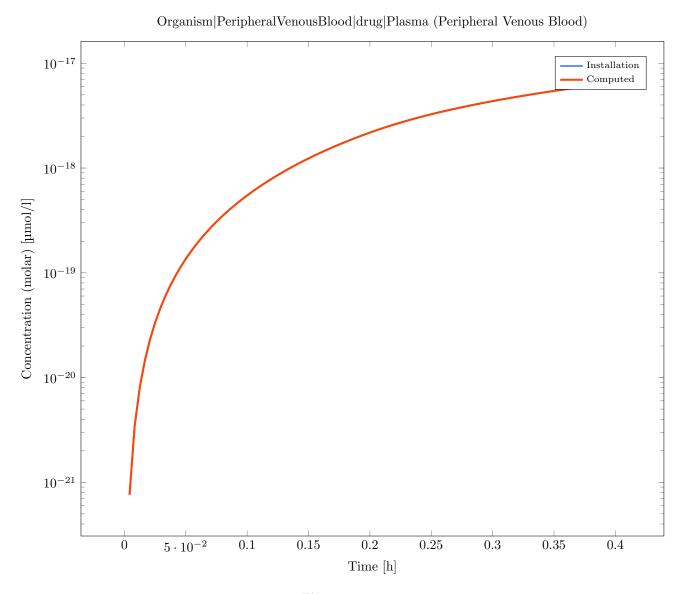
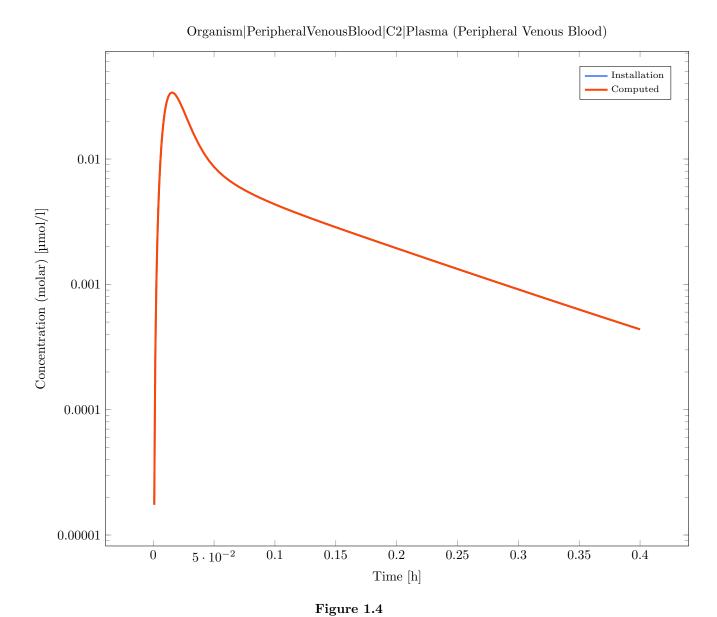


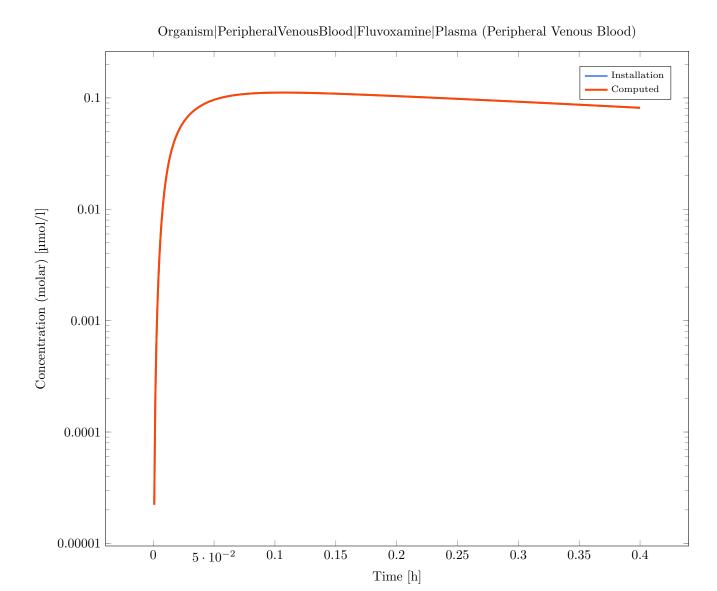
Figure 1.3

 ${\bf Simulation:\ DDI_Multiple Combinations\hbox{--}01_MM_Competitive_Competitive} \\ {\bf Result\ of\ the\ validation:\ Valid}$

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: 3.84E-4



Output Path: Organism |Peripheral Venous
Blood |Fluvoxamine |Plasma (Peripheral Venous Blood)
 Deviation: 2.00E-4



Output Path: Organism |Peripheral Venous
Blood |Itraconazole |Plasma (Peripheral Venous Blood)
 Deviation: 2.44E-4

Figure 1.5

Organism|PeripheralVenousBlood|Itraconazole|Plasma (Peripheral Venous Blood)

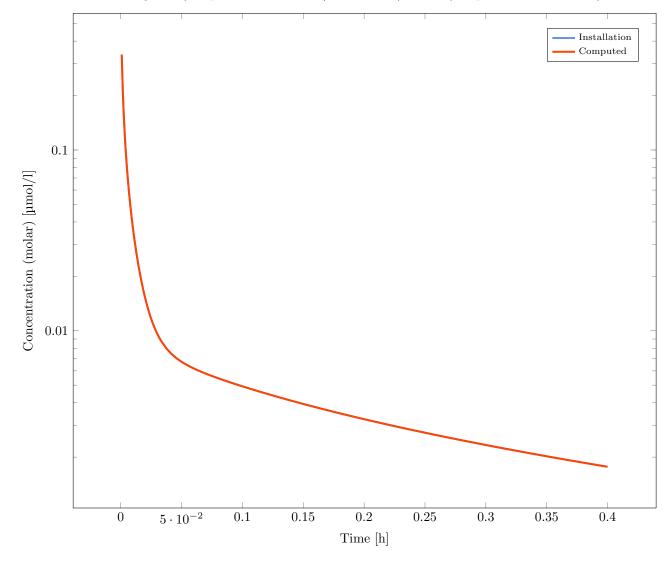


Figure 1.6

 ${\bf Simulation:\ DDI_Multiple Combinations-02_MM_Uncompetitive_Uncompetitive_Result\ of\ the\ validation:\ Valid}$

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: 3.78E-4

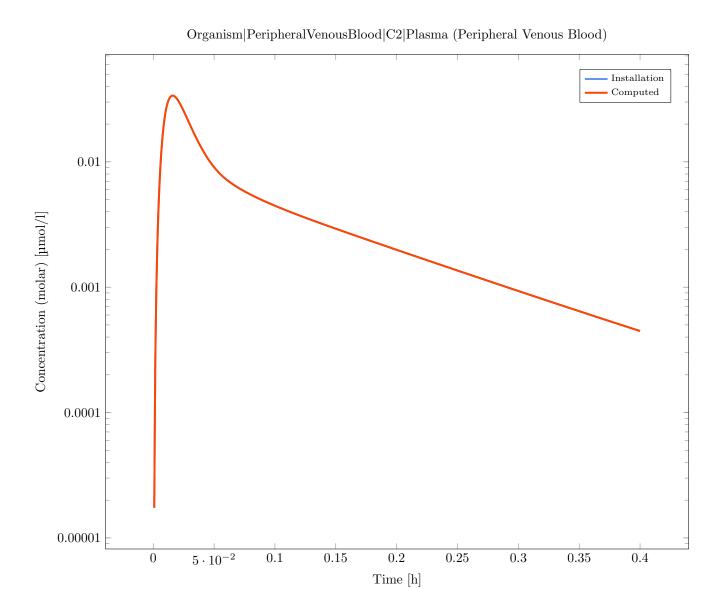


Figure 1.7

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive_CYP3A4_1|Plasma\ (PeripheralVenous\ Blood)$

Deviation: 3.93E-4

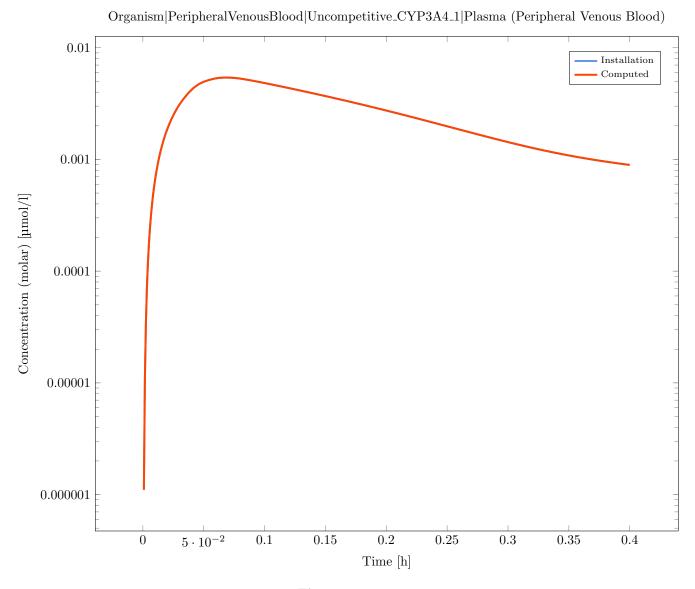
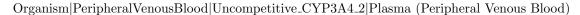


Figure 1.8

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive_CYP3A4_2|Plasma\ (PeripheralVenous\ Blood)$

Deviation: 3.69E-4



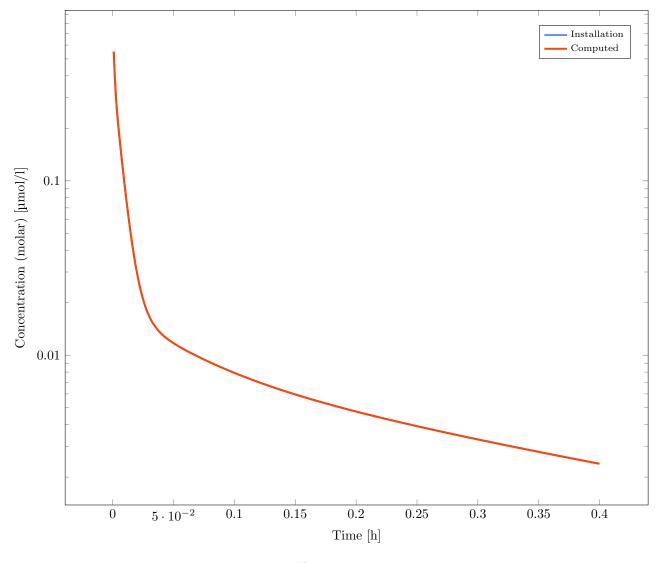


Figure 1.9

 ${\bf Simulation:\ DDI_Multiple Combinations-03_MM_Noncompetitive_N$

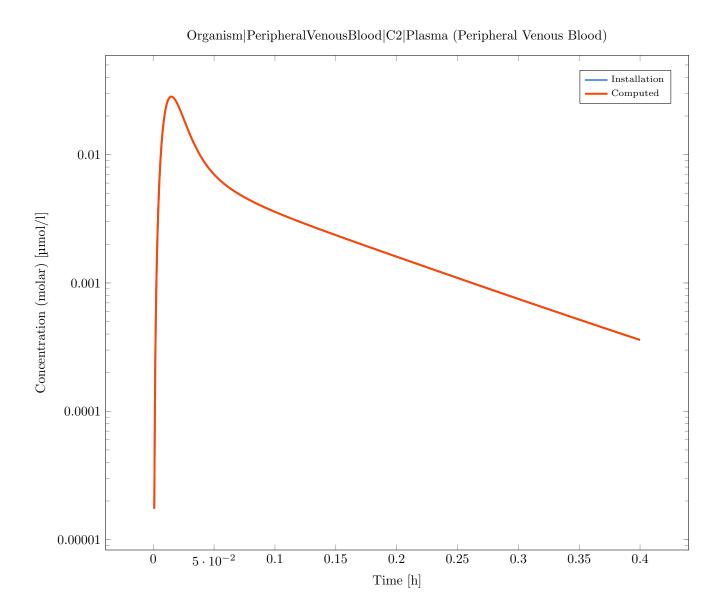


Figure 1.10

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 3.68E-4

Organism|PeripheralVenousBlood|Noncompetitive_CYP3A4_1|Plasma (Peripheral Venous Blood)

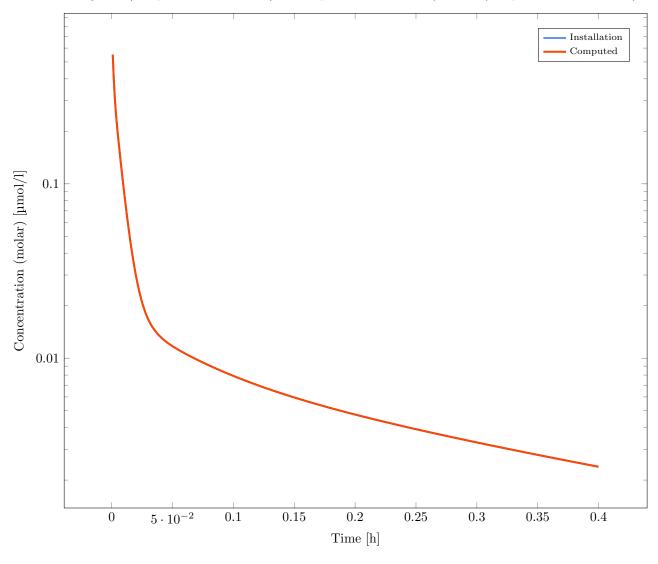


Figure 1.11

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_2|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 3.12E-4

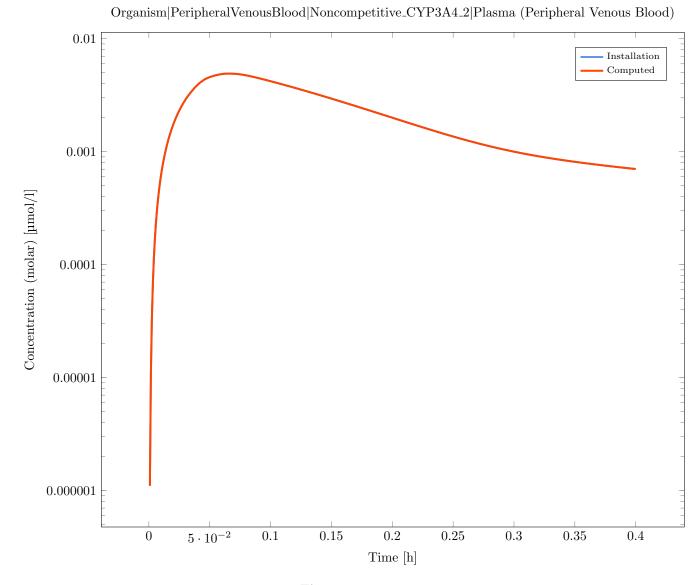


Figure 1.12

 $Simulation: \ DDI_MultipleCombinations-04_MM_Mixed_Mixed$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C2|Plasma (Peripheral Venous Blood)

Deviation: 3.82E-4

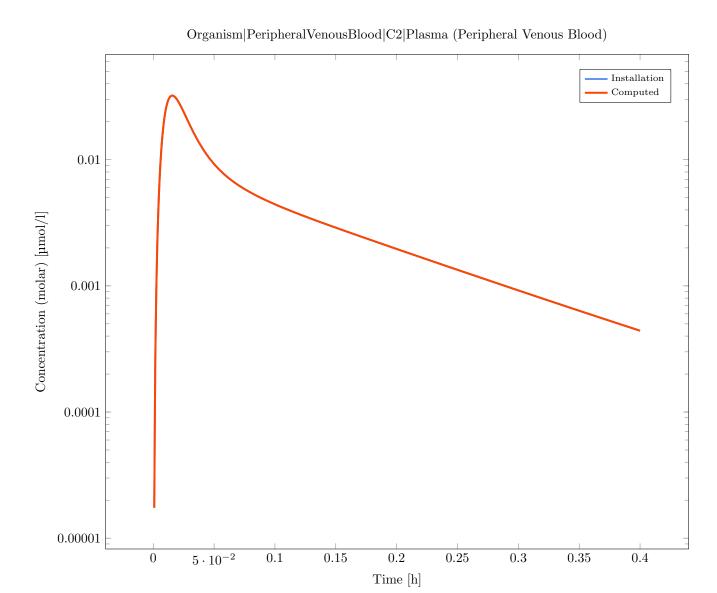


Figure 1.13

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_1|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 2.60E-4

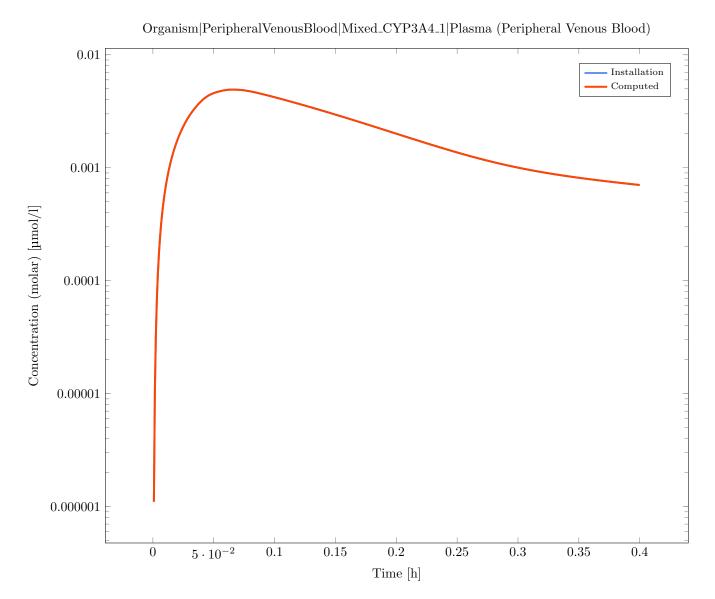


Figure 1.14

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_2|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 3.68E-4



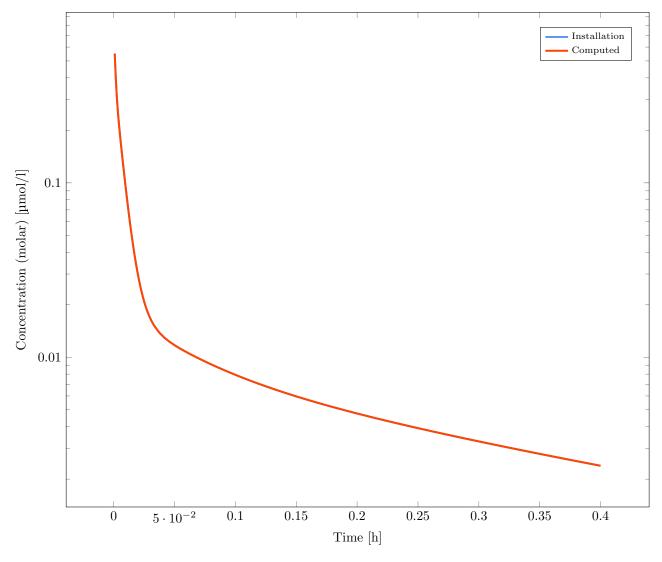


Figure 1.15

Simulation: DDI_MultipleCombinations-05_MM_Mechanismbased_Mechanismbased Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: $3.69\hbox{E-}4$

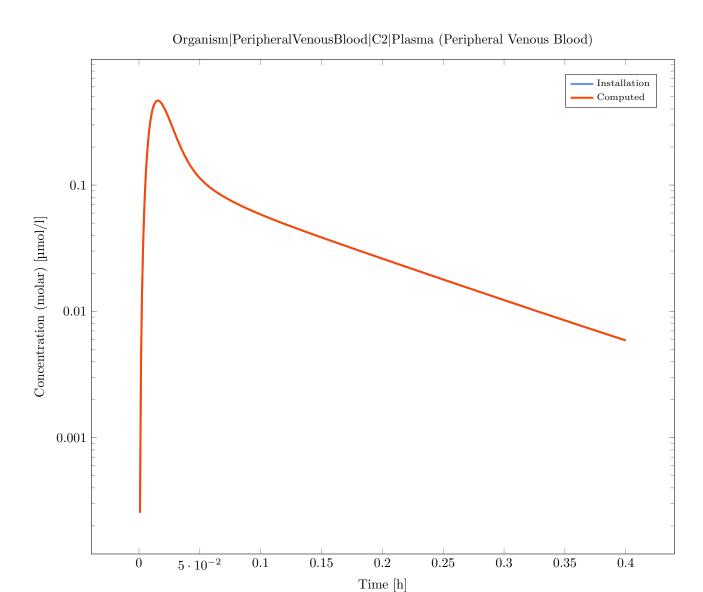
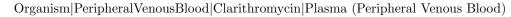


Figure 1.16

Output Path: Organism |PeripheralVenousBlood |Clarithromycin |Plasma (Peripheral Venous Blood)
 Deviation: 2.03E-4



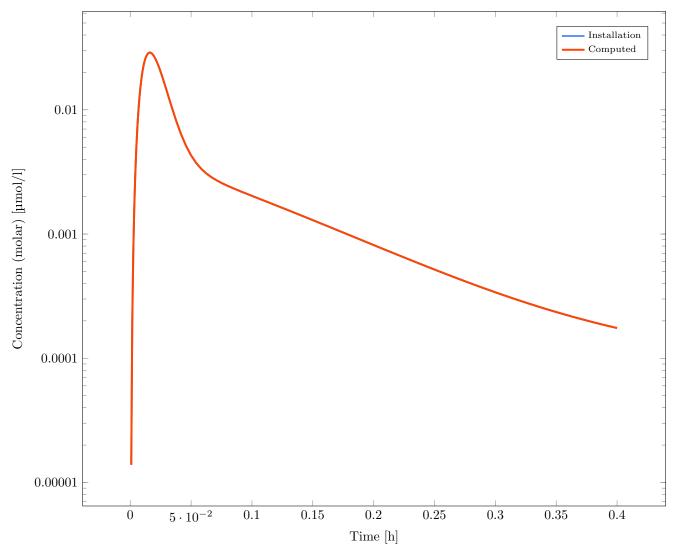
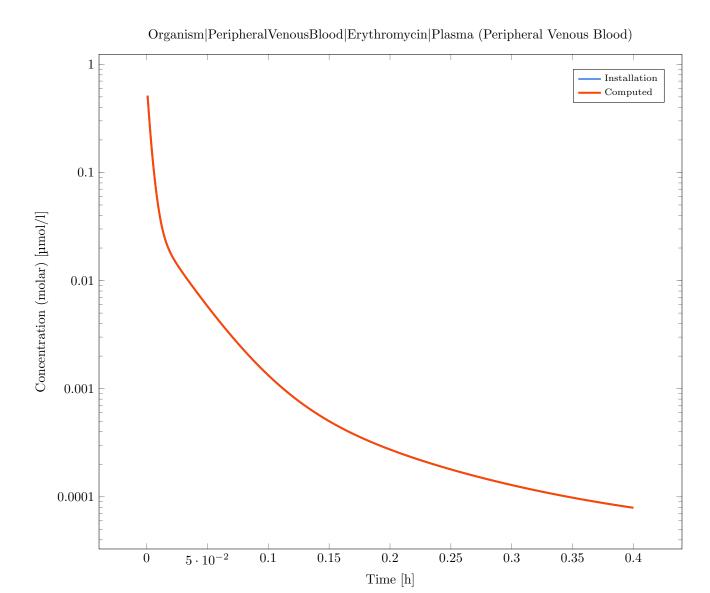


Figure 1.17

Output Path: Organism |PeripheralVenousBlood | Erythromycin |Plasma (Peripheral Venous Blood)
 Deviation: 3.61E-4



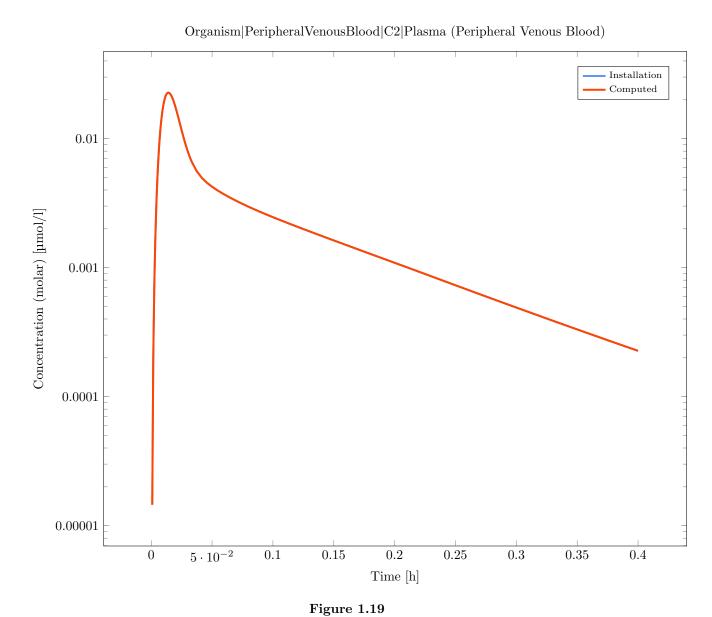
 ${\bf Simulation:\ DDI_Multiple Combinations-06_MM_Induction_Induction}$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|C2|Plasma\ (Peripheral\ Venous\ Blood)$

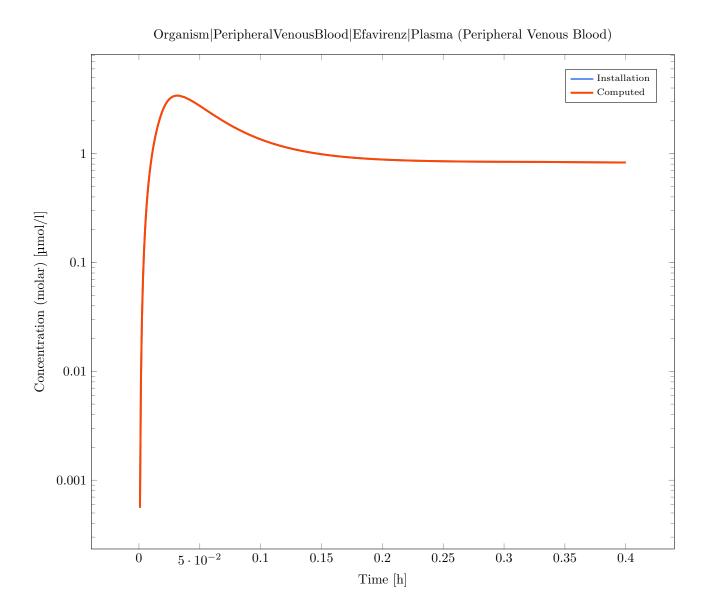
Figure 1.18

Deviation: 3.14E-4



-

Output Path: Organism|PeripheralVenousBlood|Efavirenz|Plasma (Peripheral Venous Blood) Deviation: 1.76E-4



Output Path: Organism |Peripheral Venous
Blood |Rifampicin |Plasma (Peripheral Venous Blood)
 Deviation: $3.68\hbox{E-}4$

Figure 1.20

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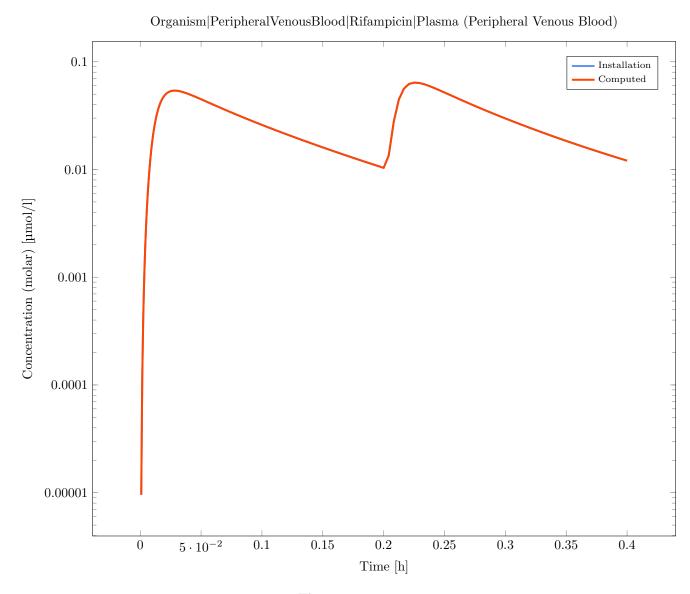
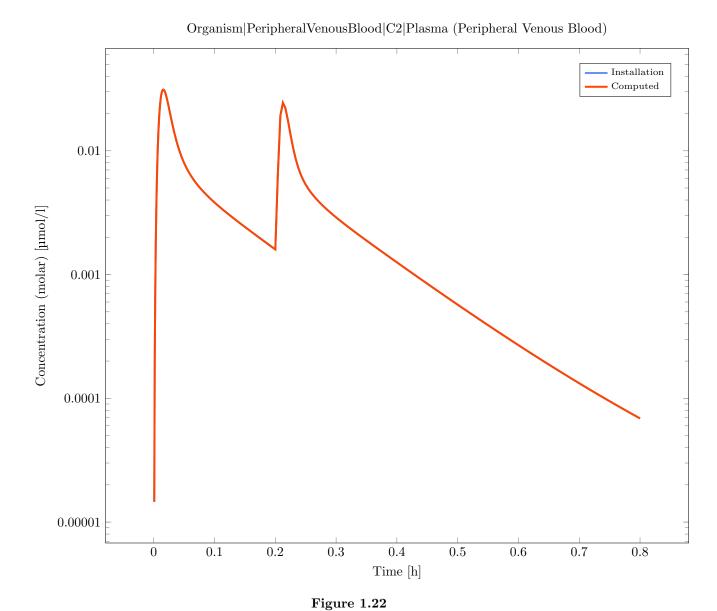


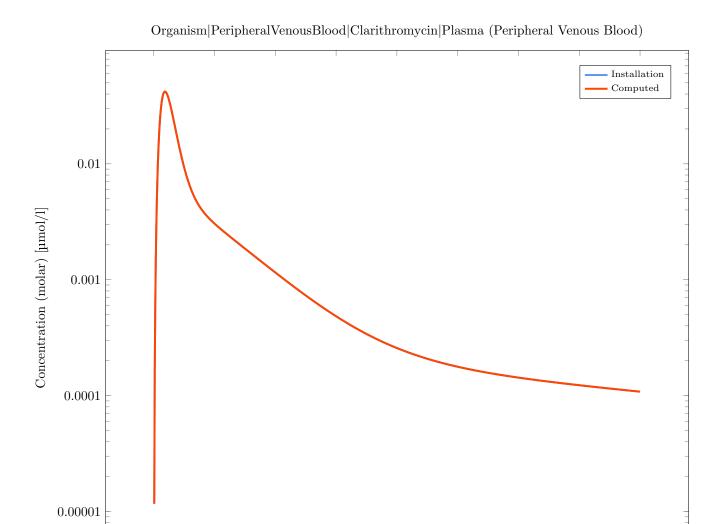
Figure 1.21

Simulation: DDI_MultipleCombinations-07_MM_Competitive_Competitive_Mechanismbased_Mechanismbased Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: 3.28E-4



Output Path: Organism |Peripheral Venous
Blood |Clarithromycin |Plasma (Peripheral Venous Blood)
 Deviation: 2.12E-4



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0.4

Time [h]

0.5

0.6

0.7

0.8

Output Path: Organism |Peripheral Venous
Blood |Erythromycin |Plasma (Peripheral Venous Blood)
 Deviation: 5.96E-4

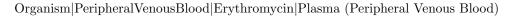
Figure 1.23

0.3

0

0.1

0.2



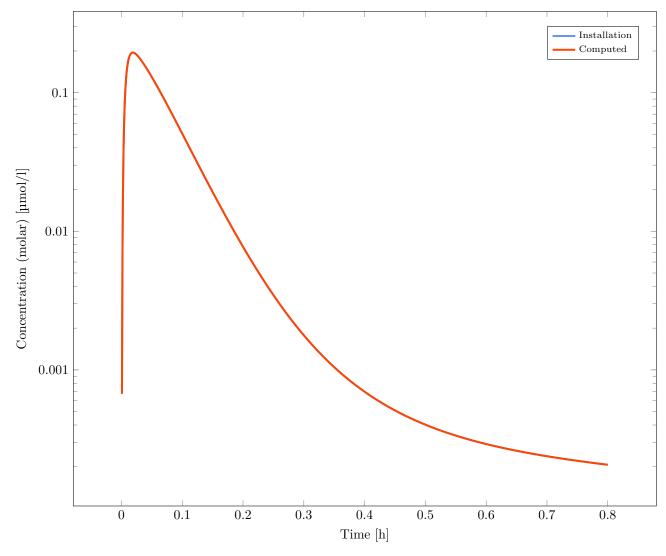
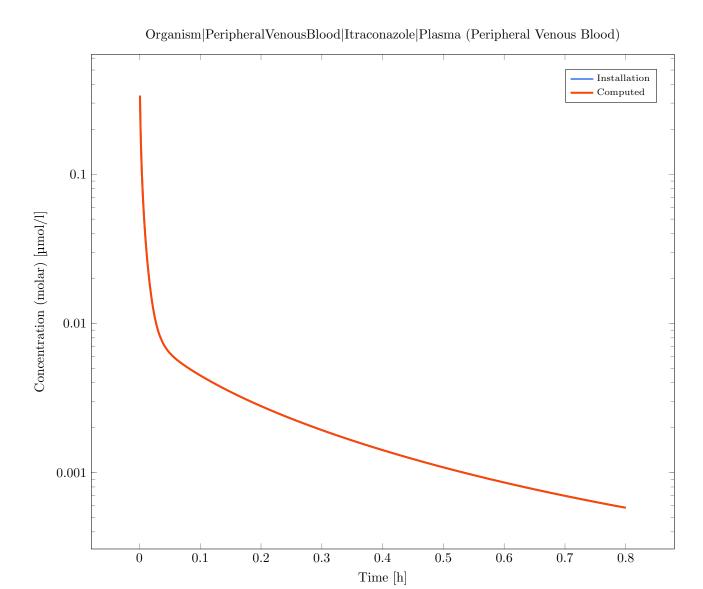


Figure 1.24

Output Path: Organism |Peripheral Venous
Blood |Itraconazole |Plasma (Peripheral Venous Blood)
 Deviation: 3.28E-4



Output Path: Organism|PeripheralVenousBlood|Rifampicin|Plasma (Peripheral Venous Blood)

Figure 1.25

Deviation: 4.68E-4

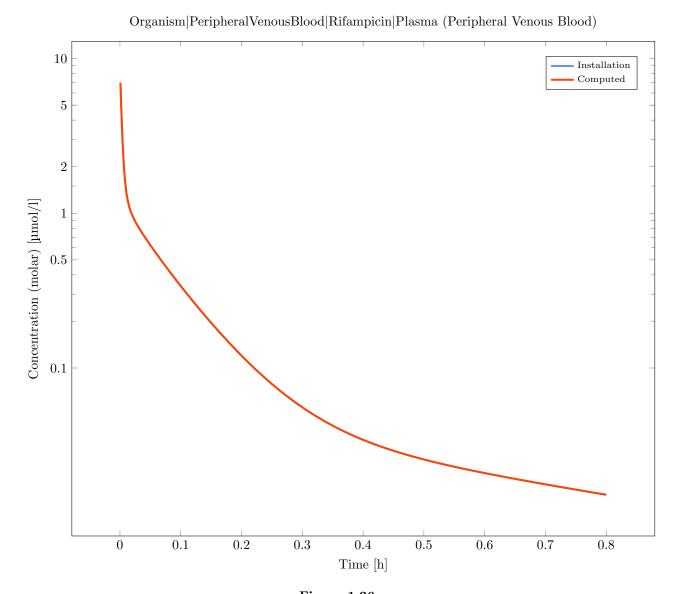


Figure 1.26

 $Simulation: \ DDI_Multiple Combinations - 08_MM_Uncompetitive_Uncompetitive_Mechanism based_Mechanism based$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|C2|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 6.01E-4

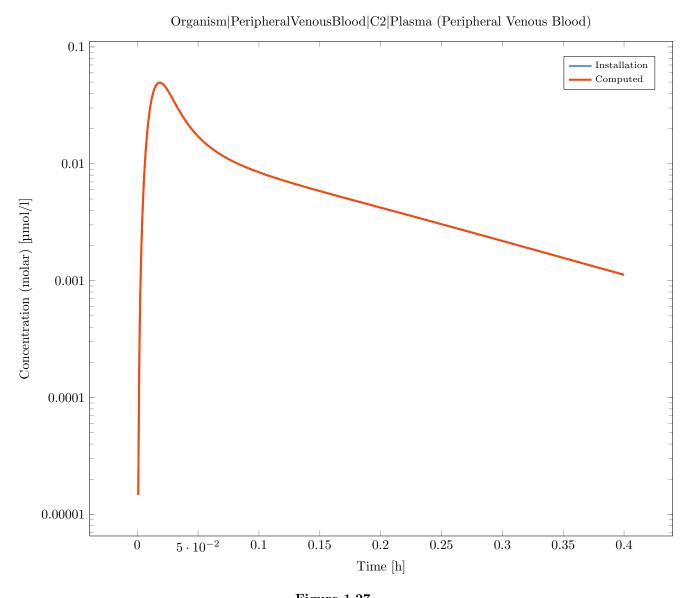


Figure 1.27

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_4|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 6.08E-4

Organism|PeripheralVenousBlood|MechanismBased_4|Plasma (Peripheral Venous Blood)

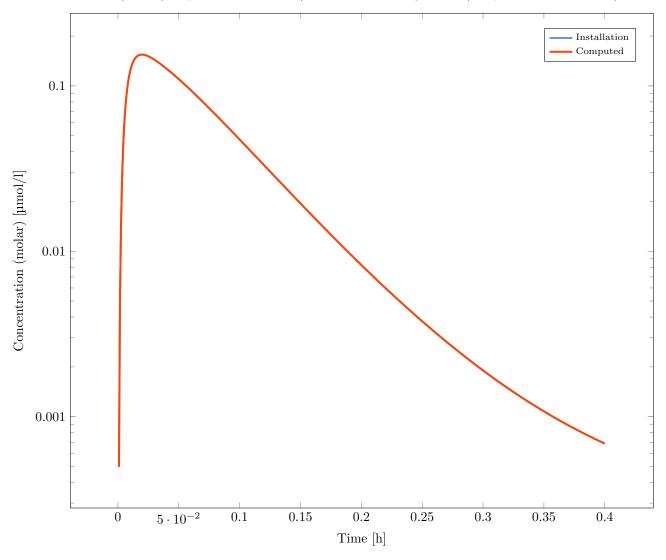
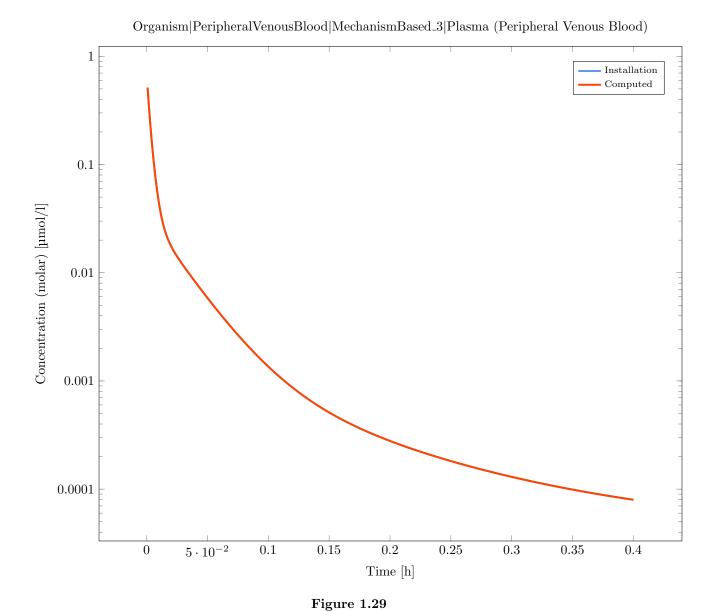


Figure 1.28

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_3|Plasma\ (Peripheral\ Venous\ Blood)$

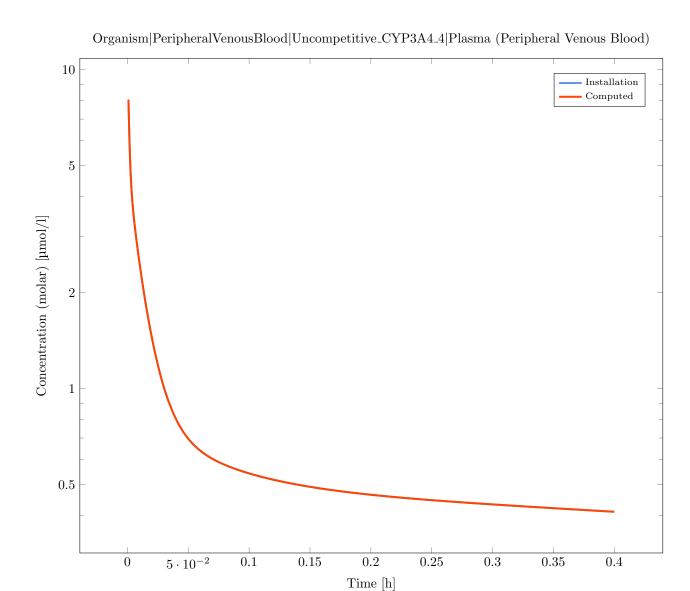
Deviation: 3.67E-4



Output Path: Organism |PeripheralVenousBlood |Uncompetitive_CYP3A4_4 |Plasma (Peripheral Venous Blood)

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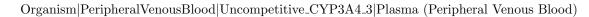
Deviation: 5.65E-5



Output Path: Organism |Peripheral VenousBlood |Uncompetitive_CYP3A4_3 |Plasma (Peripheral Venous Blood)

Figure 1.30

Deviation: 8.35E-5



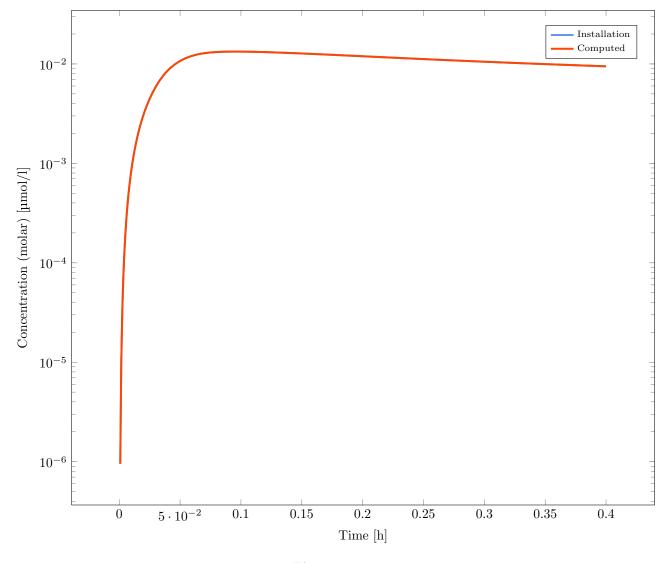


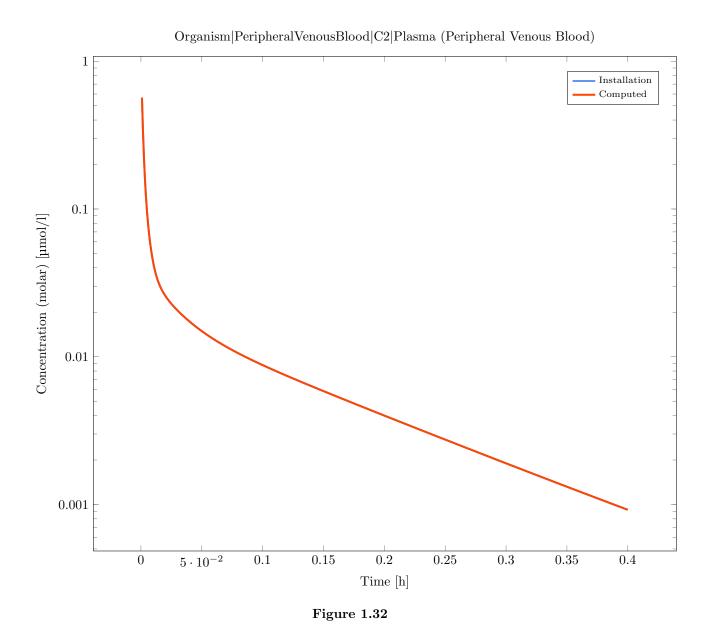
Figure 1.31

 $Simulation: \ DDI_Multiple Combinations - 09_MM_Noncompetitive_Noncompetitive_Mechanism based_Mechanism based$

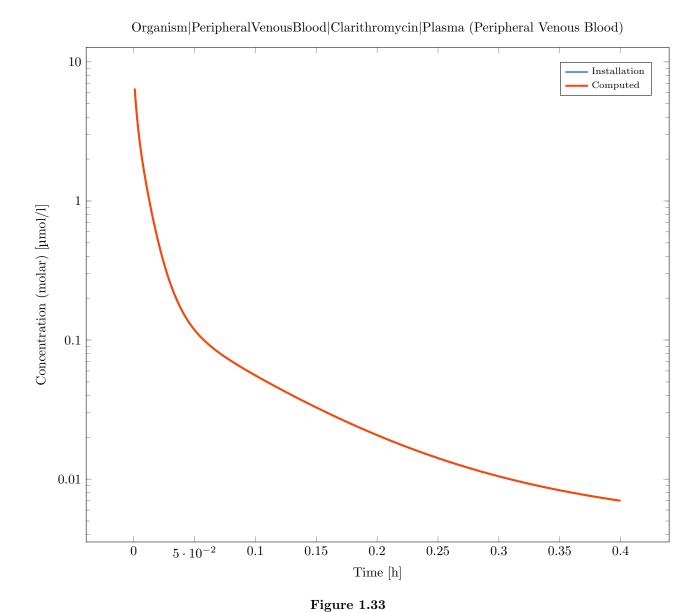
Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C2|Plasma (Peripheral Venous Blood)

Deviation: 3.09E-4



Output Path: Organism |Peripheral Venous
Blood |Clarithromycin |Plasma (Peripheral Venous Blood)
 Deviation: 2.51E-4



Output Path: Organism |Peripheral Venous
Blood |Erythromycin |Plasma (Peripheral Venous Blood)
 Deviation: 5.92E-4

Organism|PeripheralVenousBlood|Erythromycin|Plasma (Peripheral Venous Blood)

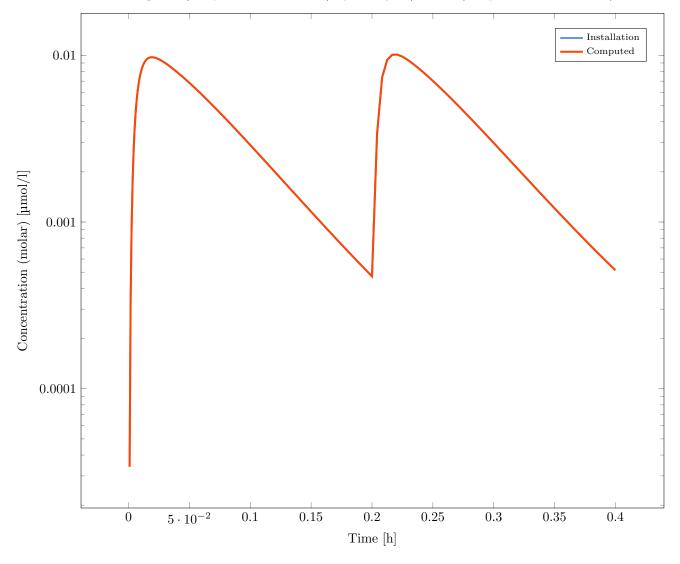
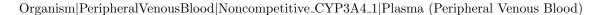


Figure 1.34

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 3.25E-4



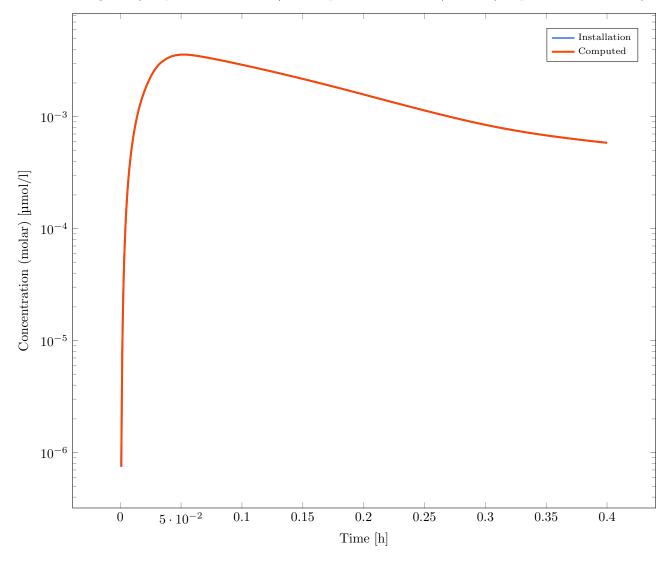


Figure 1.35

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_2|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 3.38E-4

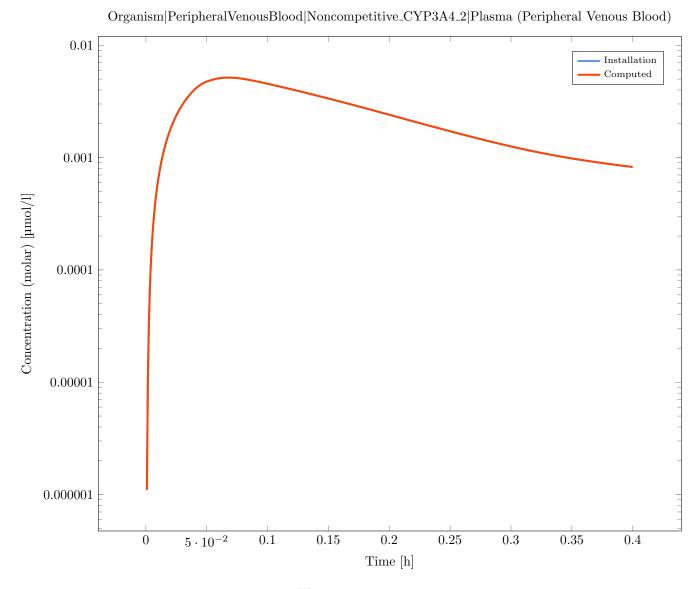
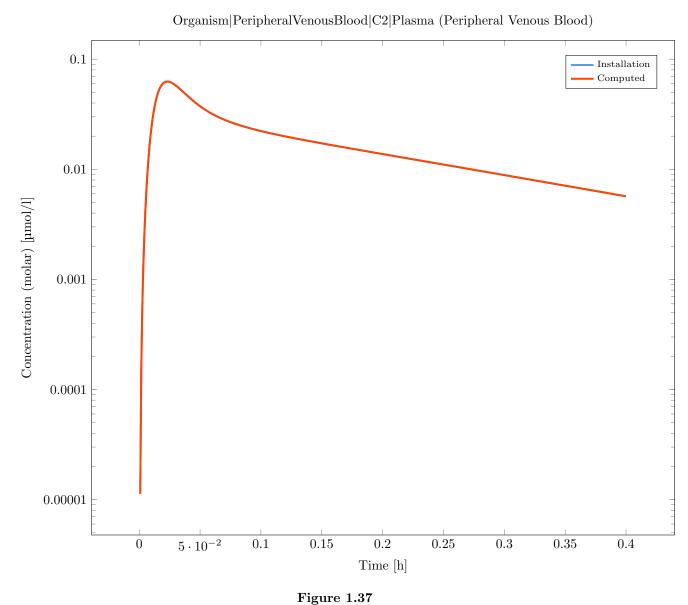


Figure 1.36

 ${\bf Simulation:\ DDI_Multiple Combinations-10_MM_Mixed_Mixed_Mechanismbased_Mech$

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: $4.92\hbox{E-}4$



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 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_4|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.67E-4

Organism|PeripheralVenousBlood|MechanismBased_4|Plasma (Peripheral Venous Blood)

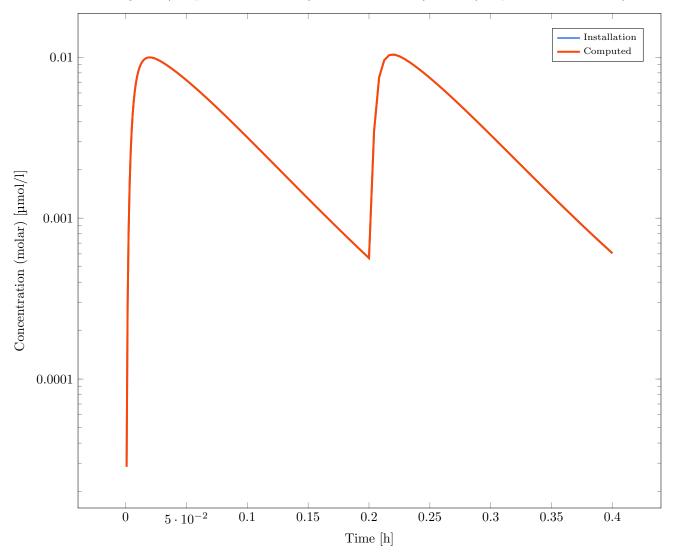


Figure 1.38

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_3|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.85E-4

Organism|PeripheralVenousBlood|MechanismBased_3|Plasma (Peripheral Venous Blood)

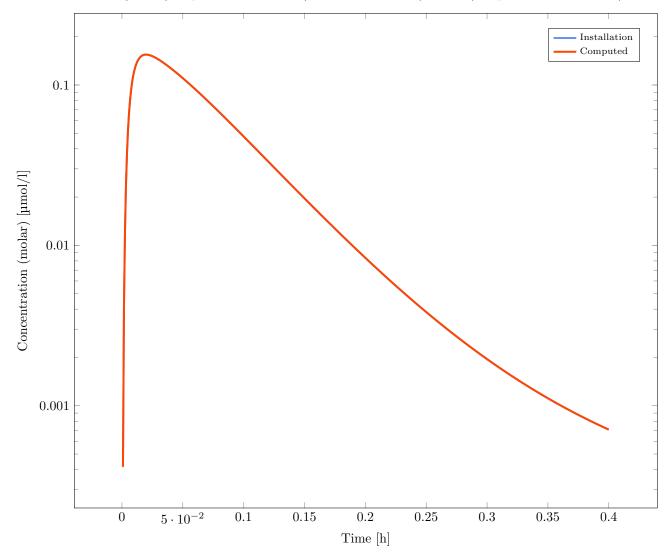
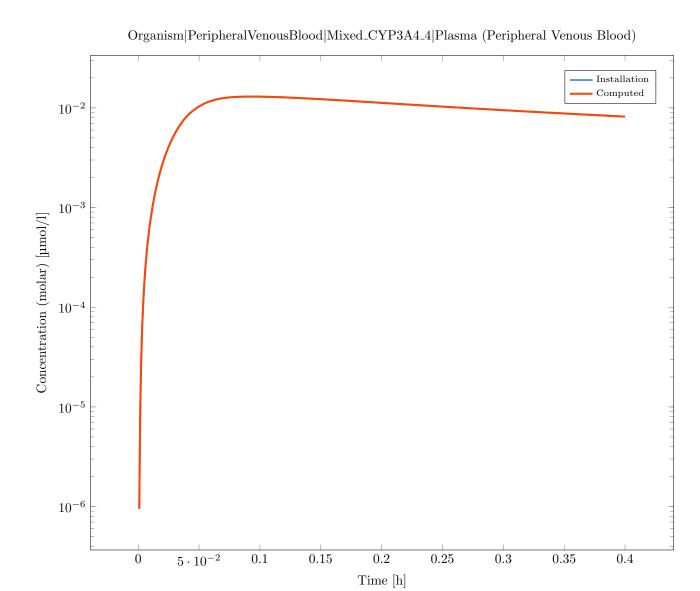


Figure 1.39

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_4|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 1.04E-4



 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_3|Plasma\ (Peripheral\ VenousBlood)$

Figure 1.40

Deviation: 1.61E-4

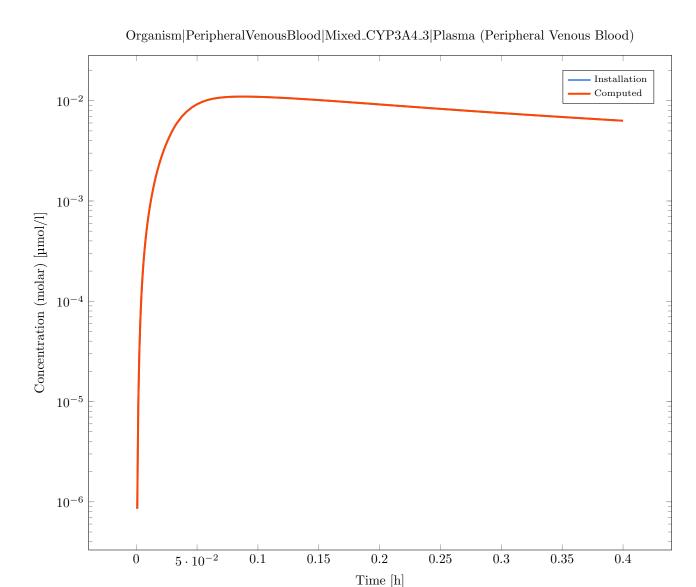
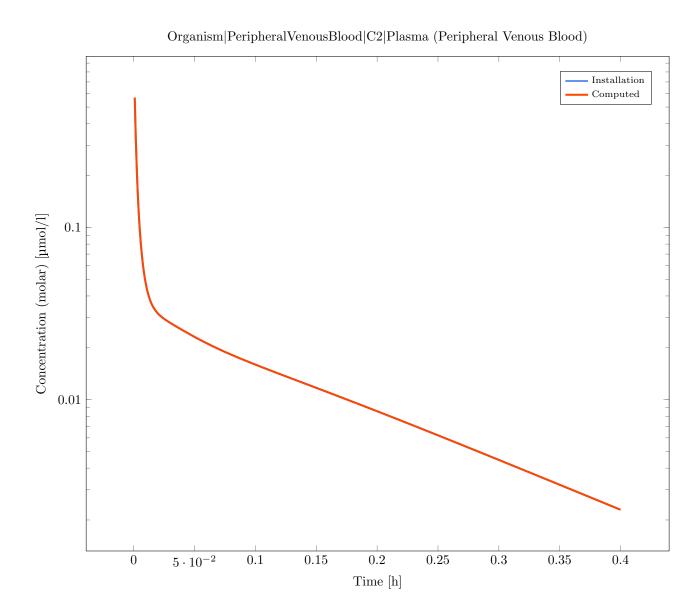


Figure 1.41

 ${\bf Simulation:} \ \ {\bf DDI_Multiple Combinations-11_MM_Mechanismbased_Mechanismbased_Induction$

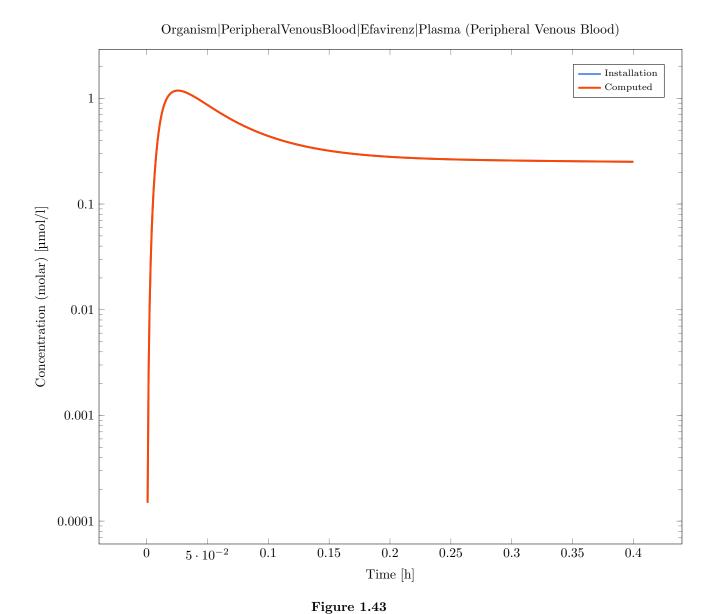
Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: $5.05\hbox{E-}4$



Output Path: Organism |Peripheral Venous
Blood |Efavirenz |Plasma (Peripheral Venous Blood)
 Deviation: 1.74E-4

Figure 1.42



 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_3|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 5.98E-4

Organism|PeripheralVenousBlood|MechanismBased_3|Plasma (Peripheral Venous Blood)

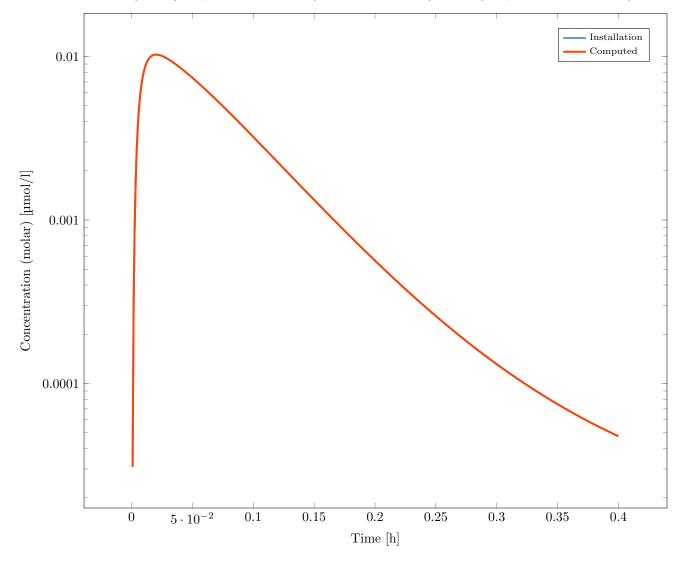


Figure 1.44

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_4|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 6.00E-4



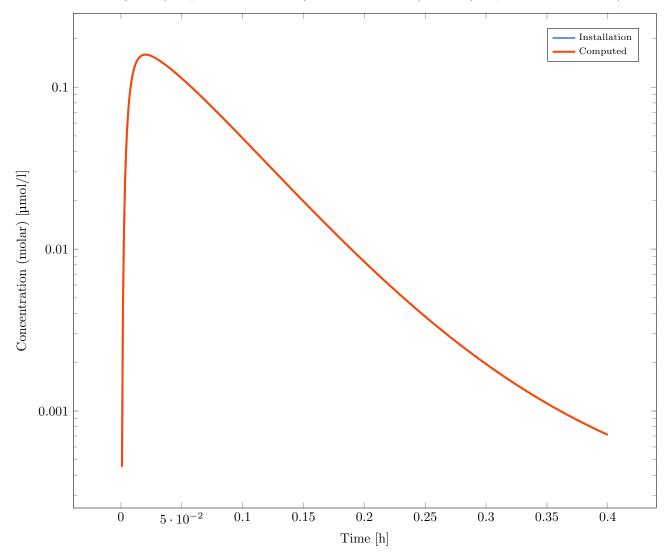


Figure 1.45

Output Path: Organism |Peripheral Venous
Blood |Rifampicin |Plasma (Peripheral Venous Blood)
 Deviation: $4.51 \hbox{E-}4$

$Organism|Peripheral Venous Blood|Rifampicin|Plasma\ (Peripheral Venous Blood)$

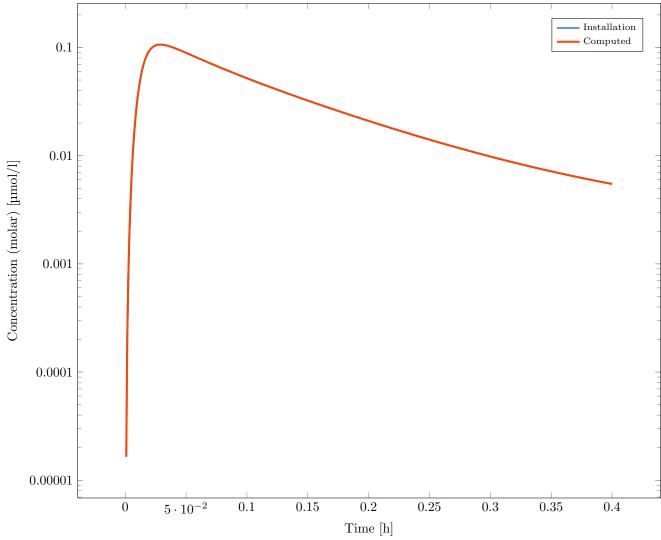


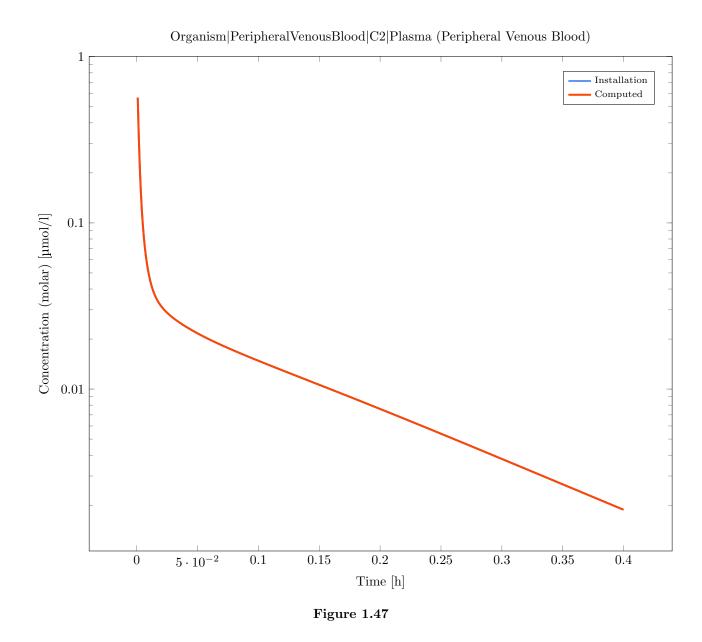
Figure 1.46

 $Simulation: \ DDI_MultipleCombinations-12_MM_All_DDI_Types$

Result of the validation: Valid

 $Output\ Path:\ Organism | Peripheral Venous Blood | C2 | Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.67E-4



Output Path: Organism |Peripheral Venous
Blood |Efavirenz |Plasma (Peripheral Venous Blood)
 Deviation: $1.92 \hbox{E-}4$

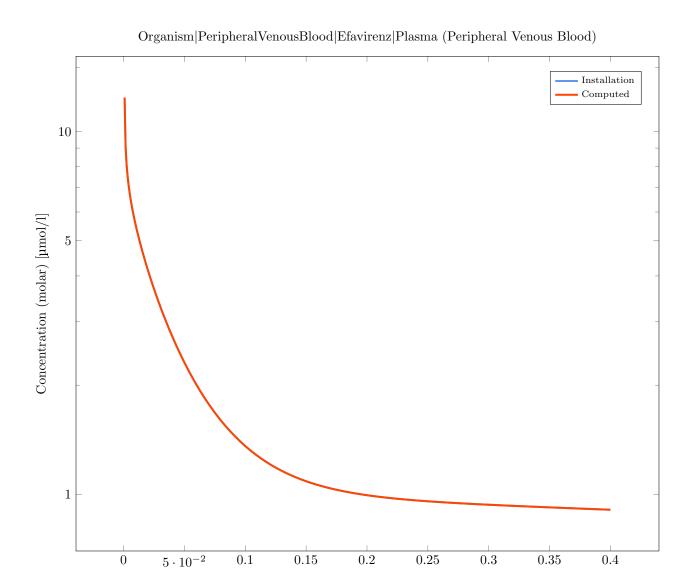
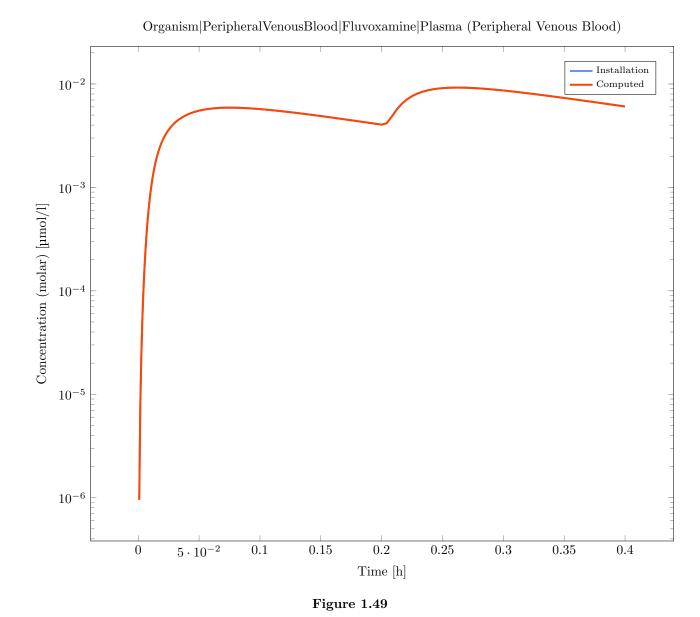


Figure 1.48

Time [h]

Output Path: Organism |Peripheral Venous
Blood |Fluvoxamine |Plasma (Peripheral Venous Blood)
 Deviation: 3.12E-4



 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_3|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.81E-4



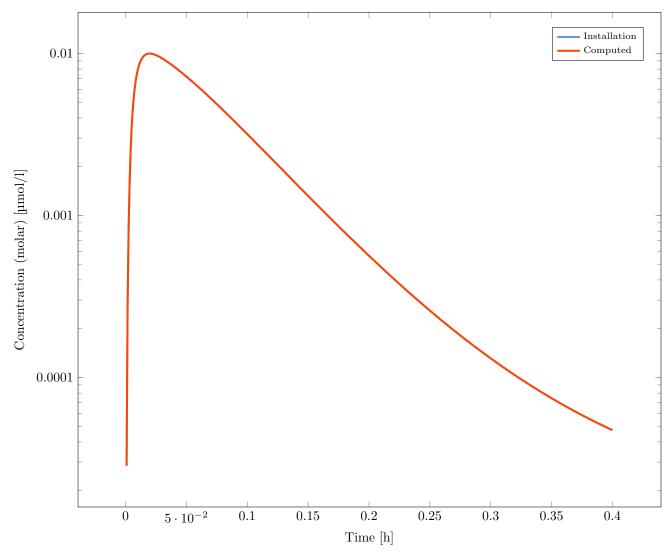


Figure 1.50

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_3|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 4.21E-4

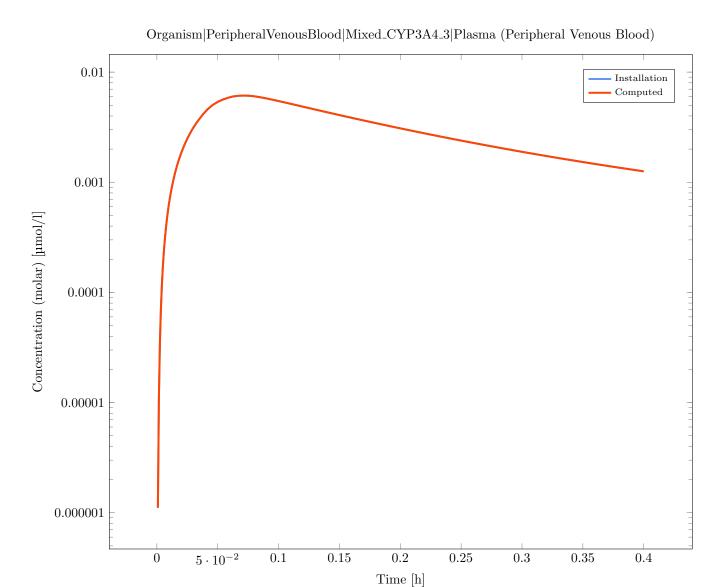
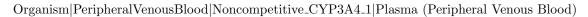


Figure 1.51

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.11E-4



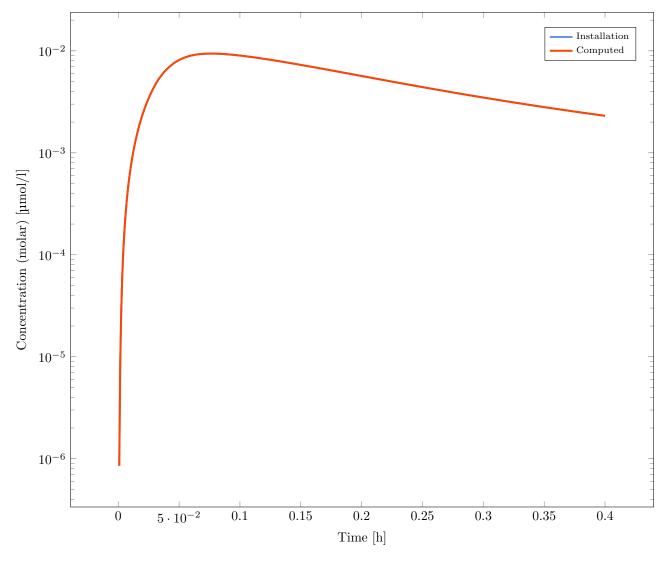


Figure 1.52

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive_CYP3A4_3|Plasma\ (PeripheralVenous\ Blood)$

Deviation: 5.31E-4

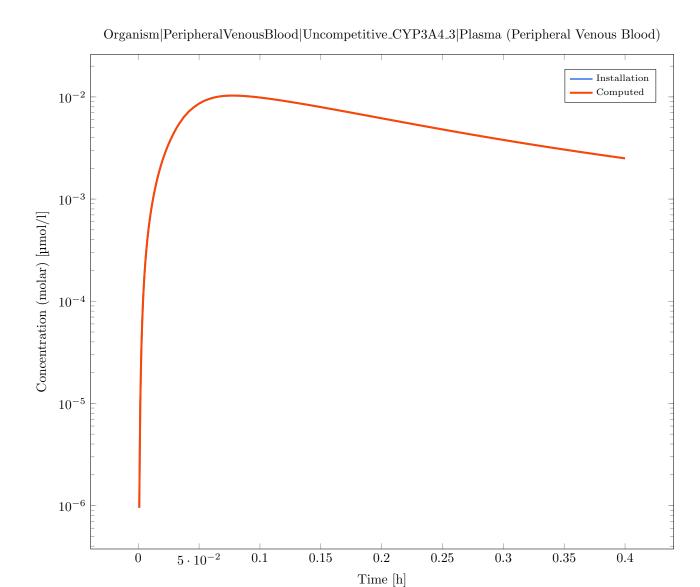
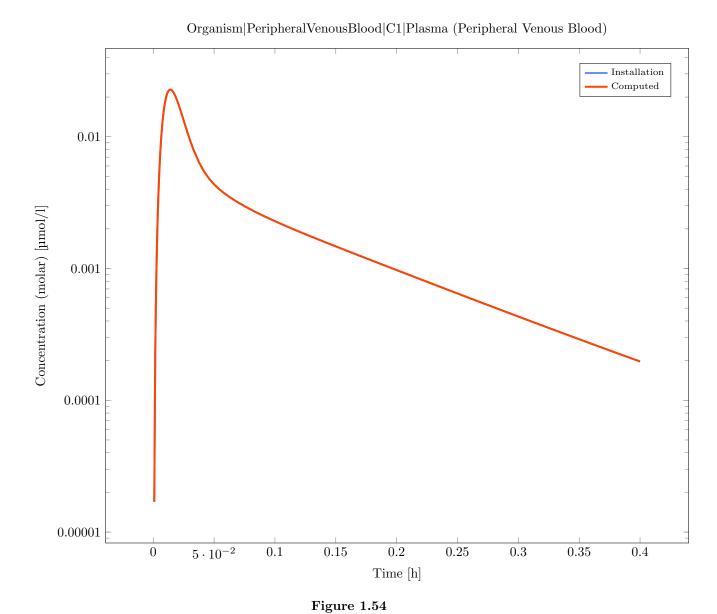


Figure 1.53

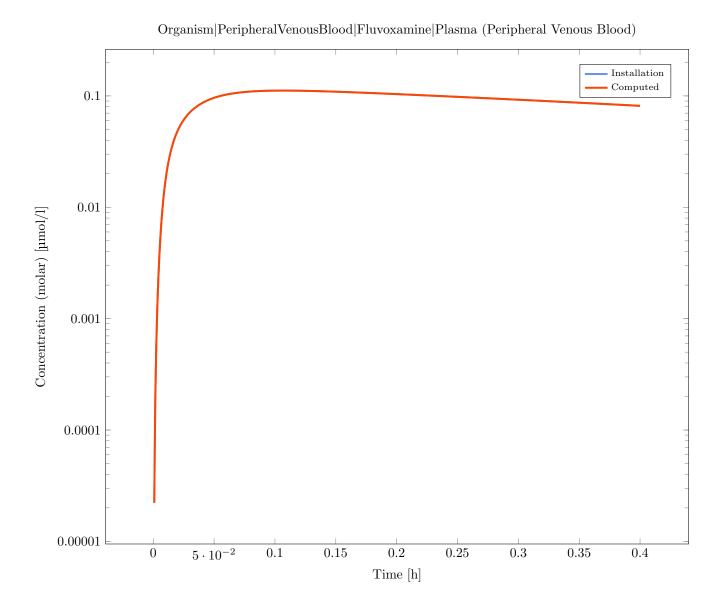
 ${\bf Simulation:\ DDI_Multiple Combinations-21_1st_Competitive_Competitive_Result\ of\ the\ validation:\ Valid}$

 $Output\ Path:\ Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 2.97E-4



Output Path: Organism |Peripheral Venous
Blood |Fluvoxamine |Plasma (Peripheral Venous Blood)
 Deviation: 2.00E-4



Output Path: Organism |Peripheral Venous
Blood |Itraconazole |Plasma (Peripheral Venous Blood)
 Deviation: 2.44E-4

Figure 1.55

Installation Computed 0.1 Concentration (molar) [µmol/l] 0.01

Organism|PeripheralVenousBlood|Itraconazole|Plasma (Peripheral Venous Blood)

Figure 1.56

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

Simulation: DDI_MultipleCombinations-23_1st_Noncompetitive_Noncompetitive Result of the validation: Valid

0.1

 $5 \cdot 10^{-2}$

 $Output\ Path:\ Organism | Peripheral Venous Blood | Noncompetitive_CYP3A4_1 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Noncompetitive_CYP3A4_1 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Noncompetitive_CYP3A4_1 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Noncompetitive_CYP3A4_1 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Noncompetitive_CYP3A4_1 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Noncompetitive_CYP3A4_1 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Noncompetitive_CYP3A4_1 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Peripheral Venous Blood$ Venous Blood)

Deviation: 3.69E-4

0

Organism|PeripheralVenousBlood|Noncompetitive_CYP3A4_1|Plasma (Peripheral Venous Blood)

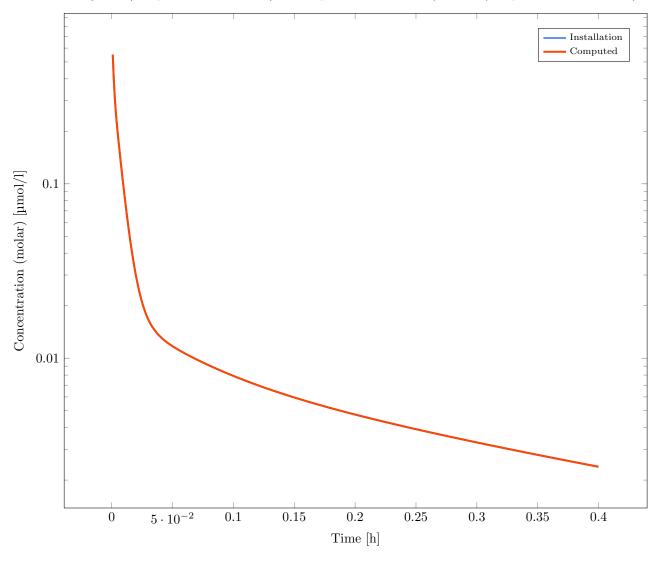


Figure 1.57

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_2|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 3.23E-4

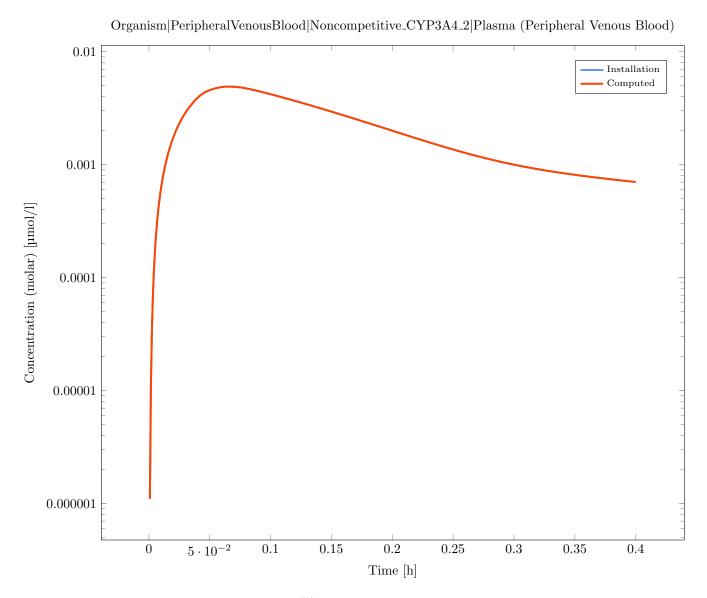


Figure 1.58

 $Output\ Path:\ Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 2.65E-4

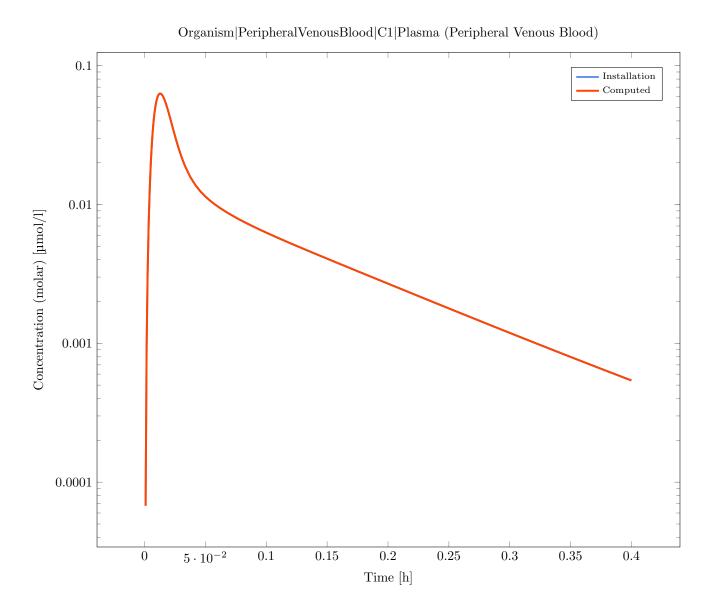


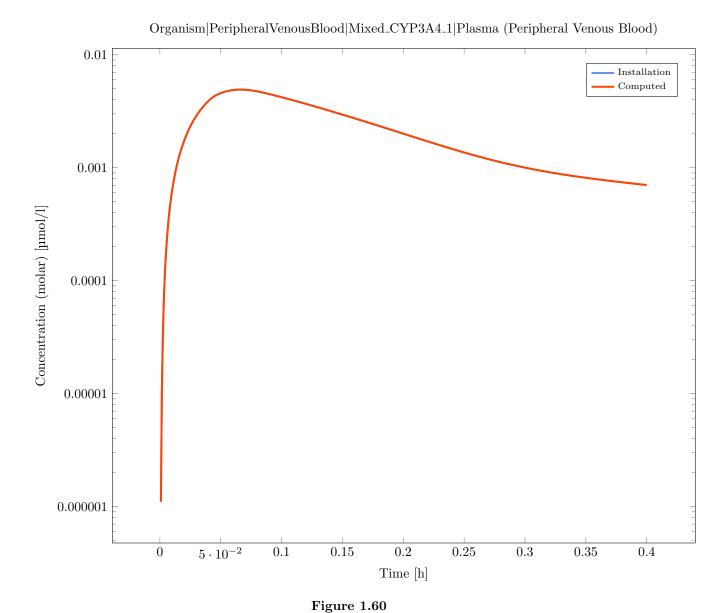
Figure 1.59

 $Simulation: \ DDI_MultipleCombinations-24_1st_Mixed_Mixed$

Result of the validation: Valid

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_1|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 2.99E-4



Output Path: Organism |PeripheralVenousBlood |Mixed_CYP3A4_2 |Plasma (Peripheral VenousBlood)

Deviation: 3.68E-4

$Organism | Peripheral Venous Blood | Mixed_CYP3A4_2 | Plasma \ (Peripheral Venous Blood)$

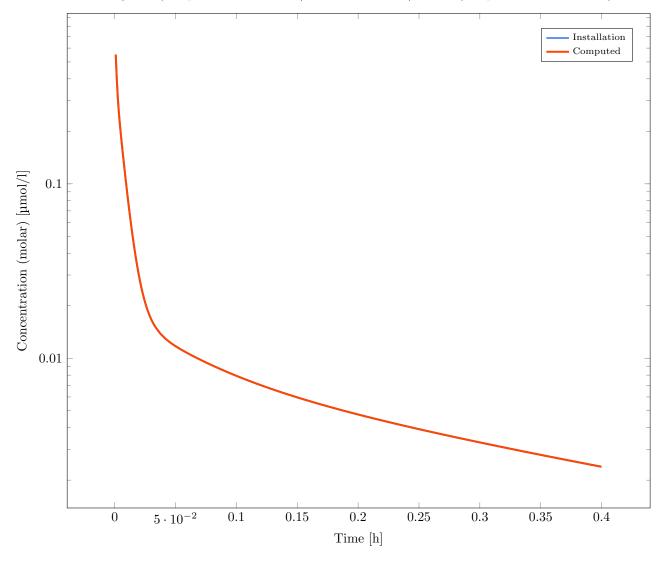


Figure 1.61

 $Output\ Path:\ Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 2.88E-4

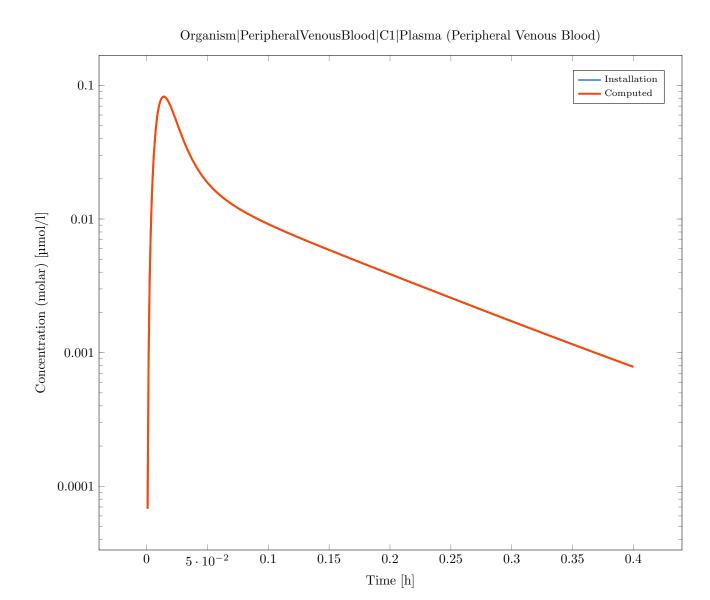
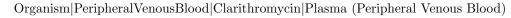


Figure 1.62

 ${\bf Simulation:\ DDI_Multiple Combinations\hbox{--}25_1st_Mechanismbased_Mechanismbased}. Result of the validation:\ Valid$

Output Path: Organism |Peripheral Venous
Blood |Clarithromycin |Plasma (Peripheral Venous Blood)
 Deviation: 2.03E-4



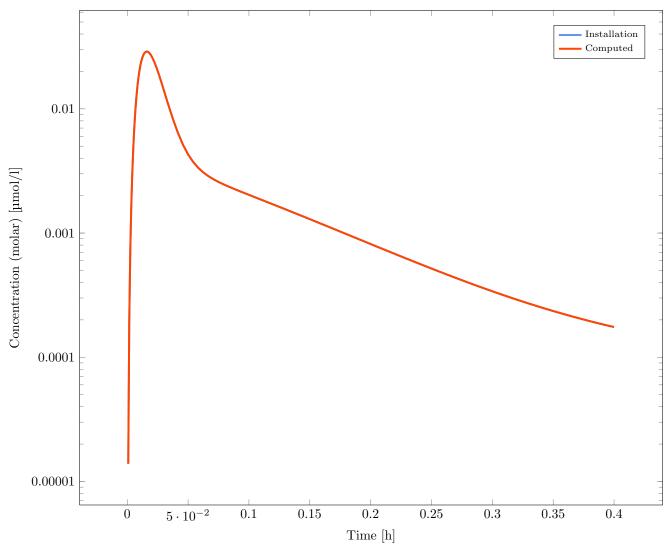


Figure 1.63

Output Path: Organism |Peripheral Venous
Blood |Erythromycin |Plasma (Peripheral Venous Blood)
 Deviation: 3.62 ± 4

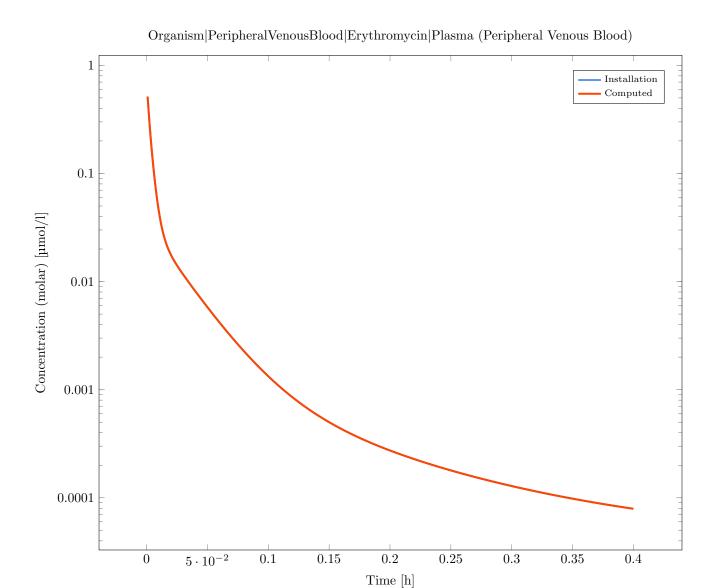


Figure 1.64

Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood)
 Deviation: 2.67E-4

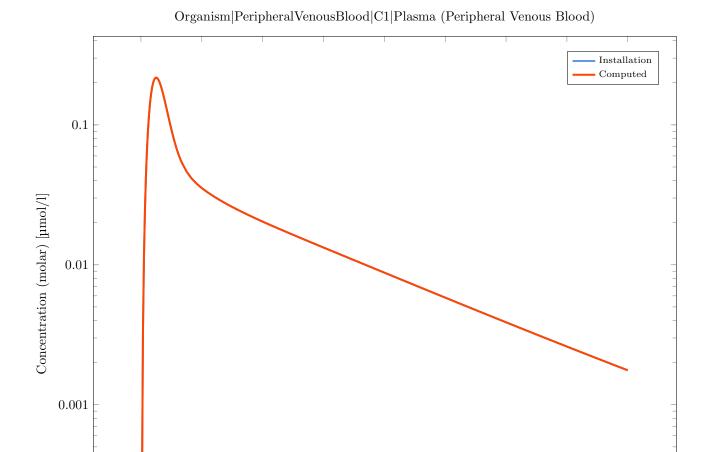


Figure 1.65

0.15

0.2

Time [h]

0.25

0.3

0.35

0.4

Simulation: DDI_MultipleCombinations-26_1st_Induction_Induction

0.1

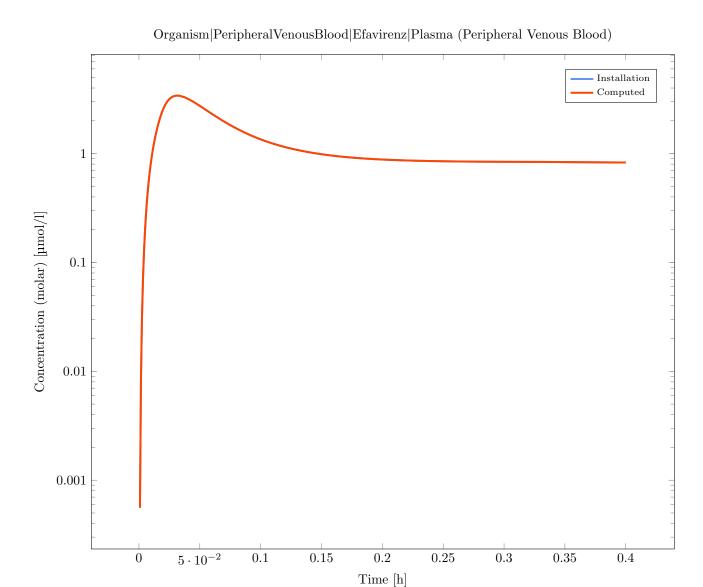
Result of the validation: Valid

0

 $5\cdot 10^{-2}$

$Output\ Path:\ Organism | Peripheral Venous Blood | Efavirenz | Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 1.67E-4



Output Path: Organism |Peripheral Venous
Blood |Rifampicin |Plasma (Peripheral Venous Blood)
 Deviation: 3.68E-4

Figure 1.66

Figure 1.67

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood)
 Deviation: $2.59\hbox{E-}4$

0.1

 $5\cdot 10^{-2}$

0

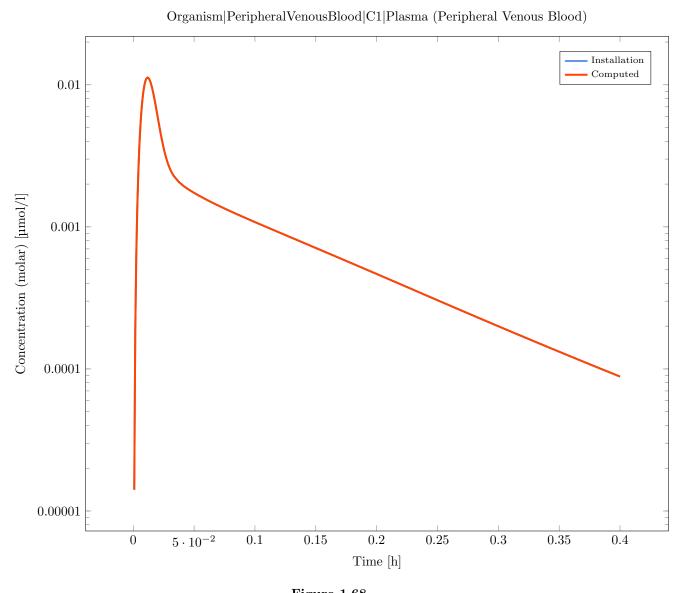
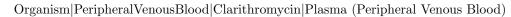


Figure 1.68

Simulation: DDI_MultipleCombinations-27_1st_Competitive_Competitive_Mechanismbased_Mechanismbased Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |Clarithromycin |Plasma (Peripheral Venous Blood)
 Deviation: 2.12E-4



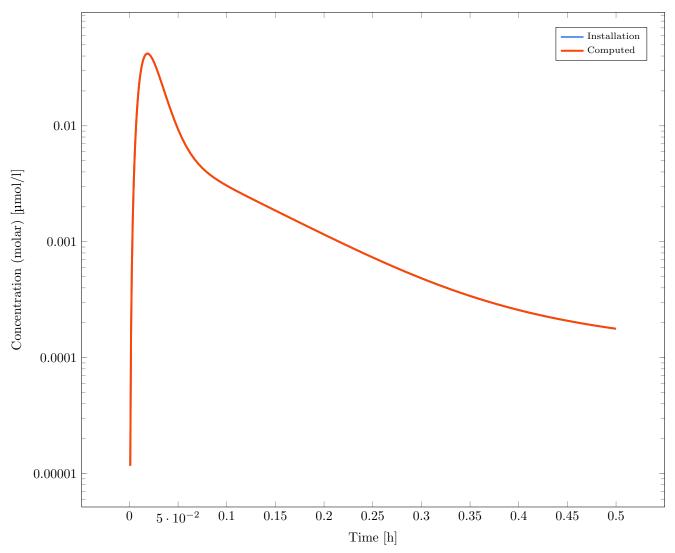


Figure 1.69

Output Path: Organism |PeripheralVenousBlood | Erythromycin |Plasma (Peripheral Venous Blood)
 Deviation: 5.96E-4

Organism|PeripheralVenousBlood|Erythromycin|Plasma (Peripheral Venous Blood)

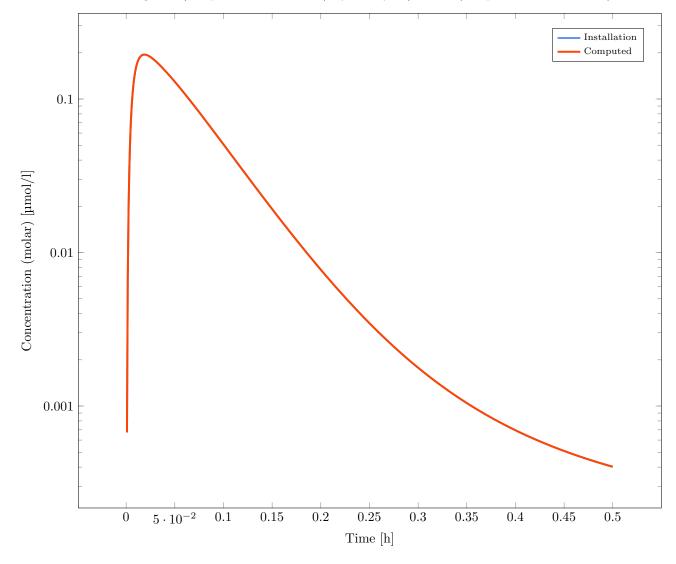


Figure 1.70

Output Path: Organism |Peripheral Venous
Blood |Itraconazole |Plasma (Peripheral Venous Blood)
 Deviation: 2.46E-4

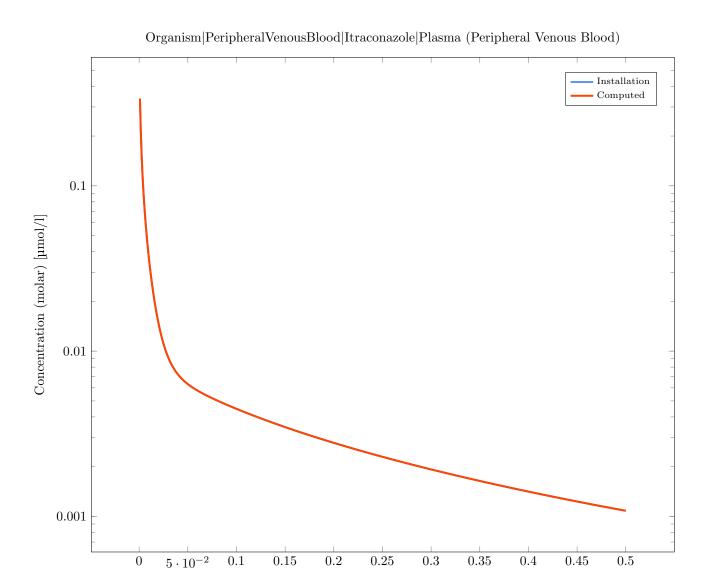


Figure 1.71

Time [h]

Output Path: Organism |Peripheral Venous
Blood |Rifampicin |Plasma (Peripheral Venous Blood)
 Deviation: $4.59\hbox{E-}4$

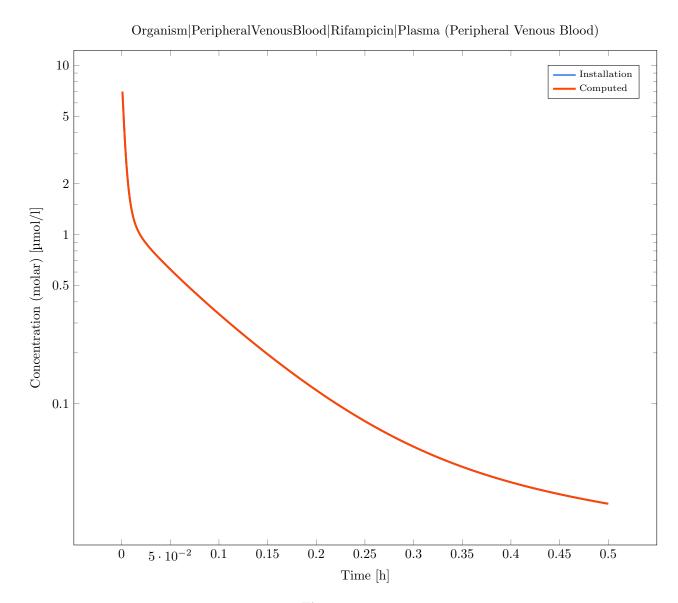


Figure 1.72

Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood)
 Deviation: 2.70E-4

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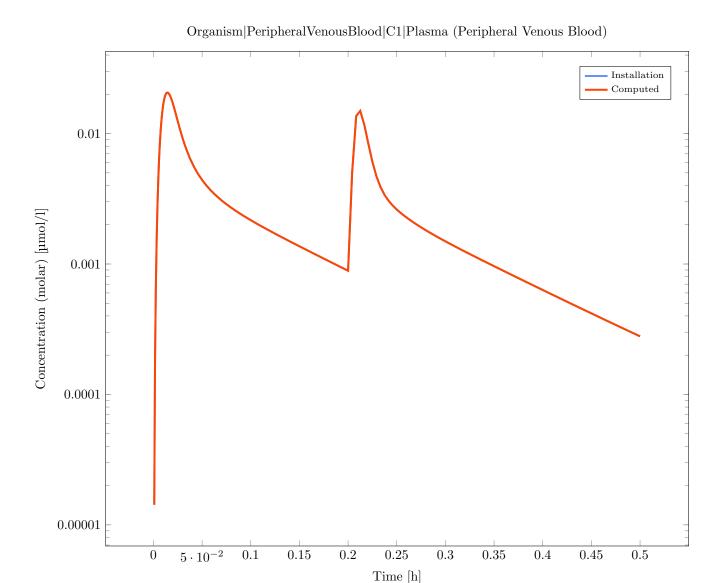


Figure 1.73

 $Simulation: \ DDI_Multiple Combinations \textbf{-} 28_1 st_Uncompetitive_Uncompetitive_Mechanism based_Mechanism based$

Result of the validation: Valid

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_4|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 6.43E-4

$Organism | Peripheral Venous Blood | Mechanism Based_4 | Plasma \ (Peripheral Venous Blood)$

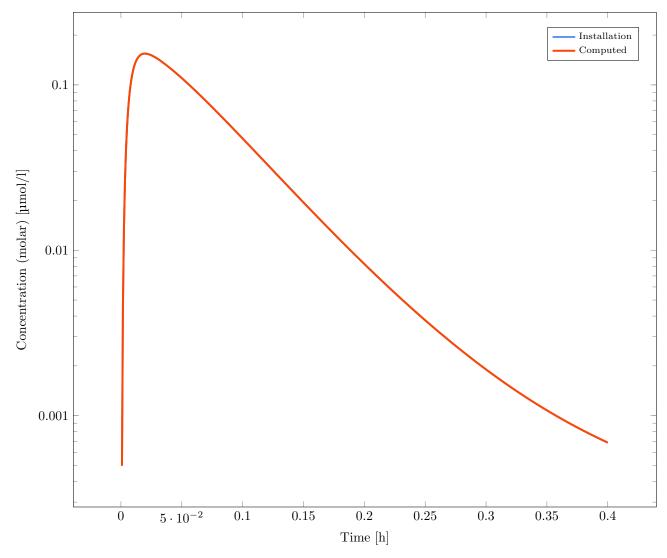


Figure 1.74

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_3|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 3.70E-4

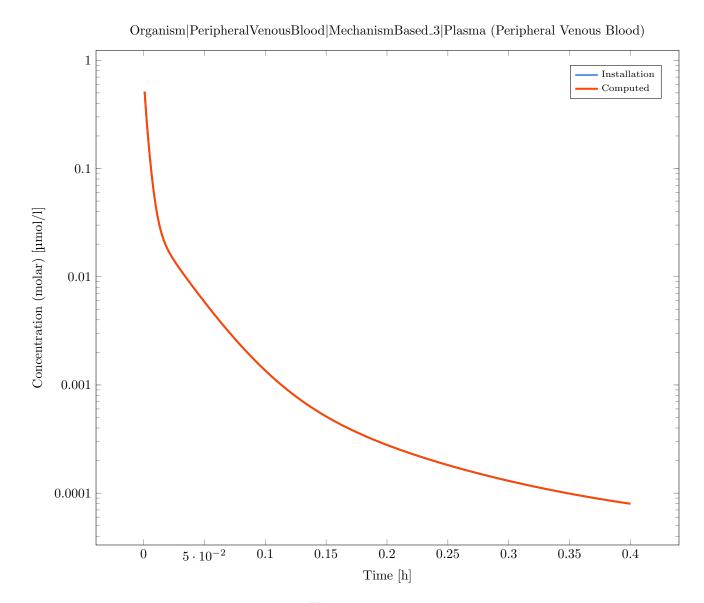


Figure 1.75

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive_CYP3A4_4|Plasma\ (PeripheralVenous\ Blood)$

Deviation: 5.75E-5

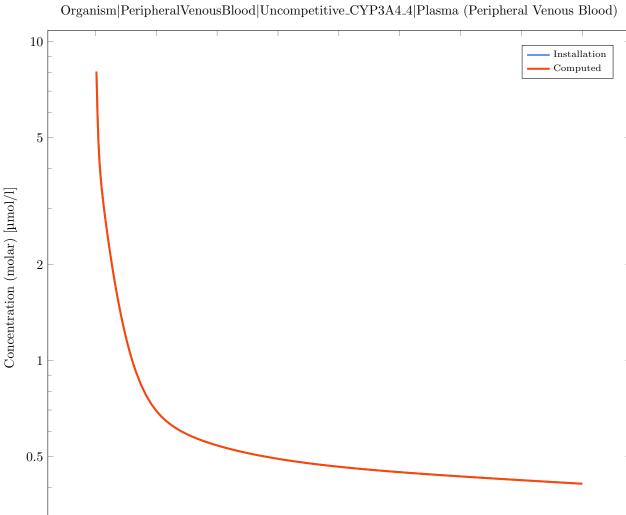


Figure 1.76

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

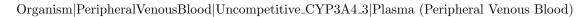
0.1

 $Output\ Path:\ Organism | Peripheral Venous Blood | Uncompetitive_CYP3A4_3 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Uncompetitive_CYP3A4_3 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Uncompetitive_CYP3A4_3 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Uncompetitive_CYP3A4_3 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Uncompetitive_CYP3A4_3 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Uncompetitive_CYP3A4_3 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Uncompetitive_CYP3A4_3 | Plasma\ (Peripheral Venous Blood) | Peripheral Venous Blood | Perip$ Venous Blood)

Deviation: 1.13E-4

0

 $5 \cdot 10^{-2}$



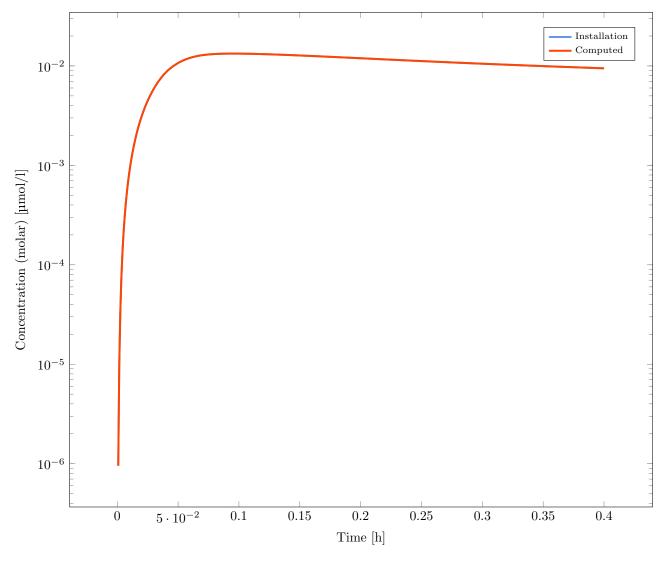


Figure 1.77

 $Output\ Path:\ Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.13E-4

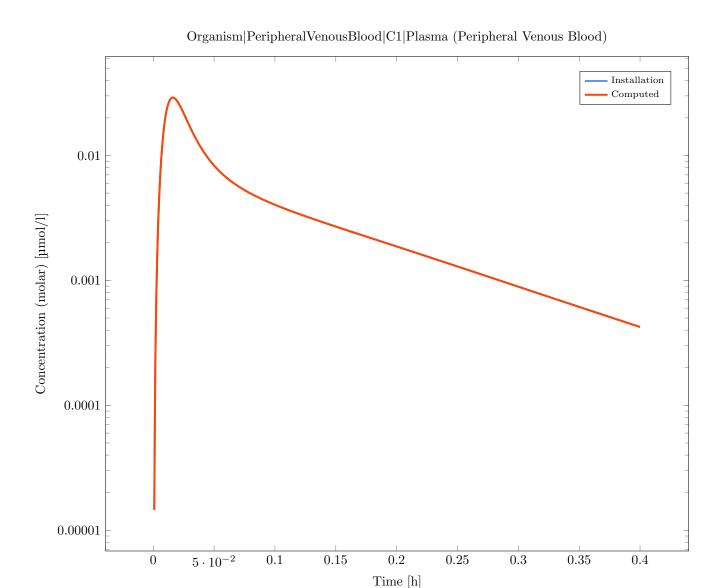


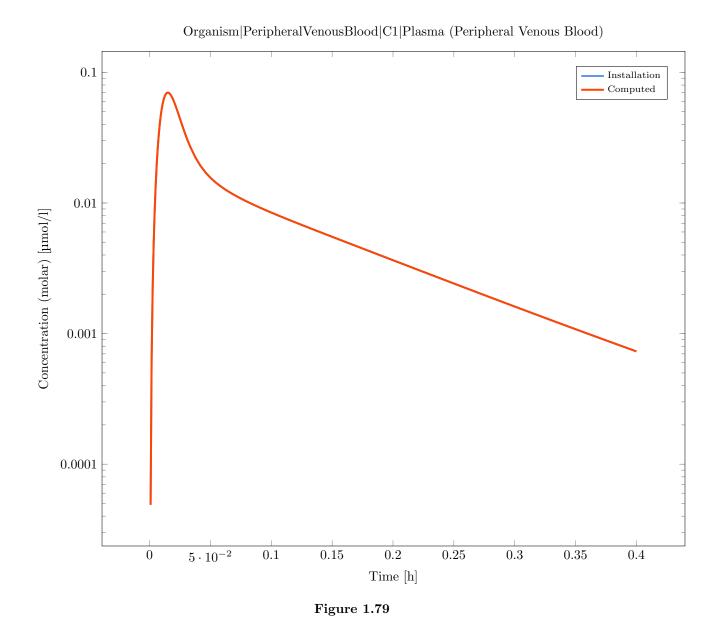
Figure 1.78

 $Simulation: \ DDI_Multiple Combinations \textbf{-} 29_1st_Noncompetitive_Noncompetitive_Mechanism based_Mechanism based$

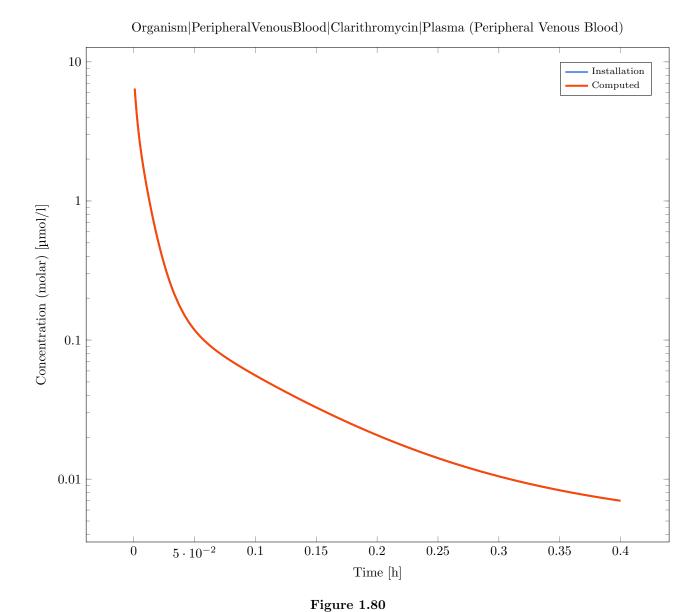
Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood)

Deviation: 2.86E-4



Output Path: Organism |Peripheral Venous
Blood |Clarithromycin |Plasma (Peripheral Venous Blood)
 Deviation: 2.45 ± 2.4



Output Path: Organism |Peripheral Venous
Blood |Erythromycin |Plasma (Peripheral Venous Blood)
 Deviation: 5.52E-4

Organism|PeripheralVenousBlood|Erythromycin|Plasma (Peripheral Venous Blood)

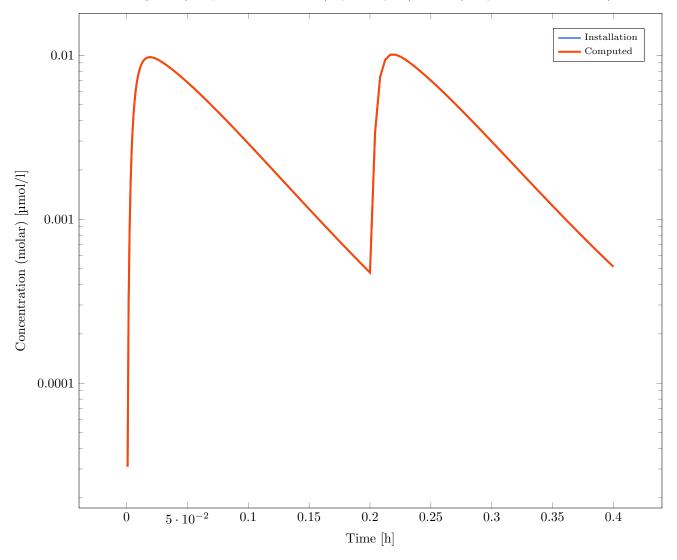


Figure 1.81

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 3.16E-4



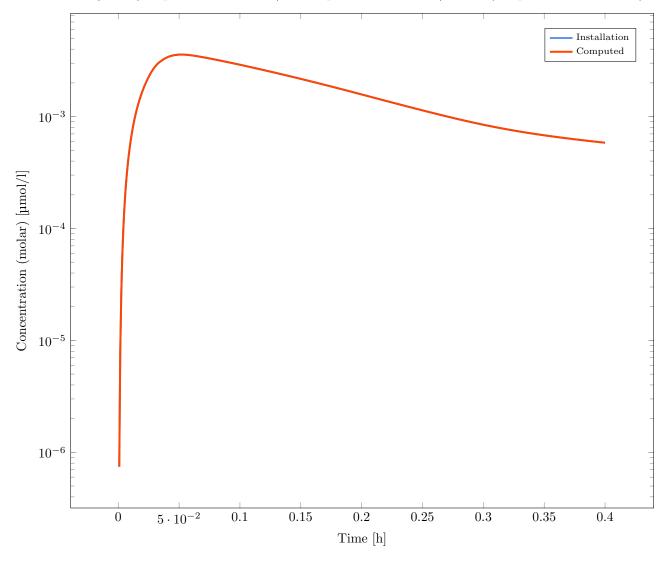


Figure 1.82

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_2|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 3.39E-4

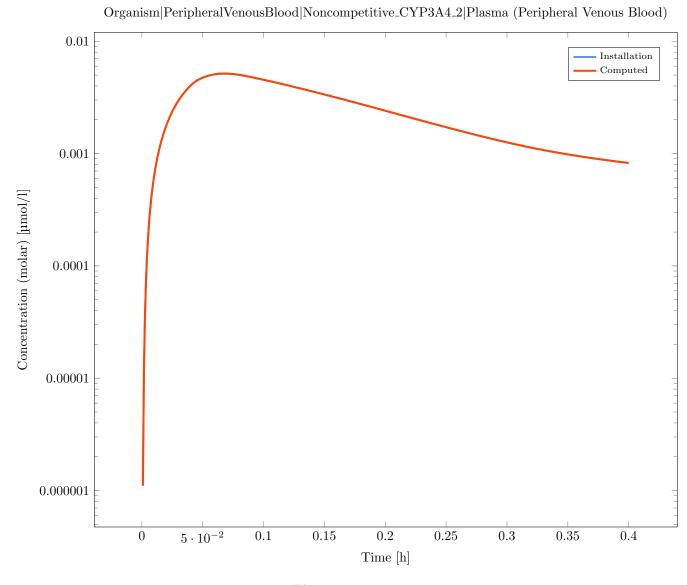


Figure 1.83

 ${\bf Simulation:\ DDI_Multiple Combinations-30_1st_Mixed_Mechanismbased_Mechanismbased_Mechanismbased_Nesult\ of\ the\ validation:\ Valid$

 $Output\ Path:\ Organism|Peripheral Venous Blood|MechanismBased_4|Plasma\ (Peripheral\ Venous Blood)$

Deviation: 5.78E-4

Organism|PeripheralVenousBlood|MechanismBased_4|Plasma (Peripheral Venous Blood)

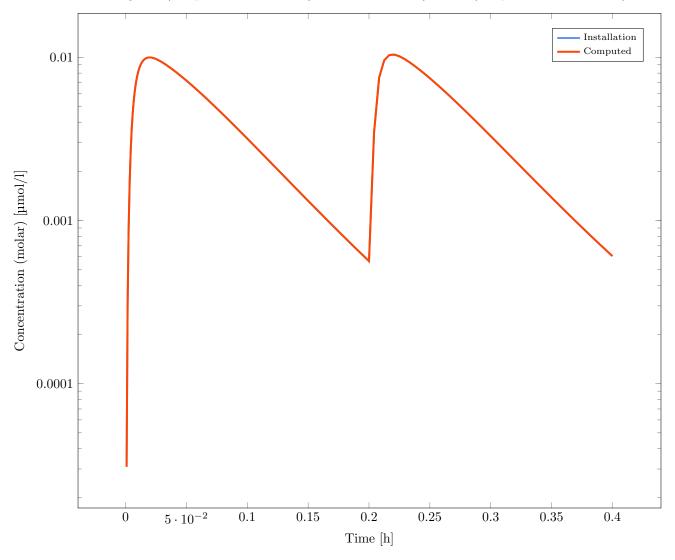


Figure 1.84

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_3|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.82E-4

$Organism | Peripheral Venous Blood | Mechanism Based_3 | Plasma \ (Peripheral Venous Blood)$

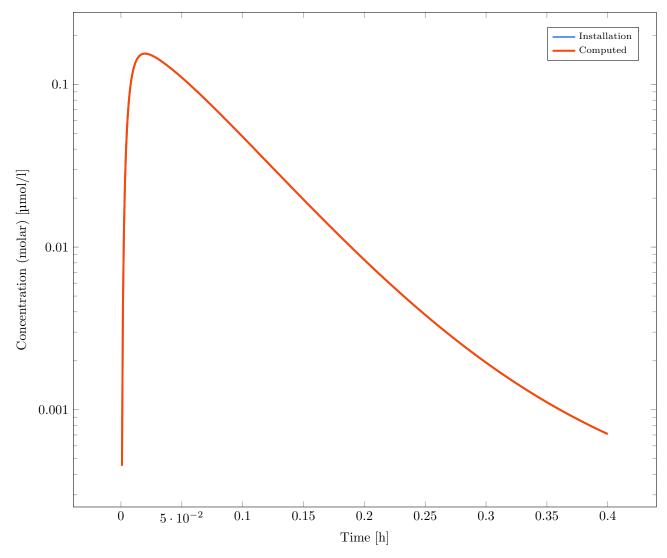
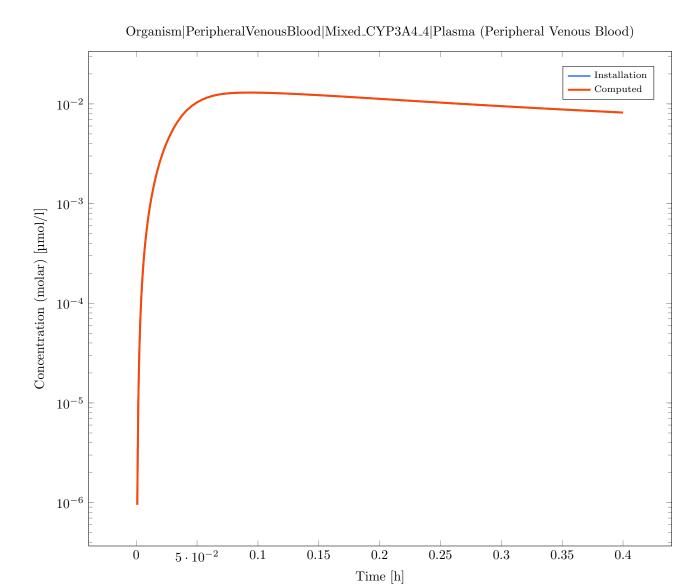


Figure 1.85

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_4|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 1.16E-4



Output Path: Organism |PeripheralVenousBlood |Mixed_CYP3A4_3 |Plasma (Peripheral VenousBlood)
 Deviation: 1.67E-4

Figure 1.86

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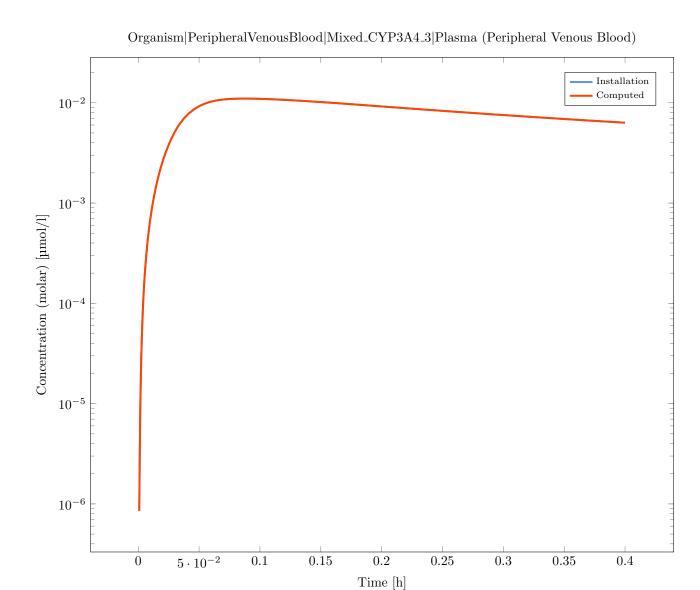


Figure 1.87

Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood)
 Deviation: $6.85\hbox{E-}4$

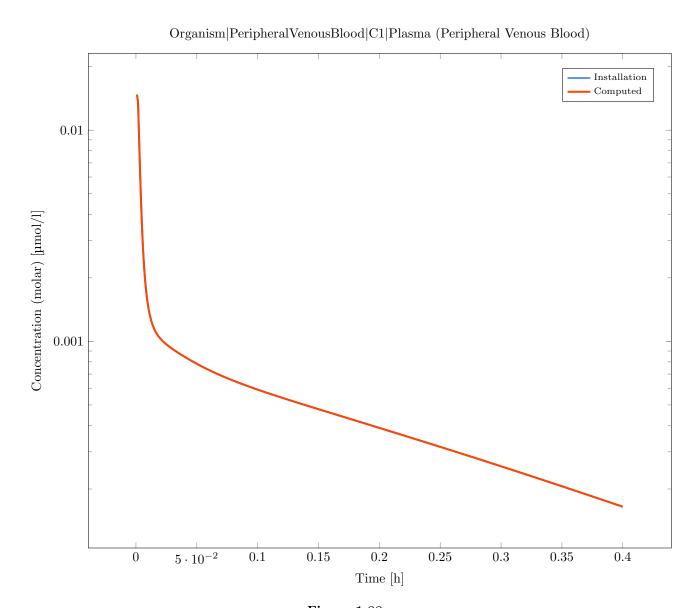
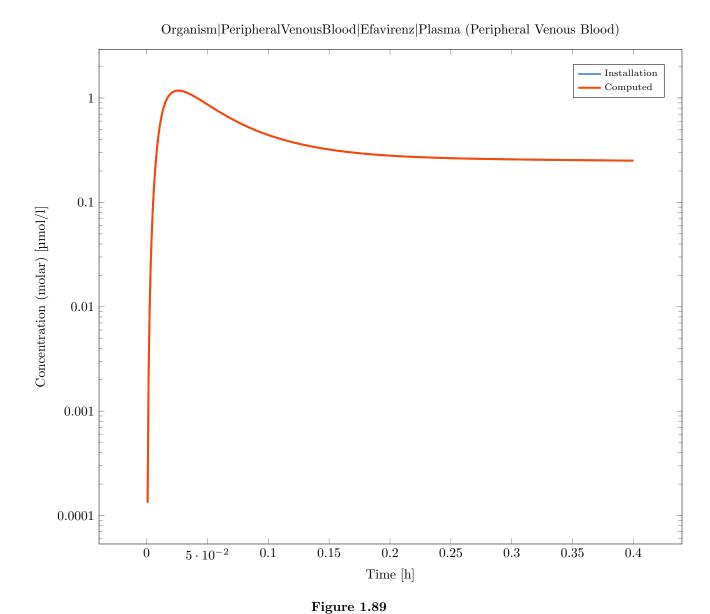


Figure 1.88

 ${\bf Simulation:\ DDI_Multiple Combinations\hbox{--}31_1st_Mechanismbased_Mechanismbased_Induction_Induction} \\ {\bf Result\ of\ the\ validation:\ Valid}$

Output Path: Organism |Peripheral Venous
Blood |Efavirenz |Plasma (Peripheral Venous Blood)
 Deviation: 1.73E-4



Output Path: Organism |PeripheralVenousBlood |MechanismBased_3 |Plasma (Peripheral Venous Blood)

Deviation: 5.97E-4

Organism|PeripheralVenousBlood|MechanismBased_3|Plasma (Peripheral Venous Blood)

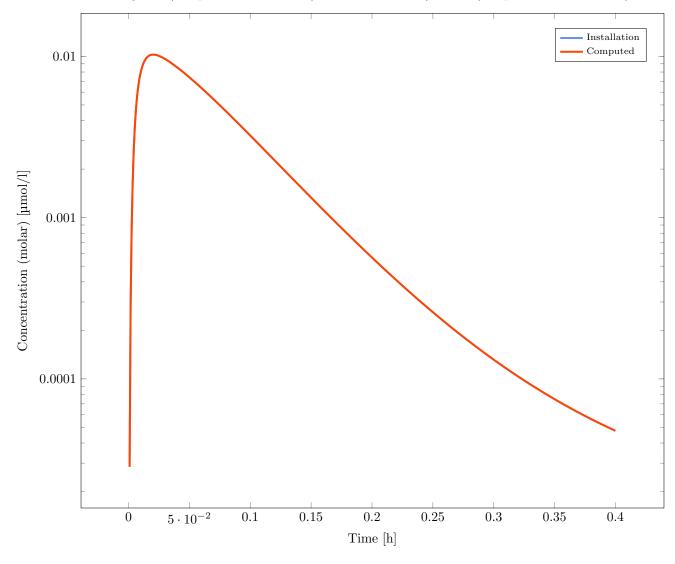


Figure 1.90

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_4|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.99E-4

Organism|PeripheralVenousBlood|MechanismBased_4|Plasma (Peripheral Venous Blood)

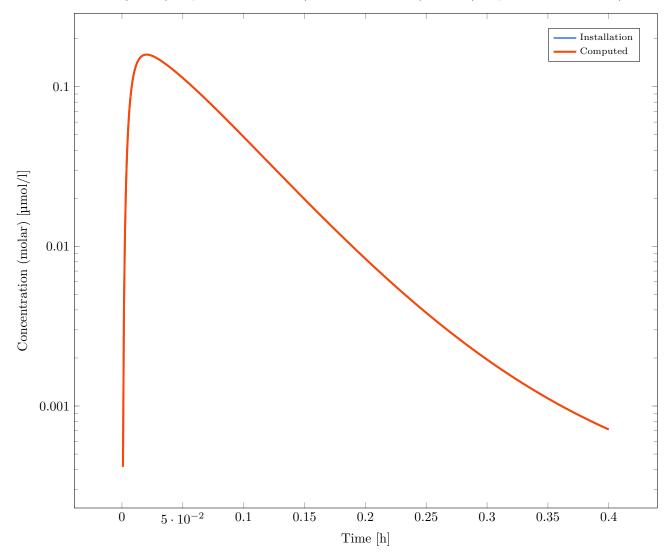


Figure 1.91

Output Path: Organism |Peripheral Venous
Blood |Rifampicin |Plasma (Peripheral Venous Blood)
 Deviation: $4.48\hbox{E-}4$

0.001

0.0001

0.00001

0

 $5\cdot 10^{-2}$

Organism|PeripheralVenousBlood|Rifampicin|Plasma (Peripheral Venous Blood) Installation Computed 0.1 0.01 Concentration (molar) $[\mu]$

Figure 1.92

0.15

0.2

Time [h]

0.25

0.3

0.35

0.4

Output Path: Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood) Deviation: 5.81E-4

0.1

Open Systems Pharmacology Suite - 12

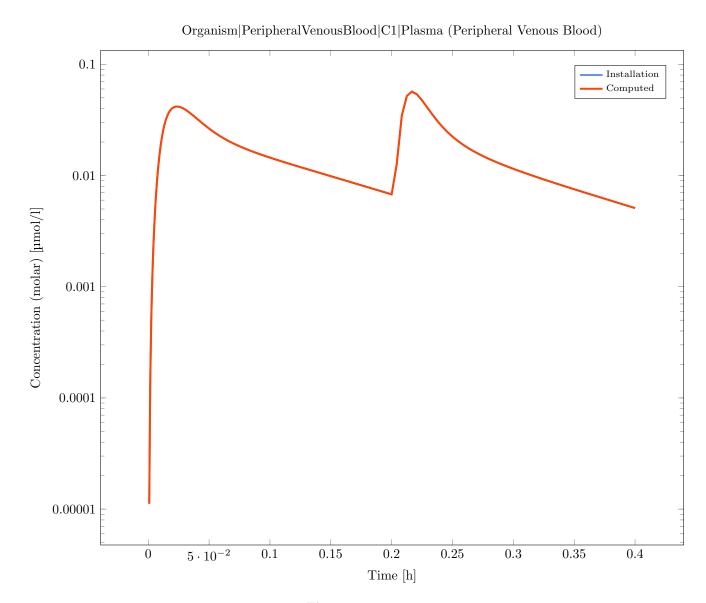


Figure 1.93

 $Simulation: \ DDI_MultipleCombinations-32_1st_All_DDI_Types$

Result of the validation: Valid

 $Output\ Path:\ Organism | Peripheral Venous Blood | Efavirenz | Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 1.92E-4

Organism|PeripheralVenousBlood|Efavirenz|Plasma (Peripheral Venous Blood)

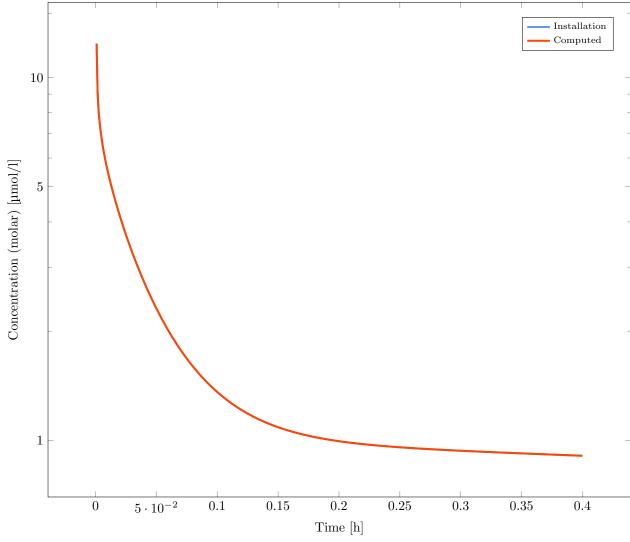
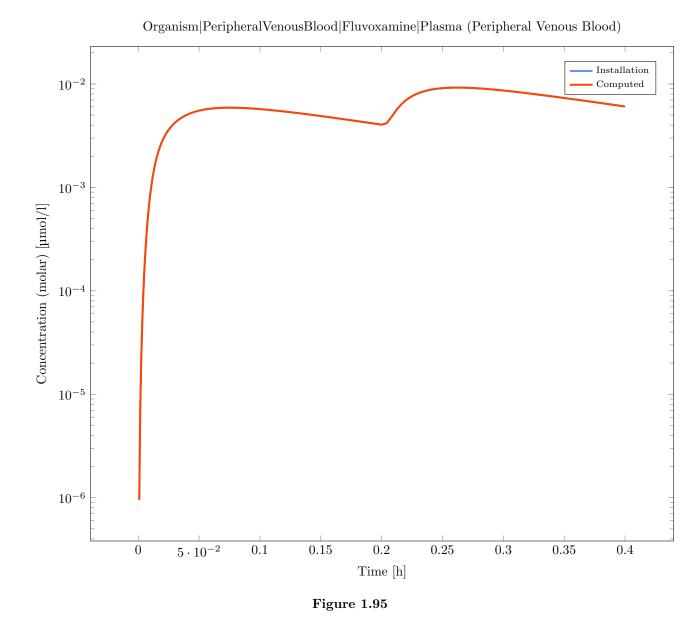


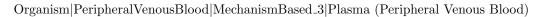
Figure 1.94

Output Path: Organism |Peripheral Venous
Blood |Fluvoxamine |Plasma (Peripheral Venous Blood)
 Deviation: 3.14E-4



 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_3|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 6.03E-4



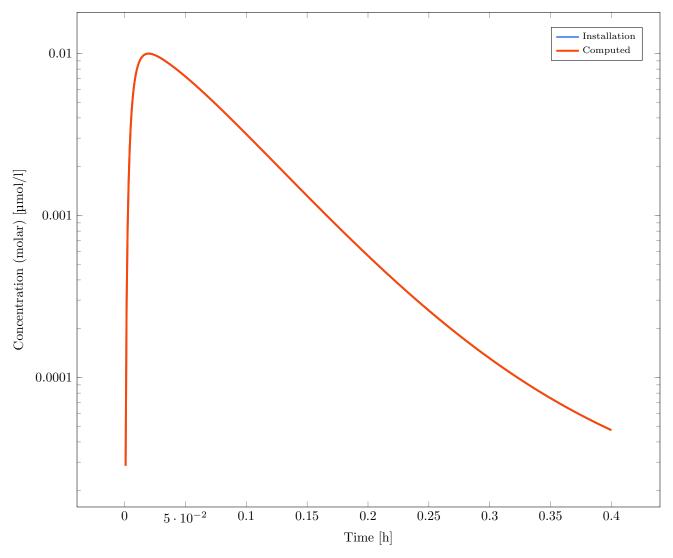


Figure 1.96

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_3|Plasma\ (Peripheral\ VenousBlood)$

Deviation: 4.10E-4

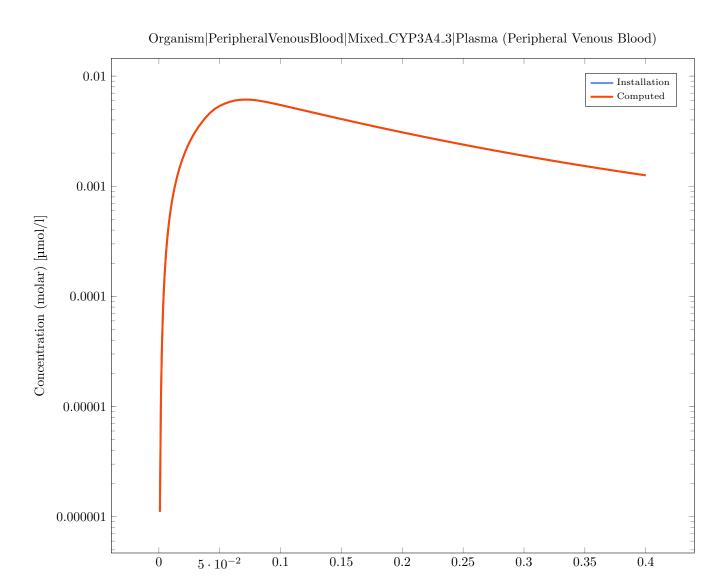
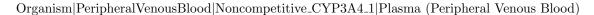


Figure 1.97

Time [h]

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive_CYP3A4_1|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 5.19E-4



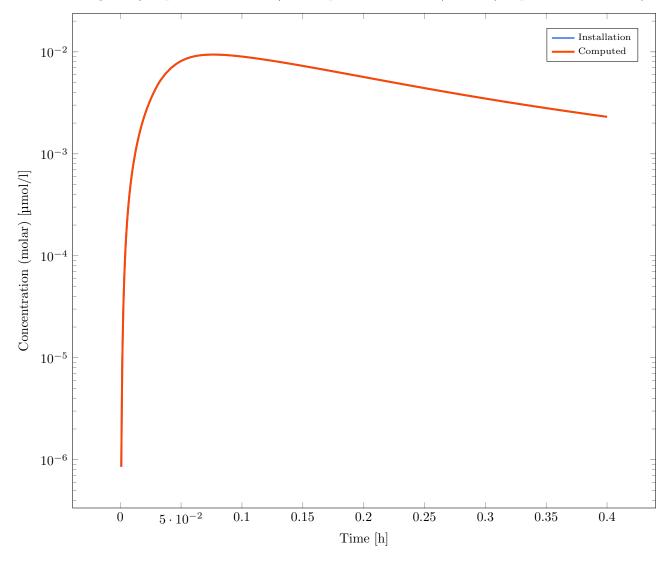
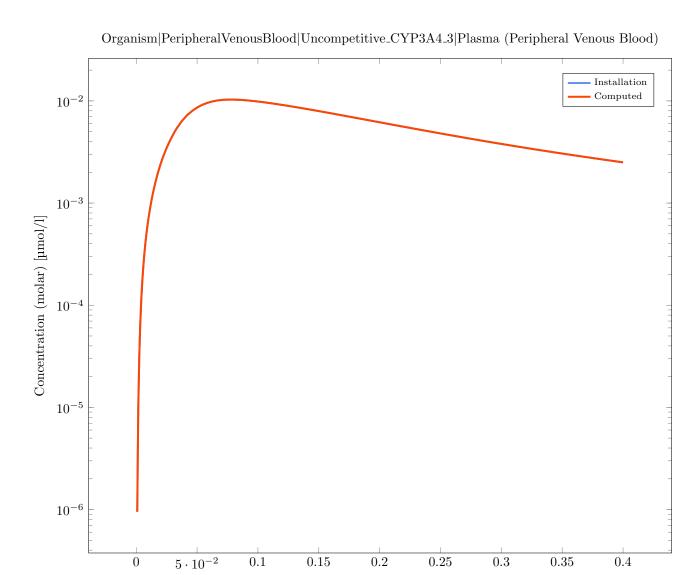


Figure 1.98

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive_CYP3A4_3|Plasma\ (PeripheralVenous\ Blood)$

Deviation: 4.97E-4



Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood)
 Deviation: $6.90\hbox{E-}4$

Time [h]

Figure 1.99

Open Systems Pharmacology Suite - $12\,$

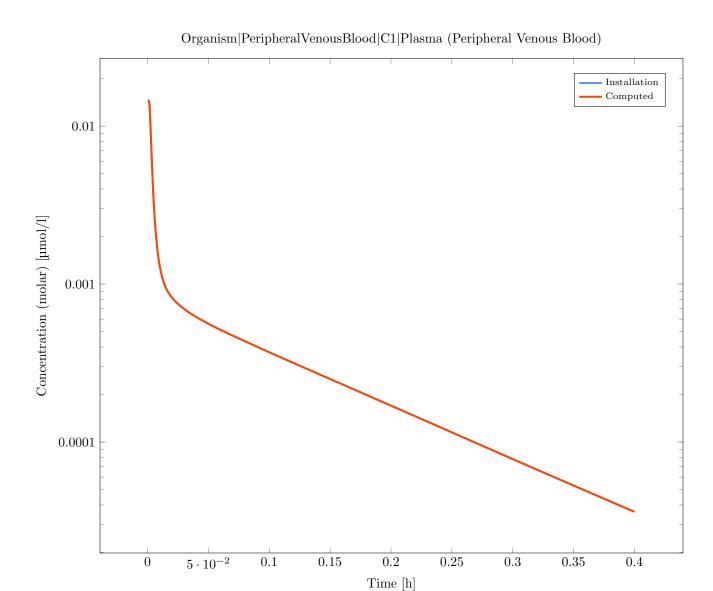


Figure 1.100

 $\begin{tabular}{ll} Simulation: $Dog_MultiORAL_12_12_Dissolved-Dog_MultiORAL_12_12_Dissolved \\ Result of the validation: Valid \\ \end{tabular}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

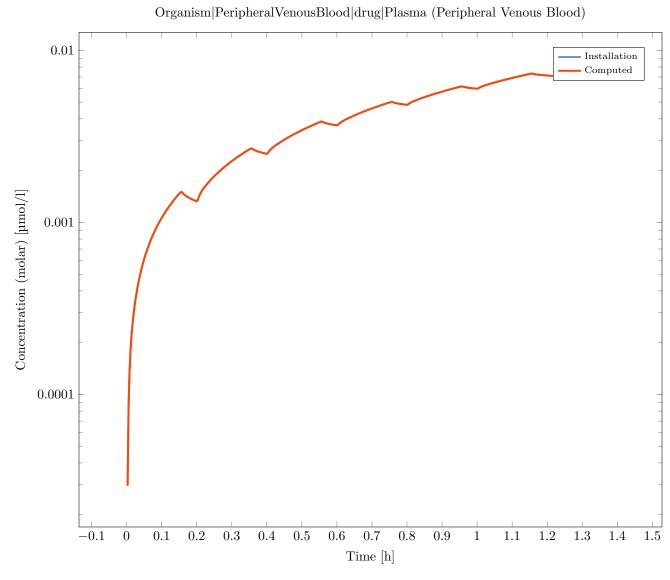


Figure 1.101

 $\begin{tabular}{ll} \bf Simulation: \begin{tabular}{ll} \bf Dog_MultiORAL_24_Dissolved-Dog_MultiORAL_24_$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

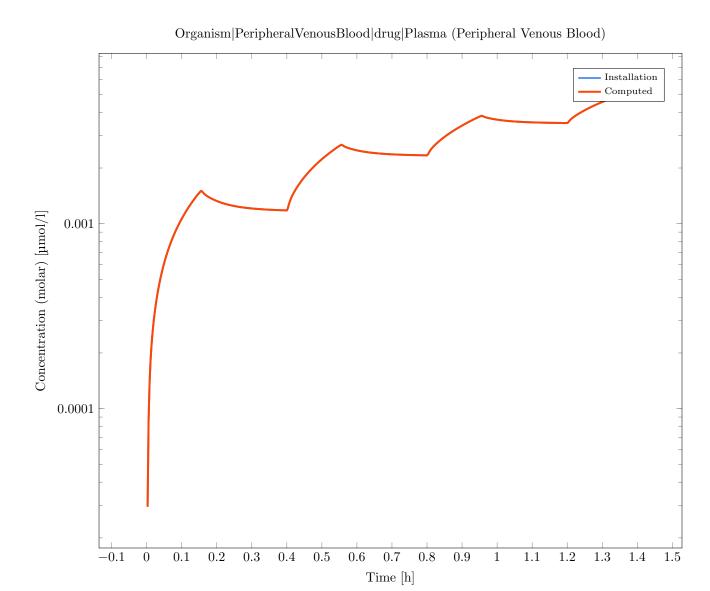
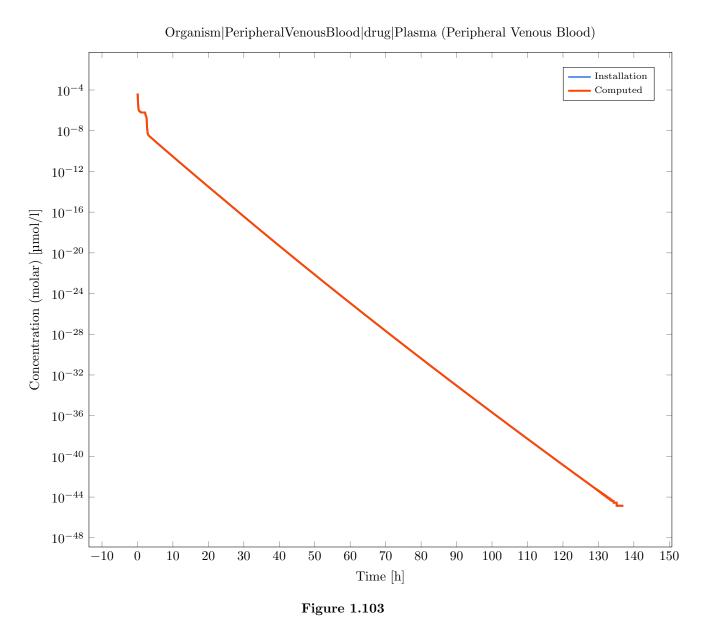


Figure 1.102

 $\begin{tabular}{ll} \bf Simulation: European_SingleORAL_Age_0_CYP3A4-European_SingleORAL_Age_0_CYP3$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: $1.56\hbox{E-}5$



 ${\bf Simulation: European_SingleORAL_Age_0_GFR-European_SingleORAL_Age_0_GFR} \\ {\bf Result of the \ validation: \ Valid}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 1.68E-5

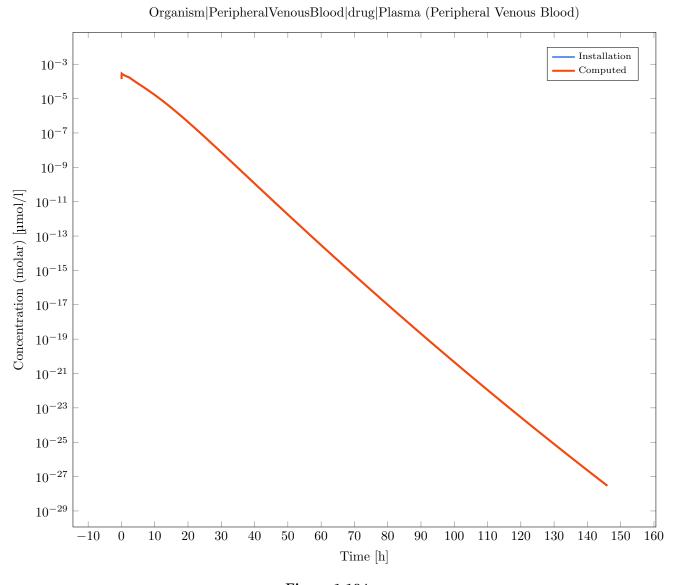
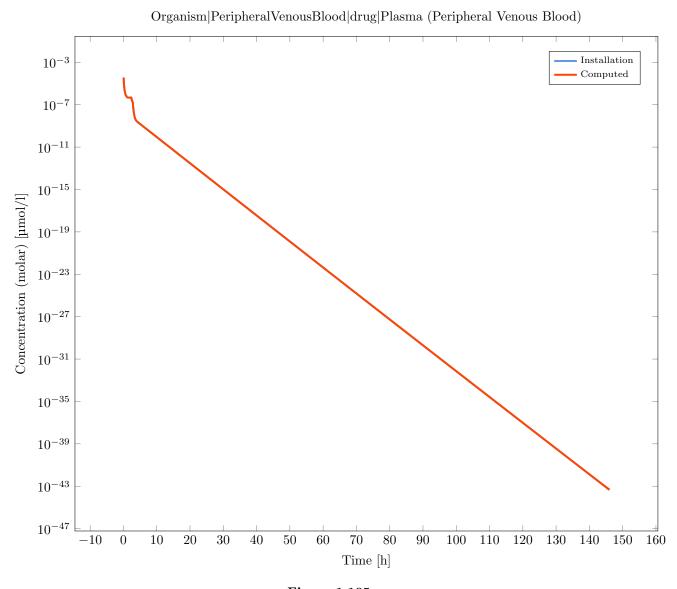


Figure 1.104

 $\begin{tabular}{ll} \bf Simulation: European_SingleORAL_Age_1_CYP3A4-European_SingleORAL_Age_1_CYP3$

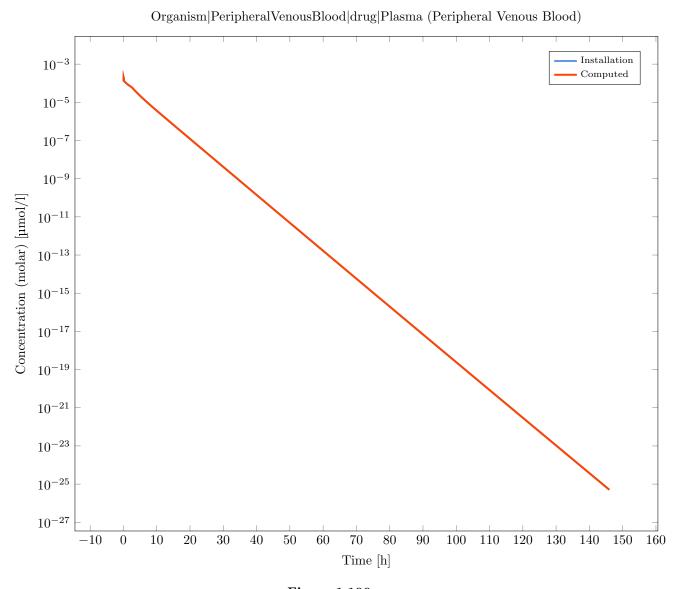
Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 1.54 ± 6



 ${\bf Figure~1.105}$

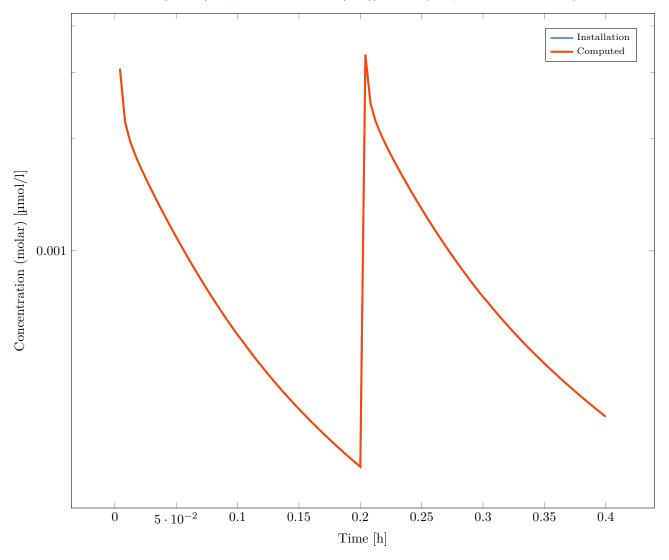
 ${\bf Simulation: European_SingleORAL_Age_1_GFR-European_SingleORAL_Age_1_GFR} \\ {\bf Result of the \ validation: \ Valid}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 1.19E-7



 ${\bf Figure~1.106}$

Simulation: Human_CompetitiveInhibition-Human_CompetitiveInhibition Result of the validation: Valid



 $Figure \ 1.107$

Output Path: Organism |PeripheralVenousBlood |
inhibitor |Plasma (Peripheral Venous Blood) | Deviation:
 0

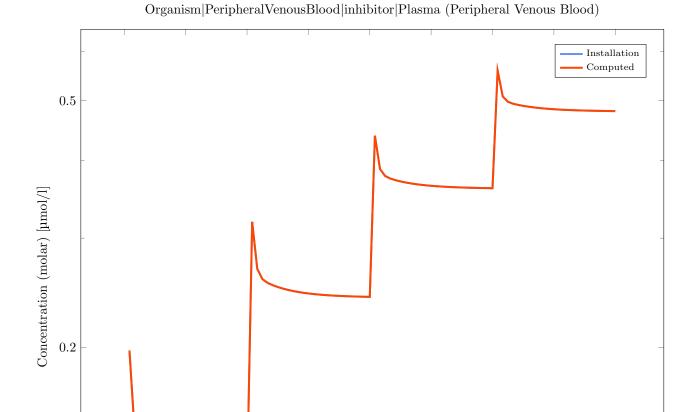


Figure 1.108

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: \ Human_ICRP_AGP-01_ICRP_0y_Male$

 $5 \cdot 10^{-2}$

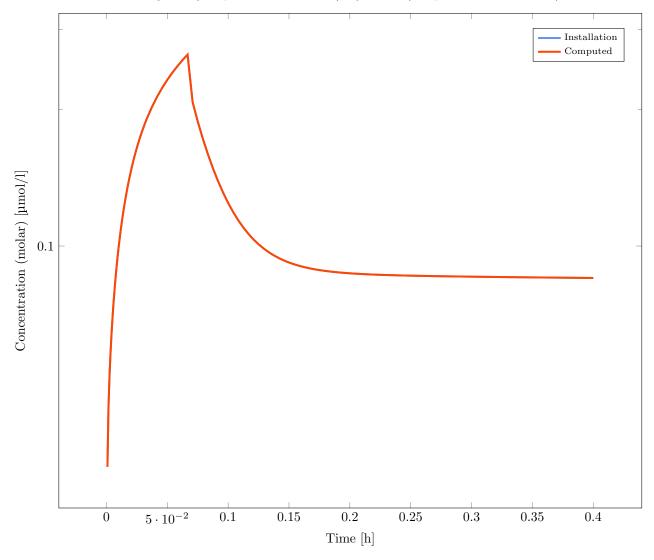
Result of the validation: Valid

0

Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

0.15

0.1



 $Figure \ 1.109$

 $Simulation: \ Human_ICRP_AGP-02_ICRP_0.05y_Female$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood) | Installation | Computed | Com

 ${\bf Figure~1.110}$

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: \ Human_ICRP_AGP-03_ICRP_0.18y_Male$

 $5\cdot 10^{-2}$

0.1

Result of the validation: Valid

0

 $Output\ Path:\ Organism|PeripheralVenousBlood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

0.15



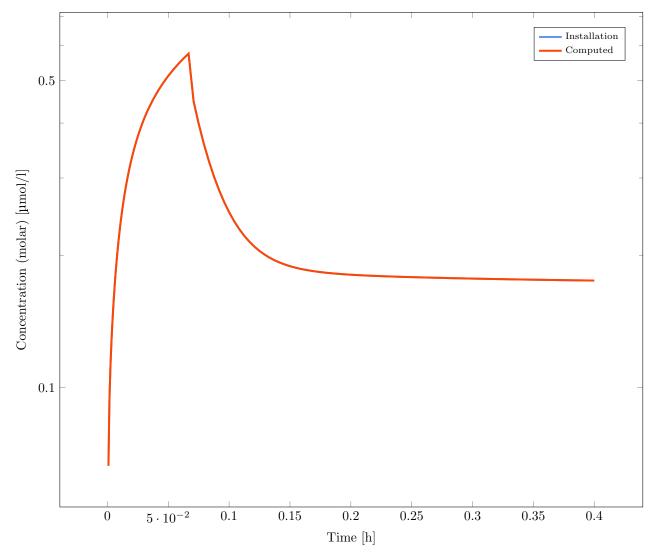


Figure 1.111

Simulation: Human_ICRP_AGP-04_ICRP_1y_Female

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

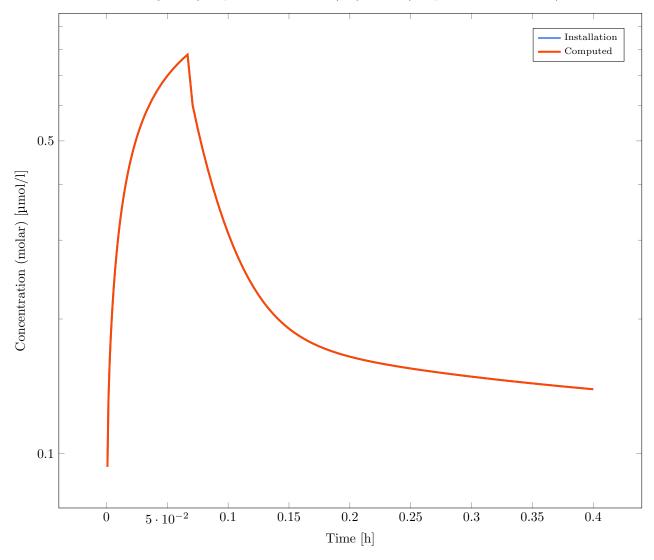


Figure 1.112

 $Simulation: \ Human_ICRP_AGP-05_ICRP_12y_Male$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood)

Deviation: 1.50E-4

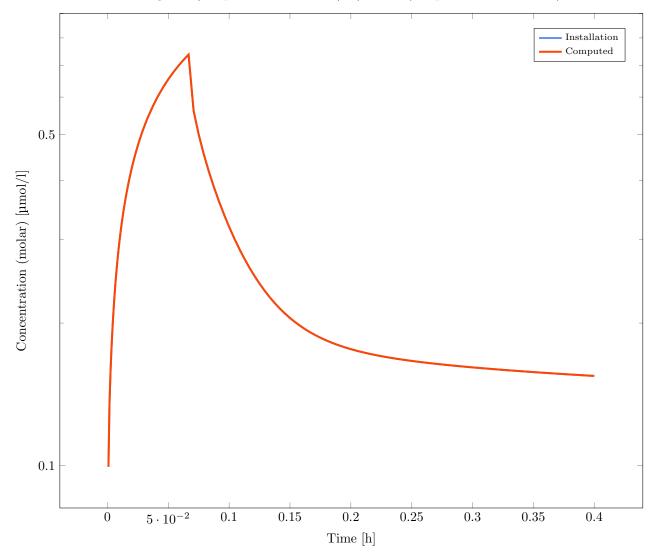


Figure 1.113

 $Simulation: \ Human_ICRP_AGP-06_ICRP_30y_Female$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

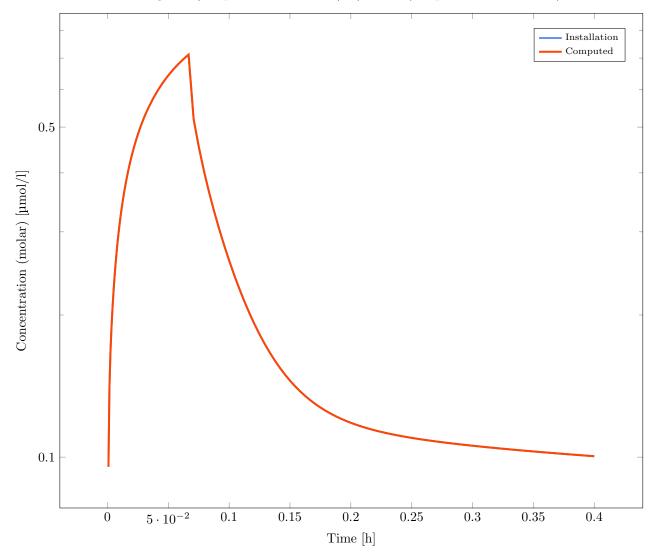


Figure 1.114

 $Simulation: \ Human_ICRP_AGP-07_ICRP_100y_Male$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral\ Venous\ Blood)$

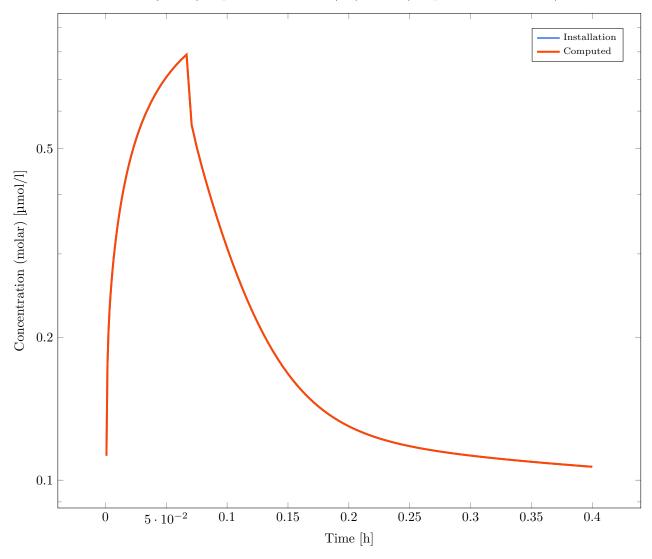
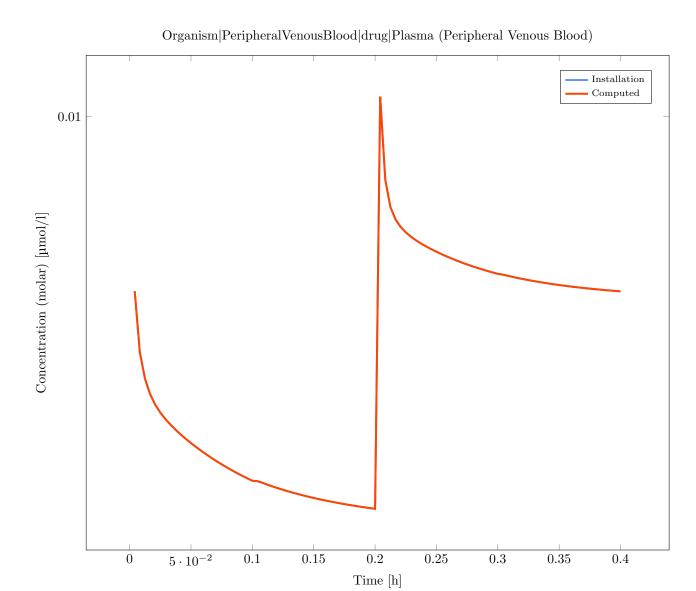


Figure 1.115

 ${\bf Simulation: \ Human_Irreversible Inhibition-Human_Irreversible Inhibition} \\ {\bf Result \ of \ the \ validation: \ Valid}$

 $Output\ Path:\ Organism|Peripheral Venous Blood|drug|Plasma\ (Peripheral\ Venous\ Blood)$



Output Path: Organism |PeripheralVenousBlood |
inhibitor |Plasma (Peripheral Venous Blood) | Deviation:
 0

Figure 1.116

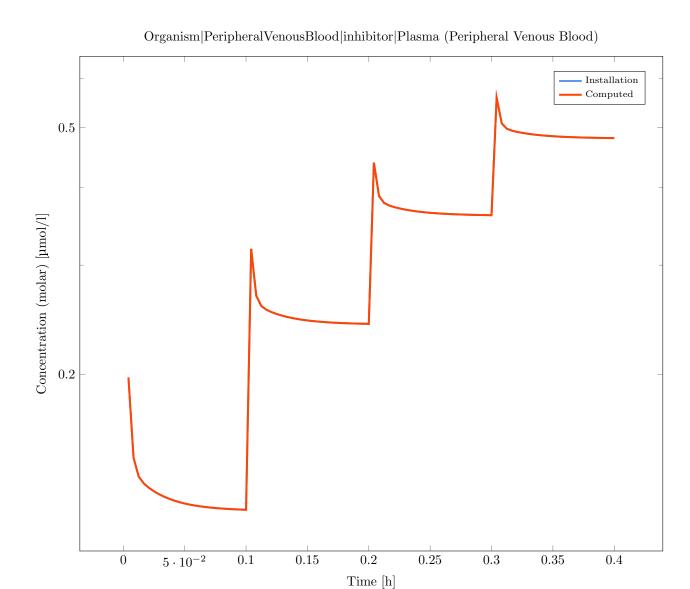


Figure 1.117

 $Simulation: \ Human_MixedInhibition-Human_MixedInhibition$

Result of the validation: Valid

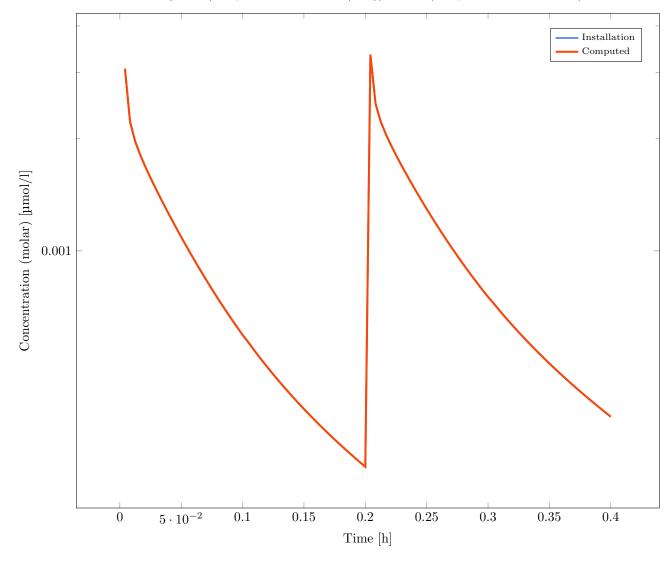


Figure 1.118

Output Path: Organism |PeripheralVenousBlood |
inhibitor |Plasma (Peripheral Venous Blood) | Deviation:
 0

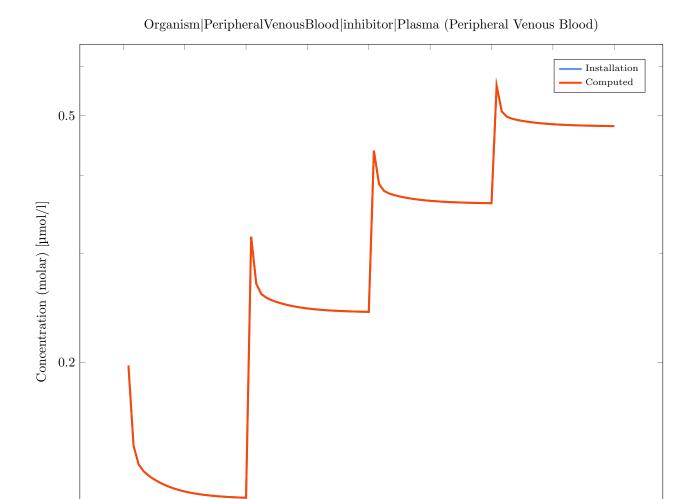


Figure 1.119

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: \ Human_MultiIV_6_6_12-Human_MultiIV_6_6_12$

0.1

Result of the validation: Valid

0

 $5 \cdot 10^{-2}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

0.15



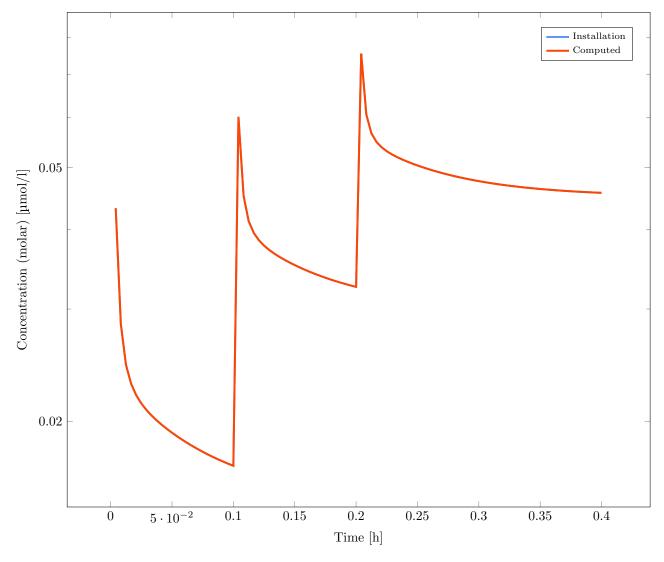


Figure 1.120

 $Simulation: \ Human_MultiORAL_6_12_12_Dissolved-Human_6_12_Dissolved-Human_6_12_$

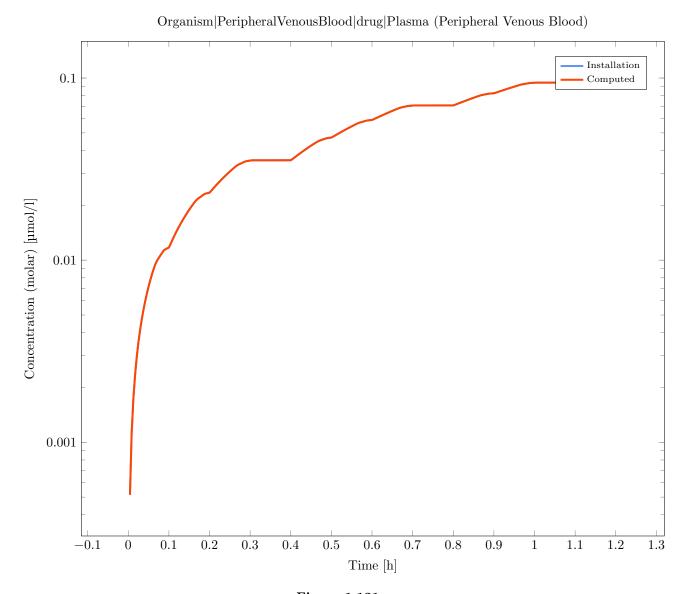


Figure 1.121

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_absorption_sink_conditions$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|drug|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 1.03E-7



Figure 1.122

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_EHC_continuous_fraction_0.5$

Result of the validation: Valid



 ${\bf Figure~1.123}$

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_EHC_continuous_fraction_1$

Result of the validation: Valid

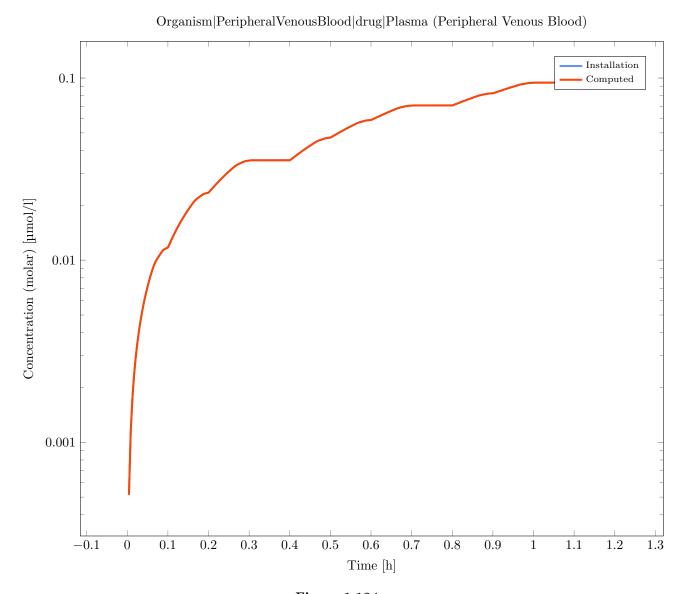
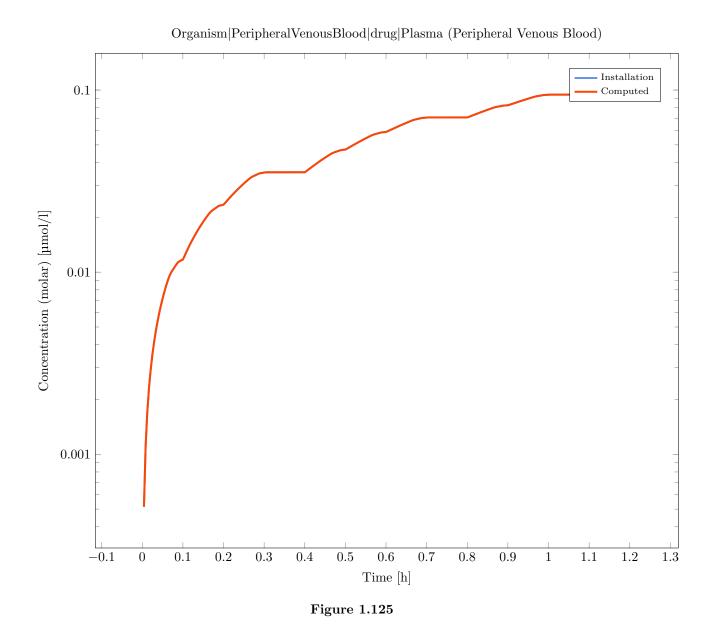


Figure 1.124

Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKadependent penalty factor Result of the validation: Valid



 $Simulation: \ Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_solubility \\ Result of the validation: \ Valid$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 1.17E-7

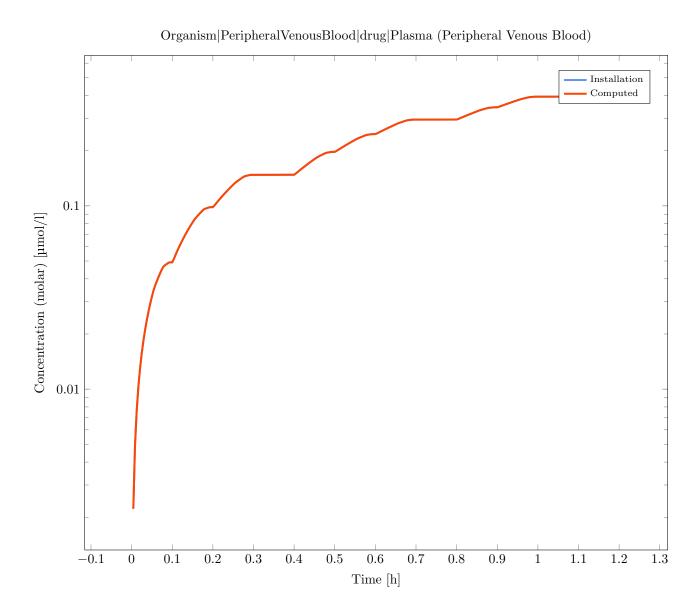


Figure 1.126

 $Simulation: \ Human_MultipleIV_Binding-Human_MultipleIV_Binding$

Result of the validation: Valid

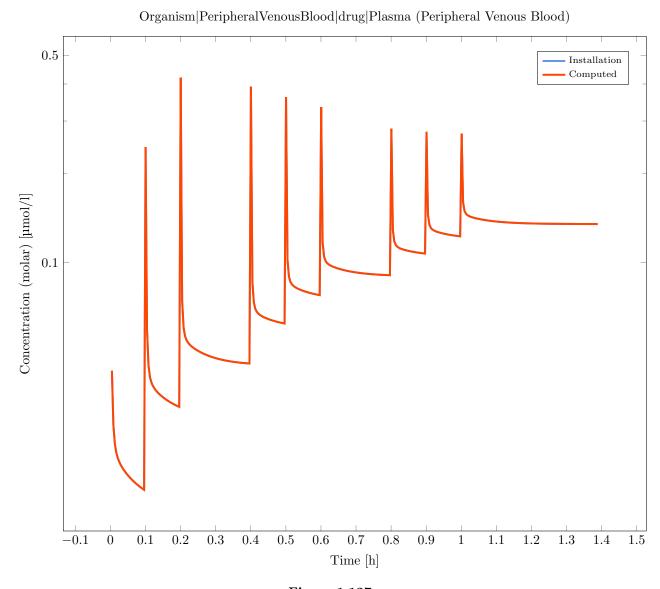


Figure 1.127

 ${\bf Simulation: \ Human_Multiple IV_Efflux Basolateral-Human_Multiple IV_Efflux Basolateral-Result \ of the \ validation: \ Valid$

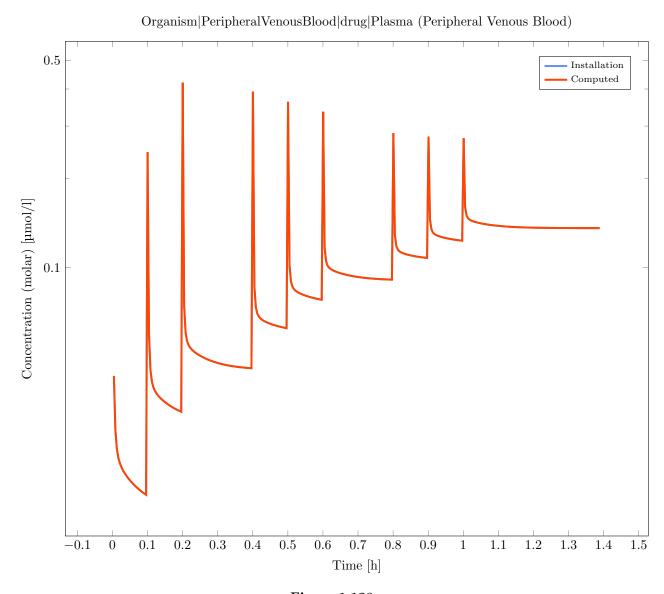


Figure 1.128

 $Simulation: \ Human_MultipleIV_Efflux-Human_MultipleIV_Efflux$

Result of the validation: Valid

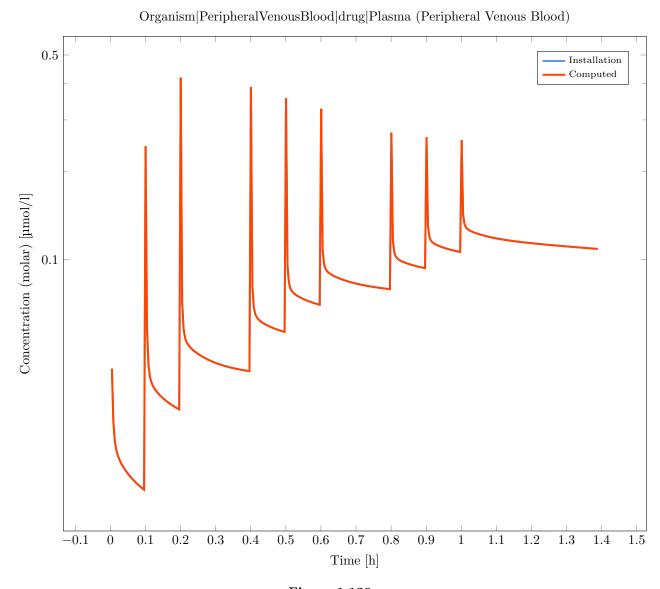
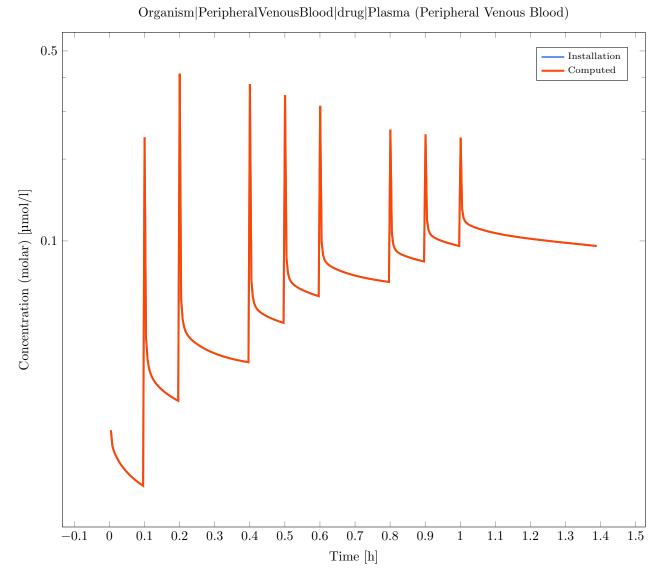


Figure 1.129

 ${\bf Simulation: \ Human_Multiple IV_Influx Basolateral-Human_Multiple IV_Influx Basolateral-Result \ of the \ validation: \ Valid$



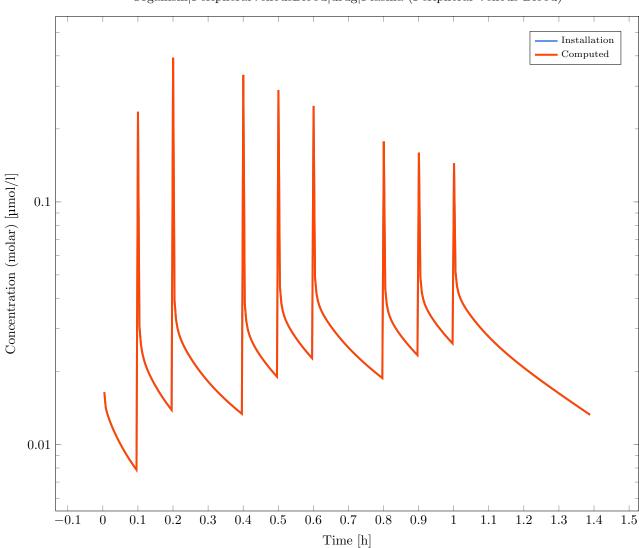
 ${\bf Figure~1.130}$

 $Simulation: \ Human_MultipleIV_Influx-Human_MultipleIV_ActiveInflux$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

Deviation: 3.47E-5



Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

Figure 1.131

 ${\bf Simulation: \ Human_Multiple IV_Metabolizm Binding-Human_Multiple IV_Metabolizm Binding \ Result \ of \ the \ validation: \ Valid }$

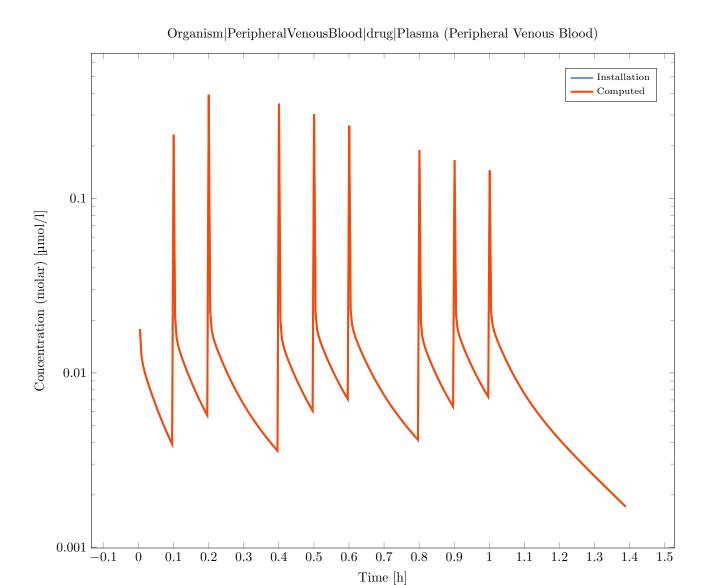


Figure 1.132

 ${\bf Simulation: \ Human_Multiple IV_Metabolizm-Human_Multiple IV_Metabolizm.} \\ {\bf Result \ of \ the \ validation: \ Valid}$

1.3

1.4

1.5

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed 0.1 Concentration (molar) $[\mu]$ 0.01 0.0010.2 0.3 0.8 0.9 1.1 1.2

Figure 1.133

0.6

0.7

Time [h]

 $Simulation: \ Human_MultipleIV_PGPB a solateral-Human_MultipleIV_PGPB a$ Result of the validation: Valid

0.5

0.4

Output Path: Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Deviation: 0

-0.1

0

0.1



Figure 1.134

 $Simulation: \ Human_MultipleIV_PGP-Human_MultipleIV_PGP$

Result of the validation: Valid

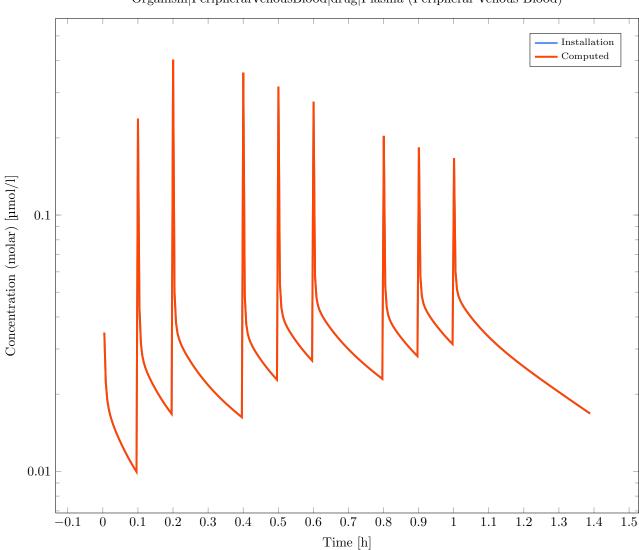
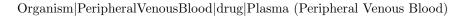
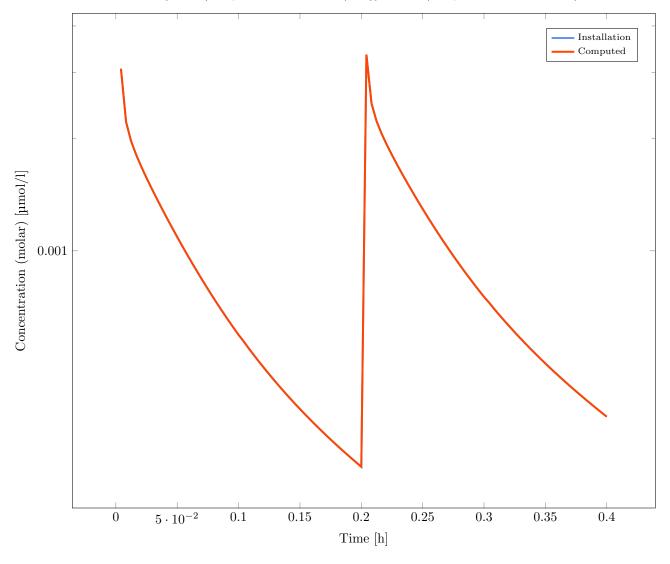


Figure 1.135

 ${\bf Simulation: \ Human_NonCompetitive Inhibition-Human_NonCompetitive Inhibition} \\ {\bf Result \ of \ the \ validation: \ Valid}$





 $Figure \ 1.136$

Output Path: Organism |PeripheralVenousBlood |
inhibitor |Plasma (Peripheral Venous Blood) | Deviation:
 0

Organism|PeripheralVenousBlood|inhibitor|Plasma (Peripheral Venous Blood) 0.5 0.2 0.2

Figure 1.137

0.2

Time [h]

0.25

0.35

0.4

0.3

 $Simulation: \ Human_Oral_BiDaily_Table Formulation-S1_suspension$

0.1

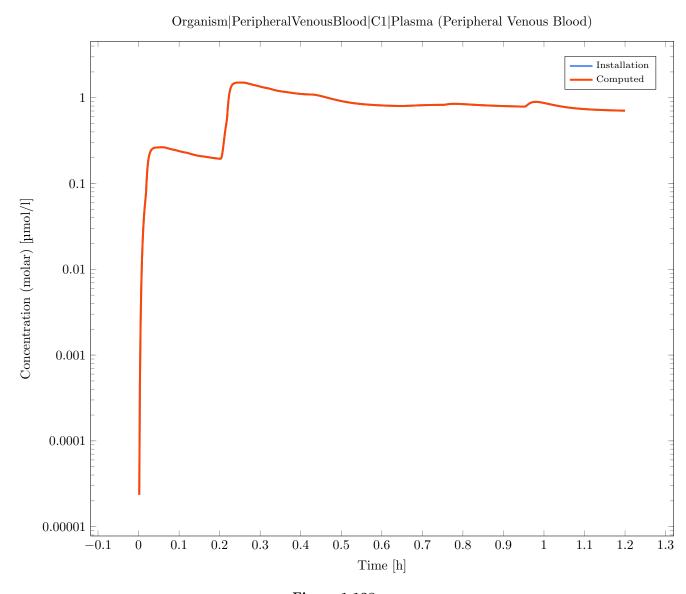
Result of the validation: Valid

0

 $5 \cdot 10^{-2}$

Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

0.15



 ${\bf Figure~1.138}$

 $Simulation: \ Human_Oral_BiDaily_Table Formulation-S2_NoSuspension$

Result of the validation: Valid

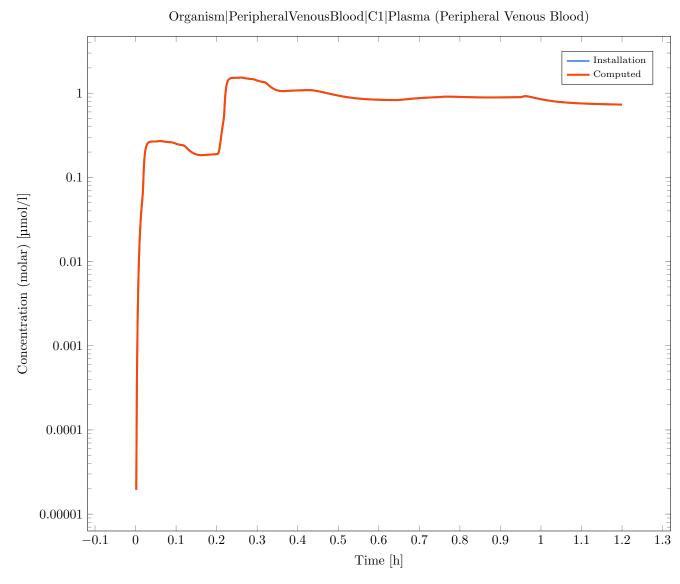


Figure 1.139

Simulation: Human_pH_SolubilityTable-S1_Table

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood)

Deviation: 9.55E-6

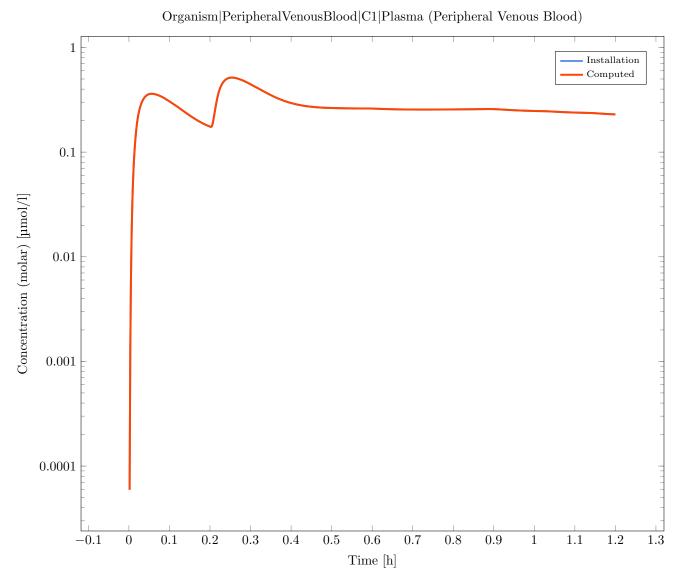


Figure 1.140

Simulation: Human_pH_SolubilityTable-S2_Measurement

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood)

Deviation: 1.64E-6

$Organism|Peripheral Venous Blood|C1|Plasma\ (Peripheral Venous\ Blood)$

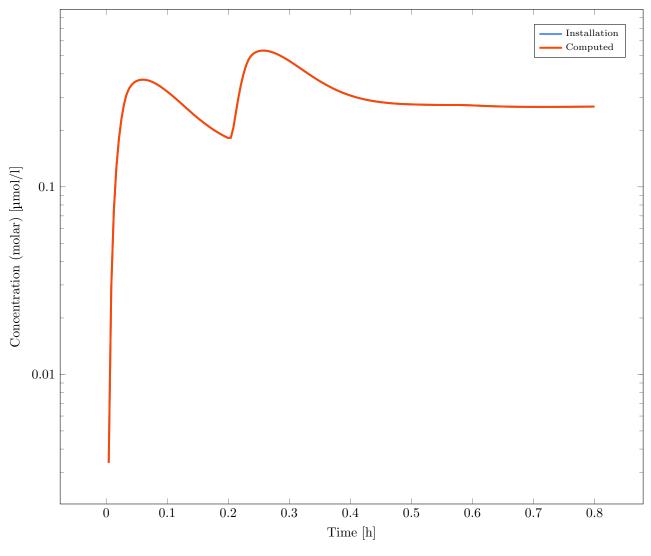


Figure 1.141

 $Simulation: \ Human_pH_SolubilityTable_SolubilityChanged$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood)

Deviation: 1.99E-5

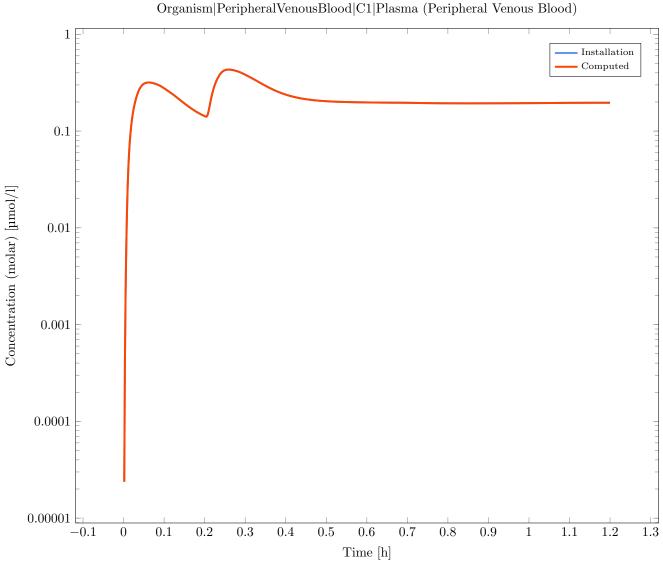


Figure 1.142

 ${\bf Simulation: \ \, Human_pH_SolubilityTable_S4_Table_SolubilityTableChanged}$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood)

Deviation: 8.54E-8

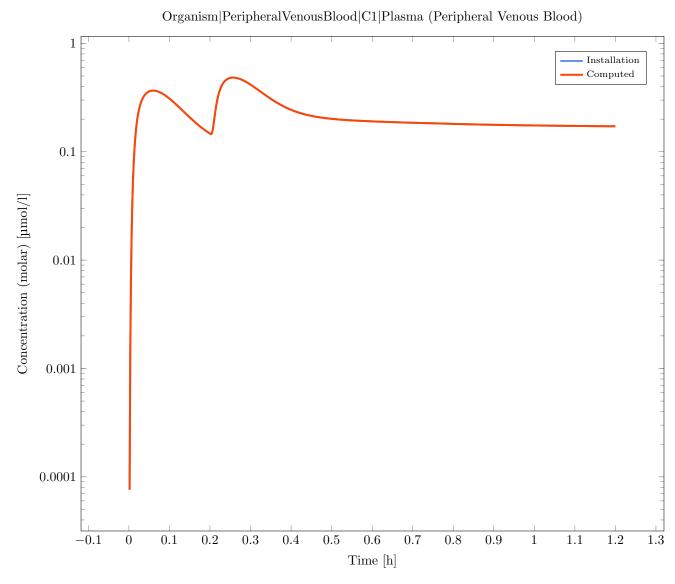


Figure 1.143

 ${\bf Simulation: \ Human_Single IV_Configuration-Human_Single IV_Configuration} \\ {\bf Result \ of \ the \ validation: \ Valid}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

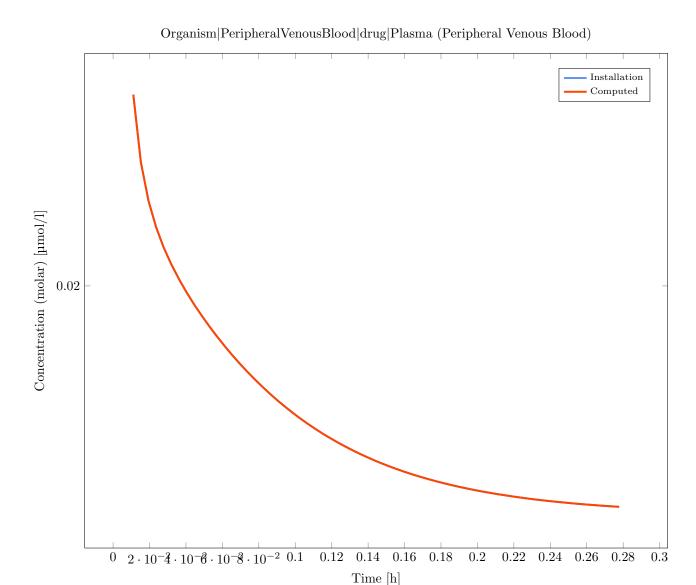


Figure 1.144

Simulation: Human_SingleIV-Human_SingleIV

Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 0

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

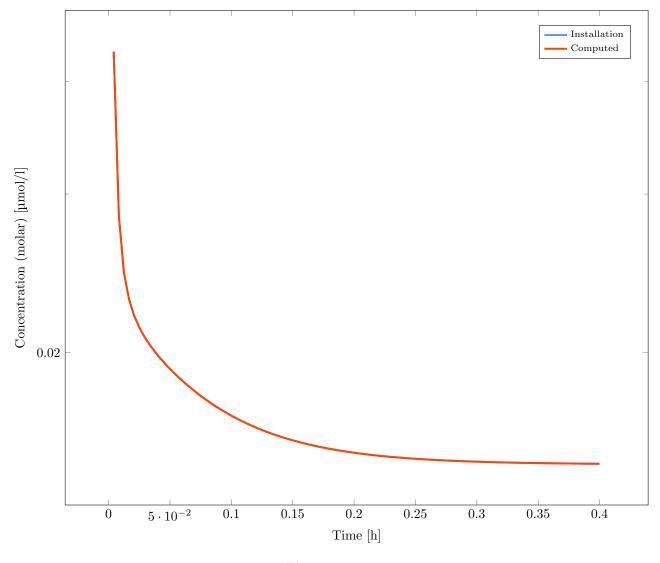


Figure 1.145

Simulation: Human_SingleIV-Human_SingleIV_MW_200_fu_0.2_LogP_5 Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

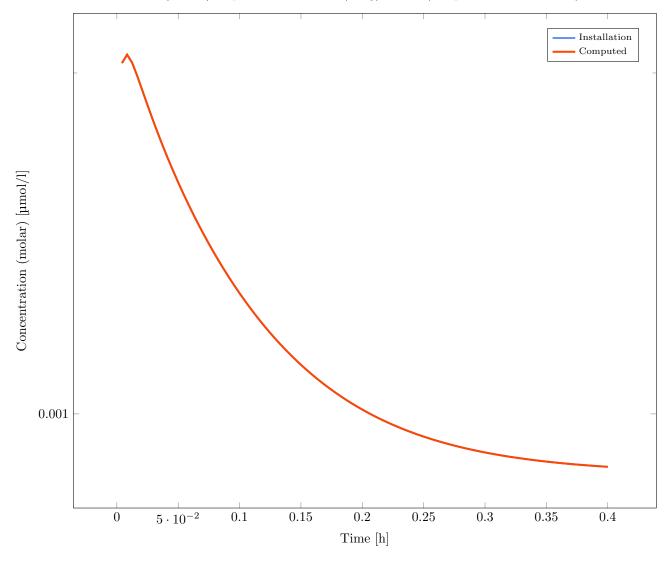


Figure 1.146

 $Simulation: \ Human_SingleIV-Human_SingleIV_MW_800_fu_0.6_LogP_-5$

Result of the validation: Valid

 $Output\ Path:\ Organism | Peripheral Venous Blood | drug | Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 1.12E-7

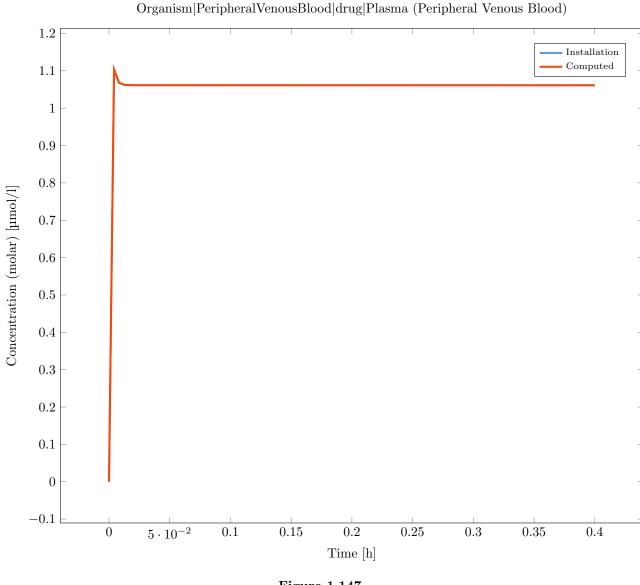
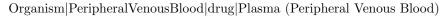


Figure 1.147

Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_SingleO

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 2.13E-7



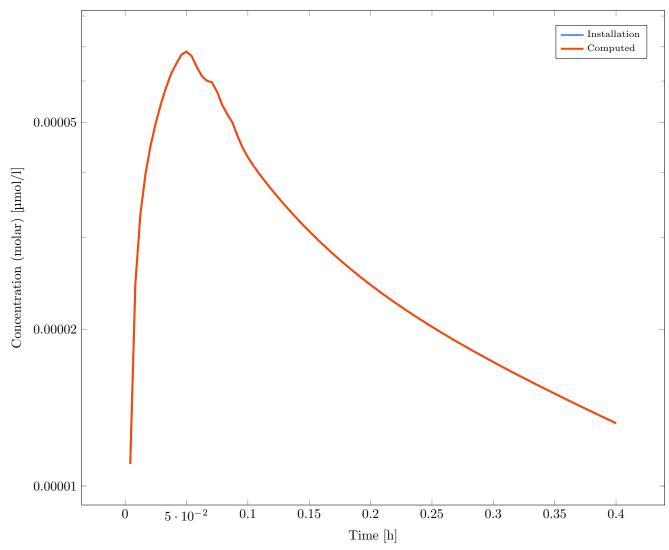


Figure 1.148

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_Singl$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

Deviation: 0



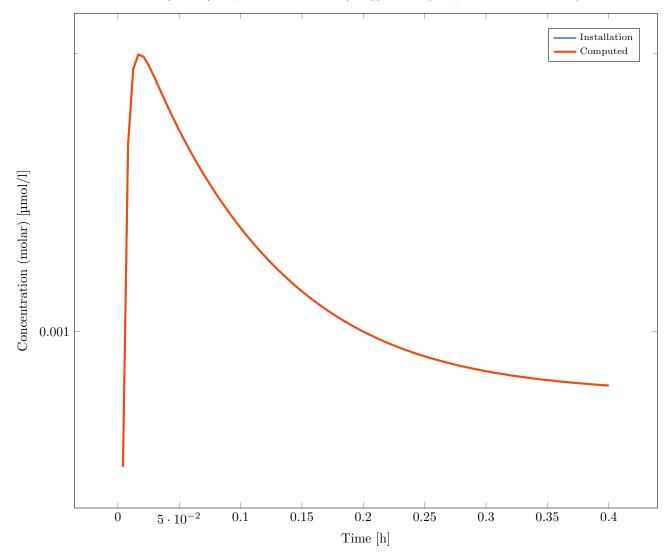


Figure 1.149

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_Singl$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

Deviation: 0

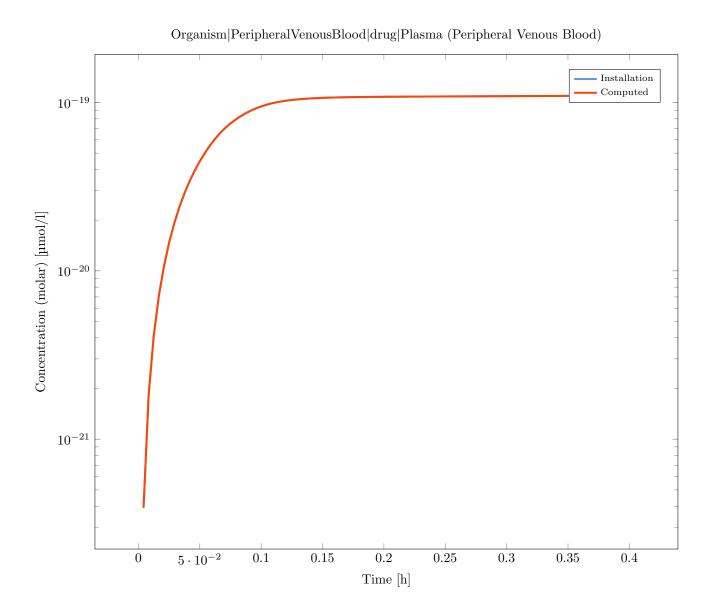


Figure 1.150

Simulation: Human_SingleORAL_Dissolved-Human_SingleORAL_Dissolved Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: $1.53 \pm .6$

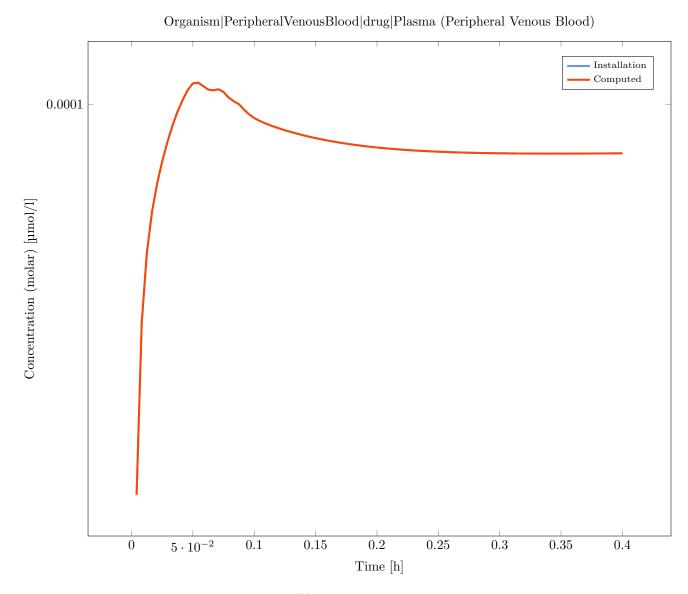


Figure 1.151

 $Simulation: Human_SingleORAL_Dissolved_Human_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$ Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |drug |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

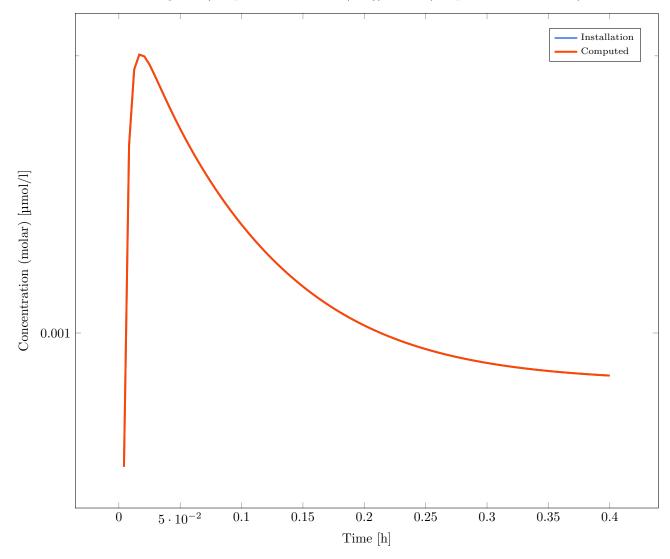
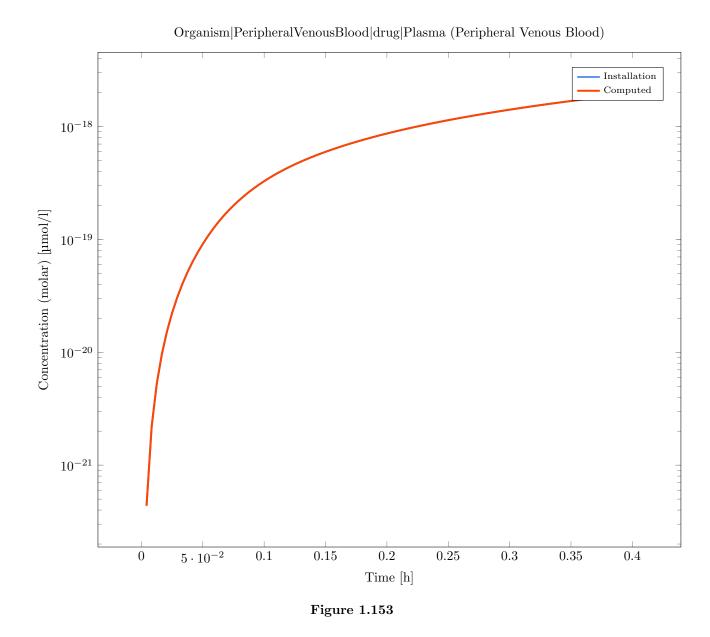


Figure 1.152

Simulation: Human_SingleORAL_Dissolved-Human_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_--5 Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |drug |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$



 ${\bf Simulation: \ Human_SingleORAL_Lint80_AsSuspention-Human_SingleORAL_Lint80_AsSuspention.} \\ {\bf Result \ of \ the \ validation: \ Valid}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

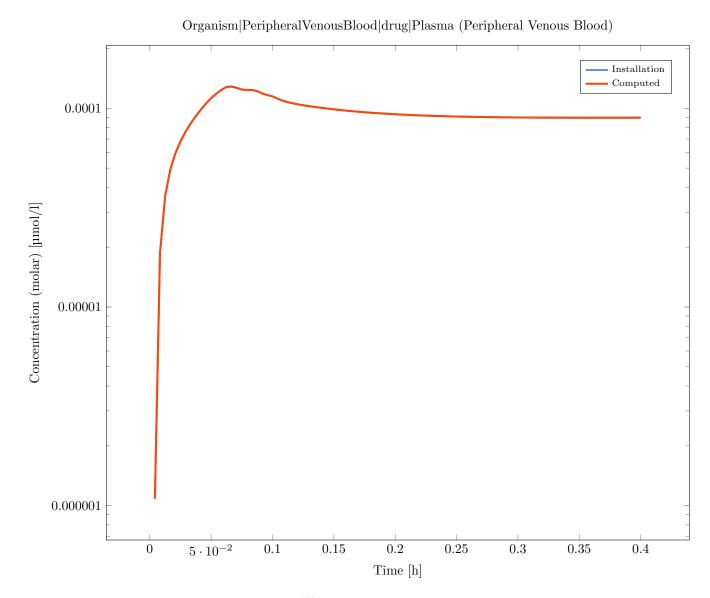


Figure 1.154

 $Simulation: \ Human_SingleORAL_Lint80-Human_SingleORAL_Lint80$

Result of the validation: Valid

 $Output\ Path:\ Organism | Peripheral Venous Blood | drug | Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 2.89E-5

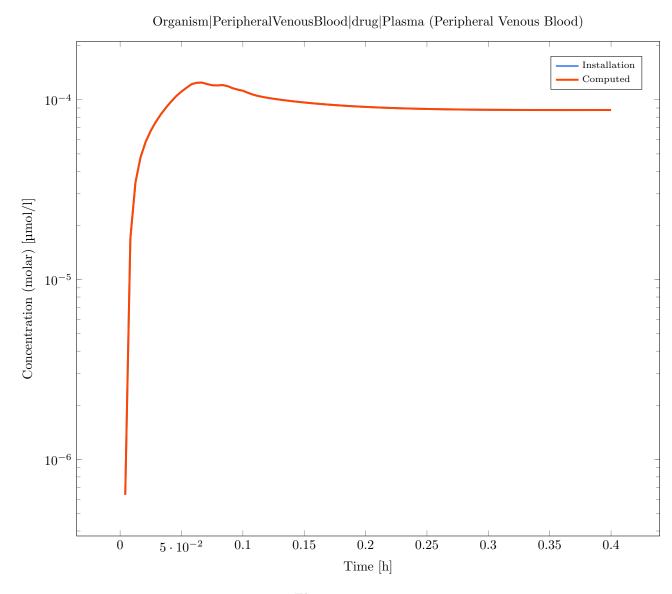


Figure 1.155

 $Simulation: Human_SingleORAL_MonoParticles_AsSuspention-Human_SingleORAL_MonoParticles_AsSuspention\\$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 0

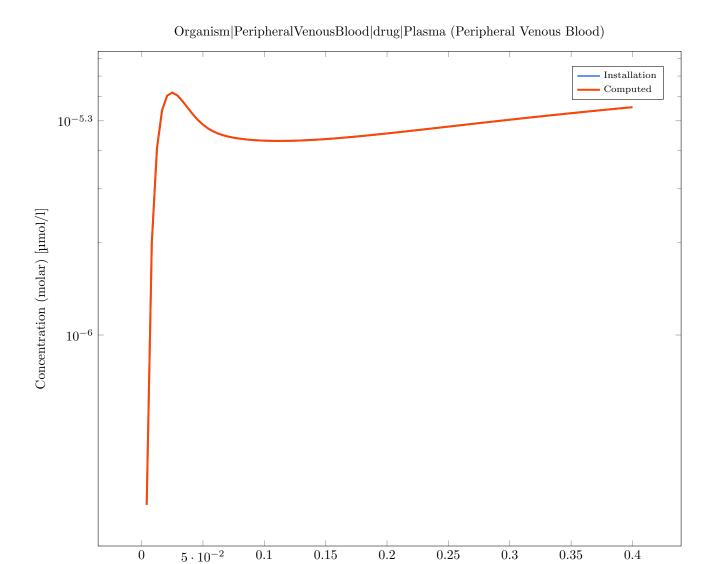


Figure 1.156

Time [h]

 $Simulation: \ Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|drug|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 2.03E-6

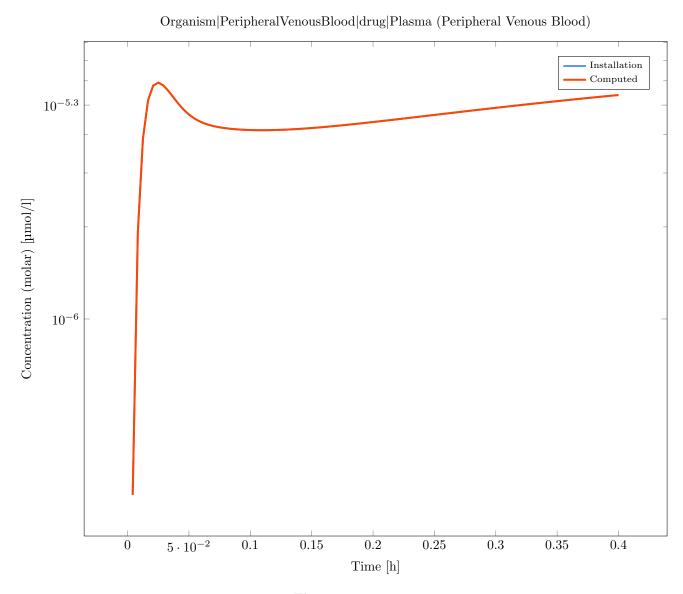


Figure 1.157

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention\\$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 0

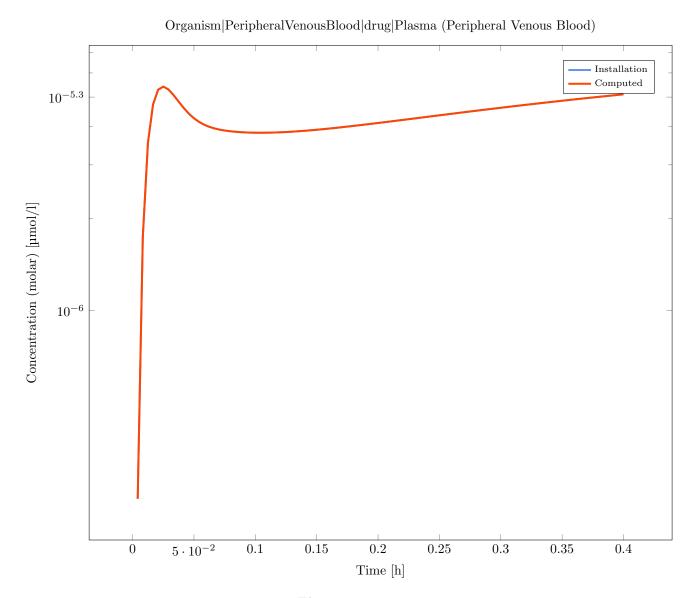


Figure 1.158

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention_dissolved_radius$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 0

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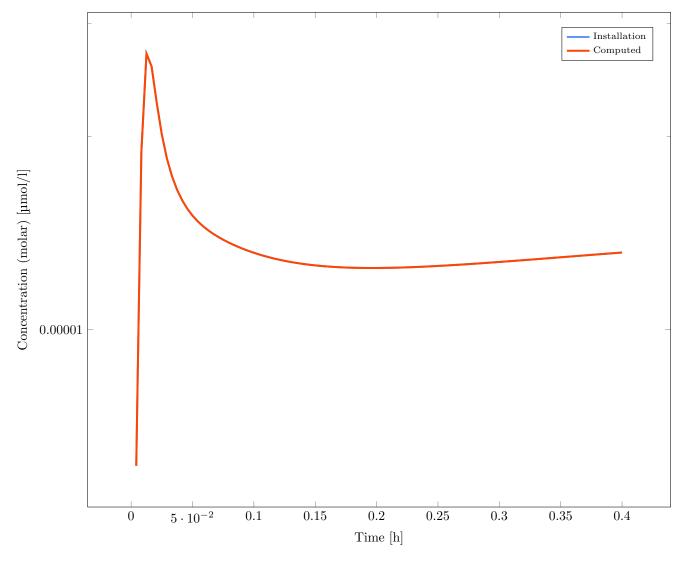


Figure 1.159

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention_treat_precipated_drug_as_soluble$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

Deviation: 0

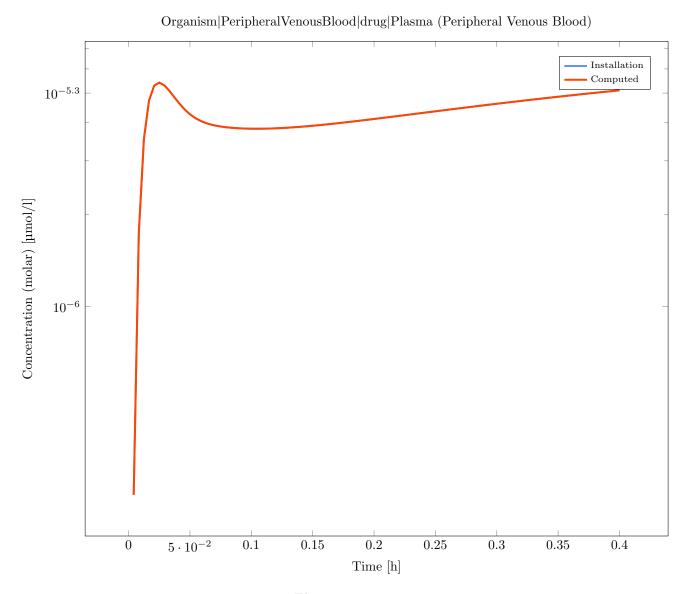


Figure 1.160

 ${\bf Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention}. \\ {\bf Result\ of\ the\ validation:\ Valid}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: $6.57\hbox{E-}6$

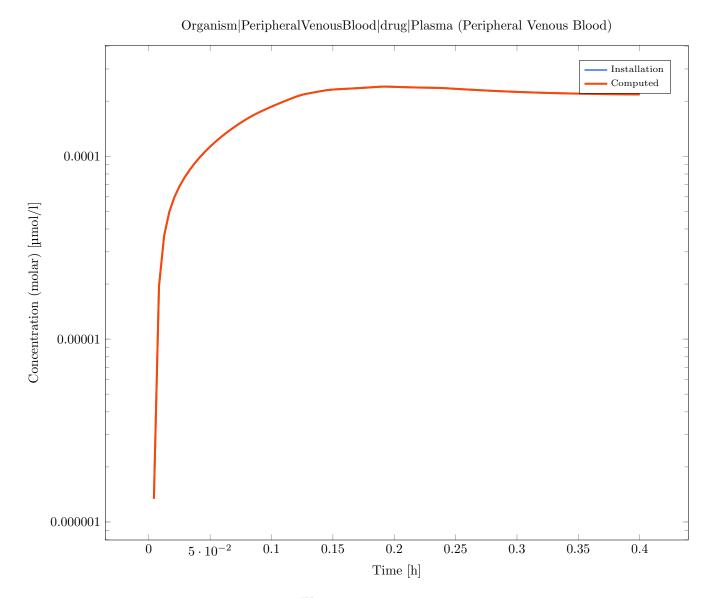


Figure 1.161

 $Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention_MW_200_fu_0.2_LogP_5\\ Result of the validation: Valid$

Output Path: Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Deviation: 1.57E-6

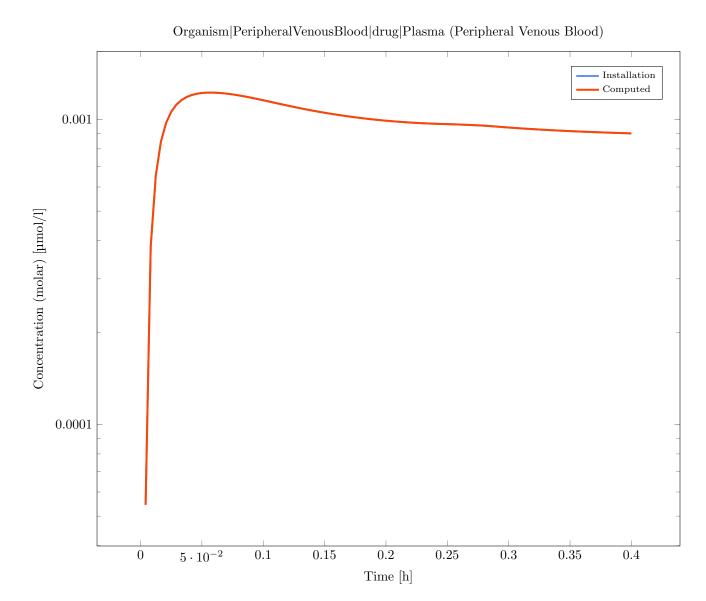
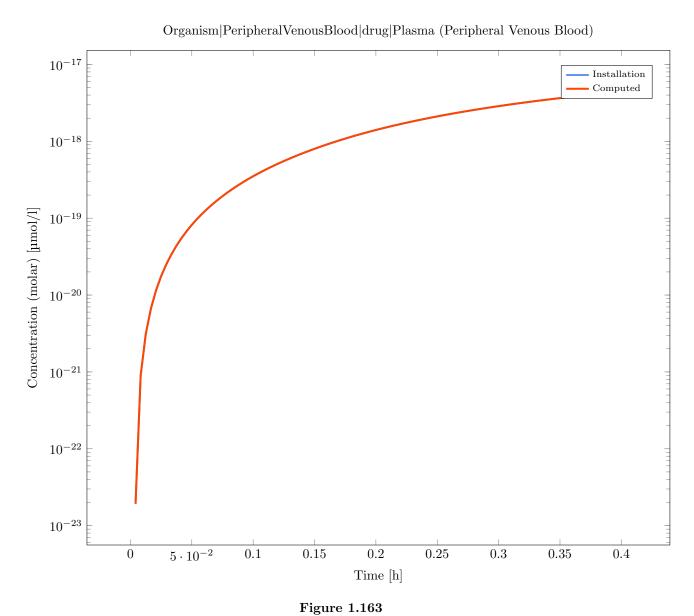


Figure 1.162

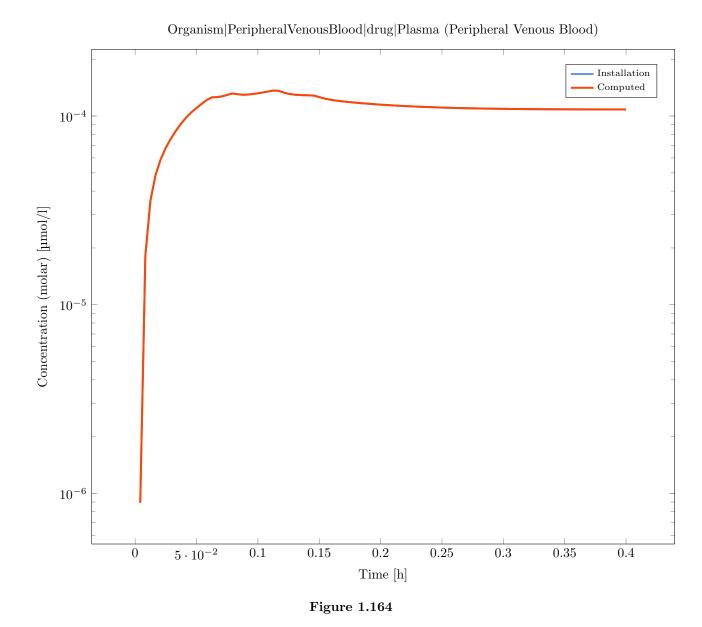
 $Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention_MW_800_fu_0.6_LogP_-5\\ Result of the validation: Valid$

Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: ${\bf 0}$



 ${\bf Simulation: \ Human_SingleORAL_Weibull-Human_SingleORAL_Weibull} \\ {\bf Result \ of \ the \ validation: \ Valid}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 1.08E-4



 $Simulation: \ Human_SingleORAL_Weibull_Human_SingleORAL_Weibull_MW_200_fu_0.2_LogP_5 \\ Result of the validation: \ Valid$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 4.05 ± 6

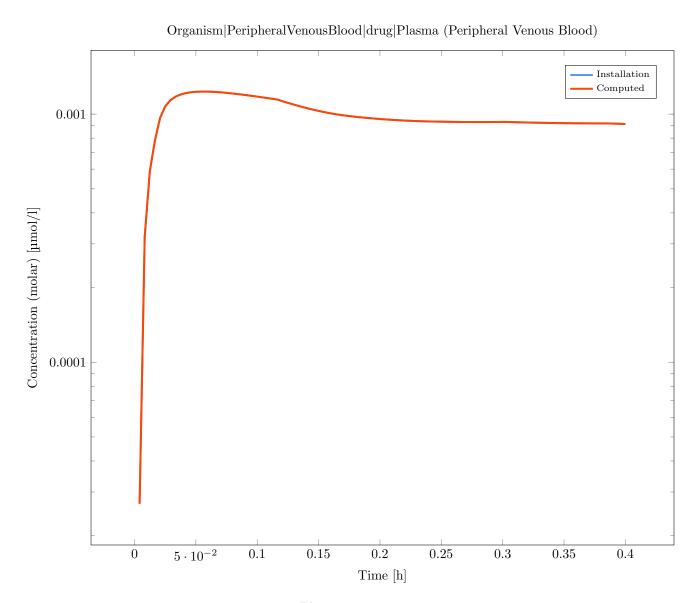


Figure 1.165

Simulation: Human_SingleORAL_Weibull-Human_SingleORAL_Weibull_MW_800_fu_0.6_LogP_5 Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: ${\bf 0}$

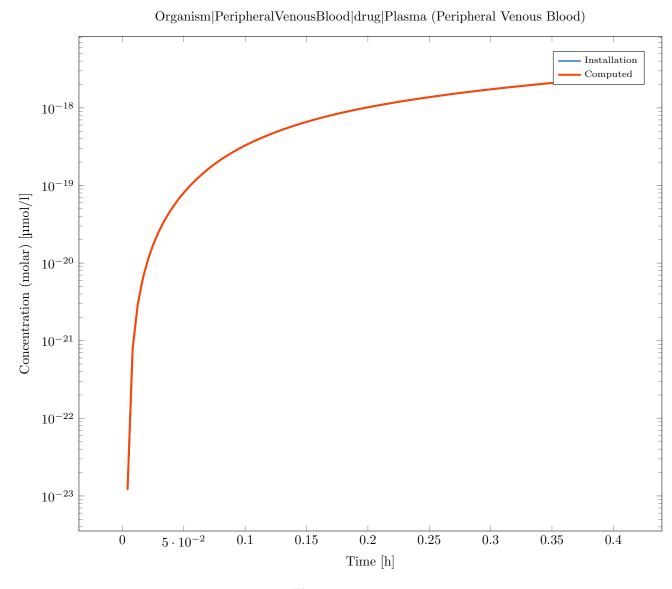


Figure 1.166

 ${\bf Simulation: Human_Uncompetitive Inhibition-Human_Uncompetitive Inhibition} \\ {\bf Result of the \ validation: \ Valid}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

$\label{eq:constraint} Organism | Peripheral Venous Blood | drug | Plasma \; (Peripheral Venous Blood)$

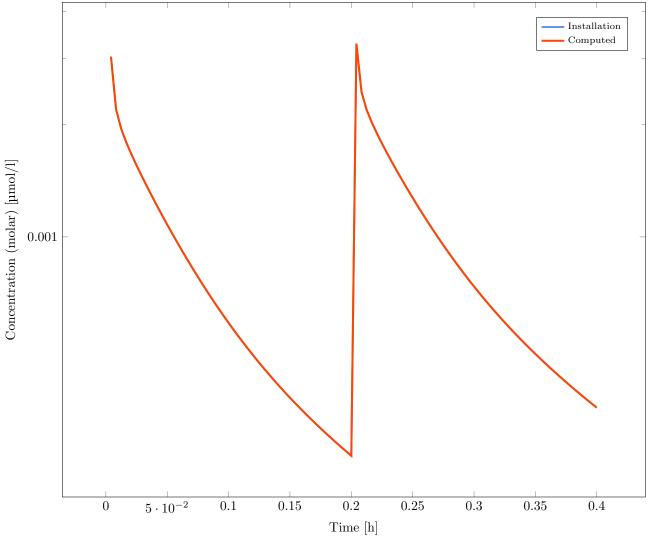


Figure 1.167

Output Path: Organism |PeripheralVenousBlood |
inhibitor |Plasma (Peripheral Venous Blood) | Deviation:
 0

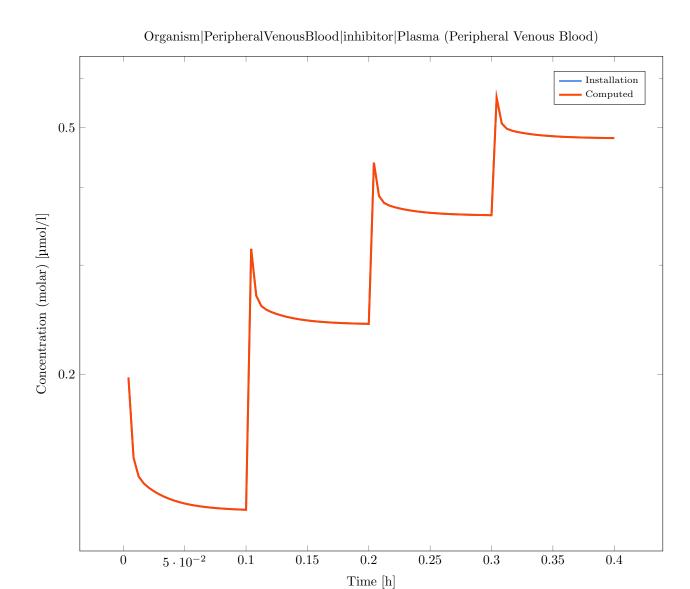
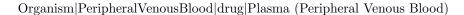


Figure 1.168

Simulation: Minipig_SingleORAL_Dissolved-Minipig_SingleORAL_Dissolved Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0



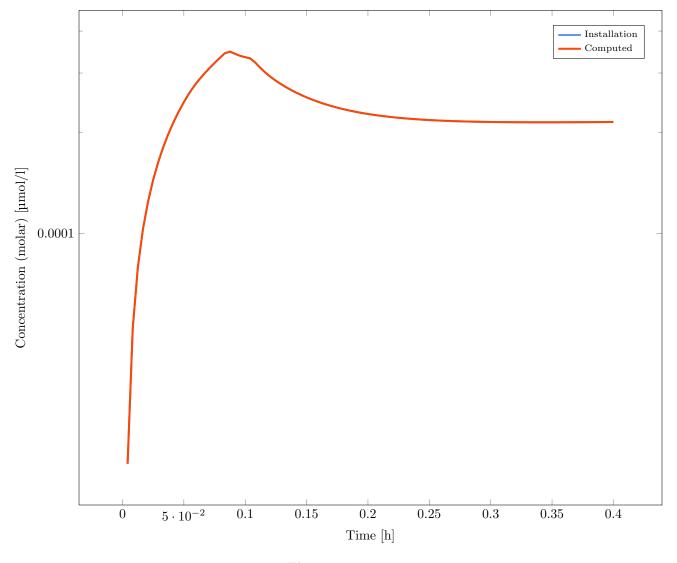


Figure 1.169

 $Simulation: \ Minipig_SingleORAL_Dissolved_Minipig_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$ Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

Deviation: 0



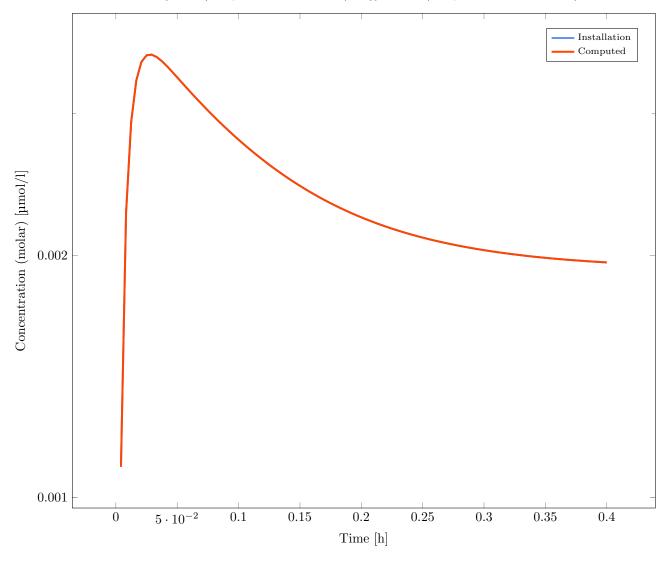


Figure 1.170

 $\label{lem:simulation:minipig_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-5 \\ Result of the validation: Valid$

Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: ${\bf 0}$



Figure 1.171

 ${\bf Simulation: \ Monkey_SingleORAL_Dissolved-Monkey_SingleORAL_Dissolved \ Result \ of \ the \ validation: \ Valid}$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed 0.001

Figure 1.172

0.2

Time [h]

0.25

0.35

0.3

0.4

0.15

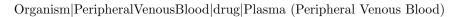
0.1

Simulation: Monkey_SingleORAL_Dissolved-Monkey_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5 Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: 0

0

 $5 \cdot 10^{-2}$



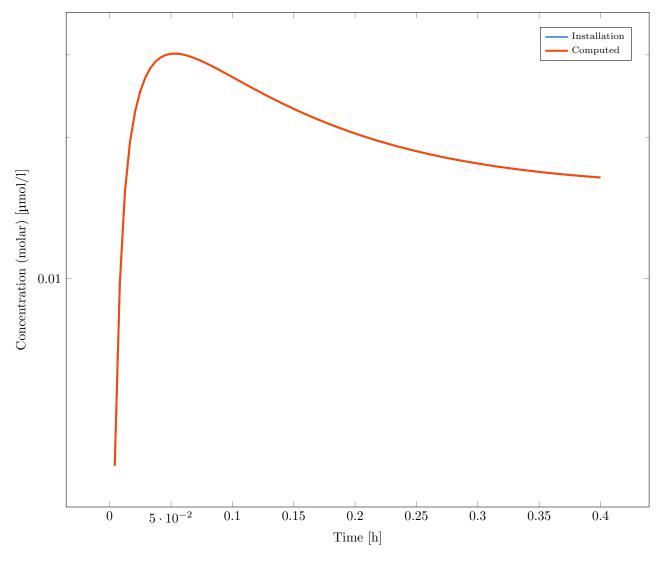


Figure 1.173

Simulation: Monkey_SingleORAL_Dissolved-Monkey_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_--5 Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: ${\bf 0}$

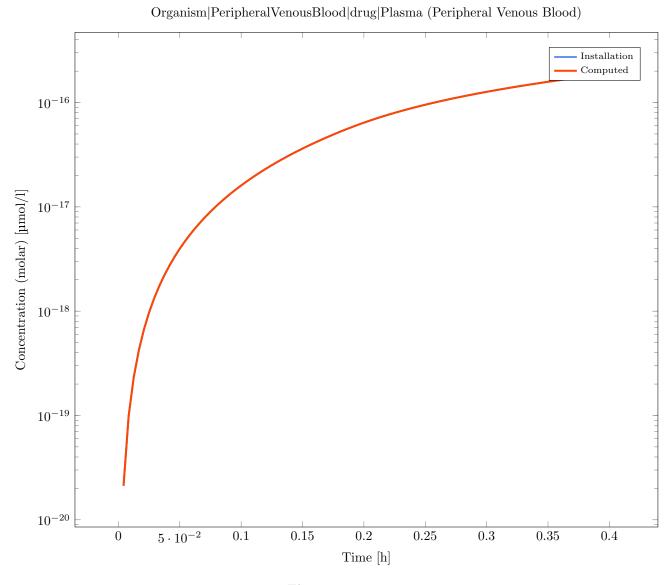


Figure 1.174

Simulation: Mouse_SingleORAL_Dissolved-Mouse_SingleORAL_Dissolved Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

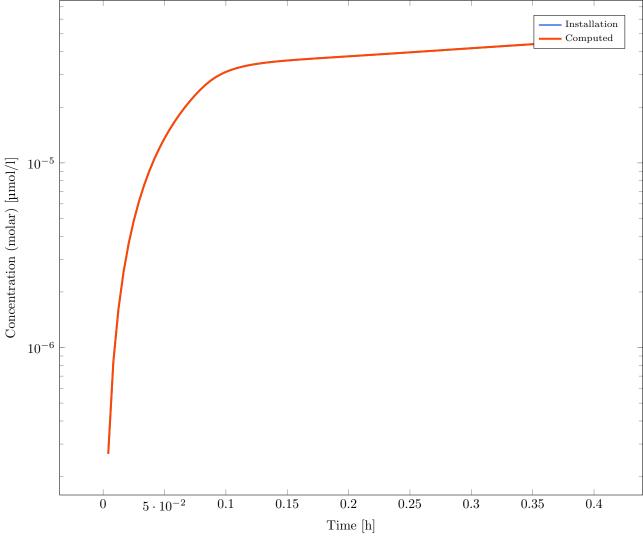


Figure 1.175

 $Simulation: Mouse_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: $\mathbf 0$

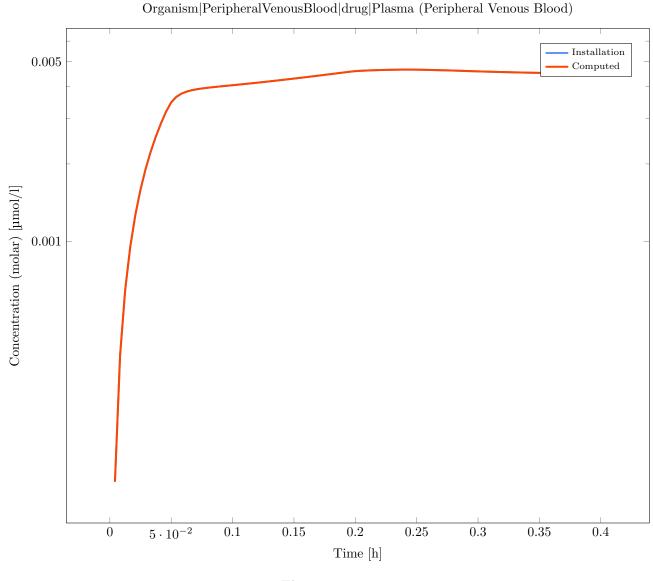


Figure 1.176

Simulation: Mouse_SingleORAL_Dissolved-Mouse_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_--5 Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: $\mathbf 0$

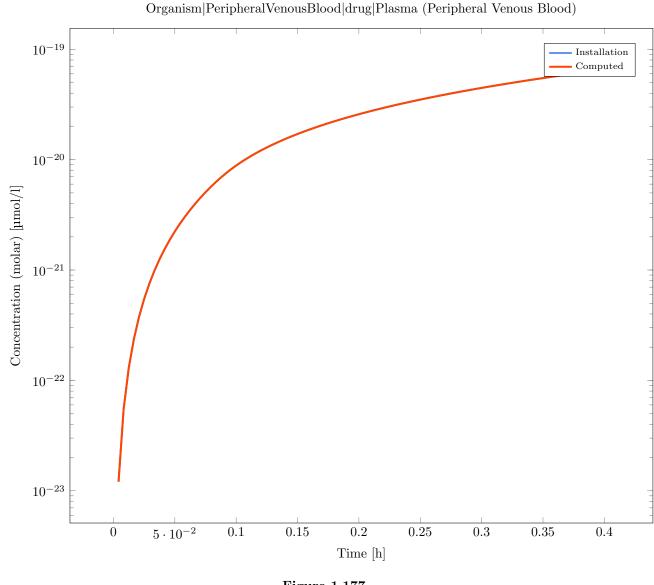
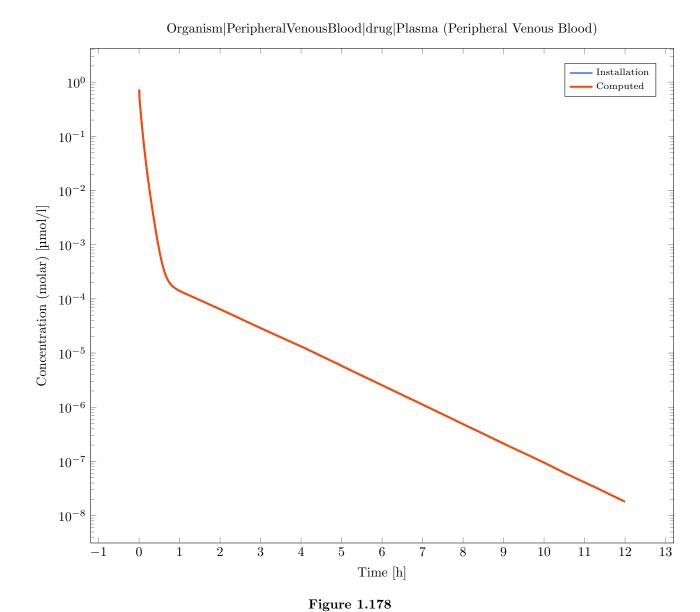


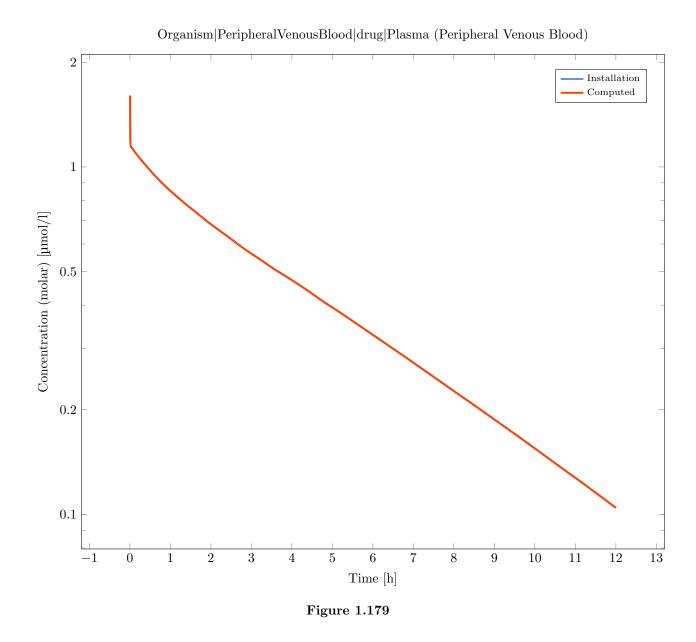
Figure 1.177

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 1.74E-4

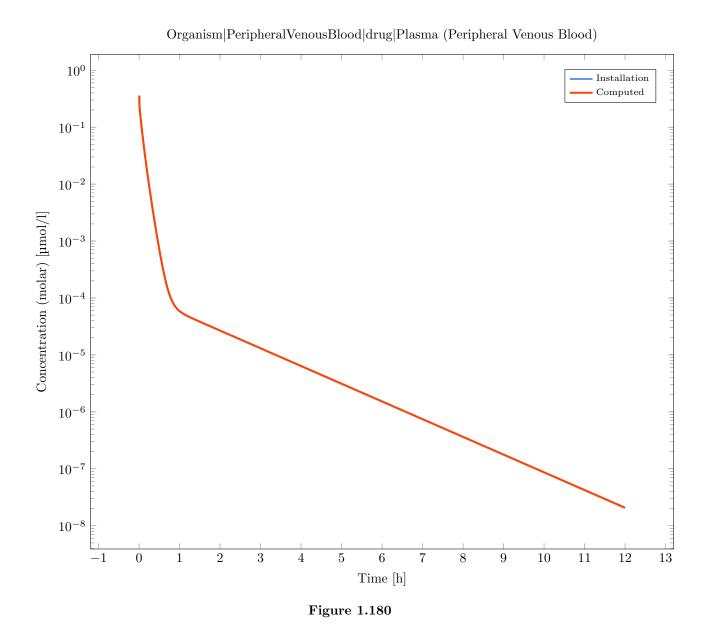


 $Simulation: \ \, Preterm_SingleIV_Age_0_GA_32_GFR-Preterm_SingleIV_Age_0_GA_32_GFR \\ Result of the validation: \ \, Valid$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 1.42E-4



 $\label{lem:condition:con$



 $Simulation: \ \, Preterm_SingleIV_Age_15_GA_32_GFR-Preterm_SingleIV_Age_15_GA_32_GFR \\ Result of the validation: \ \, Valid$

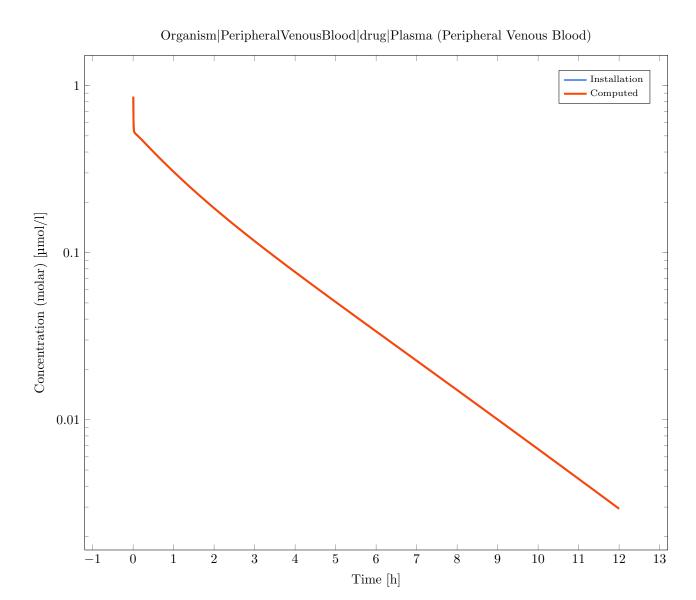


Figure 1.181

 ${\bf Simulation: Rabbit_SingleORAL_Dissolved-Rabbit_SingleORAL_Dissolved} \\ {\bf Result \ of \ the \ validation: \ Valid}$

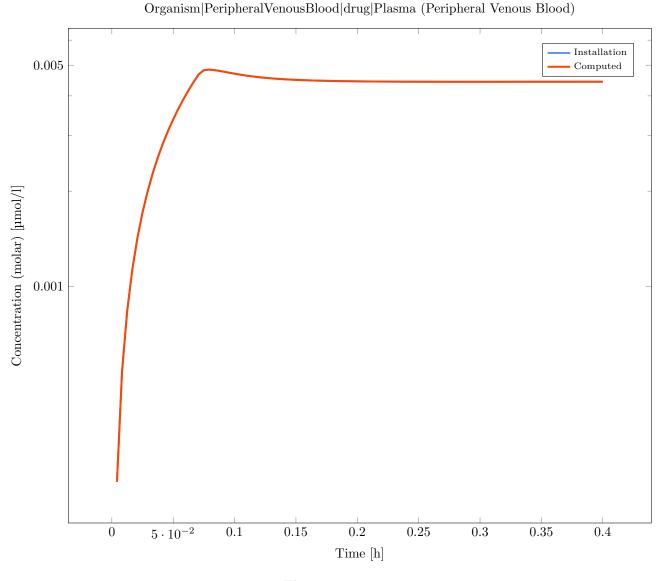
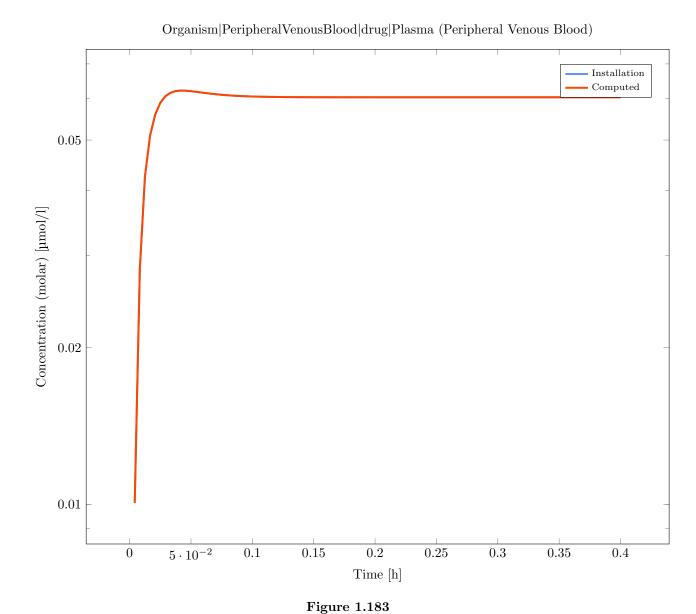


Figure 1.182

 $Simulation: Rabbit_SingleORAL_Dissolved_Rabbit_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$ Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: ${\bf 0}$



 $\label{local_simpleORAL_Dissolved_Rabbit_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_--5 \\ Result of the validation: Valid$

Output Path: Organism |PeripheralVenousBlood |drug |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

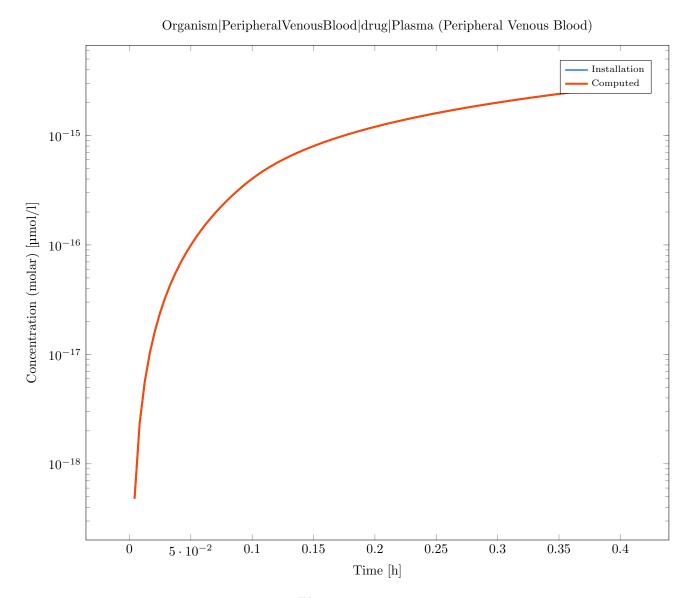
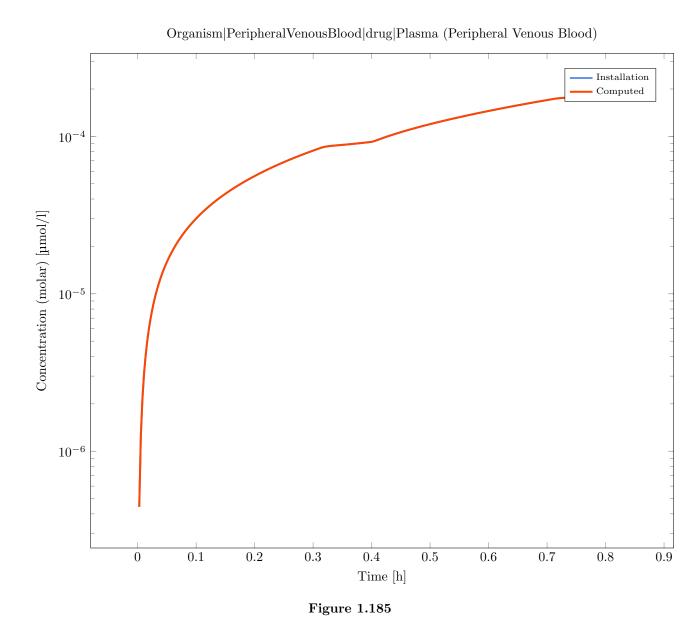


Figure 1.184

Simulation: Rat_MultiORAL_6_6_12_Dissolved-Rat_MultiORAL_6_6_12_Dissolved Result of the validation: Valid



 $Simulation: Rat_MultiORAL_6_6_6_6_Dissolved-Rat_MultiORAL_6_6_6_6_Dissolved \\ Result of the validation: Valid$

Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: ${\bf 0}$

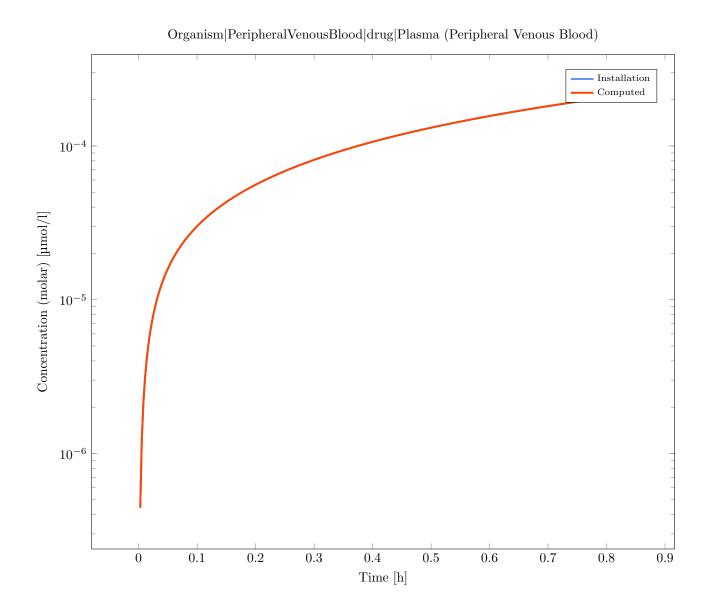


Figure 1.186

Output Path: Organism |PeripheralVenousBlood |drug |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed 10^{-4} Concentration (molar) $[\mu]$ 10^{-5} 10^{-6} 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9

Figure 1.187

Time [h]

 $Simulation: Single IV_2 Pores_Human-Single IV_2 Pores_Human$

Result of the validation: Valid

$\label{eq:constraint} Organism | Peripheral Venous Blood | drug | Plasma \; (Peripheral Venous Blood)$

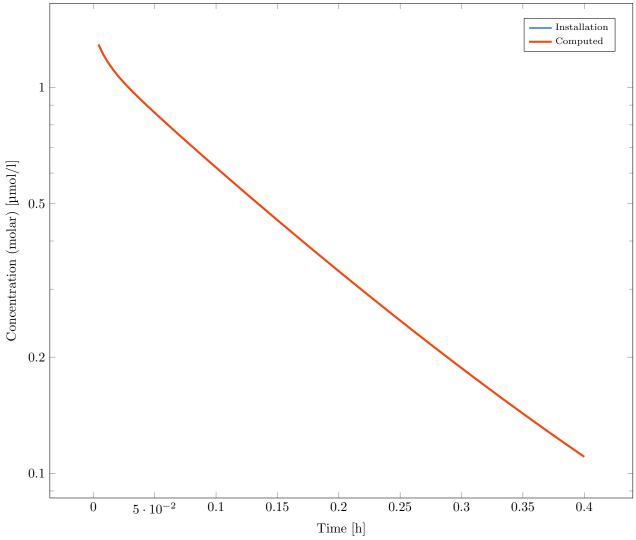


Figure 1.188

Simulation: SingleIV_2Pores_Human-SingleIV_2Pores_Human_SimulationC Result of the validation: Valid

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

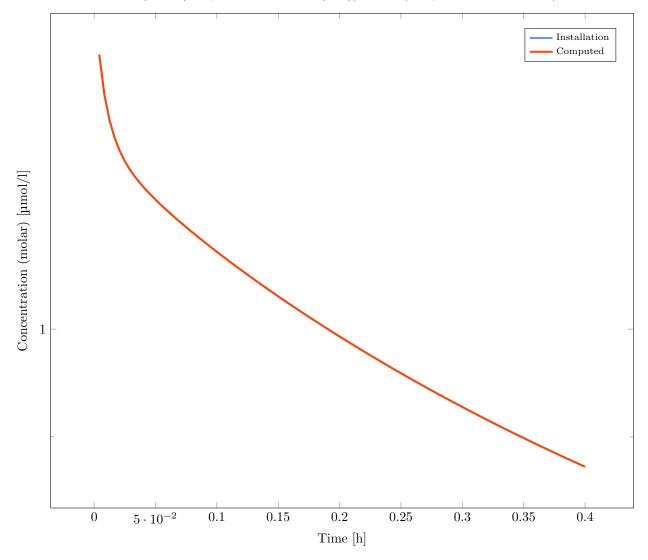


Figure 1.189

Simulation: SingleIV_2Pores_Human-SingleIV_2Pores_Human_SimulationD Result of the validation: Valid

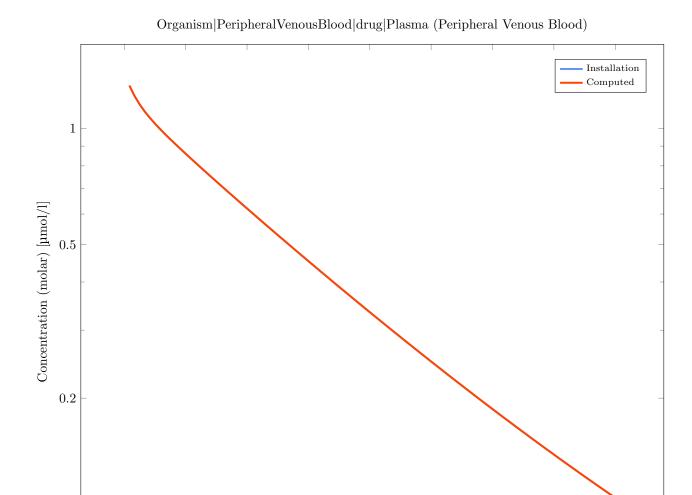


Figure 1.190

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

Simulation: SingleIV_2Pores_Human-SingleIV_2Pores_Human_SimulationF Result of the validation: Valid

0.1

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

0.1

0

 $5\cdot 10^{-2}$

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

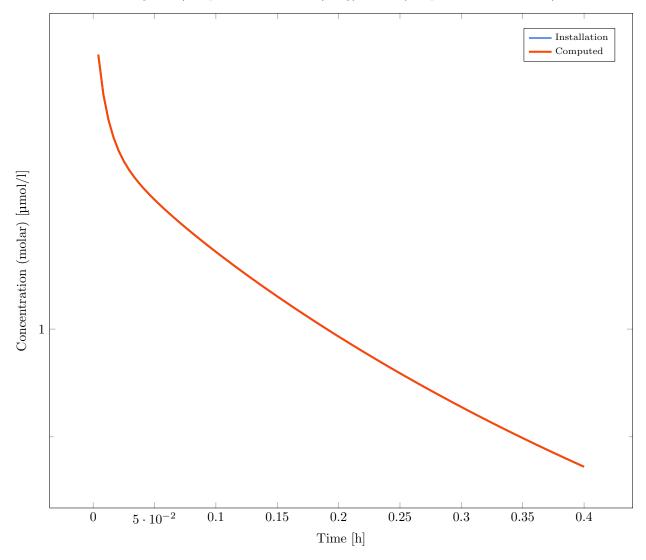


Figure 1.191

 $Simulation: Single IV_2 Pores_Monkey-Single IV_2 Pores_Monkey$

Result of the validation: Valid

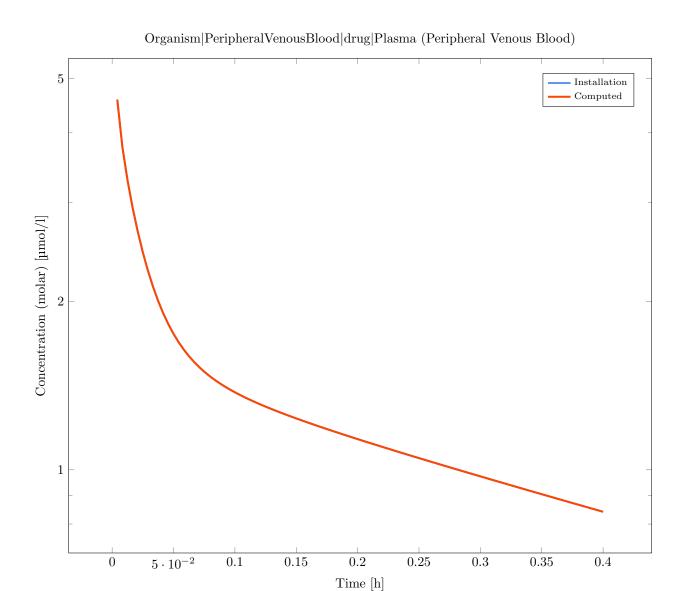


Figure 1.192

Simulation: SingleIV_2Pores_Monkey-SingleIV_2Pores_Monkey_SimulationG Result of the validation: Valid

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)

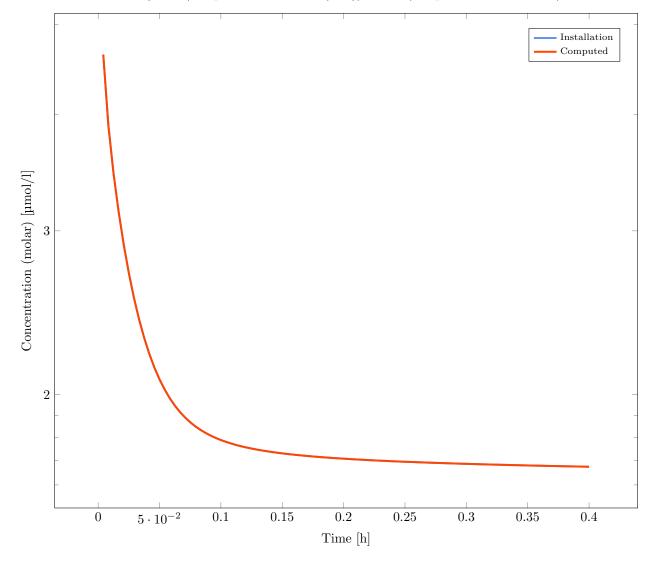


Figure 1.193

Simulation: SingleIV_2Pores_Monkey-SingleIV_2Pores_Monkey_SimulationH Result of the validation: Valid

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) | Total | Computed | Computed

Figure 1.194

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

 ${\bf Simulation: \ Single IV_2 Pores_Mouse-Single IV_2 Pores_Mouse}$

0.1

 $5\cdot 10^{-2}$

Result of the validation: Valid

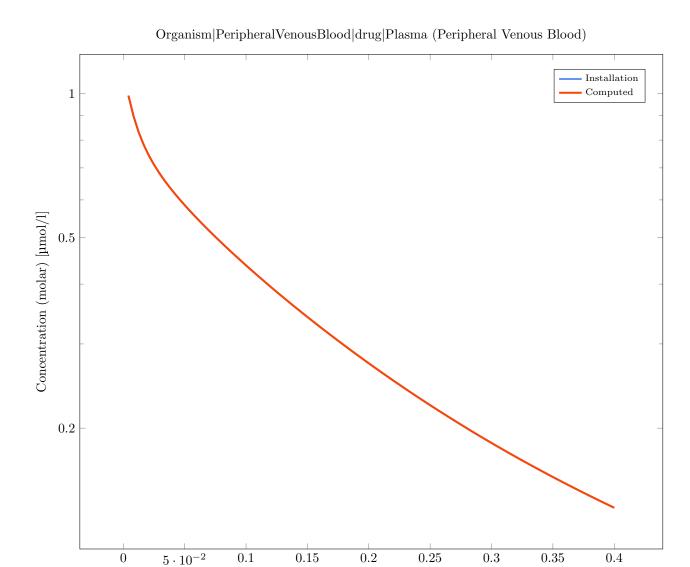


Figure 1.195

Time [h]

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse_SimulationA Result of the validation: Valid

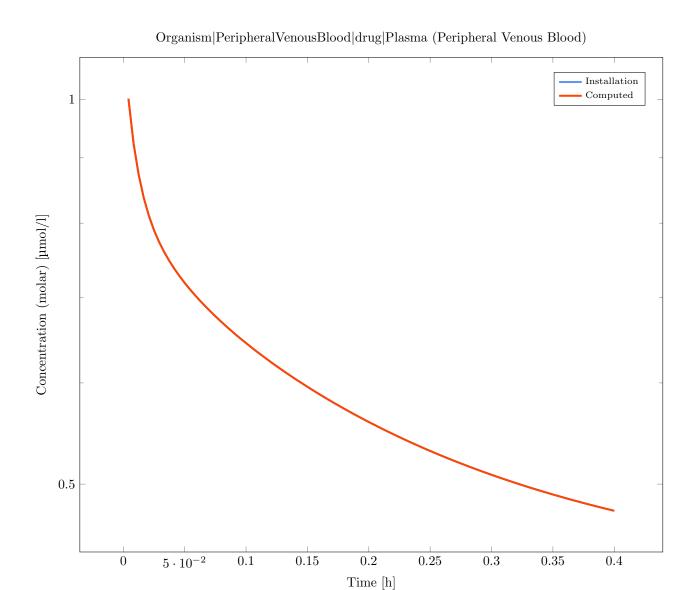


Figure 1.196

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse_SimulationB Result of the validation: Valid

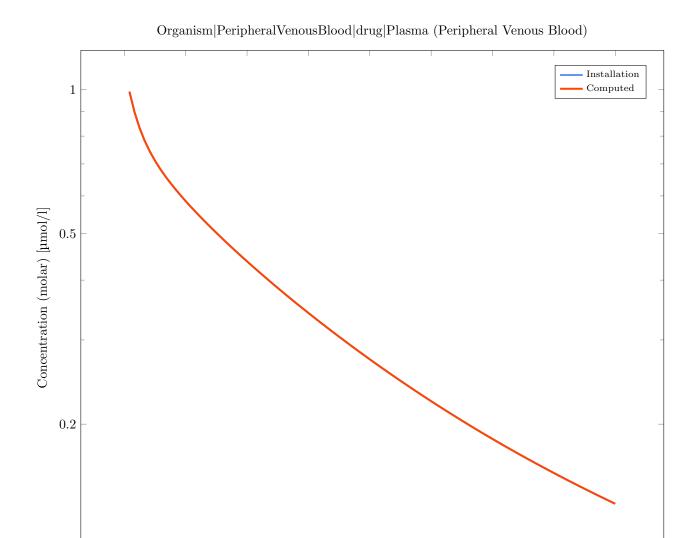


Figure 1.197

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse_SimulationE Result of the validation: Valid

0.1

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood) Deviation:
 0

0

 $5\cdot 10^{-2}$

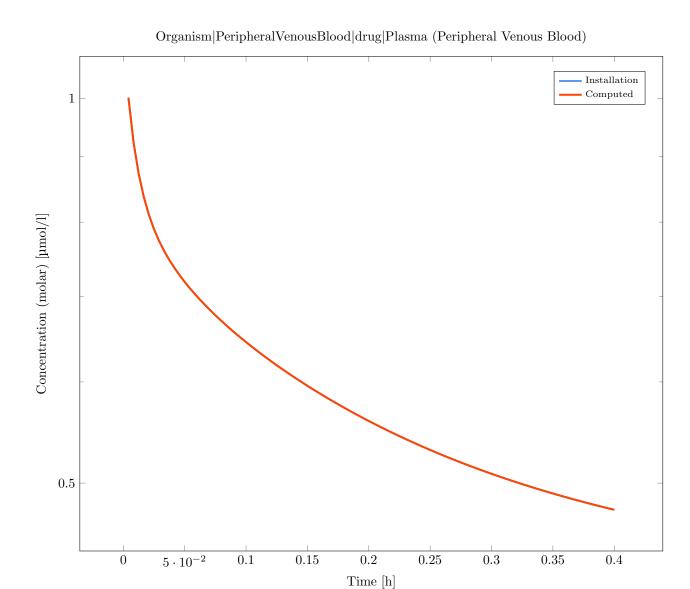


Figure 1.198

 $Simulation: Single IV_C1_4 Comp_standard_stand$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |C1|Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

${\it Organism}|{\it Peripheral Venous Blood}|{\it C1}|{\it Plasma}~({\it Peripheral Venous Blood})$

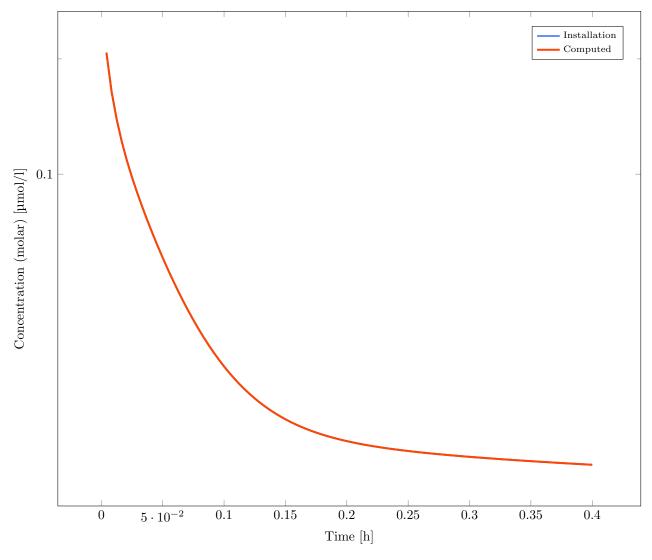


Figure 1.199

 $Simulation: Single IV_C2_4 Comp_PT_standard_st$

Organism|PeripheralVenousBlood|C2|Plasma (Peripheral Venous Blood) Installation Computed 0.2

Figure 1.200

 $Simulation: Single IV_C2_4 Comp_RR_standard_st$

0.2

Time [h]

0.25

0.35

0.4

0.3

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

0.15

0.1

0

 $5\cdot 10^{-2}$

Organism|PeripheralVenousBlood|C2|Plasma (Peripheral Venous Blood) 1.4 1.2 1.2 0.8 0.4 0.2

Figure 1.201

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single IV_C2_4 Comp_standard_schmitt_standard-Single IV_C2_4 Comp_standard_schmitt_standard\\$

Result of the validation: Valid

0

 $5\cdot 10^{-2}$

0

Output Path: Organism |PeripheralVenousBlood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

0.15

Organism|PeripheralVenousBlood|C2|Plasma (Peripheral Venous Blood) Installation Computed 0.5

Figure 1.202

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single IV_C3_4 Comp_RR_schmitt_standard-Single IV_C3_schmitt_standard-Single IV_C3_schmitt_schmitt_standard-Single IV_C3_schmitt_s$

Output Path: Organism |Peripheral Venous
Blood |C3 |Plasma (Peripheral Venous Blood) Deviation:
 0

0.15

0.1

0

 $5\cdot 10^{-2}$

Organism|PeripheralVenousBlood|C3|Plasma (Peripheral Venous Blood)

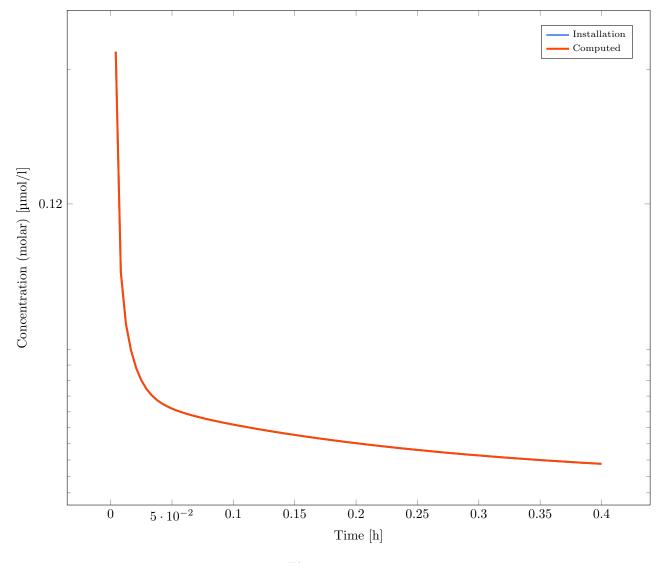


Figure 1.203

 $Simulation: Single IV_C3_4 Comp_standard_schmittnorm lized_standard-Single IV_C3_4 Comp_standard_schmittnorm lized_standard$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C3|Plasma (Peripheral Venous Blood)

Deviation: 0

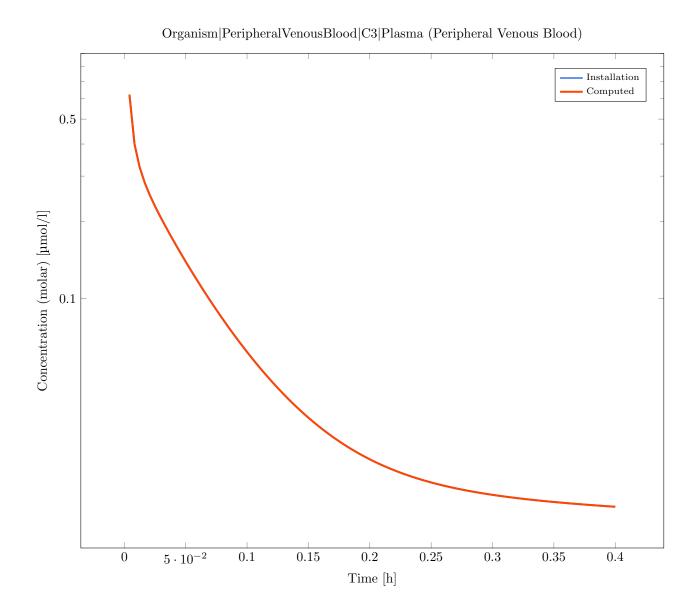


Figure 1.204

 $Simulation: Single IV_C4_2 Pores_RR_standard_s$

Output Path: Organism |Peripheral Venous
Blood |C4 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

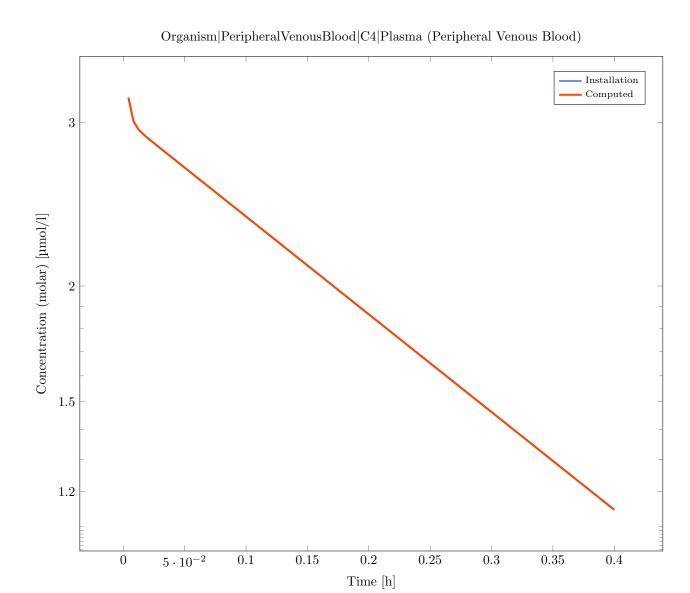


Figure 1.205

 $Simulation: Single IV_C4_4 Comp_Ber_standard_s$

Output Path: Organism |Peripheral Venous
Blood |C4 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

$Organism|Peripheral Venous Blood|C4|Plasma\ (Peripheral Venous\ Blood)$

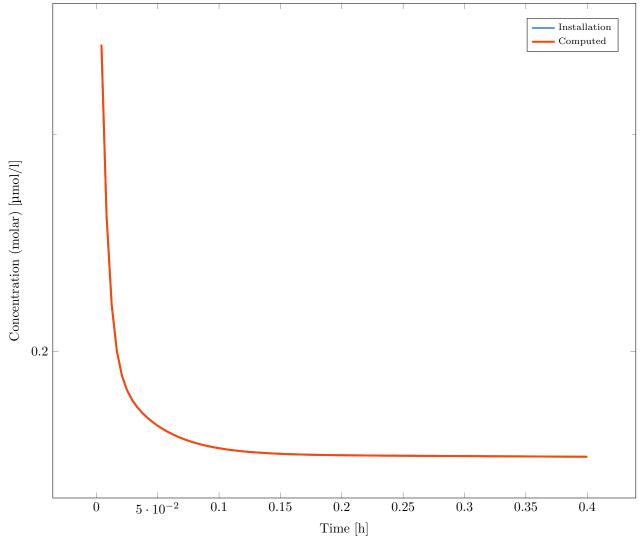


Figure 1.206

 $Simulation: Single IV_C5_2 Pores_Ber_standard_$

Organism|PeripheralVenousBlood|C5|Plasma (Peripheral Venous Blood) Installation Computed 3 Concentration (molar) $[\mu mol/1]$ 2 1.5 1.2 0.15 0.2 0.25 0.3 0.35 0 $5\cdot 10^{-2}$ 0.1 0.4

Figure 1.207

Time [h]

 $Simulation: Single IV_C5_2 Pores_PT_standard_s$

Output Path: Organism |Peripheral Venous
Blood |C5 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

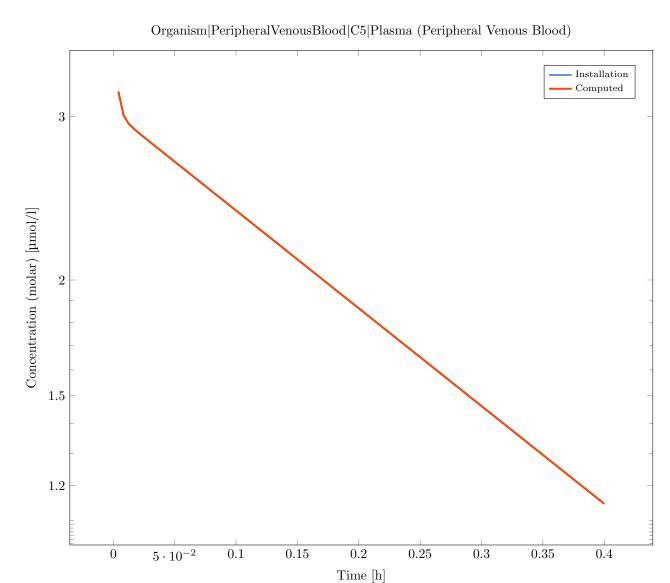


Figure 1.208

 $Simulation: SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_schmitt_schmi$

Output Path: Organism |Peripheral Venous
Blood |C5 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

Installation Computed Computed 1.5

Organism|PeripheralVenousBlood|C5|Plasma (Peripheral Venous Blood)

.

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

0.1

Figure 1.209

 $Simulation: Single IV_C6_2 Pores_standard_stan$

Result of the validation: Valid

0

 $5\cdot 10^{-2}$

 $Output\ Path:\ Organism|PeripheralVenousBlood|C6|Plasma\ (Peripheral\ Venous\ Blood)$

Deviation: 0

Organism|PeripheralVenousBlood|C6|Plasma (Peripheral Venous Blood) Installation Computed 1.5

Figure 1.210

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single IV_C7_2 Pores_standard_schmitt_standard_Single IV_C7_2 Pores_standard_schmitt_schmitt$

Result of the validation: Valid

0

 $5\cdot 10^{-2}$

Output Path: Organism |PeripheralVenousBlood |C7 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

0.15

0.5 — Installation — Computed Onto

Organism|PeripheralVenousBlood|C7|Plasma (Peripheral Venous Blood)

Figure 1.211

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single IV_C7_4 Comp_schmitt_standard_standa$

Result of the validation: Valid

0

 $5\cdot 10^{-2}$

Output Path: Organism |PeripheralVenousBlood |C7 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

0.15

Organism|PeripheralVenousBlood|C7|Plasma (Peripheral Venous Blood)

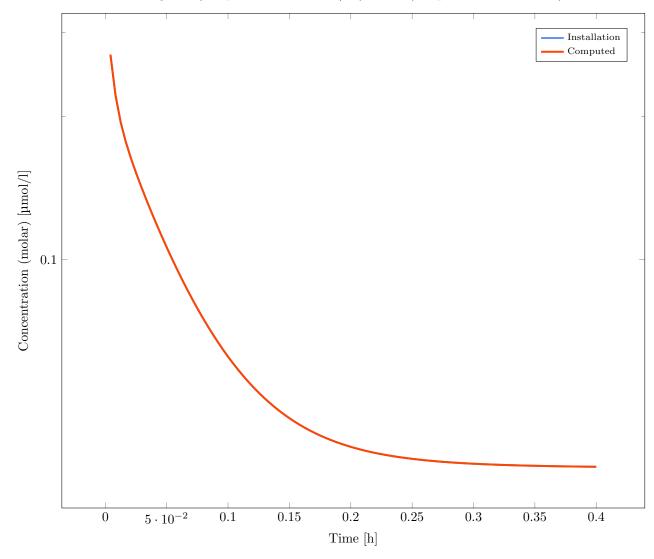


Figure 1.212

 $Simulation: Single IV_C8_2 Pores_standard_schmittnormalized_standard_Single IV_C8_2 Pores_standard_schmittnormalized_schmittnormalized_schmittnor$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C8|Plasma (Peripheral Venous Blood)

Deviation: 0

$Organism | Peripheral Venous Blood | C8 | Plasma \ (Peripheral Venous Blood)$

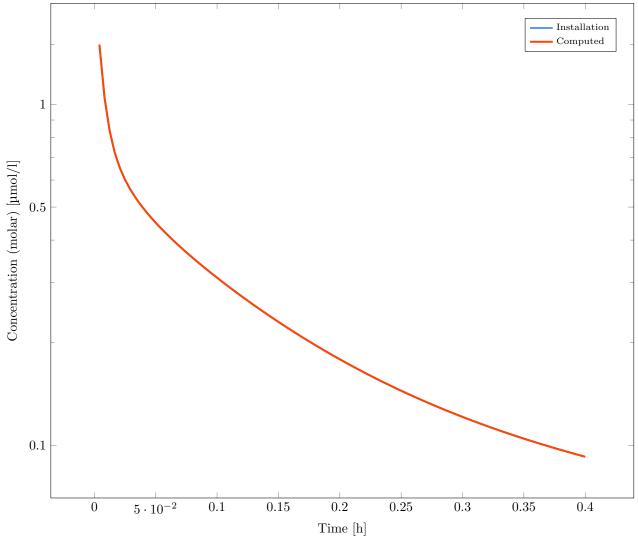


Figure 1.213

 $Simulation: Single IV_C9_2 Pores_schmitt_standard_standard_Single IV_C9_2 Pores_schmitt_standard_sta$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|C9|Plasma\ (Peripheral\ Venous\ Blood)$

Organism|PeripheralVenousBlood|C9|Plasma (Peripheral Venous Blood) Installation Computed 2 1.5

Figure 1.214

0.15

0.1

 $Simulation: Single ORAL_C10_4 Comp_PT_standard_standard-Single ORAL_C10_4 Comp_PT_standard-Single ORAL_C10_4 Comp_Single ORAL_C10_4 C00_4 C00_$

0.2

Time [h]

0.25

0.3

0.35

0.4

Result of the validation: Valid

0

 $5\cdot 10^{-2}$

1.2

Output Path: Organism |PeripheralVenousBlood |C10 |Plasma (Peripheral Venous Blood)
 Deviation: 0

Organism|PeripheralVenousBlood|C10|Plasma (Peripheral Venous Blood)

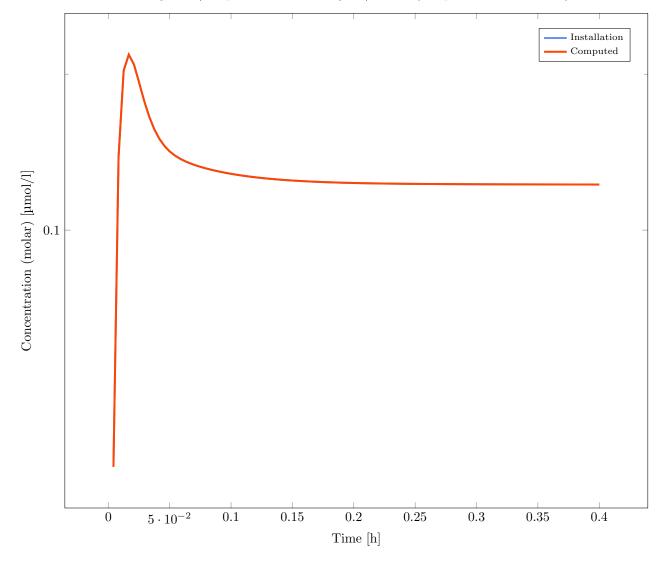


Figure 1.215

 $Simulation: Single ORAL_C11_4 Comp_schmitt_standard_standard_Single ORAL_C11_4 Comp_schmitt_standard$

Result of the validation: Valid

 $\label{eq:continuous} Output\ Path:\ Organism | Peripheral Venous Blood) \\ Peripheral Venous Blood)$

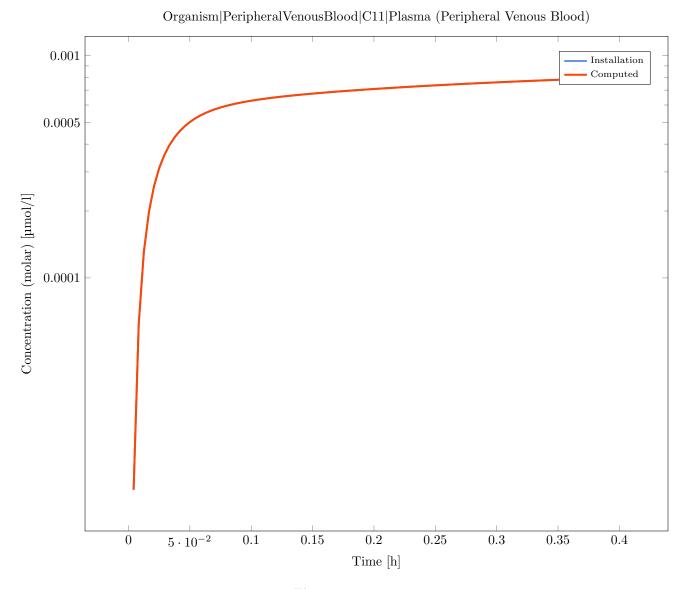


Figure 1.216

 $Simulation: Single ORAL_C11_4 Comp_standard_st$

Result of the validation: Valid

Organism|PeripheralVenousBlood|C11|Plasma (Peripheral Venous Blood)

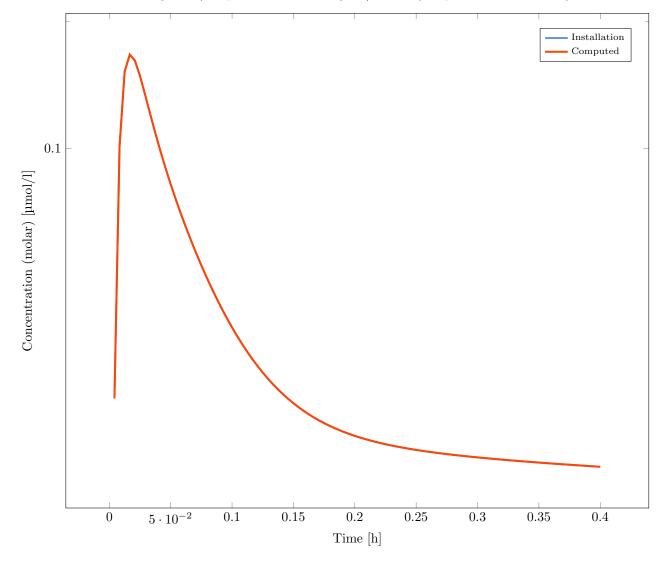


Figure 1.217

 $Simulation: Single ORAL_C12_4 Comp_standard_schmitt_standard-Single ORAL_C12_4 Comp_standard_schmitt_standard\\$

Result of the validation: Valid

 $Output \ Path: \ Organism | Peripheral Venous Blood | C12 | Plasma \ (Peripheral \ Venous \ Blood)$

Organism|PeripheralVenousBlood|C12|Plasma (Peripheral Venous Blood)

Figure 1.218

0.15

0.1

 $Simulation: Single ORAL_C13_2 Pores_schmitt_standard_st$

0.2

Time [h]

0.25

0.35

0.3

0.4

Result of the validation: Valid

0

 $5\cdot 10^{-2}$



Figure 1.219

 $Simulation: Single ORAL_C13_4 Comp_standard_schmittnormalized_schmittnormalized_sc$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |C13 |Plasma (Peripheral Venous Blood)
 Deviation: $\bf 0$





Figure 1.220

 $Simulation: Single ORAL_C14_2 Pores_PT_standard_standard_Single ORAL_C14_2 Pores_PT_standard_standar$ standard

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C14|Plasma (Peripheral Venous Blood)

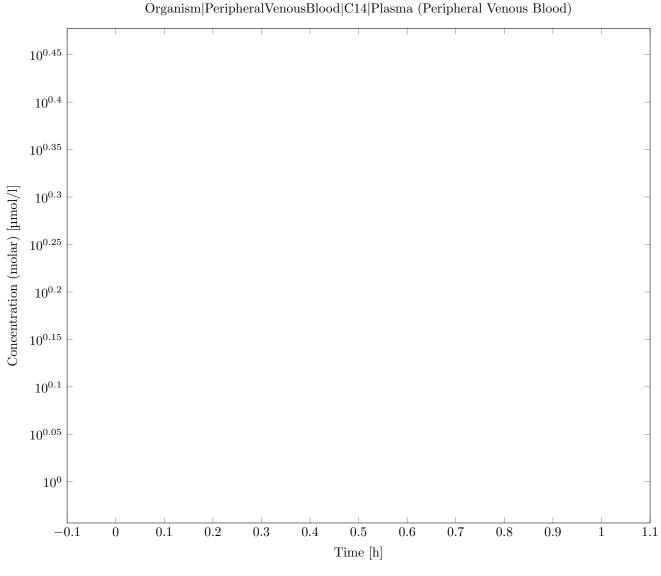
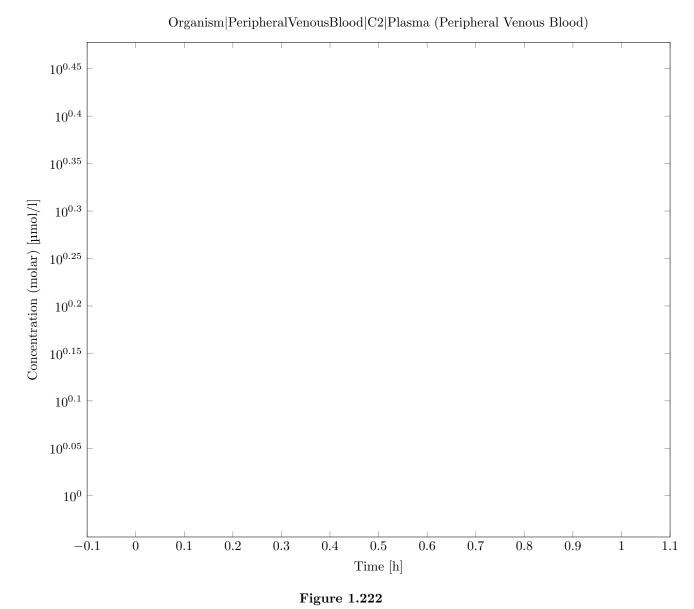


Figure 1.221

 $Simulation: Single ORAL_C2_2 Pores_standard_st$

Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood) Deviation:
 0



 $Simulation: Single ORAL_C3_2 Pores_standard_schmitt_standard-Single ORAL_C3_2 Pores_standard_schmitt_standard$

Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |C3 |Plasma (Peripheral Venous Blood) Deviation:
 0

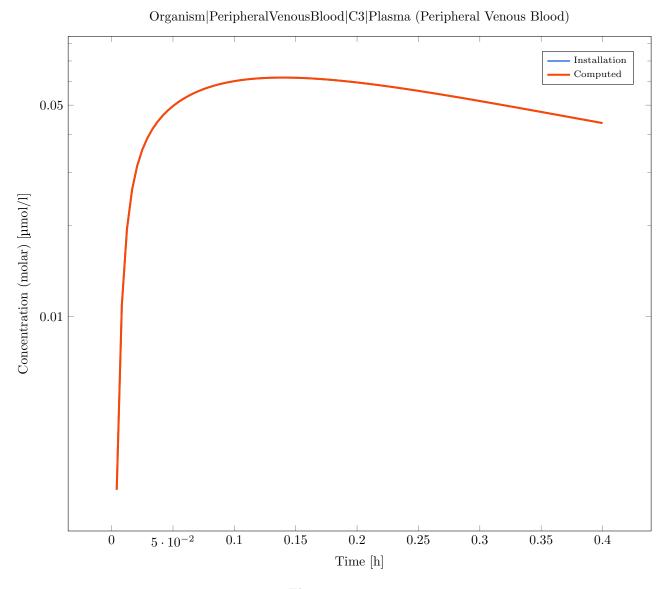


Figure 1.223

 $Simulation: Single ORAL_C4_2 Pores_standard_schmittnormalized_standard_Single ORAL_C4_2 Pores_standard_schmittnormalized_standard$

Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |C4 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

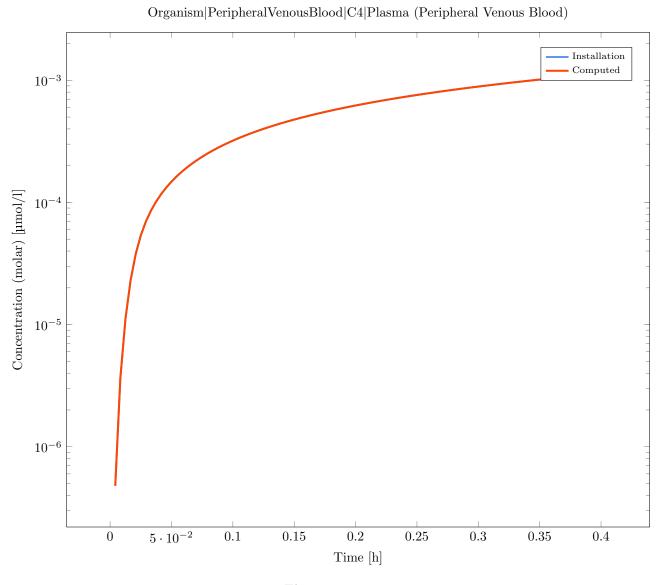


Figure 1.224

 $Simulation: Single ORAL_C6_4 Comp_Ber_standard_standard_Single ORAL_C6_4 Comp_Ber_standard_$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |C6 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$



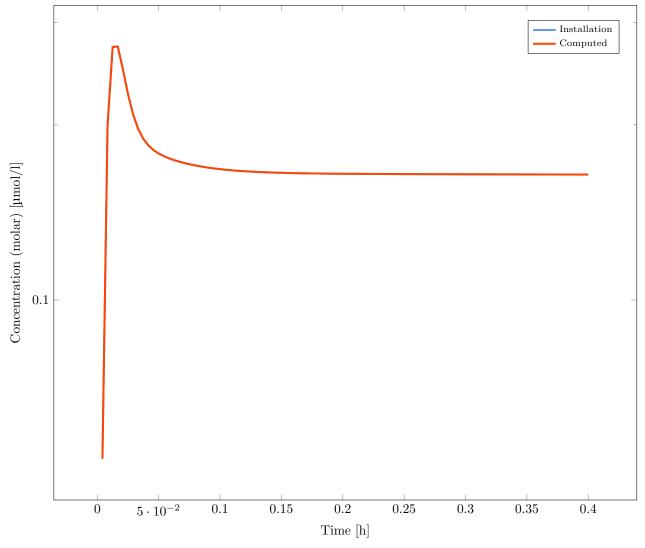


Figure 1.225

 $Simulation: Single ORAL_C6_4 Comp_RR_standard_standard_Single ORAL_C6_4 Comp_RR_standard_st$

Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|C6|Plasma\ (Peripheral\ Venous\ Blood)$

Figure 1.226

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single ORAL_C7_2 Pores_Ber_standard_standard_Single ORAL_C7_2 Pores_Ber_standard_standar$

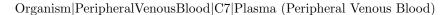
Result of the validation: Valid

0

 $5\cdot 10^{-2}$

0.1

0.15



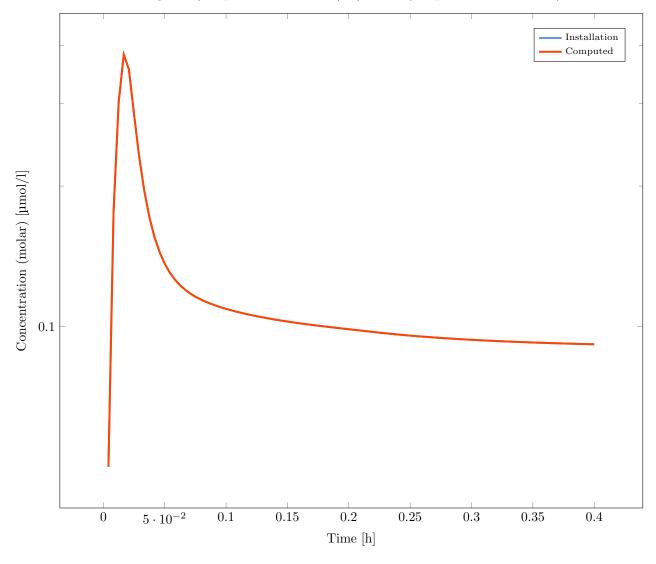


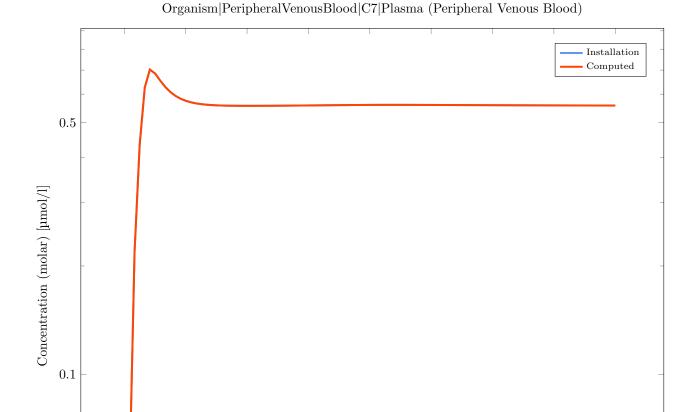
Figure 1.227

 $Simulation: Single ORAL_C7_4 Comp_RR_schmitt_standard-Single ORAL_C7_5 Comp_RR_schmitt_standard-Single ORAL_C7_5$

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C7|Plasma (Peripheral Venous Blood)

Deviation: 1.06E-7



Time [h] Figure 1.228

0.2

0.25

0.3

0.35

0.4

0.15

0.1

 $Simulation: Single ORAL_C8_2 Pores_RR_standard_standard_Single ORAL_C8_2 Pores_RR_standard_$ standard

Result of the validation: Valid

0

 $5\cdot 10^{-2}$

Output Path: Organism|PeripheralVenousBlood|C8|Plasma (Peripheral Venous Blood)

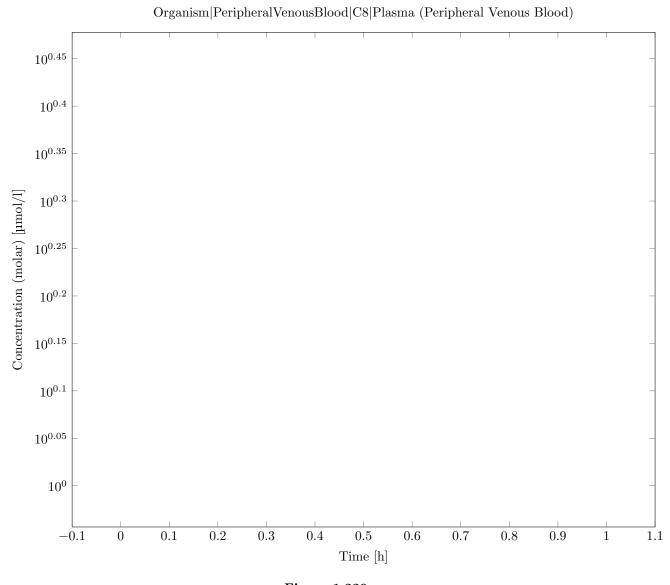
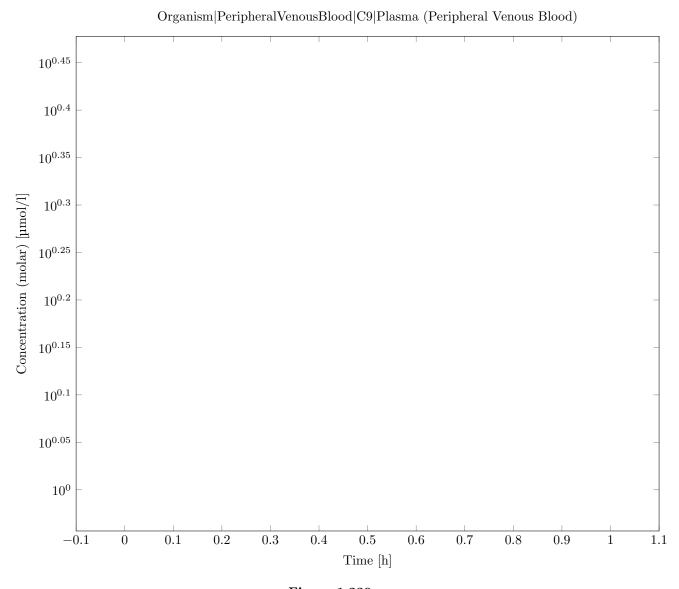


Figure 1.229

 $Simulation: Single ORAL_C9_2 Pores_RR_schmitt_standard-Single ORAL_SChmitt_standard-Single ORAL_SChmitt_standard-Single ORAL_Schmitt_Standard-Single ORAL_Schmitt_Standard-Single ORAL_Schmitt$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |C9 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$



 ${\bf Figure~1.230}$

 $Simulation: \ Test\ 18.1_I1_C1_A1_Config1-Test\ 18.1_I1_C1_A1_Config1$

Result of the validation: Valid



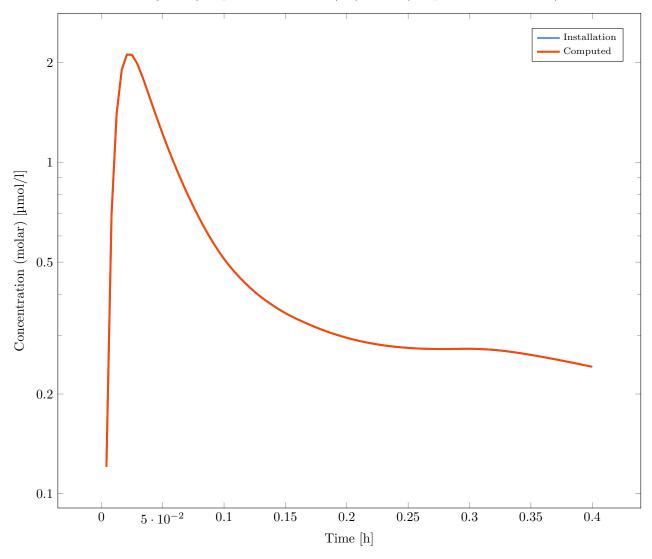
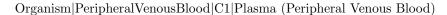


Figure 1.231

Simulation: Test 18.1_I2_C1_A1_Config2-Test 18.1_I2_C1_A1_Config2

Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$



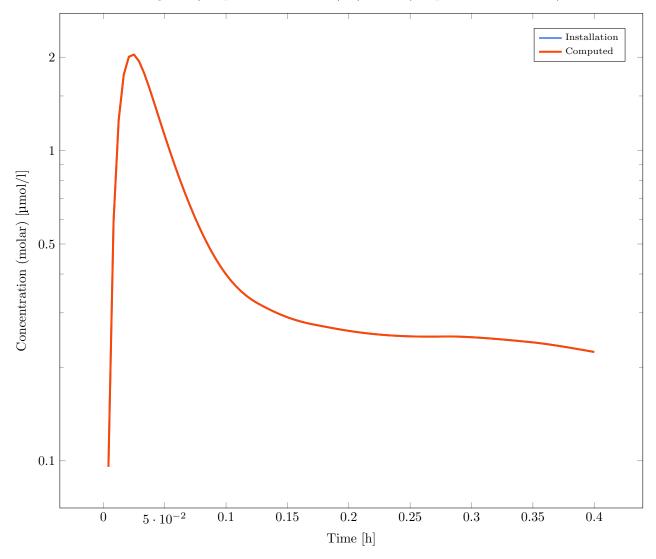


Figure 1.232

Simulation: Test 18.1_I2_C3_A1_Config2-Test 18.1_I2_C3_A1_Config2 Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C3|Plasma (Peripheral Venous Blood)

5

1

0

 $5\cdot 10^{-2}$

Installation 20 Computed 10 Concentration (molar) [µmol/1]

Organism|PeripheralVenousBlood|C3|Plasma (Peripheral Venous Blood)

Figure 1.233

0.2

Time [h]

0.25

0.3

0.35

0.4

Simulation: Test 18.1_I3_C3_A3_Config2-Test 18.1_I3_C3_A3_Config2

0.1

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C3|Plasma (Peripheral Venous Blood) Deviation: 0

0.15

$Organism|Peripheral Venous Blood|C3|Plasma\ (Peripheral Venous Blood)$

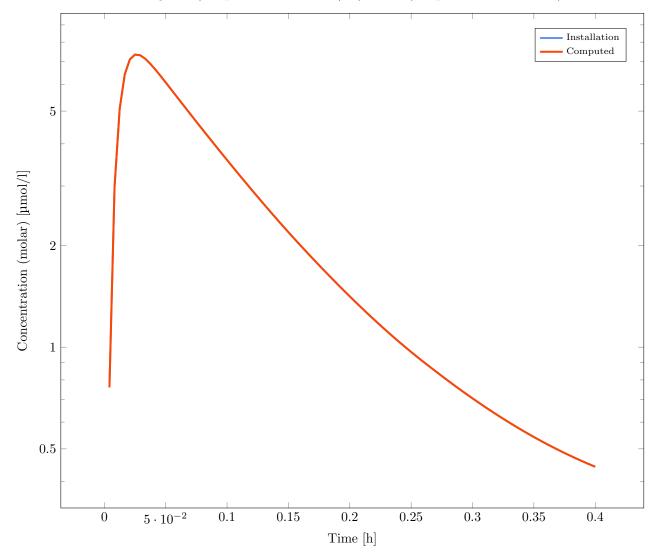


Figure 1.234