Open Systems Pharmacology Suite - 9 Installation Validation

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Chapter 1

Installation Validation Results

Overall Validation Result

Valid

1.1 Validation Summary

Run Duration

Start time: $2020-07-22\ 00:05$ End time: $2020-07-22\ 00:24$

Validation performed in 18m:32s:364ms

Input Configuration Folder

 $C: \label{lem:condition} C: \label{lem:condition} Paramacology \label{lem:condition} Inputs \label{lem:condition} BatchFiles$

Local Outputs Location

Application Versions

PK-Sim Version 9.1.2 MoBi Version 9.1.1

Computer Name

BY1056

Operating System

Windows Server 2016 Standard

Architecture

x64

Running on Virtual Machine

No

Running on Terminal Session

Yes

1.2 Comparison Results

Overall Comparison Result

Valid

Installation Folder

C:\ProgramData\Open Systems Pharmacology\InstallationValidator\9.1\Outputs\BatchFiles

Computed Folder

C:\Users\gibpk\AppData\Roaming\Open Systems Pharmacology\InstallationValidator\9.1\Outputs

1.2.1 Valid Simulations (148/148)

$Simulation: \ Beagle_SingleORAL_Dissolved-Beagle_SingleORAL_Dissolved$

Result of the validation: Valid

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

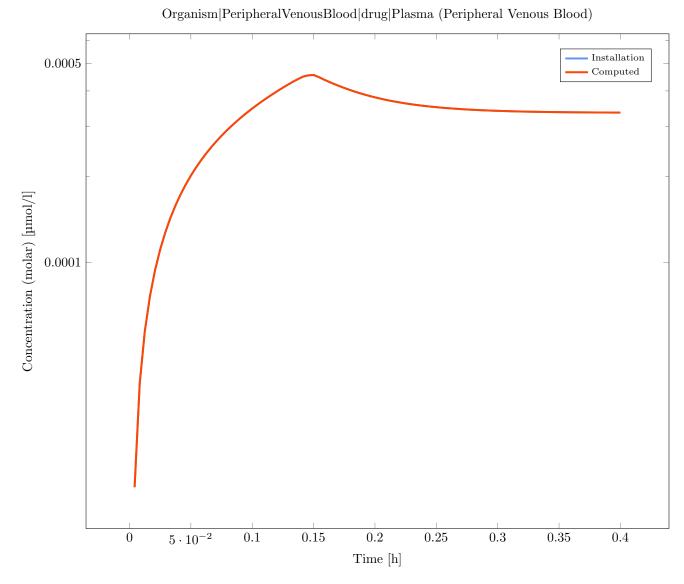


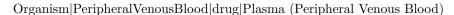
Figure 1.1

 $Simulation: Beagle_SingleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-$

Result of the validation: Valid

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

Deviation: 0



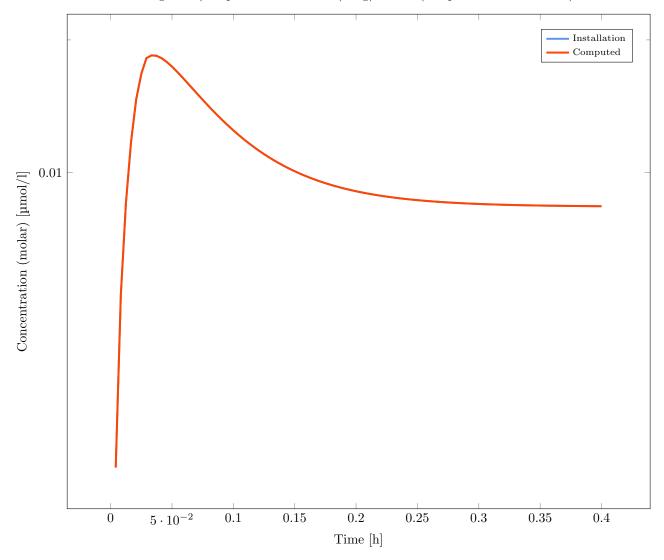


Figure 1.2

 $Simulation: Beagle_SingleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-5$

Result of the validation: Valid

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

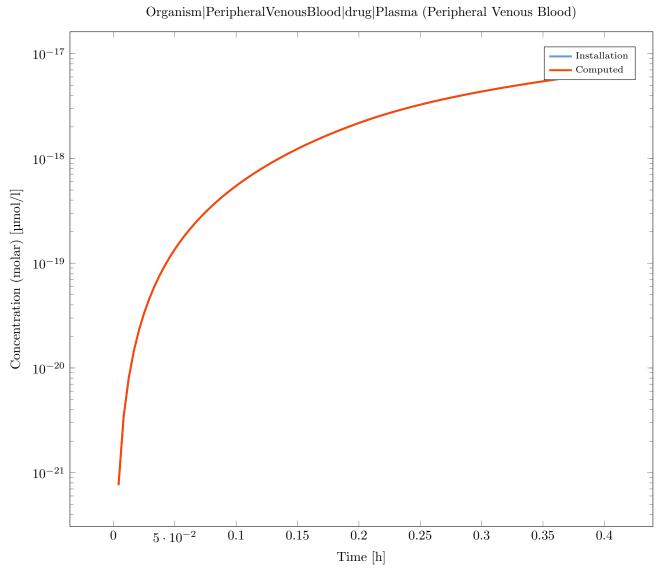
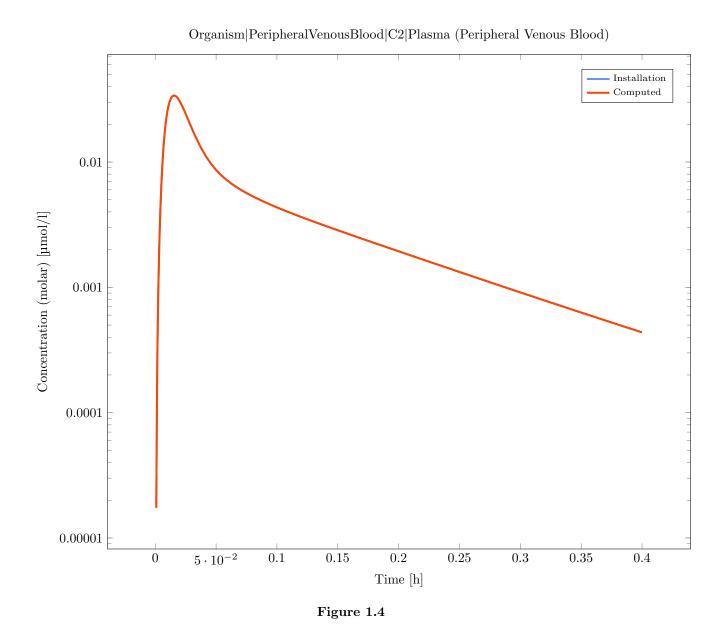


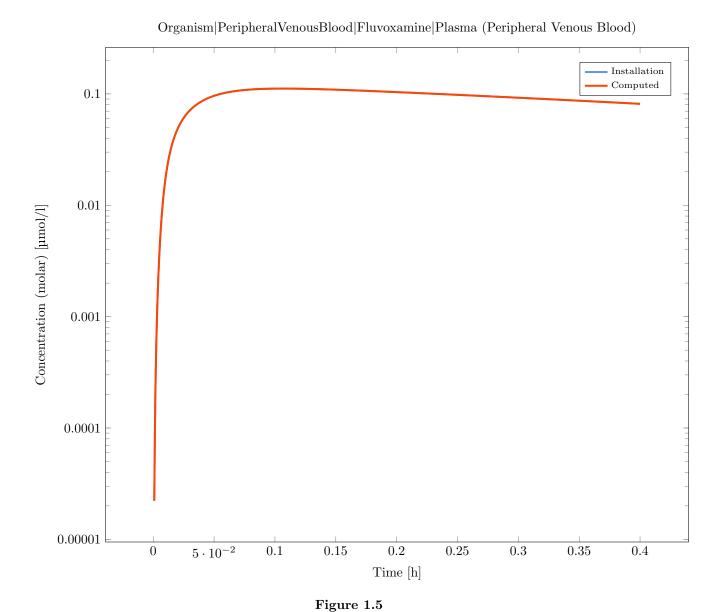
Figure 1.3

 ${\bf Simulation:\ DDI_Multiple Combinations-01_MM_Competitive_Competitive_Result\ of\ the\ validation:\ Valid}$

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



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



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

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

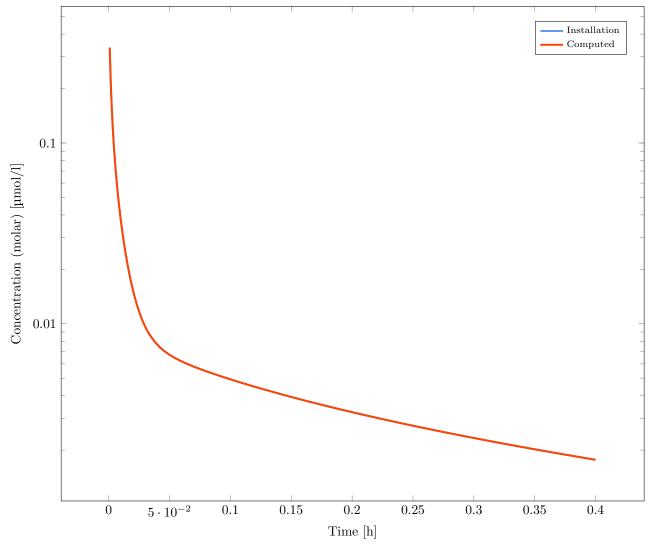
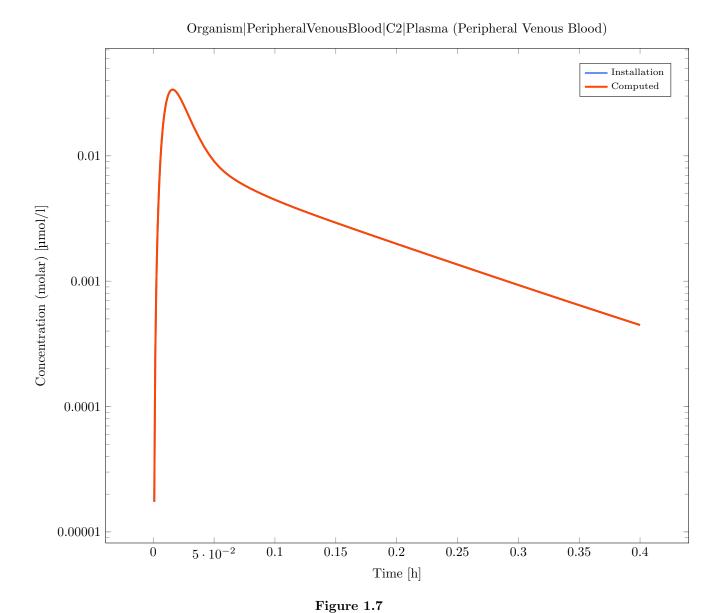


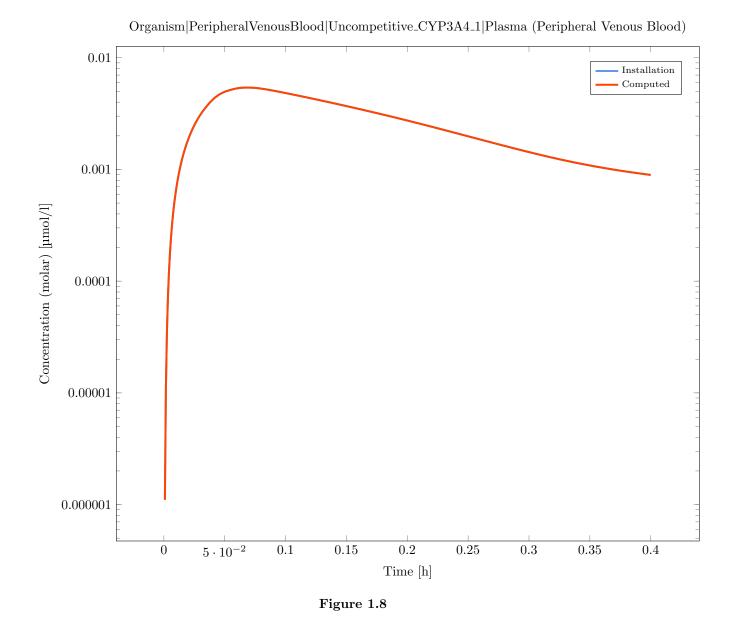
Figure 1.6

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

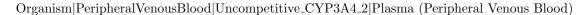
Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood) Deviation:
 $\mathbf 0$



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



Output Path: Organism |PeripheralVenousBlood |Uncompetitive_CYP3A4_2 |Plasma (Peripheral Venous Blood) | Deviation: 0



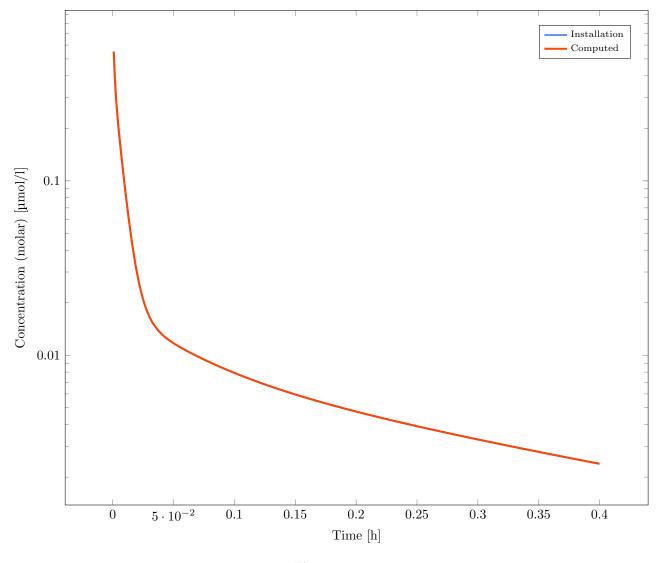


Figure 1.9

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

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

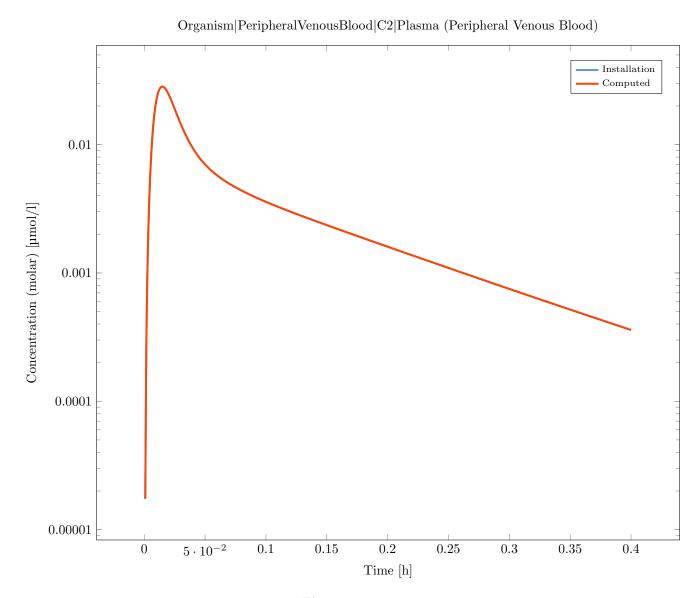


Figure 1.10

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

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

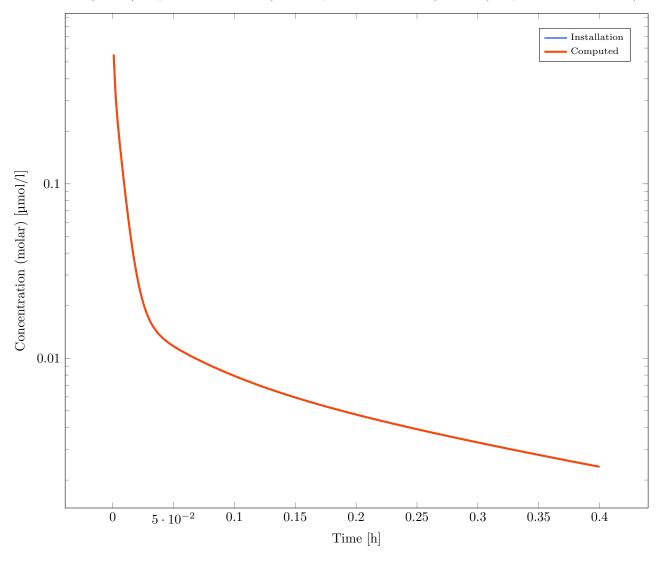


Figure 1.11

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

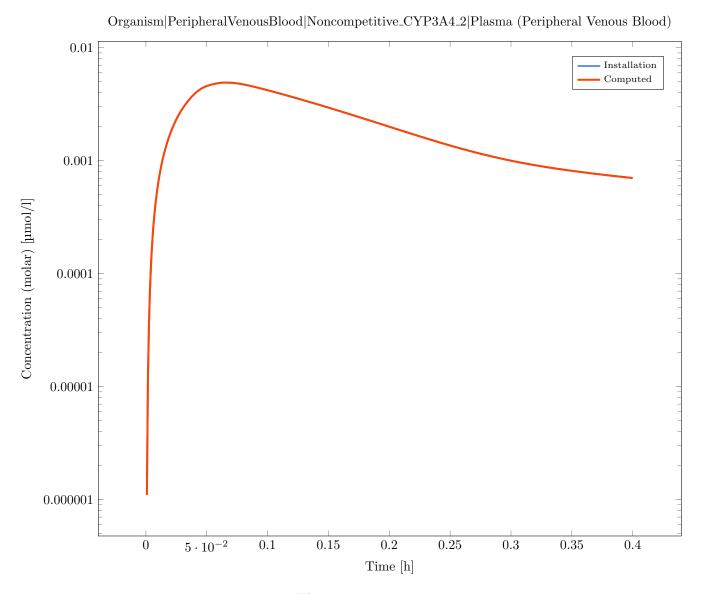
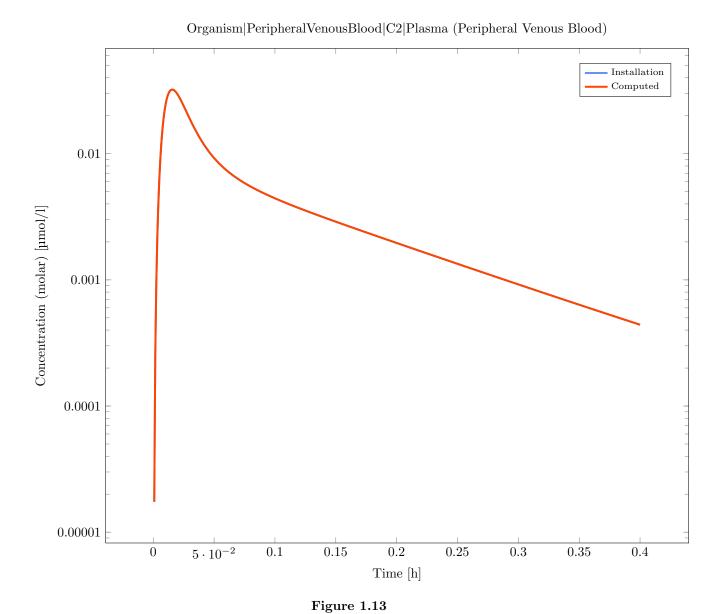


Figure 1.12

 $Simulation: DDI_MultipleCombinations-04_MM_Mixed_Mixed$

Result of the validation: Valid

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



Output Path: Organism |PeripheralVenousBlood |Mixed_CYP3A4_1 |Plasma (Peripheral VenousBlood)
 Deviation: 0

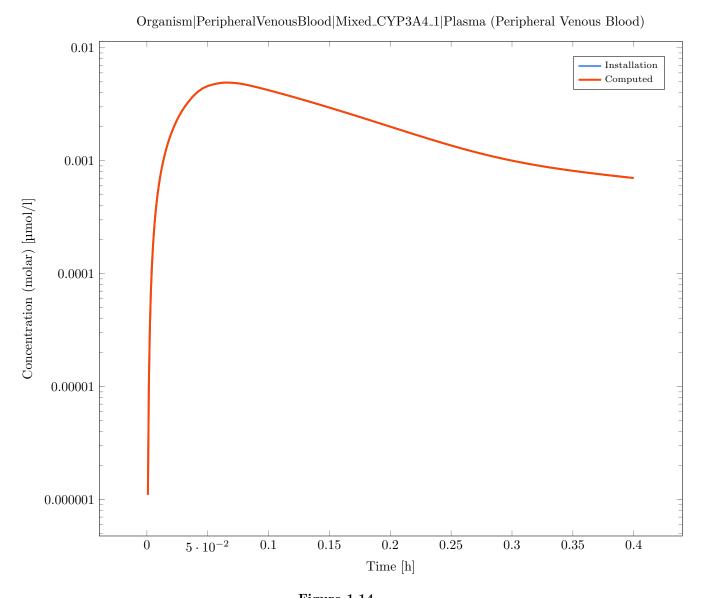
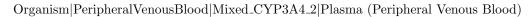


Figure 1.14

Output Path: Organism |PeripheralVenousBlood |Mixed_CYP3A4_2 |Plasma (Peripheral VenousBlood)
 Deviation: 0



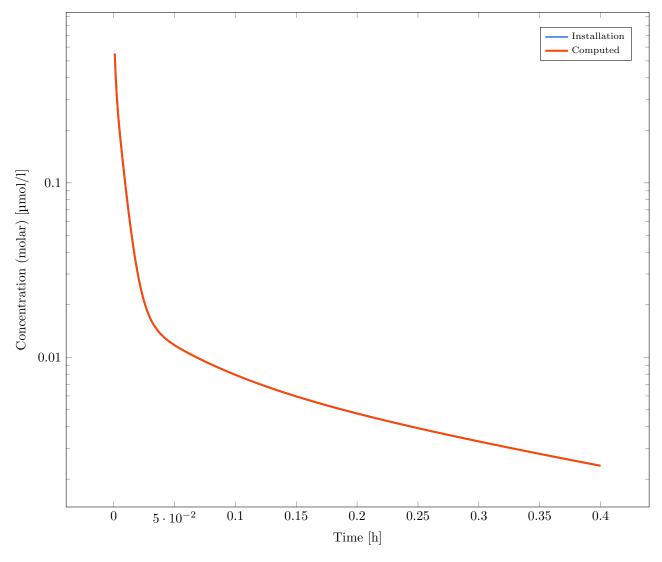
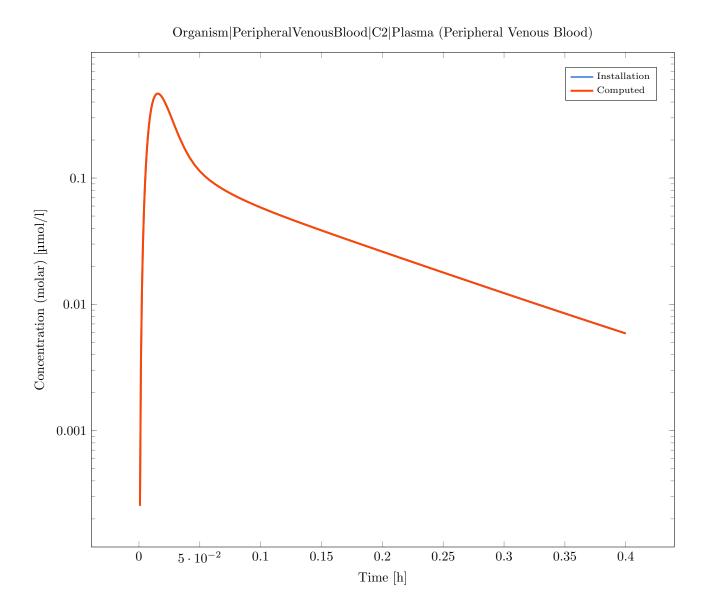


Figure 1.15

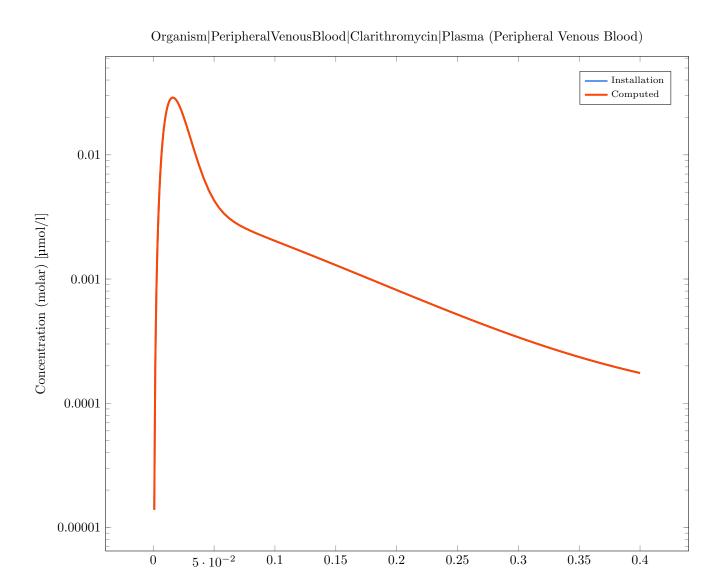
Simulation: DDI_MultipleCombinations-05_MM_Mechanismbased_Mechanismbased Result of the validation: Valid

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



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

Figure 1.16



Deviation: 0

Time [h]

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

Figure 1.17

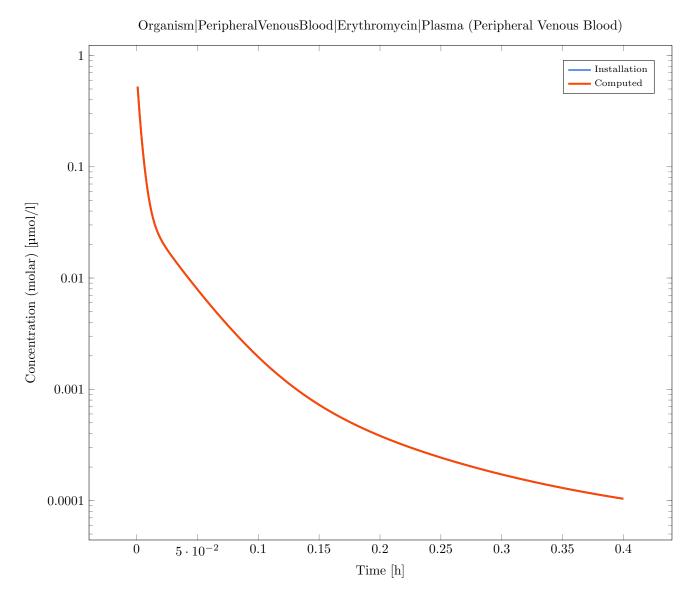
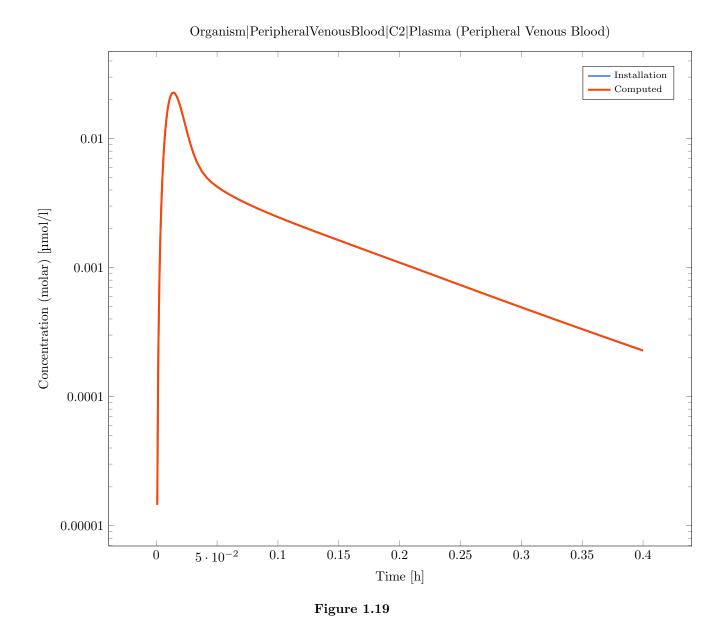


Figure 1.18

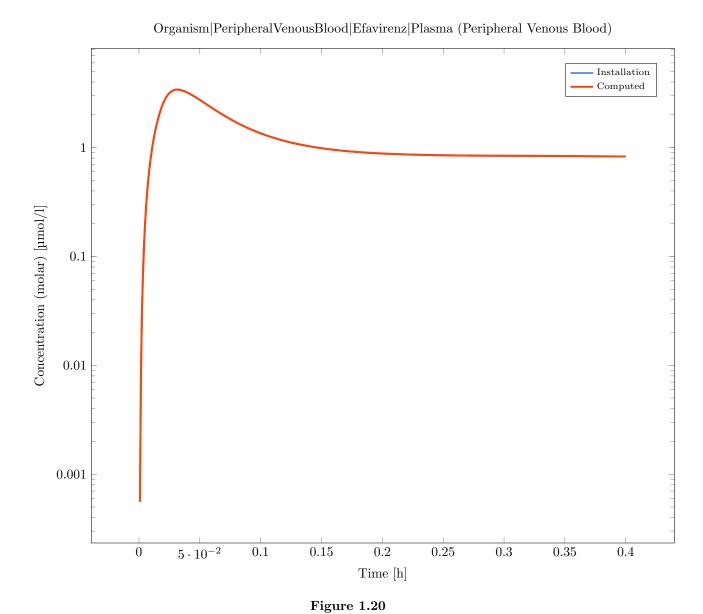
 ${\bf Simulation:\ DDI_Multiple Combinations-06_MM_Induction_Induction}$

Result of the validation: Valid

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



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



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

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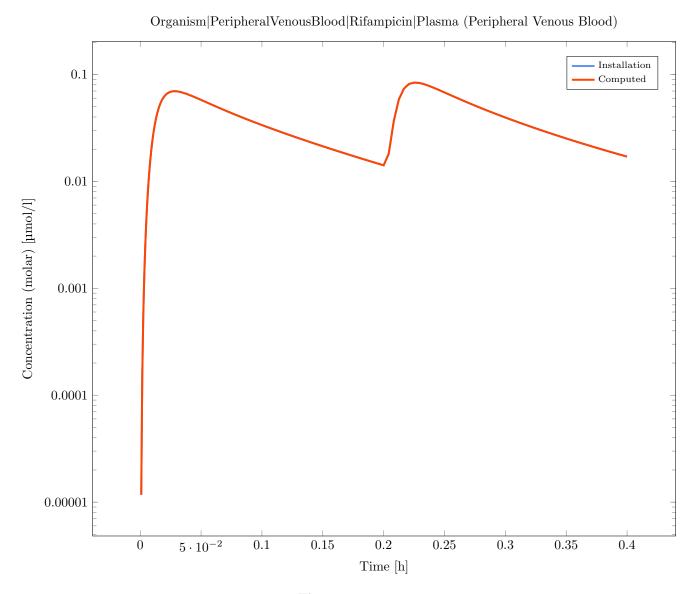
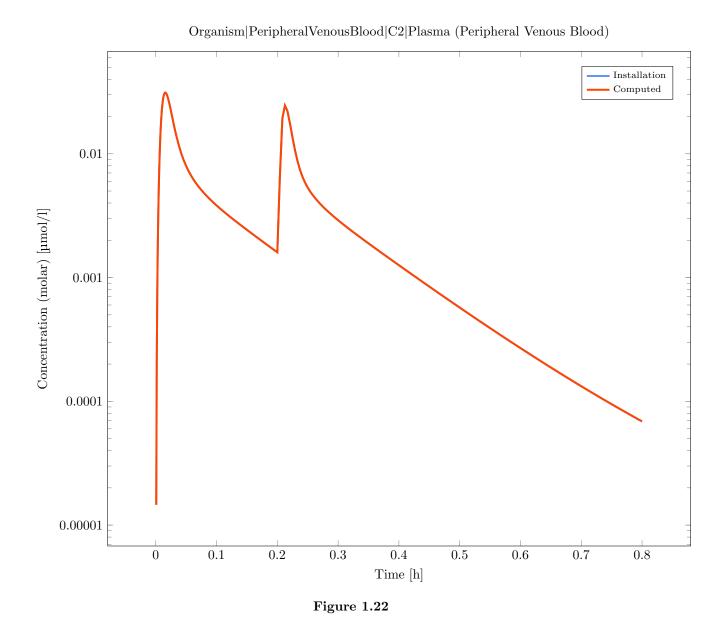


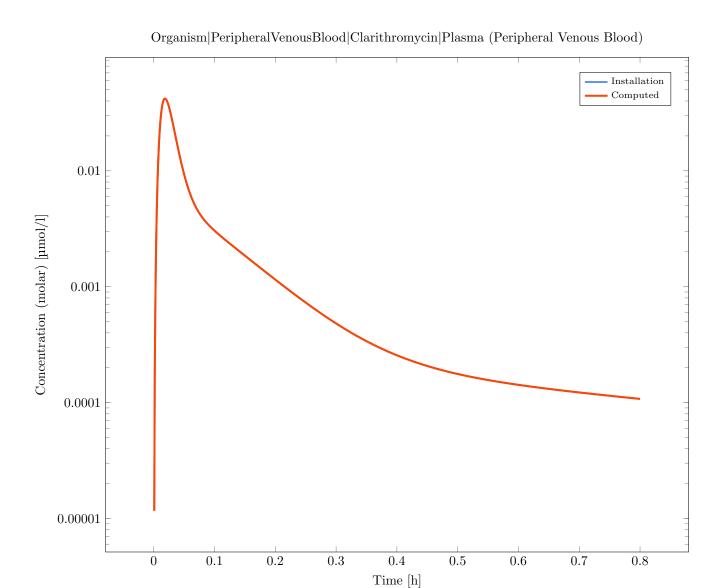
Figure 1.21

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: 0

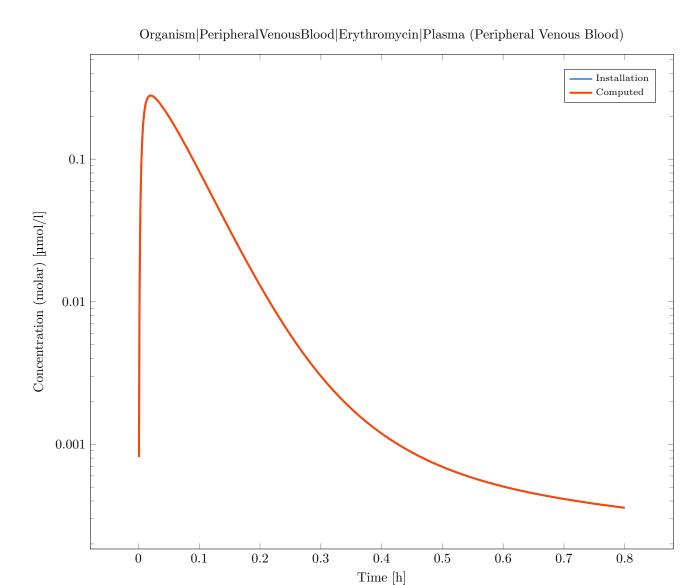


Output Path: Organism |Peripheral Venous
Blood |Clarithromycin |Plasma (Peripheral Venous Blood)
 Deviation: $\boldsymbol{0}$



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

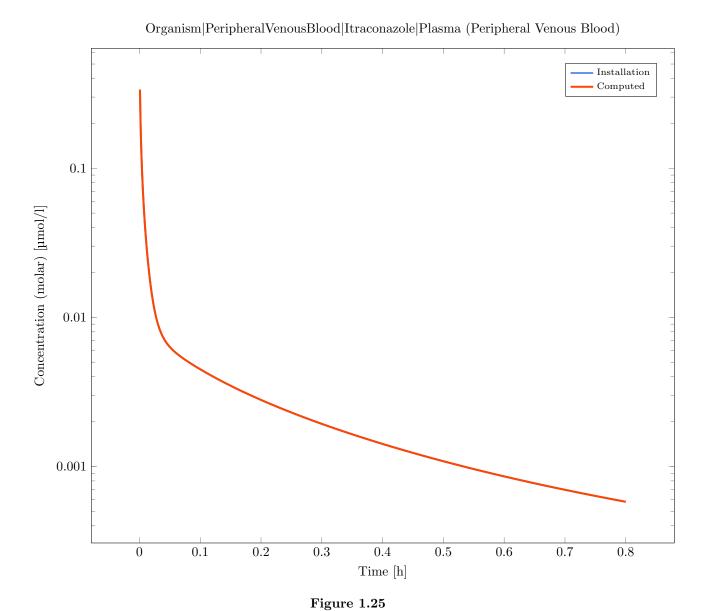
Figure 1.23



Deviation: 0

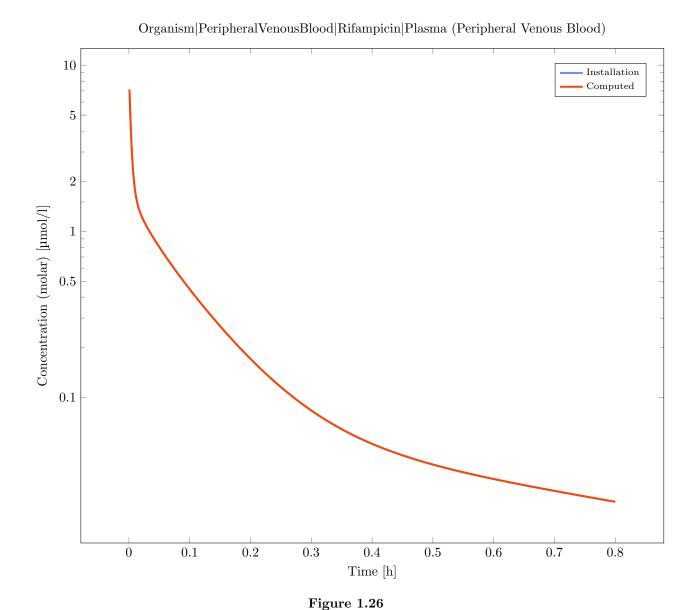
Figure 1.24

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



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

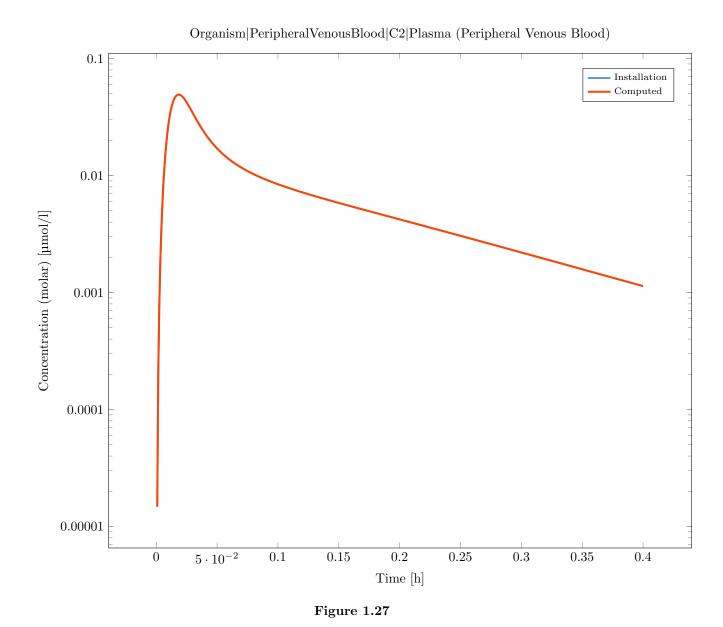
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 $Simulation: \ DDI_Multiple Combinations - 08_MM_Uncompetitive_Uncompetitive_Mechanism based_Mechanism based$

Result of the validation: Valid

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



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

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

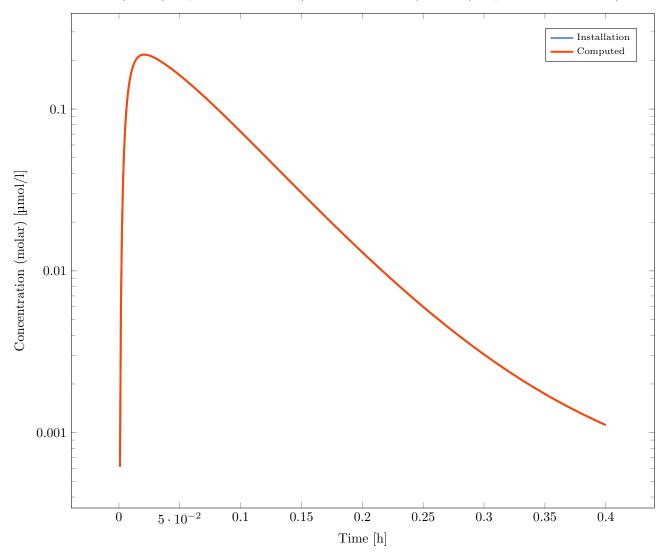
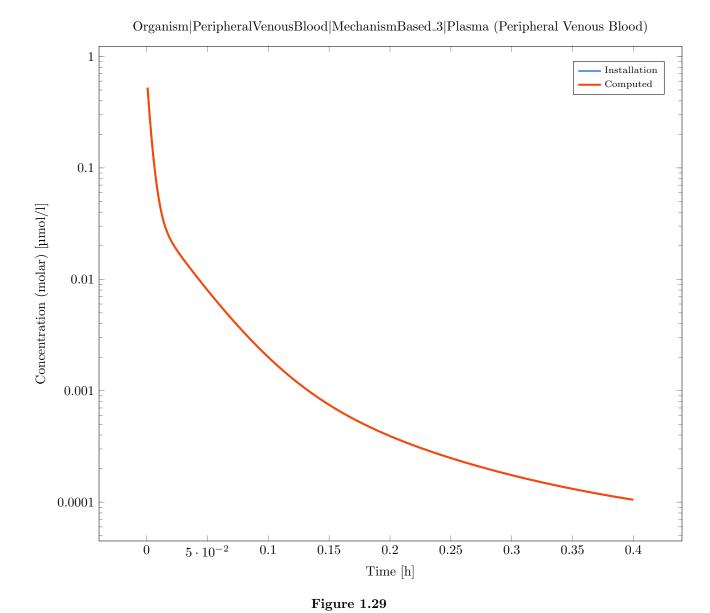
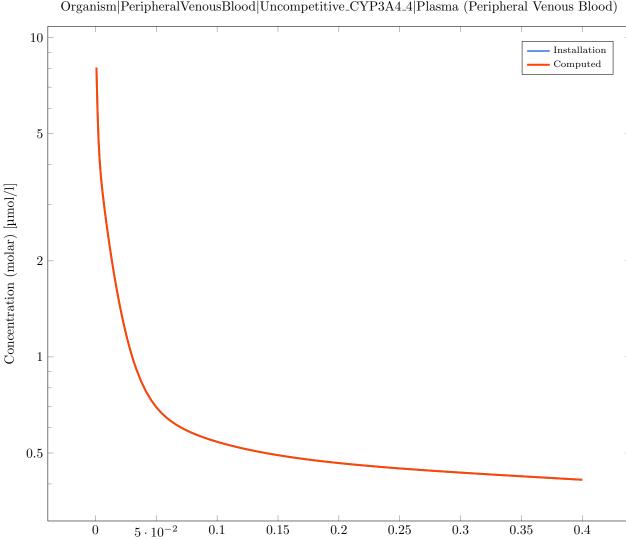


Figure 1.28

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



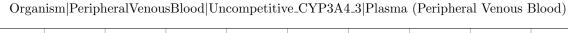


Organism|PeripheralVenousBlood|Uncompetitive_CYP3A4_4|Plasma (Peripheral Venous Blood)

Figure 1.30

Time [h]

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



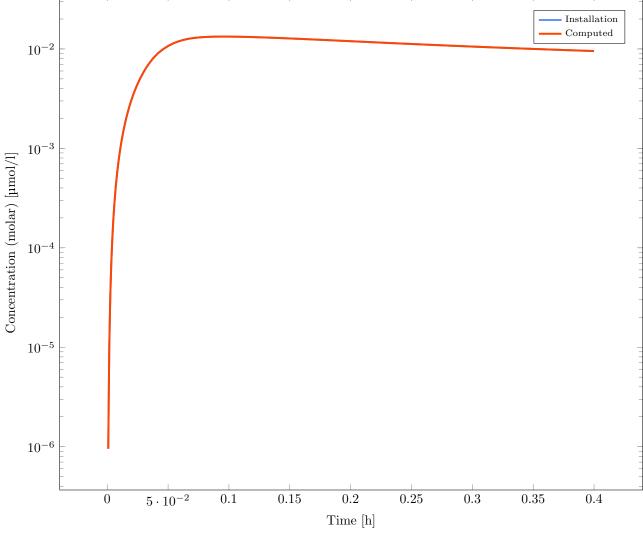
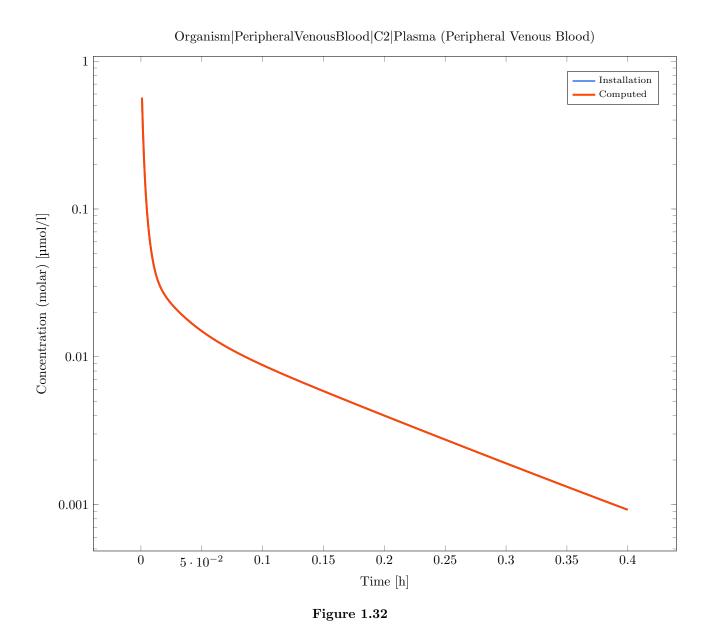


Figure 1.31

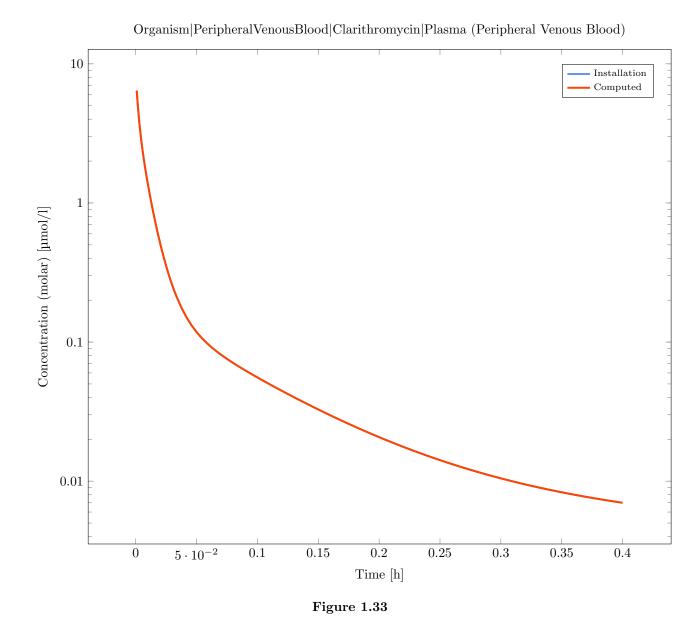
 $Simulation: \ DDI_Multiple Combinations - 09_MM_Noncompetitive_Noncompetitive_Mechanism based_Mechanism based$

Result of the validation: Valid

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



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



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

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

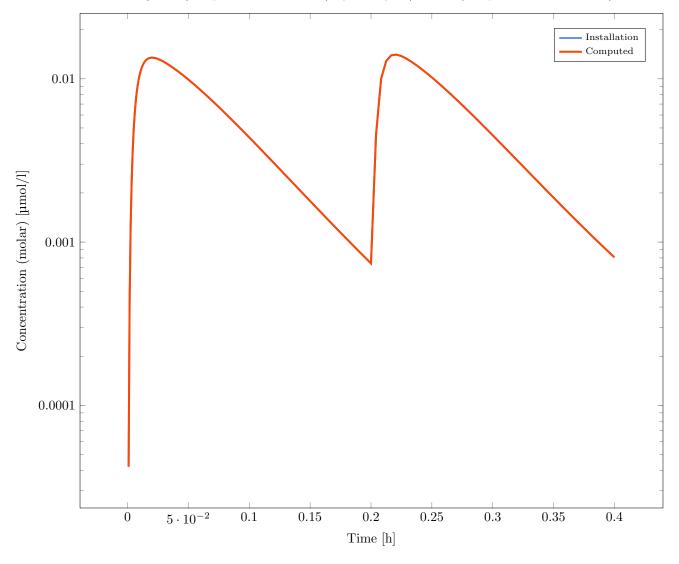


Figure 1.34

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

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

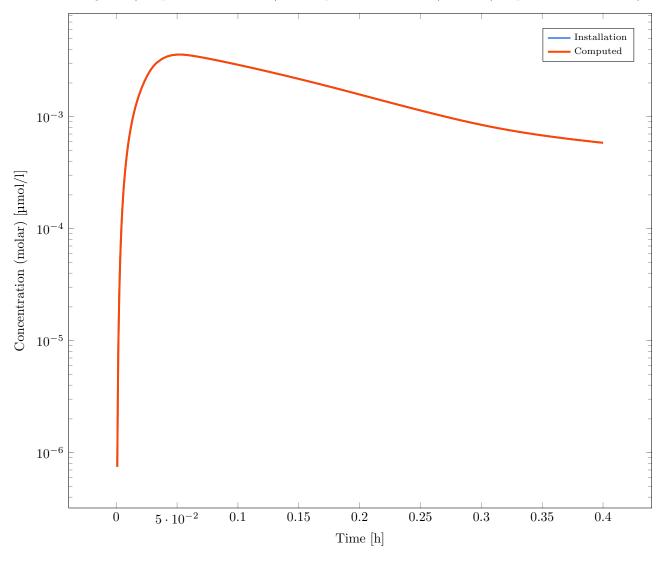


Figure 1.35

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

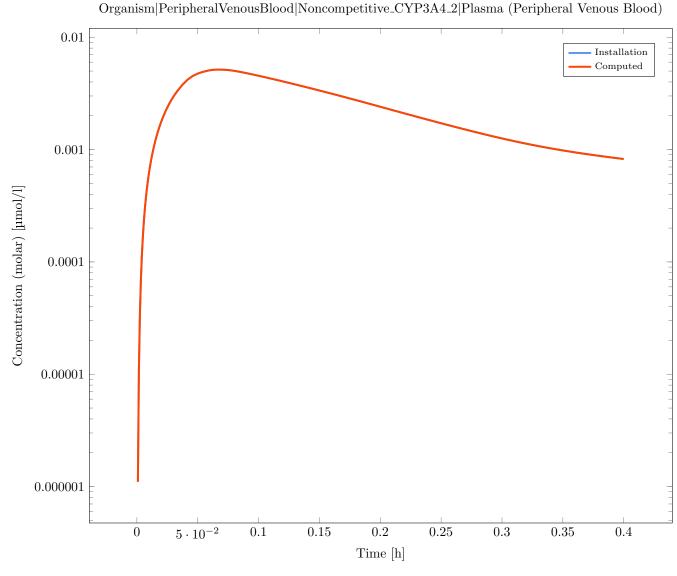
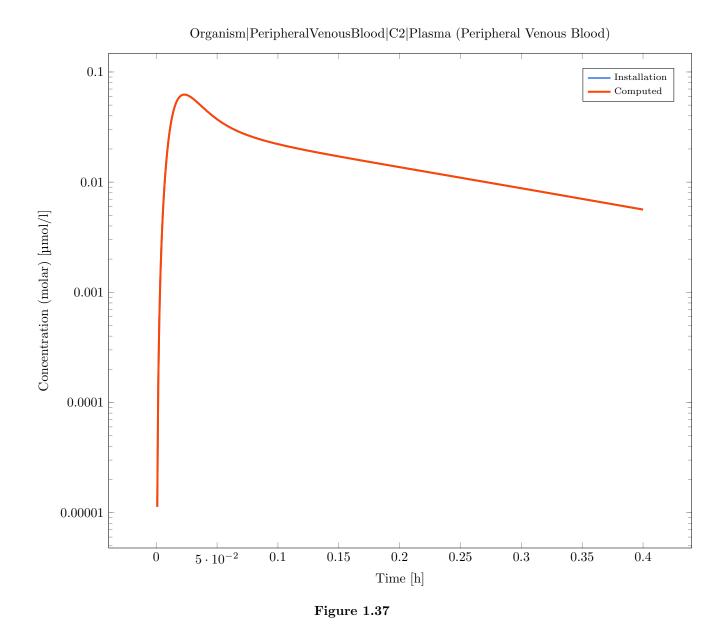


Figure 1.36

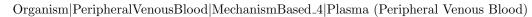
 ${\bf Simulation:\ DDI_Multiple Combinations-10_MM_Mixed_Mixed_Mechanismbased_Mech$

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



Output Path: Organism |PeripheralVenousBlood |MechanismBased_4 |Plasma (Peripheral VenousBlood)
 Deviation: 0

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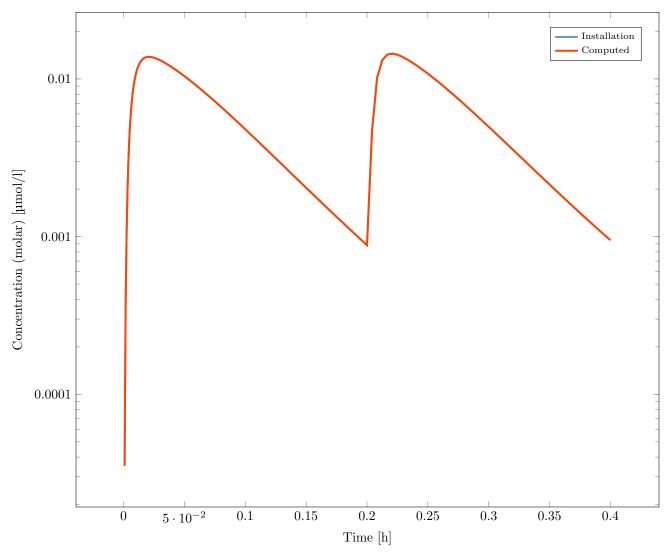


Figure 1.38

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

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

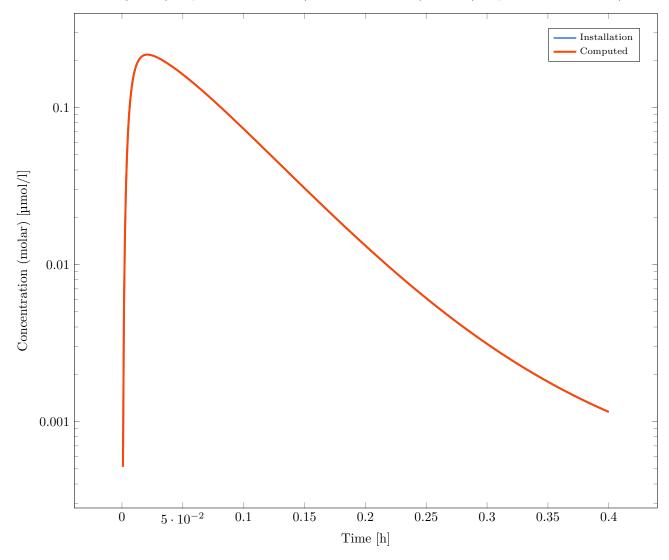
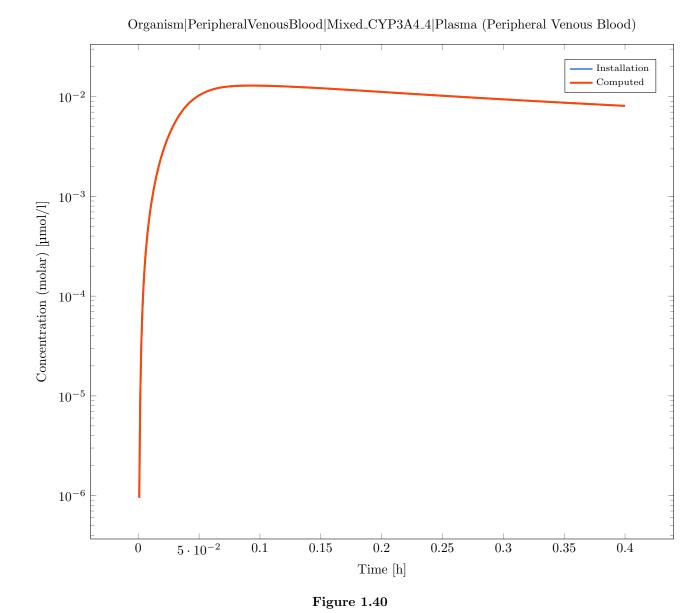


Figure 1.39

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



Output Path: Organism |PeripheralVenousBlood |Mixed_CYP3A4_3 |Plasma (Peripheral VenousBlood)
 Deviation: 0

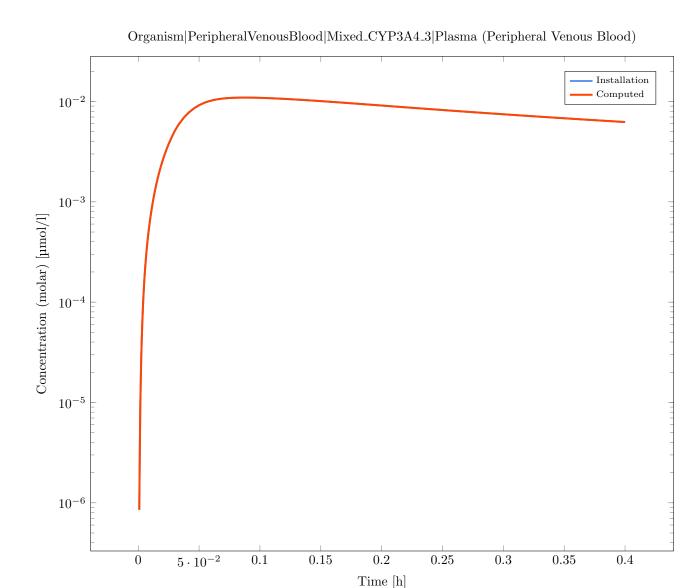
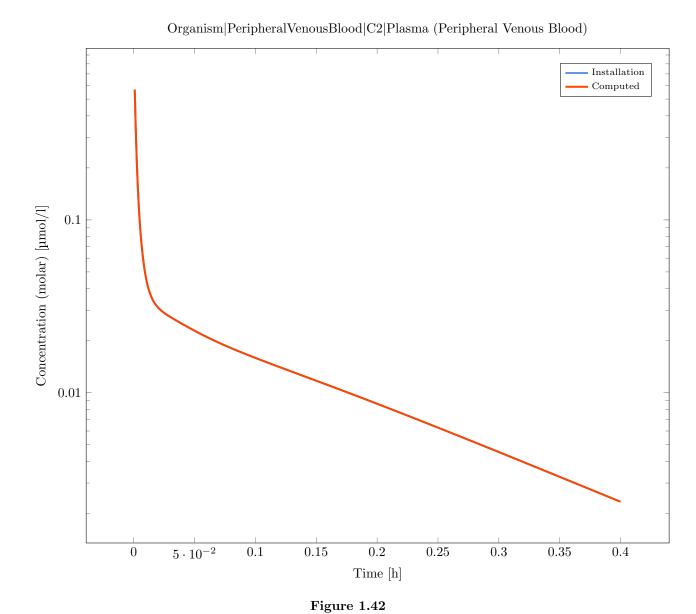


Figure 1.41

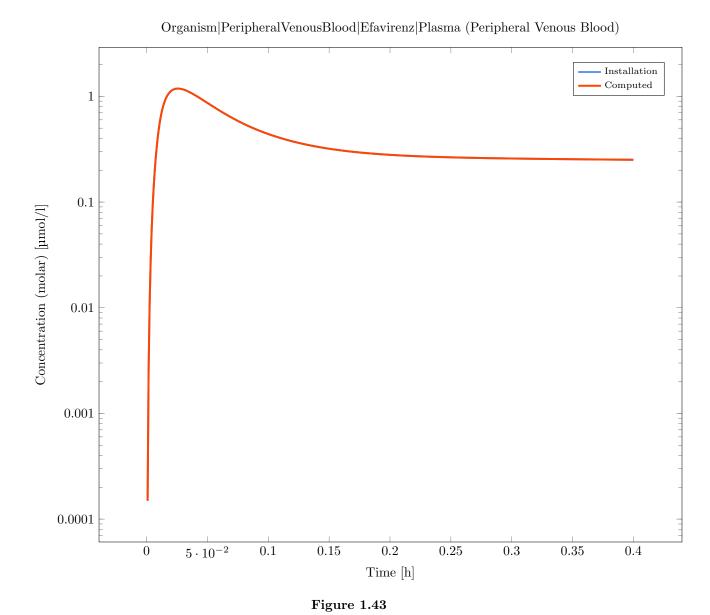
 $Simulation: \begin{tabular}{ll} DDI_Multiple Combinations-11_MM_Mechanism based_Mechanism based_Induction_Induction \end{tabular}$

Result of the validation: Valid

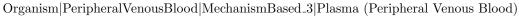
Output Path: Organism |PeripheralVenousBlood |C2|Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$



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



Output Path: Organism |PeripheralVenousBlood |MechanismBased_3 |Plasma (Peripheral VenousBlood)
 Deviation: 0



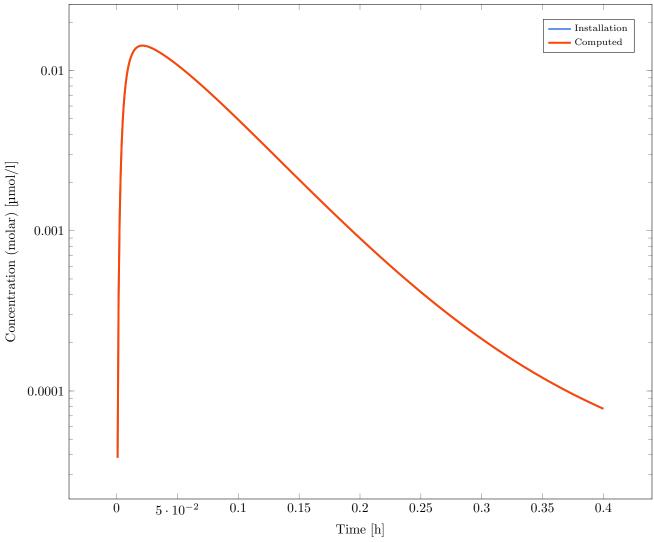


Figure 1.44

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



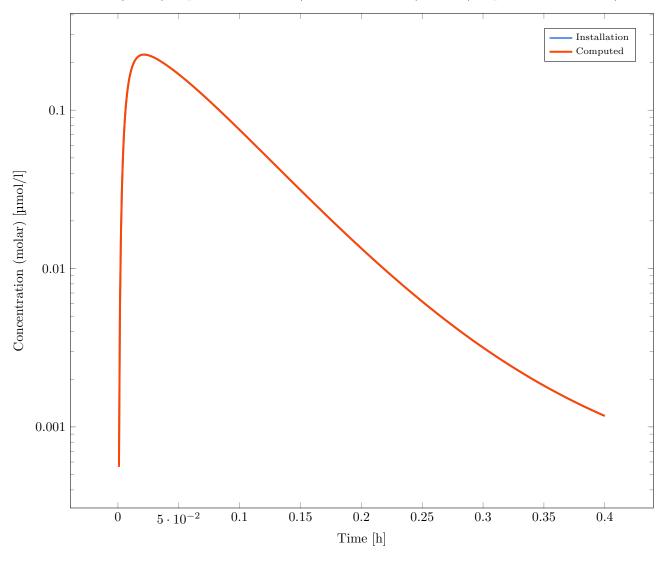


Figure 1.45

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

Organism|PeripheralVenousBlood|Rifampicin|Plasma (Peripheral Venous Blood) Installa Compt

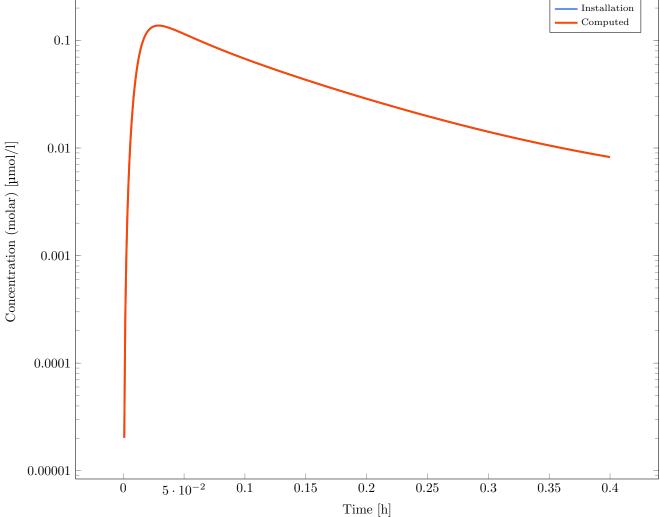
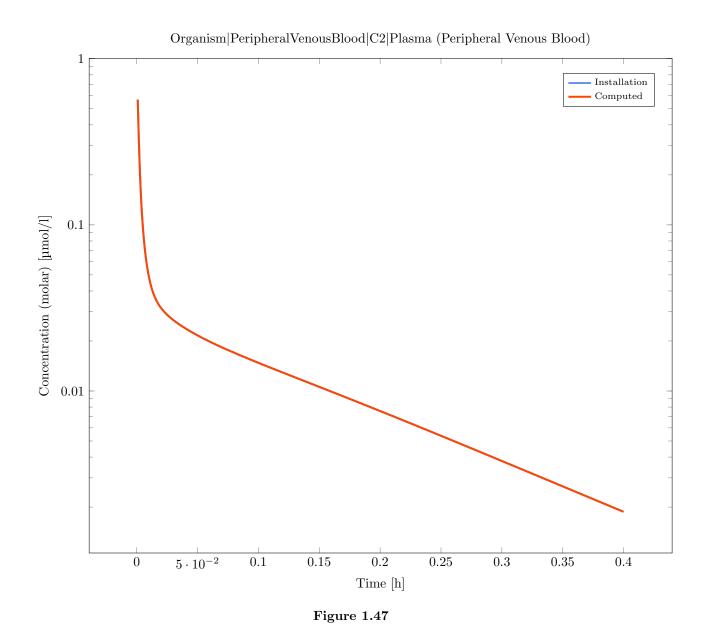


Figure 1.46

 $Simulation: \ DDI_MultipleCombinations-12_MM_All_DDI_Types$

Result of the validation: Valid

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



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

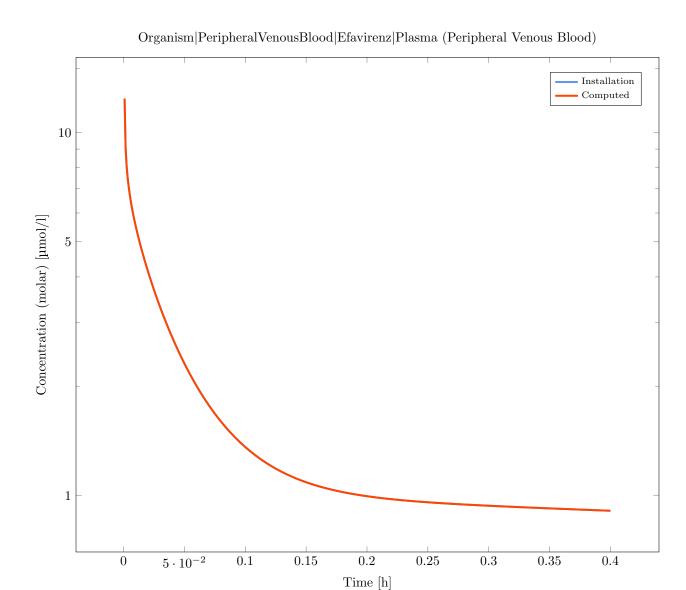
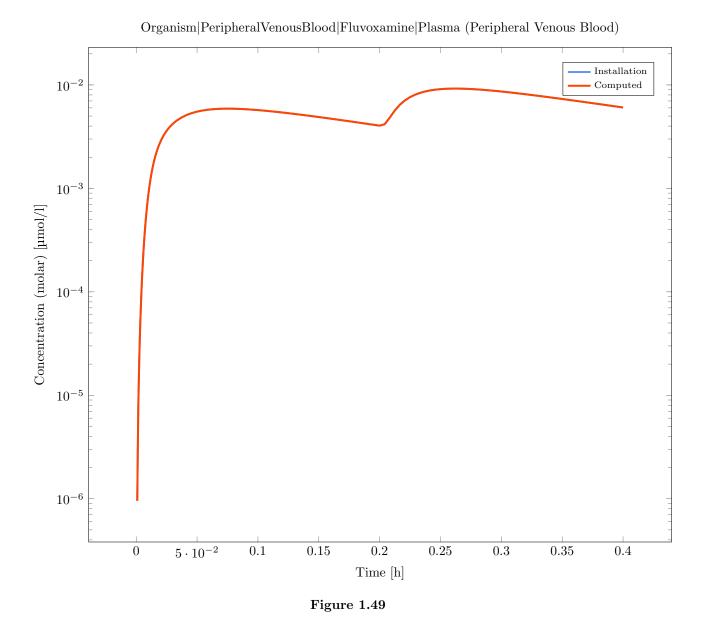
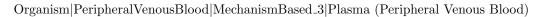


Figure 1.48

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



Output Path: Organism |PeripheralVenousBlood |MechanismBased_3 |Plasma (Peripheral VenousBlood)
 Deviation: 0



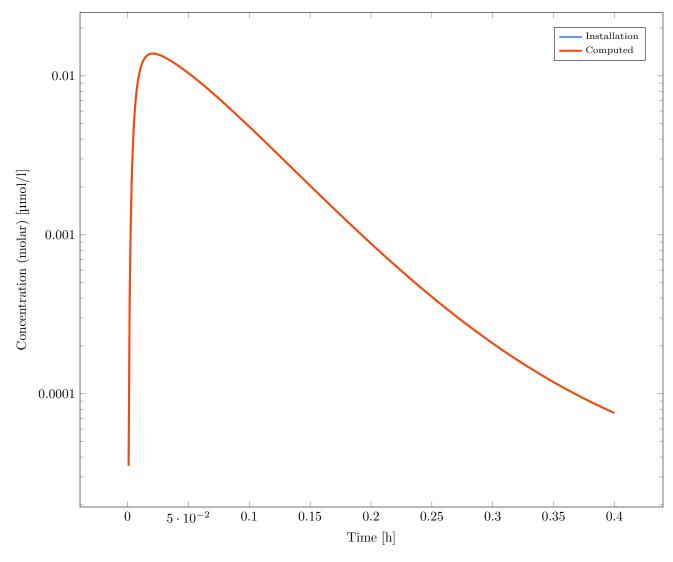


Figure 1.50

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

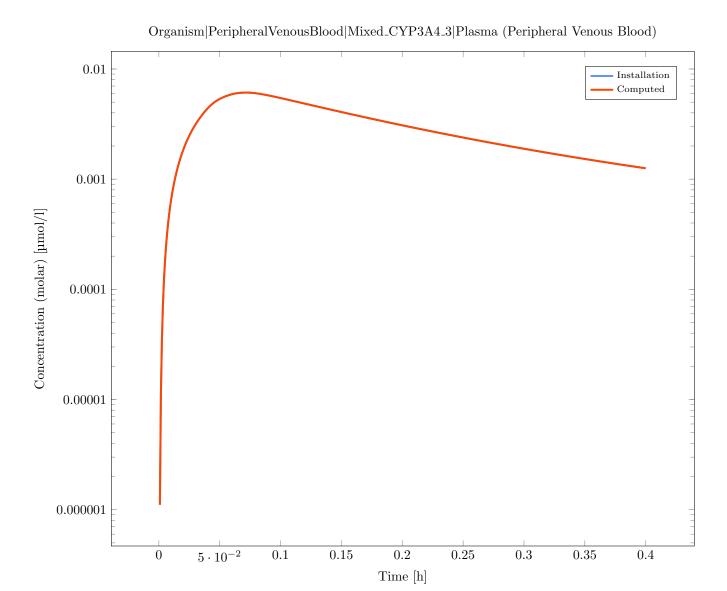
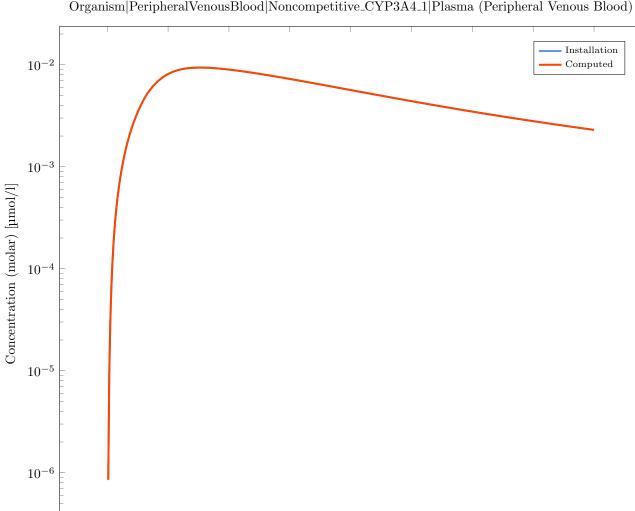


Figure 1.51

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



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

Figure 1.52

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: 0

0

 $5 \cdot 10^{-2}$

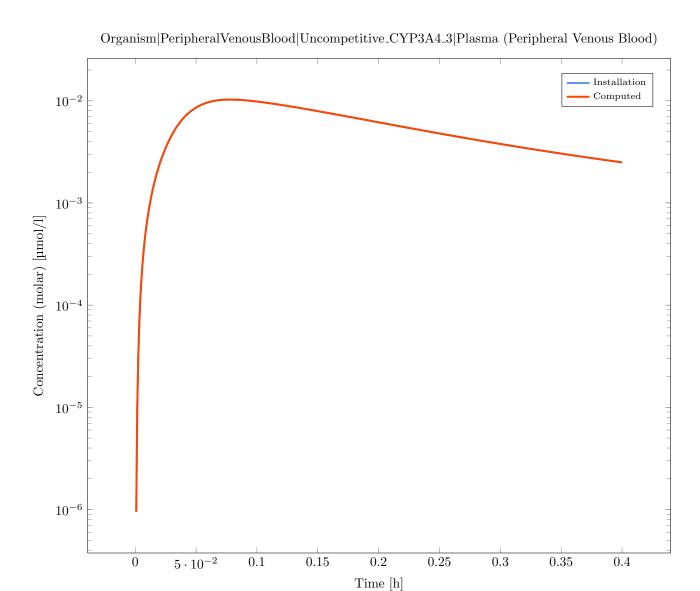
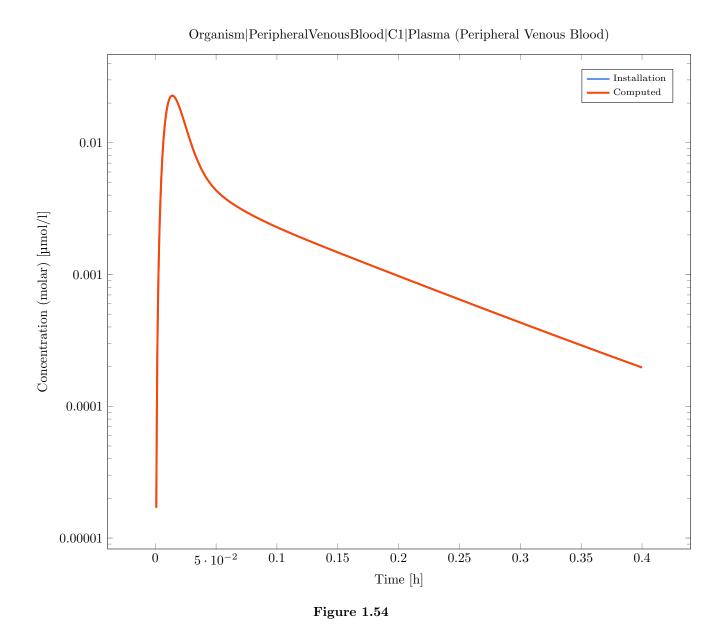


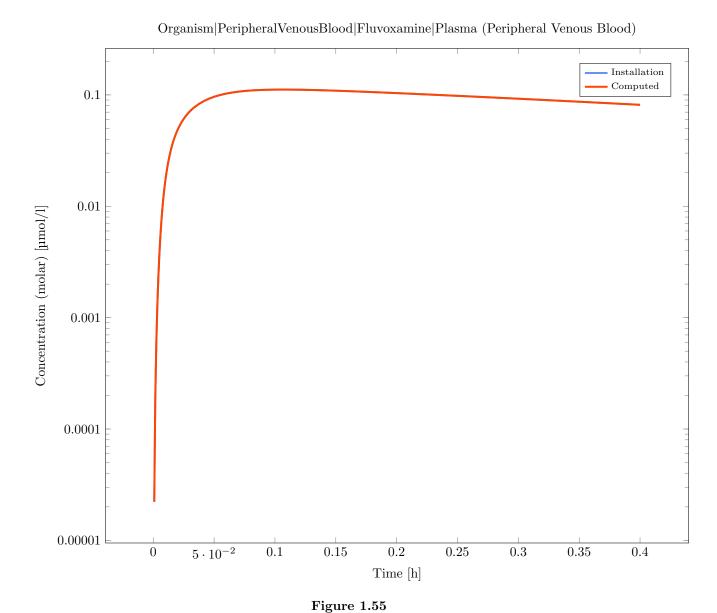
Figure 1.53

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

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



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



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

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: 0

0

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

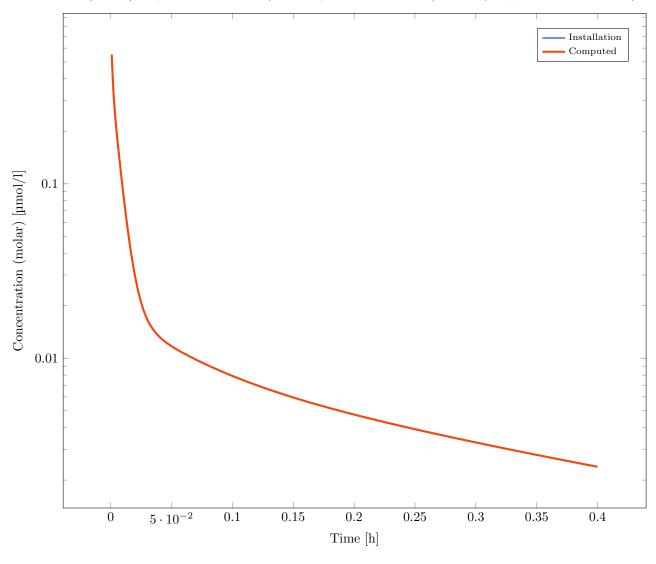
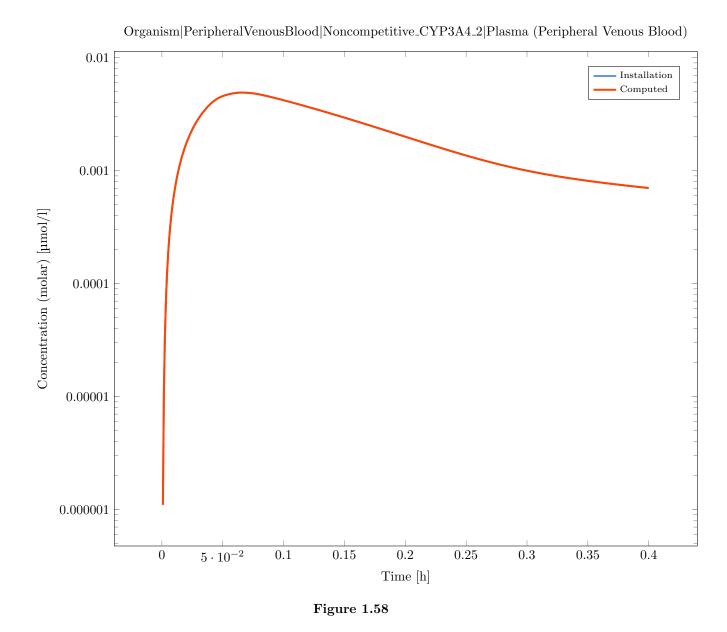


Figure 1.57

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



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

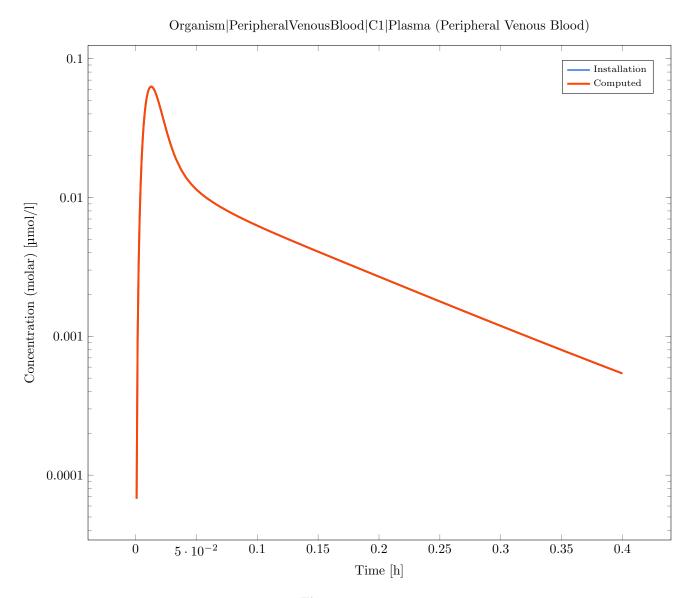
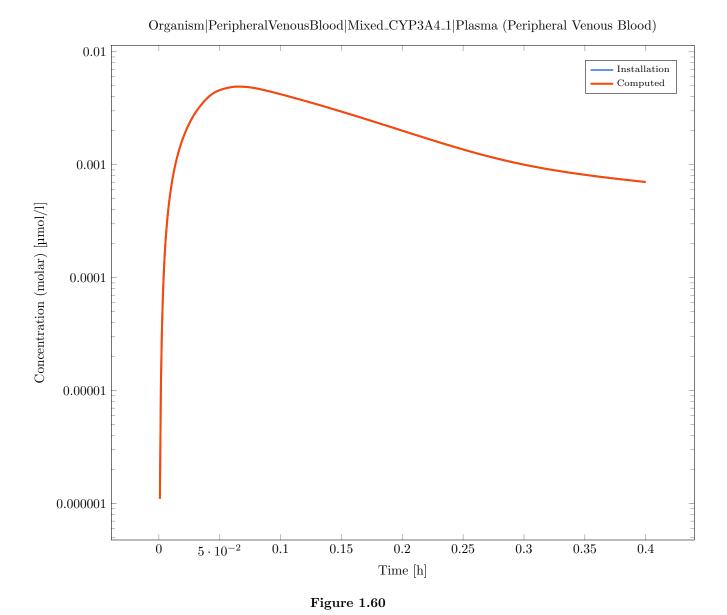


Figure 1.59

 $Simulation: \ DDI_MultipleCombinations \textbf{-} 24_1st_Mixed_Mixed$

Result of the validation: Valid

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



Output Path: Organism |PeripheralVenousBlood |Mixed_CYP3A4_2 |Plasma (Peripheral VenousBlood)
 Deviation: 0

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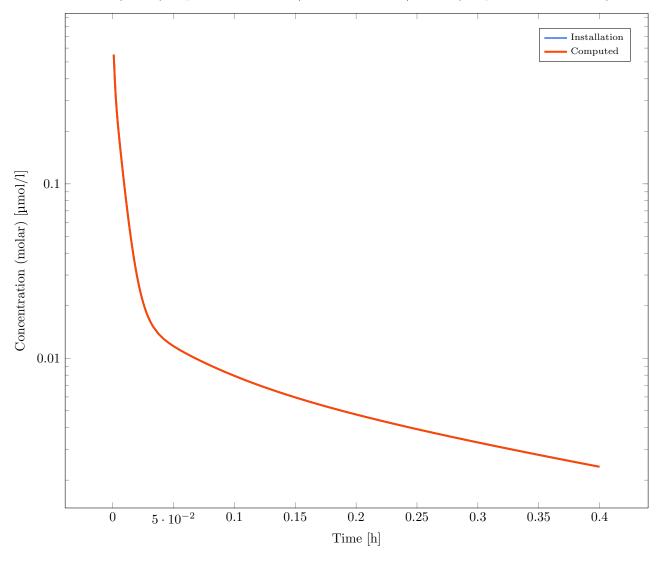
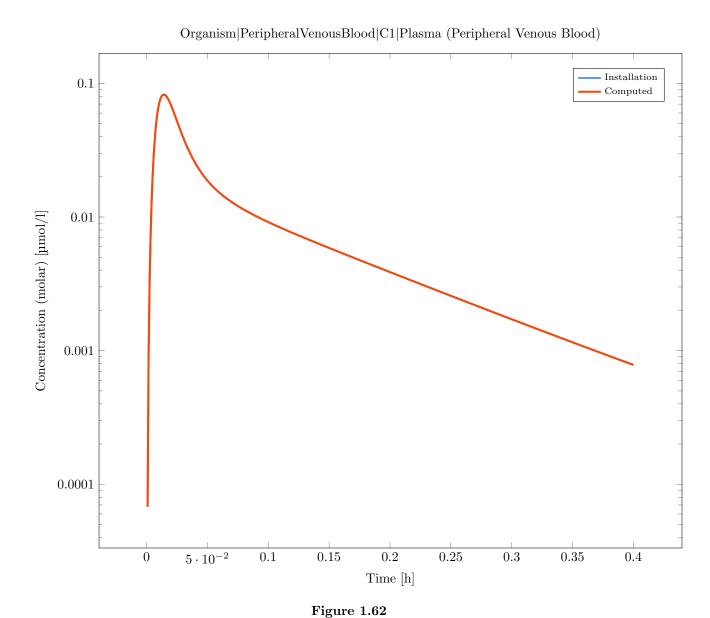


Figure 1.61

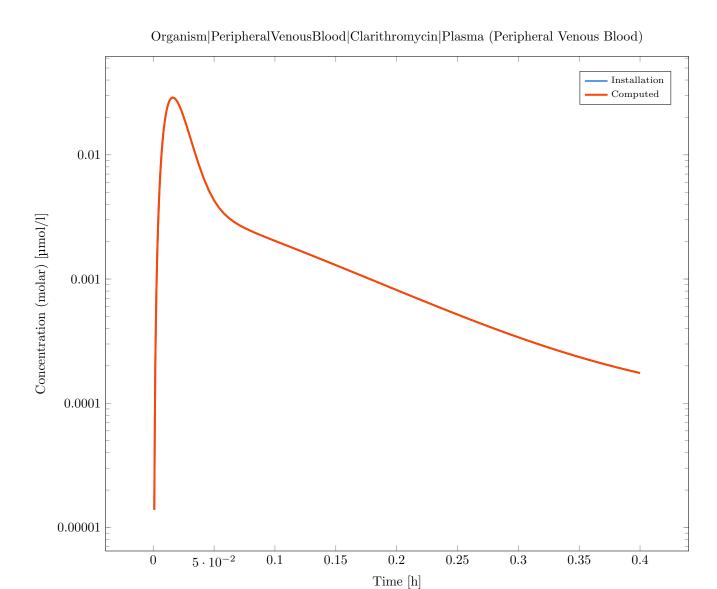
Output Path: Organism |PeripheralVenousBlood |C1|Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$



Simulation: DDI_MultipleCombinations-25_1st_Mechanismbased_Mechanismbased

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

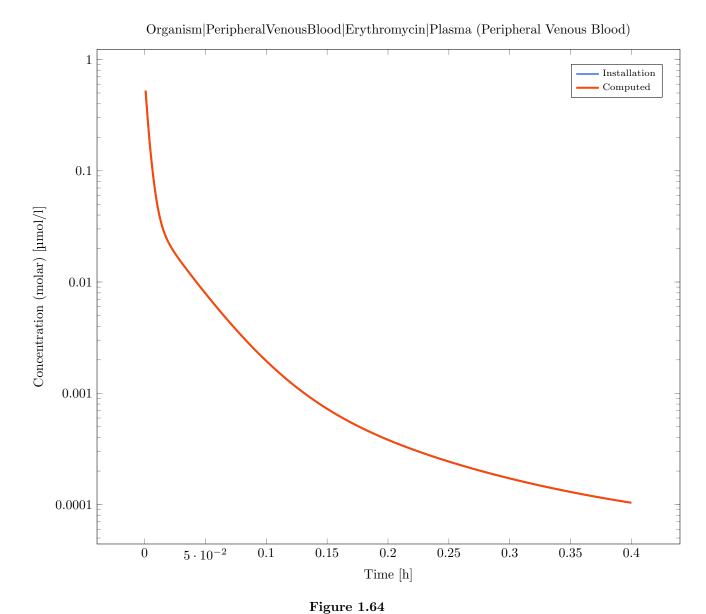
Result of the validation: Valid



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

Deviation: 0

Figure 1.63



Output Path: Organism |Peripheral Venous
Blood |C1 |Plasma (Peripheral Venous Blood) Deviation:
 0

Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood) O.1 O.001 O.001

Figure 1.65

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

 ${\bf Simulation: \ DDI_Multiple Combinations\hbox{--}26_1st_Induction_Induction}$

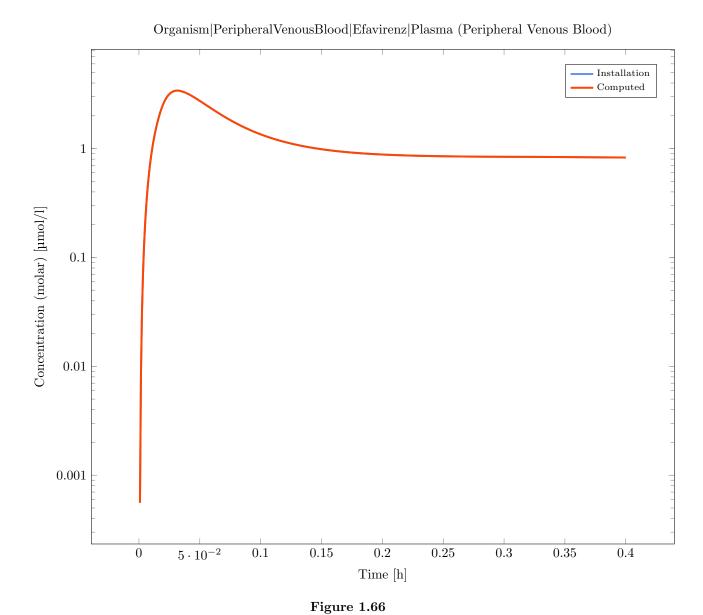
0.1

 $5 \cdot 10^{-2}$

Result of the validation: Valid

0

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



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

Deviation: 0

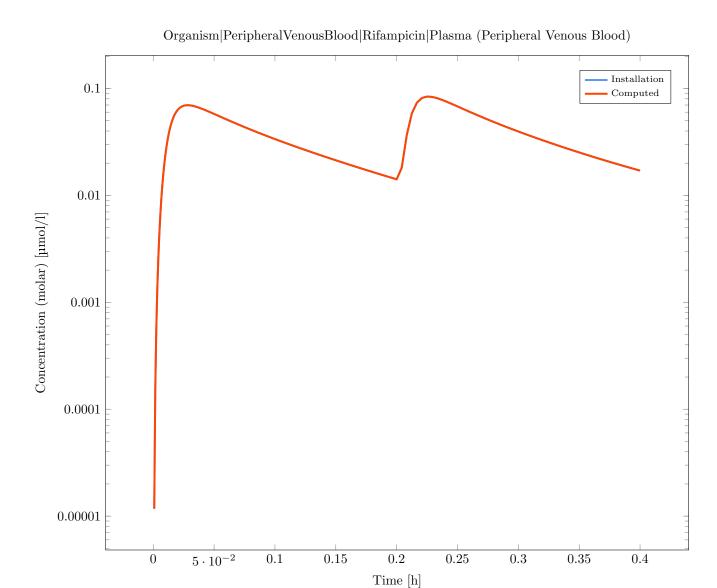
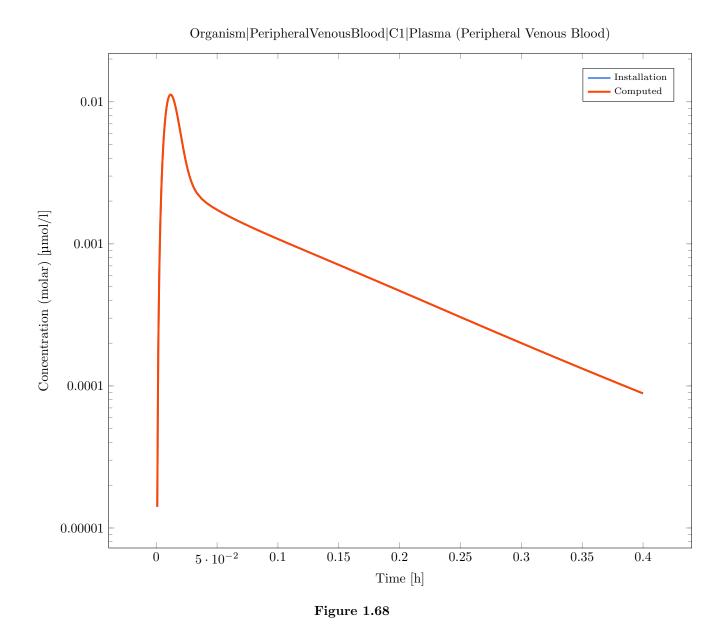


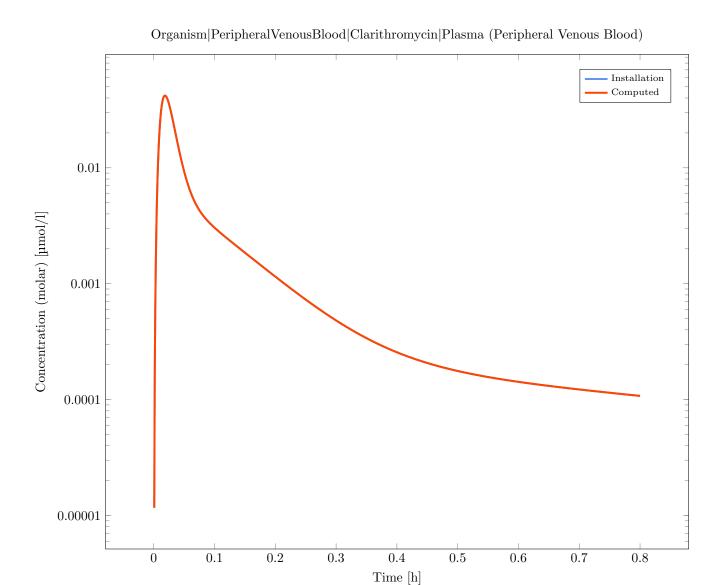
Figure 1.67

Output Path: Organism |PeripheralVenousBlood |C1|Plasma (Peripheral Venous Blood)
 Deviation: 0



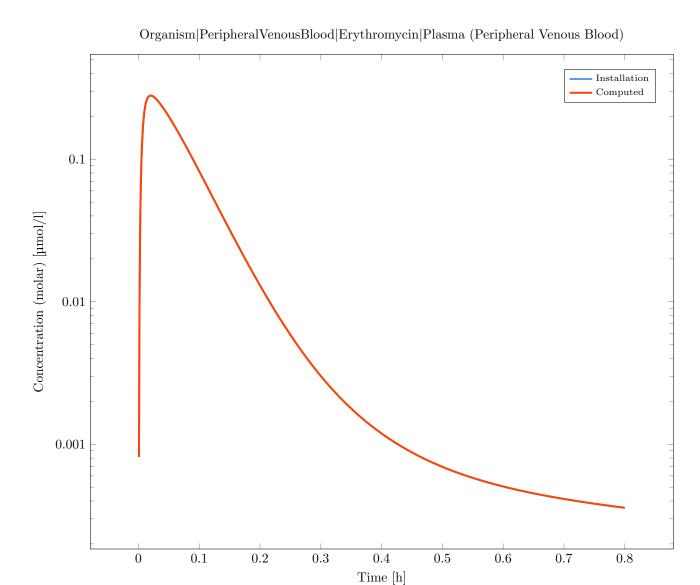
Simulation: DDI_MultipleCombinations-27_1st_Competitive_Competitive_Mechanismbased_Mechanismbased Result of the validation: Valid

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



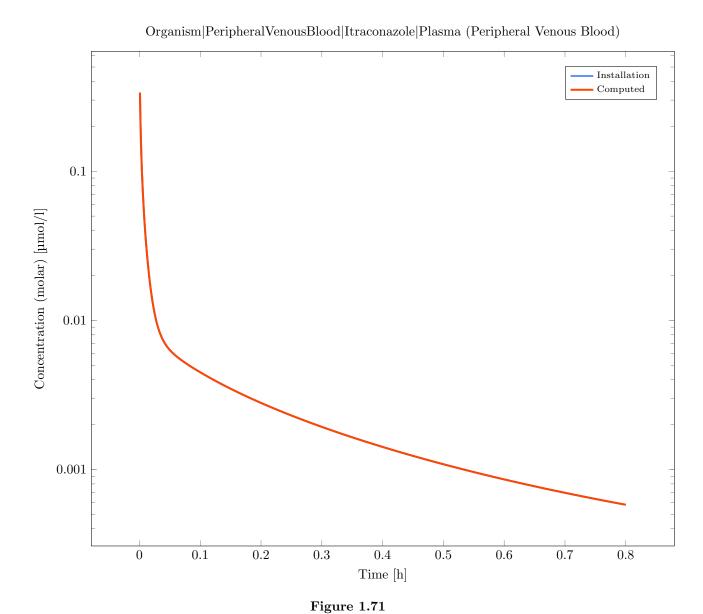
Output Path: Organism |Peripheral Venous
Blood |Erythromycin |Plasma (Peripheral Venous Blood)
 Deviation: $\boldsymbol{0}$

Figure 1.69

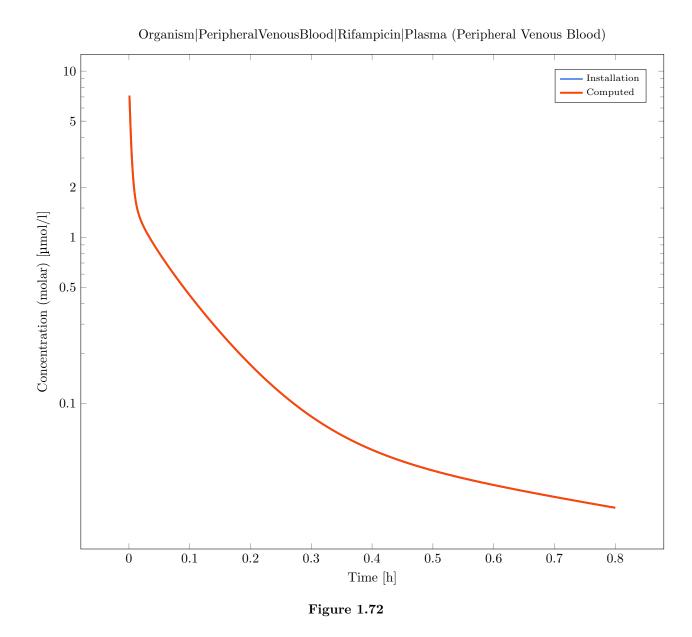


 $Output\ Path:\ Organism | Peripheral Venous Blood | Itraconazole | Plasma\ (Peripheral Venous\ Blood)$ Deviation: 0

Figure 1.70



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



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

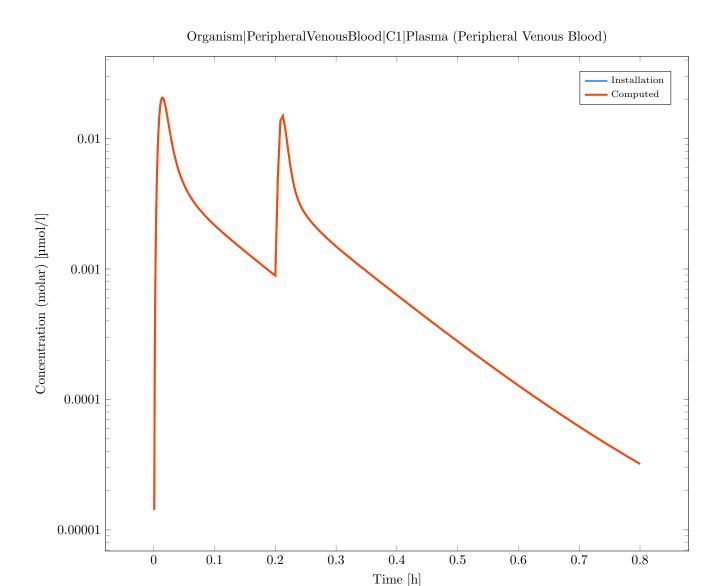


Figure 1.73

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

Result of the validation: Valid

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

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

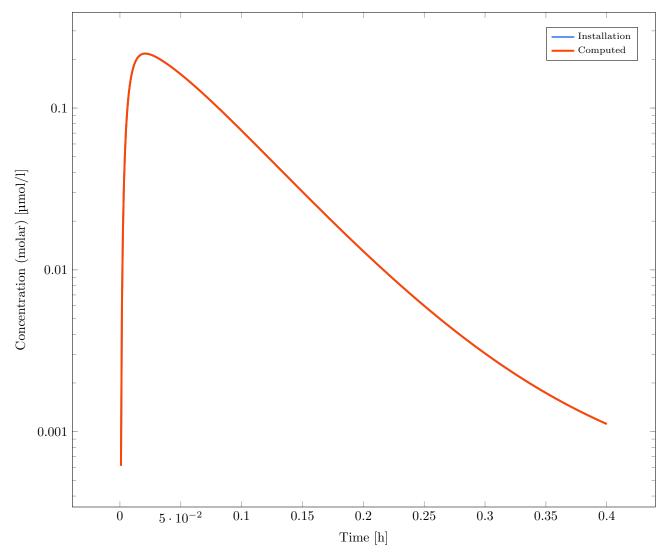
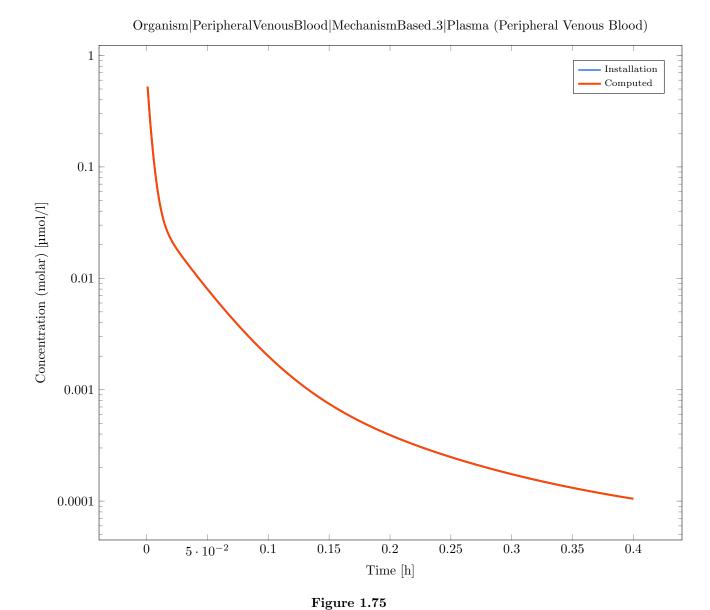
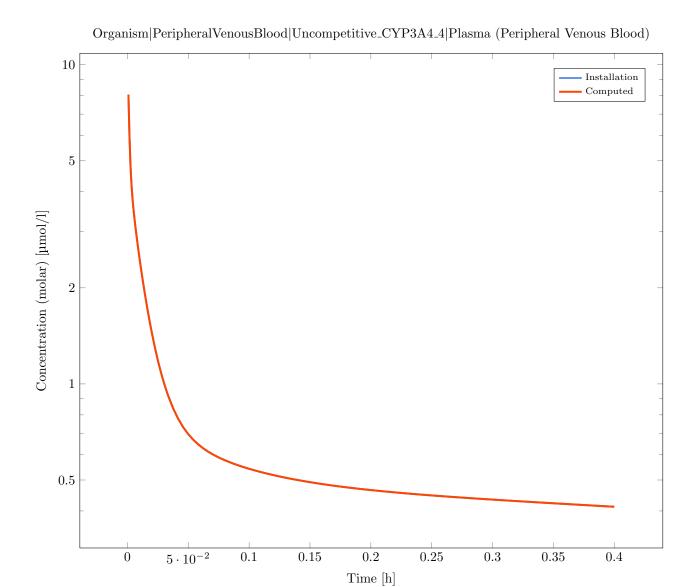


Figure 1.74

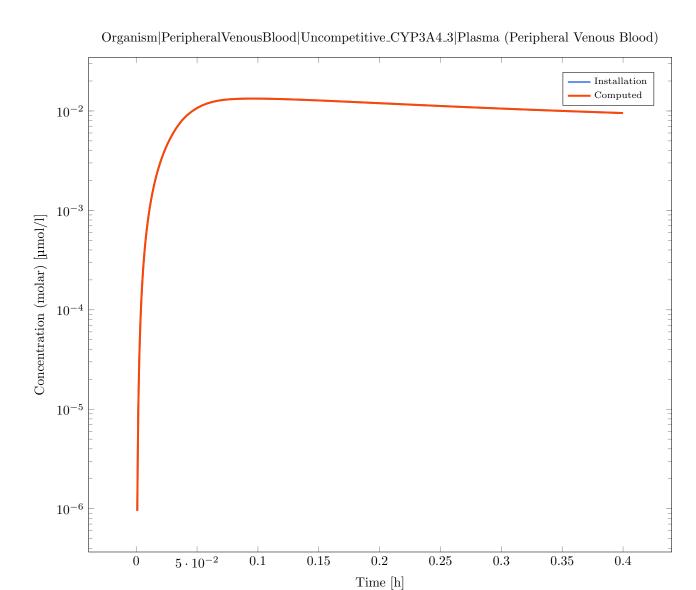
 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased_3|Plasma\ (Peripheral\ Venous\ Blood)$





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

Figure 1.76



Deviation: 0

Figure 1.77

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

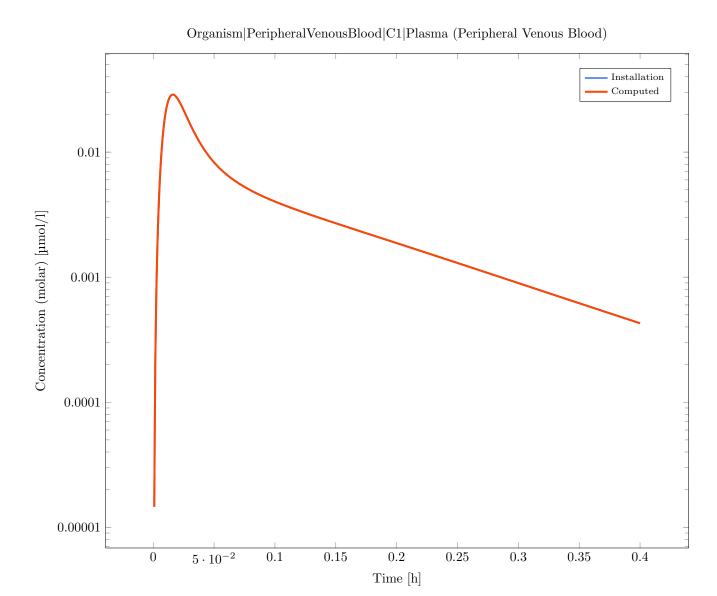
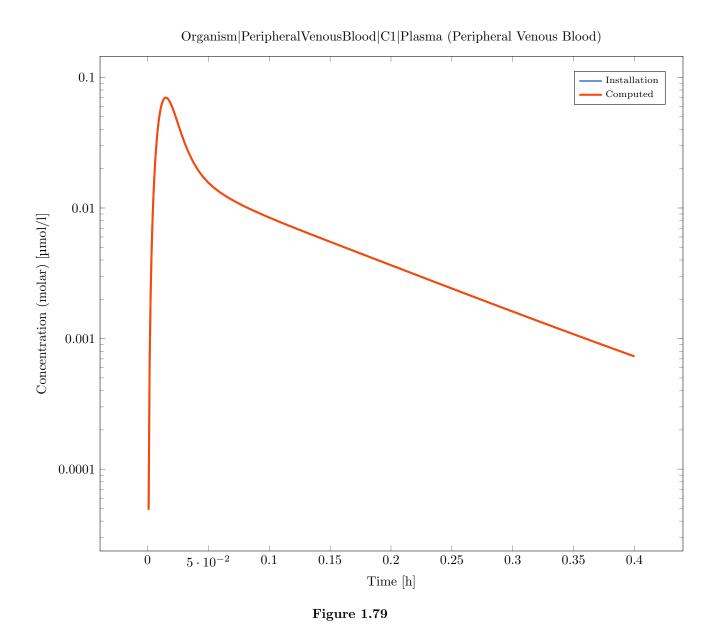


Figure 1.78

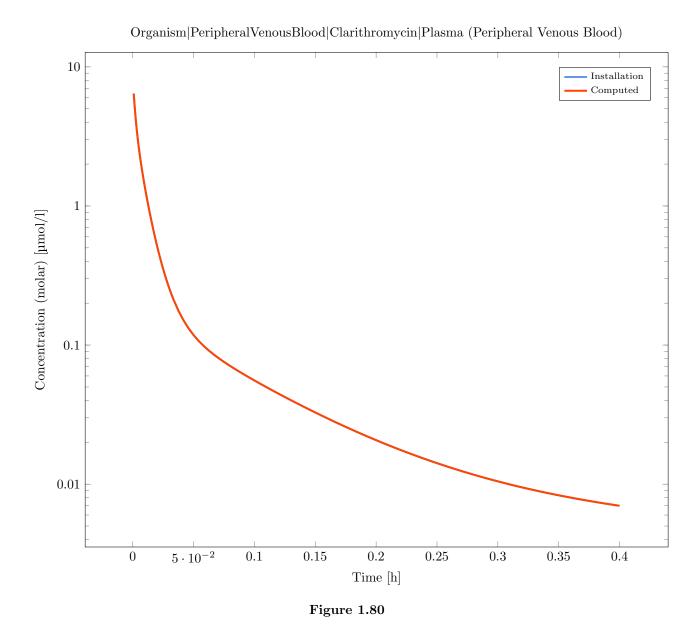
 $Simulation: \ DDI_Multiple Combinations \textbf{-} 29_1st_Noncompetitive_Noncompetitive_Mechanism based_Mechanism based$

Result of the validation: Valid

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



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



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

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

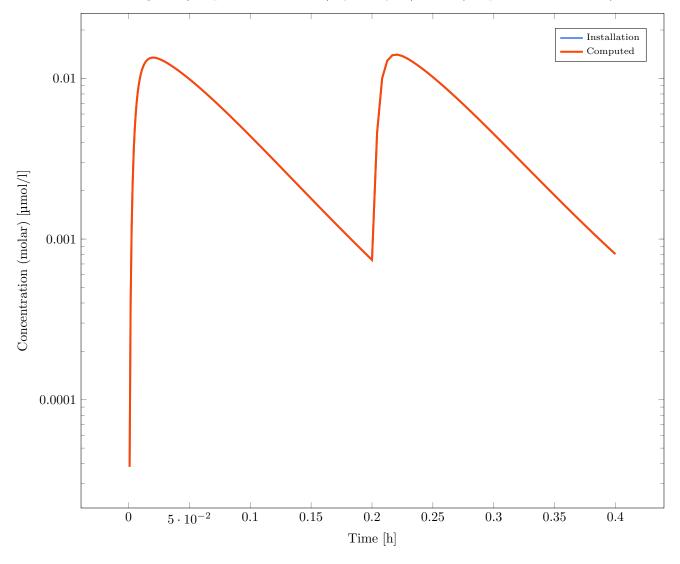


Figure 1.81

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

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

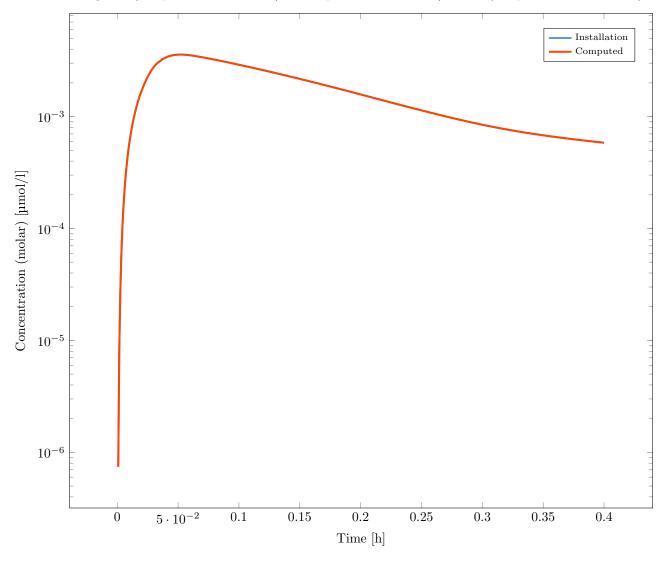


Figure 1.82

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

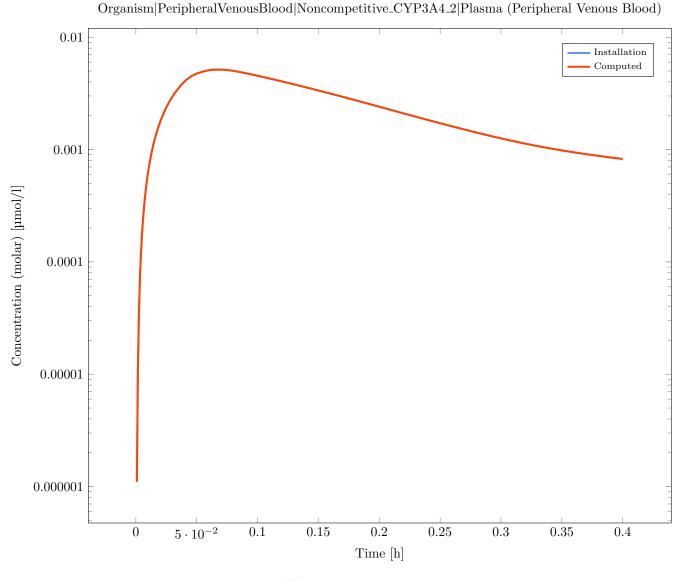


Figure 1.83

 ${\bf Simulation:\ DDI_Multiple Combinations-30_1st_Mixed_Mechanismbased_Mechanism$

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



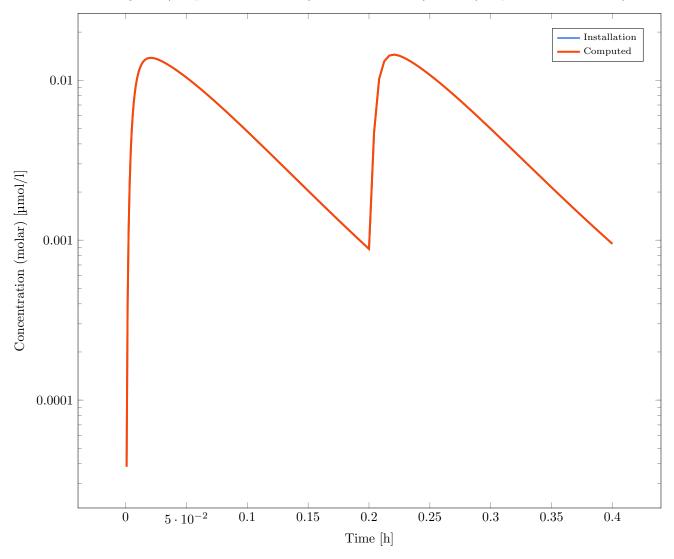


Figure 1.84

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

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

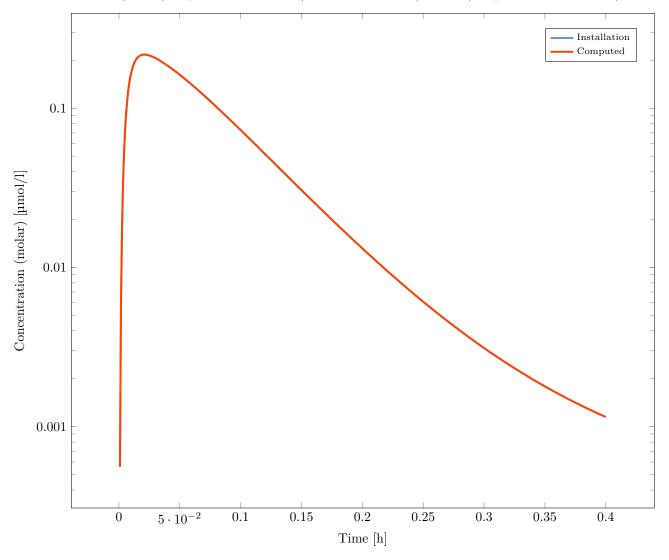
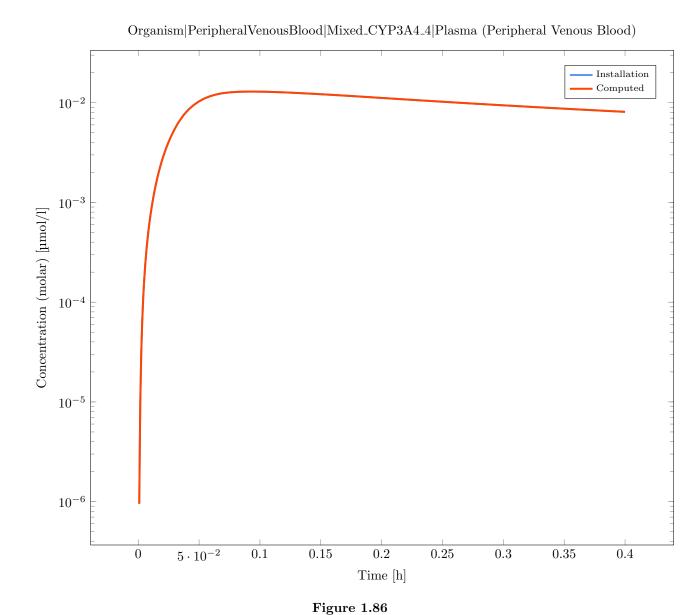
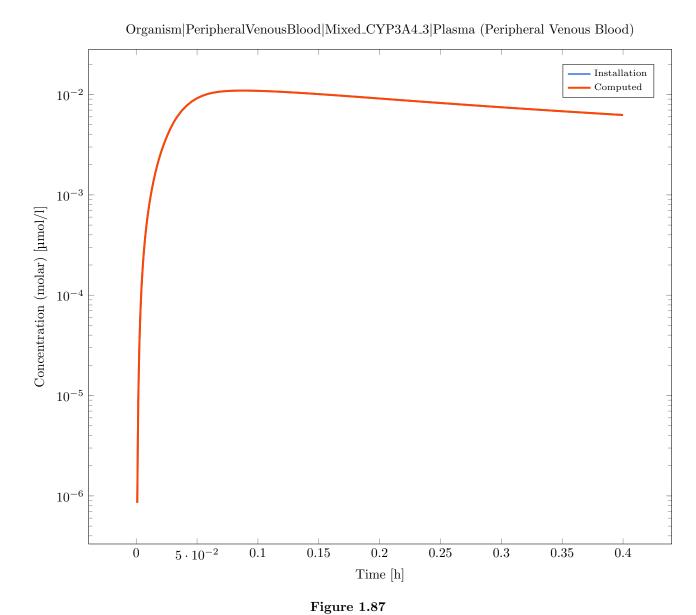


Figure 1.85

 $Output\ Path:\ Organism|Peripheral Venous Blood|Mixed_CYP3A4_4|Plasma\ (Peripheral\ Venous Blood)$



Output Path: Organism |PeripheralVenousBlood |Mixed_CYP3A4_3 |Plasma (Peripheral VenousBlood)
 Deviation: 0



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

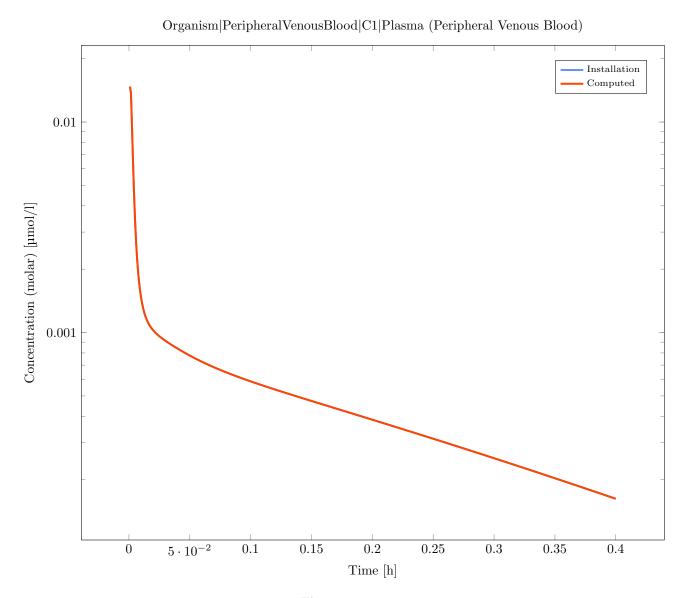
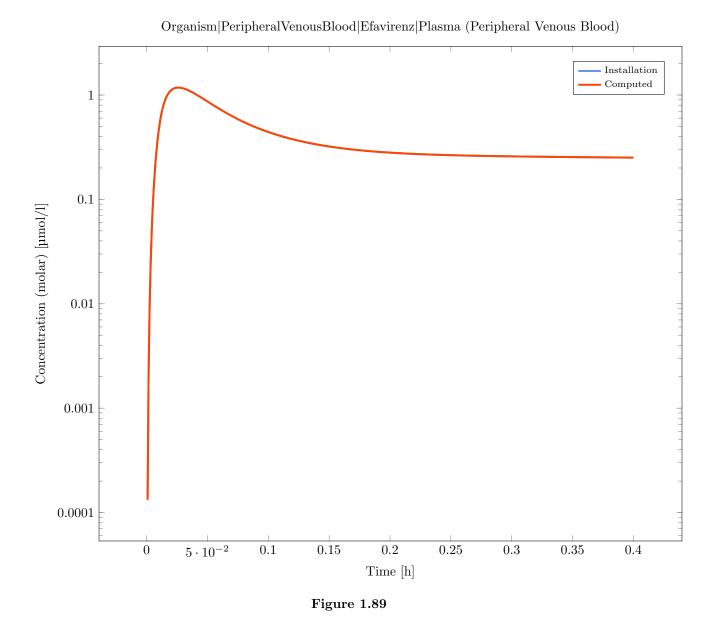


Figure 1.88

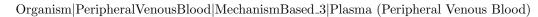
 ${\bf Simulation:\ DDI_Multiple Combinations\hbox{--}31_1st_Mechanismbased_Mechanismbased_Induction_Induction} \\ {\bf Result\ of\ the\ validation:\ Valid}$

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



Output Path: Organism |PeripheralVenousBlood |MechanismBased_3 |Plasma (Peripheral VenousBlood)
 Deviation: 0

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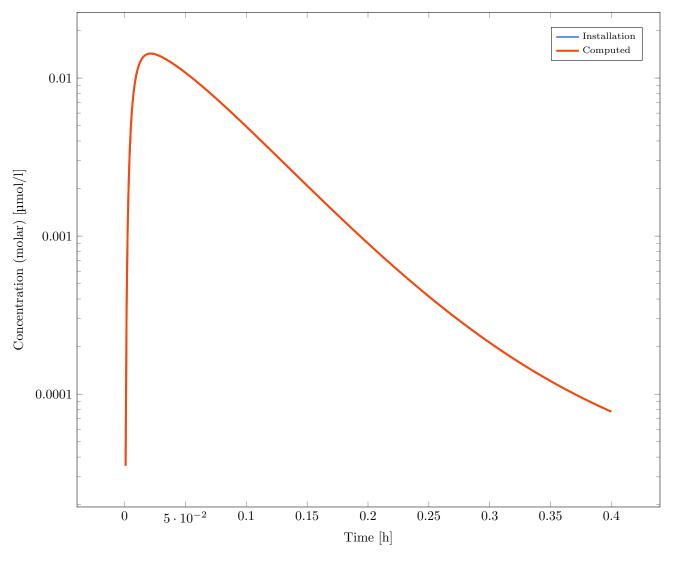
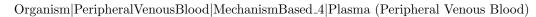


Figure 1.90

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



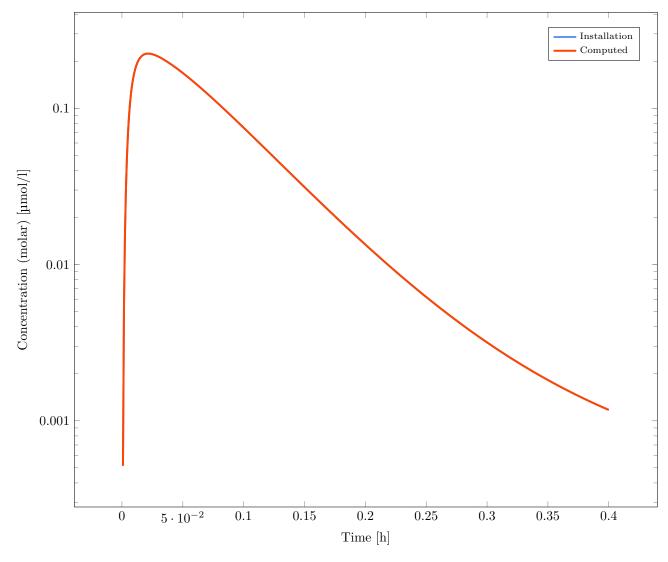


Figure 1.91

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

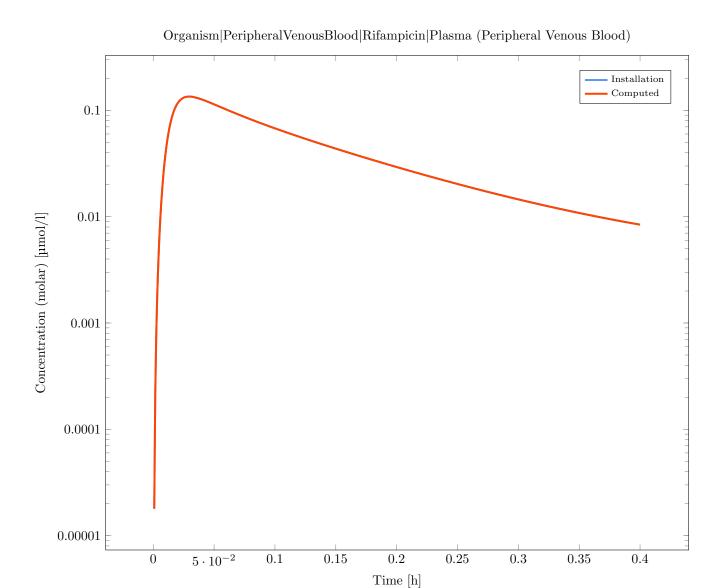


Figure 1.92

Output Path: Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood) Deviation: 0

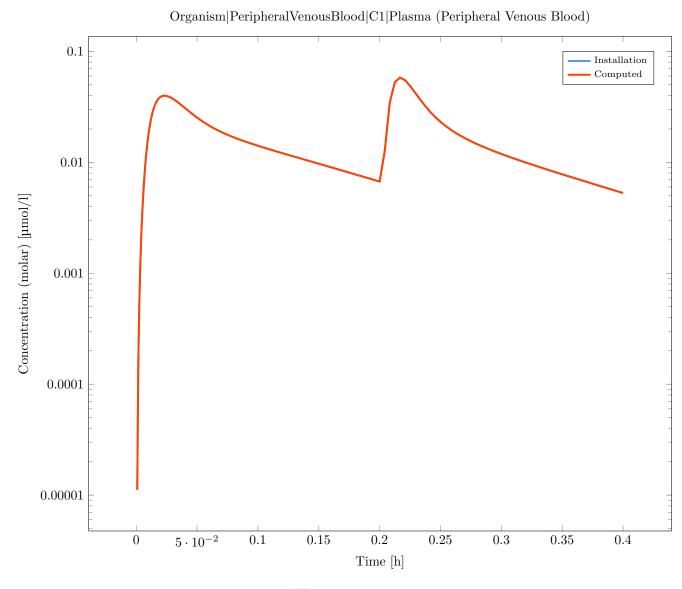
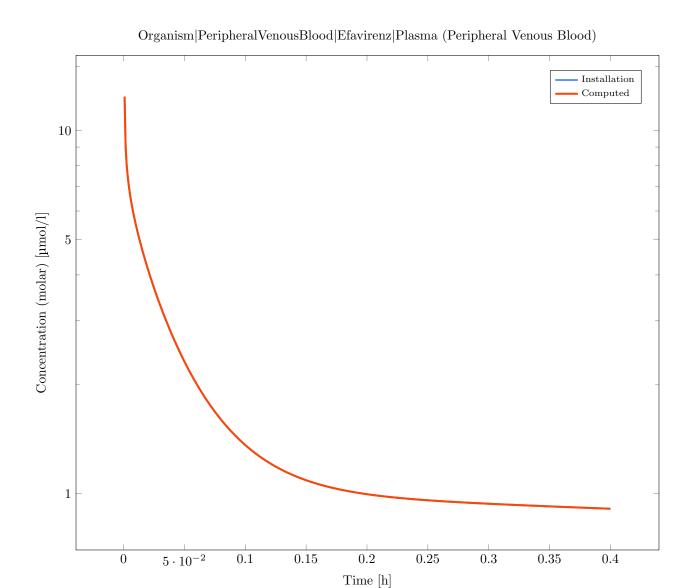


Figure 1.93

 $Simulation: \ DDI_Multiple Combinations \textbf{-32_1st_All_DDI_Types}$

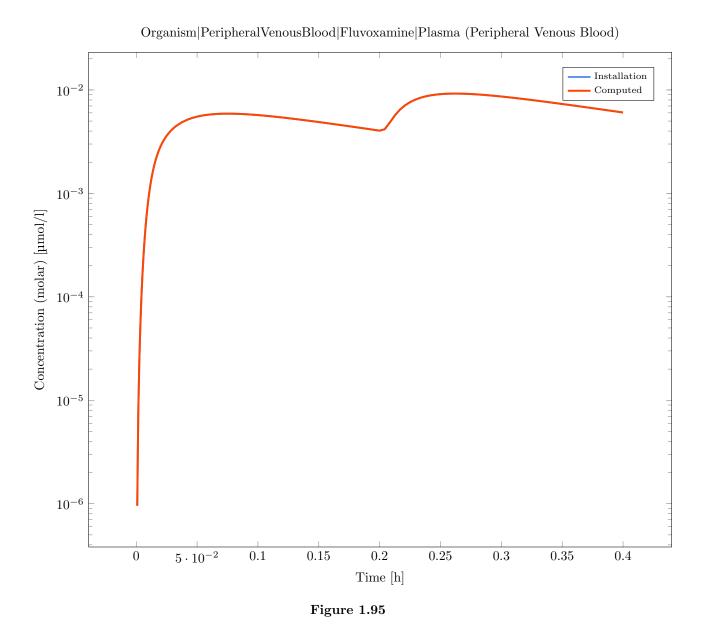
Result of the validation: Valid

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

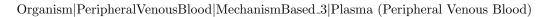


 $Output\ Path:\ Organism | Peripheral Venous Blood | Fluvoxamine | Plasma\ (Peripheral\ Venous\ Blood)$ Deviation: 0

Figure 1.94



Output Path: Organism |Peripheral VenousBlood |Mechanism
Based_3 |Plasma (Peripheral Venous Blood)
 Deviation: 0



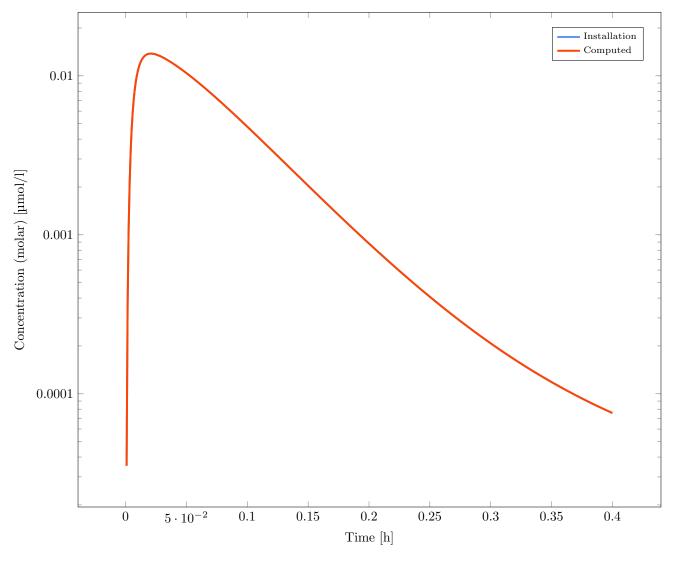


Figure 1.96

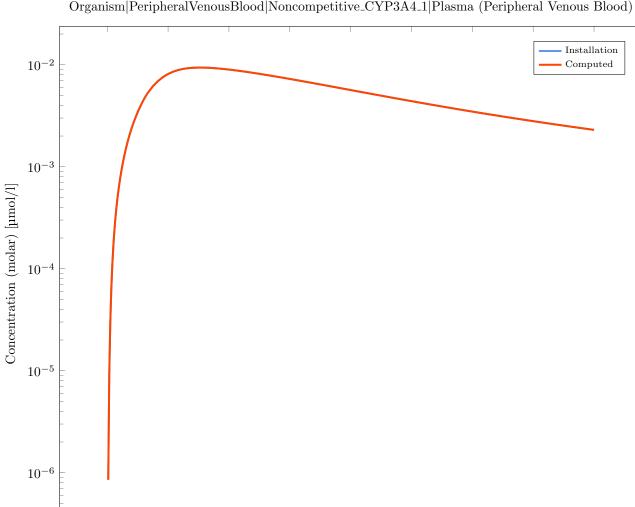
 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed_CYP3A4_3|Plasma\ (Peripheral\ VenousBlood)$

$Organism | Peripheral Venous Blood | Mixed_CYP3A4_3 | Plasma~(Peripheral Venous~Blood)$ 0.01Installation Computed 0.001 Concentration (molar) [µmol/1] 0.00010.000010.0000010 0.1 0.15 0.2 0.25 0.3 0.35 0.4 $5 \cdot 10^{-2}$

Figure 1.97

Time [h]

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



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

Figure 1.98

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

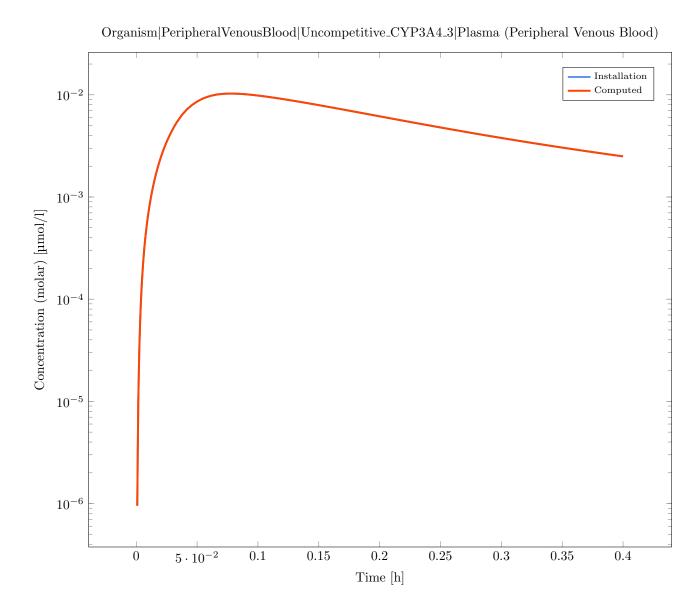
0.1

 $5\cdot 10^{-2}$

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

Deviation: 0

0



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

Figure 1.99

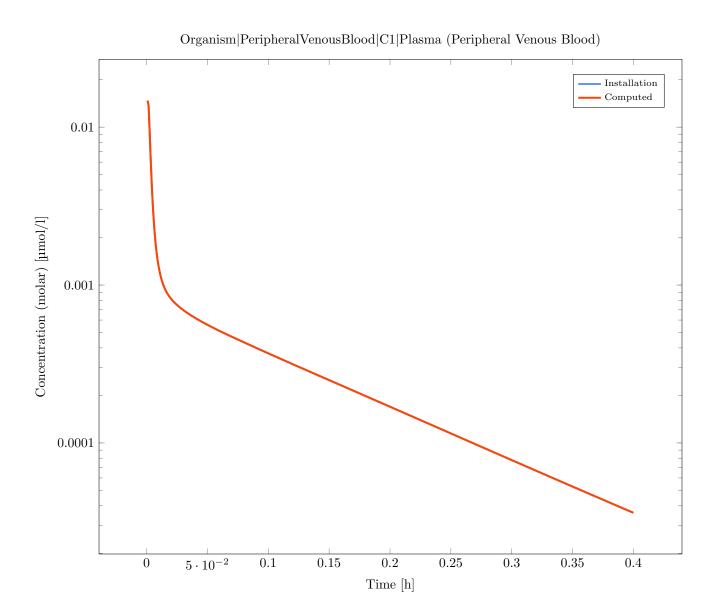


Figure 1.100

Simulation: Dog_MultiORAL_12_12_Dissolved-Dog_MultiORAL_12_12_Dissolved Result of the validation: Valid

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

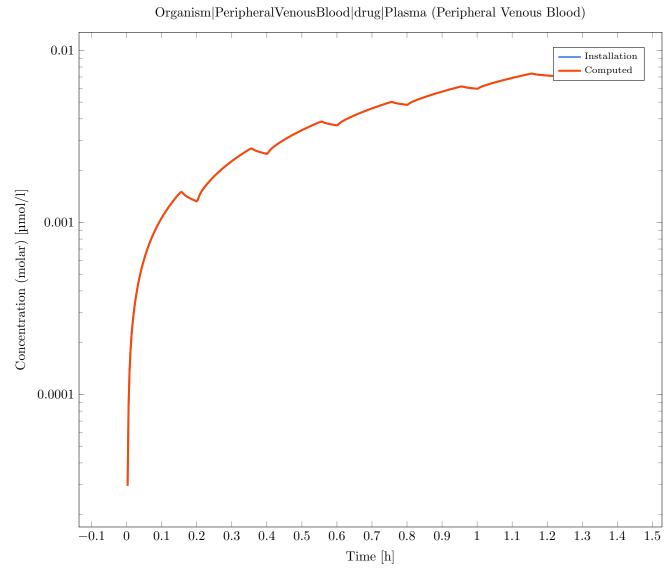


Figure 1.101

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

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

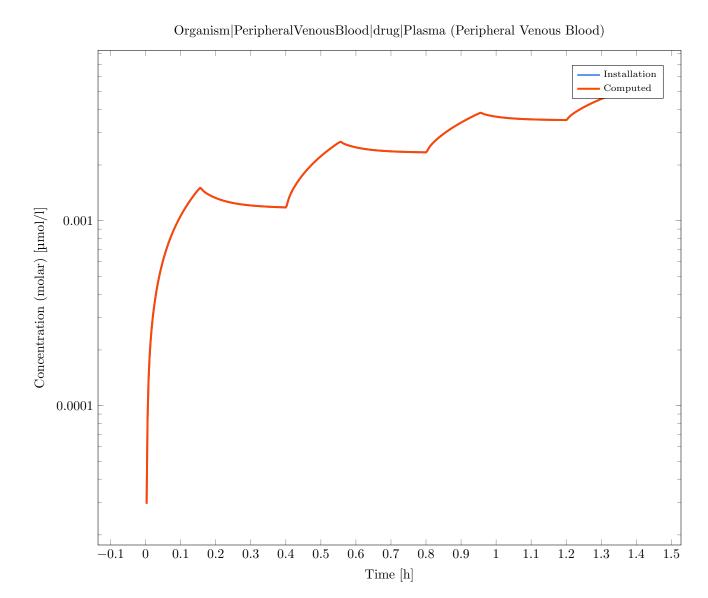
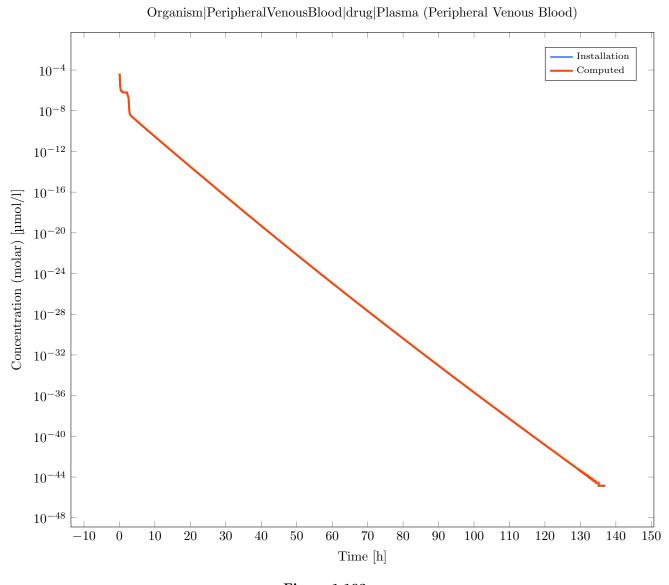


Figure 1.102

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

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



 ${\bf Figure~1.103}$

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

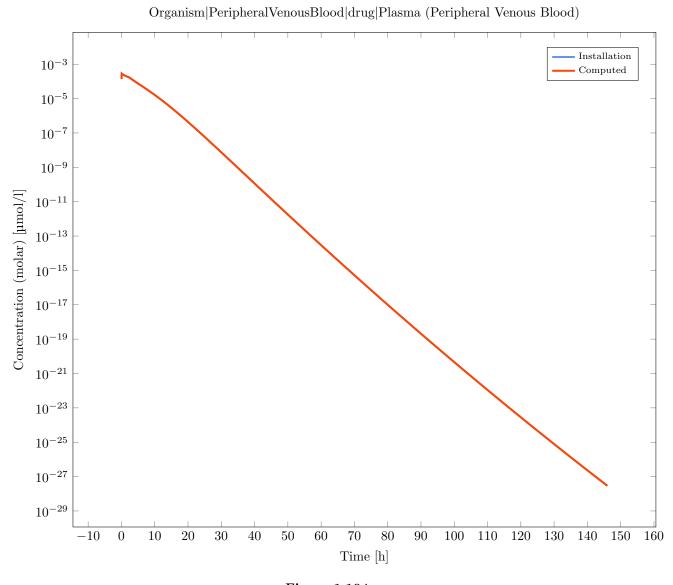
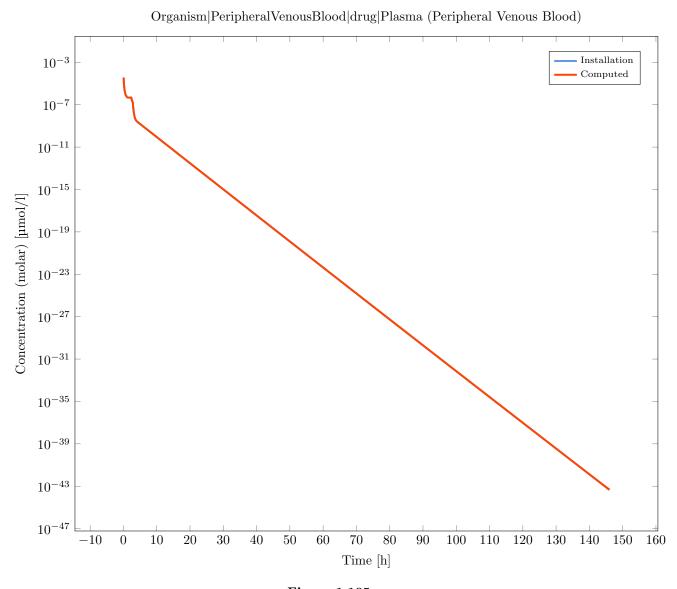


Figure 1.104

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

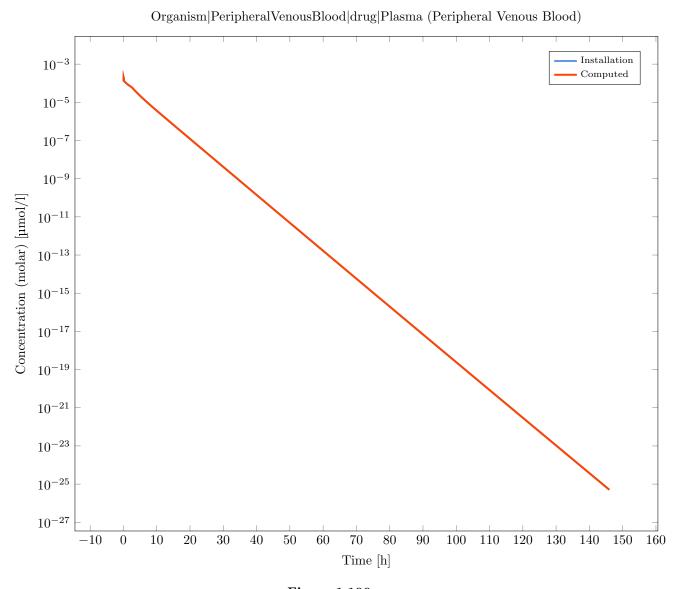
Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 2.02E-6



 ${\bf Figure~1.105}$

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

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



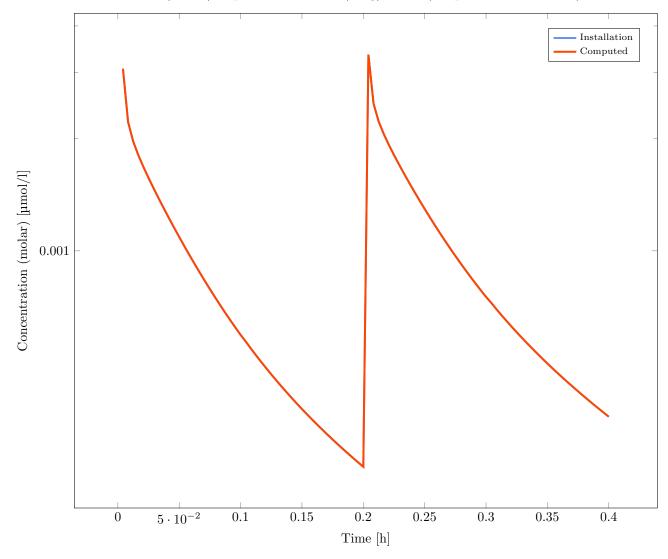


Figure 1.107

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

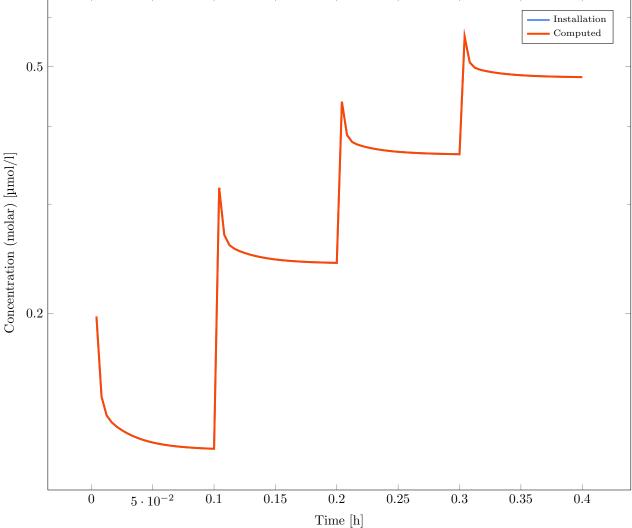


Figure 1.108

Simulation: Human_ICRP_AGP-01_ICRP_0y_Male

Result of the validation: Valid

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

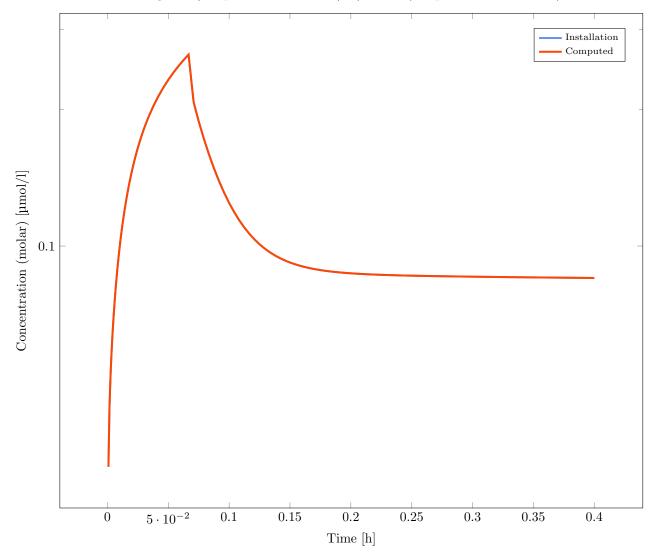


Figure 1.109

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

Result of the validation: Valid

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

Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood) O.5 Installation Computed One of the control of the cont

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

0.15

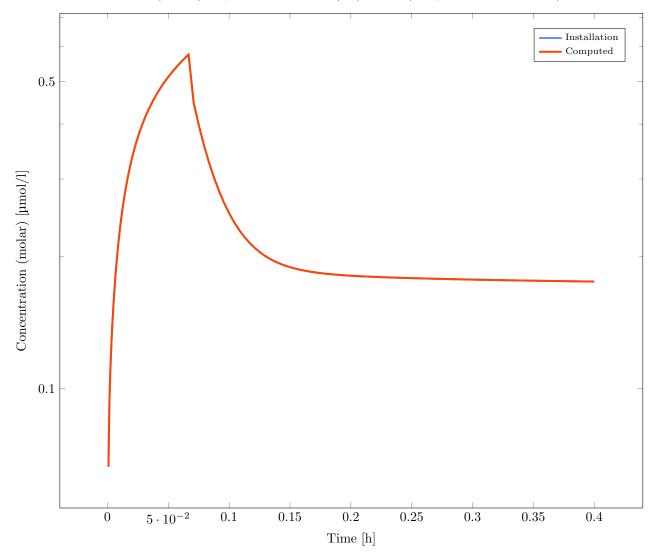


Figure 1.111

 $Simulation: \ Human_ICRP_AGP-04_ICRP_1y_Female$

Result of the validation: Valid

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

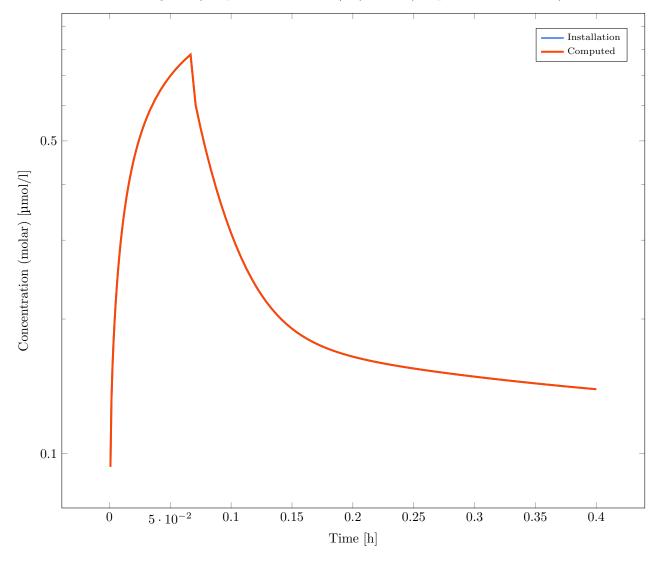


Figure 1.112

 $Simulation: \ Human_ICRP_AGP-05_ICRP_12y_Male$

Result of the validation: Valid

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

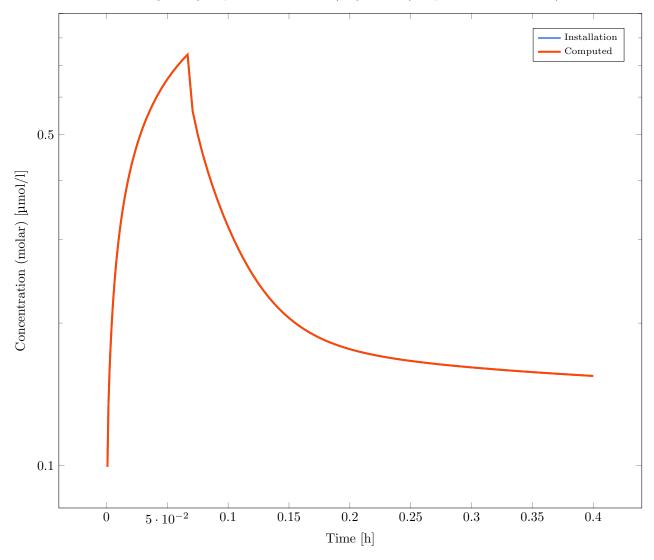


Figure 1.113

 $Simulation: \ Human_ICRP_AGP-06_ICRP_30y_Female$

Result of the validation: Valid

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



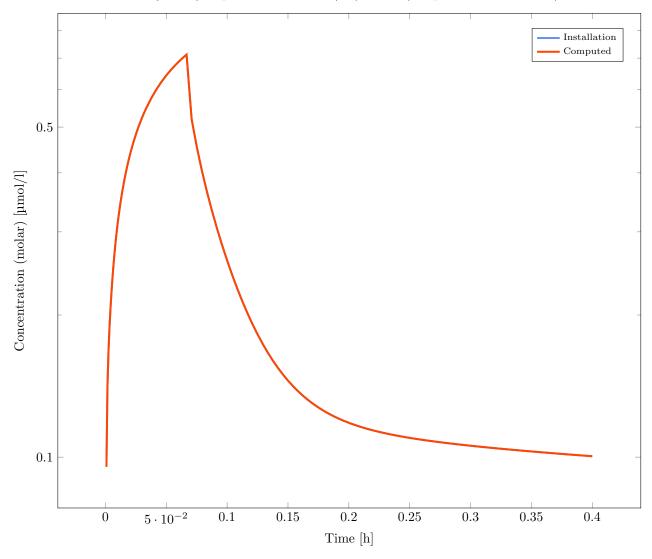


Figure 1.114

 $Simulation: \ Human_ICRP_AGP-07_ICRP_100y_Male$

Result of the validation: Valid

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

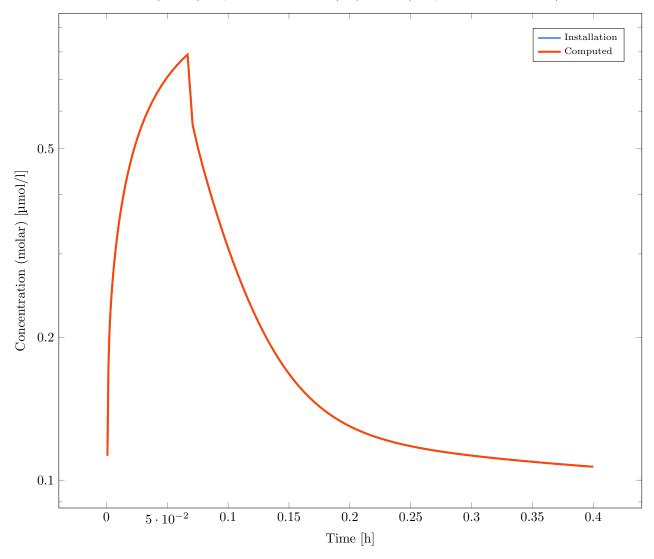
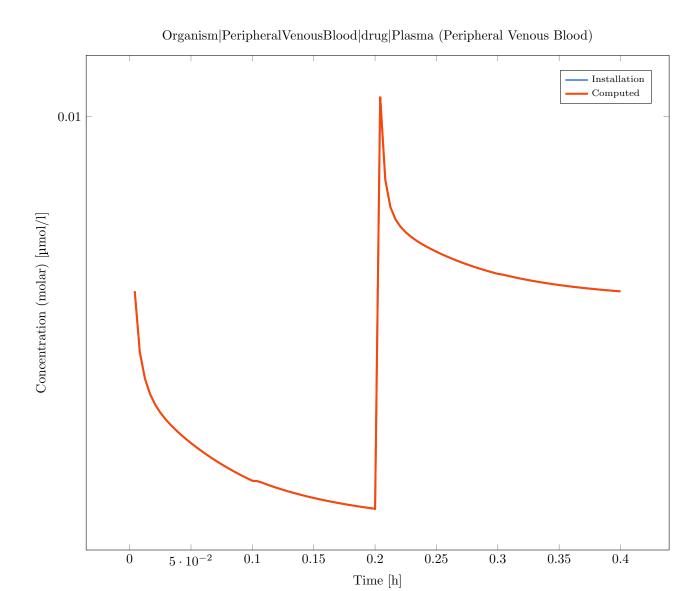


Figure 1.115

 ${\bf Simulation: \ Human_Irreversible Inhibition-Human_Irreversible Inhibition}$

Result of the validation: Valid



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

 $Figure \ 1.116$

Organism|PeripheralVenousBlood|inhibitor|Plasma (Peripheral Venous Blood) | Installation | Computed | Compute

Figure 1.117

Time [h]

 $Simulation: \ Human_MixedInhibition-Human_MixedInhibition$

Result of the validation: Valid

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

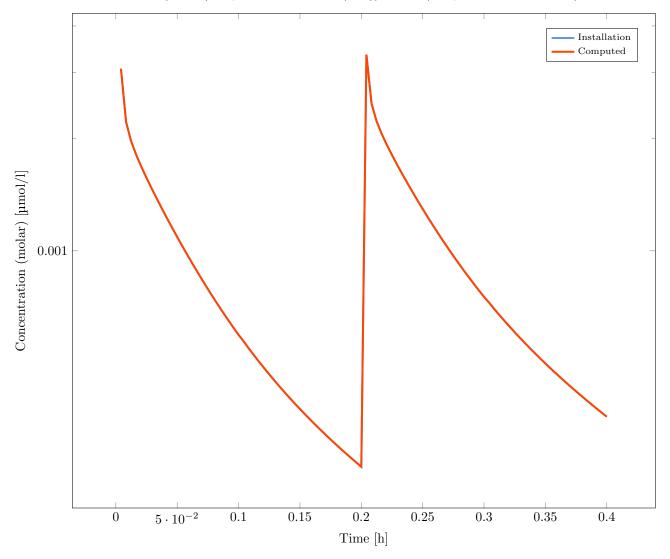


Figure 1.118

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

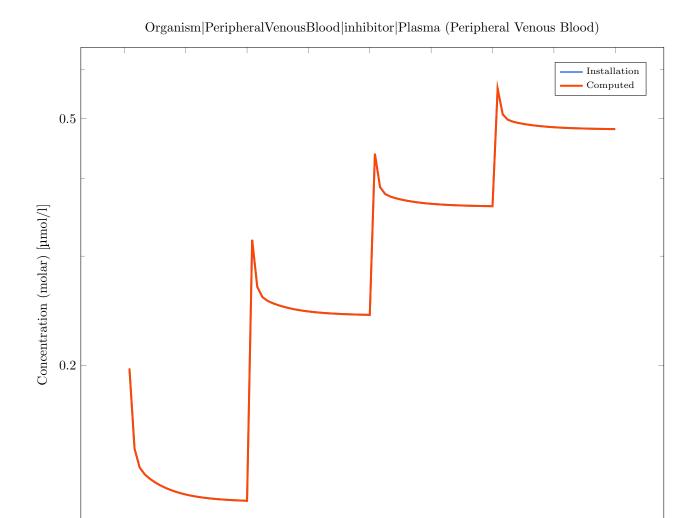


Figure 1.119

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



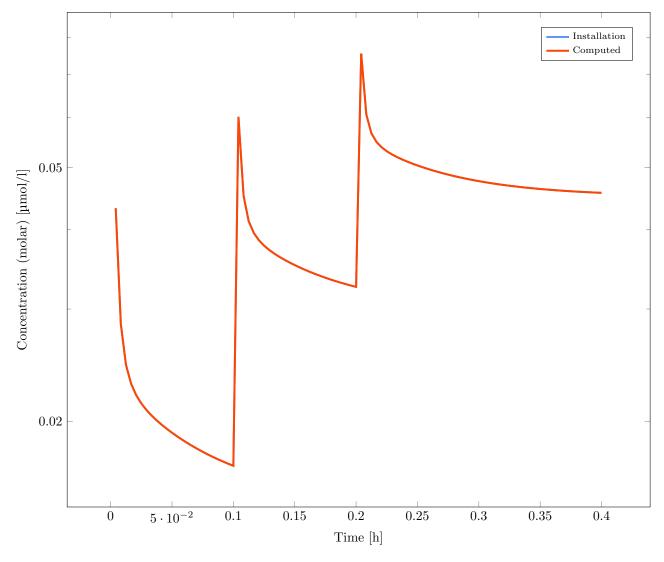


Figure 1.120

 $Simulation: \ Human_MultiORAL_6_12_12_Dissolved-Human_6_12_Dissolved-Human_6_12_$

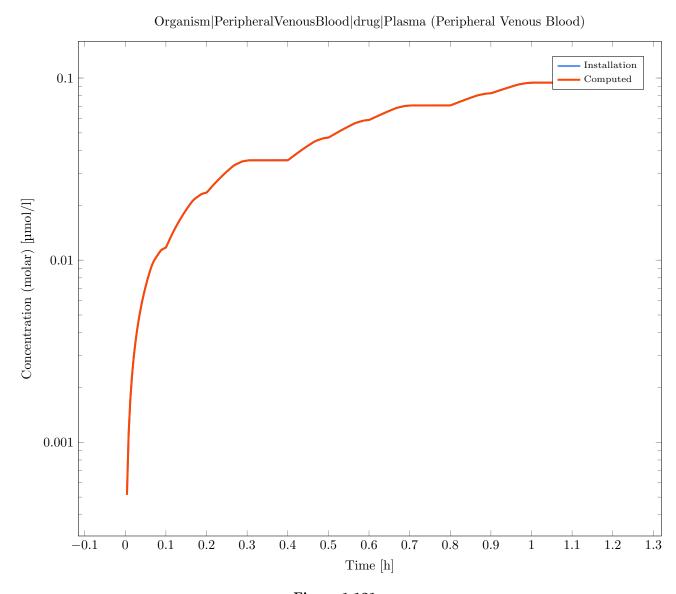
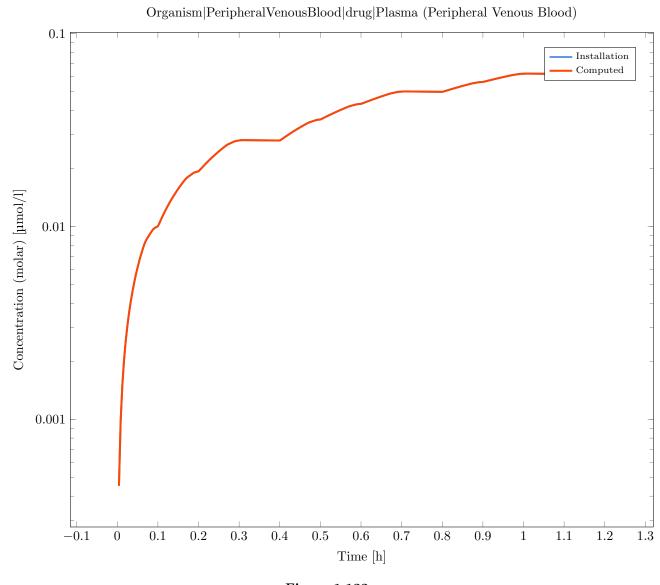


Figure 1.121

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_absorption_sink_conditions$

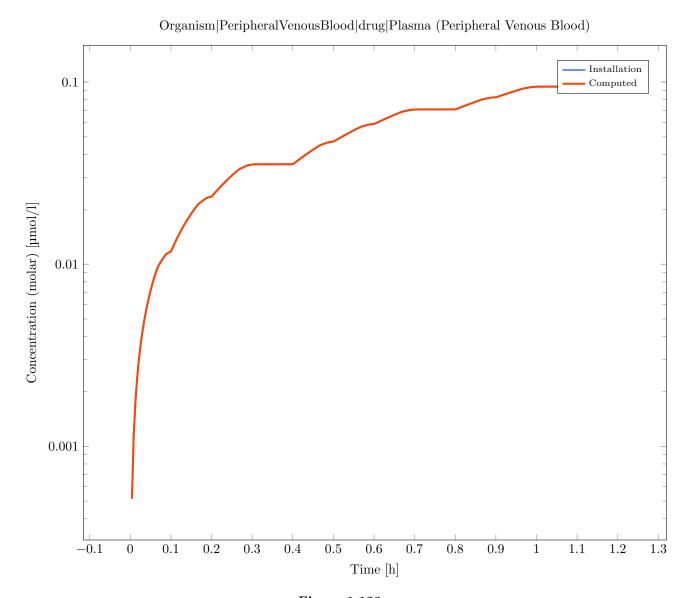
Result of the validation: Valid



 ${\bf Figure~1.122}$

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_EHC_continuous_fraction_0.5$

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

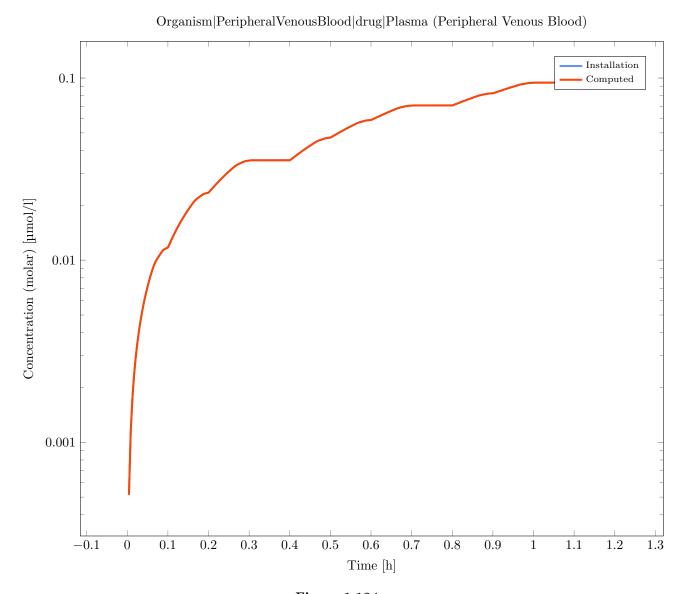
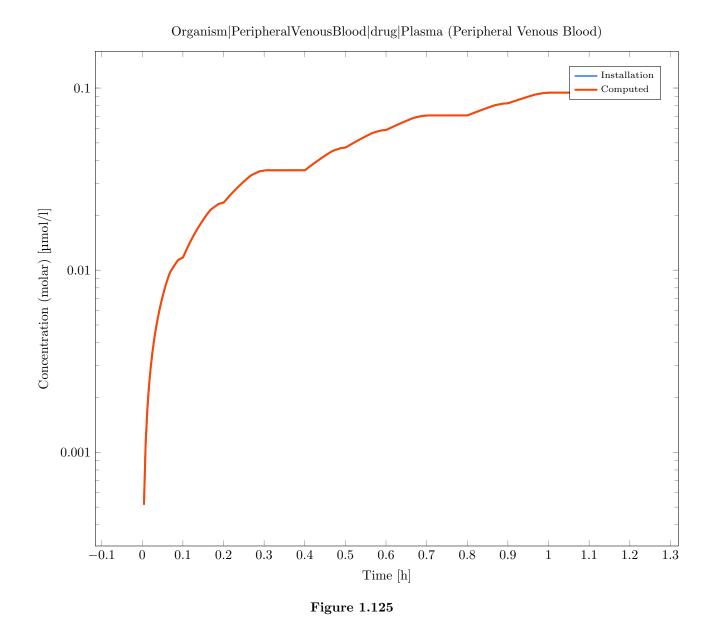
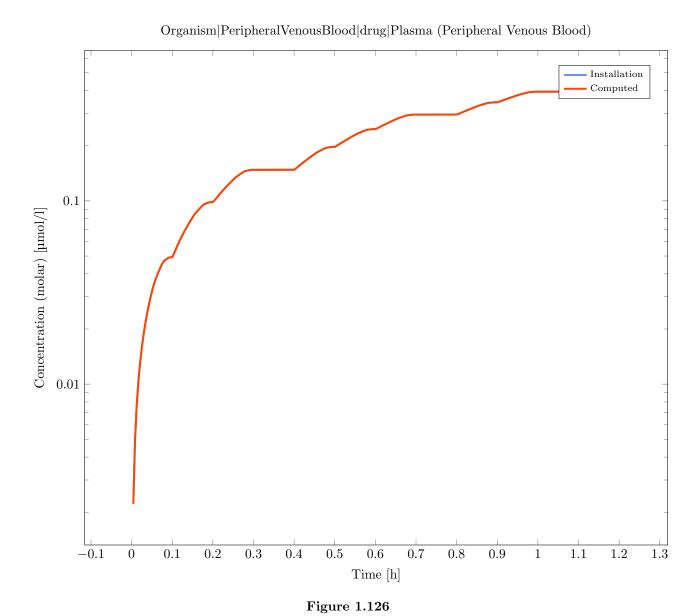


Figure 1.124

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



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



 ${\bf Simulation: \ Human_Multiple IV_All Active Processes-Human_Multiple IV_All Active Processes \ Result of the validation: \ Valid$

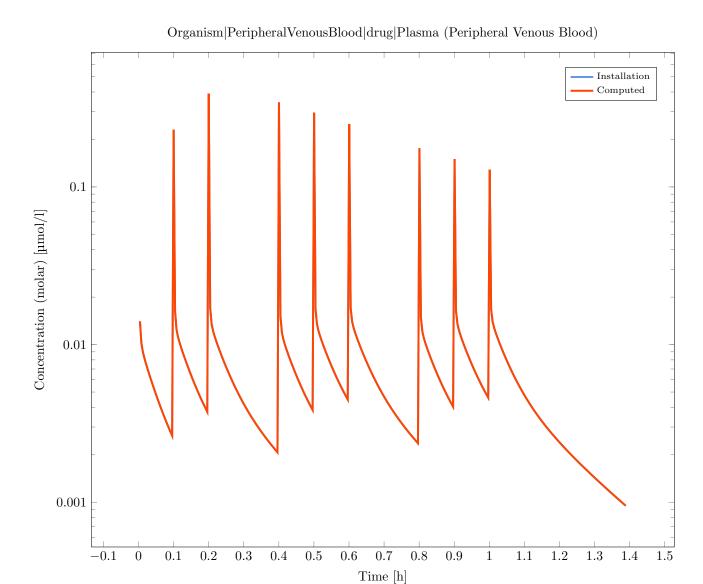


Figure 1.127

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

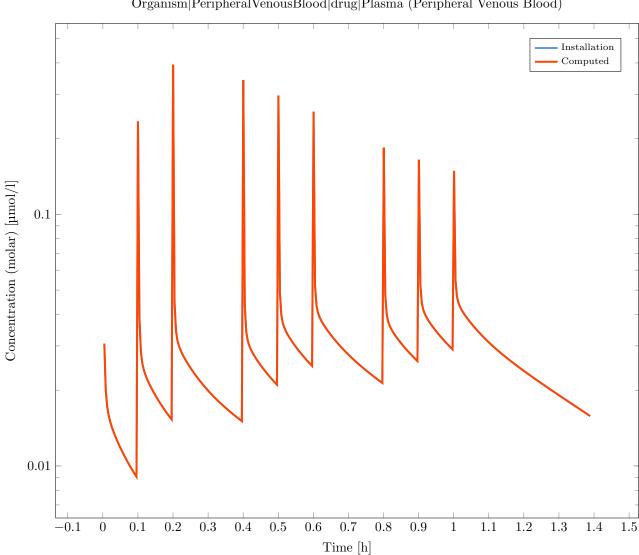
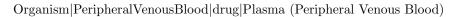
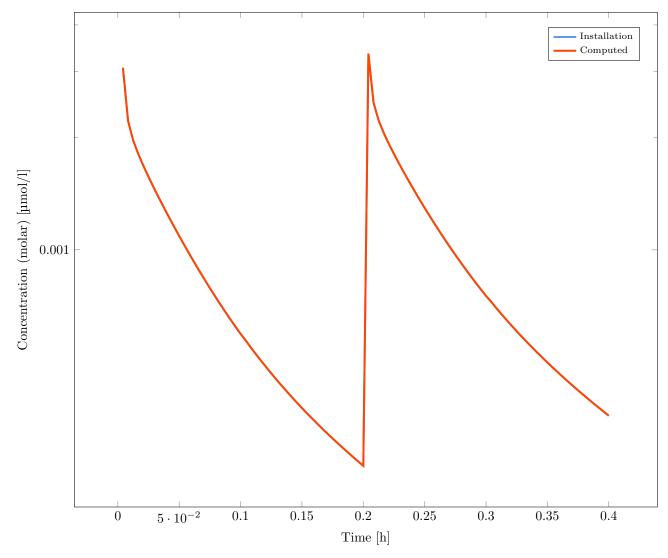


Figure 1.128

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





 $Figure \ 1.129$

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

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

Figure 1.130

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: \ Human_Oral_BiDaily_Table Formulation-S1_suspension$

0.1

Result of the validation: Valid

0

 $5 \cdot 10^{-2}$

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

0.15

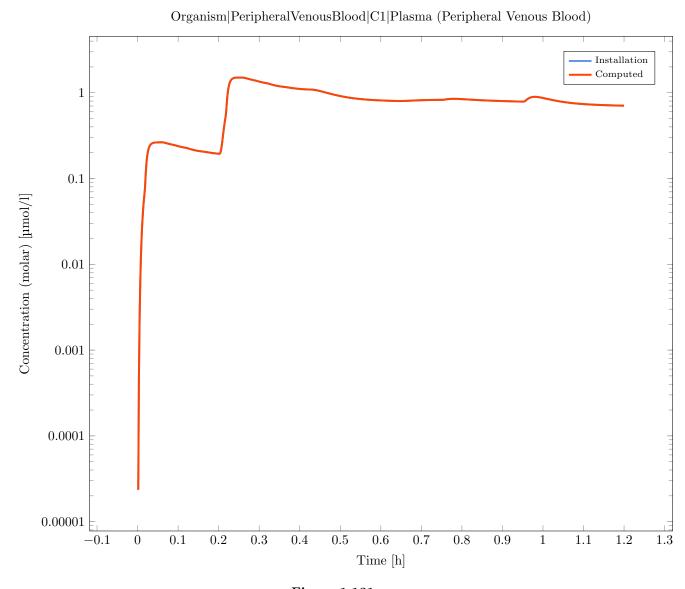
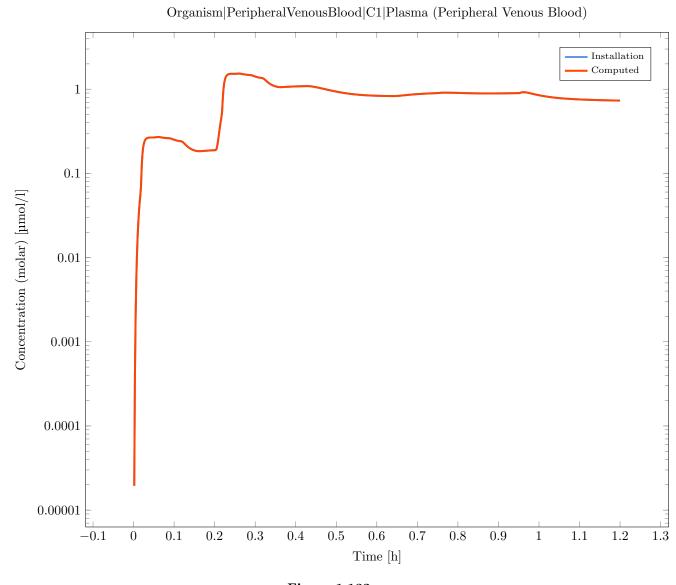


Figure 1.131

 ${\bf Simulation: Human_Oral_BiDaily_Table Formulation-S2_NoSuspension}$

Result of the validation: Valid

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



 ${\bf Figure~1.132}$

Simulation: Human_pH_SolubilityTable-S1_Table

Result of the validation: Valid

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

Deviation: 7.47E-6

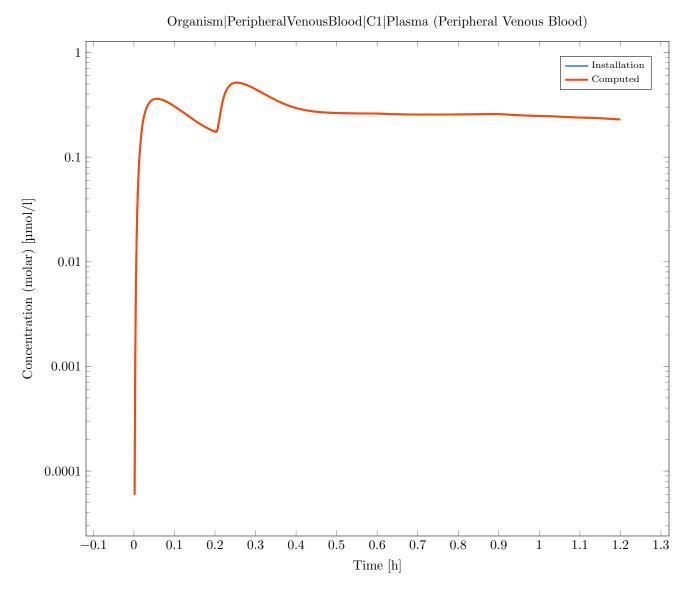


Figure 1.133

Simulation: Human_pH_SolubilityTable-S2_Measurement

Result of the validation: Valid

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

Deviation: 2.09E-6

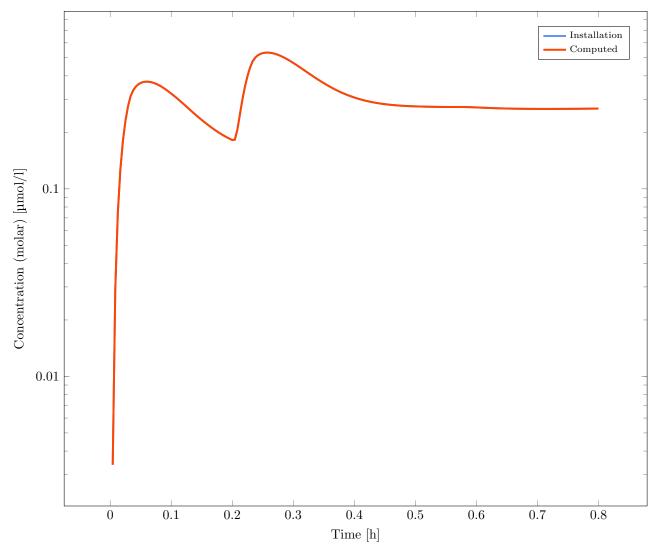


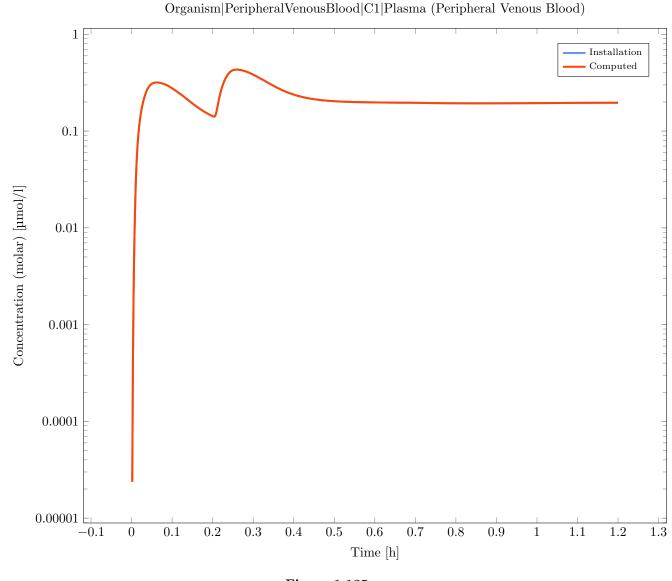
Figure 1.134

 $Simulation: \ Human_pH_SolubilityTable_SolubilityChanged$

Result of the validation: Valid

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

Deviation: 6.73E-6



 ${\bf Figure~1.135}$

 ${\bf Simulation: \ Human_pH_SolubilityTable_S4_Table_SolubilityTableChanged \ Result\ of\ the\ validation:\ Valid}$

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

Deviation: 6.13E-7

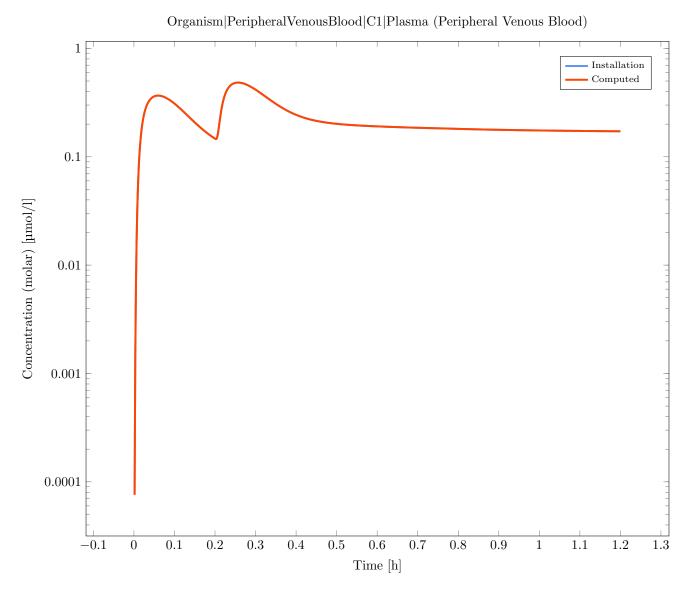


Figure 1.136

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

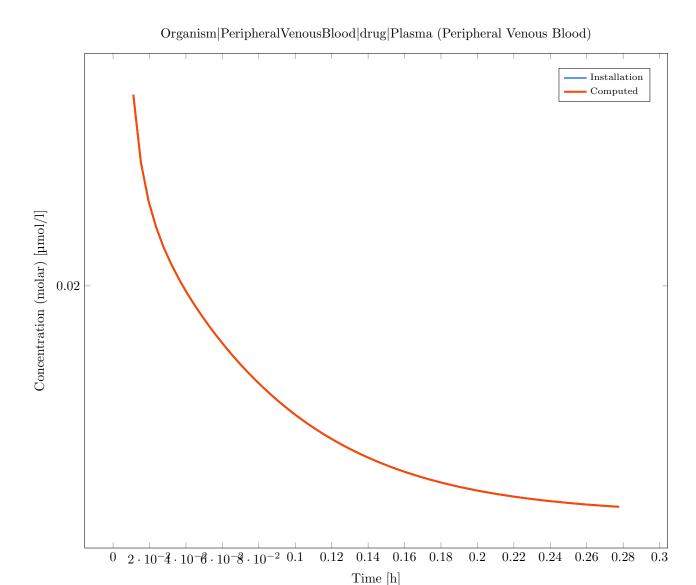


Figure 1.137

 $Simulation: \ Human_Single IV-Human_Single IV$

Result of the validation: Valid

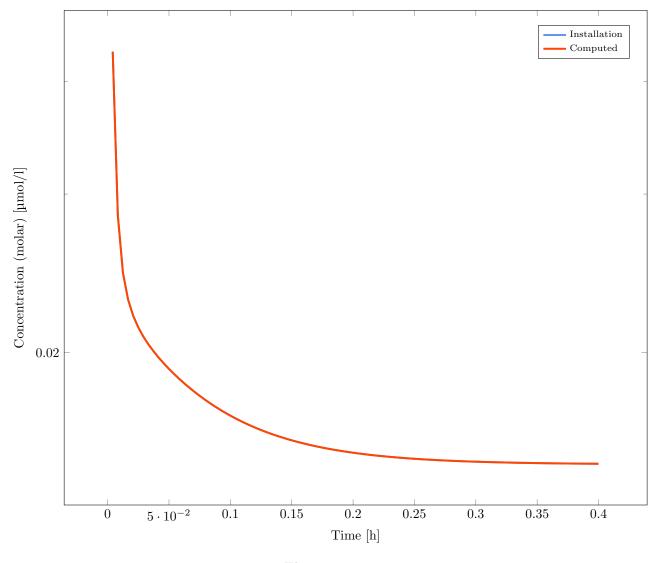


Figure 1.138

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

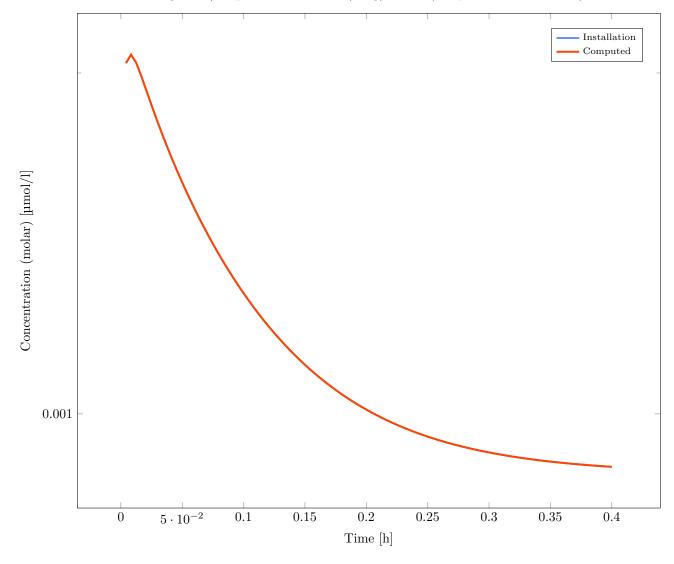


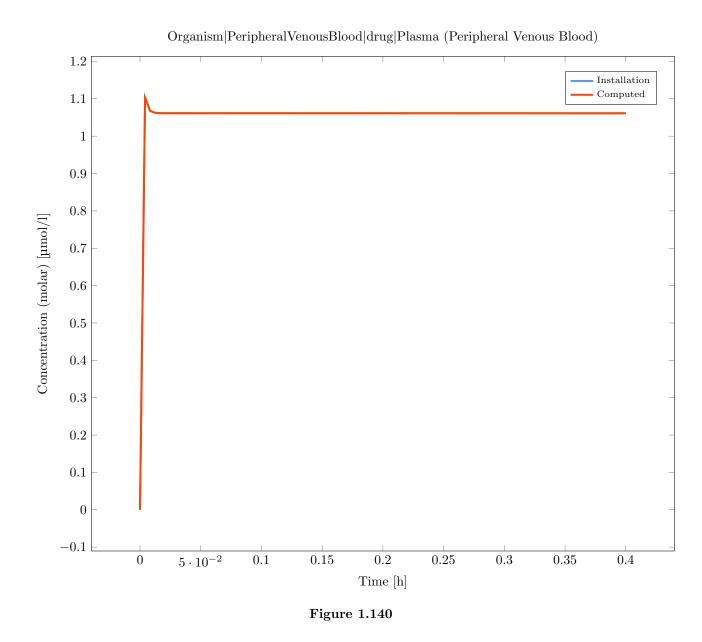
Figure 1.139

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

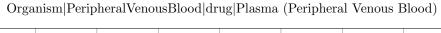
Result of the validation: Valid

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

Open Systems Pharmacology Suite - 9



Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_SingleO



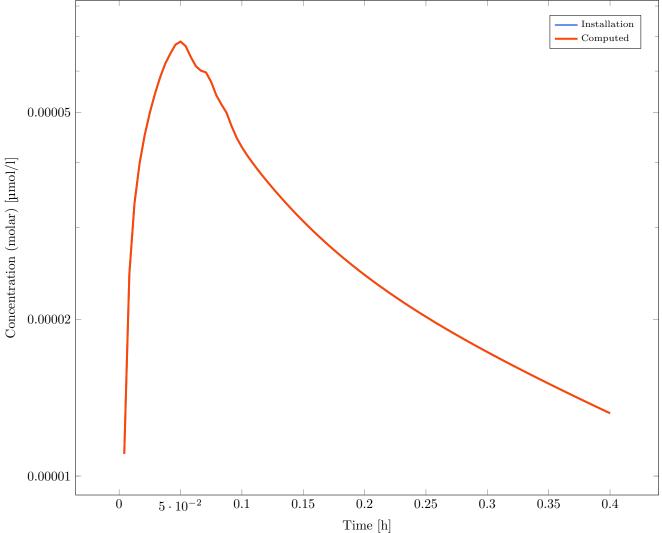
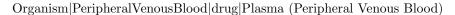


Figure 1.141

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_Singl$

Result of the validation: Valid

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



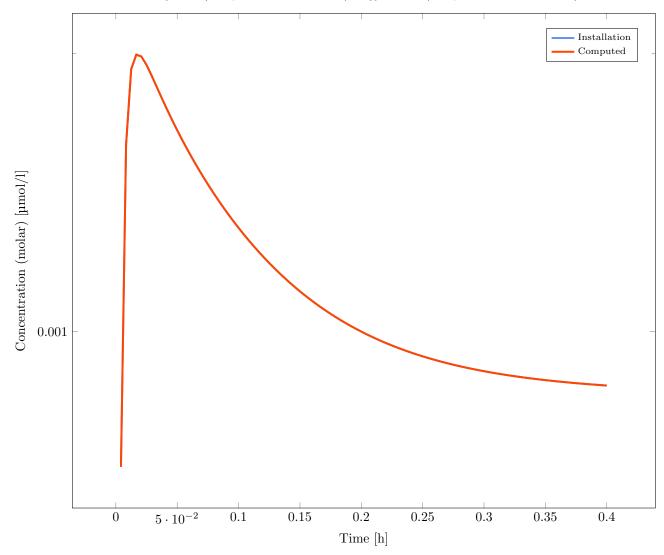


Figure 1.142

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_Singl$

Result of the validation: Valid

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

Deviation: 0

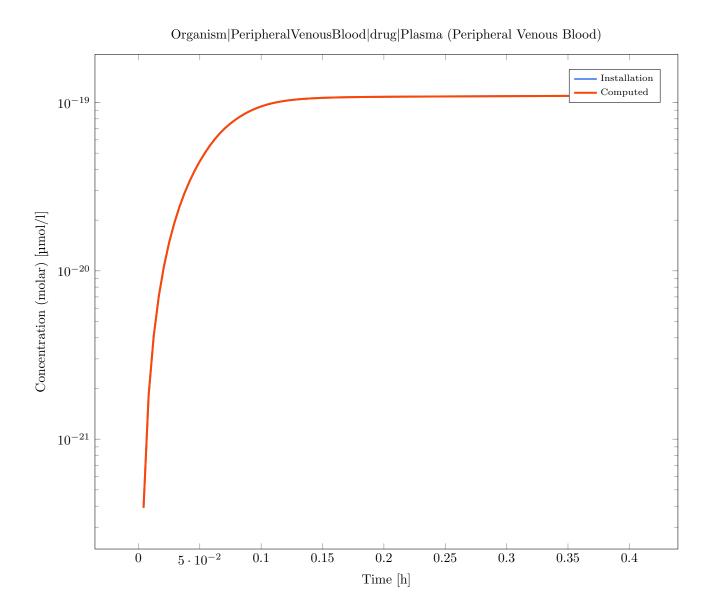


Figure 1.143

Simulation: Human_SingleORAL_Dissolved-Human_SingleORAL_Dissolved Result of the validation: Valid

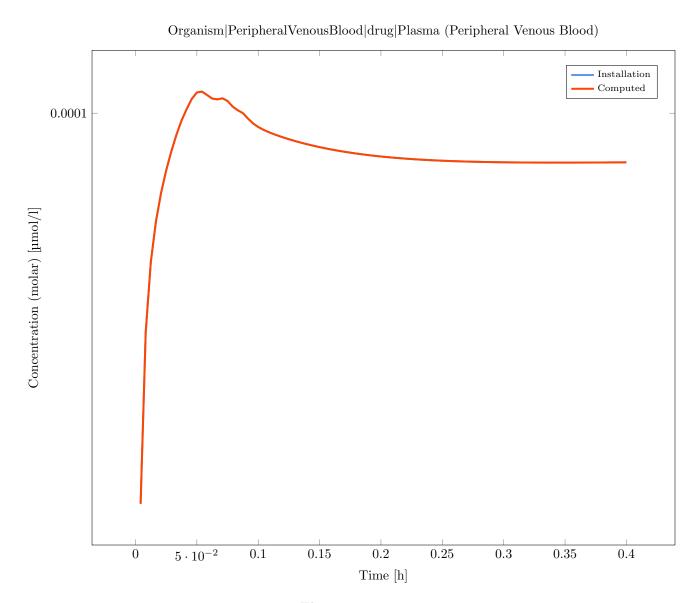


Figure 1.144

 $Simulation: \ Human_SingleORAL_Dissolved_Human_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

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

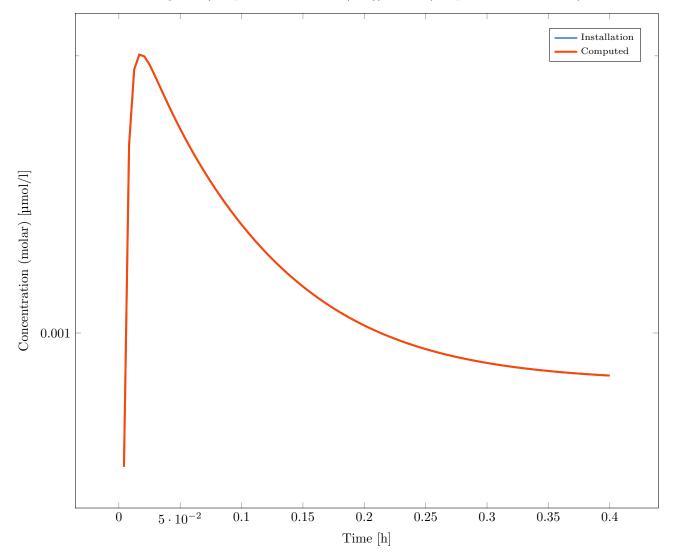
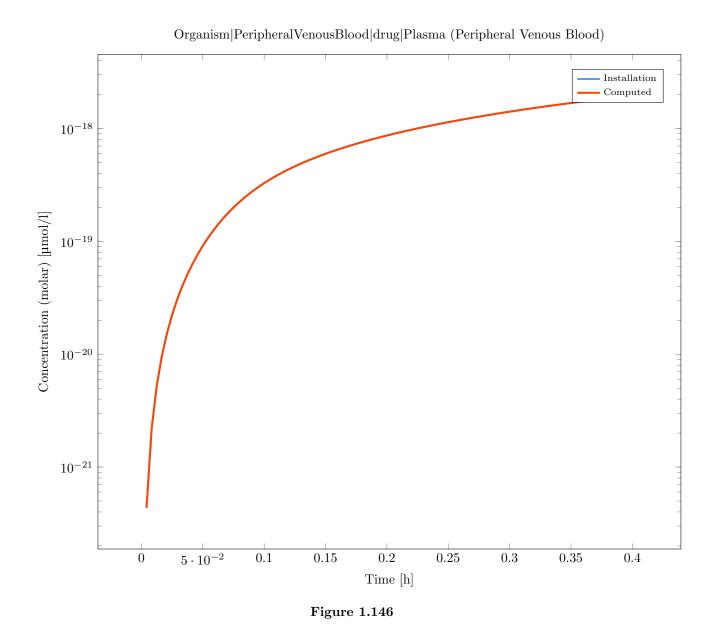


Figure 1.145

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



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

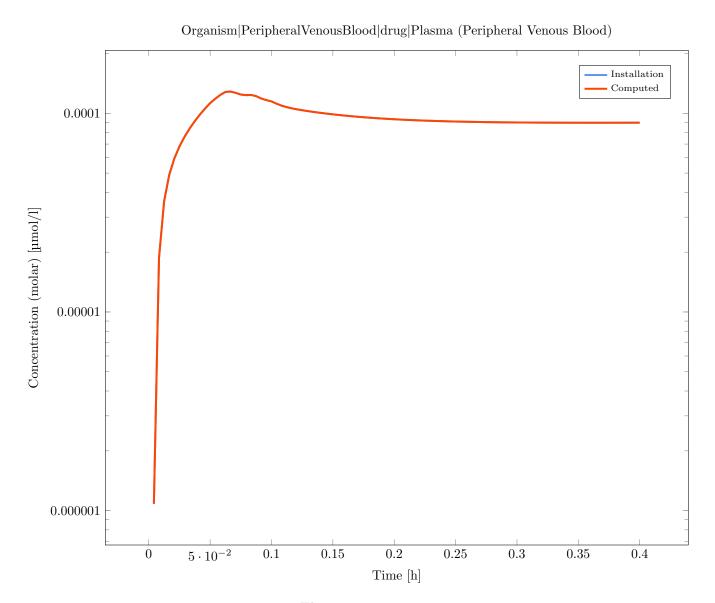


Figure 1.147

 $Simulation: \ Human_SingleORAL_Lint80-Human_SingleORAL_Lint80$

Result of the validation: Valid

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

Deviation: 0

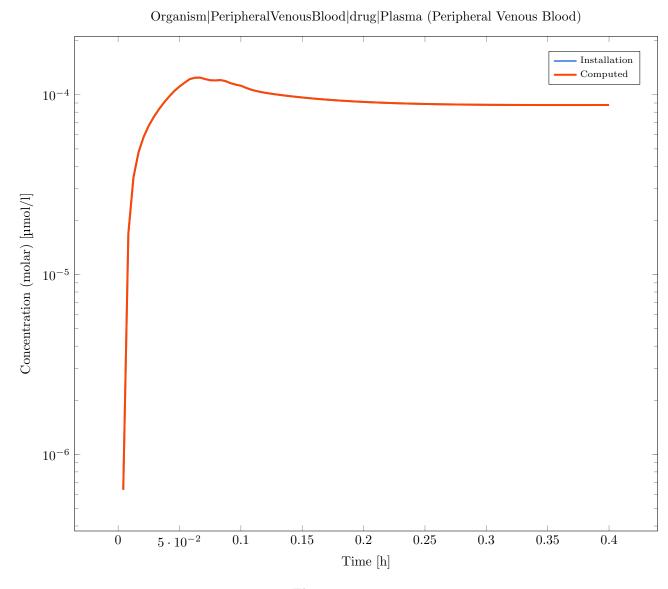


Figure 1.148

 $Simulation: Human_SingleORAL_MonoParticles_AsSuspention-Human_SingleORAL_MonoParticles_AsSuspention\\$

Result of the validation: Valid

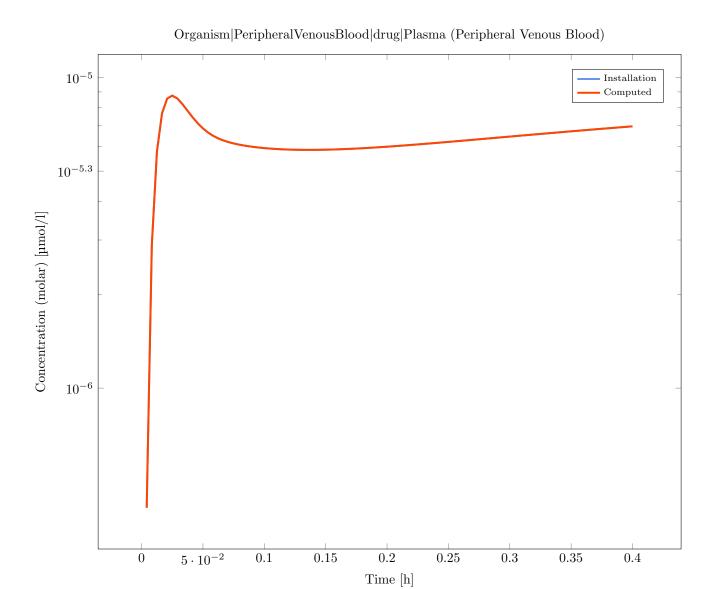
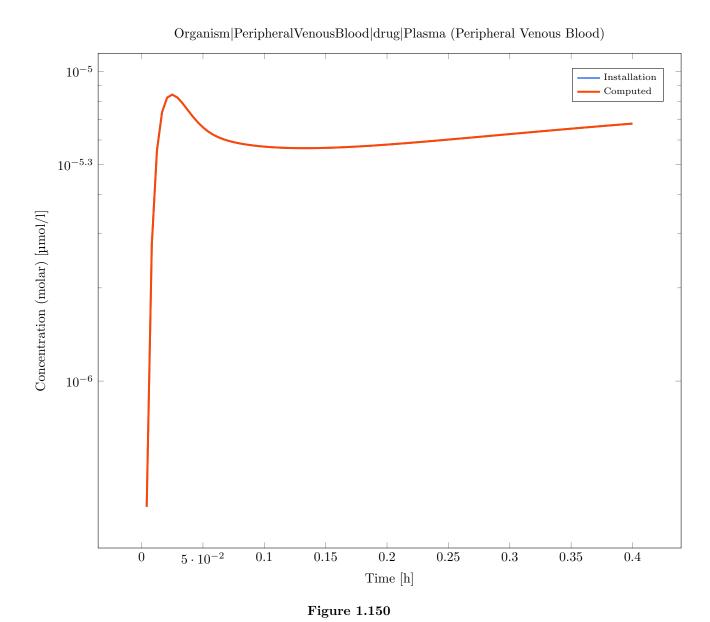


Figure 1.149

 $Simulation: \ Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention$

Result of the validation: Valid



 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNoAsSuspention\\$

Result of the validation: Valid

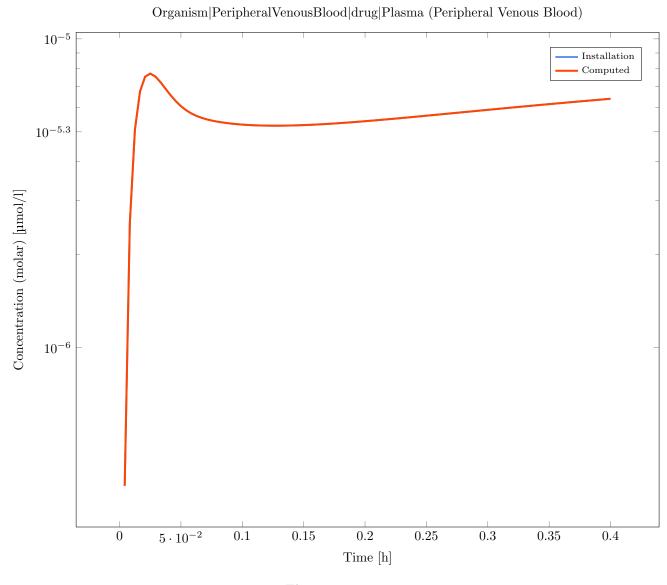


Figure 1.151

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention_dissolved_radius$

Result of the validation: Valid

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

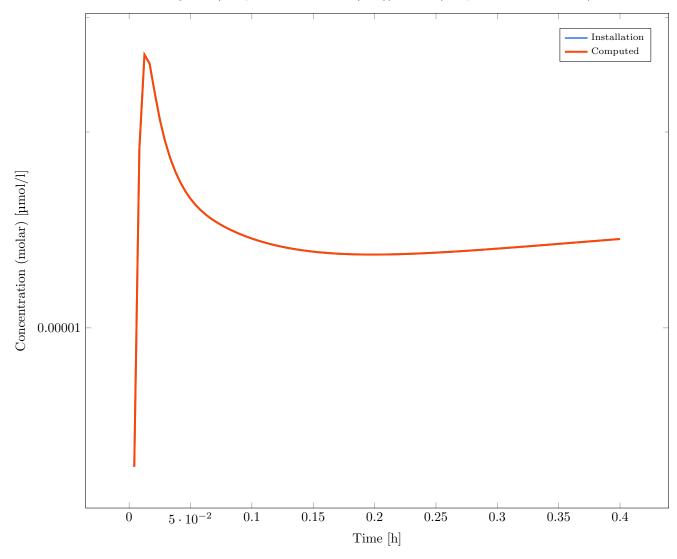


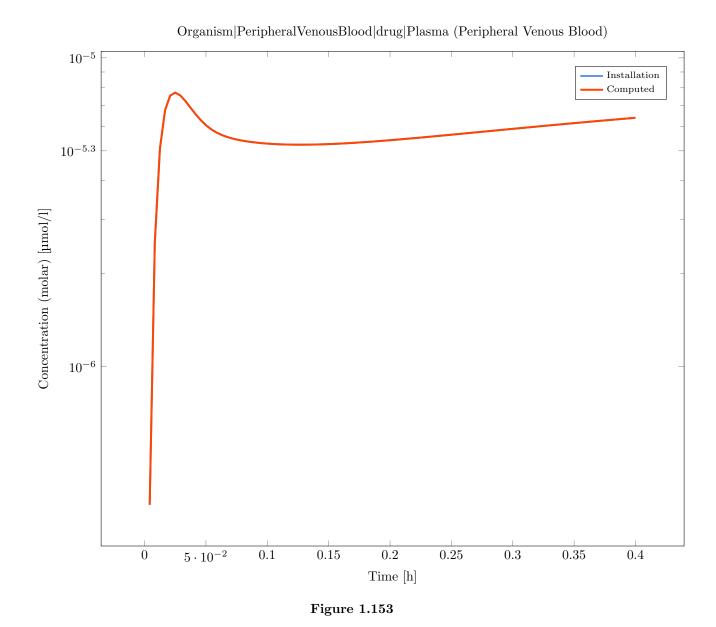
Figure 1.152

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention_treat_precipated_drug_as_soluble$

Result of the validation: Valid

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

Deviation: 0



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

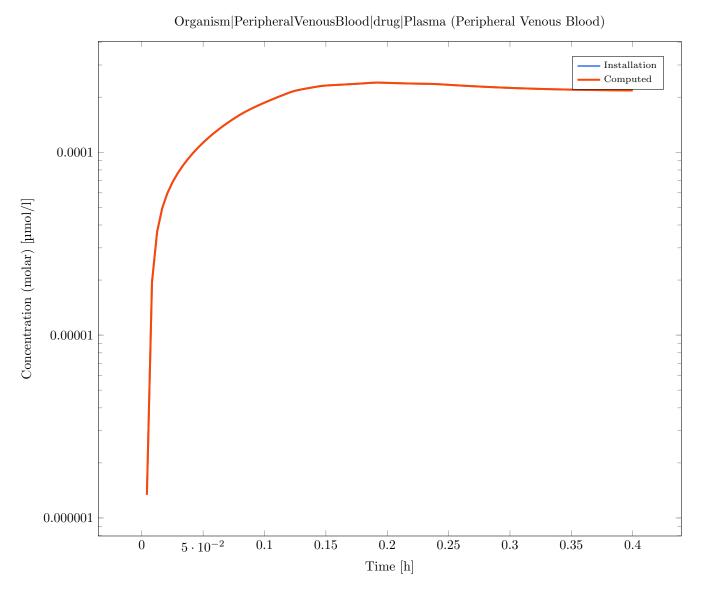


Figure 1.154

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

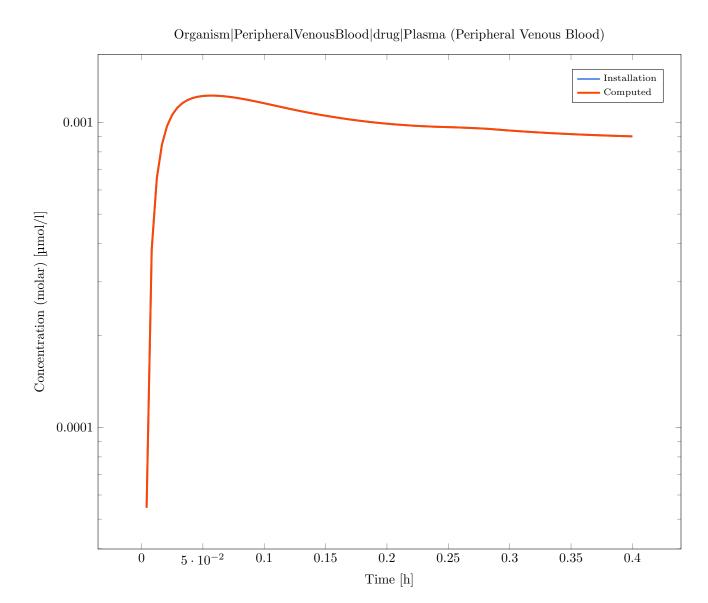
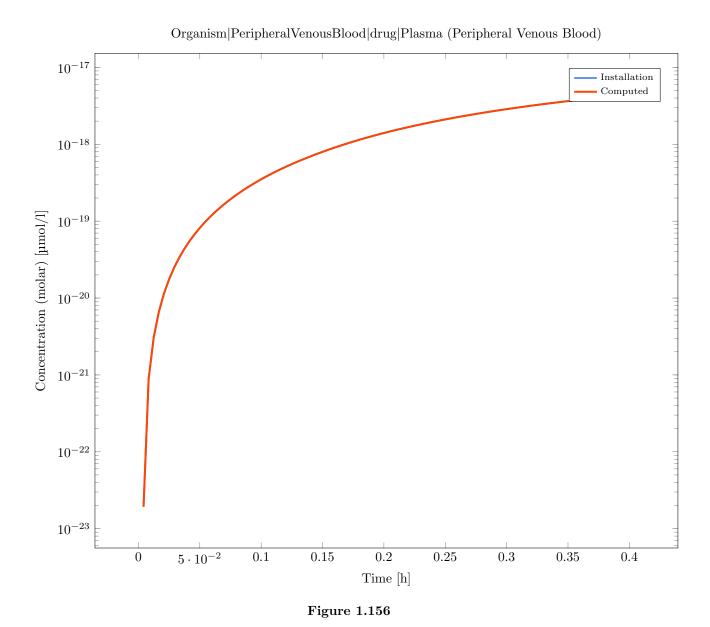
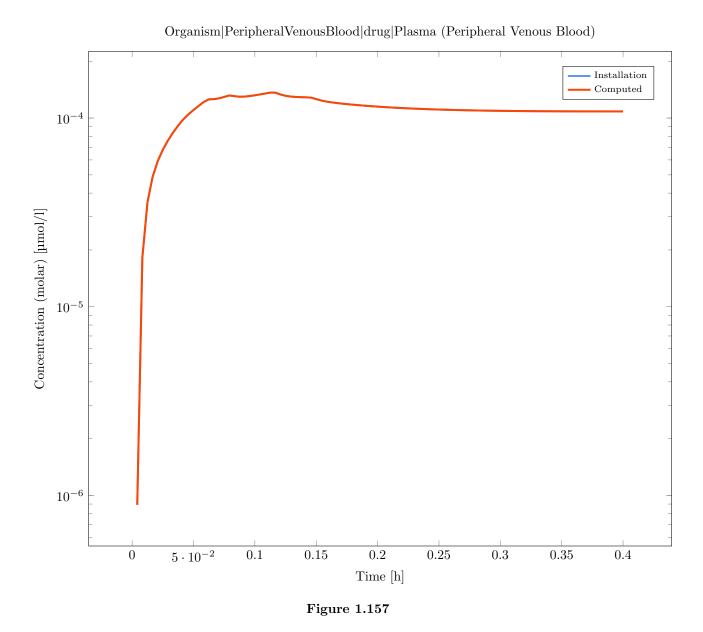


Figure 1.155

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



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



 $Simulation: \ Human_SingleORAL_Weibull-Human_SingleORAL_Weibull_MW_200_fu_0.2_LogP_5 \\ Result of the validation: \ Valid$

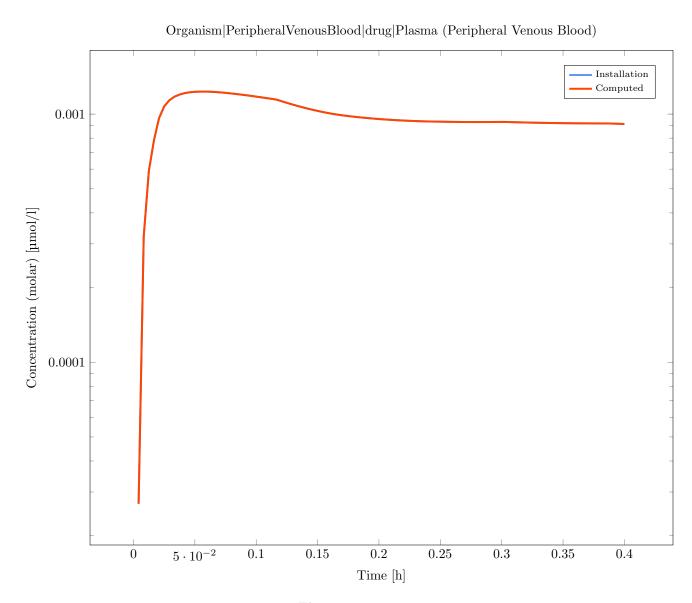


Figure 1.158

 $\label{lem:singleORAL_Weibull-Human_SingleORAL_Weibull_MW_800_fu_0.6_LogP_5 \\ Result of the validation: Valid$

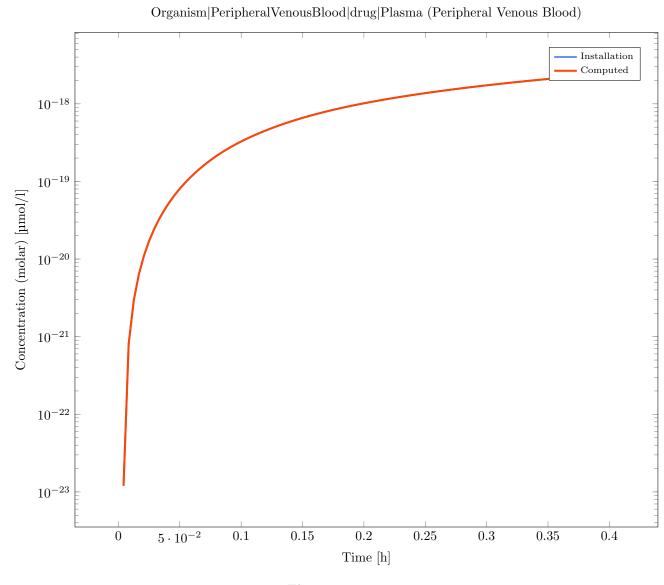


Figure 1.159

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

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

Figure 1.160

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

0.1

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

0

 $5 \cdot 10^{-2}$

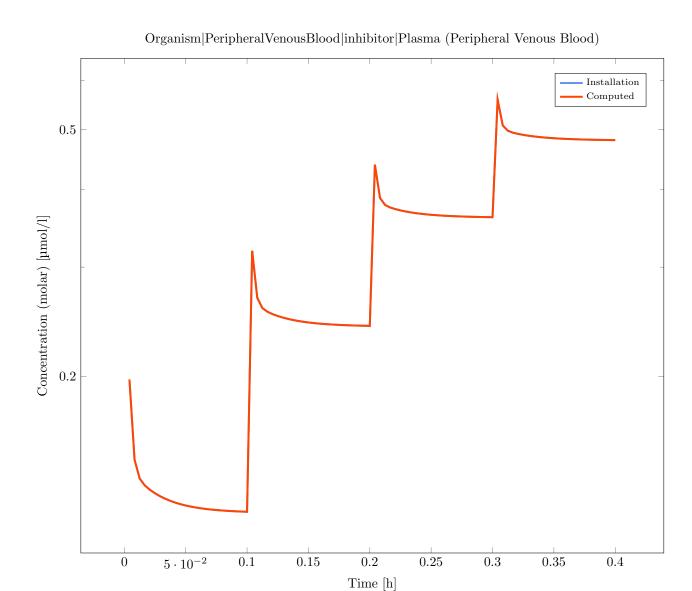
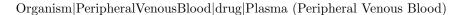


Figure 1.161

Simulation: Minipig_SingleORAL_Dissolved-Minipig_SingleORAL_Dissolved Result of the validation: Valid



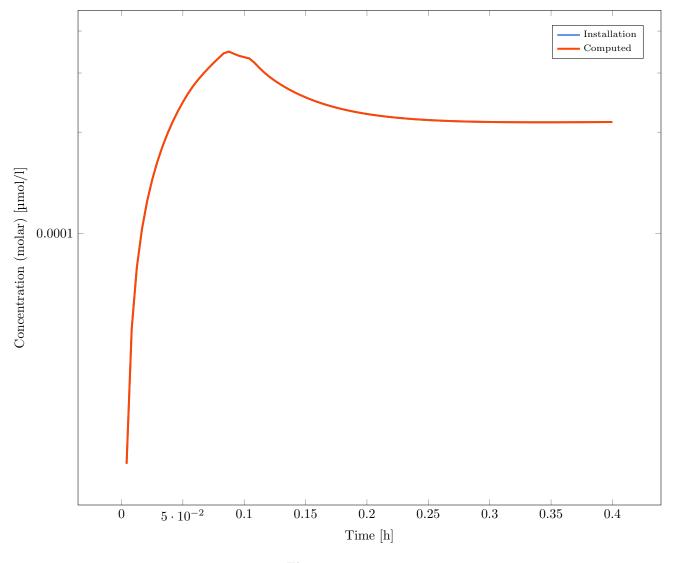


Figure 1.162

 $Simulation: Minipig_SingleORAL_Dissolved_Minipig_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

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

Deviation: 0

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

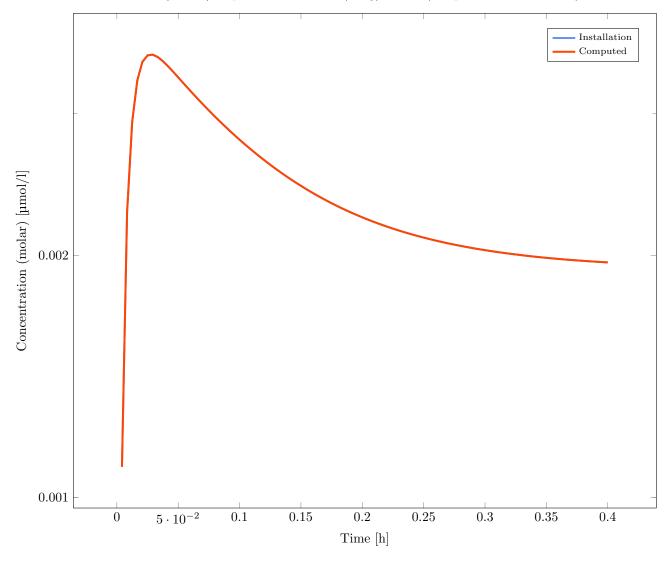


Figure 1.163

 $Simulation: \ Minipig_SingleORAL_Dissolved_Minipig_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-5$ Result of the validation: Valid

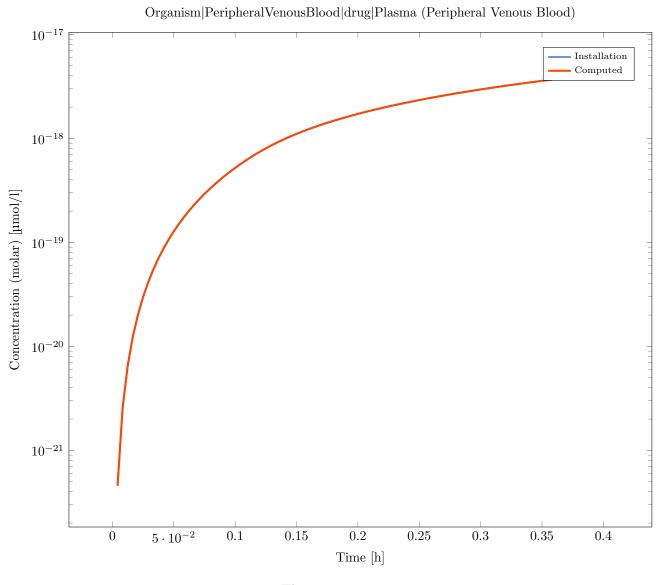


Figure 1.164

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

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

0.15 0.2

Time [h]

0.25

0.35

0.3

0.4

0.1

Figure 1.165

 $Simulation: Monkey_SingleORAL_Dissolved_Monkey_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

0

 $5 \cdot 10^{-2}$

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

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

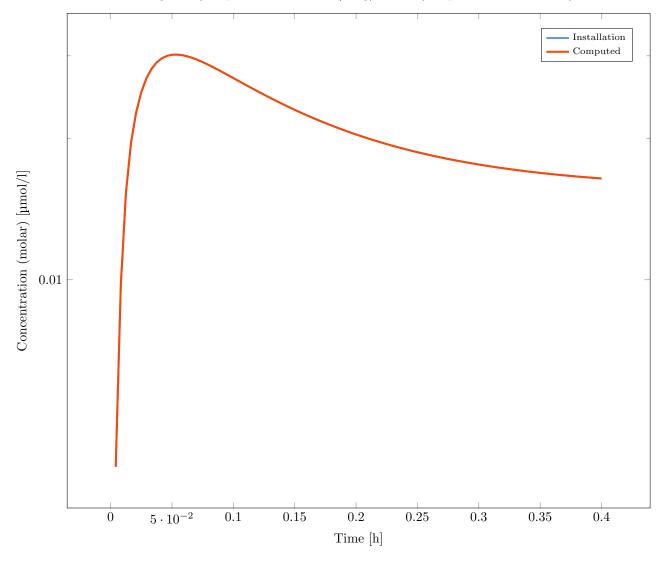


Figure 1.166

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

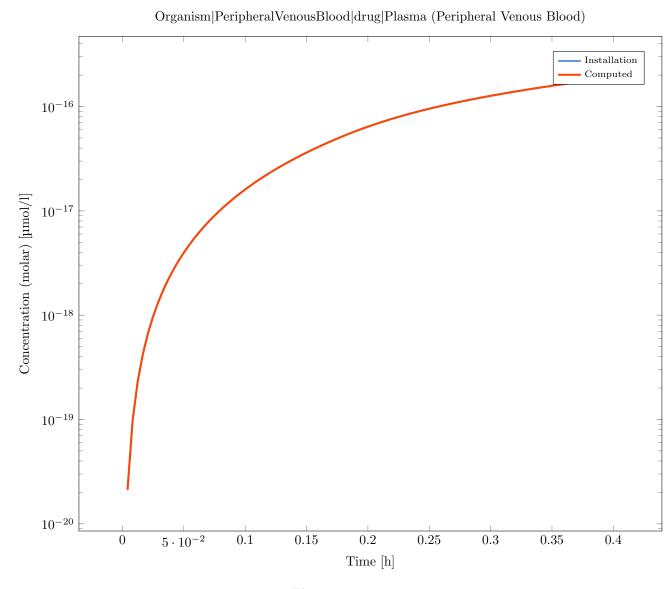


Figure 1.167

Simulation: Mouse_SingleORAL_Dissolved-Mouse_SingleORAL_Dissolved Result of the validation: Valid



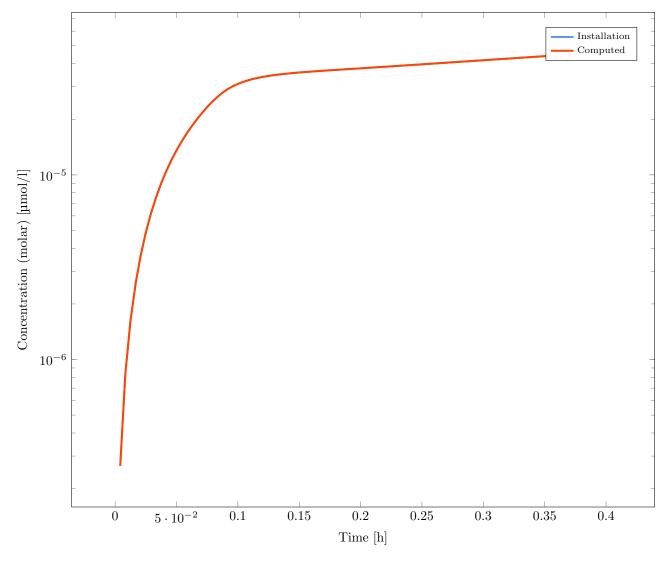


Figure 1.168

 $Simulation: Mouse_SingleORAL_Dissolved_MOUSe_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$ Result of the validation: Valid

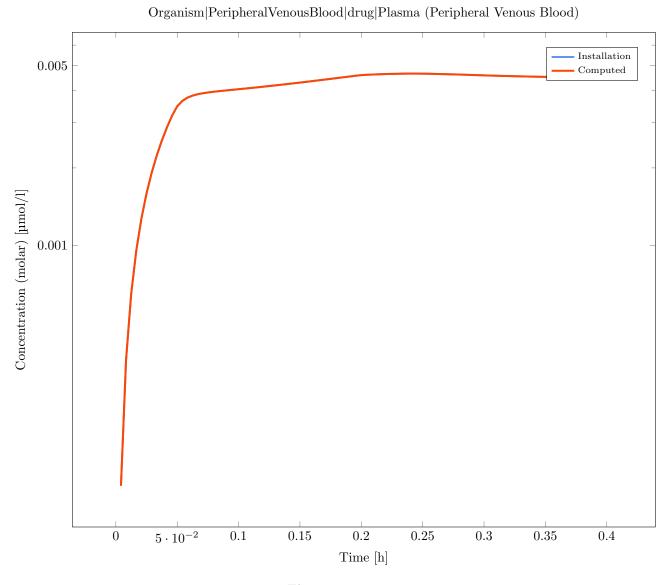
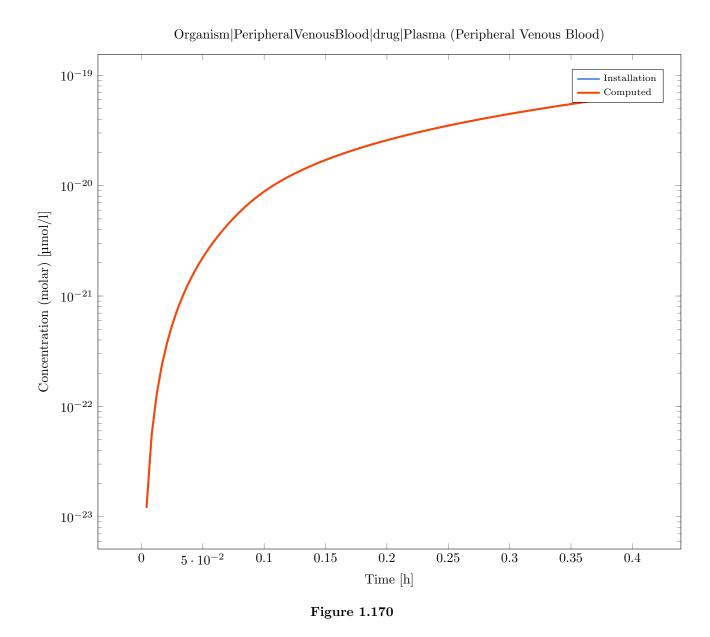
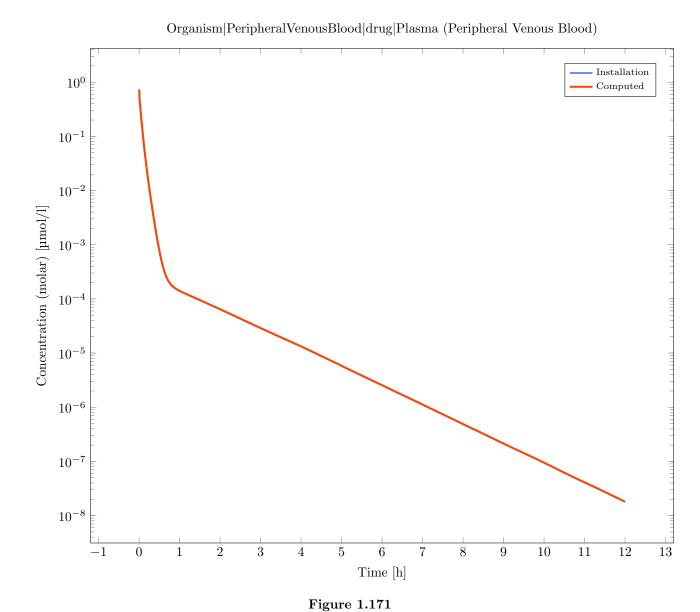
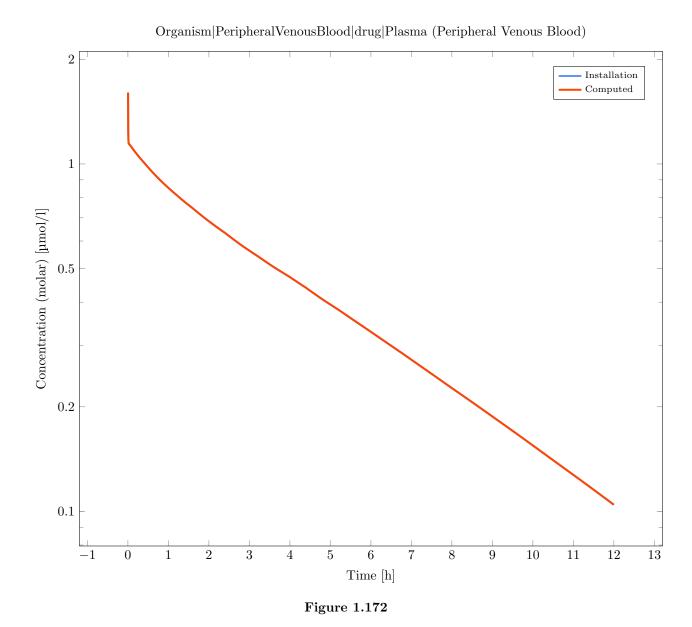


Figure 1.169

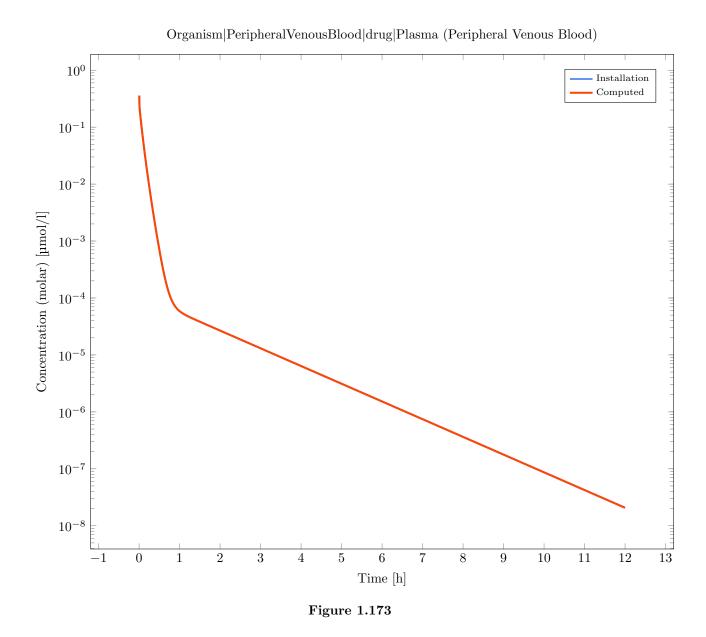
 $\label{local_simple_oral_bis} Simulation: Mouse_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-5 \\ Result of the validation: Valid$







 $\label{lem:condition:condition:preterm_SingleIV_Age_15_GA_32_CYP3A4-Preterm_SingleIV_Age_15_GA_25_CYP3A4-Preterm_SingleIV_Age_15_GA_25_CYP3A4-Preterm_SingleIV_Age_15_GA_25_CYP3A4-Preterm_SingleIV_Age_15_GA_25_CYP3A4-Preterm_SingleIV_Age_15_GA_25_CYP3A4-Preterm_SingleIV_Age_15_GA_25_CYP3A4-Preterm_SingleIV_Age_15_GA_25_CYP3A4-Preterm_SingleIV_Age_15_CYP3A4-Preterm_SingleIV_Age_$



 $\label{lem:simple_simple_simple_simple_simple} Simulation: \ Preterm_SingleIV_Age_15_GA_32_GFR-Preterm_Sin$

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed Concentration (molar) $[\mu]$ 0.1 0.01 2 3 10 -10 4 5 6 11 12 13

Figure 1.174

Time [h]

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

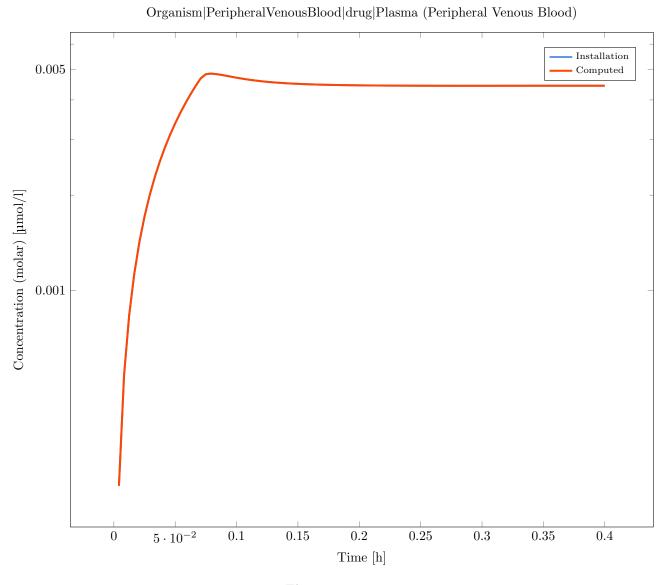


Figure 1.175

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

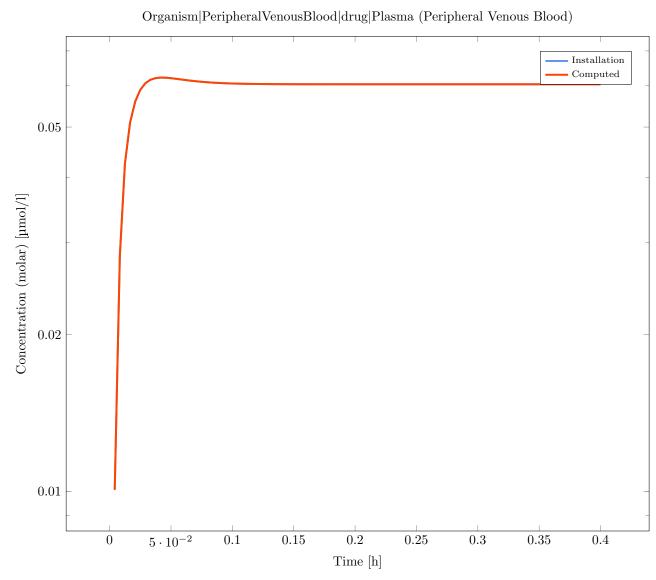


Figure 1.176

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

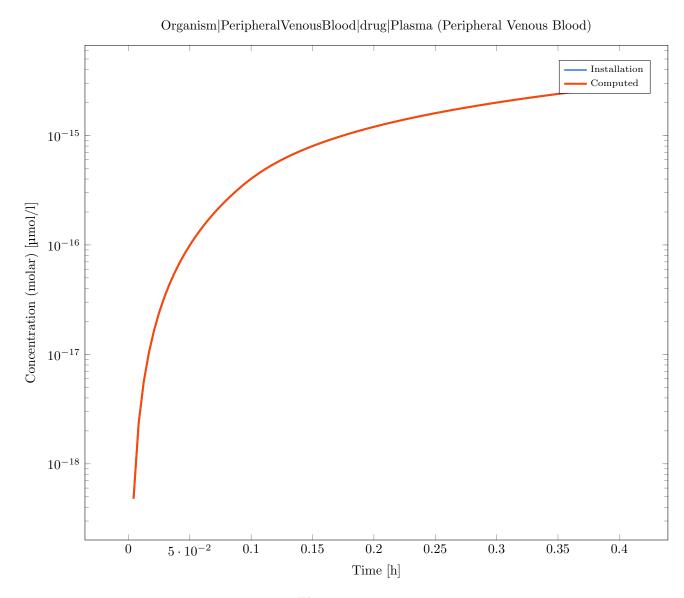
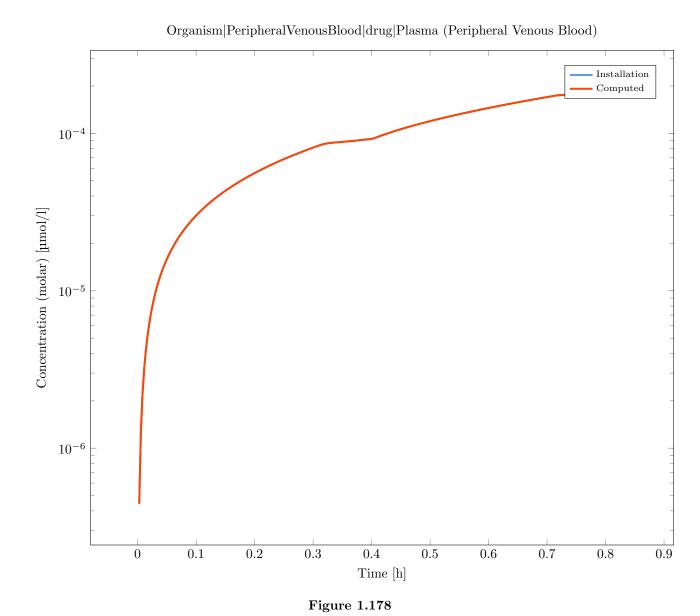


Figure 1.177

Simulation: Rat_MultiORAL_6_6_12_Dissolved-Rat_MultiORAL_6_6_12_Dissolved Result of the validation: Valid



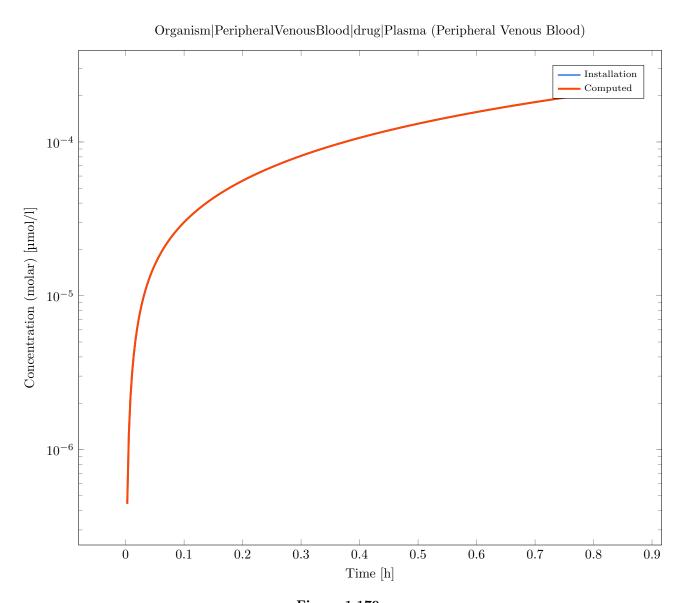


Figure 1.179

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

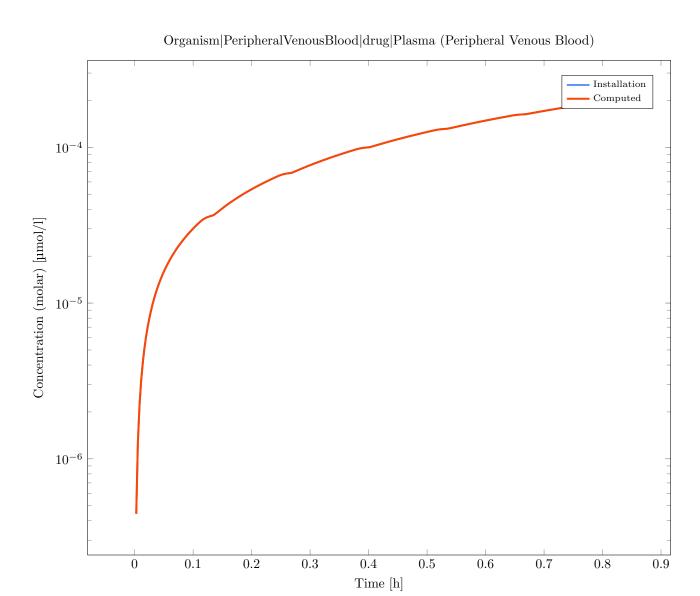


Figure 1.180

 $Simulation: Single IV_2 Pores_Human-Single IV_2 Pores_Human$

Result of the validation: Valid

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

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

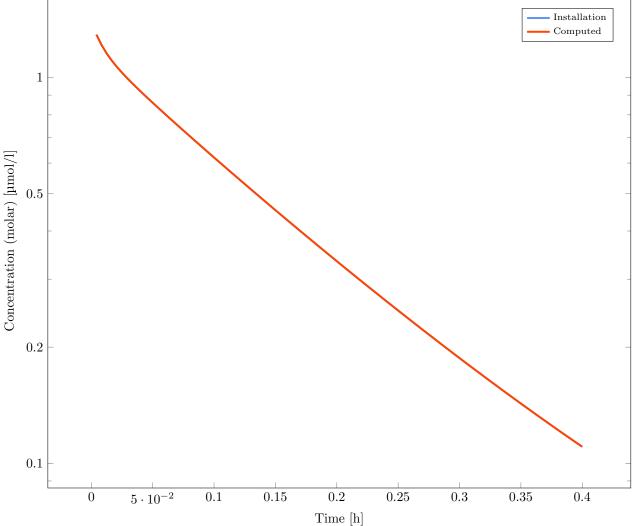


Figure 1.181

Simulation: SingleIV_2Pores_Human-SingleIV_2Pores_Human_SimulationC Result of the validation: Valid

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

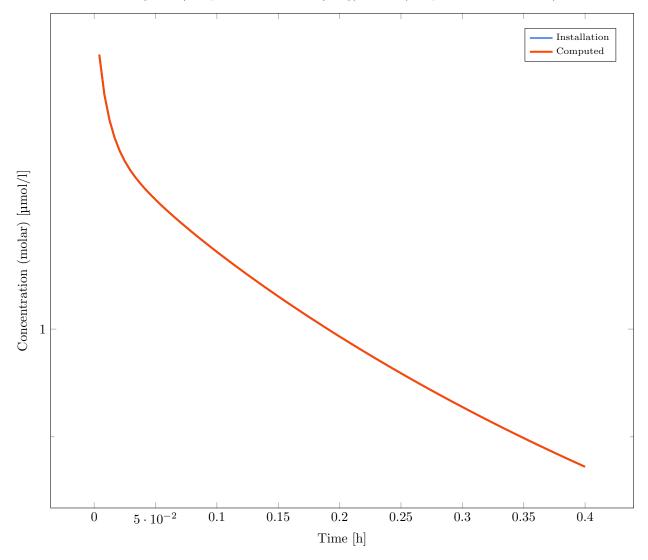


Figure 1.182

Simulation: SingleIV_2Pores_Human-SingleIV_2Pores_Human_SimulationD Result of the validation: Valid

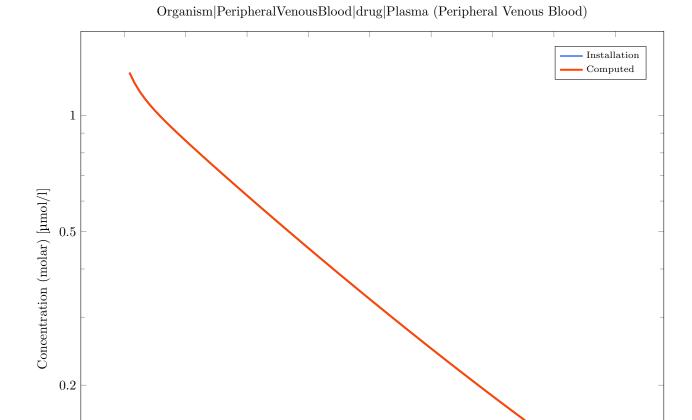


Figure 1.183

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)

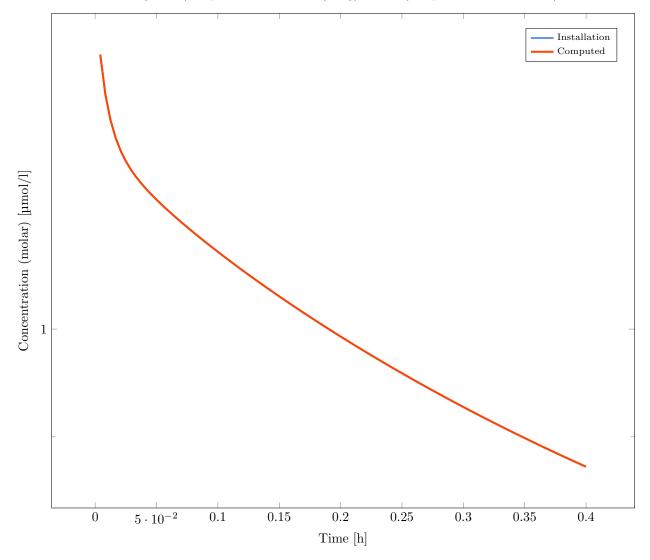


Figure 1.184

 $Simulation: Single IV_2 Pores_Monkey-Single IV_2 Pores_Monkey$

Result of the validation: Valid

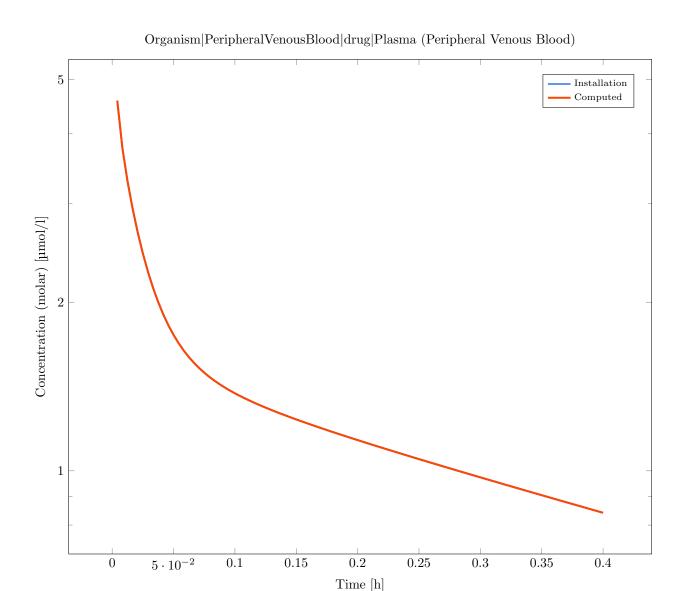


Figure 1.185

Simulation: SingleIV_2Pores_Monkey-SingleIV_2Pores_Monkey_SimulationG Result of the validation: Valid



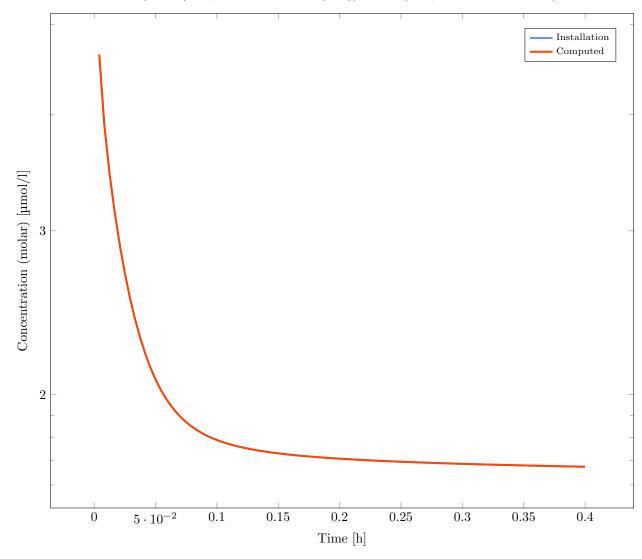


Figure 1.186

Simulation: SingleIV_2Pores_Monkey-SingleIV_2Pores_Monkey_SimulationH Result of the validation: Valid

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

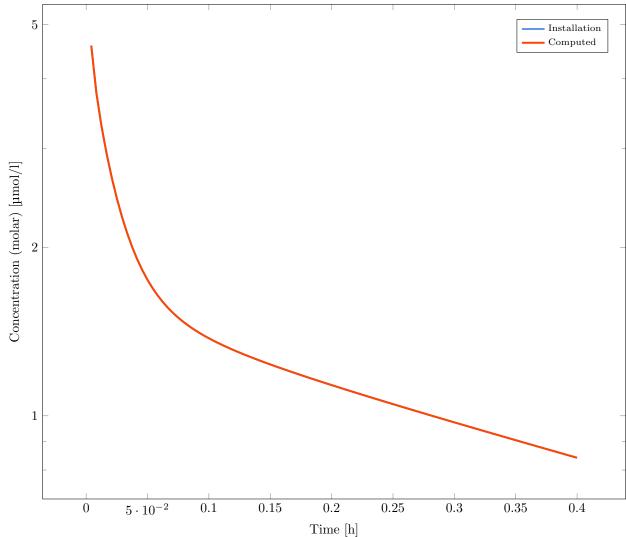


Figure 1.187

 $Simulation: Single IV_2 Pores_Mouse-Single IV_2 Pores_Mouse$

Result of the validation: Valid

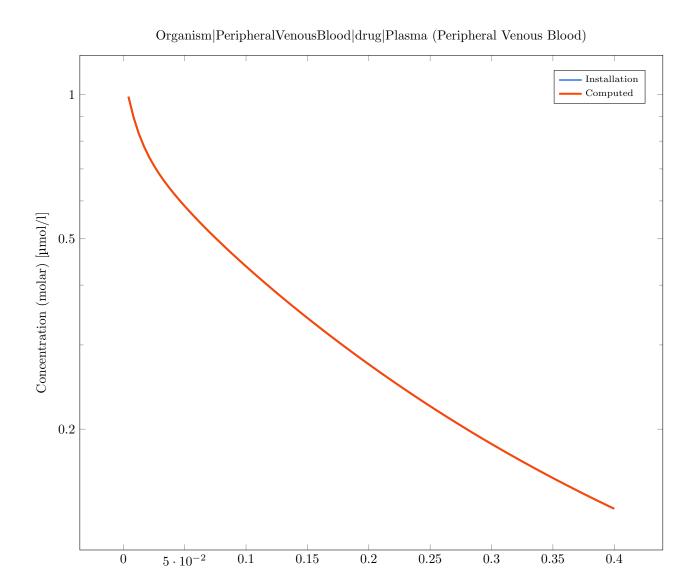


Figure 1.188

Time [h]

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse_SimulationA Result of the validation: Valid

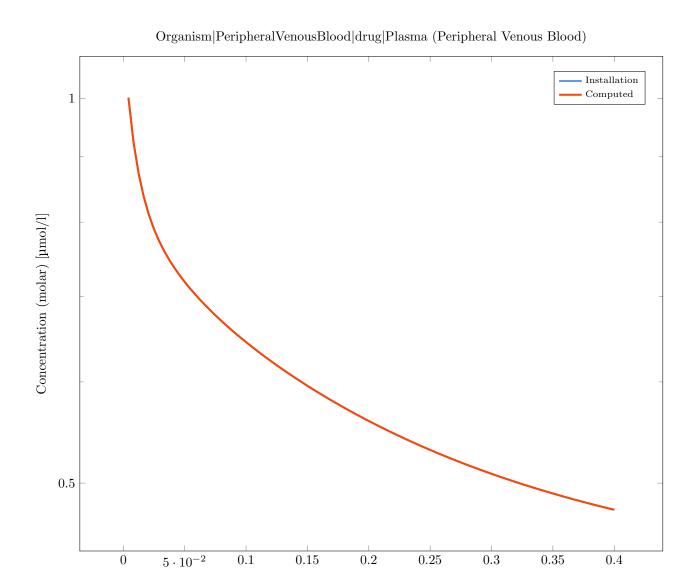


Figure 1.189

Time [h]

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse_SimulationB Result of the validation: Valid

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed O.5 O.2

Figure 1.190

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

 $5\cdot 10^{-2}$

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

Figure 1.191

 $Simulation: Single IV_C1_4 Comp_standard_stand$

Time [h]

Result of the validation: Valid

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



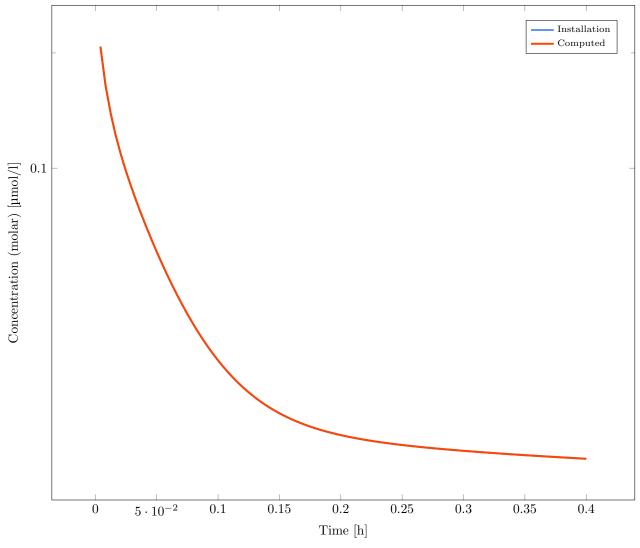


Figure 1.192

 $Simulation: Single IV_C2_4 Comp_PT_standard_st$

Organism|PeripheralVenousBlood|C2|Plasma (Peripheral Venous Blood)

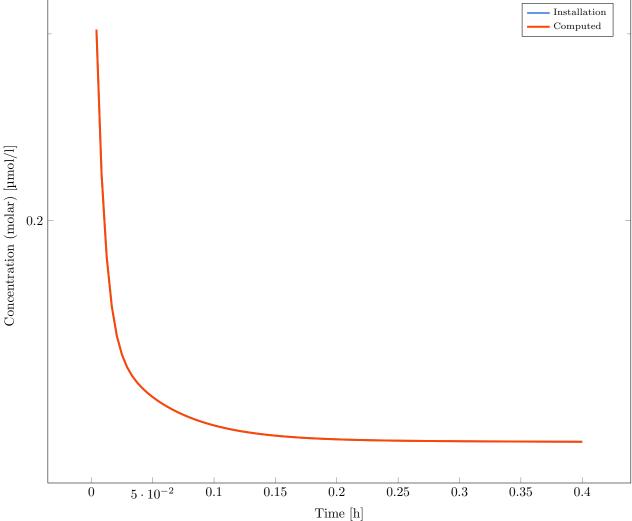


Figure 1.193

 $Simulation: Single IV_C2_4 Comp_RR_standard_st$

Output Path: Organism |Peripheral Venous
Blood |C2 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$ 1.2

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

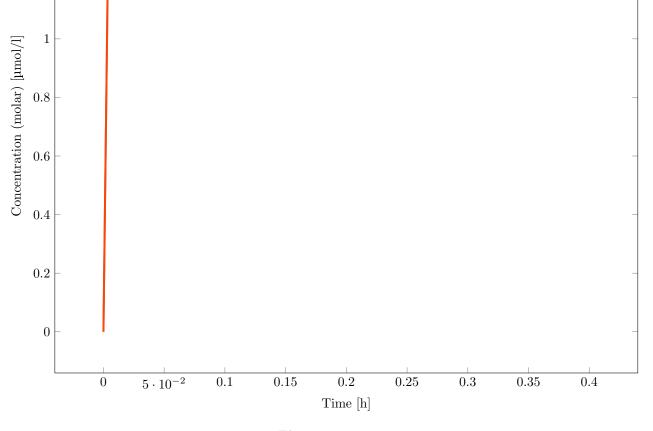


Figure 1.194

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

Result of the validation: Valid

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

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

Figure 1.195

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single IV_C3_4 Comp_RR_schmitt_standard-Single IV_C3_schmitt_standard-Single IV_C3_schmitt$

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 1.196

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

Result of the validation: Valid

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

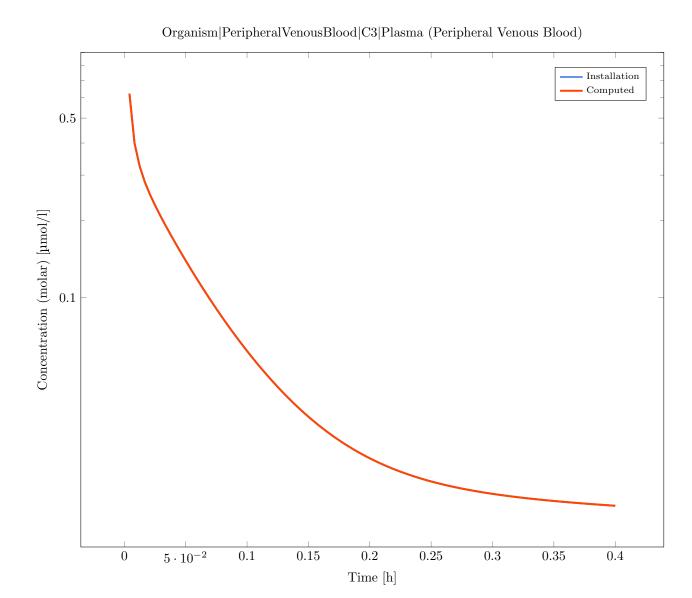


Figure 1.197

 $Simulation: Single IV_C4_2 Pores_RR_standard_s$

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

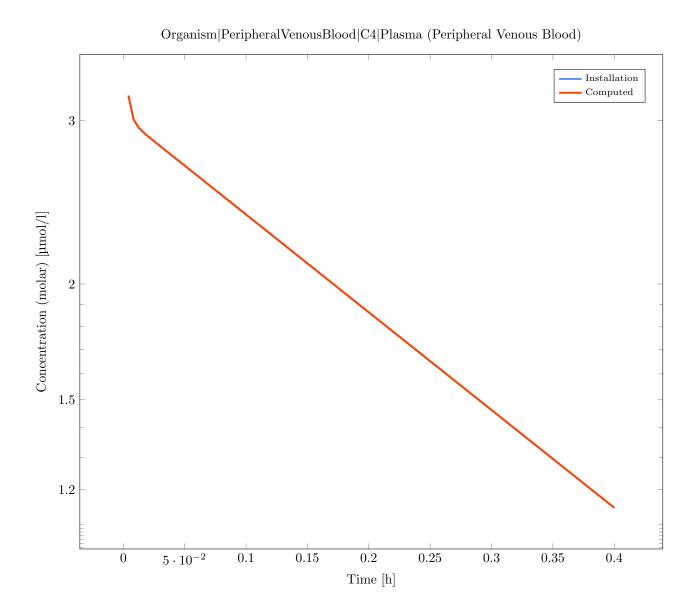


Figure 1.198

 $Simulation: Single IV_C4_4 Comp_Ber_standard_s$

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

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

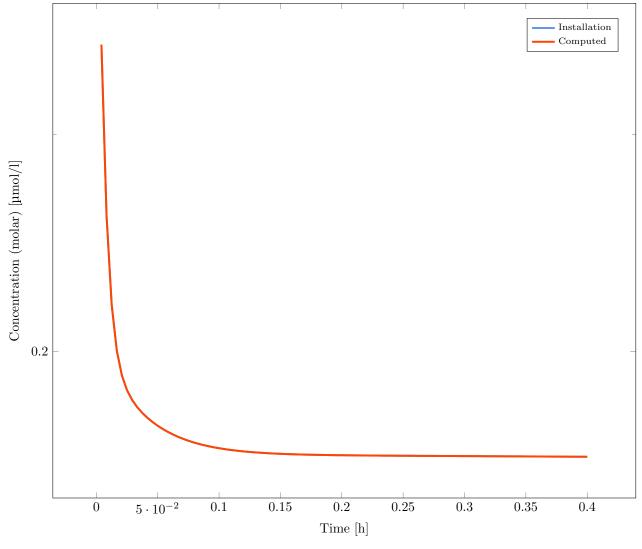
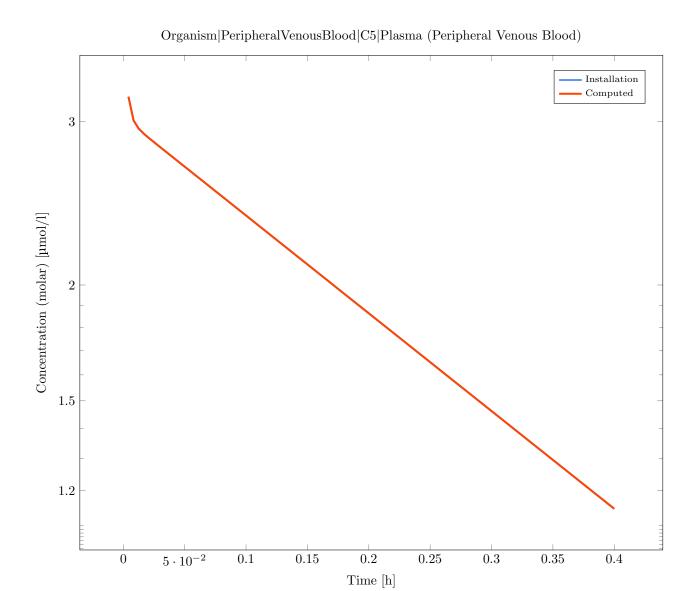


Figure 1.199

 $Simulation: Single IV_C5_2 Pores_Ber_standard_$



 $Simulation: Single IV_C5_2 Pores_PT_standard_s$

Figure 1.200

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

Result of the validation: Valid

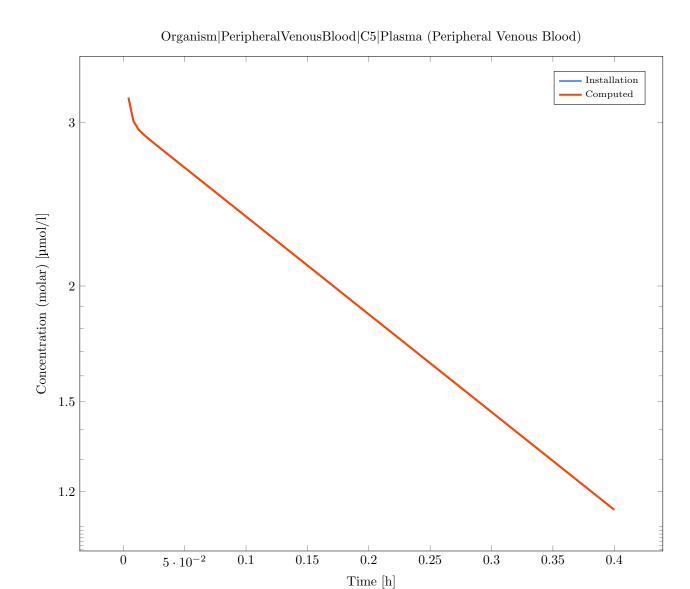


Figure 1.201

 $Simulation: SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_schmitt$

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



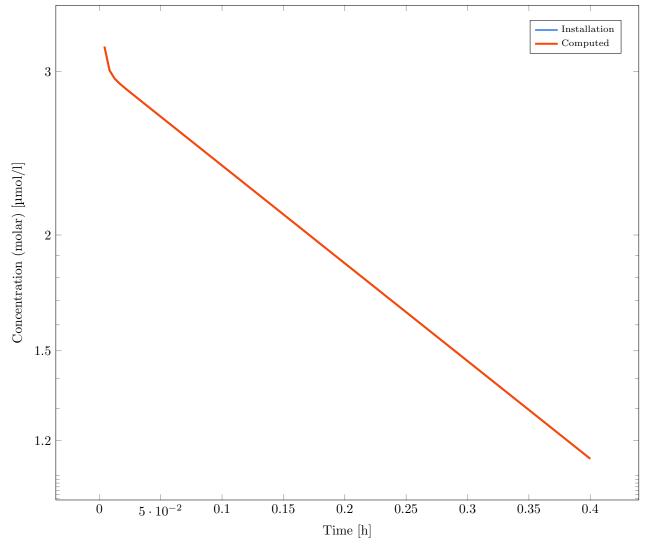


Figure 1.202

 $Simulation: Single IV_C6_2 Pores_standard_stan$

Result of the validation: Valid

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

$Organism | Peripheral Venous Blood | C6 | Plasma \ (Peripheral Venous Blood)$

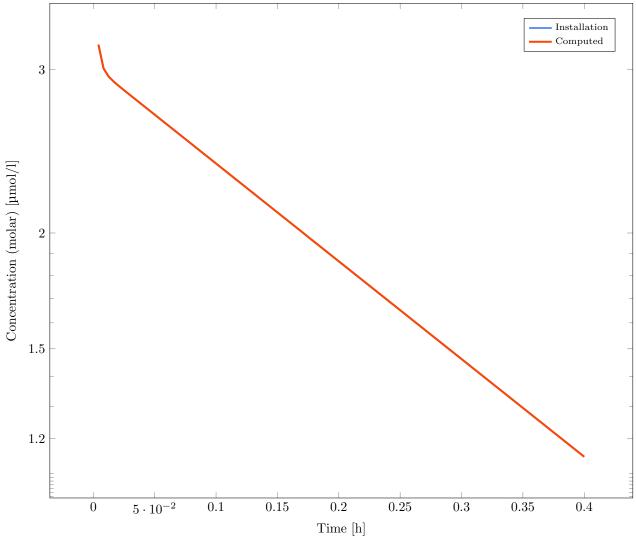


Figure 1.203

 $Simulation: Single IV_C7_2 Pores_standard_schmitt_standard_Single IV_C7_2 Pores_standard_schmitt_schmitt$

Result of the validation: Valid

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

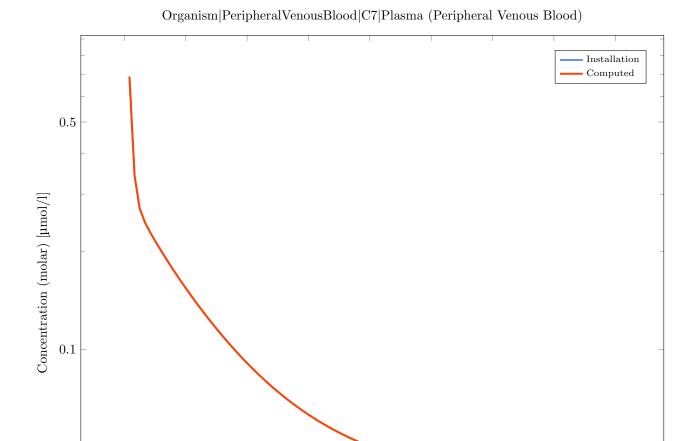


Figure 1.204

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

0.1

$Organism|Peripheral Venous Blood|C7|Plasma\ (Peripheral Venous Blood)$

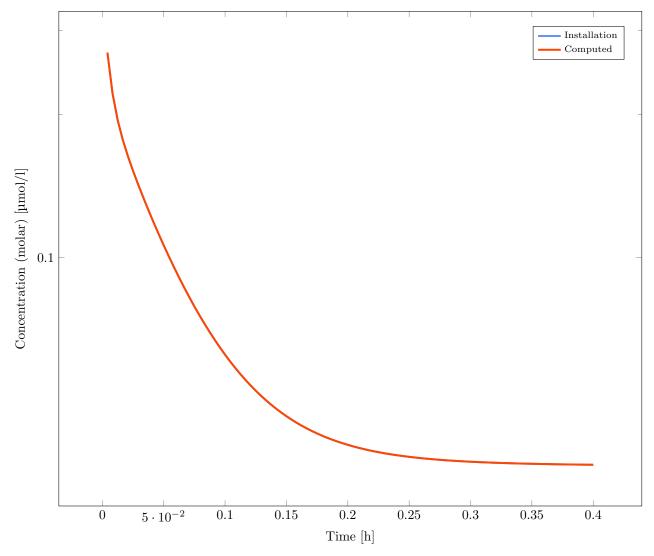
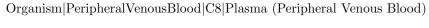


Figure 1.205

 $Simulation: Single IV_C8_2 Pores_standard_schmittnormalized_standard_Single IV_C8_2 Pores_standard_schmittnormalized_schmittnormalized_schmittnor$

Result of the validation: Valid

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



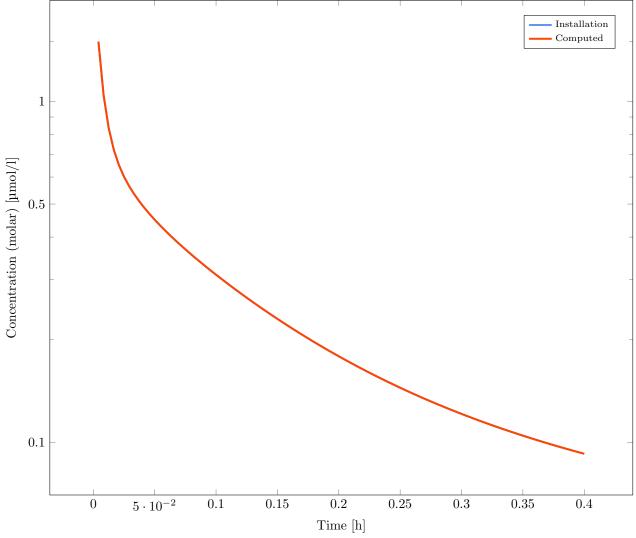


Figure 1.206

 $Simulation: Single IV_C9_2 Pores_schmitt_standard_standard_Single IV_C9_2 Pores_schmitt_standard_sta$

Result of the validation: Valid

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

Organism|PeripheralVenousBlood|C9|Plasma (Peripheral Venous Blood)

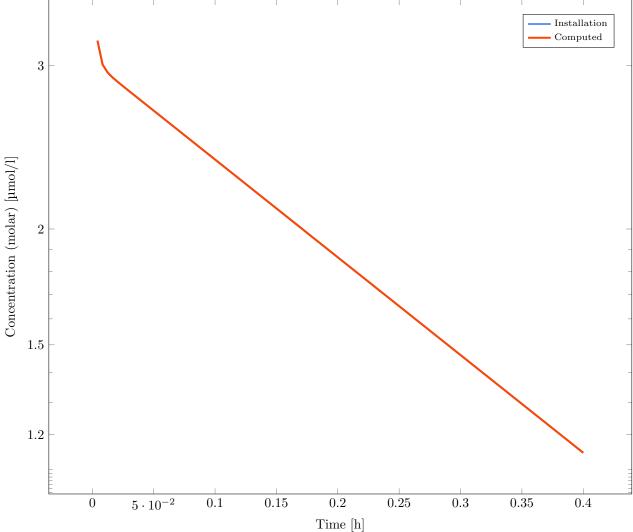


Figure 1.207

 $Simulation: Single ORAL_C10_4 Comp_PT_standard_standard_Single ORAL_C10_4 Comp_PT_standard_$

Result of the validation: Valid

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

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

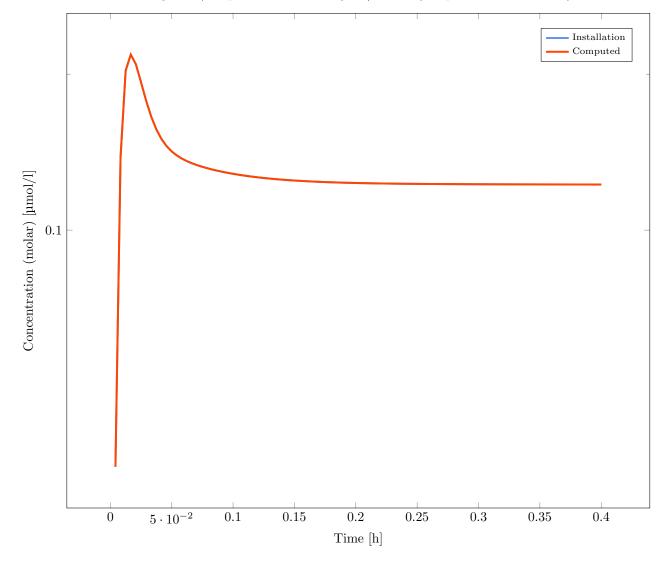


Figure 1.208

 $Simulation: Single ORAL_C11_4 Comp_schmitt_standard_standard_Single ORAL_C11_4 Comp_schmitt_standard$

Result of the validation: Valid

 $Output \ Path: \ Organism | Peripheral Venous Blood | C11 | Plasma \ (Peripheral \ Venous \ Blood)$

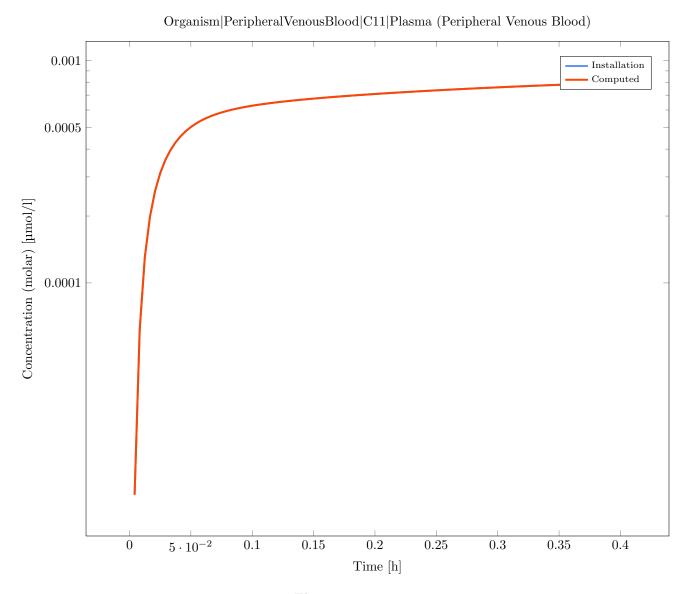


Figure 1.209

 $Simulation: Single ORAL_C11_4 Comp_standard_st$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood | C11 |Plasma (Peripheral Venous Blood)
 Deviation: 0

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

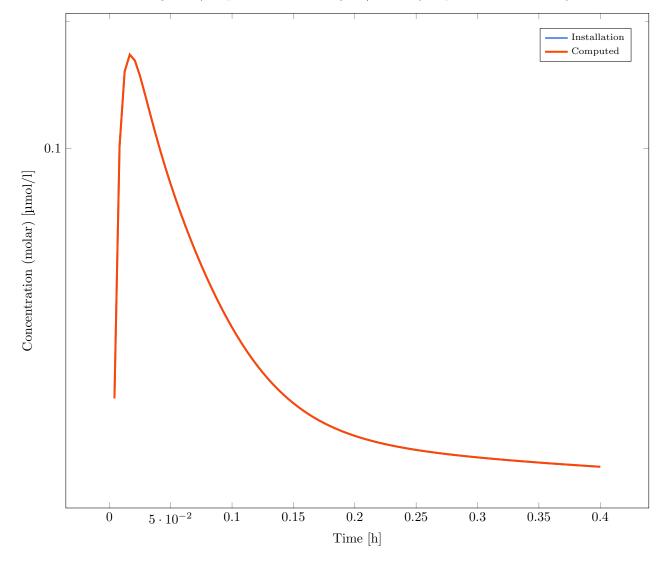


Figure 1.210

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

Result of the validation: Valid

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

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

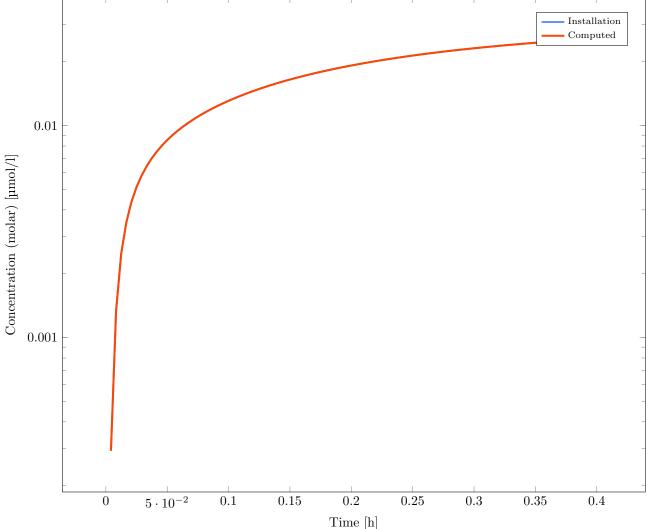
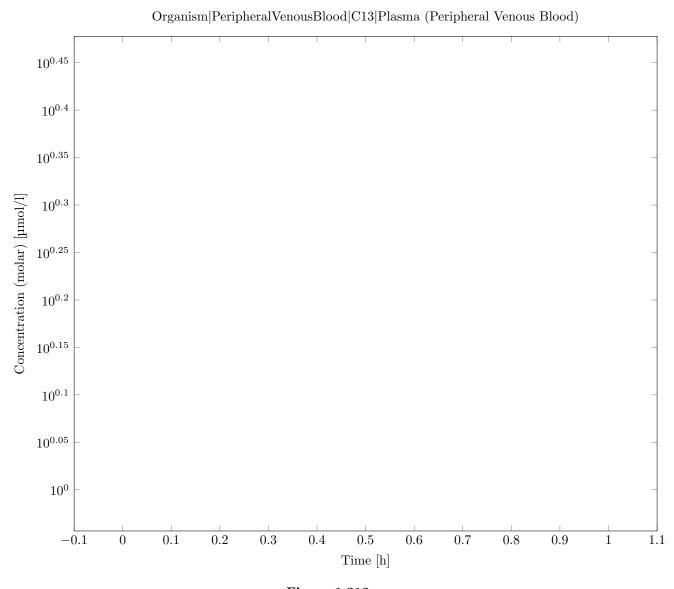


Figure 1.211

 $Simulation: Single ORAL_C13_2 Pores_schmitt_standard_st$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood | C13 |Plasma (Peripheral Venous Blood)



 $\mathbf{Figure}\ \mathbf{1.212}$

 $Simulation: Single ORAL_C13_4 Comp_standard_schmittnormalized_schmittnormalized_sc$

Result of the validation: Valid

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

Organism|PeripheralVenousBlood|C13|Plasma (Peripheral Venous Blood)

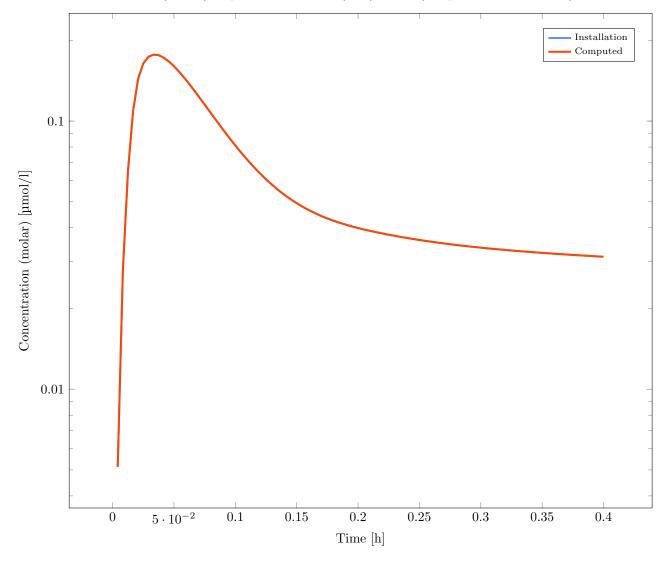


Figure 1.213

 $Simulation: Single ORAL_C14_2 Pores_PT_standard_standard_Single ORAL_C14_2 Pores_PT_standard_standar$ standard

Result of the validation: Valid

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

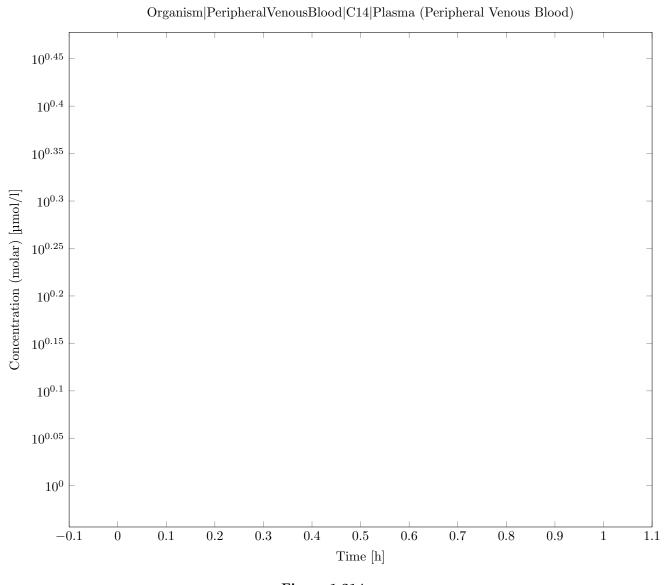
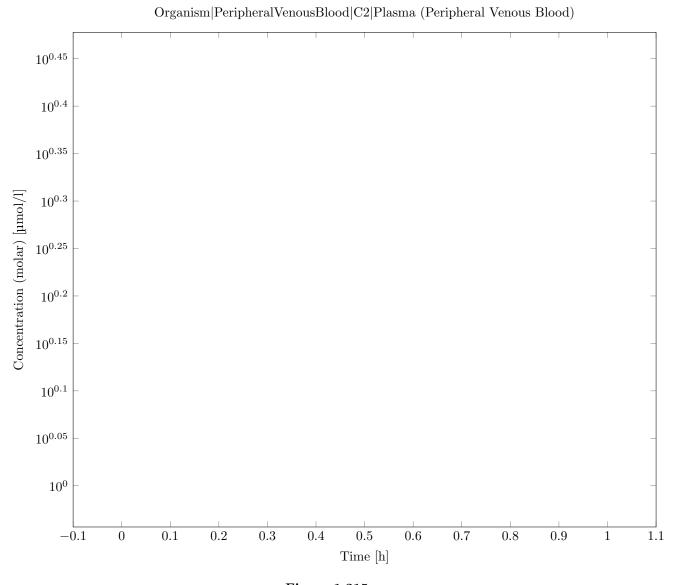


Figure 1.214

 $Simulation: Single ORAL_C2_2 Pores_standard_st$

Result of the validation: Valid

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



 ${\bf Figure~1.215}$

 $Simulation: Single ORAL_C3_2 Pores_standard_schmitt_standard-Single ORAL_C3_2 Pores_standard_schmitt_standard\\$

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |C3|Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

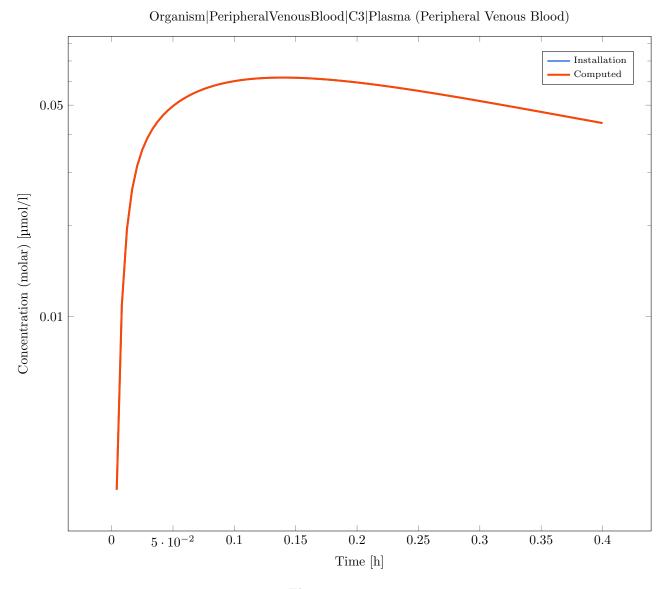


Figure 1.216

 $Simulation: Single ORAL_C4_2 Pores_standard_schmittnormalized_standard_Single ORAL_C4_2 Pores_standard_schmittnormalized_standard$

Result of the validation: Valid

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

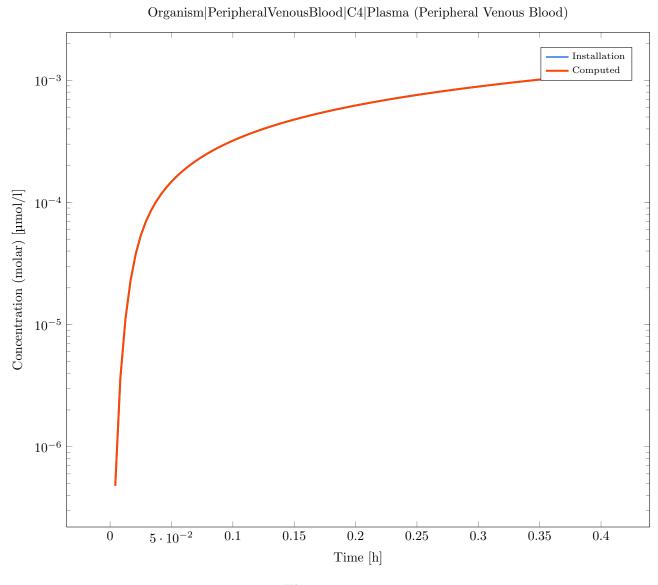


Figure 1.217

 $Simulation: Single ORAL_C6_4 Comp_Ber_standard_standard_Single ORAL_C6_4 Comp_Ber_standard_$

Result of the validation: Valid

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



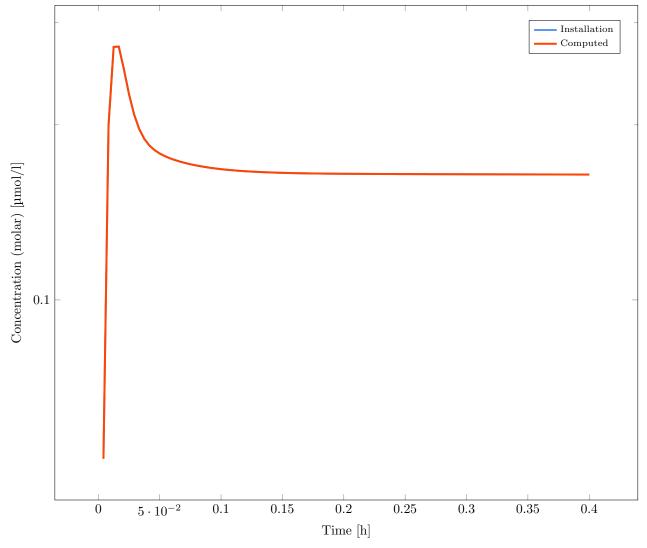


Figure 1.218

 $Simulation: Single ORAL_C6_4 Comp_RR_standard_standard_Single ORAL_C6_4 Comp_RR_standard_st$

Result of the validation: Valid

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

Organism|PeripheralVenousBlood|C6|Plasma (Peripheral Venous Blood) Installation Computed 0.05Concentration (molar) [µmol/1] 0.01

Figure 1.219

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single ORAL_C7_2 Pores_Ber_standard_standard_Single ORAL_C7_2 Pores_Ber_standard_standar$ standard

Result of the validation: Valid

0

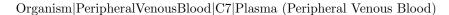
 $5\cdot 10^{-2}$

0.1

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

0.15

Deviation: 0



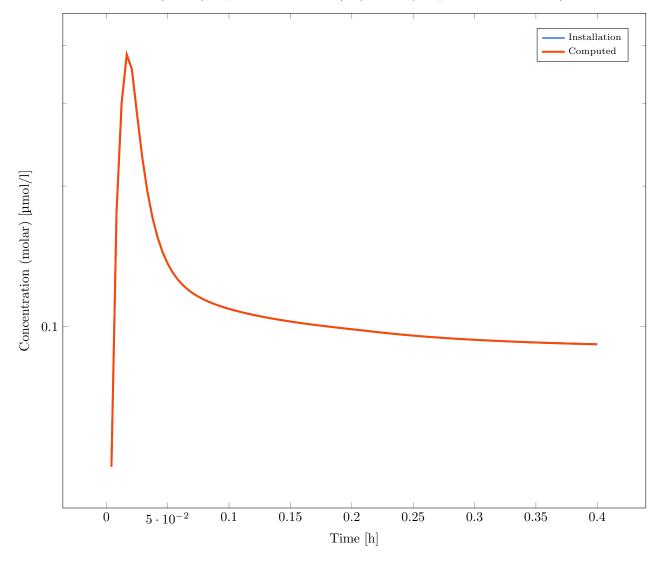


Figure 1.220

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

Result of the validation: Valid

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

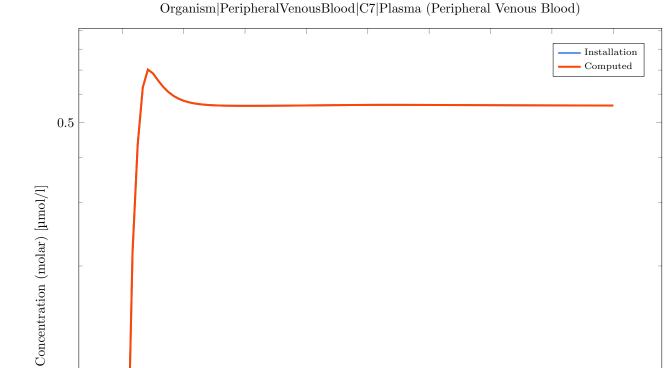


Figure 1.221

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single ORAL_C8_2 Pores_RR_standard_standard_Single ORAL_C8_2 Pores_RR_standard_$

Result of the validation: Valid

0

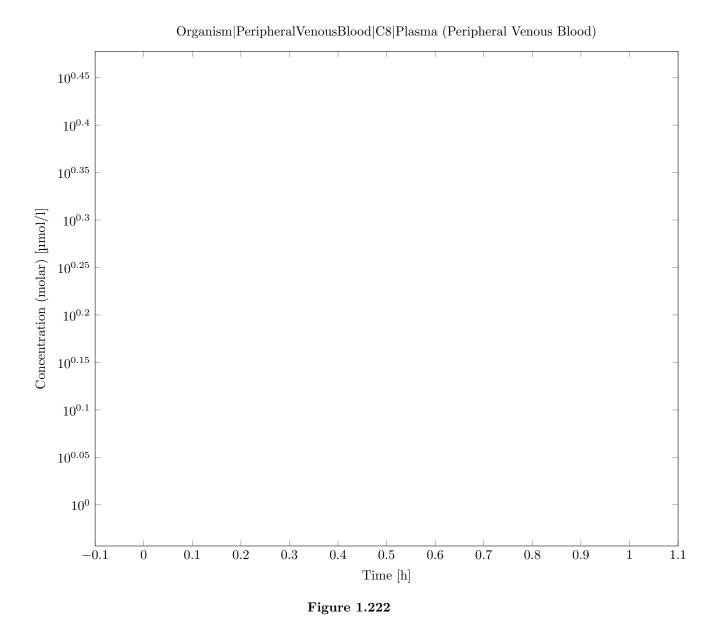
 $5\cdot 10^{-2}$

0.1

Output Path: Organism |Peripheral Venous
Blood |C8 |Plasma (Peripheral Venous Blood) Deviation:
 0

0.15

0.1



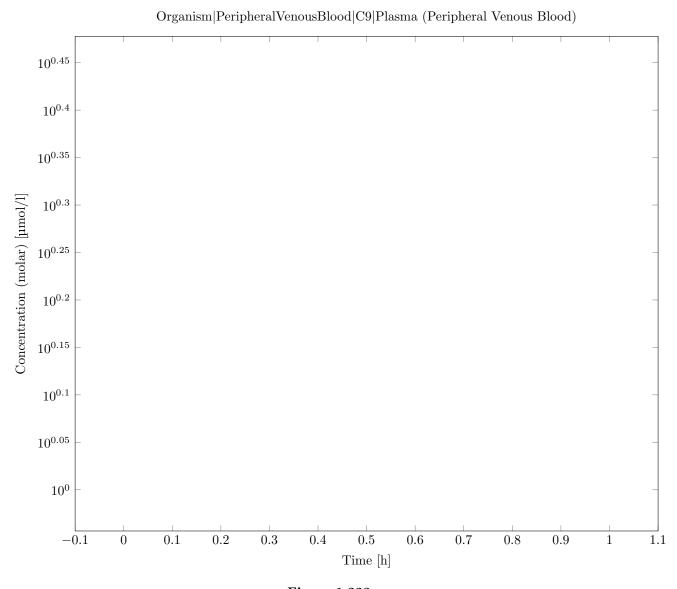
 $Simulation: Single ORAL_C9_2 Pores_RR_schmitt_standard-Single ORAL_S Pores_S Pore$

Result of the validation: Valid

standard

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

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 ${\bf Figure~1.223}$

Simulation: Test 18.1_I1_C1_A1_Config1-Test 18.1_I1_C1_A1_Config1 Result of the validation: Valid

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

Deviation: 0

Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood)

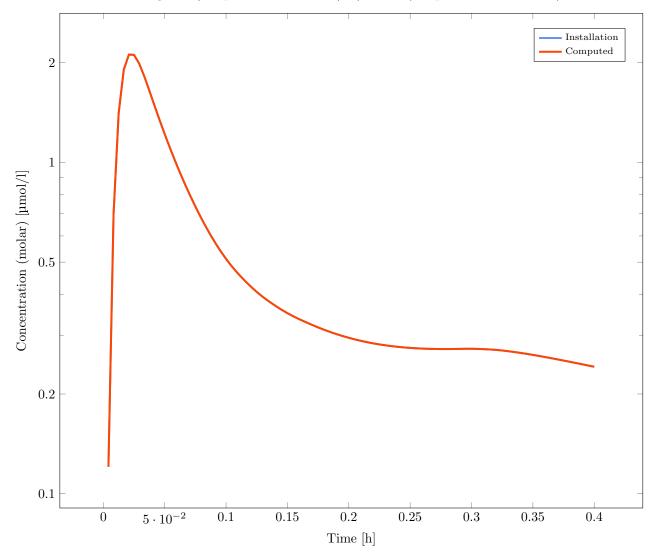
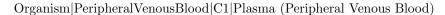


Figure 1.224

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: ${\bf 0}$



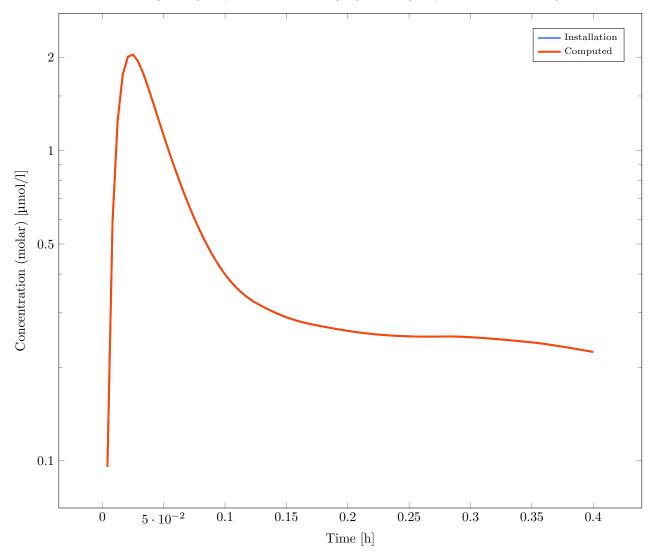


Figure 1.225

Simulation: Test 18.1_I2_C3_A1_Config2-Test 18.1_I2_C3_A1_Config2

Result of the validation: Valid

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

Deviation. 0

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

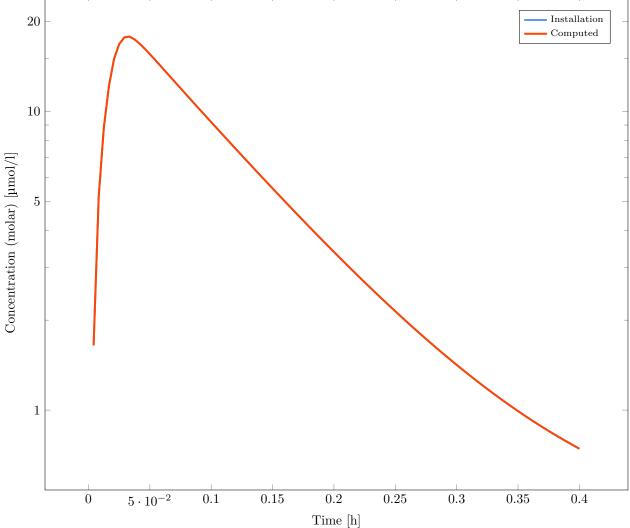


Figure 1.226

Simulation: Test 18.1_I3_C3_A3_Config2-Test 18.1_I3_C3_A3_Config2 Result of the validation: Valid

Output Path: Organism |Peripheral Venous
Blood |C3 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

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

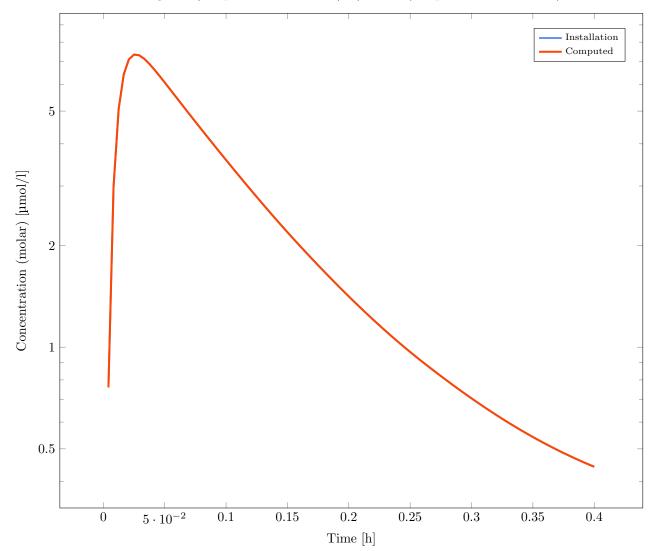


Figure 1.227