Open Systems Pharmacology Suite - 9 Installation Validation

User1

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Chapter 1

Installation Validation Results

Overall Validation Result

Valid

1.1 Validation Summary

Run Duration

Start time: 2020-06-20 16:25 End time: 2020-06-20 16:40

Validation performed in 15m:07s:45ms

Input Configuration Folder

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

Local Outputs Location

Application Versions

PK-Sim Version 9.0.170 MoBi Version 9.0.150

Computer Name

WIN-0NC3JFG157V

Operating System

Windows Server 2016 Standard

Architecture

x64

Running on Virtual Machine

Yes

Running on Terminal Session

No

1.2 Comparison Results

Overall Comparison Result

Valid

Installation Folder

C:\ProgramData\Open Systems Pharmacology\InstallationValidator\9.0\Outputs\BatchFiles

Computed Folder

1.2.1 Valid Simulations (125/125)

Simulation: Beagle_SingleORAL_Dissolved-Beagle_SingleORAL_Dissolved

Result of the validation: Valid

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

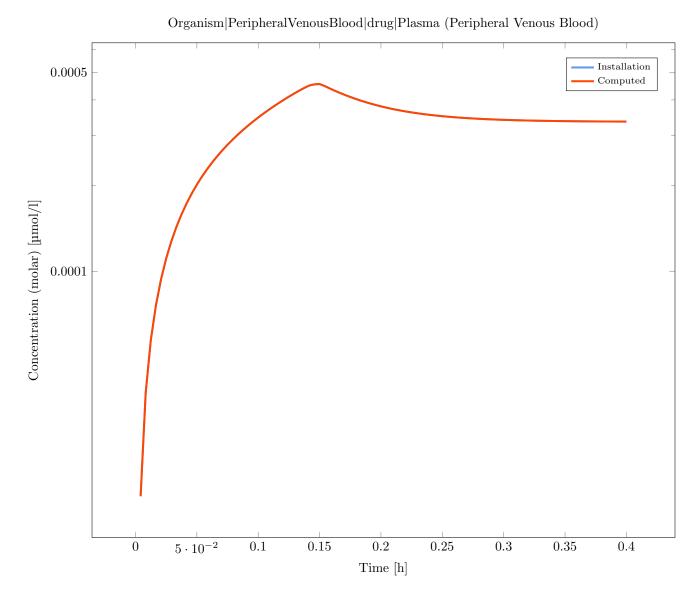


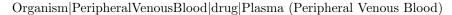
Figure 1.1

 $Simulation: Beagle_SingleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-$

Result of the validation: Valid

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

Deviation: 0



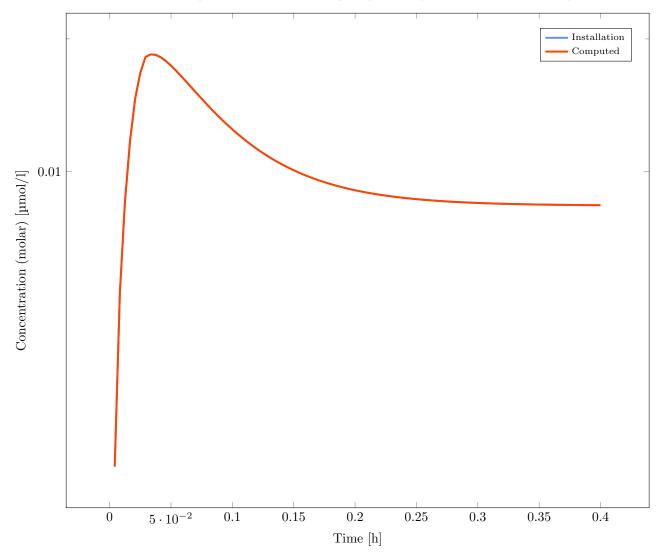


Figure 1.2

 $Simulation: Beagle_SingleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-5$

Result of the validation: Valid

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

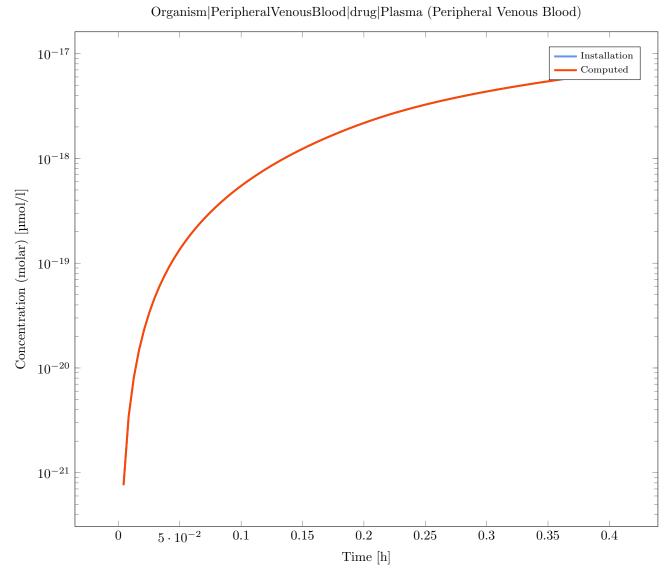


Figure 1.3

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

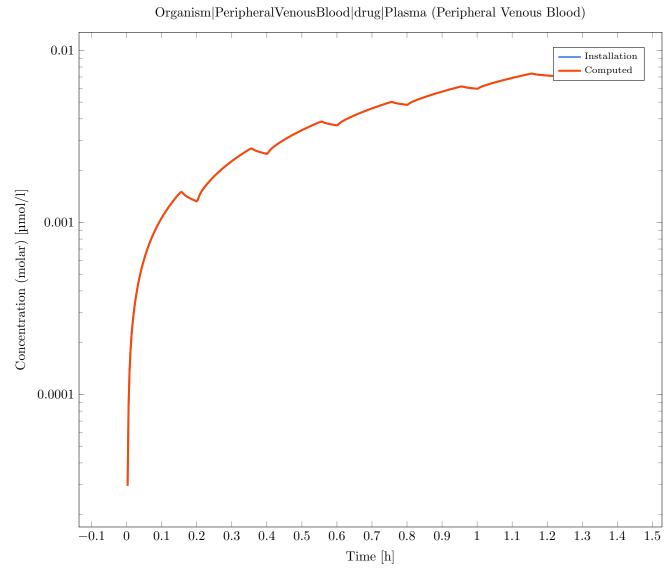


Figure 1.4

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

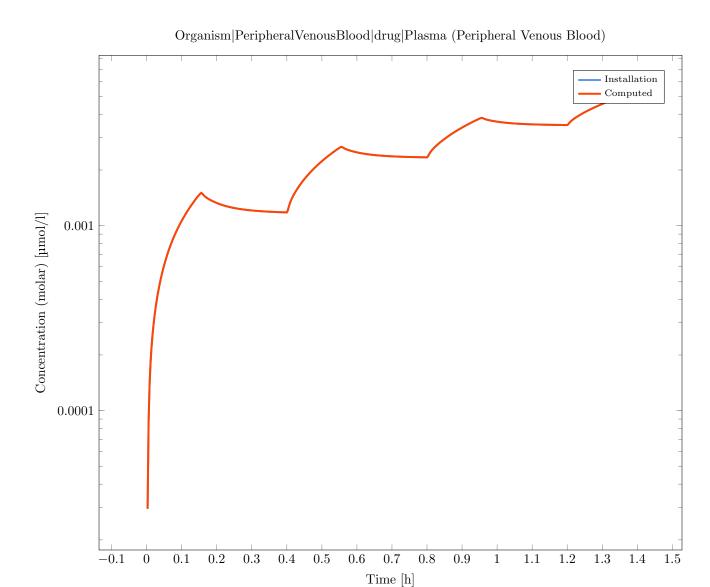
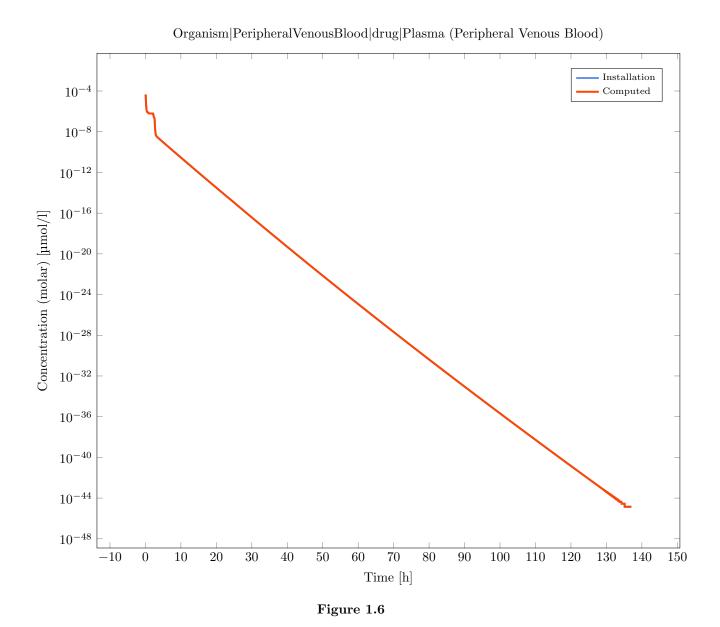


Figure 1.5

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

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 2.63E-5



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

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

Deviation: 8.28E-5

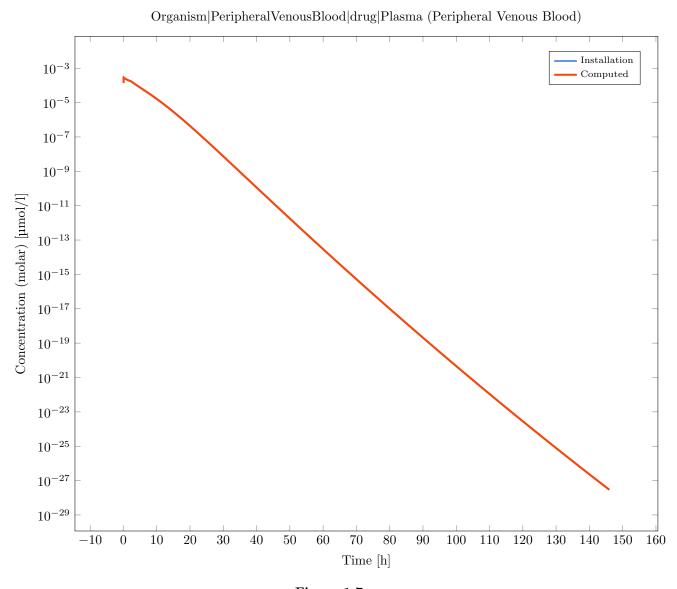


Figure 1.7

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

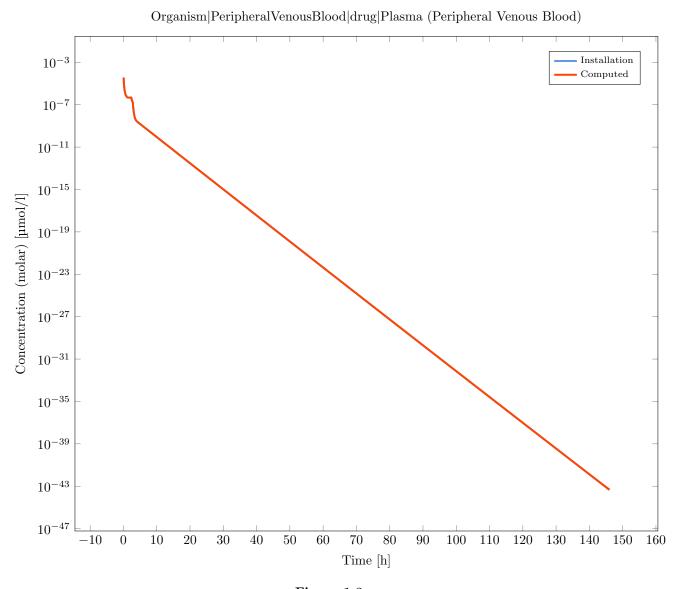


Figure 1.8

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

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

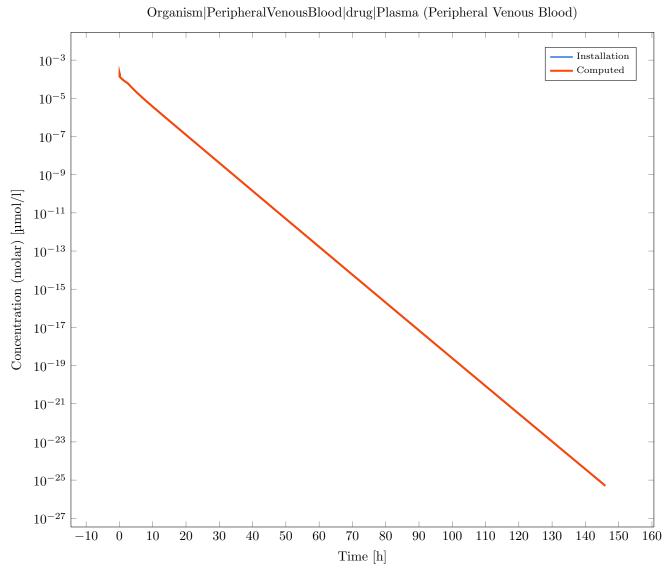


Figure 1.9

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

Result of the validation: Valid

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

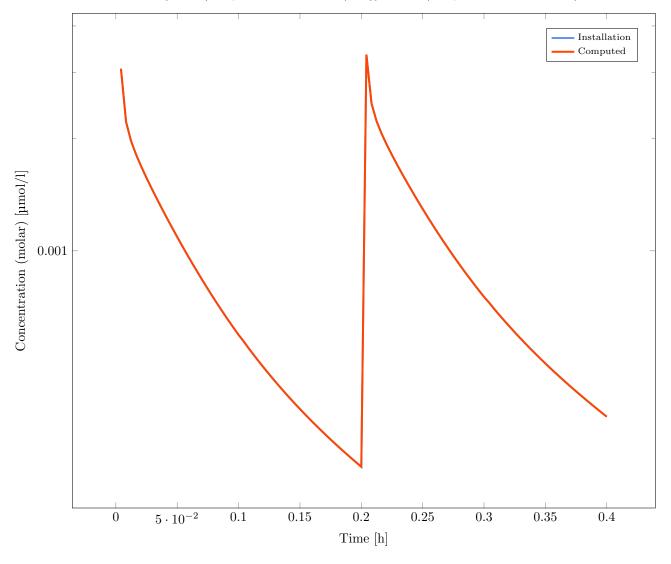


Figure 1.10

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

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

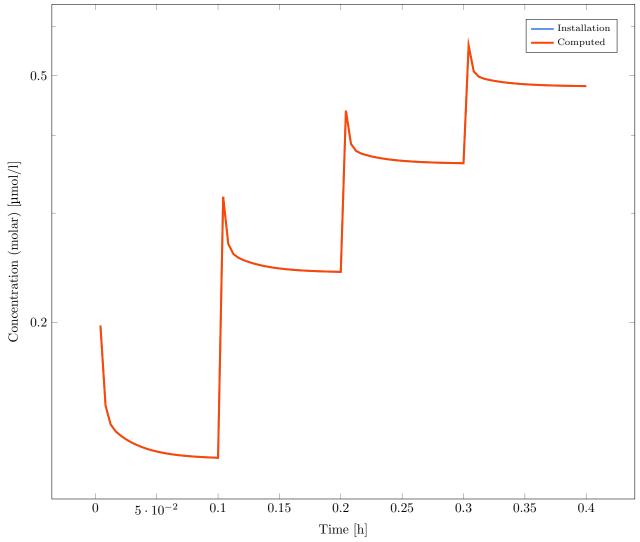


Figure 1.11

Simulation: Human_ICRP_AGP-01_ICRP_0y_Male

Result of the validation: Valid

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

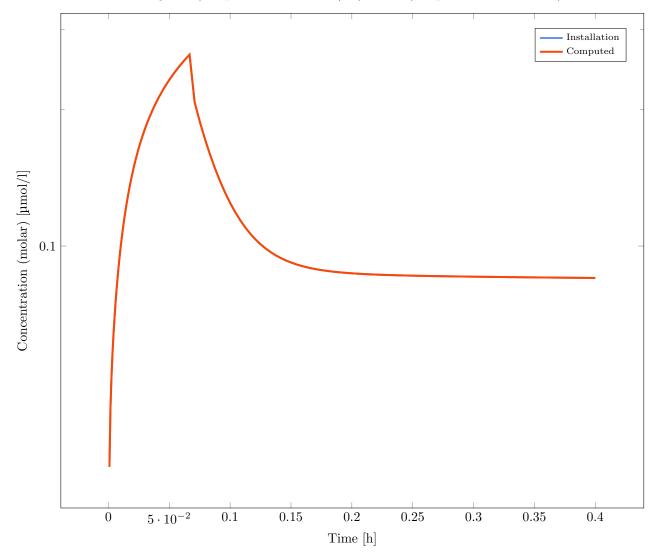


Figure 1.12

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

Result of the validation: Valid

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

Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood) O.5 Installation Computed O.0.1

Figure 1.13

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

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

0.15

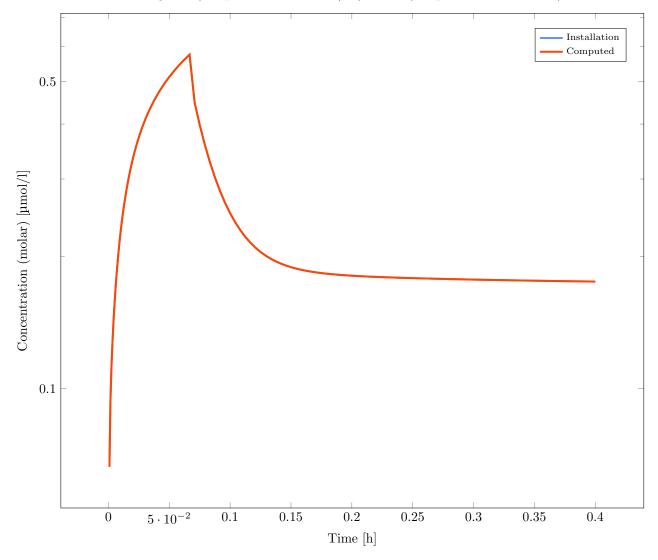


Figure 1.14

Simulation: Human_ICRP_AGP-04_ICRP_1y_Female

Result of the validation: Valid

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

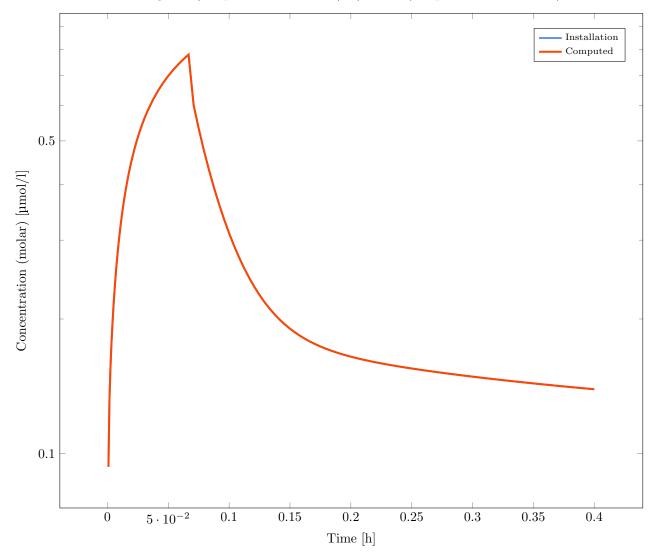


Figure 1.15

 $Simulation: \ Human_ICRP_AGP-05_ICRP_12y_Male$

Result of the validation: Valid

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

Deviation: 1.50E-4

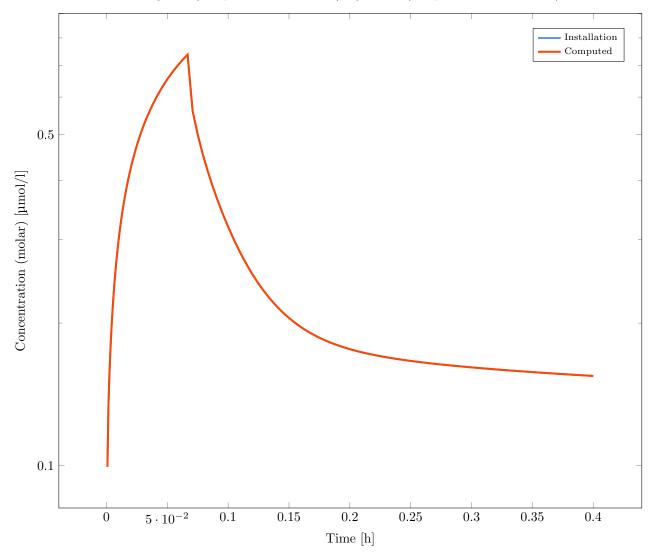


Figure 1.16

 $Simulation: \ Human_ICRP_AGP-06_ICRP_30y_Female$

Result of the validation: Valid

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

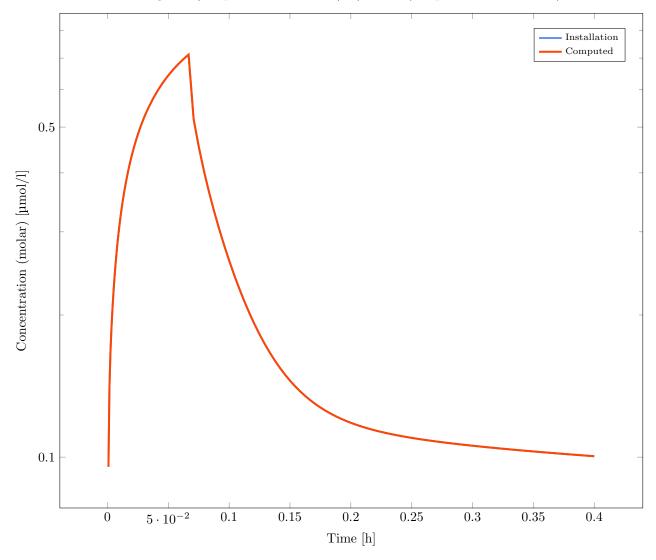
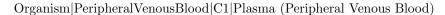


Figure 1.17

 $Simulation: \ Human_ICRP_AGP-07_ICRP_100y_Male$

Result of the validation: Valid

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



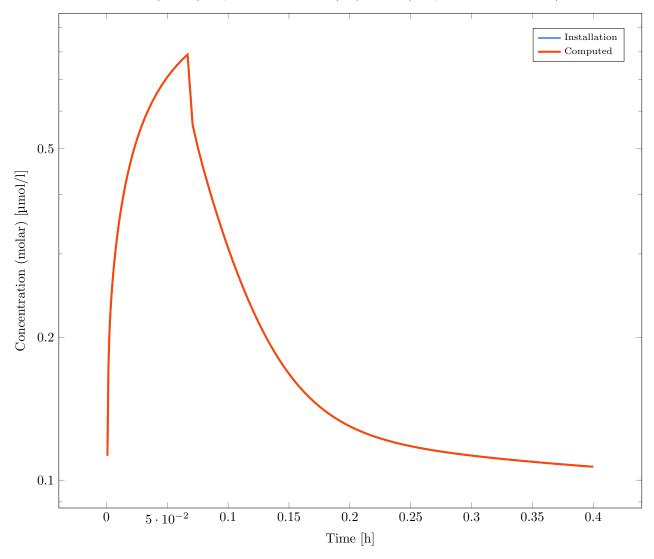
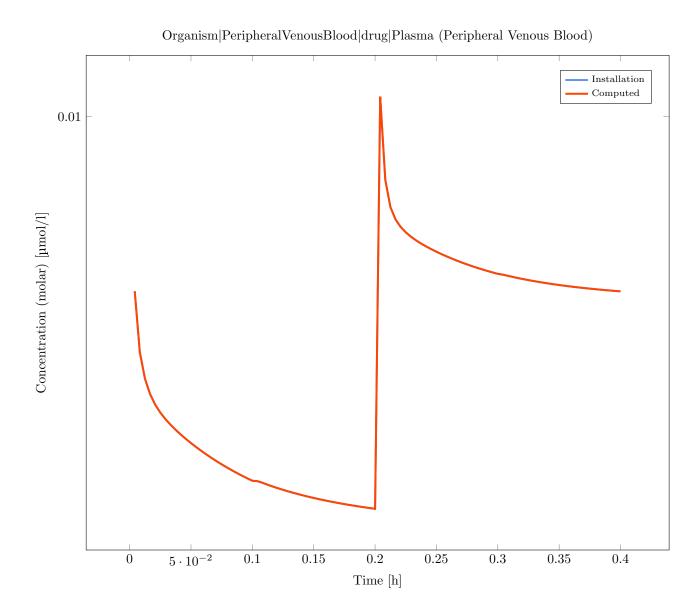


Figure 1.18

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

Result of the validation: Valid

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



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

Figure 1.19

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

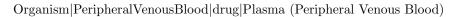
Figure 1.20

Time [h]

 $Simulation: \ Human_MixedInhibition-Human_MixedInhibition$

Result of the validation: Valid

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



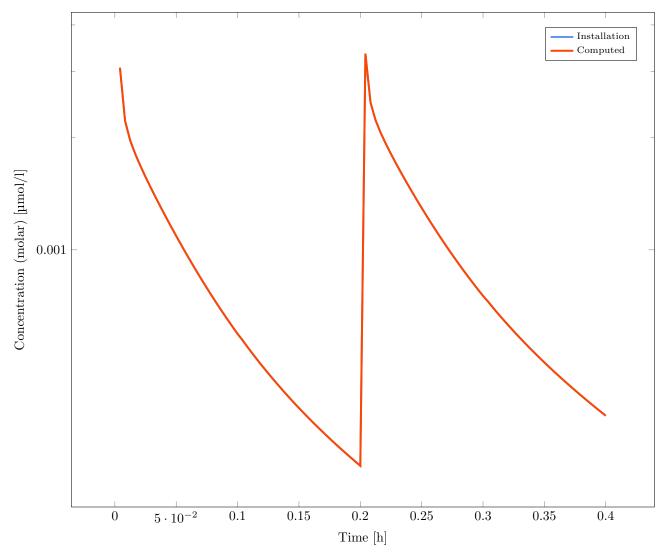


Figure 1.21

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

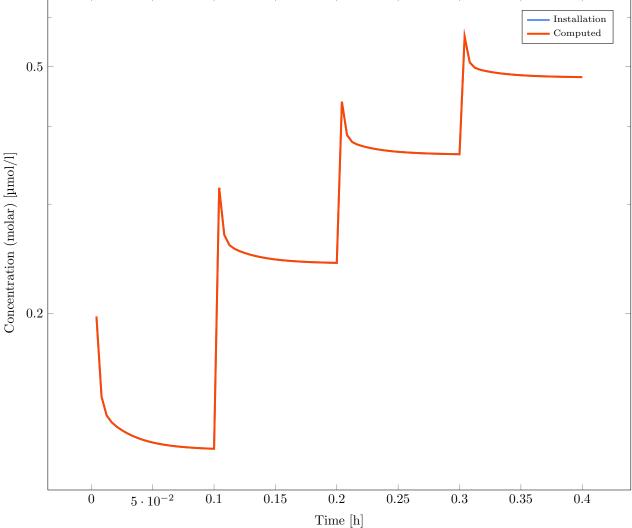


Figure 1.22

Simulation: Human_MultiIV_6_6_12-Human_MultiIV_6_6_12

Result of the validation: Valid

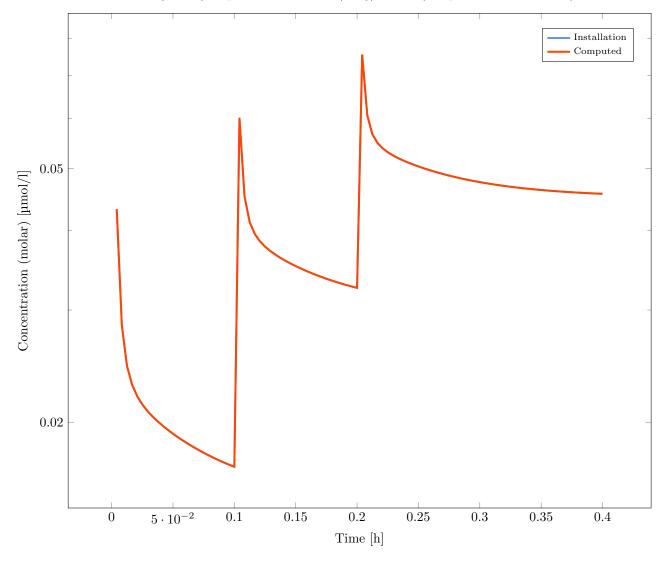


Figure 1.23

 $Simulation: \ Human_MultiORAL_6_12_12_Dissolved-Human_6_12_Dissolved-Human_6_12_$

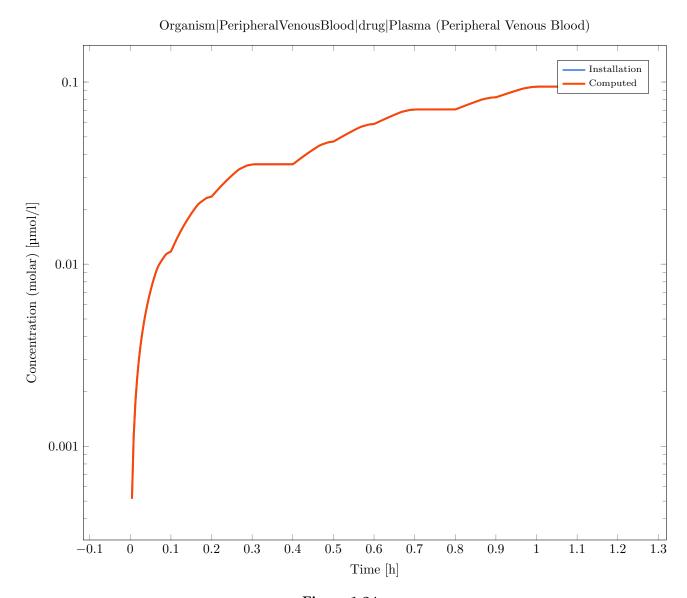


Figure 1.24

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_absorption_sink_conditions$

Result of the validation: Valid

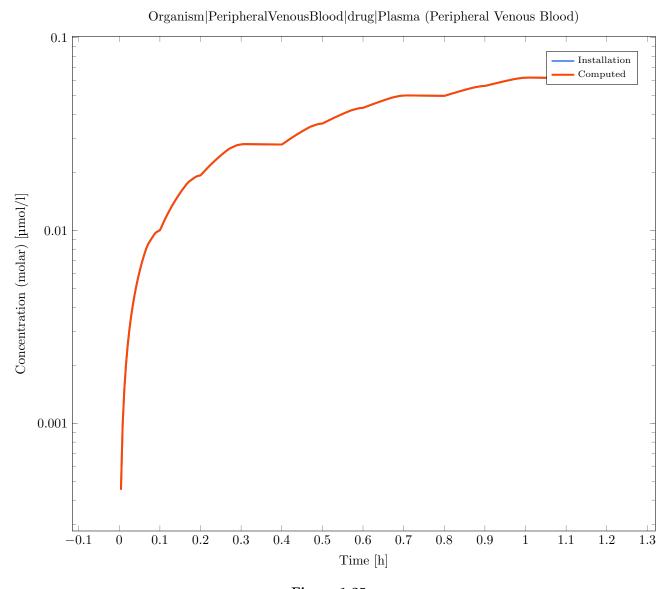


Figure 1.25

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_EHC_continuous_fraction_0.5$

Result of the validation: Valid

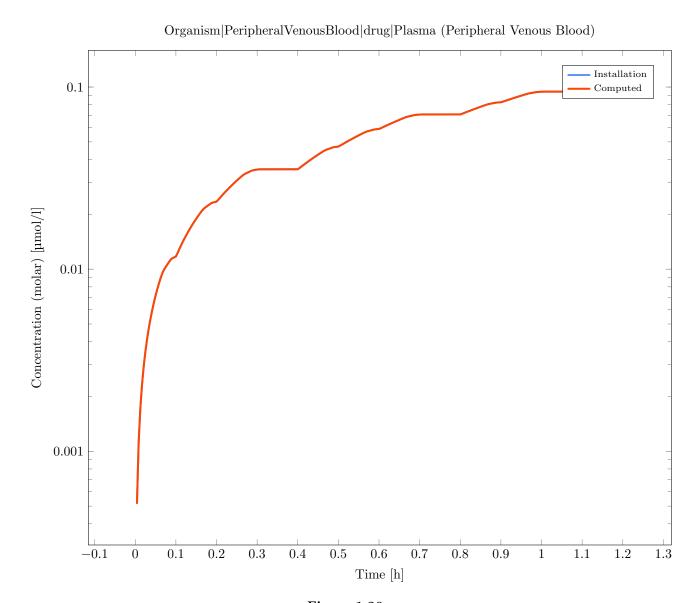


Figure 1.26

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_EHC_continuous_fraction_1$

Result of the validation: Valid

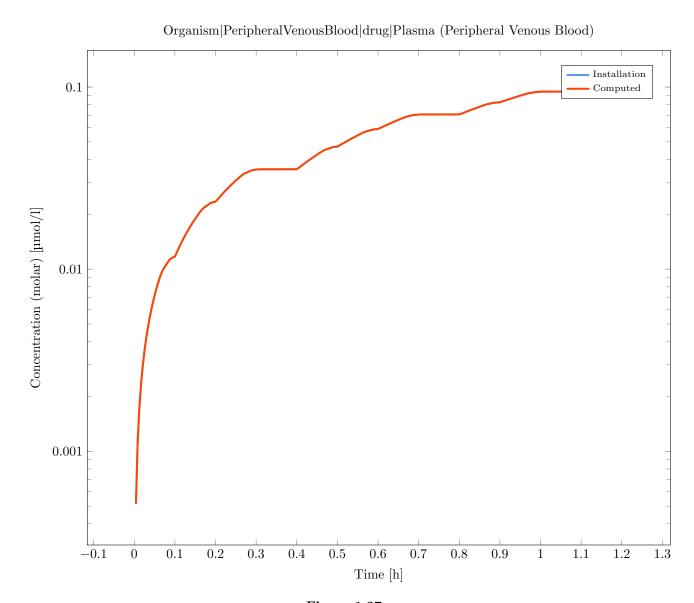


Figure 1.27

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

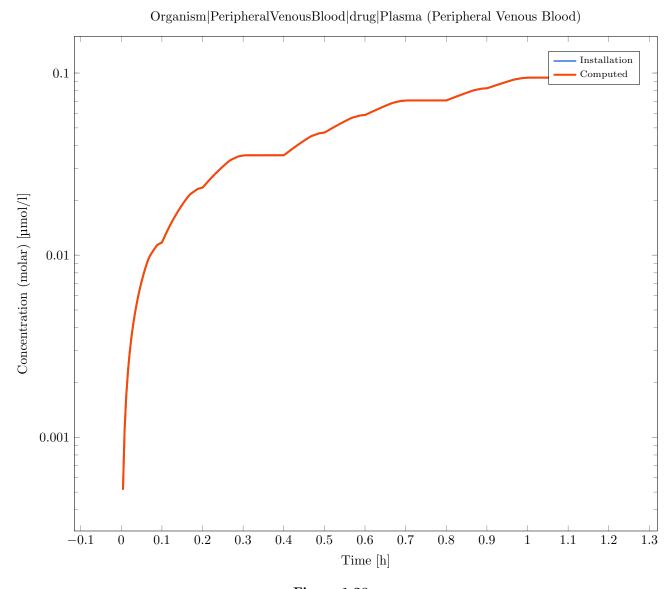


Figure 1.28

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

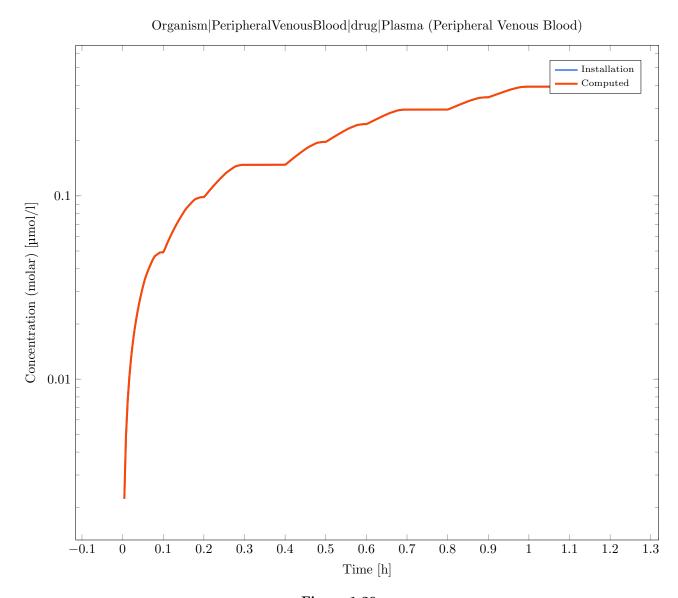


Figure 1.29

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

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 7.18E-5

Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) O.1 O.000 O.001

Figure 1.30

0.6

0.7

Time [h]

0.8

0.9

1.1

1.2

1.3

1.4

1.5

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

0.4

0.5

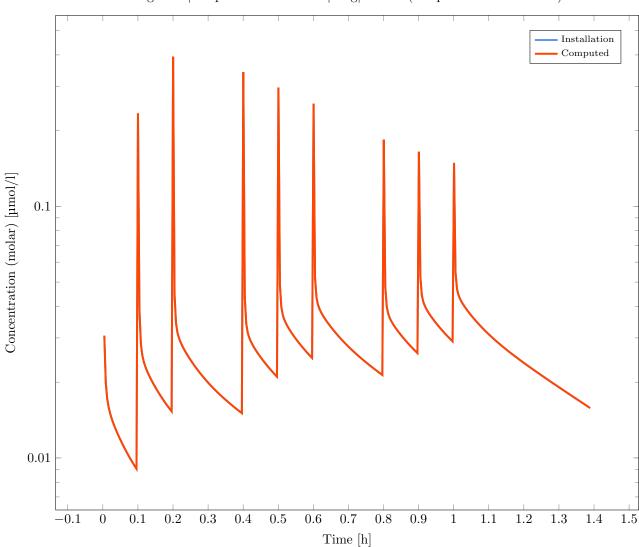
0.2

-0.1

0

0.1

0.3



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

Figure 1.31

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

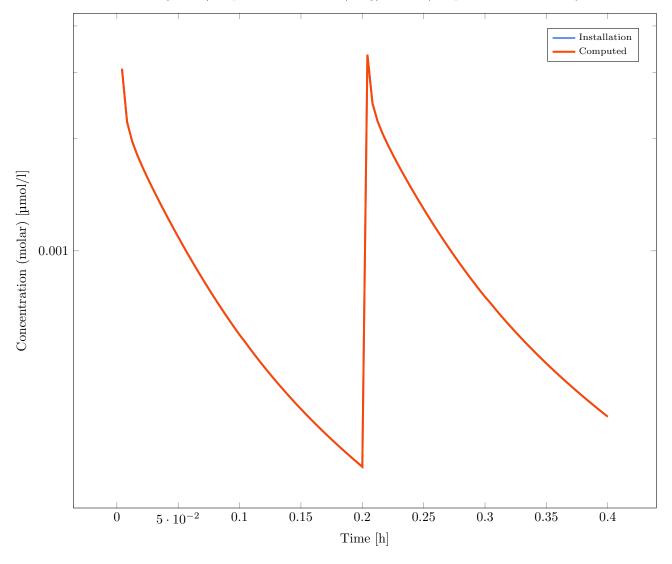


Figure 1.32

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 1.33

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

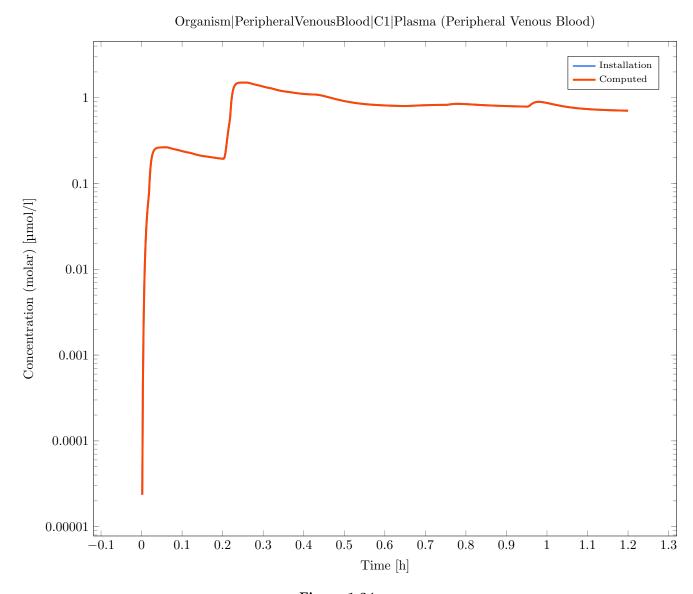


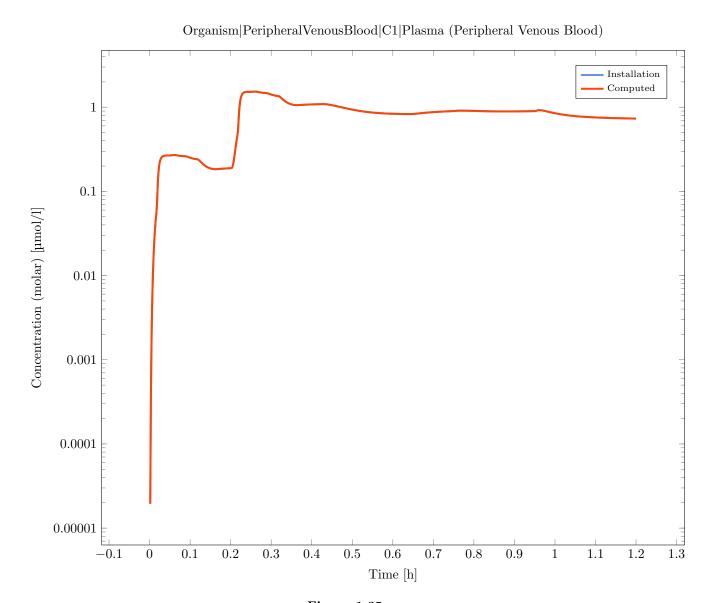
Figure 1.34

 $Simulation: Human_Oral_BiDaily_TableFormulation-S2_NoSuspension$

Result of the validation: Valid

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

Deviation: 0



 ${\bf Figure~1.35}$

Simulation: Human_pH_SolubilityTable-S1_Table

Result of the validation: Valid

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

Deviation: 4.04E-6

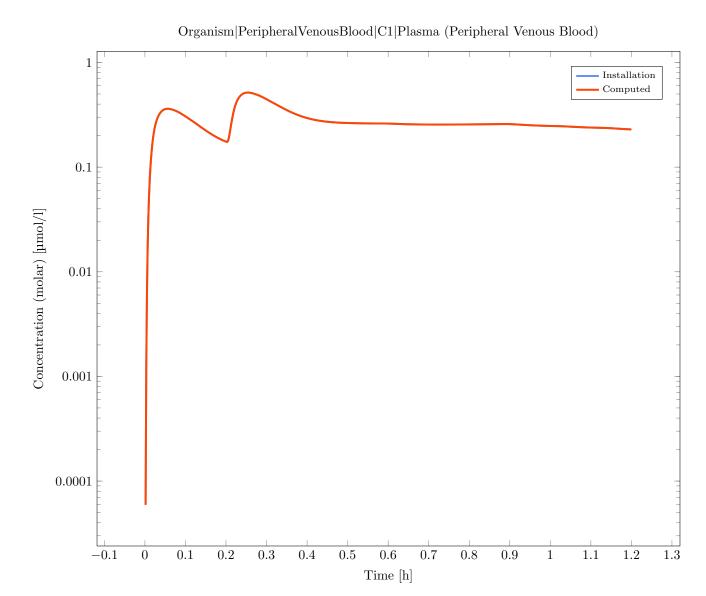


Figure 1.36

Simulation: Human_pH_SolubilityTable-S2_Measurement

Result of the validation: Valid

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

Deviation: 3.61E-6

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

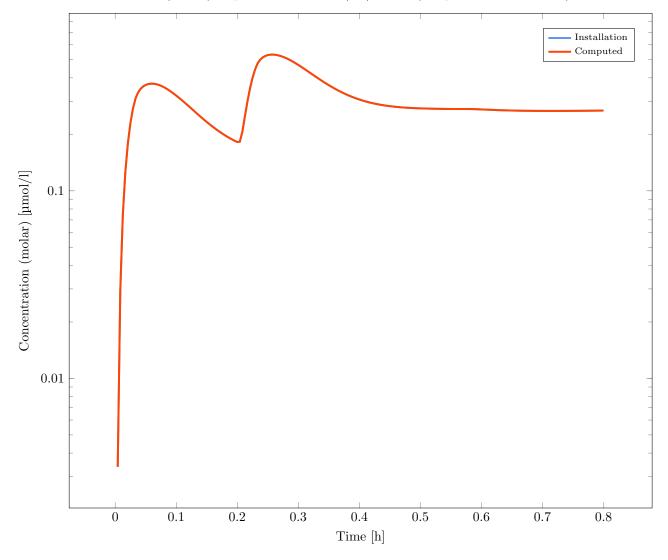


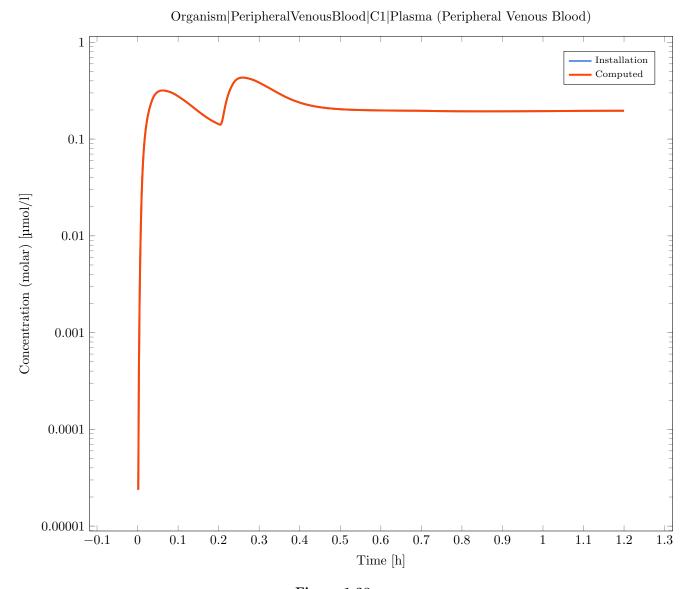
Figure 1.37

 $Simulation: \ Human_pH_SolubilityTable_SolubilityChanged$

Result of the validation: Valid

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

Deviation: 6.73E-6



 ${\bf Figure~1.38}$

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

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

Deviation: 6.13E-7

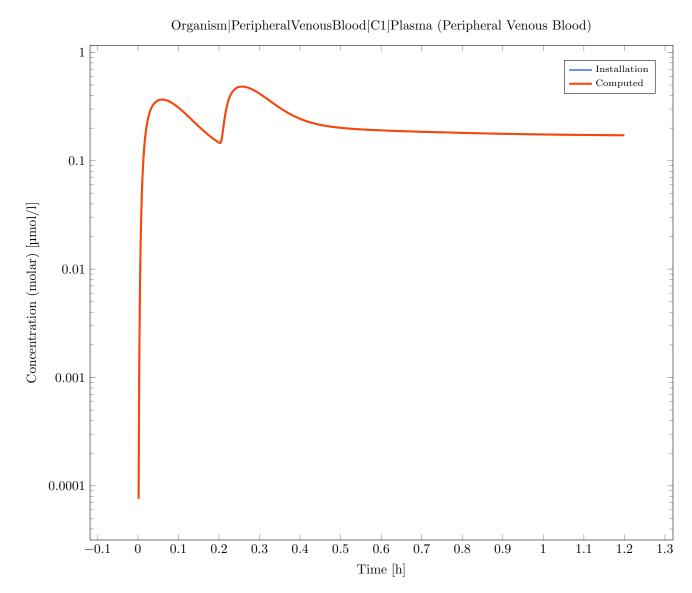


Figure 1.39

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

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

Deviation: 0

Installation Computed Computed O.002

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

Figure 1.40

0.12 0.14 0.16

Time [h]

0.2

 $0.22 \quad 0.24$

0.18

 $Simulation: \ Human_Single IV-Human_Single IV$

 $0 \quad 2 \cdot 10^{-2} \cdot 10^{-2} \cdot 10^{-2} \cdot 10^{-2} \cdot 0.1$

Result of the validation: Valid

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

Deviation: 0

0.3

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

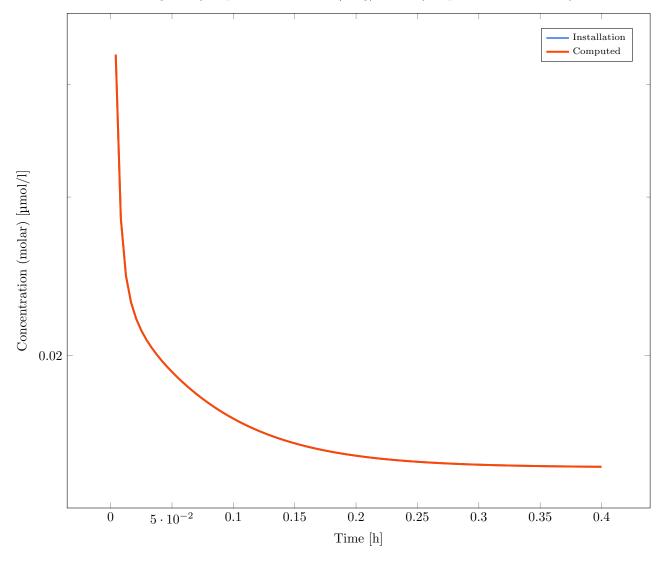


Figure 1.41

 $Simulation: Human_SingleIV_Human_SingleIV_MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

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

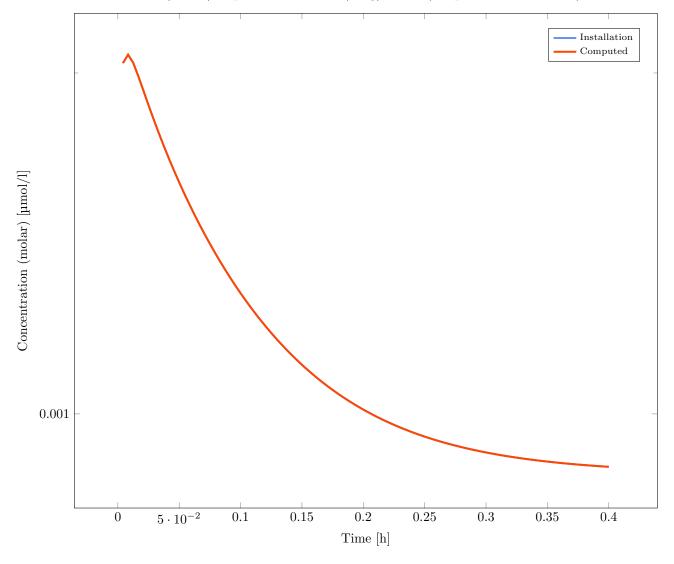
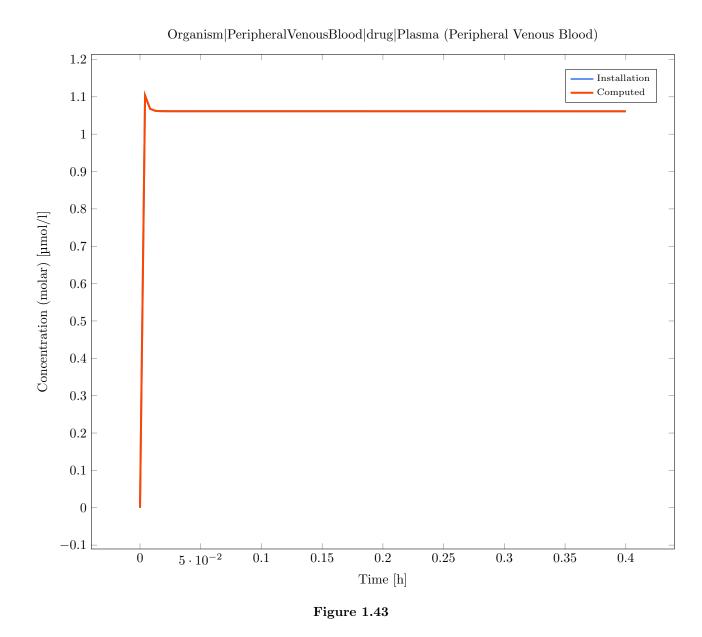


Figure 1.42

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

Result of the validation: Valid



Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_SingleO



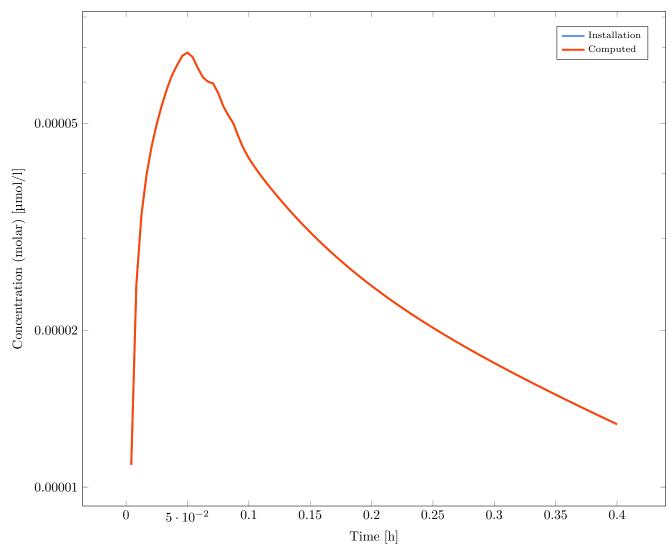


Figure 1.44

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_Singl$

Result of the validation: Valid

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

Deviation: 0



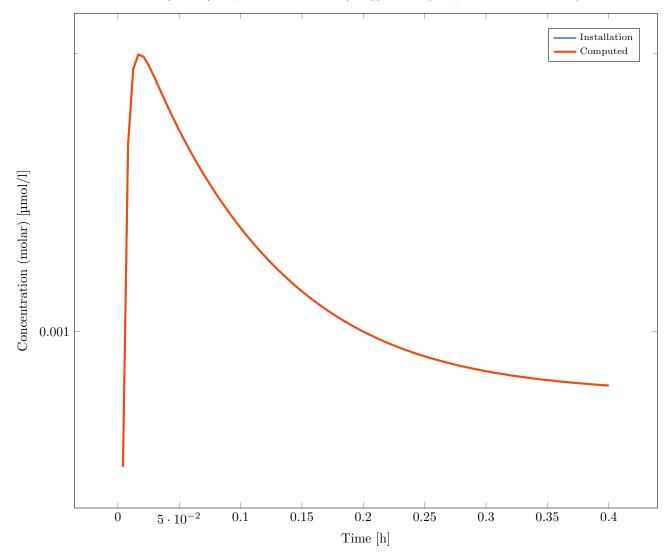


Figure 1.45

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_Singl$

Result of the validation: Valid

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

Deviation: 0

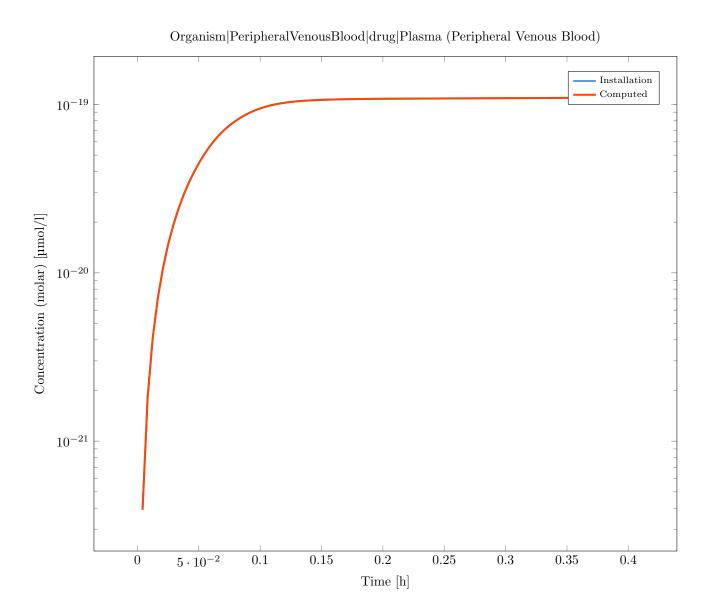


Figure 1.46

Simulation: Human_SingleORAL_Dissolved-Human_SingleORAL_Dissolved Result of the validation: Valid

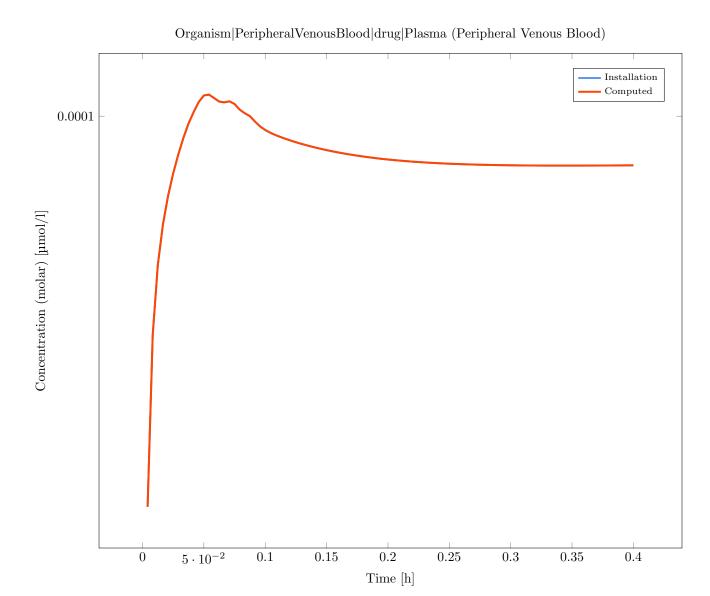


Figure 1.47

 $Simulation: \ Human_SingleORAL_Dissolved_Human_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$

Result of the validation: Valid



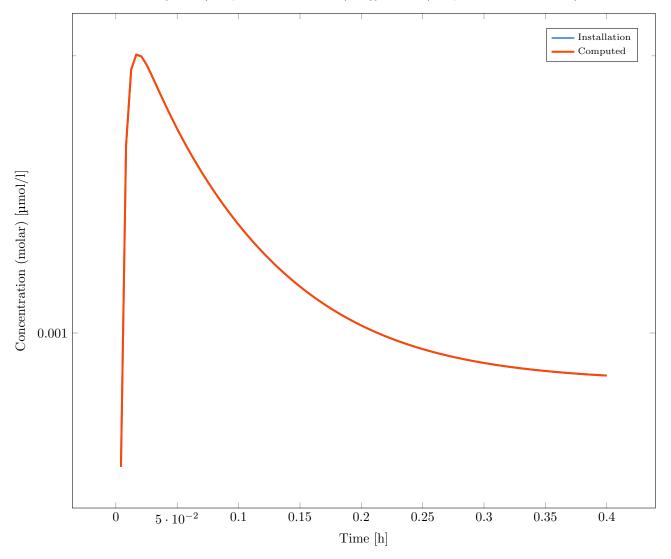
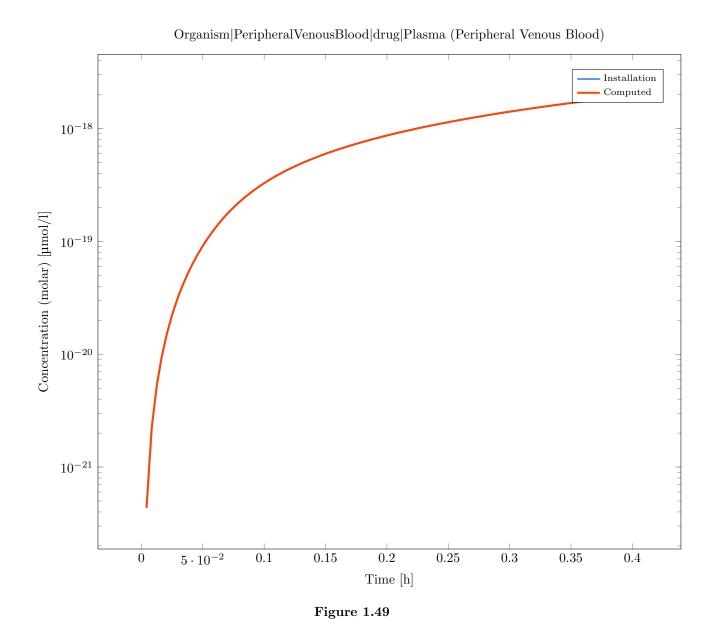


Figure 1.48

 $Simulation: Human_SingleORAL_Dissolved_Human_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-5\\ Result of the validation: Valid$

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



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

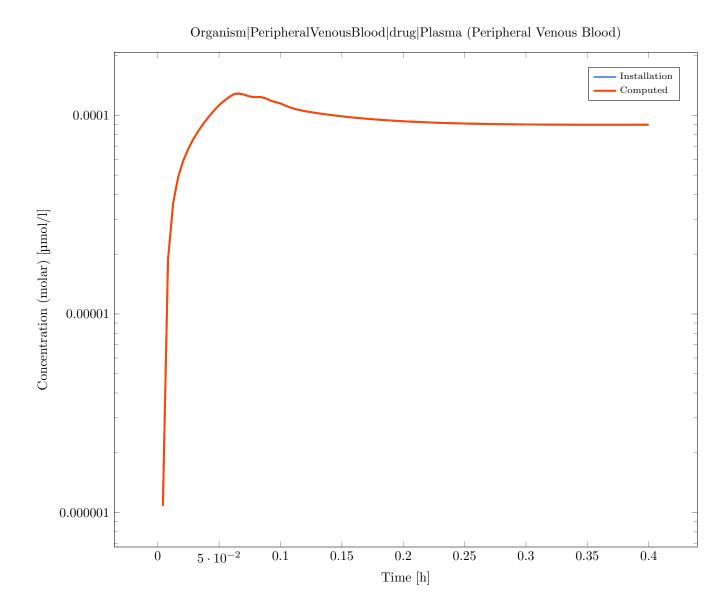


Figure 1.50

 $Simulation: \ Human_SingleORAL_Lint80-Human_SingleORAL_Lint80$

Result of the validation: Valid

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

Deviation: 0

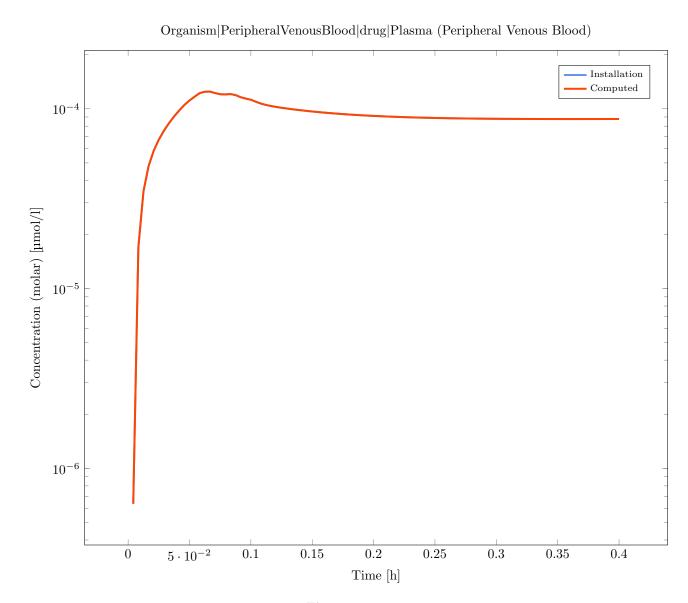


Figure 1.51

 $Simulation: Human_SingleORAL_MonoParticles_AsSuspention-Human_SingleORAL_MonoParticles_AsSuspention\\$

Result of the validation: Valid

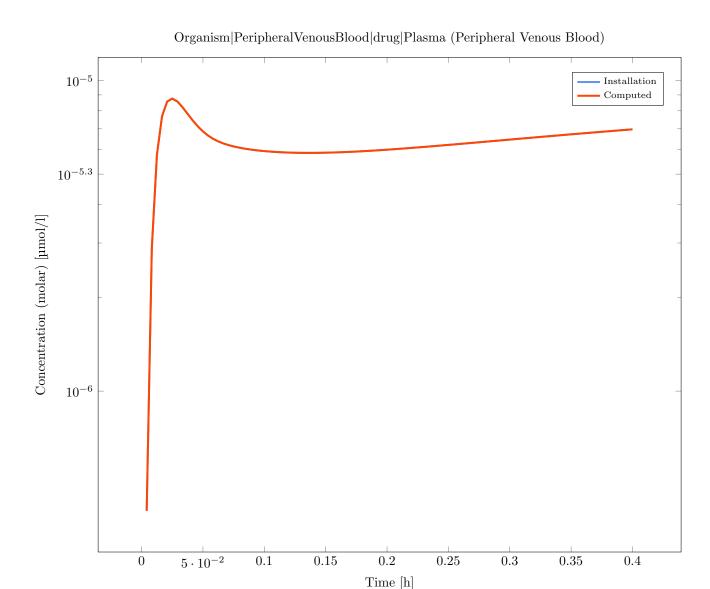


Figure 1.52

 $Simulation: \ Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention$

Result of the validation: Valid

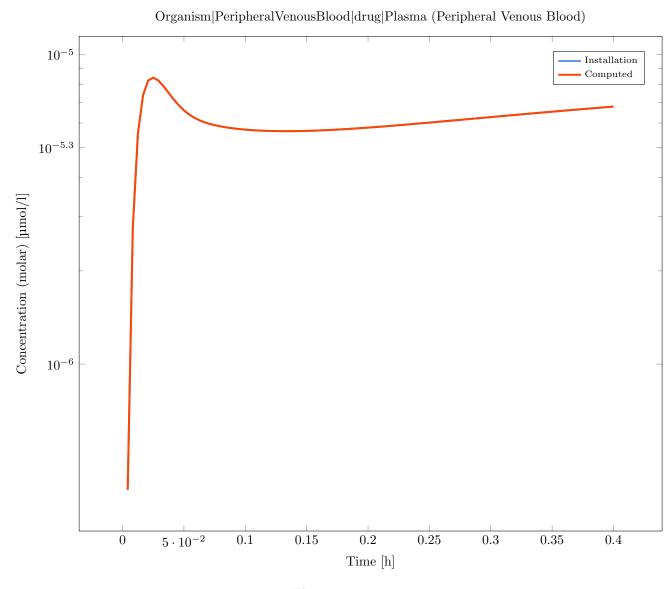


Figure 1.53

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention$

Result of the validation: Valid

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

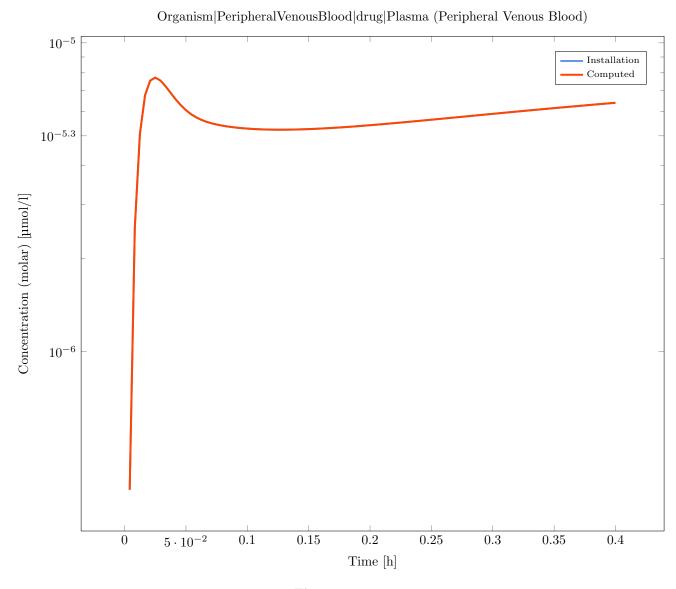


Figure 1.54

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention_dissolved_radius$

Result of the validation: Valid

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

Deviation: 6.85E-8

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

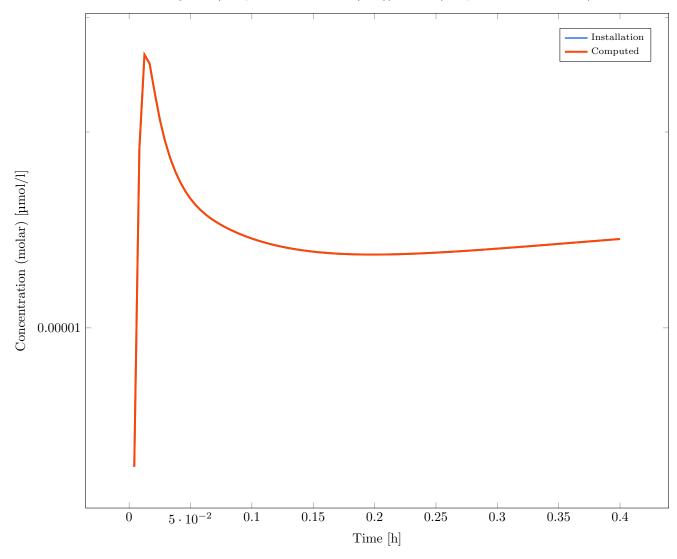


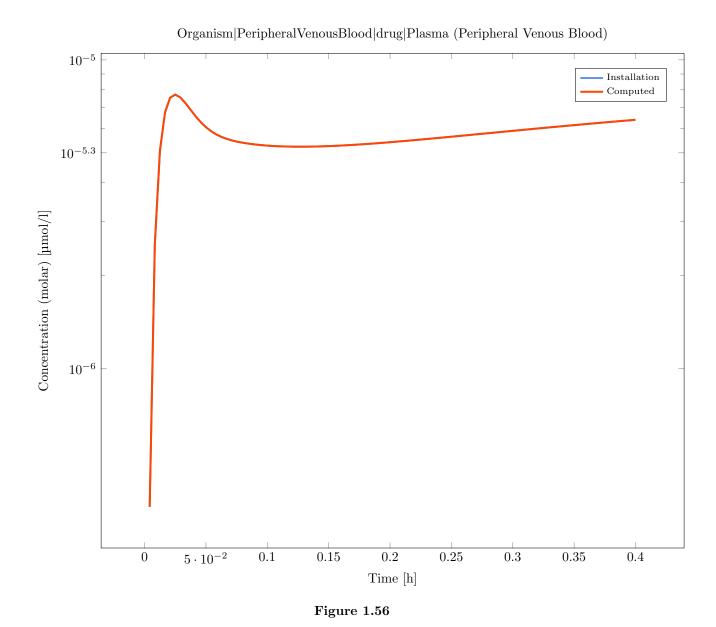
Figure 1.55

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_SingleORAL_PolyParticlesNormal_SingleORAL_PolyParticlesNormal_SingleORAL_PolyParticlesNormal_SingleORAL_PolyParticlesNormal_SingleORAL_PolyParticlesNormal_SingleORAL_PolyParticlesNormal_SingleORAL_PolyParticlesNormal_SingleORAL_Single$ $As Suspention_treat_precipated_drug_as_soluble$

Result of the validation: Valid

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

Deviation: 0



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

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 1.04E-5

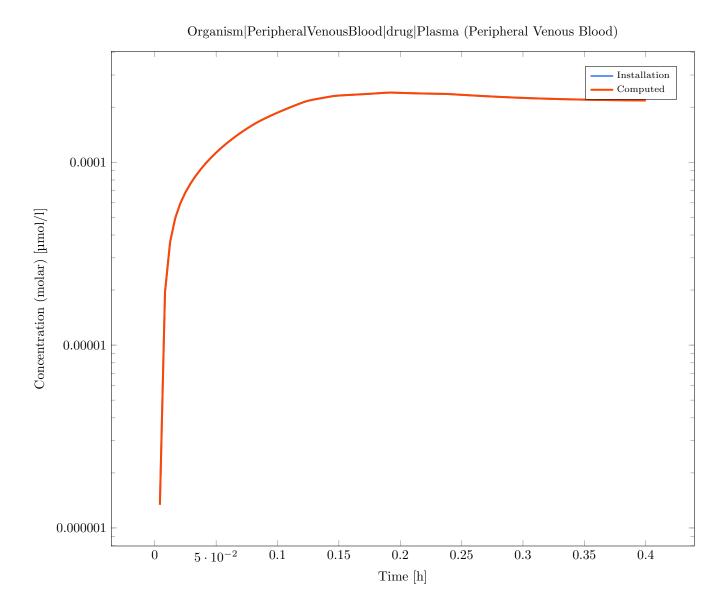


Figure 1.57

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

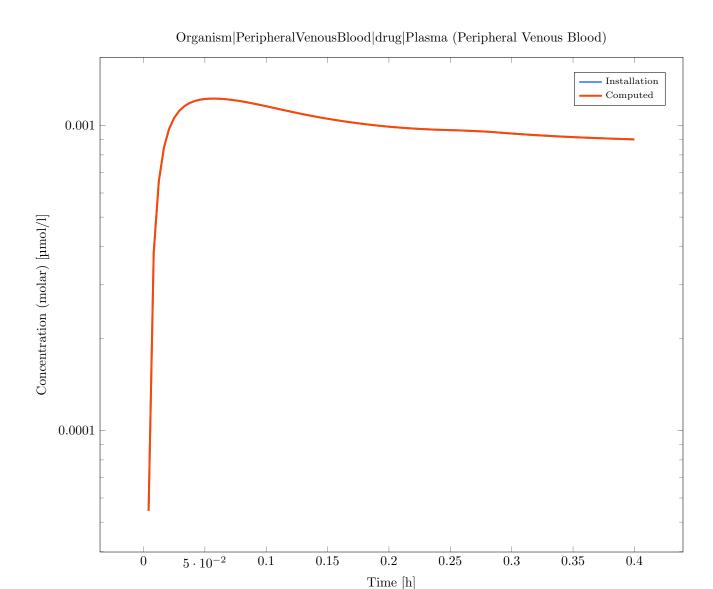
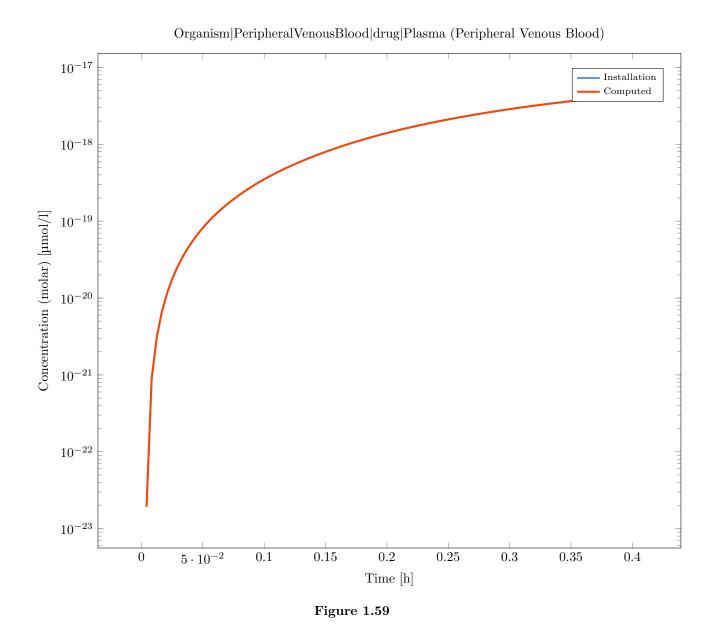


Figure 1.58

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

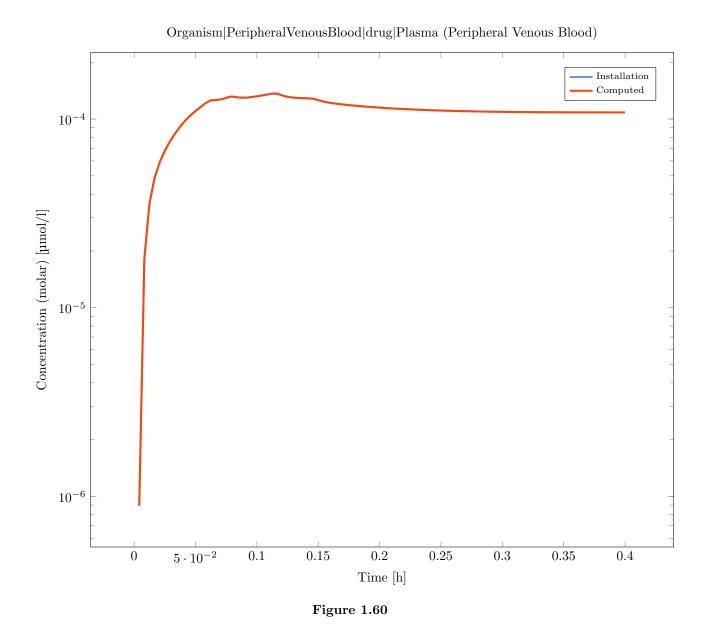
Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: ${\bf 0}$



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

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

Deviation: 3.54E-5



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

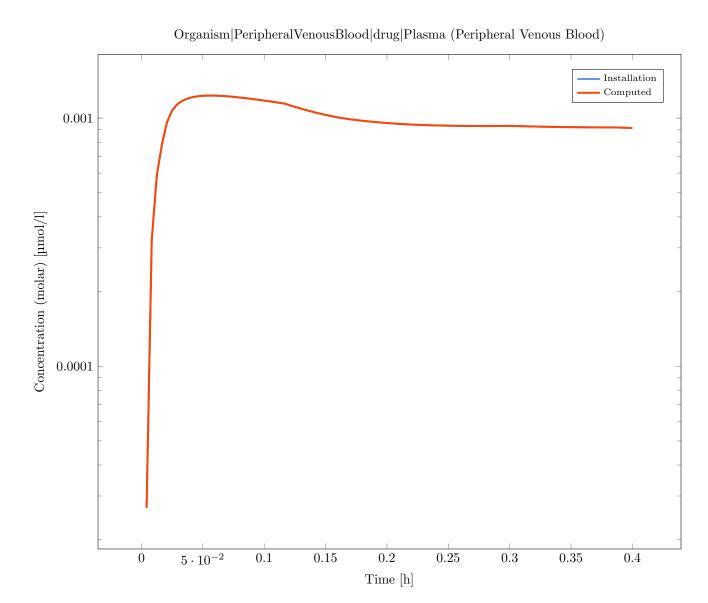
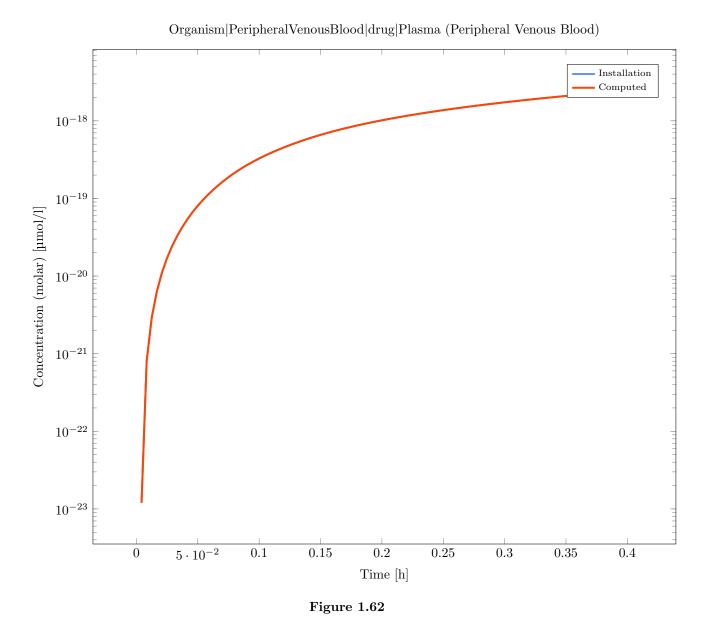


Figure 1.61

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

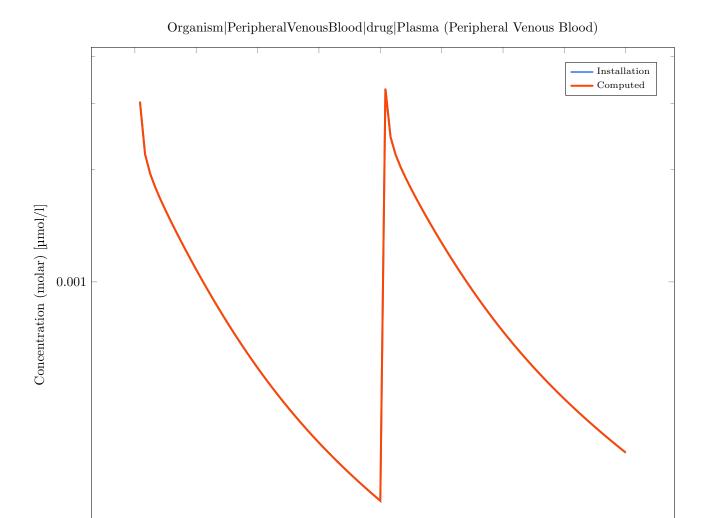
Output Path: Organism |PeripheralVenousBlood |
drug |Plasma (Peripheral Venous Blood) Deviation: ${\bf 0}$



Simulation: Human_UncompetitiveInhibition-Human_UncompetitiveInhibition

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

Result of the validation: Valid



anous Rlood linhibitor Plasma (Perinheral Venous Rloo

0.25

0.3

0.35

0.4

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

Figure 1.63

0.15

0.2

Time [h]

0.1

0

 $5 \cdot 10^{-2}$

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

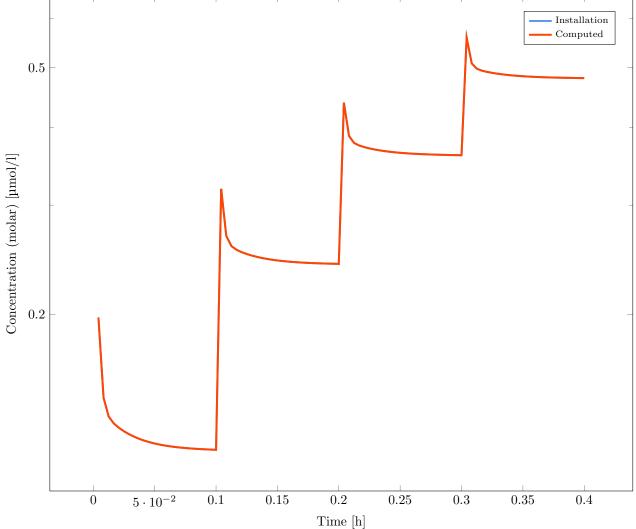


Figure 1.64

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

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 1.18E-7

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

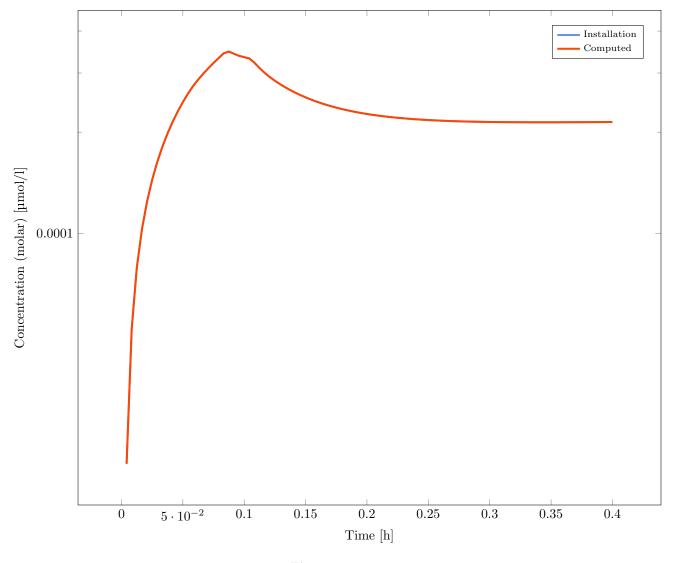


Figure 1.65

 $Simulation: Minipig_SingleORAL_Dissolved_Minipig_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-Installation: Minipig_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-Installation: Minipig_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-Installation: Minipig_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-Installation: Minipig_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-I$

Result of the validation: Valid

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

Deviation: 0

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

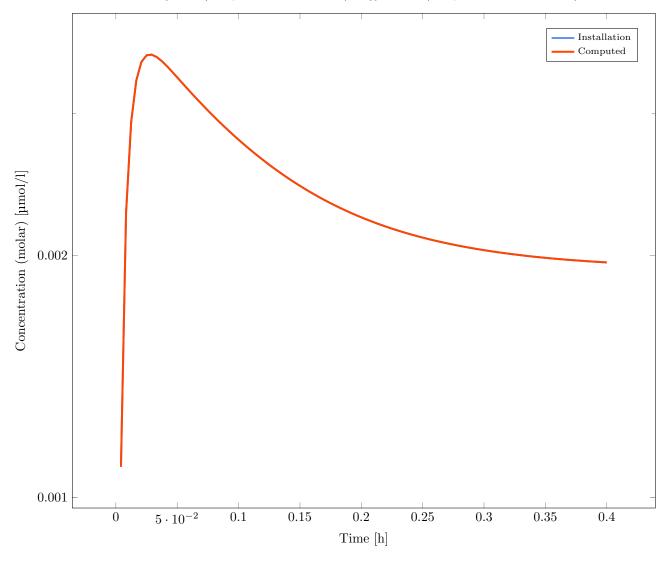


Figure 1.66

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

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

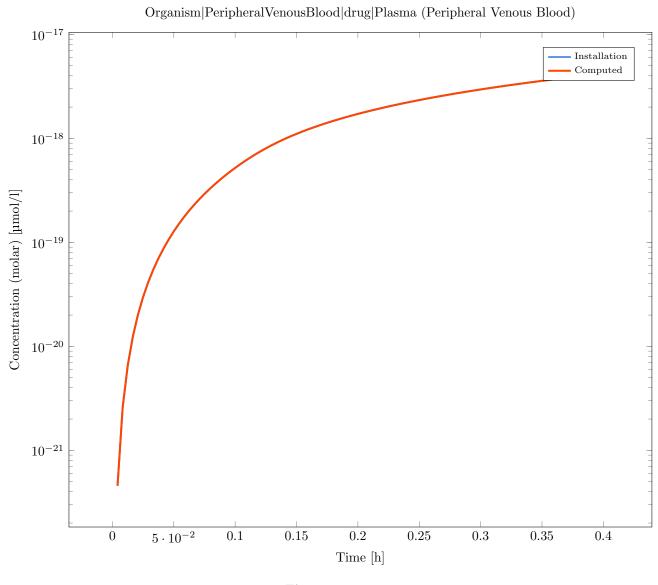


Figure 1.67

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

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

Figure 1.68

0.2

Time [h]

0.25

0.35

0.3

0.4

0.15

0.1

 $Simulation: Monkey_SingleORAL_Dissolved_Monkey_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5\\ Result of the validation: Valid$

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

0

 $5 \cdot 10^{-2}$

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

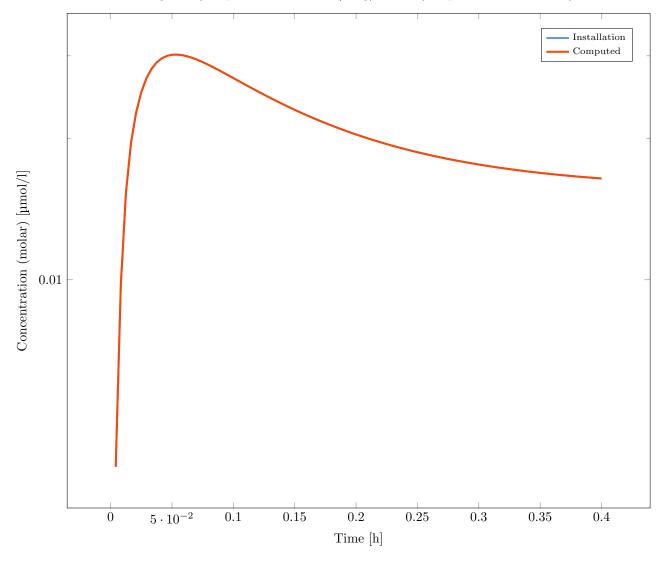


Figure 1.69

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

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

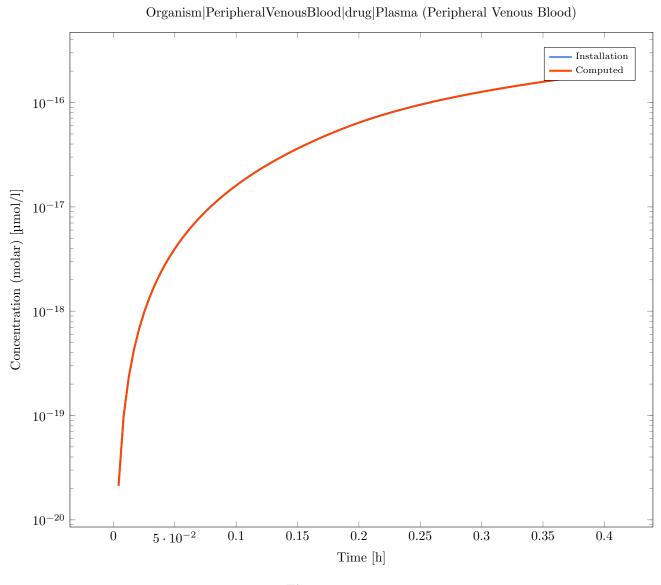


Figure 1.70

Simulation: Mouse_SingleORAL_Dissolved-Mouse_SingleORAL_Dissolved Result of the validation: Valid

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

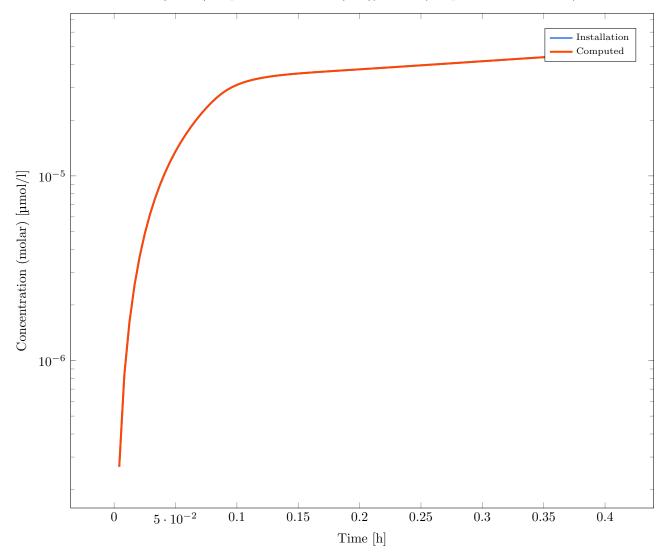


Figure 1.71

Simulation: Mouse_SingleORAL_Dissolved-Mouse_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5 Result of the validation: Valid

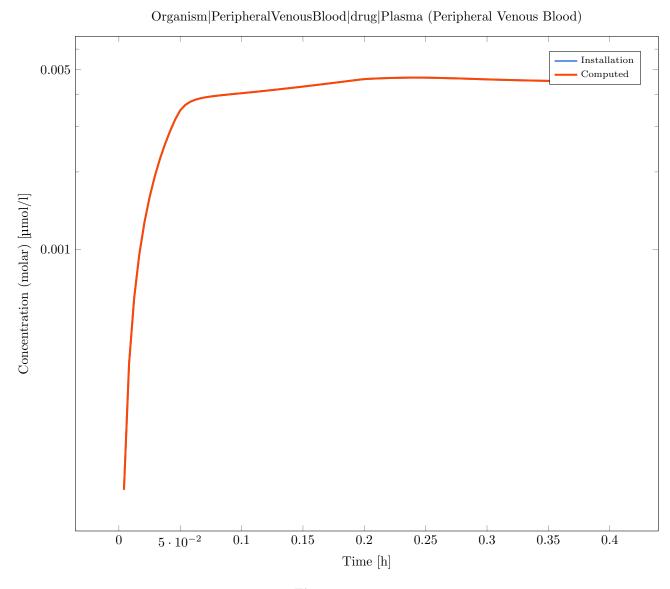
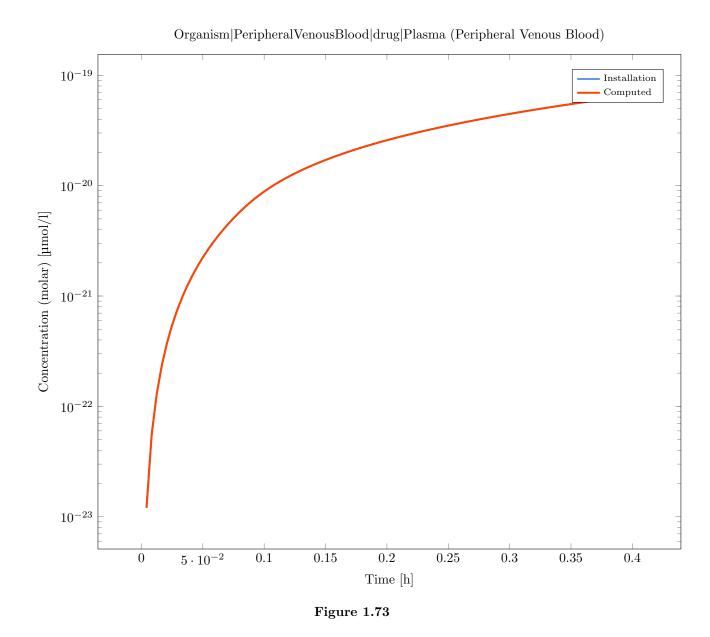


Figure 1.72

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

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



 $Simulation: \ Preterm_SingleIV_Age_0_GA_32_CYP3A4-Preterm_SingleIV_Single$

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 6.48E-8

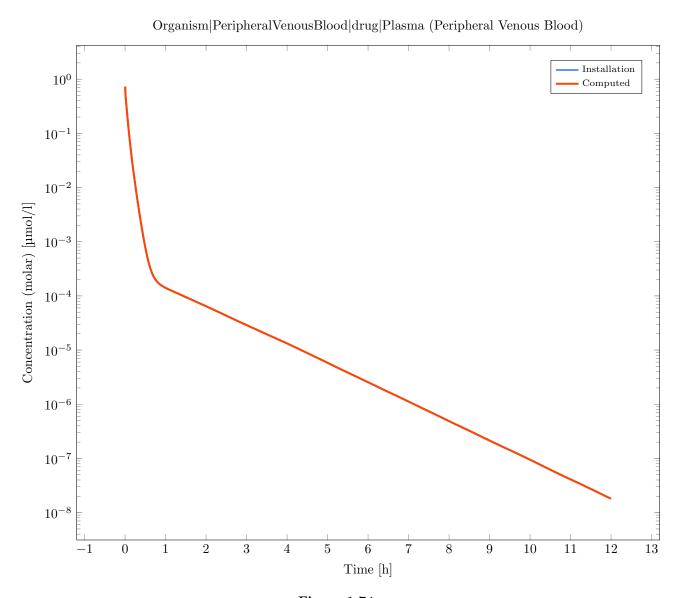
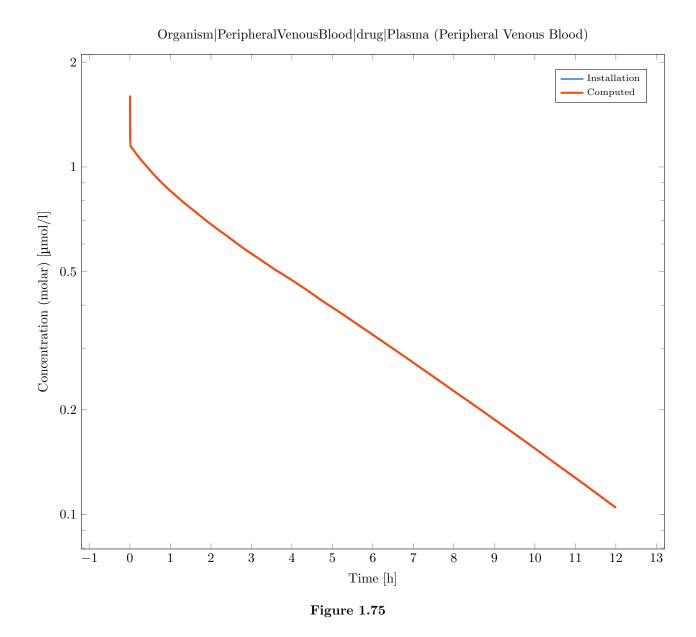
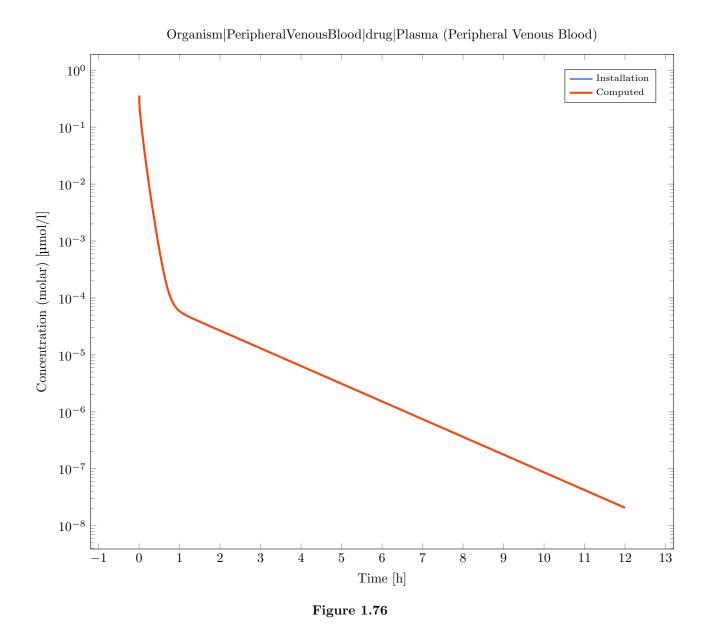


Figure 1.74

Output Path: Organism |Peripheral Venous
Blood |drug |Plasma (Peripheral Venous Blood)
 Deviation: 8.91E-5



 $\label{lem:single_index} \textbf{Simulation: Preterm_SingleIV_Age_15_GA_32_CYP3A4-Preterm_SingleIV_Age_15_CYP3A4-Pr$



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

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

Figure 1.77

Time [h]

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

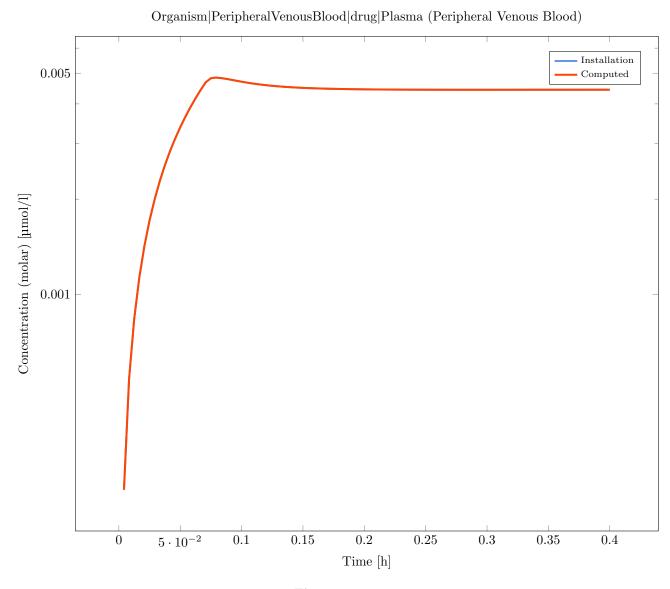
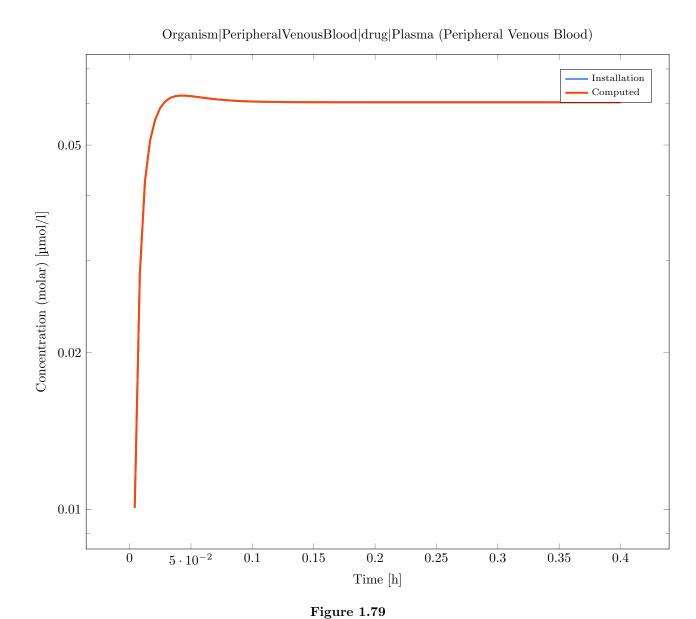


Figure 1.78

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

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



 $Simulation: Rabbit_SingleORAL_Dissolved_Rabbit_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-5$

Result of the validation: Valid

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

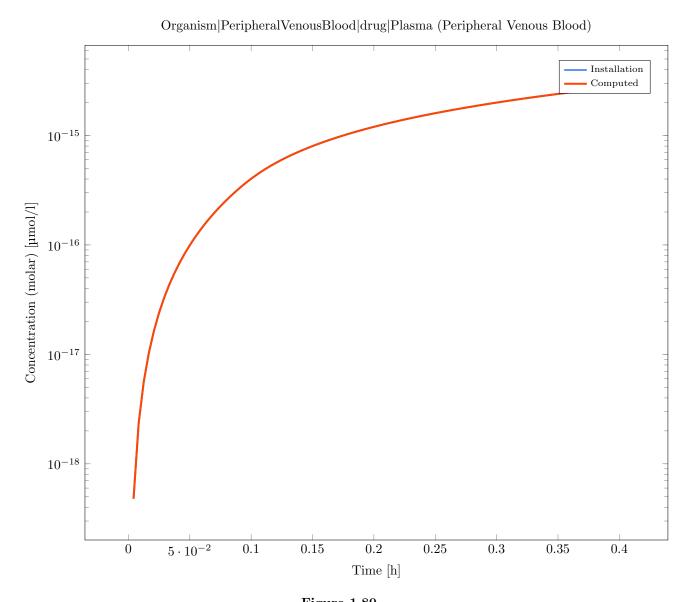
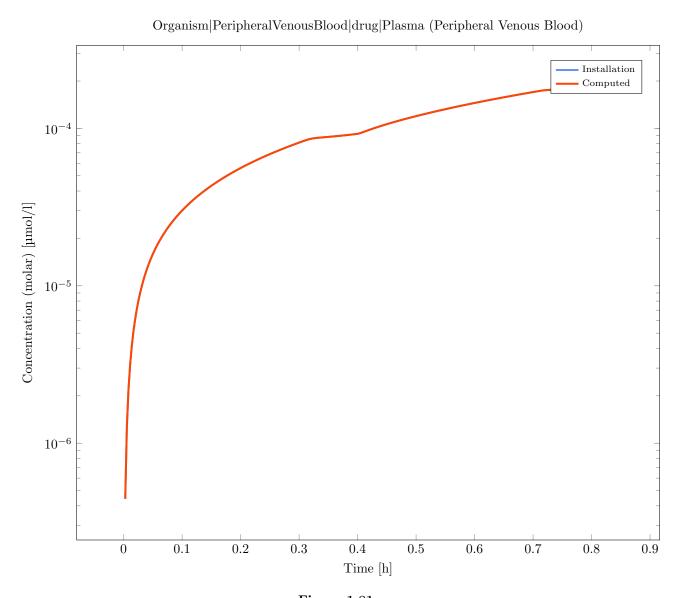


Figure 1.80

Simulation: Rat_MultiORAL_6_6_12_Dissolved-Rat_MultiORAL_6_6_12_Dissolved Result of the validation: Valid



 $\mathbf{Figure~1.81}$

 $\begin{tabular}{ll} \bf Simulation: & Rat_MultiORAL_6_6_6_6_6_0 \\ \bf Dissolved-Rat_MultiORAL_6_6_6_6_0 \\ \bf Dissolved-Rat_MultiORAL_6_6_6_0 \\ \bf Dissolved-Rat_MultiORAL_6_6_6_0 \\ \bf Dissolved-Rat_MultiORAL_6_6_6_0 \\ \bf Dissolved-Rat_MultiORAL_6_6_0 \\ \bf Dissolved-Rat_MultiORAL_6_0 \\ \bf Dissol$

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

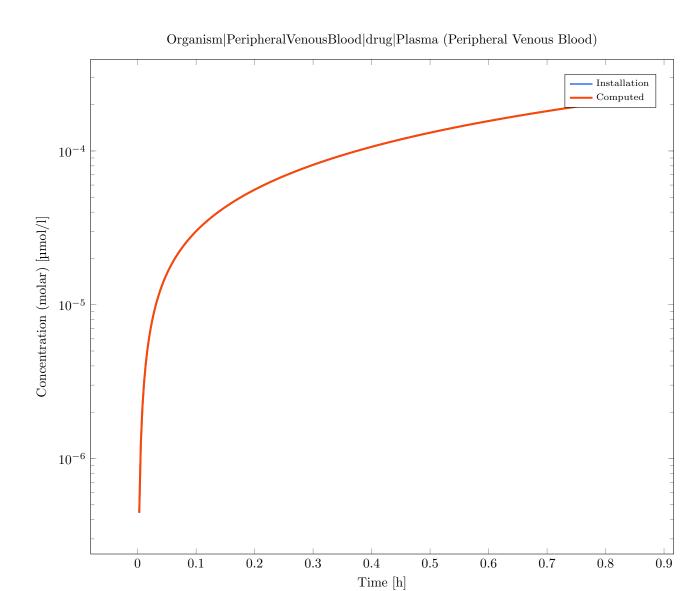


Figure 1.82

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

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

Figure 1.83

Time [h]

 $Simulation: Single IV_2 Pores_Human-Single IV_2 Pores_Human$

Result of the validation: Valid

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

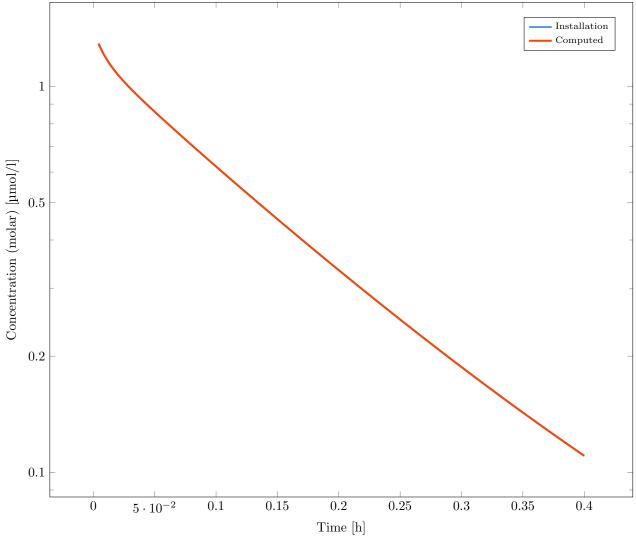


Figure 1.84

Simulation: SingleIV_2Pores_Human-SingleIV_2Pores_Human_SimulationC Result of the validation: Valid

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

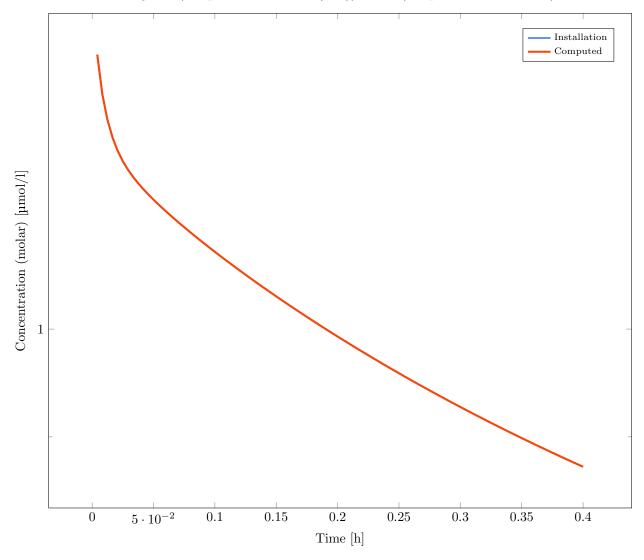
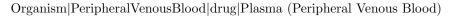


Figure 1.85

Simulation: SingleIV_2Pores_Human-SingleIV_2Pores_Human_SimulationD Result of the validation: Valid



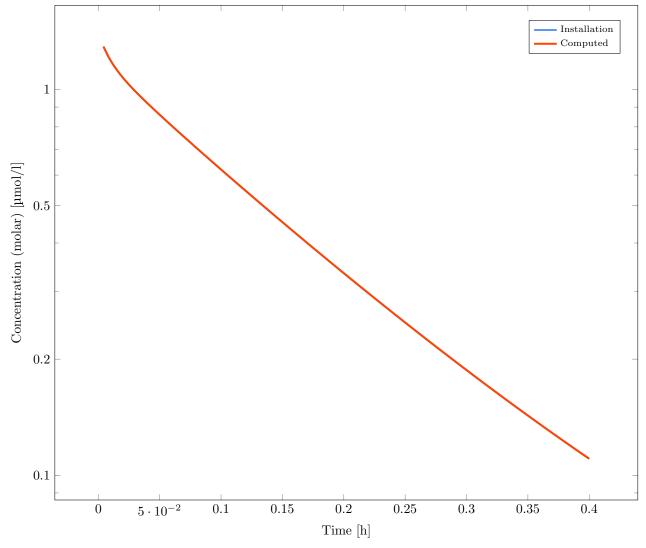


Figure 1.86

Simulation: SingleIV_2Pores_Human-SingleIV_2Pores_Human_SimulationF Result of the validation: Valid

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

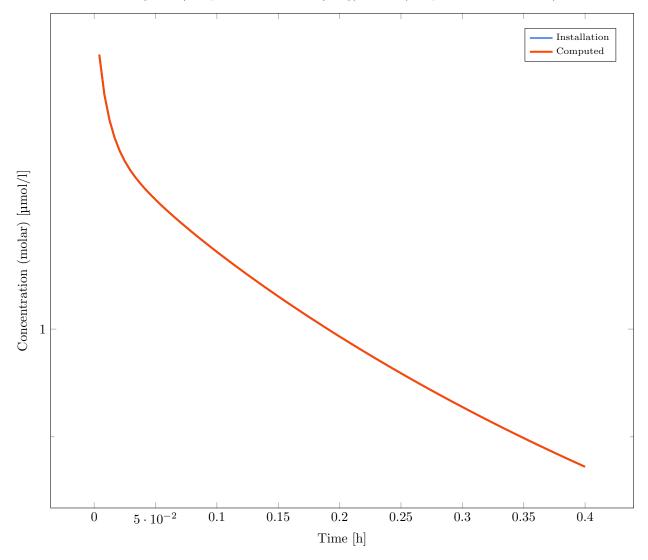


Figure 1.87

 $Simulation: Single IV_2 Pores_Monkey-Single IV_2 Pores_Monkey$

Result of the validation: Valid

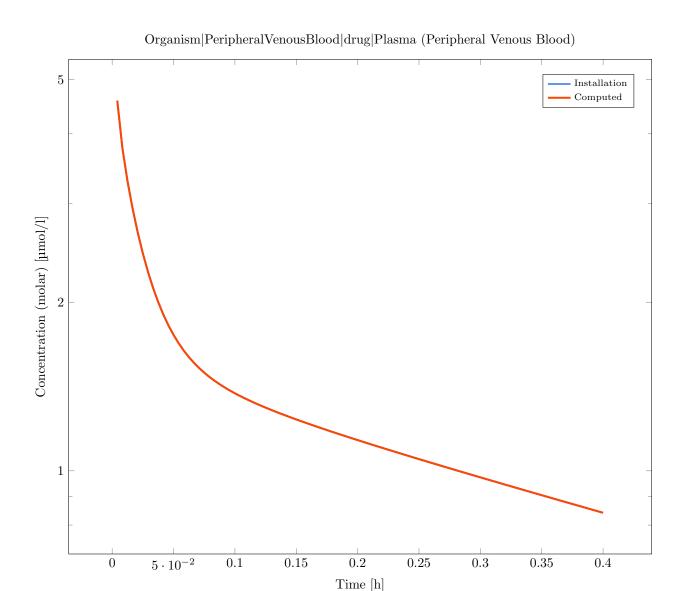


Figure 1.88

Simulation: SingleIV_2Pores_Monkey-SingleIV_2Pores_Monkey_SimulationG Result of the validation: Valid

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

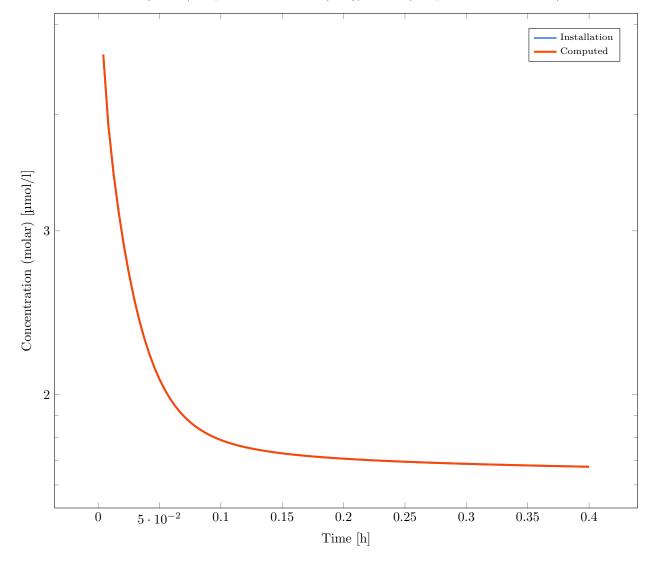


Figure 1.89

Simulation: SingleIV_2Pores_Monkey-SingleIV_2Pores_Monkey_SimulationH Result of the validation: Valid

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

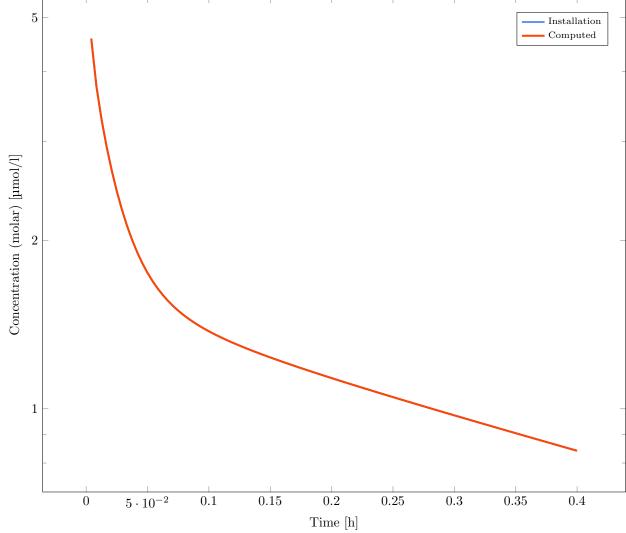


Figure 1.90

 $Simulation: Single IV_2 Pores_Mouse-Single IV_2 Pores_Mouse$

Result of the validation: Valid

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

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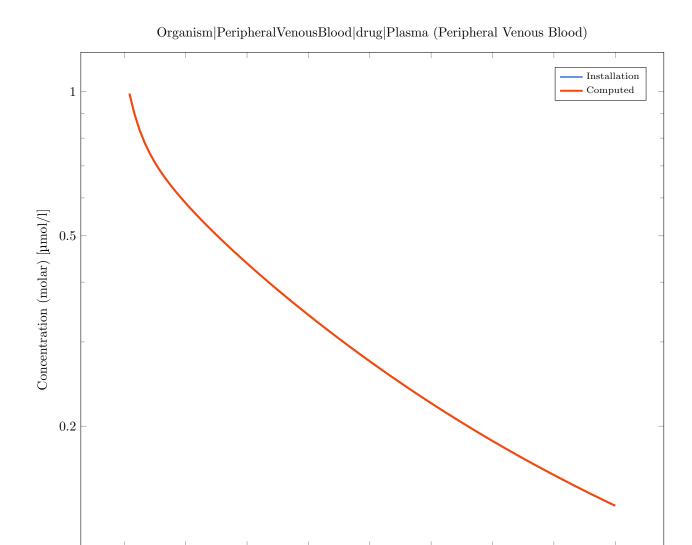


Figure 1.91

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse_SimulationA 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) Installation Computed Onsolve C

Figure 1.92

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse_SimulationB Result of the validation: Valid

0.1

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

0

 $5\cdot 10^{-2}$

0.2

0

 $5\cdot 10^{-2}$

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

Figure 1.93

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

Open Systems Pharmacology Suite - $9\,$

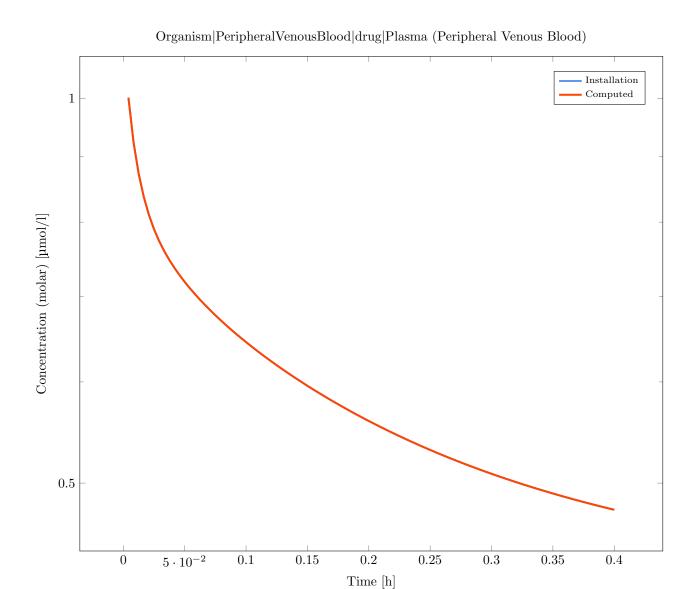
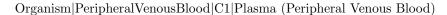


Figure 1.94

 $Simulation: Single IV_C1_4 Comp_standard_stand$

Result of the validation: Valid

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



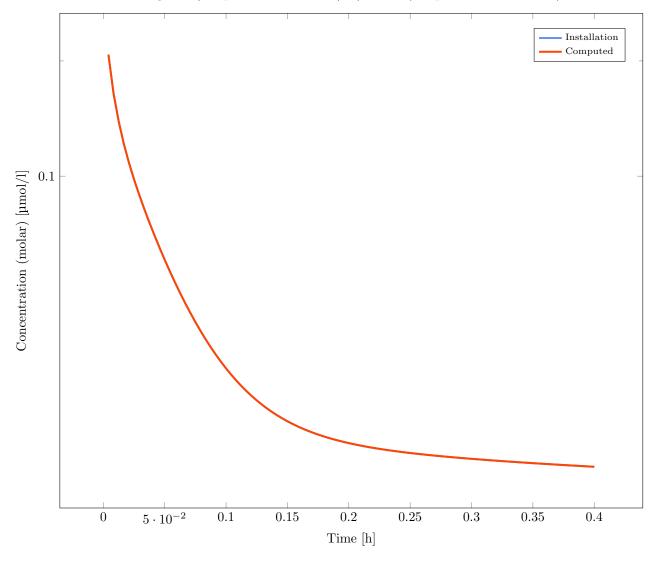


Figure 1.95

 $Simulation: Single IV_C2_4 Comp_PT_standard_st$

$Organism|Peripheral Venous Blood|C2|Plasma\ (Peripheral Venous\ Blood)$

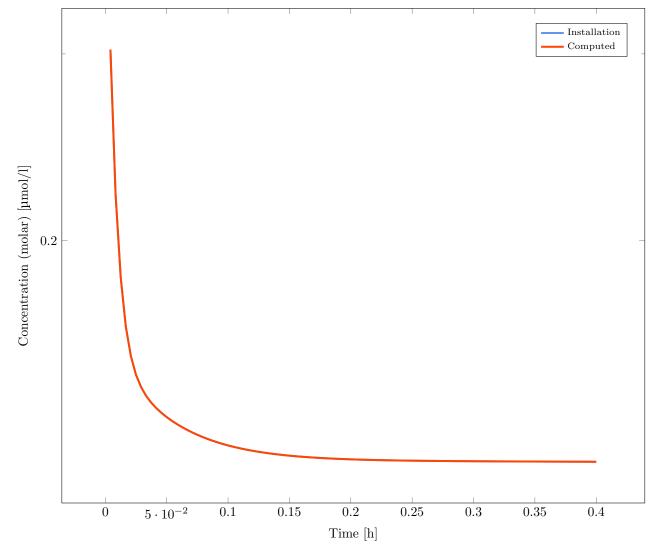


Figure 1.96

 $Simulation: Single IV_C2_4 Comp_RR_standard_st$

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

${\it Organism} | {\it Peripheral Venous Blood} | {\it C2} | {\it Plasma~(Peripheral Venous Blood)}$

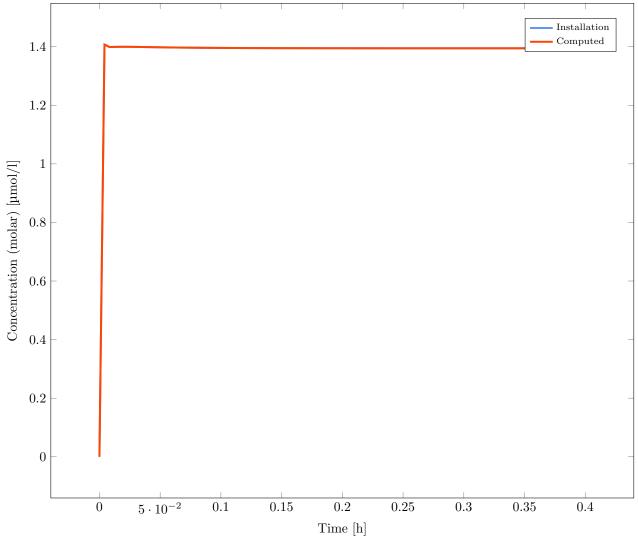


Figure 1.97

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

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 O.5

Figure 1.98

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)

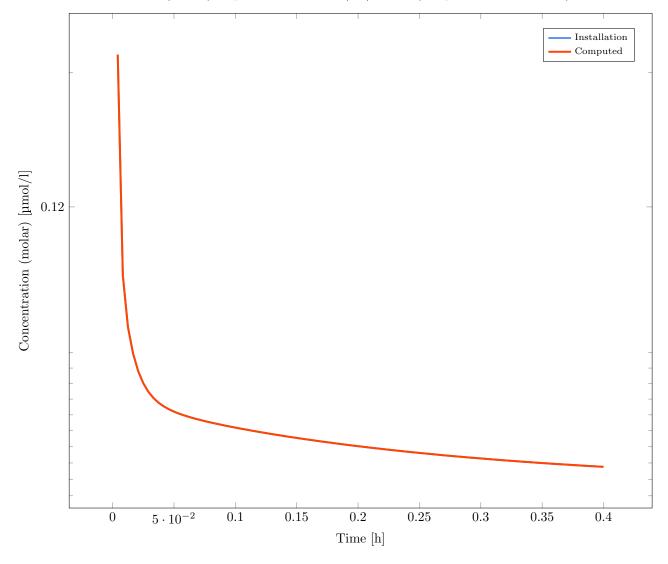


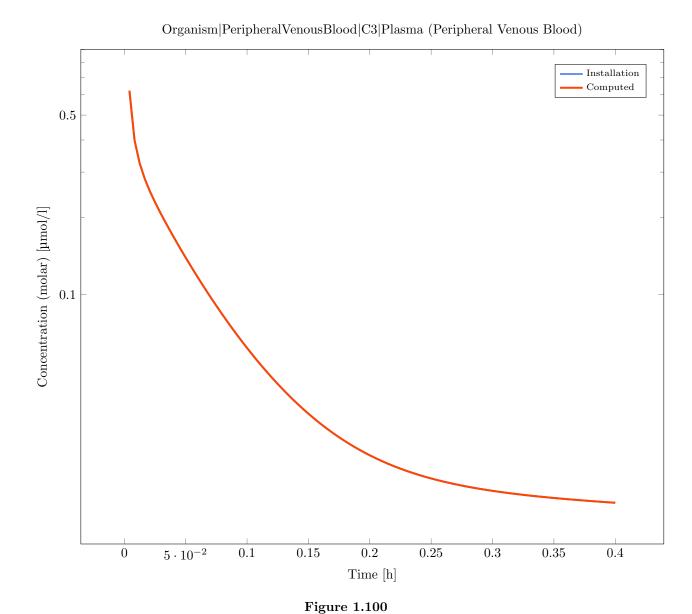
Figure 1.99

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

Result of the validation: Valid

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

Deviation: 0



 $Simulation: Single IV_C4_2 Pores_RR_standard_s$

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

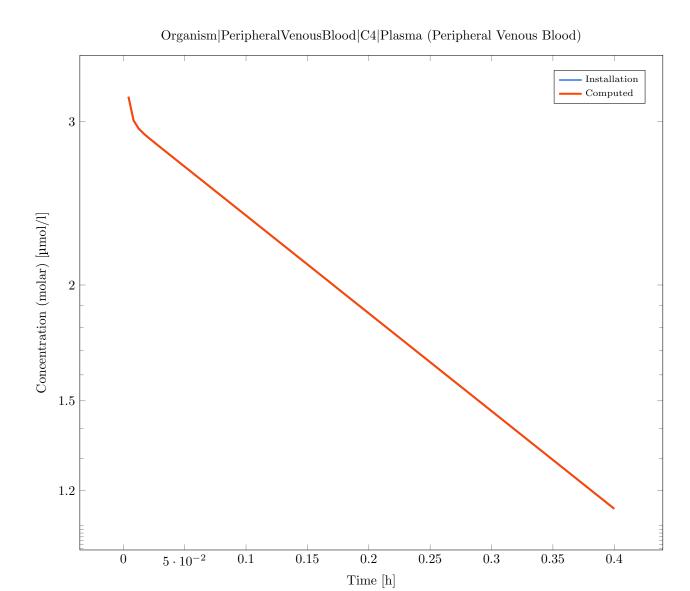


Figure 1.101

 $Simulation: Single IV_C4_4 Comp_Ber_standard_s$

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



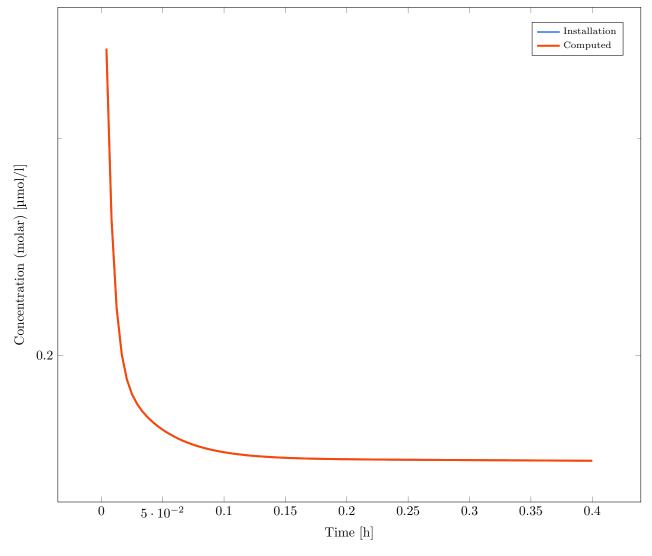


Figure 1.102

 $Simulation: Single IV_C5_2 Pores_Ber_standard_$

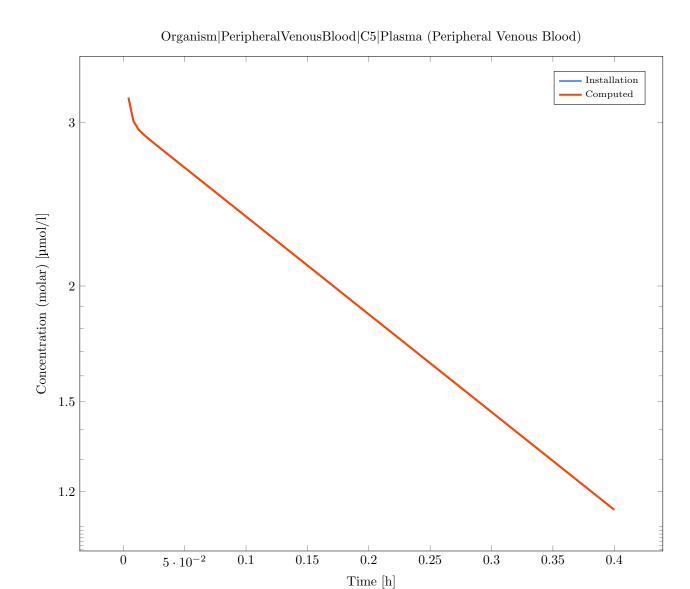


Figure 1.103

 $Simulation: Single IV_C5_2 Pores_PT_standard_s$

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

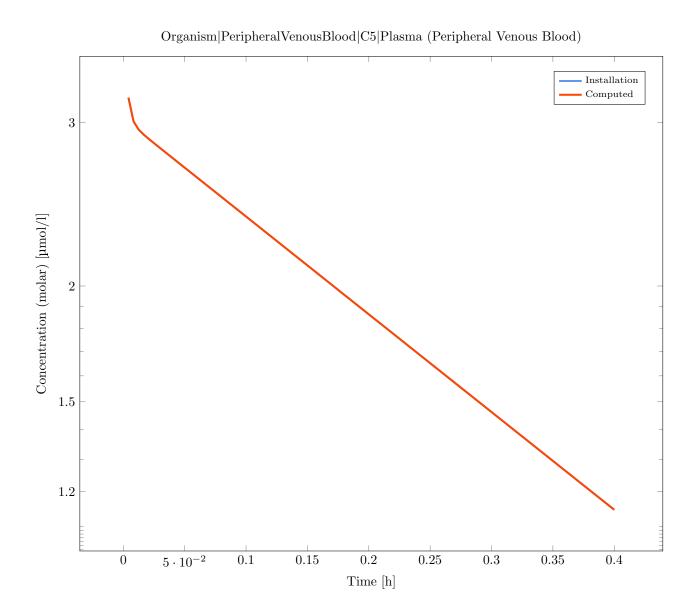
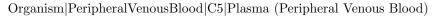


Figure 1.104

 $Simulation: SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_C5_2Pores_RR_schmitt_standard-SingleIV_SingleI$

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



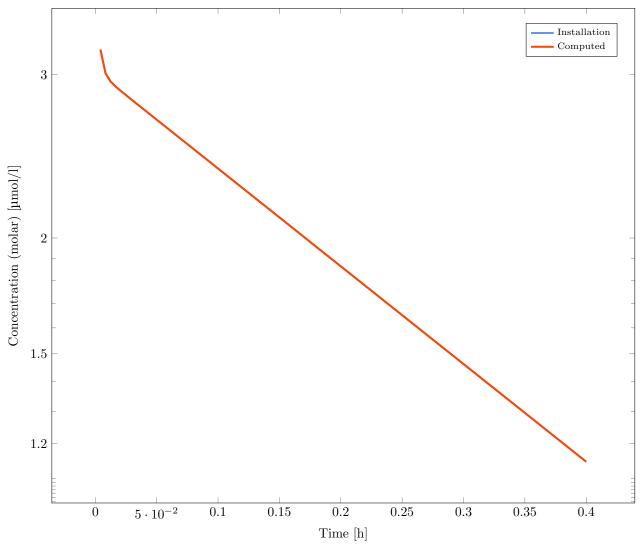


Figure 1.105

 $Simulation: Single IV_C6_2 Pores_standard_stan$

Result of the validation: Valid

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

Deviation: 0

Organism|PeripheralVenousBlood|C6|Plasma (Peripheral Venous Blood)

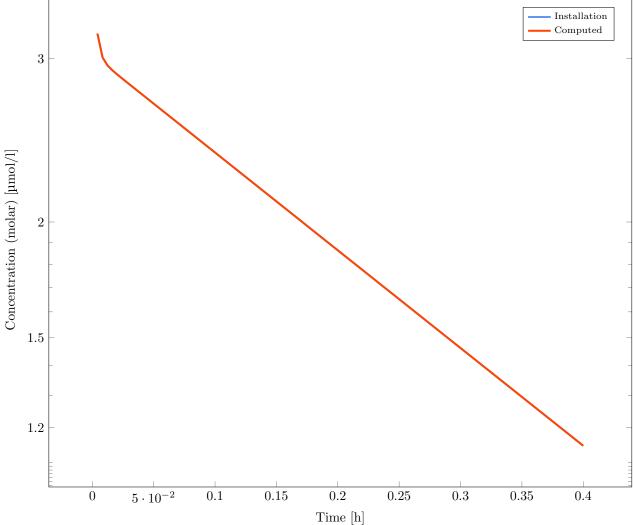


Figure 1.106

 $Simulation: Single IV_C7_2 Pores_standard_schmitt_standard_Single IV_C7_2 Pores_standard_schmitt_schmitt$

Result of the validation: Valid

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

Organism|PeripheralVenousBlood|C7|Plasma (Peripheral Venous Blood) 0.5

Figure 1.107

 $Simulation: Single IV_C7_4 Comp_schmitt_standard_standa$ standard

Result of the validation: Valid

Output Path: Organism|PeripheralVenousBlood|C7|Plasma (Peripheral Venous Blood) Deviation: 0



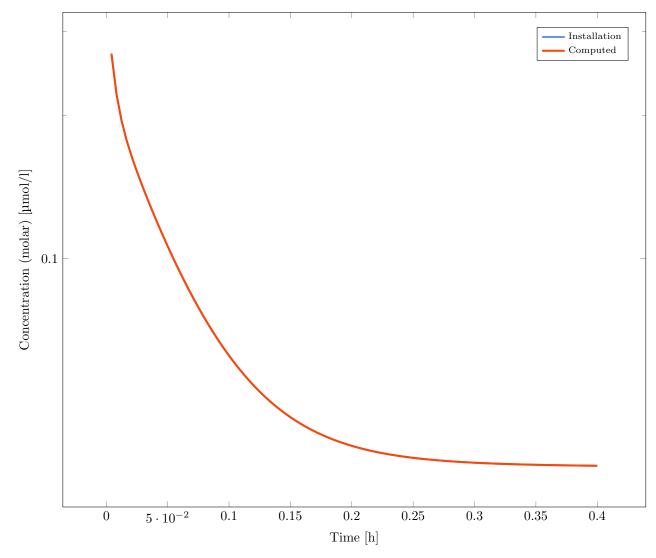


Figure 1.108

 $Simulation: Single IV_C8_2 Pores_standard_schmittnormalized_standard_Single IV_C8_2 Pores_standard_schmittnormalized_schmittnormalized_schmittnor$

Result of the validation: Valid

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

Organism|PeripheralVenousBlood|C8|Plasma (Peripheral Venous Blood)

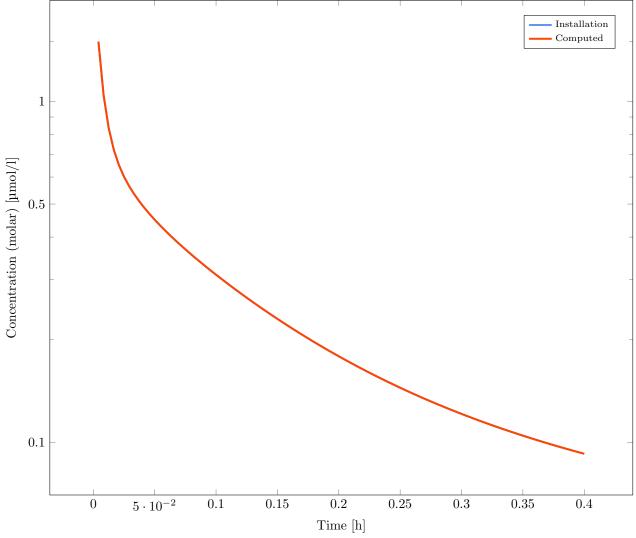


Figure 1.109

 $Simulation: Single IV_C9_2 Pores_schmitt_standard_standard_Single IV_C9_2 Pores_schmitt_standard_sta$

Result of the validation: Valid

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

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

Figure 1.110

0.15

0.1

 $Simulation: Single ORAL_C10_4 Comp_PT_standard_standard_Single ORAL_C10_4 Comp_PT_standard_$

0.2

Time [h]

0.25

0.3

0.35

0.4

Result of the validation: Valid

0

 $5\cdot 10^{-2}$

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

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

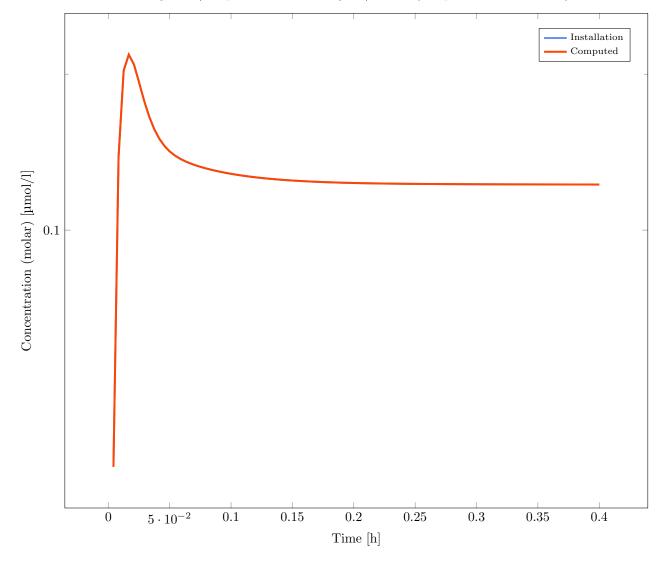


Figure 1.111

 $Simulation: Single ORAL_C11_4 Comp_schmitt_standard_standard_Single ORAL_C11_4 Comp_schmitt_standard$ $standard_standard$

Result of the validation: Valid

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

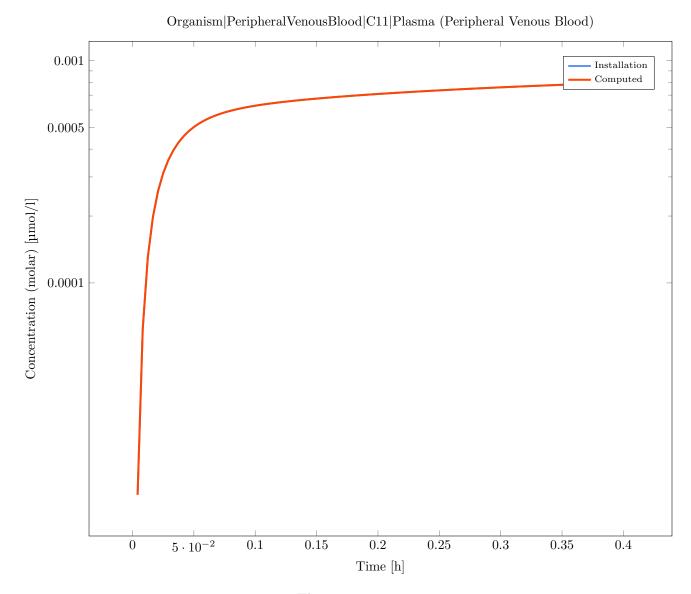
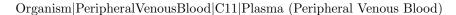


Figure 1.112

 $Simulation: Single ORAL_C11_4 Comp_standard_st$

Result of the validation: Valid

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



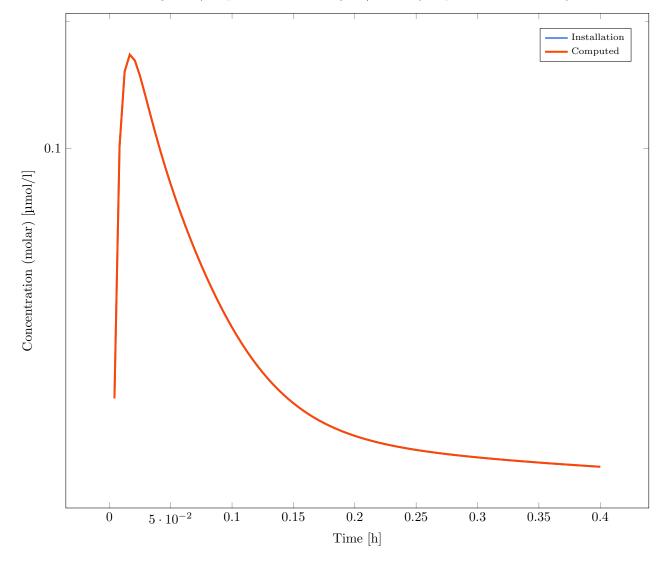


Figure 1.113

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

Result of the validation: Valid

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

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

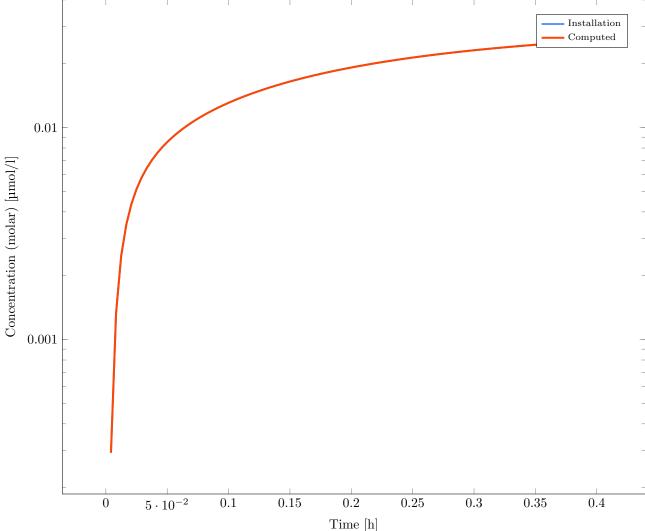


Figure 1.114

 $Simulation: Single ORAL_C13_2 Pores_schmitt_standard_st$

Result of the validation: Valid

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



Figure 1.115

 $Simulation: Single ORAL_C13_4 Comp_standard_schmittnormalized_schmittnormalized_sc$

Result of the validation: Valid

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

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

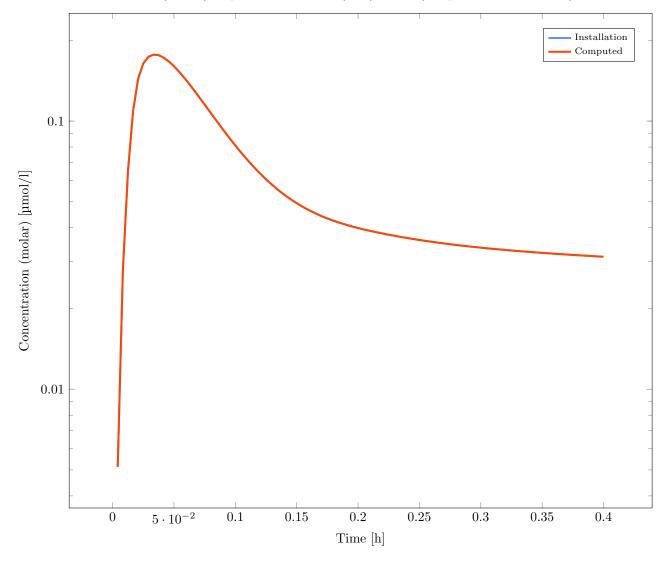


Figure 1.116

 $Simulation: Single ORAL_C14_2 Pores_PT_standard_standard_Single ORAL_C14_2 Pores_PT_standard_standar$

Result of the validation: Valid

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

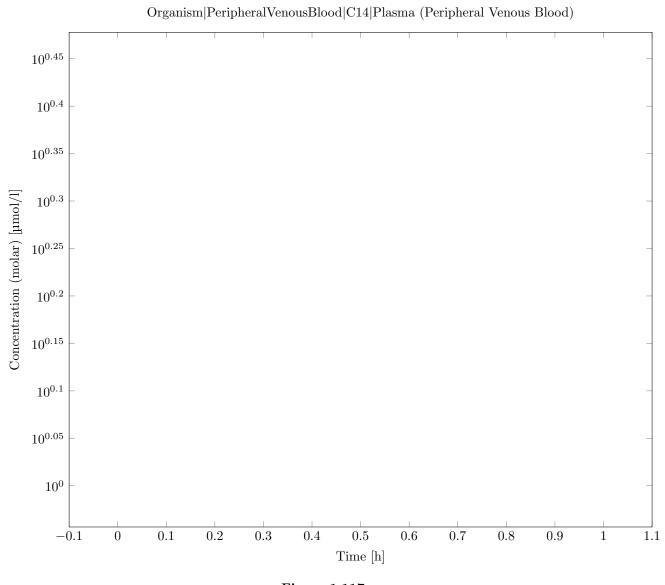


Figure 1.117

 $Simulation: Single ORAL_C2_2 Pores_standard_st$

Result of the validation: Valid

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

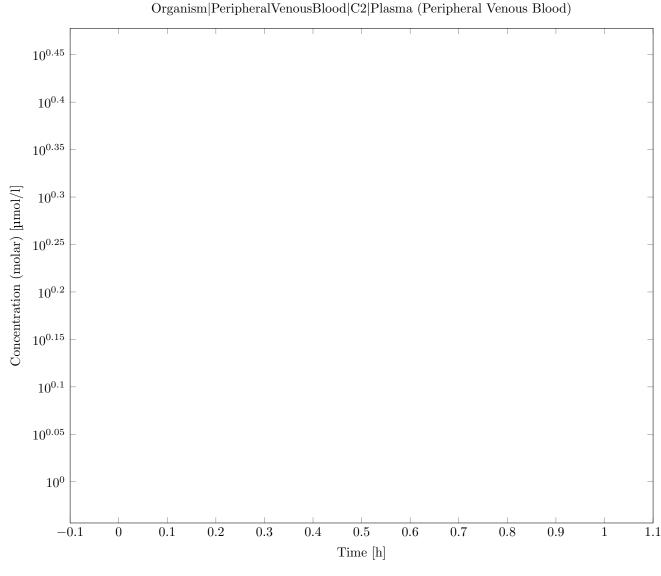


Figure 1.118

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

Result of the validation: Valid

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

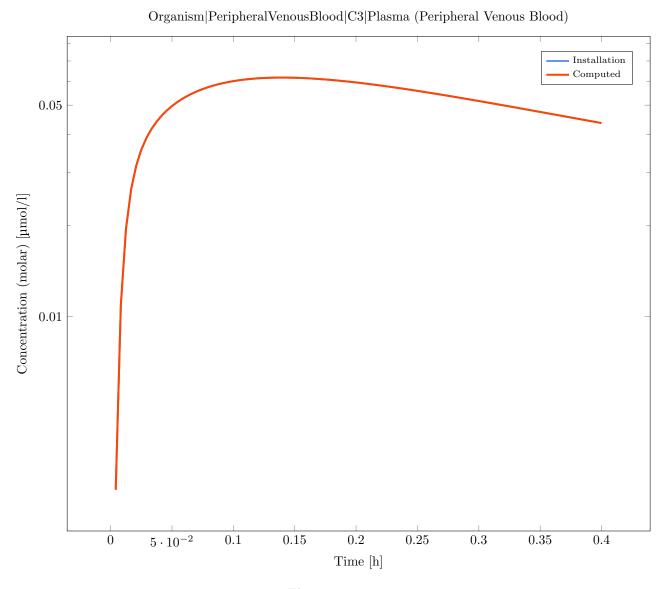


Figure 1.119

 $Simulation: Single ORAL_C4_2 Pores_standard_schmittnormalized_standard_Single ORAL_C4_2 Pores_standard_schmittnormalized_standard$

Result of the validation: Valid

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

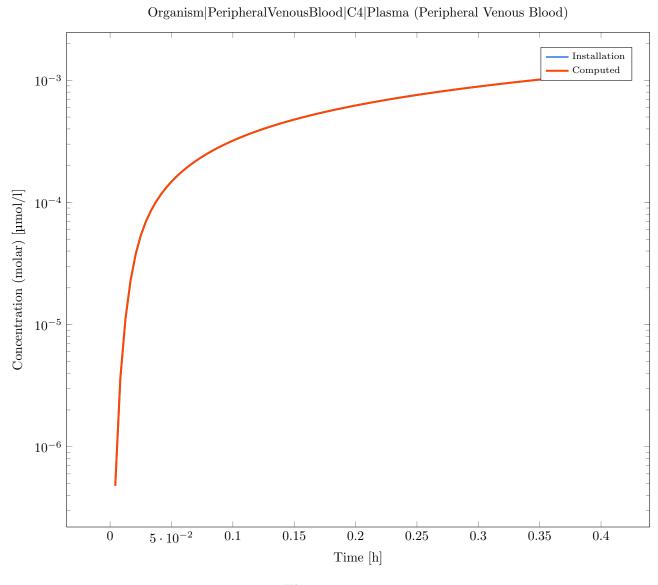


Figure 1.120

 $Simulation: Single ORAL_C6_4 Comp_Ber_standard_standard_Single ORAL_C6_4 Comp_Ber_standard_$

Result of the validation: Valid

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



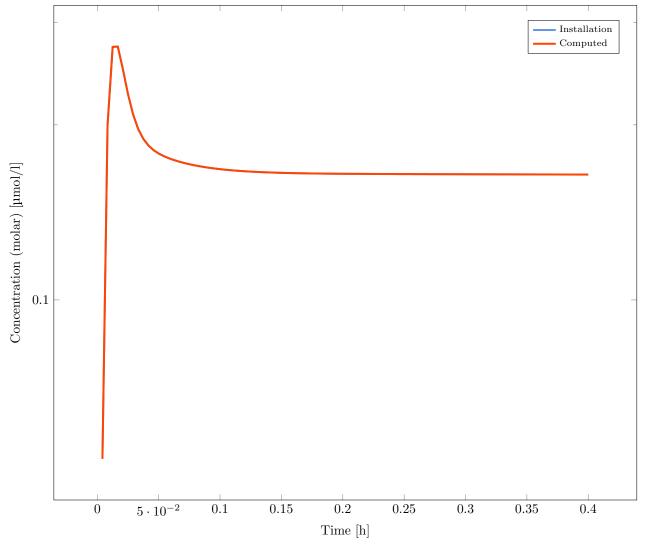


Figure 1.121

 $Simulation: Single ORAL_C6_4 Comp_RR_standard_standard_Single ORAL_C6_4 Comp_RR_standard_st$

Result of the validation: Valid

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

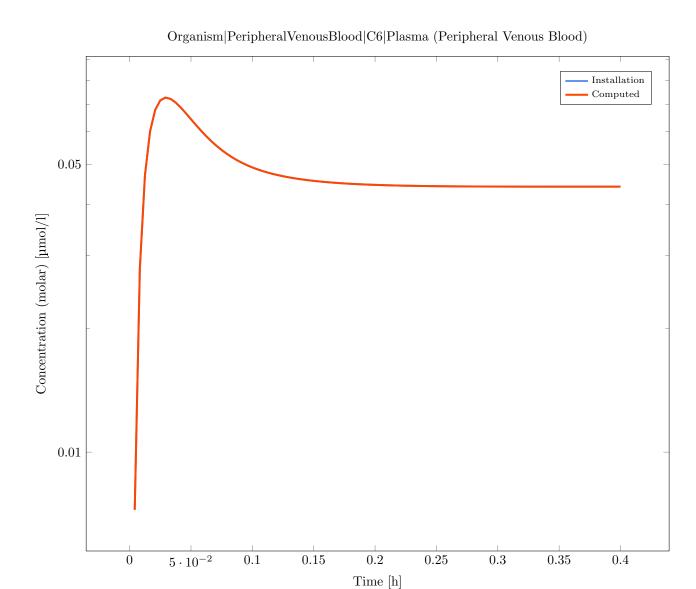


Figure 1.122

 $Simulation: Single ORAL_C7_2 Pores_Ber_standard_standard_Single ORAL_C7_2 Pores_Ber_standard_standar$

Result of the validation: Valid

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

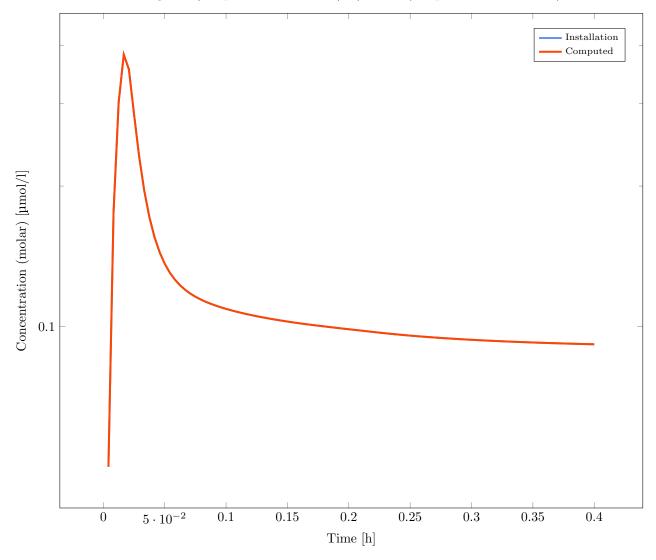


Figure 1.123

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

Result of the validation: Valid

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

Organism|PeripheralVenousBlood|C7|Plasma (Peripheral Venous Blood) Installation Computed 0.5 0.1 0.1

Figure 1.124

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

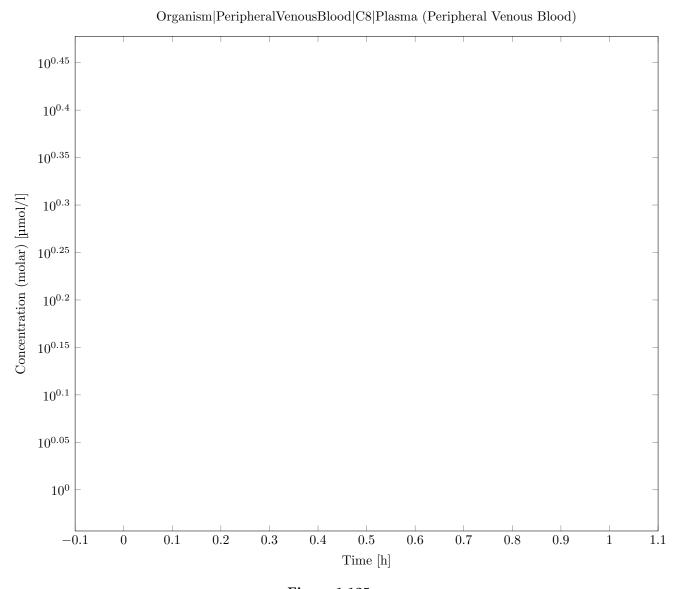
0

 $5\cdot 10^{-2}$

Output Path: Organism |PeripheralVenousBlood |C8 |Plasma (Peripheral Venous Blood)
 Deviation: ${\bf 0}$

0.15

0.1



 ${\bf Figure~1.125}$

 $Simulation: Single ORAL_C9_2 Pores_RR_schmitt_standard-Single ORAL_SCHMitt_standard-Single ORAL_SCHMit$

Result of the validation: Valid

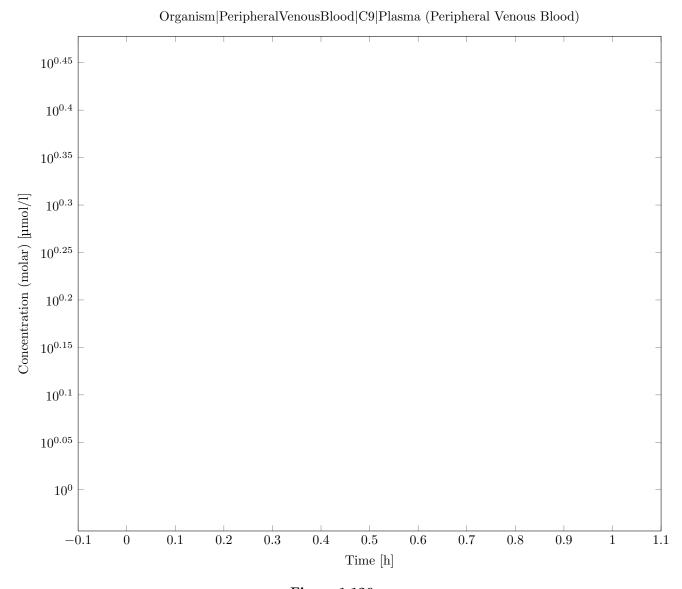


Figure 1.126

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

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

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

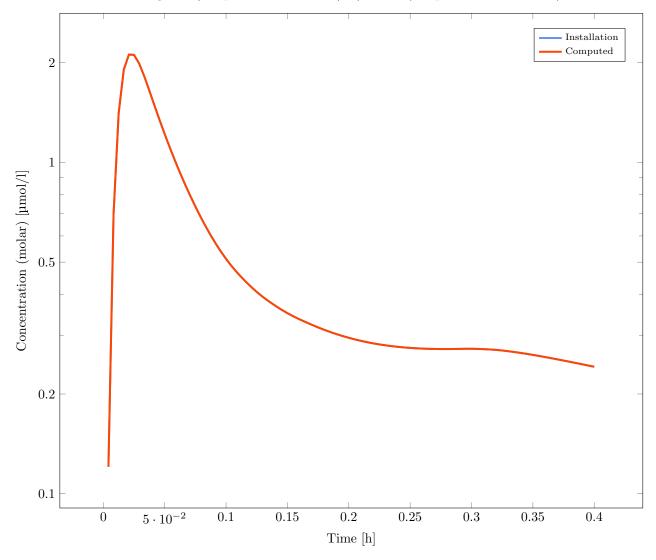


Figure 1.127

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: ${\bf 0}$



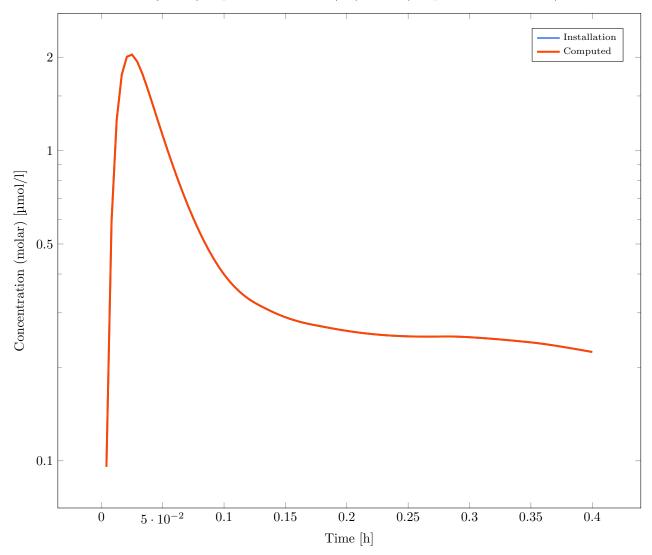


Figure 1.128

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

result of the validation. Valid

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

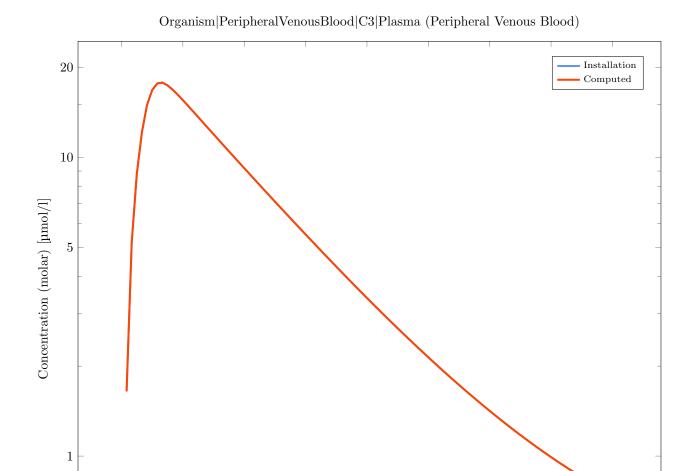


Figure 1.129

0.2

Time [h]

0.25

0.3

0.35

0.4

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

0.1

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

0.15

0

 $5\cdot 10^{-2}$

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

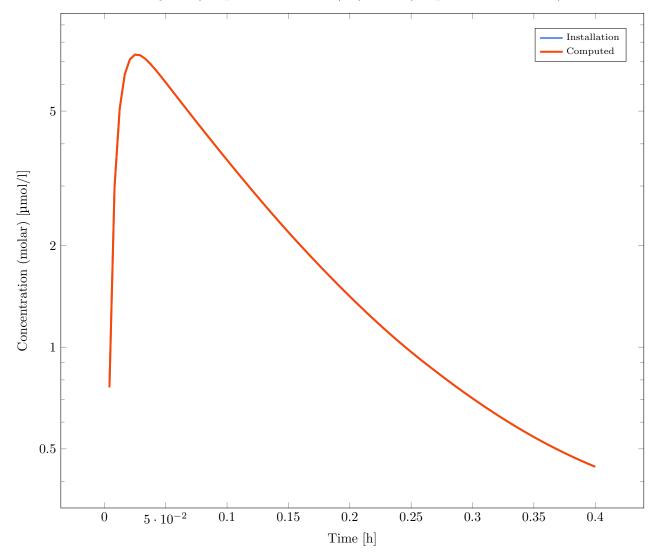


Figure 1.130