# Open Systems Pharmacology Suite - 7.3.0 Installation Validation

user

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# Chapter 1

# Installation Validation Results

### **Overall Validation Result**

Valid

### 1.1 Validation Summary

### **Run Duration**

Start time:  $2018-06-10\ 01:07$ End time:  $2018-06-10\ 01:18$ 

Validation performed in 10m:14s:625ms

### Input Configuration Folder

 $C: \label{lem:condition} C: \label{lem:condition} Paramacology \label{lem:condition} Inputs \label{lem:condition} Batch Files \label{lem:condition} Paramacology \label{lem:condition} Inputs \label{lem:condition} Paramacology \label{lem:condition} Paramacology$ 

### **Local Outputs Location**

### **Application Versions**

PK-Sim Version 7.3.0.42 MoBi Version 7.3.0.35

### Computer Name

WIN-TSALD3O4R5J

### Operating System

Windows 7 Ultimate - Service Pack 1

### 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\7.3\Outputs\BatchFiles

### Computed Folder

### 1.2.1 Valid Simulations (125/125)

### Simulation: Beagle\_SingleORAL\_Dissolved-Beagle\_SingleORAL\_Dissolved

Result of the validation: Valid

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

Deviation: 0

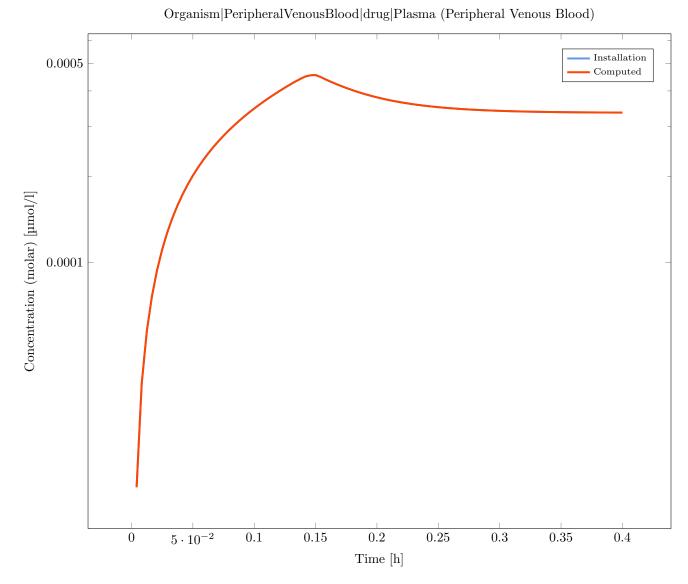


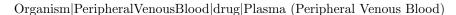
Figure 1.1

 $Simulation: Beagle\_SingleORAL\_Dissolved\_Beagle\_SingleORAL\_Dissolved\_MW\_200\_fu\_0.2\_LogP\_-$ 

Result of the validation: Valid

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

Deviation: 0



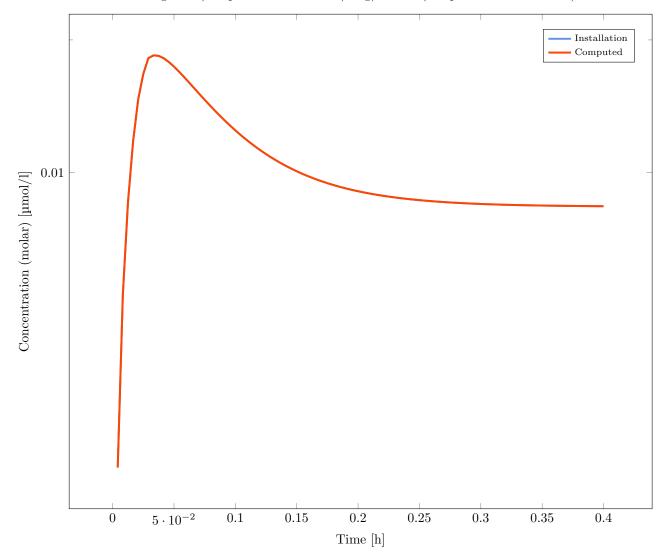


Figure 1.2

 $Simulation: Beagle\_SingleORAL\_Dissolved\_Beagle\_SingleORAL\_Dissolved\_MW\_800\_fu\_0.6\_LogP\_-5$ 

Result of the validation: Valid

### Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood) Deviation:<br/> 0

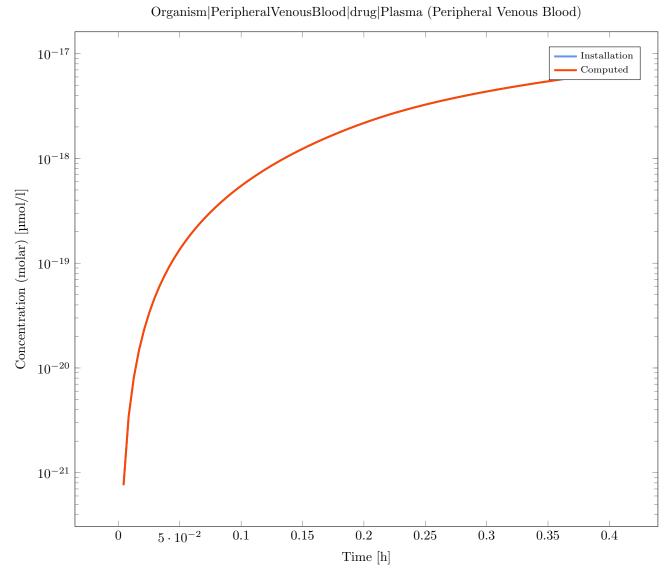


Figure 1.3

 $Simulation: \begin{tabular}{ll} Dog\_MultiORAL\_12\_12\_Dissolved-Dog\_MultiORAL\_12\_12\_Dissolved \\ Result of the validation: Valid \\ \end{tabular}$ 

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

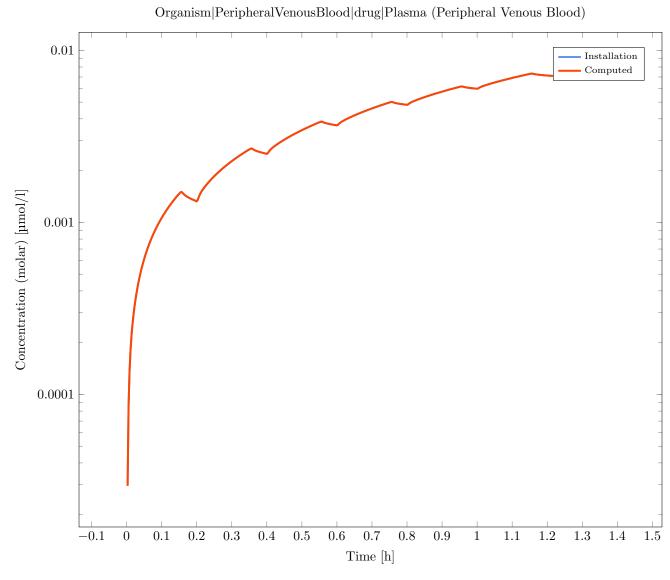


Figure 1.4

 $\begin{tabular}{ll} \bf Simulation: \begin{tabular}{ll} \bf Dog\_MultiORAL\_24\_Dissolved-Dog\_MultiORAL\_24\_$ 

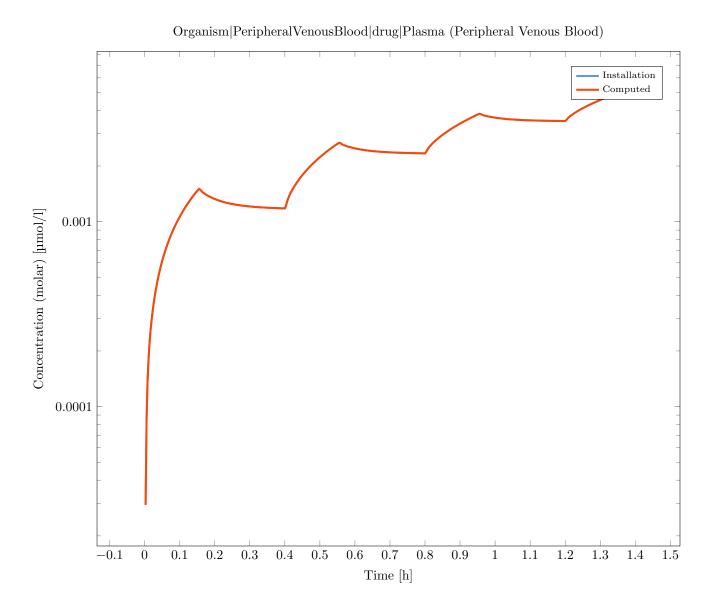
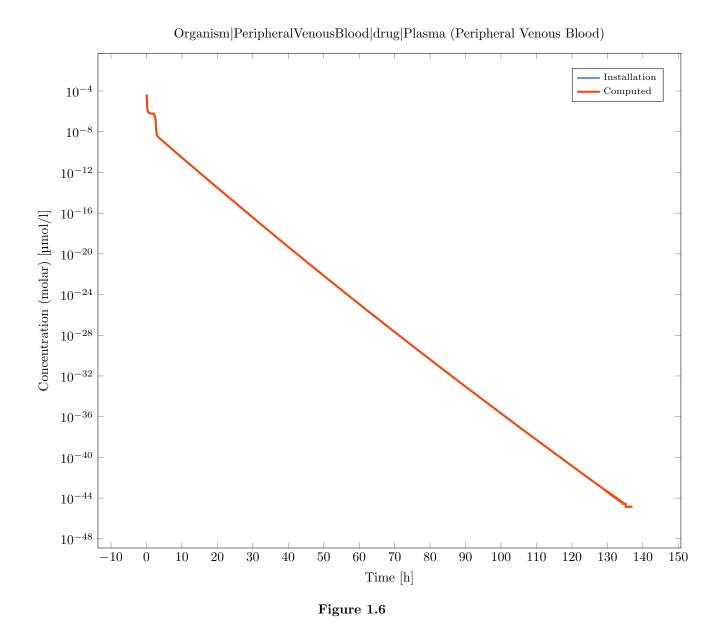


Figure 1.5

 $\begin{tabular}{ll} \bf Simulation: European\_SingleORAL\_Age\_0\_CYP3A4-European\_SingleORAL\_Age\_0\_CYP3$ 



 ${\bf Simulation: European\_SingleORAL\_Age\_0\_GFR-European\_SingleORAL\_Age\_0\_GFR} \\ {\bf Result of the \ validation: \ Valid}$ 

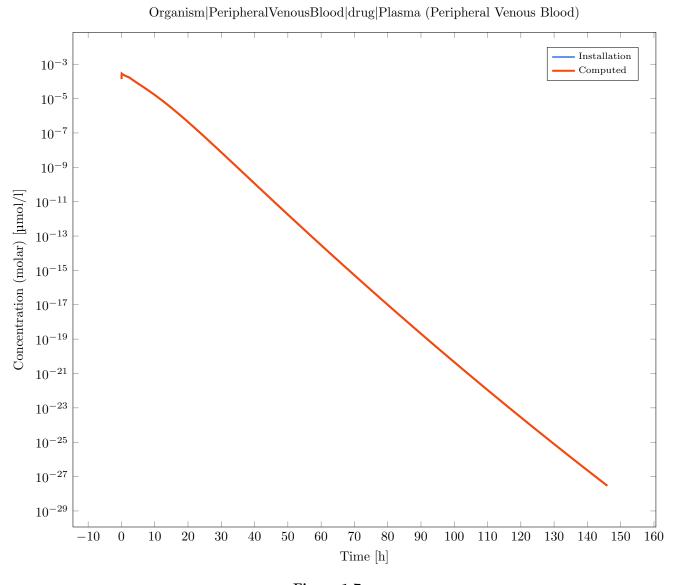


Figure 1.7

 $\begin{tabular}{ll} \bf Simulation: European\_SingleORAL\_Age\_1\_CYP3A4-European\_SingleORAL\_Age\_1\_CYP3$ 

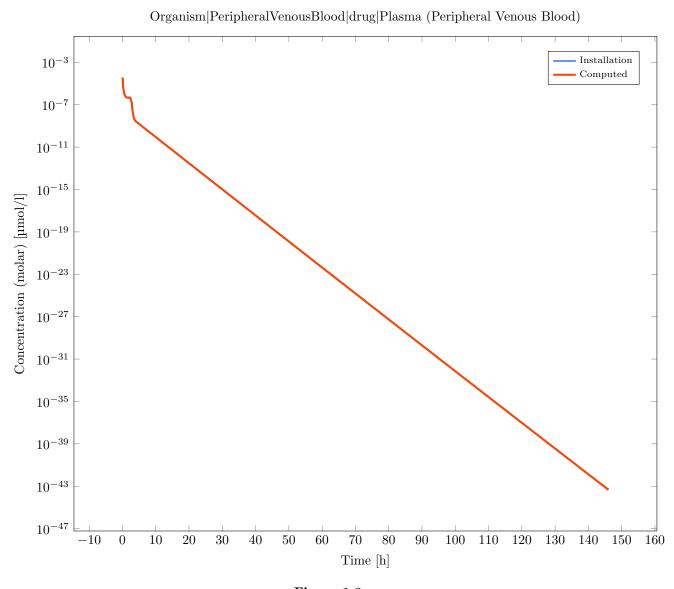


Figure 1.8

 ${\bf Simulation: European\_SingleORAL\_Age\_1\_GFR-European\_SingleORAL\_Age\_1\_GFR} \\ {\bf Result of the \ validation: \ Valid}$ 

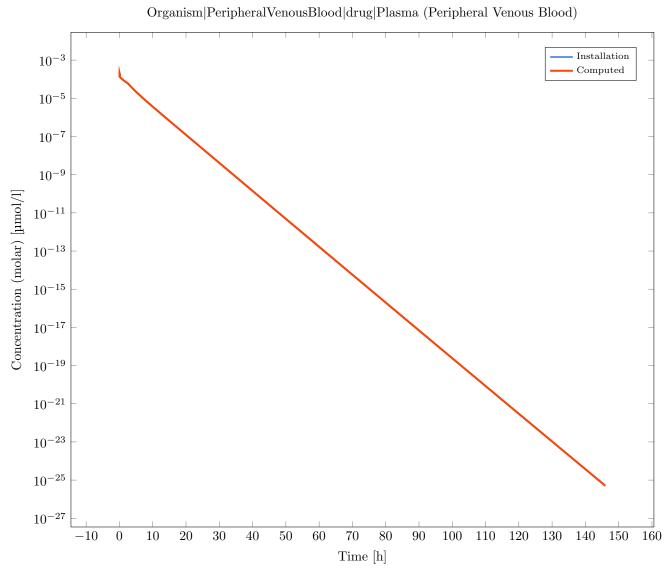


Figure 1.9

 ${\bf Simulation: Human\_Competitive Inhibition-Human\_Competitive Inhibition}$ 

Result of the validation: Valid

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

Deviation: 0

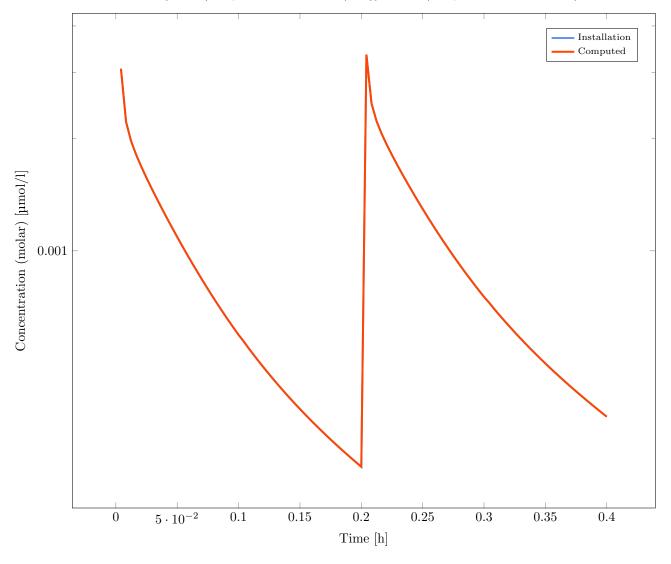


Figure 1.10

Output Path: Organism |PeripheralVenousBlood |<br/>inhibitor |Plasma (Peripheral Venous Blood) | Deviation:<br/> 0

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

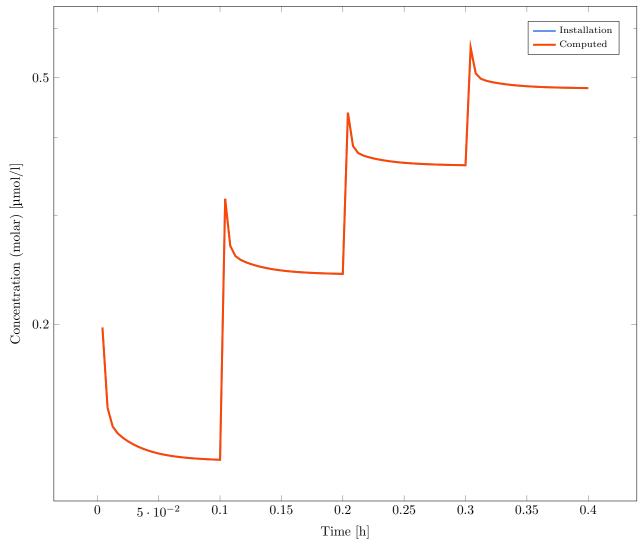


Figure 1.11

Simulation: Human\_ICRP\_AGP-01\_ICRP\_0y\_Male

Result of the validation: Valid

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

Deviation: 0

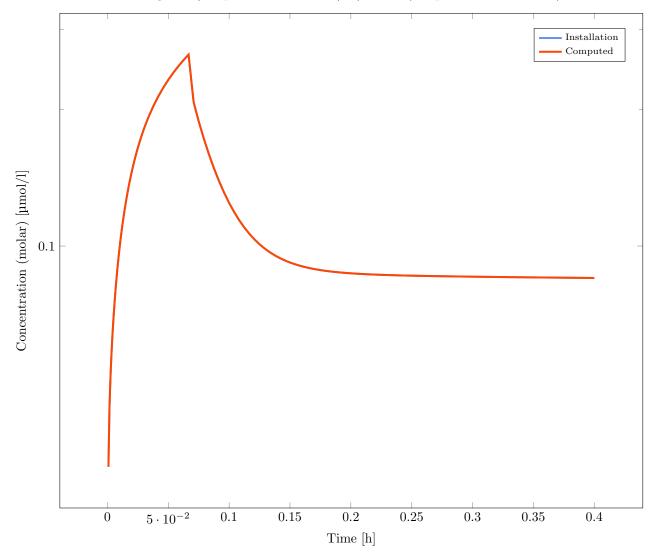


Figure 1.12

 $Simulation: \ Human\_ICRP\_AGP-02\_ICRP\_0.05y\_Female$ 

Result of the validation: Valid

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

Deviation: 0

# Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood) O.5 Installation Computed O.1 O.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<br/>Blood |C1 |Plasma (Peripheral Venous Blood)<br/> Deviation:  ${\bf 0}$ 

0.15

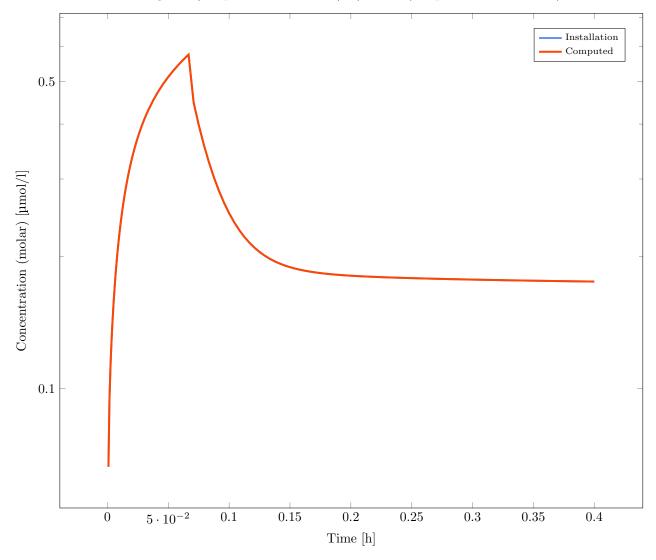


Figure 1.14

Simulation: Human\_ICRP\_AGP-04\_ICRP\_1y\_Female

Result of the validation: Valid

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

Deviation: 0

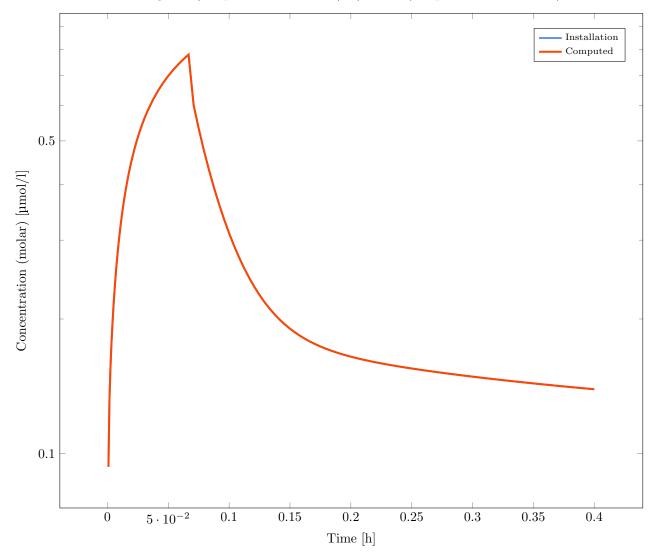


Figure 1.15

 $Simulation: \ Human\_ICRP\_AGP-05\_ICRP\_12y\_Male$ 

Result of the validation: Valid

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

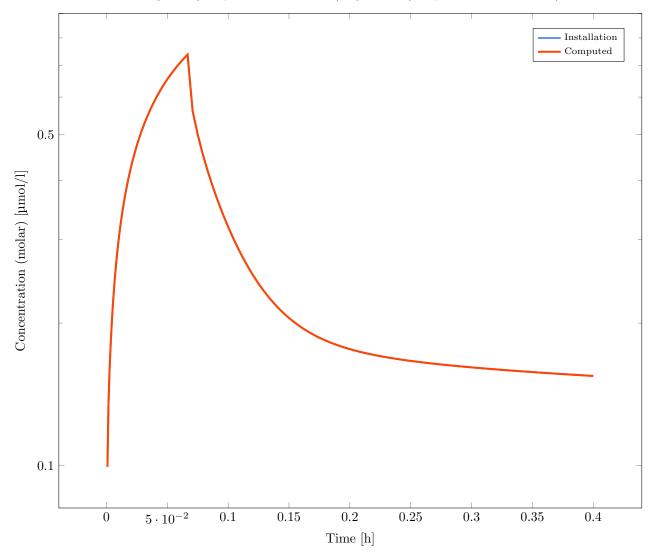


Figure 1.16

 $Simulation: \ Human\_ICRP\_AGP-06\_ICRP\_30y\_Female$ 

Result of the validation: Valid

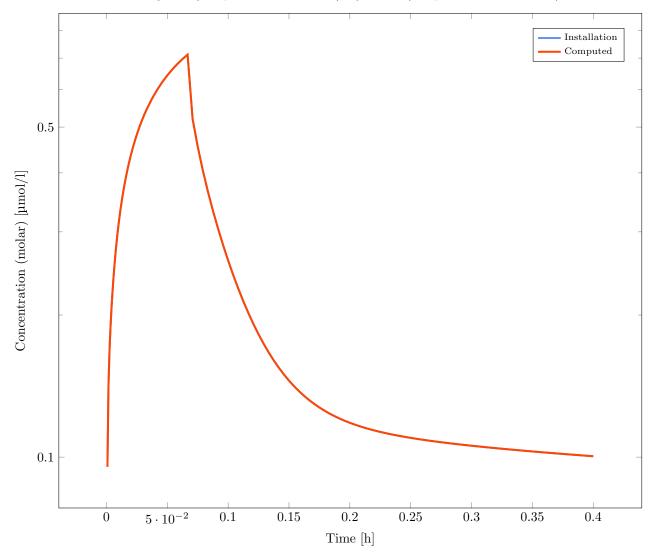


Figure 1.17

 $Simulation: \ Human\_ICRP\_AGP-07\_ICRP\_100y\_Male$ 

Result of the validation: Valid

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

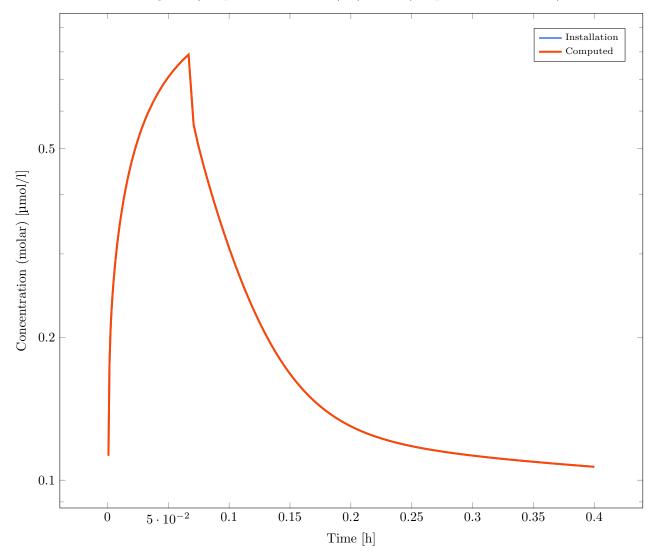


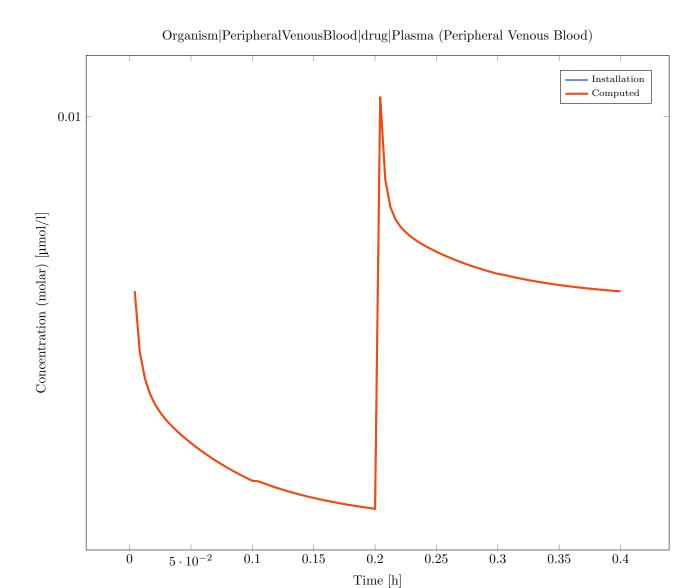
Figure 1.18

 ${\bf Simulation: \ Human\_Irreversible Inhibition-Human\_Irreversible Inhibition}$ 

Result of the validation: Valid

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

Deviation: 0



Output Path: Organism |PeripheralVenousBlood |<br/>inhibitor |Plasma (Peripheral Venous Blood) | Deviation:<br/> 0

Figure 1.19

# Organism|PeripheralVenousBlood|inhibitor|Plasma (Peripheral Venous Blood) 0.5 |[V||Ound| (xe)| (xe) | (xe

**Figure 1.20** 

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: \ Human\_MixedInhibition-Human\_MixedInhibition$ 

0.1

Result of the validation: Valid

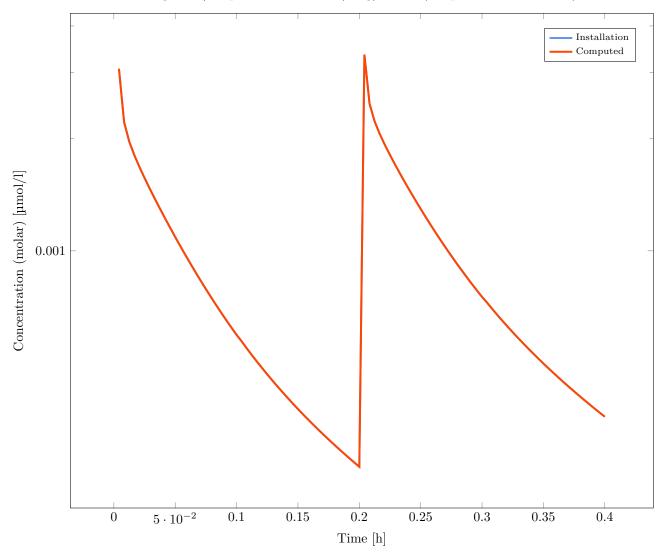
0

 $5 \cdot 10^{-2}$ 

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

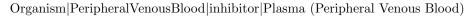
0.15

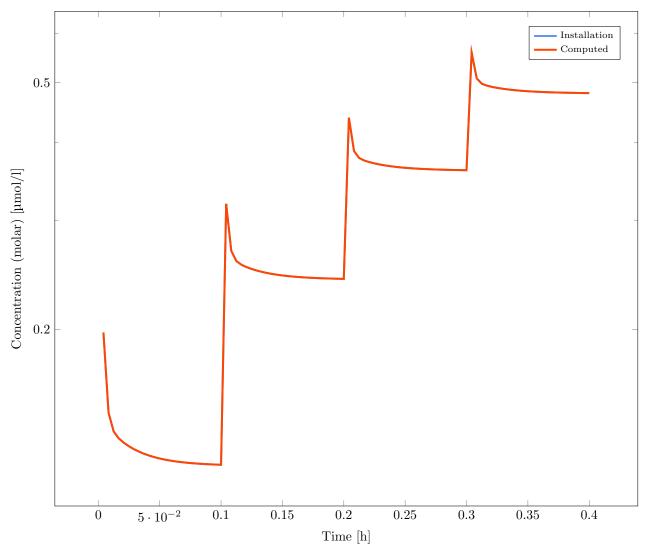
Deviation: 0



**Figure 1.21** 

Output Path: Organism |PeripheralVenousBlood |<br/>inhibitor |Plasma (Peripheral Venous Blood) | Deviation:<br/> 0





**Figure 1.22** 

Simulation: Human\_MultiIV\_6\_6\_12-Human\_MultiIV\_6\_6\_12

Result of the validation: Valid

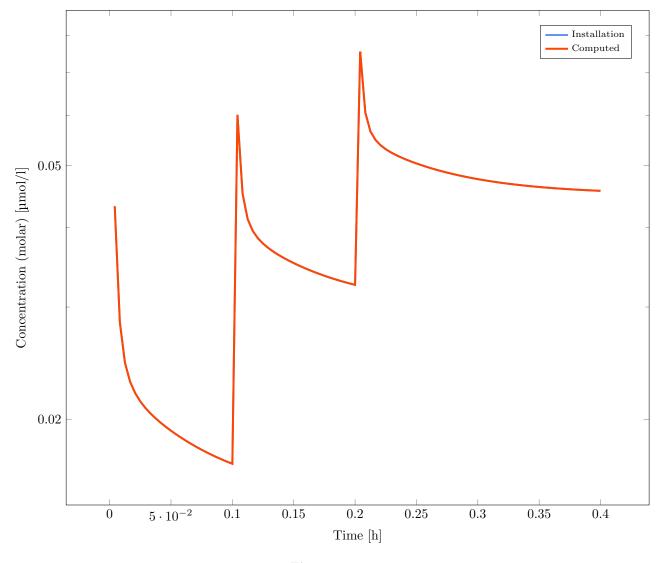


Figure 1.23

 $Simulation: \ Human\_MultiORAL\_6\_12\_12\_Dissolved-Human\_6\_12\_Dissolved-Human\_6\_12\_$ 

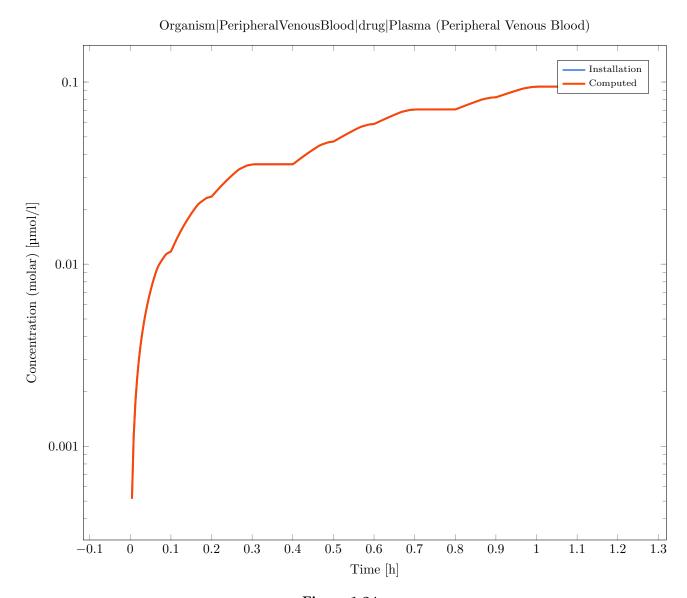


Figure 1.24

 $Simulation: Human\_MultiORAL\_6\_12\_12\_Dissolved-Human\_MultiORAL\_6\_12\_12\_Dissolved\_absorption\_sink\_conditions$ 

Result of the validation: Valid

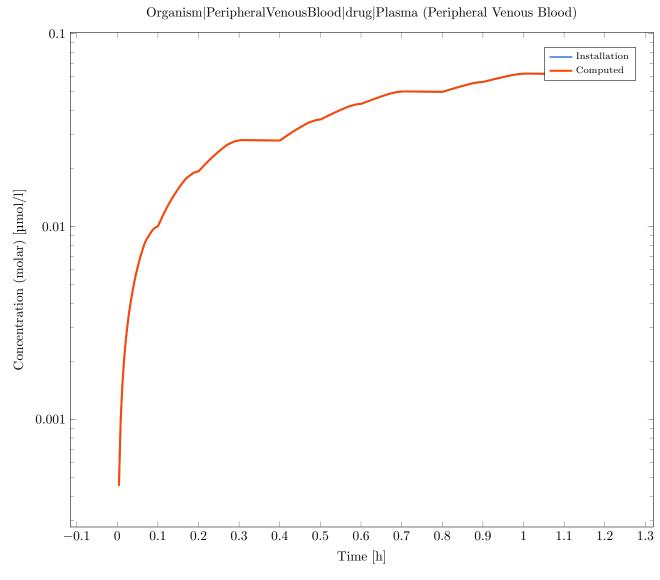
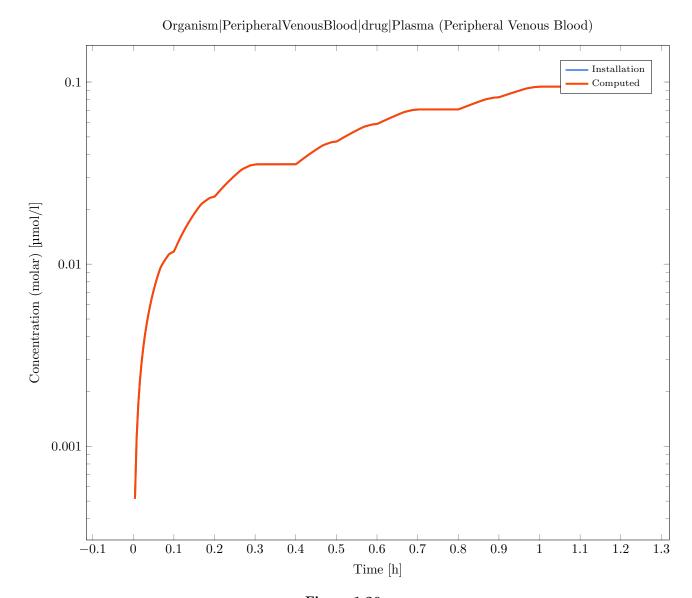


Figure 1.25

 $Simulation: Human\_MultiORAL\_6\_12\_12\_Dissolved-Human\_MultiORAL\_6\_12\_12\_Dissolved\_EHC\_continuous\_fraction\_0.5$ 

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

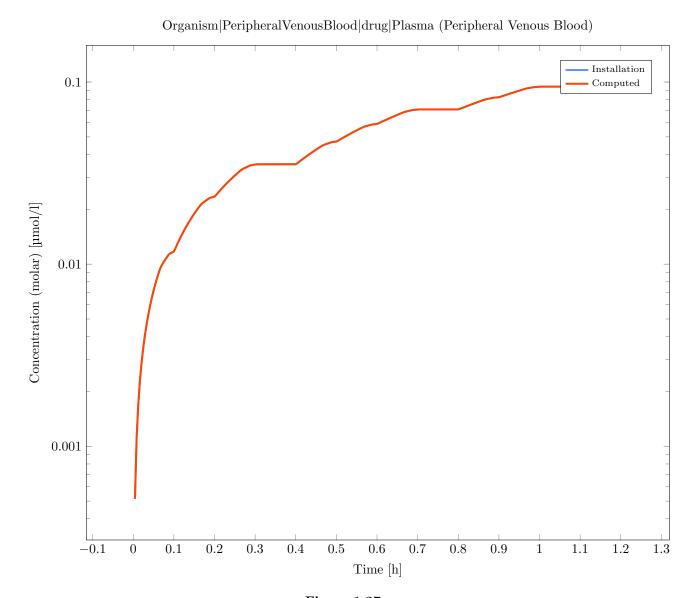
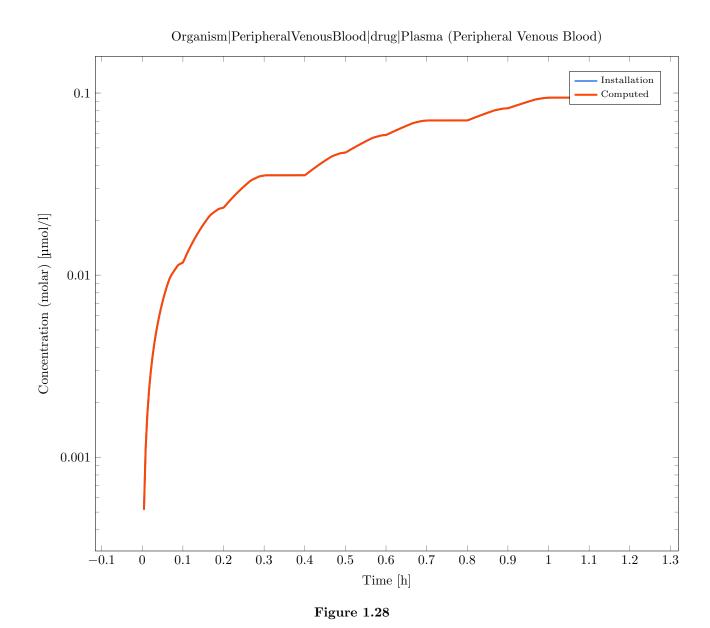


Figure 1.27

 $Simulation: \ Human\_MultiORAL\_6\_12\_12\_Dissolved-Human\_MultiORAL\_6\_12\_12\_Dissolved\_pKadependent\ penalty\ factor$  Result of the validation: Valid



 $Simulation: \ Human\_MultiORAL\_6\_12\_12\_Dissolved-Human\_MultiORAL\_6\_12\_12\_Dissolved\_solubility \ Result of the validation: \ Valid$ 

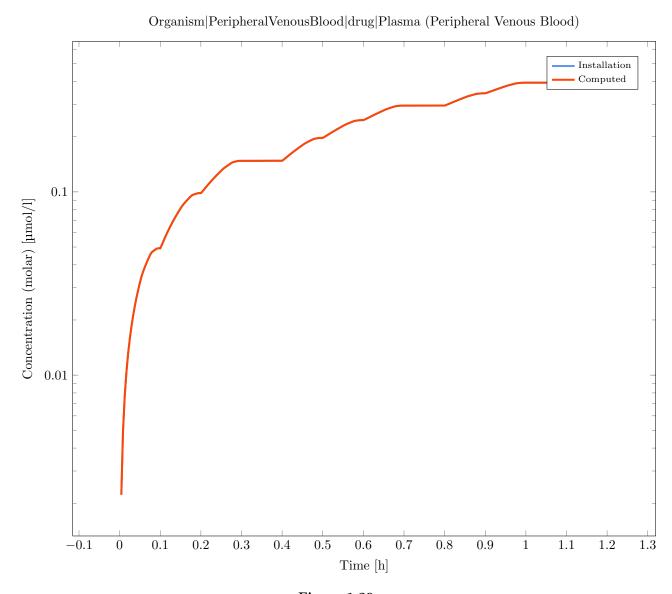


Figure 1.29

 ${\bf Simulation: \ Human\_Multiple IV\_All Active Processes-Human\_Multiple IV\_All Active Processes \ Result \ of \ the \ validation: \ Valid$ 

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

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

0.3

0.2

-0.1

0

0.1

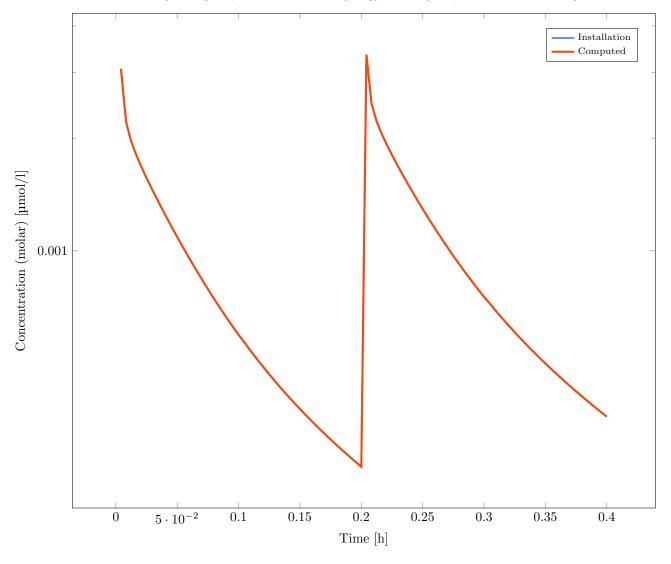
## Installation Computed Concentration (molar) $[\mu]$ 0.10.01 0.2 1.2 -0.10.1 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.1 1.3 1.4 1.5

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

Figure 1.31

Time [h]

 $Simulation: \ Human\_NonCompetitiveInhibition-Human\_NonCompetitiveInhibition$ Result of the validation: Valid



**Figure 1.32** 

Output Path: Organism |PeripheralVenousBlood |<br/>inhibitor |Plasma (Peripheral Venous Blood) | Deviation:<br/> 0

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

Figure 1.33

0.2

Time [h]

0.25

0.35

0.4

0.3

 ${\bf Simulation: Human\_Oral\_BiDaily\_TableFormulation-S1\_suspension}$ 

0.1

Result of the validation: Valid

0

 $5 \cdot 10^{-2}$ 

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

0.15

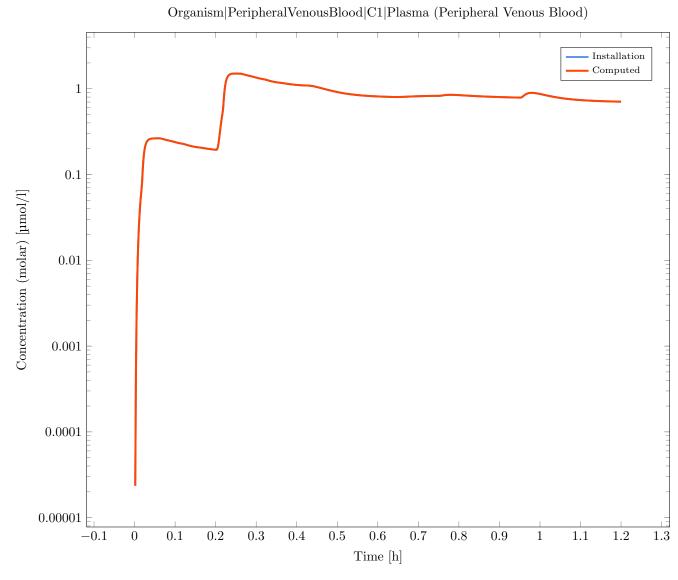


Figure 1.34

 ${\bf Simulation: Human\_Oral\_BiDaily\_Table Formulation-S2\_NoSuspension}$ 

Result of the validation: Valid

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

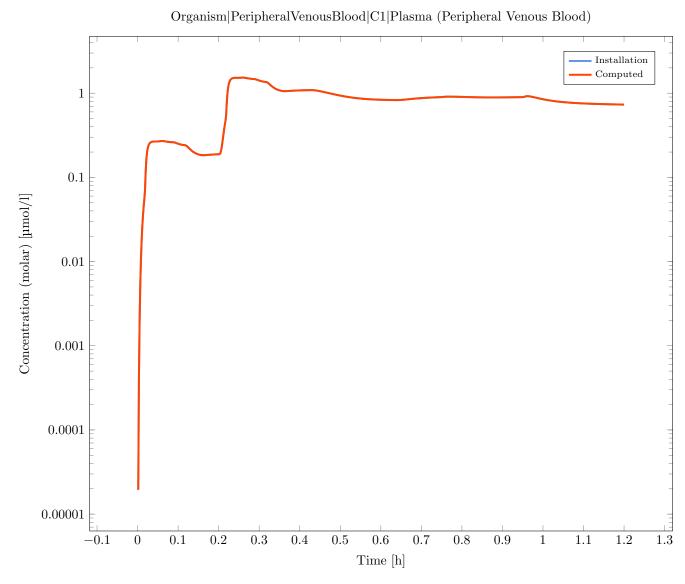


Figure 1.35

Simulation: Human\_pH\_SolubilityTable-S1\_Table

Result of the validation: Valid

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

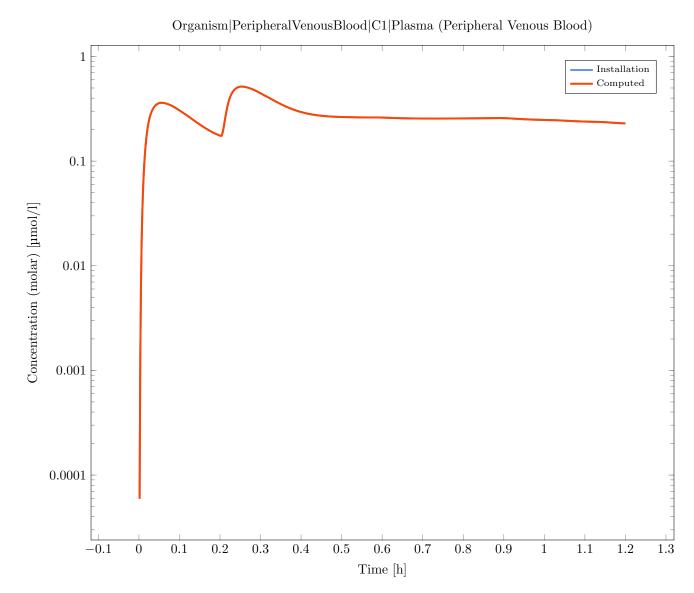


Figure 1.36

Simulation: Human\_pH\_SolubilityTable-S2\_Measurement

Result of the validation: Valid

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

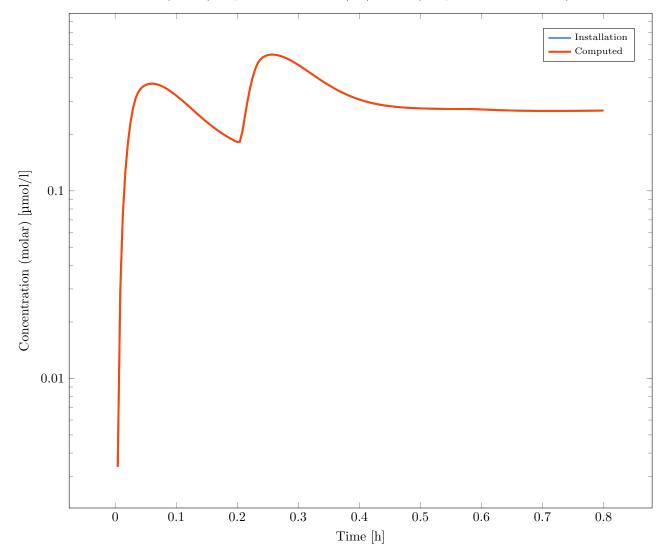


Figure 1.37

 $Simulation: \ Human\_pH\_SolubilityTable\_SolubilityChanged$ 

Result of the validation: Valid

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

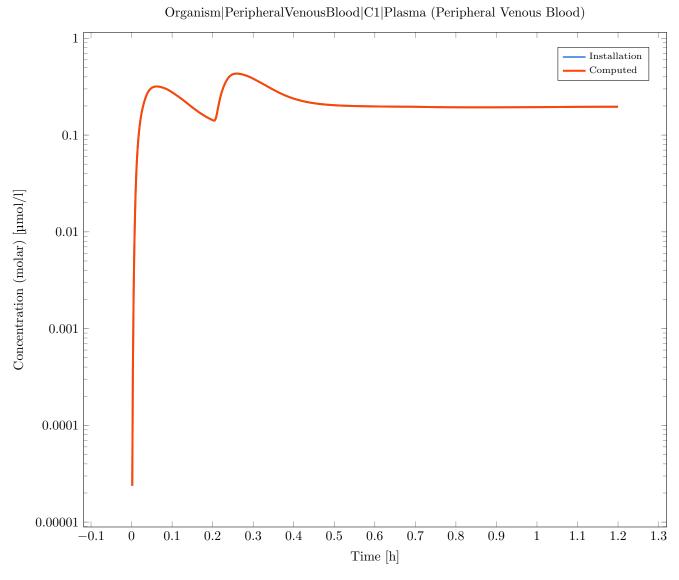


Figure 1.38

 ${\bf Simulation: \ Human\_pH\_SolubilityTable\_S4\_Table\_SolubilityTableChanged \ Result\ of\ the\ validation:\ Valid}$ 

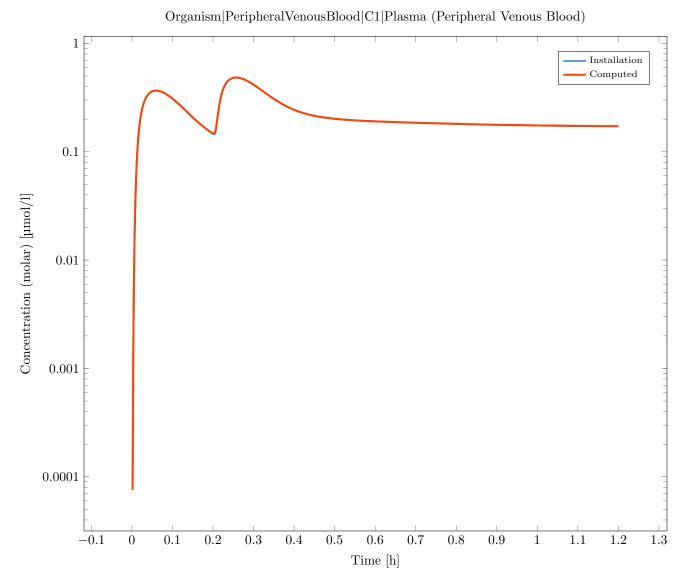


Figure 1.39

 ${\bf Simulation: \ Human\_Single IV\_Configuration-Human\_Single IV\_Configuration} \\ {\bf Result \ of \ the \ validation: \ Valid}$ 

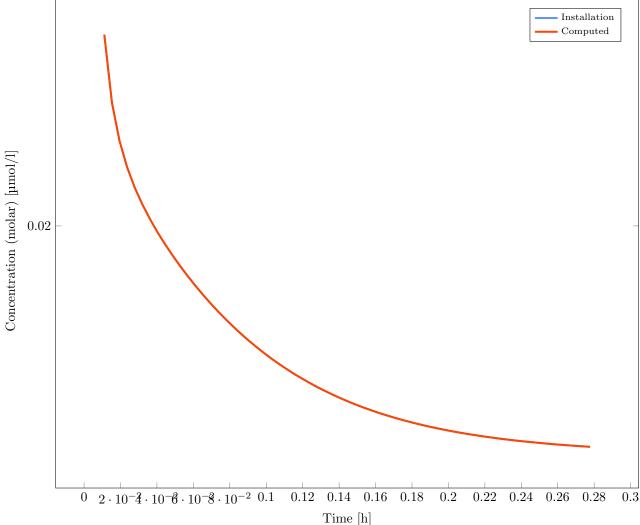


Figure 1.40

 $Simulation: \ Human\_Single IV-Human\_Single IV$ 

Result of the validation: Valid

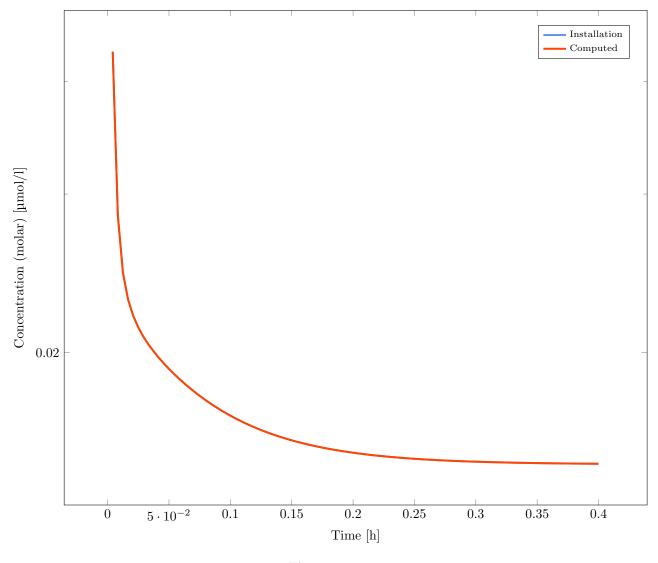
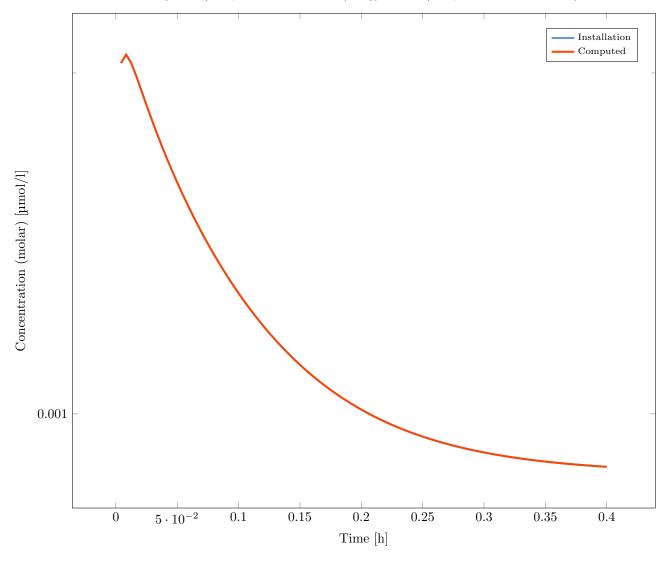


Figure 1.41

 $Simulation: Human\_SingleIV\_Human\_SingleIV\_MW\_200\_fu\_0.2\_LogP\_5$ 

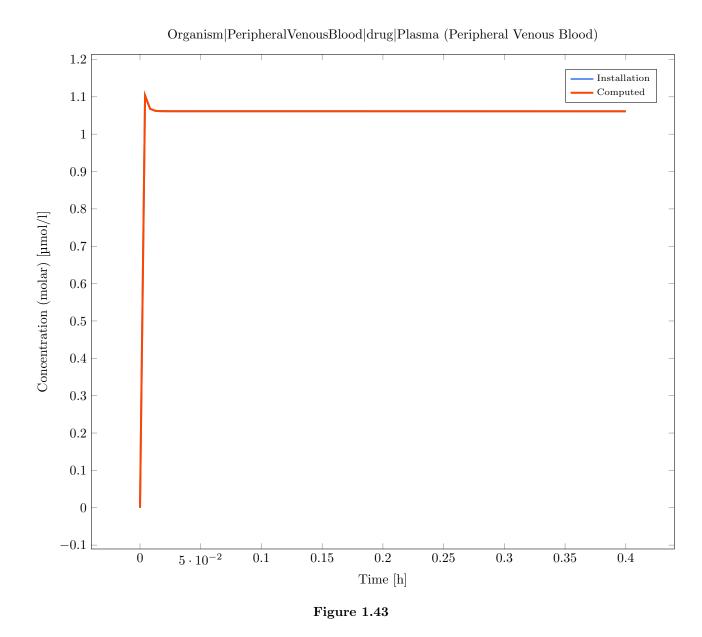
Result of the validation: Valid  $\,$ 



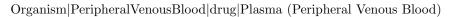
**Figure 1.42** 

 $Simulation: \ Human\_SingleIV-Human\_SingleIV\_MW\_800\_fu\_0.6\_LogP\_-5$ 

Result of the validation: Valid



Simulation: Human\_SingleORAL\_Dissolved\_PlasmaClearance-Human\_SingleO



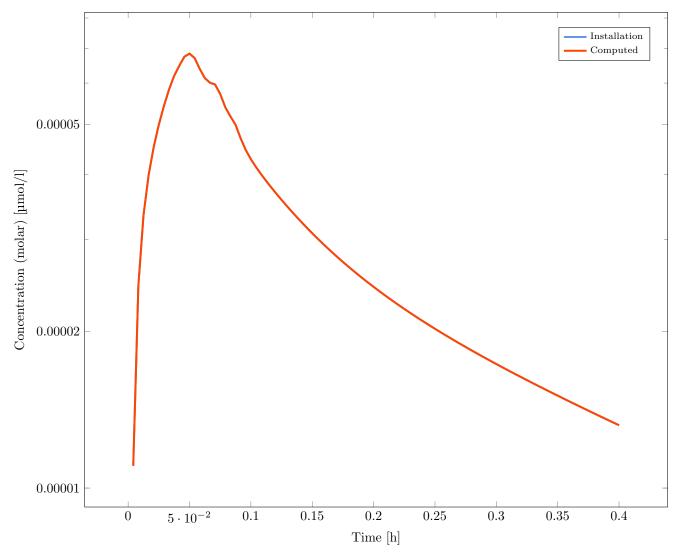


Figure 1.44

 $Simulation: Human\_SingleORAL\_Dissolved\_PlasmaClearance-Human\_Singl$ 

Result of the validation: Valid

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

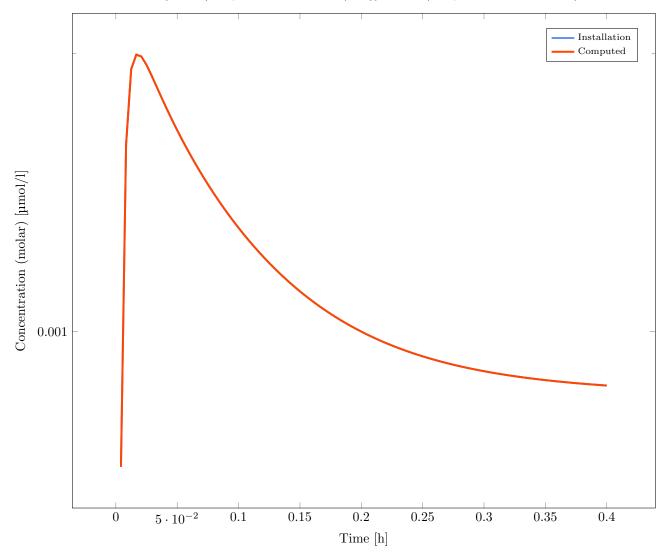
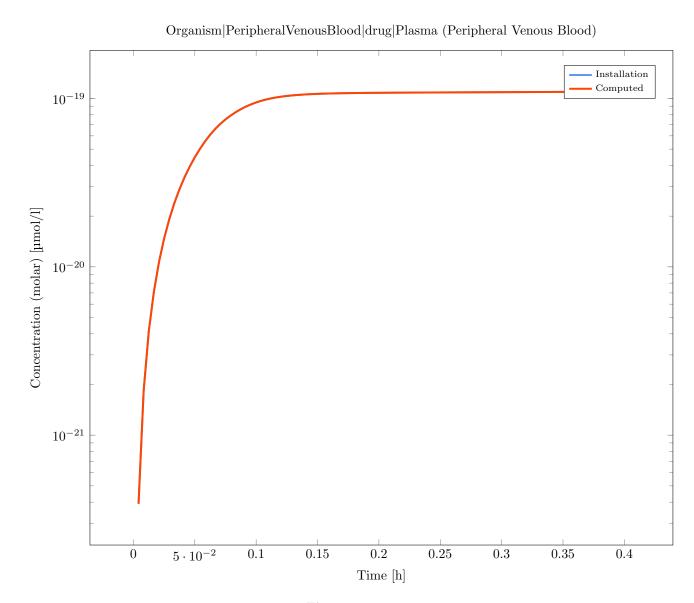


Figure 1.45

 $Simulation: Human\_SingleORAL\_Dissolved\_PlasmaClearance-Human\_Singl$ 

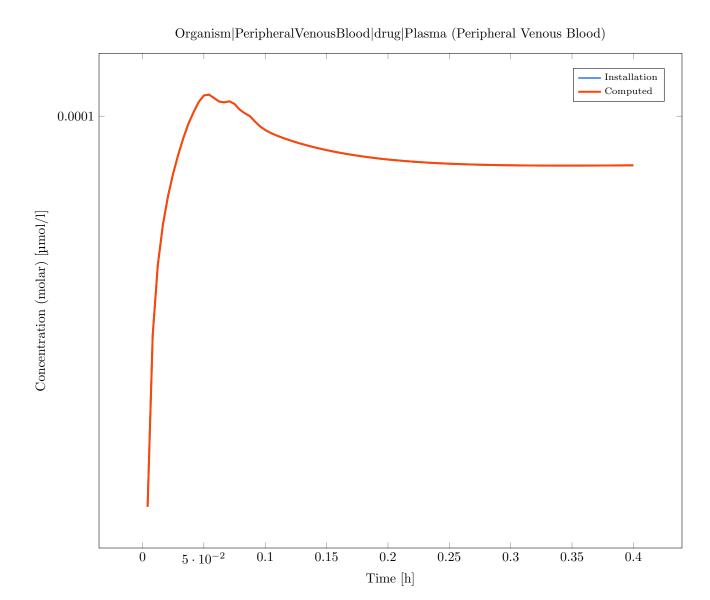
Result of the validation: Valid

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



**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

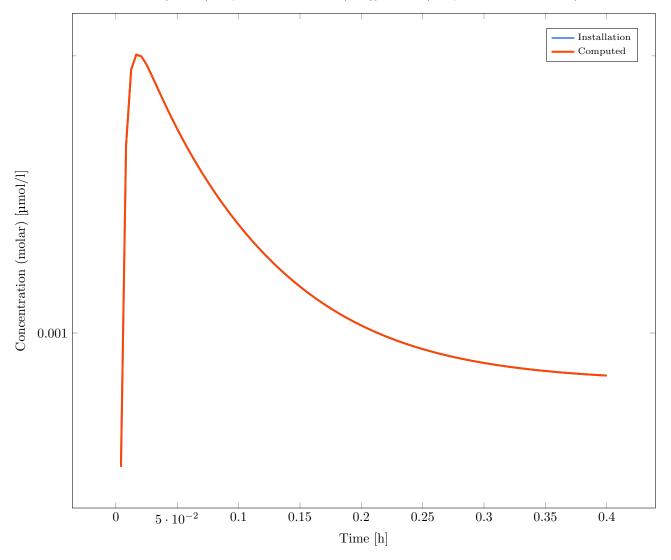
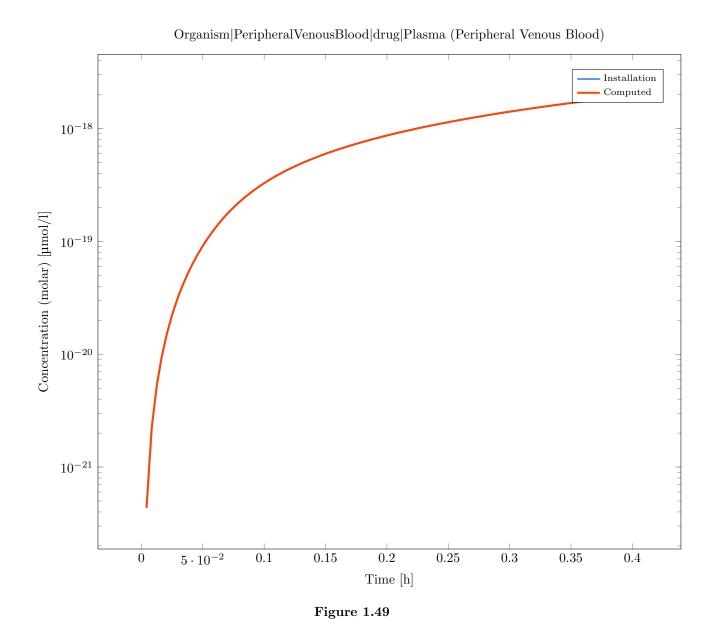


Figure 1.48

Simulation: Human\_SingleORAL\_Dissolved-Human\_SingleORAL\_Dissolved\_MW\_800\_fu\_0.6\_LogP\_--5 Result of the validation: Valid



 ${\bf Simulation: Human\_SingleORAL\_Lint80\_AsSuspention-Human\_SingleORAL\_Lint80\_AsSuspention}. \\ {\bf Result\ of\ the\ validation:\ Valid}$ 

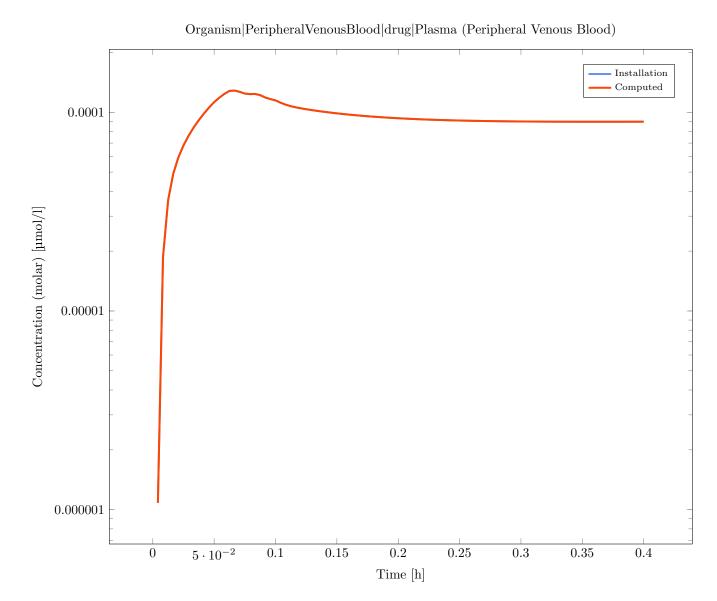


Figure 1.50

Simulation: Human\_SingleORAL\_Lint80-Human\_SingleORAL\_Lint80

Result of the validation: Valid

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

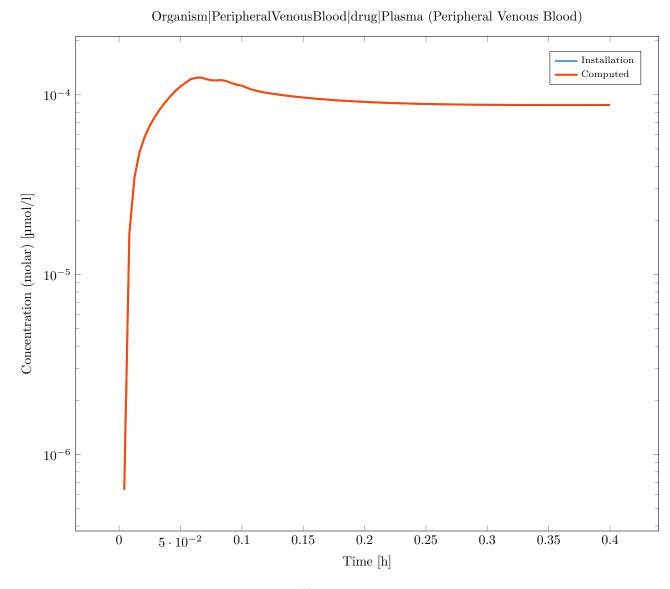


Figure 1.51

 $Simulation: Human\_SingleORAL\_MonoParticles\_AsSuspention-Human\_SingleORAL\_MonoParticles\_AsSuspention\\$ 

Result of the validation: Valid

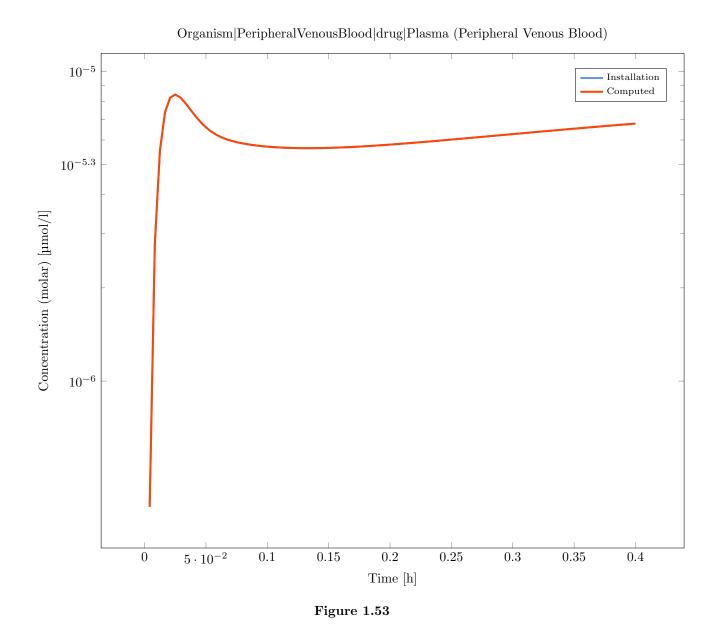
## Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) $10^{-5}$ Installation Computed $10^{-5.3}$ Concentration (molar) [µmol/1] $10^{-6}$ 0.15 0.2 0.25 0.3 0.35 0.4 0 $5\cdot 10^{-2}$ 0.1

Figure 1.52

Time [h]

 $Simulation: \ Human\_SingleORAL\_PolyParticlesLogNormal\_AsSuspention-Human\_SingleORAL\_PolyParticlesLogNormal\_AsSuspention$ 

Result of the validation: Valid



 $Simulation: Human\_SingleORAL\_PolyParticlesNormal\_AsSuspention-Human\_SingleORAL\_PolyParticlesNormal\_AsSuspention\\$ 

Result of the validation: Valid

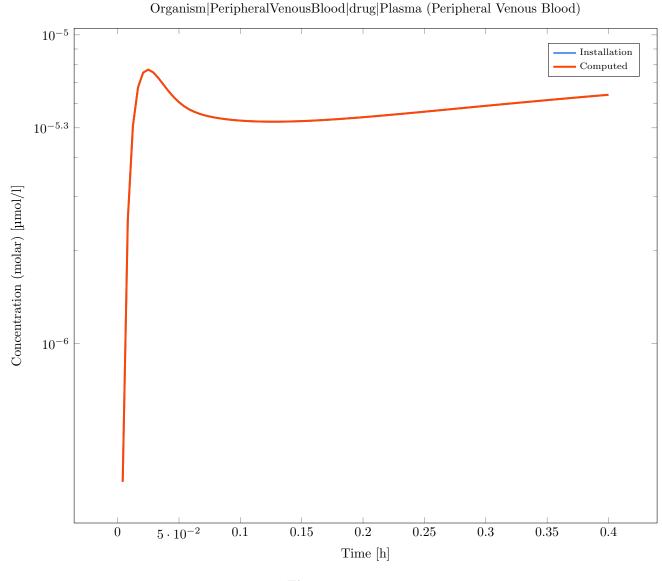


Figure 1.54

 $Simulation: Human\_SingleORAL\_PolyParticlesNormal\_AsSuspention-Human\_SingleORAL\_PolyParticlesNormal\_AsSuspention\_dissolved\_radius$ 

Result of the validation: Valid

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

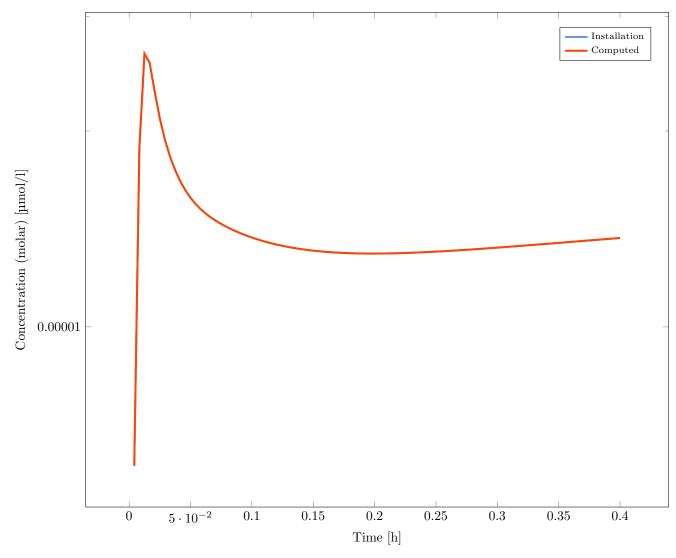
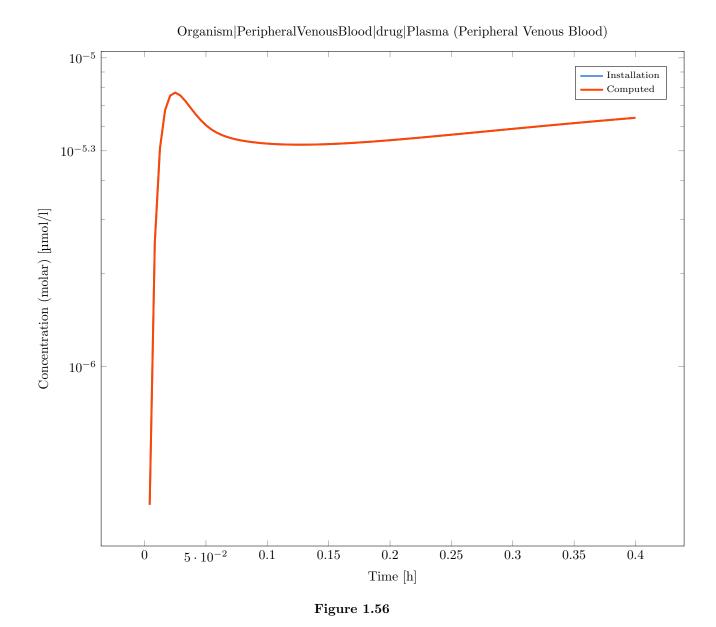


Figure 1.55

 $Simulation: Human\_SingleORAL\_PolyParticlesNormal\_AsSuspention-Human\_SingleORAL\_PolyParticlesNormal\_AsSuspention\_treat\_precipated\_drug\_as\_soluble$ 

Result of the validation: Valid

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



 ${\bf Simulation: Human\_SingleORAL\_Weibull\_AsSuspention-Human\_SingleORAL\_Weibull\_AsSuspention}. \\ {\bf Result\ of\ the\ validation:\ Valid}$ 

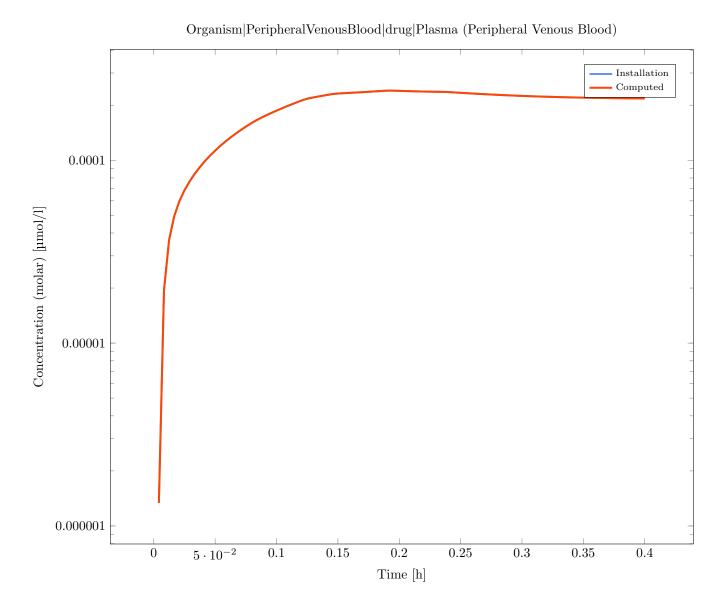


Figure 1.57

 $Simulation: Human\_SingleORAL\_Weibull\_AsSuspention-Human\_SingleORAL\_Weibull\_AsSuspention\_MW\_200\_fu\_0.2\_LogP\_5\\ Result of the validation: Valid$ 

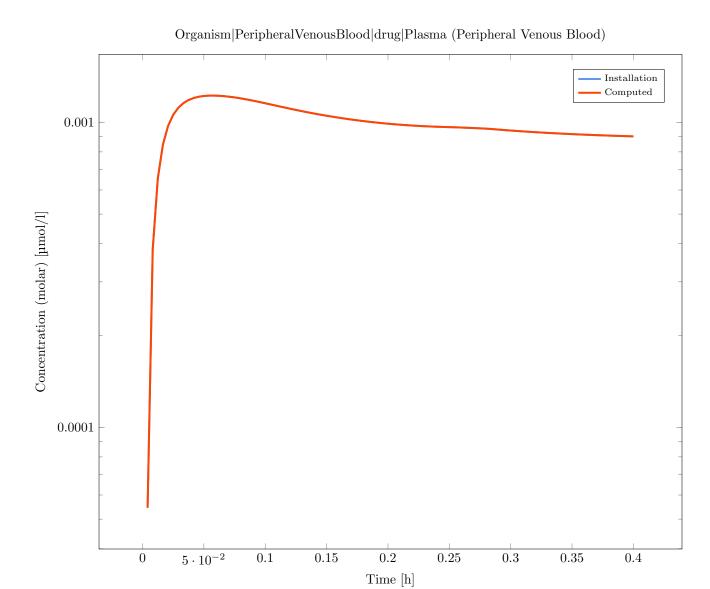


Figure 1.58

 $Simulation: Human\_SingleORAL\_Weibull\_AsSuspention-Human\_SingleORAL\_Weibull\_AsSuspention\_MW\_800\_fu\_0.6\_LogP\_-5\\ Result of the validation: Valid$ 

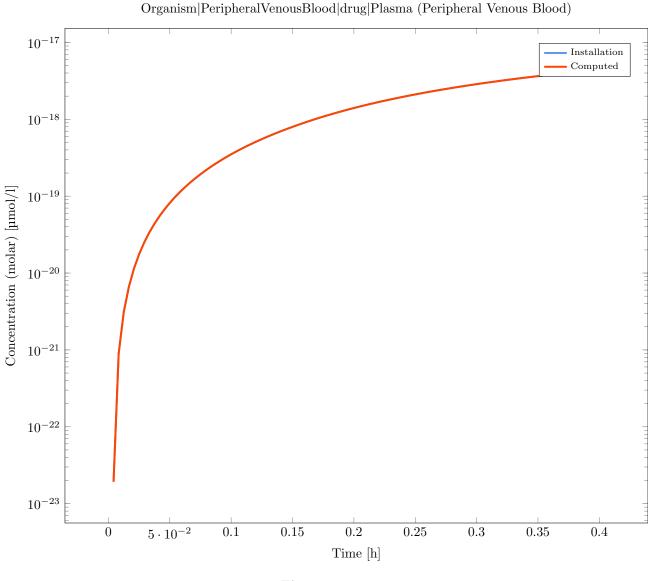
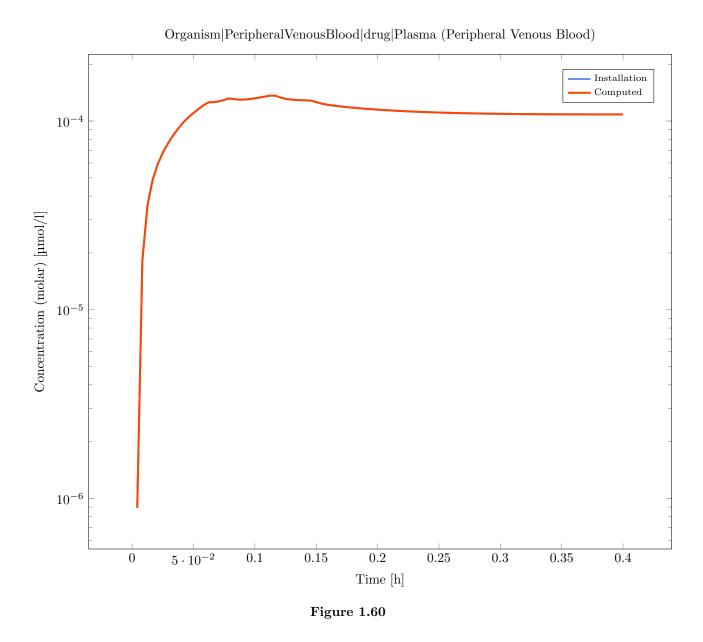


Figure 1.59

 ${\bf Simulation: \ Human\_SingleORAL\_Weibull-Human\_SingleORAL\_Weibull} \\ {\bf Result \ of \ the \ validation: \ Valid}$ 



 $Simulation: \ Human\_SingleORAL\_Weibull\_Human\_SingleORAL\_Weibull\_MW\_200\_fu\_0.2\_LogP\_5 \\ Result of the validation: \ Valid$ 

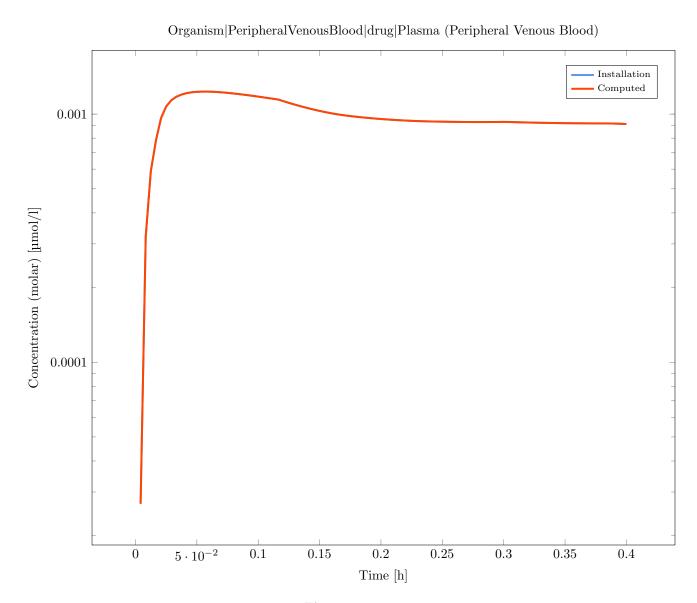
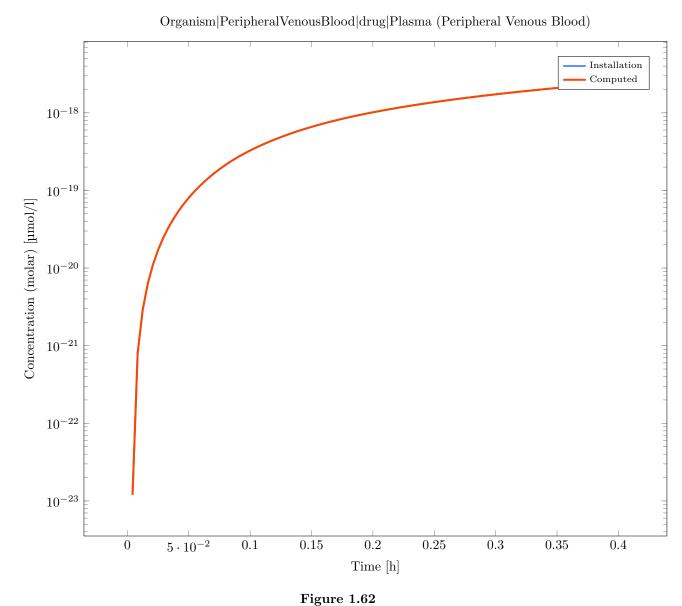


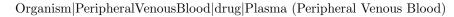
Figure 1.61

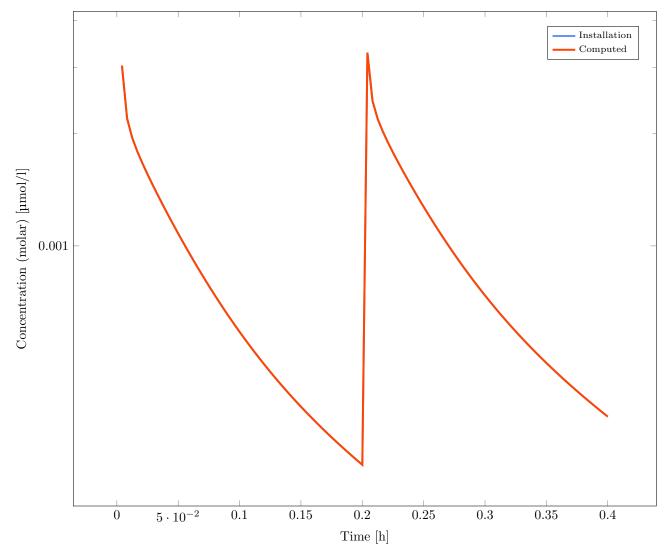
 $\label{lem:singleORAL_Weibull-Human_SingleORAL_Weibull_MW_800_fu_0.6_LogP_5 \\ Result of the validation: Valid$ 



118010 1101

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





**Figure 1.63** 

Output Path: Organism |PeripheralVenousBlood |<br/>inhibitor |Plasma (Peripheral Venous Blood) | Deviation:<br/> 0

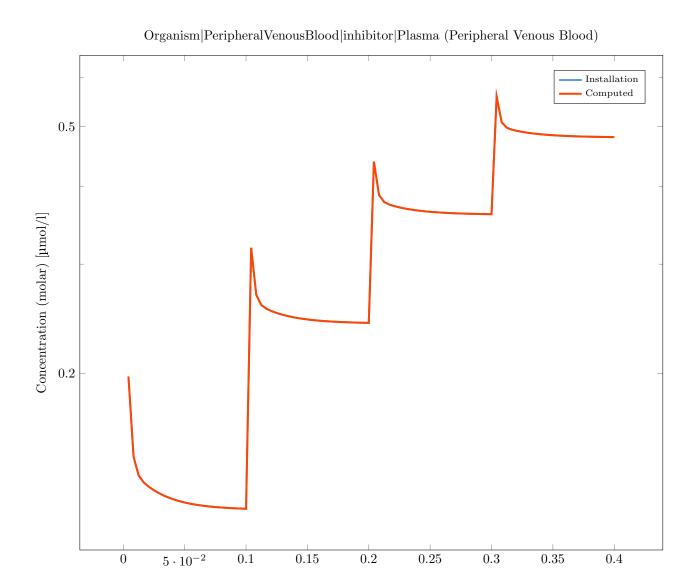
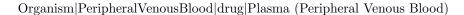
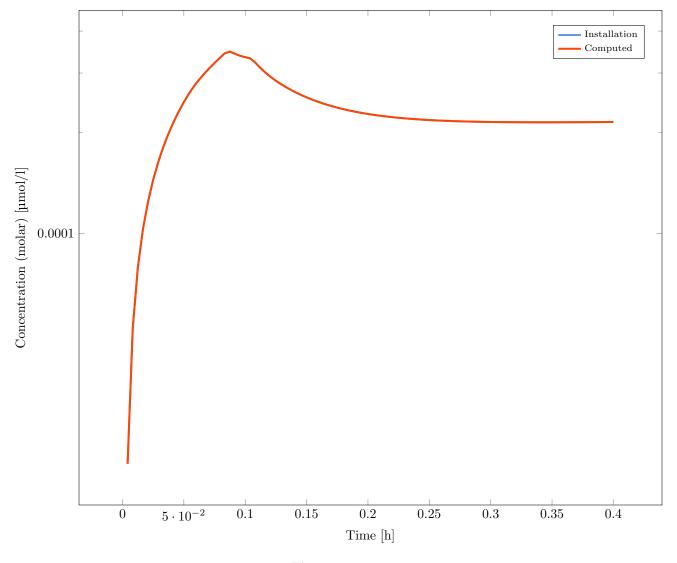


Figure 1.64

Time [h]

 ${\bf Simulation: \ Minipig\_SingleORAL\_Dissolved-Minipig\_SingleORAL\_Dissolved \ Result \ of \ the \ validation: \ Valid}$ 





**Figure 1.65** 

 $Simulation: Minipig\_SingleORAL\_Dissolved\_Minipig\_SingleORAL\_Dissolved\_MW\_200\_fu\_0.2\_LogP\_5$ 

Result of the validation: Valid

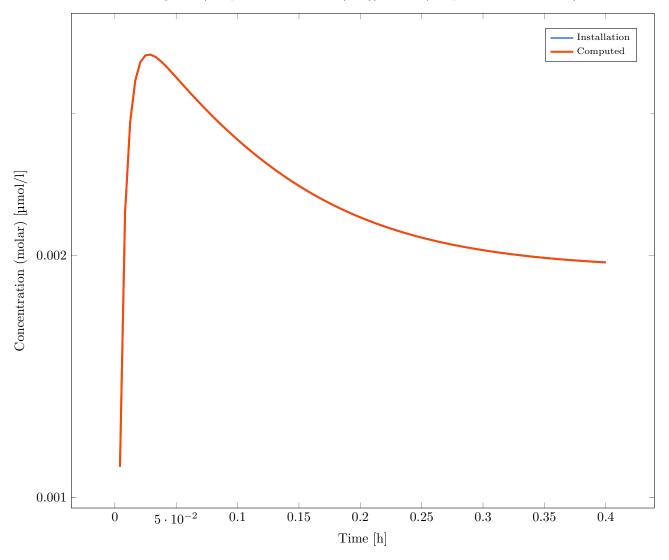
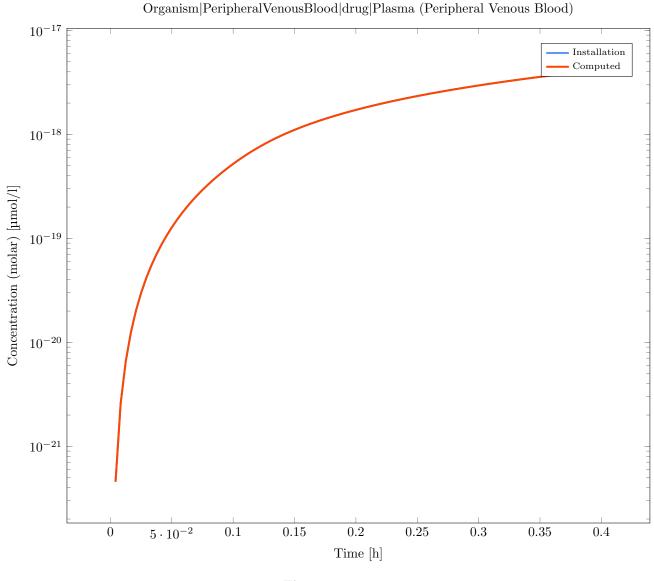


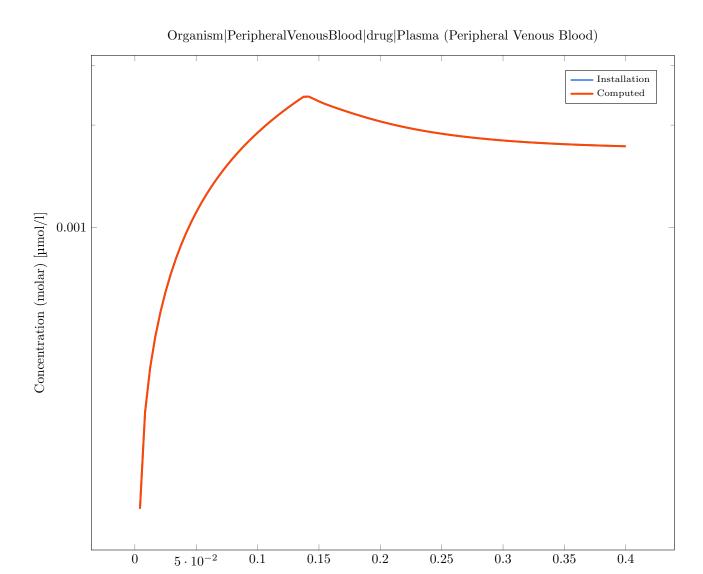
Figure 1.66

 $Simulation: \ Minipig\_SingleORAL\_Dissolved\_Minipig\_SingleORAL\_Dissolved\_MW\_800\_fu\_0.6\_LogP\_-5$  Result of the validation: Valid



**Figure 1.67** 

 ${\bf Simulation: \ Monkey\_SingleORAL\_Dissolved-Monkey\_SingleORAL\_Dissolved \ Result \ of \ the \ validation: \ Valid}$ 



Time [h] **Figure 1.68** 

Simulation: Monkey\_SingleORAL\_Dissolved-Monkey\_SingleORAL\_Dissolved\_MW\_200\_fu\_0.2\_LogP\_5 Result of the validation: Valid

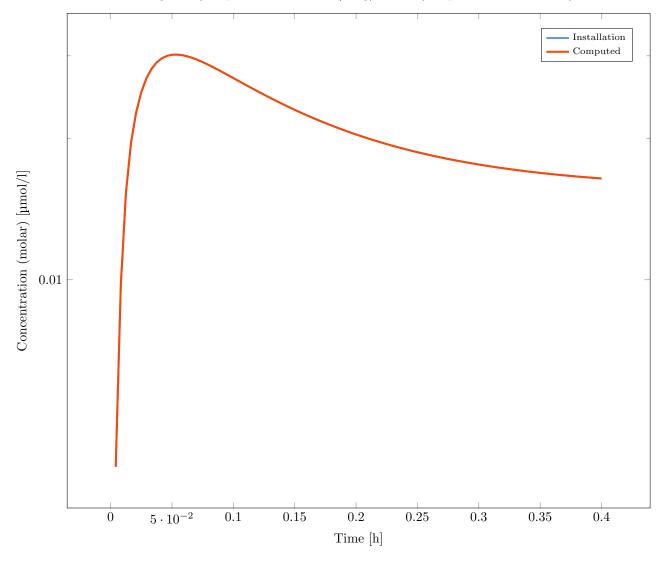
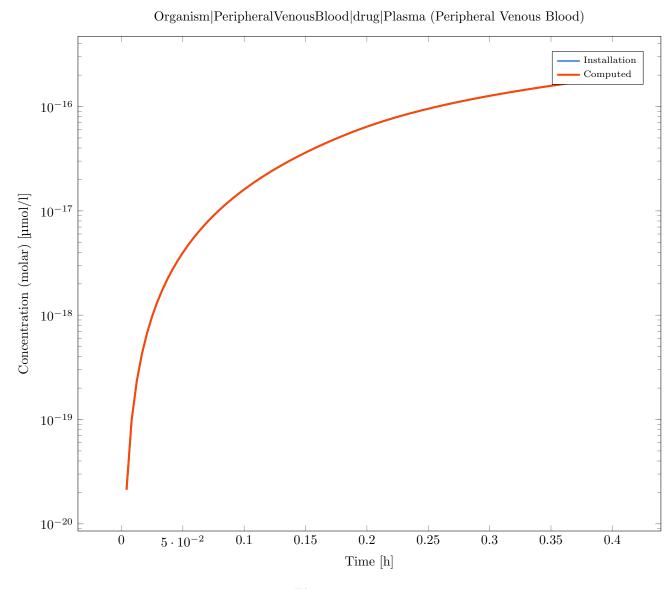


Figure 1.69

Simulation: Monkey\_SingleORAL\_Dissolved-Monkey\_SingleORAL\_Dissolved\_MW\_800\_fu\_0.6\_LogP\_--5 Result of the validation: Valid



**Figure 1.70** 

Simulation: Mouse\_SingleORAL\_Dissolved-Mouse\_SingleORAL\_Dissolved Result of the validation: Valid

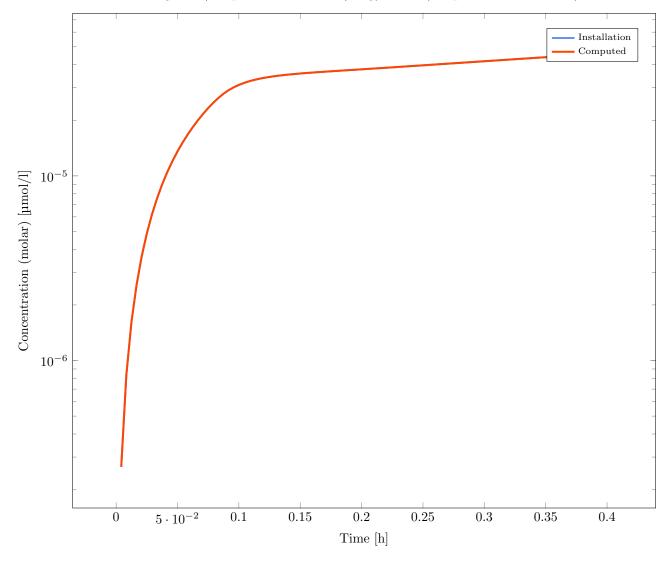
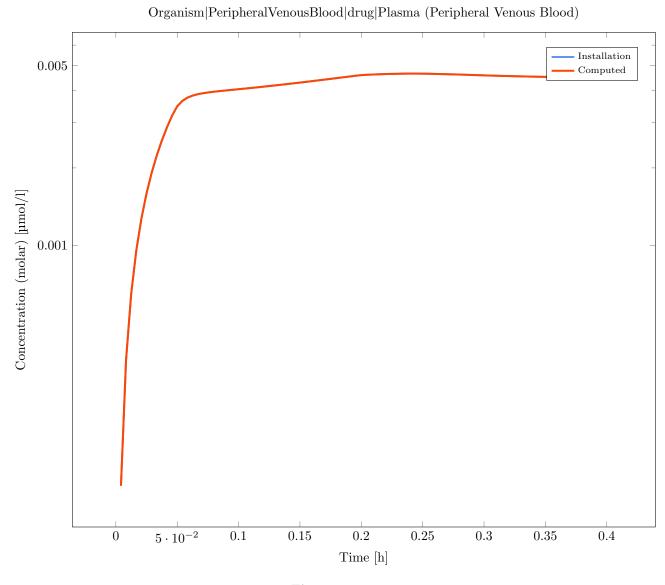


Figure 1.71

Simulation: Mouse\_SingleORAL\_Dissolved-Mouse\_SingleORAL\_Dissolved\_MW\_200\_fu\_0.2\_LogP\_5 Result of the validation: Valid

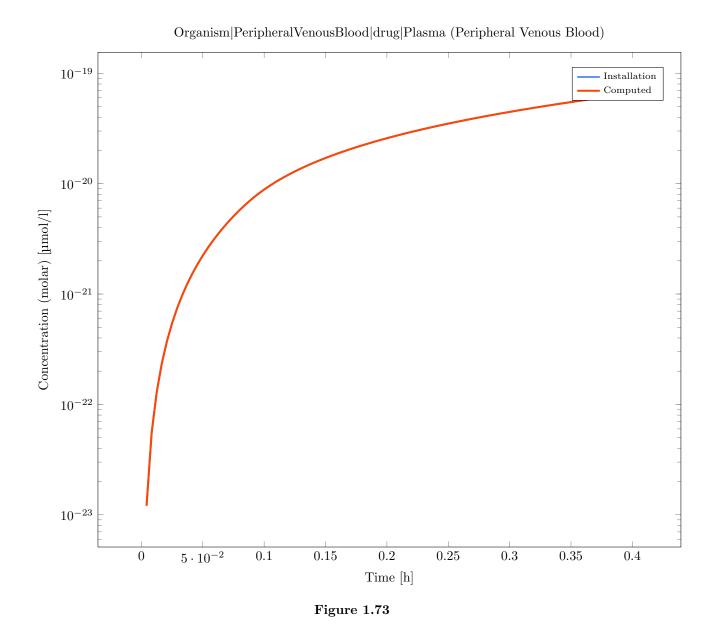
Output Path: Organism |PeripheralVenousBlood |<br/>drug |Plasma (Peripheral Venous Blood) Deviation:  ${\bf 0}$ 

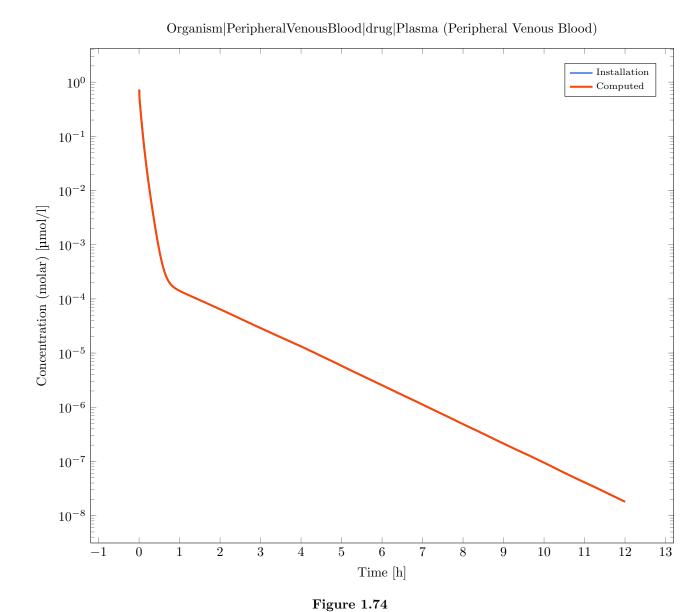


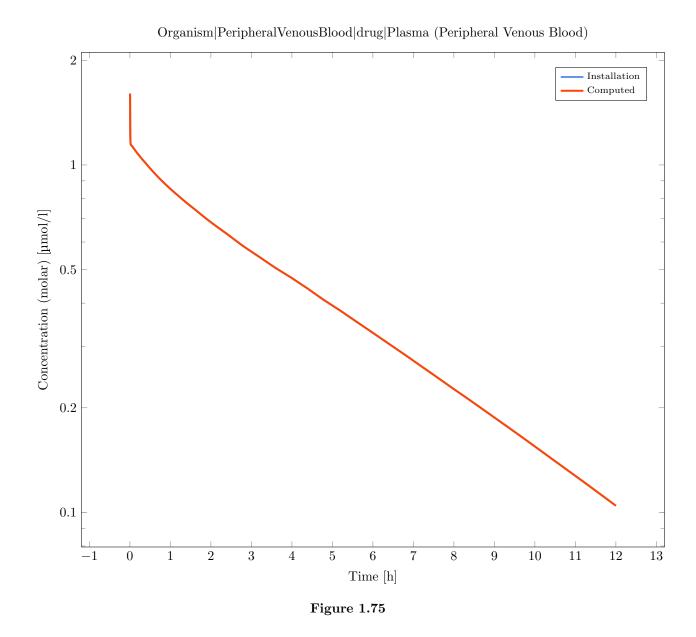
**Figure 1.72** 

Simulation: Mouse\_SingleORAL\_Dissolved-Mouse\_SingleORAL\_Dissolved\_MW\_800\_fu\_0.6\_LogP\_--5 Result of the validation: Valid

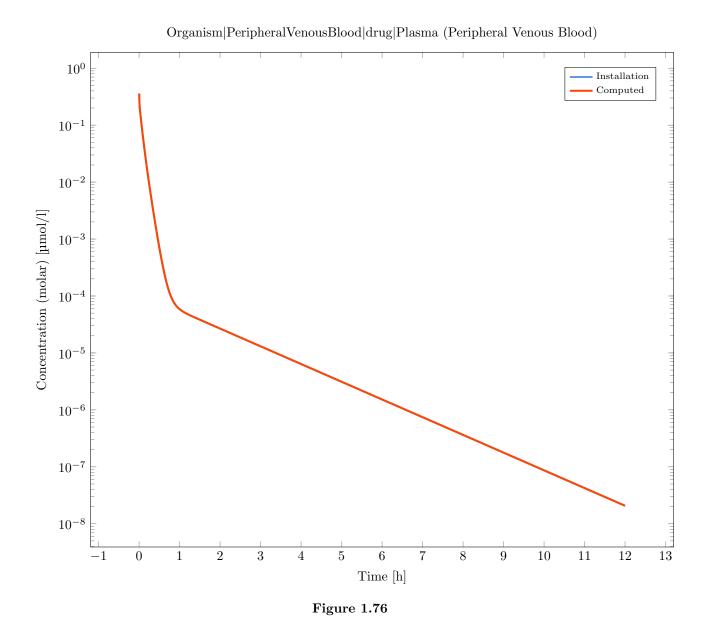
Output Path: Organism |PeripheralVenousBlood |<br/>drug |Plasma (Peripheral Venous Blood) Deviation:  ${\bf 0}$ 







 $\label{lem:single_index} \textbf{Simulation: Preterm\_SingleIV\_Age\_15\_GA\_32\_CYP3A4-Preterm\_SingleIV\_Age\_15\_CYP3A4-Pr$ 



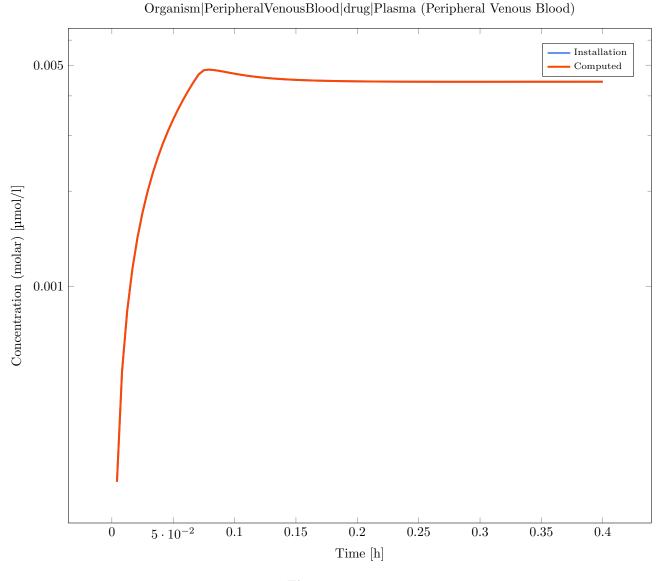
 $Simulation: \ \, Preterm\_SingleIV\_Age\_15\_GA\_32\_GFR-Preterm\_SingleIV\_Age\_15\_GA\_32\_GFR \\ Result of the validation: \ \, Valid$ 

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

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)<br/> Deviation:  ${\bf 0}$ 

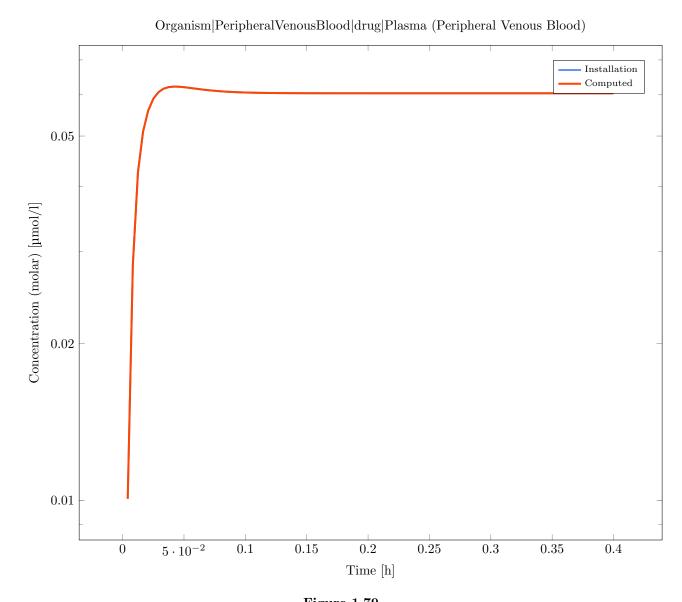


Figure 1.79

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

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

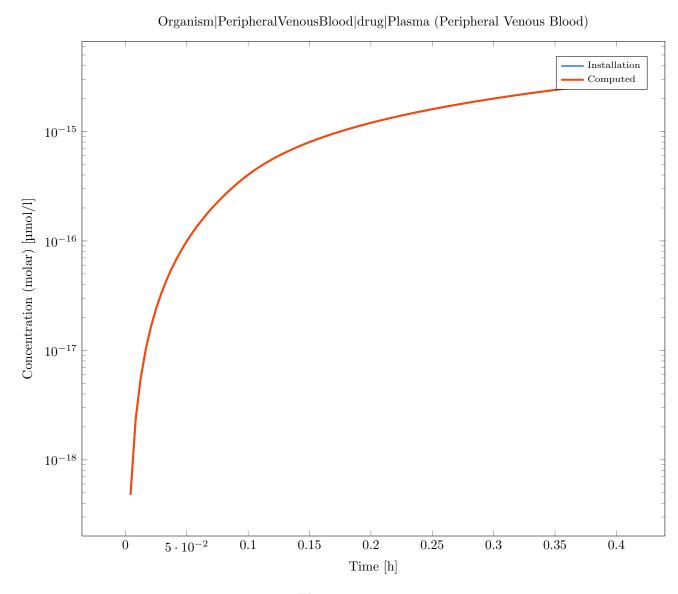


Figure 1.80

Simulation: Rat\_MultiORAL\_6\_6\_12\_Dissolved-Rat\_MultiORAL\_6\_6\_12\_Dissolved Result of the validation: Valid

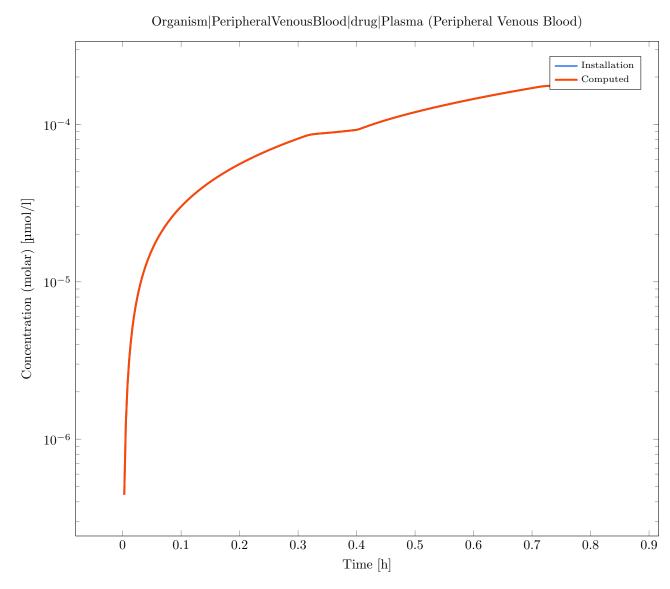


Figure 1.81

 $\begin{tabular}{ll} \bf Simulation: & Rat\_MultiORAL\_6\_6\_6\_6\_6\_0 \\ \bf Dissolved-Rat\_MultiORAL\_6\_6\_6\_6\_0 \\ \bf Dissolved-Rat\_MultiORAL\_6\_6\_6\_0 \\ \bf Dissolved-Rat\_MultiORAL\_6\_6\_6\_0 \\ \bf Dissolved-Rat\_MultiORAL\_6\_6\_6\_0 \\ \bf Dissolved-Rat\_MultiORAL\_6\_6\_0 \\ \bf Dissolved-Rat\_MultiORAL\_6\_0 \\ \bf Dissol$ 

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

## Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed $10^{-4}$ Concentration (molar) $[\mu]$ $10^{-5}$ $10^{-6}$ 0.1 0.2 0 0.3 0.4 0.50.6 0.7 0.8 0.9

Figure 1.82

Time [h]

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

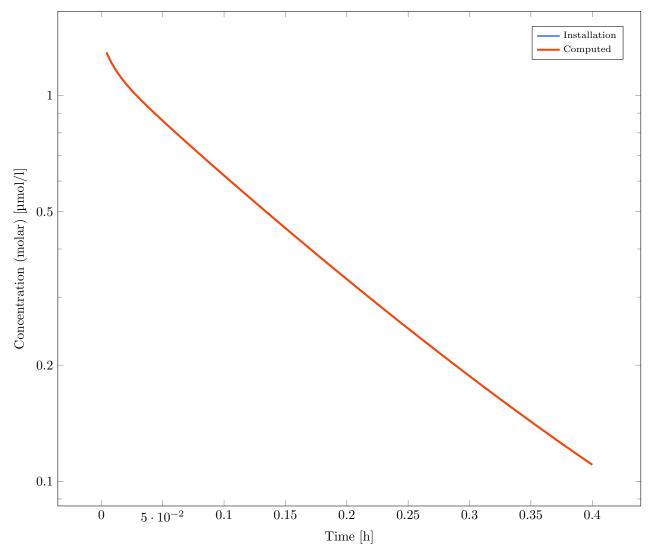
## Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed $10^{-4}$ Concentration (molar) $[\mu]$ $10^{-5}$ $10^{-6}$ 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9

Figure 1.83

Time [h]

 $Simulation: Single IV\_2 Pores\_Human-Single IV\_2 Pores\_Human$ 

Result of the validation: Valid



**Figure 1.84** 

Simulation: SingleIV\_2Pores\_Human-SingleIV\_2Pores\_Human\_SimulationC Result of the validation: Valid

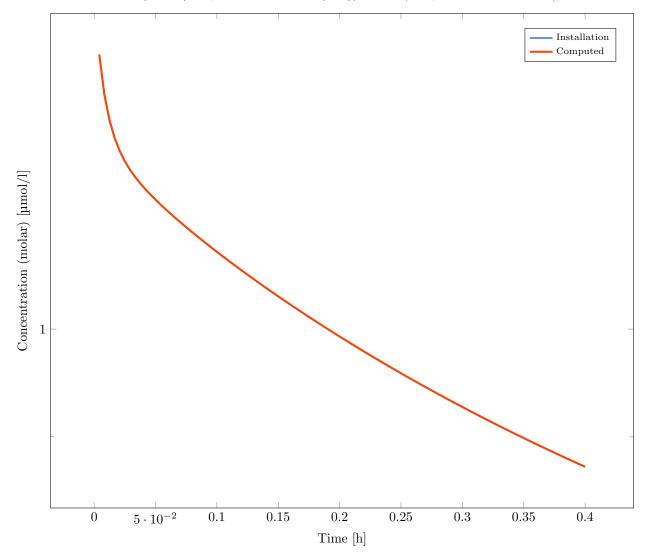
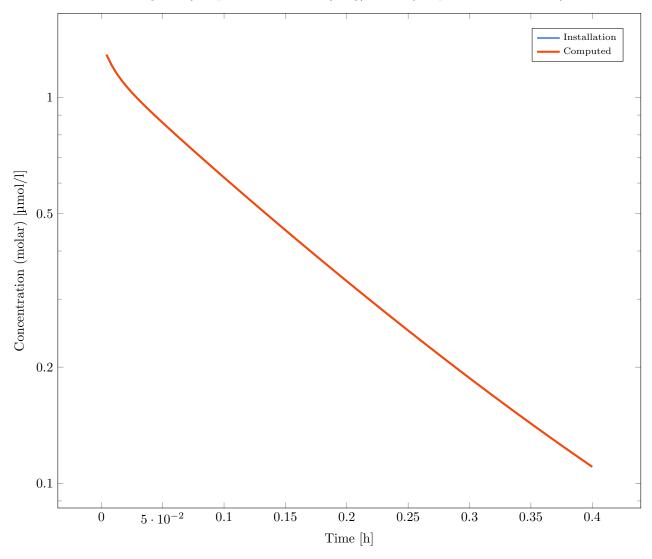


Figure 1.85

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

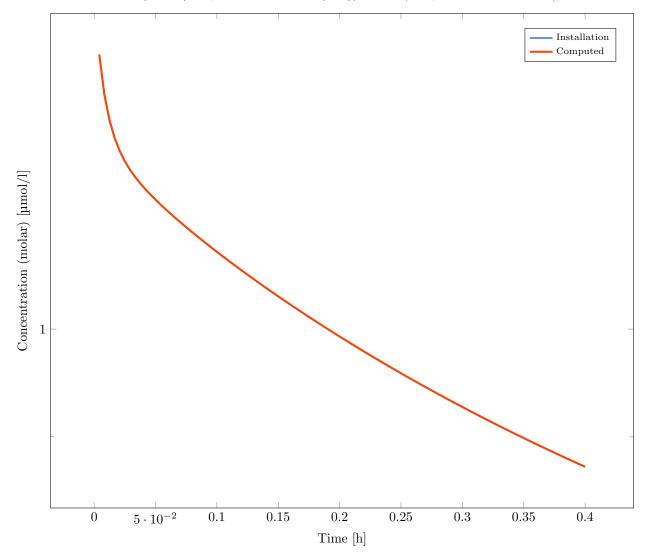


Figure 1.87

 $Simulation: Single IV\_2 Pores\_Monkey-Single IV\_2 Pores\_Monkey$ 

Result of the validation: Valid

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

Figure 1.88

0.2

Time [h]

0.25

0.3

0.35

0.4

 ${\bf Simulation: Single IV\_2 Pores\_Monkey\_Single IV\_2 Pores\_Monkey\_Simulation G} \\ {\bf Result of the \ validation: \ Valid}$ 

0.15

0.1

 $5\cdot 10^{-2}$ 

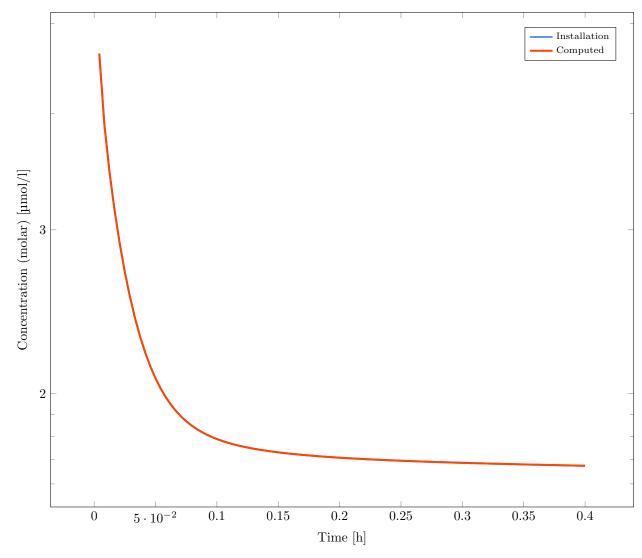


Figure 1.89

Simulation: SingleIV\_2Pores\_Monkey-SingleIV\_2Pores\_Monkey\_SimulationH Result of the validation: Valid

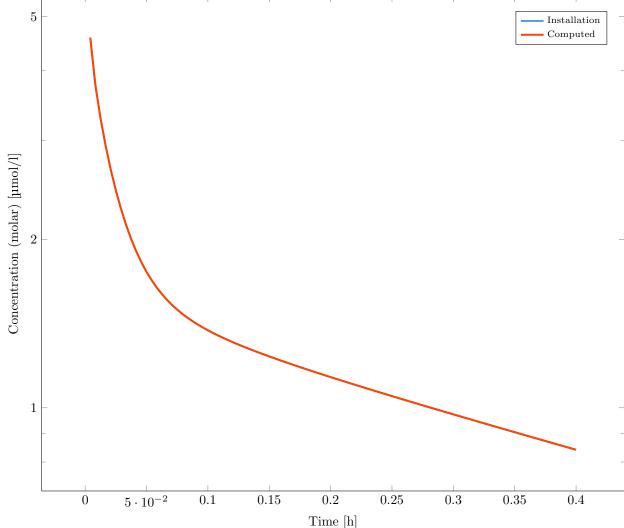


Figure 1.90

 $Simulation: Single IV\_2 Pores\_Mouse-Single IV\_2 Pores\_Mouse$ 

Result of the validation: Valid

0

 $5\cdot 10^{-2}$ 

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

Figure 1.91

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

 ${\bf Simulation: Single IV\_2 Pores\_Mouse\_Single IV\_2 Pores\_Mouse\_Simulation A} \\ {\bf Result of the \ validation: \ Valid}$ 

0.1

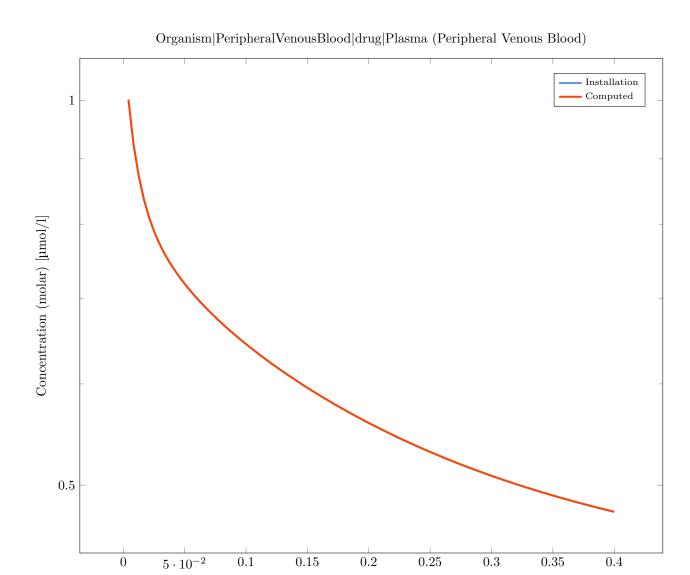


Figure 1.92

Time [h]

Simulation: SingleIV\_2Pores\_Mouse-SingleIV\_2Pores\_Mouse\_SimulationB Result of the validation: Valid

0

 $5\cdot 10^{-2}$ 

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

Figure 1.93

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

 ${\bf Simulation: \ Single IV\_2 Pores\_Mouse\_Single IV\_2 Pores\_Mouse\_Simulation E} \\ {\bf Result \ of \ the \ validation: \ Valid}$ 

0.1

# Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed O.5 - 10<sup>-2</sup> 0.1 0.15 0.2 0.25 0.3 0.35 0.4

Figure 1.94

 $Simulation: Single IV\_C1\_4 Comp\_standard\_stand$ 

Time [h]

Result of the validation: Valid

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

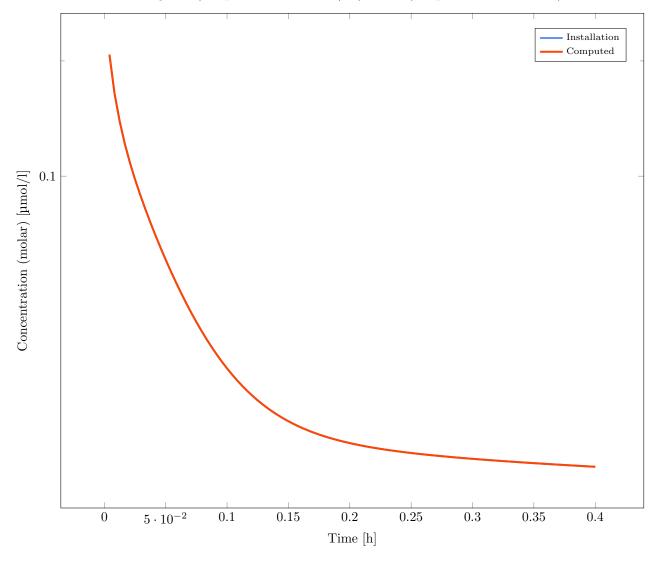


Figure 1.95

 $Simulation: Single IV\_C2\_4 Comp\_PT\_standard\_st$ 

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

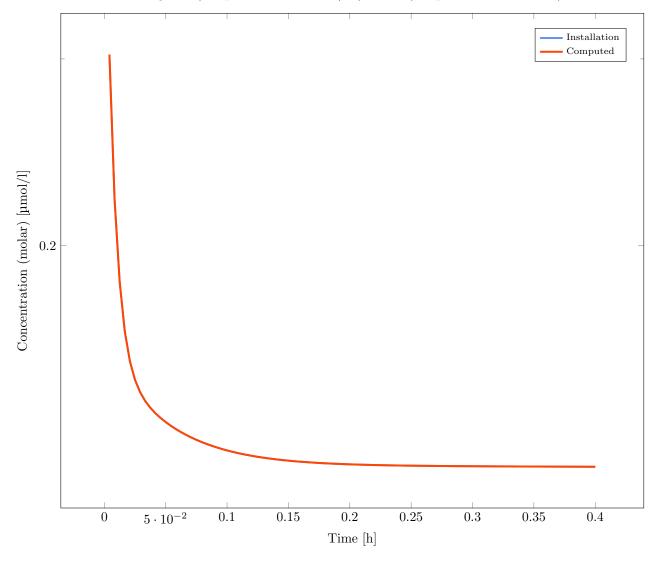


Figure 1.96

 $Simulation: Single IV\_C2\_4 Comp\_RR\_standard\_st$ 

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

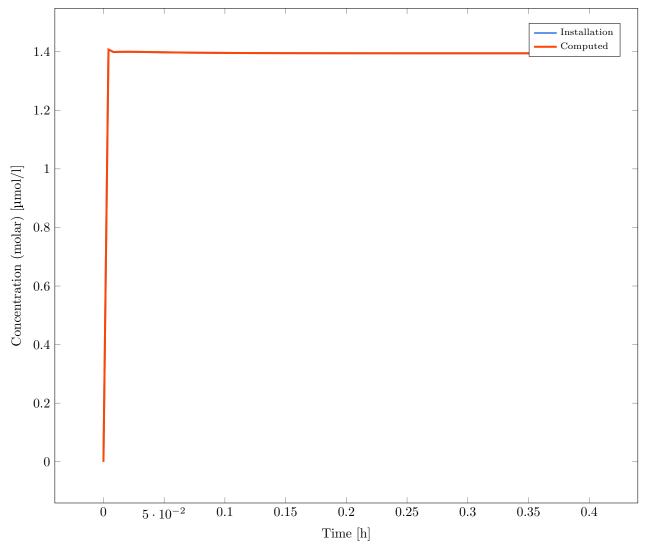


Figure 1.97

 $Simulation: Single IV\_C2\_4 Comp\_standard\_schmitt\_standard-Single IV\_C2\_4 Comp\_standard\_schmitt\_standard\\$ 

Result of the validation: Valid

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

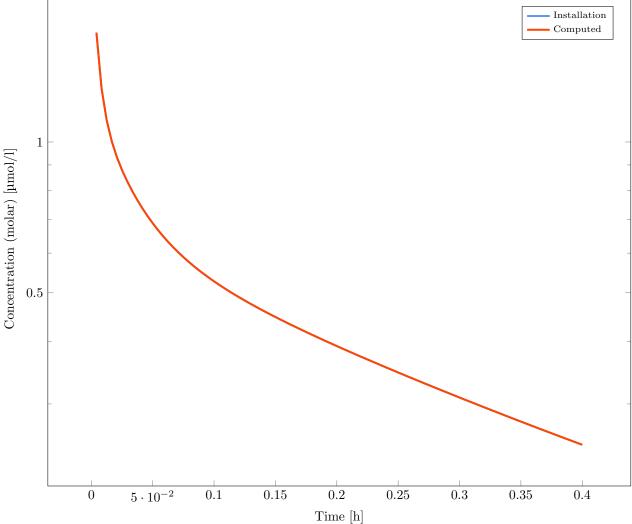


Figure 1.98

 $Simulation: Single IV\_C3\_4 Comp\_RR\_schmitt\_standard-Single IV\_C3\_schmitt\_standard-Single IV\_C3\_schmitt$ 

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

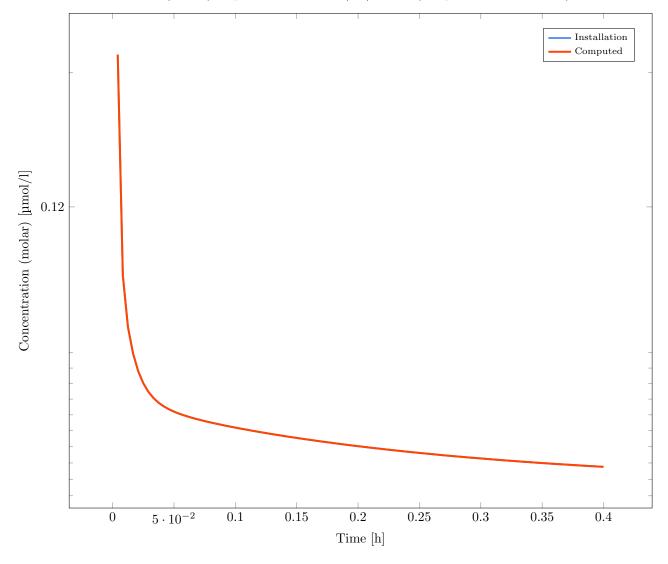


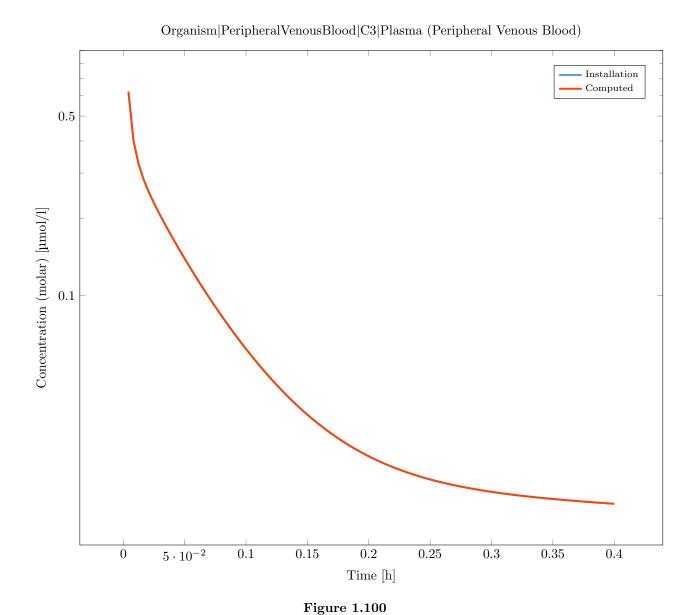
Figure 1.99

 $Simulation: Single IV\_C3\_4 Comp\_standard\_schmittnorm lized\_standard-Single IV\_C3\_4 Comp\_standard\_schmittnorm lized\_standard$ 

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<br/>Blood |C4 |Plasma (Peripheral Venous Blood)<br/> Deviation:  ${\bf 0}$ 

Result of the validation: Valid

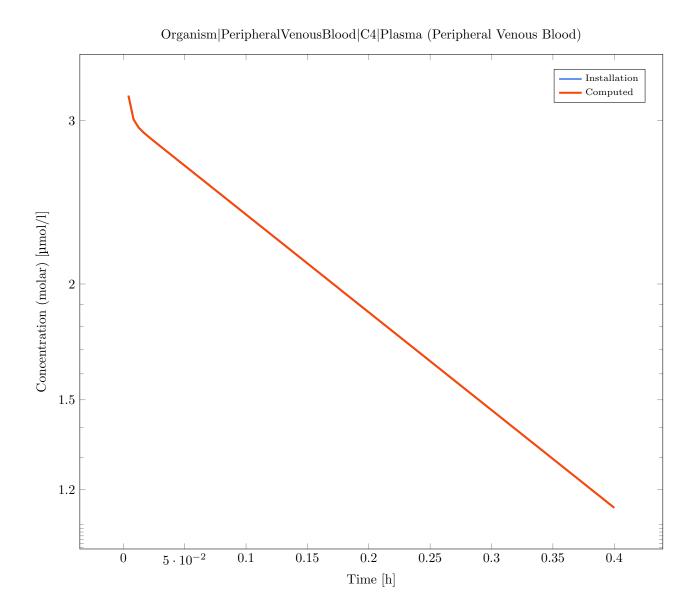


Figure 1.101

 $Simulation: Single IV\_C4\_4 Comp\_Ber\_standard\_s$ 

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



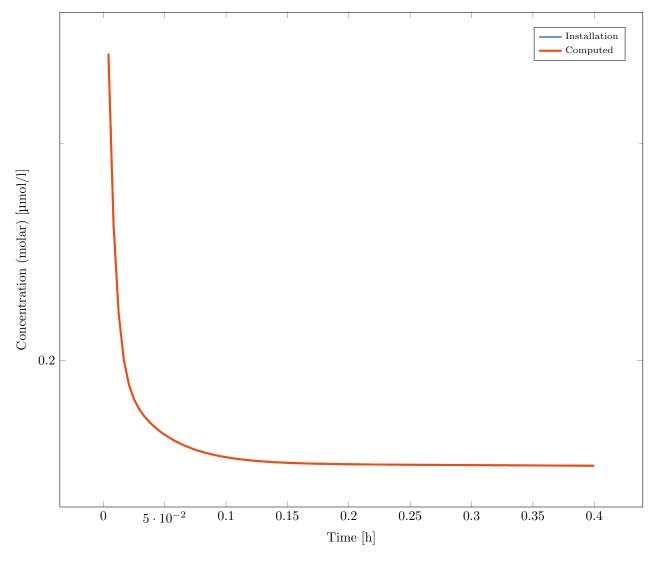


Figure 1.102

 $Simulation: Single IV\_C5\_2 Pores\_Ber\_standard\_$ 

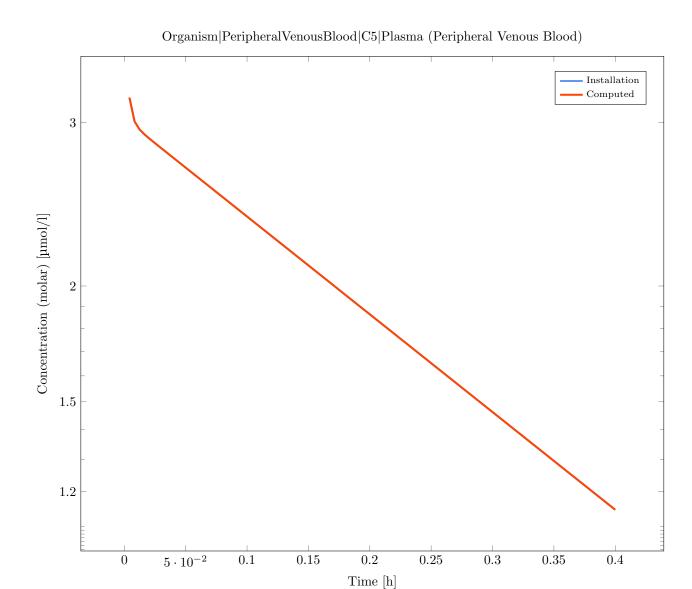


Figure 1.103

 $Simulation: Single IV\_C5\_2 Pores\_PT\_standard\_s$ 

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

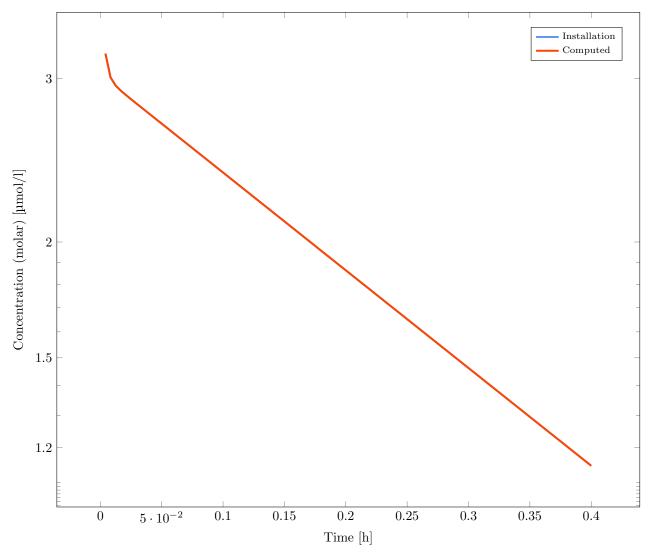
## Organism|PeripheralVenousBlood|C5|Plasma (Peripheral Venous Blood) Installation Computed 3 Concentration (molar) $[\mu mol/1]$ 2 1.5 1.2 0.15 0.2 0.25 0.3 0.35 0 $5\cdot 10^{-2}$ 0.1 0.4

**Figure 1.104** 

Time [h]

 $Simulation: SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_C5\_2Pores\_RR\_schmitt\_standard-SingleIV\_SingleI$ 

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



**Figure 1.105** 

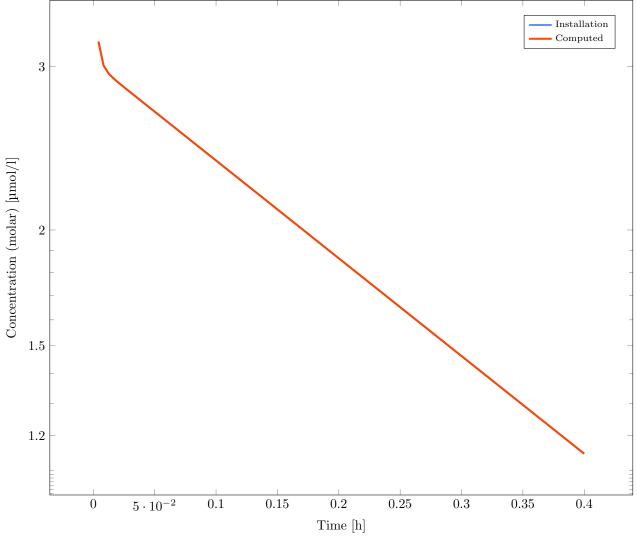
 $Simulation: Single IV\_C6\_2 Pores\_standard\_stan$ 

Result of the validation: Valid

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

Deviation: 0

# $\label{eq:constraint} Organism | Peripheral Venous Blood | C6| Plasma \ (Peripheral Venous Blood)$



**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)<br/> Deviation:  ${\bf 0}$ 

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

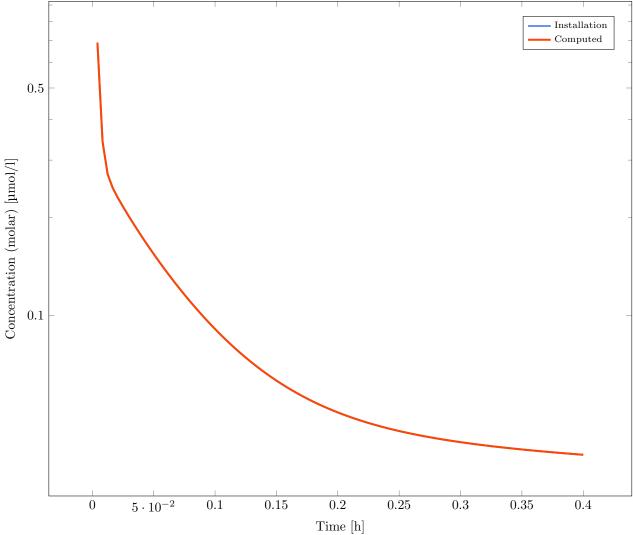


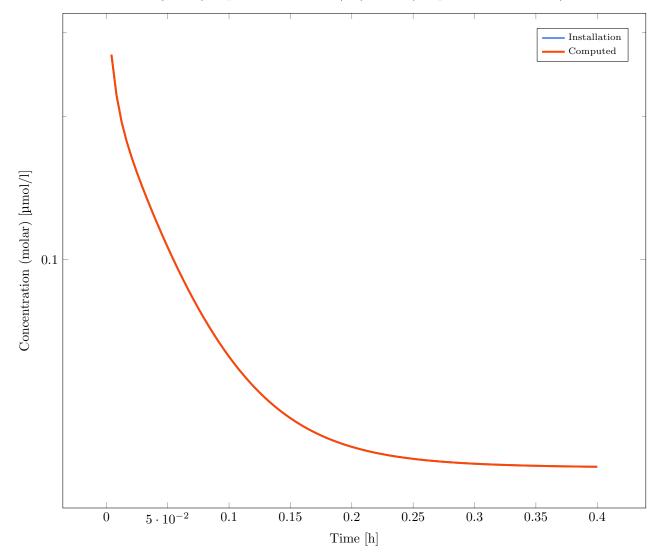
Figure 1.107

 $Simulation: Single IV\_C7\_4 Comp\_schmitt\_standard\_standa$ 

Result of the validation: Valid

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

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



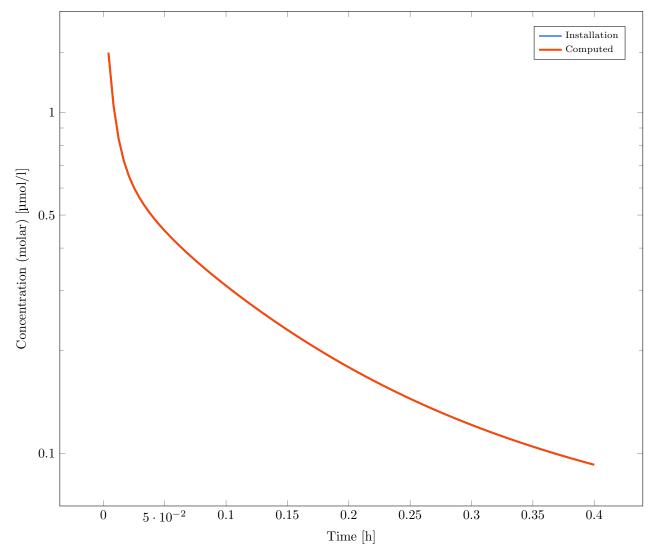
**Figure 1.108** 

 $Simulation: Single IV\_C8\_2 Pores\_standard\_schmittnormalized\_standard\_Single IV\_C8\_2 Pores\_standard\_schmittnormalized\_schmittnormalized\_s$ 

Result of the validation: Valid

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

# ${\it Organism}|{\it Peripheral Venous Blood}|{\it C8}|{\it Plasma}~({\it Peripheral Venous Blood})$



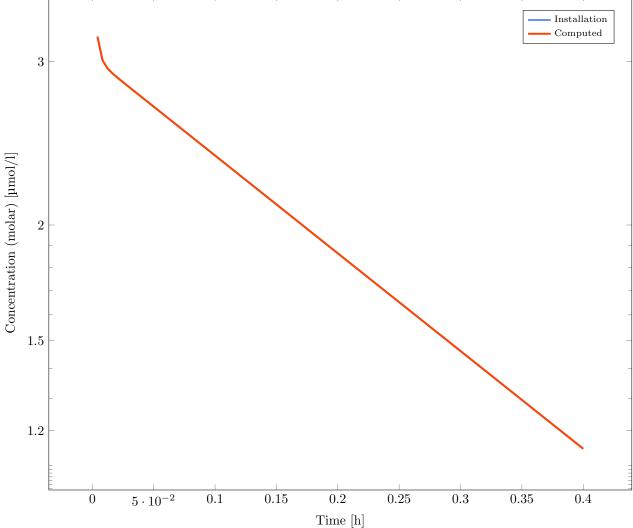
**Figure 1.109** 

 $Simulation: Single IV\_C9\_2 Pores\_schmitt\_standard\_standard\_Single IV\_C9\_2 Pores\_schmitt\_standard\_sta$ 

Result of the validation: Valid

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

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



**Figure 1.110** 

 $Simulation: Single ORAL\_C10\_4 Comp\_PT\_standard\_standard\_Single ORAL\_C10\_4 Comp\_PT\_standard\_$ 

Result of the validation: Valid

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

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

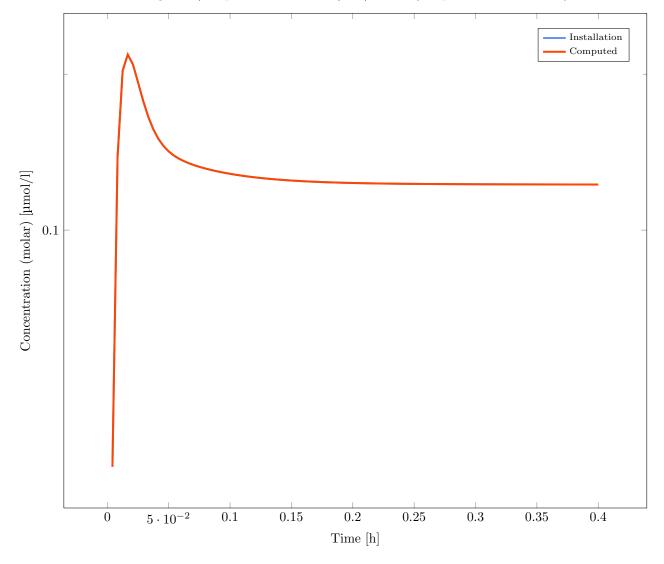
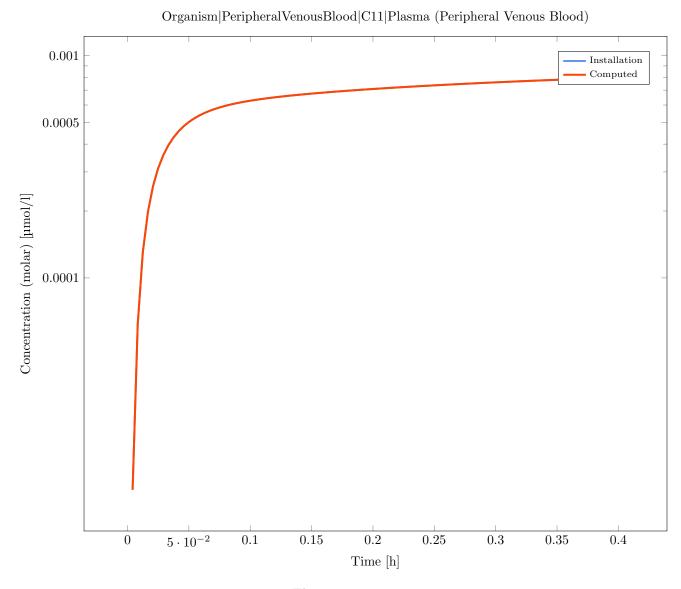


Figure 1.111

 $Simulation: Single ORAL\_C11\_4 Comp\_schmitt\_standard\_standard\_Single ORAL\_C11\_4 Comp\_schmitt\_standard$  $standard\_standard$ 

Result of the validation: Valid

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

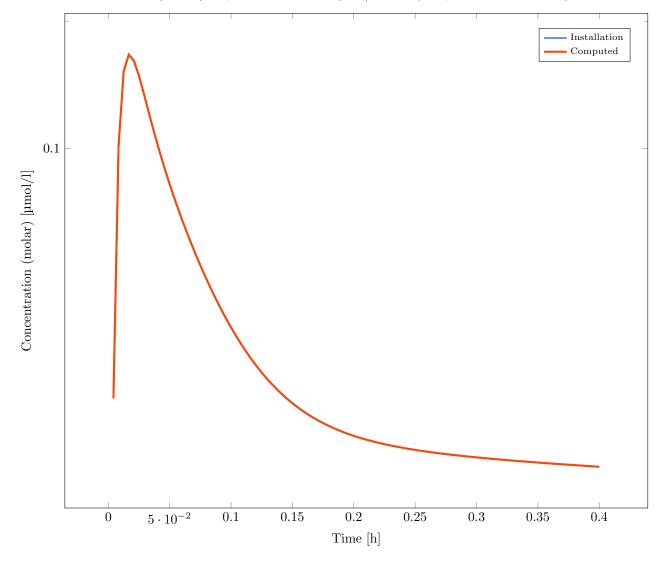


**Figure 1.112** 

 $Simulation: Single ORAL\_C11\_4 Comp\_standard\_st$ 

Result of the validation: Valid

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

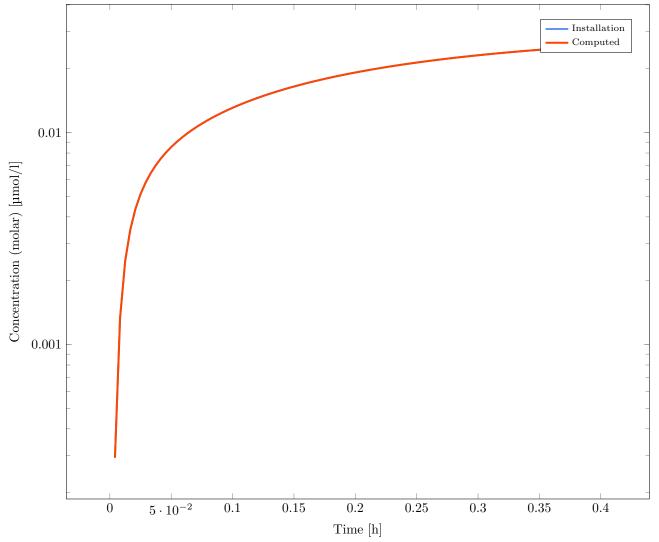


**Figure 1.113** 

 $Simulation: Single ORAL\_C12\_4 Comp\_standard\_schmitt\_standard-Single ORAL\_C12\_4 Comp\_standard\_schmitt\_standard\\$ 

Result of the validation: Valid

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



**Figure 1.114** 

 $Simulation: Single ORAL\_C13\_2 Pores\_schmitt\_standard\_standard\_Single ORAL\_C13\_2 Pores\_schmitt\_standard\_standa$  $standard\_standard$ 

Result of the validation: Valid

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



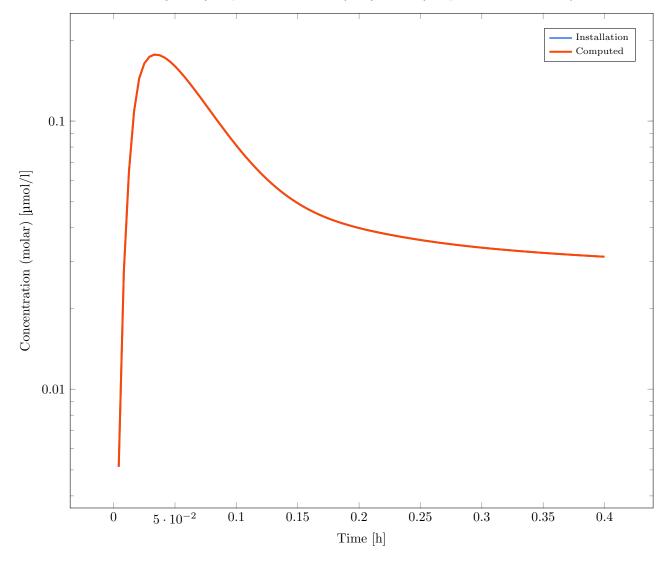
**Figure 1.115** 

 $Simulation: Single ORAL\_C13\_4 Comp\_standard\_schmittnormalized\_schmittnormalized\_sc$ 

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |C13 |Plasma (Peripheral Venous Blood)<br/> 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)

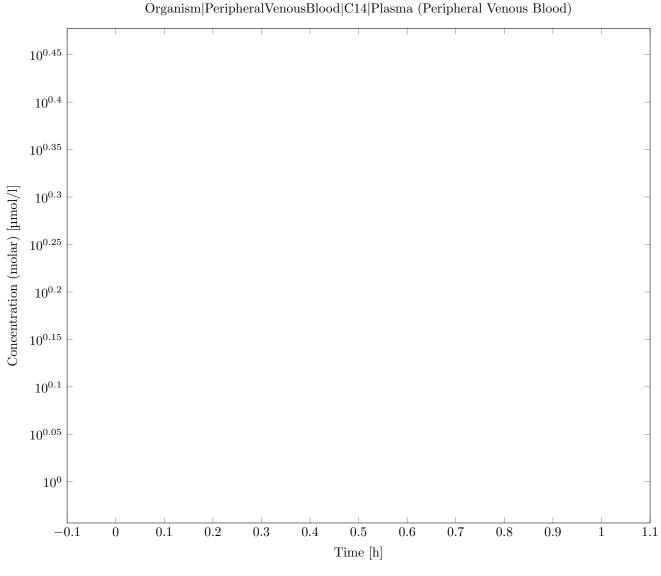
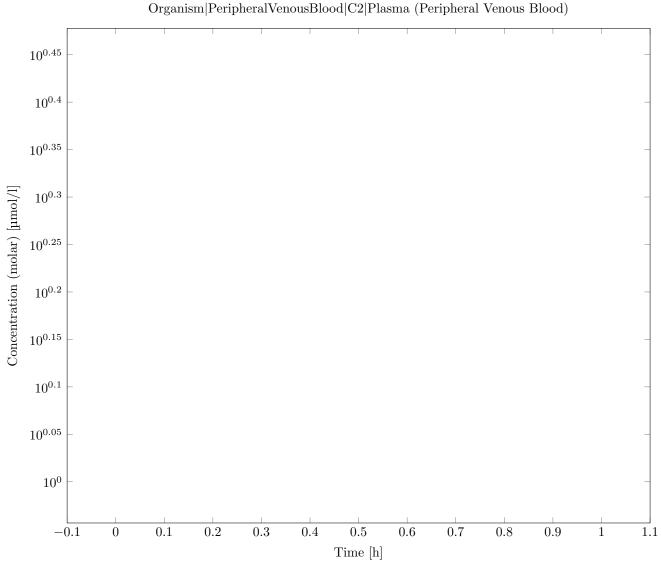


Figure 1.117

 $Simulation: Single ORAL\_C2\_2 Pores\_standard\_st$ 

Result of the validation: Valid

Output Path: Organism |Peripheral Venous<br/>Blood |C2 |Plasma (Peripheral Venous Blood) Deviation:<br/> 0

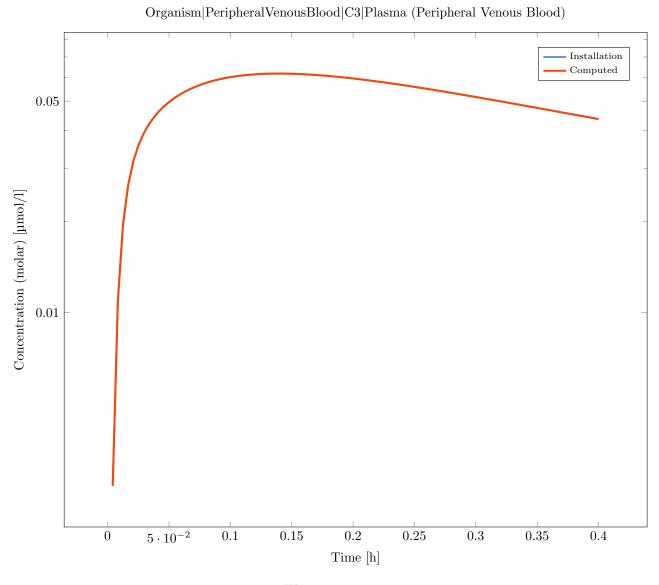


**Figure 1.118** 

 $Simulation: Single ORAL\_C3\_2 Pores\_standard\_schmitt\_standard-Single ORAL\_C3\_2 Pores\_standard\_schmitt\_standard$ 

Result of the validation: Valid

Output Path: Organism |Peripheral Venous<br/>Blood |C3 |Plasma (Peripheral Venous Blood) Deviation:<br/> 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<br/>Blood |C4 |Plasma (Peripheral Venous Blood)<br/> Deviation:  ${\bf 0}$ 

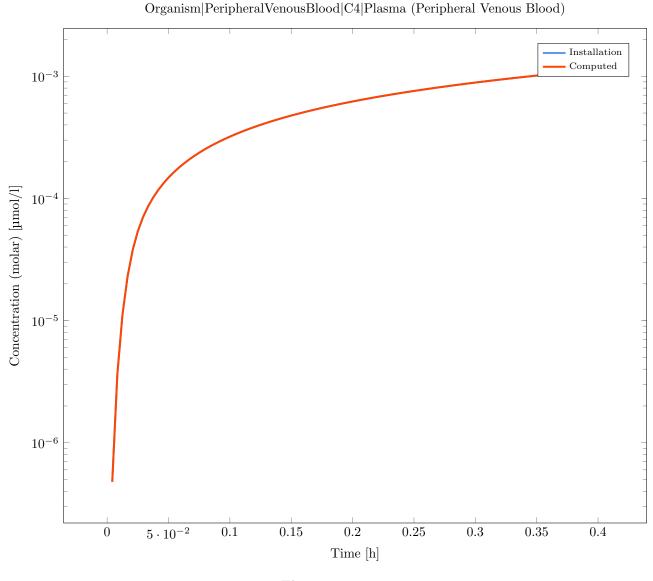


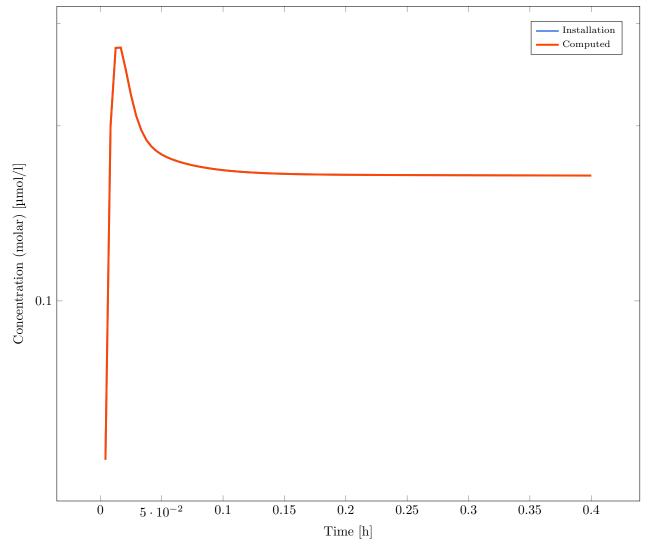
Figure 1.120

 $Simulation: Single ORAL\_C6\_4 Comp\_Ber\_standard\_standard\_Single ORAL\_C6\_4 Comp\_Ber\_standard\_$ 

Result of the validation: Valid

Output Path: Organism |PeripheralVenousBlood |C6 |Plasma (Peripheral Venous Blood)<br/> Deviation:  $\bf 0$ 

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



**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

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

# Organism|PeripheralVenousBlood|C6|Plasma (Peripheral Venous Blood) Installation Computed O.05 O.01

Figure 1.122

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single ORAL\_C7\_2 Pores\_Ber\_standard\_standard\_Single ORAL\_C7\_2 Pores\_Ber\_standard\_standar$ 

Result of the validation: Valid

0

 $5 \cdot 10^{-2}$ 

0.1

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

0.15

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

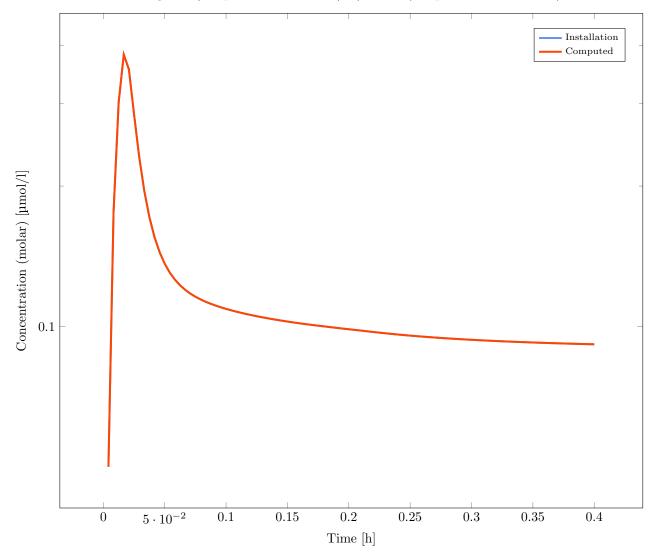


Figure 1.123

 $Simulation: Single ORAL\_C7\_4 Comp\_RR\_schmitt\_standard-Single ORAL\_C7\_5 Comp\_RR\_schmitt\_standard-Single ORAL\_C7\_5$ 

Result of the validation: Valid

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

# Organism|PeripheralVenousBlood|C7|Plasma (Peripheral Venous Blood) O.5 O.1 O.1

 $\label{eq:Time_h} \text{Time [h]}$  Figure 1.124

0.2

0.25

0.3

0.35

0.4

0.15

0.1

 $Simulation: Single ORAL\_C8\_2 Pores\_RR\_standard\_standard\_Single ORAL\_C8\_2 Pores\_RR\_standard\_$ 

Result of the validation: Valid

0

 $5\cdot 10^{-2}$ 

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

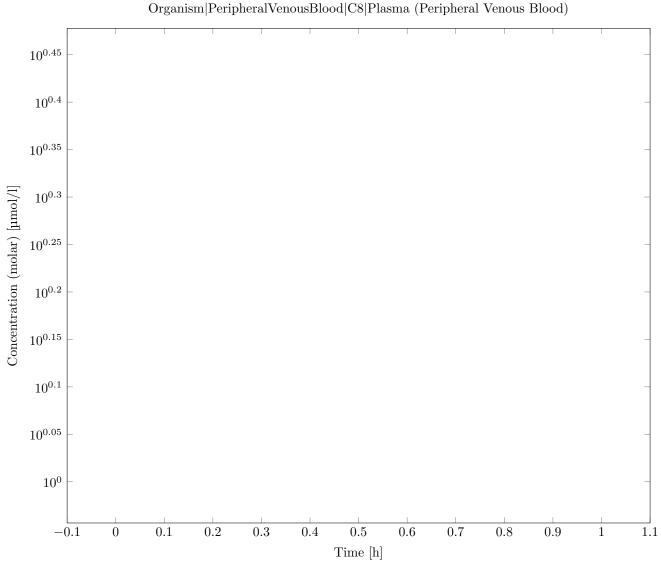


Figure 1.125

 $Simulation: SingleORAL\_C9\_2Pores\_RR\_schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_standard-SingleORAL\_Schmitt\_Schmitt\_standard-SingleORAL\_Schmitt\_$ 

Result of the validation: Valid

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

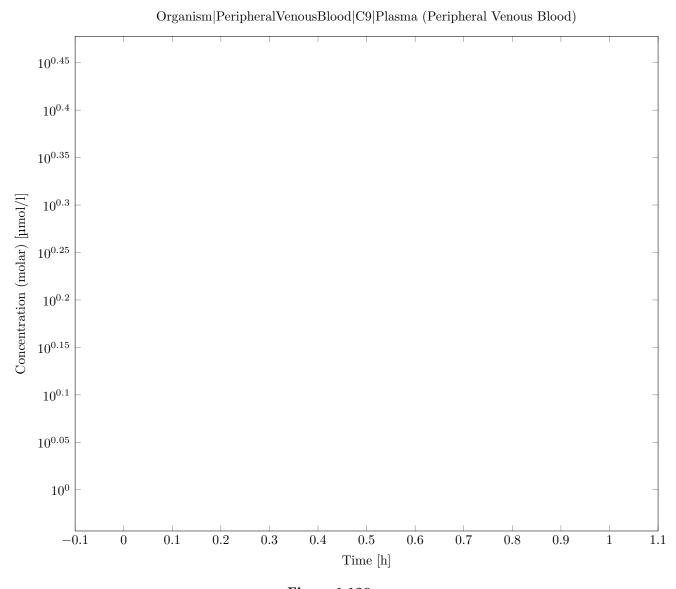


Figure 1.126

Simulation: Test 18.1\_I1\_C1\_A1\_Config1-Test 18.1\_I1\_C1\_A1\_Config1 Result of the validation: Valid

Deviation: 0

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

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

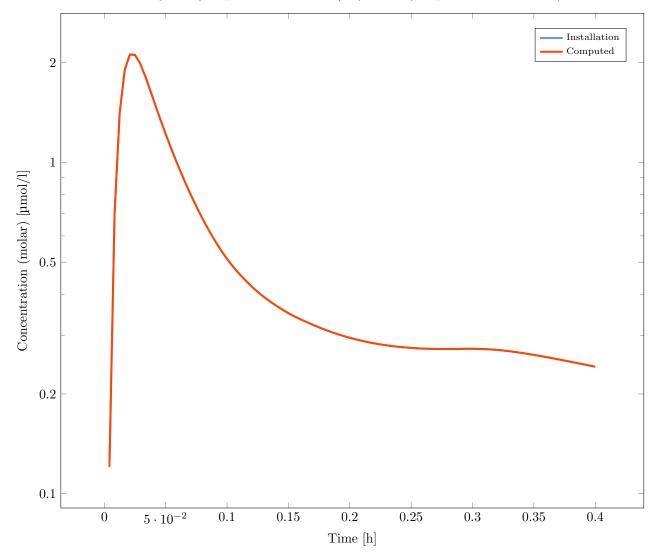


Figure 1.127

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

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

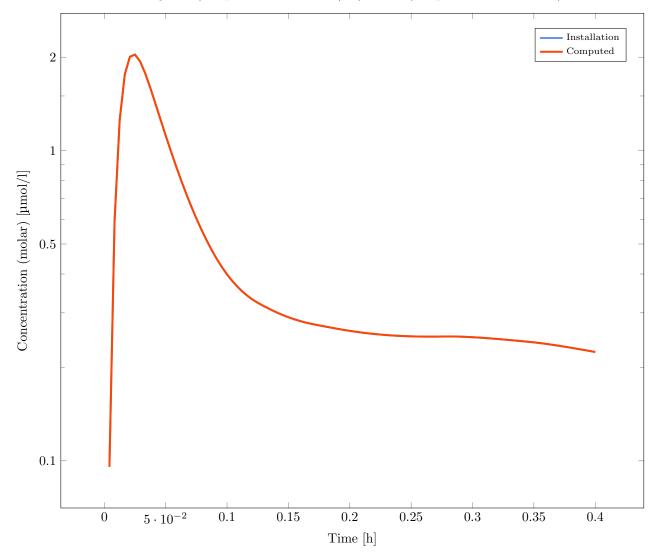


Figure 1.128

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<br/>Blood |C3 |Plasma (Peripheral Venous Blood)<br/> Deviation:  ${\bf 0}$ 

# Organism|Peripheral Venous Blood|C3|Plasma~(Peripheral Venous~Blood)

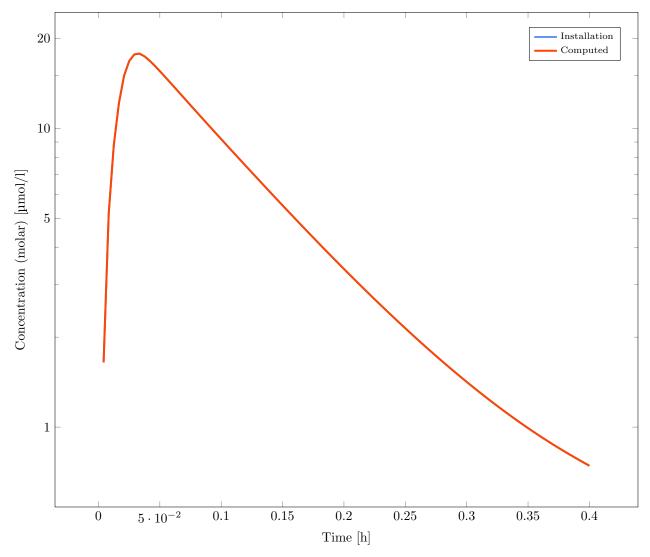


Figure 1.129

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<br/>Blood |C3 |Plasma (Peripheral Venous Blood)<br/> Deviation: 0

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

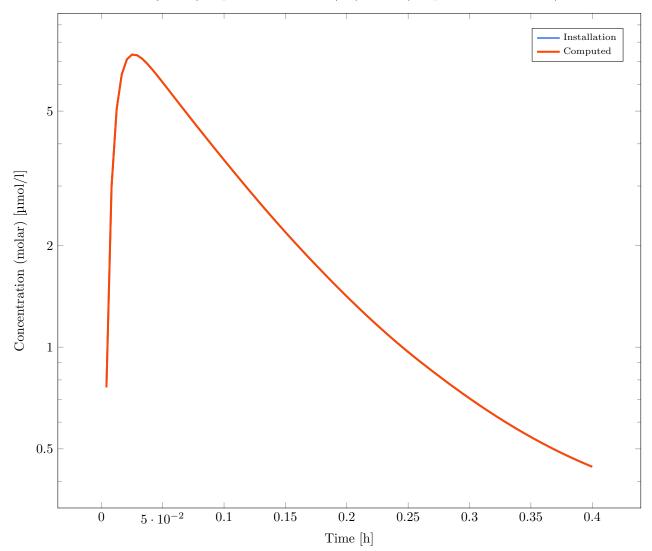


Figure 1.130