# Open Systems Pharmacology Suite - 11 Installation Validation

User1

May 19, 2022

# Contents

1 Installation Validation Results			Validation Results	2
	1.1	Valida	ion Summary	2
	1.2	Compa	rison Results	3
		1.2.1	Invalid Simulations $(1/155)$	3
		1.2.2	Valid Simulations (154/155)	6

## Chapter 1

## Installation Validation Results

#### **Overall Validation Result**

Invalid

## 1.1 Validation Summary

### Run Duration

Start time: 2022-05-19 16:43 End time: 2022-05-19 18:42

Validation performed in 01h:59m:03s:889ms

#### Input Configuration Folder

 $C: \label{lem:cology} Installation Validator \cite{C:ProgramData}. Open Systems Pharmacology \cite{C:ProgramData} Batch Files and the program Pharmacology \cite{C:ProgramData}. The program Pharmacology \cite{C:ProgramData} and the program Pharmacology \cite{C:ProgramData}. The program Pharmacology \cite{C:ProgramData} and the program Pharmacology \cite{C:ProgramData}. The program Pharmacology \cite{C:ProgramData} and the program Pharmacology \cite{C:ProgramData}. The program Pharmacology \cite{C:ProgramData} and \cite{C:ProgramData} and \cite{C:ProgramData}. The program Pharmacology \cite{C:ProgramData} and \cite{C:ProgramData} and \cite{C:ProgramData}. The program Pharmacology \cite{C:ProgramData} and \cite{C:ProgramData$ 

#### **Local Outputs Location**

#### **Application Versions**

PK-Sim Version 11.0.150 MoBi Version 11.0.138

#### Language Settings

Japanese (Japan) (ja-JP)

#### Computer Name

WIN11\_JP

#### Operating System

Windows 10 Pro

#### Architecture

x64

#### Running on Virtual Machine

Yes

#### Running on Terminal Session

No

## 1.2 Comparison Results

#### Overall Comparison Result

Invalid

#### Installation Folder

C:\ProgramData\Open Systems Pharmacology\InstallationValidator\11.0\Outputs\BatchFiles

#### Computed Folder

C:\Users\User1\AppData\Roaming\Open Systems Pharmacology\InstallationValidator\11.0\Outputs

## 1.2.1 Invalid Simulations (1/155)

#### $Simulation: \ Human\_MultiORAL\_6\_12\_12\_Dissolved-Human\_MultiORAL\_6\_12\_12\_Dissolved\_solubility$

Result of the validation: Invalid Absolute Tolerance: 1.00E-13 Relative Tolerance: 1.00E-8

# Output Path: Organism|Lumen|LowerJejunum|drug|Fraction of oral drug mass absorbed into mucosa segment

Deviation for 'Organism|Lumen|LowerJejunum|drug|Fraction of oral drug mass absorbed into mucosa segment' is 100.00% and is greater than the allowed max. tolerance of 3.00%

Deviation: 1.00

0

 $\cdot 10 \text{rg} \\ \text{å} \\ \text{nism} \\ \text{Lumen} \\ \text{LowerJejunum} \\ \text{drug} \\ \text{Fraction of oral drug mass absorbed into mucosa segment} \\$ 1 Installation Computed

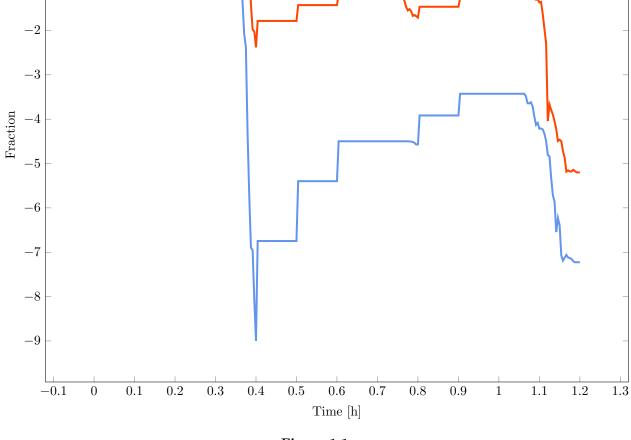


Figure 1.1

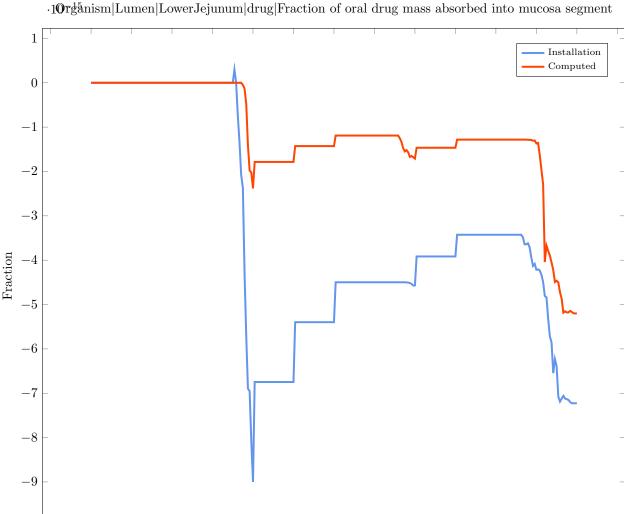


Figure 1.2

0.6

Time [h]

0.7

0.8

0.9

1.1

1.2

1.3

Output Path: Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Deviation: 9.74E-8

0.5

0.1

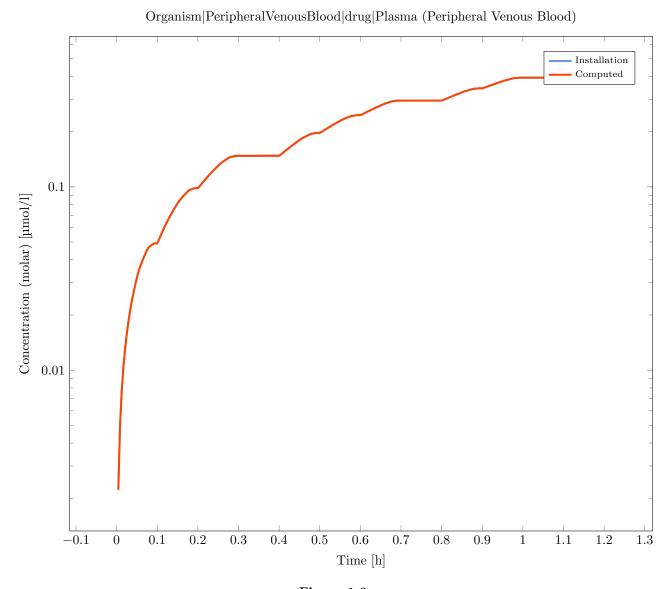
0

-0.1

0.2

0.3

0.4



#### Figure 1.3

### 1.2.2 Valid Simulations (154/155)

 $Simulation: \ Beagle\_SingleORAL\_Dissolved-Beagle\_SingleORAL\_Dissolved$ 

Result of the validation: Valid

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

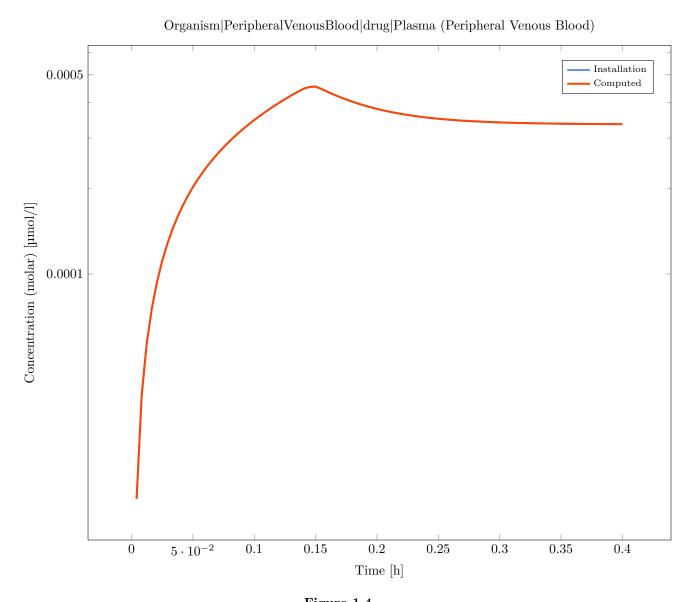
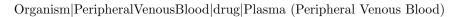


Figure 1.4

 $Simulation: Beagle\_SingleORAL\_Dissolved\_Beagle\_SingleORAL\_Dissolved\_MW\_200\_fu\_0.2\_LogP\_5$ 

Result of the validation: Valid

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



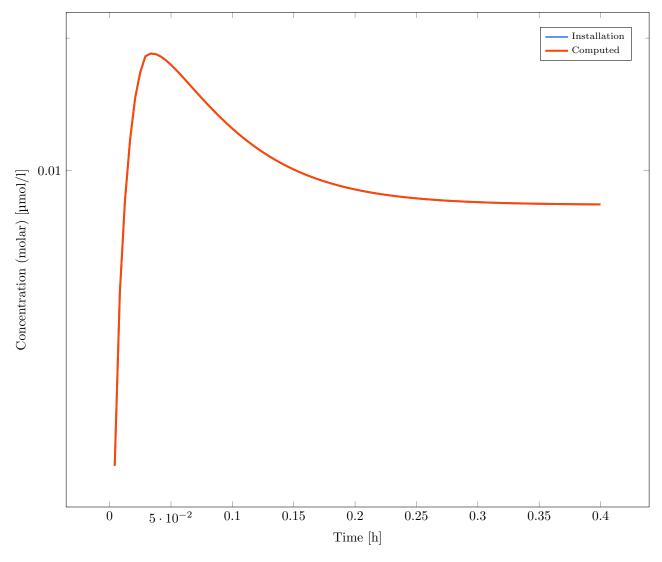


Figure 1.5

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

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

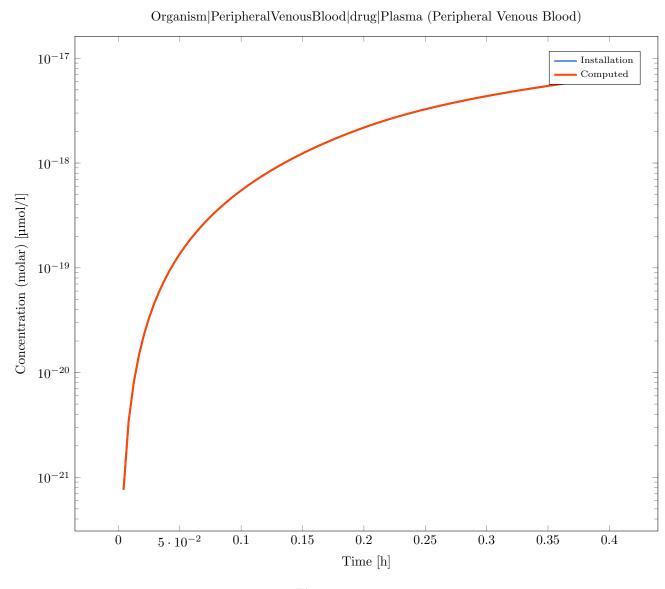
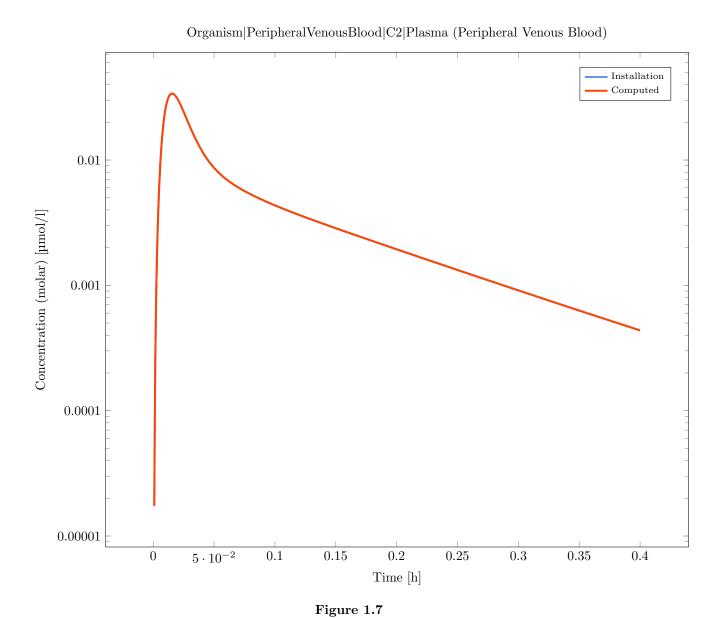


Figure 1.6

 ${\bf Simulation:\ DDI\_Multiple Combinations\hbox{--}01\_MM\_Competitive\_Competitive} \\ {\bf Result\ of\ the\ validation:\ Valid}$ 

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



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

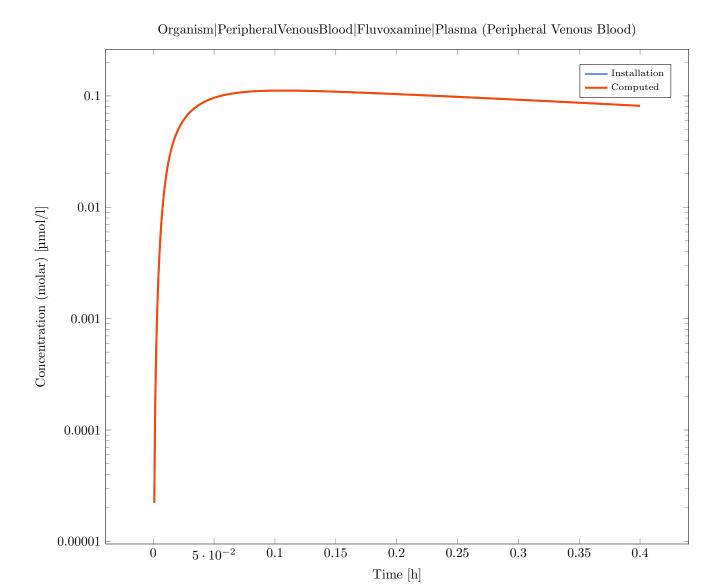


Figure 1.8

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



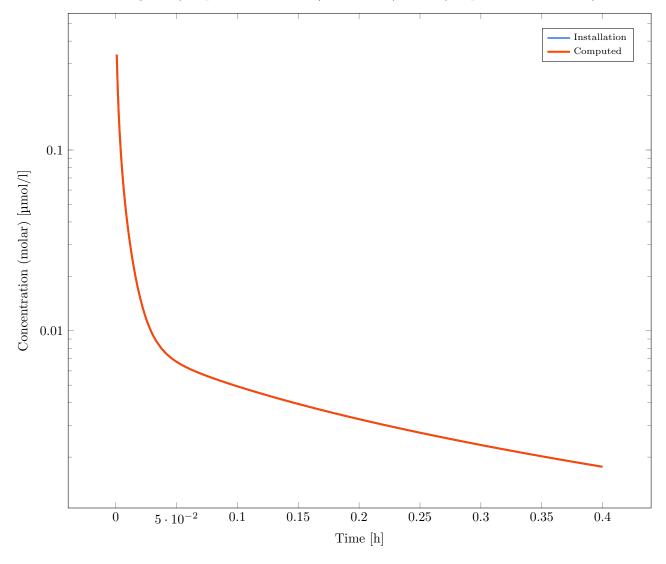


Figure 1.9

 ${\bf Simulation:\ DDI\_Multiple Combinations-02\_MM\_Uncompetitive\_Uncompetitive\_Result\ of\ the\ validation:\ Valid}$ 

Output Path: Organism |Peripheral Venous<br/>Blood |C2 |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.77E-4

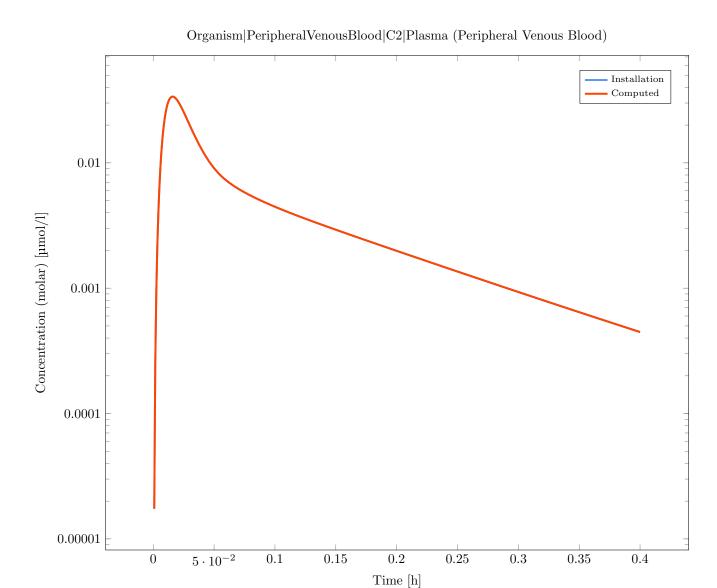


Figure 1.10

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive\_CYP3A4\_1|Plasma\ (PeripheralVenous\ Blood)\\ Venous\ Blood)$ 

Deviation: 3.69E-4

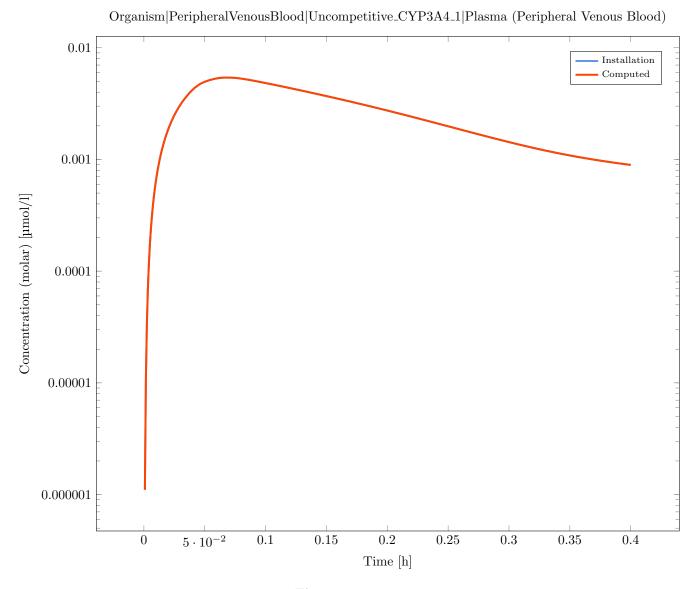
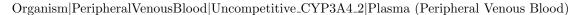


Figure 1.11

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive\_CYP3A4\_2|Plasma\ (PeripheralVenous\ Blood)$ 

Deviation: 3.69E-4



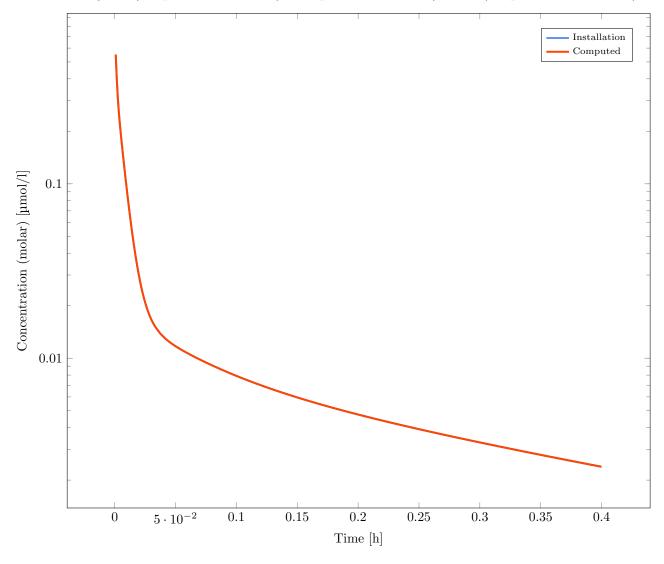


Figure 1.12

 ${\bf Simulation:\ DDI\_Multiple Combinations-03\_MM\_Noncompetitive\_N$ 

Output Path: Organism |Peripheral Venous<br/>Blood |C2 |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.58E-4

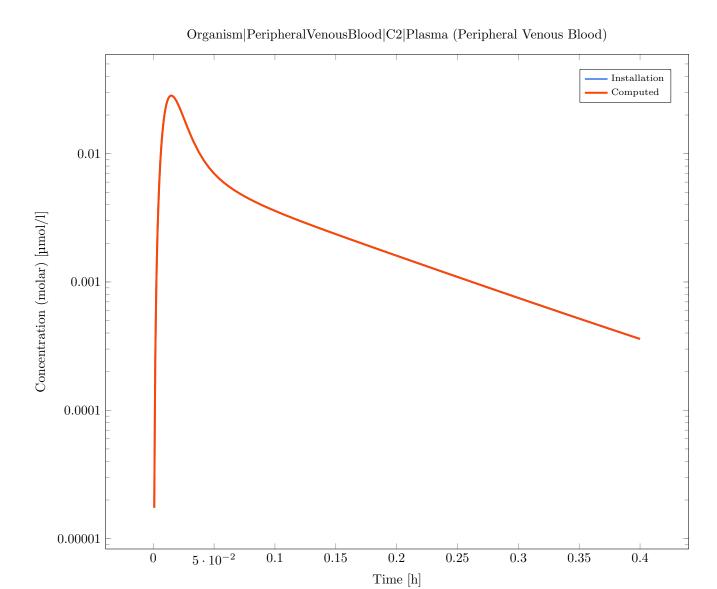


Figure 1.13

 $Output\ Path:\ Organism | Peripheral Venous Blood | Noncompetitive\_CYP3A4\_1 | Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.68E-4

Organism|PeripheralVenousBlood|Noncompetitive\_CYP3A4\_1|Plasma (Peripheral Venous Blood)

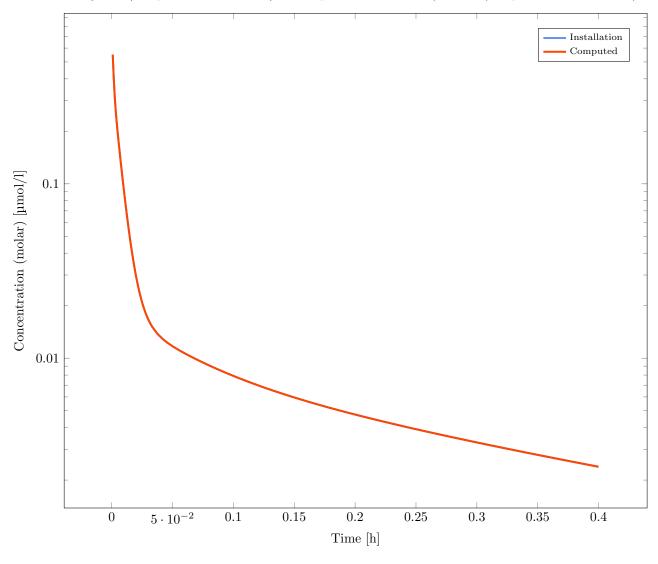


Figure 1.14

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_2|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.06E-4

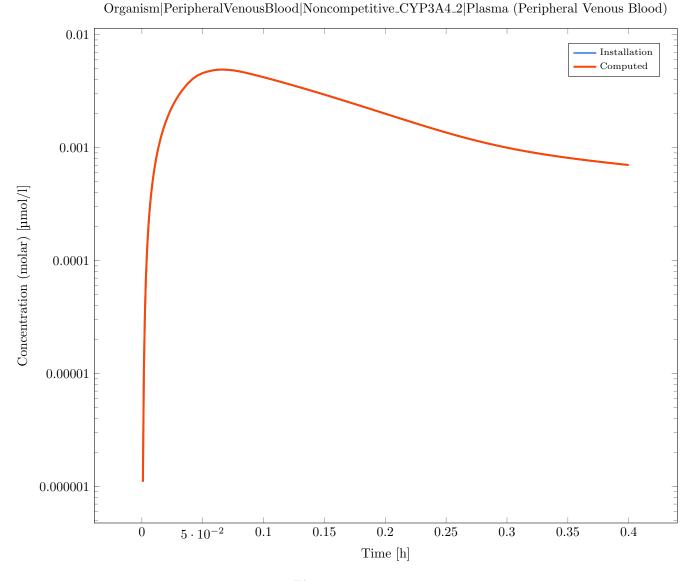


Figure 1.15

 $Simulation: \ DDI\_MultipleCombinations-04\_MM\_Mixed\_Mixed$ 

Result of the validation: Valid

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

Deviation: 3.82E-4

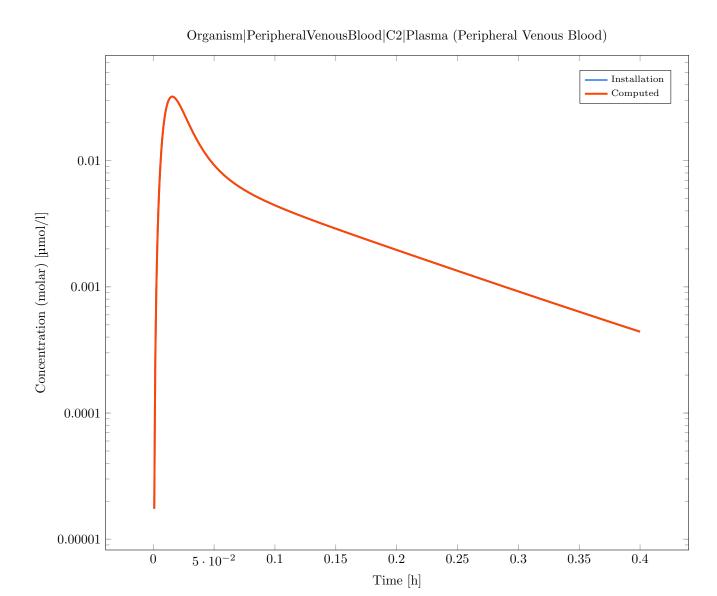


Figure 1.16

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_1|Plasma\ (Peripheral\ VenousBlood)$ 

Deviation: 3.16E-4

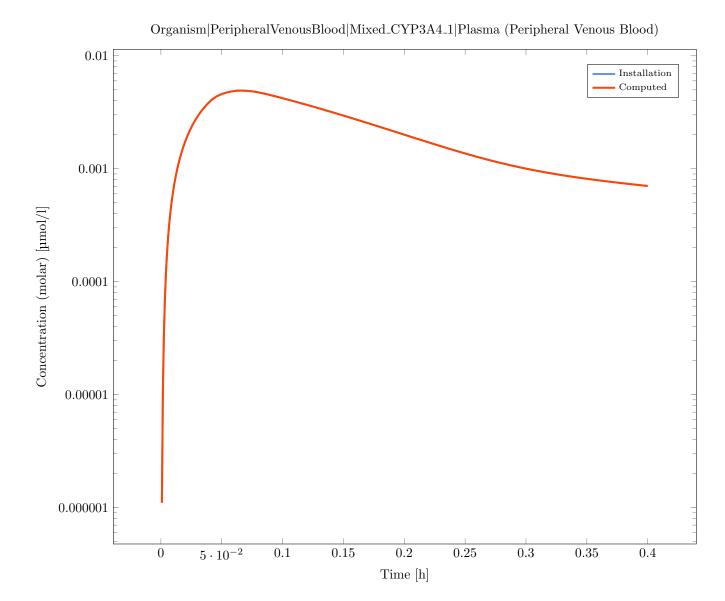


Figure 1.17

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_2|Plasma\ (Peripheral\ VenousBlood)$ 

Deviation: 3.68E-4

#### Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_2|Plasma (Peripheral Venous Blood)

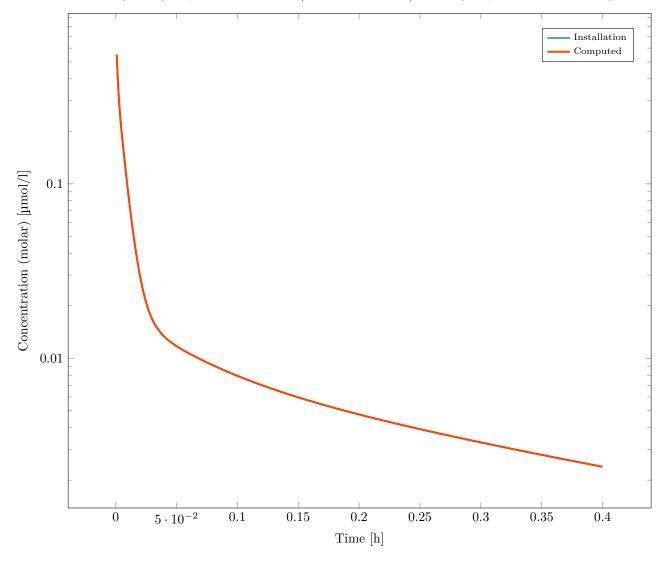


Figure 1.18

Simulation: DDI\_MultipleCombinations-05\_MM\_Mechanismbased\_Mechanismbased Result of the validation: Valid

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

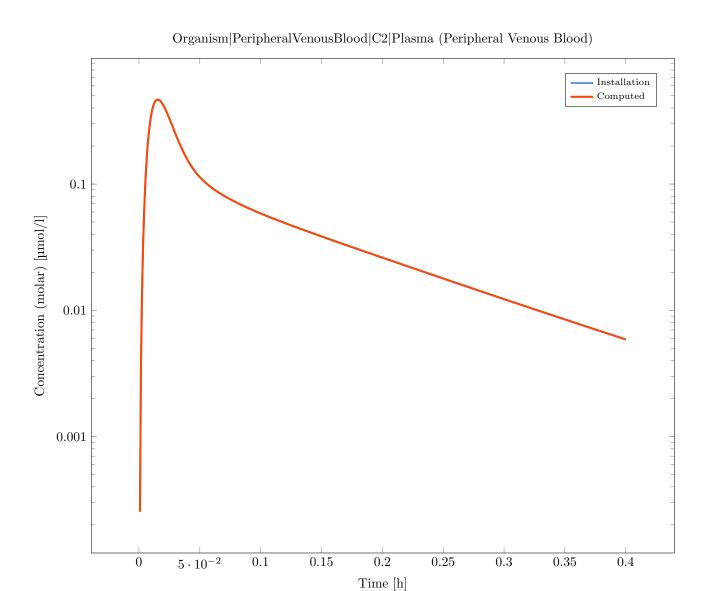
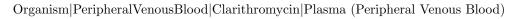
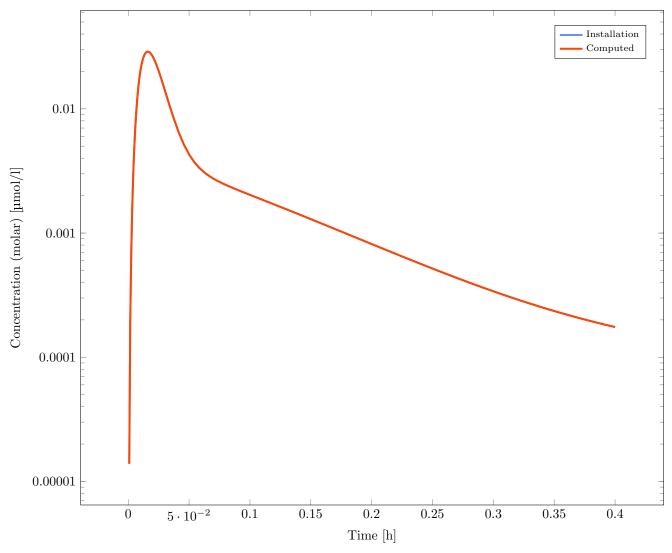


Figure 1.19

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





**Figure 1.20** 

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

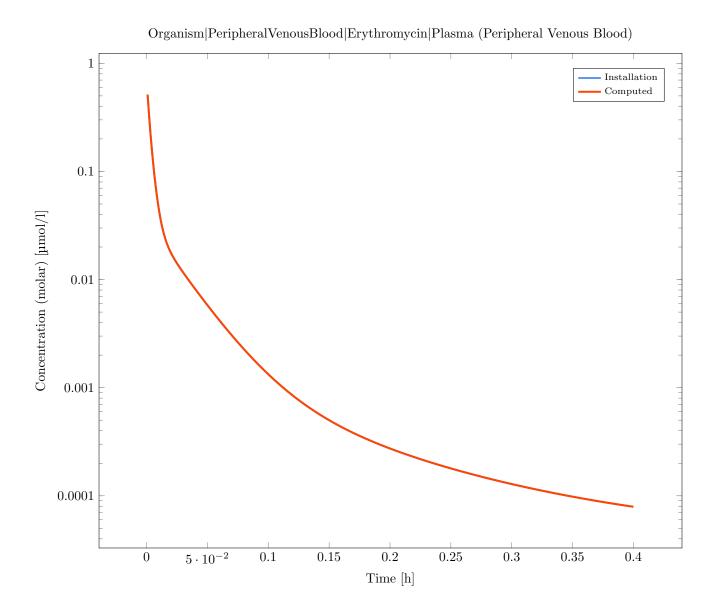


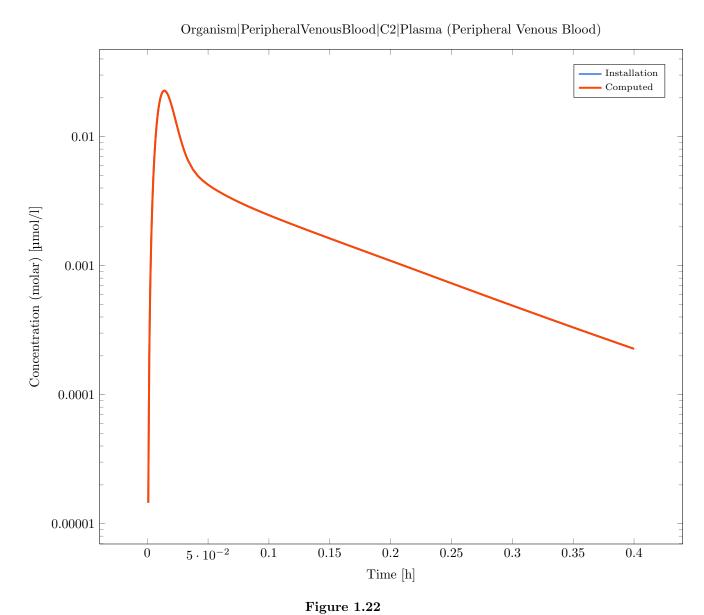
Figure 1.21

 ${\bf Simulation:\ DDI\_Multiple Combinations-06\_MM\_Induction\_Induction}$ 

Result of the validation: Valid

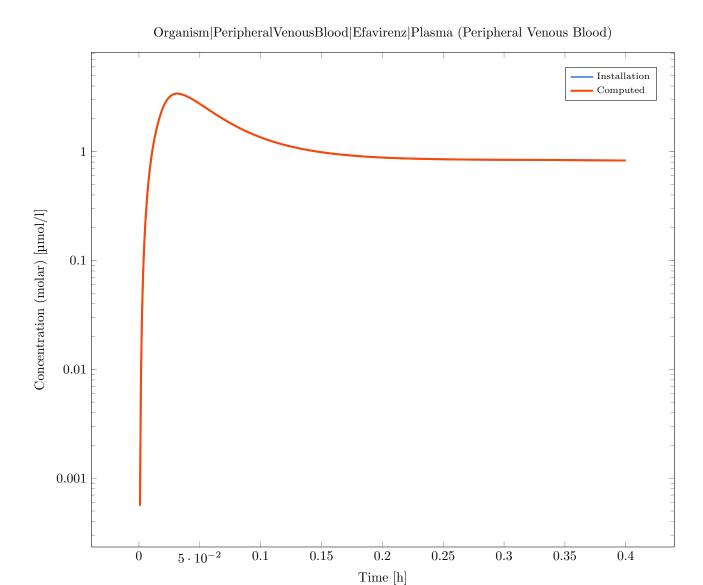
Output Path: Organism|PeripheralVenousBlood|C2|Plasma (Peripheral Venous Blood)

Deviation: 3.14E-4



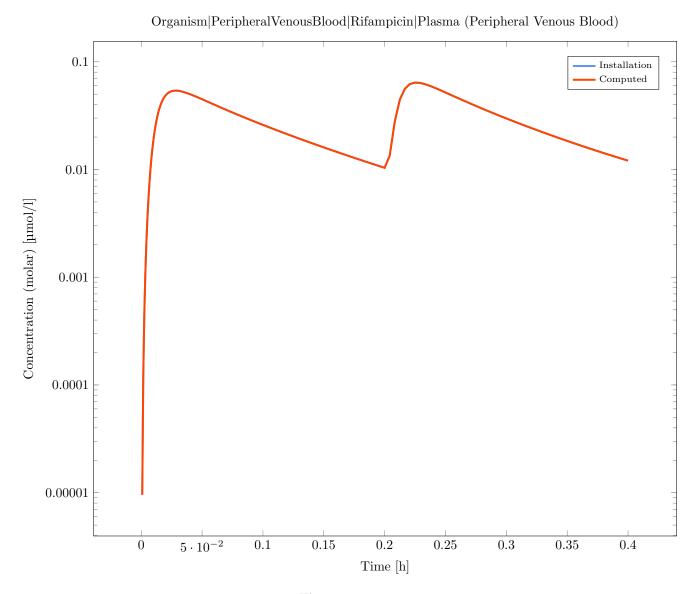
116410 1.22

Output Path: Organism|PeripheralVenousBlood|Efavirenz|Plasma (Peripheral Venous Blood) Deviation: 1.65E-4



**Figure 1.23** 

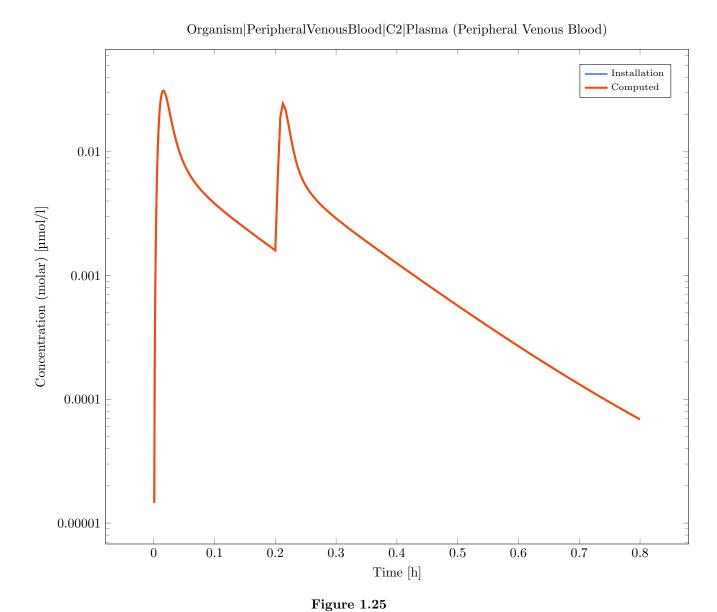
Output Path: Organism |Peripheral Venous<br/>Blood |Rifampicin |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.68E-4



**Figure 1.24** 

Simulation: DDI\_MultipleCombinations-07\_MM\_Competitive\_Competitive\_Mechanismbased\_Mechanismbased Result of the validation: Valid

Output Path: Organism |Peripheral Venous<br/>Blood |C2 |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.29E-4



Output Path: Organism |Peripheral Venous<br/>Blood |Clarithromycin |Plasma (Peripheral Venous Blood)<br/> Deviation:  $2.15 \pm .4$ 

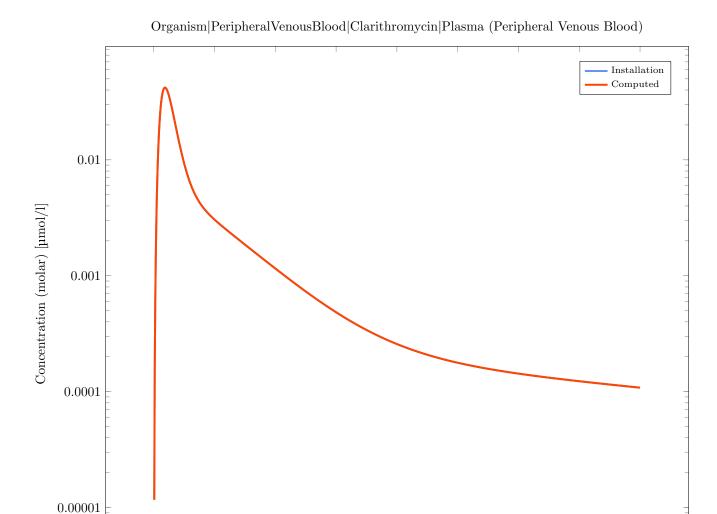


Figure 1.26

0.3

0.4

Time [h]

0.5

0.6

0.7

0.8

Output Path: Organism |Peripheral Venous<br/>Blood |Erythromycin |Plasma (Peripheral Venous Blood)<br/> Deviation: 6.44E-4

0

0.1

0.2



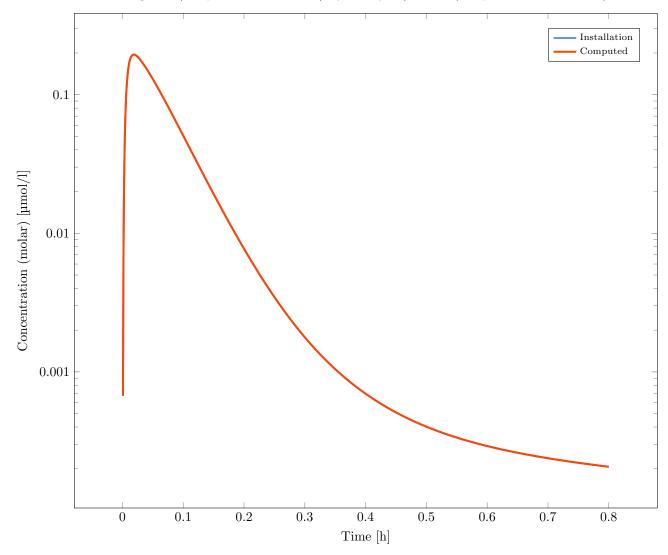
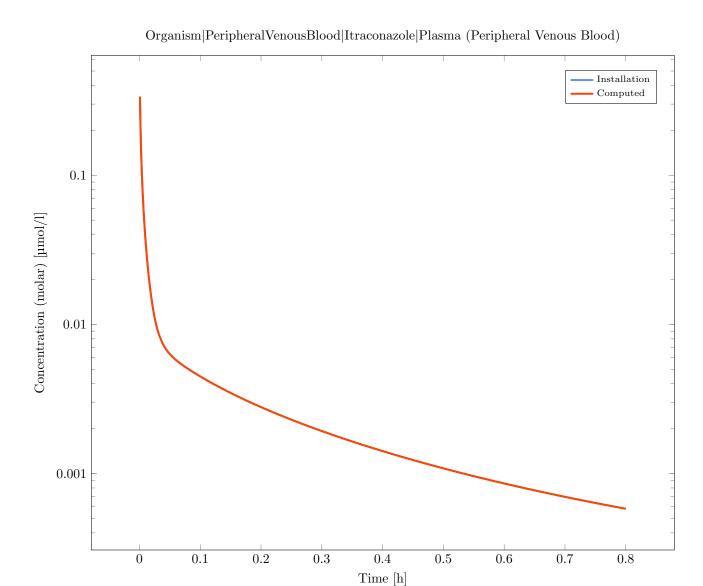


Figure 1.27

Output Path: Organism |Peripheral Venous<br/>Blood |Itraconazole |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.27E-4



Output Path: Organism |Peripheral Venous<br/>Blood |Rifampicin |Plasma (Peripheral Venous Blood)<br/> Deviation:  $4.68\hbox{E-}4$ 

Figure 1.28

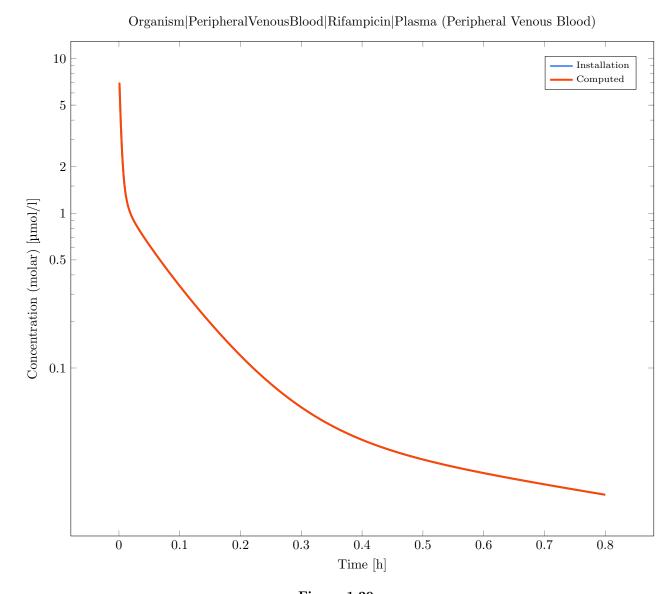


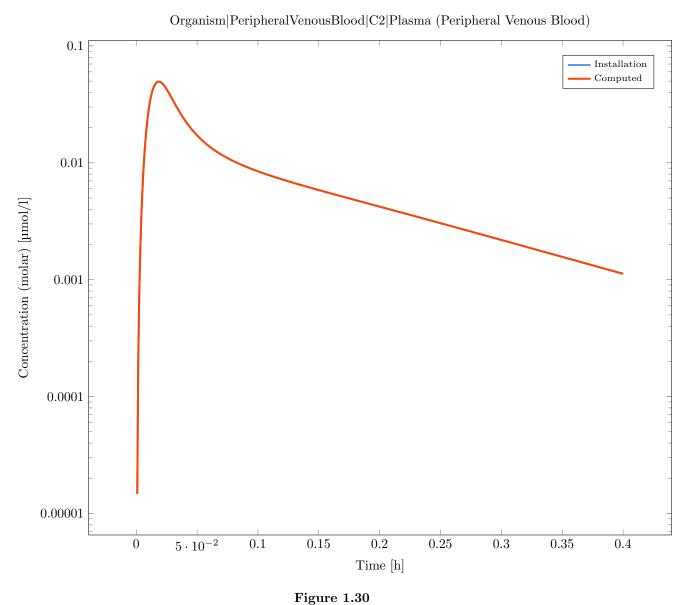
Figure 1.29

 $Simulation: \ DDI\_Multiple Combinations - 08\_MM\_Uncompetitive\_Uncompetitive\_Mechanism based\_Mechanism based$ 

Result of the validation: Valid

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

Deviation: 6.00E-4



118010 1100

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_4|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 6.00E-4

#### Organism|PeripheralVenousBlood|MechanismBased\_4|Plasma (Peripheral Venous Blood)

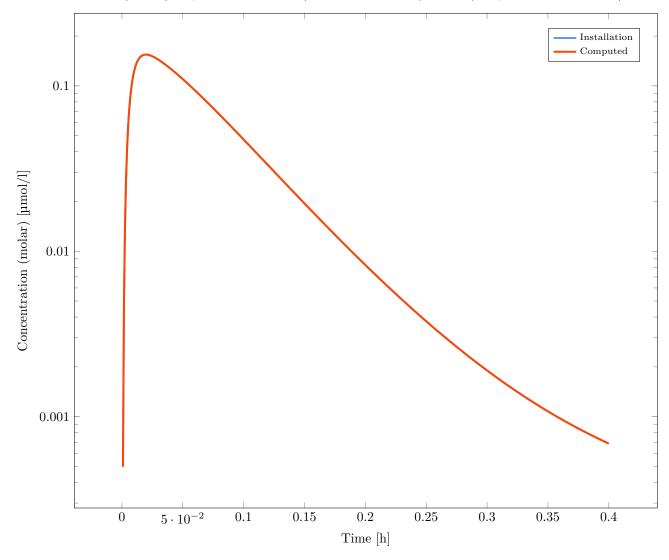
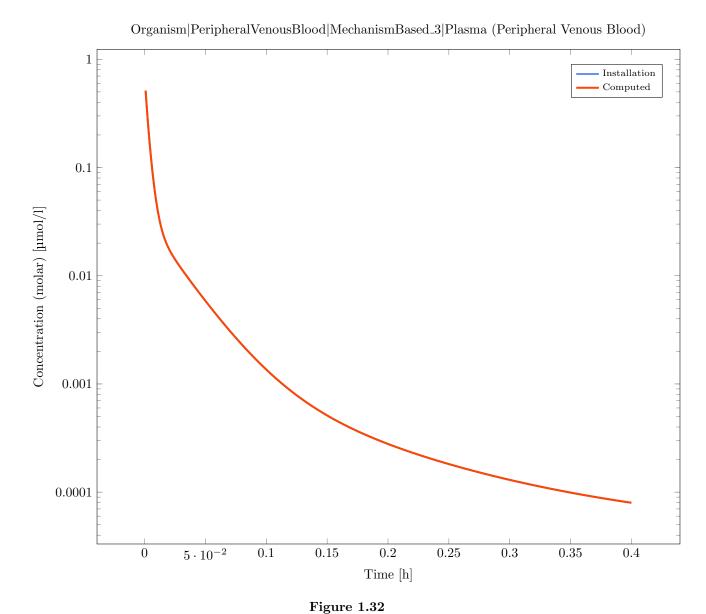


Figure 1.31

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.66E-4



 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive\_CYP3A4\_4|Plasma\ (PeripheralVenous\ Blood)$ 

Deviation: 5.77E-5

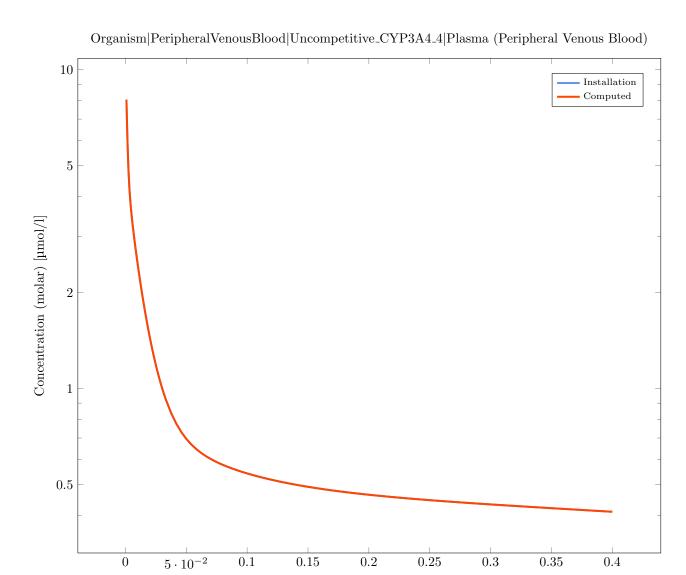
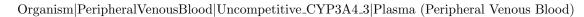


Figure 1.33

Time [h]

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive\_CYP3A4\_3|Plasma\ (PeripheralVenous\ Blood)$ 

Deviation: 1.05E-4



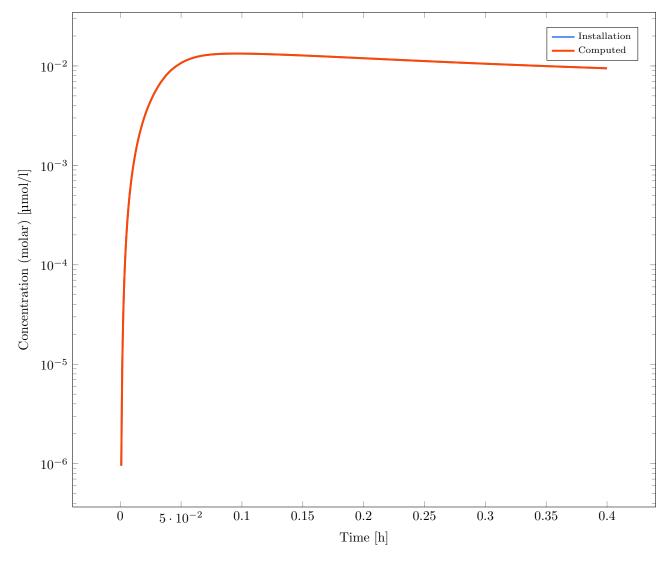


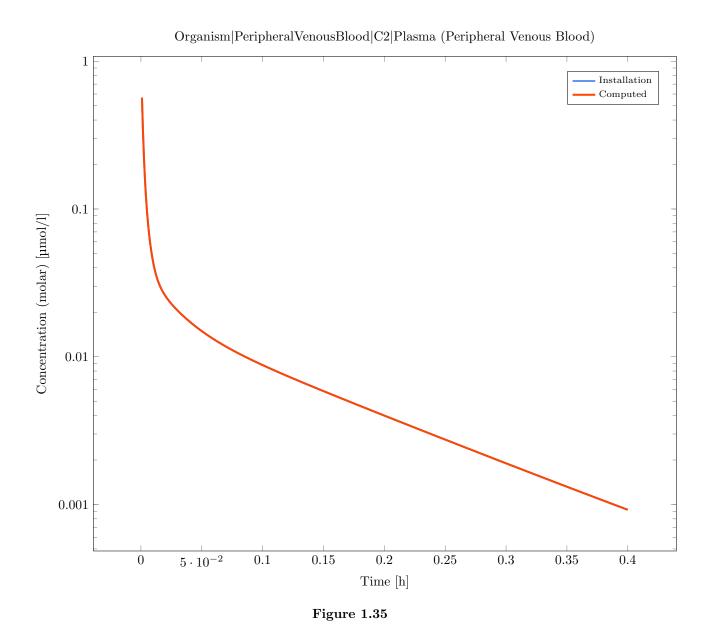
Figure 1.34

 $Simulation: \ DDI\_Multiple Combinations - 09\_MM\_Noncompetitive\_Noncompetitive\_Mechanism based\_Mechanism based$ 

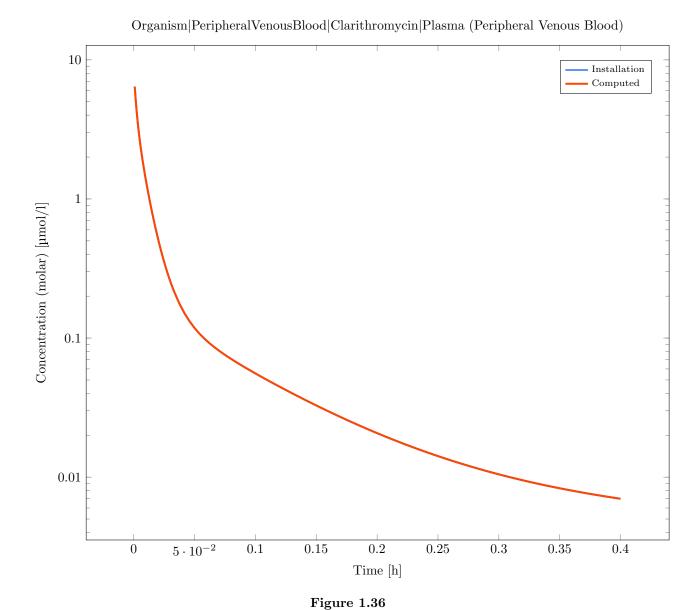
Result of the validation: Valid

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

Deviation: 3.07E-4



Output Path: Organism |Peripheral Venous<br/>Blood |Clarithromycin |Plasma (Peripheral Venous Blood)<br/> Deviation: 2.42E-4



Output Path: Organism |Peripheral Venous<br/>Blood |Erythromycin |Plasma (Peripheral Venous Blood)<br/> Deviation: 5.50E-4

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

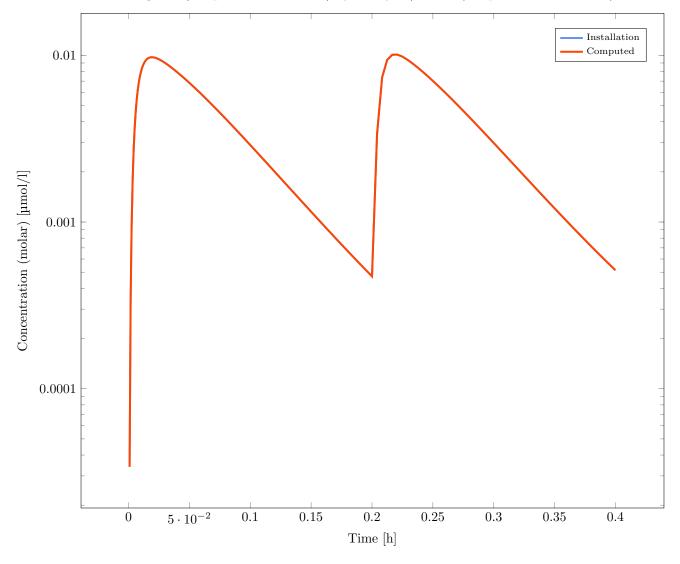
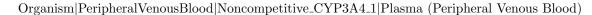


Figure 1.37

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_1|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.16E-4



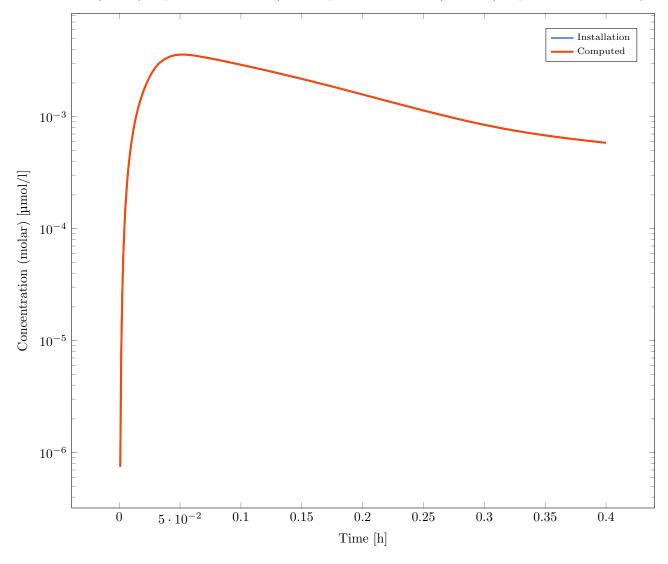


Figure 1.38

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_2|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.33E-4



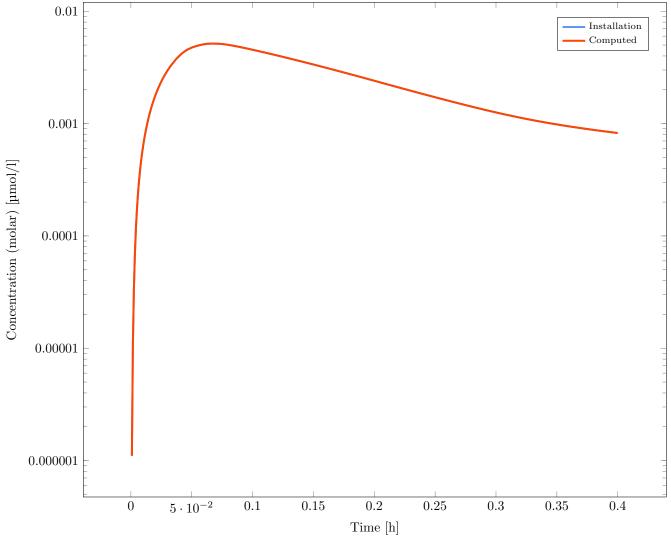


Figure 1.39

 ${\bf Simulation:\ DDI\_Multiple Combinations-10\_MM\_Mixed\_Mixed\_Mechanismbased\_Mech$ 

Output Path: Organism |Peripheral Venous<br/>Blood |C2 |Plasma (Peripheral Venous Blood)<br/> Deviation:  $4.93\hbox{E-}4$ 

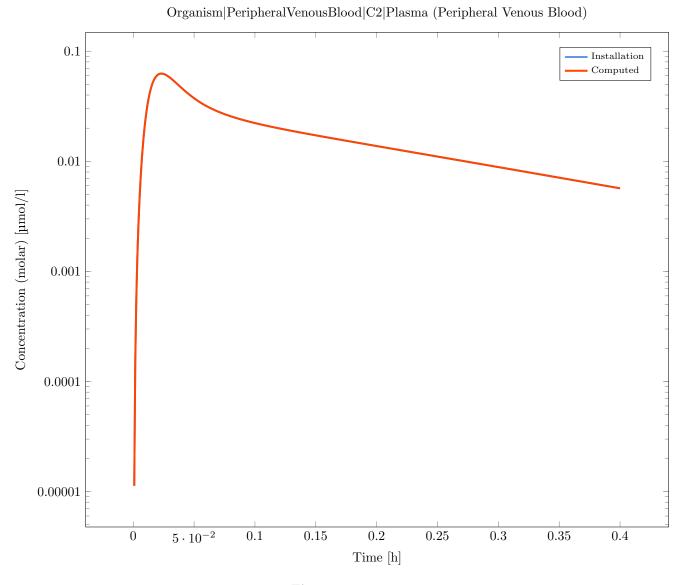


Figure 1.40

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_4|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 5.67E-4

# Organism|PeripheralVenousBlood|MechanismBased\_4|Plasma (Peripheral Venous Blood)

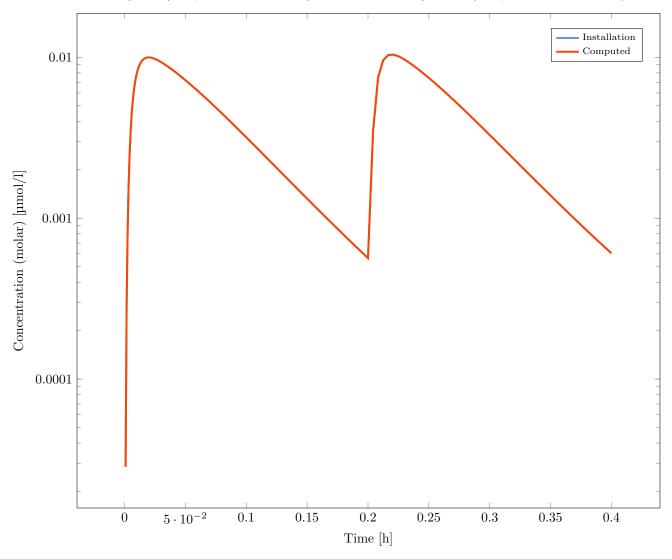
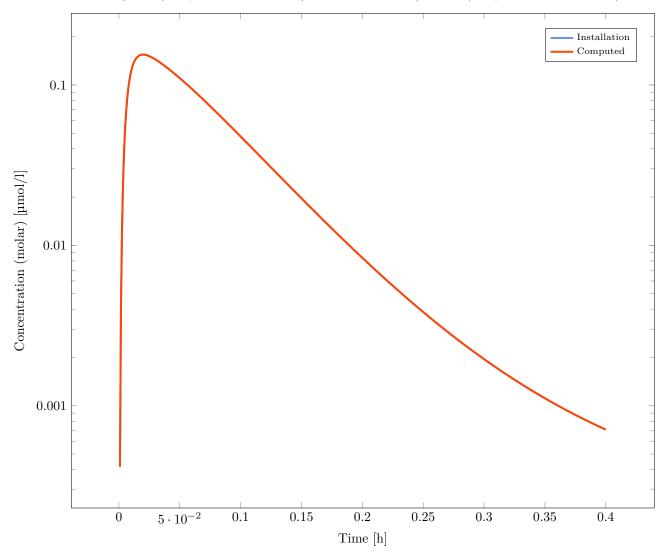


Figure 1.41

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 5.92E-4

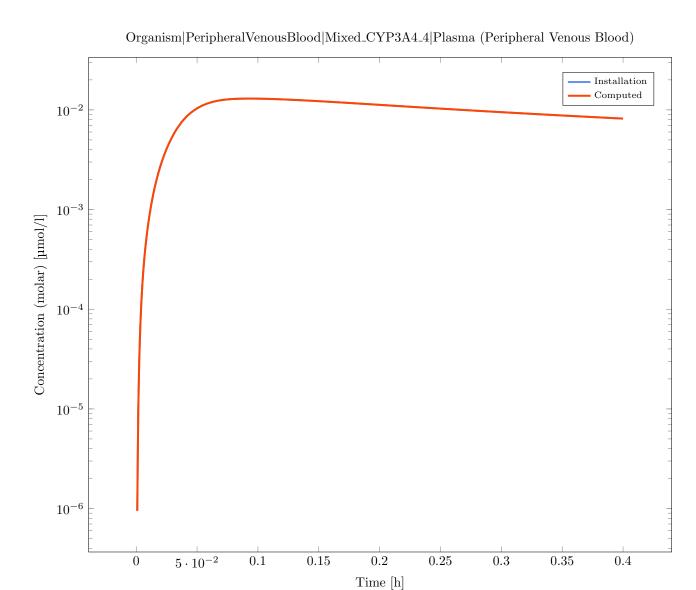
# Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma (Peripheral Venous Blood)



**Figure 1.42** 

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_4|Plasma\ (Peripheral\ VenousBlood)$ 

Deviation: 1.01E-4



 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_3|Plasma\ (Peripheral\ VenousBlood)$ 

Figure 1.43

Deviation: 1.61E-4

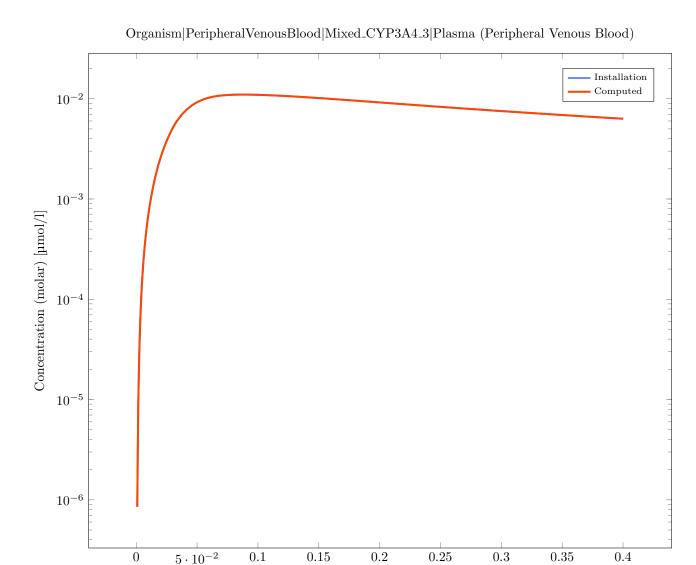


Figure 1.44

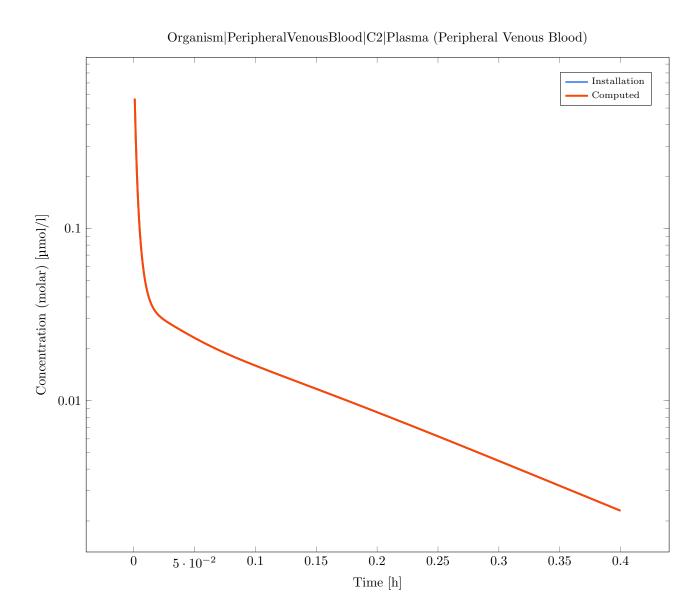
Time [h]

 $Simulation: \begin{tabular}{ll} DDI\_Multiple Combinations - 11\_MM\_Mechanism based\_Mechanism based\_Induction\_Induction \end{tabular}$ 

Result of the validation: Valid

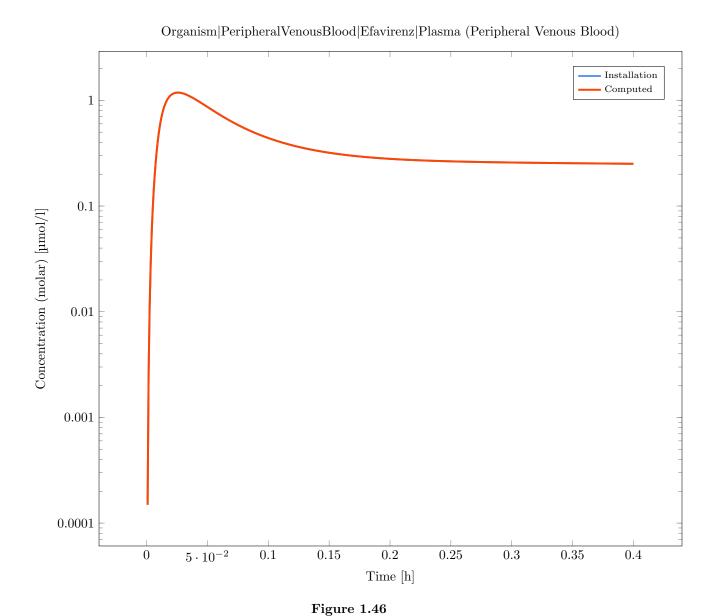
 $Output\ Path:\ Organism|Peripheral Venous Blood|C2|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 5.05E-4



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

Figure 1.45



 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 5.98E-4

# Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma (Peripheral Venous Blood)

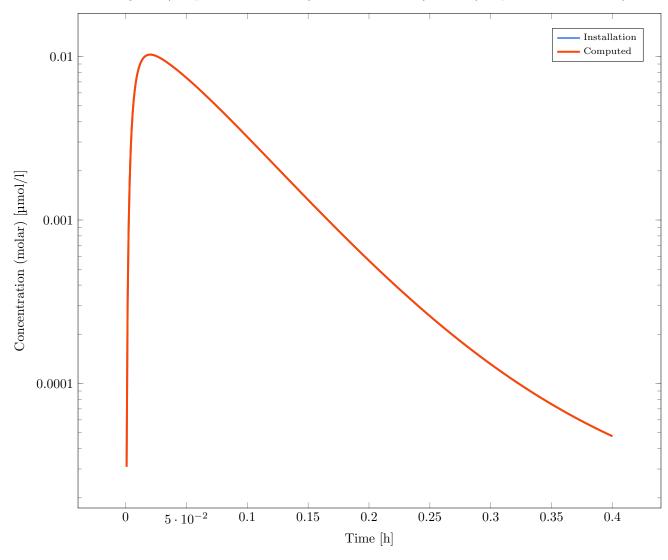
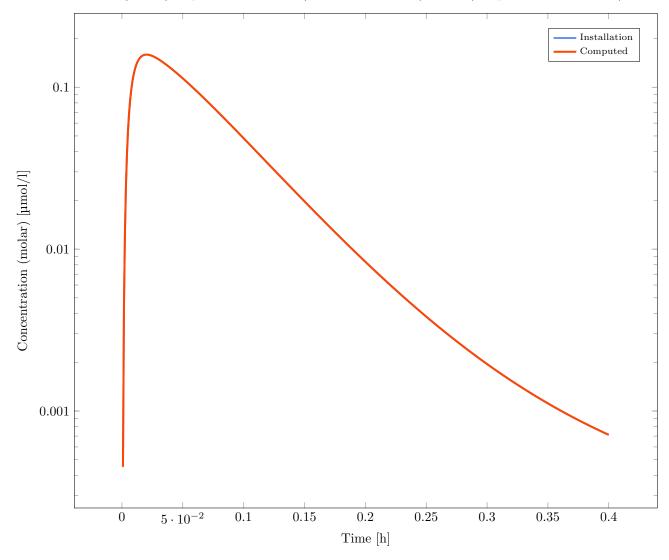


Figure 1.47

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_4|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 6.00E-4

# Organism|PeripheralVenousBlood|MechanismBased\_4|Plasma (Peripheral Venous Blood)



**Figure 1.48** 

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

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

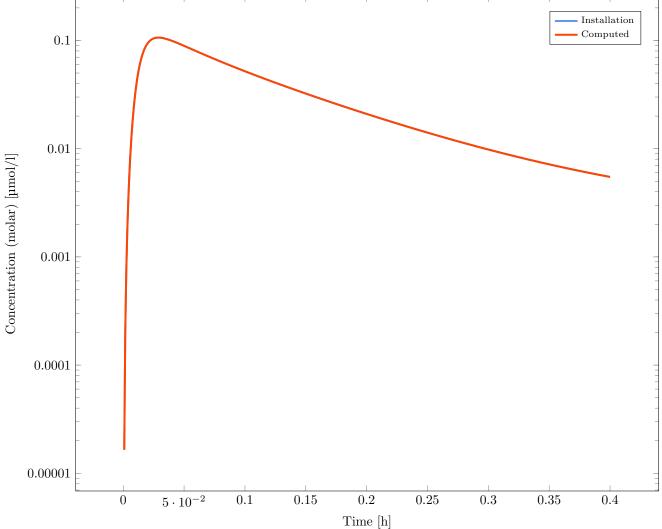


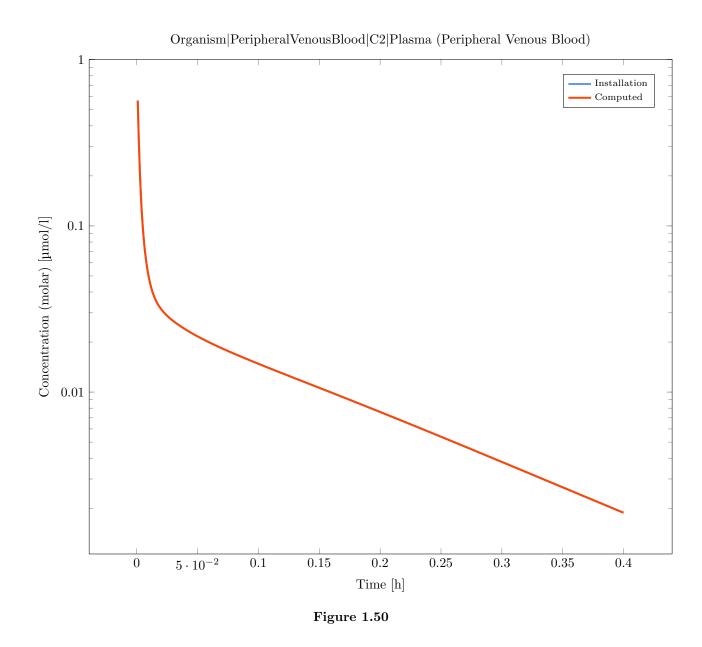
Figure 1.49

 $Simulation: \ DDI\_MultipleCombinations-12\_MM\_All\_DDI\_Types$ 

Result of the validation: Valid

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

Deviation: 5.68E-4



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

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

Figure 1.51

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

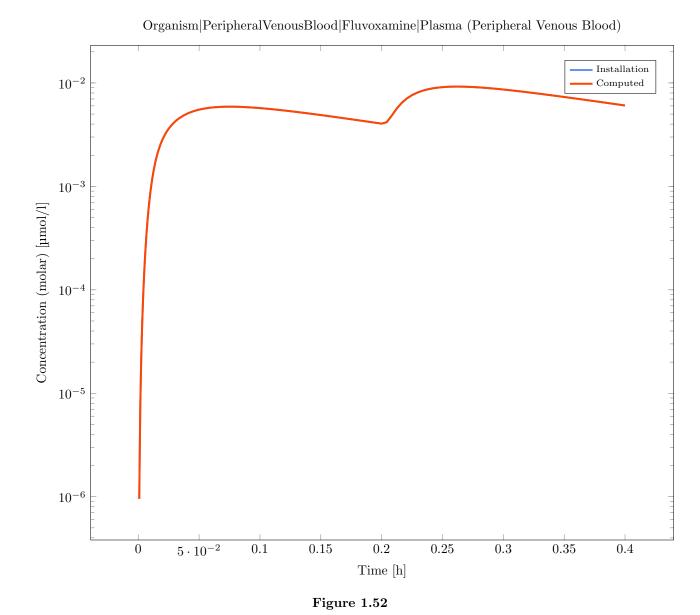
0.1

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

1

0

 $5 \cdot 10^{-2}$ 



 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 4.79E-4



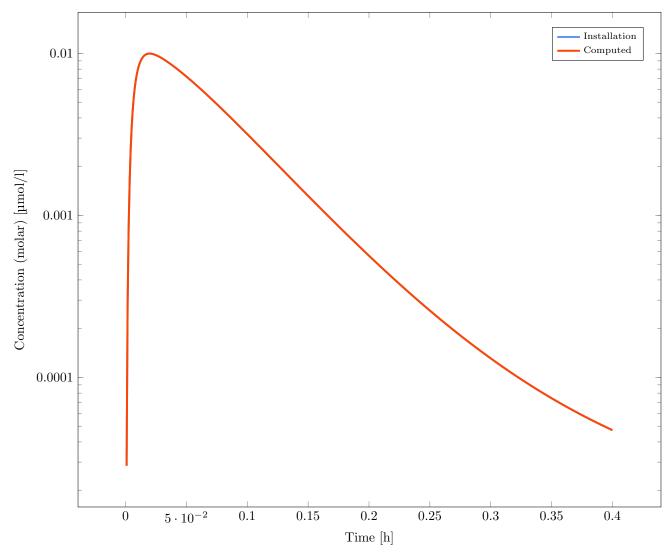


Figure 1.53

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_3|Plasma\ (Peripheral\ VenousBlood)$ 

Deviation: 4.20E-4

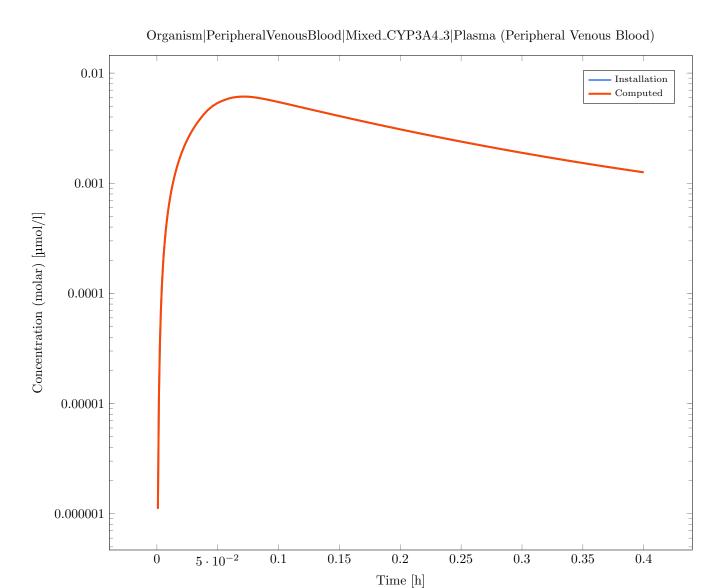
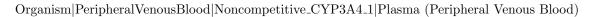


Figure 1.54

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_1|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 5.23E-4



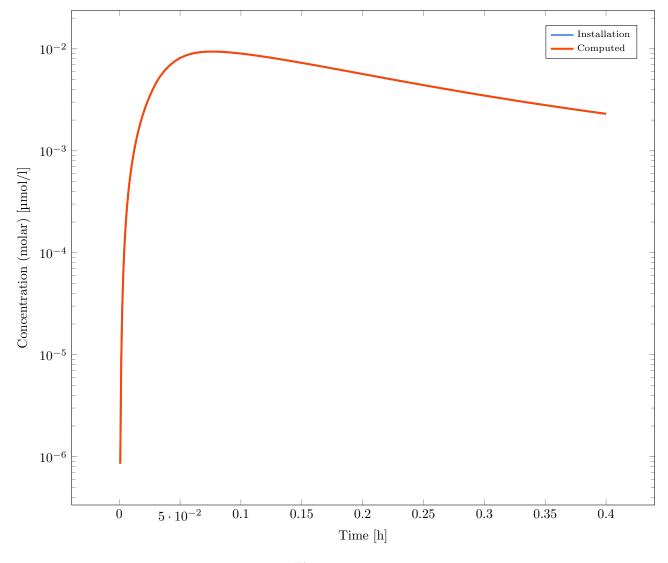


Figure 1.55

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive\_CYP3A4\_3|Plasma\ (PeripheralVenous\ Blood)$ 

Deviation: 5.07E-4

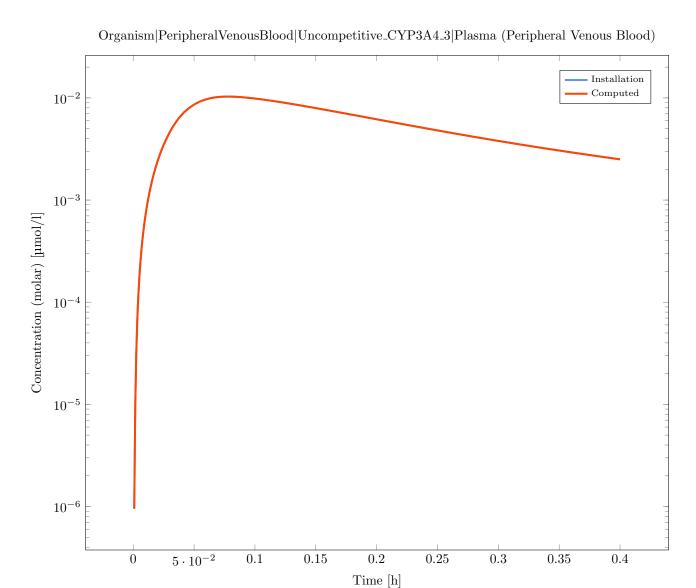
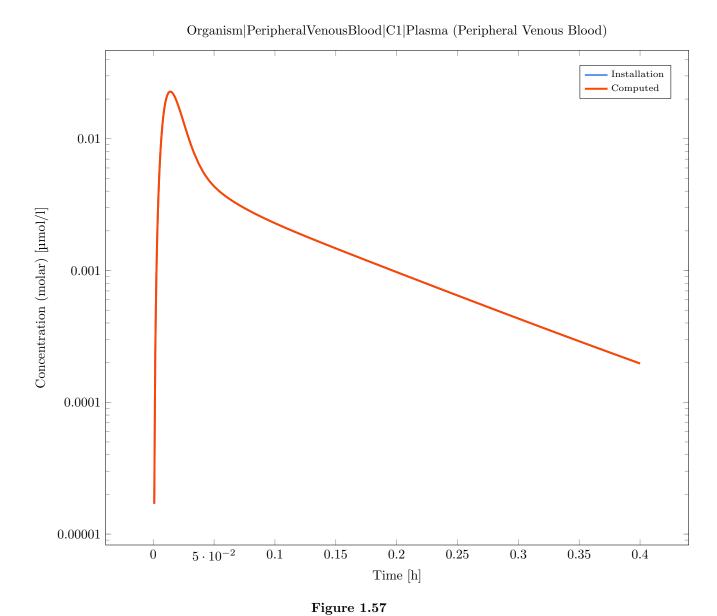


Figure 1.56

 ${\bf Simulation:\ DDI\_Multiple Combinations-21\_1st\_Competitive\_Competitive\_Result\ of\ the\ validation:\ Valid}$ 

Output Path: Organism |Peripheral Venous<br/>Blood |C1 |Plasma (Peripheral Venous Blood)<br/> Deviation: 2.97E-4



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

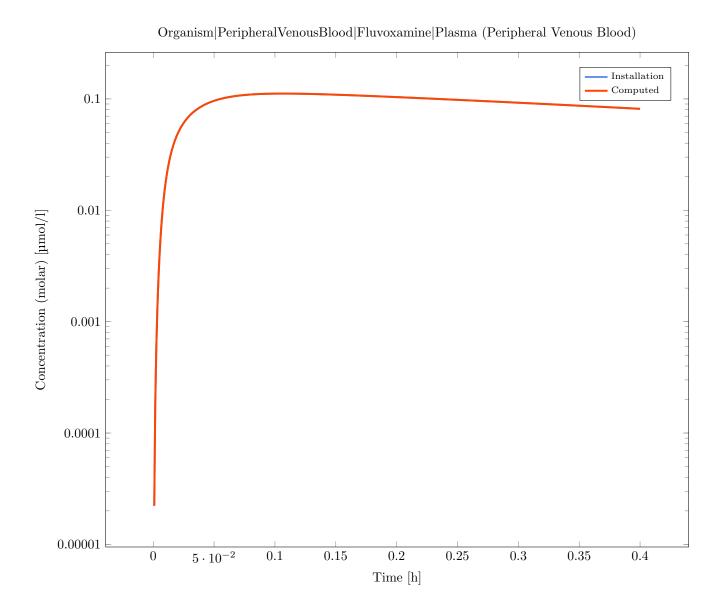


Figure 1.58

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

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

Figure 1.59

Time [h]

Simulation: DDI\_MultipleCombinations-23\_1st\_Noncompetitive\_Noncompetitive Result of the validation: Valid

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_1|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.68É-4

Organism|PeripheralVenousBlood|Noncompetitive\_CYP3A4\_1|Plasma (Peripheral Venous Blood)

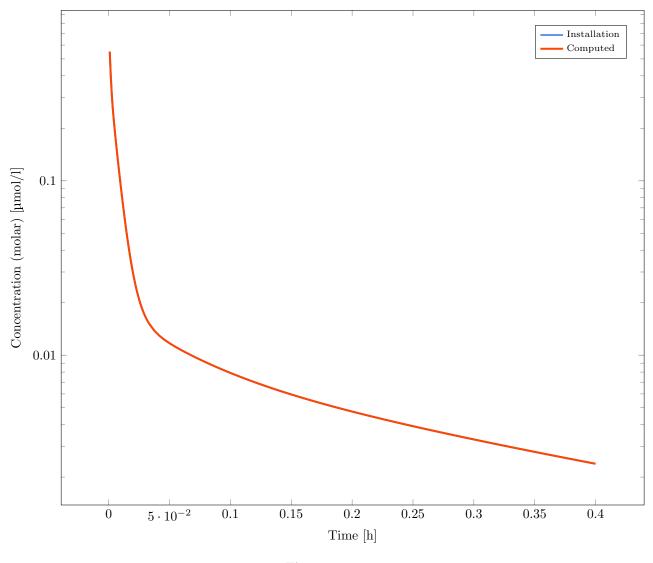


Figure 1.60

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_2|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.32E-4

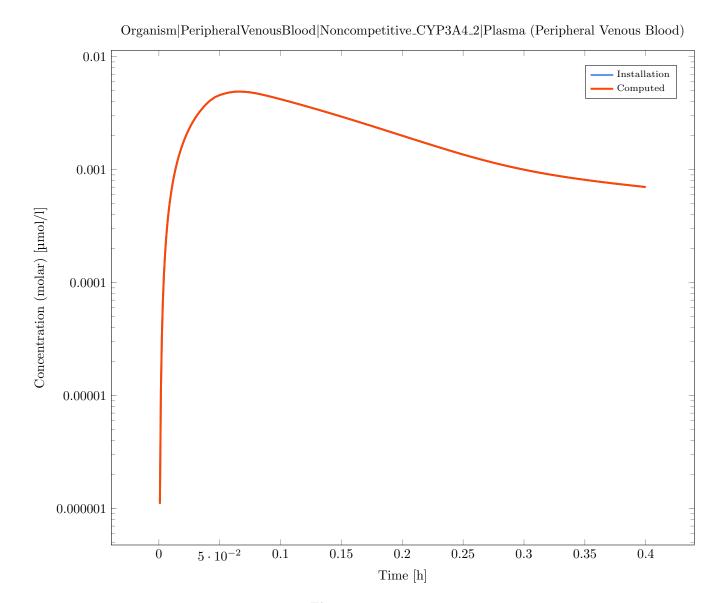
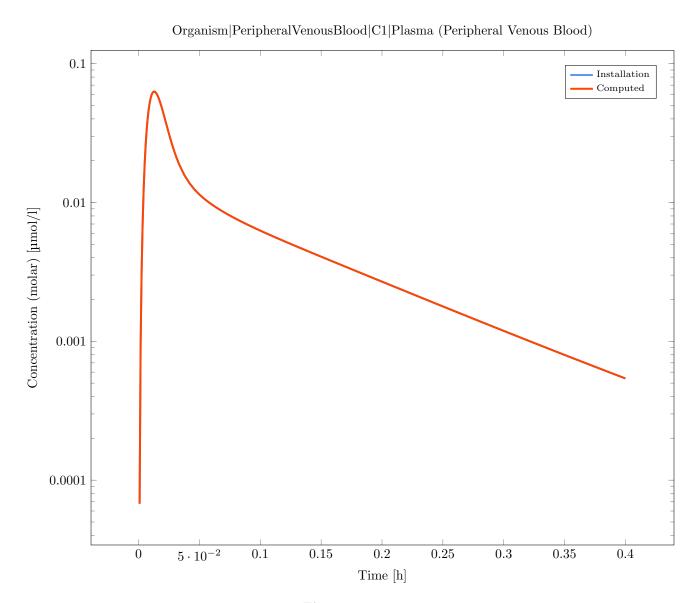


Figure 1.61

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

Deviation: 2.67E-4



**Figure 1.62** 

 $Simulation: \ DDI\_MultipleCombinations-24\_1st\_Mixed\_Mixed$ 

Result of the validation: Valid

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_1|Plasma\ (Peripheral\ VenousBlood)$ 

Deviation: 3.11E-4

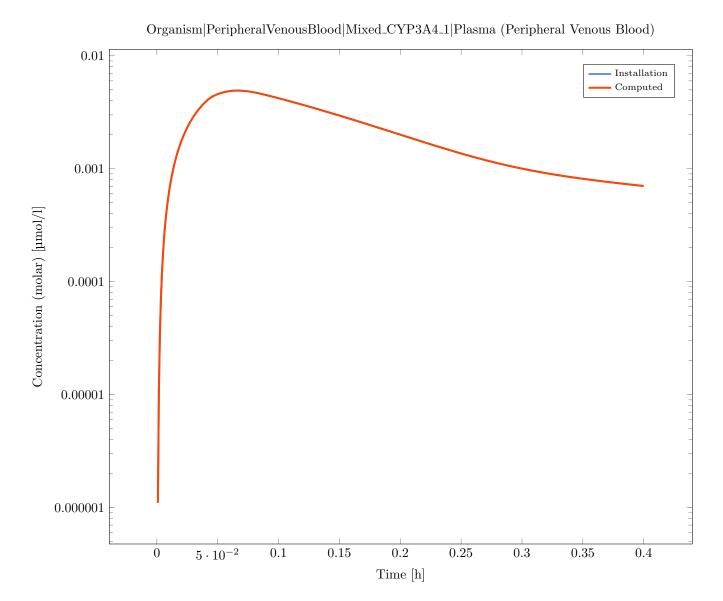
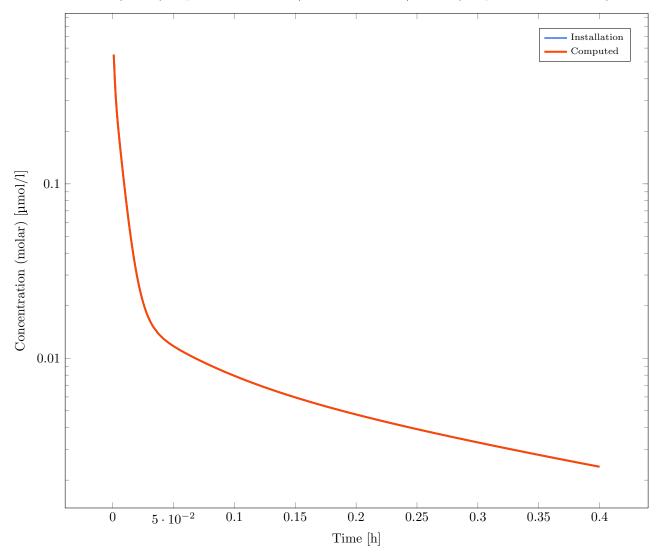


Figure 1.63

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_2|Plasma\ (Peripheral\ VenousBlood)$ 

Deviation: 3.68E-4

# Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_2|Plasma (Peripheral Venous Blood)



**Figure 1.64** 

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

Deviation: 2.84E-4

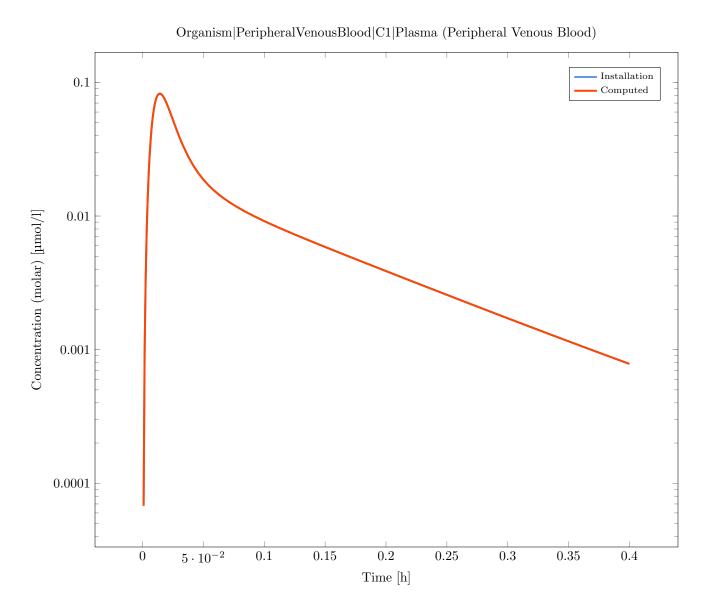
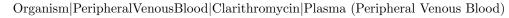


Figure 1.65

 ${\bf Simulation:\ DDI\_Multiple Combinations\hbox{--}25\_1st\_Mechanismbased\_Mechanismbased}. Result of the validation:\ Valid$ 

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



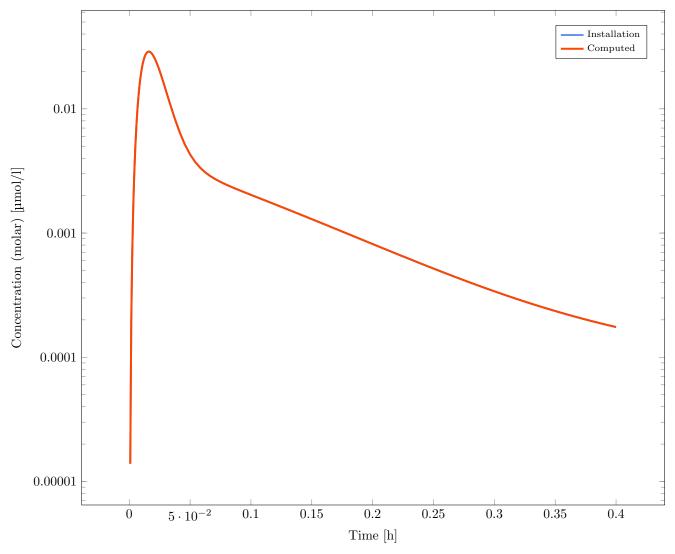


Figure 1.66

Output Path: Organism |PeripheralVenousBlood | Erythromycin |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.62E-4

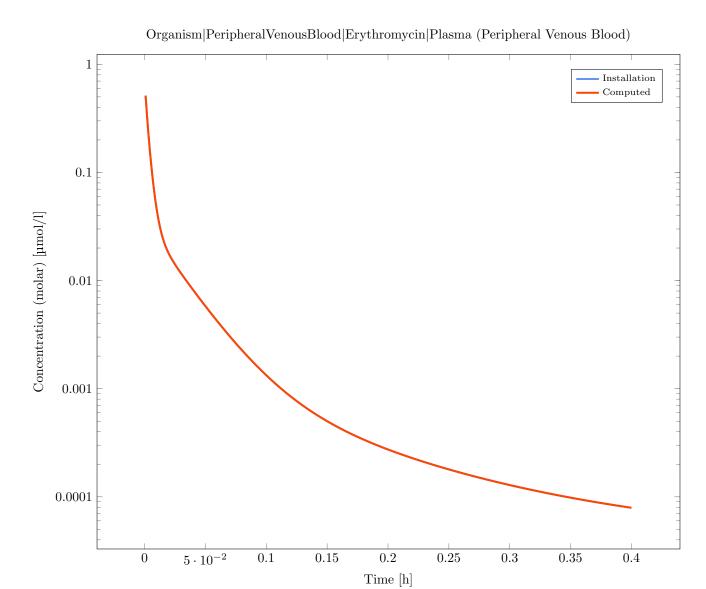


Figure 1.67

Output Path: Organism |PeripheralVenousBlood |C1|Plasma (Peripheral Venous Blood)<br/> Deviation: 2.67E-4

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

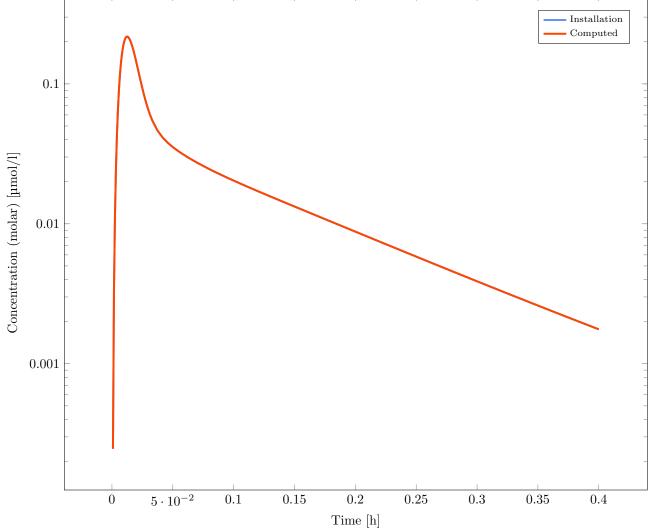


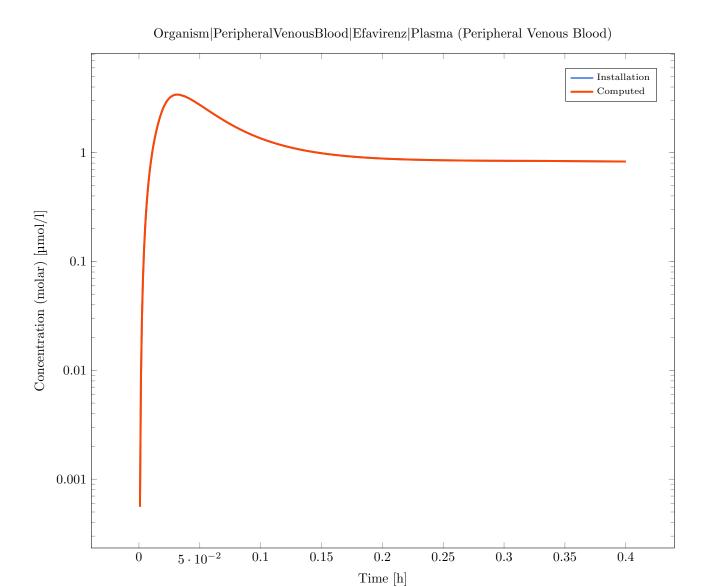
Figure 1.68

Simulation: DDI\_MultipleCombinations-26\_1st\_Induction\_Induction

Result of the validation: Valid

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

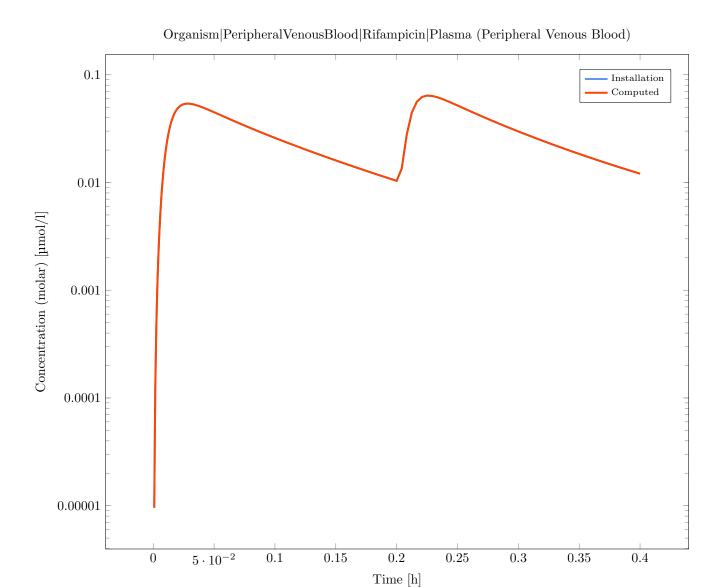
Deviation: 1.75E-4



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

Figure 1.69

Deviation: 3.68E-4



**Figure 1.70** 

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

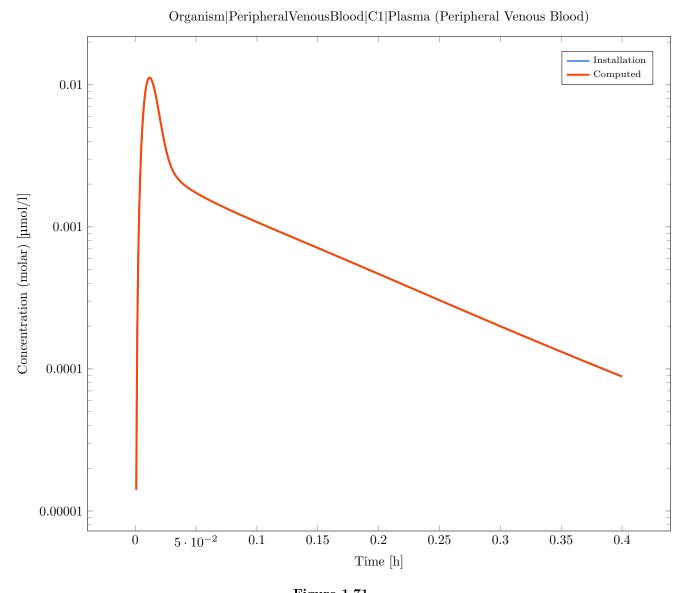
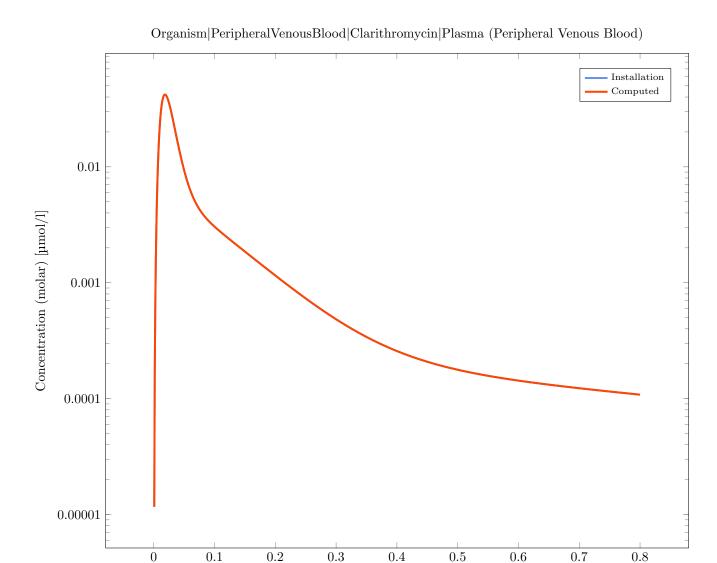


Figure 1.71

Simulation: DDI\_MultipleCombinations-27\_1st\_Competitive\_Competitive\_Mechanismbased\_Mechanismbased Result of the validation: Valid

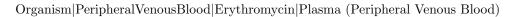
Output Path: Organism |Peripheral Venous<br/>Blood |Clarithromycin |Plasma (Peripheral Venous Blood)<br/> Deviation: 2.11E-4



 $Output\ Path:\ Organism | Peripheral Venous Blood | Erythromycin | Plasma\ (Peripheral Venous\ Blood)$ Deviation: 5.99E-4

Time [h]

**Figure 1.72** 



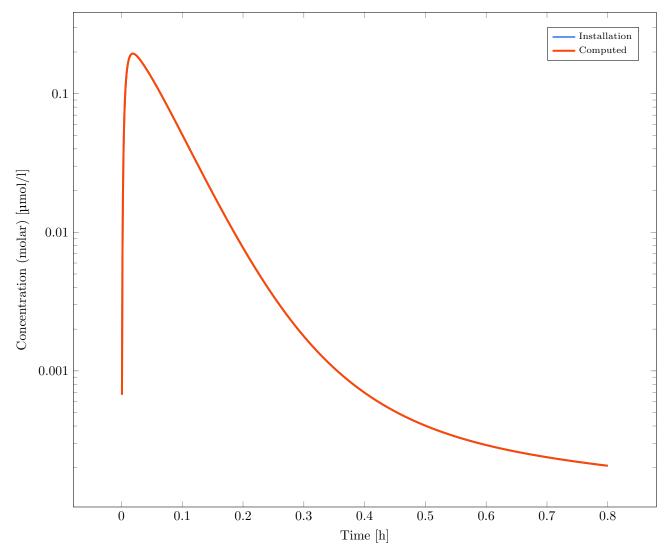


Figure 1.73

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

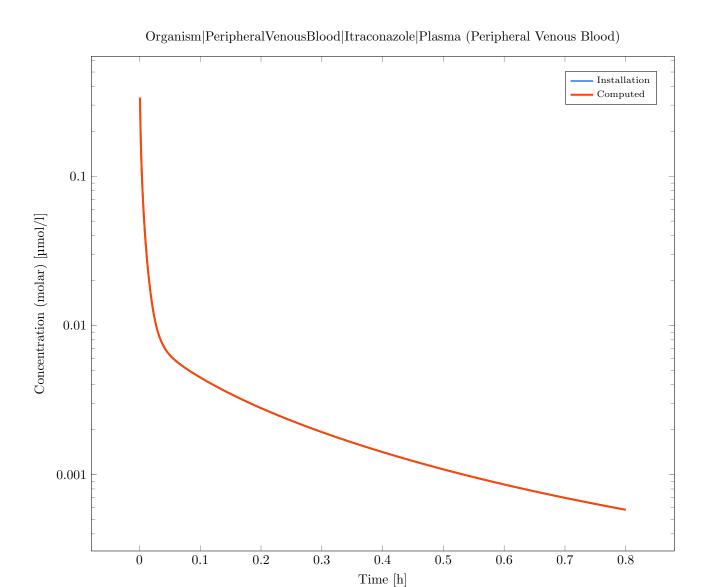
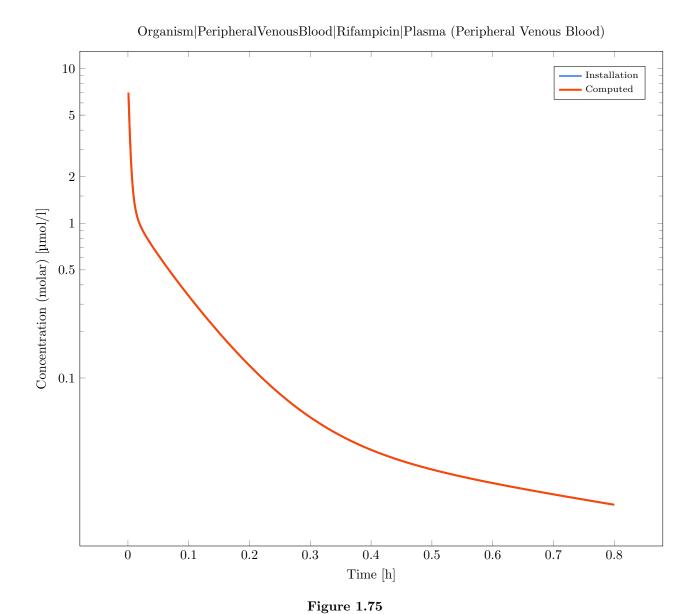


Figure 1.74

Output Path: Organism |Peripheral Venous<br/>Blood |Rifampicin |Plasma (Peripheral Venous Blood)<br/> Deviation:  $4.68 \hbox{E-}4$ 



Output Path: Organism |Peripheral Venous<br/>Blood |C1 |Plasma (Peripheral Venous Blood)<br/> Deviation:  $2.88\hbox{E-}4$ 

# Organism|PeripheralVenousBlood|C1|Plasma (Peripheral Venous Blood) O.01 O.001 O.0001 O.0001

Figure 1.76

0.4

Time [h]

0.5

0.6

0.7

0.8

0.3

 $Simulation: \ DDI\_Multiple Combinations - 28\_1 st\_Uncompetitive\_Uncompetitive\_Mechanism based\_Mechanism based$ 

Result of the validation: Valid

0

0.1

0.2

 $Output\ Path:\ Organism|Peripheral Venous Blood|MechanismBased\_4|Plasma\ (Peripheral\ Venous Blood)$ 

Deviation: 5.99E-4

0.00001

## Organism|PeripheralVenousBlood|MechanismBased\_4|Plasma (Peripheral Venous Blood)

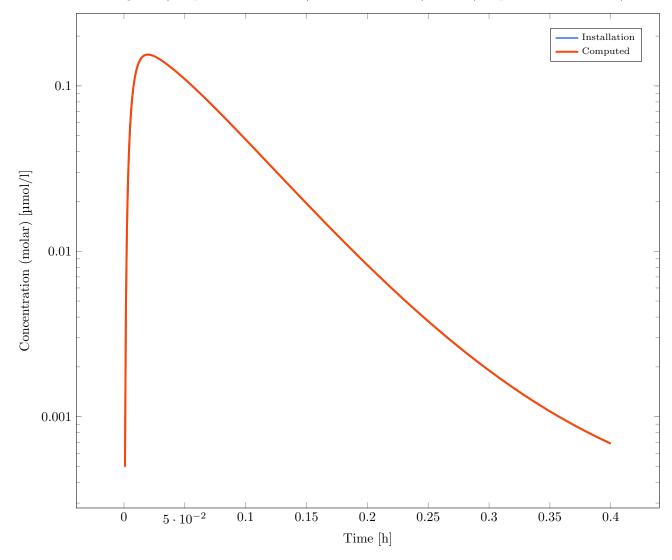
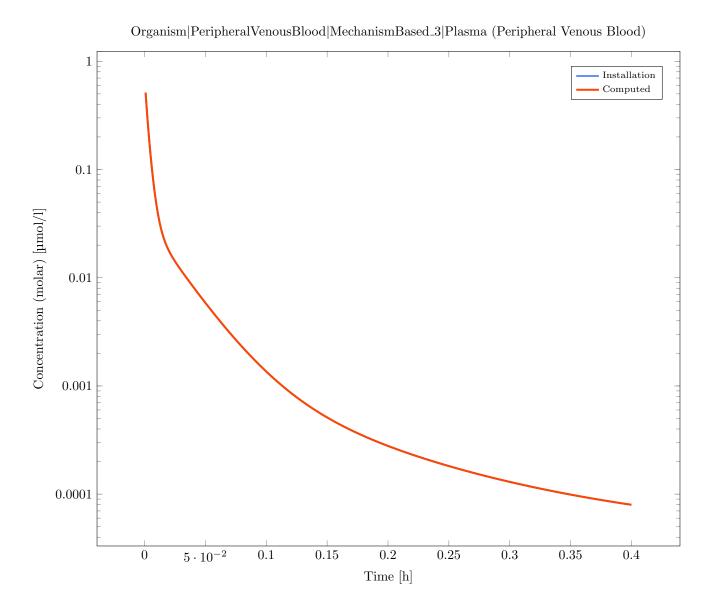


Figure 1.77

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma\ (Peripheral\ Venous\ Blood)$ 

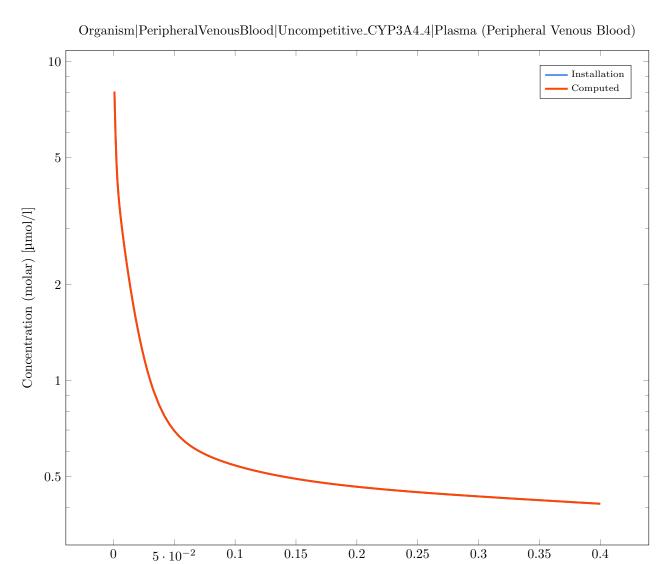
Deviation: 3.67E-4



**Figure 1.78** 

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive\_CYP3A4\_4|Plasma\ (PeripheralVenous\ Blood)$   $Venous\ Blood)$ 

Deviation: 5.72E-5

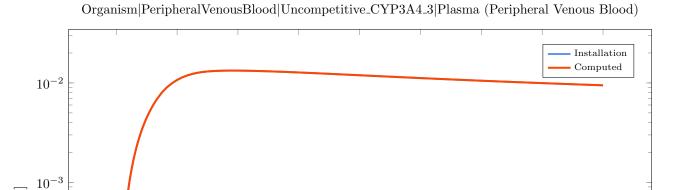


Time [h]

**Figure 1.79** 

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive\_CYP3A4\_3|Plasma\ (PeripheralVenous\ Blood)$ 

Deviation: 1.14E-4



10<sup>-6</sup>
10<sup>-6</sup>
0 5 · 10<sup>-2</sup> 0.1 0.15 0.2 0.25 0.3 0.35 0.4

Time [h]

Figure 1.80

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

Deviation: 5.07E-4

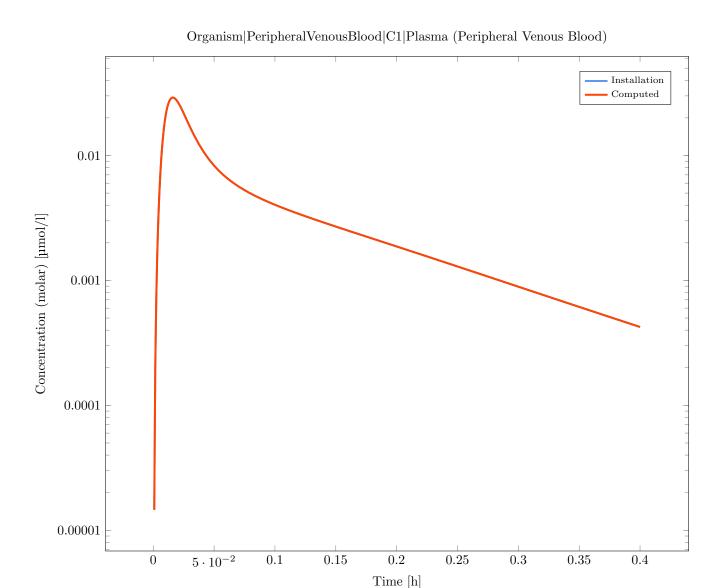


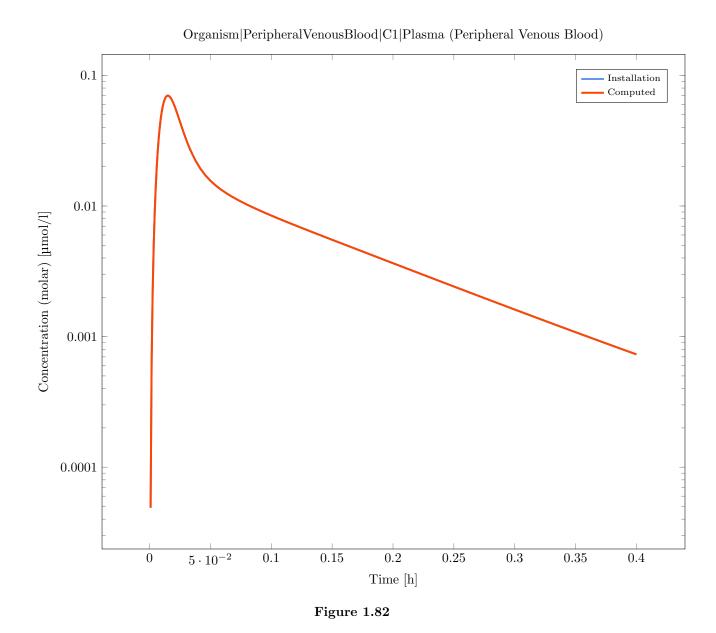
Figure 1.81

 $Simulation: \ DDI\_Multiple Combinations \textbf{-} 29\_1st\_Noncompetitive\_Noncompetitive\_Mechanism based\_Mechanism based$ 

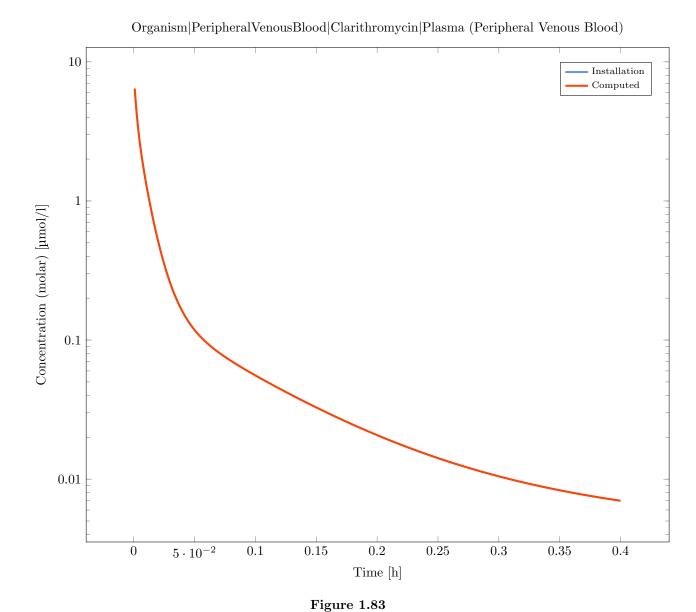
Result of the validation: Valid

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

Deviation: 2.87E-4



Output Path: Organism |Peripheral Venous<br/>Blood |Clarithromycin |Plasma (Peripheral Venous Blood)<br/> Deviation: 2.47E-4



Output Path: Organism |PeripheralVenousBlood | Erythromycin |Plasma (Peripheral Venous Blood)<br/> Deviation: 5.66E-4

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

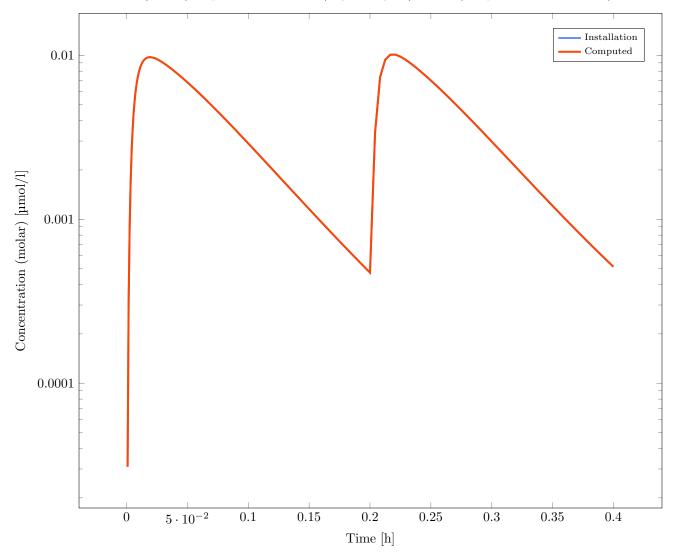
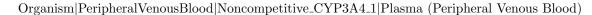


Figure 1.84

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_1|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.19E-4



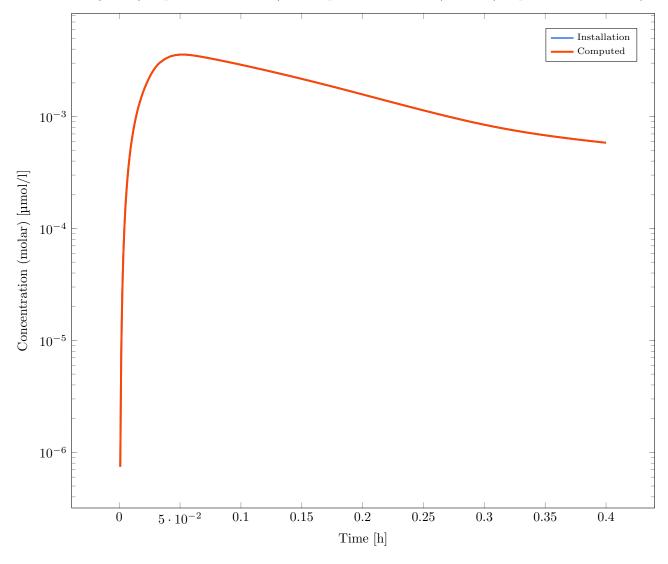


Figure 1.85

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_2|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 3.27E-4

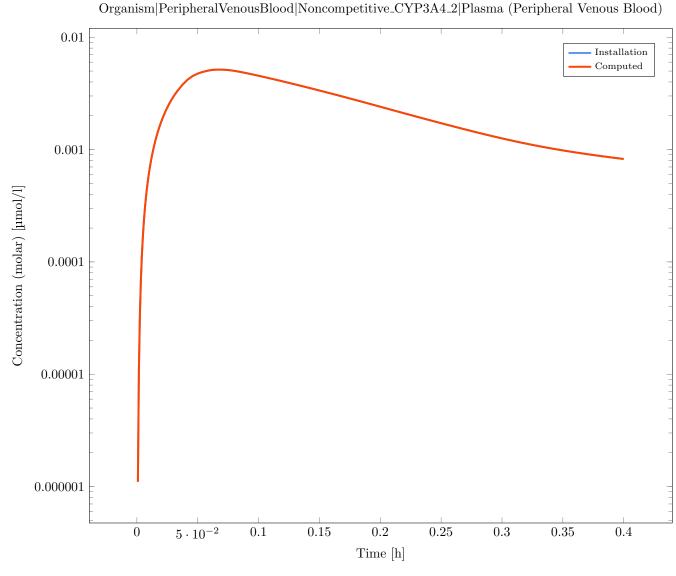


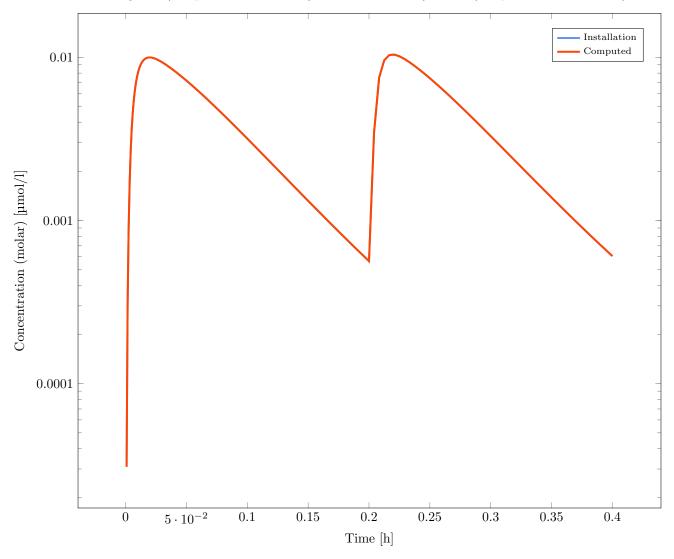
Figure 1.86

 ${\bf Simulation:\ DDI\_Multiple Combinations\text{--}30\_1st\_Mixed\_Mechanismbased\_Mechanismbased\_Mechanismbased\_Nesult\ of\ the\ validation:\ Valid$ 

 $Output\ Path:\ Organism|Peripheral Venous Blood|MechanismBased\_4|Plasma\ (Peripheral\ Venous Blood)$ 

Deviation: 5.63E-4





**Figure 1.87** 

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 5.34E-4

# $Organism | Peripheral Venous Blood | Mechanism Based\_3 | Plasma \ (Peripheral Venous Blood)$

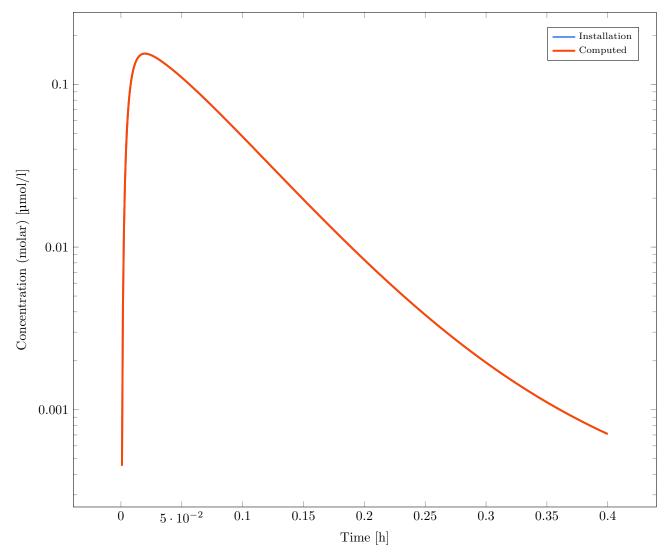
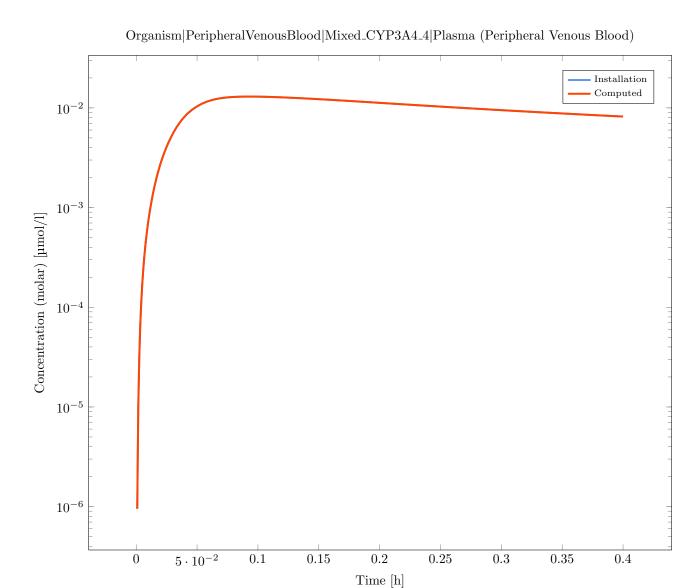


Figure 1.88

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_4|Plasma\ (Peripheral\ VenousBlood)$ 

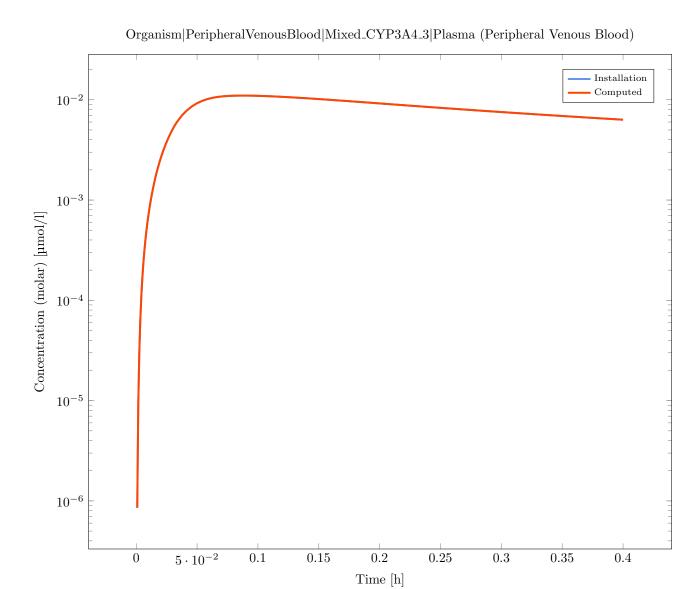
Deviation: 1.10E-4



Output Path: Organism |PeripheralVenousBlood |Mixed\_CYP3A4\_3 |Plasma (Peripheral Venous Blood)

Figure 1.89

Deviation: 1.61E-4



Output Path: Organism |Peripheral Venous<br/>Blood |C1 |Plasma (Peripheral Venous Blood)<br/> Deviation:  $6.75\hbox{E-}4$ 

Figure 1.90

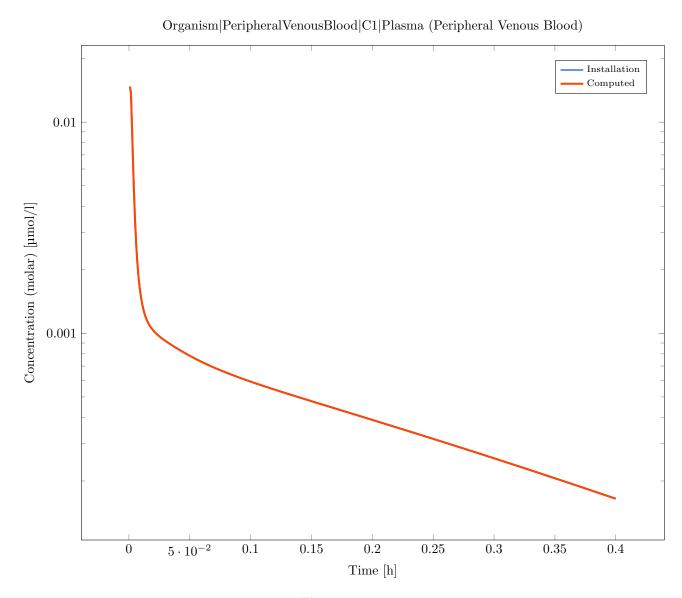
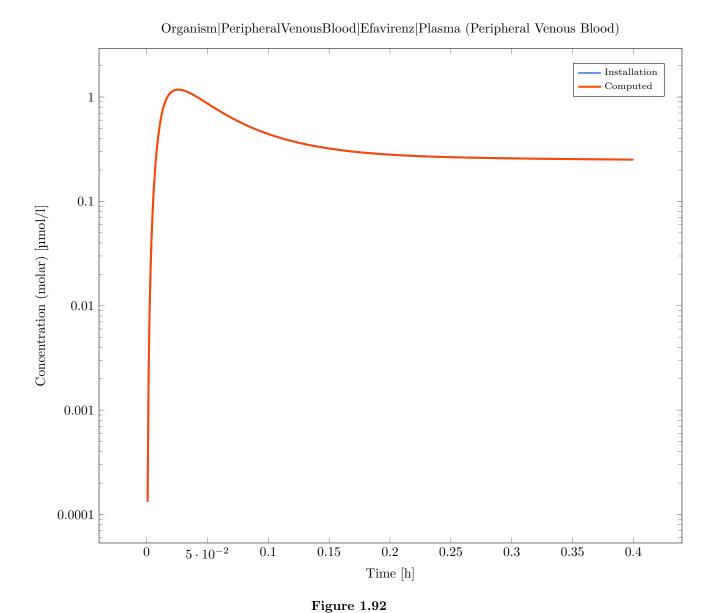


Figure 1.91

 ${\bf Simulation:\ DDI\_Multiple Combinations\hbox{--}31\_1st\_Mechanismbased\_Mechanismbased\_Induction\_Induction} \\ {\bf Result\ of\ the\ validation:\ Valid}$ 

Output Path: Organism |Peripheral Venous<br/>Blood |Efavirenz |Plasma (Peripheral Venous Blood)<br/> Deviation: 1.71E-4



 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 6.12E-4



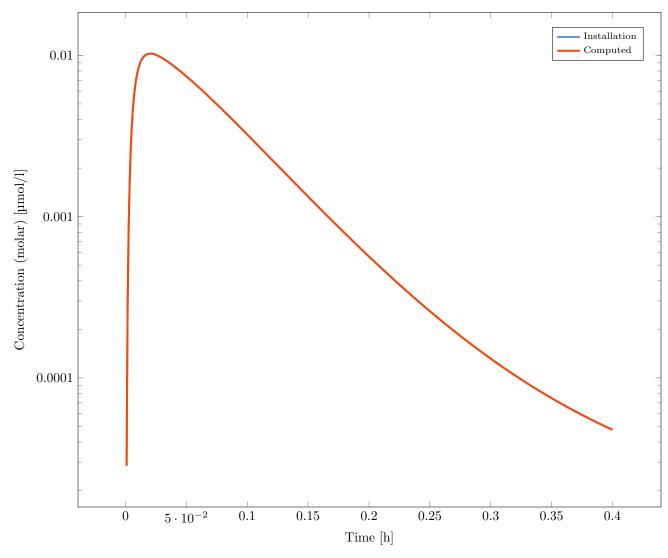
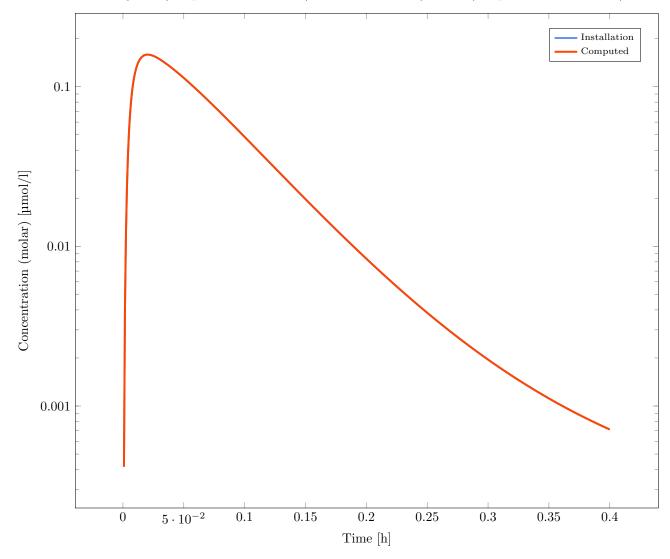


Figure 1.93

 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_4|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 6.14E-4





**Figure 1.94** 

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

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

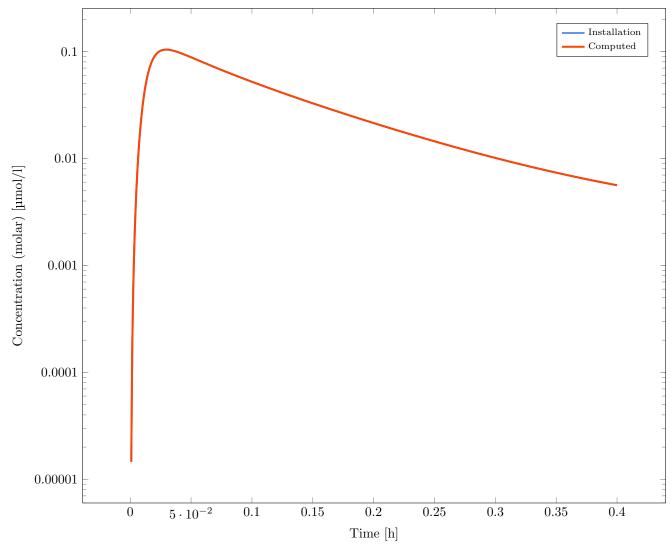


Figure 1.95

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

Deviation: 5.55E-4

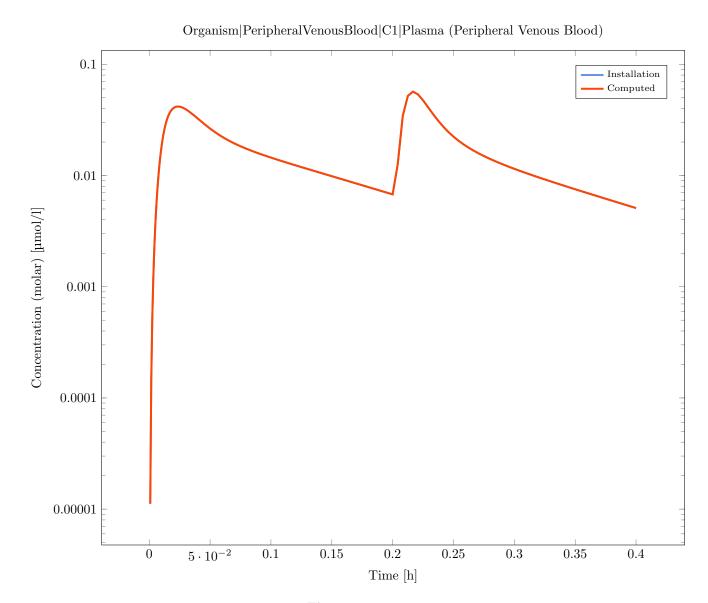


Figure 1.96

 $Simulation: \ DDI\_MultipleCombinations-32\_1st\_All\_DDI\_Types$ 

Result of the validation: Valid

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

Deviation: 1.92E-4

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

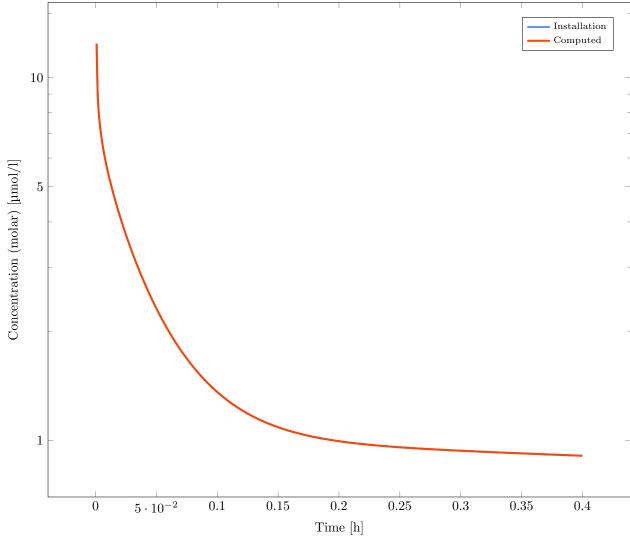
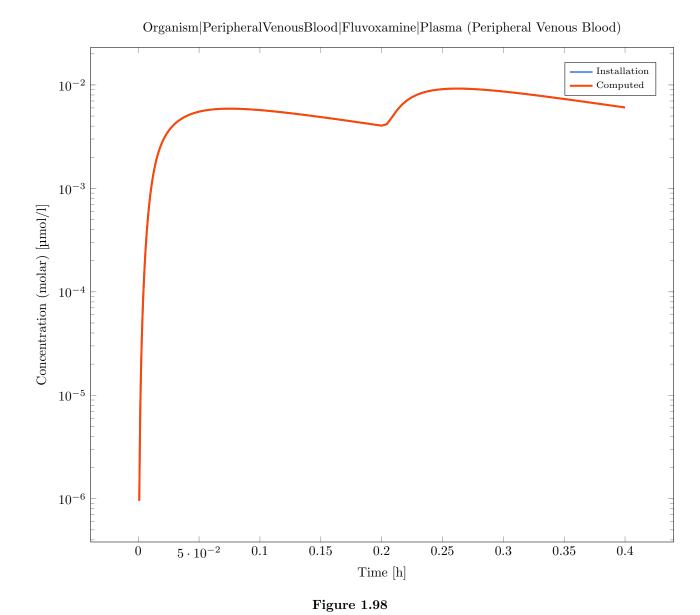


Figure 1.97

Output Path: Organism |Peripheral Venous<br/>Blood |Fluvoxamine |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.13E-4



 $Output\ Path:\ Organism|PeripheralVenousBlood|MechanismBased\_3|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 5.98E-4



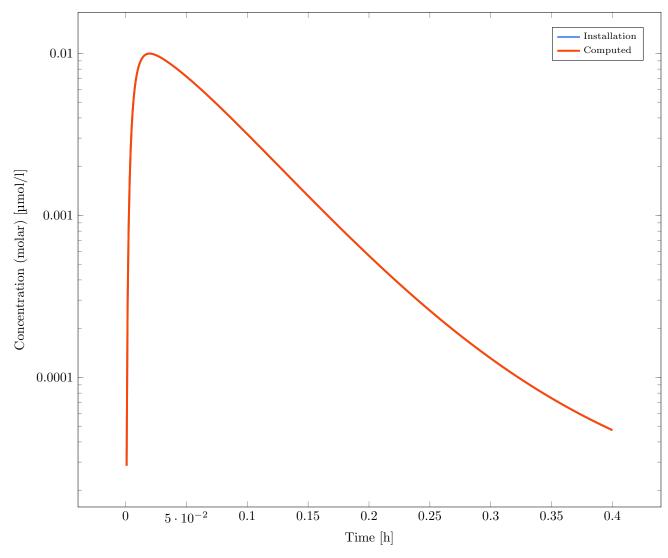


Figure 1.99

 $Output\ Path:\ Organism|PeripheralVenousBlood|Mixed\_CYP3A4\_3|Plasma\ (Peripheral\ VenousBlood)$ 

Deviation: 4.17E-4

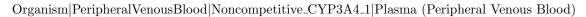
# $Organism | Peripheral Venous Blood | Mixed\_CYP3A4\_3 | Plasma \ (Peripheral Venous Blood)$ 0.01Installation Computed 0.001 Concentration (molar) [µmol/1] 0.00010.000010.0000010 0.1 0.15 0.2 0.25 0.3 0.35 0.4 $5\cdot 10^{-2}$

**Figure 1.100** 

Time [h]

 $Output\ Path:\ Organism|Peripheral Venous Blood|Noncompetitive\_CYP3A4\_1|Plasma\ (Peripheral\ Venous\ Blood)$ 

Deviation: 4.97E-4



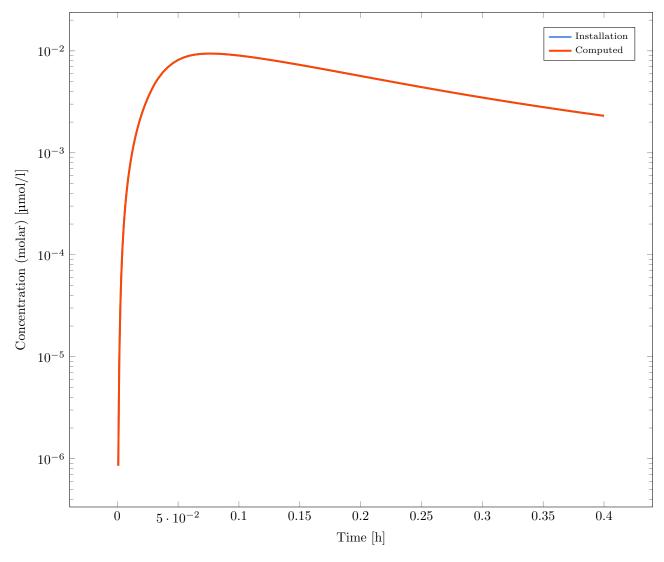
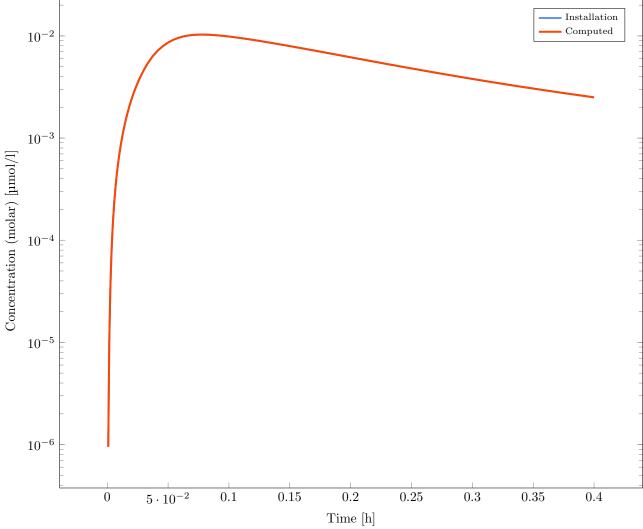


Figure 1.101

 $Output\ Path:\ Organism|PeripheralVenousBlood|Uncompetitive\_CYP3A4\_3|Plasma\ (PeripheralVenous\ Blood)$ 

Deviation: 5.01E-4

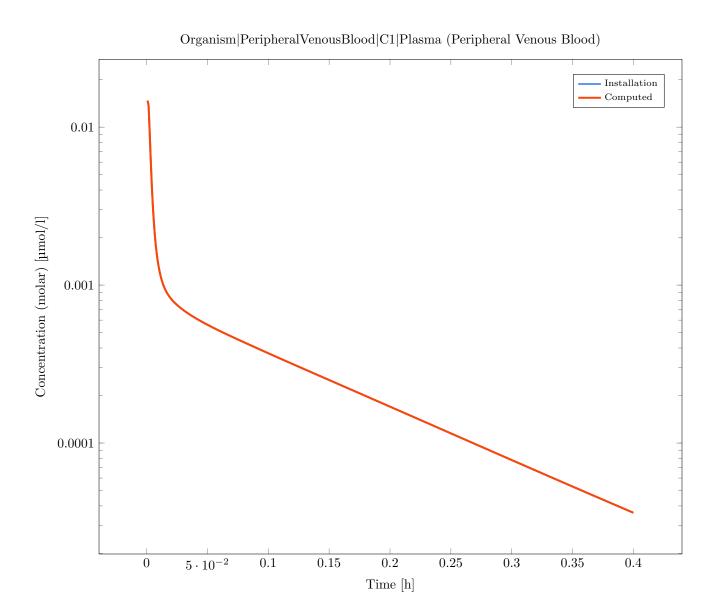




 $Figure \ 1.102$ 

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

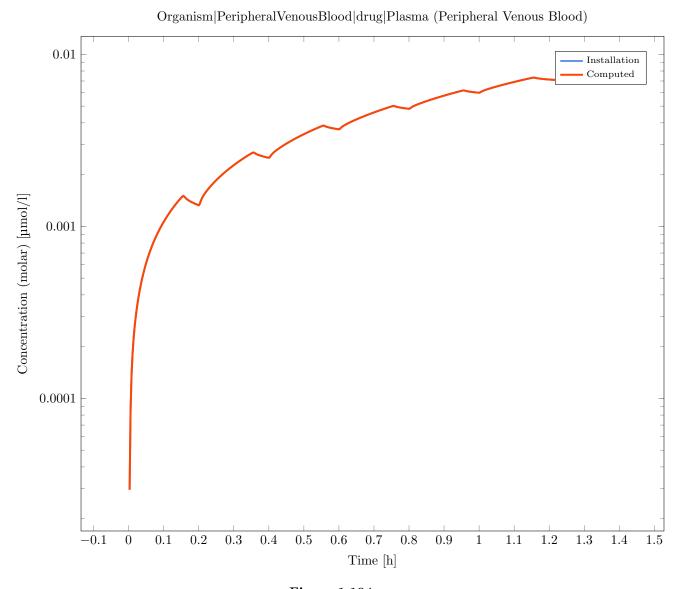
Deviation: 6.86E-4



**Figure 1.103** 

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

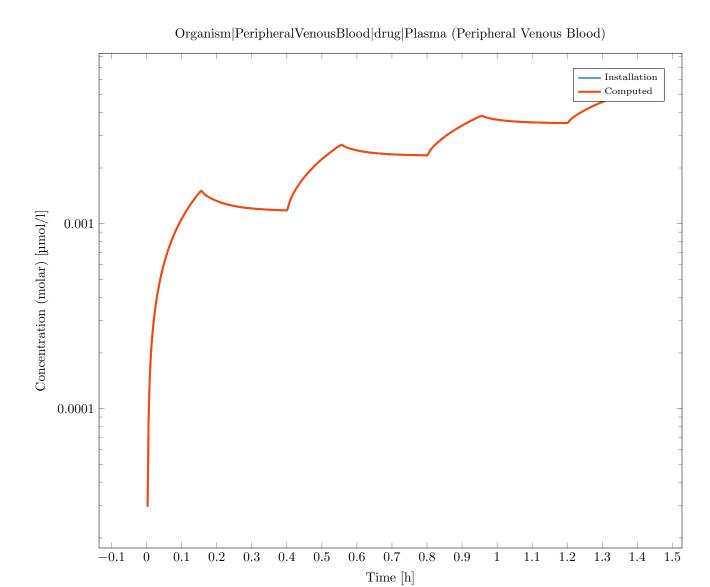
Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood) Deviation:<br/> 0



**Figure 1.104** 

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

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



**Figure 1.105** 

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

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.40E-6

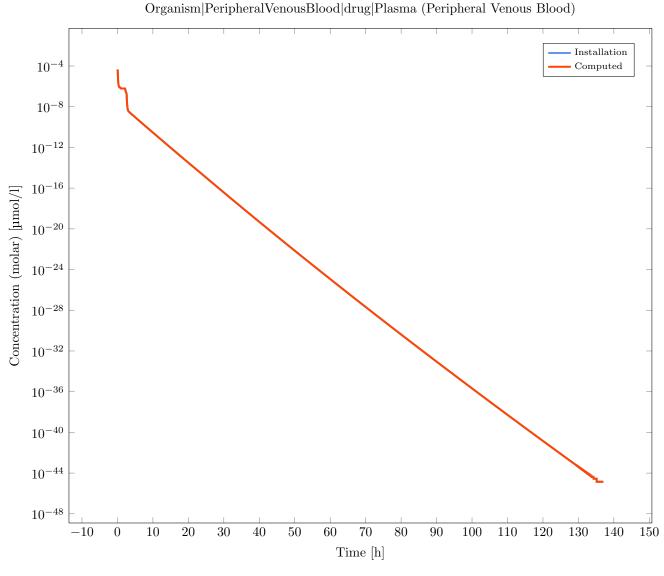


Figure 1.106

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation:  $8.37 \hbox{E-}7$ 

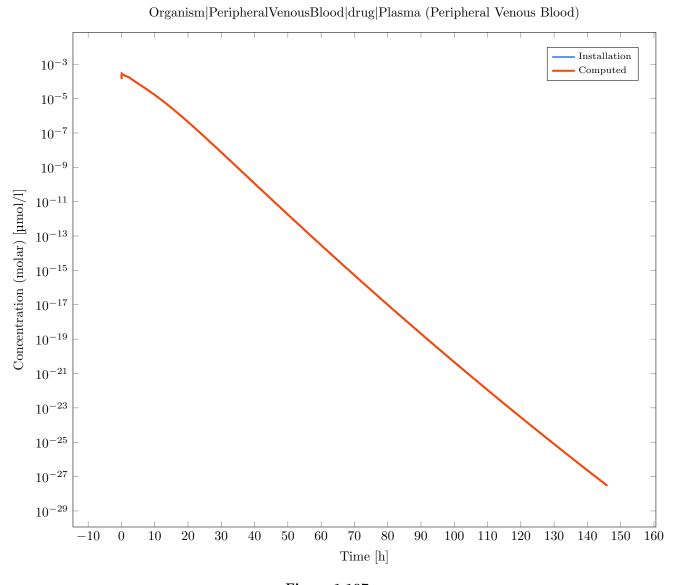
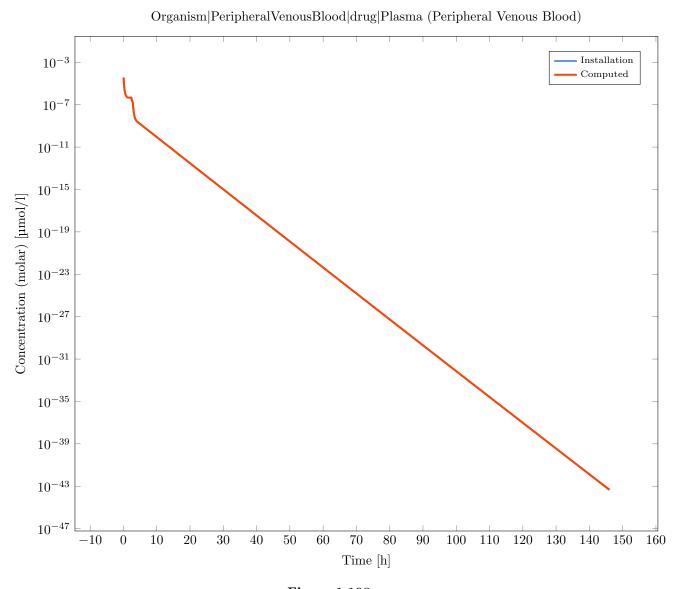


Figure 1.107

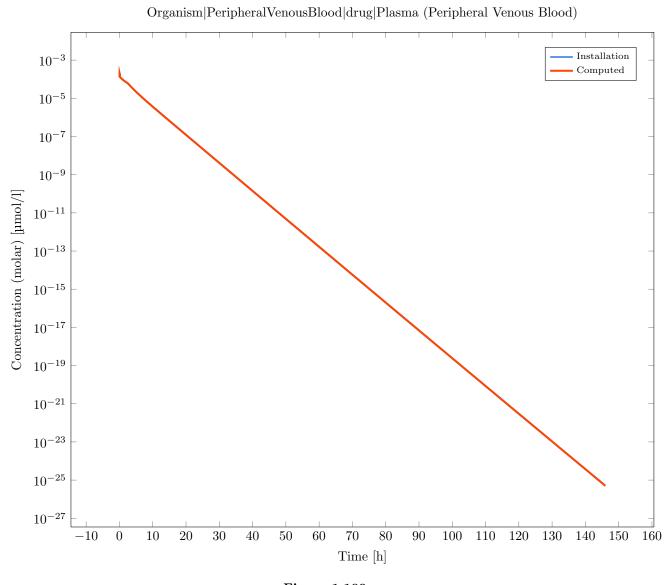
 $\begin{tabular}{ll} \bf Simulation: European\_SingleORAL\_Age\_1\_CYP3A4-European\_SingleORAL\_Age\_1\_CYP3$ 



**Figure 1.108** 

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

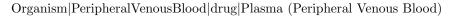
Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 1.19E-7

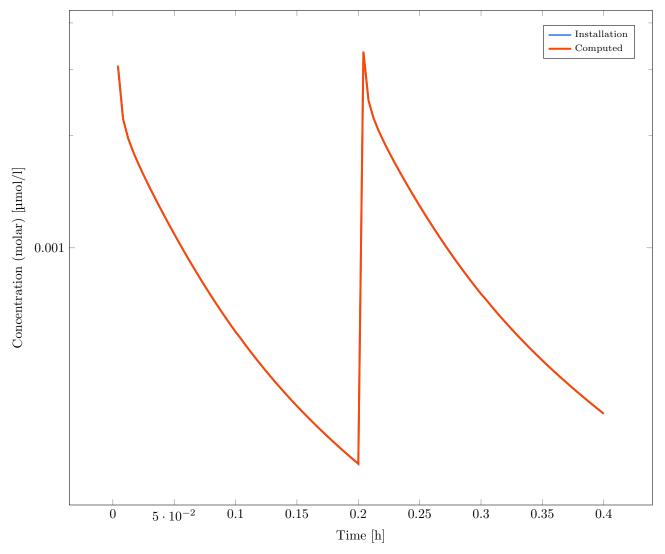


 ${\bf Figure~1.109}$ 

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

Result of the validation: Valid





 ${\bf Figure~1.110}$ 

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 1.111** 

0.2

Time [h]

0.25

0.3

0.35

0.4

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

 $5 \cdot 10^{-2}$ 

Result of the validation: Valid

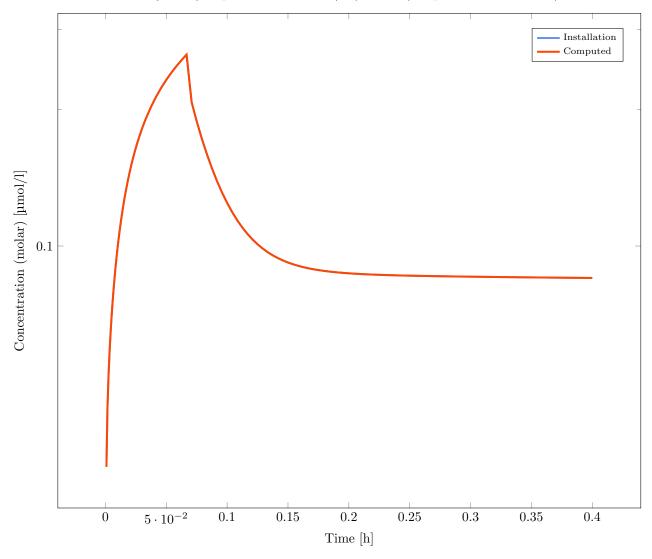
0

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

0.15

0.1





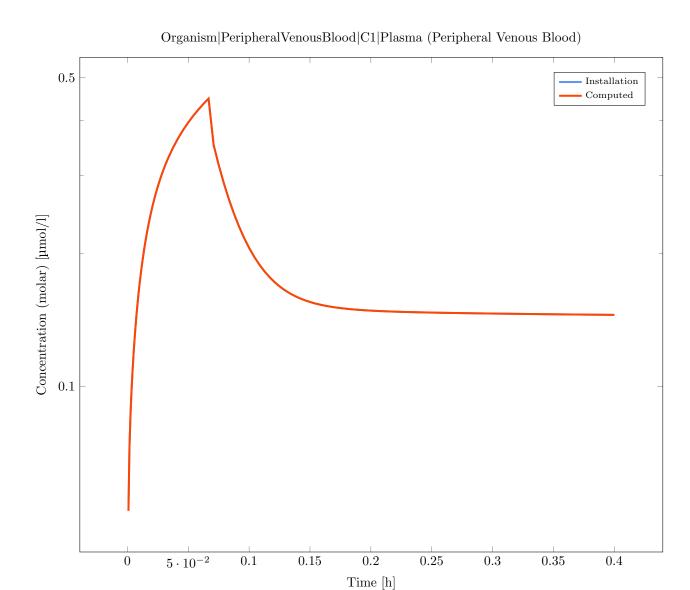
 ${\bf Figure~1.112}$ 

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

Result of the validation: Valid

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

Deviation: 0

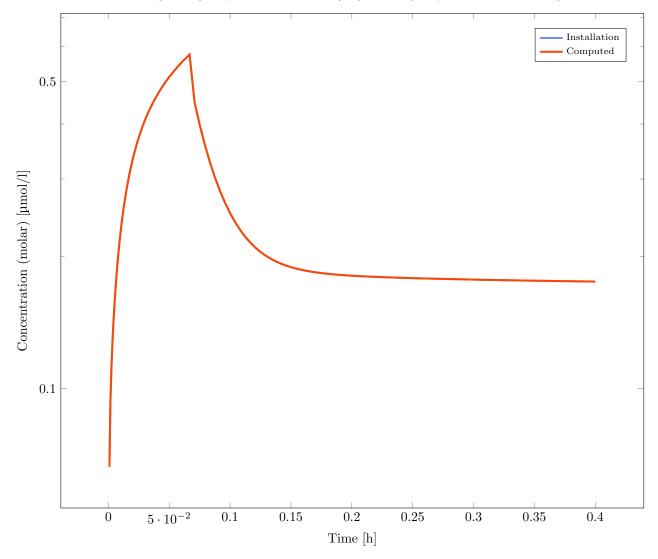


 $Figure \ 1.113$ 

 $Simulation: \ Human\_ICRP\_AGP-03\_ICRP\_0.18y\_Male$ 

Result of the validation: Valid

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



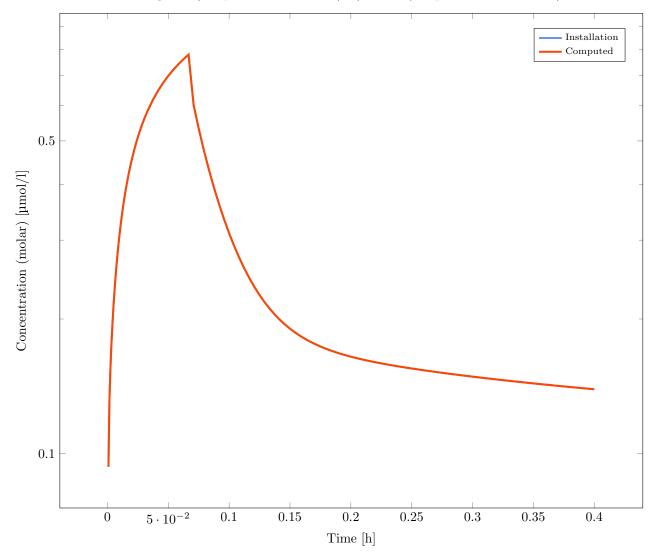
**Figure 1.114** 

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



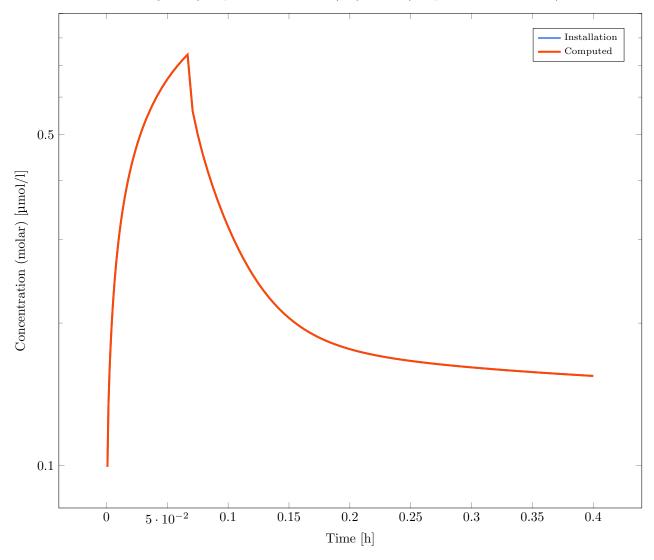
**Figure 1.115** 

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

Result of the validation: Valid

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

Deviation: 1.50E-4



**Figure 1.116** 

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

Result of the validation: Valid

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



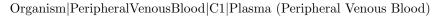
**Figure 1.117** 

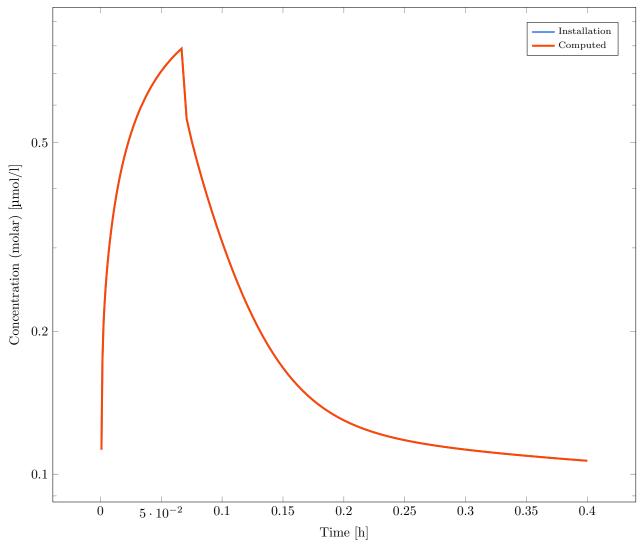
 $Simulation: \ Human\_ICRP\_AGP-07\_ICRP\_100y\_Male$ 

Result of the validation: Valid

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

Deviation: 0





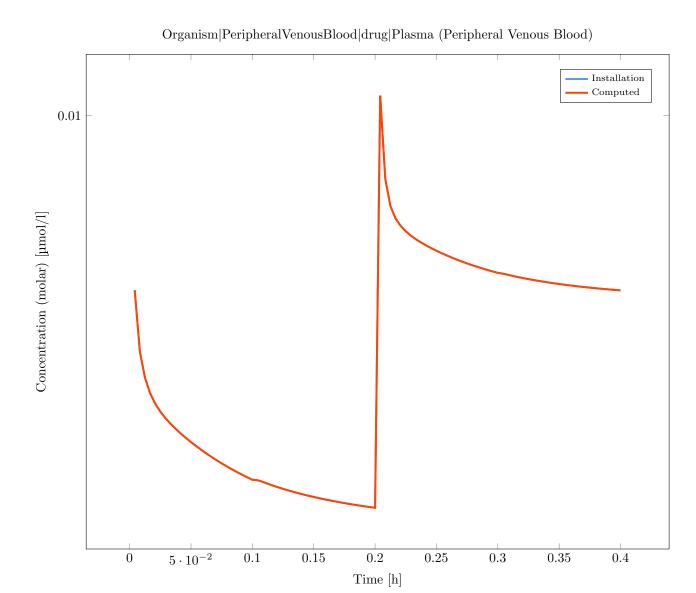
**Figure 1.118** 

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

Result of the validation: Valid

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

Deviation: 0



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

**Figure 1.119** 

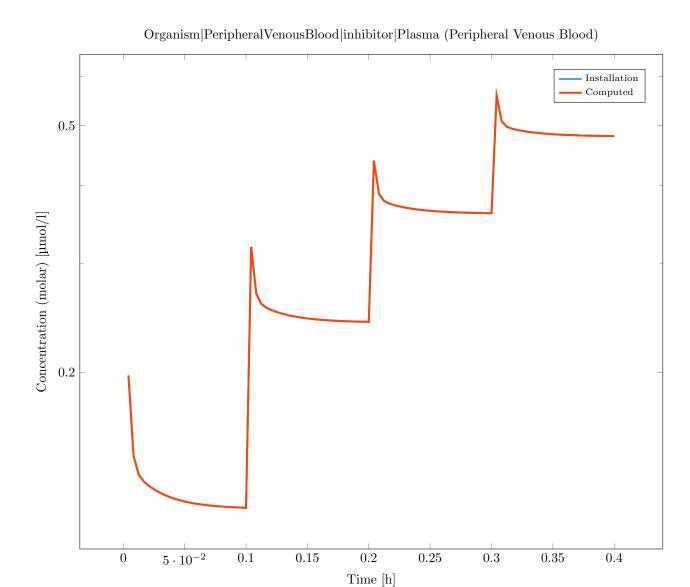
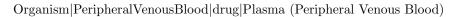
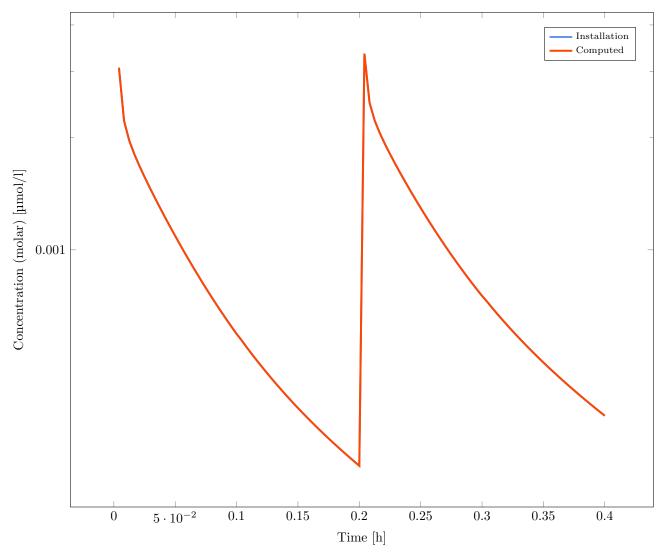


Figure 1.120

 ${\bf Simulation: Human\_MixedInhibition-Human\_MixedInhibition}$ 

Result of the validation: Valid





 $Figure \ 1.121$ 

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

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

Figure 1.122

0.2

Time [h]

0.25

0.3

0.35

0.4

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

0.1

Result of the validation: Valid

0

 $5 \cdot 10^{-2}$ 

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

0.15

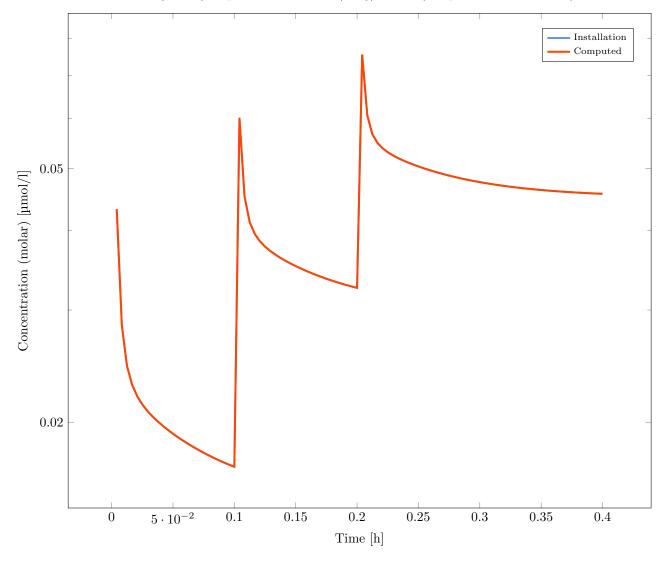


Figure 1.123

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

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation:  $1.05\mbox{E-}7$ 

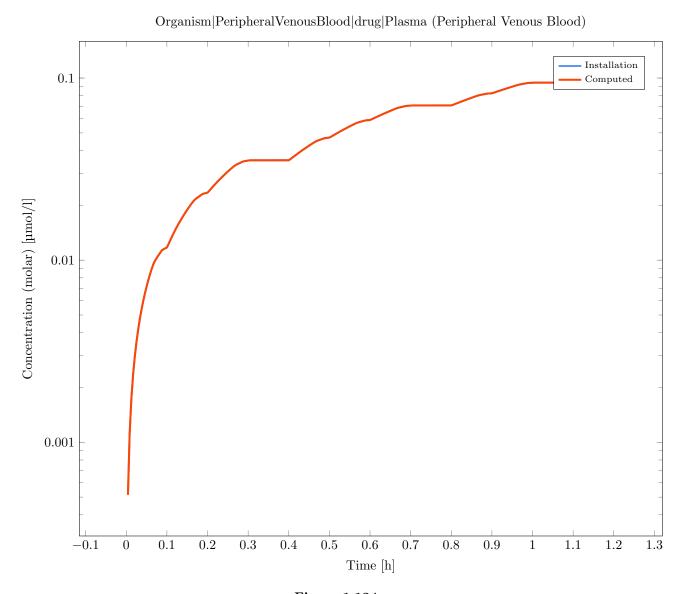


Figure 1.124

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

Result of the validation: Valid

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 6.10E-8



Figure 1.125

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

Result of the validation: Valid

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

Deviation: 1.05E-7

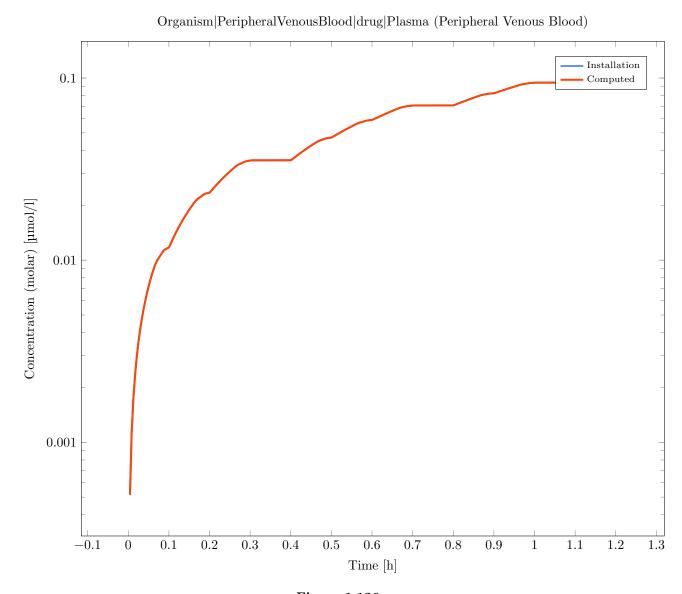


Figure 1.126

 $Simulation: Human\_MultiORAL\_6\_12\_12\_Dissolved-Human\_MultiORAL\_6\_12\_12\_Dissolved\_EHC\_continuous\_fraction\_1$ 

Result of the validation: Valid

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

Deviation: 1.05E-7

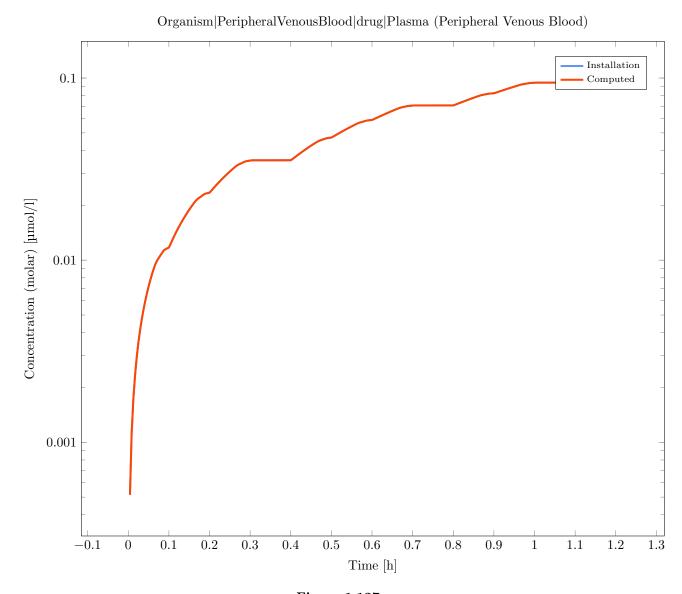


Figure 1.127

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

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation:  $1.05\mbox{E-}7$ 

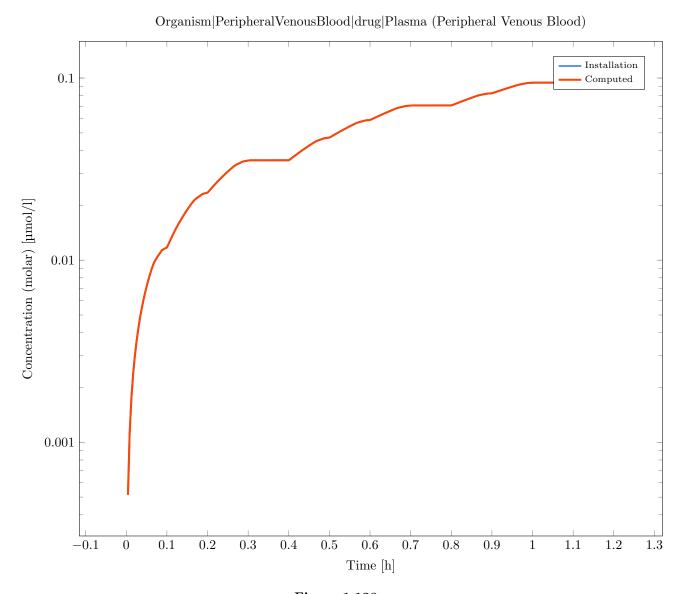


Figure 1.128

 $Simulation: \ Human\_MultipleIV\_Binding-Human\_MultipleIV\_Binding$ 

Result of the validation: Valid

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

Deviation: 0

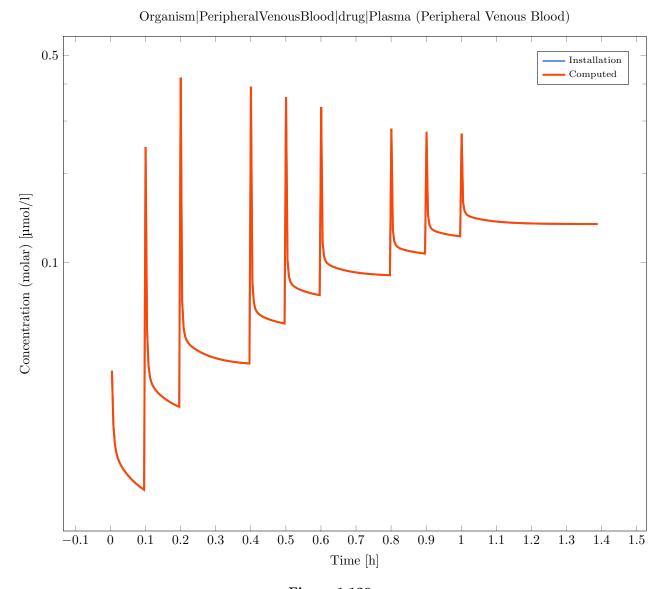
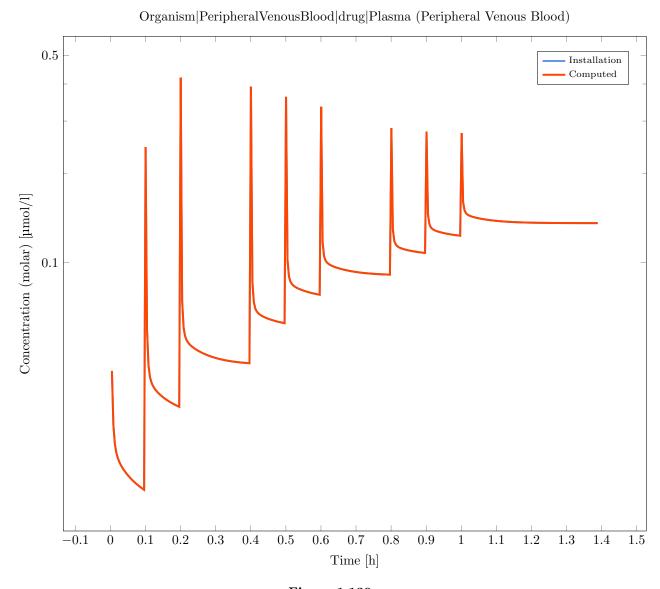


Figure 1.129

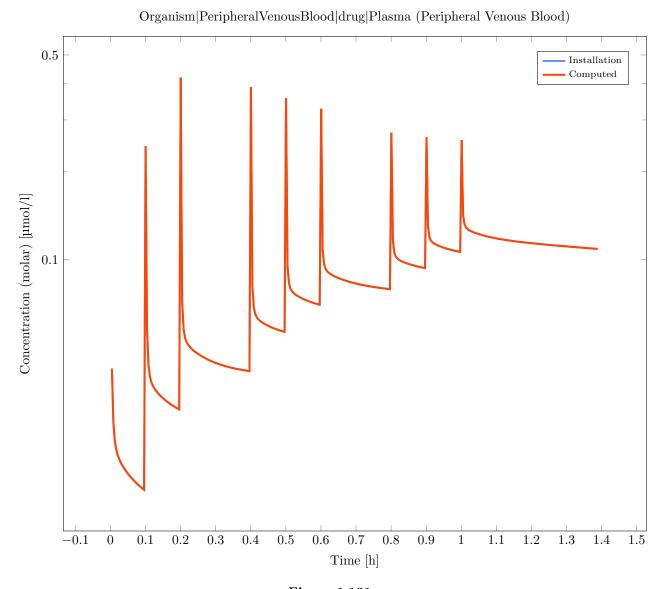
 ${\bf Simulation: \ Human\_Multiple IV\_Efflux Basolateral-Human\_Multiple IV\_Efflux Basolateral-Result \ of the \ validation: \ Valid$ 



 ${\bf Figure~1.130}$ 

 $Simulation: \ Human\_MultipleIV\_Efflux-Human\_MultipleIV\_Efflux$ 

Result of the validation: Valid



**Figure 1.131** 

 ${\bf Simulation: \ Human\_Multiple IV\_Influx Basolateral-Human\_Multiple IV\_Influx Basolateral-Result \ of the \ validation: \ Valid$ 

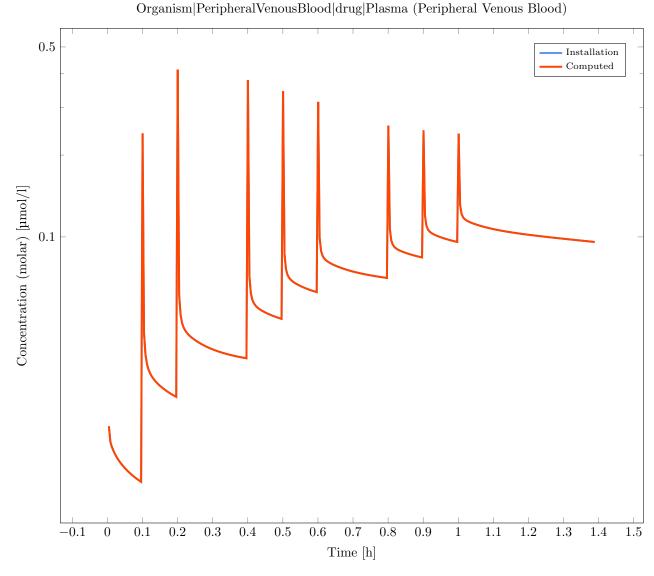


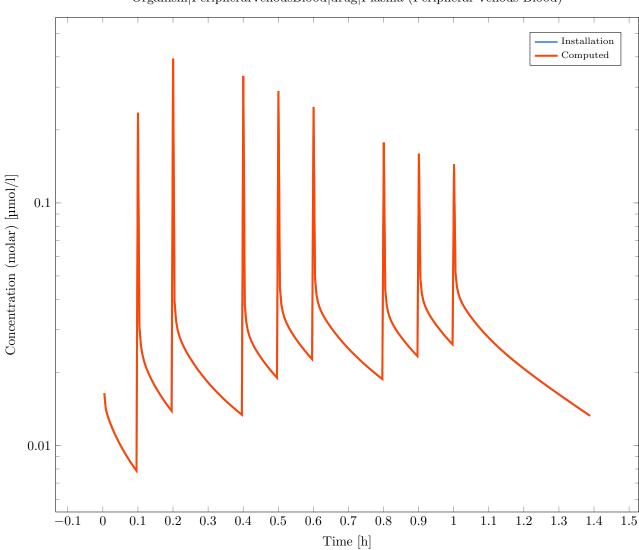
Figure 1.132

 $Simulation: \ Human\_MultipleIV\_Influx-Human\_MultipleIV\_ActiveInflux$ 

Result of the validation: Valid

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

Deviation: 3.51E-5



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

**Figure 1.133** 

 ${\bf Simulation: \ Human\_Multiple IV\_Metabolizm Binding-Human\_Multiple IV\_Metabolizm Binding \ Result \ of \ the \ validation: \ Valid }$ 

### Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed 0.1 Concentration (molar) $[\mu]$ 0.01 0.0010.2 0.3 0.7 0.8 0.9 1.1 1.2 -0.10 0.1 0.4 0.5 0.6 1.3 1.4 1.5

**Figure 1.134** 

Time [h]

 ${\bf Simulation: \ Human\_Multiple IV\_Metabolizm-Human\_Multiple IV\_Metabolizm.} \\ {\bf Result \ of \ the \ validation: \ Valid}$ 

1.3

1.4

1.5

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

**Figure 1.135** 

0.6

0.7

Time [h]

 $Simulation: \ Human\_MultipleIV\_PGPB a solateral-Human\_MultipleIV\_PGPB a$ Result of the validation: Valid

0.5

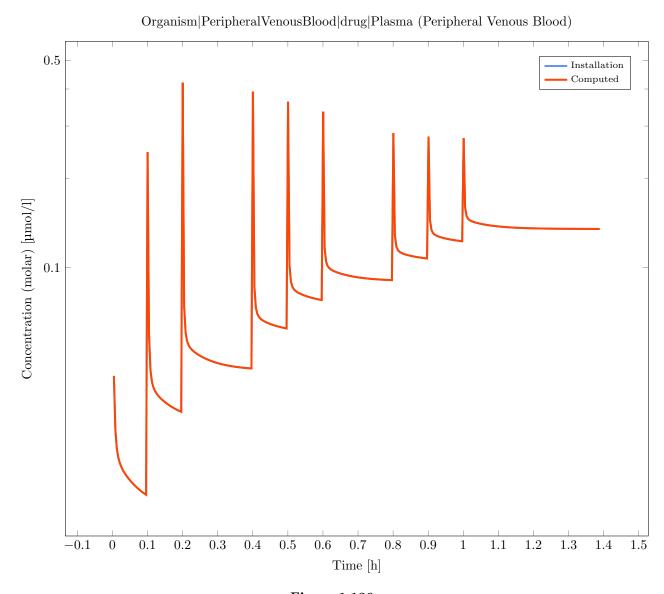
0.4

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

-0.1

0

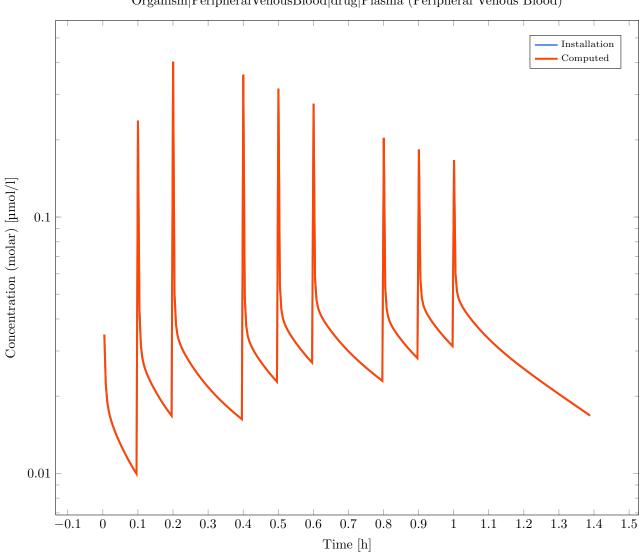
0.1



 ${\bf Figure~1.136}$ 

 $Simulation: \ Human\_MultipleIV\_PGP-Human\_MultipleIV\_PGP$ 

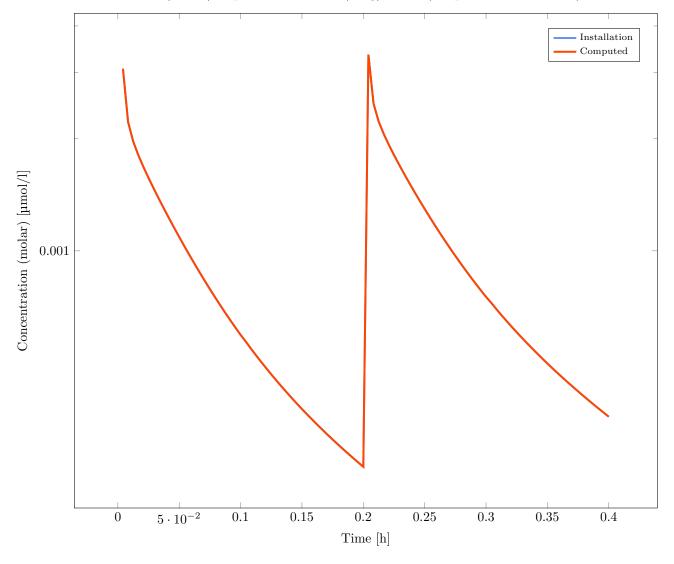
Result of the validation: Valid



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

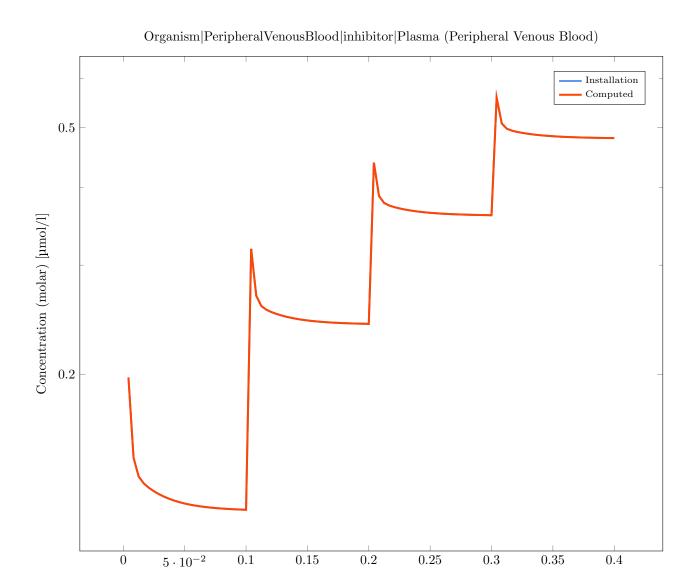
Figure 1.137

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



 $Figure \ 1.138$ 

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



**Figure 1.139** 

Time [h]

 $Simulation: \ Human\_Oral\_BiDaily\_Table Formulation-S1\_suspension$ 

Result of the validation: Valid

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

Deviation: 5.83E-5

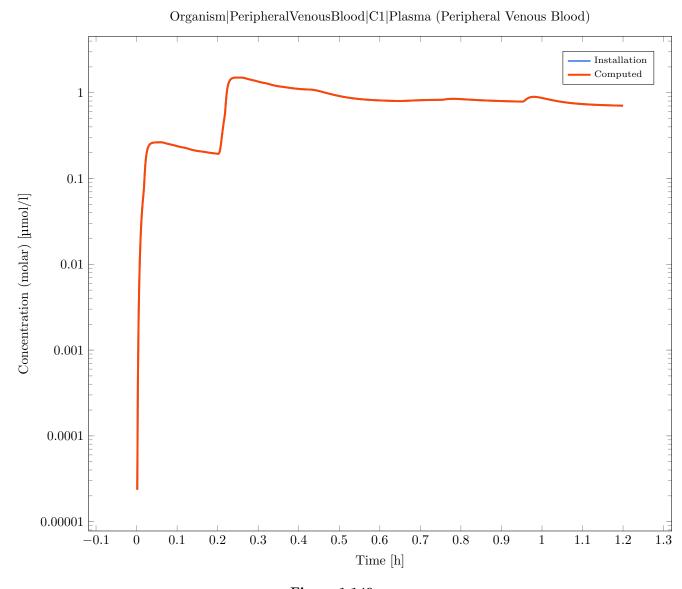
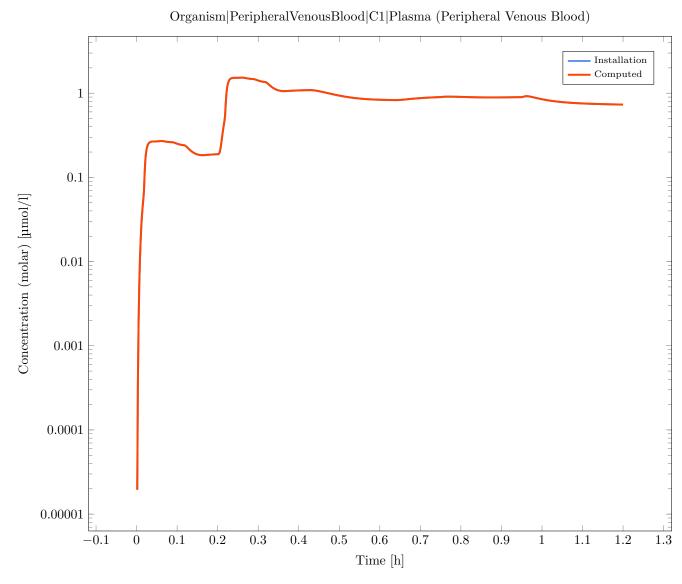


Figure 1.140

 $Simulation: Human\_Oral\_BiDaily\_TableFormulation-S2\_NoSuspension$ 

Result of the validation: Valid



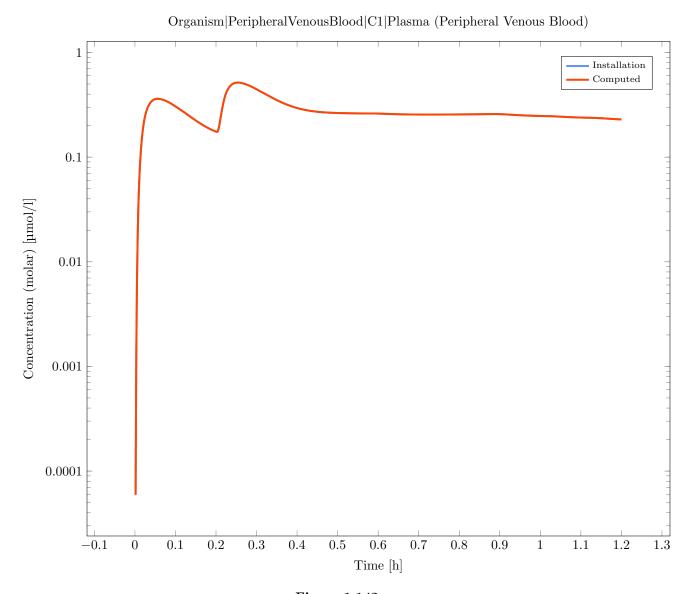
**Figure 1.141** 

Simulation: Human\_pH\_SolubilityTable-S1\_Table

Result of the validation: Valid

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

Deviation: 1.12E-5



 ${\bf Figure~1.142}$ 

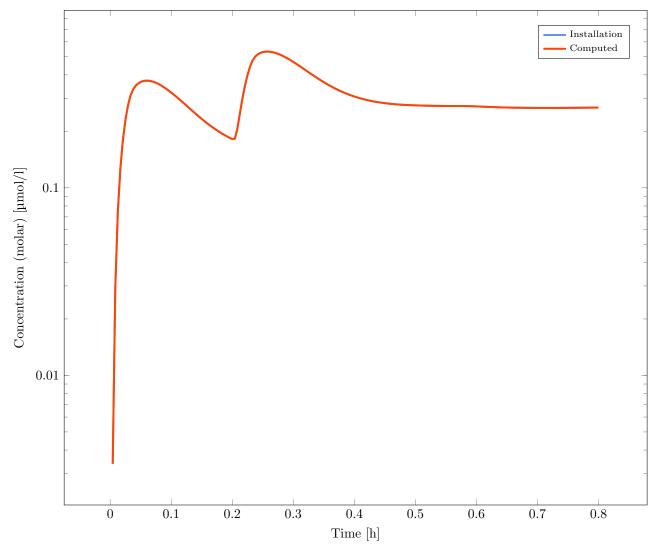
Simulation: Human\_pH\_SolubilityTable-S2\_Measurement

Result of the validation: Valid

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

Deviation: 0

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



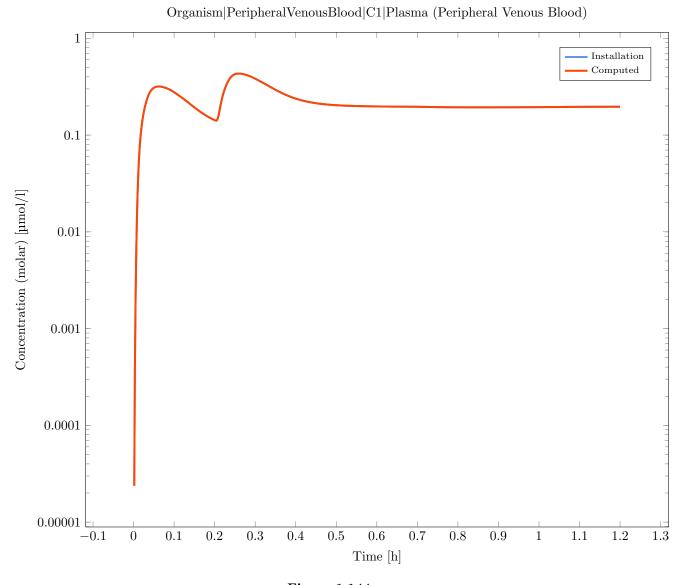
**Figure 1.143** 

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

Result of the validation: Valid

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

Deviation: 3.58E-6

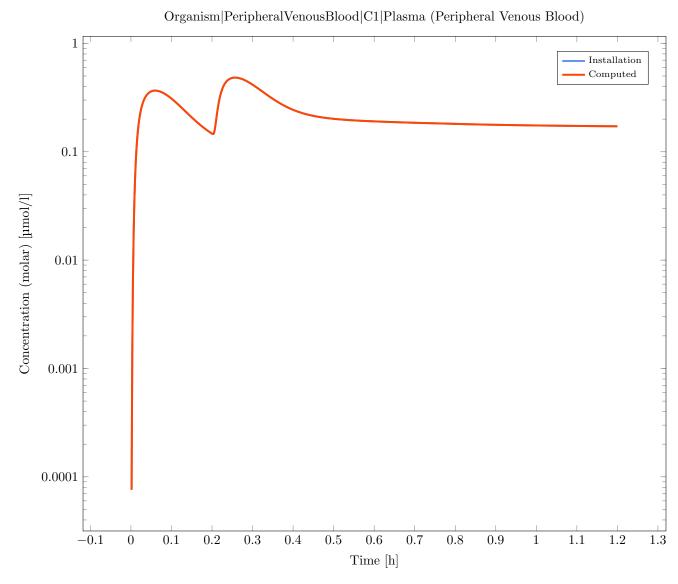


**Figure 1.144** 

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

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

Deviation: 8.65E-8



**Figure 1.145** 

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

# Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood) Installation Computed Concentration (molar) $[\mu]$ 0.02 $0 \quad 2 \cdot 10^{-2} \cdot 10^{-2} \cdot 10^{-2} \cdot 10^{-2} \cdot 0.1$

**Figure 1.146** 

0.12 0.14 0.16

Time [h]

0.2

 $0.22 \quad 0.24$ 

0.3

0.18

Simulation: Human\_SingleIV-Human\_SingleIV

Result of the validation: Valid

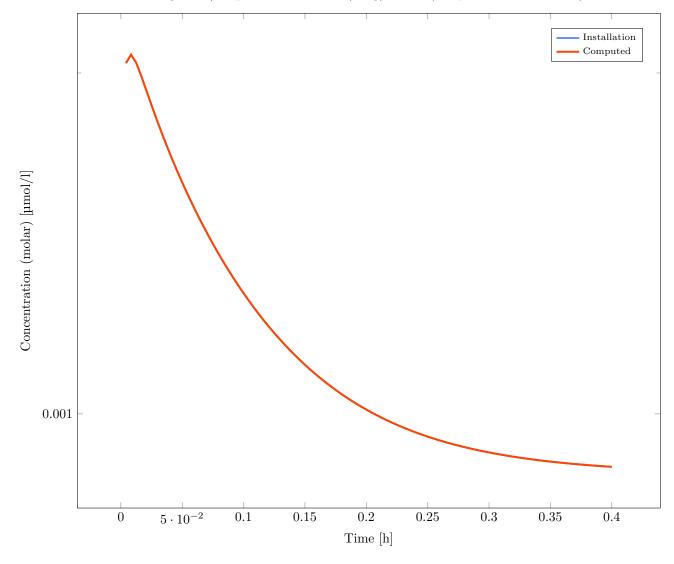
## Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)



Figure 1.147

Simulation: Human\_SingleIV-Human\_SingleIV\_MW\_200\_fu\_0.2\_LogP\_5 Result of the validation: Valid

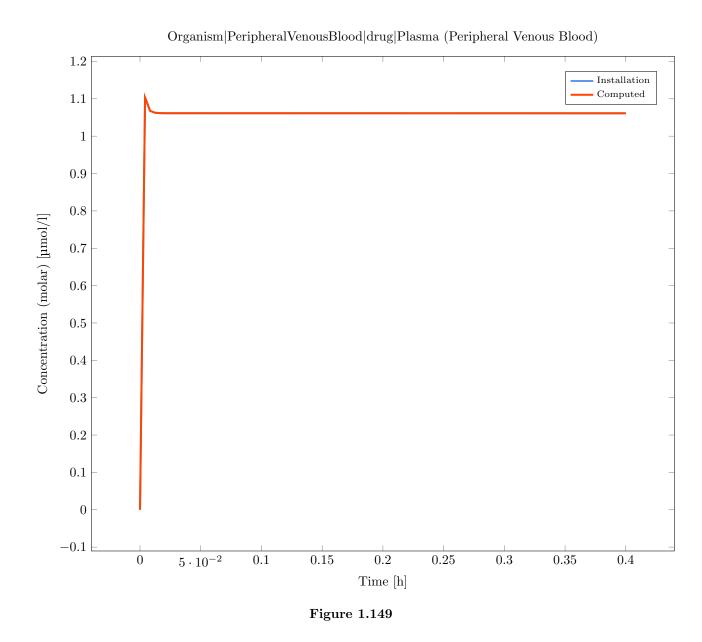
## Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)



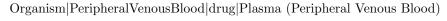
**Figure 1.148** 

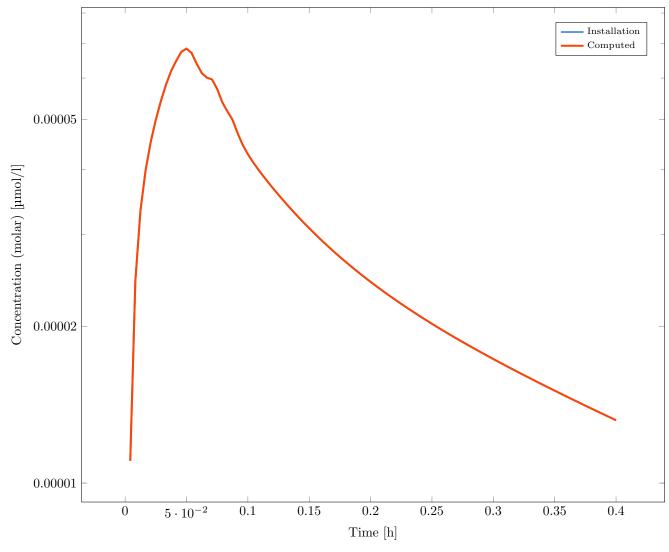
 $Simulation: \ Human\_SingleIV-Human\_SingleIV\_MW\_800\_fu\_0.6\_LogP\_-5$ 

Result of the validation: Valid



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





**Figure 1.150** 

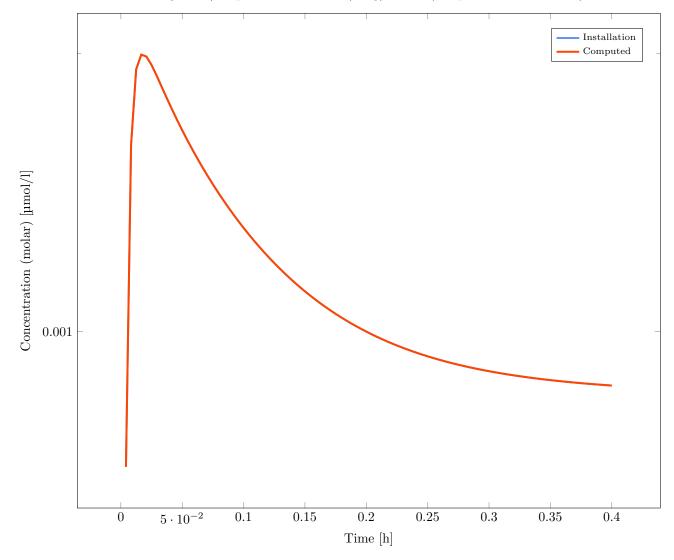
 $Simulation: Human\_SingleORAL\_Dissolved\_PlasmaClearance-Human\_Singl$ 

Result of the validation: Valid

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

Deviation: 0

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



**Figure 1.151** 

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

Result of the validation: Valid

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

Deviation: 0

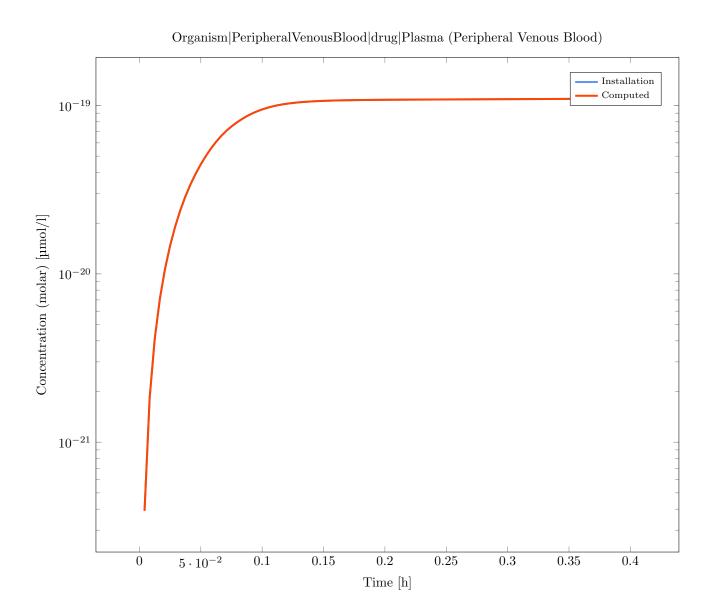


Figure 1.152

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

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 1.17E-6

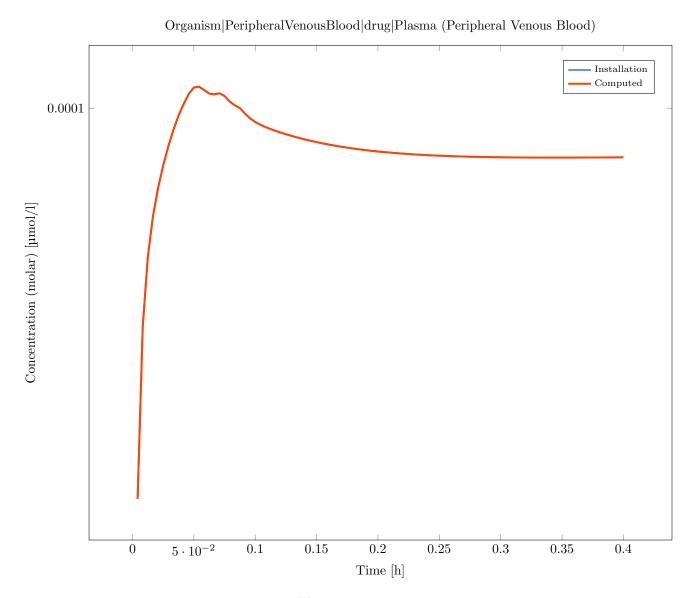
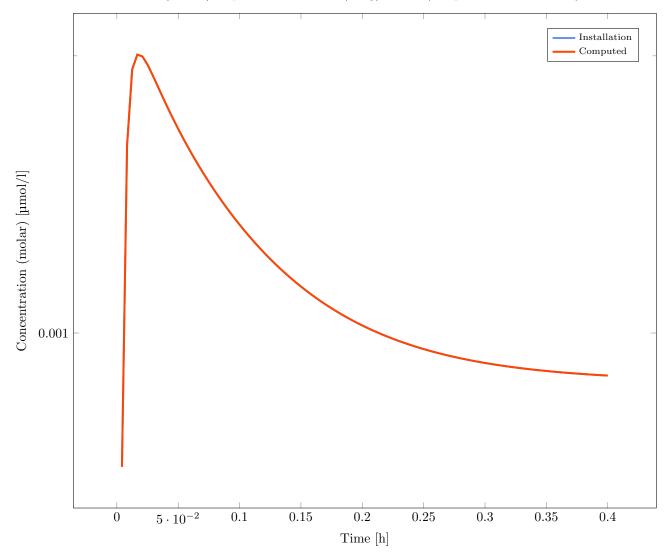


Figure 1.153

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

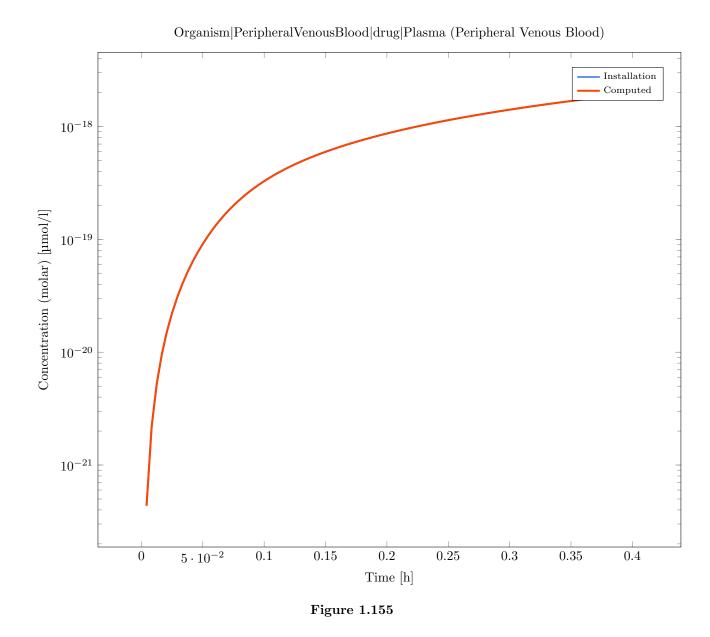
## Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)



**Figure 1.154** 

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

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



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



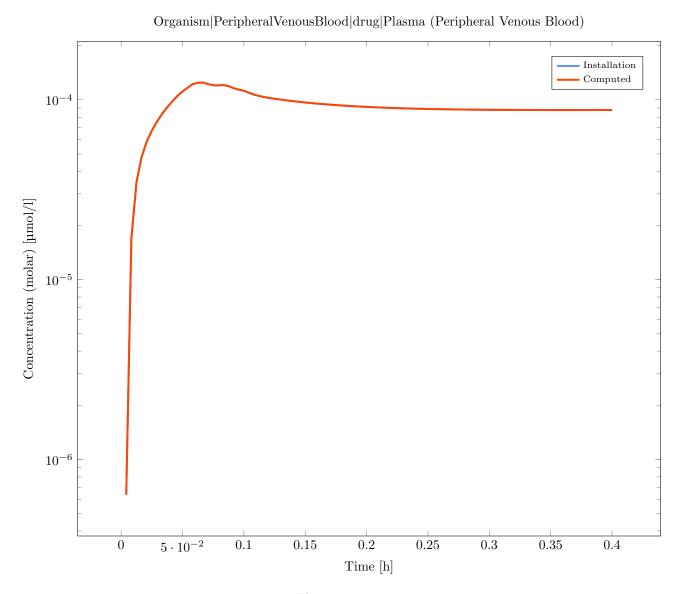
**Figure 1.156** 

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

Result of the validation: Valid

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

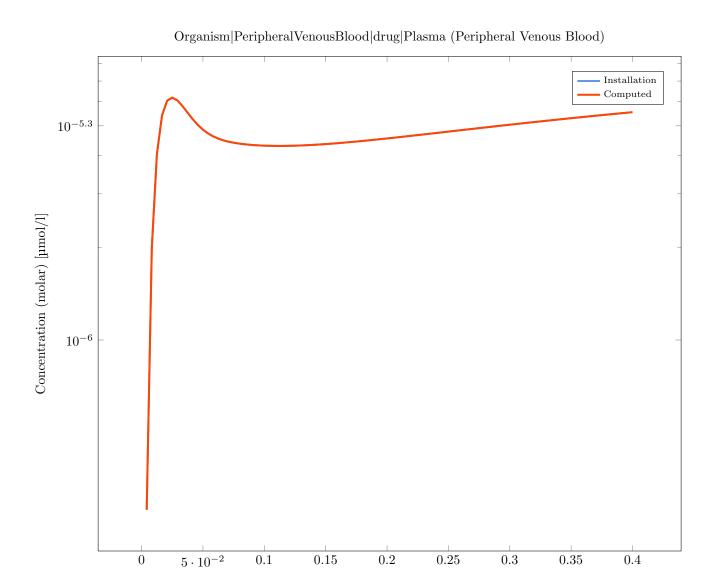
Deviation: 0



**Figure 1.157** 

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

Result of the validation: Valid



**Figure 1.158** 

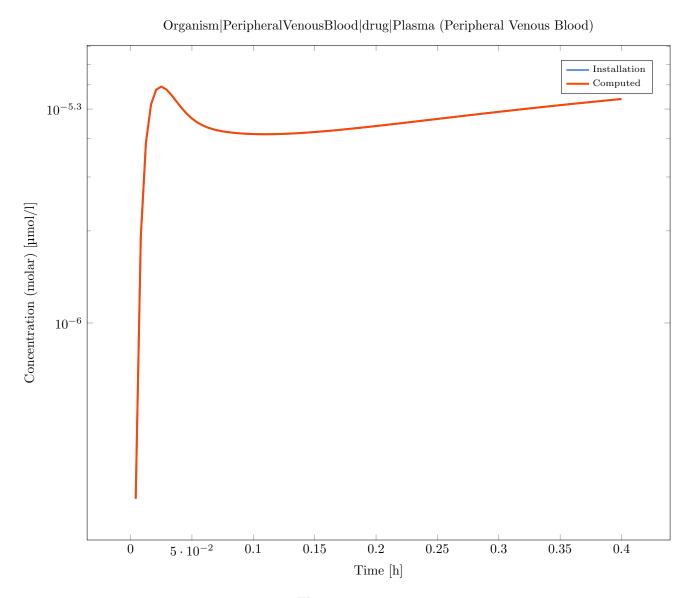
Time [h]

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

Result of the validation: Valid

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

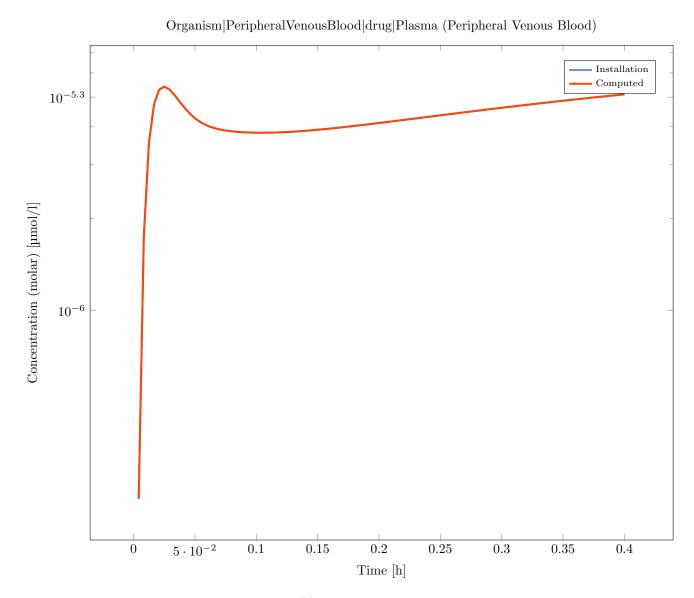
Deviation: 8.76E-8



**Figure 1.159** 

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

Result of the validation: Valid

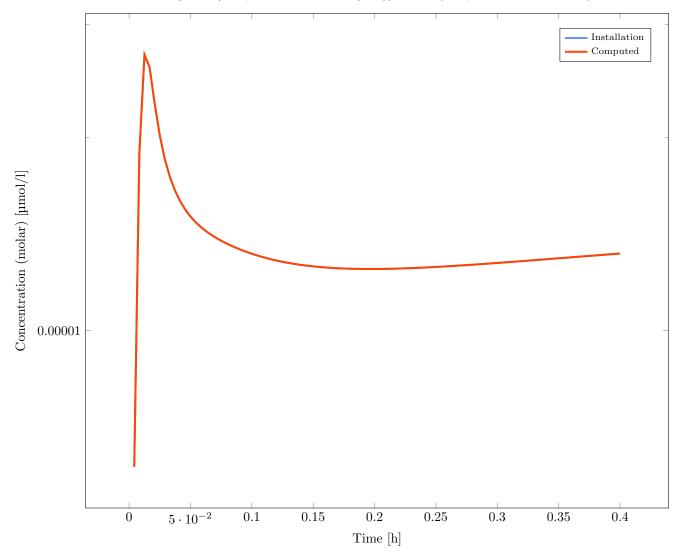


**Figure 1.160** 

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

Result of the validation: Valid

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



**Figure 1.161** 

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

Result of the validation: Valid

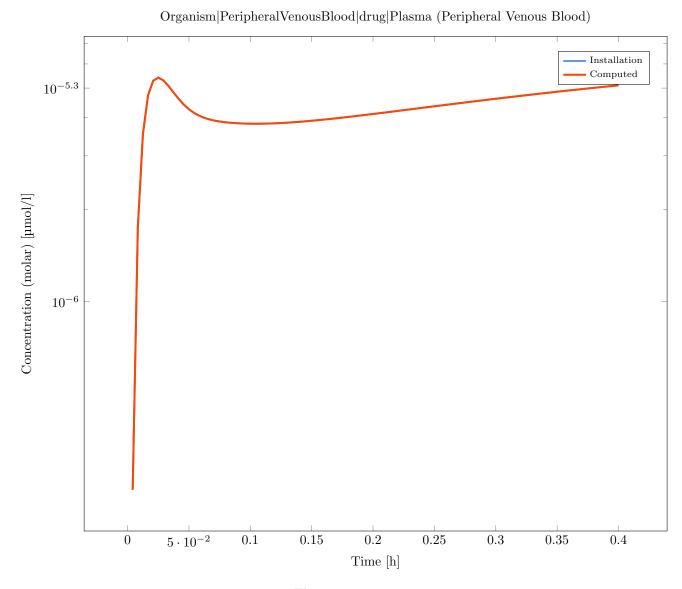
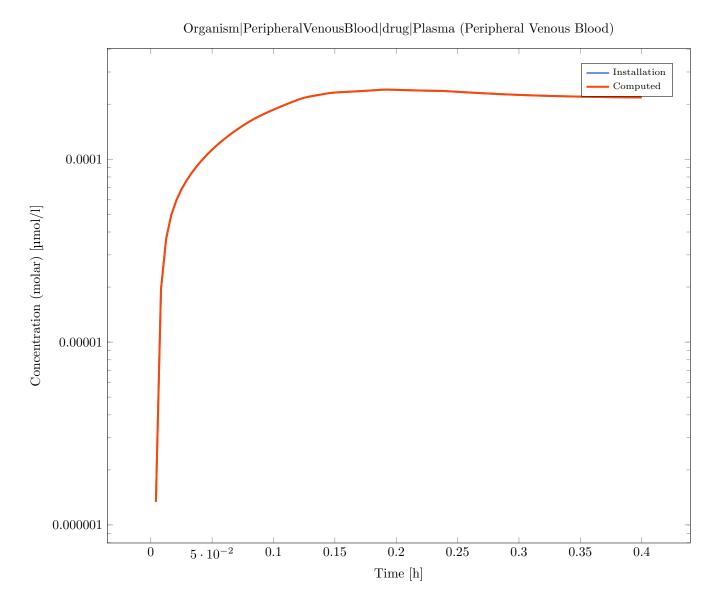


Figure 1.162

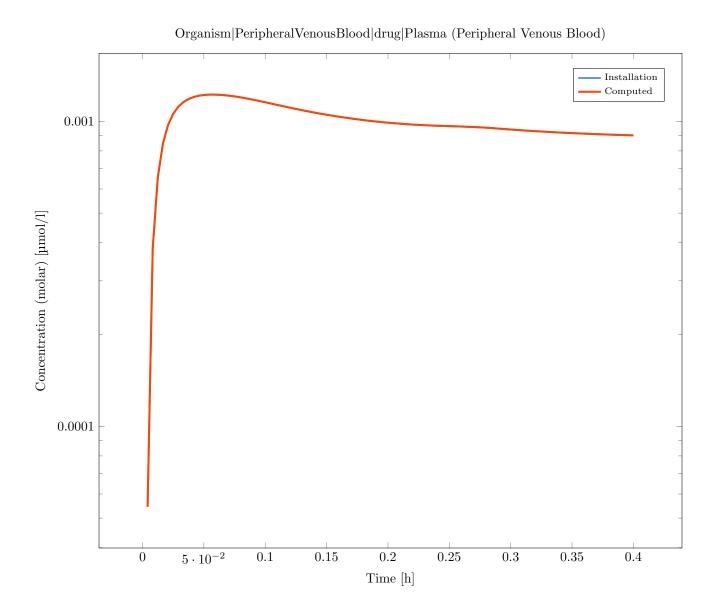
 ${\bf Simulation: Human\_SingleORAL\_Weibull\_AsSuspention-Human\_SingleORAL\_Weibull\_AsSuspention}. \\ {\bf Result\ of\ the\ validation:\ Valid}$ 

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 8.81E-7



**Figure 1.163** 

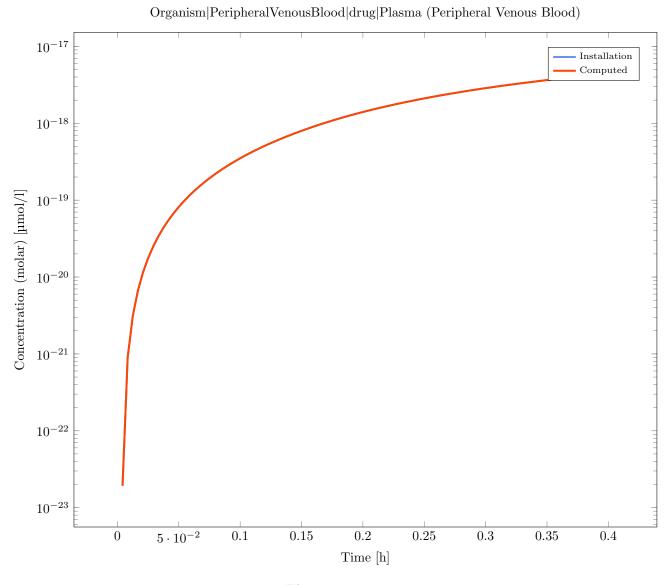
 $Simulation: Human\_SingleORAL\_Weibull\_AsSuspention-Human\_SingleORAL\_Weibull\_AsSuspention\_MW\_200\_fu\_0.2\_LogP\_5\\ Result of the validation: Valid$ 



**Figure 1.164** 

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

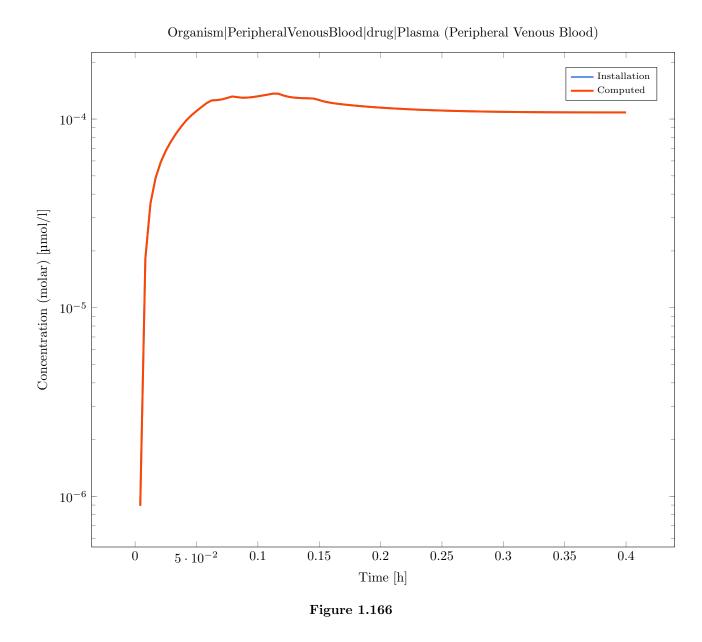
Output Path: Organism |PeripheralVenousBlood |<br/>drug |Plasma (Peripheral Venous Blood) Deviation:  ${\bf 0}$ 



**Figure 1.165** 

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

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 2.31E-4



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

Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 5.01E-6

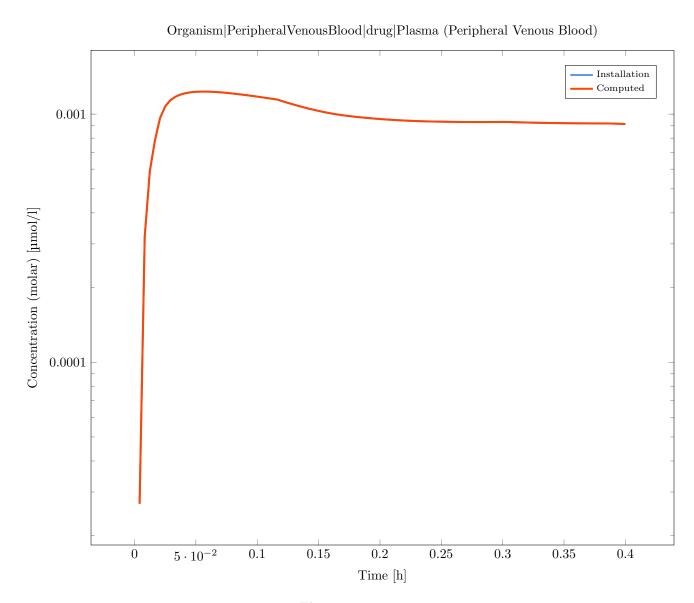
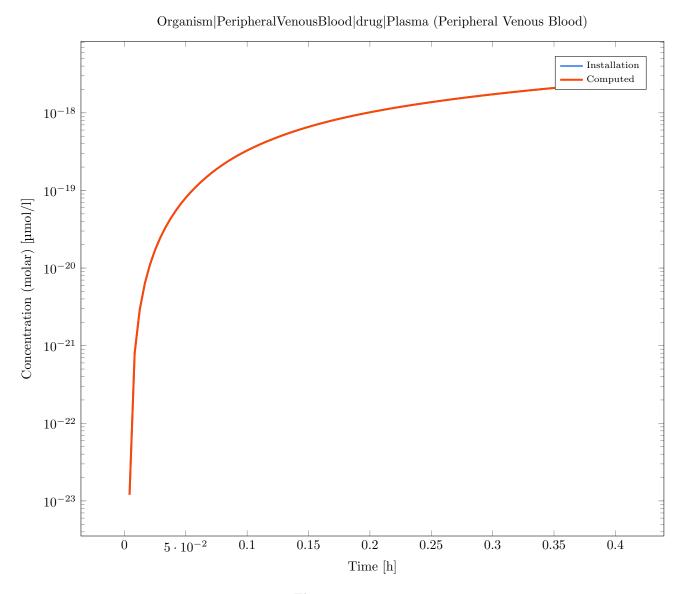


Figure 1.167

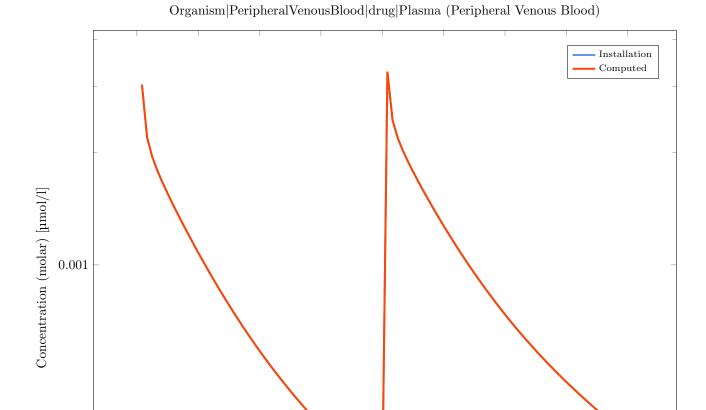
Simulation: Human\_SingleORAL\_Weibull-Human\_SingleORAL\_Weibull\_MW\_800\_fu\_0.6\_LogP\_5 Result of the validation: Valid

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



**Figure 1.168** 

Simulation: Human\_UncompetitiveInhibition-Human\_UncompetitiveInhibition Result of the validation: Valid



0.2

Time [h]

0.25

0.3

0.35

0.4

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

**Figure 1.169** 

0.15

0.1

0

 $5 \cdot 10^{-2}$ 



Figure 1.170

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



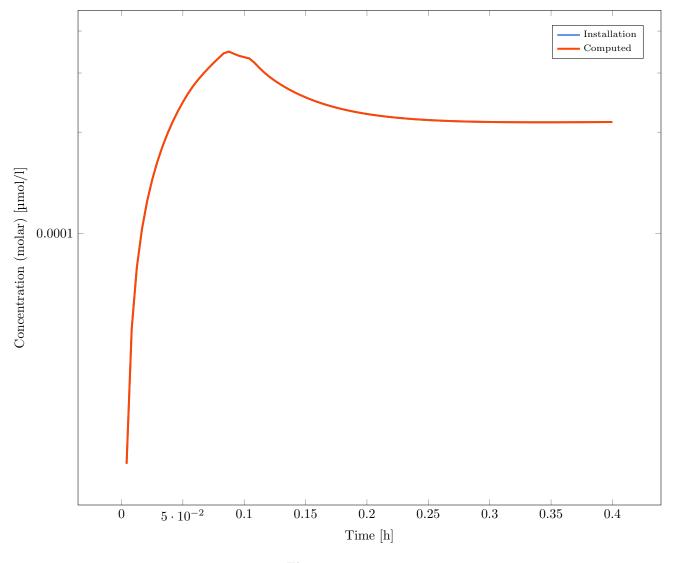


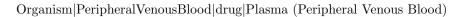
Figure 1.171

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

Result of the validation: Valid

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

Deviation: 0



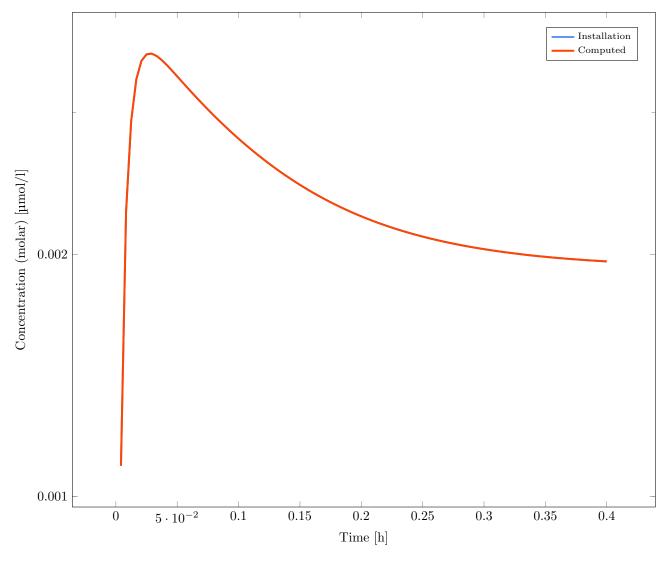


Figure 1.172

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

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

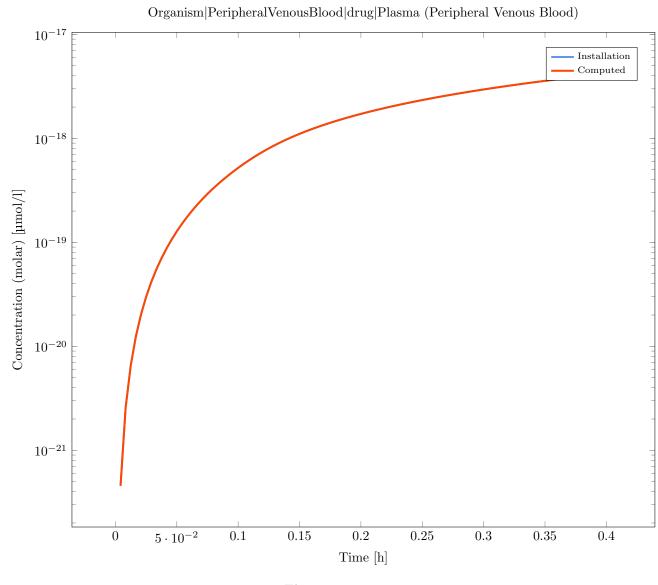


Figure 1.173

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

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

Figure 1.174

0.2

Time [h]

0.25

0.35

0.3

0.4

0.15

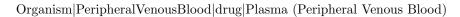
0.1

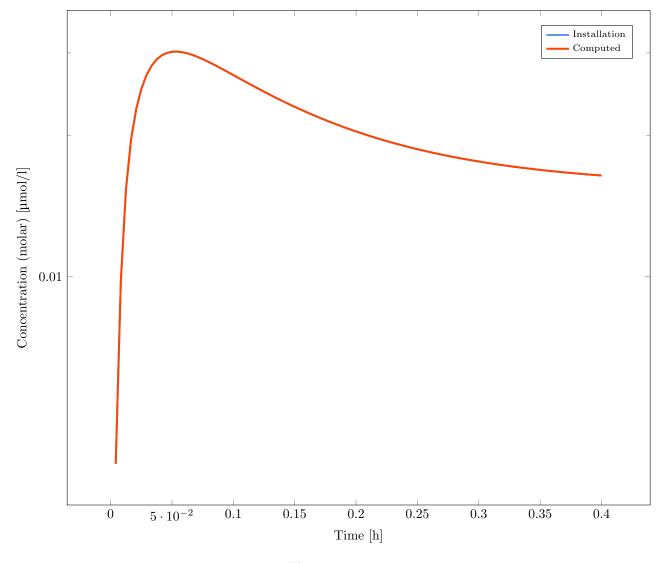
Simulation: Monkey\_SingleORAL\_Dissolved-Monkey\_SingleORAL\_Dissolved\_MW\_200\_fu\_0.2\_LogP\_5 Result of the validation: Valid

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

0

 $5 \cdot 10^{-2}$ 





**Figure 1.175** 

Simulation: Monkey\_SingleORAL\_Dissolved-Monkey\_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:  ${\bf 0}$ 

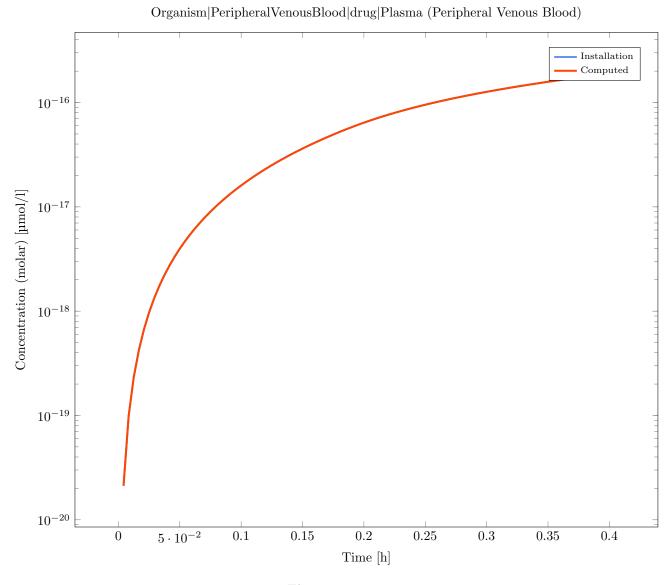


Figure 1.176

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



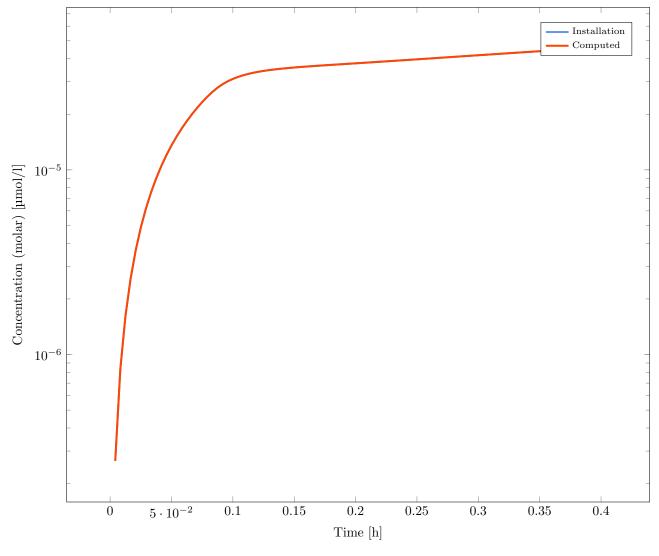
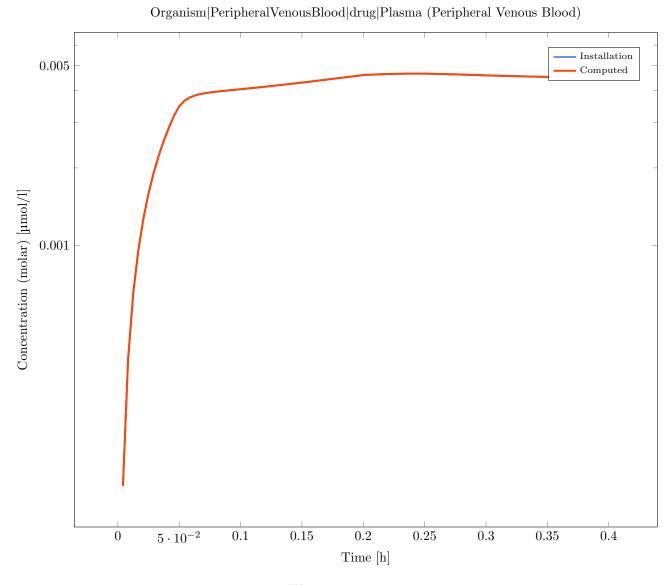


Figure 1.177

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

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

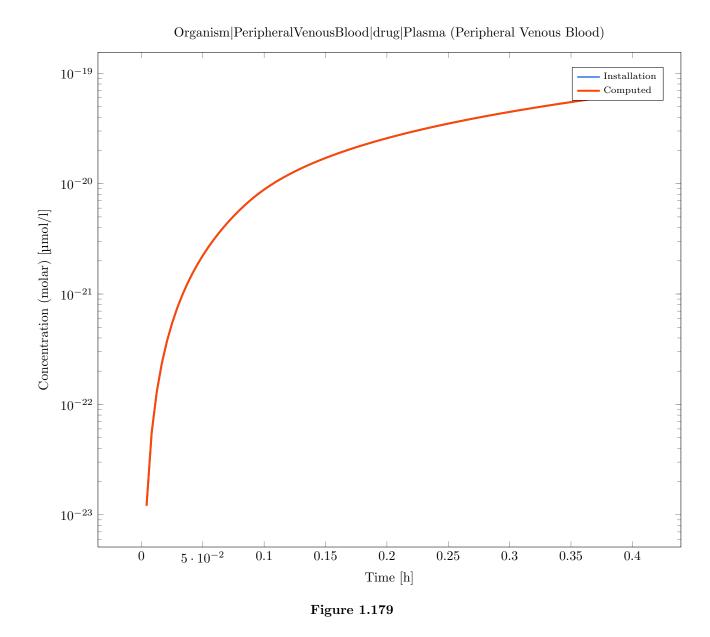
Result of the validation: Valid



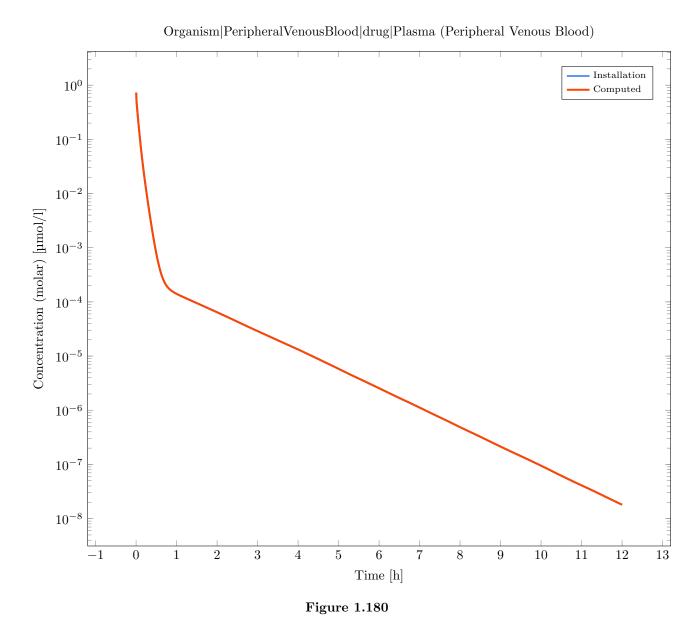
**Figure 1.178** 

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:  ${\bf 0}$ 



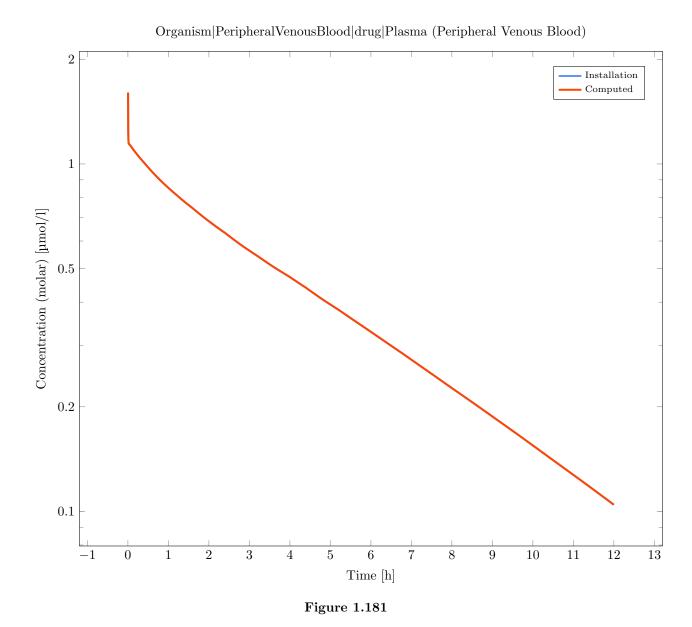
Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 1.17E-7



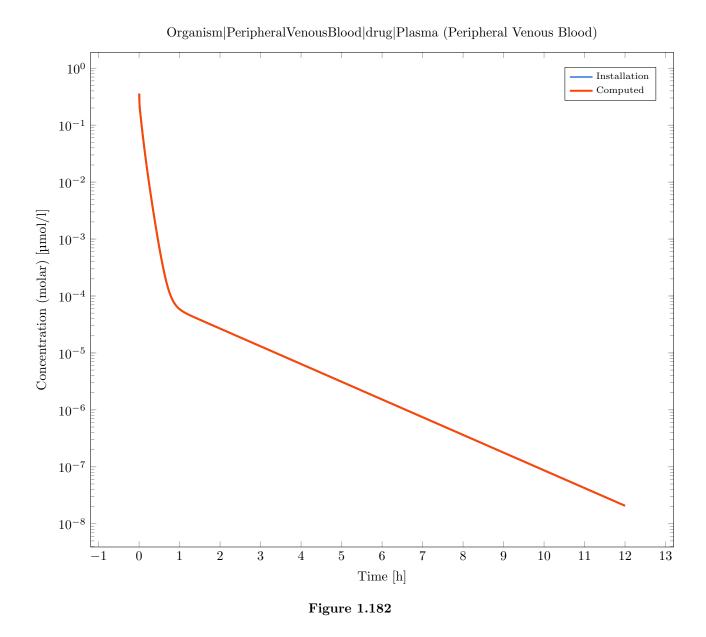
 $Simulation: \ Preterm\_SingleIV\_Age\_0\_GA\_32\_GFR-Preterm\_SingleIV\_Age\_0\_GA\_32\_GFR$ 

Result of the validation: Valid

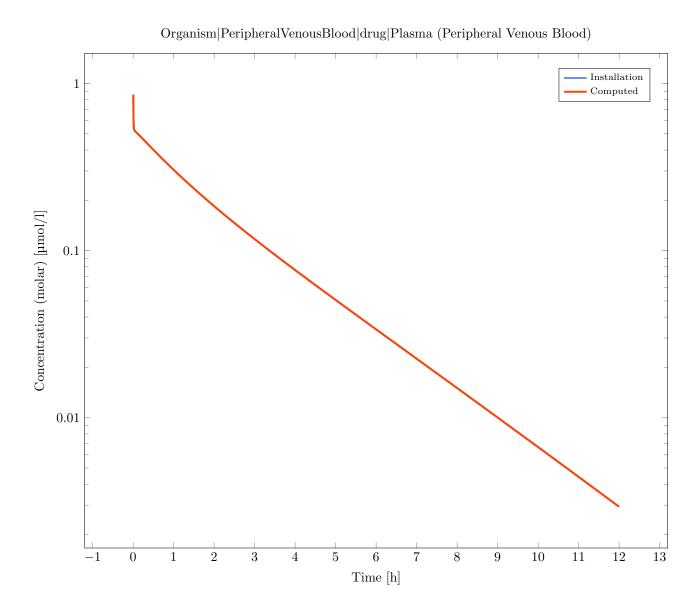
Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood)<br/> Deviation: 3.66E-5



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

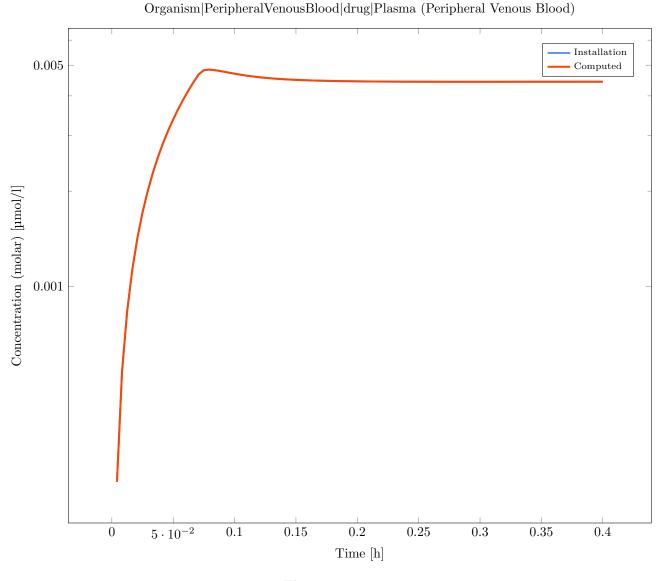


 $\label{lem:single_index} \textbf{Simulation: Preterm\_SingleIV\_Age\_15\_GA\_32\_GFR-Preterm\_SingleIV\_Age\_15\_GA\_32\_GFR} \\ \textbf{Result of the validation: Valid}$ 



**Figure 1.183** 

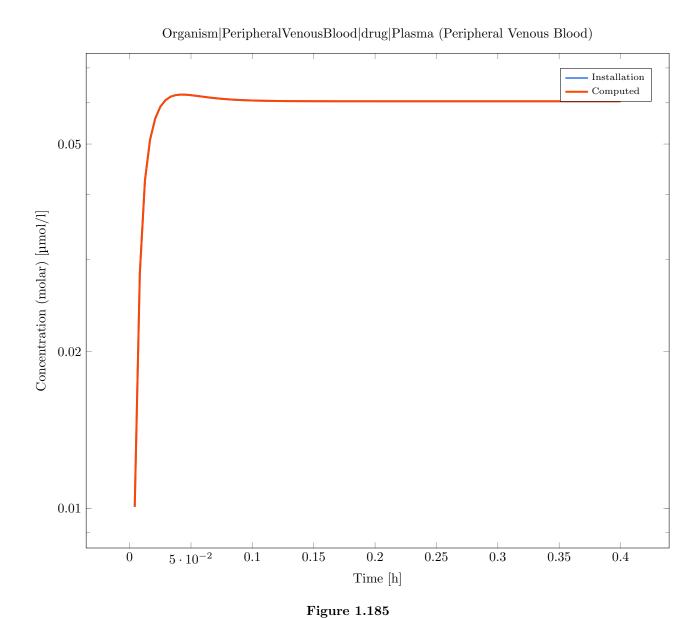
 ${\bf Simulation: Rabbit\_SingleORAL\_Dissolved-Rabbit\_SingleORAL\_Dissolved} \\ {\bf Result \ of \ the \ validation: \ Valid}$ 



**Figure 1.184** 

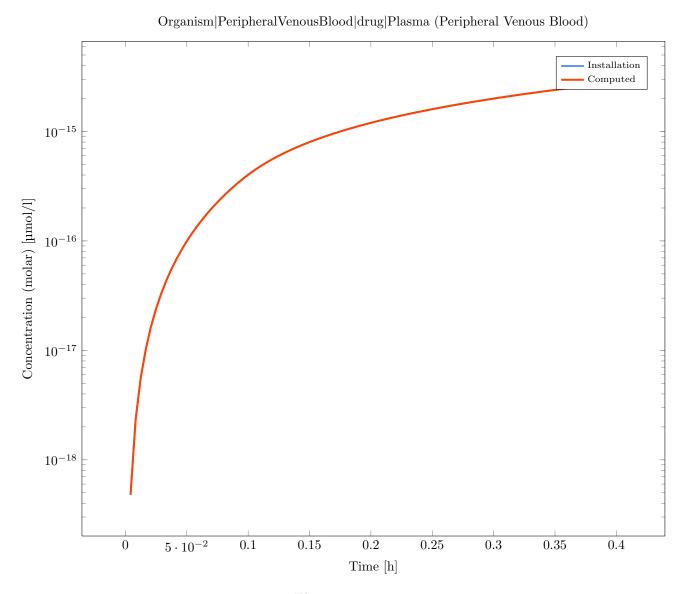
 $Simulation: Rabbit\_SingleORAL\_Dissolved\_Rabbit\_SingleORAL\_Dissolved\_MW\_200\_fu\_0.2\_LogP\_5$  Result of the validation: Valid

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



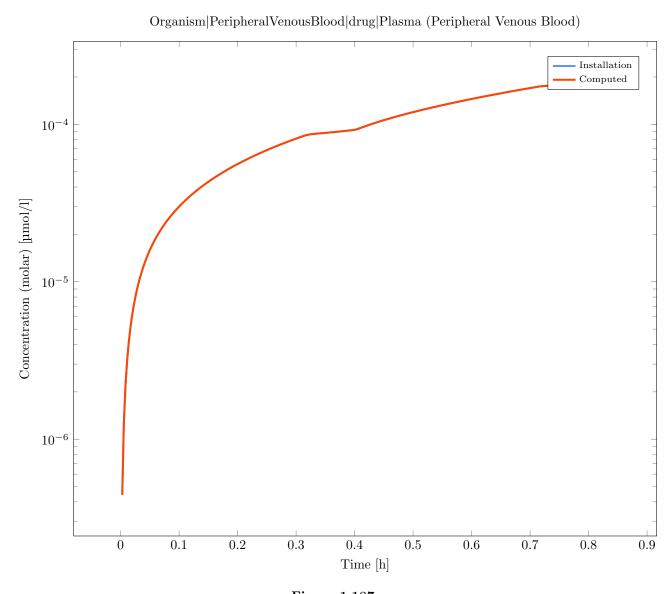
 $Simulation: Rabbit\_SingleORAL\_Dissolved\_Rabbit\_SingleORAL\_Dissolved\_MW\_800\_fu\_0.6\_LogP\_-logP\_-$ 

Result of the validation: Valid



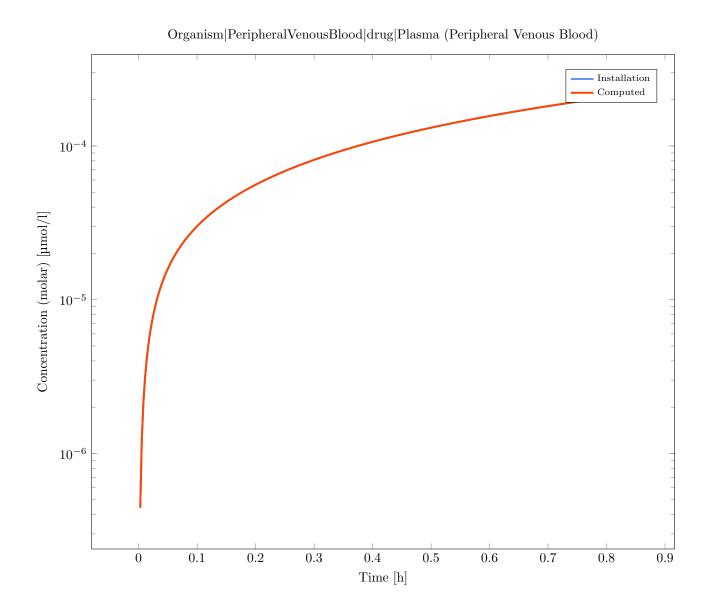
**Figure 1.186** 

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



 ${\bf Figure~1.187}$ 

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



**Figure 1.188** 

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

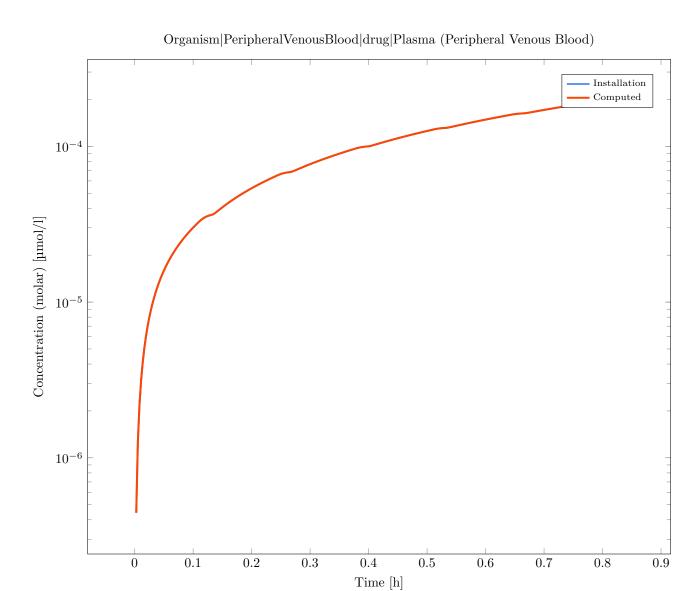


Figure 1.189

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

Result of the validation: Valid

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

**Figure 1.190** 

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

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

0.1

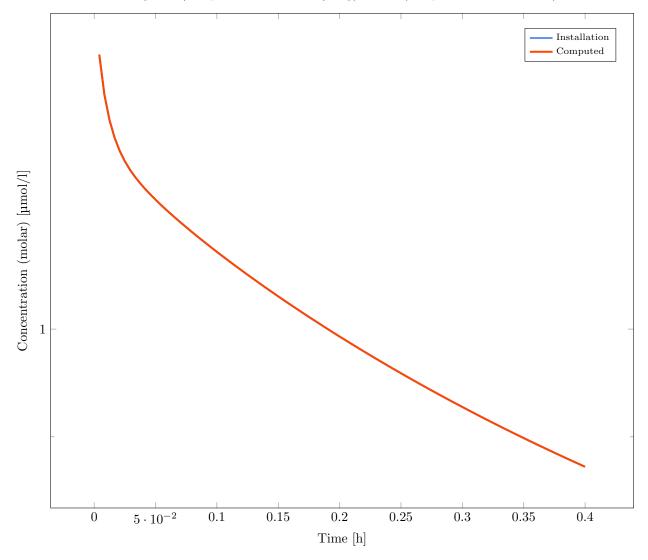
Output Path: Organism |Peripheral Venous<br/>Blood |drug |Plasma (Peripheral Venous Blood) Deviation:<br/> 0

0.1

0

 $5\cdot 10^{-2}$ 

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



**Figure 1.191** 

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

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

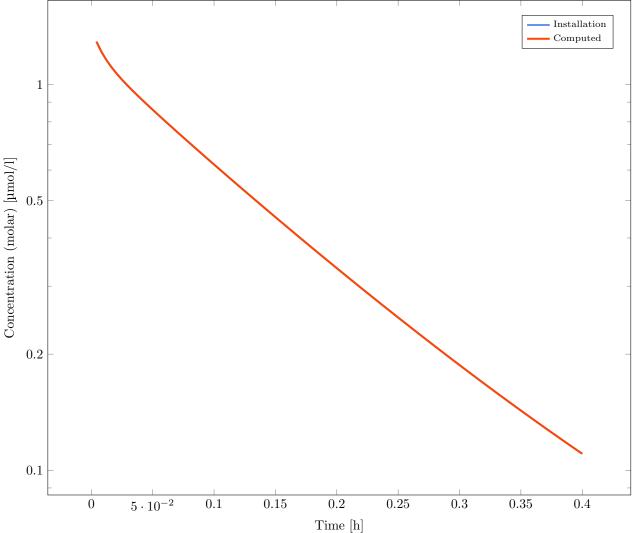


Figure 1.192

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

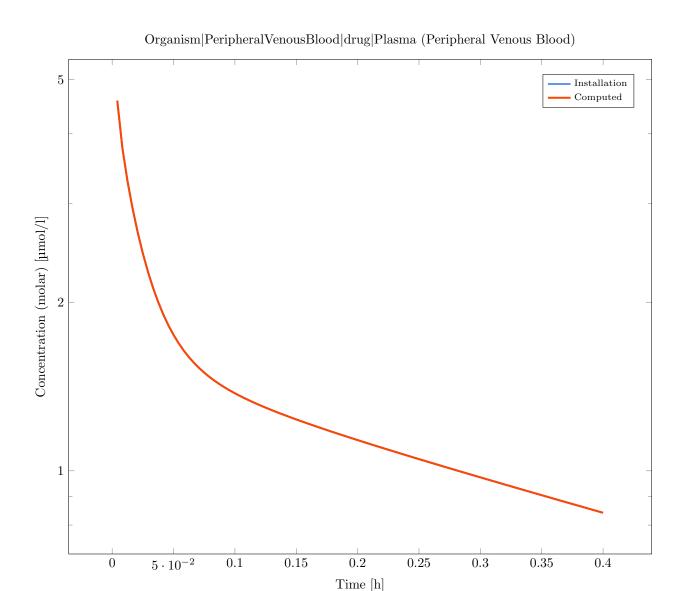
### Organism|PeripheralVenousBlood|drug|Plasma (Peripheral Venous Blood)



**Figure 1.193** 

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

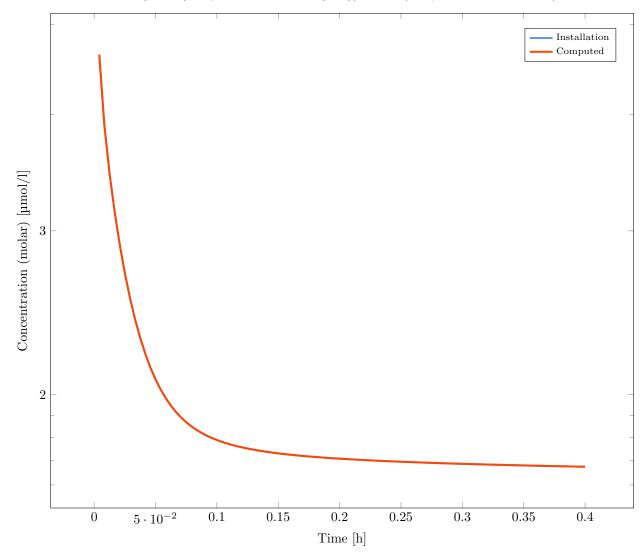
Result of the validation: Valid



**Figure 1.194** 

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





**Figure 1.195** 

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

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

**Figure 1.196** 

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

 ${\bf Simulation: \ Single IV\_2 Pores\_Mouse-Single IV\_2 Pores\_Mouse}$ 

0.1

 $5\cdot 10^{-2}$ 

Result of the validation: Valid

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

Figure 1.197

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

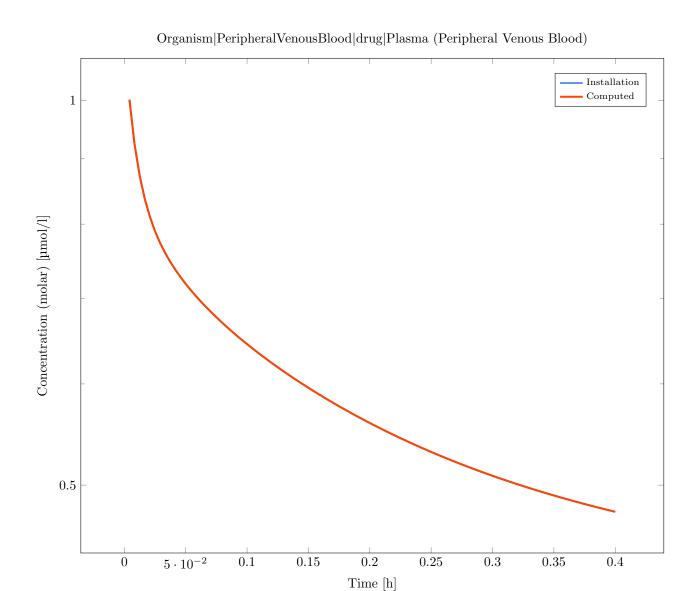
Simulation: SingleIV\_2Pores\_Mouse-SingleIV\_2Pores\_Mouse\_SimulationA Result of the validation: Valid

0.1

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

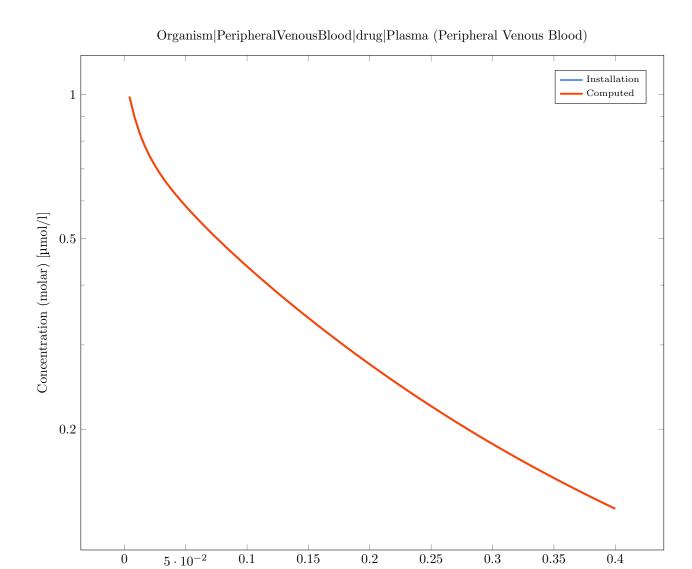
0

 $5\cdot 10^{-2}$ 



**Figure 1.198** 

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



**Figure 1.199** 

Time [h]

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

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

Figure 1.200

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

Time [h]

Result of the validation: Valid

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

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

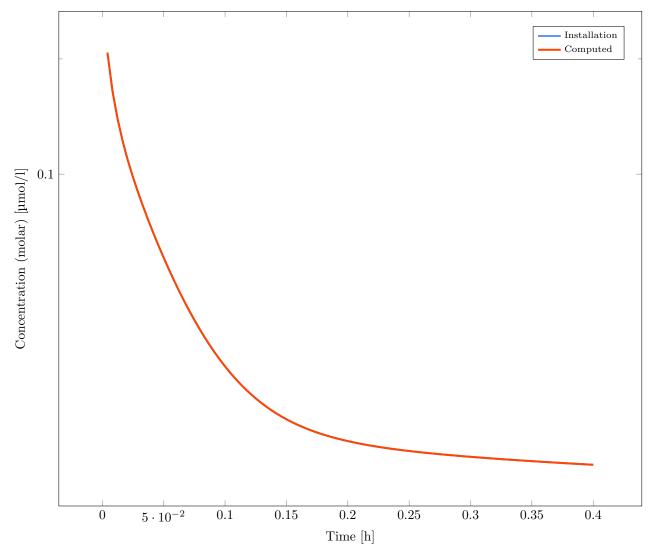


Figure 1.201

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

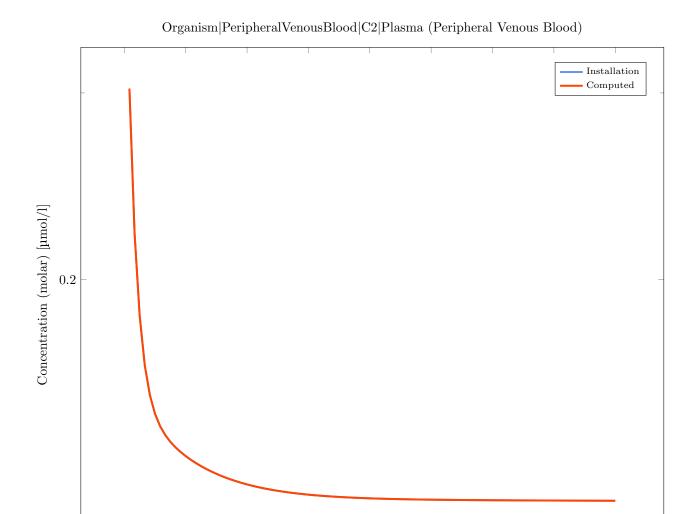


Figure 1.202

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

0.2

Time [h]

0.25

0.35

0.4

0.3

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

0.15

0.1

0

 $5\cdot 10^{-2}$ 

### 1.4 — Installation — Computed — C

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

Figure 1.203

 $Simulation: Single IV\_C2\_4 Comp\_standard\_schmitt\_standard-Single IV\_C2\_4 Comp\_standard-Single IV\_C2\_5 Comp\_standard-Single IV\_C2\_$ 

0.2

Time [h]

0.25

0.3

0.35

0.4

Result of the validation: Valid

0

 $5\cdot 10^{-2}$ 

0.2

0

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

0.15

0.1

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

Figure 1.204

0.2

Time [h]

0.25

0.3

0.35

0.4

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

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

0.15

0.1

0

 $5\cdot 10^{-2}$ 

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



Figure 1.205

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

Result of the validation: Valid

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

Deviation: 0

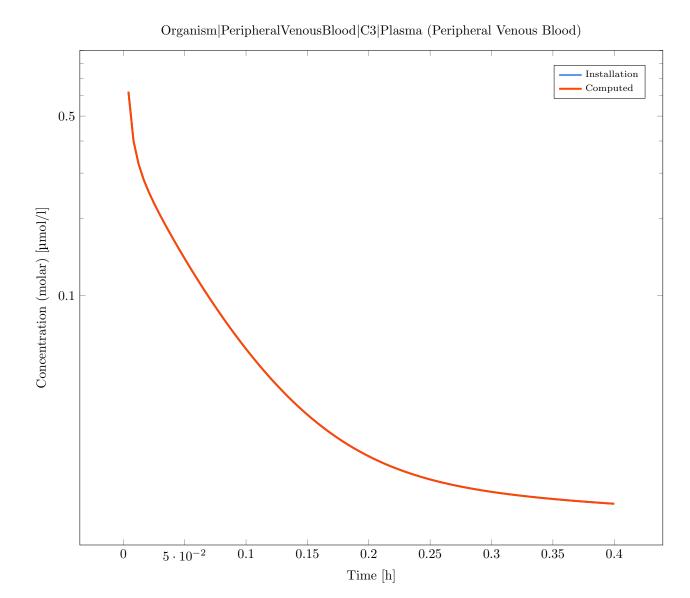


Figure 1.206

 $Simulation: Single IV\_C4\_2 Pores\_RR\_standard\_s$ 

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

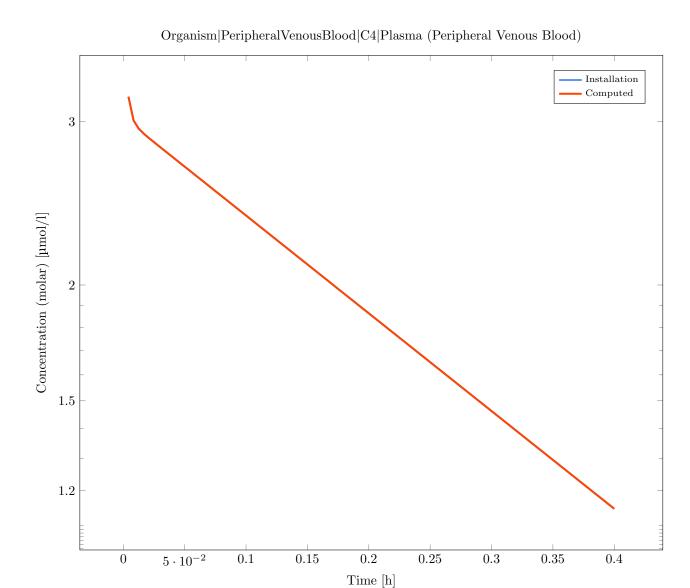


Figure 1.207

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

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

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

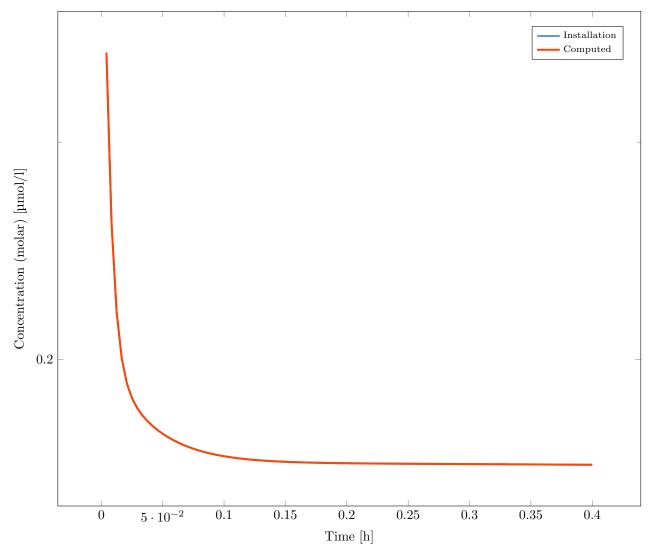


Figure 1.208

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



Figure 1.209

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

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

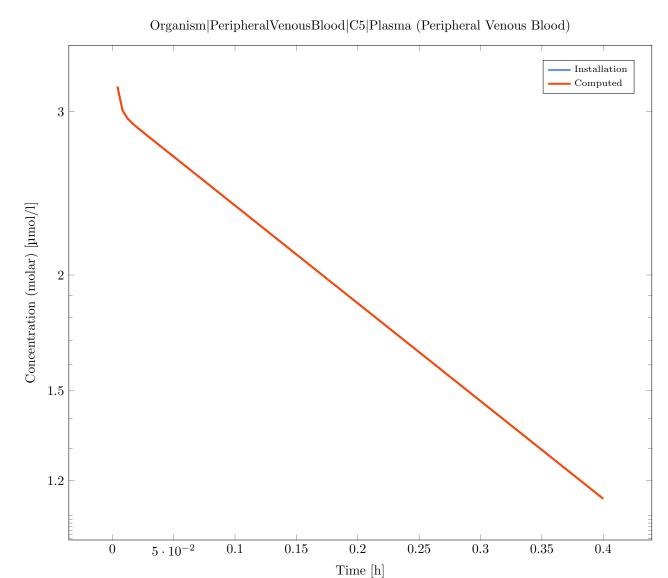


Figure 1.210

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

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

### Organism|Peripheral Venous Blood|C5|Plasma (Peripheral Venous Blood) Installation Computed Computed

**Figure 1.211** 

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

0.2

Time [h]

0.25

0.3

0.35

0.4

Result of the validation: Valid

0

 $5\cdot 10^{-2}$ 

1.2

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

0.15

0.1

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

Figure 1.212

0.2

Time [h]

0.25

0.3

0.35

0.4

 $Simulation: Single IV\_C7\_2 Pores\_standard\_schmitt\_standard\_Single IV\_C7\_2 Pores\_standard\_schmitt\_schmitt$ 

Result of the validation: Valid

0

 $5\cdot 10^{-2}$ 

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

0.15

0.1

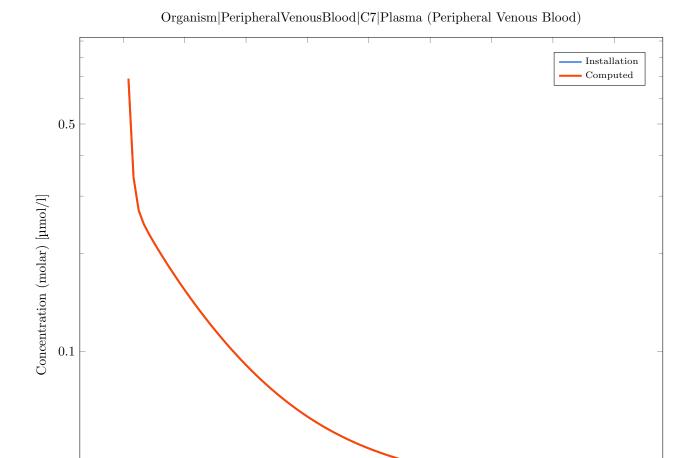


Figure 1.213

0.2

Time [h]

0.25

0.3

0.35

0.4

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

Result of the validation: Valid

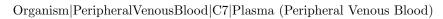
0

 $5\cdot 10^{-2}$ 

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

0.15

0.1



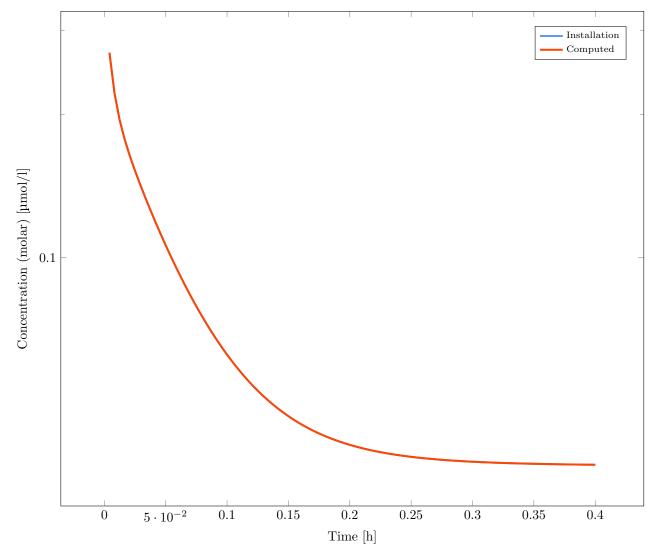


Figure 1.214

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

Result of the validation: Valid

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

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

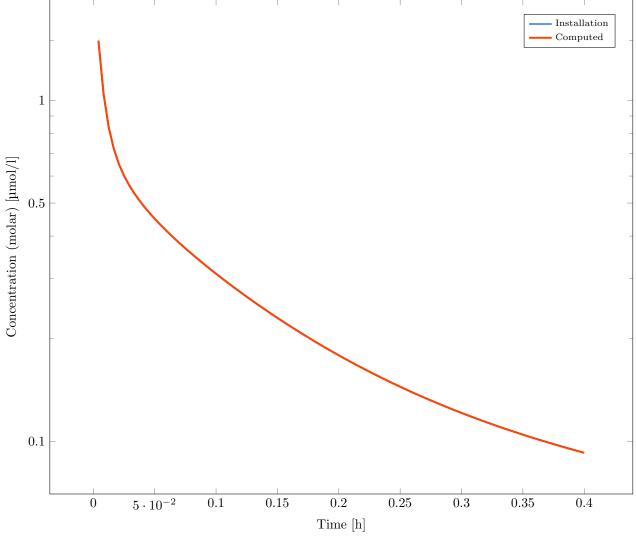


Figure 1.215

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

Result of the validation: Valid

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

# Organism|PeripheralVenousBlood|C9|Plasma (Peripheral Venous Blood) Installation Computed 3 Concentration (molar) $[\mu mol/1]$

0.15 0.2 0.25 0.3 0.35 0.4 Time [h]

Figure 1.216

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

Result of the validation: Valid

0

 $5\cdot 10^{-2}$ 

0.1

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

2

1.5

1.2

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

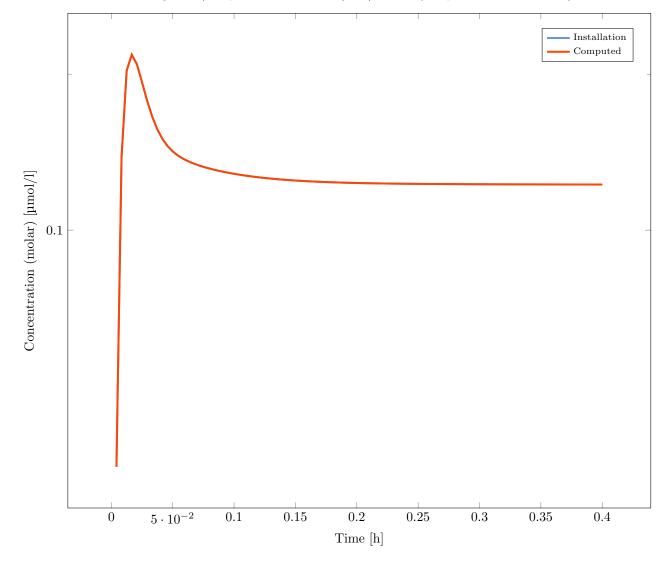


Figure 1.217

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

Result of the validation: Valid

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

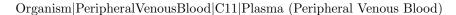


Figure 1.218

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

Result of the validation: Valid

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



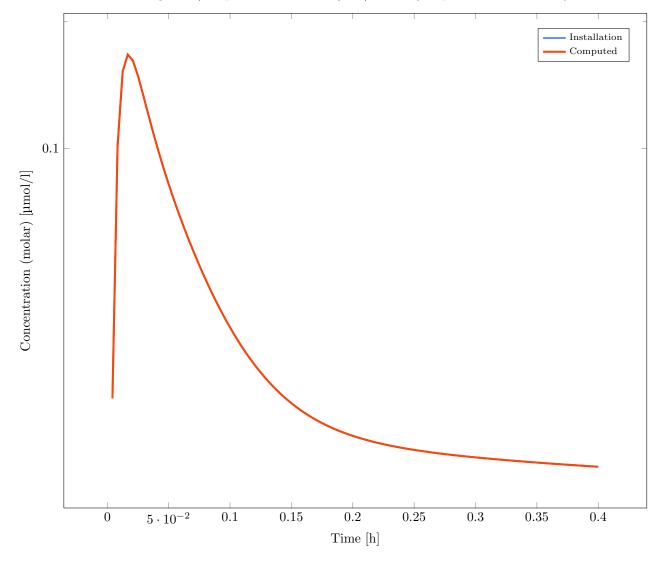


Figure 1.219

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

Result of the validation: Valid

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

# Organism|PeripheralVenousBlood|C12|Plasma (Peripheral Venous Blood) Installation Computed O.01 O.001 O.001 O.001

Figure 1.220

0.2

Time [h]

0.25

0.3

0.35

0.4

0.15

 $Simulation: Single ORAL\_C13\_2 Pores\_schmitt\_standard\_st$ 

Result of the validation: Valid

0

 $5\cdot 10^{-2}$ 

0.1

Output Path: Organism |PeripheralVenousBlood | C13 |Plasma (Peripheral Venous Blood)<br/> Deviation: 0



Figure 1.221

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

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)

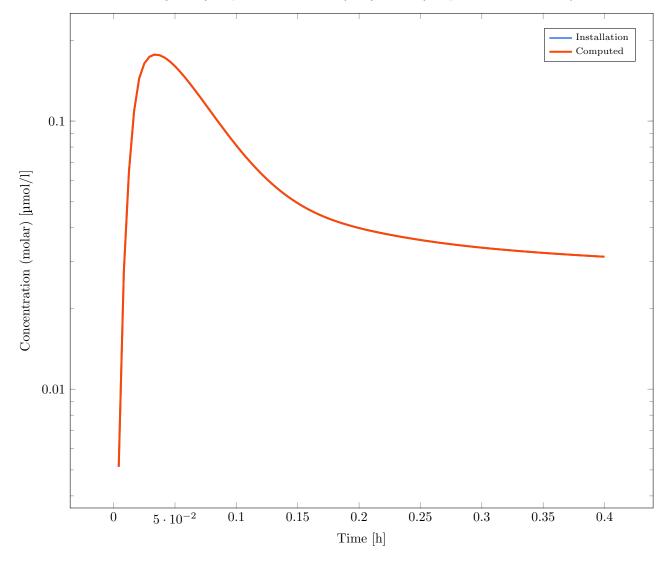
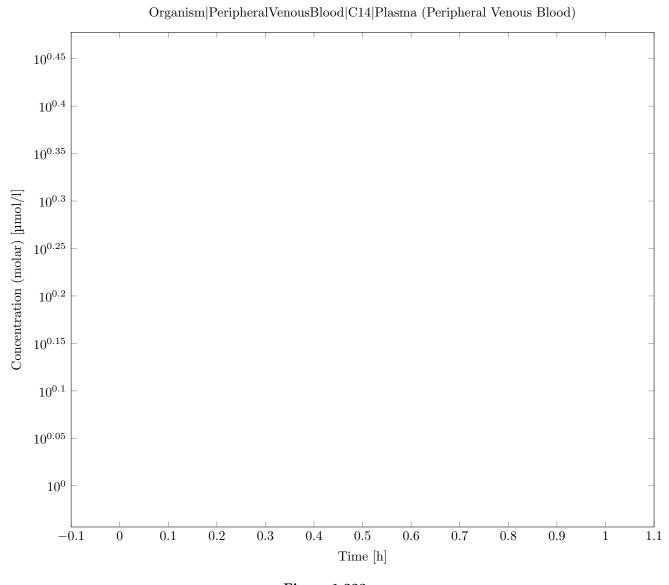


Figure 1.222

 $Simulation: Single ORAL\_C14\_2 Pores\_PT\_standard\_standard\_Single ORAL\_C14\_2 Pores\_PT\_standard\_standar$ standard

Result of the validation: Valid

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

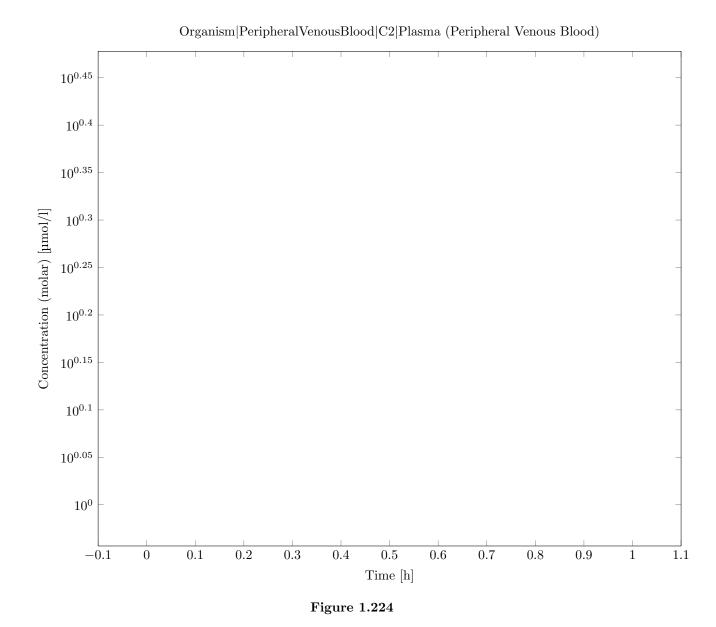


 ${\bf Figure~1.223}$ 

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

Result of the validation: Valid

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



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

Result of the validation: Valid

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



Figure 1.225

 $Simulation: Single ORAL\_C4\_2 Pores\_standard\_schmittnormalized\_standard\_Single ORAL\_C4\_2 Pores\_standard\_schmittnormalized\_standard$ 

Result of the validation: Valid

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

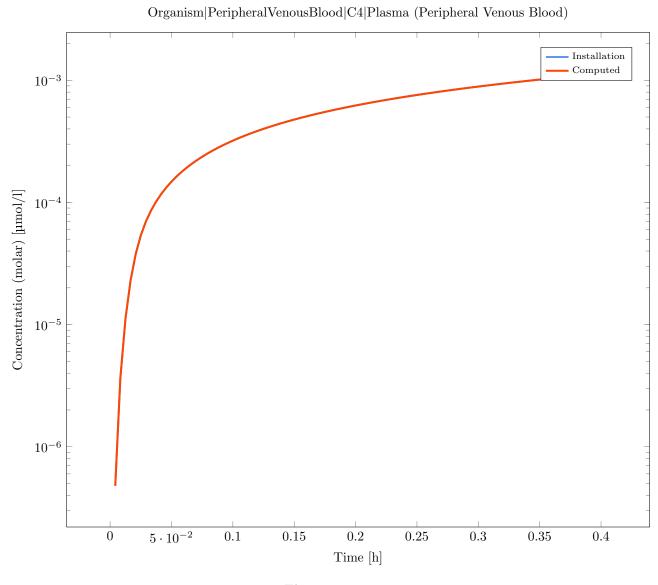


Figure 1.226

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

Result of the validation: Valid

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

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

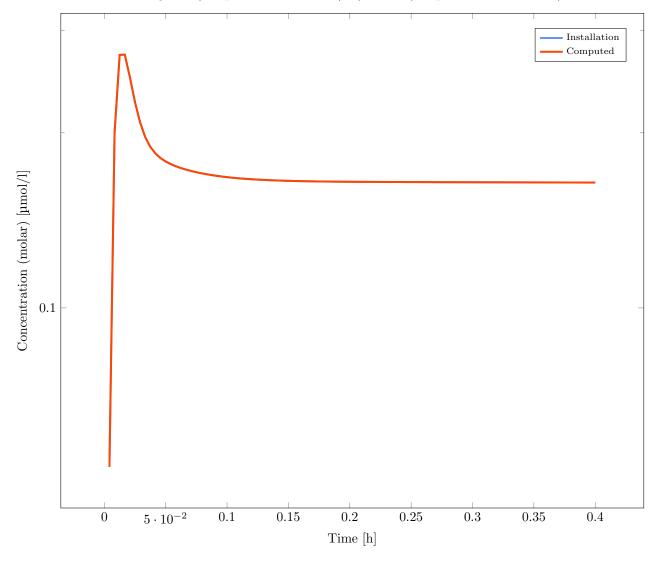


Figure 1.227

 $Simulation: Single ORAL\_C6\_4 Comp\_RR\_standard\_standard\_Single ORAL\_C6\_4 Comp\_RR\_standard\_st$ 

Result of the validation: Valid

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

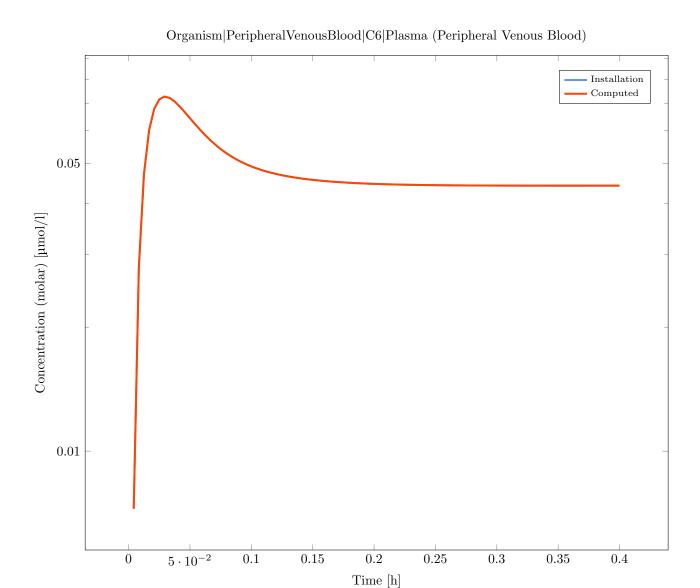


Figure 1.228

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

Result of the validation: Valid

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



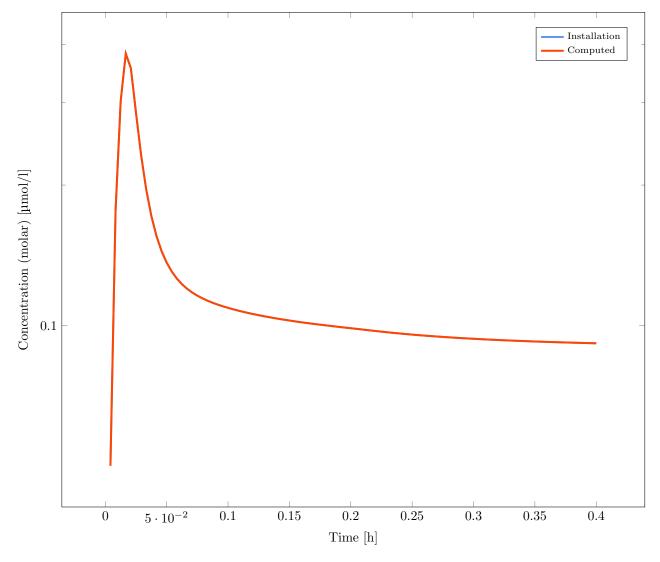


Figure 1.229

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

Result of the validation: Valid

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

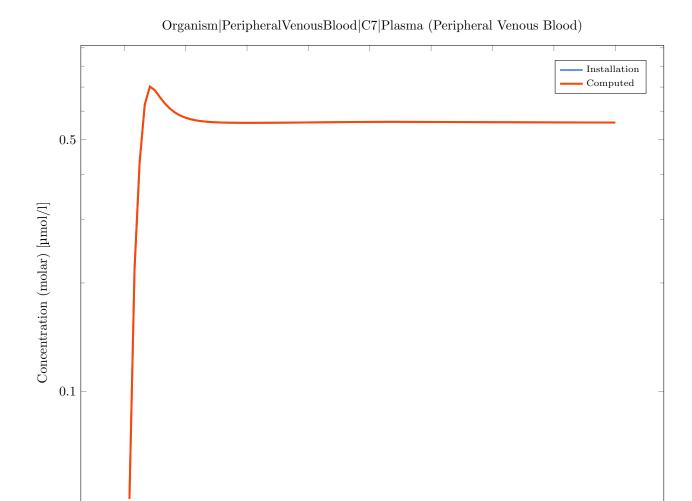


Figure 1.230

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

0.15

0.1

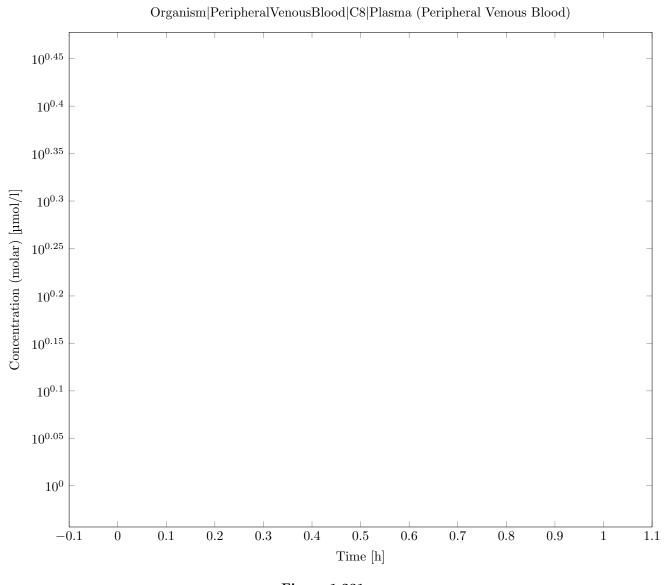
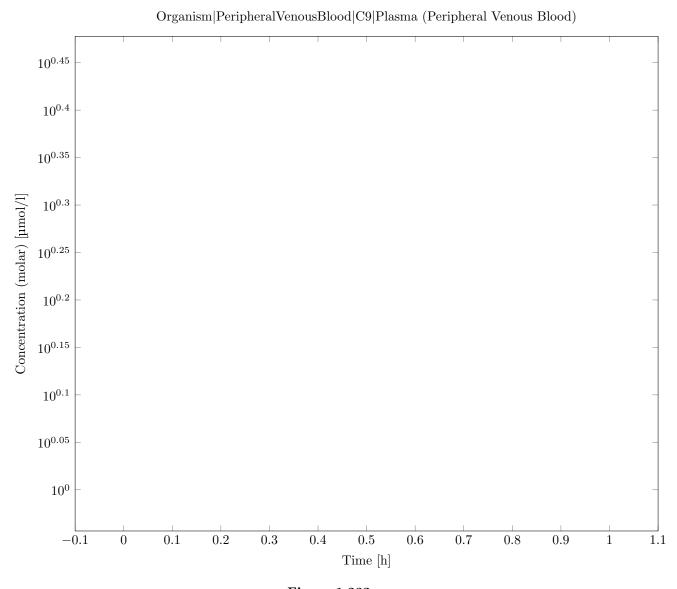


Figure 1.231

 $Simulation: Single ORAL\_C9\_2 Pores\_RR\_schmitt\_standard-Single ORAL\_SChmitt\_standard-Single ORAL\_Schmitt\_standard-Single ORAL\_Schmitt\_Standard-Single ORAL\_Schmitt\_Standard-Single ORAL\_Schmitt$ 

Result of the validation: Valid

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



 ${\bf Figure~1.232}$ 

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

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

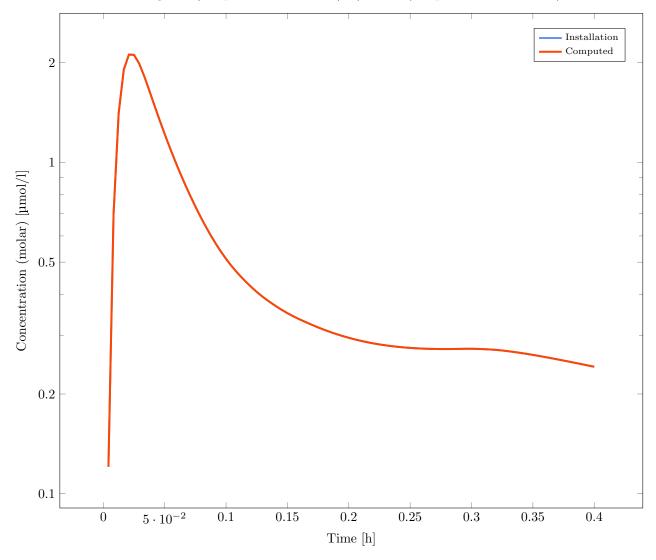


Figure 1.233

Simulation: Test  $18.1\_I2\_C1\_A1\_Config2$ -Test  $18.1\_I2\_C1\_A1\_Config2$  Result of the validation: Valid

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

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



Figure 1.234

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:  ${\bf 0}$ 

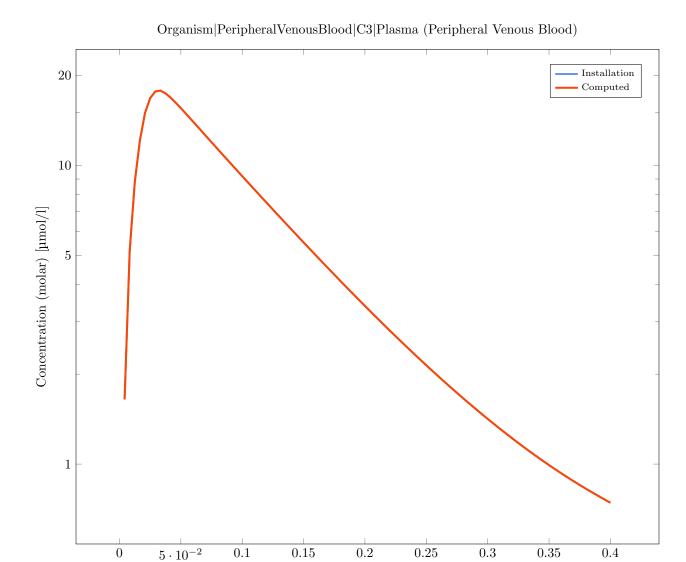


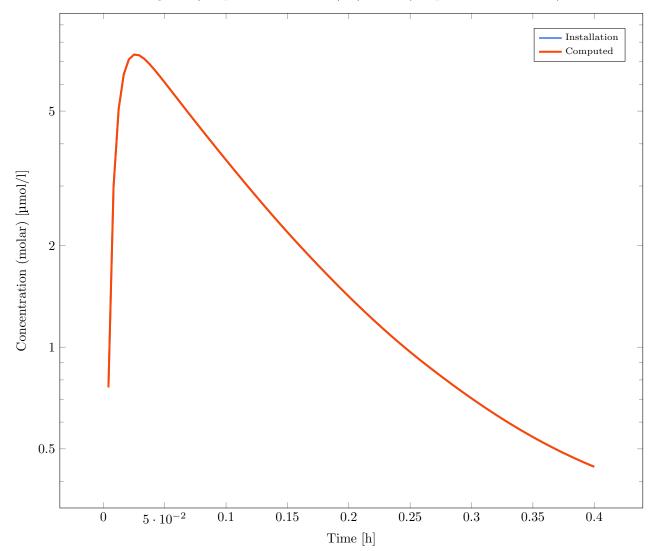
Figure 1.235

Time [h]

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:  ${\bf 0}$ 

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



 $Figure \ 1.236$