

# Pirana

The flexible modeling environment for NONMEM



## Quick Guide: Converting NONMEM differential equations to R-deSolve, Berkeley Madonna and Matlab

Version 1.1

### Scope

This Pirana Quick Guide explains how blocks of differential equations defined in \$DES can be converted to differential equations code that can be used for simulation using R/deSolve, Berkeley Madonna or Matlab.

### Introduction

- If a model contains differential equations as defined in a \$DES-block, these may be converted to R/deSolve, Berkeley Madonna or Matlab.
- This can be done by selecting a model, accessing the right-mouse-button menu and then selecting **Translate Model** (Figure 1).
- Next, files will be generated containing code to numerically solve these differential equations. The code can be used to perform simulations in these software packages.
- Pirana will automatically extract parameter values and use them in the simulation code. If the selected model has already been run in NONMEM, it will use the final parameter estimates. If a result file is not available, Pirana will use the initial parameter estimates. Note that parameter estimates are extracted for fixed effects only.
- Generated R/deSolve code will be automatically loaded in the defined R interface. Berkeley Madonna and Matlab code will be opened in the defined code editor. Examples of generated R and Berkeley Madonna code are depicted in Figures 2 and 3 respectively.
- An example of associated simulation output for the R/deSolve code is depicted in Figure 4.

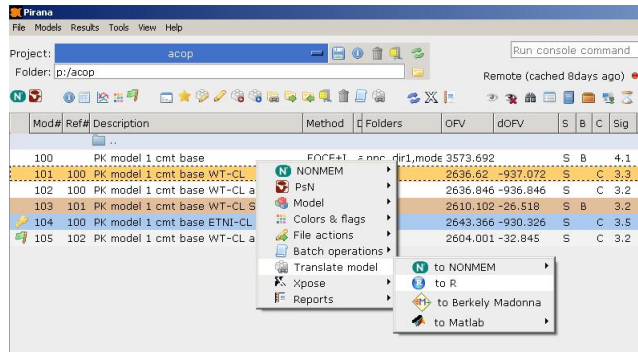


Figure 1: Translate options in Pirana

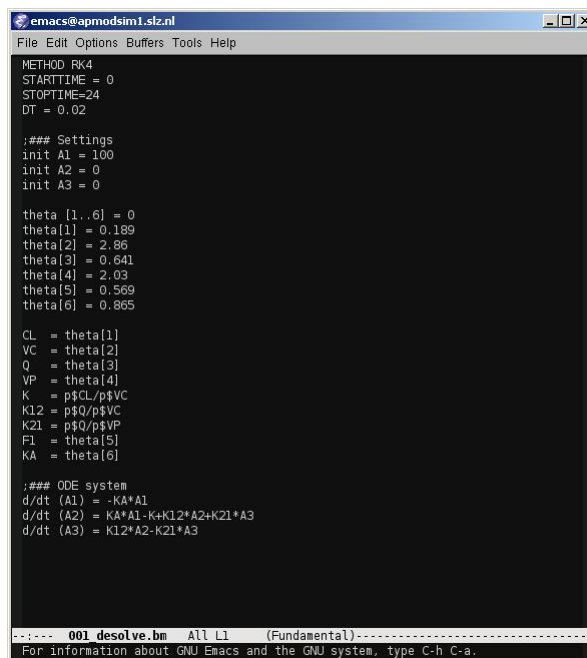


Figure 2: Generated BM code

```

emacs@apmodsim1.szl.nl
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## Pirana-generated deSolve code (RJK2011)
## Number of ODEs in system : 3
library (deSolve)
library (MASS)
library (lattice)

## Dose and time Settings
A_init <- c(0,0,0) # Initial state of ODE system
n_doses <- 3
dose_cmt <- 1
ii <- 24
dose_times <- seq (from = 0, by=ii, to=n_doses*ii)
dose_amts <- c(rep (100, n_doses), 0)
times <- seq(from=0, to=ii*n_doses, by=.5) # Integration window and steps:
obs_c <- c(1:3) # Observation compartments
n_ind <- 20
n_par <- 10

## Parameters
theta <- c(0.189, 2.86, 0.641, 2.03, 0.569, 0.865)
omega <- diag(.04, n_par) # 10% iiv in each parameter
etas <- mvrnorm(n = n_ind, mu=rep(0, n_par), Sigma=omega )

draw_params <- function (eta) {
  p <- list() # Parameter list
  p$CL <- theta[1] * exp(eta[1])
  p$VC <- theta[2] * exp(eta[2])
  p$Q <- theta[3] * exp(eta[3])
  p$VP <- theta[4] * exp(eta[4])
  p$K <- p$CL/p$VC
  p$K12 <- p$Q/p$VC
  p$K21 <- p$Q/p$VP
  p$F1 <- theta[5] * exp(eta[5])
  p$KA <- theta[6] * exp(eta[6])
  return(p)
}

## ODE system
--:-- 001_odesolve.R Top L1 (ESS[S] (none))-----

```

Figure 3: Generated R code

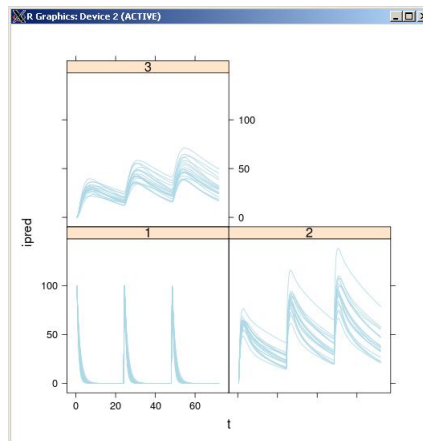


Figure 4: Graphical output of simulation R code