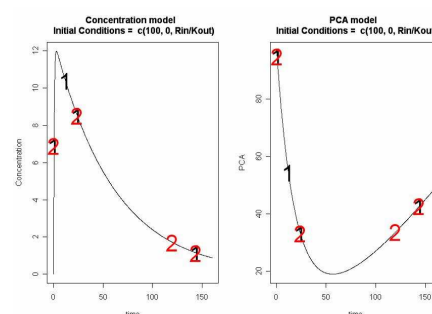
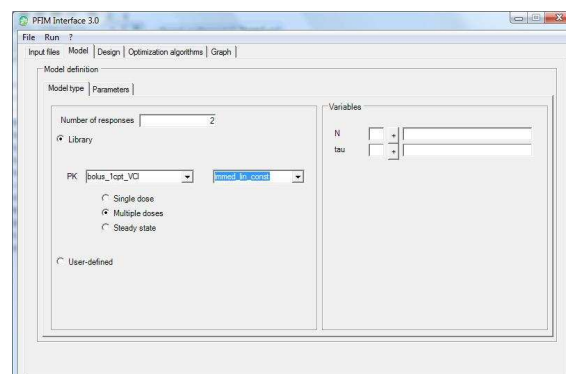




Population design evaluation and optimization with R functions

PFIM Interface 3.1

- Graphical user interface version
- Multiple response models
- Analytical form / differential équations
- Library of PK models
 - 1, 2 or 3 compartments
 - oral, IV or infusion administration
 - single or repeated doses or steady state
- Library of PD models
 - immediate response models
 - turnover models
- Optimisation Simplex/Federov-Wynn



```
PFIM 3.2
Project: Example
Date: Fri May 29 11:20:06 2009

***** INPUT SUMMARY *****

Analytical function models :
expression(log(exp(lf1) * exp(-exp(llambda1) * t) + exp(lf2) * exp(-exp(llambda2) * t))/log(10))

Population design:
Sample times for response: A      Number of subjects per group
c(1, 3, 7, 14, 28, 56)          100
c(1, 3, 7, 14, 28, 56)          100

Variance error model response A : ( 0.065 + 0 * f )^2
Between-subject variance model: Trans = 1

Covariate model :
NB: Covariates is additive on parameters
Covariate 1 : TRT ( llambda1 )
Categories References Proportions
(1)      0      *      0.5
(2)      1      *      0.5

Computation of the Fisher information matrix: option = 1

***** EXPECTED STANDARD ERRORS *****

----- Fixed Effects Parameters -----
Beta StdError CV
lf1 12.0000000 0.04066851 0.33899043 %
lf2 8.0000000 0.04124141 0.5155177 %
llambda1 -0.7000000 0.05555053 7.9357901 %
llambda2 -3.0000000 0.03943398 1.3144661 %
beta_llambda1_TRT_1 0.2623643 0.07858679 29.9533148 %

----- Variance of Random Effects -----
Omega StdError CV
lf1 0.3 0.03306247 11.02082 %
lf2 0.3 0.03396093 11.32031 %
llambda1 0.3 0.03089408 10.29469 %

----- Variance of residual error -----
SIG StdError CV
1 0.065 0.002290616 3.524025 %

***** EXPECTED POWER *****

With a Type I error equal to 0.05 :
Beta 95% CI Expected power
beta_llambda1_TRT_1 0.2623643 [0.11;0.42] 0.9159855

***** NUMBER OF SUBJECTS NEEDED *****

With a Type I error equal to 0.05 and with a given power equal to 0.8 :
Beta 95% CI Number_subjects_needed
beta_llambda1_TRT_1 0.2623643 [0.11;0.42] 140.8405
```

PFIM 3.2

- R scripts version
- Analytical form / differential équations
- Library of PK models
- Library of PD models
- Discrete covariates
- Computation of the predicted power of the Wald test
- Computation of the number of subjects needed
- Optimisation Simplex/Federov-Wynn

www.pfim.biostat.fr

UMR 738, INSERM-University Paris Diderot

Caroline Bazzoli, Sylvie Retout, Emanuelle Comets, Anne Dubois,
Hervé Le Nagard, France Mentré