Perl speaks NONMEM (PsN) and Xpose

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PsN³ Perl speaks NONMEM

http://psn.sf.net

http://xpose.sf.net

XPOSE

What is PsN?

PsN is a toolbox for population PK/PD model building using NONMEM. It has a broad functionality ranging from parameter estimate extraction from output files, data file sub setting and resampling, to advanced computer-intensive statistical methods and NONMEM job handling in large distributed computing systems. PsN includes stand-alone tools for the end-user as well as development libraries for method developers. PsN3 supports NONMEM7.

Features of PsN

- Parallel execution of multiple NONMEM runs on several systems; Sun Grid Engine, Platform LSF and Slurm (**new**). Support for NM7.2 parallelization (**new**).

- Automatic reruns with perturbed initial estimates.

- Covariate model building using the Stepwise Covariate Model building (scm), the **new** Least absolute shrinkage and selection operator (lasso) and the **new** Cross-Validation scm (xv_scm) programs. Automatic linearization (**new**) of covariate models for faster evaluation. The scm program has recently undergone a major revision for increased flexibility and stability.

- Model diagnostics using automated Numerical and Visual Predictive Check (npc/vpc). **New** features include handling of drop-out , missing observations and time-to-event models.

- Rapid sample size calculations for a likelihood ratio test-based power using the **new** mcmp program.

- Model comparisons and diagnostics using Stochastic Simulation and Estimation (sse).

- Model fit diagnostics using the Case-deletion Diagnostic, bootstrap and Log-likelihood Profiling programs.

- Creation of run records for NONMEM runs using the runrecord program.

- Replacing initial estimates in model files with final estimates from lst-files (reduced runtime) and renumbering table and msfo-file settings using program update_inits.
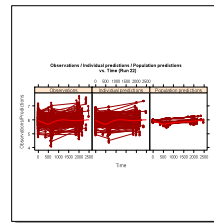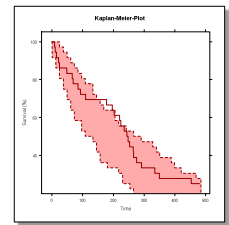
- Runs on Windows, OS X and Linux.

MCMP
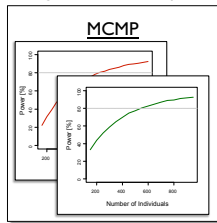
What is Xpose?

Xpose is an open-source population PK/PD model building aid for NONMEM. Xpose tries to make it easier for a modeler to use diagnostics in an intelligent manner, providing a toolkit for dataset checkout, exploration and visualization, model diagnostics, candidate covariate identification and model comparison. The current version of Xpose (4.2) supports NONMEM 7.

Features of Xpose

- Written in R – a language and environment for statistical computing and graphics similar to S-Plus. R is free, easy to use and very powerful. Because R is open source, new methods can be implemented and verified, with many methods based on peer reviewed literature.

- Simulation based diagnostics – Mirror Plots, Visual predictive Checks, Numerical predictive checks.

- Command line and menu-based interface – all functions in Xpose are available from the command line, resulting in:

  – Highly customizable, publication quality, plots

  – Scripts for automatic generation of PDF files containing goodness-of-fit plots after every NONMEM run.

  – Through the use of DCOM technology, Xpose can be run from any Windows application

- Calculation of CWRES for NONMEM VI.

Kaplan-Meier-Plot

Observations / Individual predictions / Population predictions vs. Time (Run 22)

Tools available in Xpose

- Data checkout
- Run summaries
- Diagnostic plots
- Variable summaries
- GAM covariate prediction
- Kaplan-Meier-Plots

Model Diagnostics using Cooperative Features of PsN and Xpose

Mirror Plots

- Mirror plots created by simulating data and calculating post-hoc estimates from the final model. PsN simulates, estimates and creates table files with the command:

      execute run22.mod –mirror_plots=1

- Xpose creates the mirror plots

Observations vs. Population predictions (Run 22)
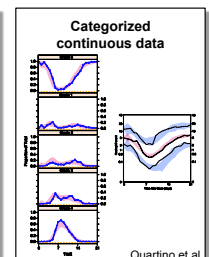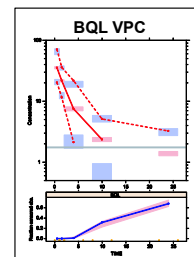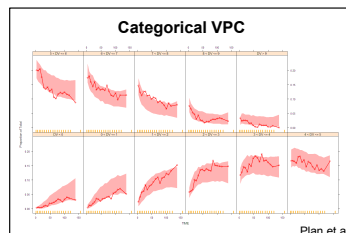Original data
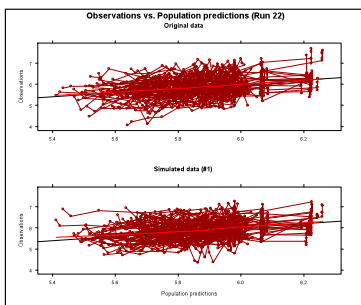
Simulated data (#1)

NPC/VPC

- PsN controls the simulation of new datasets and does the computations needed for the NPC or VPC

      vpc run22.mod –samples=1000

- Options to handle categorized data e.g.:

  - Categorical data

  - Censored continuous (e.g. BLQ) data

  - Categorized continuous data

Categorical VPC

Plan et al.

BQL VPC

Categorized continuous data

Quartino et al.

- Options to perform prediction corrected VPC (pcVPC) and prediction+variability corrected VPC (pvcVPC)

      vpc run22.mod –samples=1000 -predcorr

- Wide range of customizable binning and stratification settings

      vpc run.mod–stratify_on=DOSE

- Automatic handling of log transformed data

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