ICON: Symbol of Excellence Providing Standard of Excellence in Population Analysis Software

New Features of NONMEM® 7.4, Planned Release Date April 2017

PARALLELIZATION EXTENDED TO MORE TASKS
The evaluation of weighted residuals for the STABLE step. This can take a long time for Monte Carlo assessed EWRES and NPDE, so these would benefit from parallelization. To turn off parallelization:
$\text{STABLE ... PARAFILE=OFF}$
Evaluation of final empirical Bayes estimates of etas (EBE’s) after the estimation step (when FNLETA=1). To turn off parallelization during the FNLETA step,
$\text{FNLETA ... PARAFILE=OFF}$
Simulation can now be parallelized. Only on occasion is simulation so slow that it needs to be parallelized. So it is off by default. To turn it on:
$\text{SIM ... PARAFILE=ON}$
Permit constant seed patterns regardless of whether you choose parallelization or not with:
$\text{S$\text{SIM ... PARAFILE-ON}$}$
Nonparametric analysis can be parallelized. To turn it off,
$\text{S$\text{NONPFRAMFILE=OFF}$}$

IMPROVED SPEED FOR FOCE/ITS ANALYSES
The FAST option has been added to FOCE/ITS analysis, which can increase the speed of these analyses by up to 3-4 fold during the estimation of differential equation models, as well as speed up the covariance step by the same factor. The FAST method takes advantage of mapping analytical eta derivatives via MU referencing to evaluate theta analytical derivatives. This increases the speed and accuracy of derivatives required for FOCE estimation. For thetas that should not have inter-subject variability, provide a Mu-reference equation, and set OMEGA to 0. For example:
$\text{SPK}$
$\text{MU_1=THETA(1)+THETA(2)*LOG(AGE)}$
$\text{MU_2=THETA(3)}$
$\text{MU_3=THETA(4)}$
$\text{...}$
$\text{SOMMA BLOCK(2)}$
$\text{0.2}$
$\text{0.01 0.2}$
$\text{SOMMA (0.0 FIXED)}$
$\text{S$\text{EST METHOD=1 INTERACTION FAST ...}$}$
Consider a problem with eight parameters, three differential equations, 50 subjects. Computation Time is 3-4 fold faster with FAST option, compared to default.

IMPROVEMENTS IN IMP, SAEM, BAYES ANALYSIS
• A new kernel has been added to the Bayesian sampling of individual parameters, that reduces the correlation between Metropolis-Hastings generated samples, for BAYES and SAEM methods.
• A Hamiltonian/No U-Turn Sampling (NUTS) algorithm has been implemented for BAYES analysis, similar to that in the software Stan. This algorithm increases the efficiency of Markov-Chain Monte Carlo Bayesian sampling among population and individual parameters, by reducing the statistical correlation between samples.
• New algorithms for creating multivariate samples for importance sampling are offered, such as mixed-normal and additional t-distribution methods.
• The GRDQ option provides faster importance sampling analysis when several thetas not mu-referenced need to be gradient assessed.

BUT WAIT, THERE’S MORE...
• $\text{SSIM REWIND}$ feature allows original data set to be used for all sub-problems.
• $\text{SSIM NOSUPRESET}$ feature allows simulation seeds not to be reset with each iteration of a super-problem.
• Read MSF files generated from earlier versions of NONMEM
• Omegas and Sigmas may have inverse Wishart or gamma distribution priors.
• Thetas may have normal or t-distribution priors.

ADDITIONAL TABLE OUTPUT CONTROL
Specific table records may be excluded from being printed. A data item or defined variable may be identified on a STABLE record as an EXCLUDE_BY variable, which if not 0, will exclude the record. For example:
$\text{S$\text{PK ...}$}$
$\text{EXCL=0}$
$\text{IF(ID,GE,45,AND.ID.LE,53) EXCL=1}$
$\text{...}$
$\text{S$\text{TABLE ID TIME DV IPRED CL V1 Q V2 ETAS(1-LAST) EXCLUDE_BY EXCL NOAPPEND FILE=extendible.par NOPRINT}$}$
The table extendible.par will not list records from subjects 45 to 53. If more than one exclusion variable is listed, then if any of these have a non-zero value, the record will be excluded.

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