nonmem2rx / babelmixr2 **automatically translates** NONMEM to a **qualified** rxode^2/nlmixr^2 model/fit

A nlmixr^2 model can **generate docx/pptx, VPCs** or even **debug NONMEM** models

nlmixr2, rxode2 and NONMEM: interchangeable models using babelmixr2 and nonmem2rx

Introduction: *nlmixr2* (www.nlmixr2.org) is an open-source R package, freely available on CRAN[1] and GitHub[2]. NONMEM[3] is a commercial tool for non-linear mixed effects modeling and has been used since 1989.

Objective:
Allow bidirectional translation with nlmixr2/rxode2 and NONMEM.

Methods:
babelmixr2[4]:
- Translate nlmixr2 to mu-referenced NONMEM models
- After NONMEM has run, read in parameters and create a nlmixr2 fit
- Compare the IPRED/PRED values between nlmixr2 and NONMEM

nonmem2rx[5]:
- Parse NONMEM & create rxode2 model
- Compare IPRED/PRED/IWRES between rxode2 and NONMEM
- If nlmixr2 compatible residual specification is not captured, allow manual edits that can be Qualified as well

babelmixr2 and nonmem2rx
- Use babelmixr2 to create nlmixr2 fit from the nonmem2rx output

Validation Models of translation:
- We tested against the models in Perl Speaks NONMEM, DDMoRe, and 3 NONMEM tutorials (~400 models)

Results:
- babelmixr2 models and imported nonmem2rx mdels helped diagnose NONMEM rounding errors and could add covariances
- All but the expected (unsupported) model types were imported to rxode2:
  - Perl Speaks NONMEM validation suite[6]: 203 models (193 translated, 10 with expected errors)
  - DDMoRe model scrapings[7]: 131 models(104 translated, 27 with expected errors)
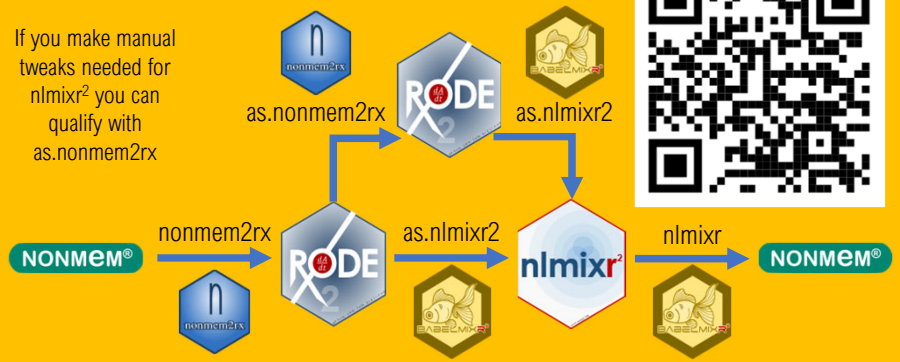 - NONMEM tutorials[8, 9, 10]: 44 models (41 translated models, 3 with expected errors)

Conclusions:
These results show that these tools can be used to speed up model development time while instantaneously knowing how well the translation tools are performing relative to one another.
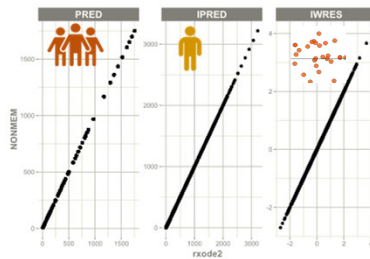
References:
[1] https://cran.r-project.org/package=nlmixr2
[2] https://github.com/nlmixr2/nlmixr2
[3] Beal SL et al. 1989-2011. NONMEM Users Guides. Icon Development Solutions, Ellicott City, Maryland, USA.
[4] https://github.com/nlmixr2/babelmixr2
[5] https://github.com/nlmixr2/nonmem2rx
[6] https://uupharmacometrics.github.io/PsN/
[7] https://github.com/dpastoor/ddmore_scraping
[8] https://doi.org/10.1002/psp4.12713
[9] https://doi.org/10.1002/psp4.12404
[10] https://doi.org/10.1002/psp4.12422

If you make manual tweaks needed for nlmixr^2 you can qualify with as.nonmem2rx

as.nonmem2rx   as.nlmixr2

NONMEM → nonmem2rx → as.nlmixr2 → nlmixr → NONMEM
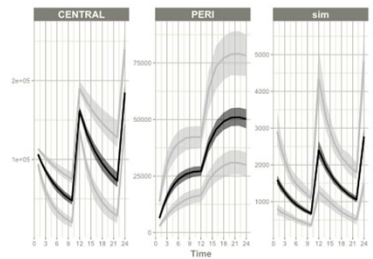

NONMEM to rxode^2/ nlmixr^2 conversion takes four functions
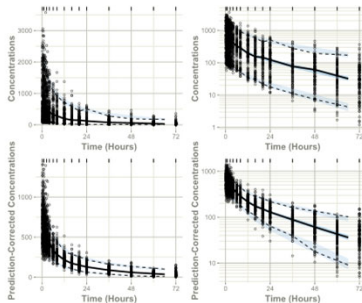
Qualified: population, individual and residual differences are small

Simulate Trials with Uncertainty & Derived Parameters

Create VPC with nlmixr2::vpcPlot() and doc/ppt with nlmixr2report::report_fit()

Read/Debug NONMEM with rounding errors & add covariance nlme::getVarCov()

I don't know if I will ever get a model without rounding errors or a covariance step

Try nonmem2rx / babelmixr2

Authors
Matthew Fidler[1,8], William S. Denney[2, 8], John Harrold[7, 8], Richard Hooijmakers[4, 8], Rik Schoemaker[3, 8], Max Taubert[1, 8], Mirjam Trame[5, 8], Theodoros Papathanasiou[6, 8], Justin Wilkins[3, 8]

[1]Novartis Pharmaceuticals, USA, [2]Human Predictions, USA, [3]Occams, The Netherlands, [4]LAP&P Consultants, The Netherlands, [5]Certara Strategic Consulting, USA, [6]GSK, Switzerland, [7]Seagen, [8]The nlmixr2 team

Sock Puppet from Myles McCoy from the Noun Project