Installing nlmixr for Windows

Rtools is required to supply the compiler for packages like nlmixr in which R code is converted to C. Rtools34.exe (version 3.3.x and later) can be downloaded from http://cran.r-project.org/bin/windows/Rtools/. Install by double-clicking the file and following the prompts. Select the default items, and make sure the toolset is installed in C:\Rtools: do not rename the directory to something else, and remove the 32 bit toolchain option (so keep "R toolset", "Cygwin DLLs", and "R 3.3.x+ 64 bit toolchain").

During the installation process, in the "Select additional tasks" window, check the box for "Edit the system path: Current value:", and ensure the path contains the following items:

```
C:\Rtools\bin;
C:\Rtools\mingw 64\bin;
```

Then install your preferred R package in the 64 bit version if not yet installed (e.g. download microsoft-r-open-3.3.1.msi, from http://mran.revolutionanalytics.com/download/, and install R by double-clicking microsoft-r-open-3.3.1.msi. Do not install the 32 bit version of R so make sure you uncheck the 32-bit option! Ensure that your path points to the R-installation directory, e.g.:

```
C:\Program Files\Microsoft\MRO-3.3.1\bin\x64\
or
C:\Program Files\R\R-3.3.1\bin\x64\
```

If you want to make use of SAEM functionality as well -at this stage- you will need to change the default permissions of the R installation directory. In the windows explorer, right click the directory (e.g. C:\Program Files\Microsoft\MRO-3.3.1\) or C:\Program Files\R\R-3.3.1\) and Select "Properties/Security", then click the "Edit" button with the shield next to it, then click "Users (ComputerName\Users)", click the check box under "Full control", click "Apply", and "OK" twice.

Then start R and run the following commands:

```
install.packages("devtools")
library(devtools)
```

and install the source code packages for RxODE and nlmixr as provided on the GitHub page using the commands below. There will be numerous warning messages but these can be ignored:

```
install_github('nlmixrdevelopment/RxODE')
install_github('nlmixrdevelopment/nlmixr')
```

This concludes the installation of nlmixr on Windows.

Installing nlmixr for OS X

Rtools is not available on OS X, and is replaced By Xcode and the command line tools, so first install Xcode 8.1 and the command line tools, then install devtools:

```
install.packages("devtools")
library(devtools)

and then run:

devtools::install_github("nlmixrdevelopment/nlmixr", repos = NULL, type =
"source")
```

```
devtools::install_github("nlmixrdevelopment/RxODE", repos = NULL, type =
"source")
```

If these steps fail, you can try the following instead:

```
devtools::install_github("hadley/devtools")
devtools::has_devel()

install.packages("Rcpp", dependencies = TRUE)
install.packages("RcppEigen")
install.packages("RcppArmadillo")
install.packages("BH")
install.packages("coda")
install.packages("brew")
install.packages("inline")
install.packages("lbfgs")

devtools::install_github("nlmixrdevelopment/nlmixr", repos = NULL, type =
"source")
devtools::install_github("nlmixrdevelopment/RxODE", repos = NULL, type =
"source")
```

Demo files

The demo files from the vignette can be run using VignetteDemo.R found at https://github.com/nlmixrdevelopment/nlmixr/tree/master/vignettes

A short demo illustrating use of nlme and SAEM is available at: https://github.com/nlmixrdevelopment/nlmixr/tree/master/inst/examples/LiveDemo

and all the nlmixr commands and files used for the nlmixr poster at AcoP7 (http://www.occams.eu/assets/pdf/PosterACoP2016.pdf) are available at: https://github.com/nlmixrdevelopment/nlmixr/tree/master/inst/examples/ACoP7poster