



# CAMPSIS: A GENERIC, EASY-TO-USE AND INTUITIVE PK/PD SIMULATION PLATFORM BASED ON R PACKAGES RXODE, RXODE2 AND MRGSOLVE

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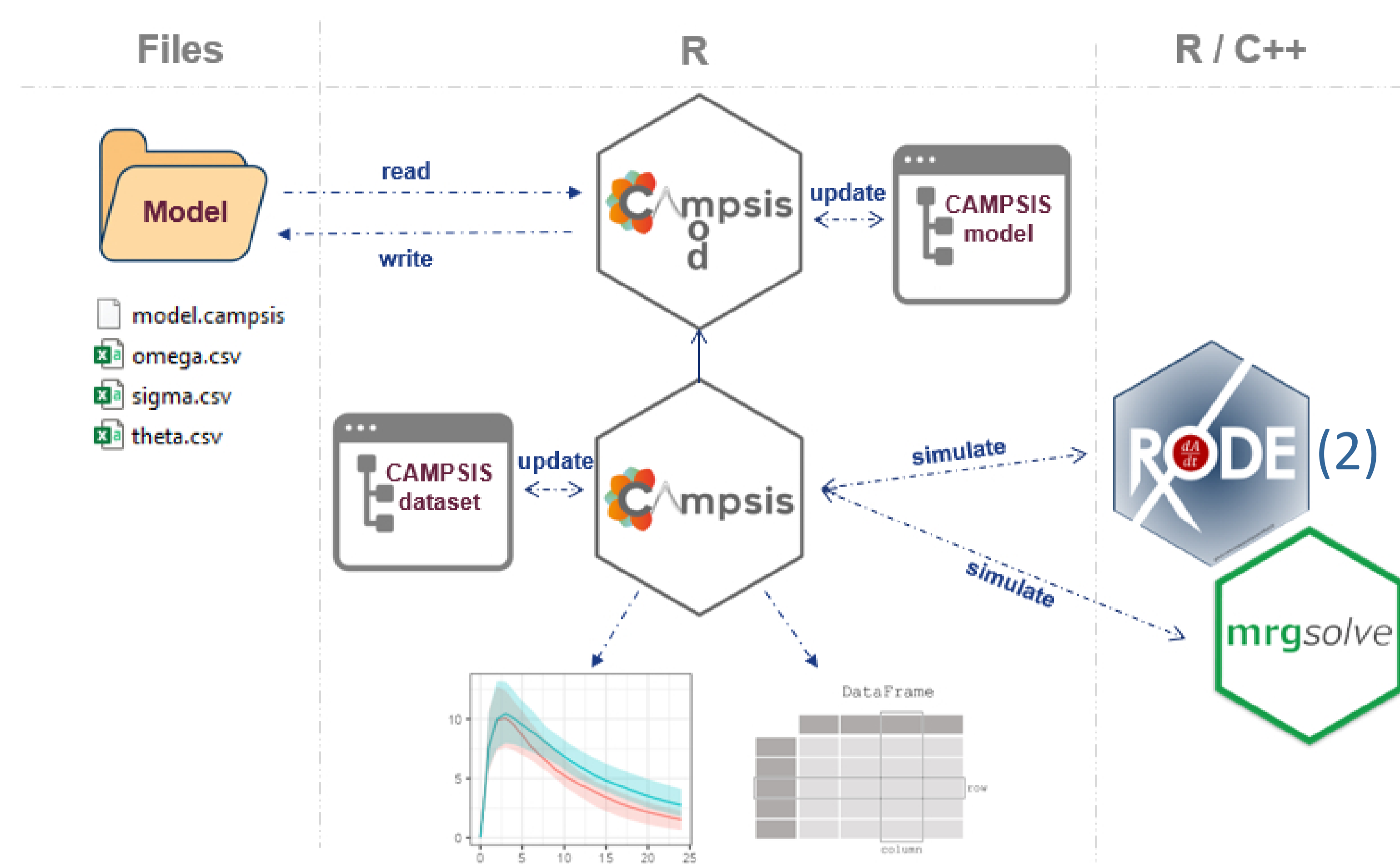
## INTRODUCTION

Campsis ([www.campsis.org](http://www.campsis.org)) is an open-source PK/PD simulation suite running in R, freely available on CRAN [1] and GitHub [2], using RxODE [3], rxode2 [4] or mrgsolve [5], and designed to facilitate the simulation of population PK/PD models.

### Objectives

Overall, the goal is to define a **common language** for performing PK/PD simulations, whatever simulation engine is chosen. This is achieved by:

- 1) Creating an **API** to work with pharmacometric models (*campsismod*)
- 2) Creating an **API** to work with pharmacometric datasets (*campsis*)
- 3) Building an **abstraction layer** on top of RxODE, rxode2 and mrgsolve



## SETUP

To fulfil the objectives, the S4 object system provided in R was used. This object system is relatively close to other object-oriented programming languages (like Java, C++/C#, Python) and allows to define classes, inheritance and generic functions, which are the building blocks to design complex software.

**A pharmacometric model** is defined as an S4 object containing a series of code records (MAIN, ODE, ERROR, etc.), similarly to NONMEM [6]. Each code record contains model statements. Model statements can be simple equations, IF-statements, comments, or ordinary differential equations (ODE's). A model also contains the definition of all the parameters (THETA, OMEGA & SIGMA) and finally all the compartment properties: infusion duration/rate, bioavailability, lag time and initial values. The model can be adapted from the files or directly in the R environment using the numerous easy-to-use functions from the API [2].

**A pharmacometric dataset**, instead of commonly being stored as tabular data, is more elaborated and implemented as a complex S4 object. This object encapsulates the whole dataset by defining a series of independent layers: one or more treatment arms, boluses and infusions to be administered, observations, model covariates (with all sorts of predefined distributions), inter-occasion variability (IOV), dose adaptation formulas and occasions. This complex dataset is organized in the background without the user realizing it.

While *campsismod* is responsible for the conversion of the Campsis model to RxODE, rxode2 or mrgsolve, the package *campsis* is in charge of exporting the Campsis dataset into tabular data and calling the simulation engine with the proper arguments, depending on the user-chosen simulation configuration. This configuration includes, among others: the variables to be output, the number of replicates to be simulated, a seed value, a list of scenarios to be run, a list of interruption events and a post-processing function to be applied on the simulation output.

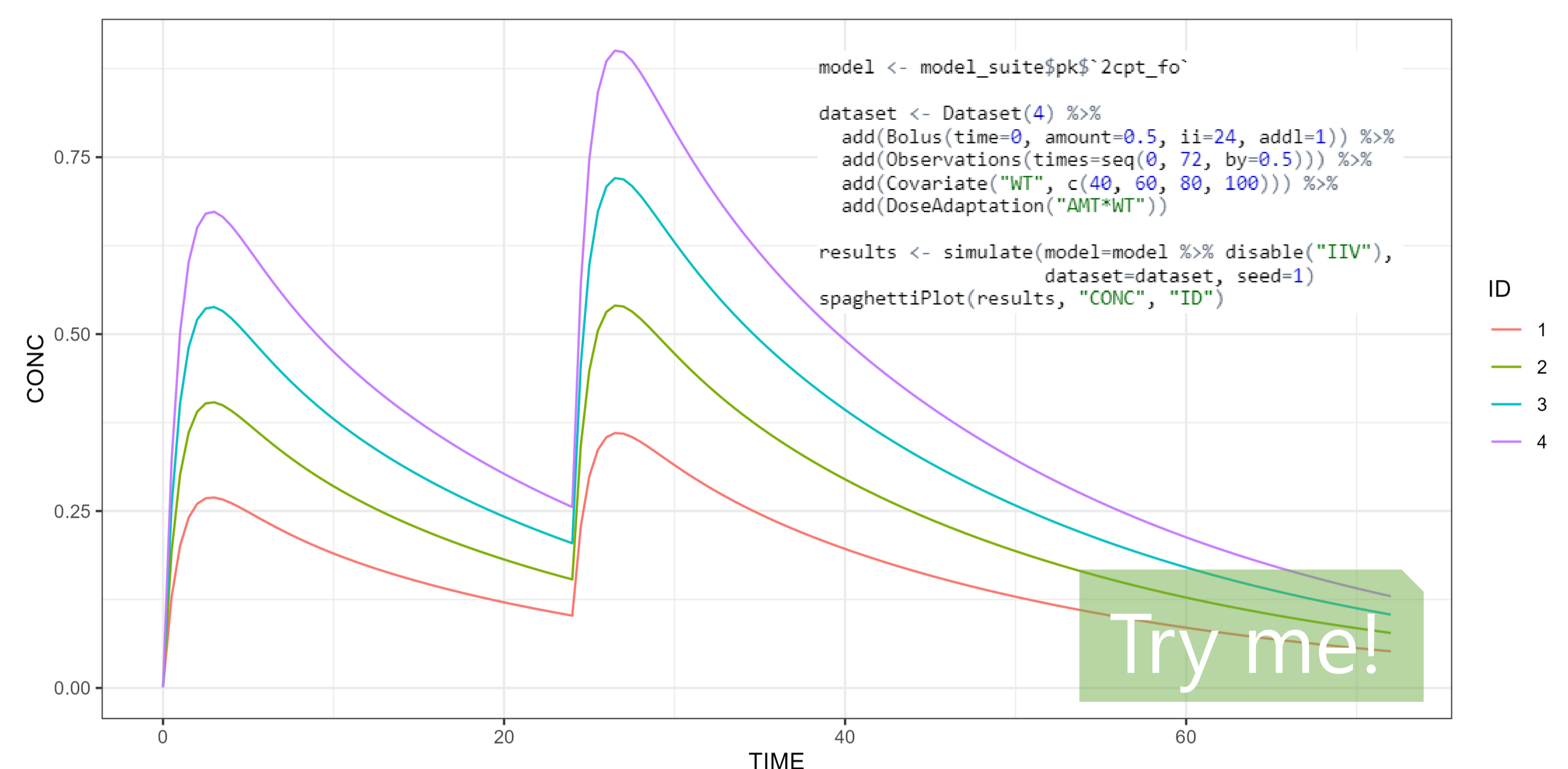
## RESULTS

Packages *campsismod* and *campsis* were released on **CRAN** for the first time in February 2022. These packages come with extensive and reproducible documentation [2] to facilitate self-learning. In addition, a **model suite** comprising more than 100 models of all kinds (PK, PD, TMDD, etc.) is available in *campsismod* for quick simulations.

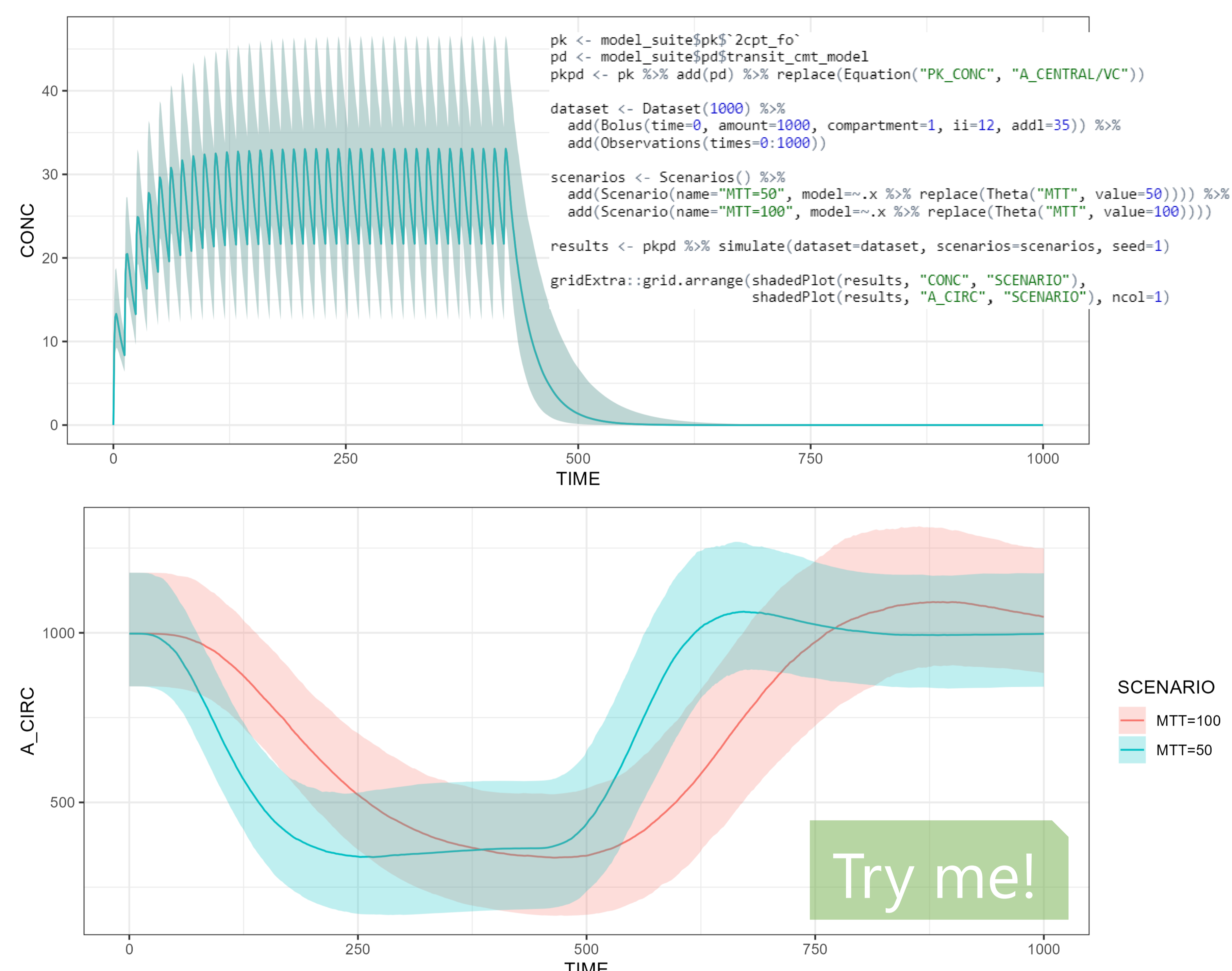
These packages are extensively tested and currently both show a code coverage of 90% [7][8], meaning almost all source code is executed during test runs. Simulation tests are executed with all three simulation engines and compared to reference results, ensuring they all provide strictly identical results.

## EXAMPLES

### 1 - Simple dose adaptation



### 2 - PK/PD simulation (maturation compartments)



## REFERENCES

- [1] <https://cran.r-project.org/web/packages/campsis/index.html>
- [2] <https://calvagone.github.io/> or [www.campsis.org](http://www.campsis.org)
- [3] <https://github.com/nlmixrdevelopment/RxODE>
- [4] <https://github.com/nlmixr2/rxode2>
- [5] <https://github.com/metrumresearchgroup/mrgsolve>
- [6] <https://www.iconplc.com/innovation/nonmem/>
- [7] <https://app.codecov.io/gh/Calvagone/campsismod>
- [8] <https://app.codecov.io/gh/Calvagone/campsis>

