R Based Shiny App To Simulate PKPD Profiles Using TMDD Models

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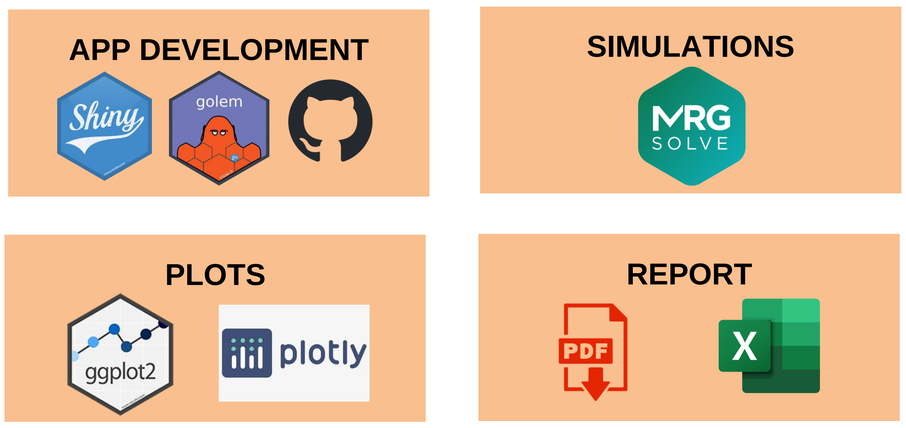
Background and Objectives

- Monoclonal antibodies (mAbs) are an important class of therapeutic agents.
- Possess a high degree of target selectivity.
- Many exhibit nonlinear distribution and elimination, influenced by binding to their target.
- Data from several sources are often combined to guide dose selection and study designs from first time in human studies.
- Target engagement (percent change in free target from baseline) is a key component that can inform dose selection for first time in human and/or Phase 2 studies.
- R shiny applications can save time, financial resources, minimize programming errors and increase reproducibility.

Objective: To develop an R Shiny application that can be used to (1) simulate and visualize PKPD profiles of mAbs to support design of PKPD studies and (2) explore possible range of initial estimates for PKPD modelling.

Methods

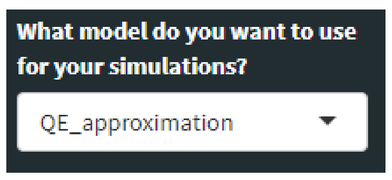
- A shiny application was developed in R software.
- Simulations are performed using the mrgsolve package.
- Golem R package was used to guide application development and structure of the back-end directories.
- Used a modular programming approach to allow reuse of application components and future expansion of the app.
- Plots were generated using ggplot2 and plotly.

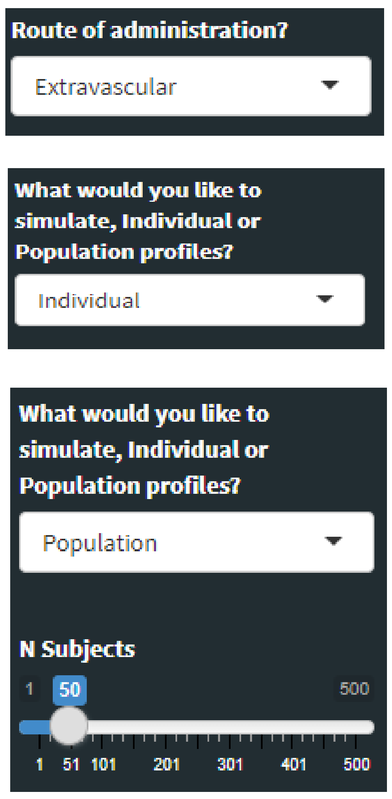


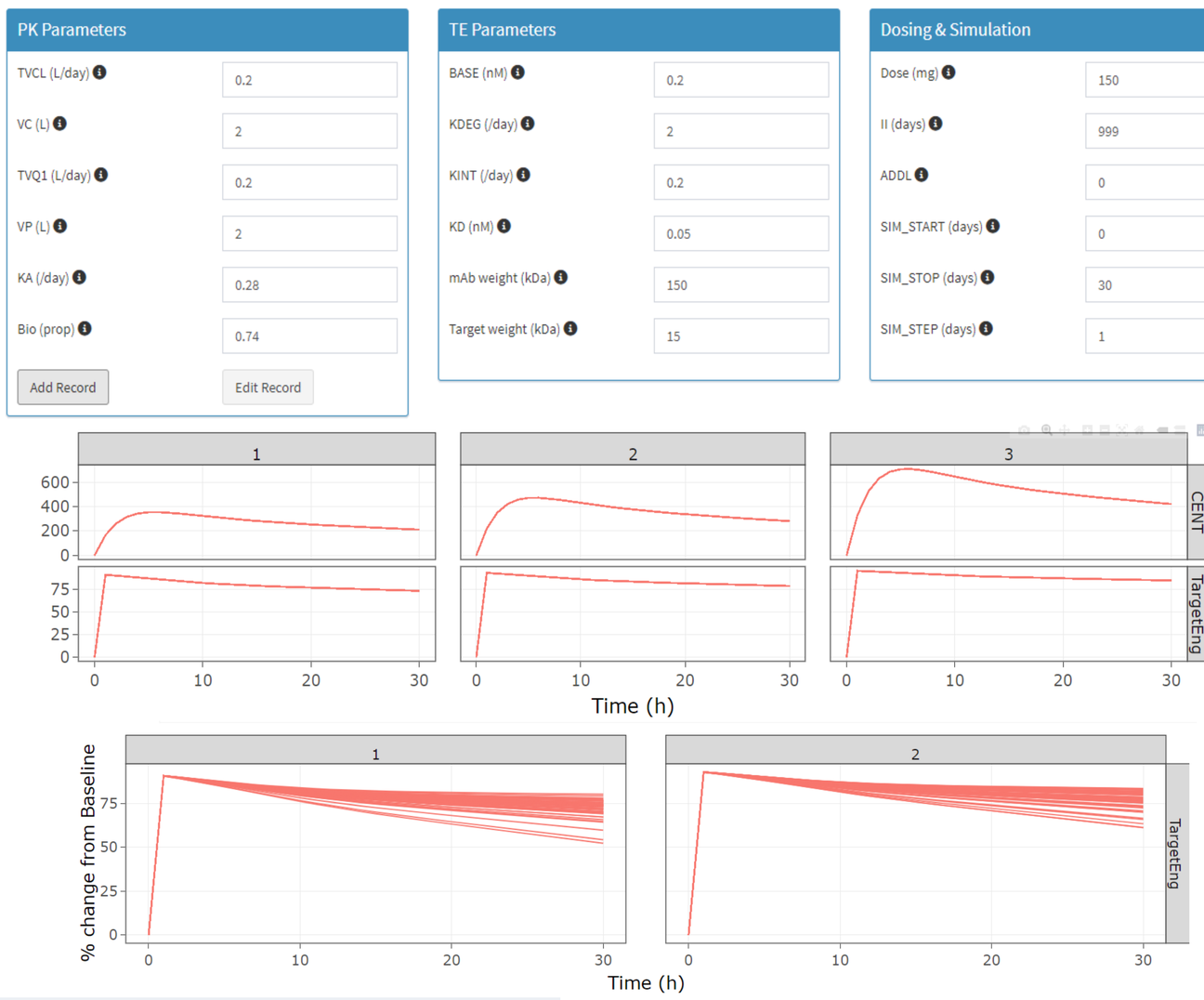
The App

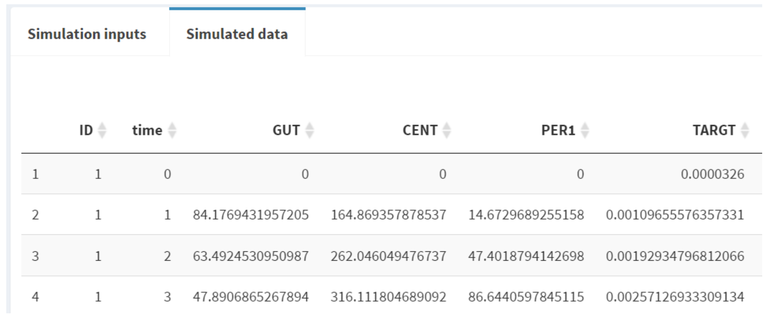
The user interface is built to accept:
- PK parameters
- PD parameters
- Dosing regimens

- Supports both IV and extravascular dosing.
- User can build and edit a data frame of dosing regimens.
- Provides flexibility for different quantities to be plotted.
- Summaries such as AUC, Cmax, Cmin, and % target engagement.
- An option to generate a report has been included as well as downloading simulated data for further manipulation.

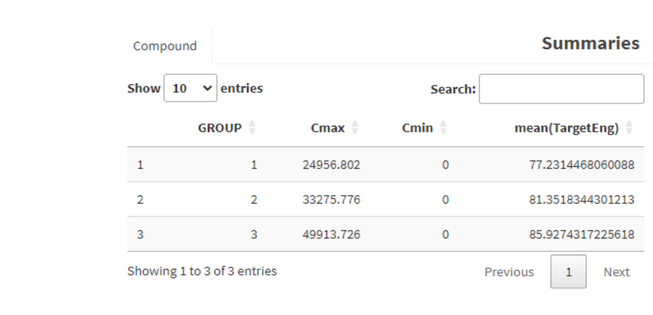








	ID	time	GUT	CENT	PER1	TARGT
1	1	0	0	0	0	0.0000326
2	1	1	84.1769431957205	164.869357878537	14.6729689255158	0.00109655576357331
3	1	2	63.4924530950987	262.046049476737	47.4018794142698	0.00192934796812066
4	1	3	47.8906865267894	316.111804689092	86.6440597845115	0.00257126933309134



	GROUP	Cmax	Cmin	mean(TargetEng)
1	1	24956.802	0	77.2314468060088
2	2	33275.776	0	81.3518344301213
3	3	49913.726	0	85.9274317225618

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Beta Testing

Interested in helping us better our app?

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Discussion and Conclusions

This app is a useful tool for modelers/ pharmacologists to support the design of clinical trials and to visualize the influence of different parameters on the PK or PD profiles following dosing of a monoclonal antibody. By comparing simulated PK data with experimental data, researchers can use realistic initial parameter estimates during model development.

Next Steps

1. Add a **library of models** of previously published mAbs
2. Use app to promote the **development of biosimilars**
3. Guide the design of **bioequivalence assessment studies**

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