Simulx - GUI: a flexible and user-friendly application for simulations

LIXOFT
A SIMULATIONS PLUS COMPANY

Monika Twarogowska (1), Géraldine Ayral (1), Pauline Traynard (1), Jonathan Chauvin (1)

(1) Lixoft, Antony, France. Contact: jonathan.chauvin@lixoft.com

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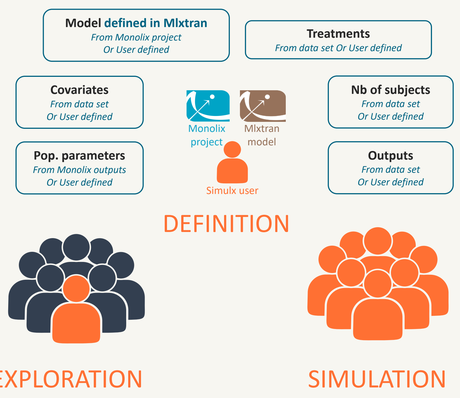
INTRODUCTION

Simulx – GUI 2020

- Advanced simulator of clinical trials and decision-making tool
- Easy-to-use and interactive interface
- Intuitive workflow
- Interconnected with MonolixSuite applications
- Flexible in building simulation scenarios
- Advanced computational capabilities with C++ engine
- Immediate visual feedback
- Export of plots and results

How does it work?



Example

Remifentanil PKPD dataset - opioid analgesic drug used for sedation tested on 65 healthy adults who received an infusion at different rates; *concentration of the drug* and *EEG measurements*

Clinical study questions:

1. What percentage of individuals reach the efficacy target at different dose levels?
2. What is the uncertainty of the result in a small size trial and how does it change if more individuals are recruited?

Methods:

Model: PKPD model from the Monolix library with the population parameters estimated in Monolix

Simulations: qualitative and quantitative comparison of two arms with different treatments and different number of subjects

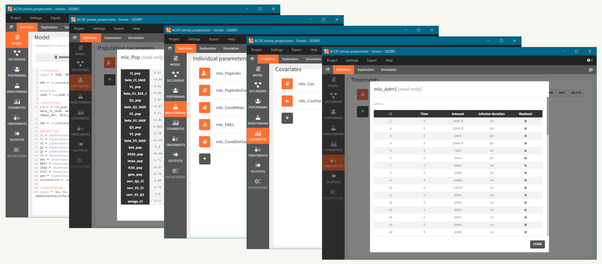
Monolix

Simulx

DEFINITION & EXPLORATION

Import from Monolix

Starting a Simulx project from a Monolix project loads automatically the model developed in Monolix and creates all simulation elements with values estimated by Monolix or read from a dataset.

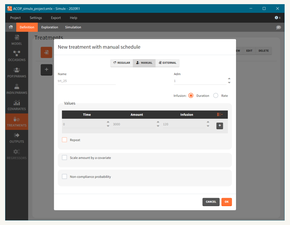


Definition of simulation elements

Creating new simulation elements is very flexible using single values, regular grids, distributions or external files.

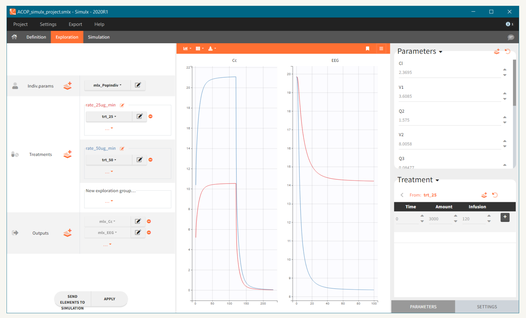
New treatment elements:

- Infusion for 2h with different infusion rates: 25 or 50 ug/min
- Definition of the infusion starting time, the dose amount and the infusion duration
- Other options: cycles, covariate scaling, non-compliance probability



Exploration

Exploration tab allows to simulate a typical individual to investigate different treatments and effects of model parameters.

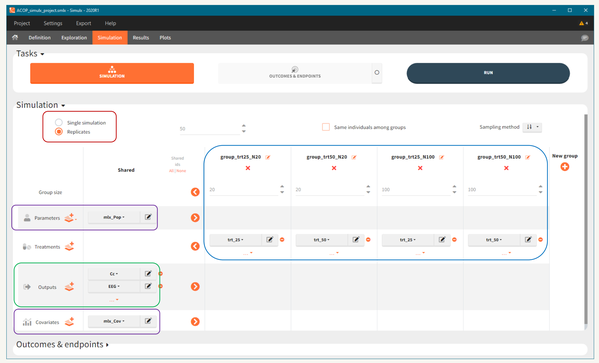


SIMULATION

Simulation of a clinical trial with two treatments

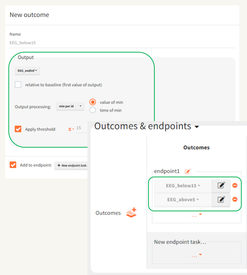
The Simulation tab aim is to simulate populations of individuals in groups, either one or several. It contains a simulation scenario builder which uses simulation elements defined in the "Definition" tab.

- Four groups with different treatments (25 or 50 µm/min infusion rate) and different number of individuals (20 or 100)
- Individual parameters simulated using population parameters estimated by Monolix and covariates from the original dataset
- Output: model predictions for the concentration and EEG
- Several simulations of the scenario (replicates) for uncertainty assessment

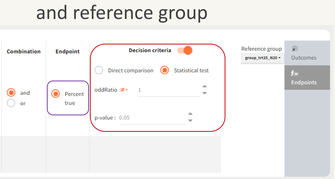


Efficacy target

The Outcomes & Endpoints task is used for post-processing of the simulation outputs. Several outcomes can be combined into an endpoint, and several endpoints can be created. Statistical tests compare endpoints between groups.



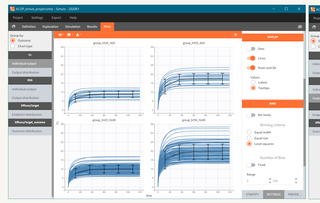
- Outcome: EEG at time 120 min in the EEG target range [5 , 15] Hz
- Efficacy endpoint: percentage of individuals in the EEG target
- Stat test: Fisher's exact test for the odds ratio between test groups and reference group



PLOTS & RESULTS

Individual output

Concentration vs time
with the mean and sd.

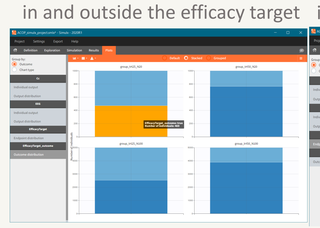


Output distribution

EEG vs time
with the efficacy target limits

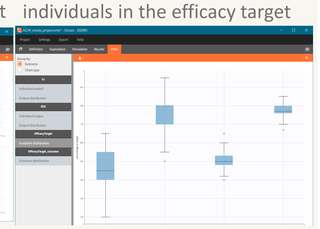
Outcome distribution

Number of individuals
in and outside the efficacy target



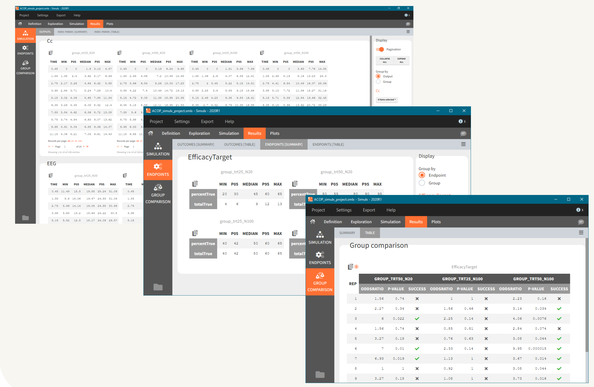
Endpoint distribution

Distribution of the percentage of individuals in the efficacy target



Results

Tables display the percentage of individuals in the EEG target for each replicates. With 20 individuals per arm, this percentage varies from 20 to 65 for the 25µm/min arm and from 50 to 95 for the 50µm/min arm. The difference between arms is significative: 36% over the clinical trial replicates. With 100 individuals per arm, the probability of success is 76% for the 50µm/min arm.



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