Instructions

This manual provides instructions on the installation and execution of the softward and a brief explanation of various input parameters and outputs of the software 'PrEP Predictor' [1]. The mathematical and technical details can be found in the main manuscript and Supplementary Notes of [1].
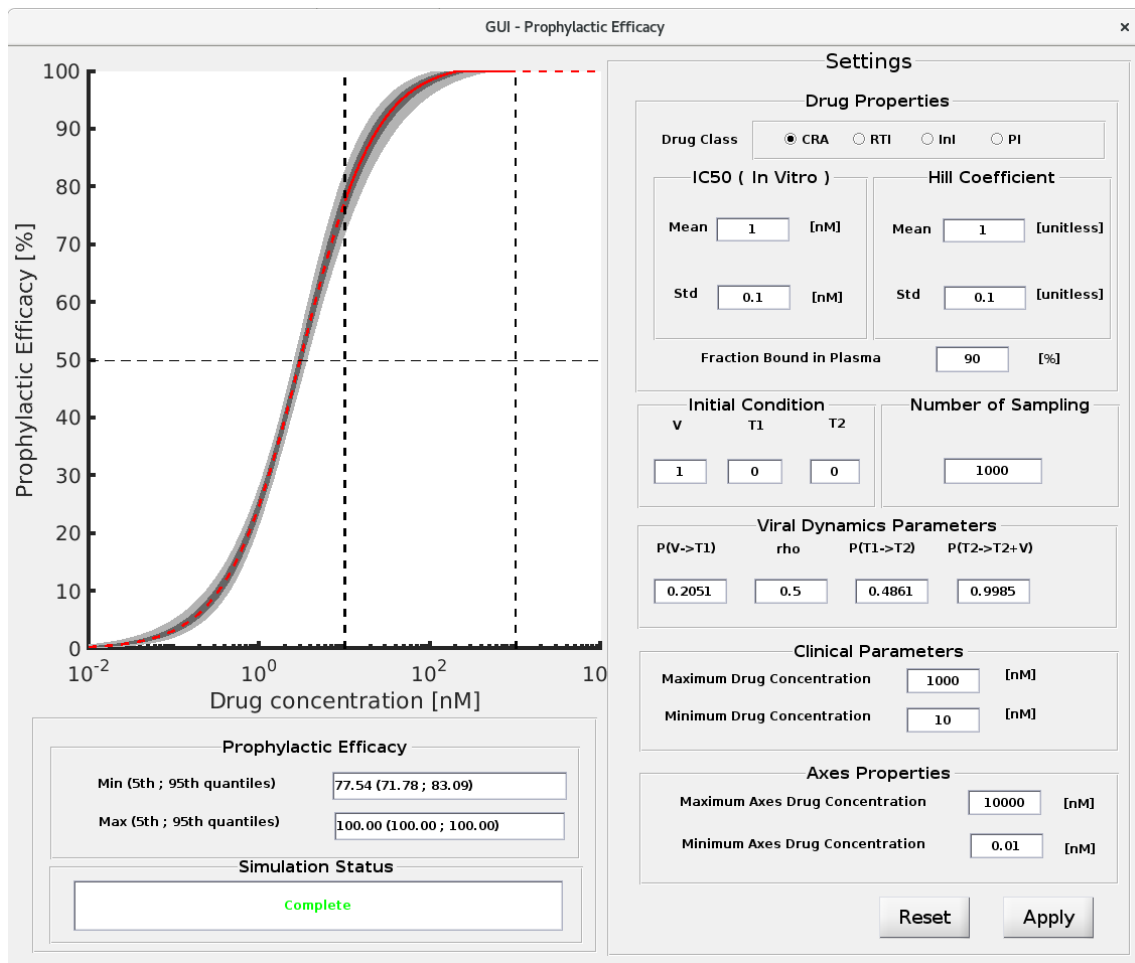

Figure 1: Graphical user interface of 'PrEP Predictor'

Installation and execution of the software

- For the windows OS, we provide an installer which upon the execution will download the *Matlab Compiler Runtime*. The *Matlab Compiler Runtime* allows a user to run the software without Matlab. The software is installed in the local computer and can be found with window starter programs.

- For the linux OS, the user needs to manually download *Matlab Compiler Runtime R2018a (MCR)*. The link to MCR is :
  https://de.mathworks.com/products/compiler/matlab-runtime.html
  The further details of executing the software can be found in 'readme.txt'.

Inputs

Drug Properties.

Figure 2: Properties related to the drug of interest.

A user can select a drug class from a list of four drug classes, namely co-receptor antagonist (CRA), reverse transcriptase inhibitor (RTI), integrase inhibitor (InI) or protease inhibitor (PI). Drug specific parameters such as the 50 % inhibitory concentration IC_{50} and a hill coefficient from single-round infectivity assays can be typed into the corresponding fields. The IC_{50} is assumed to be log normal distributed, whereas the hill coefficient is assumed to be normal distributed. The user also needs to provide the fraction of drug bound to plasma proteins in percentage.

Viral Exposure.

Figure 3: Initial condition relating to the viral exposure.

The prophylactic efficacy of the administered drug class depends on the intensity of viral exposure, herein defined by the number of free infectious viruses V, early infected T-cells T_1 and productively infected T-cells T_2 within a replication-competent compartment. Note that we do not refer to e.g. the mucosal exposure, but rather the number of viral species passing the mucosal barrier and reaching a compartment rich in target cells ($CD4^+$ immune cells). This allows the user to explore prophylactic efficacy depending on the intensity of virus exposure.

Viral dynamics parameters.

The user can specify various viral dynamics parameters. The values of these parameters correspond to a drug-free condition. The term (P(V$\rightarrow$ T1)) denotes the probability that a virus infects a T-cell and advances to early infected T-cell T_1 (after completion of reverse transcription, but before proviral integration). The term rho (ρ) denotes the probability to successfully complete reverse transcription. Similarly the term (P(T1 $\rightarrow$ T2)) and term (P(T2 $\rightarrow$ T2 + V)) denote the probability that a T_1 advances to a productively infected T-cell T_2 (after proviral integration) and

Figure 4: Viral dynamics parameters.

that a T_2 cell produces a free virus. Further details of these parameters can be found in Supplementary Text S1 of [1].

Number of samplings.

Figure 5: Number of random samplings performed for the computation of prophylactic efficacy.

The number of sampling denotes the number of realizations where an IC_{50} and a hill coefficient are randomly sampled from the user-defined distribution.

Clinically achievable drug concentration in plasma.

Figure 6: Clinically relevant drug concentration range in blood plasma.

The range of clinically achievable drug concentration in plasma can be specified, which allows to consider variability due to dosing regimen and pharmacokinetics. The unit is nanomolar [nM].

Axes concentration range.

Figure 7: Drug concentration to adjust x-axis of the concentration-prophylaxis profile plot.

This allows the user to adjust the x-axis i.e. concentration range to be displayed in the plot.
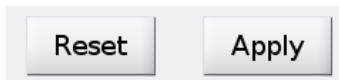
Buttons.

Figure 8: Buttons.

Pressing the button 'Apply' will perform the computation based on the user defined inputs. The button 'Reset' resets inputs variables to initially pre-defined values.
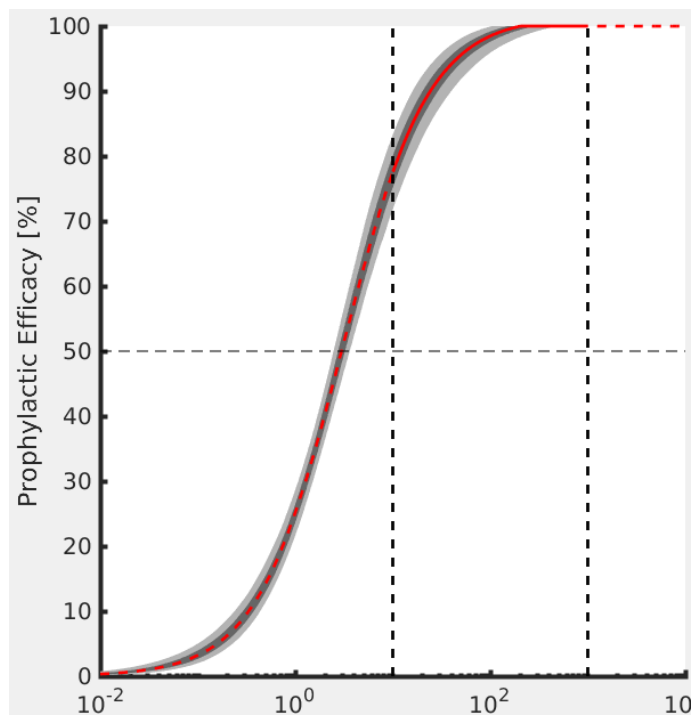
Outputs

Concentration-prophylaxis plot.

Figure 9: Concentration-prophylaxis plot.

Based on the user defined inputs, the display shows the concentration-prophylaxis profile for the drug (relative reduction in infection probability). The dashed colored line represents the median prophylactic efficacy and is plotted in one of the four colors depending on the selected drug class. The green color represents RTI, whereas red, blue and purple represent CRA, InI and PI respectively. The solid colored line denotes concentration-prophylaxis profile within the clinically achievable concentration ranges. Light and dark grey areas indicate 25th-75th and 5th-95th percentiles respectively. The horizontal dashed line marks 50% prophylactic efficacy. The two vertical dashed lines represent the drug concentration range (minimum – maximum concentrations provided by the user).

Prophylactic efficacy within concentration range.

Figure 10: Concentration-prophylactic efficacy within concentration range.

The text box shows the minimum and maximum prophylactic efficacy achieved along with their respective 5th-95th percentiles.
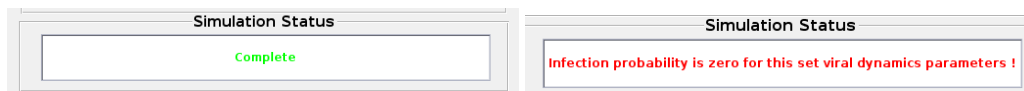
Simulation status display.

Figure 11: Text showing simulation status: The leftmost panel shows the displayed text when the simulation completed without problem. The rightmost panel shows an instance where the simulation encountered a problem.

The text box shows the end status of simulation. If the simulation executed without problem, a text in green reading 'complete' is shown. If the simulation encounters problem, a text in red is showing instructions to solve the error.

References

[1] Sulav Duwal, Laura Dickinson, Saye H. Khoo, and Max von Kleist. Mechanistic framework predicts utility of antiretroviral drugs for HIV prophylaxis. submitted for publication 2017.