

How to use

Required parameters for given drug are the following:

- Concentrations
- IC₅₀ on I_{Kr}
- IC₅₀ on I_{Ks}
- IC₅₀ on I_{CaL}

First, calculate x, y and z as written in the Description section, rounding to one decimal. Use -3 for each unknown IC₅₀ or when drug-channel interaction does not exist or is unlikely to happen. Resulting Coordinates can be outside the ranges that were provided. In that case, use the nearest value in the range (either maximum or minimum).

Then, search for the nearest to x value in the first column. This will return several possible rows. Now, search among those rows the nearest to y value in the second column, restricting the resulting data to one row. Finally, among the latter row, search nearest to z value in the first row and select the corresponding cell in the same column.

Example compound: consider compound D such as concentrations (could be therapeutic or just test concentrations) of 1 nM, IC₅₀ I_{Kr} of 1 nM, IC₅₀ I_{Ks} of 10000 nM and IC₅₀ I_{CaL} of 10 nM. Coordinates would be x=0, y=-4 and z=-1. The second should be transformed to -3, the nearest value in the simulated range. Here are the results of searching into the files (file/sheet) for the Coordinates [0,-3,-1] in the first column, the second column and the first row respectively.

APD.xlsx/Endo = 375.2 ms

APD.xlsx/Mid = 449.7 ms

APD.xlsx/Epi = 317.8 ms

QT.xlsx/QT = 422 ms

Tx_APD.xlsx/Endo = 0.200

Tx_APD.xlsx/Mid = 0.251

Tx_APD.xlsx/Epi = 0.200

Tx_QT.xlsx/QT = 0.229

This method will return the APD₉₀ or QT values of a steady-state simulation of the selected ORd (Endocardial, Mid-myocardial, Epicardial or one-dimensional Strand) under the effects of a drug with the inserted parameters.

Raw APD₉₀ or QT values give limited information about drug safety. In Romero et al. 2017 [2], it was found that compounds at therapeutic concentrations that yielded Tx values under 9.2, 8.0, 8.0 or 6.4 in Strand tissue (QT), Endocardial cells, Mid-myocardial cells or Epicardial cells respectively, were considered dangerous and could lead to Torsade-de-Pointes ventricular arrhythmia.