How to Run the PBPK Model Template

PBPK Model Template Project

Instructions for using source code and data files.

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To Run the Included Simulations

These instructions allow you to run the simulations given in the included script files for simulations of dichloromethane, methanol, and chloroform.

1. Install R, RStudio, the R packages “deSolve” and “readxl”, Rtools, and GNU MCSim on your system. Instructions can be found in “R_and_MCSim_installation_instructions.html”.
2. Open RStudio.
3. Within RStudio, open the R source code file containing the desired simulations, e.g. “DCM_IRIS_scripts.R”
4. Use the “Source” button to load the included functions.
5. If this is the first time using the template model, compile the template model by using the command PBPK_compile(). This command was loaded when sourcing the script file in step 4, and the function definition can be found in the file “run_template_model.R”.
6. Each function in the simulation script can be called from the command line to create the named figure or table from the manuscript and perform the corresponding accuracy calculations. For example, to create Figure C-3 from the U.S. EPA IRIS report for DCM, use the command “DCM.IRIS.FigC3()”. Figures will print to the figure pane in the lower right area of RStudio.

To Run Your Own Simulations Using the Model Template

These instructions allow you to run simulations using your own scripts.

1. Install R, RStudio, the R packages “deSolve” and “readxl”, Rtools, and GNU MCSim on your system. Instructions can be found in “R_and_MCSim_installation_instructions.html”.
2. Open RStudio.
3. Open “run_template_model.R”, set your working directory to the directory containing this file, and “Source” the file to load the included functions.
4. If this is the first time using the template model, compile the template model by using the command PBPK_compile().
5. Create input spreadsheets for your desired PBPK model simulation using copies of the provided blank templates. These can be found in the “Inputs” folder and are titled “BLANK_template_parameters_Model.xlsx” and “BLANK_template_parameters_Exposure.xlsx”.
6. Run the desired simulation by calling the function PBPK_run:
   PBPK_run(model.param.filename = "[Your model parameters spreadsheet filename]",
   model.param.sheetname = "[Your model parameters spreadsheet sheetname]",

exposure.param.filename = "[Your exposure parameters spreadsheet sheetname]", exposure.param.sheetname = "[Your exposure parameters spreadsheet sheetname]")

7. Output is provided in a data frame containing time-course data for all state and output variables included in the PBPK model template, and units are given in (mg, L, h).

See the included scripts and input spreadsheets for examples of how to perform simulations using the template. Additional instructions and information can be found in the "Documentation" folder.

PBPK Template Description of Files

run_template_model.R

This R source code file includes functions to run the PBPK model template. It requires the R libraries readxl (for importing parameter values) and deSolve (for methods of solving ordinary differential equations) and the R file RMCSim.R.

PBPK_template.model

This MCSim source code file defines the current model template.

PBPK_template_model.c

This C source code file defines the current model template.

PBPK_template_model.dll

This DLL file defines the current model template and can be used directly by functions in the R package deSolve.

PBPK_template_model.o

This C object code file defines the current model template.

PBPK_template_model_inits.R

This R source code file defines initialization functions for the current model template.

RMCSim.R

This R source code file defines functions for compiling, loading, and running an ODE model encoded in the GNU MCSim model specification language. The mod.exe utility must be available in the user's PATH for the compile_model function to work properly.

Data

This is a directory containing data files for each of the chemicals and example models. The directory contains sub-folders for each chemical named "Digitized_Data_X" or "Data_X" where X is the name of the chemical. The sub-folders contain .csv and .xlsx files containing data from the source publications.

Inputs

This is a directory containing input data files for each chemical. To run the current model template there must be two input spreadsheets: one for parameters in the model, and one for parameters related to the exposure scenario. Note, blank spreadsheets are included that contain the current format for the input spreadsheets.

Documentation

This is a directory containing documentation and instructional files explaining how to use the PBPK model template.

DCM_IRIS_scripts.R

This R source code file includes functions that run different simulations for dichloromethane exposures using the U.S. EPA IRIS DCM model. It requires the R file run_template_model.R.

methanol_scripts.R

This R source code file includes functions that run different simulations for methanol exposures using the U.S. EPA IRIS methanol model. It requires the R file run_template_model.R.

CF_Corley_scripts.R

This R source code file includes functions to recreate results for the Corley chloroform experiments modeled by Sasso et. al. (2013). It requires the R file run_template_model.R.

CF_Take_scripts.R

This R source code file includes functions to recreate results for the Take chloroform experiments modeled by Sasso et. al. (2013). It requires the R file run_template_model.R.

Styrene_scripts.R

This R source code file includes functions that run different simulations for styrene exposures using the Ramsey and Andersen (1984) styrene model. It requires the R file run_template_model.R.

Yoon_scripts.R

This R source code file includes functions that run different simulations for VOC exposures using the Yoon et al. (2007) PBPK model for VOCs, including vinyl chloride (VC), trichloroethylene (TCE), and carbon tetrachloride (CCl4). It requires the R file run_template_model.R.

PFAS_manuscript_scripts.R

This R source code file includes functions to recreate results included in Bernstein et al. (2021), updated to be compatible with this version of the model template. It requires the R files run_template_model.R and plot_PFAS_template_man.R.

plot_PFAS_template_man.R

This R source code file includes functions to generate the plots for results included in Bernstein et al. (2021) and is used by PFAS_manuscript_scripts.R.