MembranePlus™
March 2022

Dear MembranePlus™ User,

Thank you for your interest in MembranePlus. Our Simulations Plus development team continues to work hard to make MembranePlus the most advanced and reliable simulation of drug absorption and metabolism in cell-based assays in the world today.

1. Updates in version 3.0

· New Membrane models:
  o Modeling of diffusion through *ex vivo* skin samples – NEW!
    o Includes dermatomed skin, heat-separated epidermis, stratum corneum, full thickness skin, and simple membranes
  o Static and flowthrough diffusion cells
  o Modeling of complex topical formulations including solutions, suspensions, ointments, pastes, lotions, gels, and creams
  o Modeling of processes including evaporation, dissolution and precipitation, absorption into skin, diffusion and partitioning in skin and into receiver fluid

- ADMET Predictor® Module:
  o Updated models from ADMET Predictor version 10.3
  o Prediction of Km/Vmax for metabolism by cytochrome P450 enzymes (CYPs), including isoforms 1A2, 2C9, 2C19, 2D6, and 3A4.
  o IVIVE settings for conversion to either intestinal cell monolayers or hepatocytes.
  o Allow membrane model to be specified upon structure import.
  o New! Classification models to predict whether imported compounds are inhibitors or substrates for OATP1B3, OCT1, OCT2, OAT3, BSEP, and BCRP; as well as previous Pgp and OATP1B1 models.
  o Km values for OATP1B1, OATP1B3, OCT1, OCT2, OAT1, and OAT3.

- New Simulation Outputs:
  o New outputs for all dermal related transport quantities like mass and concentration.

- General Features:
  o Bug fixes

2. Installation of MembranePlus on your computer/network

MembranePlus is a mechanistic modeling & simulation software program designed to run on Windows 8, 10, and 11 systems, or Mac computers through Parallels (or similar Windows virtualization). MembranePlus can be installed from the *.zip package retrieved from our ShareFile online portal, either as a "standalone" installation on your computer or as a "network installation" on your local area network.

Refer to the installation manual for detailed instructions on the installation process.

Before MembranePlus can be run from your installation, it has to be activated. The activation process is handled via email with our licensing department. Should you have any questions, please contact one of our customer support representatives at: licensing@simulations-plus.com or +1-661-723-7723.

3. MembranePlus tutorial

MembranePlus includes an extensive help file with a redesigned tutorial for new users. This tutorial can be used by prospective customers during the evaluation of MembranePlus, or by new/existing customers to assist with validating a computer system (i.e., running tutorials to confirm the same results are generated on your computer versus what is reported in the tutorial).

The tutorial document contains step-by-step instructions for running MembranePlus simulations. A few standard simulations and their use in drug development are described. Data for running these simulations are also provided wherever necessary, along with the nature and source of the data. The tutorial data files are present in the Tutorials folder after installing MembranePlus on your computer.

4. Customer support

As part of our Personal Consultation Program, Simulations Plus has assigned scientists to specifically serve you in your use of MembranePlus. Feel free to contact them for advice on techniques for using the program better, for suggestions, and bug reports.

We stand ready to help you. If you need assistance in getting started, or if you would like advice on techniques for using the program most effectively in your research, please feel free to contact us.

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We look forward to serving you and assisting in any way we can.

Best regards,

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