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## New time course equations for GraphPad Prism

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### Outline

- Time course data are often described by unfamiliar equations such as the rise-and-fall equation.
- These equations have been loaded into <u>GraphPad Prism</u> in custom templates designed by Pharmechanics.
- We are grateful to Harvey Motulsky at GraphPad Software for guidance.





#### **Overview**

- Download the relevant Prism template from <u>here</u>.
- The equations can be loaded in batch or individually into your equation library as described <u>here</u> and on <u>Slide 16</u>.
- Questions? Email sam.hoare@pharmechanics.com
- The equations are supported by <u>Pharmechanics</u>, not by GraphPad.

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#### Familiar time course equations built into Prism



#### New time course equations from Pharmechanics

- New equations for rise-and-fall curves have been introduced by Pharmechanics.
- Upward and downward versions available.
- In addition, the familiar time course equations (straight line, association & dissociation curves) have been rewritten to be in the same format as these new equations.



### **Five files of equations**



Time

#### **Baseline considerations**

In some experiments, baseline signaling is recorded before compound is added.

Equations are available that incorporate this baseline run in period.

Occasionally, the baseline drifts over time.

Equations are available that incorporate this baseline drift



#### **Analysis tips**

When there is a baseline run in period, the initial value of the parameter X0 often needs to be entered manually for the fit to work. See <u>here</u>.

For the bell or U-shaped curves, K1 is the faster of the two rates and K2 is the slower. Usually, but not always, K1 is the rate of the first phase and K2 the rate of the second.

The equations are written out in the "Time course equation list" document <u>here</u> and can be viewed from the "Details" tab in the "Nonlinear regression" dialogue in Prism.





equation list

#### **Rise-and-fall equations**



#### **Rise-and-fall equations**



#### **Fall-and-rise equations**



#### **Fall-and-rise equations**



#### **Rise to steady state equations**



#### Fall to steady state equations



#### **Straight line equations**



### Loading equations into Prism from a file

GraphPad Prism contains an equation editor for the input of user-defined equations.

There are sharing methods that simplify the loading of equations written by other users.

This avoids the need to write in the equation and all the fit settings.

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First, download the files containing the equations to your computer. Here we are going to do all of the collections but you can select only the collection you need. The files are located on an open-access Google Drive at:

https://drive.google.com/drive/folders/1F5Qlyi30a3VNu9ZzCTKuTCDEmH6B4rdX?usp=sharing

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#### First, if Prism is open, close it.

Navigate to the Prism program files location on your computer.

Open the "Equations" folder.

Be very careful not to delete any of the files here – this is the equation library Prism uses.



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#### Now copy the equations files into the "Equations" folder.

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本 Rise-and-fall time course equations for AGM.pzf:Nonlin fit of Baseline then rise-and-fall to baseline - GraphPad Prism 8.4.1 (676)  $\times$ <u>File Edit View Insert Change Arrange Family Window Help</u> File She Text Prism Х Parameters: Nonlinear Regression 🖥 🗃 🖌 🗙 🕂 I Method Compare Constrain Initial values Range Output Confidence Diagnostics Flag Model Search... Click OK then close file. Now Choose an equation Data with Results Α В С Recently used  $\mathbf{A}$ New • the equation is available every User-defined equations [Pharmechanics] Baseline then rise-and-fall to baseline time course Details... Nonlin fit time you open Prism, in the Standard curves to interpolate Dose-response - Stimulation Edit... 0.03 Nonlin fit "User-defined equations" list. Dose-response - Inhibition 236 ✓ ☐ Baseline then rise Dose-response - Special, X is concentration 949 Delete Dose-response - Special, X is log(concentration) 1472 Nonlin fit Binding - Saturation 08251 Delete All Baseline then rise-709 Binding - Competitive Nonlin fit 401 Binding - Kinetics Move Up Baseline then rise- Enzyme kinetics - Inhibition 006785 📃 Nonlin fit Enzyme kinetics - Velocity as a function of substrate Move Down 05870 Exponential Table... 04231 Lines ✓ Info 002733 Polynomial 001582 Project info Gaussian New Info... ine waves 9997 Graphs curves 595 Curve: Nonlin fit of Ris 1956 ment in which effect is initiated after a baseline period Use for time coun Curve: Nonlin fit of Ris > 0 Curve: Nonlin fit of I Initial values might need man 1 > 1\*K2 K1, X at midpoint of rise phase Curve: Nonlin fit of Ba K2, X at midpoint of fall phase 2 > 0 Curve: Nonlin fit of Ba [Pharmechanics] Baseline then rise-and-fall to time course Numerical derivatives ① New Graph... Layouts Interpolate ① New Layout... Interpolate unknowns from standard curve. Confidence interval: OK Learn Cancel 34 < 35 > 36 Nonlin fit 37 < < > > **i** .....  $\sim$ QQ € Nonlin fit of Baseline then rise-  $\times$ ∂ Table of results

#### Using the new equations

- The new equations are used in the same way as the "Exponential" equations built into Prism.
- See following slides for screen clippings







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Search       >         Your data       >         Image: New Data Table       >         Image: Image: New Data Table       >         Image: Image	Model       Method       Compare       Constrain       Initial values       Range       Output       Confidence       Diagnostics       Flag         Choose an equation <ul> <li>We we change</li> <li>User-defined equations</li> <li>Dose-response : Stimulation</li> <li>Dose-response : Inhibition</li> <li>Dose-response : Special, X is log(concentration)</li> <li>Binding : Competitive</li> <li>Binding : Kinetics :</li> <li>Polynomial</li> <li>Gaussian</li> <li>Sine waves</li> <li>Growth curves</li> <li>Variation</li> <li>Polynomial</li> <li>Sine waves</li> <li>Growth curves</li> <li>Variation of fall phase</li> <li>Pharmechanical Ruse-and-fall to baseline time course</li> <li>Numerichanical Ruse-and-fall to baseline time course</li> <li>Numerichanical Ruse-and-fall curve. Confidence interval:</li> <li>Numerichanical Ruse-and-fall curve. Confidence interval:</li> <li>Numerichanical Ruse-and-fall curve.</li> <li>Learn</li> <li>Cancel</li> <li>OK</li> <li>Concel</li> <li>Concel</li></ul>					





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<ul> <li>Data Tables</li> <li>Your data</li> <li>New Data Table</li> <li>Info <ol> <li>Project info 1</li> <li>New Info</li> </ol> </li> <li>Results <ol> <li>New Analysis</li> </ol> </li> <li>Graphs <ol> <li>Your data</li> <li>New Graph</li> </ol> </li> <li>Layouts <ol> <li>New Layout</li> </ol> </li> </ul>	Equation       Rules for Initial Values       Default Constraints       Trans         [Pharmechanics] Rise-and-fall to zero time course       Tip: K1 constrained to be > K2, i.e. it is the faster rate.         Initial values might need to be entered manually:       K1, X at midpoint of rise phase       K2, X at midpoint of fall phase         C, peak Y divided by time at peak Y       Contact sam.hoare@pharmechanics.com for technical support       X: Time         Y: Y starts at zero, then goes up to a peak, then declines to       K1: Rate constant 1, units of inverse time         K2: Rate constant 2, units of inverse time       C: Initial rate of rise phase, Y units per unit time.         Y=(C/(K1-K2))*(exp(+K2*X)-exp(-K1*X))       Y=(C/(K1-K2))*(exp(-K2*X)-exp(-K1*X))	rt zero.
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Search <ul> <li>Data Tables</li> <li>Your data</li> <li>New Data Table</li> </ul> <li>Info         <ul> <li>Project info 1</li> <li>New Info</li> </ul> </li> <li>Results         <ul> <li>Nonlin fit of Your data</li> <li>New Analysis</li> </ul> </li> <li>Graphs         <ul> <li>New Graph</li> </ul> </li> <li>Layouts         <ul> <li>New Layout</li> </ul> </li>			Response		10 20	Your data	70					