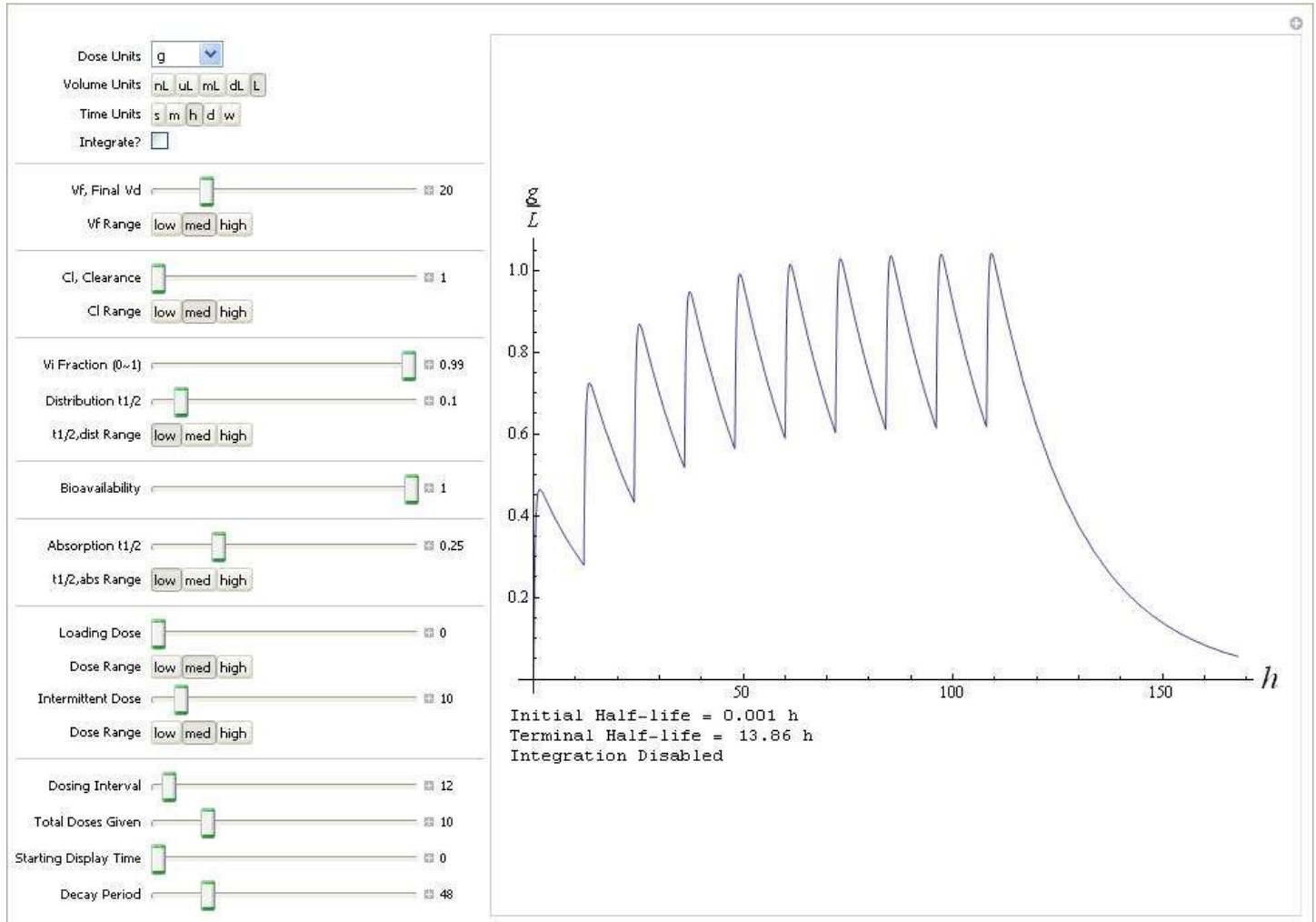


The pharmacokinetic simulators available at <http://hodsdon.com/PK> were programmed in Mathematica™ and require the free CDF Player/Plugin available from Wolfram (www.wolfram.com). Upon clicking on one of the models, you will be directed to the appropriate download page. After installing the CDF Player/Plugin, I recommend restarting your browser, although it doesn't seem to be required by the installer.

This manual can be found at <http://hodsdon.com/PK/manual.pdf>.

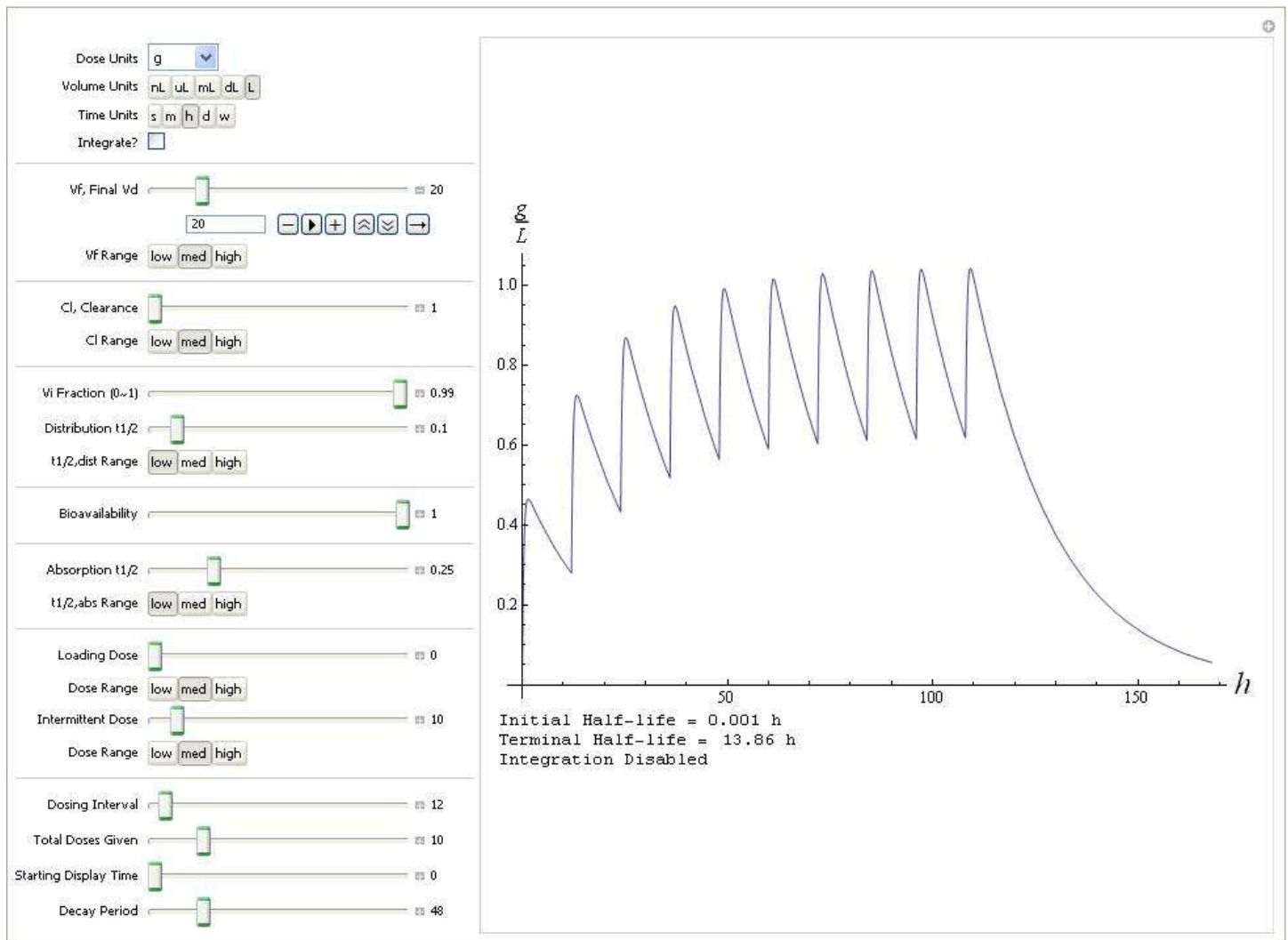
Shown below is an example simulator for the most complex model.



On the left are the adjustable controllers and on the right is a plot of drug concentration (in the “central” volume, typically blood or plasma) versus time. The units for the plot are controllable by the top three selectors. The only effect these unit selectors is the axis labels for the plot. It is up to the user to make sure that all the pharmacokinetic parameters are entered with the correct units! In the above example, with dose units in ‘g’ (grams), volume units in ‘L’ (liters), and time units in ‘h’ (hours), the volume of distribution (Vd) must be in liters, clearance (Cl) must be in in liters per hour, the distribution and absorption half-lives must be in hours, the loading and intermittent doses must be in grams, and the dosing interval, starting display time and decay period must be in hours. Of course, the Vi fraction, bioavailability and total doses are unit-less.

The sliders allow interactive adjustment of all the appropriate pharmacokinetic parameters. Each slider has a minimum and maximum, which can be changed by the button immediately below. The current value (NOT the range) is always shown on the right of the slider. If the current value is greater or lesser than the current slider minimum or maximum, respectively, a red shadow is shown next to the slider bar. This is NOT a problem until you try to move the slider and then the value will automatically reset to the current maximum of minimum for the slider.

You also have the option to directly enter any numeric value for each of the sliders, regardless of the slider's current minimum or maximum values. To do this, you need to click on the very small '+' sign in a box to the immediate right of the slider, which opens up a new menu. This is shown below for Vd:



“Opening” the slider provides multiple new control options. First, the user can now type in any numeric value in the box and then click anywhere within the simulator (note that hitting return or enter does nothing, you must click somewhere for the simulator to recognize the new value). You can type in a value that is currently outside of range of the slider, as discussed above. You can also hit the “play” button and watch an animation as the slider steps through its current range. Alternatively, you can manually hit “+” or “-” to manually step through the range of the slider. The two up arrow and down arrow buttons let you control the step size (larger and smaller, respectively) and the last button on the right cycles through three options: forward, backward, and forward-backward, which applies to the direction of the animator.

Below the plot, I provide a few calculated values, which vary with each model. You can read about them in the detailed description of the models available elsewhere (<http://hodsdon.com/PK/description.pdf>).

Lastly, there is a little Integrate selector. When enabled, a numeric integrator is applied to get the “area under the curve” (AUC). However, be warned, this slows down the calculations significantly, so I suggest turning it off when using the sliders.