LSD Pharmacokinetic Model

Kurt Bryan and SIMIODE

A worksheet to start the analysis of the two-compartment pharmacokinetic LSD model in Section 6.5.1.

First load in various helpful Maple packages:

```
> with(plots) :
  with(Optimization) :
```

The Data: Sampling times, in hours

```
> times := [1/12, 1/4, 1/2, 1, 2, 4, 8] :
```

The concentration data (mg/liter) for each subject at the seven times above is shown below (with "0" for the missing data point at time t = 4 hours for subject 3).

```
> sub[1] := [11.1, 7.4, 6.3, 6.9, 5, 3.1, 0.8] :
  sub[2] := [10.6, 7.6, 7, 4.8, 2.8, 2.5, 2] :
  sub[3] := [8.7, 6.7, 5.9, 4.3, 4.4, 0, 0.3] :
  sub[4] := [10.9, 8.2, 7.9, 6.6, 5.3, 3.8, 1.2] :
  sub[5] := [6.4, 6.3, 5.1, 4.3, 3.4, 1.9, 0.7] :
```

A plot of the subject concentration data.

```
> plts := array(1 ..5) :
   R := rand(0.0 ..1.0) : #To generate random colors to distinguish the subjects
  for j from 1 to 5 do
  plts[j] := pointplot(times, sub[j], symbol = solidcircle, symbolsize = 10, color = ColorTools:-
      Color([R( ), R( ), R( )])) :
  od:
   datplot := display(seq(plts[j], j = 1 ..5), size = [0.5, 0.8],
  legend = ["Subject 1", "Subject 2", "Subject 3", "Subject 4", "Subject 5"] , title
        = "Best Fit cP(t) to Concentration Data")
```

We use cP(t) for the plasma concentration and cT(t) as the tissue concentration we have cP(0) = 12.27 for each subject and cT(0) = 0.

The ODE Model: The model for cP(t) and cT(t) of Section 6.5.1 (equation (6.67)) is

```
> deP := 0.163·cP'(t) = (-0.163 kb - 0.163 ke) cP(t) + 0.115 ka cT(t);
  deT := 0.115 cT'(t) = 0.163 kb cP(t) - 0.115 ka cT(t)
```

where ka, kb, and ke are the constants to be determined from the concentration data.

We can have Maple solve these ODEs symbolically with initial data cP(0) = 12.27 and cT(0) = 0. The resulting solution is quite complicated, so the display is suppressed by putting a colon after dsolve (remove it if you want to see the solution.)

```
> sol := dsolve({deP, deT, cP(0) = 12.27, cT(0) = 0}, {cP(t), cT(t)}) :
```

The solution depends on ka, kb, and ke. We want to adjust these constants so that cP(t) fits the data.

```
> cPsol0 := subs(sol, cP(t)) : #Pick off the solution cP(t)
  cPsol := unapply(cPsol0, t) : #Turn it into an actual function of t
```

Fitting the Data: Construct the least squares functional that depends on ka, kb, and ke. Omit missing data point for subject 3 at time 4 hours.

```
> SS := add(add((cPsol(times[j]) - sub[k][j])^2, j = 1..7), k = 1..5) :
  SS := SS - (cPsol(times[6]) - sub[3][6])^2 : #Omit missing data point.
```

Now we need to minimize SS as a function of ka, kb, ke. The can be done by setting partial derivatives equal to zero or by using Maple's "Minimize" command as in the worksheet "paramest_demo.mw".
It may also help to specify that the variables ka, kb, and ke are all nonnegative, with the option "{0<=ka,0<=kb,0<=ke}".

```
>
```