Pharmacokinetics and pharmacodynamics

Peter Dalgaard

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The `nls` function

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Overview

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- Simple usage

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- Summary output

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- Writing self-starting models

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- The `start` argument defines which are parameters to be estimated and starting values for the iterative algorithm

Summary output

```
> summary(nlsout)

Formula: y ~ A * exp(-alpha * t)

Parameters:
      Estimate Std. Error t value Pr(>|t|)
A      4.75402    0.29408  16.166 5.88e-08 ***
alpha  0.18364    0.02023   9.079 7.95e-06 ***

Residual standard error: 0.3892 on 9 degrees of freedom

Correlation of Parameter Estimates:
           A
alpha 0.6724
```

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par(mfrow=c(2,1))
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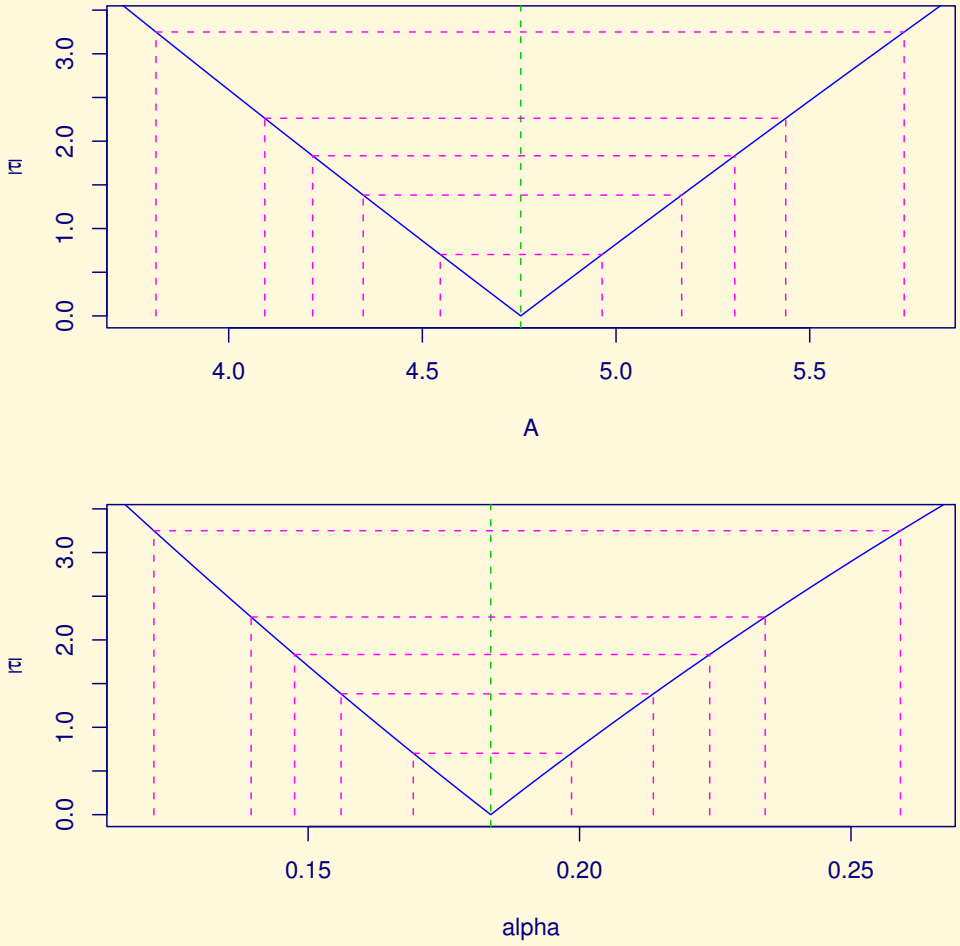
- Plots of $|t|$ with indication of approximate confidence levels (.99, .95, .90, .80, .50)

Profile plots



Confidence intervals

```
> confint(nlsout)
Waiting for profiling to be done...
            2.5%     97.5%
A      4.0931837 5.4381261
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- The same procedure as in profile plots, but showing results numerically

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```
nls(y~structure(A*exp(-alpha*t),
          gradient=cbind(A=exp(-alpha*t),
                         alpha=-A*t*exp(-alpha*5))),
    start=list(A=10,alpha=3.5))
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- The `deriv()` function can do much of the hard work for you if the model is given as a simple arithmetic expression.

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  - calculate "landmarks" as function of parameters (AUC, initial slope, position and value of maximum) estimate them empirically and solve for parameters
- Idea: Store algorithm for starting value within model object
- Standard models supplied: `SSfol`, etc.

Writing your own selfstart models

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- `data` is the modelling frame.
- Return value should be a named list.
- `selfStart()` constructor function does the rest. If used on a model formula, `deriv` is used for gradient info.

Selfstart example

```
initexp <-
function(mCall, data, LHS) {
     y <- eval(LHS,data)
     cc <- coef(lm(log(y)~t,data=data))
     l <- list(exp(cc[1]),-cc[2])
     names(l) <- mCall[c("A","a")]
     l
}

SSexp<-selfStart(~A*exp(-a*t),
                 initial = initexp,
                 parameters = c("A","a"))

summary(nls(y~SSexp(t,A,a)))
summary(nls(y~SSexp(t,B,b))) # won't work without the mCall stuff
```

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- Arrange that r.h.s. becomes a *matrix* to be multiplied by the linear parameters.

```
nls(y~cbind(exp(-a*t),exp(-b*t)),start=list(a=.3,b=.01),
    algorithm="plinear")
```

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- NB: Using `setPar()` destroys the fit. Cannot just save the fit in a different variable because of the embedded environment
- Used by the profiler, and can also be used for drawing approximate confidence regions.