Maximum likelihood estimation and analysis with the `bbmle` package

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```
## Loading required package:  methods
## Loading required package:  survival
## Loading required package:  splines
## Loading required package:  Formula
## Hmisc library by Frank E Harrell Jr
##
## Type library(help='Hmisc'), ?Overview, or ?Hmisc.Overview')
## to see overall documentation.
##
##
## Attaching package:  'Hmisc'
##
## The following object is masked from 'package:survival':
##
##    untangle.specials
##
```

```
## The following objects are masked from 'package:base':
##
##    format.pval, round.POSIXt, trunc.POSIXt, units
```

The `bbmle` package, designed to simplify maximum likelihood estimation and analysis in R, extends and modifies the `mle` function and class in the `stats4` package that comes with R by default. `mle` is in turn a wrapper around the `optim` function in base R. The maximum-likelihood-estimation function and class in `bbmle` are both called `mle2`, to avoid confusion and conflict with the original functions in the `stats4` package. The major differences between `mle` and `mle2` are:

- `mle2` is more robust, with additional warnings (e.g. if the Hessian can't be computed by finite differences, `mle2` returns a fit with a missing Hessian rather than stopping with an error)
- `mle2` uses a `data` argument to allow different data to be passed to the negative log-likelihood function
- `mle2` has a formula interface like that of (e.g.) `gls` in the `nlme` package. For relatively simple models the formula for the maximum likelihood can be written in-line, rather than defining a negative log-likelihood function. The formula interface also simplifies fitting models with categorical variables. Models fitted using the formula interface also have applicable `predict` and `simulate` methods.
- `bbmle` defines `anova`, `AIC`, `AICc`, and `BIC` methods for `mle2` objects, as well as `AICtab`, `BICtab`, `AICctab` functions for producing summary tables of information criteria for a set of models.

Other packages with similar functionality (extending GLMs in various ways) are

- on CRAN: `aods3` (overdispersed models such as beta-binomial); `vgam` (a wide range of models); `betareg` (beta regression); `pscl` (zero-inflated, hurdle models); `maxLik` (another general-purpose maximizer, with a different selection of optimizers)
- In Jim Lindsey's code repository (http://popgen.unimaas.nl/~jlindsey/rcode.html): `gnlr` and `gnlr3`

1 Example: *Orobanche*/overdispersed binomial

This example will use the classic data set on *Orobanche* germination from Crowder (1978) (you can also use `glm(...,family="quasibinomial")` or the `aods3` package to analyze these data).

1.1 Test basic fit to simulated beta-binomial data

First, generate a single beta-binomially distributed set of points as a simple test.

Load the `emdbook` package to get functions for the beta-binomial distribution (random-deviate function `rbetabinom` — these functions are also available in Jim Lindsey's `rmutil` package).

```
library(emdbook)
```

Generate random deviates from a random beta-binomial:

```
set.seed(1001)
x1 <- rbetabinom(n=1000,prob=0.1,size=50,theta=10)
```

Load the package:

```
library("bbmle")
```

Construct a simple negative log-likelihood function:

```
mtmp <- function(prob,size,theta) {
  -sum(dbetabinom(x1,prob,size,theta,log=TRUE))
}
```

Fit the model — use `data` to pass the `size` parameter (since it wasn't hard-coded in the `mtmp` function):

```
(m0 <- mle2(mtmp,start=list(prob=0.2,theta=9),data=list(size=50)))

##
## Call:
## mle2(minuslogl = mtmp, start = list(prob = 0.2, theta = 9), data = list(size = 50))
##
## Coefficients:
##    prob   theta
##  0.1031 10.0758
##
## Log-likelihood: -2724
```

The `summary` method for `mle2` objects shows the parameters; approximate standard errors (based on quadratic approximation to the curvature at the maximum likelihood estimate); and a test of the parameter difference from zero based on this standard error and on an assumption that the likelihood surface is quadratic (or equivalently that the sampling distribution of the estimated parameters is normal).

```
summary(m0)

## Maximum likelihood estimation
##
## Call:
## mle2(minuslogl = mtmp, start = list(prob = 0.2, theta = 9), data = list(size = 50))
##
## Coefficients:
##       Estimate Std. Error z value  Pr(z)
## prob   0.10310    0.00316    32.6 <2e-16 ***
## theta 10.07581    0.62133    16.2 <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## -2 log L: 5447
```

Construct the likelihood profile (you can apply `confint` directly to `m0`, but if you're going to work with the likelihood profile [e.g. plotting, or looking for confidence intervals at several different α values] then it is more efficient to compute the profile once):

```
p0 <- profile(m0)
```

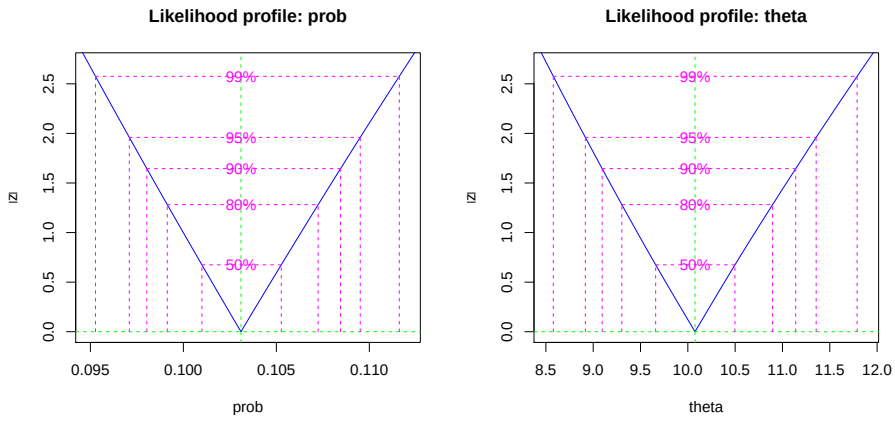
Compare the confidence interval estimates based on inverting a spline fit to the profile (the default); based on the quadratic approximation at the maximum likelihood estimate; and based on root-finding to find the exact point where the profile crosses the critical level.

```
confint(p0)

##          2.5 %  97.5 %
## prob  0.09709  0.1095
## theta 8.91708 11.3560

confint(m0,method="quad")

##        2.5 %  97.5 %
## prob  0.0969  0.1093
## theta 8.8580 11.2936

confint(m0,method="uniroot")

##        2.5 %  97.5 %
## prob  0.0971  0.1095
## theta 8.9169 11.3560
```

All three types of confidence limits are similar.

Plot the profiles:

```
par(mfrow=c(1,2))
plot(p0,plot.confstr=TRUE)
```



By default, the plot method for likelihood profiles displays the square root of the the deviance difference (twice the difference in negative log-likelihood from the best fit), so it will be V-shaped for cases where the quadratic approximation works well (as in this case). (For a better visual estimate of whether the profile is quadratic, use the `absVal=FALSE` option to the `plot` method.)

You can also request confidence intervals calculated using `uniroot`, which may be more exact when the profile is not smooth enough to be modeled accurately by a spline. However, this method is also more sensitive to numeric problems.

Instead of defining an explicit function for `minuslogl`, we can also use the formula interface. The formula interface assumes that the density function given (1) has `x` as its first argument (if the distribution is multivariate, then `x` should be a matrix of observations) and (2) has a `log` argument that will return the log-probability or log-probability density if `log=TRUE`. Some of the extended functionality (prediction etc.) depends on the existence of an `s-` variant function for the distribution that returns (at least) the mean and median as a function of the parameters (currently defined: `snorm`, `sbinom`, `sbeta`, `snbinom`, `spois`).

```
m0f <- mle2(x1~dbetabinom(prob,size=50,theta),
            start=list(prob=0.2,theta=9),data=data.frame(x1))
```

Note that you must specify the data via the `data` argument when using the formula interface. This may be slightly more unwieldy than just pulling the data from your workspace when you are doing simple things, but in the long run it makes tasks like predicting new responses much simpler.

It's convenient to use the formula interface to try out likelihood estimation on the transformed parameters:

```
m0cf <- mle2(x1~dbetabinom(prob=plogis(lprob),size=50,theta=exp(ltheta)),
             start=list(lprob=0,ltheta=2),data=data.frame(x1))
confint(m0cf,method="uniroot")

##          2.5 % 97.5 %
## lprob  -2.230 -2.096
## ltheta  2.188  2.430

confint(m0cf,method="spline")

##          2.5 % 97.5 %
## lprob  -2.230 -2.096
## ltheta  2.188  2.430
```

In this case the answers from `uniroot` and `spline` (default) methods barely differ.

1.2 Real data (*Orobanche*, Crowder (1978))

Data are copied from the `aods3` package (but a copy is saved with the package to avoid depending on the `aods3` package):

```
load(system.file("vignetteData","orob1.rda",package="bbmle"))
summary(orob1)

##   dilution       n               m
##  1/1  :6   Min.   :  7.0   Min.   : 0.0
##  1/25 :5   1st Qu.: 17.5   1st Qu.: 8.0
##  1/625:5   Median : 47.5   Median :13.5
##            Mean   : 44.2   Mean   :27.2
##            3rd Qu.: 57.5   3rd Qu.:46.2
##            Max.   :104.0   Max.   :90.0
```

Now construct a negative log-likelihood function that differentiates among groups:

```
ML1 <- function(prob1,prob2,prob3,theta,x) {
  prob <- c(prob1,prob2,prob3)[as.numeric(x$dilution)]
  size <- x$n
  -sum(dbetabinom(x$m,prob,size,theta,log=TRUE))
}
```

Results from Crowder (1978):

model	prob1	prob2	prob3	theta	sd.prob1	sd.prob2	sd.prob3	NLL
prop diffs	0.132	0.871	0.839	78.424	0.027	0.028	0.032	−34.991
full model								−34.829
homog model								−56.258

```
(m1 <- mle2(ML1,start=list(prob1=0.5,prob2=0.5,prob3=0.5,theta=1),
            data=list(x=orob1)))

##
## Call:
## mle2(minuslogl = ML1, start = list(prob1 = 0.5, prob2 = 0.5,
##     prob3 = 0.5, theta = 1), data = list(x = orob1))
##
## Coefficients:
##   prob1   prob2   prob3   theta
##  0.1318  0.8706  0.8383 73.7214
##
## Log-likelihood: -34.99
##
## Warning: optimization did not converge (code 1: )
```

Or:

```
## would prefer ~dilution-1, but problems with starting values ...
(m1B <- mle2(m~dbetabinom(prob,size=n,theta),
             param=list(prob~dilution),
             start=list(prob=0.5,theta=1),
    data=orob1))
```

The result warns us that the optimization has not converged; we also don't match Crowder's results for θ exactly. We can fix both of these problems by setting `parscale` appropriately.

Since we don't bound θ (or below, σ) we get a fair number of warnings with this and the next few fitting and profiling attempts. We will ignore these for now, since the final results reached are reasonable (and match or nearly match Crowder's values); the appropriate, careful thing to do would be either to fit on a transformed scale where all real-valued parameter values were legal, or to use `method="L-BFGS-B"` (or `method="bobyqa"` with the `optimx` package) to bound the parameters appropriately. You can also use `suppressWarnings()` if you're sure you don't need to know about any warnings (beware: this will suppress *all* warnings, those you weren't expecting as well as those you were ...)

```
(m2 <- mle2(ML1,start=as.list(coef(m1)),
          control=list(parscale=coef(m1)),
          data=list(x=orob1)))
```

```
##
## Call:
## mle2(minuslogl = ML1, start = as.list(coef(m1)), data = list(x = orob1),
##     control = list(parscale = coef(m1)))
##
## Coefficients:
##   prob1   prob2   prob3   theta
##  0.1322  0.8709  0.8393 78.4228
##
## Log-likelihood: -34.99
```

Calculate likelihood profile (restrict the upper limit of θ, simply because it will make the picture below a little bit nicer):

```
p2 <- profile(m2,prof.upper=c(Inf,Inf,Inf,theta=2000))
```

Get the curvature-based parameter standard deviations (which Crowder used rather than computing likelihood profiles):

```
round(stdEr(m2),3)

##  prob1  prob2  prob3  theta
##  0.028  0.029  0.032 74.238
```

We are slightly off Crowder's numbers — rounding error?
Crowder also defines a variance (overdispersion) parameter $\sigma^2 = 1/(1+\theta)$.

```
sqrt(1/(1+coef(m2)["theta"]))

##  theta
## 0.1122
```

Using the delta method (via the `deltavar` function in the `emdbook` package) to approximate the standard deviation of σ:

```
sqrt(deltavar(sqrt(1/(1+theta)),meanval=coef(m2)["theta"],
         vars="theta",Sigma=vcov(m2)[4,4]))

## [1] 0.05244
```

Another way to fit in terms of σ rather than θ is to compute $\theta = 1/\sigma^2 - 1$ on the fly in a formula:

```
m2b <- mle2(m~dbetabinom(prob,size=n,theta=1/sigma^2-1),
            data=orob1,
```

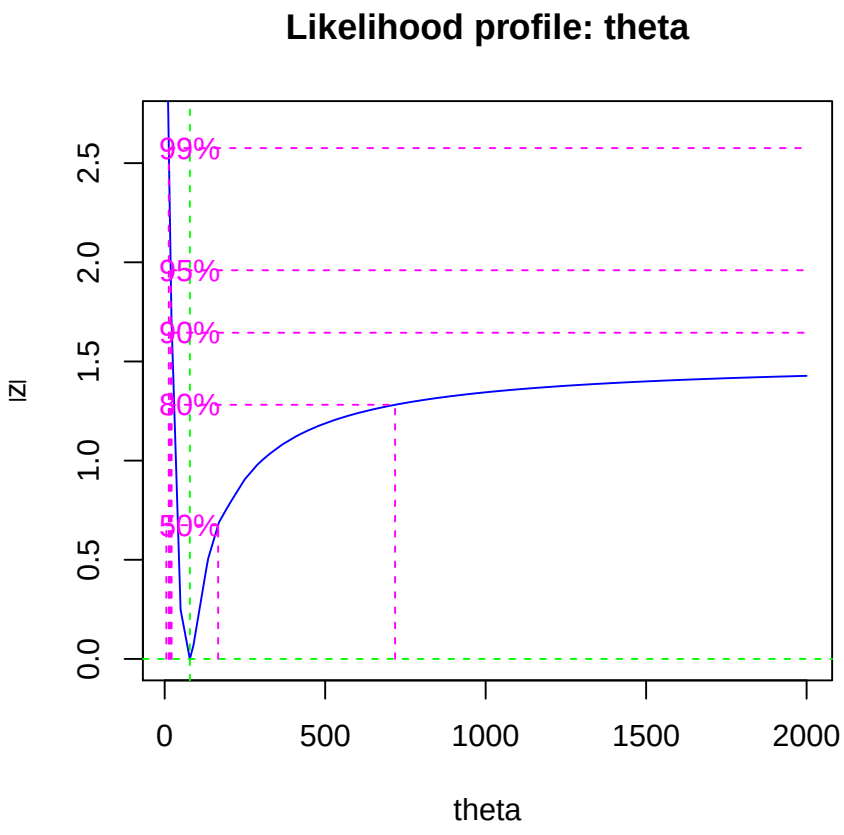
```
            parameters=list(prob~dilution,sigma~1),
            start=list(prob=0.5,sigma=0.1))
## ignore warnings (we haven't bothered to bound sigma<1)
round(stdEr(m2b)["sigma"],3)

## sigma
## 0.052

p2b <- profile(m2b,prof.lower=c(-Inf,-Inf,-Inf,0))
```

As might be expected since the standard deviation of σ is large, the quadratic approximation is poor:

```
r1 <- rbind(confint(p2)["theta",],
            confint(m2,method="quad")["theta",])
rownames(r1) <- c("spline","quad")
r1

##         2.5 % 97.5 %
## spline  19.67     NA
## quad   -67.08  223.9
```

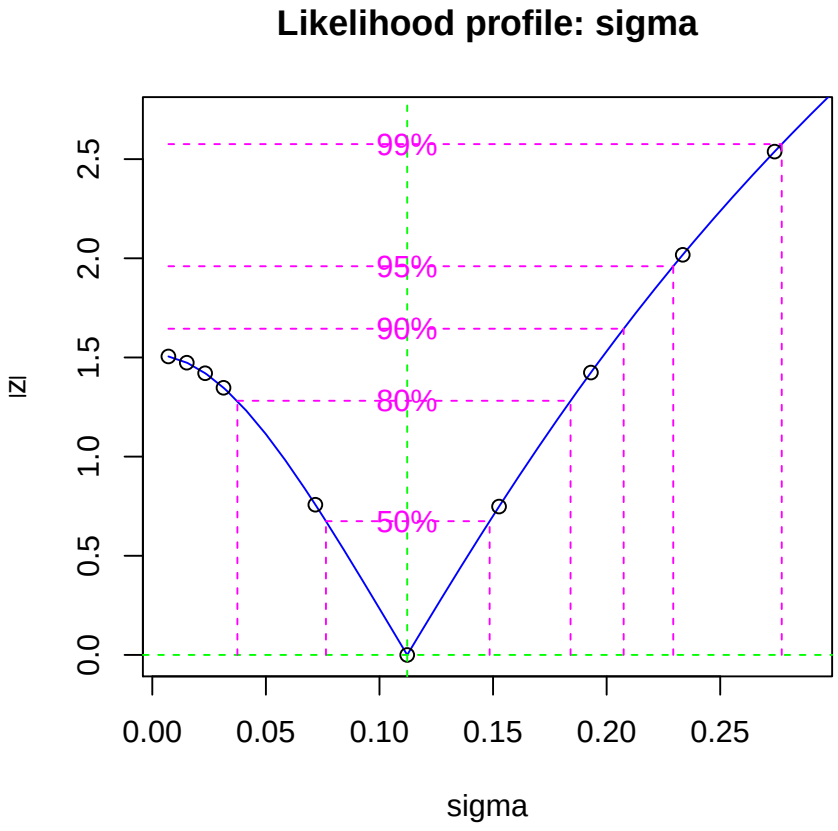
Plot the profile:

```
plot(p2,which="theta",plot.confstr=TRUE)
```



What does the profile for σ look like?

```
plot(p2b,which="sigma",plot.confstr=TRUE,
     show.points=TRUE)
```



Now fit a homogeneous model:

```
ml0 <- function(prob,theta,x) {
  size <- x$n
  -sum(dbetabinom(x$m,prob,size,theta,log=TRUE))
}
m0 <- mle2(ml0,start=list(prob=0.5,theta=100),
           data=list(x=orob1))
```

The log-likelihood matches Crowder's result:

```
logLik(m0)

## 'log Lik.' -56.26 (df=2)
```

It's easier to use the formula interface to specify all three of the models fitted by Crowder (homogeneous, probabilities differing by group, probabilities and overdispersion differing by group):

```
m0f <- mle2(m~dbetabinom(prob,size=n,theta),
            parameters=list(prob~1,theta~1),
            data=orob1,
            start=list(prob=0.5,theta=100))
m2f <- update(m0f,
              parameters=list(prob~dilution,theta~1),
              start=list(prob=0.5,theta=78.424))
m3f <- update(m0f,
              parameters=list(prob~dilution,theta~dilution),
              start=list(prob=0.5,theta=78.424))
```

`anova` runs a likelihood ratio test on nested models:

```
anova(m0f,m2f,m3f)

## Likelihood Ratio Tests
## Model 1: m0f, m~dbetabinom(prob,size=n,theta): prob~1, theta~1
## Model 2: m2f, m~dbetabinom(prob,size=n,theta): prob~dilution, theta~1
## Model 3: m3f, m~dbetabinom(prob,size=n,theta): prob~dilution,
##           theta~dilution
##   Tot Df Deviance Chisq Df Pr(>Chisq)
## 1      2      112
## 2      4       70  42.5  2    5.8e-10 ***
## 3      6       70   0.0  2          1
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The various `ICtab` commands produce tables of information criteria, optionally sorted and with model weights.

```
AICtab(m0f,m2f,m3f,weights=TRUE,delta=TRUE,sort=TRUE)

##     dAIC df weight
## m2f  0.0 4  0.88
## m3f  4.0 6  0.12
## m0f 38.5 2  <0.001

BICtab(m0f,m2f,m3f,delta=TRUE,nobs=nrow(orob1),sort=TRUE,weights=TRUE)

##     dBIC df weight
## m2f  0.0 4  0.941
## m3f  5.5 6  0.059
## m0f 37.0 2  <0.001

AICctab(m0f,m2f,m3f,delta=TRUE,nobs=nrow(orob1),sort=TRUE,weights=TRUE)
```

```
##     dAICc df weight
## m2f   0.0  4  0.9922
## m3f   9.7  6  0.0078
## m0f  35.8  2  <0.001
```

2 Example: reed frog size predation

Data from an experiment by Vonesh (Vonesh and Bolker, 2005)

```
frogdat <- data.frame(
  size=rep(c(9,12,21,25,37),each=3),
  killed=c(0,2,1,3,4,5,rep(0,4),1,rep(0,4)))
frogdat$initial <- rep(10,nrow(frogdat))
```

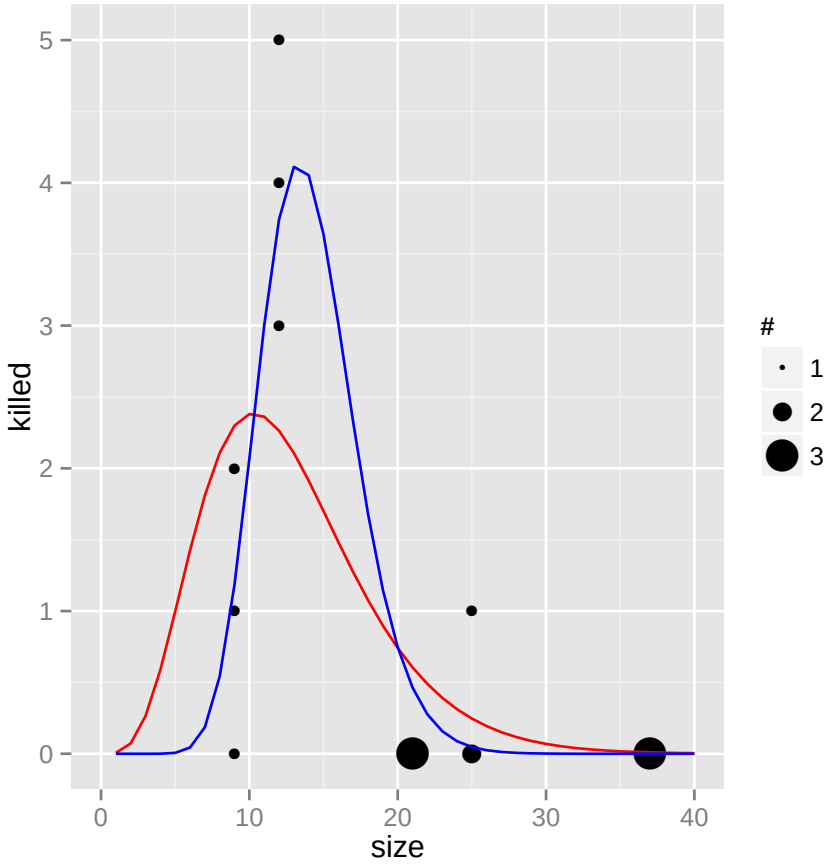
```
library(ggplot2)
```

```
gg1 <- ggplot(frogdat,aes(x=size,y=killed))+geom_point()+
      stat_sum(aes(size=factor(..n..)))+
      labs(size="#")+scale_x_continuous(limits=c(0,40))
```

```
m3 <- mle2(killed~dbinom(prob=c*(size/d)^g*exp(1-size/d),
  size=initial),data=frogdat,start=list(c=0.5,d=5,g=1))
pdat <- data.frame(size=1:40,initial=rep(10,40))
pdat1 <- data.frame(pdat,killed=predict(m3,newdata=pdat))
```

```
m4 <- mle2(killed~dbinom(prob=c*((size/d)*exp(1-size/d))^g,
  size=initial),data=frogdat,start=list(c=0.5,d=5,g=1))
pdat2 <- data.frame(pdat,killed=predict(m4,newdata=pdat))
```

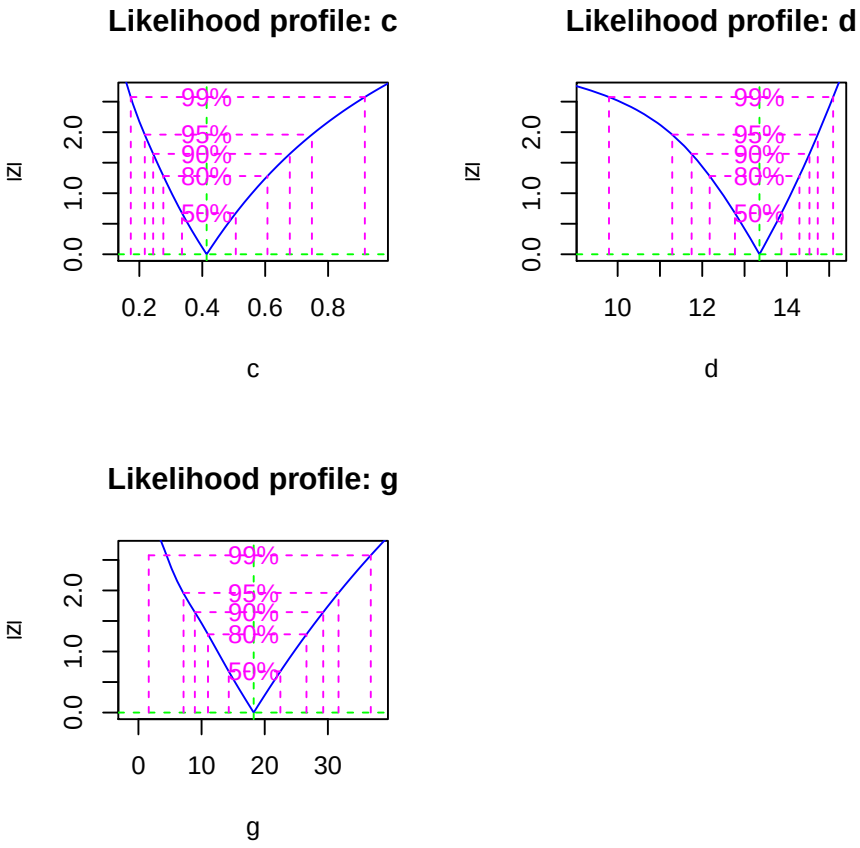
```
gg1 + geom_line(data=pdat1,colour="red")+
      geom_line(data=pdat2,colour="blue")
```




```
coef(m4)

##       c       d       g
##  0.4139 13.3518 18.2511

prof4 <- profile(m4)
```

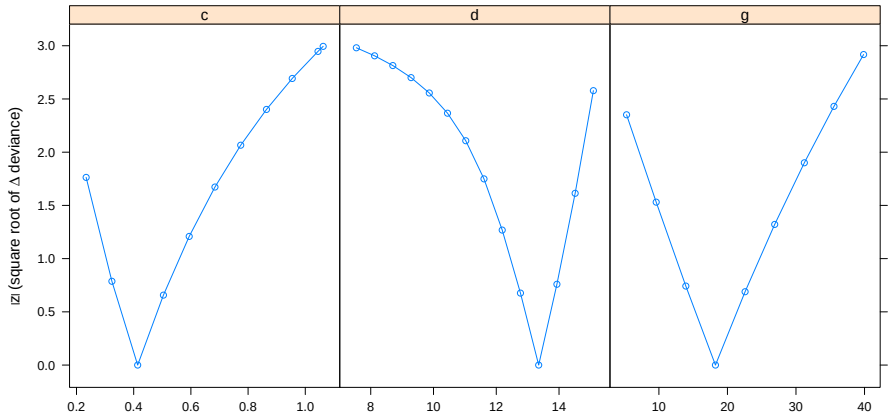
Three different ways to draw the profile:
(1) Built-in method (base graphics):

```
plot(prof4)
```



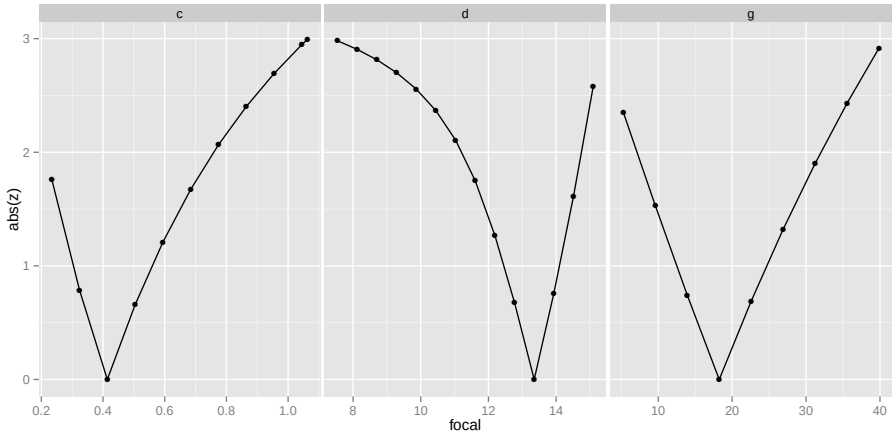
(2) Using `xyplot` from the `lattice` package:

```
prof4_df <- as.data.frame(prof4)
library(lattice)
xyplot(abs(z)~focal|param,data=prof4_df,
       subset=abs(z)<3,
        type="b",
        xlab="",
        ylab=expression(paste(abs(z),
            " (square root of ",Delta," deviance)")),
        scale=list(x=list(relation="free")),
              layout=c(3,1))
```



(3) Using `ggplot` from the `ggplot2` package:

```
ss <-subset(prof4_df,abs(z)<3)
ggplot(ss,
       aes(x=focal,y=abs(z)))+geom_line()+
      geom_point()+
      facet_grid(.~param,scale="free_x")
```



Additions/enhancements/differences from `stats4::mle`

- `anova` method
- warnings on convergence failure
- more robust to non-positive-definite Hessian; can also specify `skip.hessian` to skip Hessian computation when it is problematic

- when profiling fails because better value is found, report new values
- can take named vectors as well as lists as starting parameter vectors
- added `AICc`, `BIC` definitions, `ICtab` functions
- added `"uniroot"` and `"quad"` options to `confint`
- more options for colors and line types etc etc. The old arguments are:

```
function (x, levels, conf = c(99, 95, 90, 80, 50)/100, nseg = 50,
          absVal = TRUE, ...) {}
```

  The new one is:

```
function (x, levels, which=1:p, conf = c(99, 95, 90, 80, 50)/100, nseg = 50,
          plot.confstr = FALSE, confstr = NULL, absVal = TRUE, add = FALSE,
          col.minval="green", lty.minval=2,
          col.conf="magenta", lty.conf=2,
          col.prof="blue", lty.prof=1,
          xlabs=nm, ylab="score",
          show.points=FALSE,
          main, xlim, ylim, ...) {}
```

  `which` selects (by character vector or numbers) which parameters to plot: `nseg` does nothing (even in the old version); `plot.confstr` turns on the labels for the confidence levels; `confstr` gives the labels; `add` specifies whether to add the profile to an existing plot; `col` and `lty` options specify the colors and line types for horizontal and vertical lines marking the minimum and confidence vals and the profile curve; `xlabs` gives a vector of x labels; `ylab` gives the y label; `show.points` specifies whether to show the raw points computed.

- `mle.options()`
- `data` argument
- handling of names in argument lists
- can use alternative optimizers (`nlminb`, `nlm`, `constrOptim`, `optimx`, `optimize`)
- uses code from `numDeriv` package to compute Hessians rather than built-in optimizer code
- by default, uses `MASS::ginv` (generalized inverse) rather than `solve` to invert Hessian (more robust to positive-semidefinite Hessians ...)
- can use `vecpar=TRUE` (and `parnames()`) to use objective functions with parameters specified as vectors (for compatibility with `optim` etc.)

3 Newer stuff

To do:

- use `predict`, `simulate` etc. to demonstrate different parametric bootstrap approaches to confidence and prediction intervals
  - use `predict` to get means and standard deviations, use delta method?
  - use `vcov`, assuming quadratic profiles, with `predict(...,newparams=...)`
  - prediction intervals assuming no parameter uncertainty with `simulate`
  - both together ...

4 Technical details

4.1 Profiling and confidence intervals

This section describes the algorithm for constructing profiles and confidence intervals, which is not otherwise documented anywhere except in the code. * indicates changes from the version in `stats4:::mle`

4.1.1 Estimating standard error

In order to construct the profile for a particular parameter, one needs an initial estimate of the scale over which to vary that parameter. The estimated standard error of the parameter based on the estimated curvature of the likelihood surface at the MLE is a good guess.

- if `std.err` is missing, extract the standard error from the summary coefficient table (ultimately computed from `sqrt(diag(inverse Hessian))` of the fit)
- * a user-set value of `std.err` overrides this behavior unless the value is specified as `NA` (in which case the estimate from the previous step is used)
- * if the standard error value is still `NA` (i.e. the user did not specify it and the value estimated from the Hessian is missing or `NA`) use `sqrt(1/diag(hessian))`. This represents a (fairly feeble) attempt to come up with a plausible number when the Hessian is not positive definite but still has positive diagonal entries
- if all else fails, stop and * print an error message that encourages the user to specify the values with `std.err`

There may be further tricks that would help guess the appropriate scale: for example, one could guess on the basis of a comparison between the parameter values and negative log-likelihoods at the starting and ending points of the fits. On the other hand, (a) this would take some effort and still be subject to failure

for sufficiently pathological fits and (b) there is some value to forcing the user to take explicit, manual steps to remedy such problems, as they may be signs of poorly defined or buggy log-likelihood functions.

4.1.2 Profiling

Profiling is done on the basis of a constructed function that minimizes the negative log-likelihood for a fixed value of the focal parameter and returns the signed square-root of the deviance difference from the minimum (denoted by z). At the MLE $z = 0$ by definition; it should never be < 0 unless something has gone wrong with the original fit. The LRT significance cutoffs for z are equal to the usual two-tailed normal distribution cutoffs (e.g. $\pm \approx 1.96$ for 95% confidence regions).

In each direction (decreasing and increasing from the MLE for the focal parameter):

- fix the focal parameter
- adjust control parameters etc. accordingly (e.g. remove the entry for the focal parameter so that the remaining control parameters match the non-fixed parameters)
- controls on the profiling (which can be set manually, but for which there is not much guidance in the documentation):
  - `zmax` Maximum z to aim for. (Default: `sqrt(qchisq(1-alpha/2, p))`) The default maximum α (type I error) is 0.01. *I don't understand this criterion. It seems to expand the size of the univariate profile to match a cutoff for the multivariate confidence region of the model. The χ^2 cutoff for deviance to get the $(1-\alpha)$ multivariate confidence region (i.e., on all p of the parameters) would be* `qchisq(1-alpha,p)` *— representing a one-tailed test on the deviance. Taking the square root makes sense, since we are working with the square root of the deviance, but I don't understand (1) why we are expanding the region to allow for the multivariate confidence region (since we are computing univariate profiles) [you could at least argue that this is conservative, making the region a little bigger than it needs to be]; (2) why we are using $1-\alpha/2$ rather than $1-\alpha$.* For comparison, `MASS::profile.glm` (written by Bates and Venables in 1996, ported to R by BDR in 1998) uses `zmax=sqrt(qchisq(1-alpha,1))` *(this makes more sense to me . . .)* . On the other hand, the profiling code in `lme4a` (the `profile` method for `merMod`, in `profile.R`) uses `qchisq(1-alphamax, nptot)` . . .
  - `del` Step size (scaled by standard error) (Default: `zmax`/5.) Presumably (?) copied from `MASS::profile.glm`, which says (in `?profile.glm`): "[d]efault value chosen to allow profiling at about 10 parameter values."

  - `maxsteps` Maximum number of profiling steps to try in each direction. (Default: 100)

- While `step<maxsteps` and `abs(z) < zmax`, set the value of the focal parameter to its MLE + `sgn*step*del*std.err` where `sgn` represents the direction, `step` is the current (integer) step, and `del` and `std.err` are the step size scaling factor and standard error estimate discussed above (i.e. take steps of size (`del*std.err`) in the appropriate direction); evaluate z
- Stop the profiling:
  - if z doesn't change from the previous step (`stop_flat`) — unless `try_harder` is `TRUE`
  - * stop if z is less than `tol.newmin` (default: 0.001) units *better* than the MLE fit, i.e. $z < -$`tol.newmin` (if $-$`tol.newmin` $< z < 0$, set z to zero) (`newpars_found`)
  - if z is `NA` (`stop_na`) — unless `try_harder` is `TRUE`
  - if z is beyond `zmax` (i.e., we have reached our goal: `stop_cutoff`)
  - if `step==maxsteps`
  - if the focal parameter has hit its upper/lower bound (`stop_bound`)
- if we have hit the maximum number of steps but not reached the cutoff (`stop_maxstep` but not `stop_cutoff`), "try a bit harder": go *almost* one more `del*std.err` unit out (in intervals of 0.2, 0.4, 0.6, 0.8, 0.9) (*also seems reasonable but don't know where it comes from*)
- * if we violated the boundary but did not reach the cutoff (`!stop_cutoff && stop_bound`), evaluate z at the boundary
- if we got to the cutoff in < 5 steps, try smaller steps: start at `step=0.5` and proceed to `mxstep-0.5` in unit increments (rather than the original scale which went from 0 to `mxstep`). (*Again, it seems reasonable, but I don't know what the original justification was ...*)

4.1.3 Confidence intervals

We are looking for the values where z (signed square root deviance difference) is equal to the usual two-tailed normal distribution cutoffs for a specified α level, e.g. $z = \pm 1.96$ for 95% confidence intervals (this is equivalent to a one-tailed test on the deviance difference with the cutoff value for χ^2_1).

Spline method (default)

- If necessary (i.e. if applied to a fitted object and not to an existing profile), construct the profile

- * If the profile of the signed square root is non-monotonic, warn the user and revert to linear approximation on the profiled points to find the cutoffs:
- Otherwise, build an interpolation spline of z (signed square root deviance difference) based on profiled points (the default is $n = 3 \times L$ where L is the length of the original vector). Then use linear approximation on the y (z) and x (focal parameter value) of the spline to find the cutoffs (*Why construct a spline and then interpolate linearly? Why not use* `backSpline` *as in the profile plotting code?*)

Quad method Use a quadratic approximation based on the estimated curvature (this is almost identical to using `confint.default`, and perhaps obsolete/could be replaced by a pointer to `confint.default` ...)

Uniroot For each direction (up and down):

- start by stepping 5 σ away from the MLE, or to the box constraint on the parameter, whichever is closer (*this standard error is based on the curvature; I should allow it, or the intervals themselves, to be overridden via a* `std.err` *or* `interval` *parameter*)
- compute the difference between the deviance and the desired deviance cutoff at this point; if it is `NA`, reduce the distance in steps of 0.25 σ until it is not, until you reduce the distance to zero
- if the product of the deviance differences at the MLE and at the point you stopped at is `NA` or positive (indicating that you didn't find a root-crossing in the range $[0, 5\sigma]$), quit.
- otherwise, apply `uniroot` across this interval

`method="uniroot"` should give the most accurate results, especially when the profile is wonky (it won't care about non-smooth profiles), but it will be the slowest — and different confidence levels will have to be computed individually, whereas multiple confidence levels can be computed quickly from a single computed profile. A cruder approach would be to use profiling but decrease `std.err` a lot so that the profile points were very closely spaced.

4.1.4 Profile plotting

Plot the signed (or unsigned) square root deviance difference, and $(1 - \alpha)$ confidence regions/critical values designated by `conf` (default: $\{0.99, 0.95, 0.9, 0.8, 0.5\}$).

- * If the (signed) profile is non-monotonic, simply plot computed points with `type="l"` (i.e., with the default linear interpolation)
- Construct the interpolation spline (using `splines:::interpSpline` rather than `spline` as in the confidence interval method (*why this difference?*)

- attempt to construct the inverse of the interpolation spline (using `backSpline`)
- * if this fails warn the user (assume this was due to non-monotonicity) and try to use `uniroot` and `predict` to find cutoff values
- otherwise, use the inverse spline to find cutoff values

Why is there machinery in the plotting code to find confidence intervals? Shouldn't this call `confint`*, for consistency/fewer points of failure?*

Bugs, wishes, to do

- **WISH**: further methods and arguments: `subset`, `predict`, `resid`: `sim`?
- **WISH**: extend ICtab to allow DIC as well?
- minor **WISH**: better methods for extracting `nobs` information when possible (e.g. with formula interface)
- **WISH**: better documentation, especially for S4 methods
- **WISH**: variable-length (and shaped) chunks in argument list – cleaner division between linear model specs/list of arguments/vector equivalent
- **WISH**: limited automatic differentiation (add capability for common distributions)
- **WISH**: store `objectivefunction` and `objectivefunctiongr` (vectorized objective/gradient functions) in the `mle2` object (will break backward compatibility!!); add accessors for these and for `minuslogl`
- **WISH**: document use of the objective function in `MCMCpack` to do *post* hoc MCMC sampling (or write my own Metropolis-Hastings sampler ...)
- **WISH**: polish profile plotting, with lattice or ggplot2 methods
- **WISH**: add in/document/demonstrate "slice" capabilities
- **WISH**: refactor profiling to use stored objective functions rather than recalling `mle2` with `fixed` values mucked around with in the calls??? Strip out and make generic for vectorized objective function? (`profileModel` package only works for glm-like objects, with a linear predictor)

References

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