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Harry Southworth

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1 Introduction

This document contains the output of running the examples in the bcrm help file, as installed from CRAN on 2018-12-08. The reason is to be able to compare future versions with the current CRAN version.

Note that one of the examples (with the 3+3 design) failed to run through knitr and rmarkdown. Also, there is a final example which (on some runs) reveals a bug: there is a systematic change in the simulated trials after the 100th.

1.1 Example 1

```

startTime <- Sys.time()

seed <- 20181208
set.seed(seed)

library(bcrm)
library(ggplot2)

## Dose-escalation cancer trial example as described in Neuenschwander et al 2008.
## Pre-defined doses
dose <- c(1, 2.5, 5, 10, 15, 20, 25, 30, 40, 50, 75,
          100, 150, 200, 250)
## Pre-specified probabilities of toxicity
## [dose levels 11-15 not specified in the paper, and are for illustration only]
p.tox0 <- c(0.010, 0.015, 0.020, 0.025, 0.030, 0.040,
            0.050, 0.100, 0.170, 0.300, 0.400, 0.500,
            0.650, 0.800, 0.900)
## Data from the first 5 cohorts of 18 patients
data <- data.frame(patient=1:18,
                   dose=rep(c(1:4, 7), c(3, 4, 5, 4, 2)),
                   tox=rep(0:1, c(16, 2)))
## Target toxicity level
target.tox <- 0.30

## A 1-parameter power model is used, with standardised doses calculated using
## the plug-in prior median
## Prior for alpha is lognormal with mean 0 (on log scale)
## and standard deviation 1.34 (on log scale)
## The recommended dose for the next cohort if posterior mean is used
Power.LN.bcrm <- bcrm(stop=list(nmax=18), data=data,
                     p.tox0=p.tox0, dose=dose, ff="power",
                     prior.alpha=list(3, 0, 1.34^2),
                     target.tox=target.tox, constrain=FALSE,
                     sdose.calculate="median", pointest="mean")

##
## Stopping: Reached maximum sample size

```

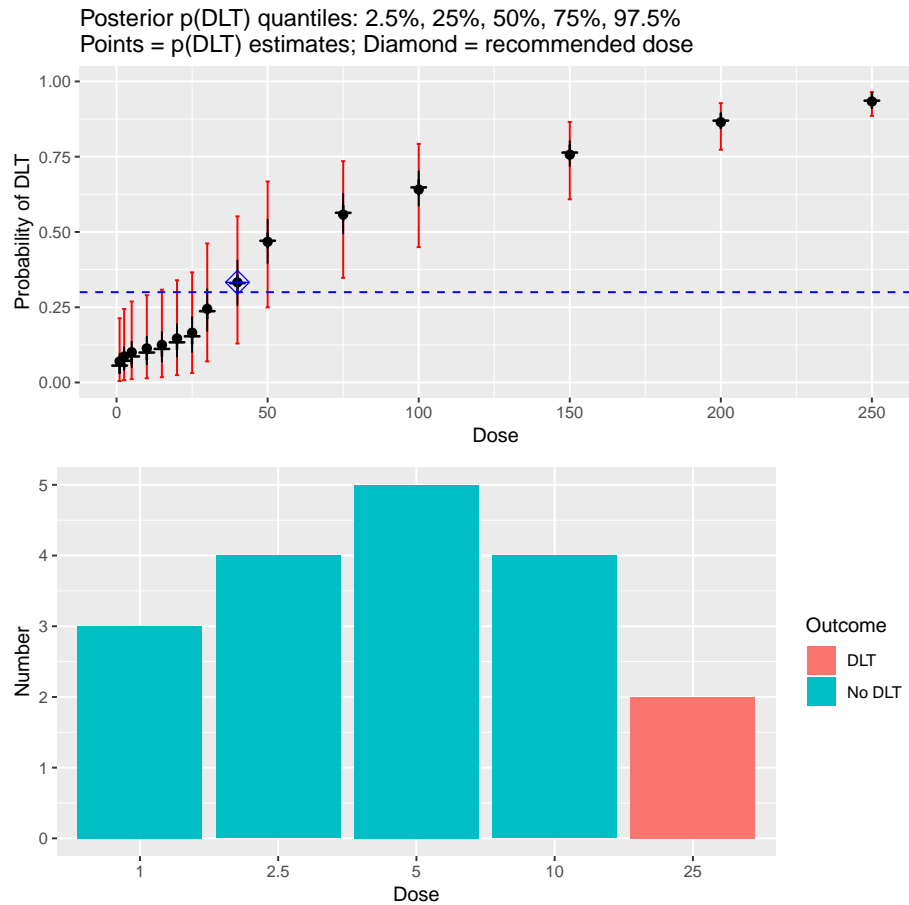
```

print(Power.LN.bcrm)
## Estimation method: exact
##
## Target toxicity level: 0.3
##
## Model: 1-parameter power
##
## Prior: Lognormal( Mean:0, Variance:1.7956)
##
## Standardised doses (skeleton):
##      1  2.5    5    10    15    20    25    30    40    50    75    100
## 0.010 0.015 0.020 0.025 0.030 0.040 0.050 0.100 0.170 0.300 0.400 0.500
##      150    200    250
## 0.650 0.800 0.900
##
## Unmodified (unconstrained) CRM used
##
## Posterior mean estimate of probability of toxicity used to select next dose
##
## Toxicities observed:
##           Doses
##           1 2.5 5 10 15 20 25 30 40 50 75 100 150 200 250
## n           3  4 5  4  0  0  2  0  0  0  0  0  0  0  0
## Toxicities 0  0 0  0  0  0  2  0  0  0  0  0  0  0  0
##
## Posterior estimates of toxicity:
##           Doses
##           1  2.5    5    10    15    20    25    30    40
## Mean    0.0702 0.0866 0.1010 0.1130 0.1250 0.1460 0.1650 0.244 0.333
## SD      0.0558 0.0630 0.0686 0.0731 0.0769 0.0831 0.0879 0.102 0.109
## Median  0.0561 0.0723 0.0865 0.0995 0.1110 0.1330 0.1530 0.237 0.330
##           Doses
##           50    75    100    150    200    250
## Mean    0.467 0.5580 0.641 0.757 0.8650 0.9330
## SD      0.108 0.0996 0.088 0.066 0.0398 0.0205
## Median  0.471 0.5640 0.648 0.764 0.8700 0.9360
##           Doses
## Quantiles 1  2.5    5    10    15    20    25    30    40
## 2.5%      0.00493 0.00787 0.0110 0.0142 0.0175 0.0244 0.0316 0.0702 0.130
## 25%       0.02860 0.03910 0.0488 0.0579 0.0667 0.0833 0.0990 0.1690 0.255
## 50%       0.05610 0.07230 0.0865 0.0995 0.1110 0.1330 0.1530 0.2370 0.330
## 75%       0.09710 0.11900 0.1380 0.1540 0.1690 0.1960 0.2190 0.3120 0.408
## 97.5%     0.21300 0.24400 0.2690 0.2900 0.3080 0.3400 0.3660 0.4620 0.552
##           Doses
## Quantiles 50    75    100    150    200    250
## 2.5%      0.249 0.347 0.450 0.608 0.773 0.886
## 25%       0.395 0.493 0.586 0.717 0.842 0.922
## 50%       0.471 0.564 0.648 0.764 0.870 0.936
## 75%       0.544 0.629 0.704 0.804 0.893 0.948

```

```
##      97.5% 0.668 0.735 0.792 0.865 0.928 0.965
##
## Next recommended dose: 40

plot(Power.LN.bcrm)
```



1.2 Example 2

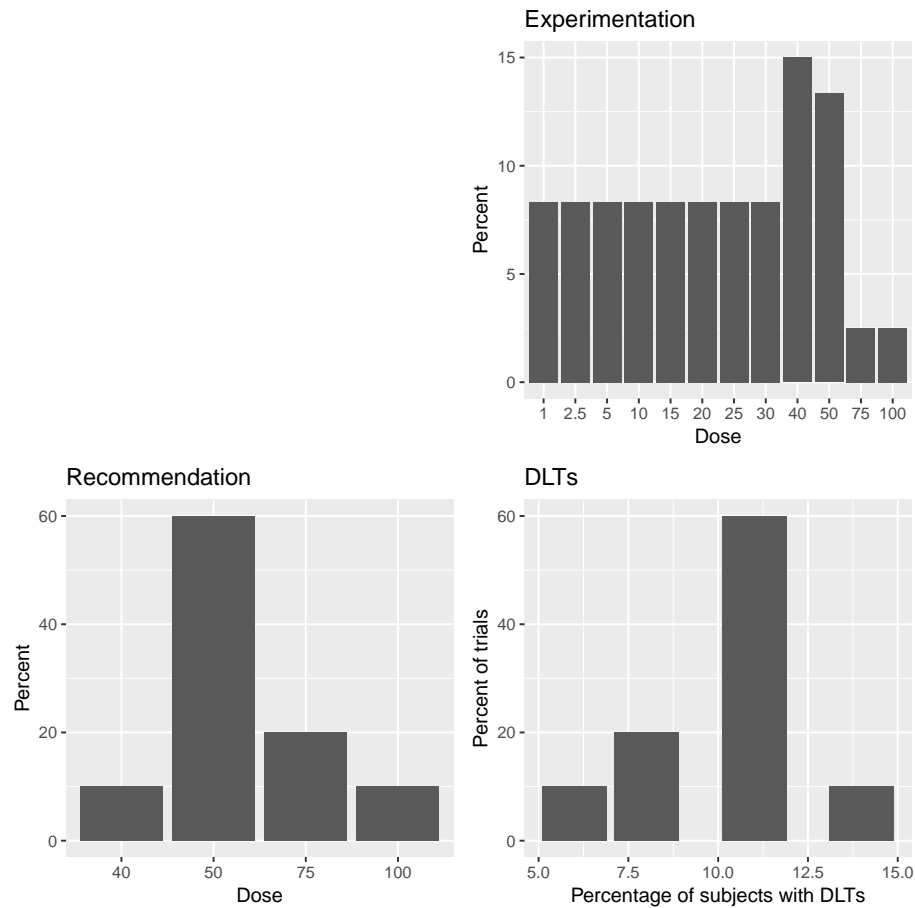
```
## Simulate 10 replicate trials of size 36 (cohort size 3) using this design
## with constraint (i.e. no dose-skipping) and starting at lowest dose
## True probabilities of toxicity are set to pre-specified probabilities (p.tox0)
Power.LN.bcrm.sim <- bcrm(stop=list(nmax=36), p.tox0=p.tox0,
  dose=dose, ff="power",
  prior.alpha=list(3, 0, 1.34^2),
  target.tox=target.tox, constrain=TRUE,
  sdose.calculate="median", pointest="mean",
  start=1, simulate=TRUE, nsims=10,
  truep=p.tox0)
```

```
## 1
## 2
## 3
## 4
## 5
## 6
## 7
## 8
## 9
## 10

print(Power.LN.bcrm.sim)

## Operating characteristics based on 10 simulations:
##
## Sample size 36
##
##           Doses
##           No dose      1      2.5      5      10      15
## Experimentation proportion      NA 0.0833 0.0833 0.0833 0.0833 0.0833
## Recommendation proportion      0 0.0000 0.0000 0.0000 0.0000 0.0000
##           Doses
##           20      25      30      40      50      75      100
## Experimentation proportion 0.0833 0.0833 0.0833 0.15 0.133 0.025 0.025
## Recommendation proportion 0.0000 0.0000 0.0000 0.10 0.600 0.200 0.100
##           Doses
##           150 200 250
## Experimentation proportion 0 0 0
## Recommendation proportion 0 0 0
##
##           Probability of DLT
##           [0,0.2] (0.2,0.4] (0.4,0.6] (0.6,0.8] (0.8,1]
## Experimentation proportion 0.817 0.158 0.025 0 0
## Recommendation proportion 0.100 0.800 0.100 0 0

plot(Power.LN.bcrm.sim)
```



1.3 Example 3

Note that in the following example, I set `threep3=FALSE` because otherwise it mysteriously never finishes executing when run through knitr or rmarkdown.

```
## Comparing this CRM design with the standard 3+3 design
## (only considering the first 12 dose levels)
Power.LN.bcrm.compare.sim <- bcrm(stop=list(nmax=36),
  p.tox0=p.tox0[1:12],
  dose=dose[1:12], ff="power",
  prior.alpha=list(3, 0, 1.34^2),
  target.tox=target.tox,
  constrain=TRUE,
  sdose.calculate="median",
  pointest="mean", start=1,
  simulate=TRUE, nsims=50,
  truep=p.tox0[1:12], threep3=FALSE,
  quietly=TRUE)

#print(Power.LN.bcrm.compare.sim, threep3=TRUE)
#plot(Power.LN.bcrm.compare.sim, threep3=TRUE)
```

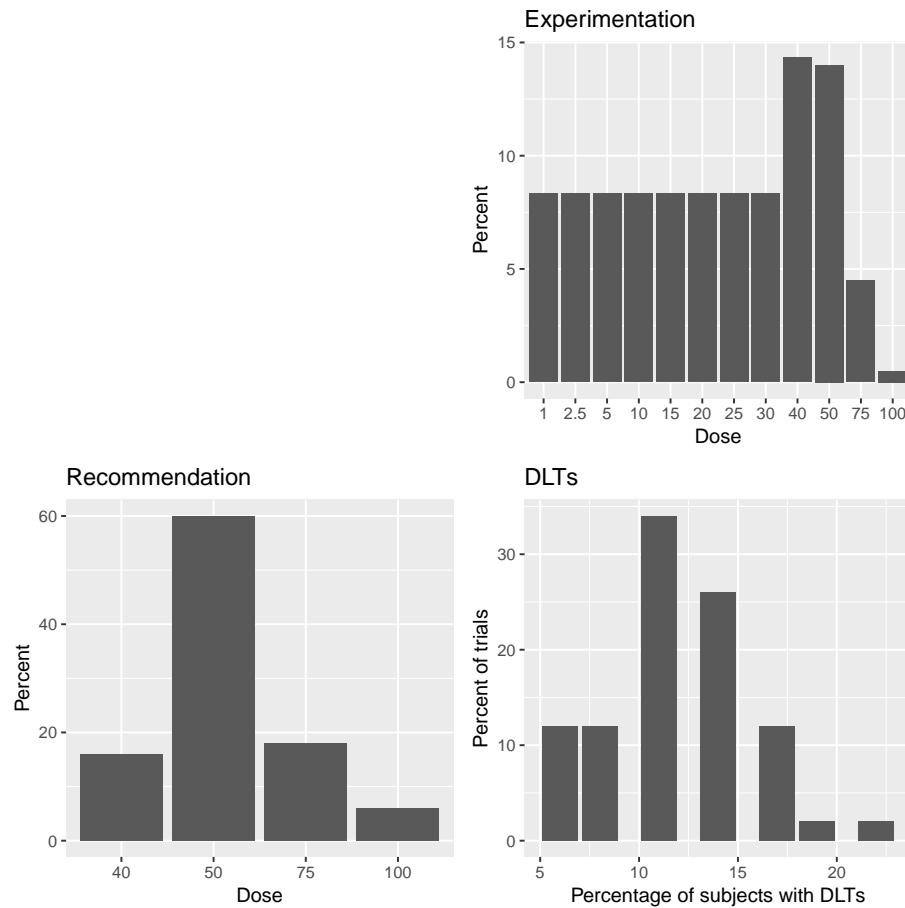
```

print(Power.LN.bcrm.compare.sim, threep3=FALSE)

## Operating characteristics based on 50 simulations:
##
##
## Sample size 36
##
##           Doses
##           No dose      1      2.5      5      10      15
## Experimentation proportion      NA 0.0833 0.0833 0.0833 0.0833 0.0833
## Recommendation proportion      0 0.0000 0.0000 0.0000 0.0000 0.0000
##           Doses
##           20      25      30      40      50      75      100
## Experimentation proportion 0.0833 0.0833 0.0833 0.143 0.14 0.045 0.005
## Recommendation proportion 0.0000 0.0000 0.0000 0.160 0.60 0.180 0.060
##
##           Probability of DLT
##           [0,0.2] (0.2,0.4] (0.4,0.6] (0.6,0.8] (0.8,1]
## Experimentation proportion      0.81      0.185      0.005      0      0
## Recommendation proportion      0.16      0.780      0.060      0      0

plot(Power.LN.bcrm.compare.sim, threep3=FALSE)

```



1.4 Example 4

```
## A 2-parameter model, using priors as specified in Neuenschwander et al 2008.
## Posterior mean used to choose the next dose
## Standardised doses using reference dose, 250mg
set.seed(20181214)

sdose <- log(dose/250)
## Bivariate lognormal prior for two parameters
mu <- c(2.15, 0.52)
Sigma <- rbind(c(0.84^2, 0.134), c(0.134, 0.80^2))
## Using rjags (requires JAGS to be installed)
TwoPLogistic.mean.bcrm <- bcrm(stop=list(nmax=18), data=data,
                                sdose=sdose, dose=dose,
                                ff="logit2",
                                prior.alpha=list(4, mu, Sigma),
                                target.tox=target.tox,
                                constrain=FALSE,
                                pointtest="mean", method="rjags")
```



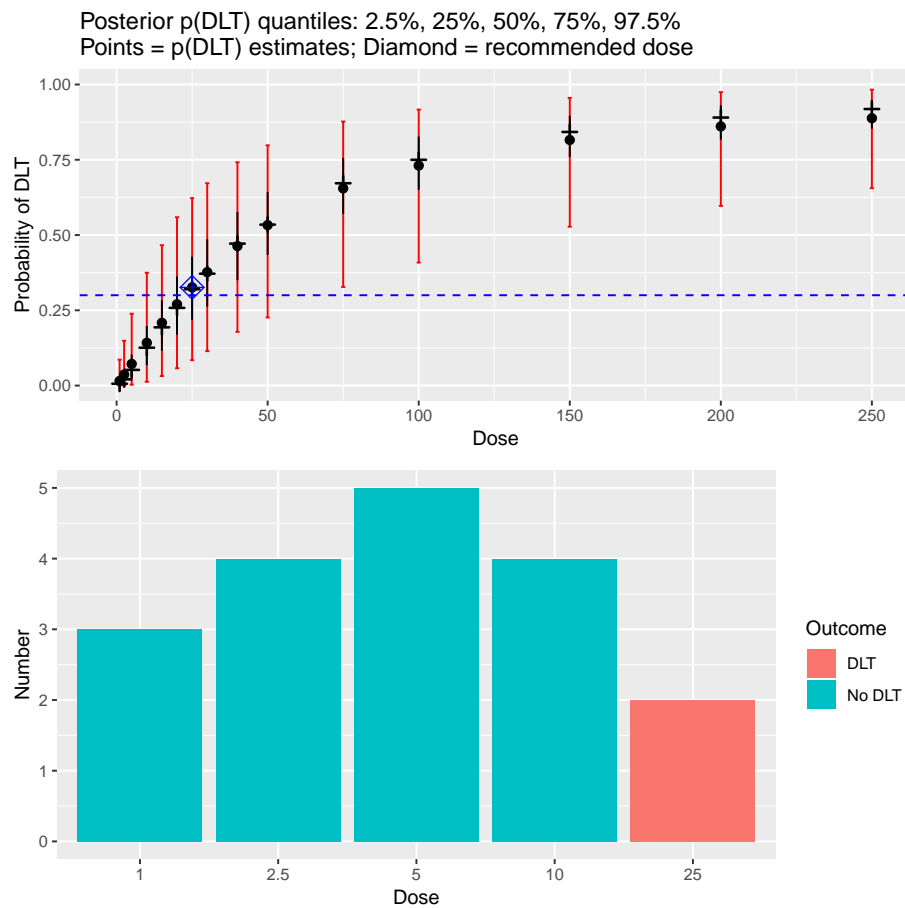
```
##
## Stopping: Reached maximum sample size

print(TwoPLogistic.mean.bcrm)

## Estimation method: rjags
##
## Target toxicity level: 0.3
##
## Model: Two-parameter logistic
##
## Prior: Log Multivariate Normal
## Mean Vector:
## [1] 2.15 0.52
##
## Variance-Covariance Matrix:
##      [,1] [,2]
## [1,] 0.7056 0.134
## [2,] 0.1340 0.640
##
## Standardised doses (skeleton):
##      1      2.5      5      10      15      20
## -5.5214609 -4.6051702 -3.9120230 -3.2188758 -2.8134107 -2.5257286
##      25      30      40      50      75      100
## -2.3025851 -2.1202635 -1.8325815 -1.6094379 -1.2039728 -0.9162907
##      150      200      250
## -0.5108256 -0.2231436 0.0000000
##
## Unmodified (unconstrained) CRM used
##
## Posterior mean estimate of probability of toxicity used to select next dose
##
## Toxicities observed:
##      Doses
##      1 2.5 5 10 15 20 25 30 40 50 75 100 150 200 250
## n      3  4 5  4  0  0  2  0  0  0  0  0  0  0  0
## Toxicities 0  0 0  0  0  0  2  0  0  0  0  0  0  0  0
##
## Posterior estimates of toxicity:
##      Doses
##      1      2.5      5      10      15      20      25      30      40      50
## Mean  0.0155 0.0365 0.0719 0.1420 0.209 0.270 0.326 0.377 0.463 0.533
## SD    0.0235 0.0412 0.0637 0.0958 0.117 0.130 0.139 0.143 0.147 0.146
## Median 0.0060 0.0205 0.0520 0.1260 0.193 0.258 0.320 0.372 0.471 0.535
##      Doses
##      75      100      150      200      250
## Mean  0.655 0.731 0.816 0.861 0.8880
## SD    0.137 0.127 0.112 0.101 0.0934
## Median 0.672 0.750 0.842 0.890 0.9180
##      Doses
```

```
## Quantiles      1      2.5      5      10      15      20      25      30
##      2.5% 6.53e-05 0.000602 0.00285 0.0127 0.0314 0.0575 0.0843 0.114
##      25%  2.02e-03 0.008370 0.02500 0.0680 0.1150 0.1690 0.2180 0.262
##      50%  6.00e-03 0.020500 0.05200 0.1260 0.1930 0.2580 0.3200 0.372
##      75%  1.91e-02 0.053000 0.10300 0.1980 0.2830 0.3620 0.4280 0.486
##      97.5% 8.61e-02 0.149000 0.23900 0.3750 0.4660 0.5590 0.6230 0.672
##      Doses
## Quantiles      40      50      75      100     150     200     250
##      2.5% 0.178 0.226 0.328 0.409 0.528 0.597 0.656
##      25%  0.350 0.434 0.570 0.651 0.759 0.817 0.854
##      50%  0.471 0.535 0.672 0.750 0.842 0.890 0.918
##      75%  0.577 0.643 0.756 0.827 0.896 0.931 0.949
##      97.5% 0.742 0.798 0.877 0.917 0.955 0.975 0.983
##
## Next recommended dose: 25

plot(TwoPLogistic.mean.bcrm)
```



1.5 Example 5

```

## A 2-parameter model, using an EWOC design with feasibility
## bound (MTD quantile)
## of 0.25 to choose the next dose
## Using rjags (requires JAGS to be installed)
TwoPLogistic.EWOC0.25.bcrm <- bcrm(stop=list(nmax=18), data=data,
                                   sdose=sdose, dose=dose,
                                   ff="logit2",
                                   prior.alpha=list(4, mu, Sigma),
                                   target.tox=target.tox,
                                   constrain=FALSE,
                                   pointest=0.25, method="rjags")

##
## Stopping: Reached maximum sample size

print(TwoPLogistic.EWOC0.25.bcrm)

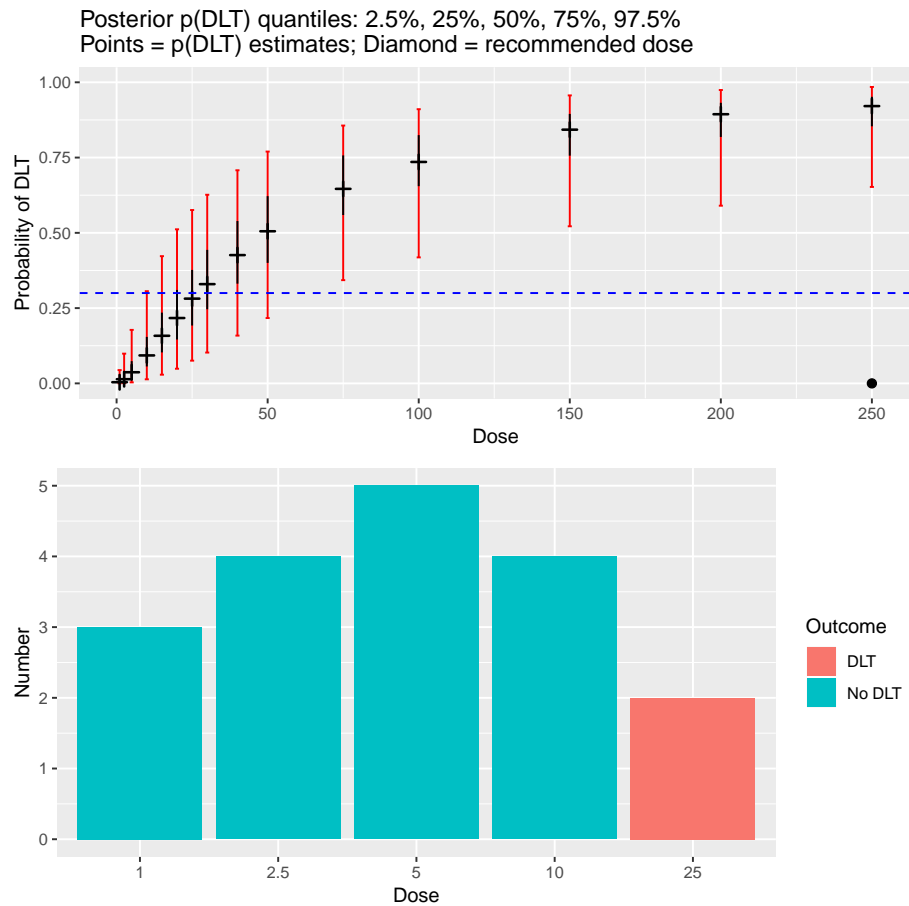
## Estimation method: rjags
##
## Target toxicity level: 0.3
##
## Model: Two-parameter logistic
##
## Prior: Log Multivariate Normal
## Mean Vector:
## [1] 2.15 0.52
##
## Variance-Covariance Matrix:
##      [,1] [,2]
## [1,] 0.7056 0.134
## [2,] 0.1340 0.640
##
## Standardised doses (skeleton):
##      1      2.5      5      10      15      20
## -5.5214609 -4.6051702 -3.9120230 -3.2188758 -2.8134107 -2.5257286
##      25      30      40      50      75      100
## -2.3025851 -2.1202635 -1.8325815 -1.6094379 -1.2039728 -0.9162907
##      150      200      250
## -0.5108256 -0.2231436 0.0000000
##
## Unmodified (unconstrained) CRM used
##
## 25 percentile of (standardised) MTD distribution used to select next dose
## 25 percentile is: -2.562308
##
## Toxicities observed:
##      Doses
##      1 2.5 5 10 15 20 25 30 40 50 75 100 150 200 250
## n      3  4 5  4  0  0  2  0  0  0  0  0  0  0  0
## Toxicities 0  0 0  0  0  0  2  0  0  0  0  0  0  0  0

```

```
##
## Posterior estimates of toxicity:
##      Doses
##           1      2.5      5      10      15      20      25      30      40      50
## Mean    0.00911 0.0248 0.0535 0.1150 0.177 0.236 0.292 0.344 0.434 0.508
## SD      0.01360 0.0288 0.0504 0.0831 0.106 0.121 0.131 0.138 0.145 0.146
## Median  0.00387 0.0139 0.0369 0.0929 0.158 0.217 0.281 0.330 0.426 0.505
##      Doses
##           75     100     150     200     250
## Mean    0.641 0.723 0.816 0.8650 0.8940
## SD      0.138 0.127 0.107 0.0928 0.0817
## Median  0.646 0.735 0.843 0.8940 0.9210
##      Doses
## Quantiles      1      2.5      5      10      15      20      25      30
## 2.5%  0.000085 0.000623 0.00331 0.0135 0.0289 0.0486 0.0755 0.102
## 25%   0.001070 0.005480 0.01970 0.0562 0.1030 0.1460 0.1920 0.246
## 50%   0.003870 0.013900 0.03690 0.0929 0.1580 0.2170 0.2810 0.330
## 75%   0.010600 0.032500 0.07380 0.1540 0.2350 0.3100 0.3770 0.443
## 97.5% 0.044100 0.098700 0.17800 0.3060 0.4230 0.5120 0.5760 0.626
##      Doses
## Quantiles      40      50      75      100     150     200     250
## 2.5%  0.159 0.217 0.343 0.418 0.522 0.590 0.652
## 25%   0.331 0.400 0.559 0.655 0.756 0.819 0.854
## 50%   0.426 0.505 0.646 0.735 0.843 0.894 0.921
## 75%   0.539 0.622 0.757 0.825 0.895 0.932 0.952
## 97.5% 0.708 0.770 0.856 0.911 0.957 0.974 0.985
##
## Next recommended dose: 20

plot(TwoPLogistic.EWOC0.25.bcrm)

## Warning: Removed 14 rows containing missing values (geom.point).
## Warning: Removed 1 rows containing missing values (geom.point).
```



1.6 Example 6

```
## A 2-parameter model, using a loss function based on
## intervals of toxicity to choose the next dose
## Using rjags (requires JAGS to be installed)
## Toxicity cut-points
tox.cutpoints <- c(0.2, 0.35, 0.6)
## Losses associated with toxicity intervals
## [0, 0.2]=1, (0.2, 0.35]=0, (0.35, 0.6]=1, (0.6, 1]=2
loss <- c(1, 0, 1, 2)
TwoPLogistic.tox.intervals.bcrm <- bcrm(stop=list(nmax=18),
                                         data=data, sdose=sdose,
                                         dose=dose, ff="logit2",
                                         prior.alpha=list(4, mu, Sigma),
                                         target.tox=target.tox,
                                         constrain=FALSE,
                                         tox.cutpoints=tox.cutpoints,
                                         loss=loss, method="rjags")
```

```
##
## Stopping: Reached maximum sample size

print(TwoPLogistic.tox.intervals.bcrm)

## Estimation method: rjags
##
## Target toxicity level: 0.3
##
## Model: Two-parameter logistic
##
## Prior: Log Multivariate Normal
## Mean Vector:
## [1] 2.15 0.52
##
## Variance-Covariance Matrix:
##      [,1] [,2]
## [1,] 0.7056 0.134
## [2,] 0.1340 0.640
##
## Standardised doses (skeleton):
##      1      2.5      5      10      15      20
## -5.5214609 -4.6051702 -3.9120230 -3.2188758 -2.8134107 -2.5257286
##      25      30      40      50      75      100
## -2.3025851 -2.1202635 -1.8325815 -1.6094379 -1.2039728 -0.9162907
##      150      200      250
## -0.5108256 -0.2231436 0.0000000
##
## Unmodified (unconstrained) CRM used
##
## Loss function given intervals of toxicity used to select next dose.
## Loss function:
## (0,0.2] (0.2,0.35] (0.35,0.6] (0.6,1]
##      1      0      1      2
##
## Toxicities observed:
##      Doses
##      1 2.5 5 10 15 20 25 30 40 50 75 100 150 200 250
## n      3  4 5  4  0  0  2  0  0  0  0  0  0  0  0
## Toxicities 0  0 0  0  0  0  2  0  0  0  0  0  0  0  0
##
## Posterior estimates of toxicity:
##      Doses
##      1      2.5      5      10      15      20      25      30      40      50
## Mean  0.01150 0.0293 0.0608 0.1260 0.190 0.250 0.306 0.358 0.447 0.520
## SD    0.01790 0.0345 0.0570 0.0899 0.112 0.126 0.134 0.139 0.143 0.142
## Median 0.00527 0.0175 0.0419 0.1020 0.165 0.229 0.288 0.342 0.435 0.525
##      Doses
##      75      100      150      200      250
## Mean  0.648 0.728 0.817 0.8640 0.8920
```

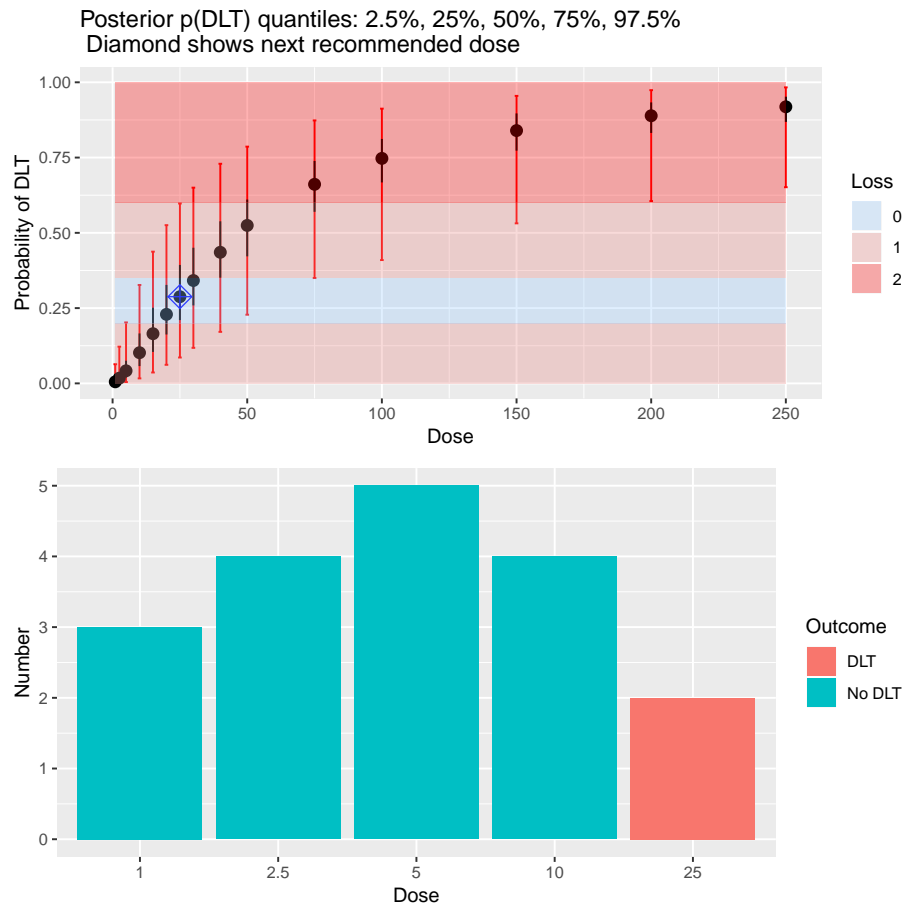
```

##      SD      0.134 0.125 0.108 0.0959 0.0865
##      Median 0.661 0.747 0.840 0.8890 0.9190
##      Doses
## Quantiles      1      2.5      5      10      15      20      25      30      40
##      2.5%  0.000133 0.00101 0.00445 0.0165 0.0362 0.0617 0.0859 0.118 0.171
##      25%   0.001310 0.00612 0.01930 0.0574 0.1040 0.1620 0.2100 0.259 0.351
##      50%   0.005270 0.01750 0.04190 0.1020 0.1650 0.2290 0.2880 0.342 0.435
##      75%   0.011900 0.03220 0.07540 0.1660 0.2510 0.3270 0.3930 0.451 0.538
##      97.5% 0.063500 0.12200 0.20200 0.3270 0.4370 0.5250 0.5970 0.650 0.729
##      Doses
## Quantiles      50      75      100      150      200      250
##      2.5%  0.228 0.350 0.410 0.532 0.605 0.652
##      25%   0.422 0.570 0.667 0.773 0.832 0.868
##      50%   0.525 0.661 0.747 0.840 0.889 0.919
##      75%   0.611 0.739 0.812 0.897 0.933 0.952
##      97.5% 0.786 0.873 0.912 0.955 0.974 0.983
##
##      Posterior expected loss at each dose:
##      1      2.5      5      10      15      20      25      30      40      50
## [1,] 0.9995 0.998 0.9745 0.832 0.707 0.6515 0.5645 0.6555 0.9575 1.1765
##      75      100      150      200      250
## [1,] 1.6695 1.838 1.939 1.974 1.983
##
##      Posterior probability of dose being in each toxicity interval
## Toxicity intervals      1      2.5      5      10      15      20      25      30
##      (0,0.2]  0.9995 0.998 0.9740 0.809 0.601 0.4380 0.2230 0.1095
##      (0.2,0.35] 0.0005 0.002 0.0255 0.168 0.293 0.3540 0.4585 0.4035
##      (0.35,0.6] 0.0000 0.000 0.0005 0.023 0.106 0.2025 0.2955 0.4280
##      (0.6,1]   0.0000 0.000 0.0000 0.000 0.000 0.0055 0.0230 0.0590
##      Doses
## Toxicity intervals      40      50      75      100      150      200      250
##      (0,0.2]  0.0440 0.0155 0.0015 0.0015 0.0000 0.0000 0.0000
##      (0.2,0.35] 0.2010 0.1060 0.0240 0.0075 0.0025 0.0015 0.0015
##      (0.35,0.6] 0.5965 0.5960 0.2810 0.1455 0.0560 0.0230 0.0140
##      (0.6,1]   0.1585 0.2825 0.6935 0.8455 0.9415 0.9755 0.9845
##
##      Next recommended dose: 25

```

`plot(TwoPLogistic.tox.intervals.bcrm)`

Doses



1.7 Example 7

```
## Greater loss associated with overdosing and unacceptable toxicity
## [0, 0.2]=1, (0.2, 0.35]=0, (0.35, 0.6]=2, (0.6, 1]=4
loss2 <- c(1, 0, 2, 4)
TwoPLogistic.tox.intervals.2.bcrm <- bcrm(stop=list(nmax=18),
                                          data=data, sdose=sdose,
                                          dose=dose, ff="logit2",
                                          prior.alpha=list(4, mu, Sigma),
                                          target.tox=target.tox,
                                          constrain=FALSE,
                                          tox.cutpoints=tox.cutpoints,
                                          loss=loss2, method="rjags")

##
## Stopping: Reached maximum sample size
print(TwoPLogistic.tox.intervals.2.bcrm)

## Estimation method: rjags
```



```

##
## Target toxicity level: 0.3
##
## Model: Two-parameter logistic
##
## Prior: Log Multivariate Normal
## Mean Vector:
## [1] 2.15 0.52
##
## Variance-Covariance Matrix:
##      [,1] [,2]
## [1,] 0.7056 0.134
## [2,] 0.1340 0.640
##
## Standardised doses (skeleton):
##      1      2.5      5      10      15      20
## -5.5214609 -4.6051702 -3.9120230 -3.2188758 -2.8134107 -2.5257286
##      25      30      40      50      75      100
## -2.3025851 -2.1202635 -1.8325815 -1.6094379 -1.2039728 -0.9162907
##      150      200      250
## -0.5108256 -0.2231436 0.0000000
##
## Unmodified (unconstrained) CRM used
##
## Loss function given intervals of toxicity used to select next dose.
## Loss function:
## (0,0.2] (0.2,0.35] (0.35,0.6] (0.6,1]
##      1      0      2      4
##
## Toxicities observed:
##      Doses
##      1 2.5 5 10 15 20 25 30 40 50 75 100 150 200 250
## n      3  4 5  4  0  0  2  0  0  0  0  0  0  0  0
## Toxicities 0  0 0  0  0  0  2  0  0  0  0  0  0  0  0
##
## Posterior estimates of toxicity:
##      Doses
##      1      2.5      5      10      15      20      25      30      40      50
## Mean  0.0105 0.0276 0.0586 0.1240 0.188 0.249 0.306 0.357 0.445 0.517
## SD    0.0156 0.0314 0.0528 0.0859 0.110 0.128 0.140 0.148 0.157 0.158
## Median 0.0047 0.0167 0.0437 0.1060 0.172 0.236 0.296 0.354 0.448 0.526
##      Doses
##      75      100      150      200      250
## Mean  0.644 0.724 0.815 0.8630 0.8920
## SD    0.149 0.135 0.111 0.0944 0.0827
## Median 0.667 0.746 0.837 0.8860 0.9140
##      Doses
## Quantiles      1      2.5      5      10      15      20      25      30
## 2.5% 6.25e-05 0.000492 0.00234 0.0100 0.0253 0.0426 0.0616 0.0847

```

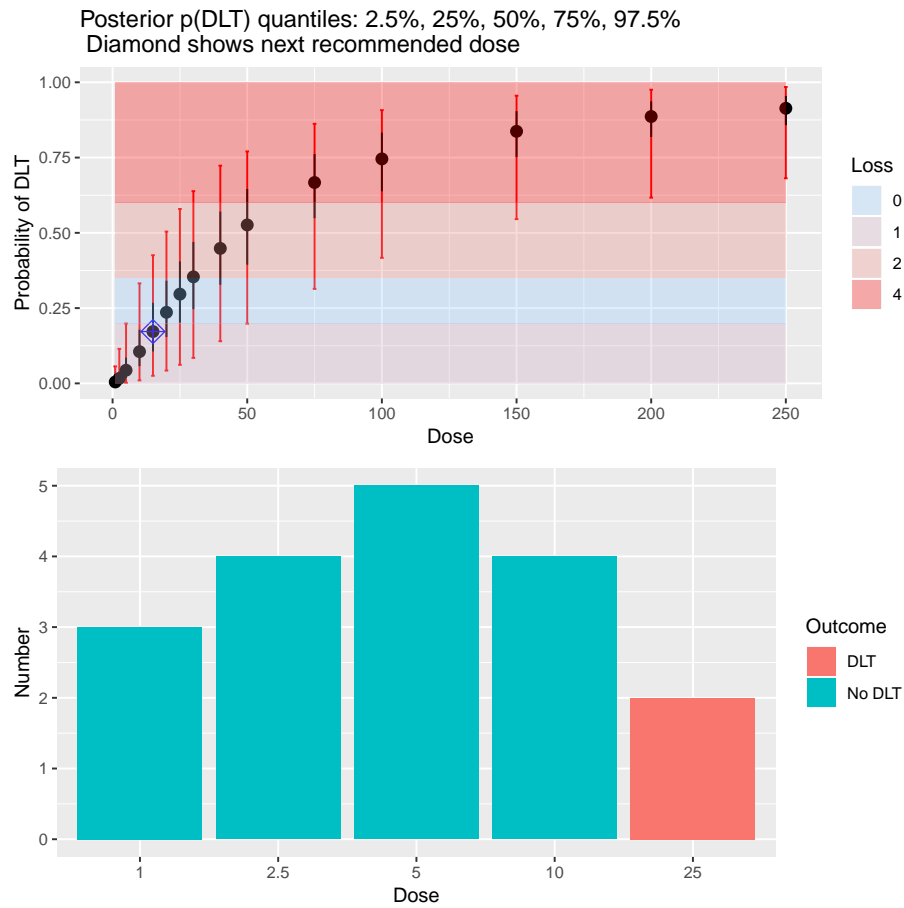
```

##      25%      1.34e-03 0.006050 0.01790 0.0572 0.1060 0.1540 0.2020 0.2470
##      50%      4.70e-03 0.016700 0.04370 0.1060 0.1720 0.2360 0.2960 0.3540
##      75%      1.26e-02 0.039100 0.08590 0.1780 0.2680 0.3410 0.4050 0.4700
##      97.5% 5.63e-02 0.115000 0.19900 0.3320 0.4260 0.5040 0.5790 0.6380
##              Doses
## Quantiles      40      50      75      100      150      200      250
##      2.5%      0.140 0.198 0.314 0.417 0.546 0.617 0.681
##      25%      0.327 0.394 0.549 0.638 0.752 0.818 0.858
##      50%      0.448 0.526 0.667 0.746 0.837 0.886 0.914
##      75%      0.571 0.646 0.762 0.833 0.904 0.937 0.955
##      97.5% 0.723 0.770 0.862 0.907 0.955 0.975 0.985
##
## Posterior expected loss at each dose:
##      1      2.5      5      10      15      20      25      30      40      50      75      100
## [1,] 1 0.998 0.9765 0.85 0.7525 0.8475 1.04 1.2825 1.863 2.436 3.179 3.612
##      150      200      250
## [1,] 3.889 3.965 3.984
##
## Posterior probability of dose being in each toxicity interval
## Toxicity intervals 1      2.5      5      10      15      20      25      30      40
##      (0,0.2]      1 0.998 0.9765 0.820 0.5825 0.3755 0.2490 0.1735 0.0630
##      (0.2,0.35] 0 0.002 0.0235 0.165 0.3325 0.3960 0.3710 0.3220 0.2165
##      (0.35,0.6] 0 0.000 0.0000 0.015 0.0850 0.2210 0.3645 0.4545 0.5410
##      (0.6,1]      0 0.000 0.0000 0.000 0.0000 0.0075 0.0155 0.0500 0.1795
##              Doses
## Toxicity intervals      50      75      100      150      200      250
##      (0,0.2]      0.0280 0.0020 0.0000 0.0000 0.0000 0.000
##      (0.2,0.35] 0.1255 0.0315 0.0115 0.0005 0.0005 0.000
##      (0.35,0.6] 0.4890 0.3445 0.1710 0.0545 0.0165 0.008
##      (0.6,1]      0.3575 0.6220 0.8175 0.9450 0.9830 0.992
##
## Next recommended dose: 15

```

plot(TwoPLogistic.tox.intervals.2.bcrm)

Doses



1.8 Example 8

```
# And a final example, not from the help file, that reveals a bug
# on some runs
dose <- 1:12
p.tox0 <- seq(.04, .5, length.out = length(dose))
target.tox <- 0.33
sdose <- log(dose/25)
mu <- c(2.15, 0.52)
Sigma <- rbind(c(0.84^2, 0.134), c(0.134, 0.80^2))

m <- bcrm::bcrm(stop=list(nmax=18), sdose=sdose,
  dose=dose, ff="logit2",
  prior.alpha=list(4, mu, Sigma),
  target.tox=target.tox,
  constrain=FALSE, quietly=TRUE,
  pointest=0.25, method="rjags",
  truep=p.tox0 * 1.5, simulate=TRUE, nsim=200)
```

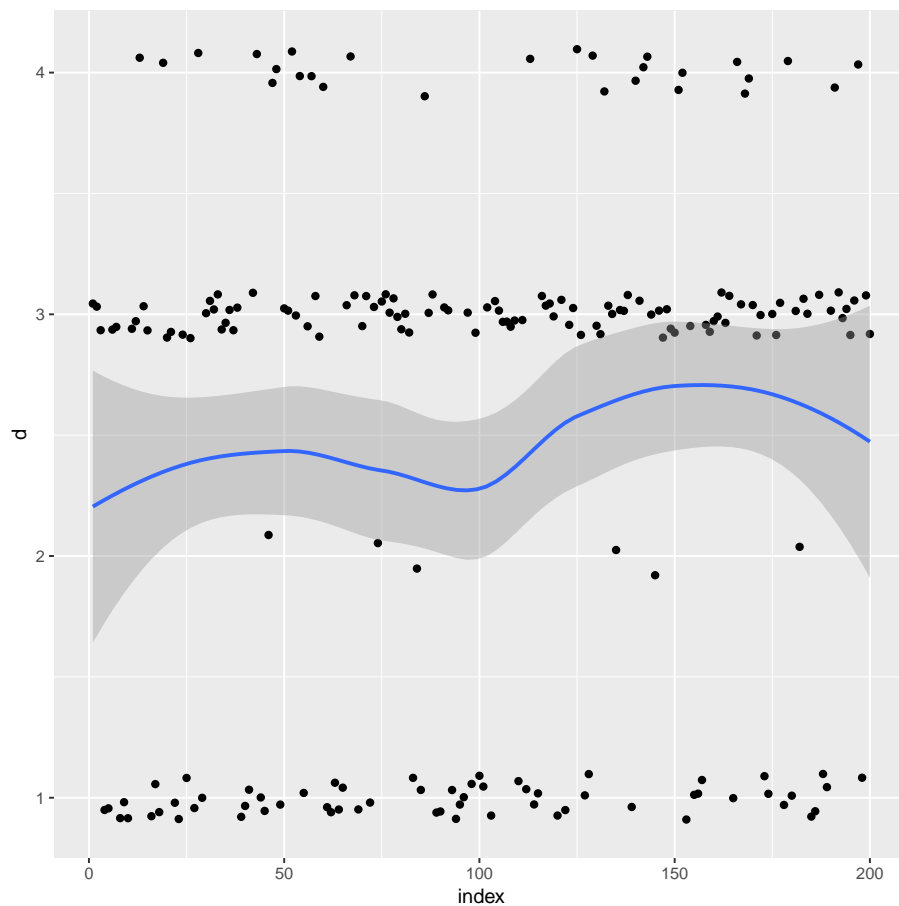
```
## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

d <- sapply(m, function(X){
  max(diff(X$data$dose))
})
d <- data.frame(d, index = 1:200)

ggplot(d, aes(index, d)) +
  geom_point(position=position_jitter(height=.1, width=0)) +
  geom_smooth()

## 'geom_smooth()' using method = 'loess' and formula 'y ~ x'
```



1.9 Example 9

This example is the same as the last one but with more simulated trials. It is to compare the times of a minimally fixed version of 4.7 (4.7.999) with 4.9.X.

```

# And a final example, not from the help file, that reveals a bug
# on some runs
dose <- 1:12
p.tox0 <- seq(.04, .5, length.out = length(dose))
target.tox <- 0.33
sdose <- log(dose/25)
mu <- c(2.15,0.52)
Sigma <- rbind(c(0.84^2,0.134),c(0.134,0.80^2))

m <- bcrm::bcrm(stop=list(nmax=18), sdose=sdose,
                dose=dose, ff="logit2",
                prior.alpha=list(4,mu,Sigma),
                target.tox=target.tox,
                constrain=FALSE, quietly=TRUE,
                pointest=0.25, method="rjags",
                truep=p.tox0 * 1.5, simulate=TRUE,
                nsim=2000)

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

```

DRAFT

```
## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

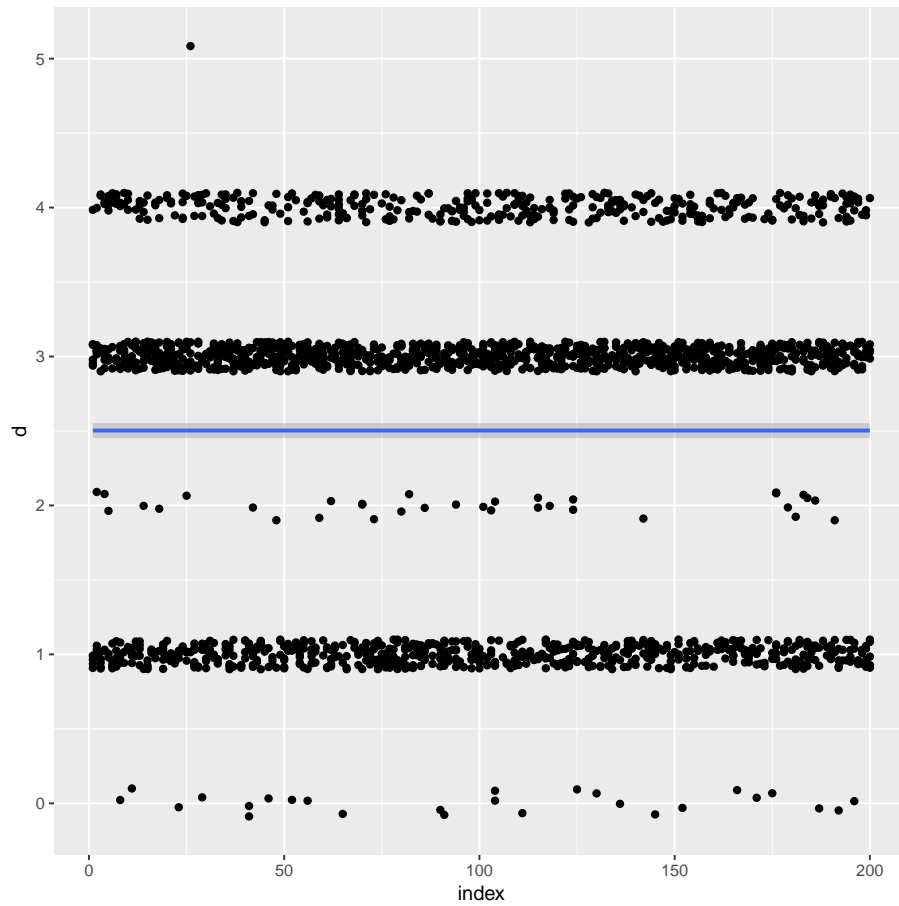
## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## NOTE: Stopping adaptation

d <- sapply(m, function(X){
  max(diff(X$data$dose))
})
d <- data.frame(d, index = 1:200)

ggplot(d, aes(index, d)) +
  geom_point(position=position_jitter(height=.1, width=0)) +
  geom_smooth()

## 'geom_smooth()' using method = 'gam' and formula 'y ~ s(x, bs =
"cs")'
```



```
Sys.time() - startTime
## Time difference of 7.231886 mins
```


2 Information on the R session

Information on the R session, in the interests of reproducibility.

- R version 3.4.4 (2018-03-15), x86_64-pc-linux-gnu
- Locale: LC_CTYPE=en_GB.UTF-8, LC_NUMERIC=C, LC_TIME=en_GB.UTF-8, LC_COLLATE=en_GB.UTF-8, LC_MONETARY=en_GB.UTF-8, LC_MESSAGES=en_GB.UTF-8, LC_PAPER=en_GB.UTF-8, LC_NAME=C, LC_ADDRESS=C, LC_TELEPHONE=C, LC_MEASUREMENT=en_GB.UTF-8, LC_IDENTIFICATION=C
- Running under: Ubuntu 18.04.1 LTS
- Matrix products: default
- BLAS: /usr/lib/x86_64-linux-gnu/blas/libblas.so.3.7.1
- LAPACK: /usr/lib/x86_64-linux-gnu/lapack/liblapack.so.3.7.1
- Base packages: base, datasets, graphics, grDevices, methods, stats, utils
- Other packages: bcrn 0.4.7.999, ggplot2 3.1.0
- Loaded via a namespace (and not attached): assertthat 0.2.0, bindr 0.1.1, bindrcpp 0.2.2, boot 1.3-20, coda 0.19-2, colorspace 1.3-2, compiler 3.4.4, crayon 1.3.4, digest 0.6.18, dplyr 0.7.8, evaluate 0.12, glue 1.3.0, grid 3.4.4, gtable 0.2.0, highr 0.7, knitr 1.20, labeling 0.3, lattice 0.20-38, lazyeval 0.2.1, magrittr 1.5, Matrix 1.2-15, mgcv 1.8-26, munsell 0.5.0, mvtnorm 1.0-8, nlme 3.1-137, pillar 1.3.0, pkgconfig 2.0.2, plyr 1.8.4, purrr 0.2.5, R2WinBUGS 2.1-21, R6 2.3.0, Rcpp 1.0.0, rjags 4-8, rlang 0.3.0.1, scales 1.0.0, stringi 1.2.4, stringr 1.3.1, tibble 1.4.2, tidyselect 0.2.5, tools 3.4.4, withr 2.1.2, yaml 2.2.0