

Output from CRAN bcrn 0.4.7

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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.

Some of the plots are slightly different (titles and point shapes) due to changes to github.com/mikesweeting/bcrm that have not been published to CRAN.

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")
```

```

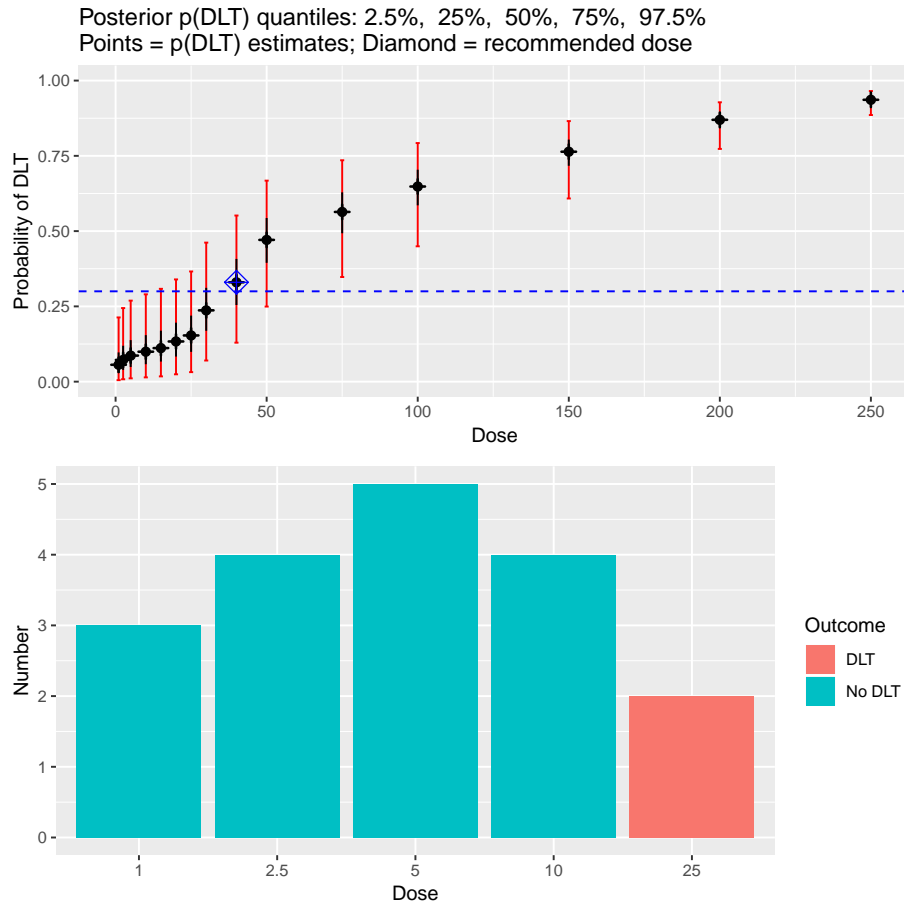
##
## Stopping: Reached maximum sample size
print(Power.LN.bcrm)

##
## 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)
```



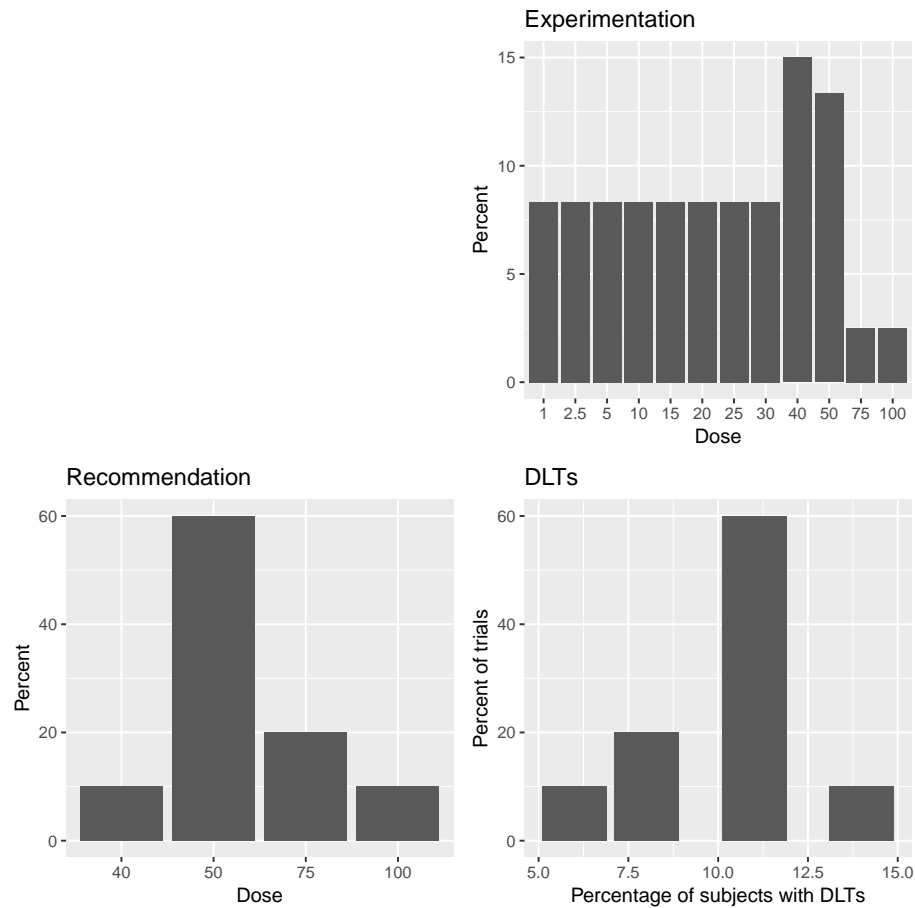
1.2 Example 2

```
## 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)
```

```
## Simulated trial: 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, `threep3=TRUE` but it won't work in the CRAN version because it prompts for a go-ahead and knitr and rmarkdown can't cope with that.

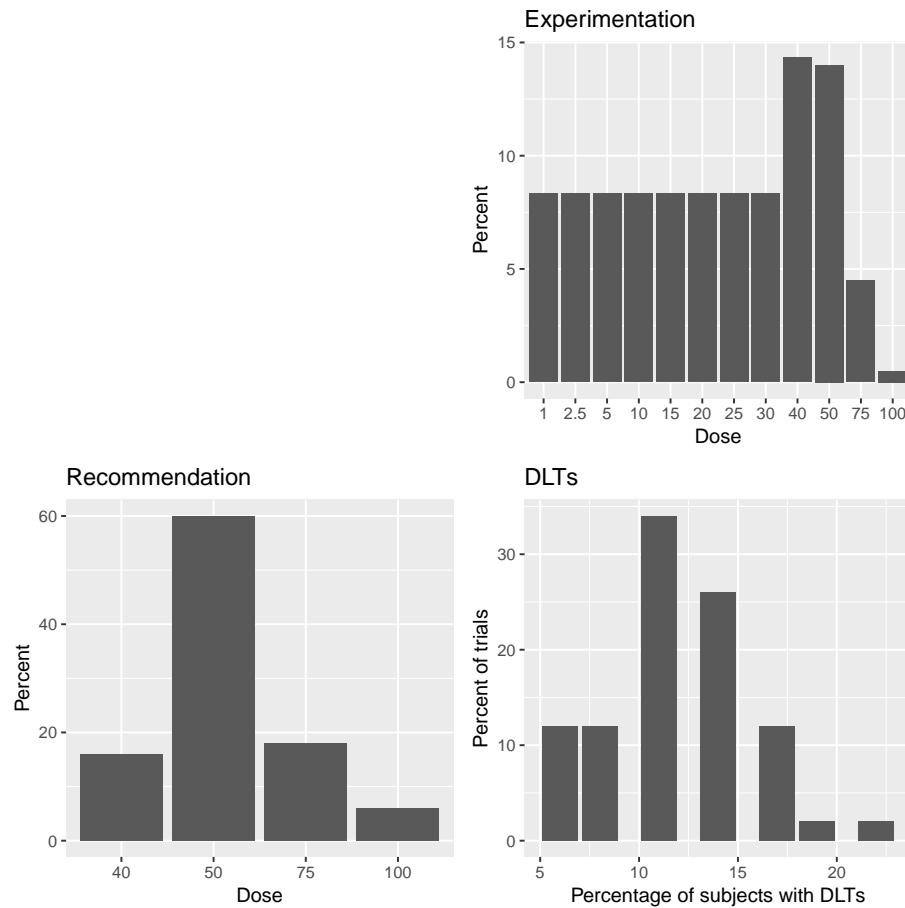
```
## Comparing this CRM design with the standard 3+3 design
## (only considering the first 12 dose levels)
Power.LN.bcrm.compare.sim <- bcrm(stop=list(nmax=36),
  p.tox0=p.tox0[1:12],
  dose=dose[1:12], ff="power",
  prior.alpha=list(3, 0, 1.34^2),
  target.tox=target.tox,
  constrain=TRUE,
  sdose.calculate="median",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

```
## Calculating operating characteristics of a standard 3+3 trial for
comparison...
## 12% complete
## 16% complete
## 20% complete
## 24% complete
## 28% complete
## 32% complete
## 36% complete
## 40% complete
## 44% complete
## 48% complete
## 52% complete
## 56% complete
## 60% complete
## 64% complete
## 68% complete
## 72% complete
## 76% complete
## 80% complete
## 84% complete
## 88% complete
## 92% complete
## 96% complete
## 100% complete

print(Power.LN.bcrm.compare.sim)

## 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)
```



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,
                                pointest="mean", method="rjags")
```



```

##
## Stopping: Reached maximum sample size
print(TwoPLogistic.mean.bcrm)

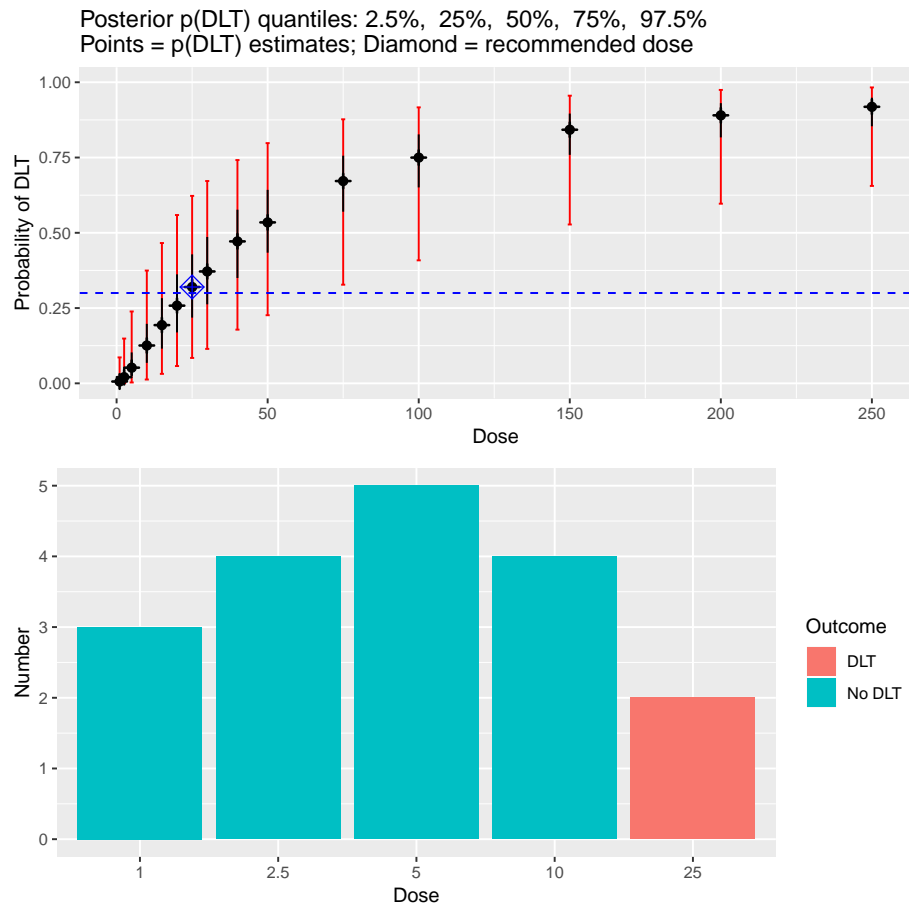
##
## Estimation method: rjags
## Target toxicity level: 0.3
## Model: Two-parameter logistic
## Prior: Log Multivariate Normal

## 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

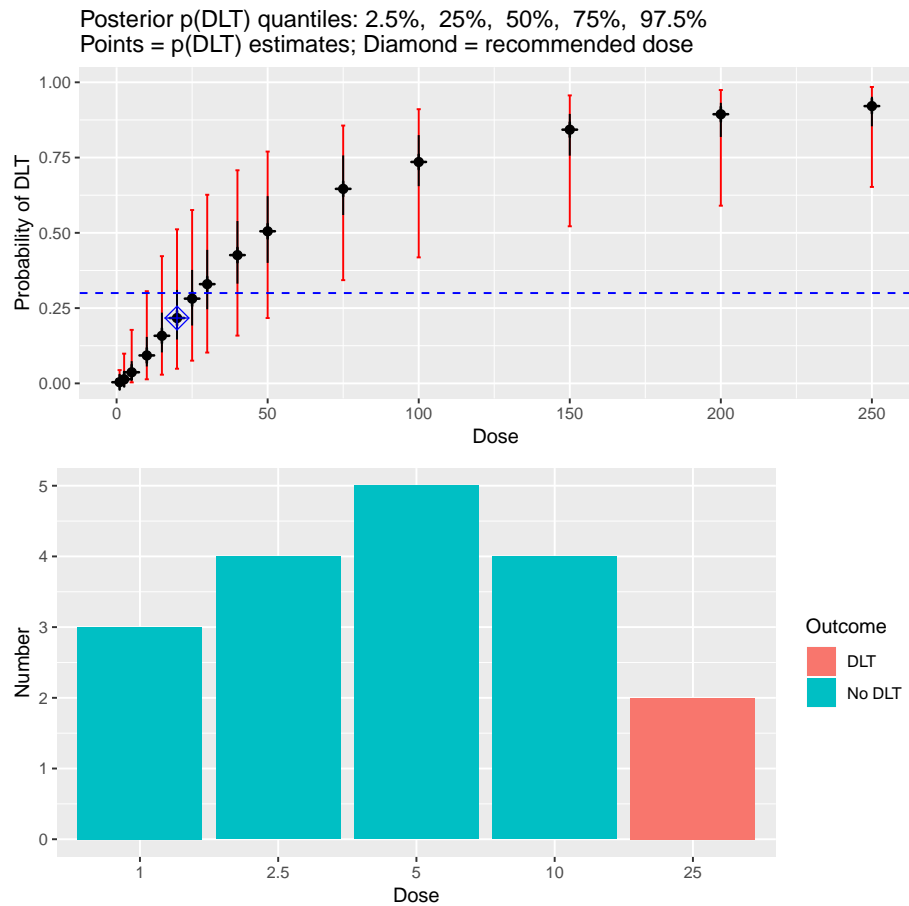
## Mean Vector:

## [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)
```



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

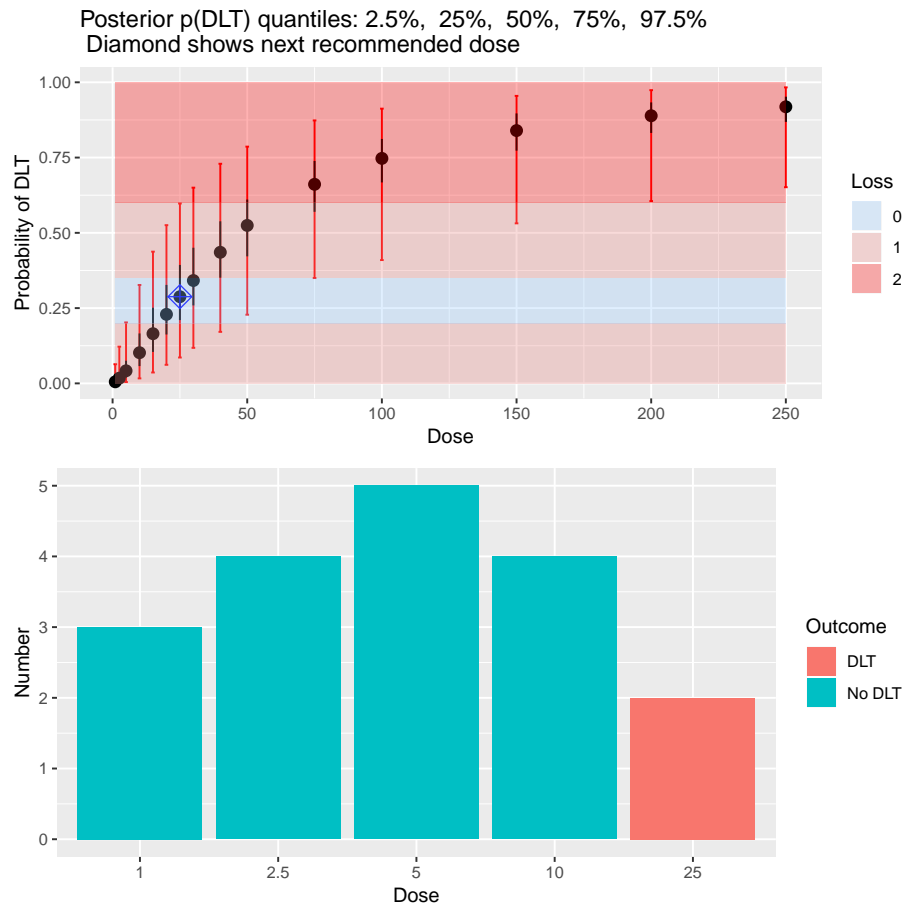
## Mean Vector:
## [1] 2.15 0.52
##
## Variance-Covariance Matrix:
##      [,1] [,2]
## [1,] 0.7056 0.134
## [2,] 0.1340 0.640
##
## Standardised doses (skeleton):
##      1      2.5      5      10      15      20
## -5.5214609 -4.6051702 -3.9120230 -3.2188758 -2.8134107 -2.5257286
##      25      30      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

```

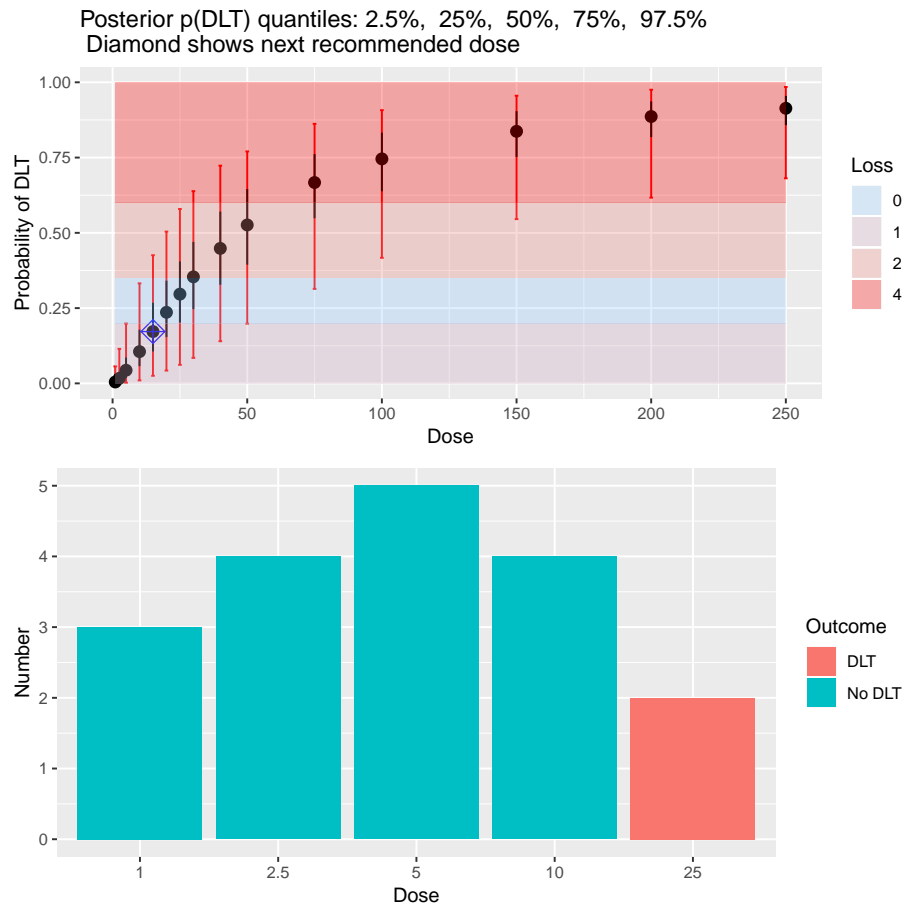
```

##      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)
```

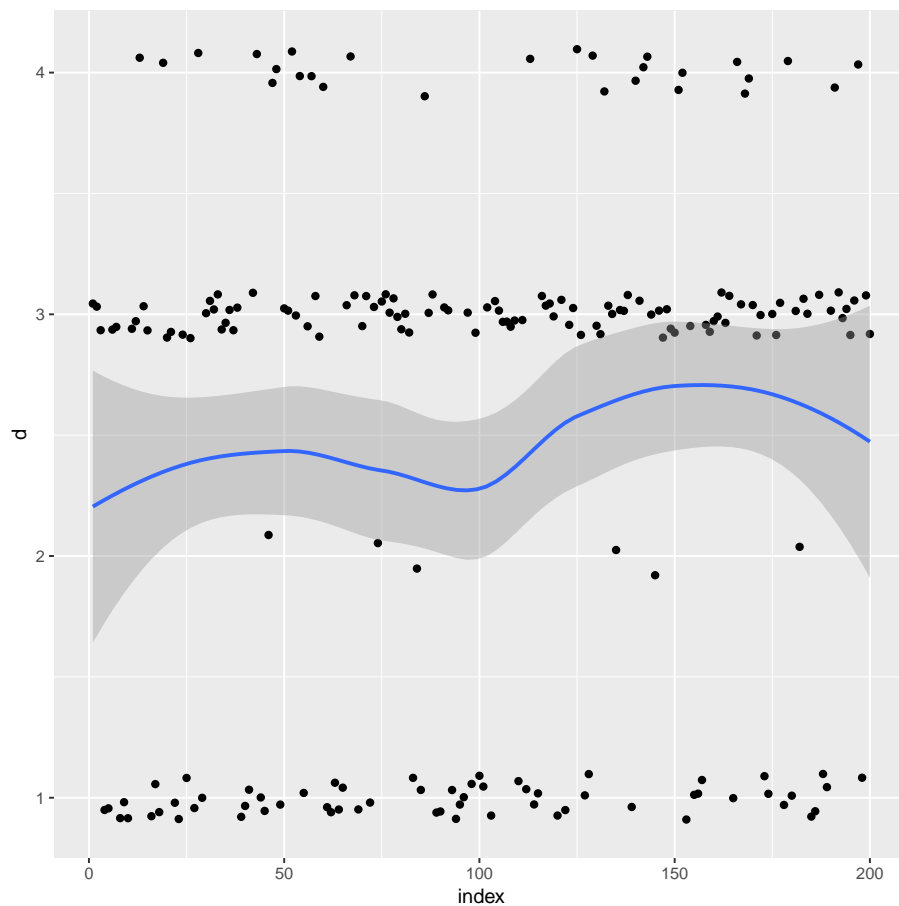
```
## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## 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'
```



```
Sys.time() - startTime

## Time difference of 1.268287 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 0.4.9.2, 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, munsell 0.5.0, mvtnorm 1.0-8, 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, tidselect 0.2.5, tools 3.4.4, withr 2.1.2, yaml 2.2.0