

The title goes here

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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.

```

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

```

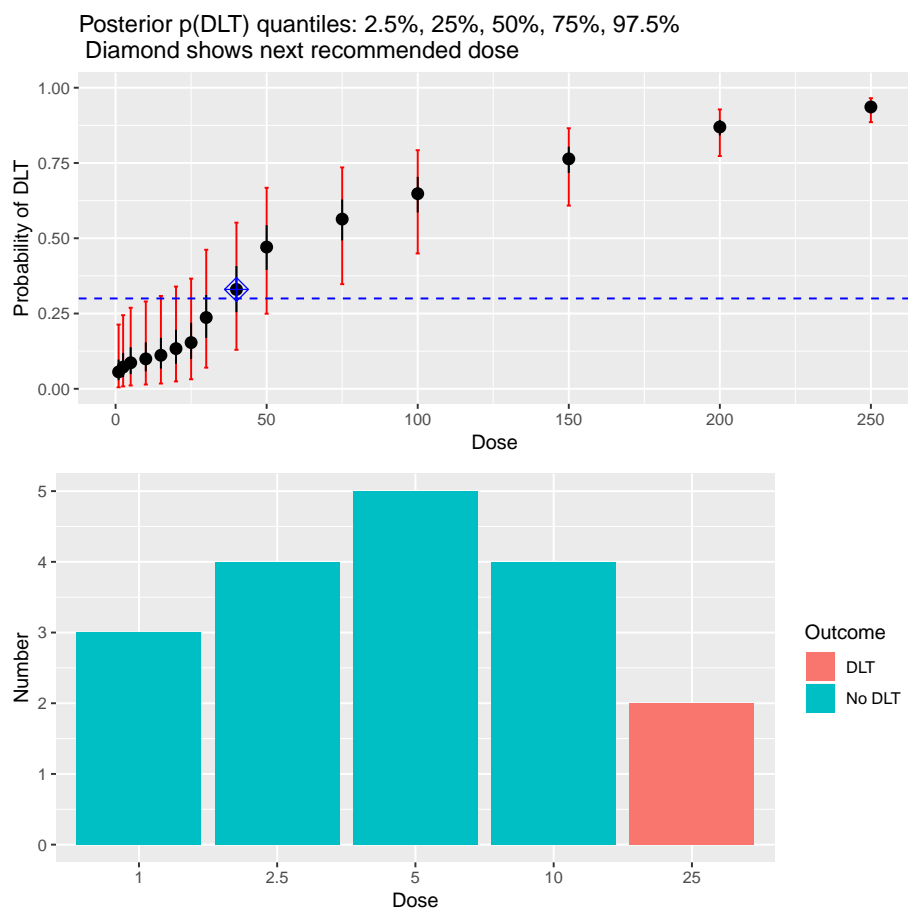
```

##
## 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)
```



```
## 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
```

```

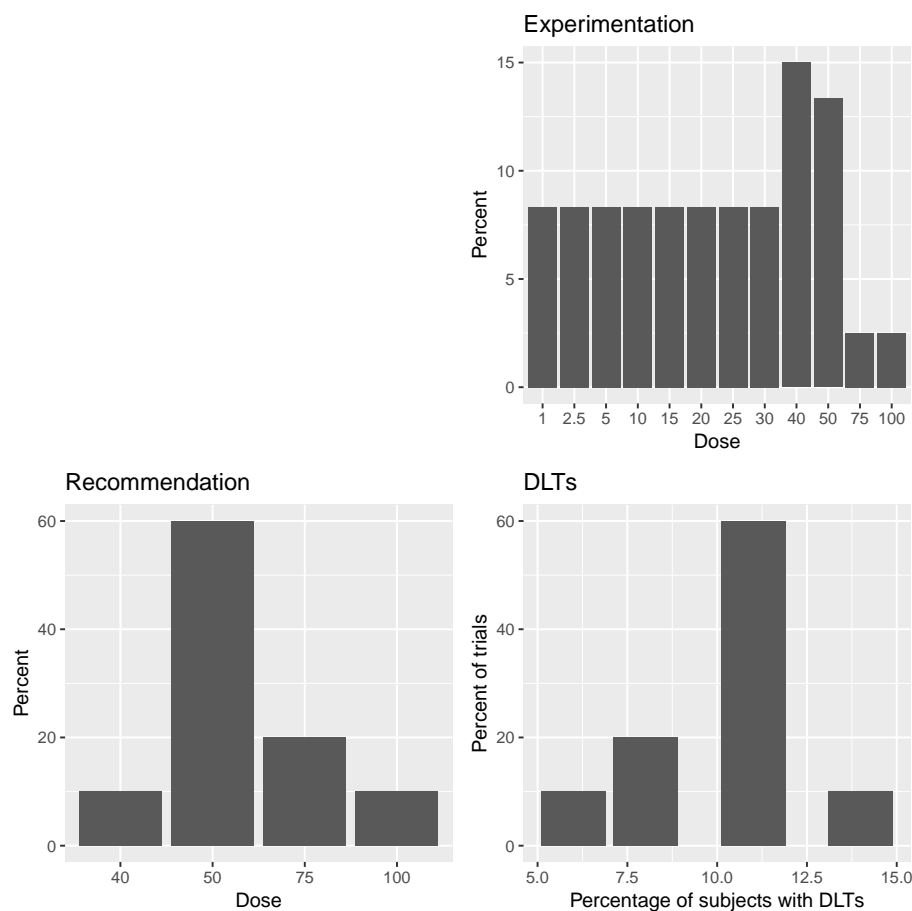
## 6
## 7
## 8
## 9
## 10

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)

```

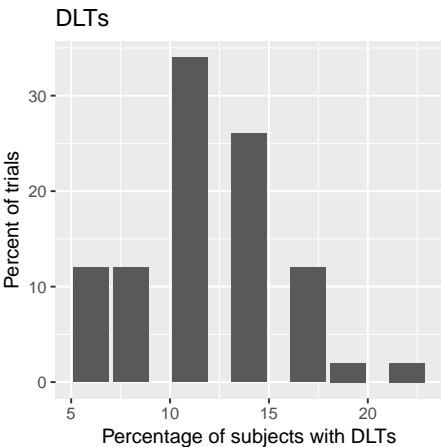
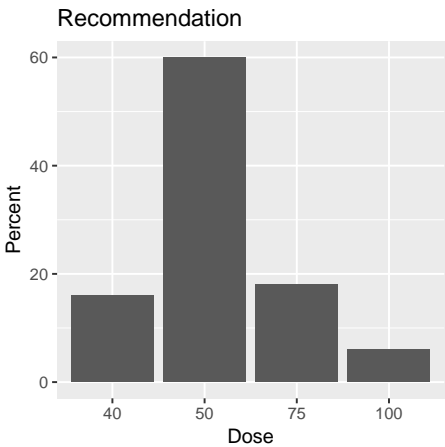
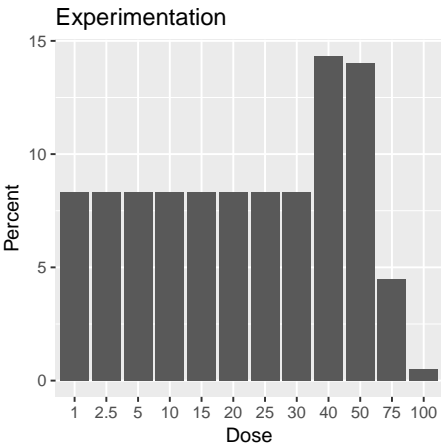


**Note that** in the following example, I set `threep3=FALSE` because otherwise it mysteriously never finishes executing when run through knitr or rmarkdown.

```
## 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)
```



```

## 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
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

```

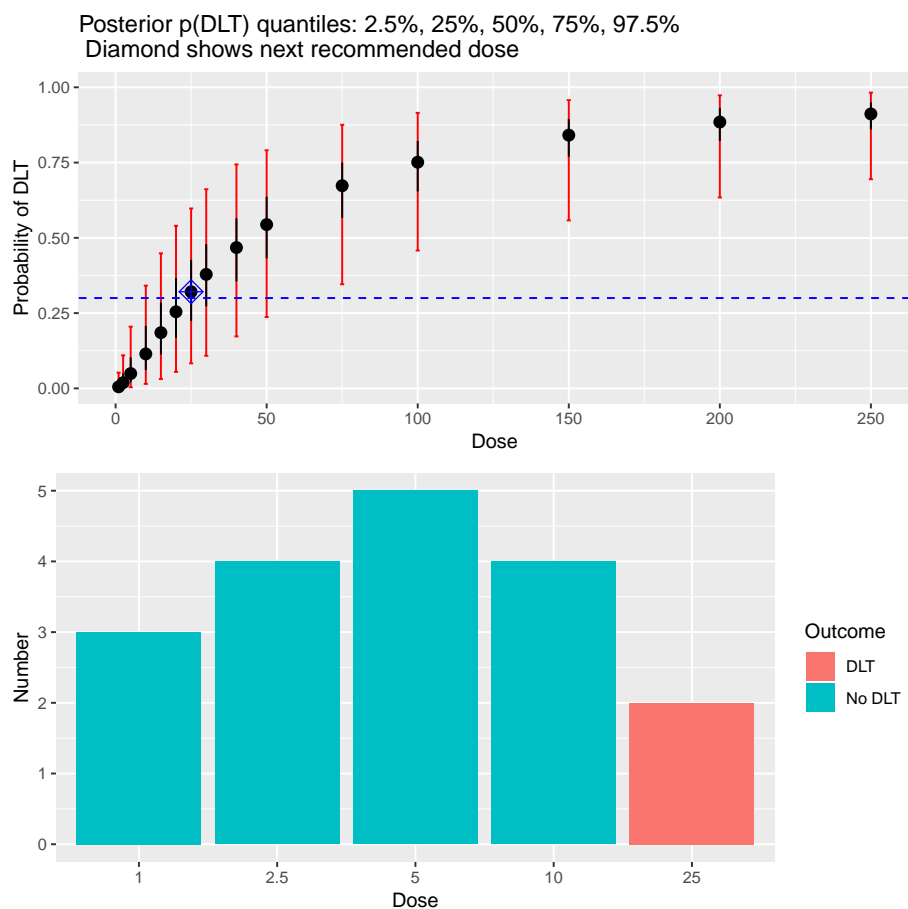


```

##           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  0.01240 0.0320 0.0662 0.1360 0.203 0.265 0.322 0.373 0.461 0.531
## SD    0.01570 0.0328 0.0559 0.0897 0.112 0.128 0.137 0.144 0.149 0.148
## Median 0.00527 0.0189 0.0493 0.1150 0.185 0.254 0.321 0.379 0.468 0.544
##      Doses
##           75    100    150    200    250
## Mean  0.655 0.732 0.820 0.8660 0.8940
## SD    0.137 0.124 0.102 0.0874 0.0769
## Median 0.673 0.751 0.841 0.8850 0.9120
##      Doses
## Quantiles      1    2.5    5    10    15    20    25    30    40
## 2.5%  7.61e-05 0.00075 0.00364 0.0149 0.0312 0.0548 0.0832 0.108 0.173
## 25%   1.44e-03 0.00693 0.02020 0.0609 0.1130 0.1680 0.2240 0.272 0.355
## 50%   5.27e-03 0.01890 0.04930 0.1150 0.1850 0.2540 0.3210 0.379 0.468
## 75%   1.89e-02 0.04890 0.10300 0.2080 0.2850 0.3670 0.4270 0.479 0.565
## 97.5% 5.22e-02 0.11000 0.20500 0.3410 0.4490 0.5400 0.5970 0.661 0.744
##      Doses
## Quantiles      50    75    100    150    200    250
## 2.5%  0.237 0.346 0.458 0.558 0.634 0.695
## 25%   0.432 0.566 0.654 0.769 0.822 0.860
## 50%   0.544 0.673 0.751 0.841 0.885 0.912
## 75%   0.637 0.750 0.822 0.895 0.932 0.950
## 97.5% 0.791 0.875 0.915 0.957 0.973 0.983
##
## Next recommended dose: 25

```

plot(TwoPLogistic.mean.bcrm)



```
## 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
```

```

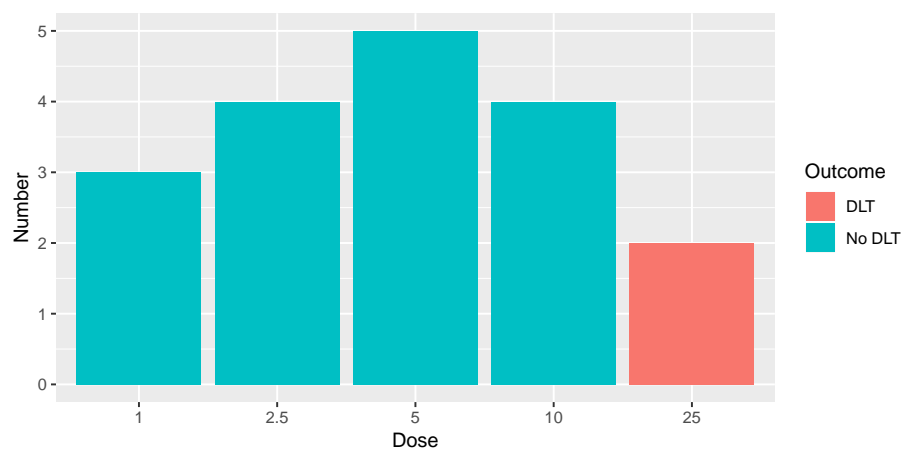
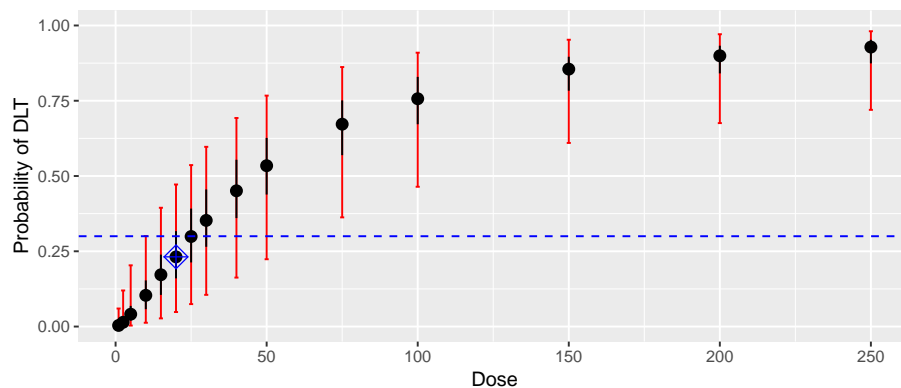
##
## Model: Two-parameter logistic
##
## Prior: Log Multivariate Normal
## Mean Vector:
## [1] 2.15 0.52
##
## Variance-Covariance Matrix:
##      [,1] [,2]
## [1,] 0.7056 0.134
## [2,] 0.1340 0.640
##
## Standardised doses (skeleton):
##      1      2.5      5      10      15      20
## -5.5214609 -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: -2.5864
##
## 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  0.00950 0.0250 0.0541 0.1180 0.1830 0.246 0.304 0.358 0.450 0.526
## SD    0.01620 0.0306 0.0493 0.0777 0.0985 0.114 0.124 0.131 0.138 0.138
## Median 0.00375 0.0143 0.0411 0.1040 0.1720 0.231 0.299 0.353 0.451 0.534
##      Doses
##      75      100      150      200      250
## Mean  0.658 0.739 0.8300 0.8760 0.9040
## SD    0.127 0.114 0.0945 0.0812 0.0715
## Median 0.672 0.757 0.8550 0.8990 0.9280
##      Doses
## Quantiles      1      2.5      5      10      15      20      25      30
## 2.5%  8.28e-05 0.000635 0.00323 0.0126 0.0271 0.0482 0.0745 0.105
## 25%   1.57e-03 0.007190 0.02020 0.0576 0.1050 0.1600 0.2130 0.265
## 50%   3.75e-03 0.014300 0.04110 0.1040 0.1720 0.2310 0.2990 0.353
## 75%   1.01e-02 0.030400 0.06870 0.1530 0.2390 0.3170 0.3920 0.455
## 97.5% 5.98e-02 0.120000 0.20300 0.3010 0.3950 0.4720 0.5360 0.597

```

```
##           Doses
## Quantiles    40    50    75   100   150   200   250
##   2.5%  0.163 0.224 0.363 0.464 0.610 0.676 0.720
##   25%   0.360 0.438 0.569 0.672 0.783 0.841 0.874
##   50%   0.451 0.534 0.672 0.757 0.855 0.899 0.928
##   75%   0.554 0.627 0.751 0.829 0.896 0.933 0.953
##  97.5% 0.693 0.767 0.862 0.910 0.953 0.971 0.981
##
## Next recommended dose:  20
```

```
plot(TwoPLogistic.EWOC0.25.bcrm)
```

Posterior p(DLT) quantiles: 2.5%, 25%, 50%, 75%, 97.5%  
Diamond shows next recommended dose



```
## 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
##

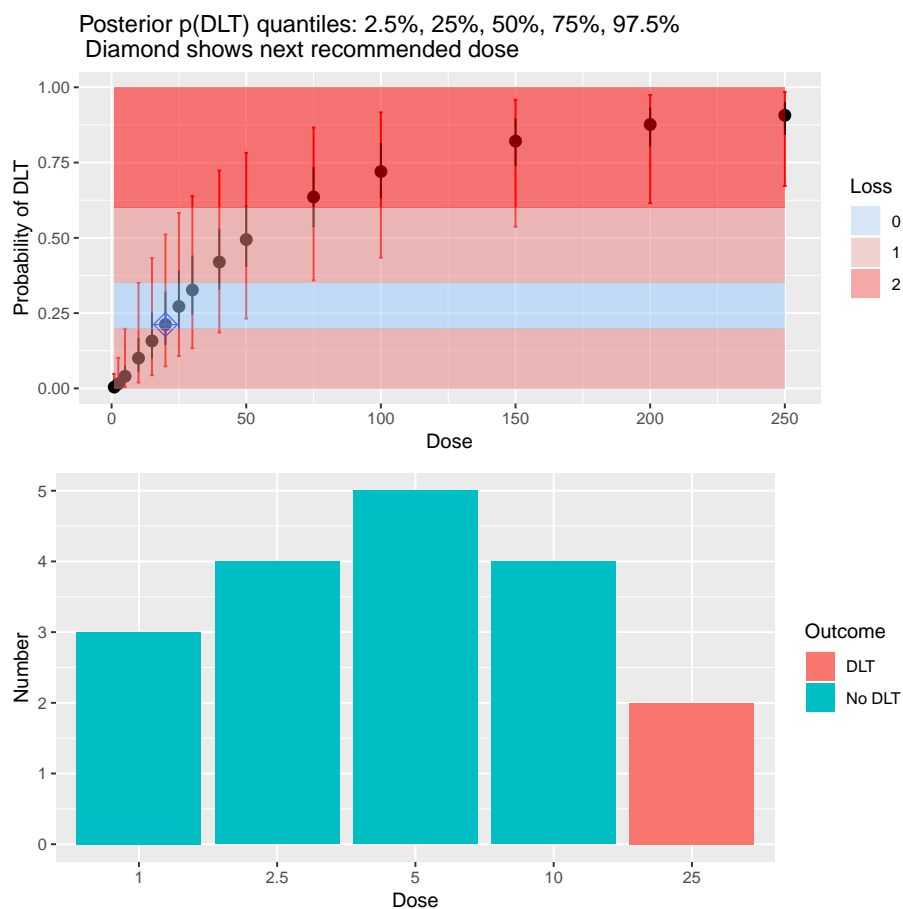
```

```

## Posterior estimates of toxicity:
##      Doses
##      1      2.5      5      10      15      20      25      30      40      50
## Mean  0.01020 0.0268 0.0569 0.1200 0.183 0.243 0.298 0.349 0.436 0.508
## SD    0.01590 0.0309 0.0515 0.0836 0.106 0.123 0.133 0.140 0.147 0.147
## Median 0.00436 0.0155 0.0403 0.1000 0.158 0.212 0.272 0.327 0.420 0.494
##      Doses
##      75      100      150      200      250
## Mean  0.635 0.715 0.807 0.8560 0.8860
## SD    0.139 0.128 0.109 0.0943 0.0839
## Median 0.636 0.720 0.821 0.8770 0.9070
##      Doses
## Quantiles      1      2.5      5      10      15      20      25      30      40
## 2.5%  0.000136 0.00105 0.0049 0.0193 0.0435 0.0733 0.107 0.134 0.186
## 25%   0.001380 0.00645 0.0184 0.0551 0.0994 0.1440 0.195 0.244 0.328
## 50%   0.004360 0.01550 0.0403 0.1000 0.1580 0.2120 0.272 0.327 0.420
## 75%   0.011800 0.03370 0.0750 0.1670 0.2530 0.3220 0.391 0.442 0.530
## 97.5% 0.047800 0.10100 0.1980 0.3500 0.4330 0.5110 0.583 0.639 0.723
##      Doses
## Quantiles      50      75      100      150      200      250
## 2.5%  0.232 0.359 0.434 0.537 0.615 0.672
## 25%   0.403 0.535 0.630 0.738 0.803 0.842
## 50%   0.494 0.636 0.720 0.821 0.877 0.907
## 75%   0.608 0.735 0.815 0.897 0.933 0.952
## 97.5% 0.782 0.866 0.917 0.958 0.975 0.985
##
## Posterior expected loss at each dose:
##      1      2.5      5      10      15      20      25      30      40      50
## [1,] 0.9995 0.9975 0.9785 0.858 0.695 0.6235 0.6305 0.6585 0.885 1.132
##      75      100      150      200      250
## [1,] 1.584 1.7965 1.964 1.981 1.986
##
## 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 0.9975 0.9785 0.833 0.618 0.4285 0.2630 0.1460
## (0.2,0.35] 0.0005 0.0025 0.0215 0.142 0.305 0.3805 0.3890 0.4015
## (0.35,0.6] 0.0000 0.0000 0.0000 0.025 0.077 0.1870 0.3285 0.3925
## (0.6,1]   0.0000 0.0000 0.0000 0.000 0.000 0.0040 0.0195 0.0600
##      Doses
## Toxicity intervals      40      50      75      100      150      200      250
## (0,0.2]  0.0305 0.0130 0.0010 0.0010 0.0000 0.0000 0.000
## (0.2,0.35] 0.2845 0.1295 0.0225 0.0090 0.0015 0.0015 0.001
## (0.35,0.6] 0.5155 0.5960 0.3700 0.1845 0.0330 0.0160 0.012
## (0.6,1]   0.1695 0.2615 0.6065 0.8055 0.9655 0.9825 0.987
##
## Next recommended dose: 20
plot(TwoPLogistic.tox.intervals.bcrm)

```

Doses



```
## 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  0.01400 0.0336 0.0675 0.1360 0.203 0.265 0.322 0.375 0.465 0.538
## SD    0.02370 0.0409 0.0631 0.0947 0.115 0.128 0.136 0.140 0.141 0.137
## Median 0.00568 0.0195 0.0496 0.1190 0.193 0.255 0.319 0.383 0.481 0.550
##      Doses
##      75      100      150      200      250
## Mean  0.666 0.745 0.8320 0.8760 0.9030
## SD    0.122 0.110 0.0927 0.0822 0.0748
## Median 0.683 0.763 0.8530 0.8970 0.9250
##      Doses
## Quantiles      1      2.5      5      10      15      20      25      30      40
## 2.5%  4.84e-05 0.000463 0.00255 0.0123 0.027 0.0455 0.0676 0.101 0.173
## 25%   1.30e-03 0.006460 0.01970 0.0550 0.103 0.1550 0.2100 0.269 0.373
## 50%   5.68e-03 0.019500 0.04960 0.1190 0.193 0.2550 0.3190 0.383 0.481

```

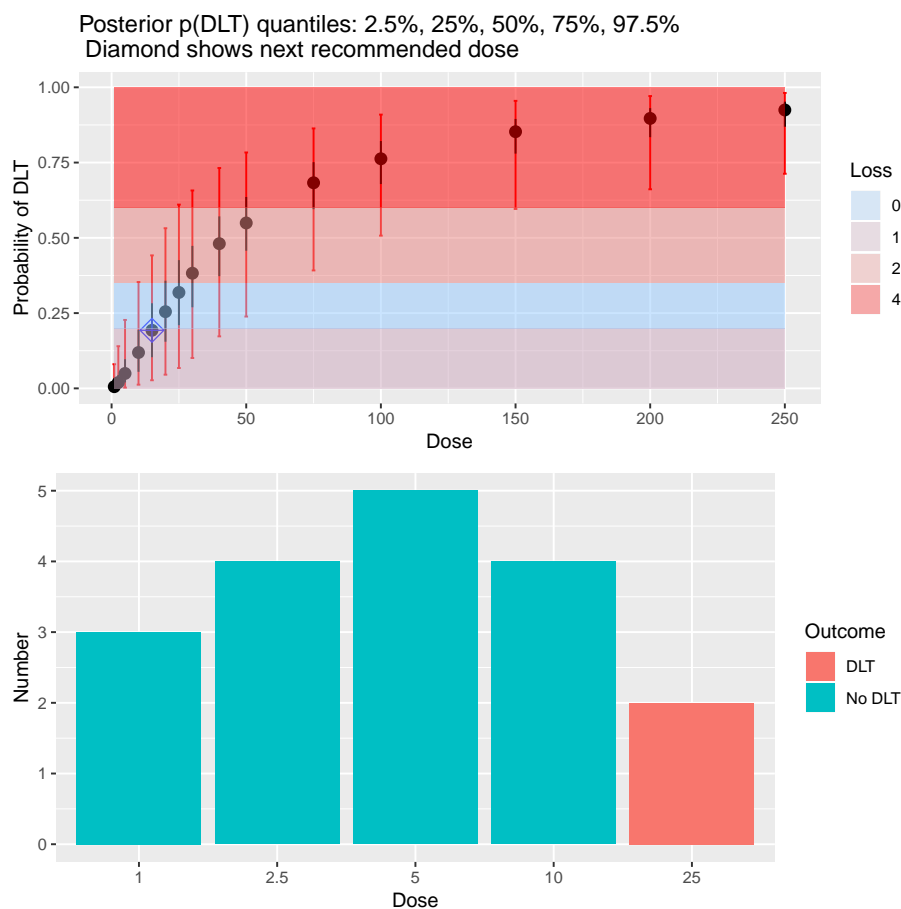


```

##      75%      1.56e-02 0.044900 0.09690 0.1940 0.283 0.3580 0.4260 0.473 0.571
##      97.5% 8.02e-02 0.140000 0.22700 0.3530 0.442 0.5320 0.6100 0.657 0.732
##      Doses
## Quantiles      50      75      100      150      200      250
##      2.5% 0.239 0.392 0.507 0.596 0.661 0.713
##      25% 0.457 0.595 0.679 0.780 0.834 0.869
##      50% 0.550 0.683 0.763 0.853 0.897 0.925
##      75% 0.636 0.751 0.822 0.895 0.931 0.952
##      97.5% 0.784 0.863 0.909 0.955 0.971 0.981
##
## Posterior expected loss at each dose:
##      1      2.5      5      10      15      20      25      30      40      50
## [1,] 0.998 0.9905 0.959 0.8145 0.77 0.865 1.0885 1.3915 1.965 2.4235
##      75      100      150      200      250
## [1,] 3.4465 3.784 3.943 3.979 3.986
##
## Posterior probability of dose being in each toxicity interval
## Toxicity intervals      1      2.5      5      10      15      20      25      30
##      (0,0.2]      0.998 0.9905 0.9540 0.7605 0.538 0.3340 0.2155 0.1175
##      (0.2,0.35] 0.002 0.0095 0.0435 0.2125 0.346 0.4075 0.3760 0.2955
##      (0.35,0.6] 0.000 0.0000 0.0025 0.0270 0.116 0.2515 0.3805 0.5370
##      (0.6,1]      0.000 0.0000 0.0000 0.0000 0.000 0.0070 0.0280 0.0500
##      Doses
## Toxicity intervals      40      50      75      100      150      200      250
##      (0,0.2]      0.0460 0.0055 0.0025 0.0000 0.0000 0.0000 0.000
##      (0.2,0.35] 0.1650 0.1100 0.0055 0.0035 0.0025 0.0020 0.002
##      (0.35,0.6] 0.6185 0.5600 0.2620 0.1010 0.0235 0.0065 0.003
##      (0.6,1]      0.1705 0.3245 0.7300 0.8955 0.9740 0.9915 0.995
##
## Next recommended dose: 15
plot(TwoPLogistic.tox.intervals.2.bcrm)

```

Doses



```
# 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)

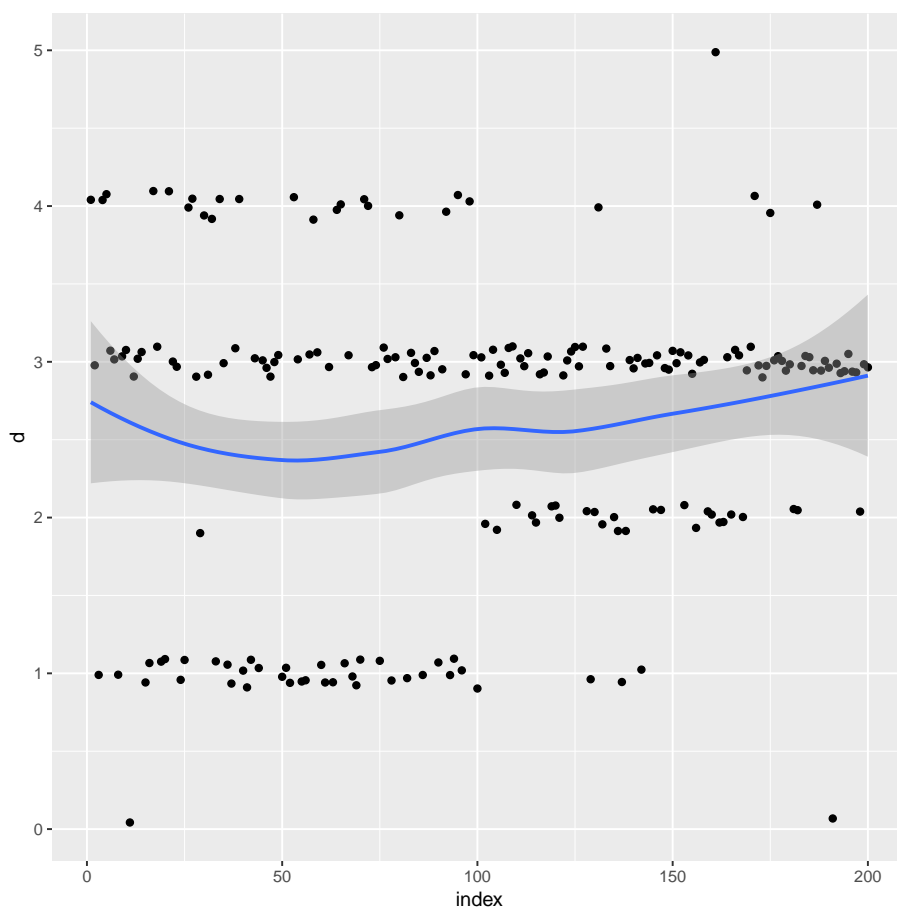
## Warning in rjags::jags.model(path.model, data = mydata, n.chains
= 2, quiet = TRUE, : Adaptation incomplete

## 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 1.419758 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, 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 0.7.7, 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, tidysselect 0.2.5, tools 3.4.4, withr 2.1.2, yaml 2.2.0