

concavex: An R package for fitting Bayesian dose-response models

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Introduction

concavex is an R package for fitting dose response curves. It conceptually borrows from the MCPMod approach to dose response curve fitting and only requires point estimates of effects and their standard errors at tested doses. Model fitting uses a fully Bayesian approach, and the **concavex** package is largely a wrapper for easily implementing and generating outputs with JAGS and the **rjags** package.

As such, **concavex** requires a working JAGS implementation, which may be downloaded from this link: <http://mcmc-jags.sourceforge.net/>.

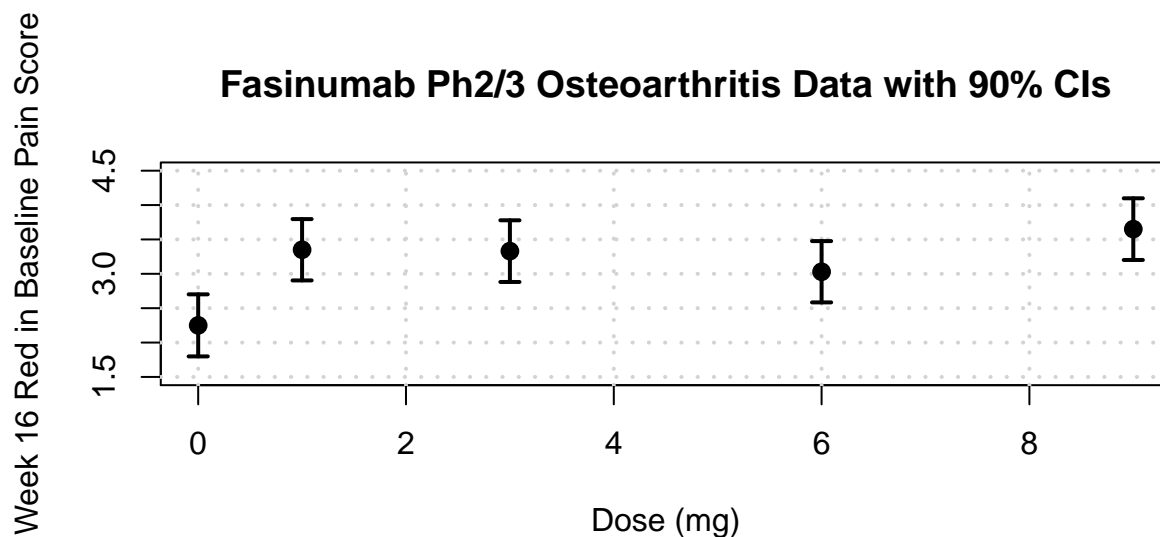
Example data

Example data comes for Regeneron Fasinumab dose ranging study published May 2, 2016.

- 421 patients with moderate-to-severe Osteoarthritis of the hip or knee randomized 1:1:1:1:1
- Primary endpoint was the WOMAC pain scale: a 0-10 scale measured after monthly treatment for 3 months

Published data is provided below. No standard error estimates were provided, but a standard deviation of 2.5 is assumed for change from baseline for all treatment arms.

	Placebo	1 mg	3 mg	6 mg	9mg
N subjects	83	85	84	85	84
Baseline pain score	6.43	6.33	6.35	6.1	6.53
Week 16 reduction in pain score	2.25	3.35	3.33	3.03	3.65



Fitting the Basic Concavex model with concavex package and JAGS

```
library(concavex)

# define fasinumab summary statistics
doses <- c(0, 1, 3, 6, 9)
n <- c(83, 85, 84, 85, 84)
week16red <- c(2.25, 3.35, 3.33, 3.03, 3.65)
stddev <- 2.5
stderr <- stddev / sqrt(n)

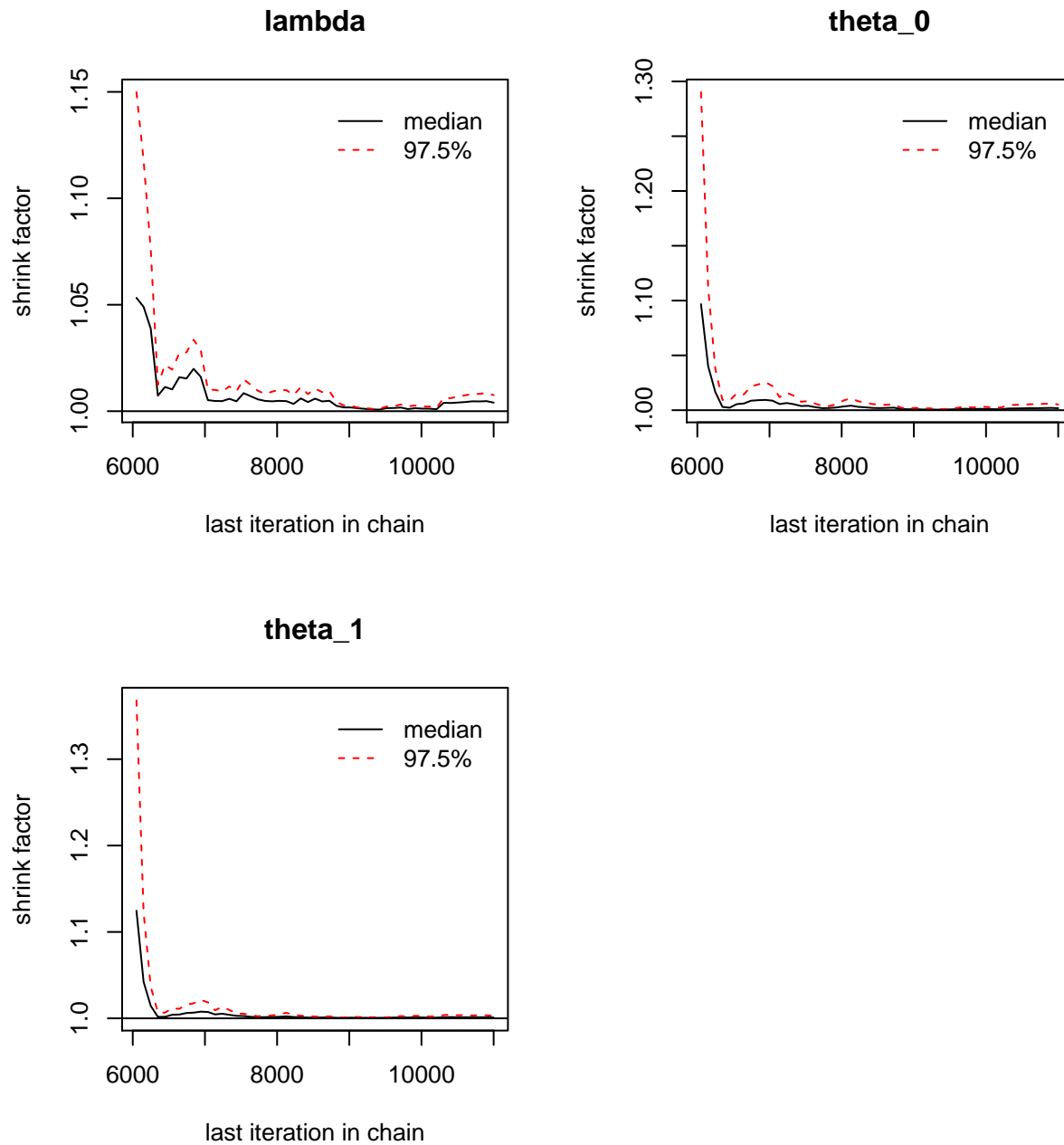
# build JAGS code for default Concavex model with weakly informative priors
ccvx.mod <- ccvx_build_jags()

# fit default concavex model
ccvx.samples <- ccvx_fit(ccvx.mod, doses = doses, mu.hat = week16red, stderr = stderr)

## Compiling model graph
##   Resolving undeclared variables
##   Allocating nodes
## Graph information:
##   Observed stochastic nodes: 5
##   Unobserved stochastic nodes: 3
##   Total graph size: 7875
##
## Initializing model
```

BGR Diagnostic plots for MCMC Gibbs sampling with coda package

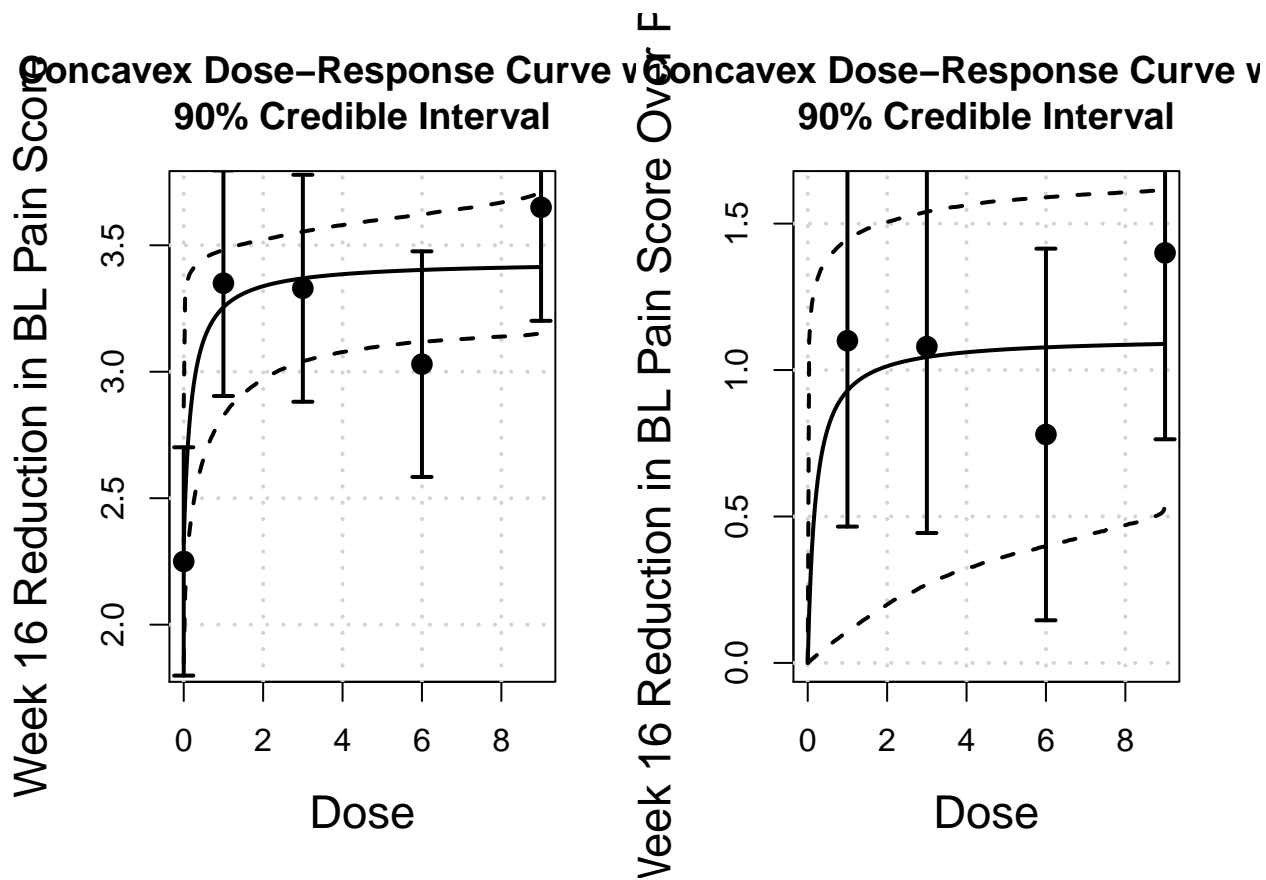
```
gelman.plot(ccvx.samples$coda.samples)
```



Assessing Concavex model fit

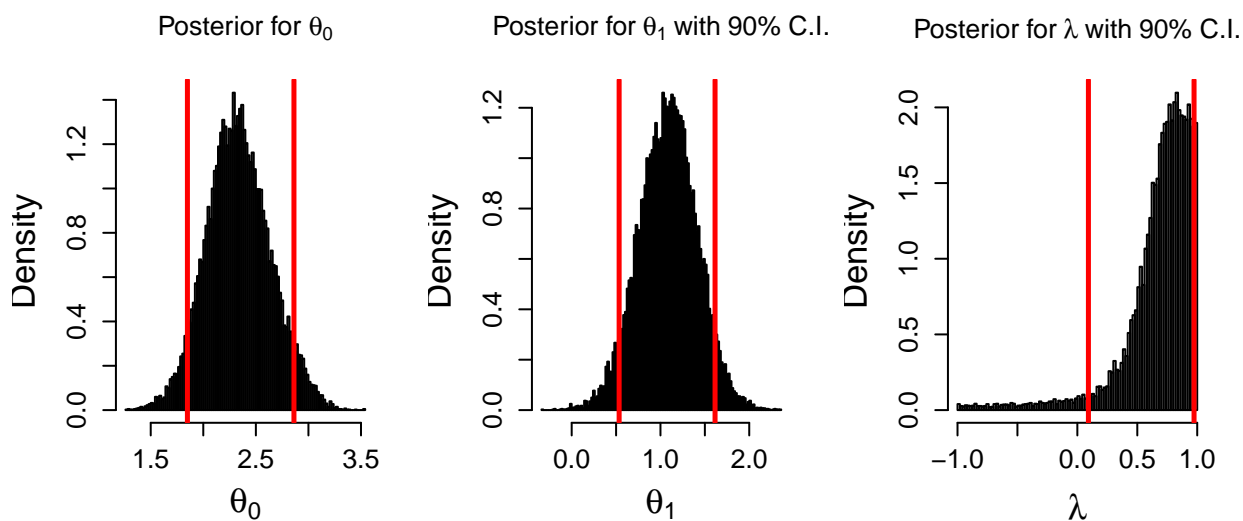
```
par(mfrow=c(1,2))

ccvx_plot_fit(ccvx.samples, placebo.adjusted = FALSE,
              title = "Concavex D-R Curve",
              ylab = "Week 16 Reduction in BL Pain Score")
ccvx_plot_fit(ccvx.samples, placebo.adjusted = TRUE,
              title = "Concavex Placebo-adjusted D-R Curve",
              ylab = "Week 16 Reduction in BL Pain Score Over Pbo")
```



Plotting and accessing model posteriors

```
par(mfrow = c(1, 3))  
ccvx_hist_post(ccvx.samples)
```



```
mean(ccvx.samples$jags.samples$theta_1 > 0)
```

```
## [1] 0.9988
```

```
mean(ccvx.samples$jags.samples$lambda > 0)
```

```
## [1] 0.95845
```

Ongoing work