2017 SISG Bayesian Statistics for Genetics
R Notes: Multinomial Sampling

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Hardy-Weinberg via Fisher's exact test

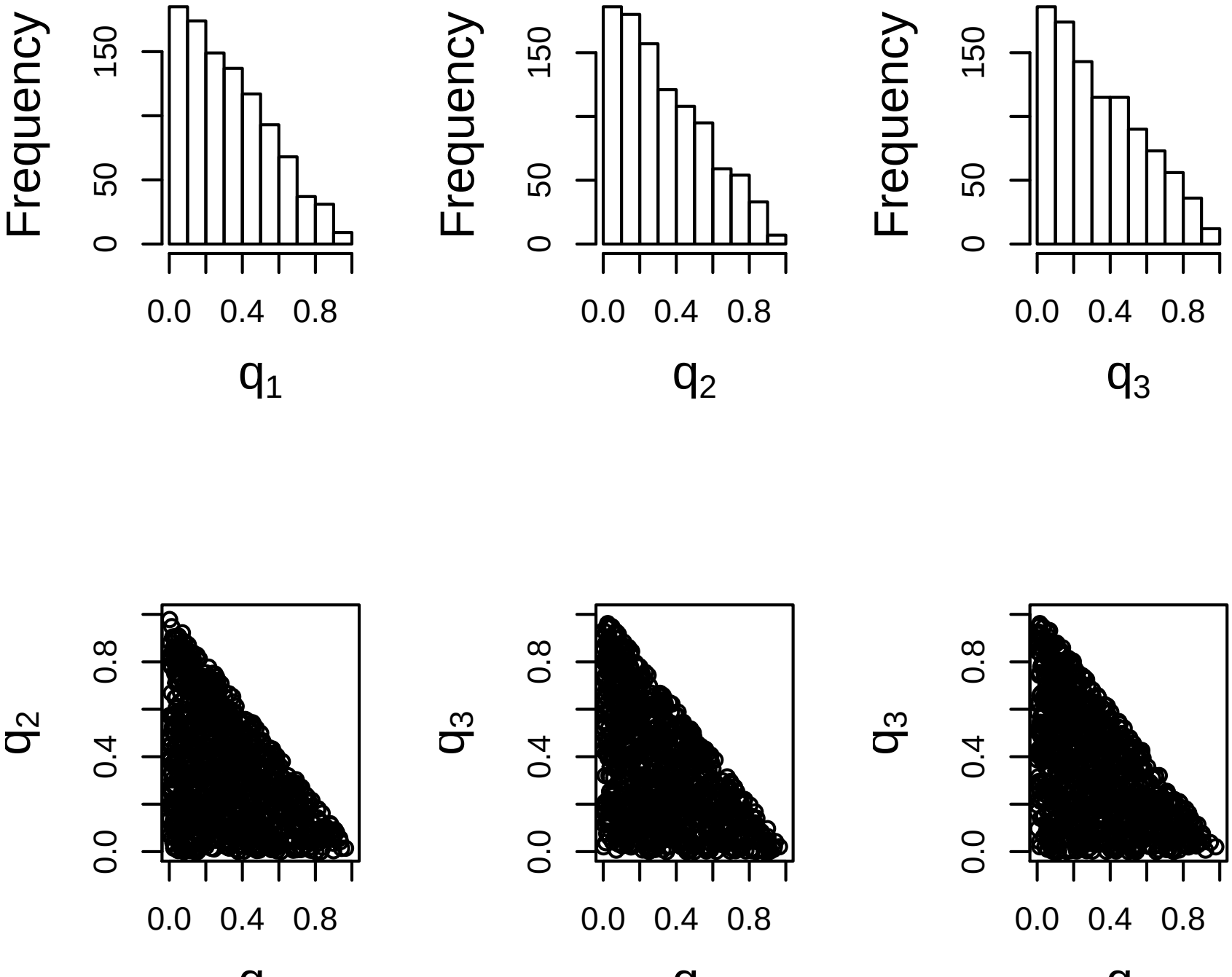
```
library(hwde)
n1 <- 88
n2 <- 10
n3 <- 2
exact <- hwexact(n1, n2, n3)
exact
## [1] 0.06544427
```

We obtain a p-value of 0.07

Displaying samples from a dirichlet(1,1,1)

```
library(VGAM)  # To access the rdiric function
nsim <- 1000
q <- rdiric(nsim, c(1, 1, 1))
# Univariate marginal representations
par(mfrow = c(2, 3))
hist(q[, 1], xlab = expression(q[1]), main = "", cex.lab = 1.5,
    xlim = c(0, 1))
hist(q[, 2], xlab = expression(q[2]), main = "", cex.lab = 1.5,
    xlim = c(0, 1))
hist(q[, 3], xlab = expression(q[3]), main = "", cex.lab = 1.5,
    xlim = c(0, 1))
# Bivariate representations
plot(q[, 1], q[, 2], xlim = c(0, 1), ylim = c(0, 1),
    xlab = expression(q[1]), ylab = expression(q[2]),
    cex.lab = 1.5)
plot(q[, 1], q[, 3], xlim = c(0, 1), ylim = c(0, 1),
    xlab = expression(q[1]), ylab = expression(q[3]),
    cex.lab = 1.5)
plot(q[, 2], q[, 3], xlim = c(0, 1), ylim = c(0, 1),
    xlab = expression(q[2]), ylab = expression(q[3]),
    cex.lab = 1.5)
```

Displaying samples from a dirichlet(1,1,1)

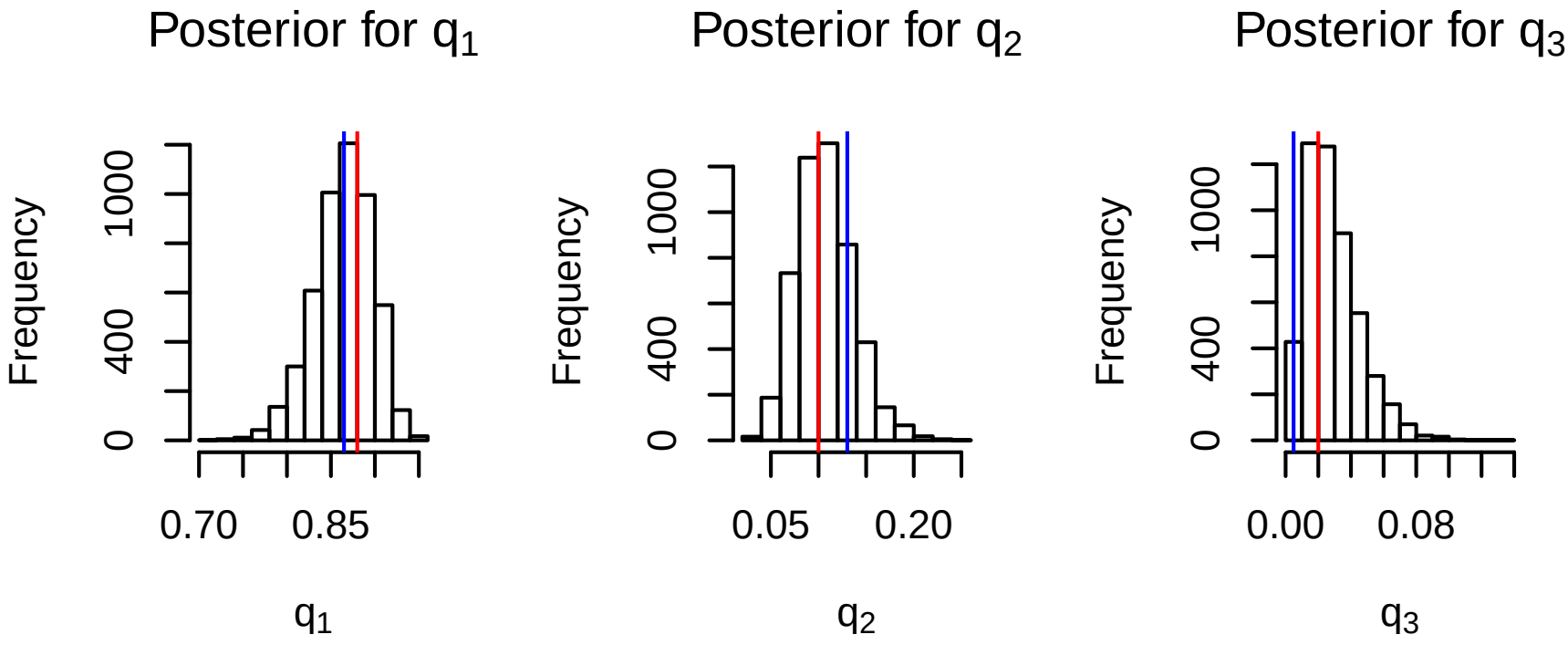


Bayes analysis of (88,10,2) data

```
n1 <- 88
n2 <- 10
n3 <- 2
p1 <- 88/100 + 0.5 * 10/100  # Estimated allele frequencies
p2 <- 2/100 + 0.5 * 10/100  # for A1 and A2
v1 <- v2 <- v3 <- 1
nsim <- 5000
q <- rdiric(nsim, c(n1 + v1, n2 + v2, n3 + v3))  # The posterior
par(mfrow = c(1, 3))
hist(q[, 1], xlab = expression(q[1]), main = expression(paste("Posterior for ",
    q[1])))
abline(v = n1/(n1 + n2 + n3), col = "red")
abline(v = p1^2, col = "blue")
hist(q[, 2], xlab = expression(q[2]), main = expression(paste("Posterior for ",
    q[2])))
abline(v = n2/(n1 + n2 + n3), col = "red")
abline(v = 2 * p1 * p2, col = "blue")
hist(q[, 3], xlab = expression(q[3]), main = expression(paste("Posterior for ",
    q[3])))
abline(v = n3/(n1 + n2 + n3), col = "red")
abline(v = p2^2, col = "blue")
```

Bayes analysis of (88,10,2) data

Univariate posterior distributions: blue lines are the MLEs in the full model, red lines under the HWE model

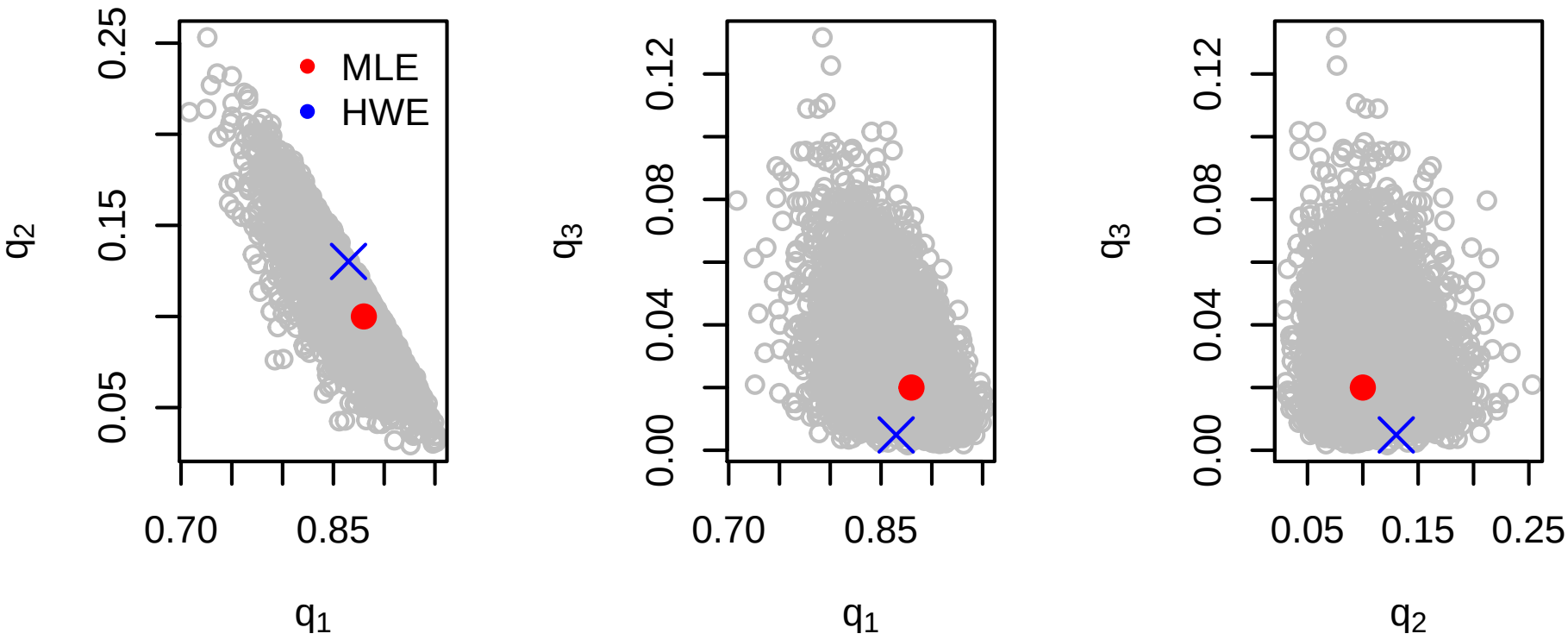


Bayes analysis of (88,10,2) data

```
par(mfrow = c(1, 3))
plot(q[, 2] ~ q[, 1], xlab = expression(q[1]), ylab = expression(q[2]),
    col = "grey")
points(n1/(n1 + n2 + n3), n2/(n1 + n2 + n3), col = "red",
    pch = 20, cex = 2)
points(p1^2, 2 * p1 * p2, col = "blue", pch = 4, cex = 2)
legend("topright", legend = c("MLE", "HWE"), col = c("red",
    "blue"), pch = c(20, 20), bty = "n")
plot(q[, 3] ~ q[, 1], xlab = expression(q[1]), ylab = expression(q[3]),
    col = "grey")
points(n1/(n1 + n2 + n3), n3/(n1 + n2 + n3), col = "red",
    pch = 20, cex = 2)
points(p1^2, p2^2, col = "blue", pch = 4, cex = 2)
plot(q[, 3] ~ q[, 2], xlab = expression(q[2]), ylab = expression(q[3]),
    col = "grey")
points(n2/(n1 + n2 + n3), n3/(n1 + n2 + n3), col = "red",
    pch = 20, cex = 2)
points(2 * p1 * p2, p2^2, col = "blue", pch = 4, cex = 2)
```

Bayes analysis of (88,10,2) data

Bivariate posterior distributions: blue lines are the MLEs in the full model, red lines under the HWE model



Functions of interest: implied priors

We assume a "dirichlet(1,1,1)"' distribution

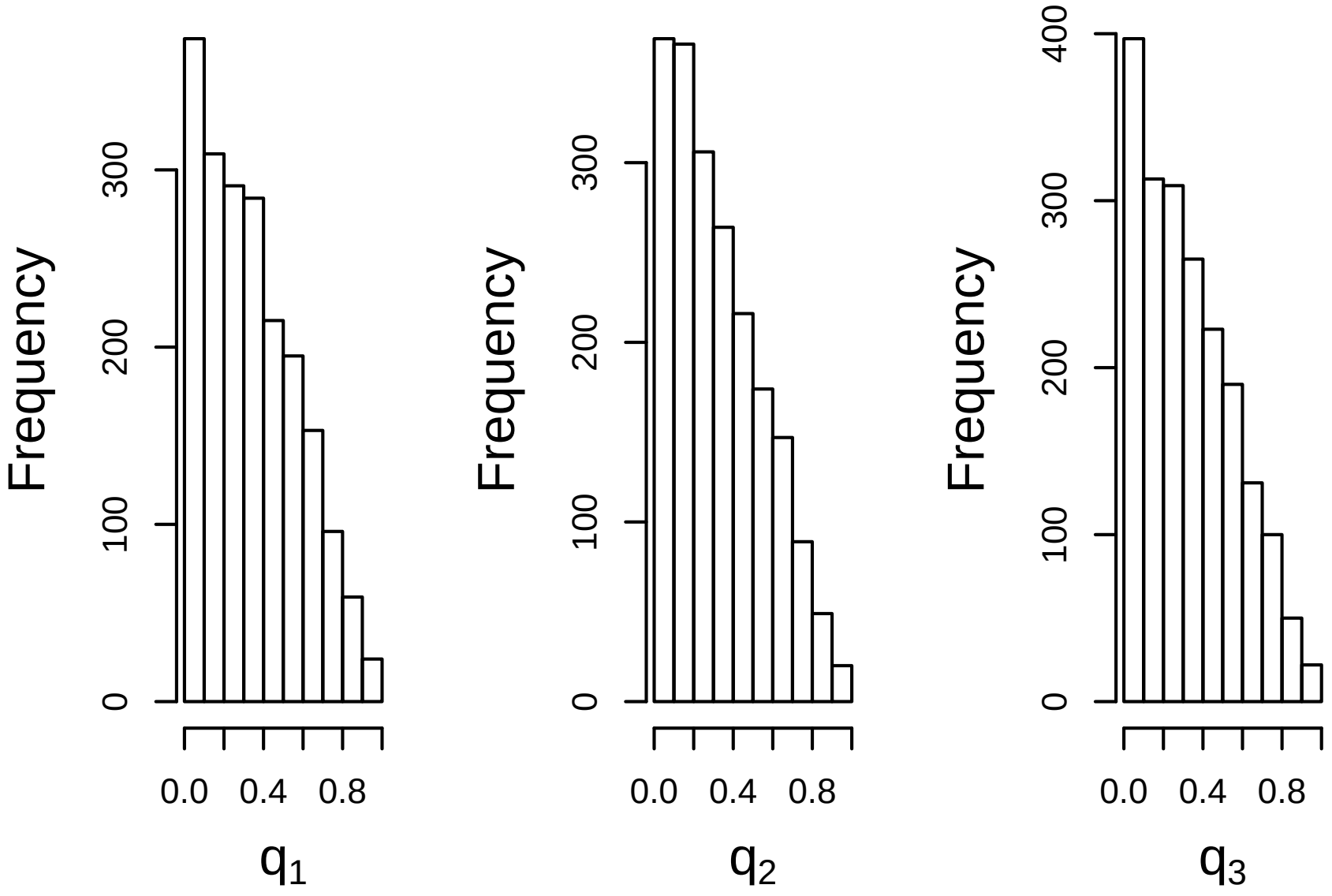
```
v1 <- v2 <- v3 <- 1
nsim <- 2000
samps <- rdiric(nsim, c(v1, v2, v3))
q1 <- samps[, 1]
q2 <- samps[, 2]
q3 <- samps[, 3]
p1 <- q1 + q2/2
p2 <- q3 + q2/2
f <- (q1 - p1^2)/(p1 * p2)
D <- q1 - p1^2
psi <- q2^2/(p1 * p2)
## Functions of interest
cat("Prior prob f>0: ", sum(f > 0)/nsim, "\n")
## Prior prob f>0:  0.6835
cat("Prior prob D>0: ", sum(D > 0)/nsim, "\n")
## Prior prob D>0:  0.6835
```

Functions of interest

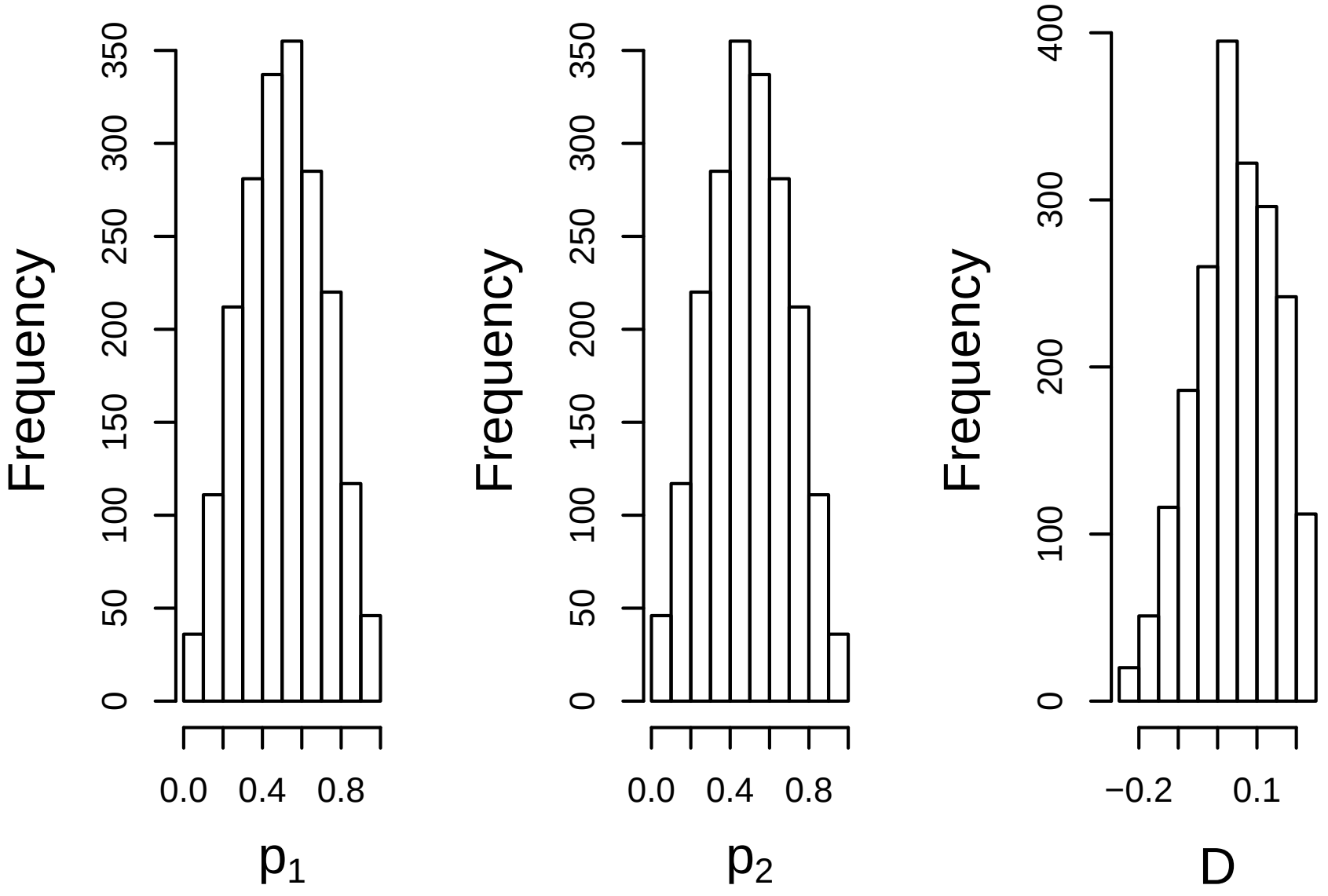
Examine prior summaries for different functions of interest.

```
par(mfrow = c(1, 3))
hist(q1, main = "", xlab = expression(q[1]), cex.lab = 1.5)
hist(q2, main = "", xlab = expression(q[2]), cex.lab = 1.5)
hist(q3, main = "", xlab = expression(q[3]), cex.lab = 1.5)
par(mfrow = c(1, 3))
hist(p1, main = "", xlab = expression(p[1]), cex.lab = 1.5)
hist(p2, main = "", xlab = expression(p[2]), cex.lab = 1.5)
hist(D, main = "", xlab = expression(D), cex.lab = 1.5)
par(mfrow = c(1, 2))
hist(f, main = "", xlab = "f", cex.lab = 1.5)
hist(psi, main = "", xlab = expression(psi), cex.lab = 1.5)
```

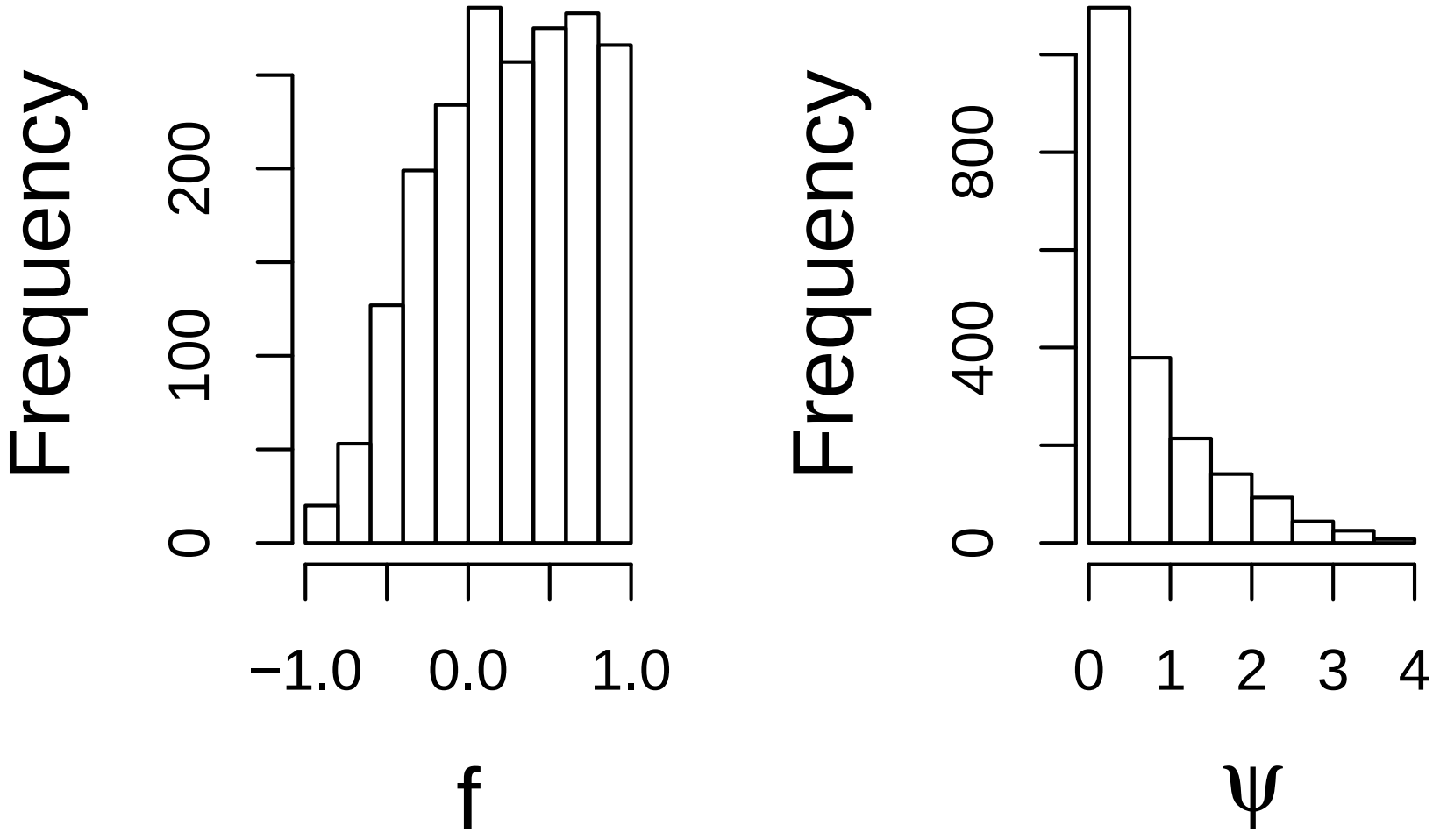
Functions of interest: prior margins on $q1, q_2, q3$.



Functions of interest: priors on p_1, p_2, D



Functions of interest: priors on f, ψ.



Inference for f

The MLE is $\hat{f} = 0.23$ with asymptotic standard error 0.17.

Hence, a 95% confidence interval is

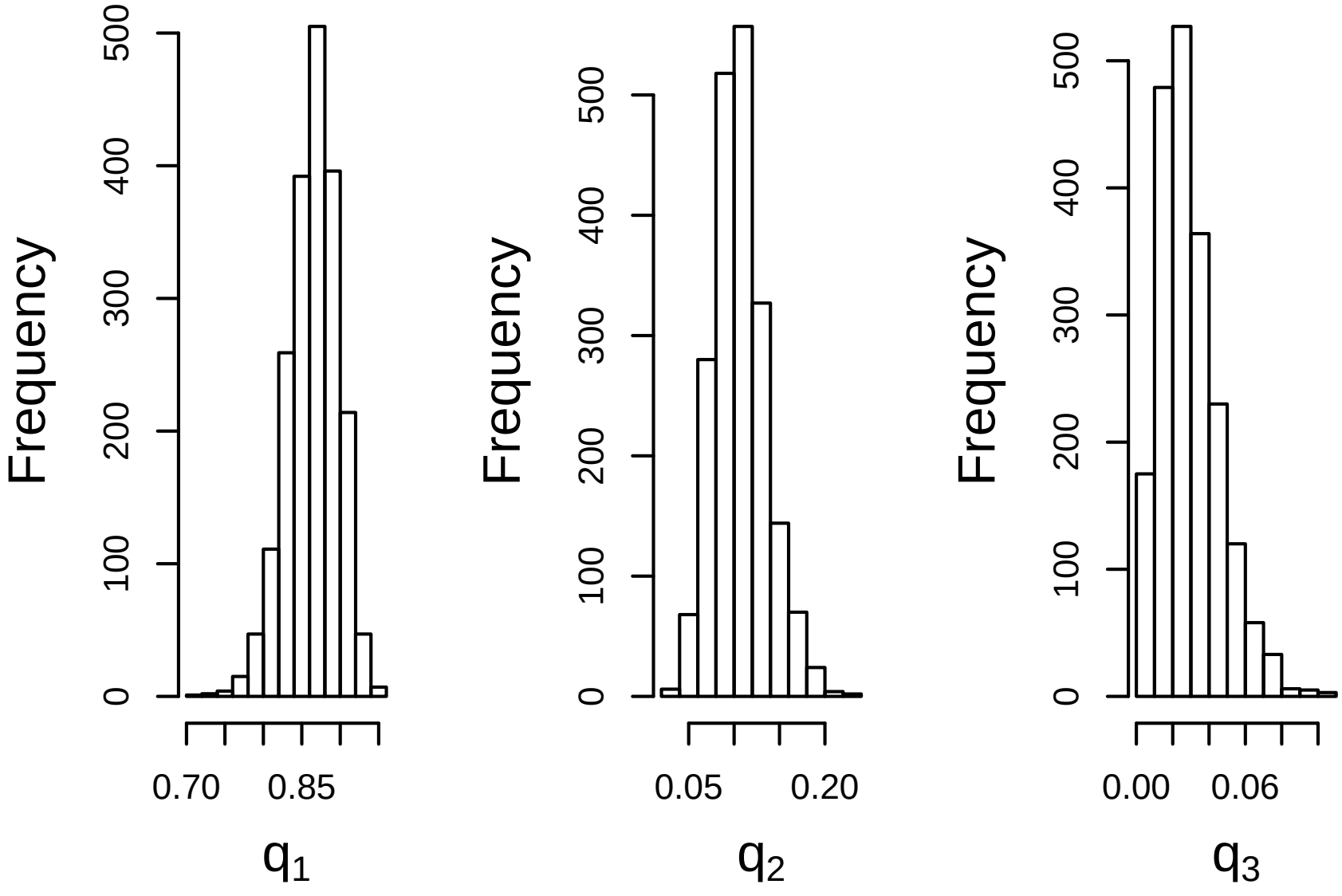
$$(0.23 - 1.96 \times 0.17, 0.23 + 1.96 \times 0.17) = (-0.1032, 0.5632).$$

The posterior median and 95% credible interval are given below.

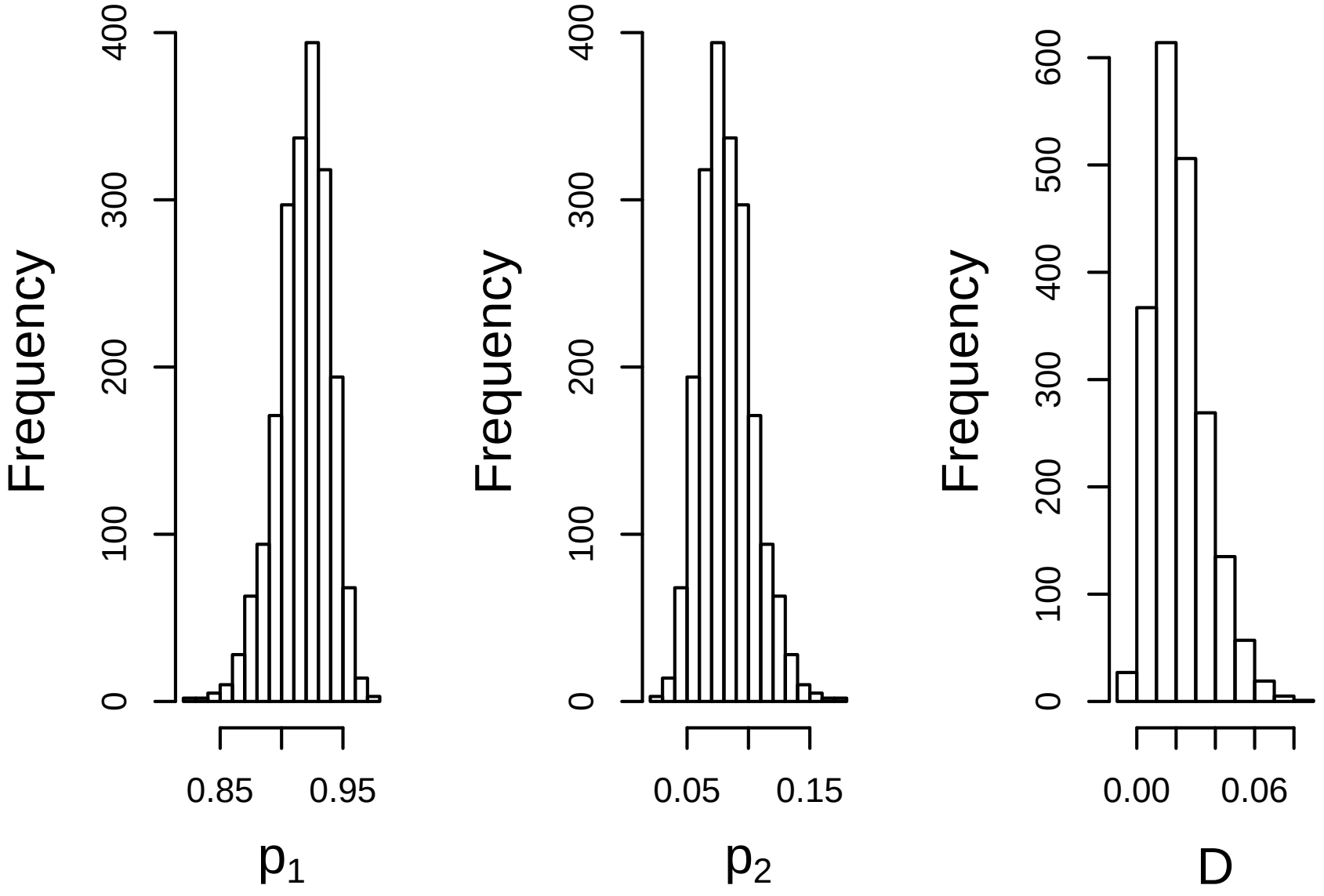
```
# Bayesian posterior quantiles are
quantile(f, c(0.025, 0.5, 0.975))
##       2.5%        50%      97.5%
## -0.6820174  0.2661336  0.9588663
```

Subsequent figures give posterior distributions on functions of interest.

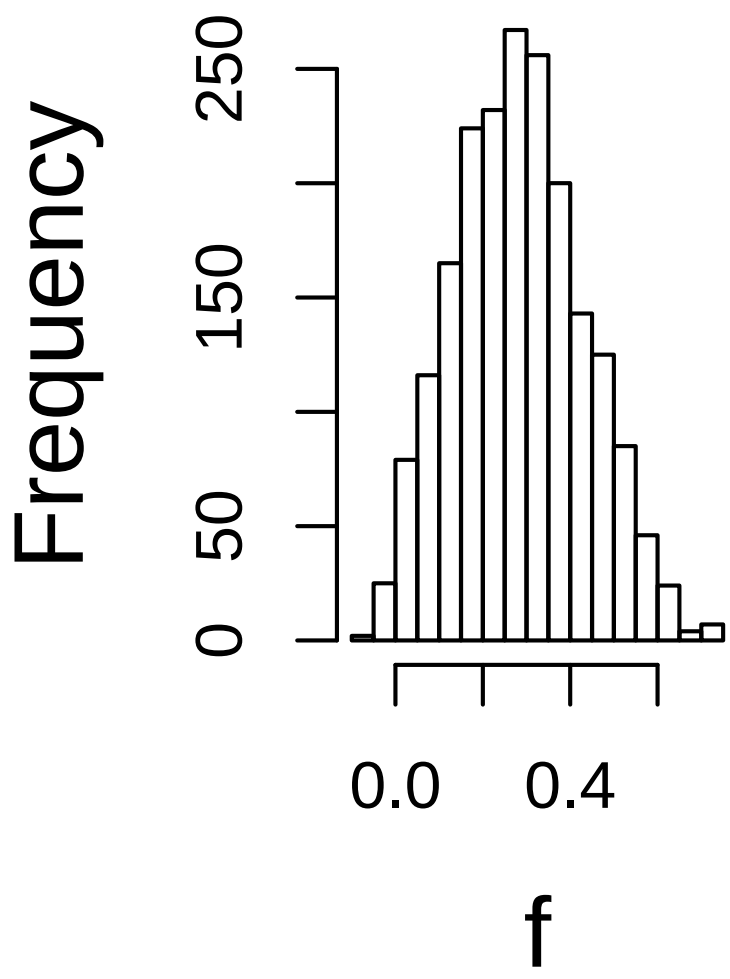
Dirichlet Posterior Distribution

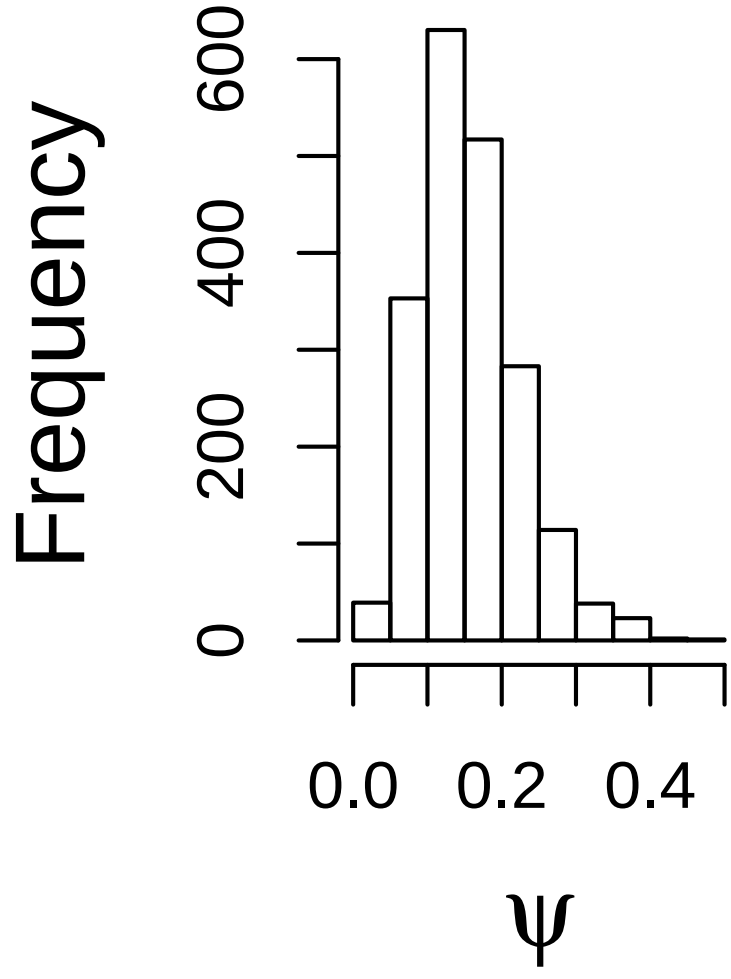


Posterior summaries



Posterior summaries





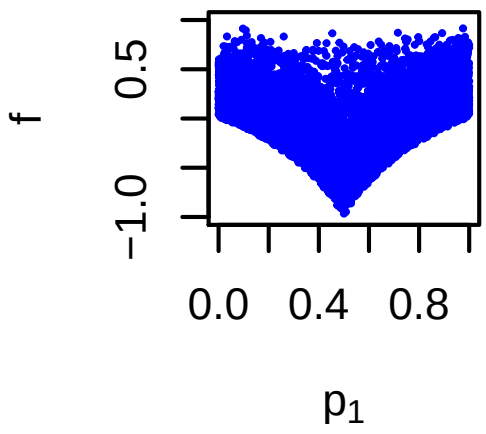
Non-conjugate analysis

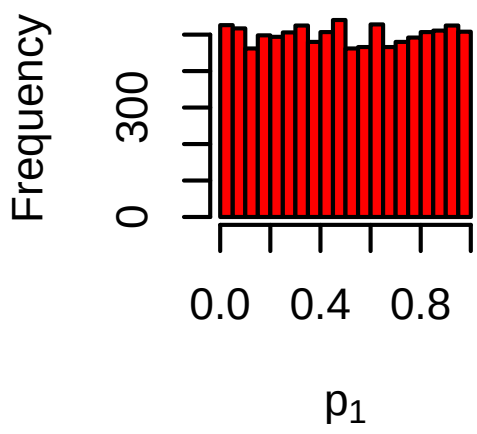
```
library(HWEBayes)
nsim <- 50000
diricvec <- c(1, 1)
Prior <- LambdaOptim(nsim, diricvec, 0, 0.5, 0.5, 0.95,
    init = c(-1, log(1)))
## lambda mu and lambda sd =  -1.239067 1.027574
nvec <- c(88, 10, 2)
nsamp <- 10000
Check <- SinglefPrior(nsamp, diricvec, Prior$lambdamu,
    Prior$lambdasd)
quantile(Check$f, p = c(0.5, 0.95))
##           50%           95%
## -0.001438567  0.506087445
```

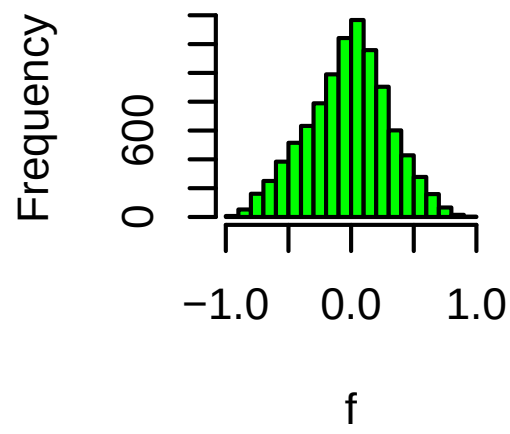
Non-conjugate analysis

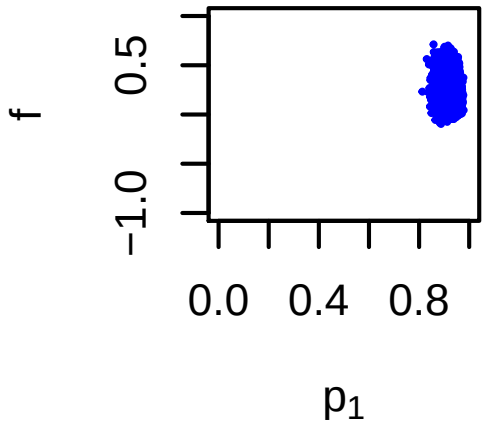
```
Out <- SinglefReject(nsamp, diricvec, Prior$lambdamu,
    Prior$lambdasd, nvec)
## Allele Marginal prob:  1 0.93
## Allele Marginal prob:  2 0.07
## Convergence =  0 (0 is successful convergence)
## Probs and f at max and fmin:
##  0.9299904 0.07000956 0.2318971 -0.07527987
## nsim norm constant (se) 95% interval:
## 10000 0.001019874 ( 7.34324e-06 ) 0.001005481 0.001034267
quantile(Out$fsamp)
##          0%         25%         50%         75%        100%
## -0.09576995  0.12064114  0.20245186  0.29412365  0.71181533
sum(Out$fsamp > 0)/nsamp
## [1] 0.983
quantile(Out$fsamp)
##          0%         25%         50%         75%        100%
## -0.09576995  0.12064114  0.20245186  0.29412365  0.71181533
```

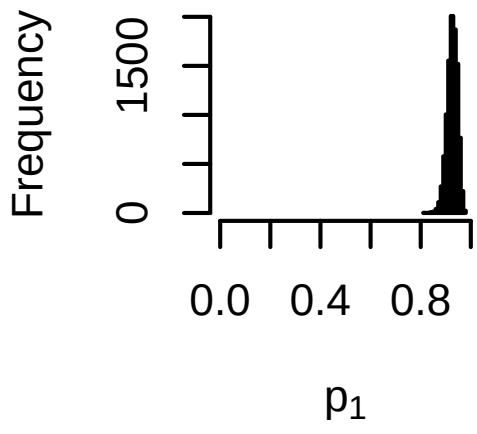
Non-conjugate analysis

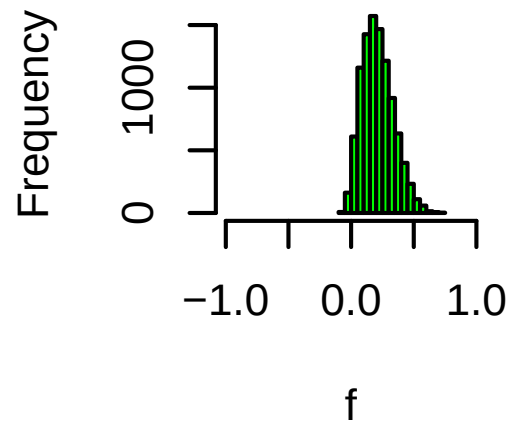












Non-conjugate analysis

```
bvec0 <- c(1, 1)
bvec1 <- c(1, 1, 1)
PrnH0 <- DirichNormHWE(nvec, bvec0)
PrnH1sat <- DirichNormSat(nvec, bvec1)
BFH0H1sat <- PrnH0/PrnH1sat
cat("H0 norm = ", PrnH0, "\n")
## H0 norm =  0.0002993684
cat("H1 (sat) norm = ", PrnH1sat, "\n")
## H1 (sat) norm =  0.0001941371
cat("Conjugate Bayes factor = ", BFH0H1sat, "\n")
## Conjugate Bayes factor =  1.542047
BFH0H1NonConj <- PrnH0/Out$PrnH1
cat("Non-Conjugate Bayes factor = ", BFH0H1NonConj,
    "\n")
## Non-Conjugate Bayes factor =  0.2935347
```

Non-conjugate analysis: Increasing Sample Sizes by 2

```
exact2 <- hwexact(2 * n1, 2 * n2, 2 * n3)
exact2
## [1] 0.008886848
nvec2 <- 2 * nvec
PrnH02 <- DirichNormHWE(nvec2, bvec0)
PrnH1sat2 <- DirichNormSat(nvec2, bvec1)
BFH0H1sat2 <- PrnH02/PrnH1sat2
cat("2x Conjugate Bayes factor = ", BFH0H1sat2, "\n")
## 2x Conjugate Bayes factor =  0.4033526
Out2 <- SinglefReject(nsamp, diricvec, Prior$lambdamu,
    Prior$lambdasd, nvec2)
## Allele Marginal prob:  1 0.93
## Allele Marginal prob:  2 0.07
## Convergence =  0 (0 is successful convergence)
## Probs and f at max and fmin:
##  0.9299904 0.07000956 0.2318971 -0.07527987
## nsim norm constant (se) 95% interval:
## 10000 0.000283962 ( 2.034317e-06 ) 0.0002799747 0.0002879492
sum(Out2$fsamp > 0)/nsamp
## [1] 0.9974
BFH0H1NonConj2 <- PrnH02/Out2$PrnH1
cat("2x Non-Conjugate Bayes factor = ", BFH0H1NonConj2,
    "\n")
## 2x Non-Conjugate Bayes factor =  0.06996925
```

Non-conjugate analysis: Increasing Sample Sizes by 5

```
exact5 <- hwexact(5 * n1, 5 * n2, 5 * n3)
exact5
## [1] 3.583063e-05
nvec5 <- 5 * nvec
PrnH05 <- DirichNormHWE(nvec5, bvec0)
PrnH1sat5 <- DirichNormSat(nvec5, bvec1)
BFH0H1sat5 <- PrnH05/PrnH1sat5
cat("5x Conjugate Bayes factor = ", BFH0H1sat5, "\n")
## 5x Conjugate Bayes factor =  0.003945016
Out5 <- SinglefReject(nsamp, diricvec, Prior$lambdamu,
    Prior$lambdasd, nvec5)
## Allele Marginal prob:  1 0.93
## Allele Marginal prob:  2 0.07
## Convergence =  0 (0 is successful convergence)
## Probs and f at max and fmin:
##  0.9299904 0.07000956 0.2318971 -0.07527987
## nsim norm constant (se) 95% interval:
## 10000 4.942458e-05 ( 3.491229e-07 ) 4.87403e-05 5.010886e-05
sum(Out5$fsamp > 0)/nsamp
## [1] 1
BFH0H1NonConj5 <- PrnH05/Out5$PrnH1
cat("5x Non-Conjugate Bayes factor = ", BFH0H1NonConj5,
    "\n")
## 5x Non-Conjugate Bayes factor =  0.0006347377
```

Non-conjugate analysis: Increasing Sample Sizes by 10

```
exact10 <- hwexact(10 * n1, 10 * n2, 10 * n3)
exact10
## [1] 5.305573e-09
nvec10 <- 10 * nvec
PrnH010 <- DirichNormHWE(nvec10, bvec0)
PrnH1sat10 <- DirichNormSat(nvec10, bvec1)
BFH0H1sat10 <- PrnH010/PrnH1sat10
cat("10x Conjugate Bayes factor = ", BFH0H1sat10, "\n")
## 10x Conjugate Bayes factor =  1.154053e-06
Out10 <- SinglefReject(nsamp, diricvec, Prior$lambdamu,
    Prior$lambdasd, nvec10)
## Allele Marginal prob:  1 0.93
## Allele Marginal prob:  2 0.07
## Convergence =  0 (0 is successful convergence)
## Probs and f at max and fmin:
##  0.9299904 0.07000956 0.2318971 -0.07527987
## nsim norm constant (se) 95% interval:
## 10000 1.257162e-05 ( 8.935165e-08 ) 1.23965e-05 1.274675e-05
sum(Out10$fsamp > 0)/nsamp
## [1] 1
BFH0H1NonConj10 <- PrnH010/Out10$PrnH1
cat("10x Non-Conjugate Bayes factor = ", BFH0H1NonConj10,
    "\n")
## 10x Non-Conjugate Bayes factor =  1.830469e-07
```

HWE analysis via Stan

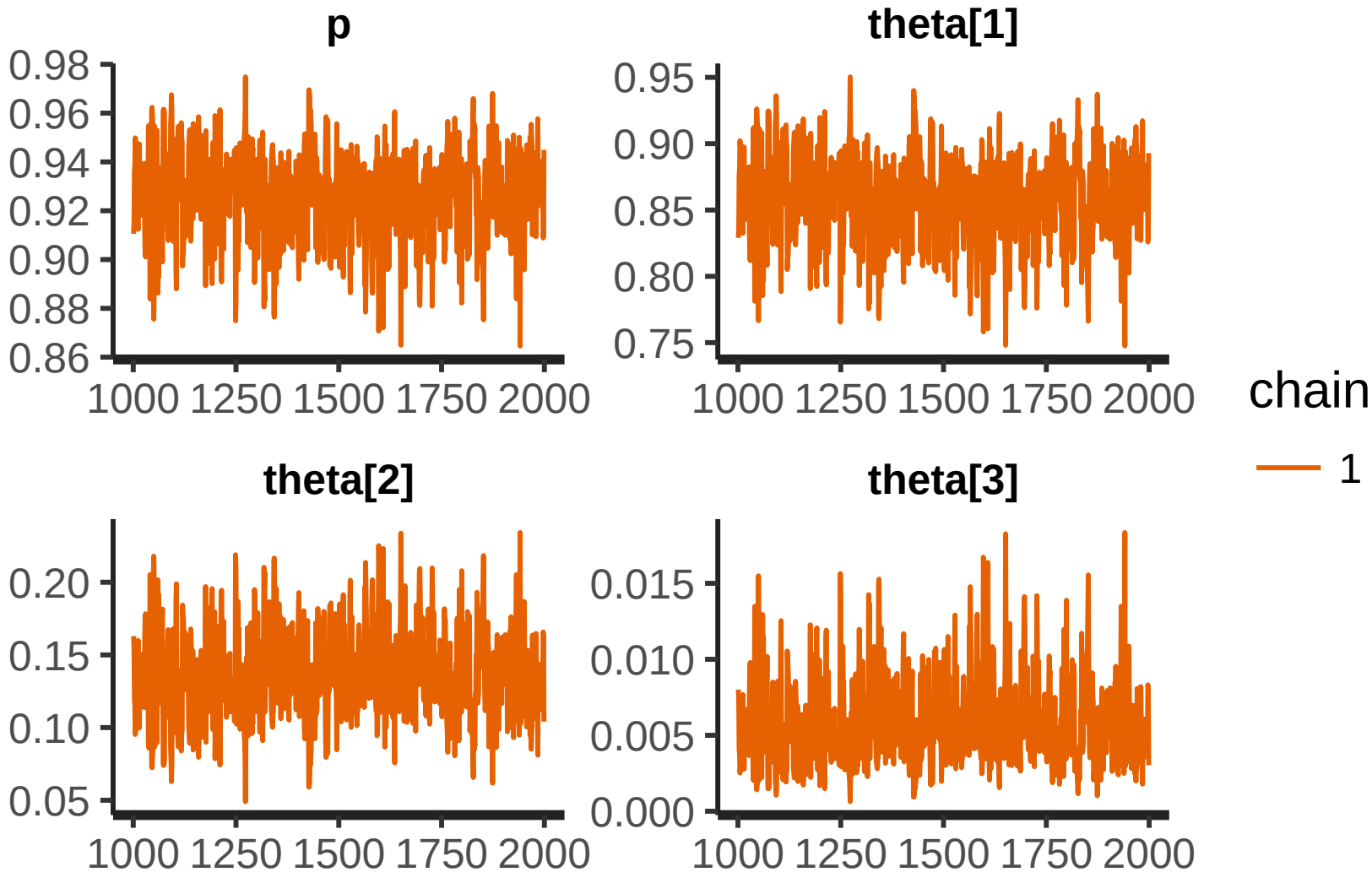
```
library(rstan)
stanexample <- stan("HWEexample.stan", data = list(y = c(88,
    10, 2)), iter = 2000, chains = 1, seed = 1234)
```

HWE analysis via Stan

```
print(stanexample)
## Inference for Stan model: HWEexample.
## 1 chains, each with iter=2000; warmup=1000; thin=1;
## post-warmup draws per chain=1000, total post-warmup draws=1000.
##
##           mean se_mean   sd   2.5%    25%    50%    75%  97.5% n_eff Rhat
## p         0.93    0.00 0.02   0.89   0.91   0.93   0.94   0.96   326    1
## theta[1]  0.86    0.00 0.03   0.79   0.83   0.86   0.88   0.92   324    1
## theta[2]  0.14    0.00 0.03   0.08   0.12   0.13   0.16   0.20   322    1
## theta[3]  0.01    0.00 0.00   0.00   0.00   0.01   0.01   0.01   413    1
## lp__    -47.00    0.04 0.70 -48.97 -47.18 -46.74 -46.56 -46.50   391    1
##
## Samples were drawn using NUTS(diag_e) at Mon Aug 28 15:05:55 2017.
## For each parameter, n_eff is a crude measure of effective sample size,
## and Rhat is the potential scale reduction factor on split chains (at
## convergence, Rhat=1).
```

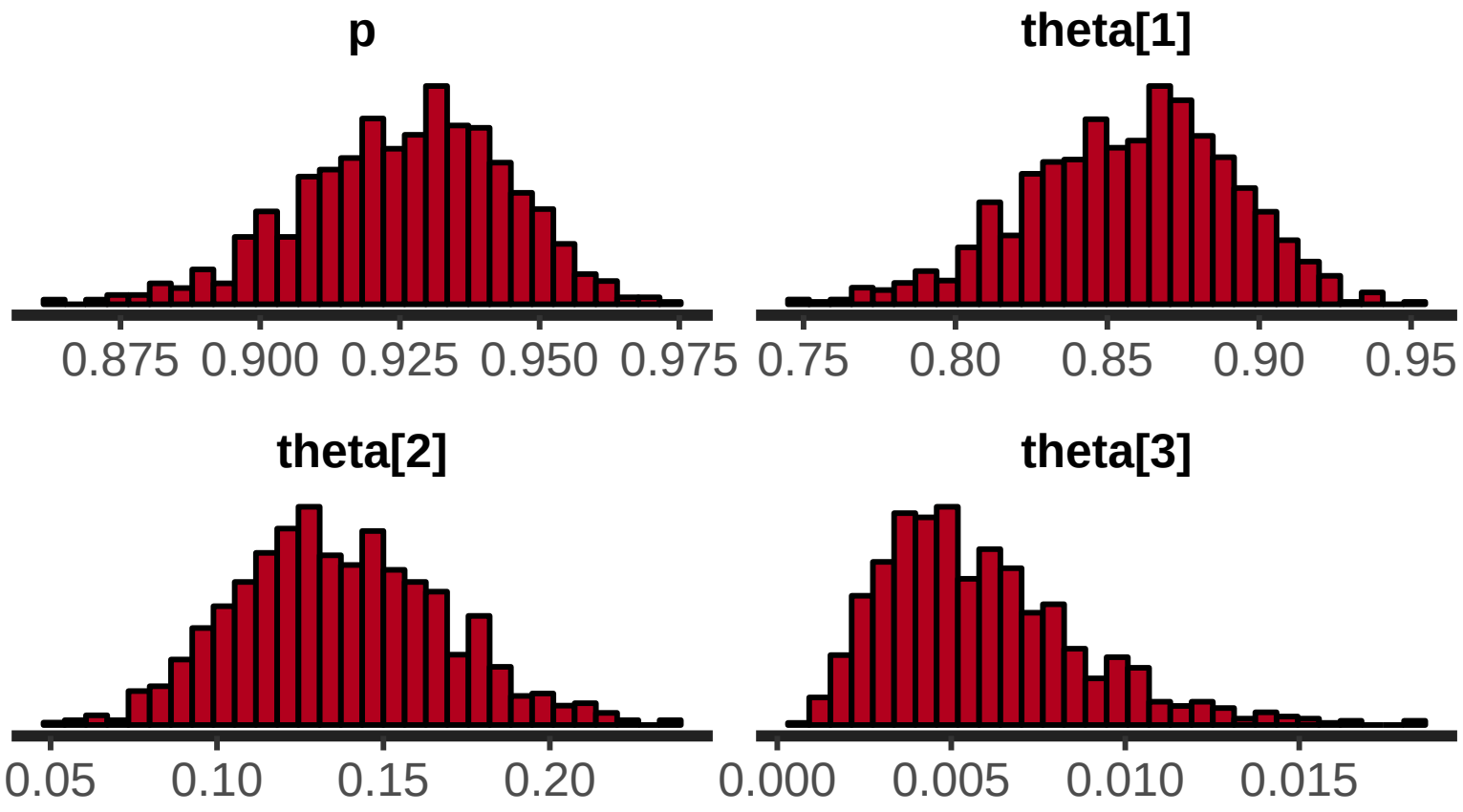
HWE analysis via Stan

```
traceplot(stanexample)
```



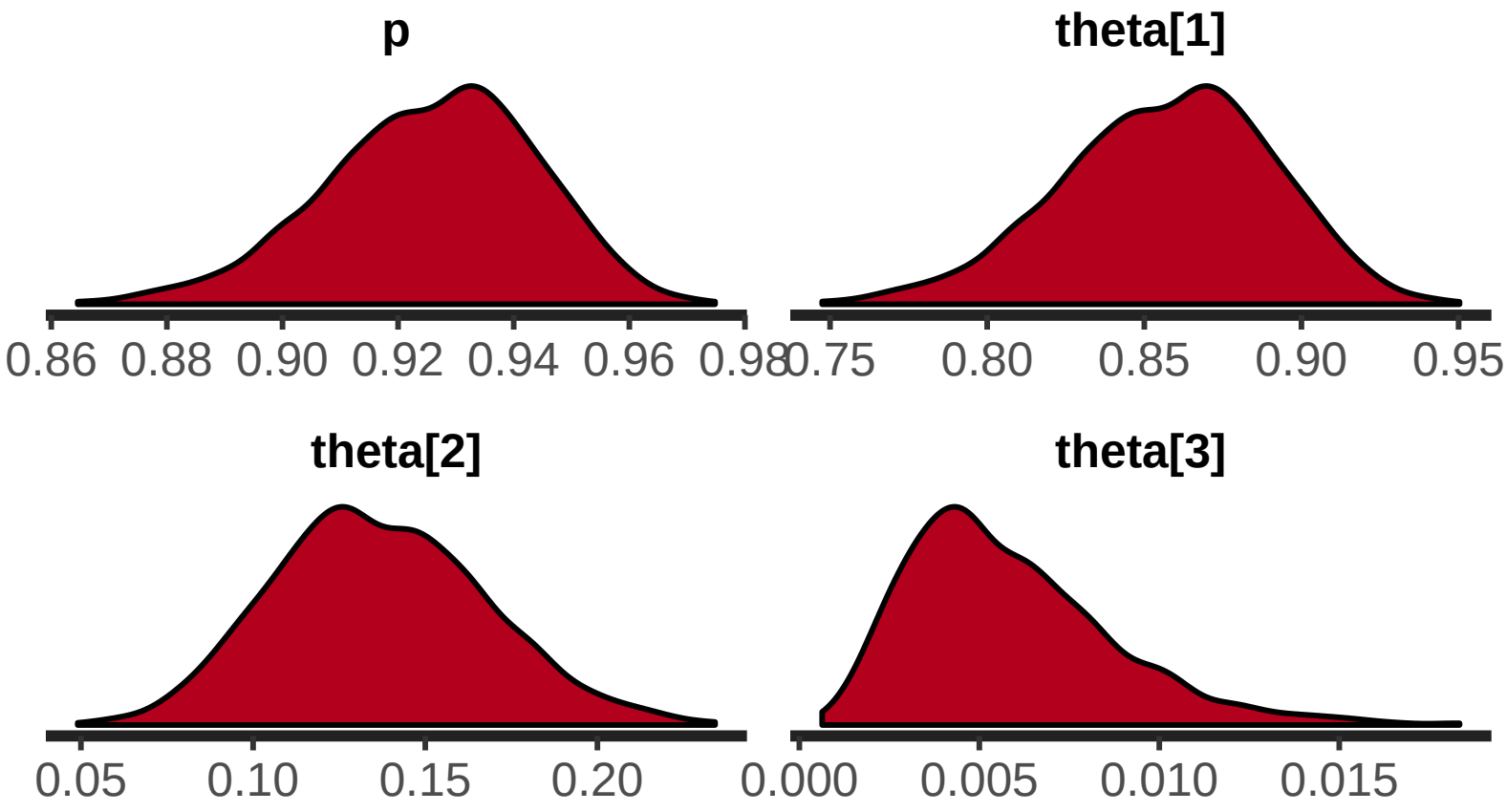
HWE analysis via Stan

```
stan_hist(stanexample)
```



HWE analysis via Stan

```
stan_dens(stanexample)
```



HWE analysis via Stan

Now run a second example with

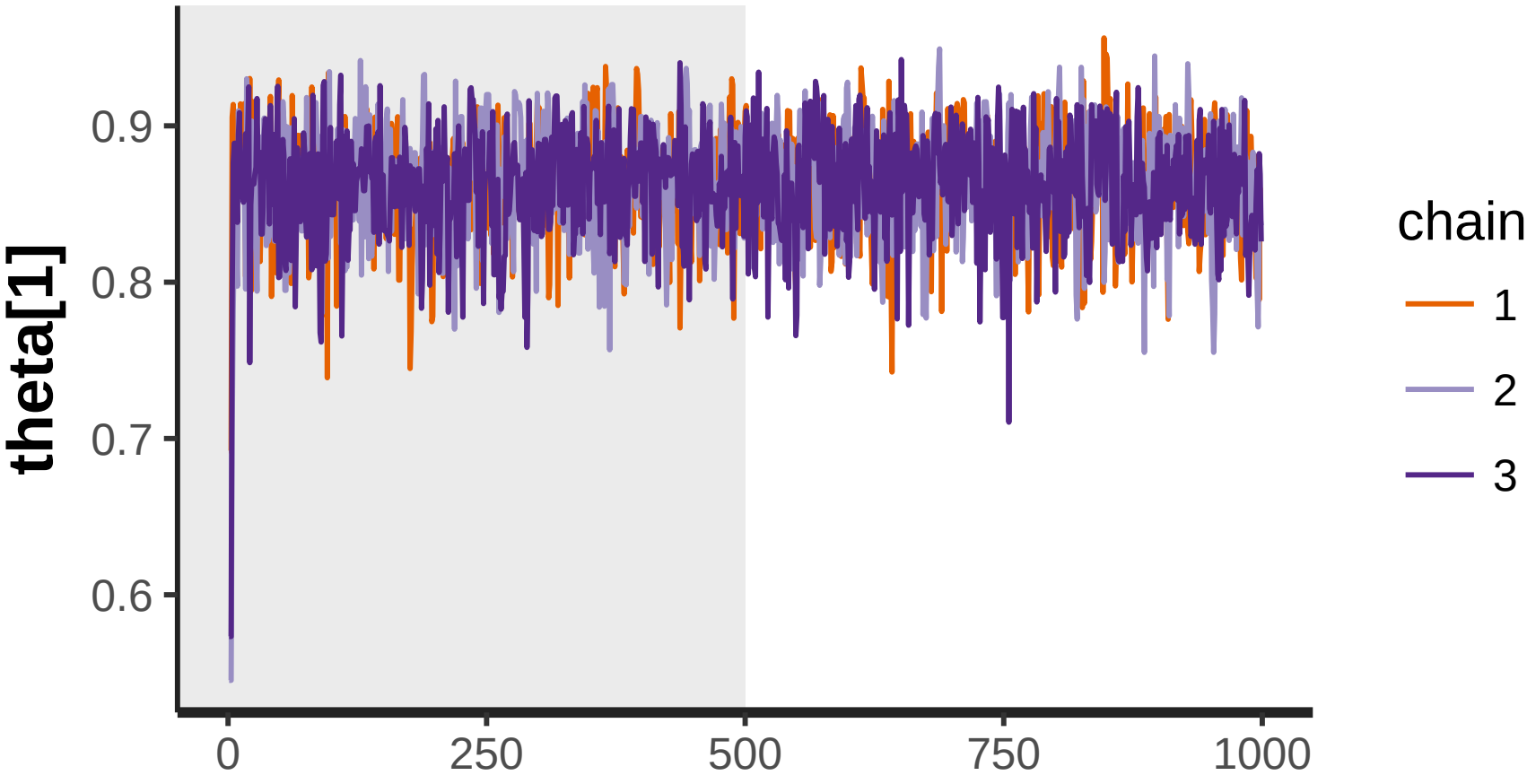
```
stanexample2 <- stan("HWEexampleSaturated.stan",
    data = list(y = c(88, 10, 2), alpha = c(1,
        1, 1)), iter = 1000, chains = 3,
    seed = 1234)
```

HWE analysis via Stan

```
summary(stanexample2)
## $summary
##                  mean      se_mean          sd          2.5%          25%
## theta[1]   0.86364137 0.0009698448 0.03204995   0.796408996   0.84297928
## theta[2]   0.10694565 0.0009071363 0.02914322   0.056216354   0.08509521
## theta[3]   0.02941297 0.0005063260 0.01634523   0.006538859   0.01735054
## lp__     -49.18671869 0.0367749137 0.93604437 -51.568059828 -49.59677209
##                  50%          75%        97.5%     n_eff     Rhat
## theta[1]   0.86540537   0.88566043   0.91828361 1092.0693 1.000051
## theta[2]   0.10506044   0.12712657   0.16505920 1032.1197 1.000564
## theta[3]   0.02652115   0.03810645   0.06719045 1042.1300 1.000420
## lp__     -48.92713551 -48.51721491 -48.24191009  647.8725 1.001987
##
## $c_summary
## , , chains = chain:1
##
##           stats
## parameter          mean          sd          2.5%          25%          50%
##   theta[1]   0.86373016 0.03125062   0.798139673   0.84400116   0.8643620
##   theta[2]   0.10647039 0.02868388   0.054506645   0.08564891   0.1051546
##   theta[3]   0.02979944 0.01607163   0.006897829   0.01757219   0.0272143
##   lp__     -49.18929202 0.94430406 -51.494728045 -49.60043191 -48.9446966
##           stats
## parameter           75%        97.5%
##   theta[1]   0.88540814   0.91779117
##   theta[2]   0.12592753   0.16232566
```

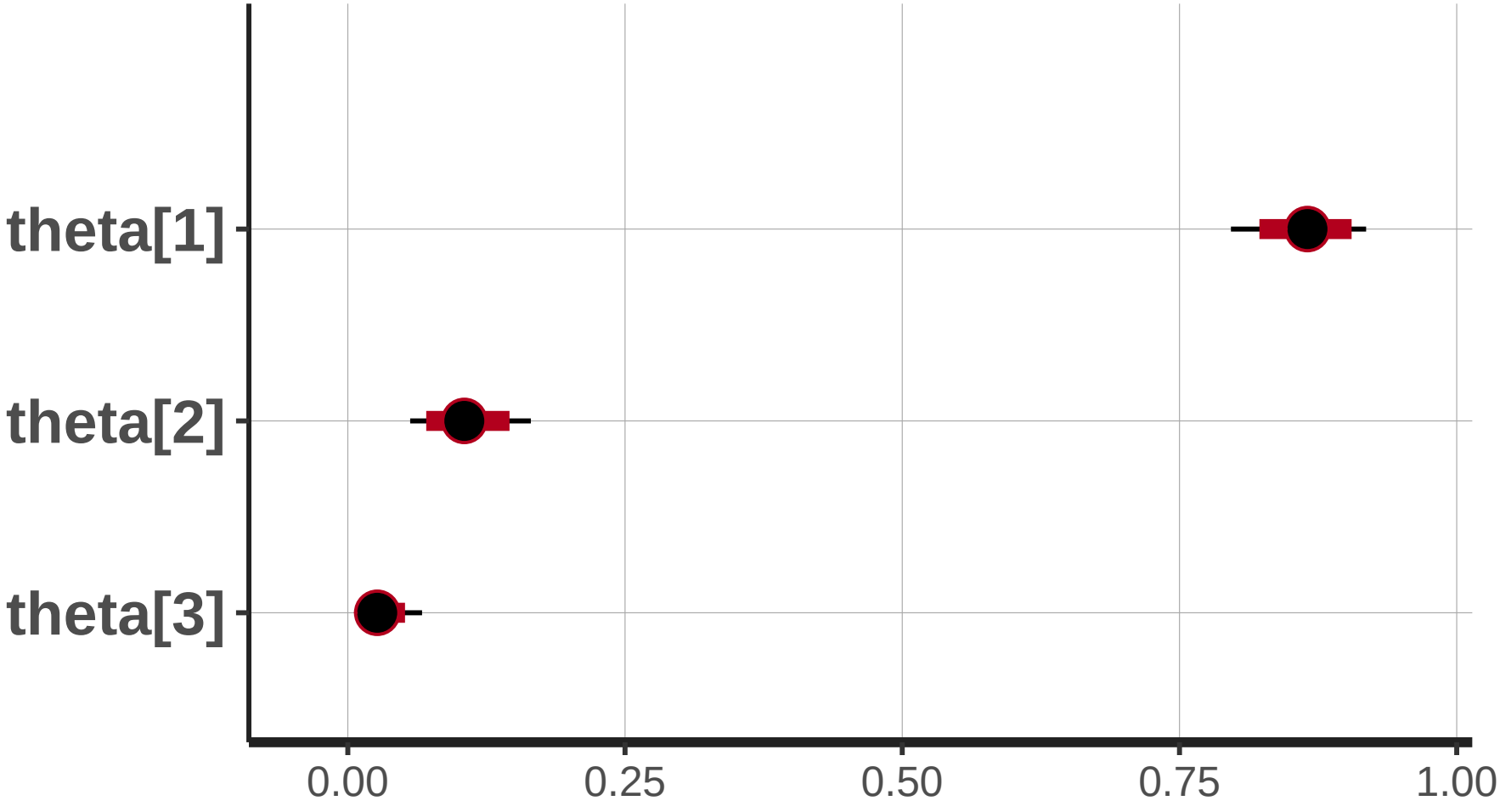
HWE analysis via Stan

```
traceplot(stanexample2, pars = c("theta[1]"), inc_warmup = TRUE)
```



HWE analysis via Stan

```
plot(stanexample2, color = "green")
```



HWE analysis via Stan

```
stan_scat(stanexample2, pars = c("theta[1]", "theta[2]"),
    color = "blue", size = 2)
```