# 2019 SISG Bayesian Statistics for Genetics
# R Notes: Binomial Sampling

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# Introduction

As we have seen there is an important duality between probability distributions and samples.

In many approaches to implementation, Bayesian inference is carried out via samples from the posterior distibution.

In this lecture we demonstrate this approach in the context of binomial sampling.

# Samples to Summarize Beta Distributions

Probability distributions can be investigated by generating samples and then examining summaries such as histograms, moments and quantiles.

```
# First look at the theoretical quantiles of a
# uniform distribution, a beta(1,1)
qbeta(p = c(0.05, 0.1, 0.5, 0.9, 0.95), 1, 1)
## [1] 0.05 0.10 0.50 0.90 0.95
# Now find the mean and quantiles from a large
# sample from a uniform
nsim <- 5000
samp <- rbeta(nsim, 1, 1)
mean(samp)
## [1] 0.50442
quantile(samp, p = c(0.05, 0.1, 0.5, 0.9, 0.95))
##        5%        10%        50%        90%        95%
## 0.04994313 0.10185837 0.50541915 0.90603164 0.95343201
# These differ slightly from the theoretical
# quantiles because of sampling variability
```
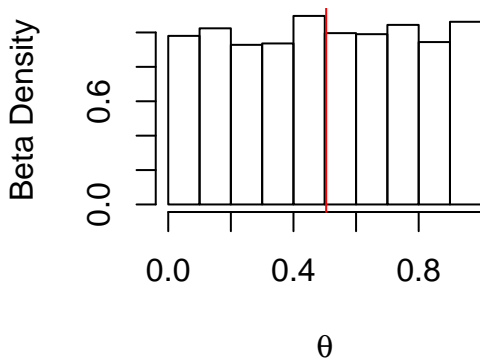
# Samples to Summarize Beta Distributions

We now examine a histogram representation of a random variable $\theta$ with a uniform distribution, and then add a vertical line at the mean.

```
hist(samp, xlab = expression(theta), ylab = "Beta Density",
    main = "a=1, b=1", freq = F, nclass = 10)
abline(v = mean(samp), col = "red")
```

# Samples to Summarize Beta Distributions



a=1, b=1

# Samples to Summarize Beta Distributions

Now we examine a beta(4,2) distribution.

We first look at the theoretical quantiles (using the `qbeta` function), and then simulate a sample and evaluate the empirical quantiles.

```
qbeta(p = c(0.05, 0.1, 0.5, 0.9, 0.95), 4, 2)
## [1] 0.3425917 0.4161096 0.6861898 0.8877650 0.9235596
samp <- rbeta(nsim, 4, 2)
mean(samp)
## [1] 0.6631277
quantile(samp, p = c(0.05, 0.1, 0.5, 0.9, 0.95))
##        5%        10%        50%        90%        95%
## 0.3457143 0.4184458 0.6822974 0.8823382 0.9188194
hist(samp, xlab = expression(theta), ylab = "Beta Density",
    main = "a=4, b=2", freq = F, nclass = 10)
abline(v = mean(samp), col = "red")
```

# Samples to Summarize Beta Distributions
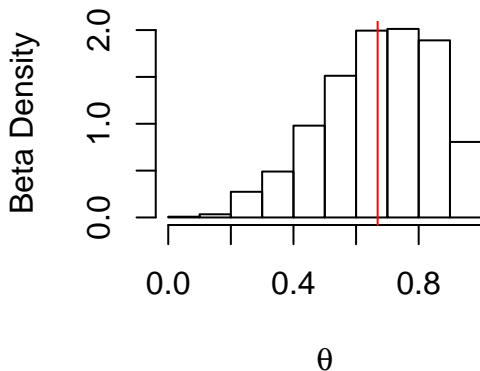
# Samples for Describing Weird Parameters

So far the samples we have generated have produced summaries we can easily obtain anyway.

But what about functions of the probability $\theta$, such as the odds $\theta/(1-\theta)$?

Once we have samples for $\theta$ we can simply transform the samples to the functions of interest.

In a prior specification context, we may have clearer prior opinions about the odds, than the probability.

Below we give a histogram representation of the prior on the odds $\theta/(1-\theta)$ when $\theta$ is `beta(10,10)`.

```
nsim <- 5000
samp <- rbeta(nsim, 10, 10)
odds <- samp/(1 - samp)
```

# Samples for Describing Weird Parameters

```
hist(odds, xlab = "Odds", main = expression(paste("Odds with ",
    theta, " from beta(10,10)")))
abline(v = mean(odds), col = "red")
```

## Odds with θ from beta(10,10)
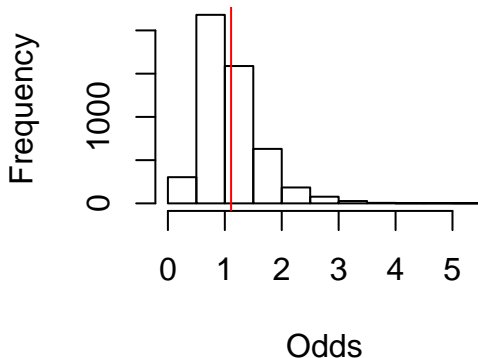
# Are Priors Really Uniform?

Suppose we have a uniform prior on $\theta$, i.e. $\theta \sim \text{beta}(1, 1)$.
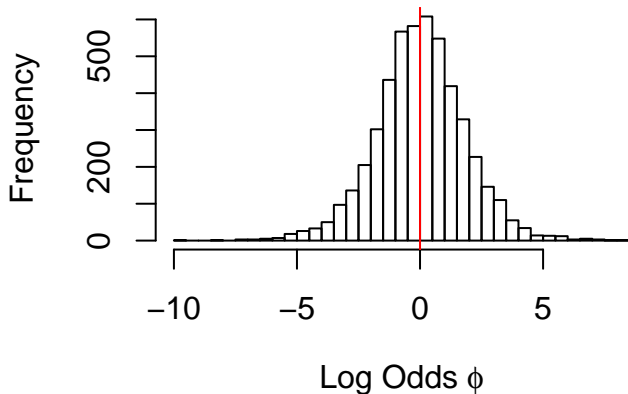
This prior is not uniform on the function

$$\phi = \log\left(\frac{\theta}{1 - \theta}\right).$$

```r
nsim <- 5000
theta <- rbeta(nsim, 1, 1)
phi <- log(theta/(1 - theta))
hist(phi, xlab = expression(paste("Log Odds ", phi)),
    nclass = 30, main = expression(paste("Log Odds with ",
        theta, " from a beta(1,1)")))
abline(v = 0, col = "red")
```

Log Odds with θ from beta(1,1)

# Beta Prior, Binomial Likelihood and Beta Posterior

We consider a beta prior for a proportion $\theta$ and a binomial likelihood and beta posterior that these choices lead to.

The prior is `beta(2,3)` the likelihood is proportional to a `binomial(7,3)` and the posterior is `beta(7+2,3+3)`.

```
a <- 2
b <- 3
N <- 10
y <- 7
thetaseq <- seq(0, 1, 0.001)
prior <- dbeta(thetaseq, a, b)
likelihood <- dbeta(thetaseq, y + 1, N - y + 1)
posterior <- dbeta(thetaseq, a + y, b + N - y)
```

# Beta Prior, Binomial Likelihood and Beta Posterior

```r
plot(posterior ~ thetaseq, xlab = expression(theta),
    type = "n", ylab = "Density")
lines(prior ~ thetaseq, type = "l", col = "red", lwd = 2,
    lty = 1)
lines(likelihood ~ thetaseq, type = "l", col = "green",
    lwd = 2, lty = 2)
lines(posterior ~ thetaseq, type = "l", col = "blue",
    lwd = 2, lty = 3)
legend("topleft", legend = c("Prior", "Likelihood",
    "Posterior"), col = c("red", "green", "blue"),
    lwd = 2, bty = "n", lty = 1:3)
```

# Beta Prior, Likelihood and Posterior
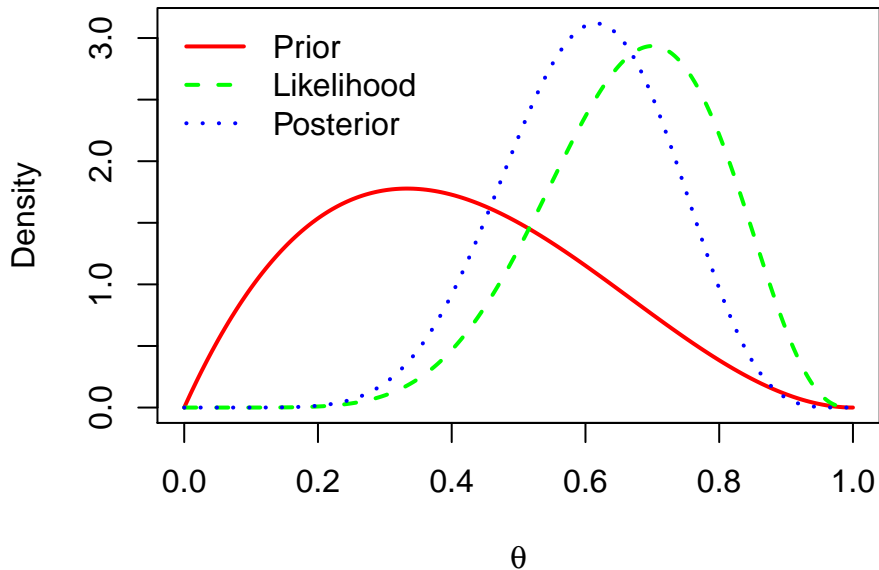
# Specifying a prior distribution

The code below finds the beta distribution, i.e. the a and the b, with 5% and 95% points of 0.1 and 0.6.

```
# Function to find a and b
priorch <- function(x, q1, q2, p1, p2) {
    (p1 - pbeta(q1, x[1], x[2]))^2 + (p2 - pbeta(q2,
        x[1], x[2]))^2
}
p1 <- 0.05
p2 <- 0.95
q1 <- 0.1
q2 <- 0.6
opt <- optim(par = c(1, 1), fn = priorch, q1 = q1,
    q2 = q2, p1 = p1, p2 = p2, control = list(abstol = 1e-08))
cat("a and b are ", opt$par, "\n")
## a and b are  2.730616 5.667462
probvals <- seq(0, 1, 0.001)
plot(probvals, dbeta(probvals, shape1 = opt$par[1],
    shape2 = opt$par[2]), type = "l", xlab = expression(theta),
    ylab = "Beta Density")
abline(v = q1, col = "red")
abline(v = q2, col = "red")
```

# Specifying a prior distribution
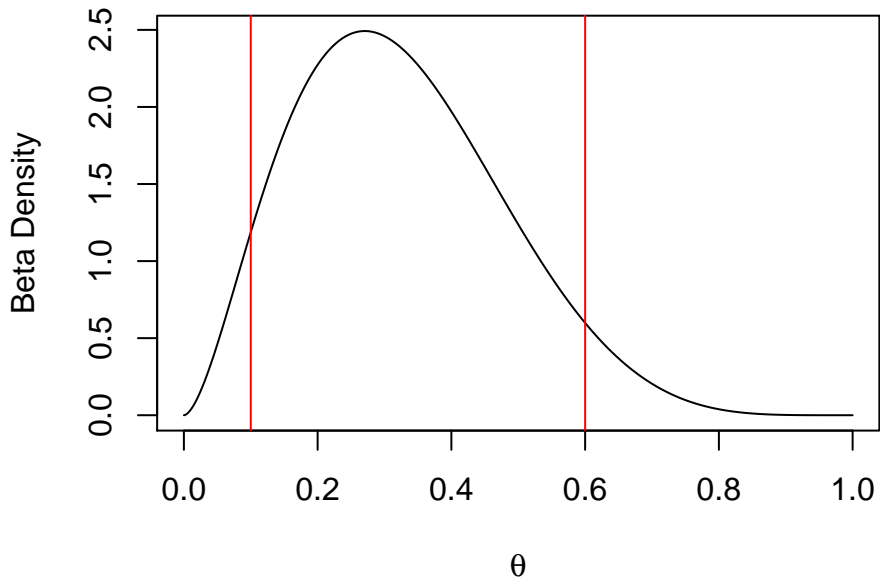
# Predictions from a Binomial Distribution

We now consider prediction.

Assume $y|\theta \sim \text{binomial}(N, \theta)$ and $\theta \sim \text{beta}(a, b)$.

We suppose we wish to predict the number of successes $Z$ from $M$ trials.

The predictive distribution is

$$\Pr(z|y) = \left( \begin{array}{c} M \\ z \end{array} \right) \frac{\Gamma(N + a + b)}{\Gamma(y + a)\Gamma(N - y + b)} \frac{\Gamma(a + y + z)\Gamma(b + N - y + M - z)}{\Gamma(a + b + N + M)}$$

for $z = 0, \ldots, M$.

# Predictions from a Binomial Distribution

We demonstrate with a uniform prior and observing $y = 2$ successes from $N = 20$ trials, and suppose we wish to predict the number of successes we will see in 10 additional trials.

```r
# User written function
binomialpred <- function(a, b, y, N, z, M) {
    lchoose(M, z) + lgamma(a + b + N) - lgamma(a +
        y) - lgamma(b + N - y) + lgamma(a + y + z) +
        lgamma(b + N - y + M - z) - lgamma(a + b +
        N + M)
}
a <- b <- 1
y <- 2
N <- 20
M <- 10
binpred <- NULL
z <- seq(0, M)
```
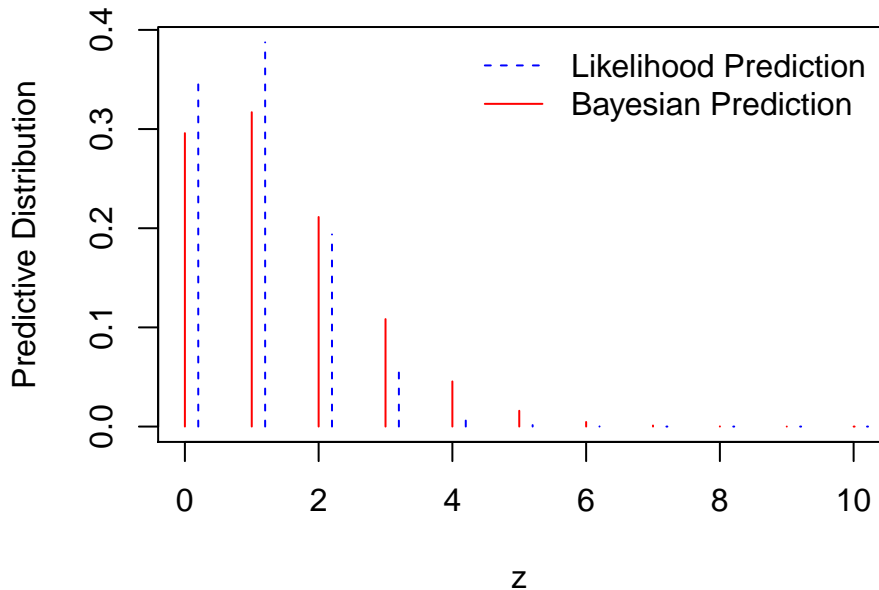
## Predictions from a Binomial Distribution

Along with the Bayesian predictive distribution, we also include a
simple approach in which we assume simply take a
binomial(M,y/N) distribution, i.e. assuming the probability is
known to be the sample fraction.

```
sumcheck <- 0
for (i in 1:(M + 1)) {
    binpred[i] <- exp(binomialpred(a, b, y, N, z[i],
        M))
    sumcheck <- sumcheck + binpred[i]
}
likpred <- dbinom(z, M, prob = y/N)
cat("Sum of probs = ", sumcheck, "\n")
## Sum of probs =  1
```

# Predictions from a Binomial Distribution

```r
plot(binpred ~ z, type = "h", col = "red", ylim = c(0,
    max(likpred, binpred)), ylab = "Predictive Distribution")
points(z + 0.2, likpred, type = "h", col = "blue",
    lty = 2)
legend("topright", legend = c("Likelihood Prediction",
    "Bayesian Prediction"), lty = 2:1, col = c("blue",
    "red"), bty = "n")
```

# Predictions from a Binomial Distribution
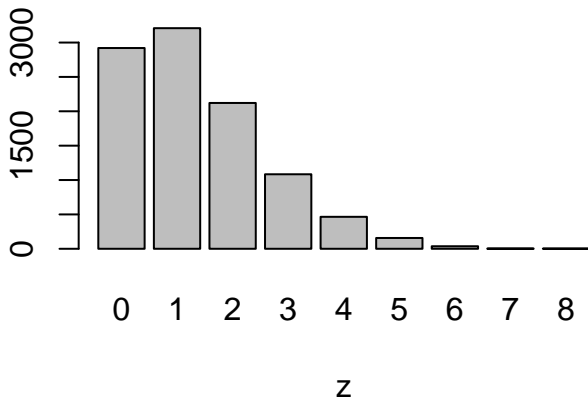
# Predictions with a Binomial Distribution

We now simulate directly via:

– Sampling from $\theta^{(s)} \sim p(\theta|y)$, $s = 1, \ldots, S$.

– Sampling from $z^{(s)} \sim p(z|\theta)$, $s = 1, \ldots, S$.

```
a <- b <- 1
y <- 2
N <- 20
M <- 10
nsim <- 10000
theta <- z <- NULL  # This is inefficient but makes method clear
for (s in 1:nsim) {
    theta[s] <- rbeta(1, a + y, b + N - y)
    z[s] <- rbinom(1, M, theta[s])
}
```

# Predictions with a Binomial Distribution

```
barplot(table(z), xlab = "z")
```

# Differences in Binomial Proportions

We consider an example in which we wish to compare allele frequencies between two populations.

Let $\theta_1$ and $\theta_2$ be the allele frequencies in the NE and US population from which the samples were drawn, respectively.

The allele frequencies were 10.69% and 13.21% with sample sizes of 650 and 265, in the NE and US samples, respectively.

We assume independent `beta(1,1)` priors on each of $\theta_1$ and $\theta_2$.

# Differences in Binomial Proportions

The $y1$ and $y2$ data (i.e. the numbers with the allele in the two populations) were reconstructed from figures in the original paper in which only the denominators and the frequencies were given, hence the `floor` function.

```
N1 <- 650
y1 <- floor(N1 * 0.1069)
N2 <- 265
y2 <- floor(N2 * 0.1321)
nsamp <- 10000
a <- b <- 1
post1 <- rbeta(nsamp, y1 + a, N1 - y1 + b)
post2 <- rbeta(nsamp, y2 + a, N2 - y2 + b)
```

# Differences in Binomial Proportions

The key step is in constructing a sample estimate of the difference in probabilities $\theta_1 - \theta_2$.

```r
par(mfrow = c(1, 3))
hist(post1, xlab = expression(theta[1]), main = "",
    cex.lab = 1.5)
hist(post2, xlab = expression(theta[2]), main = "",
    cex.lab = 1.5)
#
hist(post1 - post2, xlab = expression(paste(theta[1],
    "-", theta[2])), main = "", cex.lab = 1.5)
abline(v = 0, col = "red")
sum(post1 - post2 > 0)/nsamp
## [1] 0.123
```

# Differences in Binomial Proportions
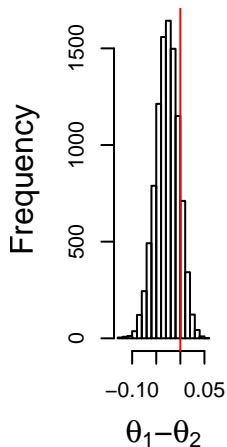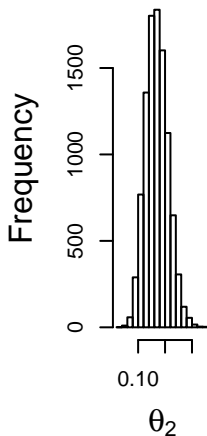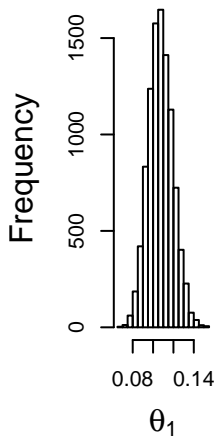
## Analysis of ASE data

```
ASEdat <- read.table("ASEgene.txt", header = TRUE)
head(ASEdat)
##      Y    N
## 1   62  107
## 2   33   59
## 3  658 1550
## 4   14   61
## 5   57  153
## 6  218  451
dim(ASEdat)
## [1] 4844    2
ngenes <- dim(ASEdat)[1]
pvals <- NULL
for (i in 1:ngenes) {
    pvals[i] <- binom.test(ASEdat$Y[i], ASEdat$N[i],
        p = 0.5, alternative = "two.sided")[["p.value"]]
}
```
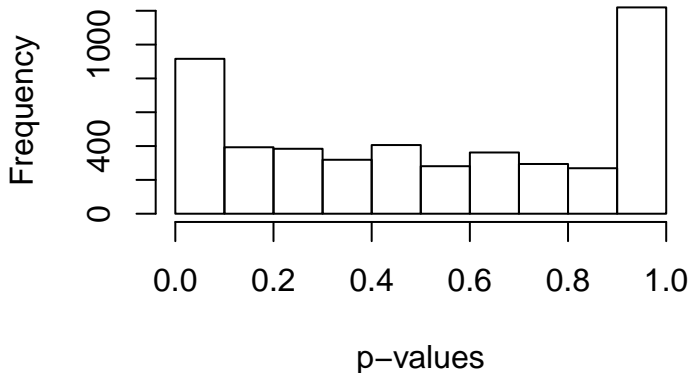
# Analysis of ASE data

```r
# Function to evaluate Bayes factors for a binomial
# likelihood and beta prior, and a point null at p0
BFbinomial <- function(N, y, a, b, p0) {
    logPrH0 <- lchoose(N, y) + y * log(p0) + (N - y) *
        log(1 - p0)
    logPrH1 <- lchoose(N, y) + gamma(a + b) - lgamma(a) -
        lgamma(b) + lgamma(y + a) + lgamma(N - y +
        b) - lgamma(N + a + b)
    logBF <- logPrH0 - logPrH1
    list(logPrH0 = logPrH0, logPrH1 = logPrH1, logBF = logBF)
}
nsim <- 5000
a <- 1
b <- 1
p0 <- 0.5
```

# Analysis of ASE data

```r
postprob <- logBFr <- rep(0, ngenes)
pcutoff <- 0.05/length(pvals)
for (i in 1:ngenes) {
    BFcall <- BFbinomial(ASEdat$N[i], ASEdat$Y[i],
        a, b, p0)
    logBFr[i] <- -BFcall$logBF
    postprob[i] <- pbeta(0.5, a + ASEdat$Y[i], b +
        ASEdat$N[i] - ASEdat$Y[i])
}
cat("log BFr > log(150) = ", sum(logBFr > log(150)),
    "\n")
## log BFr > log(150) =  197
cat("log BFr > log(20) = ", sum(logBFr > log(20)),
    "\n")
## log BFr > log(20) =  359
cat("p-values >  ", pcutoff, sum(pvals < pcutoff),
    "\n")
## p-values >   1.032205e-05 111
cat("postprobs < 0.01 and > 0.99 ", sum(postprob <
    0.01), sum(postprob > 0.99), "\n")
## postprobs < 0.01 and > 0.99  278 242
```
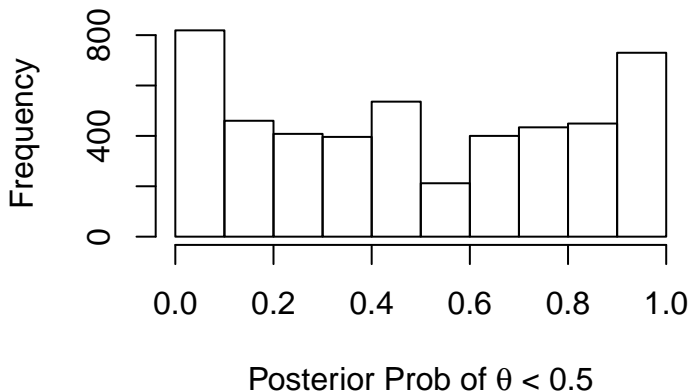
# Histogram of *p*-values for ASE data

```
hist(pvals, xlab = "p-values", main = "")
```
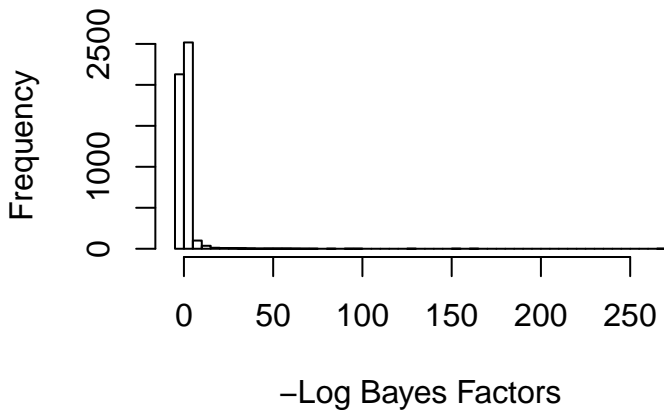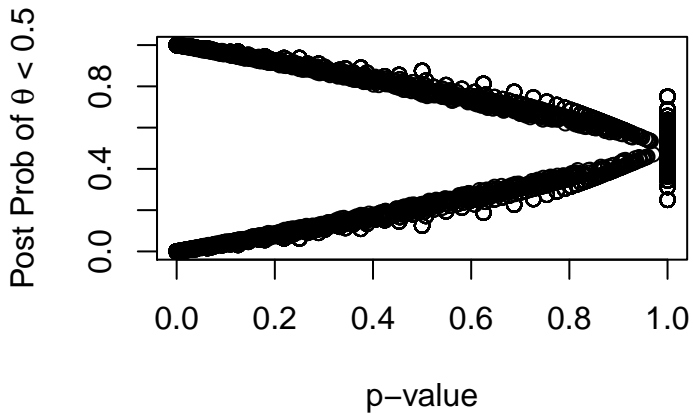
# Histogram of posterior probabilities for ASE data

```
hist(postprob, xlab = expression(paste("Posterior Prob of ",
    theta, " < 0.5")), main = "")
```



Posterior Prob of θ < 0.5

# Analysis of ASE data

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