Version 3: 4 clusters

Simulate data

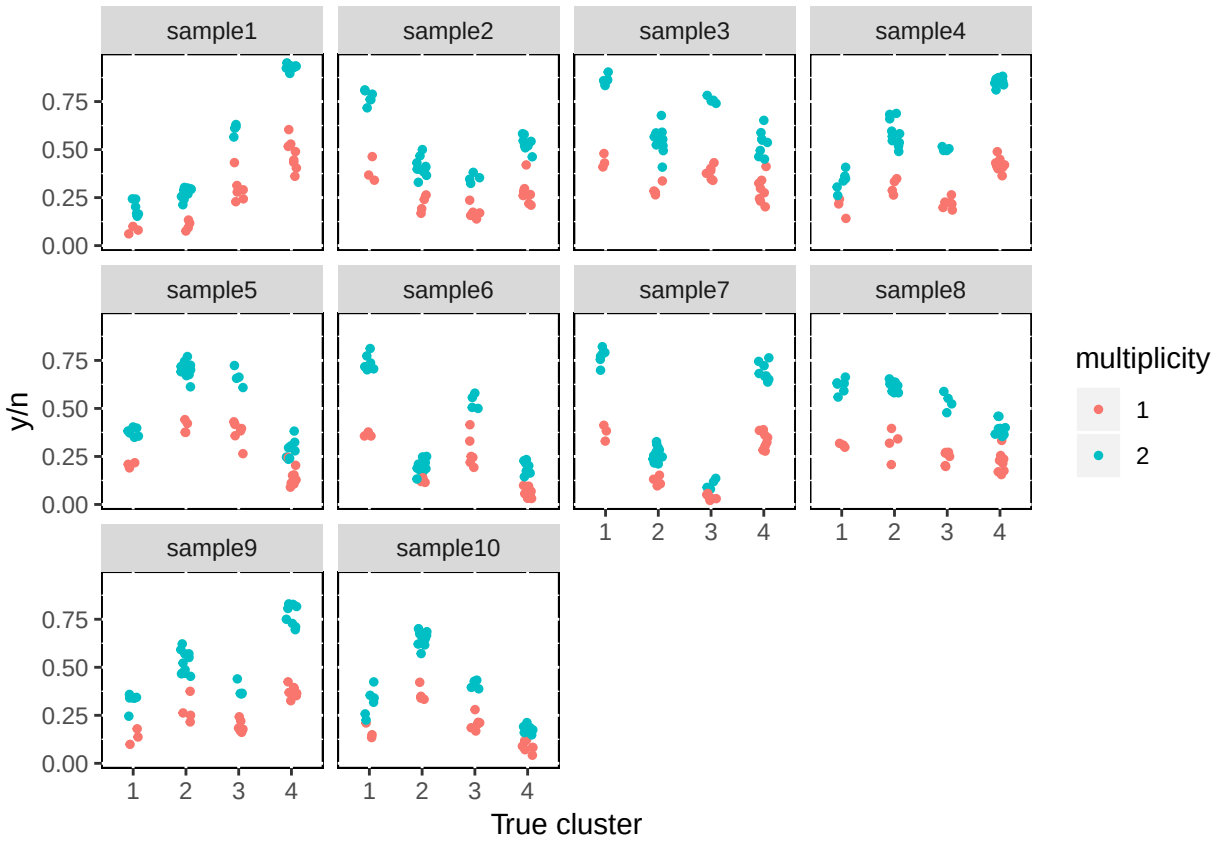
```
I <- 50
K <- 4
S <- 10

# choose diffuse priors for gamma
a_gamma <- 2
b_gamma <- 10

set.seed(123)

a <- matrix(NA, nrow=K, ncol=S)
b <- matrix(NA, nrow=K, ncol=S)
for (s in 1:S) {
  a[, s] <- rgamma(K, a_gamma, rate = 1/b_gamma)
  b[, s] <- rgamma(K, a_gamma, rate = 1/b_gamma)
}
colnames(a) <- colnames(b) <- paste0("sample", seq_len(ncol(a)))
# reorder a,b matrices to match ordering of means (U) in S1
U <- a/(a+b)
V <- a+b
ix <- order(U[, 1])
U.ordered <- U[ix, ]
a.ordered <- a[ix, ]
b.ordered <- b[ix, ]
V.ordered <- V[ix, ]

#pi <- as.vector(rdirichlet(1, rep(1, K)))
pi <- c(0.2, 0.3, 0.2, 0.3)
z <- sample(1:K, size = I, replace = T, prob = pi)

##
## omega (w) is the cancer cell fraction
## - shouldn't omega have dimension K x S
## - I'd like to be able to recover the true values of a and b
## ->  a single random ordinate drawn from this distribution
##     might not be representative
##     a an average over 1000 random ordinates guarantees that
##     we have a representative ordinate of beta(a, b)
w <- matrix(NA, nrow=K, ncol=S)
for(k in seq_len(K)){
    tmp <- rowMeans(replicate(1000,
                              rbeta(S, a.ordered[k, ],
                                    b.ordered[k, ])))
    w[k, ] <- tmp
}

tcn <- matrix(2, nrow=I, ncol=S)
```

```
m <- matrix(rep(sample(1:2, size = I, replace = T), S),
            nrow=I, ncol=S)
W <- w[z, ]
calcTheta <- function(m, tcn, w) {
  (m * w) / (tcn * w + 2*(1-w))
}
theta <- calcTheta(m, tcn, W)

n <- replicate(S, rpois(I, 100))
y <- matrix(NA, nrow=I, ncol=S)
for (i in 1:I) {
  for (s in 1:S) {
    y[i, s] <- rbinom(1, n[i, s], theta[i,s])
  }
}

test.data <- list("I" = I, "S" = S, "K" = K,
                  "y" = y, "n" = n,
                  "m" = m, "tcn" = tcn)
```

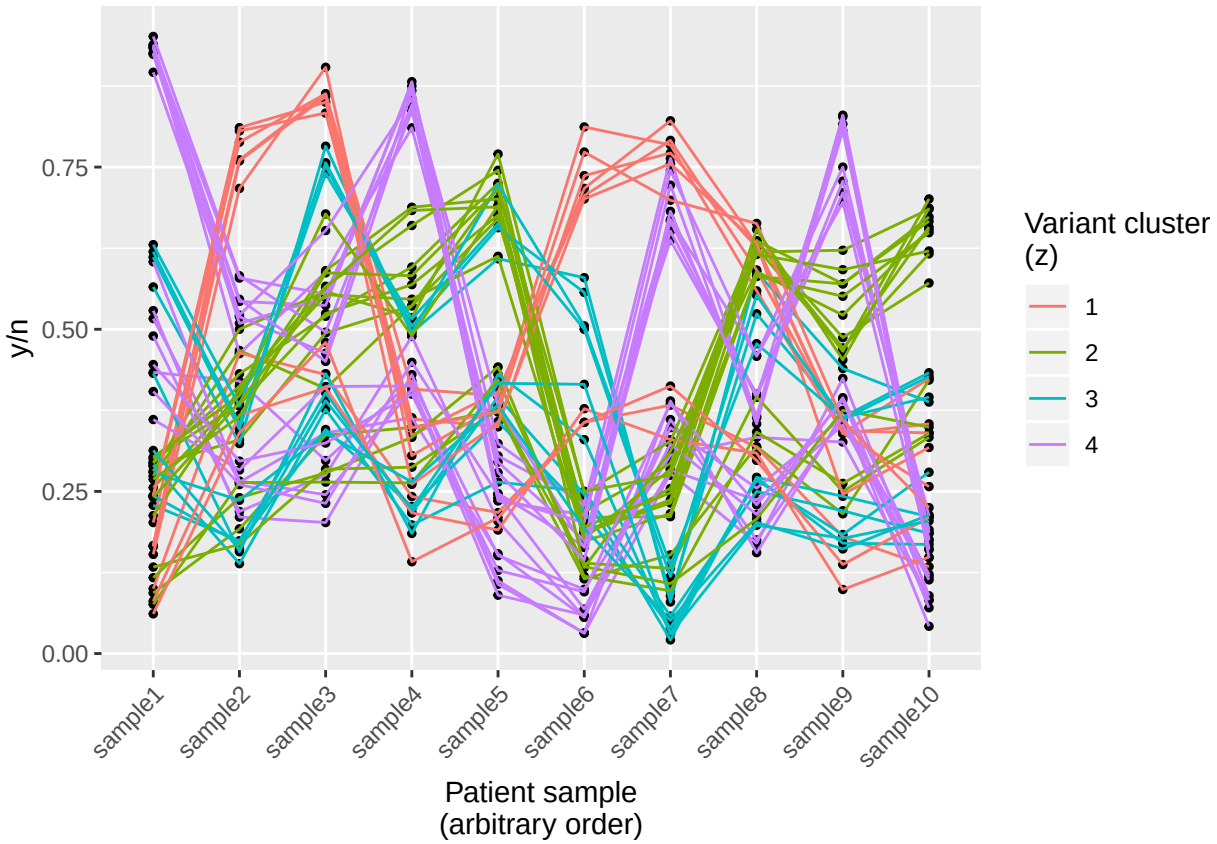
Visualize densities of simulated data

Clustering is by ω

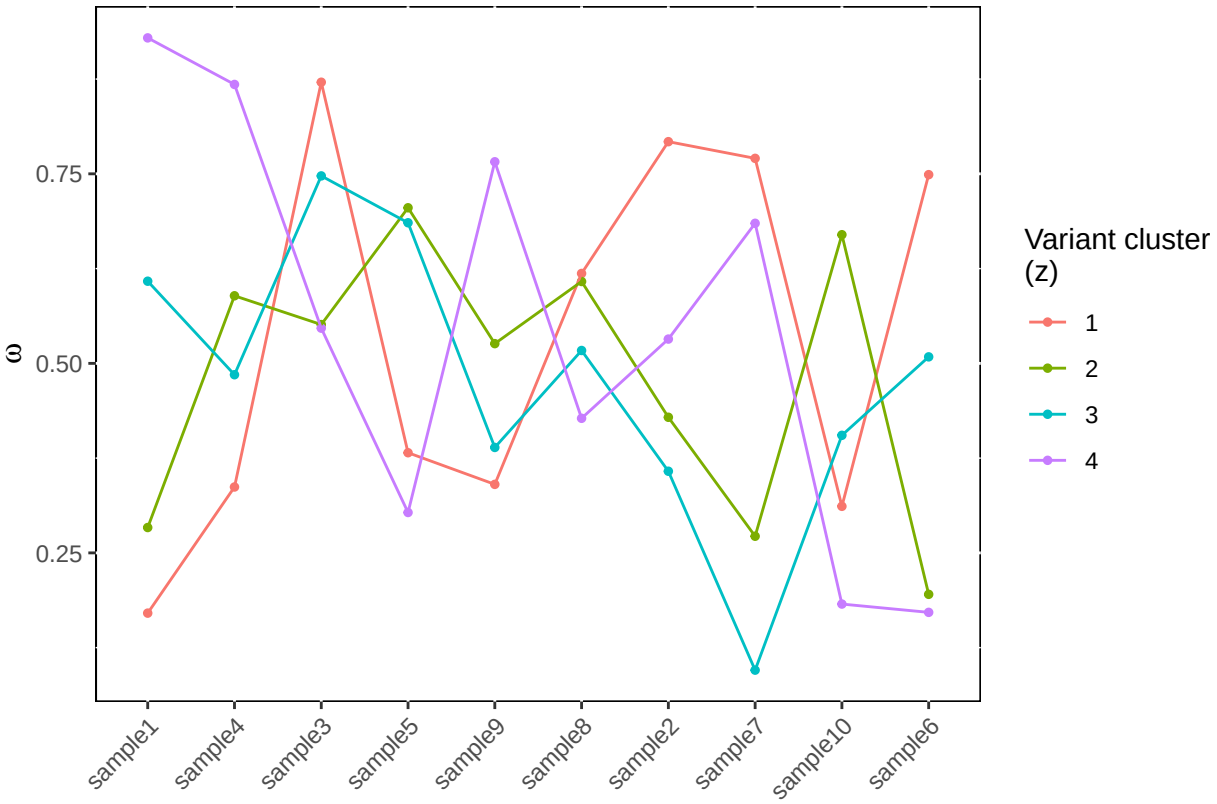
```
test.data <- list("I" = I, "S" = S, "K" = K,
                  "y" = y, "n" = n,
                  "m" = m, "tcn" = tcn)
p <- test.data$y/test.data$n
colnames(w) <- colnames(p) <- paste0("sample", seq_len(ncol(p)))
colnames(m) <- colnames(p)
m2 <- m %>%
    as_tibble() %>%
    mutate(z=factor(z),
           variant_index=seq_len(nrow(.))) %>%
    gather("sample", "multiplicity", -c(z, variant_index)) %>%
    mutate(sample=factor(sample, levels=colnames(p)))
p2 <- p %>%
    as_tibble() %>%
    mutate(z=factor(z),
           variant_index=seq_len(nrow(.))) %>%
    gather("sample", "fraction", -c(z, variant_index)) %>%
    mutate(sample=factor(sample, levels=colnames(p))) %>%
    left_join(m2, by=c("z", "variant_index", "sample")) %>%
    mutate(multiplicity=factor(multiplicity))
## what the data looks like by sample
ggplot(p2, aes(z, fraction)) +
    geom_jitter(width=0.1, size=1, aes(color=multiplicity)) +
    facet_wrap(~sample) +
    ylab("y/n") +
    xlab("True cluster") +
    theme(panel.background=element_rect(fill="white", color="black"))
```




```
## by variant
ggplot(p2, aes(sample, fraction, group=variant_index)) +
    geom_point(size=1) +
    geom_line(aes(color=z)) +
    ylab("y/n") +
    xlab("Patient sample\n(arbitrary order)") +
    theme(axis.text.x=element_text(angle=45, hjust=1)) +
    guides(color=guide_legend(title="Variant cluster\n(z)"))
```




```
##
## Cluster means and variances
##
meds   <- apply(W, 2, median)
slevels <- colnames(w)[order(meds, decreasing=TRUE)]
w2 <- w %>%
    as_tibble() %>%
    mutate(z=factor(1:K)) %>%
    ##       variant_index=seq_len(nrow(.))) %>%
    gather("sample", "omega", -z) %>%
    mutate(sample=factor(sample, levels=slevels))
##fig1 <- ggplot(w2, aes(z, omega)) +
##    geom_jitter(width=0.1, size=1) +
##    facet_wrap(~sample) +
##    ylab(expression(omega)) +
##    xlab("True cluster") +
##    theme(panel.background=element_rect(fill="white", color="black"))
fig2 <- ggplot(w2, aes(sample, omega, group=z)) +
    geom_point(size=1,  aes(color=z)) +
    geom_line(aes(color=z)) +
    ylab(expression(omega)) +
    xlab("") +
    theme(axis.text.x=element_text(angle=45, hjust=1),
          panel.background=element_rect(fill="white", color="black"),
          legend.key=element_rect(fill="white", color="white")) +
    guides(color=guide_legend(title="Variant cluster\n(z)"))
fig2
```



JAGS

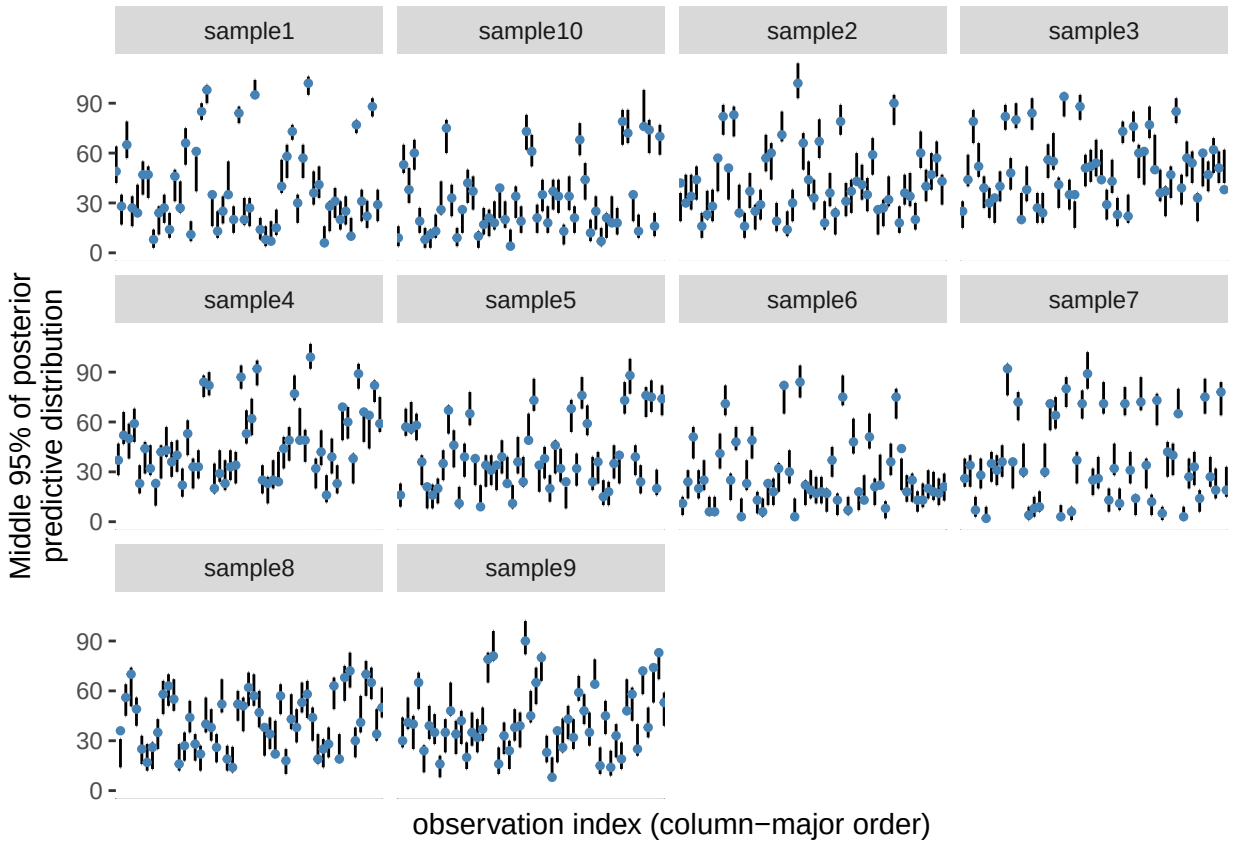
```
jags.file <- file.path(models.dir, "rs_no_constraints.jags")
inits <- list(".RNG.name" = "base::Wichmann-Hill",
              ".RNG.seed" = 123)
jags.m <- jags.model(jags.file, test.data,
                     n.chains = 1,
                     inits = inits,
                     n.adapt = 1000)
```

```
## Compiling model graph
##    Resolving undeclared variables
##    Allocating nodes
## Graph information:
##    Observed stochastic nodes: 500
##    Unobserved stochastic nodes: 671
##    Total graph size: 8010
##
## Initializing model
```

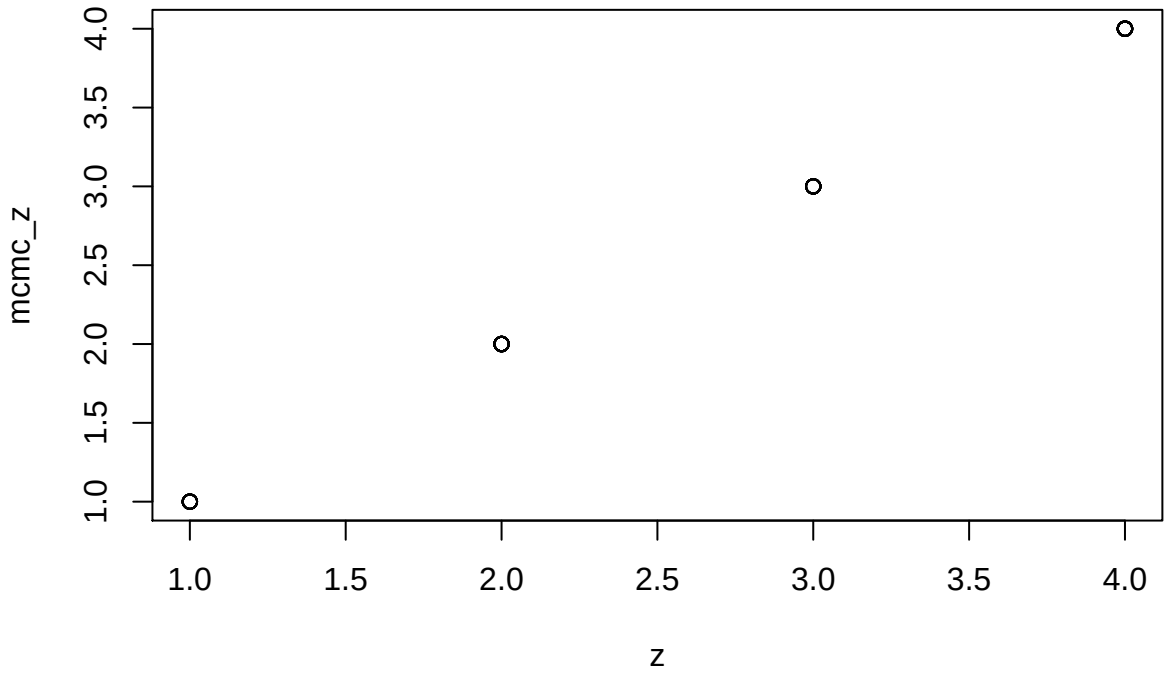
```
params <- c("z", "w", "U", "V", "ystar")
samps <- coda.samples(jags.m, params, n.iter=10000, thin=7)
jags_df <- ggs(samps)
##ggs_traceplot(jags_df, family="U")
s <- summary(samps)
#effectiveSize(samps)
#pdf(file.path(trace.dir, paste0(runName, "_trace.pdf")))
```

```
#plot(samps)
#dev.off()
```

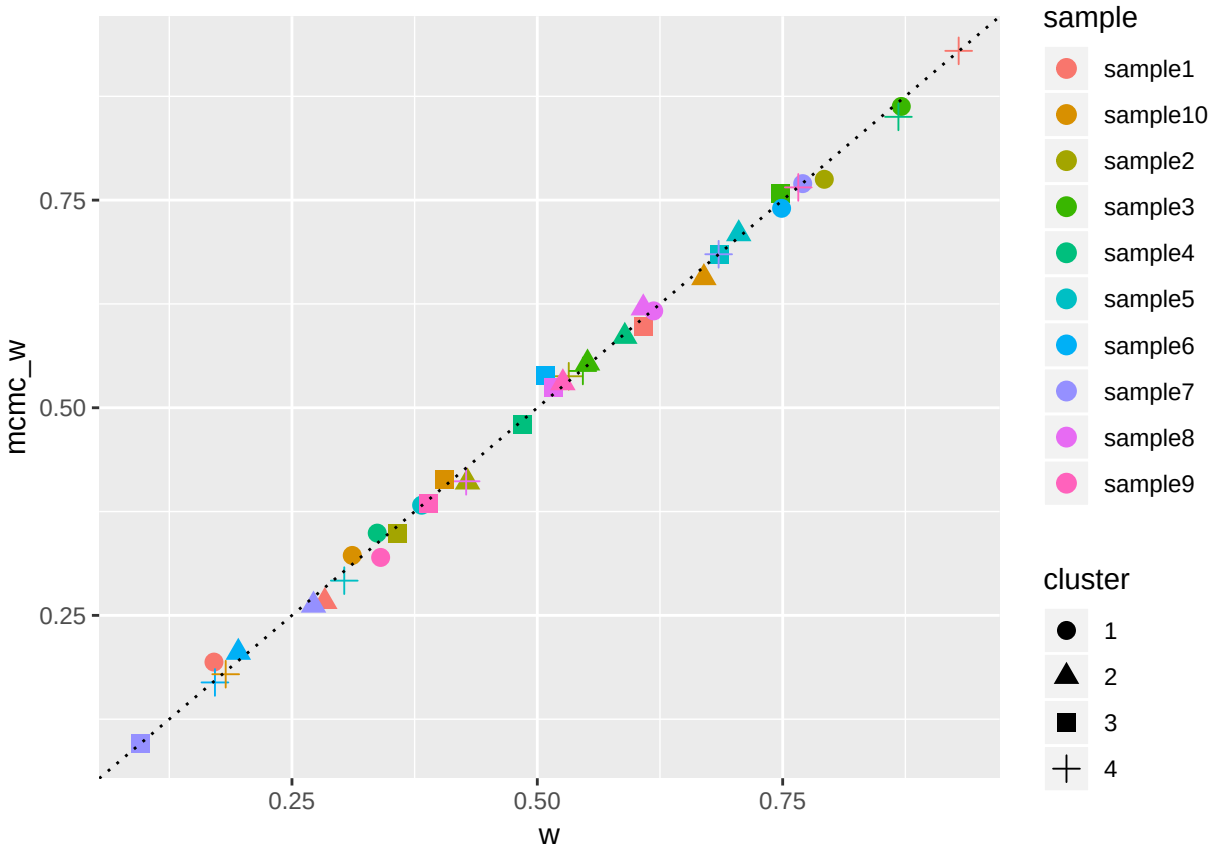
```
##
## 50 mutations x 10 samples
chains <- do.call(rbind, samps)
ystar <- chains[, grep("ystar", colnames(chains))]
## each row of MCMC is in column-major order
orig.order <- tibble(statistic=colnames(ystar))
ppd.summaries <- ystar %>%
    as_tibble() %>%
    gather("statistic", "value") %>%
    group_by(statistic) %>%
    summarize(mean=mean(value),
              q1=quantile(value, 0.025),
              q3=quantile(value, 0.975))
ppd.summaries2 <- left_join(orig.order,
                            ppd.summaries, by="statistic") %>%
    mutate(observed=as.numeric(test.data$y)) %>%
    mutate(sample=paste0("sample", rep(1:S, each=I)),
           variant=rep(1:I, S))
ggplot(ppd.summaries2, aes(x=statistic, y=mean,
                           ymin=q1,
                           ymax=q3)) +
    geom_errorbar() +
    geom_point(aes(x=statistic, y=observed),
               size=1, color="steelblue") +
    theme(axis.text.x=element_blank(),
          axis.ticks.x=element_blank(),
          panel.background=element_rect(fill="white",
                                        color="black")) +
    ylab("Middle 95% of posterior\npredictive distribution") +
    xlab("observation index (column-major order)") +
    facet_wrap(~sample)
```

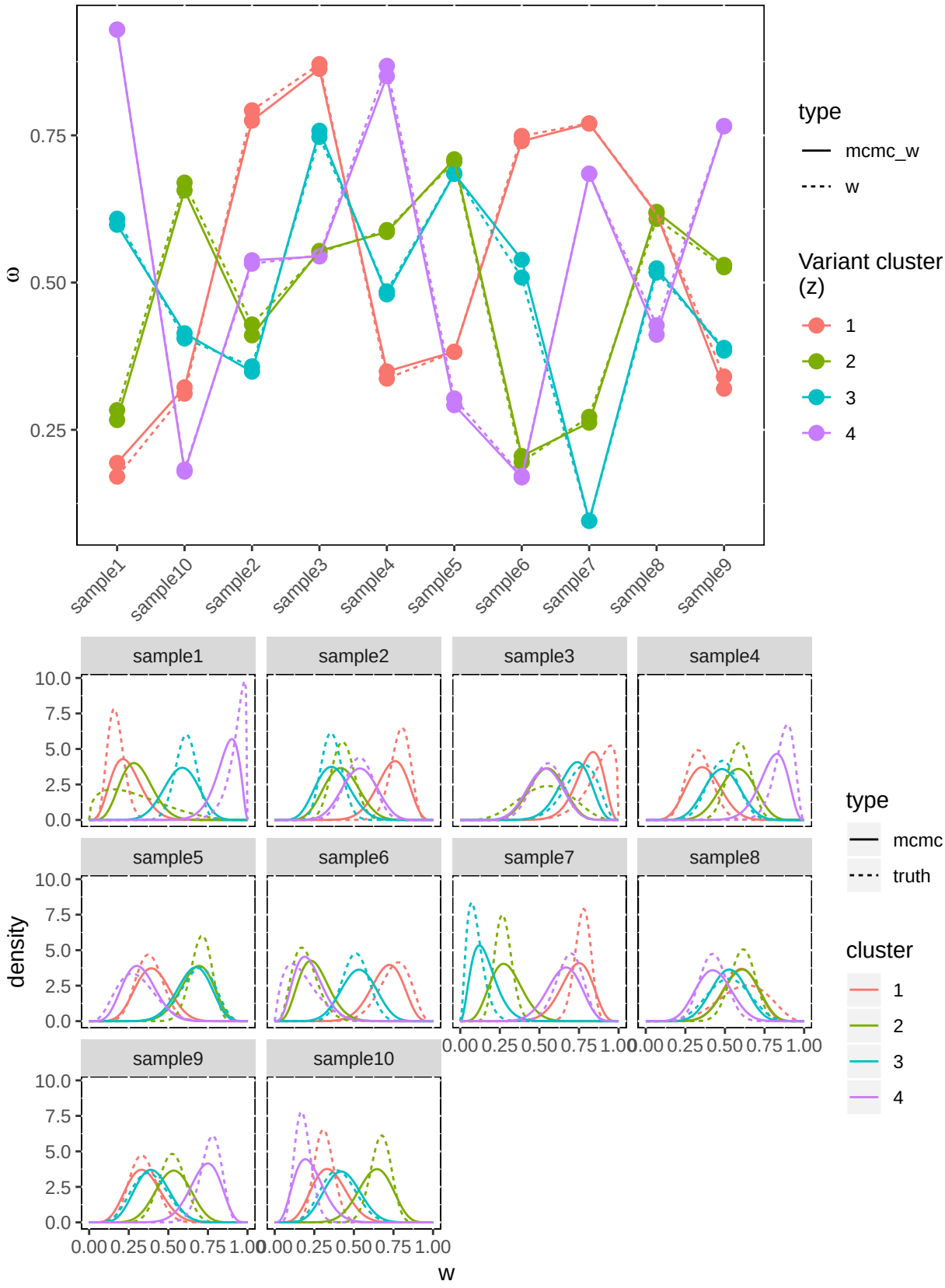

sample1
sample10
sample2
sample3
sample4
sample5
sample6
sample7
sample8
sample9
Middle 95% of posterior predictive distribution
observation index (column−major order)

Plots


mcmc_z
z

z	mcmc_z
1	1
2	2
3	3
4	4




ω
0.75
0.50
0.25
sample1
sample10
sample2
sample3
sample4
sample5
sample6
sample7
sample8
sample9
type
mcmc_w
w
Variant cluster (z)
1
2
3
4
sample1
sample2
sample3
sample4
sample5
sample6
sample7
sample8
sample9
sample10
density
10.0
7.5
5.0
2.5
0.0
0.00 0.25 0.50 0.75 1.00
w
type
mcmc
truth
cluster
1
2
3
4