

```
pvalue_scz <- SCZ[SCZ$snpid %in% snp_result,]$pval
BIP_jiaoji <- BIP[BIP$snpid %in% snp_result,]
SCZ_jiaoji <- SCZ[SCZ$snpid %in% snp_result,]
BIP_SCZ <- inner_join(BIP[,c('snpid', 'pval')], SCZ[,c('snpid', 'pval')], by="snpid")
```

```
# The parameter estimates are obtained using the EM algorithm
```

```
theta_est <- EM1(pvalue_bip, pvalue_scz, pi00_ini = 0.8, pi01_ini=0.01, pi10_ini=0.01, pi11_ini=0.1, alpha1,
theta_est
```

```
## $pi00
## [1] 0.8173783
##
## $pi01
## [1] 0.006304867
##
## $pi10
## [1] 0.001133071
##
## $pi11
## [1] 0.1751837
##
## $alpha1
## [1] 0.5985608
##
## $alpha2
## [1] 0.5039367
```

```
gamma_post <- theta_est$pi00+theta_est$pi01*theta_est$alpha2*pvalue_scz^(theta_est$alpha2-1)+theta_est$
```

```
z11_post <- theta_est$pi11*theta_est$alpha1*theta_est$alpha2*pvalue_bip^(theta_est$alpha1-1)*pvalue_scz
z01_post <- theta_est$pi01*theta_est$alpha2*pvalue_scz^(theta_est$alpha2-1)/gamma_post
z10_post <- theta_est$alpha1*pvalue_bip^(theta_est$alpha1-1)*theta_est$pi10/gamma_post
z00_post <- theta_est$pi00/gamma_post
z1_post <- z11_post+z10_post
z2_post <- z11_post+z01_post
```

```
# SNPS associated with both diseases
```

```
Z_est_11 <- assoc(z11_post, 0.1)
sum(Z_est_11)
```

```
## [1] 6956
```

```
# SNPS associated with BIP
```

```
Z_est_10 <- assoc(z1_post, 0.1)
sum(Z_est_10)
```

```
## [1] 7018
```

```
# SNPS associated with SCZ
```

```
Z_est_01 <- assoc(z2_post, 0.1)
sum(Z_est_01)
```

```
## [1] 8210
```

The coincidence of the ids of the three classes of SNPS was judged

```
snpid_bip <- BIP[BIP$snpid %in% snp_result,]$snpid
snp_bip = data.frame(snpid_bip = snpid_bip,bip_11 = Z_est_11,bip_10 = Z_est_10)
snpid_bip_11 <- snp_bip[which(snp_bip$bip_11 == 1),'snpid_bip']
snpid_bip_10 <- snp_bip[which(snp_bip$bip_10 == 1),'snpid_bip']
```

```
length(intersect(snpid_bip_11,snpid_bip_10))
```

```
## [1] 6956
```

The high degree of overlap between those associated with both diseases and those associated with BIP

```
setdiff(snpid_bip_10,snpid_bip_11)
```

```
## [1] "rs4908147" "rs387176" "rs263908" "rs10921107" "rs2270543"
## [6] "rs17017120" "rs3845684" "rs906867" "rs13386455" "rs1526645"
## [11] "rs7583278" "rs4430889" "rs1435845" "rs1161474" "rs6729882"
## [16] "rs7641289" "rs17718783" "rs9288851" "rs16825602" "rs810471"
## [21] "rs6829771" "rs2646269" "rs370831" "rs391529" "rs13128519"
## [26] "rs7733288" "rs256014" "rs9393672" "rs9275523" "rs7767277"
## [31] "rs2842625" "rs2138707" "rs1934124" "rs4357169" "rs9387090"
## [36] "rs13227417" "rs11761050" "rs6958911" "rs2196" "rs12342040"
## [41] "rs10760846" "rs7895653" "rs3858136" "rs10791838" "rs11174379"
## [46] "rs7300029" "rs11174386" "rs11109376" "rs1262775" "rs17107699"
## [51] "rs10518779" "rs16957422" "rs7190307" "rs12943984" "rs7209032"
## [56] "rs156430" "rs4277599" "rs2378249" "rs6030341" "rs11906231"
## [61] "rs2836779" "rs926761"
```

The only SNP associated with BIP but not with SCZ

```
snpid_scz <- SCZ[SCZ$snpid %in% snp_result,]$snpid
snp_scz = data.frame(snpid_scz = snpid_scz,scz_11 = Z_est_11,scz_10 = Z_est_01)
snpid_scz_11 <- snp_scz[which(snp_scz$scz_11 == 1),'snpid_scz']
snpid_scz_01 <- snp_scz[which(snp_scz$scz_10 == 1),'snpid_scz']
```

```
length(intersect(snpid_scz_11,snpid_scz_01))
```

```
## [1] 6956
```

Only the bipolar GWAS data was used for analysis

```
## Define the function that calculates the log-likelihood
# input: p, pi1, alpha
log_P_single <- function(P, pi1, alpha){
  return(sum(log(pi1*dbeta(P, alpha, 1) + (1 - pi1))))#
```

```

}
## Define functions that implement the EM algorithm for the analysis of a single dataset
# input: P, pi1_ini, alpha_ini, max_iter, tol
# output: pi1_est, alpha_est
EM_single <- function(P, pi1_ini, alpha_ini, max_iter = 1e4, tol = 1e-6){
  L_ini <- log_P_single(P, pi1_ini, alpha_ini)
  for (iter in 1:max_iter){
    if (iter == 1){
      pi1_old <- pi1_ini
      alpha_old <- alpha_ini
      L_old <- L_ini
    }

    # E step
    comp_gamma <- pi1_old*dbeta(P, alpha_old, 1)
    gamma <- comp_gamma/(comp_gamma + 1 - pi1_old)

    # M step
    pi1_new <- mean(gamma)
    alpha_new <- -sum(gamma)/sum(gamma*log(P))
    L_new <- log_P_single(P, pi1_new, alpha_new)
    # whether the algorithm converges
    if (L_new < L_old){
      print("Error: log likelihood is not increasing!")
      break
    }
    if ((L_new - L_old)/abs(L_new) < tol){
      break
    } else {
      pi1_old <- pi1_new
      alpha_old <- alpha_new
      L_old <- L_new
    }
  }

  return(list(pi1 = pi1_new, alpha = alpha_new))
}

```

```

theta_est_BIP <- EM_single(pvalue_bip, pi1_ini = 0.1, alpha_ini = 0.2)
theta_est_BIP

```

```

## $pi1
## [1] 0.2194204
##
## $alpha
## [1] 0.6628928

```

```

posterior_bip <- (theta_est_BIP$pi1*theta_est_BIP$alpha*pvalue_bip^(theta_est_BIP$alpha - 1))/(theta_est_BIP$alpha*
Z_est_bip <- assoc(posterior_bip, 0.1)
sum(Z_est_bip)

```

```

## [1] 403

```

```
snp_bip_single = data.frame(snpid_bip = snpid_bip, bip_1 = Z_est_bip)
snpid_bip_1 <- snp_bip_single[which(snp_bip_single$bip_1 == 1), 'snpid_bip']
```

```
length(intersect(snpid_bip_1, snpid_bip_10))
```

```
## [1] 387
```

Only the schizophrenia GWAS data was used for analysis

```
theta_est_SCZ <- EM_single(pvalue_scz, pi1_ini = 0.1, alpha_ini = 0.2)
theta_est_SCZ
```

```
## $pi1
## [1] 0.2419776
##
## $alpha
## [1] 0.5668053
```

```
posterior_scz <- (theta_est_SCZ$pi1*theta_est_SCZ$alpha*pvalue_scz^(theta_est_SCZ$alpha - 1))/(theta_est_SCZ$pi1 + theta_est_SCZ$alpha*pvalue_scz^(theta_est_SCZ$alpha - 1))
Z_est_scz <- assoc(posterior_scz, 0.1)
sum(Z_est_scz)
```

```
## [1] 4012
```

```
snp_scz_single = data.frame(snpid_scz = snpid_scz, scz_1 = Z_est_scz)
snpid_scz_1 <- snp_scz_single[which(snp_scz_single$scz_1 == 1), 'snpid_scz']
```

```
length(intersect(snpid_scz_1, snpid_scz_01))
```

```
## [1] 3692
```

Plot the Manhattan

```
FDR <- function(posterior, alpha){
  M      <- length(posterior)
  fdr     <- 1 - posterior
  rank.fdr <- rank(fdr)
  sort.fdr <- sort(fdr)
  cumsum.fdr <- cumsum(sort.fdr)
  sort.FDR <- cumsum.fdr/seq(1, M, 1)
  FDR     <- sort.FDR[rank.fdr]

  return(FDR)
}
```

BIP