Project 3

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Problem 8: Profile HMMs: Estimating match emission probabilities

What are the estimated match emission probabilities of the profile HMM in Figure 1?

The model

```
## The Example Data

bat <- c("A","G","-","-","-","C")
rat <- c("A","-","A","G","-","C")
cat <- c("A","G","-","-","-","C")
gnat <- c("-","G","A","A","A","C")
goat <- c("A","G","-","-","A","C")
M <- rbind(bat,rat,cat,gnat,goat)

# Alphabet
A=c("A","C","G","T")
```

Find out which positions are in Match state and which are in Insert state

```
# Get the positions which are Insertstate and Match state
match = which(colSums(M!="-")>(dim(M)[1]/2)) #Vector with Match positions
insertion = c(1:dim(M)[2])[!c(1:dim(M)[2]) %in% match] #Vector with insert positions
```

```
#Matrix of all pos???????????????
E=matrix(,0,dim(M)[2])
for (n in A){
  e<-apply(M==n,2,sum)
  E <- rbind(E,e)
}
rownames(E)=A
```

Calculate the Emission probabilities of a match

```
# Emission probabilities of match
E_match_prob=t(t(E[,match]+1)/colSums(E[,match]+1))
E_match_prob
```

```
##    [,1]  [,2]      [,3]
## A 0.625 0.125 0.1111111
## C 0.125 0.125 0.6666667
## G 0.125 0.625 0.1111111
## T 0.125 0.125 0.1111111
```

Problem 9: Estimating insert emission probabilities

What are the estimated insert emission probabilities of the profile HMM in Figure 1?

```
consecutive_in=split(insertion, cumsum(c(1, diff(insertion) != 1)))
E_cons=matrix(,length(A),0)
for (insert in consecutive_in){
  s = rowSums(E[,insert])
  E_cons = cbind(E_cons,s)
}
rownames(E_cons)=A

# Emission probabilities of insertion
E_insertion_prob=t(t(E_cons+1)/colSums(E_cons+1))
E_insertion_prob
```

```
##     s
## A 0.6
## C 0.1
## G 0.2
## T 0.1
```

Problem 10: Estimating transition probabilities

What are the estimated transmission probabilities in the profile HMM in Figure 1?

```
#Transition probabilities
counts.only=FALSE

#Get state Matrix
SM=matrix(FALSE,dim(M)[1],dim(M)[2])
SM[,match][M[,match]!='-']='M'
SM[,match][M[,match]=='-']='D'
SM[,insertion][M[,insertion]!='-']='I'

#Initate Transition Matrix
transitions <- c("MM","MD","MI","IM","ID","II","DM","DD","DI")
Tr=matrix(0,length(transitions),dim(M)[2]+1)
rownames(Tr)=transitions


#Create the Transition counts for every possible szenario
for (i in 1:dim(SM)[1]){
  prev <- 'M'
  prevStateNum <- 0
  for(j in 1:(dim(SM)[2])) {
    newState<- SM[i,j]
    if (newState==FALSE){
      prevStateNum <- j
      next
    }
    transition <- paste(prev, newState, sep="")
    Tr[transition, prevStateNum +1] <- Tr[transition, prevStateNum +1] +1
    prevStateNum <- j
    prev <- newState
  }
```

```
  transition<- paste(prev, 'M', sep="")
  Tr[transition, prevStateNum +1] <- Tr[transition, prevStateNum +1] +1
}

#Add the Insertion state columns to the corresponding match state
for (insert in rev(consecutive_in)){
  s = rowSums(Tr[,c(insert[1]-1,insert)])
  Tr[,insert[1]-1]=s
  Tr=Tr[,-insert] #Delete the insertion columns
}


#Add pseudo-count and Get the Transition probabilities
if (!counts.only) {
    Tr <- Tr+1
    for(i in 1:ncol(Tr)) {
      Tr[1:3,i] <- Tr[1:3,i] / sum(Tr[1:3,i])
      Tr[4:6,i] <- Tr[4:6,i] / sum(Tr[4:6,i])
      Tr[7:9,i] <- Tr[7:9,i] / sum(Tr[7:9,i])
    }
}

colnames(Tr)=c(0:(ncol(Tr)-1))
Tr
```

```
##            0         1         2         3
## MM 0.6250000 0.4444444 0.6000000 0.7500000
## MD 0.2500000 0.2222222 0.2000000 0.1250000
## MI 0.1250000 0.3333333 0.2000000 0.1250000
## IM 0.3333333 0.1666667 0.6666667 0.3333333
## ID 0.3333333 0.1666667 0.1666667 0.3333333
## II 0.3333333 0.6666667 0.1666667 0.3333333
## DM 0.3333333 0.4000000 0.3333333 0.3333333
## DD 0.3333333 0.2000000 0.3333333 0.3333333
## DI 0.3333333 0.4000000 0.3333333 0.3333333
```

Problem 11: Protein family membership classification

(1) Import functions

```
#Get Functions
source("./code/profileHMM.R")
```

(2) Read the two alignments

```
#Read in Data
GTP_binding_proteins = parseAlignment("./data/GTP_binding_proteins.txt")
ATPases = parseAlignment("./data/ATPases.txt")
```

(3) Parametrise two profile HMMs

Parametrise two profile HMMs for each protein family

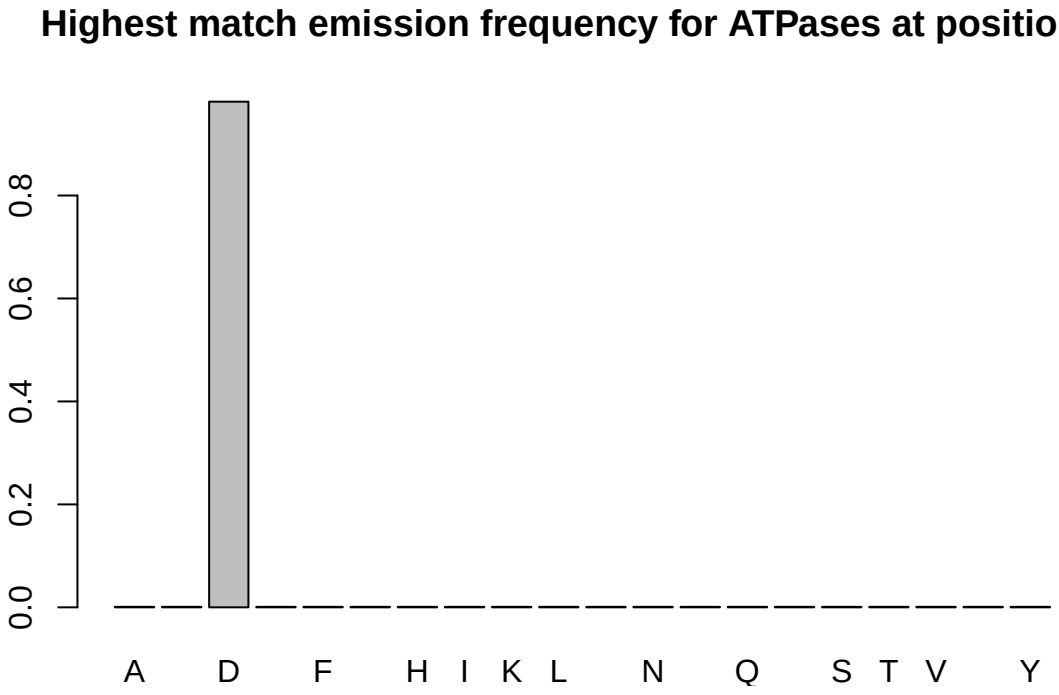
```
#Get the profile HMMS
profileHMM_GTP = learnHMM(GTP_binding_proteins)
profileHMM_ATPases = learnHMM(ATPases)
```

(4) Highest match and highest insert emission frequencies for ATPases

```
# Highest match emission frequencies
match_frequency_positions_ATPases = which(profileHMM_ATPases$mE == max(profileHMM_ATPases$mE,
    na.rm = TRUE), arr.ind = TRUE)[2]
print(match_frequency_positions_ATPases)
```

```
## [1] 8
```

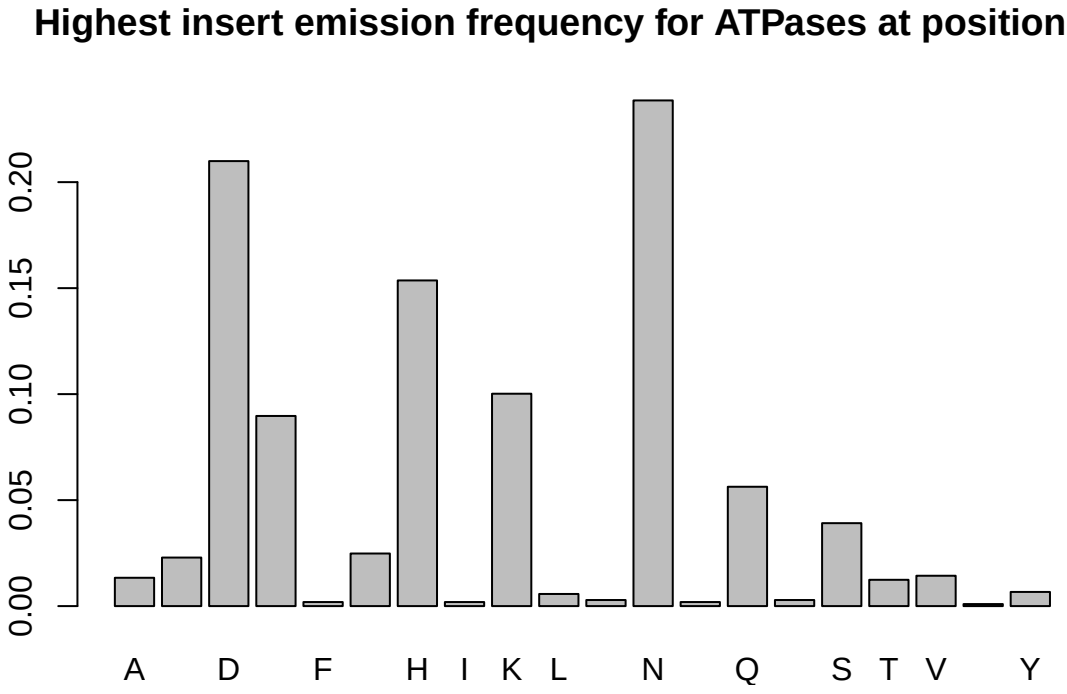
```
barplot(profileHMM_ATPases$mE[, match_frequency_positions_ATPases], names.arg = rownames(profileHMM_ATPa
    main = paste0("Highest match emission frequency for ATPases at position: ", match_frequency_positio
```




```
# Highest insert emission frequencies
insert_frequency_positions_ATPases = which(profileHMM_ATPases$iE == max(profileHMM_ATPases$iE,
    na.rm = TRUE), arr.ind = TRUE)[2]
print(insert_frequency_positions_ATPases)
```

```
## [1] 71
```

```
barplot(profileHMM_ATPases$mE[, insert_frequency_positions_ATPases], names.arg = rownames(profileHMM_ATP
    main = paste0("Highest insert emission frequency for ATPases at position: ",
        insert_frequency_positions_ATPases))
```

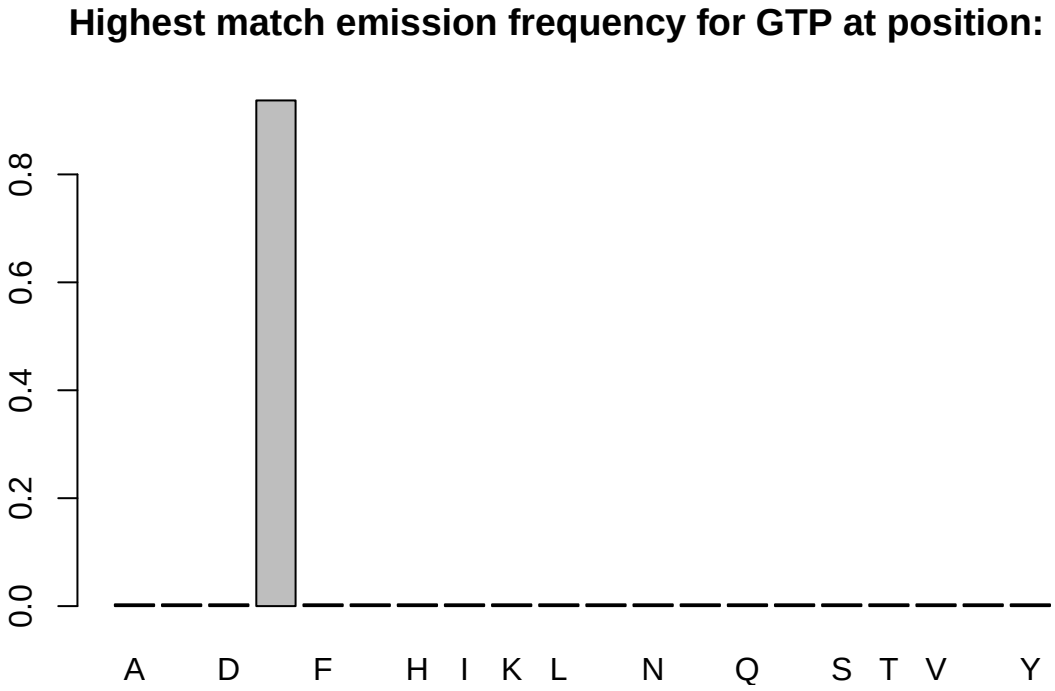


(4) Highest match and highest insert emission frequencies for GTP

```
# Highest match emission frequencies
match_frequency_positions_GTP = which(profileHMM_GTP$mE == max(profileHMM_GTP$mE,
    na.rm = TRUE), arr.ind = TRUE)[2]
print(match_frequency_positions_GTP)
```

```
## [1] 77
```

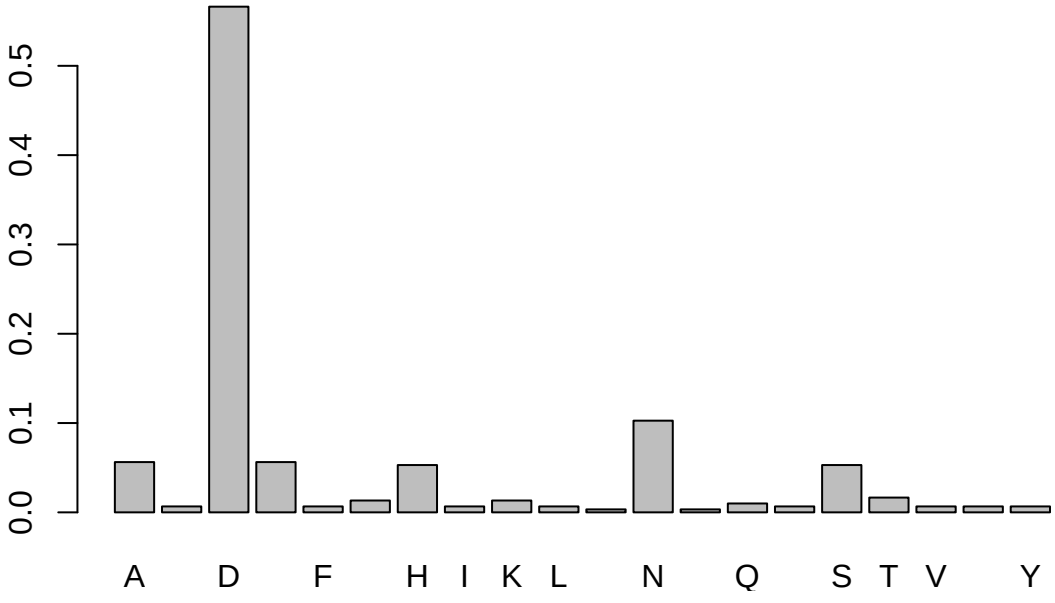
```
barplot(profileHMM_GTP$mE[, match_frequency_positions_GTP], names.arg = rownames(profileHMM_GTP),
    main = paste0("Highest match emission frequency for GTP at position: ", match_frequency_positions_G
```




```
# Highest insert emission frequencies
insert_frequency_positions_GTP = which(profileHMM_GTP$iE == max(profileHMM_GTP$iE,
    na.rm = TRUE), arr.ind = TRUE)[2]
print(insert_frequency_positions_GTP)
```

```
## [1] 50
```

```
barplot(profileHMM_GTP$mE[, insert_frequency_positions_GTP], names.arg = rownames(profileHMM_GTP),
    main = paste0("Highest insert emission frequency for GTP at position: ", insert_frequency_positions
```



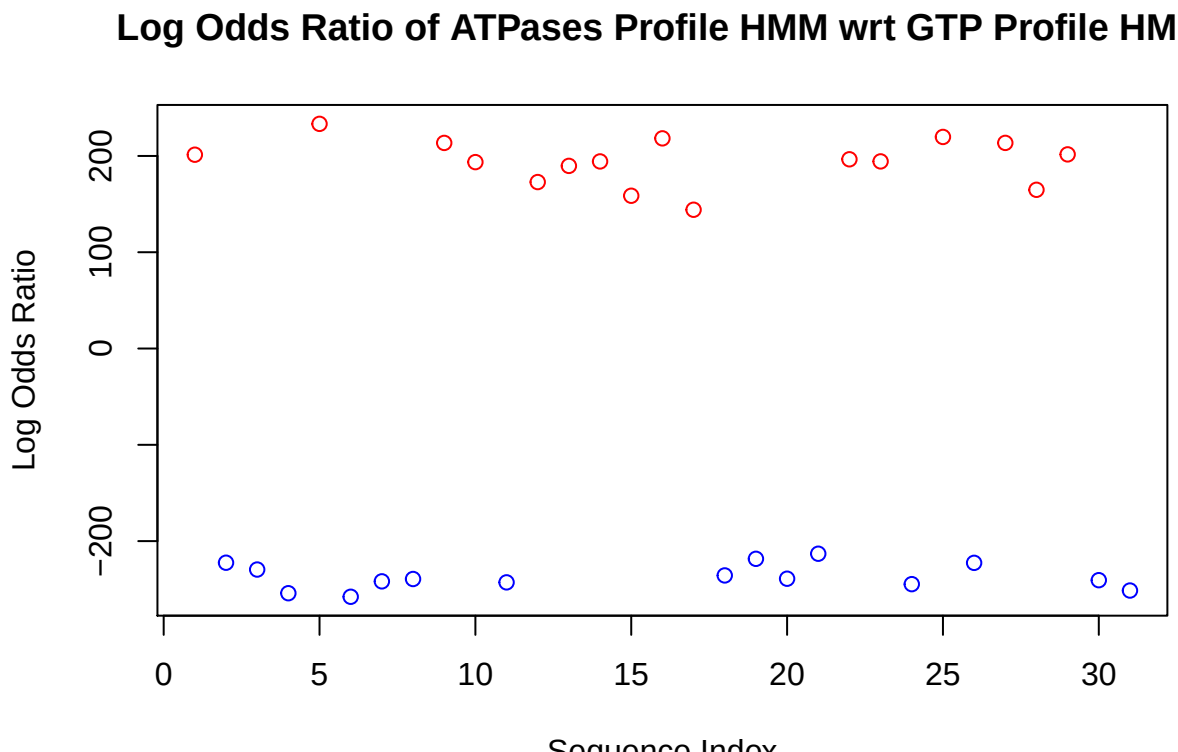
(5) Load the protein sequences into a list

```
#Load the protein sequence
unclassifiedProteins <- parseProteins(proteinsFile =
                                        "./data/Unclassified_proteins.txt" )
```

(6) Obtain the log odds ratio and plot the results

```
P_ATPases <- lapply(X = unclassifiedProteins, forward, HMM = profileHMM_ATPases)
P_GTP <- lapply(X = unclassifiedProteins, forward, HMM = profileHMM_GTP)

# Log-Odds Ratio of ATPases Profile HMM wrt GTP Profile HMM
q <- unlist(P_ATPases) - unlist(P_GTP)
plot(q, col = ifelse(q >= 0, "red", "blue"), main = "Log Odds Ratio of ATPases Profile HMM wrt GTP Profi
    ylab = "Log Odds Ratio", xlab = "Sequence Index")
```




```
unclassifiedATPases = as.numeric(which(q >= 0, arr.ind = TRUE))
no_unclassifiedATPases = length(unclassifiedATPases)
print(paste0("The number of predicted ATPases is ", no_unclassifiedATPases))
```

```
## [1] "The number of predicted ATPases is 16"
```

```
print("The unclassified proteins that are ATPases have indices")
```

```
## [1] "The unclassified proteins that are ATPases have indices"
```

```
print(unclassifiedATPases)
```

```
##  [1]  1  5  9 10 12 13 14 15 16 17 22 23 25 27 28 29
```

```r
unclassifiedGTP = as.numeric(which(q < 0, arr.ind = TRUE))
no_unclassifiedGTP = length(unclassifiedGTP)
print(paste0("The number of predicted GTPs is ", no_unclassifiedGTP))
```

```
## [1] "The number of predicted GTPs is 15"
```

```r
print("The unclassified proteins that are GTPs have indices")
```

```
## [1] "The unclassified proteins that are GTPs have indices"
```

```r
print(unclassifiedGTP)
```

```
##  [1]  2  3  4  6  7  8 11 18 19 20 21 24 26 30 31
```

```r
# #TO DO
# library(ggplot2)
#
# logsodd<-vector()
#
# #loop through all the sequences in protdd
# for(i in 1:length(Protdd)){
#   loGTP<-forward(GTPHMM,unlist(Protdd[i]))
#   loATP<-forward(ATPHMM,unlist(Protdd[i]))
#   logsodd <- c(logsodd,loGTP[[1]]-loATP[[1]])
#
# }
# logsodd
#
#
# a <- barplot(logsodd,
#              col= ifelse(logsodd < 0,"red","blue"),
#              xaxt = "n", yaxt = "n"
# )
#
#
# y<-vector(1:length(logsodd))
#
# ggplot(logsodd) +geom_histogram()
```