Class 6 function homework

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Write a function from the supplied code

```
# Can you improve this analysis code?
library(bio3d)
s1 <- read.pdb("4AKE") # kinase with drug
```

```
  Note: Accessing on-line PDB file
```

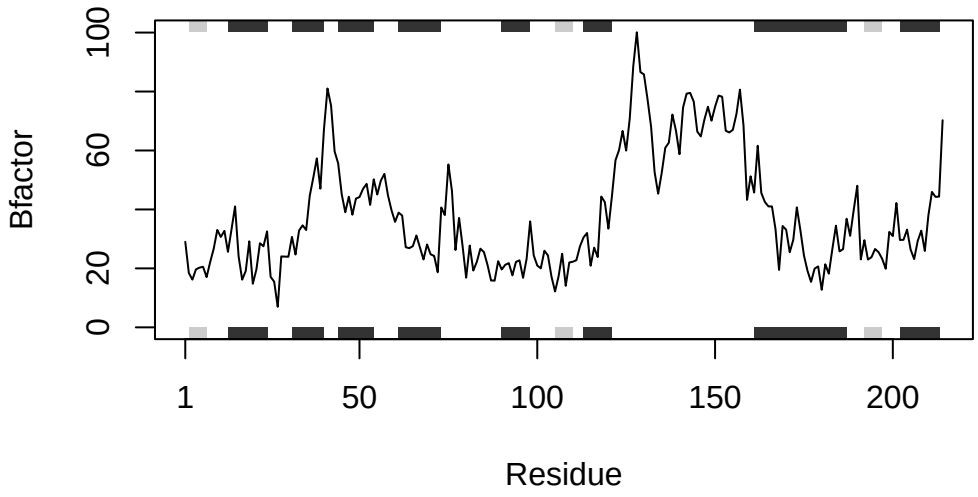
```
s2 <- read.pdb("1AKE") # kinase no drug
```

```
  Note: Accessing on-line PDB file
   PDB has ALT records, taking A only, rm.alt=TRUE
```

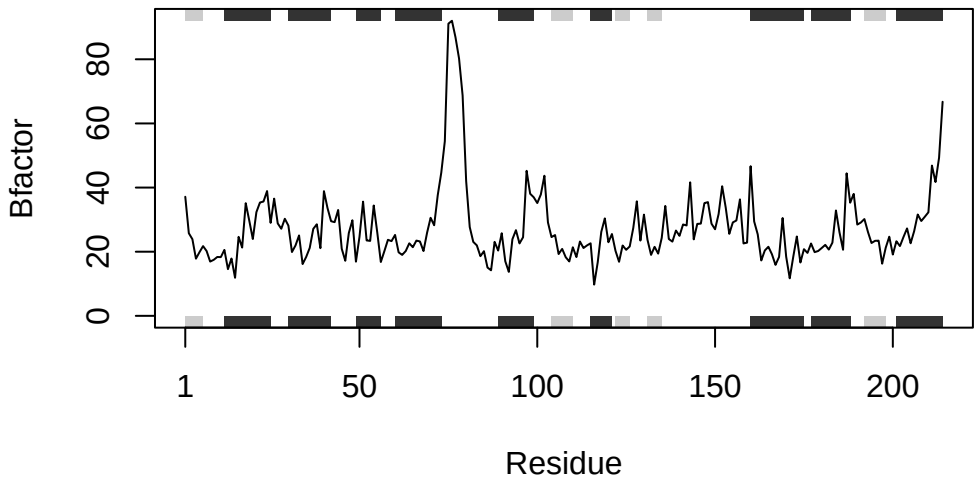
```
s3 <- read.pdb("1E4Y") # kinase with drug
```

```
  Note: Accessing on-line PDB file
```

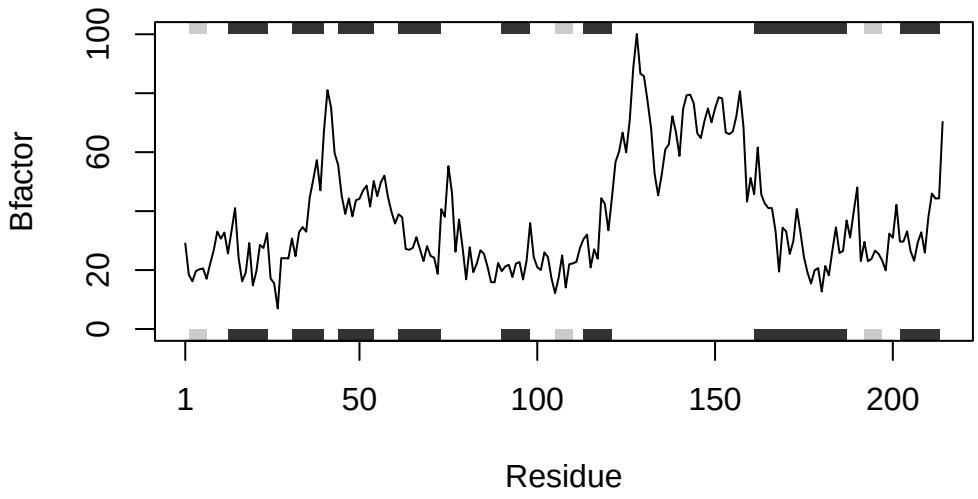
```
s1.chainA <- trim.pdb(s1, chain="A", elety="CA")
s2.chainA <- trim.pdb(s2, chain="A", elety="CA")
s3.chainA <- trim.pdb(s1, chain="A", elety="CA")

s1.b <- s1.chainA$atom$b
s2.b <- s2.chainA$atom$b
s3.b <- s3.chainA$atom$b

plotb3(s1.b, sse=s1.chainA, typ="l", ylab="Bfactor")
```




```
plotb3(s2.b, sse=s2.chainA, typ="l", ylab="Bfactor")
```



```
plotb3(s3.b, sse=s3.chainA, typ="l", ylab="Bfactor")
```



Q1. What type of object is returned from the read.pdb() function?

A `read.pdb()` returns a Protein Data Bank (PDB) coordinate file, which is a list containing data that contains atom coordinates, B-factors, residue info, sequence, etc. This object is used through the bio3d package for structural bioinformatics analyses.

```
s1
```

```
 Call:  read.pdb(file = "4AKE")

   Total Models#: 1
     Total Atoms#: 3459,  XYZs#: 10377  Chains#: 2  (values: A B)

     Protein Atoms#: 3312  (residues/Calpha atoms#: 428)
     Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)

     Non-protein/nucleic Atoms#: 147  (residues: 147)
     Non-protein/nucleic resid values: [ HOH (147) ]
```

```
   Protein sequence:
      MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
      DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDRI
      VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILGMRIILLGAPGA...<cut>...KILG

+ attr: atom, xyz, seqres, helix, sheet,
        calpha, remark, call
```

Q2. What does the trim.pdb() function do?

A `trim.pdb()` pulls out a subset of atoms from a pdb object based on a specified criteria. In this case, it is used to extract only the alpha carbon atoms (CA) from chain A.

Q3. What input parameter would turn off the marginal black and grey rectangles in the plots and what do they represent in this case?

You would turn off the sse function as `sse = NULL`. In this case, it represents the secondary structure annotations such as helices and beta pleated sheets.

```
# plotb3(s1.b, sse = NULL, type = "l", ylab = "Bfactor")
```

Q4. What would be a better plot to compare across the different proteins?

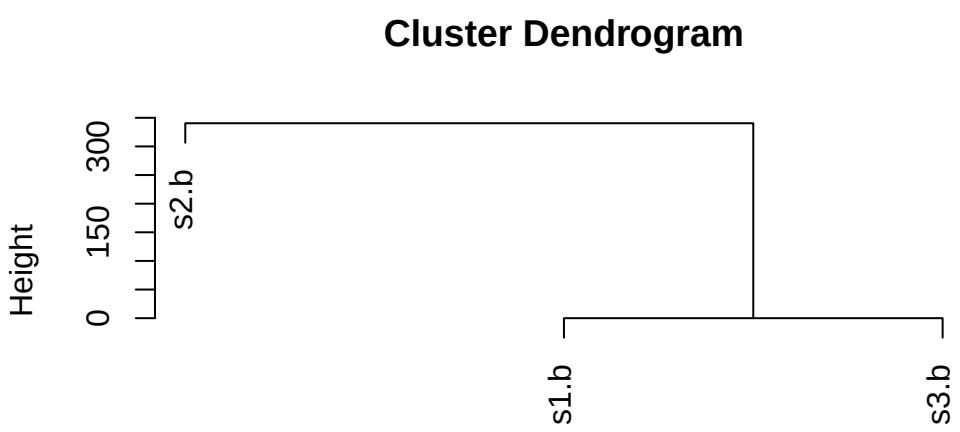
Instead of viewing plots individually side by side, we can overlay them on a single graph plot using varying colors.

Q5. Which proteins are more similar to each other in their B-factor trends. How could you quantify this? HINT: try the rbind(), dist() and hclust() functions together with a resulting dendrogram plot. Look up the documentation to see what each of these functions does.

We can utilize hierarchical clustering or `hclust()` to group the proteins based on similarity between B factor.

Based on the `hplot()` below, s1 and s3 are more similar in regards to their B factor. This makes sense because they are both kinase with drugs.

```
hc <- hclust(dist(rbind(s1.b, s2.b, s3.b)))
plot(hc)
```



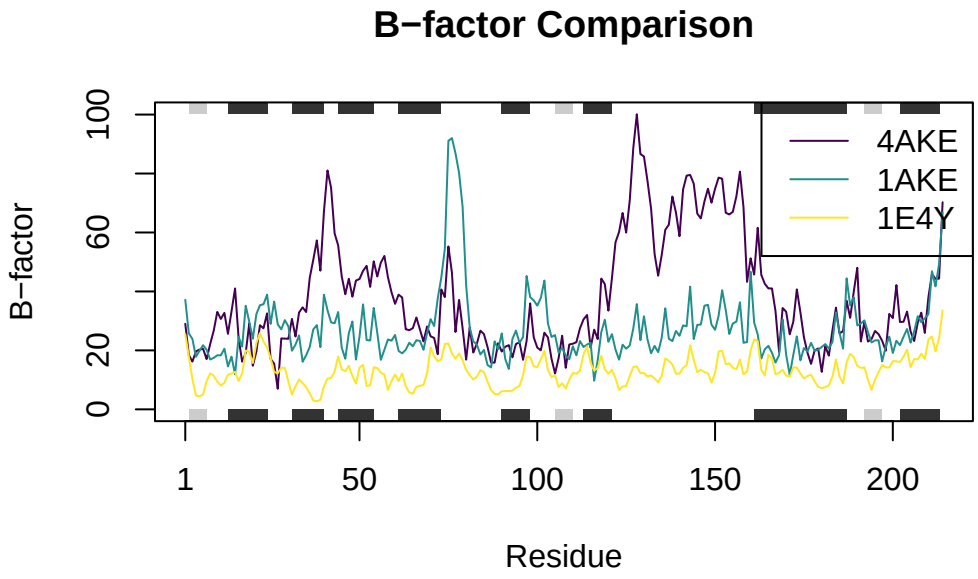
Q6. How would you generalize the original code above to work with any set of input protein structures?

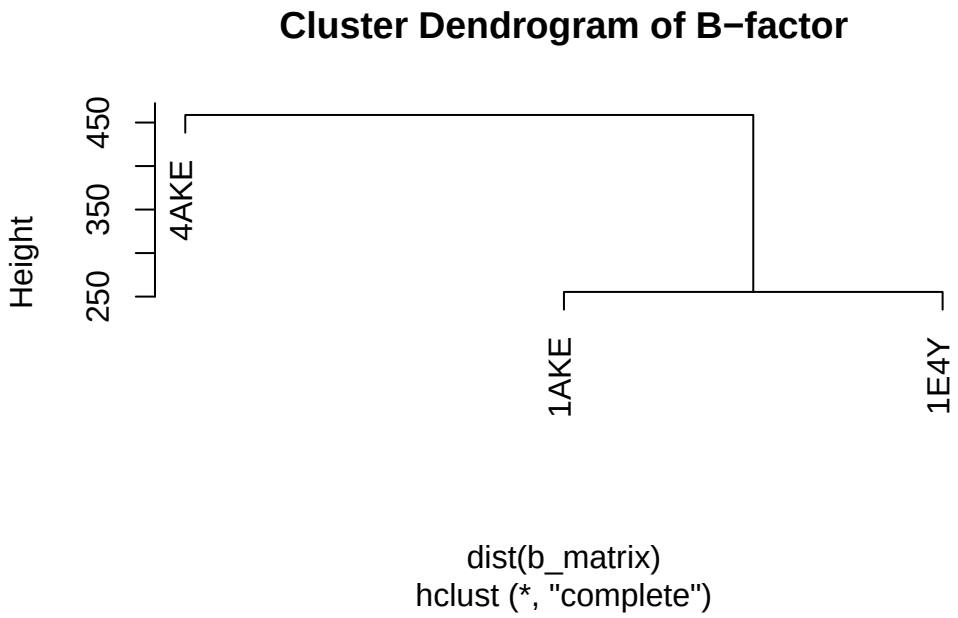
```
# Function: to analyze_bfactors
# Purpose: Download multiple PDB structures, extract B-factors for
#          alpha carbons (CA) in a specific chain, and output:
#          1) a line plot comparing B-factors
#          2) a dendrogram showing similarity across proteins
# Inputs:
#   - pdb_ids: c("4AKE", "1AKE", "1E4Y"))
#   - chain_id: chain to analyze (default = "A")
#   - elety: atom type (default = "CA")
#   - show_secondary_structure: if TRUE, include secondary structure plot
#   - compare: if TRUE, perform clustering and show dendrogram
# Output:
#   - Two plots: B-factor comparison and dendrogram (if compare = TRUE)


analyze_bfactors <- function(pdb_ids,
                             chain_id = "A",
                             elety = "CA",
                             show_secondary_structure = TRUE,
                             compare = TRUE) {
```

```r
# Load required libraries
library(bio3d)
library(viridis)

# Initialize lists for trimmed PDBs and B-factors
n <- length(pdb_ids)
bfactors <- list()
trimmed <- list()

# Loop through each PDB ID
for (i in seq_along(pdb_ids)) {
  pdb <- read.pdb(pdb_ids[i])
  trimmed[[i]] <- trim.pdb(pdb, chain = chain_id, elety = elety)
  bfactors[[i]] <- trimmed[[i]]$atom$b
}

# Use viridis color-blind friendly palette
colors <- viridis(n)

# Plot B-factors with or without secondary structure
if (show_secondary_structure) {
  plotb3(bfactors[[1]], sse = trimmed[[1]], typ = "l",
         ylab = "B-factor", col = colors[1], main = "B-factor Comparison")
  if (n > 1) {
    for (i in 2:n) {
      lines(bfactors[[i]], col = colors[i])
    }
  }
  legend("topright", legend = pdb_ids, col = colors, lty = 1)
} else {
  plot(bfactors[[1]], type = "l", col = colors[1],
       ylab = "B-factor", xlab = "Residue Index", main = "B-factor Comparison")
  if (n > 1) {
    for (i in 2:n) {
      lines(bfactors[[i]], col = colors[i])
    }
  }
  legend("topright", legend = pdb_ids, col = colors, lty = 1)
}

# Cluster B-factors
if (compare) {
```

```
    # Make sure all B-factor vectors are the same length
    min_len <- min(sapply(bfactors, length))
    b_matrix <- do.call(rbind, lapply(bfactors, function(x) x[1:min_len]))
    rownames(b_matrix) <- pdb_ids
    hc <- hclust(dist(b_matrix), method = "complete")
    plot(hc, main = "Cluster Dendrogram of B-factor")
  }
}

# Call for an output:
analyze_bfactors(c("4AKE", "1AKE", "1E4Y"))
```

```
Loading required package: viridisLite

  Note: Accessing on-line PDB file

Warning in get.pdb(file, path = tempdir(), verbose = FALSE):
/var/folders/0z/ldwmbf9n6033ylqhkpyb8h080000gn/T//RtmpsepaOD/4AKE.pdb exists.
Skipping download

  Note: Accessing on-line PDB file

Warning in get.pdb(file, path = tempdir(), verbose = FALSE):
/var/folders/0z/ldwmbf9n6033ylqhkpyb8h080000gn/T//RtmpsepaOD/1AKE.pdb exists.
Skipping download

   PDB has ALT records, taking A only, rm.alt=TRUE
  Note: Accessing on-line PDB file

Warning in get.pdb(file, path = tempdir(), verbose = FALSE):
/var/folders/0z/ldwmbf9n6033ylqhkpyb8h080000gn/T//RtmpsepaOD/1E4Y.pdb exists.
Skipping download
```


B−factor Comparison
B−factor
0
20
60
100
1
50
100
150
200
Residue
4AKE
1AKE
1E4Y


Cluster Dendrogram of B−factor
Height
250
350
450
4AKE
1AKE
1E4Y
dist(b_matrix)
hclust (*, "complete")