HW Class 6 (R Functions)

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original for A (can you improve this analysis code?)

```
df <- data.frame(a=1:10, b=seq(200,400,length=10),c=11:20,d=NA)
df$a <- (df$a - min(df$a)) / (max(df$a) - min(df$a))
df$b <- (df$b - min(df$a)) / (max(df$b) - min(df$b))
df$c <- (df$c - min(df$c)) / (max(df$c) - min(df$c))
df$d <- (df$d - min(df$d)) / (max(df$a) - min(df$d))
```

improved version of A)

```
df <- data.frame(
  a = 1:10,
  b = seq(200, 400, length.out = 10),
  c = 11:20,
  d = NA_real_
)

minmax01 <- function(x) {
```

```
  if (all(is.na(x))) return(x)              # keep all-NA columns as NA
  rng <- range(x, na.rm = TRUE)
  if (diff(rng) == 0) return(rep(0, length(x)))  # constant column -> all 0
  (x - rng[1]) / (rng[2] - rng[1])
}

cols <- c("a", "b", "c", "d")
df[cols] <- lapply(df[cols], minmax01)
df
```

```
           a         b         c  d
1  0.0000000 0.0000000 0.0000000 NA
2  0.1111111 0.1111111 0.1111111 NA
3  0.2222222 0.2222222 0.2222222 NA
4  0.3333333 0.3333333 0.3333333 NA
5  0.4444444 0.4444444 0.4444444 NA
6  0.5555556 0.5555556 0.5555556 NA
7  0.6666667 0.6666667 0.6666667 NA
8  0.7777778 0.7777778 0.7777778 NA
9  0.8888889 0.8888889 0.8888889 NA
10 1.0000000 1.0000000 1.0000000 NA
```

original for B (can you improve this analysis code?)

```
# Can you improve this analysis code?
library(bio3d)
```

```
Warning: package 'bio3d' was built under R version 4.4.3
```

```
s1 <- read.pdb("4AKE") # kinase with drug
```

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

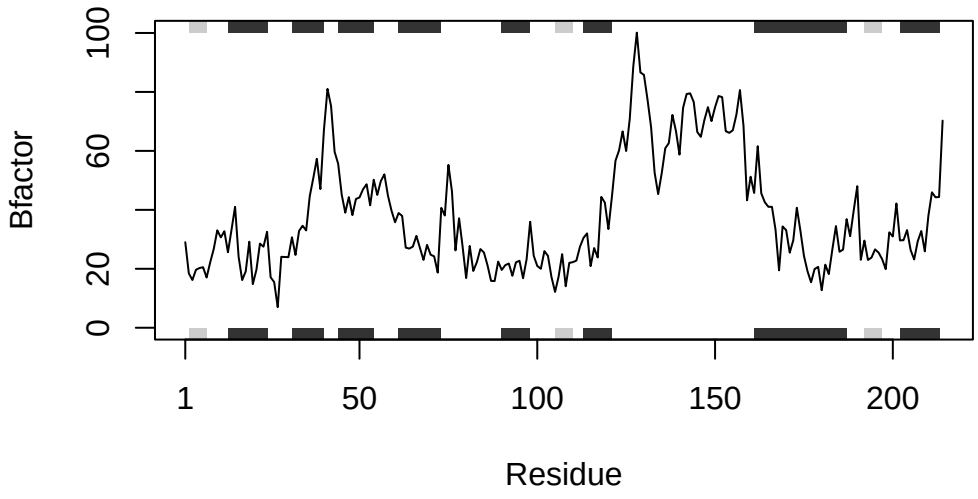
```
s2 <- read.pdb("1AKE") # kinase no drug
```

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

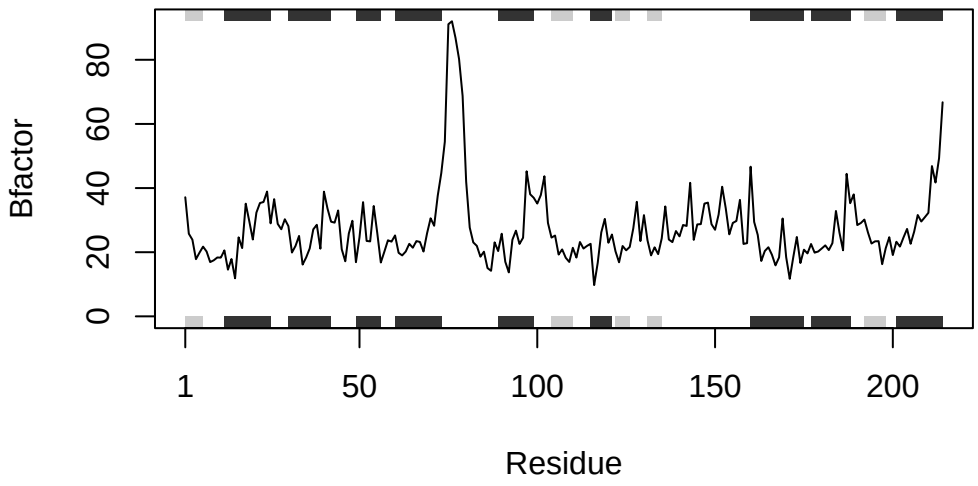
```
s3 <- read.pdb("1E4Y") # kinase with drug
```

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

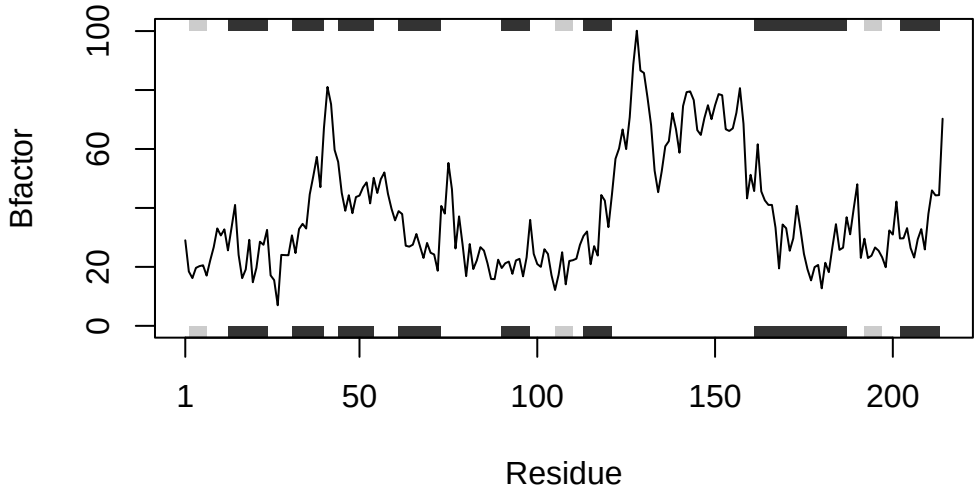
```
s1.chainA <- trim.pdb(s1, chain="A", elety="CA")
s2.chainA <- trim.pdb(s2, chain="A", elety="CA")
s3.chainA <- trim.pdb(s1, chain="A", elety="CA")
s1.b <- s1.chainA$atom$b
s2.b <- s2.chainA$atom$b
s3.b <- s3.chainA$atom$b
plotb3(s1.b, sse=s1.chainA, typ="l", ylab="Bfactor")
```




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




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

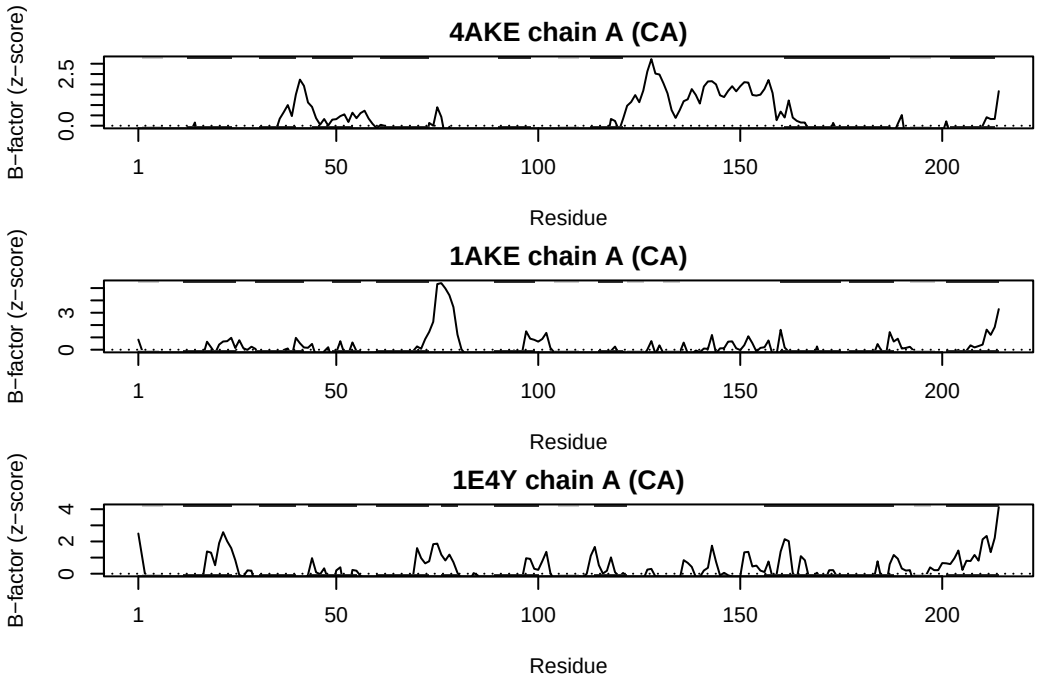


improved version of B)

```
library(bio3d)

# ---- helpers ----
get_chain_ca <- function(pdb, chain="A") {
  x <- trim.pdb(pdb, chain = chain, elety = "CA")
  if (is.null(x$atom) || nrow(x$atom) == 0) {
    stop("No CA atoms found for chain ", chain, " in this PDB.")
  }
  x
}

zscore <- function(v) (v - mean(v, na.rm = TRUE)) / sd(v, na.rm = TRUE)

# ---- read PDBs ----
pdb_ids <- c("4AKE", "1AKE", "1E4Y")
pdbs <- lapply(pdb_ids, read.pdb)
```

```
  Note: Accessing on-line PDB file

Warning in get.pdb(file, path = tempdir(), verbose = FALSE):
C:\Users\kenny\AppData\Local\Temp\Rtmpek3OXe/4AKE.pdb exists. Skipping download

  Note: Accessing on-line PDB file

Warning in get.pdb(file, path = tempdir(), verbose = FALSE):
C:\Users\kenny\AppData\Local\Temp\Rtmpek3OXe/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):
C:\Users\kenny\AppData\Local\Temp\Rtmpek3OXe/1E4Y.pdb exists. Skipping download
```

```r
# ---- trim to chain A CA ----
chainA <- lapply(pdbs, get_chain_ca, chain="A")

# ---- extract B-factors ----
braw <- lapply(chainA, function(x) x$atom$b)
bz   <- lapply(braw, zscore)

# ---- plotting ----
op <- par(mfrow = c(3, 1), mar = c(4, 4, 2, 1))
for (i in seq_along(pdb_ids)) {
  plotb3(
    bz[[i]],
    sse  = chainA[[i]],
    typ  = "l",
    ylab = "B-factor (z-score)",
    main = paste0(pdb_ids[i], " chain A (CA)")
  )
  abline(h = 0, lty = 3)
}
```




```r
par(op)
```

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

```
library(bio3d)

analyze_protein_drug <- function(pdb_inputs,
                                 chain = "A",
                                 target = 1,
                                 protein_elety = "CA",
                                 ligand_resids = NULL,
                                 contact_cutoff = 4.0,
                                 normalize_b = TRUE) {

  # ---- helpers ----
  zscore <- function(x) {
    if (!normalize_b) return(as.numeric(x))
    if (all(is.na(x))) return(as.numeric(x))
    s <- sd(x, na.rm = TRUE)
    if (is.na(s) || s == 0) return(rep(0, length(x)))
    (x - mean(x, na.rm = TRUE)) / s
  }

  get_chain_elety <- function(pdb) {
    x <- trim.pdb(pdb, chain = chain, elety = protein_elety)
    if (is.null(x$atom) || nrow(x$atom) == 0)
      stop("No ", protein_elety, " atoms found for chain ", chain, ".")
    x
  }

  ligand_idx <- function(pdb) {
    a <- pdb$atom
    if (!is.null(ligand_resids)) {
      return(which(toupper(a$resid) %in% toupper(ligand_resids)))
    }
    # heuristic ligand selection
    water <- c("HOH", "WAT")
    ions  <- c("NA","K","CL","CA","MG","ZN","MN","FE","CU","CO")
    which(a$type == "HETATM" &
            !(toupper(a$resid) %in% water) &
            !(toupper(a$resid) %in% ions))
  }
```

```r
contact_counts <- function(pdb) {
  # plotting residues (CA or chosen elety)
  sel_plot <- atom.select(pdb, chain = chain, elety = protein_elety)
  plot_atoms <- pdb$atom[sel_plot$atom, , drop = FALSE]
  counts <- integer(nrow(plot_atoms))

  # protein chain all atoms
  sel_prot <- atom.select(pdb, chain = chain, "protein")
  prot <- trim.pdb(pdb, sel_prot)

  # ligand heavy atoms
  li <- ligand_idx(pdb)
  if (length(li) == 0) return(list(counts = counts, resno = plot_atoms$resno, resid = plot_
  li <- li[toupper(pdb$atom$elety[li]) != "H"]
  if (length(li) == 0) return(list(counts = counts, resno = plot_atoms$resno, resid = plot_

  prot_xyz <- matrix(prot$xyz, ncol = 3, byrow = TRUE)
  lig_xyz  <- matrix(pdb$xyz[atom.select(pdb, atom = li)$xyz], ncol = 3, byrow = TRUE)

  d <- dist.xyz(prot_xyz, lig_xyz)
  pairs <- which(d <= contact_cutoff, arr.ind = TRUE)
  if (nrow(pairs) > 0) {
    tab <- table(prot$atom$resno[pairs[, 1]])
    plot_res <- as.character(plot_atoms$resno)
    hit <- intersect(plot_res, names(tab))
    counts[match(hit, plot_res)] <- as.integer(tab[hit])
  }

  list(
    counts = counts,
    resno = plot_atoms$resno,
    resid = plot_atoms$resid,
    ligands = unique(pdb$atom$resid[li])
  )
}

# ---- checks ----
stopifnot(is.character(pdb_inputs), length(pdb_inputs) >= 1)
stopifnot(target >= 1, target <= length(pdb_inputs))

# ---- main workflow ----
pdbs <- lapply(pdb_inputs, read.pdb)
```

```
  trimmed <- lapply(pdbs, get_chain_elety)
  b_list  <- lapply(trimmed, function(x) zscore(x$atom$b))
  cont    <- lapply(pdbs, contact_counts)

  # ---- plot target ----
  b <- b_list[[target]]
  sse <- trimmed[[target]]
  cc <- cont[[target]]$counts

  n <- min(length(b), length(cc), nrow(sse$atom))
  b <- b[1:n]; cc <- cc[1:n]; sse$atom <- sse$atom[1:n, , drop = FALSE]

  plotb3(b, sse = sse, typ = "l",
         main = paste0(pdb_inputs[[target]], " chain ", chain, ": B-factors + ligand contacts
         ylab = if (normalize_b) "B-factor (z-score)" else "B-factor")

  hits <- which(cc > 0)
  if (length(hits)) {
    rug(hits, col = "gray40")
    legend("topright",
           legend = c("B-factor", "contact residues"),
           lty = c(1, NA), pch = c(NA, 124), bty = "n")
  }

  invisible(list(
    settings = list(chain = chain, target = target, protein_elety = protein_elety,
                    ligand_resids = ligand_resids, contact_cutoff = contact_cutoff,
                    normalize_b = normalize_b),
    b_factors = b_list,
    contacts = lapply(cont, `[[`, "counts"),
    residue_map = lapply(cont, function(x) data.frame(resno = x$resno, resid = x$resid)),
    ligands_found = lapply(cont, `[[`, "ligands")
  ))
}

# Example call
res <- analyze_protein_drug(c("4AKE","1AKE","1E4Y"), chain="A", target=1)
```

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

```
Warning in get.pdb(file, path = tempdir(), verbose = FALSE):
```

```
C:\Users\kenny\AppData\Local\Temp\Rtmpek3OXe/4AKE.pdb exists. Skipping download

  Note: Accessing on-line PDB file

Warning in get.pdb(file, path = tempdir(), verbose = FALSE):
C:\Users\kenny\AppData\Local\Temp\Rtmpek3OXe/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):
C:\Users\kenny\AppData\Local\Temp\Rtmpek3OXe/1E4Y.pdb exists. Skipping download
```