Class 9: Structural Bioinformatics 1 pt.1

Sabrina Wu (PID: A16731683)

The main database for structural data is caled the PDB (Protein Data Bank). Let's see what it contains:

Data from: https://www.rcsb.org/stats/summary, download the csv file and import into this folder

```
pdbdb <- read.csv("C:/Users/sabri/Downloads/Data_Export_Summary.csv",row.names=1)
pdbdb
```

```
                         X.ray     EM    NMR Multiple.methods Neutron Other
Protein (only)         167,192 15,572 12,529              208      77    32
Protein/Oligosaccharide  9,639  2,635     34                8       2     0
Protein/NA               8,730  4,697    286                7       0     0
Nucleic acid (only)      2,869    137  1,507               14       3     1
Other                      170     10     33                0       0     0
Oligosaccharide (only)      11      0      6                1       0     4
                         Total
Protein (only)         195,610
Protein/Oligosaccharide 12,318
Protein/NA              13,720
Nucleic acid (only)      4,531
Other                      213
Oligosaccharide (only)      22
```

> Q1: What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy.

```
pdbdb$Total
```

```
[1] "195,610" "12,318"  "13,720"  "4,531"   "213"     "22"
```

I need to remove the comman and convert to numeric to do math:

```
as.numeric(sub(",","",pdbdb$Total))
```

```
[1] 195610  12318  13720   4531    213     22
```

I could trun this into a function to fix the whole table or any future table I read like this:

```
x <- pdbdb$Total
as.numeric(sub(",","",x))
```

```
[1] 195610  12318  13720   4531    213     22
```

```
comma2numeric <- function (x){
  as.numeric(sub(",","",x))
}
```

```
comma2numeric(pdbdb$X.ray)
```

```
[1] 167192   9639   8730   2869    170     11
```

```
apply(pdbdb,2,comma2numeric)
```

```
      X.ray    EM   NMR Multiple.methods Neutron Other  Total
[1,] 167192 15572 12529              208      77    32 195610
[2,]   9639  2635    34                8       2     0  12318
[3,]   8730  4697   286                7       0     0  13720
[4,]   2869   137  1507               14       3     1   4531
[5,]    170    10    33                0       0     0    213
[6,]     11     0     6                1       0     4     22
```

##Or try a different read/import function:

```
library(readr)
pdbdb <- read_csv("C:/Users/sabri/Downloads/Data_Export_Summary.csv")
```

```
Rows: 6 Columns: 8
-- Column specification --------------------------------------------------------
Delimiter: ","
chr (1): Molecular Type
dbl (3): Multiple methods, Neutron, Other
num (4): X-ray, EM, NMR, Total

i Use `spec()` to retrieve the full column specification for this data.
i Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

> Q1: What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy.

```
sum(pdbdb$`X-ray`)/sum(pdbdb$Total)*100
```

```
[1] 83.30359
```

```
sum(pdbdb$EM)/sum(pdbdb$Total)*100
```

```
[1] 10.18091
```

> Q2: What proportion of structures in the PDB are protein?

```
pdbdb$Total[1]/sum(pdbdb$Total)*100
```

```
[1] 86.39483
```

Most of database are protein and is with x-ray –> biased.

> Q3: Type HIV in the PDB website search box on the home page and determine how many HIV-1 protease structures are in the current PDB?

4,553 Structures came up in the search.

Mol*

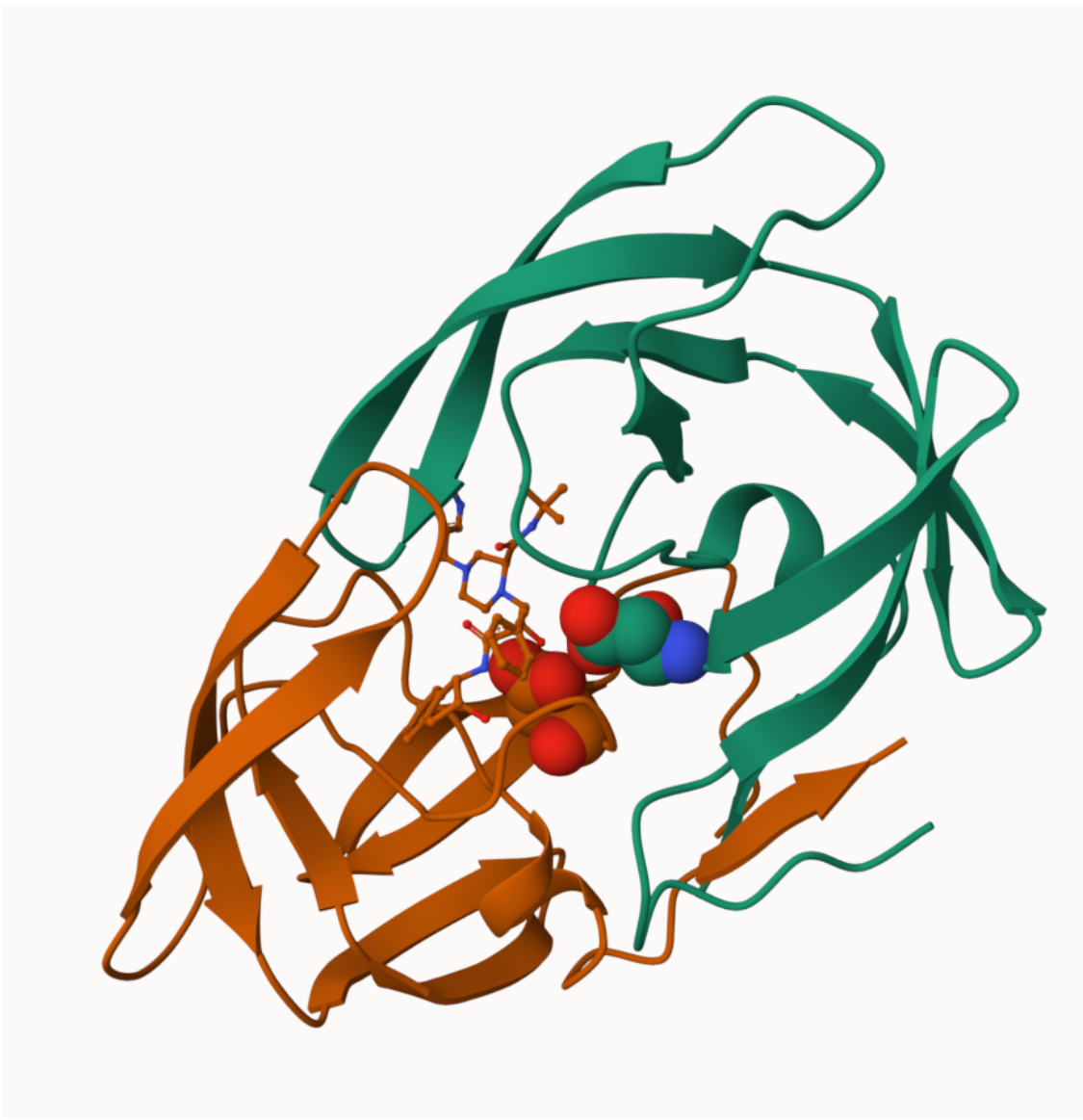
Mol* (pronounced "molstar") is a new web-based molecular viewer that we will need to learn the basics of here.

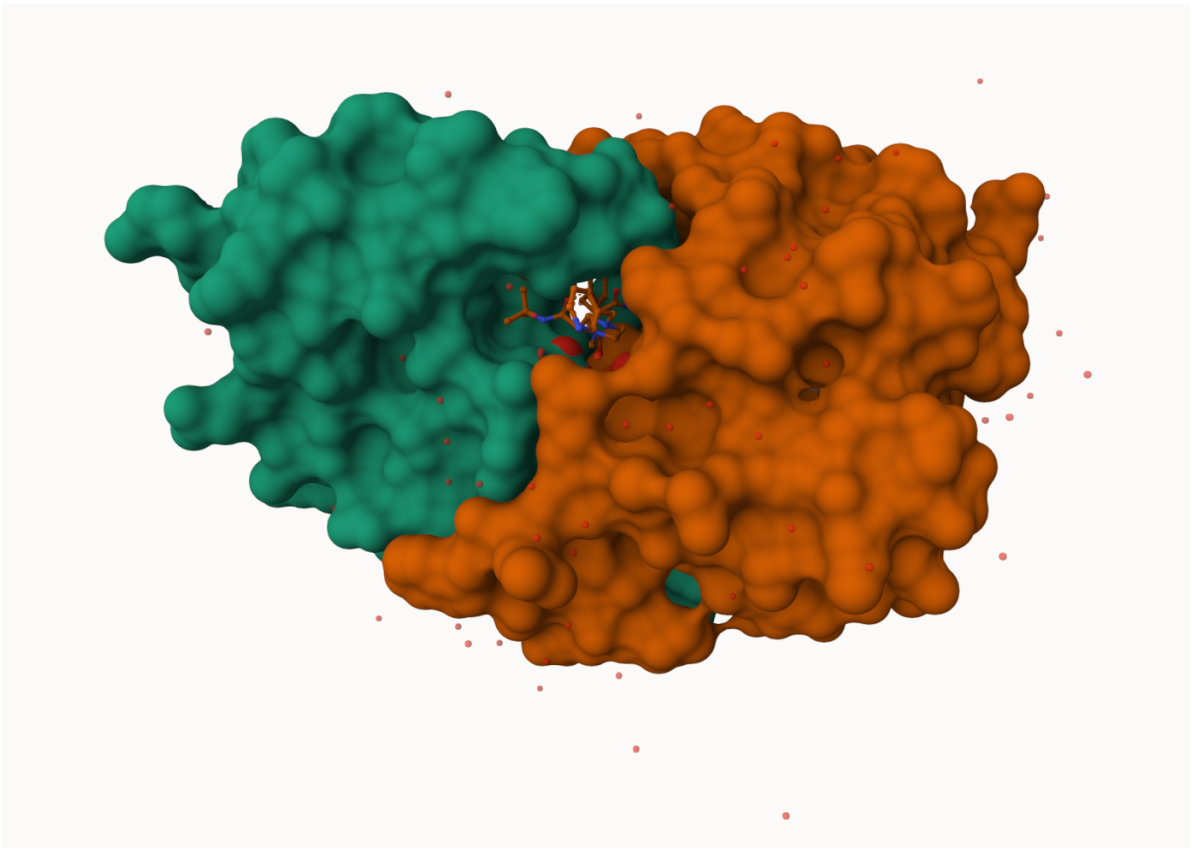
http://molstar.org/viewer/

We will use PDB code: 1HSG

Figure 1: A first image from molstar

More custome images:



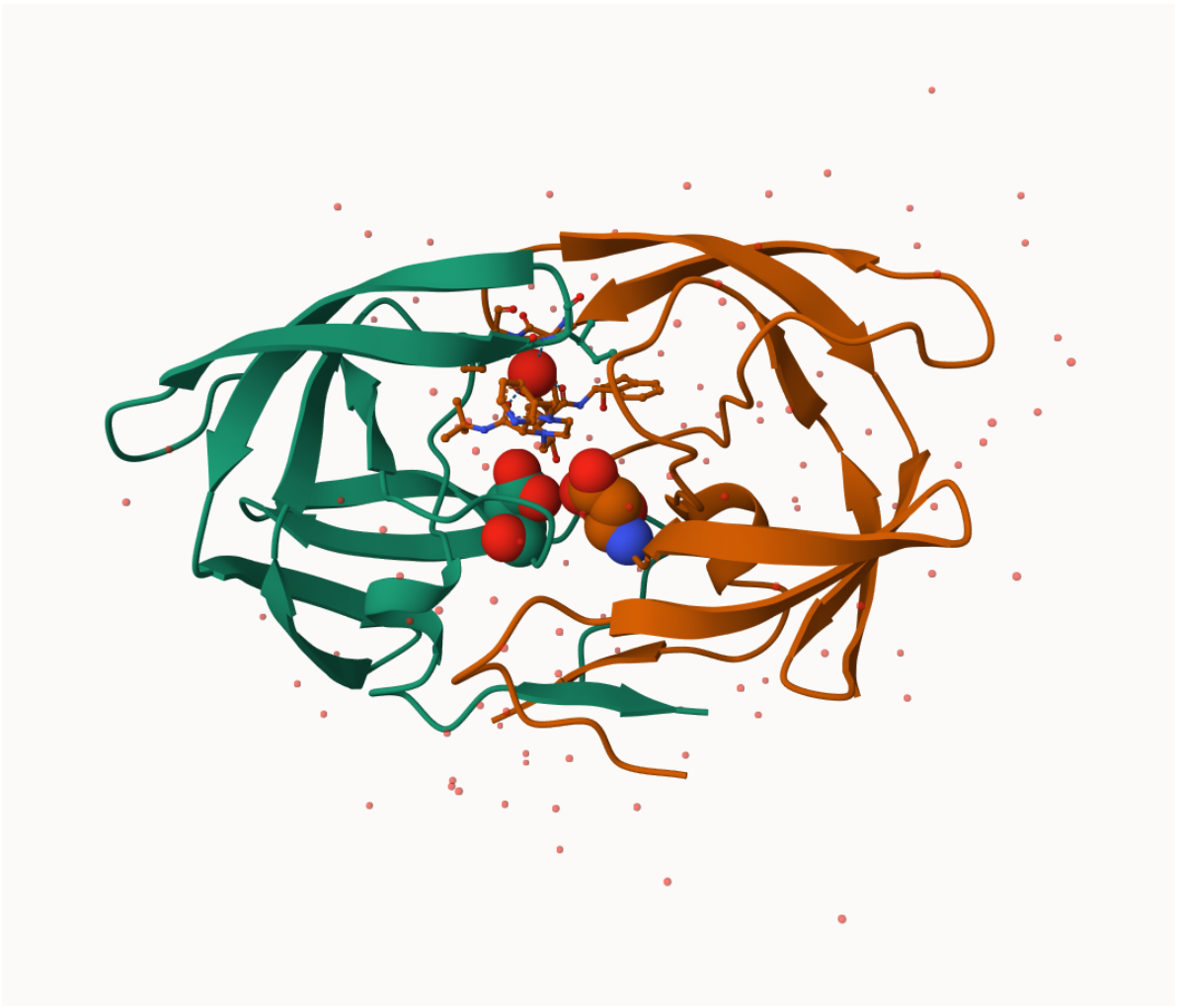


Q4: Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure?

We are just representing water as one molecule instead of seeing the individual atoms that makes up the water molecules.

Q5: There is a critical "conserved" water molecule in the binding site. Can you identify this water molecule? What residue number does this water molecule have

The water molecule is in between all the ligand and has a residue number of HOH 308.



Q6: Generate and save a figure clearly showing the two distinct chains of HIV-protease along with the ligand. You might also consider showing the catalytic residues ASP 25 in each chain and the critical water (we recommend "Ball & Stick" for these side-chains). Add this figure to your Quarto document.

Q7: [Optional] As you have hopefully observed HIV protease is a homodimer (i.e. it is composed of two identical chains). With the aid of the graphic display can you identify secondary structure elements that are likely to only form in the dimer rather than the monomer?

The Bio3D package

The bio3d package allows us to do all sorts of structural bioinformativs work in R.

Let's start with how it can read these PDB files:

```
library(bio3d)

pdb <- read.pdb("1hsg")
```

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

```
pdb
```

```
 Call:  read.pdb(file = "1hsg")

   Total Models#: 1
     Total Atoms#: 1686,  XYZs#: 5058  Chains#: 2  (values: A B)

     Protein Atoms#: 1514  (residues/Calpha atoms#: 198)
     Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)

     Non-protein/nucleic Atoms#: 172  (residues: 128)
     Non-protein/nucleic resid values: [ HOH (127), MK1 (1) ]

   Protein sequence:
      PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIGGFIKVRQYD
      QILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFPQITLWQRPLVTIKIGGQLKE
      ALLDTGADDTVLEEMSLPGRWKPKMIGGIGGFIKVRQYDQILIEICGHKAIGTVLVGPTP
      VNIIGRNLLTQIGCTLNF

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

```
attributes(pdb)
```

```
$names
[1] "atom"   "xyz"    "seqres" "helix"  "sheet"  "calpha" "remark" "call"

$class
[1] "pdb" "sse"
```

```
head(pdb$atom)
```

```
  type eleno elety  alt resid chain resno insert      x      y     z o     b
1 ATOM     1     N <NA>   PRO     A     1   <NA> 29.361 39.686 5.862 1 38.10
2 ATOM     2    CA <NA>   PRO     A     1   <NA> 30.307 38.663 5.319 1 40.62
3 ATOM     3     C <NA>   PRO     A     1   <NA> 29.760 38.071 4.022 1 42.64
4 ATOM     4     O <NA>   PRO     A     1   <NA> 28.600 38.302 3.676 1 43.40
5 ATOM     5    CB <NA>   PRO     A     1   <NA> 30.508 37.541 6.342 1 37.87
6 ATOM     6    CG <NA>   PRO     A     1   <NA> 29.296 37.591 7.162 1 38.40
  segid elesy charge
1  <NA>     N   <NA>
2  <NA>     C   <NA>
3  <NA>     C   <NA>
4  <NA>     O   <NA>
5  <NA>     C   <NA>
6  <NA>     C   <NA>
```

```
pdbseq(pdb)[25]
```

```
 25
"D"
```

Q7: How many amino acid residues are there in this pdb object?

```
sum(pdb$calpha)
```

```
[1] 198
```

```
length(pdbseq(pdb))
```

```
[1] 198
```

There are 198 amino acid residues

Q8: Name one of the two non-protein residues?

HOH and MK1

Q9: How many protein chains are in this structure?

There are two chains in the structure.

```
unique(pdb$atom$chain)
```

```
[1] "A" "B"
```

##Predicting functional motions of a single structure

Let's do a bioinformatics prediction of functional motions - i.e. the movements that one of these molecules needs to make to do tis stuff.

```
adk <- read.pdb("6s36")
```

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

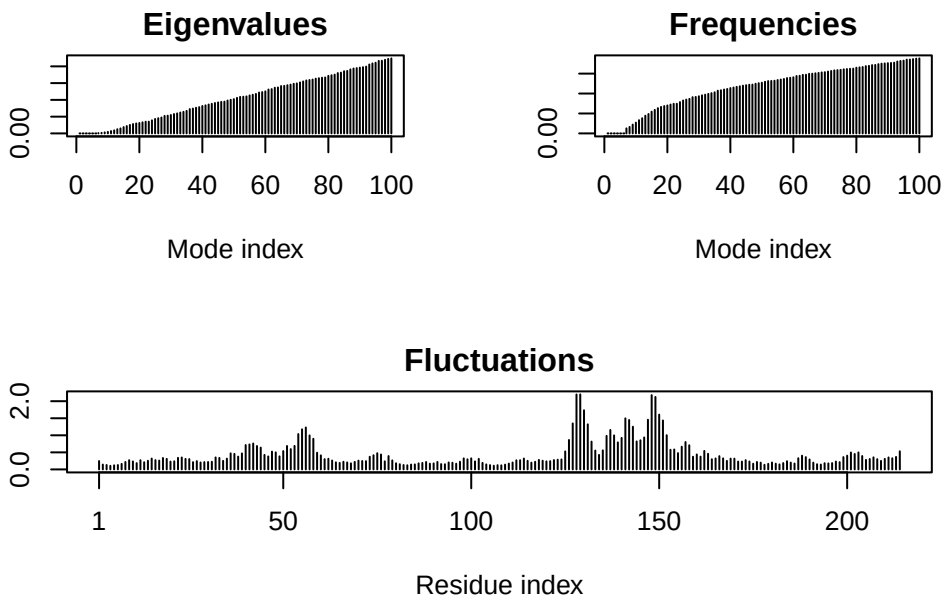
```
adk
```

```
 Call:  read.pdb(file = "6s36")

   Total Models#: 1
     Total Atoms#: 1898,  XYZs#: 5694  Chains#: 1  (values: A)

     Protein Atoms#: 1654  (residues/Calpha atoms#: 214)
     Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)

     Non-protein/nucleic Atoms#: 244  (residues: 244)
     Non-protein/nucleic resid values: [ CL (3), HOH (238), MG (2), NA (1) ]

   Protein sequence:
      MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
      DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDKI
      VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG

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

```
# Perform flexiblity prediction
m <- nma(adk)
```

```
 Building Hessian...        Done in 0.03 seconds.
 Diagonalizing Hessian...   Done in 0.31 seconds.
```

```
plot(m)
```



Write out multi-model PDB file that we can use to make an animation of the predicted motions.

```
mktrj(m, file="adk.pdb")
```

I can open this in Mol* to play the trajectory...

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comparative analysis of protein structures

```
library(bio3d)
```

Here we will find and analyze all ADK structures in the PDB database.

We will start with a single database acession id: "1ake_A"

```
id <- "1ake_A"
aa <- get.seq(id)
```

```
Warning in get.seq(id): Removing existing file: seqs.fasta
```

```
Fetching... Please wait. Done.
```

I ran these cmds in the R brain/console

install.packages("BiocManager") BiocManager::install("msa")

Q10. Which of the packages above is found only on BioConductor and not CRAN?

The `msa` package is only from BioCOnductor.

The install.packages() function is used to install packages from the main CRAN repository for R packages. BioConductor is a separate repository of R packages focused on high-throughput biomolecular assays and biomolecular data. Packages from BioConductor can be installed using the BiocManager::install() function. Finally, R packages found on GitHub or BitBucket can be installed using devtools::install_github() and devtools::install_bitbucket() functions.

Q11. Which of the above packages is not found on BioConductor or CRAN?

The package `bio3d-view`

Q12. True or False? Functions from the devtools package can be used to install packages from GitHub and BitBucket?

True

Q13. How many amino acids are in this sequence, i.e. how long is this sequence?

```
attributes(aa)
```

```
$names
[1] "id"   "ali"  "call"

$class
[1] "fasta"
```

```
aa$id
```

```
[1] "pdb|1AKE|A"
```

```
aa$ali
```

```
           [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8] [,9] [,10] [,11] [,12] [,13]
pdb|1AKE|A "M"  "R"  "I"  "I"  "L"  "L"  "G"  "A"  "P"  "G"   "A"   "G"   "K"
           [,14] [,15] [,16] [,17] [,18] [,19] [,20] [,21] [,22] [,23] [,24]
pdb|1AKE|A "G"   "T"   "Q"   "A"   "Q"   "F"   "I"   "M"   "E"   "K"   "Y"
           [,25] [,26] [,27] [,28] [,29] [,30] [,31] [,32] [,33] [,34] [,35]
pdb|1AKE|A "G"   "I"   "P"   "Q"   "I"   "S"   "T"   "G"   "D"   "M"   "L"
           [,36] [,37] [,38] [,39] [,40] [,41] [,42] [,43] [,44] [,45] [,46]
pdb|1AKE|A "R"   "A"   "A"   "V"   "K"   "S"   "G"   "S"   "E"   "L"   "G"
           [,47] [,48] [,49] [,50] [,51] [,52] [,53] [,54] [,55] [,56] [,57]
pdb|1AKE|A "K"   "Q"   "A"   "K"   "D"   "I"   "M"   "D"   "A"   "G"   "K"
           [,58] [,59] [,60] [,61] [,62] [,63] [,64] [,65] [,66] [,67] [,68]
pdb|1AKE|A "L"   "V"   "T"   "D"   "E"   "L"   "V"   "I"   "A"   "L"   "V"
           [,69] [,70] [,71] [,72] [,73] [,74] [,75] [,76] [,77] [,78] [,79]
pdb|1AKE|A "K"   "E"   "R"   "I"   "A"   "Q"   "E"   "D"   "C"   "R"   "N"
           [,80] [,81] [,82] [,83] [,84] [,85] [,86] [,87] [,88] [,89] [,90]
pdb|1AKE|A "G"   "F"   "L"   "L"   "D"   "G"   "F"   "P"   "R"   "T"   "I"
           [,91] [,92] [,93] [,94] [,95] [,96] [,97] [,98] [,99] [,100] [,101]
pdb|1AKE|A "P"   "Q"   "A"   "D"   "A"   "M"   "K"   "E"   "A"   "G"    "I"
           [,102] [,103] [,104] [,105] [,106] [,107] [,108] [,109] [,110]
pdb|1AKE|A "N"    "V"    "D"    "Y"    "V"    "L"    "E"    "F"    "D"
           [,111] [,112] [,113] [,114] [,115] [,116] [,117] [,118] [,119]
pdb|1AKE|A "V"    "P"    "D"    "E"    "L"    "I"    "V"    "D"    "R"
           [,120] [,121] [,122] [,123] [,124] [,125] [,126] [,127] [,128]
pdb|1AKE|A "I"    "V"    "G"    "R"    "R"    "V"    "H"    "A"    "P"
           [,129] [,130] [,131] [,132] [,133] [,134] [,135] [,136] [,137]
pdb|1AKE|A "S"    "G"    "R"    "V"    "Y"    "H"    "V"    "K"    "F"
           [,138] [,139] [,140] [,141] [,142] [,143] [,144] [,145] [,146]
pdb|1AKE|A "N"    "P"    "P"    "K"    "V"    "E"    "G"    "K"    "D"
           [,147] [,148] [,149] [,150] [,151] [,152] [,153] [,154] [,155]
pdb|1AKE|A "D"    "V"    "T"    "G"    "E"    "E"    "L"    "T"    "T"
           [,156] [,157] [,158] [,159] [,160] [,161] [,162] [,163] [,164]
pdb|1AKE|A "R"    "K"    "D"    "D"    "Q"    "E"    "E"    "T"    "V"
           [,165] [,166] [,167] [,168] [,169] [,170] [,171] [,172] [,173]
pdb|1AKE|A "R"    "K"    "R"    "L"    "V"    "E"    "Y"    "H"    "Q"
           [,174] [,175] [,176] [,177] [,178] [,179] [,180] [,181] [,182]
pdb|1AKE|A "M"    "T"    "A"    "P"    "L"    "I"    "G"    "Y"    "Y"
           [,183] [,184] [,185] [,186] [,187] [,188] [,189] [,190] [,191]
pdb|1AKE|A "S"    "K"    "E"    "A"    "E"    "A"    "G"    "N"    "T"
           [,192] [,193] [,194] [,195] [,196] [,197] [,198] [,199] [,200]
pdb|1AKE|A "K"    "Y"    "A"    "K"    "V"    "D"    "G"    "T"    "K"
```

```
           [,201] [,202] [,203] [,204] [,205] [,206] [,207] [,208] [,209]
pdb|1AKE|A "P"    "V"    "A"    "E"    "V"    "R"    "A"    "D"    "L"
           [,210] [,211] [,212] [,213] [,214]
pdb|1AKE|A "E"    "K"    "I"    "L"    "G"
```

```
aa$call
```

```
read.fasta(file = outfile)
```

```
ncol(aa$ali)
```

```
[1] 214
```

There are 214 amino acids in the sequence.

Ran blast against the amino sequence.Comment bc on government website.

```
#b <- blast.pdb(aa)
```

Pre-calculated results:

```
hits <- NULL
hits$pdb.id <- c('1AKE_A','6S36_A','6RZE_A','3HPR_A','1E4V_A','5EJE_A','1E4Y_A','3X2S_A','6H
```

```
#attributes(b)
#head(b$hit.tbl)
```

```
#hits <- plot(b)
```

```
#hits$pdb.id
```

Summary of what we had done: 1. get.seq("1ADK") to get amino acid sequence -> aa 2. blast.odb(aa) to find similar sequences -> b 3. get.pdb(hits) to download the tophits -> files These two line of codes does what you can do on the website.

4. pdbalm(files, fit=TRUE) superimpose all the tophits -> pdbs
5. pca(pdbs) does pca on your file (PC)

```
# Download releated PDB files
files <- get.pdb(hits$pdb.id, path="pdbs", split=TRUE, gzip=TRUE)
```

```
Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1AKE.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6S36.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6RZE.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3HPR.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1E4V.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/5EJE.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1E4Y.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3X2S.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6HAP.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6HAM.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/4K46.pdb exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3GMT.pdb exists. Skipping download
```

```
Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/4PZL.pdb exists. Skipping download
```

```
  |
  |                                                                      |   0%
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  |
  |============================================================          |  85%
  |
  |================================================================      |  92%
  |
  |======================================================================| 100%
```

Superimpose the different pdbs together to see similarities

```
# Align releated PDBs
pdbs <- pdbaln(files, fit = TRUE, exefile="msa")
```

```
Reading PDB files:
pdbs/split_chain/1AKE_A.pdb
pdbs/split_chain/6S36_A.pdb
```

```
pdbs/split_chain/6RZE_A.pdb
pdbs/split_chain/3HPR_A.pdb
pdbs/split_chain/1E4V_A.pdb
pdbs/split_chain/5EJE_A.pdb
pdbs/split_chain/1E4Y_A.pdb
pdbs/split_chain/3X2S_A.pdb
pdbs/split_chain/6HAP_A.pdb
pdbs/split_chain/6HAM_A.pdb
pdbs/split_chain/4K46_A.pdb
pdbs/split_chain/3GMT_A.pdb
pdbs/split_chain/4PZL_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
..   PDB has ALT records, taking A only, rm.alt=TRUE
....   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
...

Extracting sequences

pdb/seq: 1   name: pdbs/split_chain/1AKE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 2   name: pdbs/split_chain/6S36_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 3   name: pdbs/split_chain/6RZE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 4   name: pdbs/split_chain/3HPR_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 5   name: pdbs/split_chain/1E4V_A.pdb
pdb/seq: 6   name: pdbs/split_chain/5EJE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 7   name: pdbs/split_chain/1E4Y_A.pdb
pdb/seq: 8   name: pdbs/split_chain/3X2S_A.pdb
pdb/seq: 9   name: pdbs/split_chain/6HAP_A.pdb
pdb/seq: 10   name: pdbs/split_chain/6HAM_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 11   name: pdbs/split_chain/4K46_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 12   name: pdbs/split_chain/3GMT_A.pdb
pdb/seq: 13   name: pdbs/split_chain/4PZL_A.pdb
```

```
pdbs
```

```
                                 1        .         .         .         40
[Truncated_Name:1]1AKE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:2]6S36_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:3]6RZE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:4]3HPR_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:5]1E4V_A.pdb     ----------MRIILLGAPVAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:6]5EJE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:7]1E4Y_A.pdb     ----------MRIILLGALVAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:8]3X2S_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:9]6HAP_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:10]6HAM_A.pdb    ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:11]4K46_A.pdb    ----------MRIILLGAPGAGKGTQAQFIMAKFGIPQIS
[Truncated_Name:12]3GMT_A.pdb    ----------MRLILLGAPGAGKGTQANFIKEKFGIPQIS
[Truncated_Name:13]4PZL_A.pdb    TENLYFQSNAMRIILLGAPGAGKGTQAKIIEQKYNIAHIS
                                           **^*****  *******  *  *^ *  **
                                 1        .         .         .         40

                                41        .         .         .         80
[Truncated_Name:1]1AKE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:2]6S36_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:3]6RZE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:4]3HPR_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:5]1E4V_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:6]5EJE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDACKLVTDELVIALVKE
[Truncated_Name:7]1E4Y_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:8]3X2S_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDCGKLVTDELVIALVKE
[Truncated_Name:9]6HAP_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVRE
[Truncated_Name:10]6HAM_A.pdb     TGDMLRAAIKSGSELGKQAKDIMDAGKLVTDEIIIALVKE
[Truncated_Name:11]4K46_A.pdb     TGDMLRAAIKAGTELGKQAKSVIDAGQLVSDDIILGLVKE
[Truncated_Name:12]3GMT_A.pdb     TGDMLRAAVKAGTPLGVEAKTYMDEGKLVPDSLIIGLVKE
[Truncated_Name:13]4PZL_A.pdb     TGDMIRETIKSGSALGQELKKVLDAGELVSDEFIIKIVKD
                                  ****^*  ^* *^ **   *  ^*   ** *  ^^ ^*^^
                                41        .         .         .         80

                                81        .         .         .         120
[Truncated_Name:1]1AKE_A.pdb      RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:2]6S36_A.pdb      RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:3]6RZE_A.pdb      RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:4]3HPR_A.pdb      RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:5]1E4V_A.pdb      RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
```

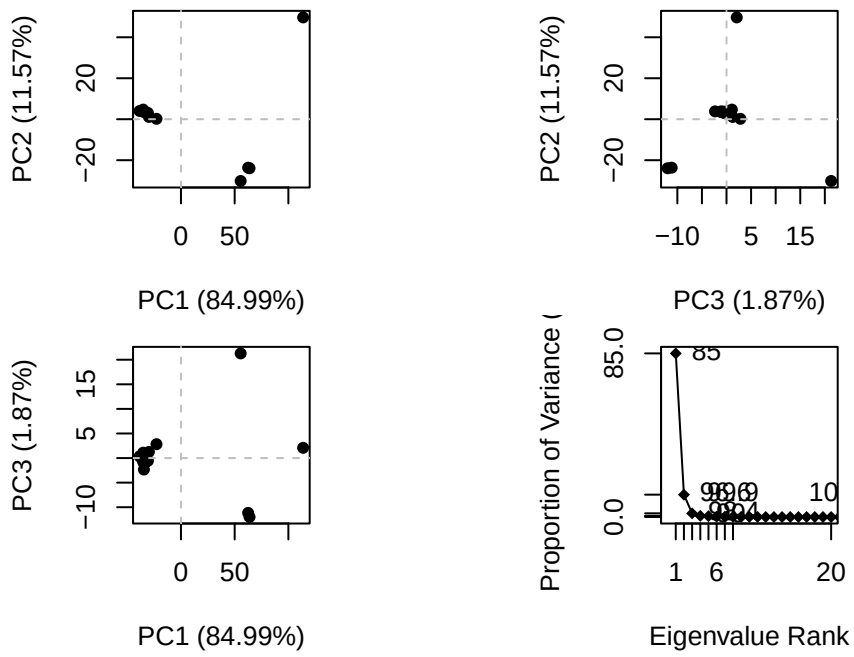
```
[Truncated_Name:6]5EJE_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:7]1E4Y_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:8]3X2S_A.pdb    RIAQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:9]6HAP_A.pdb    RICQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:10]6HAM_A.pdb   RICQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:11]4K46_A.pdb   RIAQDDCAKGFLLDGFPRTIPQADGLKEVGVVVDYVIEFD
[Truncated_Name:12]3GMT_A.pdb   RLKEADCANGYLFDGFPRTIAQADAMKEAGVAIDYVLEID
[Truncated_Name:13]4PZL_A.pdb   RISKNDCNNGFLLDGVPRTIPQAQELDKLGVNIDYIVEVD
                                *^   *   *^* ** **** **  ^   *^ ^**^^* *
                               81        .         .         .         120

                              121        .         .         .         160
[Truncated_Name:1]1AKE_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:2]6S36_A.pdb    VPDELIVDKIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:3]6RZE_A.pdb    VPDELIVDAIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:4]3HPR_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDGTG
[Truncated_Name:5]1E4V_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:6]5EJE_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:7]1E4Y_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:8]3X2S_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:9]6HAP_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:10]6HAM_A.pdb   VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:11]4K46_A.pdb   VADSVIVERMAGRRAHLASGRTYHNVYNPPKVEGKDDVTG
[Truncated_Name:12]3GMT_A.pdb   VPFSEIIERMSGRRTHPASGRTYHVKFNPPKVEGKDDVTG
[Truncated_Name:13]4PZL_A.pdb   VADNLLIERITGRRIHPASGRTYHTKFNPPKVADKDDVTG
                                *    ^^^ ^ *** *  *** **  ^*****  *** **
                              121        .         .         .         160

                              161        .         .         .         200
[Truncated_Name:1]1AKE_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:2]6S36_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:3]6RZE_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:4]3HPR_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:5]1E4V_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:6]5EJE_A.pdb    EELTTRKDDQEECVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:7]1E4Y_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:8]3X2S_A.pdb    EELTTRKDDQEETVRKRLCEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:9]6HAP_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:10]6HAM_A.pdb   EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:11]4K46_A.pdb   EDLVIREDDKEETVLARLGVYHNQTAPLIAYYGKEAEAGN
[Truncated_Name:12]3GMT_A.pdb   EPLVQRDDDKEETVKKRLDVYEAQTKPLITYYGDWARRGA
[Truncated_Name:13]4PZL_A.pdb   EPLITRTDDNEDTVKQRLSVYHAQTAKLIDFYRNFSSTNT
                                * *  * ** *^ *  **  *   *  ** ^*
```

```
                              161        .         .         .         200

                              201        .         .      227
[Truncated_Name:1]1AKE_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:2]6S36_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:3]6RZE_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:4]3HPR_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:5]1E4V_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:6]5EJE_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:7]1E4Y_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:8]3X2S_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:9]6HAP_A.pdb    T--KYAKVDGTKPVCEVRADLEKILG-
[Truncated_Name:10]6HAM_A.pdb   T--KYAKVDGTKPVCEVRADLEKILG-
[Truncated_Name:11]4K46_A.pdb   T--QYLKFDGTKAVAEVSAELEKALA-
[Truncated_Name:12]3GMT_A.pdb   E-------NGLKAPA-----YRKISG-
[Truncated_Name:13]4PZL_A.pdb   KIPKYIKINGDQAVEKVSQDIFDQLNK
                                         *
                              201        .         .      227

Call:
  pdbaln(files = files, fit = TRUE, exefile = "msa")

Class:
  pdbs, fasta

Alignment dimensions:
  13 sequence rows; 227 position columns (204 non-gap, 23 gap)

+ attr: xyz, resno, b, chain, id, ali, resid, sse, call
```

```
# Vector containing PDB codes for figure axis
ids <- basename.pdb(pdbs$id)

# Draw schematic alignment
#plot(pdbs, labels=ids)
```

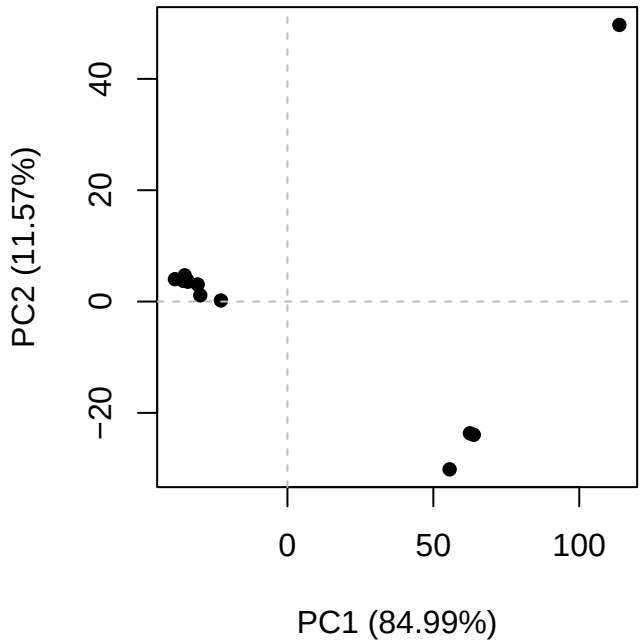
Principle Component Analysis

```
# Perform PCA
pc.xray <- pca(pdbs)
plot(pc.xray)
```



Right bottom panel: show that only 3 PC are needed to account for pretty much all the variance.

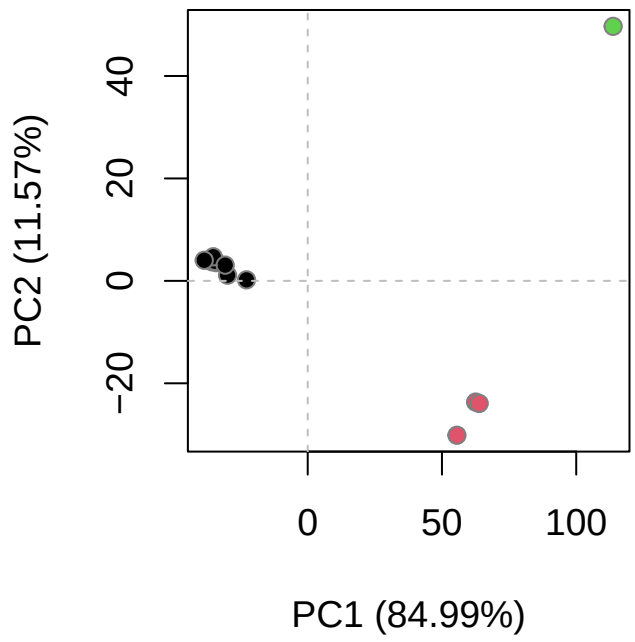
```
plot(pc.xray, pc.axes = c(1,2))
```



```
# Calculate RMSD
rd <- rmsd(pdbs)
```

```
Warning in rmsd(pdbs): No indices provided, using the 204 non NA positions
```

```
# Structure-based clustering
hc.rd <- hclust(dist(rd))
grps.rd <- cutree(hc.rd, k=3)

plot(pc.xray, 1:2, col="grey50", bg=grps.rd, pch=21, cex=1)
```



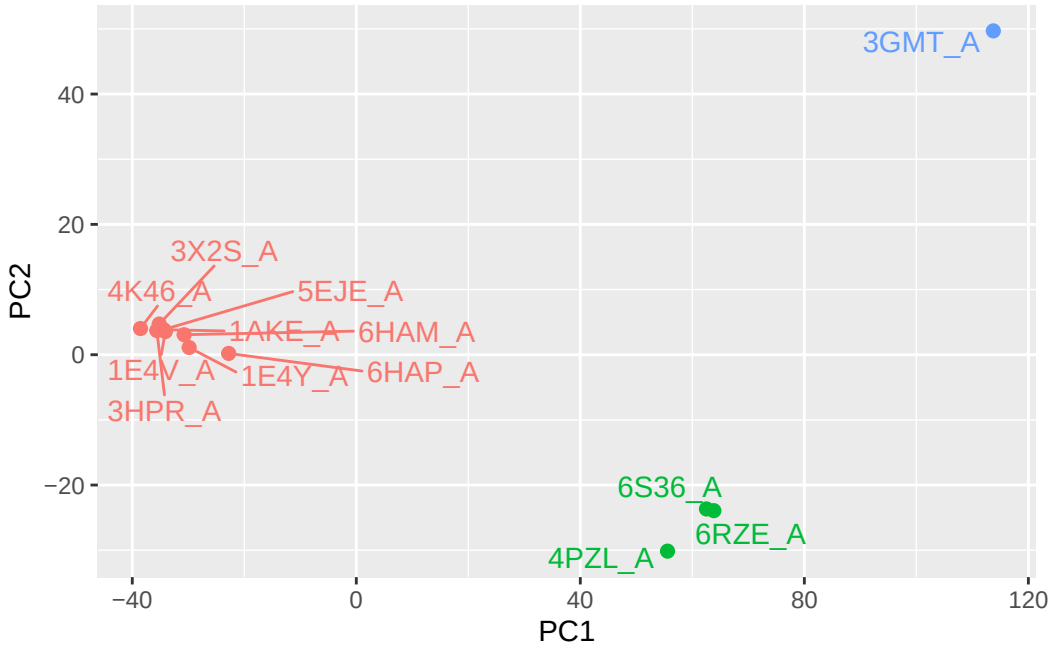
Rurther visualization

To visualize the major structural variations in the ensemble the function mktrj() can be used to generate a trajectory PDB file by interpolating along a give PC (eigenvector):

```
# Visualize first principal component
pc1 <- mktrj(pc.xray, pc=1, file="pc_1.pdb")
```

Can see this file in Molstar

```
#Plotting results with ggplot2
library(ggplot2)
library(ggrepel)

df <- data.frame(PC1=pc.xray$z[,1],
                 PC2=pc.xray$z[,2],
                 col=as.factor(grps.rd),
                 ids=ids)

p <- ggplot(df) +
  aes(PC1, PC2, col=col, label=ids) +
  geom_point(size=2) +
  geom_text_repel(max.overlaps = 20) +
  theme(legend.position = "none")
p
```



Normal Mode Analysis

```
# NMA of all structures
modes <- nma(pdbs)
```

```
Details of Scheduled Calculation:
  ... 13 input structures
  ... storing 606 eigenvectors for each structure
  ... dimension of x$U.subspace: ( 612x606x13 )
  ... coordinate superposition prior to NM calculation
  ... aligned eigenvectors (gap containing positions removed)
  ... estimated memory usage of final 'eNMA' object: 36.9 Mb


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  |
  |================================================================      |  85%
  |
  |======================================================================|  92%
  |
  |======================================================================| 100%
```
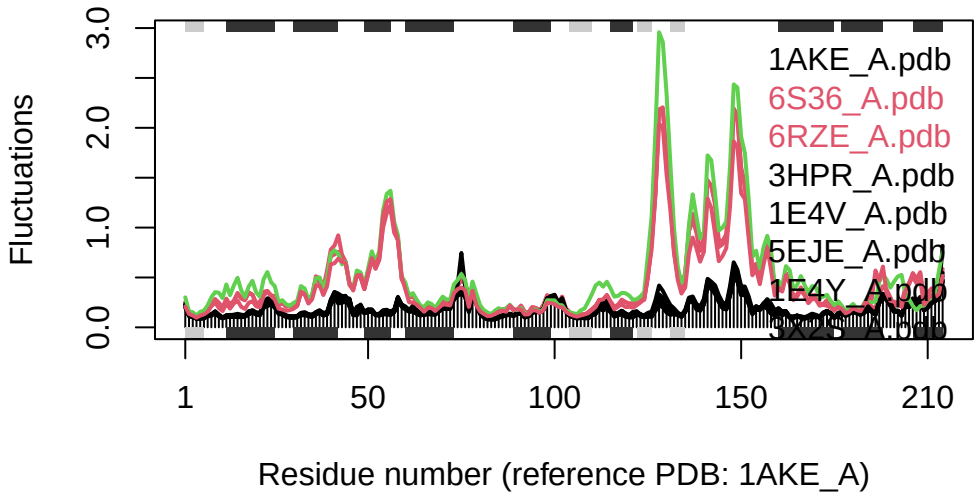

```
plot(modes, pdbs, col=grps.rd)
```

```
Extracting SSE from pdbs$sse attribute
```



Q14. What do you note about this plot? Are the black and colored lines similar or different? Where do you think they differ most and why?

The black and colored lines are pretty different in some portions. The biggest difference is between the 125-150 residue number. This is likely because there is a difference in secondary structure.

```
uniprot <- 248838887
pdb <- 195610
pdb/uniprot*100
```

```
[1] 0.0786091
```

Know way more sequences than structures bc structure determination is expensive.