Class 9: Structural Bioinformatics 1

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The main database for structural data is called PDB (Protein Databank), let's see what it contains

Data from: https://www.rcsb.org/stats

```
pdbdb<- read.csv("PDB_stats.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
```

```
pdbdb$Total
```

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

I need to remove the commas and convert to numberic in order to do math:

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

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

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

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

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

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

Test it

```
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("PDB_stats.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.
```

```
pdbdb
```

```
```

```
# A tibble: 6 × 8
  `Molecular Type`   `X-ray`    EM   NMR `Multiple methods` Neutron Other  Total
  <chr>                <dbl> <dbl> <dbl>              <dbl>   <dbl> <dbl>  <dbl>
1 Protein (only)      167192 15572 12529                208      77    32 195610
2 Protein/Oligosacc…    9639  2635    34                  8       2     0  12318
3 Protein/NA            8730  4697   286                  7       0     0  13720
4 Nucleic acid (onl…    2869   137  1507                 14       3     1   4531
5 Other                  170    10    33                  0       0     0    213
6 Oligosaccharide (…      11     0     6                  1       0     4     22
```

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
```

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

```
percentage <- (pdbdb[1, 8] / sum(pdbdb$Total)) * 100
percentage
```

```
     Total
1 86.39483
```

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?

There are currently 4,563 structures of HIV-1 in PDB database.

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

Accessed via: https://molstar.org/viewer/.

We will use PDB code: 1HSG

Figure 1: A first image from molestar of HIV-1 protease

Some more images from molestar:

Figure 2: A second image from molestar with D25 amino acid displayed

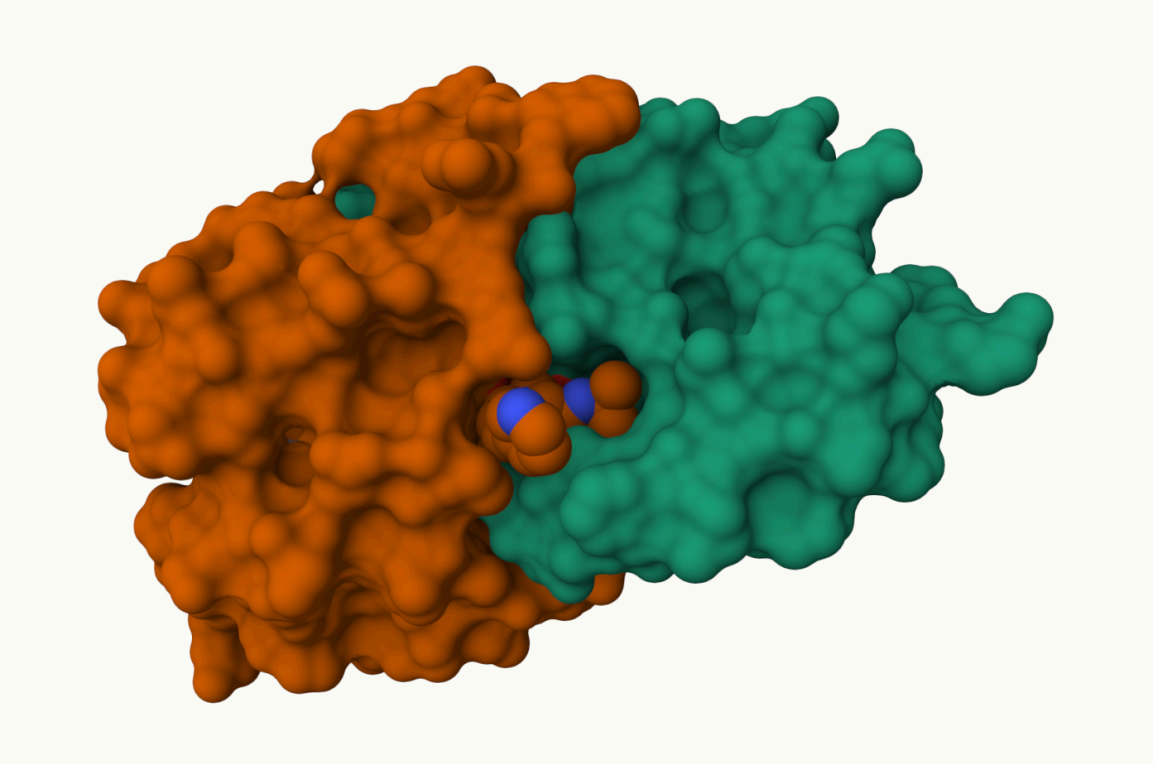


Figure 3: A third image from molestar with spacefill added to show tight binding sight with drug

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

We do not see the hydrogen atoms of the water molecules and only see the oxygen atoms because if we were to see all the atoms, including the hydrogen atoms on all the other molecules of the protein structure, it would make the visual way to crowded and complicated, obscuring the view of the important structures such as side chains and binding pockets. Furthermore, we can still identify bonds as the hydrogens contribute very little to the specific interactions formed within the protein structure.

> 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

This is water molecule 308 and is critical within the binding site as it bind/stabilizes the ligand within the protein.

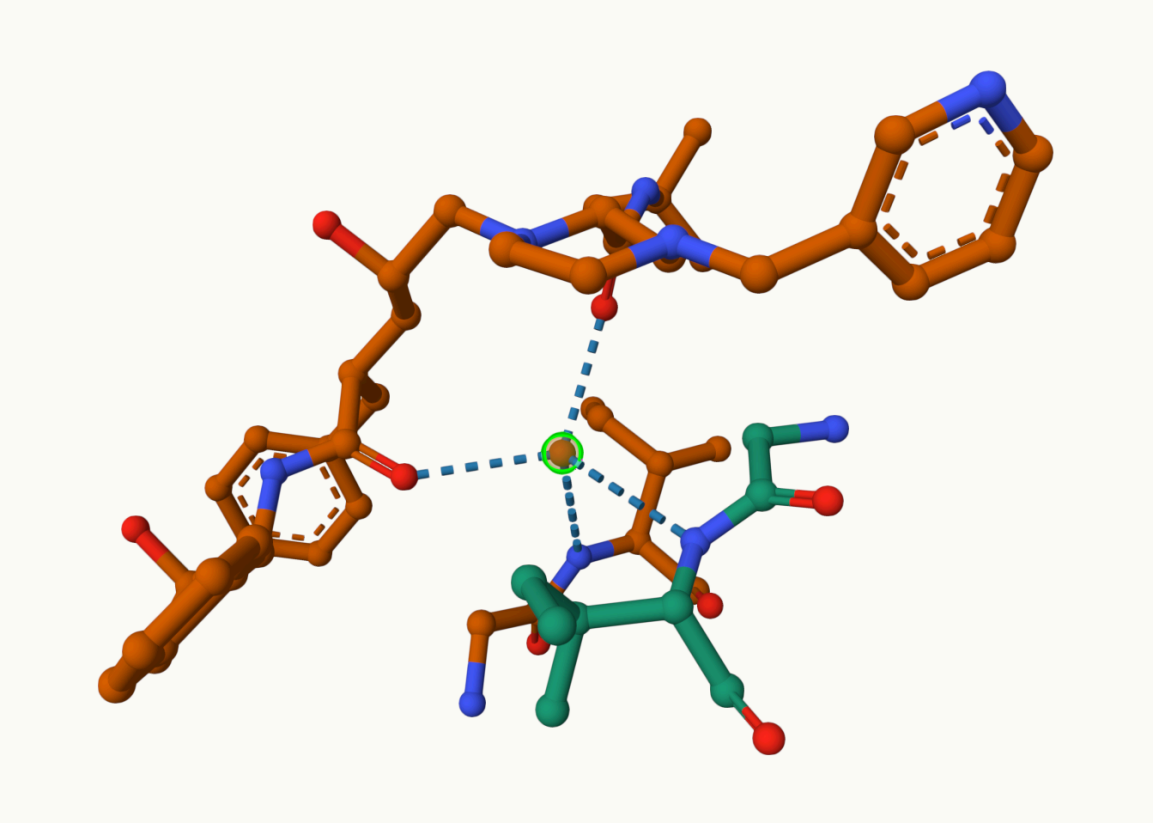


Figure 4: An image identifying the critical water molecule in the binding site

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.

Figure 5: An image identifying the critical water, both chains, the ligand, and D25 residues of both chains

The Bio3D package

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

Lets start with how it can read these PDB files:

```
library(bio3d)
```

```
Warning: package 'bio3d' was built under R version 4.3.3
```

```
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
```

This pdb object has 198 amino acid residues

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

HOH and MK1 are the two non-protein residues

Q9: How many protein chains are in this structure?

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

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

2 protein chains are in this structure

Predicting functional motions of a single structure

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

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

```
adk
```

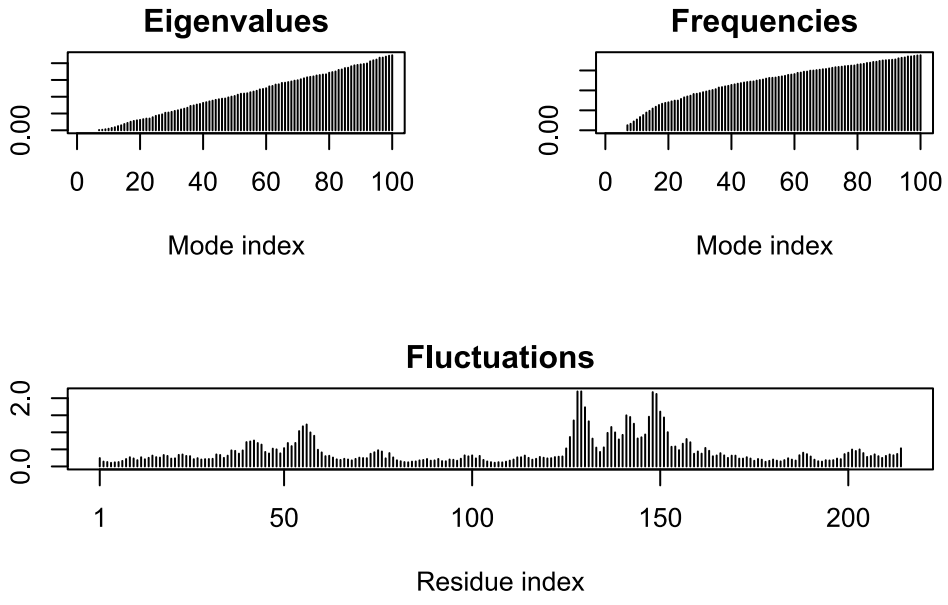
```

 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 0.34 seconds.
```

```
plot(m)
```



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

```
mktrj(m, file="adk_m7.pdb")
```

I can open this in Mol* to play the trajectory

Comparative Structure Analysis of Adenylate Kinase

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

Package “msa” only found on BioConductor

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

Package “Bio3d” not found on either BioConductor or CRAN

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

True

```
library(bio3d)
aa <- get.seq("1ake_A")
```

```
Warning in get.seq("1ake_A"): Removing existing file: seqs.fasta
```

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

```
aa
```

```
             1        .         .         .         .         .         60
pdb|1AKE|A   MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
             1        .         .         .         .         .         60

            61        .         .         .         .         .         120
pdb|1AKE|A   DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDRI
            61        .         .         .         .         .         120

           121        .         .         .         .         .         180
pdb|1AKE|A   VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
           121        .         .         .         .         .         180

           181        .         .         .   214
```

```
pdb|1AKE|A   YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG
           181        .         .         .   214

Call:
  read.fasta(file = outfile)

Class:
  fasta

Alignment dimensions:
  1 sequence rows; 214 position columns (214 non-gap, 0 gap)

+ attr: id, ali, call
```

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

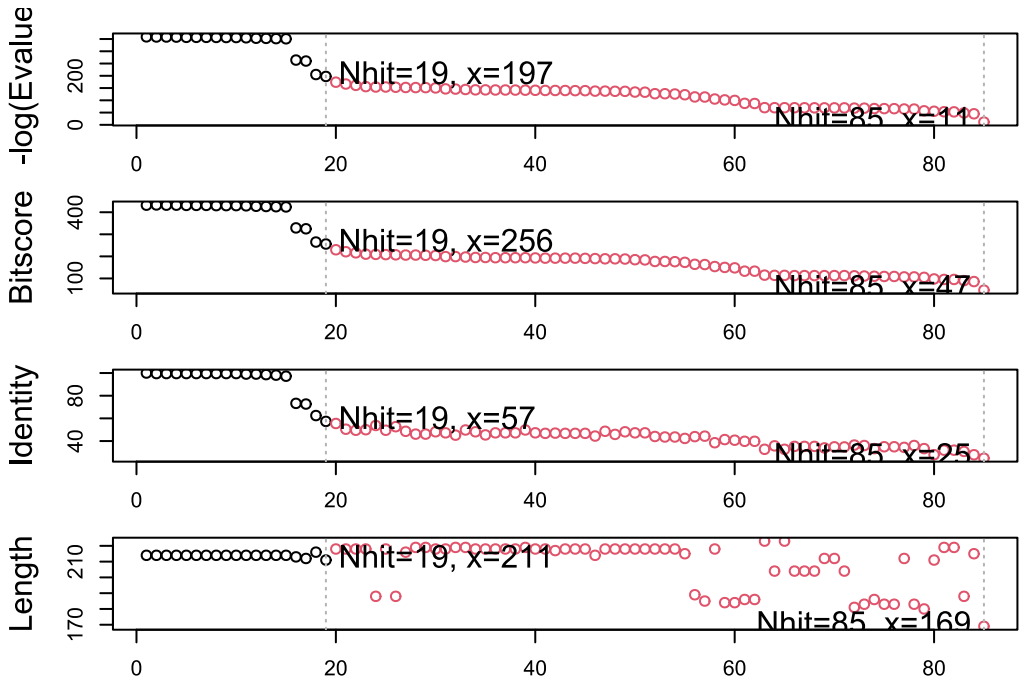
There are 214 amino acids that make up the sequence according to the output seq above.

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

```
 Searching ... please wait (updates every 5 seconds) RID = JGYYM7N6016
 ....
 Reporting 85 hits
```

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

```
  * Possible cutoff values:    197 11
            Yielding Nhits:    19 85

  * Chosen cutoff value of:    197
            Yielding Nhits:    19
```




```
head(hits$pdb.id)
```

```
[1] "1AKE_A" "8BQF_A" "4X8M_A" "6S36_A" "8Q2B_A" "8RJ9_A"
```

```
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/8BQF.pdb exists. Skipping download
```

```
Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/4X8M.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/8Q2B.pdb exists. Skipping download
```

```
Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/8RJ9.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/4X8H.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/4NP6.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
```

```
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  |
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```

```
  |
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```

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

```
Reading PDB files:
pdbs/split_chain/1AKE_A.pdb
pdbs/split_chain/8BQF_A.pdb
pdbs/split_chain/4X8M_A.pdb
pdbs/split_chain/6S36_A.pdb
pdbs/split_chain/8Q2B_A.pdb
pdbs/split_chain/8RJ9_A.pdb
pdbs/split_chain/6RZE_A.pdb
pdbs/split_chain/4X8H_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/4NP6_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
..   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/8BQF_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 3   name: pdbs/split_chain/4X8M_A.pdb
pdb/seq: 4   name: pdbs/split_chain/6S36_A.pdb
```

```
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 5   name: pdbs/split_chain/8Q2B_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 6   name: pdbs/split_chain/8RJ9_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 7   name: pdbs/split_chain/6RZE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 8   name: pdbs/split_chain/4X8H_A.pdb
pdb/seq: 9   name: pdbs/split_chain/3HPR_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 10   name: pdbs/split_chain/1E4V_A.pdb
pdb/seq: 11   name: pdbs/split_chain/5EJE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 12   name: pdbs/split_chain/1E4Y_A.pdb
pdb/seq: 13   name: pdbs/split_chain/3X2S_A.pdb
pdb/seq: 14   name: pdbs/split_chain/6HAP_A.pdb
pdb/seq: 15   name: pdbs/split_chain/6HAM_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 16   name: pdbs/split_chain/4K46_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 17   name: pdbs/split_chain/4NP6_A.pdb
pdb/seq: 18   name: pdbs/split_chain/3GMT_A.pdb
pdb/seq: 19   name: pdbs/split_chain/4PZL_A.pdb
```

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

# Draw schematic alignment (Will not format to pdf - only code shown)
##plot(pdbs, labels=ids)
```

```
#Annotate PDB Structures
anno <- pdb.annotate(ids)
unique(anno$source)
```

```
[1] "Escherichia coli"
[2] "Escherichia coli K-12"
[3] "Escherichia coli O139:H28 str. E24377A"
[4] "Escherichia coli str. K-12 substr. MDS42"
[5] "Photobacterium profundum"
[6] "Vibrio cholerae O1 biovar El Tor str. N16961"
[7] "Burkholderia pseudomallei 1710b"
[8] "Francisella tularensis subsp. tularensis SCHU S4"
```

```
anno
```

```
       structureId chainId macromoleculeType chainLength experimentalTechnique
1AKE_A        1AKE       A           Protein         214                 X-ray
8BQF_A        8BQF       A           Protein         234                 X-ray
4X8M_A        4X8M       A           Protein         214                 X-ray
6S36_A        6S36       A           Protein         214                 X-ray
8Q2B_A        8Q2B       A           Protein         214                 X-ray
8RJ9_A        8RJ9       A           Protein         214                 X-ray
6RZE_A        6RZE       A           Protein         214                 X-ray
4X8H_A        4X8H       A           Protein         214                 X-ray
3HPR_A        3HPR       A           Protein         214                 X-ray
1E4V_A        1E4V       A           Protein         214                 X-ray
5EJE_A        5EJE       A           Protein         214                 X-ray
1E4Y_A        1E4Y       A           Protein         214                 X-ray
3X2S_A        3X2S       A           Protein         214                 X-ray
6HAP_A        6HAP       A           Protein         214                 X-ray
6HAM_A        6HAM       A           Protein         214                 X-ray
4K46_A        4K46       A           Protein         214                 X-ray
4NP6_A        4NP6       A           Protein         217                 X-ray
3GMT_A        3GMT       A           Protein         230                 X-ray
4PZL_A        4PZL       A           Protein         242                 X-ray
       resolution       scopDomain                                      pfam
1AKE_A      2.000 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
8BQF_A      2.050             <NA> Adenylate kinase, active site lid (ADK_lid)
4X8M_A      2.600             <NA> Adenylate kinase, active site lid (ADK_lid)
6S36_A      1.600             <NA> Adenylate kinase, active site lid (ADK_lid)
8Q2B_A      1.760             <NA>                      Adenylate kinase (ADK)
8RJ9_A      1.590             <NA> Adenylate kinase, active site lid (ADK_lid)
6RZE_A      1.690             <NA>                      Adenylate kinase (ADK)
4X8H_A      2.500             <NA> Adenylate kinase, active site lid (ADK_lid)
3HPR_A      2.000             <NA> Adenylate kinase, active site lid (ADK_lid)
1E4V_A      1.850 Adenylate kinase                      Adenylate kinase (ADK)
5EJE_A      1.900             <NA> Adenylate kinase, active site lid (ADK_lid)
1E4Y_A      1.850 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
3X2S_A      2.800             <NA>                      Adenylate kinase (ADK)
6HAP_A      2.700             <NA>                      Adenylate kinase (ADK)
6HAM_A      2.550             <NA> Adenylate kinase, active site lid (ADK_lid)
4K46_A      2.010             <NA> Adenylate kinase, active site lid (ADK_lid)
4NP6_A      2.004             <NA>                      Adenylate kinase (ADK)
3GMT_A      2.100             <NA> Adenylate kinase, active site lid (ADK_lid)
4PZL_A      2.100             <NA>                      Adenylate kinase (ADK)
             ligandId
1AKE_A            AP5
8BQF_A            AP5
4X8M_A           <NA>
6S36_A CL (3),NA,MG (2)
8Q2B_A     AP5,SO4,MPO
8RJ9_A         ADP (2)
6RZE_A   NA (3),CL (2)
```

```
4X8H_A             <NA>
3HPR_A              AP5
1E4V_A              AP5
5EJE_A           AP5,CO
1E4Y_A              AP5
3X2S_A   JPY (2),AP5,MG
6HAP_A              AP5
6HAM_A              AP5
4K46_A      ADP,AMP,PO4
4NP6_A             <NA>
3GMT_A          SO4 (2)
4PZL_A       CA,FMT,GOL
                                                                                ligandName
1AKE_A                                                                BIS(ADENOSINE)-5'-
PENTAPHOSPHATE
8BQF_A                                                                BIS(ADENOSINE)-5'-
PENTAPHOSPHATE
4X8M_A                                                                                <NA>
6S36_A                                        CHLORIDE ION (3),SODIUM ION,MAGNESIUM
ION (2)
8Q2B_A   BIS(ADENOSINE)-5'-PENTAPHOSPHATE,SULFATE   ION,3[N-MORPHOLINO]PROPANE
SULFONIC ACID
8RJ9_A                                                                    ADENOSINE-5'-
DIPHOSPHATE (2)
6RZE_A                                                       SODIUM ION (3),CHLORIDE
ION (2)
4X8H_A                                                                            <NA>
3HPR_A                                                                BIS(ADENOSINE)-5'-
PENTAPHOSPHATE
1E4V_A                                                                BIS(ADENOSINE)-5'-
PENTAPHOSPHATE
5EJE_A                                     BIS(ADENOSINE)-5'-PENTAPHOSPHATE,COBALT
(II) ION
1E4Y_A                                                                BIS(ADENOSINE)-5'-
PENTAPHOSPHATE
3X2S_A              N-(pyren-1-ylmethyl)acetamide       (2),BIS(ADENOSINE)-5'-
PENTAPHOSPHATE,MAGNESIUM ION
6HAP_A                                                                BIS(ADENOSINE)-5'-
PENTAPHOSPHATE
6HAM_A                                                                BIS(ADENOSINE)-5'-
PENTAPHOSPHATE
4K46_A              ADENOSINE-5'-DIPHOSPHATE,ADENOSINE MONOPHOSPHATE,PHOSPHATE
ION
4NP6_A                                                                            <NA>
3GMT_A                                                                         SULFATE
ION (2)
4PZL_A                                                                CALCIUM ION,FORMIC
ACID,GLYCEROL
```

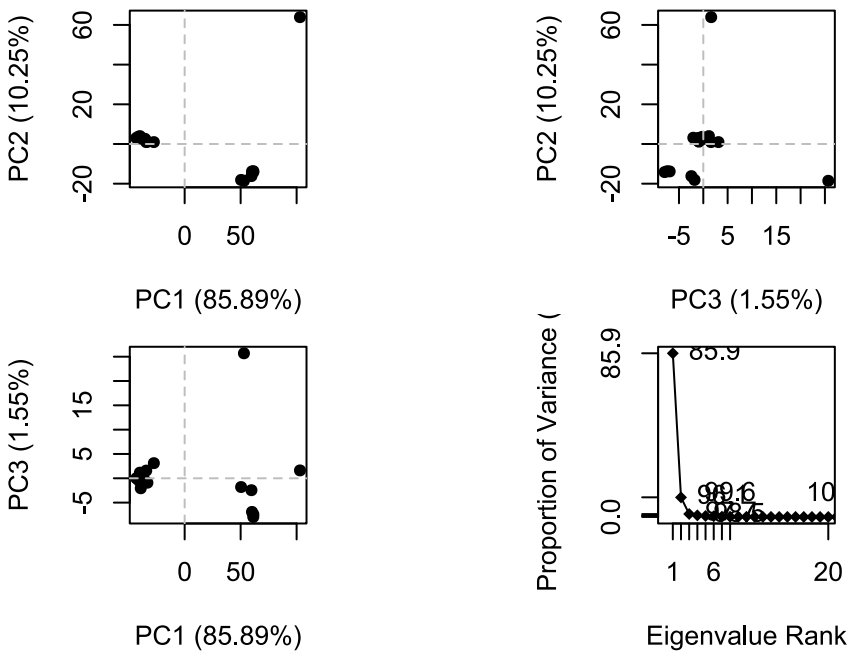
```
                                                source
1AKE_A                                  Escherichia coli
8BQF_A                                  Escherichia coli
4X8M_A                                  Escherichia coli
6S36_A                                  Escherichia coli
8Q2B_A                                  Escherichia coli
8RJ9_A                                  Escherichia coli
6RZE_A                                  Escherichia coli
4X8H_A                                  Escherichia coli
3HPR_A                               Escherichia coli K-12
1E4V_A                                  Escherichia coli
5EJE_A            Escherichia coli O139:H28 str. E24377A
1E4Y_A                                  Escherichia coli
3X2S_A          Escherichia coli str. K-12 substr. MDS42
6HAP_A            Escherichia coli O139:H28 str. E24377A
6HAM_A                               Escherichia coli K-12
4K46_A                            Photobacterium profundum
4NP6_A     Vibrio cholerae O1 biovar El Tor str. N16961
3GMT_A                   Burkholderia pseudomallei 1710b
4PZL_A Francisella tularensis subsp. tularensis SCHU S4

structureTitle
1AKE_A STRUCTURE OF THE COMPLEX BETWEEN ADENYLATE KINASE FROM ESCHERICHIA COLI
AND THE INHIBITOR AP5A REFINED AT 1.9 ANGSTROMS RESOLUTION: A MODEL FOR A
CATALYTIC TRANSITION STATE
8BQF_A
Adenylate Kinase L107I MUTANT
4X8M_A
Crystal structure of E. coli Adenylate kinase Y171W mutant
6S36_A
Crystal structure of E. coli Adenylate kinase R119K mutant
8Q2B_A                                                          E. coli Adenylate
Kinase variant D158A (AK D158A) showing significant changes to the stacking of
catalytic arginine side chains
8RJ9_A                                                                  E. coli
adenylate kinase Asp84Ala variant in complex with two ADP molecules as a result
of enzymatic AP4A hydrolysis.
6RZE_A
Crystal structure of E. coli Adenylate kinase R119A mutant
4X8H_A
Crystal structure of E. coli Adenylate kinase P177A mutant
3HPR_A                                                                  Crystal
structure of V148G adenylate kinase from E. coli, in complex with Ap5A
1E4V_A
Mutant G10V of adenylate kinase from E. coli, modified in the Gly-loop
5EJE_A                                                                  Crystal
structure of E. coli Adenylate kinase G56C/T163C double mutant in complex with
Ap5a
```

```
1E4Y_A
Mutant P9L of adenylate kinase from E. coli, modified in the Gly-loop
3X2S_A
Crystal structure of pyrene-conjugated adenylate kinase
6HAP_A
Adenylate kinase
6HAM_A
Adenylate kinase
4K46_A
Crystal Structure of Adenylate Kinase from Photobacterium profundum
4NP6_A
Crystal Structure of Adenylate Kinase from Vibrio cholerae O1 biovar eltor
3GMT_A
Crystal structure of adenylate kinase from burkholderia pseudomallei
4PZL_A                                                                  The crystal
structure of adenylate kinase from Francisella tularensis subsp. tularensis SCHU
S4
                                                        citation rObserved   rFree
1AKE_A                 Muller, C.W., et al. J Mol Biol (1992)   0.19600      NA
8BQF_A   Scheerer, D., et al. Proc Natl Acad Sci U S A (2023)   0.22073 0.25789
4X8M_A                Kovermann, M., et al. Nat Commun (2015)   0.24910 0.30890
6S36_A                  Rogne, P., et al. Biochemistry (2019)   0.16320 0.23560
8Q2B_A                Nam, K., et al. J Chem Inf Model (2024)   0.18320 0.22440
8RJ9_A                         Nam, K., et al. Sci Adv (2024)   0.15190 0.20290
6RZE_A                  Rogne, P., et al. Biochemistry (2019)   0.18650 0.23500
4X8H_A                Kovermann, M., et al. Nat Commun (2015)   0.19610 0.28950
3HPR_A  Schrank, T.P., et al. Proc Natl Acad Sci U S A (2009)   0.21000 0.24320
1E4V_A                   Muller, C.W., et al. Proteins (1993)   0.19600      NA
5EJE_A  Kovermann, M., et al. Proc Natl Acad Sci U S A (2017)   0.18890 0.23580
1E4Y_A                   Muller, C.W., et al. Proteins (1993)   0.17800      NA
3X2S_A                Fujii, A., et al. Bioconjug Chem (2015)   0.20700 0.25600
6HAP_A               Kantaev, R., et al. J Phys Chem B (2018)   0.22630 0.27760
6HAM_A               Kantaev, R., et al. J Phys Chem B (2018)   0.20511 0.24325
4K46_A                    Cho, Y.-J., et al. To be published    0.17000 0.22290
4NP6_A                       Kim, Y., et al. To be published    0.18800 0.22200
3GMT_A Buchko, G.W., et al. Biochem Biophys Res Commun (2010)   0.23800 0.29500
4PZL_A                       Tan, K., et al. To be published    0.19360 0.23680
         rWork spaceGroup
1AKE_A 0.19600  P 21 2 21
8BQF_A 0.21882  P 2 21 21
4X8M_A 0.24630    C 1 2 1
6S36_A 0.15940    C 1 2 1
8Q2B_A 0.18100   P 1 21 1
8RJ9_A 0.15010  P 21 21 2
6RZE_A 0.18190    C 1 2 1
4X8H_A 0.19140    C 1 2 1
3HPR_A 0.20620  P 21 21 2
1E4V_A 0.19600  P 21 2 21
```

```
5EJE_A 0.18630  P 21 2 21
1E4Y_A 0.17800   P 1 21 1
3X2S_A 0.20700 P 21 21 21
6HAP_A 0.22370    I 2 2 2
6HAM_A 0.20311       P 43
4K46_A 0.16730 P 21 21 21
4NP6_A 0.18600       P 43
3GMT_A 0.23500   P 1 21 1
4PZL_A 0.19130       P 32
```

Principle Component Analysis

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

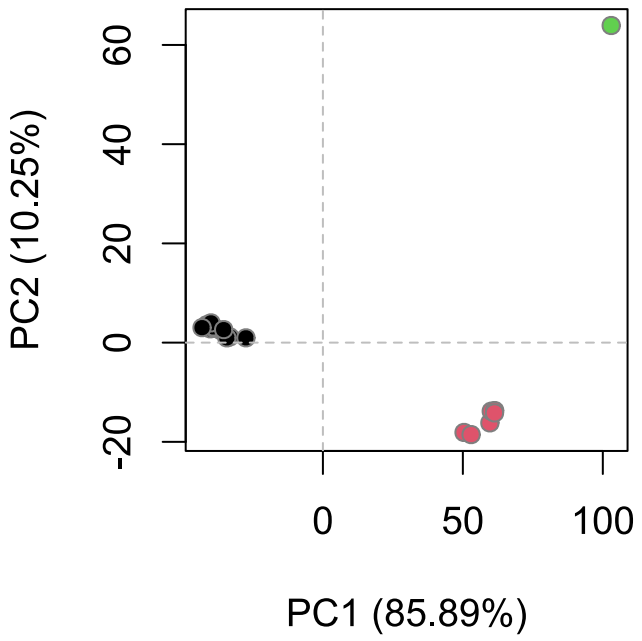



```
# Calculate RMSD
rd <- rmsd(pdbs)
```

```
Warning in rmsd(pdbs): No indices provided, using the 199 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)
```




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

```
Warning: package 'ggplot2' was built under R version 4.3.3
```

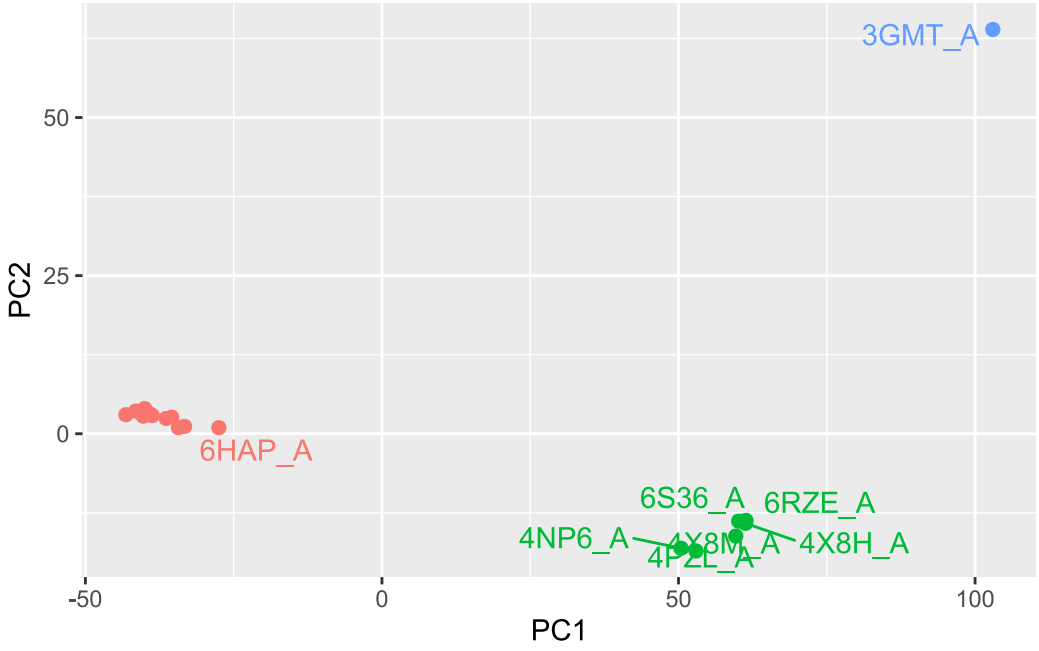
```
library(ggrepel)
```

```
Warning: package 'ggrepel' was built under R version 4.3.3
```

```
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
```

```
Warning: ggrepel: 11 unlabeled data points (too many overlaps). Consider
increasing max.overlaps
```




```
# Normal Mode Analysis of all structures
modes <- nma(pdbs)
```

```
Warning in nma.pdbs(pdbs): 8BQF_A.pdb might have missing residue(s) in structure:
   Fluctuations at neighboring positions may be affected.
```

```
Details of Scheduled Calculation:
  ... 19 input structures
  ... storing 591 eigenvectors for each structure
  ... dimension of x$U.subspace: ( 597x591x19 )
  ... coordinate superposition prior to NM calculation
  ... aligned eigenvectors (gap containing positions removed)
  ... estimated memory usage of final 'eNMA' object: 51.3 Mb


  |
```

```
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  |======================================================================| 100%
```
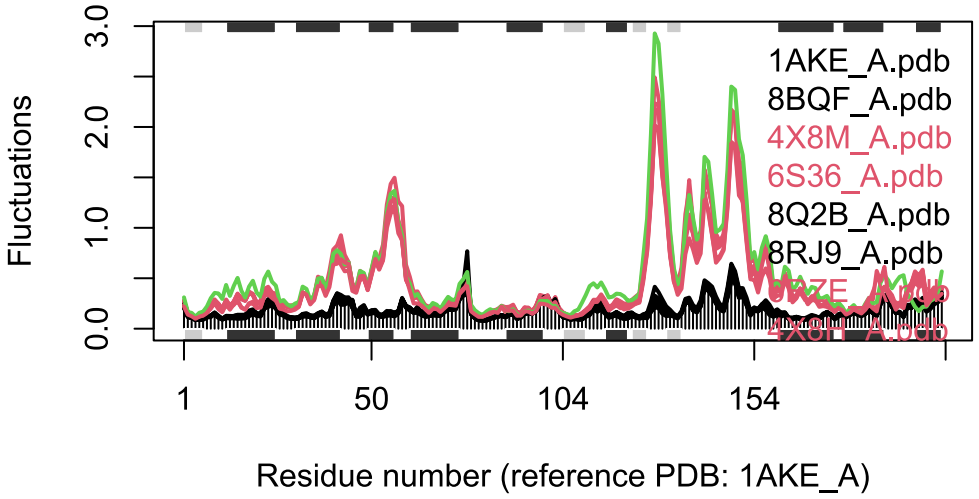

```
plot(modes, pdbs, col=grps.rd)
```

```
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?

I notice that this plot may show distinct configurations of the protein of interest based on the activities of the black and colored lines. These lines are different as the colored lines represent more peaks and troughs compared to the black line which exhibits much less fluctuations and peak variability. This difference could be in leu of the greater conformations present in one region versus the other as we saw previously where certain structures of the protein are flexible and can change its conformation and possibly alter its activity as well.