Class 10: Structural Bioinformatics (Pt. 1)

Clarissa Savko (PID:A69028482)

```
pdb_data <- read.csv("Data Export Summary.csv")
```

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

```
pdb_data$Total <- as.numeric(sub("," ,"" , pdb_data$Total))
pdb_data$X.ray <- as.numeric(sub("," ,"" , pdb_data$X.ray))
pdb_data$EM <- as.numeric(sub("," ,"" , pdb_data$EM))
total_structures <- sum(pdb_data$Total)
total_X.ray <- sum(pdb_data$X.ray)
total_EM <- sum(pdb_data$EM)
(total_X.ray + total_EM) / total_structures * 100
```

```
[1] 93.15962
```

93.16% of structures in the PDB are solved by X-ray and electron microscopy.

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

```
(pdb_data$Total[1]/total_structures) *100
```

```
[1] 86.67026
```

86.67% of structures in the PDB are protein.

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 7,434 HIV-1 protease structures in the current PDB.

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

Mol* is only showing the oxygen atom.

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

H20 308 seems to be the most involved 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.

```
library(imager)
```

```
Warning: package 'imager' was built under R version 4.3.2
```

```
Loading required package: magrittr
```

```

Attaching package: 'imager'
```

```
The following object is masked from 'package:magrittr':

    add
```

```
The following objects are masked from 'package:stats':

    convolve, spectrum
```

```
The following object is masked from 'package:graphics':

    frame
```

```
The following object is masked from 'package:base':

    save.image
```

```
molstar <- load.image("1HSG.png")
molstar
```

```
Image. Width: 1280 pix Height: 720 pix Depth: 1 Colour channels: 4
```

```
library(bio3d)
```

```
Warning: package 'bio3d' was built under R version 4.3.2
```

```
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
```

Q7: How many amino acid residues are there in this pdb object? There are 128 amino acid residues. Q8: Name one of the two non-protein residues? Mk1 is a non-protein residue. Q9: How many protein chains are in this structure? There are 2 protein chains in this structure.

```
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>
```

```
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) ]

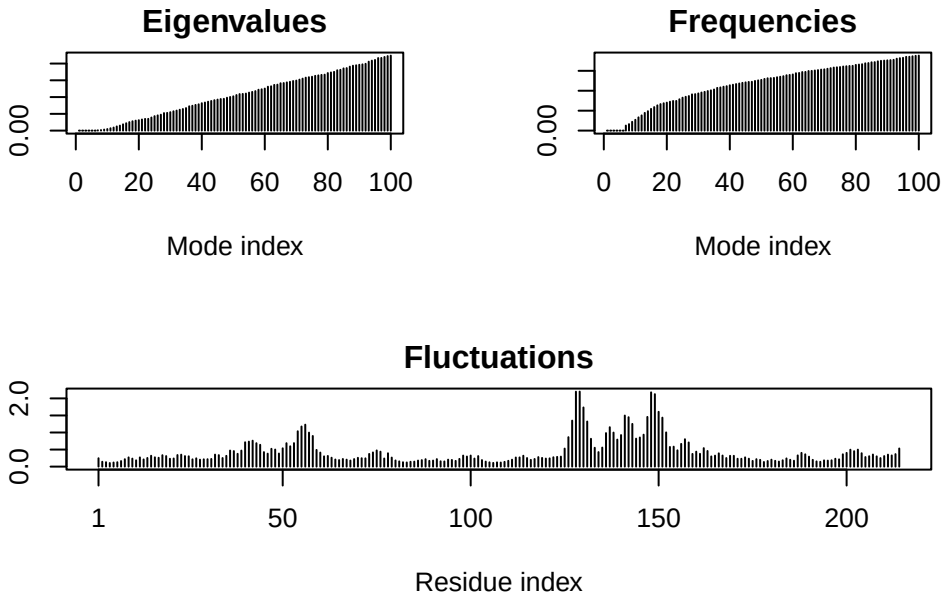
   Protein sequence:
      MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
      DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDKI
      VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG

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

```
m <- nma(adk)
```

```
 Building Hessian...        Done in 0.01 seconds.
 Diagonalizing Hessian...   Done in 0.26 seconds.
```

```
plot(m)
```



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

Q10. Which of the packages above is found only on BioConductor and not CRAN? "msa" is found only on Bioconductor and not CRAN. Q11. Which of the above packages is not found on BioConductor or CRAN?: Grantlab/bio3d-view 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")
```

```
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?

214 amino acids are in this sequence.

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

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

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

```
[1] "1AKE_A" "6S36_A" "6RZE_A" "3HPR_A" "1E4V_A" "5EJE_A"
```

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

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```

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

```
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
```

```
ids <- basename.pdb(pdbs$id)
```

```
#plot(pdbs, labels=ids)
```

```
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] "Burkholderia pseudomallei 1710b"
[7] "Francisella tularensis subsp. tularensis SCHU S4"
```

```
anno
```

```
       structureId chainId macromoleculeType chainLength experimentalTechnique
1AKE_A        1AKE       A           Protein         214                X-ray
6S36_A        6S36       A           Protein         214                X-ray
6RZE_A        6RZE       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
3GMT_A	3GMT	A	Protein	230		X-ray
4PZL_A	4PZL	A	Protein	242		X-ray

	resolution	scopDomain	pfam	ligandId	ligandName
1AKE_A	2.00	Adenylate kinase	Adenylate kinase (ADK)	AP5	BIS(ADENOSINE)-5'-PENTAPHOSPHATE
6S36_A	1.60	<NA>	Adenylate kinase (ADK)	CL (3),MG (2),NA	CHLORIDE ION (3),MAGNESIUM ION (2),SODIUM ION
6RZE_A	1.69	<NA>	Adenylate kinase (ADK)	NA (3),CL (2)	SODIUM ION (3),CHLORIDE ION (2)
3HPR_A	2.00	<NA>	Adenylate kinase (ADK)	AP5	BIS(ADENOSINE)-5'-PENTAPHOSPHATE
1E4V_A	1.85	Adenylate kinase	Adenylate kinase (ADK)	AP5	BIS(ADENOSINE)-5'-PENTAPHOSPHATE
5EJE_A	1.90	<NA>	Adenylate kinase (ADK)	AP5,CO	BIS(ADENOSINE)-5'-PENTAPHOSPHATE,COBALT (II) ION
1E4Y_A	1.85	Adenylate kinase	Adenylate kinase (ADK)	AP5	BIS(ADENOSINE)-5'-PENTAPHOSPHATE
3X2S_A	2.80	<NA>	Adenylate kinase (ADK)	JPY (2),AP5,MG	N-(pyren-1-ylmethyl)acetamide (2),BIS(ADENOSINE)-5'-PENTAPHOSPHATE,MAGNESIUM ION
6HAP_A	2.70	<NA>	Adenylate kinase (ADK)	AP5	BIS(ADENOSINE)-5'-PENTAPHOSPHATE
6HAM_A	2.55	<NA>	Adenylate kinase (ADK)	AP5	BIS(ADENOSINE)-5'-PENTAPHOSPHATE
4K46_A	2.01	<NA>	Adenylate kinase (ADK)	PO4,ADP,AMP	PHOSPHATE ION,ADENOSINE-5'-DIPHOSPHATE,ADENOSINE MONOPHOSPHATE
3GMT_A	2.10	<NA>	Adenylate kinase (ADK)	SO4 (2)	SULFATE ION (2)
4PZL_A	2.10	<NA>	Adenylate kinase (ADK)	CA,FMT,GOL	CALCIUM ION,FORMIC ACID,GLYCEROL

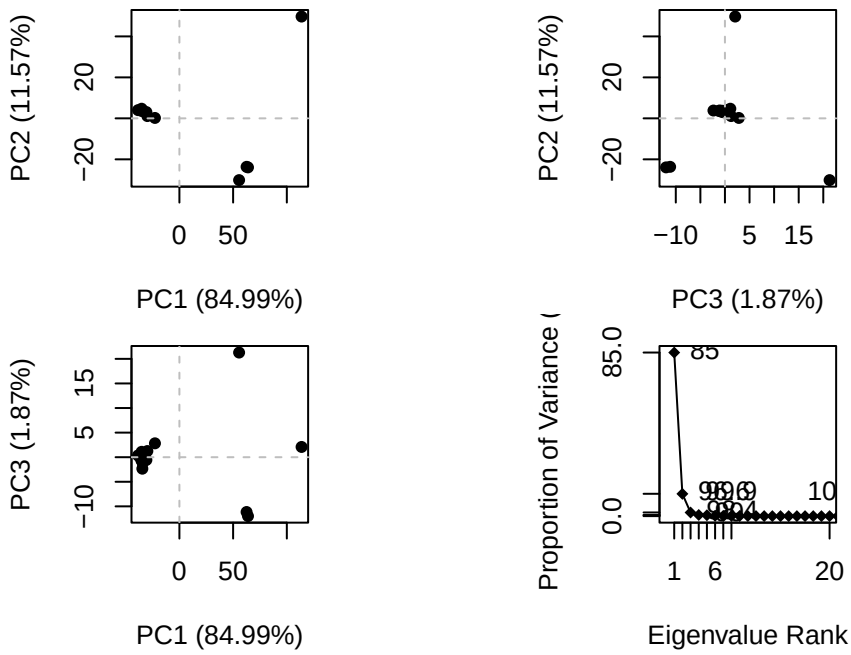
	source
1AKE_A	Escherichia coli
6S36_A	Escherichia coli
6RZE_A	Escherichia coli
3HPR_A	Escherichia coli K-12
1E4V_A	Escherichia coli
5EJE_A	Escherichia coli O139:H28 str. E24377A
1E4Y_A	Escherichia coli
3X2S_A	Escherichia coli str. K-12 substr. MDS42
6HAP_A	Escherichia coli O139:H28 str. E24377A

```
6HAM_A                            Escherichia coli K-12
4K46_A                          Photobacterium profundum
3GMT_A                   Burkholderia pseudomallei 1710b
4PZL_A Francisella tularensis subsp. tularensis SCHU S4

1AKE_A STRUCTURE OF THE COMPLEX BETWEEN ADENYLATE KINASE FROM ESCHERICHIA COLI AND THE INHIBI
6S36_A
6RZE_A
3HPR_A
1E4V_A
5EJE_A                                                                          Cryst
1E4Y_A
3X2S_A
6HAP_A
6HAM_A
4K46_A
3GMT_A
4PZL_A                                                                      The cryst
                                                    citation rObserved   rFree
1AKE_A                 Muller, C.W., et al. J Mol Biol (1992)   0.19600      NA
6S36_A                  Rogne, P., et al. Biochemistry (2019)   0.16320 0.23560
6RZE_A                  Rogne, P., et al. Biochemistry (2019)   0.18650 0.23500
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
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
6S36_A 0.15940    C 1 2 1
6RZE_A 0.18190    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
3GMT_A 0.23500   P 1 21 1
4PZL_A 0.19130       P 32
```

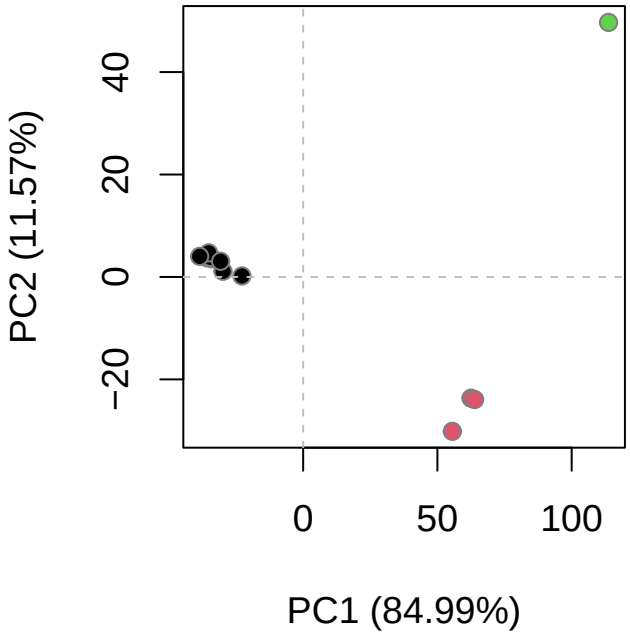
```
pc.xray <- pca(pdbs)
plot(pc.xray)
```




```
rd <- rmsd(pdbs)
```

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

```
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)
```

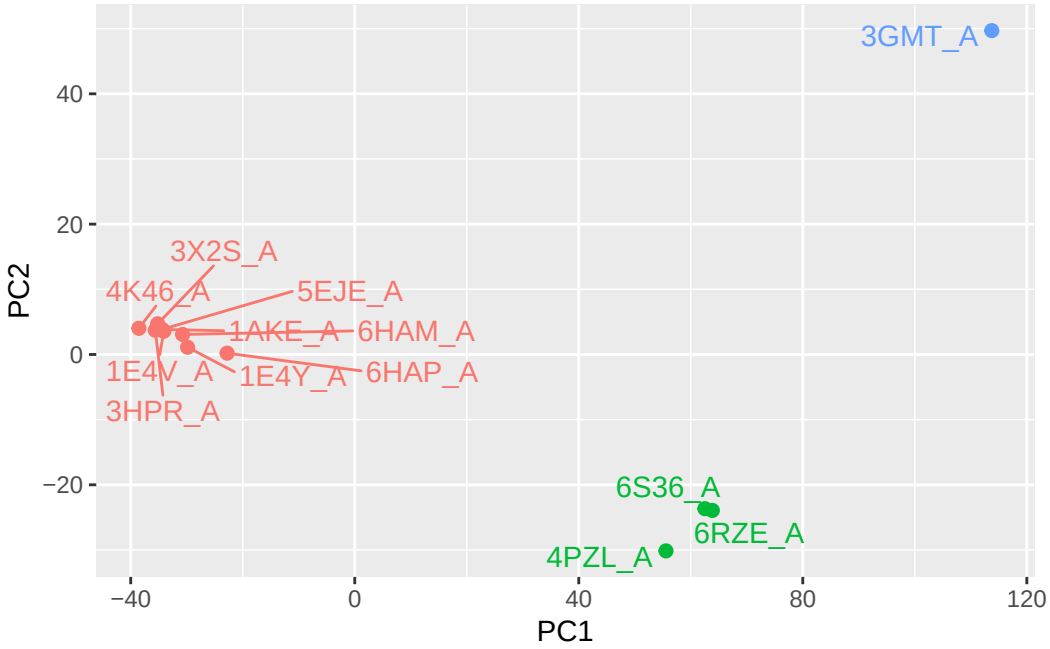



```
pc1 <- mktrj(pc.xray, pc=1, file="pc_1.pdb")
```

```
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
```




```
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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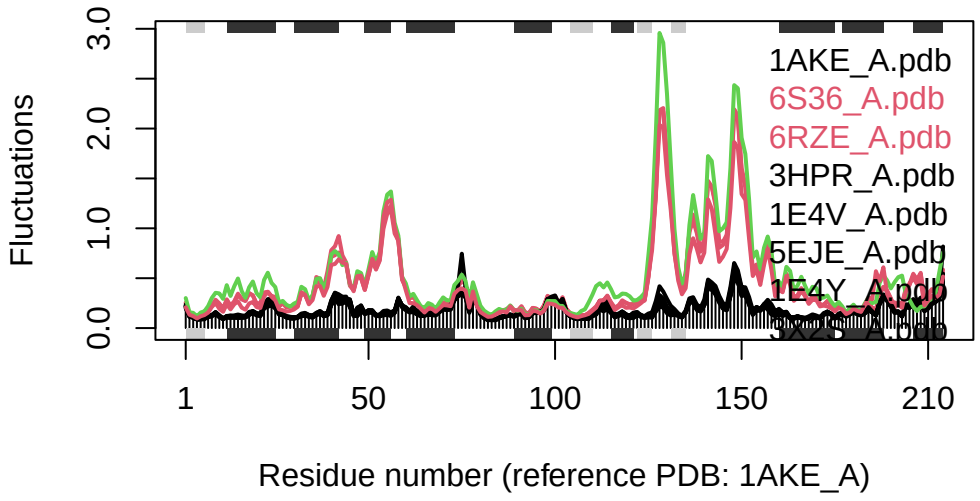
```

```
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? They are different. They seem to differ the most in between residues 104 and 154 where the colored lines reach the highest peaks (fluctuations). I think this means those residues are the most flexible.