Structural Bioinformatics Part1

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what is in the PDB anyway?

The main database of biomolecular structures is called PDB and is available at www.rcsb.org.

Let's begin by seeing what is in this database.

```
pdbstats <- read.csv("PDB.csv", row.names=1)
head(pdbstats)
```

```
                          X.ray    EM    NMR Multiple.methods Neutron Other
Protein (only)          152,809 9,421 12,117               191      72    32
Protein/Oligosaccharide   9,008 1,654     32                 7       1     0
Protein/NA                8,061 2,944    281                 6       0     0
Nucleic acid (only)       2,602    77  1,433                12       2     1
Other                       163     9     31                 0       0     0
Oligosaccharide (only)       11     0      6                 1       0     4
                          Total
Protein (only)          174,642
Protein/Oligosaccharide  10,702
Protein/NA               11,292
Nucleic acid (only)       4,127
Other                       203
Oligosaccharide (only)       22
```

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

```
# have to set as numeric, use `gsub()` function indicating what you want to remove and wha
n.xray <- sum(as.numeric(gsub(",","", pdbstats$X.ray)))
n.em <- sum(as.numeric(gsub(",","", pdbstats$EM)))
n.total <- sum(as.numeric(gsub(",","", pdbstats$Total)))
```

```
((n.xray+n.em)/n.total)*100
```

```
[1] 92.92047
```

```
# can also do
p.xray <- (n.xray/n.total)*100
p.em <- (n.em/n.total)*100

#round to 2 s.f.
round(p.xray,2)
```

```
[1] 85.9
```

```
round(p.em,2)
```

```
[1] 7.02
```

There are 1.72654×10^5 protein structures (85.9%) and 1.4105×10^4 (7.02%) EM structures in the PDB database

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

```
as.numeric(gsub(",","",pdbstats$Total))/n.total*100
```

```
[1] 86.89175473  5.32469600  5.61824587  2.05335642  0.10100105  0.01094593
```

86.89% are protein only

> 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?

It is not very straightforward to find all HIV-1 protease structures using plain text searching on the database.

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

Hydrogen is too small, need a finer resolution

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

H308

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.

A wee pic of HIV-1 Protease from Molstar How to insert: `1[*caption*](*filename*)`

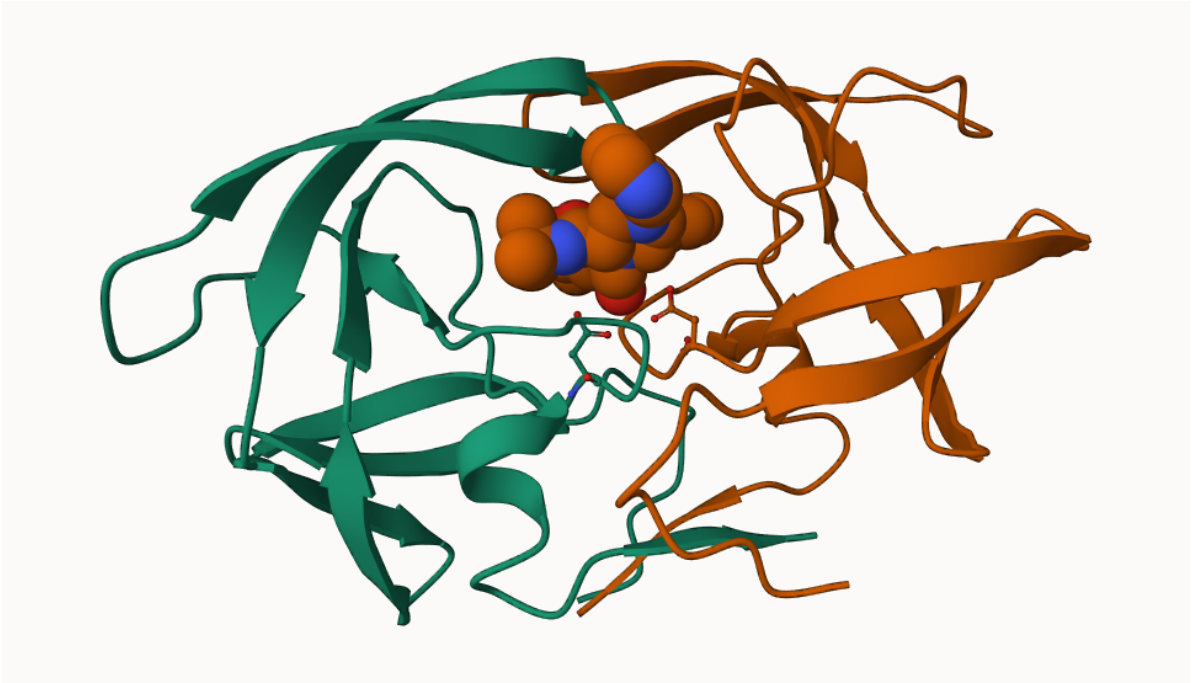


Figure 1: A image I like whilst learning how to break Molstar

Working with structure data in R

We will use the `bio3d` package for this

```
library(bio3d)
```

Read a PDB file form the online database

```
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
```

```
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>
```

What is the first residue 3 letter code?

```
pdb$atom$resid[1]
```

```
[1] "PRO"
```

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

198

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

HOH

Q9: How many protein chains are in this structure?

2

```
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>
```

Predicting functional motions of a single structure

Let's read a new PDB structure of Adenylate Kinase and perform a normal mode analysis

```
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
```

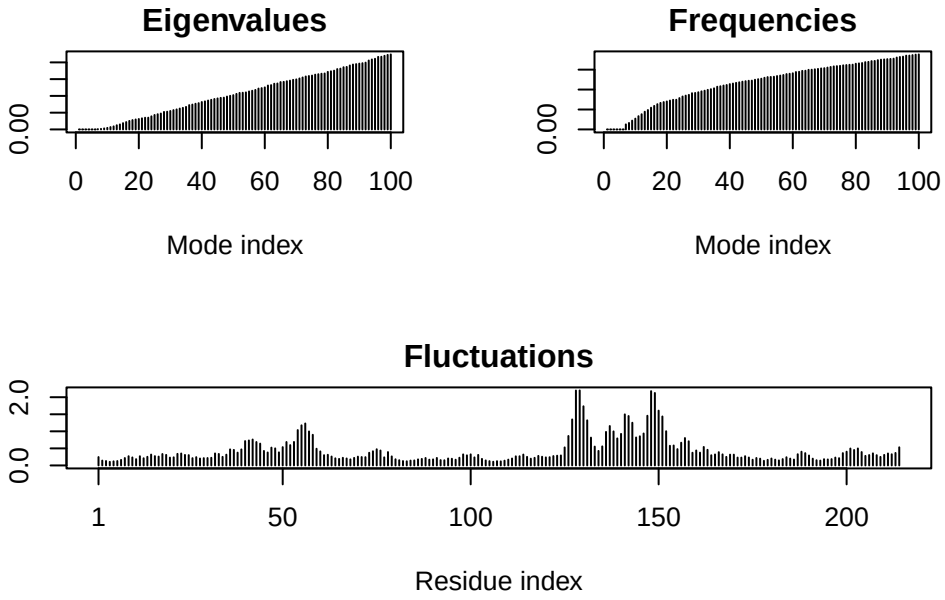
Normal mode analysis (NMA) is a structural bioinformatics method to predict protein flexibility and potential functional motions (a.k.a. conformational changes).

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

```
 Building Hessian...        Done in 0.05 seconds.
 Diagonalizing Hessian...   Done in 0.33 seconds.
```

And plot it

```
plot(m)
```



To view a "movie" of these predicted motions we can generate a molecular "trajectory" with the mktrj() function.

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

Now we can load the resulting "adk_m7.pdb" PDB into Mol* with the "Open Files" option on the right side control panel. Once loaded click the "play" button to see a movie (see image below). We will discuss how this method works at the end of this lab when we apply it across a large set of homologous structures.

Section 4. Comparative Structure Analysis

Today we are continuing where we left off last day, building towards completing the loop from biomolecular structural data to our new analysis methods like PCA and clustering.

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

"msa" is a package that is not found on CRAN and only on BioConductor.

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

"bio3d-view" (same as molstar)

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

True

We will begin with getting the protein sequence of the protein family of interest

```
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?

214 amino acids

Now we can use this sequence as a query to BLAST search the PDB to find similar sequences and structures.

```
# Blast or hmmer search (use # to prevent it to run over and over again)
#b <- blast.pdb(aa)
```

I could save and load my blast results next time so that I don't need to run the search every time.

```
#saveRDS(b, file="blast_results.RDS")
```

Next time if I want to load it, I can use

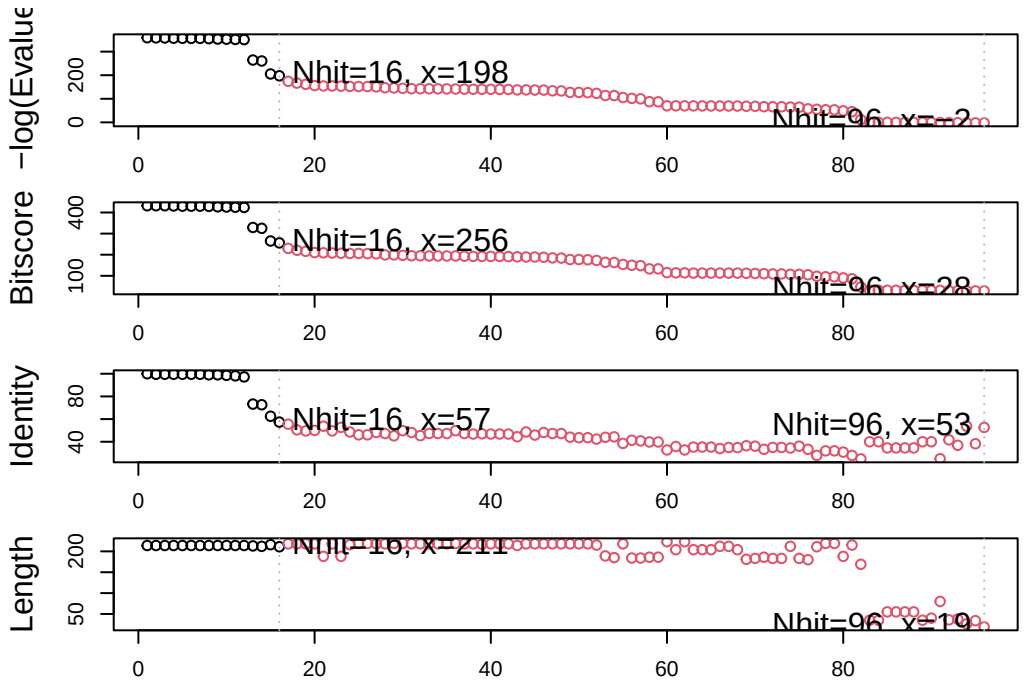
```
b <- readRDS("blast_results.RDS")
```

A summary plot of our BLAST results

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

```
  * Possible cutoff values:    197 -3
            Yielding Nhits:    16 96

  * Chosen cutoff value of:    197
            Yielding Nhits:    16
```




```
hits$pdb.id
```

```
[1] "1AKE_A" "4X8M_A" "6S36_A" "6RZE_A" "4X8H_A" "3HPR_A" "1E4V_A" "5EJE_A"
[9] "1E4Y_A" "3X2S_A" "6HAP_A" "6HAM_A" "4K46_A" "4NP6_A" "3GMT_A" "4PZL_A"
```

```
# 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/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/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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  |====================================================                  |  75%
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  |
  |================================================================      |  88%
  |
  |====================================================================  |  94%
  |
  |======================================================================| 100%
```

Next we are going to align and superpose all of the structures

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

```
Reading PDB files:
```

```
pdbs/split_chain/1AKE_A.pdb
pdbs/split_chain/4X8M_A.pdb
pdbs/split_chain/6S36_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
....

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/4X8M_A.pdb
pdb/seq: 3   name: pdbs/split_chain/6S36_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 4   name: pdbs/split_chain/6RZE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 5   name: pdbs/split_chain/4X8H_A.pdb
pdb/seq: 6   name: pdbs/split_chain/3HPR_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 7   name: pdbs/split_chain/1E4V_A.pdb
pdb/seq: 8   name: pdbs/split_chain/5EJE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 9   name: pdbs/split_chain/1E4Y_A.pdb
pdb/seq: 10   name: pdbs/split_chain/3X2S_A.pdb
pdb/seq: 11   name: pdbs/split_chain/6HAP_A.pdb
```

```
pdb/seq: 12   name: pdbs/split_chain/6HAM_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 13   name: pdbs/split_chain/4K46_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 14   name: pdbs/split_chain/4NP6_A.pdb
pdb/seq: 15   name: pdbs/split_chain/3GMT_A.pdb
pdb/seq: 16   name: pdbs/split_chain/4PZL_A.pdb
```

Run `pdbs`

```
pdbs
```

```
                                 1        .         .         .        40
[Truncated_Name:1]1AKE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:2]4X8M_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:3]6S36_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:4]6RZE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:5]4X8H_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:6]3HPR_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:7]1E4V_A.pdb     ----------MRIILLGAPVAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:8]5EJE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:9]1E4Y_A.pdb     ----------MRIILLGALVAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:10]3X2S_A.pdb    ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:11]6HAP_A.pdb    ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:12]6HAM_A.pdb    ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:13]4K46_A.pdb    ----------MRIILLGAPGAGKGTQAQFIMAKFGIPQIS
[Truncated_Name:14]4NP6_A.pdb    --------NAMRIILLGAPGAGKGTQAQFIMEKFGIPQIS
[Truncated_Name:15]3GMT_A.pdb    ----------MRLILLGAPGAGKGTQANFIKEKFGIPQIS
[Truncated_Name:16]4PZL_A.pdb    TENLYFQSNAMRIILLGAPGAGKGTQAKIIEQKYNIAHIS
                                           **^*****  *******  *  *^ *  **
                                 1        .         .         .        40

                                41        .         .         .        80
[Truncated_Name:1]1AKE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:2]4X8M_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:3]6S36_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:4]6RZE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:5]4X8H_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:6]3HPR_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:7]1E4V_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:8]5EJE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDACKLVTDELVIALVKE
[Truncated_Name:9]1E4Y_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
```

```
[Truncated_Name:10]3X2S_A.pdb   TGDMLRAAVKSGSELGKQAKDIMDCGKLVTDELVIALVKE
[Truncated_Name:11]6HAP_A.pdb   TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVRE
[Truncated_Name:12]6HAM_A.pdb   TGDMLRAAIKSGSELGKQAKDIMDAGKLVTDEIIIALVKE
[Truncated_Name:13]4K46_A.pdb   TGDMLRAAIKAGTELGKQAKSVIDAGQLVSDDIILGLVKE
[Truncated_Name:14]4NP6_A.pdb   TGDMLRAAIKAGTELGKQAKAVIDAGQLVSDDIILGLIKE
[Truncated_Name:15]3GMT_A.pdb   TGDMLRAAVKAGTPLGVEAKTYMDEGKLVPDSLIIGLVKE
[Truncated_Name:16]4PZL_A.pdb   TGDMIRETIKSGSALGQELKKVLDAGELVSDEFIIKIVKD
                                ****^*  ^* *^ **   *  ^*   ** *  ^^ ^^^^
                               41        .         .         .         80

                               81        .         .         .         120
[Truncated_Name:1]1AKE_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:2]4X8M_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:3]6S36_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:4]6RZE_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:5]4X8H_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:6]3HPR_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:7]1E4V_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:8]5EJE_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:9]1E4Y_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:10]3X2S_A.pdb   RIAQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:11]6HAP_A.pdb   RICQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:12]6HAM_A.pdb   RICQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:13]4K46_A.pdb   RIAQDDCAKGFLLDGFPRTIPQADGLKEVGVVVDYVIEFD
[Truncated_Name:14]4NP6_A.pdb   RIAQADCEKGFLLDGFPRTIPQADGLKEMGINVDYVIEFD
[Truncated_Name:15]3GMT_A.pdb   RLKEADCANGYLFDGFPRTIAQADAMKEAGVAIDYVLEID
[Truncated_Name:16]4PZL_A.pdb   RISKNDCNNGFLLDGVPRTIPQAQELDKLGVNIDYIVEVD
                                *^   *   *^* ** **** **  ^   *^ ^**^^* *
                               81        .         .         .         120

                              121        .         .         .         160
[Truncated_Name:1]1AKE_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:2]4X8M_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:3]6S36_A.pdb    VPDELIVDKIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:4]6RZE_A.pdb    VPDELIVDAIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:5]4X8H_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:6]3HPR_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDGTG
[Truncated_Name:7]1E4V_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:8]5EJE_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:9]1E4Y_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:10]3X2S_A.pdb   VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:11]6HAP_A.pdb   VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:12]6HAM_A.pdb   VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
```

```
[Truncated_Name:13]4K46_A.pdb   VADSVIVERMAGRRAHLASGRTYHNVYNPPKVEGKDDVTG
[Truncated_Name:14]4NP6_A.pdb   VADDVIVERMAGRRAHLPSGRTYHVVYNPPKVEGKDDVTG
[Truncated_Name:15]3GMT_A.pdb   VPFSEIIERMSGRRTHPASGRTYHVKFNPPKVEGKDDVTG
[Truncated_Name:16]4PZL_A.pdb   VADNLLIERITGRRIHPASGRTYHTKFNPPKVADKDDVTG
                                *    ^^^ ^ *** *  *** **  ^*****  *** **
                               121        .         .         .         160

                               161        .         .         .         200
[Truncated_Name:1]1AKE_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:2]4X8M_A.pdb    EELTTRKDDQEETVRKRLVEWHQMTAPLIGYYSKEAEAGN
[Truncated_Name:3]6S36_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:4]6RZE_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:5]4X8H_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAALIGYYSKEAEAGN
[Truncated_Name:6]3HPR_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:7]1E4V_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:8]5EJE_A.pdb    EELTTRKDDQEECVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:9]1E4Y_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:10]3X2S_A.pdb   EELTTRKDDQEETVRKRLCEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:11]6HAP_A.pdb   EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:12]6HAM_A.pdb   EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:13]4K46_A.pdb   EDLVIREDDKEETVLARLGVYHNQTAPLIAYYGKEAEAGN
[Truncated_Name:14]4NP6_A.pdb   EDLVIREDDKEETVRARLNVYHTQTAPLIEYYGKEAAAGK
[Truncated_Name:15]3GMT_A.pdb   EPLVQRDDDKEETVKKRLDVYEAQTKPLITYYGDWARRGA
[Truncated_Name:16]4PZL_A.pdb   EPLITRTDDNEDTVKQRLSVYHAQTAKLIDFYRNFSSTNT
                                * *  * ** *^ *  **  ^   *  ** ^*
                               161        .         .         .         200

                               201        .         .      227
[Truncated_Name:1]1AKE_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:2]4X8M_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:3]6S36_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:4]6RZE_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:5]4X8H_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:6]3HPR_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:7]1E4V_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:8]5EJE_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:9]1E4Y_A.pdb    T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:10]3X2S_A.pdb   T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:11]6HAP_A.pdb   T--KYAKVDGTKPVCEVRADLEKILG-
[Truncated_Name:12]6HAM_A.pdb   T--KYAKVDGTKPVCEVRADLEKILG-
[Truncated_Name:13]4K46_A.pdb   T--QYLKFDGTKAVAEVSAELEKALA-
[Truncated_Name:14]4NP6_A.pdb   T--QYLKFDGTKQVSEVSADIAKALA-
[Truncated_Name:15]3GMT_A.pdb   E-------NGLKAPA-----YRKISG-
```

```
[Truncated_Name:16]4PZL_A.pdb   KIPKYIKINGDQAVEKVSQDIFDQLNK
                                           *
                               201         .          .      227

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

Class:
  pdbs, fasta

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

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

Can visualize, white = not aligned

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

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

And collect annotation for each array

```
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"
```

```
head(anno)
```

```
      structureId chainId macromoleculeType chainLength experimentalTechnique
```

```
1AKE_A        1AKE       A           Protein         214                X-ray
4X8M_A        4X8M       A           Protein         214                X-ray
6S36_A        6S36       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
       resolution       scopDomain                   pfam         ligandId
1AKE_A       2.00 Adenylate kinase Adenylate kinase (ADK)              AP5
4X8M_A       2.60             <NA> Adenylate kinase (ADK)             <NA>
6S36_A       1.60             <NA> Adenylate kinase (ADK) CL (3),NA,MG (2)
6RZE_A       1.69             <NA> Adenylate kinase (ADK)    NA (3),CL (2)
4X8H_A       2.50             <NA> Adenylate kinase (ADK)             <NA>
3HPR_A       2.00             <NA> Adenylate kinase (ADK)              AP5
                                          ligandName               source
1AKE_A              BIS(ADENOSINE)-5'-PENTAPHOSPHATE      Escherichia coli
4X8M_A                                          <NA>      Escherichia coli
6S36_A CHLORIDE ION (3),SODIUM ION,MAGNESIUM ION (2)      Escherichia coli
6RZE_A               SODIUM ION (3),CHLORIDE ION (2)      Escherichia coli
4X8H_A                                          <NA>      Escherichia coli
3HPR_A              BIS(ADENOSINE)-5'-PENTAPHOSPHATE Escherichia coli K-12

1AKE_A STRUCTURE OF THE COMPLEX BETWEEN ADENYLATE KINASE FROM ESCHERICHIA COLI AND THE INHIBI
4X8M_A
6S36_A
6RZE_A
4X8H_A
3HPR_A
                                                 citation rObserved  rFree
1AKE_A                Muller, C.W., et al. J Mol Biol (1992)    0.1960     NA
4X8M_A               Kovermann, M., et al. Nat Commun (2015)    0.2491 0.3089
6S36_A                 Rogne, P., et al. Biochemistry (2019)    0.1632 0.2356
6RZE_A                 Rogne, P., et al. Biochemistry (2019)    0.1865 0.2350
4X8H_A               Kovermann, M., et al. Nat Commun (2015)    0.1961 0.2895
3HPR_A Schrank, T.P., et al. Proc Natl Acad Sci U S A (2009)    0.2100 0.2432
        rWork spaceGroup
1AKE_A 0.1960  P 21 2 21
4X8M_A 0.2463    C 1 2 1
6S36_A 0.1594    C 1 2 1
6RZE_A 0.1819    C 1 2 1
4X8H_A 0.1914    C 1 2 1
3HPR_A 0.2062  P 21 21 2
```

```
pdbs$xyz
```

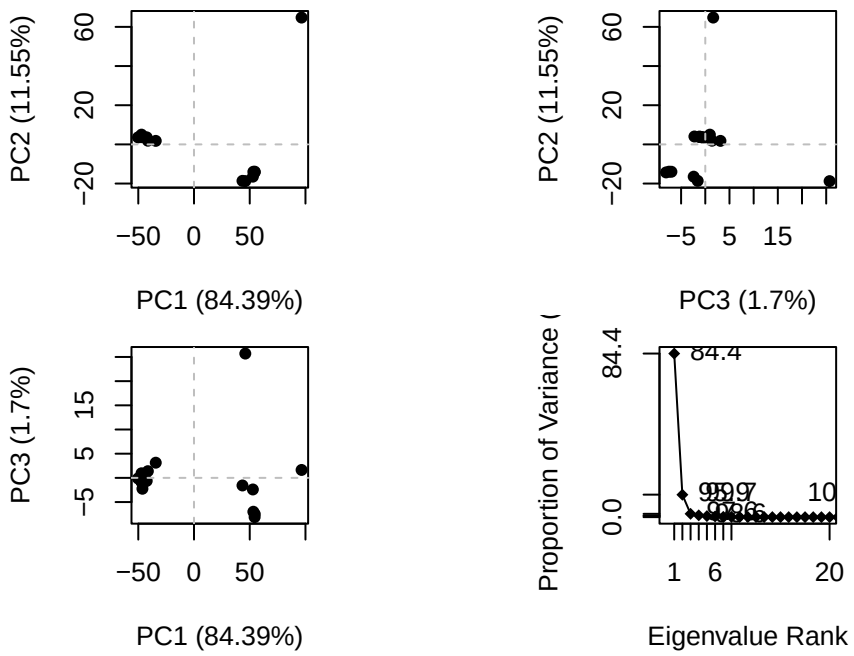
```
   Total Frames#: 16
   Total XYZs#:   681,  (Atoms#:  227)

    [1]  NA  NA  NA  <...>  15.818  46.771  47.7  [10896]

+ attr: Matrix DIM = 16 x 681
```

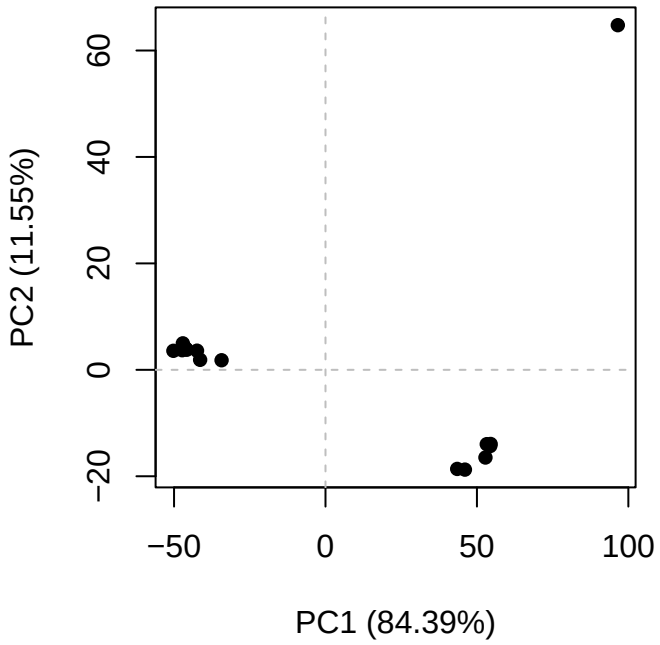
Time for PCA. We will use not the `prcomp()` function from base R but the `pca()` function from the `bio3d` package as this one is designed to work nicely with biomolecular data.

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



We can now focus in on PC1 vs PC2

```
plot(pc.xray, 1:2)
```

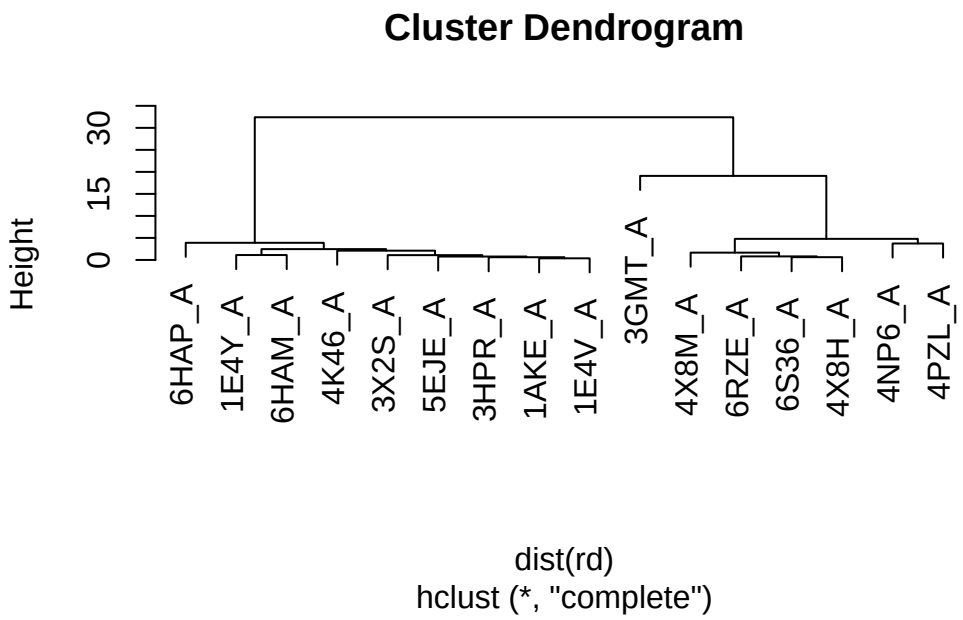


Lets cluster our data

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

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

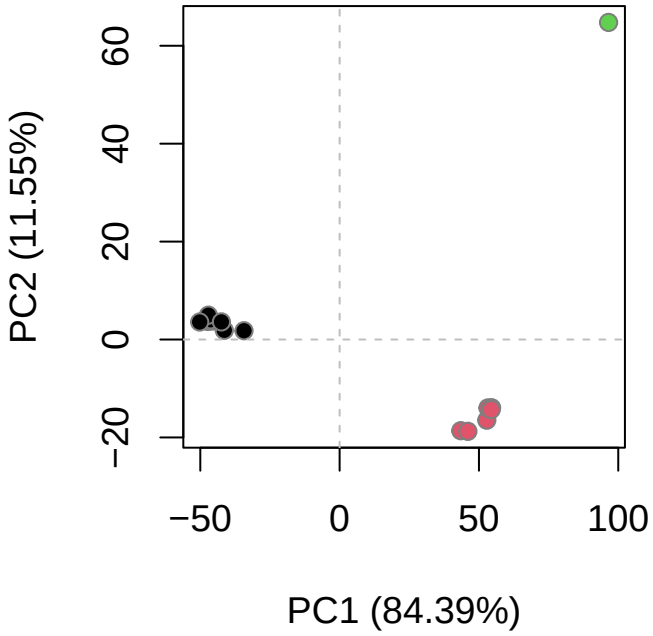
```
# Structure-based clustering, 3 groups so k=3
hc.rd <- hclust(dist(rd))
plot(hc.rd)
```



And now my PC plot colored by cluster

```
grps.rd <- cutree(hc.rd, k=3)

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



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")
```

We can now open this trajectory file in Molstar to view a wee movie of the major differences (i.e. displacements of atoms) in the structure set