Lab09: Structural Bioinformatics 1

Matthew

What is in the PDB anyway?

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

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

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

```
pdbstats <- read.csv("PDB.csv")
head(pdbstats)
```

```
##            Molecular.Type   X.ray    EM    NMR Multiple.methods Neutron Other
## 1          Protein (only) 152,809 9,421 12,117              191      72    32
## 2 Protein/Oligosaccharide   9,008 1,654     32                7       1     0
## 3              Protein/NA   8,061 2,944    281                6       0     0
## 4     Nucleic acid (only)   2,602    77  1,433               12       2     1
## 5                   Other     163     9     31                0       0     0
## 6  Oligosaccharide (only)      11     0      6                1       0     4
##     Total
## 1 174,642
## 2  10,702
## 3  11,292
## 4   4,127
## 5     203
## 6      22
```

```
pdbstats$X.ray
```

```
## [1] "152,809" "9,008"   "8,061"   "2,602"   "163"     "11"
```

```
gsub(",", "",pdbstats$X.ray)
```

```
## [1] "152809" "9008"   "8061"   "2602"   "163"    "11"
```

```
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)))
```

```
round(n.em/n.Total,4)
```

```
## [1] 0.0702
```

For EM, it is 7.02%

round((n.xray)/n.Total,2)

```
round(n.xray/n.Total,5)
```

```
## [1] 0.85903
```

For X.ray, it is 85.90%

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

```
as.numeric(gsub(",", "",pdbstats[1,8]))/n.Total
```

```
## [1] 0.8689175
```

Around 0.8689

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?

200,988 structures. It is not straightforward to find a ll 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?

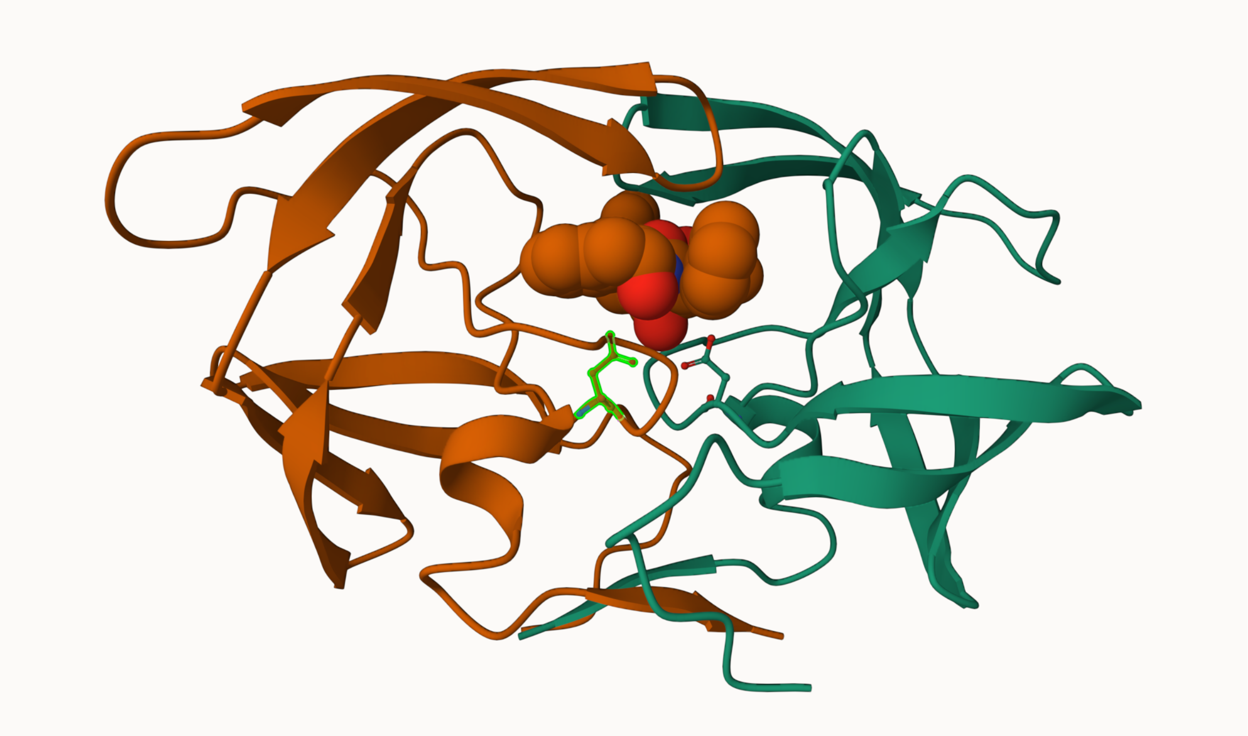
It is because we are only observing the Oxygen molecule. The Hydrogen molecules were too small to be be observed.

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 reside number of the water molecule is 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.

A picture of HIV-1 Protease from Molstar



Working with structure data in R

We will use the 'bio3d' package for this:

```
library(bio3d)
```

Read a PDB file from 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
```

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

198

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

water (HOH)

Q9: How many protein chains are in this structure?

2

```
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 and 1 letter code?

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

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

```
aa321(pdb$atom$resid[1])
```

```
## [1] "P"
```

Predicting functional motions of a single structure

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

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

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

```
adk
```

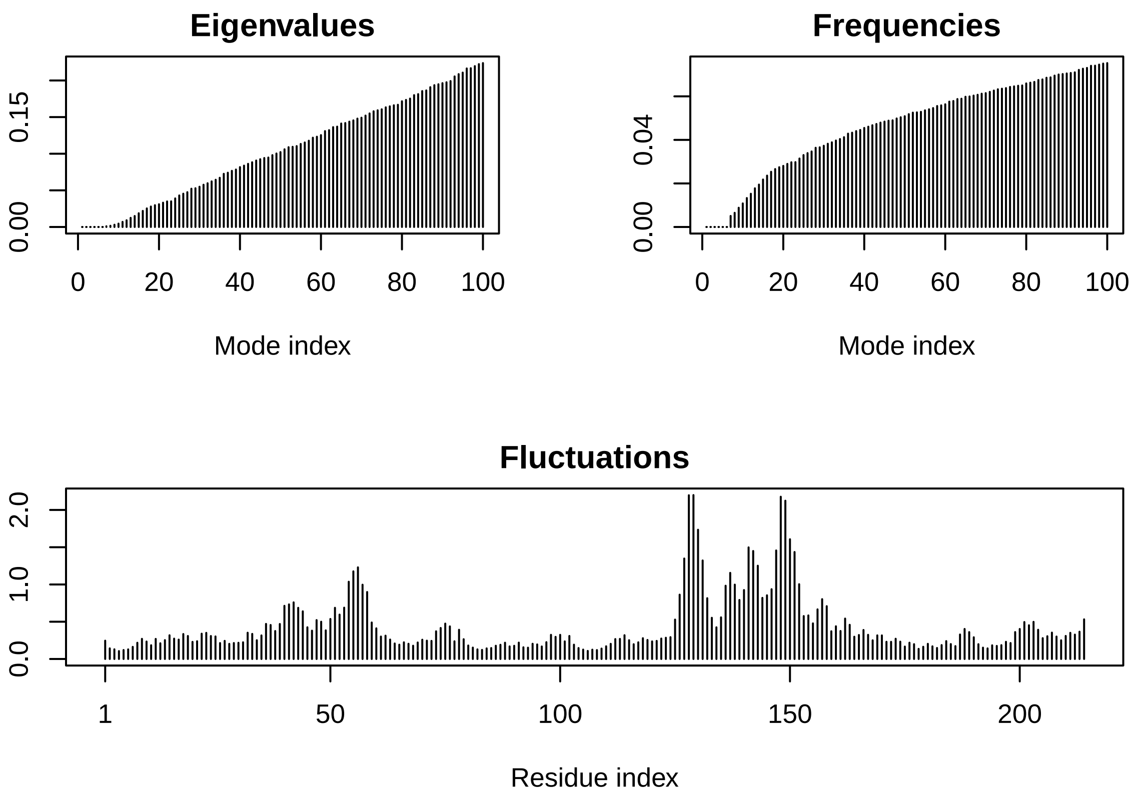
```
## 
##  Call:  read.pdb(file = "6s36")
## 
##    Total Models#: 1
##      Total Atoms#: 1898,  XYZs#: 5694  Chains#: 1  (values: A)
## 
##      Protein Atoms#: 1654  (residues/Calpha atoms#: 214)
##      Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)
## 
##      Non-protein/nucleic Atoms#: 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).

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

```
##  Building Hessian...     Done in 0.035 seconds.
##  Diagonalizing Hessian...    Done in 0.332 seconds.
```

```r
plot(m)
```



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

Section 4. Comparative Structure Analaysis of Adenylate Kinase

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

We begin with getting a single protein sequence for a protein family of interest.

```r
library(bio3d)
```

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

MSA

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

bio3d-view

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

TRUE

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

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

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

```r
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

```
# Blast or hmmer search
#b <- blast.pdb(aa)
```

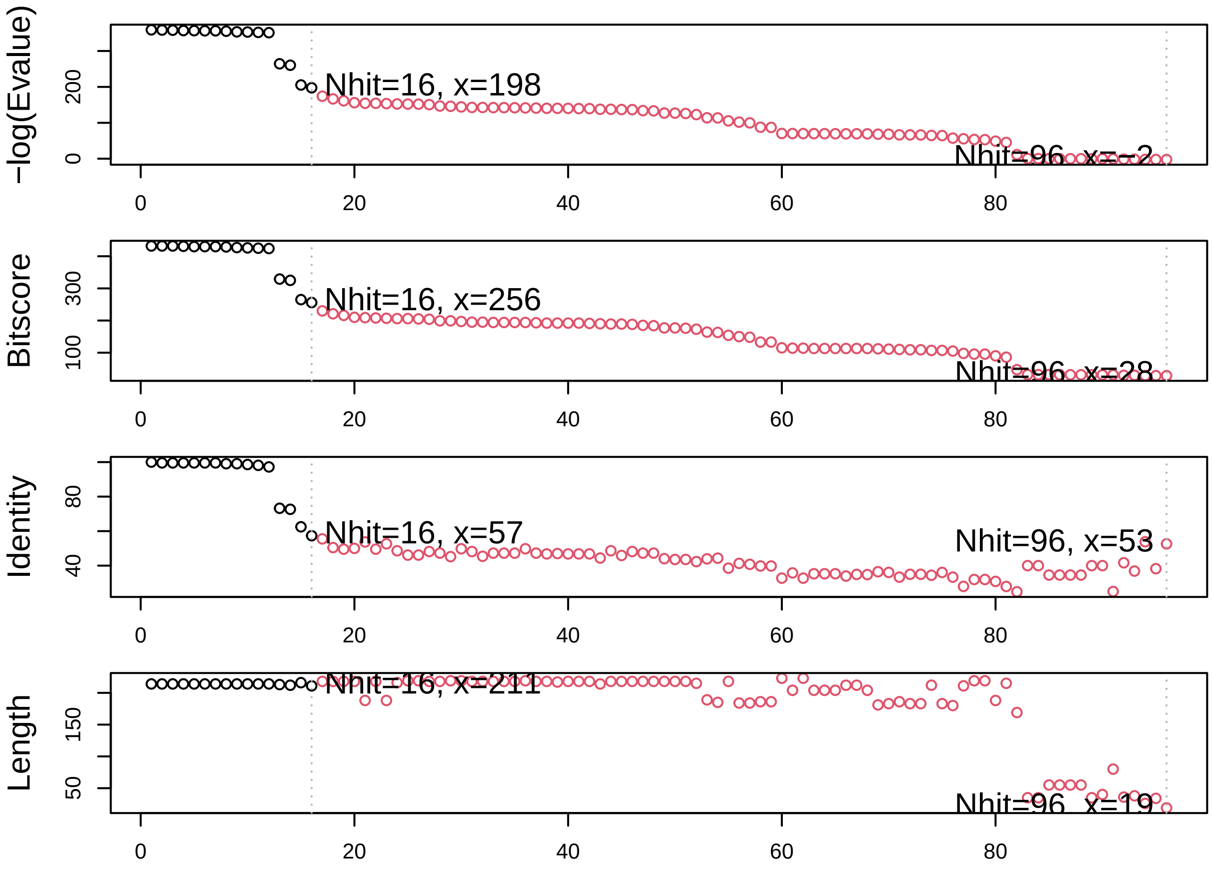
I could save and load my blast results next time so I don't ened to run the serach every time.

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

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

```
# Plot a summary of search results
hits <- plot(b)
```

```
##   * Possible cutoff values:    197 -3
##             Yielding Nhits:    16 96
##
##   * Chosen cutoff value of:    197
##             Yielding Nhits:    16
```



```
hits
```

```
## $hits
##    pdb.id   acc      group
## 1  "1AKE_A" "1AKE_A" "1"
## 2  "4X8M_A" "4X8M_A" "1"
## 3  "6S36_A" "6S36_A" "1"
## 4  "6RZE_A" "6RZE_A" "1"
## 5  "4X8H_A" "4X8H_A" "1"
## 6  "3HPR_A" "3HPR_A" "1"
## 7  "1E4V_A" "1E4V_A" "1"
## 8  "5EJE_A" "5EJE_A" "1"
## 9  "1E4Y_A" "1E4Y_A" "1"
## 10 "3X2S_A" "3X2S_A" "1"
## 11 "6HAP_A" "6HAP_A" "1"
## 12 "6HAM_A" "6HAM_A" "1"
## 13 "4K46_A" "4K46_A" "1"
## 14 "4NP6_A" "4NP6_A" "1"
## 15 "3GMT_A" "3GMT_A" "1"
## 16 "4PZL_A" "4PZL_A" "1"
##
## $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"
##
## $acc
##  [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"
##
## $inds
##  [1]  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE
## [13]  TRUE  TRUE  TRUE  TRUE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [25] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [37] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [49] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [61] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [73] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [85] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
##
## attr(,"class")
## [1] "blast"
```

```r
# List out some 'top hits'
head(hits$pdb.id)
```

```
## [1] "1AKE_A" "4X8M_A" "6S36_A" "6RZE_A" "4X8H_A" "3HPR_A"
```

```r
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"
```

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

```
## Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
## pdbs/1AKE.pdb.gz exists. Skipping download
## Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
## pdbs/4X8M.pdb.gz exists. Skipping download

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

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

## Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
## pdbs/4X8H.pdb.gz exists. Skipping download

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

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

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

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

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

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

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

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

## Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
## pdbs/4NP6.pdb.gz exists. Skipping download

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

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

##   |                                                                              |
```

Next we are going to align and superpose all the structures

```r
# 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
```

```
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
```

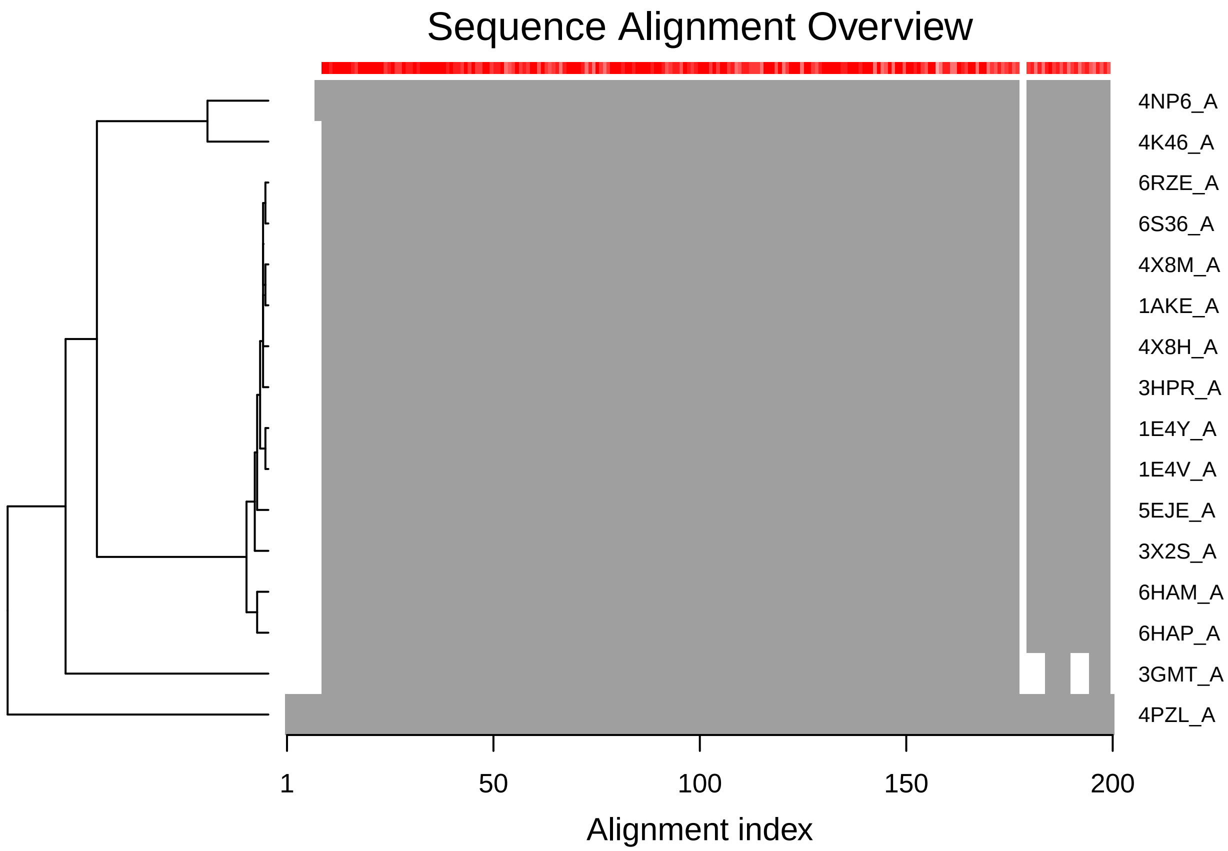
```
pdbs$xyz
```

```
##
##    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
```

Some annotations of the PDBs we have collected

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

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



And collect annotations from each entry

```
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"
```

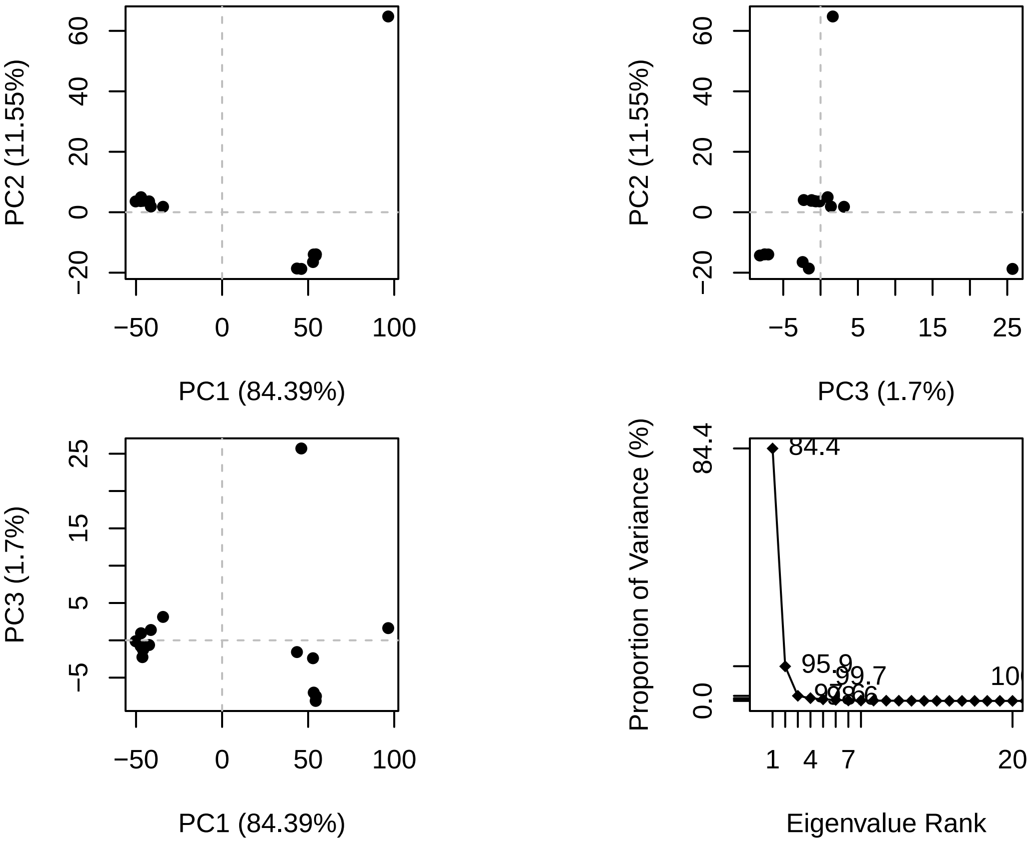
```
head(anno)
```

```
##        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 INHIBITOR AP5A
## 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
```

Principal Component Analysis

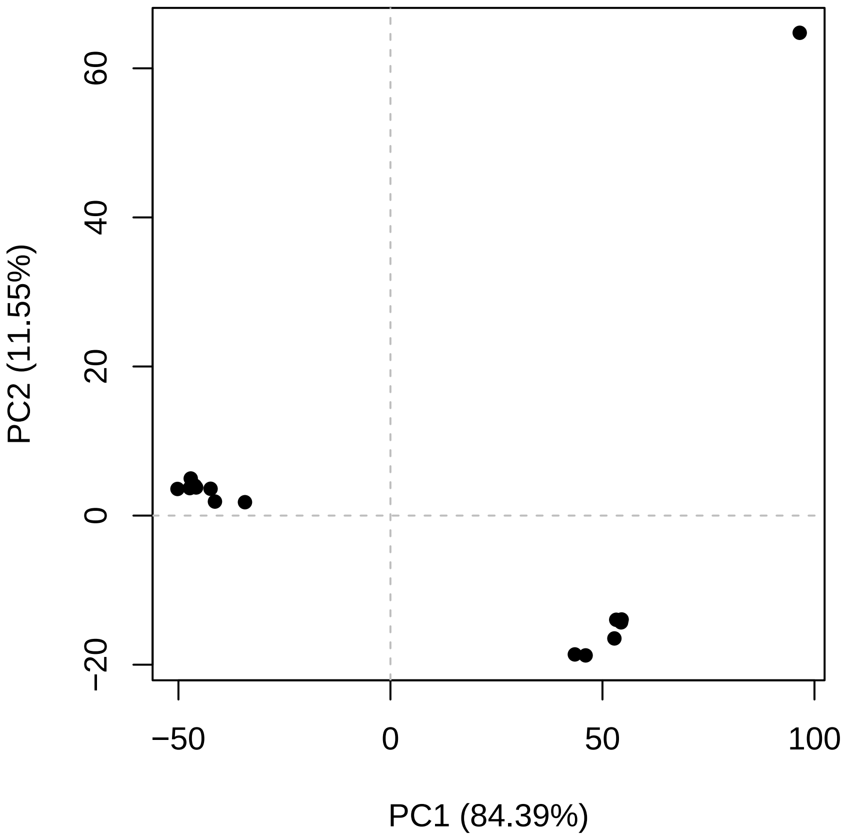
Time for PCA. We will not use the ‘prcomp()’ function from bas R but the ‘pca()’ function from the ‘bio3d’ package as this one is designed to work nicely with biomolecular data.

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



We can now focus in on PC1 vs PC2

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

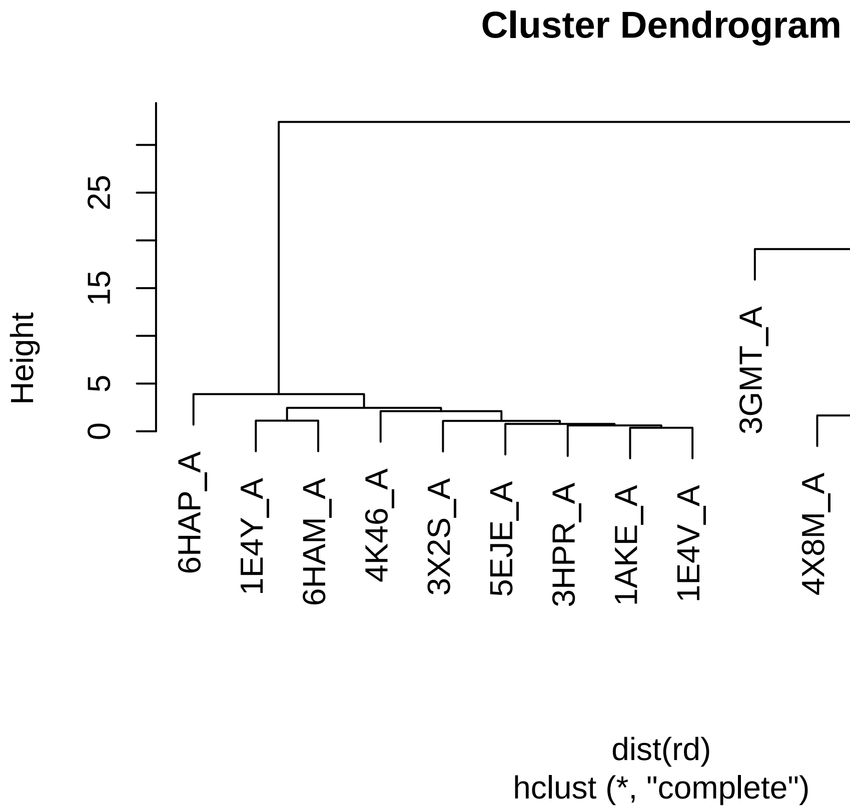


Let's cluster our structures

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

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

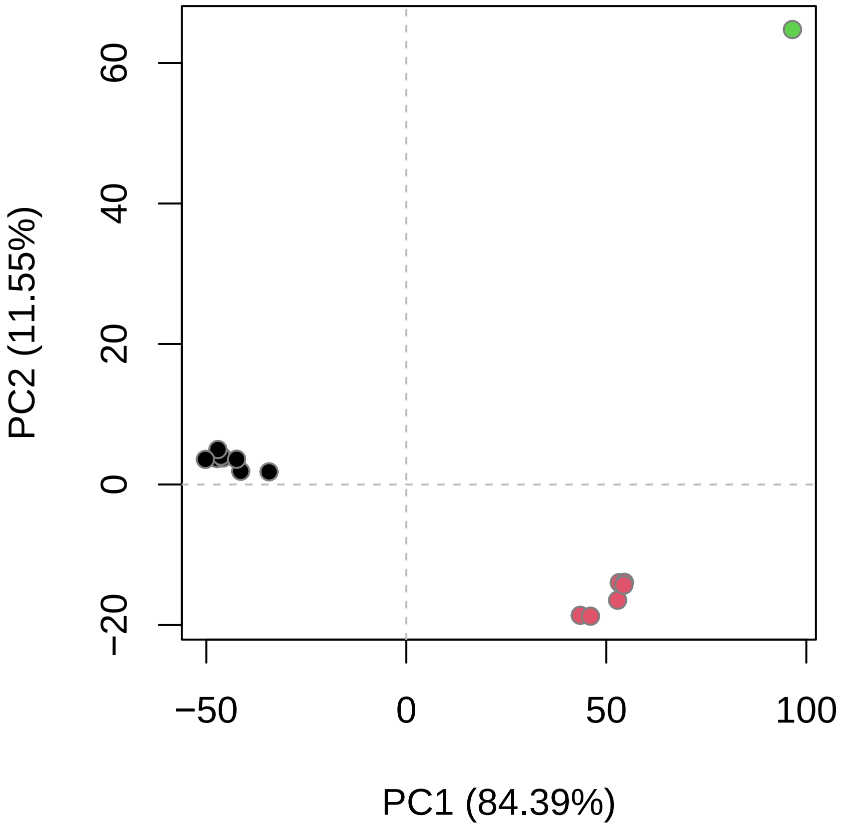
```
# Structure-based clustering
hc.rd <- hclust(dist(rd))
grps.rd <- cutree(hc.rd, k=3)
plot(hc.rd)
```



And now my PC plot colored by clustering group

```
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):

```
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 (ie displacements) in the structure set as we move along PC1.