class09

Christina Mac

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: fna.data <- "WisconsinCancer.csv"

```
pdbstats <- read.csv("Data Export Summary.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. X-Ray = 85.9% EM = 7.02%

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

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

```
sumxray <- sum(as.numeric(gsub(",", "", pdbstats$X.ray)))
sumem <-sum(as.numeric(gsub(",", "", pdbstats$EM)))
sumnmr <-sum(as.numeric(gsub(",", "", pdbstats$NMR)))
sumtotal <- sum(as.numeric(gsub(",", "", pdbstats$Total)))
round((sumxray/(sumtotal))*100,2)
```

```
[1] 85.9
```

```
round((sumem/(sumtotal))*100,2)
```

```
[1] 7.02
```

Q2: What proportion of structures in the PDB are protein? 86.89%

```
as.numeric(gsub(",", "", pdbstats$Total))/sumtotal
```

```
[1] 0.8689175473 0.0532469600 0.0561824587 0.0205335642 0.0010100105
[6] 0.0001094593
```

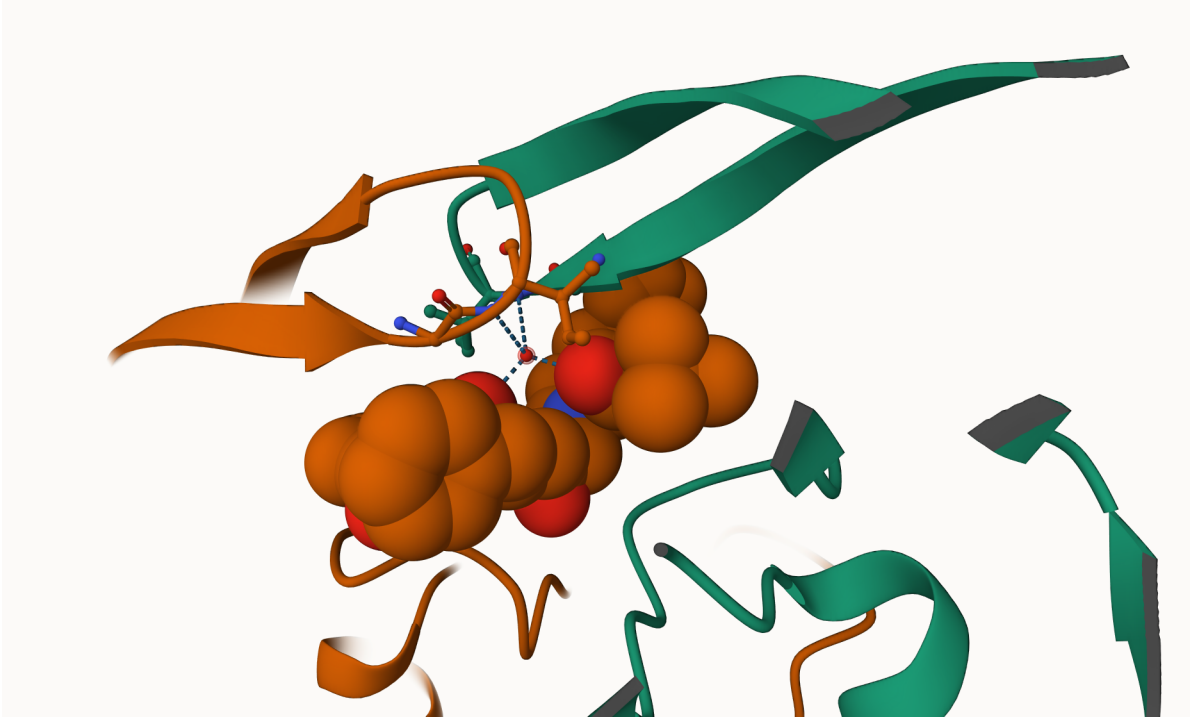
```
as.numeric(gsub(",", "", pdbstats$Total[1]))/sumtotal
```

```
[1] 0.8689175
```

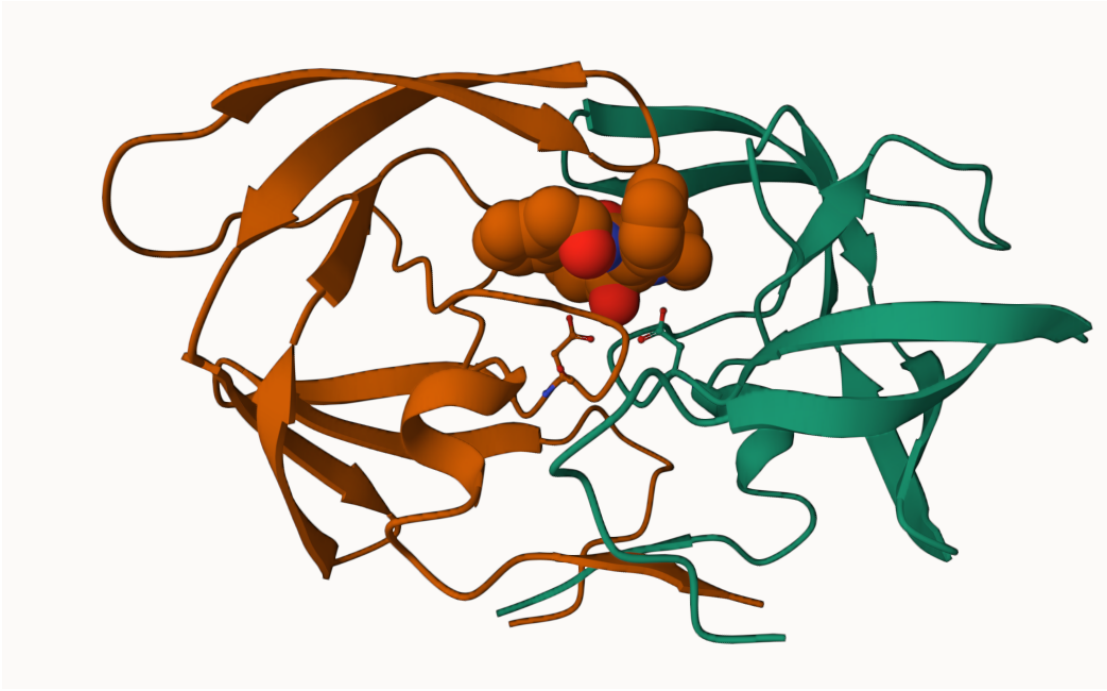
Q3: Type HIV in the PDB website search box on the home page and determine how many HIV-1 protease structures are in the current PDB? It is not straightforward to find all HIV-1 protease structures using plain text searching on the database.

Q4: Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure? The resolution of the image is at 2 angstrom, which is not high enough to see the tiny hydrogen atoms.

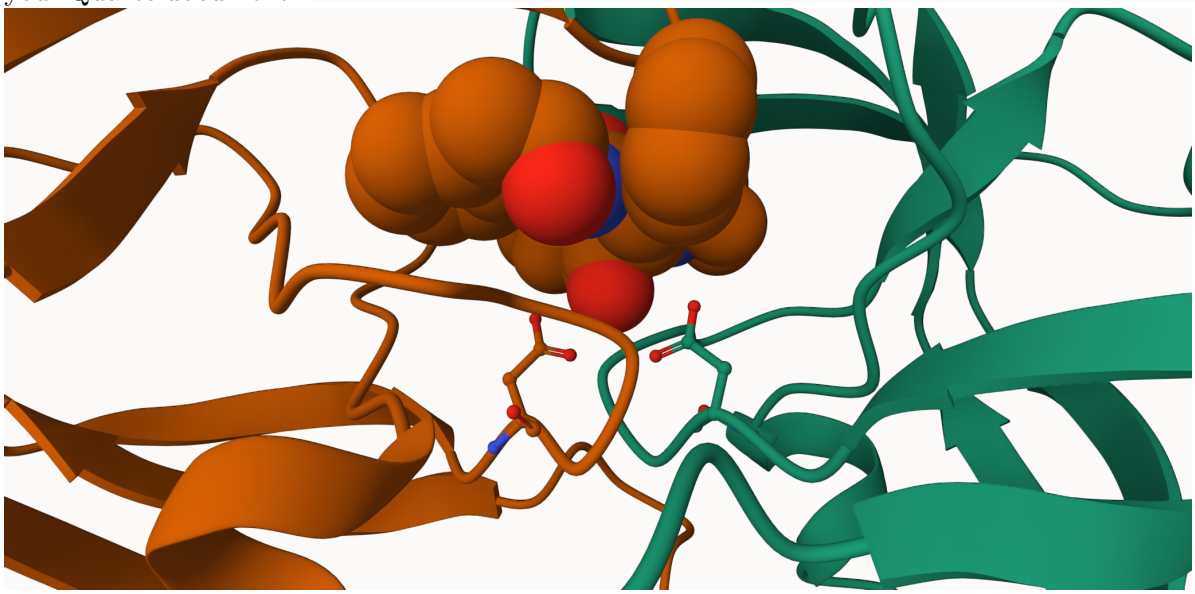
Q5: There is a critical "conserved" water molecule in the binding site. Can you identify this water molecule? What residue number does this water molecule have This is HOH 308:



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



your Quarto document.



Working with structure daa in R

We will use the `bio3d` package for this:

```
library(bio3d)
```

Read a PDB file from the online accession:

```
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
```

```
#atom records
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? "PRO" and P"

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

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

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

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

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

Predicting fuctional motions of a single structure

Let's read a new PDB structure of Adenylate Kinase (PDB code:6s36)

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

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

```
adk
```

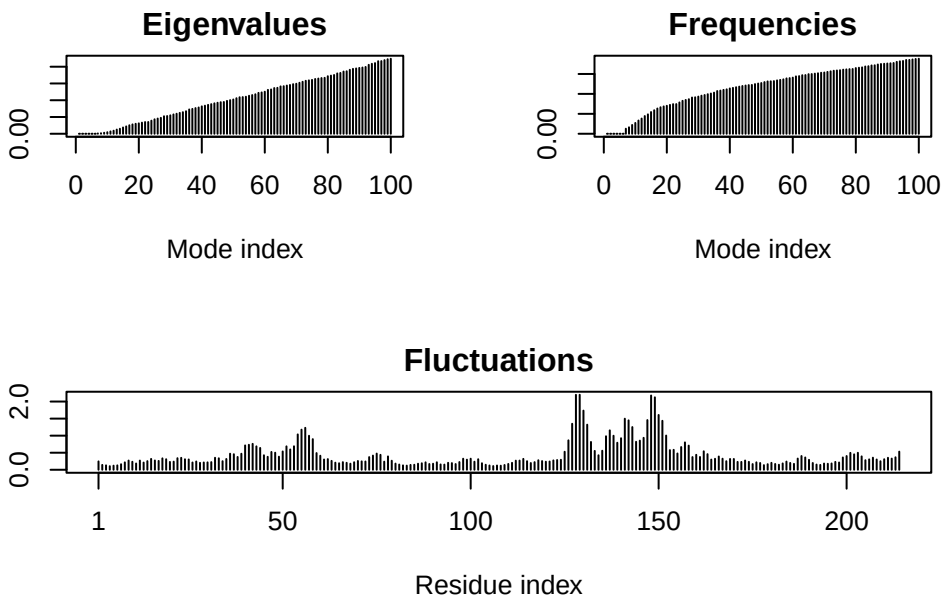
```
 Call:  read.pdb(file = "6s36")

   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 0.03 seconds.
 Diagonalizing Hessian...   Done in 0.32 seconds.
```

```
plot(m)
```




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

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

Section 4. Comparative structure analysis

Today, we are continuing where we left off last time, 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.

```
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

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

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

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

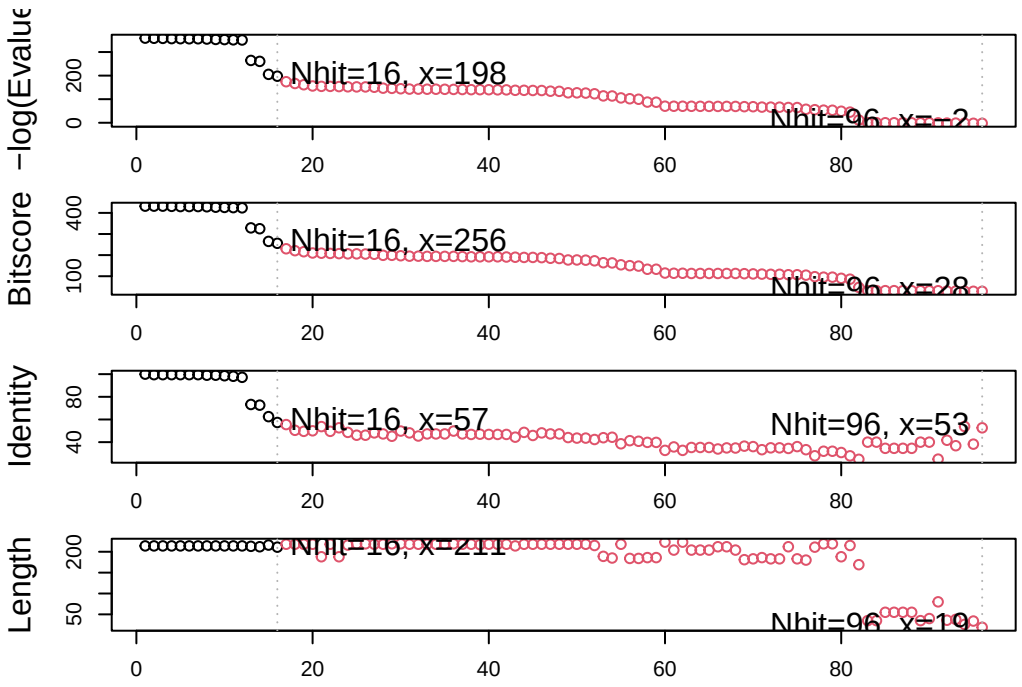
```
  #saveRDS(b, file = "blast_results.RDS")
```

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

A summary plot of our BLAST results.

```
# 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
```



The hits that are way at the top of the plot are actually the ones with the smallest E values.

```
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"
```

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

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

Next we are going to align and superpose all these structures.

```
# Align related 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
```

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

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

And collect annotation for 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)
```

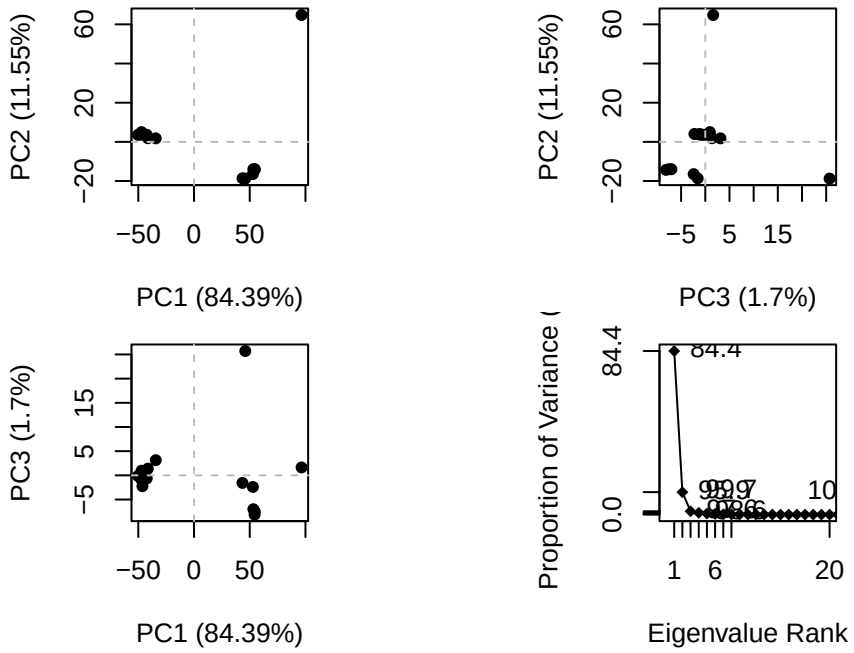
```
       structureId chainId macromoleculeType chainLength experimentalTechnique
1AKE_A        1AKE       A           Protein         214                 X-ray
4X8M_A        4X8M       A           Protein         214                 X-ray
6S36_A        6S36       A           Protein         214                 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 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
```

#Principal Component Analysis

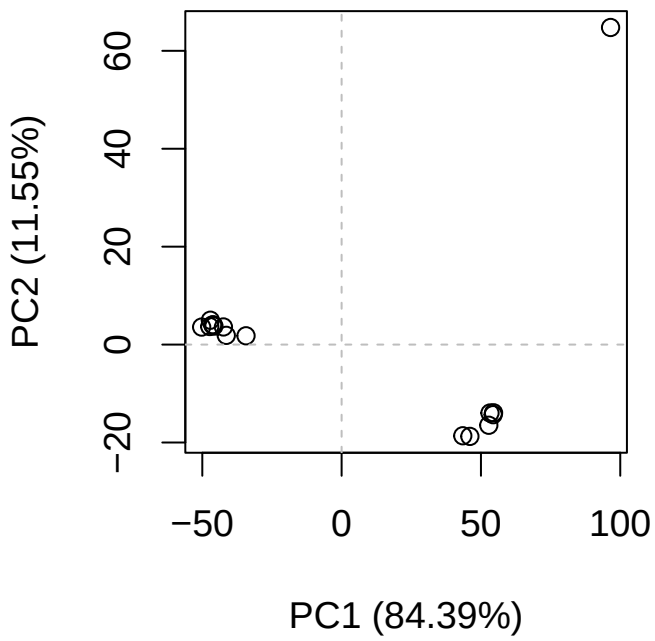
Time for PCA. We will use not the `prcomp()` function from base R but the `pca()` function from the `bio3d` package as this one is desgined to work nicely with biomolecular data.

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



We can now focus on PC1 vs PC2:

```
plot(pc.xray, 1:2, pch=21, cex=1)
```



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)
```

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 on Molstar to view a wee movie of the differences (i.e. displacements) in the structure set as we move along PC1.