Class 09

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1. Introduction to the RCSB Protein Data Bank

```
pdbStats <- read.csv("DataExportSummary.csv")
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
```

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

```
pdbStats$X.ray
```

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

These values are returned with quotations and must be coded as characters. This means 'sum(pdbStats[,1])' will not work because. We must change the values from characters to numerals before any analysis can be done. The function 'as.numeric()' can make the column readable as numeric values rather than characters.

```
as.numeric(pdbStats$X.ray)
```

```
Warning: NAs introduced by coercion
```

```
[1]  NA  NA  NA  NA 163  11
```

'as.numeric()' cannot process the commas that are included in the larger values (ex. the amount of 'protein-only' imaged by method of X ray is '152,809') We need to remove these commas to work with the data.

We can use 'gsub()' to remove the commas. The 'gsub()' function requires "pattern", "replacement" and "x". x is our data.frame, the pattern we would like to remove is the commas. and the replacement is nothing.

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

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

After removing the commas and changing the values to numeric, we can sum values of each column and figure out what proportion of structures were solved by EM and X ray diffraction.

```
n.xray <- (sum(as.numeric(gsub(",","", pdbStats$X.ray))))
n.xray
```

```
[1] 172654
```

```
n.em <- (sum(as.numeric(gsub(",","", pdbStats$EM))))
n.em
```

```
[1] 14105
```

```
n.total <- (sum(as.numeric(gsub(",","", pdbStats$Total))))
n.total
```

```
[1] 200988
```

```
p.em <- (n.em/ n.total) *100
p.em
```

```
[1] 7.017832
```

```
p.xray <- (n.xray/n.total) *100
p.xray
```

```
[1] 85.90264
```

7% of the structures were solved by EM and 85.9% of the structures were solved by X-Ray diffraction. Together, 92.9% of the structures were solved by these two methods.

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

Similarly, we need to remove the commas and change the values from characters. If we were going to be doing a longer analysis, we would write a function to make the code more readable.

```
n.protein <- (sum(as.numeric(gsub(",","", pdbStats[1,8]))))

(n.protein/n.total)*100
```

```
[1] 86.89175
```

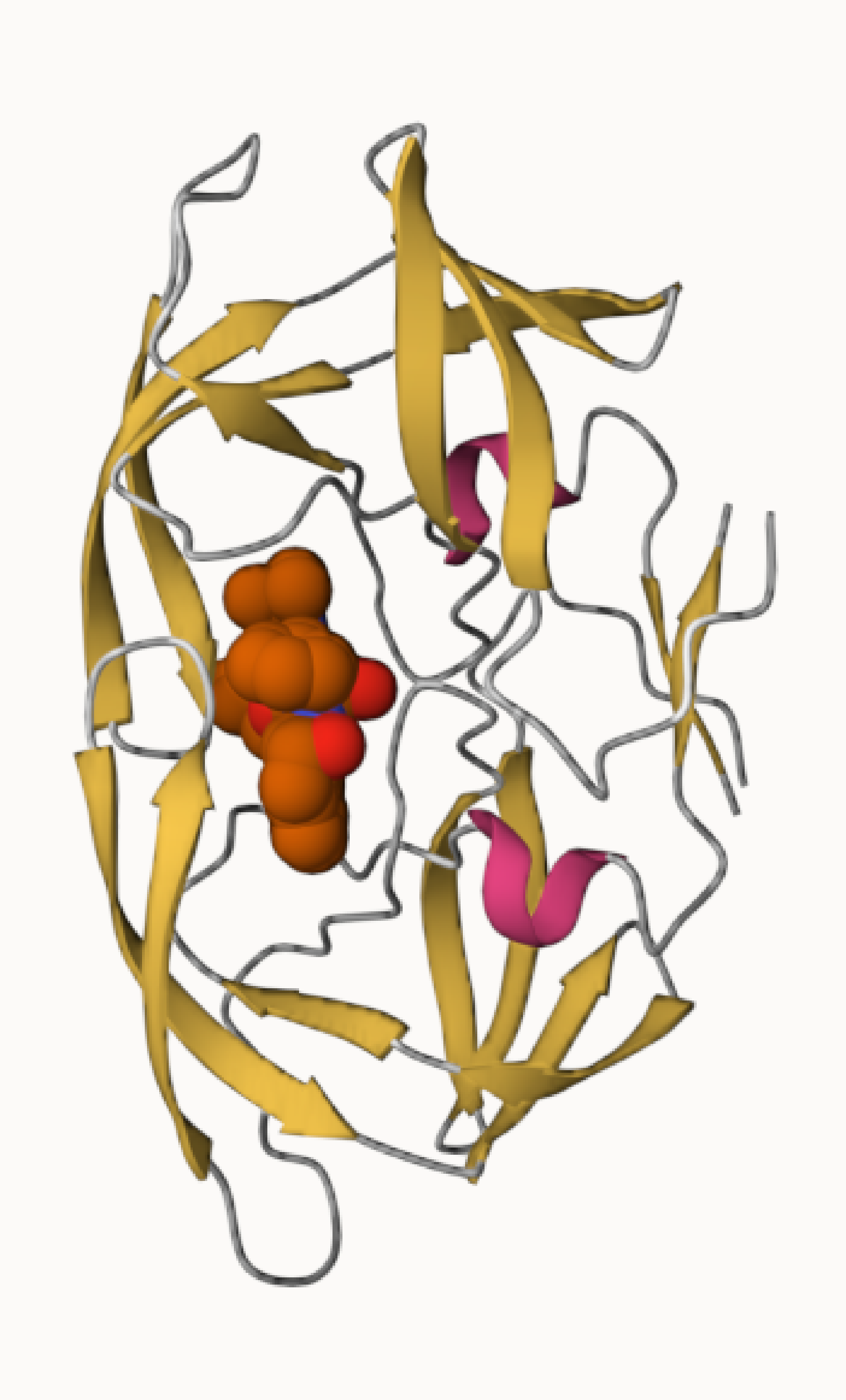
Approximately 86.9% of the structures are proteins.

> 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?

4,791 structures are in the current PDB

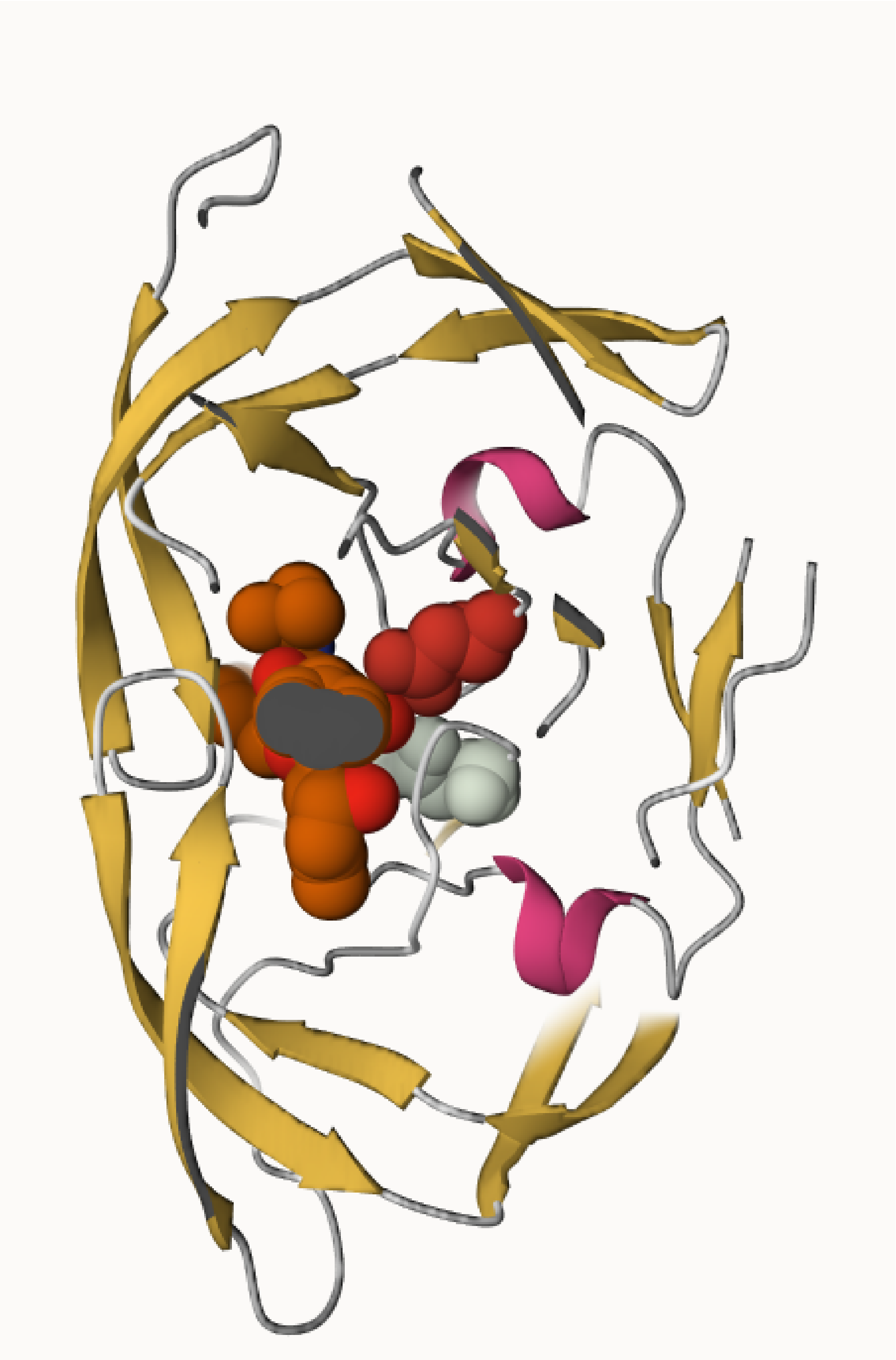
Visualizing the HIV-1 Protease Structure

Here is the 3D image of HIV-1:

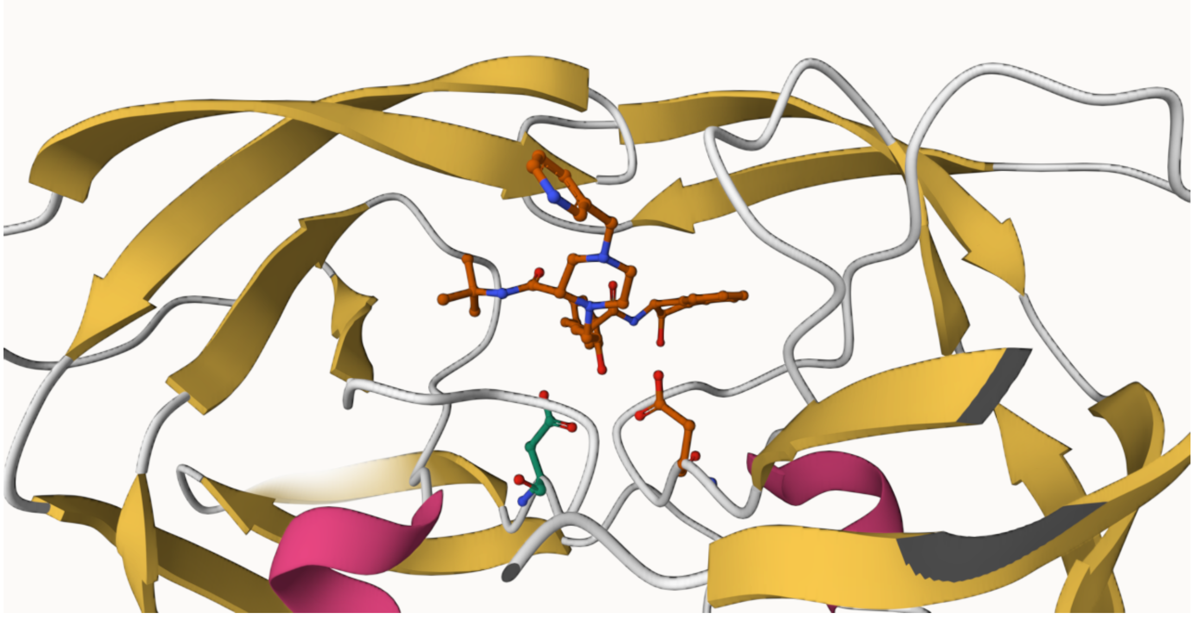


Here are 3D images of Asp-25 on each subunit of HIV-1:

spacefill representation:



ball and stick representation:



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

HIV-1 is overall positively charged and so any interactions between the polymer and water is through oxygen(which has a partial negative charge), so they only show one atom per water molecule for simplicity's sake.

> 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

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.

Call up bio3d and access online PDB file:

```
library(bio3d)

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?

HOH (or MK1)

> Q9: How many protein chains are in this structure?

2

Learn about the attributes of this object:

```
attributes(pdb)
```

```
$names
[1] "atom"   "xyz"    "seqres" "helix"  "sheet"  "calpha" "remark" "call"

$class
[1] "pdb" "sse"
```

Access the 'atom' attribute:

```
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

Access new online pdb file:

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

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

```
adk
```

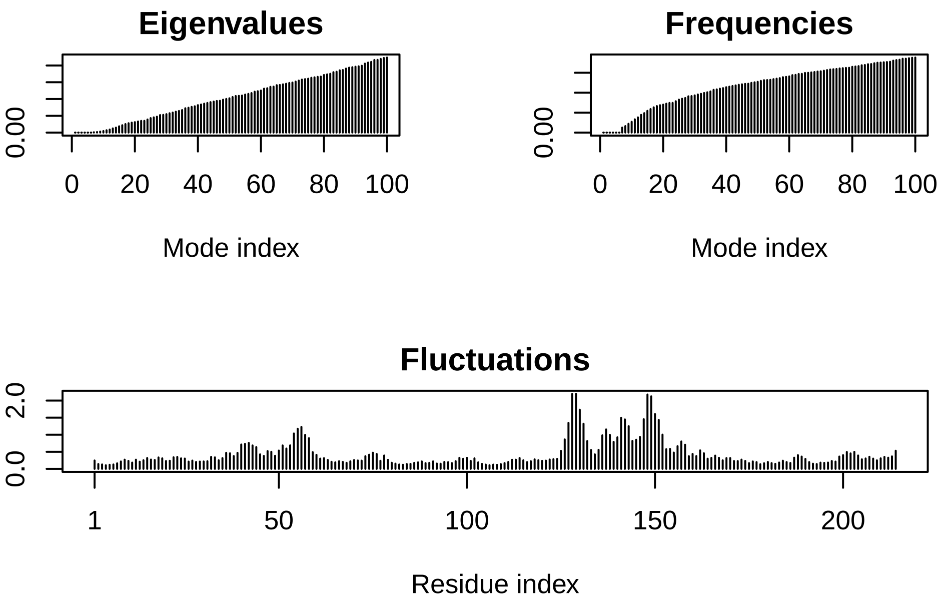
```
 Call:  read.pdb(file = "6s36")

   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
```

‘nma()’ stands for “normal mode analysis” and predicts protein flexibility and potential conformational changes

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

```
Building Hessian...        Done in 0.099 seconds.
Diagonalizing Hessian...   Done in 0.556 seconds.
```

```
plot(m)
```



Now we will view the predicted motions and conformational changes of the protein using ‘mktrj()’. It shows the predicted trajectories and therefore enables us to watch a “movie” of the predicted motions.

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

This file can be uploaded into mol to view the movement of the protein.

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 package

> 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
library(bio3d)

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 amino acids

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

```
#blast 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 and this work stays reproducible.

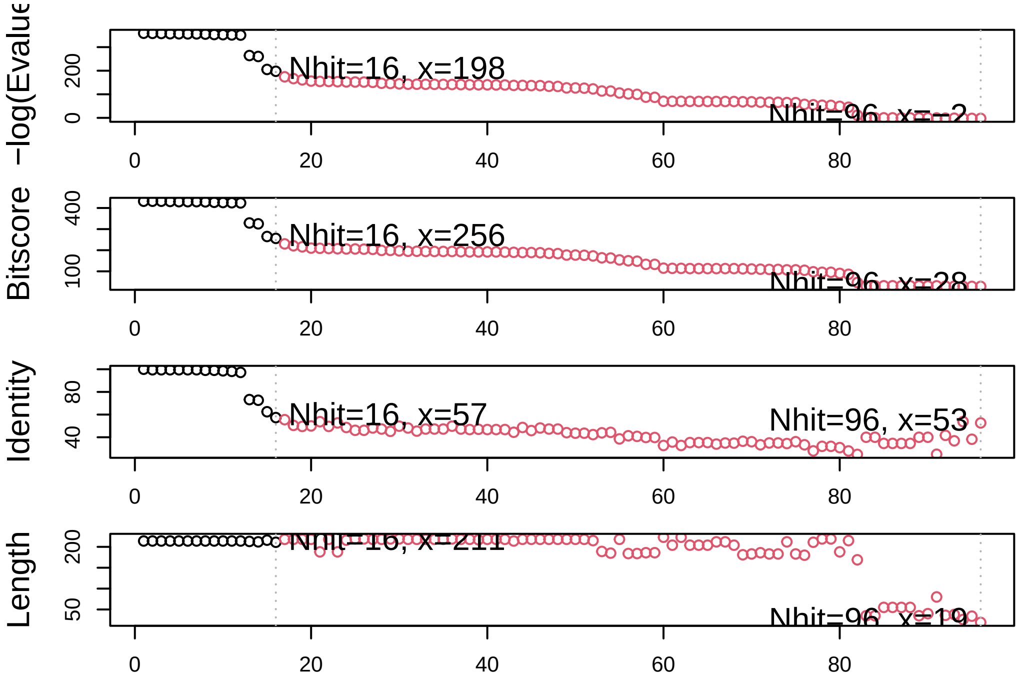
```
#saveRDS(b, file = "blast_results.RDS")
```

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

A summary plot of search results:

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

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

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



List out some 'top hits':

```
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"
```

```
#downlaod related 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
```

```
  |
  |                                                                      |   0%
  |
  |====                                                                  |   6%
  |
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  |=============                                                         |  19%
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  |=============================================================         |  88%
  |
  |==================================================================    |  94%
  |
  |======================================================================| 100%
```

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
```

```
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
```

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

#draw schematic alignment
#plot(pdbs, labels=ids)

#R Error Avoided: figure margins too large to render in pdf. Still reproducible in code.
```

```
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"
```

```r
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
```

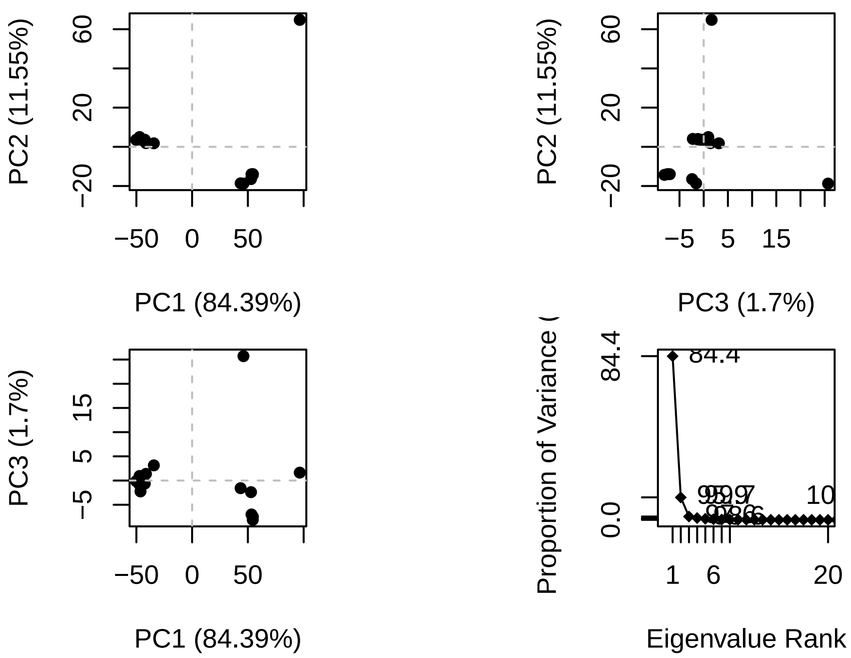
```
3HPR_A Schrank, T.P., et al. Proc Natl Acad Sci U S A (2009)    0.2100 0.2432
        rWork spaceGroup
1AKE_A 0.1960  P 21 2 21
4X8M_A 0.2463    C 1 2 1
6S36_A 0.1594    C 1 2 1
6RZE_A 0.1819    C 1 2 1
4X8H_A 0.1914    C 1 2 1
3HPR_A 0.2062  P 21 21 2
```

#Principal Component Analysis

Time for PCA. We will not use 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.

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

plot(pc.xray)
```

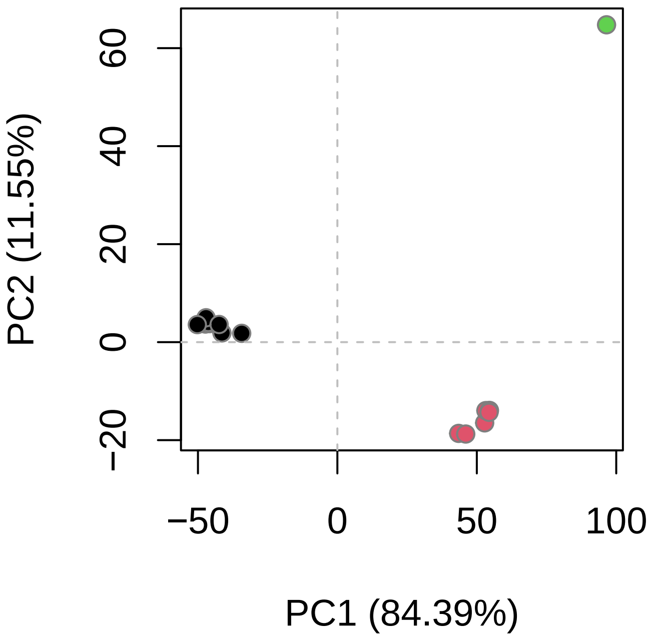


```
#calculate RMSD
rd <- rmsd(pdbs)
```

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

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

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



Further Visualization

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 ("pc_1.pdb") to view a movie of the major differences (i.e. displacements) in the structure set as we move along PC1.