Structural Bioinfomatics Pt1

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

```
##            Molecular.Type   X.ray     EM    NMR Multiple.methods Neutron Other
## 1          Protein (only) 167,317 15,698 12,534              208      77    32
## 2 Protein/Oligosaccharide   9,645  2,639     34                8       2     0
## 3              Protein/NA   8,735  4,718    286                7       0     0
## 4     Nucleic acid (only)   2,869    138  1,507               14       3     1
## 5                   Other     170     10     33                0       0     0
## 6  Oligosaccharide (only)      11      0      6                1       0     4
##     Total
## 1 195,866
## 2  12,328
## 3  13,746
## 4   4,532
## 5     213
## 6      22
```

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

```
#For x-ray:
188747/226707*100
```

```
## [1] 83.25592
```

```
#For electron microscopy:
23203/226707*100
```

```
## [1] 10.2348
```

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

```
195866/226707
```

```
## [1] 0.863961
```

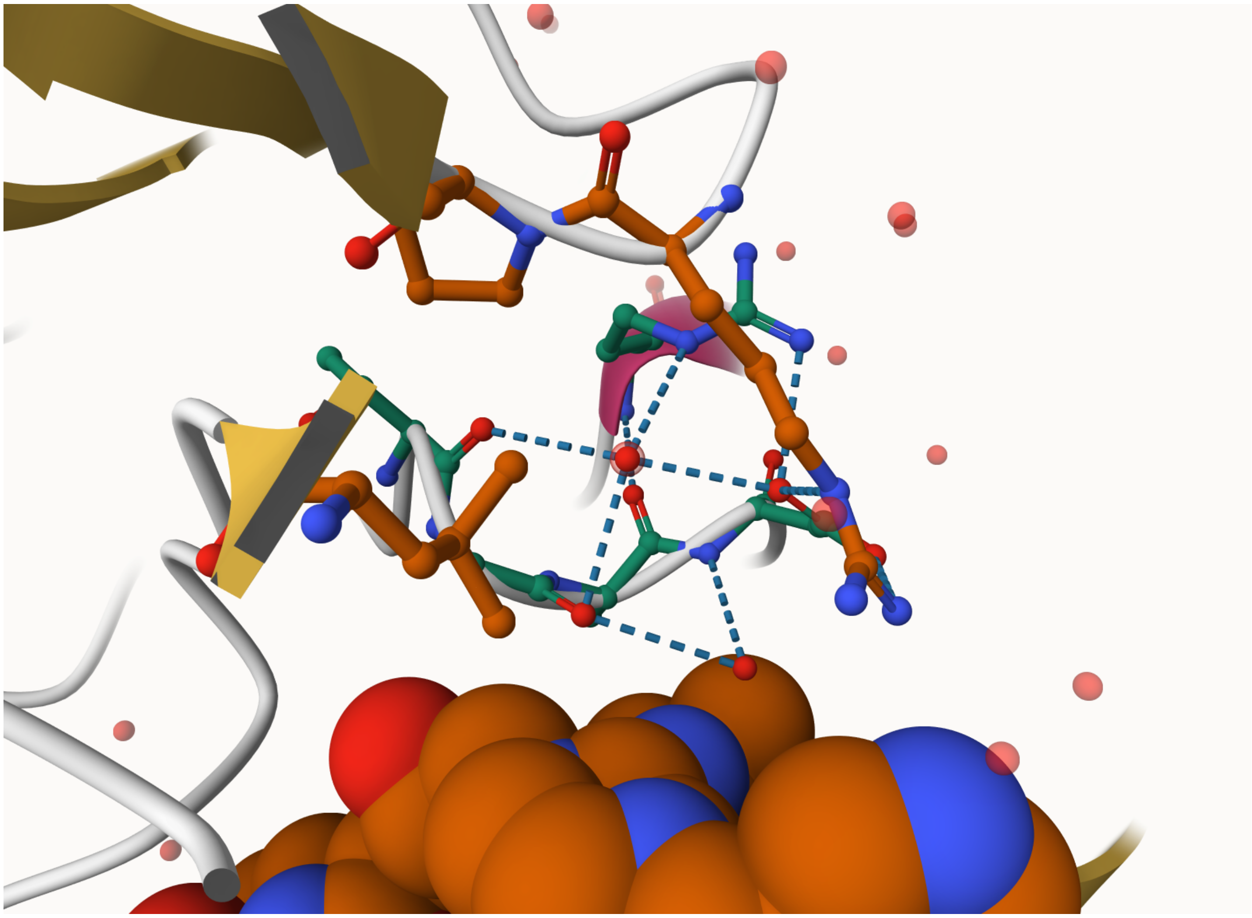
Q3: Type HIV in the PDB website search box on the home page and determine how many HIV-1 protease structures are in the current PDB? ANS: 4,563 Structures

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

ANS: We use Ball and Stick. Hydrogens aren't shown in this mode and Oxygen is represented by a red dot .

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 ANS:HOH at 324

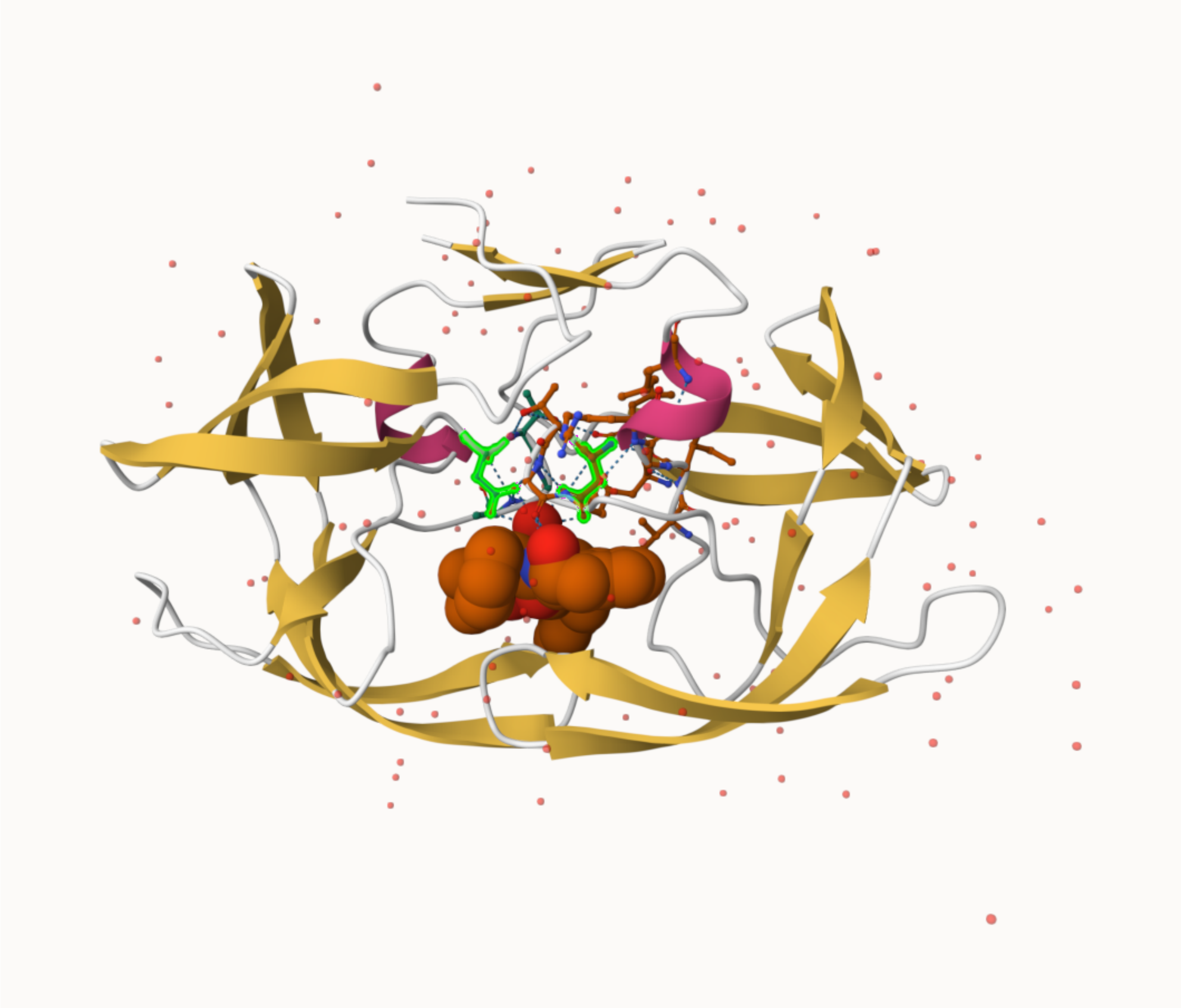
```r
knitr::include_graphics("conservedH.png")
```



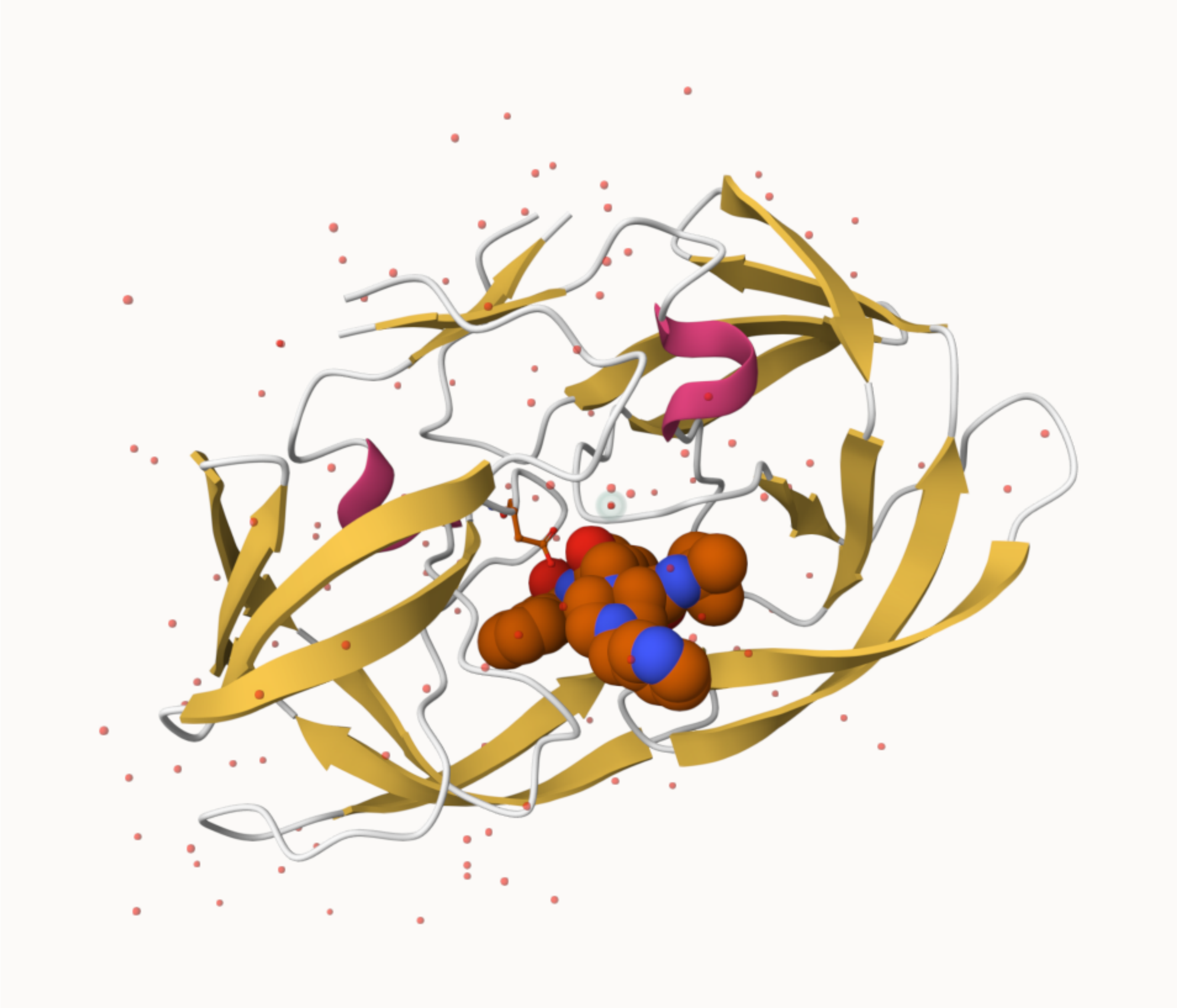
Q6: Generate and save a figure clearly showing the two distinct chains of HIV-protease along with the ligand. You might also consider showing the catalytic residues ASP 25 in each chain and the critical water (we recommend "Ball & Stick" for these side-chains). Add this figure to your Quarto document.

ANS:Chain A ASP25 on the right, Chain B ASP25 on the right.

```r
knitr::include_graphics("1HSGall.png")
```



```r
knitr::include_graphics("1HSGwater.png")
```



>Conserved water molecule with a halo.

Reading PDB file data into R

```
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? ANS:198

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

Q9: How many protein chains are in this structure? ANS:2

```r
attributes(pdb)
```

```
## $names
## [1] "atom"   "xyz"    "seqres" "helix"  "sheet"  "calpha" "remark" "call"
##
## $class
## [1] "pdb" "sse"
```

```r
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>
```

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

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

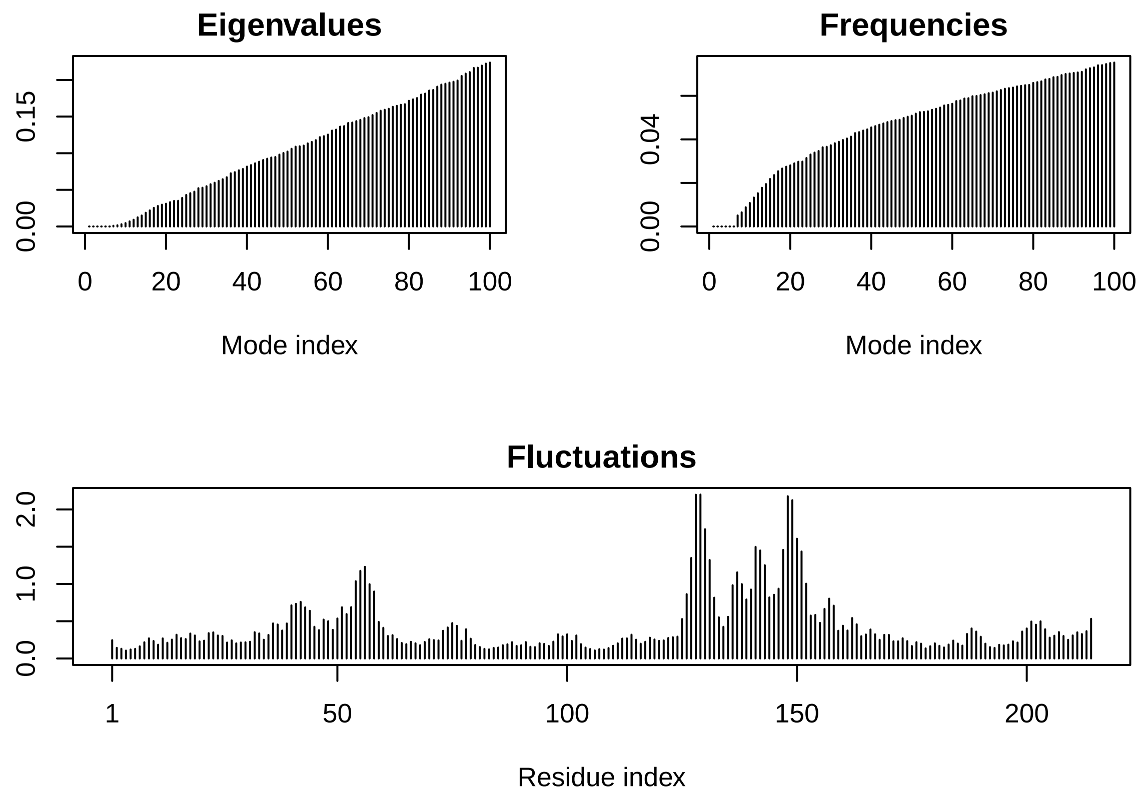
```r
adk
```

```
##
##  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
```

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

```
##  Building Hessian...     Done in 0.08 seconds.
##  Diagonalizing Hessian...    Done in 0.39 seconds.
```

```
plot(m)
```



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

Comparative structure analysis of Adenylate Kinase

```
# Install packages in the R console NOT your Rmd/Quarto file

#install.packages("bio3d")
#install.packages("devtools")
#install.packages("BiocManager")
```

```r
#BiocManager::install("msa")
#devtools::install_bitbucket("Grantlab/bio3d-view")
```

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

Q11. Which of the above packages is not found on BioConductor or CRAN?: ANS:bio3d-view

Q12. True or False? Functions from the devtools package can be used to install packages from GitHub and BitBucket? ANS: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? ANS:214

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

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



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

```
hits <- NULL
hits$pdb.id <- c('1AKE_A','6S36_A','6RZE_A','3HPR_A','1E4V_A','5EJE_A','1E4Y_A','3X2S_A','6HAP_A','6HAM_
```

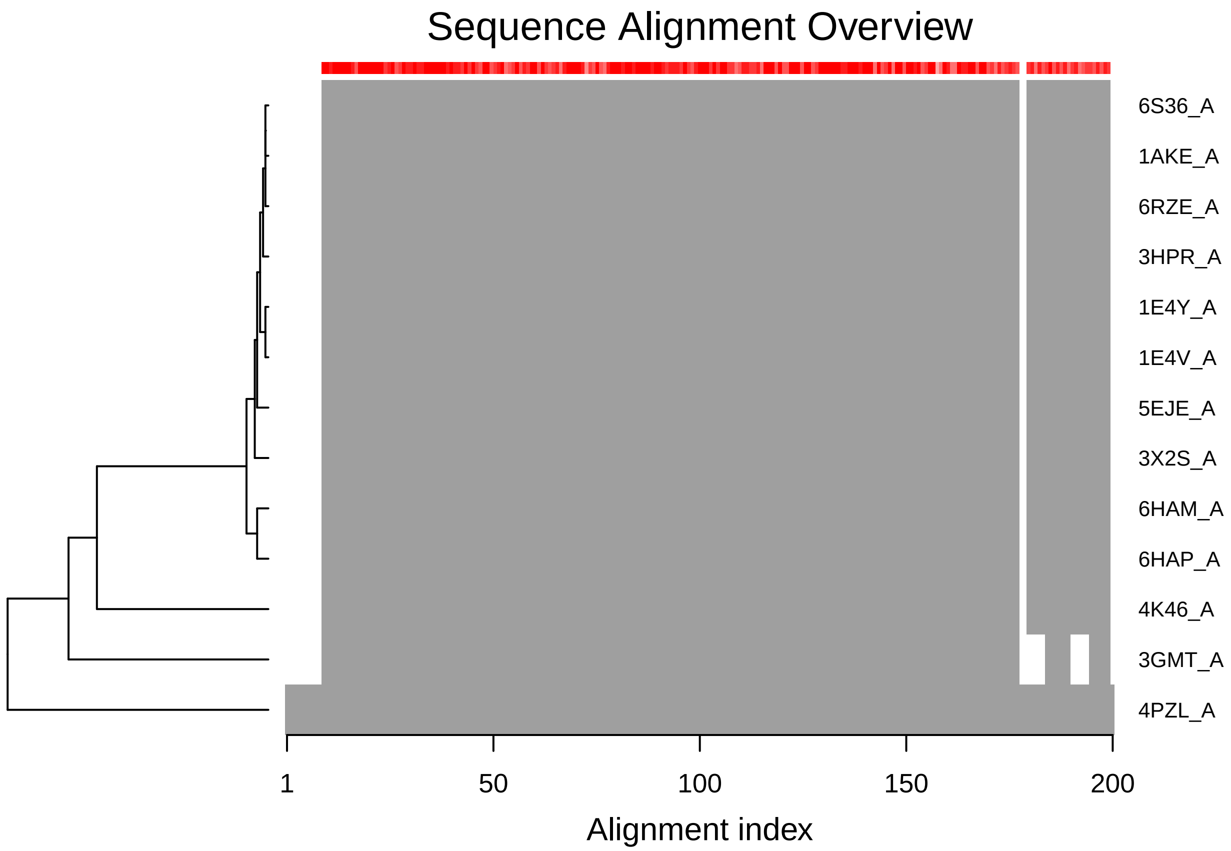
```
# Download releated PDB files

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/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/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/3GMT.pdb exists. Skipping download

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

##   |                                                                               |
```

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

```
## Reading PDB files:
## pdbs/split_chain/1AKE_A.pdb
## pdbs/split_chain/6S36_A.pdb
## pdbs/split_chain/6RZE_A.pdb
## pdbs/split_chain/3HPR_A.pdb
## pdbs/split_chain/1E4V_A.pdb
## pdbs/split_chain/5EJE_A.pdb
## pdbs/split_chain/1E4Y_A.pdb
## pdbs/split_chain/3X2S_A.pdb
## pdbs/split_chain/6HAP_A.pdb
## pdbs/split_chain/6HAM_A.pdb
## pdbs/split_chain/4K46_A.pdb
## pdbs/split_chain/3GMT_A.pdb
## pdbs/split_chain/4PZL_A.pdb
##    PDB has ALT records, taking A only, rm.alt=TRUE
## .   PDB has ALT records, taking A only, rm.alt=TRUE
## .   PDB has ALT records, taking A only, rm.alt=TRUE
## .   PDB has ALT records, taking A only, rm.alt=TRUE
## ..   PDB has ALT records, taking A only, rm.alt=TRUE
## ....   PDB has ALT records, taking A only, rm.alt=TRUE
## .   PDB has ALT records, taking A only, rm.alt=TRUE
## ...
##
## Extracting sequences
##
## pdb/seq: 1   name: pdbs/split_chain/1AKE_A.pdb
##    PDB has ALT records, taking A only, rm.alt=TRUE
## pdb/seq: 2   name: pdbs/split_chain/6S36_A.pdb
##    PDB has ALT records, taking A only, rm.alt=TRUE
## pdb/seq: 3   name: pdbs/split_chain/6RZE_A.pdb
##    PDB has ALT records, taking A only, rm.alt=TRUE
## pdb/seq: 4   name: pdbs/split_chain/3HPR_A.pdb
##    PDB has ALT records, taking A only, rm.alt=TRUE
## pdb/seq: 5   name: pdbs/split_chain/1E4V_A.pdb
## pdb/seq: 6   name: pdbs/split_chain/5EJE_A.pdb
##    PDB has ALT records, taking A only, rm.alt=TRUE
## pdb/seq: 7   name: pdbs/split_chain/1E4Y_A.pdb
## pdb/seq: 8   name: pdbs/split_chain/3X2S_A.pdb
## pdb/seq: 9   name: pdbs/split_chain/6HAP_A.pdb
## pdb/seq: 10   name: pdbs/split_chain/6HAM_A.pdb
##    PDB has ALT records, taking A only, rm.alt=TRUE
## pdb/seq: 11   name: pdbs/split_chain/4K46_A.pdb
##    PDB has ALT records, taking A only, rm.alt=TRUE
## pdb/seq: 12   name: pdbs/split_chain/3GMT_A.pdb
## pdb/seq: 13   name: pdbs/split_chain/4PZL_A.pdb
```

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

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



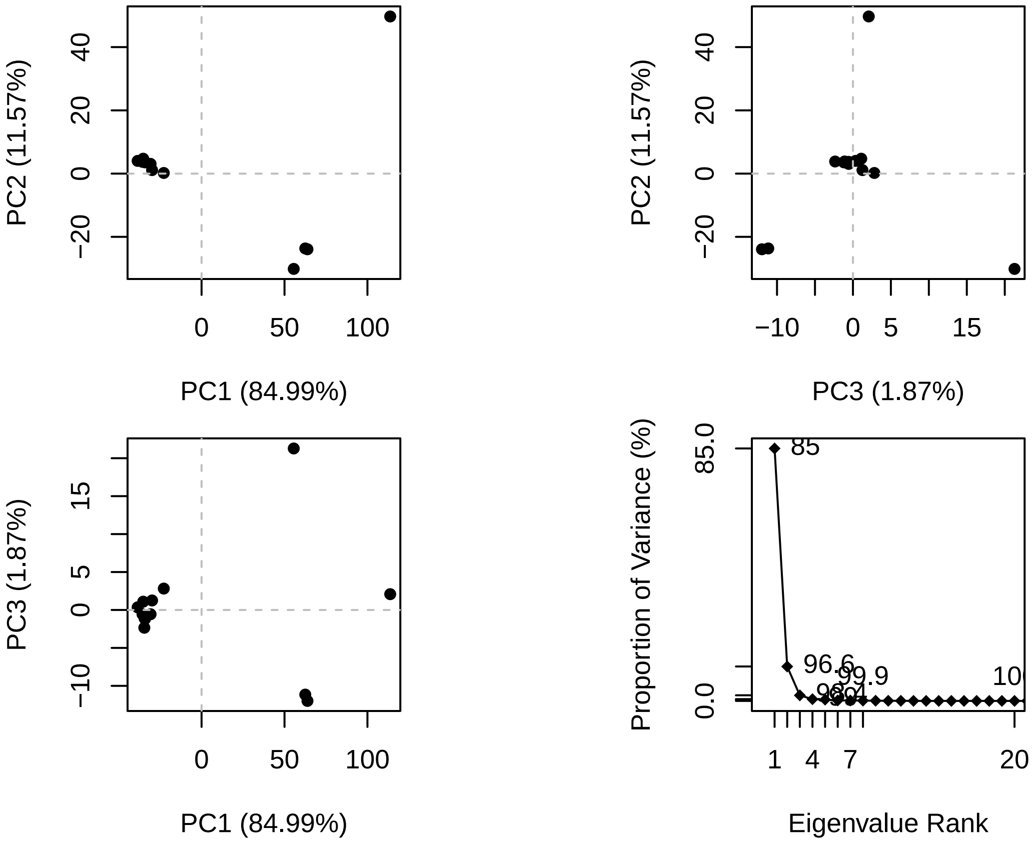
```
anno <- pdb.annotate(ids)
unique(anno$source)
```

```
## [1] "Escherichia coli"
## [2] "Escherichia coli K-12"
## [3] "Escherichia coli O139:H28 str. E24377A"
## [4] "Escherichia coli str. K-12 substr. MDS42"
## [5] "Photobacterium profundum"
## [6] "Burkholderia pseudomallei 1710b"
## [7] "Francisella tularensis subsp. tularensis SCHU S4"
```

```
anno
```

```
##        structureId chainId macromoleculeType chainLength experimentalTechnique
## 1AKE_A        1AKE       A           Protein         214                 X-ray
## 6S36_A        6S36       A           Protein         214                 X-ray
## 6RZE_A        6RZE       A           Protein         214                 X-ray
## 3HPR_A        3HPR       A           Protein         214                 X-ray
## 1E4V_A        1E4V       A           Protein         214                 X-ray
## 5EJE_A        5EJE       A           Protein         214                 X-ray
## 1E4Y_A        1E4Y       A           Protein         214                 X-ray
## 3X2S_A        3X2S       A           Protein         214                 X-ray
## 6HAP_A        6HAP       A           Protein         214                 X-ray
## 6HAM_A        6HAM       A           Protein         214                 X-ray
## 4K46_A        4K46       A           Protein         214                 X-ray
## 3GMT_A        3GMT       A           Protein         230                 X-ray
## 4PZL_A        4PZL       A           Protein         242                 X-ray
##        resolution       scopDomain                                        pfam
## 1AKE_A       2.00 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
## 6S36_A       1.60             <NA> Adenylate kinase, active site lid (ADK_lid)
## 6RZE_A       1.69             <NA>                      Adenylate kinase (ADK)
## 3HPR_A       2.00             <NA> Adenylate kinase, active site lid (ADK_lid)
## 1E4V_A       1.85 Adenylate kinase                      Adenylate kinase (ADK)
## 5EJE_A       1.90             <NA> Adenylate kinase, active site lid (ADK_lid)
## 1E4Y_A       1.85 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
## 3X2S_A       2.80             <NA>                      Adenylate kinase (ADK)
## 6HAP_A       2.70             <NA>                      Adenylate kinase (ADK)
## 6HAM_A       2.55             <NA> Adenylate kinase, active site lid (ADK_lid)
## 4K46_A       2.01             <NA> Adenylate kinase, active site lid (ADK_lid)
## 3GMT_A       2.10             <NA> Adenylate kinase, active site lid (ADK_lid)
## 4PZL_A       2.10             <NA>                      Adenylate kinase (ADK)
##                ligandId
## 1AKE_A              AP5
## 6S36_A CL (3),NA,MG (2)
## 6RZE_A    NA (3),CL (2)
## 3HPR_A              AP5
## 1E4V_A              AP5
## 5EJE_A           AP5,CO
## 1E4Y_A              AP5
## 3X2S_A   JPY (2),AP5,MG
## 6HAP_A              AP5
## 6HAM_A              AP5
## 4K46_A      AMP,PO4,ADP
## 3GMT_A          SO4 (2)
## 4PZL_A       CA,FMT,GOL
##                                                                               ligandName
## 1AKE_A                                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE
## 6S36_A                                     CHLORIDE ION (3),SODIUM ION,MAGNESIUM ION (2)
## 6RZE_A                                                   SODIUM ION (3),CHLORIDE ION (2)
## 3HPR_A                                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE
## 1E4V_A                                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE
## 5EJE_A                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE,COBALT (II) ION
## 1E4Y_A                                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE
## 3X2S_A N-(pyren-1-ylmethyl)acetamide (2),BIS(ADENOSINE)-5'-PENTAPHOSPHATE,MAGNESIUM ION
## 6HAP_A                                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE
## 6HAM_A                                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE
## 4K46_A                    ADENOSINE MONOPHOSPHATE,PHOSPHATE ION,ADENOSINE-5'-DIPHOSPHATE
## 3GMT_A                                                                   SULFATE ION (2)
## 4PZL_A                                                  CALCIUM ION,FORMIC ACID,GLYCEROL
##                                                  source
## 1AKE_A                                 Escherichia coli
## 6S36_A                                 Escherichia coli
## 6RZE_A                                 Escherichia coli
## 3HPR_A                            Escherichia coli K-12
## 1E4V_A                                 Escherichia coli
## 5EJE_A           Escherichia coli O139:H28 str. E24377A
## 1E4Y_A                                 Escherichia coli
## 3X2S_A         Escherichia coli str. K-12 substr. MDS42
## 6HAP_A           Escherichia coli O139:H28 str. E24377A
## 6HAM_A                            Escherichia coli K-12
## 4K46_A                         Photobacterium profundum
## 3GMT_A                  Burkholderia pseudomallei 1710b
## 4PZL_A Francisella tularensis subsp. tularensis SCHU S4
## 
## 1AKE_A STRUCTURE OF THE COMPLEX BETWEEN ADENYLATE KINASE FROM ESCHERICHIA COLI AND THE INHIBITOR AP5
## 6S36_A
## 6RZE_A
## 3HPR_A
## 1E4V_A
## 5EJE_A                                                                                  Crystal stru
## 1E4Y_A
## 3X2S_A
## 6HAP_A
## 6HAM_A
## 4K46_A
## 3GMT_A
## 4PZL_A                                                                              The crystal stru
##                                                       citation rObserved   rFree
## 1AKE_A                 Muller, C.W., et al. J Mol Biol (1992)   0.19600      NA
## 6S36_A                  Rogne, P., et al. Biochemistry (2019)   0.16320 0.23560
## 6RZE_A                  Rogne, P., et al. Biochemistry (2019)   0.18650 0.23500
## 3HPR_A  Schrank, T.P., et al. Proc Natl Acad Sci U S A (2009)   0.21000 0.24320
## 1E4V_A                   Muller, C.W., et al. Proteins (1993)   0.19600      NA
## 5EJE_A  Kovermann, M., et al. Proc Natl Acad Sci U S A (2017)   0.18890 0.23580
## 1E4Y_A                   Muller, C.W., et al. Proteins (1993)   0.17800      NA
## 3X2S_A                Fujii, A., et al. Bioconjug Chem (2015)   0.20700 0.25600
## 6HAP_A               Kantaev, R., et al. J Phys Chem B (2018)   0.22630 0.27760
## 6HAM_A               Kantaev, R., et al. J Phys Chem B (2018)   0.20511 0.24325
## 4K46_A                    Cho, Y.-J., et al. To be published    0.17000 0.22290
## 3GMT_A Buchko, G.W., et al. Biochem Biophys Res Commun (2010)   0.23800 0.29500
## 4PZL_A                       Tan, K., et al. To be published    0.19360 0.23680
##          rWork spaceGroup
## 1AKE_A 0.19600  P 21 2 21
## 6S36_A 0.15940    C 1 2 1
## 6RZE_A 0.18190    C 1 2 1
## 3HPR_A 0.20620  P 21 21 2
## 1E4V_A 0.19600  P 21 2 21
## 5EJE_A 0.18630  P 21 2 21
## 1E4Y_A 0.17800   P 1 21 1
## 3X2S_A 0.20700 P 21 21 21
## 6HAP_A 0.22370    I 2 2 2
## 6HAM_A 0.20311       P 43
## 4K46_A 0.16730 P 21 21 21
## 3GMT_A 0.23500   P 1 21 1
## 4PZL_A 0.19130       P 32
```

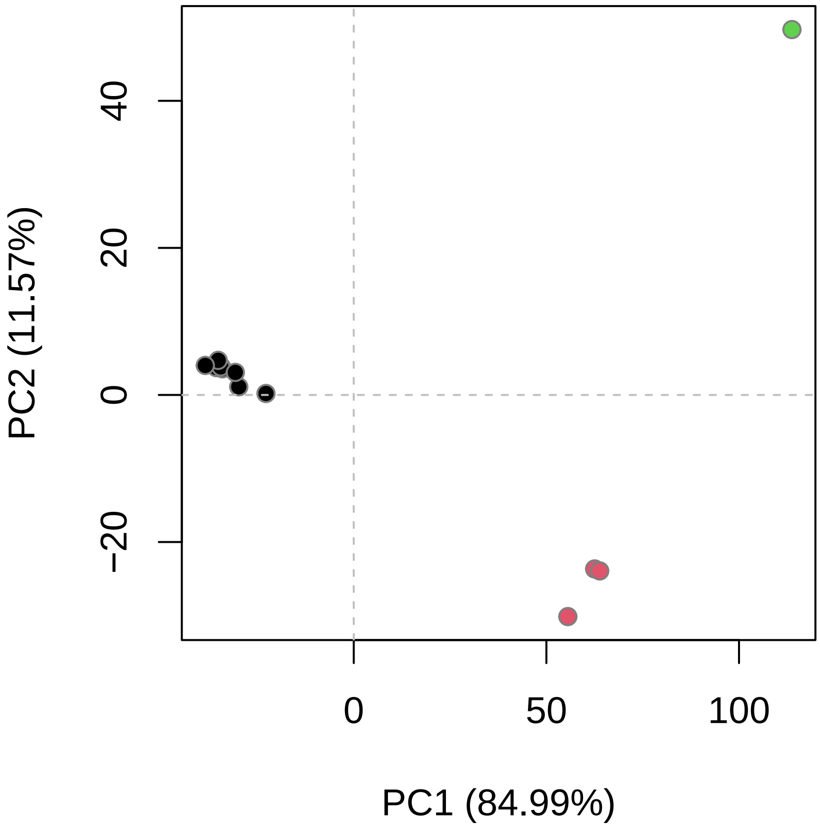
```r
# Perform PCA
pc.xray <- pca(pdbs)
plot(pc.xray)
```



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

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

```r
# Structure-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)
```


PC2 (11.57%)
40
20
0
−20
0
50
100
PC1 (84.99%)