class10_structural bioinformatics

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1. Introduction to the RCSB Protein Data Bank (PDB)

```
Data_file <- "Data Export Summary.csv"
pdbstats= read.csv(Data_file, row.names=1)
summary(pdbstats)
```

```
   X.ray               EM               NMR            Multiple.methods
 Length:6           Length:6           Length:6           Min.   :  0.00
 Class :character   Class :character   Class :character   1st Qu.:  2.50
 Mode  :character   Mode  :character   Mode  :character   Median :  7.50
                                                          Mean   : 38.33
                                                          3rd Qu.: 12.50
                                                          Max.   :200.00
   Neutron          Other            Total
 Min.   : 0.00   Min.   : 0.000   Length:6
 1st Qu.: 0.00   1st Qu.: 0.000   Class :character
 Median : 1.00   Median : 0.500   Mode  :character
 Mean   :13.17   Mean   : 6.167
 3rd Qu.: 2.75   3rd Qu.: 3.250
 Max.   :74.00   Max.   :32.000
```

```
head(pdbstats)
```

```
                        X.ray     EM    NMR Multiple.methods Neutron Other
Protein (only)        161,663 12,592 12,337              200      74    32
Protein/Oligosaccharide 9,348  2,167     34                8       2     0
Protein/NA              8,404  3,924    286                7       0     0
Nucleic acid (only)     2,758    125  1,477               14       3     1
```

```
Other                        164      9     33                0       0     0
Oligosaccharide (only)        11      0      6                1       0     4
                            Total
Protein (only)            186,898
Protein/Oligosaccharide    11,559
Protein/NA                 12,621
Nucleic acid (only)         4,378
Other                         206
Oligosaccharide (only)         22
```

```
# code extract function
  commasum <- function(x) {
    # Remomve comma, convert to numeric and sum
    sum(as.numeric(gsub(",", "", x)))
  }
```

```
commasum((pdbstats$X.ray))
```

```
[1] 182348
```

Q1: What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy. **A1:** X.ray: 84.54 % and EM: 8.72%

```
round(apply(pdbstats, 2, commasum)/commasum(pdbstats$Total)*100, 2)
```

```
          X.ray              EM             NMR Multiple.methods
          84.54            8.72            6.57            0.11
        Neutron           Other           Total
           0.04            0.02          100.00
```

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

A2: 97.86%

```
protein_structures_total <- pdbstats[1:3,7]
protein_structures_total
```

```
[1] "186,898" "11,559"  "12,621"
```

```
round(commasum(protein_structures_total)/commasum(pdbstats$Total)*100, 2)
```

```
[1] 97.86
```

Q. How does the total number of protein structures iN the PDB relate to the total number of protein sequences in Uniport?

```
186898/250322721*100
```

```
[1] 0.07466282
```

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?

A3: There are 486 HIV-1 protease structures

2. Visualizing the HIV-1 protease structure

Q4: Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure? **A4:** The resolution is not high enough to see H.

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 **A5:**Yes, HOH308

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.

3. Introduction to Bio3D in R

```
library(bio3d)
hiv <- read.pdb("1hsg")
```

```
Note: Accessing on-line PDB file
```

```
hiv
```

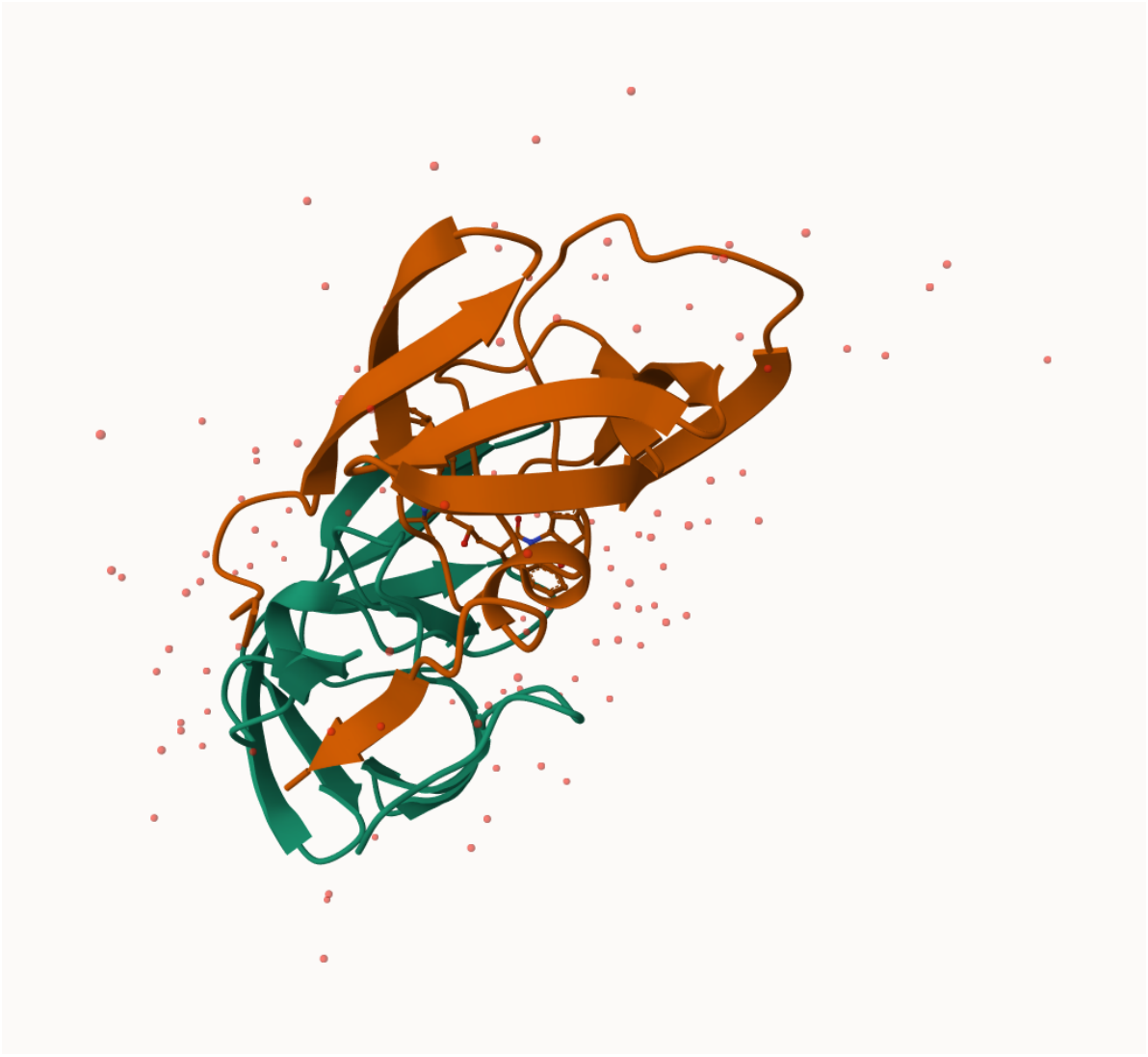


Figure 1: snapshot of 1HSG

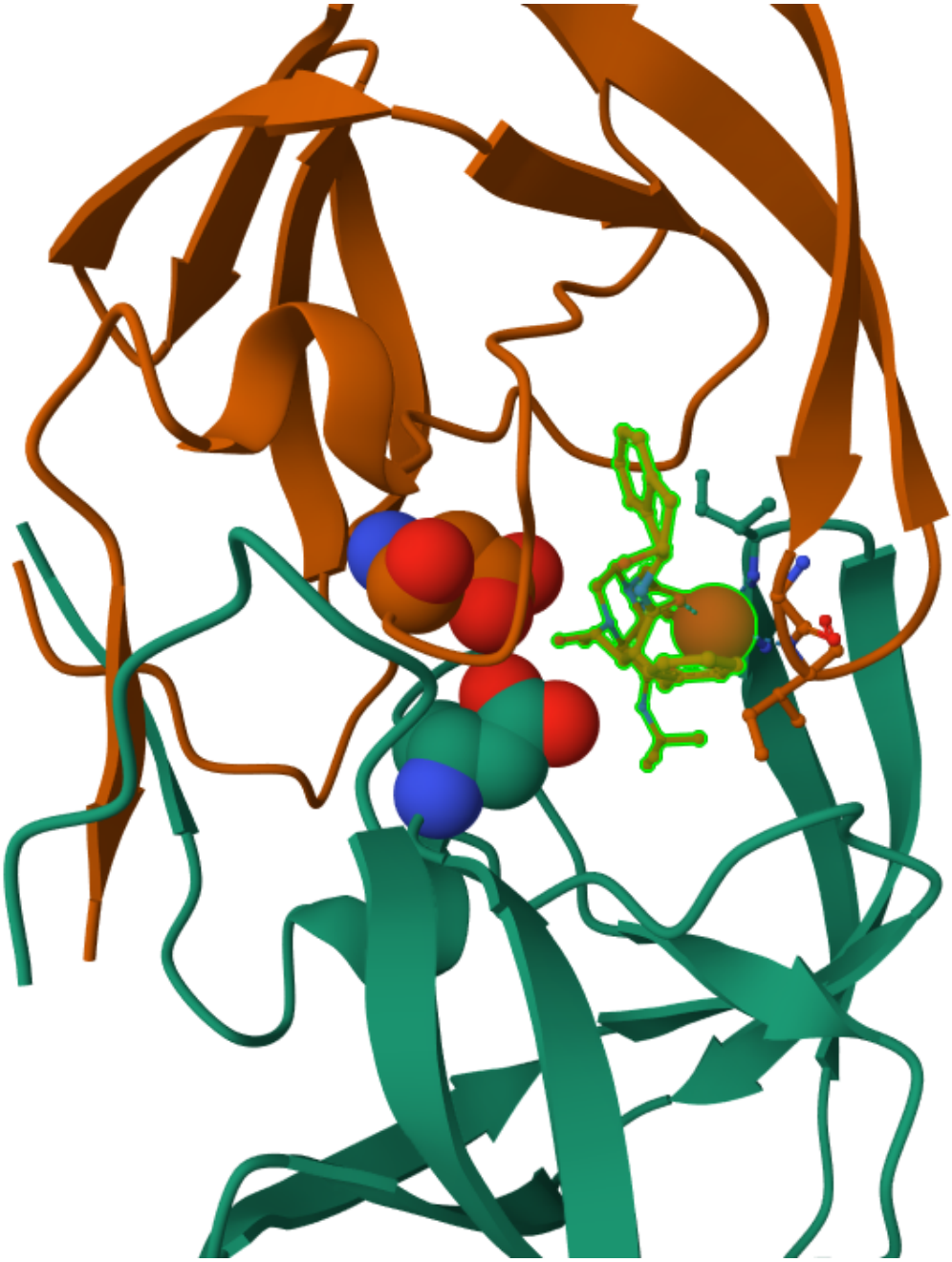


Figure 2: a nice display showing ASP 25 in the MK1 ligand

```
 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
```

```
attributes(hiv)
```

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

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

```
aa123(pdbseq(hiv)[25])
```

```
[1] "ASP"
```

```
head(hiv$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>
```

4. Reading PDB file data into R

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

A7: There are 198 amino acid

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

A8: HOH/MK1

Q9: How many protein chains are in this structure?

A9: There are 2 protein chains

```
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)
```

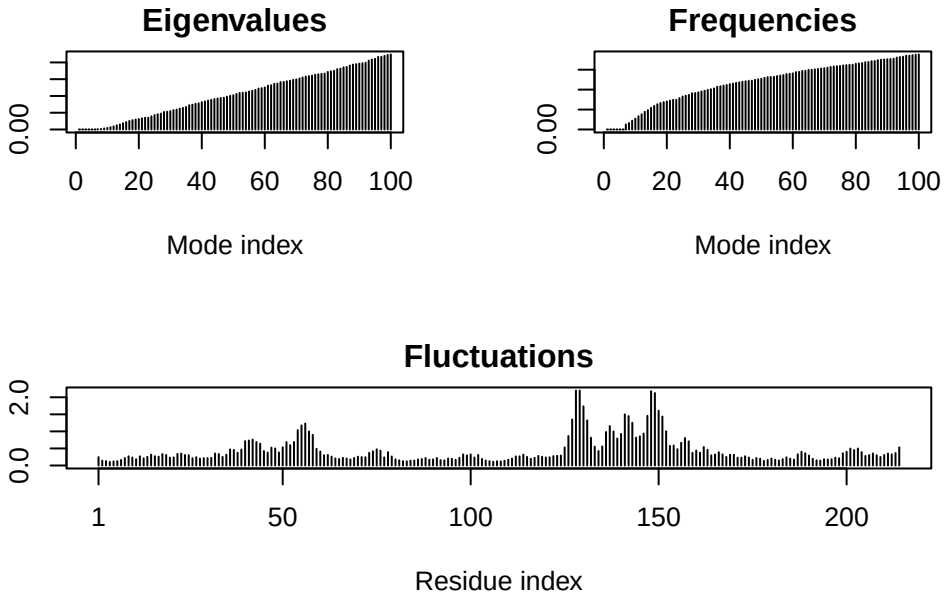
```
     Non-protein/nucleic Atoms#: 244  (residues: 244)
     Non-protein/nucleic resid values: [ CL (3), HOH (238), MG (2), NA (1) ]

   Protein sequence:
      MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
      DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDKI
      VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG

+ attr: atom, xyz, seqres, helix, sheet,
        calpha, remark, call
```

normal mode analysis(nma) a bioinformatic method to predict functional motions and large-scale structure changes

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

```
 Building Hessian...        Done in 0.05 seconds.
 Diagonalizing Hessian...   Done in 0.34 seconds.
```

```
plot(m)
```



make a wee movie

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

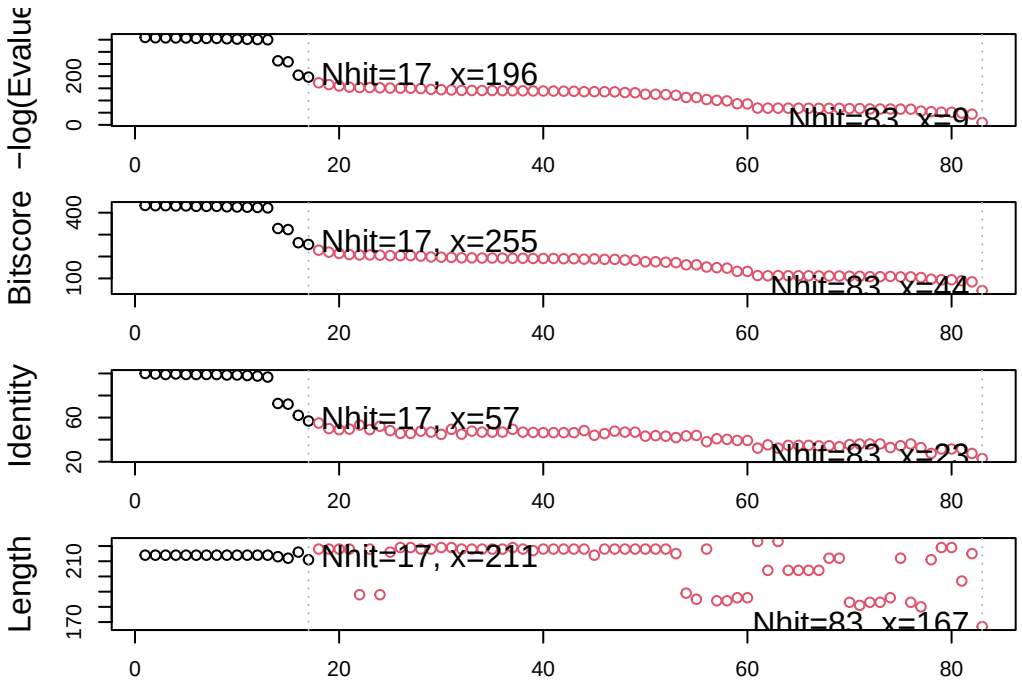
Extract a sequence and run a blast

```
s <- pdbseq(adk)
blast <- blast.pdb(s)
```

```
Searching ... please wait (updates every 5 seconds) RID = WH2A1VV301N
.
Reporting 83 hits
```

```
plot(blast)
```

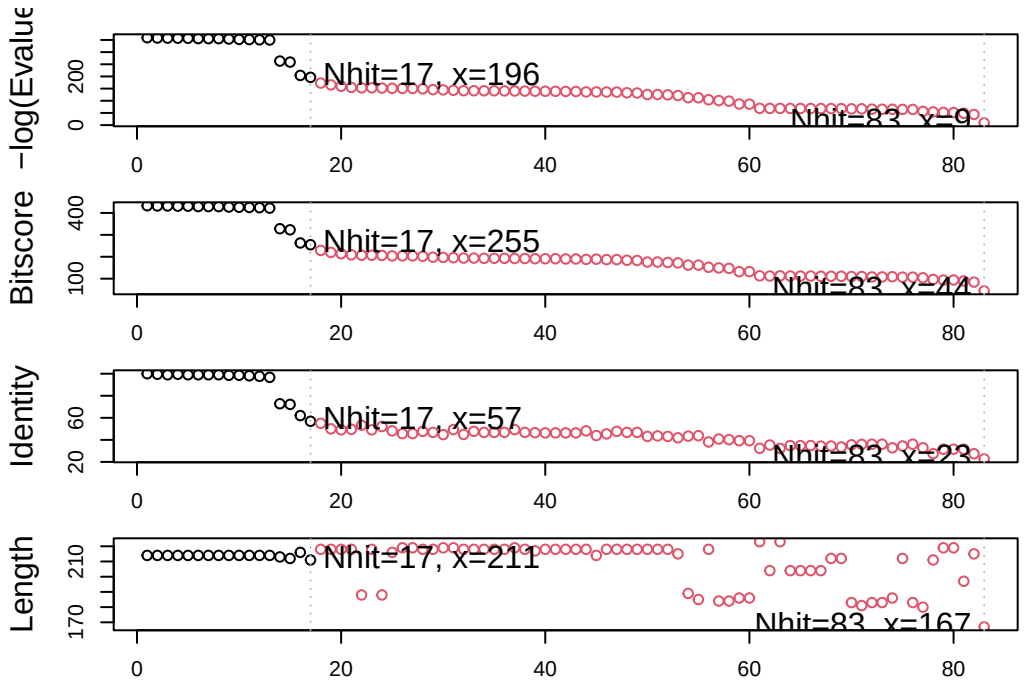
```
 * Possible cutoff values:    196 9
           Yielding Nhits:    17 83

 * Chosen cutoff value of:    196
           Yielding Nhits:    17
```



get the results from BLAST and download all the top hits.

```
hits <- plot(blast)
```

```
* Possible cutoff values:    196 9
          Yielding Nhits:    17 83

* Chosen cutoff value of:    196
          Yielding Nhits:    17
```




```
hits
```

```
$hits
   pdb.id   acc      group
1  "6S36_A" "6S36_A" "1"
2  "1AKE_A" "1AKE_A" "1"
3  "8BQF_A" "8BQF_A" "1"
4  "6RZE_A" "6RZE_A" "1"
5  "4X8M_A" "4X8M_A" "1"
6  "4X8H_A" "4X8H_A" "1"
```

```
7  "1E4V_A" "1E4V_A" "1"
8  "3HPR_A" "3HPR_A" "1"
9  "5EJE_A" "5EJE_A" "1"
10 "1E4Y_A" "1E4Y_A" "1"
11 "3X2S_A" "3X2S_A" "1"
12 "6HAP_A" "6HAP_A" "1"
13 "6HAM_A" "6HAM_A" "1"
14 "4K46_A" "4K46_A" "1"
15 "4NP6_A" "4NP6_A" "1"
16 "3GMT_A" "3GMT_A" "1"
17 "4PZL_A" "4PZL_A" "1"

$pdb.id
 [1] "6S36_A" "1AKE_A" "8BQF_A" "6RZE_A" "4X8M_A" "4X8H_A" "1E4V_A" "3HPR_A"
 [9] "5EJE_A" "1E4Y_A" "3X2S_A" "6HAP_A" "6HAM_A" "4K46_A" "4NP6_A" "3GMT_A"
[17] "4PZL_A"

$acc
 [1] "6S36_A" "1AKE_A" "8BQF_A" "6RZE_A" "4X8M_A" "4X8H_A" "1E4V_A" "3HPR_A"
 [9] "5EJE_A" "1E4Y_A" "3X2S_A" "6HAP_A" "6HAM_A" "4K46_A" "4NP6_A" "3GMT_A"
[17] "4PZL_A"

$inds
 [1]  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE  TRUE
[13]  TRUE  TRUE  TRUE  TRUE  TRUE 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

attr(,"class")
[1] "blast"
```

```
hits$pdb.id
```

```
 [1] "6S36_A" "1AKE_A" "8BQF_A" "6RZE_A" "4X8M_A" "4X8H_A" "1E4V_A" "3HPR_A"
 [9] "5EJE_A" "1E4Y_A" "3X2S_A" "6HAP_A" "6HAM_A" "4K46_A" "4NP6_A" "3GMT_A"
[17] "4PZL_A"
```

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

```
BiocManager::install("msa")
```

```
Bioconductor version 3.18 (BiocManager 1.30.22), R 4.3.2 (2023-10-31 ucrt)
```

```
Warning: package(s) not installed when version(s) same as or greater than current; use
  `force = TRUE` to re-install: 'msa'
```

```
Installation paths not writeable, unable to update packages
  path: C:/Program Files/R/R-4.3.2/library
  packages:
    cluster, foreign, lattice, MASS, Matrix, mgcv, nlme, rpart
```

```
devtools::install_bitbucket("Grantlab/bio3d-view")
```

```
Skipping install of 'bio3d.view' from a bitbucket remote, the SHA1 (dd153987) has not changed
  Use `force = TRUE` to force installation
```

4. Comparative structure analysis of Adenylate Kinase

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

A10. The package "msa" is found only on Bioconductor and not on CRAN

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

A11. The package "bio3d-view" installed using devtools::install_bitbucket("Grantlab/bio3d-view") is not from Bioconductor or CRAN.

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

A12. True

PCA of all these

```
# Perform PCA
library(bio3d)
aa <- get.seq("1ake_A")
```

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

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

```
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/6S36.pdb exists. Skipping download
```

```
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/8BQF.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/4X8M.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/1E4V.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/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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```

```
pdbs <- pdbaln(files, fit = TRUE, exefile="msa")
```

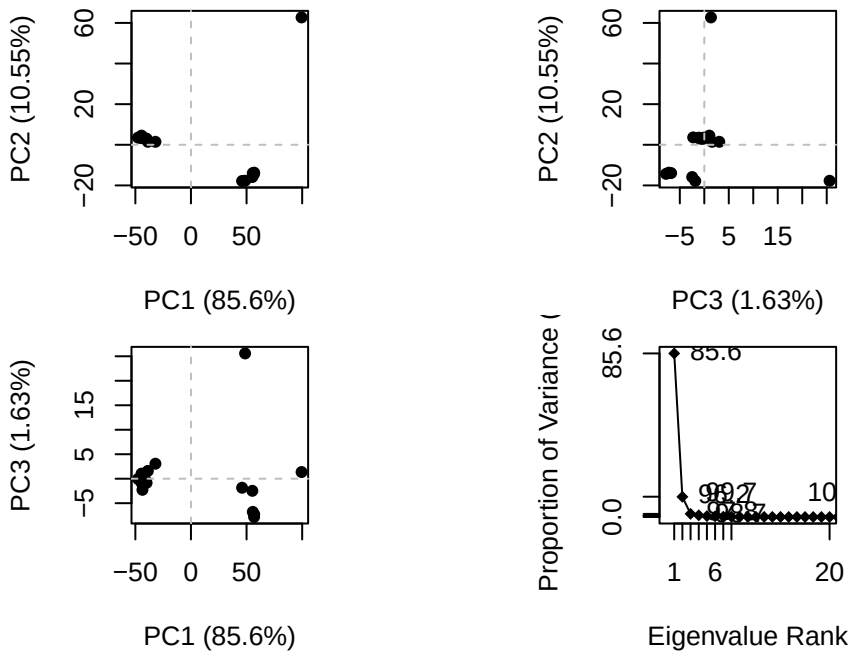
```
Reading PDB files:
pdbs/split_chain/6S36_A.pdb
pdbs/split_chain/1AKE_A.pdb
pdbs/split_chain/8BQF_A.pdb
pdbs/split_chain/6RZE_A.pdb
pdbs/split_chain/4X8M_A.pdb
pdbs/split_chain/4X8H_A.pdb
pdbs/split_chain/1E4V_A.pdb
pdbs/split_chain/3HPR_A.pdb
pdbs/split_chain/5EJE_A.pdb
pdbs/split_chain/1E4Y_A.pdb
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
.   PDB has ALT records, taking A only, rm.alt=TRUE
....

Extracting sequences

pdb/seq: 1   name: pdbs/split_chain/6S36_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 2   name: pdbs/split_chain/1AKE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 3   name: pdbs/split_chain/8BQF_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/4X8M_A.pdb
pdb/seq: 6   name: pdbs/split_chain/4X8H_A.pdb
pdb/seq: 7   name: pdbs/split_chain/1E4V_A.pdb
pdb/seq: 8   name: pdbs/split_chain/3HPR_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 9   name: pdbs/split_chain/5EJE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 10   name: pdbs/split_chain/1E4Y_A.pdb
pdb/seq: 11   name: pdbs/split_chain/3X2S_A.pdb
pdb/seq: 12   name: pdbs/split_chain/6HAP_A.pdb
pdb/seq: 13   name: pdbs/split_chain/6HAM_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 14   name: pdbs/split_chain/4K46_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 15   name: pdbs/split_chain/4NP6_A.pdb
pdb/seq: 16   name: pdbs/split_chain/3GMT_A.pdb
pdb/seq: 17   name: pdbs/split_chain/4PZL_A.pdb
```

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




```
mktrj(pc.xray, file = "pca_movie.pdb")
```

Q13. How many amino acids are in this sequence, i.e. how long is this sequence?

A13. 214 aa