Class 09: Structural Bioinformatics

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Table of contents

Visualizing the HIV-1 protease structure

The importance of water

Q4

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

We can only see the oxygen atom because the resolution on this viewer is too large for the hydrogen to be shown.

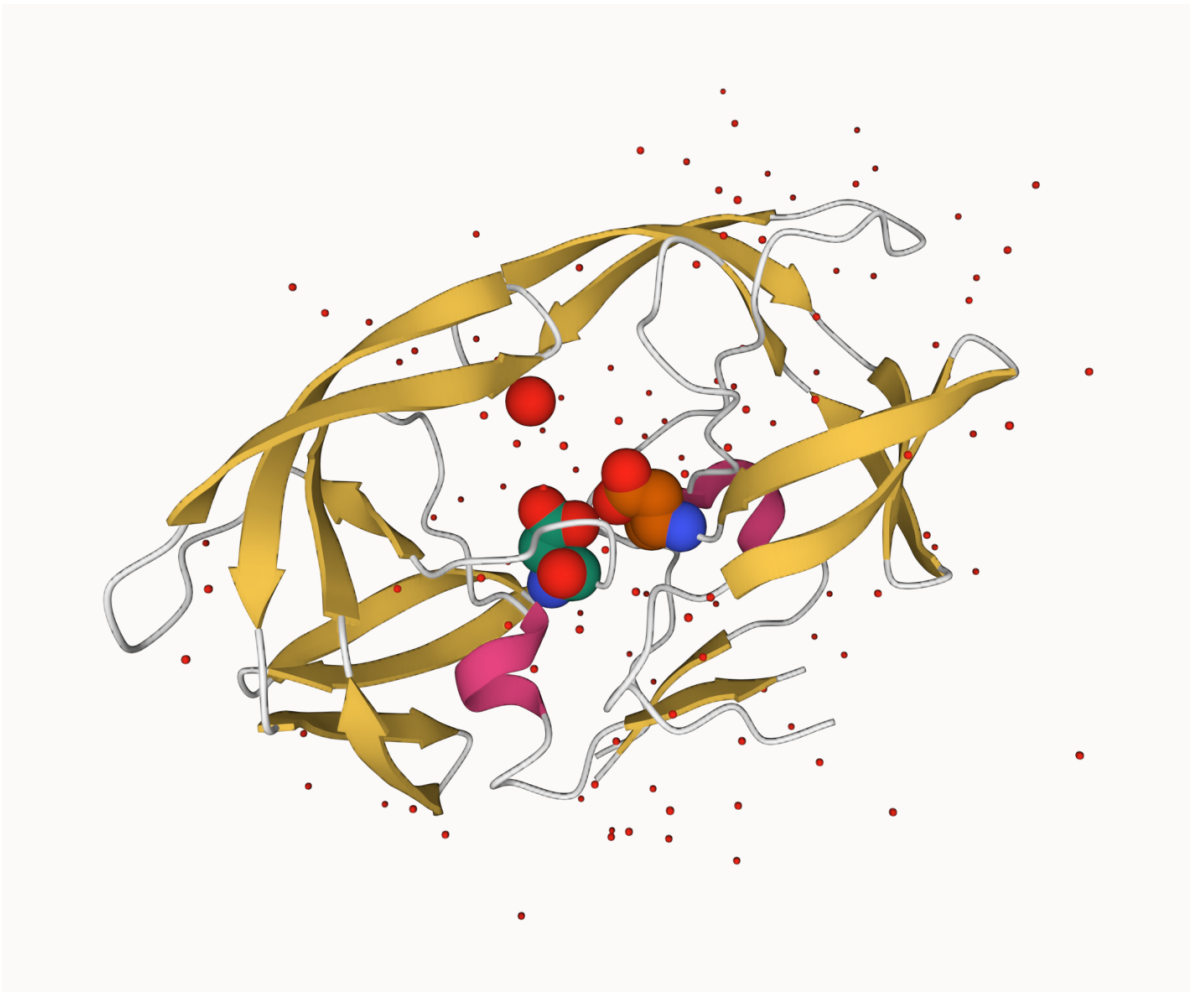
Q5

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

The hydrogen bond of the water is able to interact with both Asp25 residues which can bind better than the ligand (when it does not have the ability to H-bond)

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.



Reading and working with strutures in R

The `bio3d` package for structural bioinformatics has lots of features for reading adn working with bimolecular sequences and structures.

```
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?

There are 198 amino acids in the protein,

Q8

Name one of the two non-protein residues?

MK1 - Merck 1

Q9

How many protein chains are in this structure?

There are 2 chains in this structure

```
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>
```

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

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

```
adk
```

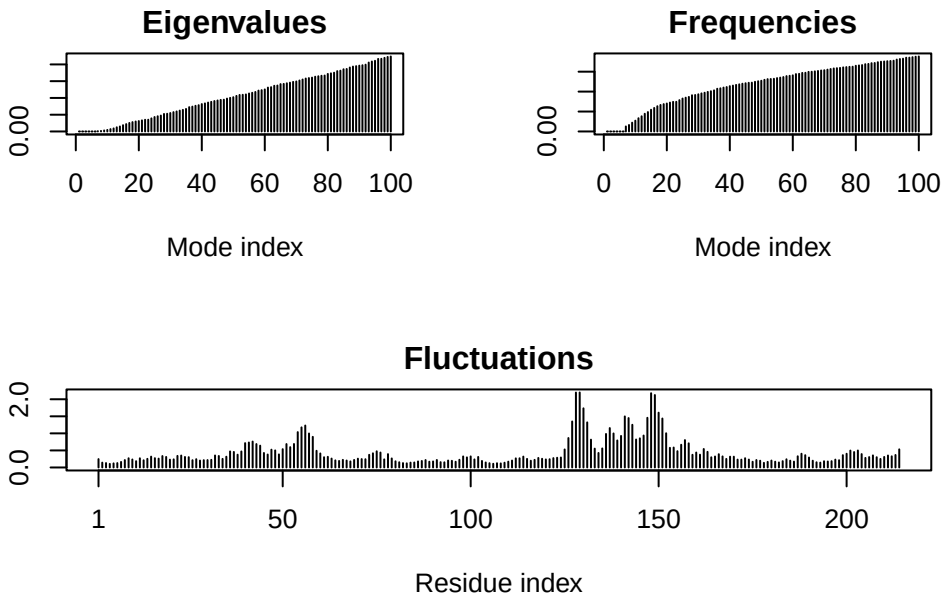
```
 Call:  read.pdb(file = "6s36")

   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 bioinformatics method for predicting functional motions, It will show us the parts of the protein that are "flexible"

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

```
 Building Hessian...        Done in 0.086 seconds.
 Diagonalizing Hessian...   Done in 0.258 seconds.
```

```
plot(m)
```



Make a "movie" of this thing moving.

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

Comparative Analysis of all ADK structures

First we get the sequence of ADK and use this to search the PDB database.

Software Installs

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

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

Q10

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

BiocManager

Q11

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

BitBucket

Q12

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

True

```
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?

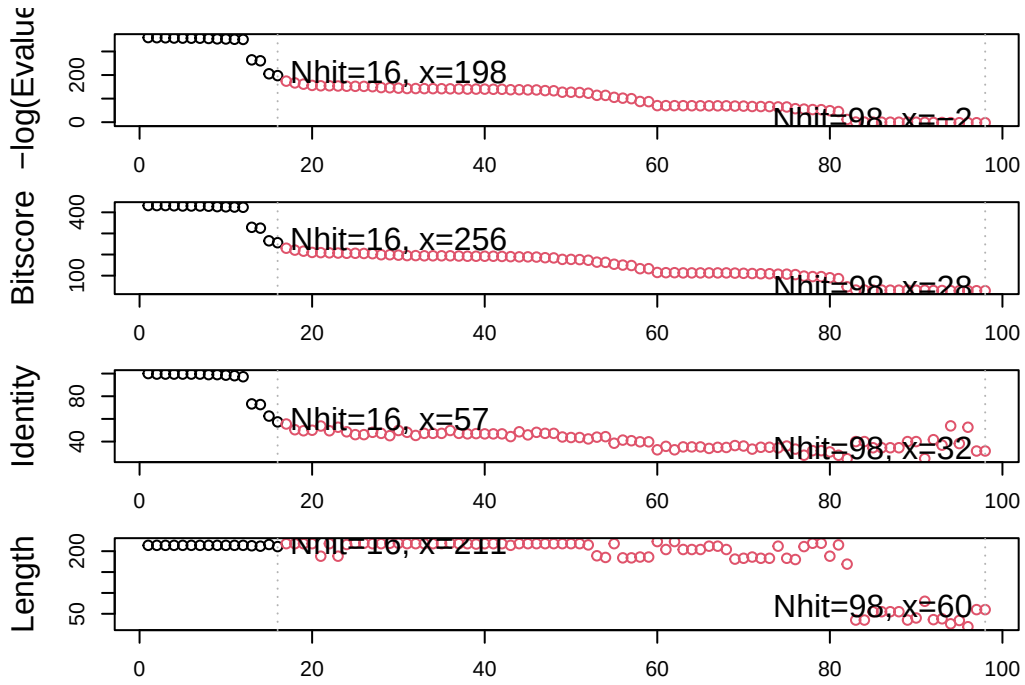
There are 214 amino acids in this sequence

```
b <- blast.pdb(aa)
```

```
Searching ... please wait (updates every 5 seconds) RID = NKFHB8JH013
.....................
Reporting 98 hits
```

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

```
* Possible cutoff values:    197 -3
          Yielding Nhits:    16 98

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




```
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"
```

```
pdb.annotate(hits$pdb.id)
```

```
       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
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
4NP6_A        4NP6       A           Protein         217                 X-ray
3GMT_A        3GMT       A           Protein         230                 X-ray
4PZL_A        4PZL       A           Protein         242                 X-ray
       resolution       scopDomain                                      pfam
1AKE_A      2.000 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
4X8M_A      2.600             <NA> Adenylate kinase, active site lid (ADK_lid)
6S36_A      1.600             <NA> Adenylate kinase, active site lid (ADK_lid)
6RZE_A      1.690             <NA> Adenylate kinase, active site lid (ADK_lid)
4X8H_A      2.500             <NA> Adenylate kinase, active site lid (ADK_lid)
3HPR_A      2.000             <NA> Adenylate kinase, active site lid (ADK_lid)
1E4V_A      1.850 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
5EJE_A      1.900             <NA> Adenylate kinase, active site lid (ADK_lid)
1E4Y_A      1.850 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
3X2S_A      2.800             <NA> Adenylate kinase, active site lid (ADK_lid)
6HAP_A      2.700             <NA> Adenylate kinase, active site lid (ADK_lid)
6HAM_A      2.550             <NA> Adenylate kinase, active site lid (ADK_lid)
4K46_A      2.010             <NA> Adenylate kinase, active site lid (ADK_lid)
4NP6_A      2.004             <NA> Adenylate kinase, active site lid (ADK_lid)
3GMT_A      2.100             <NA> Adenylate kinase, active site lid (ADK_lid)
4PZL_A      2.100             <NA> Adenylate kinase, active site lid (ADK_lid)
               ligandId
1AKE_A              AP5
4X8M_A             <NA>
6S36_A CL (3),NA,MG (2)
6RZE_A    NA (3),CL (2)
4X8H_A             <NA>
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      ADP,AMP,PO4
4NP6_A             <NA>
```

```
3GMT_A          SO4 (2)
4PZL_A       CA,FMT,GOL
                                                                                ligandName
1AKE_A                                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE
4X8M_A                                                                              <NA>
6S36_A                                     CHLORIDE ION (3),SODIUM ION,MAGNESIUM ION (2)
6RZE_A                                                  SODIUM ION (3),CHLORIDE ION (2)
4X8H_A                                                                              <NA>
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-5'-DIPHOSPHATE,ADENOSINE MONOPHOSPHATE,PHOSPHATE ION
4NP6_A                                                                              <NA>
3GMT_A                                                                   SULFATE ION (2)
4PZL_A                                                  CALCIUM ION,FORMIC ACID,GLYCEROL
                                                 source
1AKE_A                                Escherichia coli
4X8M_A                                Escherichia coli
6S36_A                                Escherichia coli
6RZE_A                                Escherichia coli
4X8H_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
4NP6_A     Vibrio cholerae O1 biovar El Tor str. N16961
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 INHIBI
4X8M_A
6S36_A
6RZE_A
4X8H_A
3HPR_A
```

```
1E4V_A
5EJE_A                                                                                                    Crys
1E4Y_A
3X2S_A
6HAP_A
6HAM_A
4K46_A
4NP6_A
3GMT_A
4PZL_A                                                                                                The crys
                                                          citation rObserved   rFree
1AKE_A                 Muller, C.W., et al. J Mol Biol (1992)   0.19600      NA
4X8M_A                Kovermann, M., et al. Nat Commun (2015)   0.24910 0.30890
6S36_A                  Rogne, P., et al. Biochemistry (2019)   0.16320 0.23560
6RZE_A                  Rogne, P., et al. Biochemistry (2019)   0.18650 0.23500
4X8H_A                Kovermann, M., et al. Nat Commun (2015)   0.19610 0.28950
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
4NP6_A                        Kim, Y., et al. To be published   0.18800 0.22200
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
4X8M_A 0.24630    C 1 2 1
6S36_A 0.15940    C 1 2 1
6RZE_A 0.18190    C 1 2 1
4X8H_A 0.19140    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
4NP6_A 0.18600       P 43
3GMT_A 0.23500   P 1 21 1
```

```
4PZL_A 0.19130       P 32
```

```
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

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```

Viewing all these structures looks like a hot mess! We need to try something else...

We will align and supperpose these structures.

```
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
```

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

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

Annotate PDB Structures

```r
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"
```

```
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
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
4NP6_A        4NP6       A           Protein         217                 X-ray
3GMT_A        3GMT       A           Protein         230                 X-ray
4PZL_A        4PZL       A           Protein         242                 X-ray
       resolution       scopDomain                                    pfam
1AKE_A      2.000 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
4X8M_A      2.600             <NA> Adenylate kinase, active site lid (ADK_lid)
6S36_A      1.600             <NA> Adenylate kinase, active site lid (ADK_lid)
6RZE_A      1.690             <NA> Adenylate kinase, active site lid (ADK_lid)
4X8H_A      2.500             <NA> Adenylate kinase, active site lid (ADK_lid)
3HPR_A      2.000             <NA> Adenylate kinase, active site lid (ADK_lid)
1E4V_A      1.850 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
5EJE_A      1.900             <NA> Adenylate kinase, active site lid (ADK_lid)
1E4Y_A      1.850 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
3X2S_A      2.800             <NA> Adenylate kinase, active site lid (ADK_lid)
6HAP_A      2.700             <NA> Adenylate kinase, active site lid (ADK_lid)
6HAM_A      2.550             <NA> Adenylate kinase, active site lid (ADK_lid)
4K46_A      2.010             <NA> Adenylate kinase, active site lid (ADK_lid)
4NP6_A      2.004             <NA> Adenylate kinase, active site lid (ADK_lid)
3GMT_A      2.100             <NA> Adenylate kinase, active site lid (ADK_lid)
4PZL_A      2.100             <NA> Adenylate kinase, active site lid (ADK_lid)
```

```
              ligandId
1AKE_A              AP5
4X8M_A            <NA>
6S36_A CL (3),NA,MG (2)
6RZE_A    NA (3),CL (2)
4X8H_A            <NA>
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      ADP,AMP,PO4
4NP6_A            <NA>
3GMT_A         SO4 (2)
4PZL_A       CA,FMT,GOL
                                                                                ligandName
1AKE_A                                                        BIS(ADENOSINE)-5'-PENTAPHOSPHATE
4X8M_A                                                                                  <NA>
6S36_A                                          CHLORIDE ION (3),SODIUM ION,MAGNESIUM ION (2)
6RZE_A                                                           SODIUM ION (3),CHLORIDE ION (2)
4X8H_A                                                                                  <NA>
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-5'-DIPHOSPHATE,ADENOSINE MONOPHOSPHATE,PHOSPHATE ION
4NP6_A                                                                                  <NA>
3GMT_A                                                                       SULFATE ION (2)
4PZL_A                                                        CALCIUM ION,FORMIC ACID,GLYCEROL
                                                 source
1AKE_A                                 Escherichia coli
4X8M_A                                 Escherichia coli
6S36_A                                 Escherichia coli
6RZE_A                                 Escherichia coli
4X8H_A                                 Escherichia coli
3HPR_A                          Escherichia coli K-12
1E4V_A                                 Escherichia coli
5EJE_A           Escherichia coli O139:H28 str. E24377A
```

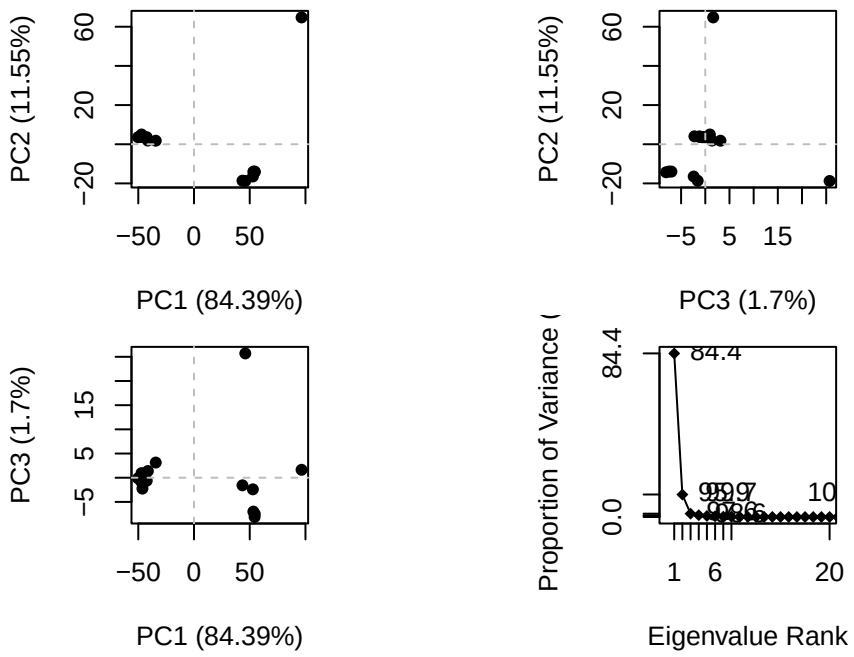
```
1E4Y_A                                  Escherichia coli
3X2S_A          Escherichia coli str. K-12 substr. MDS42
6HAP_A            Escherichia coli O139:H28 str. E24377A
6HAM_A                              Escherichia coli K-12
4K46_A                           Photobacterium profundum
4NP6_A      Vibrio cholerae O1 biovar El Tor str. N16961
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 INHIBI
4X8M_A
6S36_A
6RZE_A
4X8H_A
3HPR_A
1E4V_A
5EJE_A                                                                          Cryst
1E4Y_A
3X2S_A
6HAP_A
6HAM_A
4K46_A
4NP6_A
3GMT_A
4PZL_A                                                                      The cryst
                                                    citation rObserved   rFree
1AKE_A                 Muller, C.W., et al. J Mol Biol (1992)   0.19600      NA
4X8M_A                Kovermann, M., et al. Nat Commun (2015)   0.24910 0.30890
6S36_A                  Rogne, P., et al. Biochemistry (2019)   0.16320 0.23560
6RZE_A                  Rogne, P., et al. Biochemistry (2019)   0.18650 0.23500
4X8H_A                Kovermann, M., et al. Nat Commun (2015)   0.19610 0.28950
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
4NP6_A                       Kim, Y., et al. To be published   0.18800 0.22200
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
4X8M_A 0.24630    C 1 2 1
6S36_A 0.15940    C 1 2 1
6RZE_A 0.18190    C 1 2 1
4X8H_A 0.19140    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
4NP6_A 0.18600       P 43
3GMT_A 0.23500   P 1 21 1
4PZL_A 0.19130       P 32
```

Principal Component Analysis

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

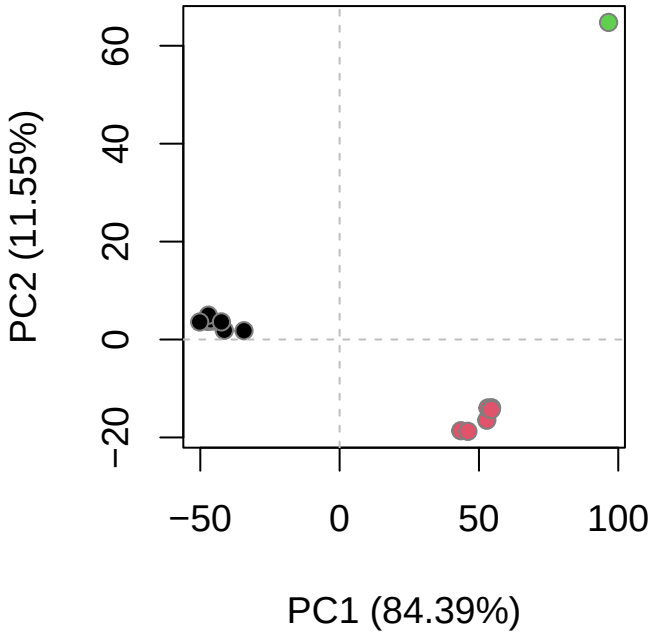



```
# Calculate RMSD
rd <- rmsd(pdbs)
```

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

```
# 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)
```

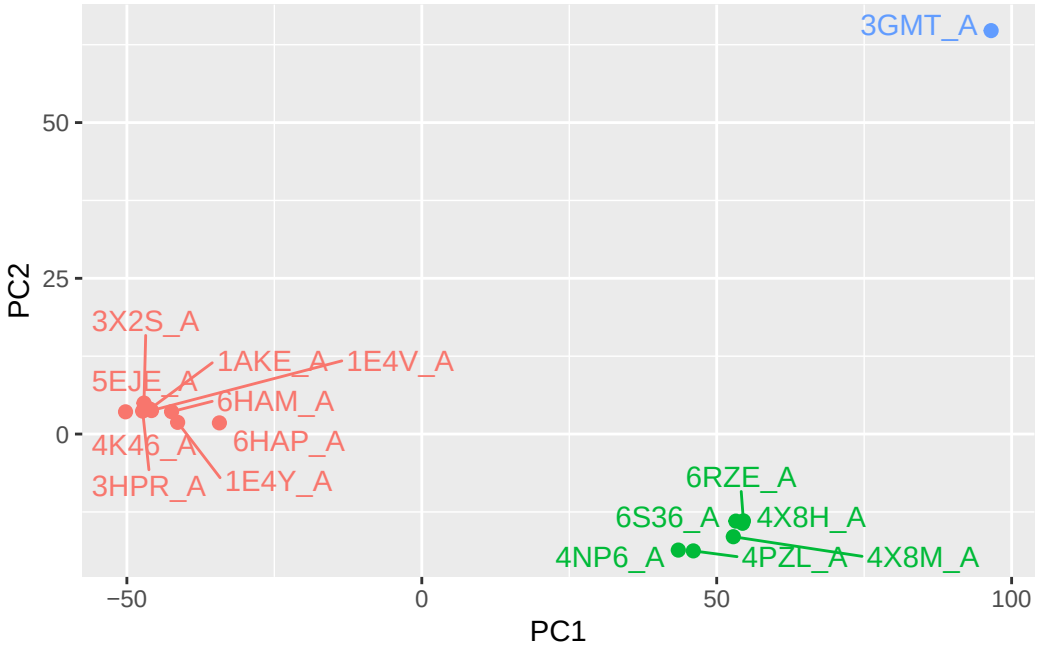



```
pc1 <- mktrj(pc.xray, pc=1, file="pc_1.pdb")
```

```
#Plotting results with ggplot2
library(ggplot2)
library(ggrepel)

df <- data.frame(PC1=pc.xray$z[,1],
                 PC2=pc.xray$z[,2],
                 col=as.factor(grps.rd),
                 ids=ids)

p <- ggplot(df) +
  aes(PC1, PC2, col=col, label=ids) +
  geom_point(size=2) +
  geom_text_repel(max.overlaps = 20) +
  theme(legend.position = "none")
p
```



Normal Mode Analysis

```
# NMA of all structures
modes <- nma(pdbs)
```

```
Details of Scheduled Calculation:
  ... 16 input structures
  ... storing 606 eigenvectors for each structure
  ... dimension of x$U.subspace: ( 612x606x16 )
  ... coordinate superposition prior to NM calculation
  ... aligned eigenvectors (gap containing positions removed)
  ... estimated memory usage of final 'eNMA' object: 45.4 Mb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```

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  |============================================================          |  81%
  |
  |================================================================      |  88%
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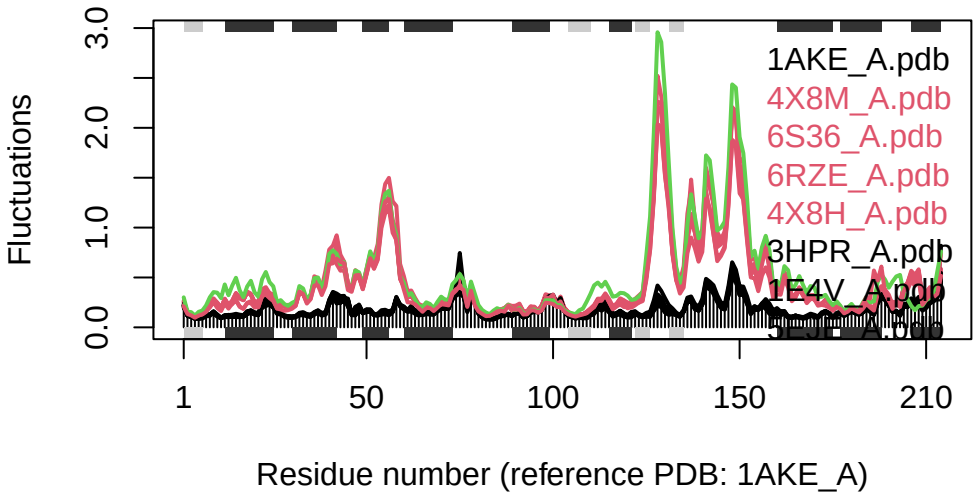
  |======================================================================|  94%
  |
  |======================================================================| 100%
```

```
plot(modes, pdbs, col=grps.rd)
```

```
Extracting SSE from pdbs$sse attribute
```



Q14

What do you note about this plot? Are the black and colored lines similar or different? Where do you think they differ most and why?

The black lines and colored lines share similar shapes, but the colored lines fluctuate more than the black lines and the differ most around the 130-150 range where the colored lines really spike more than the black ones. These residues correspond well to the ones we saw "moving" in the animated version on Mol Viewer.