# class09

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## The PDB database

The main repository for biomolecular structure data is the Protein Data Bank (PDB) https://www.rcsb.org

Let's have a quick look at the composition of this database:

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

```r
read.csv("Data Export Summary.csv")
```

```
           Molecular.Type   X.ray     EM    NMR Integrative Multiple.methods
1          Protein (only) 176,378 20,438 12,709         342              221
2 Protein/Oligosaccharide  10,284  3,396     34           8               11
3              Protein/NA   9,007  5,931    287          24                7
4     Nucleic acid (only)   3,077    200  1,554           2               15
5                   Other     174     13     33           3                0
6  Oligosaccharide (only)      11      0      6           0                1
  Neutron Other   Total
1      83    32 210,203
2       1     0  13,734
3       0     0  15,256
4       3     1   4,852
5       0     0     223
6       0     4      22
```

```r
stats <- read.csv("Data Export Summary.csv")
stats
```

```
           Molecular.Type   X.ray     EM    NMR Integrative Multiple.methods
1          Protein (only) 176,378 20,438 12,709         342              221
2 Protein/Oligosaccharide  10,284  3,396     34           8               11
3              Protein/NA   9,007  5,931    287          24                7
4     Nucleic acid (only)   3,077    200  1,554           2               15
5                   Other     174     13     33           3                0
6  Oligosaccharide (only)      11      0      6           0                1
  Neutron Other   Total
1      83    32 210,203
2       1     0  13,734
3       0     0  15,256
4       3     1   4,852
5       0     0     223
6       0     4      22
```

```
as.numeric(sub(",", "", stats$X.ray))
```

```
[1] 176378  10284   9007   3077    174     11
```

This is annoying, lets try a different import function form the **readr** package. First step `install.packages("readr")`

```
library(readr)

stats <- read_csv("Data Export Summary.csv")
```

```
Rows: 6 Columns: 9
-- Column specification --------------------------------------------------------
Delimiter: ","
chr (1): Molecular Type
dbl (4): Integrative, Multiple methods, Neutron, Other
num (4): X-ray, EM, NMR, Total

i Use `spec()` to retrieve the full column specification for this data.
i Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

```
stats
```

```
# A tibble: 6 x 9
  `Molecular Type`    `X-ray`    EM   NMR Integrative `Multiple methods` Neutron
  <chr>                 <dbl> <dbl> <dbl>       <dbl>              <dbl>   <dbl>
1 Protein (only)       176378 20438 12709         342                221      83
2 Protein/Oligosacch~   10284  3396    34           8                 11       1
3 Protein/NA             9007  5931   287          24                  7       0
4 Nucleic acid (only)    3077   200  1554           2                 15       3
5 Other                   174    13    33           3                  0       0
6 Oligosaccharide (o~      11     0     6           0                  1       0
# i 2 more variables: Other <dbl>, Total <dbl>
```

Percent X-ray

```
n.total <- sum(stats$Total)
n.xray <-sum(stats$`X-ray`)
n.em <- sum(stats$EM)

round((n.xray/n.total)*100,2)
```

```
[1] 81.43
```

```
round(n.em/n.total *100, 2)
```

```
[1] 12.27
```

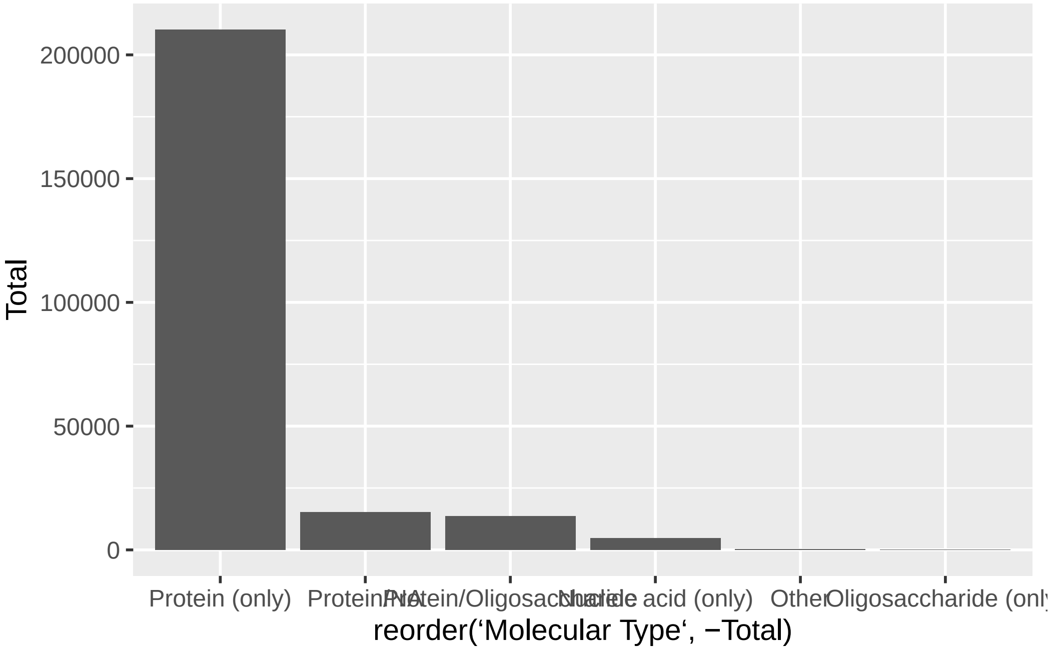
Q2: What proportion of structures in the PDB are protein?

```
protein <- stats$Total[1]/n.total
protein
```

```
[1] 0.860465
```

Q3. Make a bar plot overview of a Molecular type composition using ggplot

```
library(ggplot2)
ggplot(stats,
       aes(reorder(`Molecular Type`,-Total), Total)) +
         geom_col()
```



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

This is just a default setting in molstar

> 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

##Visualizing structure data

> 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.

The Mol* viewer is embeded in many bioinformatics websites. The homepage is https://molstar.org

I can insert any figure or image file using markdown format `![](image name)`

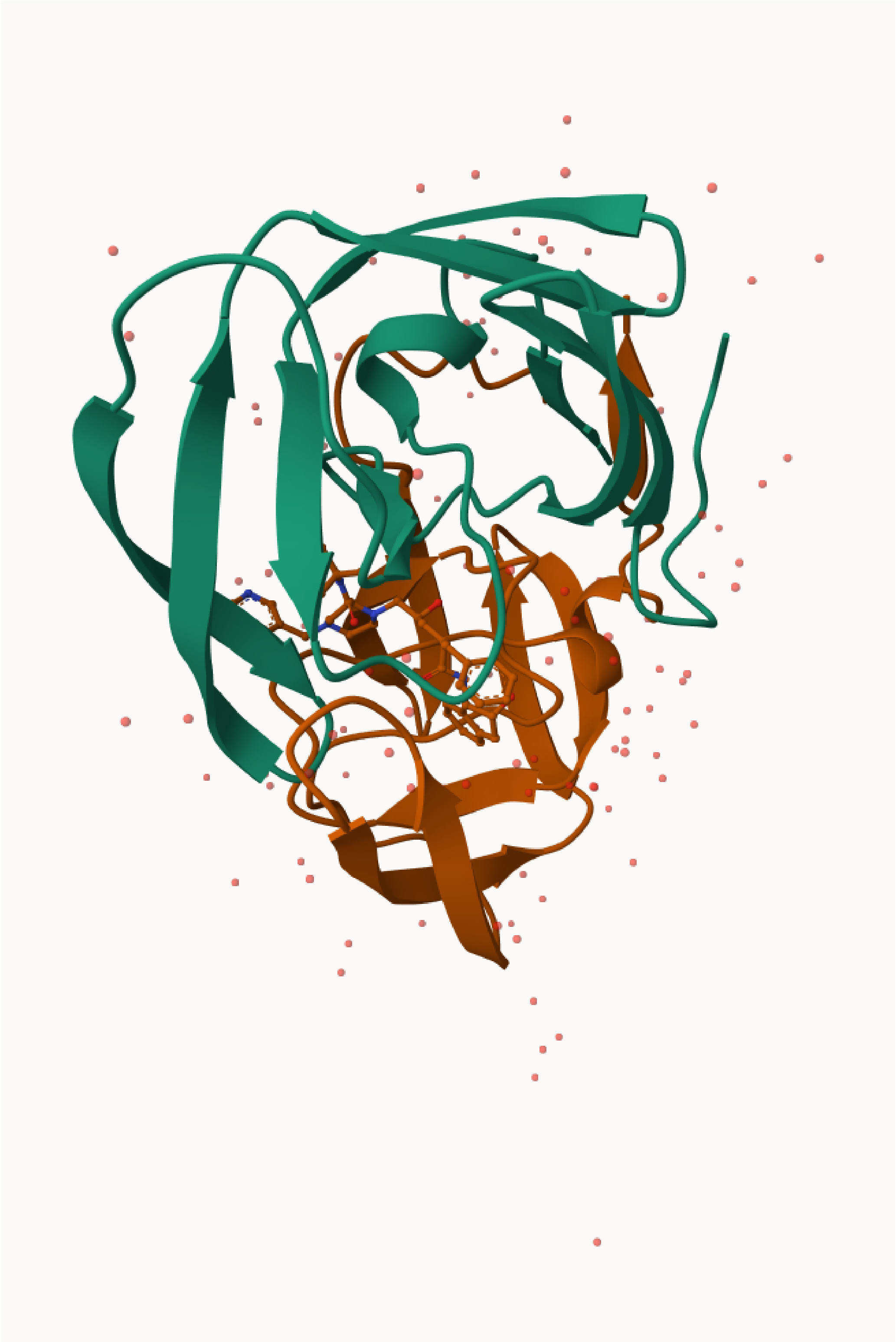
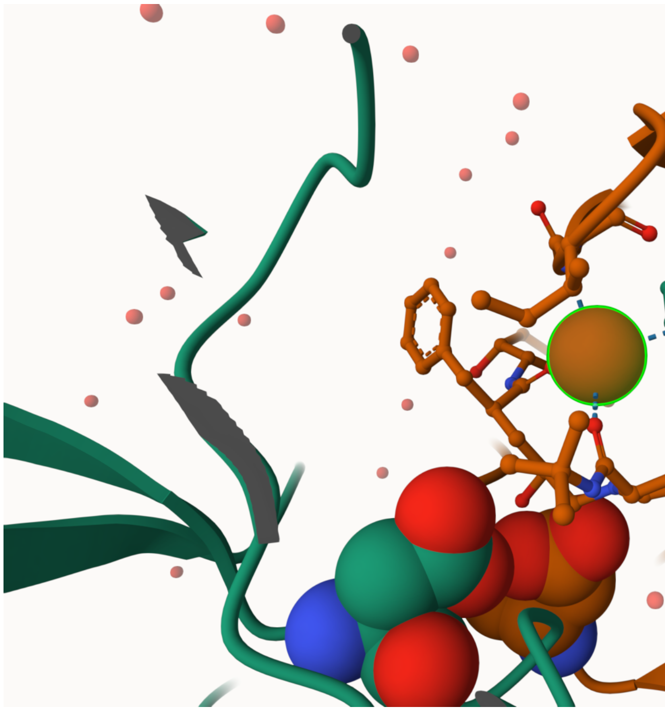


Figure 1: The HIV-Pr dimer with bound inhibitor

Image of HIV-Pr dimer with water molecule 308 highlighted 

## Bio3D package for structural bioinformatics

We can use the bio3d package to read and analyze biomolecular data in R:

```
library(bio3d)

hiv <- read.pdb("1HSG")
```

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

```
hiv
```

```

 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
```

```r
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>
```

Let's get the sequence:

```r
pdbseq(hiv)
```

```
  1   2   3   4   5   6   7   8   9  10  11  12  13  14  15  16  17  18  19  20 
"P" "Q" "I" "T" "L" "W" "Q" "R" "P" "L" "V" "T" "I" "K" "I" "G" "G" "Q" "L" "K" 
 21  22  23  24  25  26  27  28  29  30  31  32  33  34  35  36  37  38  39  40 
"E" "A" "L" "L" "D" "T" "G" "A" "D" "D" "T" "V" "L" "E" "E" "M" "S" "L" "P" "G" 
 41  42  43  44  45  46  47  48  49  50  51  52  53  54  55  56  57  58  59  60 
"R" "W" "K" "P" "K" "M" "I" "G" "G" "I" "G" "G" "F" "I" "K" "V" "R" "Q" "Y" "D" 
 61  62  63  64  65  66  67  68  69  70  71  72  73  74  75  76  77  78  79  80 
```

```
"Q" "I" "L" "I" "E" "I" "C" "G" "H" "K" "A" "I" "G" "T" "V" "L" "V" "G" "P" "T"
 81  82  83  84  85  86  87  88  89  90  91  92  93  94  95  96  97  98  99   1
"P" "V" "N" "I" "I" "G" "R" "N" "L" "L" "T" "Q" "I" "G" "C" "T" "L" "N" "F" "P"
  2   3   4   5   6   7   8   9  10  11  12  13  14  15  16  17  18  19  20  21
"Q" "I" "T" "L" "W" "Q" "R" "P" "L" "V" "T" "I" "K" "I" "G" "G" "Q" "L" "K" "E"
 22  23  24  25  26  27  28  29  30  31  32  33  34  35  36  37  38  39  40  41
"A" "L" "L" "D" "T" "G" "A" "D" "D" "T" "V" "L" "E" "E" "M" "S" "L" "P" "G" "R"
 42  43  44  45  46  47  48  49  50  51  52  53  54  55  56  57  58  59  60  61
"W" "K" "P" "K" "M" "I" "G" "G" "I" "G" "G" "F" "I" "K" "V" "R" "Q" "Y" "D" "Q"
 62  63  64  65  66  67  68  69  70  71  72  73  74  75  76  77  78  79  80  81
"I" "L" "I" "E" "I" "C" "G" "H" "K" "A" "I" "G" "T" "V" "L" "V" "G" "P" "T" "P"
 82  83  84  85  86  87  88  89  90  91  92  93  94  95  96  97  98  99
"V" "N" "I" "I" "G" "R" "N" "L" "L" "T" "Q" "I" "G" "C" "T" "L" "N" "F"
```

Let's trim to chain A and get just it's sequence

```r
chainA <-trim.pdb(hiv, chain="A")
chainA.seq <- pdbseq(chainA)
```

Let's blast

```r
blast <- blast.pdb(chainA.seq)
```

```
 Searching ... please wait (updates every 5 seconds) RID = GJBG4FB1016
 ..
 Reporting 249 hits
```

```r
head(blast$hit.tbl)
```

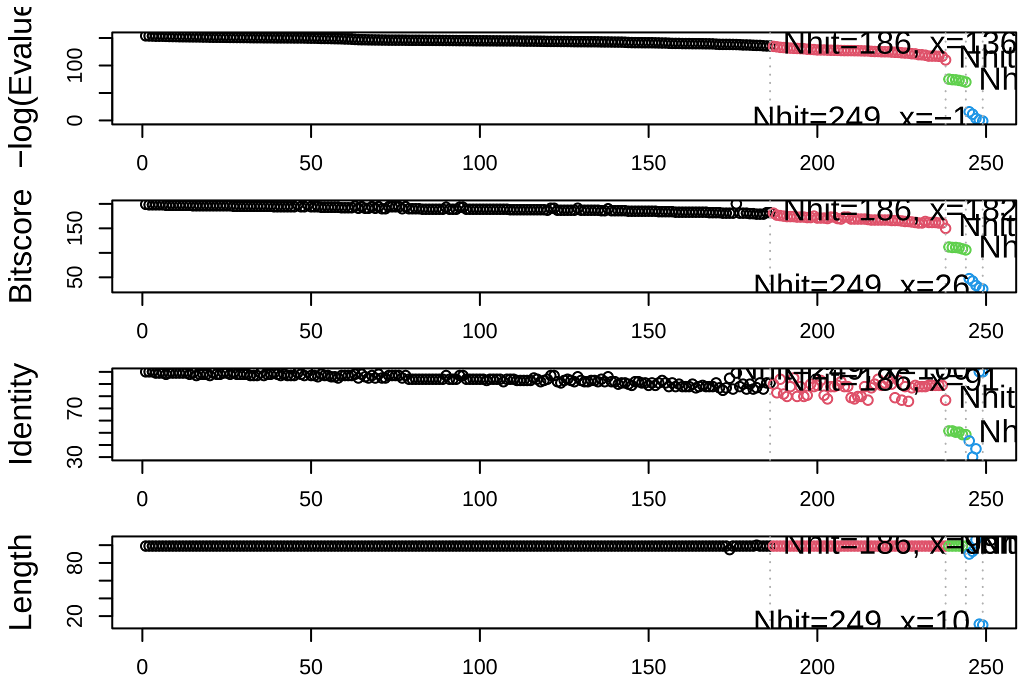
```
        queryid subjectids identity alignmentlength mismatches gapopens q.start
1 Query_2872261     1W5V_A   100.00              99          0        0       1
2 Query_2872261     2FDE_A   100.00              99          0        0       1
3 Query_2872261     1AJV_A   100.00              99          0        0       1
4 Query_2872261     2R38_A    98.99              99          1        0       1
5 Query_2872261     2R3T_A    98.99              99          1        0       1
6 Query_2872261     1HXB_A    98.99              99          1        0       1
  q.end s.start s.end   evalue bitscore positives mlog.evalue pdb.id    acc
1    99      12   110 1.38e-67      199       100    153.9511 1W5V_A 1W5V_A
2    99       2   100 1.70e-67      198       100    153.7426 2FDE_A 2FDE_A
3    99       1    99 1.99e-67      198       100    153.5851 1AJV_A 1AJV_A
```

```
4     99        1     99 2.50e-67       198         100     153.3569 2R38_A 2R38_A
5     99        1     99 2.50e-67       198         100     153.3569 2R3T_A 2R3T_A
6     99        1     99 2.50e-67       198         100     153.3569 1HXB_A 1HXB_A
```

Plot a quick overview of blast results

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

```
  * Possible cutoff values:    135 110 69 -2
            Yielding Nhits:    186 238 244 249

  * Chosen cutoff value of:    69
            Yielding Nhits:    244
```



```
hits$pdb.id
```

```
 [1] "1W5V_A" "2FDE_A" "1AJV_A" "2R38_A" "2R3T_A" "1HXB_A" "1BV9_A" "1AAQ_A"
 [9] "1AXA_A" "1HVS_A" "1ZP8_A" "2QHC_A" "1A8G_A" "2O4L_A" "5COK_A" "1TCX_A"
[17] "2Z54_A" "1D4S_A" "1BV7_A" "1BWA_A" "1A9M_A" "2FLE_A" "1ODY_A" "1GNN_A"
[25] "1GNM_A" "5YRS_B" "1HEF_E" "1ODX_A" "4QGI_A" "1BVE_A" "2AZ8_A" "1A30_A"
[33] "6DH6_A" "6DHO_A" "2I4D_A" "6OOS_A" "1RL8_A" "5YRS_A" "1ZSF_A" "2Q64_A"
```

```
 [41] "6DH3_A" "2NPH_A" "2Q63_A" "1LZQ_A" "1FB7_A" "1G6L_A" "1HIV_A" "6OOU_A"
 [49] "1HVC_A" "2I4V_A" "2AZ9_A" "6OOT_A" "2P3B_B" "5KAO_A" "2WL0_A" "6OPT_A"
 [57] "1IZI_A" "1MRX_A" "2PYM_A" "2PYN_A" "1DMP_A" "4K4P_A" "1LV1_A" "1AID_A"
 [65] "1LV1_A" "1ZBG_A" "3TKG_A" "1HVC_A" "5YOK_A" "1G6L_A" "1FGC_C" "3K4V_A"
 [73] "3KT5_A" "3KT5_A" "4QLH_A" "4QLH_A" "2F3K_A" "4Q5M_A" "2AOC_A" "3B80_A"
 [81] "3VF5_A" "2AVQ_A" "1DW6_C" "1KZK_A" "2HS1_A" "1K6C_A" "1MTB_A" "4Q1X_A"
 [89] "4Q1W_A" "4Q5M_A" "3D1X_A" "2AVM_A" "3PWM_A" "3KT2_A" "3KT2_A" "1SDV_A"
 [97] "3JVW_A" "3OY4_A" "1A94_A" "2HS2_A" "4EJ8_A" "2FGU_A" "2AVV_A" "3JW2_A"
[105] "3BVA_A" "1FFF_C" "3S43_B" "2NXD_A" "1FG6_C" "1EBK_C" "4Q1Y_A" "3EL4_A"
[113] "1F7A_A" "1K2B_A" "2FGV_A" "1Z8C_A" "2G69_A" "3EL9_A" "3OXV_A" "1BDR_A"
[121] "3N3I_A" "3N3I_A" "3OXW_A" "3S43_A" "3EM3_A" "3CYW_A" "5KQX_A" "2B60_A"
[129] "7DOZ_A" "1K2C_A" "1MT7_A" "3EM4_A" "4QJ9_A" "1BDL_A" "3LZS_A" "5T84_A"
[137] "4DQB_A" "7DOZ_A" "4QJ2_A" "3LZV_A" "1SGU_A" "2FXE_A" "1BDQ_A" "3U71_A"
[145] "2R5P_A" "4OBD_A" "7MAS_A" "3IXO_A" "3D3T_A" "5YOJ_A" "3LZU_A" "4NJS_A"
[153] "3EKP_A" "1B6J_A" "3EKQ_A" "2RKF_A" "1C6X_A" "7MAR_A" "4DQF_A" "1RPI_A"
[161] "3OU1_B" "3PJ6_A" "2P3A_A" "6OGQ_A" "3OQ7_A" "5KR1_A" "3OQD_A" "4RVI_A"
[169] "3OQA_A" "1B6K_A" "3OUD_B" "6MK9_A" "3SO9_A" "1Q9P_A" "6I45_A" "7SEP_A"
[177] "4NJT_A" "3BXR_A" "4YOA_A" "4DQC_A" "2FDD_A" "2RKG_A" "4DQH_A" "2P3C_A"
[185] "4EP2_A" "4EP2_A" "4EQ0_A" "4NPT_A" "6OPU_A" "4NPU_A" "3U7S_A" "3HAW_A"
[193] "2AZB_A" "3TTP_A" "3HBO_A" "3GGU_A" "7N6T_A" "6OPV_A" "4EQ0_A" "6OPX_A"
[201] "2O4N_A" "5T2E_A" "3UCB_A" "3KA2_A" "3FSM_A" "6OPW_A" "2AZC_A" "3FSM_A"
[209] "3HLO_A" "2P3D_A" "3T3C_A" "7MYP_A" "6O54_X" "6OPY_A" "4Z4X_A" "6OPZ_A"
[217] "2JE4_A" "1DAZ_C" "7MAP_A" "7MAQ_A" "1K1U_A" "2B7Z_A" "3MWS_A" "1K1T_A"
[225] "8DCH_A" "3I2L_A" "6P9A_A" "2FXD_A" "2J9J_A" "3DCK_A" "2J9J_B" "3NXE_A"
[233] "2O40_A" "2O40_A" "3NXE_A" "3KA2_A" "3HLO_A" "5B18_A" "1SIP_A" "2SAM_A"
[241] "1AZ5_A" "1SIV_A" "1HII_A" "1IVP_A"
```

##Prediction of functional motions

We can run a Normal Mode Analysis (NMA) to predict large scale motions/flexibility/dynamics of any biomolecule that we can read into R

Let's look at ADK and chain A only!

```
adk <-read.pdb("1ake")
```

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

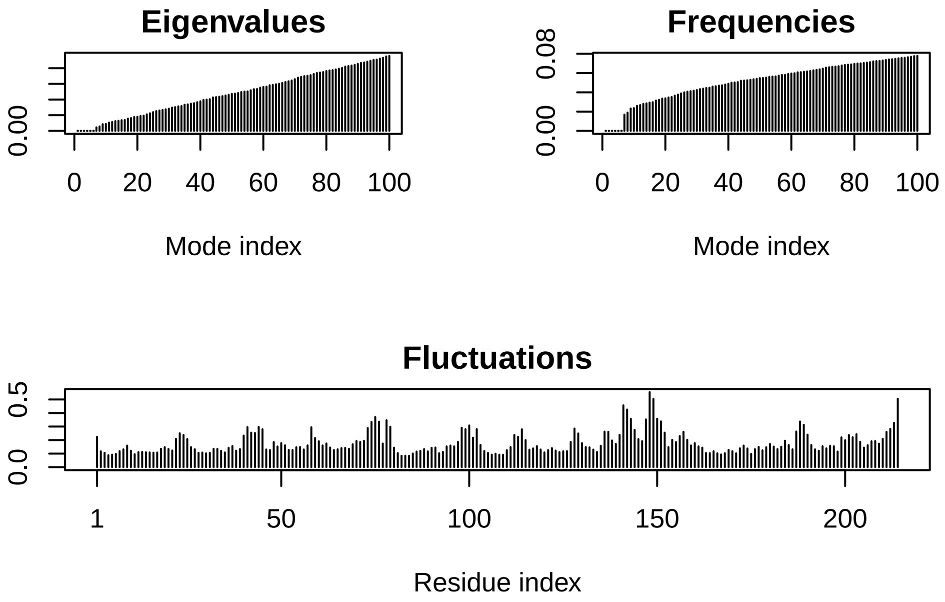
```
adk_A <- trim.pdb(adk, chain ="A")
adk_A
```

```
 Call:  trim.pdb(pdb = adk, chain = "A")

   Total Models#: 1
     Total Atoms#: 1954,  XYZs#: 5862  Chains#: 1  (values: A)

     Protein Atoms#: 1656  (residues/Calpha atoms#: 214)
     Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)

     Non-protein/nucleic Atoms#: 298  (residues: 242)
     Non-protein/nucleic resid values: [ AP5 (1), HOH (241) ]

   Protein sequence:
      MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
      DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDRI
      VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG

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

```
m <- nma(adk_A)
```

```
 Building Hessian...        Done in 0.009 seconds.
 Diagonalizing Hessian...   Done in 0.175 seconds.
```

```
plot(m)
```



Let's write out a "trajectory" of predicted motion

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

## Play with 3D viewing in R

We can use the new **bio3dview** package, which is not yet on CRAN, to render interactive 3D view in R and HTML quarto output reports.

To install from GitHub we can use the **pak** package.

```
library(bio3d)
#view.pdb(adk)
```

## Reading PDB file data into R

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

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

```
Warning in get.pdb(file, path = tempdir(), verbose = FALSE):
/var/folders/46/s1zr4cld6l9gnt7h6p8xt4km0000gn/T//RtmpBbpjBq/1hsg.pdb exists.
Skipping download
```

```
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

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

2

```
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>
```

### Predicting functional motions of a single structure

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

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

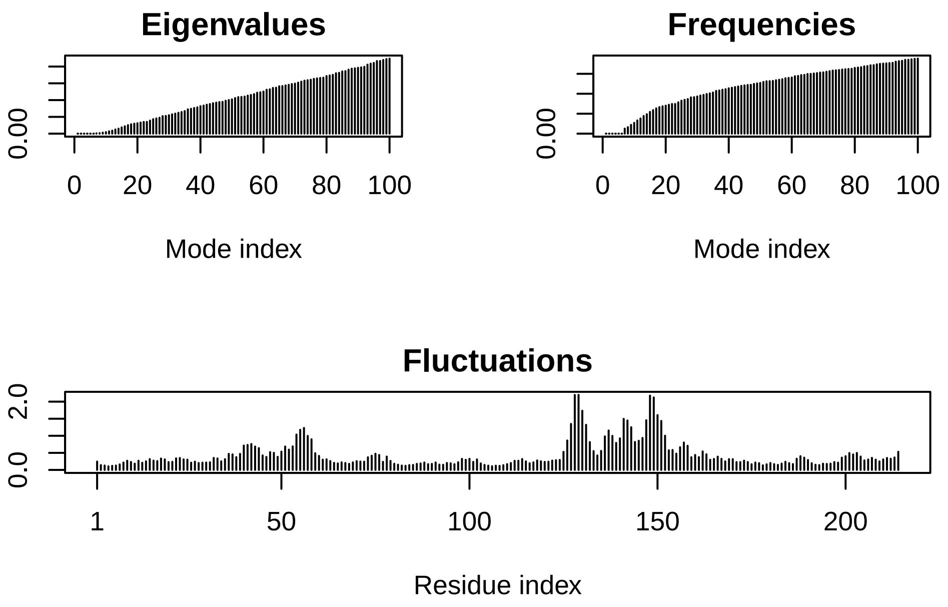
```r
adk
```

```

 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
```

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

```
 Building Hessian...        Done in 0.009 seconds.
 Diagonalizing Hessian...   Done in 0.172 seconds.
```

```r
plot(m)
```



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

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

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> 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 and colored lines are different in magnitude but show similar patterns. They seem to differ most around residue number 50 and 150, this might be due to there being two sites that show distinct fluctuations and flexibility.