Class 9: Structural Bioinformatics pt. 1

Selma Cifric (PID A69042976)

Table of contents

The PDB format

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:

```r
raw.data <- "Data Export Summary.csv"
protein.df <- read.csv(raw.data)
```

```r
protein.df
```

```
           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
```

We can substitute a comma with a space to change the chr to number.

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

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

This is annoying, let's try a different import function from the **reaadr** package. We install this package into our console.

```
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>
```

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

Percent x-ray

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

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

```
[1] 81.43
```

81.43% of structures in the PDB are solved by X-Ray.

Percent EM

```r
n.em <- sum(stats$EM)
round((n.em/n.total)*100, digits = 2)
```

```
[1] 12.27
```

12.27% of structures in the PDB are solved by EM.

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

```r
n.prot <- sum(stats$Total[1])
row.total <- sum(stats$Total)
round((n.prot/row.total)*100, digits = 2)
```

```
[1] 86.05
```

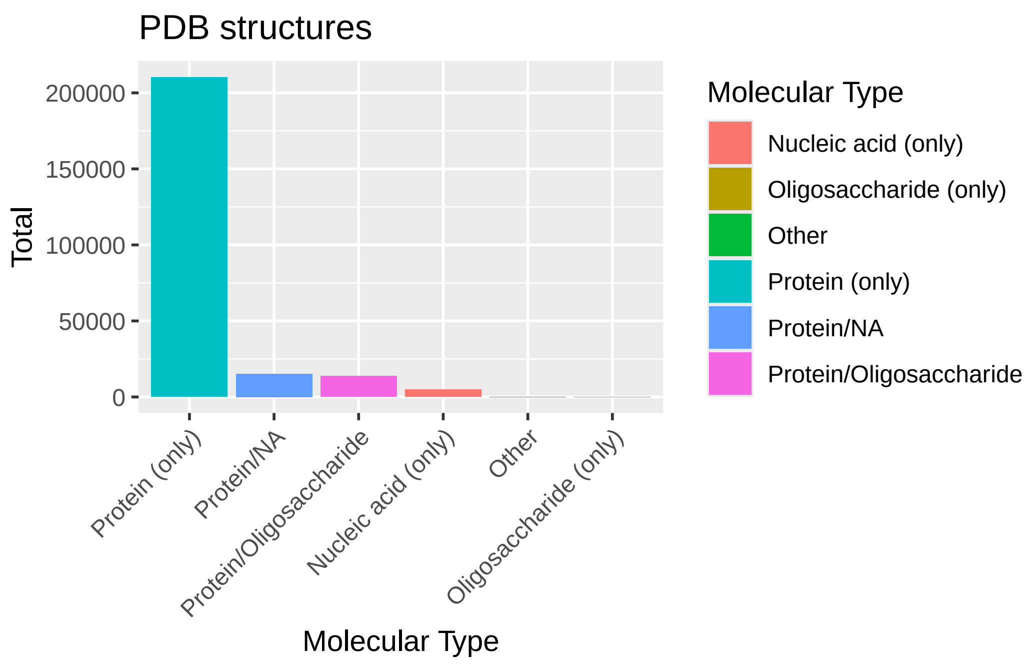
86.05% of structures in the PDB are protein.

> 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?

As of November 1 2025 there are 1150 structures of HIV-1 proteases (no filters applied).

OPTIONAL - extra credit - generating a plot

```r
library(ggplot2)

ggplot(stats) +
  aes(reorder(`Molecular Type`, - Total), Total, fill = `Molecular Type`) +
  geom_col() +
  labs(x = "Molecular Type", y = "Total", title = "PDB structures") +
  theme(axis.text.x = element_text (angle = 45, hjust = 1))
```



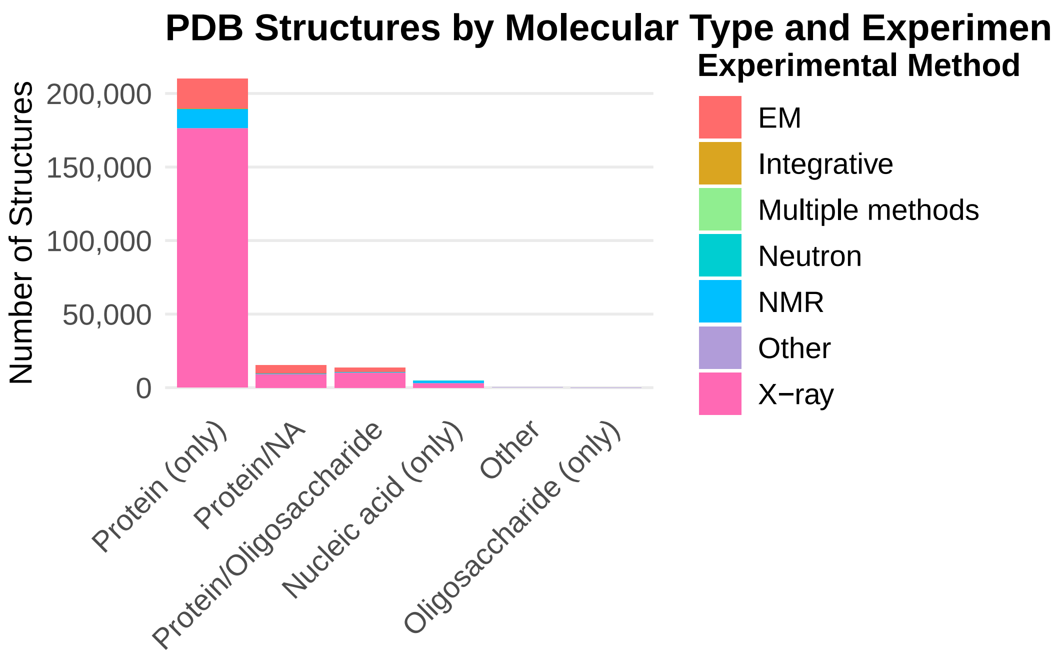
Converting wide to long data frame:

```r
library(ggplot2)
library(dplyr)
```

```


Attaching package: 'dplyr'


The following objects are masked from 'package:stats':

    filter, lag
```

```
The following objects are masked from 'package:base':

    intersect, setdiff, setequal, union
```

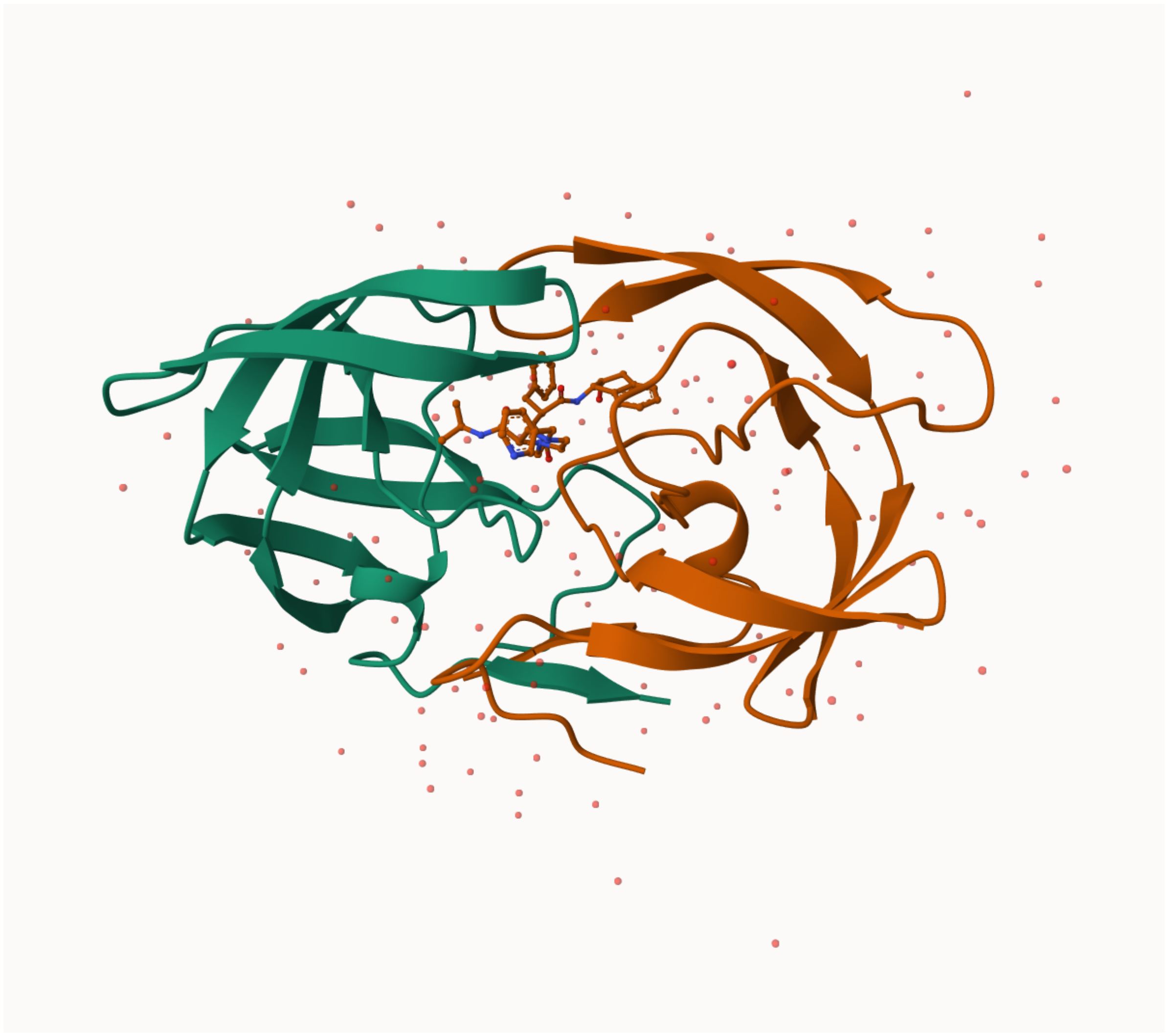
```r
library(tidyr)
library(readr)
library(forcats)

# Convert to long format and clean up the data
data_long <- stats %>%
  pivot_longer(
    cols = -c(`Molecular Type`, Total),
    names_to = "experimental_method",
    values_to = "count"
  ) %>%
  mutate(
    count = as.numeric(gsub(",", "", count))
  ) %>%
  select(-Total)

# Calculate total for each Molecular Type and reorder
data_long <- data_long %>%
  group_by(`Molecular Type`) %>%
  mutate(total = sum(count)) %>%
  ungroup() %>%
  mutate(`Molecular Type` = fct_reorder(`Molecular Type`, total, .desc = TRUE))

colors <- c("X-ray" = "#FF69B4",
            "Other" = "#B19CD9",
            "NMR" = "#00BFFF",
            "Neutron" = "#00CED1",
            "Multiple methods" = "#90EE90",
            "Integrative" = "#DAA520",
            "EM" = "#FF6B6B")

# Create the plot
ggplot(data_long, aes(x = `Molecular Type`, y = count, fill = experimental_method)) +
  geom_col() +
  scale_fill_manual(values = colors) +
  scale_y_continuous(labels = scales::comma_format(),
                     breaks = seq(0, 220000, 50000)) +
  labs(
    title = "PDB Structures by Molecular Type and Experimental Method",
    x = NULL,
    y = "Number of Structures",
    fill = "Experimental Method"
  ) +
  theme_minimal() +
  theme(
    axis.text.x = element_text(angle = 45, hjust = 1, size = 11),
    axis.text.y = element_text(size = 11),
    axis.title.y = element_text(size = 12, angle = 90),
    plot.title = element_text(size = 14, face = "bold"),
    legend.title = element_text(size = 12, face = "bold"),
    legend.text = element_text(size = 11),
    panel.grid.major.x = element_blank(),
    panel.grid.minor = element_blank()
  )
```



Visualizing structure data

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

I can insert any figure or image file using markdown format.



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

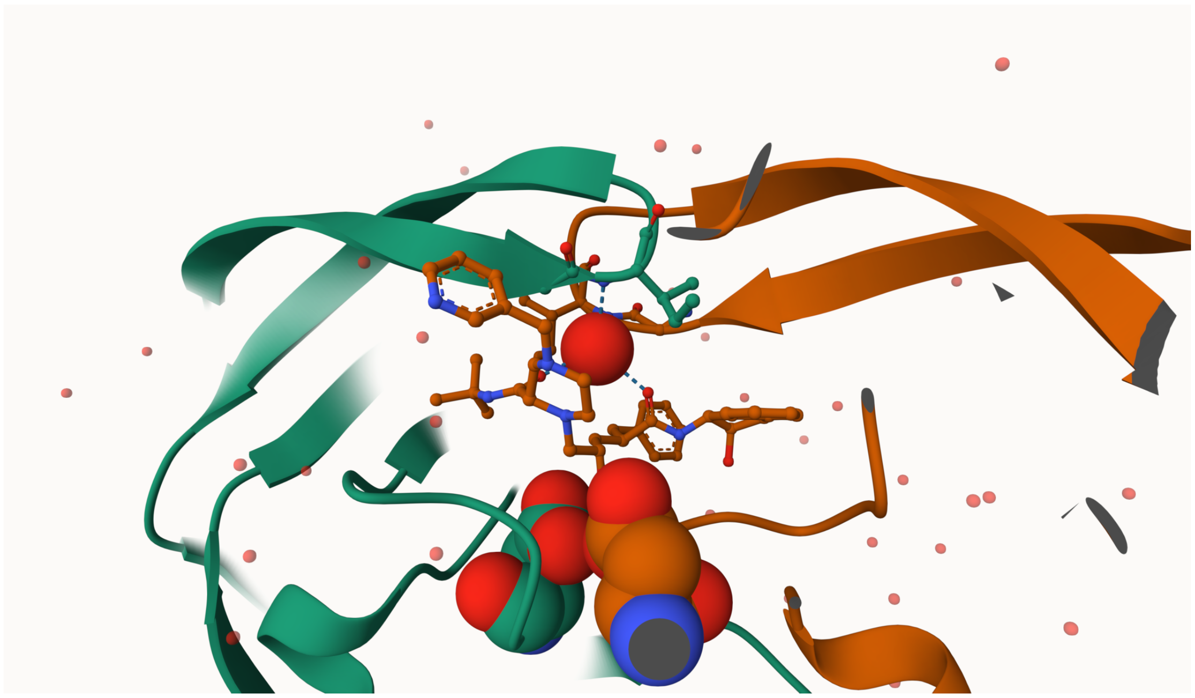
Hydrogen is a small and ligh element, not easily picked up by X-ray crystallography which is why it does not show in H2O structure. Oxygen, on the other hand, is heavier element and shows up in biological structures on PDB.

> 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

Yes, its HOH 306 shown as a single red ball in the picture below.

> 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.



Bio3D package for structural bioinformatics

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

```r
library(bio3d)

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

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

```r
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
```

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

There is 198 amino acid residues/Calpha atoms.

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

HOH 127 and MK1 1.

Q9: How many protein chains are in this structure?

Two, chains A and B.

```
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 chain A.

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

```
 Searching ... please wait (updates every 5 seconds) RID = GFX45VRW014 
 .......................................................................................
 Reporting 249 hits
```

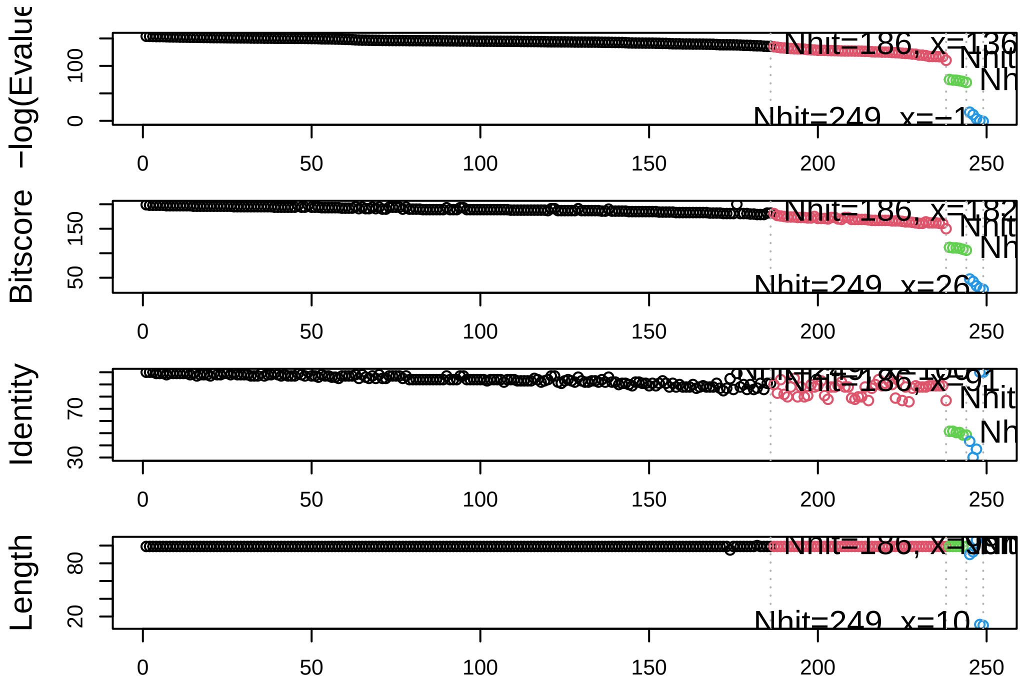
```r
head(blast$hit.tbl)
```

```
        queryid subjectids identity alignmentlength mismatches gapopens q.start
1 Query_6618617     1W5V_A   100.00              99          0        0       1
2 Query_6618617     2FDE_A   100.00              99          0        0       1
3 Query_6618617     1AJV_A   100.00              99          0        0       1
4 Query_6618617     2R38_A    98.99              99          1        0       1
5 Query_6618617     2R3T_A    98.99              99          1        0       1
6 Query_6618617     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.

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

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

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



```r
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" "6DH0_A" "2I4D_A" "6O0S_A" "1RL8_A" "5YRS_A" "1ZSF_A" "2Q64_A"
 [41] "6DH3_A" "2NPH_A" "2Q63_A" "1LZQ_A" "1FB7_A" "1G6L_A" "1HIV_A" "6O0U_A"
 [49] "1HVC_A" "2I4V_A" "2AZ9_A" "6O0T_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" "3S09_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] "2O4O_A" "2O4O_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 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
```

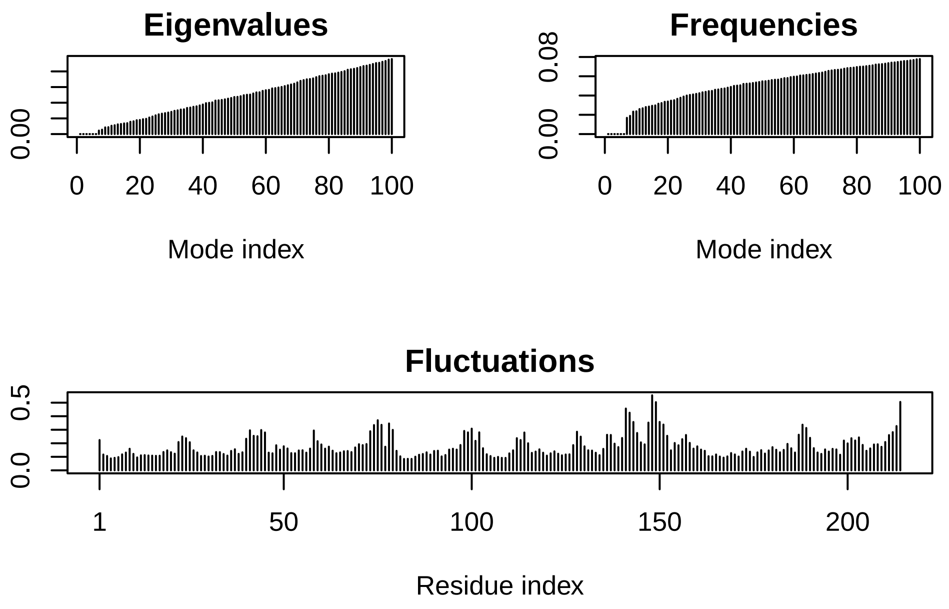
```
adk_A <- trim.pdb(adk, chain="A")
adk_A
```

```

 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
```

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

```
 Building Hessian...        Done in 0.02 seconds.
 Diagonalizing Hessian...   Done in 0.446 seconds.
```

```r
plot(m)
```



Let’s write out a “trajectory” of predicted motion.

```r
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 views in R and HTML quarto output reports. To install from GitHub we can use the **pak** package. We install it in the console.

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

#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?

msa

> Q11. 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