Class 09: Structural Bioinformatics pt. 1

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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:

```r
pdb_stats <- read.csv("Data Export Summary.csv", row.names=1)
tail(pdb_stats)
```

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

```
Other                           0      0      223
Oligosaccharide (only)          0      4       22
```

I need to convert to numeric

```r
# This was my strategy but it sounds like Barry has a different approach

# pdb_stats$X.ray <- as.numeric(gsub(",", "", pdb_stats$X.ray))
# pdb_stats$EM <- as.numeric(gsub(",", "", pdb_stats$EM))
# pdb_stats$Total <- as.numeric(gsub(",", "", pdb_stats$Total))

# Barry's approach

# install("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.
```

```r
head(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.

```
totstructures <- sum(stats$Total)
xray <- sum(stats$"X-ray")
em <- sum(stats$EM)

round((xray)/totstructures * 100, 2)
```

```
[1] 81.43
```

```
round(em/totstructures * 100, 2)
```

```
[1] 12.27
```

Xray methods are 81.43 % and EM methods are 12.27% of structures.

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

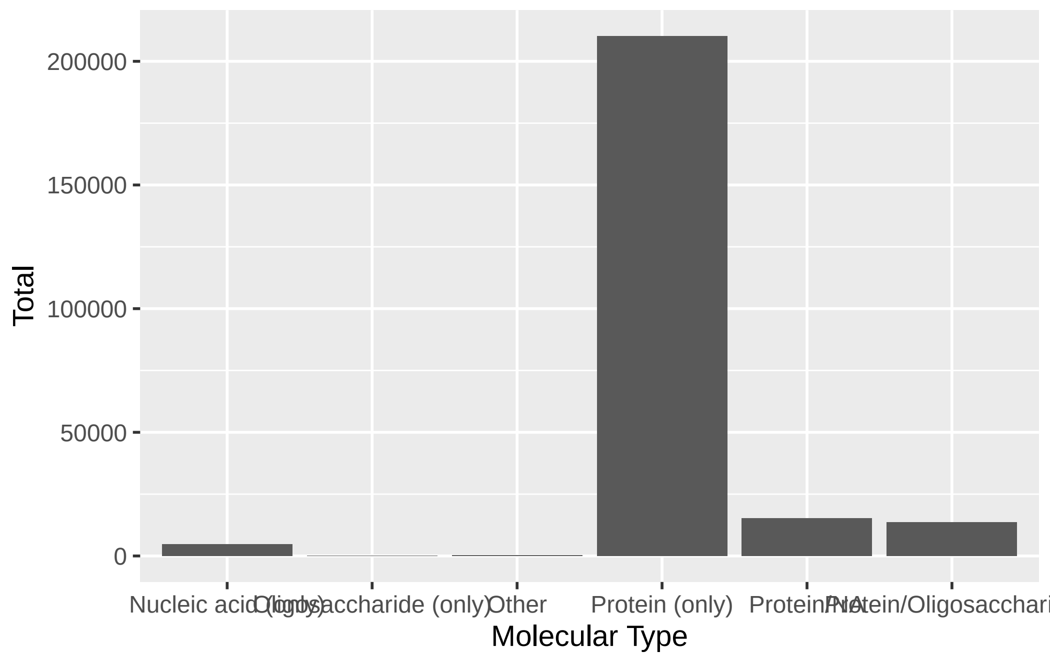
```
pdb_proteins <- stats$Total[1]
round(pdb_proteins/totstructures * 100,2)
```

```
[1] 86.05
```

> Q3: Make a bar plot overview of molecular type composition using gplot

```
library(ggplot2)

ggplot(stats) + aes(x=`Molecular Type`, y=Total) + geom_col()
```



Extra exercise:

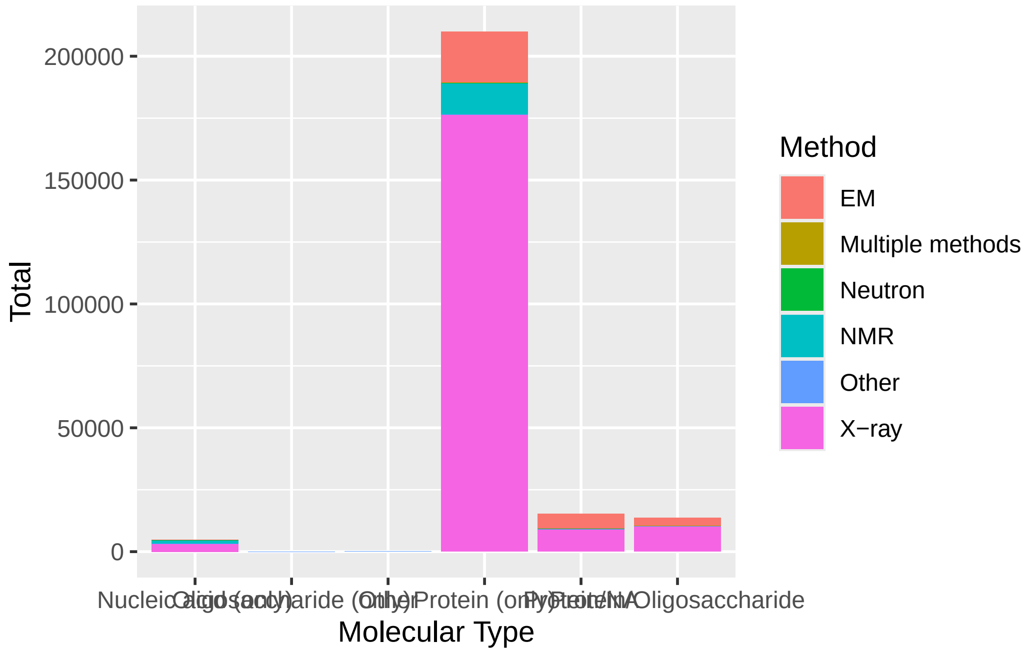
```r
library(tidyr)

# Pivot to long format
df_long <- pivot_longer(
  stats,
  cols = c("X-ray", "EM", "NMR", "Multiple methods", "Neutron", "Other"),
  names_to = "Method",
  values_to = "Count"
)

head(df_long)
```

```
# A tibble: 6 x 5
  `Molecular Type` Integrative  Total Method           Count
  <chr>                  <dbl>  <dbl> <chr>            <dbl>
1 Protein (only)           342 210203 X-ray           176378
2 Protein (only)           342 210203 EM               20438
3 Protein (only)           342 210203 NMR              12709
4 Protein (only)           342 210203 Multiple methods   221
5 Protein (only)           342 210203 Neutron             83
6 Protein (only)           342 210203 Other               32
```

```
ggplot(df_long) + aes(x=`Molecular Type`, y= Count, fill= Method) + geom_bar(stat = "identity
```



Visualizing structure data

The mol* viewer is embedded in many bioinformatics websites. The homepage is https://molstar.org

I can insert/render any figure or image file using markdown format:

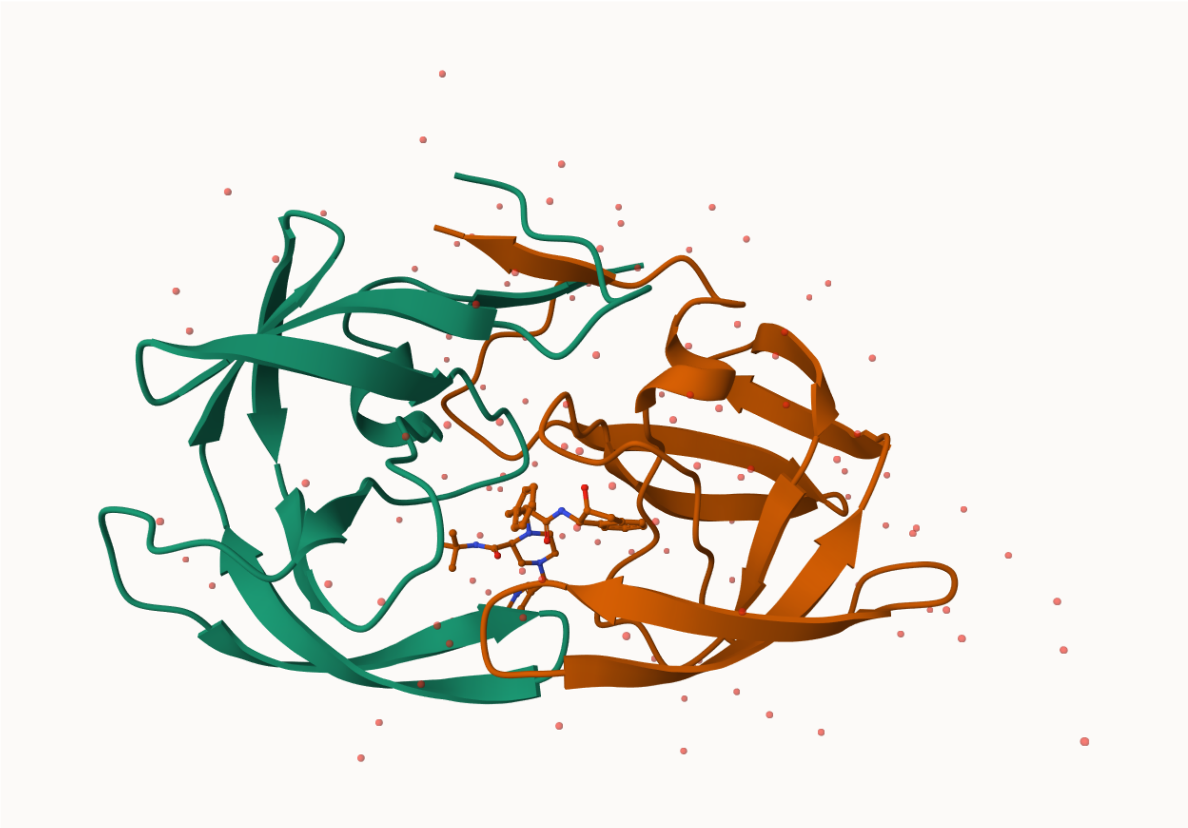


Figure 1: The HIV-Pr dimer with bound inbibitor

Figure 2: The HIV-Pr dimer, reactive aspartic acid (D25) and important H20 (308) are highlighted

Bio3D package for structural bioinformativs

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
```

```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
```

```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 just chain A and get just that chain's sequence:

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

```
  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 
"P" "V" "N" "I" "I" "G" "R" "N" "L" "L" "T" "Q" "I" "G" "C" "T" "L" "N" "F" 
```

I want to blast it

```r
# the above extra code is useful if you'll need to render the document but you don't want to
blast <- blast.pdb(HIV_A.seq)
```

```
 Searching ... please wait (updates every 5 seconds) RID = G5FAV7EF014
 ..............
 Reporting 249 hits
```

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

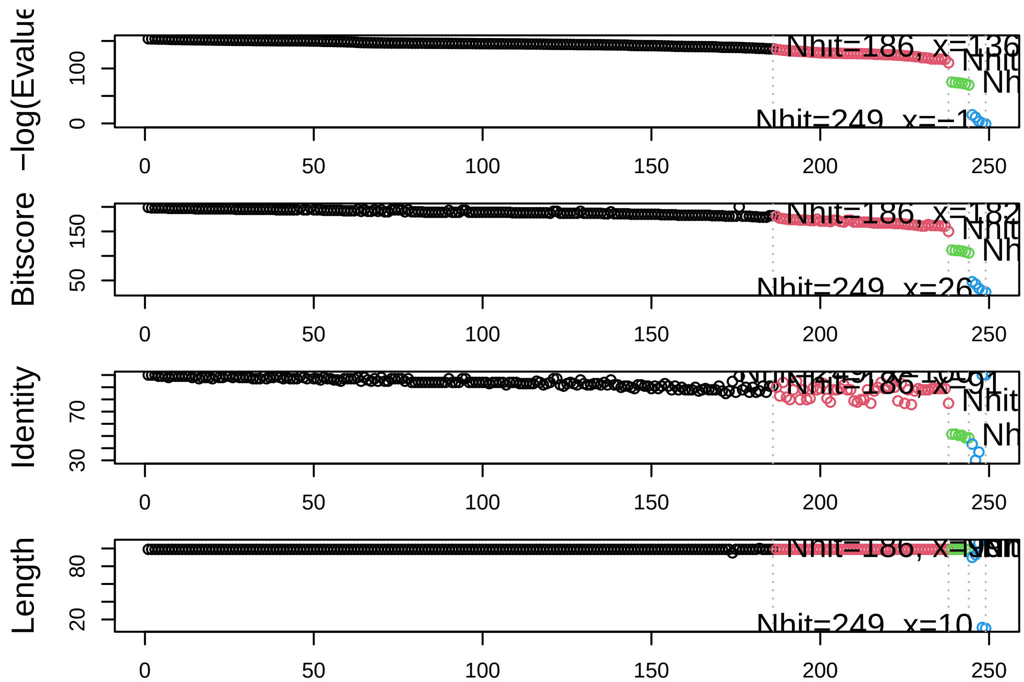
```
        queryid subjectids identity alignmentlength mismatches gapopens q.start
1 Query_3578775     1W5V_A   100.00              99          0        0       1
2 Query_3578775     2FDE_A   100.00              99          0        0       1
3 Query_3578775     1AJV_A   100.00              99          0        0       1
4 Query_3578775     2R38_A    98.99              99          1        0       1
5 Query_3578775     2R3T_A    98.99              99          1        0       1
6 Query_3578775     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
```

What if you plot the 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
```




```
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" "2WLO_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 at ADK

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

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

```r
adk_A <- trim(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
```

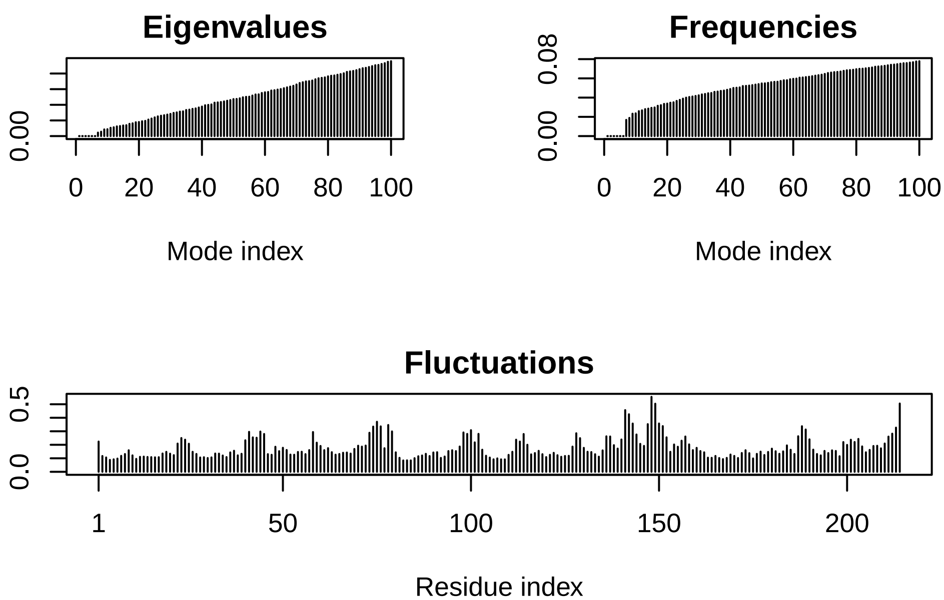
```
      DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDRI
      VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG

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

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

```
 Building Hessian...        Done in 0.012 seconds.
 Diagonalizing Hessian...   Done in 0.268 seconds.
```

```r
plot(m)
```



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

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

You can load this into molstar and play the movie!

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.

```
# install.packages("pak")
#
# pak::pak("bioboot/bio3dview")
```