Class 9: 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:

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

```
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! Let's use a different import function from the **readr** package.

```
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>
```

```
n.total <- sum(stats$Total)
n.xray <- sum(stats$`X-ray`)
n.em <- sum(stats$EM)
pct.both <- round((n.xray + n.em) / n.total * 100, 2)
pct.xray <- round(n.xray / n.total * 100, 2)
pct.em <- round(n.em / n.total * 100, 2)
pct.both
```

```
[1] 93.7
```

```
pct.xray
```

```
[1] 81.43
```

```
pct.em
```

```
[1] 12.27
```

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

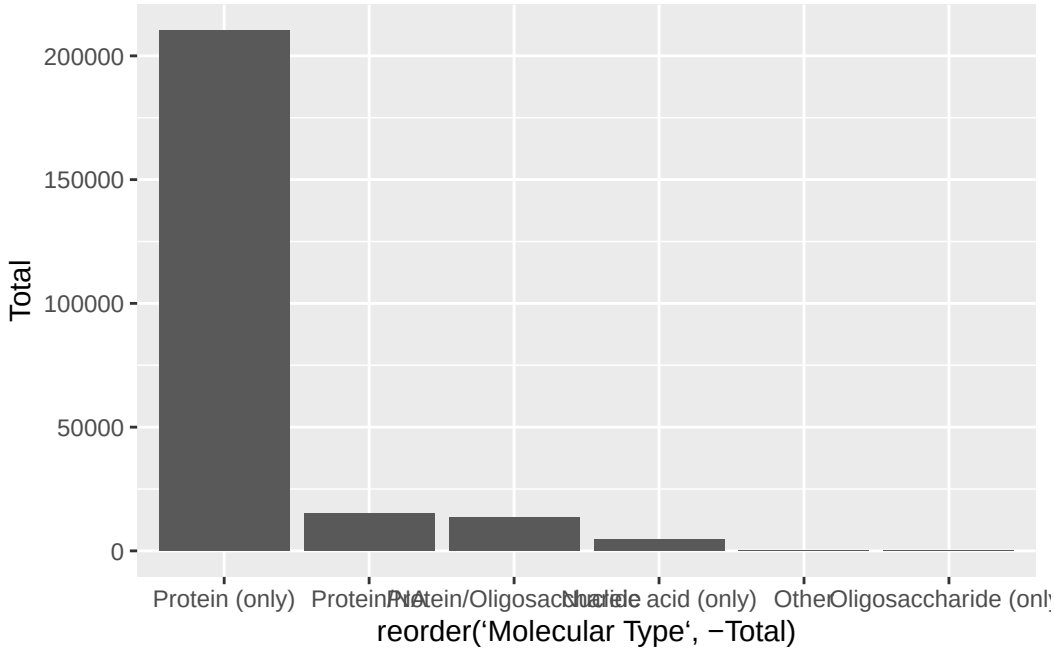
```
library(dplyr)
```

```
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
```

```
library(ggplot2)

stats %>%
  summarise(prop = sum(Total[`Molecular Type` == "Protein (only)"]) / sum(Total)) %>%
  pull(prop)
```

```
[1] 0.860465
```

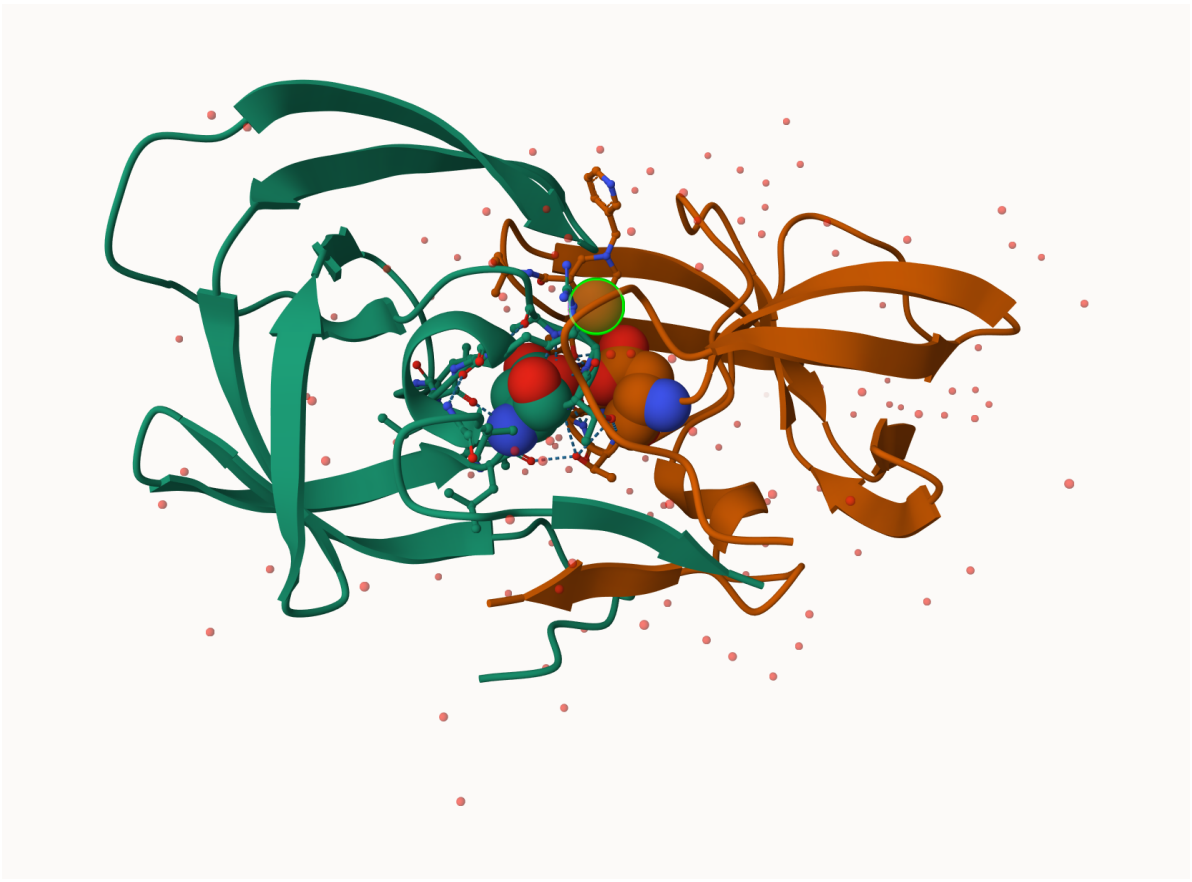
```
ggplot(stats)+
  aes(reorder(`Molecular Type`, -Total), Total) +
  geom_col()
```



Visualizing structure data

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.



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
```

```
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 trim to chain A and get just it's sequence:

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

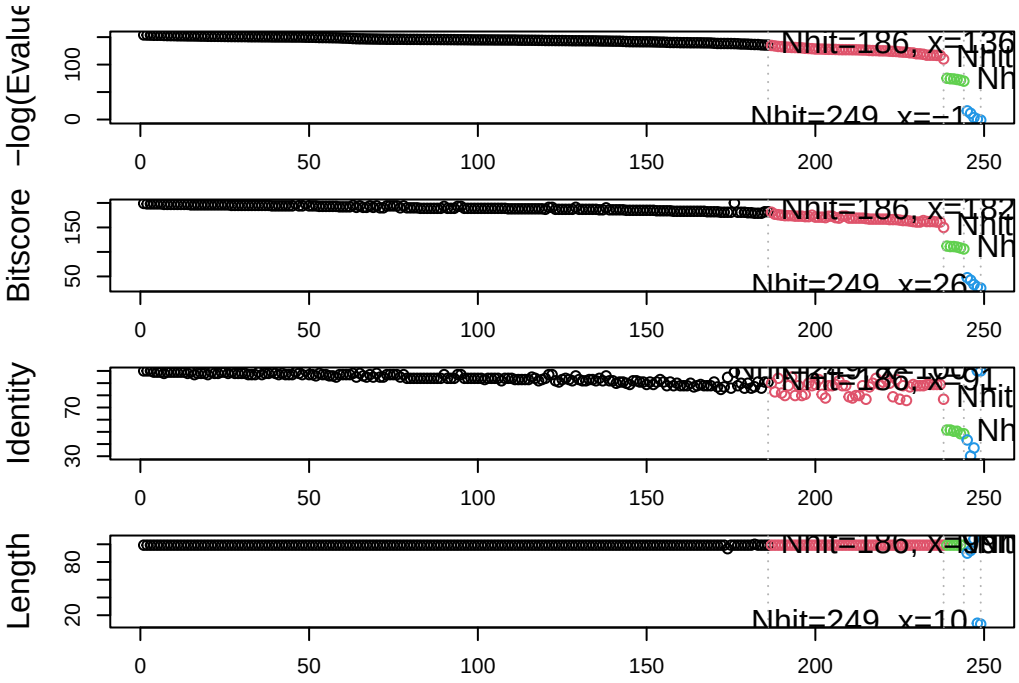
Let's blast this sequence against the PDB database to find similar structures:

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

```
 Searching ... please wait (updates every 5 seconds) RID = GREY9X3T014
 .......
 Reporting 249 hits
```

```
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" "6DH0_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's chain A.

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

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

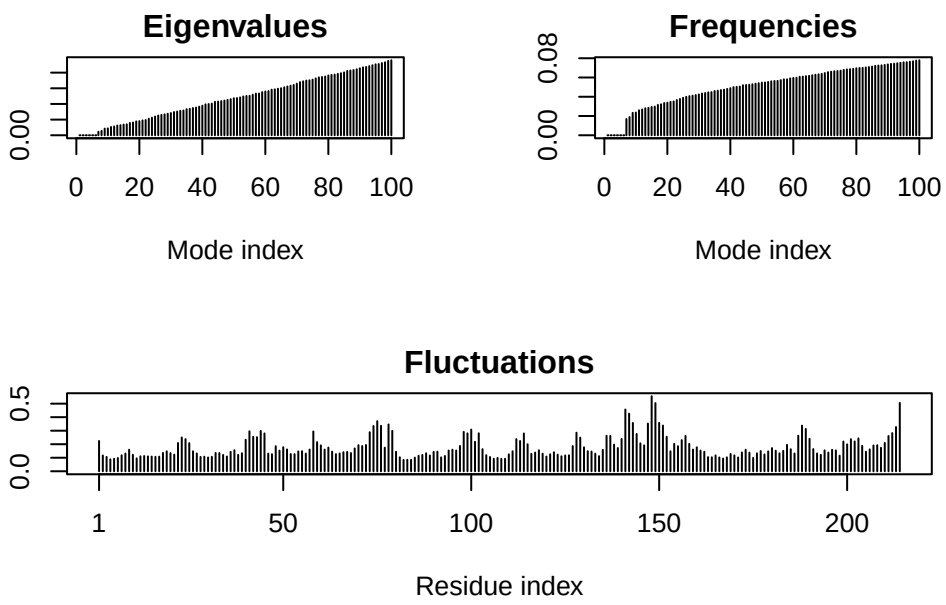
```
adk_A <-trim.pdb(adk, chain="A")
adk_A
```

```
 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 0.021 seconds.
 Diagonalizing Hessian...   Done in 0.485 seconds.
```

```
plot(m)
```



Let's writr 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 views inR and HTML quarto output reports.

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

```
library(bio3dview) view.pdb(adk_A)
```