Class 9: Structural Bioinformatics (pt 1)

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The PDB database

The main data base for structural biology is called the PDB. Lets have a look at what it contains:

Download a CSV file from the PDB site (accessible from **"Analyze" > "PDB Statistics" > "by Experimental Method and Molecular Type"**). Move this CSV file into your RStudio project and use it to answer the following questions:

```
stats <- read.csv("Data Export Summary.csv", row.names = 1)
head(stats)
```

```
                        X.ray     EM    NMR Integrative
Multiple.methods
Protein (only)        176,204 20,299 12,708         342
218
Protein/Oligosaccharide  10,279  3,385     34           8
11
Protein/NA                9,007  5,897    287          24
7
Nucleic acid (only)       3,066    200  1,553           2
15
Other                       173     13     33           3
0
Oligosaccharide (only)       11      0      6           0
1
                      Neutron Other   Total
Protein (only)             83    32 209,886
Protein/Oligosaccharide     1     0  13,718
Protein/NA                  0     0  15,222
Nucleic acid (only)         3     1   4,840
Other                       0     0     222
Oligosaccharide (only)      0     4      22
```

> **Q1:** What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy. Give your answer in 2 s.f.

```
stats$Total
```

```
[1] "209,886" "13,718"  "15,222"  "4,840"   "222"     "22"
```

Oh, these are characters not numeric...

```
sum( stats$Neutron)
```

```
[1] 87
```

```
SumTotal <- as.numeric(sub(",", "", stats$Total))
```

Long coding, inefficient

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

```
# A tibble: 6 × 9
  `Molecular Type`    `X-ray`    EM   NMR Integrative
`Multiple methods` Neutron
  <chr>                 <dbl> <dbl> <dbl>       <dbl>
<dbl>   <dbl>
1 Protein (only)       176204 20299 12708         342
218      83
2 Protein/Oligosacch…   10279  3385    34           8
11       1
3 Protein/NA             9007  5897   287          24
7        0
4 Nucleic acid (only)    3066   200  1553           2
15       3
5 Other                   173    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)
```

```
stats$`X-ray`
```

```
[1] 176204  10279   9007   3066    173     11
```

```
n.xray <- sum(stats$`X-ray`)
percent.xray <- n.xray / n.total * 100
```

```
percent.xray
```

```
[1] 81.48087
```

There are 81.48 percent Xray structures in the PDB

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

```
(209886 + 13718 + 15222)/ (209886 + 13718 + 15222 +4840 + 222 +
```

```
[1] 0.9791562
```

97.9%

> 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?

2406

Exploring PDB structures

Package for structural bioinformatics

```
library(bio3d)

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

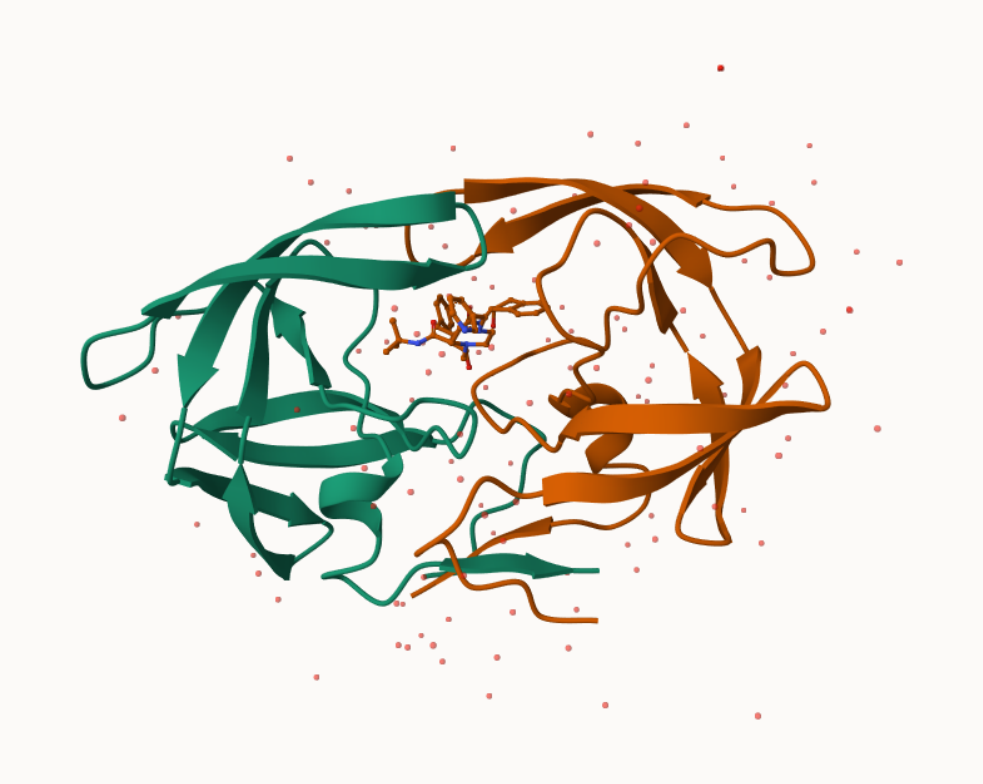
```
  Note: Accessing on-line PDB file
```

```
hiv
```

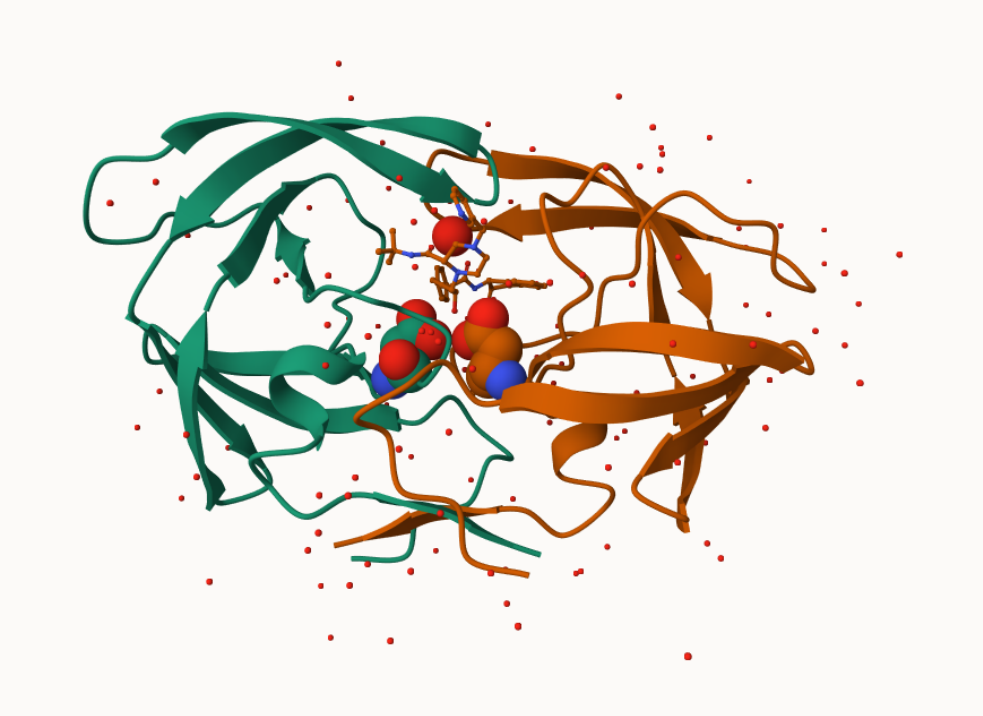
```
 Call:  read.pdb(file = "1hsg")

   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
```

Let's first use the Mol* viewer to explore this structure.



My first view of HIV-Pr



My first view of HIV-Pr

PDB objects in 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>
```

Extract the sequence

```
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"
```

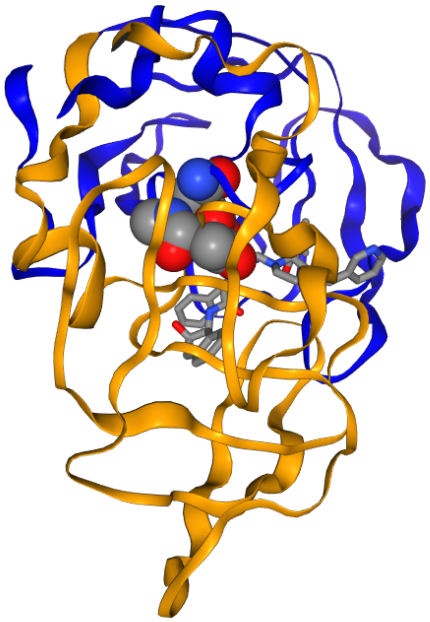
```
chainA_seq <- pdbseq( trim.pdb(hiv, chain = "A") )
```

I can interactively view these PDB objects in R iwth the new **bio3dview** package. This is not yet on CRAN.

```
pak::pak("bioboot/bio3dview")
```

```
! Using bundled GitHub PAT. Please add your own PAT using
`gitcreds::gitcreds_set()`.

ℹ Loading metadata database

✔ Loading metadata database ... done




ℹ No downloads are needed

✔ 1 pkg + 40 deps: kept 39 [6.8s]
```

```
library(bio3dview)


sel <- atom.select(hiv, resno=25)


view.pdb(hiv, highlight = sel,
         highlight.style = "spacefill",
         colorScheme = "chain",
         col = c("blue", "orange"),
         backgroundColor = "pink")
```



Predict protein flexibility

We can run a bioinformatics calculation to predict protein dynamics - i.e. functional motions.

We will use the `nma()` function:

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

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

```
adk
```

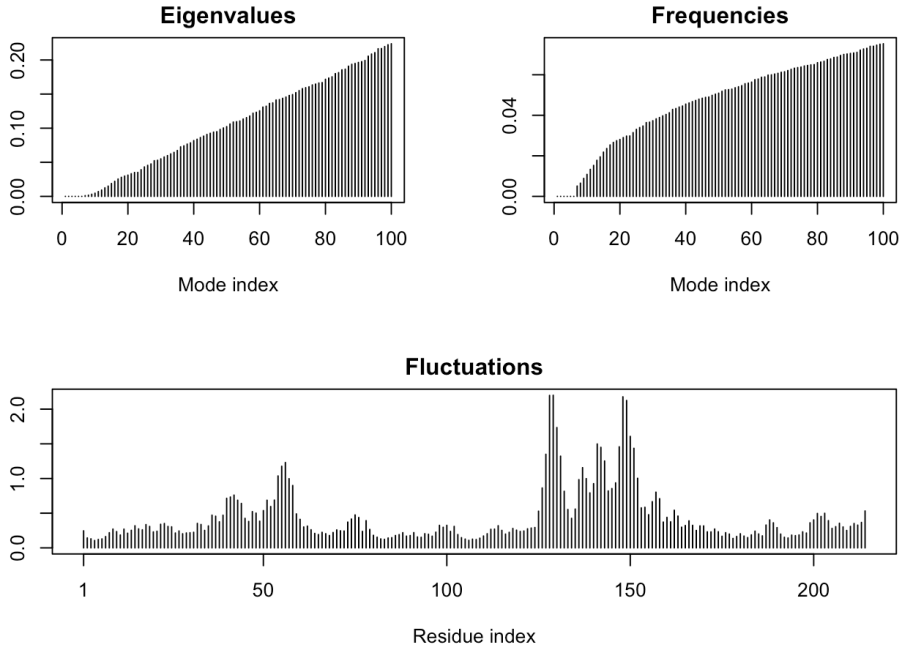
```
Call:  read.pdb(file = "6s36")

  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
```

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

```
 Building Hessian...        Done in 0.021 seconds.
 Diagonalizing Hessian...   Done in 0.454 seconds.
```

```
plot(m)
```



Generate a “trajectory” of predicted motion.

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