Class 10: Structural Bioinformatics (pt1)

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1: Introduction to the RCSB Protein Data Bank (PDB)

PDB statistics

First let's see what is in the PDB database - the main repository of protein structure.

Downloaded composition stats from: https://www.rcsb.org/stats/summary

```
stats <- read.csv("PDBstats.csv", row.names = 1)
stats
```

```
                         X.ray     EM    NMR Multiple.methods Neutron Other
Protein (only)         158,844 11,759 12,296              197      73    32
Protein/Oligosaccharide  9,260  2,054     34                8       1     0
Protein/NA               8,307  3,667    284                7       0     0
Nucleic acid (only)      2,730    113  1,467               13       3     1
Other                      164      9     32                0       0     0
Oligosaccharide (only)      11      0      6                1       0     4
                         Total
Protein (only)         183,201
Protein/Oligosaccharide  11,357
Protein/NA               12,265
Nucleic acid (only)       4,327
Other                       205
Oligosaccharide (only)       22
```

There is a problem here due to commas in the numbers. This causes R to treat them as characters.

```
rm.comma <- function(x) {
  as.numeric(gsub(",","",x))
}
```

```
rm.comma(stats$EM)
```

```
[1] 11759  2054  3667   113     9     0
```

I can use `apply()` to fix the whole table

```
pdbstats <- apply(stats, 2, rm.comma)
rownames(pdbstats) <- rownames(stats)
pdbstats
```

```
                        X.ray    EM   NMR Multiple.methods Neutron Other
Protein (only)         158844 11759 12296              197      73    32
Protein/Oligosaccharide  9260  2054    34                8       1     0
Protein/NA               8307  3667   284                7       0     0
Nucleic acid (only)      2730   113  1467               13       3     1
Other                     164     9    32                0       0     0
Oligosaccharide (only)     11     0     6                1       0     4
                        Total
Protein (only)         183201
Protein/Oligosaccharide  11357
Protein/NA               12265
Nucleic acid (only)       4327
Other                      205
Oligosaccharide (only)      22
```

```
totals <-  apply(pdbstats, 2, sum)
totals
```

```
         X.ray             EM            NMR Multiple.methods
        179316          17602          14119            226
      Neutron          Other          Total
           77             37         211377
```

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

```
round(totals/totals["Total"] * 100, 2)
```

```
        X.ray            EM           NMR Multiple.methods
        84.83          8.33          6.68             0.11
      Neutron         Other         Total
         0.04          0.02        100.00
```

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

```
round(pdbstats[,"Total"]/ sum(pdbstats[,"Total"]) * 100, 2)
```

```
      Protein (only) Protein/Oligosaccharide              Protein/NA
               86.67                    5.37                    5.80
Nucleic acid (only)                   Other Oligosaccharide (only)
                2.05                    0.10                    0.01
```

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?

Skipped.

Protein structures in PDB as a fraction of UniProt sequences. See: https://www.uniprot.org/help/release-statistics

```
round((pdbstats[1, "Total"]/251600768)*100,2)
```

```
[1] 0.07
```

2. Visualizing the HIV-1 protease structure

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

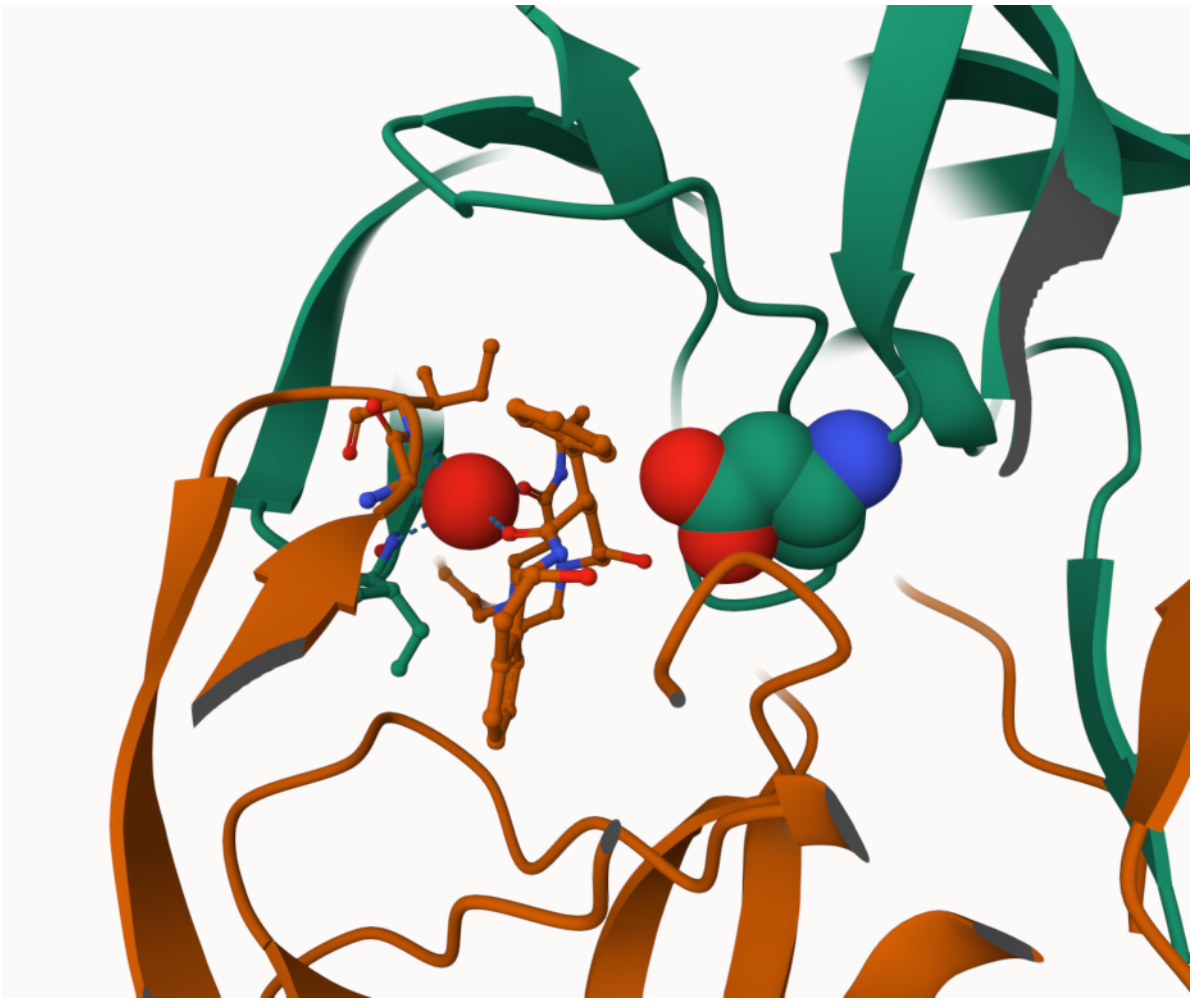
Resolution of the structure is 2 A, hydrogen is smaller so only oxygen is visible.

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

Water HOH 308

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.

Here is a lovely figure of HIV-Pr with the cathalitic ASP residues, the MK1 compound and all the important water 308



The bio3d package for structural bioinformatics

```
library(bio3d)

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

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

```
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
```

```
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

Let's finish today with a bioinformatics calculation to predict the functional motions of a PDB structure.

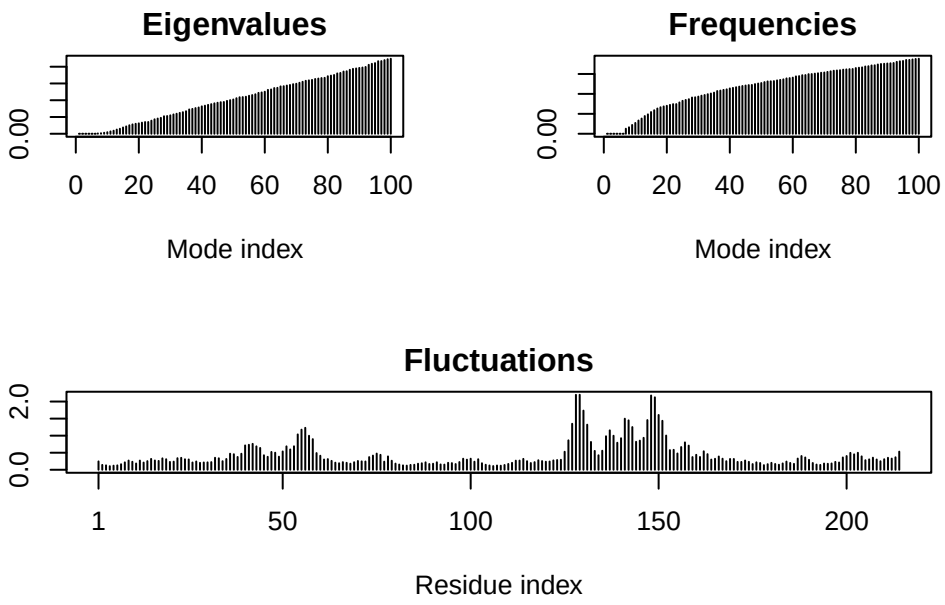
```
adk <- read.pdb("6s36")
```

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

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

```
Building Hessian...        Done in 0.11 seconds.
Diagonalizing Hessian...   Done in 0.7 seconds.
```

```
plot(m)
```




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