Class 10 Structural Bioinformatics Pt1

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the PDB database

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

PDB contains contains only 183,201

```
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 the commas in the numbers. This causes R to treat them as characters

```
x <- stats$X.ray
x
```

```
[1] "158,844" "9,260"   "8,307"   "2,730"   "164"     "11"
```

```
as.numeric( gsub(",", "", x) )
```

```
[1] 158844   9260   8307   2730    164     11
```

```
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) <- row.names(stats)
head(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
```

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

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

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
```

x-ray = 84.83% EM = 8.33%

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

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

```
[1] 87
```

87% of the 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?

SKIPPED

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

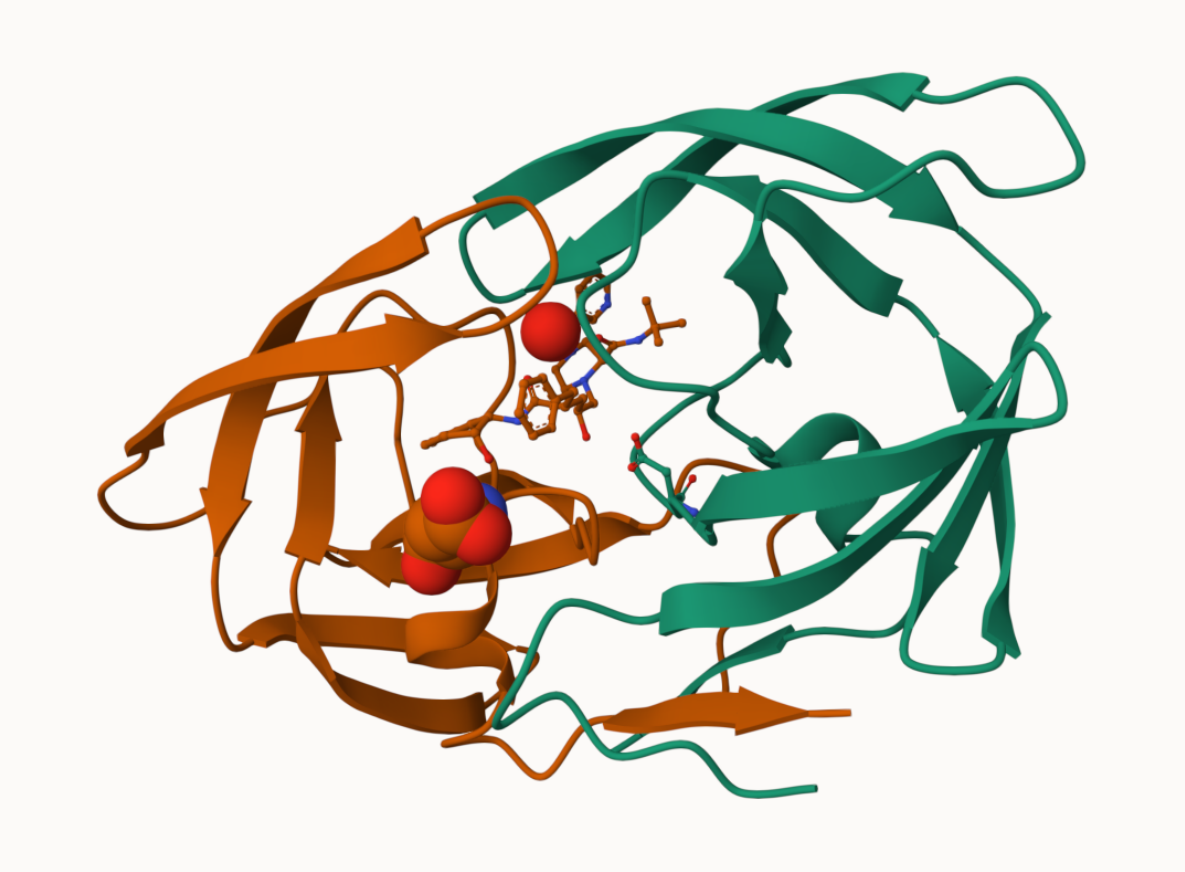
We can not see water in the structure because water is smaller than the resolution of 2 Angstroms. We would need the resolution to be 1 Angstrom or better to see hydrogen

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 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 the HIP-Pr with the catalytic ASp residues, the MK1 compund and the all important water 308



> Discussion Topic: Can you think of a way in which indinavir, or even larger ligands and substrates, could enter the binding site?

Larger ligands and substrates could enter the binding site by changing their orientation and perhaps rearranging hydrogen bonds on the chains so it can fit

The bio3d package for structural bioinofrmatics

```
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

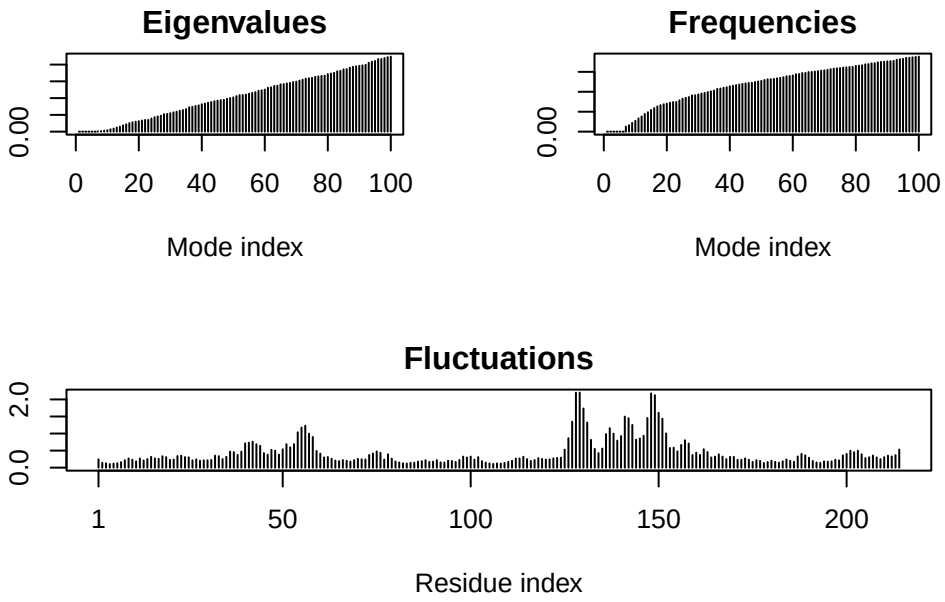
```
adk <- read.pdb("6s36")
```

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

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

```
 Building Hessian...        Done in 0.03 seconds.
 Diagonalizing Hessian...   Done in 0.331 seconds.
```

```
plot(m)
```




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