Class 09: Structural Bioinformatics (pt. 1)

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

First, let's see what is in the PDC database– the main repository of protein structures.

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

For context: Release 2023_04 of 13-Sept-2023 of UniProt/TrEMBL contains 251600,768 sequence entries. The PDB only contains 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's 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) <- rownames(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
```

Without the `row.names=1`, it would make the column values `NA`. Save this matric to a vector & reinsert the rownames using `rownames()`.

This can also be done using the `readr` package.

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
```

93.16% of structures in the PDB are solved by X-ray & EM.

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
```

86.67% of thructures 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

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? This is a 2 Angstrom structure and Hydrogen is not visible at this resolution. You need 1A or better to view the entirety of the water molecule.

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? This water molecule is 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 HIP-Pr with the catalytic ASP residues, the MK compound and the all important water 308.

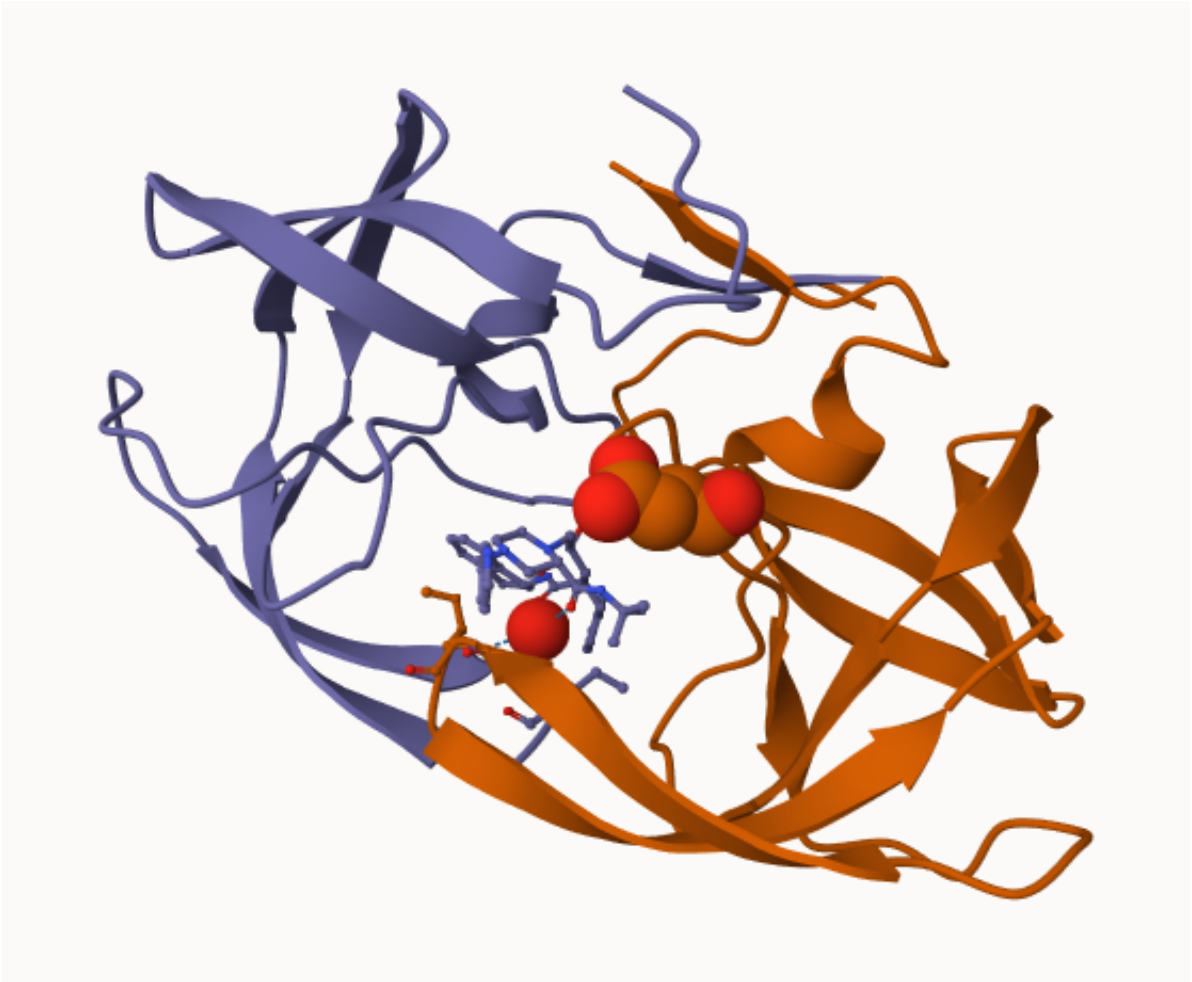


Figure 1: Figure caption

3. Introduction to Bio3D in R

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
```

Q7: How many amino acid residues are there in this pdb object? There are 198 AA residues in this pdb object.

Q8: Name one of the two non-protein residues? The non-protein residues are HOH & MK1

Q9: How many protein chains are in this structure? There are 2 protein chains.

```
attributes(pdb)
```

```
$names
[1] "atom"   "xyz"    "seqres" "helix"  "sheet"  "calpha" "remark" "call"

$class
[1] "pdb" "sse"
```

```
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.

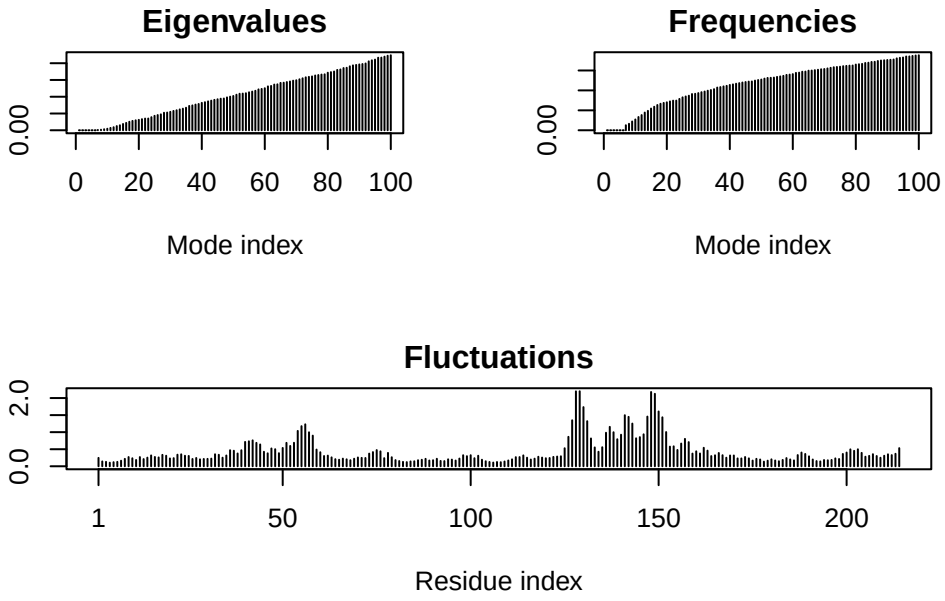
```
adk <- read.pdb("6s36")
```

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

```
# Perform flexiblity prediction
m <- nma(adk)
```

```
Building Hessian...         Done in 0.03 seconds.
Diagonalizing Hessian...    Done in 0.39 seconds.
```

```
plot(m)
```




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