Class 10

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The main repository of structural data is the PDB. Let's examine what it contains.

I download the composition stats from:https://www.rcsb.org/stats/summary

At the time of writting there are 183,201 protein structures. In UniProt there are 251,600,768 protein structures.

```
round(183201/251600768*100,2)
```

```
[1] 0.07
```

0.07 coverage

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

Because of the comma, the number above is character.

```
#string <- c("10", "100", 1, "1,000")
#as.numeric(string) + 1
```

Q. Write a function to fix this non numeric table...

Write a function to fix it. `apply()` We can use the `gsub()` function.

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

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

```
     X.ray    EM   NMR Multiple.methods Neutron Other  Total
[1,] 158844 11759 12296              197      73    32 183201
[2,]   9260  2054    34                8       1     0  11357
[3,]   8307  3667   284                7       0     0  12265
[4,]   2730   113  1467               13       3     1   4327
[5,]    164     9    32                0       0     0    205
[6,]     11     0     6                1       0     4     22
```

Will add the rownames from the original wee table...

```
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
```

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
```

84.83% and 8.33% are solved X ray and Electron Microscopy, respectively.

Q2-3 Let's skip these

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

```
totalrow <- apply(pdbstats, 1, sum)
percent <- round(totalrow/sum(totalrow)*100, 2)
percent
```

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

```
sum(percent[c(1,2,3)])
```

```
[1] 97.84
```

86.67% structures in PDB are Protein (only). 97.84% structures in PDB are proteins.

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?

419.

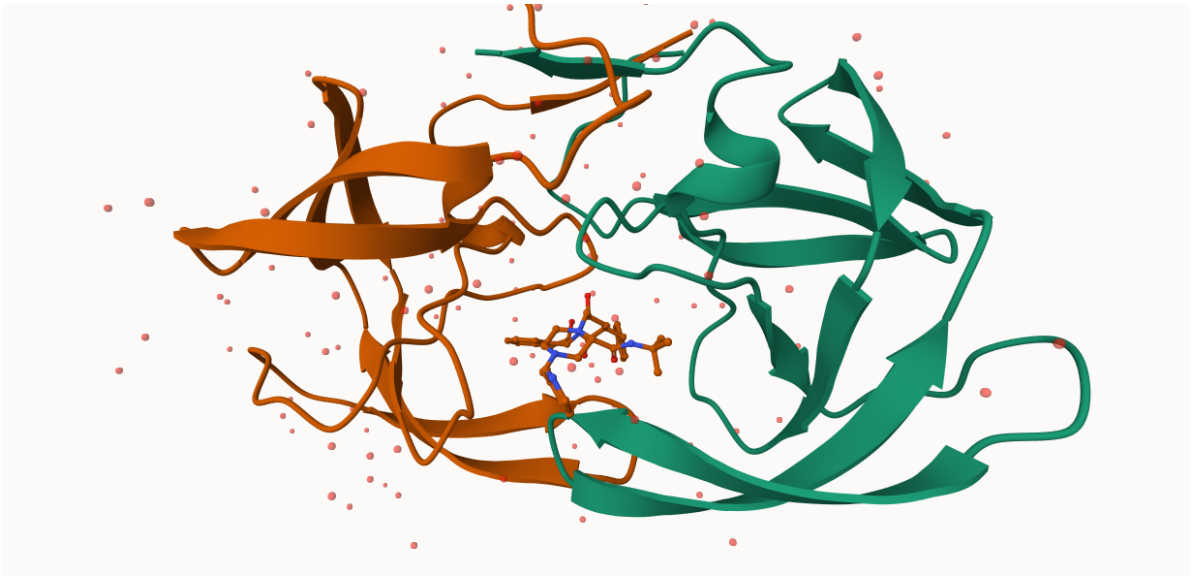
Q4: Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure?

The resolution of 1HSG is Angstrom, so the hydrogen atoms are invisible.

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

#Using Mol* to examine HIV-Pr

Here is a rubbish pic of HIV-Pr that is not very useful yet.

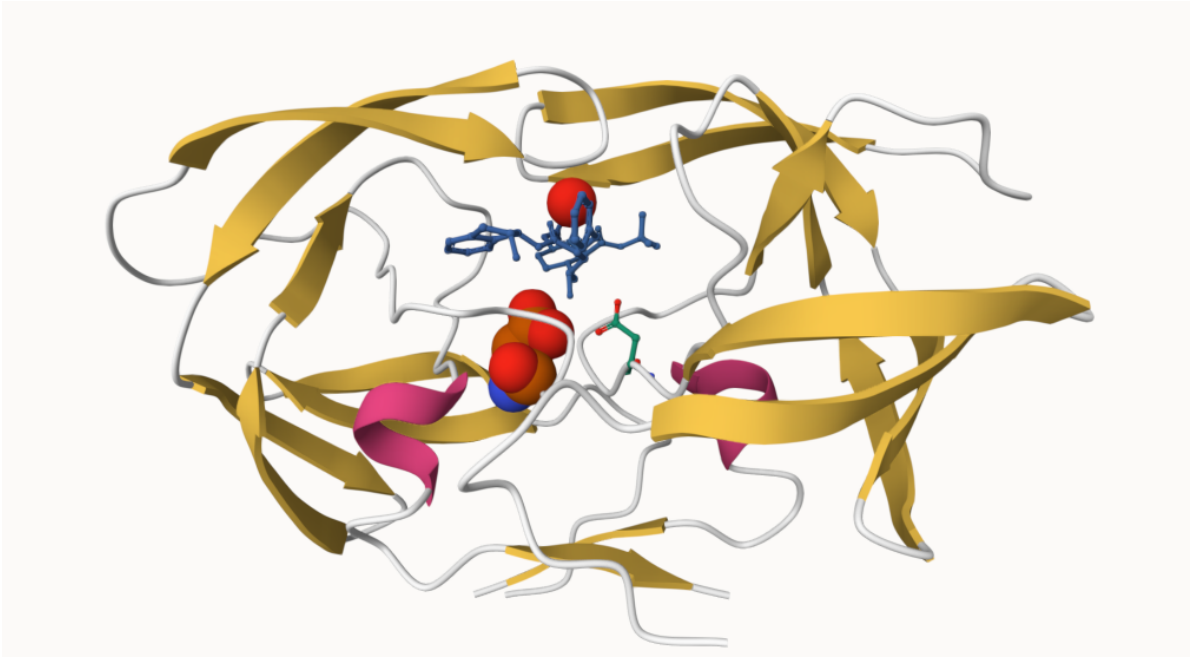


Q6: Generate and save a figure clearly showing the two distinct chains of HIV-protease along with the ligand. You might also consider showing the catalytic residues ASP 25 in each chain and the critical water (we recommend "Ball & Stick" for these side-chains). Add this figure to your Quarto document.

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

Conformational changes of the structures may create larger space for entry.

Q7: [Optional] As you have hopefully observed HIV protease is a homodimer (i.e. it is composed of two identical chains). With the aid of the graphic display can you identify secondary structure elements that are likely to only form in the dimer rather than the monomer?



Using ghd bio3d package

```
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
```

```
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>
```

```
head(pdb$atom$resid)
```

```
[1] "PRO" "PRO" "PRO" "PRO" "PRO" "PRO"
```

```
pdb$atom$resid[pdb$calpha]
```

```
  [1] "PRO" "GLN" "ILE" "THR" "LEU" "TRP" "GLN" "ARG" "PRO" "LEU" "VAL" "THR"
 [13] "ILE" "LYS" "ILE" "GLY" "GLY" "GLN" "LEU" "LYS" "GLU" "ALA" "LEU" "LEU"
 [25] "ASP" "THR" "GLY" "ALA" "ASP" "ASP" "THR" "VAL" "LEU" "GLU" "GLU" "MET"
 [37] "SER" "LEU" "PRO" "GLY" "ARG" "TRP" "LYS" "PRO" "LYS" "MET" "ILE" "GLY"
 [49] "GLY" "ILE" "GLY" "GLY" "PHE" "ILE" "LYS" "VAL" "ARG" "GLN" "TYR" "ASP"
 [61] "GLN" "ILE" "LEU" "ILE" "GLU" "ILE" "CYS" "GLY" "HIS" "LYS" "ALA" "ILE"
 [73] "GLY" "THR" "VAL" "LEU" "VAL" "GLY" "PRO" "THR" "PRO" "VAL" "ASN" "ILE"
 [85] "ILE" "GLY" "ARG" "ASN" "LEU" "LEU" "THR" "GLN" "ILE" "GLY" "CYS" "THR"
 [97] "LEU" "ASN" "PHE" "PRO" "GLN" "ILE" "THR" "LEU" "TRP" "GLN" "ARG" "PRO"
[109] "LEU" "VAL" "THR" "ILE" "LYS" "ILE" "GLY" "GLY" "GLN" "LEU" "LYS" "GLU"
[121] "ALA" "LEU" "LEU" "ASP" "THR" "GLY" "ALA" "ASP" "ASP" "THR" "VAL" "LEU"
[133] "GLU" "GLU" "MET" "SER" "LEU" "PRO" "GLY" "ARG" "TRP" "LYS" "PRO" "LYS"
[145] "MET" "ILE" "GLY" "GLY" "ILE" "GLY" "GLY" "PHE" "ILE" "LYS" "VAL" "ARG"
[157] "GLN" "TYR" "ASP" "GLN" "ILE" "LEU" "ILE" "GLU" "ILE" "CYS" "GLY" "HIS"
[169] "LYS" "ALA" "ILE" "GLY" "THR" "VAL" "LEU" "VAL" "GLY" "PRO" "THR" "PRO"
[181] "VAL" "ASN" "ILE" "ILE" "GLY" "ARG" "ASN" "LEU" "LEU" "THR" "GLN" "ILE"
[193] "GLY" "CYS" "THR" "LEU" "ASN" "PHE"
```

```
aa321(pdb$atom$resid[pdb$calpha])
```

```
  [1] "P" "Q" "I" "T" "L" "W" "Q" "R" "P" "L" "V" "T" "I" "K" "I" "G" "G" "Q"
 [19] "L" "K" "E" "A" "L" "L" "D" "T" "G" "A" "D" "D" "T" "V" "L" "E" "E" "M"
 [37] "S" "L" "P" "G" "R" "W" "K" "P" "K" "M" "I" "G" "G" "I" "G" "G" "F" "I"
 [55] "K" "V" "R" "Q" "Y" "D" "Q" "I" "L" "I" "E" "I" "C" "G" "H" "K" "A" "I"
 [73] "G" "T" "V" "L" "V" "G" "P" "T" "P" "V" "N" "I" "I" "G" "R" "N" "L" "L"
 [91] "T" "Q" "I" "G" "C" "T" "L" "N" "F" "P" "Q" "I" "T" "L" "W" "Q" "R" "P"
[109] "L" "V" "T" "I" "K" "I" "G" "G" "Q" "L" "K" "E" "A" "L" "L" "D" "T" "G"
[127] "A" "D" "D" "T" "V" "L" "E" "E" "M" "S" "L" "P" "G" "R" "W" "K" "P" "K"
[145] "M" "I" "G" "G" "I" "G" "G" "F" "I" "K" "V" "R" "Q" "Y" "D" "Q" "I" "L"
[163] "I" "E" "I" "C" "G" "H" "K" "A" "I" "G" "T" "V" "L" "V" "G" "P" "T" "P"
[181] "V" "N" "I" "I" "G" "R" "N" "L" "L" "T" "Q" "I" "G" "C" "T" "L" "N" "F"
```

#Predicting functional motions of a single structure

Run a Normal Mode Analysis (NMA) - a bioinformatics method to predict functional motions.

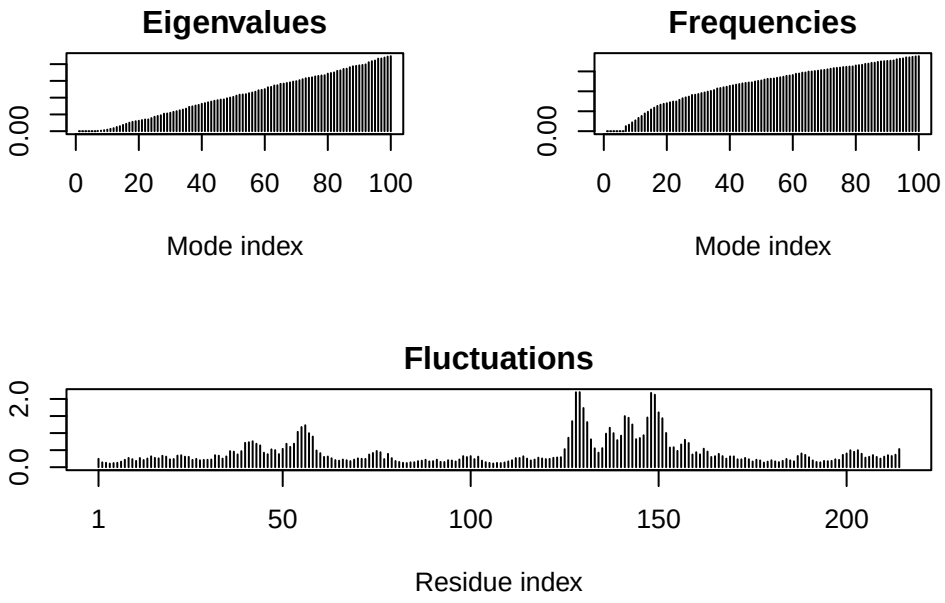
```
adk <- read.pdb("6s36")
```

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

```
modes <- nma(adk)
```

```
Building Hessian...        Done in 0.07 seconds.
Diagonalizing Hessian...   Done in 0.55 seconds.
```

```
plot(modes)
```




```
mktrj(modes, file="modes.pdb")
```

```
mktrj(modes, pdb=adk, file="modes.pdb")
```