Class10: Structural Bioinformatics 1

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PDB statistics

THe Protein Data Bank (PDB)is the main repository of biomolecular strucutres. Let's see what it contains:

Download a CSV file from the PDB site (accessible from "Analyze" > "PDB Statistics" > "by Experimental Method and Molecular Type"

```
stats <- read.csv("Data Export Summary.csv")
stats
```

```
           Molecular.Type   X.ray     EM    NMR Integrative Multiple.methods
1          Protein (only) 178,795 21,825 12,773         343               226
2 Protein/Oligosaccharide  10,363  3,564     34           8                11
3              Protein/NA   9,106  6,335    287          24                 7
4     Nucleic acid (only)   3,132    221  1,566           3                15
5                   Other     175     25     33           4                 0
6  Oligosaccharide (only)      11      0      6           0                 1
  Neutron Other   Total
1      84    32 214,078
2       1     0  13,981
3       0     0  15,759
4       3     1   4,941
5       0     0     237
6       0     4      22
```

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

```
#sum(stats$X.ray)
```

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

```
[1] 88
```

The comma in these number leads to the numbers here being read as characters

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

```
Rows: 6 Columns: 9
── Column specification ────────────────────────────────────────────────────────
Delimiter: ","
```

```
chr (1): Molecular Type
dbl (4): Integrative, Multiple methods, Neutron, Other
num (4): X-ray, EM, NMR, Total

ℹ Use `spec()` to retrieve the full column specification for this data.
ℹ Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

```
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)       178795 21825 12773         343                 226      84
2 Protein/Oligosacch…   10363  3564    34           8                  11       1
3 Protein/NA             9106  6335   287          24                   7       0
4 Nucleic acid (only)    3132   221  1566           3                  15       3
5 Other                   175    25    33           4                   0       0
6 Oligosaccharide (o…      11     0     6           0                   1       0
# ℹ 2 more variables: Other <dbl>, Total <dbl>
```

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

```
(sum(stats$`X-ray`) + sum(stats$EM))/sum(stats$Total)
```

```
[1] 0.937892
```

THe structures of X-ray and Electron Microscopy make up 93.78% of the data.

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

```
(stats[1,9])/sum(stats$Total)
```

```
      Total
1 0.8596889
```

The proportion is 85%

> Q3: SKIP... Looking up HIV structures including 1HSG

Visualizing the HIV-1 protease structure

We can use the Molstar viewer online: https://molstar.org/viewer/

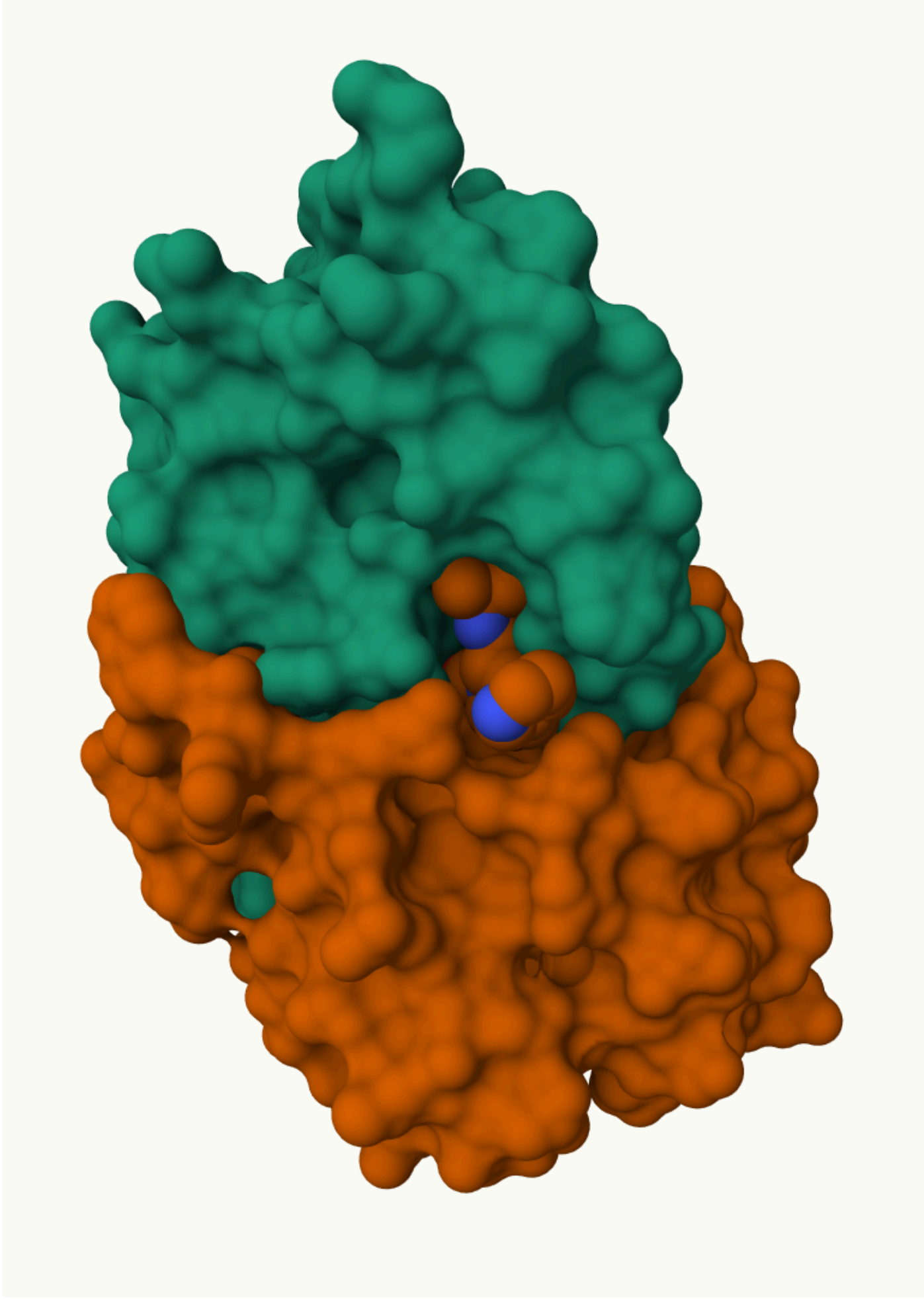


Figure 1: HIV Protease

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

This is because the molecular model is only showing the central oxygen atom of the water, not the two additional hydrogens

> 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 has a residue number of 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.

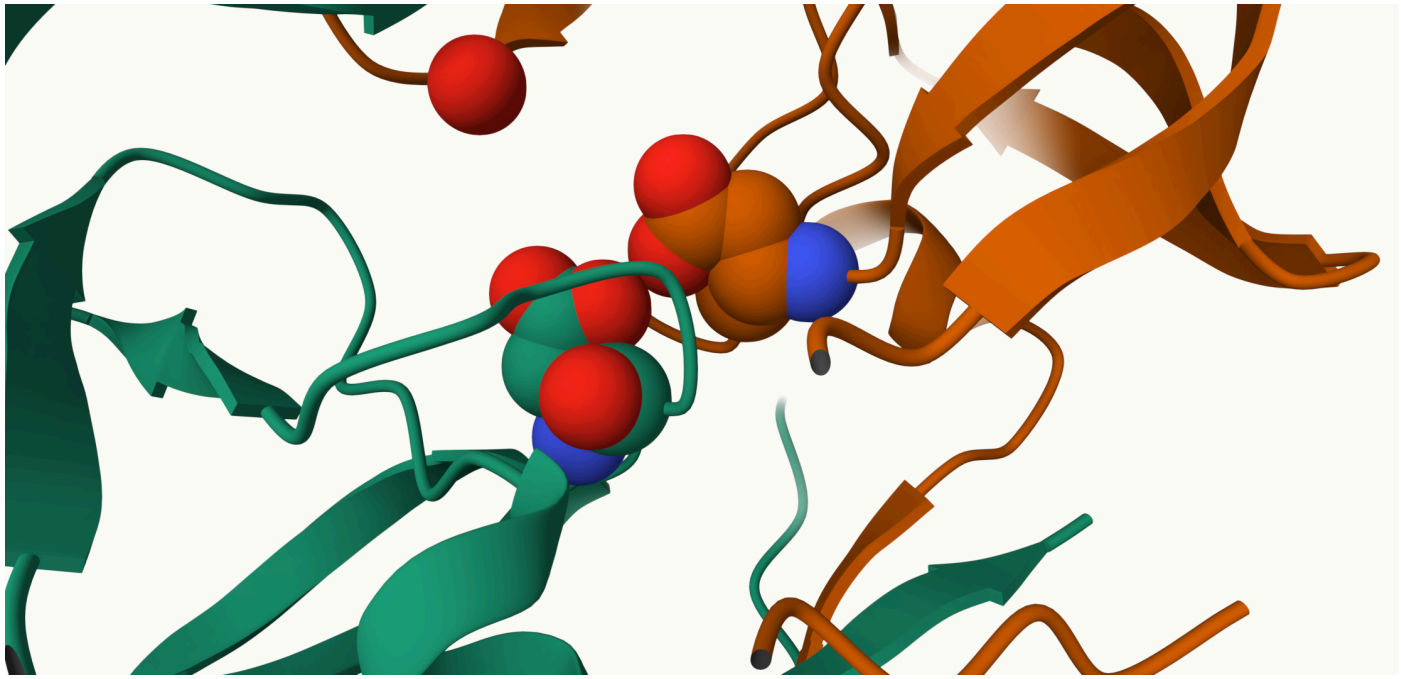


Figure 2: ASP 25 and the important active site water molecule

Introduction to Bio3D in R

```
library(bio3d)
```

```
Warning: package 'bio3d' was built under R version 4.4.3
```

```
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 128 amino acids

> Q8: Name one of the two non-protein residues?

There is both water molecules and MK1, merk 1

> Q9: How many protein chains are in this structure?

There are 2 protein chains

```
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

Read an ADK structure from the pdb database

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

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

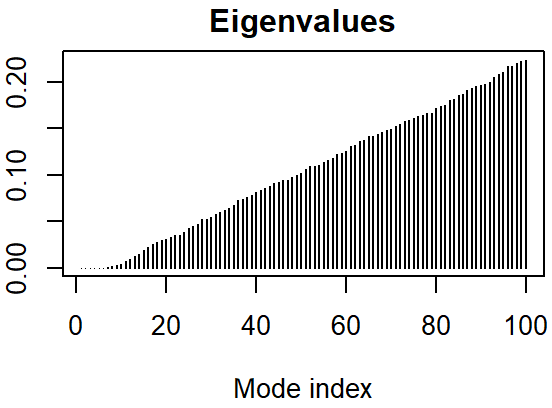
```
adk
```

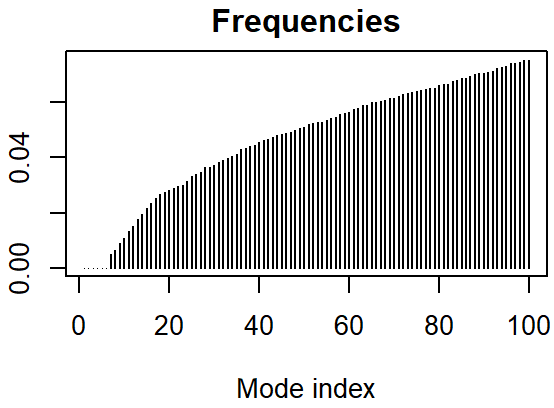
```
Call:  read.pdb(file = "6s36")

  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
```

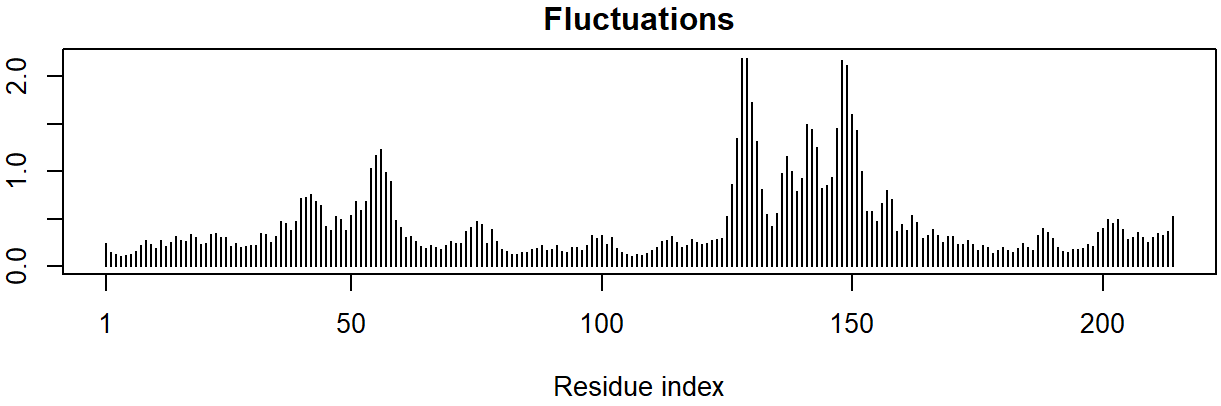
```
m <- nma(adk)
```

```
 Building Hessian...        Done in 0.02 seconds.
 Diagonalizing Hessian...   Done in 0.34 seconds.
```

```
plot(m)
```







Write our our results as a new trajectory/movie of predicted motions using `mktrj`

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