Structural Bioinformatics (Pt 1)

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The PDB archive is the major repository of information about the 3D structures of large biological molecules, including proteins and nucleic acids. Understanding the shape of these molecules helps to understand how they work. This knowledge can be used to help deduce a structure's role in human health and disease, and in drug development. The structures in the PDB range from tiny proteins and bits of DNA or RNA to complex molecular machines like the ribosome composed of many chains of protein and RNA.

The PDB database

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

Downloaded composition stats from https://tinyurl.com/statspdb

```r
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 above due to the commas in the numer. This causes R to treat them as characters.

```
stats$X.ray
```

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

Removing the comma from the dataset by using `gsub()` to replace commas. We use `lapply()` to apply `gsub()` to each column:

```
#stats <- as.data.frame(lapply(stats, function(x) gsub(",", "", x)))
#stats
```

Here is another way to remove the commas using a function

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

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
```

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

```r
total <- apply(pdbstats,2,sum)
total
```

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

```r
round(total/total["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?

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

```
[1] 86.67
```

```r
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 because of time constraints

> 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 1 Angstrom or better to be able to see such small atoms like 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 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.

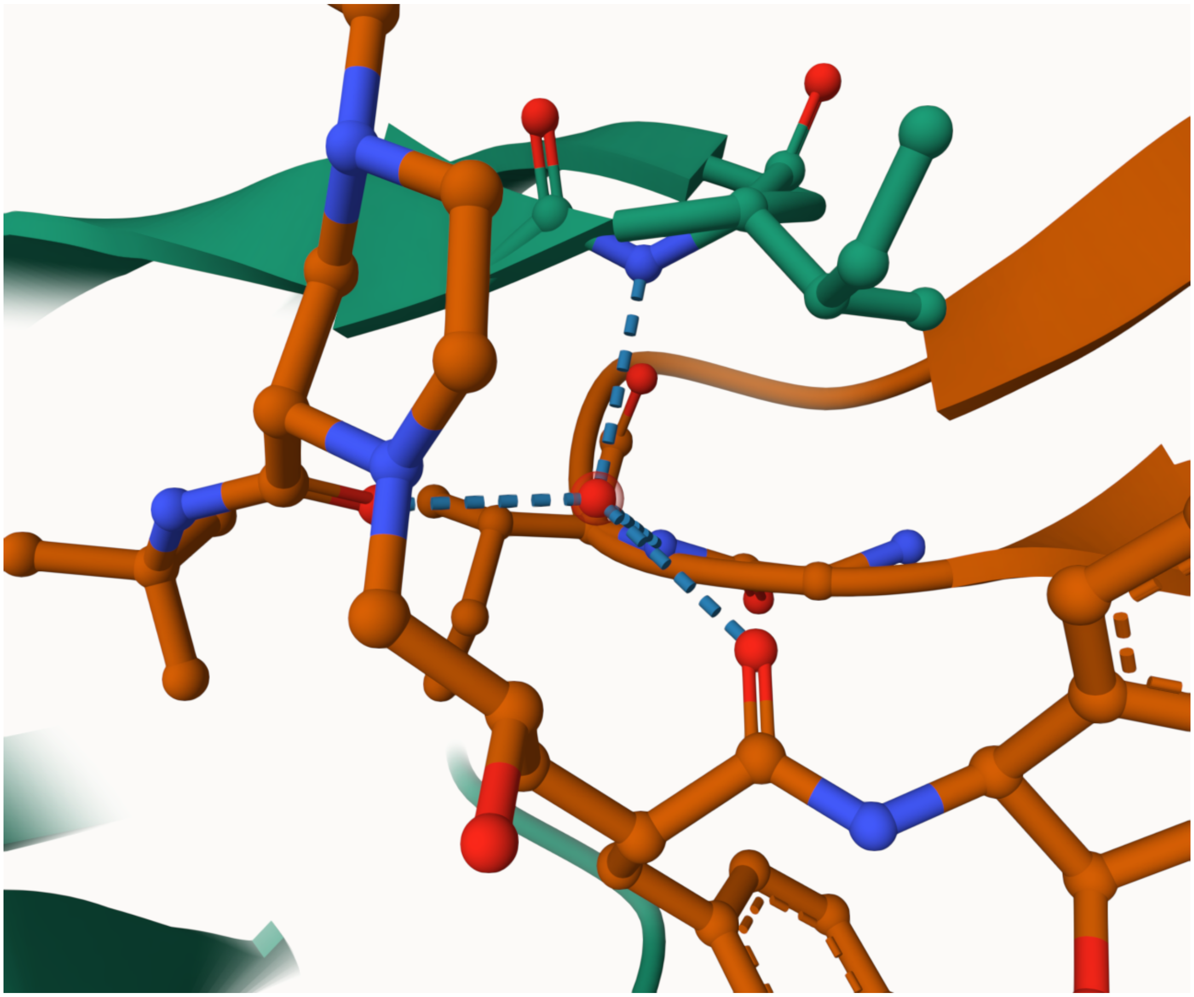


Figure 1: Here is a figure of HIP-Pr with the catalytic ASP residues, the MK1 compound and the all important water 308

Another perspective of it

One more picture!

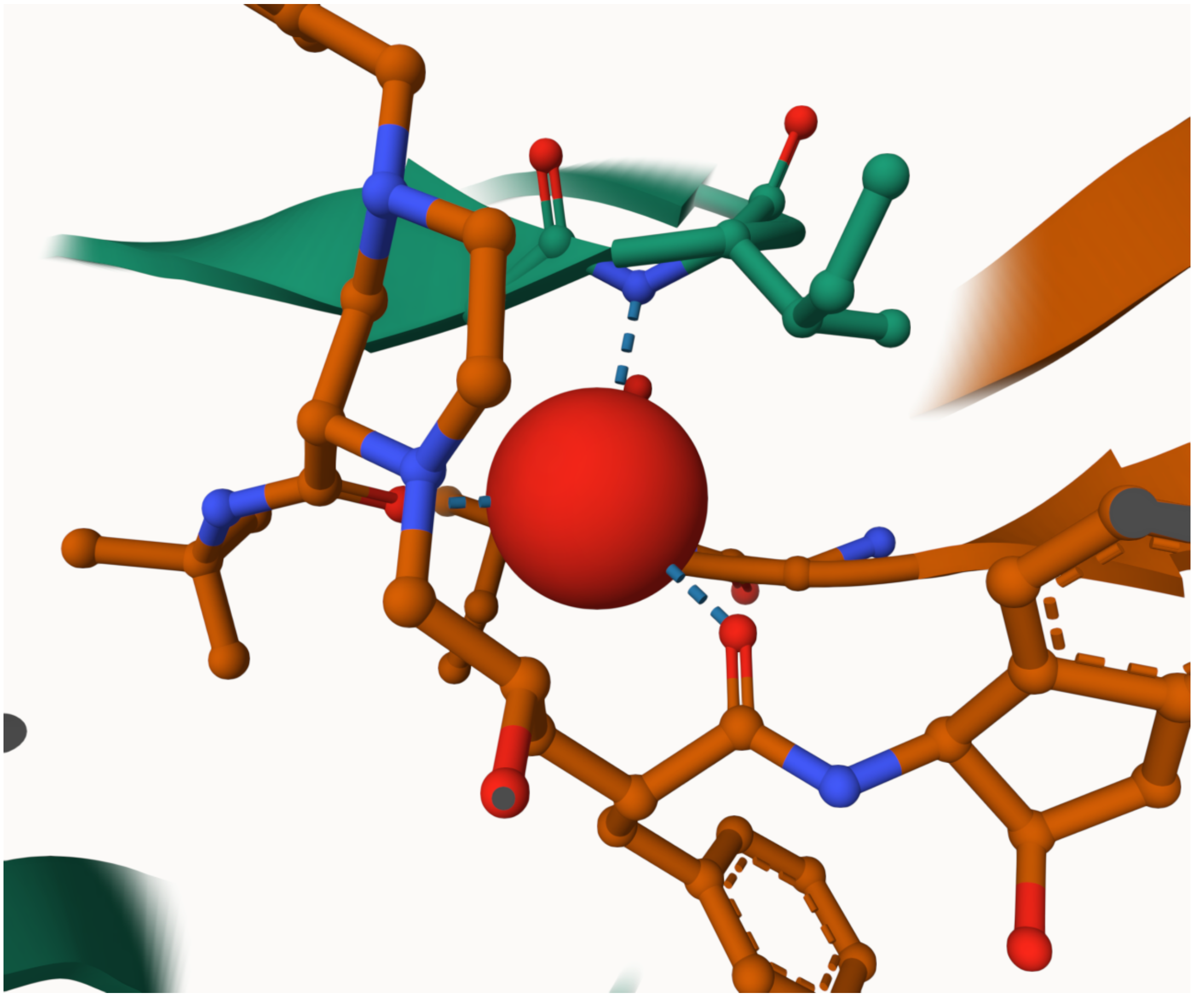


Figure 2: Another picture of the water

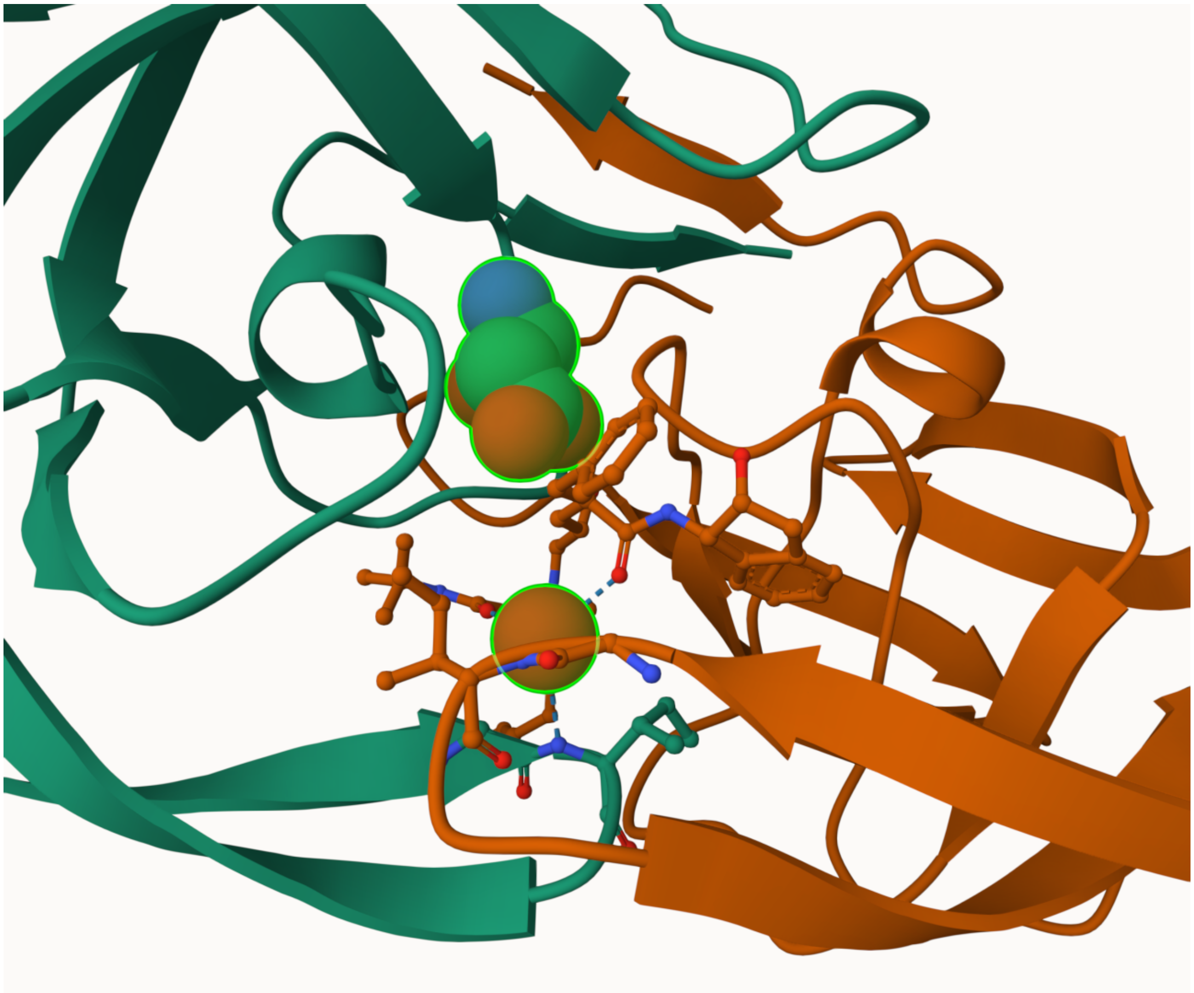


Figure 3: Uno Mas!

The bio3d package for structural bioinformatics

```r
library(bio3d)

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

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

```r
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
```

```r
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 ttoday 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
```

```
adk
```

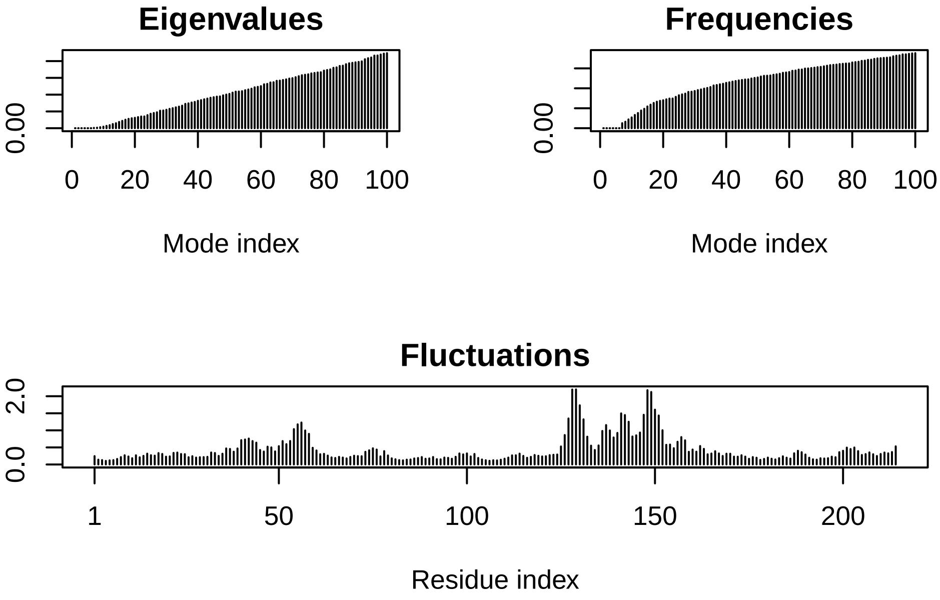
```
Call:  read.pdb(file = "6s36")

  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
```

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

```
 Building Hessian...        Done in 0.021 seconds.
 Diagonalizing Hessian...   Done in 0.456 seconds.
```

```r
plot(m)
```



```r
mktrj(m, file="adk_m7.pdf")
```