Class 10: Structural Bioinformatics

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Table of contents

Structural Bioinformatics

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

The PDB Database & PDB Statistics

The main repository of biomolecular structure data is called PDB found at https://www.rcsb.org

Let's see what this database contains. I went to PDB > Analyze > PDB Statistics > By Experimental Method and Molecular Type.

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

```
           Molecular.Type   X.ray     EM    NMR Multiple.methods Neutron Other
1          Protein (only) 169,563 16,774 12,578              208      81    32
2 Protein/Oligosaccharide   9,939  2,839     34                8       2     0
3              Protein/NA   8,801  5,062    286                7       0     0
4     Nucleic acid (only)   2,890    151  1,521               14       3     1
5                   Other     170     10     33                0       0     0
6  Oligosaccharide (only)      11      0      6                1       0     4
    Total
1 199,236
2  12,822
3  14,156
4   4,580
5     213
6      22
```

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

```
pdbstats$X.ray
```

```
[1] "169,563" "9,939"   "8,801"   "2,890"   "170"     "11"
```

The comma in these numbers is causing them to be read as character rather than numeric. I can fix this by replacing "," for nothing, " " with the `sub()` function:

```
x <- pdbstats$X.ray
as.numeric( sub(",", "", x) )
```

```
[1] 169563   9939   8801   2890    170     11
```

```
sum(as.numeric( sub(",", "", x) ))
```

```
[1] 191374
```

Or I can use the **readr** package and the `read_csv()` function.

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

```
Rows: 6 Columns: 8
-- Column specification --------------------------------------------------------
Delimiter: ","
chr (1): Molecular Type
dbl (3): 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.
```

```
pdbstats
```

```
# A tibble: 6 x 8
  `Molecular Type`   `X-ray`    EM   NMR `Multiple methods` Neutron Other  Total
  <chr>                <dbl> <dbl> <dbl>              <dbl>   <dbl> <dbl>  <dbl>
1 Protein (only)      169563 16774 12578                208      81    32 199236
2 Protein/Oligosacc~    9939  2839    34                  8       2     0  12822
3 Protein/NA            8801  5062   286                  7       0     0  14156
4 Nucleic acid (onl~    2890   151  1521                 14       3     1   4580
5 Other                  170    10    33                  0       0     0    213
6 Oligosaccharide (~      11     0     6                  1       0     4     22
```

I want to clean the column names so they are all lower case and don't have spaces in them.

```
colnames(pdbstats)
```

```
[1] "Molecular Type"   "X-ray"            "EM"               "NMR"
[5] "Multiple methods" "Neutron"          "Other"            "Total"
```

```
library(janitor)
```

```
Attaching package: 'janitor'

The following objects are masked from 'package:stats':

    chisq.test, fisher.test
```

```
df <- clean_names(pdbstats)
df
```

```
# A tibble: 6 x 8
  molecular_type         x_ray    em   nmr multiple_methods neutron other  total
  <chr>                  <dbl> <dbl> <dbl>            <dbl>   <dbl> <dbl>  <dbl>
1 Protein (only)        169563 16774 12578              208      81    32 199236
2 Protein/Oligosacchar~   9939  2839    34                8       2     0  12822
3 Protein/NA              8801  5062   286                7       0     0  14156
4 Nucleic acid (only)     2890   151  1521               14       3     1   4580
5 Other                    170    10    33                0       0     0    213
6 Oligosaccharide (onl~     11     0     6                1       0     4     22
```

Total number of X-ray structures

```
sum(df$x_ray)
```

```
[1] 191374
```

Total number of structures

```
sum(df$total)
```

```
[1] 231029
```

The percentage of structures in the PDB that are solved by X-Ray and Electron Microscopy are the following:

Percent of X-ray structures

```
sum(df$x_ray) / sum(df$total) * 100
```

```
[1] 82.83549
```

Percent of EM structures

```
sum(df$em) / sum(df$total) * 100
```

```
[1] 10.75017
```

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

```
sum(df[1,8])/sum(df$total)
```

```
[1] 0.8623852
```

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?

Around 131 HIV-1 protease structures are in the current PDB.

2. Visualizing the HIV-1 protease structure

Using Mol* and The important role of water

The main Mol* homepage at https://molstar.org/viewer/ We can input our own PDB files or just give it a PDB database accession code (4 letter PDB code).

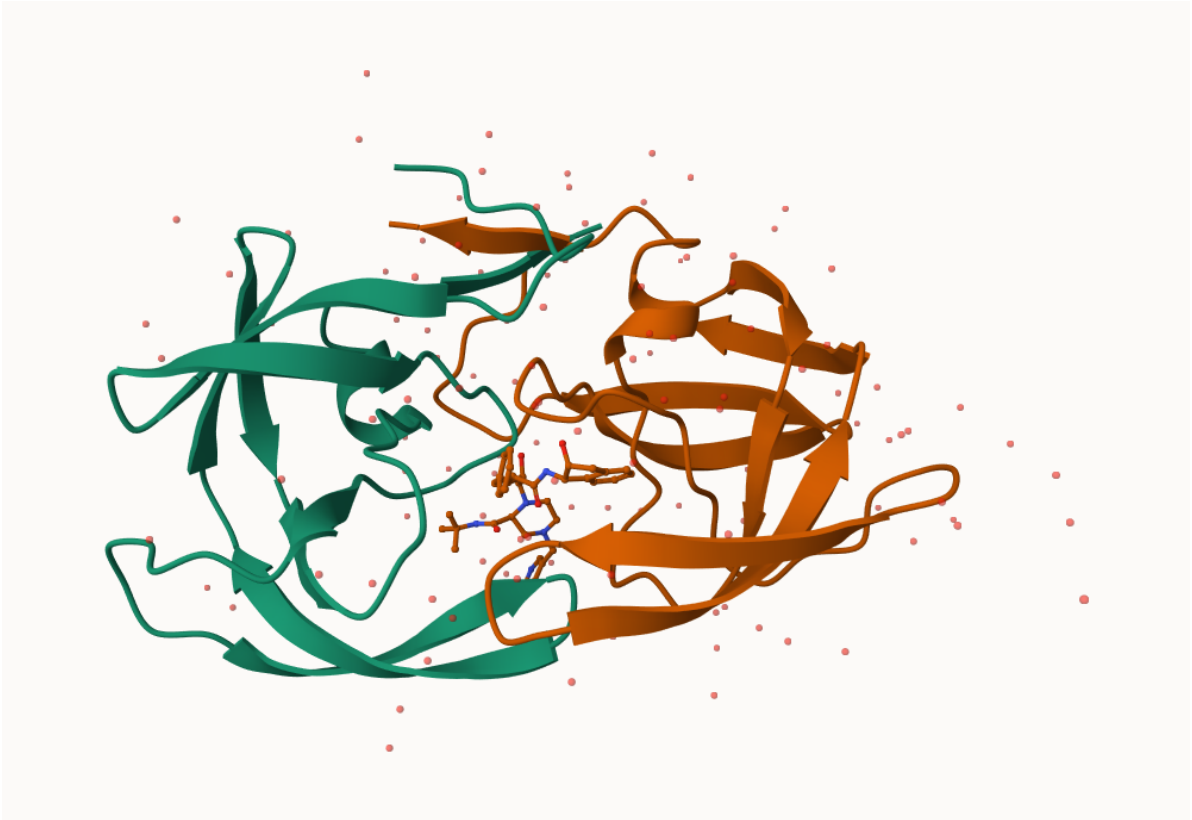


Figure 1: Molecular view of 1HSG

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

For simplification purposes and to show that bonding is only to the oxygen part of the water molecule rather than the whole molecule.

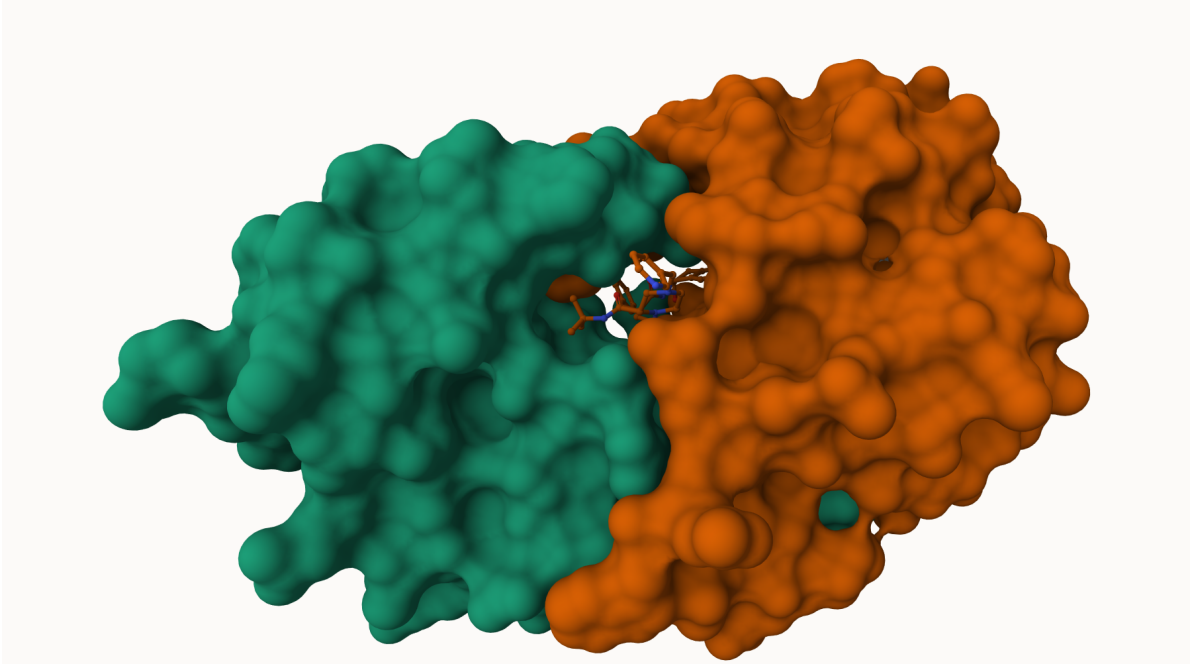


Figure 2: Surface represntation showing binding

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.

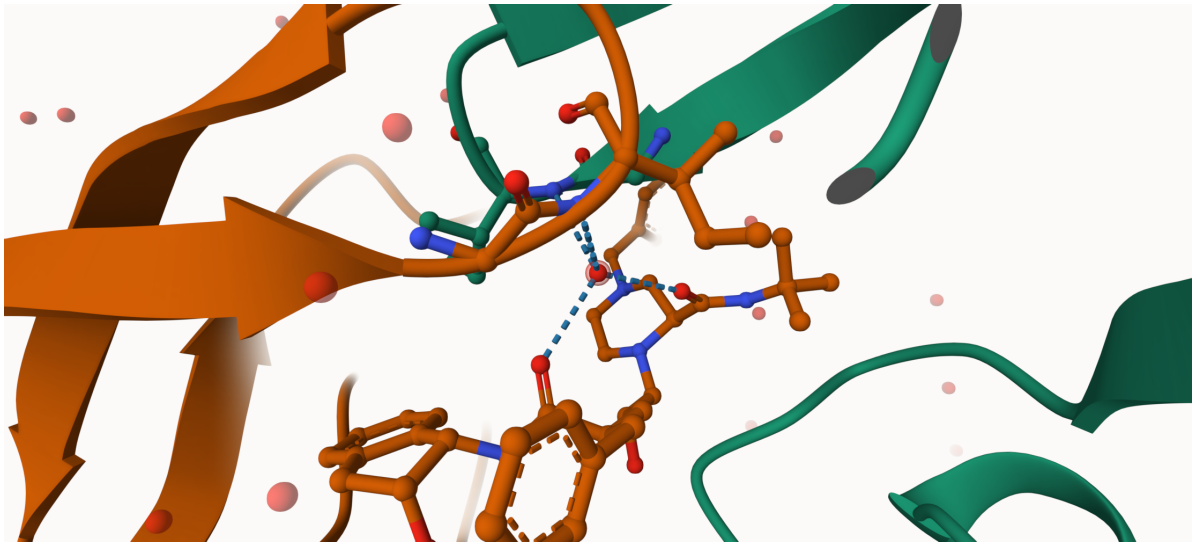


Figure 3: Water 308 in the binding site

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.

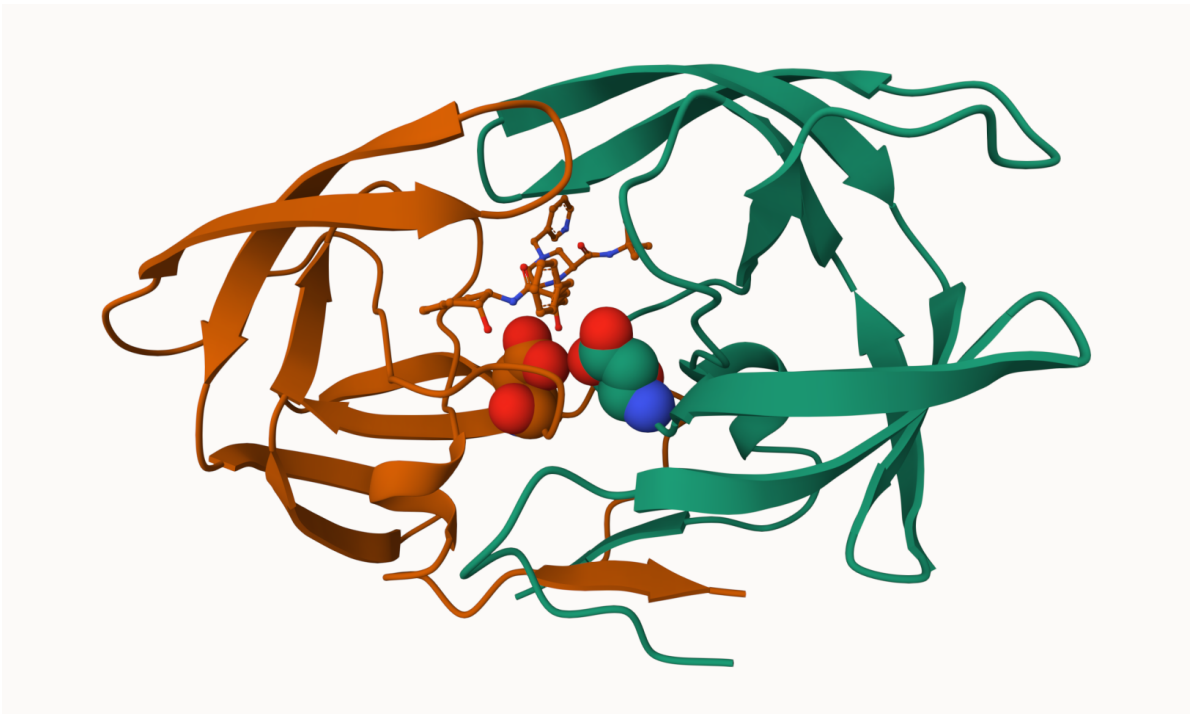


Figure 4: The important ASP25 amino-acids

3. Introduction to Bio3D in R

Reading PDB file data into R

We can use the **bio3d** package for structural bioinformatics to read PDB data into R

```
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?

198

or

```
length(pdbseq(pdb))
```

```
[1] 198
```

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

HOH

Q9: How many protein chains are in this structure?

2 chains A and B

Looking at the `pdb` object in more detail

```
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>
```

Let's try a new function not yet in the bio3d package. It requires the **r3dmol** package that we need to install with `install.packages("r3dmol")`

```
source("https://tinyurl.com/viewpdb")
#view.pdb(pdb, backgroundColor = "pink")
```

Predicting functional motions of a single structure

We can use the `nma()` function in bio3d to predict the large-scale functional motions of biomolecules.

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

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

```
adk
```

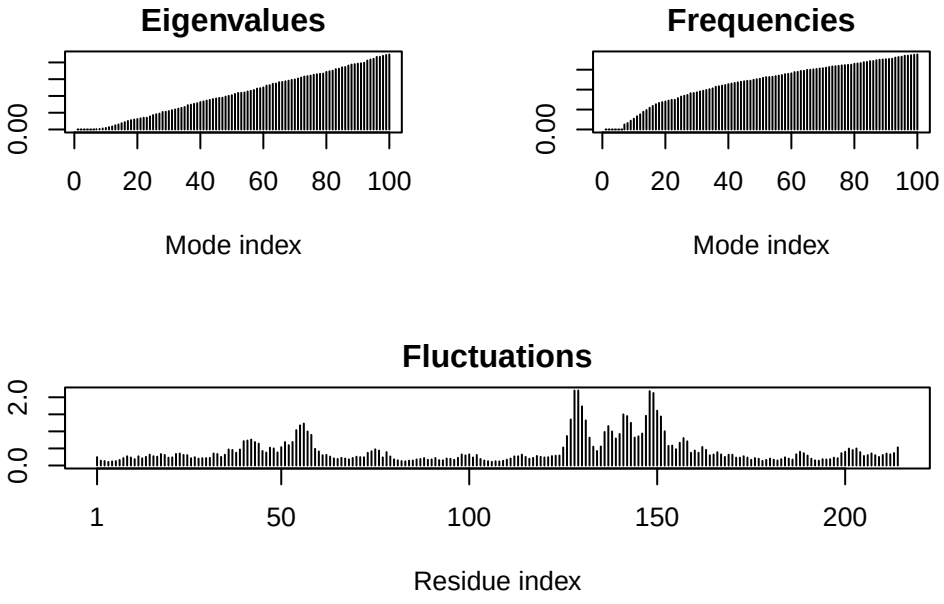
```

 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 0.021 seconds.
 Diagonalizing Hessian...   Done in 0.45 seconds.
```

```
plot(m)
```



Write out a trajectory of the predicted molecular motion:

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

4. Comparative structure analysis of Adenylate Kinase

Q10. Which of the packages above is found only on BioConductor and not CRAN?

Msa is a package that is found only on BioConductor and not CRAN.

Q11. Which of the above packages is not found on BioConductor or CRAN?:

Bio3d-view is a package not found on BioConductor or CRAN.

Q12. True or False? Functions from the devtools package can be used to install packages from GitHub and BitBucket?

True, functions from the devtools package can be used to install packages from GitHub and BitBucket

Q13. How many amino acids are in this sequence, i.e. how long is this sequence?

214 amino acids are in this sequence.