Class 9: Structural Bioinformatics pt.1

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The main database for structural data is called the PBD (Protein Data Bank). Let's see what it contains:

Data from: https://www.rcsb.com/stats

Read this into R

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

and answer the following questions:

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

```
pdbdb$Total
```

```
[1] "195,610" "12,318"  "13,720"  "4,531"   "213"     "22"
```

I need to remove the comma and convert to numeric to do math:

```
as.numeric( sub(",","", pdbdb$Total) )
```

```
[1] 195610  12318  13720   4531    213     22
```

I could turn this into a function to fix the whole table or any future table I read like this:

```
x <- pdbdb$Total
as.numeric( sub(",","",x))
```

```
[1] 195610  12318  13720   4531    213     22
```

```
comma2numeric <- function(x) {
  as.numeric( sub(",","", x))
}
```

Test it

```
comma2numeric(pdbdb$X.ray)
```

```
[1] 167192   9639   8730   2869    170     11
```

```
apply(pdbdb, 2, comma2numeric)
```

```
Warning in FUN(newX[, i], ...): NAs introduced by coercion
```

```
     Molecular.Type  X.ray    EM   NMR Multiple.methods Neutron Other  Total
[1,]             NA 167192 15572 12529              208      77    32 195610
[2,]             NA   9639  2635    34                8       2     0  12318
[3,]             NA   8730  4697   286                7       0     0  13720
[4,]             NA   2869   137  1507               14       3     1   4531
[5,]             NA    170    10    33                0       0     0    213
[6,]             NA     11     0     6                1       0     4     22
```

Or try a different read/import function:

```
library(readr)
pdbdb <- 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.
```

```
sum(pdbdb$Total)
```

```
[1] 226414
```

```
sum(pdbdb$`X-ray`)/sum(pdbdb$Total) * 100
```

```
[1] 83.30359
```

```
sum(pdbdb$EM)/sum(pdbdb$Total) * 100
```

```
[1] 10.18091
```

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

```
pdbdb$Total[1]/ sum(pdbdb$Total) * 100
```

```
[1] 86.39483
```

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?

Mol*

Mol* (pronounced "molstar") is a new web-based molecular viewer than we will need to learn the basics of here.

https://molstar.org/viewer/

We will use PDB code: 1HSG

Figure 1: First image from the start

Some more custom images:

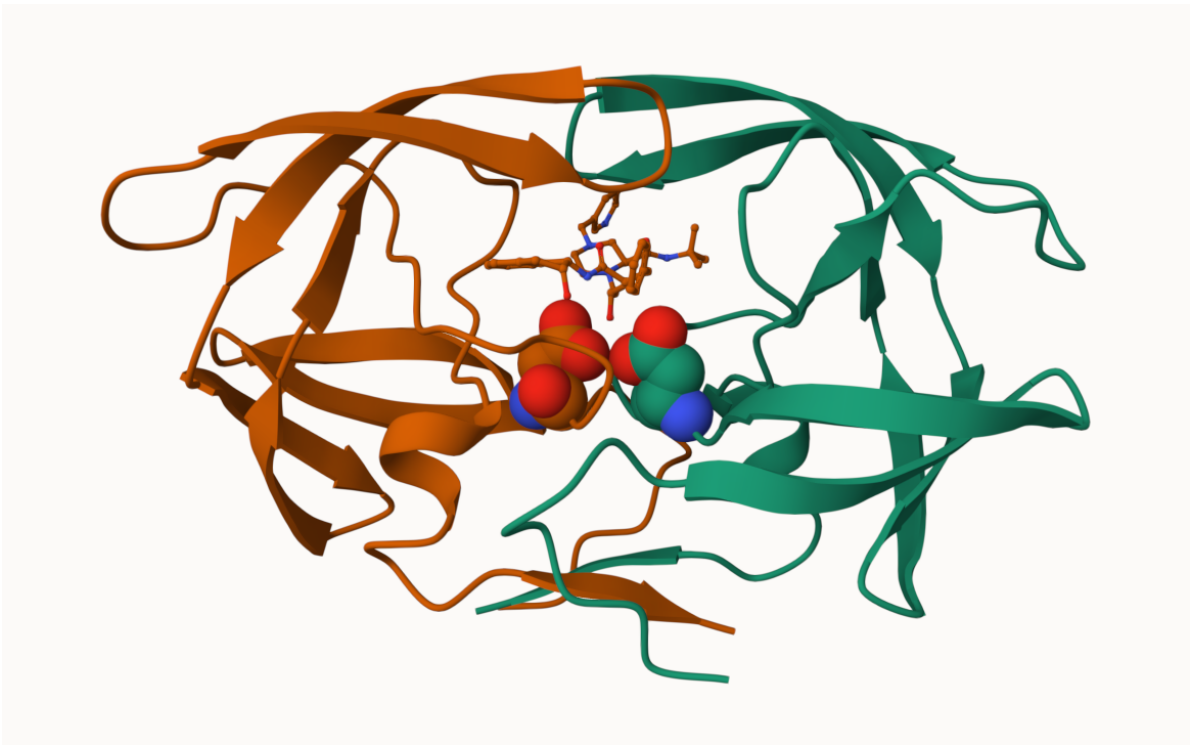


Figure 2: The all important catalytic ASP25 amino acids

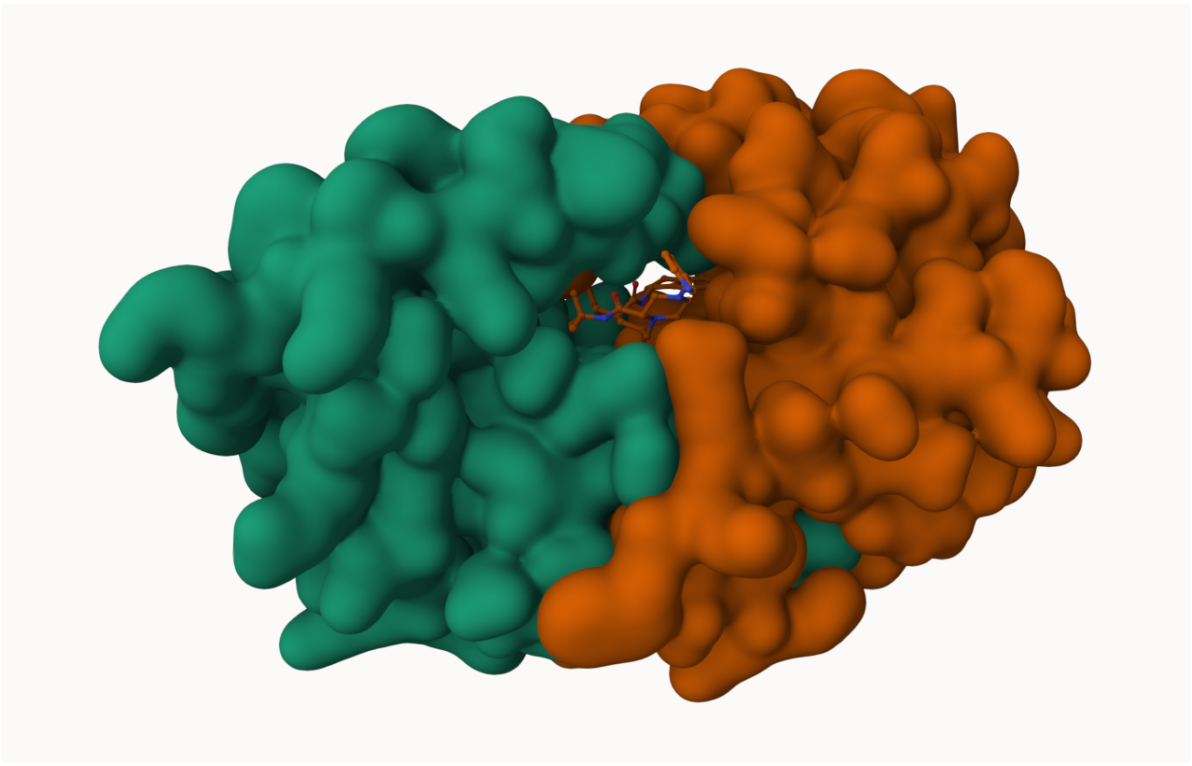


Figure 3: Surface display showing Merk compound in the peptide binding pocket

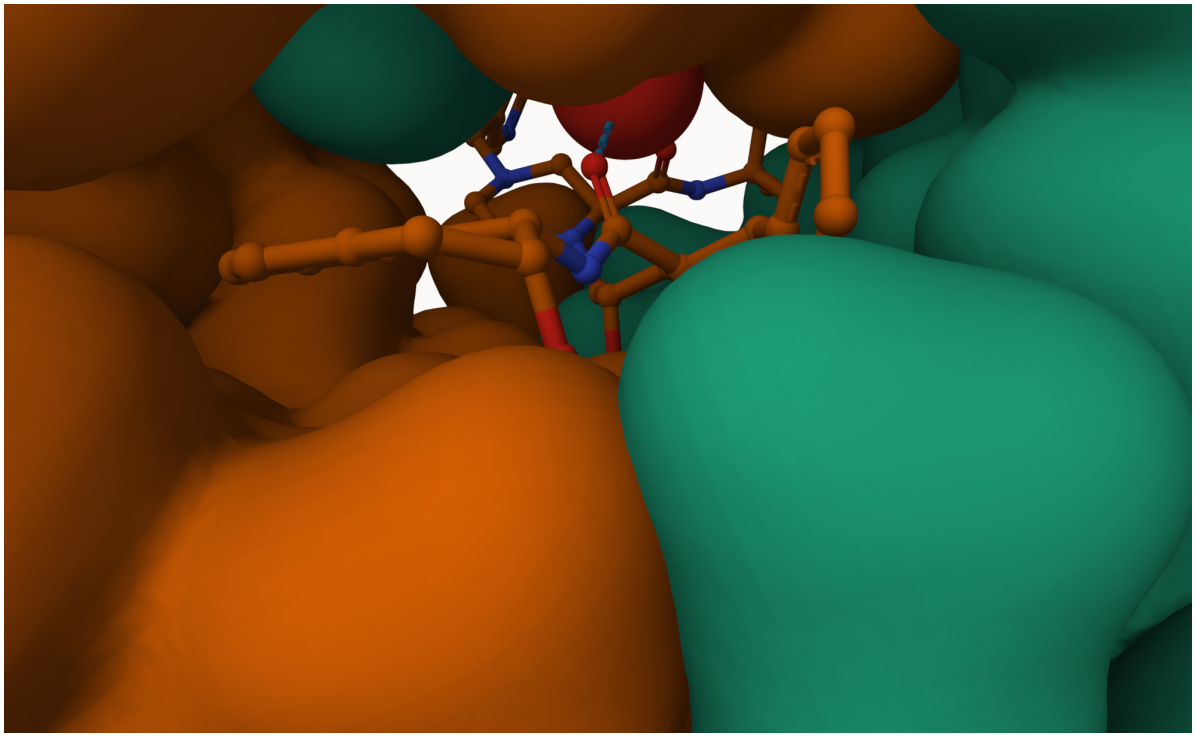


Figure 4: Close up view of binding site with drug and HOH 308

The Bio3D package

The bio3d package allows us to do all sorts of structural bioinformatics work in R.

Let's start with how it can read these PDB files:

```
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>
```

```
pdbseq(pdb)[25]
```

```
 25
"D"
```

Q7. How many amino acid residues are there in this pdb object?

```
sum(pdb$calpha)
```

```
[1] 198
```

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

```
[1] 198
```

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

HOH and MK1

Q9. How many protein chains are in this structure?

2

```
unique(pdb$atom$chain)
```

```
[1] "A" "B"
```

Predicting functional motions of a single structure

Let's do a bioinformatics prediction of functional motions - i.e. the movements that one of these molecules needs to make to do its stuff

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

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

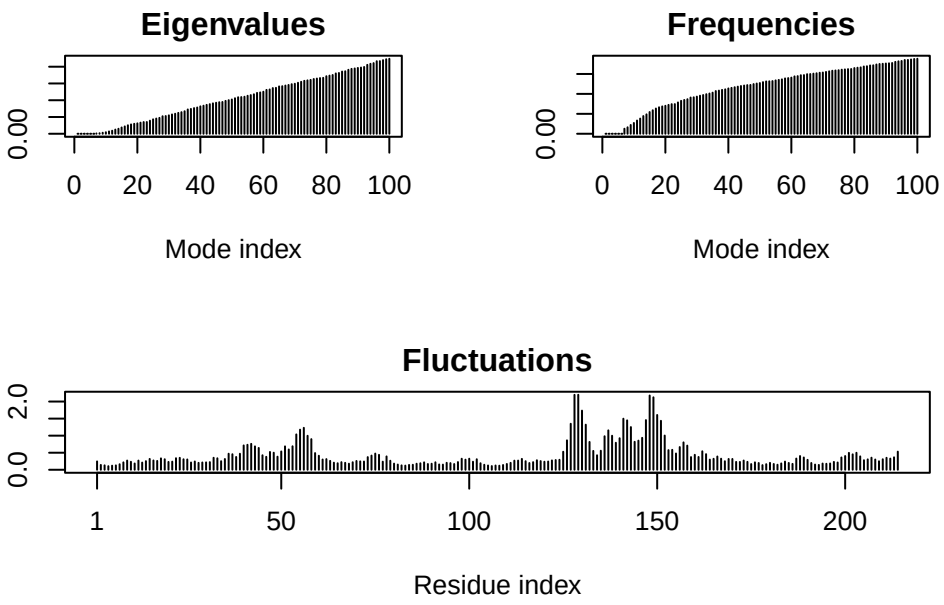
```
adk
```

```
 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
```

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

```
 Building Hessian...        Done in 0.013 seconds.
 Diagonalizing Hessian...   Done in 0.259 seconds.
```

```
plot(m)
```



Write out multi-model PDB file that we can use to make an animation of the predicted motions.

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

I can open this in Mol* to play the trajectory…