Class 11: Structural Bioinformatics pt2

Mai Tamura (PID: A18594079)

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AlphaFold DB

The EBI maintains the largest database of AlphFold structure prediction models at: https://alphafold.ebi.ac.uk

From last class (before Halloween), we saw that the PDB had 244,290 (Oct 2025)

The total number of protein sequences in UniProtKB is 199,579,901

> **Key point**: This is a fraction of sequence space that has structural coverage (0.12%)

```
244290/199579901 * 100
```

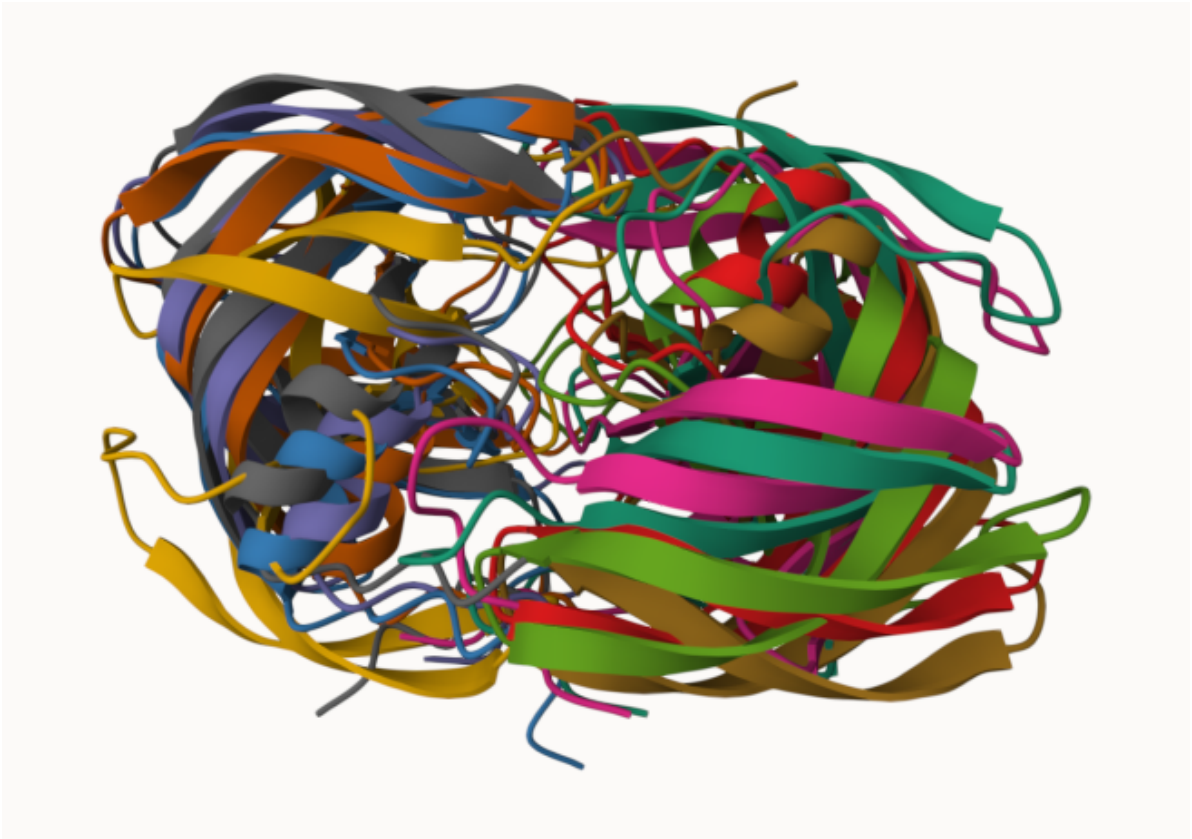
```
[1] 0.1224021
```

AFDB is attempting to address this gap...

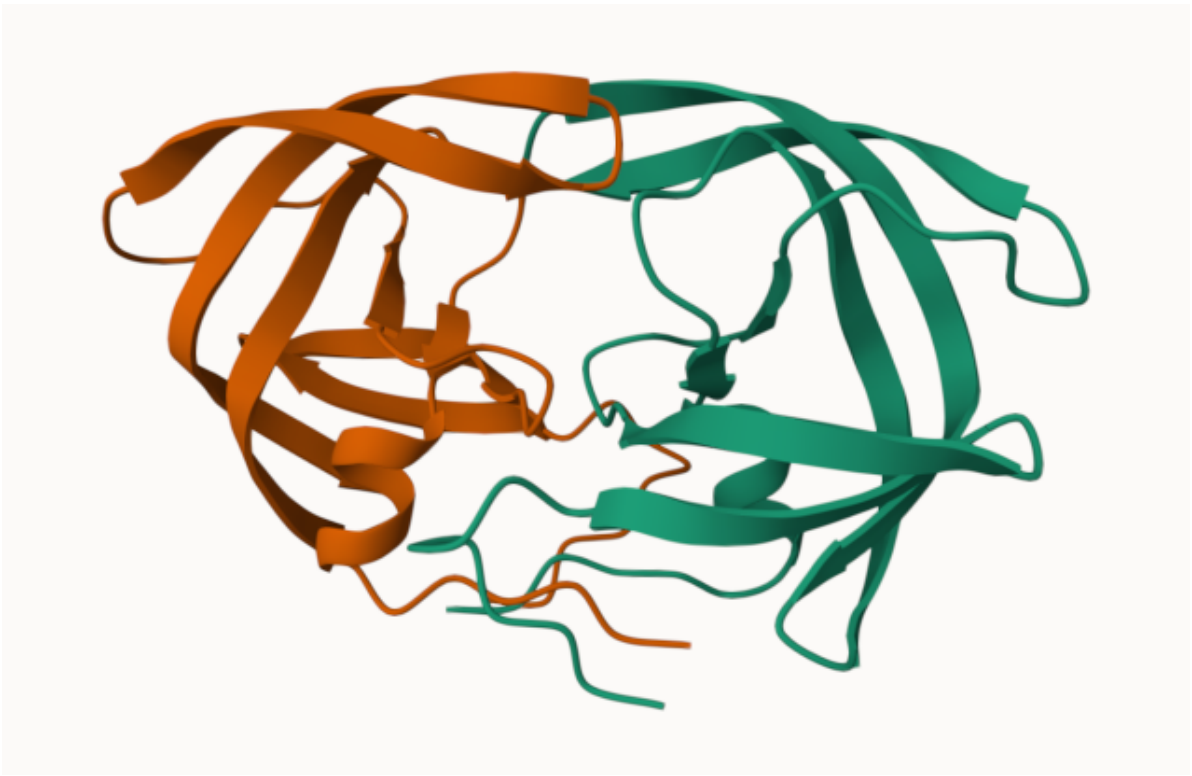
There are Two "Quality Scores" from AlphaFold one for residues (i.e. each amino acid) called **pLDDT score**. The other **PAE** score that measures the confidence in the relative position of two residues (i.e. a score for every pair of residues).

Generating Your own structure predictions

Figures of 5 generated HIV-PR models

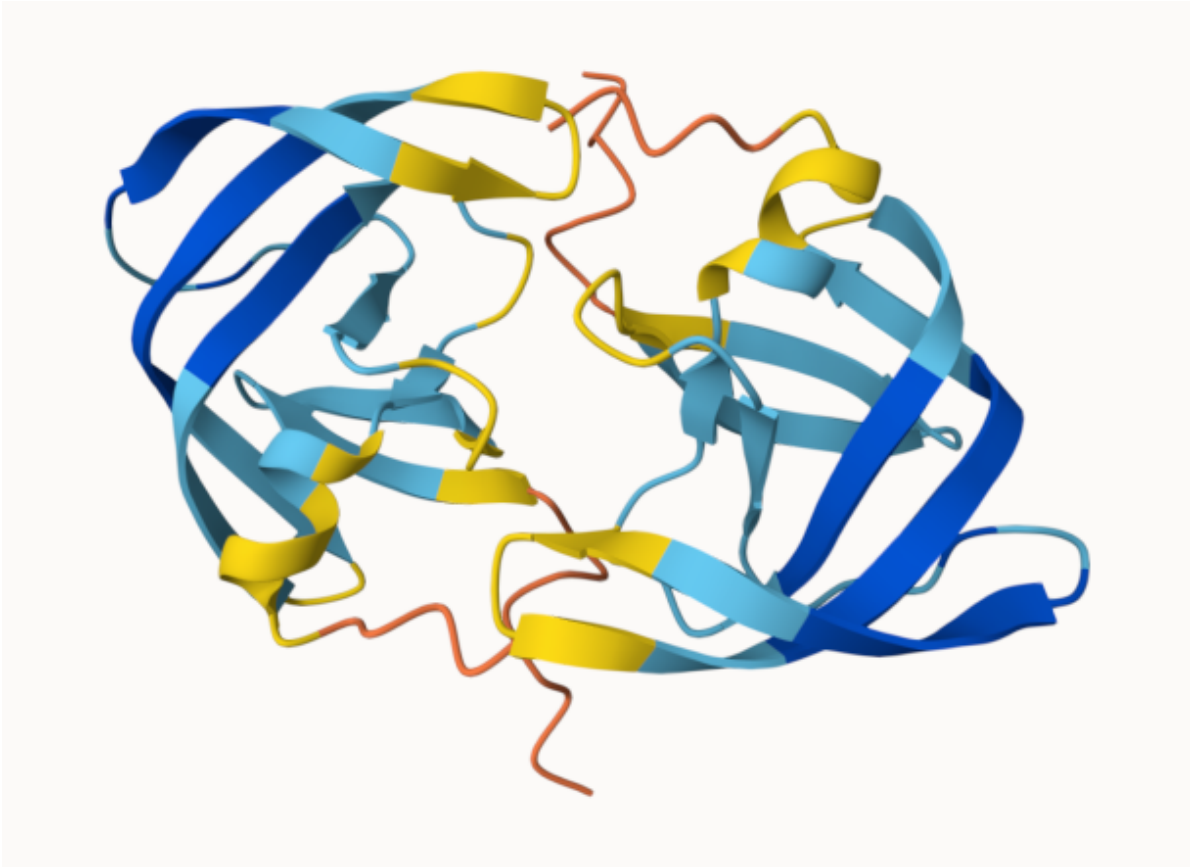


At the top model



model 1

and model 5



```
unzip("HIVPR_dimer_23119.result.zip")
```

Custom Analysis of resulting models in R

Read key result files into R. The first thing I need to know is what my results directory/folder is called (i.e. its name is different from)

```
results_dir <- "HIVPR_dimer_23119"
pdb_files <- list.files(path=results_dir,
                        pattern="*.pdb",
                        full.names = TRUE)
basename(pdb_files)
```

```
[1] "HIVPR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_4_seed_000.pdb"
[2] "HIVPR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_000.pdb"
[3] "HIVPR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_5_seed_000.pdb"
```

```
[4] "HIVPR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.pdb"
[5] "HIVPR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.pdb"
```

```
library(bio3d)

pdbs <- pdbaln(pdb_files, fit=TRUE, exefile="msa")
```

```
Reading PDB files:
HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_4_seed_00
HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_00
HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_5_seed_00
HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_00
HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_00
.....

Extracting sequences

pdb/seq: 1   name: HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer
pdb/seq: 2   name: HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer
pdb/seq: 3   name: HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer
pdb/seq: 4   name: HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer
pdb/seq: 5   name: HIVPR_dimer_23119/HIVPR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer
```

```
pdbs
```

```
                                 1        .         .         .         .         50
[Truncated_Name:1]HIVPR_dime   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:2]HIVPR_dime   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:3]HIVPR_dime   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:4]HIVPR_dime   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:5]HIVPR_dime   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
                               **************************************************
                               1        .         .         .         .         50

                              51        .         .         .         .         100
[Truncated_Name:1]HIVPR_dime   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:2]HIVPR_dime   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:3]HIVPR_dime   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:4]HIVPR_dime   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:5]HIVPR_dime   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
                               **************************************************
```

```
                            51        .         .         .         .         100

                           101        .         .         .         .         150
[Truncated_Name:1]HIVPR_dime   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:2]HIVPR_dime   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:3]HIVPR_dime   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:4]HIVPR_dime   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:5]HIVPR_dime   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
                               **************************************************
                           101        .         .         .         .         150

                           151        .         .         .         .       198
[Truncated_Name:1]HIVPR_dime   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:2]HIVPR_dime   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:3]HIVPR_dime   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:4]HIVPR_dime   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:5]HIVPR_dime   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
                               **************************************************
                           151        .         .         .         .       198

Call:
  pdbaln(files = pdb_files, fit = TRUE, exefile = "msa")

Class:
  pdbs, fasta

Alignment dimensions:
  5 sequence rows; 198 position columns (198 non-gap, 0 gap)

+ attr: xyz, resno, b, chain, id, ali, resid, sse, call
```

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

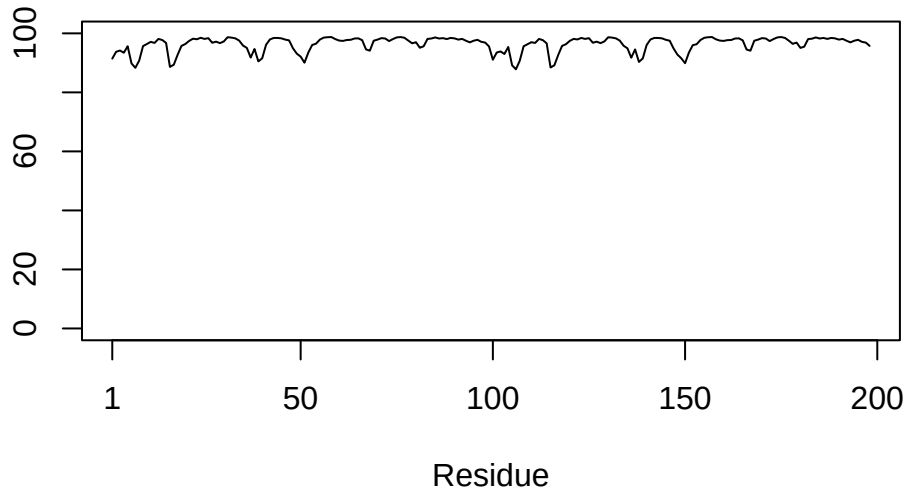
```
  Note: Accessing on-line PDB file
```

```
m1 <- read.pdb(pdb_files[1])
m1
```

```

 Call:  read.pdb(file = pdb_files[1])
```

```
   Total Models#: 1
     Total Atoms#: 1514,  XYZs#: 4542  Chains#: 2  (values: A B)

     Protein Atoms#: 1514  (residues/Calpha atoms#: 198)
     Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)

     Non-protein/nucleic Atoms#: 0  (residues: 0)
     Non-protein/nucleic resid values: [ none ]

   Protein sequence:
      PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIGGFIKVRQYD
      QILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFPQITLWQRPLVTIKIGGQLKE
      ALLDTGADDTVLEEMSLPGRWKPKMIGGIGGFIKVRQYDQILIEICGHKAIGTVLVGPTP
      VNIIGRNLLTQIGCTLNF

+ attr: atom, xyz, calpha, call
```

```
plot.bio3d(m1$atom$b[m1$calpha], typ="l", ylim=c(0,100))
```



Residue conservation from alignment file

Find the large AlphaFold alignment file

```
aln_file <- list.files(path=results_dir,
                       pattern=".a3m$",
                        full.names = TRUE)
aln_file
```

```
[1] "HIVPR_dimer_23119/HIVPR_dimer_23119.a3m"
```

Read this into R

```
aln <- read.fasta(aln_file[1], to.upper = TRUE)
```

```
[1] " ** Duplicated sequence id's: 101 **"
[2] " ** Duplicated sequence id's: 101 **"
```

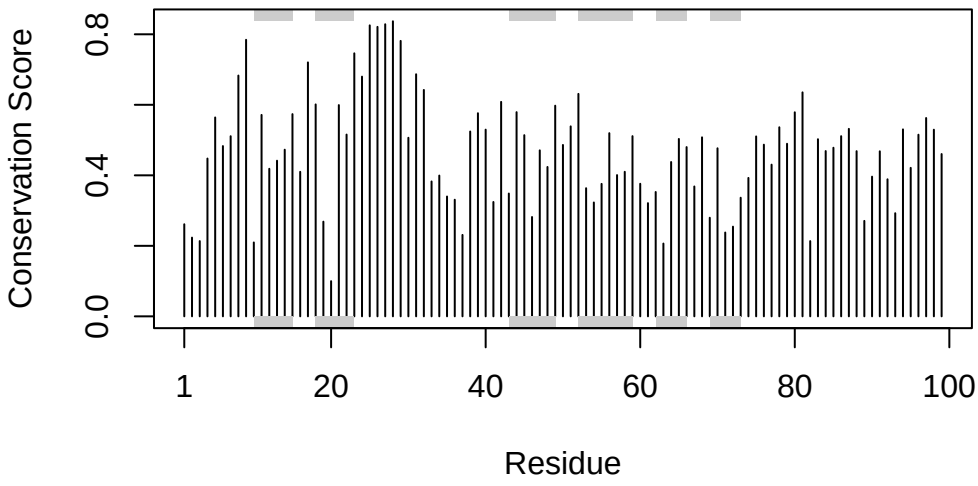
How many sequences are in this alignment

```
dim(aln$ali)
```

```
[1] 5397  132
```

We can score residue conservation in the alignment with the `conserv()` function.

```
sim <- conserv(aln)

plotb3(sim[1:99], sse=trim.pdb(pdb, chain="A"),
       ylab="Conservation Score")
```


Conservation Score
0.0
0.4
0.8
1
20
40
60
80
100
Residue