Class 09: Structural Bioinformatics Part 1

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

```
PDB_file <- "Data Export Summary.csv"

PDB = read.csv(PDB_file, row.names=1)
head(PDB)
```

```
                         X.ray     EM    NMR Multiple.methods
Neutron Other
Protein (only)         167,317 15,698 12,534              208
77    32
Protein/Oligosaccharide   9,645  2,639     34                8
2     0
Protein/NA                8,735  4,718    286                7
0     0
Nucleic acid (only)       2,869    138  1,507               14
3     1
Other                       170     10     33                0
0     0
Oligosaccharide (only)       11      0      6                1
0     4
                         Total
Protein (only)         195,866
Protein/Oligosaccharide  12,328
Protein/NA               13,746
Nucleic acid (only)       4,532
Other                       213
Oligosaccharide (only)       22
```

> Q1: What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy. A. 93.49072

```
library(dplyr)
```

```
Attaching package: 'dplyr'

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

    filter, lag

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

    intersect, setdiff, setequal, union
```

```
# Clean numeric columns by removing commas
PDB <- PDB %>%
  mutate(across(c(X.ray, EM, NMR, Multiple.methods, Neutron, Ot
                ~ as.numeric(gsub(",", "", .))))

# Sum the X-ray and Electron Microscopy and Total values
total_xray <- sum(PDB$X.ray, na.rm = TRUE)
total_em <- sum(PDB$EM, na.rm = TRUE)
total <- sum(PDB$Total, na.rm = TRUE)

# Print the Total Percent of Structures by EM and Xray
Percent_EM_Xray <- ((total_em + total_xray)/ total) * 100
Percent_EM_Xray
```

```
[1] 93.49072
```

> Q2: What proportion of structures in the PDB are protein? A. 86.3961% of structures are Protein (only). However there are more strucutres with Protein/Oligosaccharide and Protein/NA and this accounts for 97.89729%.

```
Protein_only <- PDB$Total[1]
Proportion_protein_only <- Protein_only/total * 100
Proportion_protein_only
```

```
[1] 86.3961
```

```
Protein_oligos <- PDB$Total[2]
```

```
Protein_na <- PDB$Total[3]
Proportion_all_protein <- (Protein_only + Protein_oligos + Prot
Proportion_all_protein
```

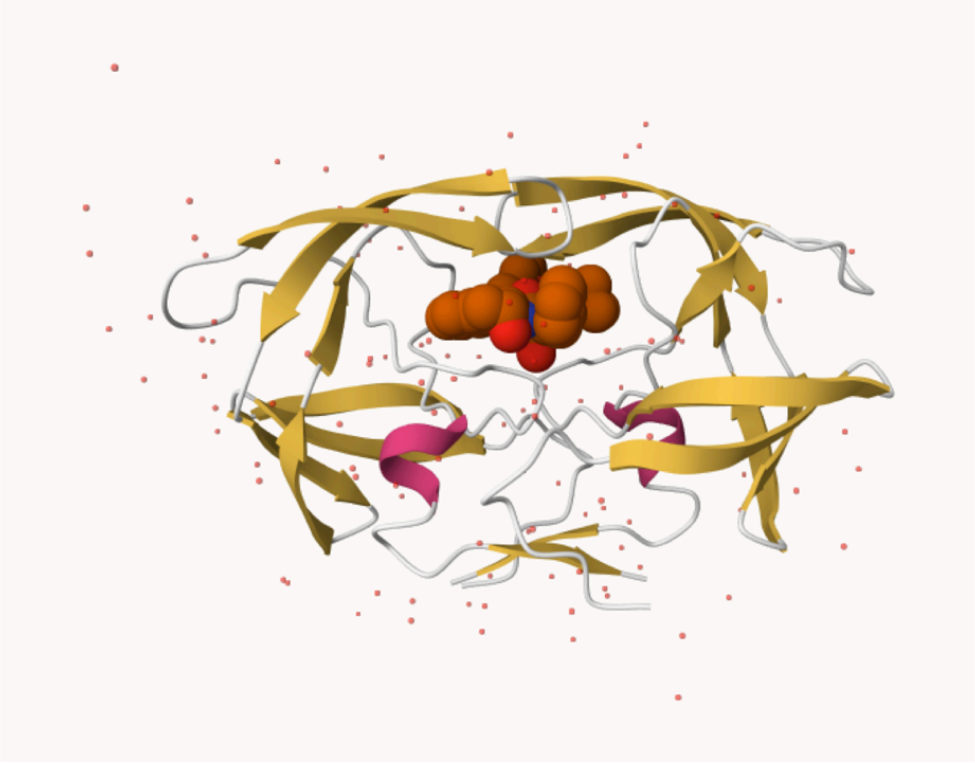
```
[1] 97.89729
```

> 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? A. This query matches 4,563 Structures in HIV search.

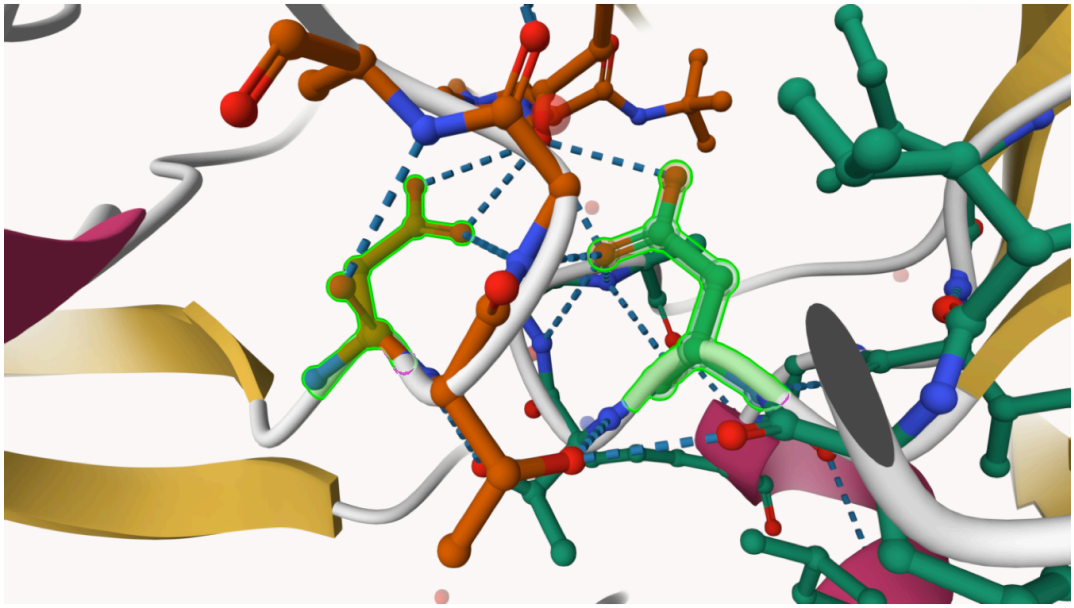
2. Visualizing the HIV-1 protease structure

#Using Mol*

```
library(grid)

img <- rasterGrob(png::readPNG("1HSG.png"), interpolate=TRUE)
grid.newpage()
grid.draw(img)
```



```
img2 <- rasterGrob(png::readPNG("1HSG-3.png"), interpolate=TRUE
grid.newpage()
grid.draw(img2)
```



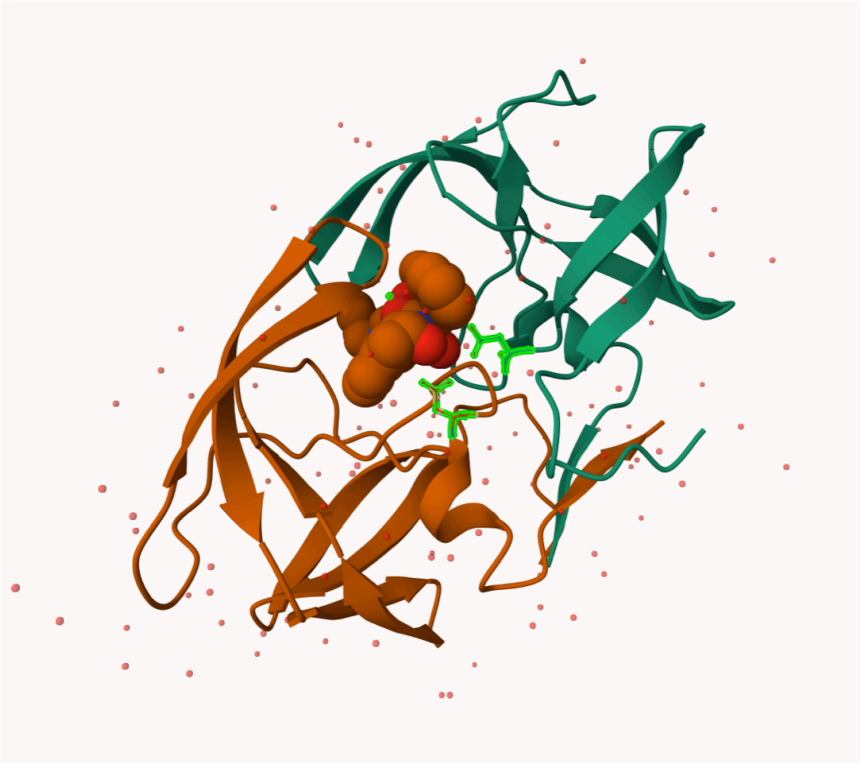
> Q4: Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure? A. In this strucutre we only see the Oxygen atom from the water, which is what makes the binding.

> 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 A. HOH 308

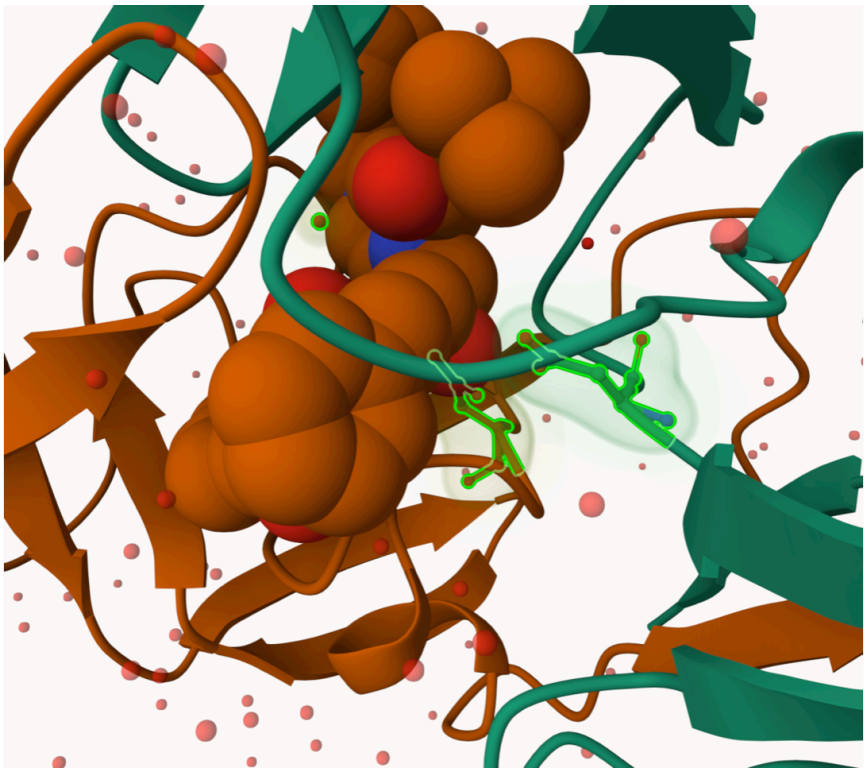
> Q6. Generate and save a figure clearly showing the two distinct chains of HIV-protease along with the ligand. You might also consider showing the catalytic residues ASP 25 in each chain and the critical water (we recommend “Ball & Stick” for these side-chains). Add this figure to your Quarto document.

```
img3 <- rasterGrob(png::readPNG("1HSG-4.png"), interpolate=TRUE
```

```
grid.newpage()
grid.draw(img3)
```



```
img4 <- rasterGrob(png::readPNG("1HSG-5.png"), interpolate=TRUE
grid.newpage()
grid.draw(img4)
```



Introduction to bio3D in R

```
library(bio3d)
```

```
Warning: package 'bio3d' was built under R version 4.3.3
```

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

```
 Call:  read.pdb(file = "1hsg.pdb")

   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? A. 198 amino acid residues. Q8: Name one of the two non-protein residues? A. HOH Q9: How many protein chains are in this structure? A. There are 2 chains.

```
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>
```

Predicting functional motions of a single structure

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

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

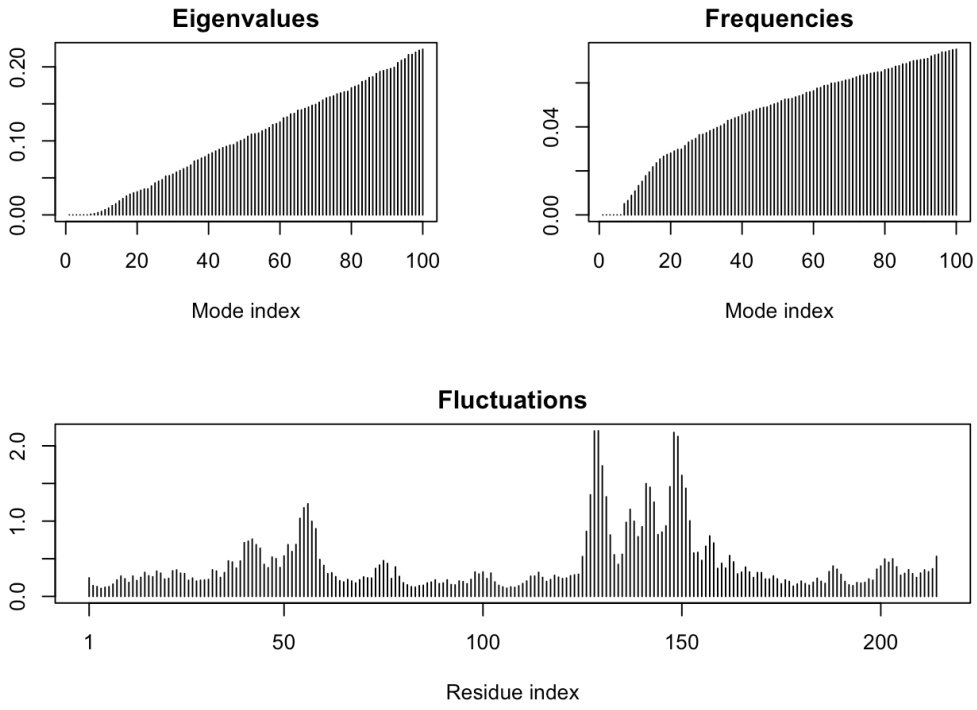
```
adk
```

```
 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
```

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

```
Building Hessian...     Done in 0.022 seconds.
Diagonalizing Hessian...   Done in 0.451 seconds.
```

```
plot(m)
```




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

4. Comparative structure analysis of Adenylate Kinase

```
# Install packages in the R console NOT your Rmd/Quarto file

#install.packages("bio3d")
#install.packages("devtools")
#install.packages("BiocManager")

#BiocManager::install("msa")
```

```
#devtools::install_bitbucket("Grantlab/bio3d-view")
```

> Q10. Which of the packages above is found only on BioConductor and not CRAN? A. The package msa is found only on BioConductor and not on CRAN

> Q11. Which of the above packages is not found on BioConductor or CRAN?: A. The package bio3d-view is not found on BioConductor or CRAN; it is available through BitBucket.

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

Search and retrieve ADK structures

```
library(bio3d)
aa <- get.seq("1ake_A")
```

```
Warning in get.seq("1ake_A"): Removing existing file:
seqs.fasta

Fetching... Please wait. Done.
```

```
aa
```

```
            1        .        .        .        .
.         60
pdb|1AKE|A
MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
            1        .        .        .        .
.         60

           61        .        .        .        .
.        120
pdb|1AKE|A
DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDRI
           61        .        .        .        .
.        120

          121        .        .        .        .
```

```
.         180
pdb|1AKE|A
VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
           121       .         .         .         .
.         180

           181       .         .         .   214
pdb|1AKE|A   YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG
           181       .         .         .   214

Call:
  read.fasta(file = outfile)

Class:
  fasta

Alignment dimensions:
  1 sequence rows; 214 position columns (214 non-gap, 0 gap)

+ attr: id, ali, call
```

> Q13. How many amino acids are in this sequence, i.e. how long is this sequence? A. 214 amino acids.

```
# Blast or hmmer search
#b <- blast.pdb(aa)
```

```
# Plot a summary of search results
#hits <- plot(b)
```

```
# List out some 'top hits'
#head(hits$pdb.id)
```

```
hits <- NULL
hits$pdb.id <- c('1AKE_A','6S36_A','6RZE_A','3HPR_A','1E4V_A','
# Download related PDB files
files <- get.pdb(hits$pdb.id, path="pdbs", split=TRUE, gzip=TRU
```

```
Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/1AKE.pdb.gz exists. Skipping download
```

```
Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/6S36.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/6RZE.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/3HPR.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/1E4V.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/5EJE.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/1E4Y.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/3X2S.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/6HAP.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/6HAM.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/4K46.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
gzip = TRUE):
pdbs/3GMT.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE,
```

```
gzip = TRUE):
pdbs/4PZL.pdb.gz exists. Skipping download


  |
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|   0%
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|  77%
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|  85%
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  |
```
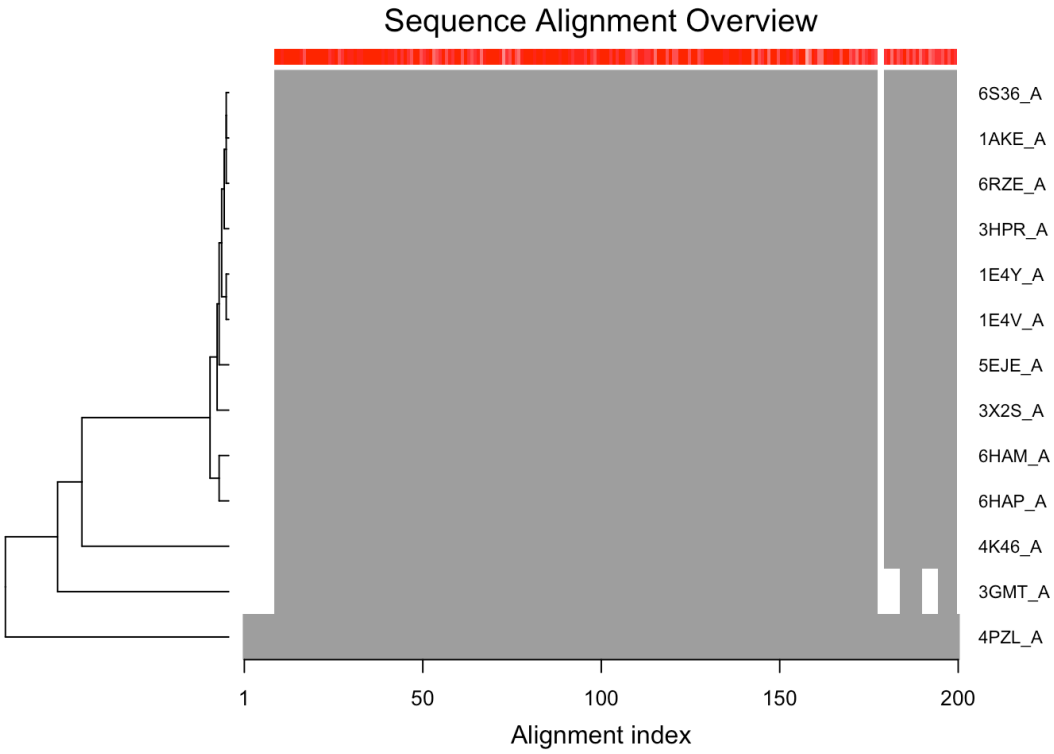

```
|=============================================================
=========| 100%
```

```
# Align releated PDBs
pdbs <- pdbaln(files, fit = TRUE, exefile="msa")
```

```
Reading PDB files:
pdbs/split_chain/1AKE_A.pdb
pdbs/split_chain/6S36_A.pdb
pdbs/split_chain/6RZE_A.pdb
pdbs/split_chain/3HPR_A.pdb
pdbs/split_chain/1E4V_A.pdb
pdbs/split_chain/5EJE_A.pdb
pdbs/split_chain/1E4Y_A.pdb
pdbs/split_chain/3X2S_A.pdb
pdbs/split_chain/6HAP_A.pdb
pdbs/split_chain/6HAM_A.pdb
pdbs/split_chain/4K46_A.pdb
pdbs/split_chain/3GMT_A.pdb
pdbs/split_chain/4PZL_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
..   PDB has ALT records, taking A only, rm.alt=TRUE
....   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
...

Extracting sequences

pdb/seq: 1   name: pdbs/split_chain/1AKE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 2   name: pdbs/split_chain/6S36_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 3   name: pdbs/split_chain/6RZE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 4   name: pdbs/split_chain/3HPR_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 5   name: pdbs/split_chain/1E4V_A.pdb
pdb/seq: 6   name: pdbs/split_chain/5EJE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 7   name: pdbs/split_chain/1E4Y_A.pdb
```

```
pdb/seq: 8   name: pdbs/split_chain/3X2S_A.pdb
pdb/seq: 9   name: pdbs/split_chain/6HAP_A.pdb
pdb/seq: 10   name: pdbs/split_chain/6HAM_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 11   name: pdbs/split_chain/4K46_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 12   name: pdbs/split_chain/3GMT_A.pdb
pdb/seq: 13   name: pdbs/split_chain/4PZL_A.pdb
```

```
# Vector containing PDB codes for figure axis
ids <- basename.pdb(pdbs$id)

# Draw schematic alignment
plot(pdbs, labels=ids)
```



Annotate collected PDB Structures

```
anno <- pdb.annotate(ids)
unique(anno$source)
```

```
[1] "Escherichia coli"
```

```
[2] "Escherichia coli K-12"
[3] "Escherichia coli O139:H28 str. E24377A"
[4] "Escherichia coli str. K-12 substr. MDS42"
[5] "Photobacterium profundum"
[6] "Burkholderia pseudomallei 1710b"
[7] "Francisella tularensis subsp. tularensis SCHU S4"
```

```
#We can view all available annotation data:
anno
```

```
       structureId chainId macromoleculeType chainLength
experimentalTechnique
1AKE_A        1AKE       A           Protein         214
X-ray
6S36_A        6S36       A           Protein         214
X-ray
6RZE_A        6RZE       A           Protein         214
X-ray
3HPR_A        3HPR       A           Protein         214
X-ray
1E4V_A        1E4V       A           Protein         214
X-ray
5EJE_A        5EJE       A           Protein         214
X-ray
1E4Y_A        1E4Y       A           Protein         214
X-ray
3X2S_A        3X2S       A           Protein         214
X-ray
6HAP_A        6HAP       A           Protein         214
X-ray
6HAM_A        6HAM       A           Protein         214
X-ray
4K46_A        4K46       A           Protein         214
X-ray
3GMT_A        3GMT       A           Protein         230
X-ray
4PZL_A        4PZL       A           Protein         242
X-ray
       resolution       scopDomain
pfam
1AKE_A       2.00 Adenylate kinase Adenylate kinase, active
site lid (ADK_lid)
6S36_A       1.60             <NA> Adenylate kinase, active
site lid (ADK_lid)
```

```
6RZE_A       1.69             <NA>
Adenylate kinase (ADK)
3HPR_A       2.00             <NA> Adenylate kinase, active
site lid (ADK_lid)
1E4V_A       1.85 Adenylate kinase
Adenylate kinase (ADK)
5EJE_A       1.90             <NA> Adenylate kinase, active
site lid (ADK_lid)
1E4Y_A       1.85 Adenylate kinase Adenylate kinase, active
site lid (ADK_lid)
3X2S_A       2.80             <NA>
Adenylate kinase (ADK)
6HAP_A       2.70             <NA>
Adenylate kinase (ADK)
6HAM_A       2.55             <NA> Adenylate kinase, active
site lid (ADK_lid)
4K46_A       2.01             <NA> Adenylate kinase, active
site lid (ADK_lid)
3GMT_A       2.10             <NA> Adenylate kinase, active
site lid (ADK_lid)
4PZL_A       2.10             <NA>
Adenylate kinase (ADK)
               ligandId
1AKE_A              AP5
6S36_A CL (3),NA,MG (2)
6RZE_A    NA (3),CL (2)
3HPR_A              AP5
1E4V_A              AP5
5EJE_A           AP5,CO
1E4Y_A              AP5
3X2S_A   JPY (2),AP5,MG
6HAP_A              AP5
6HAM_A              AP5
4K46_A      ADP,AMP,PO4
3GMT_A          SO4 (2)
4PZL_A       CA,FMT,GOL

ligandName
1AKE_A
BIS(ADENOSINE)-5'-PENTAPHOSPHATE
6S36_A                                    CHLORIDE ION
(3),SODIUM ION,MAGNESIUM ION (2)
6RZE_A                                                 SODIUM
ION (3),CHLORIDE ION (2)
3HPR_A
```

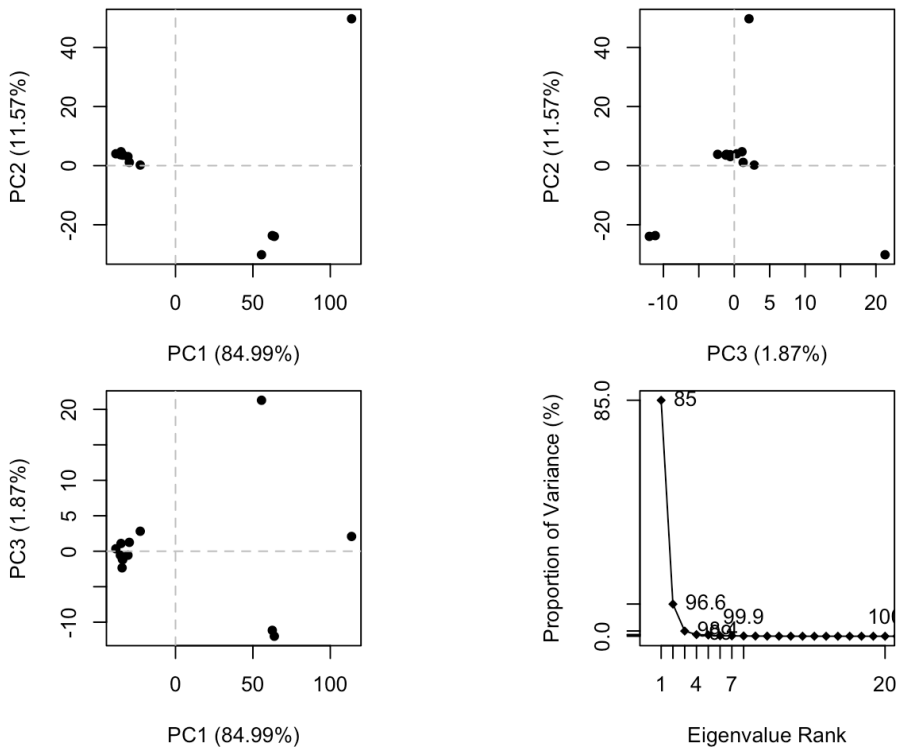
```
BIS(ADENOSINE)-5'-PENTAPHOSPHATE
1E4V_A
BIS(ADENOSINE)-5'-PENTAPHOSPHATE
5EJE_A                                  BIS(ADENOSINE)-5'-
PENTAPHOSPHATE,COBALT (II) ION
1E4Y_A
BIS(ADENOSINE)-5'-PENTAPHOSPHATE
3X2S_A N-(pyren-1-ylmethyl)acetamide (2),BIS(ADENOSINE)-5'-
PENTAPHOSPHATE,MAGNESIUM ION
6HAP_A
BIS(ADENOSINE)-5'-PENTAPHOSPHATE
6HAM_A
BIS(ADENOSINE)-5'-PENTAPHOSPHATE
4K46_A                    ADENOSINE-5'-DIPHOSPHATE,ADENOSINE
MONOPHOSPHATE,PHOSPHATE ION
3GMT_A
SULFATE ION (2)
4PZL_A                                                    CALCIUM
ION,FORMIC ACID,GLYCEROL
                                                    source
1AKE_A                                  Escherichia coli
6S36_A                                  Escherichia coli
6RZE_A                                  Escherichia coli
3HPR_A                               Escherichia coli K-12
1E4V_A                                  Escherichia coli
5EJE_A            Escherichia coli O139:H28 str. E24377A
1E4Y_A                                  Escherichia coli
3X2S_A          Escherichia coli str. K-12 substr. MDS42
6HAP_A            Escherichia coli O139:H28 str. E24377A
6HAM_A                               Escherichia coli K-12
4K46_A                           Photobacterium profundum
3GMT_A                    Burkholderia pseudomallei 1710b
4PZL_A Francisella tularensis subsp. tularensis SCHU S4

structureTitle
1AKE_A STRUCTURE OF THE COMPLEX BETWEEN ADENYLATE KINASE FROM
ESCHERICHIA COLI AND THE INHIBITOR AP5A REFINED AT 1.9
ANGSTROMS RESOLUTION: A MODEL FOR A CATALYTIC TRANSITION STATE
6S36_A
Crystal structure of E. coli Adenylate kinase R119K mutant
6RZE_A
Crystal structure of E. coli Adenylate kinase R119A mutant
3HPR_A
Crystal structure of V148G adenylate kinase from E. coli, in
complex with Ap5A
```

```
1E4V_A
Mutant G10V of adenylate kinase from E. coli, modified in the
Gly-loop
5EJE_A
Crystal structure of E. coli Adenylate kinase G56C/T163C
double mutant in complex with Ap5a
1E4Y_A
Mutant P9L of adenylate kinase from E. coli, modified in the
Gly-loop
3X2S_A
Crystal structure of pyrene-conjugated adenylate kinase
6HAP_A
Adenylate kinase
6HAM_A
Adenylate kinase
4K46_A
Crystal Structure of Adenylate Kinase from Photobacterium
profundum
3GMT_A
Crystal structure of adenylate kinase from burkholderia
pseudomallei
4PZL_A
The crystal structure of adenylate kinase from Francisella
tularensis subsp. tularensis SCHU S4
                                                        citation
rObserved   rFree
1AKE_A                Muller, C.W., et al. J Mol Biol (1992)
0.19600      NA
6S36_A                 Rogne, P., et al. Biochemistry (2019)
0.16320 0.23560
6RZE_A                 Rogne, P., et al. Biochemistry (2019)
0.18650 0.23500
3HPR_A  Schrank, T.P., et al. Proc Natl Acad Sci U S A (2009)
0.21000 0.24320
1E4V_A                  Muller, C.W., et al. Proteins (1993)
0.19600      NA
5EJE_A  Kovermann, M., et al. Proc Natl Acad Sci U S A (2017)
0.18890 0.23580
1E4Y_A                  Muller, C.W., et al. Proteins (1993)
0.17800      NA
3X2S_A               Fujii, A., et al. Bioconjug Chem (2015)
0.20700 0.25600
6HAP_A              Kantaev, R., et al. J Phys Chem B (2018)
0.22630 0.27760
6HAM_A              Kantaev, R., et al. J Phys Chem B (2018)
```

```
0.20511 0.24325
4K46_A                    Cho, Y.-J., et al. To be published
0.17000 0.22290
3GMT_A Buchko, G.W., et al. Biochem Biophys Res Commun (2010)
0.23800 0.29500
4PZL_A                       Tan, K., et al. To be published
0.19360 0.23680
         rWork spaceGroup
1AKE_A 0.19600  P 21 2 21
6S36_A 0.15940    C 1 2 1
6RZE_A 0.18190    C 1 2 1
3HPR_A 0.20620  P 21 21 2
1E4V_A 0.19600  P 21 2 21
5EJE_A 0.18630  P 21 2 21
1E4Y_A 0.17800   P 1 21 1
3X2S_A 0.20700 P 21 21 21
6HAP_A 0.22370    I 2 2 2
6HAM_A 0.20311       P 43
4K46_A 0.16730 P 21 21 21
3GMT_A 0.23500   P 1 21 1
4PZL_A 0.19130       P 32
```

#Principal component analysis

```
# Perform PCA
pc.xray <- pca(pdbs)
plot(pc.xray)
```

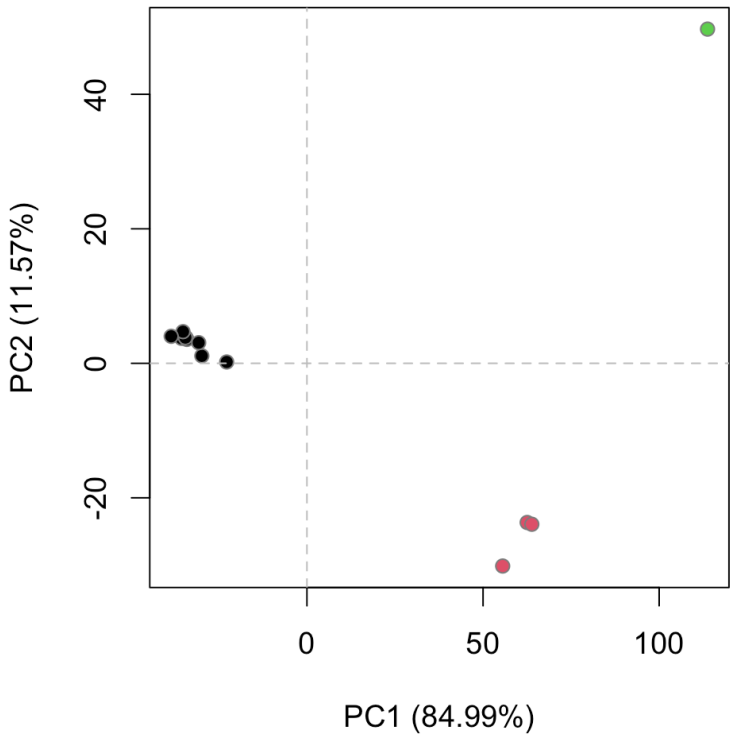


#clustering analysis based on the pairwise structural deviation

```
# Calculate RMSD
rd <- rmsd(pdbs)
```

```
Warning in rmsd(pdbs): No indices provided, using the 204 non
NA positions
```

```
# Structure-based clustering
hc.rd <- hclust(dist(rd))
grps.rd <- cutree(hc.rd, k=3)

plot(pc.xray, 1:2, col="grey50", bg=grps.rd, pch=21, cex=1)
```



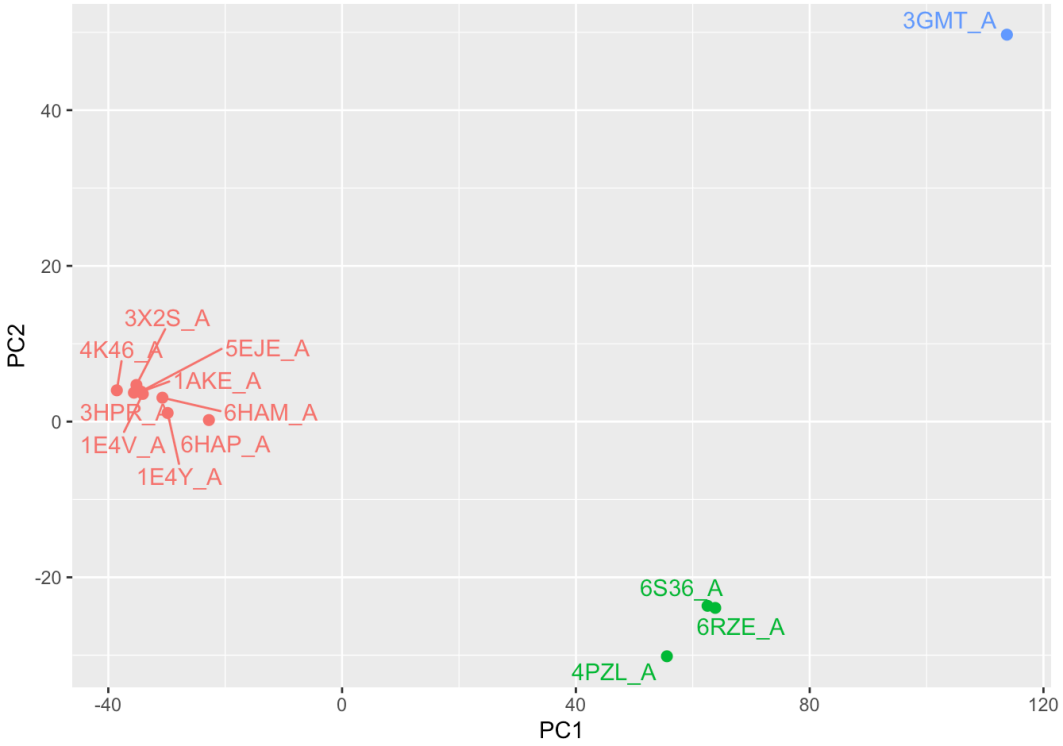
5. Optional further visualization

```
# Visualize first principal component
pc1 <- mktrj(pc.xray, pc=1, file="pc_1.pdb")
```

We can also plot our main PCA results with ggplot:

```
#Plotting results with ggplot2
library(ggplot2)
library(ggrepel)

df <- data.frame(PC1=pc.xray$z[,1],
                 PC2=pc.xray$z[,2],
                 col=as.factor(grps.rd),
                 ids=ids)

p <- ggplot(df) +
  aes(PC1, PC2, col=col, label=ids) +
  geom_point(size=2) +
  geom_text_repel(max.overlaps = 20) +
  theme(legend.position = "none")
```

```
p
```



6. Normal mode analysis [optional]

```
# NMA of all structures
modes <- nma(pdbs)
```

```
Details of Scheduled Calculation:
  ... 13 input structures
  ... storing 606 eigenvectors for each structure
  ... dimension of x$U.subspace: ( 612x606x13 )
  ... coordinate superposition prior to NM calculation
  ... aligned eigenvectors (gap containing positions removed)
  ... estimated memory usage of final 'eNMA' object: 36.9 Mb


  |
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  |
```

```
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  |==============================================
|  69%
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|  77%
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|  85%
  |

|======================================================================
====     |  92%
  |

|======================================================================
=========| 100%
```
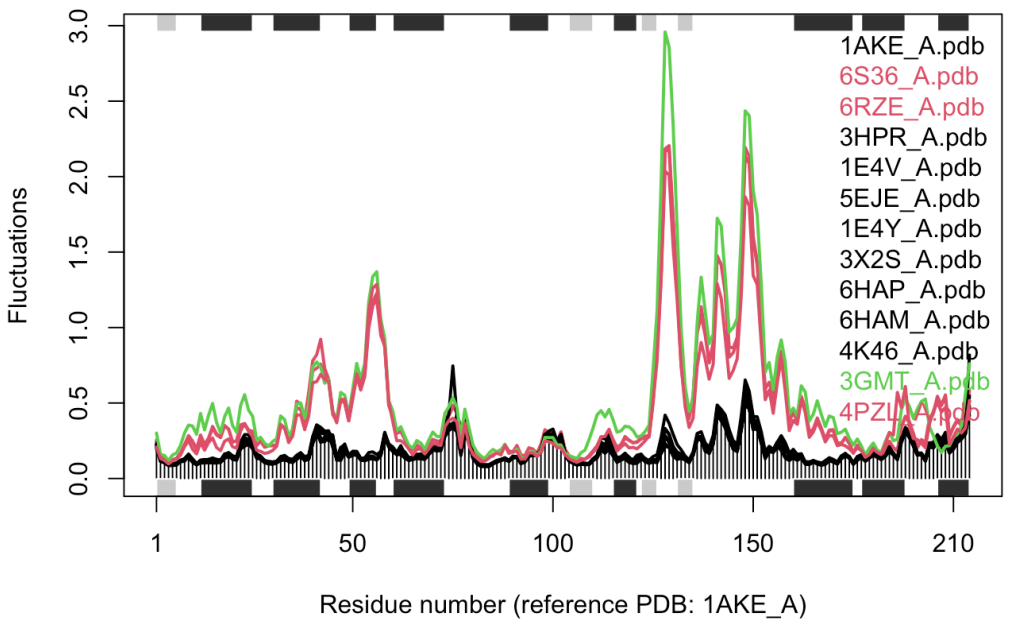

```
plot(modes, pdbs, col=grps.rd)
```

```
Extracting SSE from pdbs$sse attribute
```



> Q14. What do you note about this plot? Are the black and colored lines similar or different? Where do you think they differ most and why? A. The black and colored lines are different, they contain different peaks. They are two different structural conformations of Adk and differ by a collective low frequency displacement of two nucleotide-binding site regions that display distinct flexibilities upon nucleotide binding.