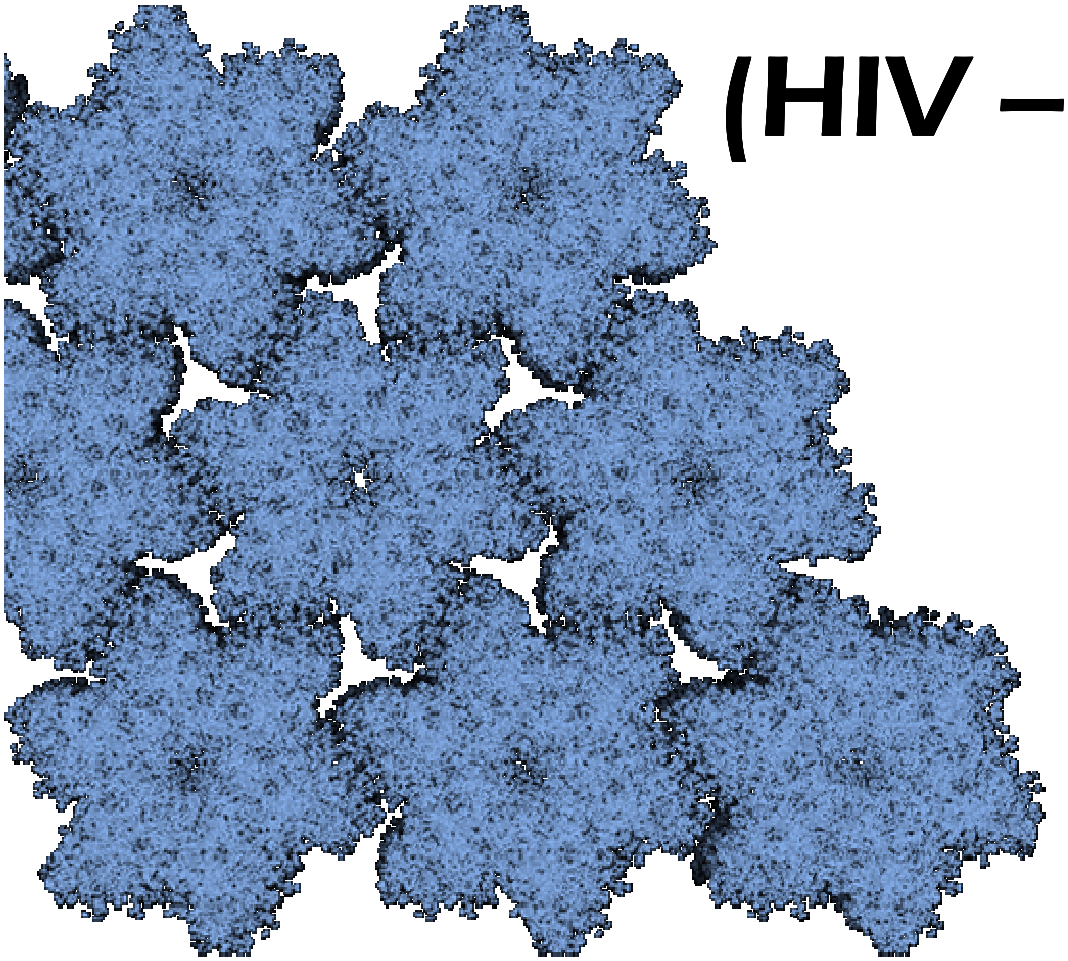
CAPSIDS OF VIRUSES

Human inmunodeficiency virus 1 (HIV – 1)



Irene Durán
Laura Gaspa
Alba Paula Navarro
Josep Mª Agustín

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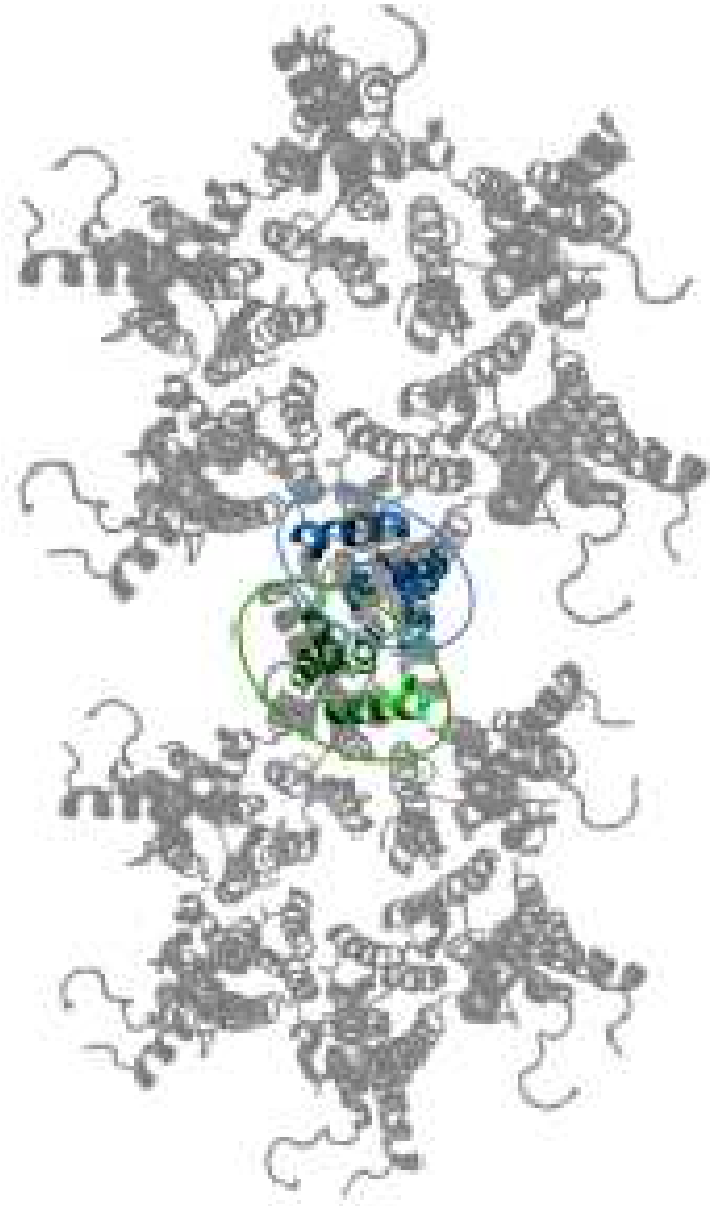


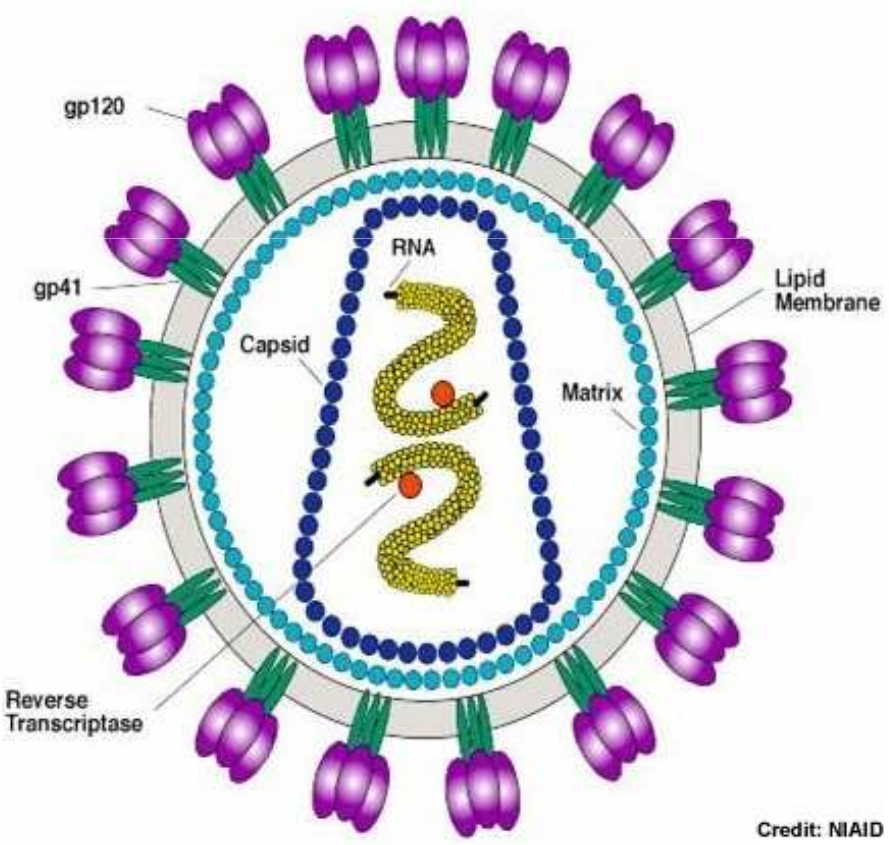
1.INTRODUCTION

Human Immunodeficiency virus -1 (HIV-1)

Family: Retroviridae
Genus: Lentivirus

Structure

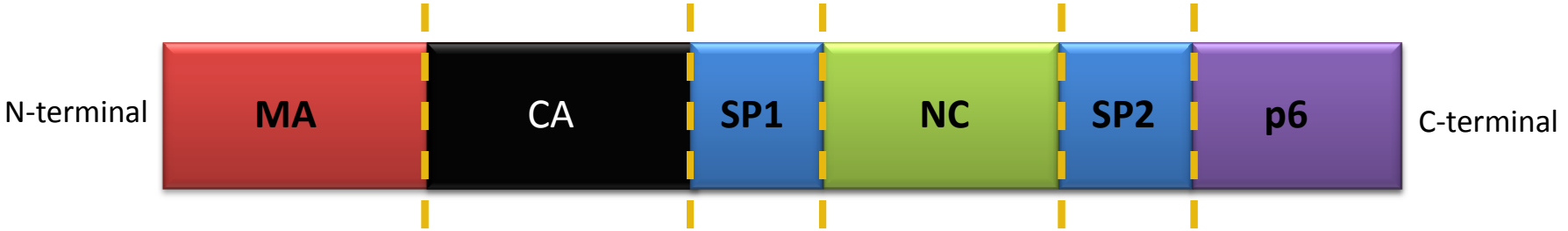
- ssRNA
- Nucleocapsid (p7)
- Capsid (p24)
- Matrix (p17)
- Envelope
  - Gp 120
  - Gp 41

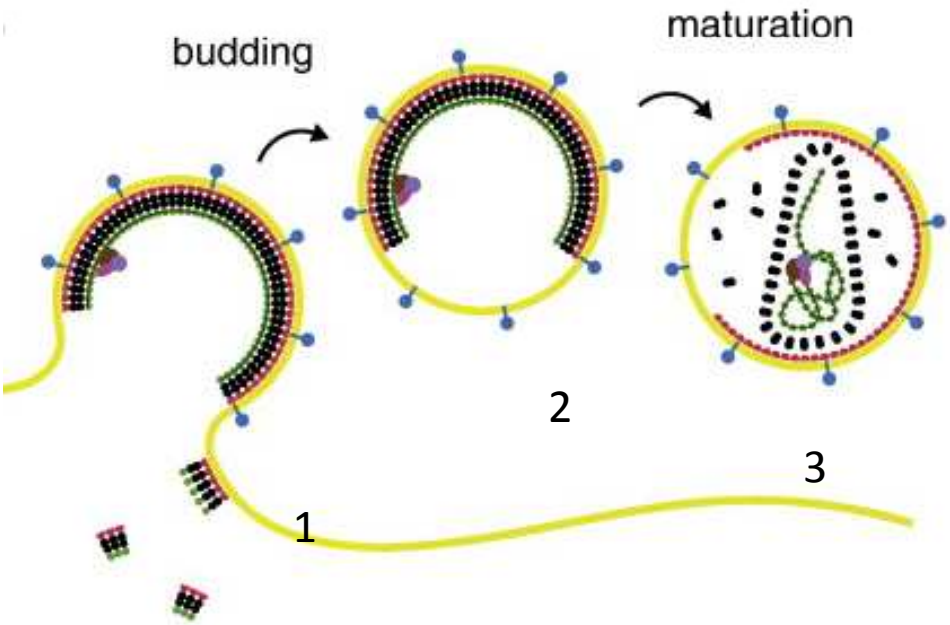


Infected cells
CD4+ T cells
Macrophages
Microglial cells

1.INTRODUCTION

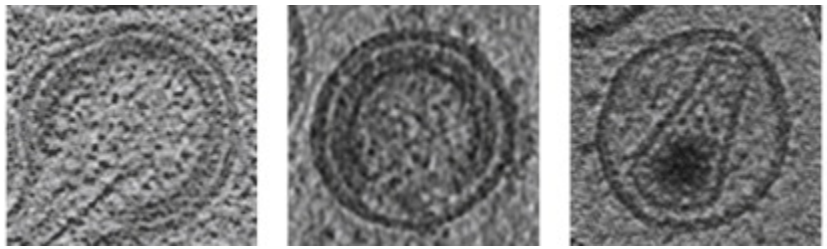
GAG POLYPROTEIN





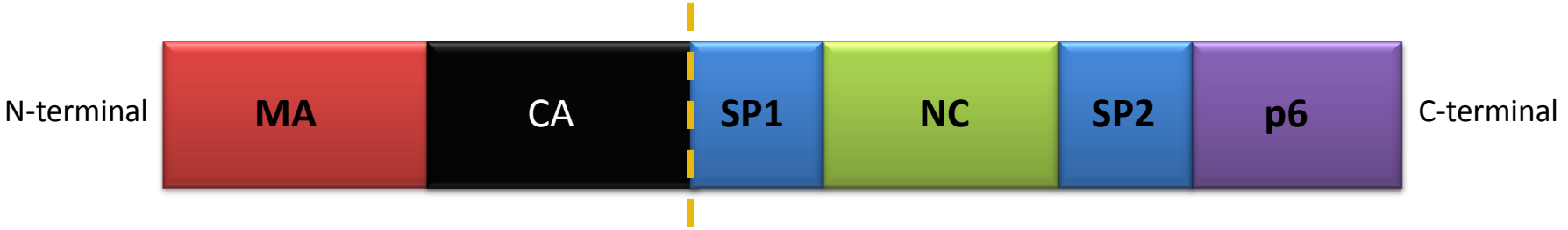
MA: Matrix
CA: Capsid
NC: Nucleocapside

1 - budding
2 – proteolytic maturation
3 – Mature CA formed



1.INTRODUCTION

“Protein structure prediction programs suggest that the last 7 residues of the CA domain and the first 7 residues of SP1 might form an α-helix”




```
# PSIPRED HFORMAT (PSIPRED V2.3 by David Jones)

Conf: 667765454217888766788778887634777532277403421457602478999999
Pred: HHHHHHHHHHCCCCCCCHHHHHHHHHHHHHHHHHHHCCCCEEEECCCCCCHHHHHHHHHH
  AA: STLQEQIAWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSILDIKQGPKEPFRDYVDRF
            250       260       270       280       290       300

Conf: 997423344478885422103530799867889974274246899998850478841567
Pred: HHHHHHHHHHHHHHHHHHHHEEEEECCCCCHHHHHHHCCCHHHHHHHHHHHHCCCCCHHHH
  AA: YKTLRAEQASQEVKNWMTETLLVQNSNPDCKTILKALGPAATLEEMMTACQGVGGPSHKA
            310       320       330       340       350       360

Conf: 889999876200002333157520112641121047766320014576100112304477
Pred: HHHHHHHHHHHCCCEEEECCCCCCHHCCCCEEEECCCCCCCCCCCCCCCCHHCHHHHCCCC
  AA: RILAEAMSQVTNSAAIMMQKGNFRKQRNSVKCFNCGKEGHVARNCRAPRKKGCWKCGKEG
            370       380       390       400       410       420
```

Confidence level	
Secondary structure	
CTD	SP1

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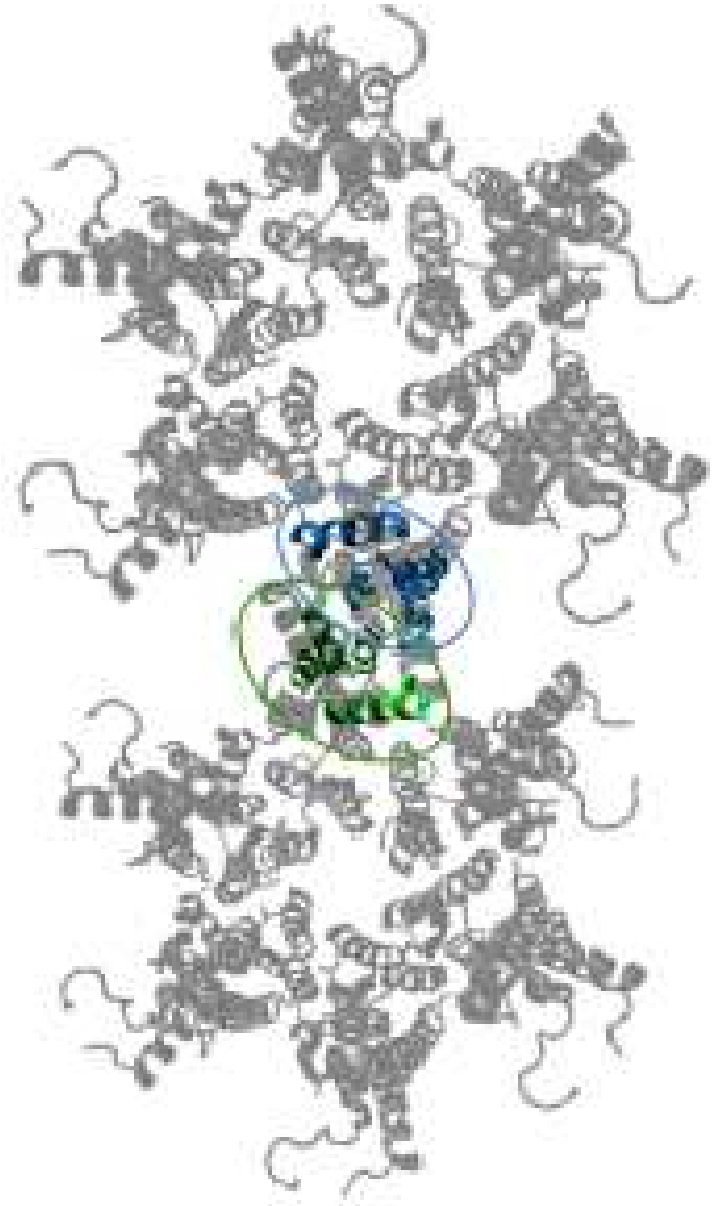
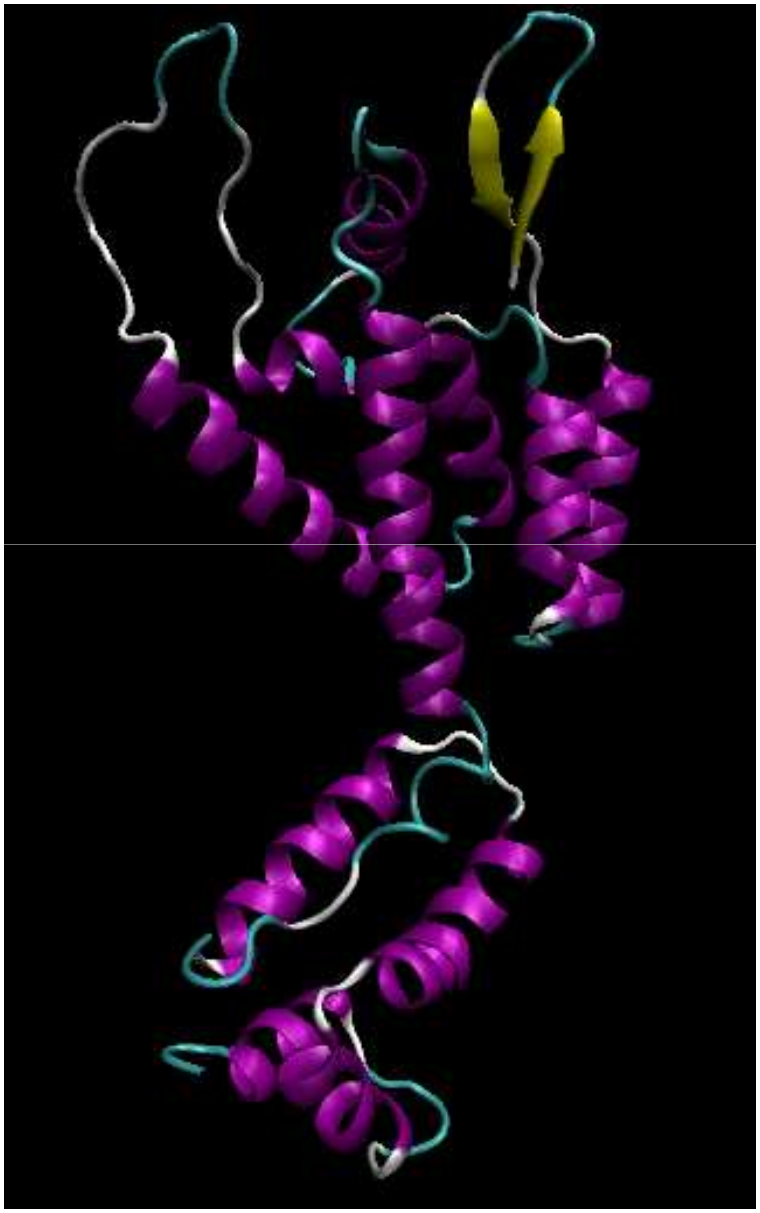


2.CA-MONOMER



2. CA-MONOMER

The two domains of CA belong to different superfamilies

NTD domain Superfamily: Retrovirus capsid protein, N-terminal core domain

1. Root: scop
2. Class: All alpha proteins [46456]
3. Fold: Retrovirus capsid protein, N-terminal core domain [47942]
   core: 5 helices; bundle
4. Superfamily: Retrovirus capsid protein, N-terminal core domain [47943]
   Superfamily
5. Family: Retrovirus capsid protein, N-terminal core domain [47944]

Protein Domains:

1. HIV-1 capsid protein [47945]
   1. Human immunodeficiency virus type 1 [TaxId: 11676] [47946] (16)
2. EIAV capsid protein p26 [47947]
   1. Equine infectious anemia virus [TaxId: 11665] [47948] (2)
3. HTLV-I capsid protein [47949]
   1. Human T-cell leukemia virus type 1 [TaxId: 11908] [47950] (2)
4. RSV capsid protein [47951]
   1. Rous sarcoma virus [TaxId: 11886] [47952] (3)
5. AKV capsid [116949]
   1. AKV murine leukemia virus [TaxId: 11791] [116950] (1)
      SQ P03336 215-345 # fragment of the core shell protein p30 (215-477)

CTD domain Superfamily: Retrovirus capsid dimerization domain-like

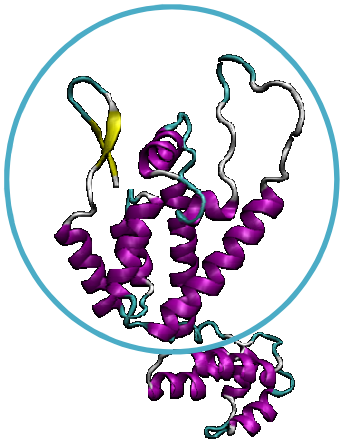
1. Root: scop
2. Class: All alpha proteins [46456]
3. Fold: Acyl carrier protein-like [47335]
   4 helices, bundle; helix 3 is shorter than others; up-and-down
4. Superfamily: Retrovirus capsid dimerization domain-like [47353]
   Superfamily
5. Family: Retrovirus capsid protein C-terminal domain [47354]

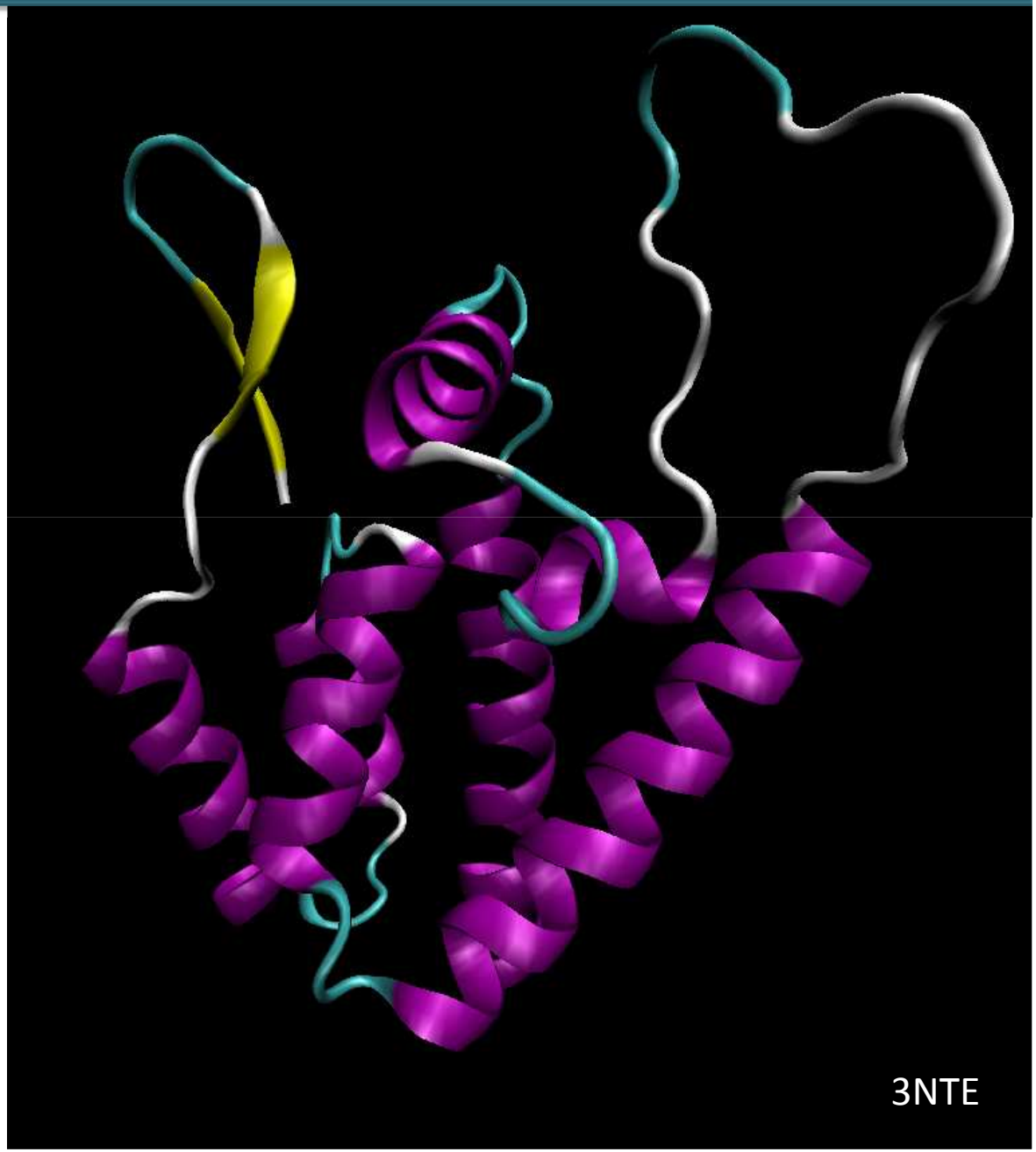
Protein Domains:

1. EIAV capsid protein p26 [47355]
   1. Equine infectious anemia virus [TaxId: 11665] [47356] (2)
2. HTLV-I capsid protein [47357]
   1. Human T-cell leukemia virus type 1 [TaxId: 11908] [47358] (1)
3. HIV capsid protein, dimerisation domain [47359]
   1. Human immunodeficiency virus type 1 [TaxId: 11676] [47360] (7)
4. RSV capsid protein [47361]
   1. Rous sarcoma virus [TaxId: 11886] [47362] (2)

2.1. NTD

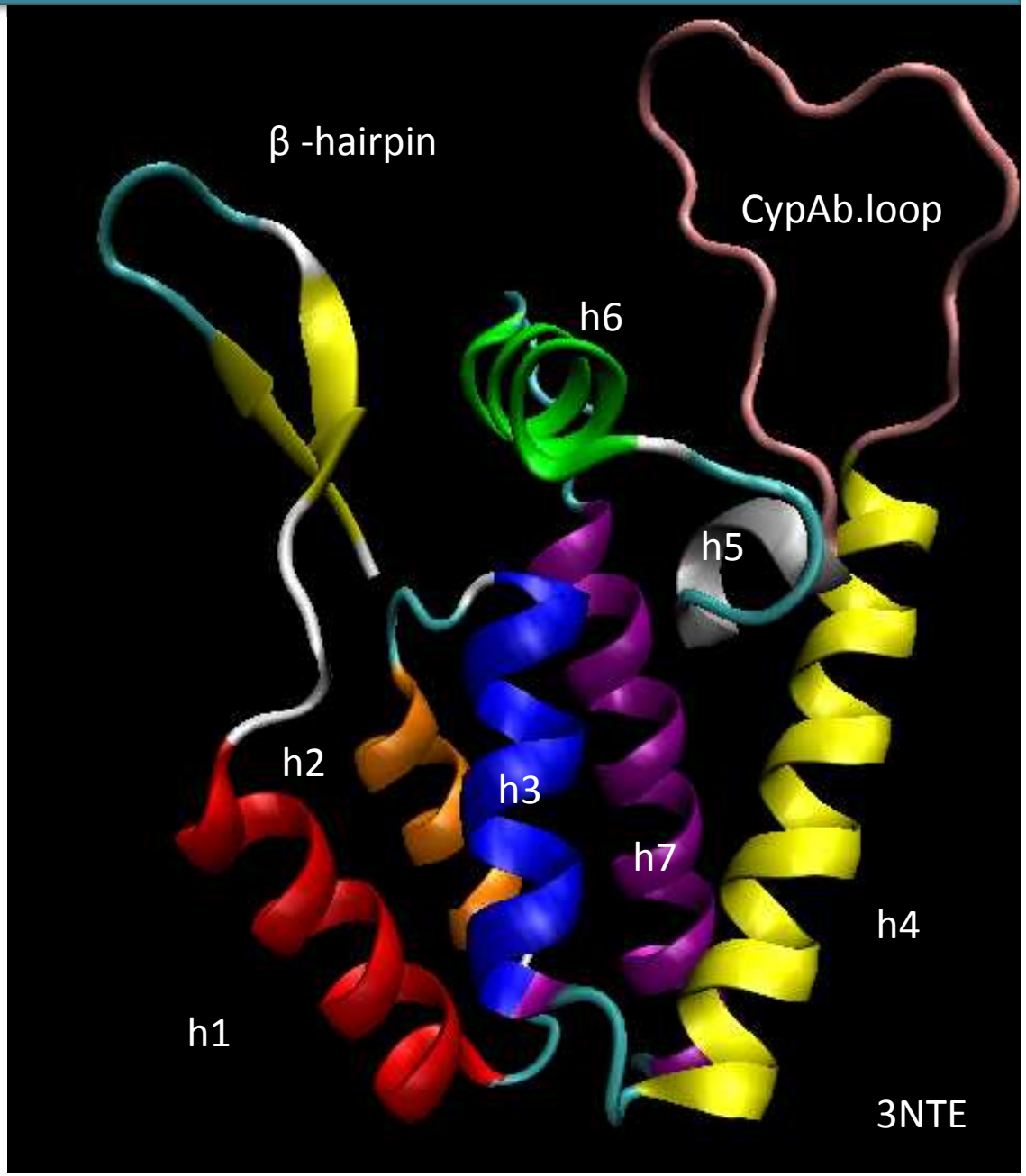
Residues: 1-146
Dimensions: 18x35x45 Å





2.1. NTD

β–hairpin	(1-13)
Helix 1	(17-29)
Helix2	(36-43)
Helix3	(49-58)
Helix4	(63-83)
CypAb.l.	(85-99)
Helix5	(101-104)
Helix6	(111-118)
Helix7	(126-145)



2.1. NTD

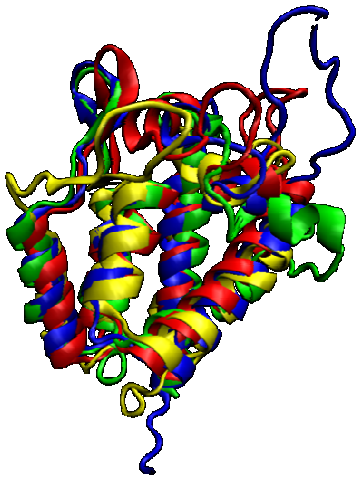
STAMP NTD superfamily

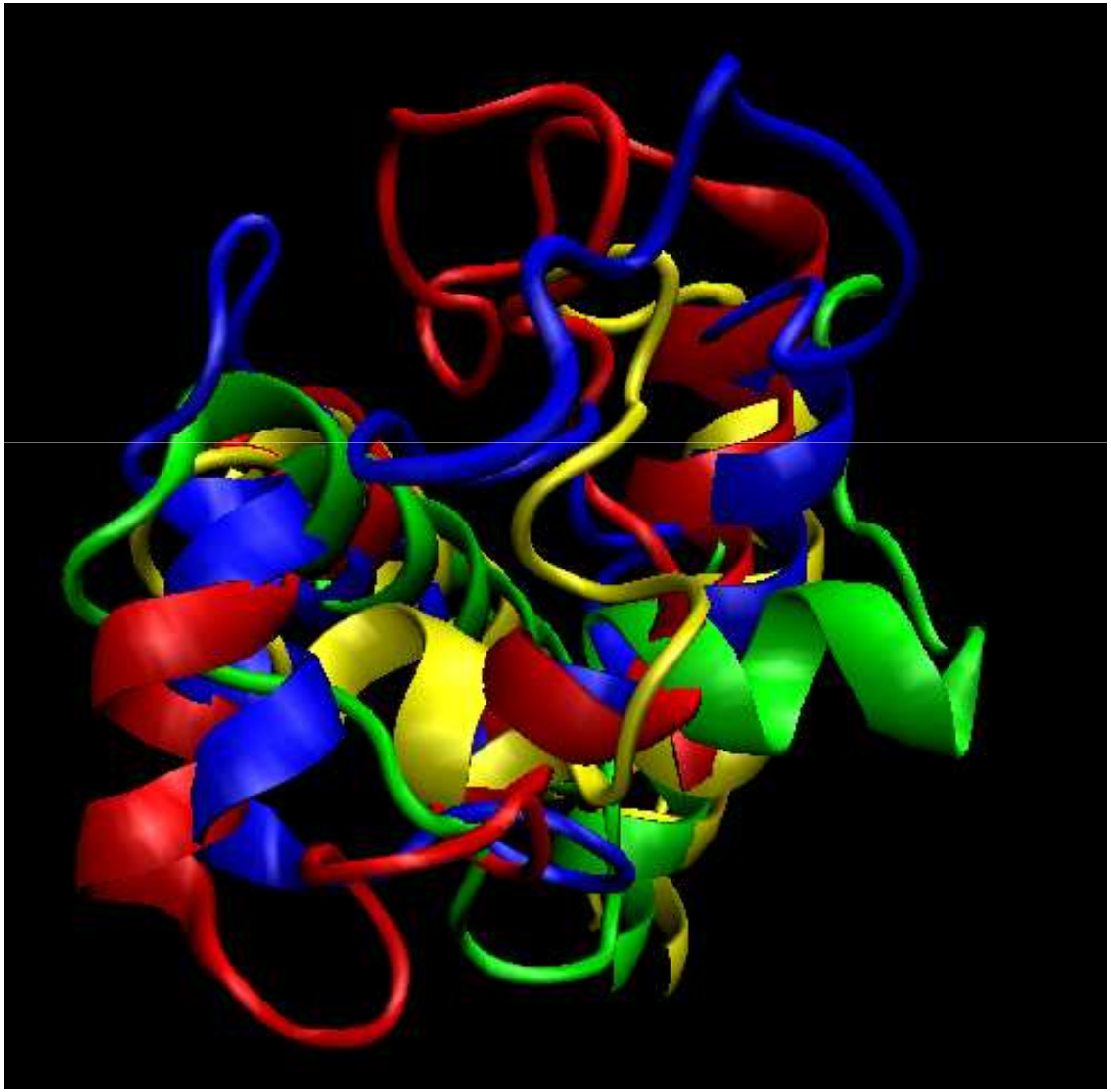
```
./1EM9.pdb 1EM9 ( ALL
   0.12363    -0.84230     0.52464          40.67896
  -0.95800     0.03656     0.28444          19.58468
  -0.25876    -0.53777    -0.80240          34.43766  )
./1G03.pdb 1G03 ( ALL
   0.84367    -0.50092     0.19312          22.12993
  -0.50440    -0.61644     0.60464           9.44606
  -0.18383    -0.60752    -0.77274          11.85248  )
./2Y4Z.pdb 2Y4Z ( ALL
   0.99515    -0.03853    -0.09047          -1.50927
   0.07430     0.89727     0.43520          -4.91943
   0.06441    -0.43981     0.89578           3.27455  )
./1GWP.pdb 1GWP ( ALL
  -0.61849    -0.72056    -0.31346          22.55360
  -0.76571     0.46303     0.44642          -0.78172
  -0.17653     0.51613    -0.83812          11.56435  )


Alignment score  Sc = 5.178694
Alignment length Lp = 335
RMS deviation after fitting on 86 atoms =  2.209671
Secondary structures are from DSSP
```

Blue: HIV-1
Green: MLV
Yellow: HTLV-1
Red: RSV

2.1. NTD



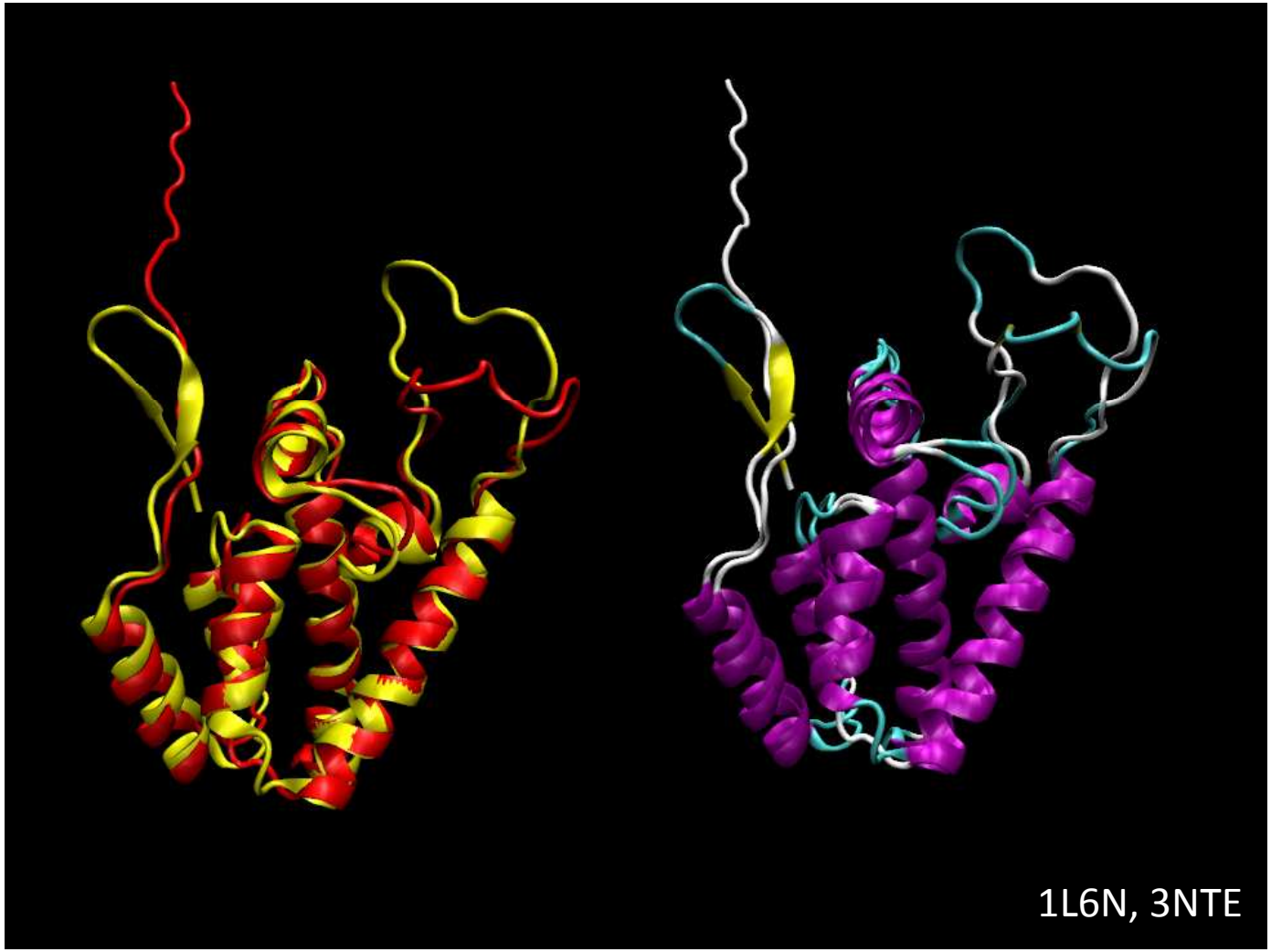


Why the region h4 to h6 is more flexible than the others?

No assembly interactions!!!!

2.1. NTD

STAMP MATURE vs IMMATURE NTD



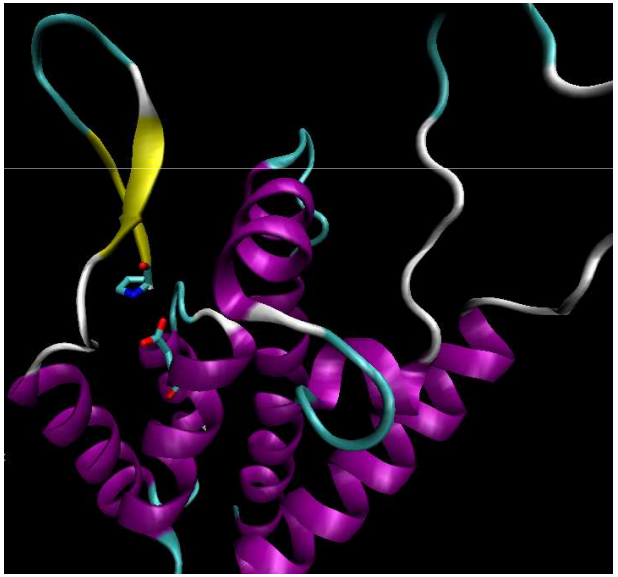
Red: immature
Yellow: mature

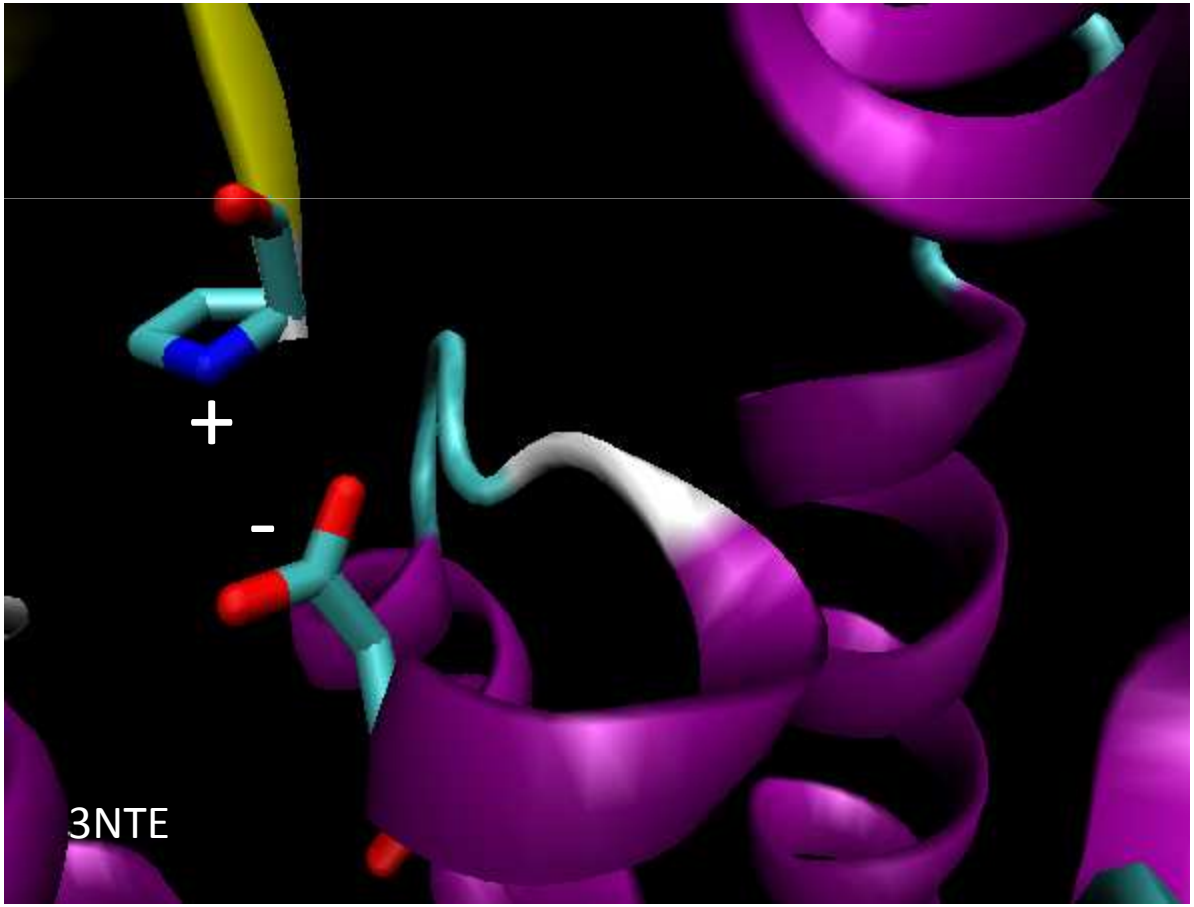
2.1. NTD

β-hairpin

Three types of interactions:
1. Salt bridge P1 – D51
2. Inter B-hairpin H-bonds
3. Interactions with surrounding strucutres

1. Salt bridge P1 – D51



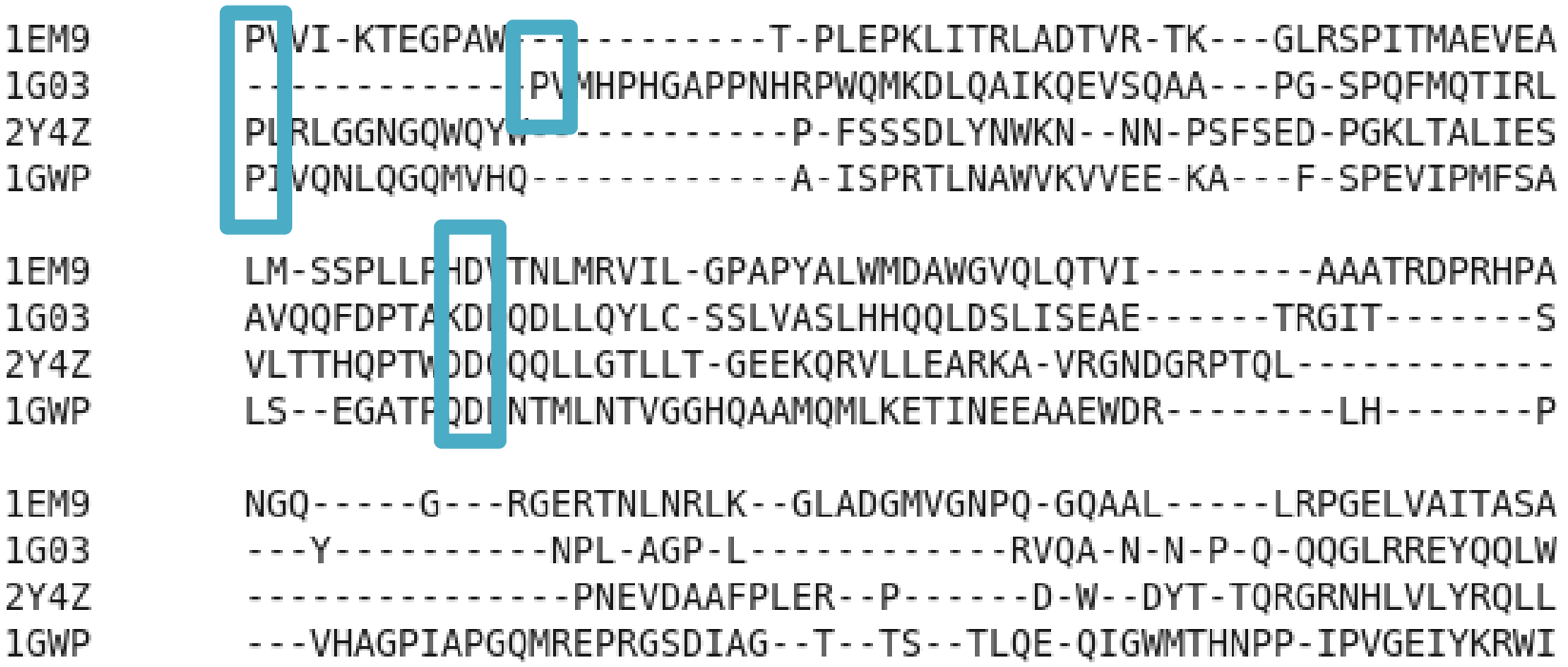


2.1. NTD

β-hairpin

Highlyght conserved P1 and D51 in the members of the superfamily

Structural alignment



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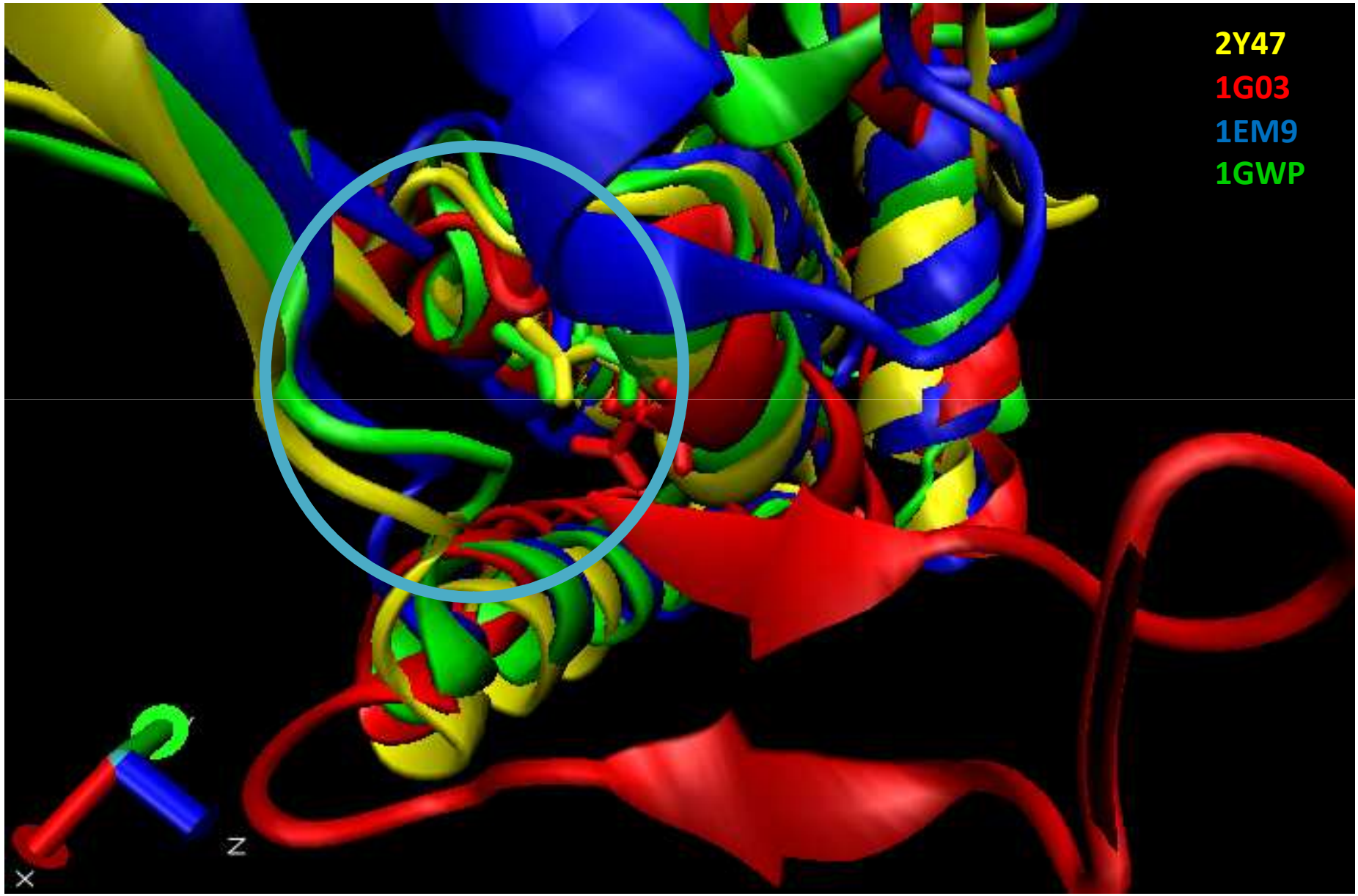

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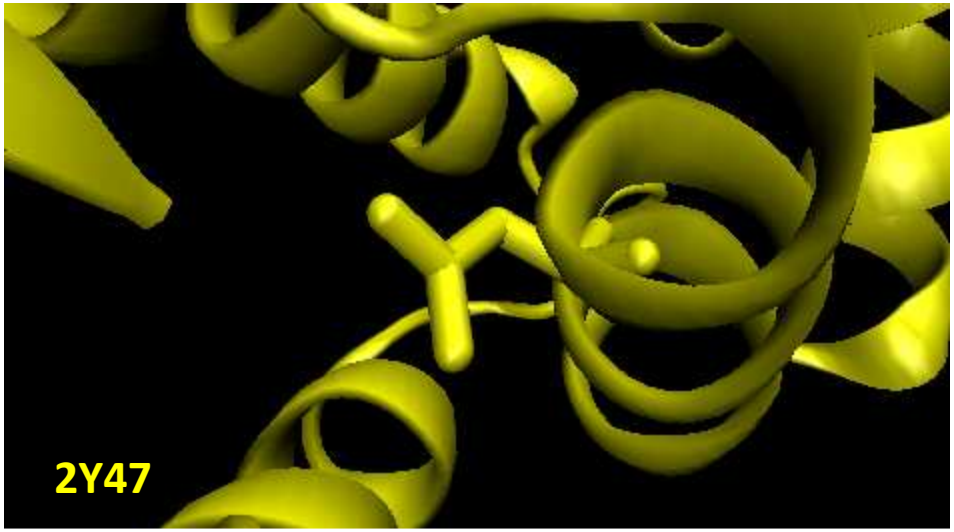
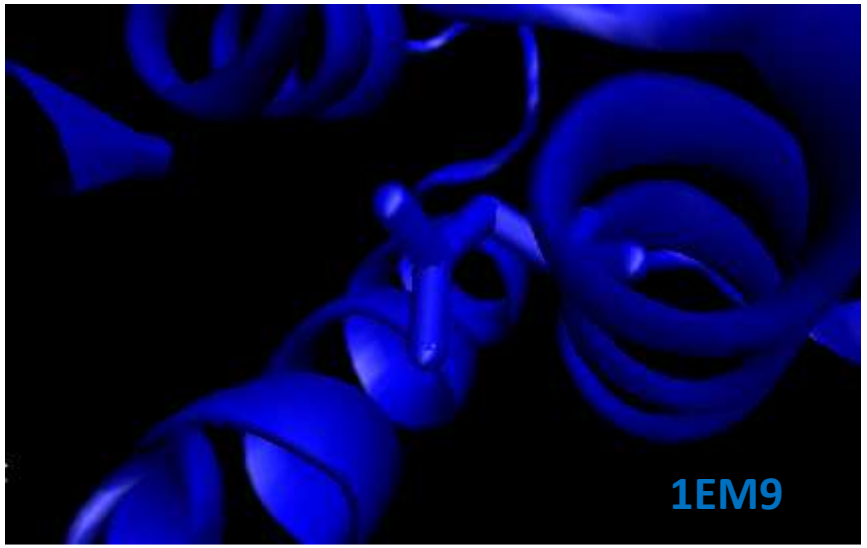
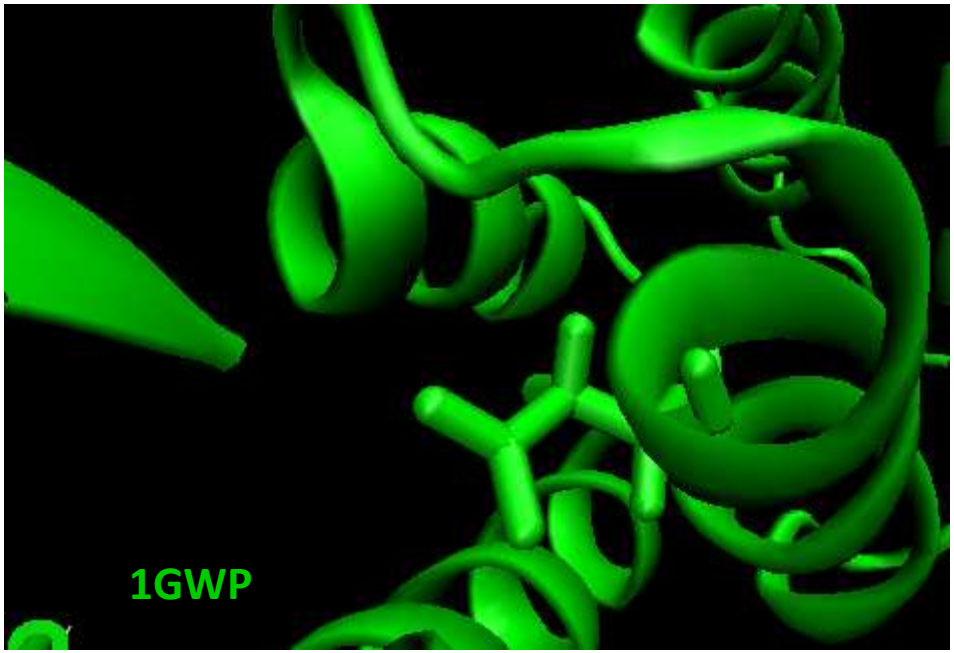


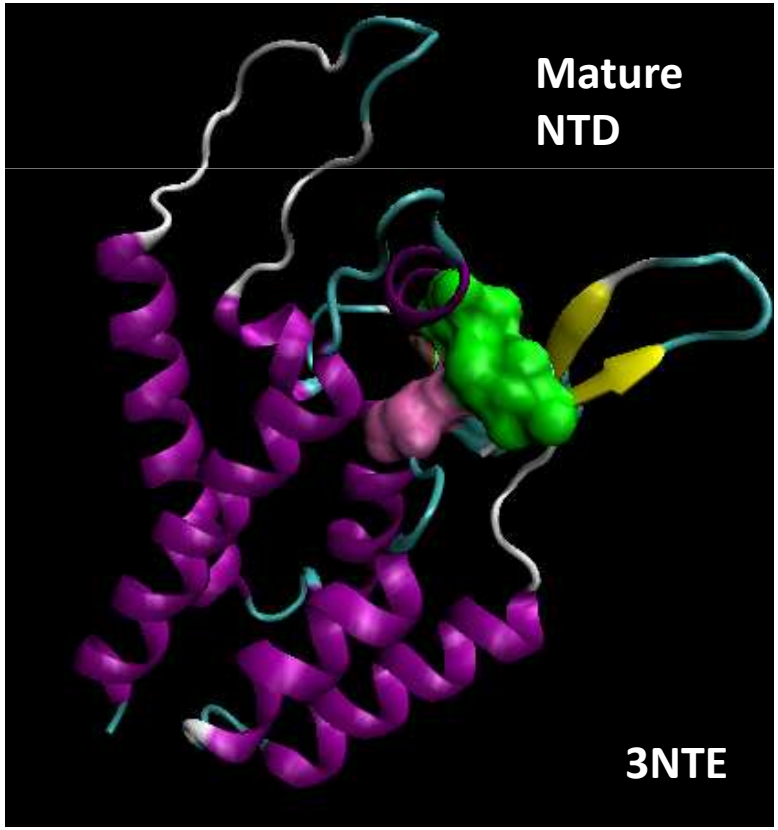


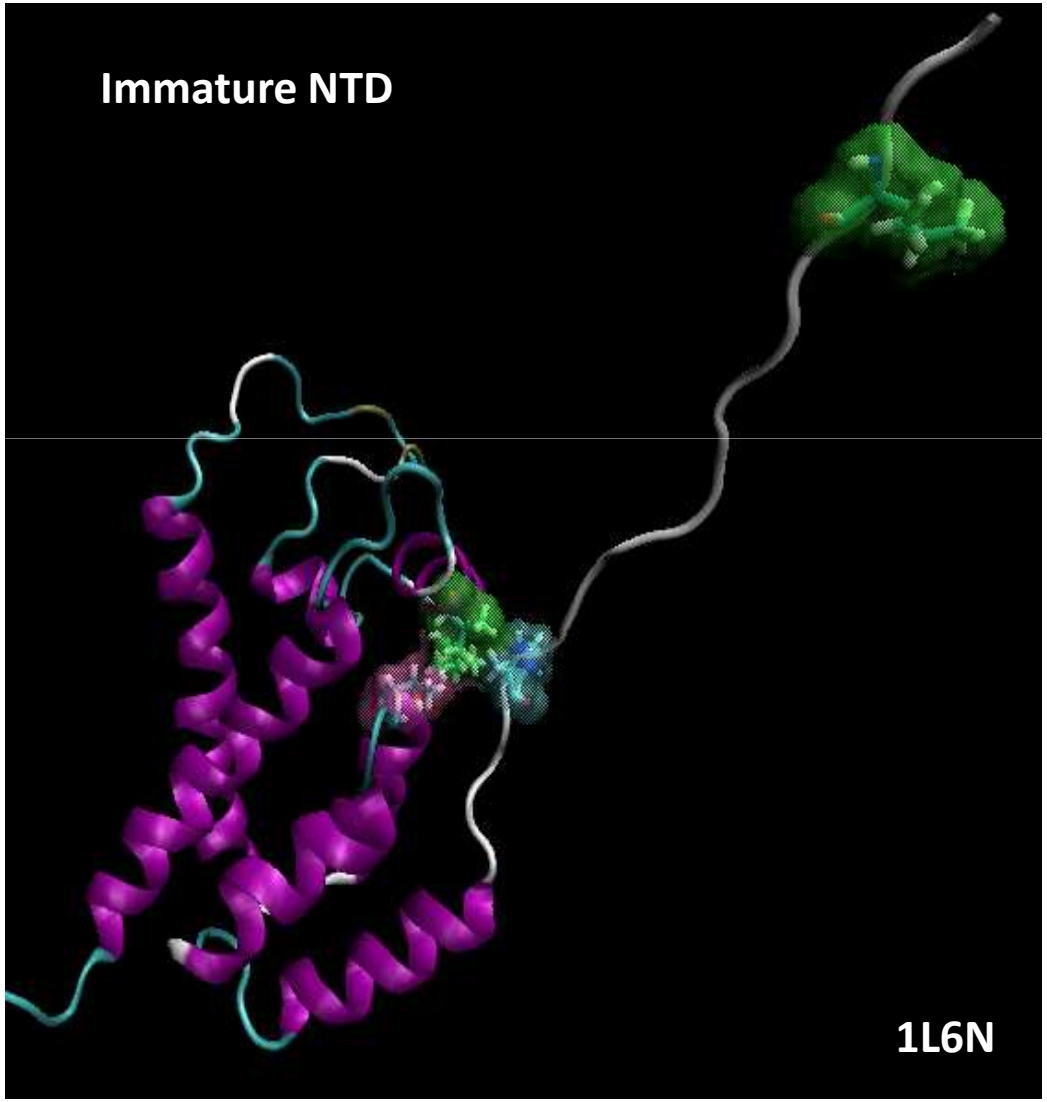


2.1. NTD

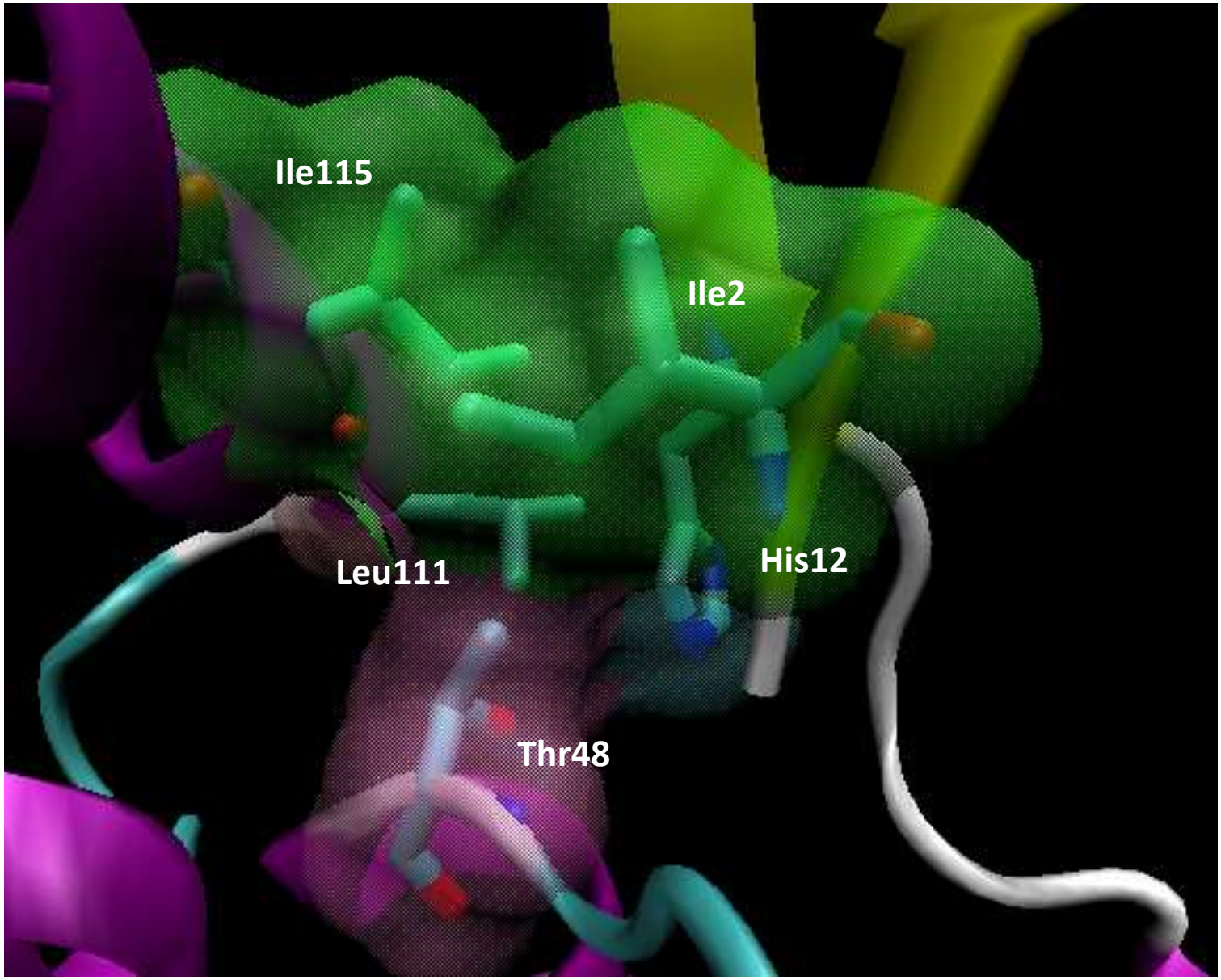
β-hairpin

2. Hidrophobic interactions

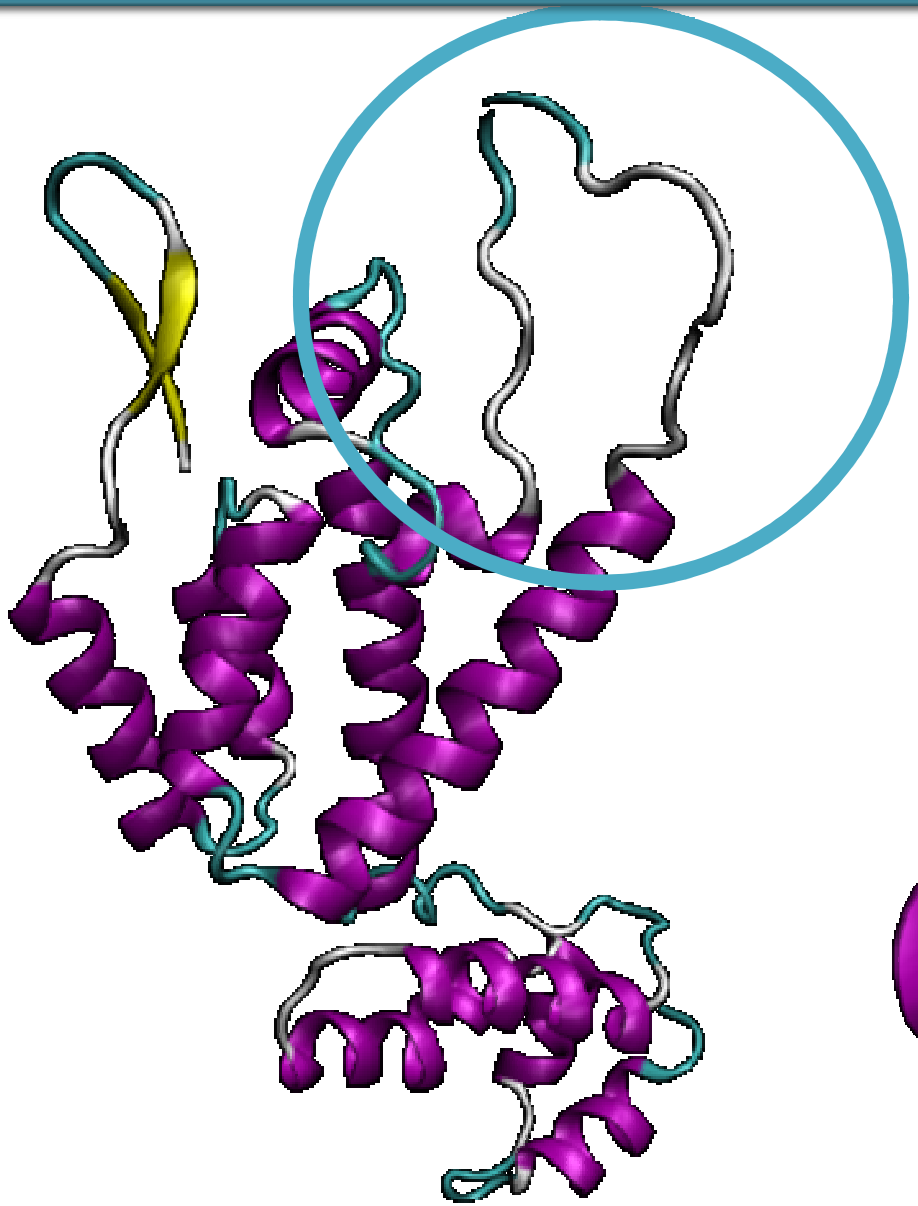




2.1. NTD

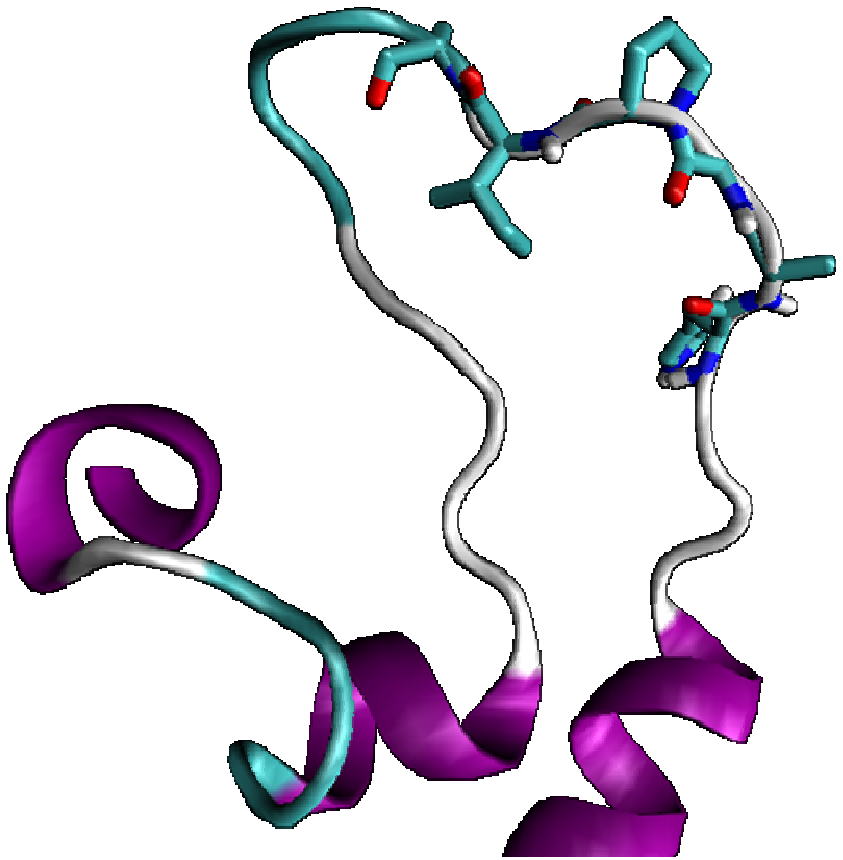


2.1. NTD

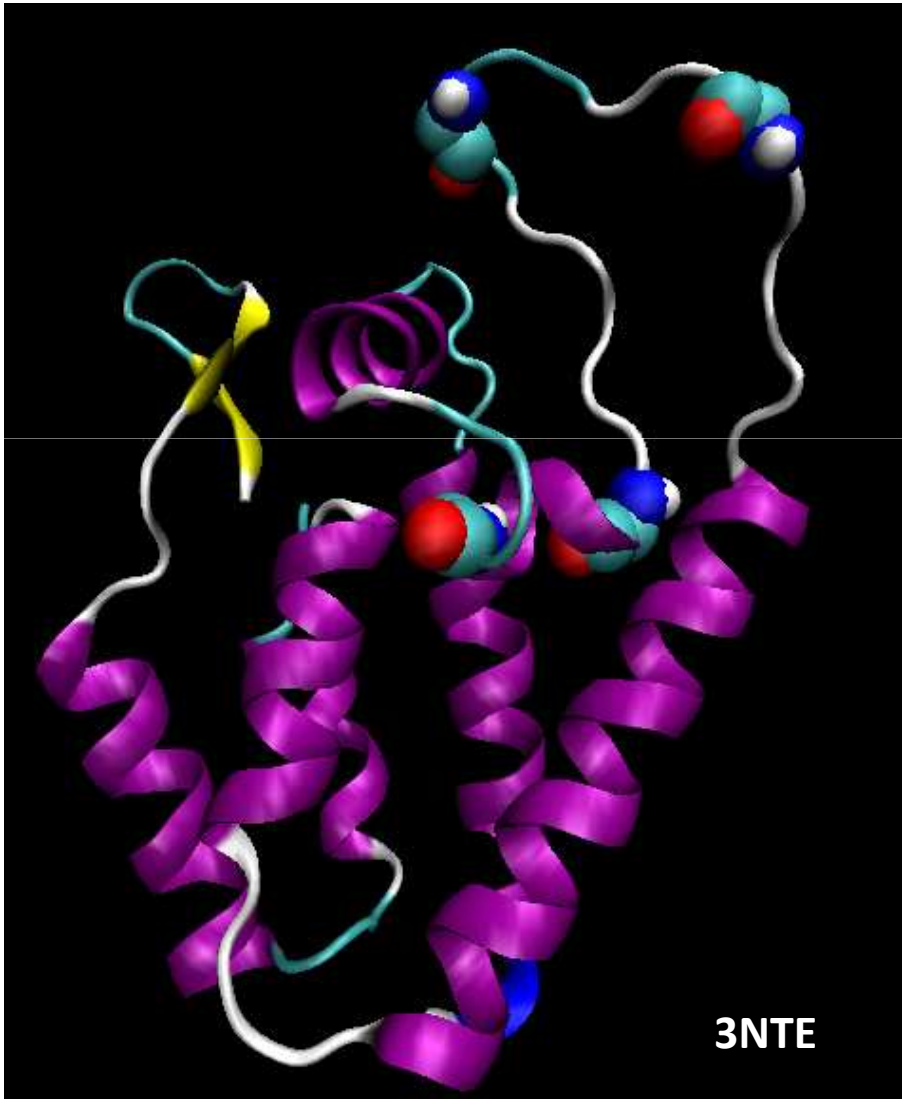


CyPA-bindingloop

^{87}HAGPIA^{92}

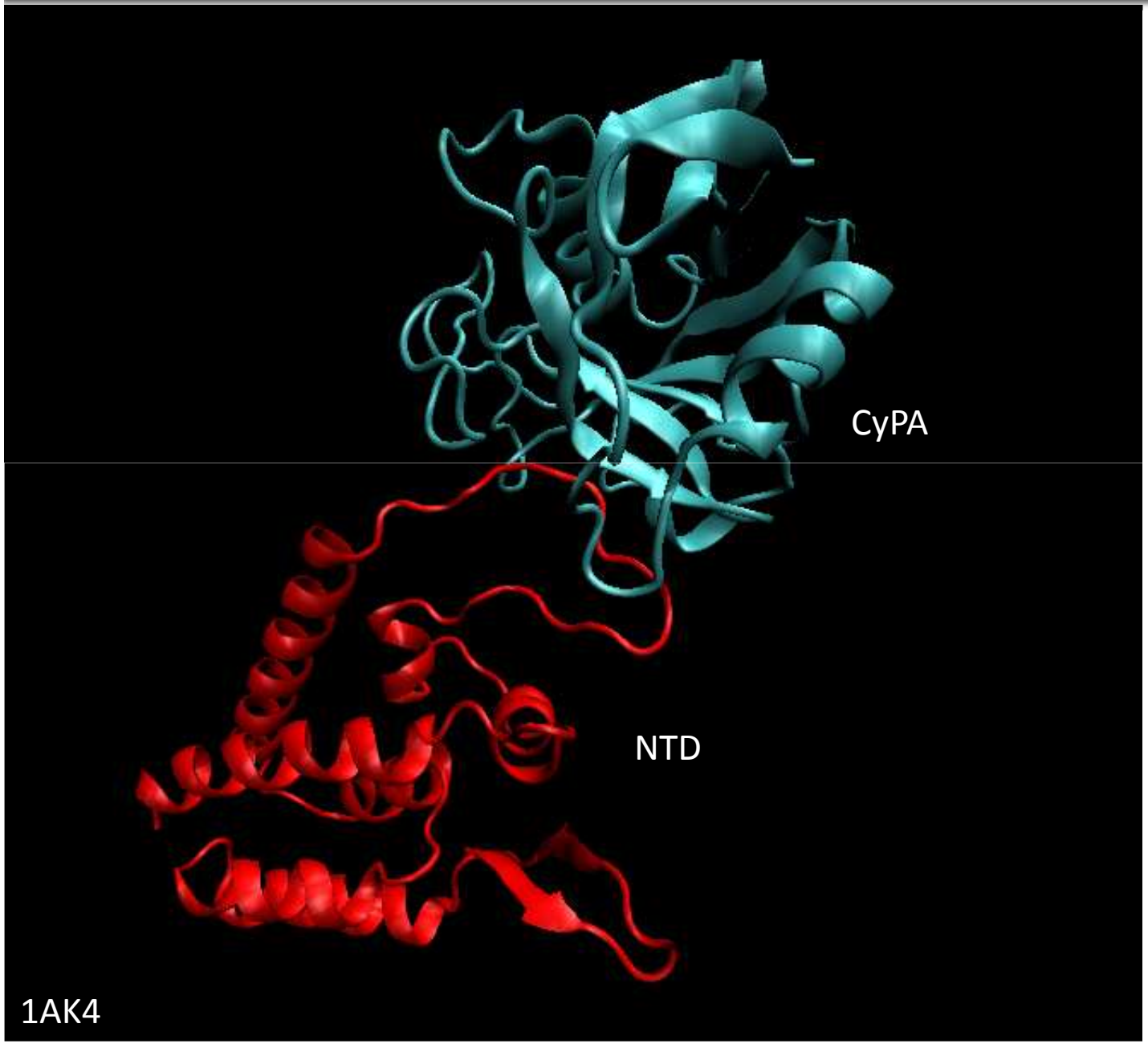


2.1. NTD



The high flexibility of the loop between alfa helices 4 and 5 is consistent with its:
1. Gly-rich composition
2. High degree of solvent accessibility
3. Lack of tertiary contacts with the protein core

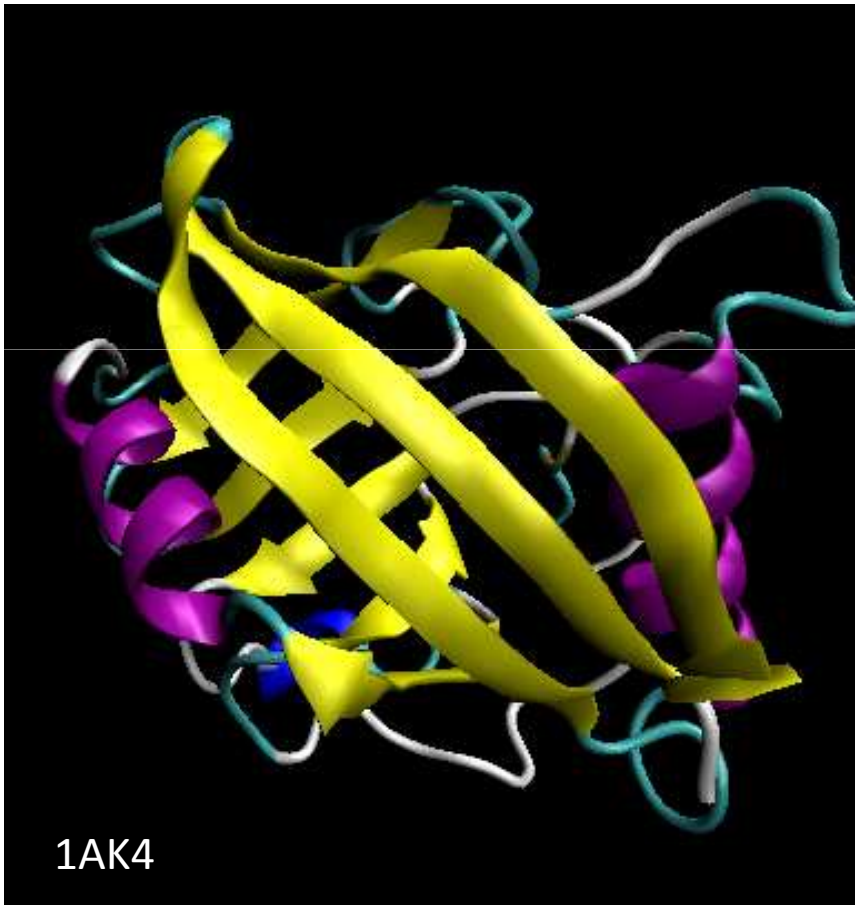
2.1. NTD



Interaction CyPA-NTD

2.1. NTD

CyPA



165 residues
B-barrel Structure
- 8 antiparallel beta chains
- 2 helix alfa

Hydrophobic pocket on the surface

Terapeutic target: Ciclosporina A

IMPORTANCE

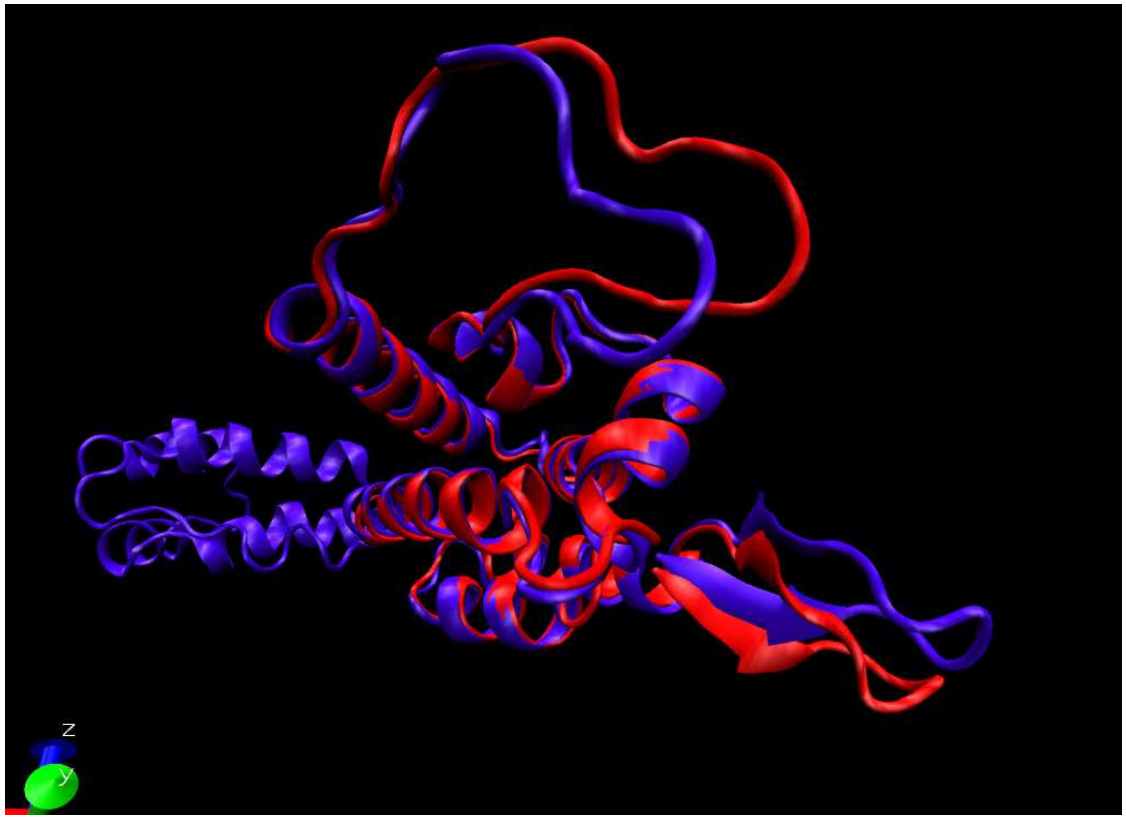
peptidyl-prolyl-cis-trans isomerization

Unknown Function – correct folding of p24

2.1. NTD

Relevant conformational changes in beta hairpin and Cyclophilin bindingloop

STAMP NTD CyPA/no-CyPA



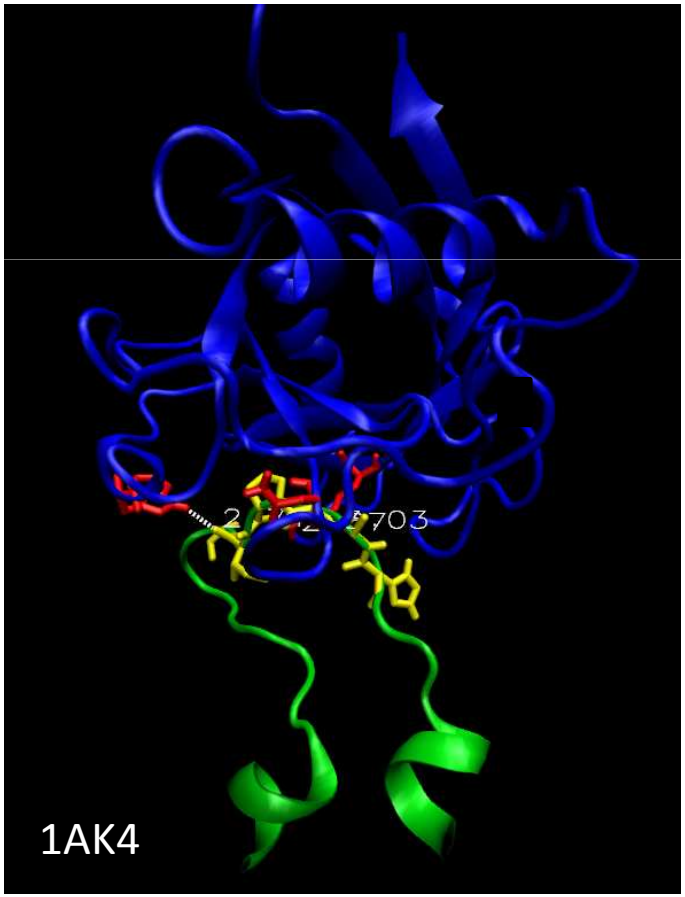

```
STAMP Structural Alignment of Multiple Proteins
 by Robert B. Russell & Geoffrey J. Barton
 Please cite PROTEINS, v14, 309-323, 1992

Running roughfit.

    Sc = STAMP score, RMS = RMS deviation, Align = alignment length
    Len1, Len2 = length of domain, Nfit = residues fitted
    Secs = no. equivalent sec. strucs. Eq = no. equivalent residues
    %I = seq. identity, %S = sec. str. identity
    P(m)  = P value (p=1/10) calculated after Murzin (1993), JMB, 230, 689-694

     No.  Domain1         Domain2         Sc     RMS    Len1 Len2  Align NFit Eq. Se
%I   %S   P(m)
Pair   1  NTD1            NTD2            5.70   0.97    145  221   145  133 132    (
98.48 100.00 0.00e+00
Reading in matrix file NTD.mat...
Doing cluster analysis...
Cluster:  1 (    NTD1  &     NTD2 ) Sc  5.70 RMS   0.96 Len 145 nfit 132
 See file NTD.1 for the alignment and transformations
```

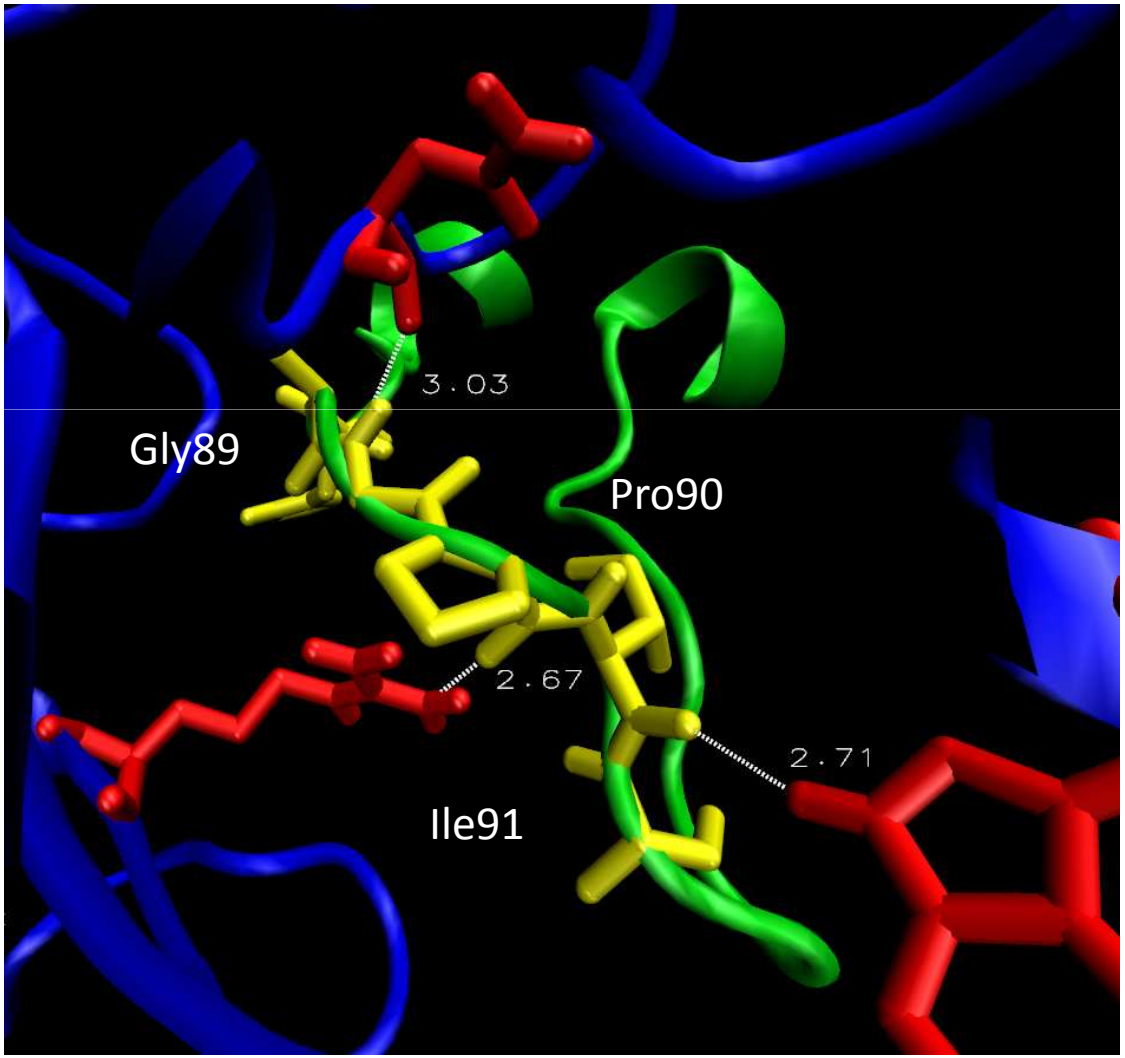
Blue: NTD not bound to CyPA
Red: NTD bound to CyPA

2.1. NTD

Interaction Cyclophilin-binding loop and CyPA

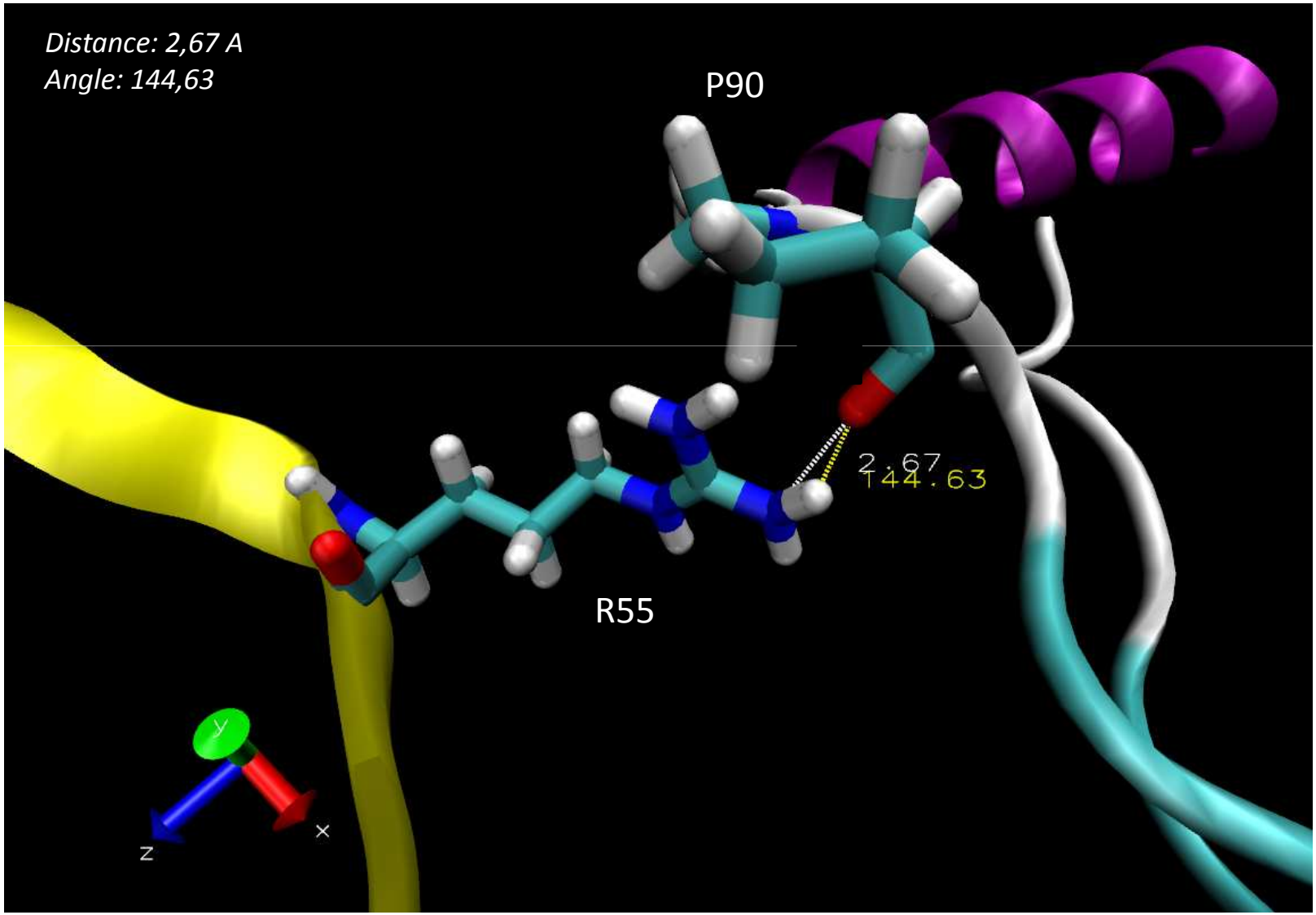
HBONDS





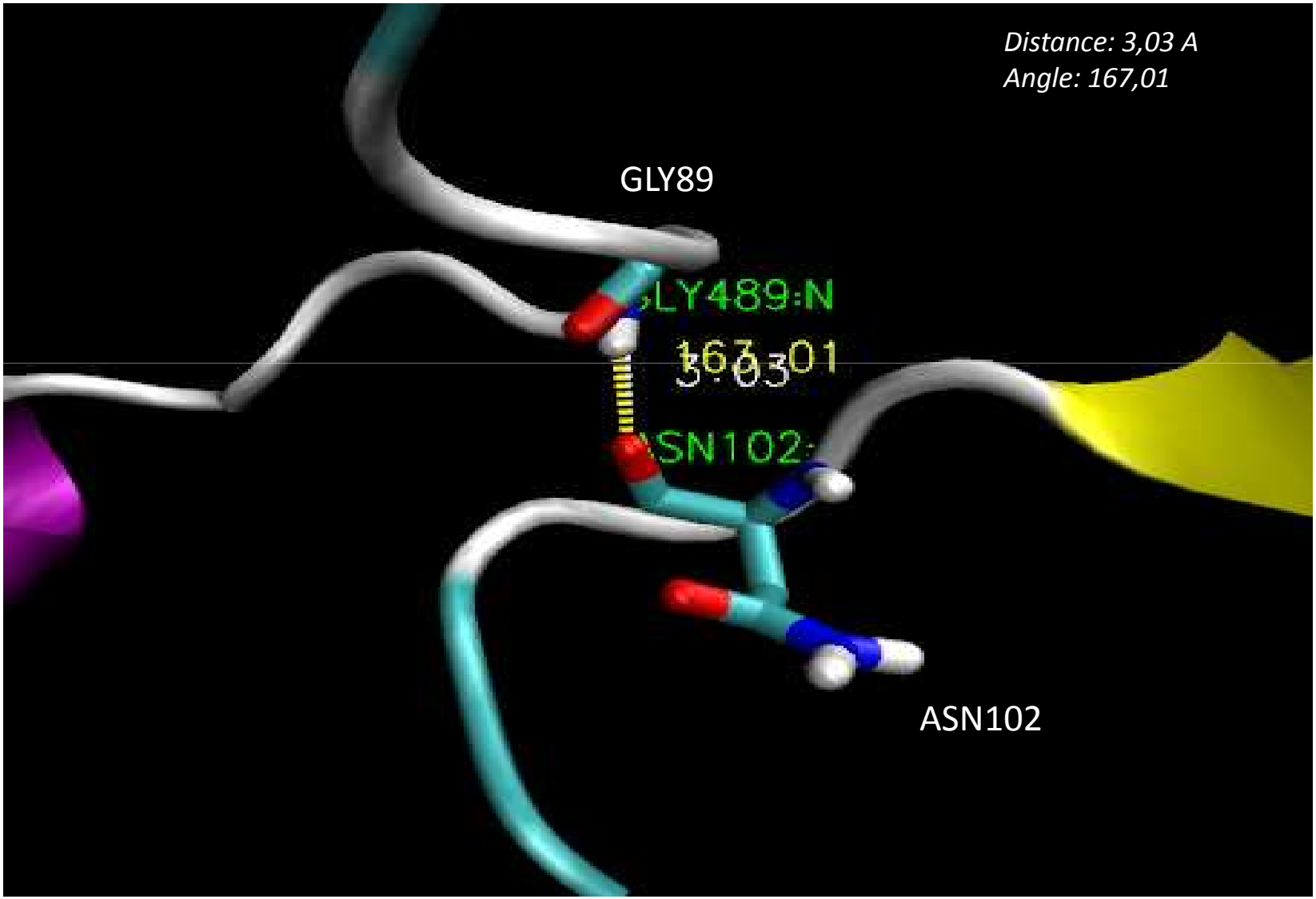
2.1. NTD

Hydrogen bond R55 of CyPA and P90 of CA



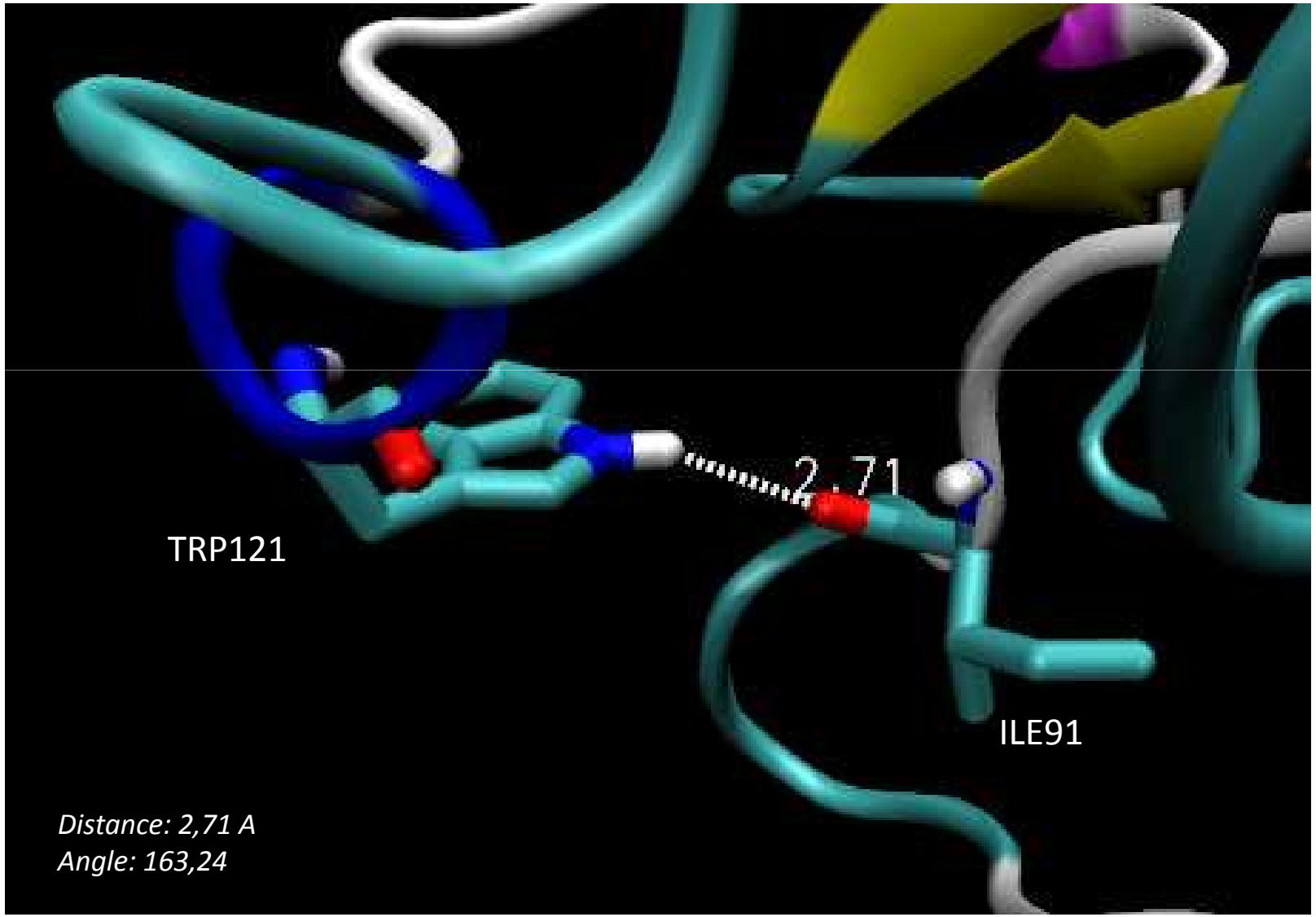
2.1. NTD

Hydrogen bond ASN102 of CyPA and GLY of CA



2.1. NTD

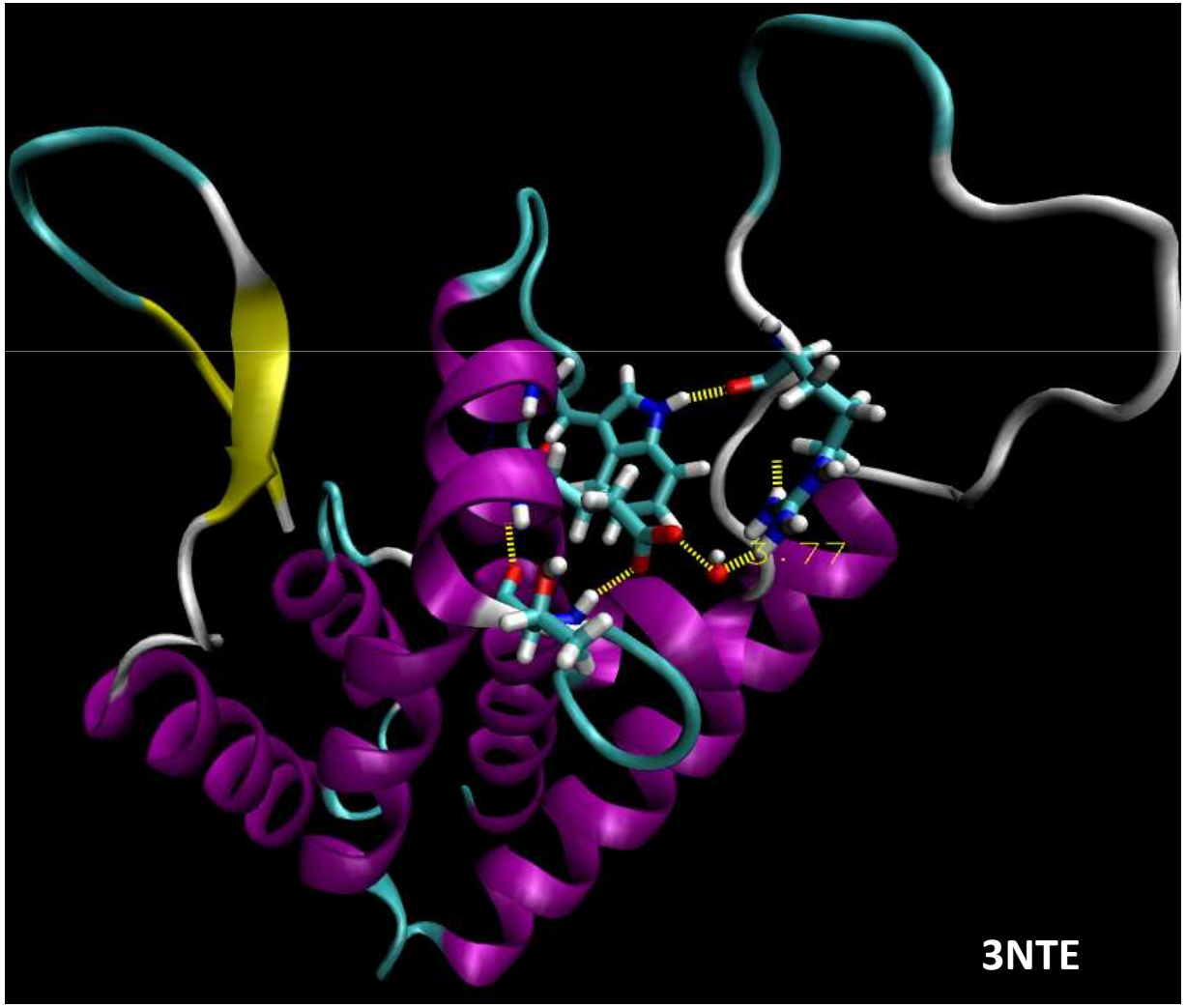
Hydrogenbond TRP121 of CyPA and ILE91 of CA



2.1. NTD

Helix6- CyPA binding loop

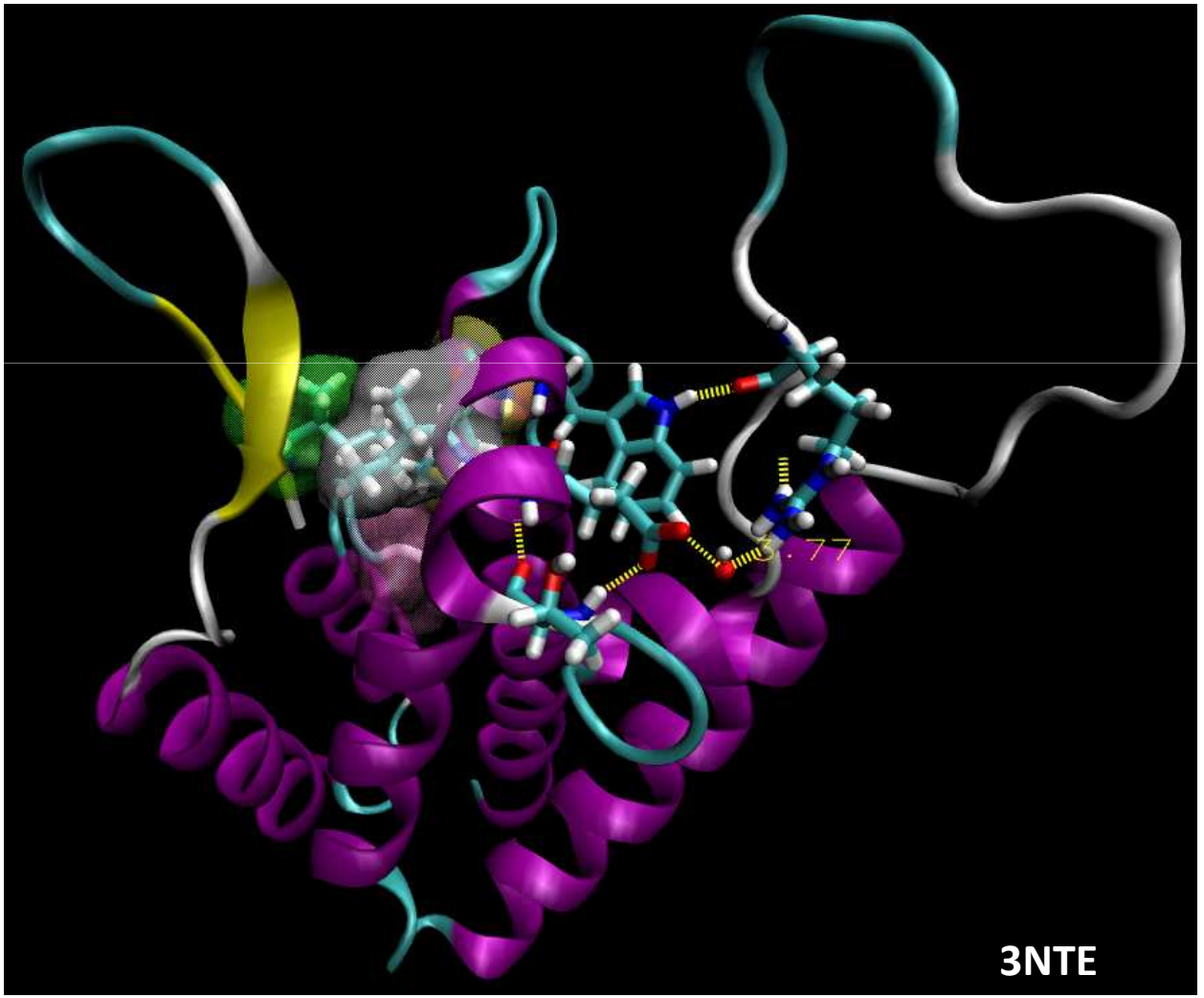
Hydrogen bonds between H6 and CypA binding loop



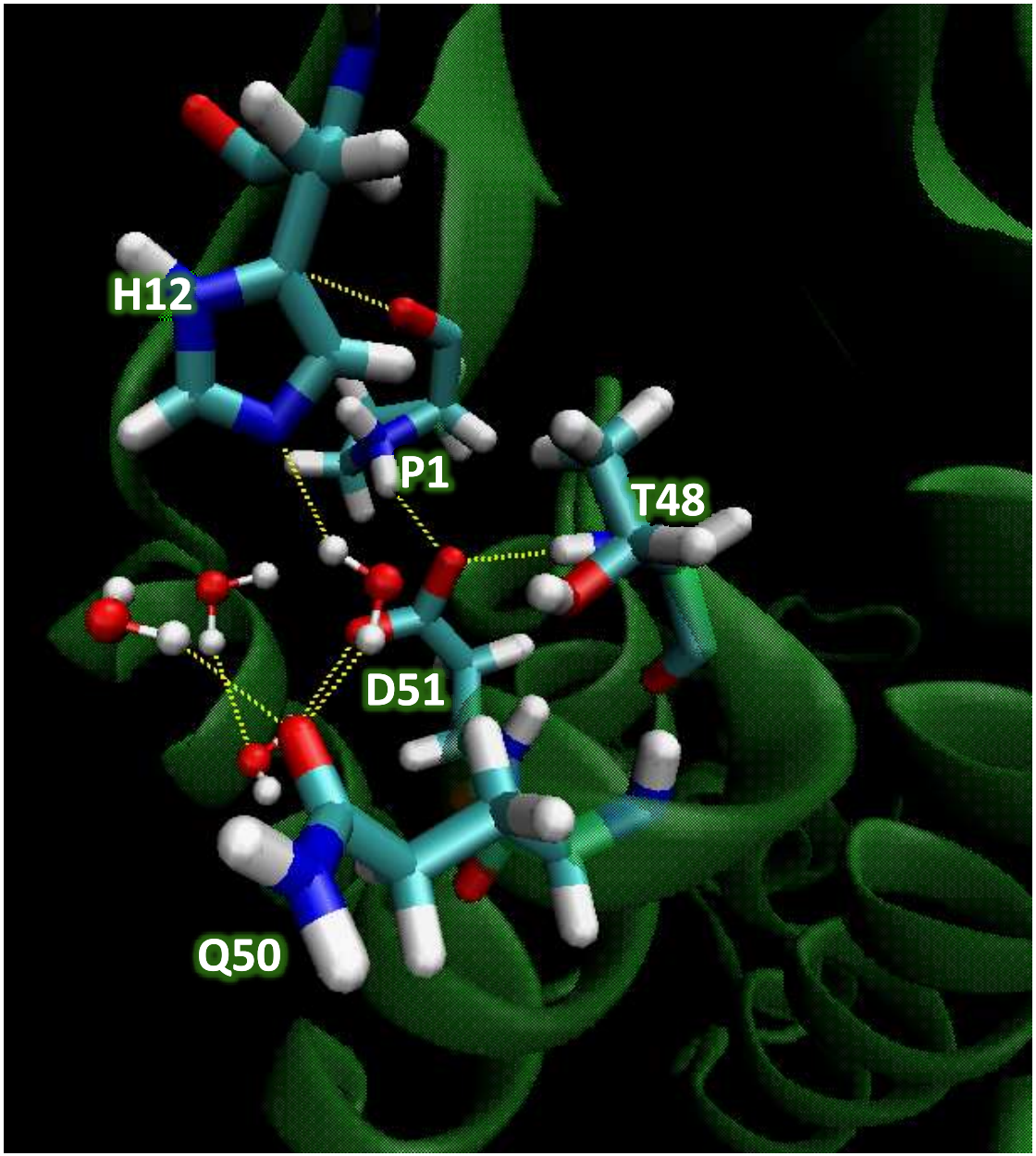
2.1. NTD

B-hairpin-Helix6- CyPA binding loop

Hydrogen bonds between B-hairpin - H6 and CypAbindingloop



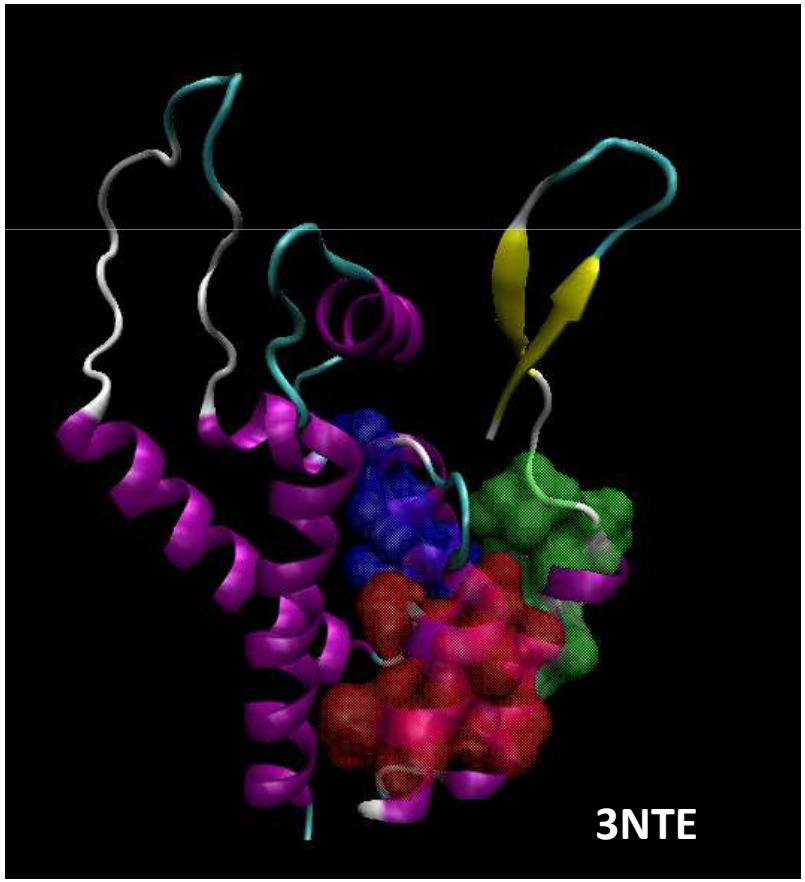
2.1. NTD

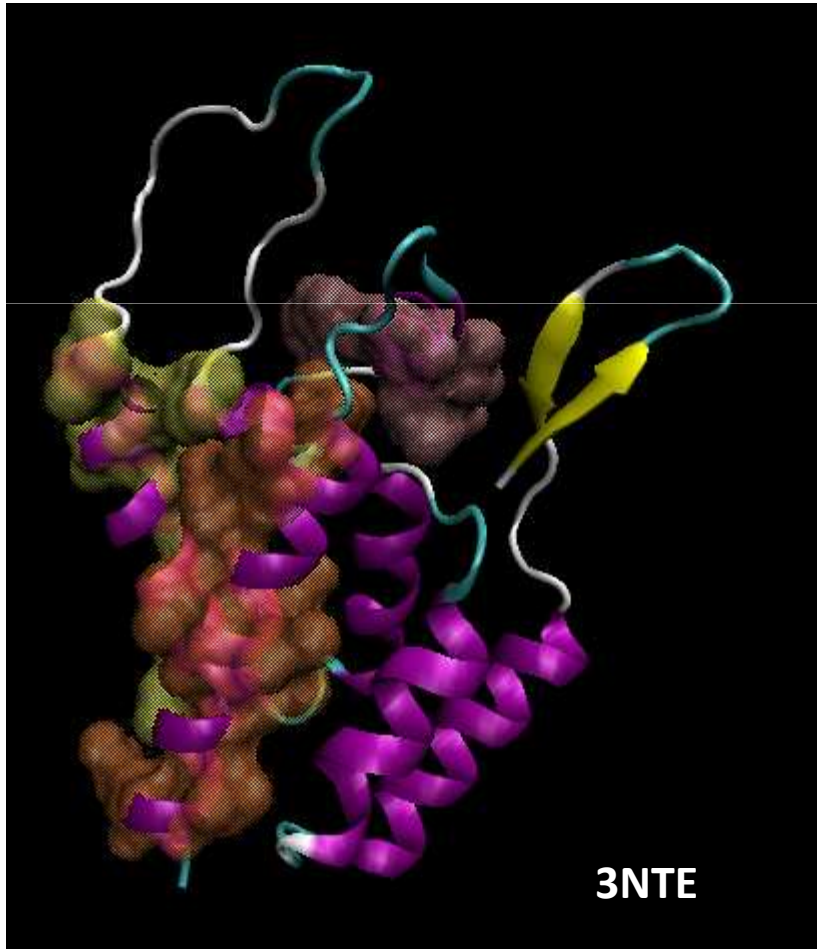


Hbonds mediated by water molecules.

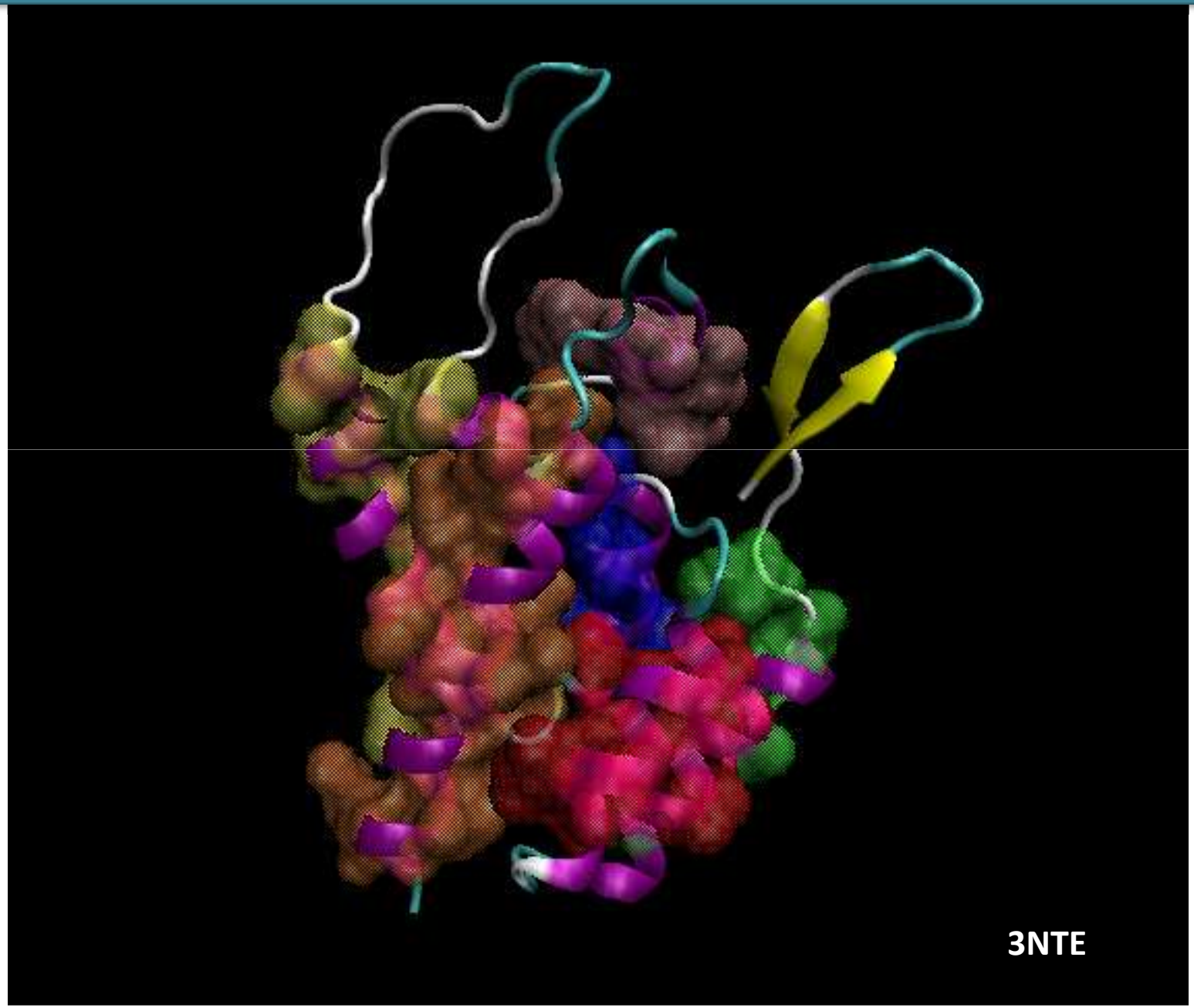
2.1 NTD

Hydrophobic interactions





Domini NTD



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- Capsid subunit (hexamer)
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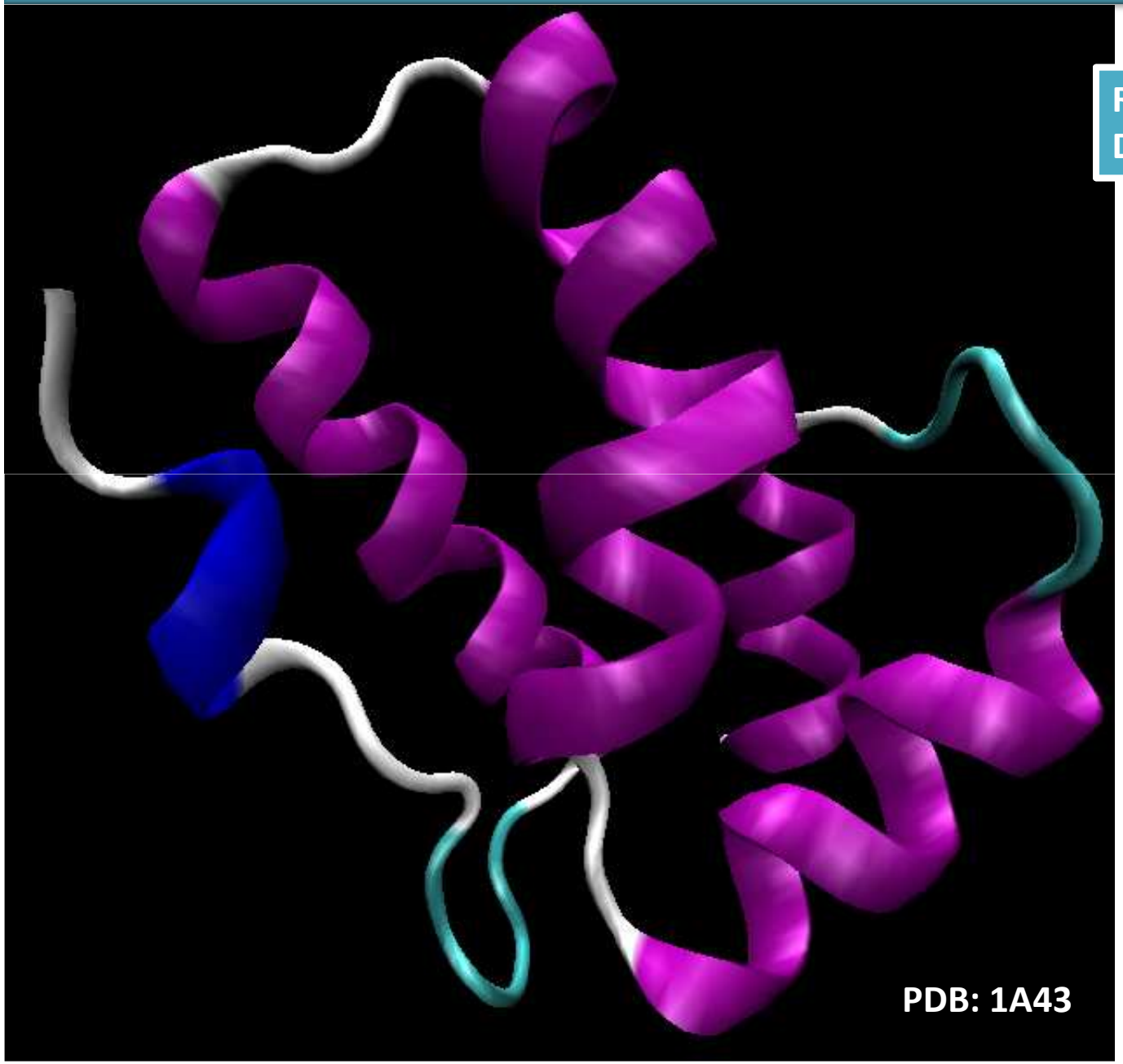
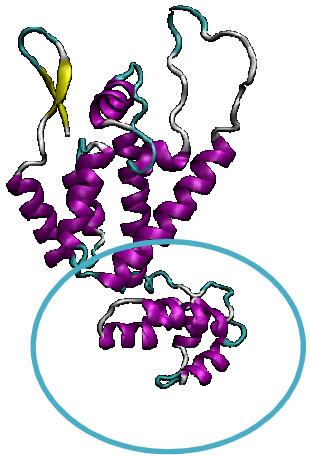
- Lattice model

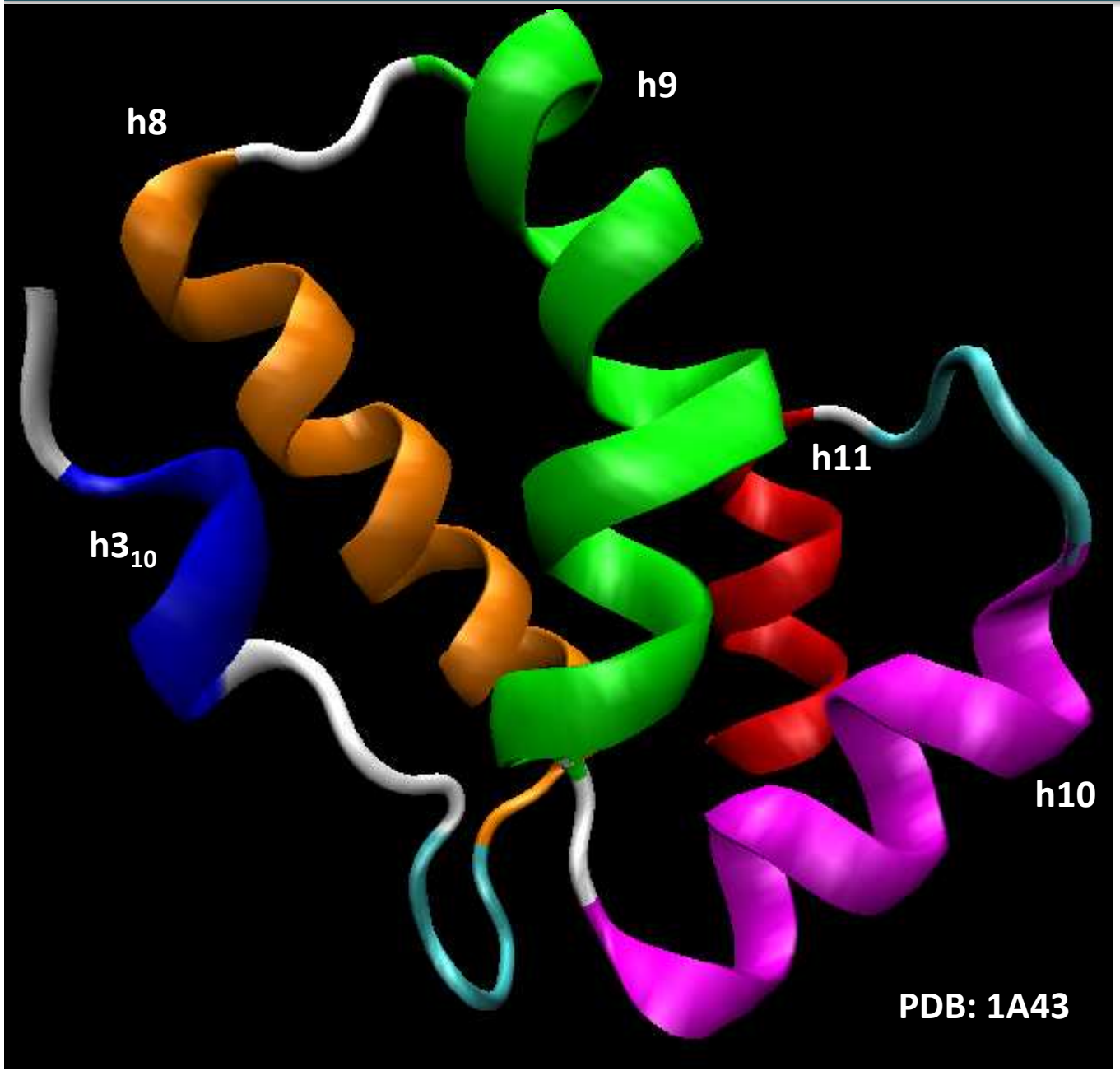
2.2.Domini CTD



Residues: 150-231
Dimensions: 29x36x28 Å



2.2.Domini CTD



3_{10}-helix (150-152)
α-helix 8 (160–176)
α-helix 9 (179–195)
α-helix 10 (196–206)
α-helix 11 (211-219)
220-231 disordered

Glycine –rich motif "GVGGP"

2.2.Domini CTD

The two domains of CA belong to different superfamilies

CTD domain Superfamily: Retrovirus capsid dimerization domain-like

4. Superfamily: Retrovirus capsid dimerization domain-like [47353]
   Superfamily
5. Family: Retrovirus capsid protein C-terminal domain [47354]

Protein Domains:

1. EIAV capsid protein p26 [47355]
   1. Equine infectious anemia virus [TaxId: 11665] [47356] (2)
2. HTLV-I capsid protein [47357]
   1. Human T-cell leukemia virus type 1 [TaxId: 11908] [47358] (1)
3. HIV capsid protein, dimerisation domain [47359]
   1. Human immunodeficiency virus type 1 [TaxId: 11676] [47360] (7)
4. RSV capsid protein [47361]
   1. Rous sarcoma virus [TaxId: 11886] [47362] (2)

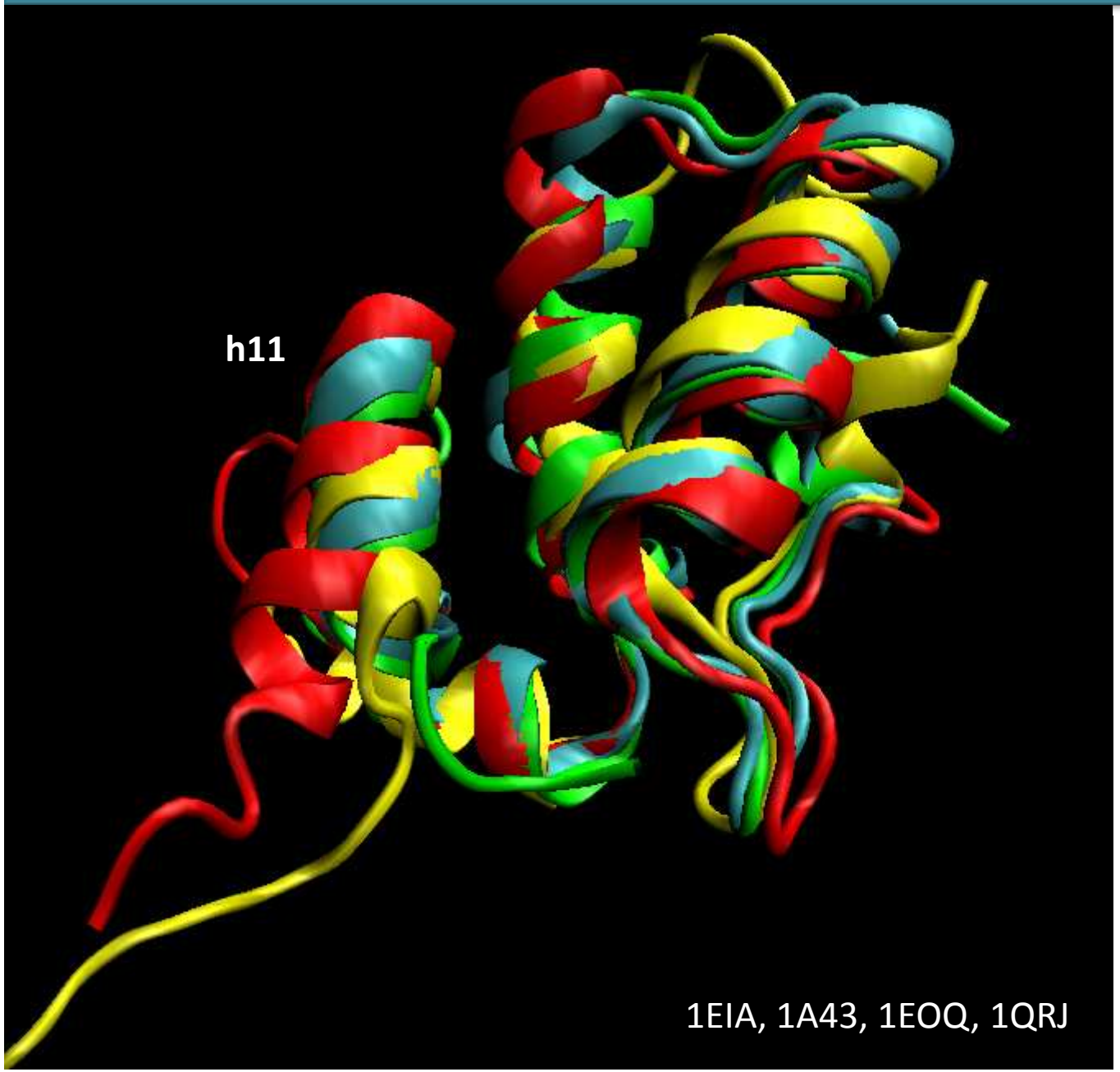
NTD domain Superfamily: Retrovirus capsid protein, N-terminal core domain

4. Superfamily: Retrovirus capsid protein, N-terminal core domain [47943]
   Superfamily
5. Family: Retrovirus capsid protein, N-terminal core domain [47944]

Protein Domains:

1. HIV-1 capsid protein [47945]
   1. Human immunodeficiency virus type 1 [TaxId: 11676] [47946] (16)
2. EIAV capsid protein p26 [47947]
   1. Equine infectious anemia virus [TaxId: 11665] [47948] (2)
3. HTLV-I capsid protein [47949]
   1. Human T-cell leukemia virus type 1 [TaxId: 11908] [47950] (2)
4. RSV capsid protein [47951]
   1. Rous sarcoma virus [TaxId: 11886] [47952] (3)
5. AKV capsid [116949]
   1. AKV murine leukemia virus [TaxId: 11791] [116950] (1)
      SQ P03336 215-345 # fragment of the core shell protein p30 (215-477)

2.2.Domini CTD



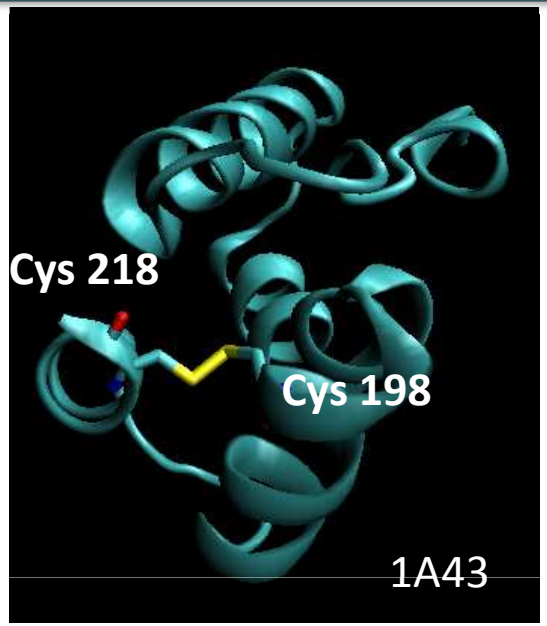
Superfamily

STAMP CTD of members of the superfamily

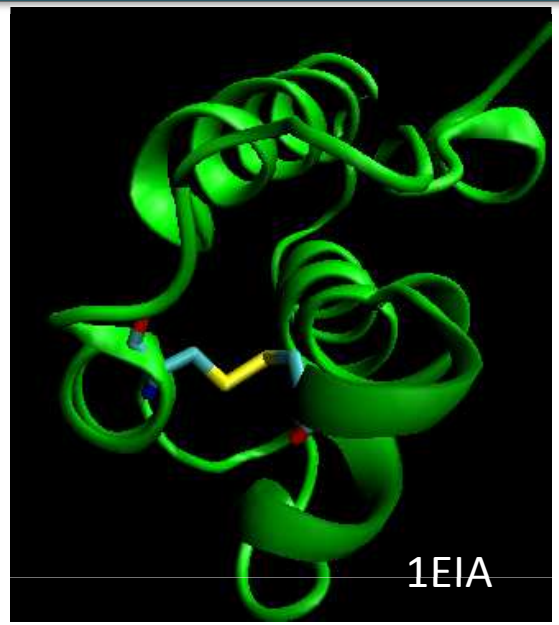
Blue: HIV-1
Green: EIAV
Yellow: HTLV-1
Red: RSV

2.2.Domini CTD

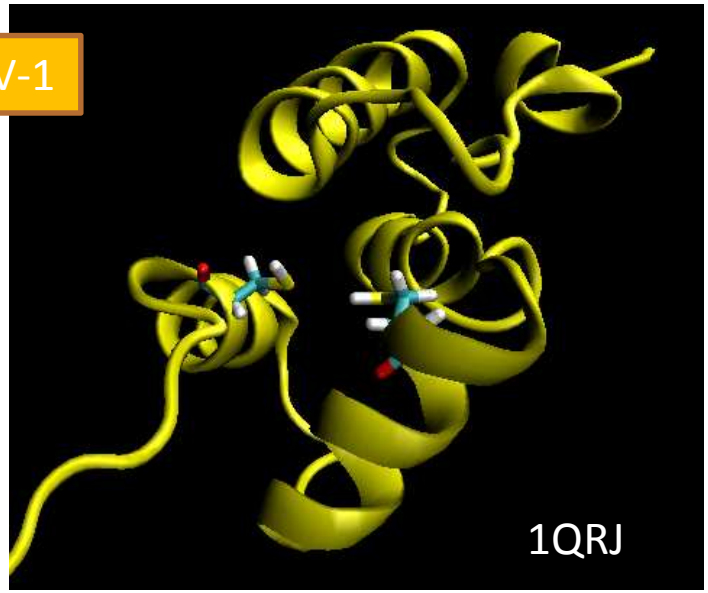
HIV-1



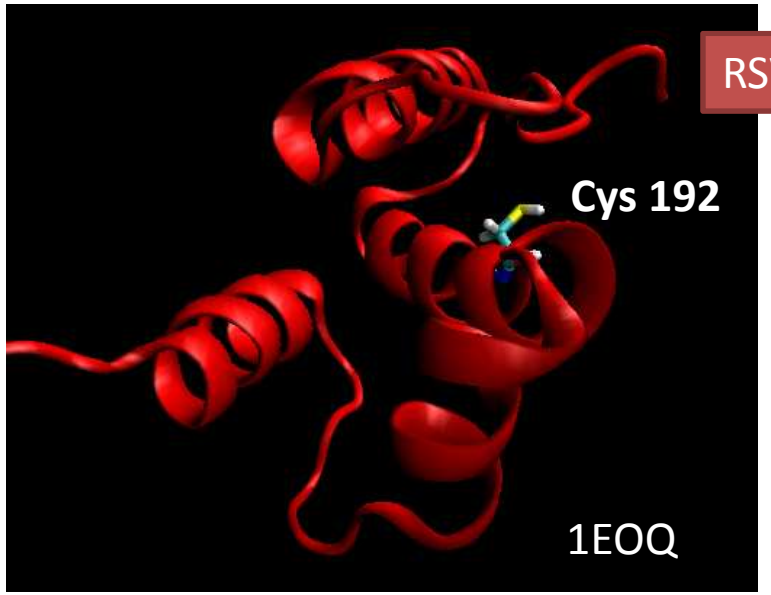
EIAV



HTLV-1



RSV



2.2.Domini CTD

Superfamily-Sequence alignment with HHM

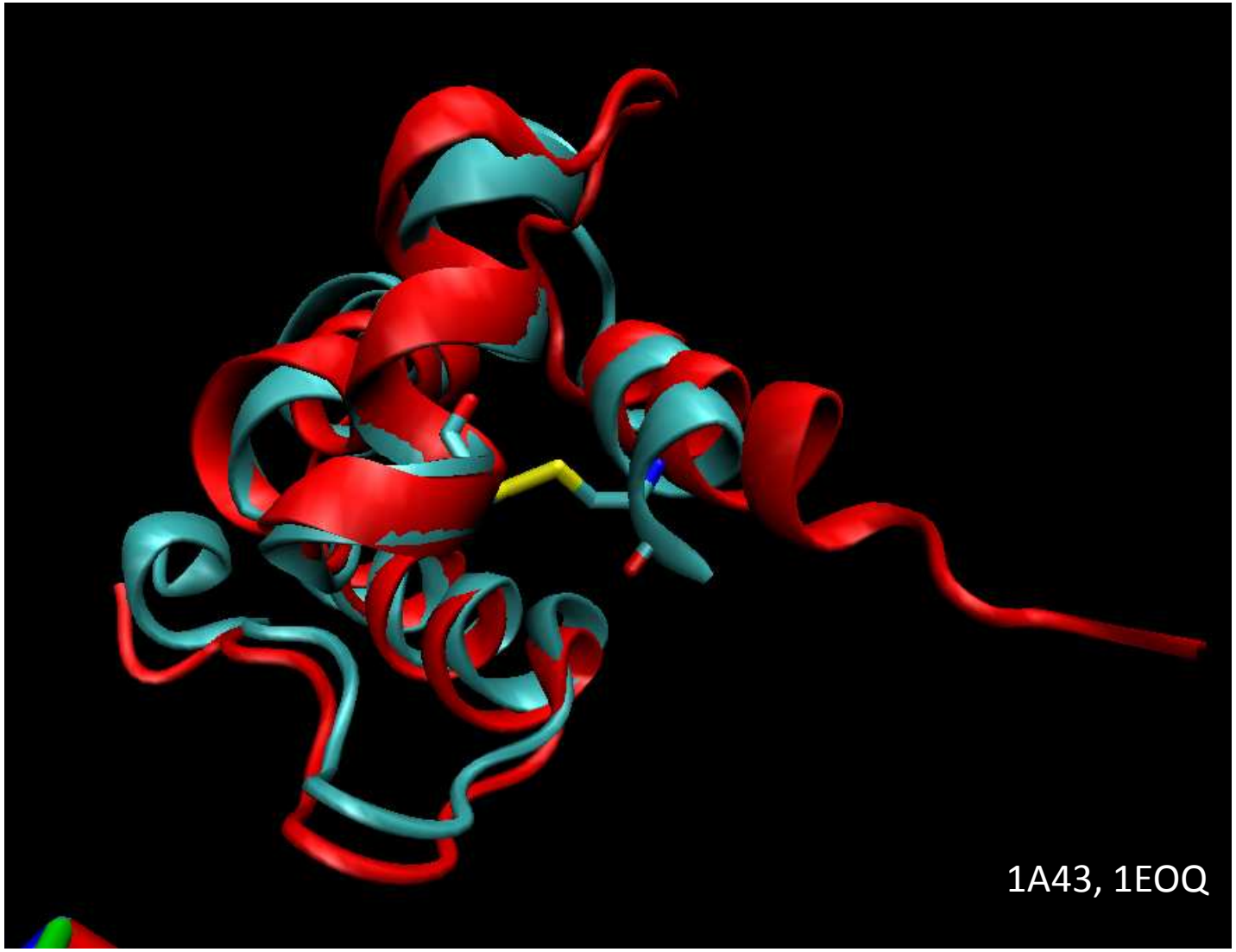
```
1A43          mspt-SILDIRQGPKEPFRDYVDRFYKTLRAEQ--ASQEVKNWMTETLLV
1EIA          ....PKAQNIRQGAKEPYPEFVDRLLSQIKSEG--HPQEISKFLTDTLTI
1EOQ          ....---MDIMQGPSESFVDFANRLIKAVEGSD--LPPSARAPVIIDCFR
1QRJ          ..kdPSWASILQGLEEPYHAFVERLNIALDNGLPEG--TPKDPILRSLAY
#=GC RF       ....xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

1A43          QNANPDCKTILKA--LGPGATLEEMMTAC-QG-VGGPghkarvl.....
1EIA          QNANEECRNAMRH--LRPEDTLEEKMYAC-RD-IG--............
1EOQ          QKSQPDIQQLIRT-APSTLTTPGEIIKYVLDRQ-KTAPltdqgiaaamss
1QRJ          SNANKECQKLLQARGHT-NSPLGDMLRAC-QTWTPKDktkvl.......
#=GC RF       xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx.............

1A43          .......
1EIA          .......
1EOQ          aiqplim
1QRJ          .......
#=GC RF       .......
//
```

1A43: HIV-1
1EIA: EIAV
1EOQ: RSV
1QRJ: HTLV-1

2.2.Domini CTD



Superfamily

STAMP CTD of HIV and RSV

Blue: HIV-1
Red: RSV

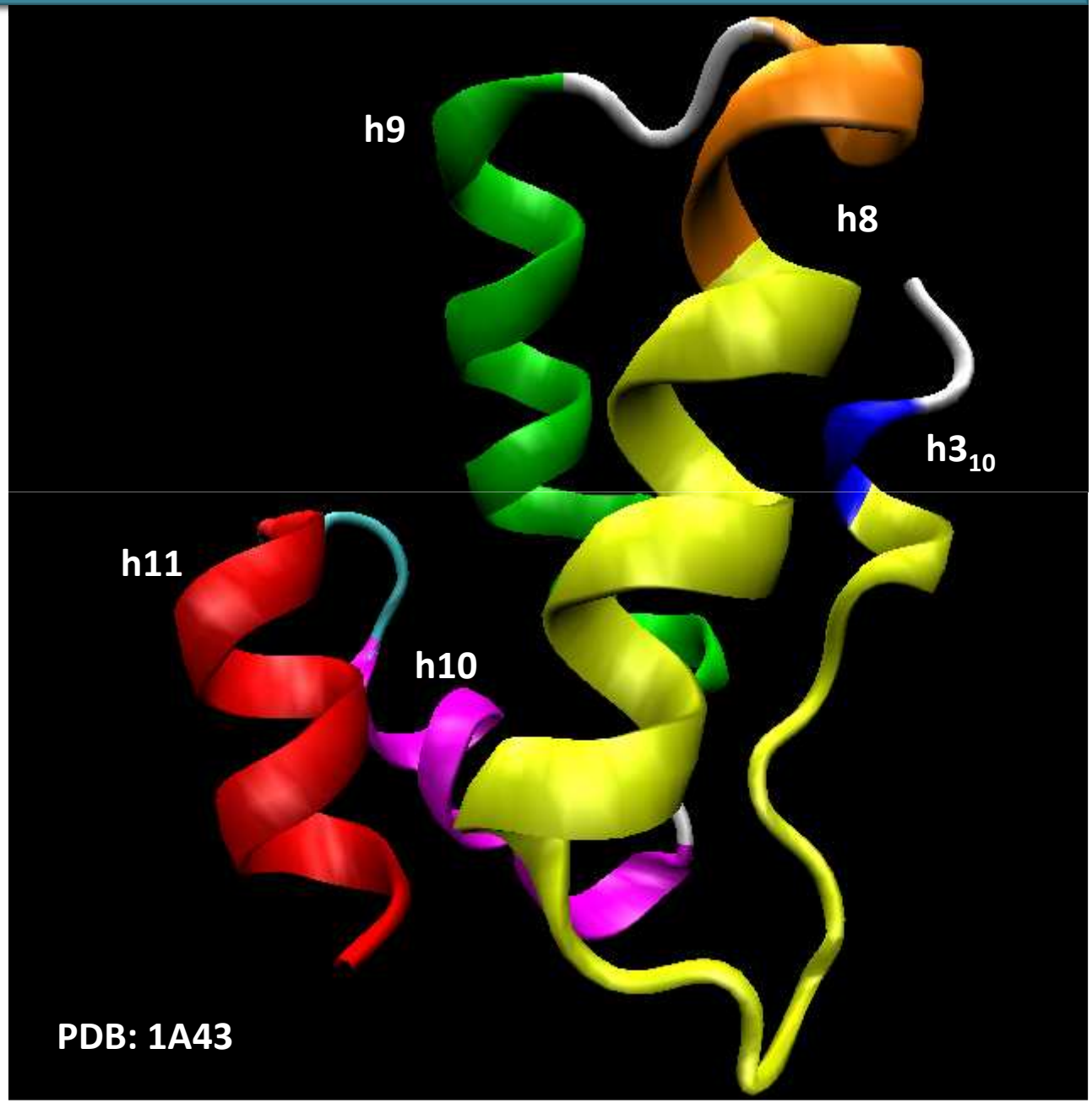
2.2.Domini CTD

The Major Homology Region

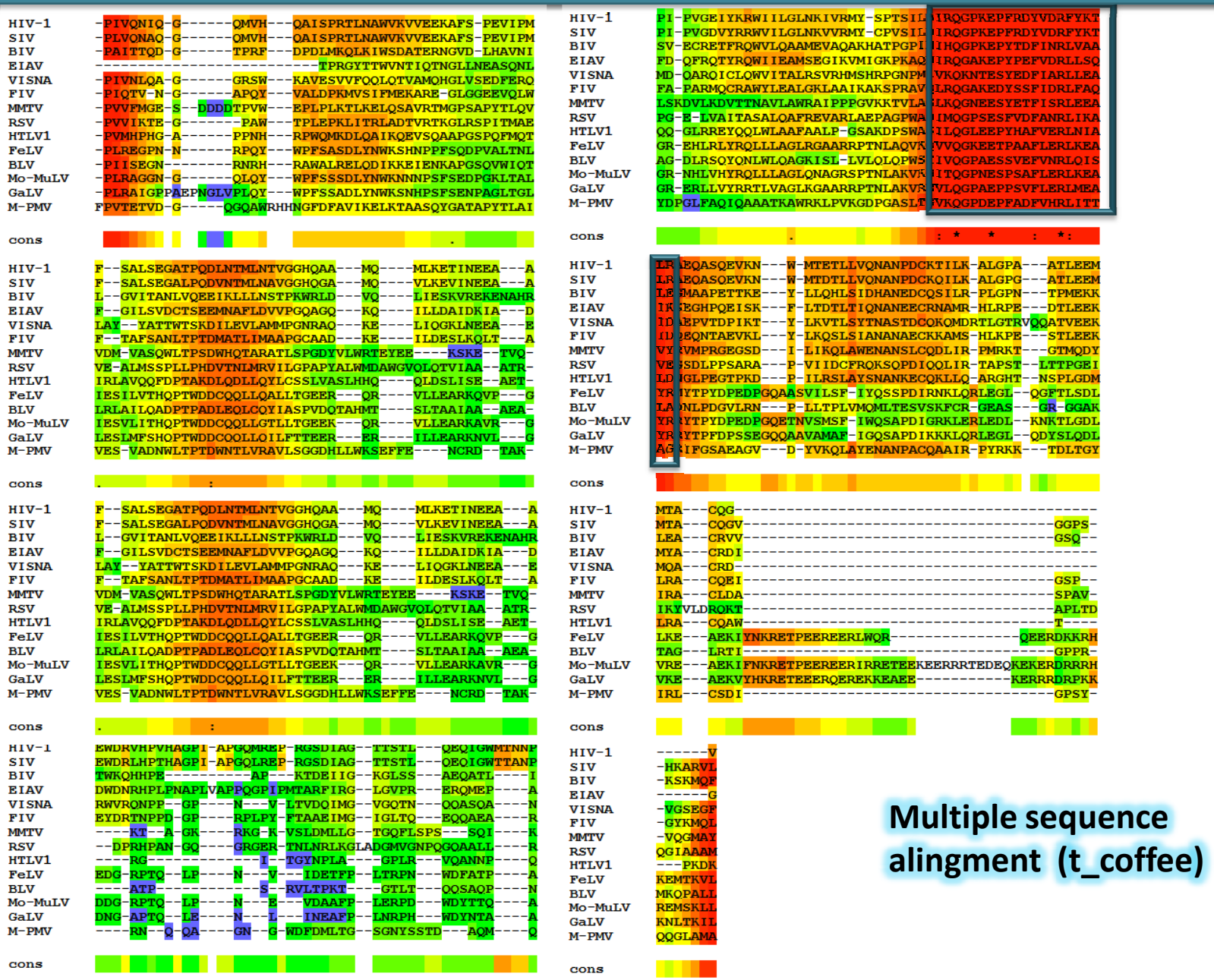
MHR

Residus: 152 to 172
Strand-turn-helix motif

This region is highly conserved among the Retroviridae family



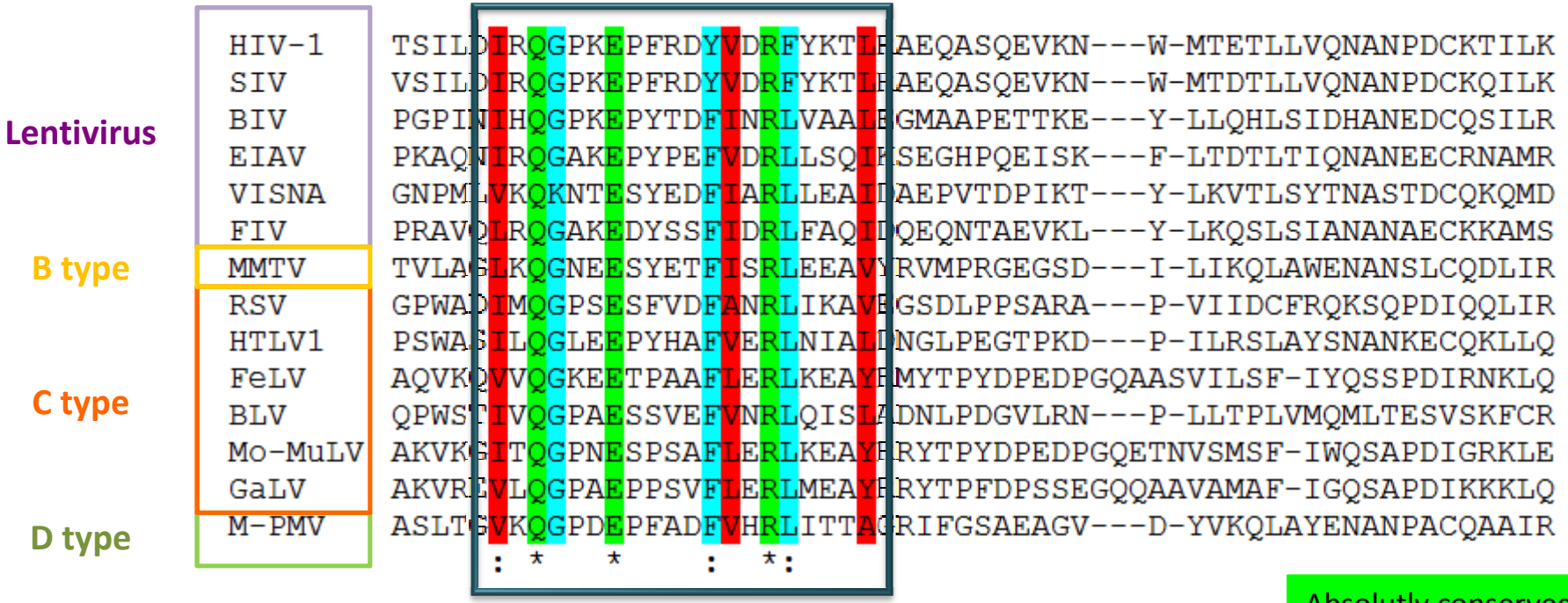
2.2.Domini CTD



Multiple sequence alingment (t_coffee)

2.2.Domini CTD

Multiple sequence alingment (t_coffee)



Absolutly conserved

Conservative mutation

Hydrophobic

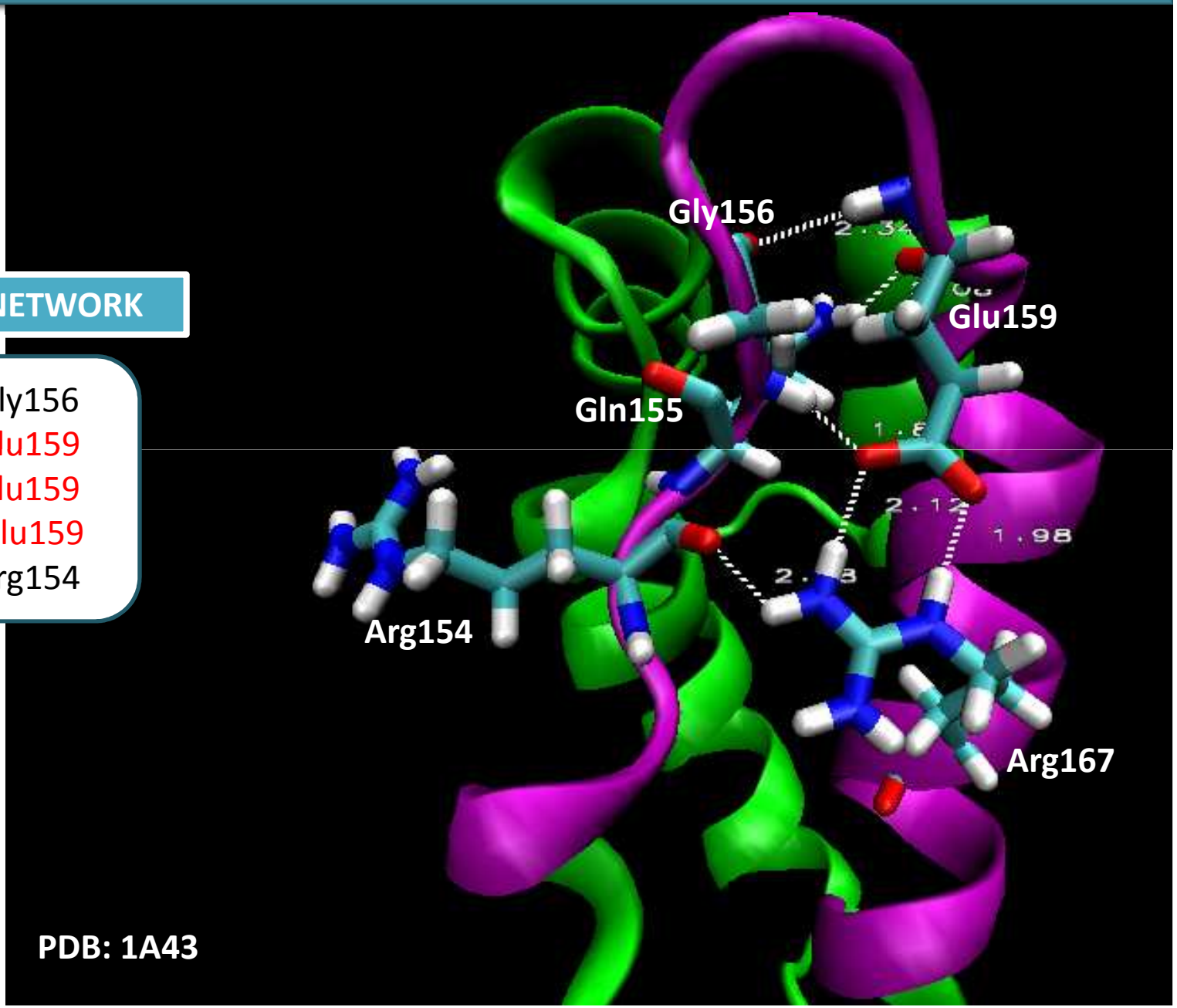
HYDROGEN NETWORK (Q155,E159, R167 and G156)
HYDROPHOBIC INTERACTIONS

2.2.Domini CTD

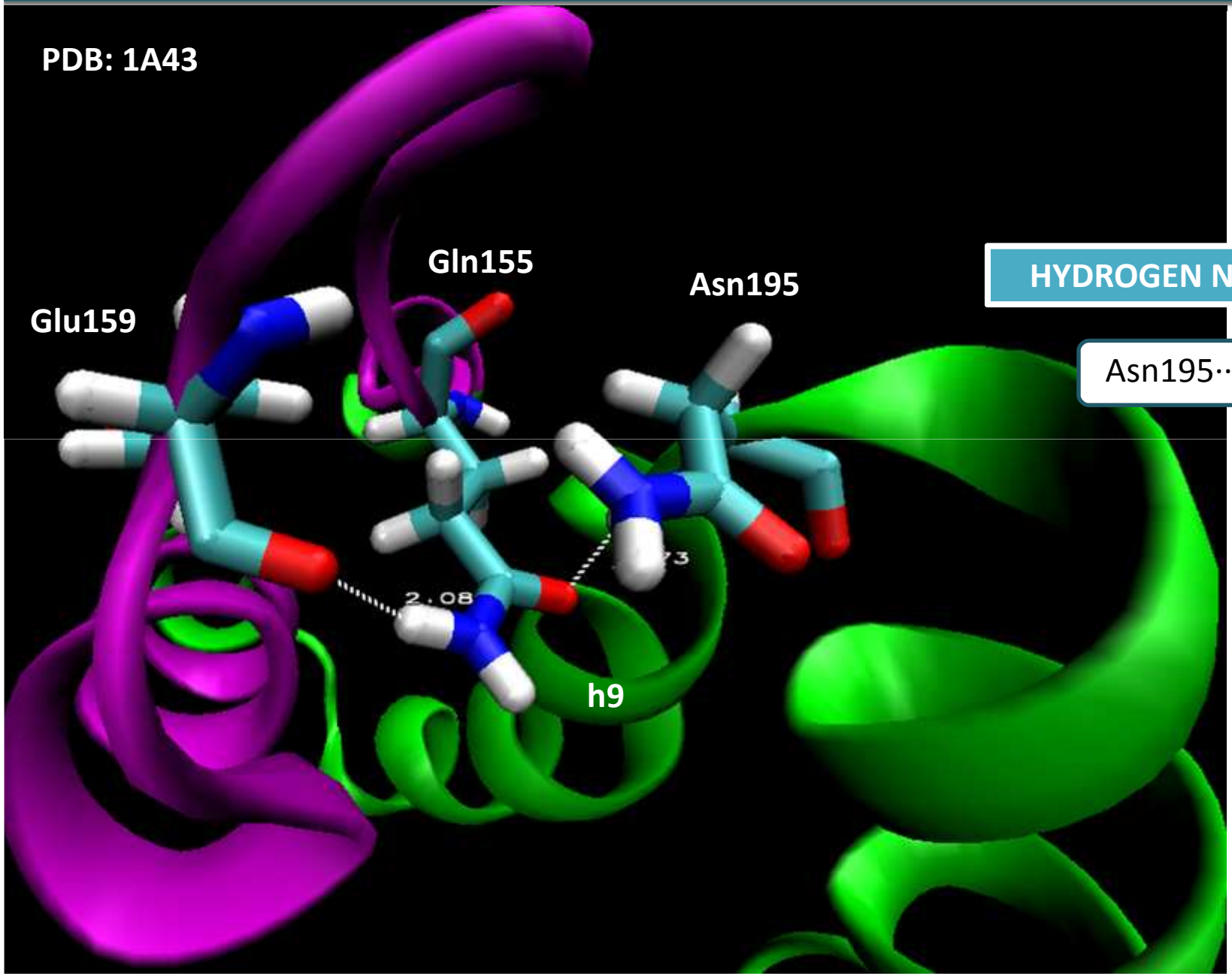
Major Homology Region

HYDROGEN NETWORK

Glu159···Gly156
Gln155···Glu159
Arg167···Glu159
Arg167···Glu159
Arg167···Arg154



2.2.Domini CTD



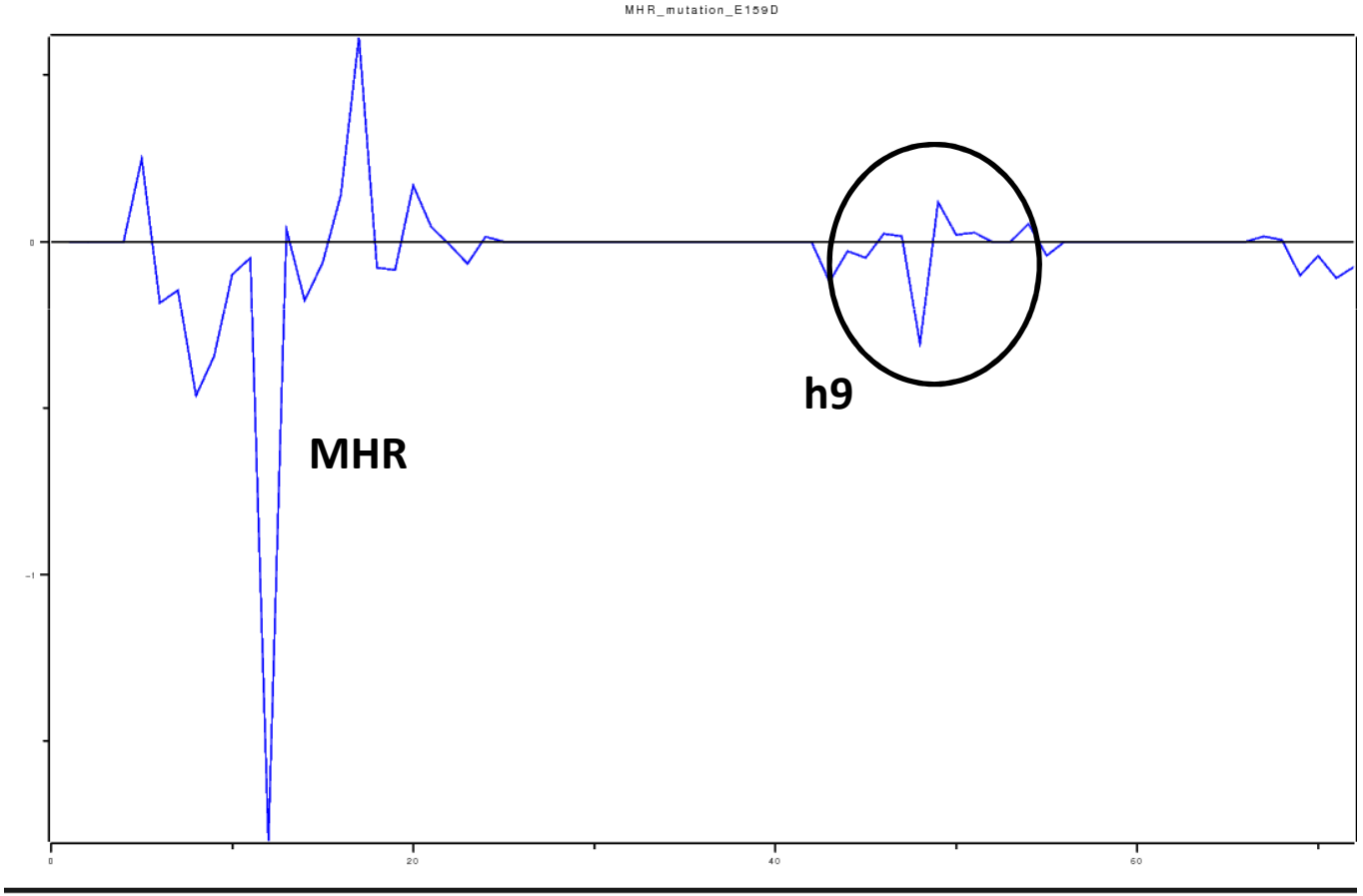
Major Homology Region

HYDROGEN NETWORK

Asn195···Gln155

2.2.Domini CTD

Mutació E159A

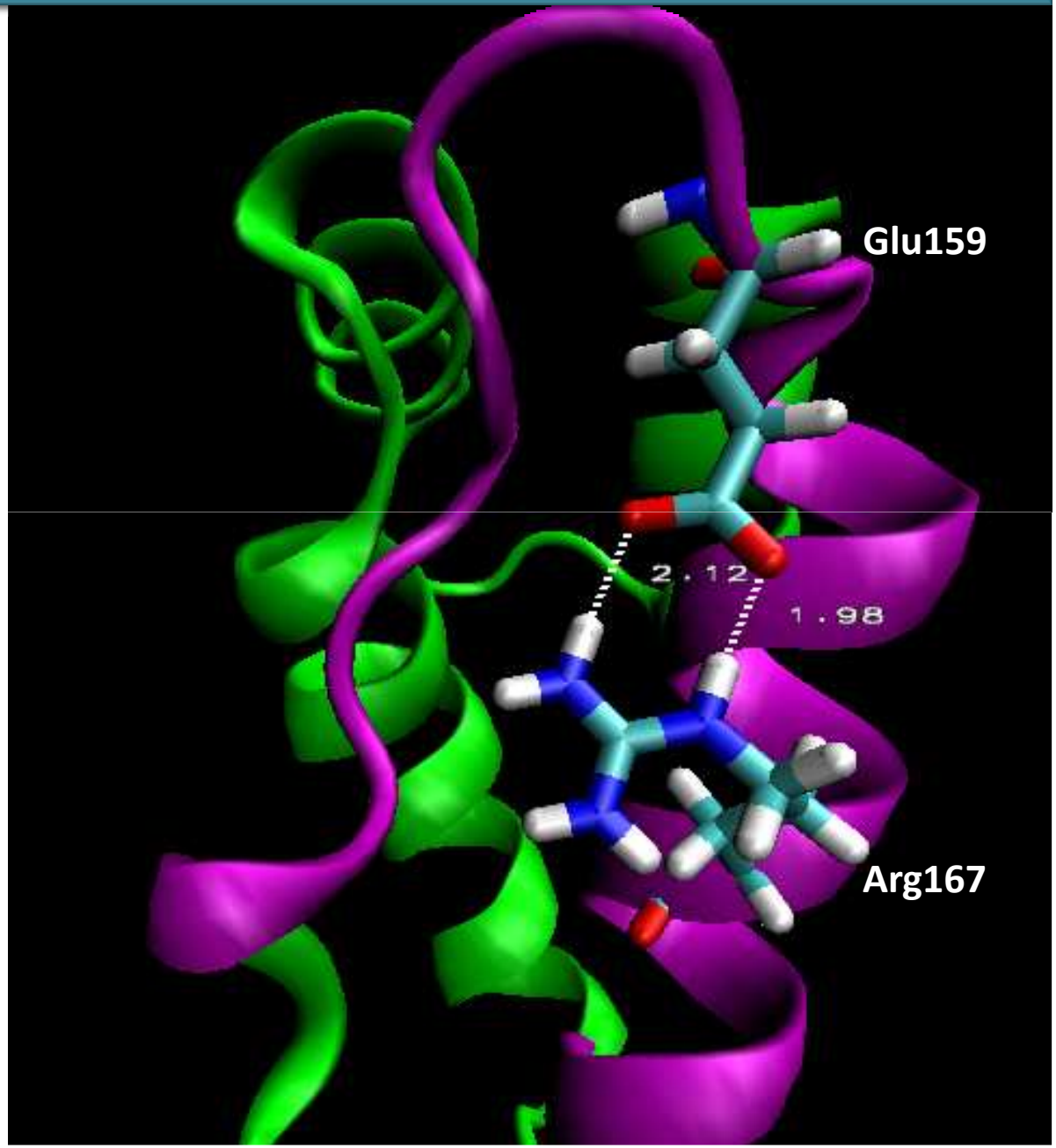


2.2.Domini CTD

Major Homology Region

SALT BRIDGE

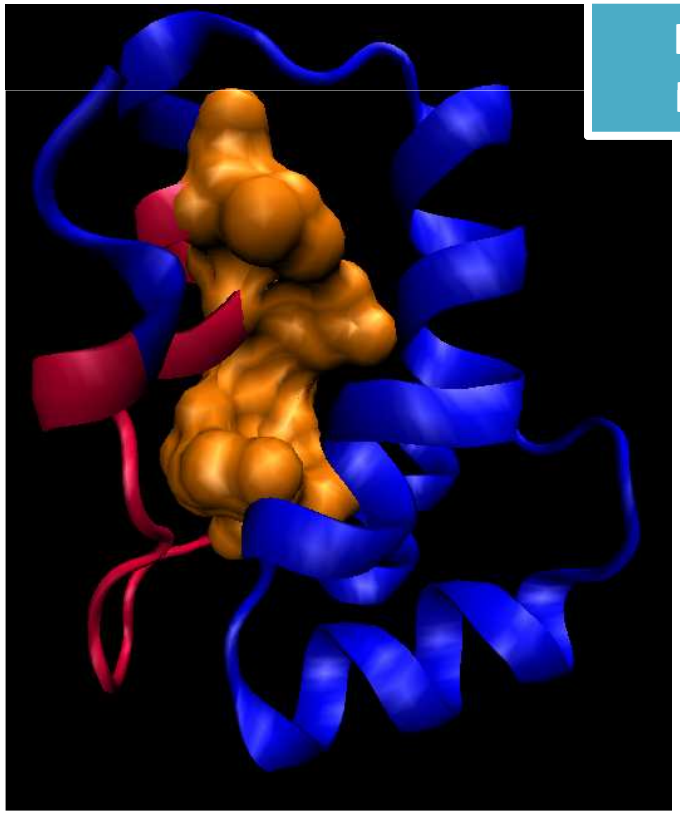
Arg167···Glu159



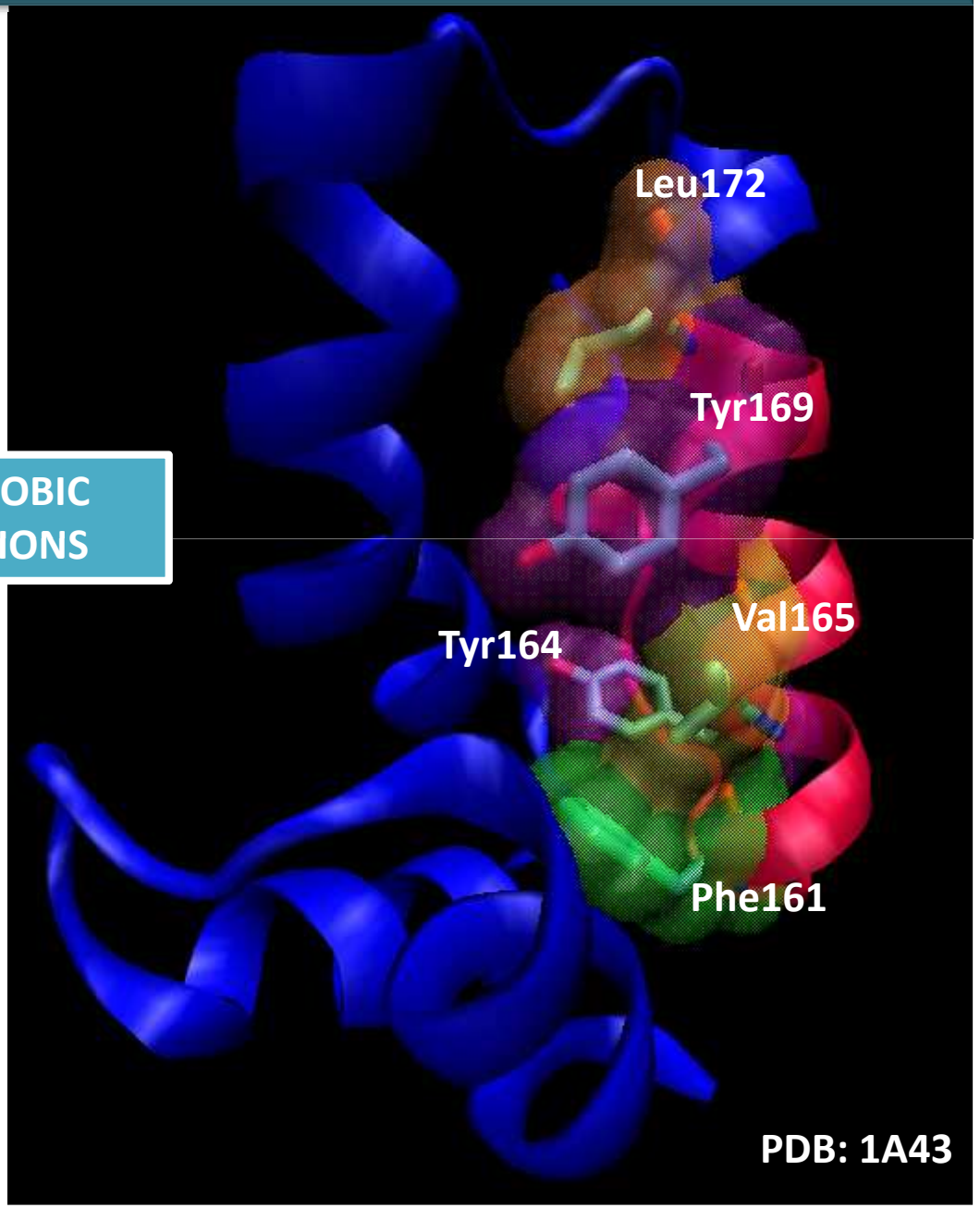
2.2.Domini CTD

Major Homology Region

Phe 161
Tyr 164/169
Val 165
Leu 172



HYDROPHOBIC INTERACTIONS



2.2.Domini CTD

Major Homology Region

Why is this region so conserved among retrovirus?

- The contribution of the **hydrogen network** to the dimerization between CTDs
- The participation of some of the residues to **NTD-CTD interactions**
- The hydrophobic residues of this region mediates the contacts in the **domain-swapped dimer** of the CTDs protein

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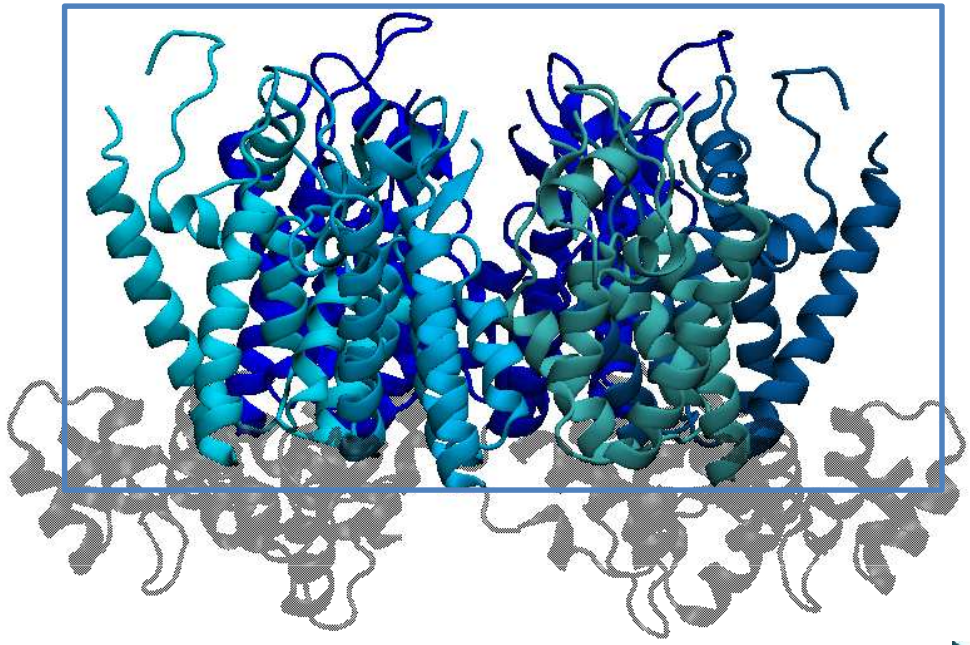
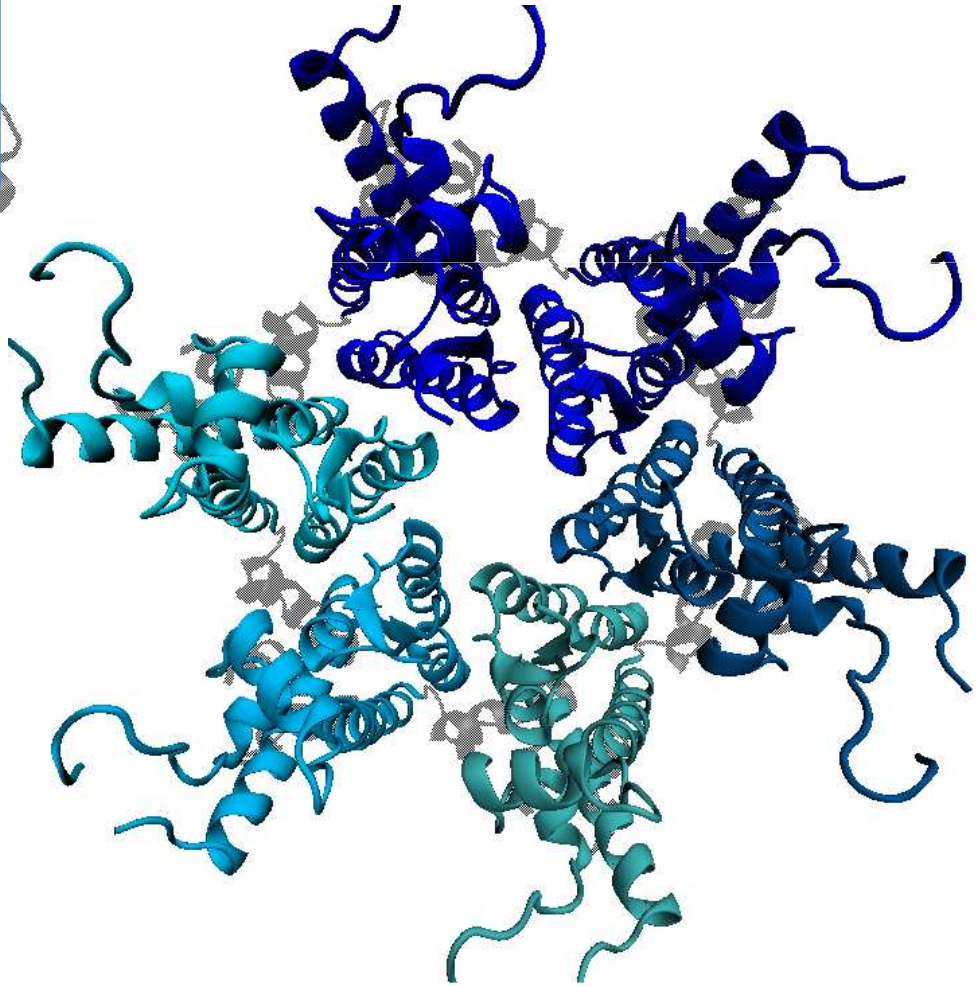
Capsid subunit



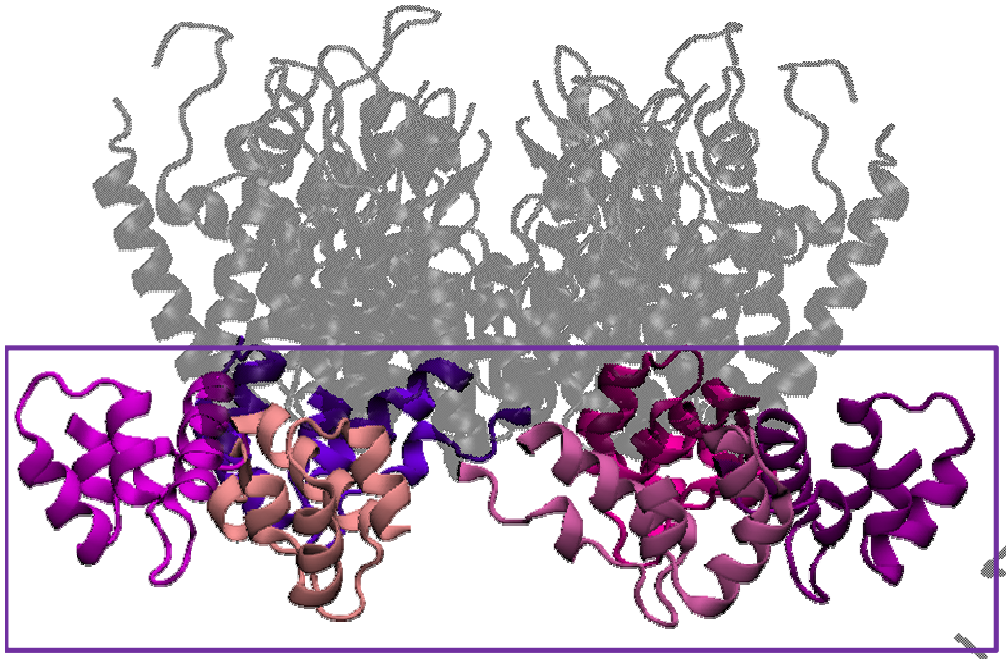
HEXAMERS:

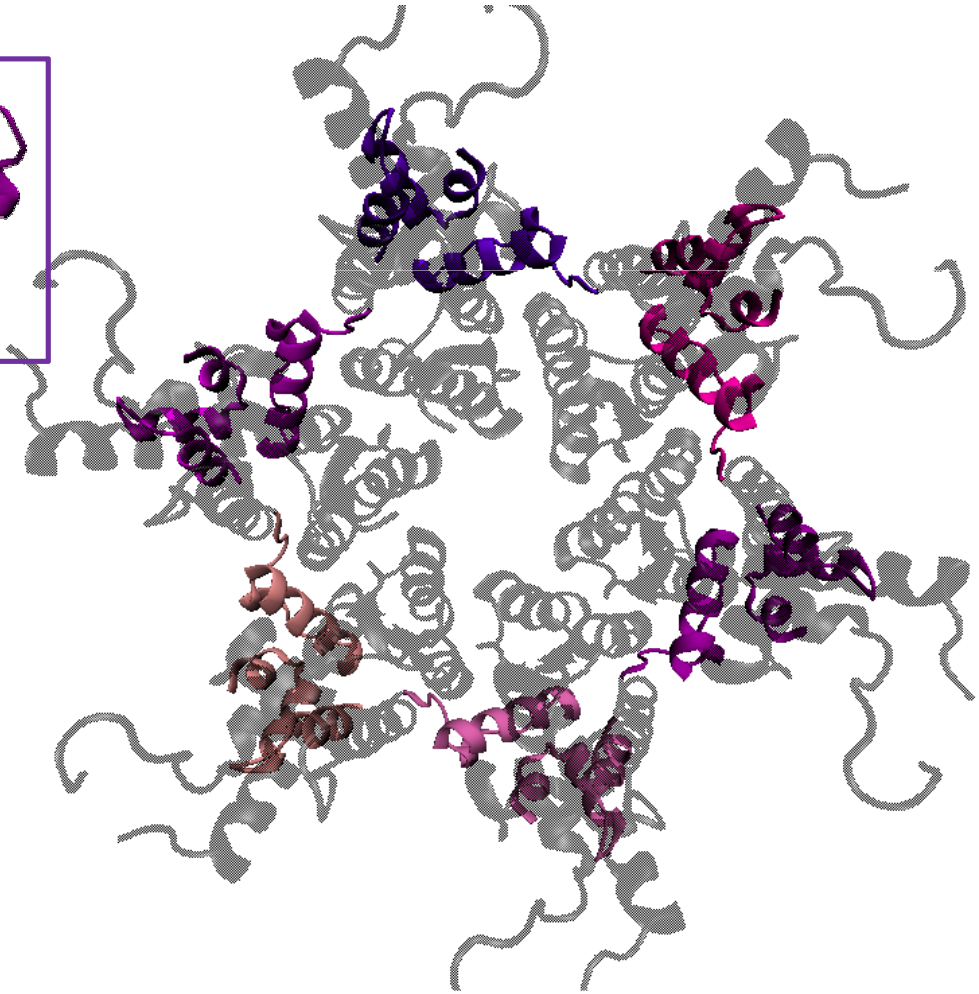


Hexamers are formed by six monomers such that form two rings.

NTDs domains form a ring on the top of hexamer

Capsid subunit

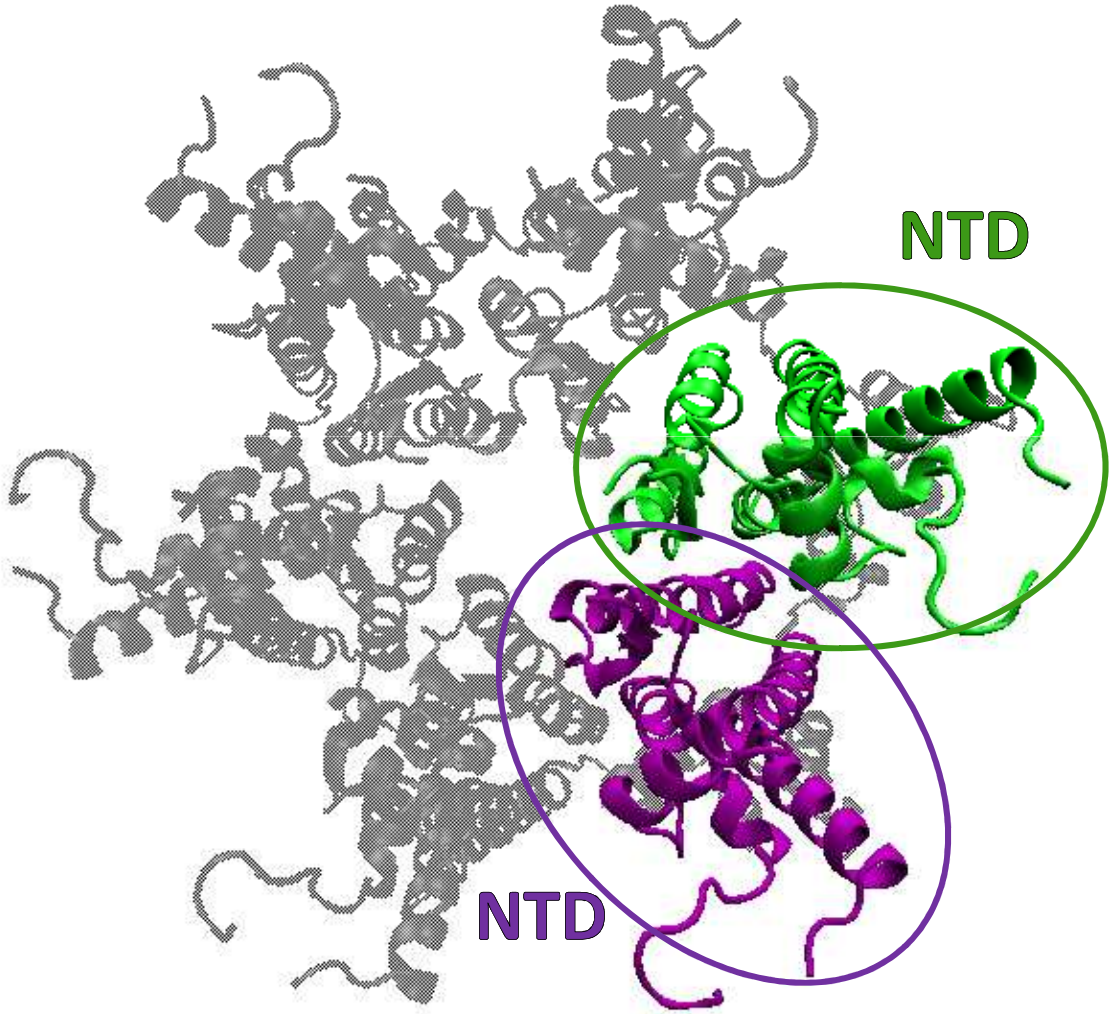




CTDs form a ring below the NTDs one.

Each CTD placed under following NTD

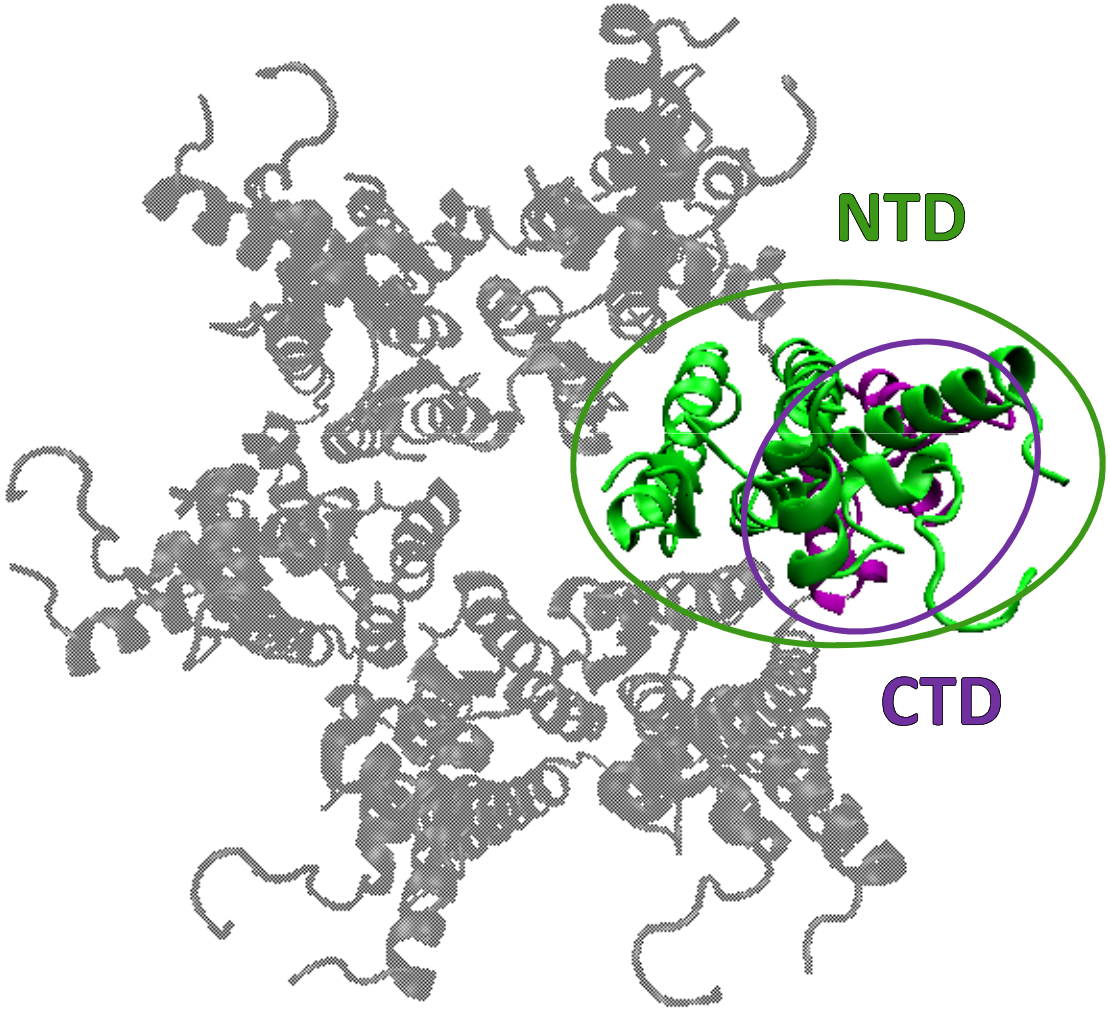
Capsid subunit



Capsid can be formed by three different types of interfaces:

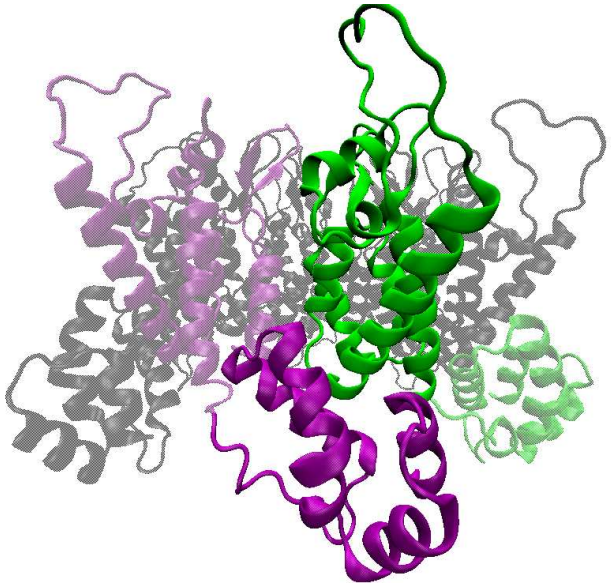
- NTD – NTD
- NTD – CTD
- CTD - CTD

Capsid subunit

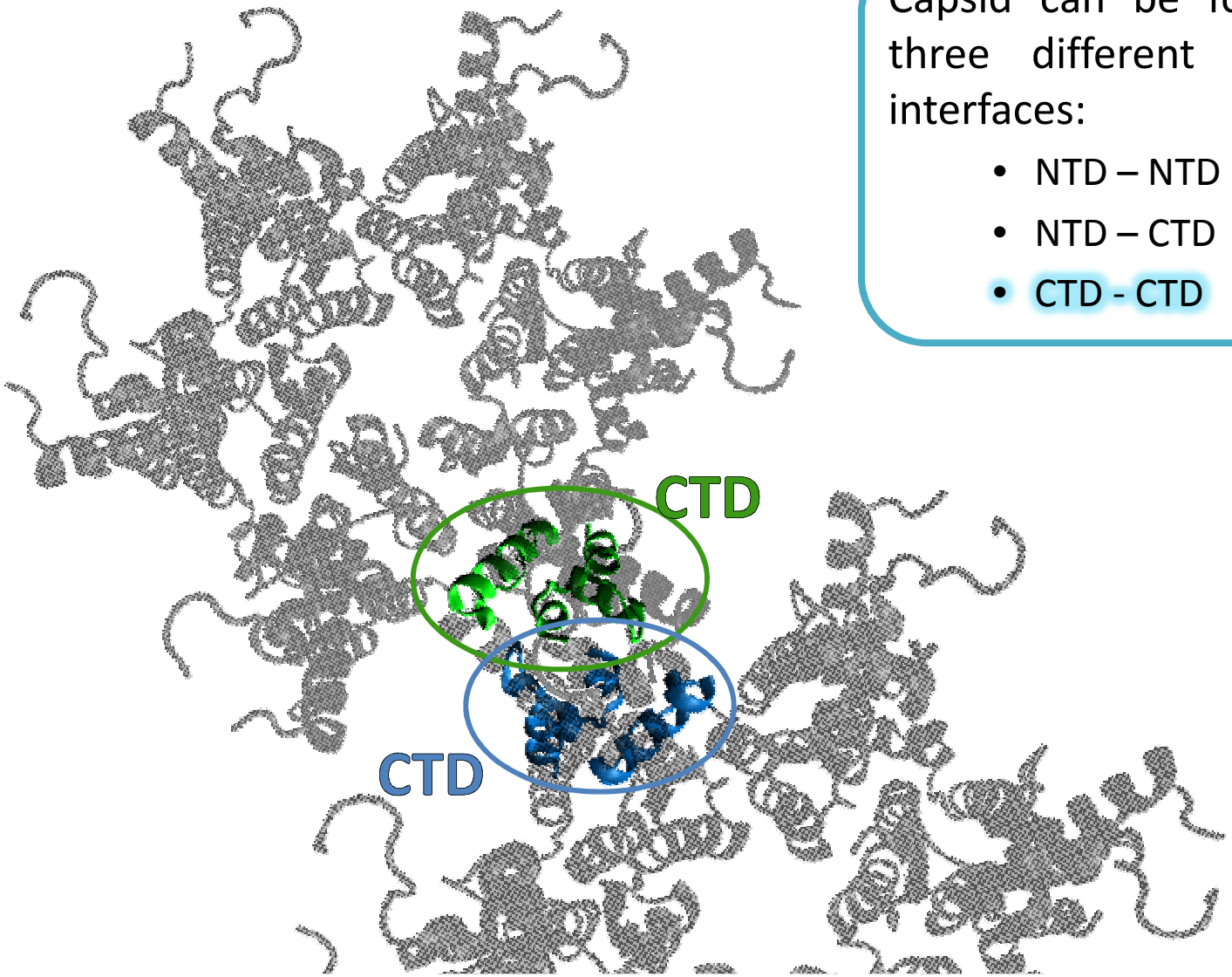


Capsid can be formed by three different types of interfaces:

- NTD – NTD
- NTD – CTD
- CTD - CTD



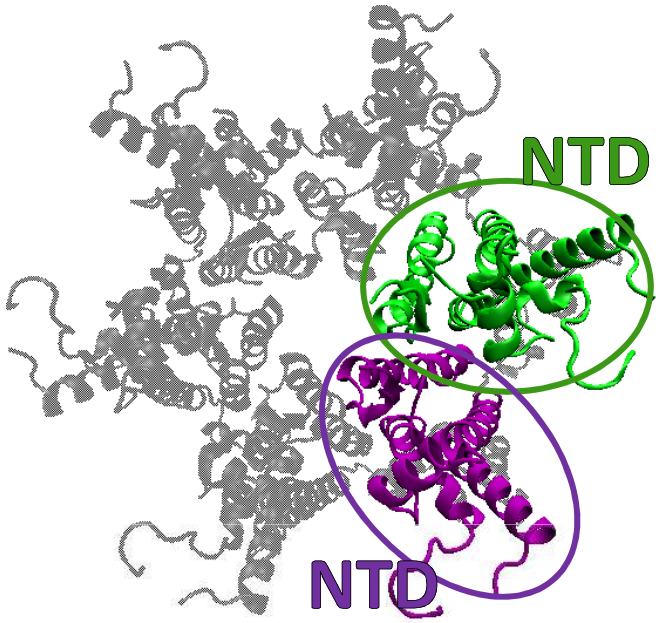
Capsid subunit

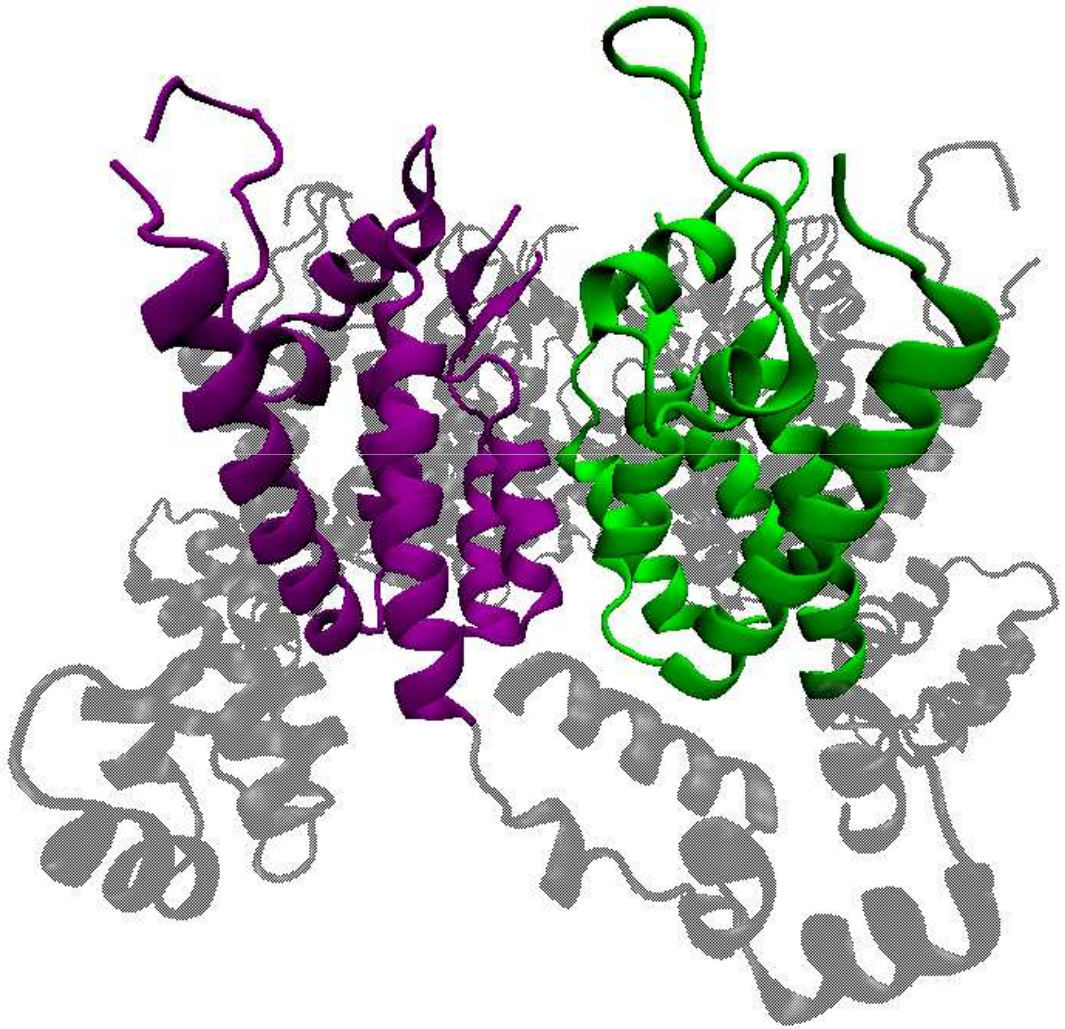


Capsid can be formed by three different types of interfaces:

- NTD – NTD
- NTD – CTD
- CTD - CTD

NTD-NTD interface

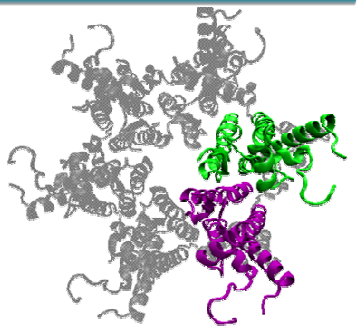


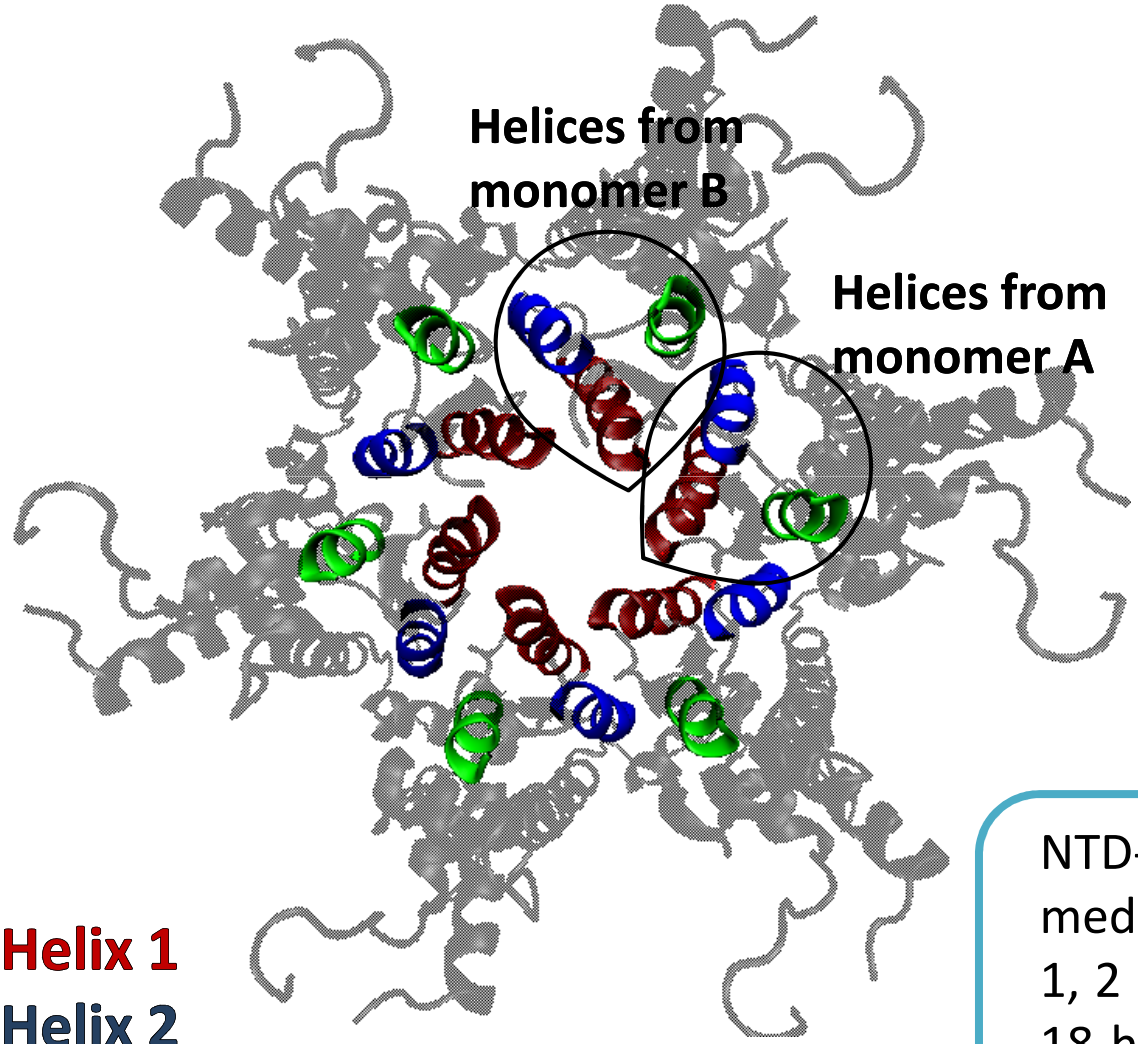


There are two kind of interactions:

- Hydrophobic contacts
- Polar (water mediated) contacts

NTD-NTD interface

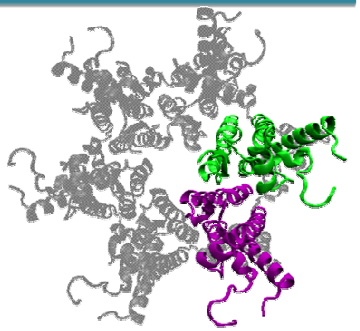


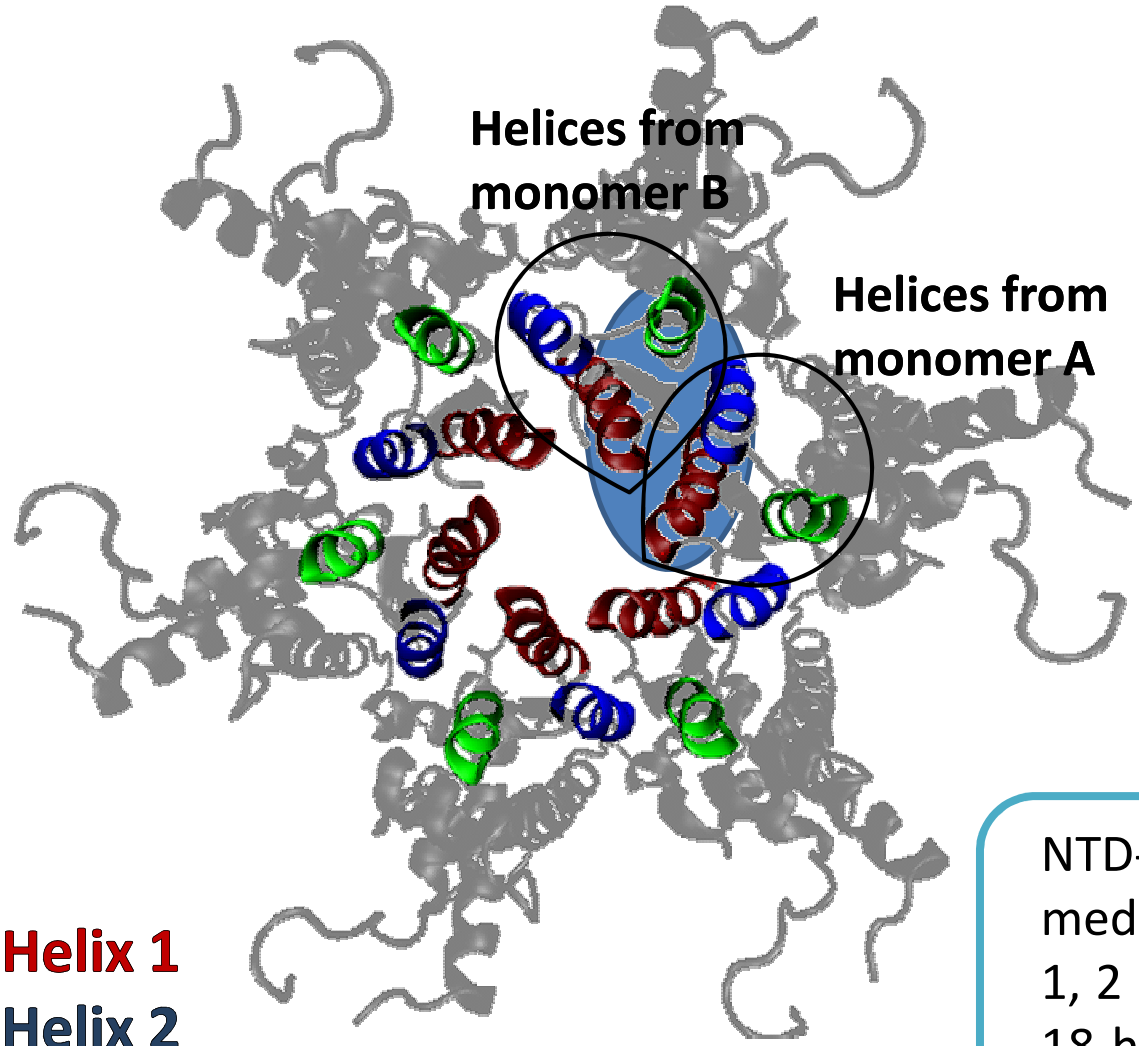


Helix 1
Helix 2
Helix 3

NTD-NTD interactions are mediated through helices 1, 2 and 3 (associate as an 18-helix bundle).

NTD-NTD interface



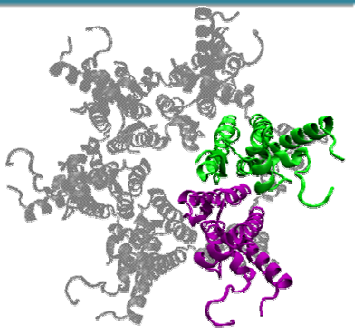


Helix 1
Helix 2
Helix 3

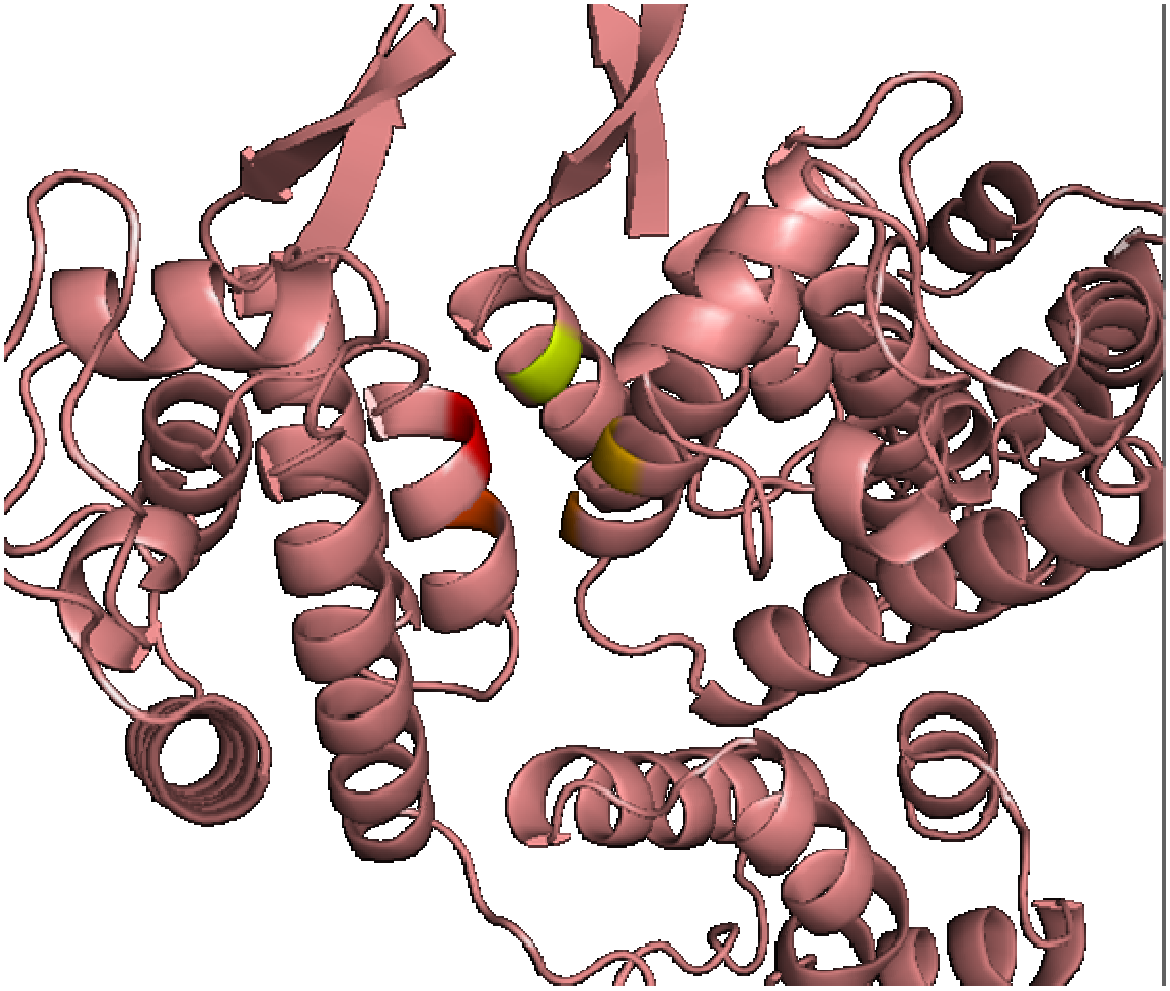
Contact interface

NTD-NTD interactions are mediated through helices 1, 2 and 3 (associate as an 18-helix bundle).

NTD-NTD interface



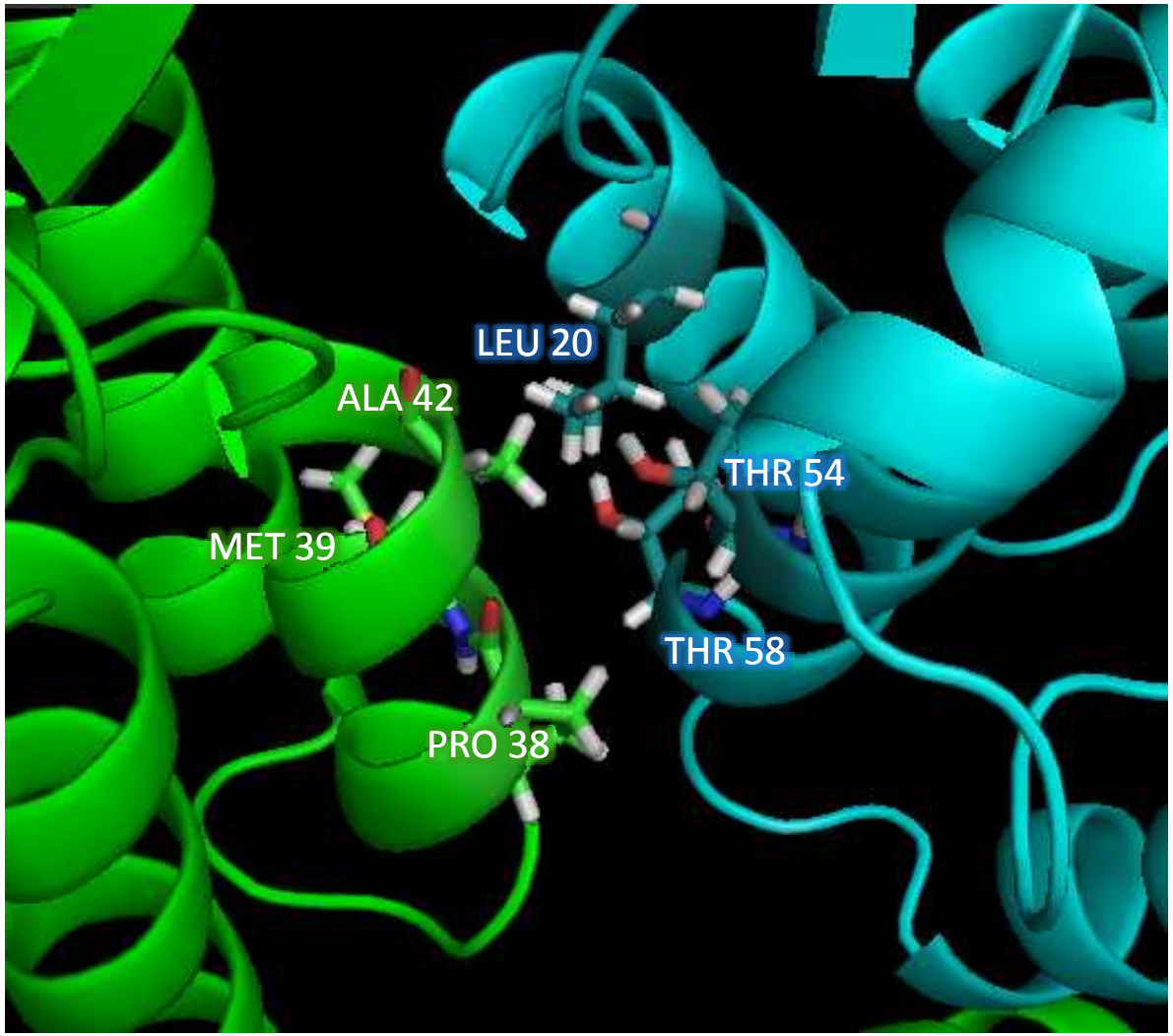
HYDROPHOBIC CONTACTS:

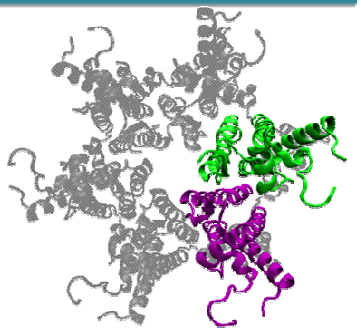


Residues in helix 2 and helices 1 and 3 form a hydrophobic core with aliphatic side chains.

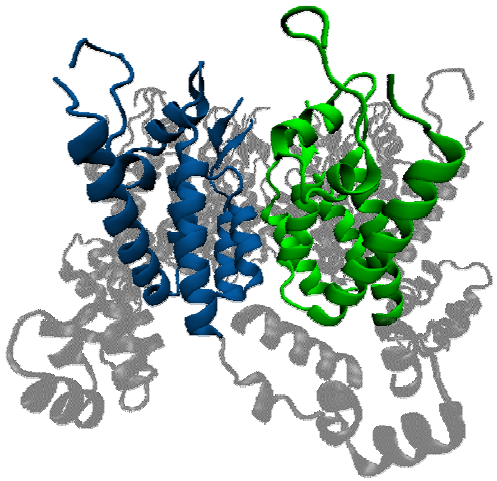
NTD-NTD interface

HYDROPHOBIC CONTACTS:



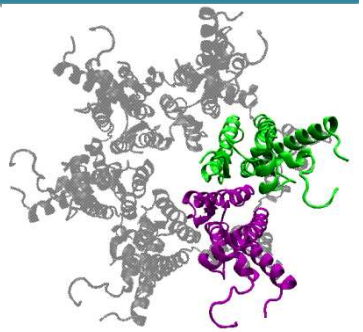


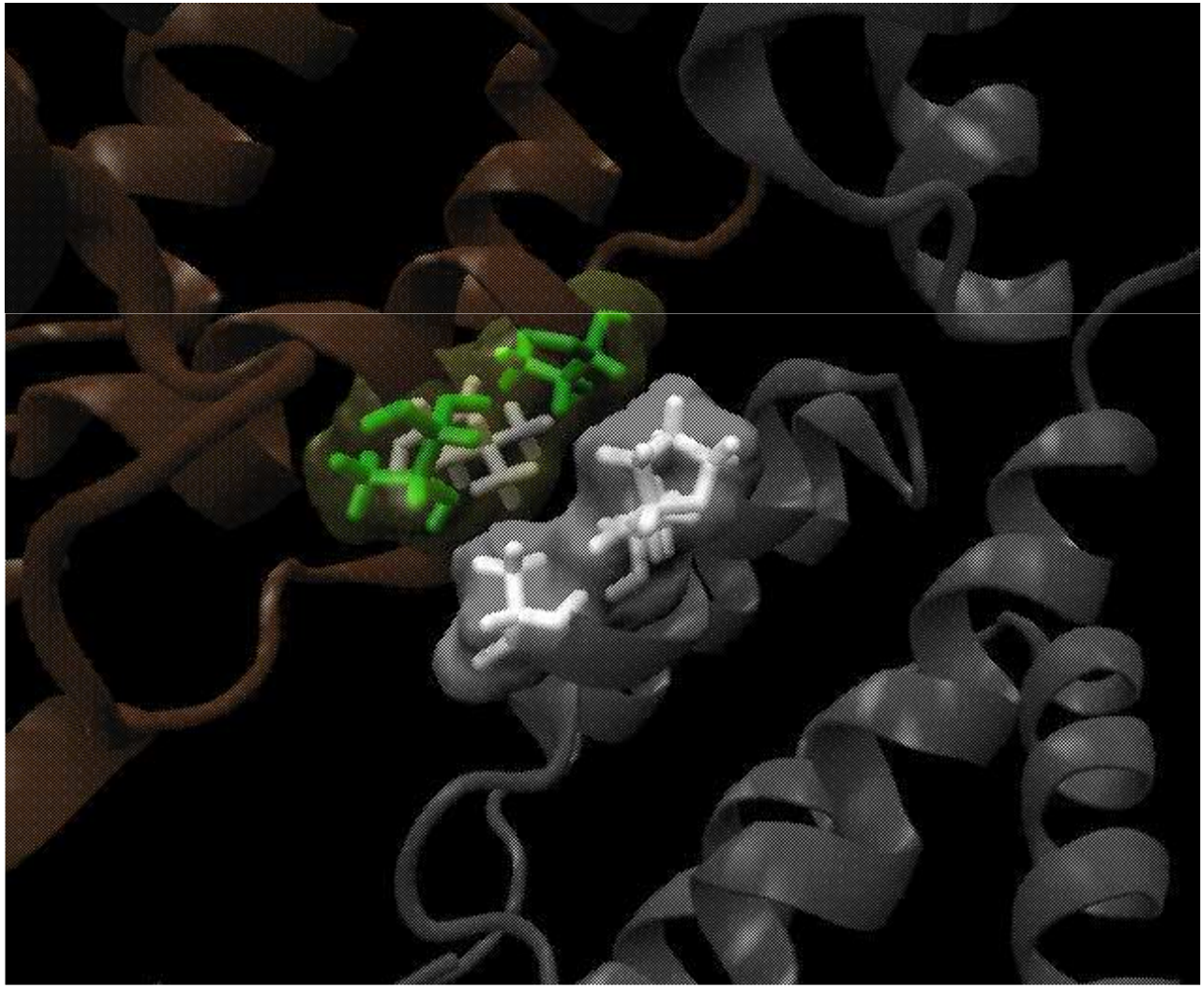
· A42, M39, P38 (helix 2)
· L20 (helix 1)
· T54 and T58 (helix 3)

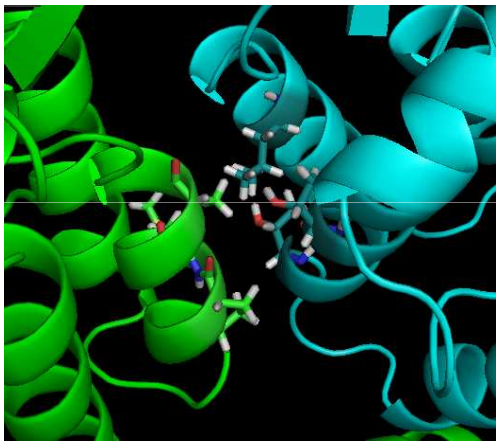


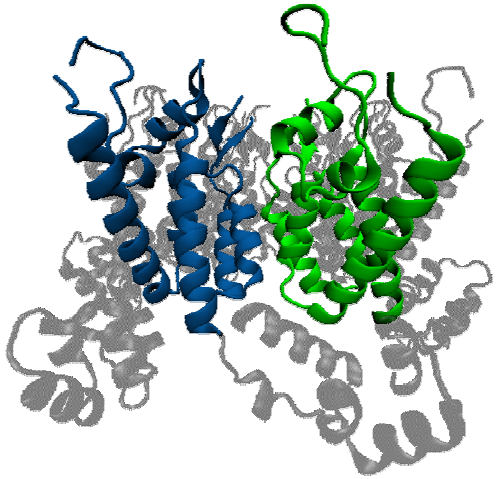
NTD-NTD interface

HYDROPHOBIC CONTACTS:





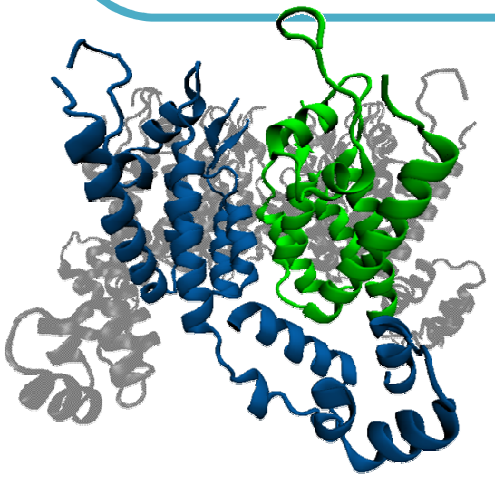


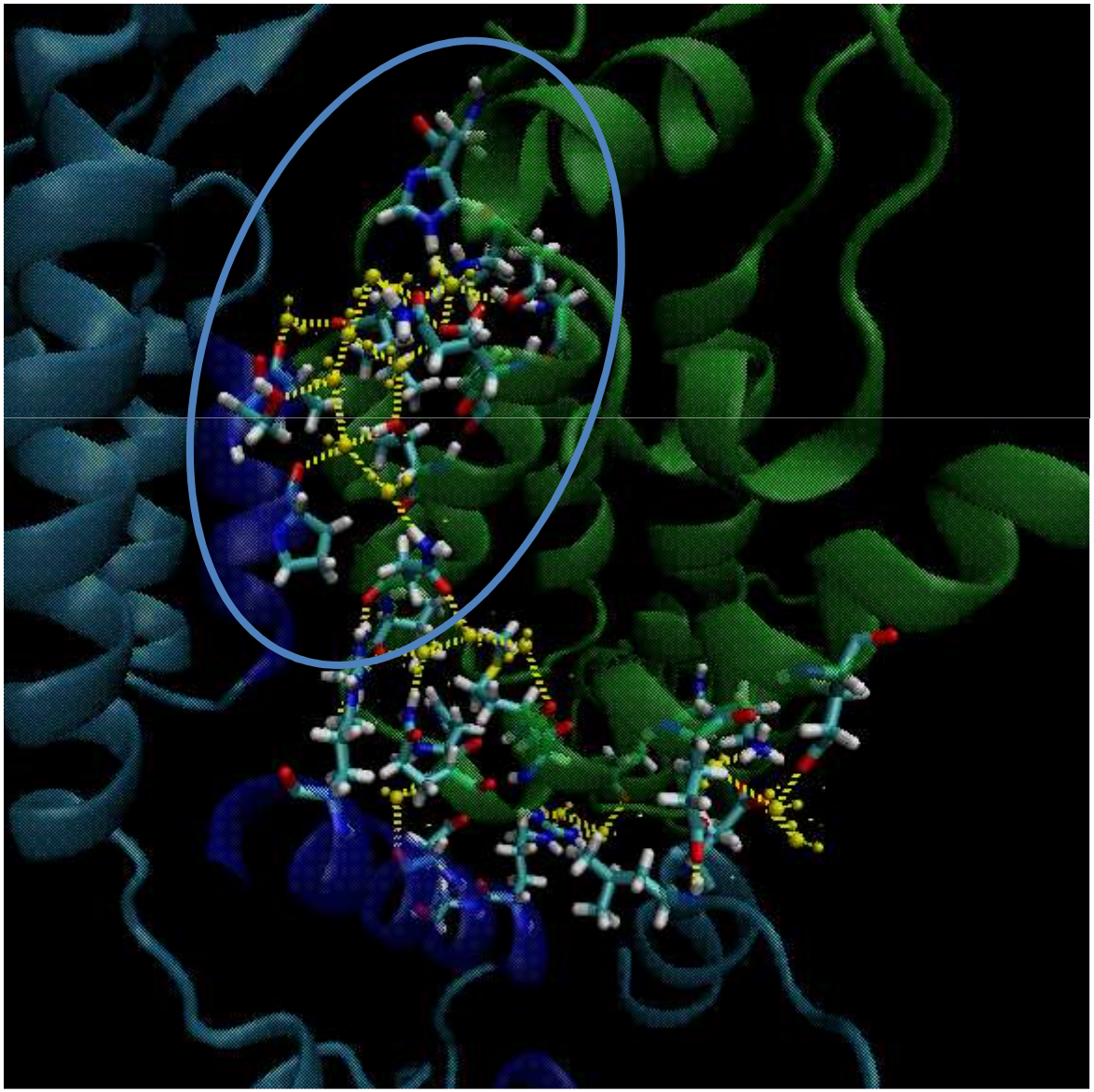


NTD-NTD interface

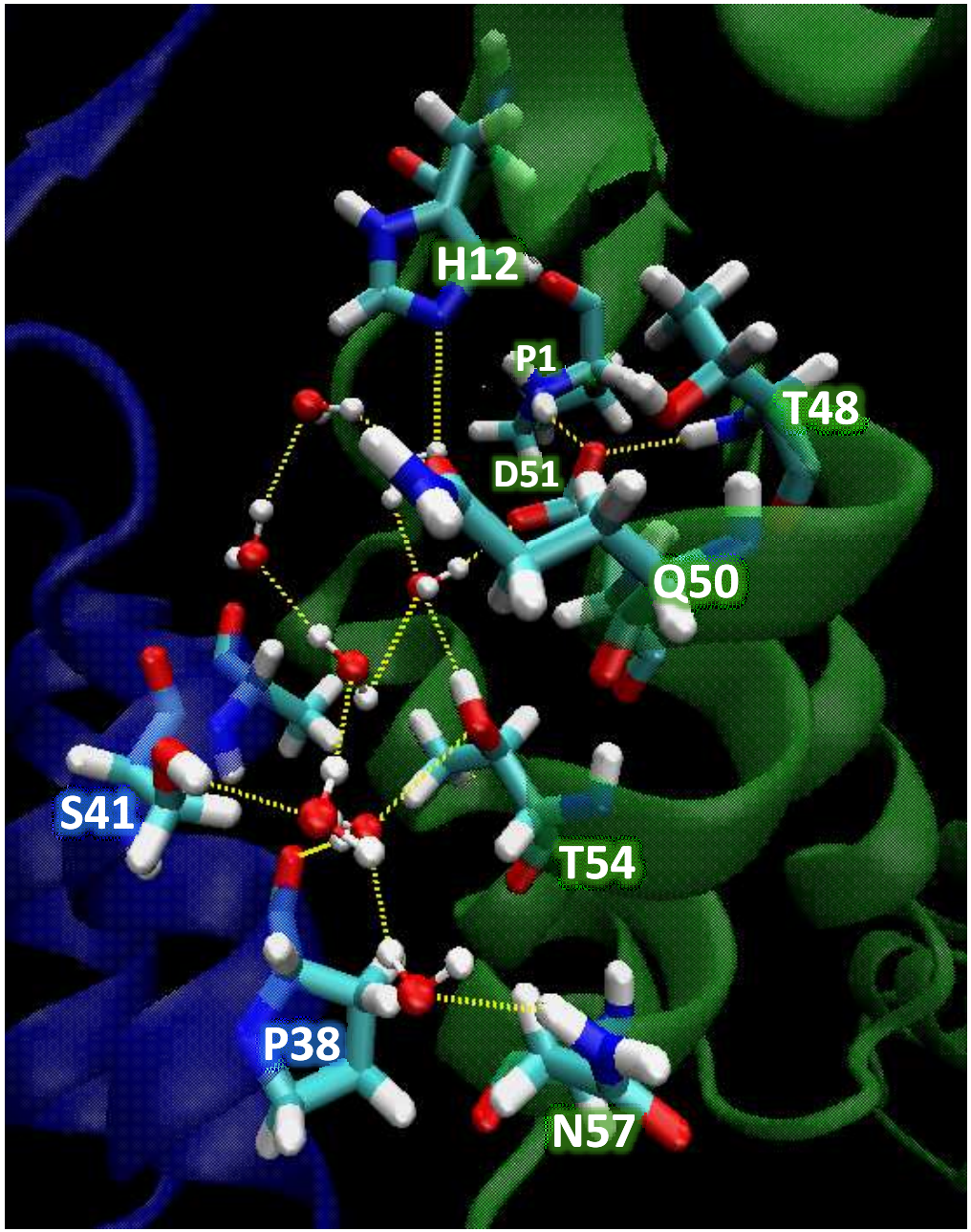
POLAR CONTACTS: Water mediated.

The most relevant interactions are polar contacts. Most of them are water mediated. We would find them both in NTD – NTD as CTD – NTD interfaces.



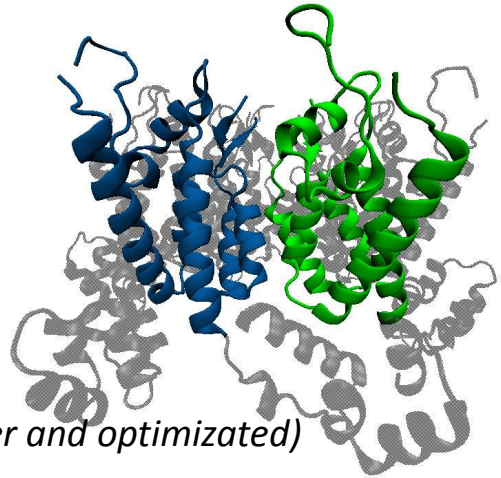


NTD-NTD interface



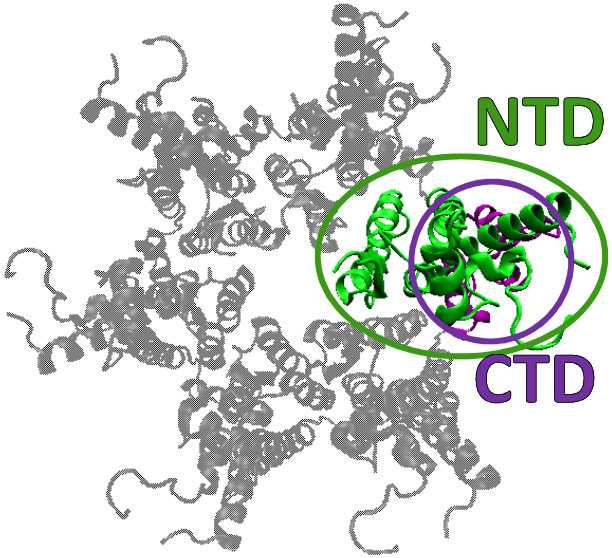
POLAR CONTACTS: Water mediated.

- Residues that are involved in water mediated contacts:
  - P1
  - H12
  - P38
  - S41
  - T48
  - Q50
  - D51
  - T54
  - N57



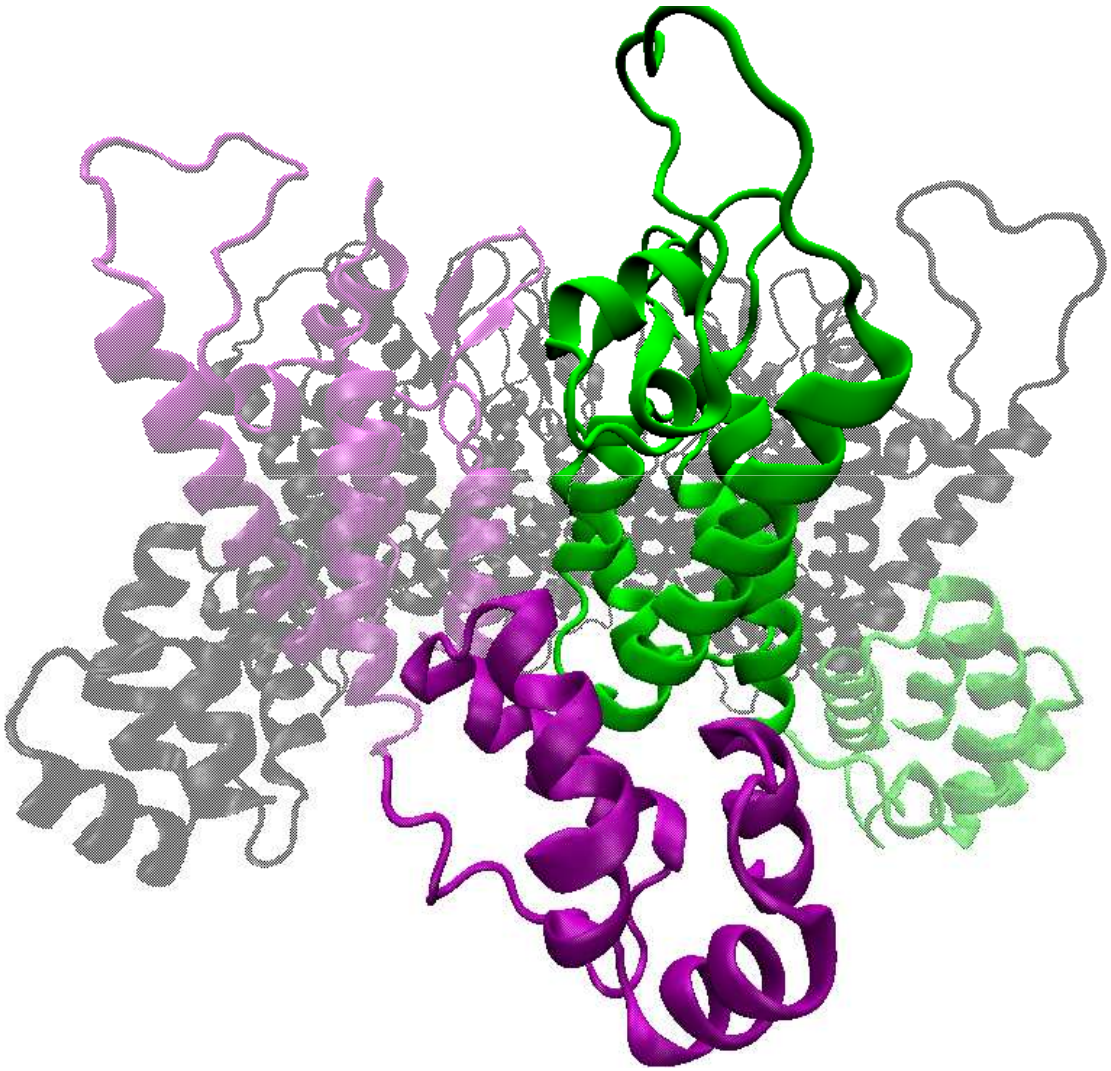
Pdb: 3H47 (added water and optimizated)

NTD-CTD interface



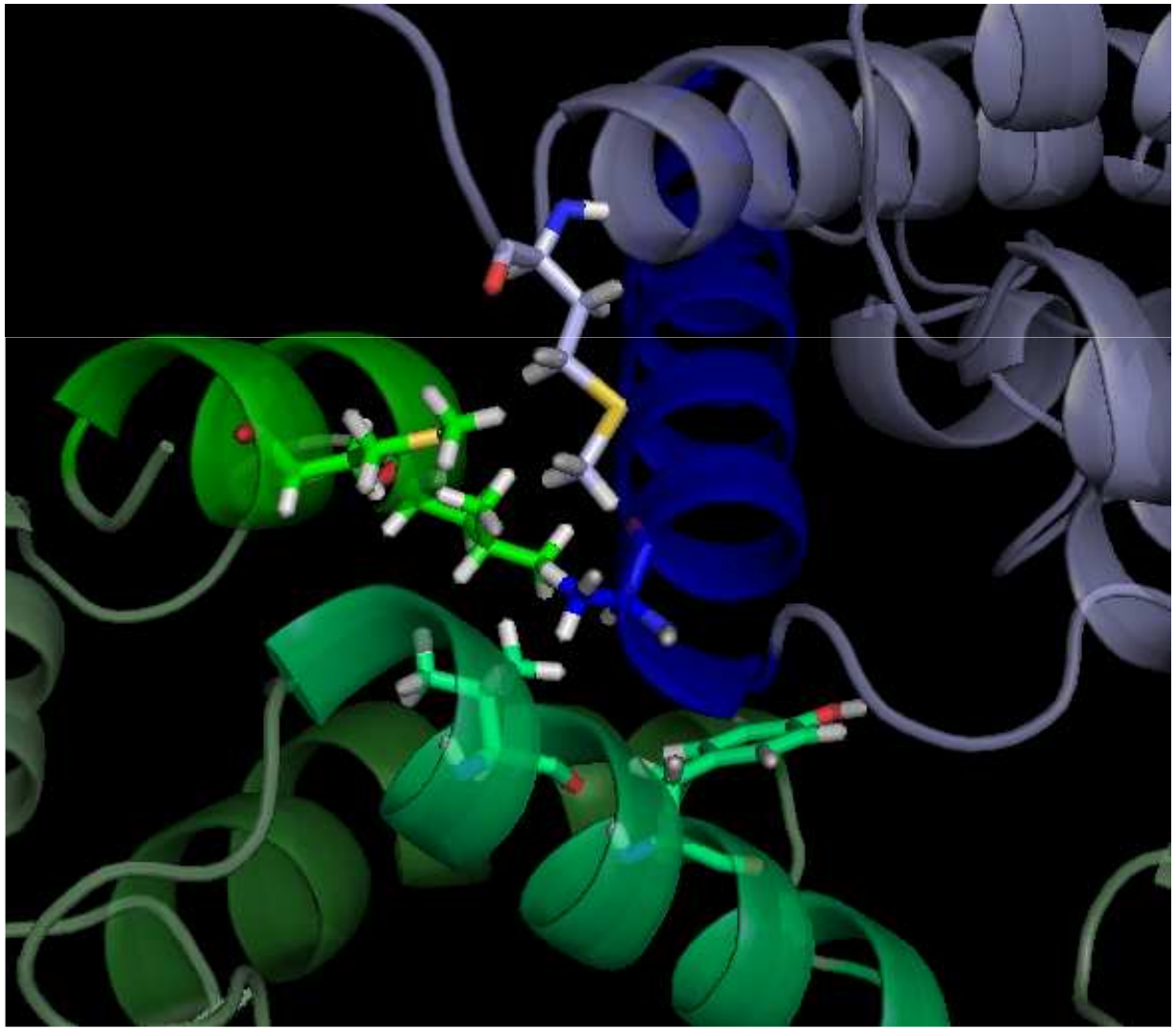
There are three kind of interactions:

- Hydrophobic
- Polar (water mediated)
- Helix capping

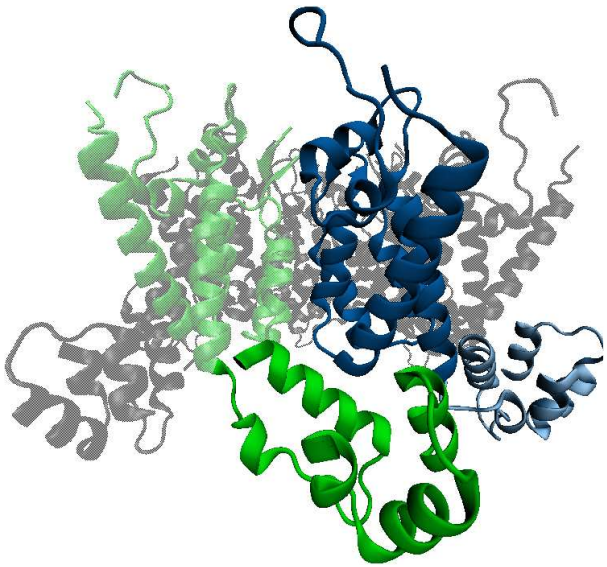


NTD-CTD interface

HYDROPHOBIC CONTACTS:

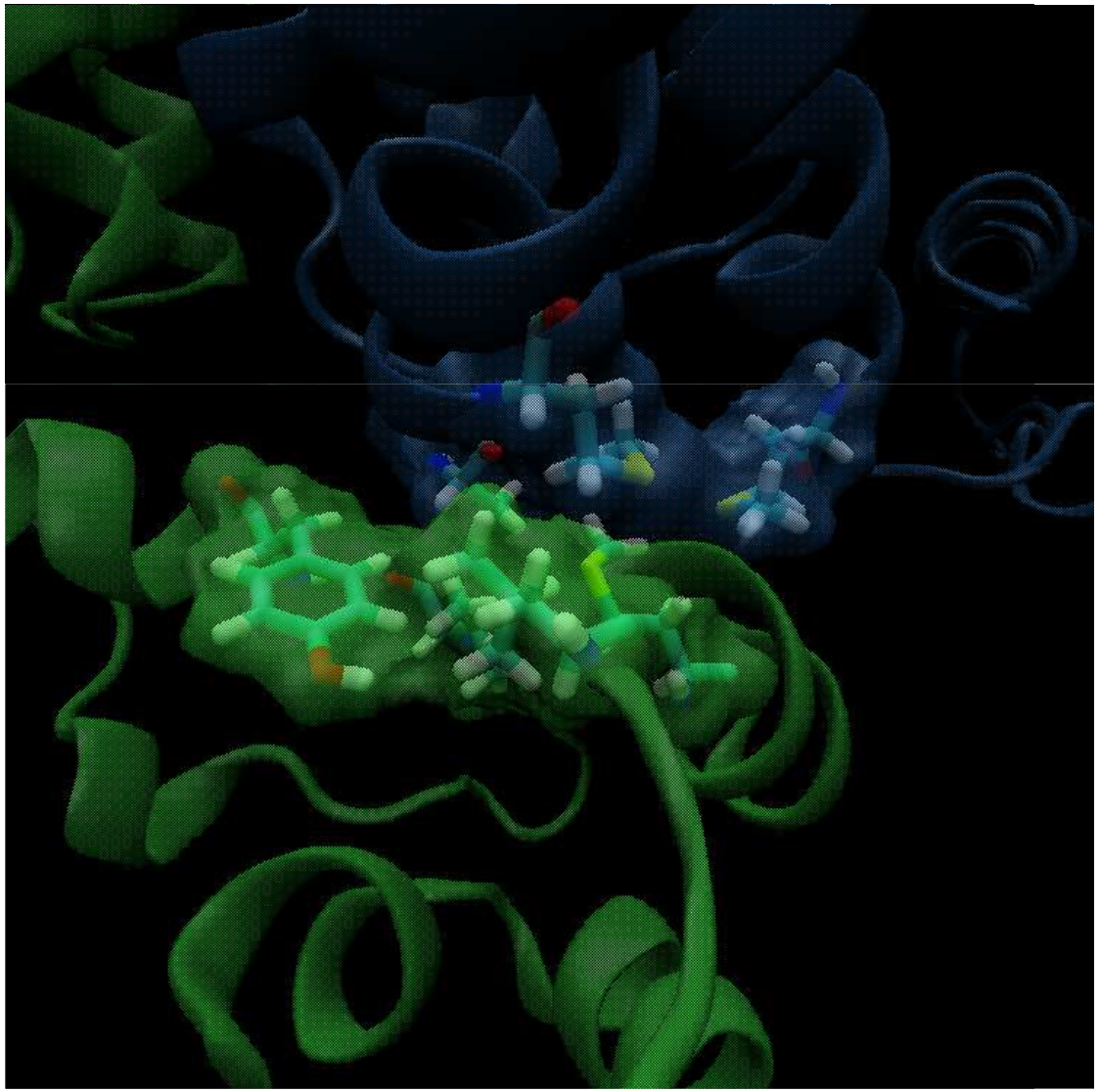


Residues on helix 4 (blue) and helices 8 and 11 (green) are involved in hydrophobic core formation.



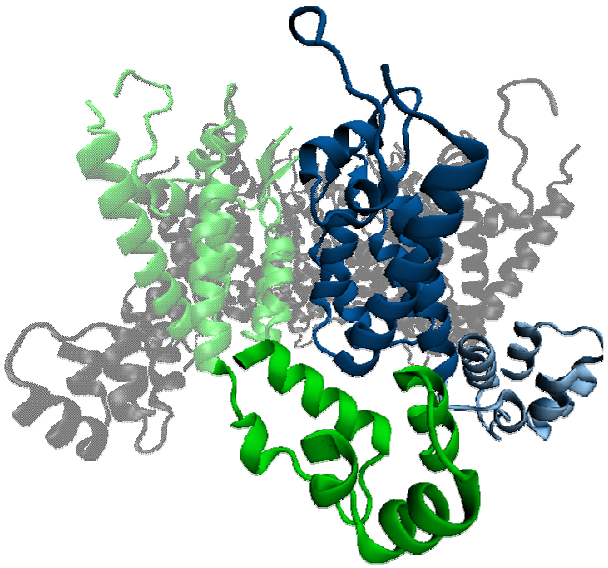
NTD-CTD interface

HYDROPHOBIC CONTACTS:



Residues that are involved:

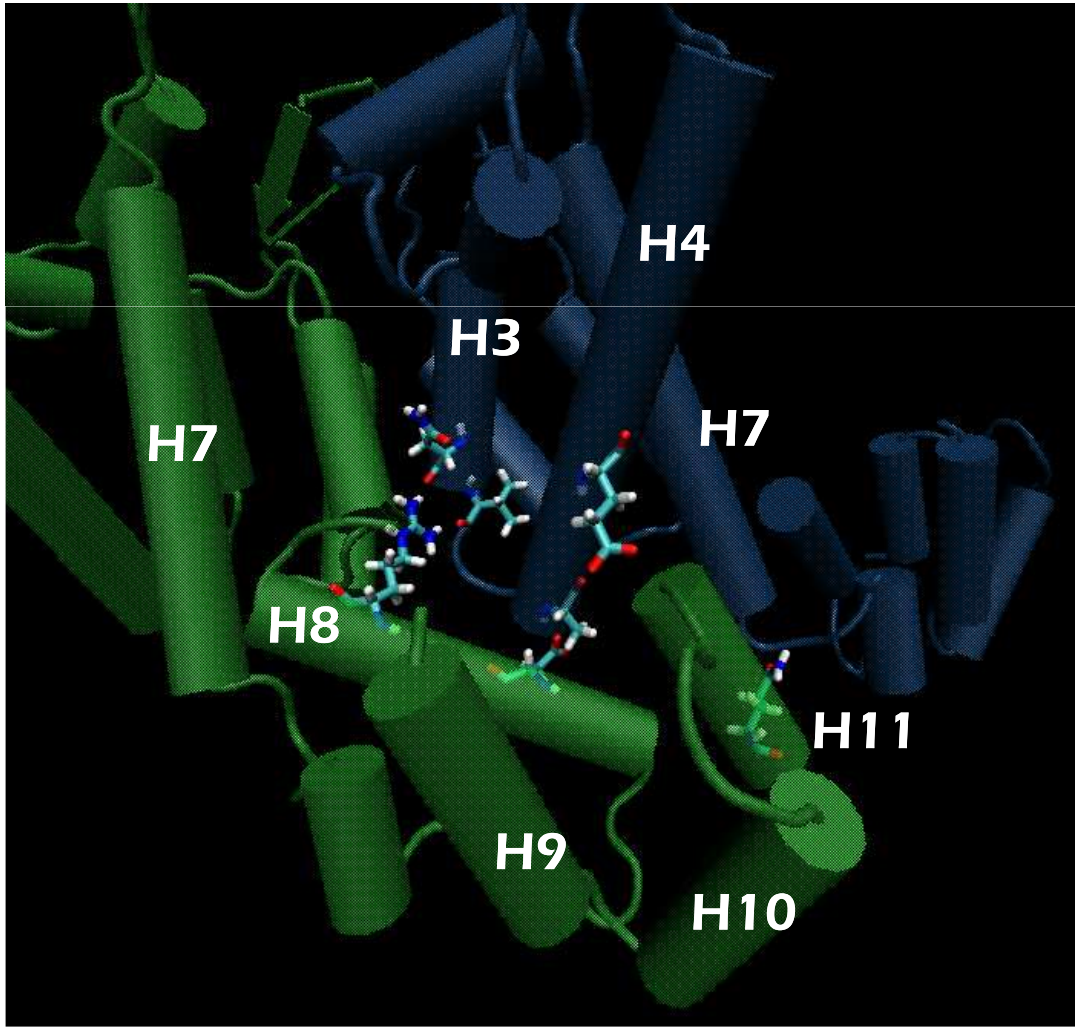
Y169	A64
V165	M68
M215	M144
L211	



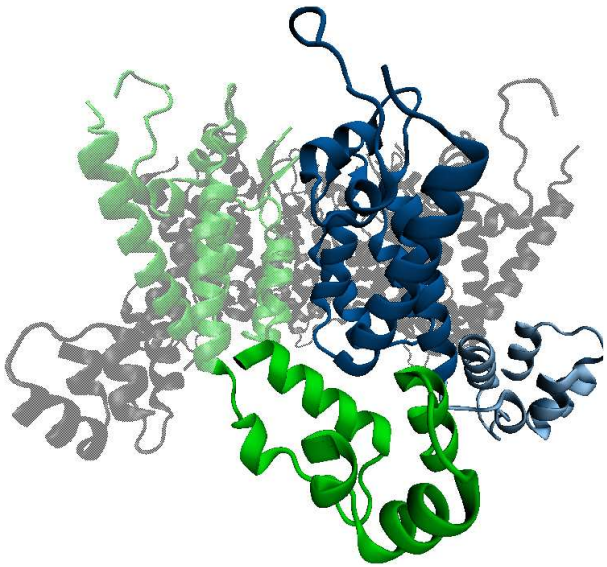
NTD-CTD interface

POLAR AND WATER MEDIATED CONTACTS:

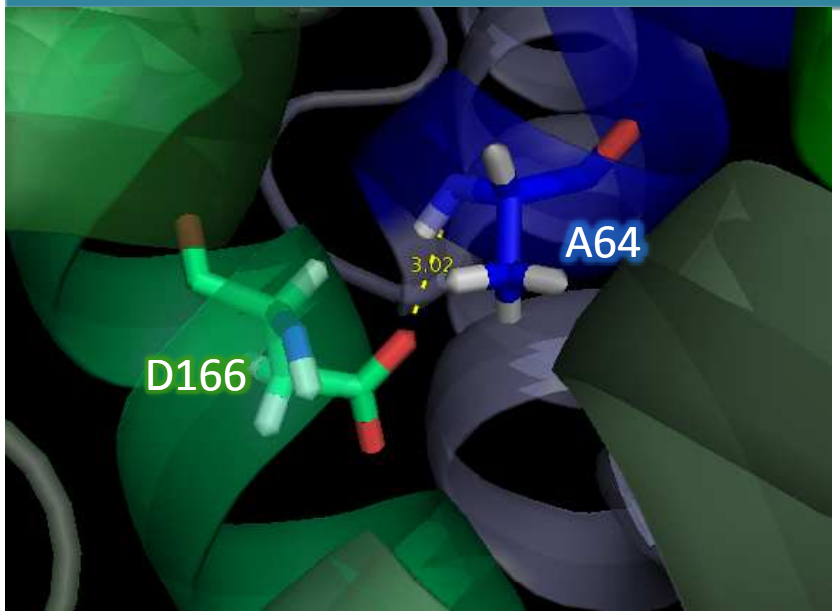
- Capping interactions

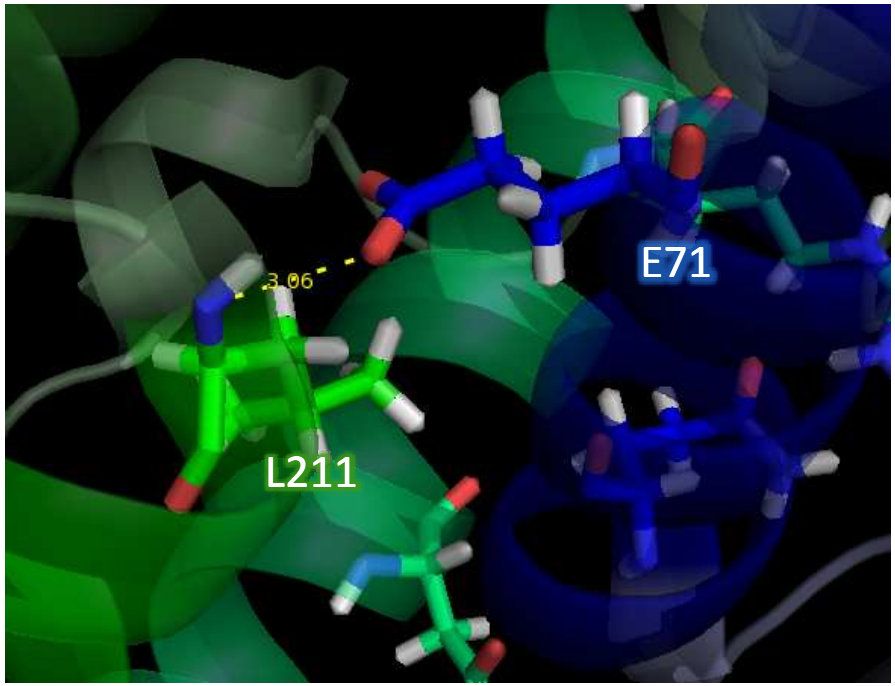


Capping interactions are the most important ones.
A side chain from a residue interact with the last residue from a helix (cap residue).



NTD-CTD interface





POLAR AND WATER MEDIATED CONTACTS:

- Capping interactions

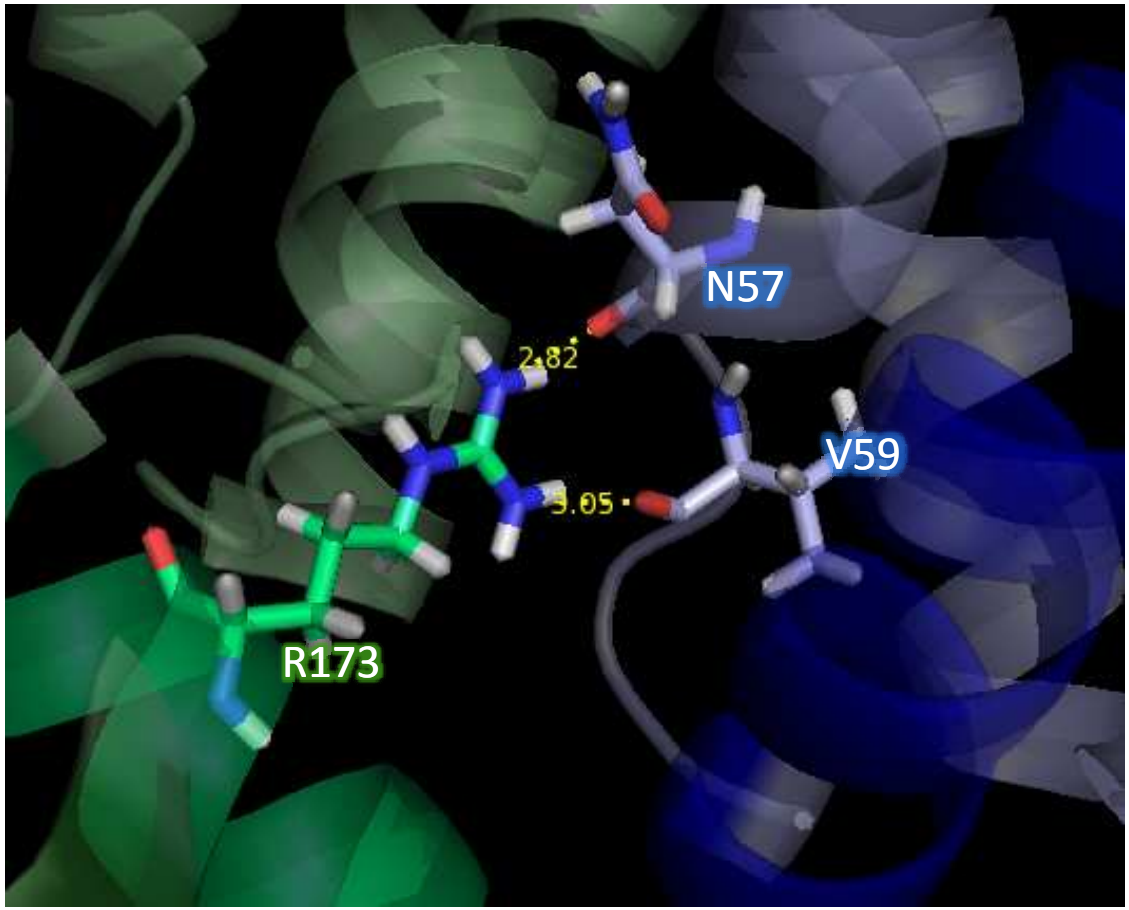
- E71 – L211
- A64 – D166
- N57 + V59 – R173

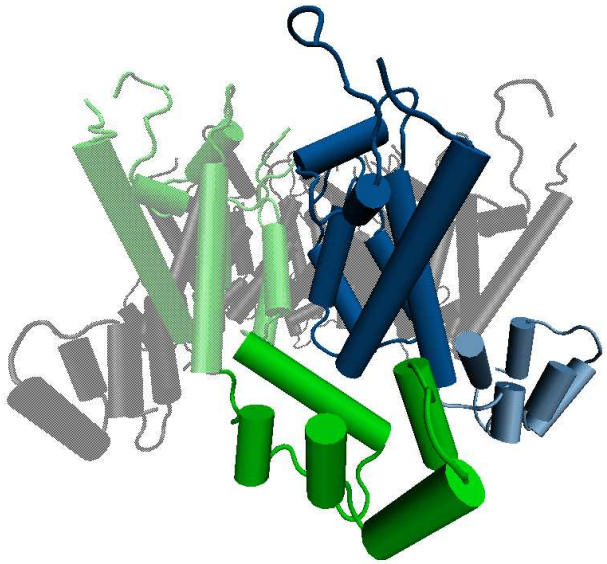
NTD-CTD interface

POLAR AND WATER MEDIATED CONTACTS:

- Capping interactions

- E71 – L211
- D166 – A64
- R173 – N57 + V59

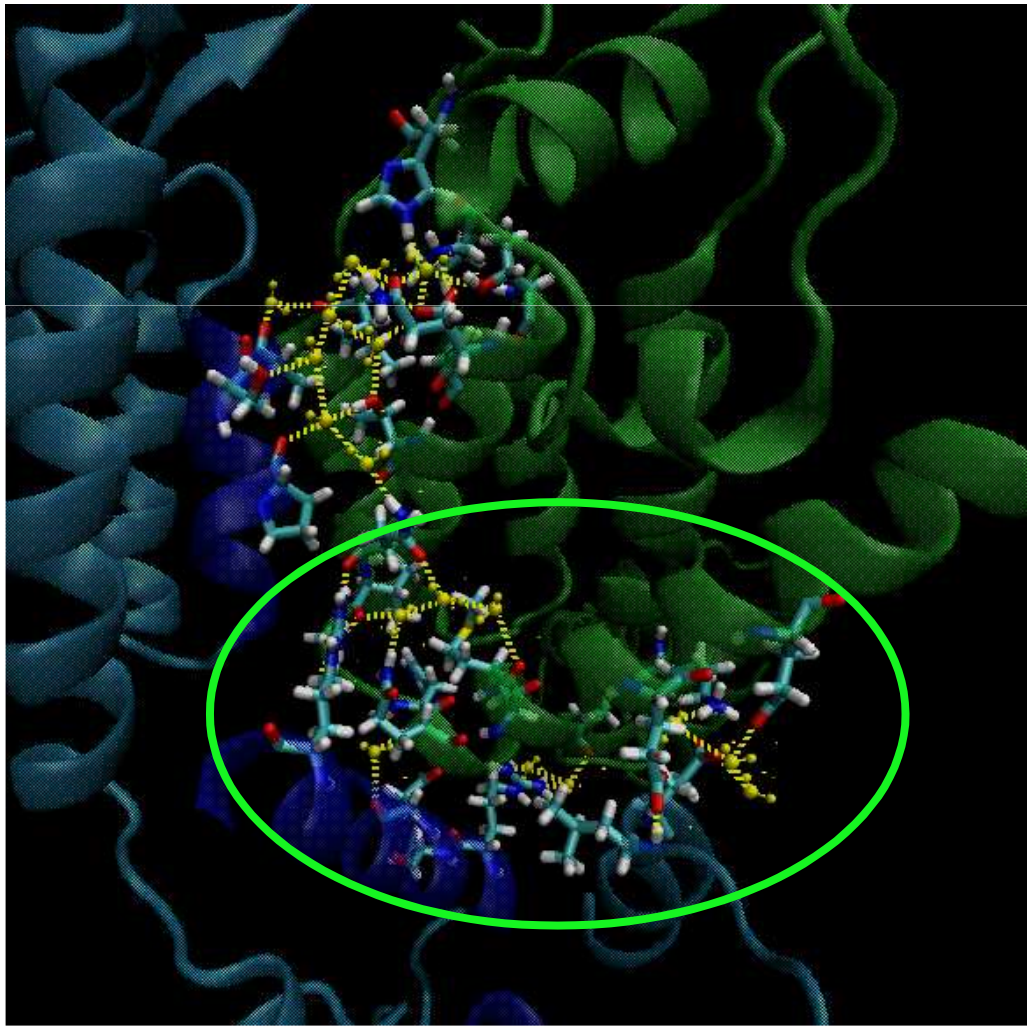




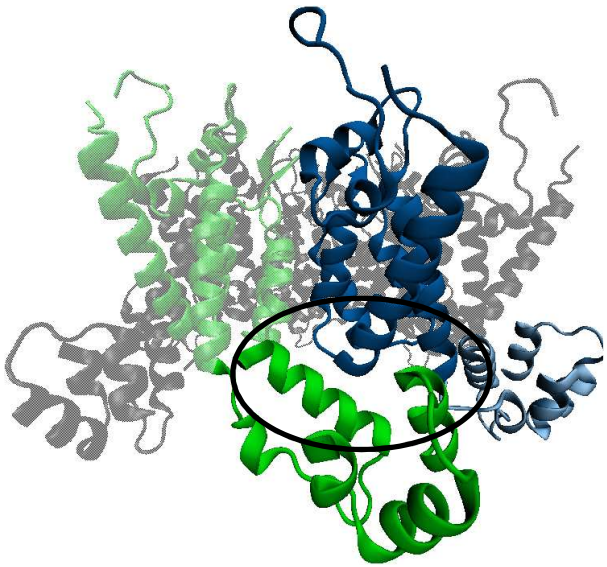
NTD-CTD interface

POLAR AND WATER MEDIATED CONTACTS:

- Water mediated contacts:



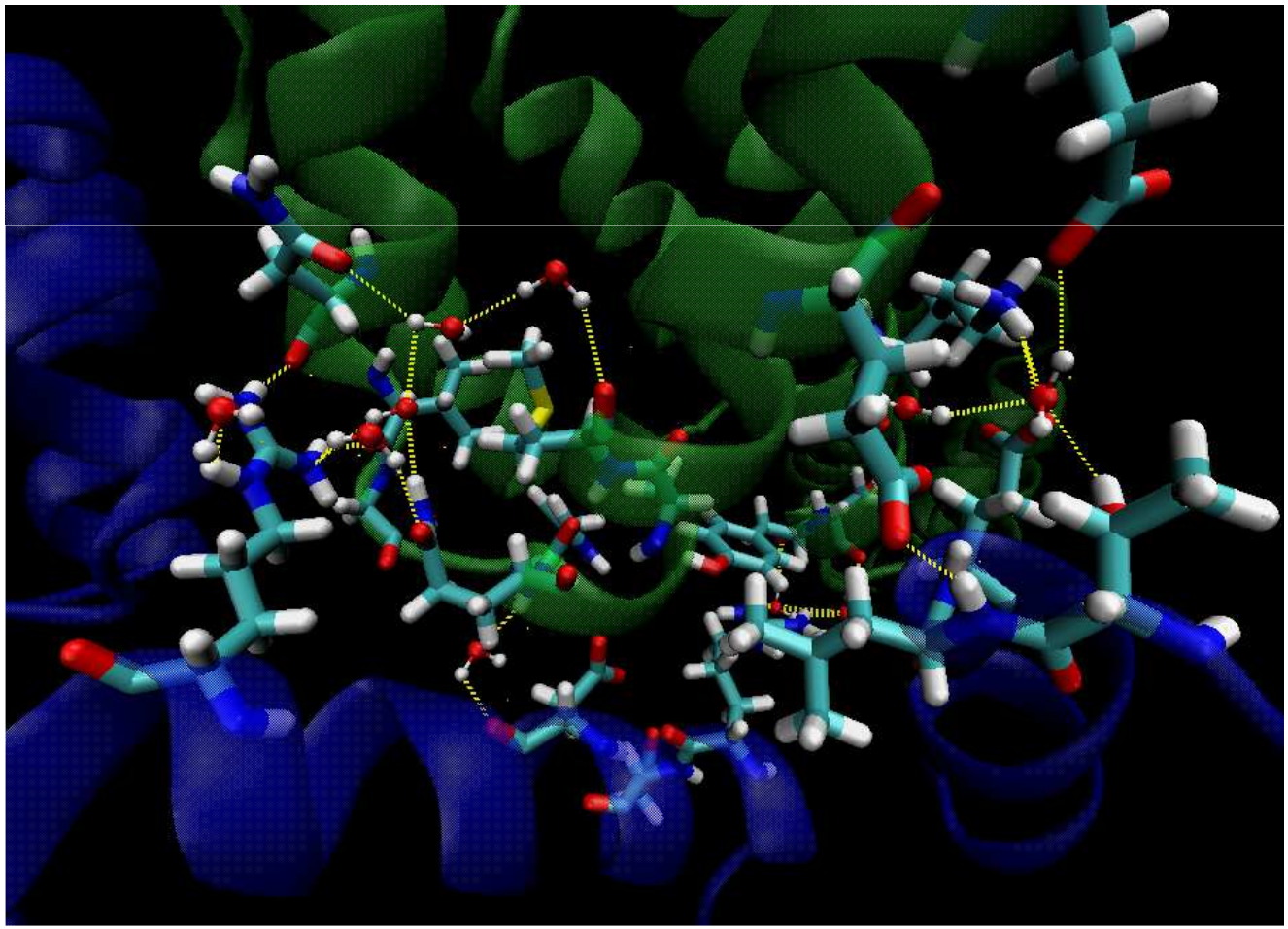
There are also water mediated contacts.
They involved helices 8, 11 (blue) and 4 and 7 (gree).



NTD-CTD interface

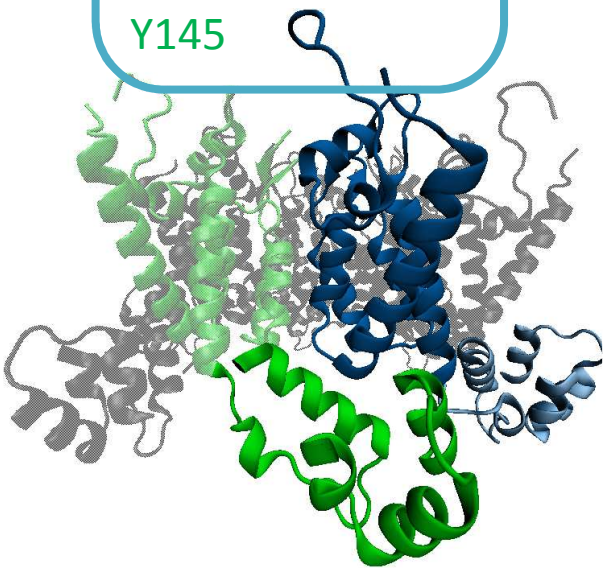
POLAR AND WATER MEDIATED CONTACTS:

- Water mediated contacts:

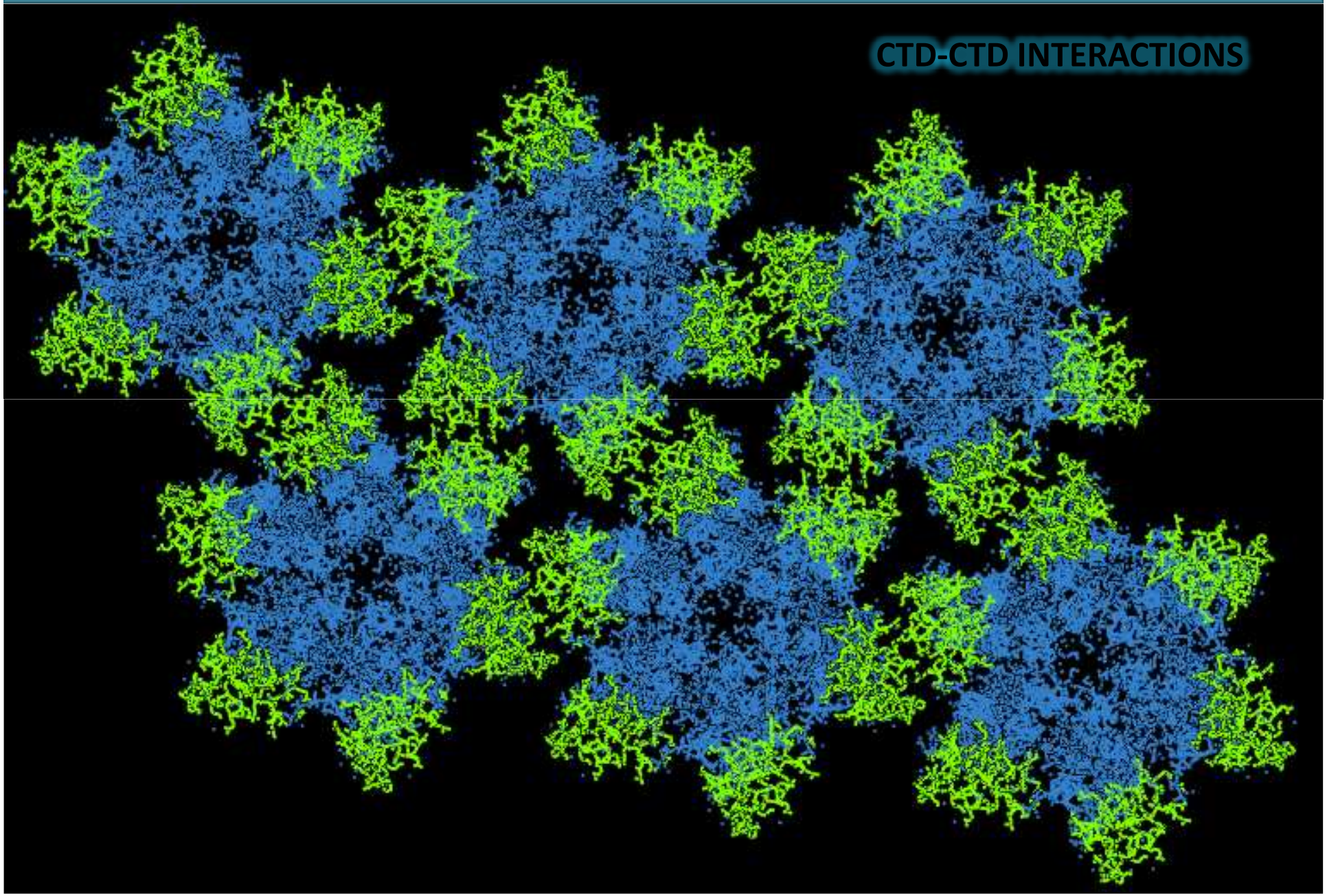


Residues involved:

G60	R173
H62	D166
Q63	R162
A65	D163
M66	T210
N57	L211
V59	E212
K140	
E71	
E75	
P146	
Y145	

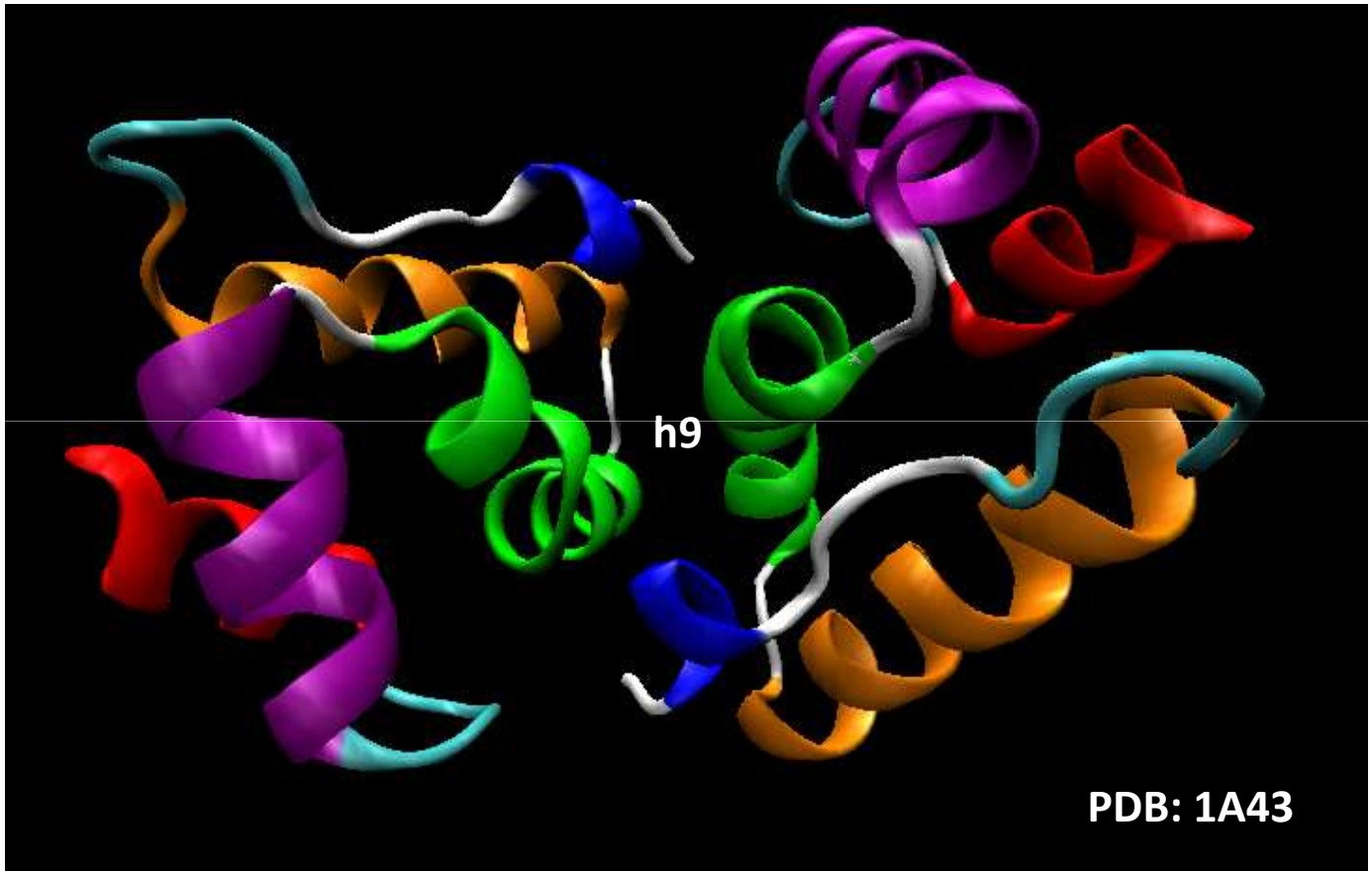


3.1.HEXAMERS



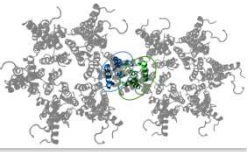
3.1.HEXAMERS

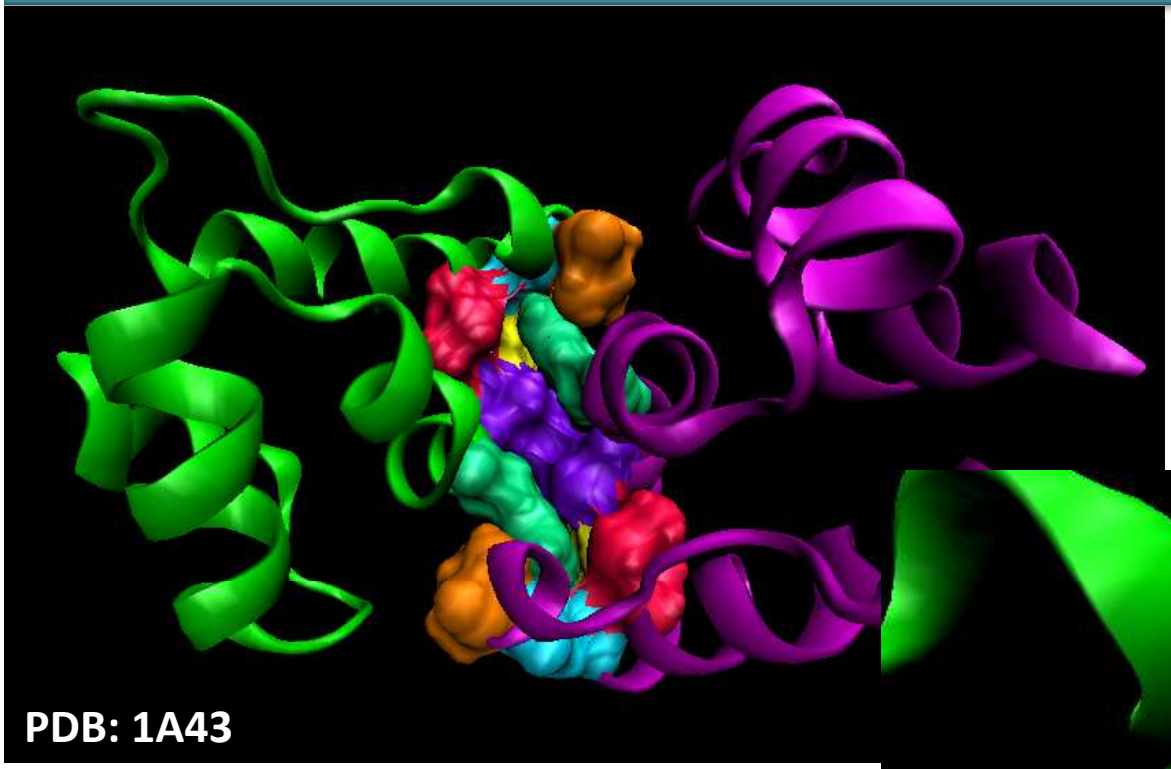
CTD-CTD INTERACTIONS



HYDROPHOBIC INTERACTIONS
POLAR INTERACTIONS: 4 hidrogen bonds and 2 salt bridges

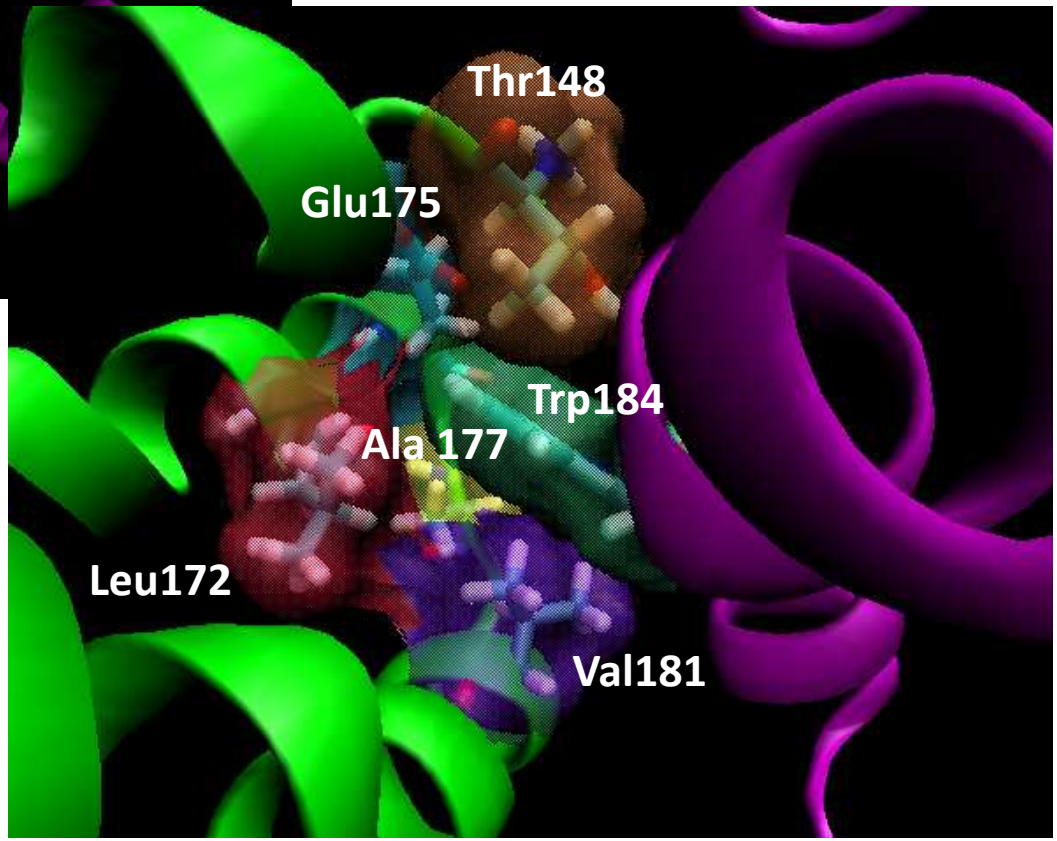
3.1.HEXAMERS





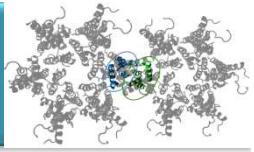
CTD-CTD INTERACTIONS

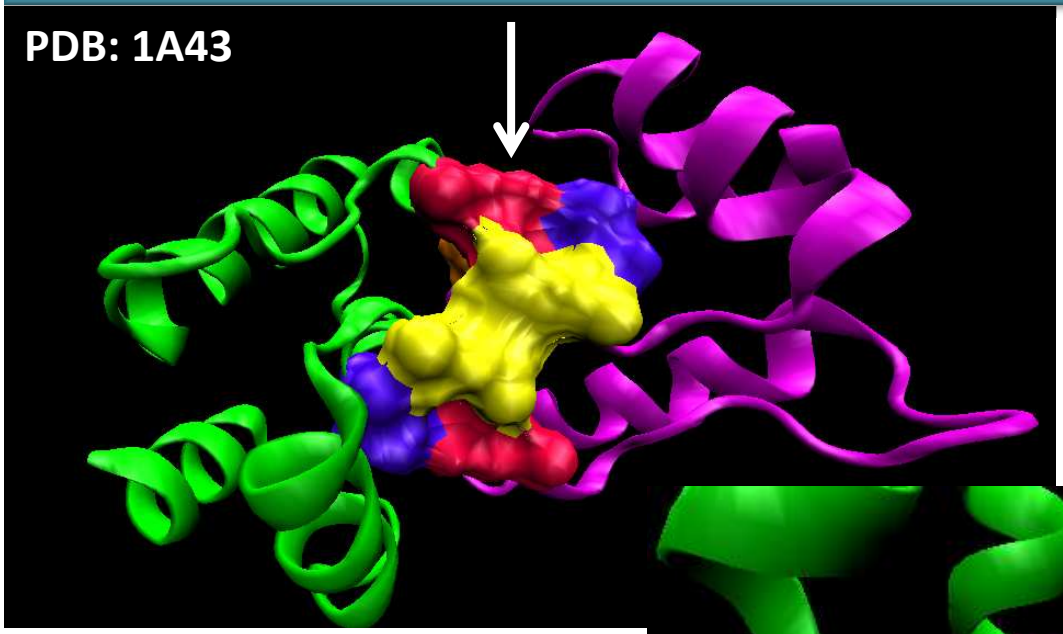
HYDROPHOBIC INTERACTIONS



Trp 184 helix 9' against:
Thr 148
Leu 172
Glu 175
Ala 177
Val 181
From helix 9"

3.1.HEXAMERS

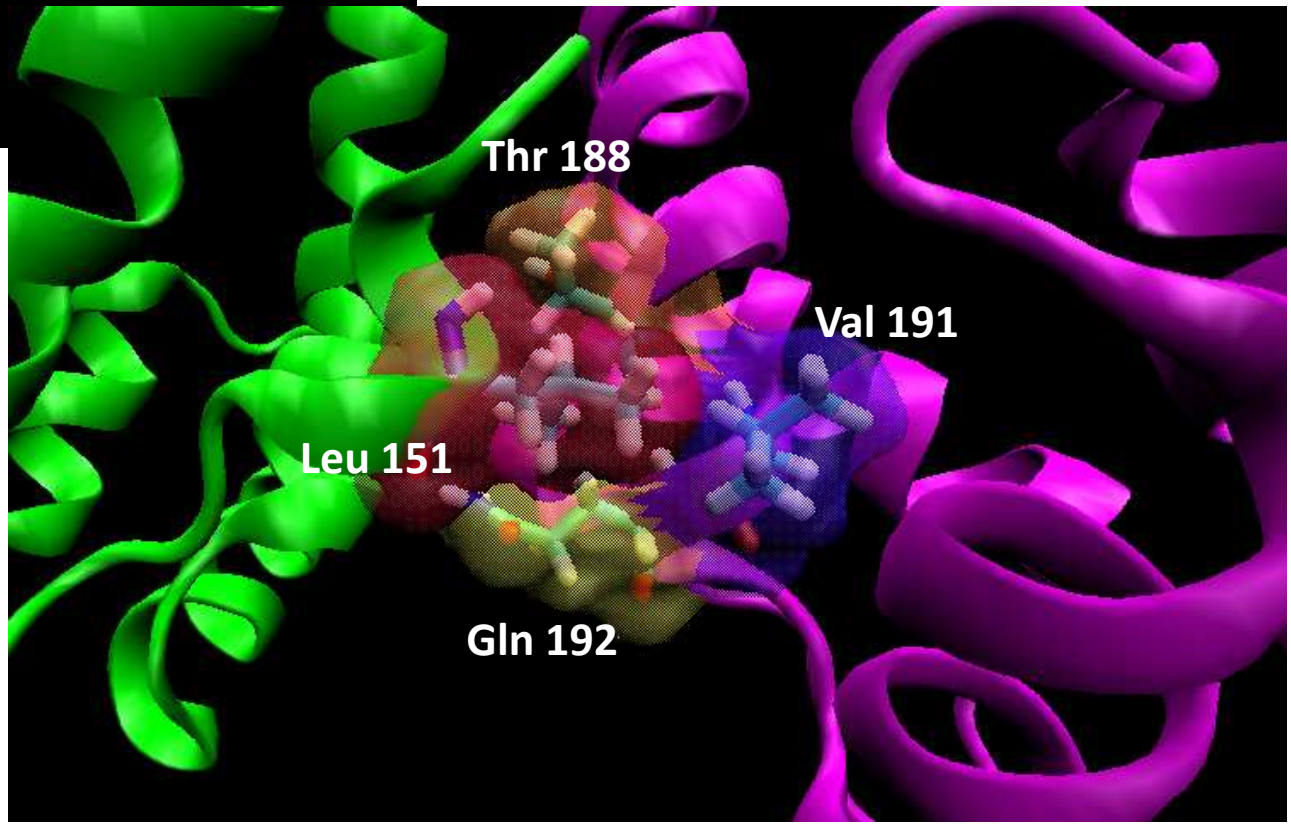




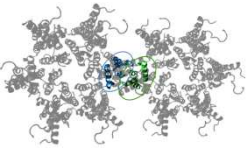
CTD-CTD INTERACTIONS

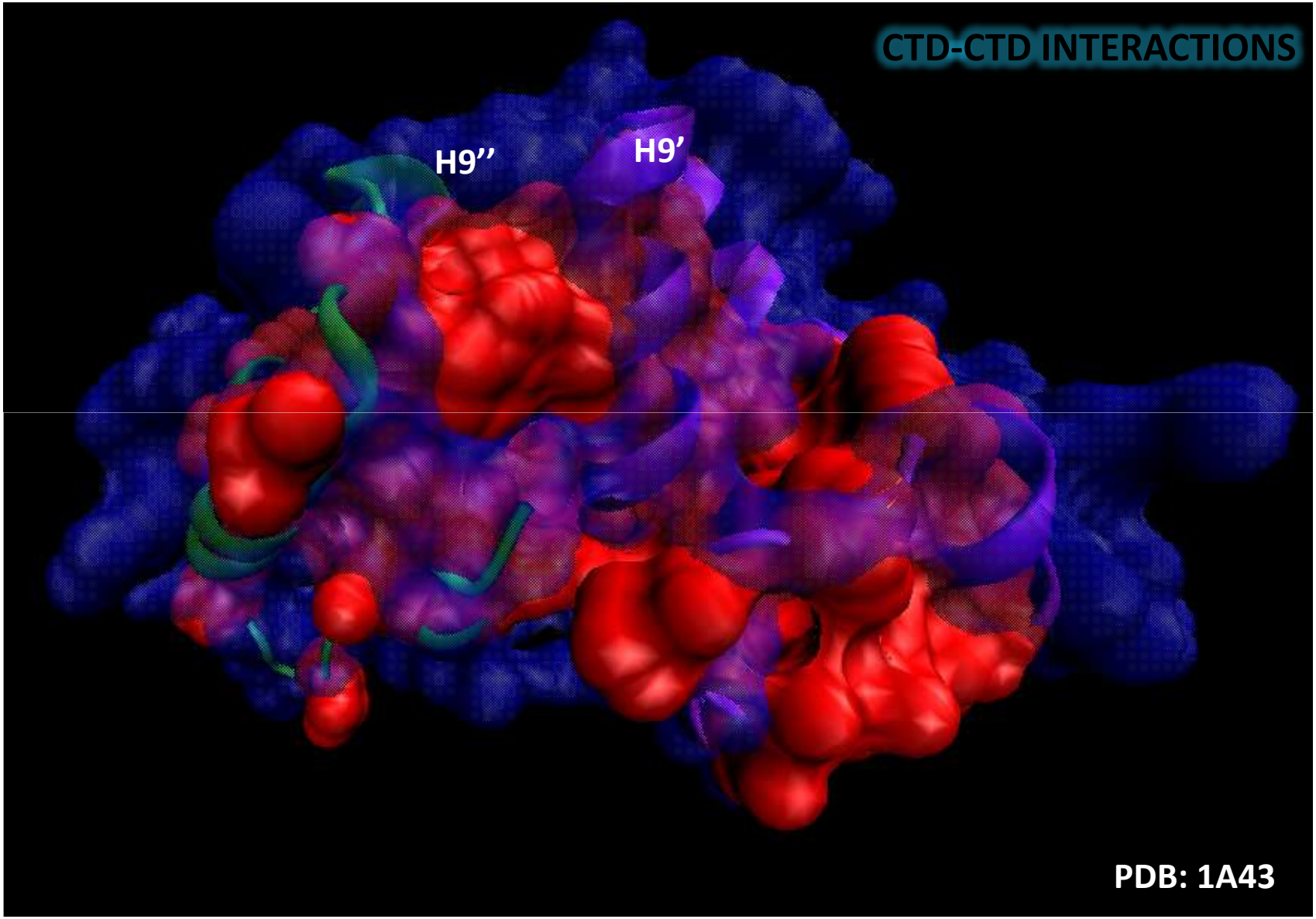
HYDROPHOBIC INTERACTIONS

Leu 151 from 3_{10} helix against:
Thr 188
Val 191
Gln 192
Met 185
from helix 9''

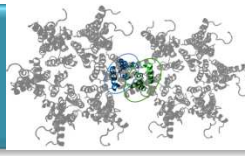


3.1.HEXAMERS

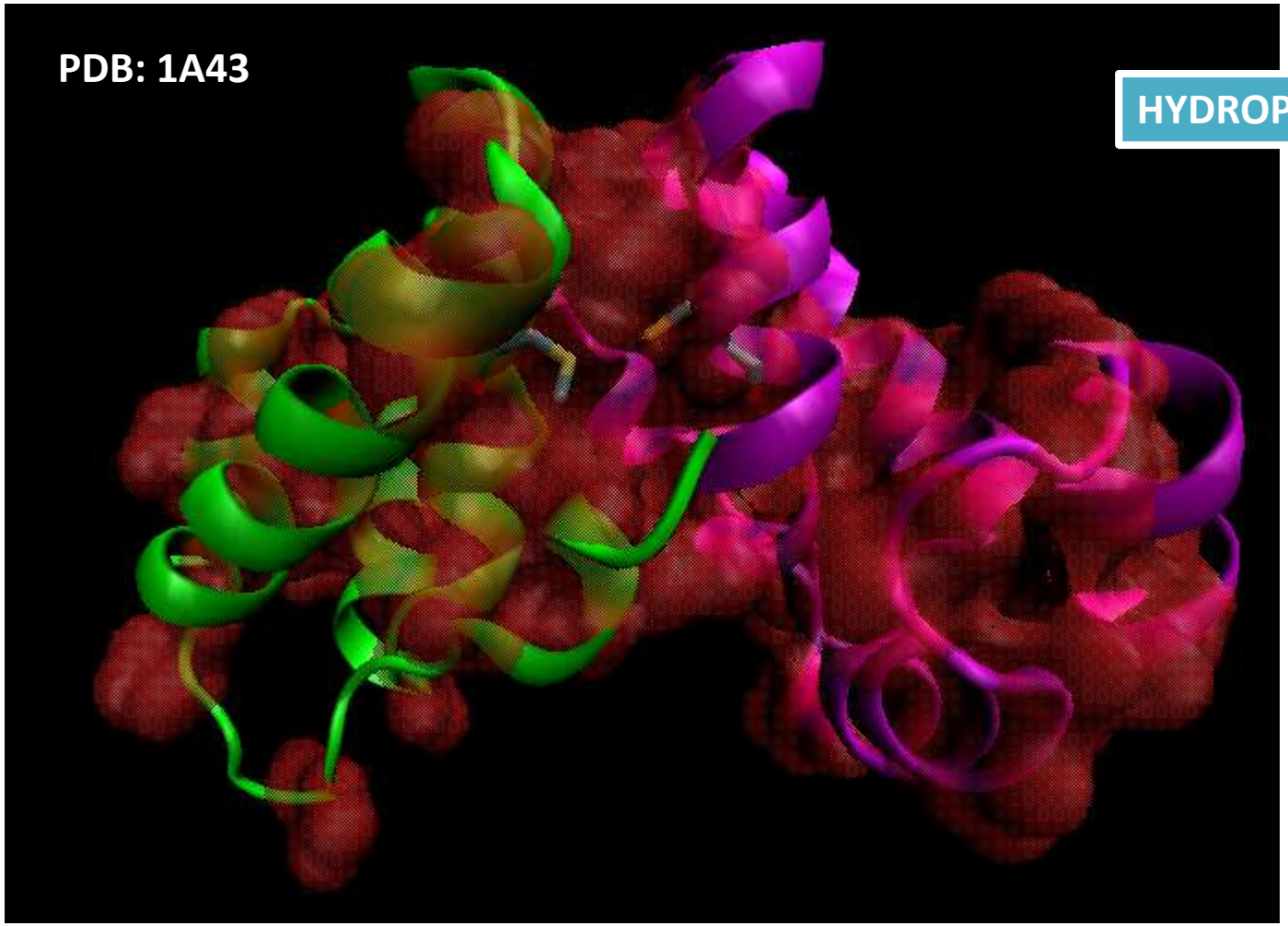




3.1.HEXAMERS



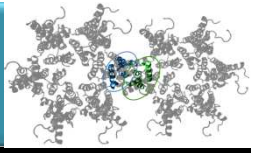
CTD-CTD INTERACTIONS



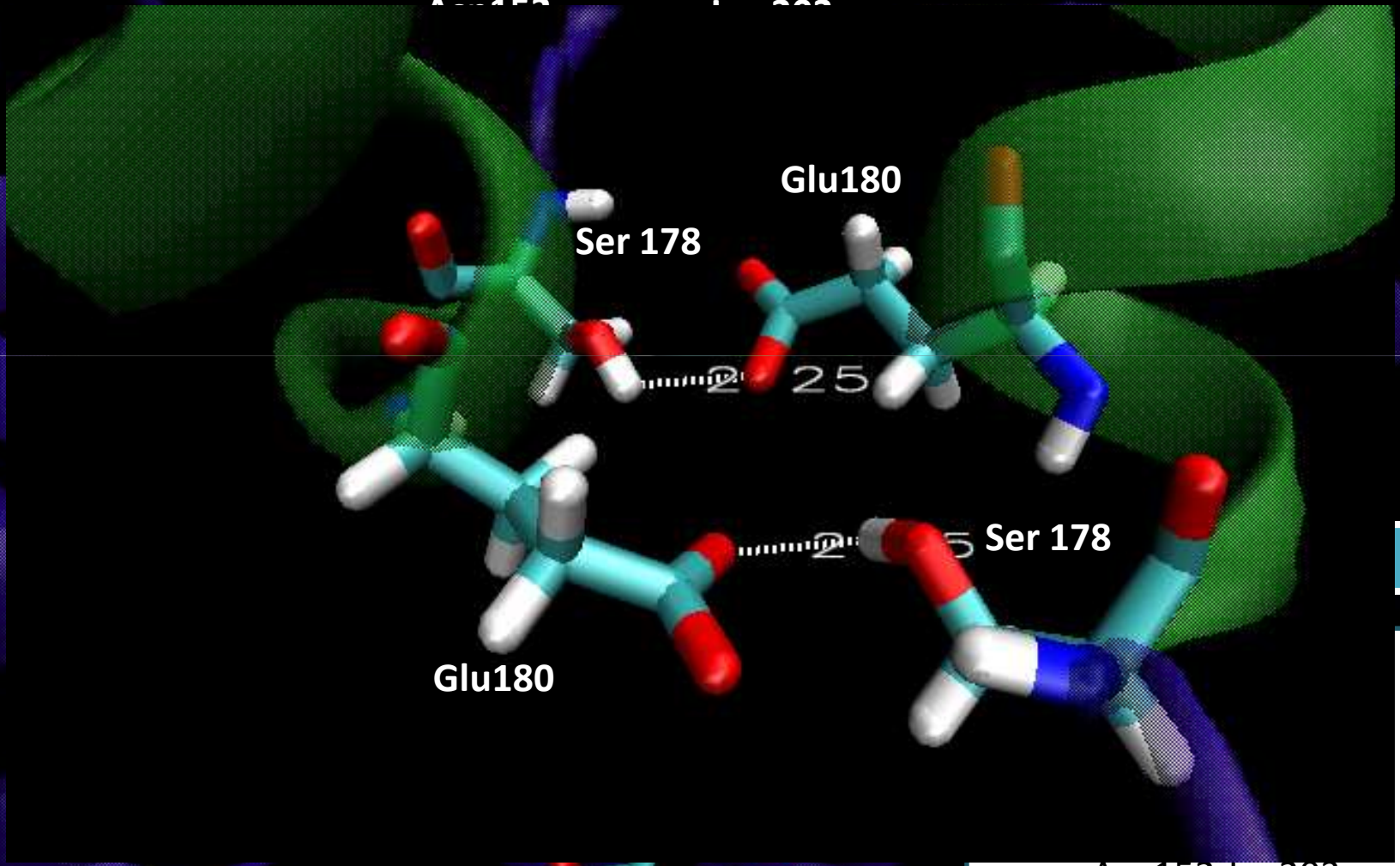
HYDROPHOBIC INTERACTIONS

Met 185

3.1.HEXAMERS



CTD-CTD INTERACTIONS



Asp152-Lys203

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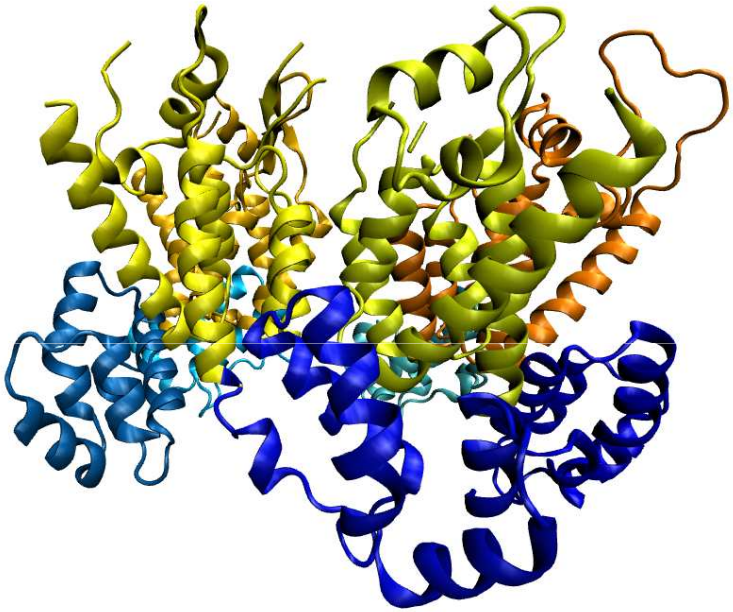
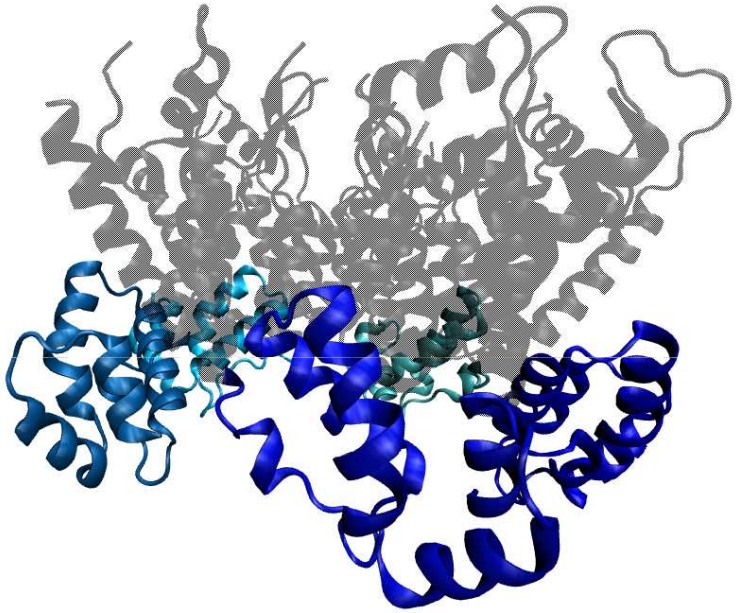
- Introduction
- CA (monomer)
  - NTD
  - CTD
- Capsid subunits
  - Hexamers
  - Pentamers
- Capsid curvature
- Current situation

3.2. PENTAMERS



CA is packed in the same way

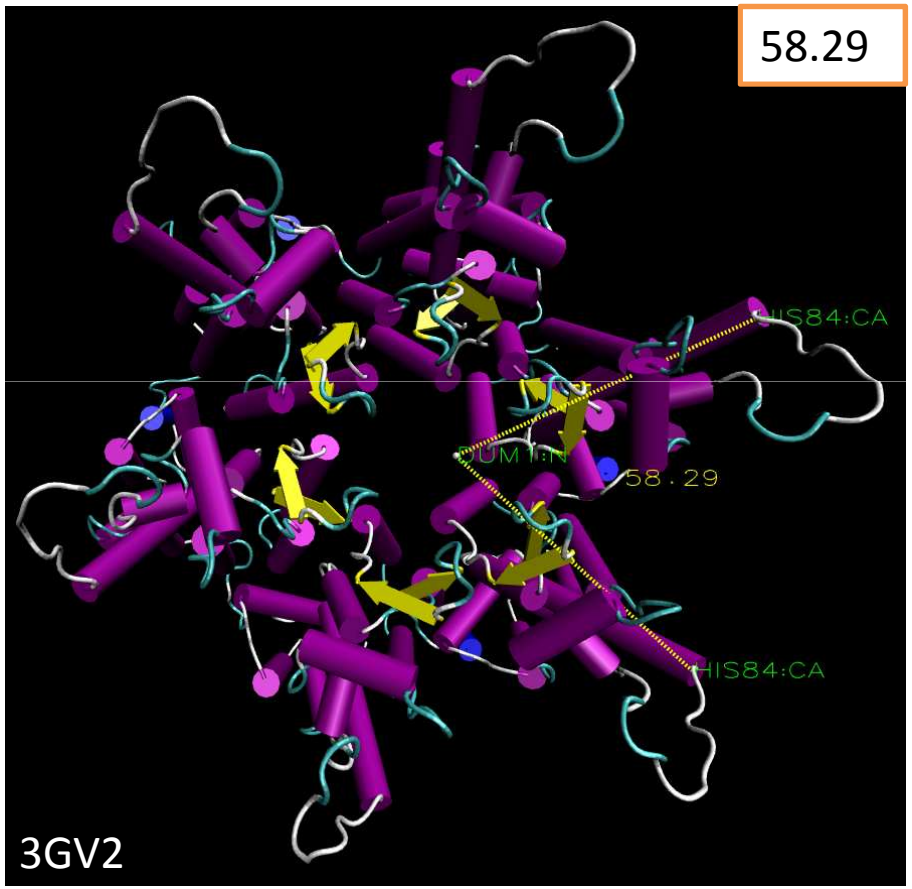


NTD inner ring, CTD outer ring

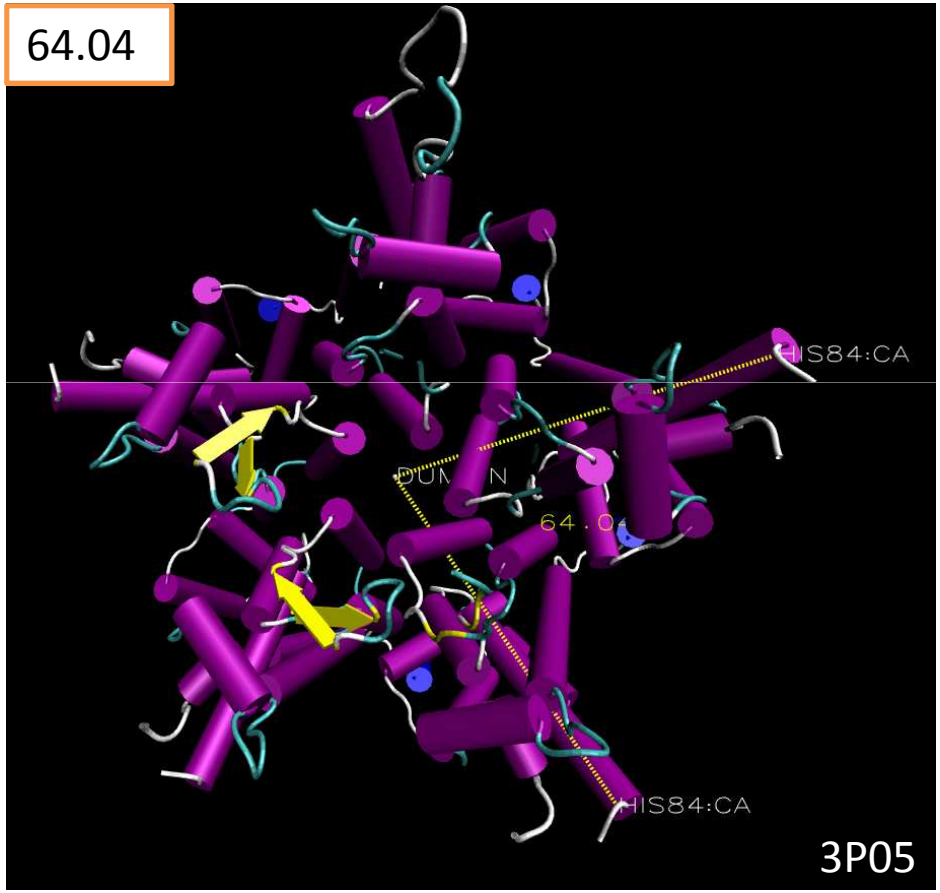
NTD: yellow
CTD: blue

3.2. PENTAMERS

HEXAMER



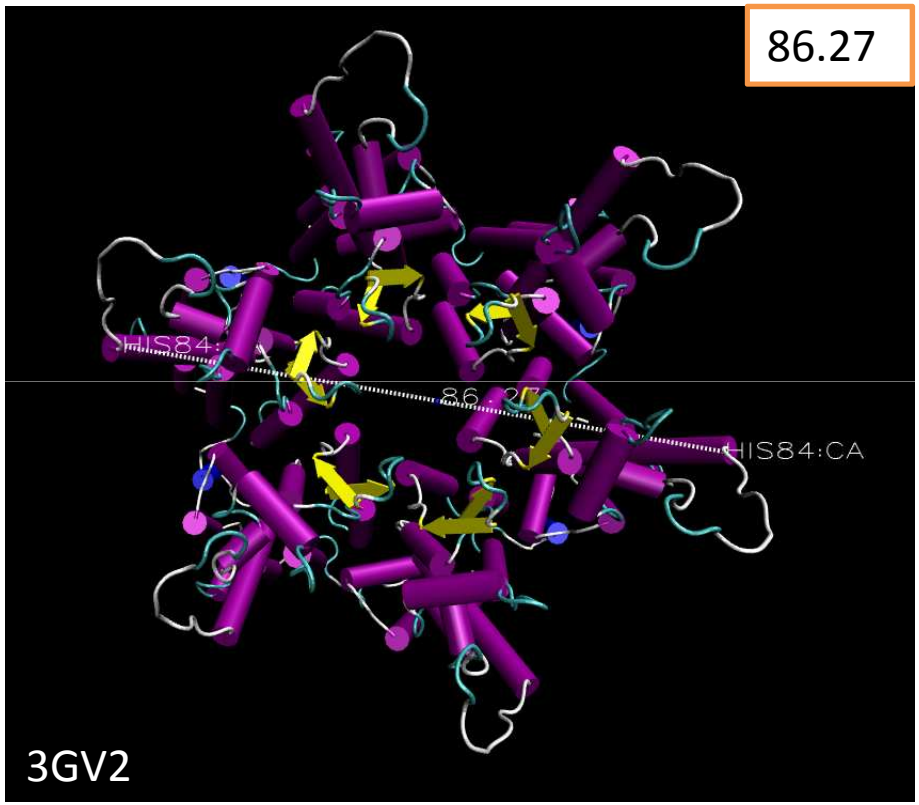
PENTAMER



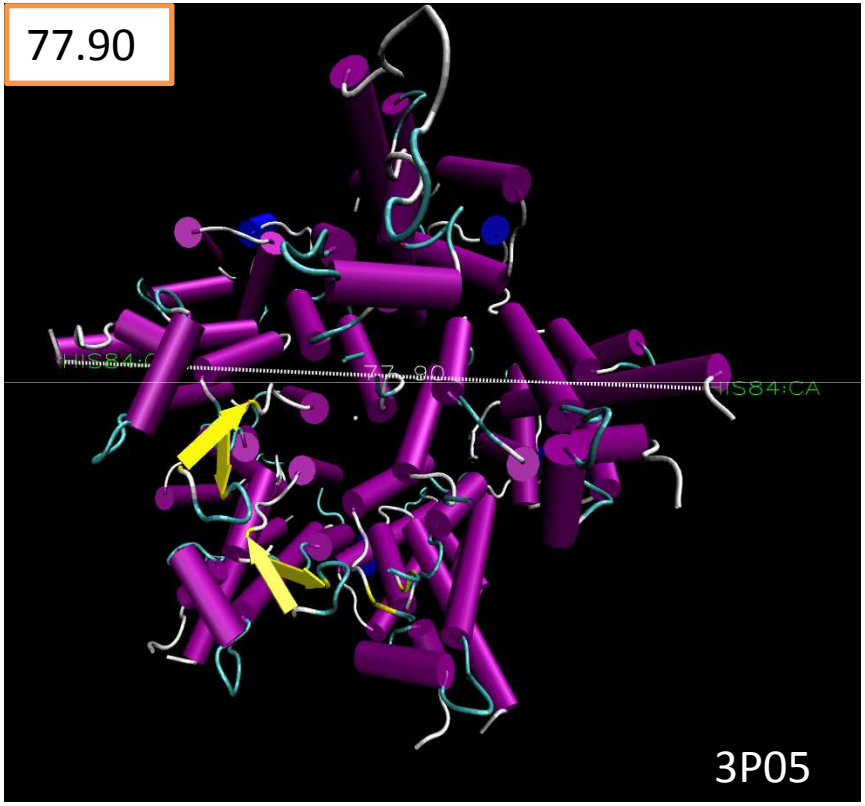
Differences in the angle between monomers

3.2. PENTAMERS

HEXAMER



PENTAMER

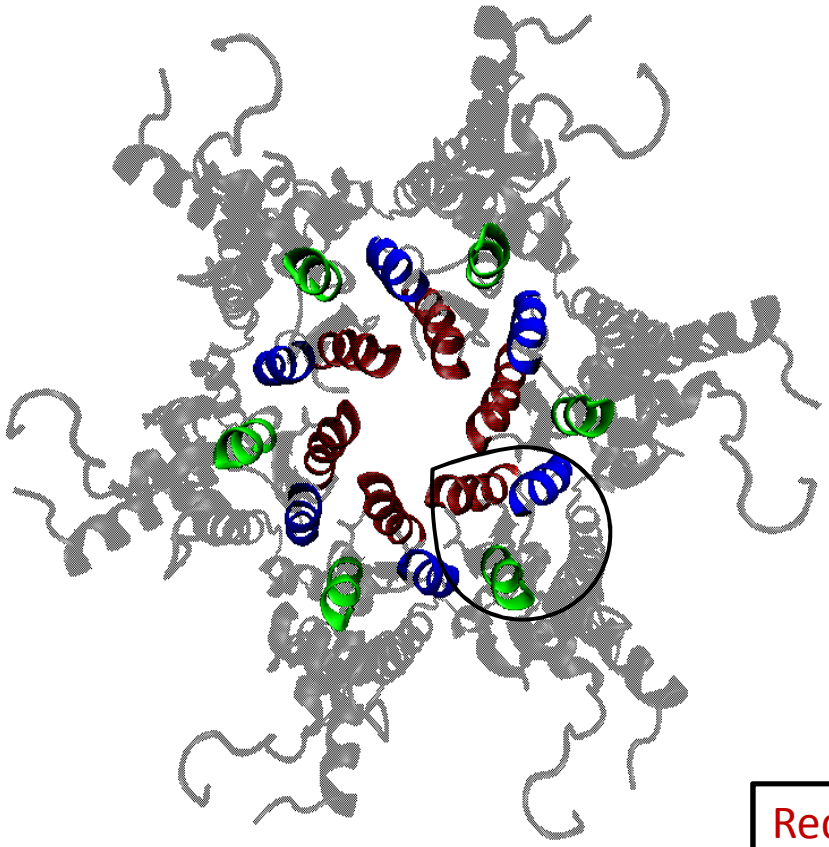


Differences in the diameter

3.2. PENTAMERS

NTD-NTD interface

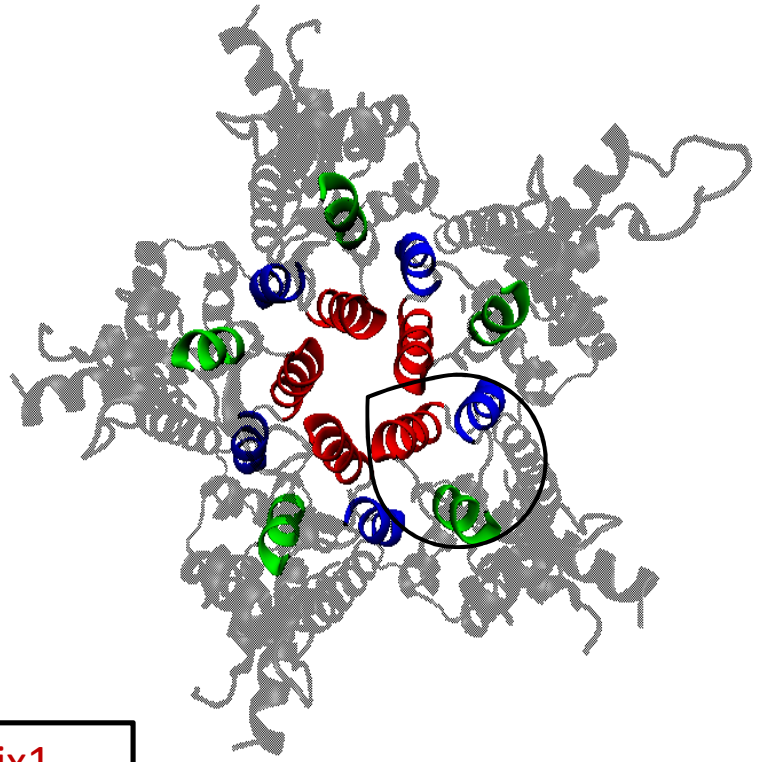
18-helix bundle



HEXAMER

Red: helix1
Blue: helix2
Green: helix3

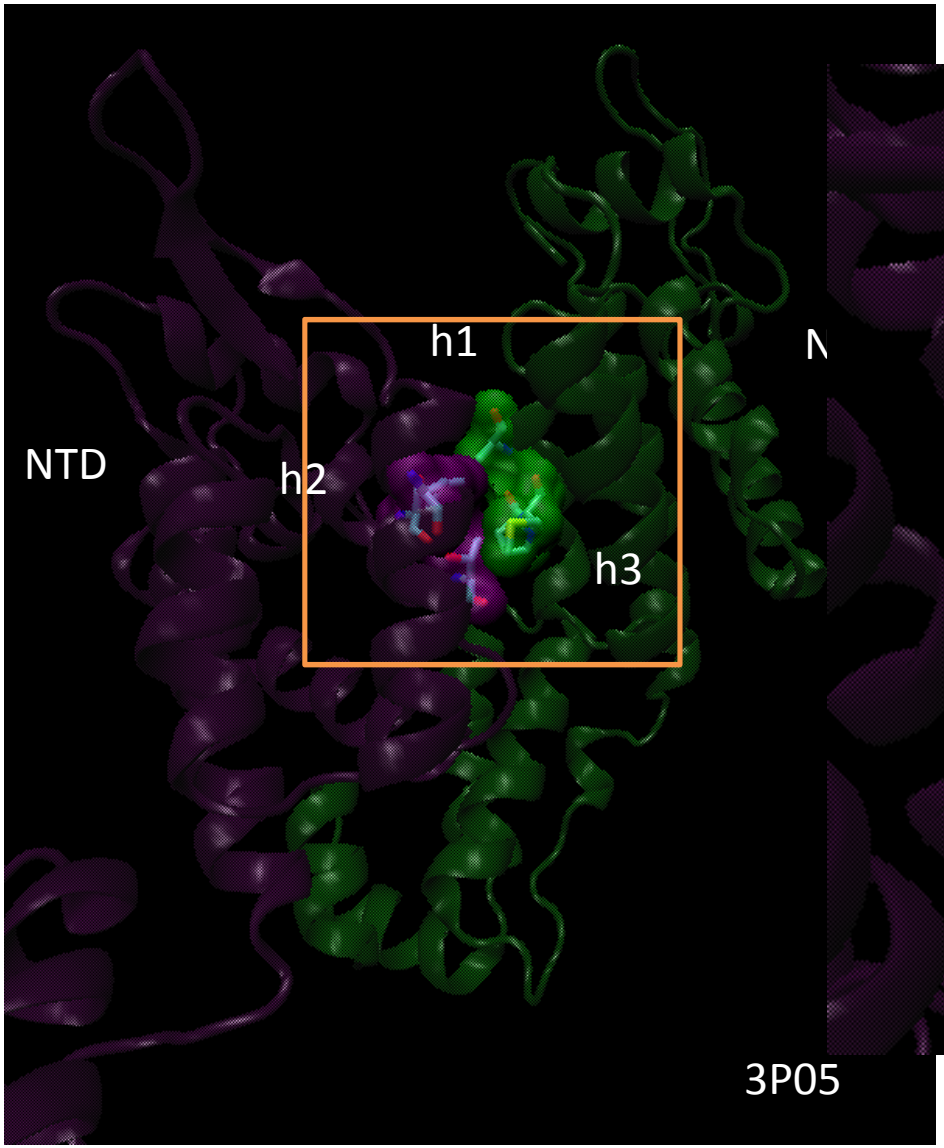
15-helix bundle



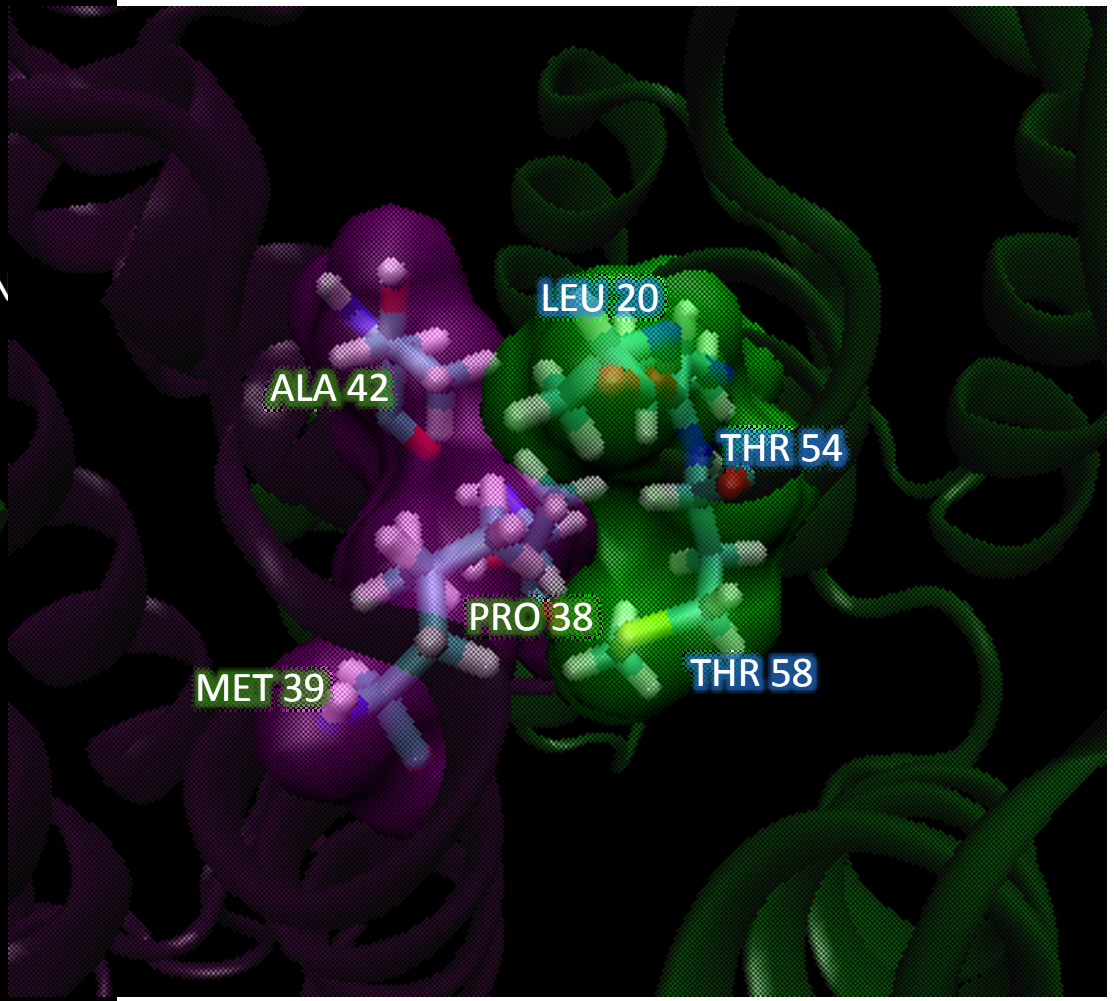
PENTAMER

3.2. PENTAMERS

NTD-NTD interface

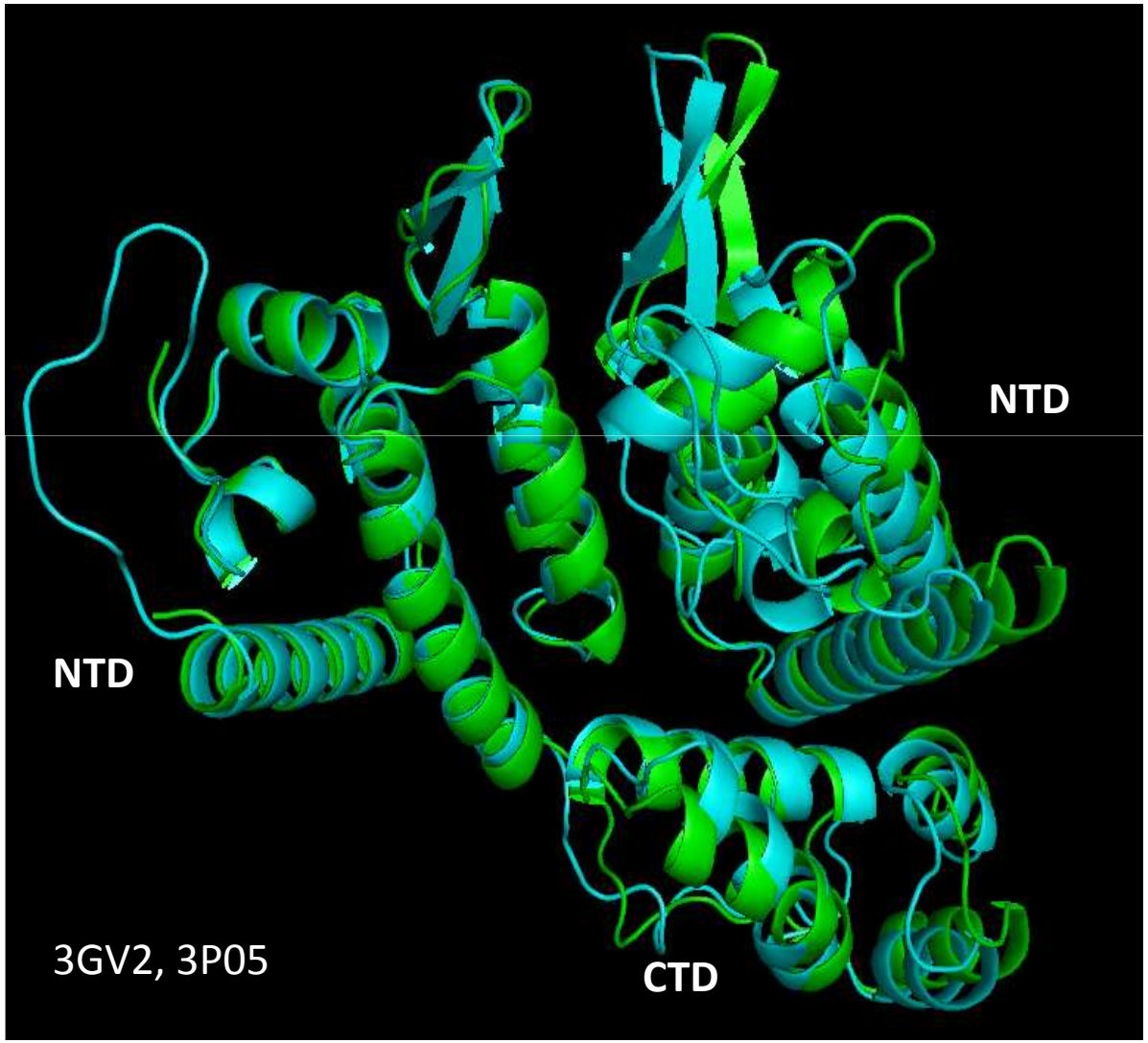


hydrophobic interactions



3.2. PENTAMERS

NTD-NTD interface



STAMP Hexamer and Pentamer

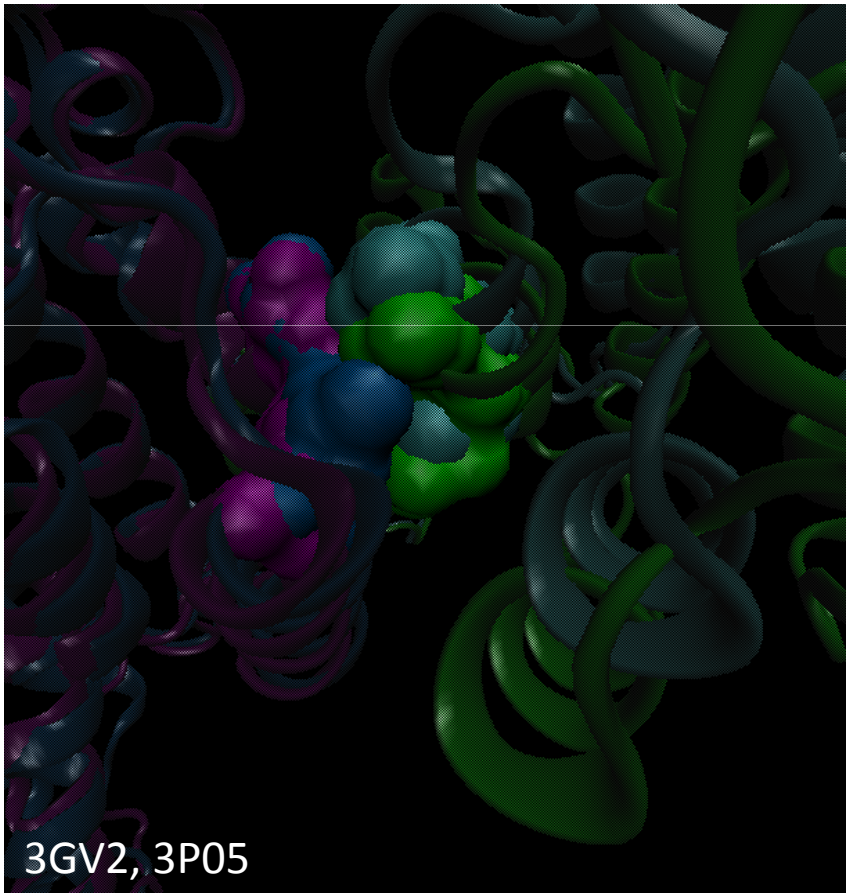
Blue: hexamer
Green: pentamer

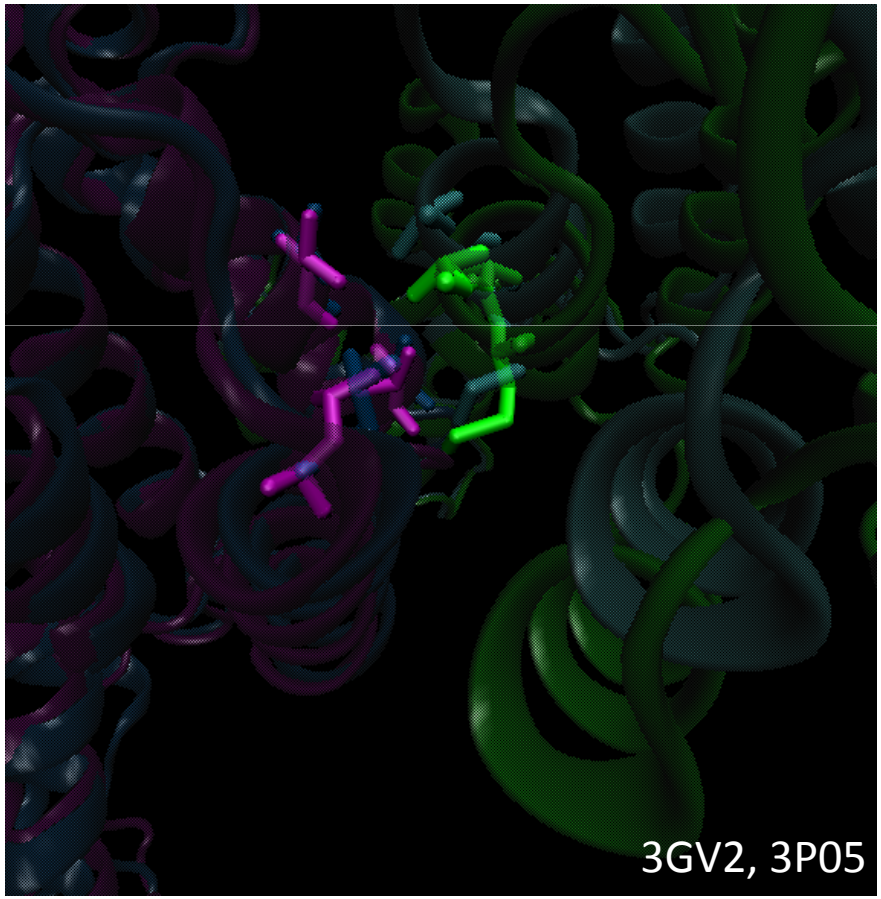
3.2. PENTAMERS

NTD-NTD interface

hydrophobic interactions

STAMP Hexamer and Pentamer



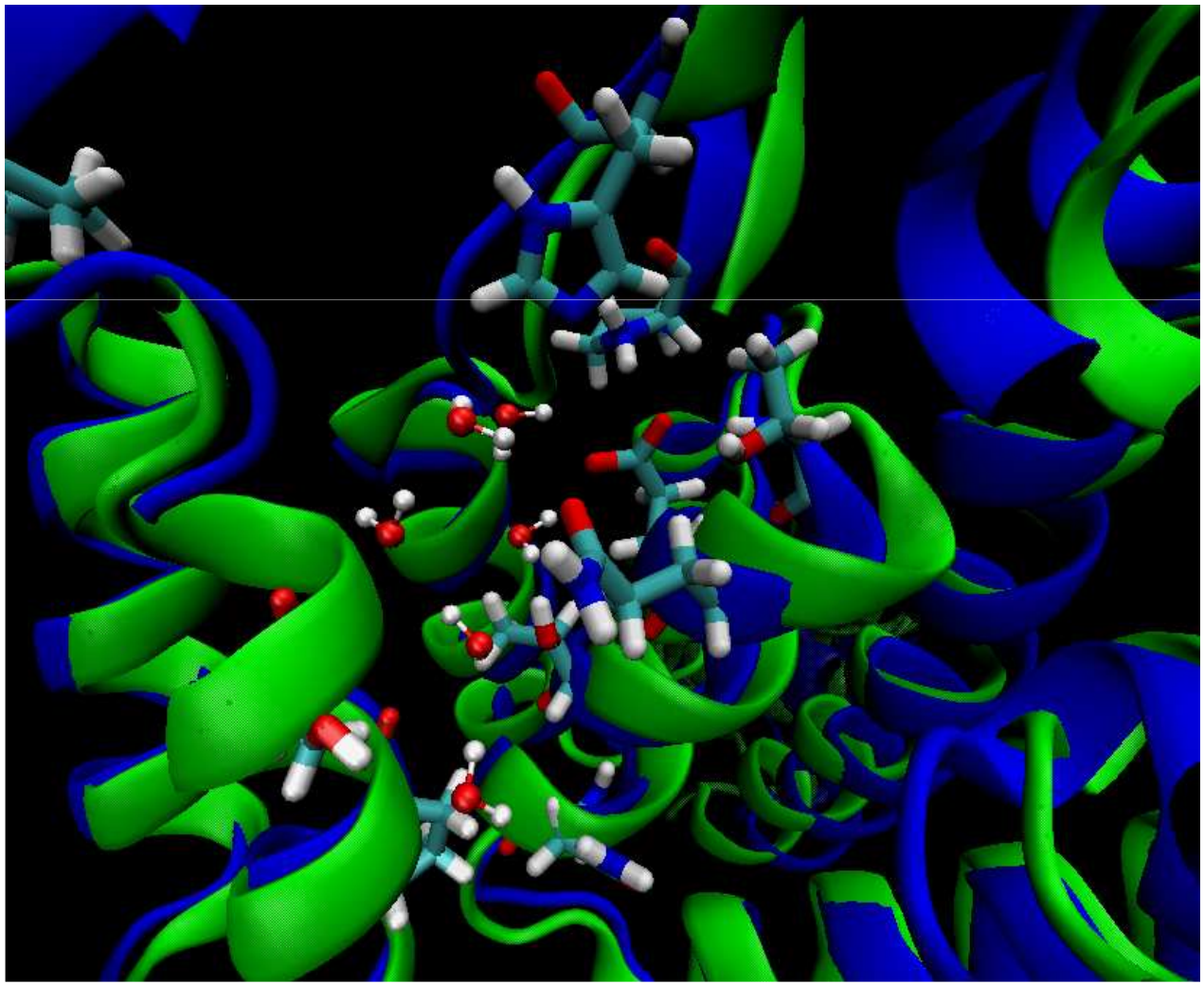


Hydrophobic interactions are conserved

3.2. PENTAMERS

NTD-NTD interface

polar interactions – water mediated



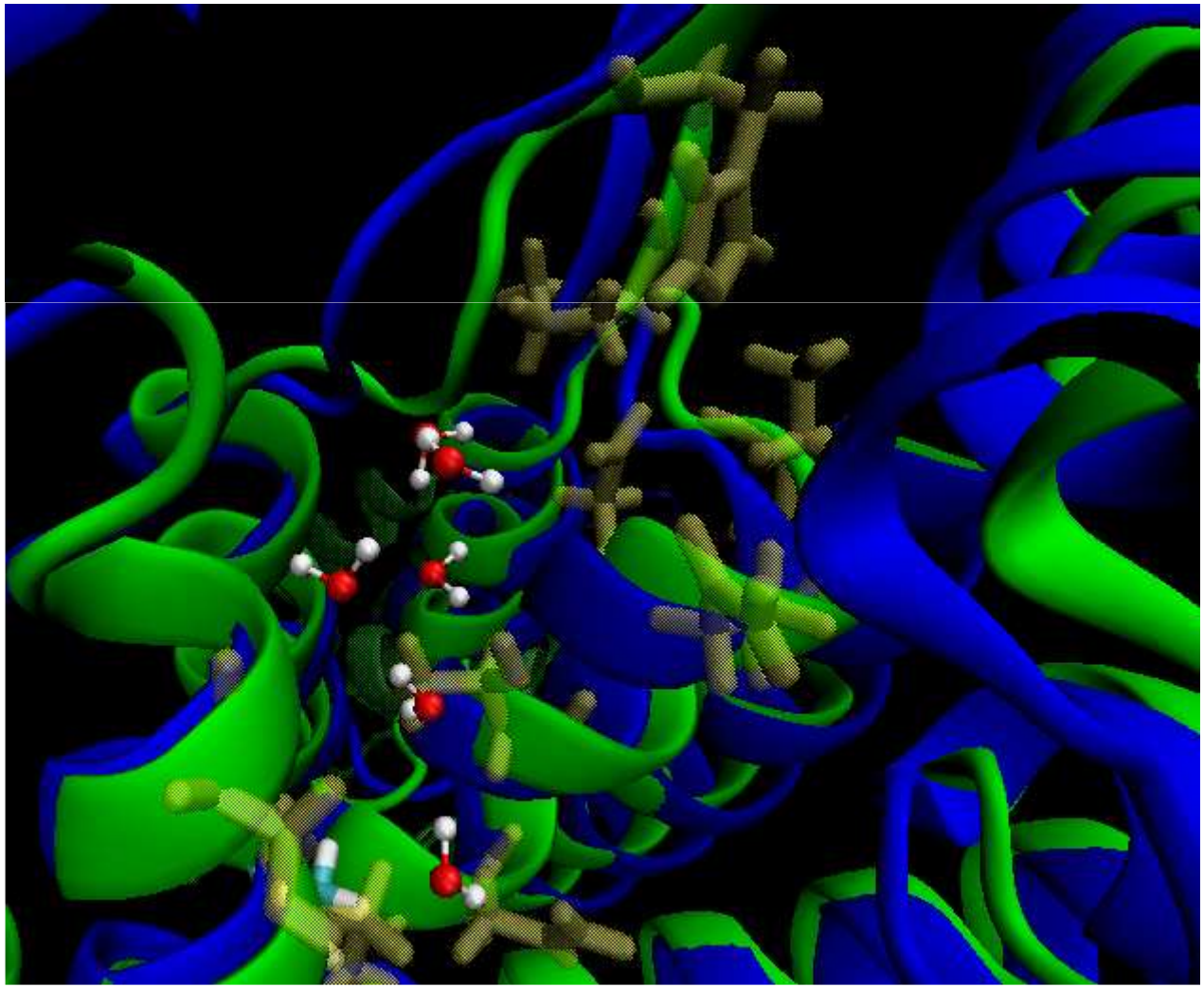
STAMP Hexamer and Pentamer

Blue: hexamer
Green: pentamer

3.2. PENTAMERS

NTD-NTD interface

polar interactions – water mediated



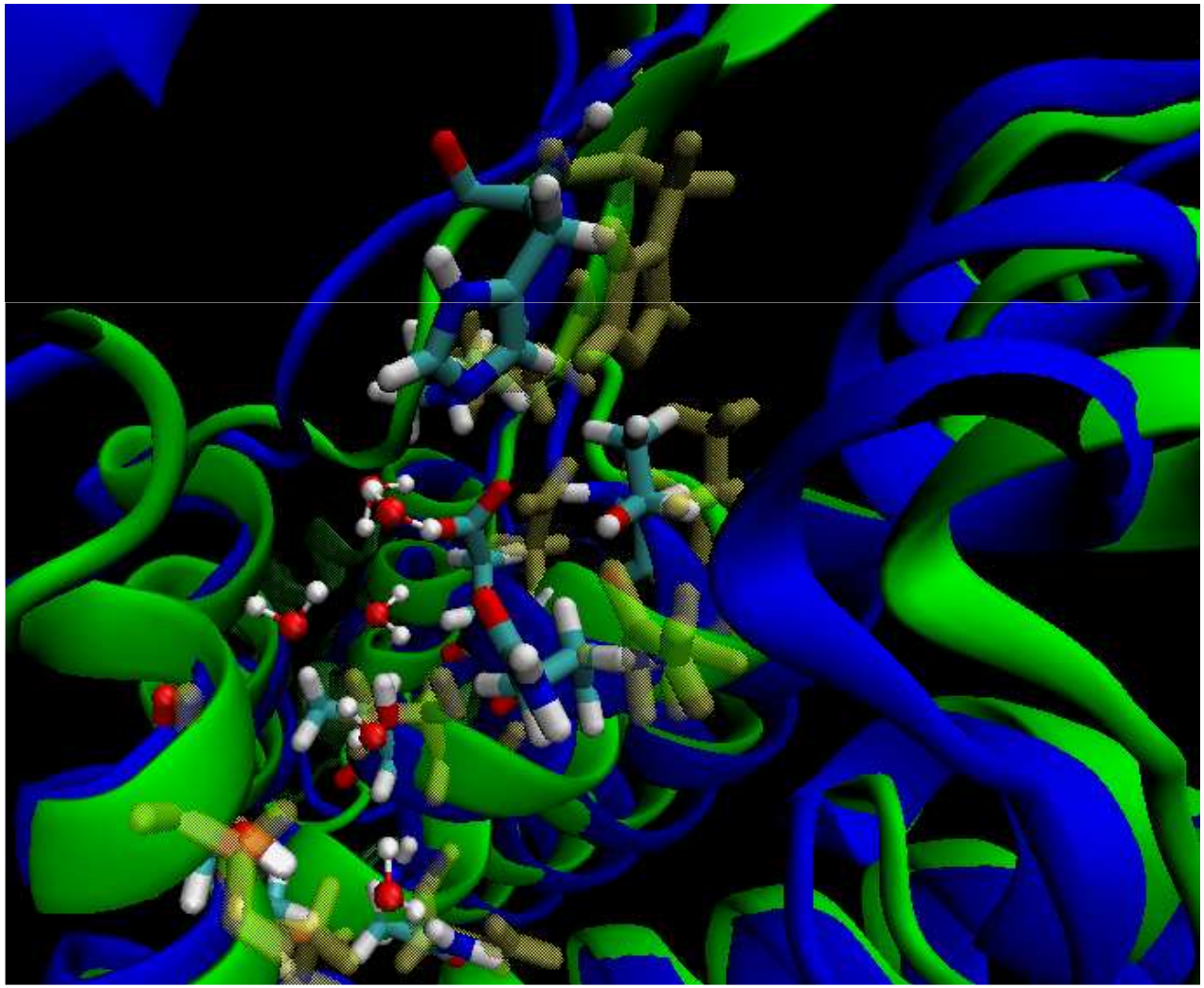
STAMP Hexamer and Pentamer

Blue: hexamer
Green: pentamer

3.2. PENTAMERS

NTD-NTD interface

polar interactions – water mediated



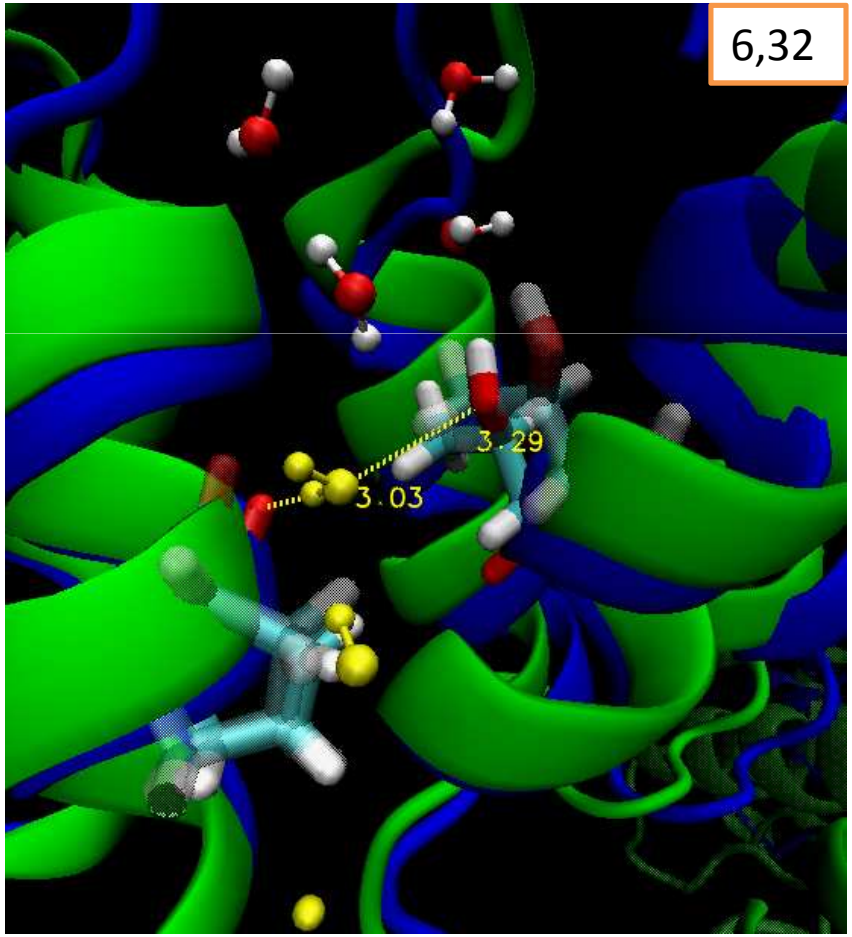
STAMP Hexamer and Pentamer

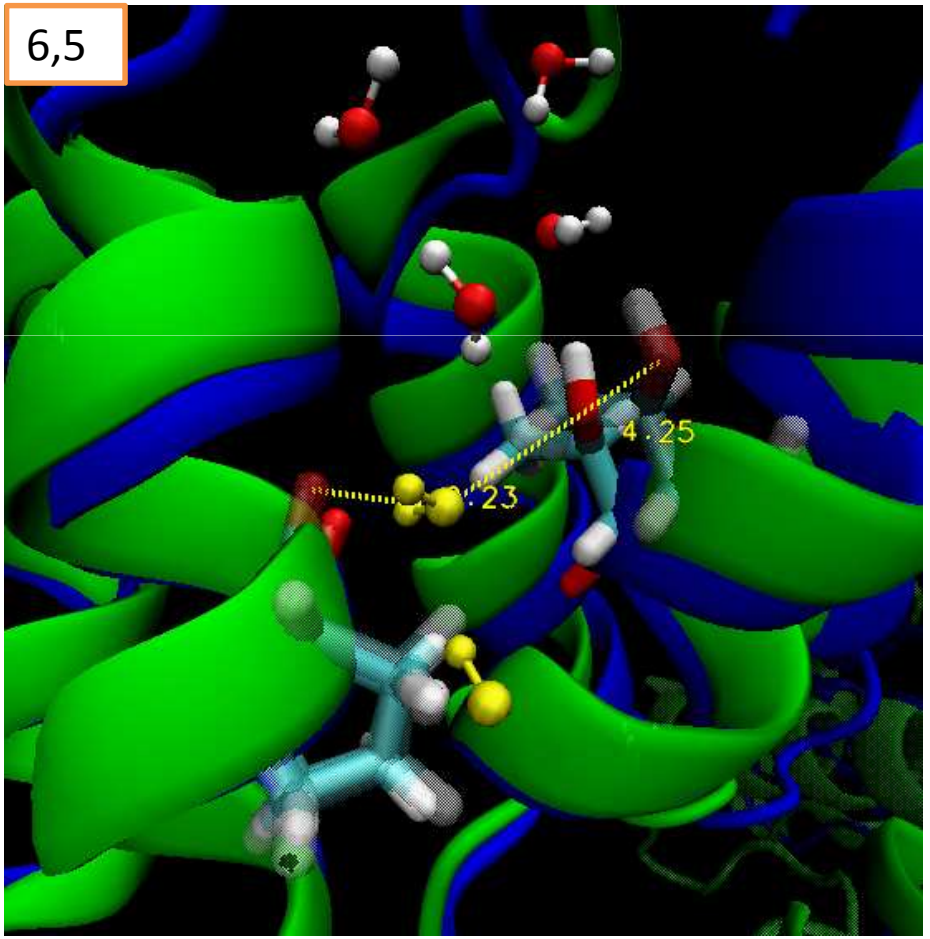
Blue: hexamer
Green: pentamer

3.2. PENTAMERS

NTD-NTD interface

polar interactions – water mediated



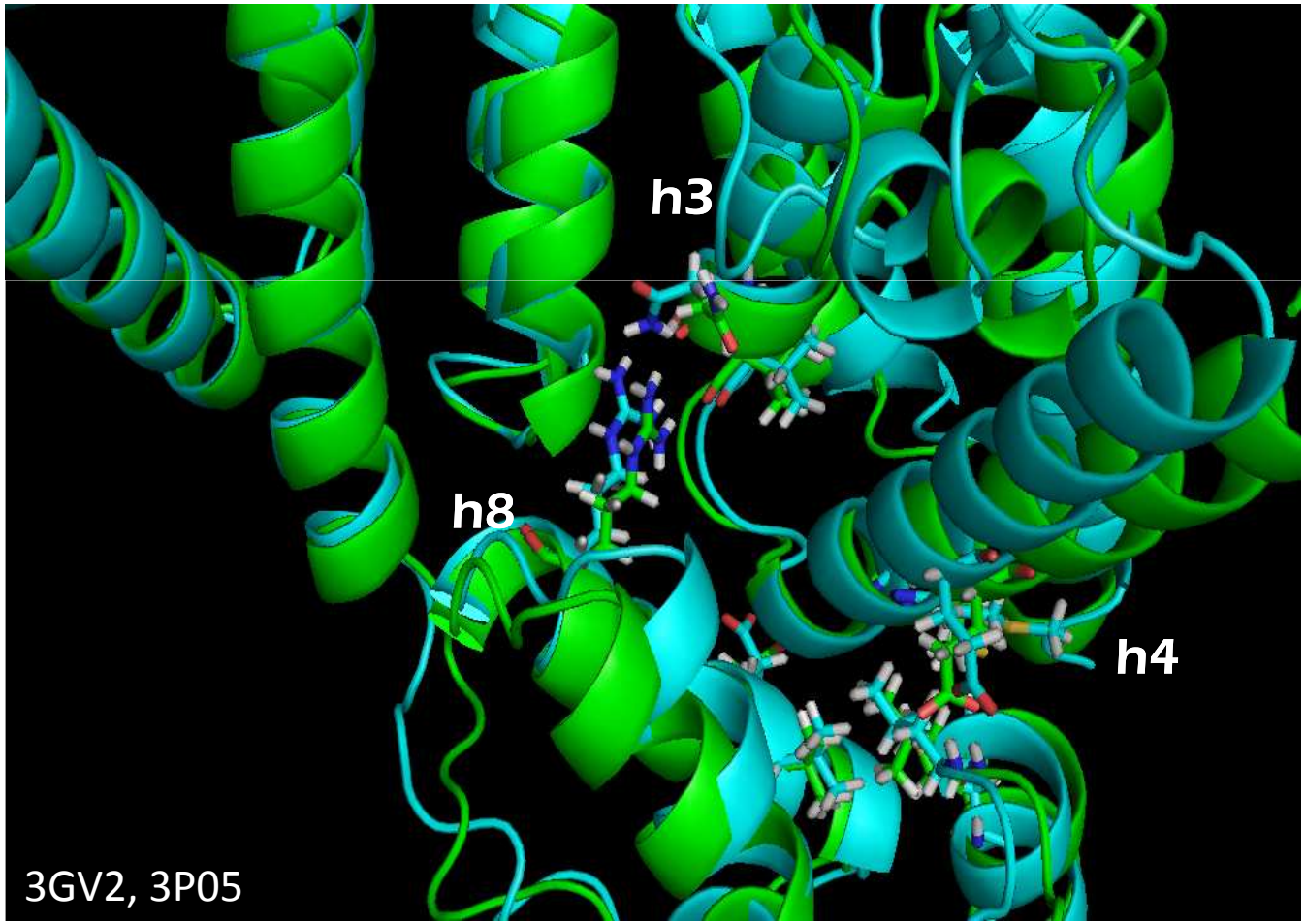


3.2. PENTAMERS

NTD-CTD INTERFACE:

POLAR CONTACTS:

- Capping interactions



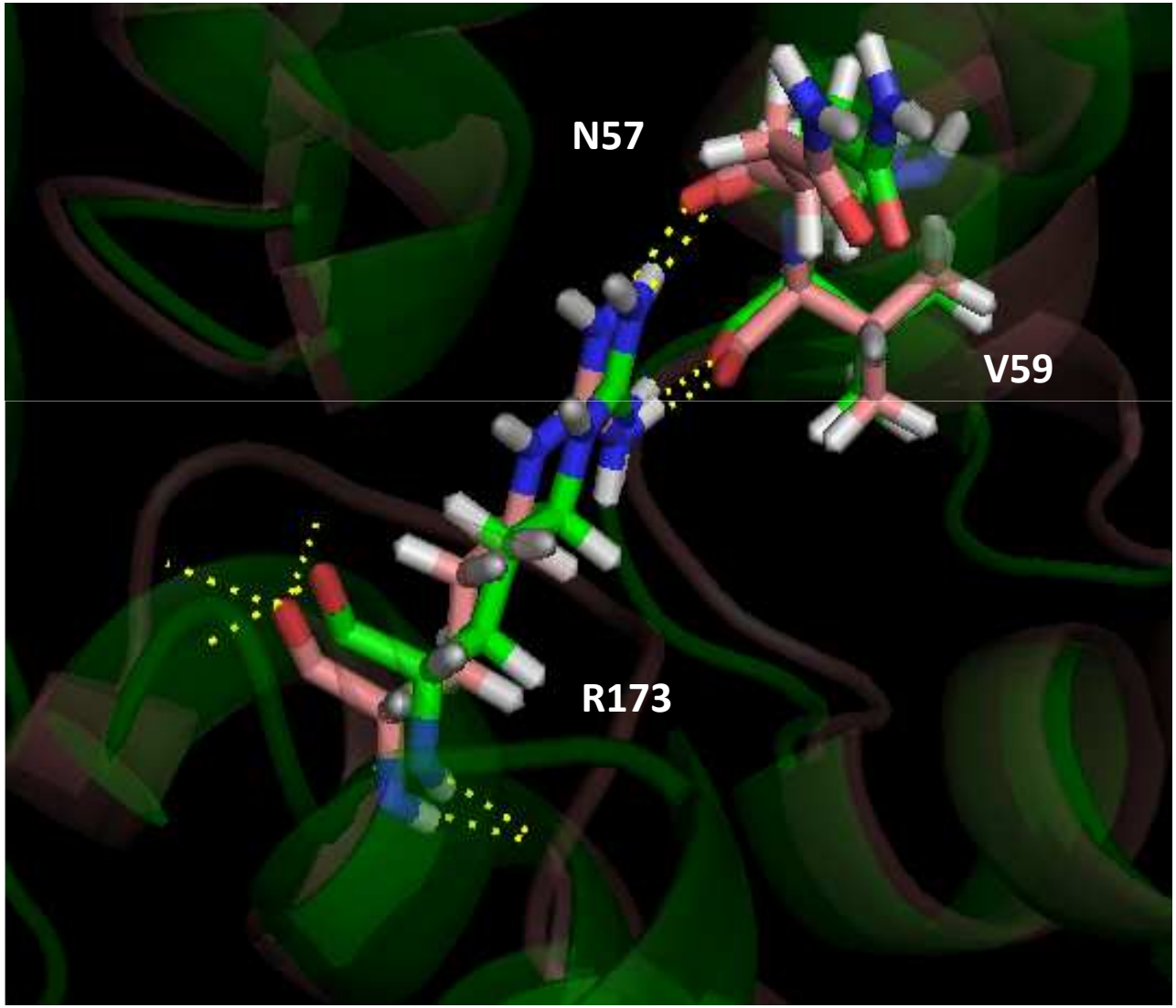
STAMP Hexamer and Pentamer

- E71 – L211
- A64 – D166
- N57 + V59 – R173

Blue: hexamer
Green: pentamer

3.2. PENTAMERS

NTD-CTD INTERFACE:



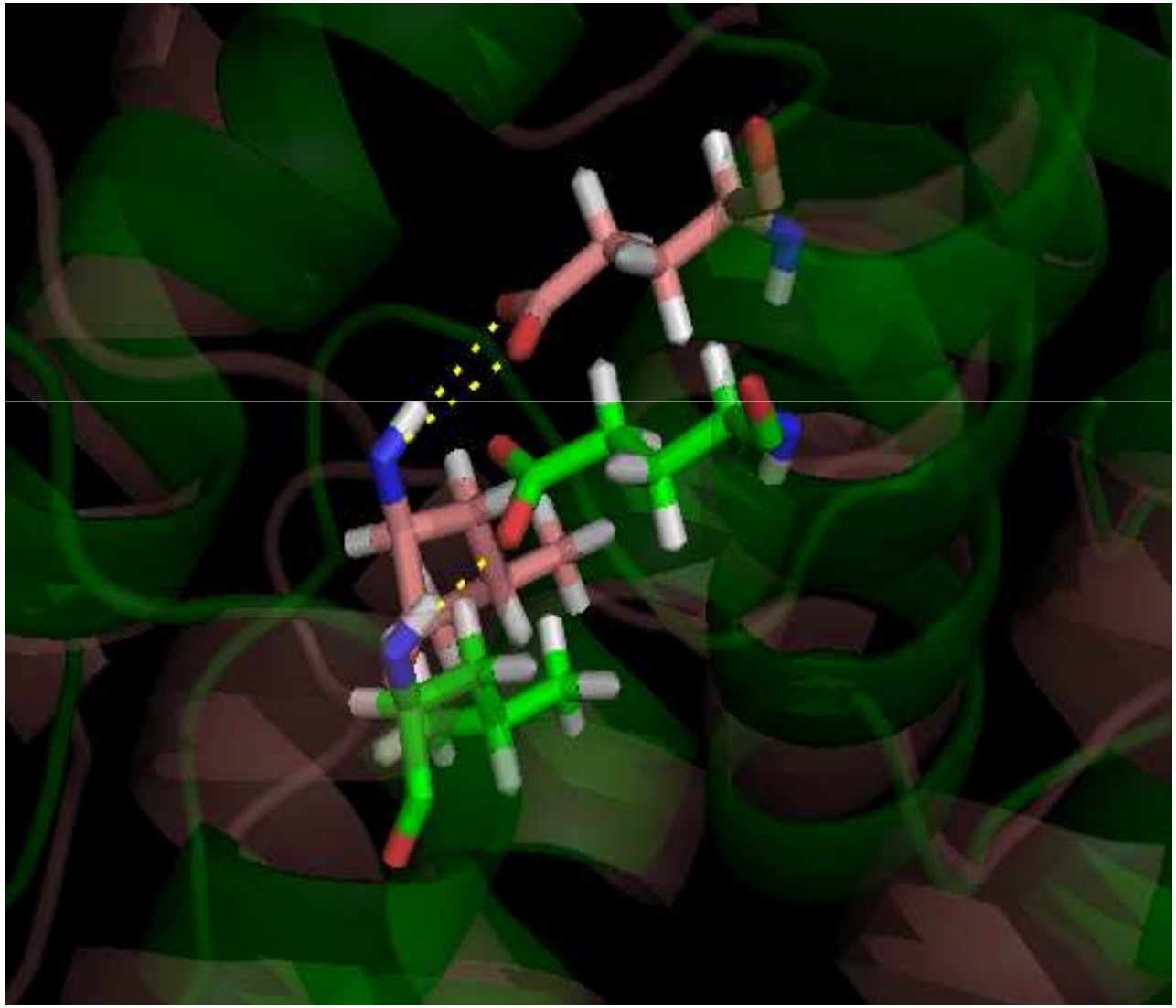
POLAR CONTACTS:

- Capping interactions

H-bonds interactions are conserved

3.2. PENTAMERS

NTD-CTD INTERFACE:



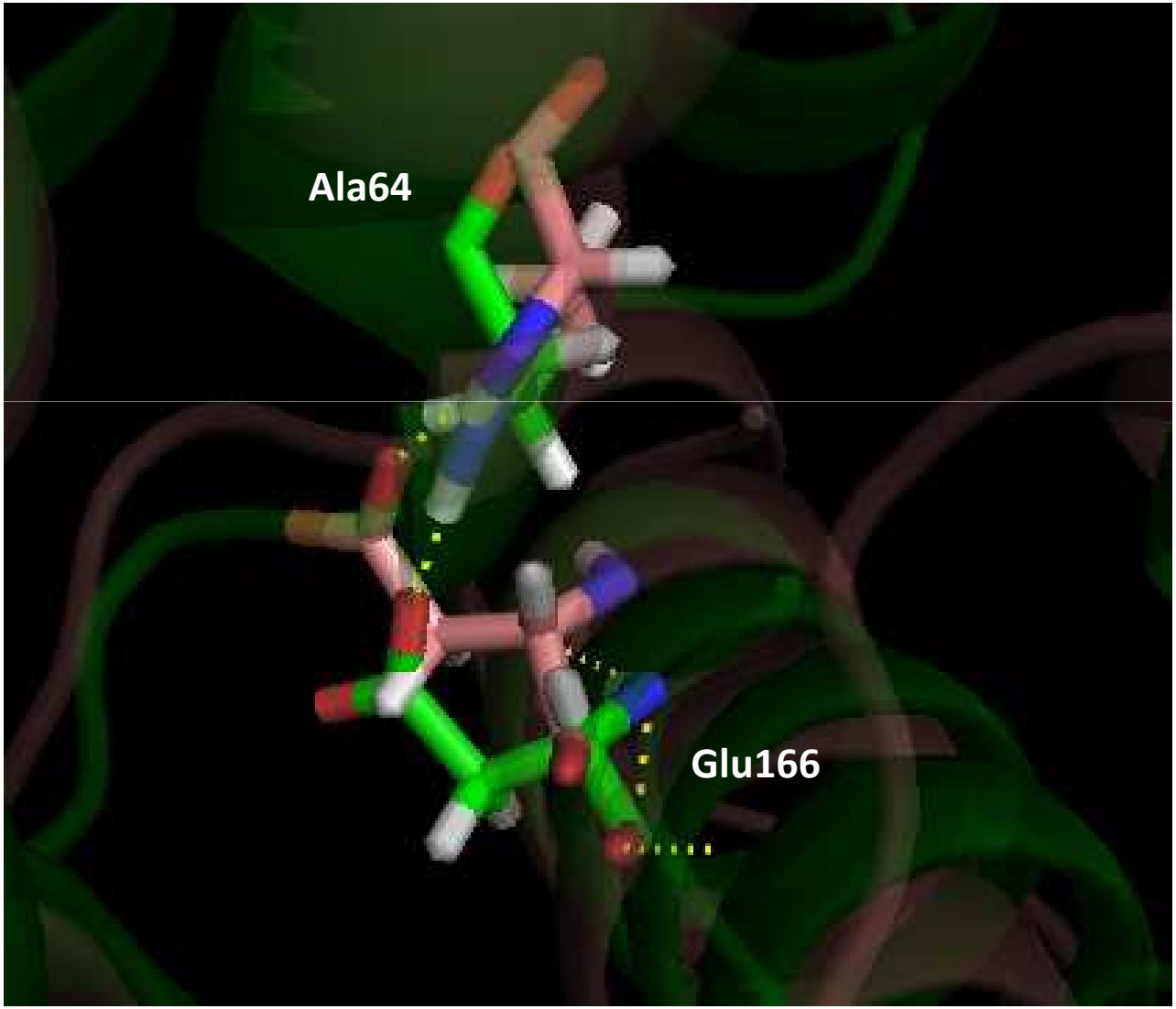
POLAR CONTACTS:

- Capping interactions

H-bonds interactions are conserved

3.2. PENTAMERS

NTD-CTD INTERFACE:



POLAR CONTACTS:

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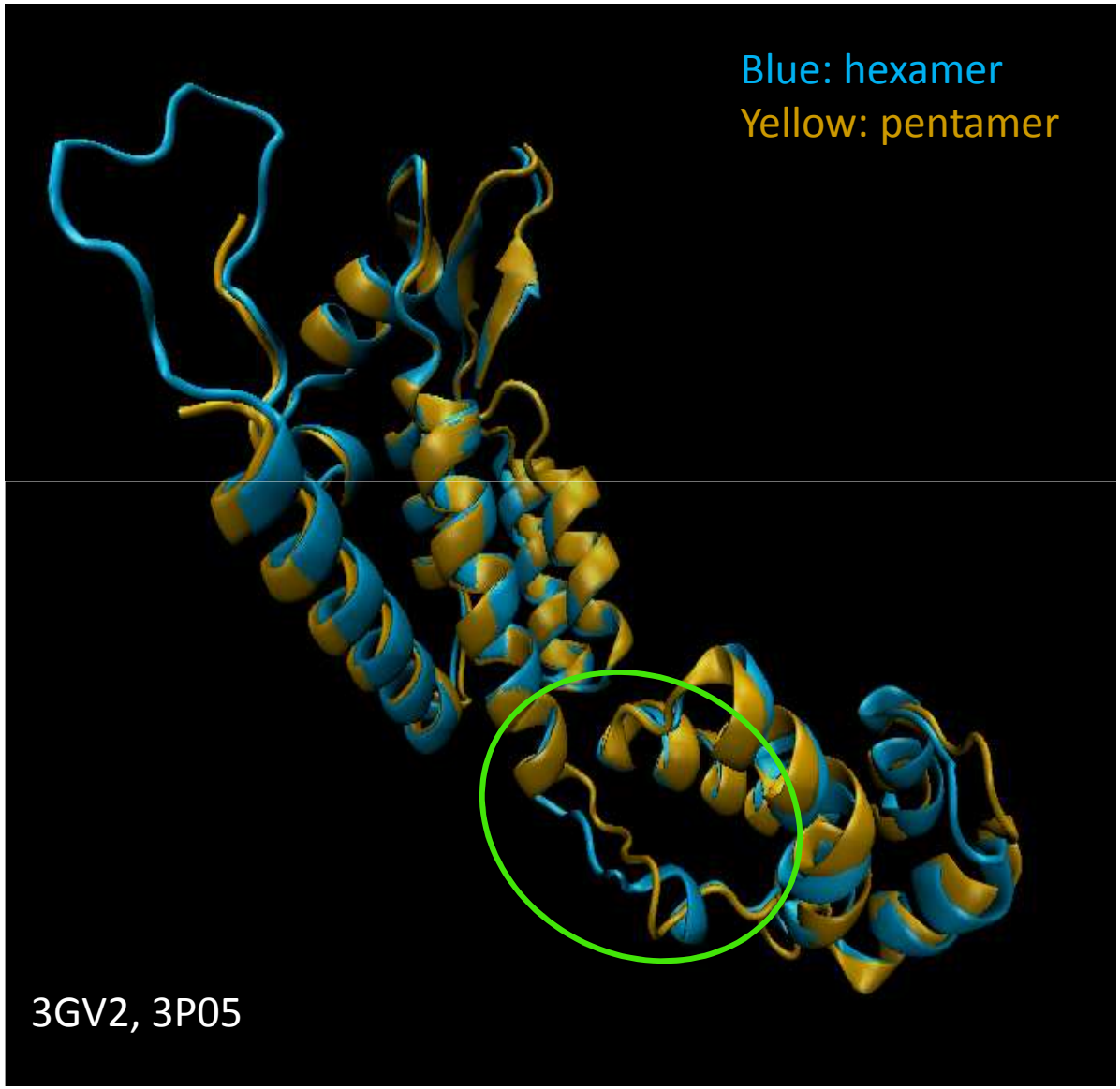
3.2. PENTAMERS



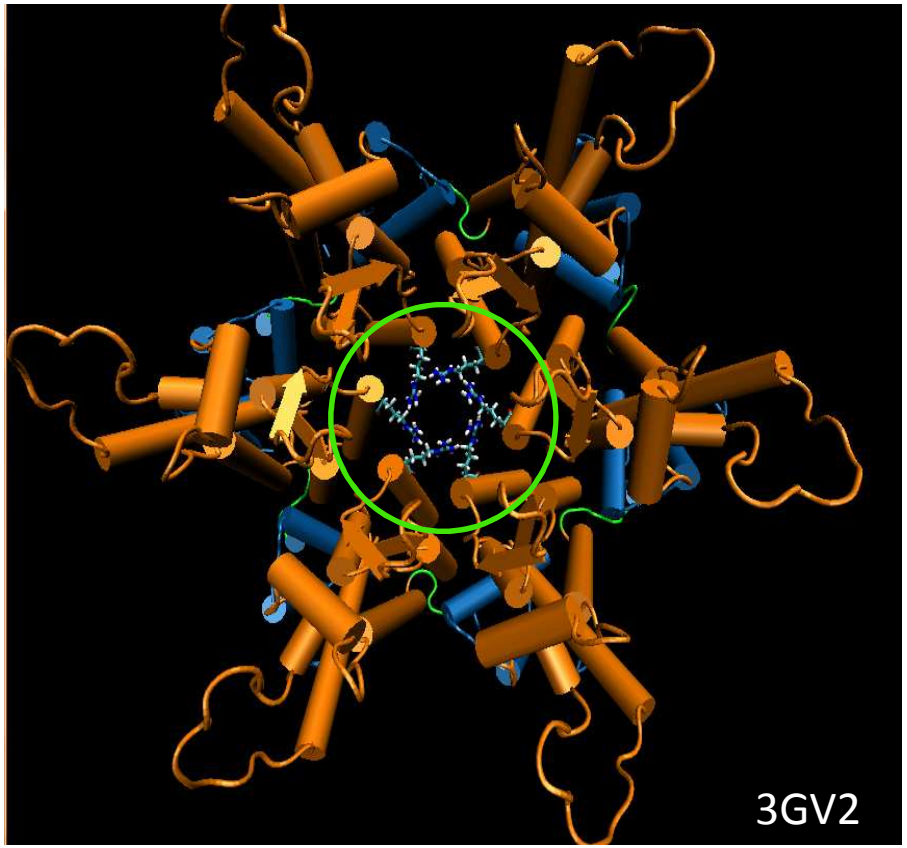
Flexible linker

STAMP Hexamer and Pentamer

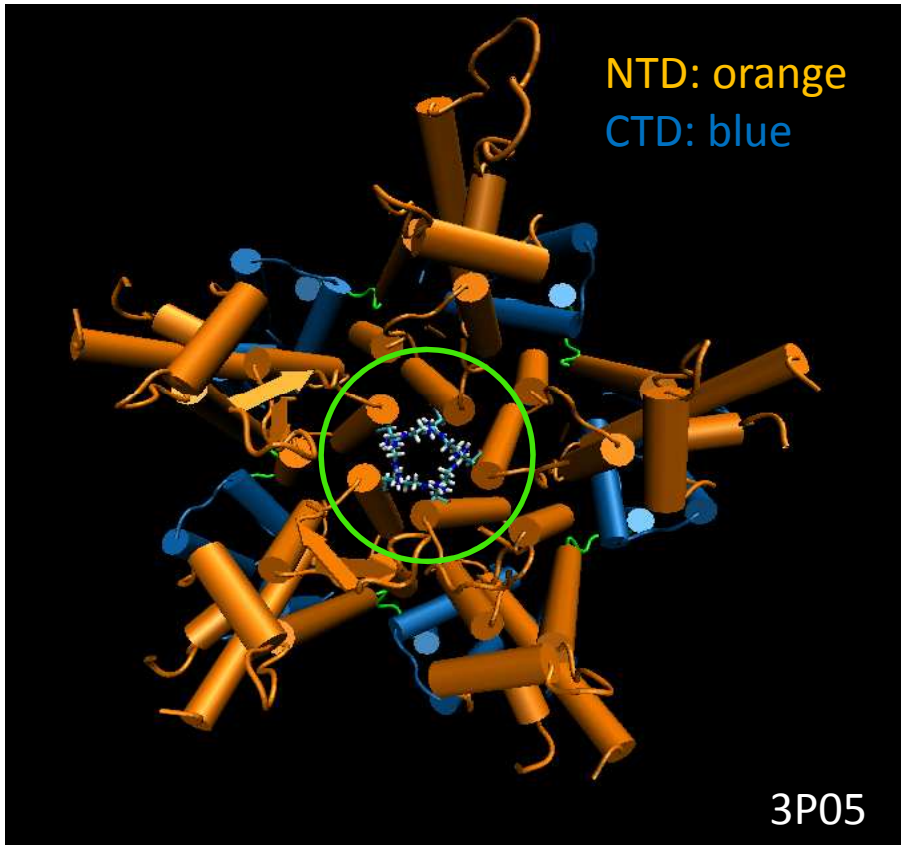
Allows movement of the CTD relative to the NTD

3.2. PENTAMERS

ELECTROSTATIC SWITCH – Arg18

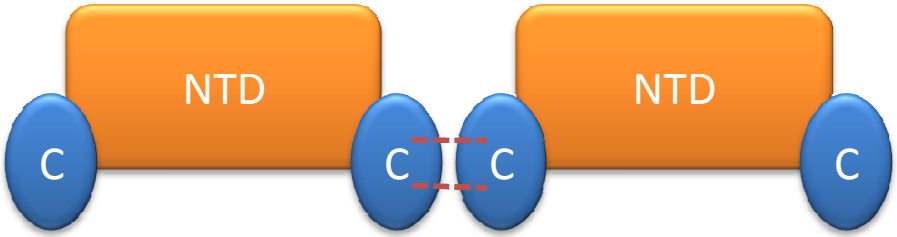


HEXAMER

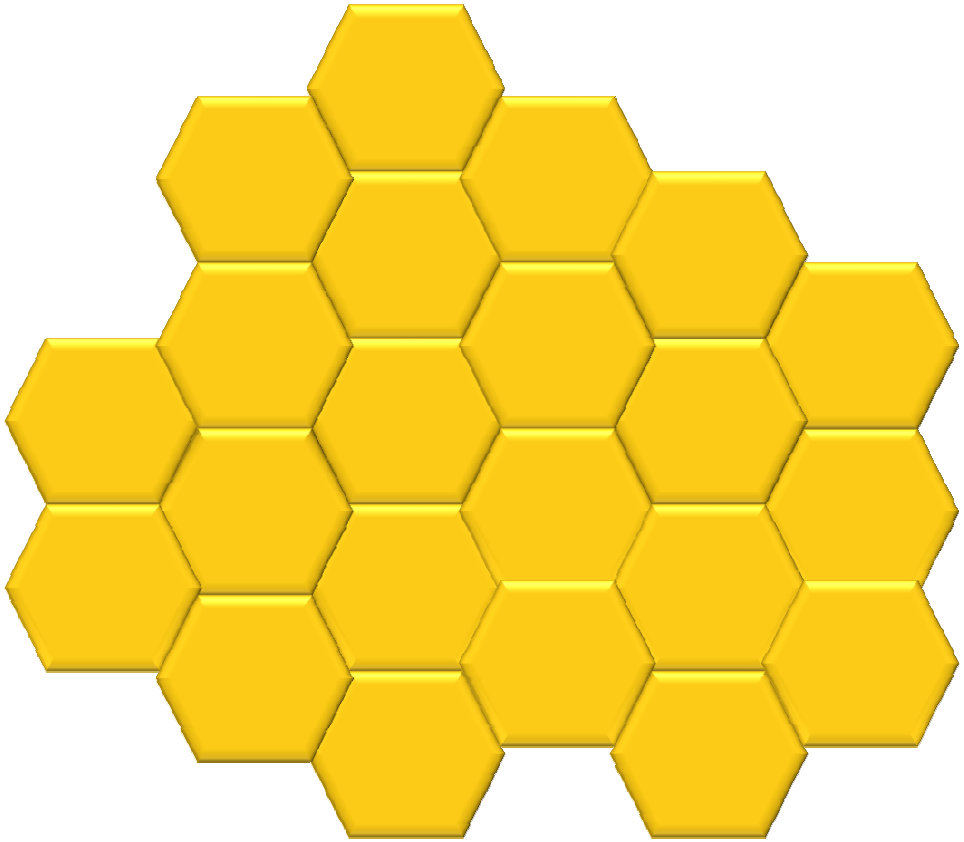


PENTAMER

4.CAPSID CURVATURE

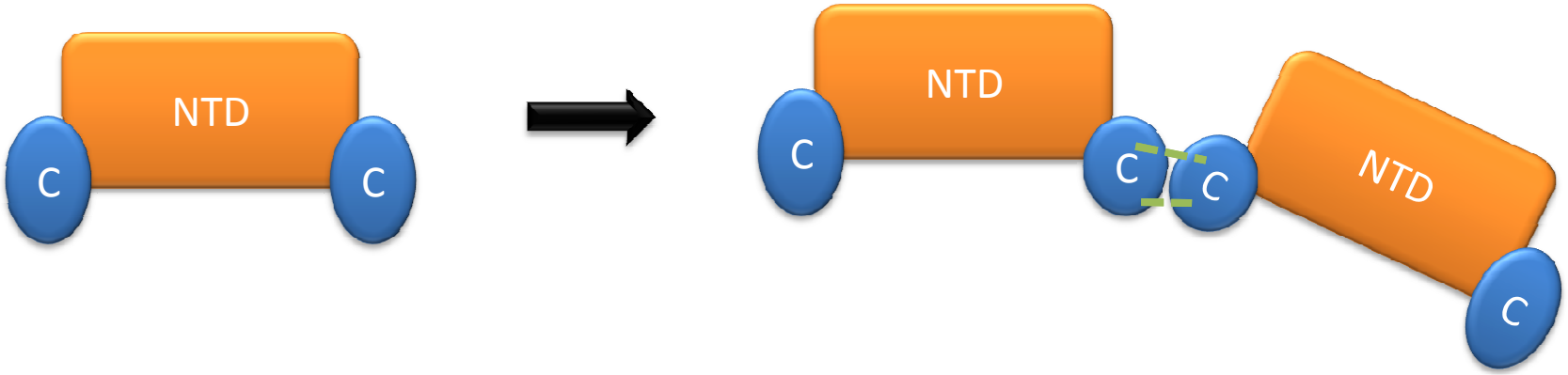


BUT, HOW A LATTICE OF HEXAMERS CAN FORM A CONICAL SHAPE?

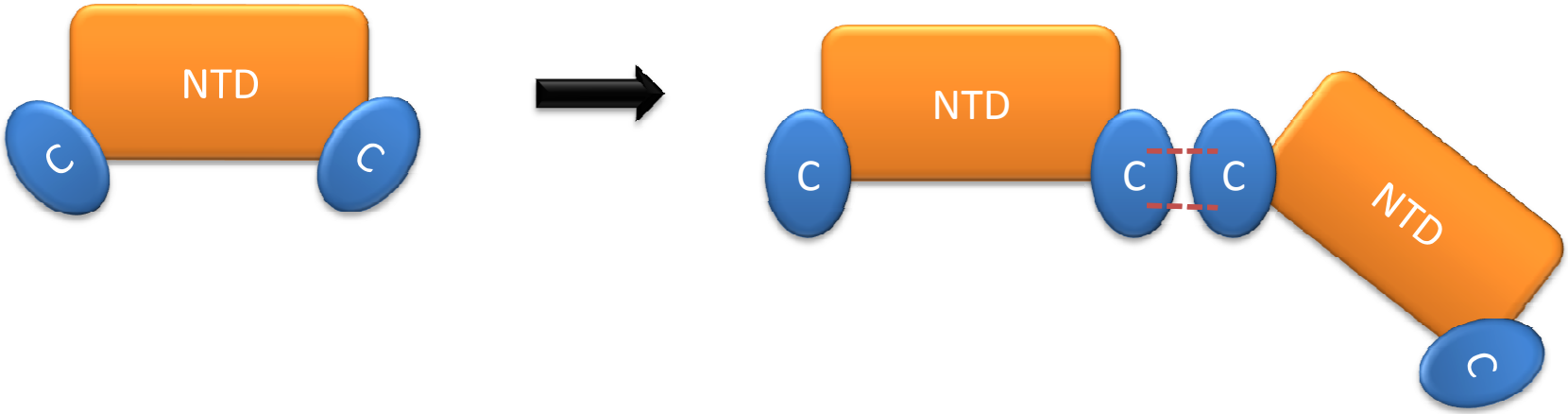


4.CAPSID CURVATURE

1. CTD flexibility

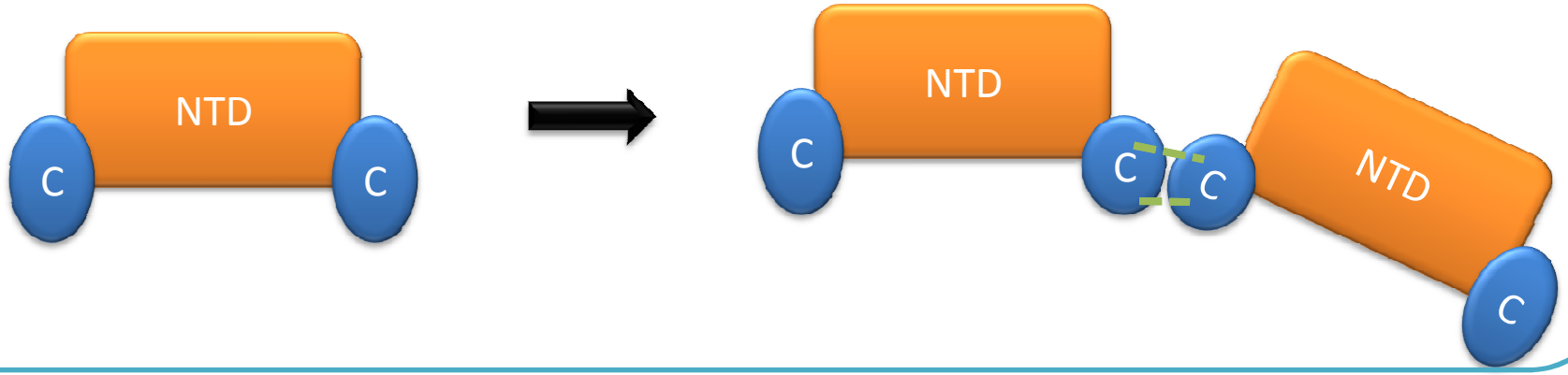


2. Rigid-body motions

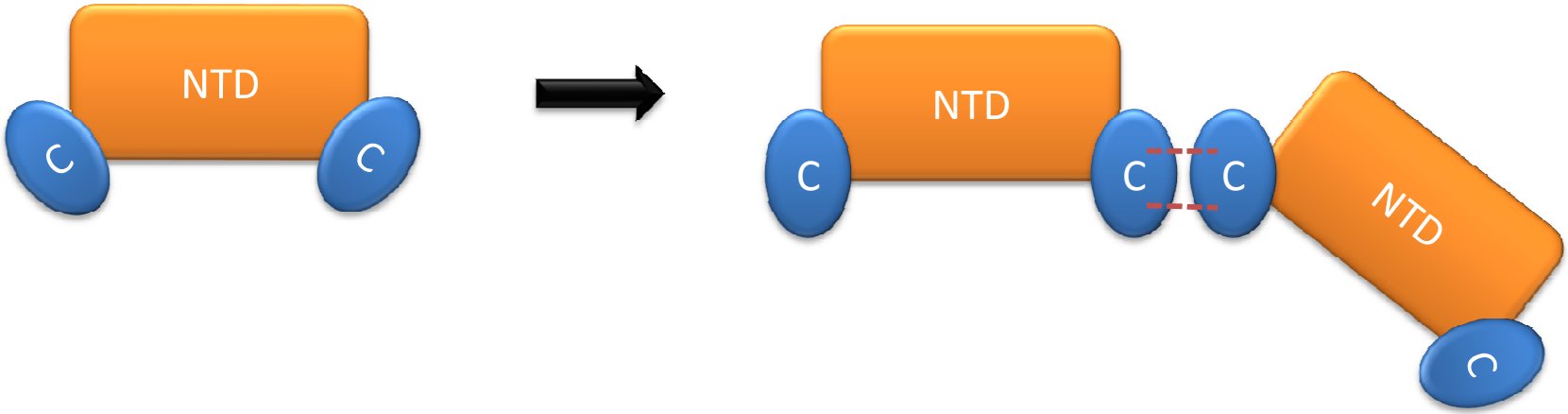


4.CAPSID CURVATURE

1. CTD flexibility

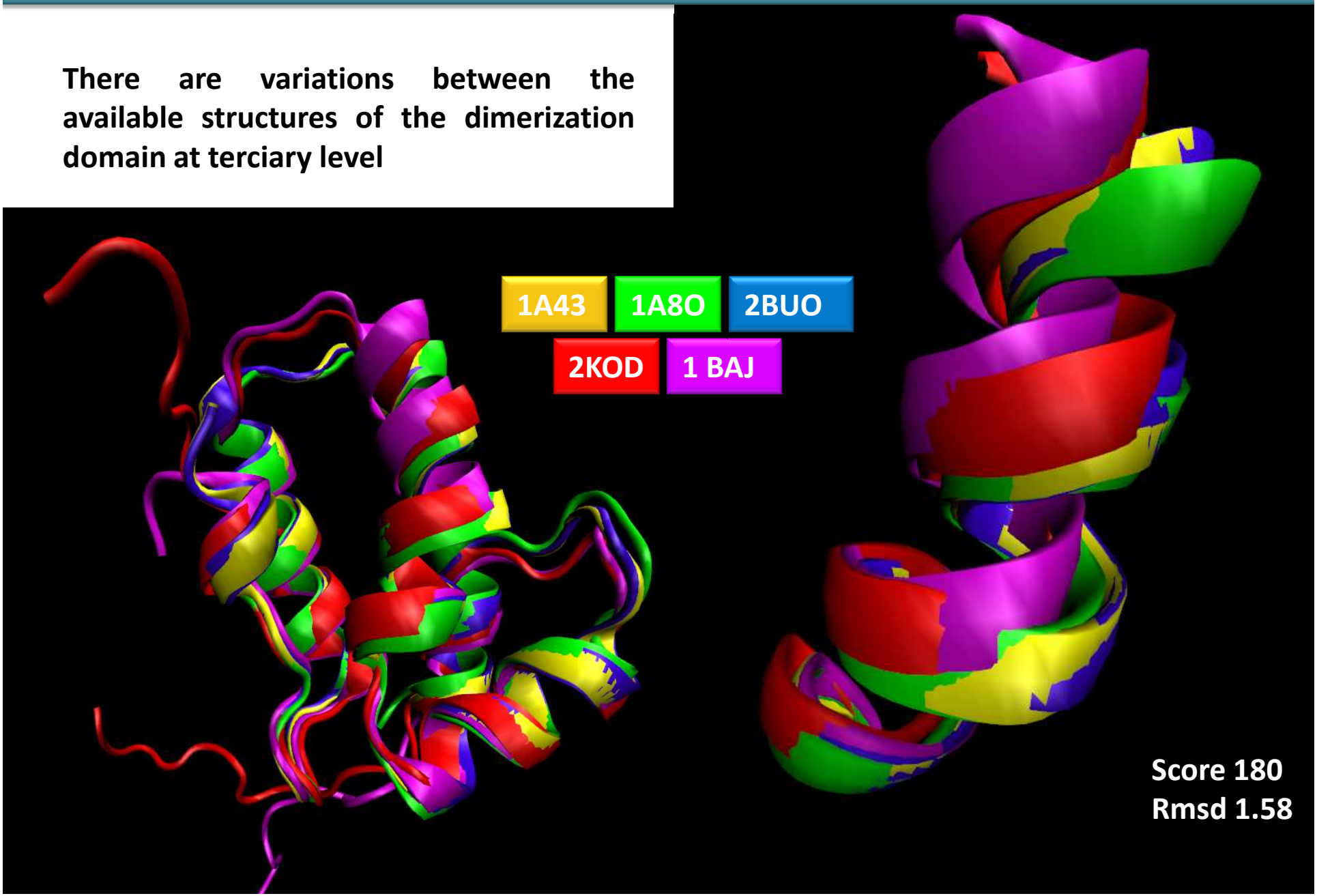


2. Rigid-body motions



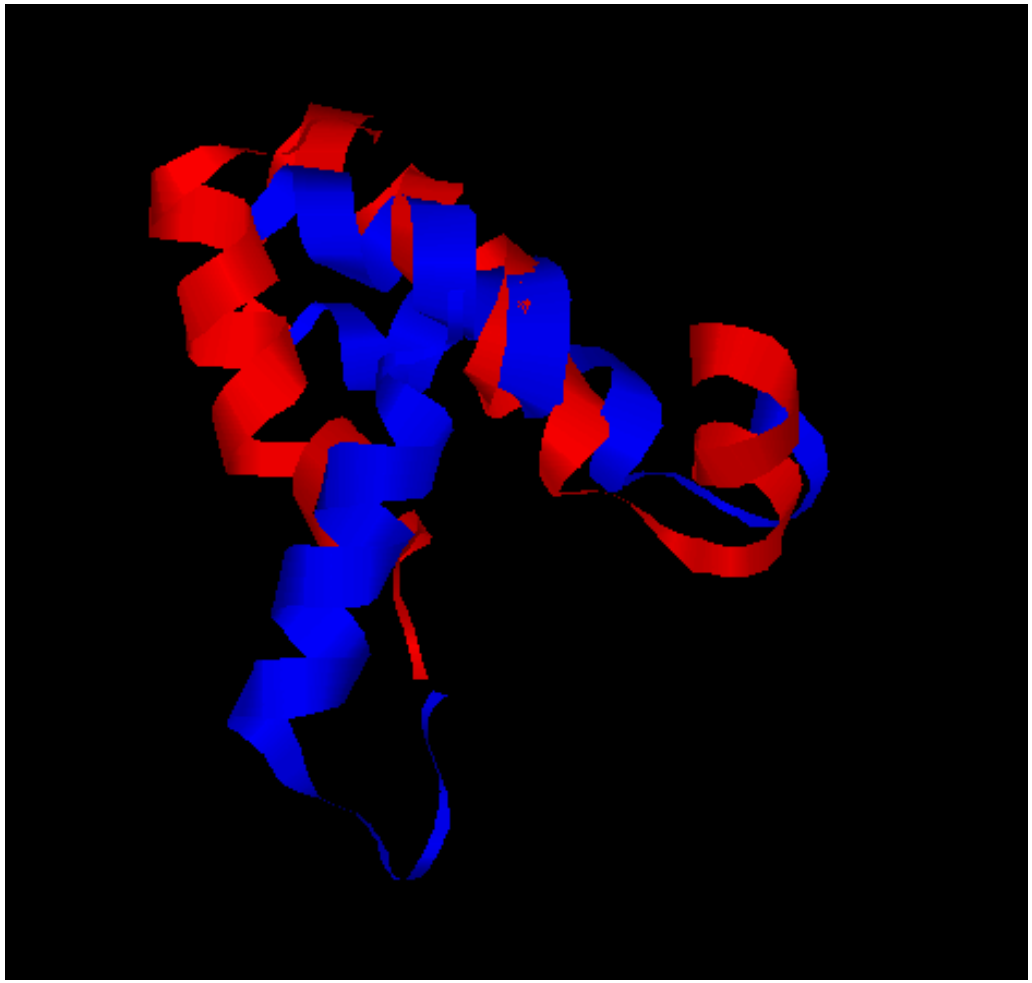
4.1. CTD FLEXIBILITY

There are variations between the available structures of the dimerization domain at terciary level



4.1. CTD FLEXIBILITY

There are also variations between the structure at quaternay level

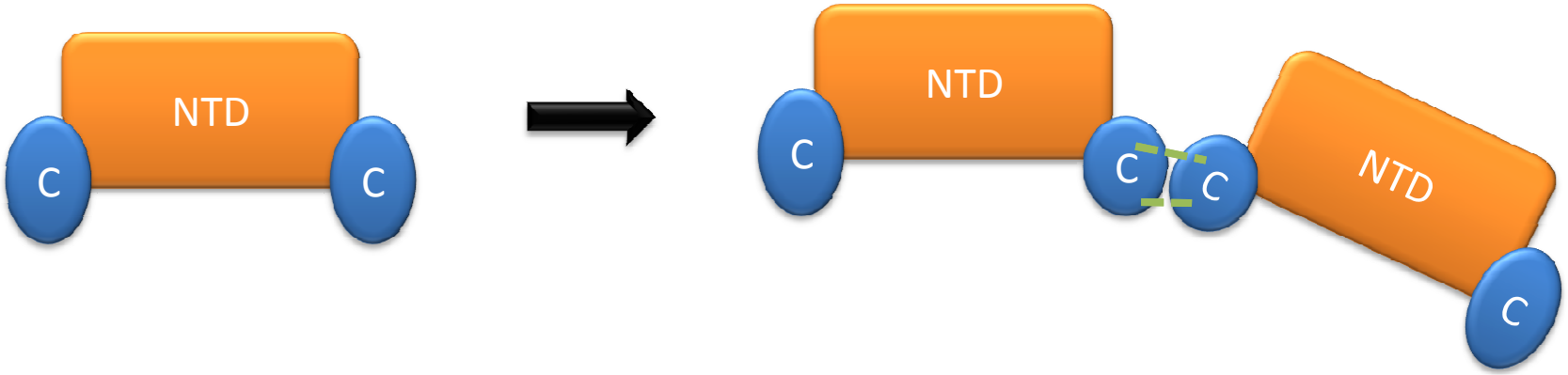


1A43

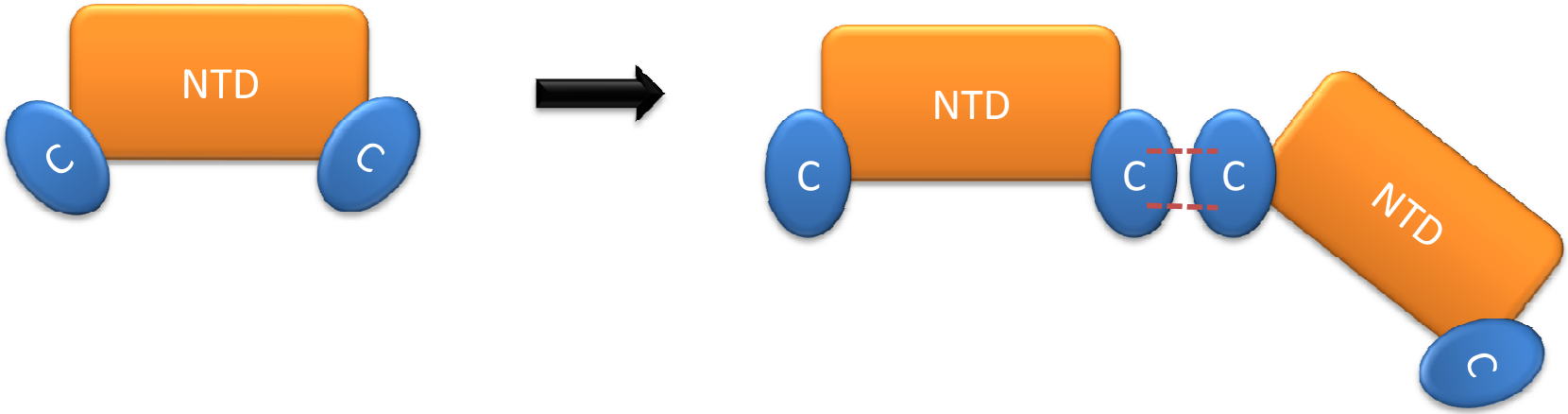
2KOD

4.CAPSID CURVATURE

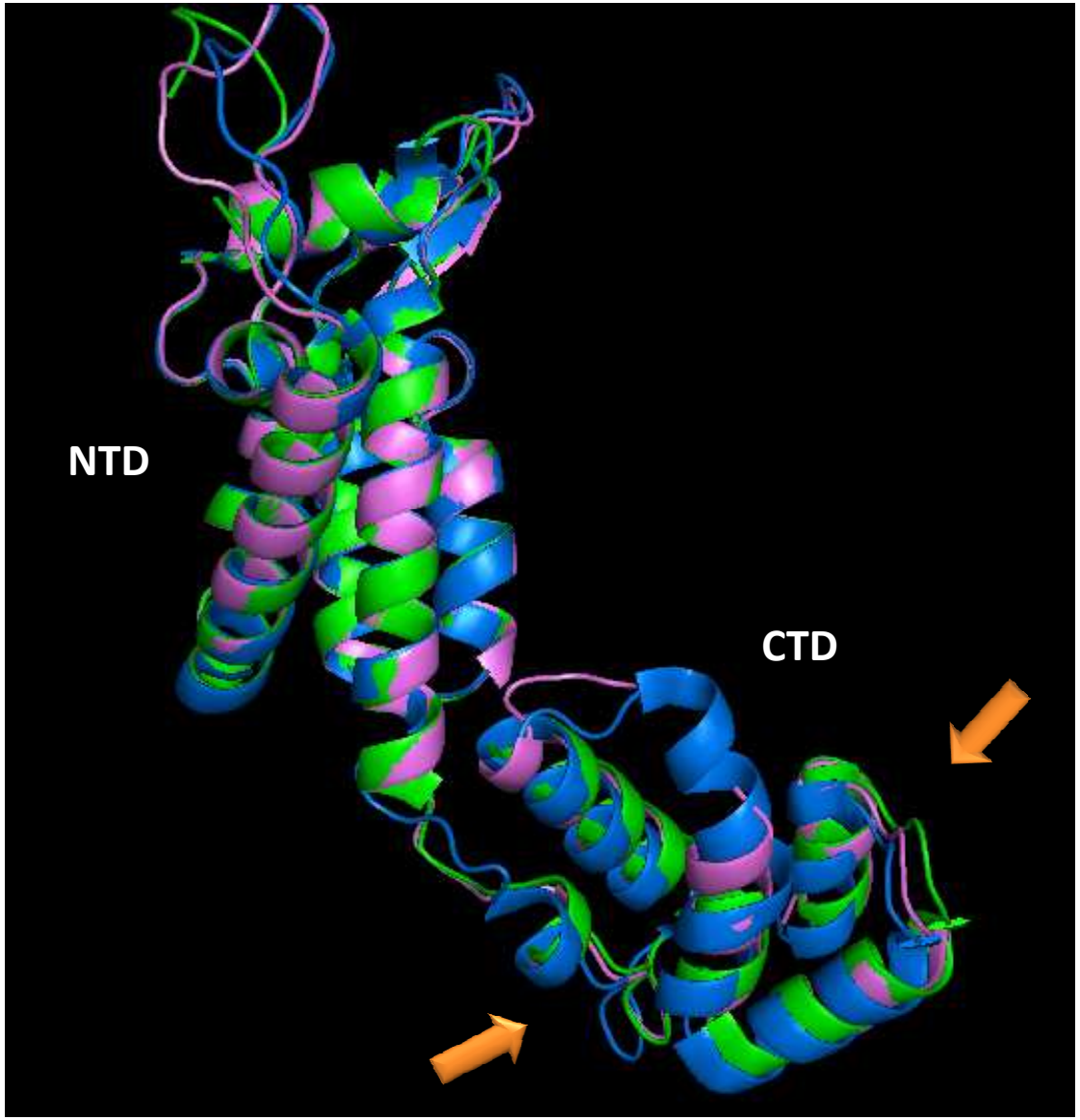
1. CTD flexibility



2. Rigid-body motions

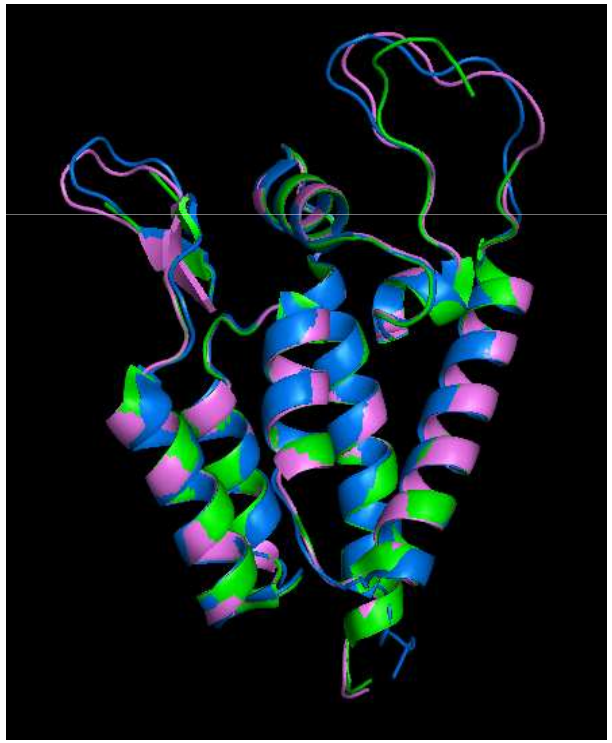


4.2. RIGID-BODY MOTIONS



STAMP
3 Hexamers

Pdb 3h47
Pdb 3GV2
Pdb 3H4E

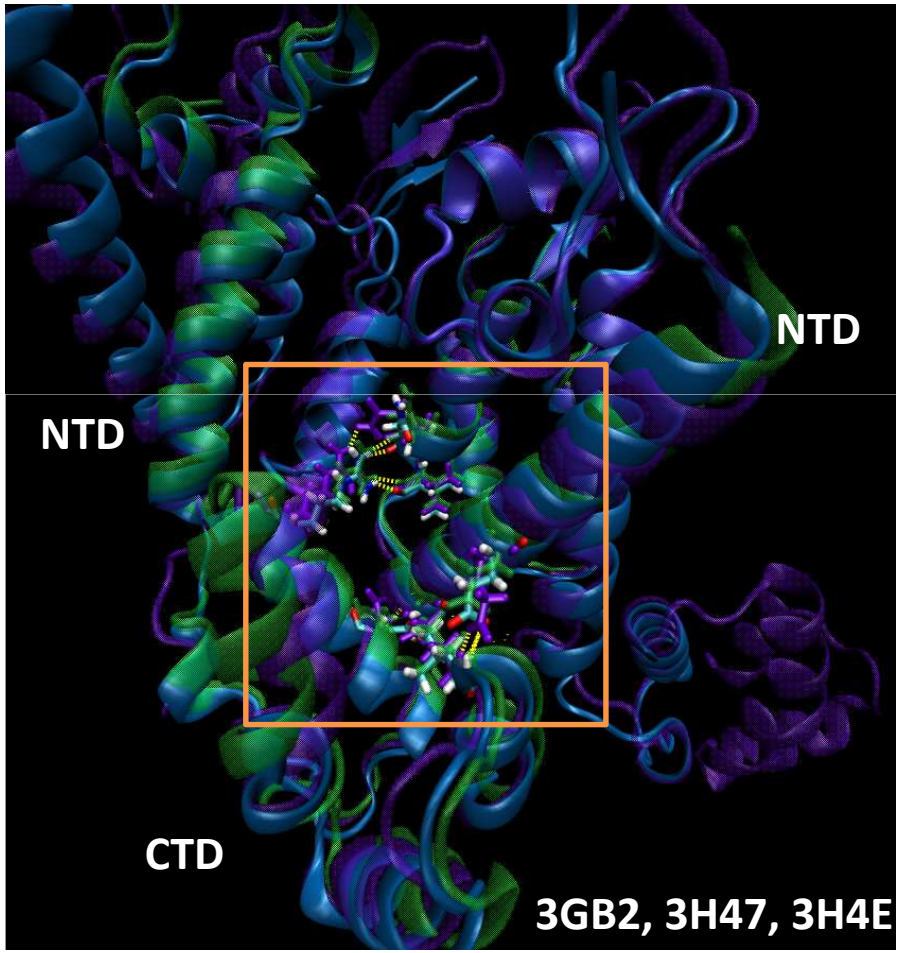


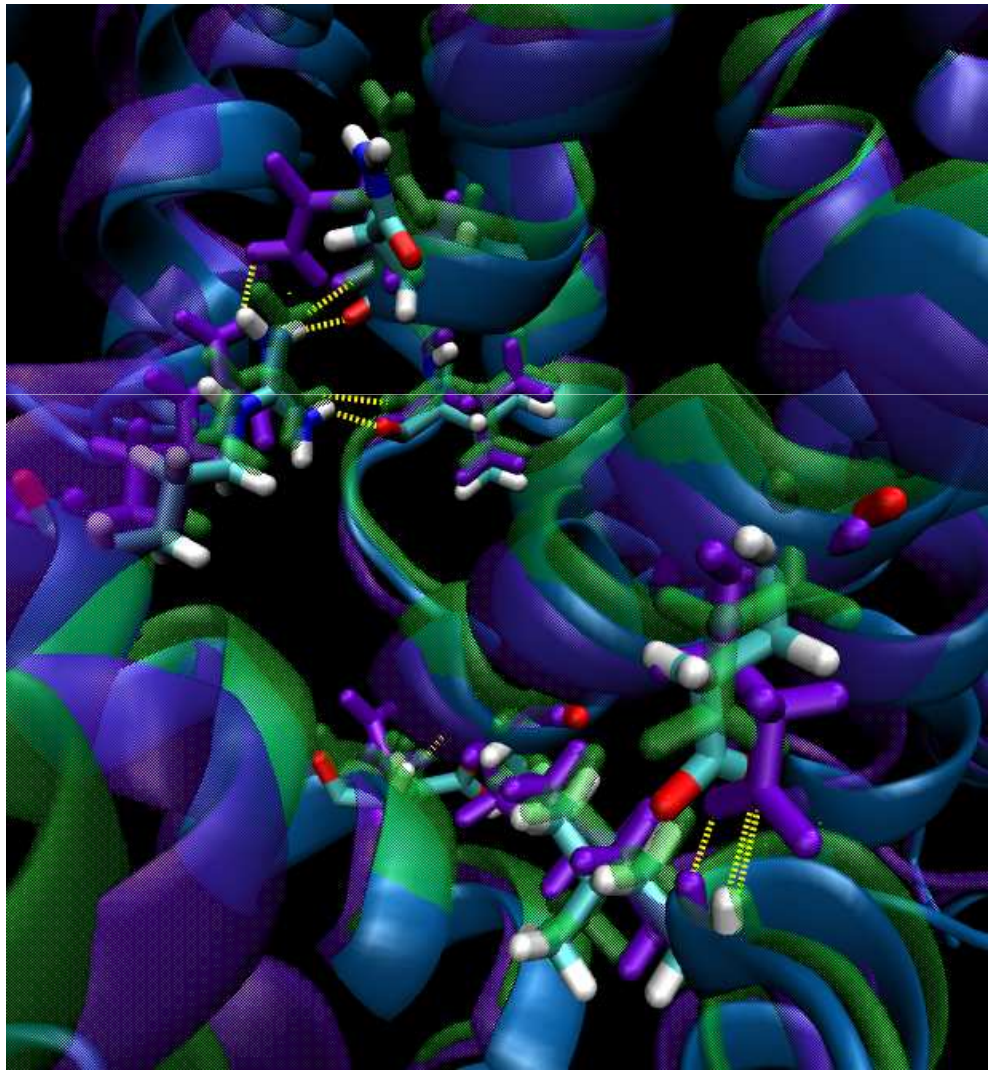
- NTD
  - Helix 1, 2, 3, 4
  - Cyp binding loop
  - Helix 5, 6

- **Pdb 3h47**: resolution: 1,90 Å
- **Pdb 3GV2**: resolution 7 Å (some variability)
- **Pdb 3H4E**: resolutin: 2,70 Å

4.2. RIGID-BODY MOTIONS

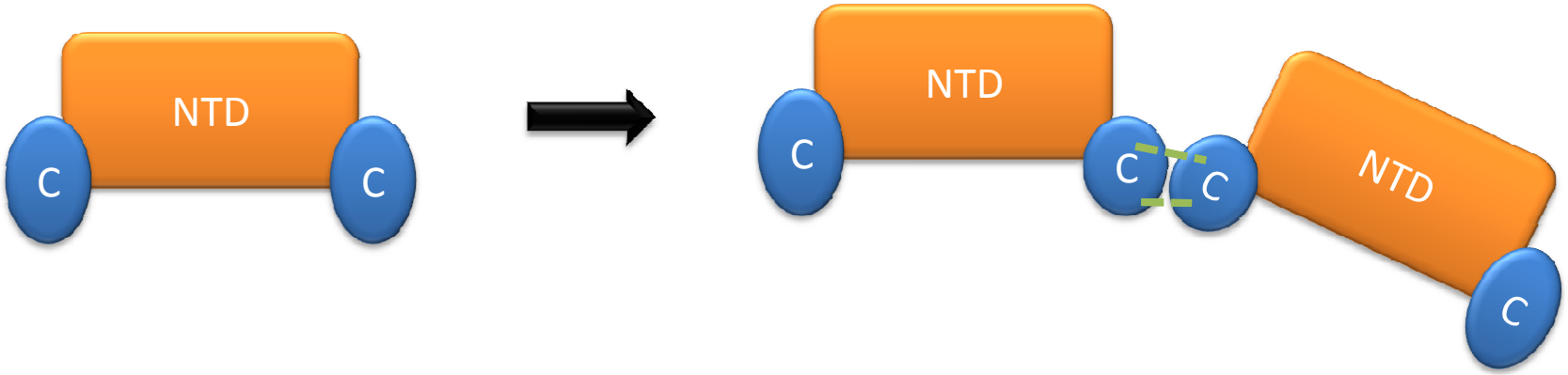
STAMP 3Hexamer





4.CAPSID CURVATURE

1. CTD flexibility



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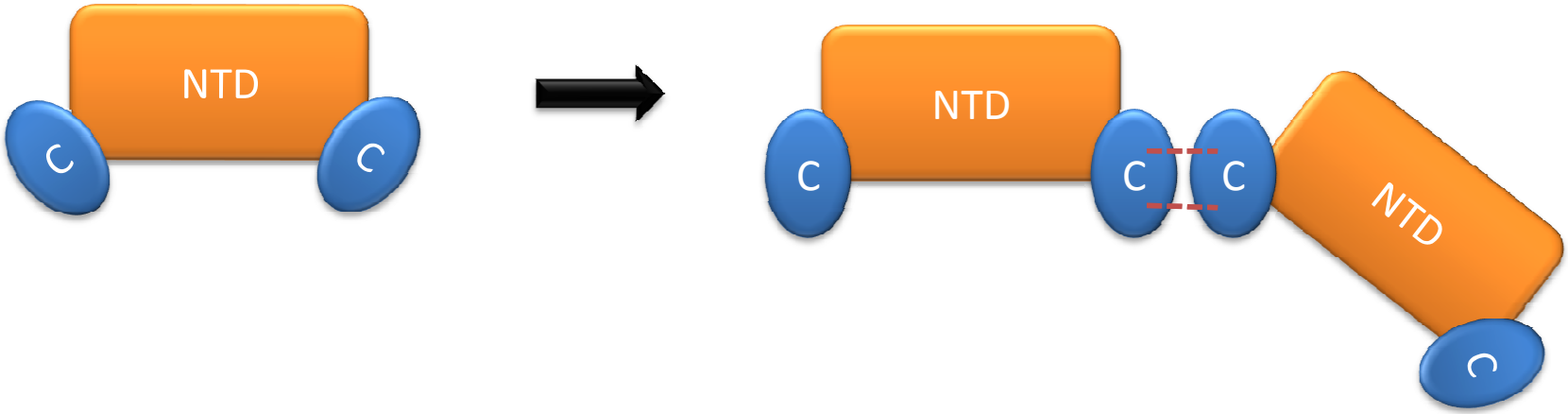
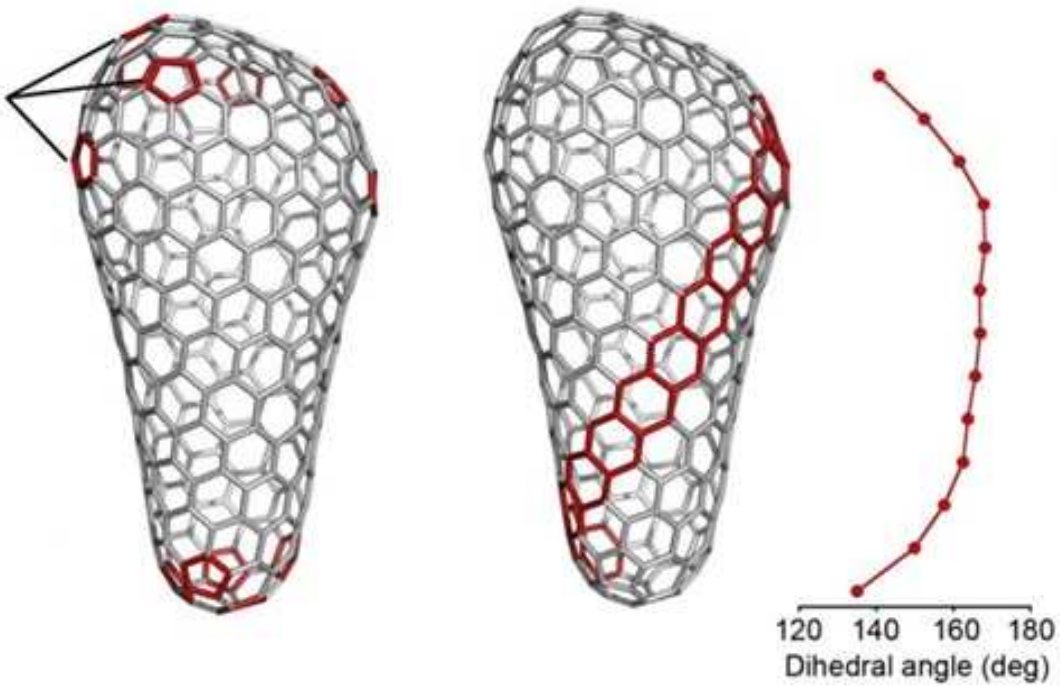


Index

- Introduction
- CA (monomer)
  - NTD
  - CTD
- Capsid subunits
  - Hexamers
  - Pentamers
- Capsid curvature
- Current situation

5. Current situation

Pentamers introduce sharp declinations



Countinuously changing curvature in the hexameric lattics

Figure from: Pornillos et al, 2011

5. Current situation

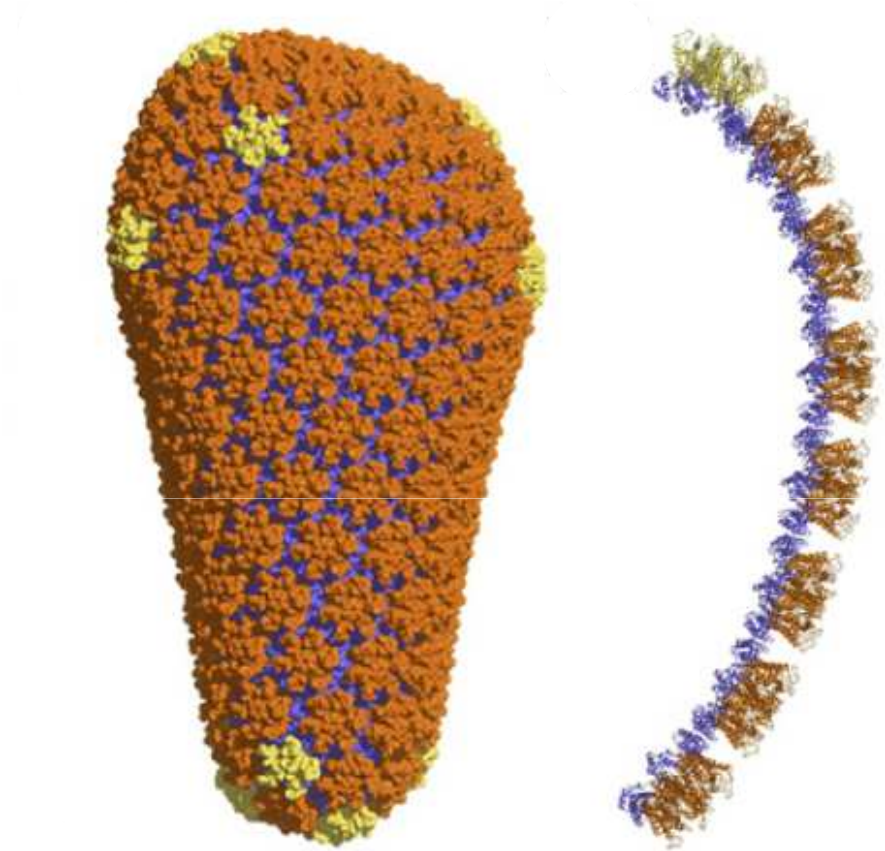
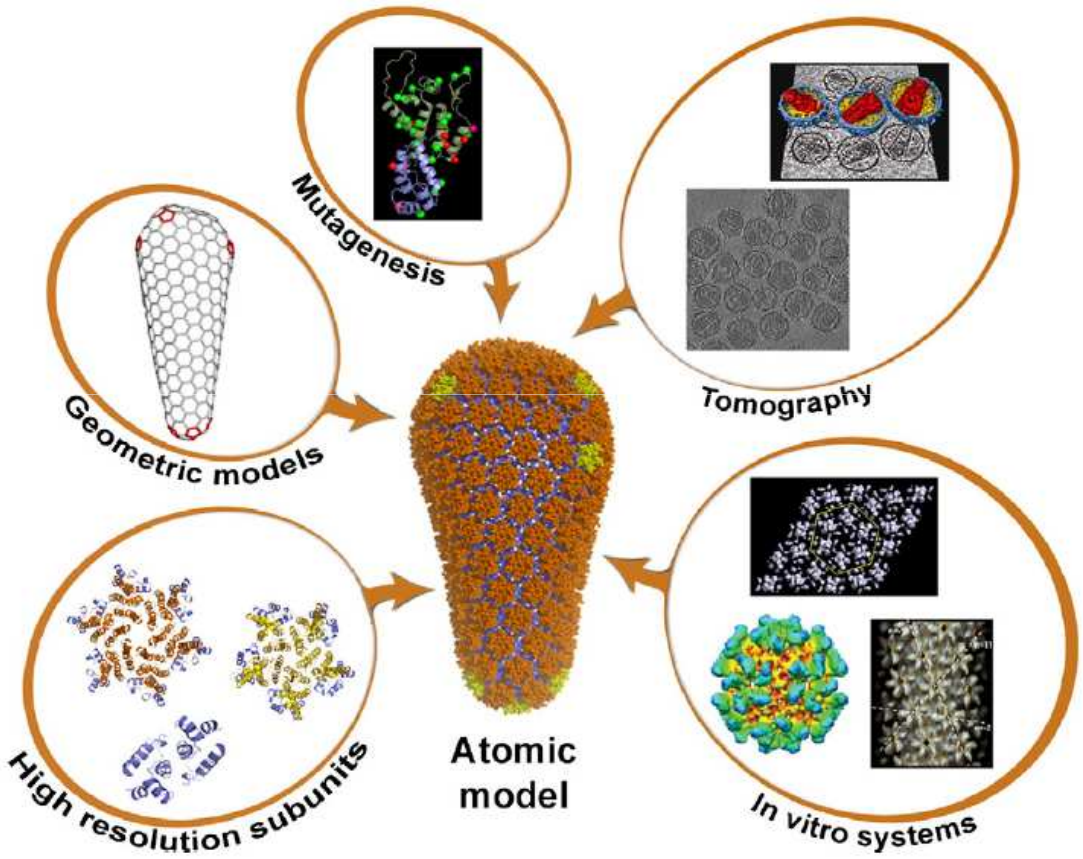


Figure from: Pornillos et al, 2011

Capsid – model



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THANK YOU FOR YOUR ATTENTION!