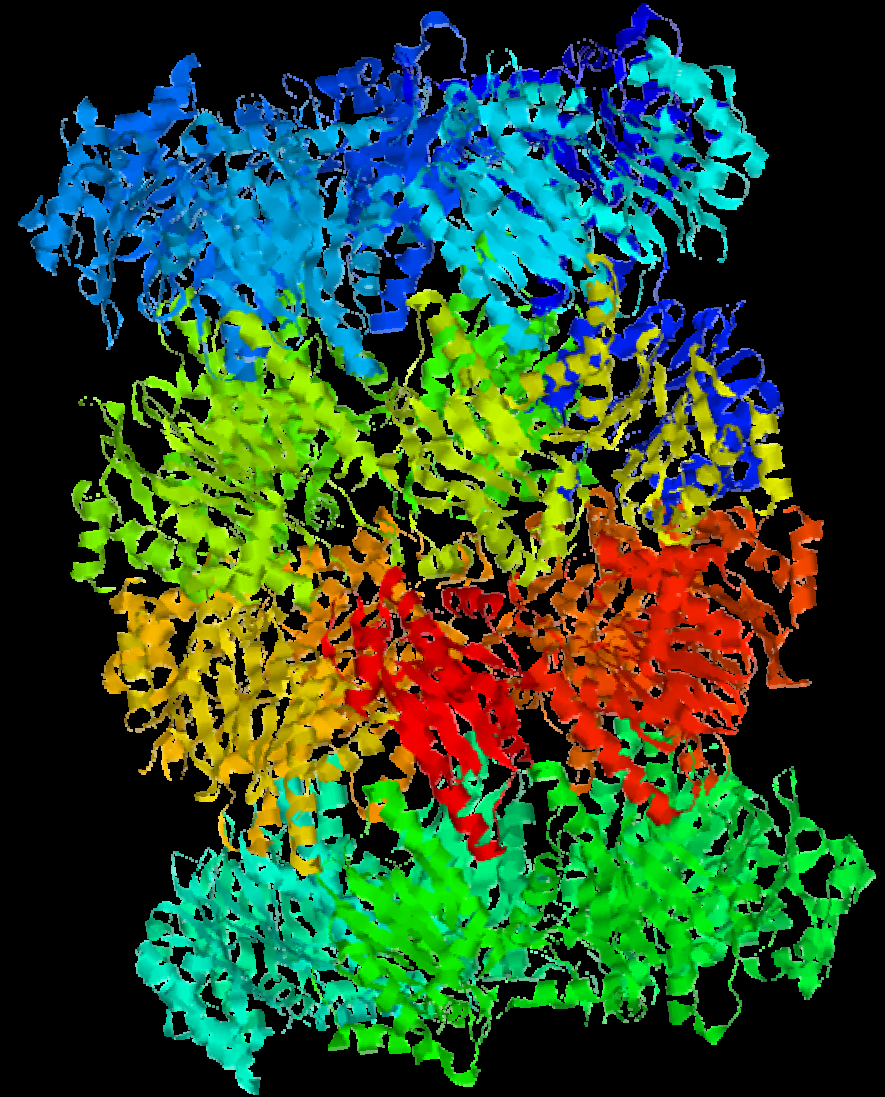


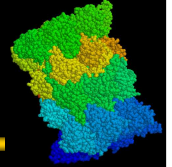
EL PROTEOSOMA



Cristina Gómez, Manuel Gómez, Anna González, Sonia Laguna

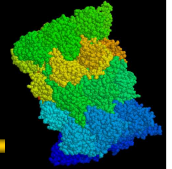
Ciències de la Salut i de la Vida, UPF

Barcelona 2007



1. Característiques generals
2. Comparació d'estructures:
 - *Thermoplasma acidophilum*
 - *Saccharomyces cerevisiae*
3. Mecanisme d'acció
4. Ensenyament
5. Estudi evolutiu
6. Caps reguladors del proteosoma

Característiques generals



El proteosoma:

Complex macromolecular responsable de la major part de la degradació de proteïnes.

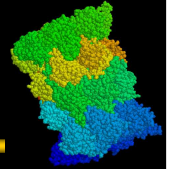
Localització:

Citoplasma i nucli d'eucariotes i procariotes.

Es troba implicat en:

- Resposta a l'estrés oxidatiu
- Control del cicle cel·lular
- Presentació d'antígens

Características generales



Estructura:

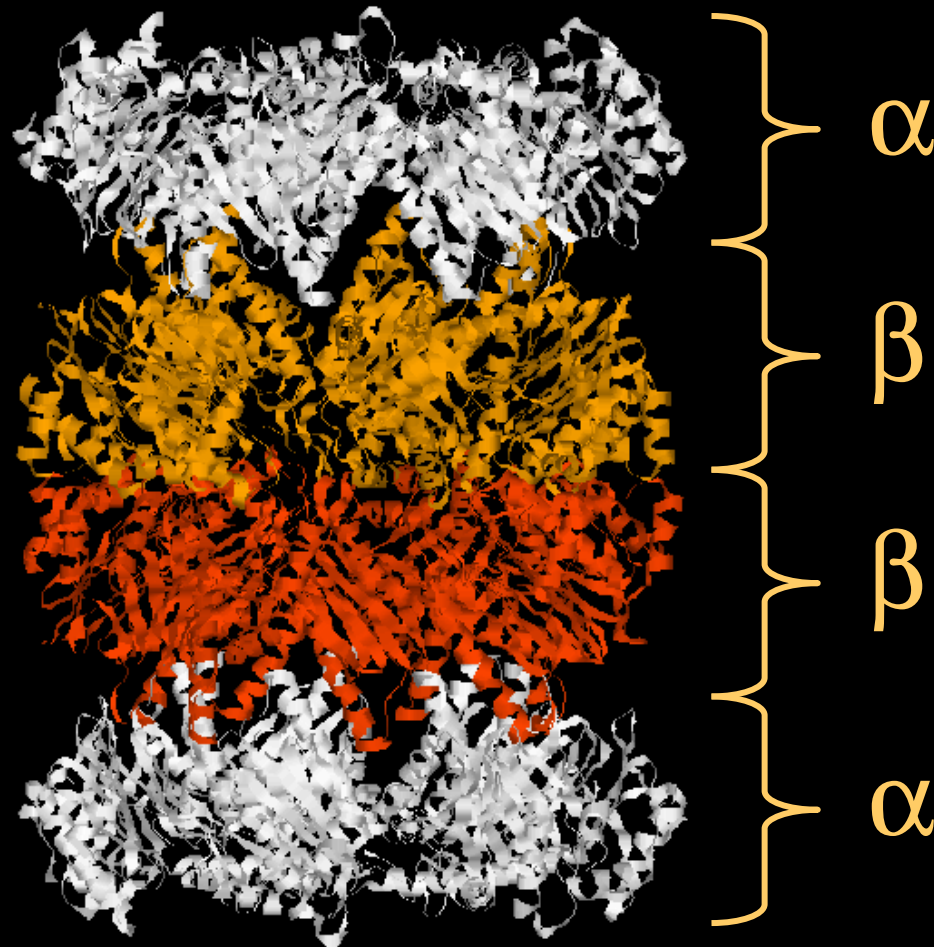
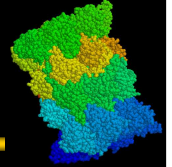
115-150 Å

113 Å



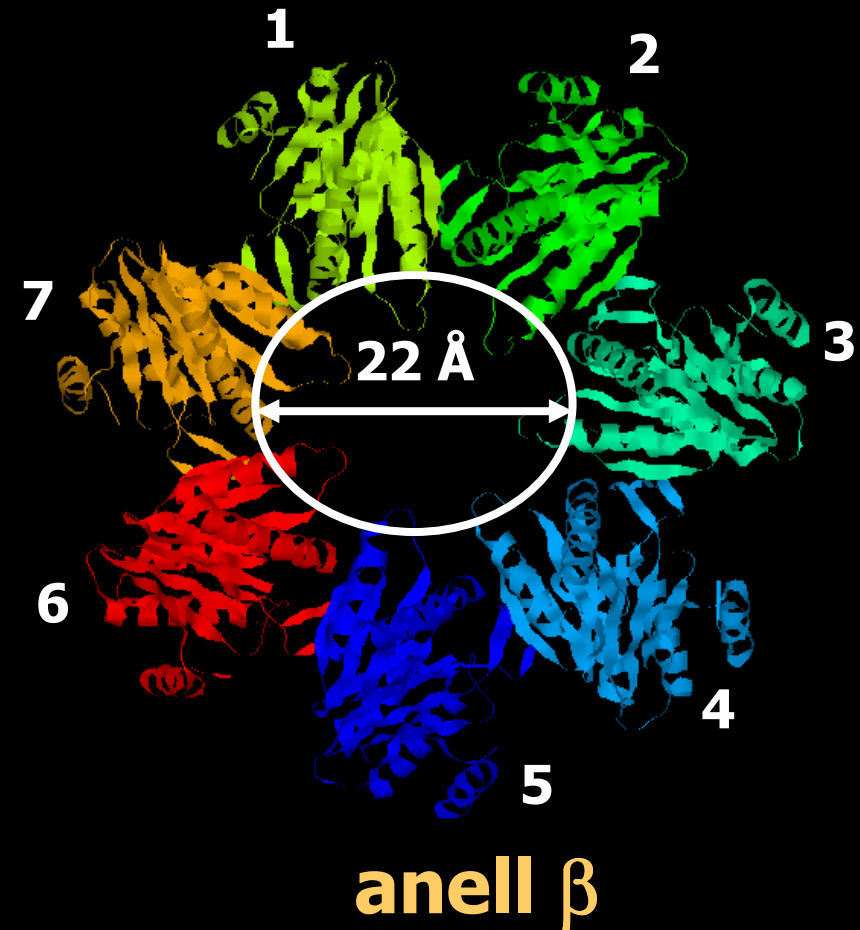
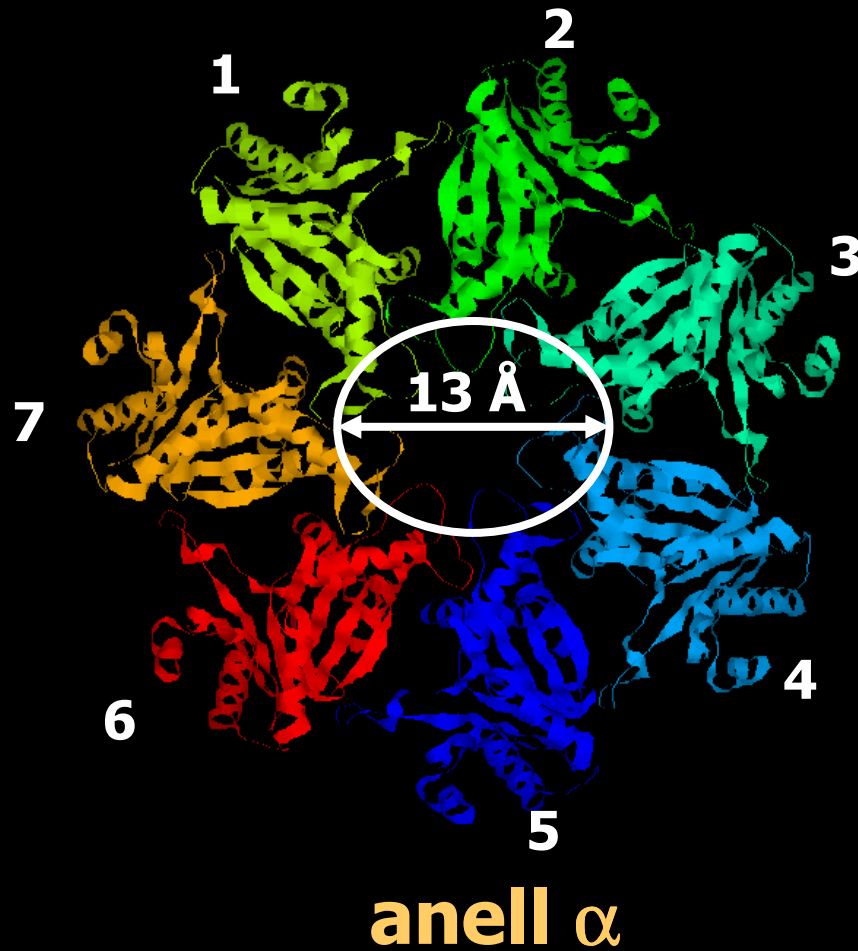
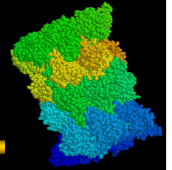
1PMA.pdb

Características generales



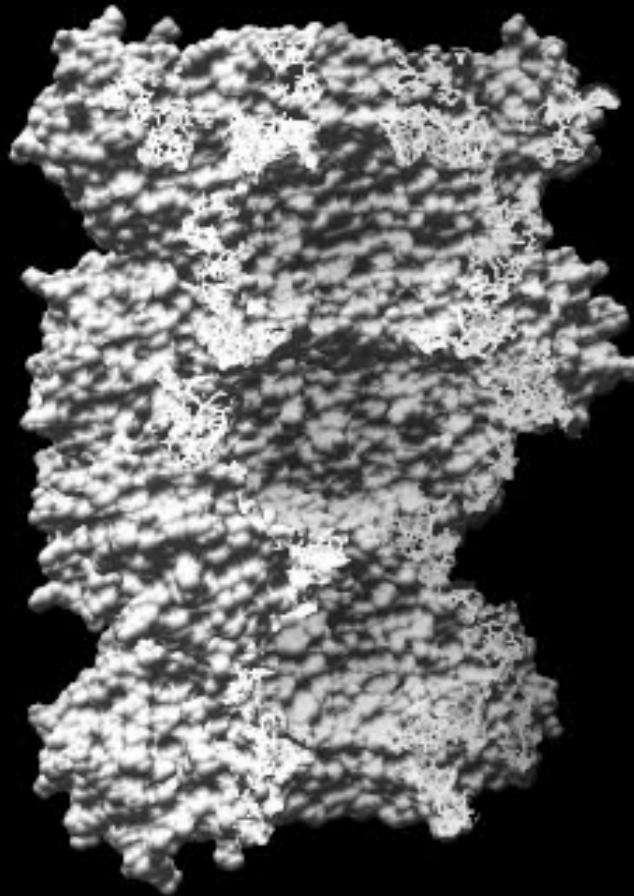
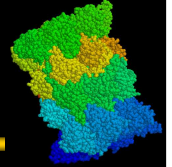
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Característiques generals



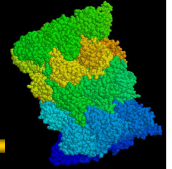
1PMA.pdb

Caractéristiques générales



1PMA.pdb

Classificació SCOP



- **CLASSE:**

Alpha and beta proteins (a+b)

- **PLEGAMENT:**

Ntn hydrolase-like

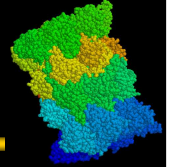
- **SUPERFAMÍLIA:**

N-terminal nucleophile aminohydrolases (Ntn hydrolases)

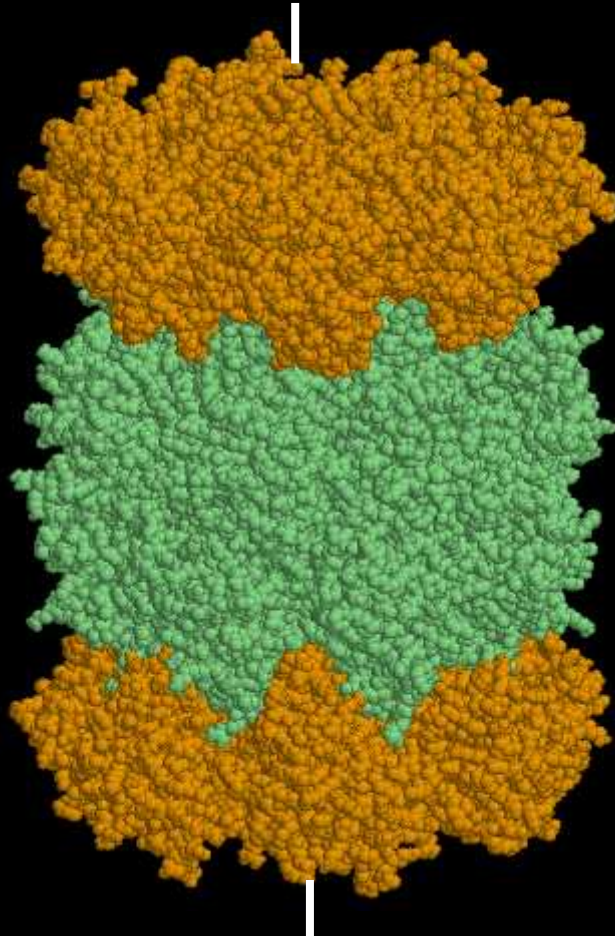
- **FAMÍLIA:**

Proteasome subunits

Simetria: *T. acidophilum* vs *S. cerevisiae*

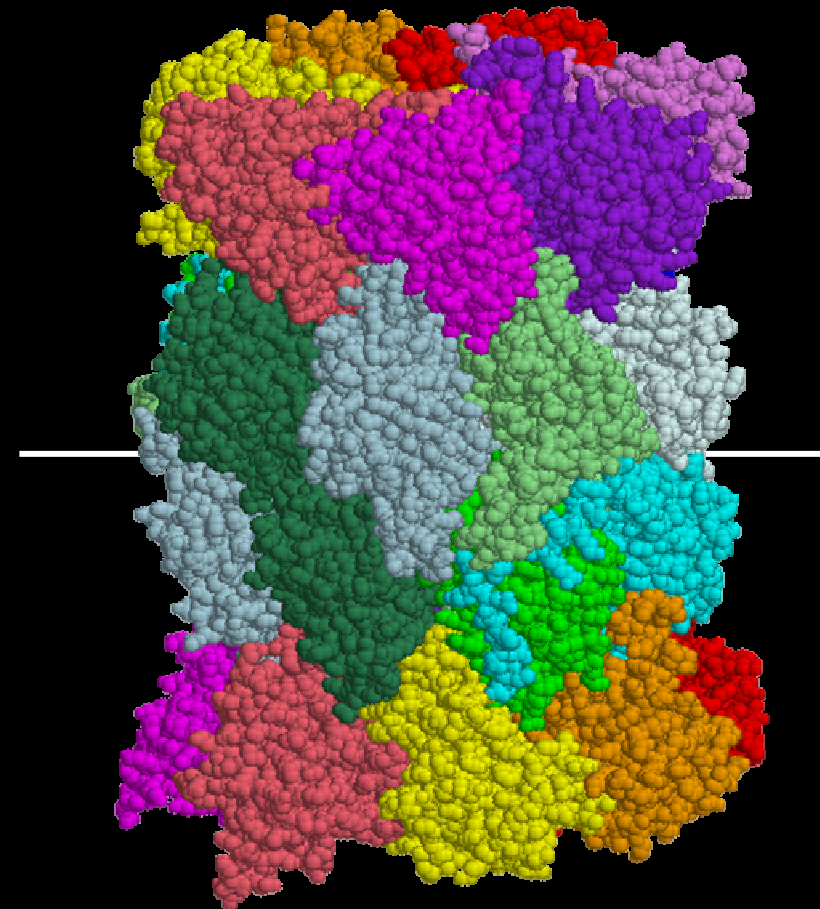


Simetria D7



T. acidophilum

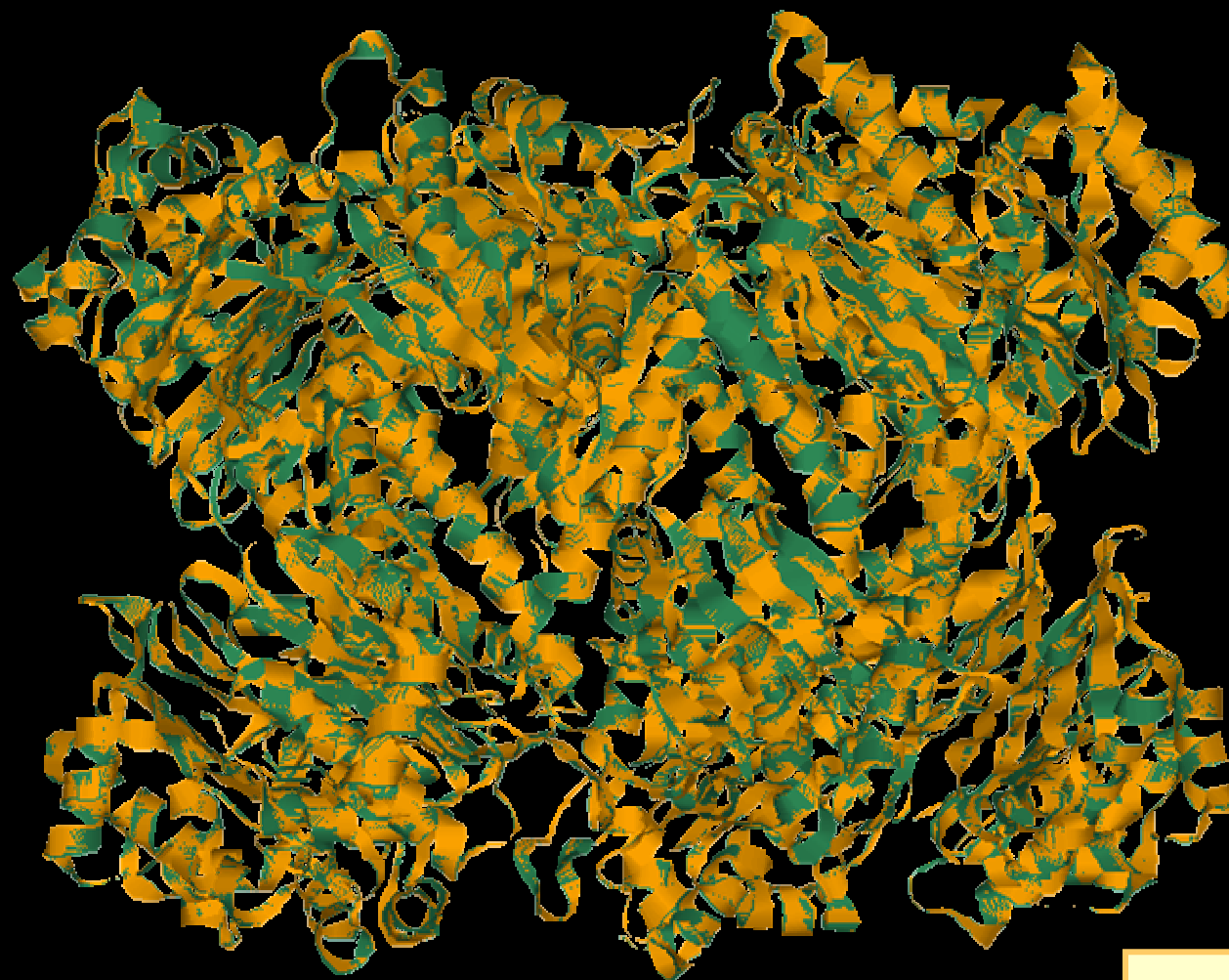
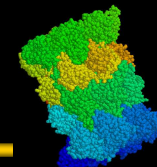
Simetria C2



S. cerevisiae

Thermoplasma acidophilum

T. acidophilum: Estudi de simetria

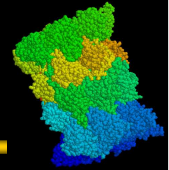


1PMA.pdb

Score: 9,77

RMS: 0,19

T. acidophilum: Estructura de les subunitats



1. Entre α i β

CLUSTAL W(1.60) multiple sequence alignment

```
beta1  -----TTTVGITLKDAVIMATERRVTMENFI--M-HK-NGKKL
alfa1  TVFSPDGRLFQVEYAREAVKKGSTALGMKFANGVLLISDKK-----VRSRLIEQNSIEKI

beta1  FQIDTYTGMTIAGLVGDAQVLVRYMKAELELYRLQRRVNMPIEAVATLLSNMLNQV--K-
alfa1  QLIDDYVAAVTSGLVADARVLVDFARISAQQQEKVTYGSLVNIENLVKRVADQMQQYTQYG

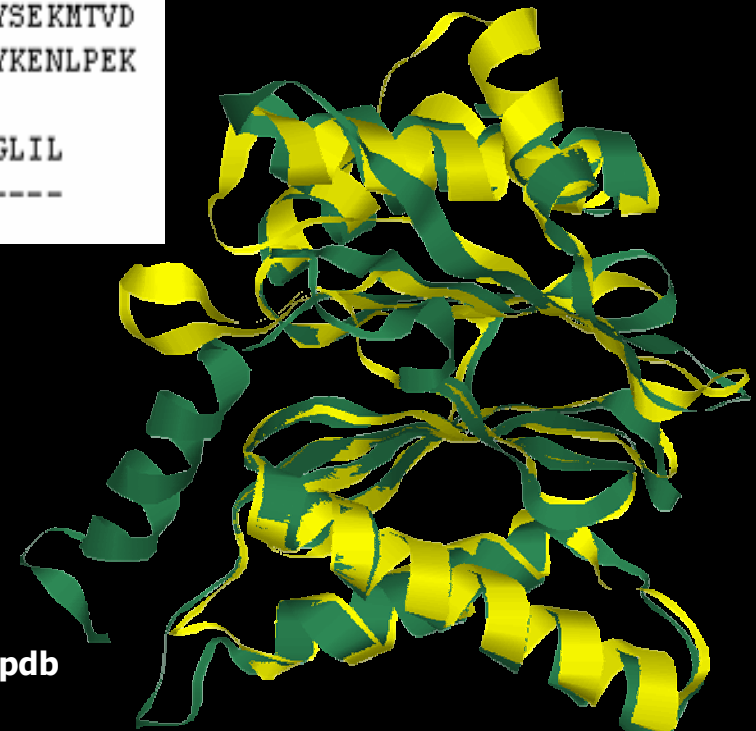
beta1  -YMPYMVQLLVGGI-DTAPHVFSIDAAGGSVEDIYASTGSGSPFVYGVLESQYSEKMTVD
alfa1  GVRPYGVSLIFAGIDQIGPRLFDCDPAGTINEYKATAIGSGKDAVVSFLEREYKENLPEK

beta1  EGVDLVIRAISAAKQRDSA--SGGMIDVAVITRKDGYVQLPTDQIESRIRKLGLIL
alfa1  EAVTLGIKALKSSLE-E--GEELKAPEIASITVGNKYRIYDQEEVKKFL-----
```

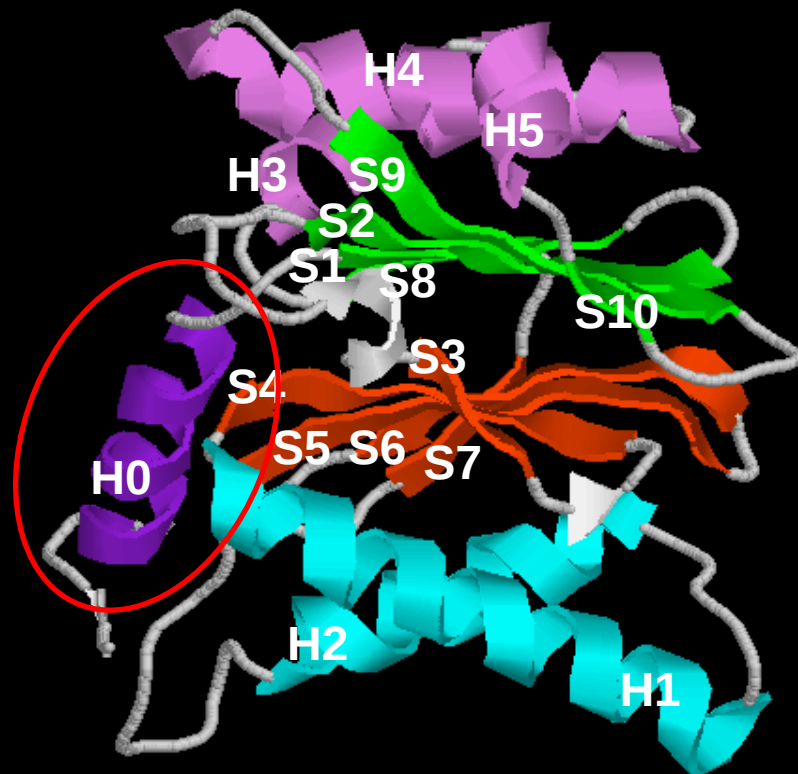
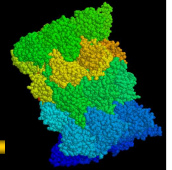
Score: 6,46

RMS: 1,33

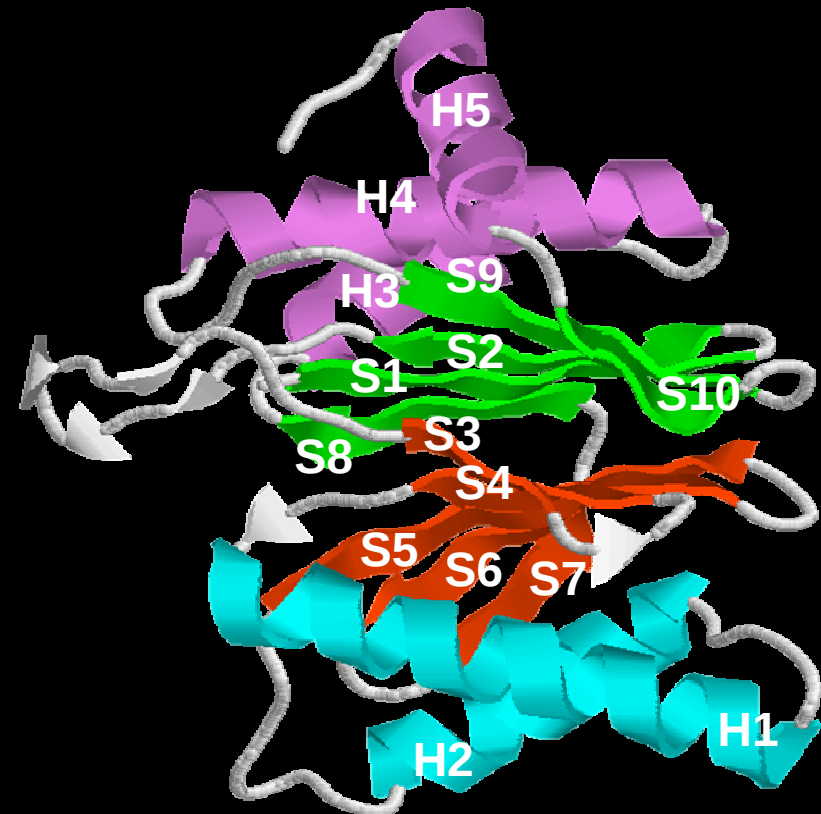
1PMA.pdb



T. acidophilum: Estructura de les subunitats

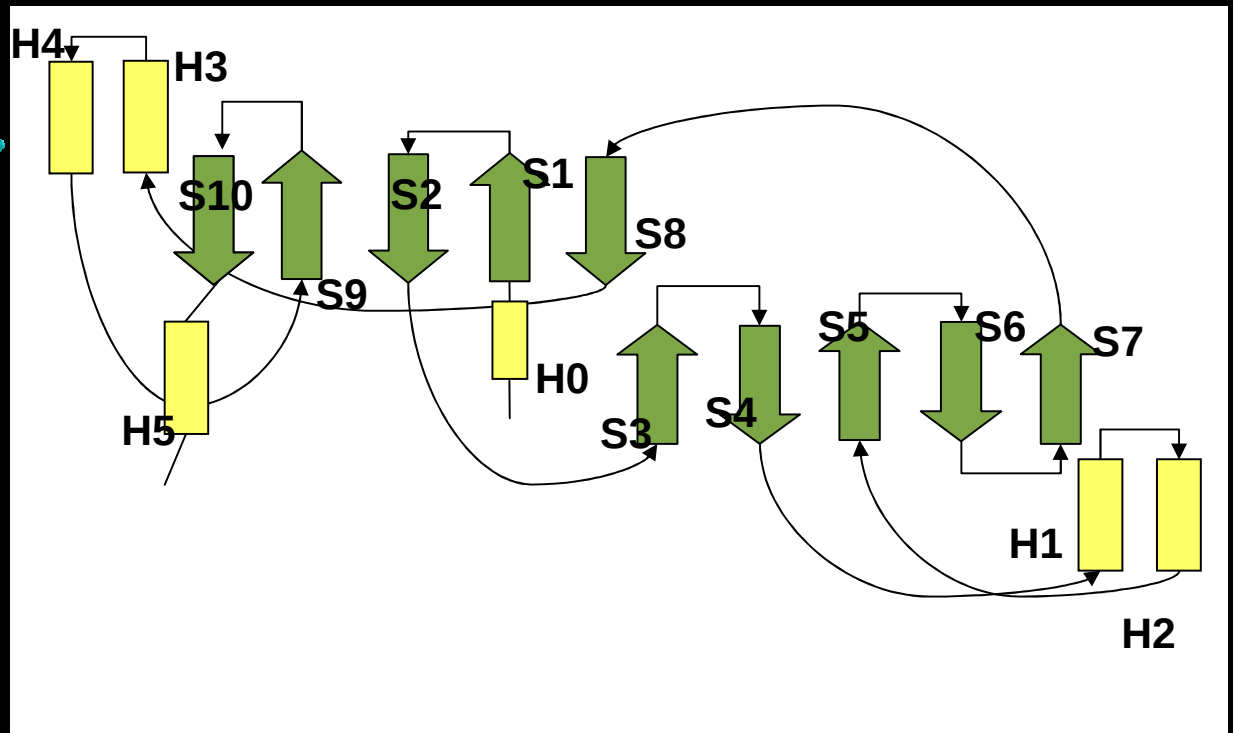
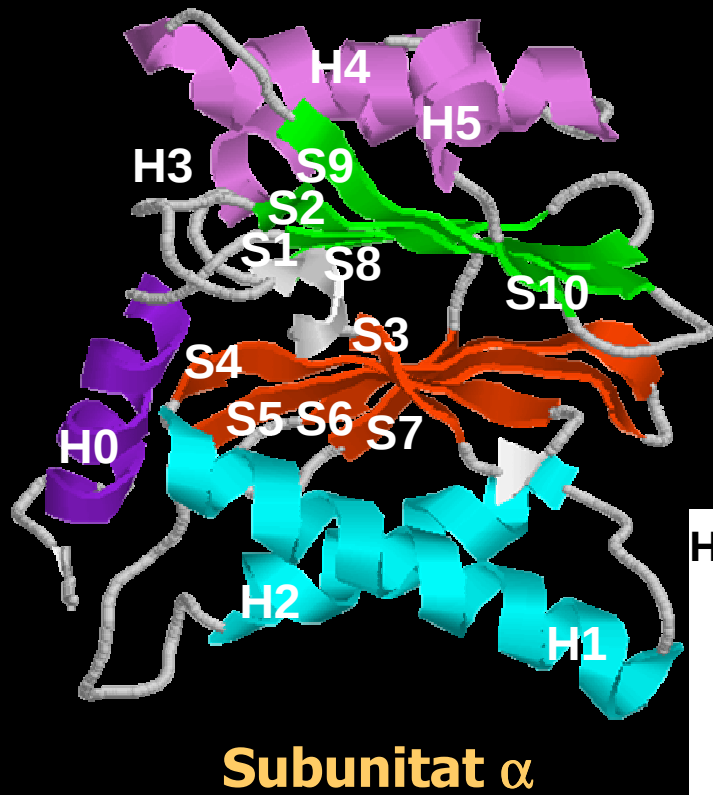
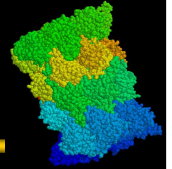


Subunitat α

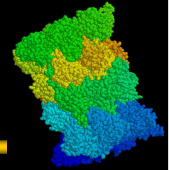


Subunitat β

T. acidophilum: Estructura de les subunitats



T. acidophilum: Estructura de les subunitats



2. Entre α i α

CLUSTAL W(1.60) multiple sequence alignment

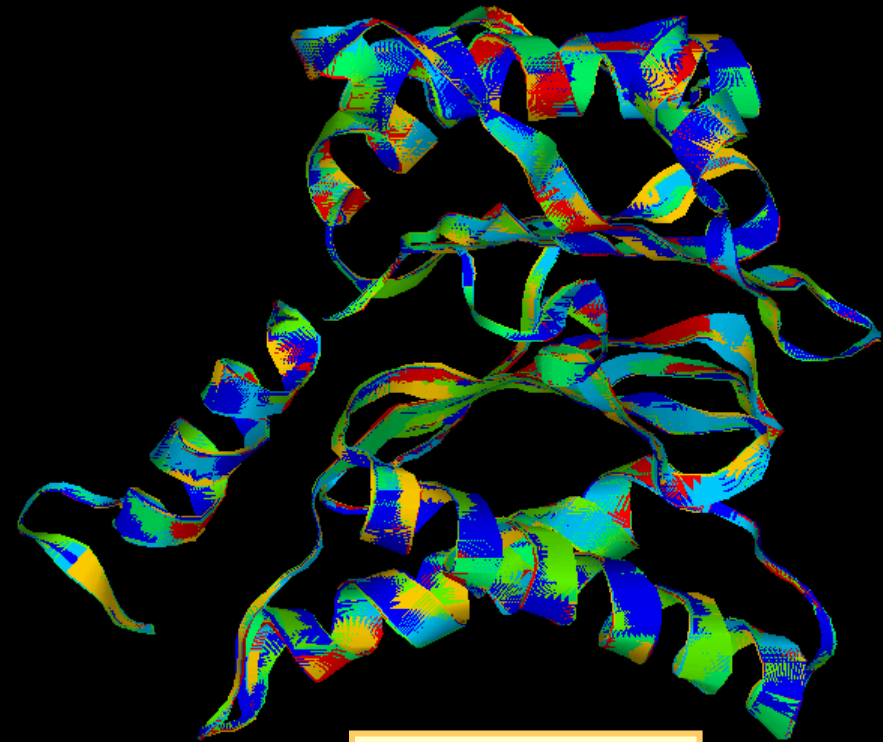
```

                H0      S1      S2      S3
alfa 2  TVFSPDGRLFQVEYAREAVKKGSTALGMKFANGVLLISDKKVRSLIEQNSIEKIQLIDD
alfa 1  TVFSPDGRLFQVEYAREAVKKGSTALGMKFANGVLLISDKKVRSLIEQNSIEKIQLIDD
alfa 5  TVFSPDGRLFQVEYAREAVKKGSTALGMKFANGVLLISDKKVRSLIEQNSIEKIQLIDD
alfa 6  TVFSPDGRLFQVEYAREAVKKGSTALGMKFANGVLLISDKKVRSLIEQNSIEKIQLIDD
alfa 3  TVFSPDGRLFQVEYAREAVKKGSTALGMKFANGVLLISDKKVRSLIEQNSIEKIQLIDD
alfa 7  TVFSPDGRLFQVEYAREAVKKGSTALGMKFANGVLLISDKKVRSLIEQNSIEKIQLIDD

                S4      H1      H2
alfa 2  YVAAVTSGLVADARVLVD FARISAQQEKVTYGSLVNIE NLVKRVADQM QYTQYGGVRPY
alfa 1  YVAAVTSGLVADARVLVD FARISAQQEKVTYGSLVNIE NLVKRVADQM QYTQYGGVRPY
alfa 5  YVAAVTSGLVADARVLVD FARISAQQEKVTYGSLVNIE NLVKRVADQM QYTQYGGVRPY
alfa 6  YVAAVTSGLVADARVLVD FARISAQQEKVTYGSLVNIE NLVKRVADQM QYTQYGGVRPY
alfa 3  YVAAVTSGLVADARVLVD FARISAQQEKVTYGSLVNIE NLVKRVADQM QYTQYGGVRPY
alfa 7  YVAAVTSGLVADARVLVD FARISAQQEKVTYGSLVNIE NLVKRVADQM QYTQYGGVRPY

                S5      S6      S7      S8      H3      H4
alfa 2  GVS LIFAGIDQIGPRLFD CDPAGTINEYKATAIGSGKDAVVSFLEREYKENLPEKEAVTL
alfa 1  GVS LIFAGIDQIGPRLFD CDPAGTINEYKATAIGSGKDAVVSFLEREYKENLPEKEAVTL
alfa 5  GVS LIFAGIDQIGPRLFD CDPAGTINEYKATAIGSGKDAVVSFLEREYKENLPEKEAVTL
alfa 6  GVS LIFAGIDQIGPRLFD CDPAGTINEYKATAIGSGKDAVVSFLEREYKENLPEKEAVTL
alfa 3  GVS LIFAGIDQIGPRLFD CDPAGTINEYKATAIGSGKDAVVSFLEREYKENLPEKEAVTL
alfa 7  GVS LIFAGIDQIGPRLFD CDPAGTINEYKATAIGSGKDAVVSFLEREYKENLPEKEAVTL

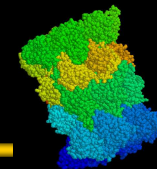
                S9      S10     H5
alfa 2  GIKALKS SLEEGEELKAPEIASITVG NKYRIYD QEEVKKFL
alfa 1  GIKALKS SLEEGEELKAPEIASITVG NKYRIYD QEEVKKFL
alfa 5  GIKALKS SLEEGEELKAPEIASITVG NKYRIYD QEEVKKFL
alfa 6  GIKALKS SLEEGEELKAPEIASITVG NKYRIYD QEEVKKFL
alfa 3  GIKALKS SLEEGEELKAPEIASITVG NKYRIYD QEEVKKFL
alfa 7  GIKALKS SLEEGEELKAPEIASITVG NKYRIYD QEEVKKFL
```



Score: 9,86

RMS: 0,09

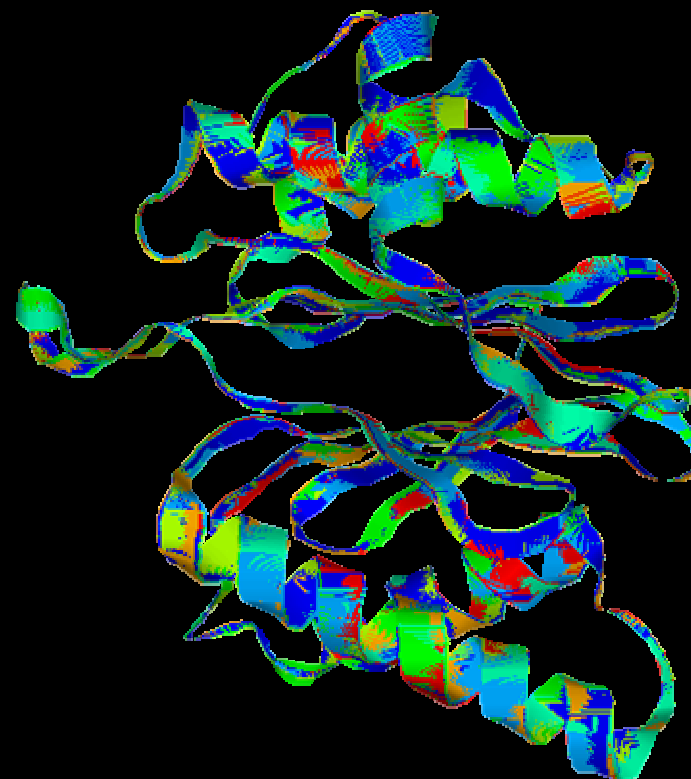
T. acidophilum: Estructura de les subunitats



3. Entre β i β

CLUSTAL W(1.60) multiple sequence alignment

	S1	S2	S3	S4	H1
beta1	TTTVG	ITLKD	AVIMATE	RRVTMEN	FIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
beta2	TTTVG	ITLKD	AVIMATE	RRVTMEN	FIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
beta3	TTTVG	ITLKD	AVIMATE	RRVTMEN	FIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
beta4	TTTVG	ITLKD	AVIMATE	RRVTMEN	FIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
beta5	TTTVG	ITLKD	AVIMATE	RRVTMEN	FIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
beta6	TTTVG	ITLKD	AVIMATE	RRVTMEN	FIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
beta7	TTTVG	ITLKD	AVIMATE	RRVTMEN	FIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
	H2	S5	S6	S7	
beta1	AELELYRLQRRVNMP	IEAVATLLSNMLN	QVKYMPYMW	QLLVGGIDTAPHVFSIDAAGGSV	
beta2	AELELYRLQRRVNMP	IEAVATLLSNMLN	QVKYMPYMW	QLLVGGIDTAPHVFSIDAAGGSV	
beta3	AELELYRLQRRVNMP	IEAVATLLSNMLN	QVKYMPYMW	QLLVGGIDTAPHVFSIDAAGGSV	
beta4	AELELYRLQRRVNMP	IEAVATLLSNMLN	QVKYMPYMW	QLLVGGIDTAPHVFSIDAAGGSV	
beta5	AELELYRLQRRVNMP	IEAVATLLSNMLN	QVKYMPYMW	QLLVGGIDTAPHVFSIDAAGGSV	
beta6	AELELYRLQRRVNMP	IEAVATLLSNMLN	QVKYMPYMW	QLLVGGIDTAPHVFSIDAAGGSV	
beta7	AELELYRLQRRVNMP	IEAVATLLSNMLN	QVKYMPYMW	QLLVGGIDTAPHVFSIDAAGGSV	
	S8	H3	H4	S9	
beta1	EDIYASTGSGSPFVYGV	LESQYSEKMT	VDEGVDLVIRAI	SAAKQRDSASGGMIDVAVITR	
beta2	EDIYASTGSGSPFVYGV	LESQYSEKMT	VDEGVDLVIRAI	SAAKQRDSASGGMIDVAVITR	
beta3	EDIYASTGSGSPFVYGV	LESQYSEKMT	VDEGVDLVIRAI	SAAKQRDSASGGMIDVAVITR	
beta4	EDIYASTGSGSPFVYGV	LESQYSEKMT	VDEGVDLVIRAI	SAAKQRDSASGGMIDVAVITR	
beta5	EDIYASTGSGSPFVYGV	LESQYSEKMT	VDEGVDLVIRAI	SAAKQRDSASGGMIDVAVITR	
beta6	EDIYASTGSGSPFVYGV	LESQYSEKMT	VDEGVDLVIRAI	SAAKQRDSASGGMIDVAVITR	
beta7	EDIYASTGSGSPFVYGV	LESQYSEKMT	VDEGVDLVIRAI	SAAKQRDSASGGMIDVAVITR	
	S10	H5			
beta1	KDGYVQLPTDQIESRIRKL	GLIL			
beta2	KDGYVQLPTDQIESRIRKL	GLIL			
beta3	KDGYVQLPTDQIESRIRKL	GLIL			
beta4	KDGYVQLPTDQIESRIRKL	GLIL			
beta5	KDGYVQLPTDQIESRIRKL	GLIL			
beta6	KDGYVQLPTDQIESRIRKL	GLIL			
beta7	KDGYVQLPTDQIESRIRKL	GLIL			



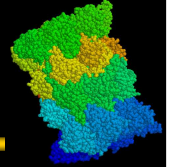
Score: 9,88

RMS: 0,10

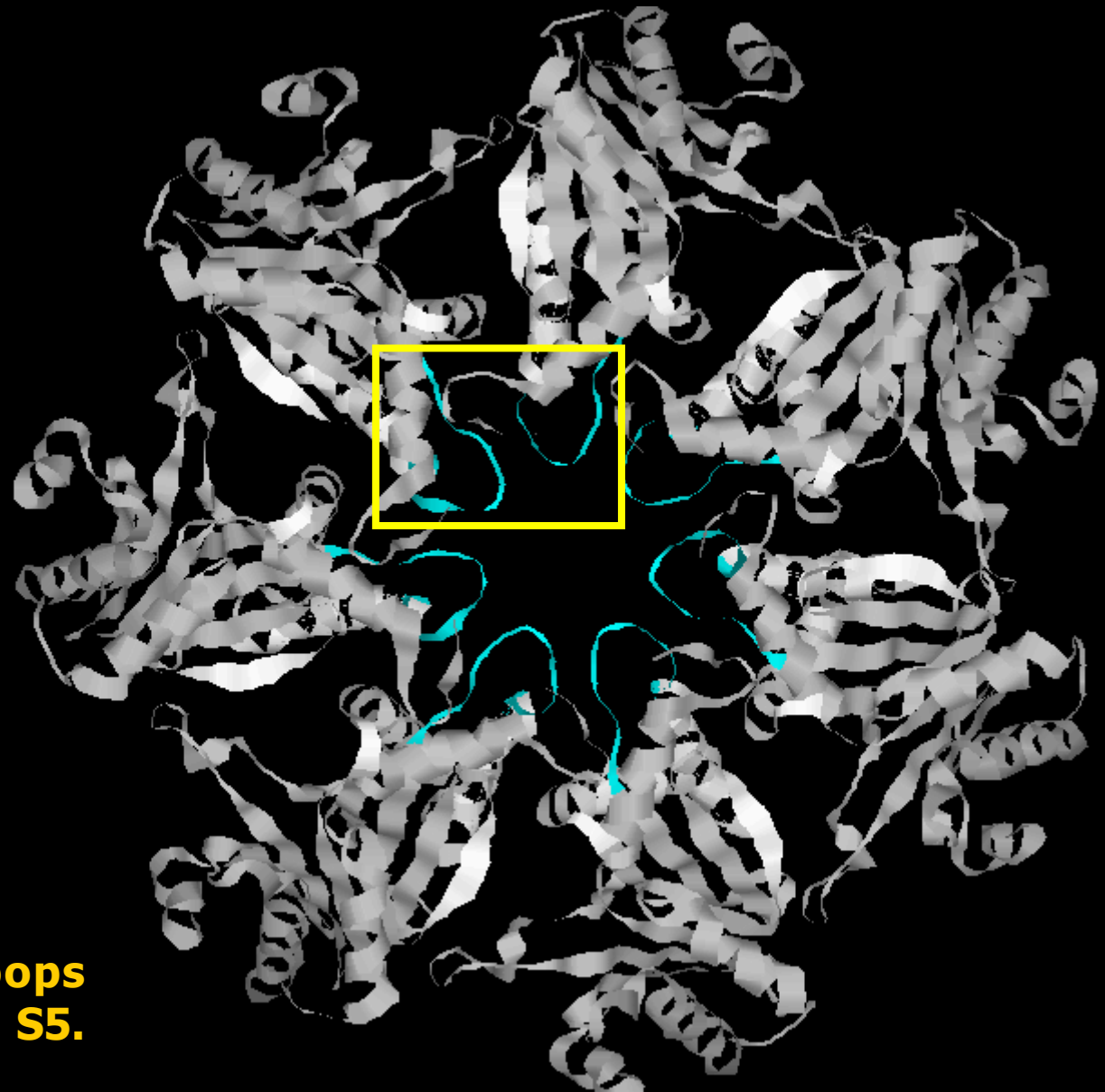
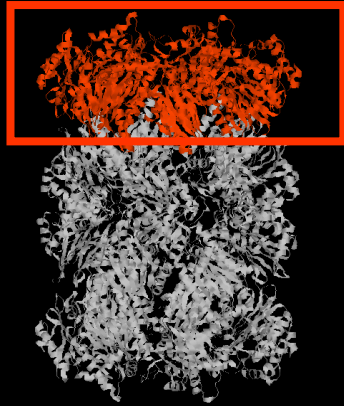
SUBUNITATS α

[illegible]

T. acidophilum: Interaccions

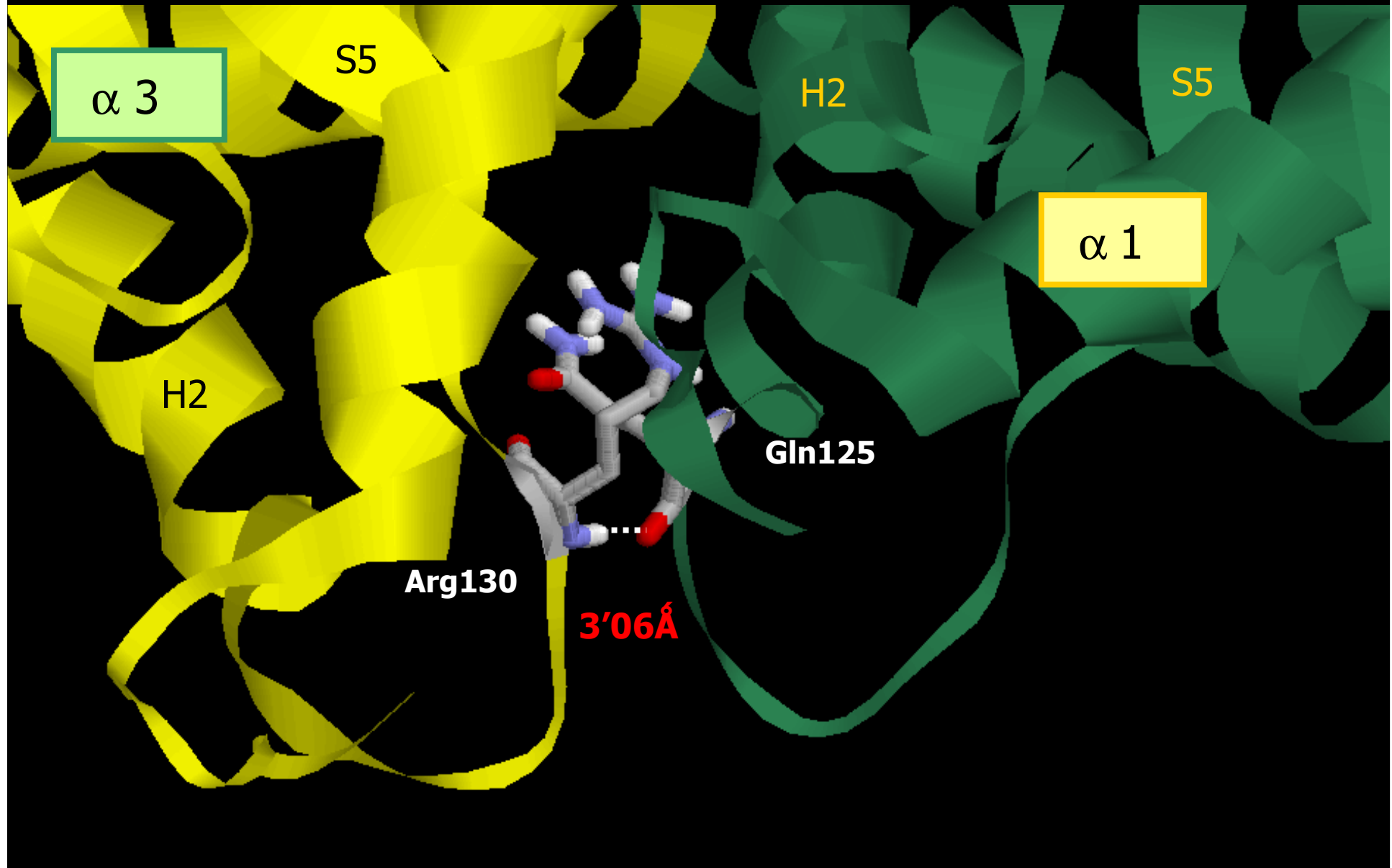
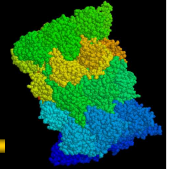


1. Entre α i α

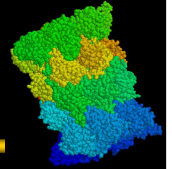


**Interacció entre els loops
que es formen entre H2 i S5.**

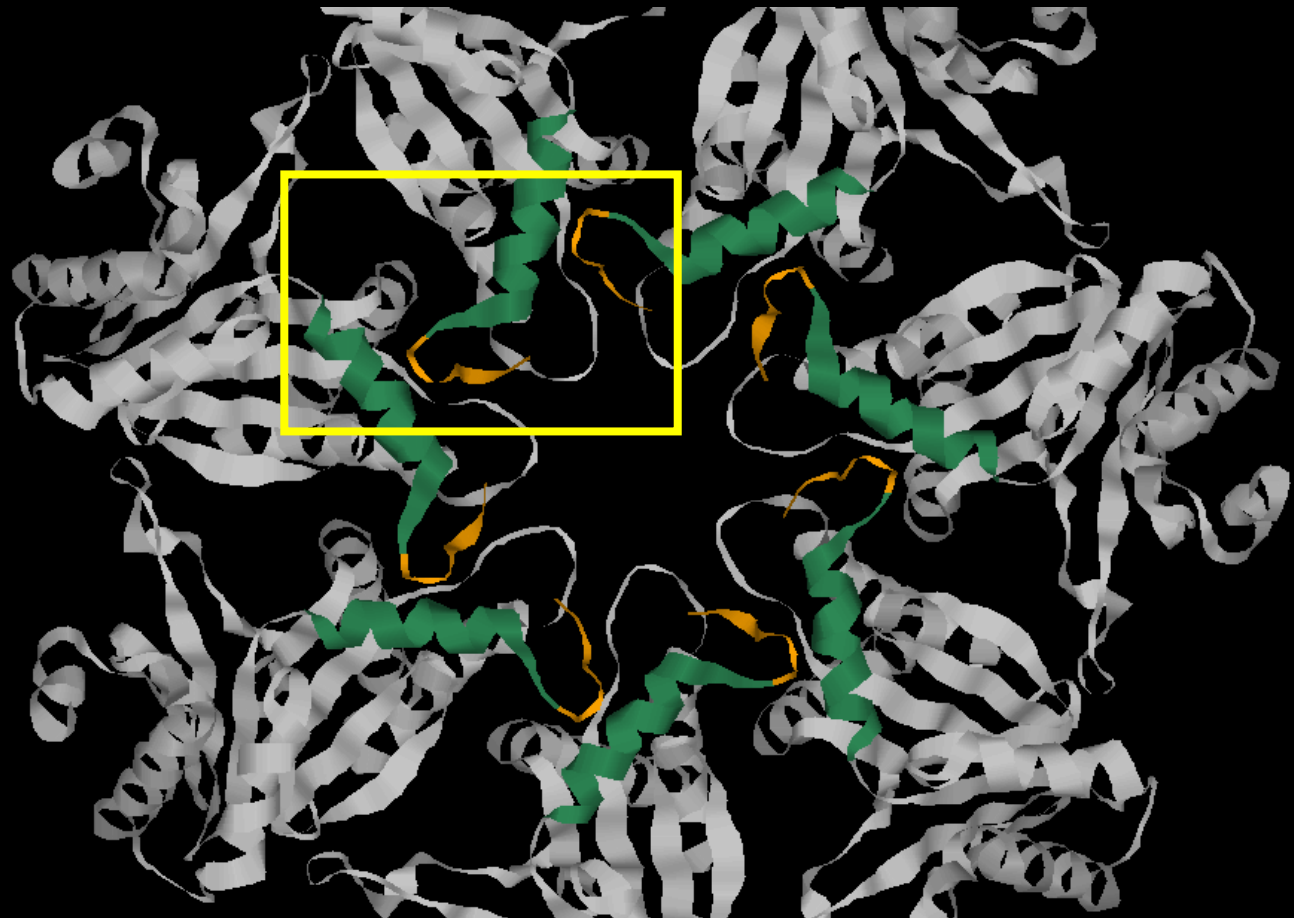
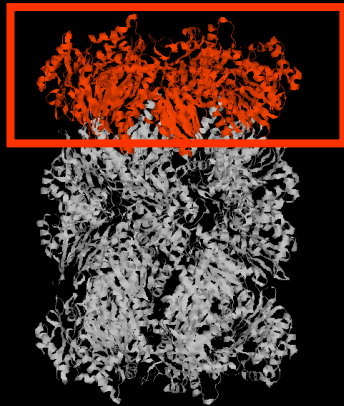
T. acidophilum: Interaccions



T. acidophilum: Interaccions

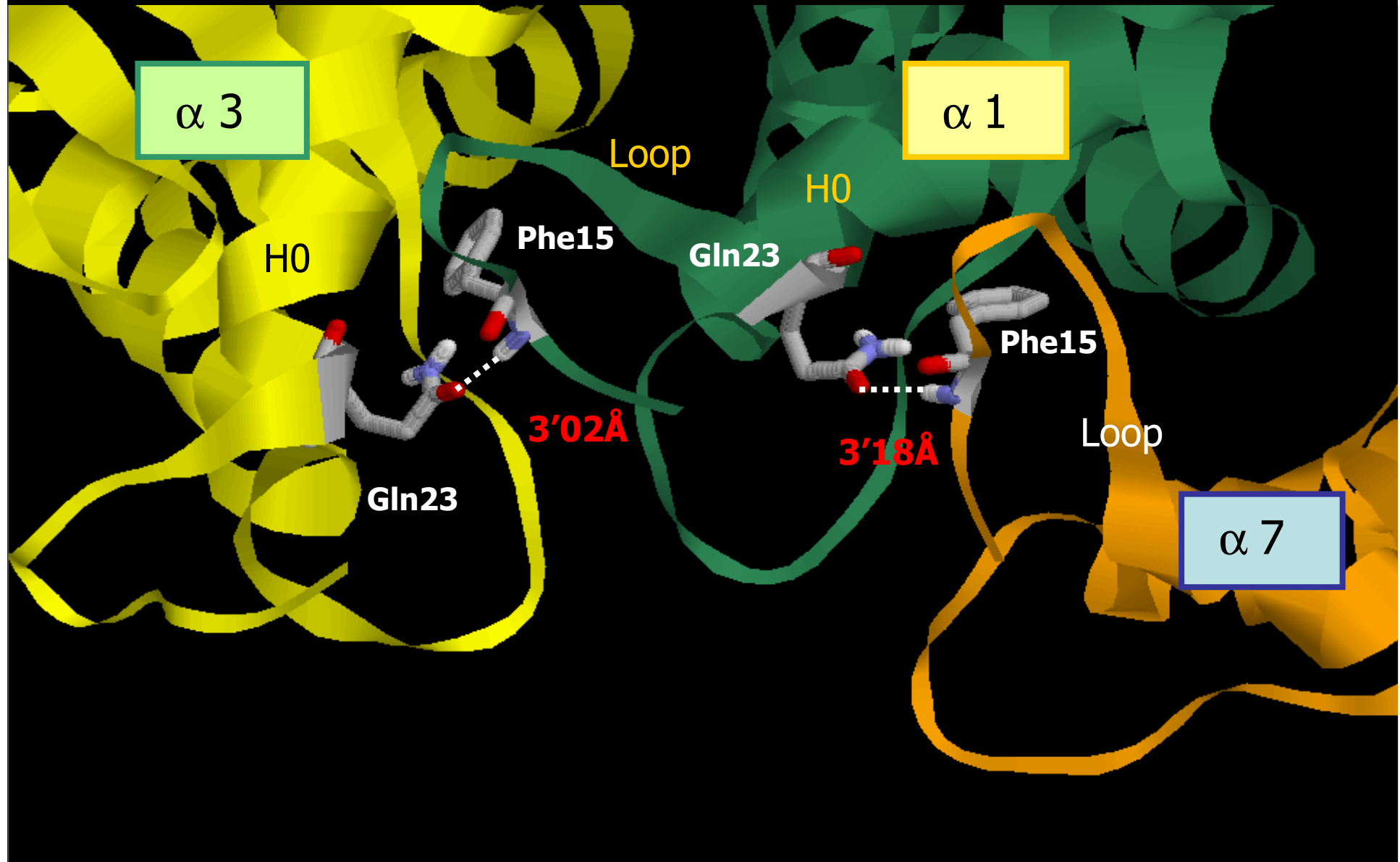
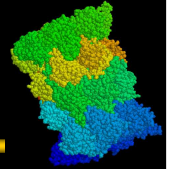


1. Entre α i α

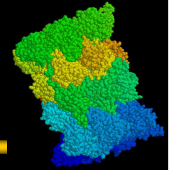


**Interacció entre el loop inicial i
la H0 de la subunitat següent**

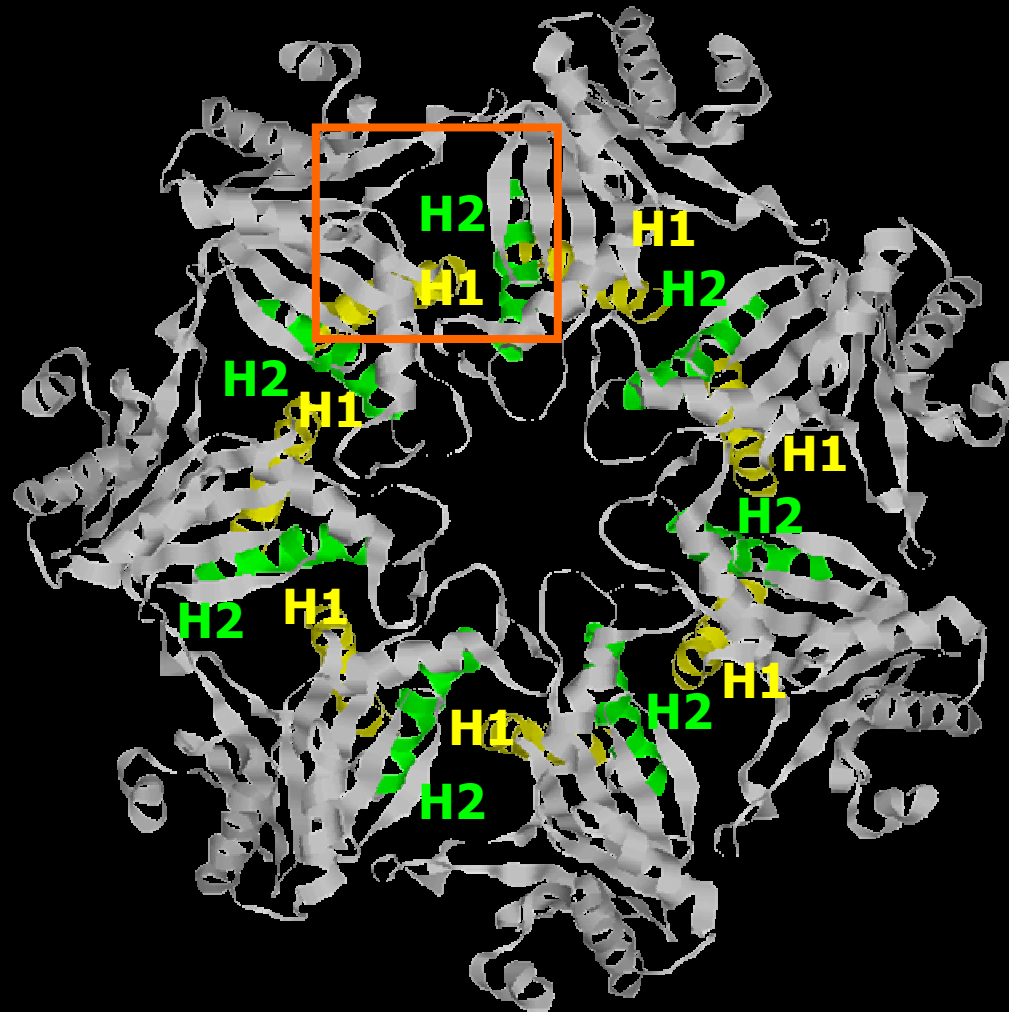
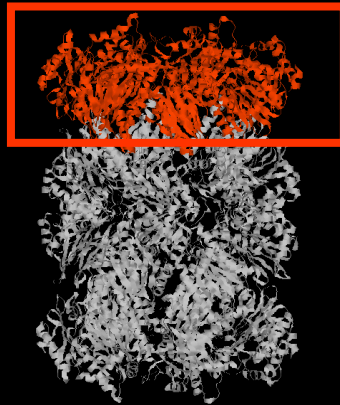
T. acidophilum: Interaccions



T. acidophilum: Interaccions

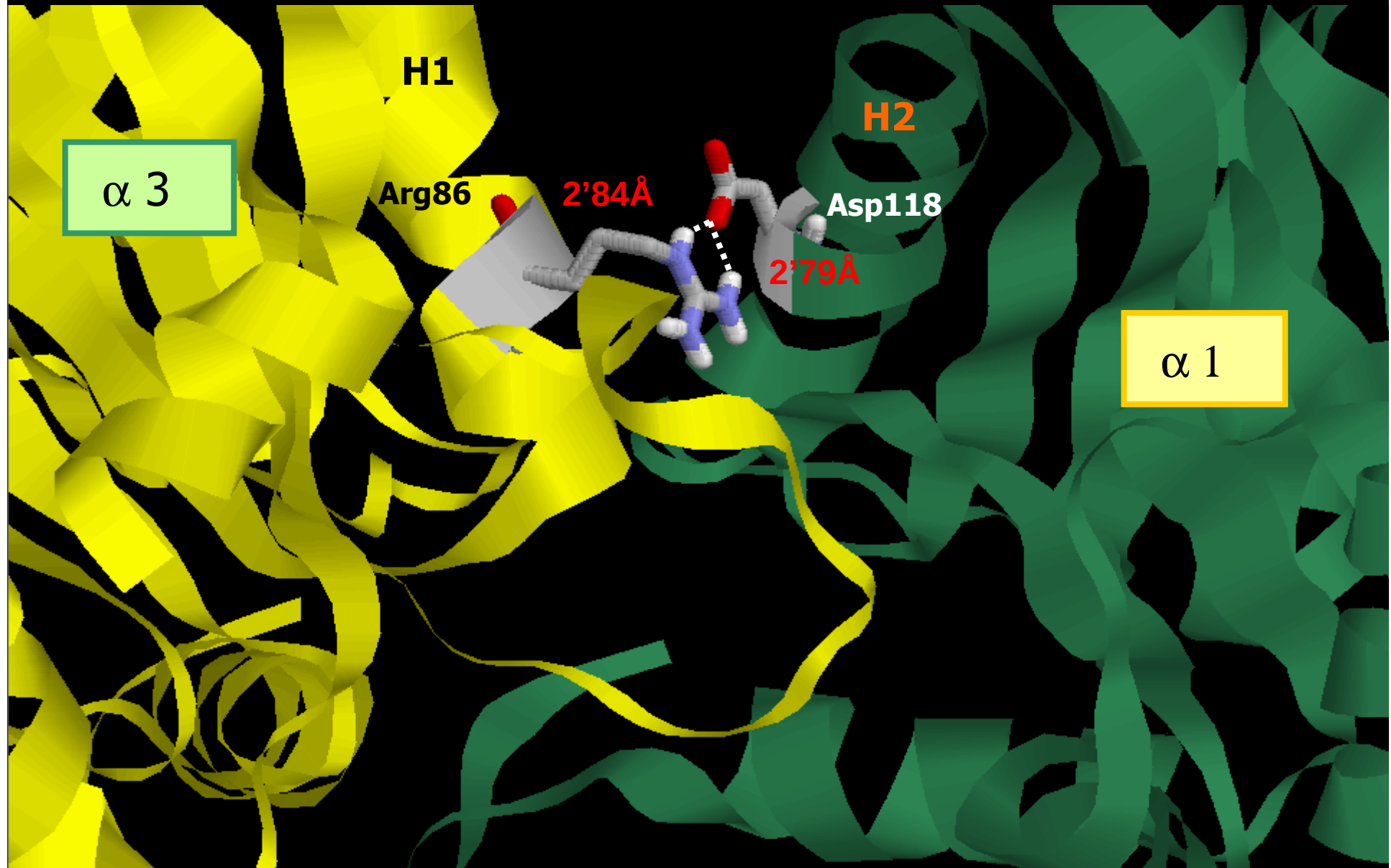
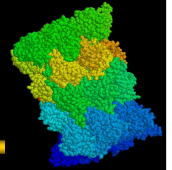


1. Entre α i α

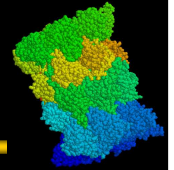


Interacció entre H1 i H2

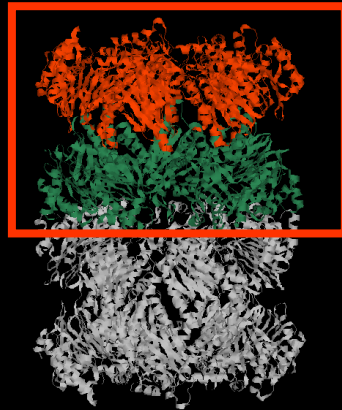
T. acidophilum: Interaccions



T. acidophilum: Interaccions



2. Entre α i β



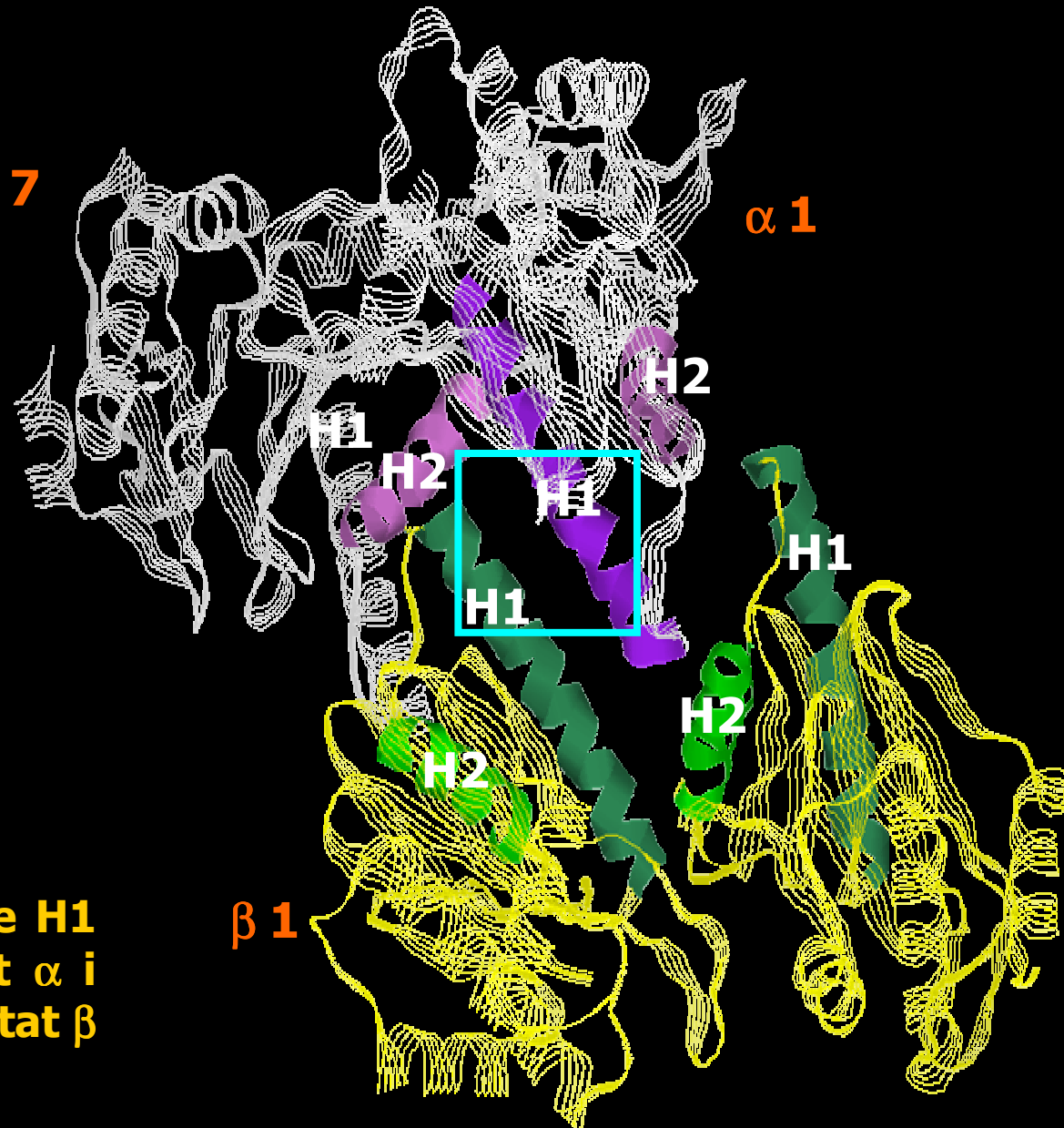
α 7

α 1

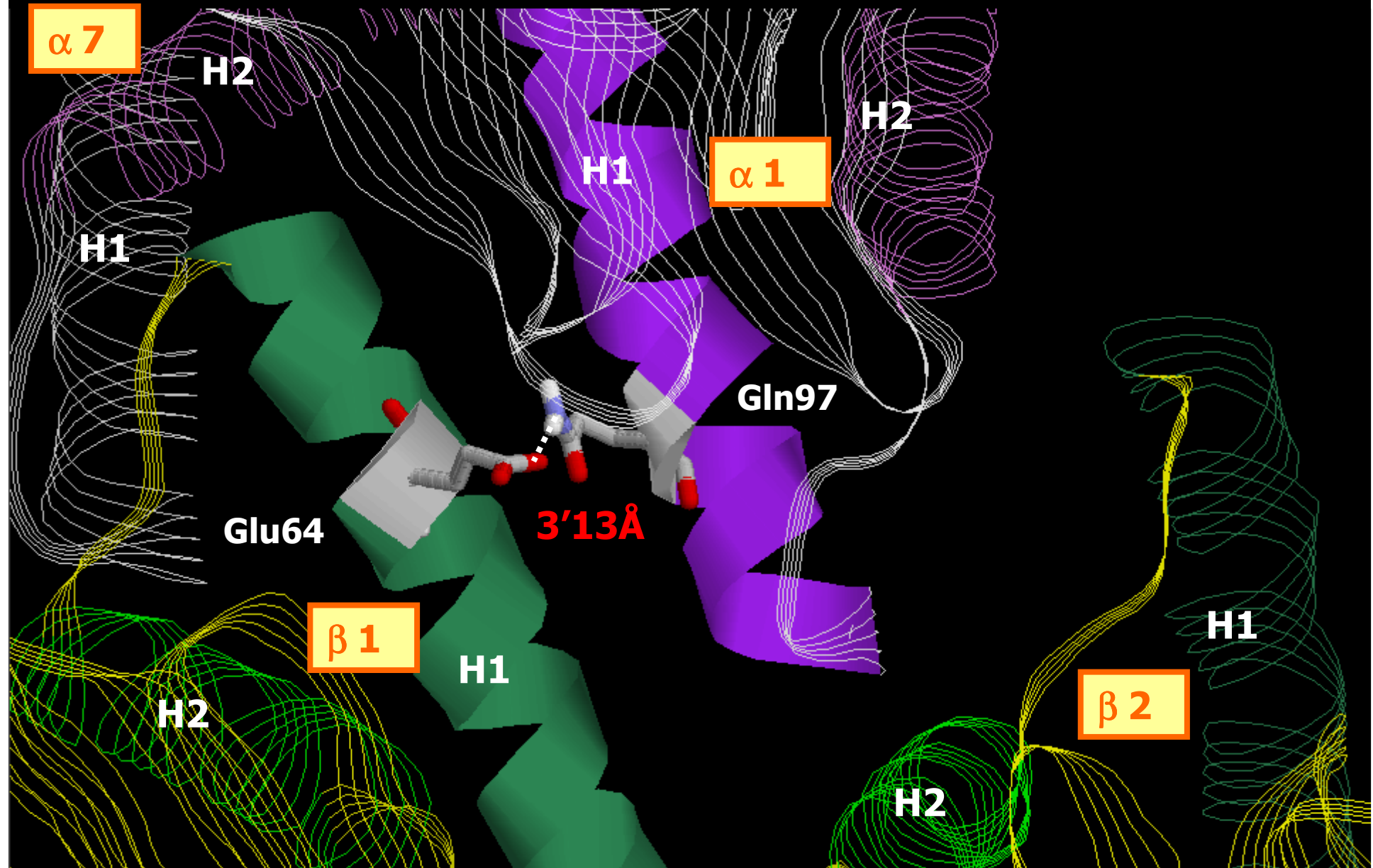
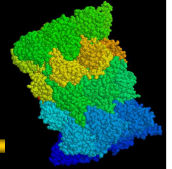
β 1

β 2

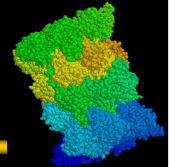
Interacció entre H1
de la subunitat α i
H1 de la subunitat β



T. acidophilum: Interaccions



T. acidophilum: Interaccions



SUBUNITATS β

CLUSTAL W(1.60) multiple sequence alignment

```
1PMA      -----TTT
METTH     -----MNDKNTLKGTIT
METJA     -----MDVMKGTIT
SULSO     -----MGNELQLENKILKGTIT
SPIOL     MKLDTSGLESTAPIFRR--SDFVFDGLQMTSPFDLPNPTD FDCGFKRAVQMVKPAKGTIT
ARATH     MKLDTSGFETSMPMIGFGSSSDMLDELSSVPSFDLPRTKE FDCGFKKAKDMLKHAKTIT
                                     ***
```

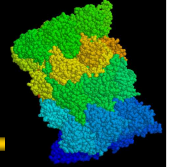
```
                26                51
1PMA      VGITLRDAVIMATERRVTMENFIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMKAEI
METTH     VGITCRDGVWFATERRASMGNLIAHKATDKIFKIDEHIAATIAGSVADAQSLMKYLKAEI
METJA     VGLICDDAVILATDKRASLGNLVADKEAKFLYKIDDIAMTIAGSVGDAQAIVRLLIARI
SULSO     VGIKVNDCVILAADDRASAGFFVANKMVKRVLYITDKIGITTAGSVADLQFIYDVLRNIY
SPIOL     LAFIFKHGVNVAADSASMGGYISSQSVKKIIEINPYMLGTMAAGGADCQFWHRNLGKIC
ARATH     LAFIFKHGVNVAADSASMGGYISSQSVKKIIEINPYMLGTMAAGGADCQFWHRNLGKIC
                *  *  *  *  *  *  *  *  *  *  *  *  *
```

```
                84                91
1PMA      ELYRLQRRVNMPIEAVATLLENMNLNQVRYPMVQLLVGGIDT--APHVFSIDAAGGSVE
METTH     ALYRMPNS EKISIRAAAALANILHSSRFYPIVQITLLCGVDE-NGAKIYSLDPSCGMIP
METJA     KLYRMRTGPNIPPLACATLLENILHSSRMFPFLTQIIIGGYDLLEGAKLFSLDPLCGMNE
SULSO     HYNSTIKYGPISIKGLATRLANVL SATRYFPYIVQILIGGYDD--QPRLFNLDYLGDIIE
SPIOL     RLHELANKRRISVTGASKLANILYNYRCMGLSVGTMIAGWDE-TGPGLYYVDS ECGRLK
ARATH     RLHELANKRRISVSGASKLANMLYSYRCMGLSVGTMIAGWDE-TGPGLYYVDNECGRLK
                .  .  *  .  .  .  .  *  .  .  *  *
```

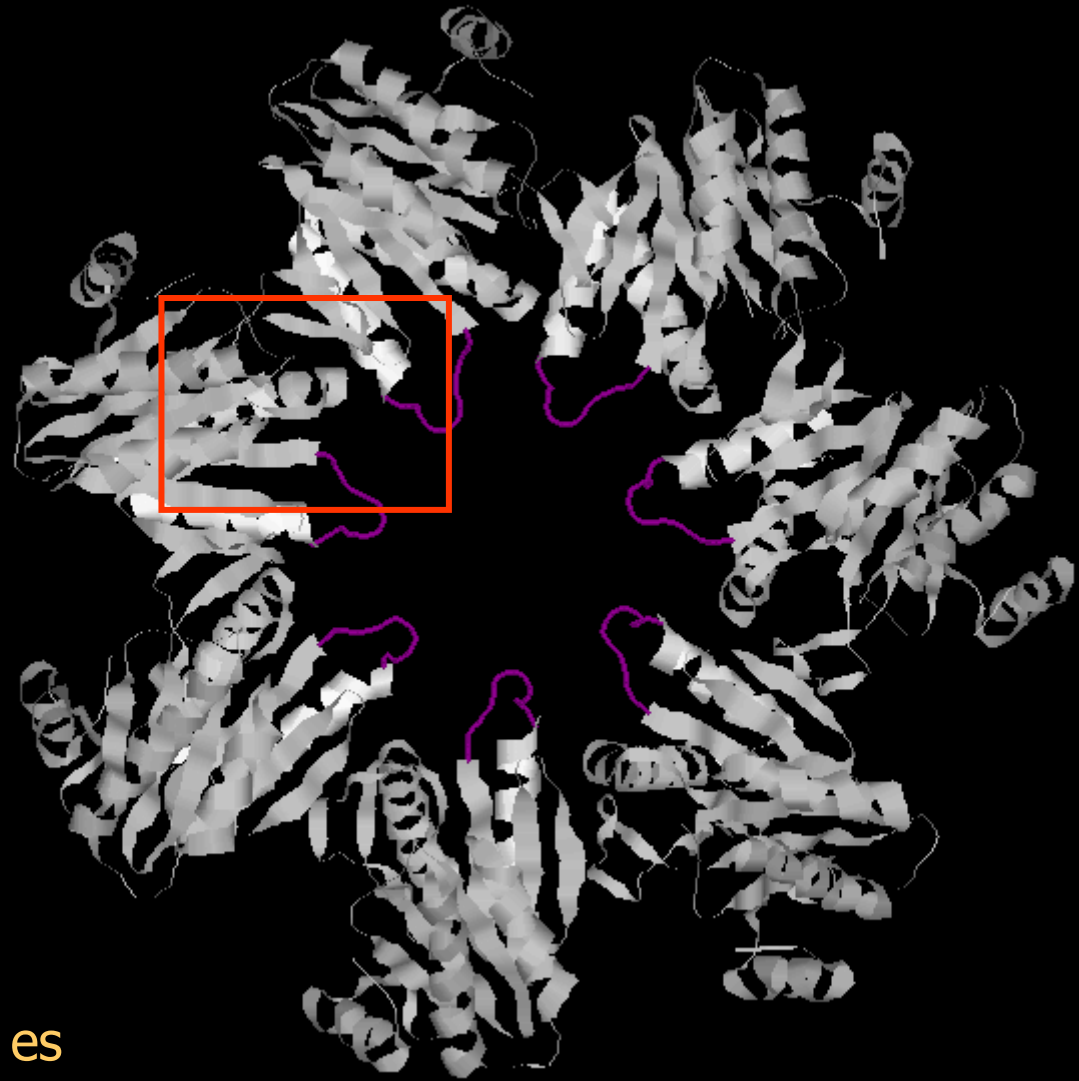
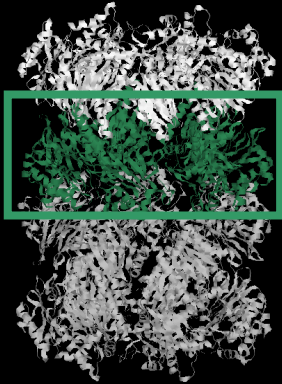
```
                139                165 166
1PMA      -DIYASTGSGSPFVYGVLESQYSEKMTWDEGVDLWIRAISSAAKQRDSASGGMIDVAVITR
METTH     -DKFVSTGSGSPVAYGVLED RYSD ELYVD EAVDVAI RAIKSAMERDTYS GNGILVATVTE
METJA     EKTFTATGSGSP IAYGVLEAGYDRDMSVEEGIKLALNALKSAMERDTFS GNGISLAVIT-
SULSO     -ENYVATGSGSPVAMGVLEDEYNPKMTLD EAADLAKRAVFSAIK RDSFTGCGVIVAKTH-
SPIOL     -GMRFSVGSGSPYAYGVLDNGYKYDMTVEEASELARRAIYHATYRDCASGGVSVYHV-
ARATH     -GDRFSVGSGSPYAYGVLDSCYKYDMSVEEASELARRSIYHATFRDCASGGVASVYHV-
                .  ****  **  *  .  .  .  .  *  **  *
```

```
1PMA      KDCYVQLPTDQIESRIRKLGLIL-----
METTH     EEGFRMLS EE EIKRIENLN-----
METJA     KDGVKIFED EIEKILDSMKAKPKKKTTRPSRRKSK-
SULSO     SKGHEELEFYLNKKM-----
SPIOL     PDGWRKVTGDVGD LHFQYYPVVPATVEQEMVEVVG-
ARATH     PEGWTKLSGDVGC ELHYHYYPVAPATARQVMEERATAE
                *
```

T. acidophilum: Interaccions

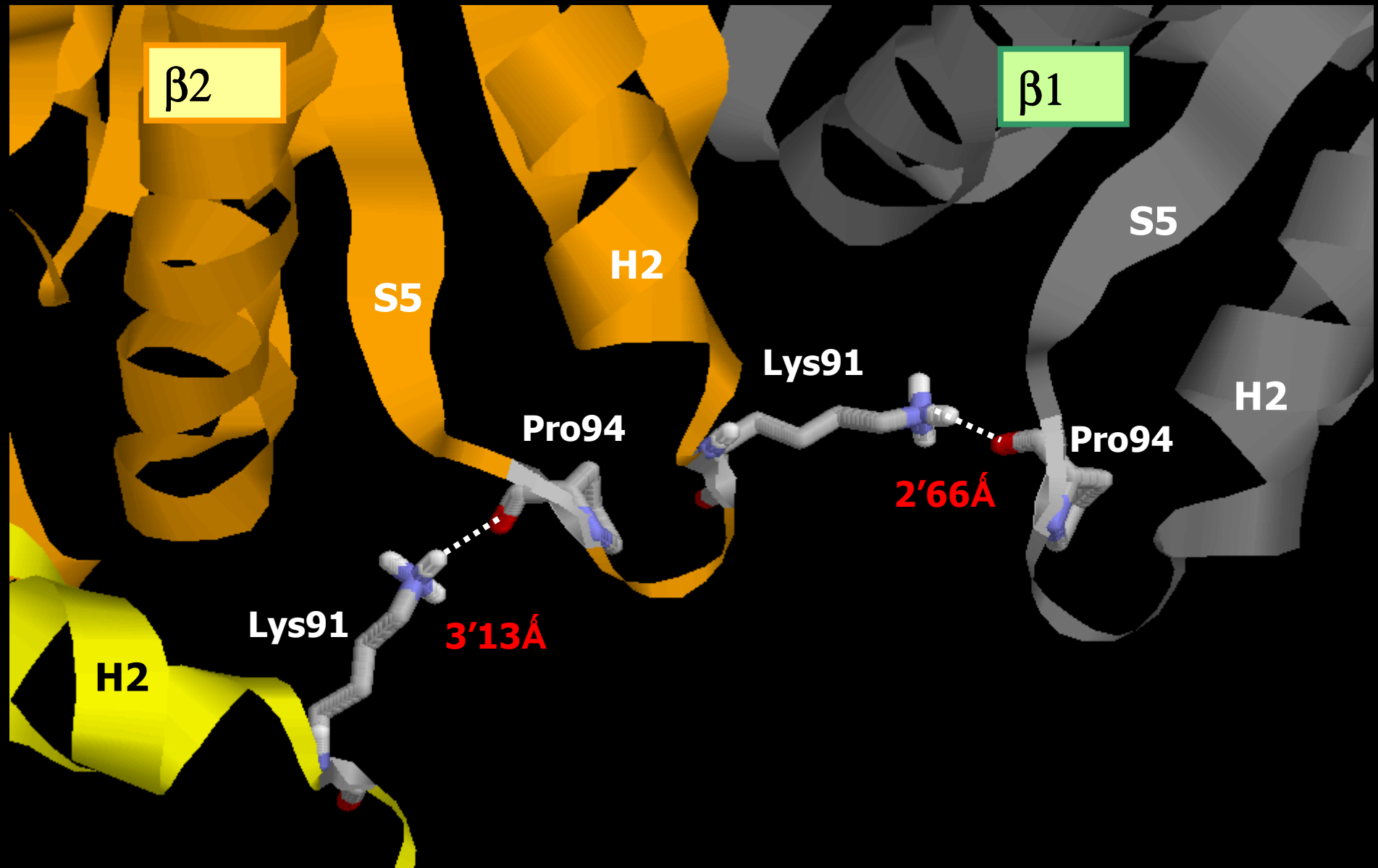
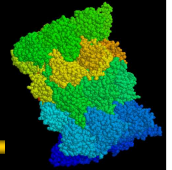


3. Entre β i β

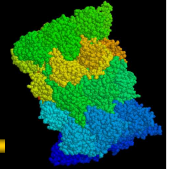


Interacció entre els loops que es formen entre H2 i S5.

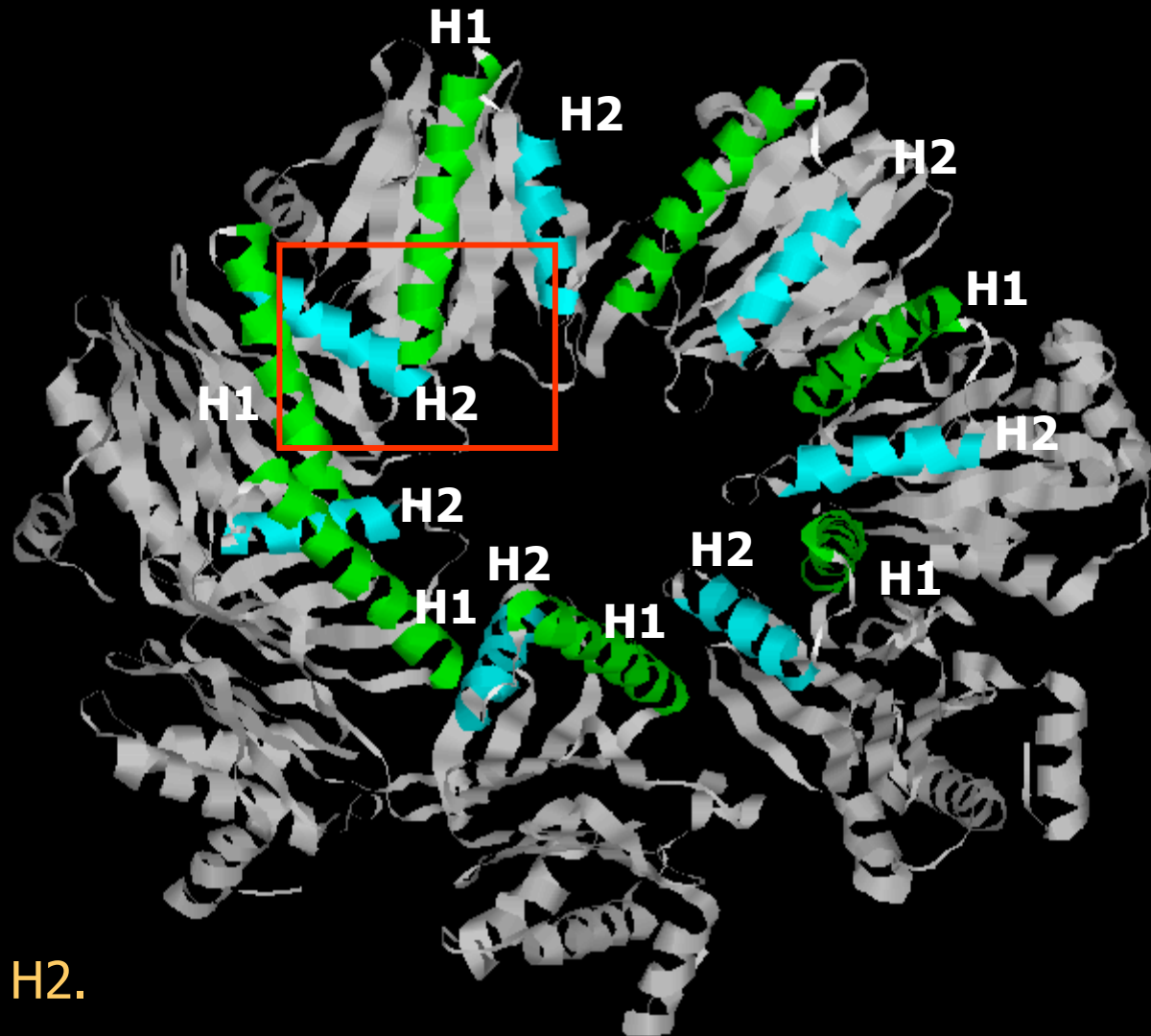
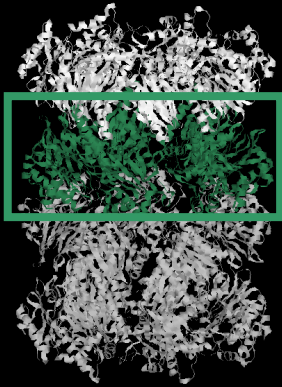
T. acidophilum: Interacciones



T. acidophilum: Interaccions

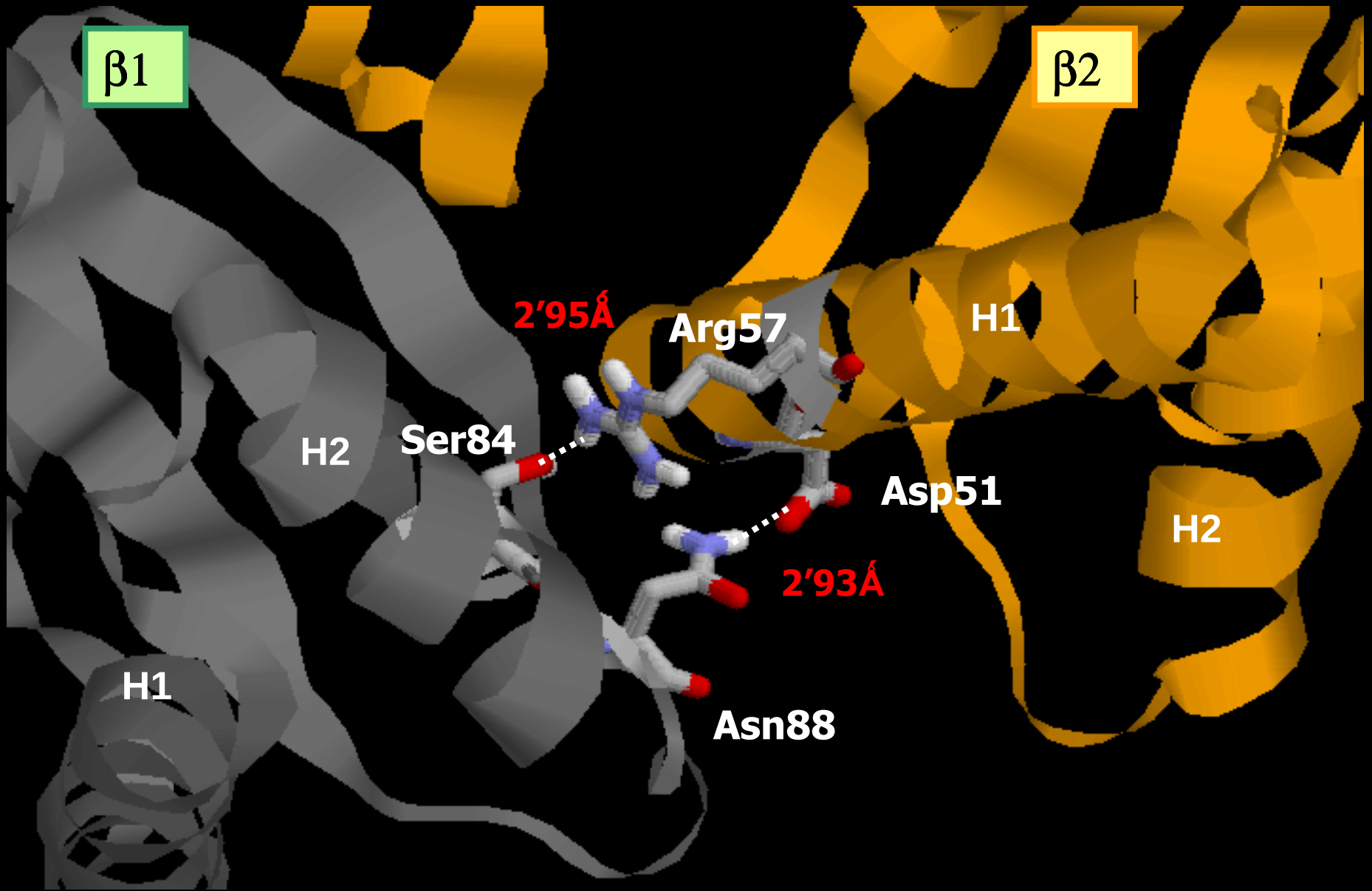
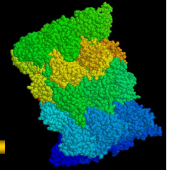


3. Entre β i β

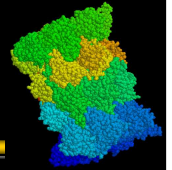


Interacció entre H1 i H2.

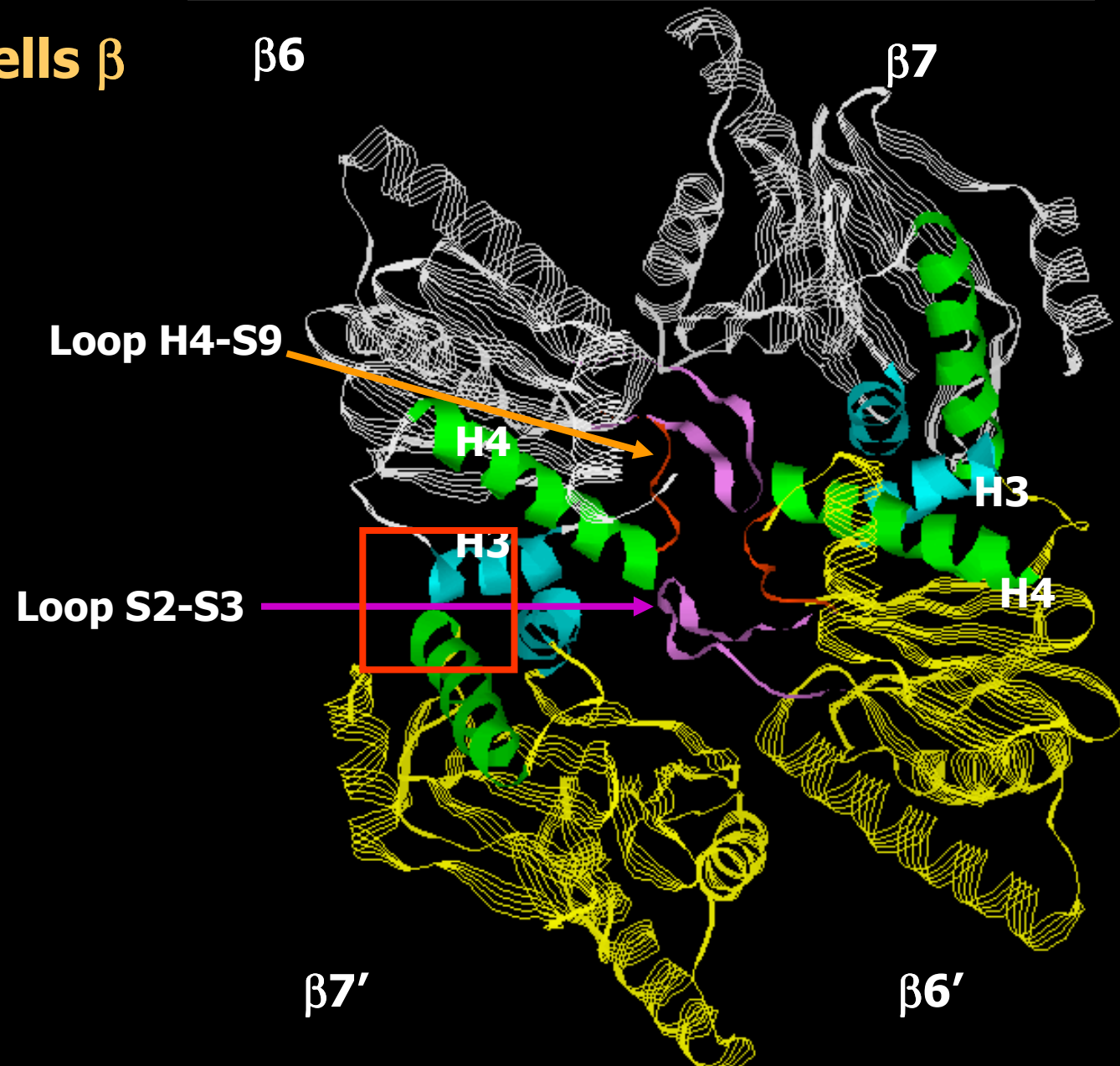
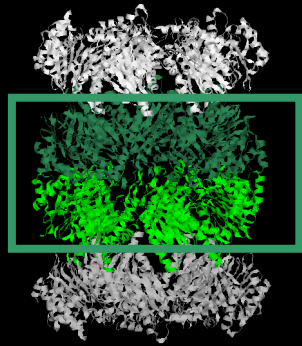
T. acidophilum: Interacciones



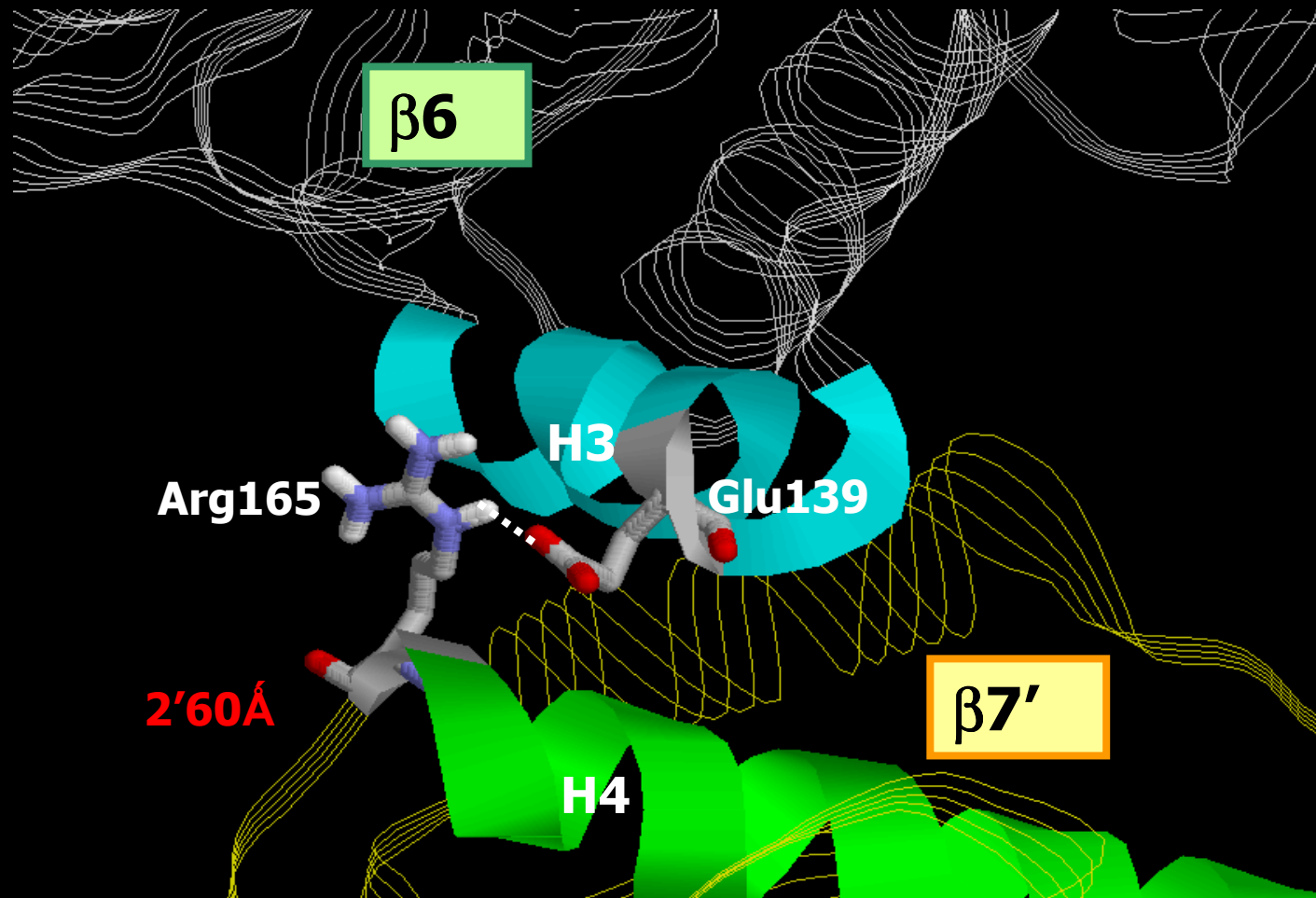
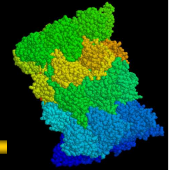
T. acidophilum: Interaccions



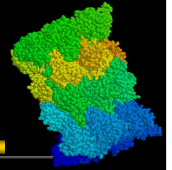
4. Entre anells β



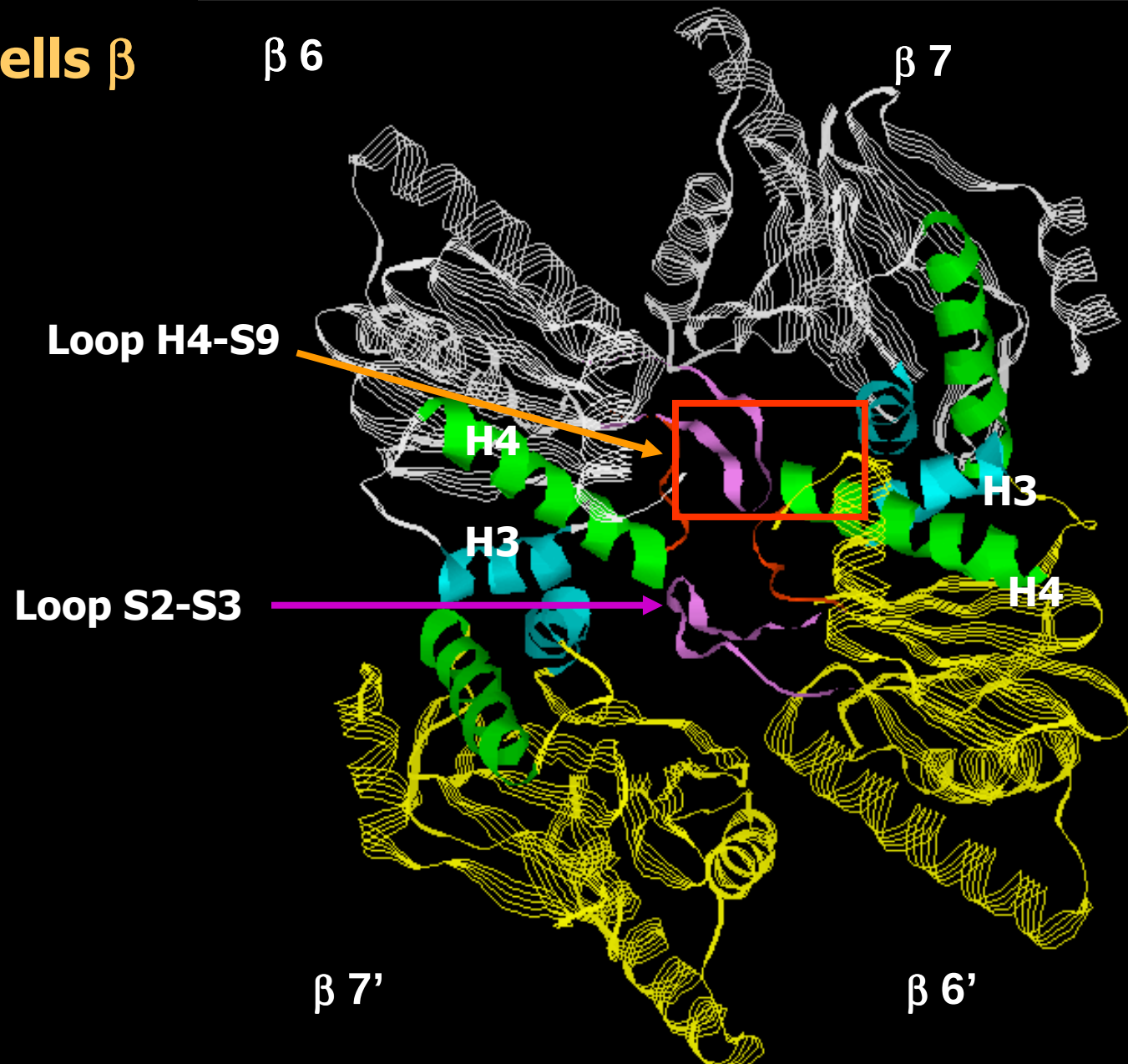
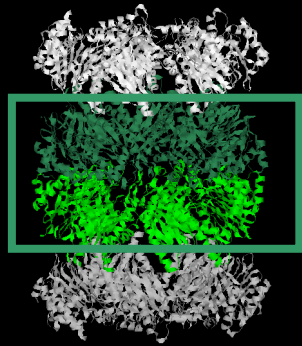
T. acidophilum: Interaccions



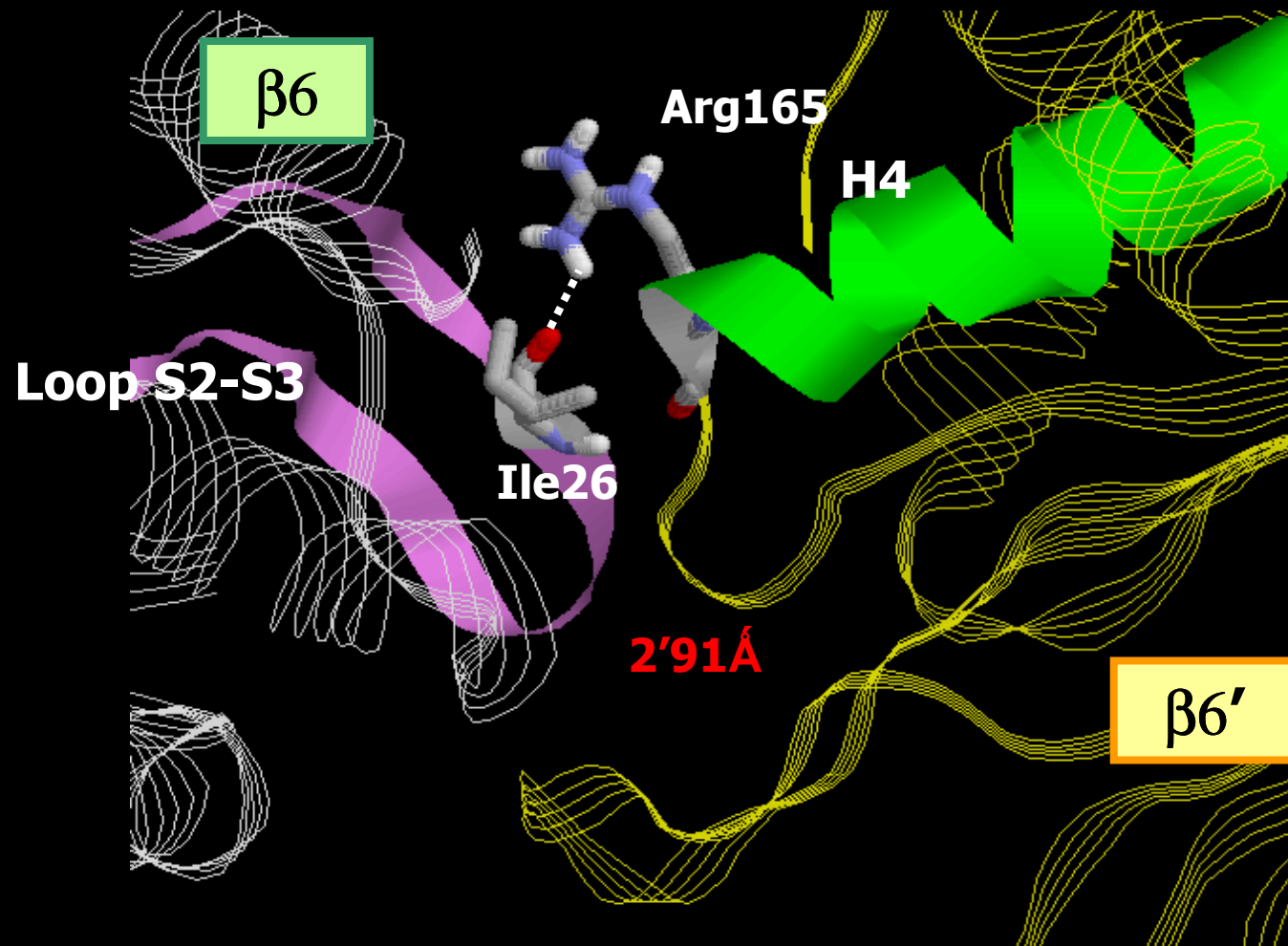
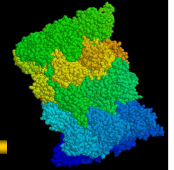
T. acidophilum: Interaccions



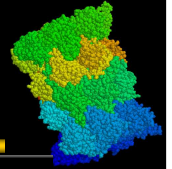
4. Entre anells β



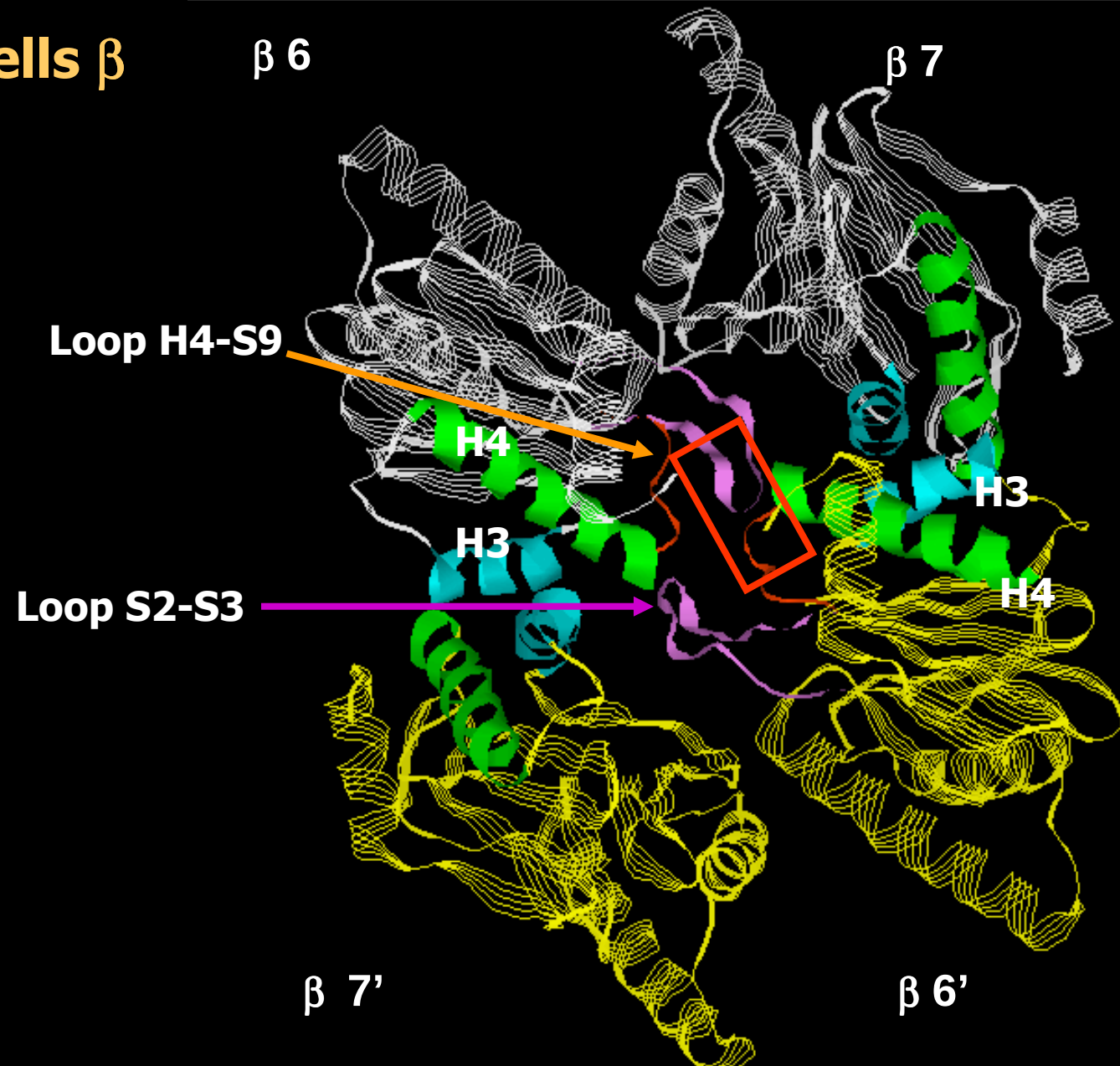
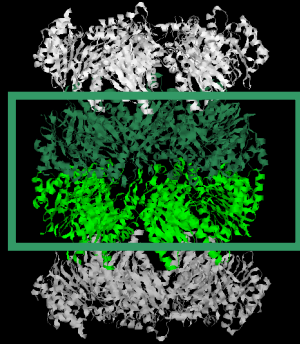
T. acidophilum: Interacciones



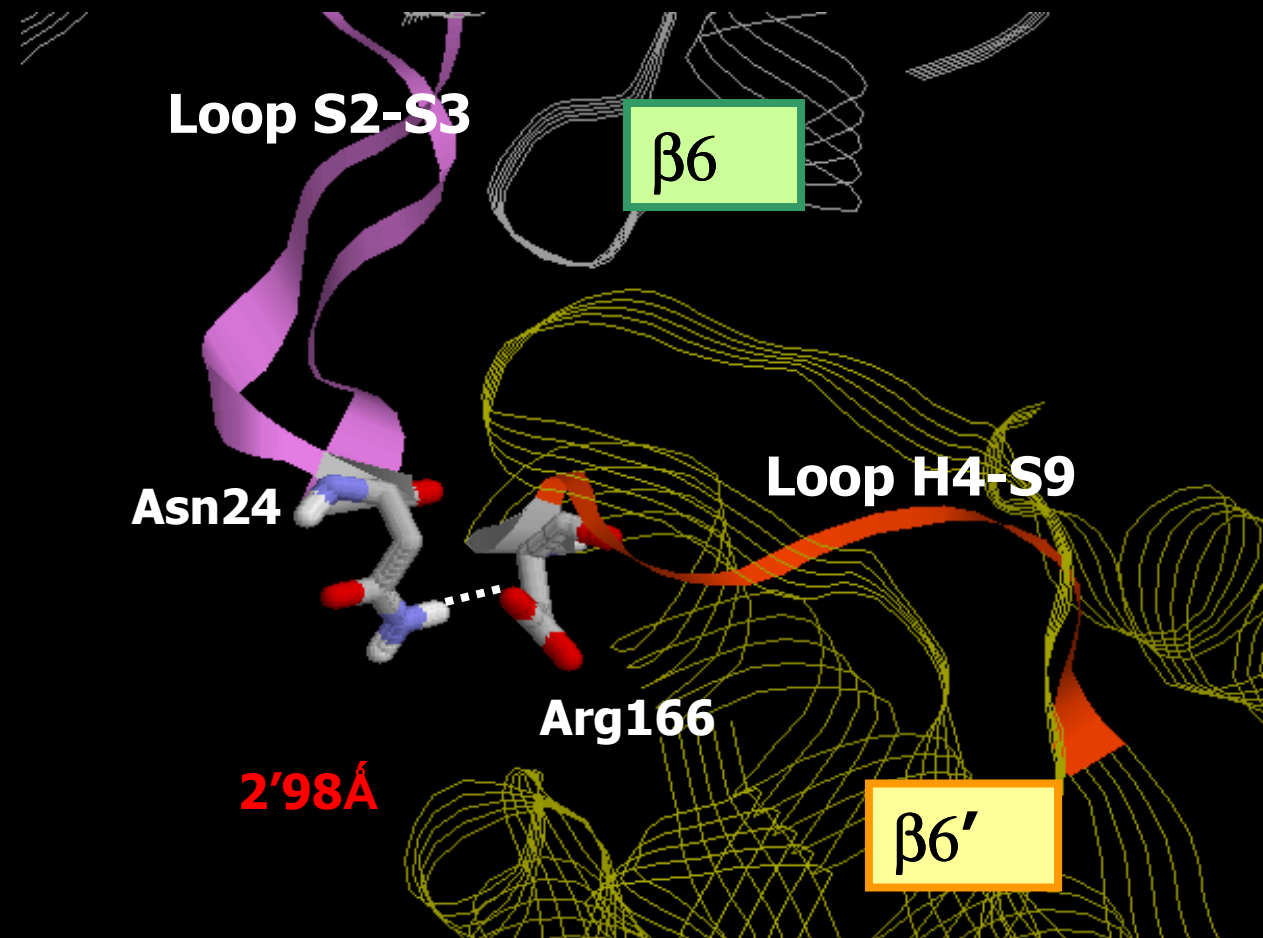
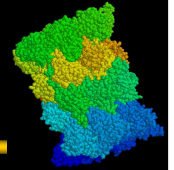
T. acidophilum: Interaccions



4. Entre anells β

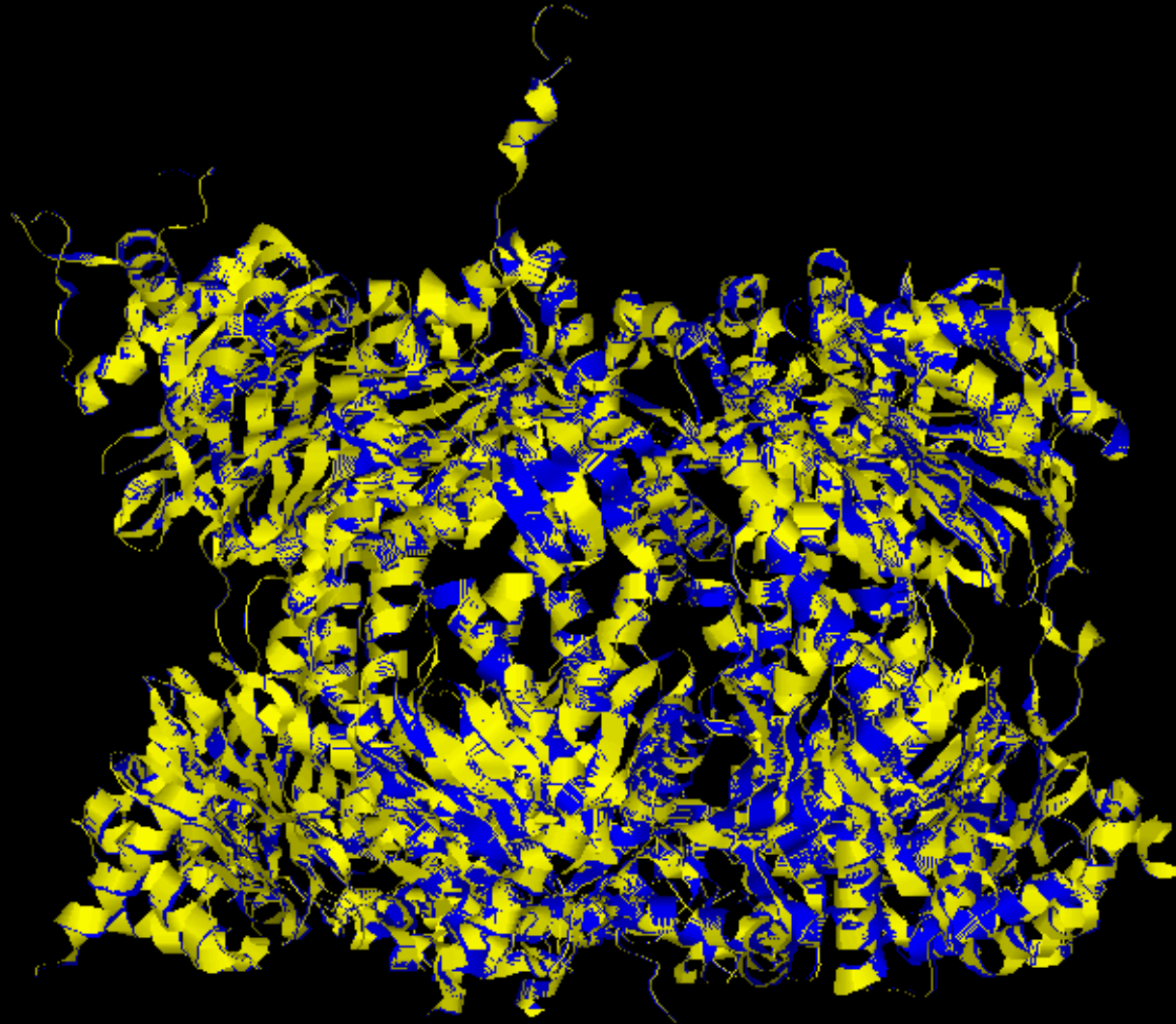
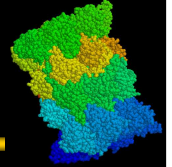


T. acidophilum: Interacciones



Saccharomyces cerevisiae

S. cerevisiae: Estudi de simetria

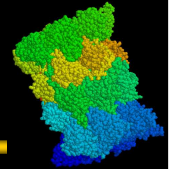


1RYP.pdb

Score: 0,20

RMS: 9,77

S.cerevisiae: Estructura de les subunitats



1. Entre α i β

CLUSTAL W(1.60) multiple sequence alignment

```
alfa1  AGYDRHITIFSPEGRLYQVEYAFKATNQTNINSLAV-R-GKDC-----TVVISQKKV
beta3  -----SDPSSINGGIVVAMTGKD---C-VAIAC-DLRLGS-QSLGVS NKFEK--I---

alfa1  PDKLLDP-TT--VSYIFC-I--SRT--IGMVVNG-----PIPD A-RNA
beta3  -----FHYGHVFLG--ITGLATDVTT-----LNEMFRYKTNLYKLKEERAIE-PETF

alfa1  -ALRAKAEAAEFYKYGYDMPCDVLAKRMANLSQIYTQRAY-----M-RPLGVILTFV
beta3  TQLVSSSLYER----RFGPYFV-GP-----VVAGINSKSG-KPF IAGFD

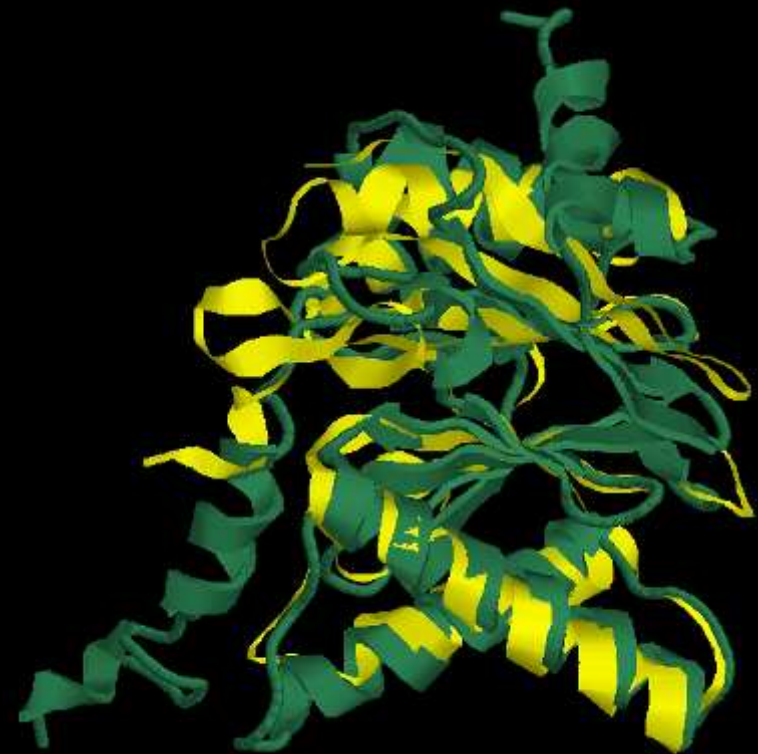
alfa1  SVDEELGPS--I-YKTD PAG-YYVG-----YK--AT---AT-----GP-K-QQEITT-NL
beta3  -----LIGCIDEA--KDF-IVSGTASDQLFGMCESL-YEPNLEPEDLFETISQAL-

alfa1  ENHFKKSKIDH-INEESWEKVVEFA-----ITHMIDALGTEFSKNDLEVGVA
beta3  -L-----NAADRDA---LSGUGAVVYIIKKDEVVKRY--L-----

alfa1  TKDKFFTL SAENIEERLVAIAEQD---
beta3  -----KMRQD
```

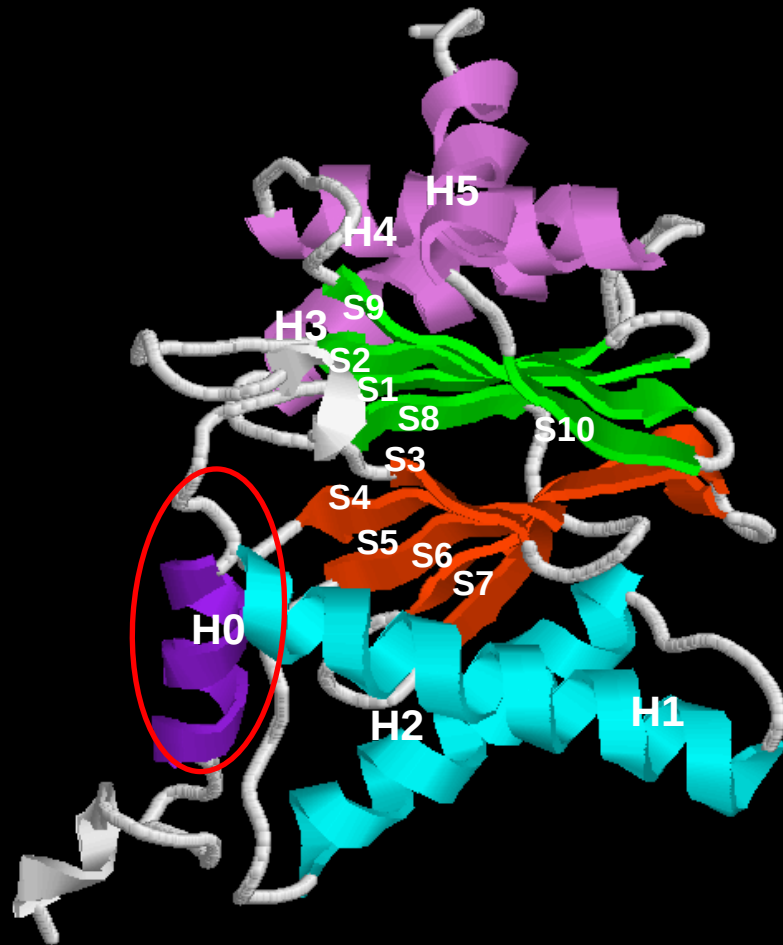
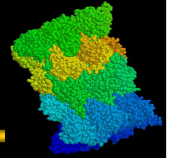
Score: 5,15

RMS: 1,77

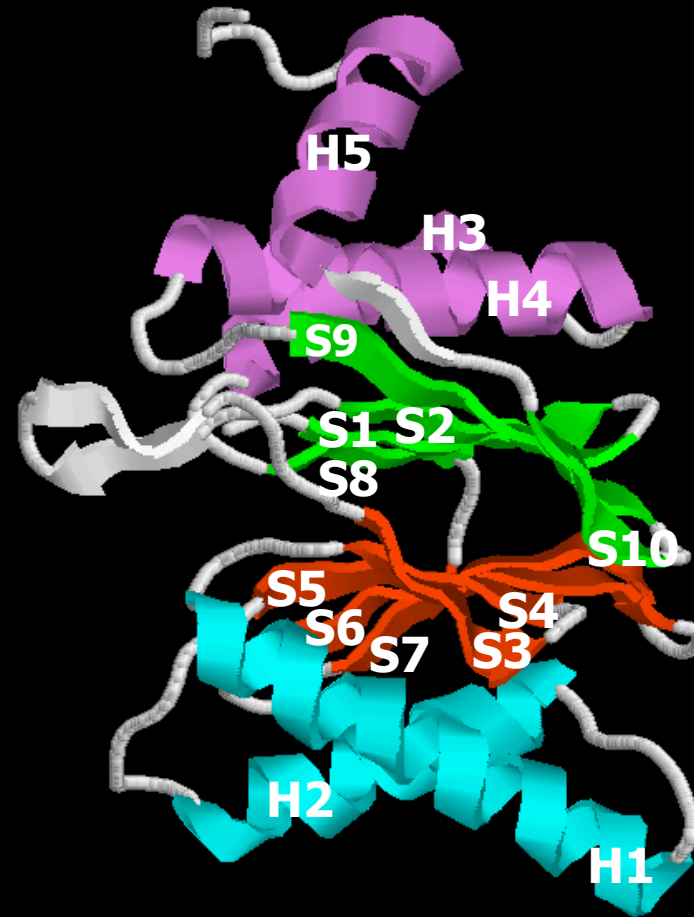


1RYP.pdb

S. cerevisiae : Estructura de les subunitats

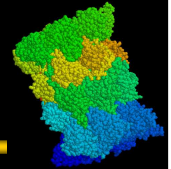


Subunitat α



Subunitat β

S.cerevisiae: Estructura de les subunitats



2. Entre α i α

CLUSTAL W(1.60) multiple sequence alignment

```

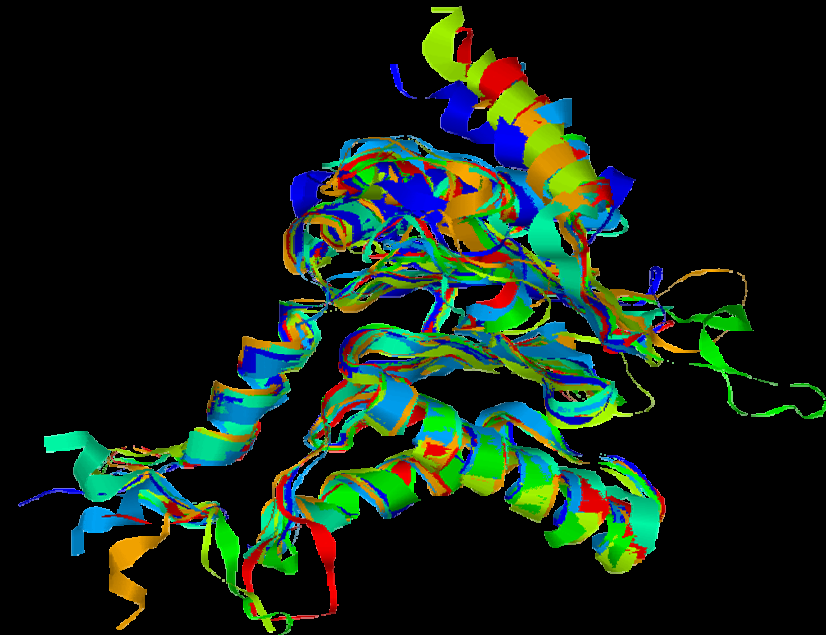
alfa 7  --C--TCGY-DLNSVSPDGRNFQVEYAVKAYE-NGTTSIGIKCNDGVVFAVEKLIITSKL
alfa 1  -----AGYDRITITFSPEGRLYQVEYAFKATNQTNINSLAVRGKDCITVVISQKKVDPRL
alfa 6  ---FPMNYD-GMTVTFSPTCGRLFQVEYALEAKIKQ-CSVTVGLRPNTHAVLVALKRNADRL
alfa 2  MTDRY---S-FSLTTFSPSGKLGQIDYALTAVKQ-CVTELCIKATNCVVLAIEKKSSSPL
alfa 4  ---GYD---RLLSIFSPDGHIFQVEYALEAVKR-CTCAVGVGRKNCVVLCGERSTLKL
alfa 3  -CSARY--D-SRTTFSPEGRLYQVEYALESLISH-AGTAIGIMASDGIVLAAEKVSTL
alfa 5  -----D-RVSTFSPEGRLFQVEYSLEAKKL-CSTAIGIATKEGVVLCVEKRAT SPL

alfa 7  LVPQK-NVKIQVDRHIGCVYSGLIPDGRHLVNRGRREA-ASFKKLYKTPIPIPAFADRL
alfa 1  LD-PTTVSYIFCISRTIGMVVNGPIPDARNAALRAKAEA-AEFYKYCYDMPCDVLAKRM
alfa 6  SS---YQKKIICDEHMGSLSLAGLAPDARVLSNYLRQOC-NYSSLVFNPKLAVERAGHLL
alfa 2  AM-SETLSKVSLLTPDIGAVYSGMGPDYRVLVDKSRKVAHTSYKRIYGEYPPTKLLVSEV
alfa 4  QDTRITPSKVS KIDSHVLSFSGLNADSRILIEKARVEAQ-SHRLTLEDPTVTEYLT RYV
alfa 3  LEQDTST EKLYKLNDRKLA VAVAGLTADAELINTARIHAQ-NYLKTYNEDI PV EILVRRL
alfa 5  LES-DSIEKIVEIDRHIGCAMSGLTADARSMIEHARTAAV-THNLYYDEDINVESLTQSV

alfa 7  GQYVQA-----HTLYNSVRPFQVSTIFG-GWDK-NGAHLYMLEPSCSYWGYKGAAT
alfa 1  ANLSQIY-----TDRAYMRPLGVILTFVS-VDEELGPSIYKTDPAQYVVGKATAT
alfa 6  CDKAQW-----TQSYGCRPYGVGLLIIC-YD-KSGAHLLFPQSGNVT ELYGTAI
alfa 2  AKIMQEA-----TQSGCVRPFQVSLIAG-HDEFNGFSLYQVDPSCSYFPWKATAI
alfa 4  AGVQQPYT-----QSGCVRPFQVSTLIAGFDPRDD EPKLYQT EPGSIYSSWSAQTI
alfa 3  SDIKQCYTQ-----H-CGLRPFQVSTFIYAGY-DDRYCYQLYTSNPSGNYTGWKAISV
alfa 5  CDLALP--FGEASCEERLM-SRPFQVALLIAGH-DADDGYQLFHAEPSCGFYRYNAKAI

alfa 7  GKGRQSAKAELEK-LV-DH-HPEG--LSAREAVKQAAKIITLHEDMKERD---FLEIS
alfa 1  GPRQQEITTNLENHFKKSKIDHIN-RESWEKVVVEFAITHMIDAE---LG-TEFSKNOLEVG
alfa 6  GARSQGARTYLERT-LD-TF--IKIDGDPDLIKACVRAISQS---LRDESLTVDNL SIA
alfa 2  GKGSVAARTFL EKR-W---N--DE--LLLEDAIHIALLT LKES---V-EGEFNGDTIELA
alfa 4  GRNSKTVRE FLEKN-Y--DR-KEPP-AVVEECVKLTVPSSL EY---VQTG-AKMI EIT
alfa 3  GANTSAAQTLQMD-Y--K--D-DM--HVDDAIEIALKTL SKT---TDSSALTYDRL EFA
alfa 5  GSCSEGAQAE LLNE-W--H--S--ST---LKEAELLVLKILKQV---ME-EKIDENNAQLS

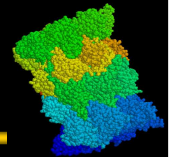
alfa 7  WCSLS--ET-----NGIHKFV-KGDL LQRAIDPAQKEIN--
alfa 1  V-----AT-----K-DIFFFLSA-ENIEERLVLAIEQD---
alfa 6  I-----VG-----KDTIFTIYDG-EAVAKYI-----
alfa 2  II-----GQENPDLLGYTCIPTDKGPIFRKLTS-QEINDRLEAL-
alfa 4  VV-----KQ-----DSHVALSS-EEINQYVTCIEQEKQEQ
alfa 3  TIHK-GAND-----EVYQKIFKP-QEIKDILVET--GIT--
alfa 5  CIT-----K-----QDQFKIYDN-EKTAEILKELKEKAAE
    
```



Score: 8,14

RMS: 1,05

S. cerevisiae : Estructura de les subunitats



3. Entre β i β

CLUSTAL W(1.60) multiple sequence alignment

```

Beta7  --TQ--QP--IVT-GTSVI SMKYNQGVIIAADNLGSGYSLRFGNVERLIPVGDNTVVGI
Beta2  -----TIVGVKFMNGVWIAADTRSTQGPPIVADKNCARLHRI SPKIWCAG
Beta4  -----MDIILGIRVQDSVILAS SKAVTRGISVLKDSDDKTQLSPHTLMSF
Beta5  -----TTLAFRFQGGIIVAVDS RATACNWVASQTVKRVIEINPFLLGTM
Beta6  QFNP---Y---GDNGGII LGLAGEDFAVLACDTRNIIDYSINSRYEPRVFDCGDNIWMSA
Beta1  ---LKKGE--VSLGASIMAVTFKDCVILGADSRITTCAYIANRVTDKLT RVHDKIWCCR
Beta3  ---S--D--PSSINGGIVVAMTCKDCVAILACDLRLGSSQLGVSNKFEKIF-HYCHVFLGI

Beta7  SCDISDMQHI ERLLKDLVTENAY--DNPLADAEAL EPSYIF EYLA TVMYQRRSKMNPLOW
Beta2  ACTAADTEAVTQLIGSNIELHSL--YTS-----REPRVSA LQMLKQHLFKY--Q-CHIGA
Beta4  ACEAGDTVQFAEYIQANIQLYSIH--ED-----YELSPQAVSS FVRQELAKSI RSRRPYQV
Beta5  ACCAADCQFWETWLGSCQCRLEHLE--EK-----ERISVAAASKILSNLVYQYK--GACLSM
Beta6  NCFAADG DALVKRFRNSVKWYHFLHND-----KKLSINSAARNIQHL LYCKR--FFPYV
Beta1  SCGAADTQAIADIVQVHLELYTSC--Y-----GTPSTE TAASVFKELCYENK--D-NLTA
Beta3  TGLATDVT TLNEMFRYKTNLYKLE--E-----RAIEPETF TQLVSSSLYERR--FCPYFV

Beta7  AIIIVACVQ--SNGDQFLRYVNLGVTY--SSPTLATCFGAHMANP LLEPKV-----
Beta2  YLIVACVD--P-TCSHLFSIHAGSTD--VGYLSLGSGSLAAMAVLESH-----
Beta4  NVLIGCYDKRKNRP ELYQIDYLGTRV--ELPYGAHCYSGFYTFSLLDH-----
Beta5  GTMICYTR--KEGPTIYYVDSGTRLRK--GDIFCVGSGQTFAYGVLDSE-----
Beta6  HTIIAGL--DEDCRCAVYSFDPVCSYER--EQCRAGCAAA SLIMPFLDNQVNFKNQYEPG TN
Beta1  GIIIVACYDDK--NKG EYVYTIPLGGSVHKL--PYALACSGSTFIYGYCDKMF-----
Beta3  GPVVAGINSKSGKPFIA GFDLIGCIDKARDFIVSGTASDQLFGMCESLY-----

Beta7  ---VDRESIPKTTVQVAE EAIWNAMRVLYYRDARSSRNFLA IIDKNTGLT--FK-KNL-
Beta2  ---W---K-QDLTKKEAIKLASDAIQAGIWDNLCSG SNVDVCVMEIGKDAE--YLRNYL-
Beta4  ---Y---R-PDMTEEGLDL LKLCVQELEKRPMDFKCVIVKIVD--KDGIR--QV-DDF-
Beta5  ---Y---K-WDLSVEDALYLGRSILAAAHRDAYS GCGSVNLYHVT--EDGWIYHG--NHD
Beta6  GKVRK--PL-KYLSVEEVIKLVDSFTSATEPHIQVGDGLEI LIVT--KDCVRK--E--FY-
Beta1  -----R--ENMSKEETVDFIKHSLSQAIKWDGSGGVI RMVVL T--AACVER--L--IFY
Beta3  -----E--PNLEPEDL FETISQAL LNAARD DALSGWCAVYIIR--KDEVRK--R--YLR

Beta7  QVE--I-----M---KMDFAKDIKGYGTQKI
Beta2  --TPNTR EKKQKSYKFPFGTTAVLKESIVNICD--
Beta4  -QAQ-----
Beta5  VGE--IFWKVKREEGSPNNVIC-----
Beta6  --ELKID-----
Beta1  -PDE--E-QL-----
Beta3  ---MRD-----
    
```

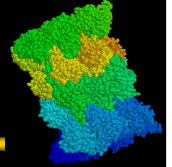


Score: 7,38

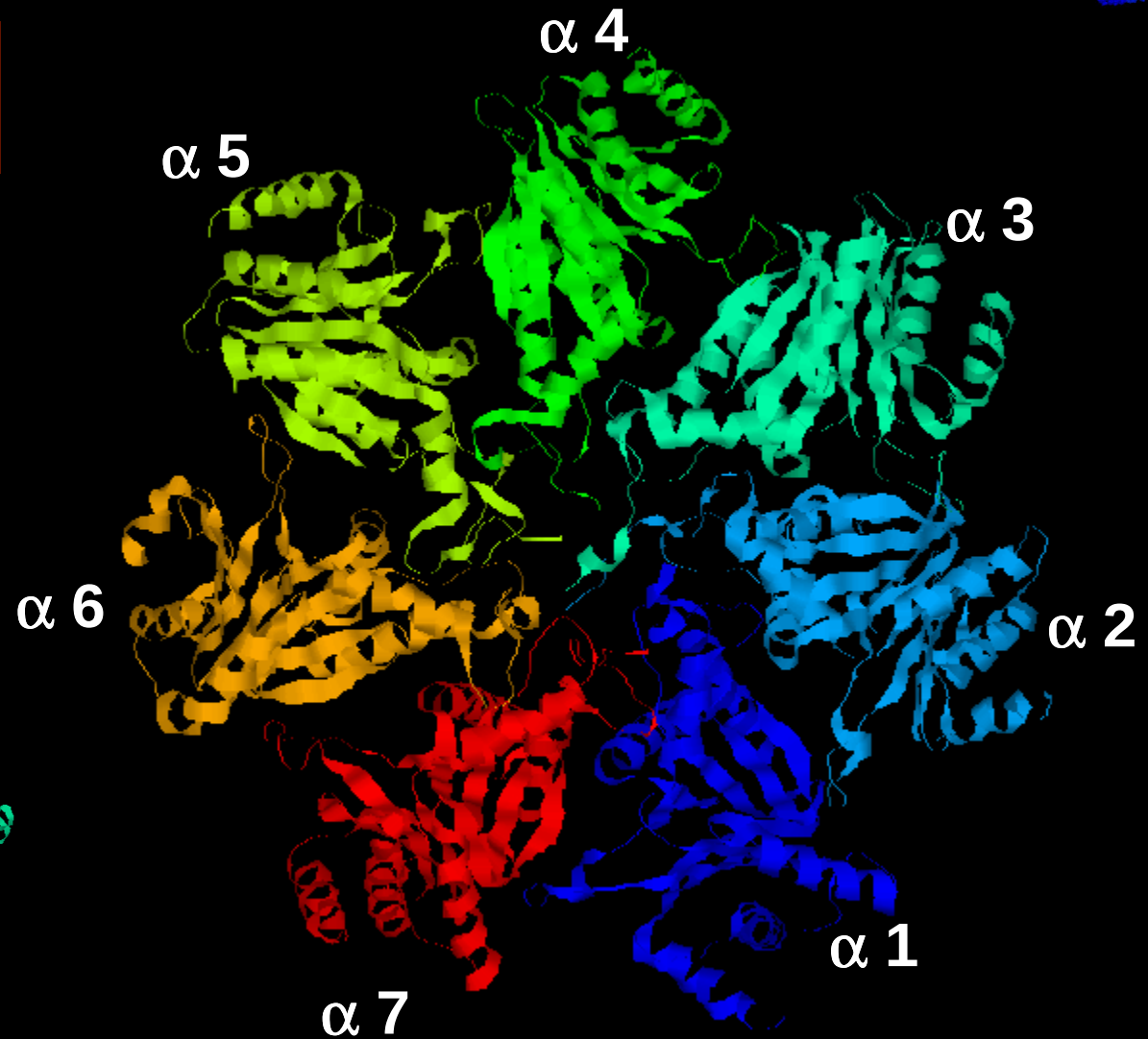
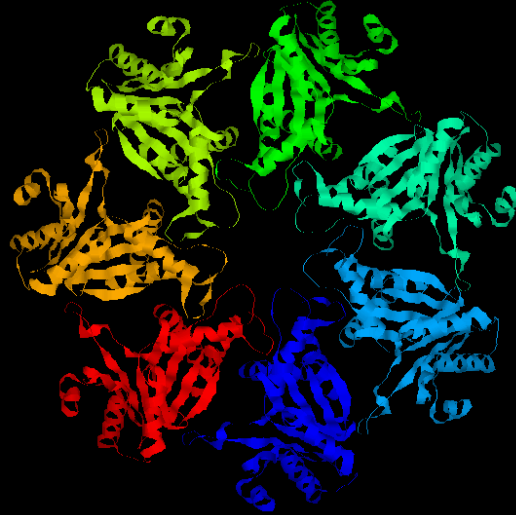
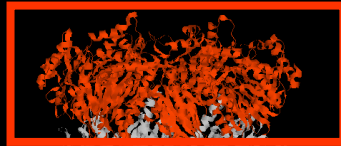
RMS: 1'47

1RYP.pdb

S.cerevisiae: Estructura de les subunitats



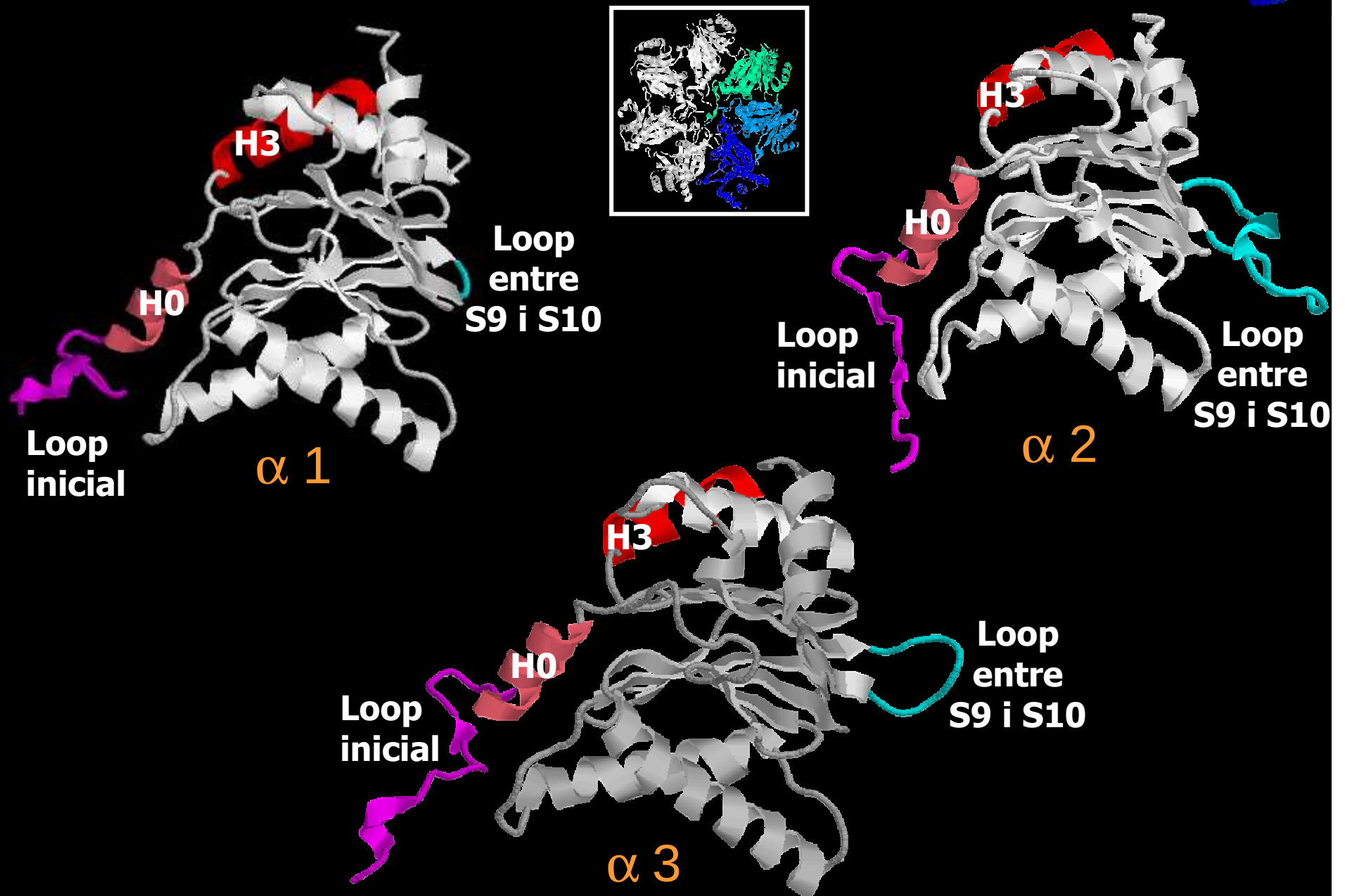
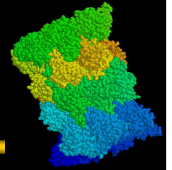
SUBUNITATS α



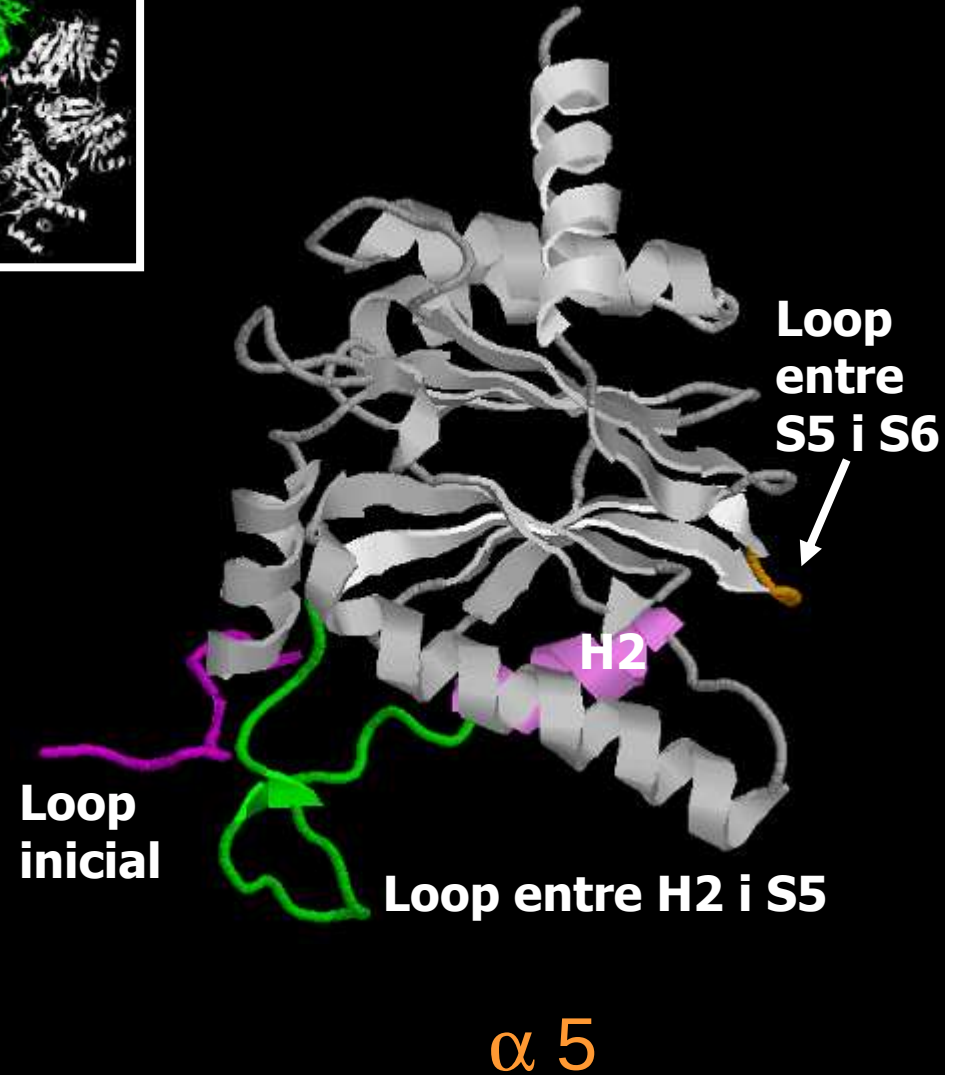
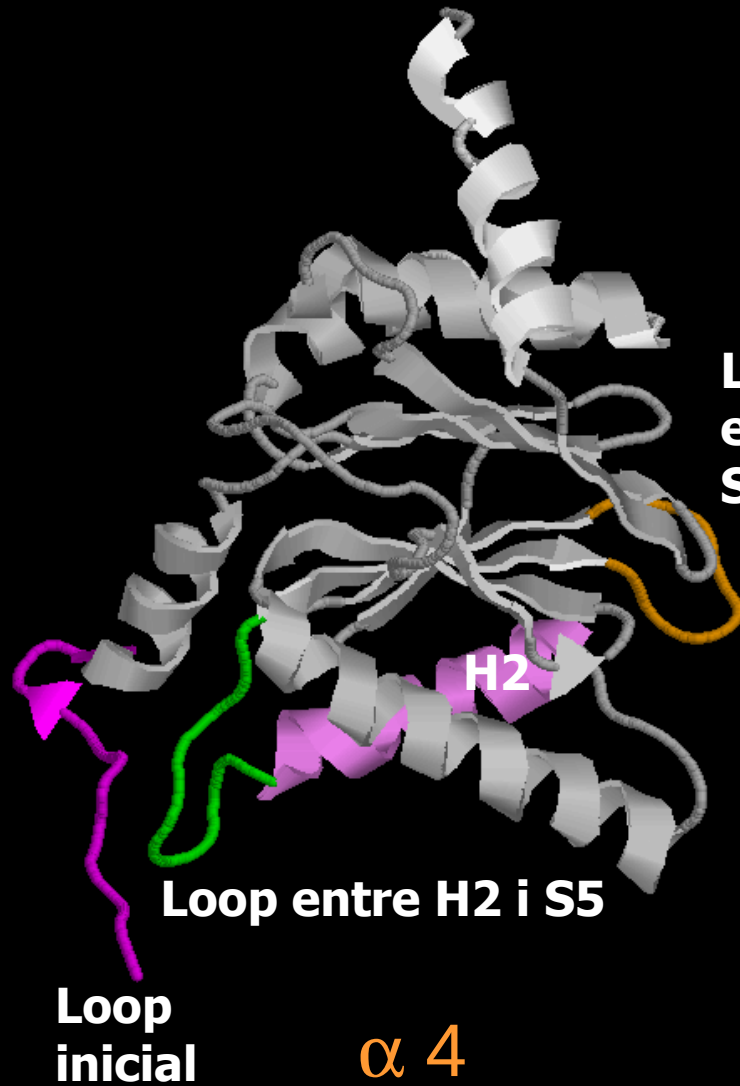
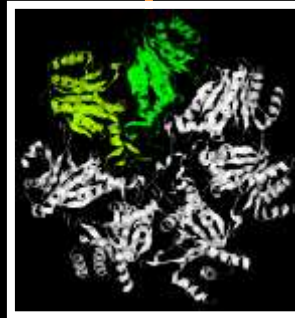
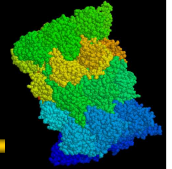
1PMA.pdb

1RYP.pdb

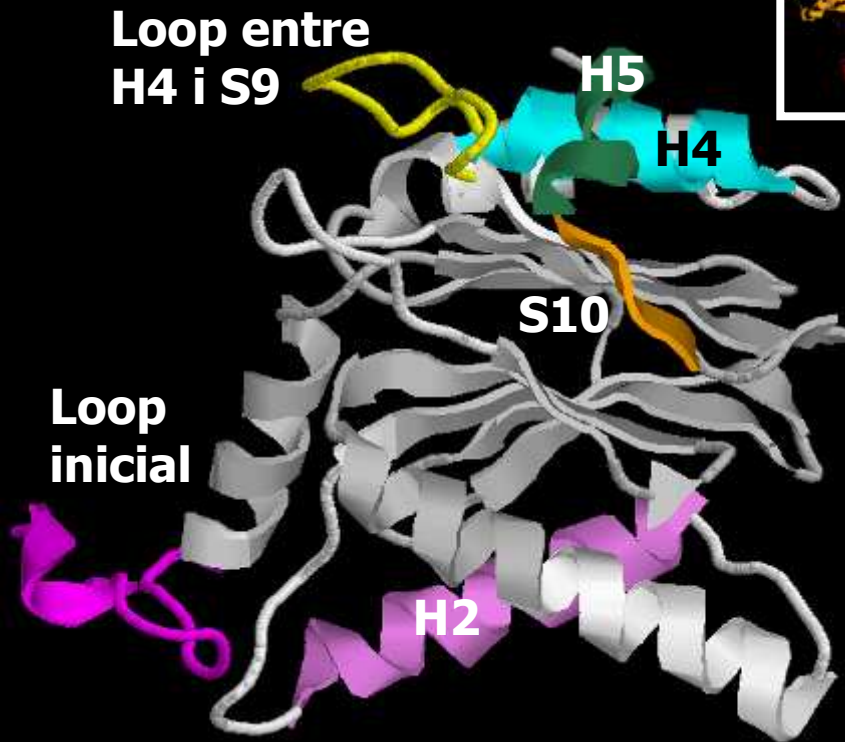
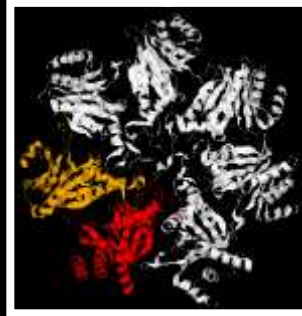
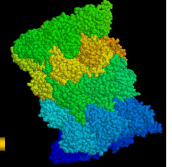
S.cerevisiae: Estructura de les subunitats



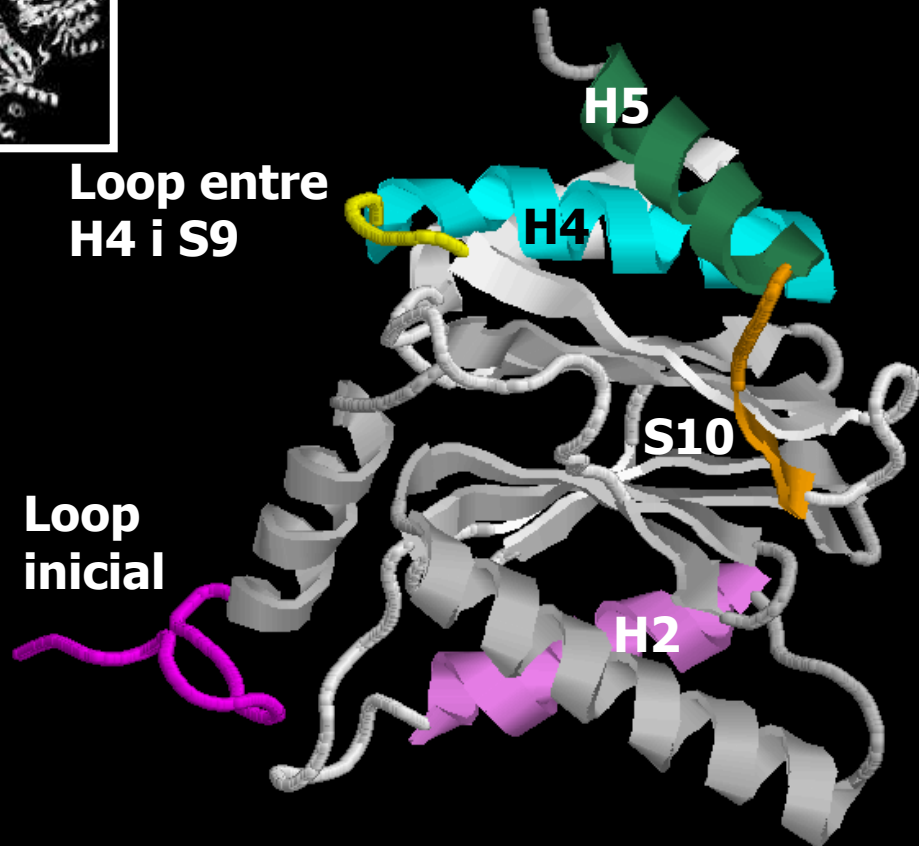
S.cerevisiae: Estructura de les subunitats



S.cerevisiae: Estructura de les subunitats

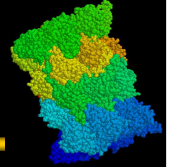


$\alpha 6$

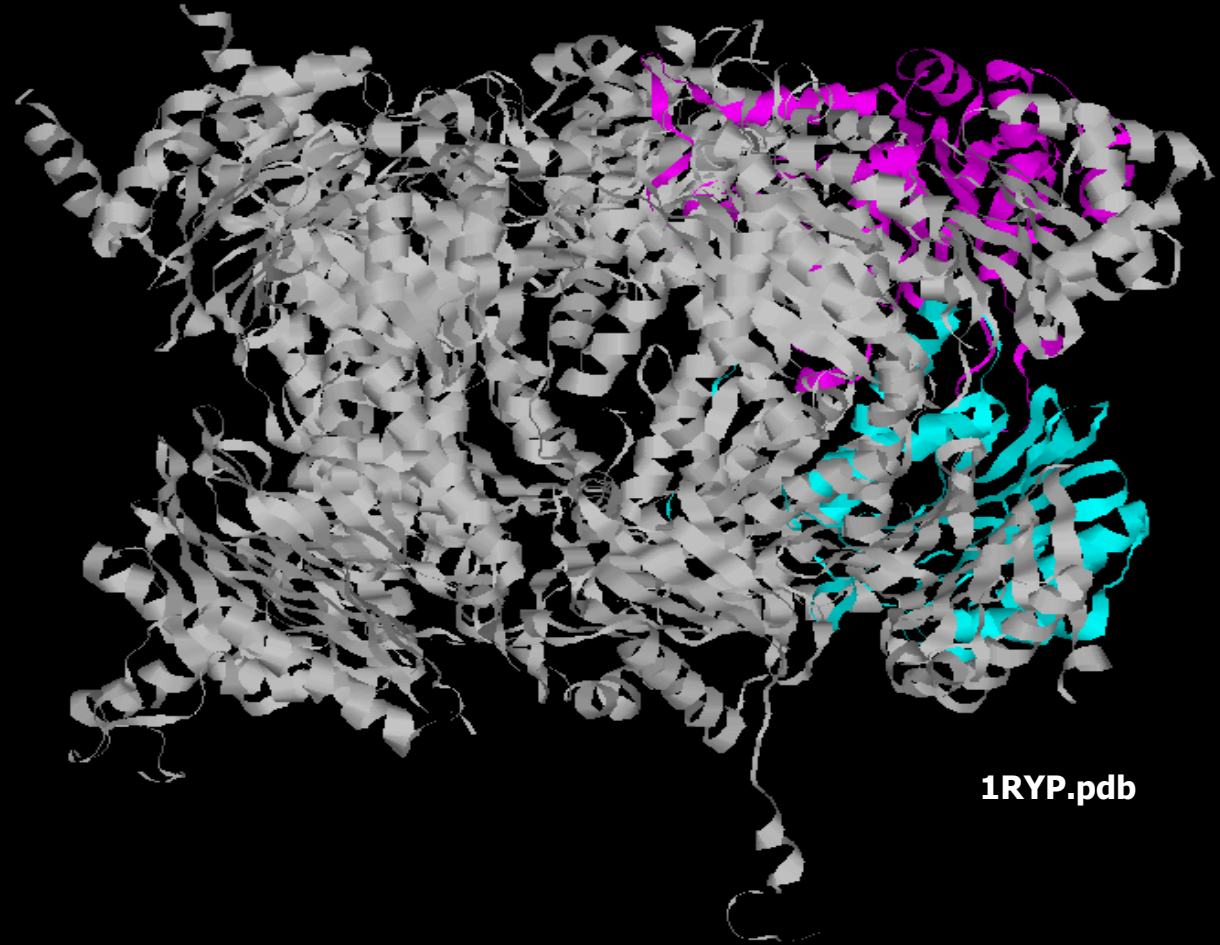
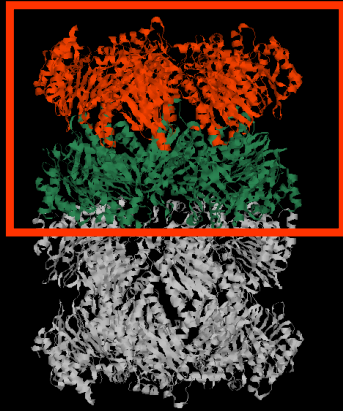


$\alpha 7$

S.cerevisiae: Interaccions



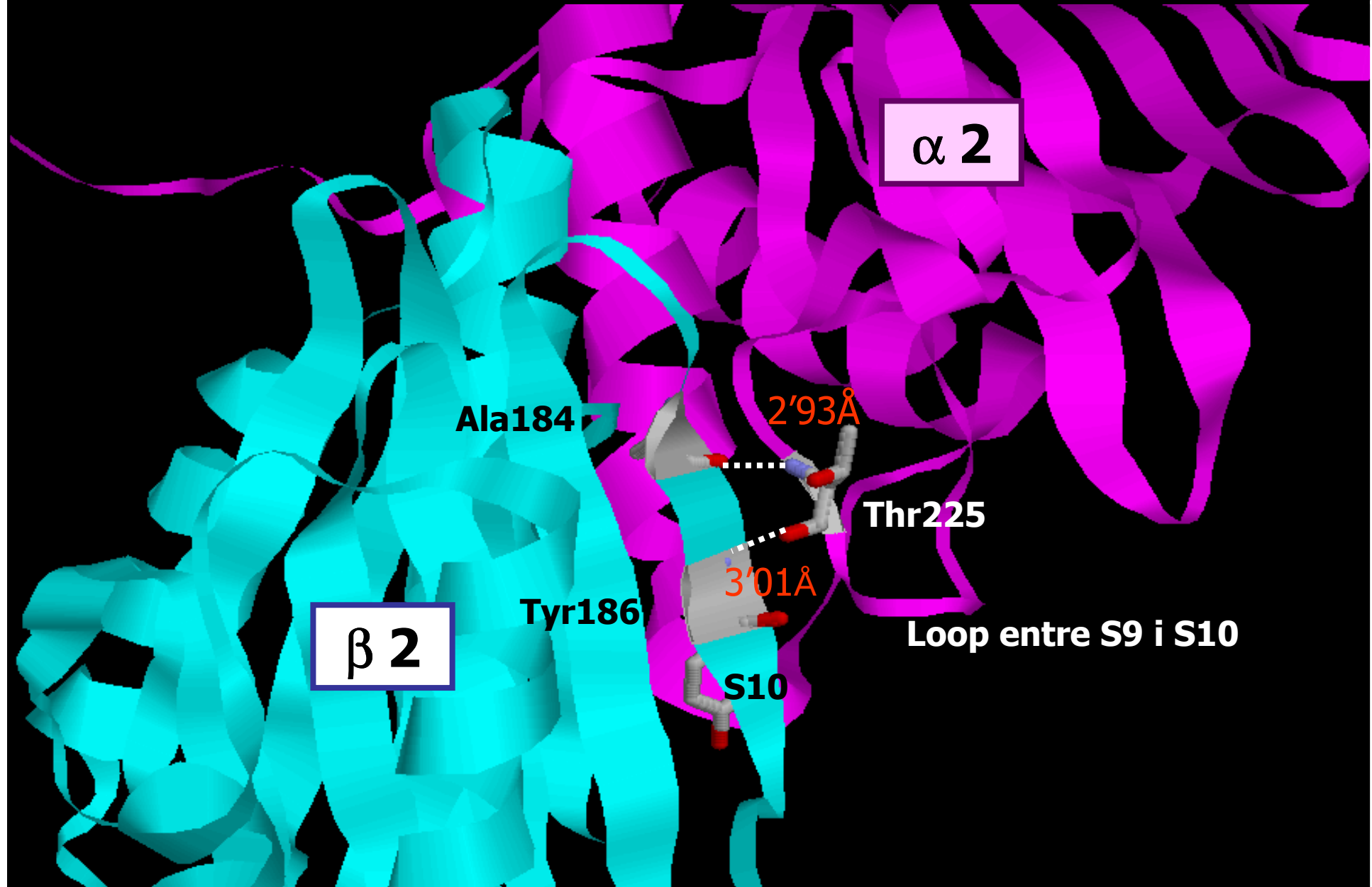
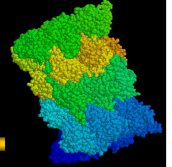
Entre α i β



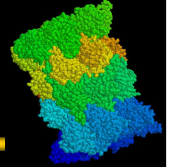
1RYP.pdb

Interacció entre $\alpha 2$ i $\beta 2$

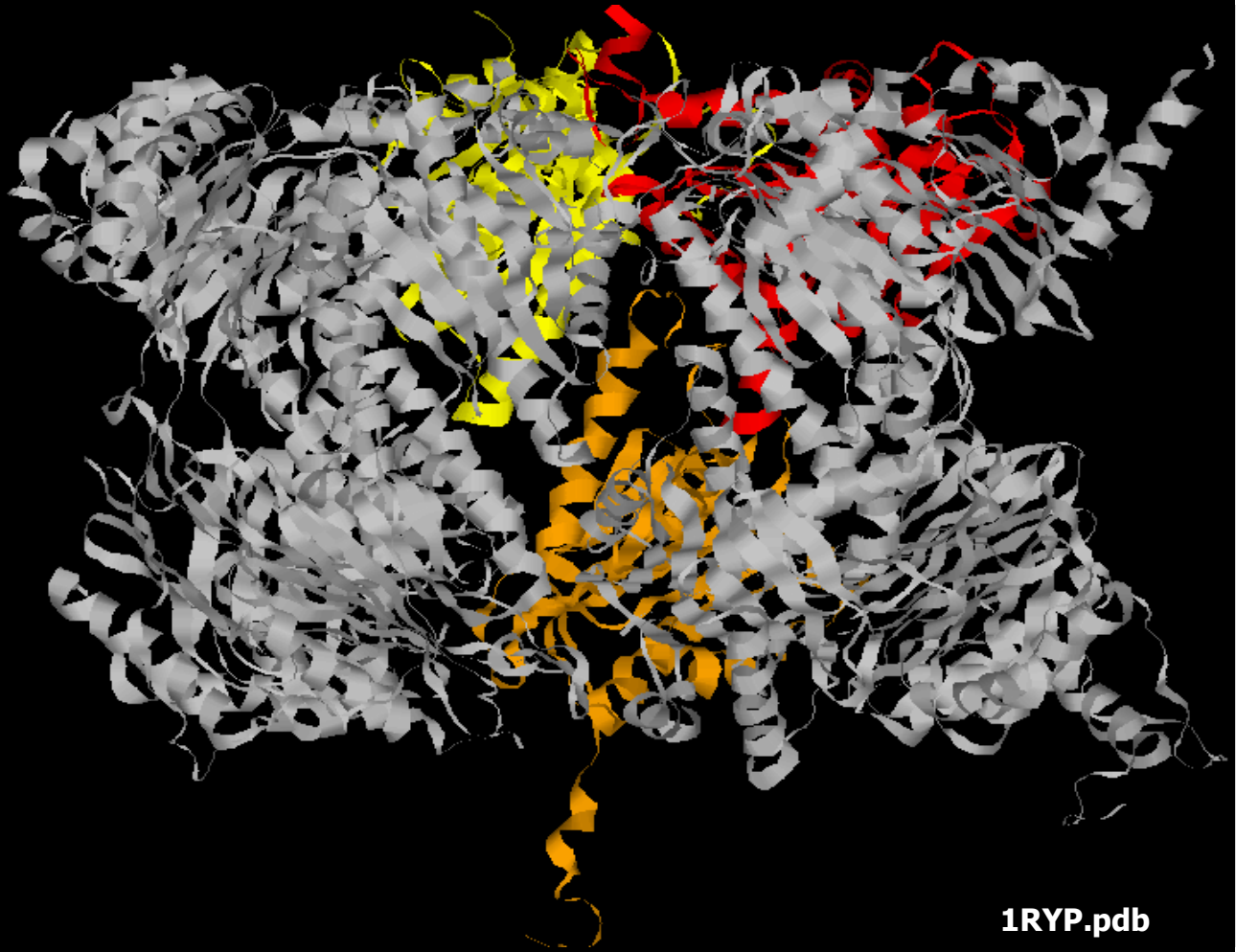
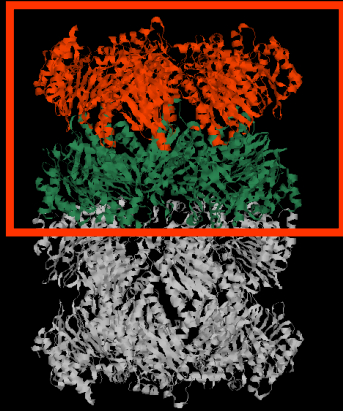
S.cerevisiae: Interaccions



S.cerevisiae: Interaccions



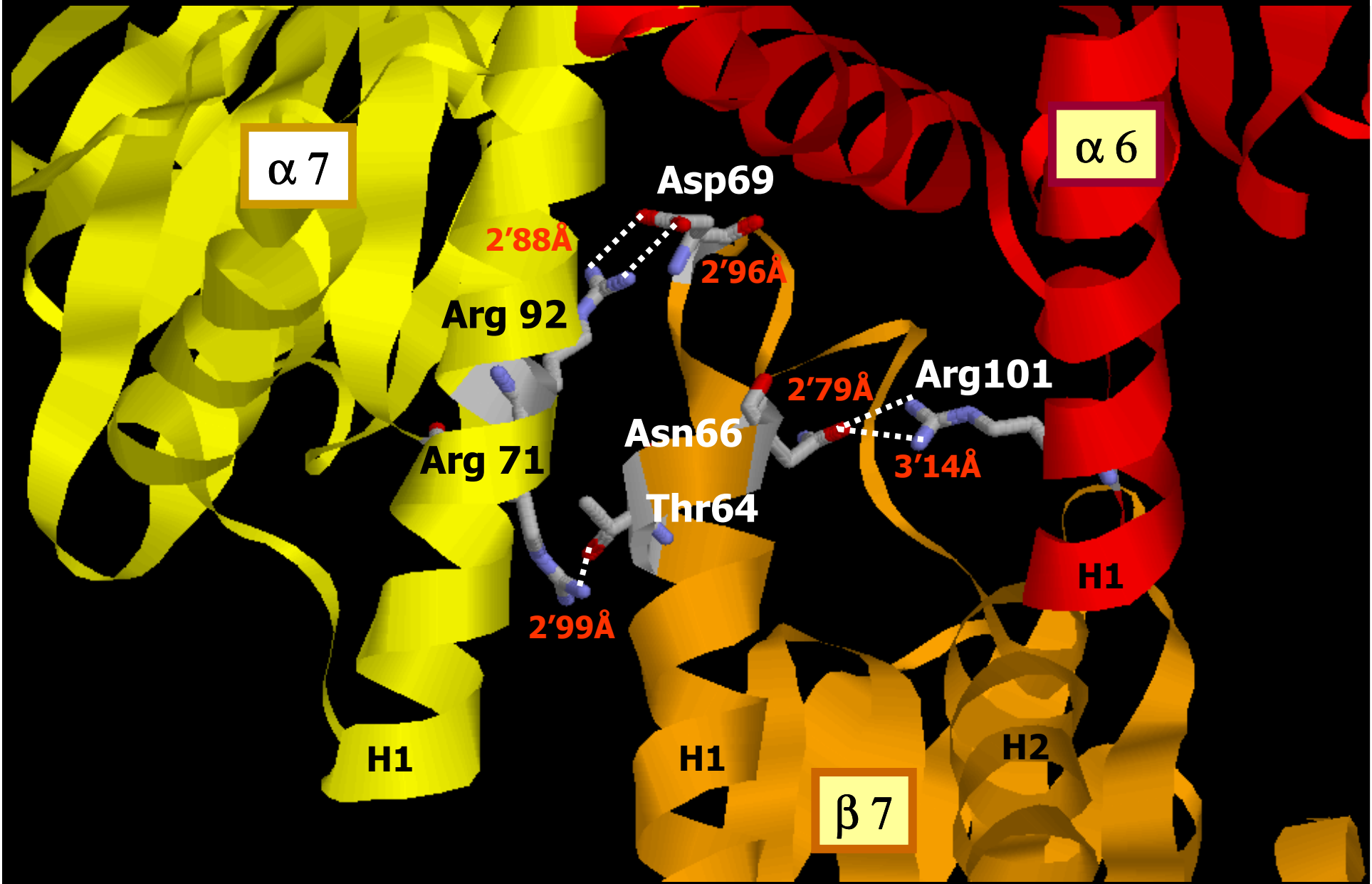
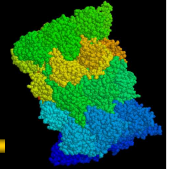
Entre α i β



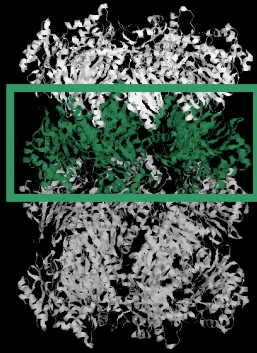
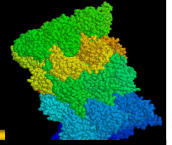
1RYP.pdb

Interacció entre $\alpha 6$, $\alpha 7$ i $\beta 7$

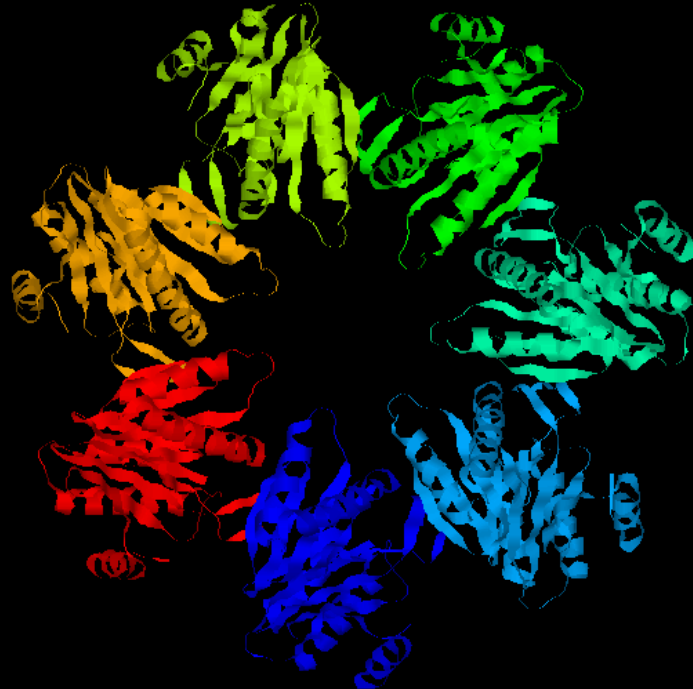
S.cerevisiae: Interaccions



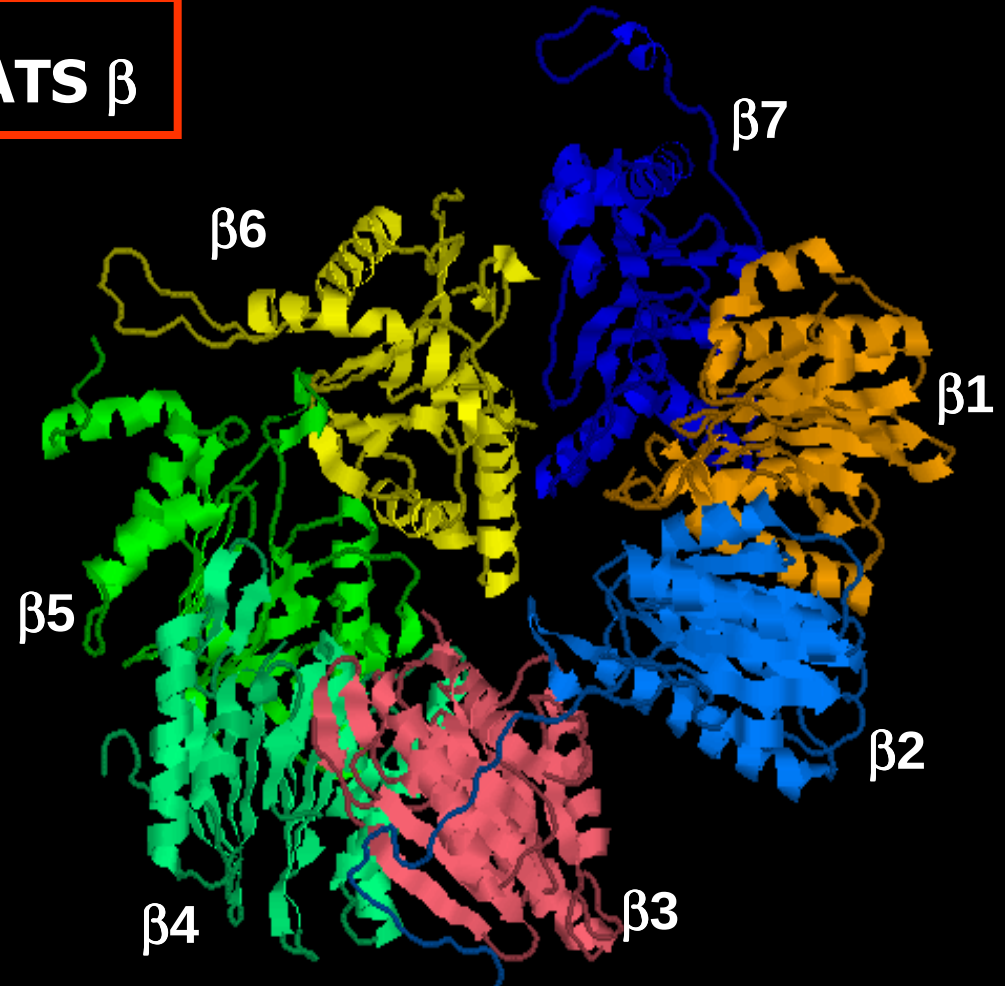
S. cerevisiae : Estructura de les subunitats



SUBUNITATS β

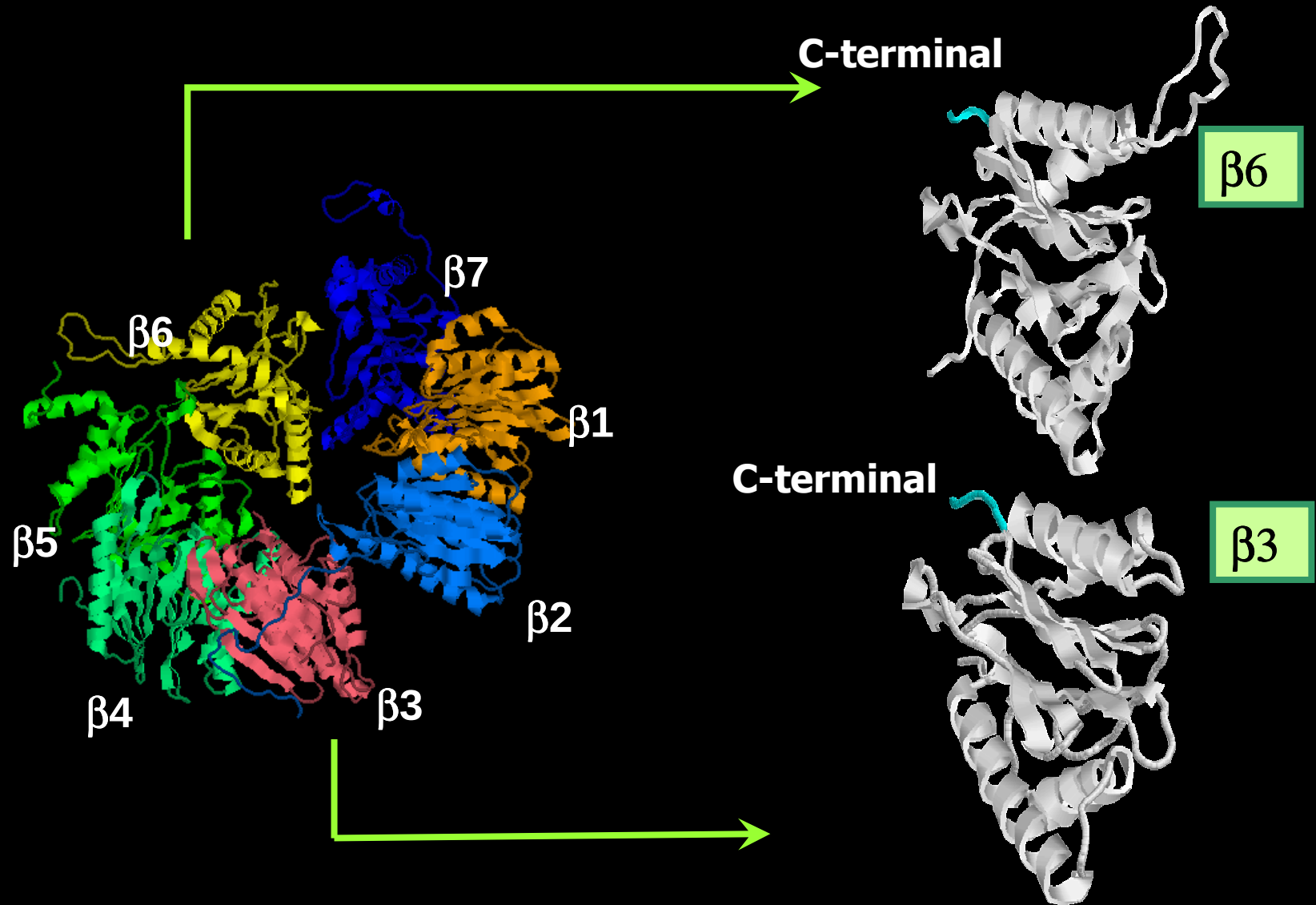
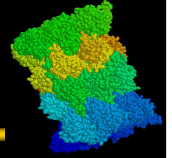


1PMA.pdb

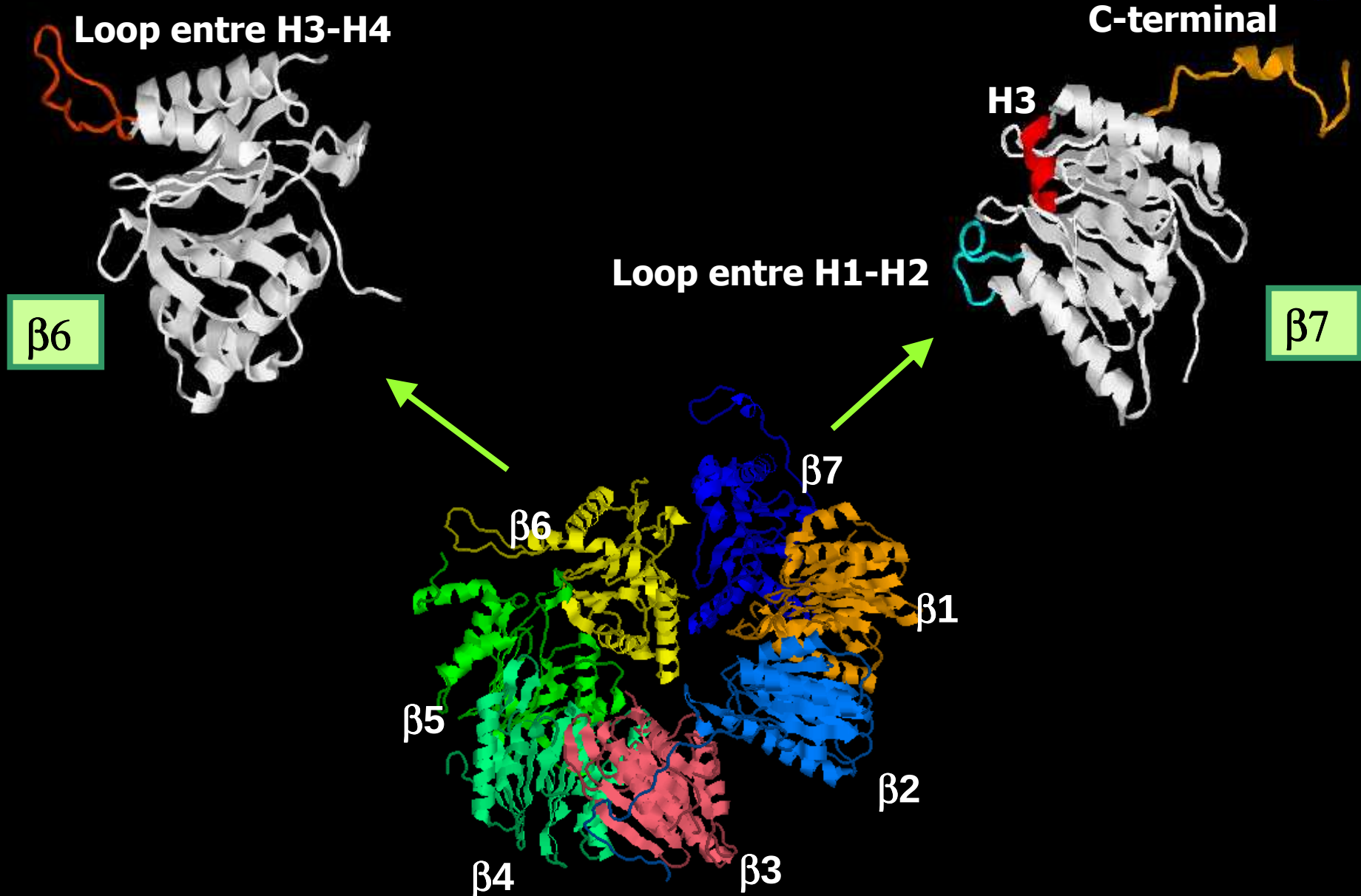
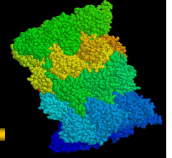


1RYP.pdb

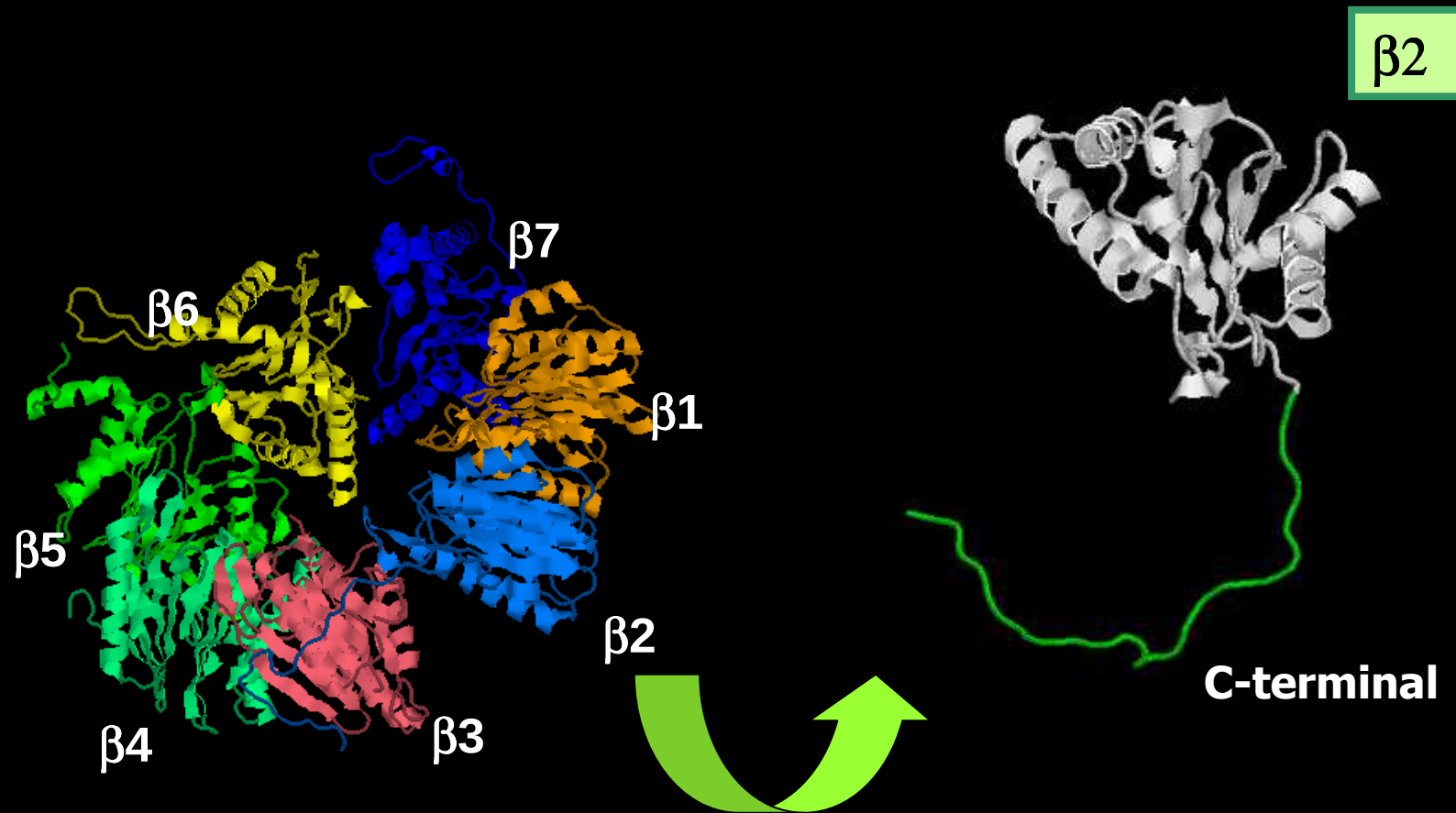
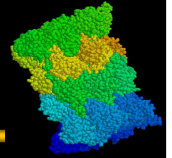
S. cerevisiae : Estructura de les subunitats



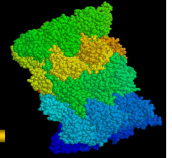
S. cerevisiae : Estructura de les subunitats



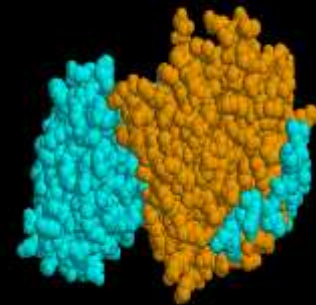
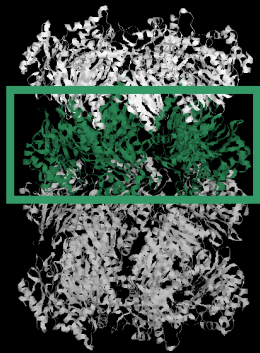
S. cerevisiae : Estructura de les subunitats



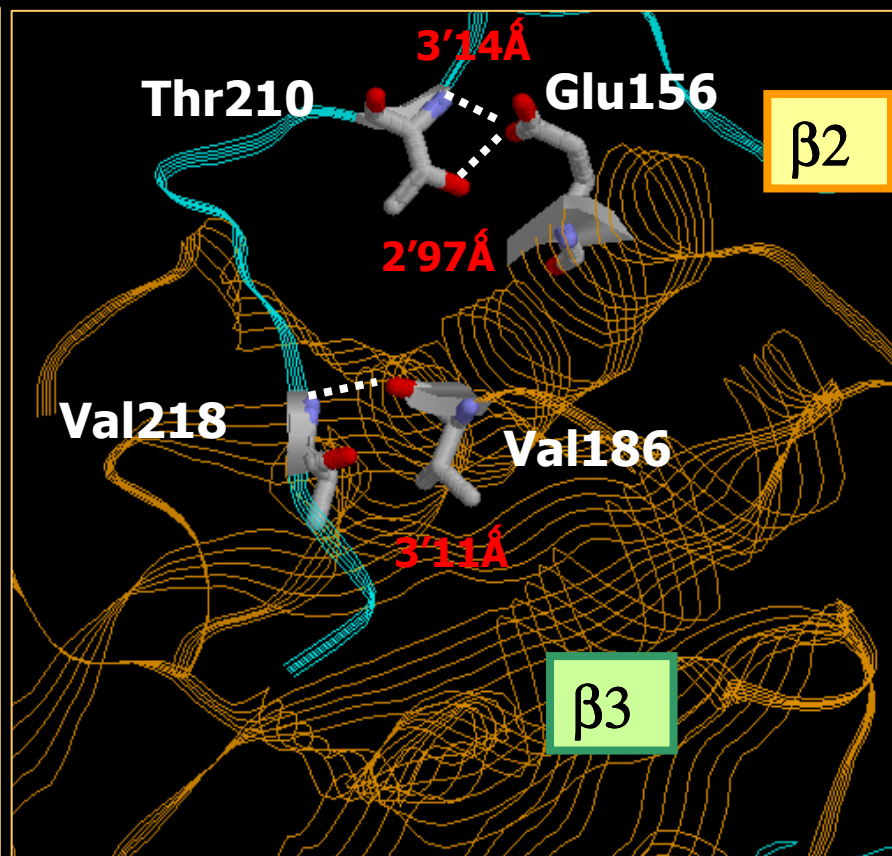
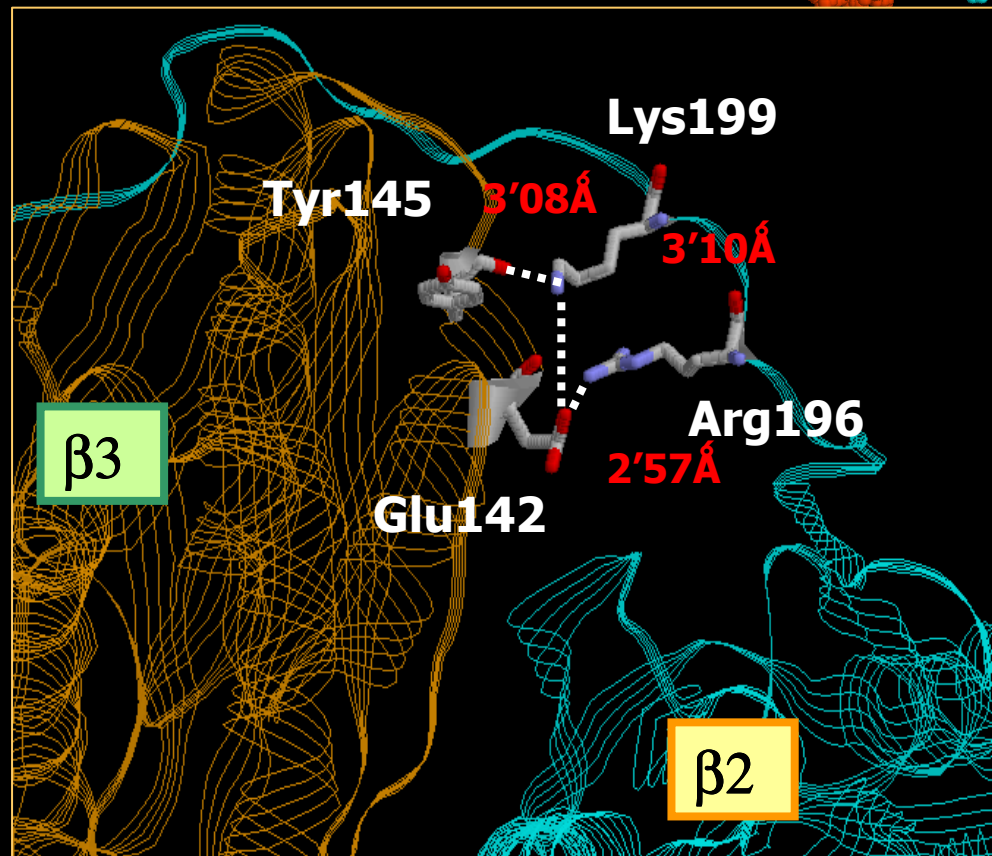
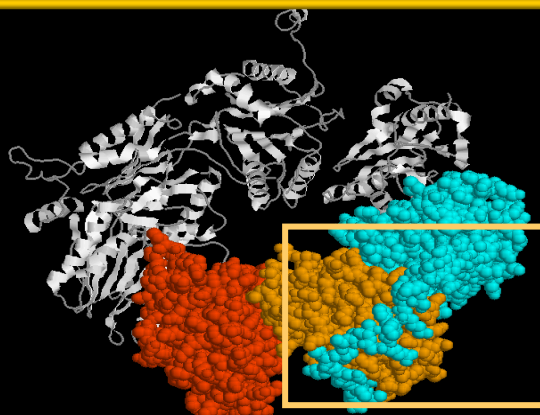
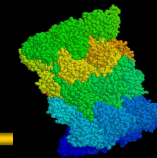
S. cerevisiae : Interaccions



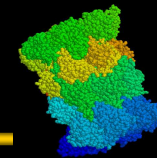
Entre β i β



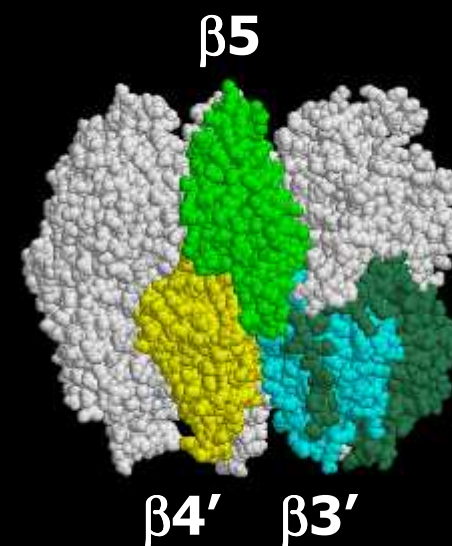
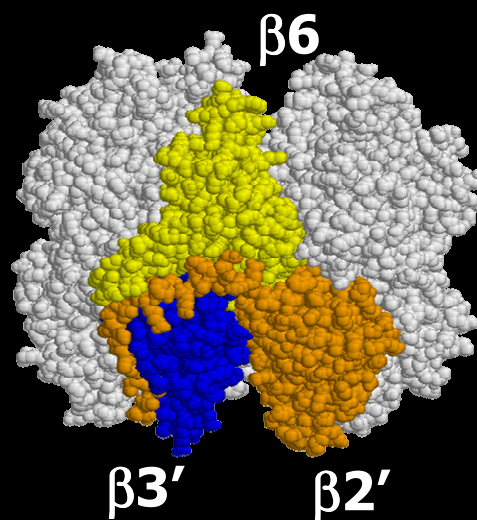
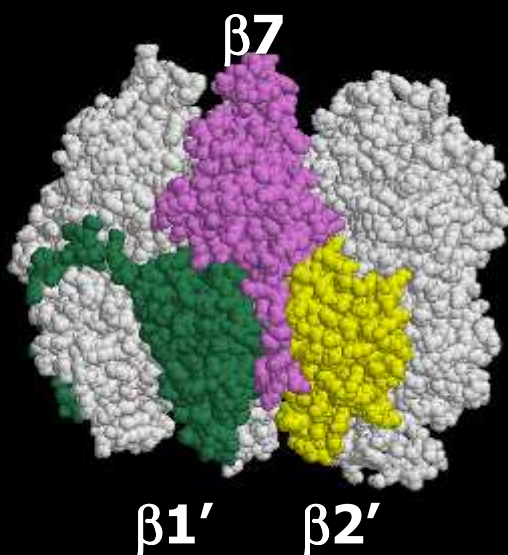
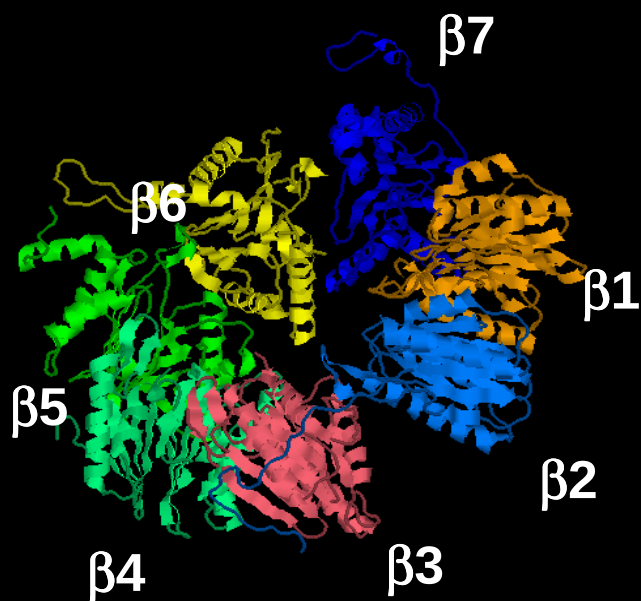
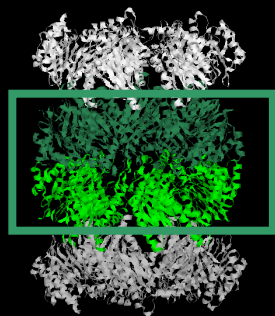
S. cerevisiae : Interaccions

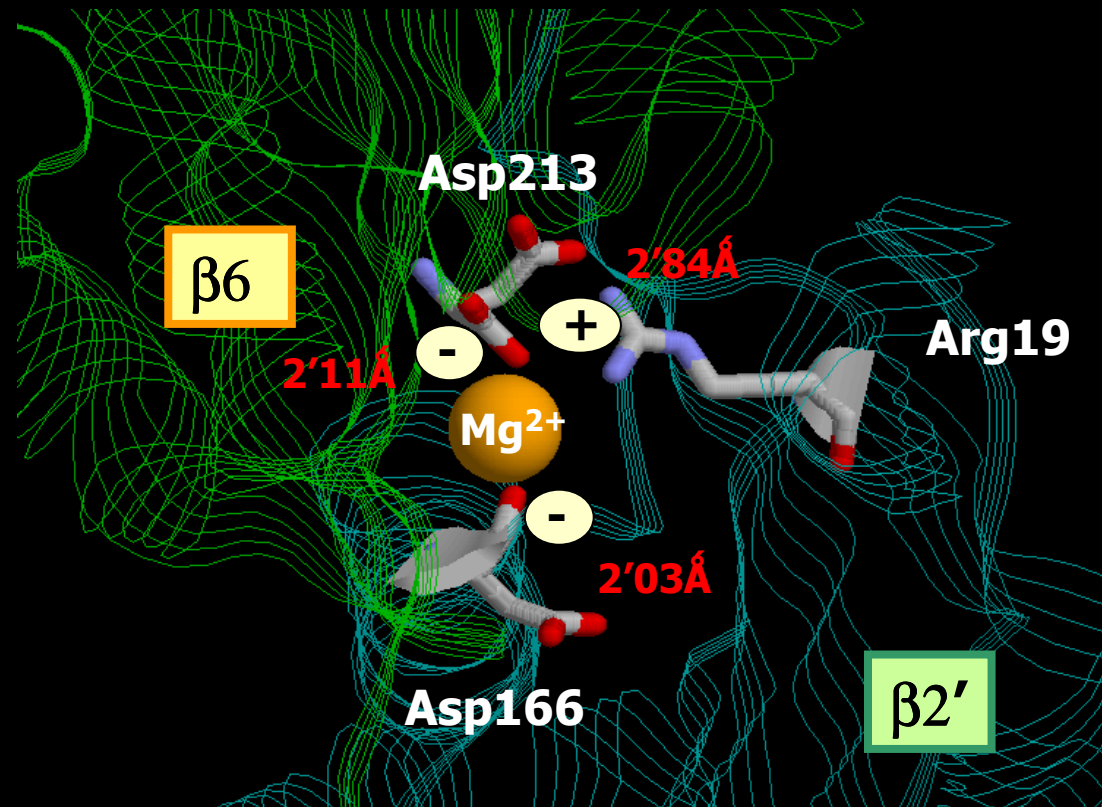
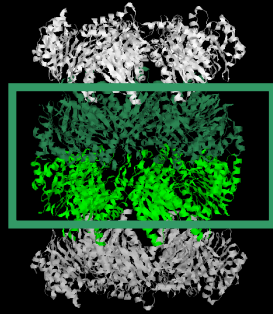


S. cerevisiae : Interaccions

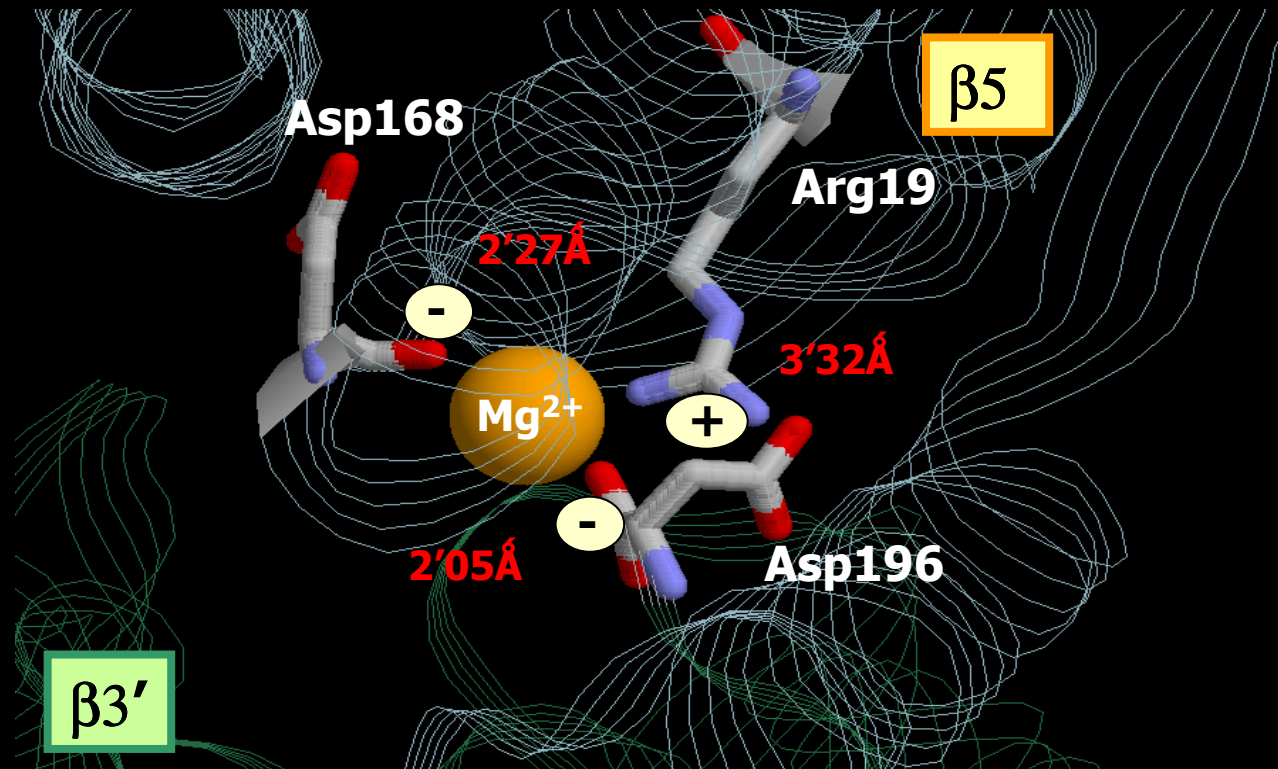
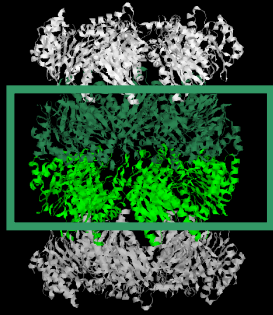
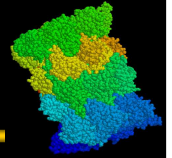


Entre anells β



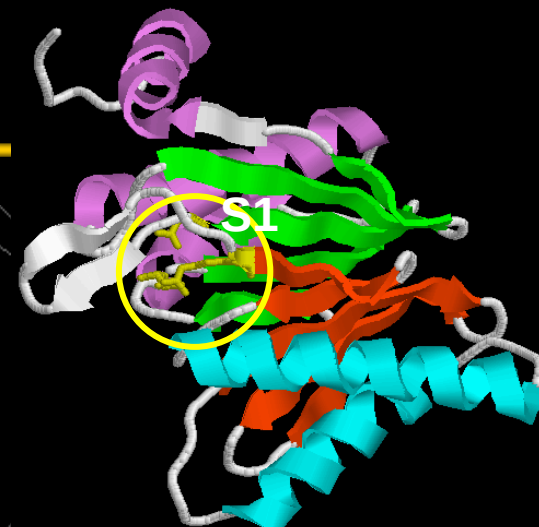


S. cerevisiae : Interaccions



Mecanisme d'acció

T. acidophilum: Tríada catalítica

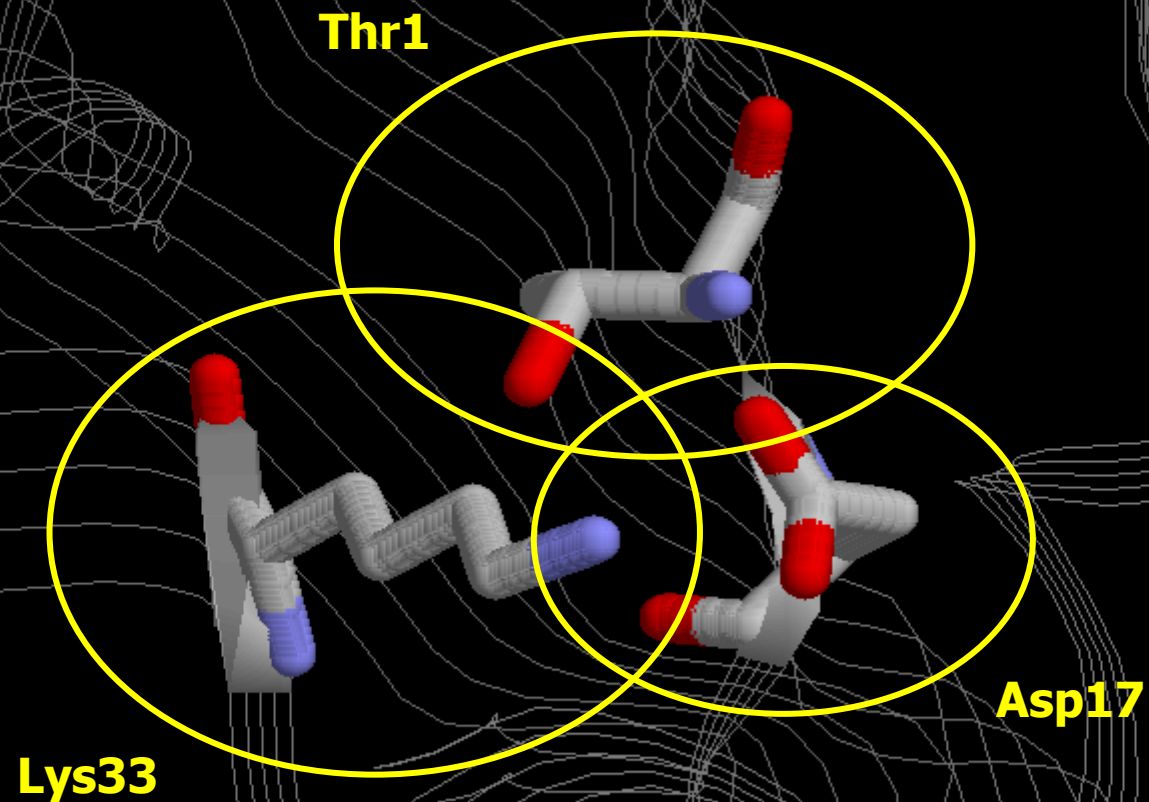
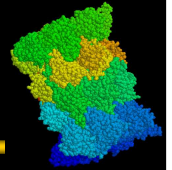


Thr1

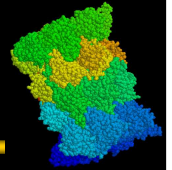
Lys33

Glu17

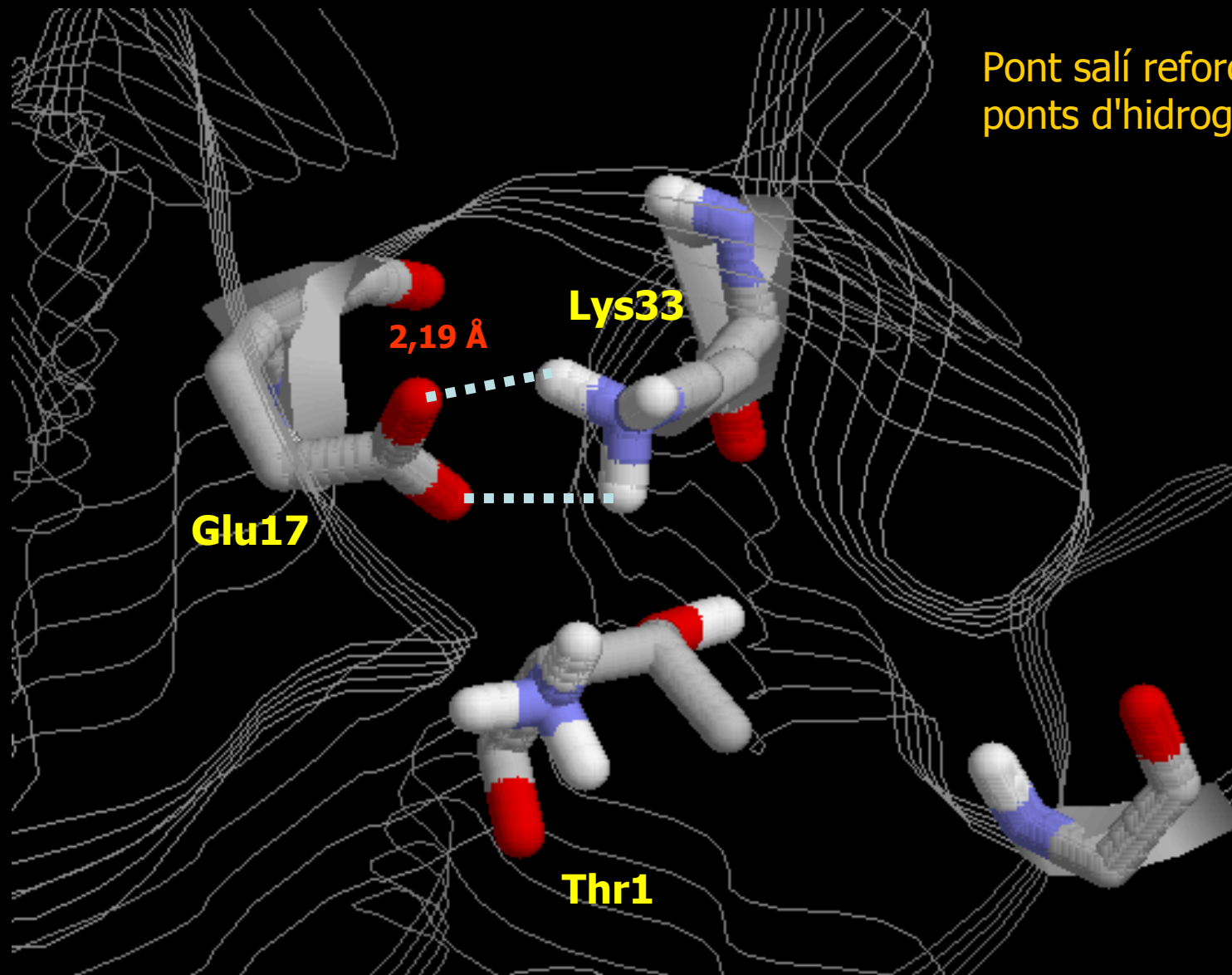
S.cerevisiae: Tríada catalítica



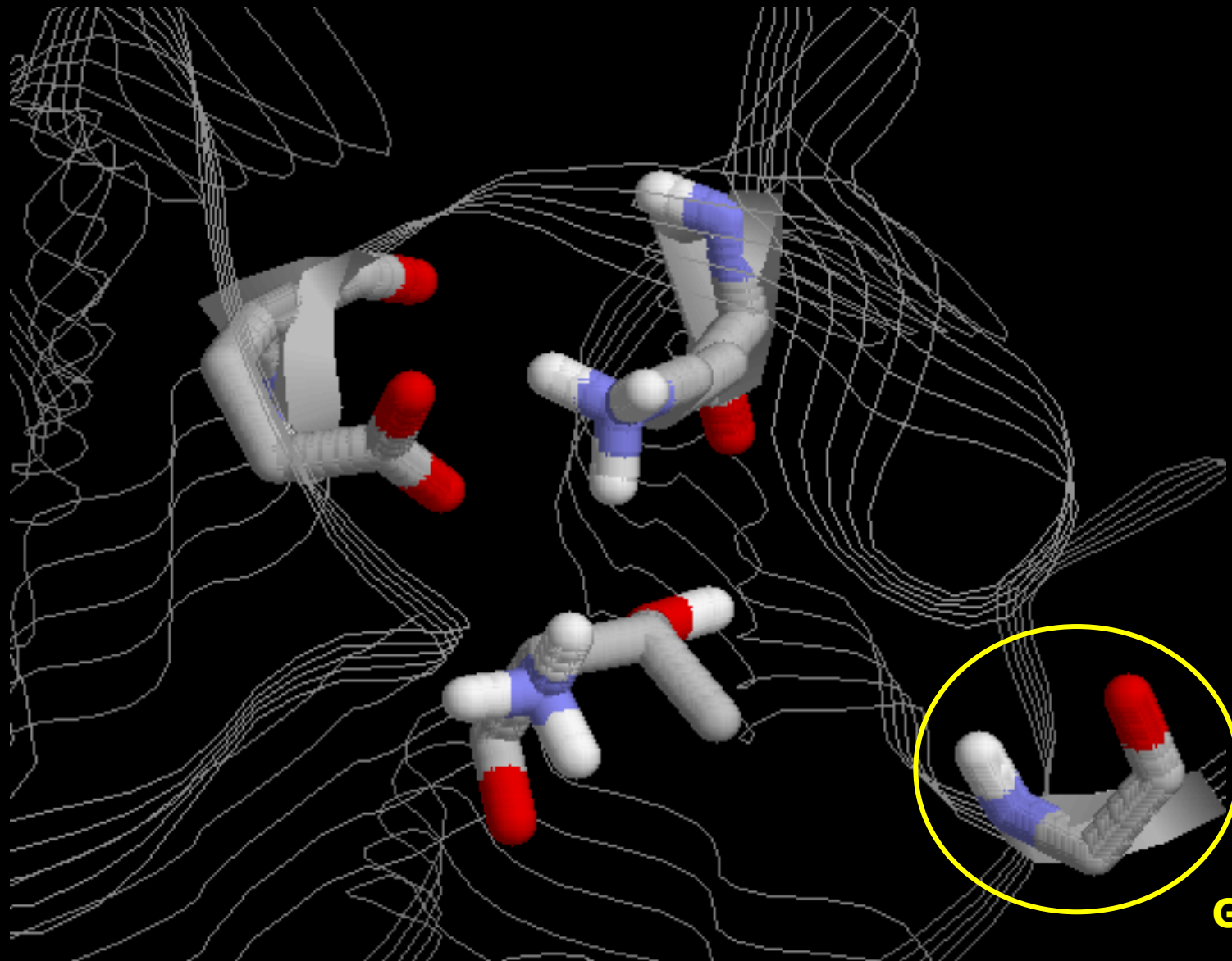
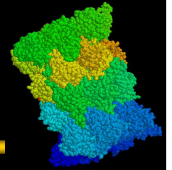
Interacció de la tríada catalítica



Pont salí reforçat per dos ponts d'hidrogen



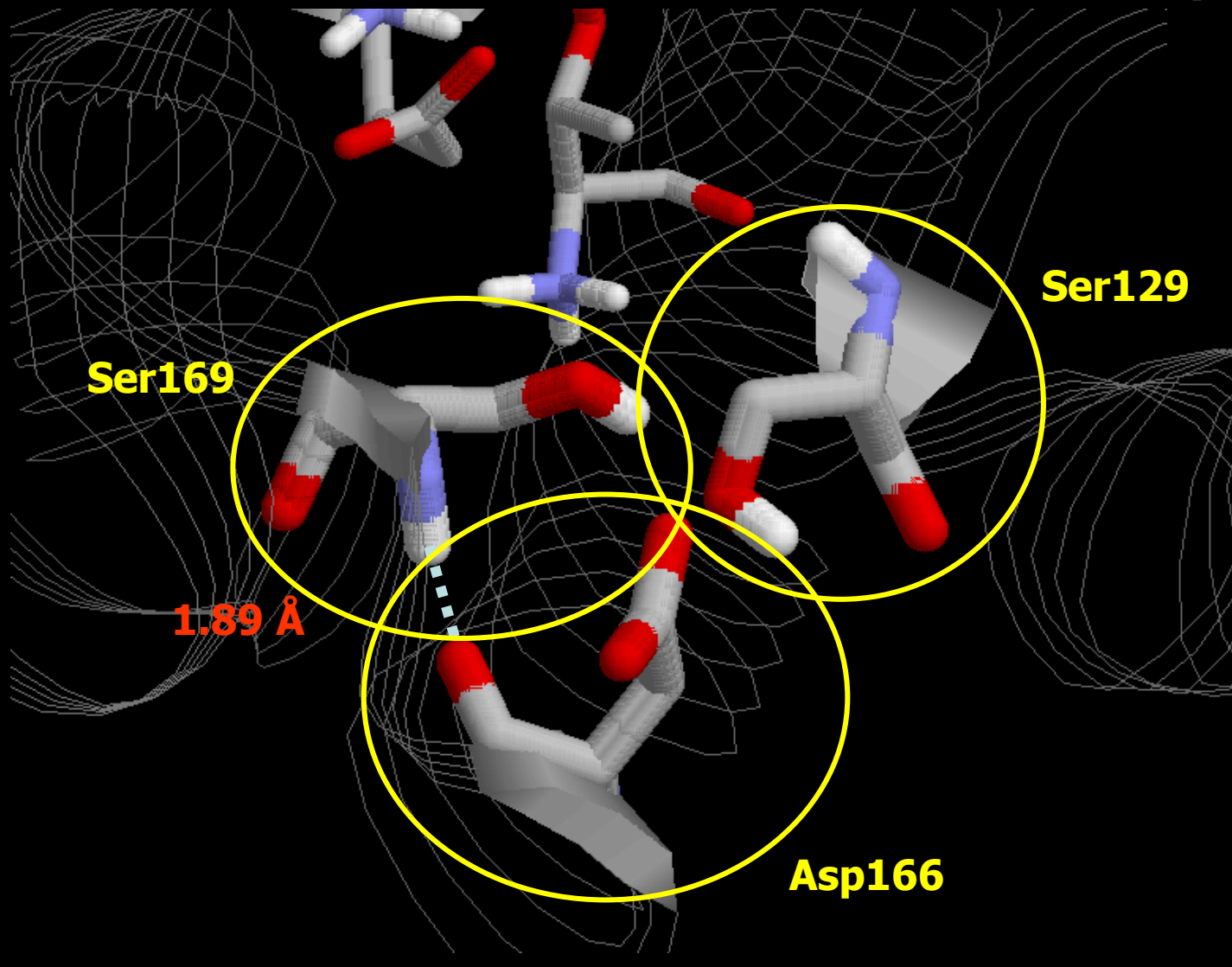
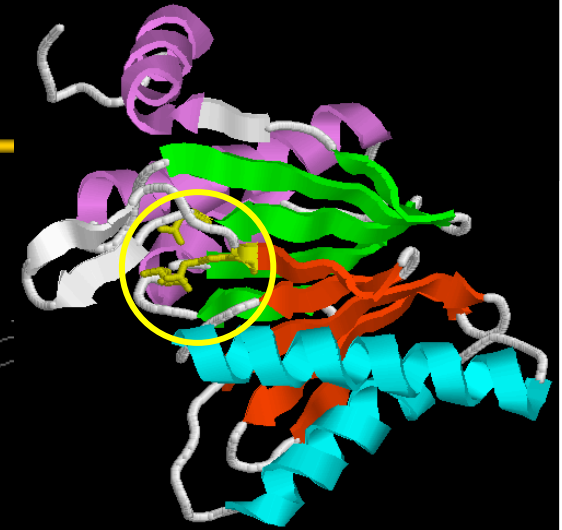
Forat de l'oxianió



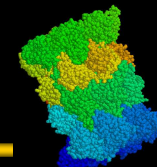
Gly47

Interaccions del centre actiu

Mantenen la integritat estructural del centre actiu



Conservació de residus



CLUSTAL W (1.60) multiple sequence alignment

```

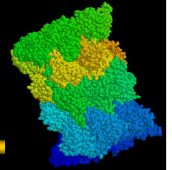
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1gOuN  TSIMAVTFKDGIVLGADSRTTTGAYIANRVTDKLTRVHDKIWCCRS GSAADTQAIADIVQ
1iruH  TTIMAVQFDGGVVLGADSRTTTGSYIANRVTDKLTPIHDRIFCCRS GSAADTQAVADAVT
1iruI  TTIAGVVYKDGIVLGADTRATEGMVVADKNCSKIHFISPNIYCCGAGTAADTDMTTQLIS
1iruL  TTTLAFKFRHGVIVAADSRATAGAYIASQTVKKVIEINPYLLGTMAGGAADCSFWERLLA
1pmaB  TTVGITLKD A VIMATERVTMENFIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
      * .      . . . * * . . . . * . . . .

1gOuH  SNIELHSLYTSREPRVVSALQMLKQHLFKYQGH-IGAYLIVAGVDPT-GSHLFSIHANGS
1gOuK  SQCRHELREKERISVAAASKILSNLVYQYKGAGLSMGTMICGYTRKEGPTIYYVDS DGT
1gOuN  YHLELYTSQYG-TPSTETAASVFKELCYENKDN-LTAGIIVAGYDDKNKGEVYTIPLGGS
1iruH  YQLGFHSIELNEPPLVHTAASLFKEMCYRYRED-LMAGIIIAGWDPQEGGQVYSVPMGGM
1iruI  SNLEHSLSTGR LPRVVTANRMLKQMLFRYRGY-IGAALVLGGVDVT-GPHLYSIYPHGS
1iruL  RQCRIYELRNKERISVAAASKLLANMVYQYKGMGLSMGTMICGWD-KRGPGLYYVDSEGN
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      . . . . . * . . . *

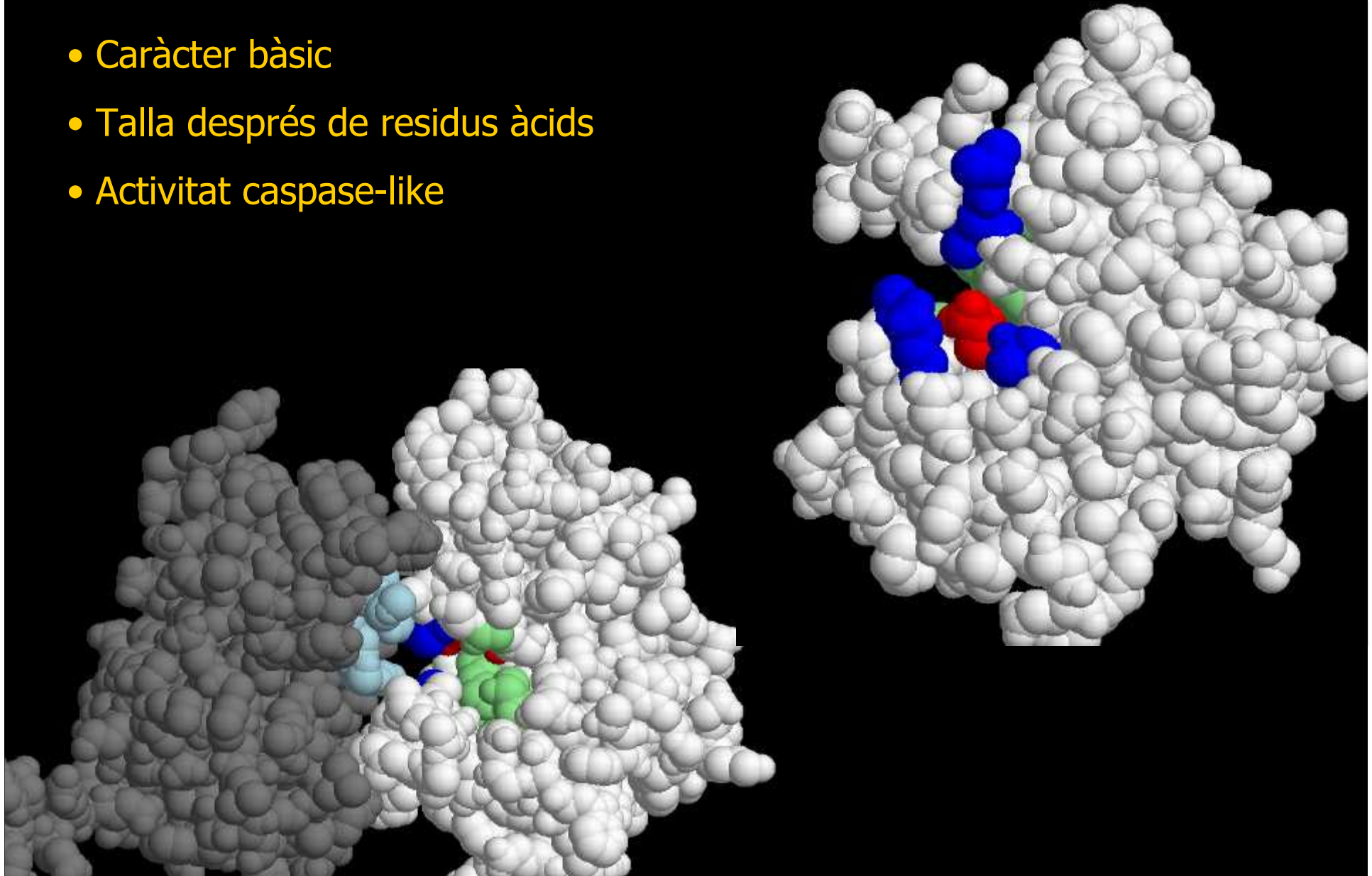
      129      166 169
1gOuH  TDVGYYSLSL GSGSLAAMAVLESHWKQDLTKEEAIKLASDAIQAGIWN DLGSGSNVDVCVM
1gOuK  RLKGDIFCV GSGQTFAYGVLD S NYKWDLSVEDALYLGKRSILAAAHRDAYS GGSVNLYHV
1gOuN  VHKL PYAIA GSGSTFIYGYCDKNFRENMSKEETVDFIKHSLSQA IKWDGSSGGVIRMVVL
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1iruI  TDKLPYVTM GSGSLAAMAVFEDKFRPDMEEEEAKNLVSE AIAAGIFNDLGSGSNIDL CVI
1iruL  RISGATFSV GSGSVYAYGVMDRGYSYDLEVEQAYDLARRAIYQATYRDAYS GGGAVNLYHV
1pmaB  SVEDIYAST GSGSPFVYGVLESQYSEKMTVDEGVDLVIRAI SAAKQRDSASGGMIDVAVI
      *** . . . . * ** . . .

1gOuH  EIGKDAEYLRNYLTPNVREEKQKSYKFPRGTTAVLKESIVNICD
1gOuK  TE---DGWIYHGNH-DVGELFWKVKEEGSFNNVIG-----
1gOuN  TA---AGVERLIFYPDEYEQL-----
1iruH  AE---SGVERQVLLGDQIPKFAVATL-----
1iruI  SK-NKLDFLRPYTPVNKKGTRLGRYRCEKGT TAVLTEKITPLE-
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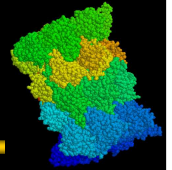
Butxaca $\beta 1$



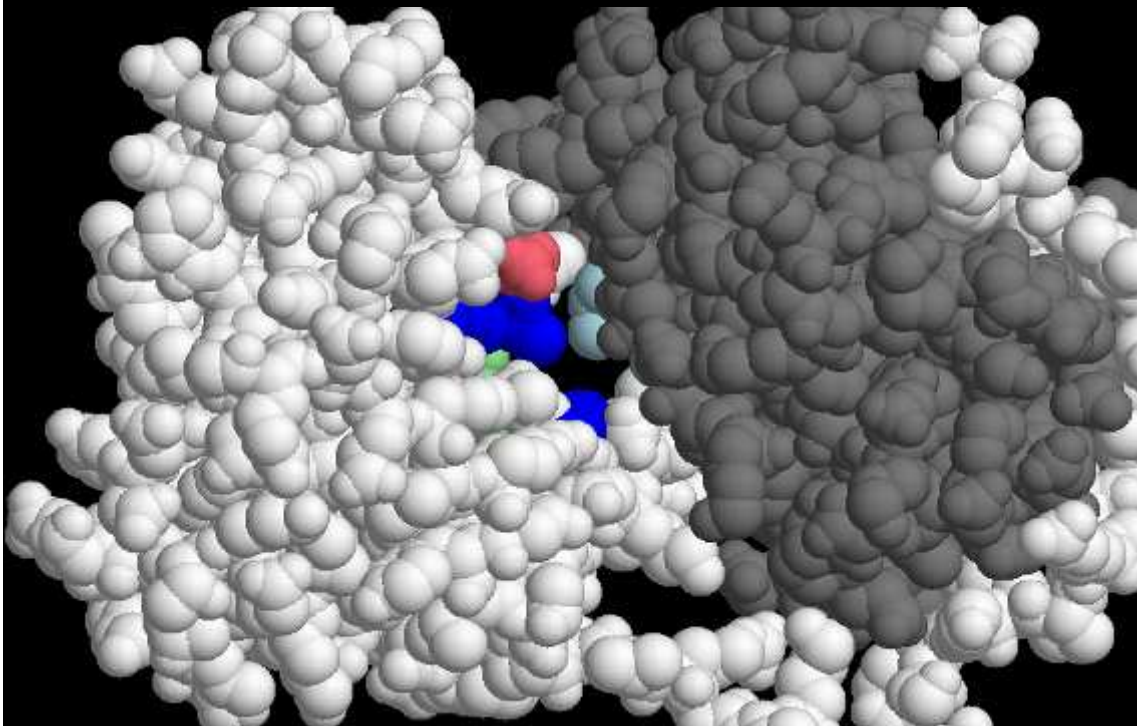
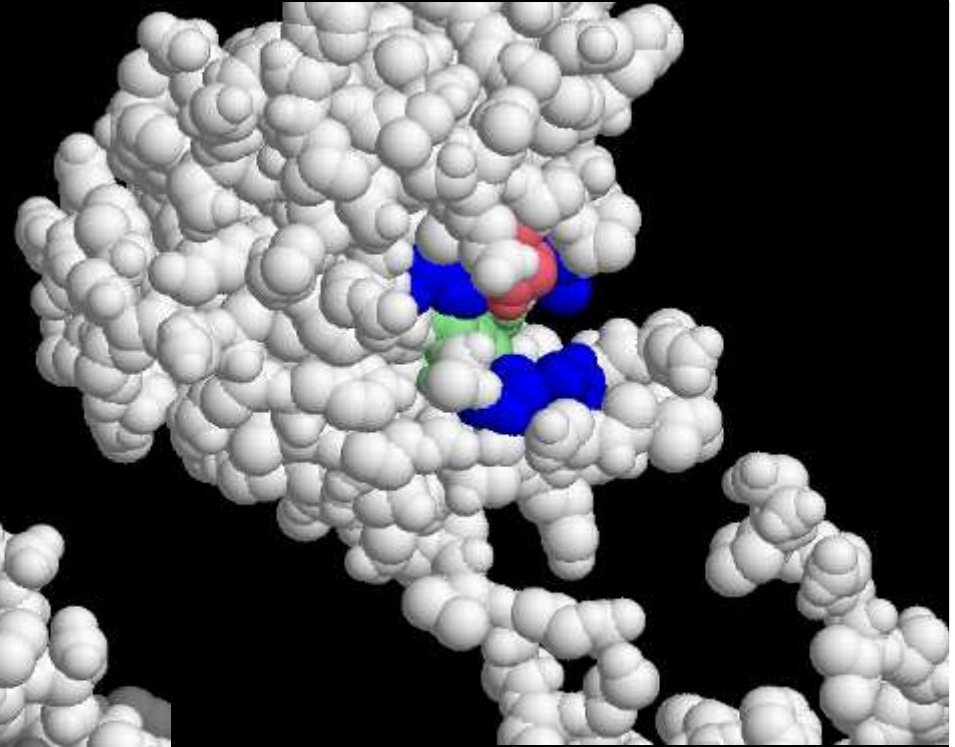
- Caràcter bàsic
- Talla després de residus àcids
- Activitat caspase-like



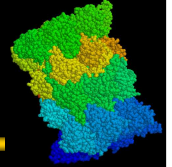
Butxaca $\beta 2$



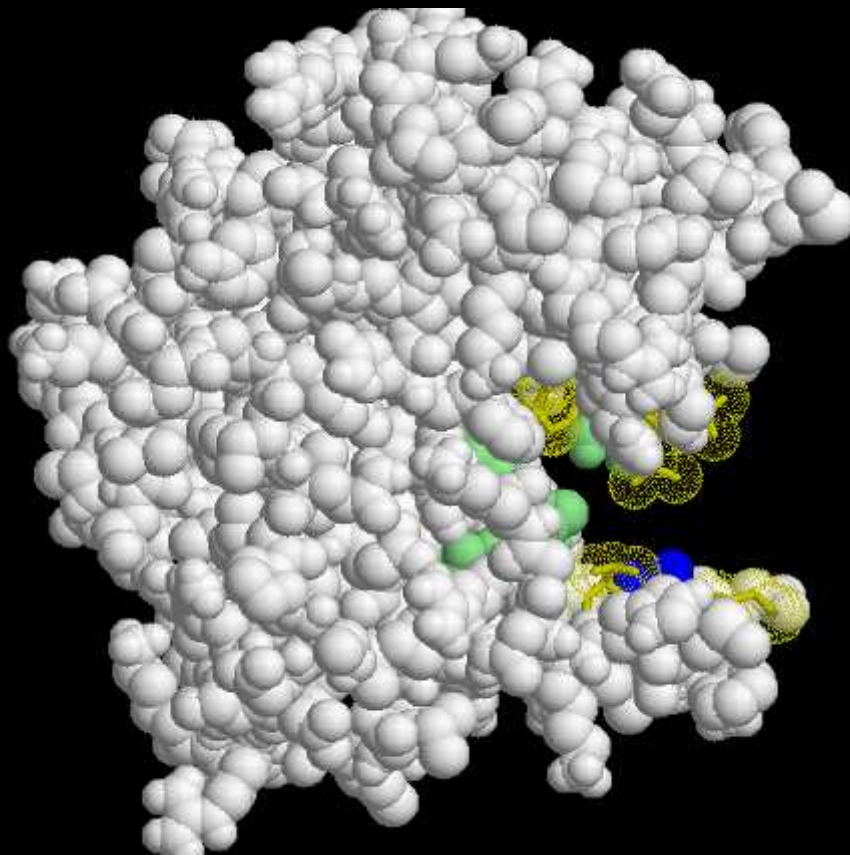
- Caràcter àcid
- Talla després de residus bàsics
- Activitat trypsin-like



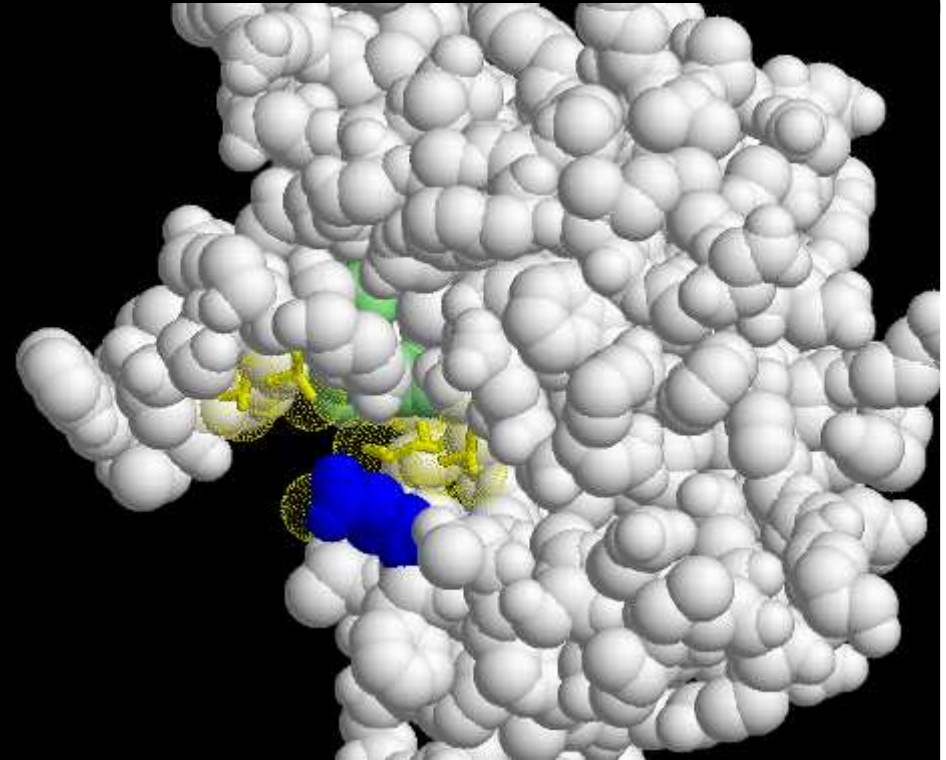
Butxaca $\beta 5$



- Caràcter hidrofòbic
- Talla després de residus hidrofòbics
- Activitat chymotrypsin-like

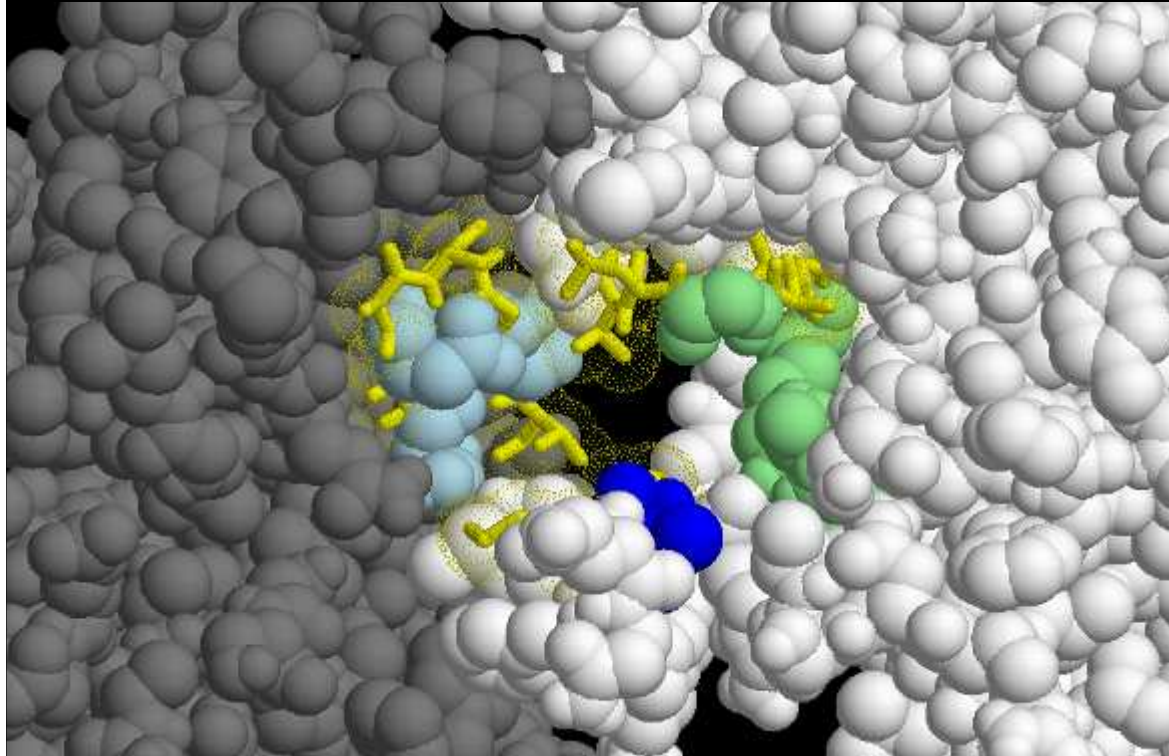
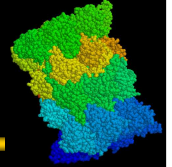


T. acidophilum



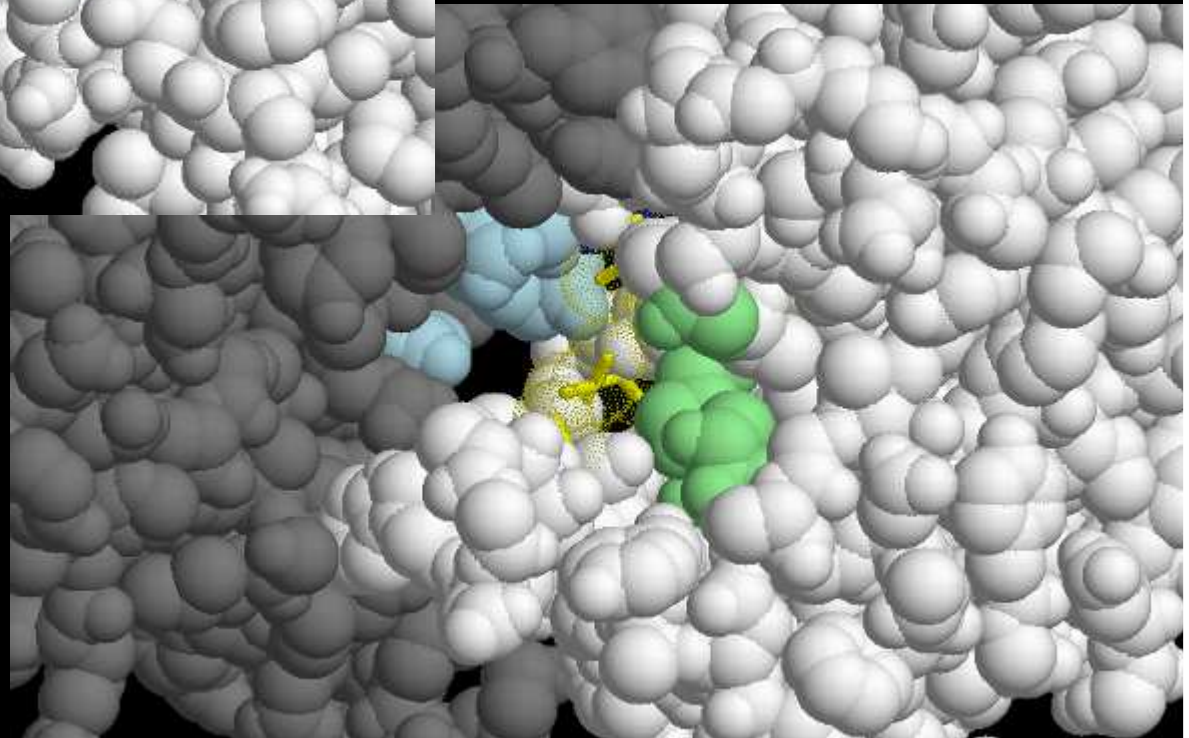
S. cerevisiae

Butxaca $\beta 5$

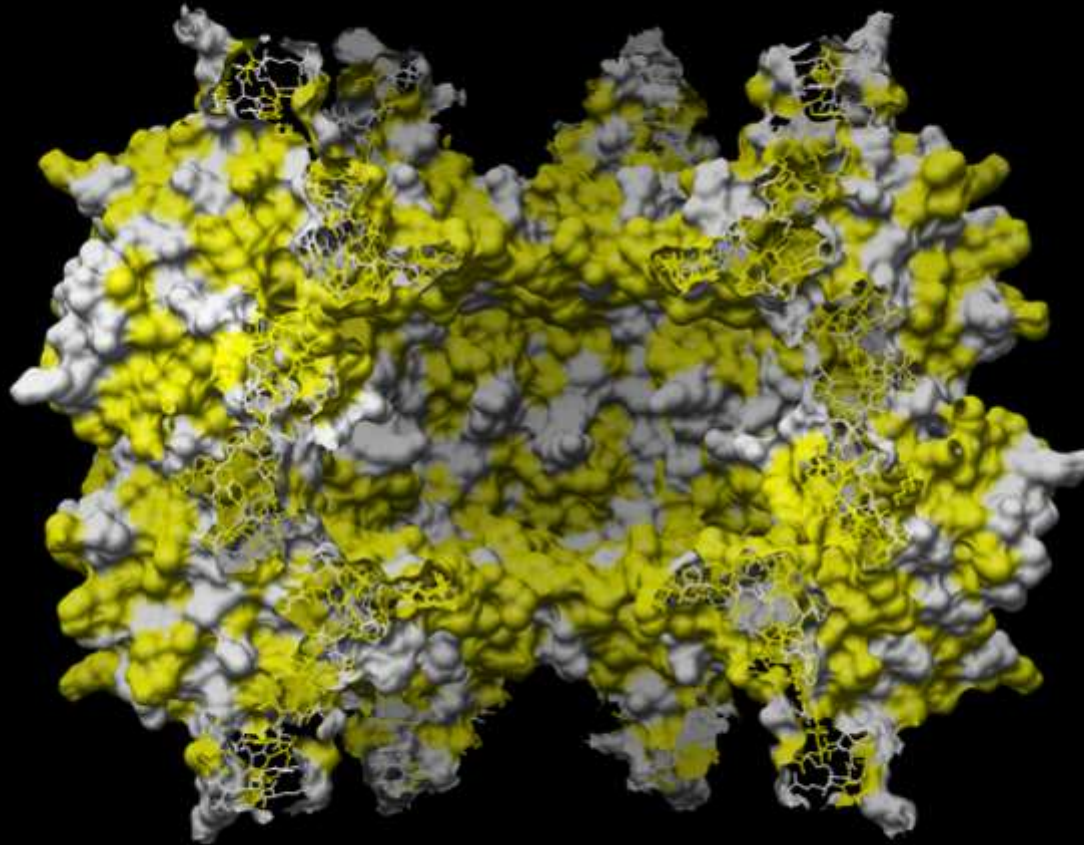
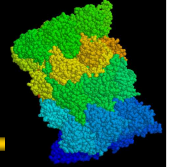


T. acidophilum

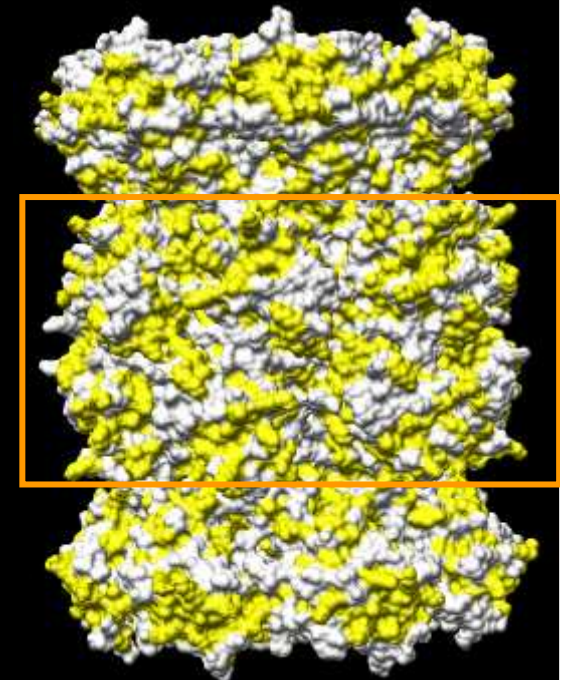
S. cerevisiae



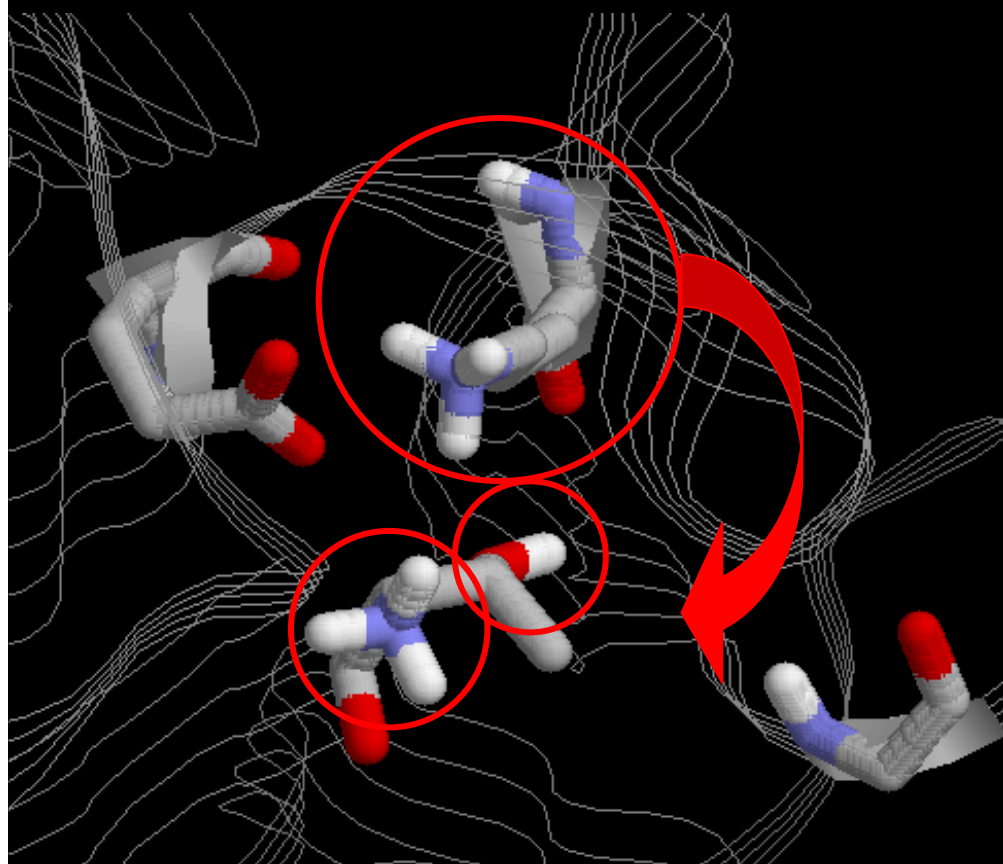
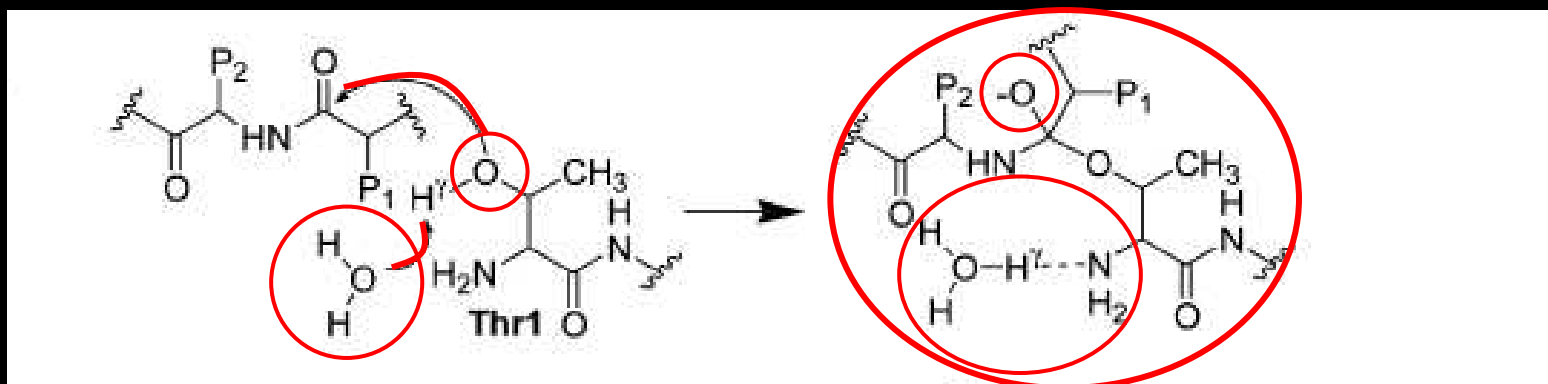
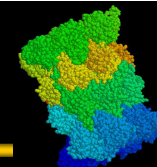
Mecanisme d'acció



Entorn hidrofòbic del nucli del proteosoma
fa que les interaccions electrostàtiques
siguin més fortes.

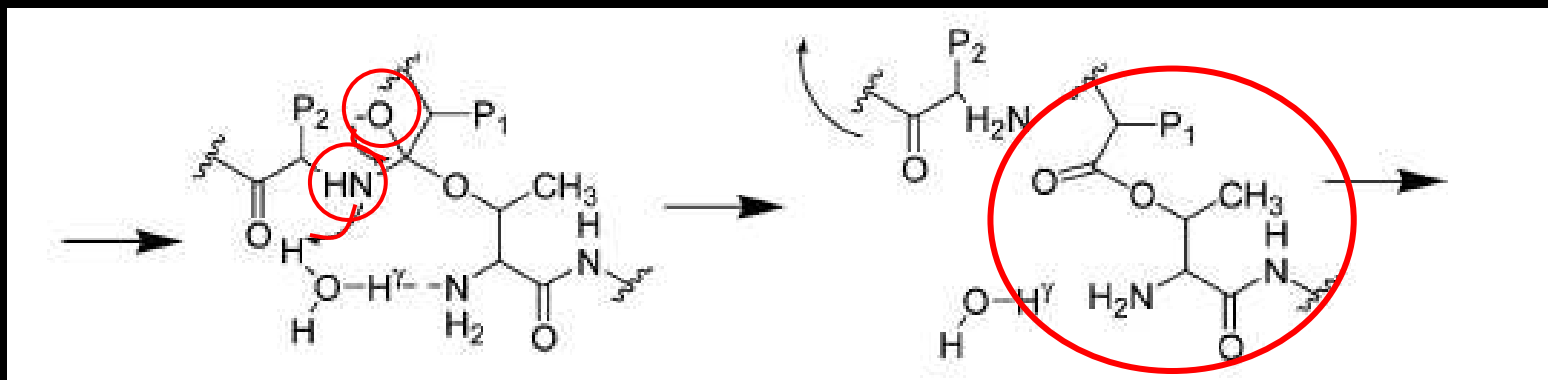
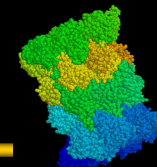


Mecanisme d'acció - Pas 1

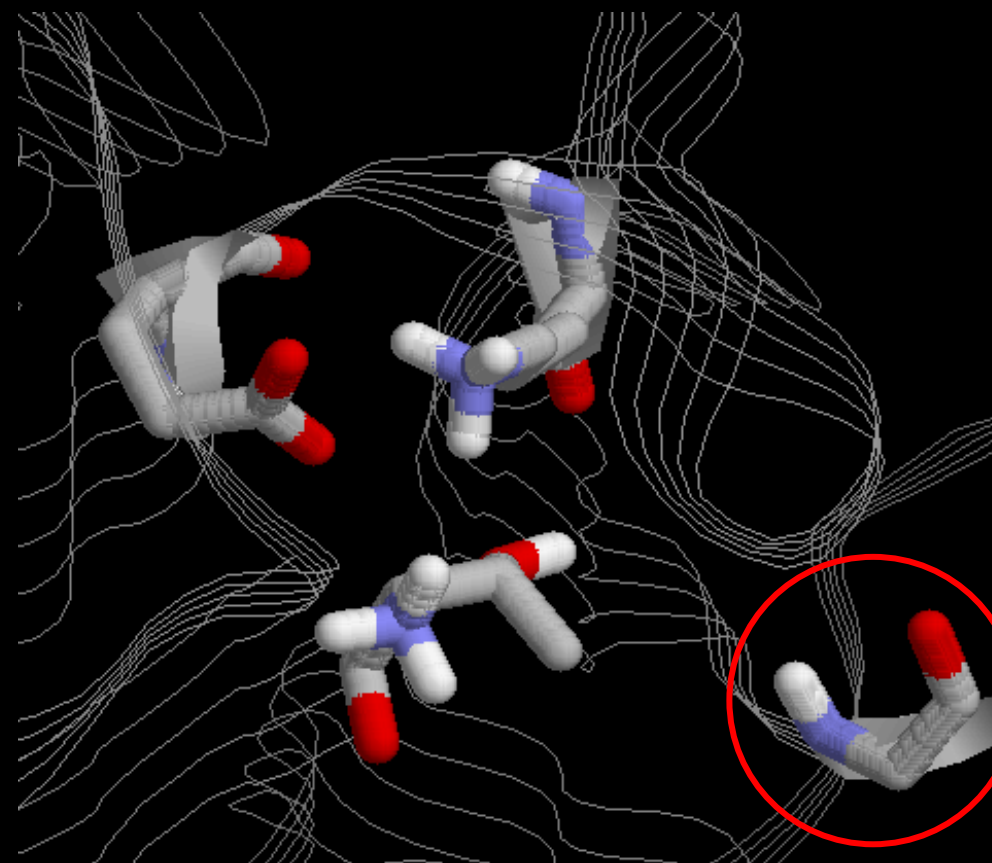


1. La Lys33 potencia la nucleofilitat de la Thr1.
2. L'O de Thr1 ataca nucleofílicament al C carbonil de l'enllaç a trencar.
3. El grup amino N-terminal de la Thr1 accepta el H^+ , directament o mitjançant H_2O .
4. Es forma l'intermediari tetraèdric amb un oxanió.

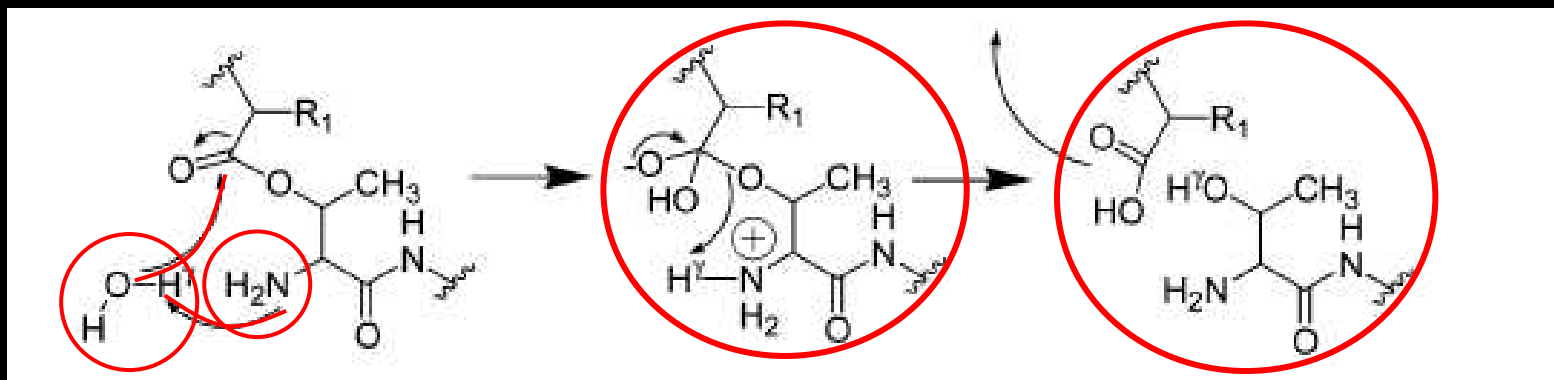
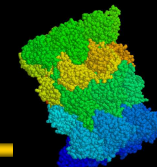
Mecanisme d'acció - Pas 2



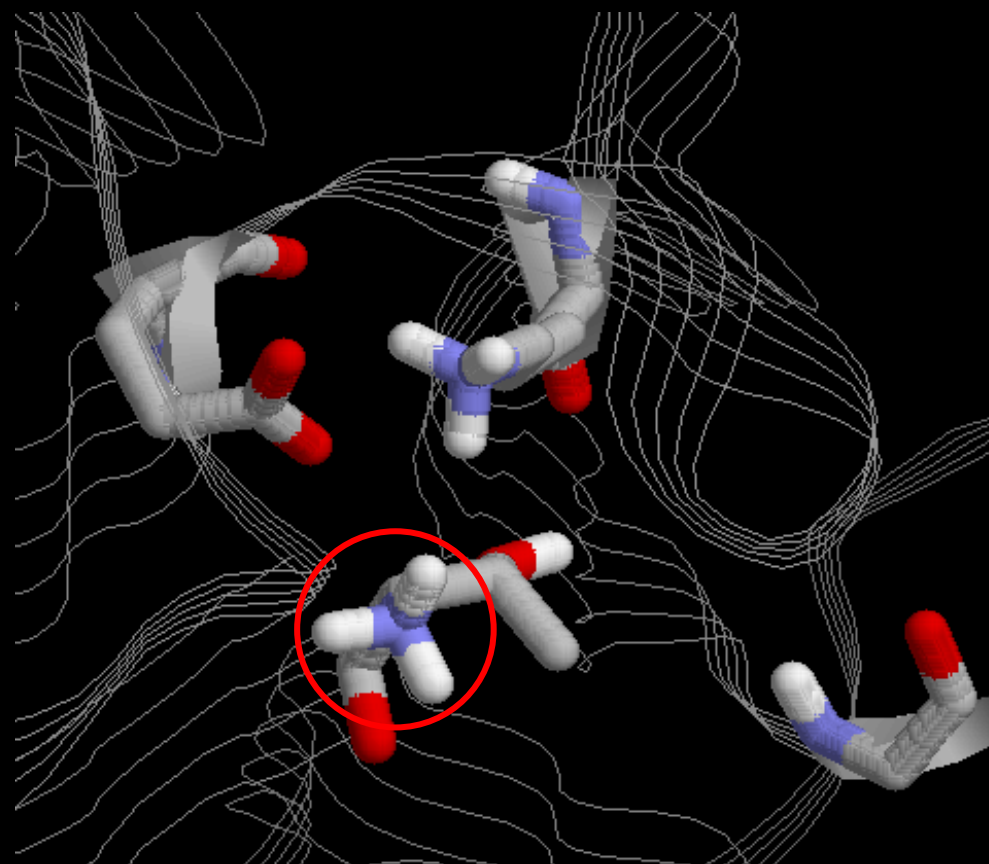
1. Oxianió establitzat per la cadena principal de Gly47 (forat oxianió).
2. Atac del grup amino del pèptid a un H de l'H₂O.
3. L'oxianió ataca al C carbonil.
4. Formació de l'intermediari acil-enzim.



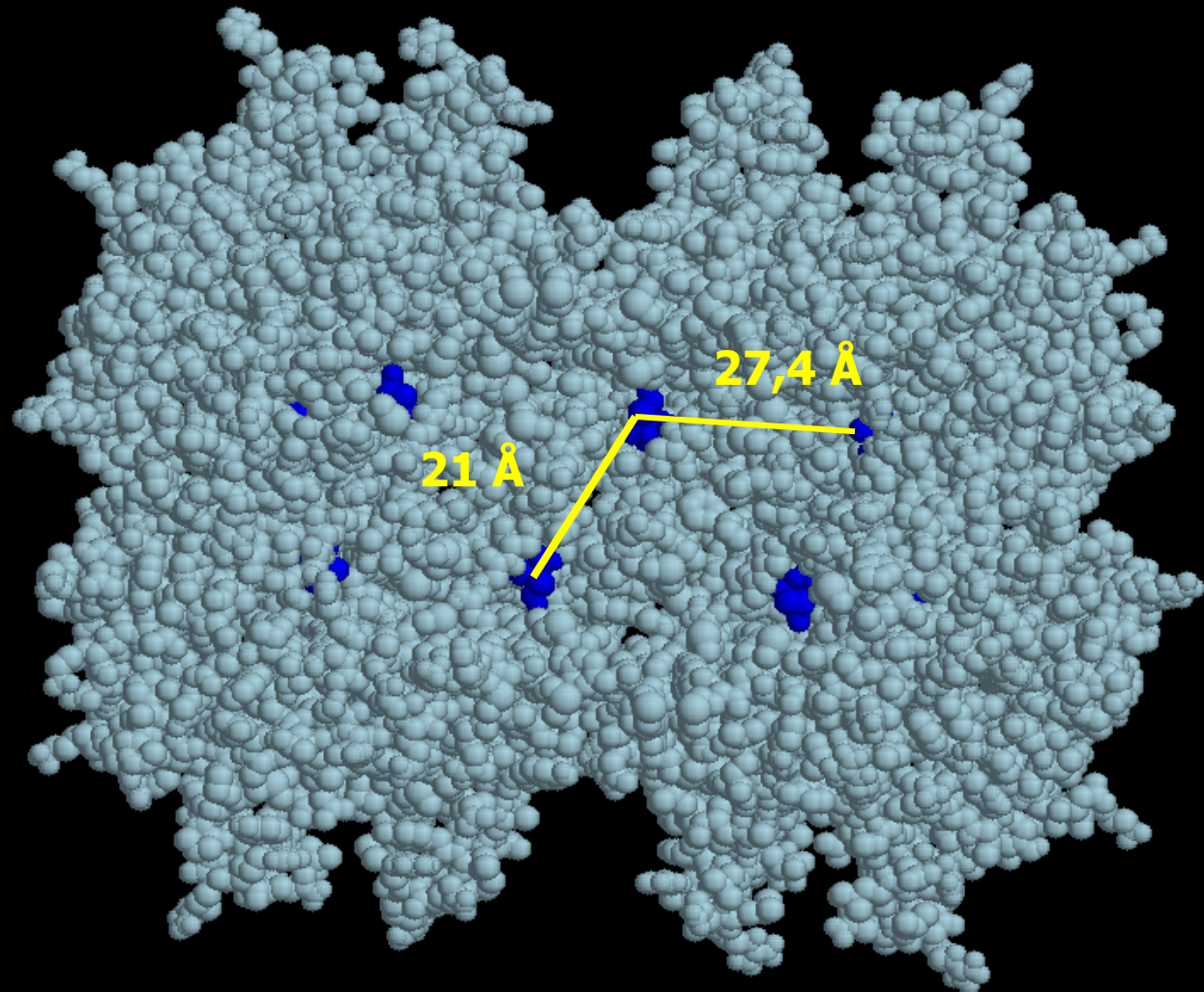
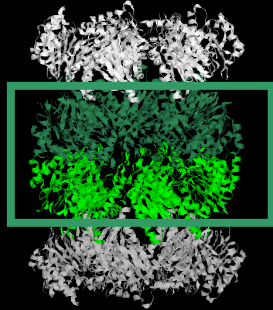
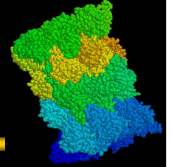
Mecanisme d'acció - Pas 3 i 4



1. La desacilació de l'O de la Thr1 està catalitzada pel N desprotonat de la Thr1.
2. S'afegeix una molècula d'H₂O nucleofílica a l'intermediari acil-enzim.
3. Es reverteix l'intermediari acil-enzim per formar un segon intermediari tetraèdric.
4. Es trenca l'enllaç i s'allibera la Thr1.

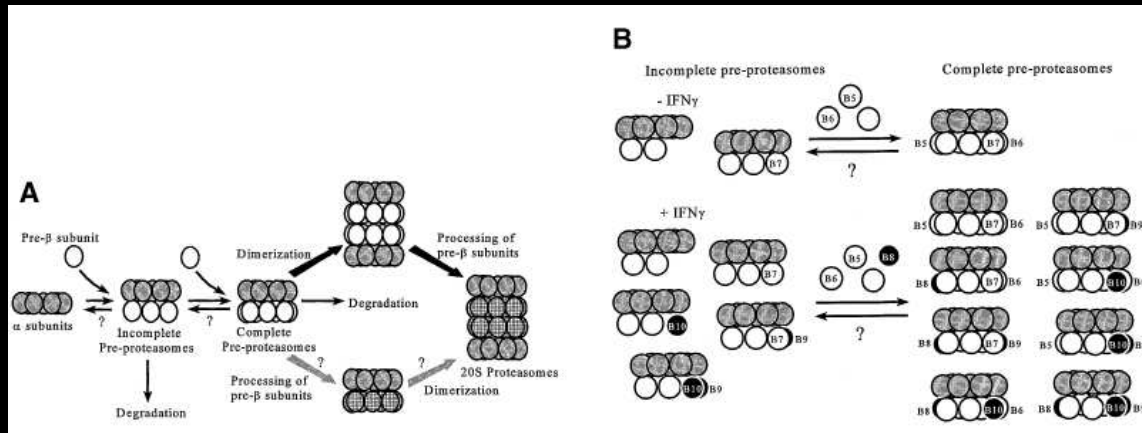


Mecanisme d'acció

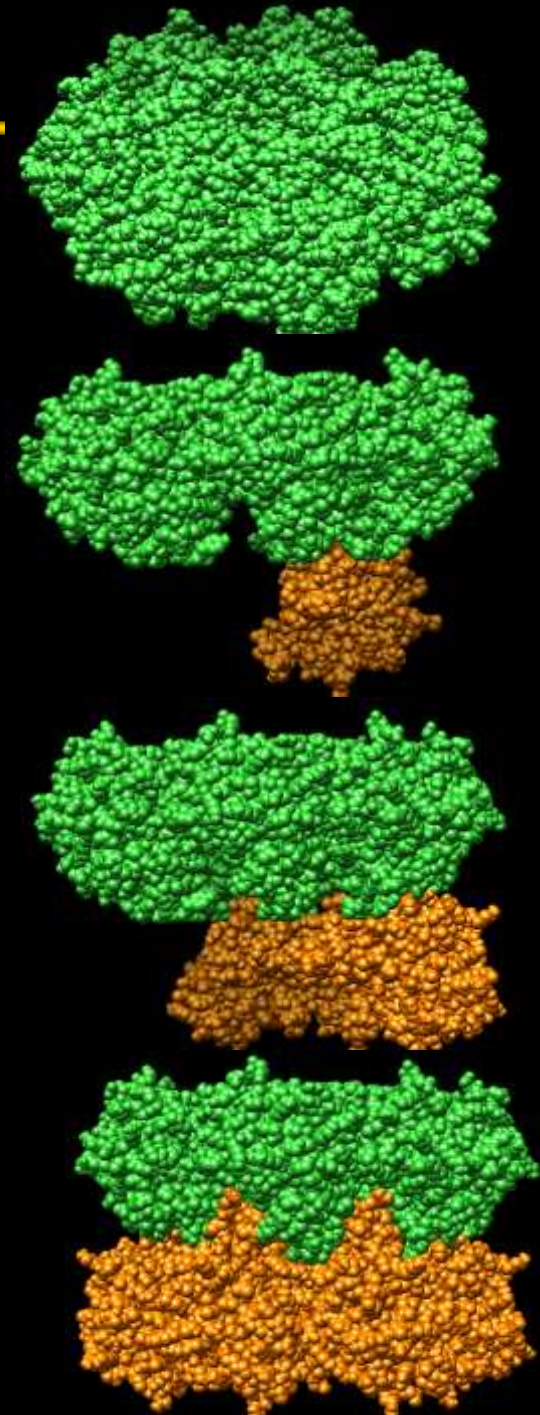


S'alliberen productes peptídics de 8-9 residus, determinat per la distància entre els centres actius de les subunitats veïnes.

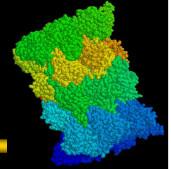
Ensemblatge



- Procés molt complicat que inclou formes precursors.
- Subunitats- β requereixen d'un procés de maduració per eliminar els pro-pèptids N-terminals i exposar la Thr1.
- Les subunitats- α tenen una gran afinitat entre elles.
- La formació de l'anell- α , possibilita la incorporació de les subunitats- β primerenques i en segon lloc les "β-tardanes".



Pro-pèptids i activitat endopeptidasa

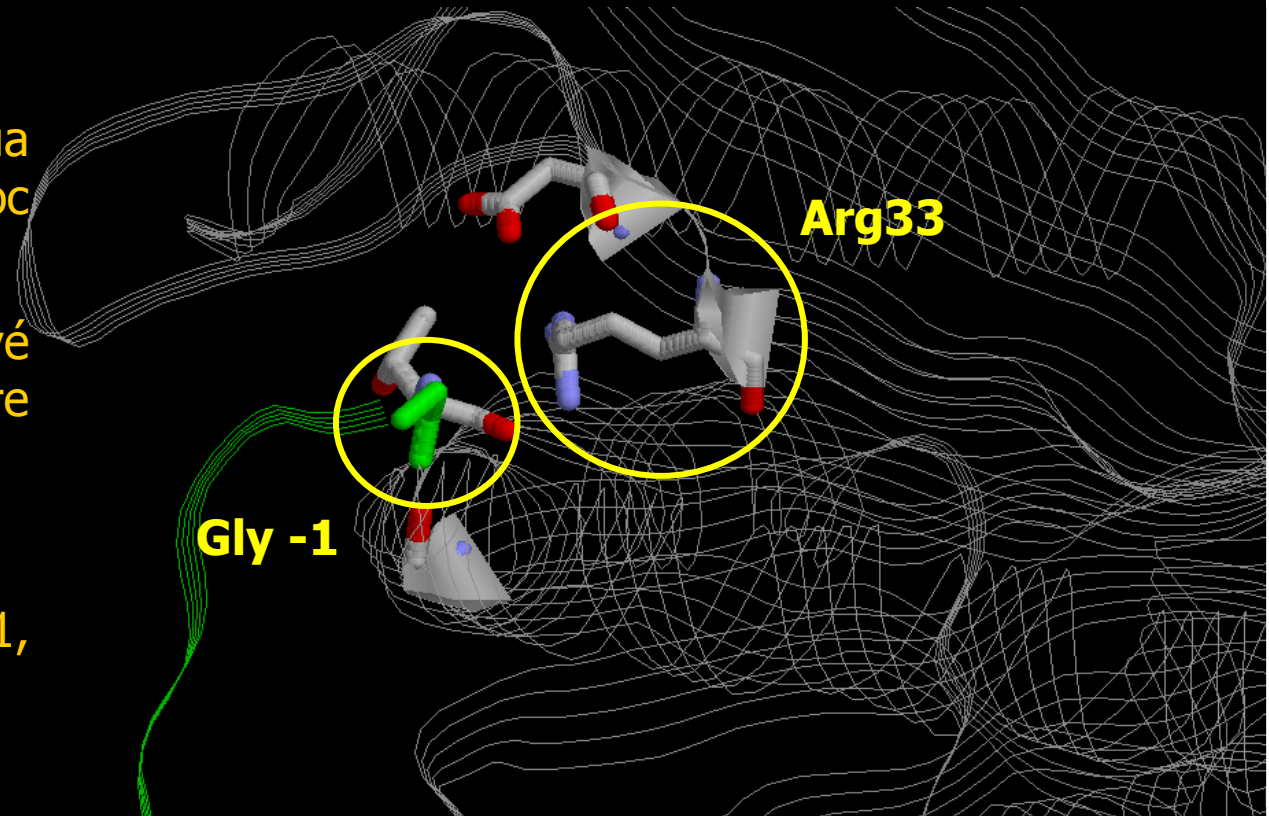


TQQPIVT**GT**SVISMKYDNGVIAA**D**NLGSYGSLRLFNGVER**R**LIPVGDNTVVGIS**G**DISDMQHIERLLKDLVTENAYDNPL
ADAEAEALPSYIFEYLATVMYQRRSKMNPLWNAIIVAGVQSNQDQFLRYVNLLGVTYSSPTLATGFGAHMANPLL RKVVD
RES DIPKTTVQVAEEAIVNAMRVLYYRDARSSRNFS LAIDKNTGLTFKKNLQVENMKWDFAKDIKGYGTQKI

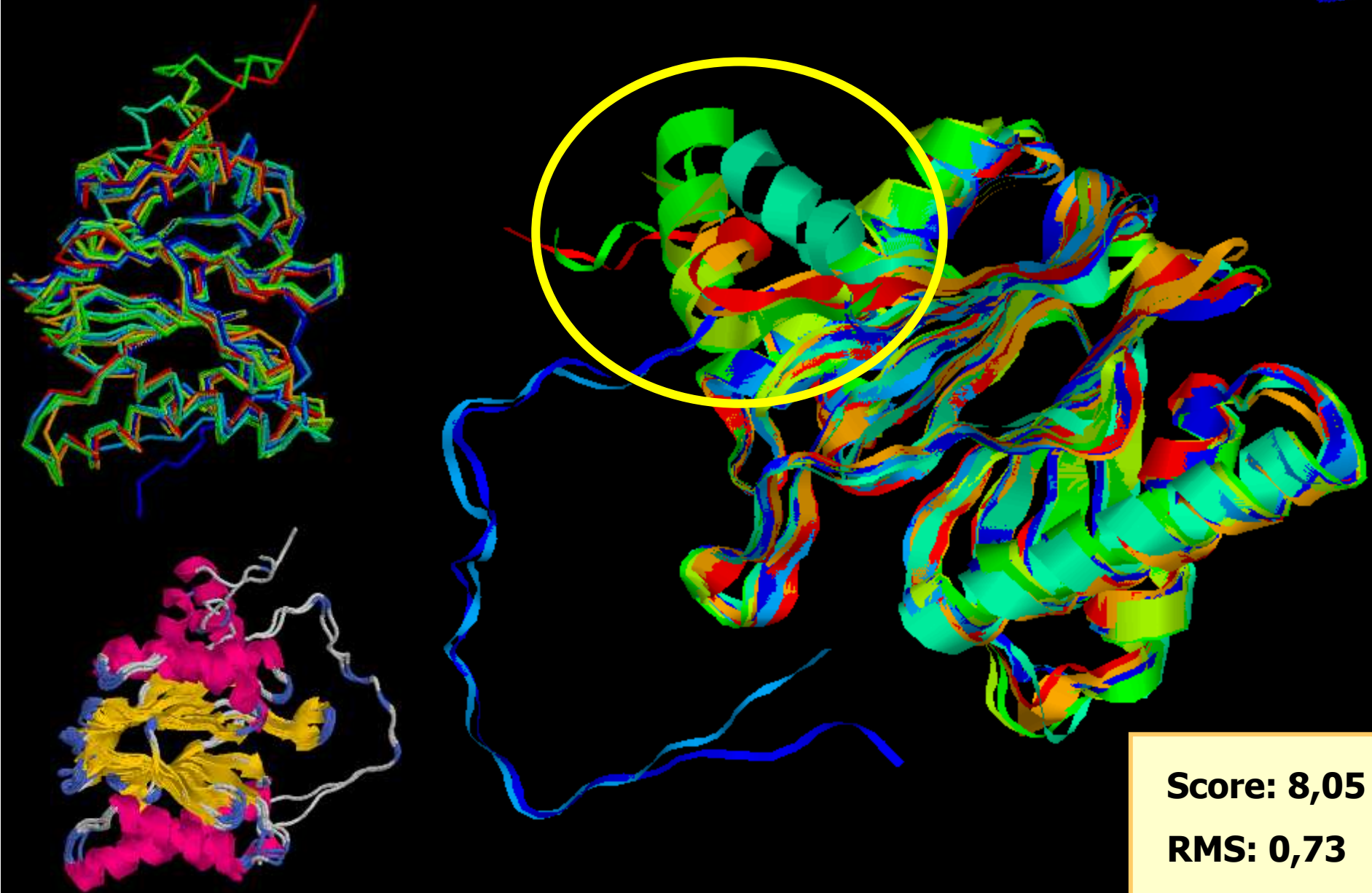
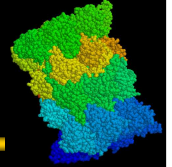


Autòlisi

- Una H_2O catalítica actua com acceptora de H^+ , enlloc de Thr1 N.
- Aquesta H_2O també intervé com un pont pel H^+ entre Thr1 O i Thr1 N.
- La Gly -1 és essencial.
- Amb l'alliberació de la Thr1, la subunitat es torna activa.



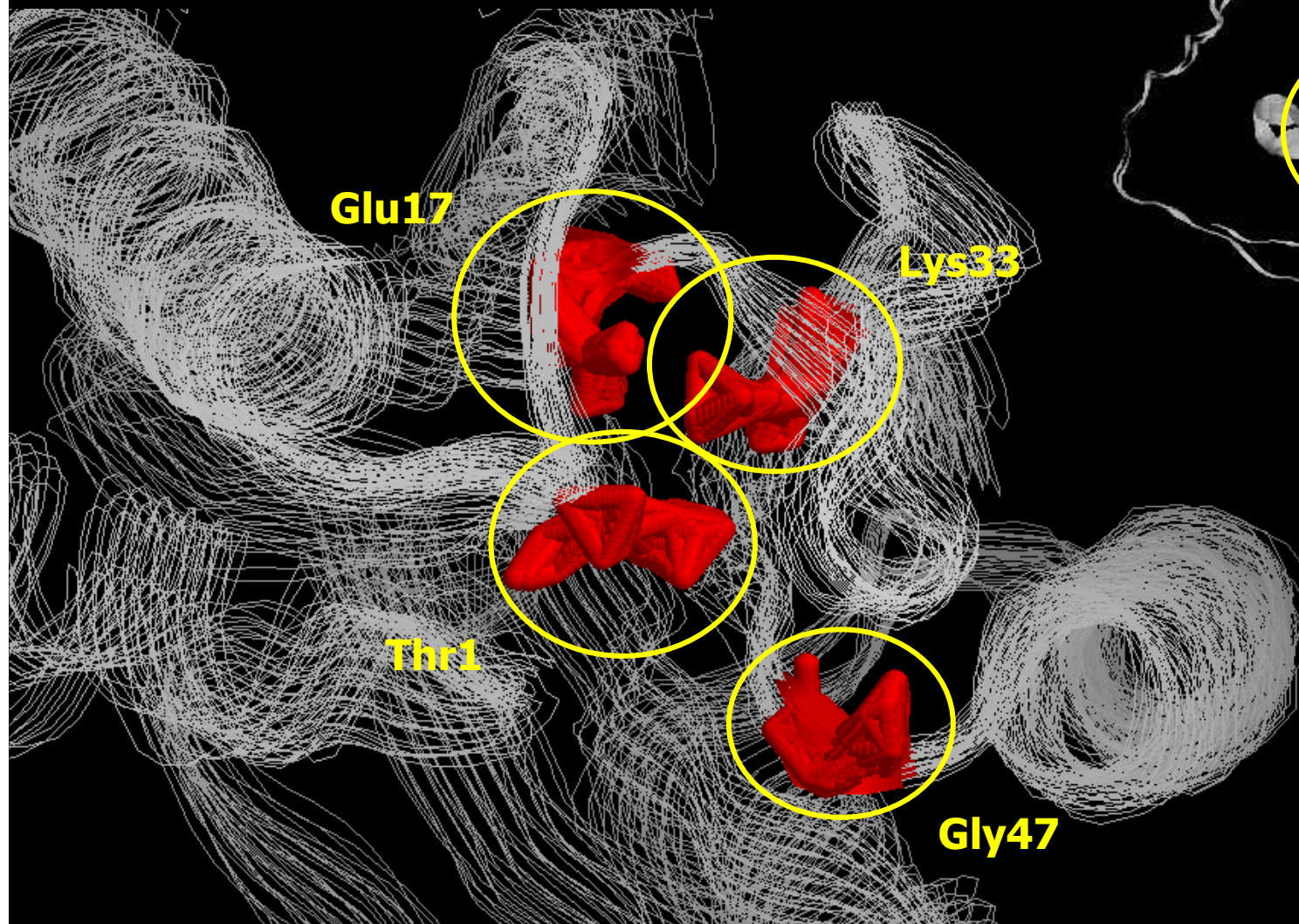
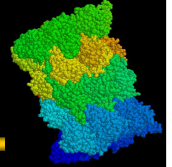
Conservació estructural



Score: 8,05

RMS: 0,73

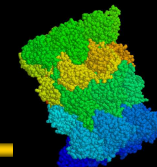
Conservació estructural



Score: 8,05

RMS: 0,73

Conservació estructural



Alineament estructural

CLUSTAL W (1.60) multiple sequence alignment

```

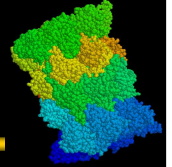
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1iruI  TTIAGVVYKDGIVLGADTRATEGMVVADKNCSKIHFISPNIYCCGAGTAADTDMTTQLIS
1pmaB  TTTVGITLKDAVIMATERRVTMENFIMHKNGKKLFQIDTYTGMTIAGLVGDAQVLVRYMK
1GOUK  TTTLAFRFQGGIIVAVDSRATAGNWWASQTVKKVIEINPFLLGTMAGGAADCQFWETWLG
1iruL  TTTLAFKFRHGVIVAADSRTAGAYIASQTVKKVIEINPYLLGTMAGGAADCSFWERLLA
1GOUN  TSIMAVTFKDGVLGADSRTTTGAYIANRVTDKLTRVHDKIWCCRSRSAADTQAIADIVQ
1iruH  TTIMAVQFDGGVVLGADSRTTTGSYIANRVTDKLTPIHDRIFCCRSRSAADTQAVADAVT

1GOUH  SNIELHSLYTSREPRVVSALQMLKQHLFKYQ-GHIGAYLIVAGVD-PTGSHLFSIHAGS
1iruI  SNLELHSLSTGRLPRVVTANRMLKQMLFRYR-GYIGAALVLGGVD-VTGPHLYSIYPHGS
1pmaB  AELELYRLQRRVNMPIEAVATLLSNMLNQVKYMPYMVQLLVGGI-D-TAPHVFSIDAAGG
1GOUK  SQCRLHELREKERISVAAAASKILSNLVYQYKAGLSMGTMICGYTRKEGPTIYYVDSGDT
1iruL  RQCRIYELRNKERISVAAAASKLLANMVYQYKGMGLSMGTMICGW-DKRGPGLYYVDSEGN
1GOUN  YHLELYTSQY-GTPSTETAASVFKELCYENKD-NLTAGIIVAGYDDKNKGEVYTIPLGGS
1iruH  YQLGFHSIELNEPPLVHTAASLFKEMCYRYRE-DLMAGIIAGWDPQEGGQVYSVPMGGM

      129          166 169
1GOUH  TDVGYYSLSGSGSLAAMAVLESHWKQDLTKEEAIKLASDAIQAGIWNDLGSGSNVDVCVM
1iruI  TDKLPYVTMGSGSLAAMAVFEDKFRPDMEEEEAKNLVSEAIAGIFNDLGSNSNIDLCVI
1pmaB  SVEDIYASTGSGSPFVYGVLESQYSEKMTVDEGVDLVIRAIISAAKQRDSASGGMIDVAVI
1GOUK  RLKGDIFCVGSGQTFAYGVLDSDNYKWDLSVEDALYLGKRSILAAAHRDAYSGGSVNLYHV
1iruL  RISGATFSVGSQSVYAYGVMDRGYSYDLEVEQAYDLARRAIYQATYRDAYSGGAVNLYHV
1GOUN  VHKLPPYAIAGSGSTFIYGYCDKNFRENMSKEETVDFIKHLSQAIAKWDGSSGGVIRMVVL
1iruH  MVRQSFAIGSGSSYIYGYVDATYREGMTKEECLOFTANALALAMERDGSAGGVIRLAAI

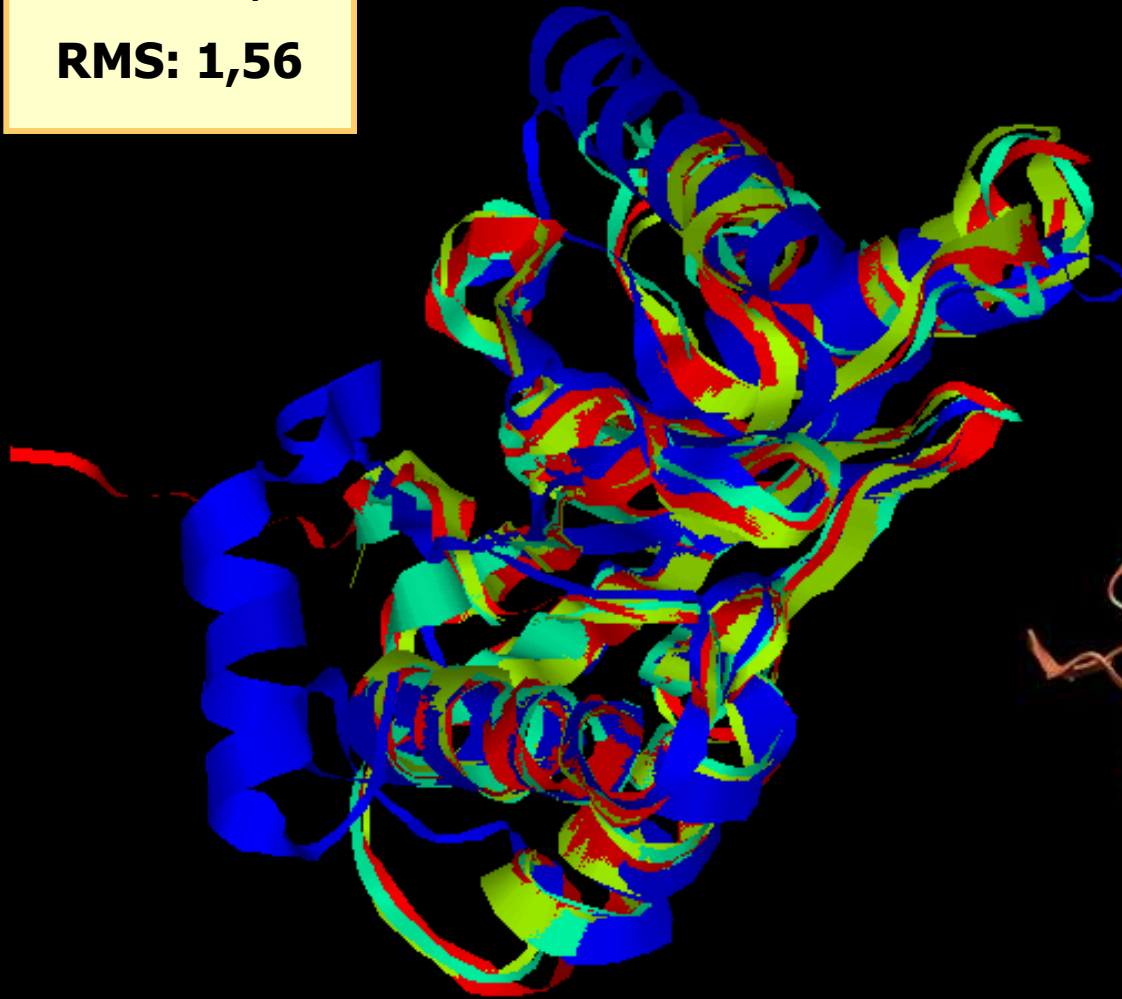
1GOUH  EI-GKDAE-YLR-NYLTP-----NVREEKQKSYKFRGTTAVLKESIVNI
1iruI  S--KNKLD-FLR-PYTV-----NKKGTRLGRYRCEKGTAVLTEKITPL
1pmaB  -TRKDGIVQL-PTDQI--ESR-IRKL-----GLIL-----
1GOUK  -TE-DGWIYH-G--NHDVGE-LFWKVKEEGSFNNVIG-----
1iruL  -RE-DGWIRV-S--SDNVAD-LHEKYS-----
1GOUN  -TA-AGVER--L--IFY-PDEY--EQ-----L-----
1iruH  -AE-SGVER--Q--VLL-GDQI--PK-----FAVATL-----
```

Homologia amb HslV



Score: 7,60

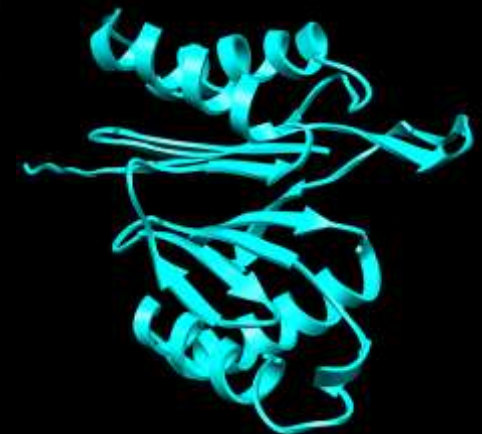
RMS: 1,56



- Homòleg del proteosoma a alguns procariotes.
- No forma proteosomes 20S.
- És un homodecàmer amb un nucli proteolític.
- Comparteix plegament i mecanisme catalític.

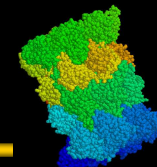


1e94.pdb



1ned.pdb

Homologia amb HslV



Alineament estructural

CLUSTAL W (1.60) multiple sequence alignment

```

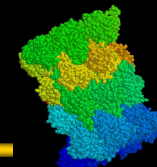
      1              17              33              47
1pma  TTTVGITLKD A VIMATERRVTMENFIMHKNGKKLFQI-DTYTGMTIAGLVGDAQVLVR-Y
1ga4  TTIVSVRRNGHVVIAGDGGQATLGNTVMKGNVKKVRRLYNDKVIAGFAGGTADAFTLFLFELF
1e94  TTIVSVRRNGHVVIAGDGGQATLGNTVMKGNVKKVRRLYNDKVIAGFAGGTADAFTLFLFEL-
1ned  TTIVSVRRNGHVVIAGDGGQATLGNTVMKGNVKKVRRLYNDKVIAGFAGGTADAFTLFLFEL-

1pma  MKAELELYRLQRRVNMPI-EAVATLLSNMLNQVKY---MPYMVQLLVGGIDTAPHVFSID
1ga4  ER-KL-E-----M-HQGHLVKAAVELAKDWRT--DRMLRKLEALLAVAD--E-TASLIIT
1e94  FERKLEM-----H-QGHLV-KAAVELAKDWRT-DRML-RKLEALLAVAD--E-TASLIIT
1ned  FERKLEM-----H-QGHLV-KAAVELAKDWRT-DRML-RKLEALLAVAD--E-TASLIIT

      129              166 169
1pma  AAGGSVE-D-IYASTGSGSPFVYGVLESQ--YSEKMTVDEGVDLVIRAI SAAKQRDSASG
1ga4  GNGDVVQPENDLIAIGSGGPYAQAAARALLEN-TE---LSAREIAEKALDIAGDICIYTN
1e94  GNGDVVQPENDLIAIGSGGPYAQAAARALLEN-TE---LSAREIAEKALDIAGDICIYTN
1ned  GNGDVVQPENDLIAIGSGGPYAQAAARALLEN-TE---LSAREIAEKALDIAGDICIYTN

1pma  GMIDVAVITRKDGYVQLPTDQIESRIRKLGIL
1ga4  HFHTIEELSY-----
1e94  HFHTIEELSYK-----
1ned  HFHTIEELSYKAEFHHH-----
```

Homologia amb HslV



CLUSTAL W(1.60) multiple sequence alignment

```

1          17          33          47
1e94A      TTIVSVRRNGHVVIAGDGGQATLGNTVMKGNVKKVRRRLYNDKVIAGFAGGTAD-AF--TLF
1gOuK      TTTLAFRFQGGIIVAVDSRATAGNWVASQTVKKVIEI-NPFLLGTMAGGAADCQFWETWL
1nedA      TTIVSVRRNGHVVIAGDGGQATLGNTVMKGNVKKVRRRLYNDKVIAGFAGGTAD-AF--TLF
1pmaB      TTTVGITLKDAVIMATERRTMENFIMHKNGKKLFQI-DTYTGMTIAGLVGDAQVLVRYM
1g4aB      TTIVSVRRNGHVVIAGDGGQATLGNTVMKGNVKKVRRRLYNDKVIAGFAGGTAD-AF--TLF
          ** .          ...* . . * * . . ** .          ** *

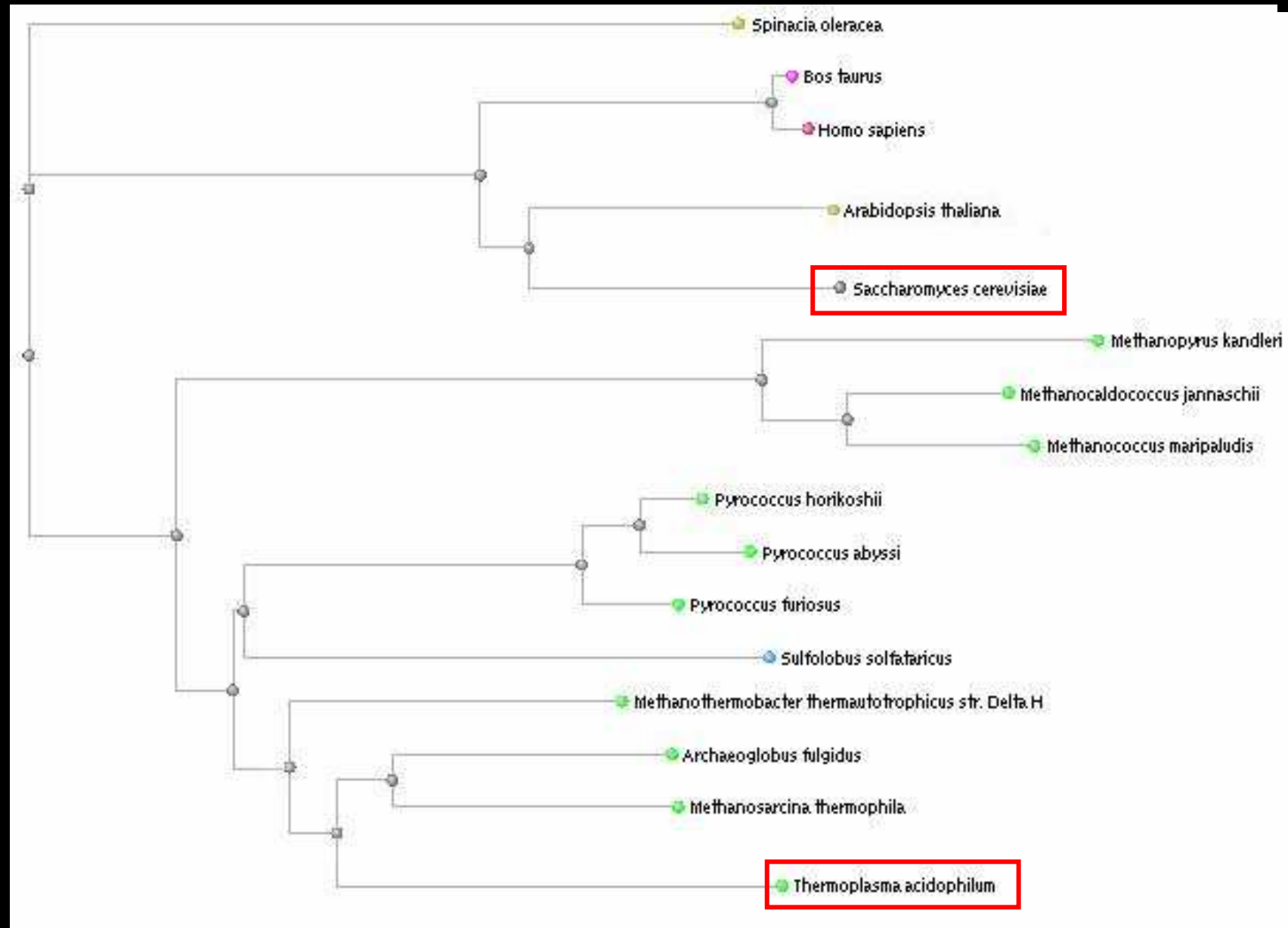
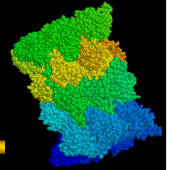
1e94A      ELFERKLEMHQGH--LVKAAVELAKDWRTDRMLRKLEALLAVADETAS---LIITGNGDV
1gOuK      GSQCRLHELREKERISVAAAASKILSNLVYQYKGAGLSMGTMICGYTRKEGPTIYYVDSGD
1nedA      ELFERKLEMHQGH--LVKAAVELAKDWRTDRMLRKLEALLAVADETAS---LIITGNGDV
1pmaB      KAELELYRLQRRVNMPIEAVATLLSNMLNQVKYMPYMQVQLLVGGIDTAP--HVFSIDAAG
1g4aB      ELFERKLEMHQGH--LVKAAVELAKDWRTDRMLRKLEALLAVADETAS---LIITGNGDV
          . .          . *          .

          129          166  169
1e94A      VQPENDLIAIGSGGPYAQAAAR-----ALLENTELSAREIAEKAL-DIA--GDICIYT
1gOuK      TRLKGDIFCVGSGQTFAVGVLDSNYKWDLSVEDALYLGKRSILAAAHRDAYSGGSVNLYH
1nedA      VQPENDLIAIGSGGPYAQAAAR-----ALLENTELSAREIAEKAL-DIA--GDICIYT
1pmaB      GSVEDIYASTGSGSPFVYGVLSEYSEKMTVDEGVDLVIRAISAAKQORDSASGGMIDVAV
1g4aB      VQPENDLIAIGSGGPYAQAAAR-----ALLENTELSAREIAEKAL-DIA--GDICIYT
          . *** .          . . . * * *          * * . .

1e94A      N-----H-FHTIEELSYK-----
1gOuK      VTEDGWIYHGNHVDVGELFWKVKEEGSFNNVIG
1nedA      N-----H-FHTIEELSYKAEFHHH-----
1pmaB      ITR-----K-DGYVQLPTDQIESRIRKLGLIL-
1g4aB      N-----H-FHTIEELSY-----
          . .
    
```

Alineament de seqüència

Estudi evolutiu



Estudi evolutiu

CLUSTAL W (1.60) multiple sequence alignment

```
PRCE_YEAST      MQAIADSFSPNRLVKELQYDNEQNLESDFVTGASQFQRLAPSLTVPPIASPPQFLRAHT
PRCD_HUMAN      -----MAATLLAARGAGPAPAWGPEAFTPDW
PRCB_THEAC      -----M
PRCE_SPIOL      -----MKLDTSGLESTAPIFRR--SDFVFDGLQMTSPFDLPNPTDFDGFQKEAV
PRCE_ARATH      -----MKLDTSGFETSMPMIGFGSSSDMLDELSVPSFDLPRTKEFDGFQKKAK
PRCB_METTH      -----MN
PRCB_METJA      -----
PRCB_SULSO      -----MGNELQL
PRCA_PYRHO      -----MAFVPPQAGYDRAITVFSPDGRLFQV
```

```
PRCE_YEAST      DDSRNPDCIKIAHGTTTTLAFRFQGGIIVAVDSRATAGNWWASQTVKKVIEINPFLGTM
PRCD_HUMAN      E-----SREVSTGTTIMAVQFDGGVVLGADSRTTGTSGYIANRVTDKLTPIHDRIFCCR
PRCB_THEAC      N-----QTLETGTTTVGITLKDAVIMATERVTMENFIMHKNGKKLFQIDTYTGMTI
PRCE_SPIOL      Q-----MVKPAKGTTTLAFIFKHGVMVAADSRASMGGYISSQSVKKIIEINPYMLGTM
PRCE_ARATH      D-----MLKHAKGTTTLAFIFKGGVMVAADSRASMGGYISSQSVKKIIEINPYMLGTM
PRCB_METTH      D-----KNTLKGTTTVGITCKDGVVFATERRASMGNLIAHKATDKIFKIDEHIAATI
PRCB_METJA      -----MDVMKGTTTVGLICDDAVILATDKRASLGNLVADKEAKKLYKIDDYIAMTI
PRCB_SULSO      E-----NKILKGTTTVGIRVNDGVILAADDRASAGFFVANKMVRKVLYITDKIGITT
PRCA_PYRHO      N-----YAREAVKRGATAVGVKCNEGVVLAVEKRITSR-LIEPESYEKIFQIDDHIAAAS
```

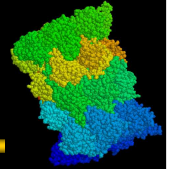
```
                *  *      .      *  .      *  *      *  *
PRCE_YEAST      AGGAADCQFWETWLGSQLHELREKE---RISVAAASKILSNLVYQYKGAGLSMGTMI
PRCD_HUMAN      SGSAADTQAVADAVTYQLGFHSIELNE---PPLVHTAASLFKEMCYRYR-EDLMAGIII
PRCB_THEAC      AGLVGDAQVLVRYMKAELLYRLQRRV---NMPIEAVATLLSNMLNQVKYMPYVQLLV
PRCE_SPIOL      AGGAADCQFWHRNLGIKRLHELANKR---RISVTGASKLLANILYNYRGMGLSVGTMI
PRCE_ARATH      AGGAADCQFWHRNLGIKRLHELANKR---RISVSGASKLLANMLYSYRGMGLSVGTMI
PRCB_METTH      AGSVADAQSLMKYLKAEAAALYMRNSE---KISIEAAAALAANILHSSRFYFIVQTLI
PRCB_METJA      AGSVGDAQIAIVRLLIAEAKLYKMRTGR---NIPPLACATLLSNILHSSRMFPFLTQIII
PRCB_SULSO      AGSVADLQFIYDVLKNIYHYNSITKYG---PISIKGIATRLANVLSATKYFPYIVQILI
PRCA_PYRHO      SGIIADARVLNRRARLEAQIHLTYGEPAPLAVIVKKICDLQMHQYGGVVRPFGAALLM
```

```
                *  *      .      .      .      .      .      .
PRCE_YEAST      CGYTRKEGPTIIYYVDSGTRLK-GDIFCVGSGQTFAYGVLDSNYKWDLSVEDALYLGKRS
PRCD_HUMAN      AGWDPQEGGQGYSVPMGGMMVR-QSFAIGGSGSSYIYGVDATYREGMTKEECLQFTANA
PRCB_THEAC      GGIDT--APHVFSIDAAGGSVE-DIYASTGSGSPFVYGVLESQYSEKMTVDEGDLVIRA
PRCE_SPIOL      AGWD-ETGPGLYYVDSEGGRLK-GMRFSVSGSPYAYGVLDNGYKYDMTVEEASELARRA
PRCE_ARATH      AGWD-ETGPGLYYVDNEGGRLK-GDRFSVSGSPYAYGVLDSGYKYDMSVEEASELARRS
PRCB_METTH      GGVDE-NGAKIYSLDPSGGMIP-DKFVSTGSGSPYAYGVLEDYSDELYVDEAVDVAIRA
PRCB_METJA      GGYDLLLEGAKLFSLDPLGGMNEEKTFTATGSGSPIAYGVLEAGYDRDMSVEEGIKLALNA
PRCB_SULSO      GGYDD--QPRLFNLDYLGDIITE-ENYVATGSGSPVAMGVLEDEYNPKMTLDEAADLAKRA
PRCA_PYRHO      AGVNE--KPELYETDPSGAYFA-WKAVAIGSGRNTAMAFEEKYKDDMSLEEAIKLAIFA
                *      .      *      ***      .      *      .      .
```

```
PRCE_YEAST      ILAAAHRDAYSGGSVNLYHVT--EDGWIYHGNDVGEFLFWKVK---E-EEGSFNNVIG-
PRCD_HUMAN      LALAMERDGSGGVIRLAAIAESGVERQVLLGDQIPKFAVATLPPA-----
PRCB_THEAC      ISAAKQRDSASGGMIDVAVITR-KDGYVQLPTDQIESRIRKLGIL-----
PRCE_SPIOL      IYHATYRDGASGGVSVYHVG--PDGWKKVTGDDVGDHLHFQYYPVPVATVEQEMVEVVG
PRCE_ARATH      IYHATFRDGASGGVASVYHVG--PEGWTKLGGDDVGELHYHYYPVAPATAEQVMEEATAE
PRCB_METTH      IKSAMERDTSNGGILVATVTE-EEGFRLMSEEEIQKRIENLN-----
PRCB_METJA      LKSAMERDTFSGNGISLAVIT--KDGVKIFEDEEIEKILDSMKAKPKKTKRSRRKSK-
PRCB_SULSO      VFSAIKRDSTGTGVIVAKIH--SKGHEELEFYLNKKM-----
PRCA_PYRHO      LAKTMEKPSAENIEVAITVK--DKKFRKLSREEIEKYLNEVMKEVEEEVKEEEDYSE
                .      .      .      .      .      .
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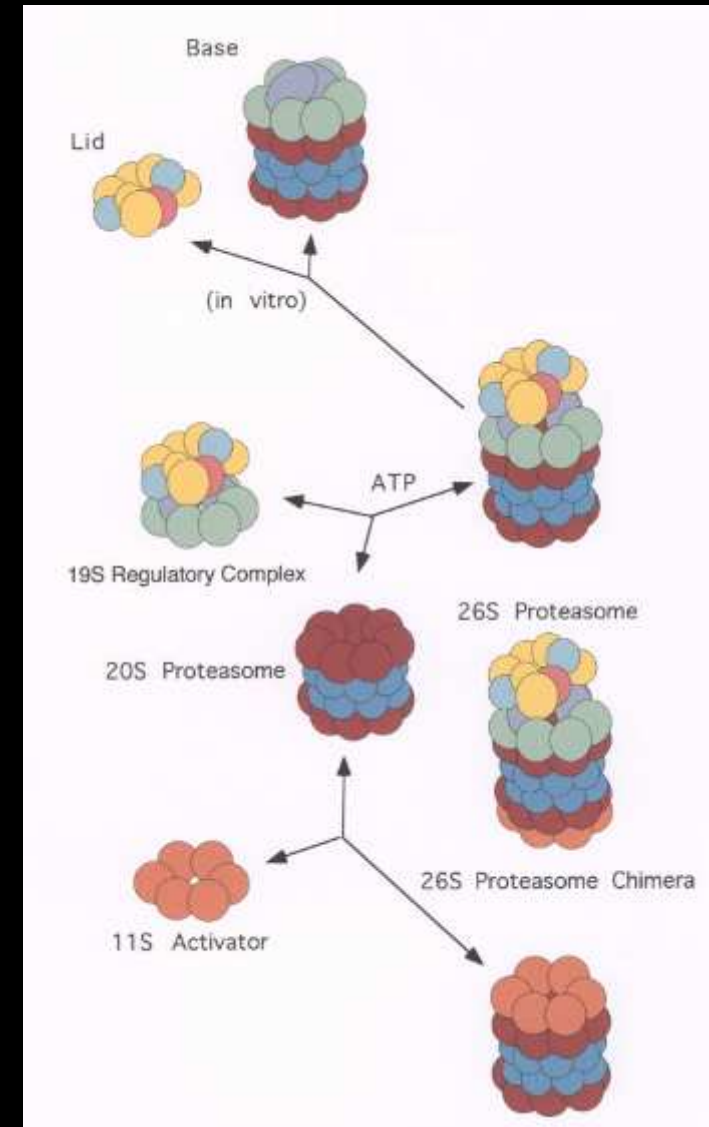
Caps reguladors del proteosoma

Tipus d'activadors

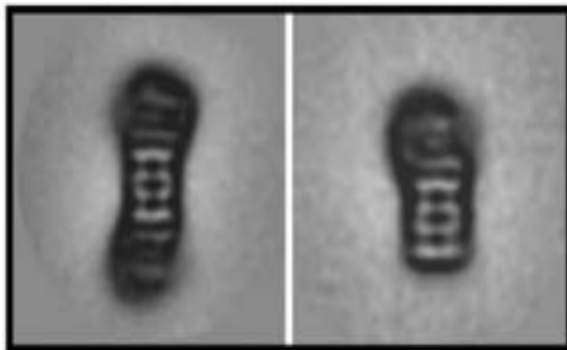
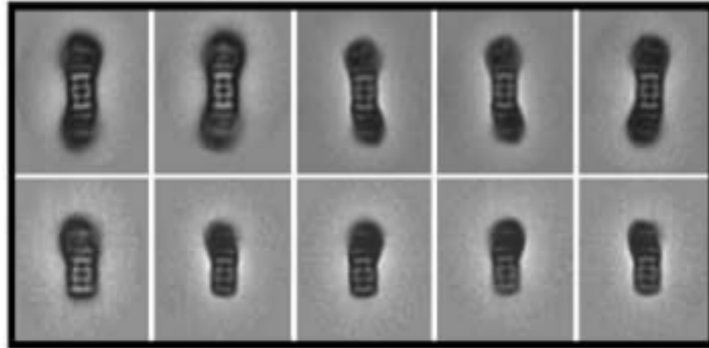
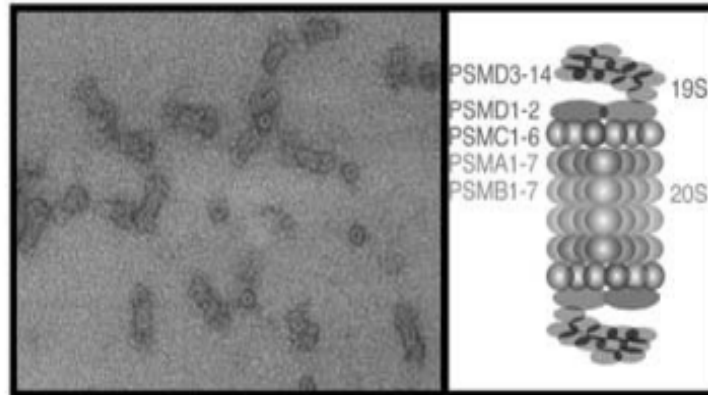
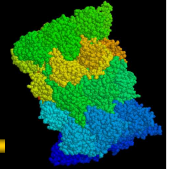


Existeixen tres tipus de subunitats reguladores:

- **19S** (PA700) → ATP-dependent
- **11S** (PA26, PA28, REG) → ATP-independent
- **PA200**



Cap regulador 19S

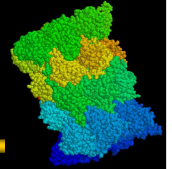


Molecular Cell 23, 875–885, September 15, 2006

- El cap 19S no ha estat cristal·litzat.
- S'ha observat per microscopia electrònica.
- Consta de 17 subunitats (separades en LID i BASE) les quals han estat purificades i seqüenciades.
- Es troba implicat en un gran nombre de funcions.

Microscopia electrònica
50000x
4,2 Å/pixel

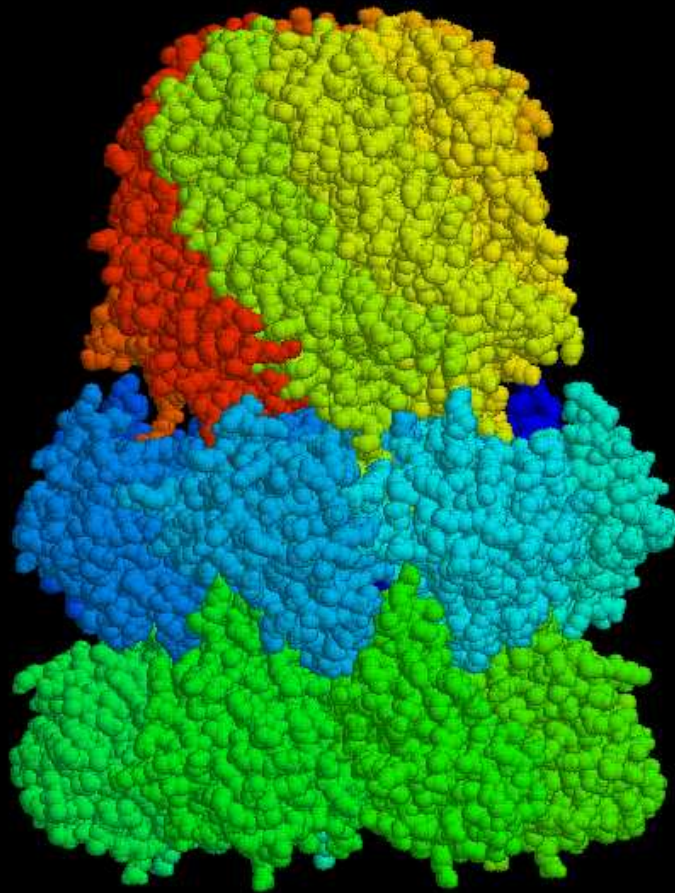
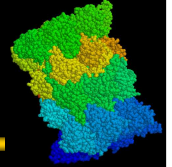
Cap regulador 19S



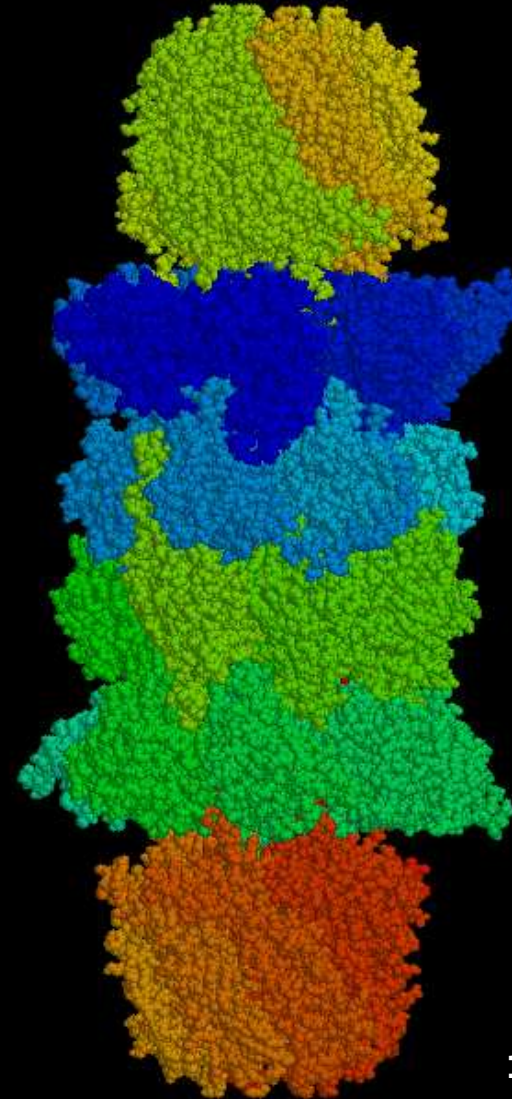
FUNCIONS

- Activació del proteosoma
- Reconeixement del substrat
- Desubiquitinació del substrat
- Desestabilització de l'estructura terciària de les proteïnes plegades
- Translocació del substrat

Cap regulador 11S

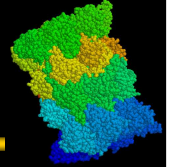


1YA7.pdb



1FNT.pdb

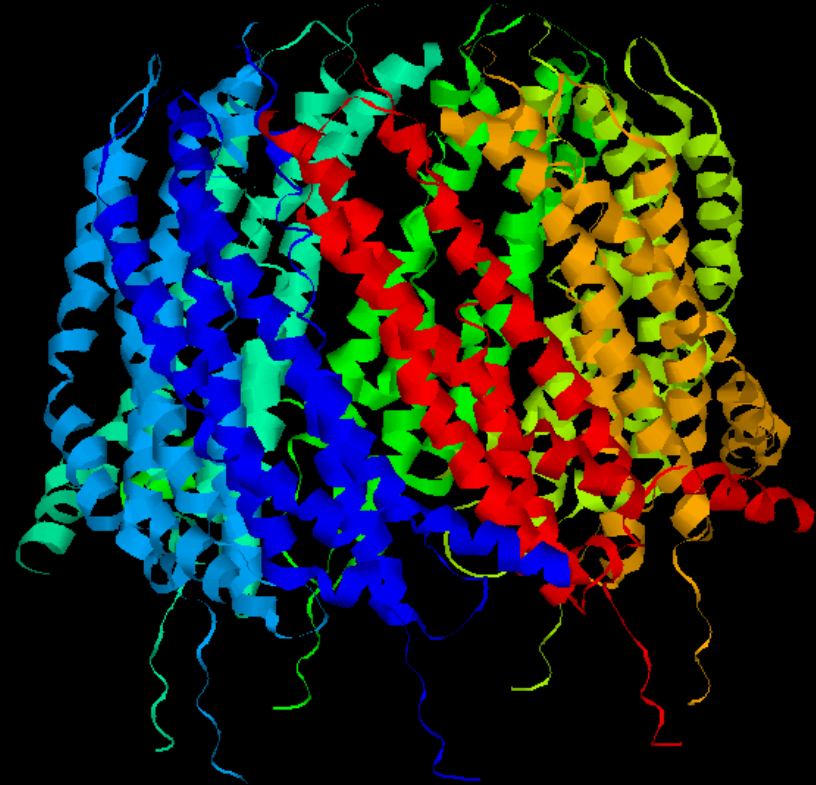
Cap regulador 11S



- El regulador 11S forma un barril heptamèric.
- És ATP-independent.
- Els diferents reguladors 11S activen els proteasomes 20S de diferents espècies.

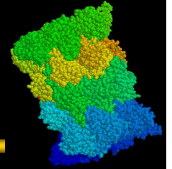
FUNCIONS

- Activació del proteosoma 20S.
- Permetre la obertura i facilitar l'entrada del substrat.
- Intervé en la generació de pèptids per la presentació al SI.

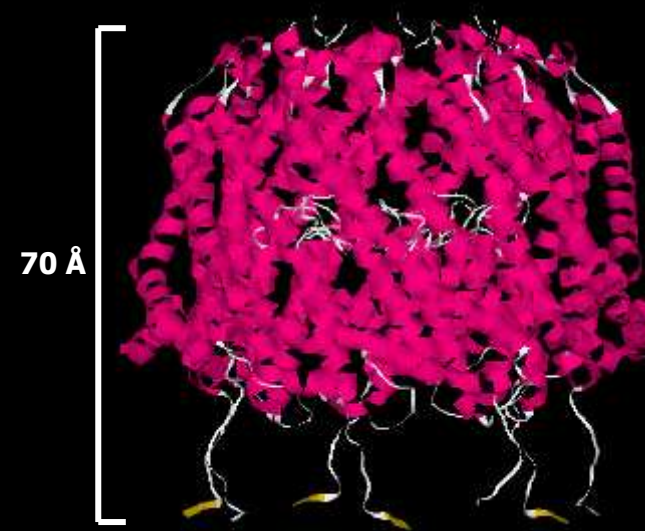
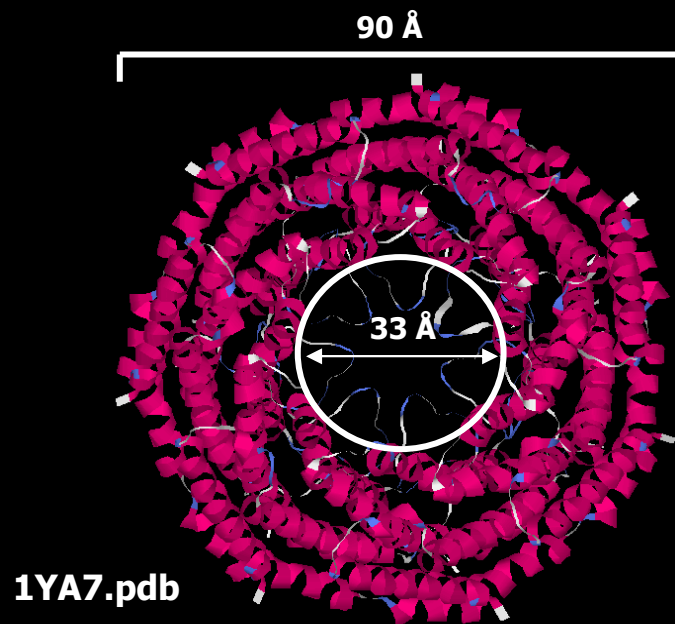


1YA7.pdb

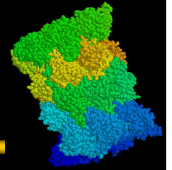
Cap regulador 11S



- Barril format per 7 monòmers.
- Similar a la subunitat humana (PA28).
- Dos barrils de PA26 s'associen pels seus eixos al proteosoma 20S, un a cada extrem.

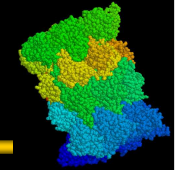


Cap regulador 11S

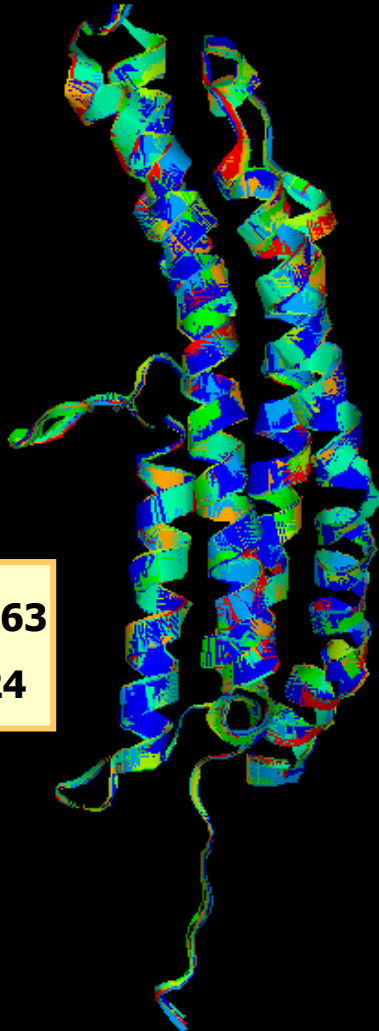


1YA7.pdb

Cap regulador 11S



STAMP Subunitats



Score: 9,63

RMS: 0,24

1YAU.pdb

CLUSTAL W(1.60) multiple sequence alignment

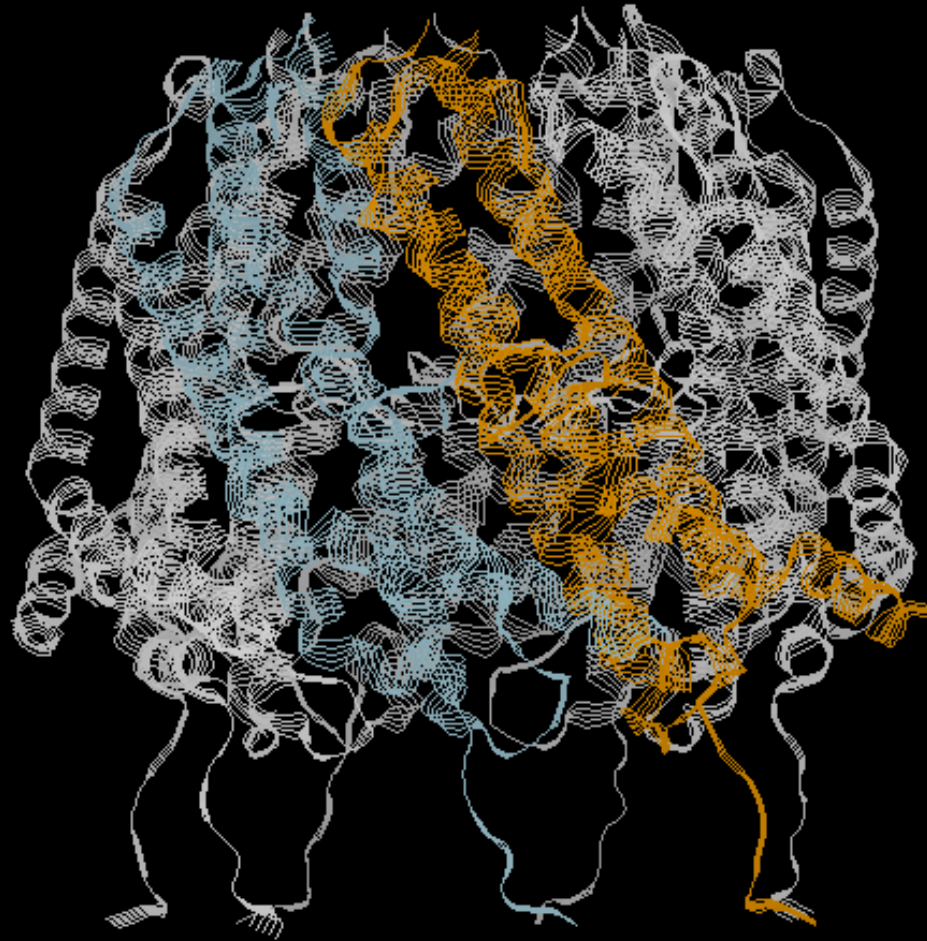
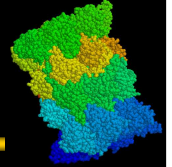
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1yauR  KRAALIQNLRDSYTETSSFAVIEEWAAGTLQEIEGIAKAAAEAHGVIRNSTYGRAQAEKS
1yauU  KRAALIQNLRDSYTETSSFAVIEEWAAGTLQEIEGIAKAAAEAHGVIRNSTYGRAQAEKS
1yauP  KRAALIQNLRDSYTETSSFAVIEEWAAGTLQEIEGIAKAAAEAHGVIRNSTYGRAQAEKS
1yauS  KRAALIQNLRDSYTETSSFAVIEEWAAGTLQEIEGIAKAAAEAHGVIRNSTYGRAQAEKS
1yauO  KRAALIQNLRDSYTETSSFAVIEEWAAGTLQEIEGIAKAAAEAHGVIRNSTYGRAQAEKS
1yauQ  KRAALIQNLRDSYTETSSFAVIEEWAAGTLQEIEGIAKAAAEAHGVIRNSTYGRAQAEKS
```

```
1yauT  PEQLLGVLQRYQDLCHNVYCQAETIRTVIAIRIPEHKEEDNLGVAVQHAVLKIIDELEIK
1yauR  PEQLLGVLQRYQDLCHNVYCQAETIRTVIAIRIPEHKEEDNLGVAVQHAVLKIIDELEIK
1yauU  PEQLLGVLQRYQDLCHNVYCQAETIRTVIAIRIPEHKEEDNLGVAVQHAVLKIIDELEIK
1yauP  PEQLLGVLQRYQDLCHNVYCQAETIRTVIAIRIPEHKEEDNLGVAVQHAVLKIIDELEIK
1yauS  PEQLLGVLQRYQDLCHNVYCQAETIRTVIAIRIPEHKEEDNLGVAVQHAVLKIIDELEIK
1yauO  PEQLLGVLQRYQDLCHNVYCQAETIRTVIAIRIPEHKEEDNLGVAVQHAVLKIIDELEIK
1yauQ  PEQLLGVLQRYQDLCHNVYCQAETIRTVIAIRIPEHKEEDNLGVAVQHAVLKIIDELEIK
```

```
1yauT  TLGSGEKSGSGGAPTPIGMYALREYLSARSTVEDKLLGGGSQSPSLLLELRQIDADFMLK
1yauR  TLGSGEKSGSGGAPTPIGMYALREYLSARSTVEDKLLGGGSQSPSLLLELRQIDADFMLK
1yauU  TLGSGEKSGSGGAPTPIGMYALREYLSARSTVEDKLLGGGSQSPSLLLELRQIDADFMLK
1yauP  TLGSGEKSGSGGAPTPIGMYALREYLSARSTVEDKLLGGGSQSPSLLLELRQIDADFMLK
1yauS  TLGSGEKSGSGGAPTPIGMYALREYLSARSTVEDKLLGGGSQSPSLLLELRQIDADFMLK
1yauO  TLGSGEKSGSGGAPTPIGMYALREYLSARSTVEDKLLGGGSQSPSLLLELRQIDADFMLK
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```

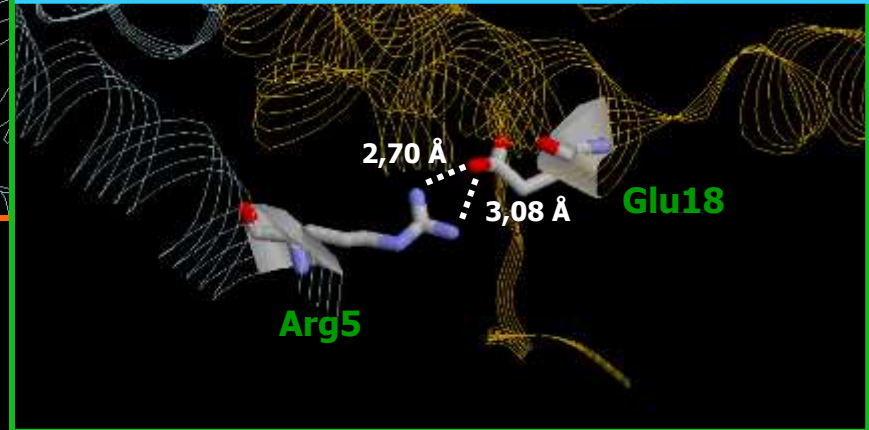
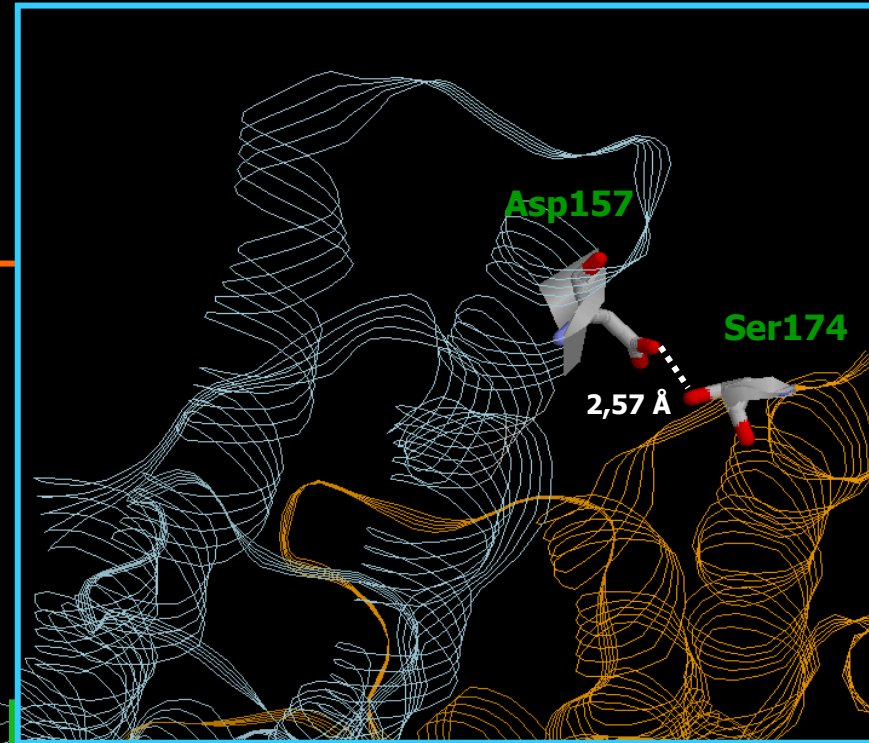
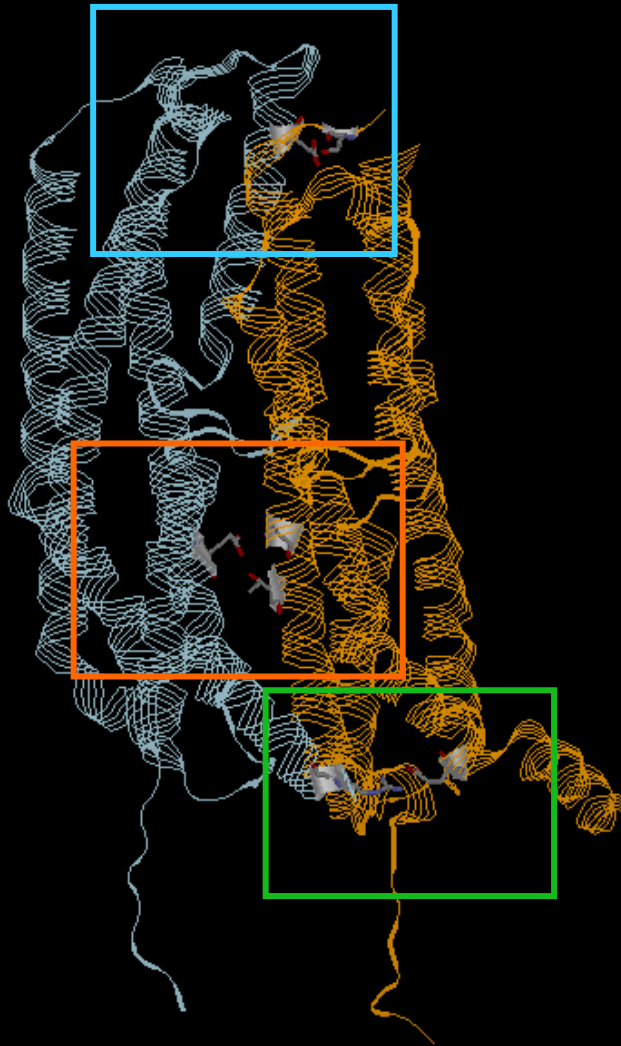
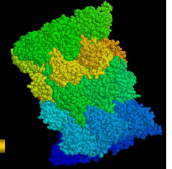
```
1yauT  VELATTHLSTMVRVINAYLLNWKKLIQPRTGSDHMVS
1yauR  VELATTHLSTMVRVINAYLLNWKKLIQPRTGSDHMVS
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1yauP  VELATTHLSTMVRVINAYLLNWKKLIQPRTGSDHMVS
1yauS  VELATTHLSTMVRVINAYLLNWKKLIQPRTGSDHMVS
1yauO  VELATTHLSTMVRVINAYLLNWKKLIQPRTGSDHMVS
1yauQ  VELATTHLSTMVRVINAYLLNWKKLIQPRTGSDHMVS
```

Interacciones



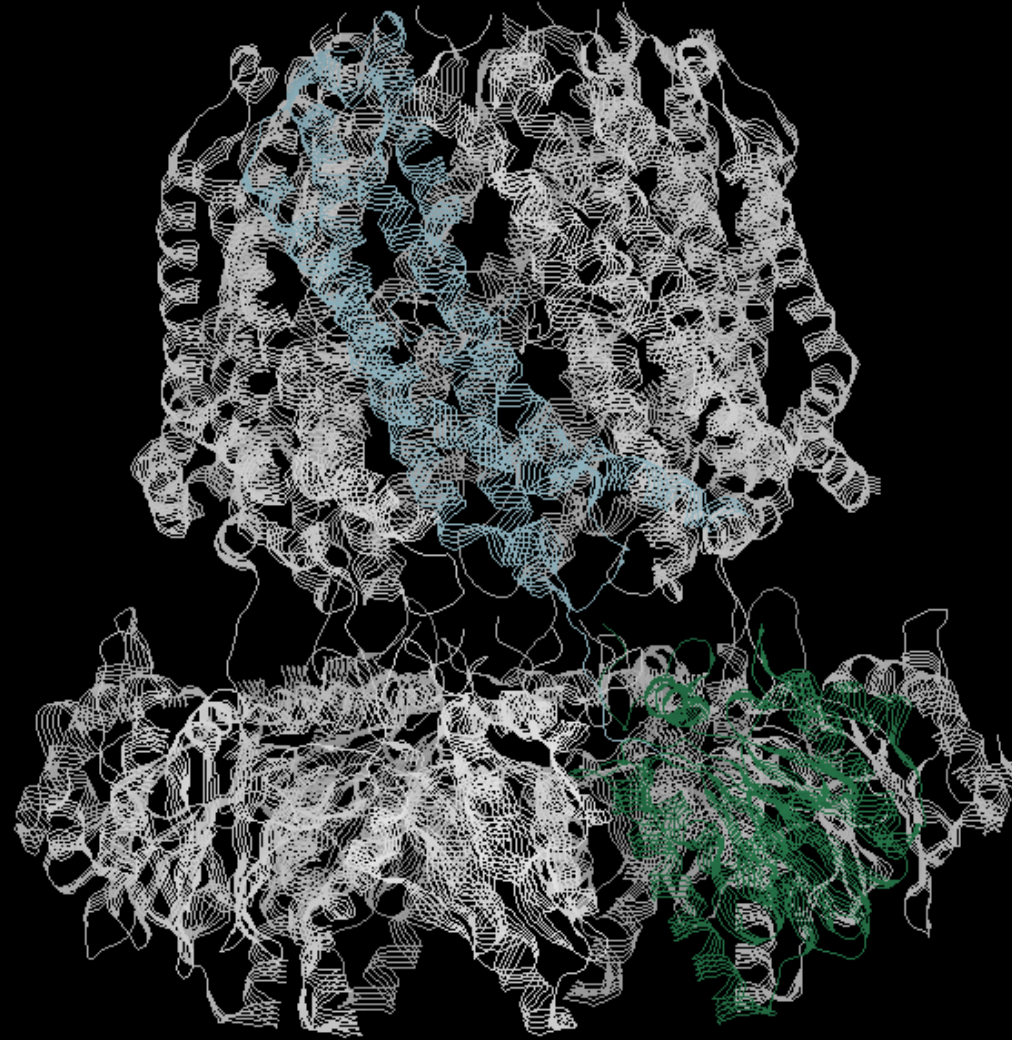
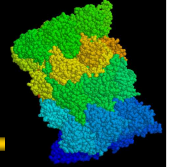
1YA7.pdb

Interacciones



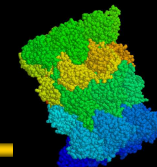
1YA7.pdb

Interacciones



1YA7.pdb

Interacciones



CLUSTAL W(1.60) multiple sequence alignment

```

1PMA      -----TVFSPDGRLFQVEYAREAVKKGSTALGMKFANGVLLI SDKKVR SRL
PYRHO     MAFVPPQAGYDRAITVFS PDGRLFQVNYAREAVKRGATAVGVCNEGVVLAVEKRIT SRL
METH      -MQPLQSAGYDRAITVFS PDGRLFQVEYAREAVKRGTT SLGVKSKEGIVLVVDKRPT SKL
METJA     -MQMVPPSAYDRAITVFS PEGRLYQVEYAREAVRRGTTAIGIACKDGVVLAVDRRIT SKL
LYCES     -----MARYDRAITVFS PDGHLFQVEYAMEAVRKGNAAVGVRGTDTVVLGVEKKST PKL
ARCFU     --MHLPMQGYDRAITVFS PDGRLFQVEYAREAVKRGATAIGIKCKEGVILIADKRVGSKL
ORYSA     -----MARYDRAITVFS PDGHLFQVEYALEAVRKGNAAVGVRGTDTVVLGVEKKST PKL
          *****.*.*.** ** ***.** ..*..* ..* ..* ..*
    
```

66

```

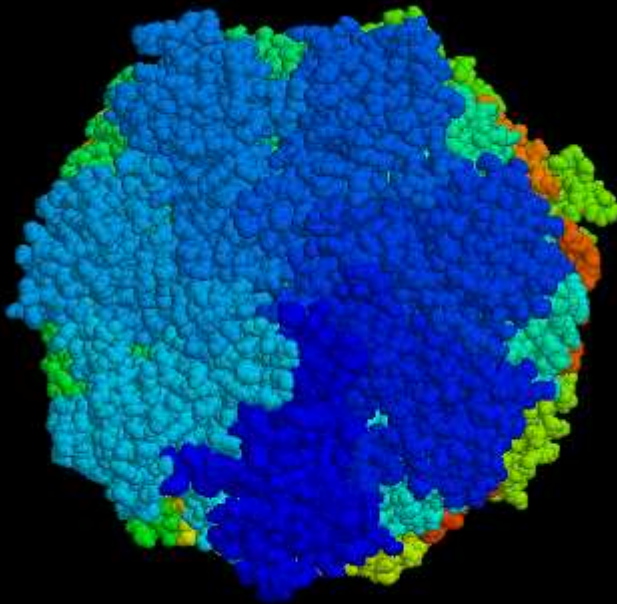
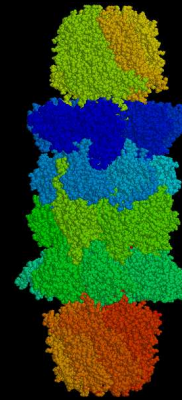
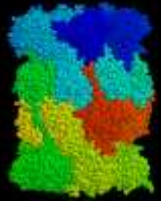
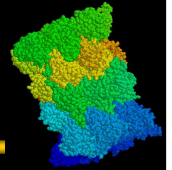
1PMA      IEQNSIEKIQ LIDDYVA AVTSGLVADARVLVDFARI SAQQEKVTYGS LVNIENLVKRVAD
PYRHO     IEPESYEKIFQIDDHIAAASSGIIADARVLVNRARLEAQIHRLTYGE PA PLAVIVKKICD
METH      VEPKSIEKIFQIDEHIGAATSGLVADARAIIEKARLEAQINRITYNEPIRVE SLAKKICD
METJA     VKIRSIEKIFQIDDHVAAATSGLVADARVLIDRARLEAQIYRLTYGEEI SI EMLAKKICD
LYCES     QDSRSVRKIVNLDDHIALACAGLKADARVLVNKARIECQSHRLTVEDPVTVEYITRYIAG
ARCFU     LEADTIEKIIYKIDEHICAATSGLVADARVLIDRARIEAQINRLTYDEPITVKELAKKICD
ORYSA     QDSRSMRKIASLDTHIALACAGLKADARVLINRARVEQC SHRLTVEDPVTVEYITRYIAG
          . ** . * . . * . **** . . ** . * . * . . . .
    
```

2,67 Å

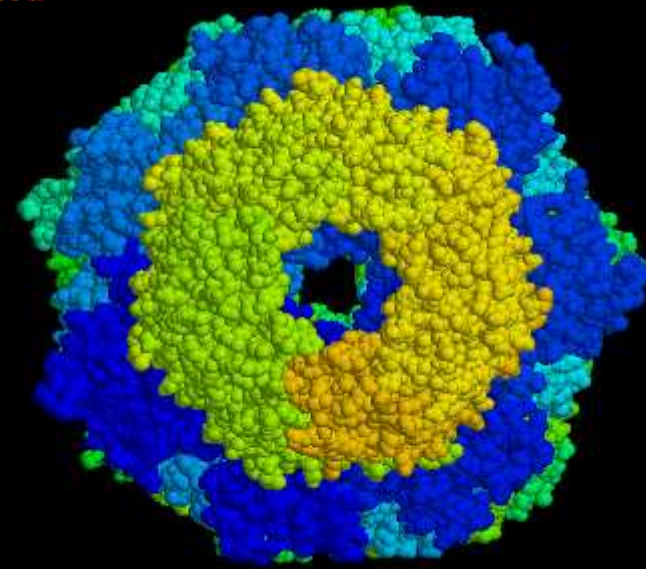
Lys66

1YA7.pdb

Obertura de l'anell

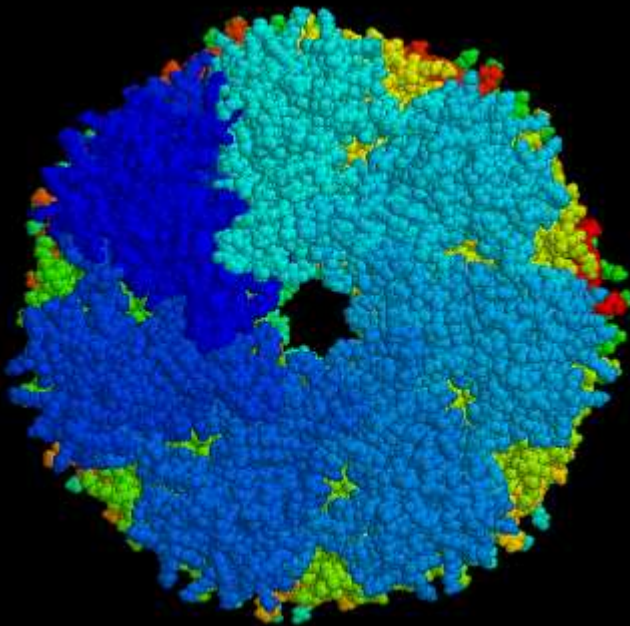
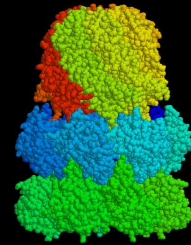
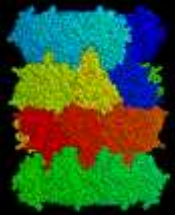
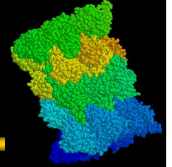


1RYP.pdb

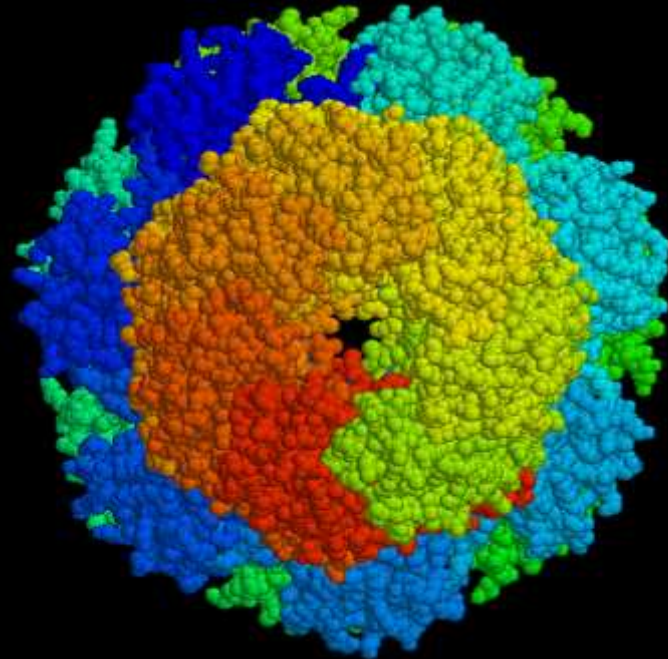


1FNT.pdb

Obertura de l'anell

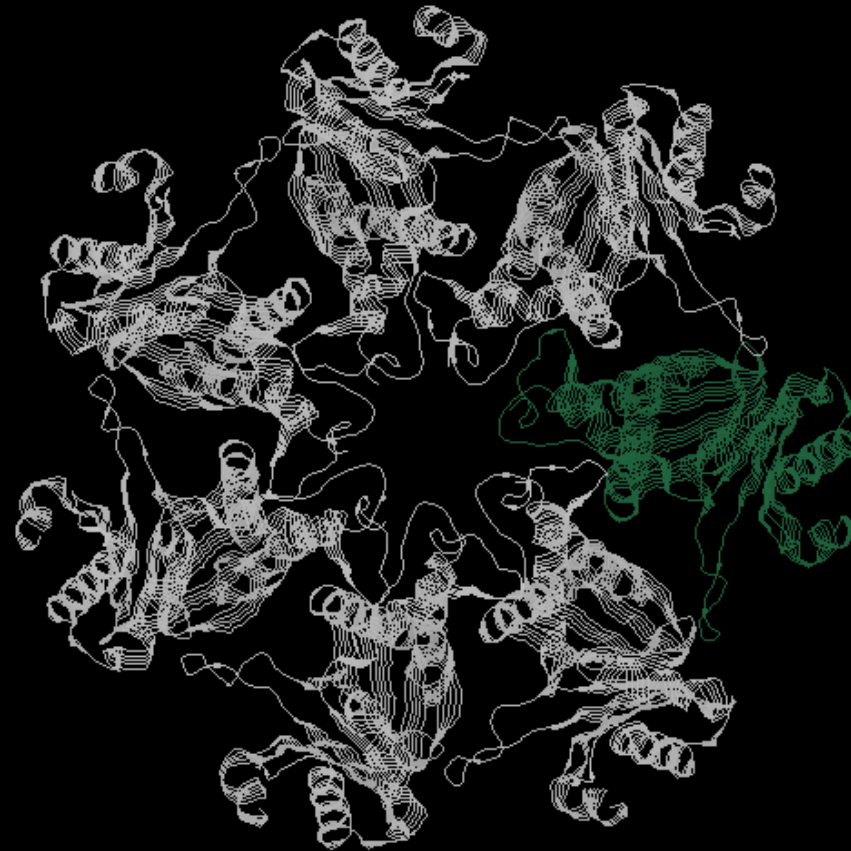
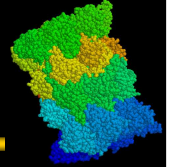


1PMA.pdb



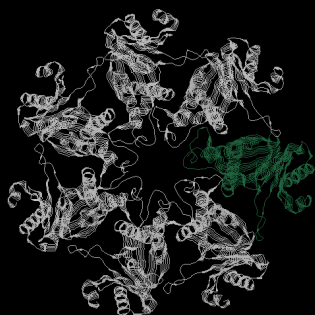
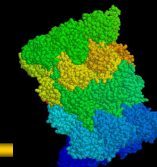
1YA7.pdb

Obertura de l'anell



1PMA.pdb

Obertura de l'anell



CLUSTAL W(1.60) multiple sequence alignment

```

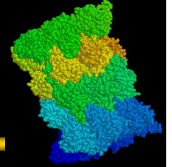
                                17      26
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PYRHO     MAFVPPQAGYDRAITVFS PDGRLFQVNYAREAVKRGATAVGVKNEGVLAVEKRIT SRL
METTH     -MQPLQSAGYDRAITVFS PDGRLFQVEYAREAVKRGTTSLGVKSKEGIVLVVDKRPT SKL
METJA     -MQMVPPSAYDRAITVFS PEGRLYQVEYAREAVRRGTTAIGIACKDGVVLAVDRRIT SKL
LYCES     -----MARYDRAITVFS PDGHLFQVEYAMEAVRKGNAAVGVRGTDTVVLGVEKKST PKL
ARCFU     --MHL PQMGYDRAITVFS PDGRLFQVEYAREAVKRGATAIGIKCKEGVILIADKRVG SKL
ORYSA     -----MARYDRAITVFS PDGHLFQVEYALEAVRKGNAAVGVRGTDTVVLGVEKKST PKL
                                *****

```



1PMA.pdb

Obertura de l'anell



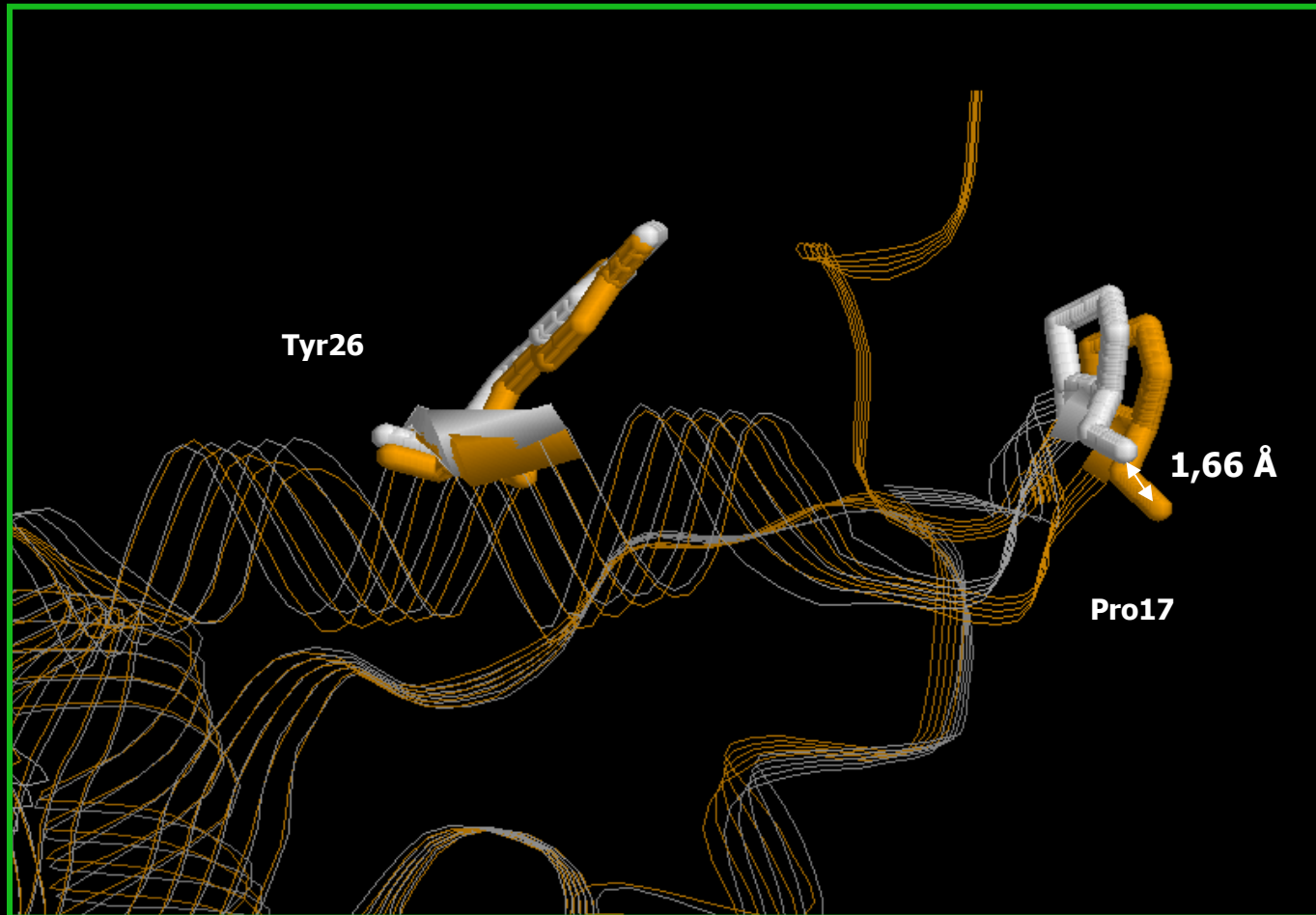
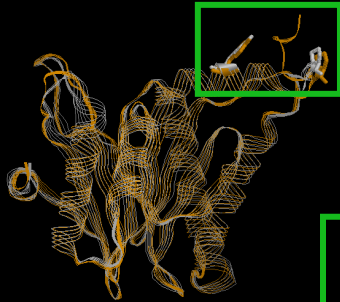
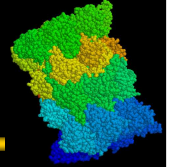
Score: 9,13

RMS: 0,67

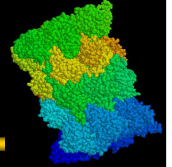
1PMA.pdb

1YA7.pdb

Obertura de l'anell



Conclusions



- L'estructura està més conservada que la seqüència.
- El proteosoma és una estructura molt complexa.
- És un tipus de proteasa amb una Thr al centre actiu.
- Sembla tenir una activitat important, ja que es troba tant en eucariotes com en procariotes.
- L'evolució ha afegit complexitat a l'estructura del proteosoma.
- Existeixen molts caps reguladors amb diferents activitats.

Preguntes PEM:

1. Quina de les afirmacions següents és correcta?
 - a) *T.acidophilum* presenta una simetria D7
 - b) *S.cerevisiae* presenta una simetria C2.
 - c) les dues anteriors**
 - d) El proteosoma NO és simètric
 - e) totes les anteriors

2. Quina de les afirmacions següents és incorrecta?
 - a) El proteosoma és un complex macromolecular responsable de la major part de la degradació de proteïnes
 - b) Es localitza al citoplasma i nucli d'eucariotes i procariotes
 - c) les dues anteriors
 - d) Està format per 4 anells beta**
 - e) totes les anteriors

3. Quina és la principal diferència entre la subunitat alfa i beta del proteosoma?
 - a) La subunitat beta té la hèlix 0 (H0) i la alfa no
 - b) La subunitat alfa té la hèlix 0 (H0) i la beta no**
 - c) La subunitat beta té una estructura beta sandwich i la alfa no
 - d) La subunitat alfa té una estructura beta sandwich i la beta no
 - e) No hi ha cap diferència entre les dues subunitats

4. Quantes subunitats diferents presenten el proteosoma de *T. Acidophilum* i el de *S. Cerevisiae* respectivament?
 - a) 7 i 7
 - b) 2 i 14**
 - c) 14 i 28
 - d) 14 i 14
 - e) Cap de les anteriors és correcta.

5. Quin tipus de plegament presenten les subunitats del proteosoma?
- a) Beta sandwich format per 2 làmines de 5 cadenes beta cada una, envoltades per 2 hèlix a la part superior i 2 a la part inferior.
 - b) Beta sandwich format per dues làmines de 10 cadenes beta cada una.
 - c) a i b són falses.
 - d) Beta sandwich format per 2 làmines de 5 cadenes beta cada una, envoltades per 3 hèlix a la part superior i 2 a la part inferior.**
 - e) Cap de les anteriors.
6. Respecte als caps reguladors del proteosoma, digues quina afirmació és la correcta:
- a) existeixen molts tipus de subunitats reguladores
 - b) totes són ATP-dependents
 - c) el cap 19S està implicat en un gran nombre de funcions**
 - d) tots han estat cristal·litzats
 - e) totes són correctes
7. A quines parts del proteosoma s'uneixen els caps reguladors?
- a) a l'anell d'alfes**
 - b) a l'anell de betes
 - c) les dues anteriors
 - d) no s'uneixen directament al proteosoma
 - e) s'uneix a alfes i betes

8. L'entorn hidrofòbic del nucli del proteosoma fa que les interaccions electrostàtiques que es donen siguin:

- a) menys fortes
- b) més fortes**
- c) més hidrofòbiques
- d) iguals
- e) cap de les anteriors

9. Respecte a les subunitats actives del proteosoma, digues quines son falses:

- 1. Requereixen d'un procés de maduració per eliminar uns residus C-terminal i exposar la Thr1.
- 2. Al ser una treonin-proteasa no té cap residu que constitueixi el forat del oxianió.
- 3. La tríada catalítica de les subunitats alfa està formada per la Thr1, Lys33 i (Asp-Glu)17.
- 4. Les butxaques S1, son responsables de la especificitat de les diferents subunitats.

- a) 1, 2 i 3**
- b) 1 i 3
- c) 2 i 4
- d) 4
- e) 1, 2, 3 i 4

10. El proteosoma, senyala l'afirmació correcta:

- a) És encarregat de la major part de la degradació de proteïnes.
- b) Està molt conservat estructuralment.
- c) L'evolució ha afegit complexitat al proteosoma.
- d) És un tipus de proteasa amb una Thr1 al centre actiu.
- e) Totes les afirmacions són certes.**