

PROTEOMIKA

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- Proteinové interakce – 10.11.
 - jak spolu proteiny interagují?
 - interaktom
- Proteinové komplexy – 24.11.
 - protein-proteinové interakce a komplexy
 - komplexom, architektura a funkce komplexů

anketa

CG030 – Struktura a funkce proteinových komplexů

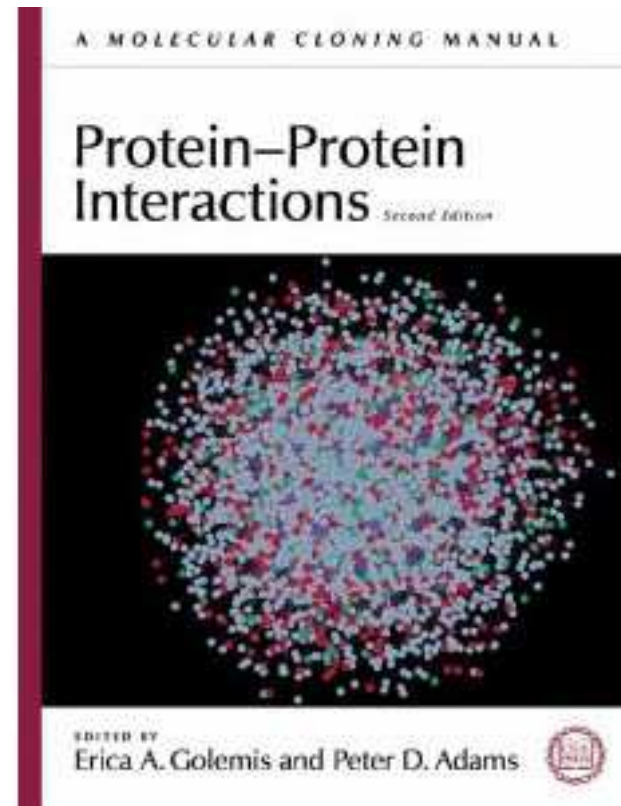
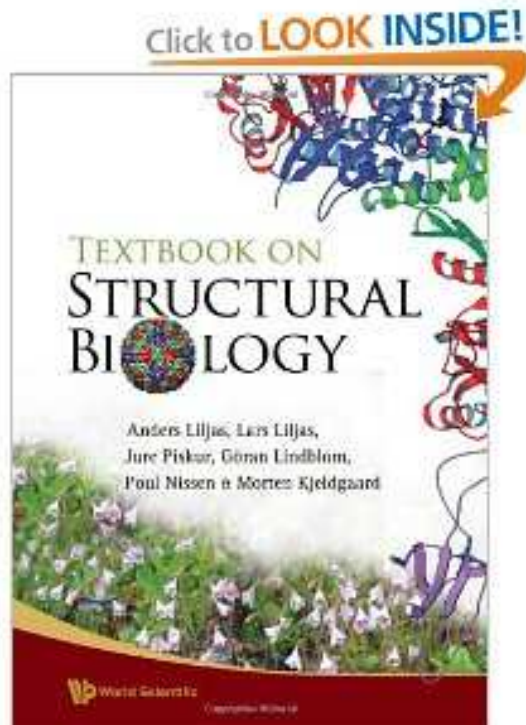
**CG031 – cvičení z modelování proteinových komplexů
(jarní semestr)**

Informační zdroje

Alberts a spol: Molecular biology of the Cell (2008 ...)

Liljas a spol: Structural biology (2009) ...

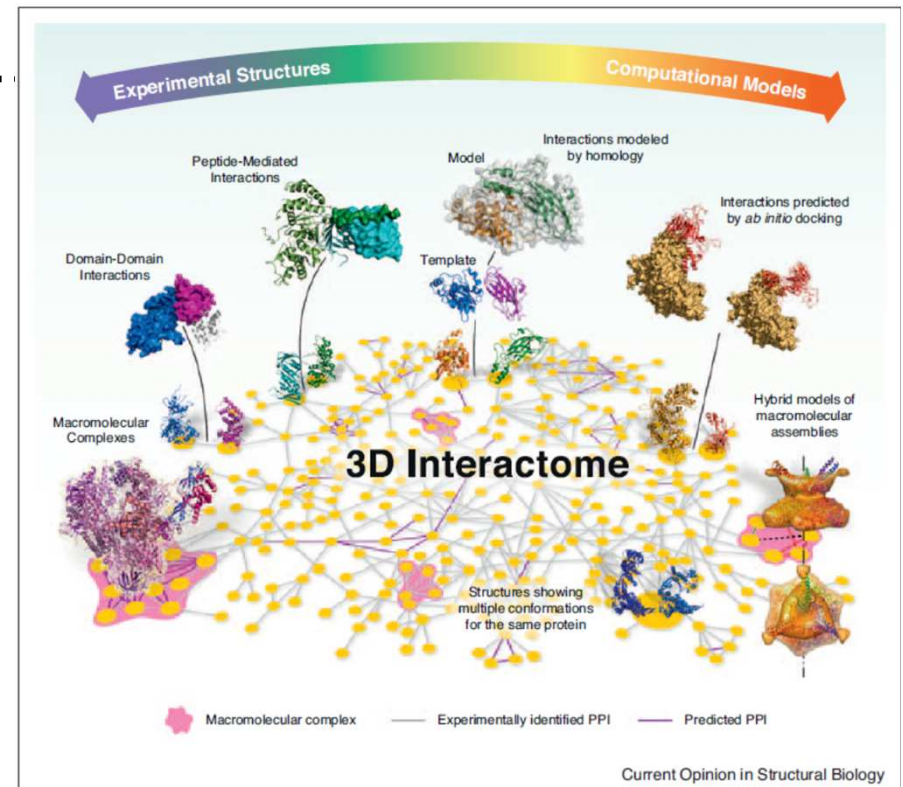
... nejnovější články z časopisů Cell, Nature, Science, PLoS ...

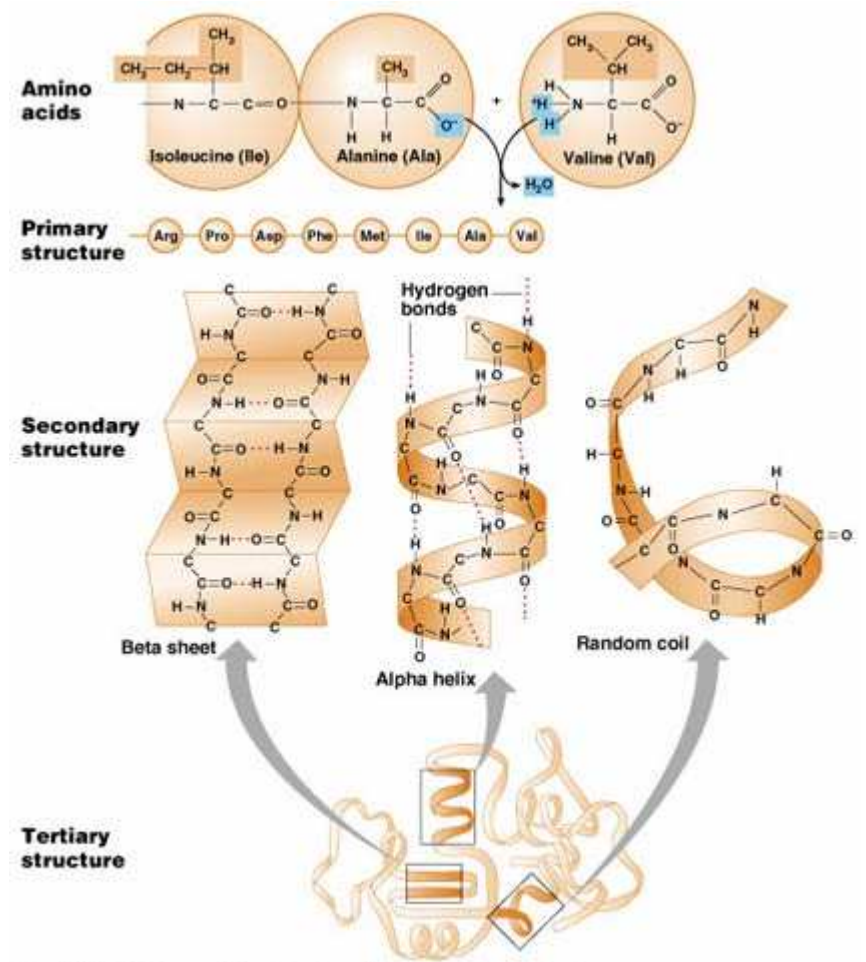
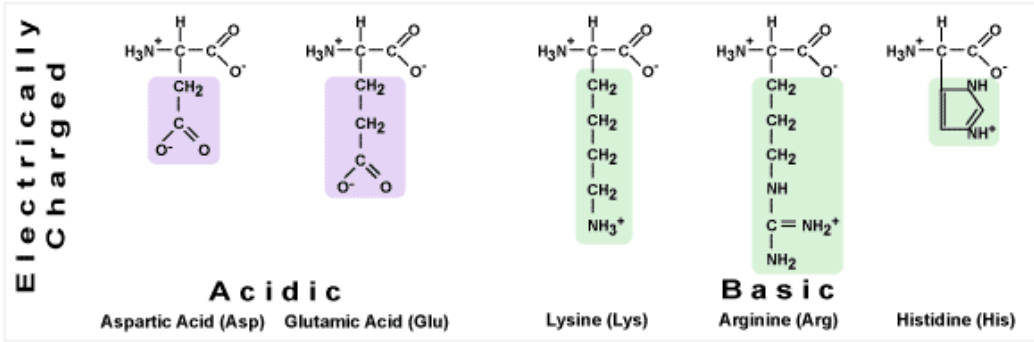
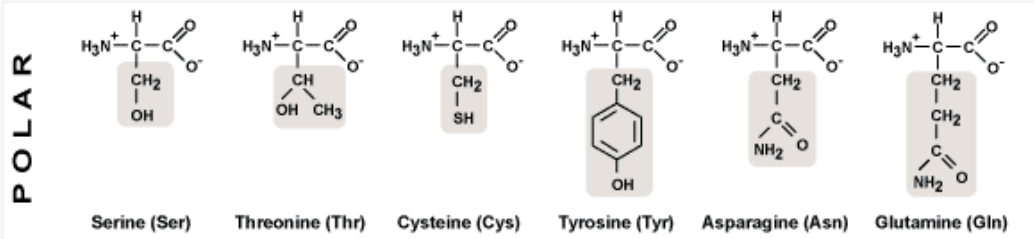
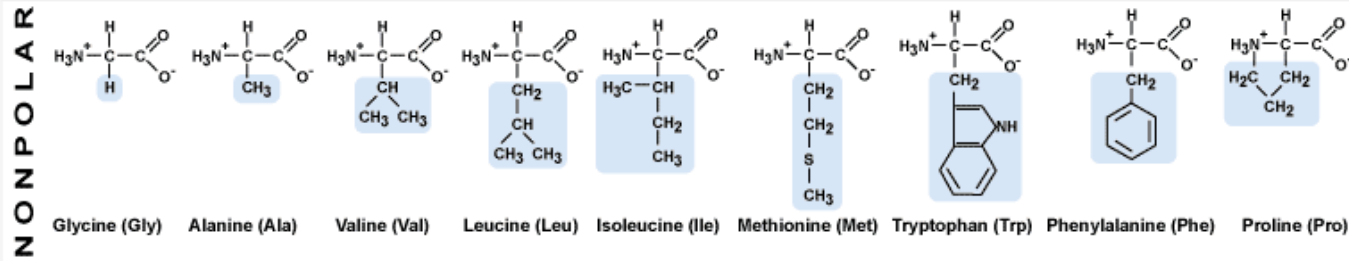


Databáze proteinových struktur: <http://www.rcsb.org/pdb/home/home.do>,
<http://www.ebi.ac.uk/pdbsum/>

Database protein-proteinových interakcí: <http://string-db.org/newstring.cgi> ...
<http://www.ebi.ac.uk/intact/?conversationContext=1>

- Proteinové interakce – 10.11.
 - Interakce: od primární po terciární strukturu
 - Typy vazeb: pohled chemický, geometrický ...
 - Informatika:
 - databáze struktur, interakcí ...
 - docking ...
 - motivy, evoluční aspekty ...
 - nástroje ...
 - interaktom ...



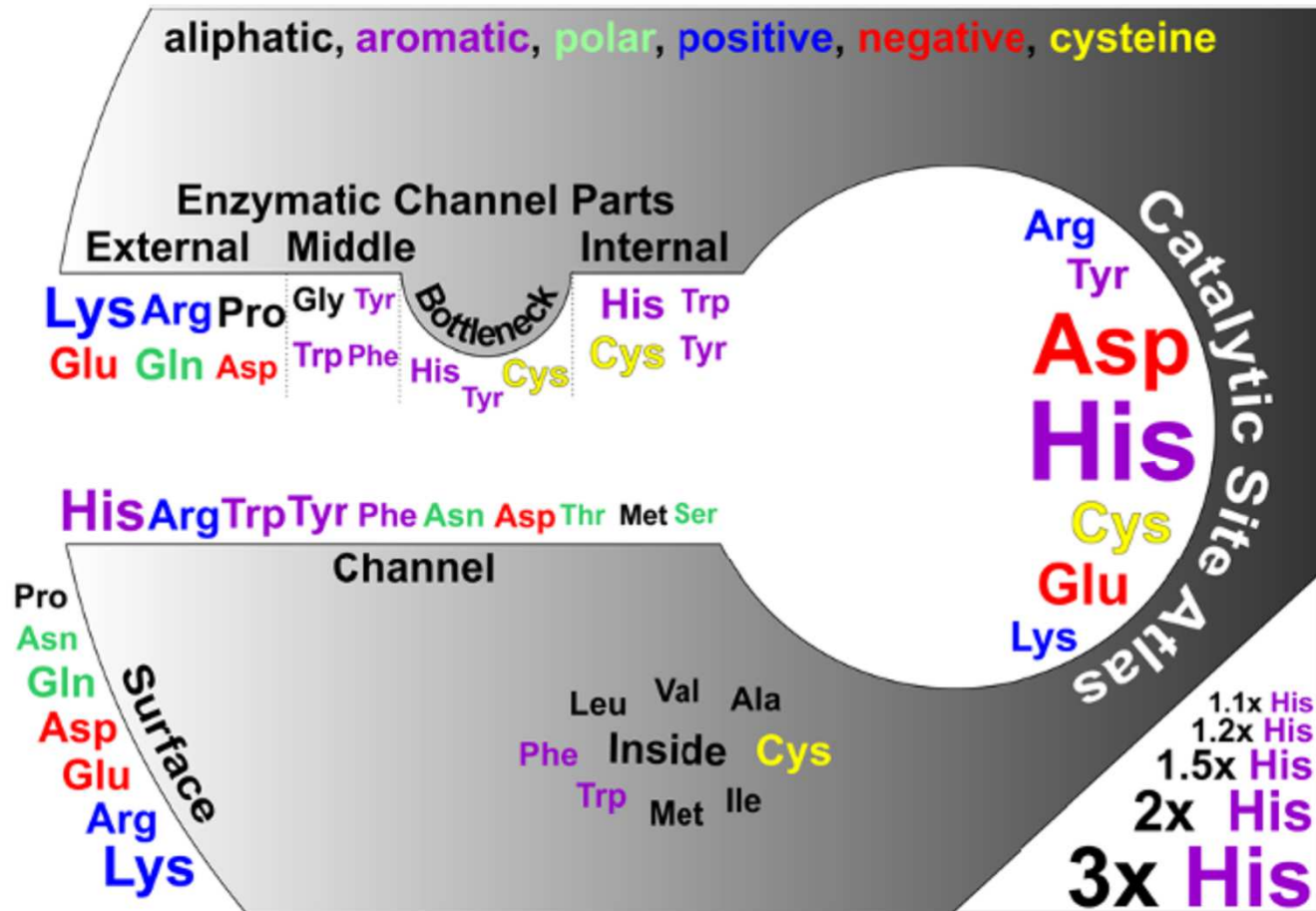


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Základní proteinové charakteristiky

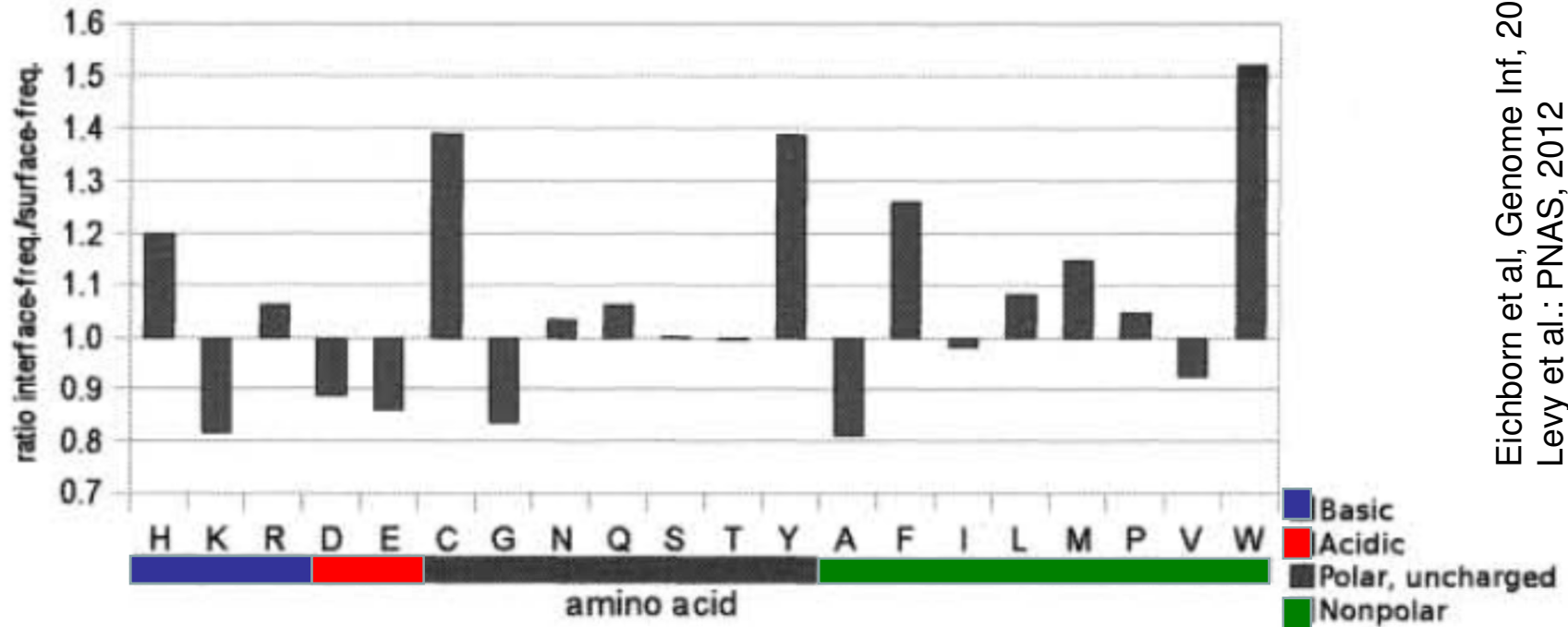
- Primární
- Sekundární
- Terciární
- Kvarterní – dva proteiny a více ...

Podíl AMK (primární struktury) na proteinových interakcích

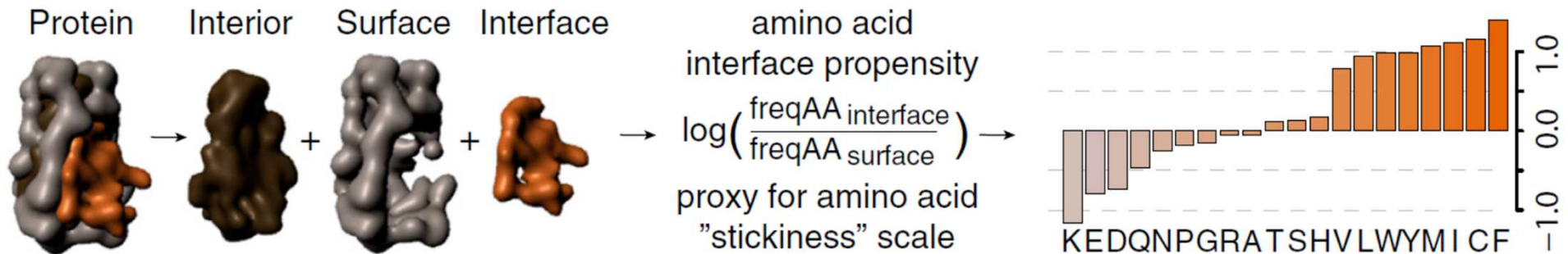


- uvnitř hydrofobní, povrch polární/nabitý (do solventu/vody), ale katalytická centra (tunely) jsou také polární a nabité (katalýza biochemické reakce)

PPI od primární struktury ...



Eichborn et al, Genome Inf, 2009
Levy et al.: PNAS, 2012



poměr mezi výskytem AMK na „intaktním“ povrchu a interakčním povrchu – polární a nabité do solventu tj. povrchu - hydrofobní na povrchu nejčastěji vytváří protein-proteinové interakce

Typy vazeb v PPI

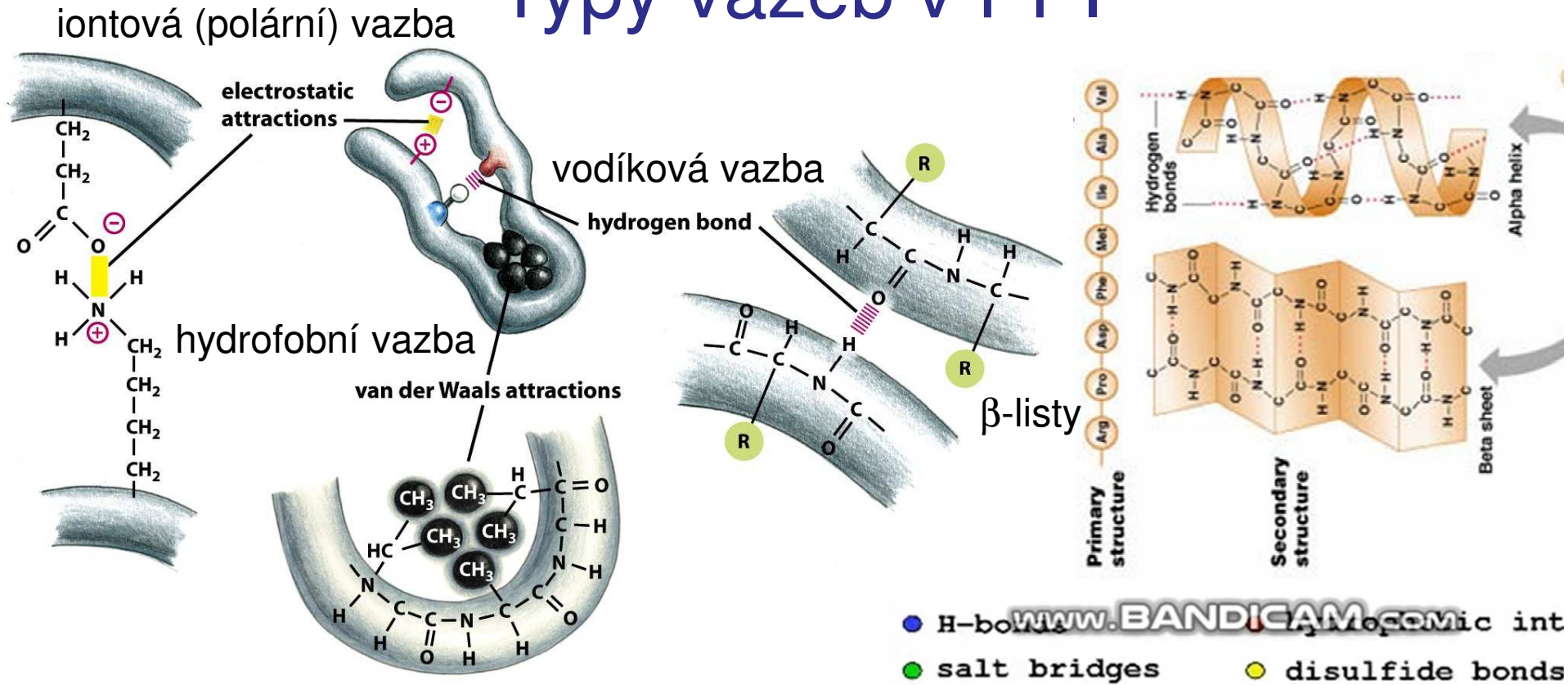
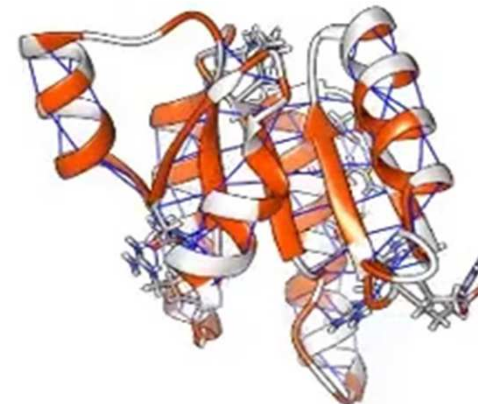


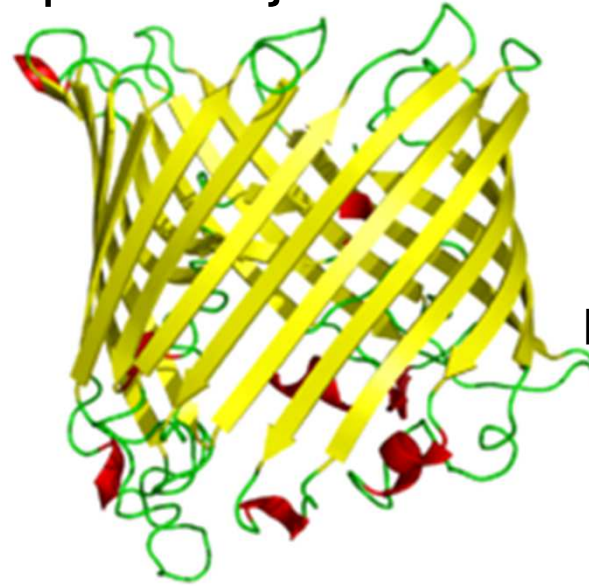
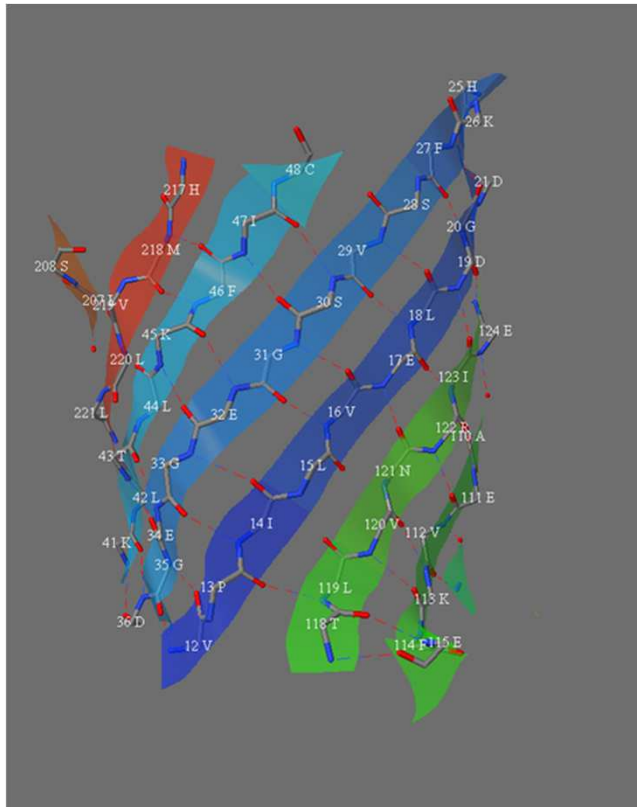
Figure 3-4 *Molecular Biology of the Cell* (© Garland Science 2008)

Kovalentní vazba = **modifikace**
 vyjimečně např. disulfidické můstky nebo jiné
 posttranslační modifikace (ubikvitinace,
 SUMOylace)



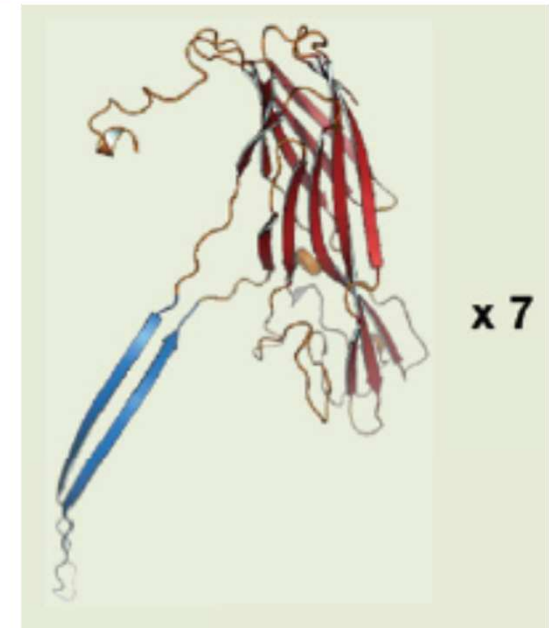
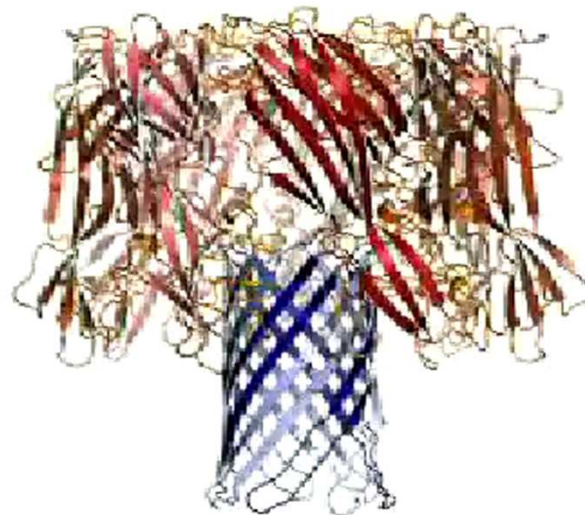
... sekundární struktury ...

V interakcích beta-listů převažují vodíkové vazby (peptidového řetězce)



Porin
(1 ORF - polypeptid
prostup mitochondriální
membrány)

Podobný „pór“ vzniká
interakcí 7 podjednotek

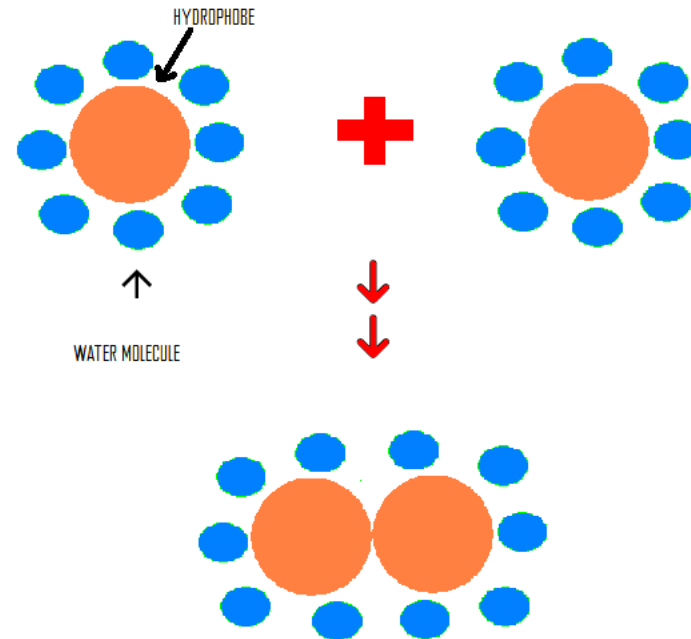
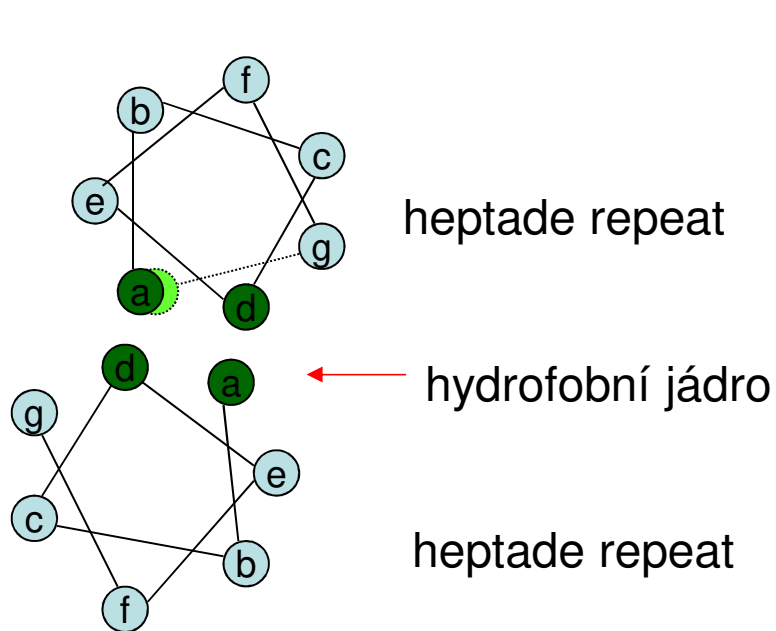


... sekundární struktury ...

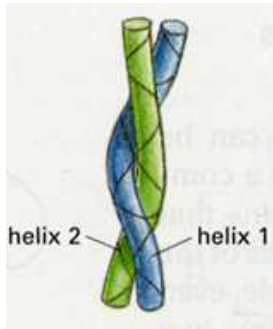
- šroubovice se vůči sobě orientují různým způsobem
- skládání slabých vazeb ovlivňuje sílu a specifitu celkové vazby

coiled-coil struktura

- dvě šroubovice s tzv. heptádovou repeticí (hxxhxxx – hydrofobní zbytky vytváří rozsáhlý povrch a tedy silnou vazbu)

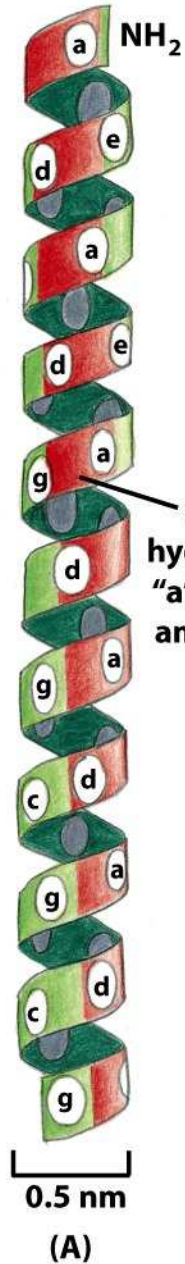


...LKSLHNQLRDLEESLTH...

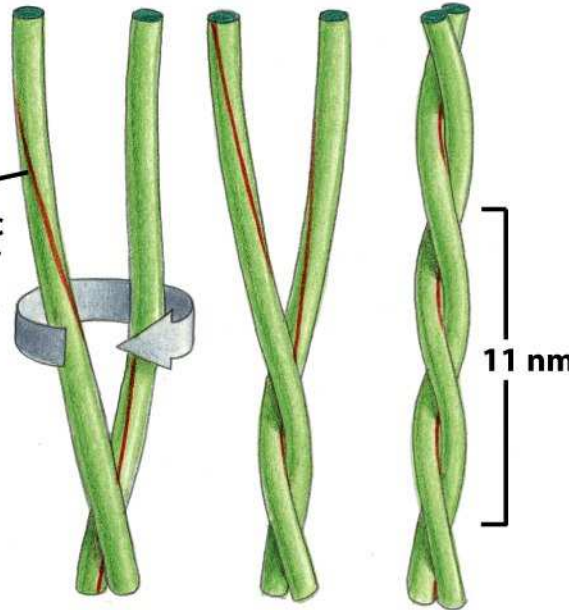


coiled-coil struktura

- dvě šroubovice s tzv. heptádovou repeticí (hxxhxxx – hydrofobní zbytky vytváří rozsáhlý povrch)



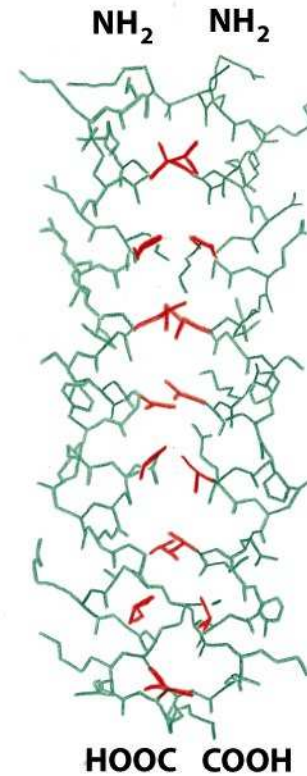
stripe of hydrophobic "a" and "d" amino acids



hydrofobní jádro

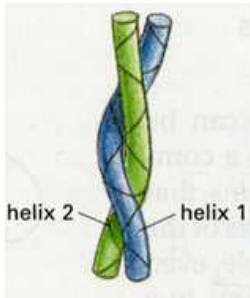
...LKS**L**HN**Q**L**R**D**L**EES**L**TH...

(B)



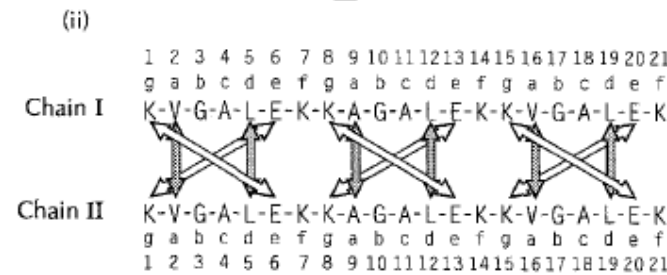
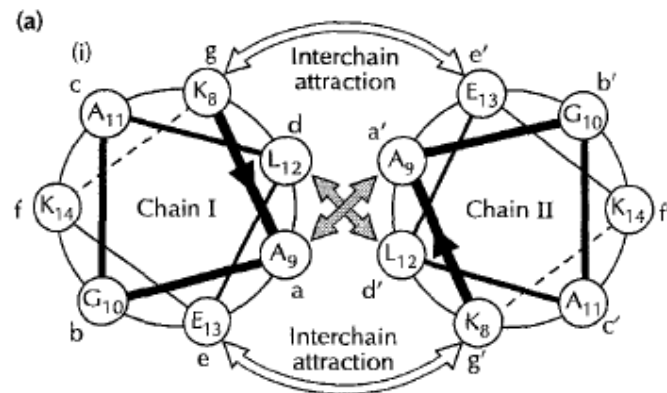
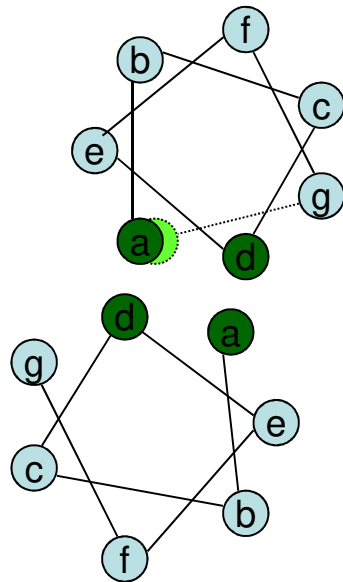
paralelní šroubovice

(C)

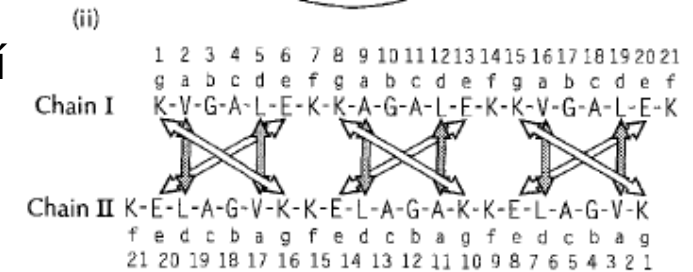
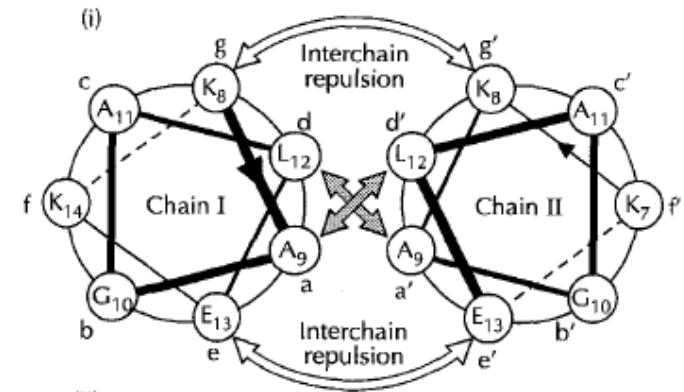


coiled-coil struktura

Síla interakce může být ovlivněna sousedními AMK

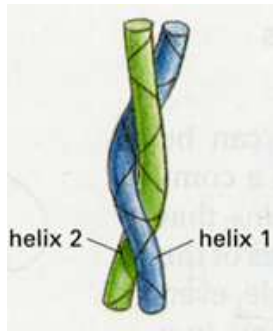


Sousední AMK stabilizují interakce šroubovic



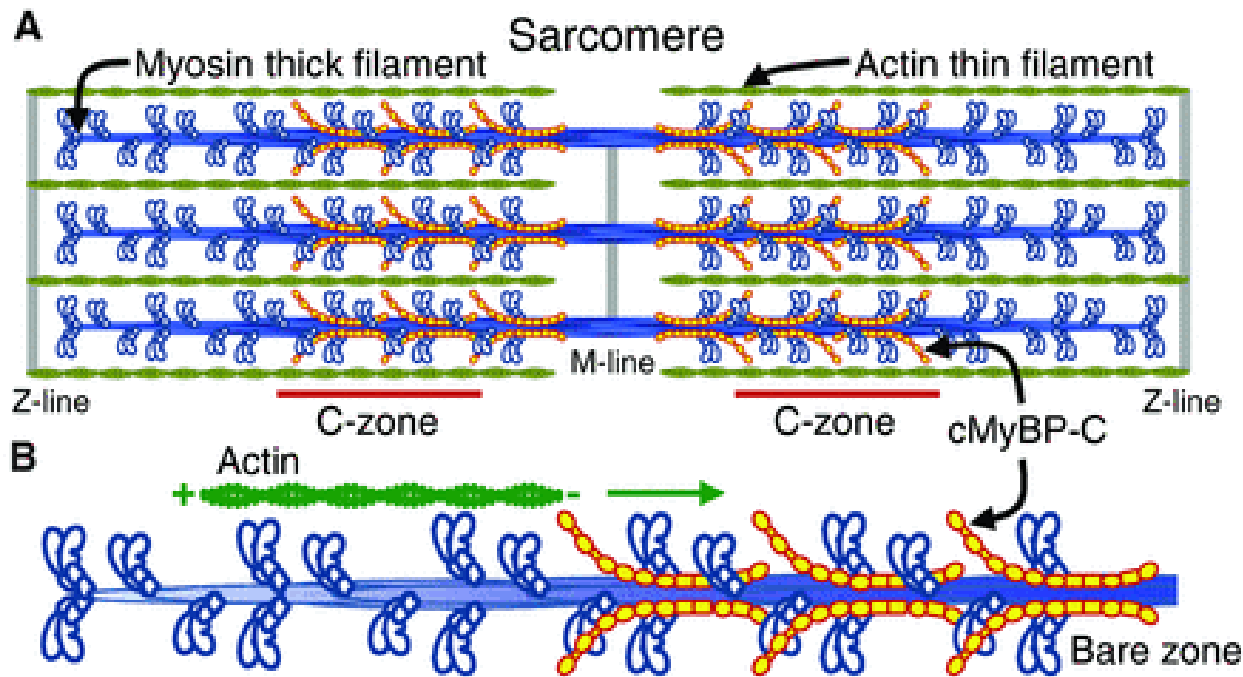
Sousední AMK destabilizují interakce šroubovic

Adamson et al.: CO in Biotech, 1993
Ivanov et al., PLoS One, 2017

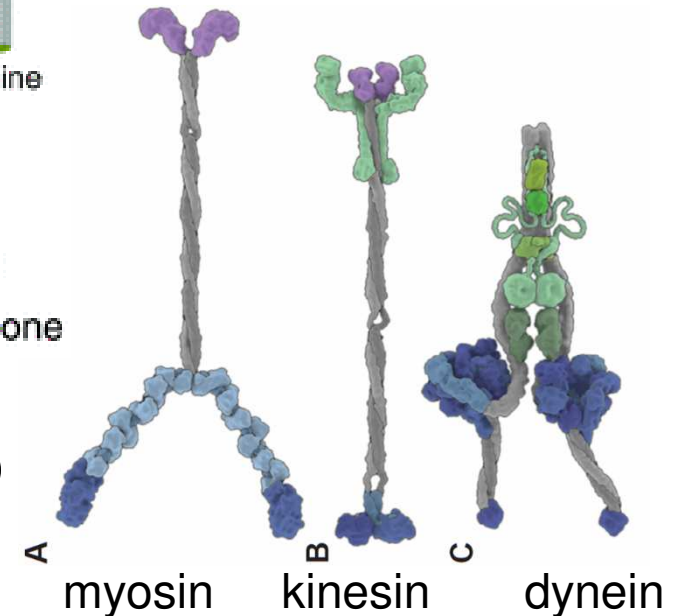


coiled-coil struktura

-dlouhé CC (>100AMK) vytváří vláknité struktury (myosin tvoří vlákna - svaly)



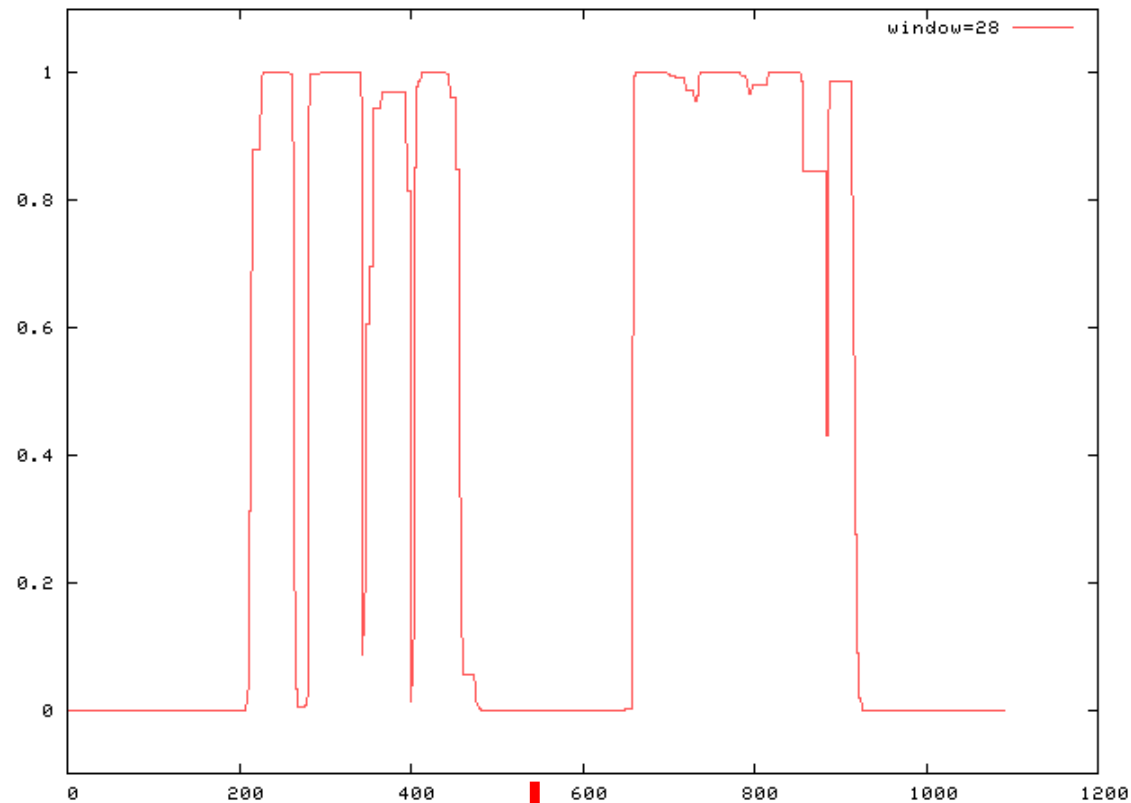
- CC v myosinu je intermolekulární (paralelní)



coiled-coil struktura

- program COIL: http://www.ch.embnet.org/software/COILS_form.html

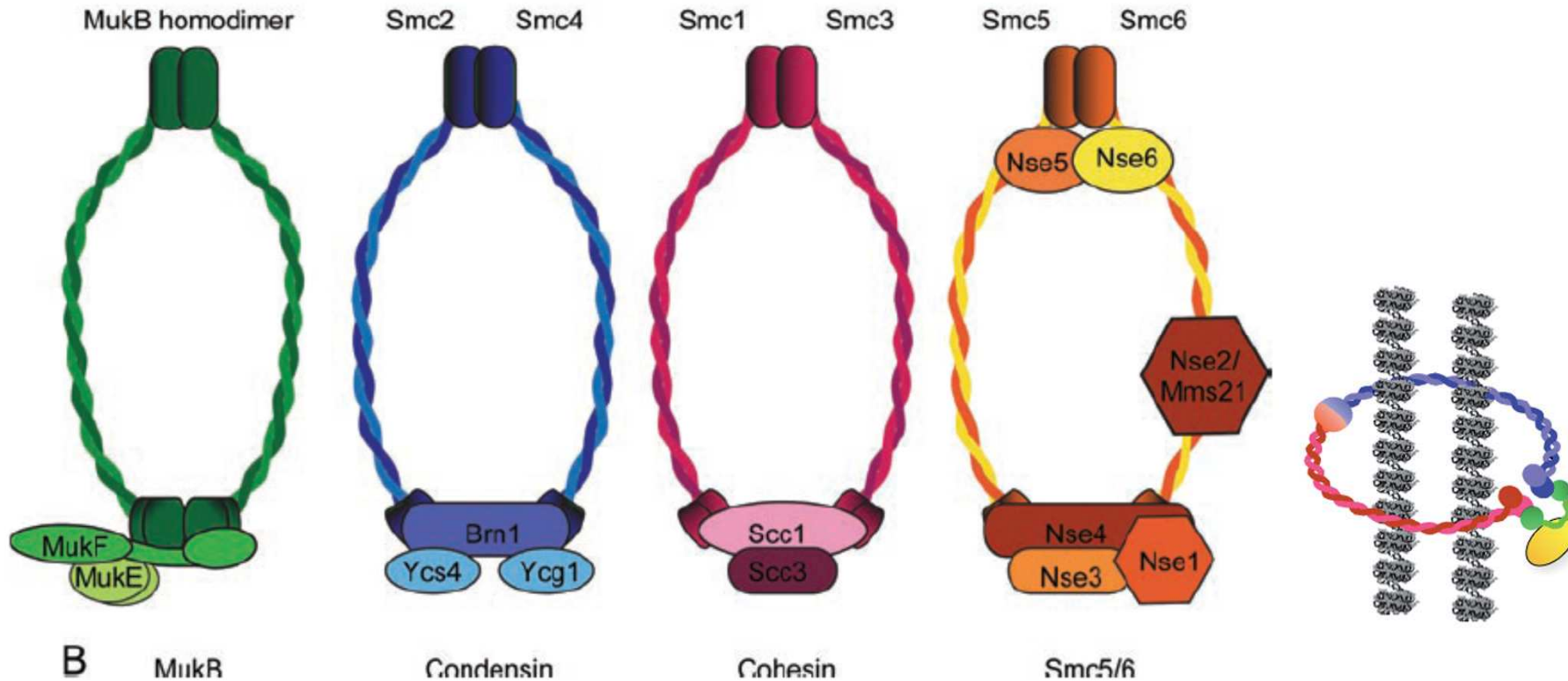
profil SMC6



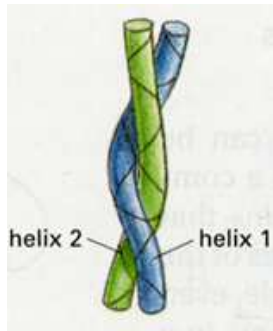
- CC v SMC proteinech jsou intramolekulární (antiparalelní)

coiled-coil struktura

-dlouhé CC (>100AMK) vytváří vláknité struktury (SMC kruhy obejmou DNA)

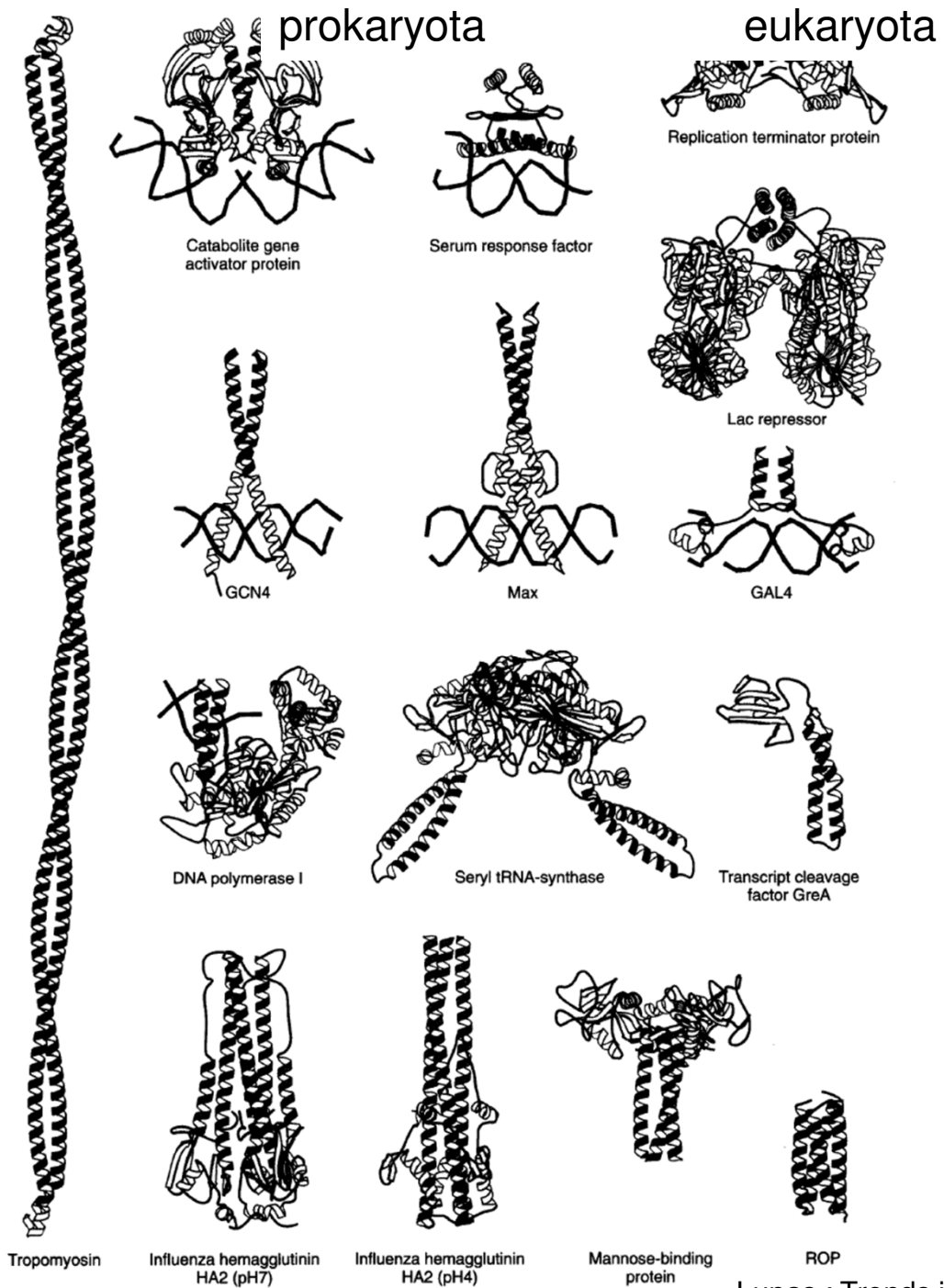


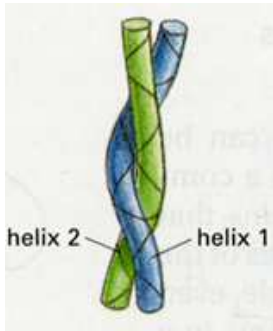
- CC v SMC proteinech jsou intramolekulární (antiparalelní)



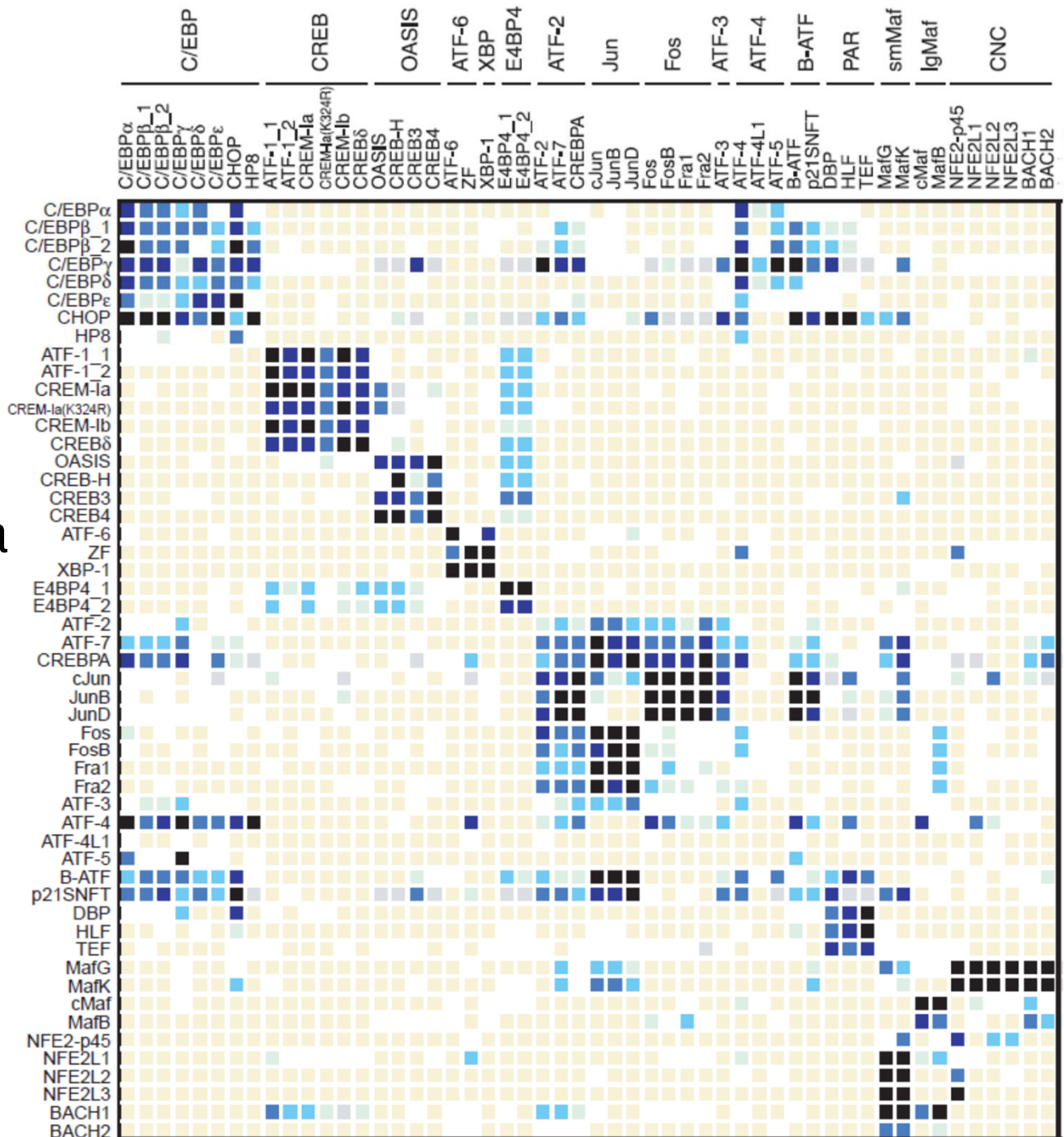
Coiled-coil
doména je
významným
dimerizačním
modulem u mnoha
proteinů (GCN4,
Max ...)

Intermolekulární -
homo- či
heterodimery
(oligomery)

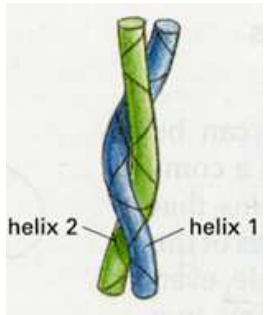




Coiled-coil
doména je
významným
dimerizačním
modulem u mnoha
proteinů: bZIP
transkripční
faktory vytváří
homo- i
heterodimery



Interakce šroubovic

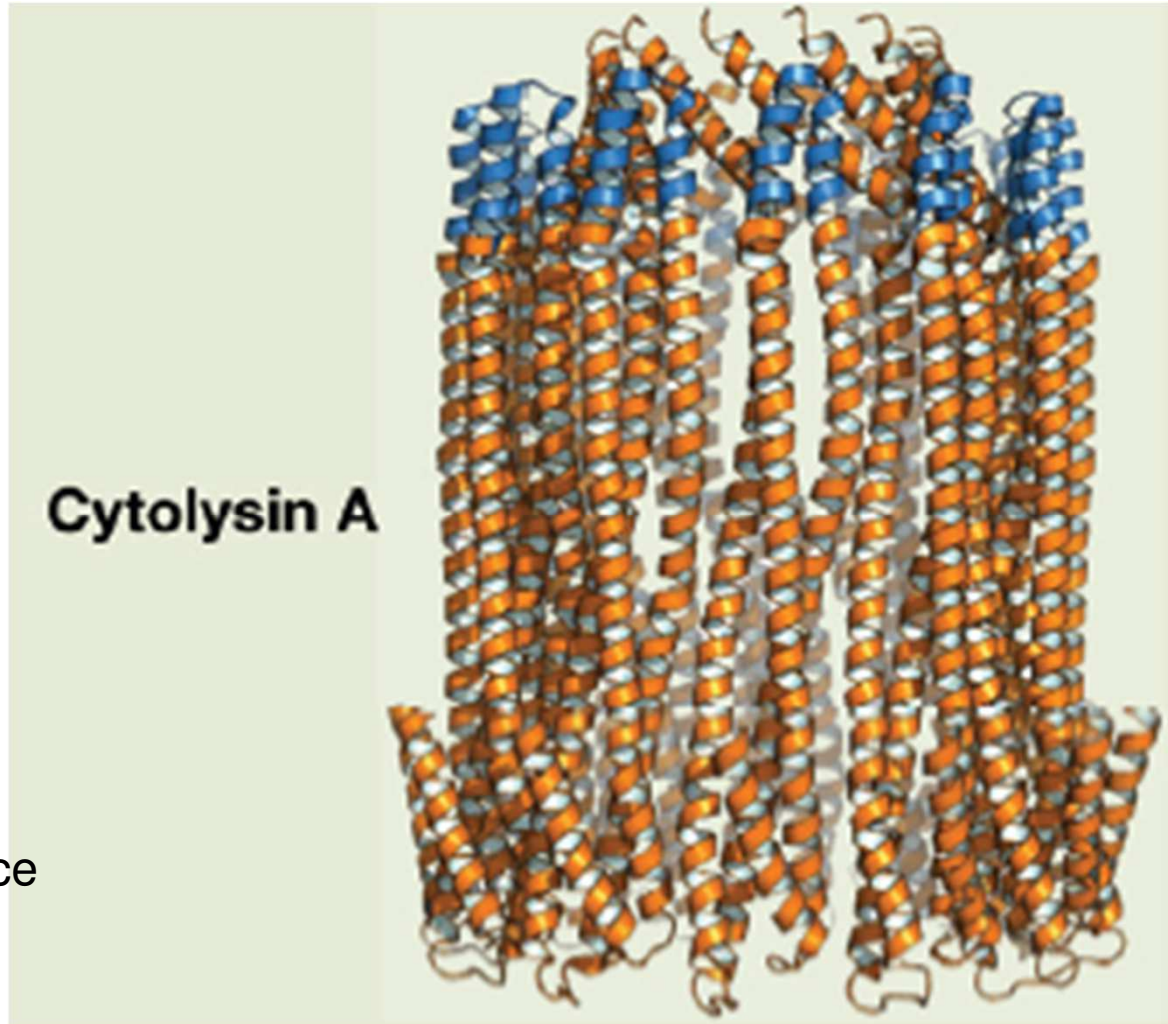


3 šroubovice



Influenza hemagglutinin

4 šroubovice



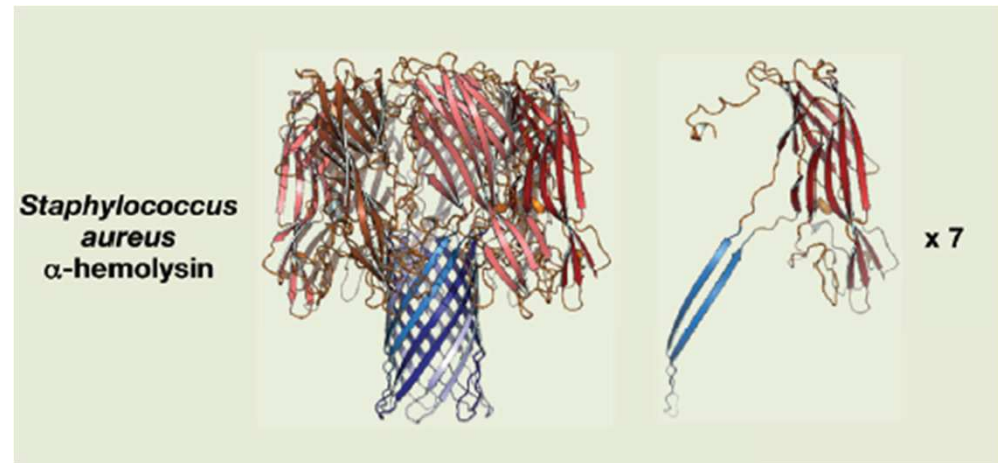
Cytolysin A

Cytolysin vytváří póry v membránách cizích buněk

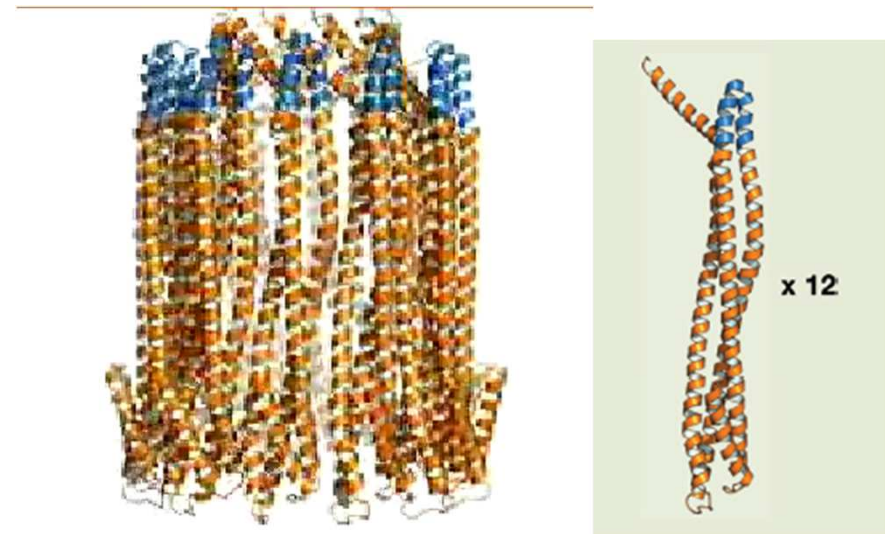
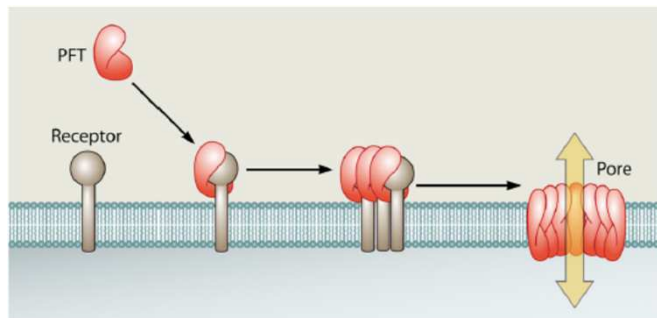
Šroubovice se pod určitým úhlem dotýkají - obtáčejí Mueller & Ban, Cell, 2010; 1QOY, 2WCD

... sekundární struktury ...

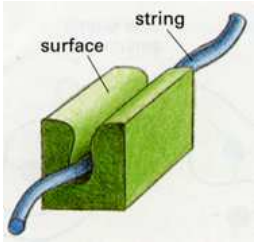
- **listy, šroubovice, smyčky**
... se podílí na protein-proteinových interakcích (PPI) podobným způsobem jako při skládání proteinu do 3D – podobné sterické faktory (listy vůči sobě, šroubovice vůči sobě)



- **foldingskládání** ... struktura některých „disordered“ proteinů se utváří až v rámci interakce s druhým proteinem

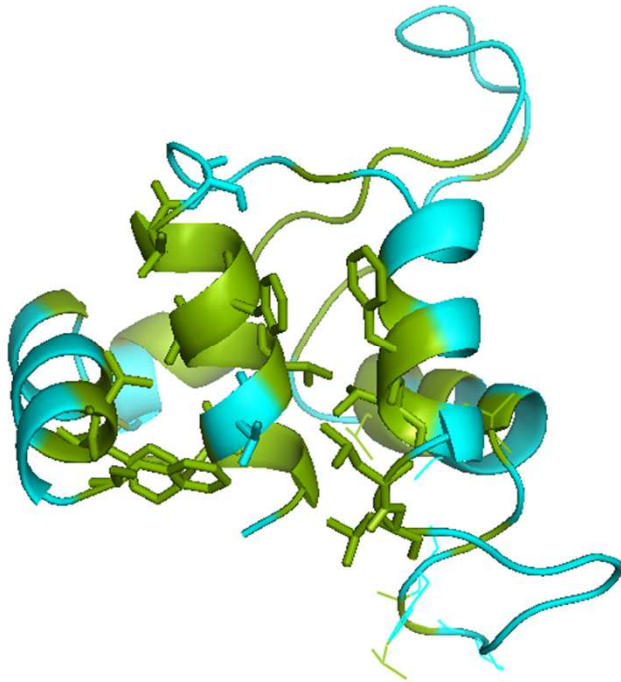
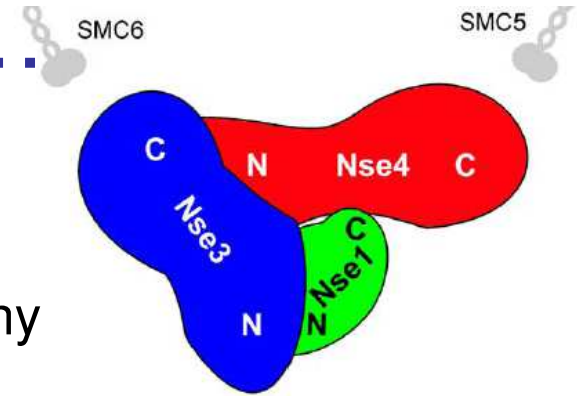


Toxiny – podjednotky se skládají tj. vytváří pór až v místě působení (neublíží původní buňce)

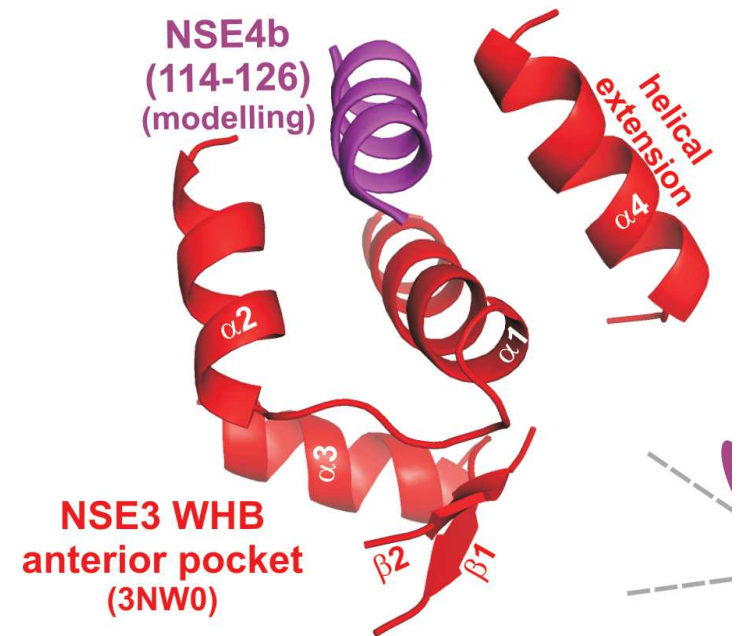


... terciární struktura ... kapsa-peptid

sekundární struktury (šroubovice, beta-listy)
interagují pod různými úhly a vytváří různé povrchy

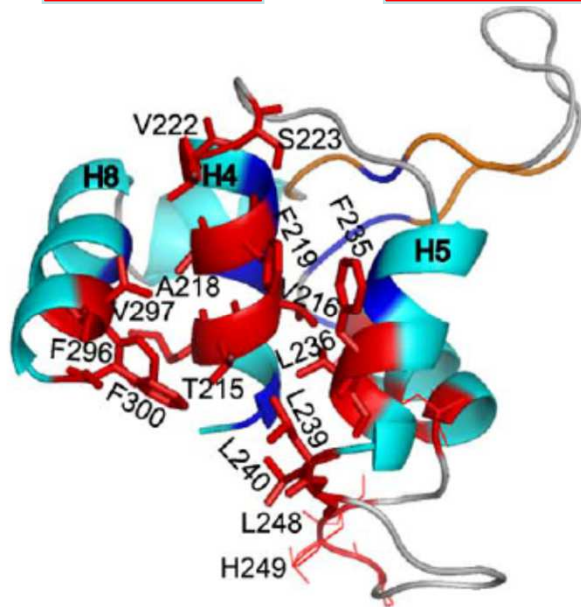
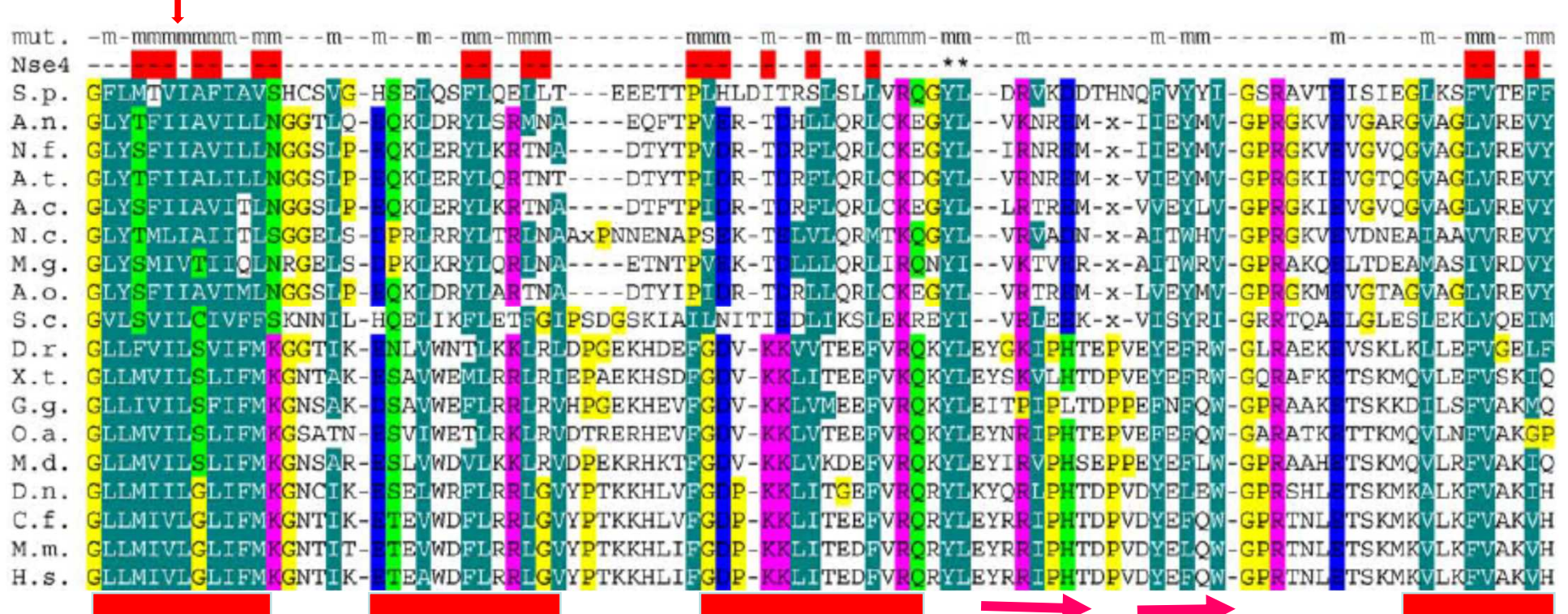


hlubší prohlubně na povrchu
mohou tvořit kapsy pro vazbu
partnera (šroubovice, peptid)

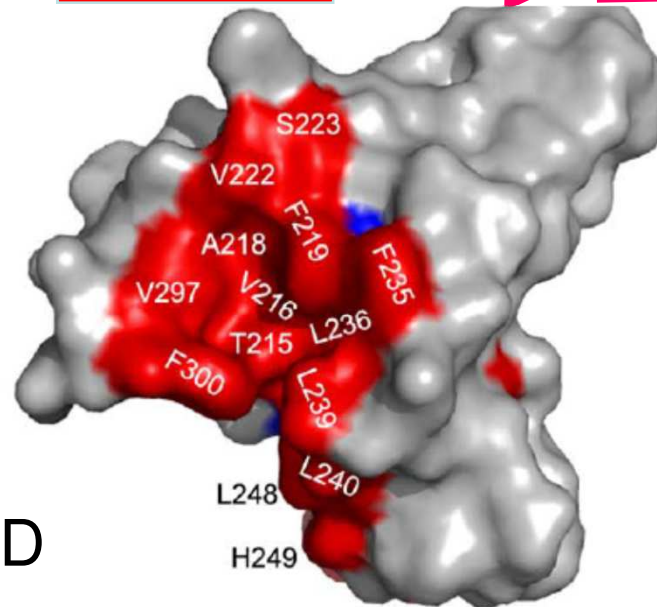


hydrofobní interakce mezi Nse3 a Nse4

Tato hydrofobní šroubovice není transmembránová, ale podílí se na protein-proteinové interakci (NSE3-NSE4)



WHD



Interakce
mapována
mutagenezí

v PDBsum můžete hledat kapsy (povrchy vhodné pro vazbu partnera) – musí mít **komplementární tvar a charakter** (terciární)

MAGEA4

PDBsum

Go to PDB code: 2wa0 go

Top page Protein **Clefts** Tunnels Links

Cleft analysis for: 2wa0 PDB id: 2wa0

WHD

View options

- Binding-site(s)
- Binding-surface(s)

Coloured by

- cleft (as in table below)
- closest atom type
- residue type
- residue conservation

Jmol RasMol

Clefts	Volume	R1 ratio	Accessible vertices	Buried vertices	Average depth	Residue type	Ligands			
1	2370.52	0.98	65.15	1	10.55	1	10.50	1	8 6 5 15 4 4 1	

největší kapsa

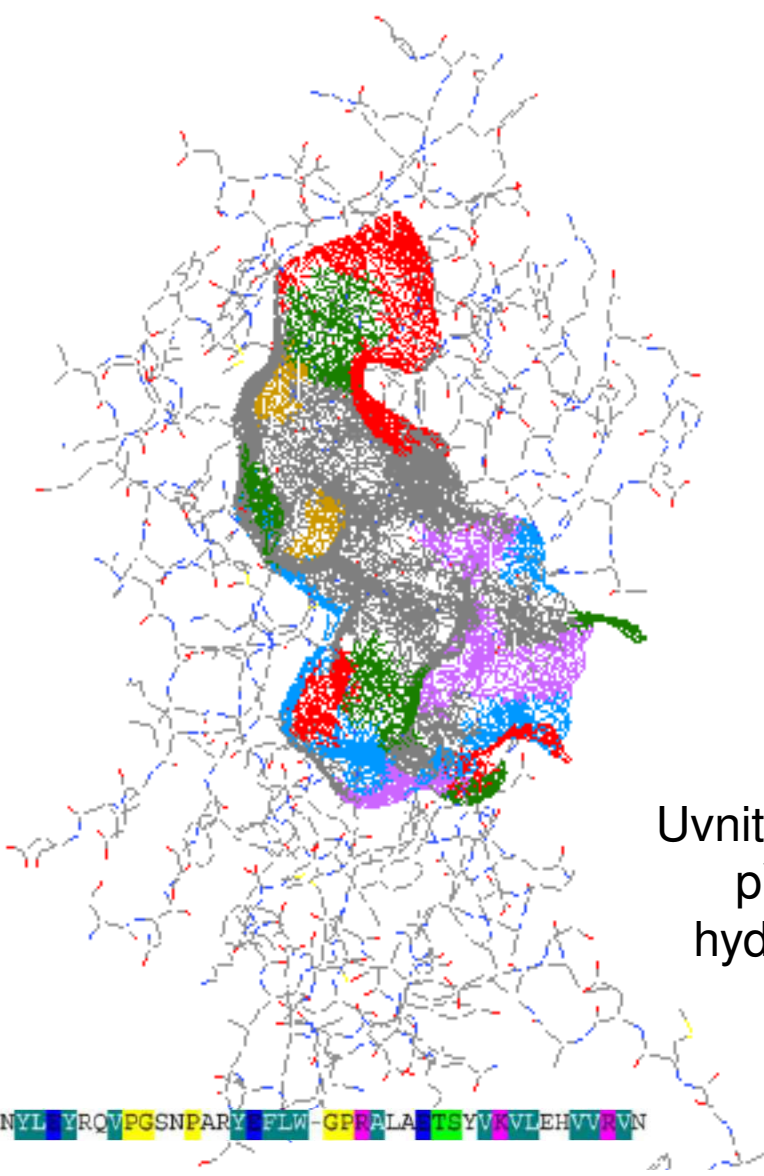
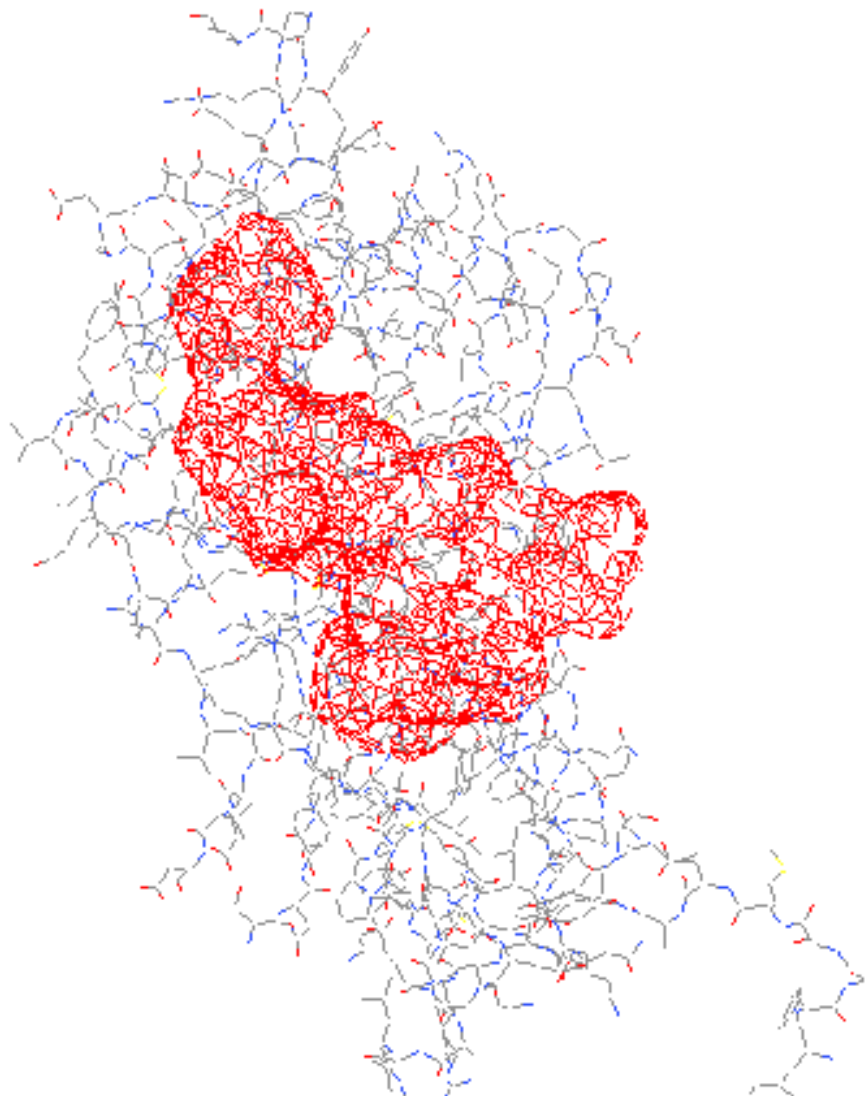
<http://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/>

Laskowski et al.: Prot Sci, 2018

Residue-type colouring						
Positive	Negative	Neutral	Aliphatic	Aromatic	Pro & Gly	Cysteine
H,K,R	D,E	S,T,N,Q	A,V,L,I,M	F,Y,W	P,G	C

Binding site

Binding surface



Uvnitř kapsy
převládá
hydrofobní
povrch

A4 GLLIIVLGTIAMEGDSAS-EEIWEELGVVGVYDGREHTVYGF-RKLLTQDWVQENYLVRQVPGSNPARYFLW-GPRALANTSYVAVLEHVVRVN

Residue-type colouring						
Positive	Negative	Neutral	Aliphatic	Aromatic	Pro & Gly	Cysteine
H,K,R	D,E	S,T,N,Q	A,V,L,I,M	F,Y,W	P,G	C


HADDOCK
Software web portal

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WELCOME TO THE UTRECHT BIOMOLECULAR INTERACTION WEB PORTAL >>


PROFILE >>

Universiteit Utrecht

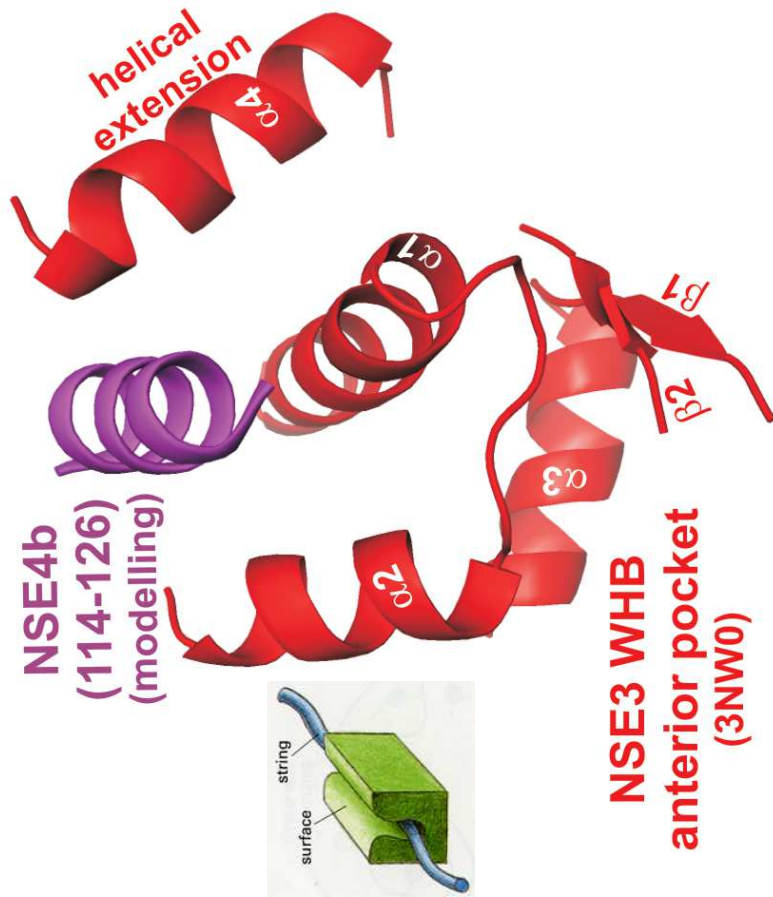


The Utrecht Biomolecular Interactions software portal provides access to software tools developed in the Computational Structural Biology group / NMR Research Group of Utrecht University with a main focus on the characterization of biomolecular interactions. Please note that this site is in active development.

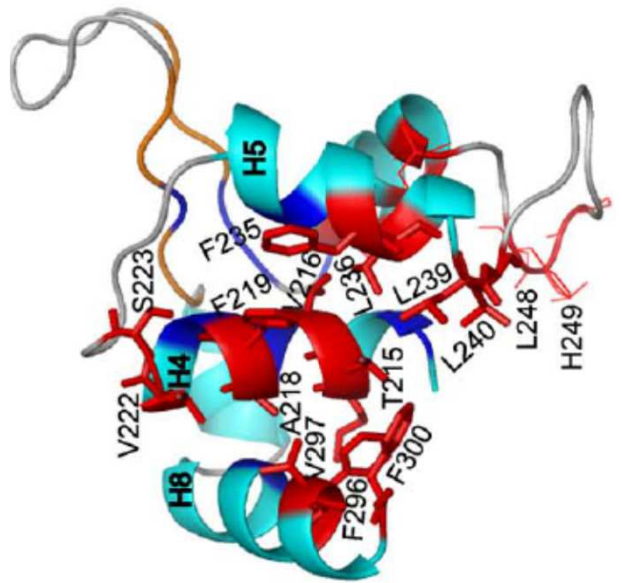
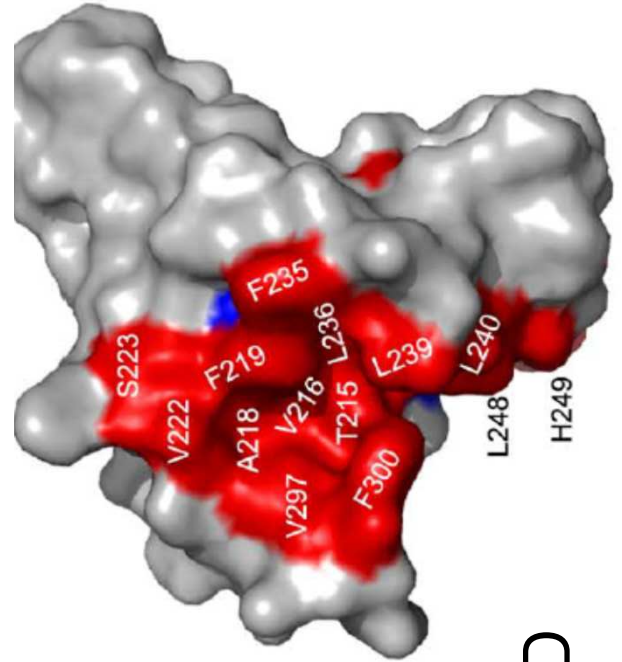
HADDOCK WEB DOCKING



HADDOCK (High Ambiguity Driven protein-protein DOCKing) is an information-driven flexible docking approach for the modeling of biomolecular complexes. HADDOCK distinguishes itself from ab-initio docking methods in the fact that it encodes



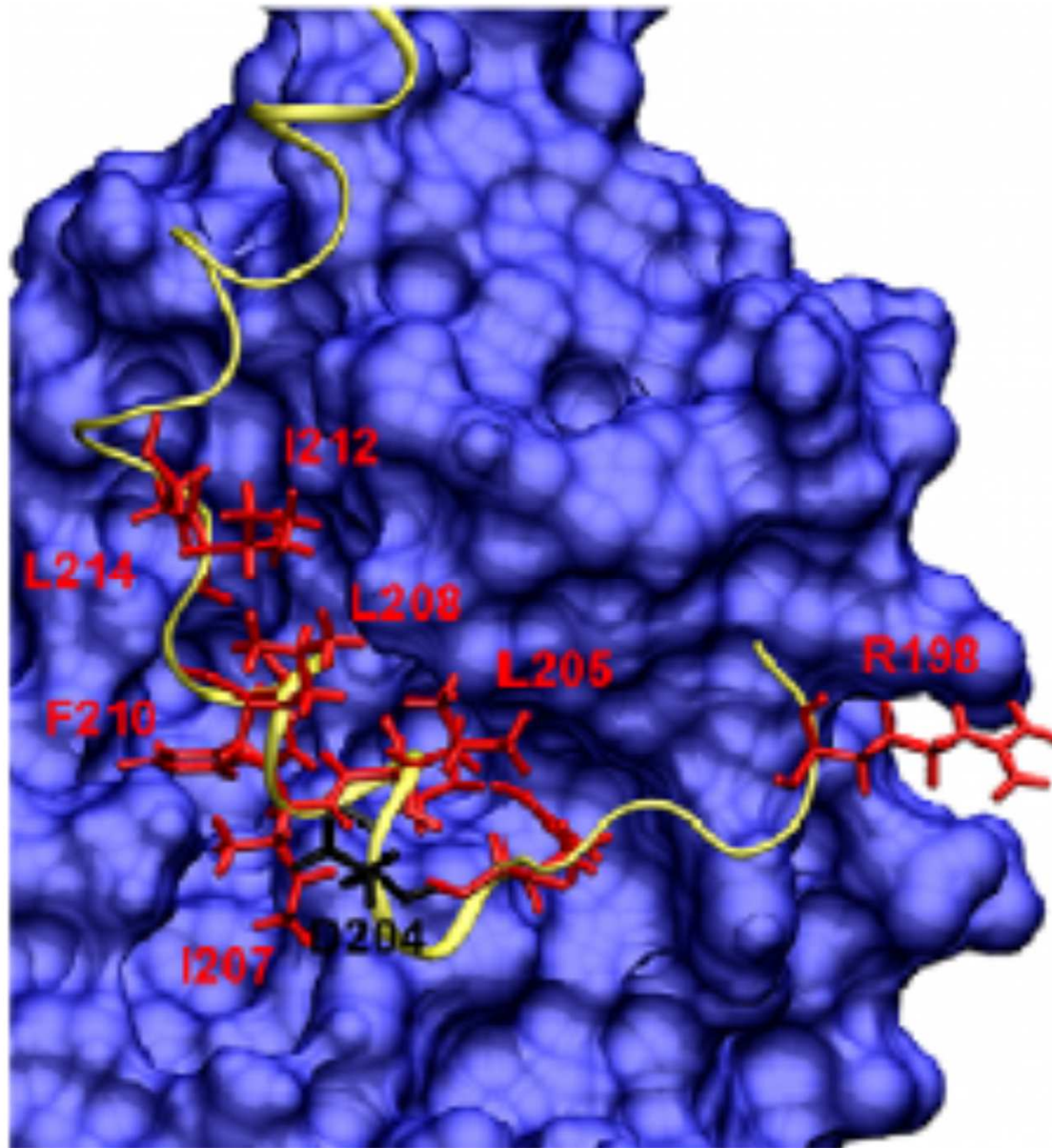
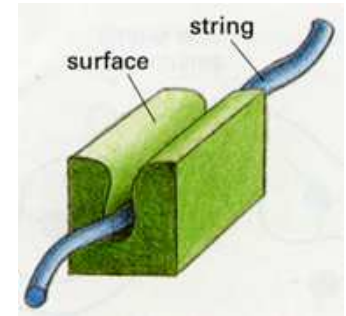
Docking



WHD

Interakce
mapována
mutagenézí

Hudson et al.: PLoS One, 2011
Guerineau et al.: PLoS One, 2012



de novo docking partnera
(HEX docking a
molekulární dynamika):
do hydrofobní kapsy
proteinu byl nadockován
„jednoduchý“ peptid (*de
novo* docking větších
povrchů je nespolehlivý)

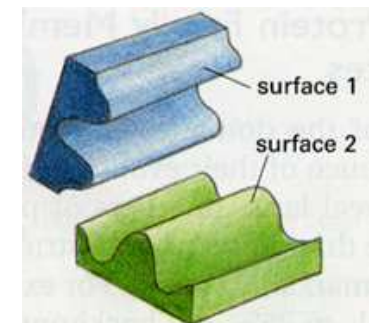
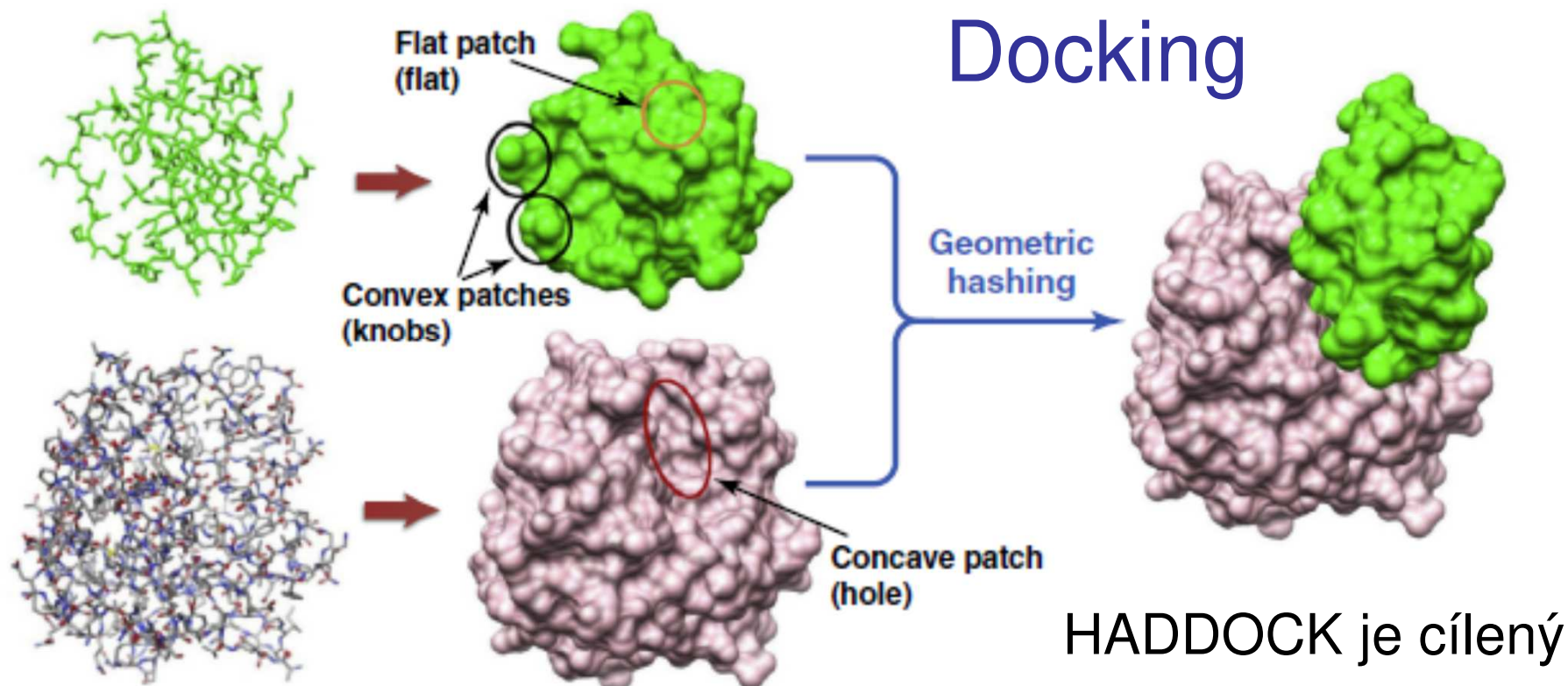
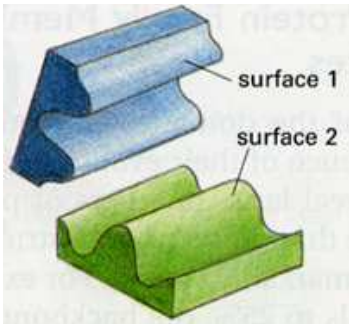


TABLE 1

Search strategies in protein-protein docking

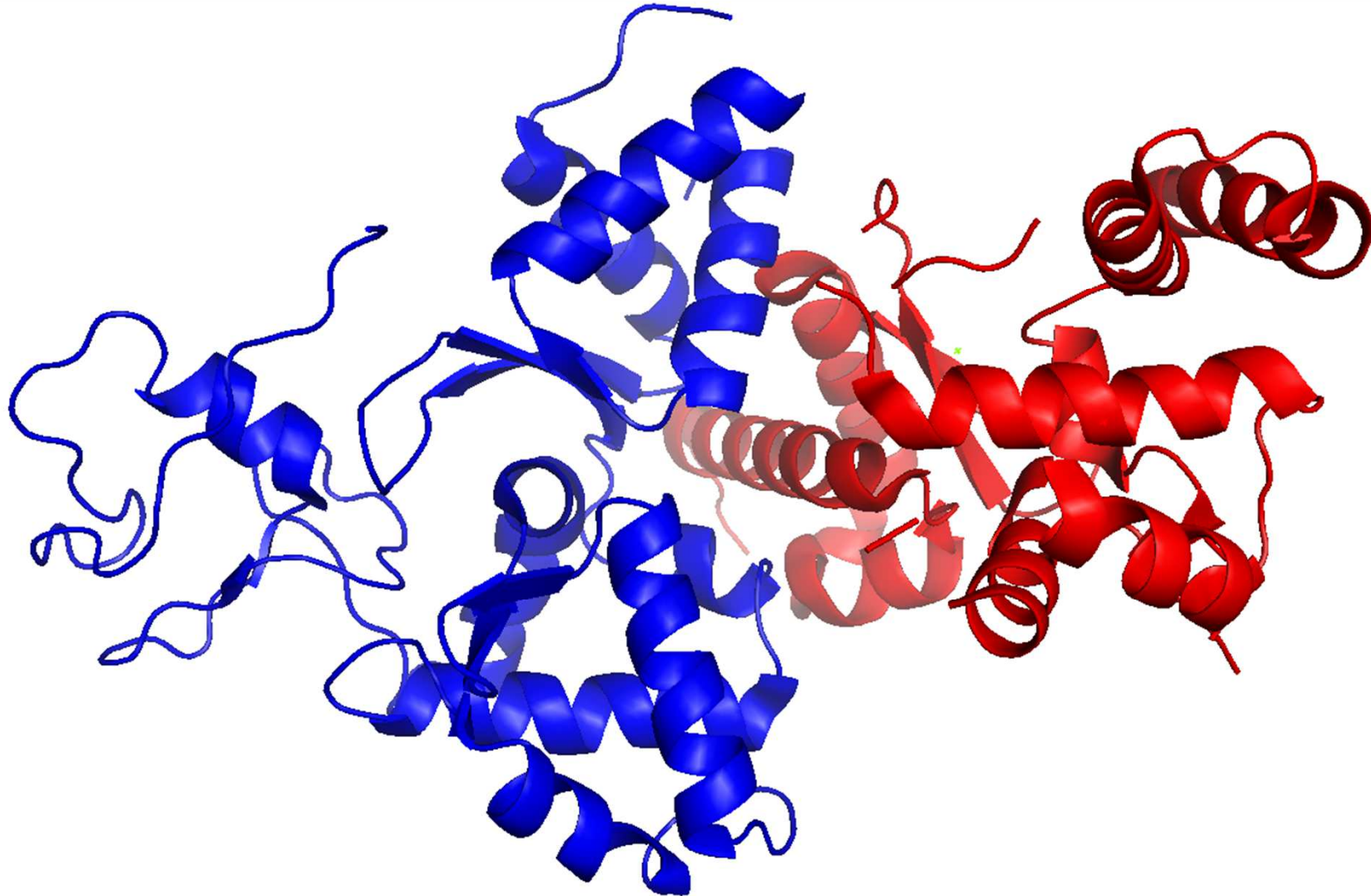
Search algorithms	Examples of docking programs	Refs
Exhaustive global search		
FFT-based search	FTDock, GRAMM, DOT, ZDOCK, MolFit, PIPER, F2DOCK, SDOCK, ASPDock, Cell-Dock	[25–41]
Spherical Fourier transform-based search	HEX, FRODOCK	[45–47]
Direct search in Cartesian space	SOFTDOCK, BIGGER, SKE-DOCK	[49–51]
Local shape feature matching		
Distance geometry algorithm	DOCK	[52]
Geometric hashing	PatchDock, SymmDock, LZerD	[53–56]
Genetic algorithm	GAPDOCK	[57]
Randomized search		
Monte Carlo search	RosettaDock, ICM-DISCO, ATTRACT, HADDOCK	[61–71]
Particle swarm optimization	SwarmDock	[72]
Genetic algorithm	AutoDock	[73]
Post-docking approach		
Using advanced scoring functions	RPScore, ZRANK, PyDock, EMPIRE, DARS, DECK, SIPPER, PIE, MDockPP, etc.	[81–94]
Considering protein flexibility	MultiDock, SmoothDock, RDOCK, FireDock, FiberDock, EigenHex, etc.	[95–104]
Other ranking protocols	SDU, CyClus, CONSRANK, etc.	[105–111]

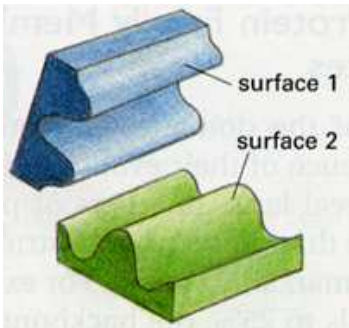




DOMÉNY - šroubovice, β -listy ... interagují pod různými úhly a vytváří různé vazebné motivy s rozsáhlými vazebnými povrchy

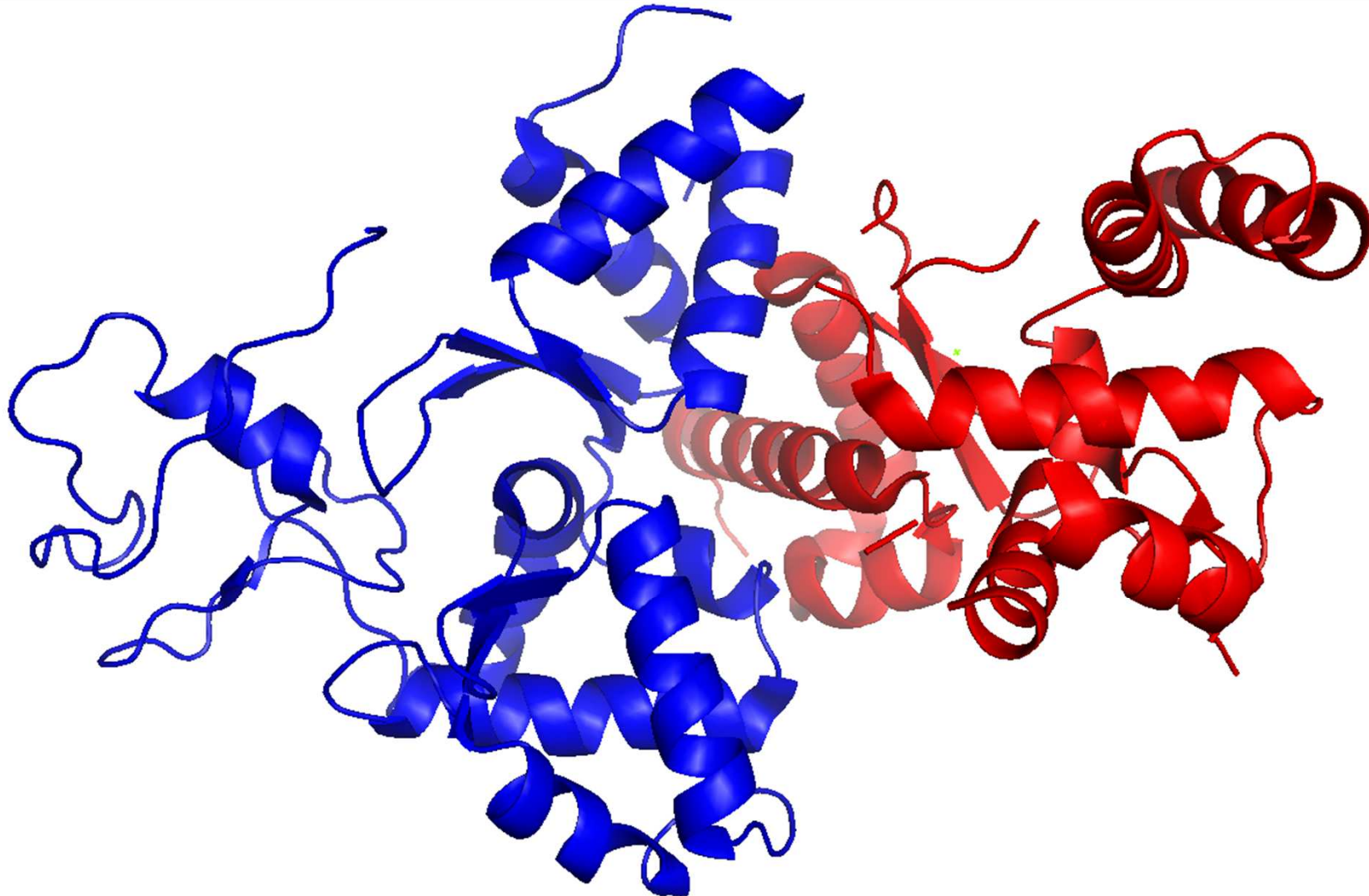
(kokrystal NSE1-NSE3 proteinů)





nejlépe lze získat info (vizuální, o typech vazby)
z vyřešených struktur (PDBsum, 3DID - databáze)

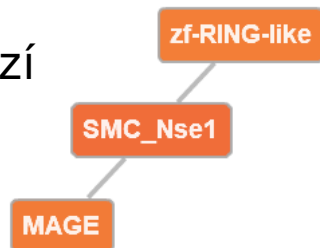
(kokrystal NSE1-NSE3 proteinů)



Domain SMC_Nse1 (Pfam: PF07574.11)

GO terms: P GO:0006281 DNA repair C GO:0030915 Smc5-Smc6 complex

integrace PDB,
PFAM a GO databází



D F C P Default color scheme

Interacting domains (2 domains)

MAGE

zf-RING-like

HMM profile interface residues in SMC_Nse1 (2 interfaces)

HMM prof. interface res.

Binding partner(s)

MAGE

zf-RING-like

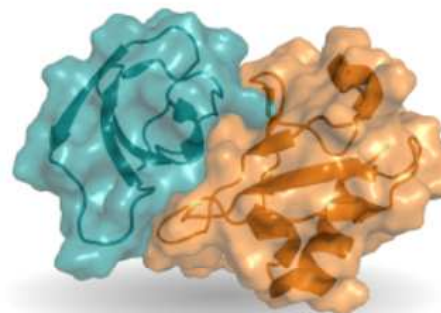
Search motif by name or keyword: ?

Motif name (e.g. SH2_LIG_0)

Search motif



<https://3did.irbbarcelona.org/>

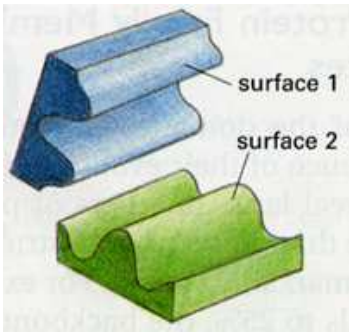


- > **Overview** General information on 3did
- > **Getting Started** Help for new users
- > **Technical Information** Linking to 3did
- > **Download** data files or MySQL tables

Statistics

Pfam version	30.0
PDB version	2017_06
Domain-domain interactions	11200
Motifs in interactions of known 3D structure	702

3DID kategorizuje doména-doména interakce z PDB (06/2017 – cca 10000 doména-doména komplexů/100000 struktur) – topologie ne detaily



PDBsum – detailní info

<http://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/GetPage.pl?pdbcode=index.html>

(kokrystal NSE1-NSE3 proteinů)

[Top page](#)
[Protein](#)
[Metals](#)
Prot-prot
[Clefs](#)
[Tunnels](#)
[Links](#)
PDB id 3nw0

Protein-protein interface: A}B

Protein-protein interface: A}B
NSE1-NSE3

Chain A
Chain B

Key:

— Salt bridges

— Disulphide bonds

— Hydrogen bonds

— Non-bonded contacts

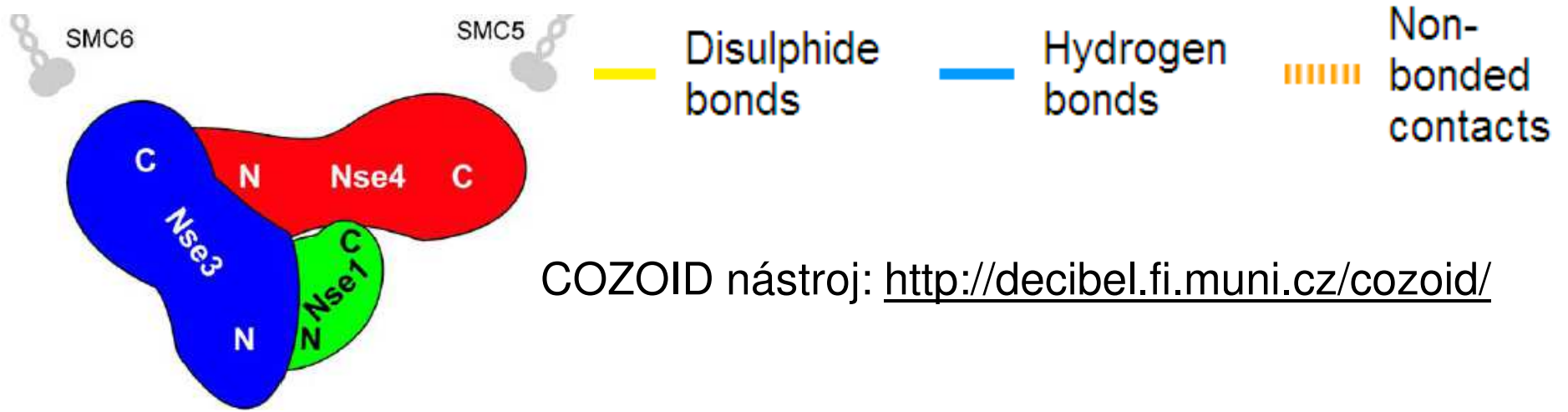
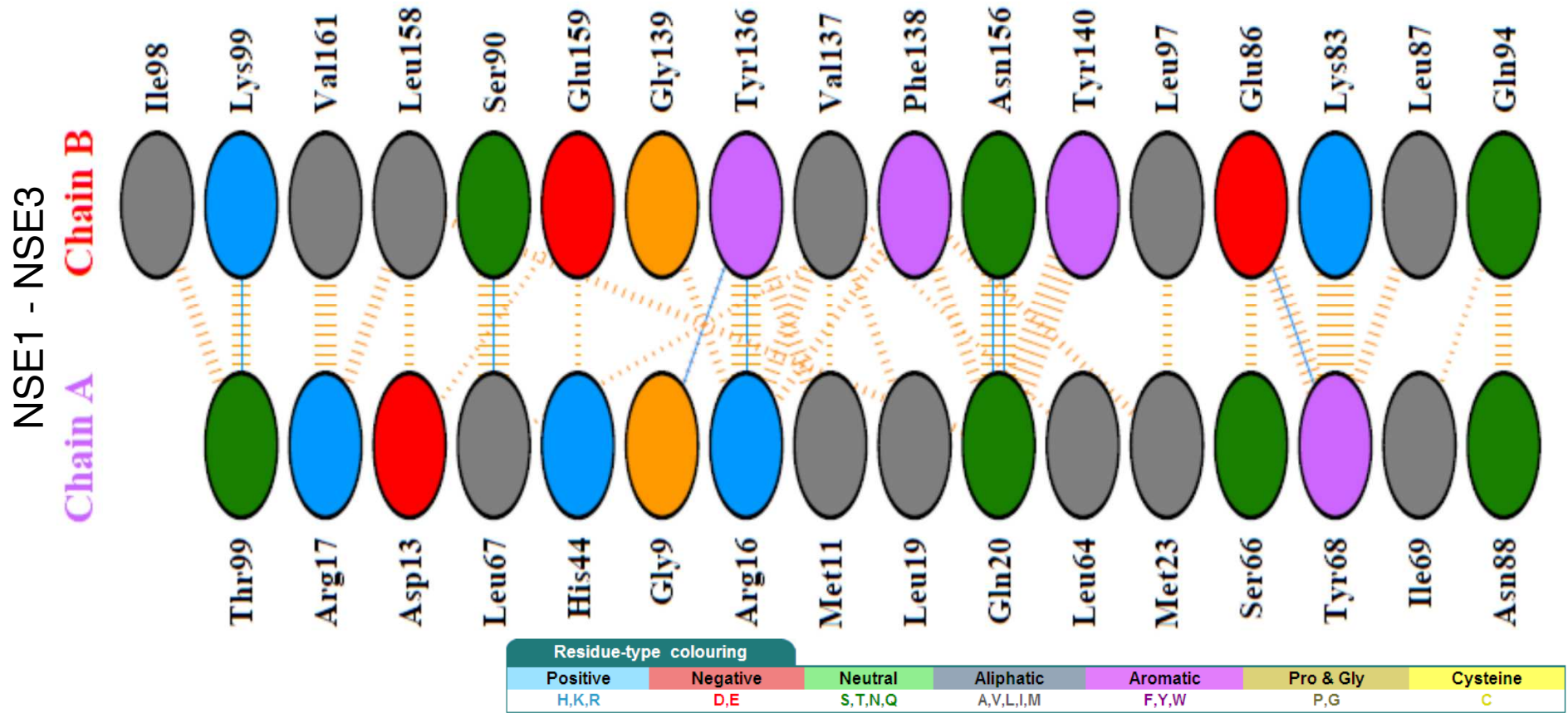
Interfaces

A}B (16:17 res)

Interface statistics

Chain	No. of interface residues	Interface area (Å ²)	No. of salt bridges	No. of disulphide bonds	No. of hydrogen bonds	No. of non-bonded contacts
A	16	1015	-	-	7	100
B	17	1003	-	-		

Silná interakce mezi NSE1 (chain A) a NSE3 (chain B)



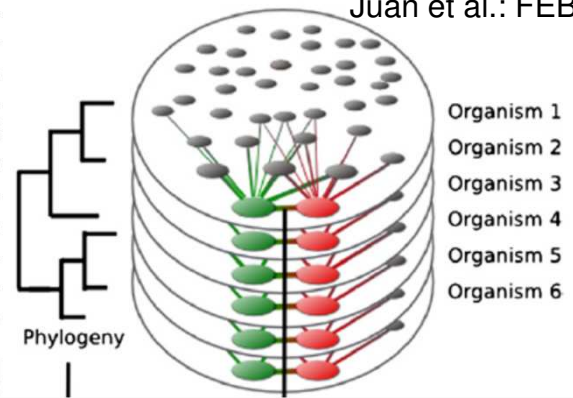
COZOID nástroj: <http://decibel.fi.muni.cz/cozoid/>

```

A1CCH2_ASPCL/14-216   NRAFLQAFM.ARSTMTFAEAKPVLAAIF.SAH.....
A2Q7K6_ASPNC/15-218   NRAFLQAFM.ARSTMTFTQAKPVLAAIF.SIR.....
B8NLA5_ASPFN/14-216   NRAFLQAFM.ARSTMTFAEARPVLAAIF.SVH.....
B6QTR9_TALMQ/14-217   NRAFLQAFM.ARSTMTFDEAKPVLAAIF.SAQ.....
V5FED6_BYSSN/14-236   NRAFLQAFM.ARSTMTFEEAKPVLAAIF.SAHGAQSTIFFDS
S7Z8E9_PENO1/8-209    HRAFLQAFM.ARSTMTFEDAQPVLAAII.SAH.....
B6H9Q9_PENRW/8-210    NRAFLQAFM.ARSCMTFEDAQPILAAIL.TVS.....
H6C926_EXODN/14-207   NRAFLQAFM.ARSVLTLETAKPILAAS.TFQ.....
U1GD89_ENDPU/11-202   NRAFLQAFM.ARGTLTYETSKPLLASIF.TVH.....
C5GY37_AJEDR/11-207   HRAFLQAFM.ARSTMTYEQAKPVLAAIF.SAR.....
C6H5E2_AJECH/11-203   HRALLOAFM.ARSTMTYEOAKPVLAAIF.TAR.....

```

Juan et al.: FEBS Lett, 2008



Browser address bar: http://pfam.xfam.org/family/PF07574#tabview=tab1

EMBL-EBI  **PFAM – databáze proteinových motivů** 

Nse1 motiv


Family: **SMC_Nse1 (PF07574)**


16 architectures | 522 sequences | 2 interactions | 443 species | 1 structure


- Summary
 - Domain organisation**
 - Clan
 - Alignments
 - HMM logo
 - Trees
 - Curation & model
 - Species
 - Interactions
 - Structures
- Jump to...

Domain organisation

Below is a listing of the unique domain organisations or architectures in which this domain is found. [More...](#)

There are 393 sequences with the following architecture: SMC_Nse1, zf-RING-like
[W9YTD0_9EURO](#) [Capronia epimyces CBS 606.96] Uncharacterized protein {ECO:0000313|EMBL:EXJ92910.1} (323 residues)

[Show](#) all sequences with this architecture.

There are 102 sequences with the following architecture: SMC_Nse1
[R1GGR5_BOTPV](#) [Botryosphaeria parva (strain UCR-NP2) (Grapevine canker fungus) (Neofusicoccum parvum)] Putative dna repair protein {ECO:0000313|EMBL:EOD47456.1} (255 residues)

[Show](#) all sequences with this architecture.

There are 6 sequences with the following architecture: SMC_Nse1 x 2, zf-RING-like
[NSE1_XENTR](#) [Xenopus tropicalis (Western clawed frog) (Silurana tropicalis)] Non-structural maintenance of chromosomes element 1 homolog EC=6.3.2.- (270 residues)

[Show](#) all sequences with this architecture.

There are 2 sequences with the following architecture: DAO, SMC_Nse1, zf-RING-like
[B8MNY1_TALSN](#) [Talaromyces stipitatus (strain ATCC 10500 / CBS 375.48 / QM 6759 / NRRL 1006) (Penicillium stipitatum)] FAD dependent oxidoreductase superfamily {ECO:0000313|EMBL:EEF14330.1} (744 residues)

A1CCH2_ASPCL/14-216	NRAFLQAFM	ARSTMTFAEAKPVLAALIF.SAH.....EG.....QPVSA...DDVTE
A2Q7K6_ASPNC/15-218	NRAFLQAFM	ARSTMTFTQAKPVLAALIF.SIR.....DD.....EQVSP...EDITE
B8NLA5_ASPFN/14-216	NRAFLQAFM	ARSTMTFAEARPVLAALIF.SVH.....EG.....EPVSA...EDVTE
B6QTR9_TALMQ/14-217	NRAFLQAFM	ARSTMTFDEAKPVLAALIF.SAQ.....EN.....REVLA...EDITQ
V5FED6_BYSSN/14-236	NRAFLQAFM	ARSTMTFEEAKPVLAALIF.SAHGAQSTIFFDSSSYVEKEIANLYLATER.....RPVLA...EDITQ
S7Z8E9_PENO1/8-209	HRAFLQAFM	ARSTMTFEDAQPVLAAII.SAH.....EG.....RTVDP...DEVTE
B6H9Q9_PENRW/8-210	NRAFLQAFM	ARSCMTFEDAQPILAAIL.TVS.....EG.....RTVDP...DEVGE
H6C926_EXODN/14-207	NRAFLQAFM	ARSVLTLETAKPILAALIS.TFQ.....DG.....REVQP...QDMTV
U1GD89_ENDPU/11-202	NRAFLQAFM	ARSTMTYEQAQPVLAALIF.SAR.....DH.....QDTLP...EDITQ
C5GY37_AJEDR/11-207	HRALLQAFM	ARSTMTYEQAQPVLAALIF.TAR.....DN.....QETLP...EDITQ
C6H5E2_AJECH/11-203	HRAFLQAFM	SRSTMTLEEAKPVLAALIF.TVS.....EG.....REILP...GDITQ
F2PT91_TRIEC/10-199	HRAFLQAFM	ARSTMTLNEAKPILAAIL.SVK.....DG.....REVLP...EDVTQ
E9DEJ9_COCPS/13-202	HRAFLQAFM	ARSVLTFEEAQPILAAIL.TAH.....EG.....RPTLP...ADITT
R7Z157_CONA1/13-202	HRALVQAFM	ARSSMTGEELLGVVTAIH.GVE.....NPEEP...TETTL
U4LU38_PYROM/8-205	HRTFLQALL	IRPFIDIEEGQELLAALIA.SAE.....SG.....TDVPA...NSITV
S8AAF4_DACHA/9-208	HRAFLQALL	IRPFIDVQEGRELLAAIK.SAE.....AG.....SDVSI...ESVPP
G1X2Y0_ARTOA/8-207	SKFLLQYVL	RRGVCSEKALAKAKLTL.....ERDG.....EQLEDSETE
C5DCF6_LACTC/23-226	ARYLLQYLL	CRGICHENMLLVLDKL.....QK.....YTQDPTSQVCS.T
C5DQF6_ZYGR/37-240	RHLLRYIM	SEGICHENMLLLALYAL.....NLDYSGDCQQEVLA.....
I2H1A9_TETBL/24-252	RYLLQYLL	CGICNESFMLLALMRLH.....LTDGSSSDDFYRLNMVELN
G8C139_TETPH/22-276	RIVLQYIL	SRGIVGENILLALMRL.....QGDT...ETND...VQELY
G8ZVJ6_TORDC/16-236	RYLLQYIL	ARGICHENALVVALMRL.....YMDL...GCFDDAWQIDQWL
H2ATC7_KAZAF/7-237	RYLLQYIL	ARGICHENNLILALMKL.....ETDA.....SKWSTEQWT
J5S7B7_SACK1/17-253	RYLLQYIL	ARGICHENALILALMRL.....ETDA...STLNTXSIQQWV
E7NKI9_YEASO/18-258	RYLLQYIL	ARGICHENALILALMRL.....ETDA...LRFDAERSMQQWI
J8PZG2_SACAR/18-258	RYLLQYIL	ARGVCHENALVVALMRL.....KVDS...NTIDPQWTISDWL
G0W7Y8_NAUDC/22-268	RYLLQYIL	ARGVCHENALMLALMRL.....KVDS...HDVNAHWTISDWL
G0V5G7_NAUCC/25-272	RYLLQYIL	ARGVCHENSLLAALMHL.....SLDLDPHSVSTR.SLDEWS
J7S9R2_KAZNA/85-303	RYLLQYIL	CRGICHENALLVLIKL.....DKDSVDEEGSPNRTFEDYL
A7TJ64_VANPO/8-260	RYLLQYIL	CRGICHENALLVLIKL.....DKDSVDEEGSPNRTFEDYL

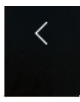
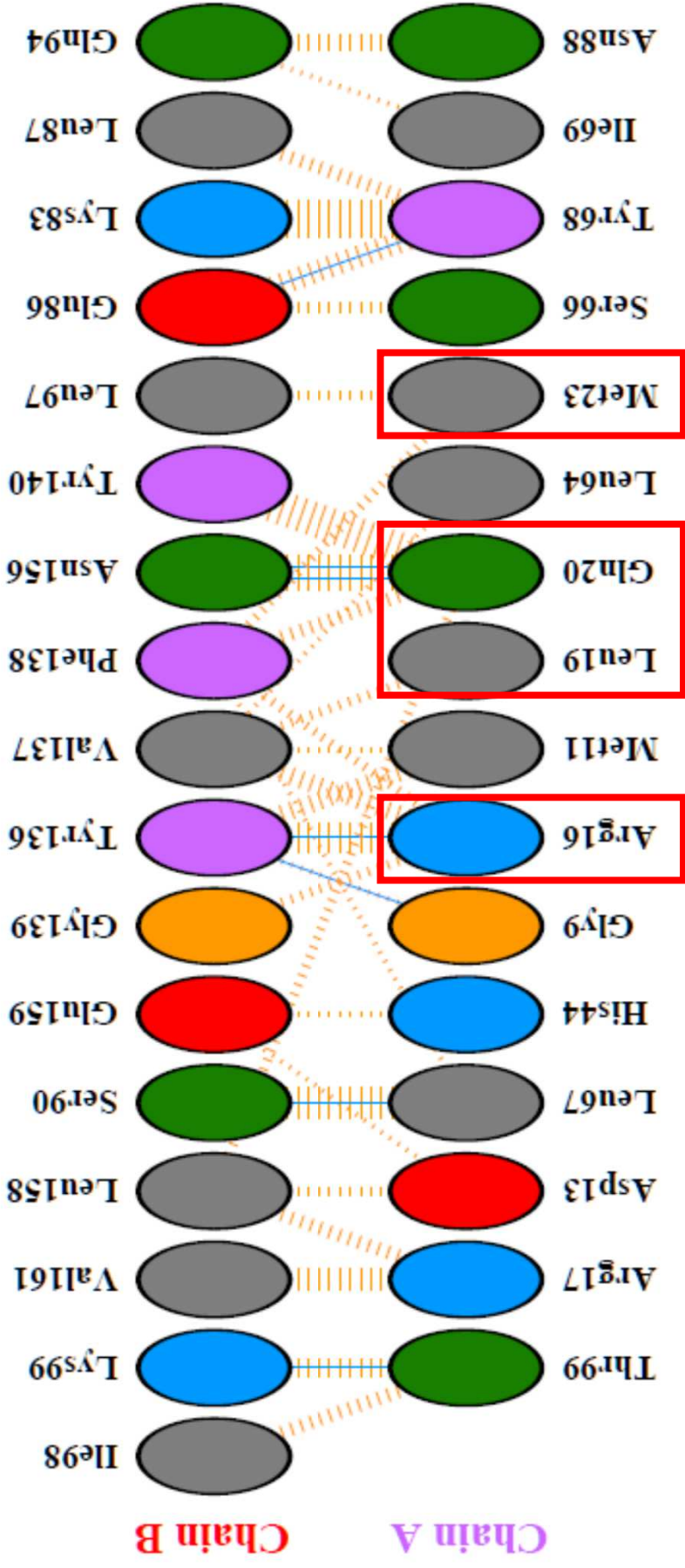
Konzervované AMK svědčí o důležitosti jejich funkce:

- důležité pro proteinovou strukturu
- důležité pro funkci proteinu:
 - enzymy – aktivní centra
 - komplexy – PPI
 - regulační funkce – AMK posttranslačně modifikovaná

A1CCH2 ASPCL/14-216
 A2Q7K6 ASPNC/15-218
 B8NLA5 ASPFN/14-216
 B6QTR9 TALMQ/14-217
 V5FED6 BYSSN/14-236
 S7Z8E9 PEN01/8-209
 B6H9Q9 PENRW/8-210
 H6C926 EXODN/14-207
 U1GD89 ENDPU/11-202
 C5GY37 AJEDR/11-207
 C6H5E2 AJECH/11-203
 F2PT91 TRIEC/10-199
 E9DEJ9 COCPN/13-202
 R7Z157 CONA1/13-202
 U4LU38 PYROM/8-205
 S8AAF4 DACHA/9-208
 G1X2Y0 ARTOA/8-207
 C5DCF6 LACTC/23-226

NRAFLQAFM ARSTMTFAEAKPVLAAIF SAH
 NRAFLQAFM ARSTMTFTQAKPVLAAIF SIR
 NRAFLQAFM ARSTMTFAEARPVLAAIF SVH
 NRAFLQAFM ARSTMTFDEAKPVLAAIF SAQ
 NRAFLQAFM ARSTMTFEEAKPVLAAIF SAHGAQSTIFFDSSYVEKEIANLYLATER
 NRAFLQAFM ARSTMTFEDAQPVLAAII SAH
 NRAFLQAFM ARSCMTFEDAQPILAAIIL TVS
 NRAFLQAFM ARSVLTLETAKPILAAIS TFQ
 NRAFLQAFM ARGTLTYETSKPLLASIF TVH
 NRAFLQAFM ARSTMTYEQAKPVLAAIF SAR
 NRAFLQAFM ARSTMTYEQAKPVLAAIF TAR
 NRAFLQAFM SRSTMTLEEAKPVLAAIF TVS
 NRAFLQAFM ARSTMTLNEAKPILAAIIL SVK
 NRAFLQAFM ARSVLTFEEAQPILAAIIL TAH
 NRAFLQAFM ARSSMTGEEILGVTVAIH GVE
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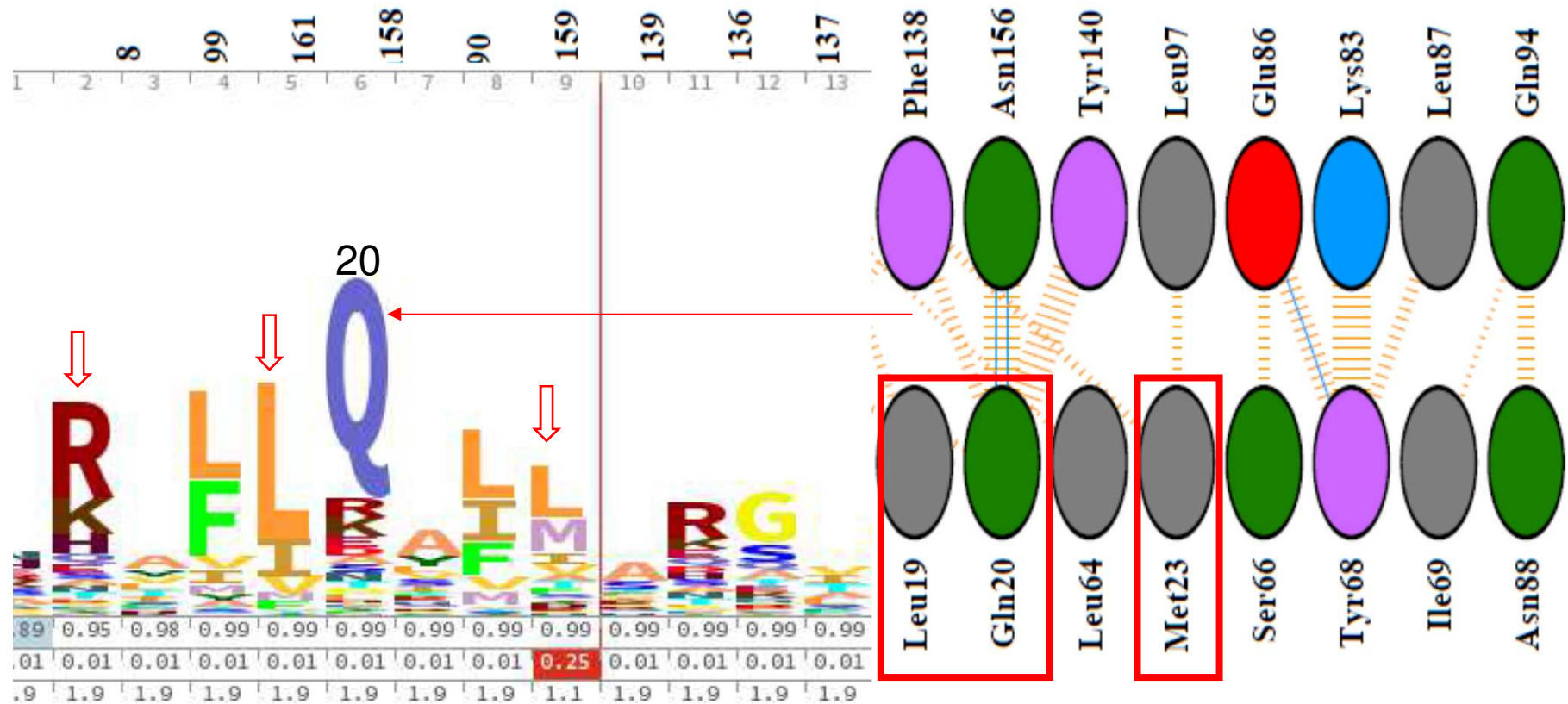
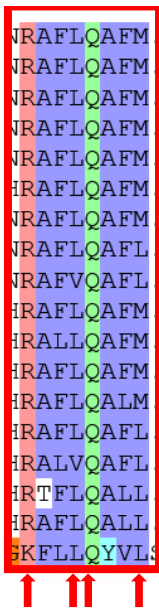
EG...QPVSA...DDVTE
 DD...EQVSP...EDITE
 EG...EPVSA...EDVTE
 EN...REVLAA...EDITQ
 EG...RPVLA...EDITQ
 EG...RTVDF...DEVTDQ
 EG...RTVDF...DEVGE
 DG...REVQP...QDMTV
 EG...REILP...NDITE
 DH...QDTLP...EDITQ
 DN...QETLP...EDITQ
 EG...REILP...GEDITQ
 DG...REVLP...EDVTQ
 EG...RPTLP...ADITT
 SG...NPEEP...TETTL
 AG...TDVPA...NSITV
 AG...SDVSI...ESVPP
 ERDG...EQLEDESETE



```

A1CCH2_ASPCL/14-216 NRAFLQAFM ARSTMTFAEAKPVLAALIF.SAH.....EG.....QPVSA...DDVTE
A2Q7K6_ASPNC/15-218 NRAFLQAFM ARSTMTFTQAKPVLAALIF.SIR.....DD.....EQVSP...EDITE
B8NLA5_ASPFN/14-216 NRAFLQAFM ARSTMTFAEARPVLAALIF.SVH.....EG.....EPVSA...EDVTE
B6QTR9_TALMQ/14-217 NRAFLQAFM ARSTMTFDEAKPVLAALIF.SAQ.....EN.....REVLA...EDITQ
V5FED6_BYSSN/14-236 NRAFLQAFM ARSTMTFEEAKPVLAALIF.SAHGAQSTIFFDSSYVEKEIANLYLATER.....RPVLA...EDITQ
S7Z8E9_PENO1/8-209 NRAFLQAFM ARSTMTFEDAQPVLAAII.SAH.....EG.....RTVDP...DEVTQ
B6H9Q9_PENRW/8-210 NRAFLQAFM ARSCMTFEDAQPILAAIL.TVS.....EG.....RTVDP...DEVGE
H6C926_EXODN/14-207 NRAFLQAFM ARSVLTLETAKPILAALIS.TFQ.....DG.....REVQP...QDMTV
U1GD89_ENDPU/11-202 NRAFLQAFM ARSVLTLETAKPILAALIS.TFQ.....DG.....REVQP...QDMTV
C5GY37_AJEDR/11-207 NRAFLQAFM ARSTMTYEQAKPVLAALIF.SAR.....DH.....QDTLP...EDITQ
C6H5E2_AJECH/11-203 HRALLQAFM ARSTMTYEQAKPVLAALIF.TAR.....DN.....QETLP...EDITQ
F2PT91_TRIEC/10-199 NRAFLQAFM SRSTMTLEEAKPVLAALIF.TVS.....EG.....REILP...GDITQ
E9DEJ9_COCPS/13-202 NRAFLQAFM ARSTMTLNEAKPILAAIL.SVK.....DG.....REVLP...EDVTQ
R7Z157_CONA1/13-202 NRAFLQAFM ARSVLTFEEAQPILAAIL.TAH.....EG.....RPTLP...ADITT
U4LU38_PYROM/8-205 HRALVQAFM ARSSMTGEELLGVVTAIH.GVE.....NPEEP...TETTL
S8AAF4_DACHA/9-208 HRTFLQALL IRPFIDIEEGQELLAALIA.SAE.....SG.....TDVPA...NSITV
G1X2Y0_ARTOA/8-207 NRAFLQALL IRPFIDVQEGRELLAAIK.SAE.....AG.....SDVSI...ESVPP
C5DCF6_LACTC/23-226 SKFLLQYVLSRRGVCSEKALAKKTL.....ERDG.....EQLEDSETE

```





Structures Overview
Structure Selections
3D View Controls

Visualization



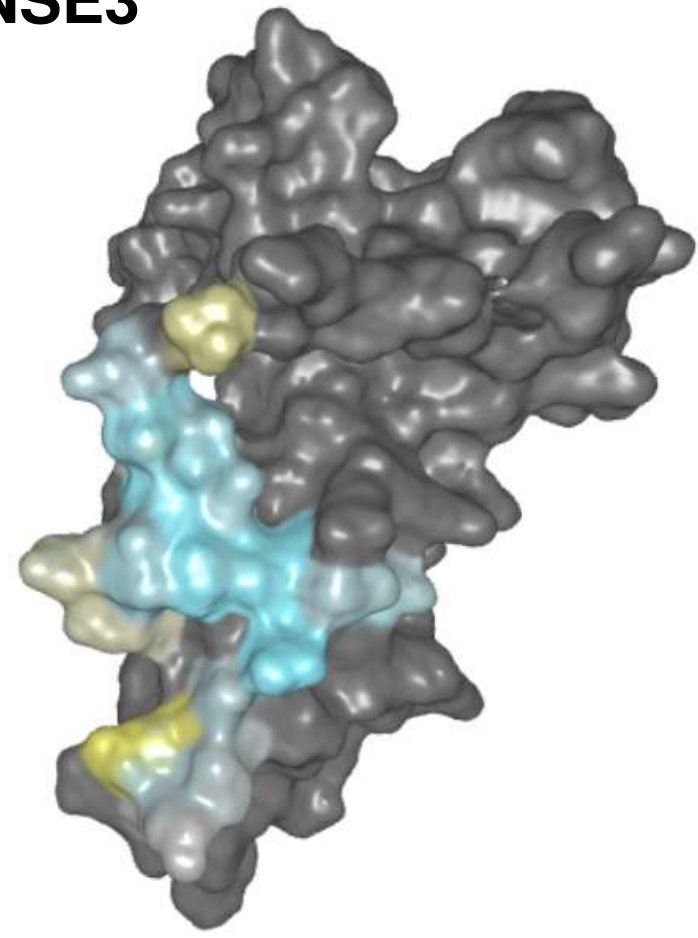
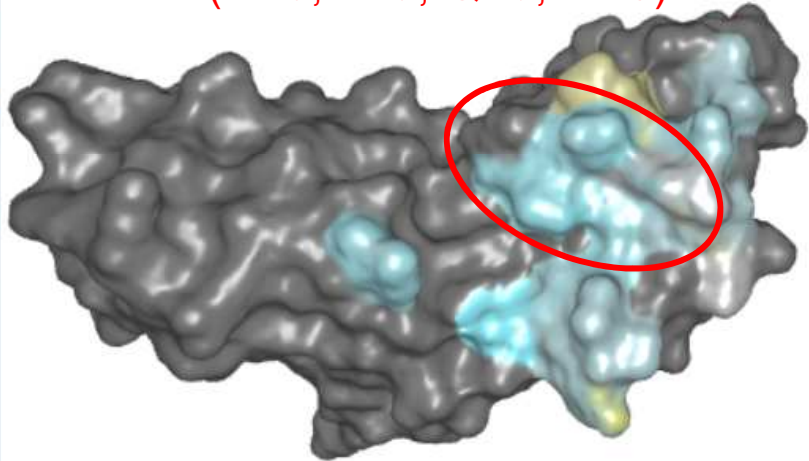
Residue Matrix

Primary Structure: 3

Sort by: Conservati

NSE1 - NSE3

Hot spot
(R16, L19, Q20, M23)



N88
Q20
M23
T99
L64
L19
D13
I69
L67
Y68
H44
S66
M11
R16
G9
R17

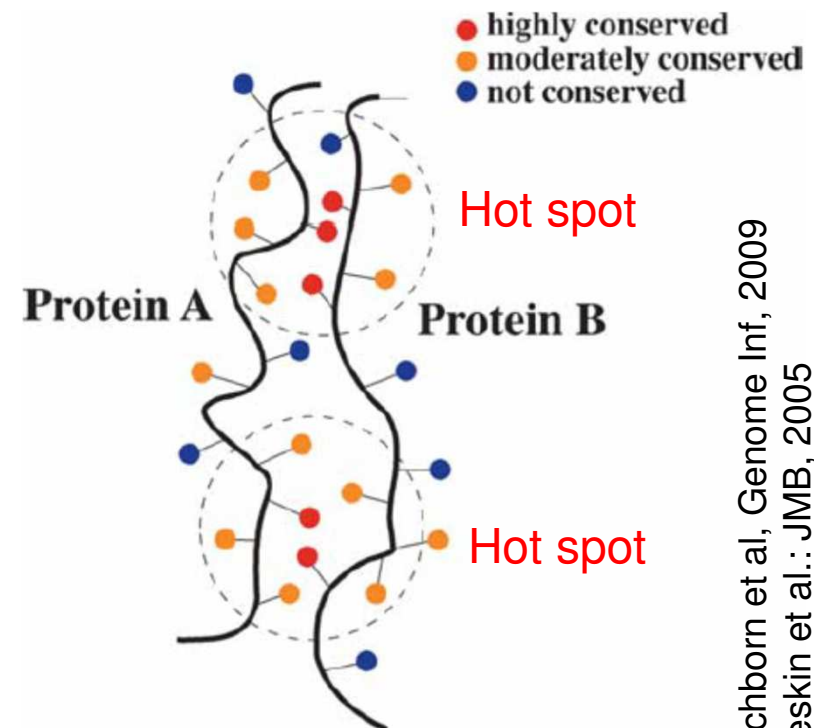
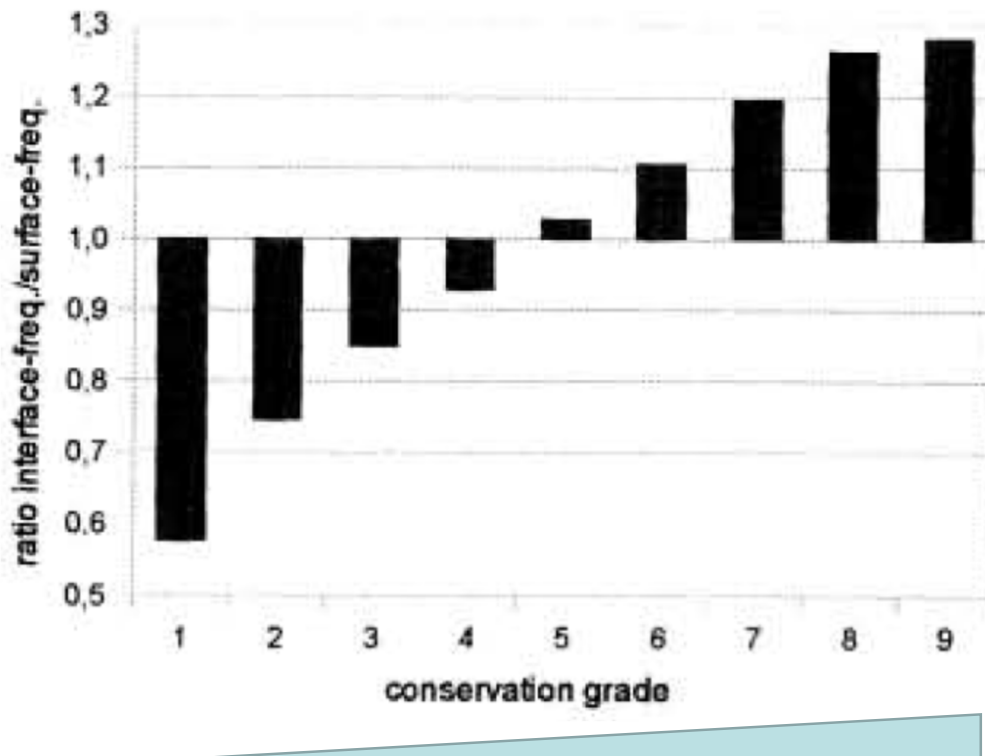


Structure Sequence x

Compact View Selection in All Structures

Silné/důležité interakce (komplexy) jsou evolučně konzervované

- jako jsou proteiny (jejich funkce) evolučně konzervované, tak i jejich interakce jsou evolučně konzervované (zajišťují funkci)
- graf** – povrchové AMK jsou málo konzervované (grade1), zatímco interakční povrchy jsou hodně konzervované (grade9)





Search Results

Gene / Identifier Search

nse3



GO

All Organisms

Your search for **NSE3** produced the following **4** results:Results matching **official symbol / systematic name** - 2 total proteins:**NSE3 (YDR288W)**

Component of the SMC5-SMC6 complex; this complex plays a key role in the removal of X-shaped DNA structures that arise between sister chromatids during DNA replication and repair; protein abundance increases in response to DNA replication stress

PHO*Saccharomyces cerevisiae* (S288c)

407 unique interactors

497 raw interactions

1 post-translational modification

NSE3 (SPCC645.04)

Smc5-6 complex non-SMC subunit Nse3

Schizosaccharomyces pombe (972h)

10 unique interactors

24 raw interactions

NSE1 | YLR007W







5 2

Component of the SMC5-SMC6 complex; this complex plays a key role in the removal of X-shaped DNA structures that arise between sister chromatids during DNA replication and repair

[\[details\]](#)

Experimental Evidence Code	Role	Dataset	Throughput	Curated By	Notes
Affinity Capture-MS	HIT	Hazbun TR (2003)	High	BioGRID	-
Reconstituted Complex	HIT	Hudson JJ (2011)	Low	BioGRID	-
Two-hybrid	HIT	Hazbun TR (2003)	High	BioGRID	-
	HIT	Hu B (2005)	Low	BioGRID	-
	BAIT/HIT	Duan X (2009)	Low	BioGRID	-
Dosage Rescue	HIT	Magtanong L (2011)	High	BioGRID	
Negative Genetic	BAIT/HIT	Costanzo M (2016)	High	BioGRID	

BioGRID – databáze interakcí (včetně genetických) pro různé organismy pučící kvasinky *S. cerevisiae*, pohlivé kvasinky *S. pombe*, octomilky *D. melanogaster*, člověka *H. sapiens* ...

Experimental Evidence Code	Role	Dataset	Throughput	Curated By	Notes
člověka <i>H. sapiens</i> ... Affinity Capture-MS \oplus	HIT	Doyle JM (2010)	Low	BioGRID	-
	BAIT	Taylor EM (2008)	Low	BioGRID	-
	BAIT	Huttlin EL (2015)	High	BioGRID	 
	BAIT	Huttlin EL (2017)	High	BioGRID	 
Affinity Capture-Western \oplus	BAIT	Doyle JM (2010)	Low	BioGRID	-
	BAIT/HIT	Taylor EM (2008)	Low	BioGRID	-
	HIT	Hudson JJ (2011)	Low	BioGRID	-
Co-crystal Structure \oplus	HIT	Newman JA (2016)	Low	BioGRID	-
Co-fractionation \oplus	BAIT	Taylor EM (2008)	Low	BioGRID	-
	BAIT	Wan C (2015)	High	BioGRID	 
Reconstituted Complex \oplus	BAIT/HIT	Doyle JM (2010)	Low	BioGRID	-

NSE1 | YLR007W

pučící kvasinky *S. cerevisiae*

5 2

Component of the SMC5-SMC6 complex; this complex plays a key role in the removal of X-shaped DNA structures that arise between sister chromatids during DNA replication and repair

[\[details\]](#)

Experimental Evidence Code	Role	Dataset	Throughput	Curated By	Notes
Affinity Capture-MS \oplus	HIT	Hazbun TR (2003)	High	BioGRID	-
Reconstituted Complex \oplus	HIT	Hudson JJ (2011)	Low	BioGRID	-
Two-hybrid \oplus	HIT	Hazbun TR (2003)	High	BioGRID	-
	HIT	Hu B (2005)	Low	BioGRID	-
	BAIT/HIT	Duan X (2009)	Low	BioGRID	-

NSE1 | SPCC550.05

poltivé kvasinky *S. pombe*

4

Smc5-6 complex ubiquitin-protein ligase E3 subunit 1

[\[details\]](#)

Experimental Evidence Code	Role	Dataset	Throughput	Curated By	Notes
Affinity Capture-Western \oplus	BAIT	Pebernard S (2004)	Low	BioGRID	-
Reconstituted Complex \oplus	BAIT	Sergeant J (2005)	Low	BioGRID	-
Two-hybrid \oplus	BAIT	Pebernard S (2004)	Low	BioGRID	-
	HIT	Hudson JJ (2011)	Low	BioGRID	-

Kde najít další informace o PPI?

The screenshot shows a Windows Internet Explorer browser window displaying the website for the Finley Lab, Center for Molecular Medicine and Genetics. The page title is "Links to Protein Interaction Databases". The main content area lists several databases:

- Finley Lab Interactions Databases:
 - Drosophila Interactions Database (DroID)***
 - Campylobacter jejuni Interactions Databases***
- Gene or Protein Interactions Databases in the research community:
 - BioGRID** - A Database of Genetic and Physical Interactions
 - DIP** - Database of Interacting Proteins
 - IntAct** - EMBL-EBI Protein Interaction Database
 - MINT** - A Molecular Interactions Database
 - MIPS** - Comprehensive Yeast Protein-Protein Interactions
 - Yeast Protein Interactions** - Yeast two-hybrid results
 - BRITE** - Biomolecular Relations in Information Transmission
 - The PIM Database** - by Hybrigenics
 - Mouse Protein-Protein Interactions**
 - Human Protein Reference Database**

The left sidebar contains navigation links for Projects, People, Bioinformatics, Papers, Positions, Proteomics, Protein Interaction DB links, Protocols/Reagents, and Molecular Biology links. The Wayne State University School of Medicine logo and contact information are also visible.

Na základě PPI v jednom organismu a homologii proteinů v jiných organismech lze odhadnout, zda proteiny interagují i v jiných organismech (lze dovodit i podle genových fúzí)

<http://proteome.wayne.edu/PIDBL.html>

Více Dr. Potěšil

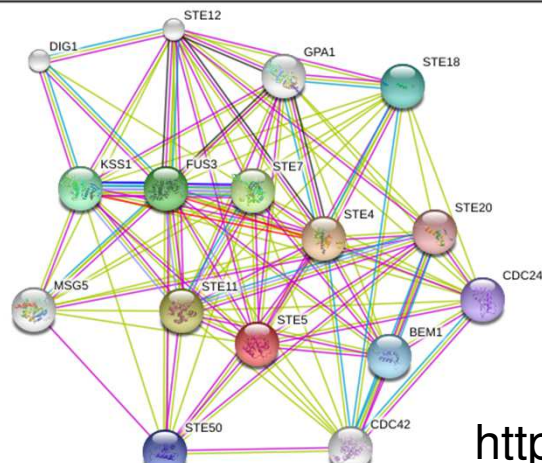
Informační zdroje PPI

Table 2. Databases Available for Searching and/or Downloading Data Related to Protein Interactions

Database	Proteins/Domains	Type	Number of Interactions
DIP ^a , LiveDIP	P	E,S	55,733
BIND ^a	P	E,C,S	83,517
MPact/MIPS ^a	P	E,C,F	15,488 (4,300) ^b
STRING	P ←	E,P,F	730,000 (proteins)
MINT ^a	P	E,C	71,854
IntAct ^a	P ←	E,C	68,165
BioGRID ^a	P ←	E,C	116,000 (30,000) ^b
HPRD	P	E,C	33,710
ProtCom	P,D	S,H	1,770
3did, Interprets	D	S,H	3,304
Pibase, ModBase	D	S,H	2,387
CBM	D	S	2,784
SCOPPI	D	S	3,358
iPfam	D	S	3,019
InterDom	D	P	30,037
DIMA	D	F,S	—
Prolinks	P	F	—

Table 3. URLs and Primary Citations for Protein Interaction-Related Databases

Database	URL/FTP
DIP [102], LiveDIP[103]	http://dip.doe-mbi.ucla.edu
BIND [105]	http://bind.ca
MPact/MIPS [97]	http://mips.gsf.de/services/ppi
STRING [119]	http://string.embl.de
MINT [120]	http://mint.bio.uniroma2.it/mint
IntAct [121]	http://www.ebi.ac.uk/intact
BioGRID [122]	http://www.thebiogrid.org
HPRD [123]	http://www.hprd.org
ProtCom [124]	http://www.ces.clemson.edu/compbio/ProtCom
3did [108], Interprets[125]	http://gatealoy.pcb.ub.es/3did/
Pibase [107], ModBase [126]	http://alto.compbio.ucsf.edu/pibase
CBM [26]	ftp://ftp.ncbi.nlm.nih.gov/pub/cbm
SCOPPI [111]	http://www.scoppi.org/
iPfam [127]	http://www.sanger.ac.uk/Software/Pfam/iPfam
InterDom [128]	http://interdom.lit.org.sg
DIMA [129]	http://mips.gsf.de/genre/proj/dima/index.html
Prolinks [104]	http://prolinks.doe-mbi.ucla.edu/cgi-bin/functionator/pronav/



STRING

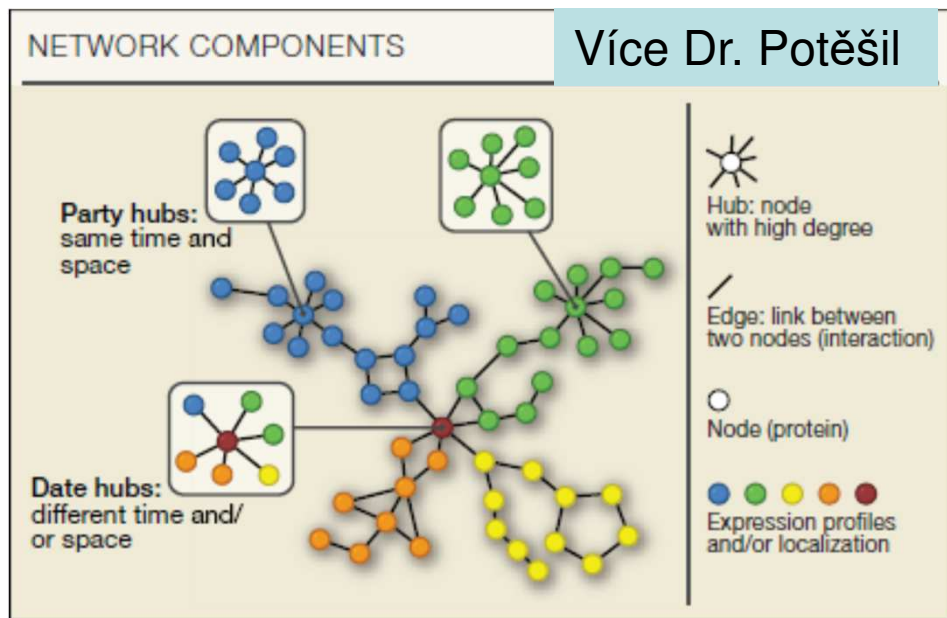
informace o binárních interakcích v databázích – zobrazeny jako sítě (různé výsledky = různé čáry)

Shoemaker and Panchenko, PLoS Comp Biol, 2007

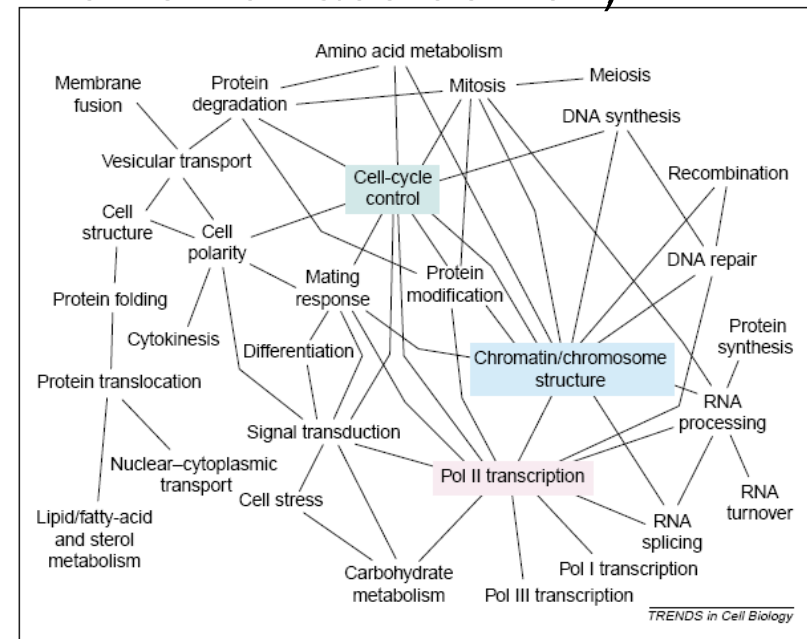
<http://string-db.org> Andreani and Guerois, ABB, 2014

Protein-proteinové interakce

- stabilní (velké plochy, většinou součástí komplexů)
- přechodné/slabe (součást dynamických procesů – předávání signálů, modifikace)
- posttranslační modifikace mohou změnit vazebné vlastnosti povrchu (fosforylace, metylace, hydroxylace, SUMO)
- souhrn proteinových interakcí = **interaktom**
(modularita díky interakcím domén – různé kombinace domén)



Seebacher & Gavin, Cell (SNAP SHOT), 2011



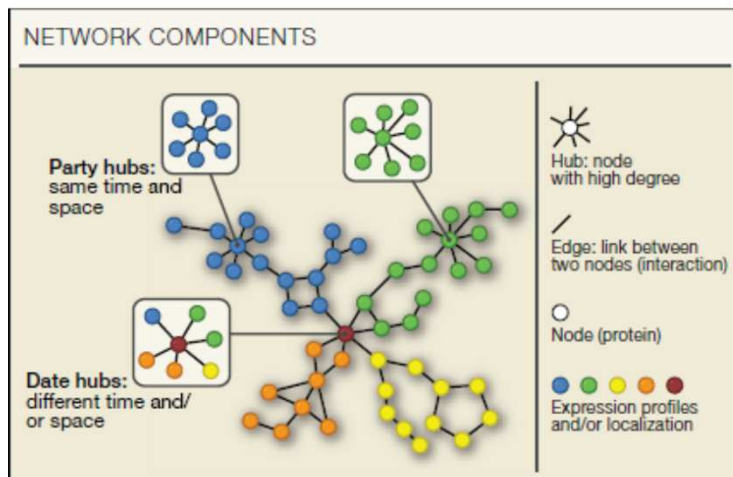
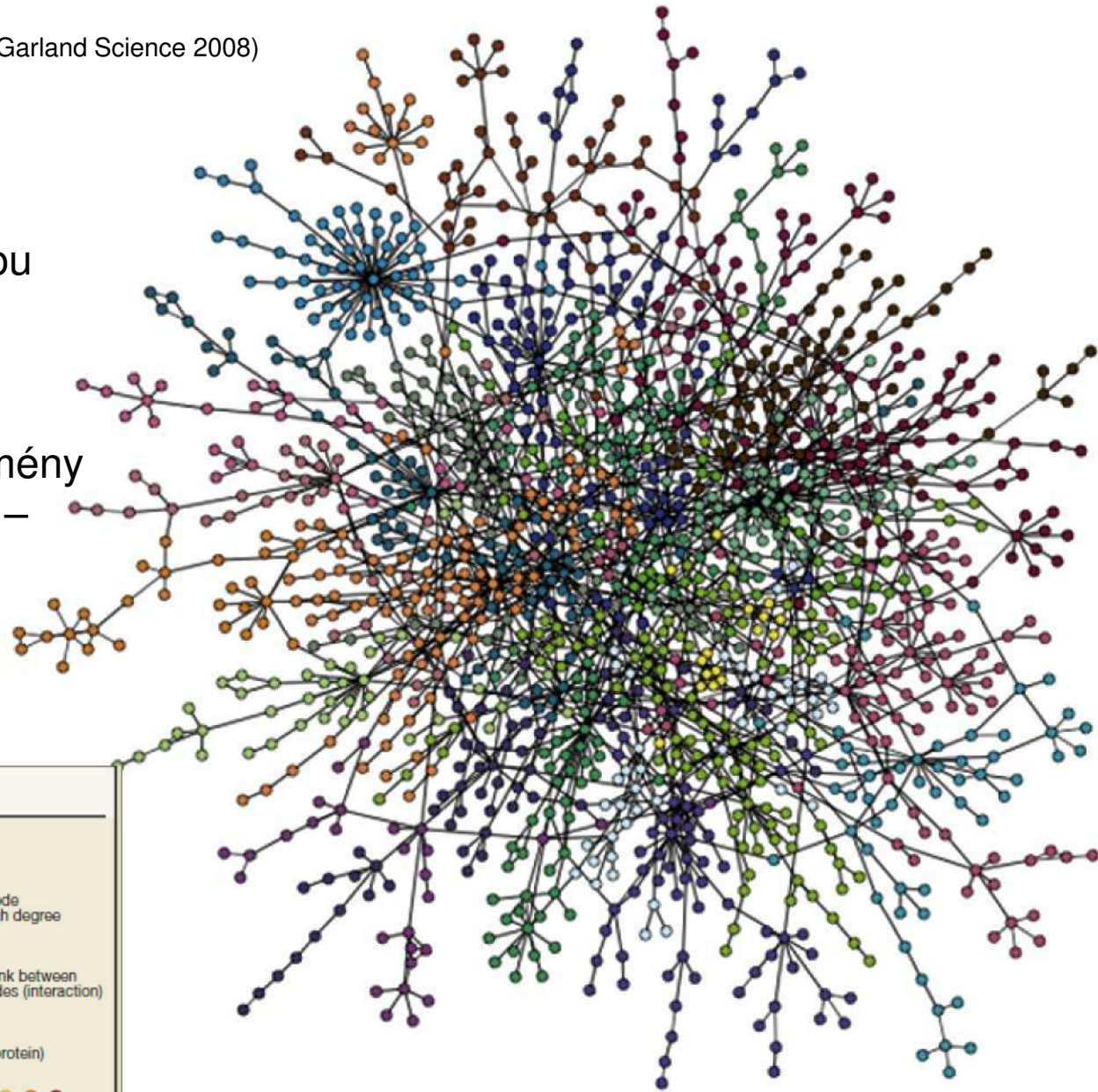
Network/síť naznačuje funkční vztahy
Tucker et al, TiCB, 2001

Interaktom x komplexom

Figure 3-83 *Molecular Biology of the Cell* (© Garland Science 2008)

Naznačují funkční vztahy
(např. buněčný cyklus –
struktura chromatinu ... jsou
zprostředkovány PPIs)

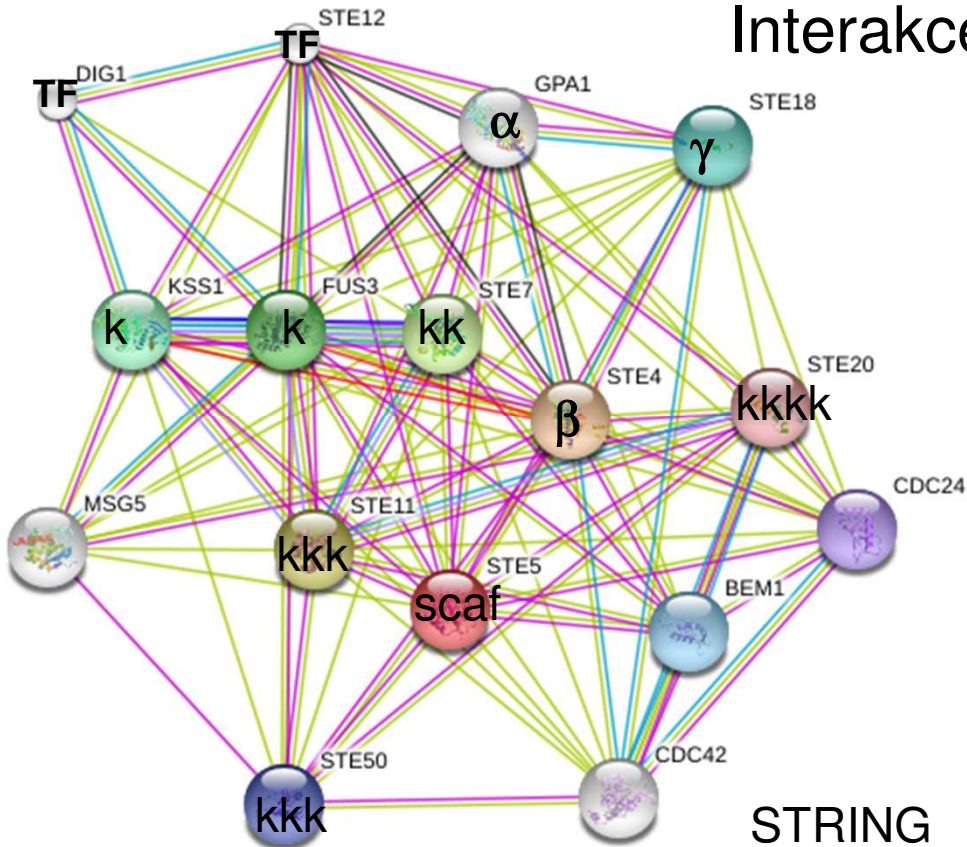
Modularita – interagují domény
(jeden protein více domén –
zapojení do více procesů)



Seebacher & Gavin, *Cell* (SNAP SHOT), 2011

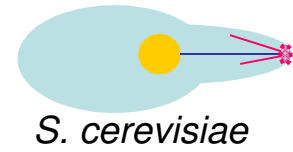
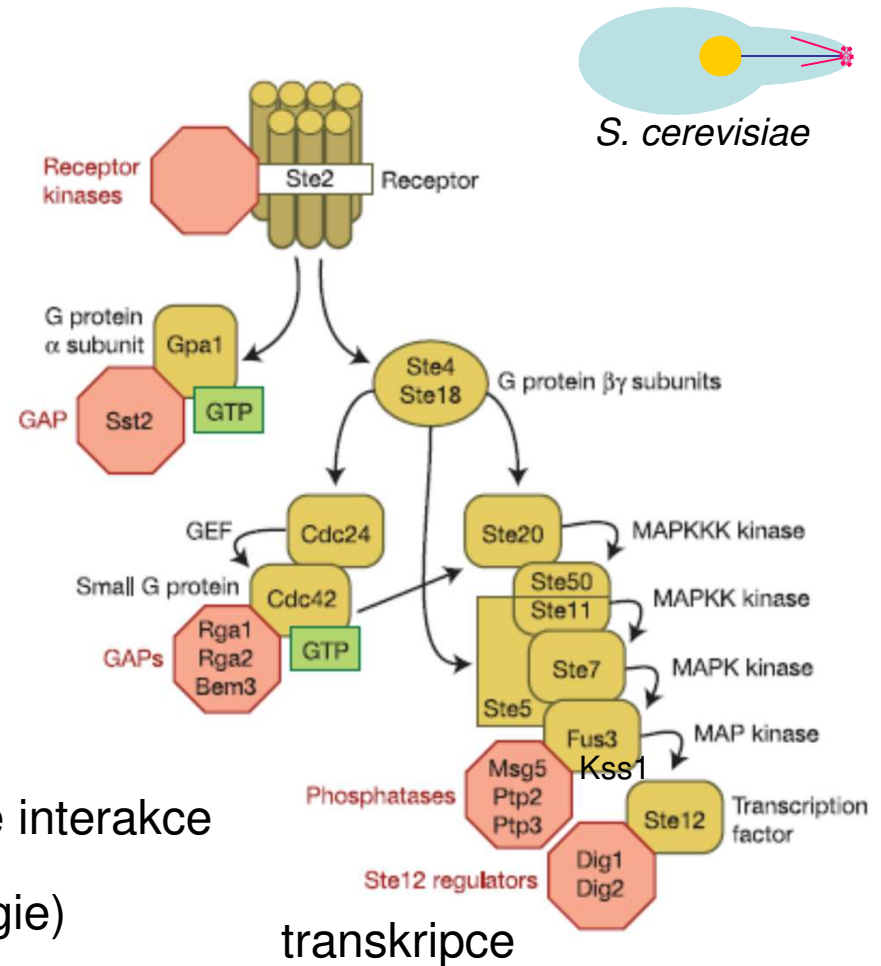
proteinové sítě – chybí info o posloupnosti, síle ... interakcí

Interakce x signální dráha



STRING

- Experiments Y2H, colP ... genetické interakce
- Databases Funkční vztahy (ontologie)
- Textmining
- Gene Fusion Svědčí o potřebě PPI
- Coexpression Potřeba výskytu ve stejném okamžiku a společná translace

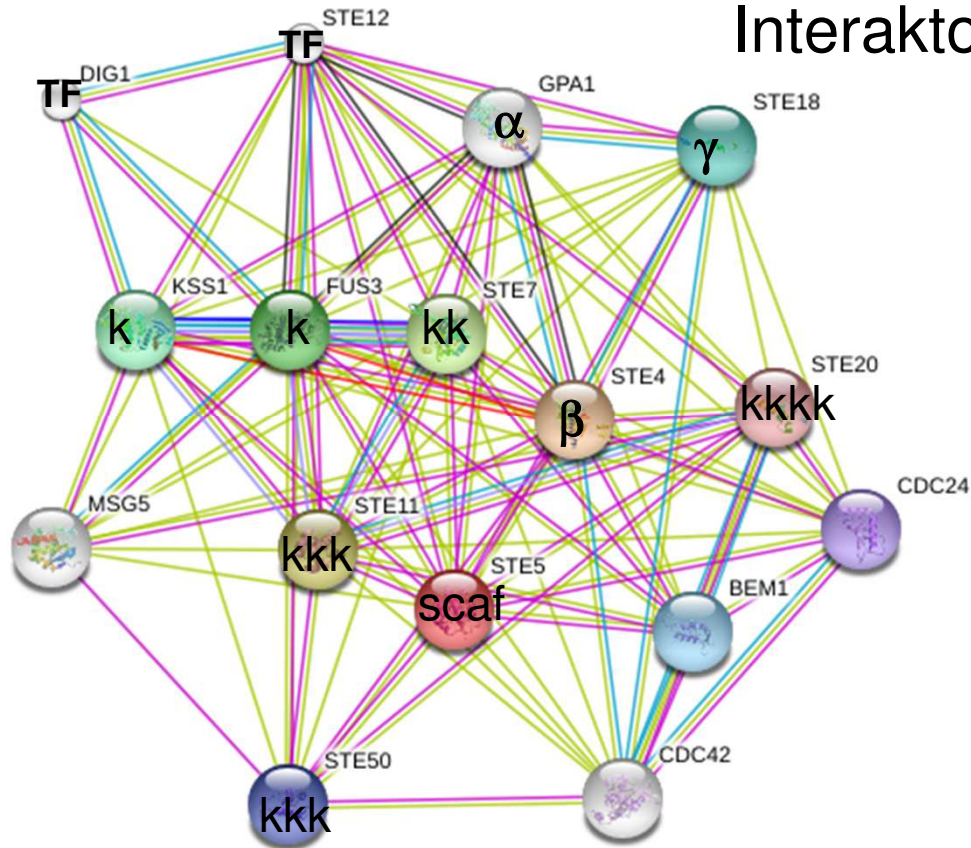


S. cerevisiae

transkripce

proteinové sítě – chybí info o lokalizaci, komplexech ...

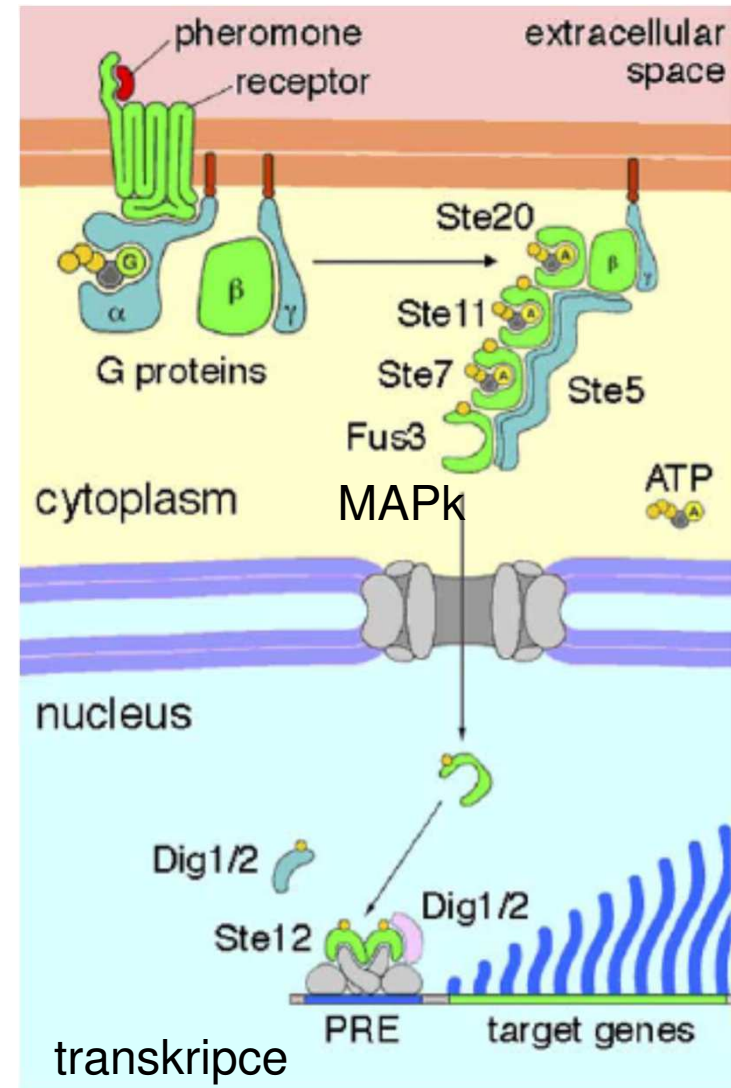
Interaktom x komplexom



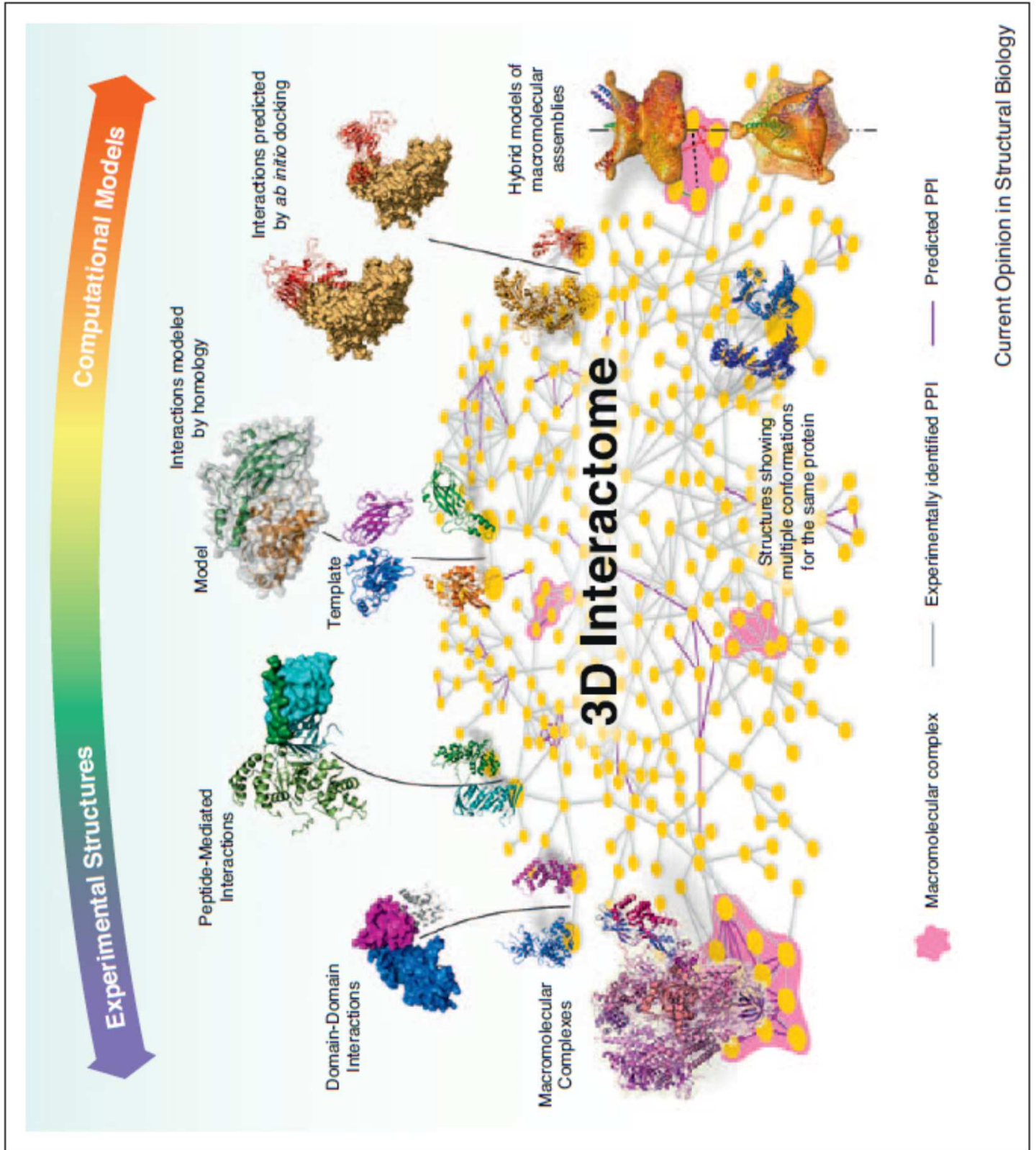
- Experiments
- Databases
- Textmining
- Gene Fusion
- Coexpression

Síť neznamená komplex,
ale vztahy

souhrn proteinových
komplexů = **komplexom**



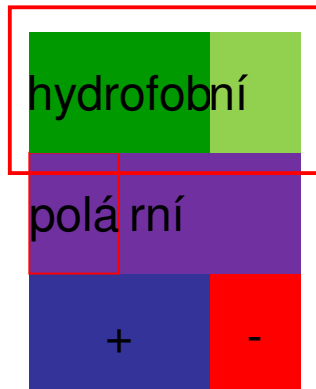
Wang et al., Nature, 2004



Souhrn - protein-proteinové interakce

- proteiny jsou troj-rozměrné - mají různé tvary a více domén => mají více vazebných míst na povrchu => komplexy a "sítě"
- části proteinů/domény/motivy interagují s partnery
 - domény mají určitou strukturu, která do značné míry determinuje tvar jejího povrchu, ale ...
 - charakter (hydrofobicitu, polaritu, náboj) povrchu určují postraní řetězce aminokyselin směřujících do solventu, takže ...
 - interakce proteinu je determinována povrchem, který musí mít tvar i charakter komplementární s interakčním partnerem (typy interakcí: ...)

primární struktura



sekundární a terciární struktura

