

- Protein-proteinové interakce – 21.10.
 - jak spolu proteiny interagují?
 - interaktom
- Proteinové komplexy – 4.11.
 - protein-proteinové interakce a komplexy
 - komplexom, architektura a funkce komplexů

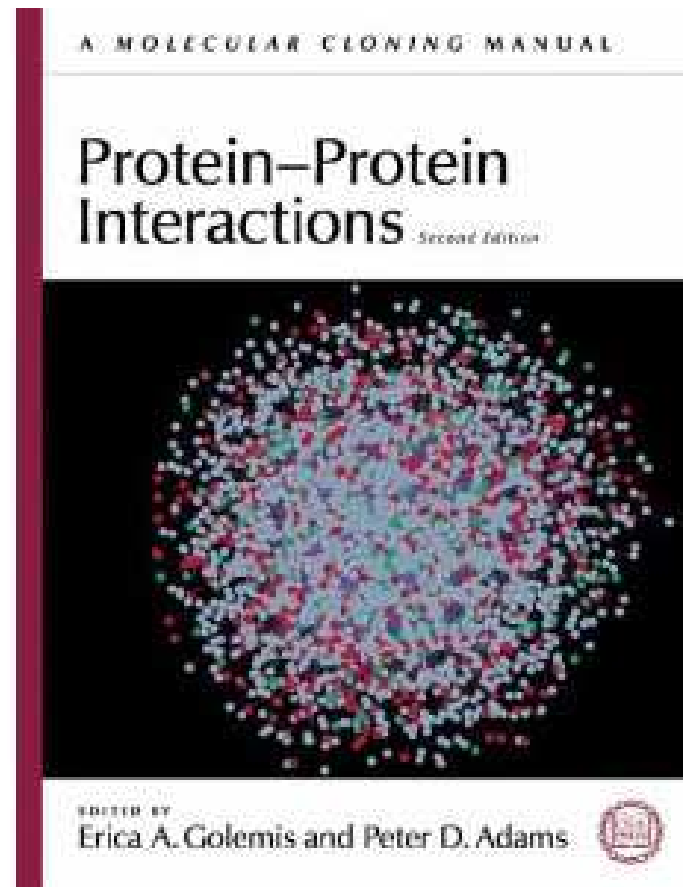
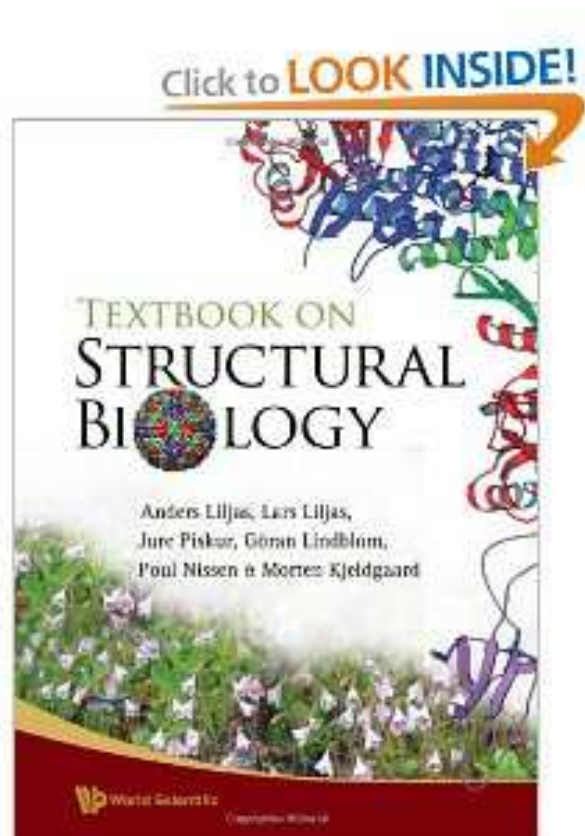
CG030 – Struktura a funkce proteinových komplexů

Informační zdroje

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

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

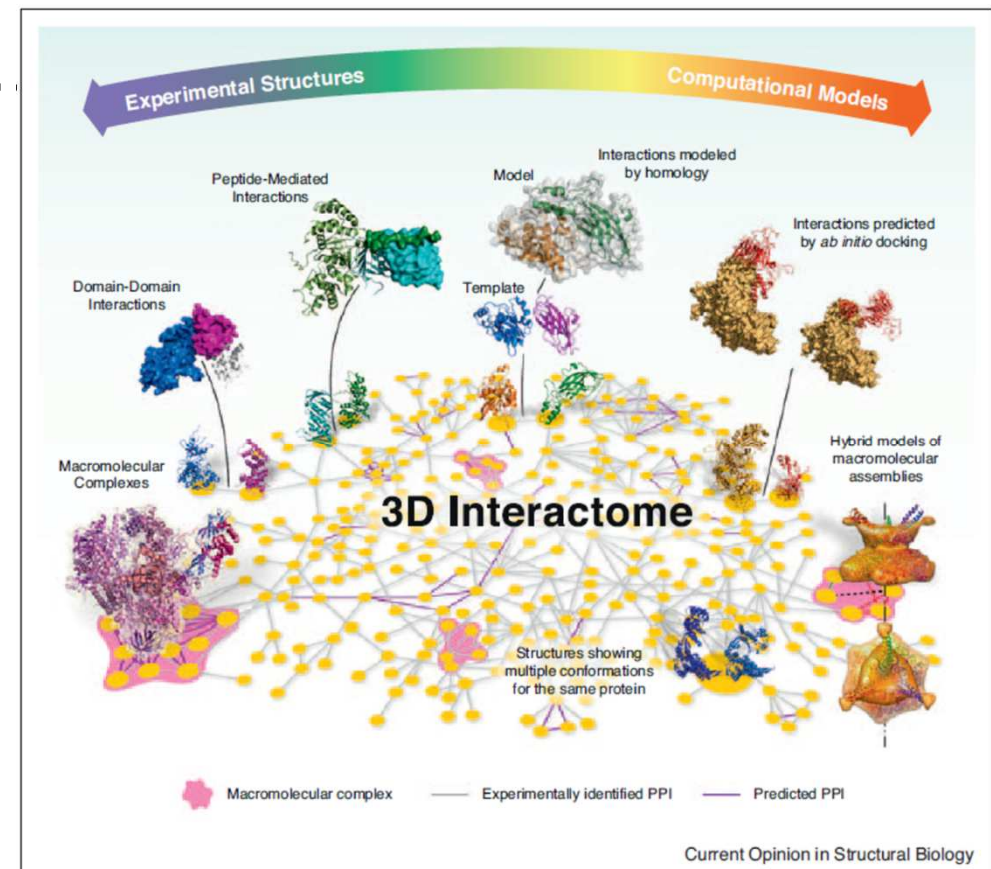
... nejnovější články z časopisů Nature, ...

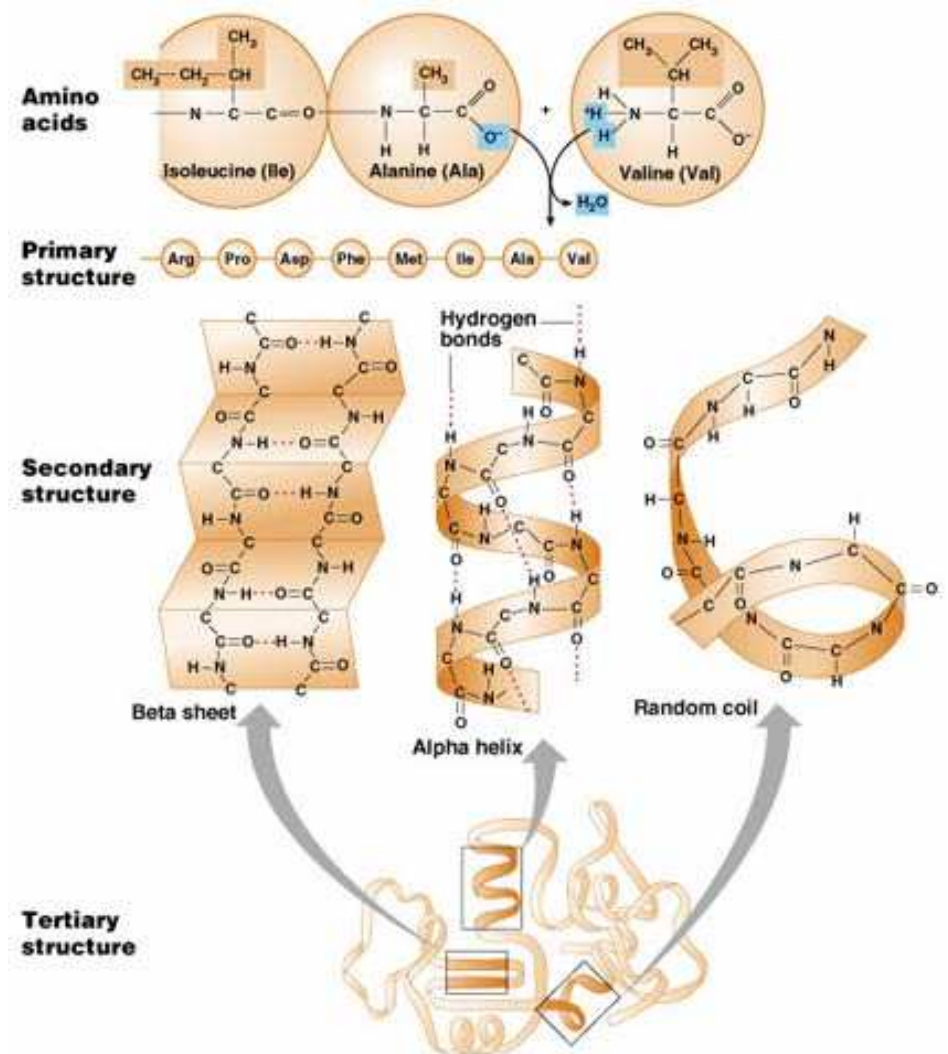
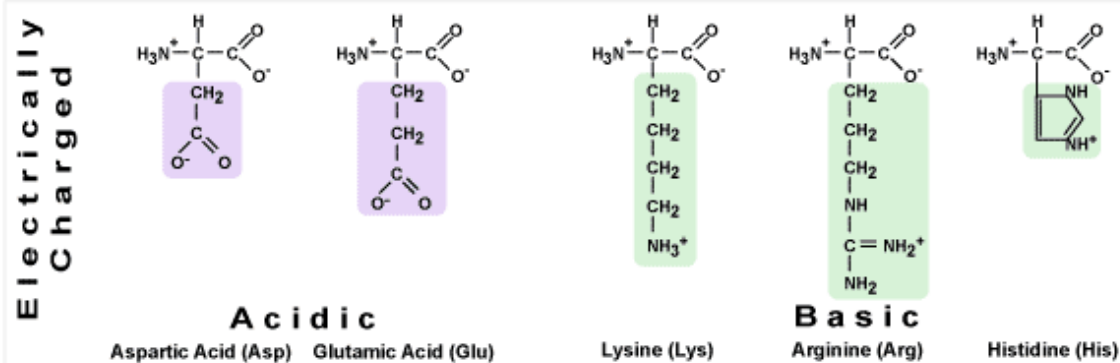
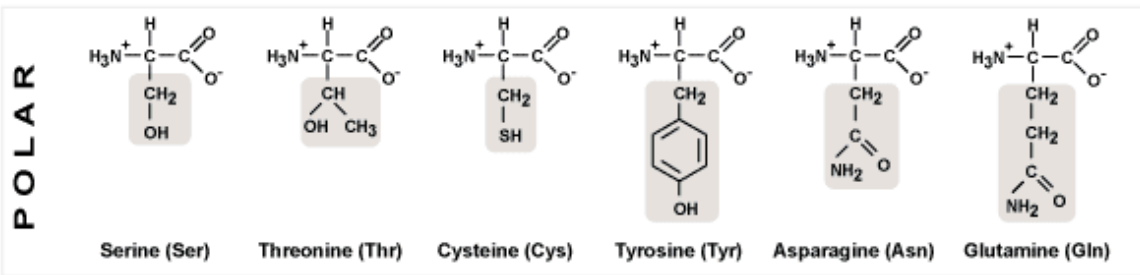
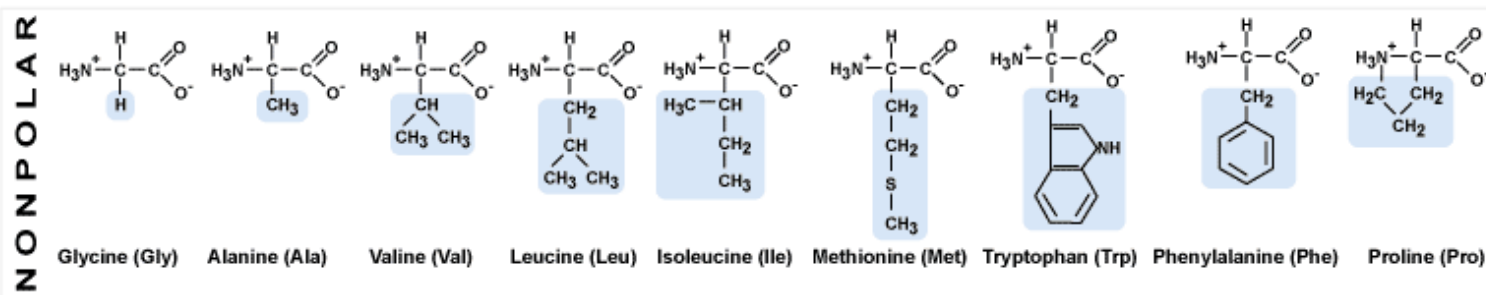


Databáze proteinových struktur: <http://www.rcsb.org/pdb/home/home.do>,
<http://www.ebi.ac.uk/pdbsum/>

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

- Protein-proteinové interakce – 21.10.
 - Interakce: od primární po terciární strukturu
 - Typy vazeb ...
 - Informatika:
 - databáze struktur, interakcí ...
 - docking, predikce ...
 - motivy, evoluční aspekty ...
 - Interaktom ...
 - síť
 - 3D interaktom





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Základní proteinové charakteristiky

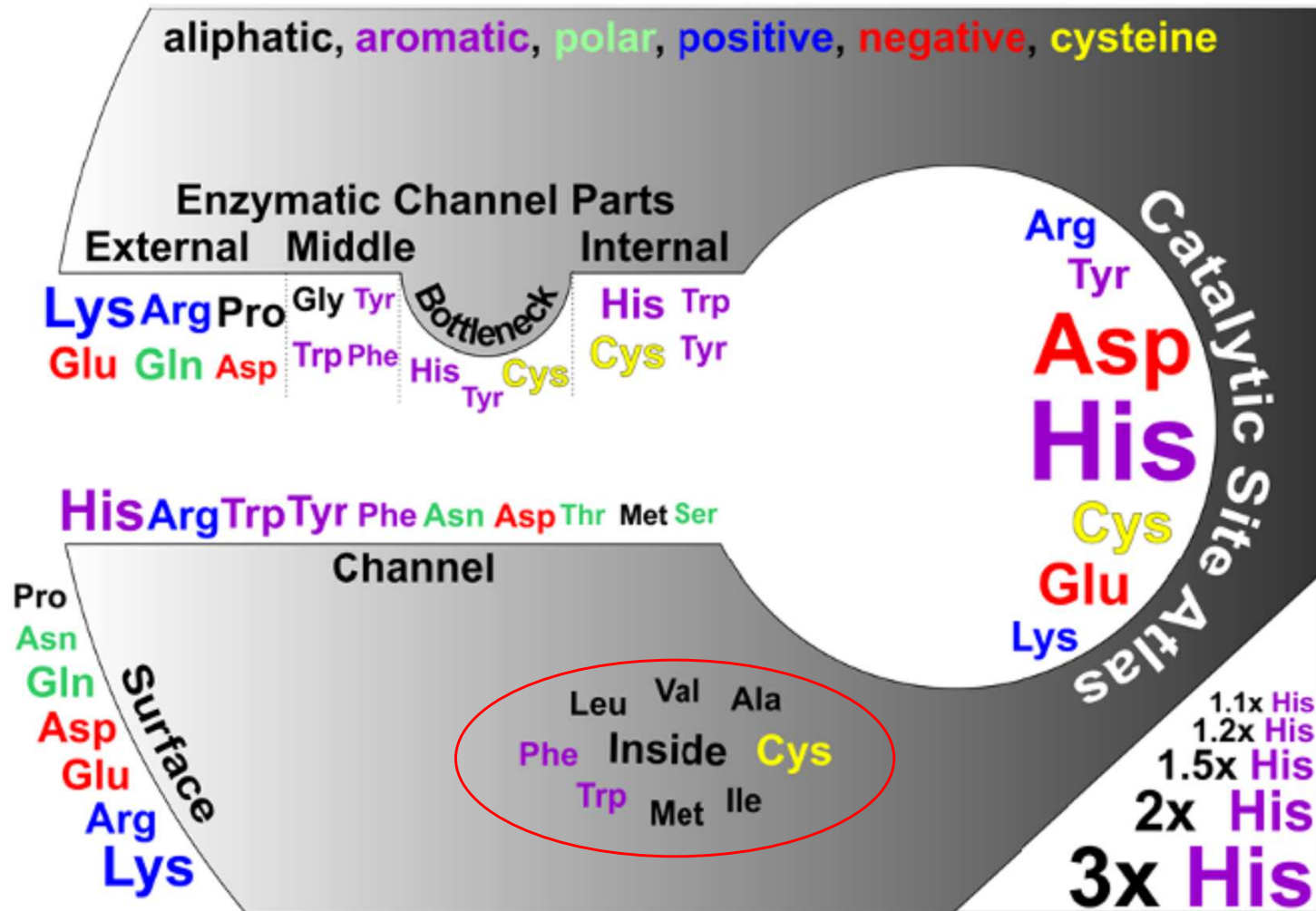
Primární

Sekundární

Terciární

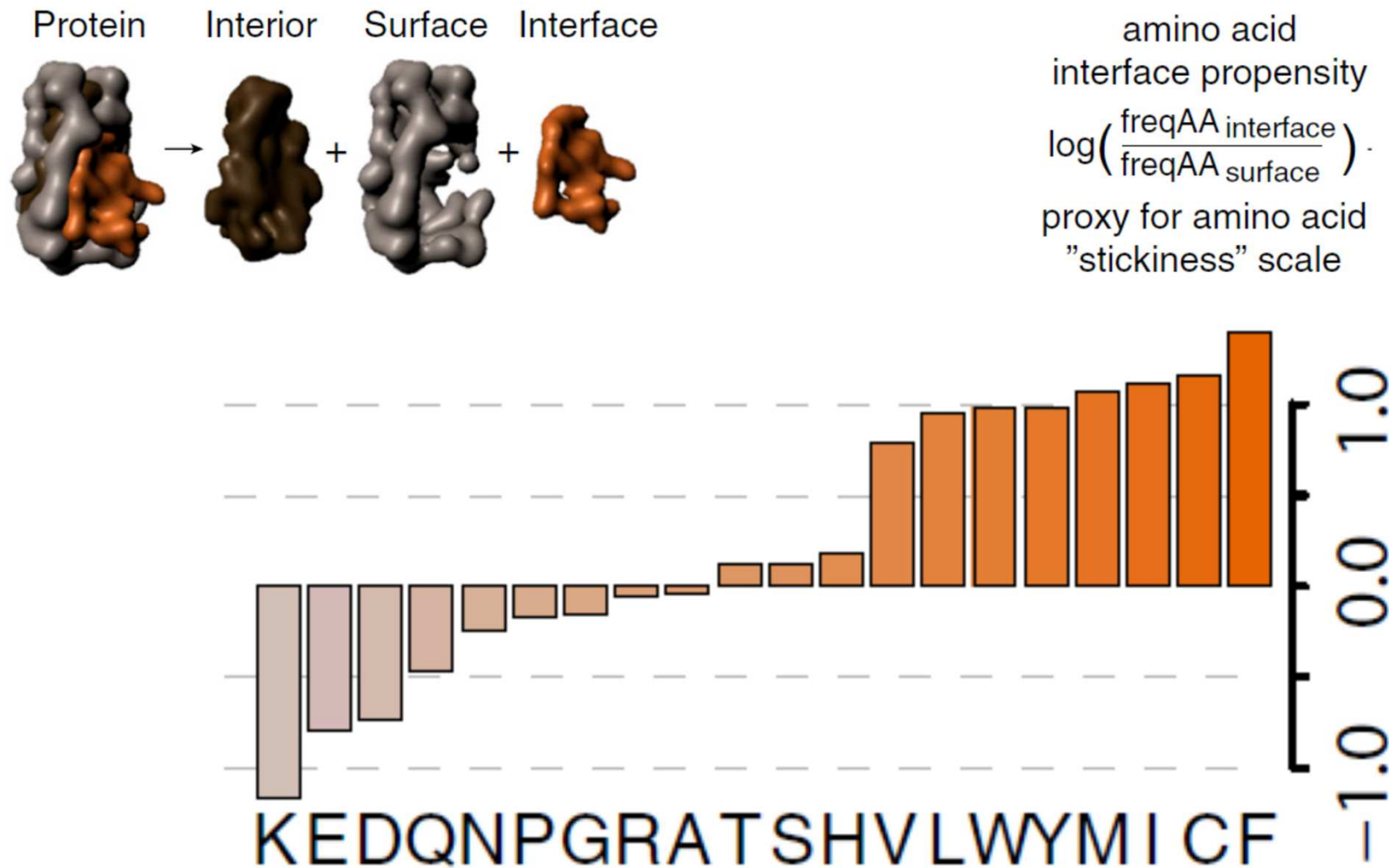
Kvarterní – dva proteiny a více ...

Podíl AMK (primární struktury) na proteinových interakcích



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

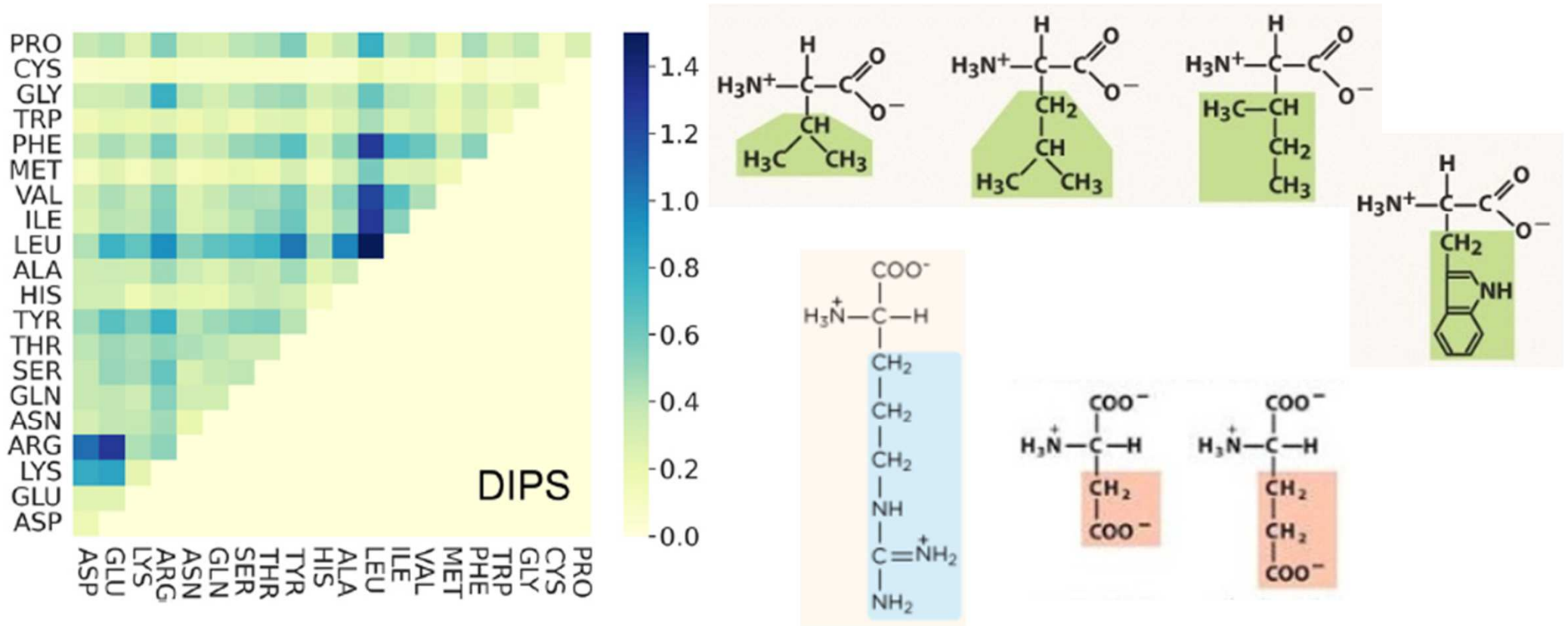
PPI od primární struktury ...



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

PPI od primární struktury ...

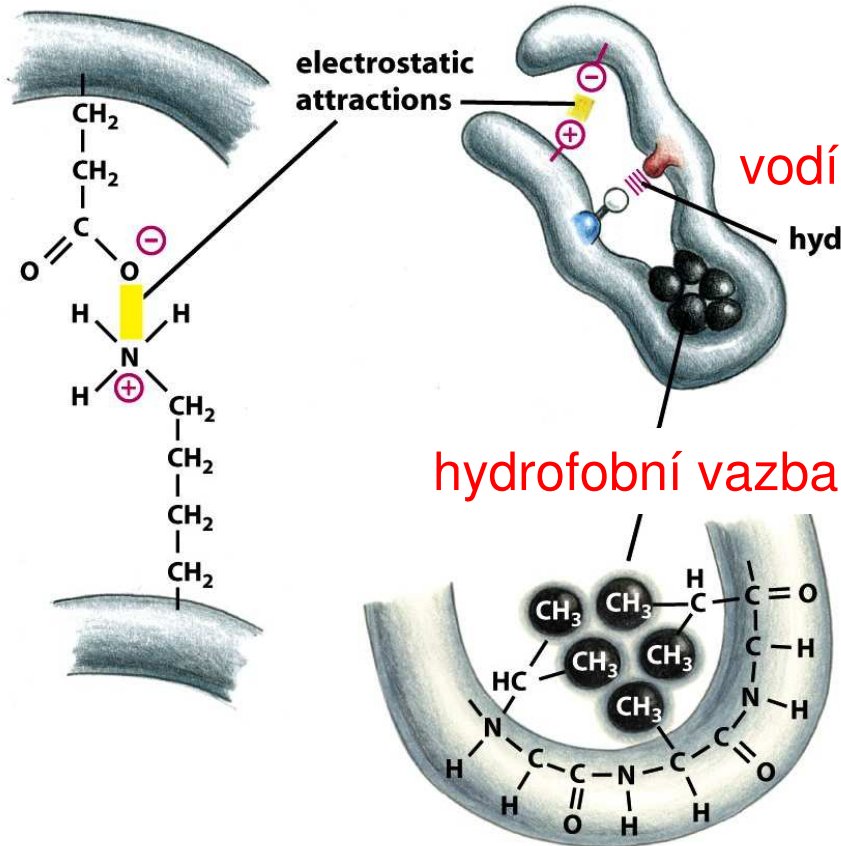


Leu s Ile, Leu, Val a Phe = hydrofobní AMK

Arg(+) s Asp(-) a Glu(-) = nabité AMK

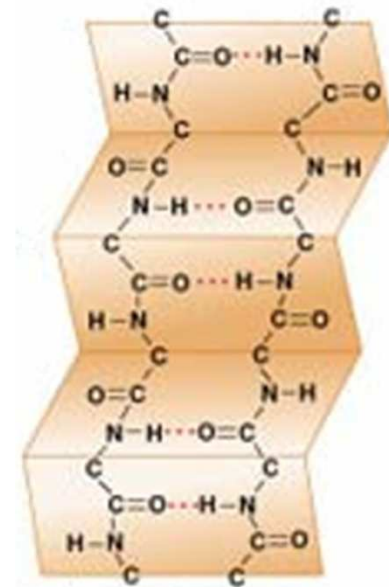
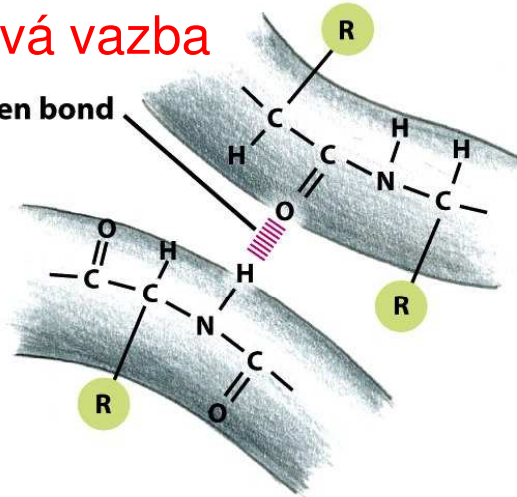
Typy vazeb v PPI

iontová (polární) vazba



vodíková vazba

hydrogen bond



β-listy

● H-bonds
● salt bridges
● disulfide bonds

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

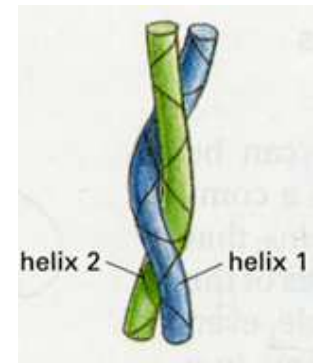
Která z těchto vazeb převažuje v PPI?

Kovalentní vazba = modifikace (nikoli PPI)
vyjimečně např. disulfidické můstky
posttranslační modifikace (ubikvitinylace,
SUMOylace)



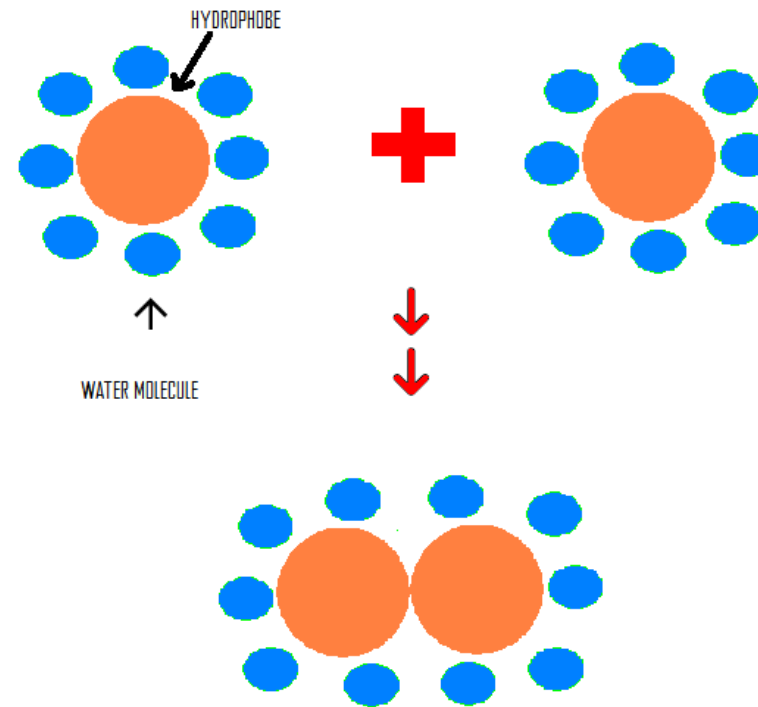
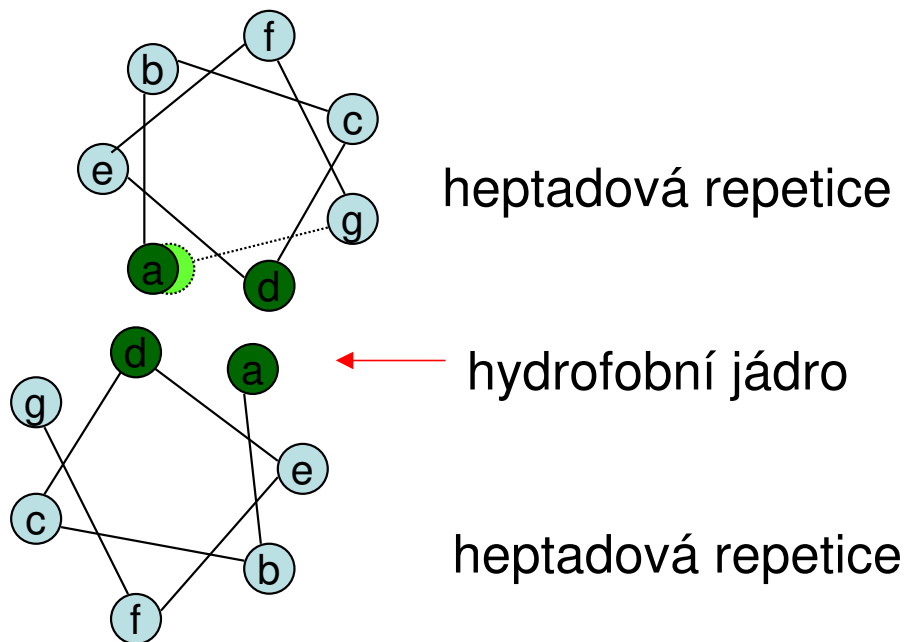
... sekundární struktury ...

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



coiled-coil struktura

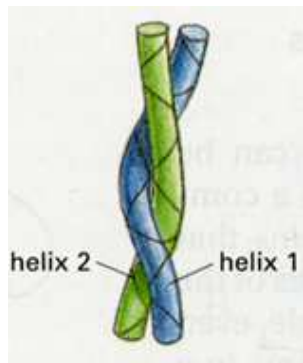
- dvě šroubovice s tzv. heptádovou repeticí (hxxhxxx – hydrofobní zbytky vytváří rozsáhlý povrch a tedy silnou vazbu)



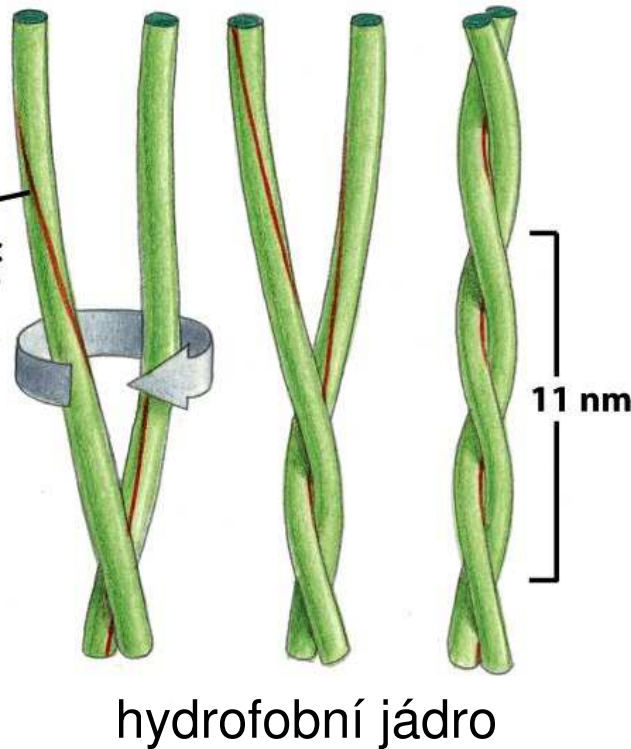
...LKS**L**HNQ**L**RD**L**EES**L**TH...

coiled-coil struktura

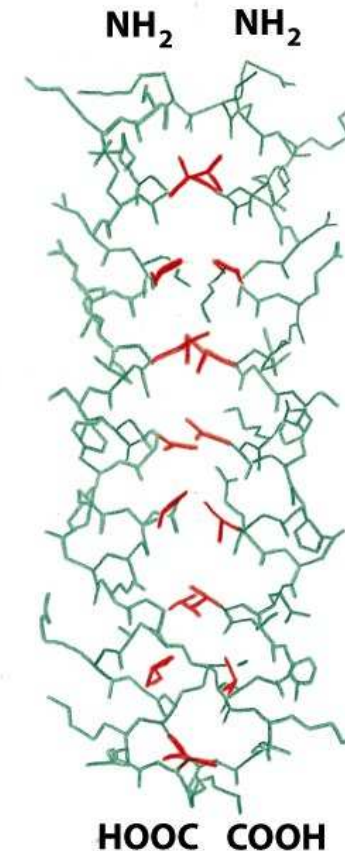
- dvě šroubovice s tzv. heptádovou repeticí (hxxhxxx – hydrofobní zbytky vytváří rozsáhlý povrch)



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

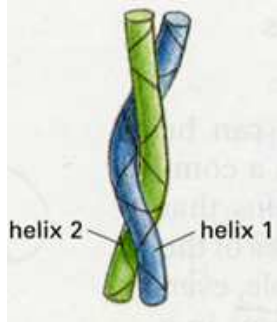


...LKSLHNQLRDLEESLTH...



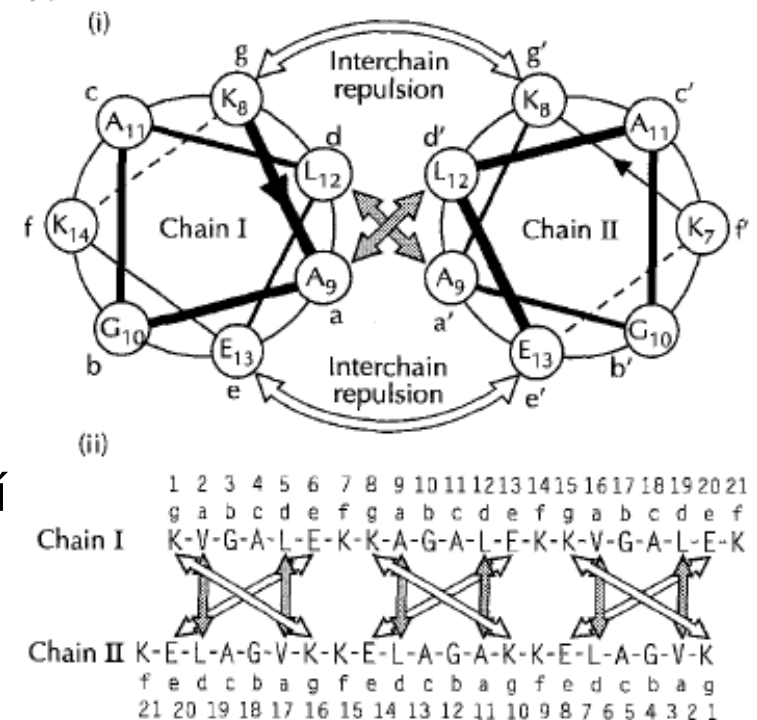
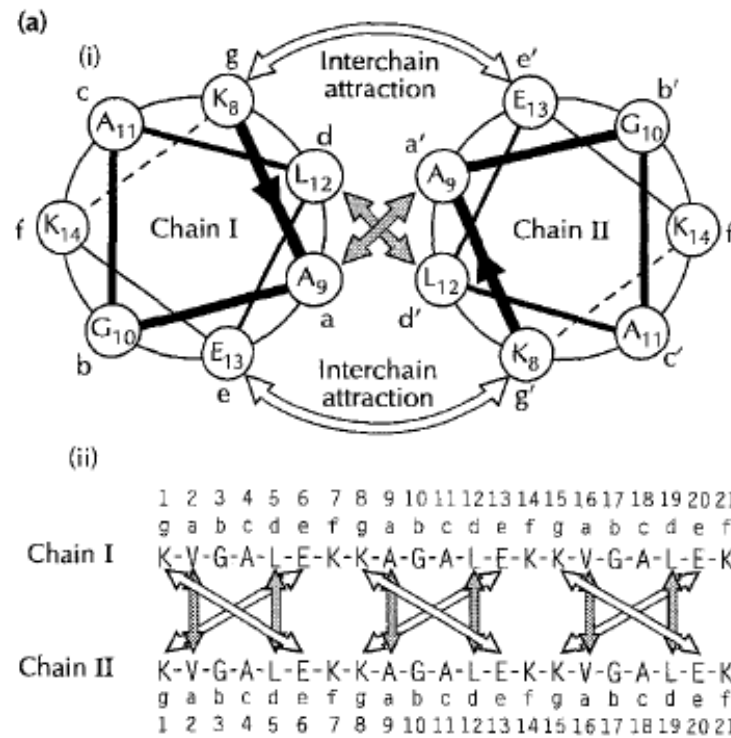
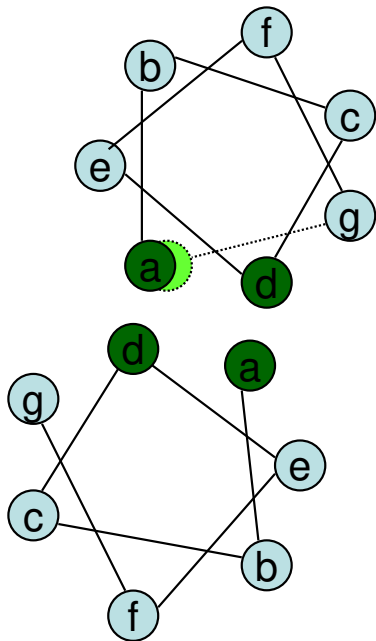
paralelní šroubovice

coiled-coil struktura



Síla interakce může být ovlivněna sousedními AMK

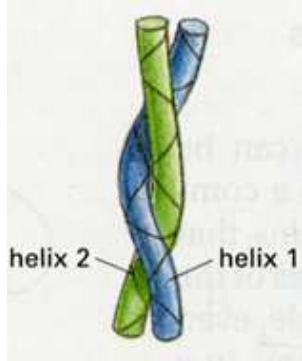
Sousední AMK stabilizují interakce šroubovic



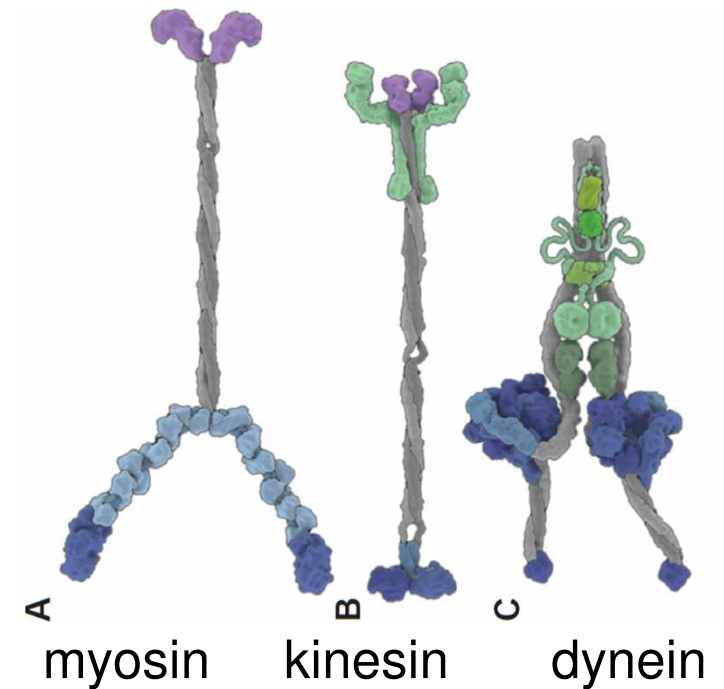
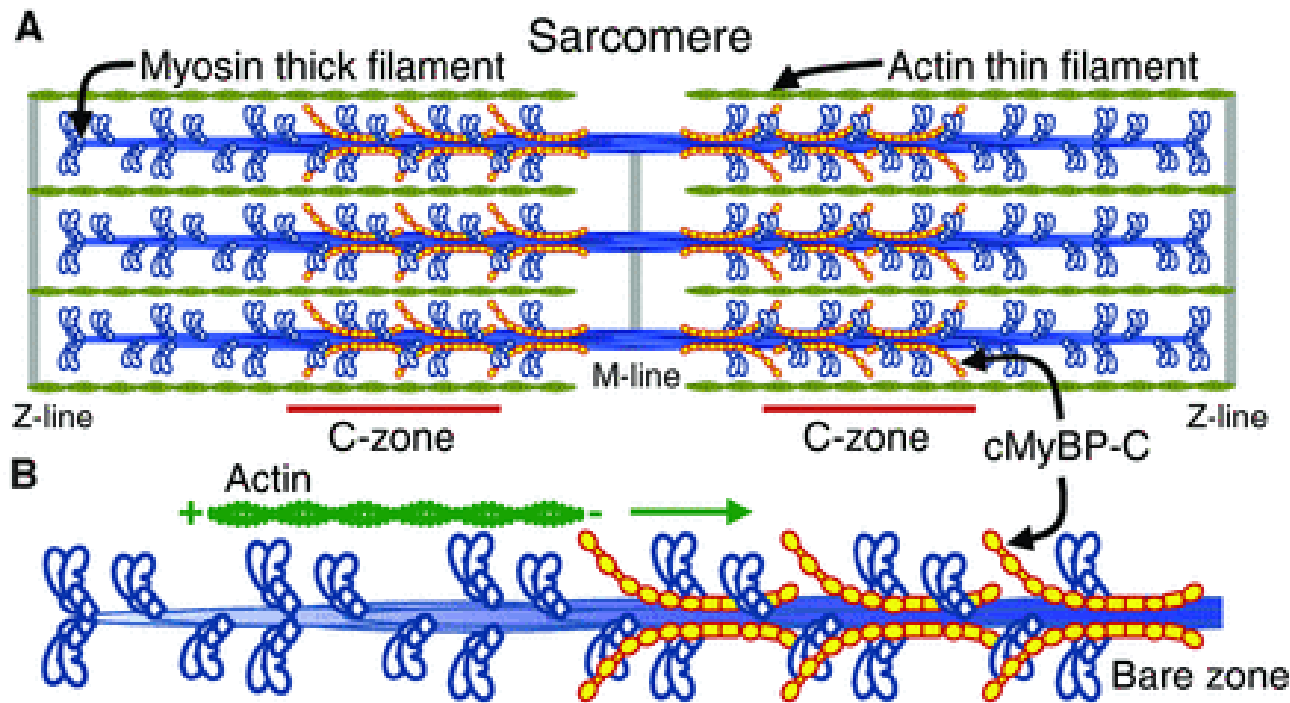
Sousední AMK destabilizují interakce šroubovic

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

coiled-coil struktura



-dlouhé CC ($>100\text{AMK}$) vytváří vláknité struktury (myosin tvoří vlákna - svaly)



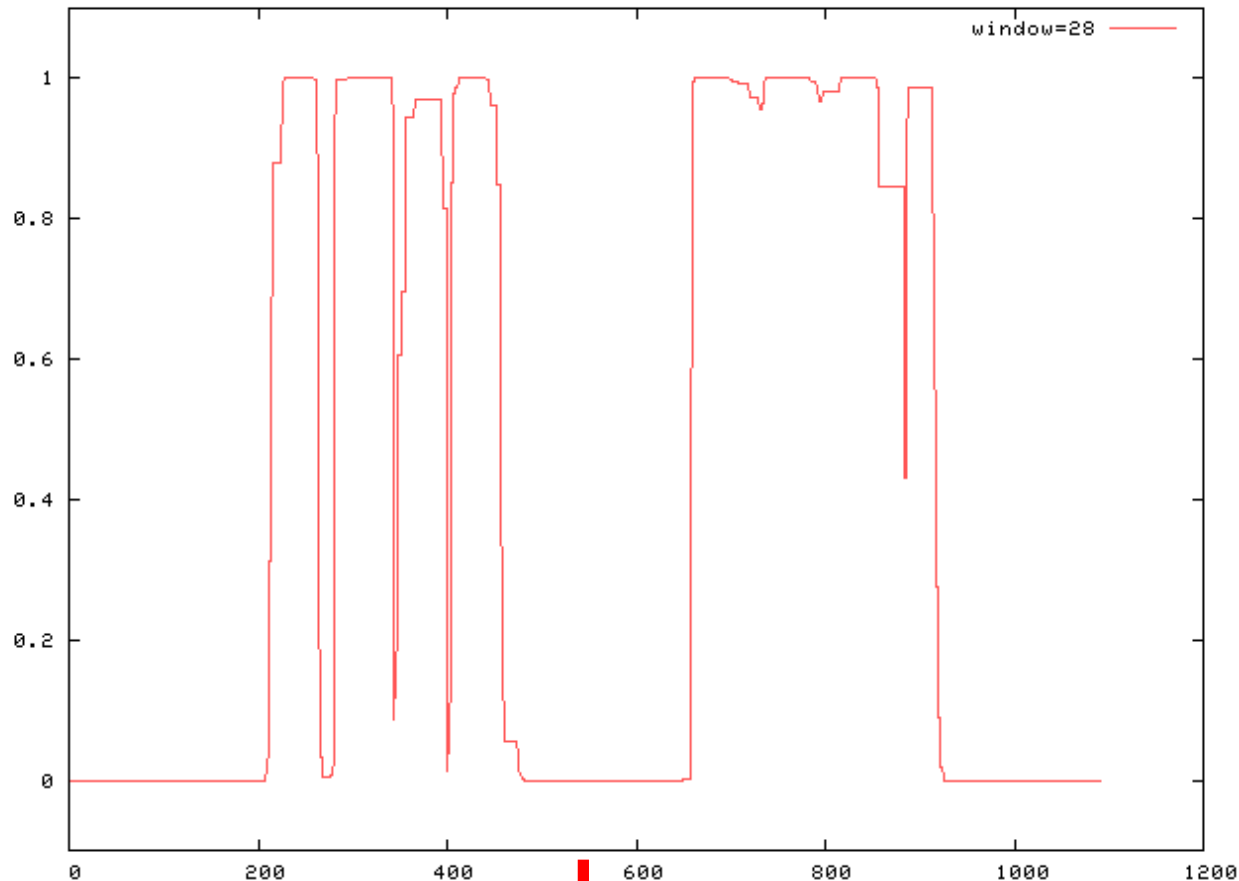
- CC v myosinu je intermolekulární (paralelní)

coiled-coil struktura

- program COIL: <https://toolkit.tuebingen.mpg.de/tools/deepcoil>

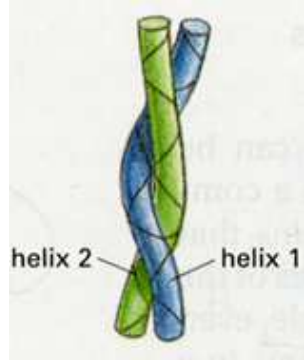
profil SMC6

Ludwiczek et al, BioInformatics, 2019



- CC jako jedna ze sekundárních struktur (viz. Dr. Klumpler)

- CC v SMC proteinech jsou intramolekulární (antiparalelní)



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



Tropomyosin



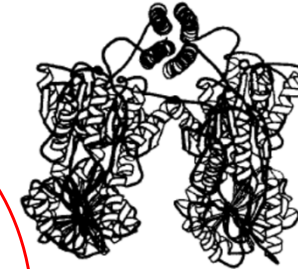
Catabolite gene
activator protein



Serum response factor



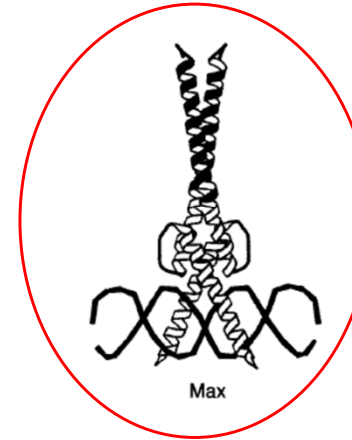
Replication terminator protein



Lac repressor



GCN4

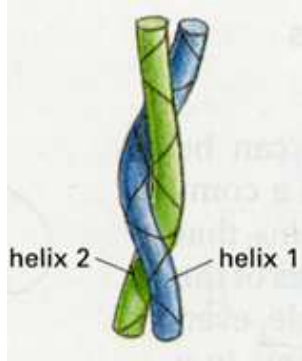


Max



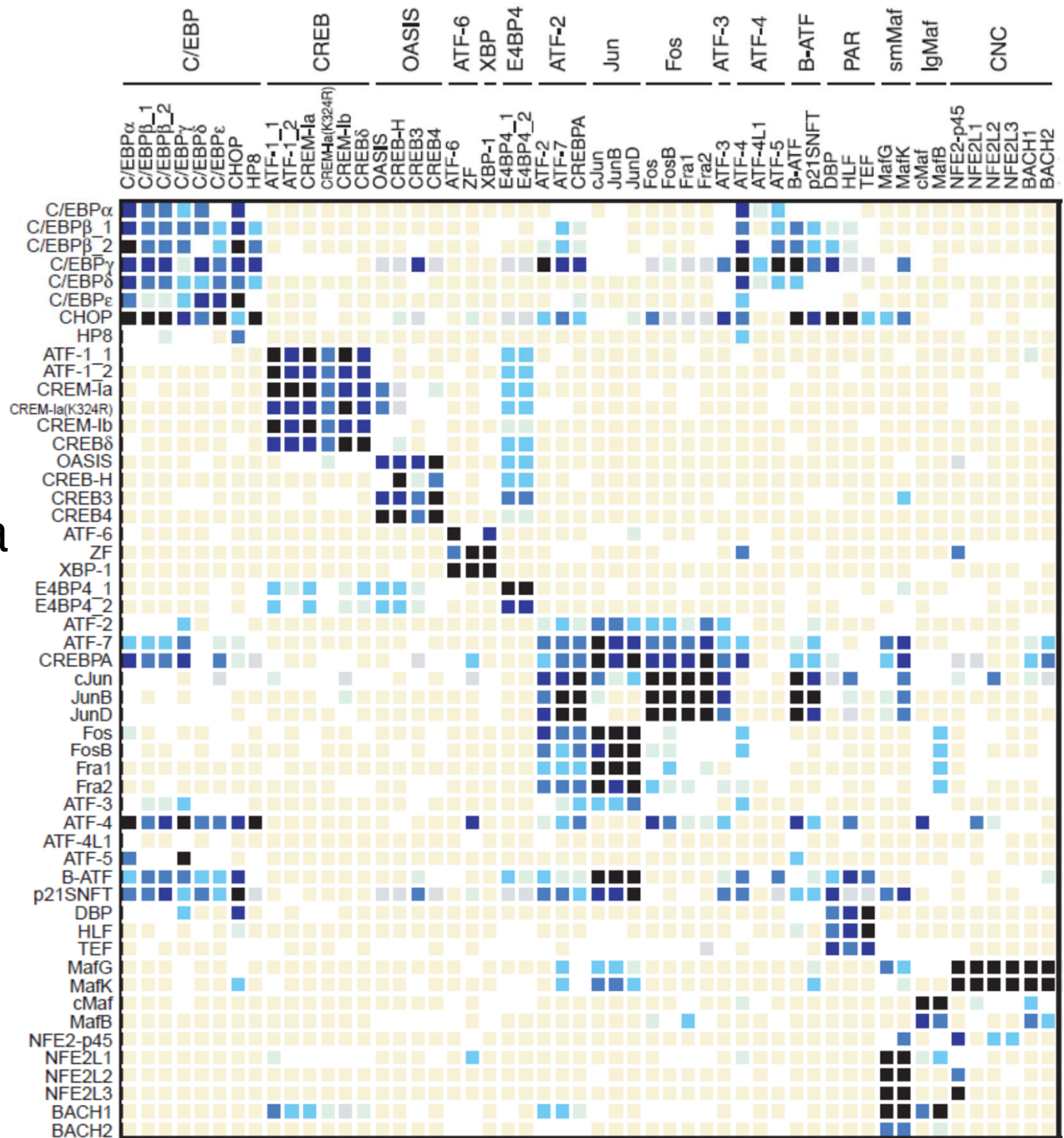
GAL4

Intermolekulární - homo- či heterodimery
(oligomery)



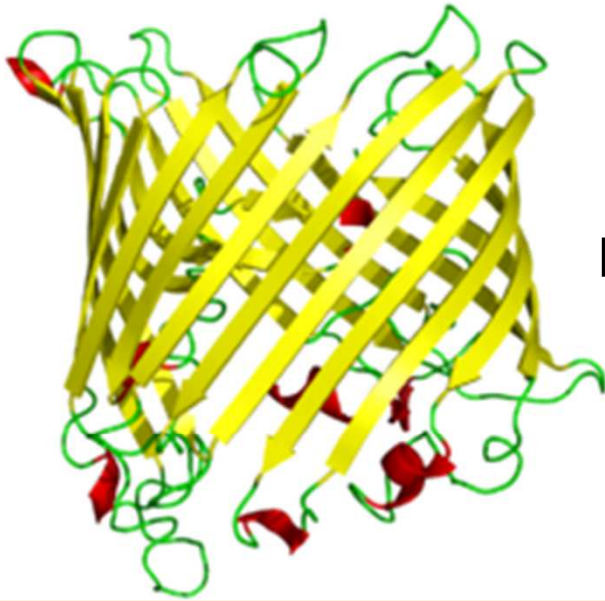
Coiled-coil
doména je
významným
dimerizačním
modulem u mnoha
proteinů: bZIP
transkripční
faktory vytváří
homo- i
heterodimery

variabilita

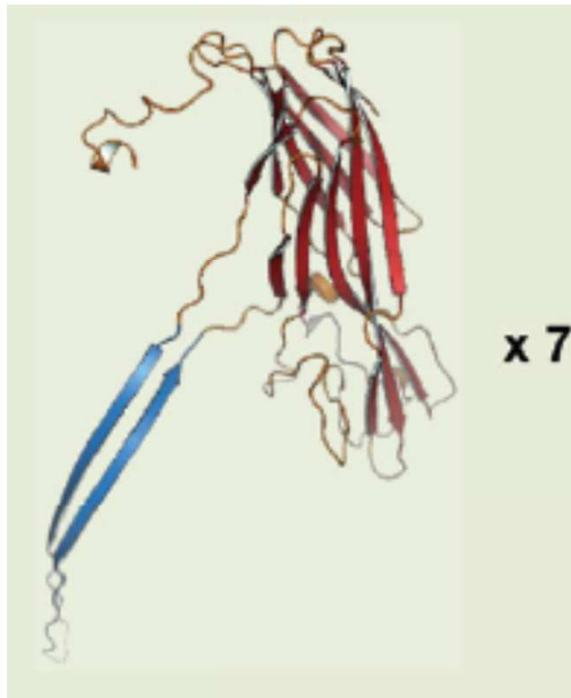
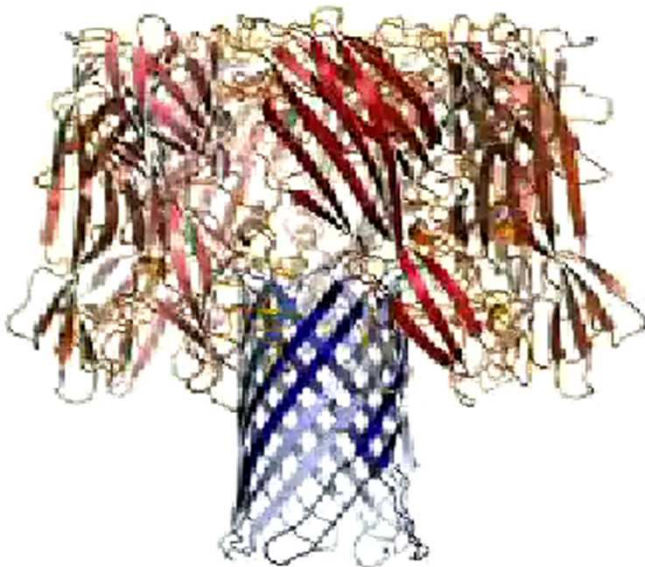
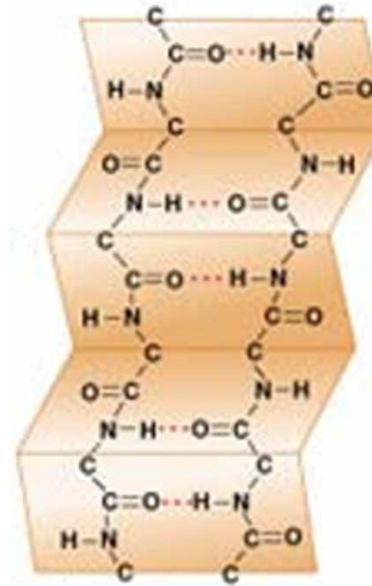


... sekundární struktury ...

v interakcích β -listů převažují **vodíkové vazby** (peptidového řetězce)



Porin
(1 ORF - polypeptid
prostup mitochondriální
membrány)

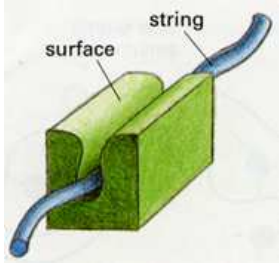


tento „pór“ vzniká interakcí
7 podjednotek

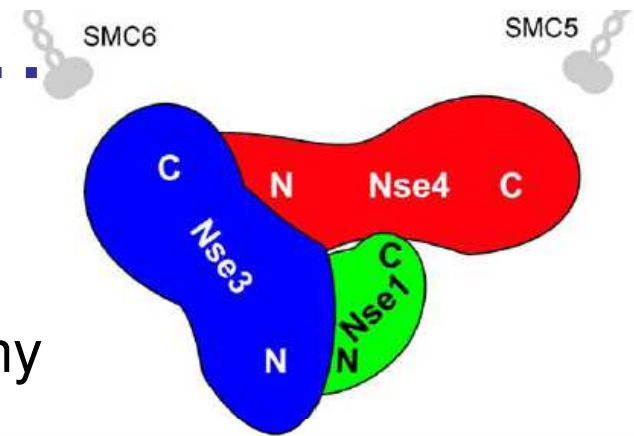
por se používá v NGS
(nanopore) technologii

Mueller & Ban, Cell, 2010
Los a spol, MMBR, 2013

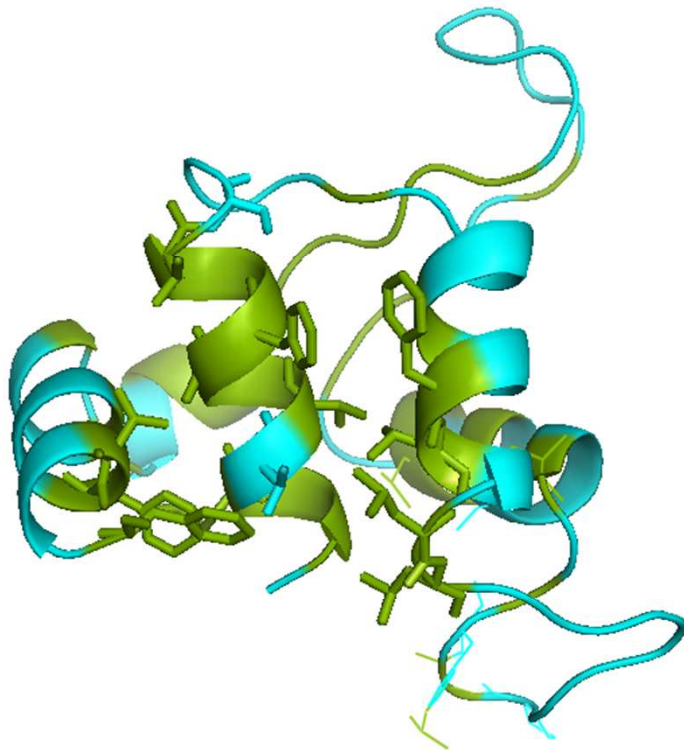
... terciární struktura ... kapsa-peptid



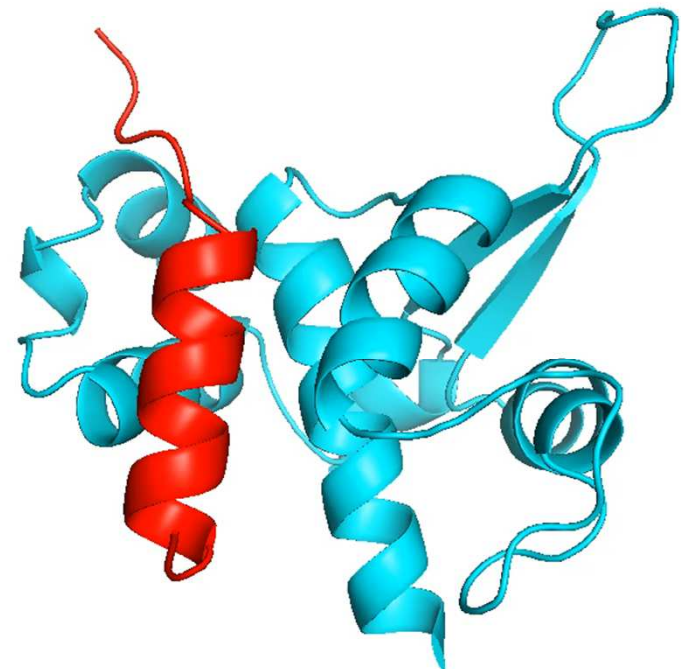
sekundární struktury (šroubovice, beta-listy)
interagují pod různými úhly a vytváří různé povrchy



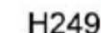
hlubší prohlubně na povrchu
mohou tvořit kapsy pro vazbu
partnera (šroubovice, peptid)



161 166 171 176 181 186 191 196 201 206 211 216 221 226 231 236 241 246 /D/107 111 116 1
ESAIWEMLRRLRIEFGEMHSEFGDVKKLVTEEFVKQKYLEYNRKIKQKDPKSMITQYKDAQE HMTVFDPTSFADLL
ining)



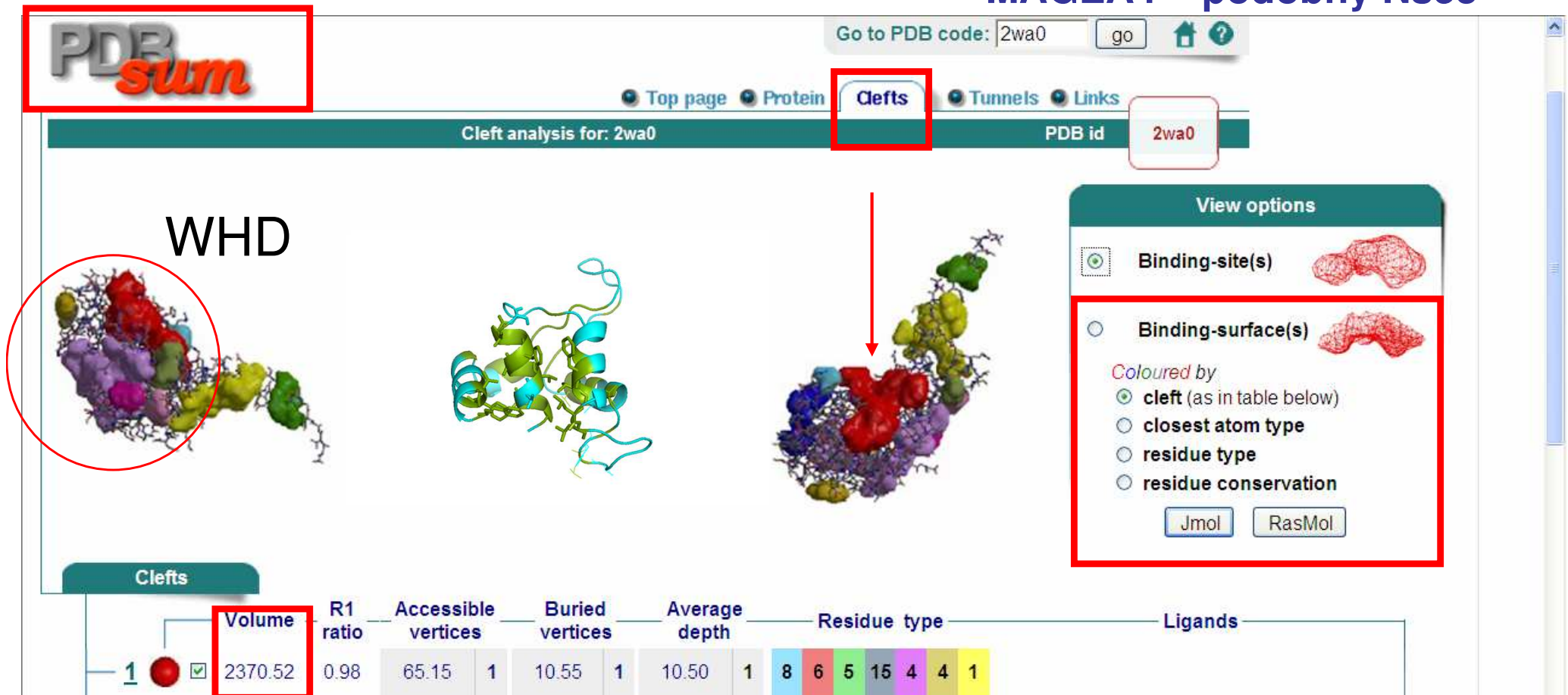
hydrofobní interakce mezi Nse3 a Nse4



Hudson et al.: PLoS One, 2011

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

MAGEA4 – podobný Nse3



největší kapsa

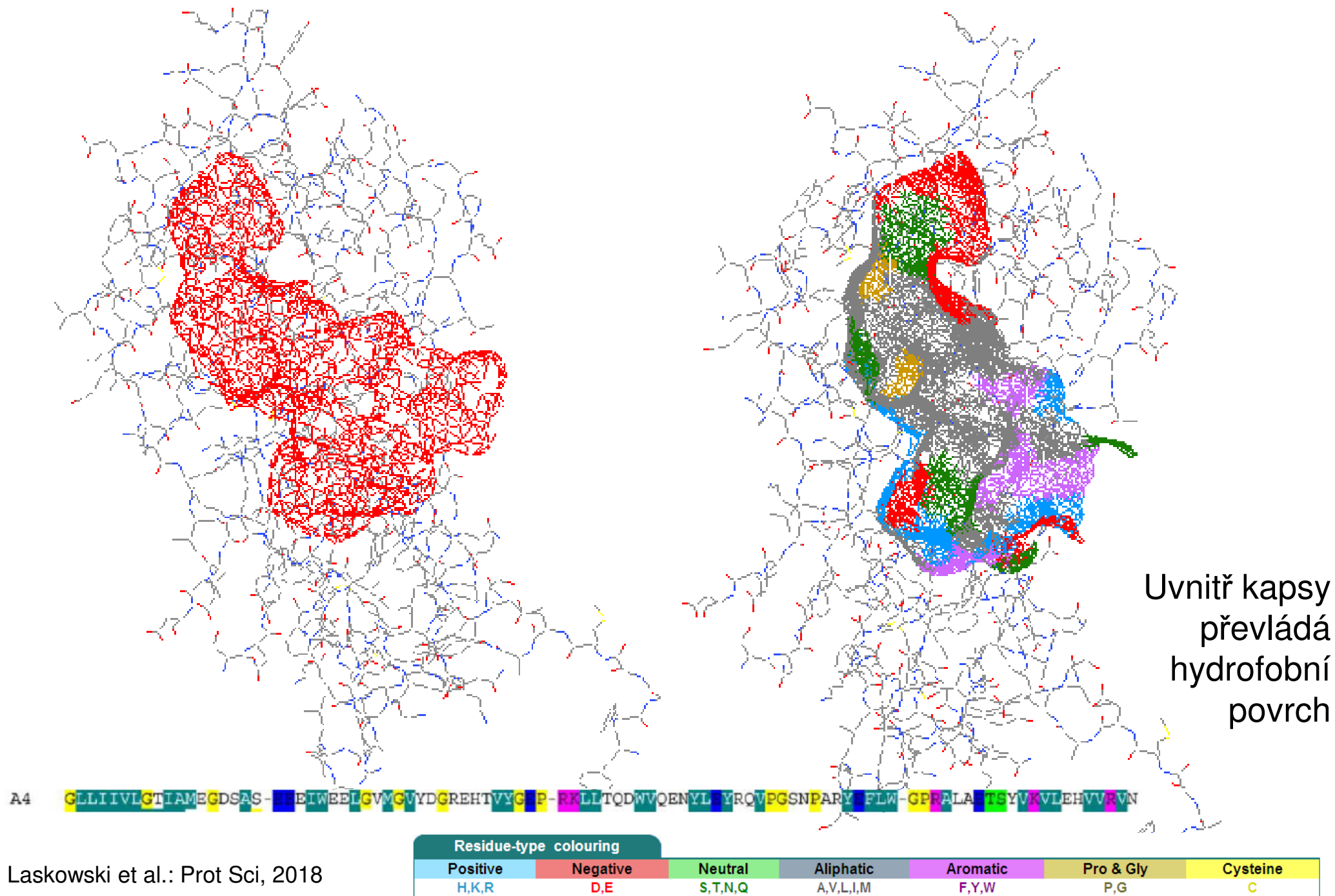
<https://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/GetPage.pl?pdbcode=index.html> /

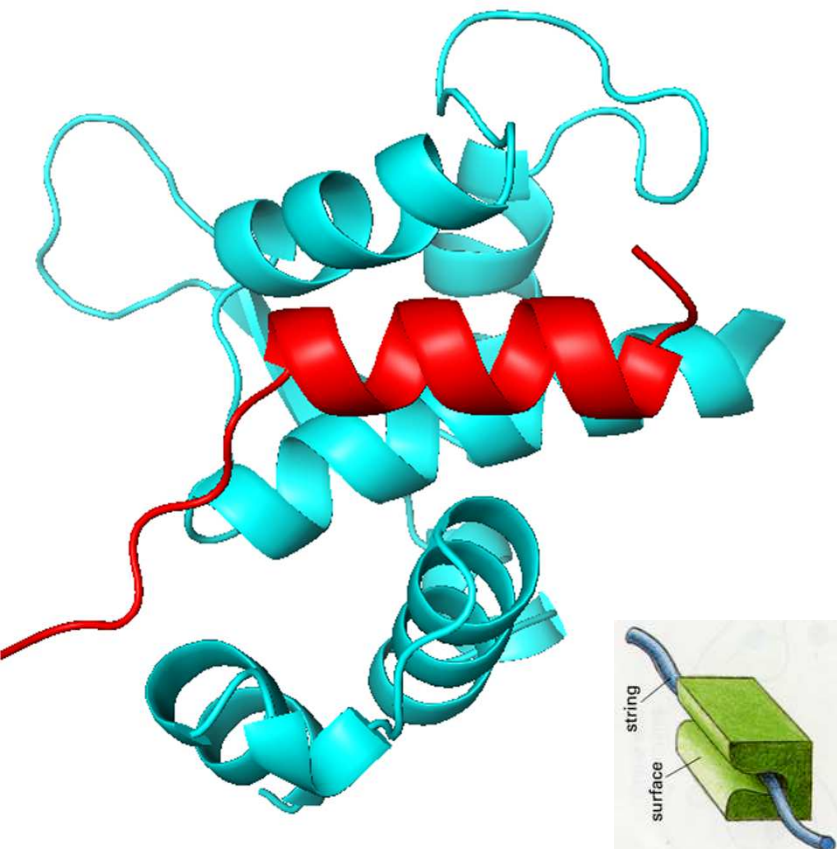
Laskowski et al.: Prot Sci, 2018

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





HADDOCK

Software web portal

Home HADDOCK Whispy CPDRT DNA SQUEEZE Publications HADDOCK CONTACT

WELCOME TO THE UTRECHT BIOMOLECULAR INTERACTION WEB PORTAL >>

PROFILE >>

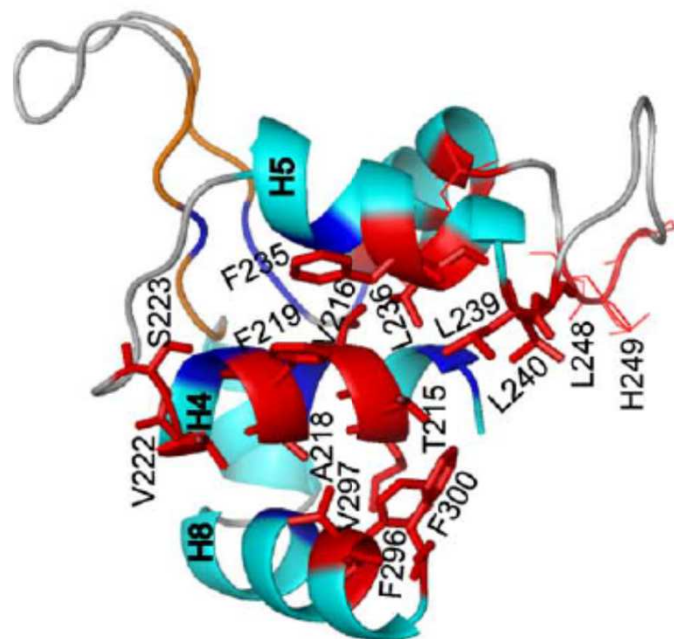
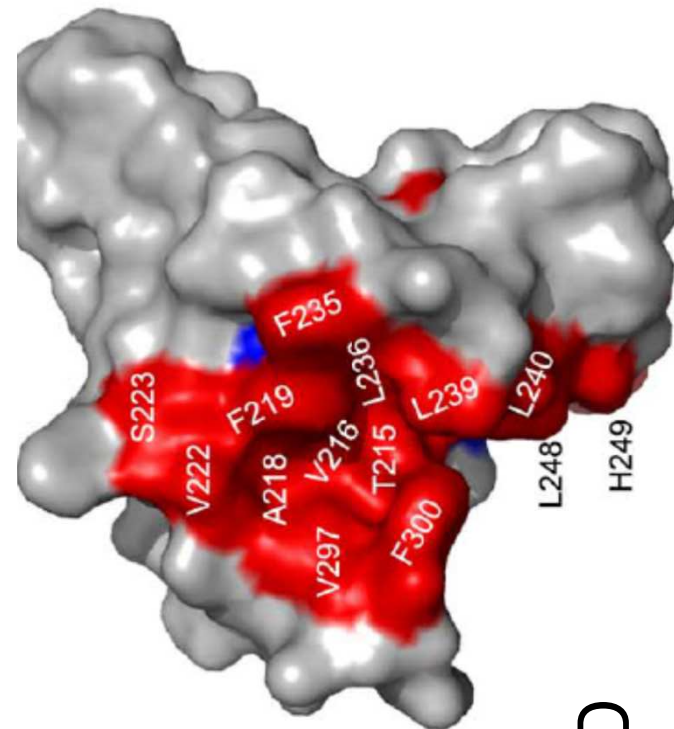
Universiteit Utrecht

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

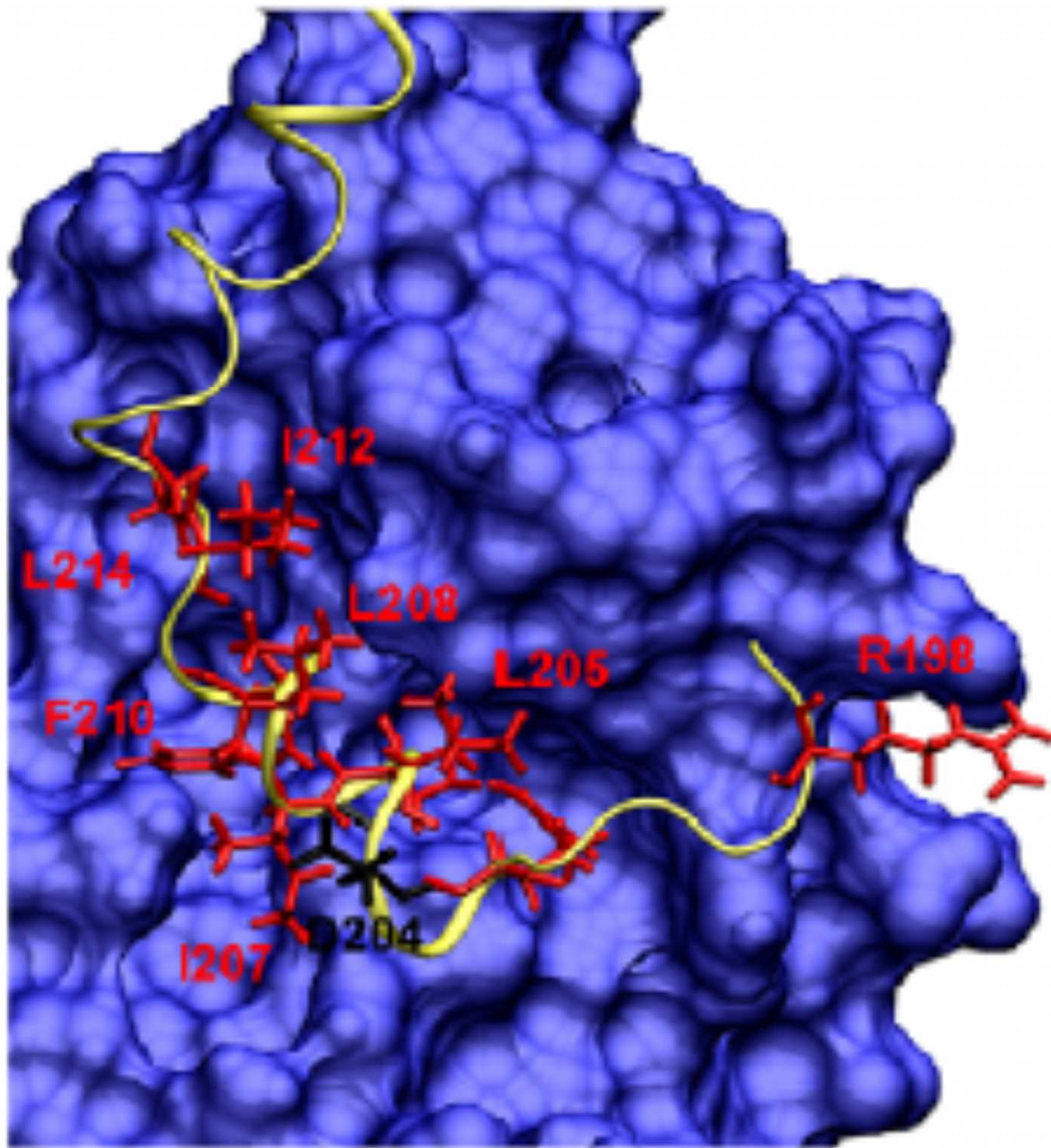
Docking



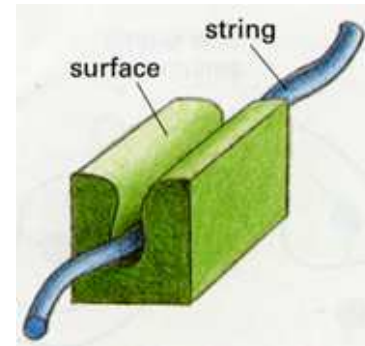
WHD

Interakce
mapována
mutagenezí

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



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)

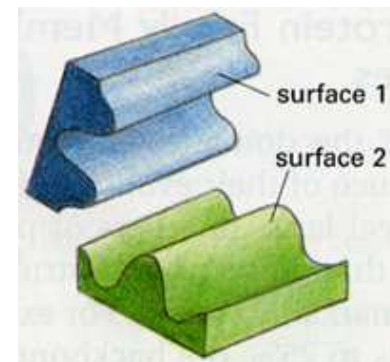
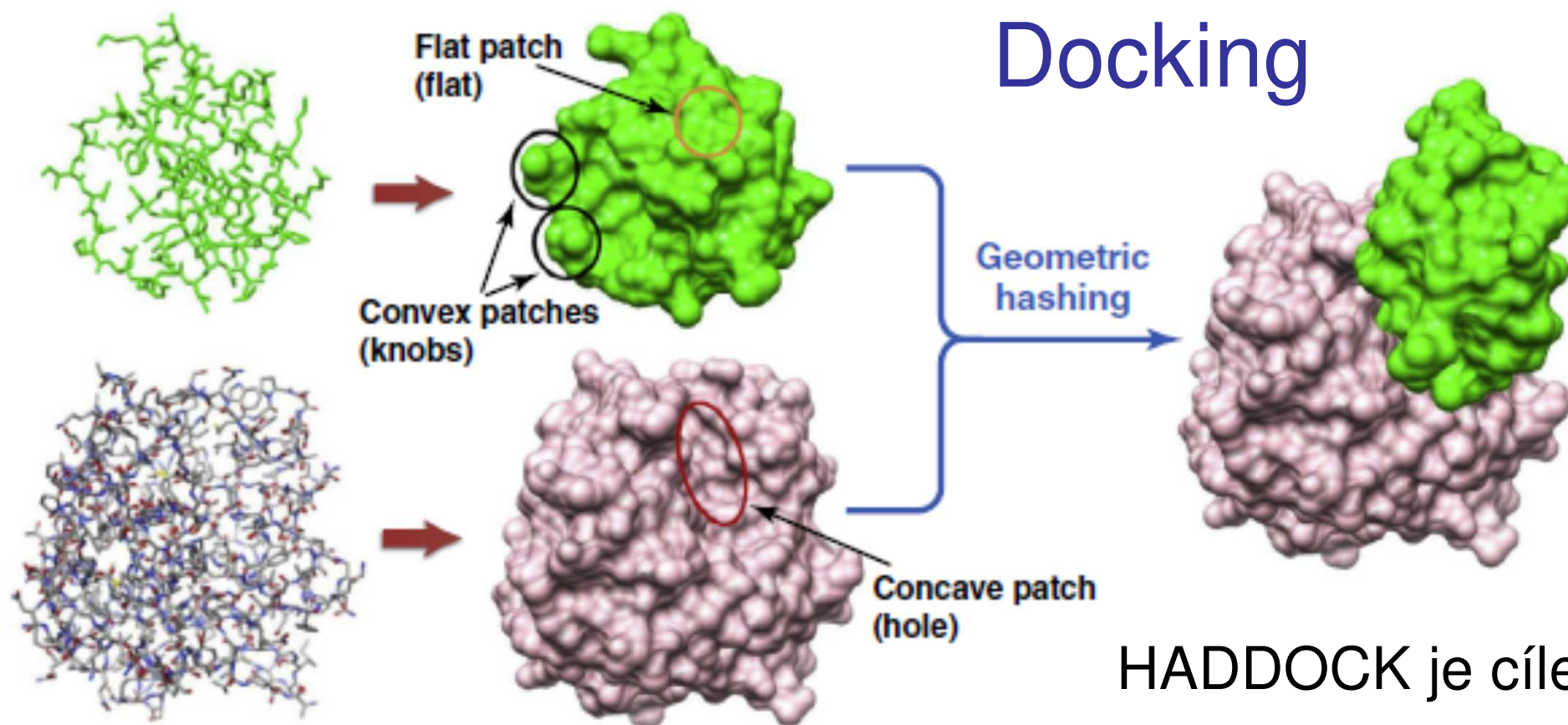


TABLE 1

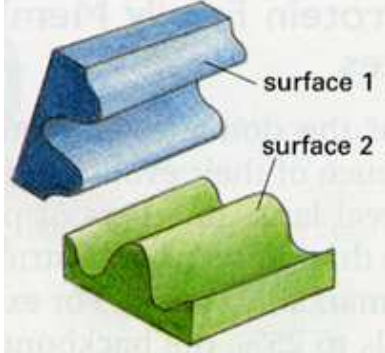
Search strategies in protein–protein docking

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]



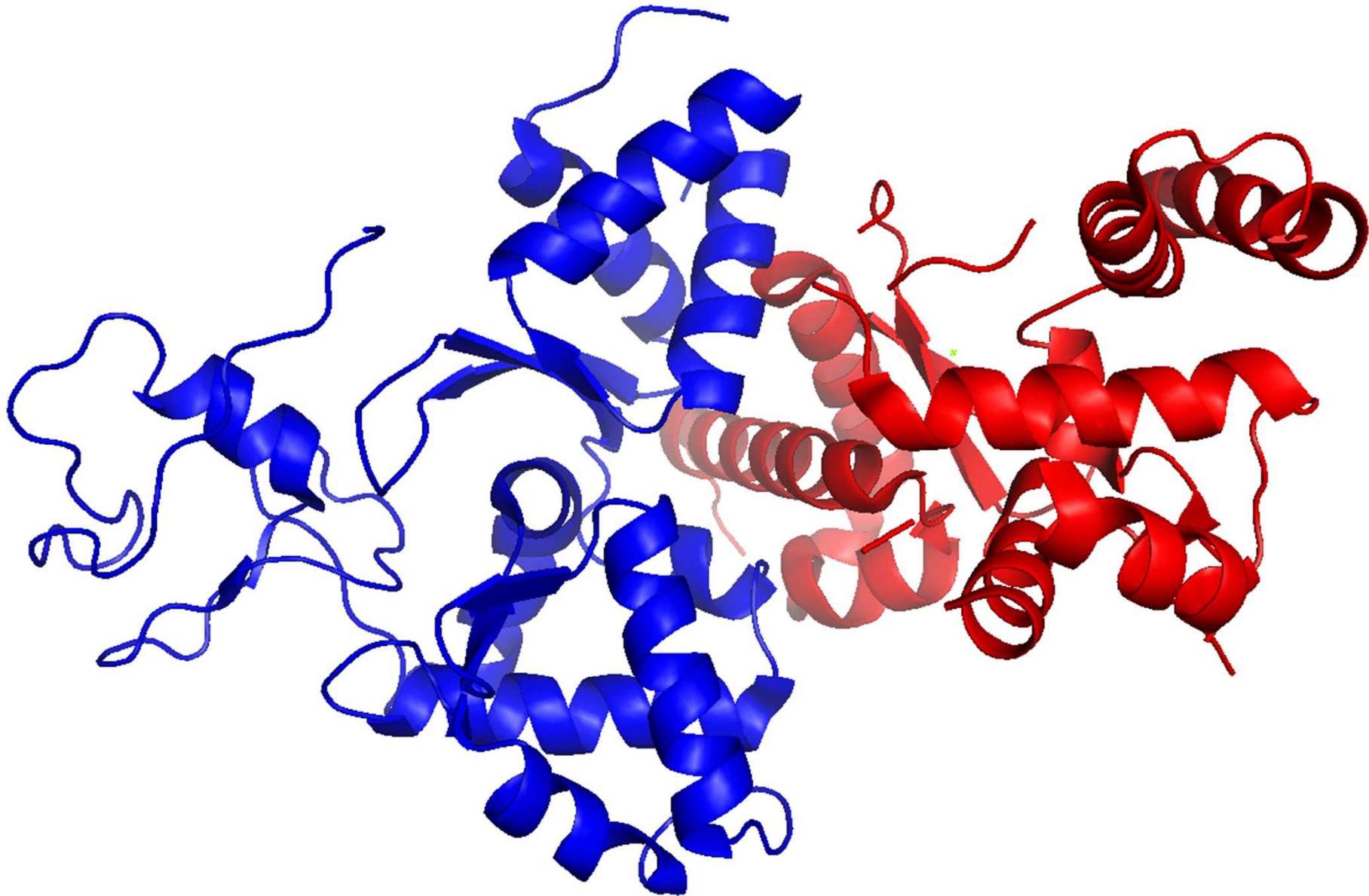
Docking

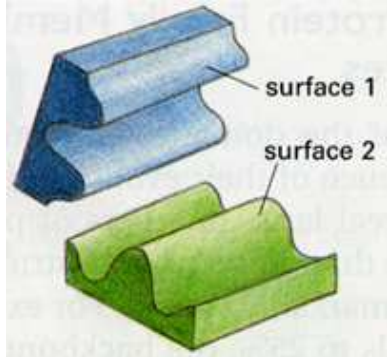
HADDOCK je cílený



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

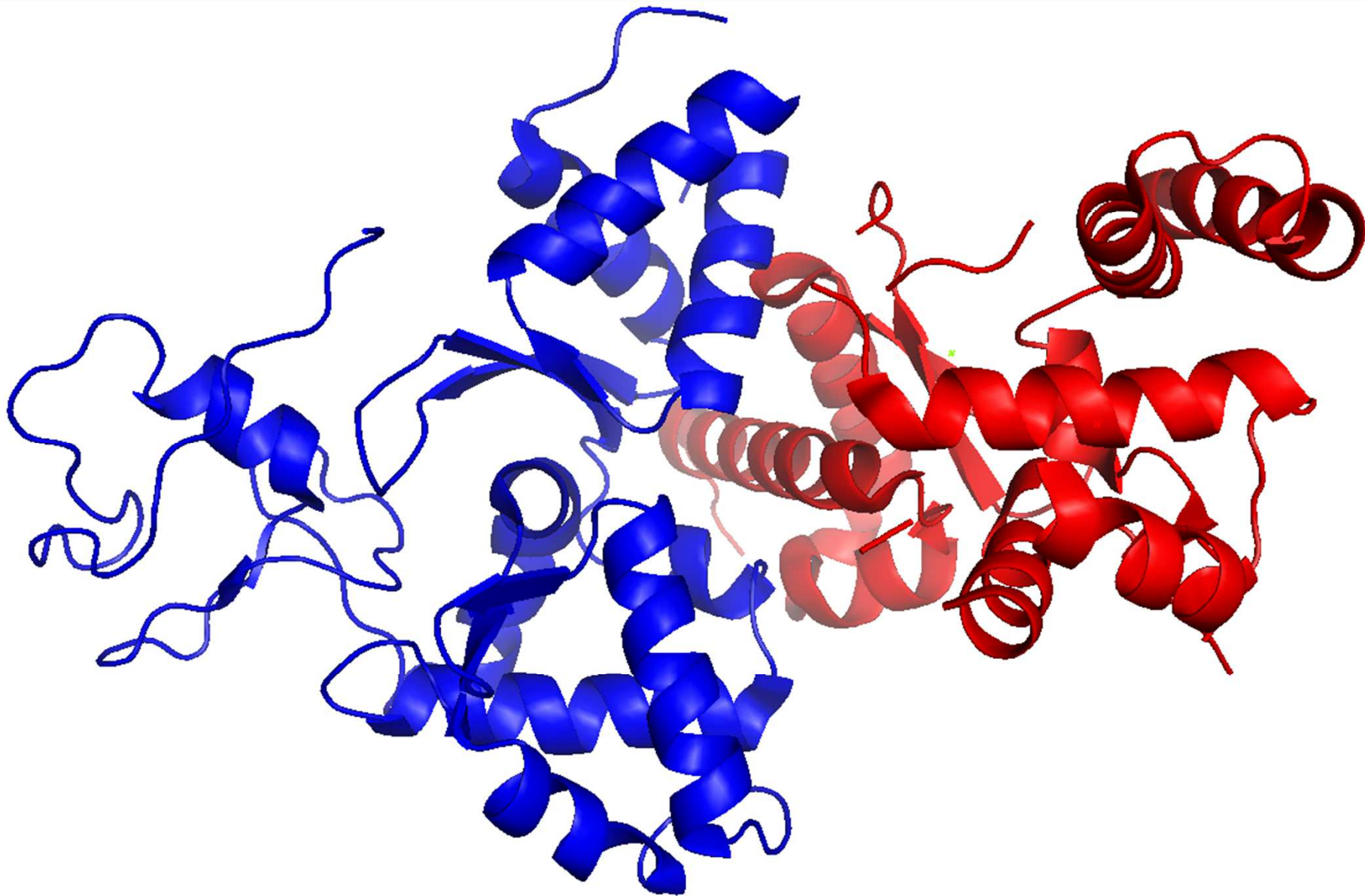
(kokrystal NSE1-NSE3 proteinů)





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

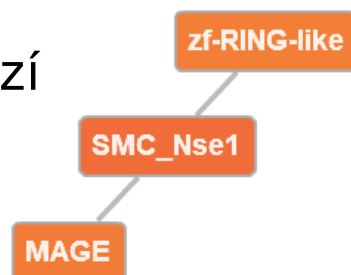
(kokrystal NSE1-NSE3 proteinů)



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



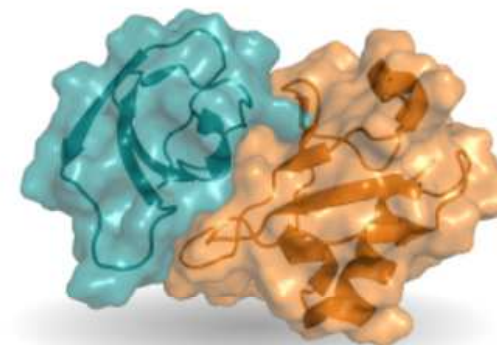
Search motif by name or keyword: ?

Motif name (e.g. SH2_LIG_0)

Search motif



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

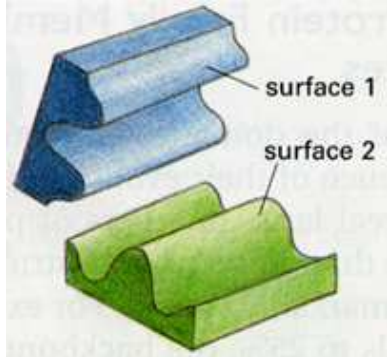


- > **Overview** General information on 3did
- > **Getting Started** Help for new users
- > **Technical Information** Linking to 3did
- > **Download** data files or MySQL tables

Statistics

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

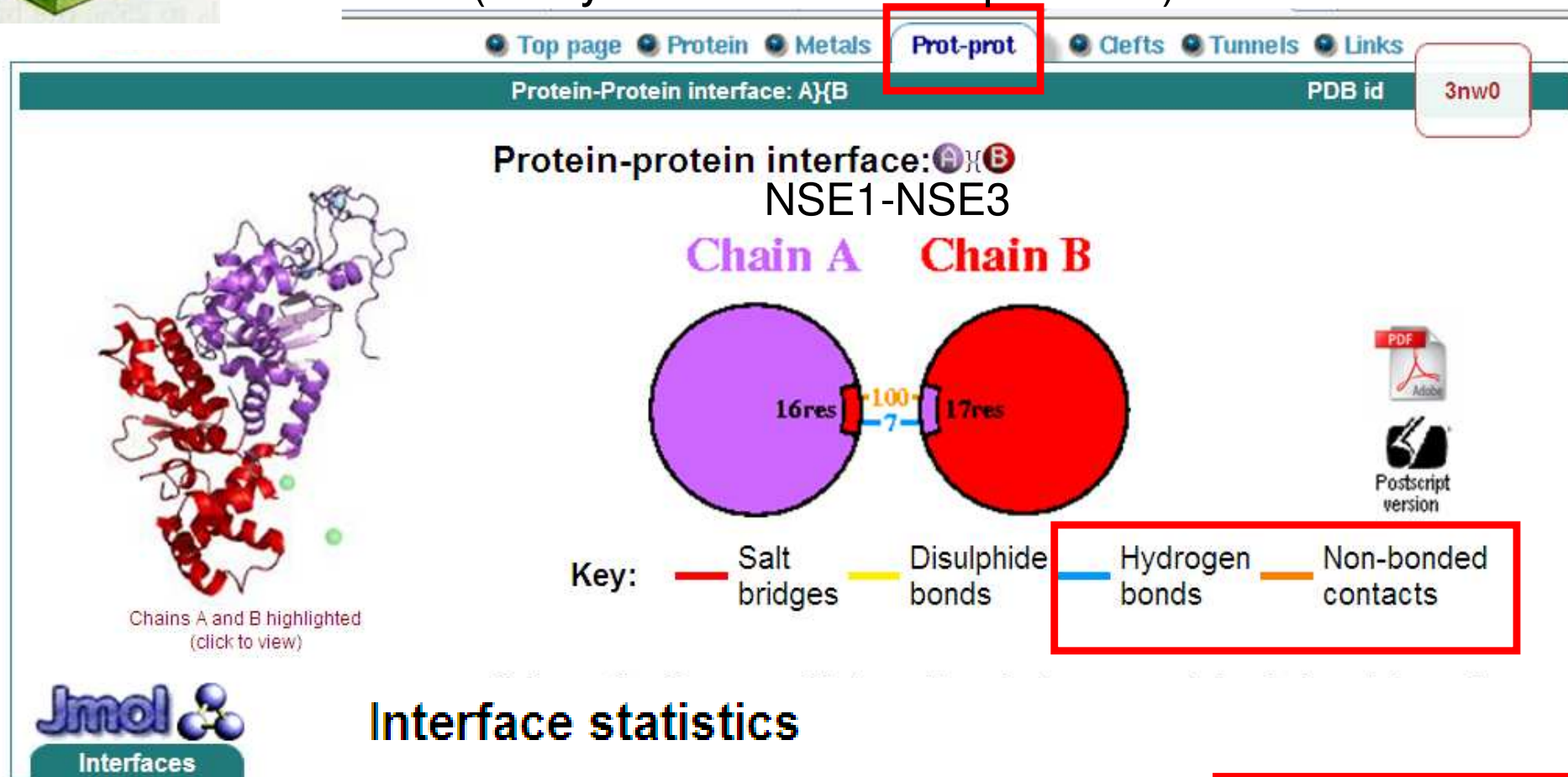
3DID kategorizuje doména-doména interakce z PDB (06/2017 – cca 10000 doména-doména komplexů/100000 struktur) – topologie ne detaily



PDBsum – detailní info

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

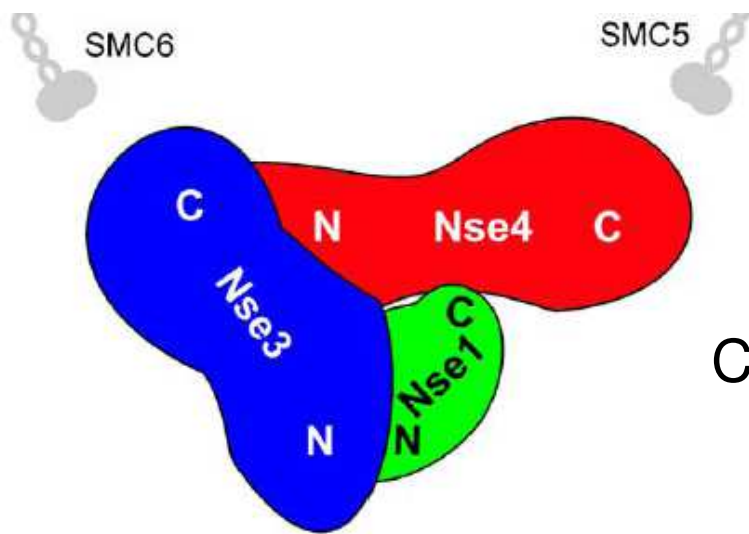
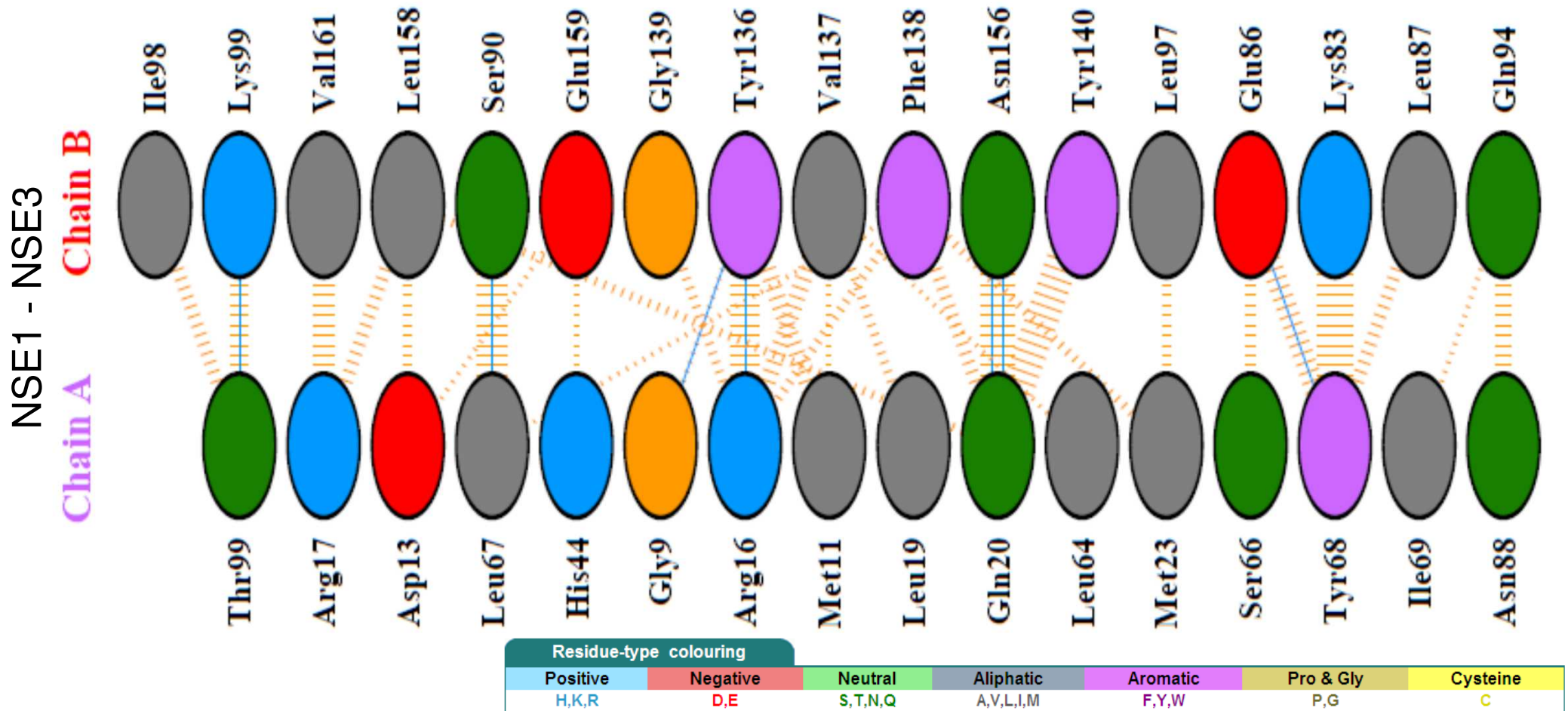
(kokrystal NSE1-NSE3 proteinů)



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)

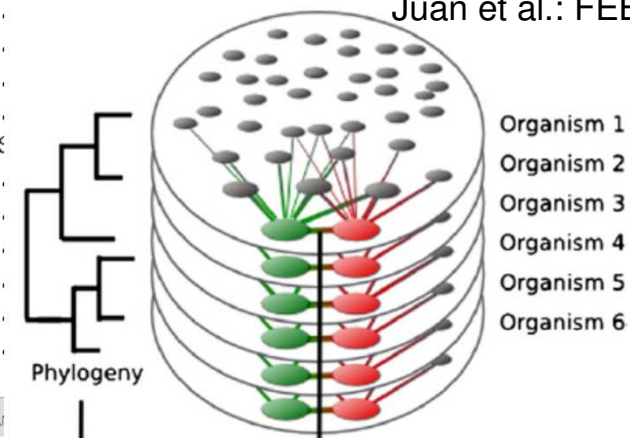


— Hydrogen bonds

||||| Non-bonded contacts

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.ARSTMTFAEAKPVLAAIF.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.ARSVLTLETAKPILAAIS.TFQ.....
 U1GD89_ENDPU/11-202 NRAFVQAFM.ARGTLTYETSKPLLASIF.TVH.....
 C5GY37_AJEDR/11-207 HRAFLQAFM.ARSTMTYEQAKPVLAAIF.SAR.....
 C6H5E2_AJECH/11-203 HRAFLQAFM.ARSTMTYEQAKPVLAAIF.TAR.....



<http://pfam.xfam.org/family/PF07574#tabview=tab1>
 x Najít: plot Předchozí Další Možnosti



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...

enter ID/acc

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:FEF14320.1} (744 residues)

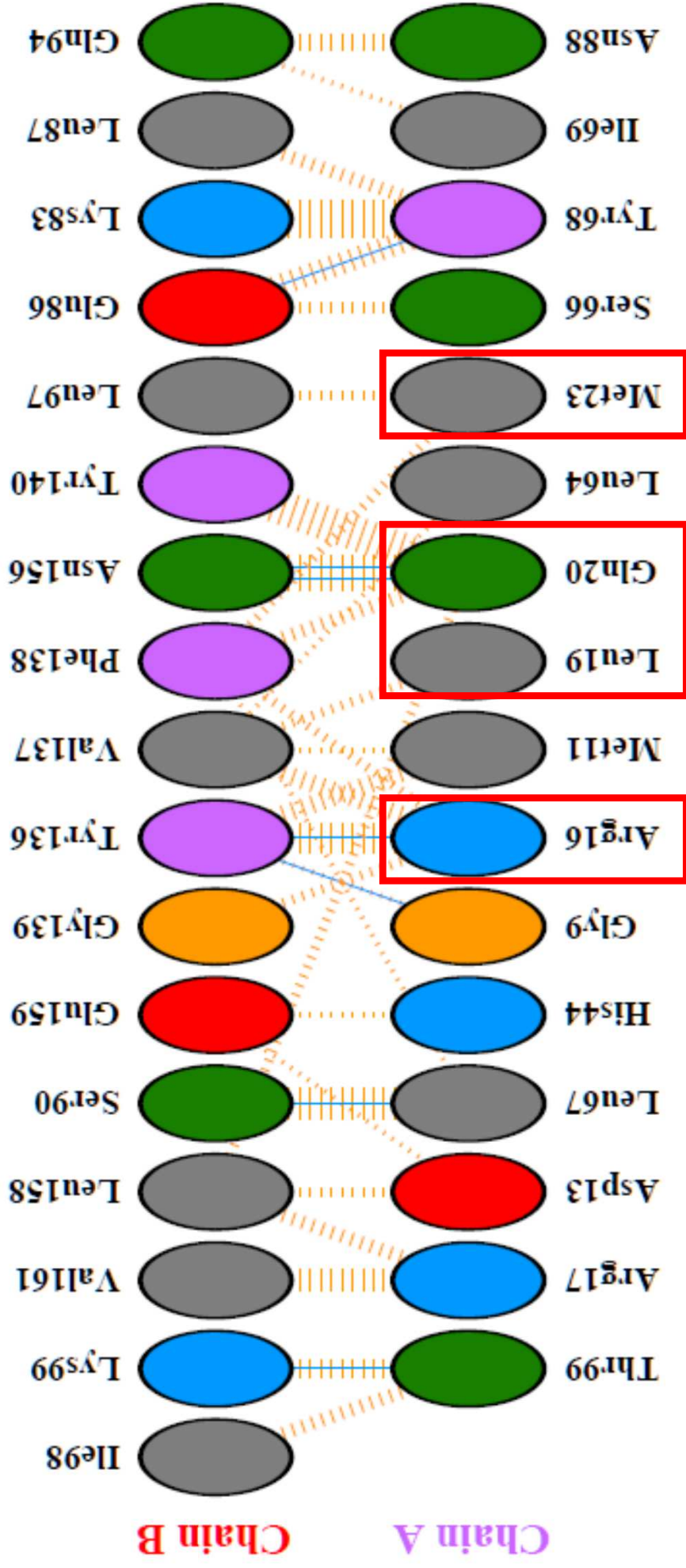
160%

A1CCH2_ASPCL/14-216	NRAFLQAFM	ARSTMTFAEAKPVLA	IF.SAH.....	EG.....	QPVSA...DDVTE
A2Q7K6_ASPNC/15-218	NRAFLQAFM	ARSTMTFTQAKPVLA	IF.SIR.....	DD.....	EQVSP...EDITE
B8NLA5_ASPFN/14-216	NRAFLQAFM	ARSTMTFAEAKPVLA	IF.SVH.....	EG.....	EPVSA...EDVTE
B6QTR9_TALMQ/14-217	NRAFLQAFM	ARSTMTFDEAKPVLA	IF.SAQ.....	EN.....	REVL...EDITQ
V5FED6_BYSSN/14-236	NRAFLQAFM	ARSTMTFEEAKPVLA	IF.SAHGAQSTIFFDSS	YVEKEIANLYLATER	RPVLA...EDITQ
S7Z8E9_PENO1/8-209	HRAFLQAFM	ARSTMTFEDAQPVL	AAII.SAH.....	EG.....	RTVDP...DEVTE
B6H9Q9_PENRW/8-210	NRAFLQAFM	ARSCMTFEDAQPIL	AAIL.TVS.....	EG.....	RTVDP...DEVGE
H6C926_EXODN/14-207	NRAFLQAFM	ARSVLTLETAKPIL	AAS.TFQ.....	DG.....	REVQP...QDMTV
U1GD89_ENDPU/11-202	NRAFLQAFM	ARGTLTYETSKPL	LASIF.TVH.....	EG.....	REILP...NDITE
C5GY37_AJEDR/11-207	HRAFLQAFM	ARSTMTYEQAKPV	LAAIF.SAR.....	DH.....	QDTLP...EDITQ
C6H5E2_AJECH/11-203	HRAFLQAFM	ARSTMTYEQAKPV	LAAIF.TAR.....	DN.....	QETLP...EDITQ
F2PT91_TRIEC/10-199	HRAFLQAFM	SRSTMTLEEAKPV	LAAIF.TVS.....	EG.....	REILP...GDITQ
E9DEJ9_COCPS/13-202	HRAFLQAFM	ARSTMTLNEAKP	LAAIL.SVK.....	DG.....	REVL...EDVTQ
R7Z157_CONA1/13-202	HRAFLQAFM	ARSVLTFFEAQP	LAAIL.TAH.....	EG.....	RPTLP...ADITT
U4LU38_PYROM/8-205	HRAFLQAFM	ARSSMTGEELLG	VVTAIH.GVE.....		NPEEP...TETTL
S8AAF4_DACHA/9-208	HRTFLQALL	IRPFIDIEEGQEL	LAAIA.SAE.....	SG.....	TDVPA...NSITV
G1X2Y0_ARTOA/8-207	HRAFLQALL	IRPFIDVQEGREL	LAAIK.SAE.....	AG.....	SDVSI...ESVPP
C5DCF6_LACTC/23-226	SKFLLQYVLS	RRGVCSEKALAK	KLTL.....	ERD.....	EQLEDSETE
C5DQF6_ZYGR/37-240	ARYLLQYLL	CRGICHENMLLV	LDKL.....	QK.....	YTQDPTSQVCS.T
I2H1A9_TETBL/24-252	RYLLRYIMASE	GICHENMLLLAL	YAL.....	NLDYS.....	GDCQEVLA.....
G8C139_TETPH/22-276	RYLLQYLL	CRGICHENMLLV	LDKL.....	LTD.....	GSSSDDFYRLNMVELN
G8ZVJ6_TORDC/16-236	RYLLQYLL	CRGICHENMLLV	LDKL.....	QGD.....	ETND...VQELY
H2ATC7_KAZAF/7-237	RYLLQYLL	CRGICHENMLLV	LDKL.....	YMDL.....	GCFDDAWQIDQWL
J5S7B7_SACK1/17-253	RYLLQYLL	CRGICHENMLLV	LDKL.....	ETDA.....	SKWSTEQWT
E7NKI9_YEASO/18-258	RYLLQYLL	CRGICHENMLLV	LDKL.....	ETDA.....	STLNTXSQQWV
J8PZG2_SACAR/18-258	RYLLQYLL	CRGICHENMLLV	LDKL.....	ETDA.....	LRFDAERSMQQWI
G0W7Y8_NAUDC/22-268	RYLLQYLL	CRGICHENMLLV	LDKL.....	KVDS.....	NTIDPQWTISDWL
G0V5G7_NAUCC/25-272	RYLLQYLL	CRGICHENMLLV	LDKL.....	KVDS.....	HDVNAHWTISDWL
J7S9R2_KAZNA/85-303	RYLLQYLL	CRGICHENMLLV	LDKL.....	SLDL.....	PHSVSTR.SLDEWS
A7TJ64_VANPO/8-260	RYLLQYLL	CRGICHENMLLV	LDKL.....	DKDSVDEE	GSNRTFEDYL

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

URAFLOAFM	ARSTMTFAEAKPVLAAIF	SAH	EG	QFVSA	DDVTE
URAFLOAFM	ARSTMTFTQAKPVLAAIF	SIR	DD	EQVSP	EDITE
URAFLOAFM	ARSTMTFAEAKPVLAAIF	SVH	EG	EFVSA	EDVTE
URAFLOAFM	ARSTMTFDEAKPVLAAIF	SAQ	EN	REVL	EDITQ
URAFLOAFM	ARSTMTFEEAKPVLAAIF	SAHGAQSTIFFDSSYEKEIANLYLATER	EN	RPVLA	EDITQ
URAFLOAFM	ARSTMTFEDAQPVLAAII	SAH	EG	RTVDP	DEVTEQ
URAFLOAFM	ARSCMTFEDAQPILAAAIL	TVS	EG	RTVDP	DEVGE
URAFLOAFM	ARSVLTLTETAKPILAAIS	TFQ	DG	REVQP	QDMTV
URAFVQAFM	ARGTLTYETSKPILLASIF	TVH	EG	REILP	NDITE
URAFLOAFM	ARSTMTYEQAKPVLAAIF	SAR	DH	QDTLP	EDITQ
URALLQAFM	ARSTMTYEQAKPVLAAIF	TAR	DN	QETLP	EDITQ
URAFLOAFM	SRSTMTLEEAKPVLAAIF	TVS	EG	REILP	GEDITQ
URAFLOAFM	ARSTMTLINEAKPILAAAIL	SVK	DG	REVL	EDVTQ
URAFLOAFM	ARSVLTFEEAQPILAAAIL	TAH	EG	RPTLP	ADITT
URAFLOAFM	ARSSMTGEEILGVVTAIH	GVE		NPEEP	TETTL
URTFLOAFM	IRPFIDIEEGQELLAAIA	SAE	SG	TDVPA	NSITV
URAFLOAFM	IRPFIDVQEGRELLAAIK	SAE	AG	SDVSI	ESVPP
SKFLLQYVLS	RRGVCSEKALAKAIKTL		ERDG		EQLEDSETE





Visualization



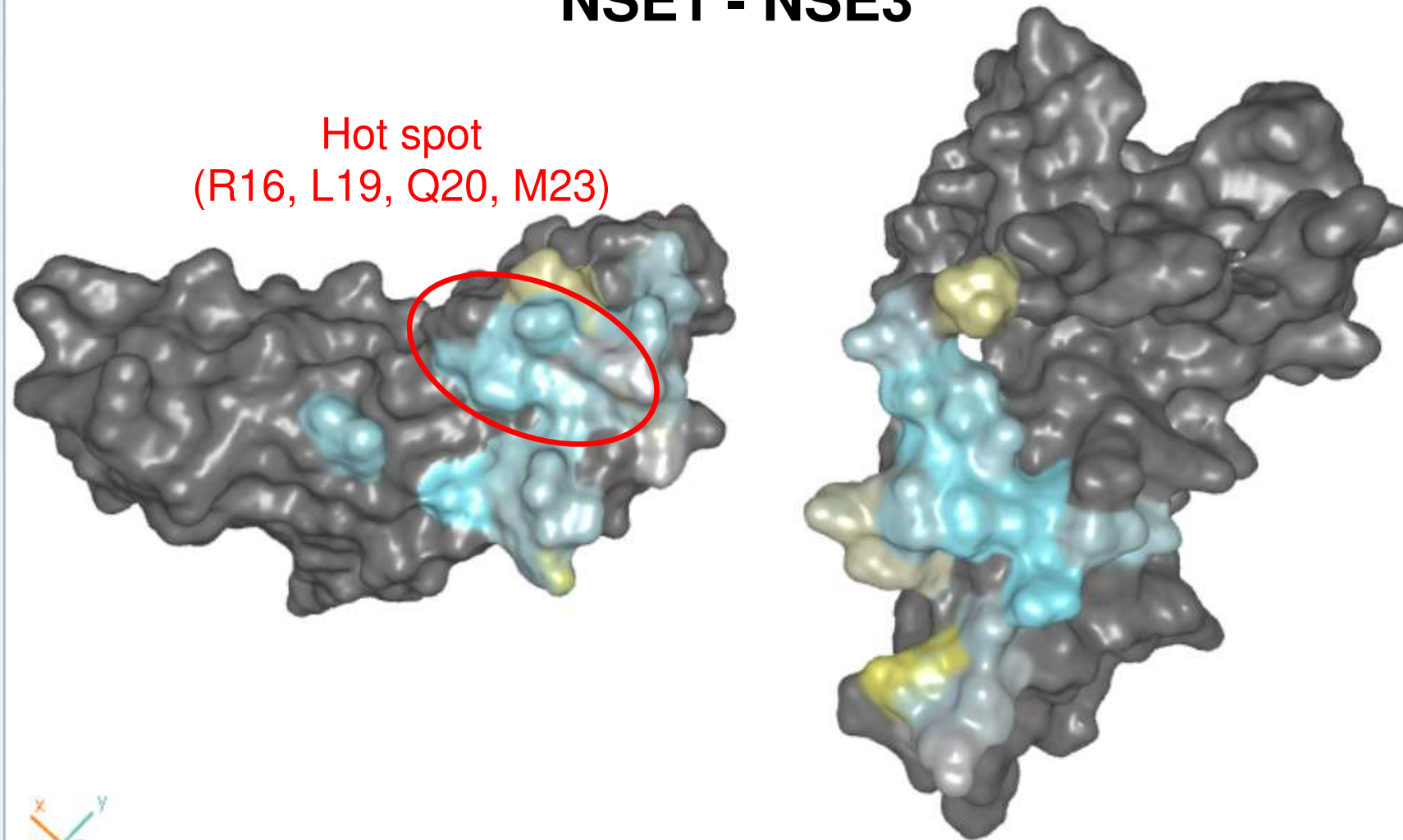
Residue Matrix

Primary Structure: 3

Sort by: Conservation

NSE1 - NSE3

Hot spot
(R16, L19, Q20, M23)



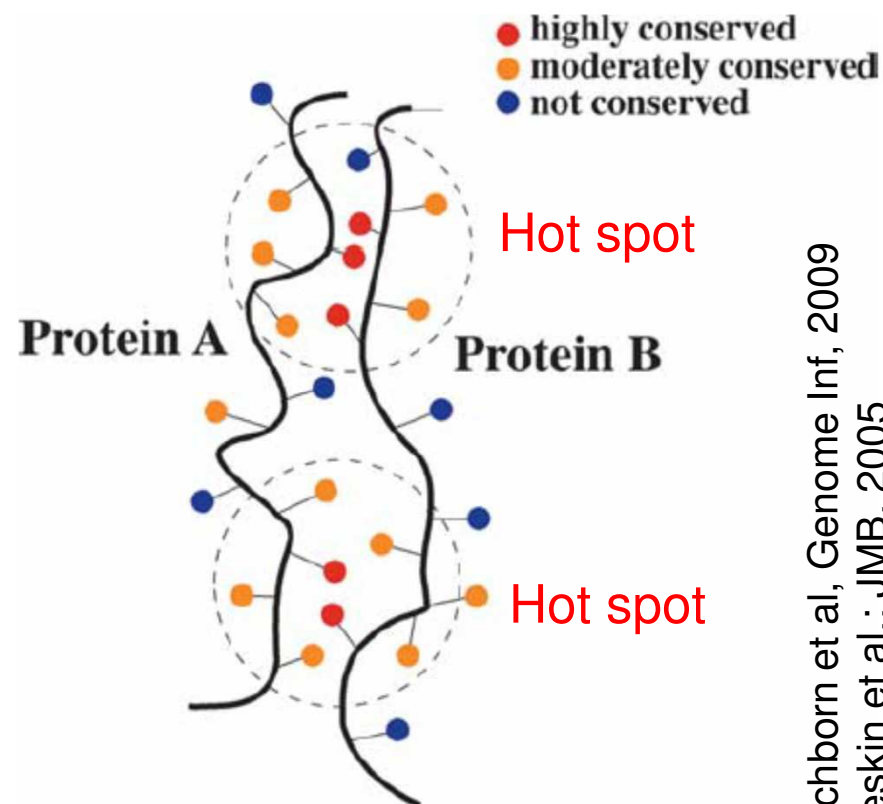
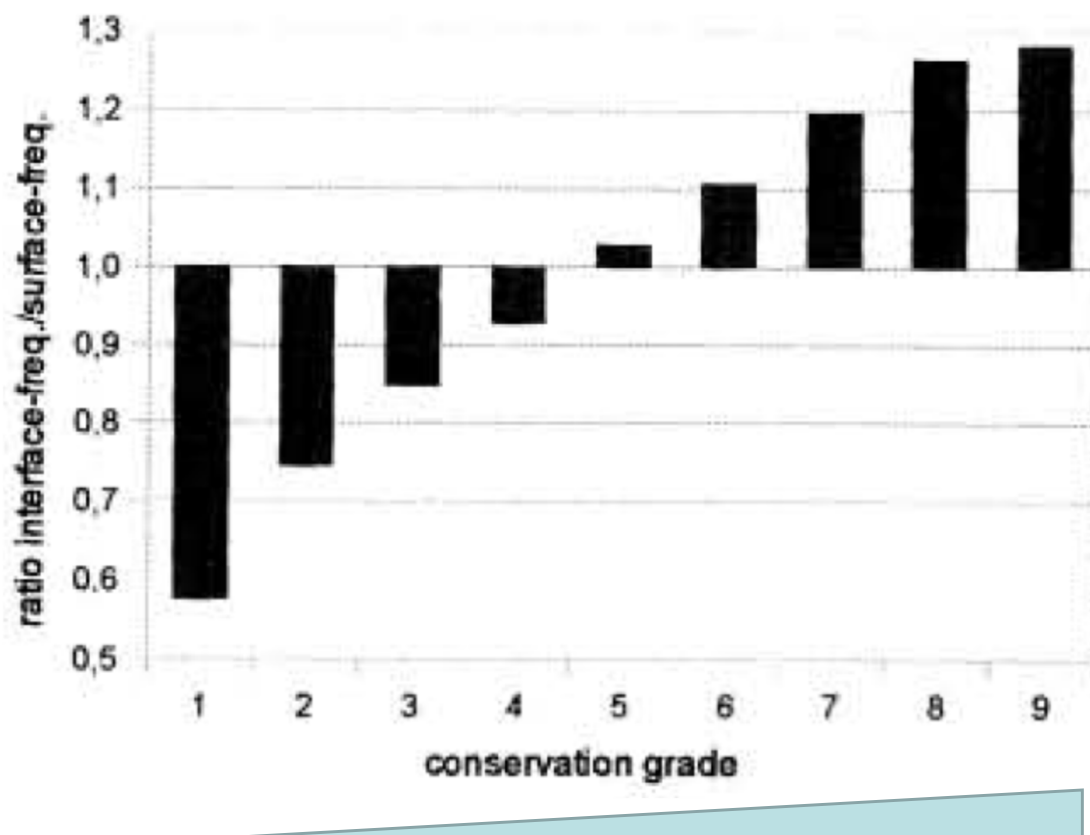
N88
Q20
M23
T99
L64
L19
D13
I69
L67
Y68
H44
S66
M11
R16
G9
R17

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** – (obecně) povrchové AMK jsou málo konzervované (grade1), zatímco interakční povrchy jsou hodně konzervované (grade9)



AlphaFold 3

Nobelova cena za chemii 2024

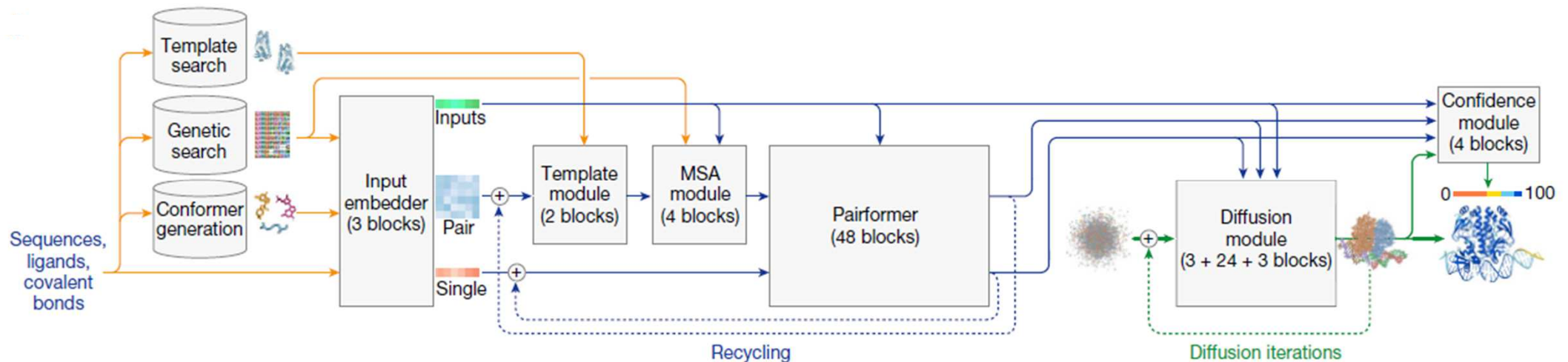


J.M. Jumper

AF2: „váží“ konzervovanost/evoluci AMK a jejich (vzájemnou) pozici ve známých strukturách (vstupy: MSA a PDB)

AF3: interakce – podobně „váží“ koevoluci AMK (více proteinů) a struktury

BindCraft: de novo design nových interakčních partnerů (AF2)



Abrams et al., Nature, 2024
Pacesa et al., Nature 2025

Kde najít další informace o PPI?

The screenshot shows a Windows Internet Explorer browser window displaying the website of the Finley Lab, Center for Molecular Medicine and Genetics. The address bar shows the URL <http://proteome.wayne.edu/PIDBL.html>. The website has a green header with the lab name and navigation links. A sidebar on the left contains a menu with categories like Projects, People, Bioinformatics, Papers, Positions, Proteomics, Protein Interaction DB links, Protocols/Reagents, and Molecular Biology links. The main content area is titled 'Links to Protein Interaction Databases' and lists various databases under two headings: 'Finley Lab Interactions Databases' and 'Gene or Protein Interactions Databases in the research community'. The first list includes *Drosophila Interactions Database (DroID)* and *Campylobacter jejuni Interactions Databases*. The second list includes BioGRID, DIP, IntAct, MINT, MIPS, Yeast Protein Interactions, BRITE, The PIM Database, Mouse Protein-Protein interactions, and Human Protein Reference Database. The Windows taskbar at the bottom shows several open applications, including Microsoft Office Word, Outlook, and EndNote.

Finley Lab
Center for Molecular Medicine and Genetics

protein interaction DB links

Links to Protein Interaction 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
- **MINT** - A Molecular Interactions Database
- **MIPS** - Comprehensive Yeast Protein-Protein interactions
- **Yeast Protein Interactions** - Yeast two-hybrid results
- **BRITE** - Biomolecular Relations in Information Transduction
- **The PIM Database** - by Hybrigenics
- **Mouse Protein-Protein interactions**
- **Human Protein Reference Database**

Wayne State University
SCHOOL OF MEDICINE

Center for Molecular Medicine and Genetics
Wayne State University School of Medicine
540 E. Canfield
Detroit, MI 48201

Internet 100%

Start 4 Microsoft Of... Doručená pošta... Interactions Da... 2 Microsoft Of... EndNote X1 - [5... nature-Rual05... Prot Cell - Feng... 2 Microsoft Of... CS 15:34

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

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

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

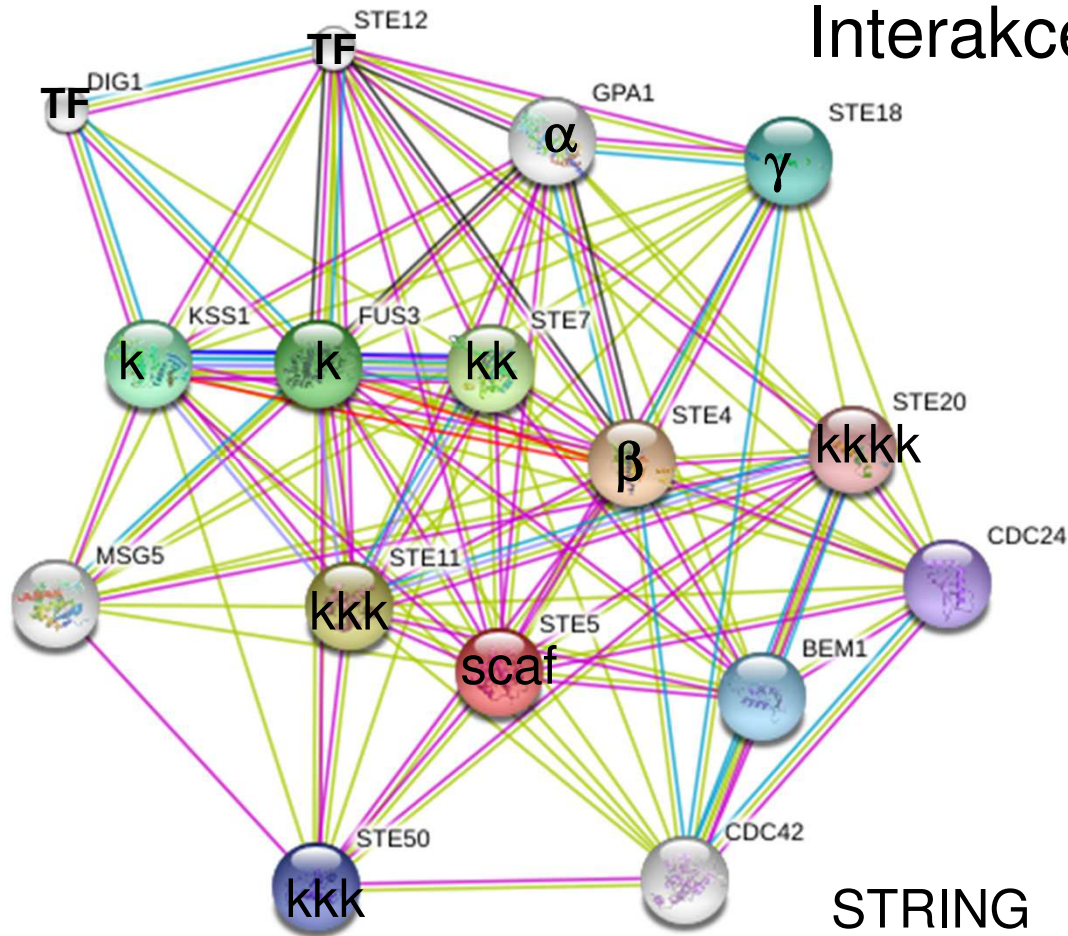
5 2[\[details\]](#)

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*, poltivé kvasinky *S. pombe*, octomilky *D. melanogaster*, člověka *H. sapiens* ...

proteinové sítě – víc než PPI vs dynamika interakcí ...

Interakce x signální dráha



STRING

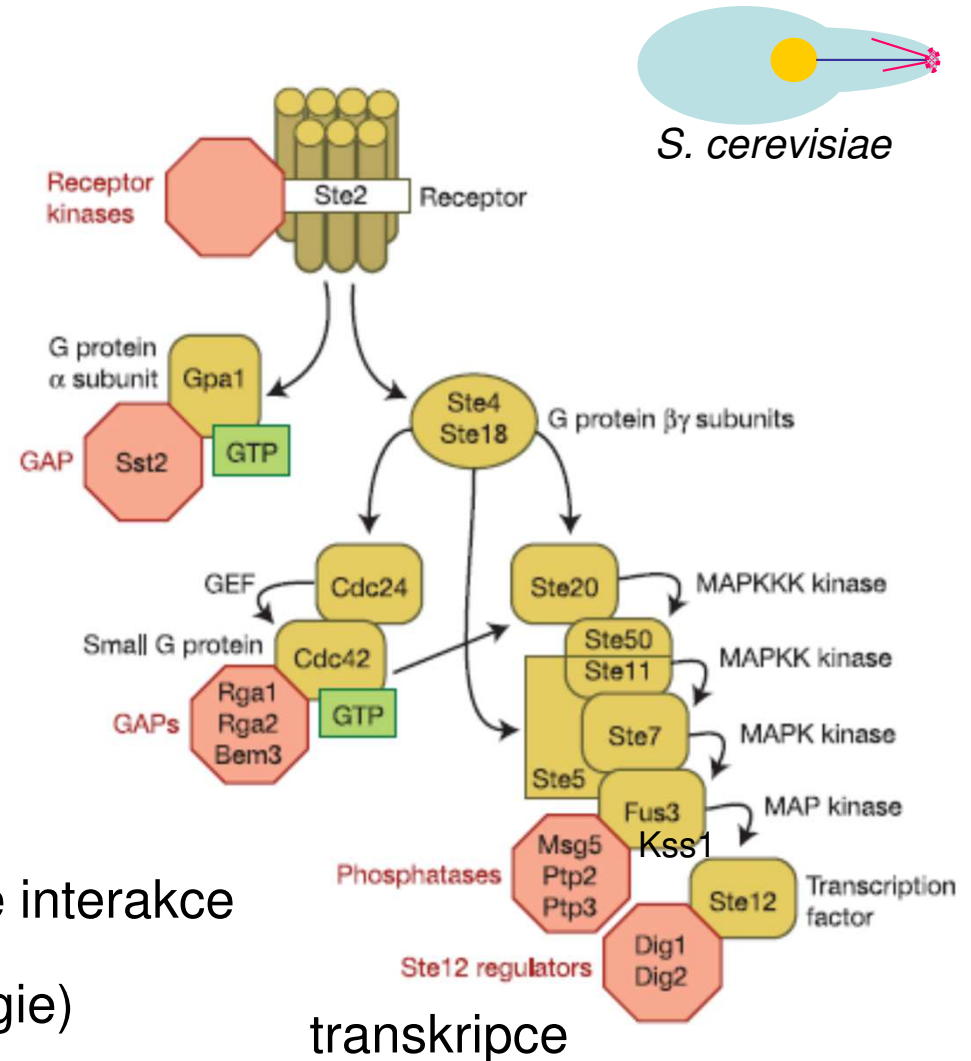
- Experiments
- Databases
- Textmining
- Gene Fusion
- Coexpression

Y2H, colP ... genetické interakce

Funkční vztahy (ontologie)

Svědčí o potřebě PPI

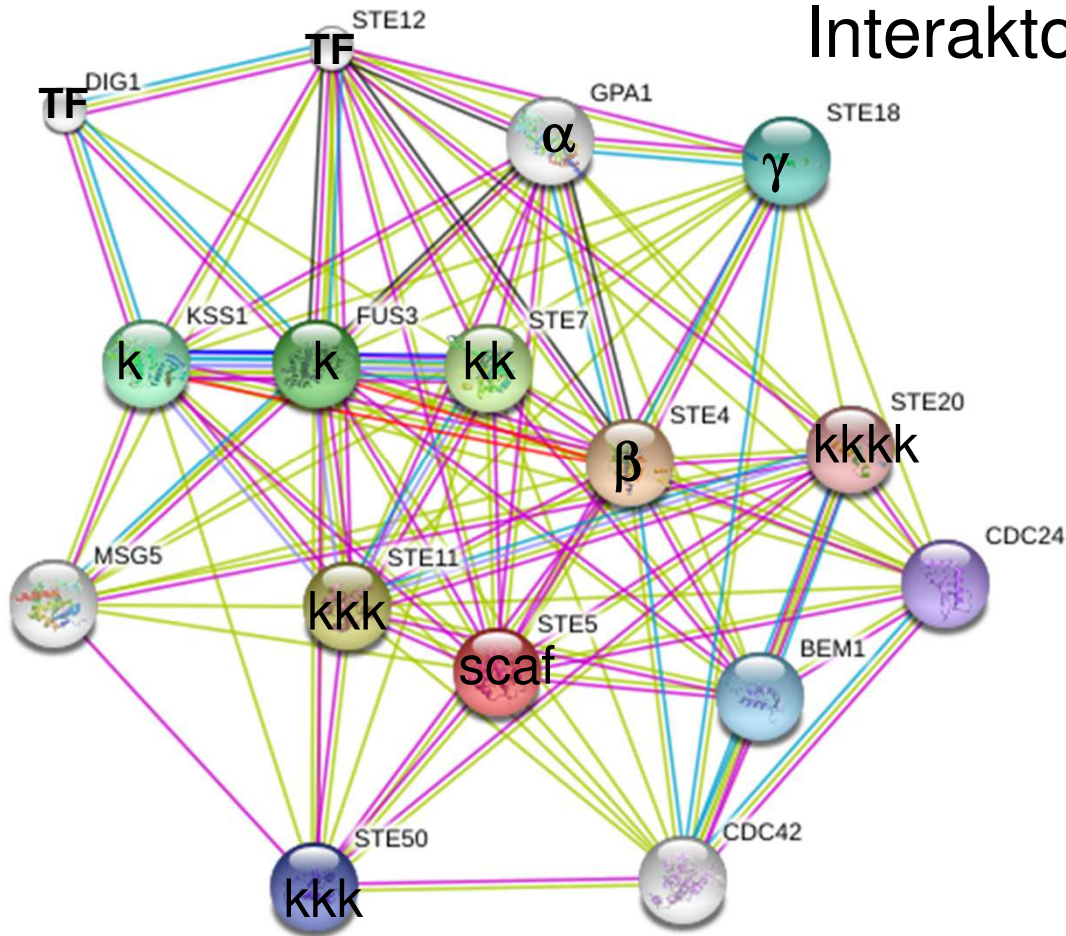
Potřeba výskytu ve stejném okamžiku a společná translace



transkripce

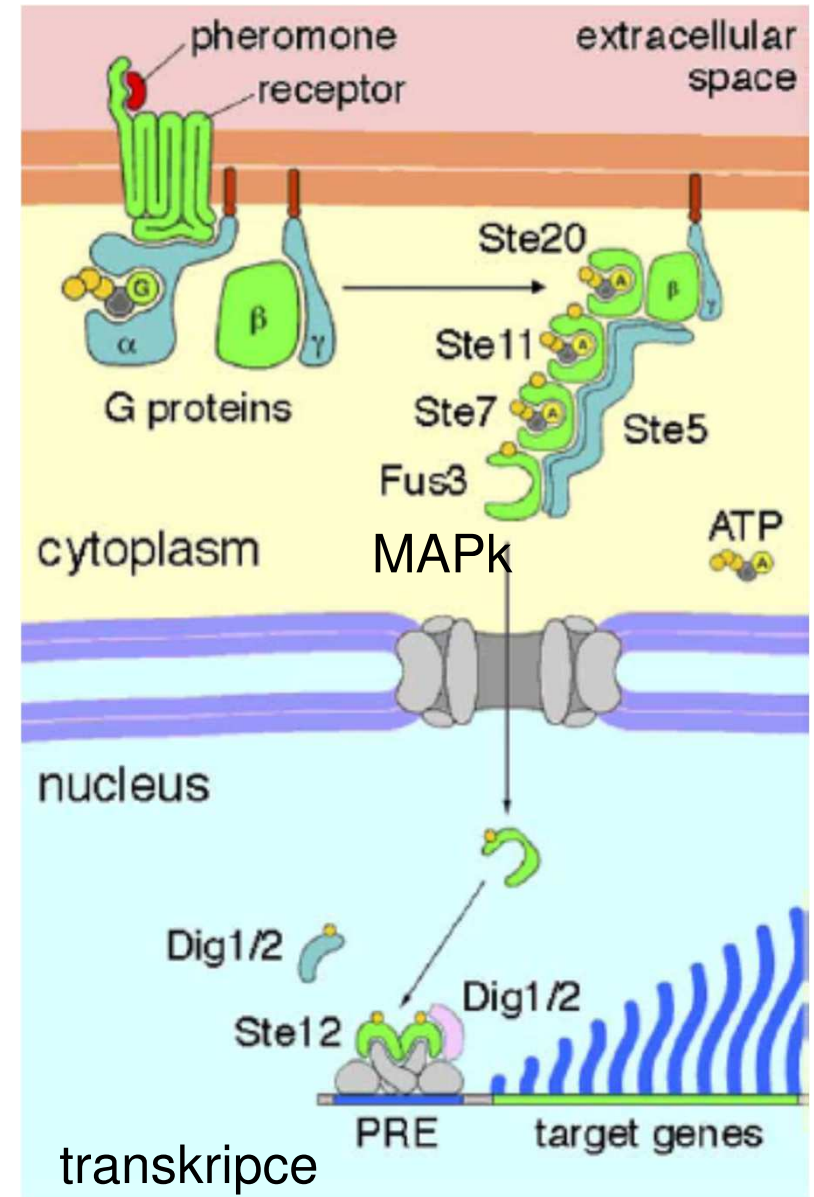
proteinové sítě – schéma vs realita

Interaktom x komplexom



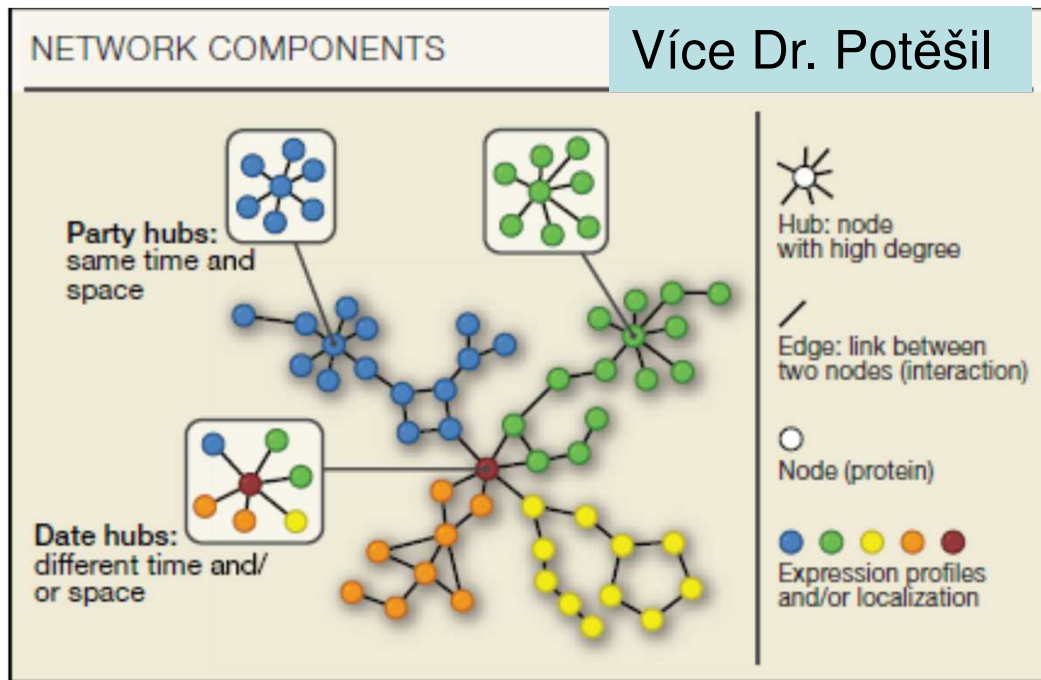
- Experiments
- Databases
- Textmining
- Gene Fusion
- Coexpression

Síť neznamená komplex,
ale vztahy
souhrn proteinových:
interakcí = **interaktom**
komplexů = **komplexom**

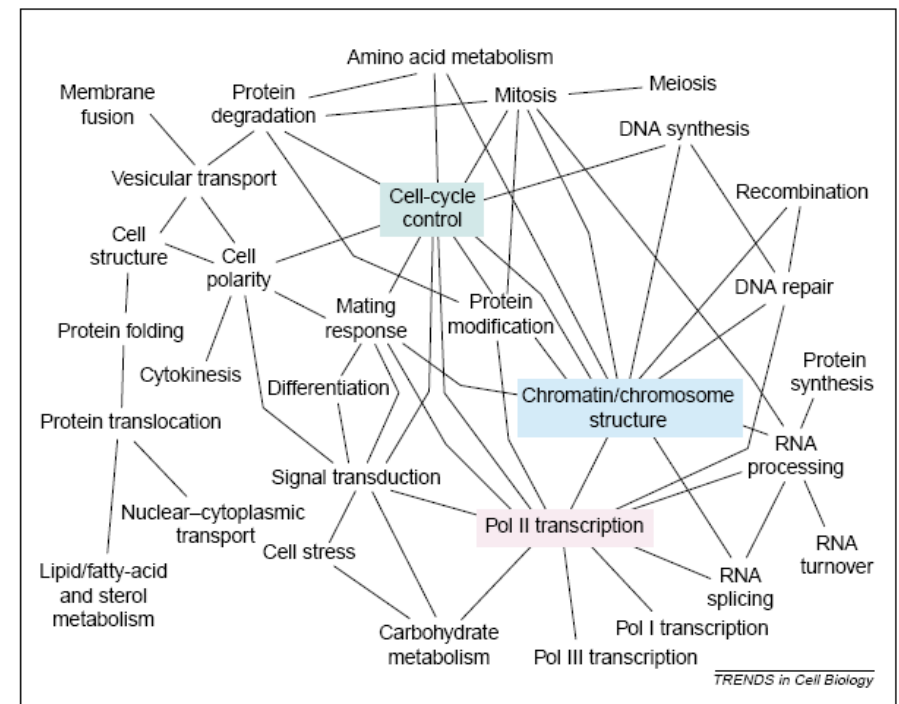


Protein-proteinové interakce

- stabilní (velké plochy, většinou součástí komplexů)
 - přechodné/slabé (součást dynamických procesů – předávání signálů, modifikace)
 - posttranslační modifikace mohou změnit vazebné vlastnosti povrchu (fosforylace, metylace, SUMOylace)
- (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)

více interakcí jedné **domény** =
různé povrchy (3D) nebo v
různém čase stejný povrch

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

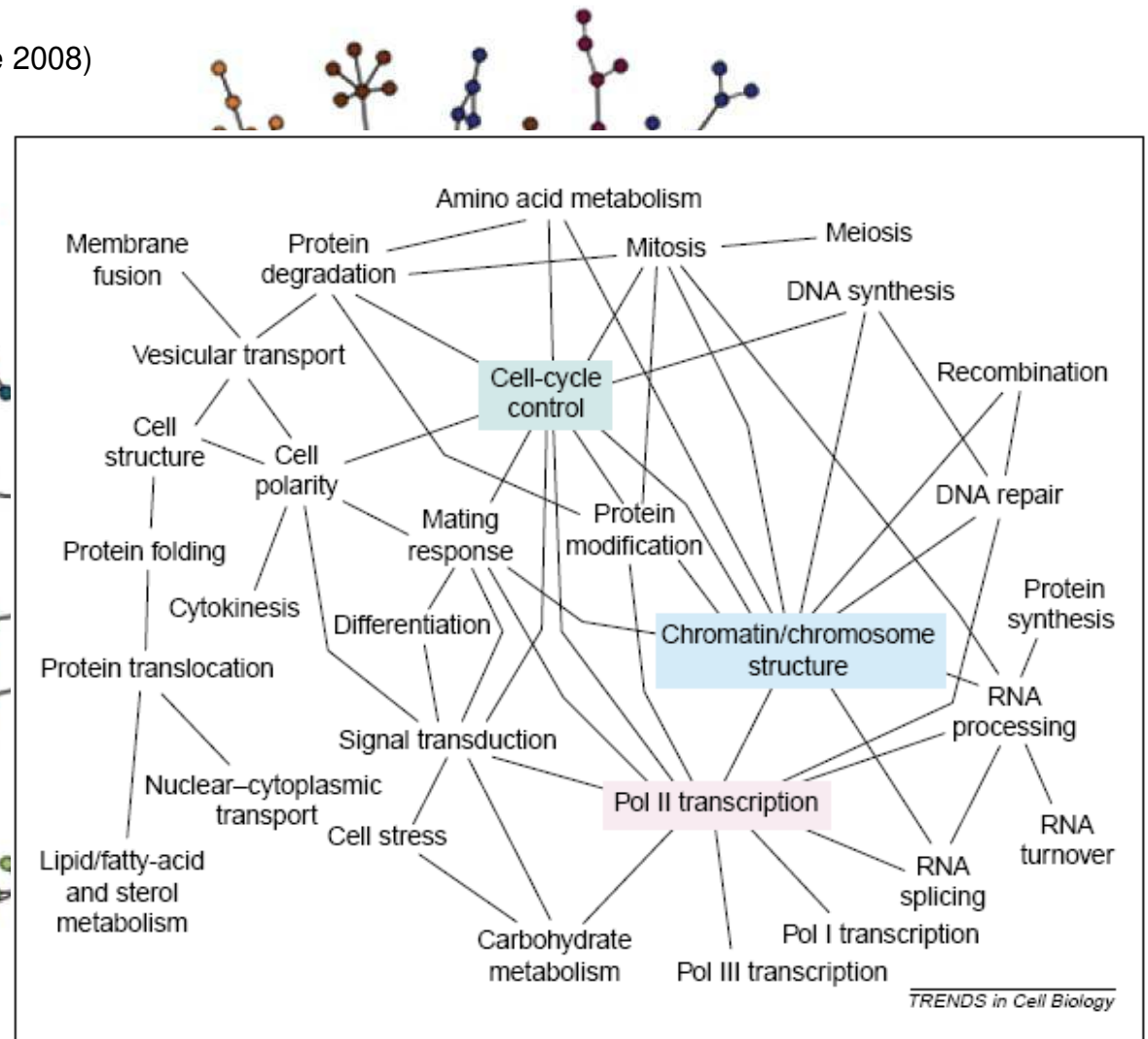
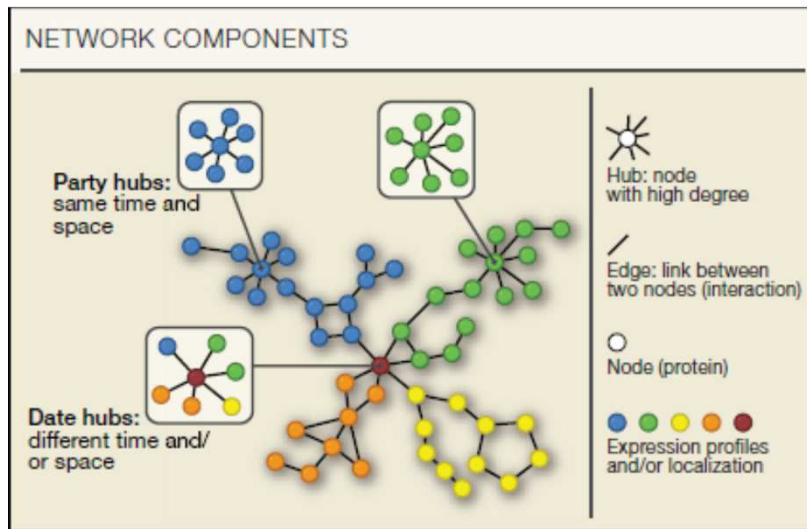
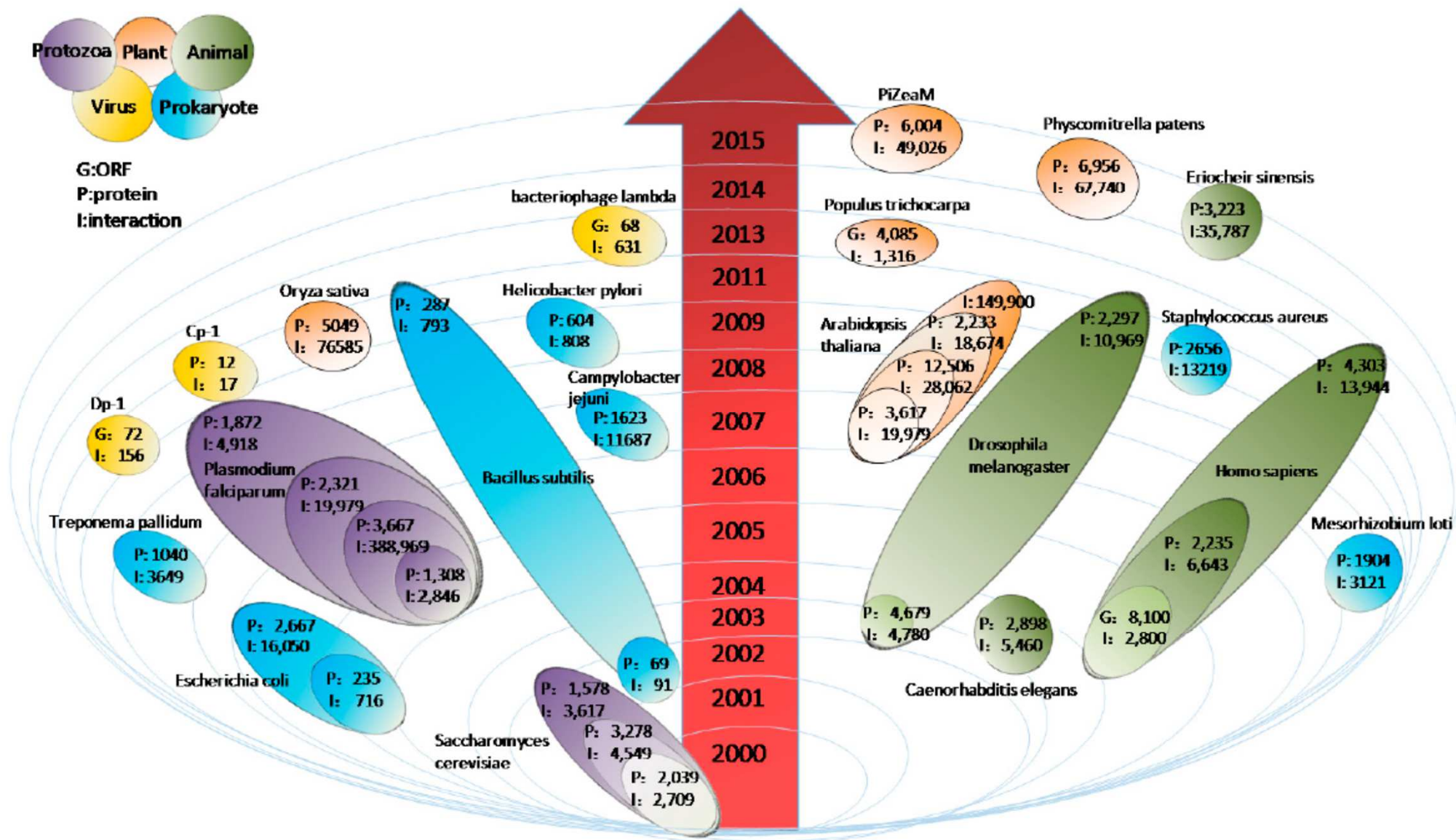


Fig. 2. Functional group interaction map based on Fig. 1 (modified from Ref. 10). Shown are interactions between functional groups of yeast proteins. Each line indicates that there are 15 or more interactions between proteins of the connected groups. Connections with fewer than 15 interactions are not shown because one or a few interactions occur between almost all groups and often tend to be spurious – that is, based on false positives in two-hybrid screens or other assays. Note that only proteins with known function are included and that about one-third of all yeast proteins belong to several classes.

High-throughput screens – interaktomy organismů



Kvasinkový dvoj-hybridní systém
TAP-tag s MS analýzou

HEK293 (human embryonal kidney) vs HCT116 (human colon cancer)

při 70% překryvu proteinů sdílí pouze 50% interakcí

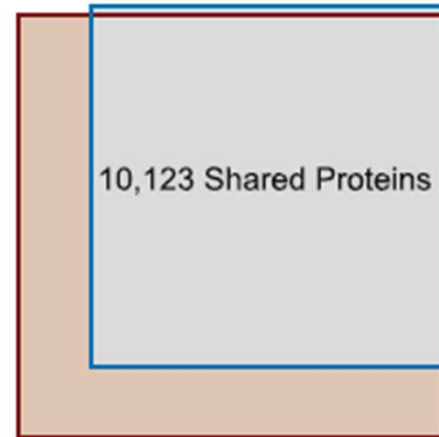
„jádra“ komplexů jsou stejná
liší se „přídavnými“ moduly

klíčové/konzervované komplexy
jsou v obou liniích (jejich exprese
je podobná)

specifické interakce zodpovídají
za rozdílné funkce („fenotypy“)
- jsou častěji mutované (nemoci)

Network Overlap: Proteins

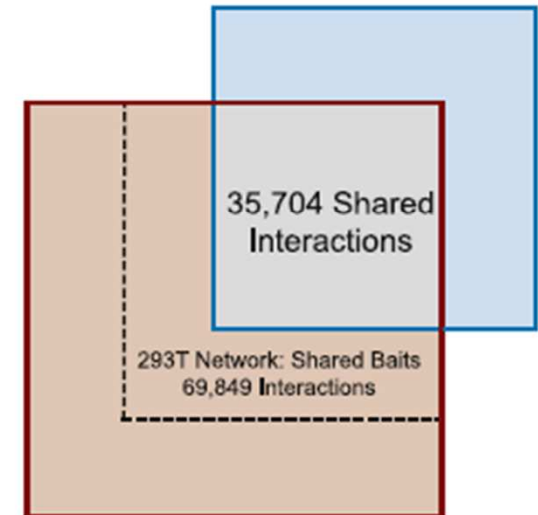
HCT116 Network (10,531 Proteins)



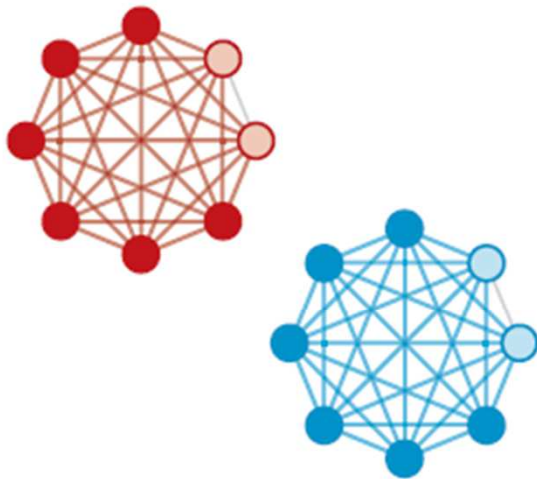
293T Network (14,586 Proteins)

Network Overlap: Interactions

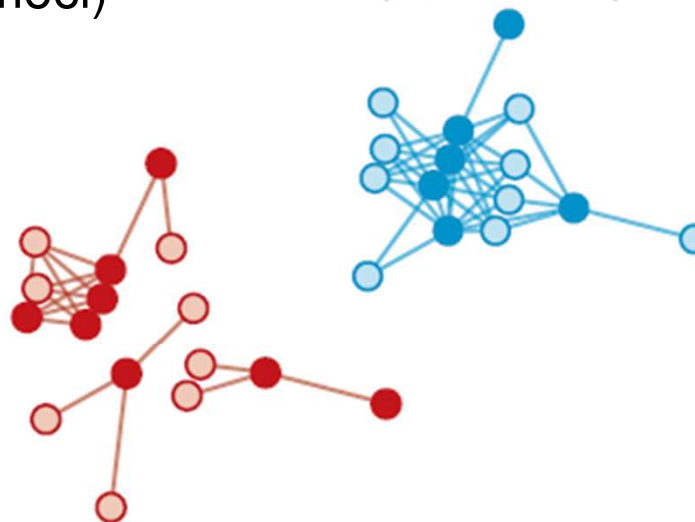
HCT116 Network (70,966 Interactions)



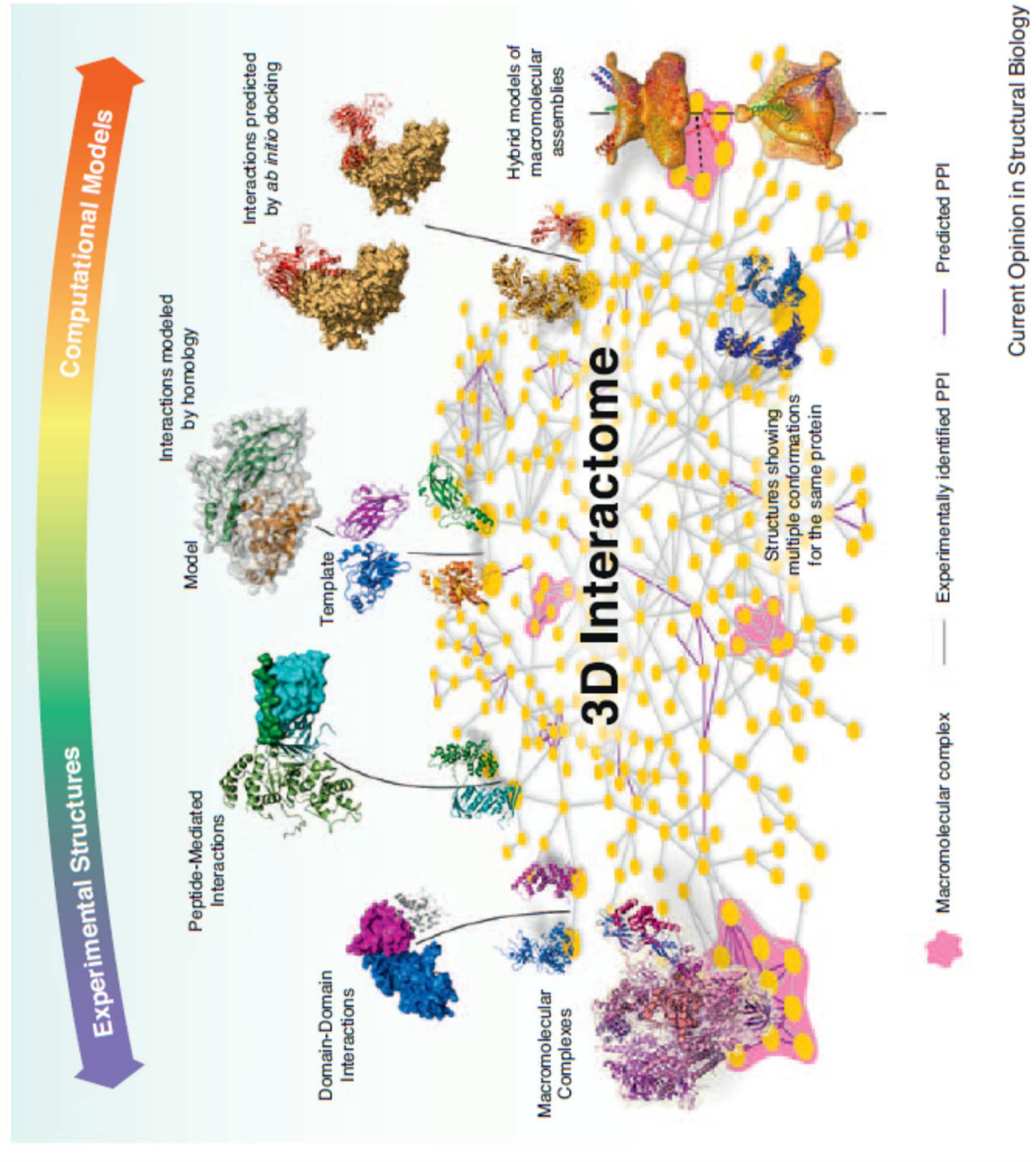
293T Network (118,162 Interactions)



Core Complexes
Are Identical



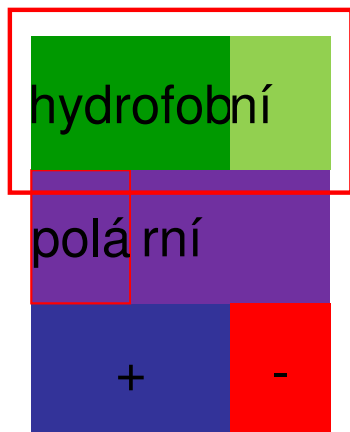
Network Remodeling
Reflects Specialized Biology



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

