

Homologické modelování proteinů

predikce neznámé 3D struktury na základě její podobnosti ke 3D struktuře známé

Vícesupňový proces:

- 1) nalezení podobných 3D struktur
- 2) zvolení vhodného výchozího modelu
- 3) vlastní homologické modelování (= „zmutování“ modelu na hledanou strukturu)
- 4) ověření „správnosti“ modelu numerickými kontrolními kritérii

literatura: např. http://en.wikipedia.org/wiki/Homology_modeling

Vstupy: veškeré dostupné informace o hledaném proteinu, přinejmenším 1D struktura

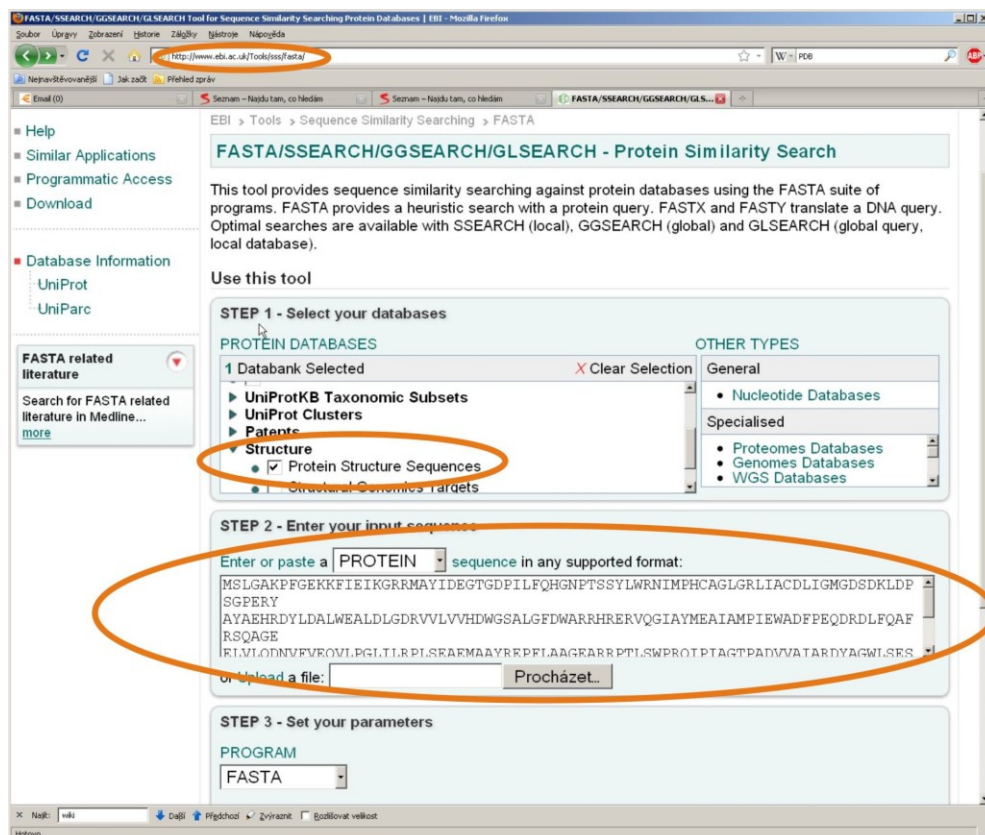
Nástroje:

- 1) <http://www.ebi.ac.uk/Tools/fasta33/index.html> - nástroj FASTA pro vyhledávání podobných AA sekvencí
- 2) PDB , databáze známých proteinových struktur, <http://www.rcsb.org/pdb/home/home.do>
- 3) WWW servery pro hledání struktur proteinů s podobnou 3D strukturou, např. PDBeFold <http://www.ebi.ac.uk/msd-srv/ssm/>
- 4) WWW servery pro homologické modelování
- 5) Vizualizace výsledků

Servery pro homologické modelování – nový test „kvality“ CASP 10 bude zveřejněn v prosinci 2012: <http://predictioncenter.org/casp10/index.cgi>

Postup:

- 1) hledání pomocí nástroje FASTA, identifikace PDB identifikátorů struktur s podobnou primární strukturou



FASTA Results

Alignments

Align	DBID	Source	Length	Score	Identical	Positives	SI
1	PDB 1D07_A	Hydrolytic haloalkane dehalogenase from <i>Sphingomonas paucimobis</i> UT26 with 1.3 Å resolution, a product of dechlorination of dibromopropane, at 2.0 Å resolution	296	2041	100.0	100.0	6.4E-138
2	PDB 1D07_A	Hydrolytic haloalkane dehalogenase from <i>Sphingomonas paucimobis</i> UT26 with 1.3 Å resolution, a product of dechlorination of dibromopropane, at 2.0 Å resolution	296	2041	100.0	100.0	6.4E-138

RCSB PDB: Structure Summary for 1D07 - Hydrolytic haloalkane dehalogenase from sphingomonas paucimobis UT26

Biological Assembly

2) PDB: databáze 3D struktur proteinů

3) hledání prostorově (3D) podobných proteinů

Structure Similarity

Submission Form for pairwise 3D alignment

Query: PDB entry 1D07

Target: Whole PDB archive

Lowest acceptable match (%) 70

Submit your query

Structure Alignment Results

Query: pdb entry 1d07A, 293 residues

Target: HYDROLYTIC HALOALKANE DEHALOGENASE LINB FROM SPHINGOMONAS PAUCIMOBIS UT26 WITH 1,3-PROPANEDIOL, A PRODUCT OF DEBROMINATION OF DIBROMOPROPANE, AT 2.0 Å RESOLUTION

Examined 76732 entries (190780 chains).
Matches 41-60 of 104.

##	Scoring			Rmsd	Nalign	Ng	%seq	Query	Target (PDB entry)	Title
	Q	P	Z							
41	0.68	22.1	14.0	1.17	262	10	44	81	3a2n:R	CRYSTAL STRUCTURE OF DBJA (WILD TYPE TYPE II P21)
42	0.68	23.4	14.6	1.17	262	10	43	90	3a4i:R	CRYSTAL STRUCTURE OF DBJA (HIS-DBJA)
43	0.67	18.1	12.7	1.23	265	9	45	76	2p9f:A	CRYSTAL STRUCTURES OF THE LUCIFERASE AND GREEN FLUORESCENT PROTEIN FROM RENILIA RENIFORMIS
44	0.67	18.1	12.7	1.90	249	14	29	76	1xt0:A	DEHALOGENASE DPPA FROM PLESIOCYSTIS PACIFICA SIR-I
45	0.43	8.0	9.5	2.43	237	18	22	71	1va4:R	PSEUDOMONAS FLUORESCENS ESTERASE COMPLEXED TO THE R-ENANTIOMER OF A SULFONATE TRANSITION STATE ANALOG
46	0.43	8.0	9.5	2.49	239	15	21	71	1va4:R	PSEUDOMONAS FLUORESCENS ARYL ESTERASE
47	0.43	9.3	9.4	2.39	235	18	22	71	1va4:R	PSEUDOMONAS FLUORESCENS ARYL ESTERASE
48	0.43	9.3	9.4	2.39	235	18	22	71	3a2:R	PSEUDOMONAS FLUORESCENS ESTERASE COMPLEXED TO THE R-ENANTIOMER OF A SULFONATE TRANSITION STATE ANALOG
49	0.43	9.5	9.5	2.47	238	15	22	71	3h4:R	SWITCHING CATALYSIS FROM HYDROLYSIS TO PERHYDROLYSIS IN P. FLUORESCENS ESTERASE
50	0.43	9.2	9.4	2.44	237	17	22	71	1va4:R	PSEUDOMONAS FLUORESCENS ARYL ESTERASE
51	0.43	9.3	9.4	2.34	233	18	22	71	3a2:R	PSEUDOMONAS FLUORESCENS ESTERASE COMPLEXED TO THE R-ENANTIOMER OF A SULFONATE TRANSITION STATE ANALOG
52	0.42	8.7	9.2	2.38	237	15	21	71	3fob:R	CRYSTAL STRUCTURE OF BROMOPEROXIDASE FROM BACILLUS ANTHRACIS
53	0.42	8.3	9.0	2.40	235	18	22	71	1va4:R	PSEUDOMONAS FLUORESCENS ARYL ESTERASE
54	0.42	9.2	9.4	2.40	235	18	22	71	1va4:R	PSEUDOMONAS FLUORESCENS ARYL ESTERASE
55	0.42	9.5	9.4	2.44	236	15	22	71	3a2:R	PSEUDOMONAS FLUORESCENS ESTERASE COMPLEXED TO THE R-ENANTIOMER OF A SULFONATE TRANSITION STATE ANALOG
56	0.42	8.4	9.0	2.49	238	15	22	71	3h4:R	SWITCHING CATALYSIS FROM HYDROLYSIS TO PERHYDROLYSIS IN P. FLUORESCENS ESTERASE
57	0.42	9.5	9.4	2.43	235	17	22	71	3h4:R	SWITCHING CATALYSIS FROM HYDROLYSIS TO PERHYDROLYSIS IN P. FLUORESCENS ESTERASE
58	0.42	8.5	9.3	2.38	233	18	22	71	3a2:R	PSEUDOMONAS FLUORESCENS ESTERASE COMPLEXED TO THE R-ENANTIOMER OF A SULFONATE TRANSITION STATE ANALOG
59	0.42	9.1	9.3	2.41	234	19	22	71	3hea:R	THE L29P/L124I MUTATION OF PSEUDOMONAS FLUORESCENS ESTERASE
60	0.42	8.4	9.3	2.44	235	18	22	71	3hea:R	THE L29P/L124I MUTATION OF PSEUDOMONAS FLUORESCENS ESTERASE

Examined 76732 entries (190780 chains).
Matches 41-60 of 104.

Query PDB 1d07:A				Alignment (44 of 104)				Target PDB 2xt0:A			
Nres	%res	Nsse	%sse	Q	P	RMSD	Nalign	Nres	%res	Nsse	%sse
293	85	21	76	0.509	18.14	1.895	249	297	84	22	73
HYDROLYTIC HALOALKANE DEHALOGENASE LINB FROM SPHINGOMONAS PAUCIMOBIS UT26 WITH 1,3-PROPANEDIOL, A PRODUCT OF DEBROMINATION OF DIBROMPROPANE, AT 2.0A RESOLUTION				%seq	Z	Nsse	N gaps	DEHALOGENASE DPPA FROM PLESIOCYSTIS PACIFICA SIRI			
				29.3	12.67	1.6	14				

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Secondary Structure Alignment
 1d07:A -SSShhS-KSHShhRRHSHaRH
 2xt0:A hSSShhShShSh-hhHSHSHaRH

Query PDB 1d07:A				Target PDB 2xt0:A								
11SD	31A	LYS	12	ILE	14	<->	21SD	31A	HIS	22	LEU	24
21SD	61A	MEI	21	GLU	26	<->	31SD	61A	MEI	35	GLU	40
31SD	51A	PRO	31	GLN	35	<->	41SD	51A	THR	48	LEU	52
41HS	61A	SER	41	ARG	46	<->	51HS	61A	TRP	58	ARG	63
61SD	51A	ARG	57	CYS	61	<->	71SD	51A	ARG	75	PRO	79
71H1	161A	ALA	81	LEU	96	<->	91H1	171A	THR	97	GLN	113
81SD	61A	VAL	102	HIS	107	<->	101SD	51A	VAL	117	CYS	121
91H1	141A	ASP	108	HIS	121	<->	111H1	151A	GLN	122	ARG	136
101SD	91A	VAL	125	ALA	133	<->	121SD	71A	VAL	140	MET	146
141H1	101A	SER	153	GLU	192	<->	151H1	101A	THR	187	ALA	196
151H1	111A	ARG	201	ILE	211	<->	161H1	71A	LYS	204	PHE	210
161H1	181A	PRO	217	SER	234	<->	171H1	161A	GLY	222	GLN	236
171SD	81A	LYS	238	PRO	245	<->	181SD	61A	THR	241	GLY	246
181H1	91A	THR	250	ARG	258	<->	191H1	131A	GLY	253	ILE	264
201HS	51A	PHE	273	ASF	277	<->	201HS	51A	PHE	279	HIS	283
211H1	171A	SER	278	ARG	294	<->	221H1	121A	GLY	284	PHE	295

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Rotation-translation matrix
 (to be applied to the target)

0.212	0.095	-0.973	X	55.988
0.643	-0.763	0.066	Y	6.467
-0.736	-0.639	-0.223	Z	65.814

3D Structural alignment

PDB 1d07:A	SI	Dist. (A)	PDB 2xt0:A
			- A:MET 1
			+ A:GLU 2
			- A:PHE 3
			- A:VAL 4

3D Structural alignment

PDB 1d07:A	SI	Dist. (A)	PDB 2xt0:A
			- A:MET 1
			+ A:GLU 2
			- A:PHE 3
			- A:VAL 4
			+ A:ARG 5
			+ A:THR 6
			H+ A:PRO 7
			H+ A:ASP 8
			H+ A:ASP 9
			H+ A:ARG 10
			H+ A:PHE 11
			H+ A:ALA 12
			+ A:ASP 13
			- A:LEU 14
-	A:GLY 4		- A:LEU 15
-	A:ALA 5	2.00	+ A:PRO 16
+ A:LYS 6		1.78	+ A:ASP 16
+ A:PRO 7		0.62	+ A:PRO 17
- A:PHE 8		5.19	+ A:PRO 18
- A:GLY 9		2.31	+ A:TYR 19
+ A:GLU 10		1.67	- A:ALA 20
+ A:LYS 11		1.27	+ A:PRO 21
S+ A:LYS 12		1.82	S+ A:HIS 22
S- A:PHE 13		0.96	S- A:TYR 23
S- A:ILE 14		1.40	S- A:LEU 24
- A:GLU 15		0.60	- A:GLU 25
- A:ILE 16			- A:GLU 26
			- A:LEU 27
			+ A:PRO 28
			- A:GLY 29
			- A:PHE 30
+ A:LYS 17		2.79	+ A:GLU 31
- A:GLY 18		2.71	- A:GLY 32
+ A:ARG 19		1.16	- A:LEU 33
- A:ARG 20		1.23	- A:ARG 34
S- A:MET 21		0.68	S- A:MET 35
S- A:ALA 22		0.59	S+ A:HIS 36
S- A:TYR 23		0.66	S- A:TYR 37
S- A:ILE 24		0.90	S- A:VAL 38
S+ A:ASP 25		0.90	S+ A:ASP 39
S+ A:GLU 26		1.16	S+ A:GLU 40
- A:GLY 27		1.55	- A:GLY 41
- A:THR 28		2.15	+ A:PRO 42
- A:GLY 29			+ A:ARG 43
			+ A:ASP 44
			- A:ALA 45
			+ A:GLU 46
+ A:SER 30		3.46	+ A:HIS 47
S+ A:PRO 31		1.42	S- A:THR 48

4) Omezení sekvence na oblasti se známými 3D analogy, homologické modelování na vybraném serveru

5) Vizualizace PDB souborů a pozorování (+interpretace) strukturních rozdílů - např. s nástrojem Swiss Pdb Viewer

