B cell epitope prediction

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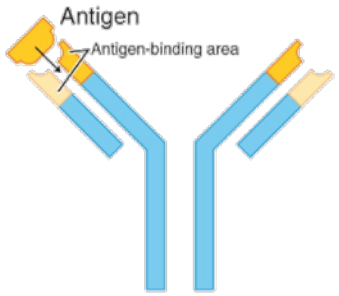
IEDB Workshop, 2018

Outline

- **B cell epitopes**: Discontinuous And linear epitopes
- **Schema** of B cell epitope prediction tools on IEDB
- **Sequence-based epitope prediction methods:**
  - Linear epitope prediction methods
- **3D Structure-based epitope prediction methods:**
  - Discontinuous epitope prediction methods
- **Computational antibody design**
  - Antigen and Antibody structure modelling
  - Antibody-protein docking



B cell epitopes

Antigen
Hemagglutinin HA1 Chain
from Influenza A Virus

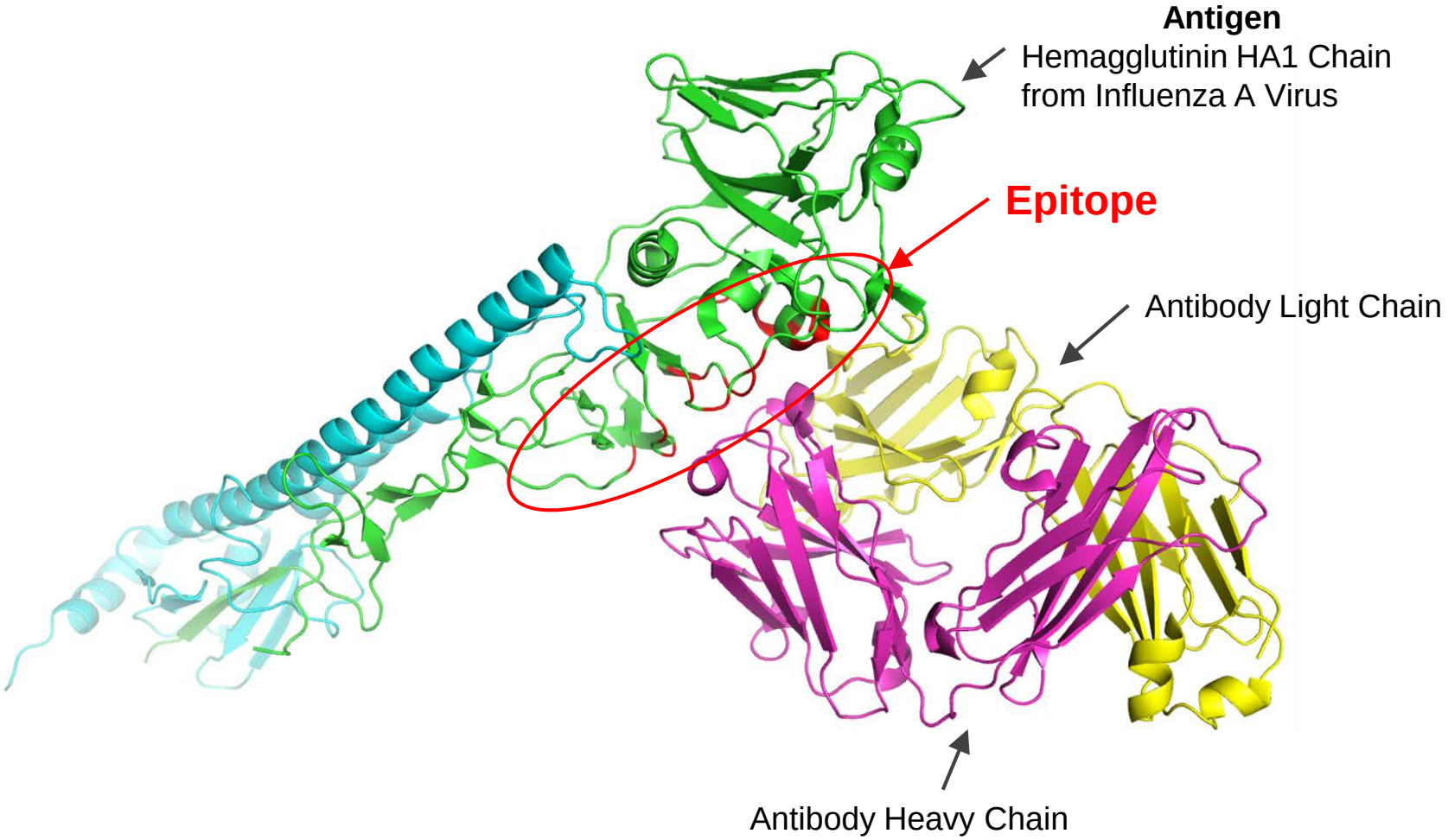
Hemagglutinin HA2 Chain

Antibody Light Chain

Antibody Heavy Chain

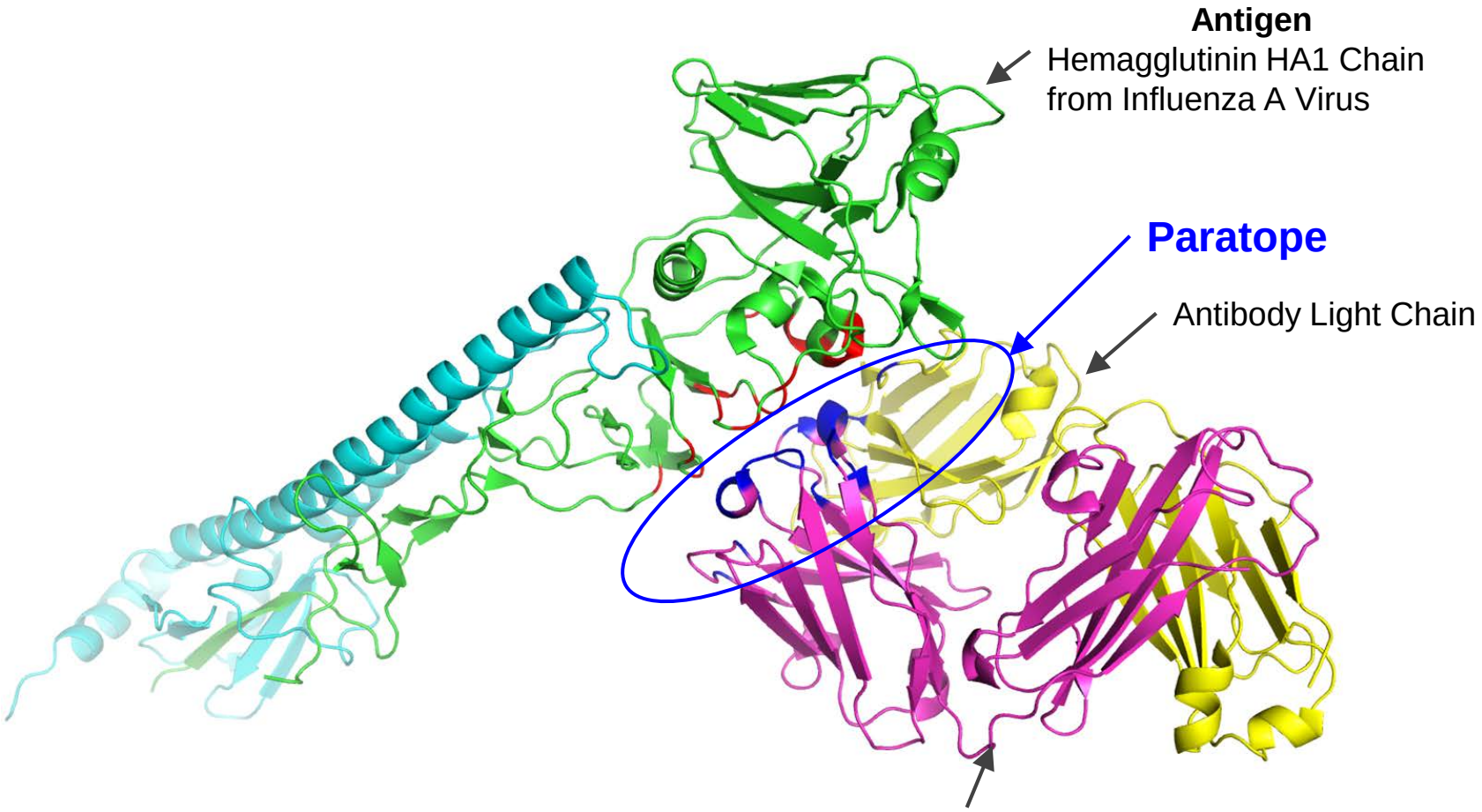
PDB ID: 1EO8

Discontinuous Epitope



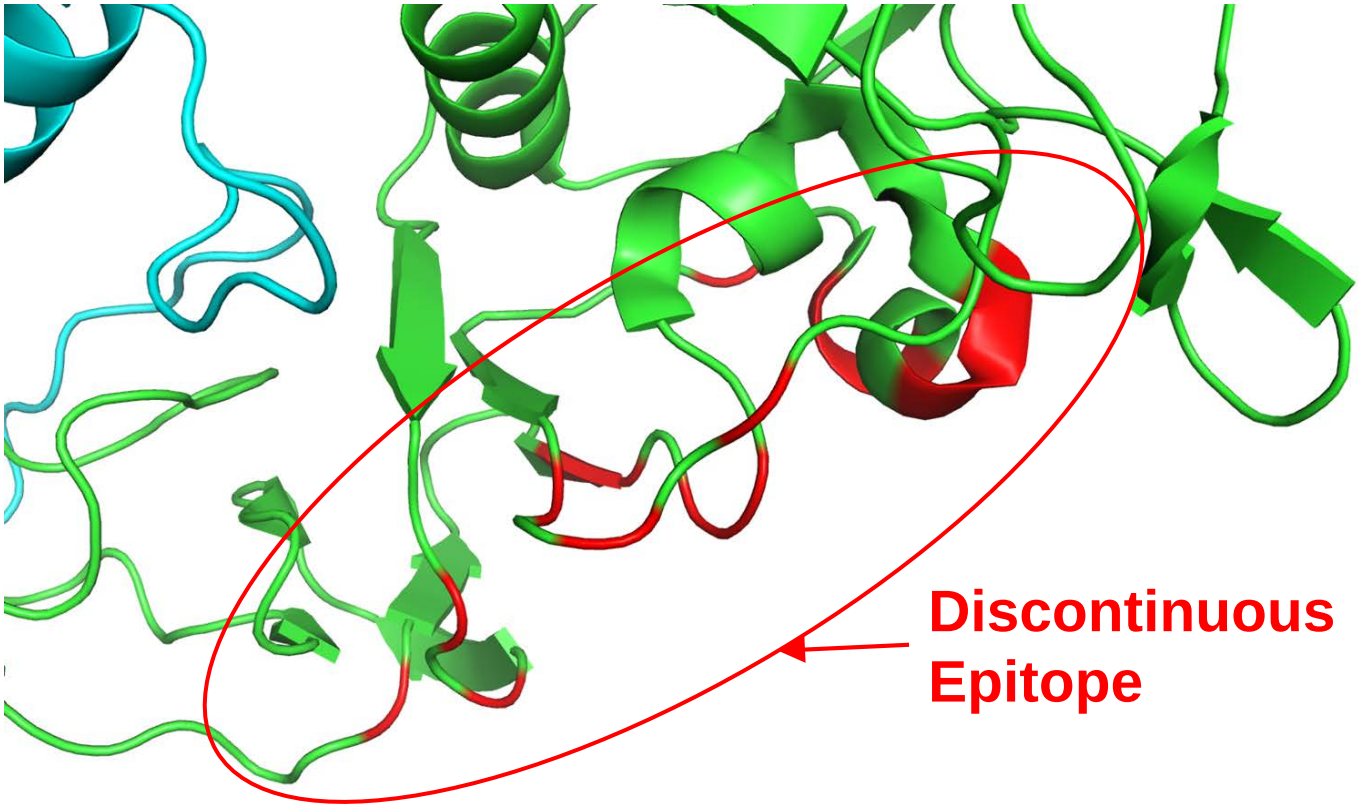
PDB ID: 1EO8

Discontinuous Epitope



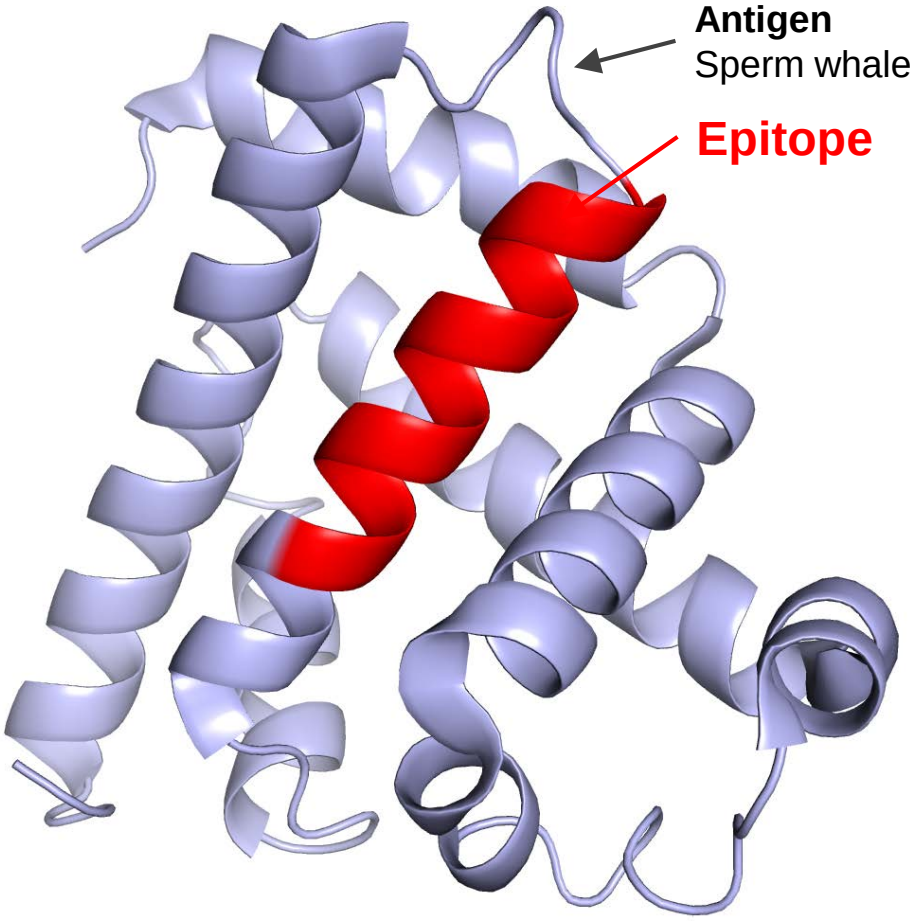
PDB ID: 1EO8

Discontinuous Epitope



PDB ID: 1EO8

B cell epitopes



PDB ID: 1VXG

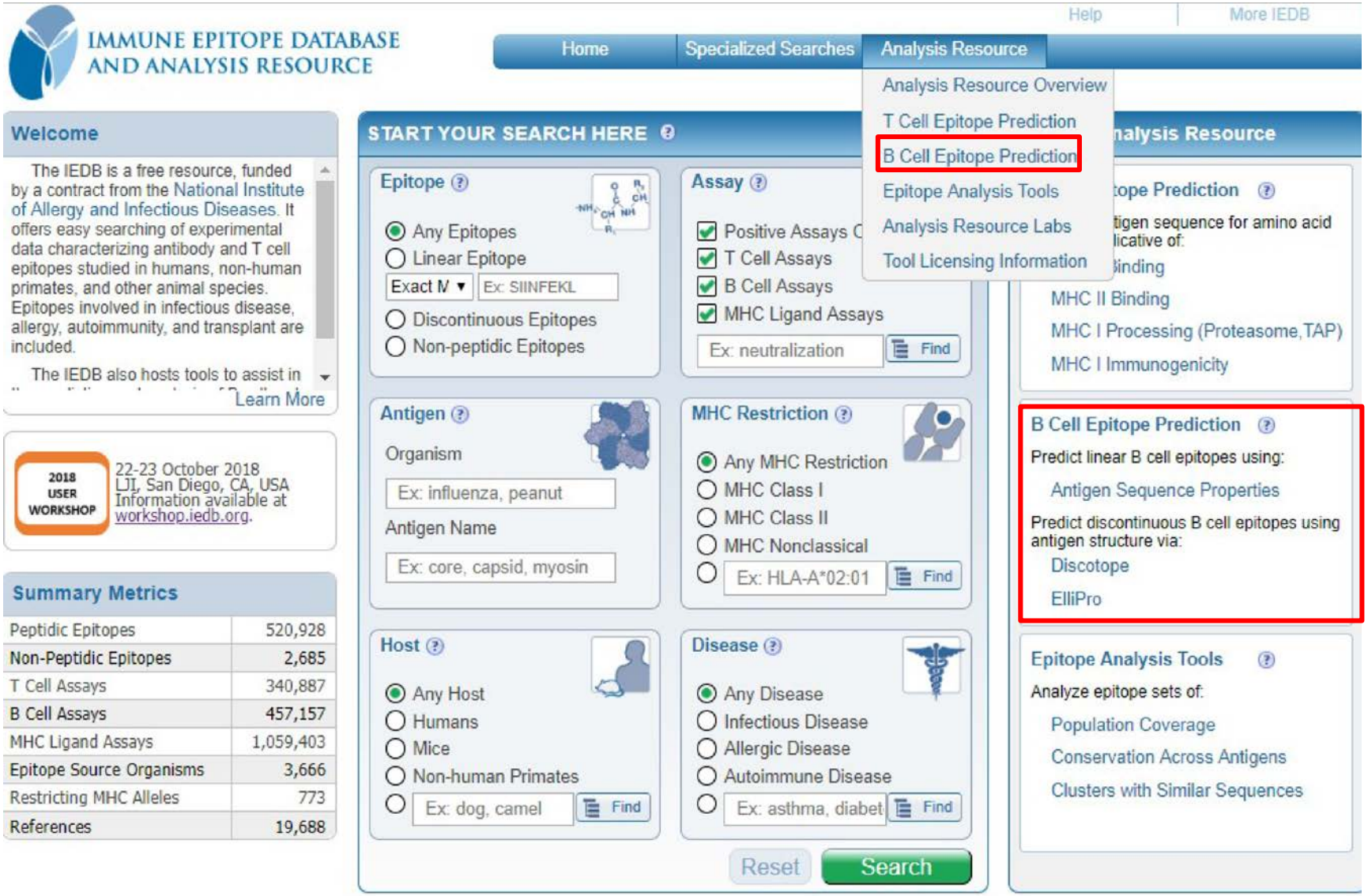
- Protein antigens usually contain both linear (aka sequential or continuous) epitopes that may still bind to the antibody even when that protein is denatured
- and discontinuous (aka non-sequential or conformational) epitopes
- **More than 90% of the B cell epitopes are estimated to be discontinuous*.**

*Barlow et al, Nature. 1986.
*Van Regenmortel, Methods. 1996.

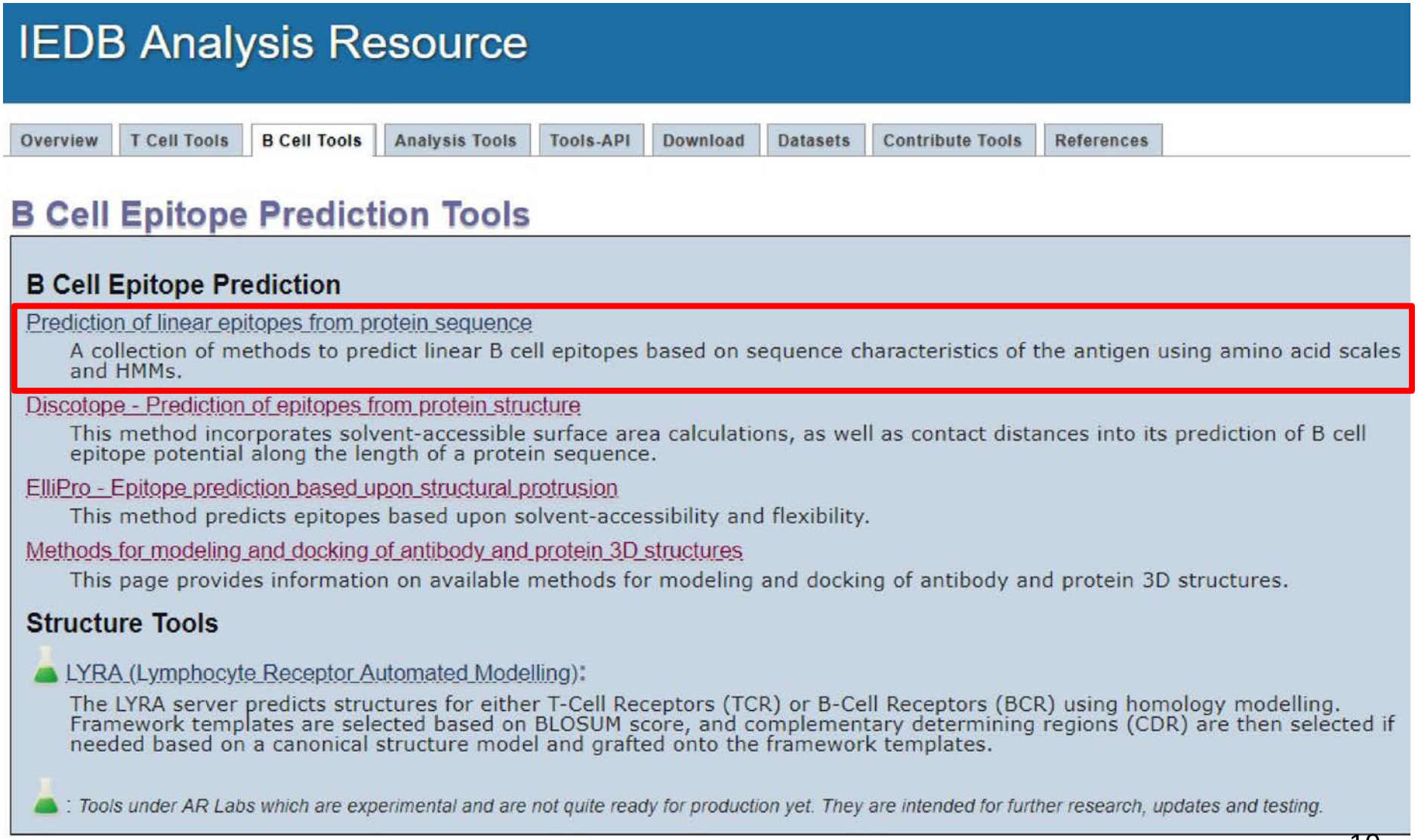
Schema of B cell epitope prediction tools

Walk through

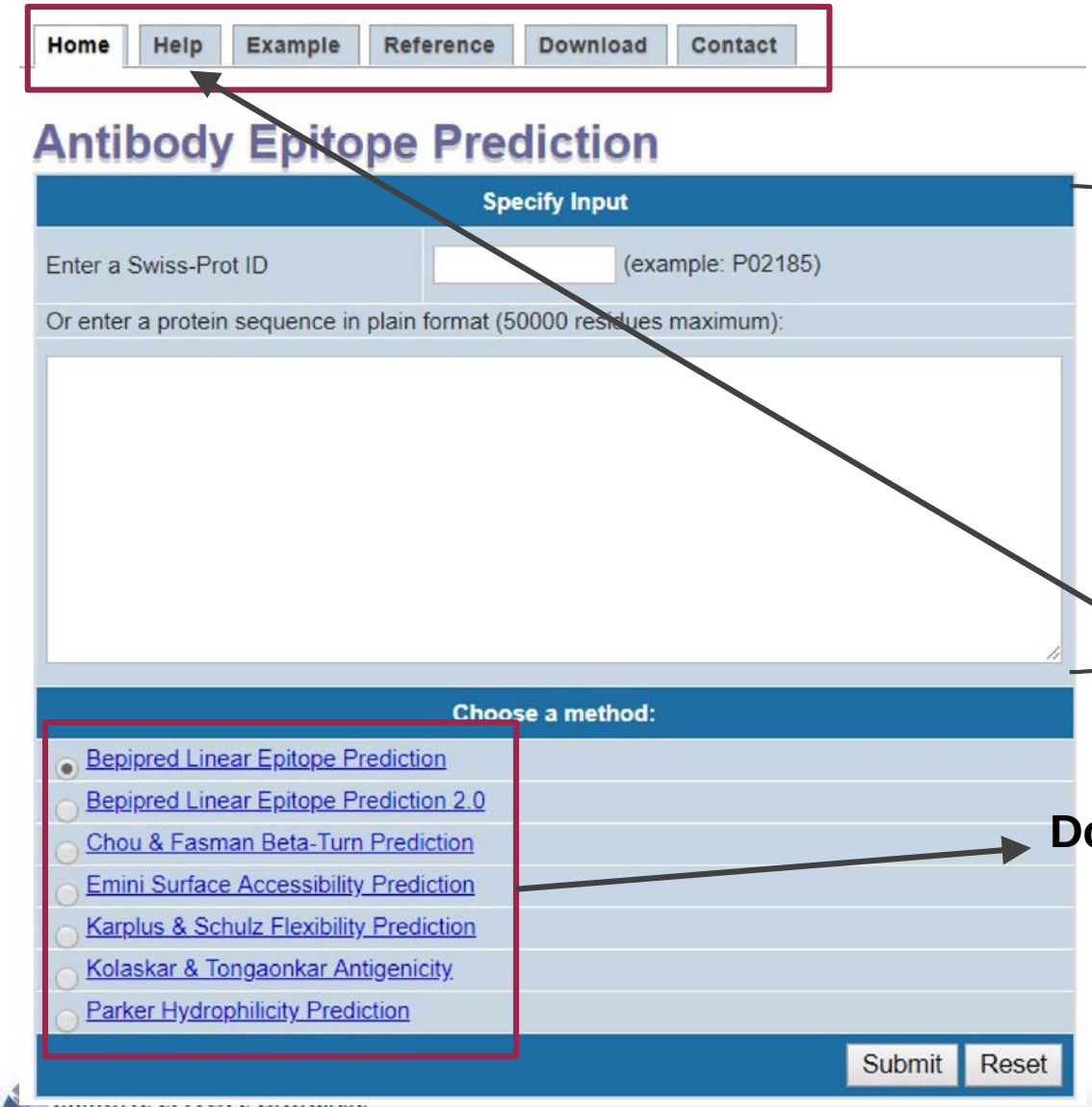
Schema of B cell epitope prediction tools



Schema of B cell epitope prediction tools



Schema of B cell epitope prediction tools



Input fields

Do you know these methods?

Click “Help”, if you want to know more about a prediction method

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Antibody Epitope Prediction - Tutorial

I. Methods for predicting continuous antibody epitope from protein sequences

General basis: Parameters such as hydrophilicity, flexibility, accessibility, turns, exposed surface, polarity and antigenic propensity of polypeptides chains ha allow the position of continuous epitopes to be predicted from certain features of the protein sequence. All prediction calculations are based on propensity scal the basis of their relative propensity to possess the property described by the scale.

General method: When computing the score for a given residue *i*, the amino acids in an interval of the chosen length, centered around residue *i*, are consider compute the score for residue *i*. Unless specified, the score for residue *i* is the average of the scale values for these amino acids (see table 1 for specific meth be antigenic.

Interpretation of output graphs and tables: On the graphs, the Y-axes depicts for each residue the correspondent score (averaged in the specified window residue positions in the sequence. The tables provide values of calculated scores for each residue. The larger score for the residues might be interpreted as th graphs). However, the presented methods do not predict the epitopes per se, either linear or discontinuous, -- they might only guide the researchers to further

Table 1. Implemented methods

Method
Chou and Fasman beta turn prediction • Reference: Chou PY, Fasman GD. Prediction of the secondary structure of proteins from their amino acid sequence. Adv Enzymol Relat Areas Mol Biol. • Description: The rationale for predicting turns to predict antibody epitopes is based on the paper by Pellequer et al, Immunology Letters, 36 (1993) 83-99. I Chou and Fasman scale which is commonly used to predict beta turns as described in the reference link above.

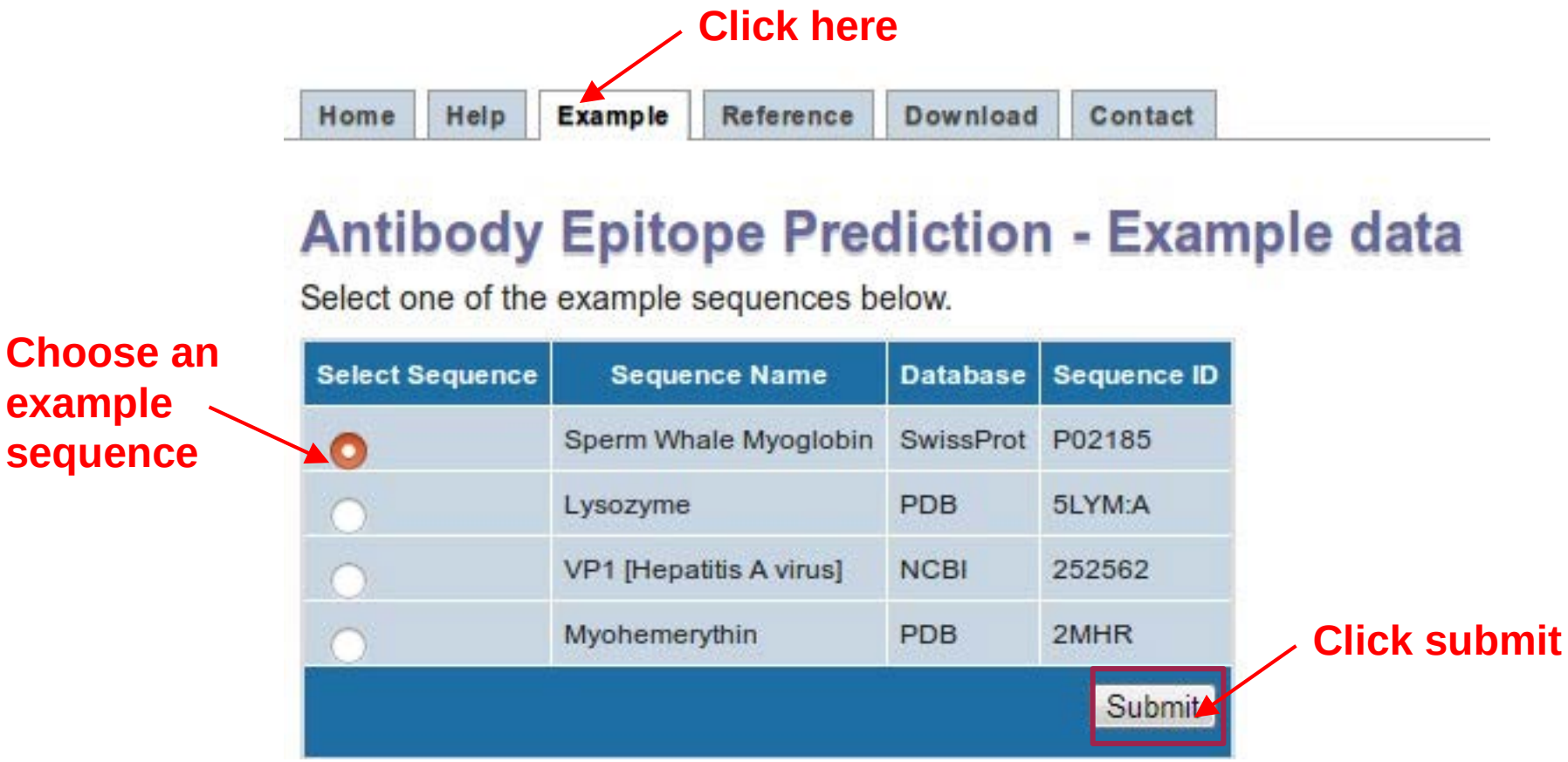
Scale:

A	C	D	E	F	G	H	I	K	L	M	N	P	Q	R	S	T	V	W	Y
0.66	1.19	1.46	0.74	0.6	1.56	0.95	0.47	1.01	0.59	0.6	1.56	1.52	0.98	0.95	1.43	0.96	0.5	0.96	1.14

Emini surface accessibility scale

- Reference: Emini EA, Hughes JV, Perlow DS, Boger J. Induction of hepatitis A virus-neutralizing antibody by a virus-specific synthetic peptide. J Virol. 19
- Description: The calculation was based on surface accessibility scale on a product instead of an addition within the window. The accessibility profile was c probability value, and i vary from 1 to 6. A hexapeptide sequence with Sn greater than 1.0 indicates an increased probability for being found on the surface

Do you want to see how the result page of a prediction method looks?



Citations

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References

Chou & Fasman Beta-Turn Prediction:
Chou PY, Fasman GD. 1978. Prediction of the secondary structure of proteins from their amino acid sequence. *Adv Enzymol Relat Areas Mol Biol* **47**:45-148.
PMID: 364941

Emini Surface Accessibility Prediction:
Emini EA, Hughes JV, Perlow DS, Boger J. 1985. Induction of hepatitis A virus-neutralizing antibody by a virus-specific synthetic peptide. *J Virol* **55**:836-839.
PMID: 2991600

Karplus & Schulz Flexibility Prediction:
Karplus PA, Schulz GE. 1985. Prediction of chain flexibility in proteins. *Naturwissenschaften* **72**:212-213.
Naturwissenschaften

Kolaskar & Tongaonkar Antigenicity:
Kolaskar AS, Tongaonkar PC. 1990. A semi-empirical method for prediction of antigenic determinants on protein antigens. *FEBS Lett***276**:172-174.
PMID: 1702393

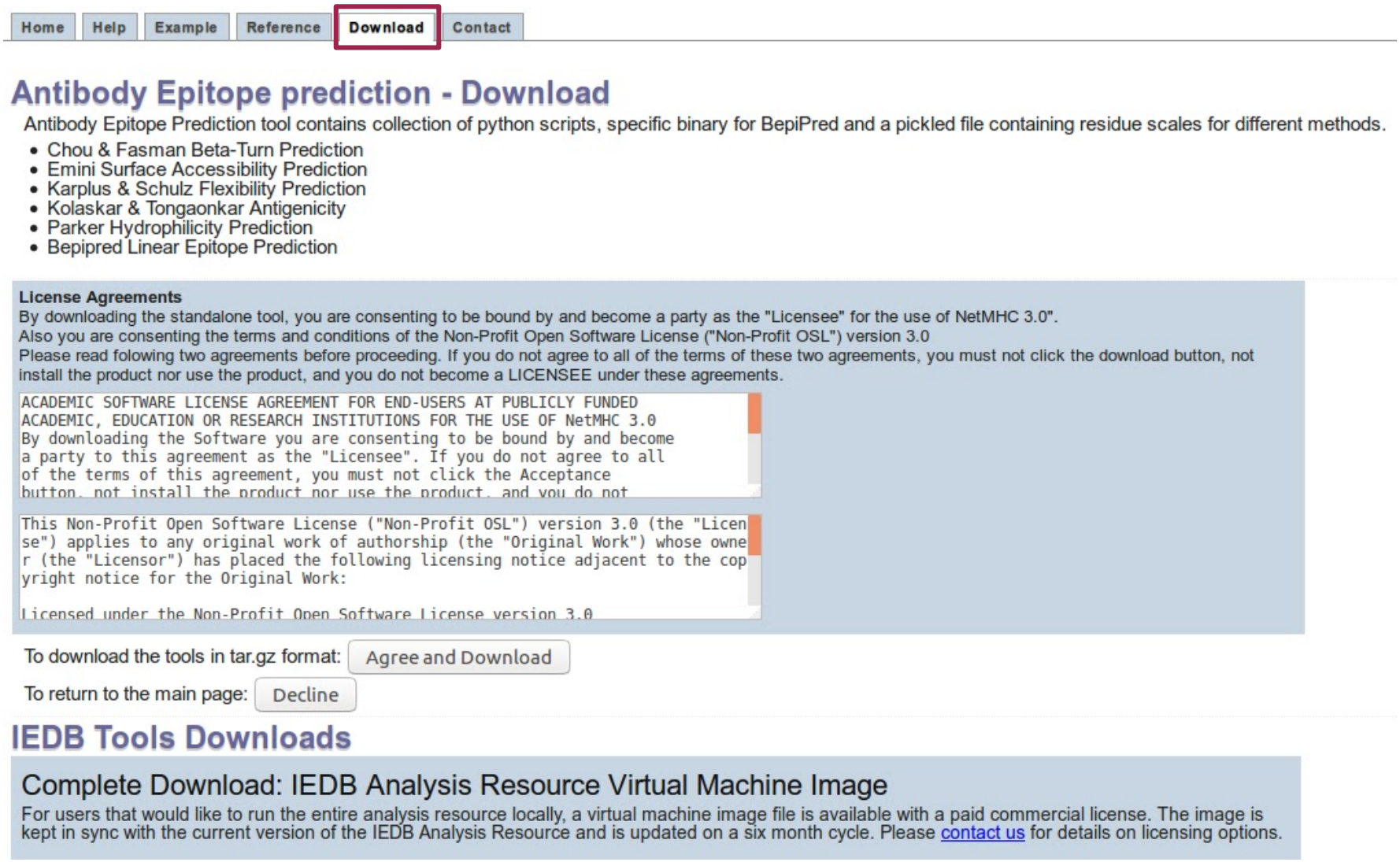
Parker Hydrophilicity Prediction:
Parker JM, Guo D, Hodges RS. 1986. New hydrophilicity scale derived from high-performance liquid chromatography peptide retention data: correlation of predicted surface residues with antigenicity and X-ray-derived accessible sites. *Biochemistry* **25**:5425-5432.
PMID: 2430611

Bepipred Linear Epitope Prediction:
Larsen JE, Lund O, Nielsen M. 2006. Improved method for predicting linear B-cell epitopes. *Immunome Res* **2**:2.
PMID: 16635264

Ponomarenko JV, Bourne PE. 2007. Antibody-protein interactions: benchmark datasets and prediction tools evaluation. *BMC Struct Biol* **7**:64.
PMID: 17910770
Video presentation on SciViee site

Haste Andersen P, Nielsen M, Lund O. 2006. Prediction of residues in discontinuous B-cell epitopes using protein 3D structures. *Protein Sci* **15**:2558-2567.
PMID: 17001032

Do you need standalone versions?



"Help will always be given at ~~Hogwarts~~ **IEDB** to those who ask for it."

IEDB solution Center
help@iedb.org

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- **Schema** of B cell epitope prediction tools on IEDB
- **Sequence-based epitope prediction methods:**
  - Linear epitope prediction methods
    - Amino acid physicochemical property-based methods
    - Machine learning approaches
- **3D Structure-based epitope prediction methods:**
  - Discontinuous epitope prediction methods
- **Computational antibody design**
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Epitope prediction

- **When to use epitope prediction methods?**

- When you have verified thoroughly that **no information is available in the IEDB** on the antigen of your interest or
- When you want to **know all the candidate antigenic determinants** in an antigen of your interest other than epitopes provided in the IEDB

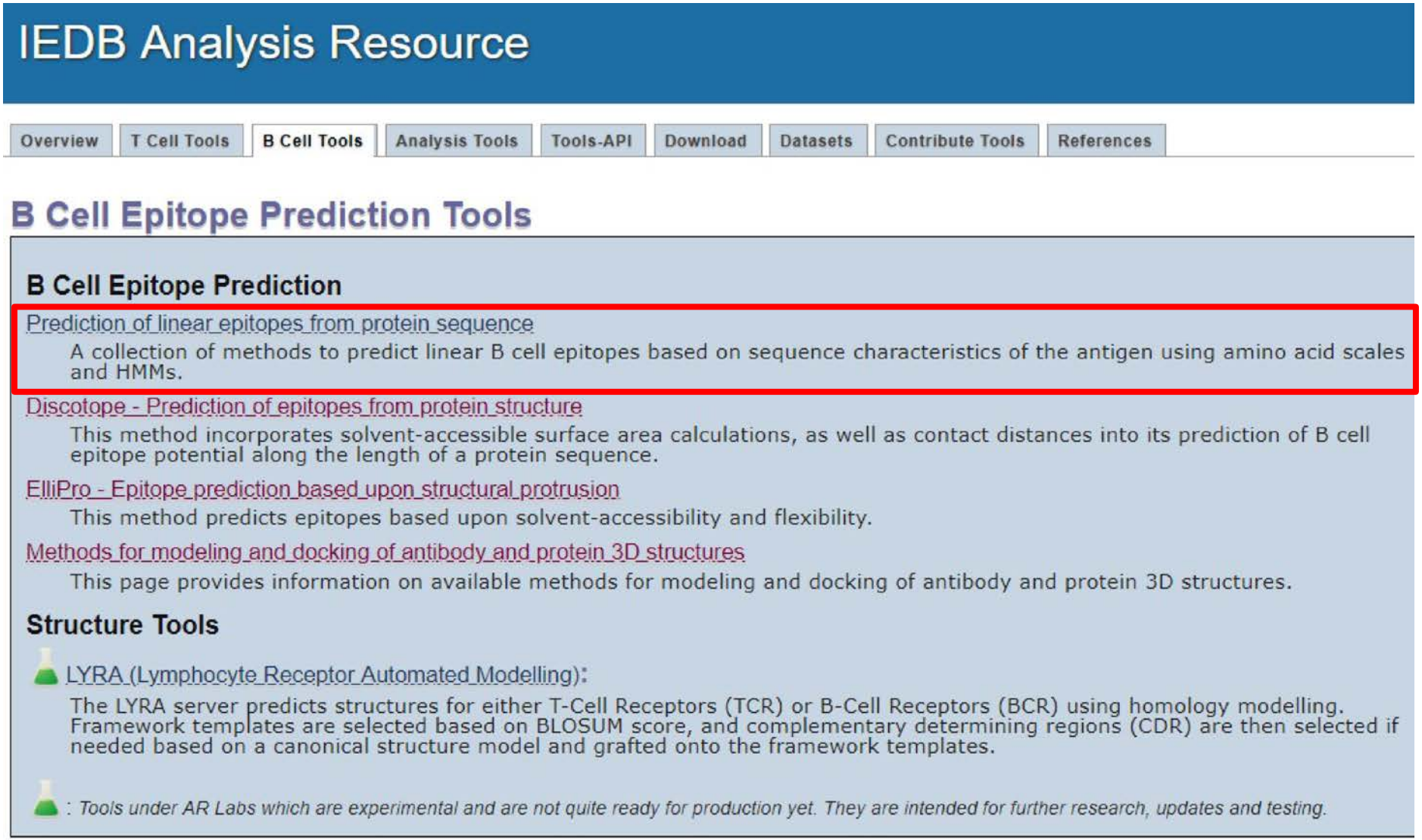
Sequence-based epitope prediction

- **Linear epitope prediction:**
  - **Amino acid physicochemical properties-based methods:**
    - Features which have been correlated with the location of continuous epitopes
    - **β**-Turns (**Chou & Fasman**),
    - Surface Accessibility (**Emini**),
    - Flexibility (**Karplus & Schulz**),
    - antigenic propensity: occurrence of residues in epitopes (**Kolaskar & Tongaonkar**),
    - Hydrophilicity (**Parker**).
  - Only provide information on protein regions which might be of interest for antibody binding.
  - These are not prediction methods in a strict sense.

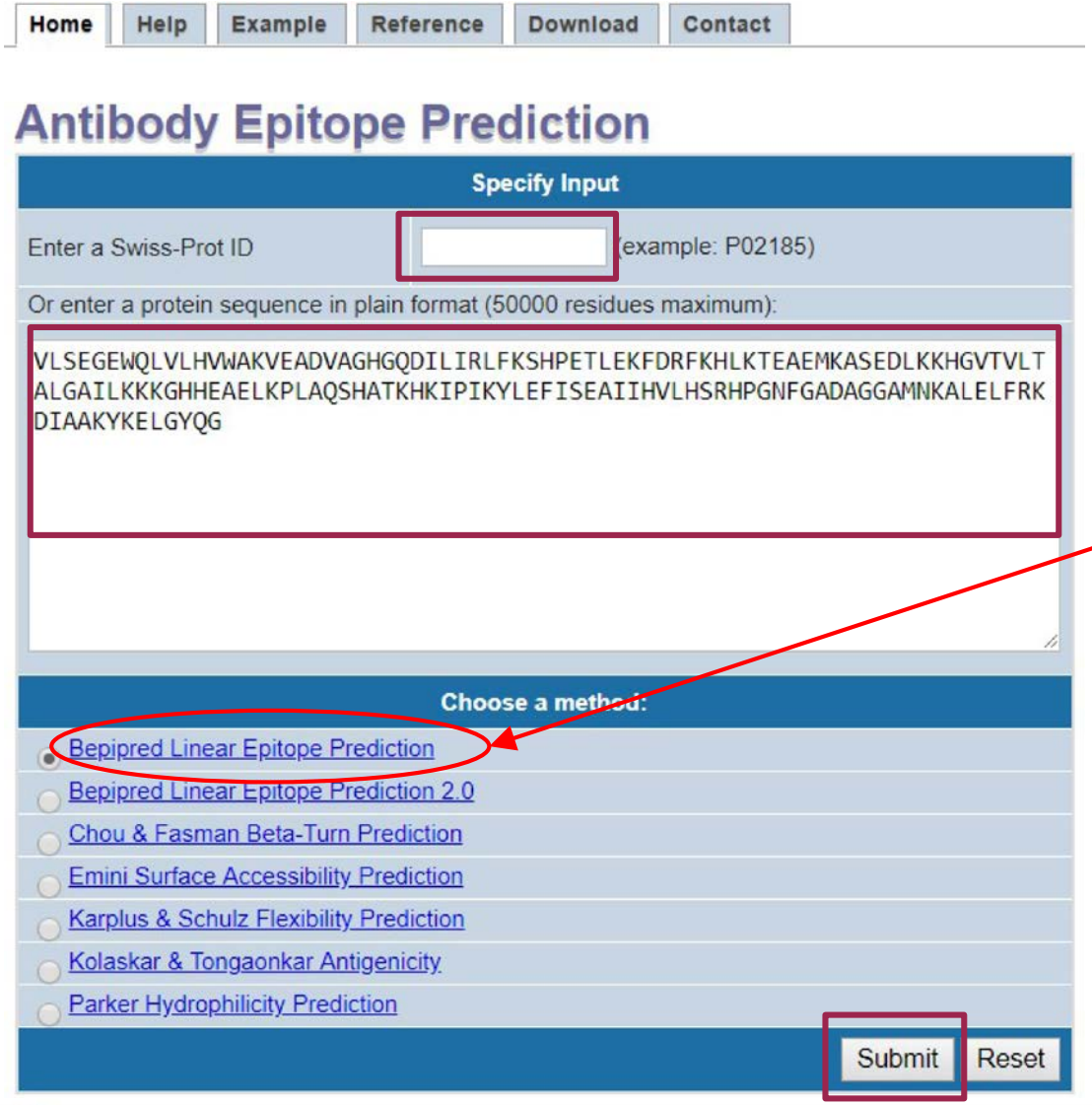
Linear epitope prediction

- **Linear epitope prediction methods:**
  - **Machine learning algorithms**
    - Positive and negative training datasets are used
    - Combination of one or more amino acid scales are used as an input to one of the machine learning algorithms
      - Random Forest (**BepiPred-2.0**)
      - ANN: Artificial Neural Network (ABCpred)
      - SVM: Support Vector Machine (BCpred, FBCpred)
    - Prediction accuracy is optimized

B cell epitope prediction tools



Linear epitope prediction



- **BepiPred** is the default and recommended method.
- It is based on a combination of Hidden Markov model (**HMM**) and two amino acid scales,
- **Parker's** hydrophilicity scale and **Levitt's** secondary structure scale.
- Reported AUC was **0.66.** (Larsen et al., 2006)

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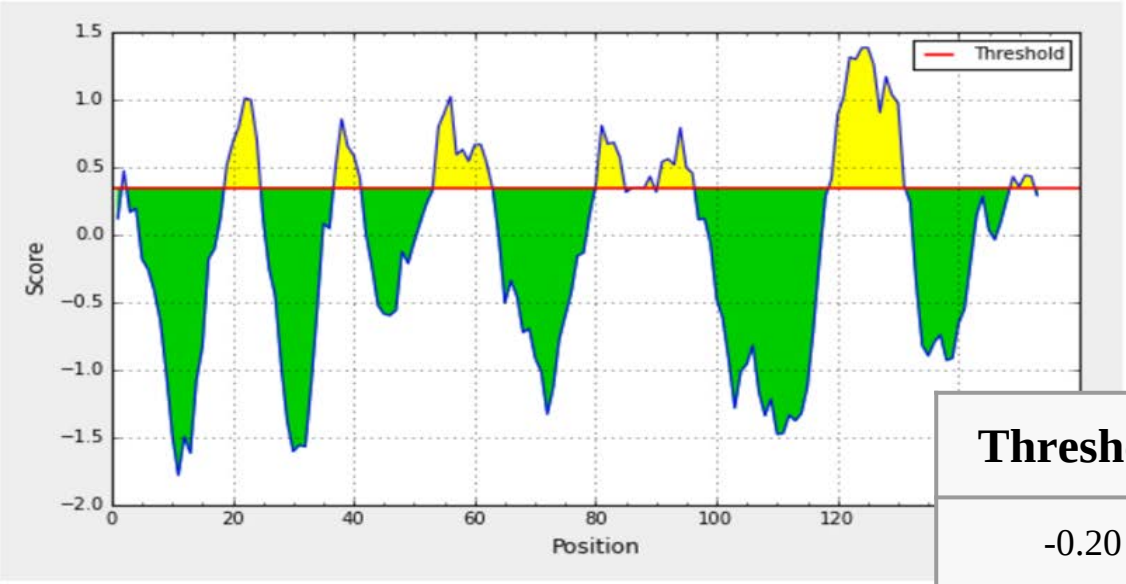
Bepipred Linear Epitope Prediction Results

Input Sequences

```
  1 VLSEGEWQLV LHVWAKVEAD VAGHGQDILI RLFKSHPETL EKFDRFKHLK TEAEMKASED
 61 LKKHGVTVLT ALGAILKKKG HHEAELKPLA QSHATKHKIP IKYLEFISEA IIHVLHSRHP
121 GNFGADAGGA MNKALELFRK DIAAKYKELG YQG
```

Center position: 4 Window size: 7 Threshold: 0.35 Recalculate



Average: -0.105 **Minimum:** -1.784 **Maximum:** 1.390

Predicted peptides:

No.	Start	End	Peptide	Length
1	2	2	L	1
2	19	24	ADVAGH	6
3	37	41	PETLE	5
4	54	62	EMKASEDLK	9
5	80	84	GHHEA	5
6	87	87	K	1
7	89	89	L	1

Threshold	Sensitivity	Specificity
-0.20	0.75	0.50
0.20	0.56	0.68
0.35	**0.49**	**0.75**
0.90	0.25	0.91
1.30	0.13	0.96

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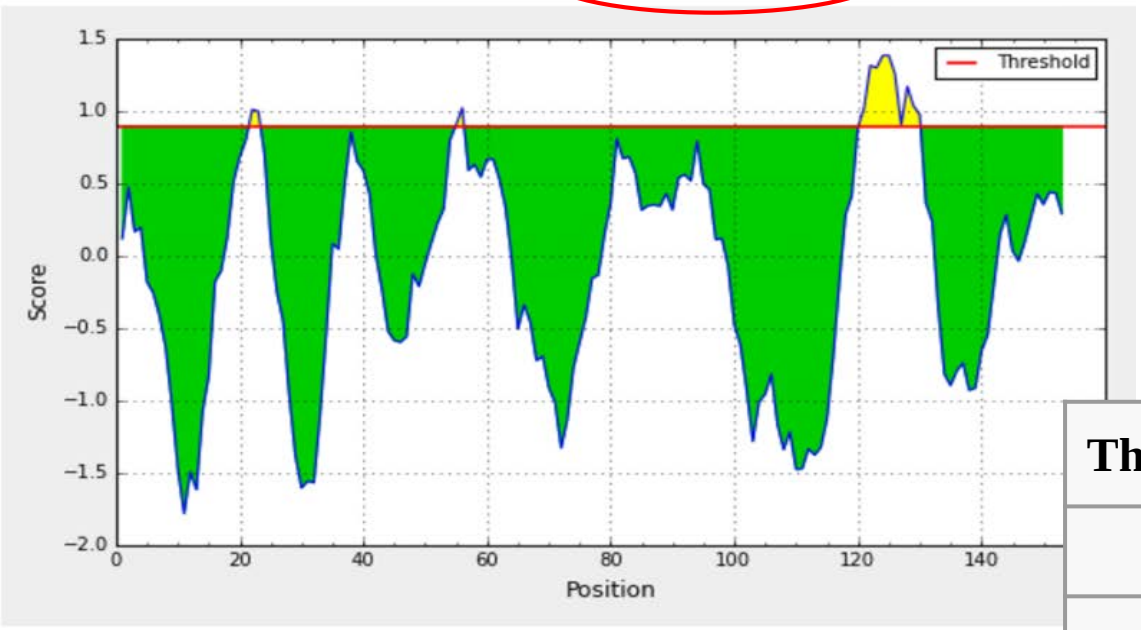
Bepipred Linear Epitope Prediction Results

Input Sequences

```
  1 VLSEGEWQLV LHVWAKVEAD VAGHGQDILI RLFKSHPETL EKFDRFKHLK TEAEMKASED
 61 LKKHGVTVLT ALGAILKKKG HHEAELKPLA QSHATKHKIP IKYLEFISEA IIHVLHSRHP
121 GNFGADAGGA MNKALELFRK DIAAKYKELG YQG
```

Center position: 4 **Window size:** 7 **Threshold:** 0.9 Recalculate



Average: -0.105 **Minimum:** -1.784 **Maximum:** 1.390

Predicted peptides:

No.	Start	End	Peptide	Length
1	22	23	AG	2
2	55	56	MK	2
3	121	130	GNFGADAGGA	10

Predicted residue scores:

Position	Residue	Score	Assignment
1	V	0.121	.

Threshold	Sensitivity	Specificity
-0.20	0.75	0.50
0.20	0.56	0.68
0.35	0.49	0.75
0.90	**0.25**	**0.91**
1.30	0.13	0.96

Predicted peptides:

No.	Start	End	Peptide	Length
1	2	2	L	1
2	19	24	ADVAGH	6
3	37	41	PETLE	5
4	54	62	EMKASEDLK	9
5	80	84	GHHEA	5
6	87	87	K	1
7	89	89	L	1
8	91	96	QSHATK	6
9	119	131	HPGNFGADAGGAM	13
10	149	152	LGYQ	4

Predicted residue scores:

Position	Residue	Score	Assignment
1	V	0.121	.
2	L	0.476	E
3	S	0.168	.
4	E	0.198	.
5	G	-0.180	.
6	E	-0.255	.
7	W	-0.412	.
8	Q	-0.631	.
9	L	-1.022	.
10	V	-1.482	.
11	L	-1.784	.
12	H	-1.496	.

Sequence-based epitope prediction

146	**Y**	-0.035	.
147	**K**	0.098	.
148	**E**	0.265	.
149	**L**	0.433	E
150	**G**	0.357	E
151	**Y**	0.442	E
152	**Q**	0.436	E
153	**G**	0.292	.

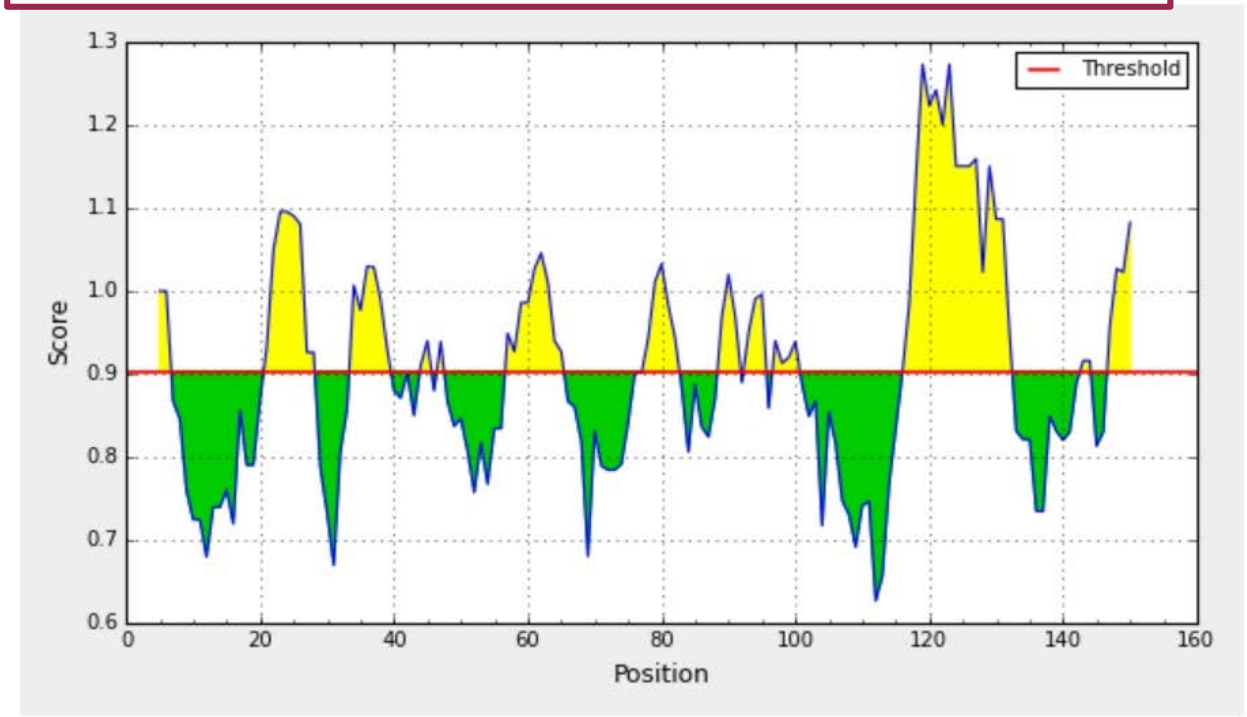
Download result 

Chou & Fasman Beta-Turn Prediction

Input Sequences

```
  1 VLSEGEWQLV LHVWAKVEAD VAGHGQDILI RLFKSHPETL EKFDRFKHLK TEAEMKASED
 61 LKKHGVTVLT ALGAILKKKG HHEAELKPLA QSHATKHKIP IKYLEFISEA IIHVLHSRHP
121 GNFGADAGGA MNKALELFRK DIAAKYKELG YQG
```

Center position: 4 **Window size:** 7 **Threshold:** 0.903 Recalculate



Average: 0.903 **Minimum:** 0.626 **Maximum:** 1.274

Average score of a protein is chosen as a threshold by default.

Predicted residue scores:

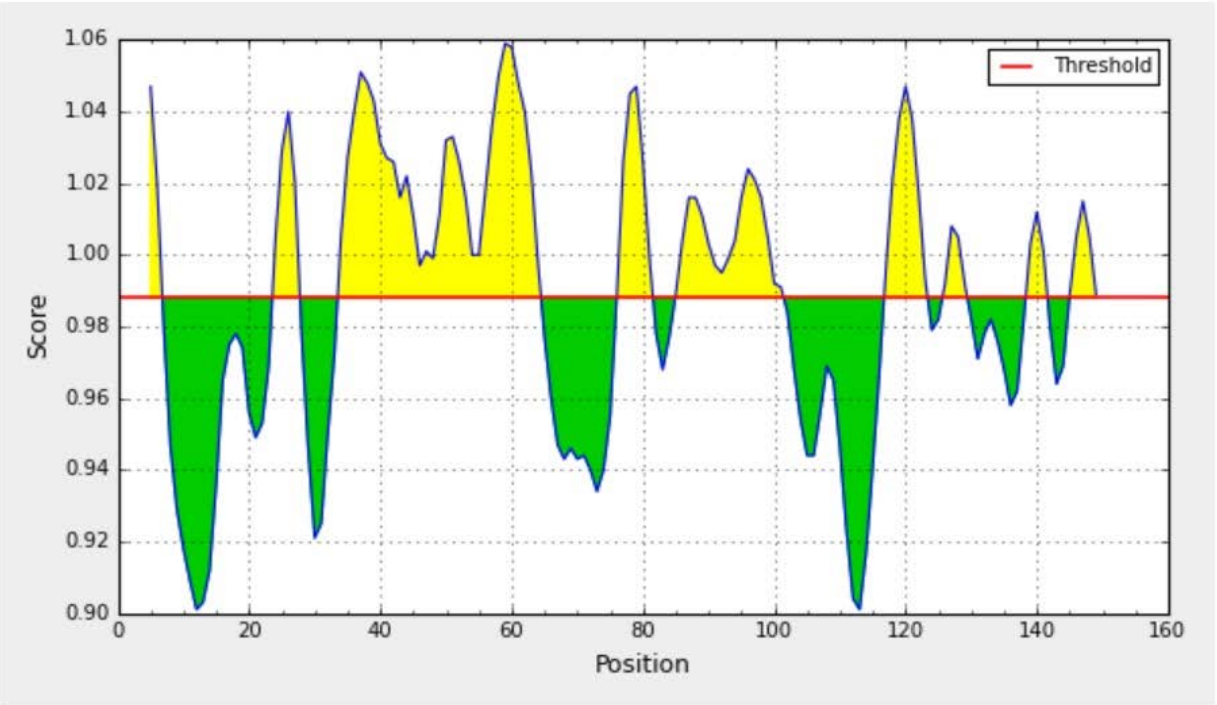
Position	Residue	Start	End	Peptide	Score
4	E	1	7	VLSEGEW	0.931
5	G	2	8	LSEGEWQ	1.0
6	E	3	9	SEGEWQL	1.0

Karplus & Schulz Flexibility Prediction Prediction

Input Sequences

```
  1 VLSEGEWQLV LHVWAKVEAD VAGHGQDILI RLFKSHPETL EKFDRFKHLK TEAEMKASED
 61 LKKHGVTVLT ALGAILKKKG HHEAELKPLA QSHATKHKIP IKYLEFISEA IIHVLHSRHP
121 GNFGADAGGA MNKALELFRK DIAAKYKELG YQG
```

Center position: 4 **Window size:** 7 **Threshold:** 0.988 Recalculate



Average: 0.988 **Minimum:** 0.901 **Maximum:** 1.059

Predicted residue scores:

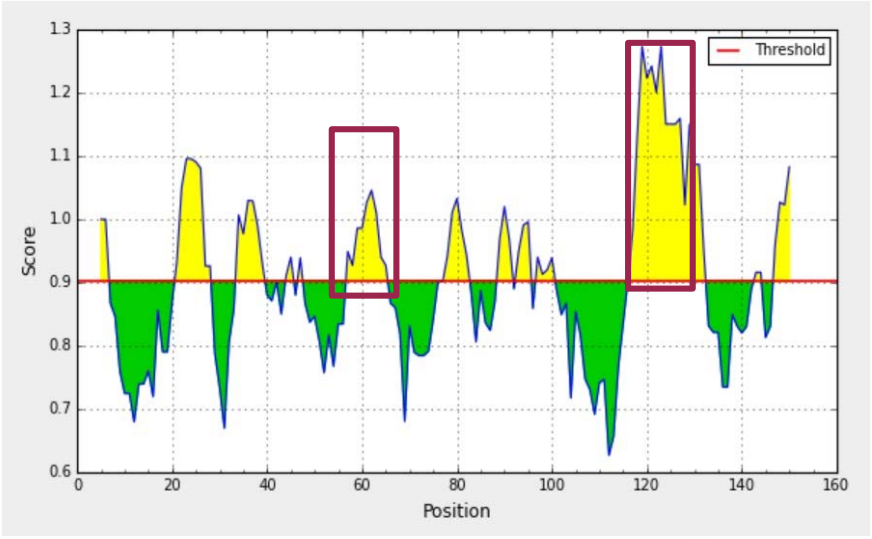
Position	Residue	Start	End	Peptide	Score
4	E	1	7	VLSEGEW	1.053
5	G	2	8	LSEGEWQ	1.047
6	E	3	9	SEGEWQL	1.02

Chou & Fasman Beta-Turn Prediction

Input Sequences

```
  1 VLSEGEWQLV LHVWAKVEAD VAGHGQDILI RLFKSHPETL EKFDRFKHLK TEAEMKASED
 61 LKKHGVTVLT ALGAILKKKG HHEAELKPLA QSHATKHKIP IKYLEFISEA IIHVLHSRHP
121 GNFGADAGGA MNKALELFRK DIAAKYKELG YQG
```

Center position: 4 **Window size:** 7 **Threshold:** 0.903 Recalculate

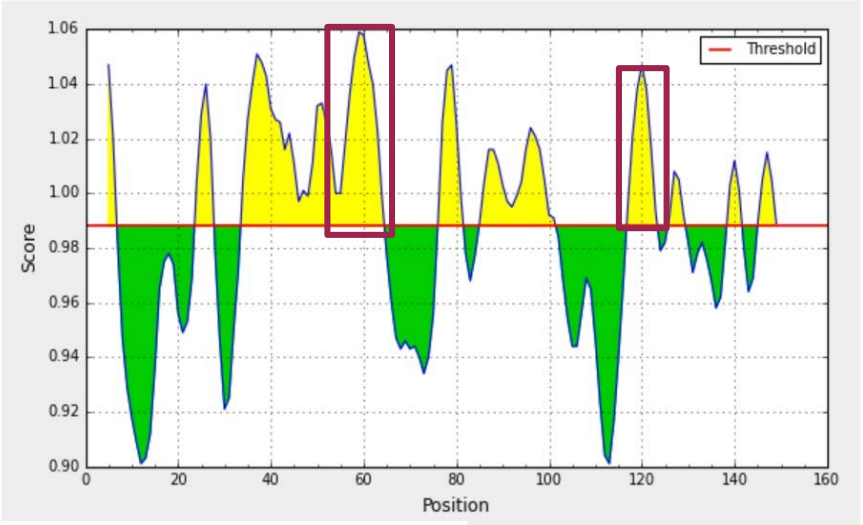


Karplus & Schulz Flexibility Prediction

Input Sequences

```
  1 VLSEGEWQLV LHVWAKVEAD VAGHGQDILI RLFKSHPETL EKFDRFKHLK TEAEMKASED
 61 LKKHGVTVLT ALGAILKKKG HHEAELKPLA QSHATKHKIP IKYLEFISEA IIHVLHSRHP
121 GNFGADAGGA MNKALELFRK DIAAKYKELG YQG
```

Center position: 4 **Window size:** 7 **Threshold:** 0.988 Recalculate

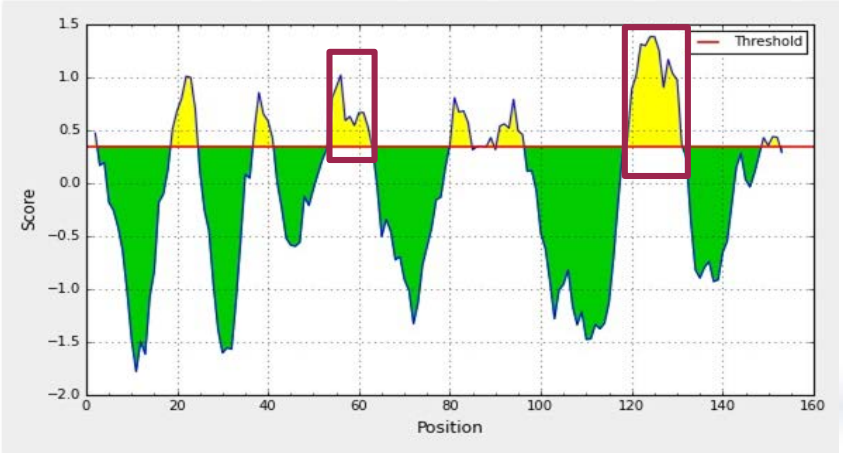


Bepipred Linear Epitope Prediction

Input Sequences

```
  1 VLSEGEWQLV LHVWAKVEAD VAGHGQDILI RLFKSHPETL EKFDRFKHLK TEAEMKASED
 61 LKKHGVTVLT ALGAILKKKG HHEAELKPLA QSHATKHKIP IKYLEFISEA IIHVLHSRHP
121 GNFGADAGGA MNKALELFRK DIAAKYKELG YQG
```

Center position: 4 **Window size:** 7 **Threshold:** 0.35 Recalculate



- It is better to use **consensus** of different methods rather than relying on a single method.

Sequence-based epitope **prediction**

- Evaluation of amino acid scales (Greenbaum et al., 2007): **No method gave AUC above 0.60.**
- Poor performance might be explained by the benchmark datasets containing long 15-25 aa peptides which along with epitope residues contain non-epitope residues.

15-mer AVVLYHNSACCPKWA

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3D Structures of Ab-Ag complexes

Methods for 3D structure determination:

- **X-ray crystallography** (This method provides the most accurate identification of epitopes)
- **Nuclear magnetic resonance** (NMR)
- **Electron microscopy** (EM)

- **Where to get 3D Ab-Ag complexes??**

  IEDB 3D export (1791 3D BCR assays)

- **Where to get 3D coordinates of proteins?**

  Biomolecular 3D structural data is deposited into **PDB (Protein Data Bank)**

www.rcsb.org PDB: Protein DataBank

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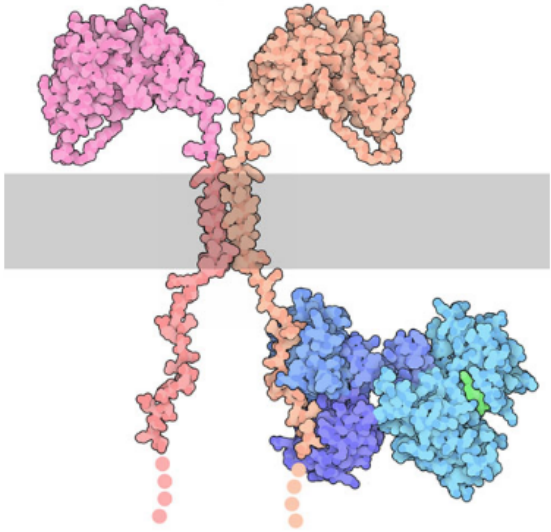
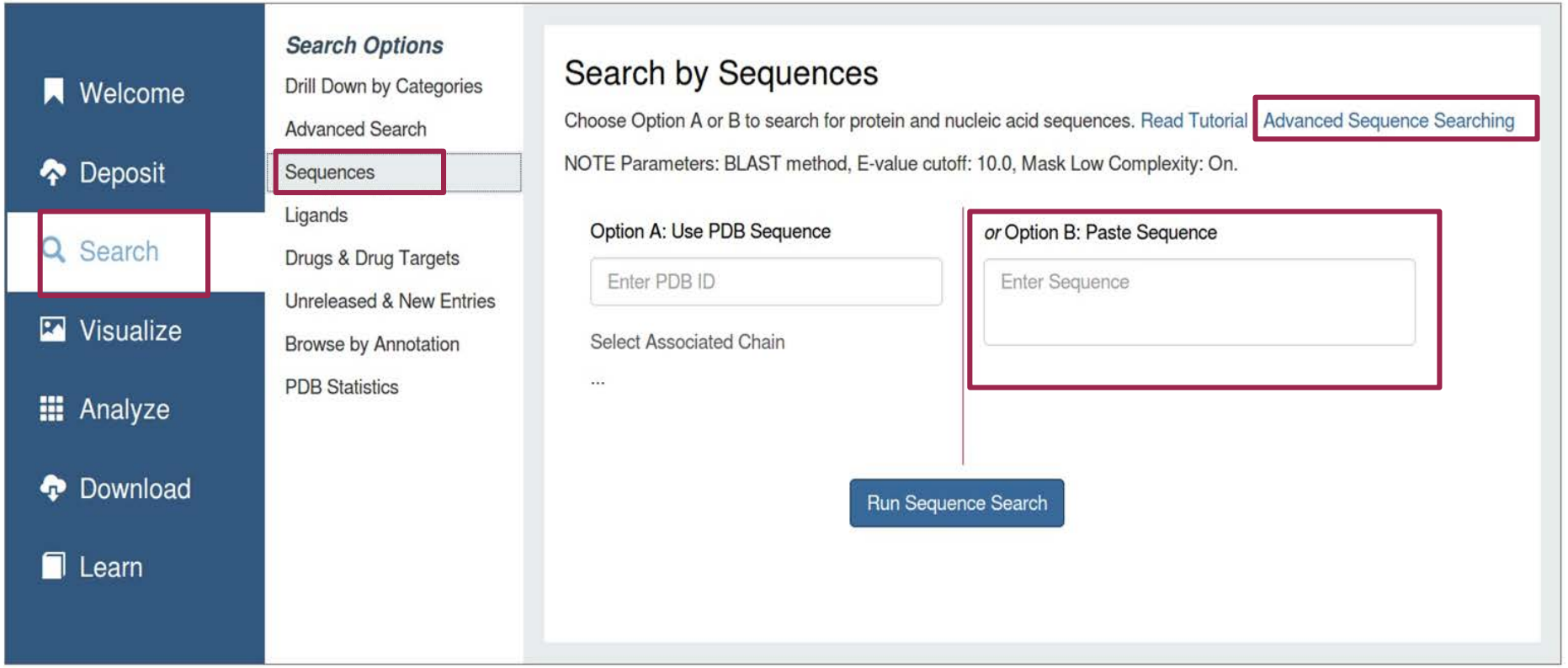


Chimeric Antigen Receptors

Search in PDB

Search in PDB



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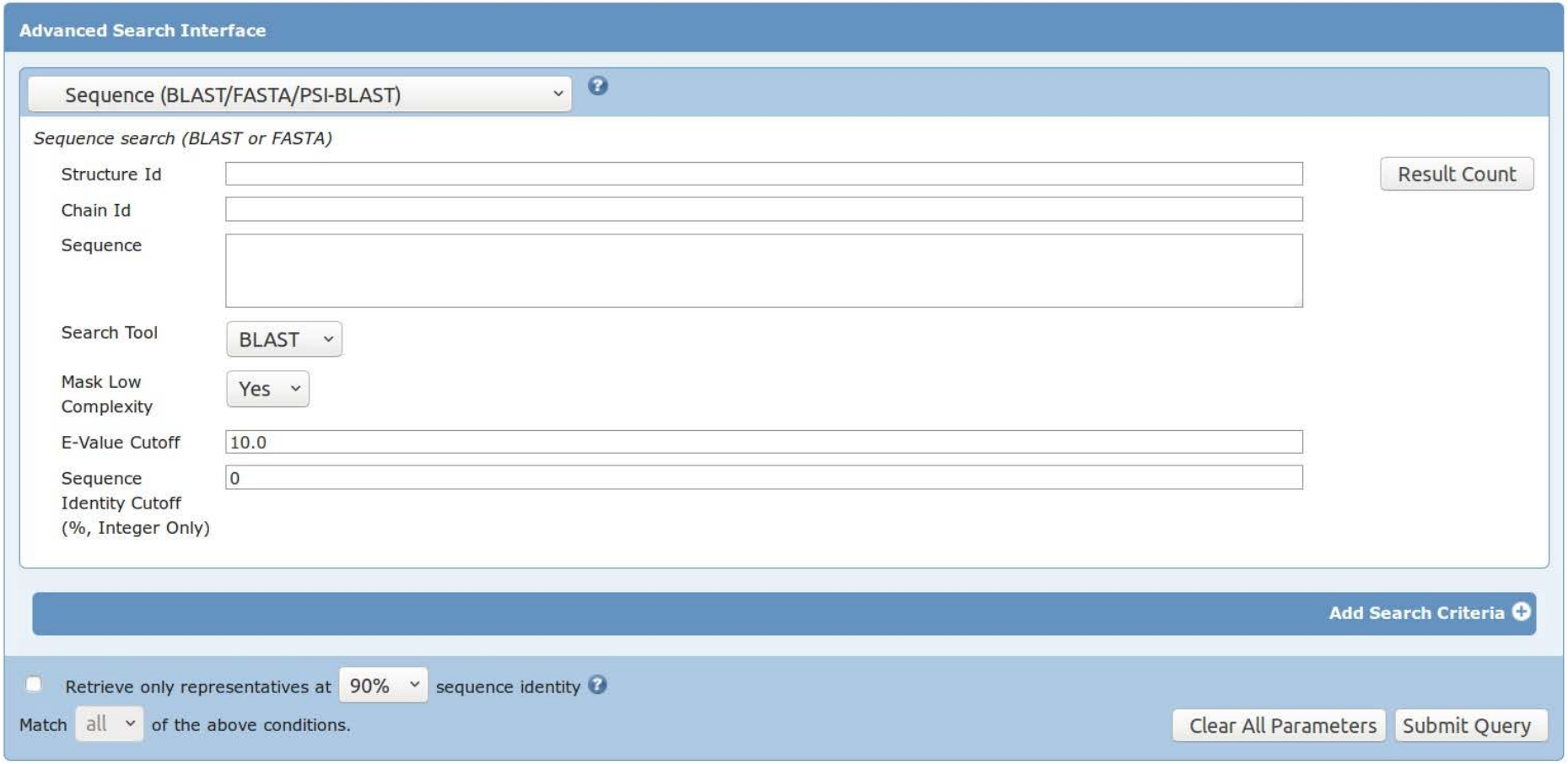
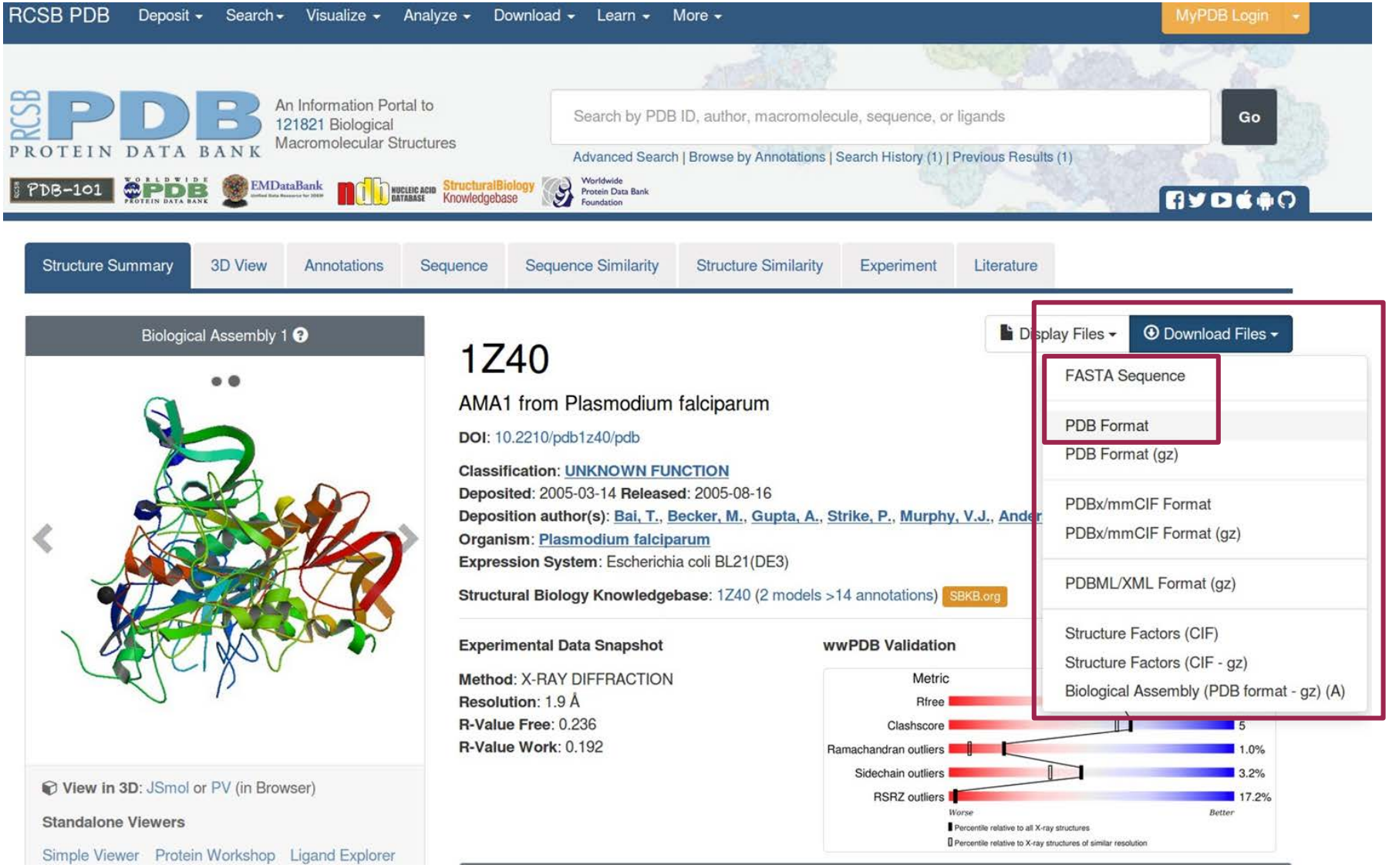
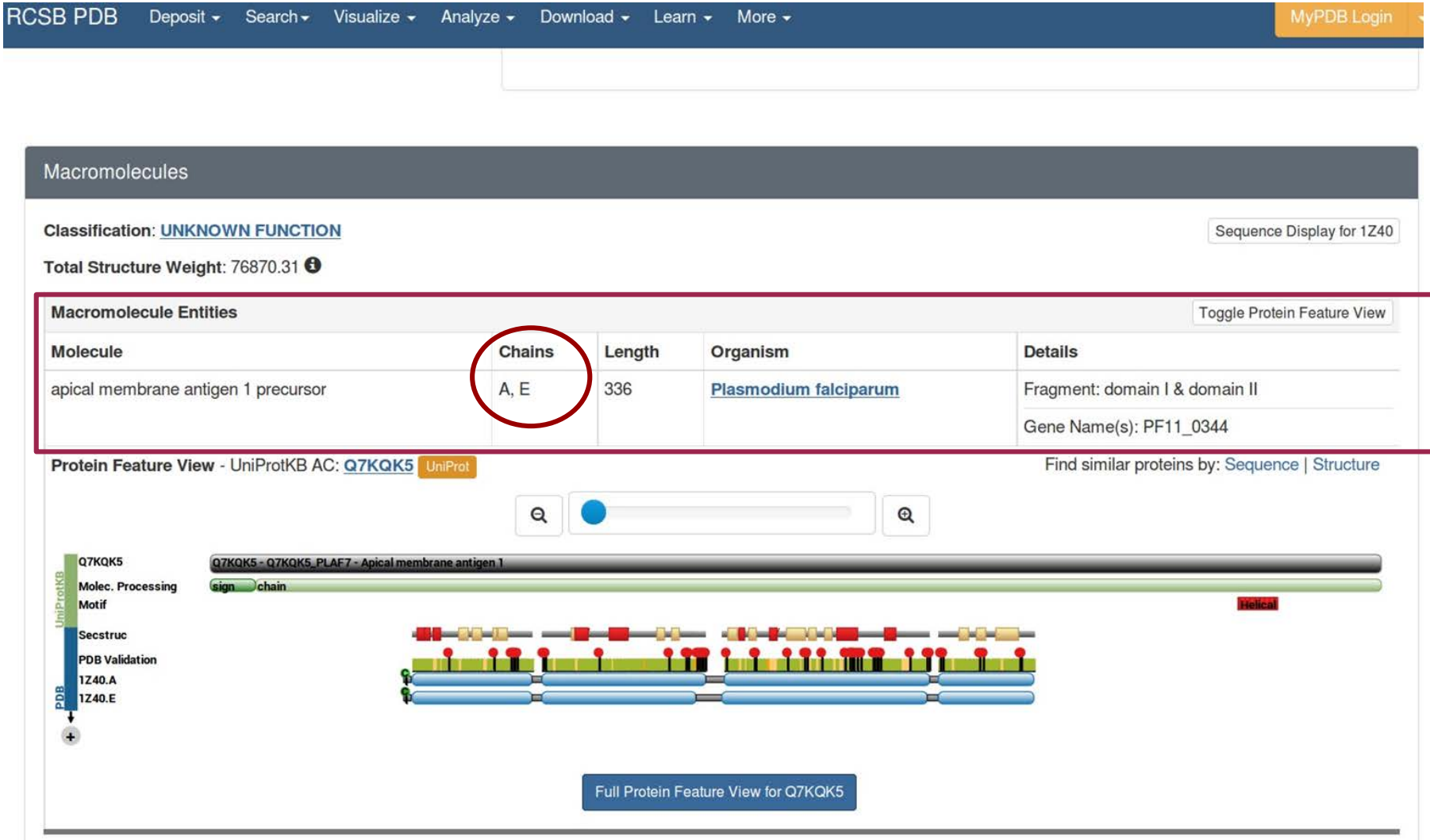


Downloading a PDB file



Protein Chains



What if the 3D structure of a protein of your interest is not available in PDB?

- **Homology or comparative modeling methods, servers and databases**

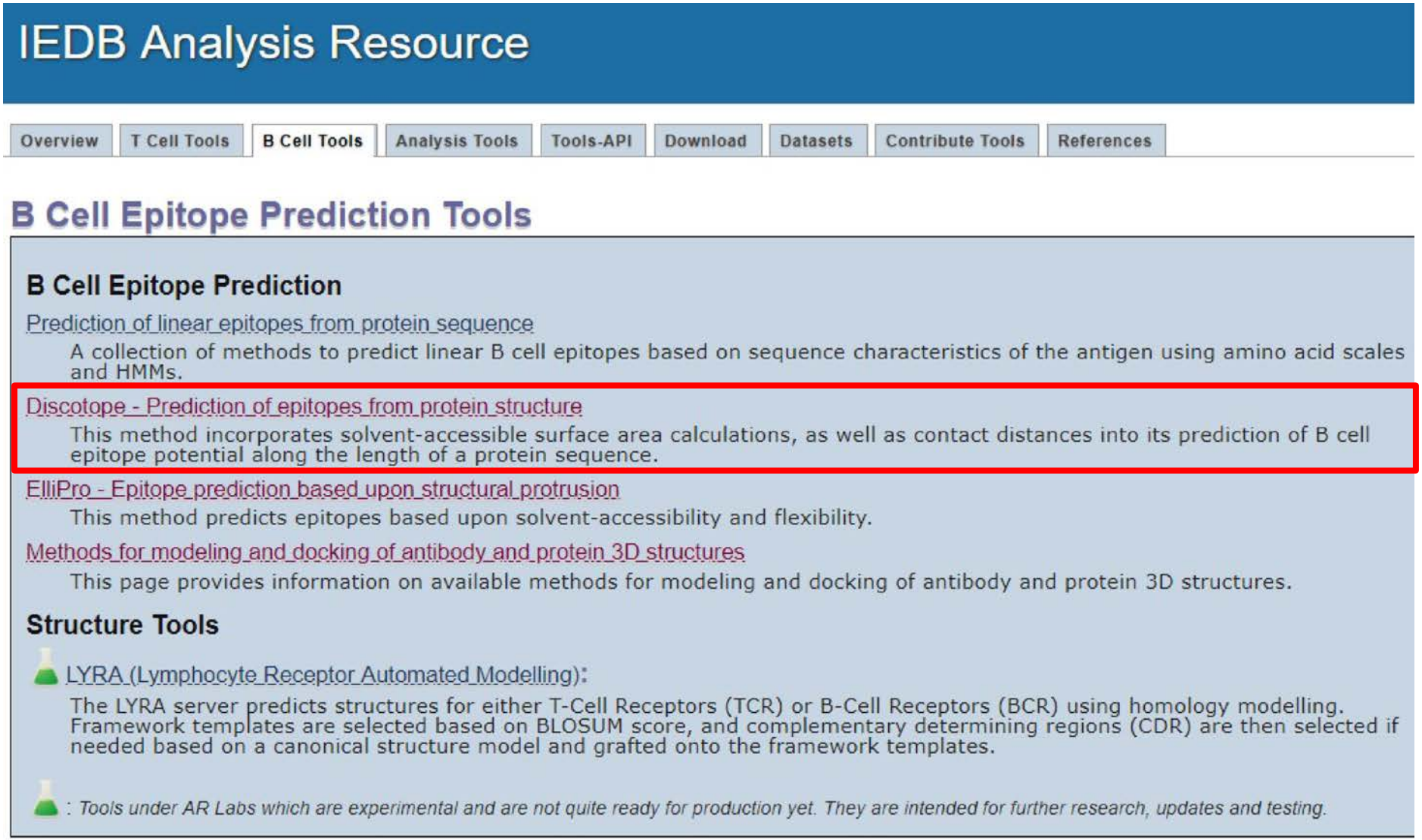
3D Structure-based epitope prediction

- **Discontinuous epitope prediction**
  - Structure-based epitope prediction using:
    - Geometrical properties combined with amino acid scales (**DiscoTope, ElliPro,** CEP)
    - Geometrical properties and amino acid scales used as input to machine learning approaches (EPSVR)
    - Protein-protein docking algorithms
  - Sequence-based epitope prediction using
    - machine learning approaches (CBTope)

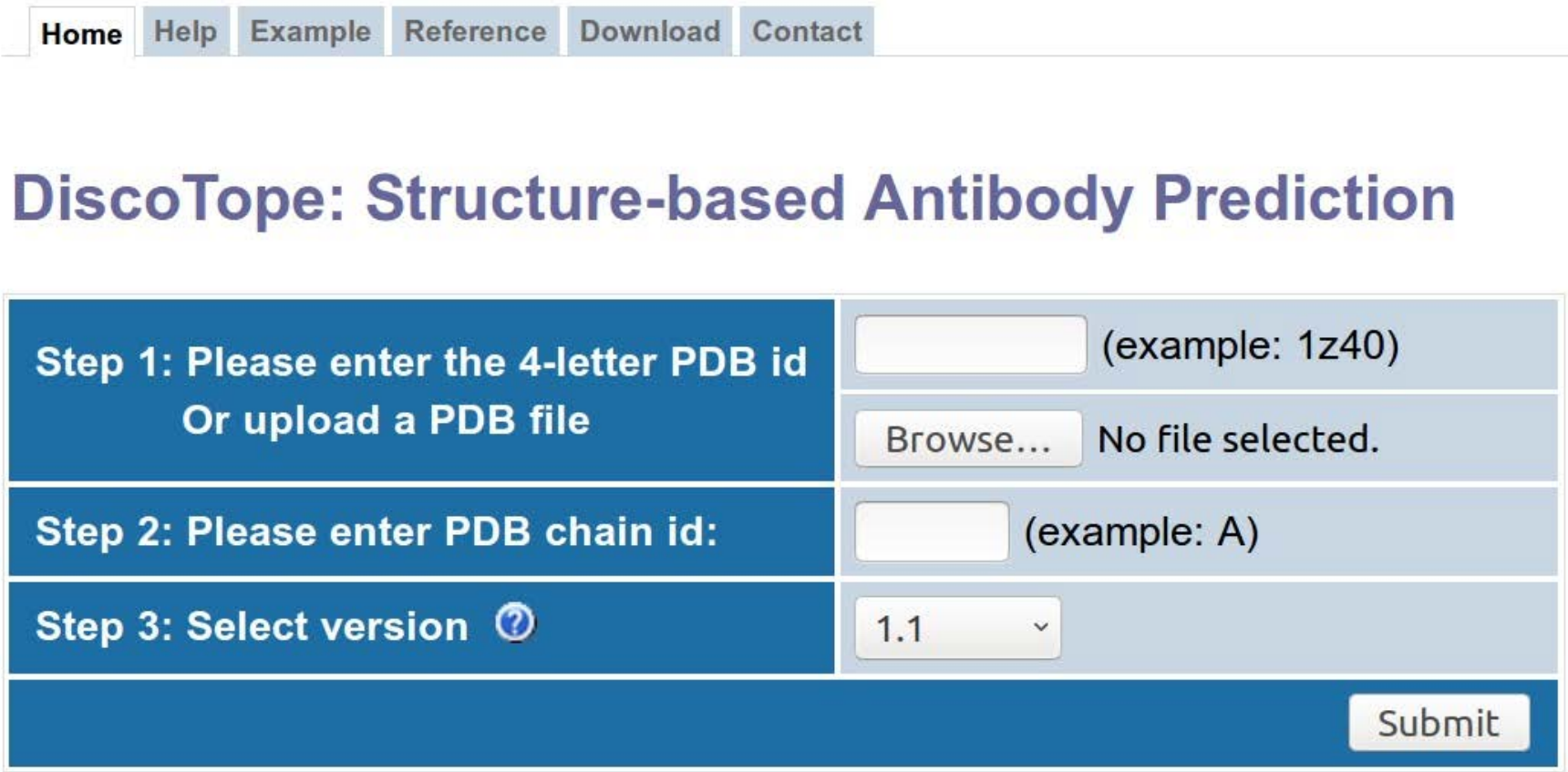
3D Structure-based epitope prediction

- **DiscoTope:**
  - DiscoTope 1 – Andersen *et al*, 2006, Protein Science
    DiscoTope 2 – Kringelum *et al*, 2012, PLoS Comp. Biol.
  - Trained on 75 X-ray structures of antibody-protein complexes (DiscoTope 2 took into account multiple epitopes in an antigen).
  - Assigns each residue a score value calculated as a linear combination of normalized values from
    - Parker's hydrophilicity scale,
    - amino acid occurrence,
    - the number of contacts within 10Å, and
    - the area of relative solvent accessibility.
  - AUC 0.71 for DiscoTope 1 and 0.73 for DiscoTope 2

3D Structure-based epitope prediction

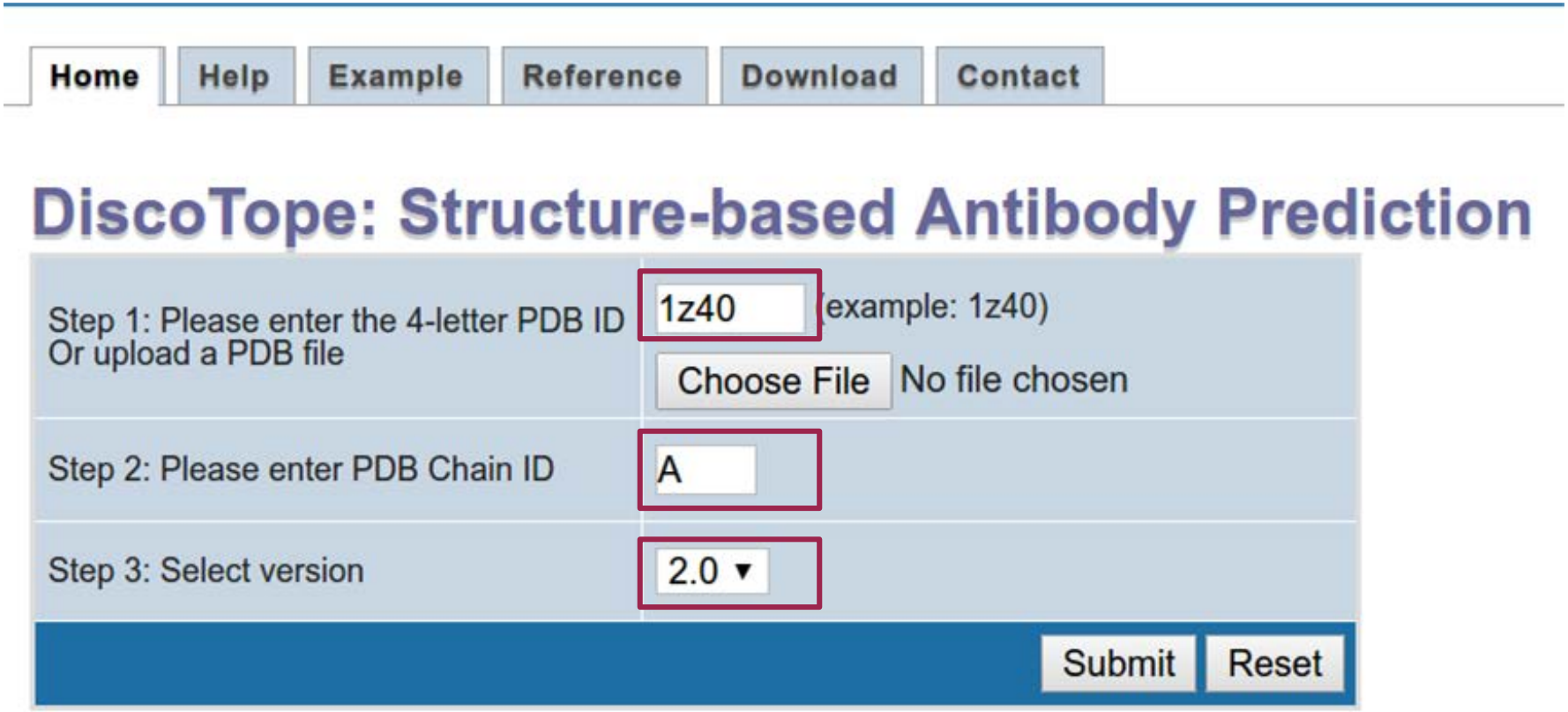


DiscoTope



Please cite this reference when using DiscoTope.

DiscoTope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Download
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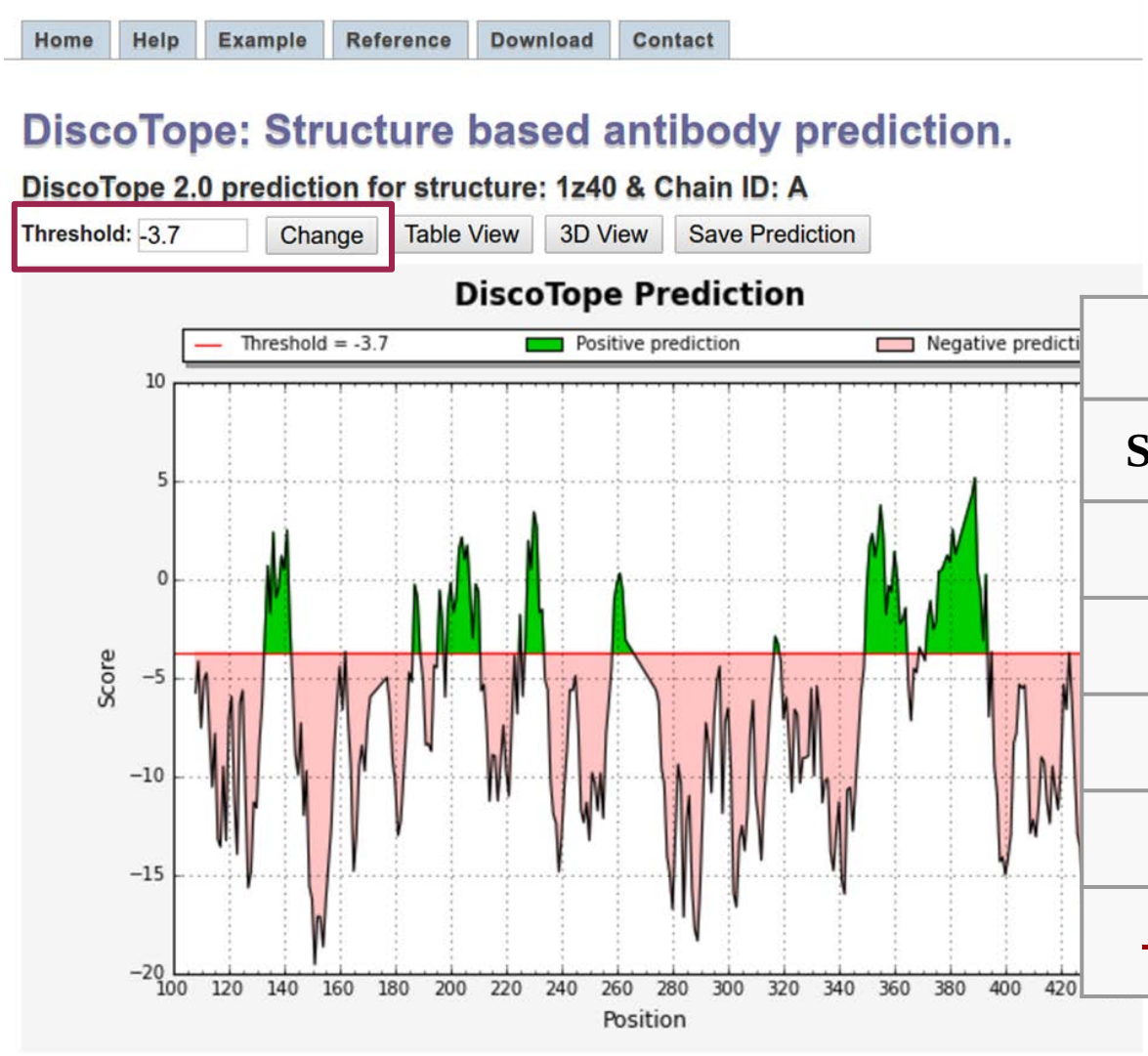
DiscoTope: Structure-based Antibody Prediction
Step 1: Please enter the 4-letter PDB ID
Or upload a PDB file
1z40
(example: 1z40)
Choose File
No file chosen
Step 2: Please enter PDB Chain ID
A
Step 3: Select version
2.0
Submit
Reset

DiscoTope Chart View



DiscoTope 2		
Score	**Sensitivity**	**Specificity**
1.9	0.17	0.95
0.5	0.23	0.90
-1.0	0.30	0.85
-2.5	0.39	0.80
-3.7	**0.47**	**0.75**

DiscoTope Table View

DiscoTope - Result

DiscoTope 2.0 prediction for structure: 1z40 & Chain ID: A

The positive predictions are displayed in green.

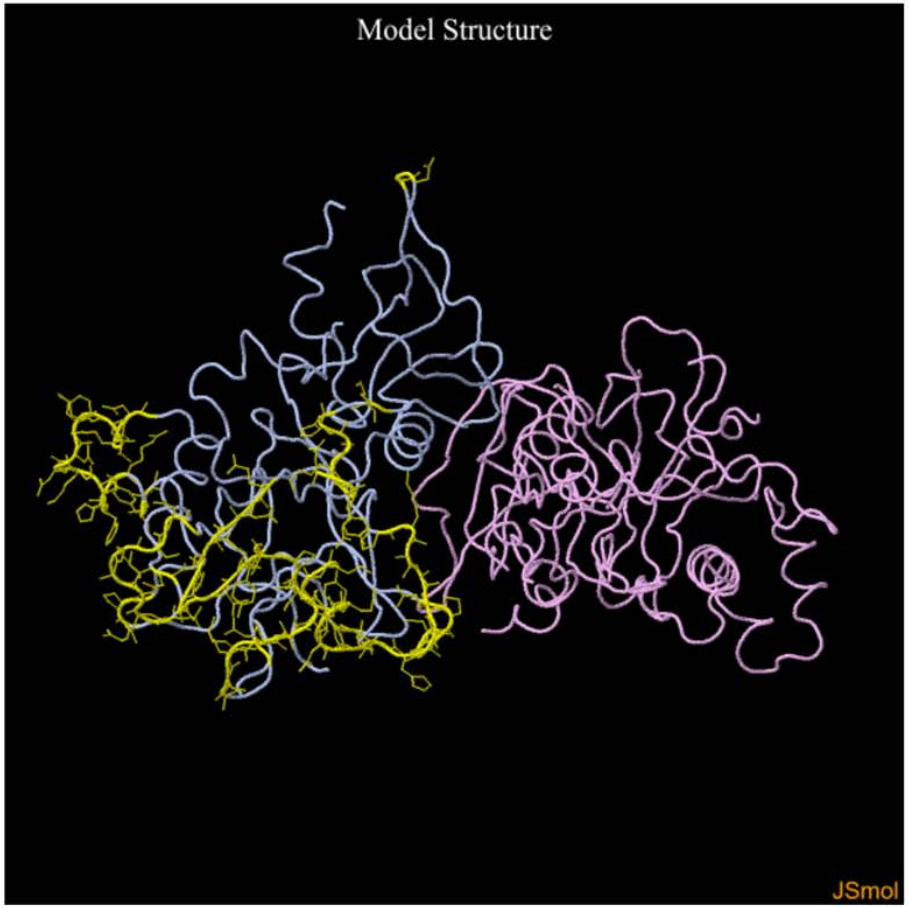
Chart View | 3D View | Save Prediction

Chain ID	Residue ID	Residue Name	Contact Number	Propensity Score	Discotope Score
A	108	ASN	17	-4.287	-5.749
A	109	PRO	7	-3.77	-4.141
A	110	TRP	23	-5.522	-7.532
A	111	THR	4	-5.226	-5.085
A	112	GLU	2	-5.1	-4.744
A	113	TYR	20	-5.97	-7.584
A	114	MET	20	-9.295	-10.526
A	115	ALA	10	-7.532	-7.816
A	116	LYS	23	-11.888	-13.166
A	117	TYR	33	-11.038	-13.564
A	118	ASP	12	-9.15	-9.478
A	119	ILE	35	-10.419	-13.246
A	120	GLU	10	-6.657	-7.042
A	121	GLU	13	-5.019	-5.937
A	122	VAL	30	-8.676	-11.129
A	123	HIS	43	-10.161	-13.938
A	124	GLY	17	-4.876	-6.27
A	125	SER	25	-3.112	-5.629
A	126	GLY	33	-8.05	-10.92
A	127	ILE	39	-12.601	-15.637
A	128	ARG	27	-13.272	-14.85
A	129	VAL	25	-9.506	-11.288
A	130	ASP	39	-8.027	-11.589
A	131	LEU	29	-5.732	-8.408
A	132	GLY	30	-3.241	-6.318
A	**133**	**GLU**	**20**	**-0.565**	**-2.8**
A	**134**	**ASP**	**19**	**3.255**	**0.695**
A	**135**	**ALA**	**28**	**1.707**	**-1.709**

DiscoTope 3D View

JSmol-Rendered PDB Structure

Chart View | Table View | Save Prediction

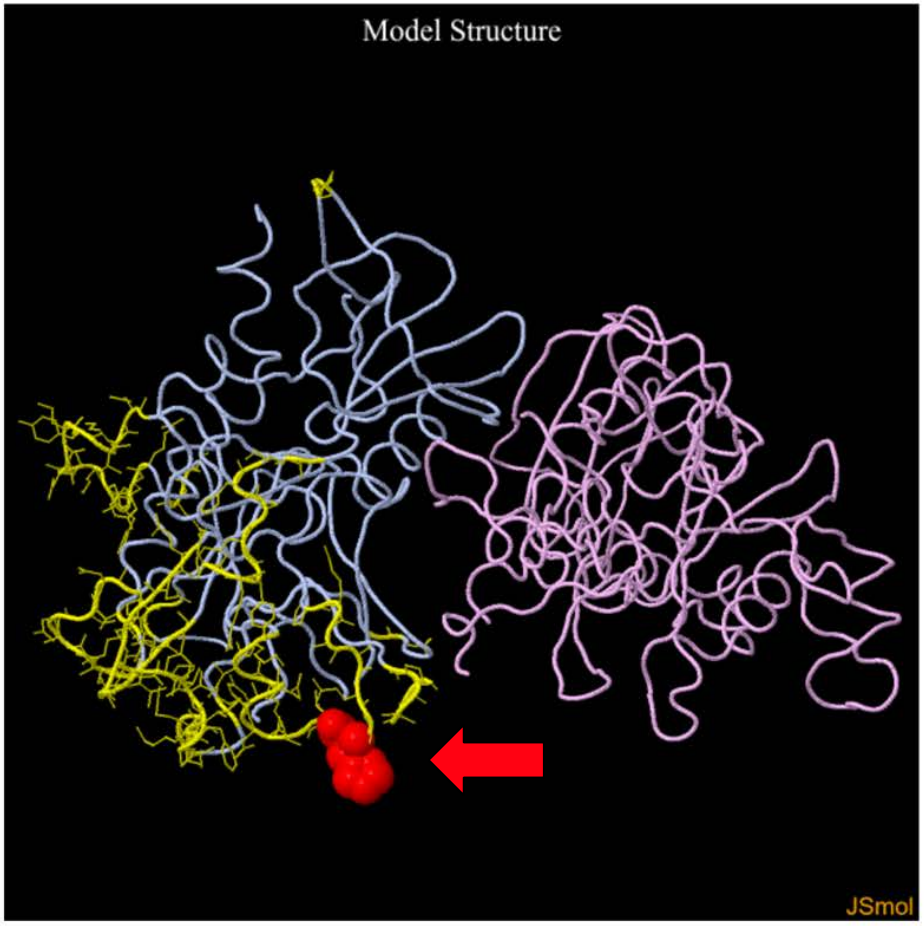


Chain ID	Residue ID	Residue Name	Contact Number	Propensity Score	Discotope Score	View
A	133	GLU	20	-0.565	-2.8	CPK
A	134	ASP	19	3.255	0.695	CPK
A	135	ALA	28	1.707	-1.709	CPK
A	136	GLU	9	3.871	2.391	CPK
A	137	VAL	26	2.342	-0.917	CPK
A	138	ALA	14	1.33	-0.433	CPK
A	139	GLY	6	2.141	1.204	CPK
A	140	THR	23	3.529	0.478	CPK
A	141	GLN	12	4.393	2.508	CPK
A	142	TYR	31	1.669	-2.088	CPK
A	162	ASN	1	-4.008	-3.662	CPK
A	187	GLU	0	-0.296	-0.262	CPK
A	188	PRO	10	0.275	-0.907	CPK
A	196	ASP	2	-0.359	-0.548	CPK
A	197	GLU	16	-0.325	-2.128	CPK
A	199	ARG	10	-0.233	-1.356	CPK
A	200	HIS	9	0.977	-0.171	CPK
A	201	PHE	23	1.105	-1.667	CPK
A	202	TYR	27	2.394	-0.986	CPK
A	203	LYS	4	2.272	1.551	CPK
A	204	ASP	1	2.544	2.136	CPK

DiscoTope 3D View

JSmol-Rendered PDB Structure

Chart View | Table View | Save Prediction



Chain ID	Residue ID	Residue Name	Contact Number	Propensity Score	Discotope Score	View
A	133	GLU	20	-0.565	-2.8	CPK
A	134	ASP	19	3.255	0.695	CPK
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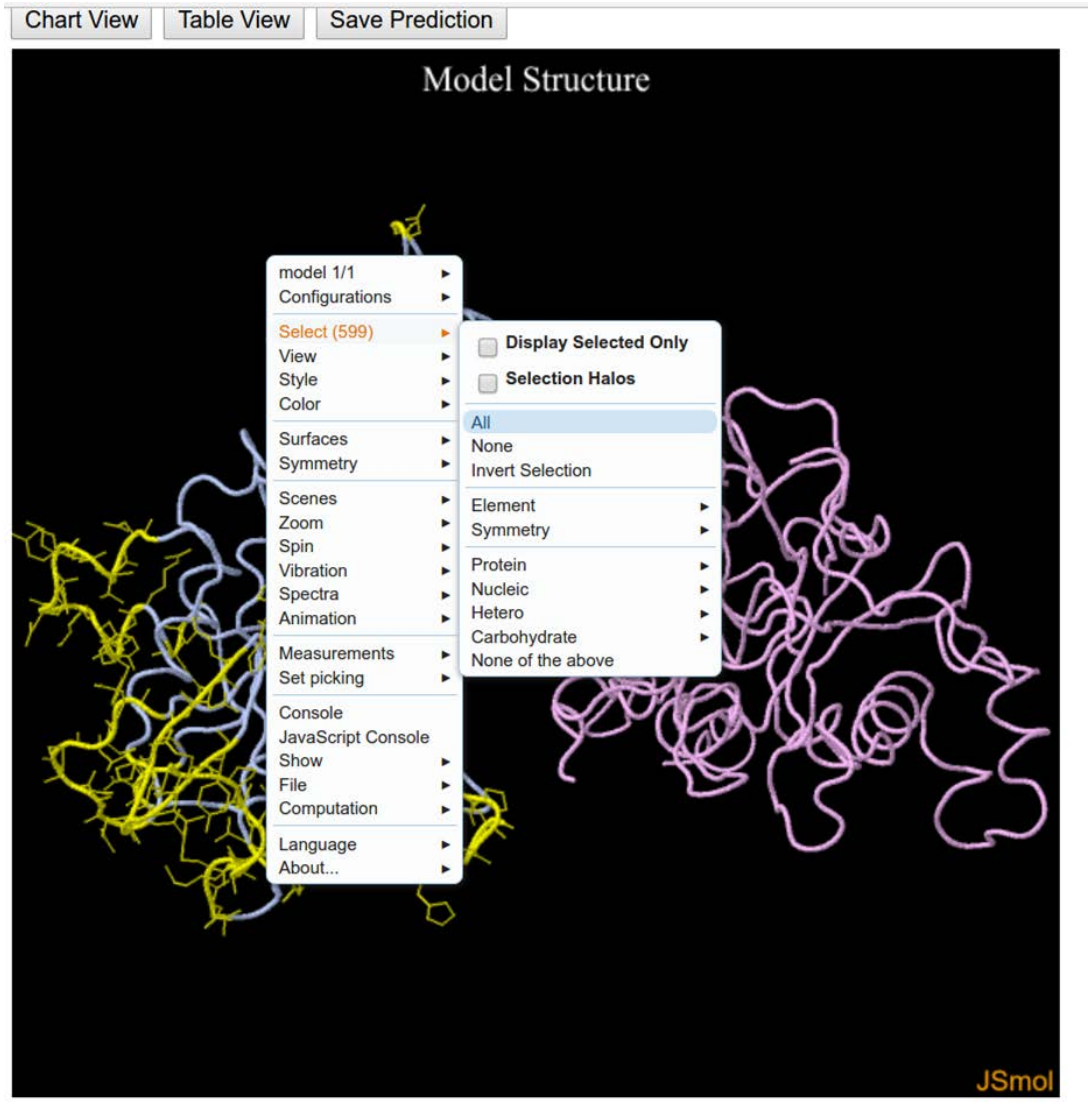
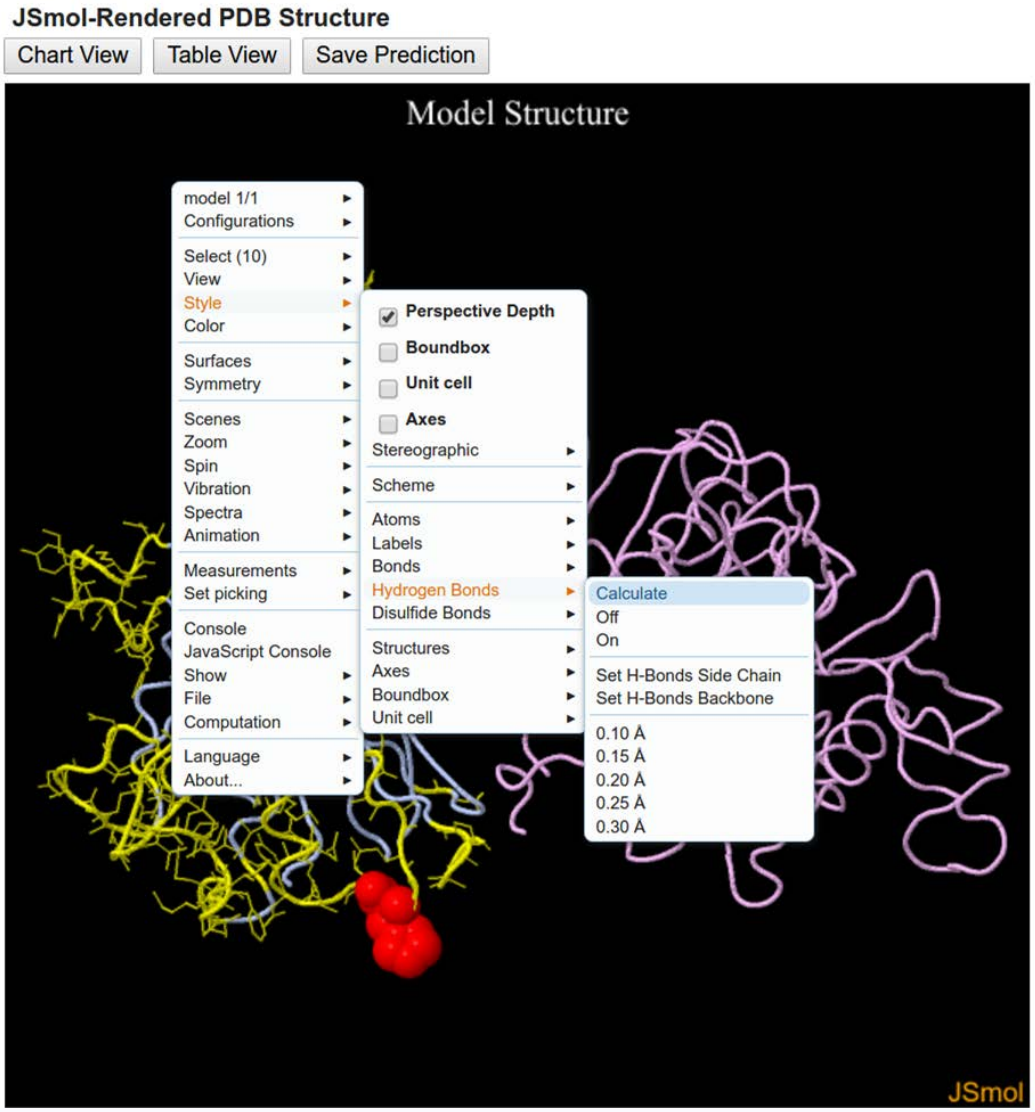
DiscoTope 3D View

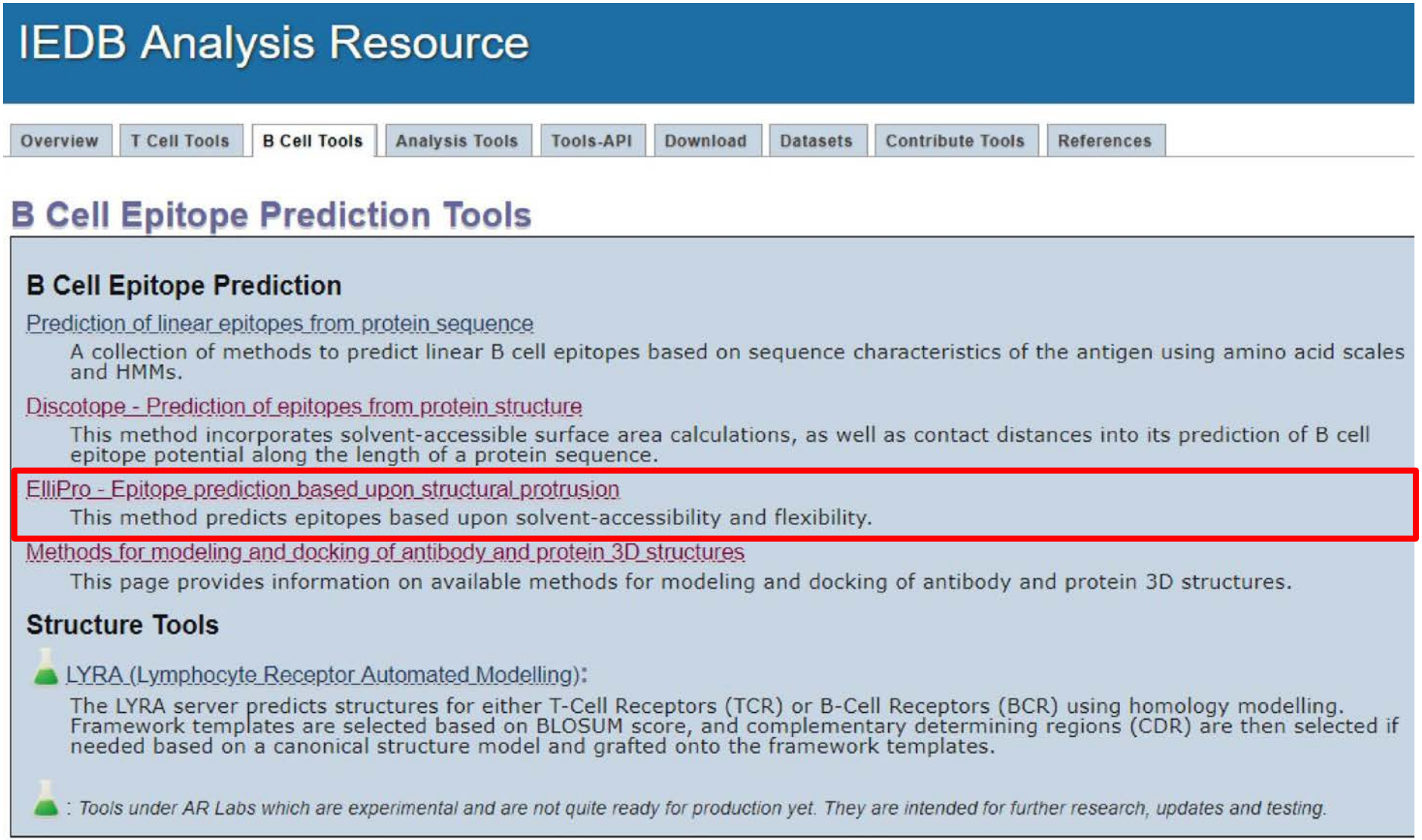


DiscoTope 3D View

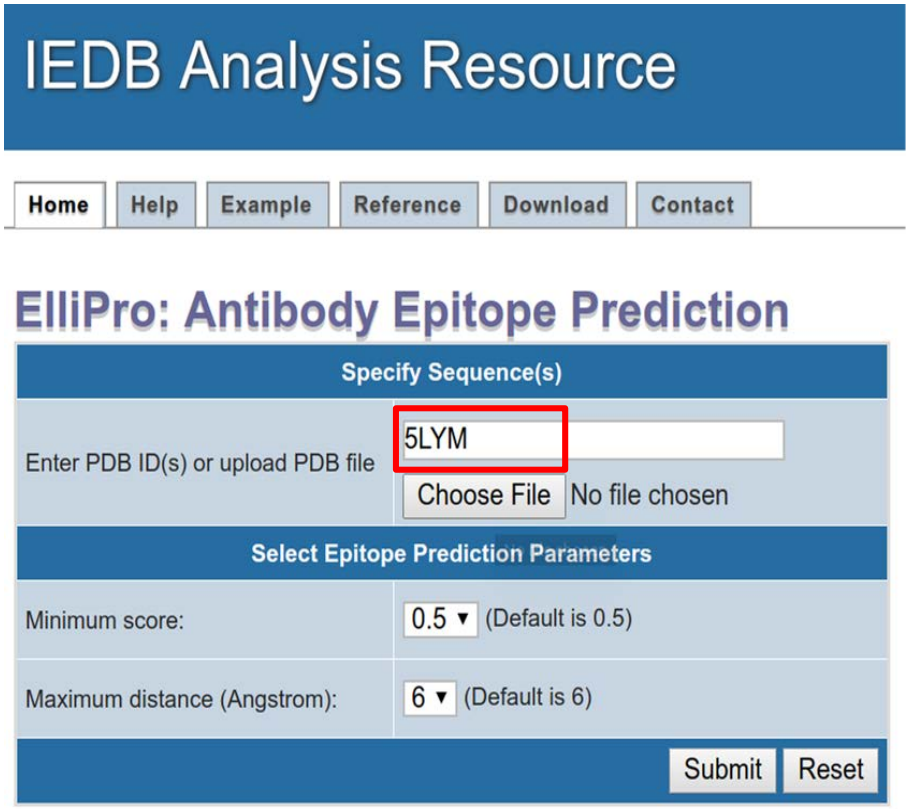


DiscoTope 3D View

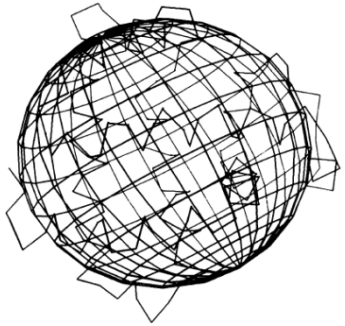
3D Structure-based epitope prediction



ElliPro

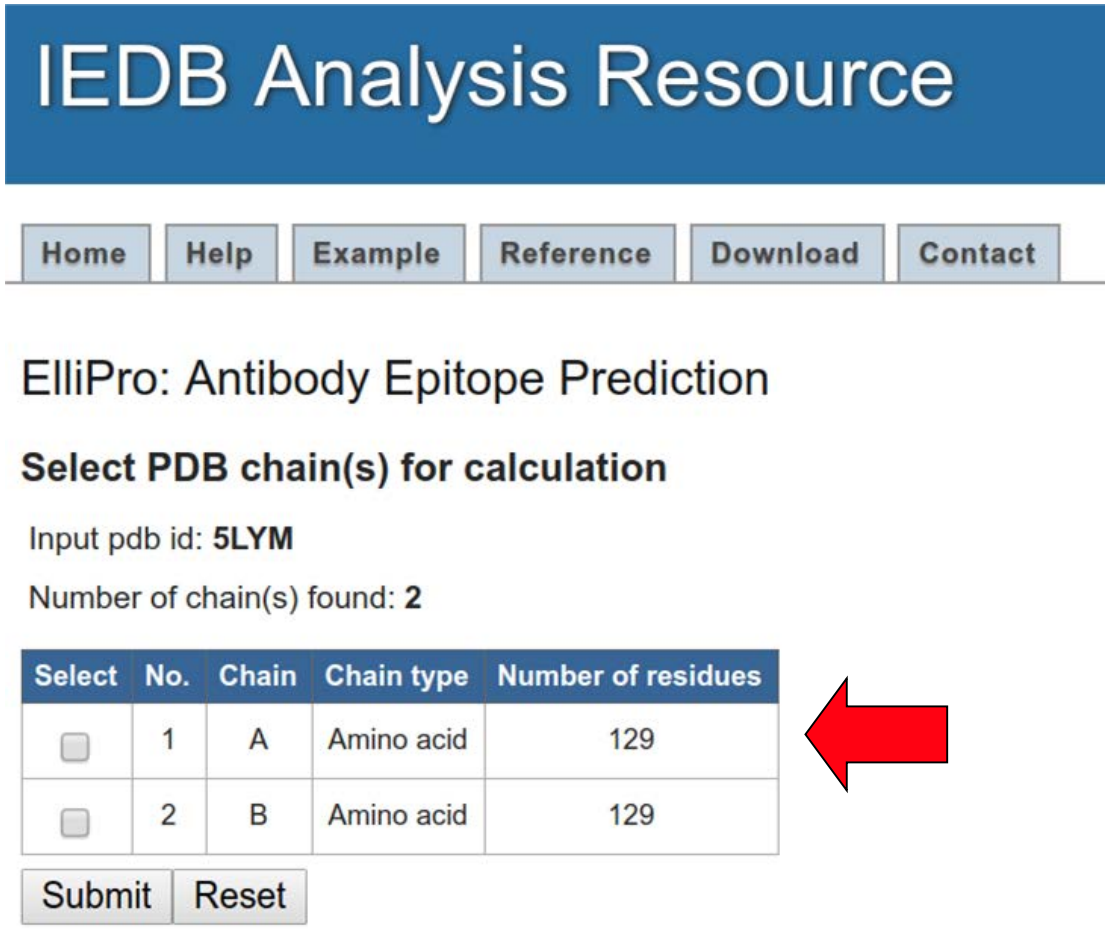


- Implements three algorithms:
  - approximation of the protein shape as an ellipsoid
  - calculation of the residue protrusion index (PI)
  - clustering of neighboring residues based on PI values



Ponomarenko *et al*, BMC Bioinformatics 2008.
Thornton *et al*, EMBO J. 1986.

ElliPro Input



ElliPro Output

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Input Sequences: 5LYM

Chain: **A**

```
  1 KVFGRCELAA AMKRHGLDNY RGYSLGNWVC AAKFESNFNT QATNRNTDGS TDYGILQINS
 61 RWWCNDGRTP GSRNLCNIPC SALLSSDITA SVNCAKKIVS DGNGMNAWVA WRNRCKGTDV
121 QAWIRGCRL
```

Predicted Linear Epitope(s):

No.	Chain	Start	End	Peptide	Number of residues	Score	3D structure
1	A	45	50	RNTDGS	6	0.78	View
2	A	112	129	RNRCKGTDVQAWIRGCRL	18	0.771	View
3	A	100	103	SDGN	4	0.76	View
4	A	64	81	CNDGRTPGSRNLCNIPCS	18	0.666	View
5	A	1	7	KVFGRCE	7	0.597	View
6	A	13	23	KRHGLDNYRGY	11	0.574	View
7	A	85	88	SSDI	4	0.504	View

Click to view 3D structure in JSMol

Predicted Discontinuous Epitope(s):

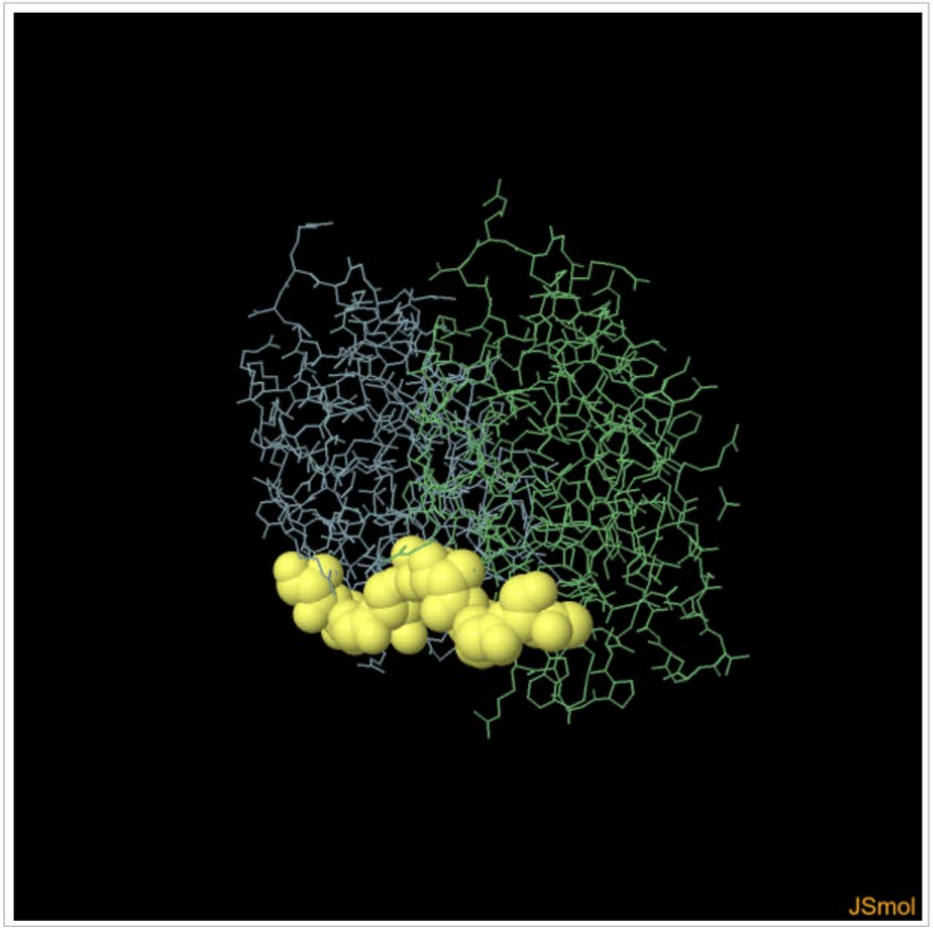
No.	Residues	Number of residues	Score	3D structure
1	A:S100, A:D101, A:G102, A:N103, A:N106	5	0.727	View
2	A:K1, A:V2, A:F3, A:G4, A:R5, A:C6, A:E7, A:F38, A:N39, A:T40, A:Q41, A:A42, A:S85, A:S86, A:D87, A:I88, A:R112, A:N113, A:R114, A:C115, A:K116, A:G117, A:T118, A:D119, A:Q121, A:A122, A:I124, A:R125, A:G126, A:C127, A:R128, A:L129	32	0.657	View
3	A:R45, A:N46, A:T47, A:D48, A:G49, A:S50, A:N59, A:S60, A:R61, A:W62, A:W63, A:C64, A:N65, A:D66, A:G67, A:R68, A:T69, A:P70, A:G71, A:S72, A:R73, A:N74, A:L75, A:C76, A:N77, A:I78, A:P79, A:S81	28	0.648	View

ElliPro Output

ElliPro: Epitope 3D Structures for 5LYM

No.	Residues	Number of residues	Score
1	A:S100, A:D101, A:G102, A:N103, A:N106	5	0.727

JSmol-Rendered PDB Structure



ElliPro Output

Predicted Linear Epitope(s):

No.	Chain	Start	End	Peptide	Number of residues	Score	3D structure
1	A	45	50	RNTDGS	6	0.78	View
2	A	112	129	RNRCKGTDVQAWIRGCRL	18	0.771	View
3	A	100	103	SDGN	4	0.76	View
4	A	64	81	CNDGRTPGSRNLCNIPCS	18	0.666	View
5	A	1	7	KVFGRCE	7	0.597	View
6	A	13	23	KRHGLDNYRGY	11	0.574	View
7	A	85	88	SSDI	4	0.504	View

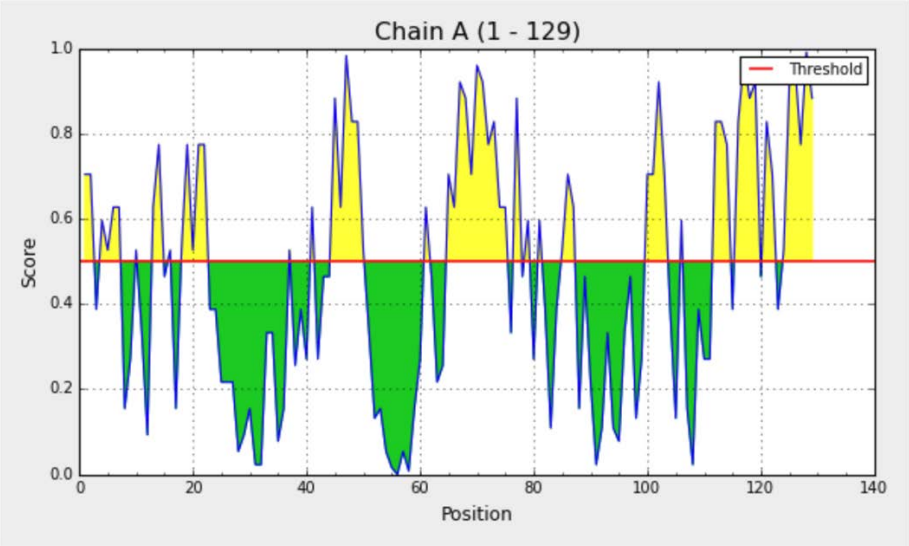
Predicted Discontinuous Epitope(s):

No.	Residues	Number of residues	Score	3D structure
1	A:S100, A:D101, A:G102, A:N103, A:N106	5	0.727	View
2	A:K1, A:V2, A:F3, A:G4, A:R5, A:C6, A:E7, A:F38, A:N39, A:T40, A:Q41, A:A42, A:S85, A:S86, A:D87, A:I88, A:R112, A:N113, A:R114, A:C115, A:K116, A:G117, A:T118, A:D119, A:Q121, A:A122, A:I124, A:R125, A:G126, A:C127, A:R128, A:L129	32	0.657	View
3	A:R45, A:N46, A:T47, A:D48, A:G49, A:S50, A:N59, A:S60, A:R61, A:W62, A:W63, A:C64, A:N65, A:D66, A:G67, A:R68, A:T69, A:P70, A:G71, A:S72, A:R73, A:N74, A:L75, A:C76, A:N77, A:I78, A:P79, A:S81	28	0.648	View
4	A:A10, A:K13, A:R14, A:G16, A:L17, A:D18, A:N19, A:Y20, A:R21, A:G22, A:Y23, A:S24	12	0.564	View

Click here to view residue scores

ElliPro Output

ElliPro: 2D Score Chart(s) for 5LYM



Data table

No.	Chain	Residue number	Residue name	Score
1	A	1	LYS	0.705
2	A	2	VAL	0.705
3	A	3	PHE	0.388
4	A	4	GLY	0.597
5	A	5	ARG	0.527
6	A	6	CYS	0.628
7	A	7	GLU	0.628
8	A	8	LEU	0.155
9	A	9	ALA	0.271

Exercise

- Use BepiPred and DiscoTope to predict B cell epitopes of dengue 2 virus envelope glycoprotein.
- Download crystal structure and sequence of dengue 2 virus envelope glycoprotein from PDB (PDB ID: 4UTC).

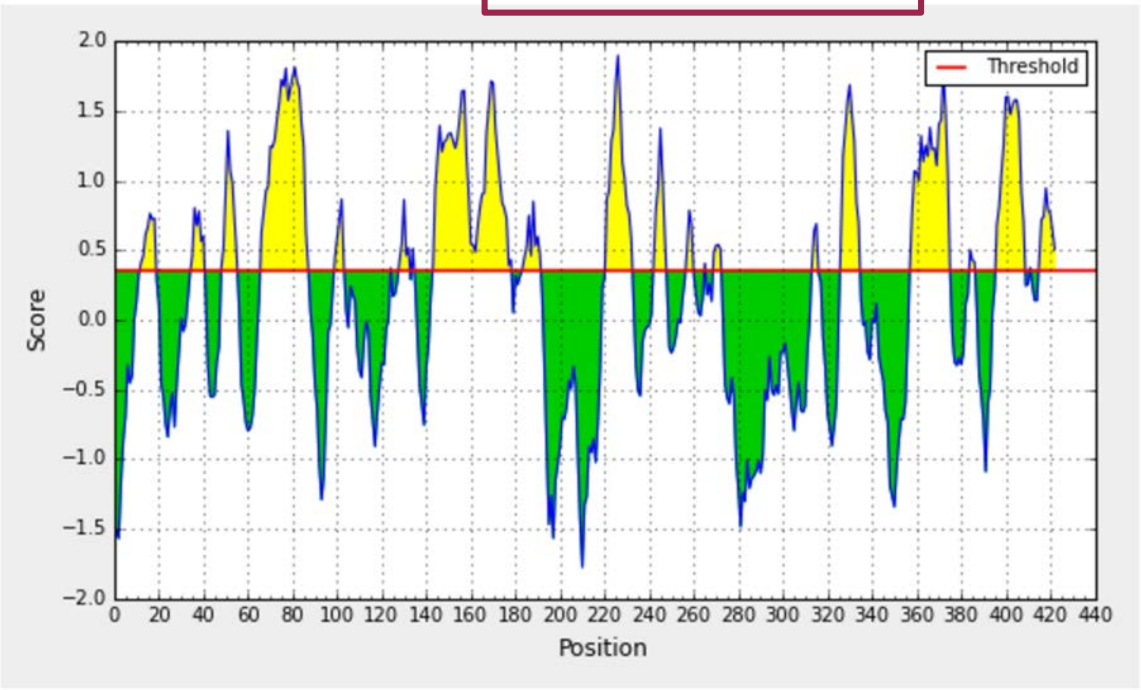
Exercise

Bepipred Linear Epitope Prediction Results

Input Sequences

```
  1 MRCIGISNRD FVEGVSGGSW VDIVLEHGSC VTTMAKNKPT LDFELIKTEA KQPATLRKYC
 61 IEAKLTNTTT ESRCPTQGEP SLNEEQDK RFICKHSMVD RGWGNGCGLF GKGGIVTCAK
121 FTCKKNMEGK IVQPENLEYT IVITPHSGEE HAVGNDTGKH GK EIKITP QSSTTEAELT
181 GYGTVTMECS PRTGLDFNEM VLLQMEDKAW LVHRQWFLDL PLPWLPGADT QGSNWIQKET
241 LVTF KNPH AKKQDVVVLG SQEGAMHTAL TGATEIQMSS GNLLFTGHLK CRLRMDKLQL
301 KGMSYSMCTG KFKIVKEIAE TQHGTI VI RVQYEGDGSP CKIPFEITDL EKRHVLGRLI
361 TVNPIVTEKD SPVNIEAEPP FGDSYIIVGV EPGQLKLNWL RPLESRGP FEGKPIPNPL
421 LGLDSTRTGH HH
```

Center position: 4 **Window size:** 7 **Threshold:** 0.35 Recalculate



Average: 0.188 **Minimum:** -1.776 **Maximum:** 1.900

Too many epitope candidates?

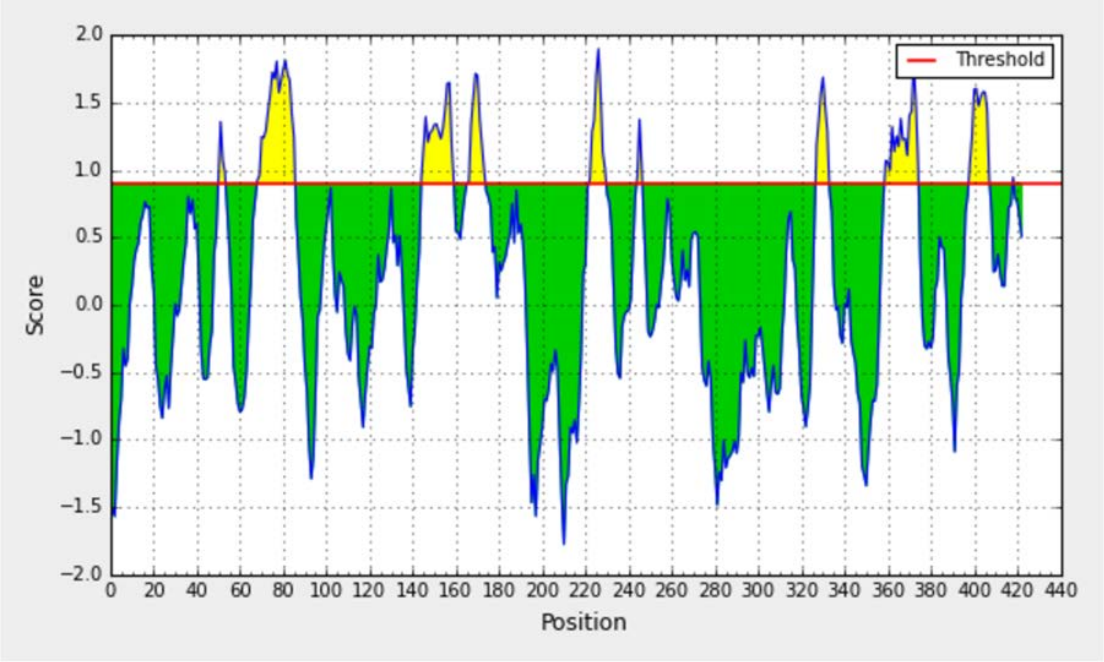
Exercise

Bepipred Linear Epitope Prediction Results

Input Sequences

```
  1 MRCIGISNRD FVEGVSGGSW VDIVLEHGSC VTTMAKNKPT LDFELIKTEA KQPATLRKYC
 61 IEAKLTNTTT ESRCPTQGEP SLNEEQDK RFICKHSMVD RGWGNGCGLF GKGGIVTCAK
121 FTCKKNMEGK IVQPENLEYT IVITPHSGEE HAVGNDTGKH GK EIKITP QSSTTEAELT
181 GYGTVTMECS PRTGLDFNEM VLLQMEDKAW LVHRQWFLDL PLPWLPGADT QGSNWIQKET
241 LVTF KNPH AKKQDVVVLG SQEGAMHTAL TGATEIQMSS GNLLFTGHLK CRLRMDKLQL
301 KGMSYSMCTG KFKIVKEIAE TQHGTI VI RVQYEGDGSP CKIPFEITDL EKRHVLGRLI
361 TVNPIVTEKD SPVNIEAEPP FGDSYIIVGV EPGQLKLNWL RPLESRGP FEGKPIPNPL
421 LGLDSTRTGH HH
```

Center position: 4 **Window size:** 7 **Threshold:** 0.9 Recalculate



Average: 0.188 **Minimum:** -1.776 **Maximum:** 1.900

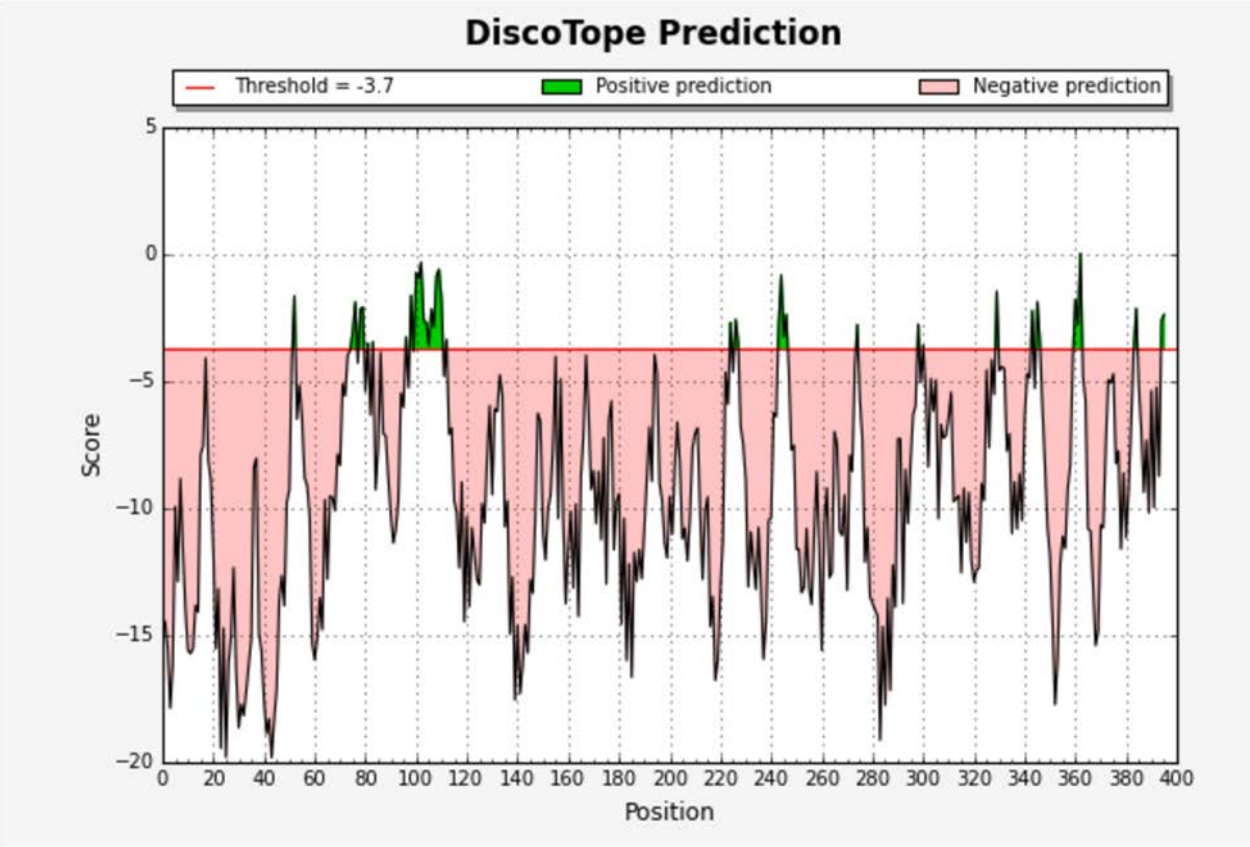
Score threshold of 0.9 corresponds to 90% specificity

Exercise

DiscoTope: Structure based antibody prediction.

DiscoTope 2.0 prediction for structure: 4utc & Chain ID: A

Threshold: -3.7 | Change | Table View | 3D View | Save Prediction



Did you notice the length difference between **BepiPred** (length **422**) and **DiscoTope** (length **391**) outputs?

Exercise

- There might be missing residues in PDB coordinate file compared to the sequence file provided by PDB.
- These missing residues are not resolved properly in the structure.
  - e.g. flexible loops

Exercise

```
4UTC_A_BepiPred     1 MRCIGISNRDFVEGVSGGSWVDIVLEHGSCVTTMAKNKPTLDFELIKTEA   50
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope    1 MRCIGISNRDFVEGVSGGSWVDIVLEHGSCVTTMAKNKPTLDFELIKTEA   50

4UTC_A_BepiPred    51 KQPATLRKYCIEAKLTNTTTESRCPTQGEPSLNEEQDKRFICKHSMVDRG  100
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope   51 KQPATLRKYCIEAKLTNTTTESRCPTQGEPSLNEEQDKRFICKHSMVDRG  100

4UTC_A_BepiPred   101 WGNGCGLFGKGGIVTCAKFTCKKNMEGKIVQPENLEYTIVITPHSGEEHA  150
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope  101 WGNGCGLFGKGGIVTCAKFTCKKNMEGKIVQPENLEYTIVITPHSGEEHA  150

4UTC_A_BepiPred   151 VGNDTGKHGKEIKITPQSSTTEAELTGYGTVTMECSPRTGLDFNEMVLLQ  200
                      ||||||||||||||||||||||||||||||||||||||||  |||||||||
4UTC_A_DiscoTope  151 VGNDTGKHGKEIKITPQSSTTEAELTGYGTVTMECSPRT--DFNEMVLLQ  198

4UTC_A_BepiPred   201 MEDKAWLVHRQWFLDLPLPWLPGADTQGSNWIQKETLVTFKNPHAKKQDV  250
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope  199 MEDKAWLVHRQWFLDLPLPWLPGADTQGSNWIQKETLVTFKNPHAKKQDV  248

4UTC_A_BepiPred   251 VVLGSQEGAMHTALTGATEIQMSSGNLLFTGHLKCRLRMDKLQLKGMSYS  300
                      ||||||||||||||||||||||||||||  ||||||||||||||||||||
4UTC_A_DiscoTope  249 VVLGSQEGAMHTALTGATEIQMSSGNLLF--HLKCRLRMDKLQLKGMSYS  296

4UTC_A_BepiPred   301 MCTGKFKIVKEIAETQHGTIVIRVQYEGDGSPCKIPFEITDLEKRHVLGR  350
                      ||||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope  297 MCTGKFKIVKEIAETQHGTIVIRVQYEGDGSPCKIPFEITDLEKRHVLGR  346

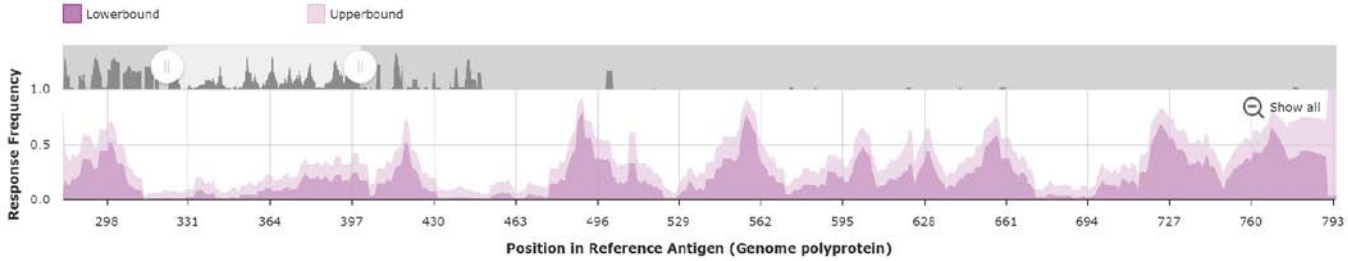
4UTC_A_BepiPred   351 LITVNPIVTEKDSPVNIEAEPPFGDSYIIVGVEPGQLKLNWLRPLESRGP  400
                      ||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope  347 LITVNPIVTEKDSPVNIEAEPPFGDSYIIVGVEPGQLKLNWLRPL-----  391

4UTC_A_BepiPred   401 FEGKPIPNPLLGLDSTRTGHHH    422
```

Predicted

Correctly predicted

Epitope residues from 3D B cell assay 3319631 (PDB ID: 2R69) were mapped on Dengue envelope glycoprotein.

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4UTC_A_BepiPred     1 MRCIGISNRDFVEGVSGGSWVDIVLEHGSCVTTMAKNKPTLDFELIKTEA   50
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4UTC_A_DiscoTope    1 MRCIGISNRDFVEGVSGGSWVDIVLEHGSCVTTMAKNKPTLDFELIKTEA   50

4UTC_A_BepiPred    51 KQPATLRKYCIEAKLTNTTTESRCPTQGEPSLNEEQDKRFICKHSMVDRG  100
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope   51 KQPATLRKYCIEAKLTNTTTESRCPTQGEPSLNEEQDKRFICKHSMVDRG  100

4UTC_A_BepiPred   101 WGNGCGLFGKGGIVTCAKFTCKKNMEGKIVQPENLEYTIVITPHSGEEHA  150
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope  101 WGNGCGLFGKGGIVTCAKFTCKKNMEGKIVQPENLEYTIVITPHSGEEHA  150

4UTC_A_BepiPred   151 VGNDTGKHGKEIKITPQSSTTEAELTGYGTVTMECSPRTGLDFNEMVLLQ  200
                      |||||||||||||||||||||||||||||||||||  |||||||||
4UTC_A_DiscoTope  151 VGNDTGKHGKEIKITPQSSTTEAELTGYGTVTMECSPRT--DFNEMVLLQ  198

4UTC_A_BepiPred   201 MEDKAWLVHRQWFLDLPLPWLPGADTQGSNWIQKETLVTFKNPHAKKQDV  250
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope  199 MEDKAWLVHRQWFLDLPLPWLPGADTQGSNWIQKETLVTFKNPHAKKQDV  248

4UTC_A_BepiPred   251 VVLGSQEGAMHTALTGATEIQMSSGNLLFTGHLKCRLRMDKLQLKGMSYS  300
                      ||||||||||||||||||||||||||  ||||||||||||||||||
4UTC_A_DiscoTope  249 VVLGSQEGAMHTALTGATEIQMSSGNLLF--HLKCRLRMDKLQLKGMSYS  296

4UTC_A_BepiPred   301 MCTGKFKIVKEIAETQHGTIVIRVQYEGDGSPCKIPFEITDLEKRHVLGR  350
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope  297 MCTGKFKIVKEIAETQHGTIVIRVQYEGDGSPCKIPFEITDLEKRHVLGR  346

4UTC_A_BepiPred   351 LITVNPIVTEKDSPVNIEAEPPFGDSYIIVGVEPGQLKLNWLRPLESRGP  400
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
4UTC_A_DiscoTope  347 LITVNPIVTEKDSPVNIEAEPPFGDSYIIVGVEPGQLKLNWLRPL-----  391

4UTC_A_BepiPred   401 FEGKPIPNPLLGLDSTRTGHHH    422

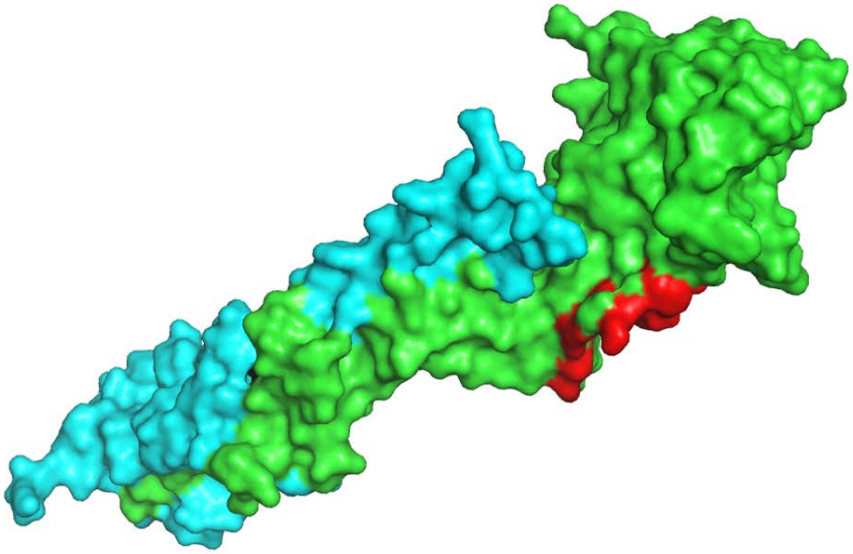
4UTC_A_DiscoTope  392 ----------------------    391
```

Predicted

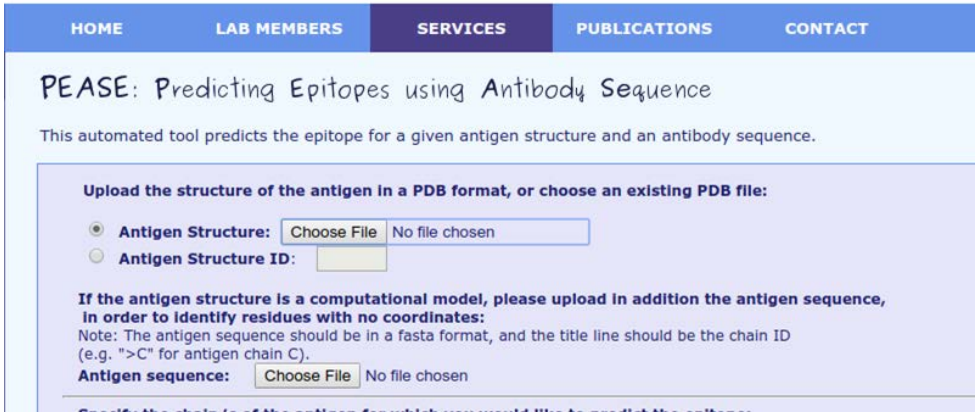
Correctly predicted

Epitope residues from the IEDB in Dengue envelope glycoprotein.

3D Structure-based epitope prediction



http://www.ofranlab.org/PEASE



- **Theoretically, the whole exposed surface of an antigen can be targeted by different antibodies.**

- Therefore, antibody sequence based B cell epitope prediction method called PEASE was developed.
  - Users must provide antigen structure and antibody sequence.

Sela-Culang *et al*, Bioinformatics 2015.

Benchmark on 42 X-ray structures of Ab-protein complexes (Ponomarenko & Bourne, 2008)

Average AUC values

- **0.73 ElliPro** (Ponomarenko et al., 2008)
- **0.65 Epitopia** (Rubinstein et al., 2008)
- **0.63 PEPITO** (Sweredoski & Baldi, 2008)
- **0.60 DiscoTope 1** (Andersen et al, 2006)

- **0.59 DOT** (1st model, bound **Ab-protein docking**)
- **0.58 PatchDock** (1st model, bound **Ab-protein docking**)

Benchmark on 52 X-ray structures of Ab-protein complexes (Kringelum et al., 2012, *PLoS Comp. Biol.*)

Average AUC values

(* means p-value < 0.05 in comparison with DiscoTope 2)

- **0.73 DiscoTope 2** (Kringelum et al., 2012)
- **0.73 PEPITO** (Sweredoski & Baldi, 2008)
- **0.73 Epitopia** (Rubinstein et al., 2008)
- **0.72 SEPPA** (Sun et al., 2009)
- **0.71 DiscoTope 1** (Andersen et al, 2006)
- **0.69* ElliPro** (Ponomarenko et al., 2008)
- **0.65* EPCES** (Liang et al., 2009)
- **0.59* EPSVR** (Liang et al., 2010)

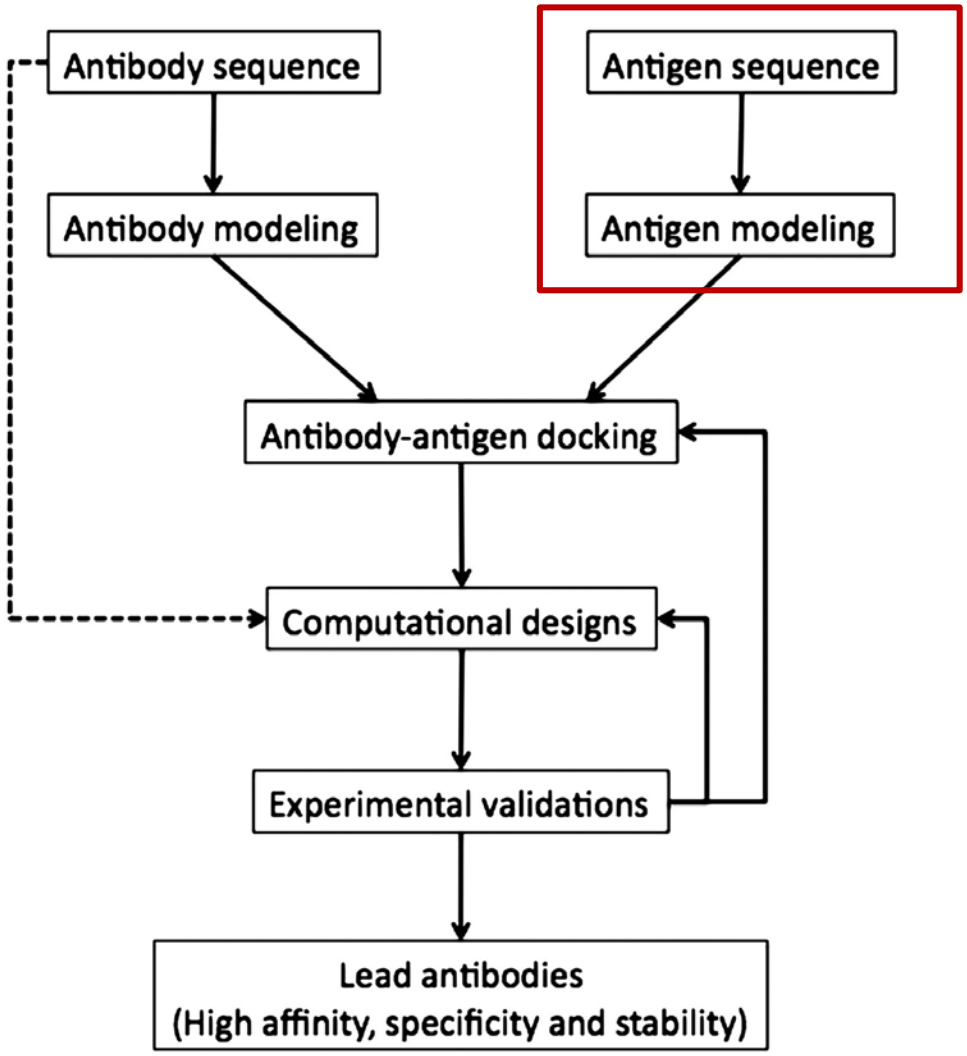
3D Structure-based epitope prediction

- The reason for the relatively poor performance is in the quality of the benchmark datasets.
  - structural information on the entire ‘‘biological unit‘‘ is often not available
  - existence of well characterized epitopes from very few antigens

Outline

- **B cell epitopes**: Discontinuous And linear epitopes
- **Schema** of B cell epitope prediction tools on IEDB
- **Sequence-based epitope prediction methods:**
  - Linear epitope prediction methods
    - Amino acid physicochemical property-based methods
    - Machine learning approaches
- **3D Structure-based epitope prediction methods:**
  - Discontinuous epitope prediction methods
- **Computational antibody design**
  - Antigen and Antibody structure modelling
  - Antibody-protein docking

Computational antibody design



Kuroda D *et al*, PEDS 2012.

What if the 3D structure of a protein of your interest is not available in PDB?

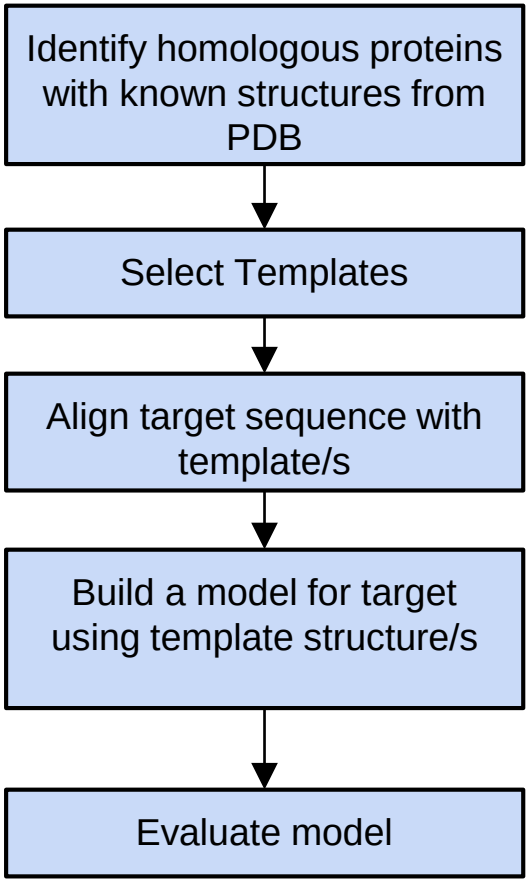
- Protein structures are more conserved than protein sequences
- Homologous proteins have similar structures
- **Homology or comparative modeling:**

  method,

  databases (**PMP**, ModBase) and

  web-servers (**I-TASSER**, ROBETTA, HHPred).

Homology modeling algorithm



Protein Modeling Portal
(www.proteinmodelportal.org)

PSI | The Protein Model Portal

Home | Interactive Modeling | Quality Estimation | Protein Modeling 101 | More | Please enter your query

Welcome to the

Protein Model Portal (PMP)

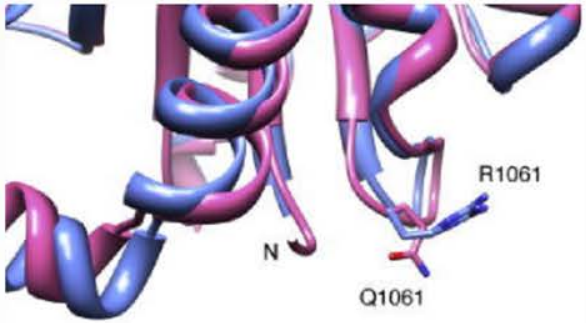
PMP gives access to various models computed by comparative modeling methods provided by different partner sites, and provides access to various interactive services for model building, and quality assessment.

EDWGPCTEHGEHRIRTPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGNTRVSW
PKFAVPNLQSLTNLLSSNLSWLSLDVSAAFYHLPLHPAAMPHLLVGSSGLSRYVARLSS
NSRIINNQHRTMQNLHNSCSRNLYVSLMLLYKTYGRKLHLYSHPIILGFRKIPMGVGLSP
FLLAQFTSAICSVVRRAFPHCLAFSYMDDVVLGAKSVQHLESLYAAVTNFLLSLGIHLNP
HKTKRWGYSLNFMGYVIGGWGTLPQEHIVQKIKMCFRKLPVNRPIDWKVCQRIVGLLG

Search

Examples: [UniProt AC] [UniProt ID] [RefSeq] [PDBID] [Sequence] [Free Text]

Modeling Highlights (Show all)

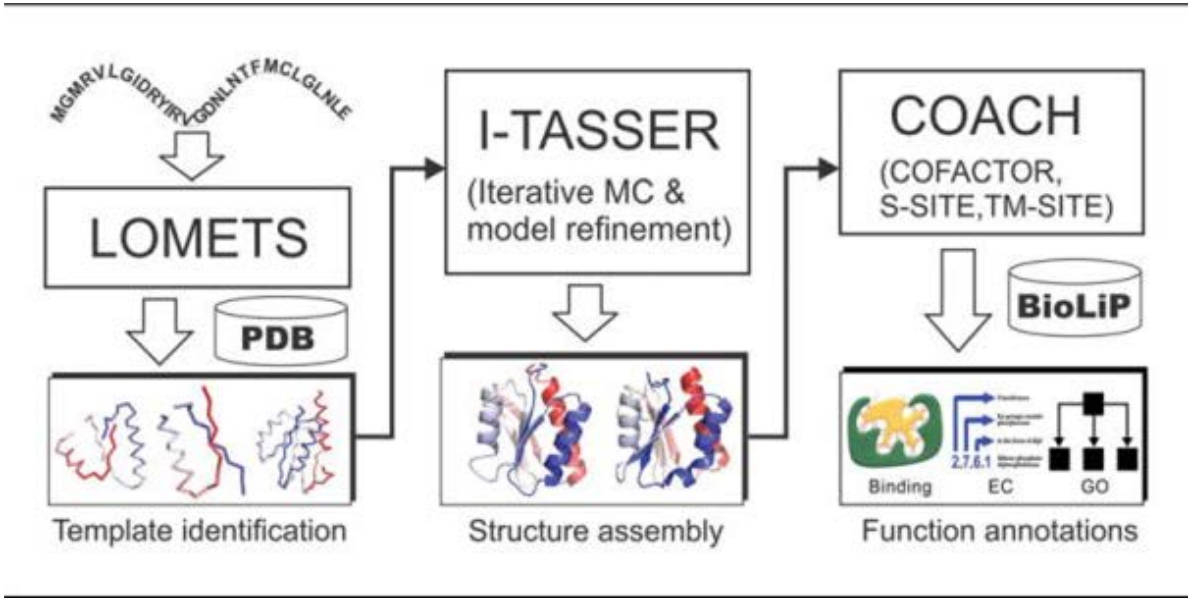


A Structure of a Collagen VI VWA Domain Displays N and C Termini at Opposite Sides of the Protein

Becker AA. *Structure* (2014) 22(2), 199–208

Haas *et al*, Database 2013

I-TASSER



- One of the best server for protein structure prediction in recent community-wide CASP7 to CASP12 experiments.
- Ranked as the best for function prediction in CASP9.
- Relatively simple user interface and parameters to understand.

Homology modeling

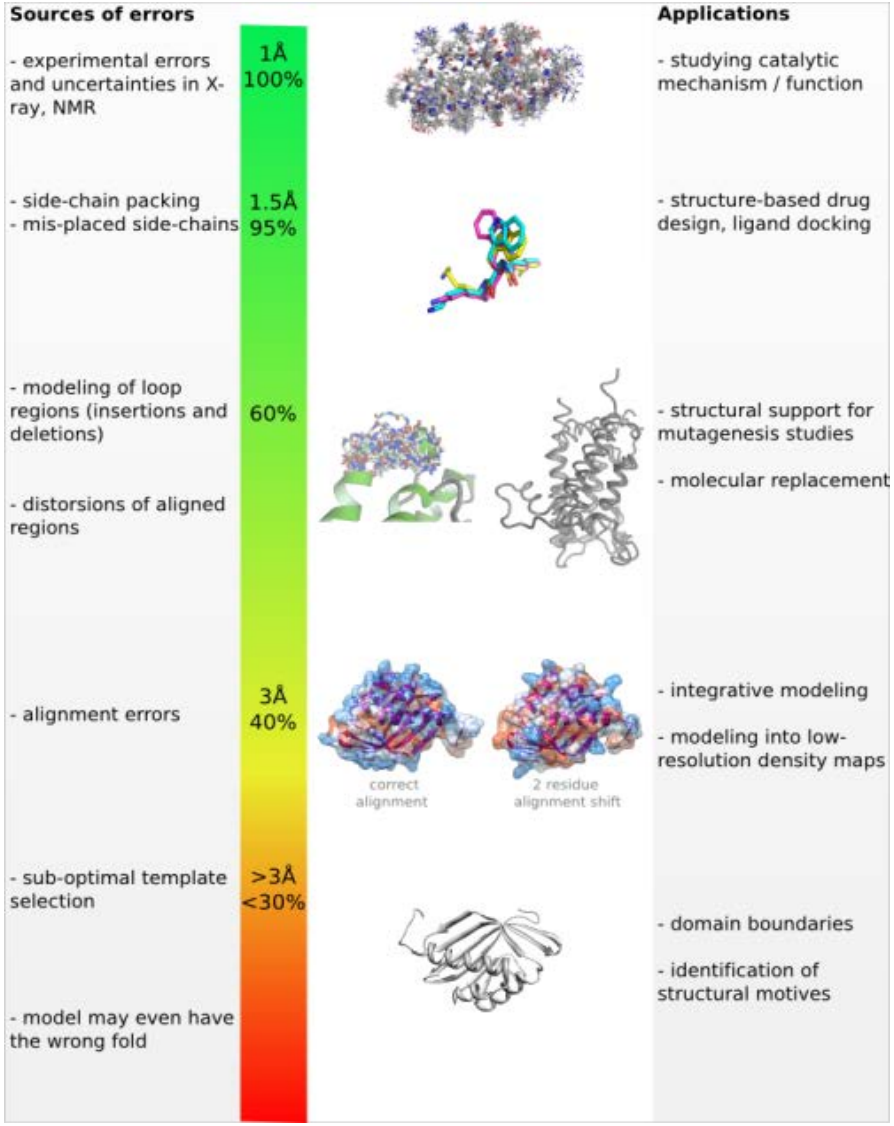
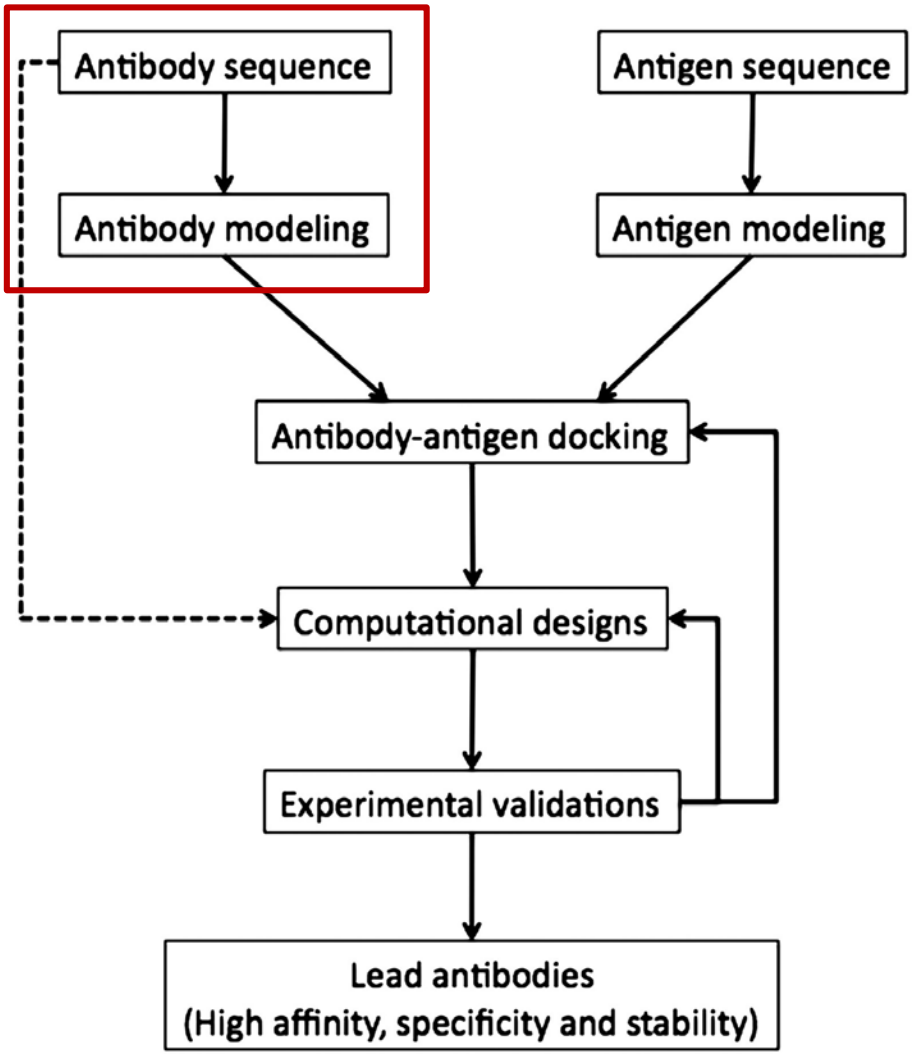


Image from PMP website

- Models can have errors if target to template sequence identity < 30%
- If the antigen model quality is good then it can used for B cell epitope prediction using Discotope and ElliPro.

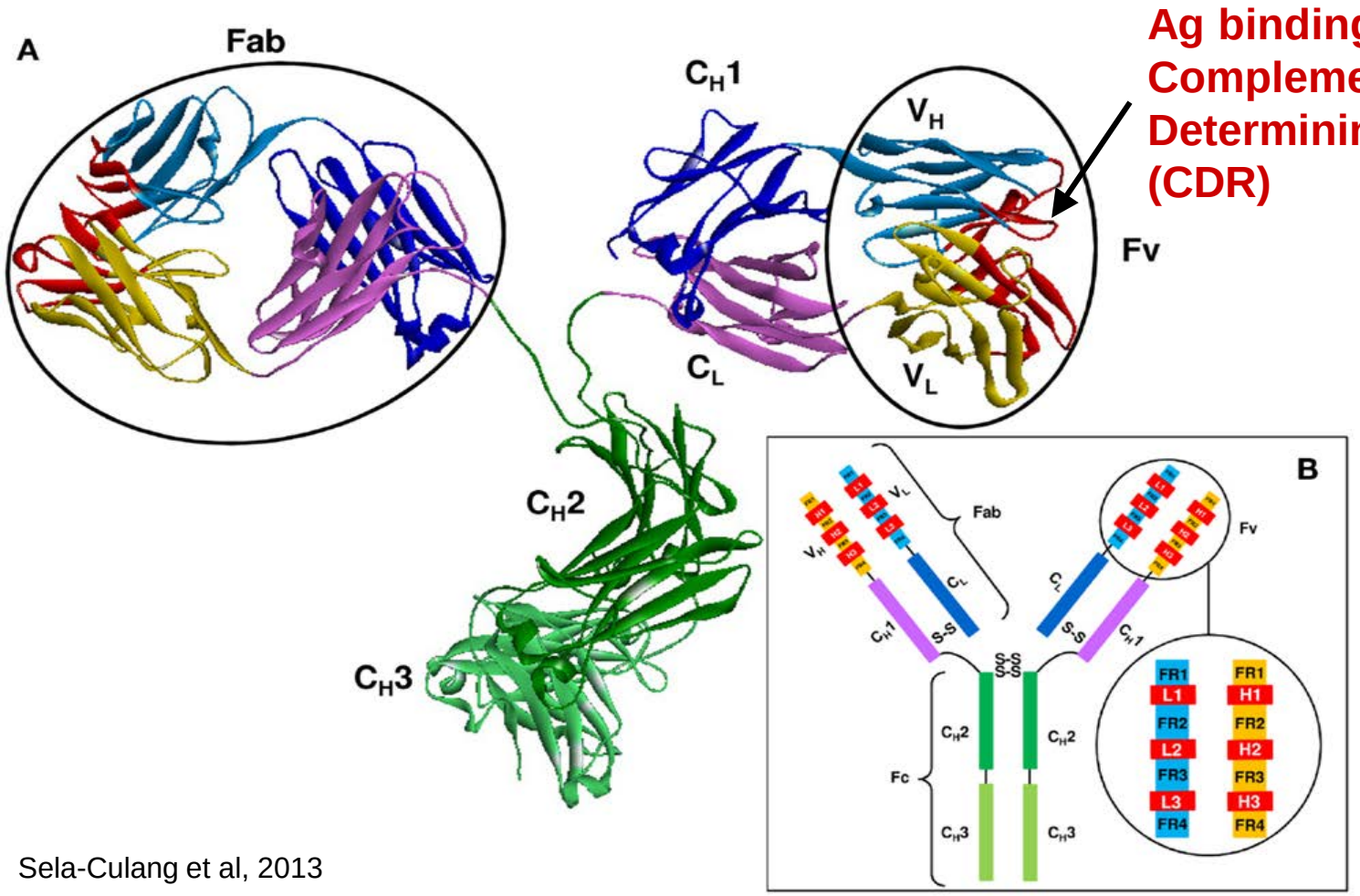
Rost 1999; Martí-Renom *et al*. 2000

Computational antibody design



Kuroda D *et al*, PEDS 2012.

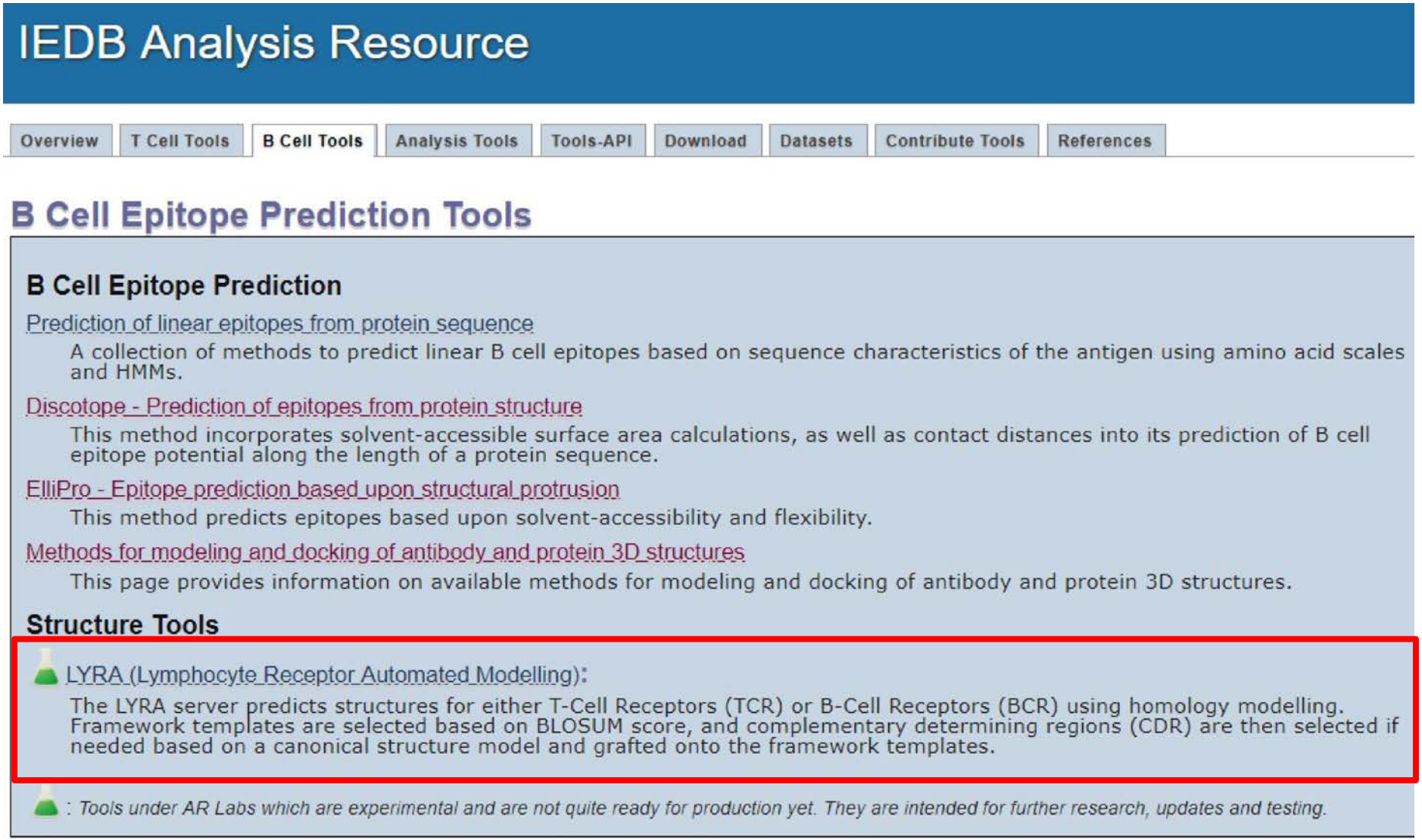
Antibody structure



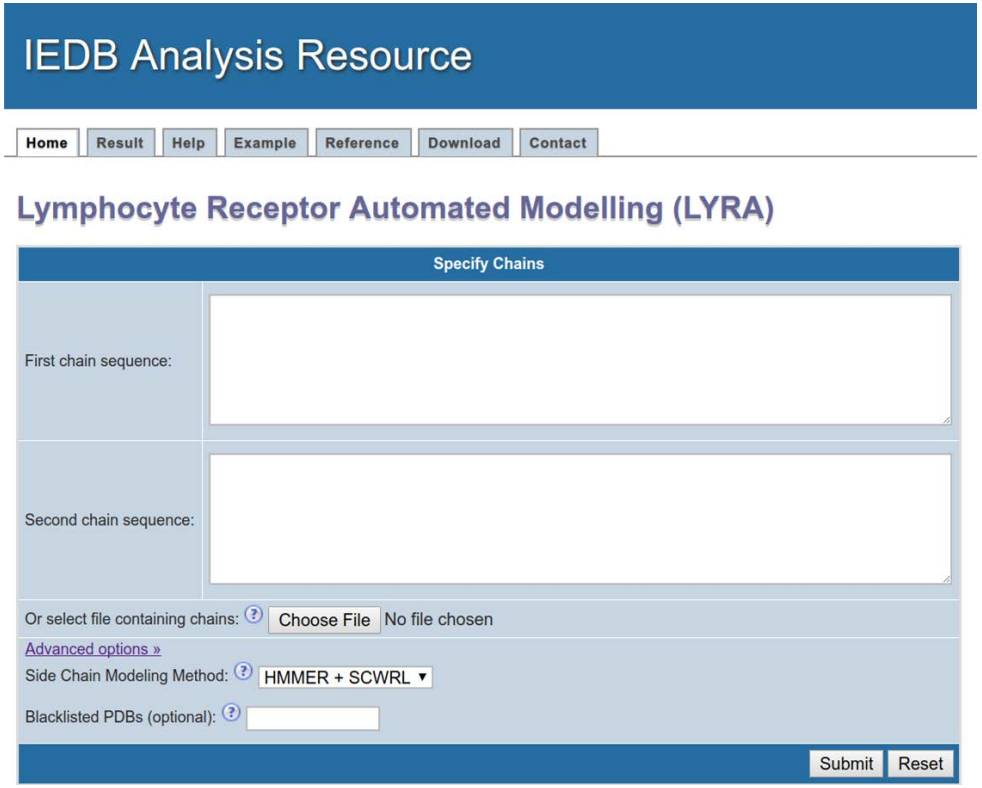
Ag binding region: Complementarity Determining Region (CDR)

Sela-Culang et al, 2013

3D Structure-based epitope prediction



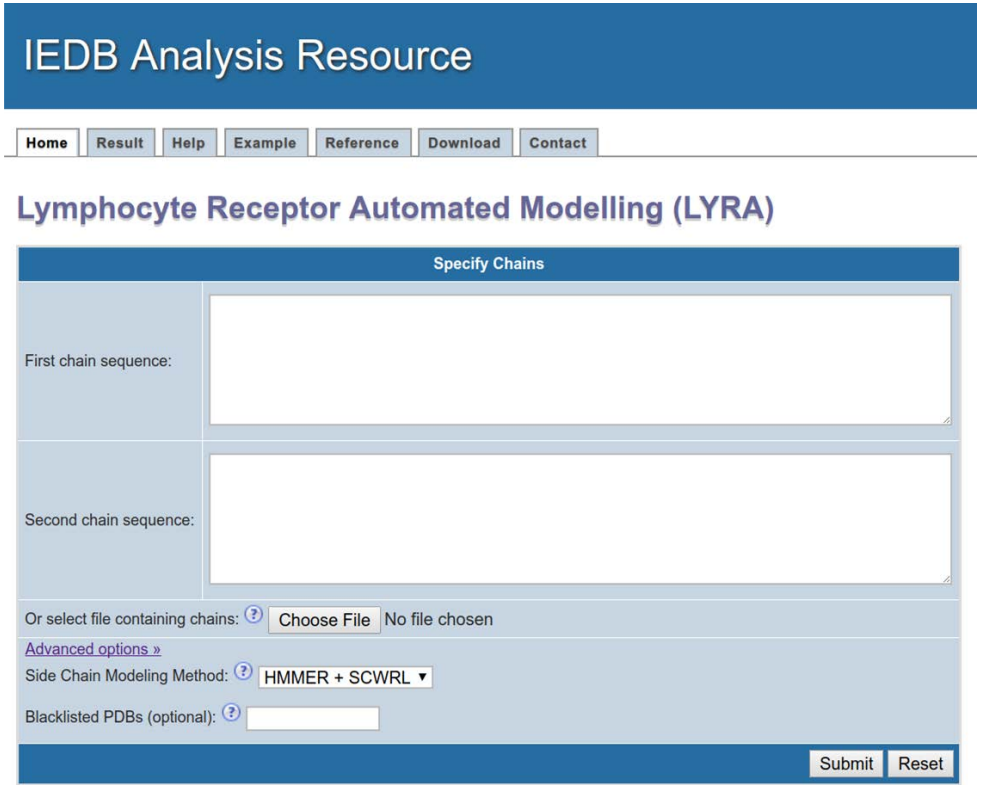
LYRA: Lymphocyte Receptor Automated Modeling



- B- and T-cell receptor structure modeling
- **Canonical structures (CS)**: The hypervariable CDR loops can only assume a limited number of conformations (Chothia & Lesk, JMB 1987).
- Canonical structures can usually be identified by specific sequence features

Klausen MS *et al*, NAR 2015.

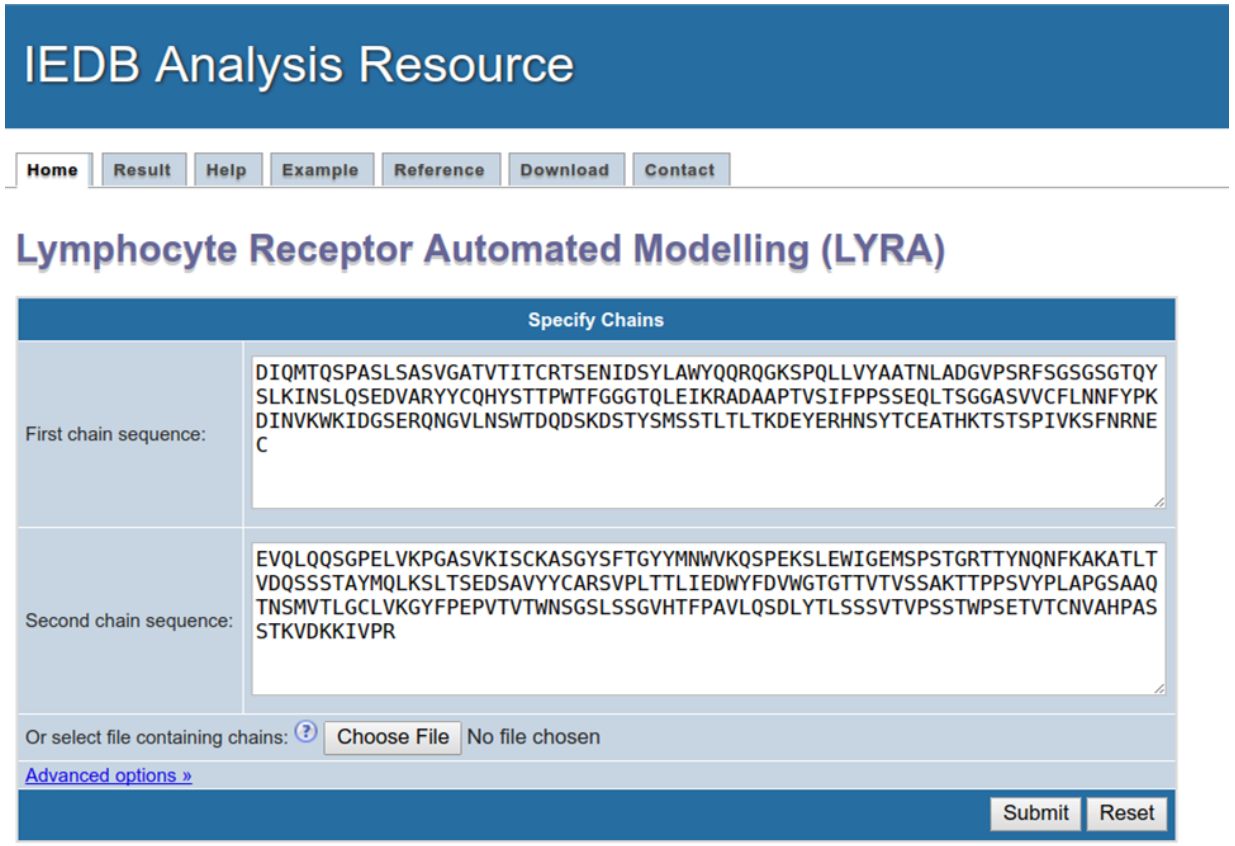
LYRA: Lymphocyte Receptor Automated Modeling



- Templates are identified using BLOSUM62 scores
- Loop modeling: If the canonical structure of target and template loops do not match then the highest scoring identical canonical structure loops from other structures are selected.

Klausen MS *et al*, NAR 2015.

LYRA


IEDB Analysis Resource
Home
Result
Help
Example
Reference
Download
Contact
Lymphocyte Receptor Automated Modelling (LYRA)
Specify Chains
First chain sequence:
DIQMTQSPASLSASVGATVTITCRTSENIDSYLAWYQQRQGKSPQLLVYAATNLADGVPSRFSGSGSGTQY
SLKINSLQSEDVARYYCQHYSTTPWTFGGGTQLEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPK
DINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE
C
Second chain sequence:
EVQLQQSGPELVKPGASVKISCKASGYSFTGYYMNWVKQSPEKSLEWIGEMSPSTGRTTYNQNFKAKATLT
VDQSSSTAYMQLKSLTSEDSAVYYCARSVPLTTLIEDWYFDVWGTGTTVTVSSAKTTPPSVYPLAPGSAAQ
TNSMVTLGCLVKGYFPEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLSSSVTVPSSTWPSETVTCNVAHPAS
STKVDKKIVPR
Or select file containing chains:
Choose File
No file chosen
Advanced options »
Submit
Reset

LYRA

Lyra results

Contents [hide]

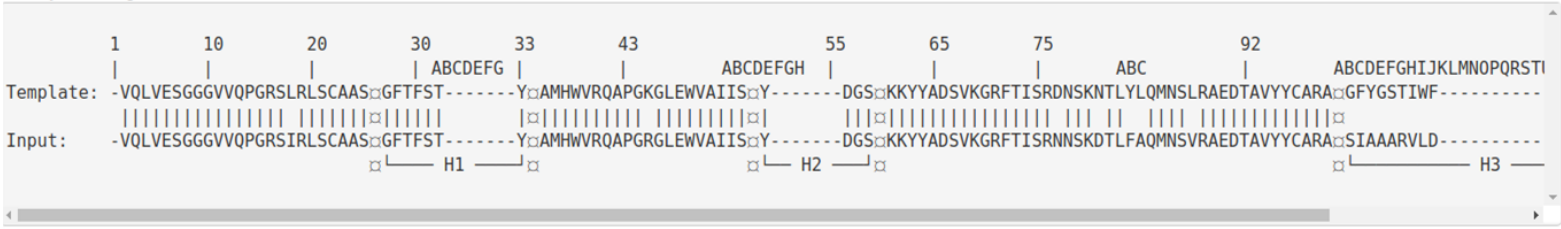
Input Sequences

Name	Sequence
First chain sequence:	DVVMTQTPLSISVTLGQPASISCKSSQSVLDTFAIWVFQRPGQSPRKLIFLISKRDSGVPDRFTGS ASGTDFTLKISRVEVEDVGVYYCWQGTHFPHTVGGGTKLEIA
Second chain sequence:	GVQLVESGGGVVQPGRSIRLSCAASGFTFSTYAMHWVRQAPGRGLEWVAIISYDGSKKYYADS VKGRFTISRNNSKDTLFAQMNSVRAEDTAVYYCARASIAAARVLDDYWGRGTMVTVSS

Summary of modelled BCR

	Heavy chain			Kappa Light chain		
	Template	Template CS	Predicted CS	Template	Template CS	Predicted CS
Framework	1NL0			1NLD		
Loop 1	1NL0	1	1	1QLR	6	6
Loop 2	1NL0	4	4	1NLD	1	1
Loop 3	3I9G	22	22	1NLD	1	1
Packing	1NLD					

Alignment:
Heavy chain alignment:



LYRA

Structure 3D View

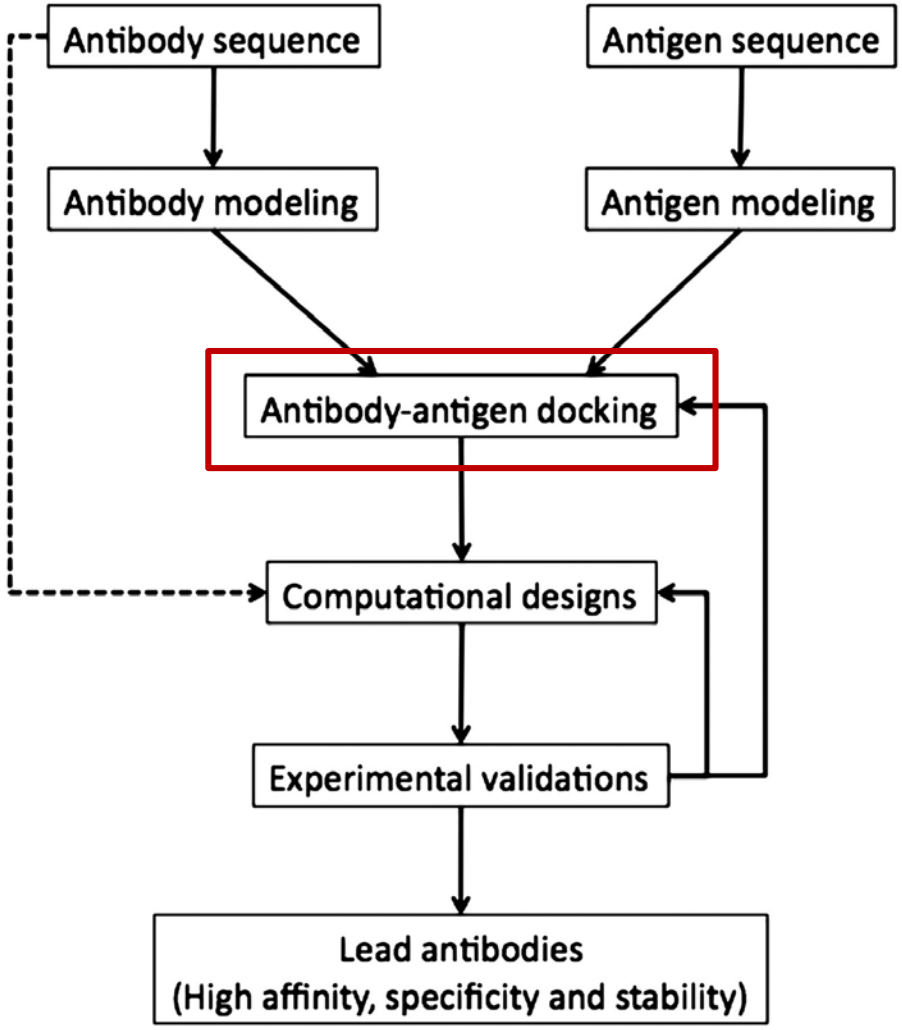
Chains: Heavy chain Kappa Light chain

Loops: H1 H2 H3 K1 K2 K3

Download PDB model file:

Download

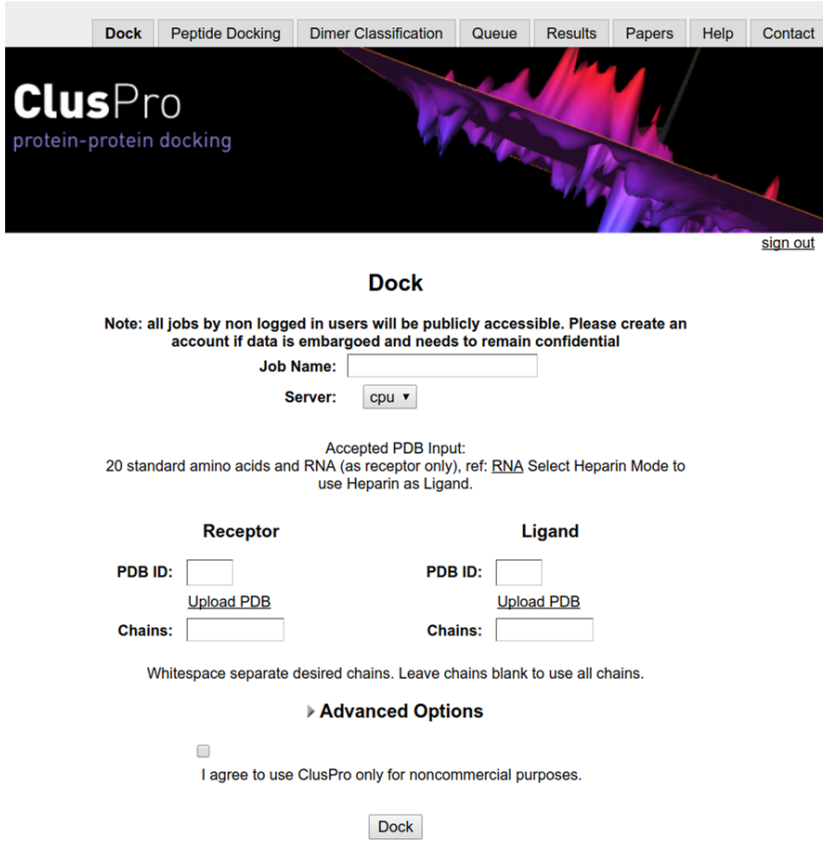
Computational antibody design



Kuroda D *et al*, PEDS 2012.

ClusPro

https://cluspro.bu.edu

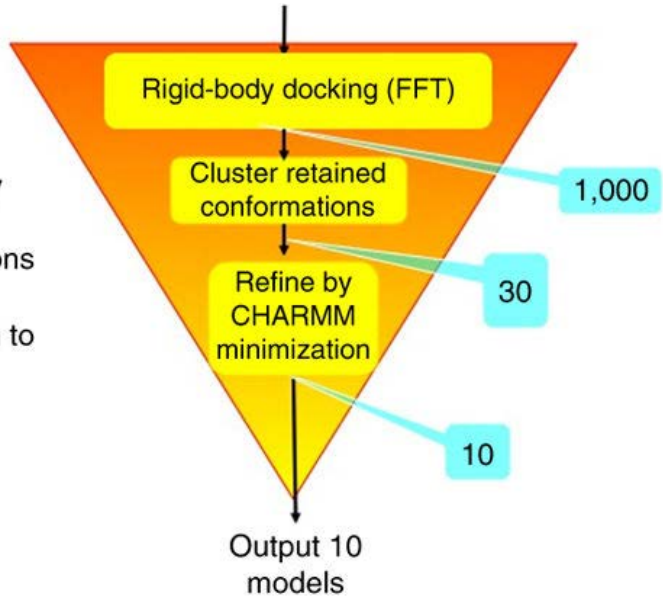


- **Consistently successful in CAPRI experiments (Critical Assessment of Protein Interactions)**

FFT-based global sampling on a grid using PIPER

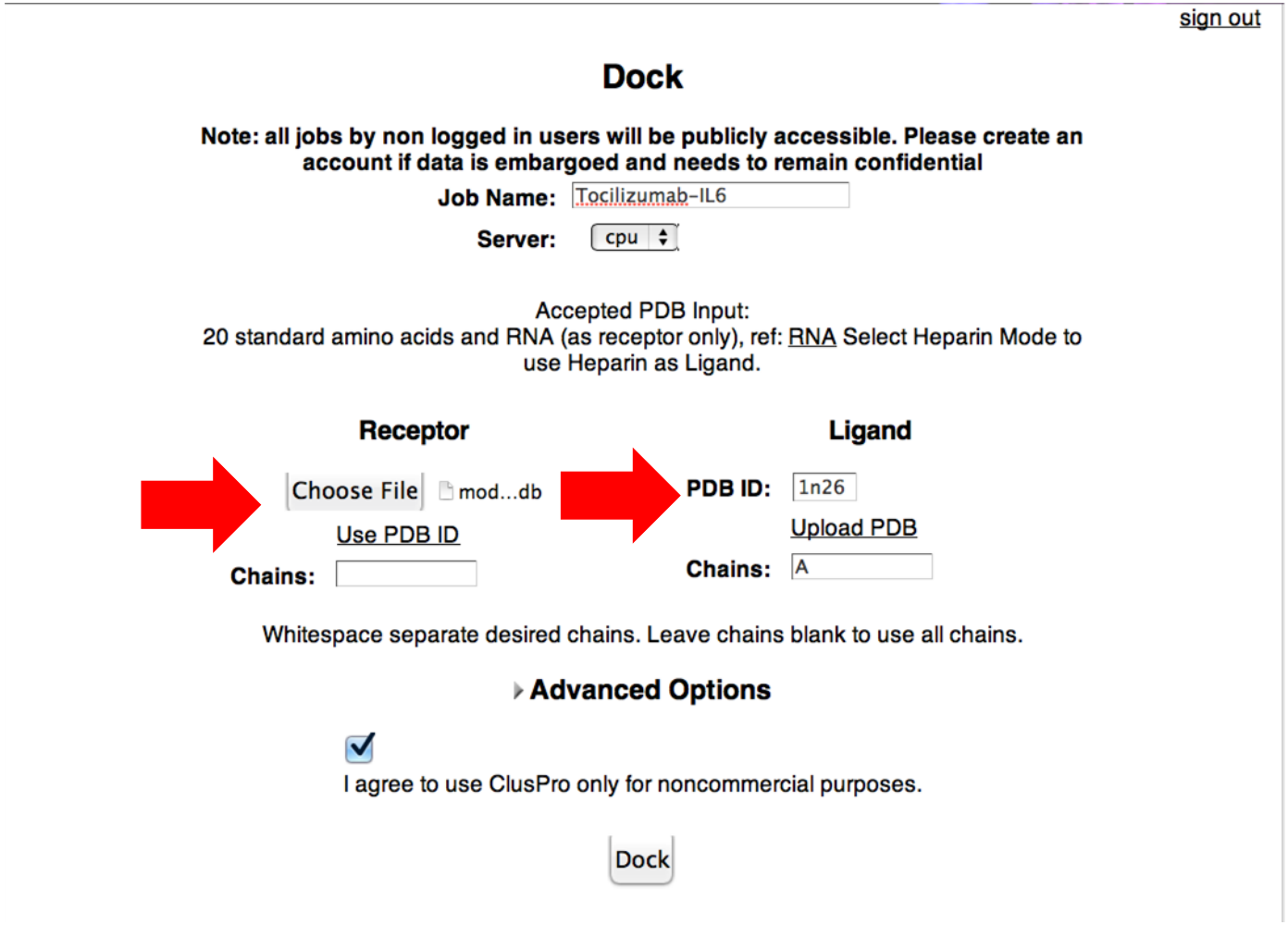
Clustering to find highly populated clusters of low-energy conformations

CHARMM minimization to remove steric clashes

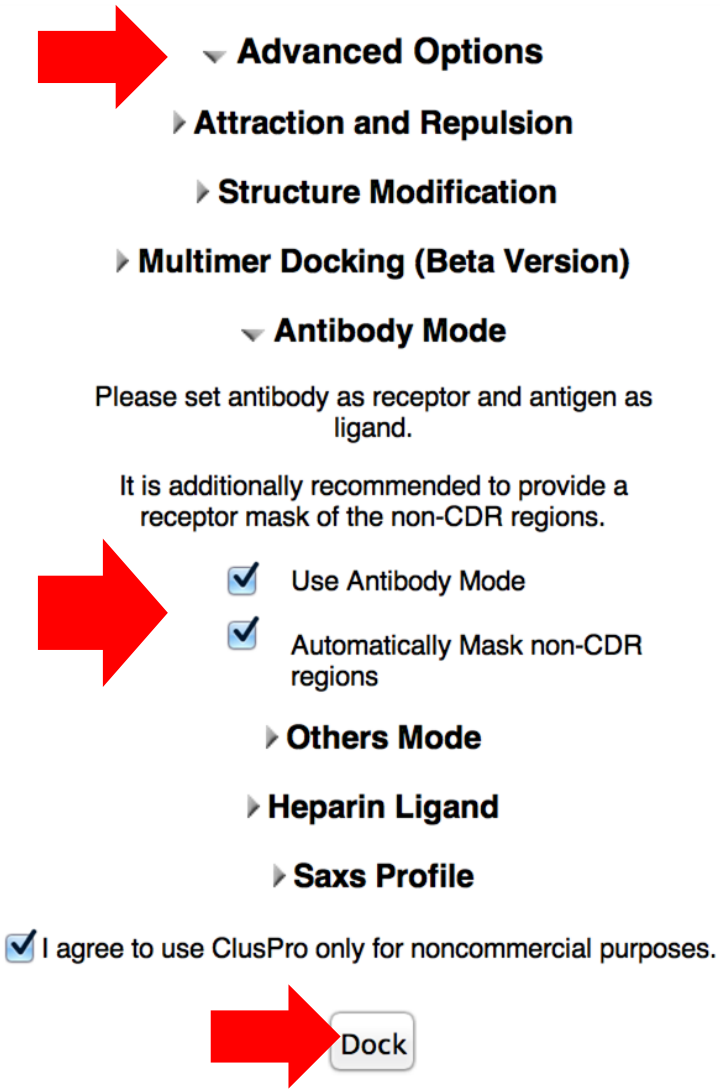


Kozakov et al, Nature Protocols 2017; Brenke *et al*, Bioinformatics 2012.

ClusPro


sign out
Dock
Note: all jobs by non logged in users will be publicly accessible. Please create an account if data is embargoed and needs to remain confidential
Job Name: Tocilizumab-IL6
Server: cpu
Accepted PDB Input:
20 standard amino acids and RNA (as receptor only), ref: RNA Select Heparin Mode to use Heparin as Ligand.
Receptor
Choose File
mod...db
Use PDB ID
Chains:
Ligand
PDB ID: 1n26
Upload PDB
Chains: A
Whitespace separate desired chains. Leave chains blank to use all chains.
Advanced Options
I agree to use ClusPro only for noncommercial purposes.
Dock

ClusPro


Advanced Options
Attraction and Repulsion
Structure Modification
Multimer Docking (Beta Version)
Antibody Mode
Please set antibody as receptor and antigen as ligand.
It is additionally recommended to provide a receptor mask of the non-CDR regions.
Use Antibody Mode
Automatically Mask non-CDR regions
Others Mode
Heparin Ligand
Saxs Profile
I agree to use ClusPro only for noncommercial purposes.
Dock

ClusPro

View Model Scores

Download all Models for all Coefficients

Antibody Mode

Display Models: 10

Download Displayed Models

If you us these models in a paper, please cite our papers

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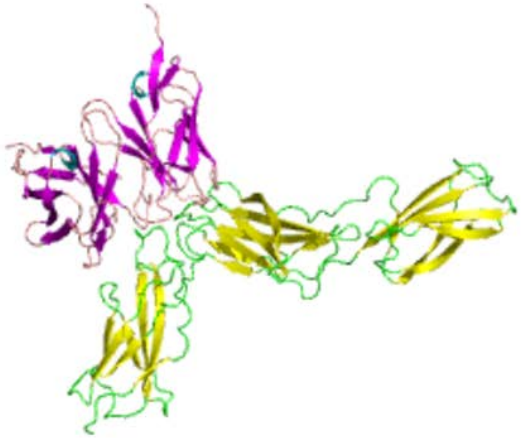
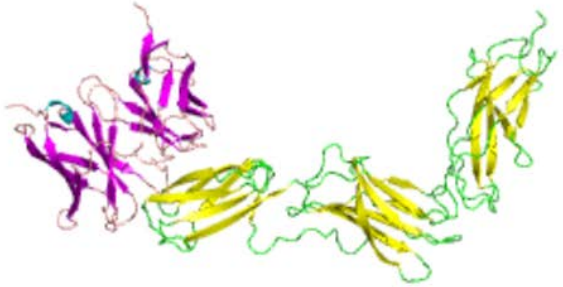


1



ClusPro

View Models

Balanced | Electrostatic-favored | Hydrophobic-favored | VdW+Elec

Download Model Scores for this Coefficient

Coefficient Weights

See *Kozakov et. al.* in Papers for a description of these terms

$$E = 0.40E_{rep} + -0.40E_{att} + 600E_{elec} + 1.00E_{DARS}$$

Cluster Scores

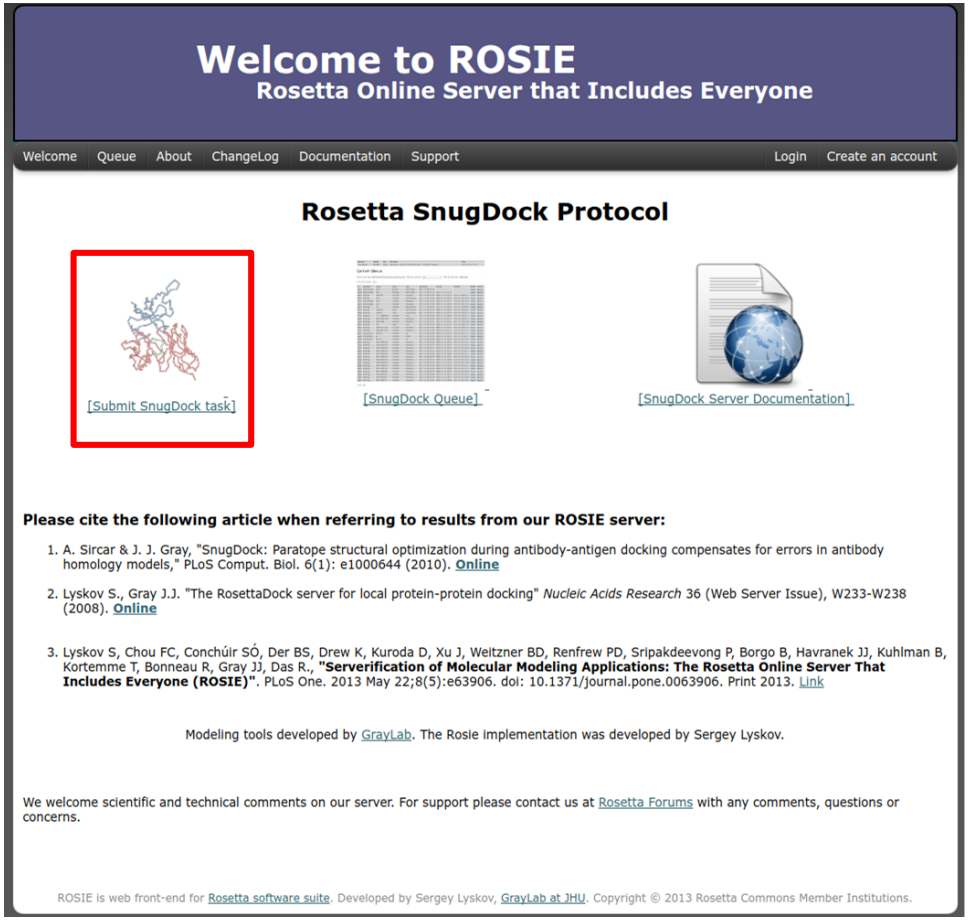
We strongly encourage you to read the FAQ related to these scores before using them.

Cluster	Members	Representative	Weighted Score
0	224	Center	-847.9
		Lowest Energy	-847.9
1	96	Center	-676.8
		Lowest Energy	-820.9
2	91	Center	-690.0
		Lowest Energy	-851.4
3	59	Center	-657.2
		Lowest Energy	-841.4
4	55	Center	-675.3
		Lowest Energy	-786.9
5	51	Center	-841.2
		Lowest Energy	-841.2
6	50	Center	-647.8
		Lowest Energy	-798.3

- Number of cluster members are used to get the best docked models
- Weighted scores should not be used to get the best models.

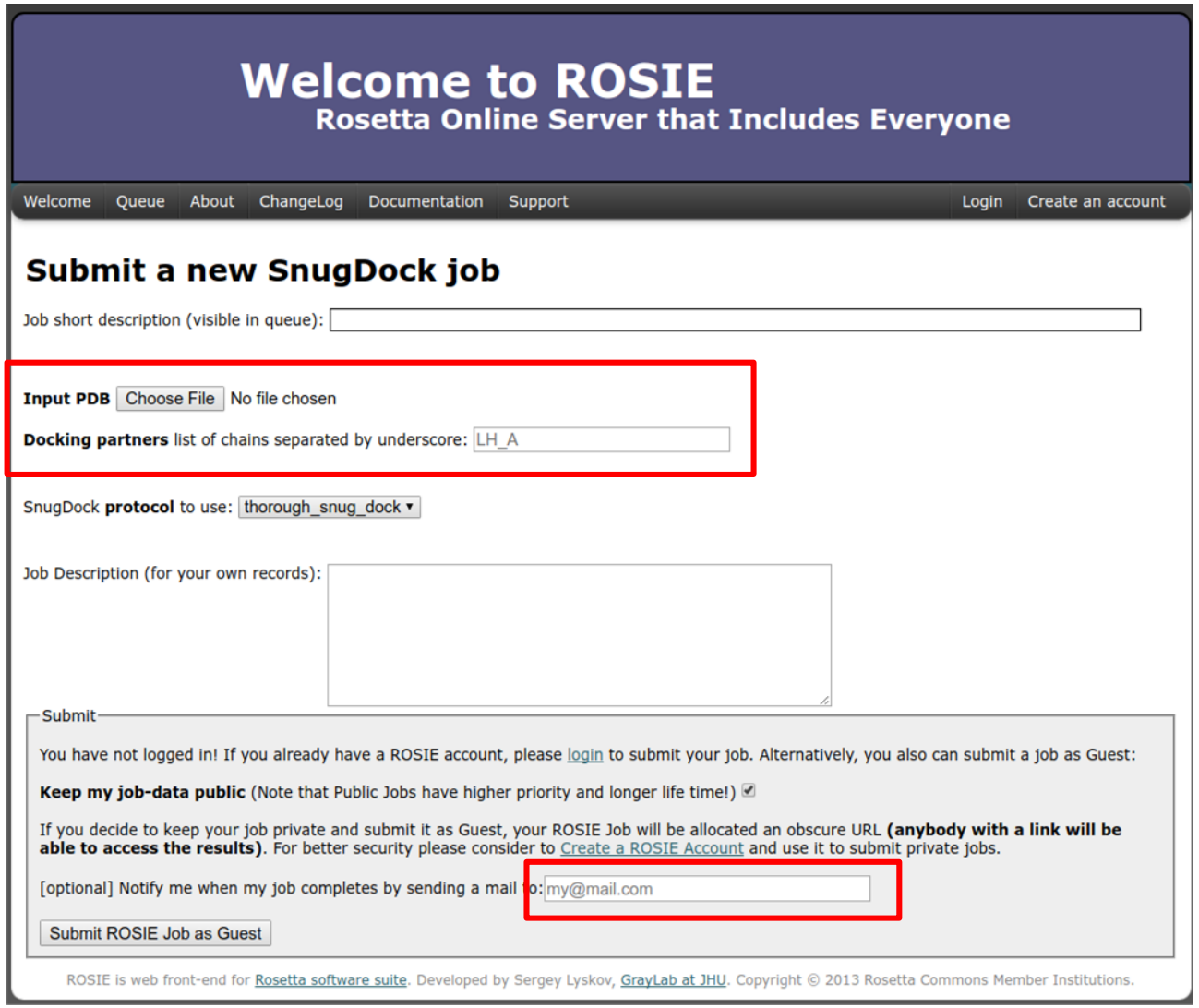
SnugDock

http://rosie.rosettacommons.org/snug_dock



- Uses RosettaDock
- Simultaneously optimizes
  - antibody-antigen position,
  - CDR loops conformation and
  - heavy and light chain relative position
- Drawback: Requires one or more days to complete job
- Assessment: Weitzner *et al*, Nature Protocols 2017.

SnugDock

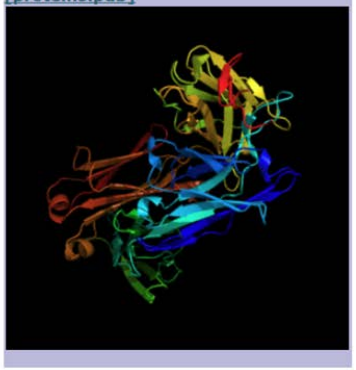

Welcome to ROSIE
Rosetta Online Server that Includes Everyone
Welcome
Queue
About
ChangeLog
Documentation
Support
Login
Create an account
Submit a new SnugDock job
Job short description (visible in queue):
Input PDB
Choose File
No file chosen
Docking partners list of chains separated by underscore:
LH_A
SnugDock protocol to use:
thorough_snug_dock
Job Description (for your own records):
Submit
You have not logged in! If you already have a ROSIE account, please login to submit your job. Alternatively, you also can submit a job as Guest:
Keep my job-data public (Note that Public Jobs have higher priority and longer life time!)
If you decide to keep your job private and submit it as Guest, your ROSIE Job will be allocated an obscure URL (anybody with a link will be able to access the results). For better security please consider to Create a ROSIE Account and use it to submit private jobs.
[optional] Notify me when my job completes by sending a mail to:
my@mail.com
Submit ROSIE Job as Guest
ROSIE is web front-end for Rosetta software suite. Developed by Sergey Lyskov, GrayLab at JHU. Copyright © 2013 Rosetta Commons Member Institutions.

SnugDock

SnugDock Job 2b1aclean 「№35368」 Details

Inputs

[proteins.pdb]



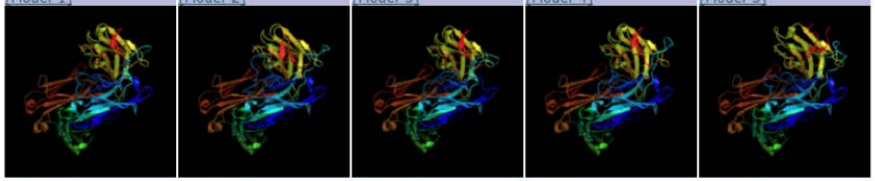
Status

Job ID	35368
Job Name	2b1aclean
Visibility	**PUBLIC**
Protocol	SnugDock
CPU hours used	75.2
user	jessye
Status	**Finished**
Description	
docking_partners	LH_P
protocol	thorough_snug_dock
Submitted time	2017-09-22 07:29
Start time	2017-09-22 08:22
End time	2017-09-22 18:21
Daemon	GrayLab.Jazz

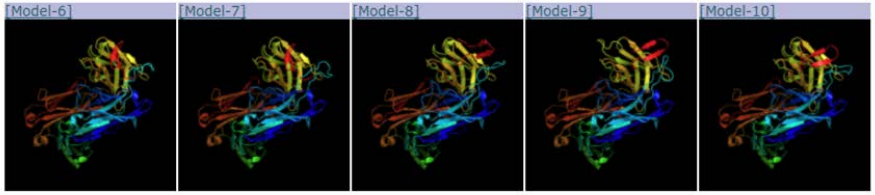
Results

Ten lowest-interface-energy structures created in the docking run:

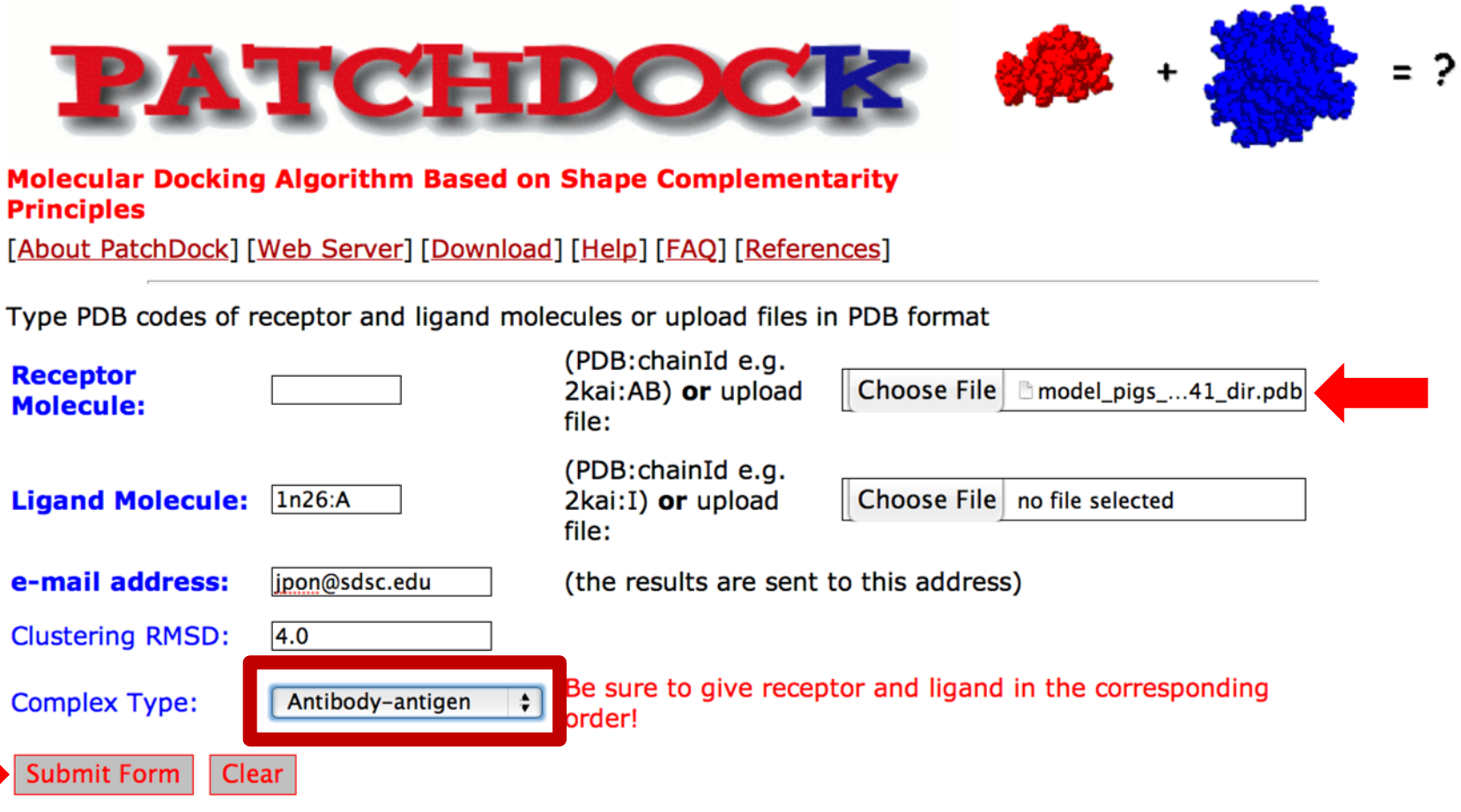
[Model-1] [Model-2] [Model-3] [Model-4] [Model-5]



[Model-6] [Model-7] [Model-8] [Model-9] [Model-10]

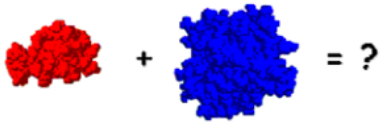


https://bioinfo3d.cs.tau.ac.il/PatchDock/



Schneidman-Duhovny *et al*, NAR 2005.

PATCHDOCK



Molecular Docking Algorithm Based on Shape Complementarity Principles

[About PatchDock] [Web Server] [Download] [Help] [FAQ] [References]

Receptor	Ligand	Complex Type	Clustering RMSD	User e-mail	Receptor Site	Ligand Site	Distance Constraints
model_pigs_de4241_dir.pdb	1n26A	AA	4.0	jpon@sdsc.edu	CDR	-	-

Solution No	Score	Area	ACE	Transformation	PDB file of the complex
1	13410	1900.90	202.79	-1.94 -1.08 2.05 24.73 107.88 63.00	result.1.pdb
2	12948	1731.60	-240.76	1.29 0.87 2.10 -10.48 70.22 38.19	result.2.pdb
3	12770	1655.80	-192.09	0.33 1.24 -2.98 -15.46 65.89 49.76	result.3.pdb
4	11584	1251.70	-26.96	-2.35 0.82 2.55 41.50 17.24 126.21	result.4.pdb
5	11570	1609.00	28.24	2.21 0.04 -1.09 76.26 77.02 40.59	result.5.pdb
6	11348	1407.10	-190.78	-1.57 0.12 -3.13 19.21 88.61 101.82	result.6.pdb
7	11300	1878.80	-225.56	2.48 -1.14 -0.04 49.28 97.02 55.91	result.7.pdb
8	11154	1813.50	-150.37	1.27 0.53 2.01 -10.16 68.70 31.29	result.8.pdb
9	10972	1479.60	47.91	1.17 0.53 2.07 -9.12 72.92 27.93	result.9.pdb
10	10872	1631.70	-316.73	-2.72 0.73 -1.53 27.15 81.70 102.14	result.10.pdb
11	10852	1512.40	-37.31	-1.25 -0.95 2.79 11.50 79.14 115.20	result.11.pdb
12	10848	1336.90	-95.71	-1.41 -0.56 2.68 14.57 79.48 123.92	result.12.pdb
13	10780	1503.70	-119.41	1.15 1.05 2.53 -14.96 65.76 41.33	result.13.pdb
14	10698	1717.60	13.31	3.09 1.53 1.37 -29.84 23.86 101.92	result.14.pdb
15	10696	1584.70	-180.44	0.64 1.01 2.79 -13.04 74.70 40.65	result.15.pdb
16	10680	1377.50	-140.37	-1.02 0.61 -1.48 0.49 60.66 55.36	result.16.pdb
17	10652	1590.40	-200.87	-1.32 1.12 -0.49 -24.09 20.10 109.61	result.17.pdb
18	10646	1502.70	-79.45	0.29 -0.81 -0.18 13.65 40.36 3.49	result.18.pdb
19	10600	1702.10	-319.87	-0.13 1.09 -2.08 -14.18 54.69 49.89	result.19.pdb
20	10484	1641.80	-65.84	-0.19 -0.33 2.38 46.01 63.28 81.06	result.20.pdb

show next 20 »»

NEW: Jmol view

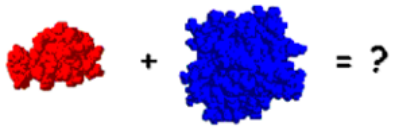
DOWNLOAD best solutions as a ZIP file: 10 (solutions number, from 2 to 100) GO (this takes few seconds, please wait patiently)

DOWNLOAD solutions table transformations file

REFINE best solutions with FireDock: 10 (solutions number, from 1 to 1000) GO

This option is recommended for protein-protein docking only!

PATCHDOCK



Molecular Docking Algorithm Based on Shape Complementarity Principles

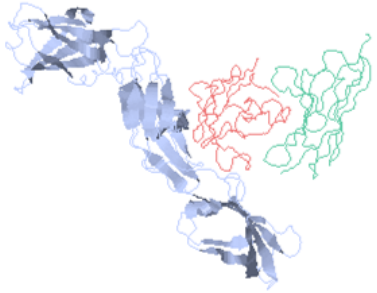
[About PatchDock] [Web Server] [Download] [Help] [FAQ] [References]

Receptor	Ligand	Complex Type	Clustering RMSD	User e-mail	Receptor Site	Ligand Site	Distance Constraints
model_pigs_de4241_dir.pdb	1n26A	AA	4.0	jpon@sdsc.edu	CDR	-	-

Solution No	Score	Area	ACE	PDB file of the complex	show/hide
1	13410	1900.90	202.79	result.1.pdb	☑
2	12948	1731.60	-240.76	result.2.pdb	☐
3	12770	1655.80	-192.09	result.3.pdb	☐
4	11584	1251.70	-26.96	result.4.pdb	☐
5	11570	1609.00	28.24	result.5.pdb	☐
6	11348	1407.10	-190.78	result.6.pdb	☐
7	11300	1878.80	-225.56	result.7.pdb	☐
8	11154	1813.50	-150.37	result.8.pdb	☐
9	10972	1479.60	47.91	result.9.pdb	☐
10	10872	1631.70	-316.73	result.10.pdb	☐
11	10852	1512.40	-37.31	result.11.pdb	☐
12	10848	1336.90	-95.71	result.12.pdb	☐
13	10780	1503.70	-119.41	result.13.pdb	☐
14	10698	1717.60	13.31	result.14.pdb	☐
15	10696	1584.70	-180.44	result.15.pdb	☐
16	10680	1377.50	-140.37	result.16.pdb	☐
17	10652	1590.40	-200.87	result.17.pdb	☐
18	10646	1502.70	-79.45	result.18.pdb	☐
19	10600	1702.10	-319.87	result.19.pdb	☐
20	10484	1641.80	-65.84	result.20.pdb	☐

show next 20 »»

☐ show all/hide all



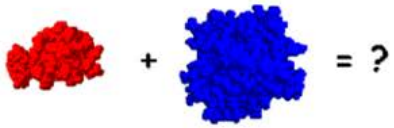
Jmol

DOWNLOAD best solutions as a ZIP file: 10 (solutions number, from 2 to 100) GO (this takes few seconds, please wait patiently)

DOWNLOAD solutions table transformations file

REFINE best solutions with FireDock: 10 (solutions number, from 1 to 1000) GO

PATCHDOCK



Molecular Docking Algorithm Based on Shape Complementarity Principles

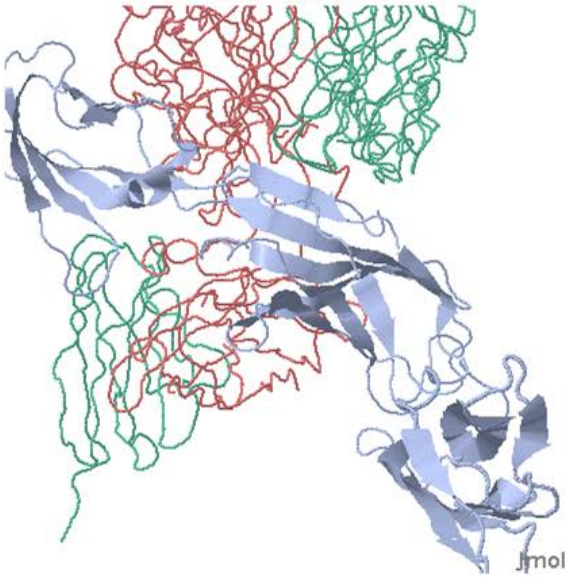
[About PatchDock] [Web Server] [Download] [Help] [FAQ] [References]

Receptor	Ligand	Complex Type	Clustering RMSD	User e-mail	Receptor Site	Ligand Site	Distance Constraints
model_pigs_de4241_dir.pdb	1n26A	AA	4.0	jpon@sdsc.edu	CDR	-	-

Solution No	Score	Area	ACE	PDB file of the complex	show/hide
1	13410	1900.90	202.79	result.1.pdb	✓
2	12948	1731.60	-240.76	result.2.pdb	✓
3	12770	1655.80	-192.09	result.3.pdb	✓
4	11584	1251.70	-26.96	result.4.pdb	
5	11570	1609.00	28.24	result.5.pdb	
6	11348	1407.10	-190.78	result.6.pdb	
7	11300	1878.80	-225.56	result.7.pdb	
8	11154	1813.50	-150.37	result.8.pdb	
9	10972	1479.60	47.91	result.9.pdb	
10	10872	1631.70	-316.73	result.10.pdb	
11	10852	1512.40	-37.31	result.11.pdb	
12	10848	1336.90	-95.71	result.12.pdb	
13	10780	1503.70	-119.41	result.13.pdb	
14	10698	1717.60	13.31	result.14.pdb	
15	10696	1584.70	-180.44	result.15.pdb	
16	10680	1377.50	-140.37	result.16.pdb	
17	10652	1590.40	-200.87	result.17.pdb	
18	10646	1502.70	-79.45	result.18.pdb	
19	10600	1702.10	-319.87	result.19.pdb	
20	10484	1641.80	-65.84	result.20.pdb	

show next 20 »»

show all/hide all

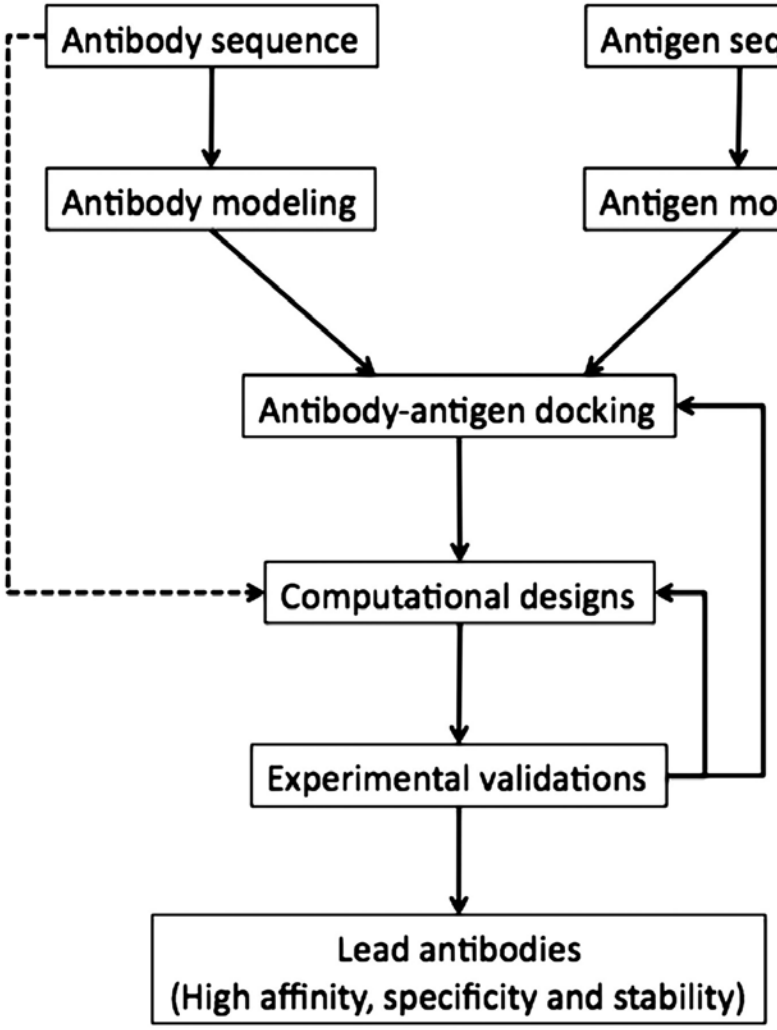


DOWNLOAD best solutions as a ZIP file: 10 (solutions number, from 2 to 100) GO (this takes few seconds, please wait patiently)

DOWNLOAD solutions table transformations file

REFINE best solutions with FireDock: 10 (solutions number, from 1 to 1000) GO

Computational antibody design



LYRA
RosettaAntibody

PDB
PMP
I-TASSER

ClusPro
SnugDock
PocketMatch

Kuroda D *et al*, PEDS 2012.

IMMUNE EPITOPE DATABASE AND ANALYSIS RESOURCE

Thank you!

Questions?