LASSOPROT DATABASE

1. In these two papers Lasso motif is defined and described, and LassoProt database and server is introduced:

   Niemyska, W., Dabrowski-Tumanski, P., Kadlof, M. et al. COMPLEX LASSO: NEW ENTANGLED MOTIFS IN PROTEINS. Sci Rep 6, 36895 (2016).

   Pawel Dabrowski-Tumanski, Wanda Niemyska, Pawel Pasznik, Joanna I. Sulkowska, LASSOPROT: SERVER TO ANALYZE BIOPOLYMERS WITH LASSOS, Nucleic Acids Research, Volume 44, Issue W1, 8 July 2016, Pages W383–W389

   On LassoProt webpage you can find as well its introduction, description of used methods, instructions how to interpret data and how to use server, examples: https://lassoprot.cent.uw.edu.pl/introduction

2. Open the LassoProt.
   Database statistics: over 400.000 deposited chains (all from PDB, also with gaps and non-Xray), around 10.000 chains with complex lassos. The database is updated every week (but we confirm all the structures which takes time, so we are a bit behind, the newest lasso is from one month ago). Lassoprot detects automatically disulfide and other types of linkages based on a header of a PDB file.

3. First lets have a look at **single structure presentation**. We may use "Search by PDB ID" field in the top right corner, and choose e.g. leptine, human obesity protein, PDB code 1AX8.

   [EXAMPLE-1: Database, 1AX8], https://lassoprot.cent.uw.edu.pl/view/1AX8/A/?bridgeType=ssbridge%2Camide%2Cester%2Cthioester%2Cothers

Button "**iHelp**" describes options:
a. **rotate** the structure,
b. **zoom** in and out,
c. buttons "**Surface**" and "**Smooth**" (smoothing as long as lasso type is not changed)
d. button "**Download**" (files that enable visualization of the structure with the surface in VMD and Mathematica -> check the gallery, coordinates of a chain and smoothed chain in XYZ and PDB formats)

Chymotrypsin inhibitor (PDB code 4TLP) in standard, smoothed and smoothed for VMD version.
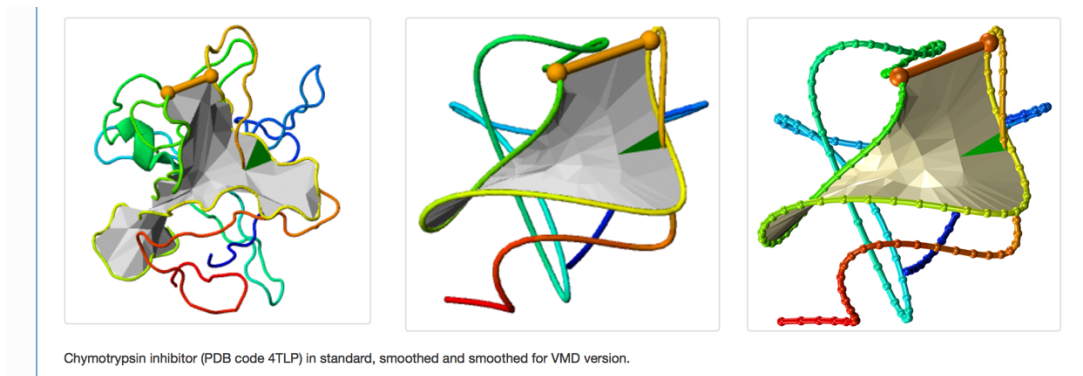
Other options:
a. button "**view details**" is useful when we have more loops in one chain;
b. **blue information bar** – orange square indicates that the bridge is cysteine, loop range=indices of atoms forming bridge and closing loop, N-term and C-term crossings list indices of atoms that cross the surface along the N-terminus tail and C-terminus, +- signs indicate direction of crossings and other information;
c. button "**+show shallow lasso**" – it shows in red indices of atoms that also cross the surface but that we do not take into account recognizing the knot type since for example they are located very close to each other – as in leptine, helice crosses the surface back and forth, but actually we would rather say that it crosses the surface significantly only once (blue and gray triangles on the surface, gray correspond with reduced crossings).

hide shallow lasso		Bridge type	Loop range	Loop length	N-term crossings	C-term crossings	N-end length	C-end length	Lasso loop area
view details	📍 🟧 ⚮ L+1N	96-146	51	(+50), (-51), (+53), (-55), +57		93	0	761	SINGLE LASSO

d. **chain sequence in the bottom** – loop and crossings aminoacids are underlined; dashes mean gap in the structure; **the gap** is indicated with the symbol below the fingerprint in top left corner, and as well on the previous screen with the list of chains; the gap is outside of the loop, and the part of tail that crosses the surface, this is why we do not treat that lasso as artificial one.
e. **Tabs in the top**: "Chain information summary", "Similar chains (by sequence)", "Similar chains (by sequence)"

[EXAMPLE-2: Database, 1ASL],
https://lassoprot.cent.uw.edu.pl/view/4ASL/A/
different complex loops, check lasso fingerprint, have a look at LL1,1, colors of crossings, similar chains with no loop.
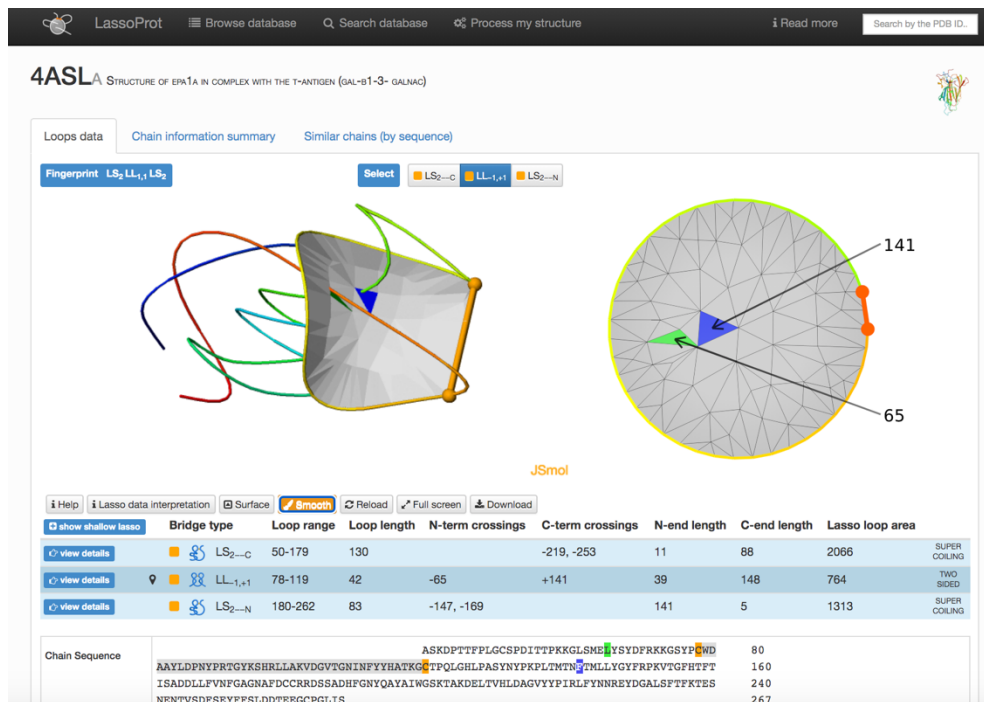
[EXAMPLE-3: Database, 1ZDO],
https://lassoprot.cent.uw.edu.pl/view/1ZD0/A
Supercoiling, smooth, no "+ show shallow lasso" button.

4. Now let's browse and search database. First click on "**Browse database**" in top left corner or bottom left corner.
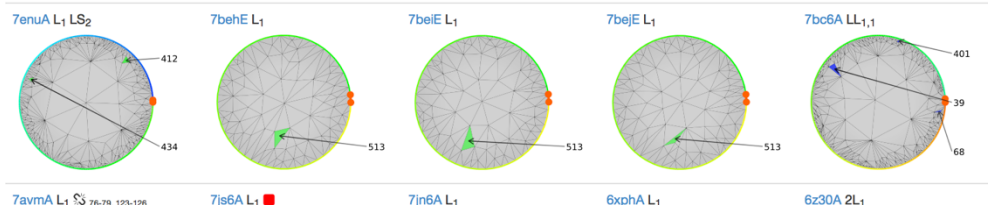https://lassoprot.cent.uw.edu.pl/browse/

List of chains with complex lassos – lasso fingerprints, symbols indicating gaps or different bonds closing loop than cysteine bridge. You can click at any of these chains.
You can display the list also in other ways – four blue buttons in the top.

Now let's search the database - click on "**Search database**" in top or bottom of the page:
https://lassoprot.cent.uw.edu.pl/search/

The database classifies protein chains first according to the **type of chemical interaction**, which form a covalent loop, second to its **entanglement type** i.e. number and the direction of threading. Based on these results, the lasso type is prescribed to every closed loop and the overal topology (**lasso fingerprint**) to the protein chain. For further analysis, LassoProt also presents **many biological and geometrical statistics**. The database contains all the protein structures deposited in Protein Data Bank (you can filter only **non redundant protein chains or all chains**) and is automatically updated every Wednesday.

5. Api: https://lassoprot.cent.uw.edu.pl/api

display list of Non-redundant protein chains with lasso type L_1 and all kinds of bridges:

https://lassoprot.cent.uw.edu.pl/browse/?lassoType=L1&set=0&bridgeType=ssbridge%2Camide%2Cester%2Cthioester%2Cothers

display list of Non-redundant protein chains with lasso type L_2 and loop length between 25 and 30 atoms:

https://lassoprot.cent.uw.edu.pl/browse/?lassoType=L2&set=0&loop_len=25;30&raw=0
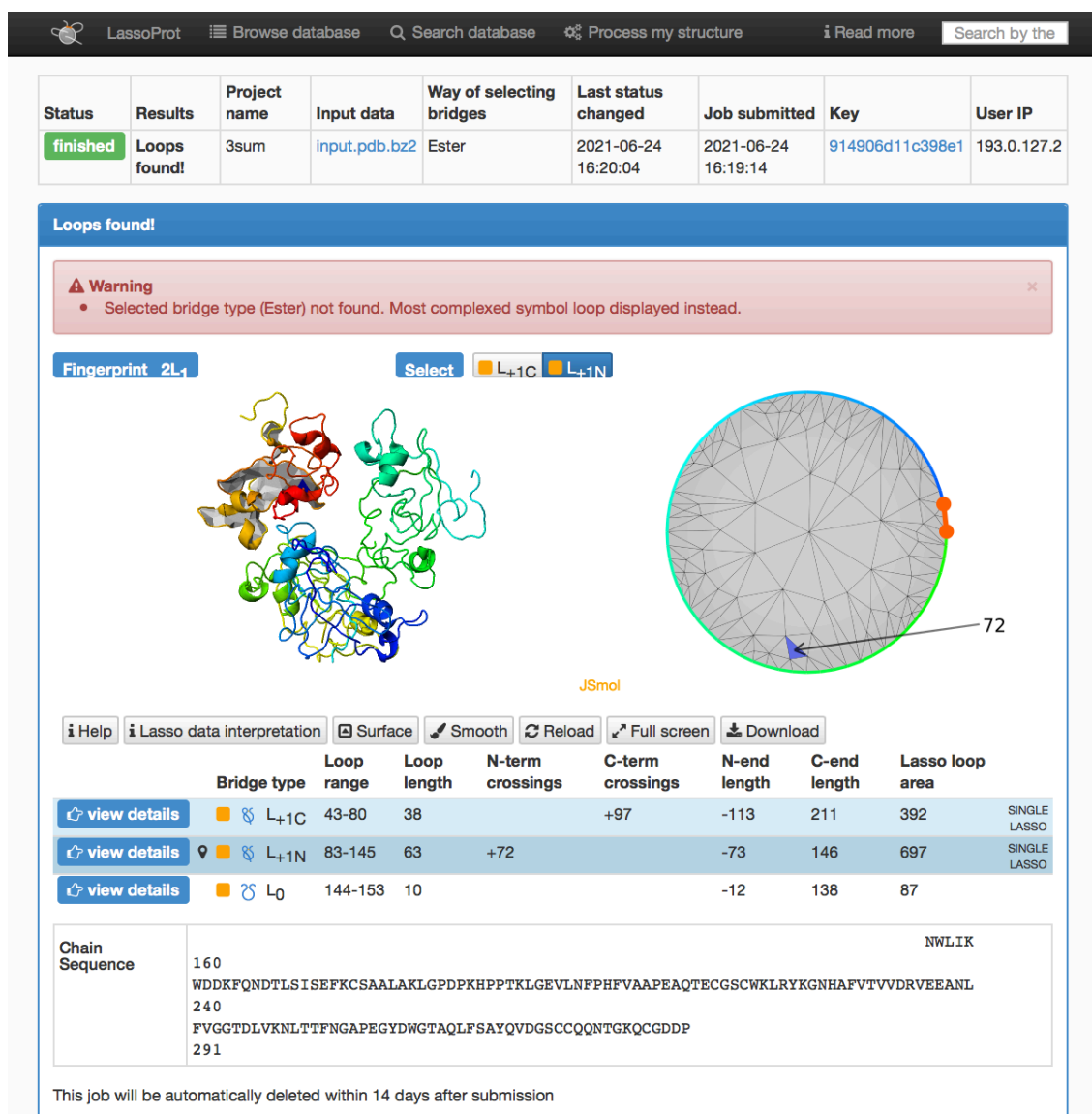
LASSOPROT - SERVER

6. Server – single chains

3sum – try amide bridges:
[EXAMPLE-4: Server, 3sum.pdb, amide bridges],
Result: https://lassoprot.cent.uw.edu.pl/compute/914906d11c398e1

[EXAMPLE-5: Server, `05_01_q_part200.xy`, defined bridges: 10-40, 30-80],
Result: https://lassoprot.cent.uw.edu.pl/compute/6db18e6d18a82eb
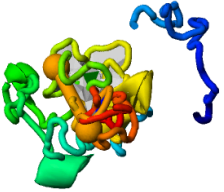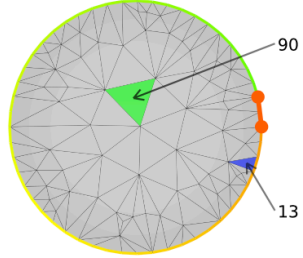
Status	Results	Project name	Input data	Way of selecting bridges	Last status changed	Job submitted	Key	User IP
finished	Loops found!	2kum	view.pdb.gz	loops typed	2021-06-24 16:20:04	2021-06-24 16:15:09	6db18e6d18a82eb	193.0.127.2

Loops found!

Fingerprint 2LL$_{1,1}$ Select LL$_{-1,-1}$ LL$_{+1,-1}$

JSmol

i Help | i Lasso data interpretation | ⬚ Surface | ✎ Smooth | ⟳ Reload | ⤢ Full screen | ⬇ Download

	Bridge type	Loop range	Loop length	N-term crossings	C-term crossings	N-end length	C-end length	Lasso loop area	
⟳ view details	LL$_{-1,-1}$	10-40	31	-5	-166	9	-40	20	TWO SIDED
⟳ view details 📍	LL$_{+1,-1}$	30-80	51	+13	-90	29	-80	50	TWO SIDED

show shallow lasso

This job will be automatically deleted within 14 days after submission

How to cite

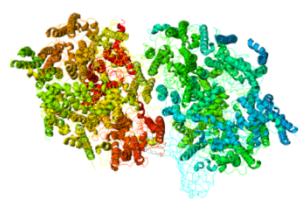LassoProt | Interdisciplinary Laboratory of Biological Systems Modelling

[EXAMPLE-6: Server, 7d1u.pdb, advanced options – distance between crossings changed to 5, no loops],
Result: https://lassoprot.cent.uw.edu.pl/compute/14e39a4338258b7

| Status	Results	Project name	Input data	Way of selecting bridges	Last status changed	Job submitted	Key	User IP
finished	No loops found!	1d1u	input.pdb.bz2	automatic	2021-06-24 16:25:05	2021-06-24 16:22:02	14e39a4338258b7	193.0.127.2

No loops found!

JSmol

i Help | i Lasso data interpretation | ⟳ Reload | ⤢ Full screen | ⬇ Download

Chain Sequence		
ANLWERFCNWVTSTDNRLYVGWFGVIMIPTLLAATICFVIAFIAAPPVDIDGIREPV	400	
SGSLLYGNNIITGAVVPSSNAIGLHFYPIWEAASLDEWLYNGGPYQLIIFHFLLGASCYMGRQWELSYRLGMRPWICVAY	480	
SAPLASAFAVFLIYPIGQGSFSDGMPLGISGTFNFMIVFQAEHNILMHPFHQLGVAGVFGGALFCAMHGSLVTSSLIRET	560	
TETESANYGYKFGQEEETYNIVAAHGYFGRLIFQYASFNNSRSLHFFLAAWPVVGVWFAALGISTMAFNLNGFNFNHSVI	640	
DAKGNVINTWADIINRANLGMEVMHERNAHNFPLDLA	677	

This job will be automatically deleted within 14 days after submission

[EXAMPLE-7: Server, 7d1u.pdb, CHAIN O, advanced options – distance between crossings changed to 5, no loops],
Result: https://lassoprot.cent.uw.edu.pl/compute/534968a7f1f505b
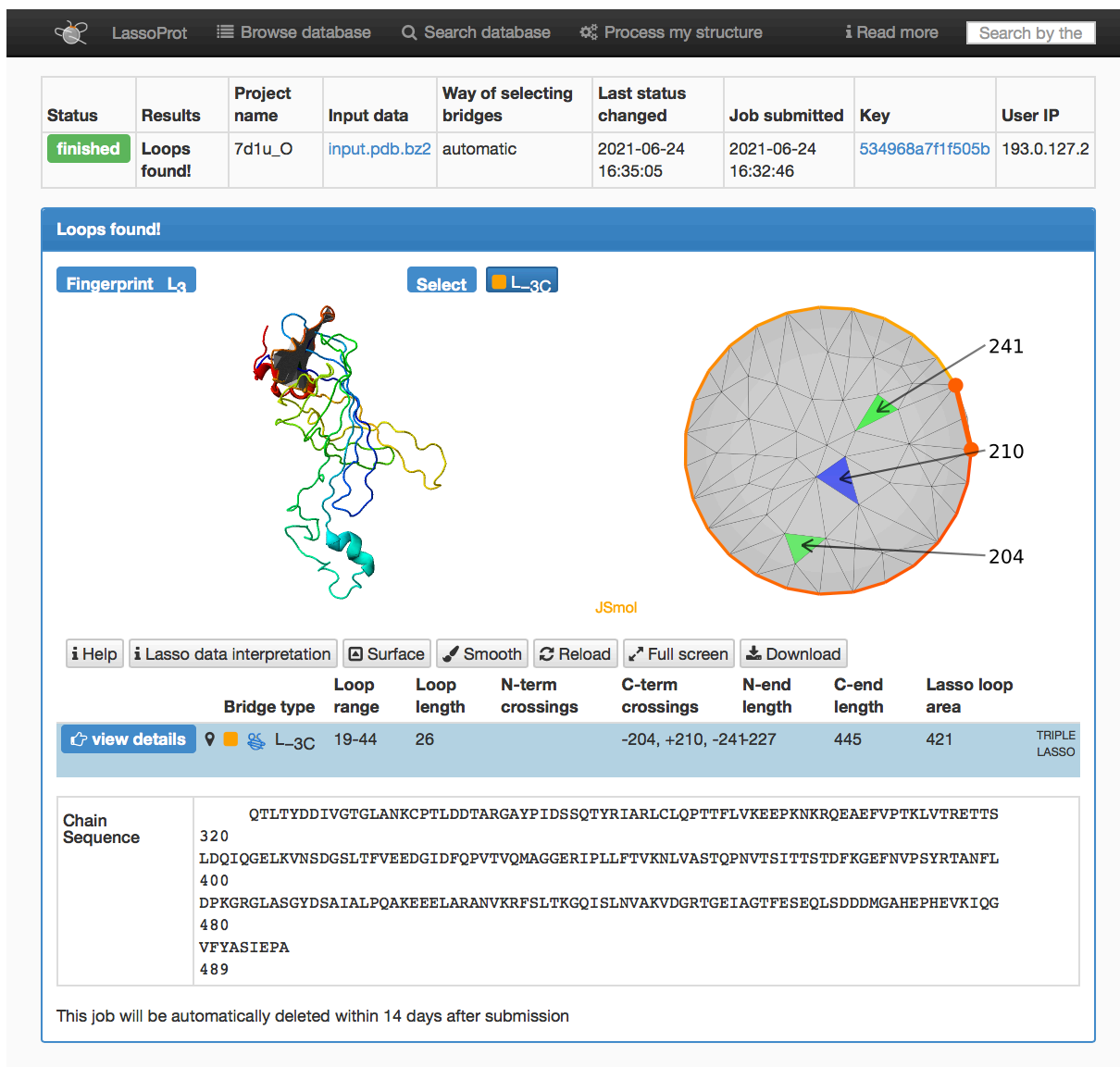
In database L1 – 2 crossings reduced. You are welcome to compute GLN in this case, using for instance PyLasso plugin to Pymol or Python package Topoly.

7. Server – trajectories

[EXAMPLE-8: Server, `short trajectory`],
https://lassoprot.cent.uw.edu.pl/compute/trajectory

[EXAMPLE-9: Server, `long trajectory`],
https://lassoprot.cent.uw.edu.pl/compute/traj-long
- zoom blue region of second plot and think how the lasso was formed