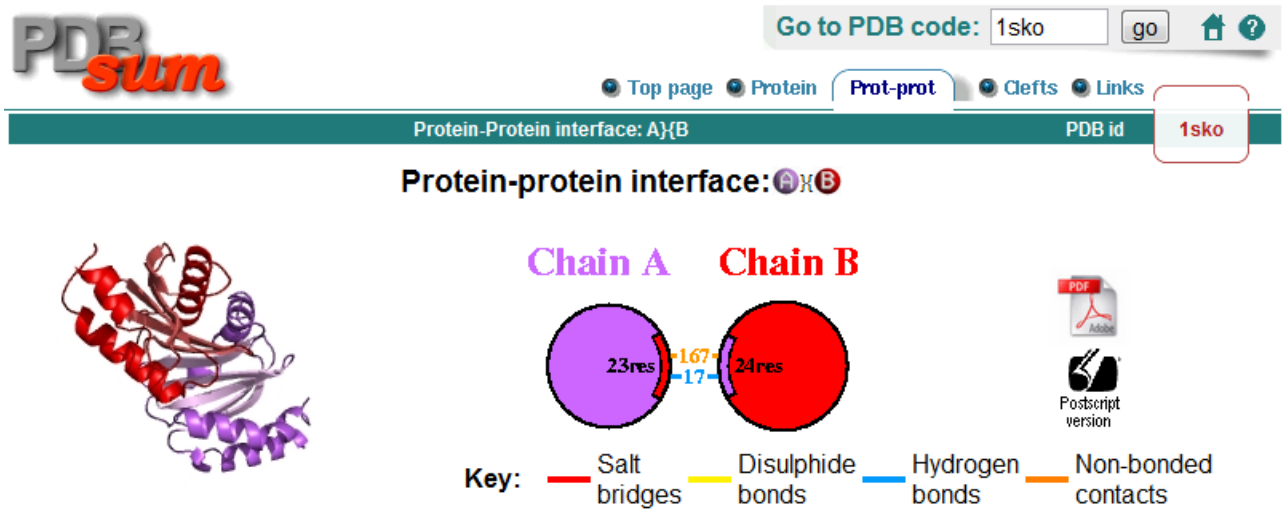
Compare a protein-protein complex with 2P2Idb dataset:

Example : Mp1-p14 complex (PDB code 1SKO)

*(**Important notice** : In this example Mp1 is considered as the target and p14 as the partner)*

1- Retrieve Chain Id for each partner of the interaction

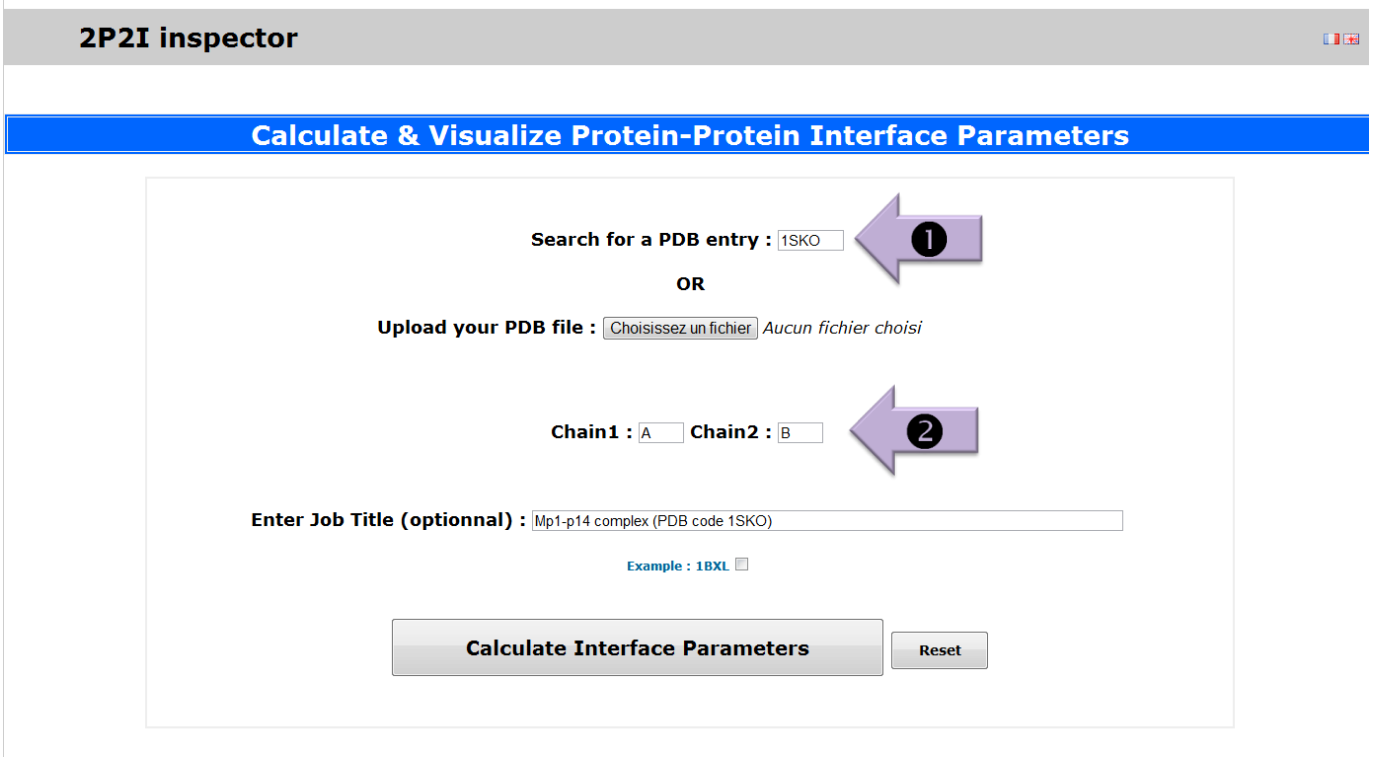
This information can be found on the **PDBSum** server (http://www.ebi.ac.uk/pdbsum/) in the Prot-prot Tab



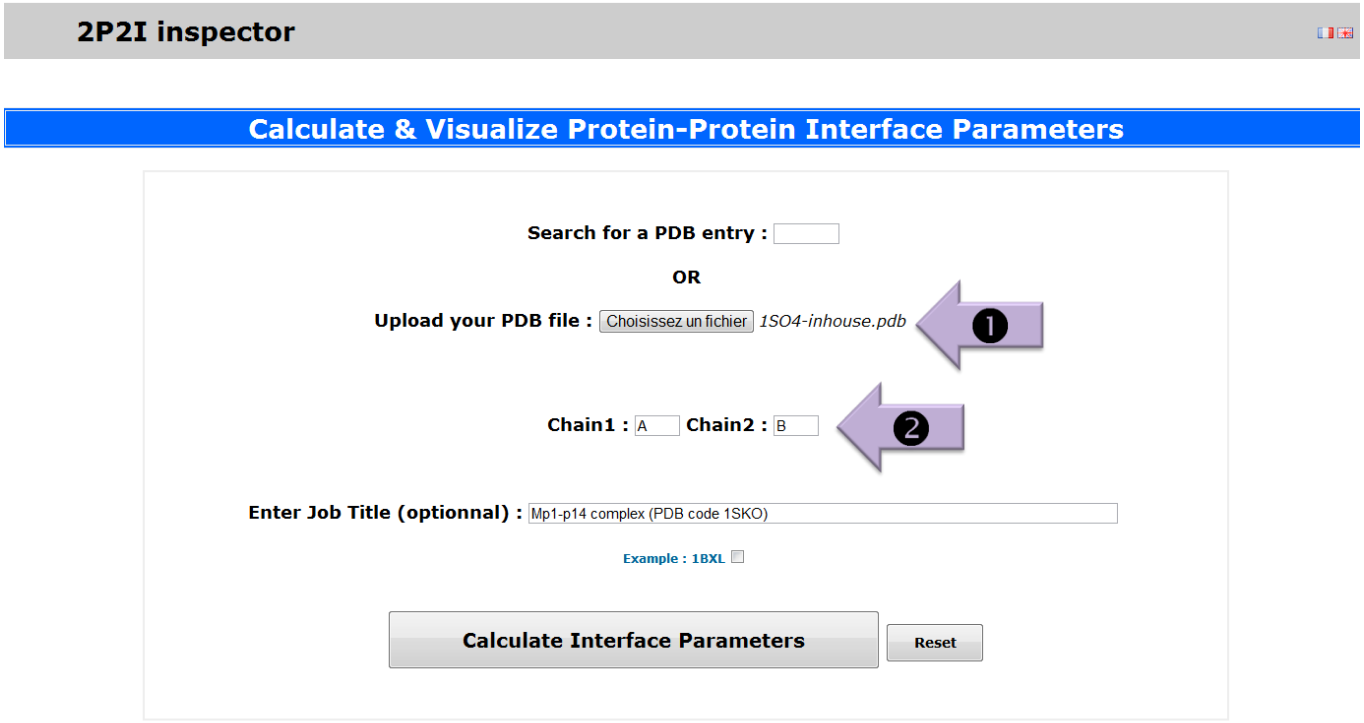
⇨ **Interacting Chains : A (Target) and B (Partner)**

1- Use 2P2I inspector Tool on this website to calculate key parameters

Option 1 : ❶ Enter PDB 4-letter Code, ❷ Enter Chain Ids then **Submit**



Option 2 : ❶ Upload a local PDB File, ❷ enter Chain Ids then **Submit**



3- Get Values for key parameters

Interface Properties for 1SKO Complex

Summary Properties

Total Interface Area (Å^2)	2479.2
Gap Volume (Å^3)	3780.00
% Charged Residues	13.0
Total Nb of Segments	6
Nb of non-bonded contacts List	167
Nb of hydrogen bonds List	11
Nb of salt bridges List	0
Total Nb of Disulfide bonds	0
Secondary Structure at Interface	Alpha/Beta

1. Total Interface Area **2479.2**
2. Gap Volume **3780.0**
3. % Charged Residues **13.0**
4. Number of Hydrogen Bonds **11**

Number of Interface Segments

A	Number of Segments: 2	5 Target (Chain A)
B	Number of Segments: 4	6 Partner (Chain B)

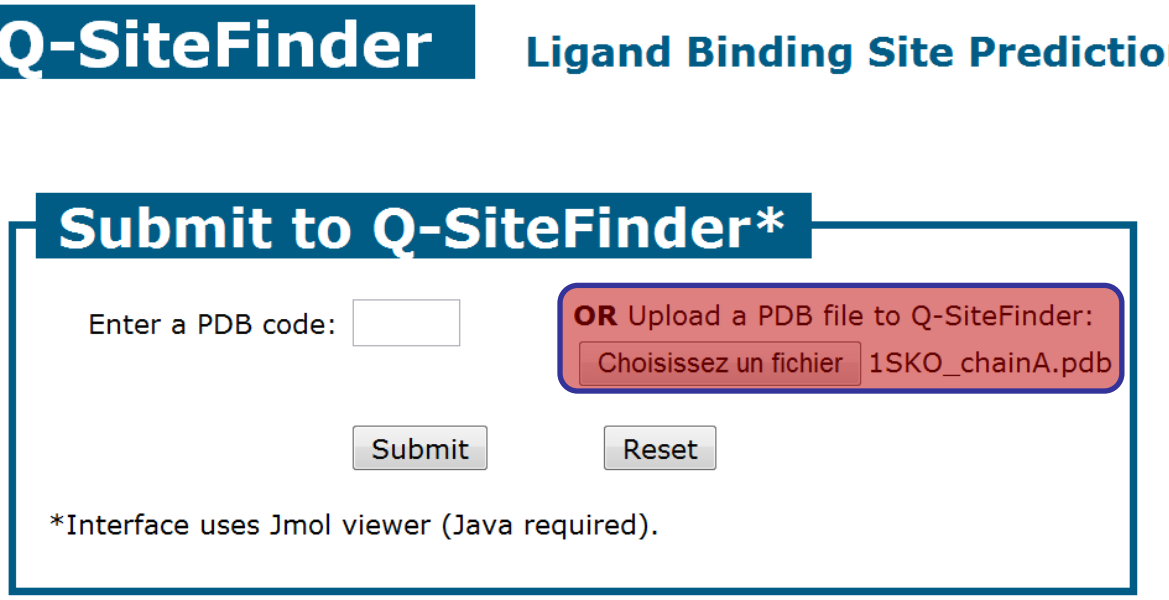
4- <u>Create a PDB file containing only the target protein (Chain A in this example)</u>

1SKO_chainA.pdb

(PDB File Containing Chain A Only)

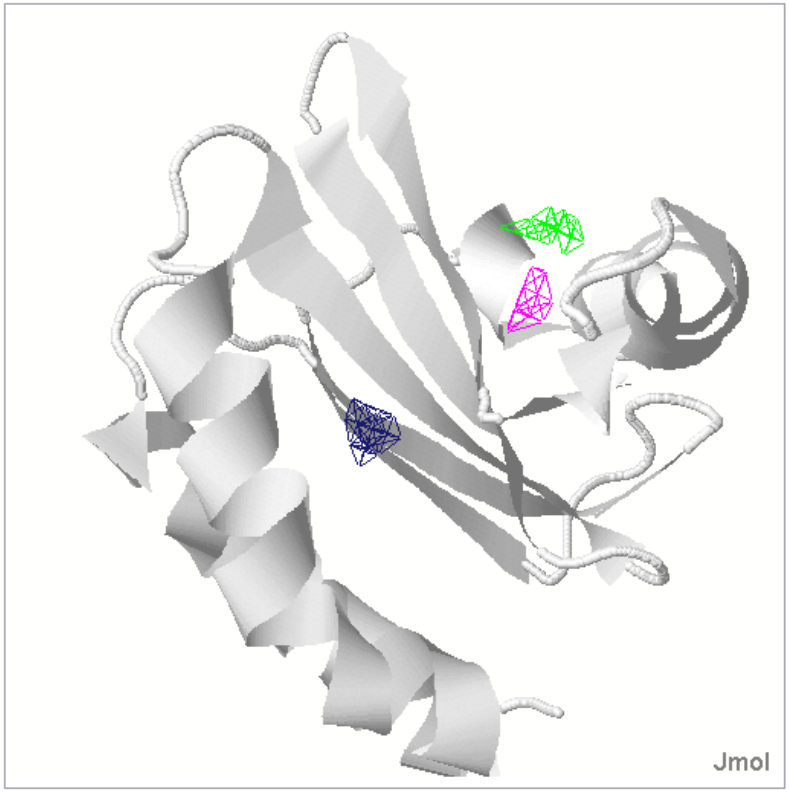
5- Go to Q-SiteFinder (http://www.modelling.leeds.ac.uk/qsitefinder/)

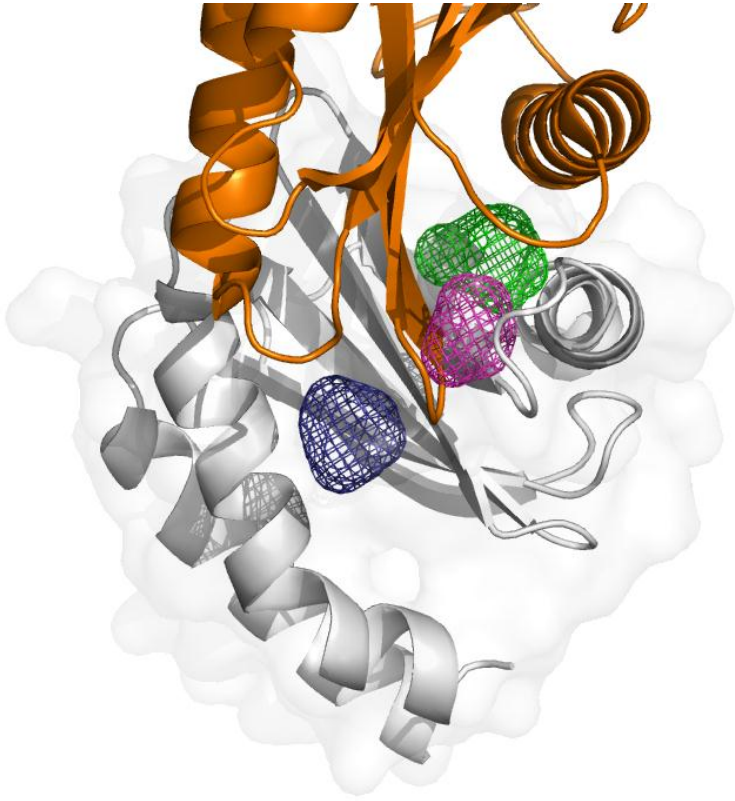
- Upload the target protein (**1SKO_chainA.pdb**) and Submit



6- Get Predicted Pockets at interface and total volume

Download the PDB file containing the target protein and the predicted pockets (***Right-Click*** *in Jmol window*). Superimpose chain A in the protein and the complex to visualize the pockets present at the interface.





Three pockets are present at the interface from sites **2** (green), **5** (magenta) and **7** (blue)

2P2I$_{SCORE}$ Help File

In **Q-SiteFinder** select the binding sites (2, 5 and 7) to get an estimate of the **cavity volume**

Display Sites

☐ Site 1	☐ Toggle Surface
☑ Site 2	☐ Toggle Surface
☐ Site 3	☐ Toggle Surface
☐ Site 4	☐ Toggle Surface
☑ Site 5	☐ Toggle Surface
☐ Site 6	☐ Toggle Surface
☑ Site 7	☐ Toggle Surface
☐ Site 8	☐ Toggle Surface
☐ Site 9	☐ Toggle Surface
☐ Site 10	☐ Toggle Surface

Volume Site 2: 117 Cubic Angstroms

Volume Site 5: 77 Cubic Angstroms

Volume Site 7: 73 Cubic Angstroms

Total Pocket Volume: 267 Cubic Angstroms

7- Report all calculated values in 2P2Iscore

Gap Volume (Å^3) 3780.0 [1]

Total ASA (Å^2) 2479.2 [1]

Charged Residues (%) 13.0 [1]

Number of Hydrogen Bonds 11 [1]

Pocket Volume (Å^3) 267 [2]

Number of Interface Segments

TARGET 2 [1]

PARTNER 4 [1]

[1] Recommended site 2P2I inspector
[2] Recommended site Q-SiteFinder

Compare with 2P2Idb Dataset

8- Compare with 2P2Idb dataset parameters

This complex belongs to Cluster Class 2 (protein/protein)

Parameters	User Values	2P2I$_{DB}$	Comment	
Gap Volume (Å^3)	3780.0	5545.8 ±2506.4	inferior	(-0.7 σ)
ASA (Å^2)	2479.2	1729.8 ±686.8	superior	(1.09 σ)
% Charged Residues	13.0	30.3 ±12.6	inferior	(-1.37 σ)
Segments	6	8.4 ±2.1	inferior	(-1.14 σ)
H-Bonds Number	11	3.8 ±2.9	superior	(2.48 σ)
Pocket Volume (Å^3)	267	107.2 ±64	superior	(2.5 σ)

- **1 Parameter with high score** (Pocket Volume)
- **3 Parameters with reasonnable score** (Gap Volume; ASA; Segments)
- **2 Parameters with low score** (% Charged Res.; HBonds)

User Values are color-coded according to their standard deviation to the 2P2I dataset values.

In this example, the presence of **3 large pockets** for a **total volume of 267 cubic Angstroms** and the **3 parameters** with a reasonable score make 1SKO a potential druggable complex (considering Chain A as the Target).