

# Algorithms in Structural Bioinformatics

Final Project  
***INTERVOR***

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# Paper of presentation

- Cazals, F. "Geometric, topological and contact analysis of interfaces in macro-molecular complexes: from the atomic scale to the complex scale using interval." *Rapport de recherche INRIA 5864* (2006).

# Related Work and Bibliography

- Lorient, Sébastien, and Frédéric Cazals. "Modeling macro-molecular interfaces with Intervor." *Bioinformatics* 26.7 (2010): 964-965.
- Bouvier, Benjamin, et al. "Shelling the Voronoi interface of protein-protein complexes reveals patterns of residue conservation, dynamics, and composition." *Proteins: structure, function, and bioinformatics* 76.3 (2009): 677-692.
- Cazals, Frederic. "Revisiting the Voronoi description of protein-protein interfaces: Algorithms." *Pattern Recognition in Bioinformatics*. Springer Berlin Heidelberg, 2010. 419-430.
- Cazals, Frederic. "Modeling Macro-Molecular Complexes and Assemblies" *May 2013 presentation @ University of Athens*.
- Cazals, Frederic. "Modeling Macro-Molecular Complexes and Assemblies with Voronoi Diagrams" *presentation 2012 @ INRIA Sophia-Antipolis*.
- Cazals, Frédéric, et al. "Revisiting the Voronoi description of protein-protein interfaces." *Protein Science* 15.9 (2006): 2082-2092
- Janin, Joël, Ranjit P. Bahadur, and Pinak Chakrabarti. "Protein-protein interaction and quaternary structure." *Quarterly reviews of biophysics* 41.02 (2008): 133-180.
- Jones, Susan, and Janet M. Thornton. "Principles of protein-protein interactions." *Proceedings of the National Academy of Sciences* 93.1 (1996): 13-20.

# Qs 2 b Answered

1. Can one bridge the gap from atoms loosing solvent accessibility to interface pairs?
2. Is the interface flat or curvy?
3. Is it connected or not (does it have a multi-patch structure)?
4. Is a connected component of the interface simply connected or not (does it have a hole)?
5. What is precisely the role played by interface structural water?

# Reason

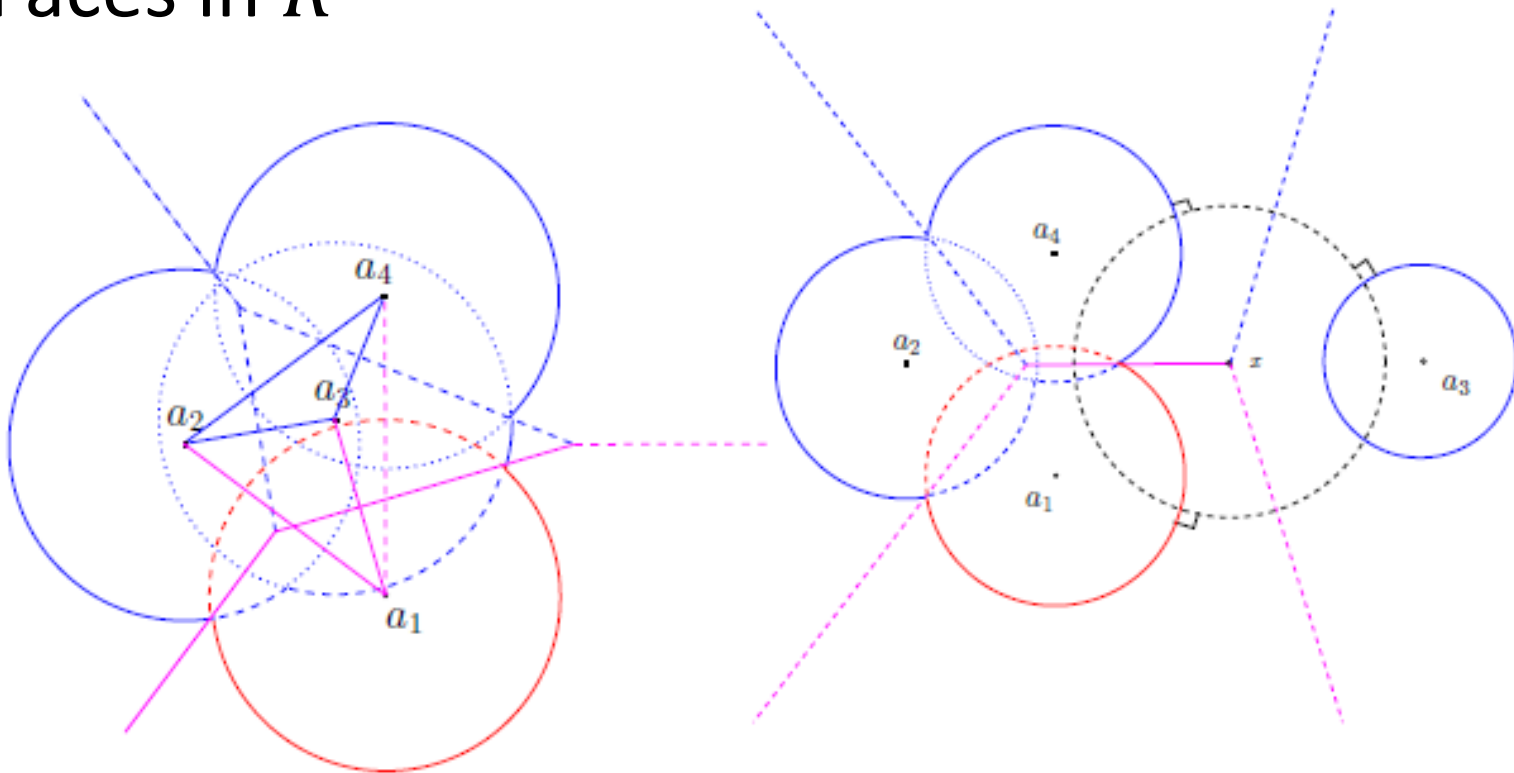
- In need of an interface model which unifies most (if not all) the statistics used so far to describe interfaces in macro-molecular complexes
  - Constructed only from a PDB file.
- Why?
  - Address questions such as the role played by interface atoms and in particular structural water, the flexibility issues involved in complex formation, or the specificity of recognition mechanisms

# Previous knowledge on the topics ...

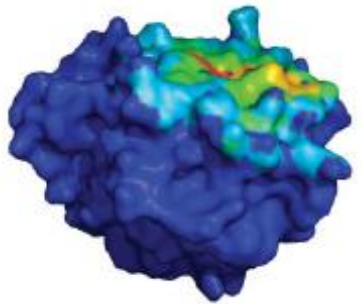
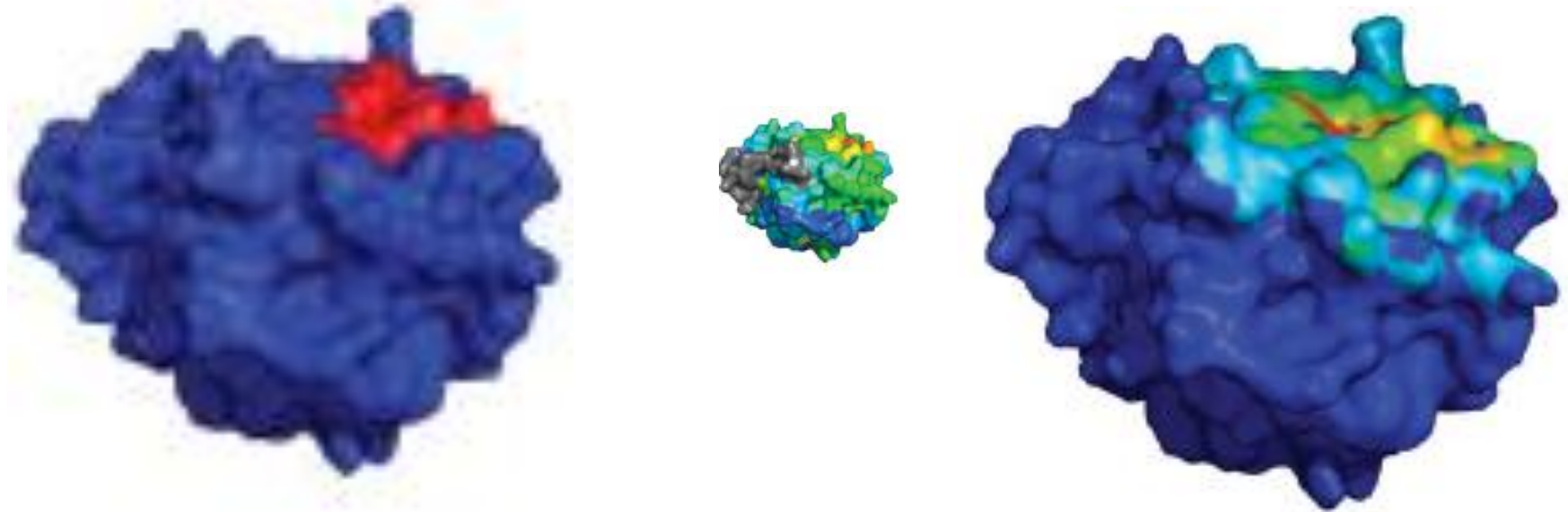
- Van der Waals models
- Convex-Hull
  - i.e. needed for buried or exposed atoms
- Delaunay Triangulation / Voronoi Diagrams
- $\alpha$ -shapes /  $\alpha$ -complex

# D.T. / V.D. / $\alpha$ -complex / 0-complex

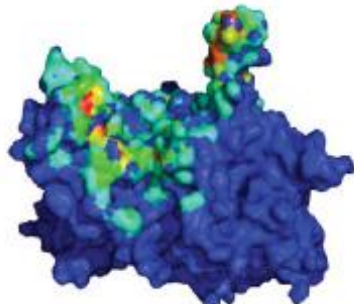
 Faces in  $R^d$



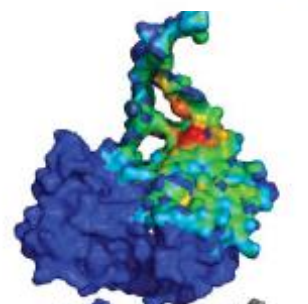
# Crystals and Structural Water: AB & ABW models



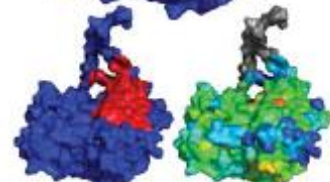
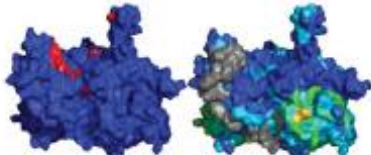
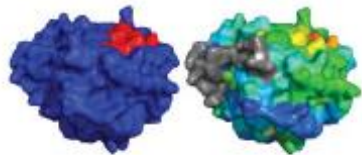
1E2D



1L5W



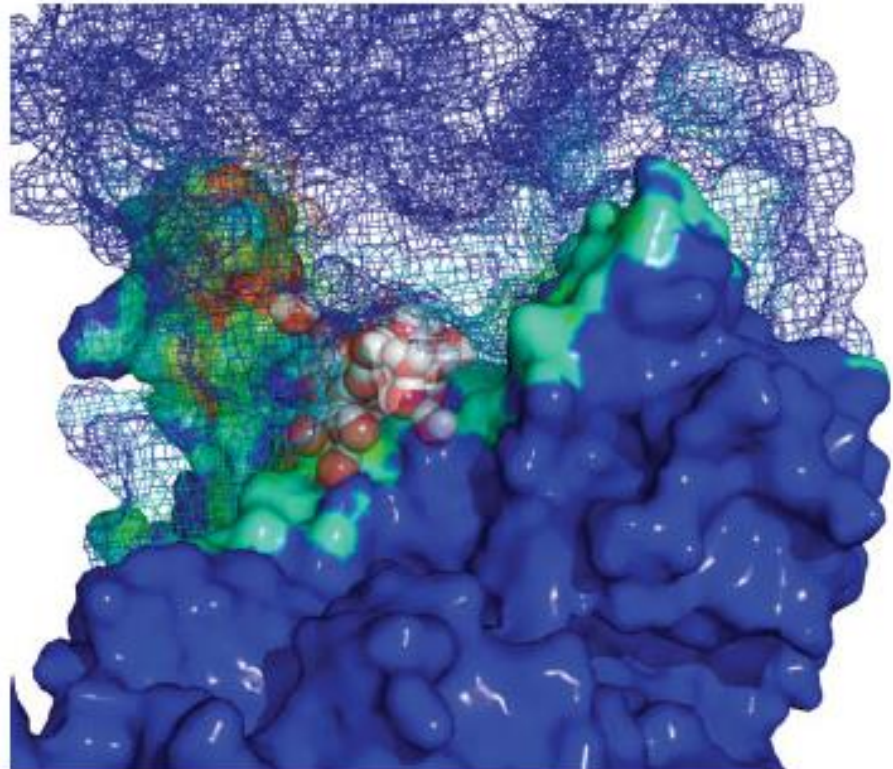
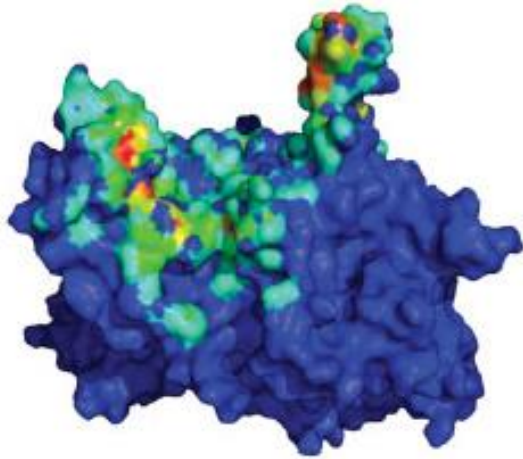
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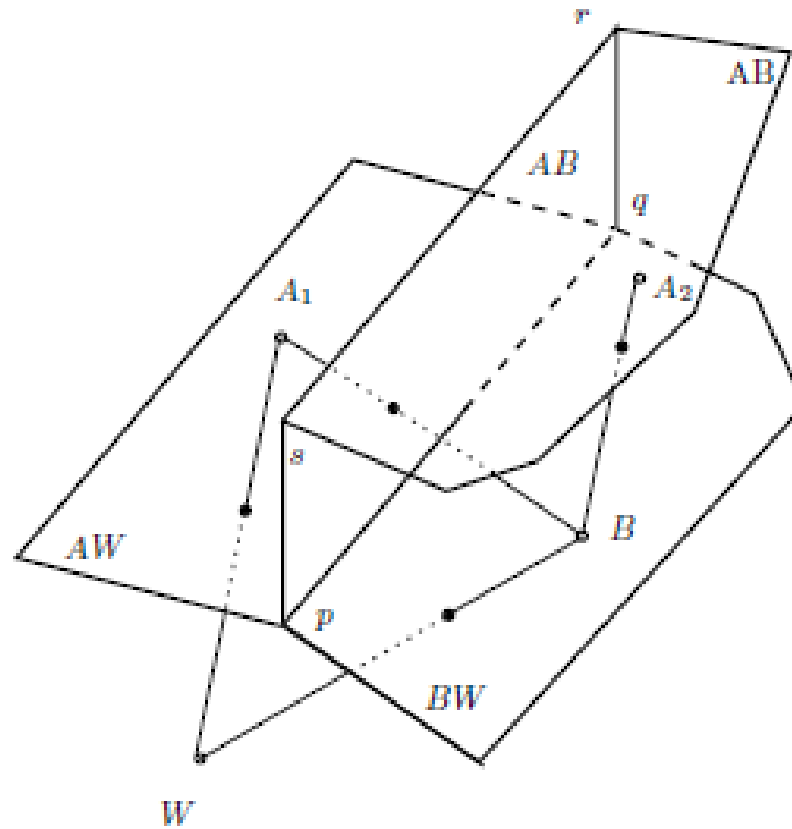
# Water



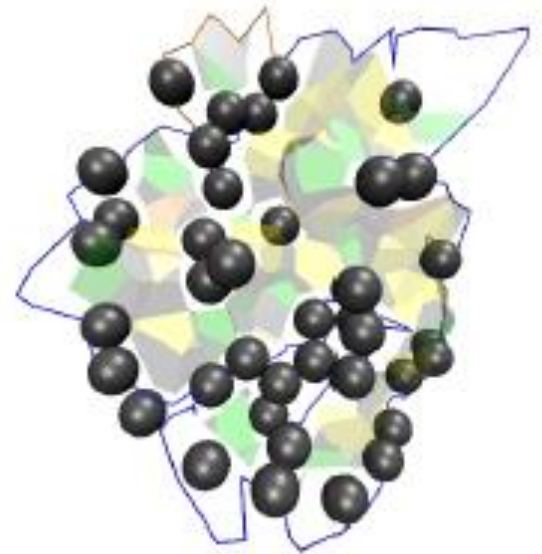
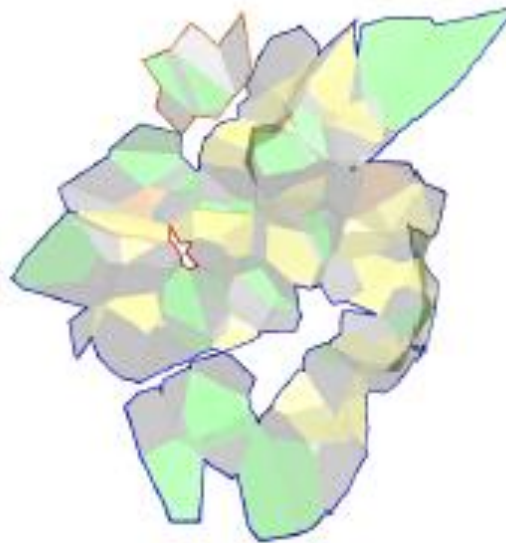
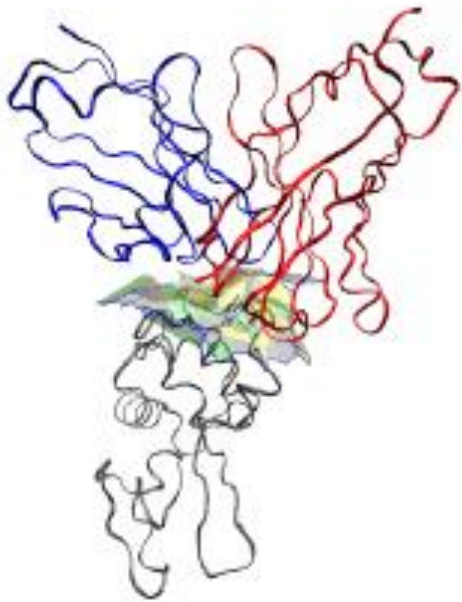
# $\{A^*W^*_*B^*W^*\}$ definitions

- **AB** interface: the interface specified by **edges of type AB**. This interface describes the contacts between both partners.
- **AW–BW** interface: the interface specified by **edges of type AW or BW**. This interface describes the contacts between the **partners and structural water**.
- **ABW** interface: the **union** of the **AB** and **AW–BW** interfaces. This interface positions relatively to one another the previous two interfaces.

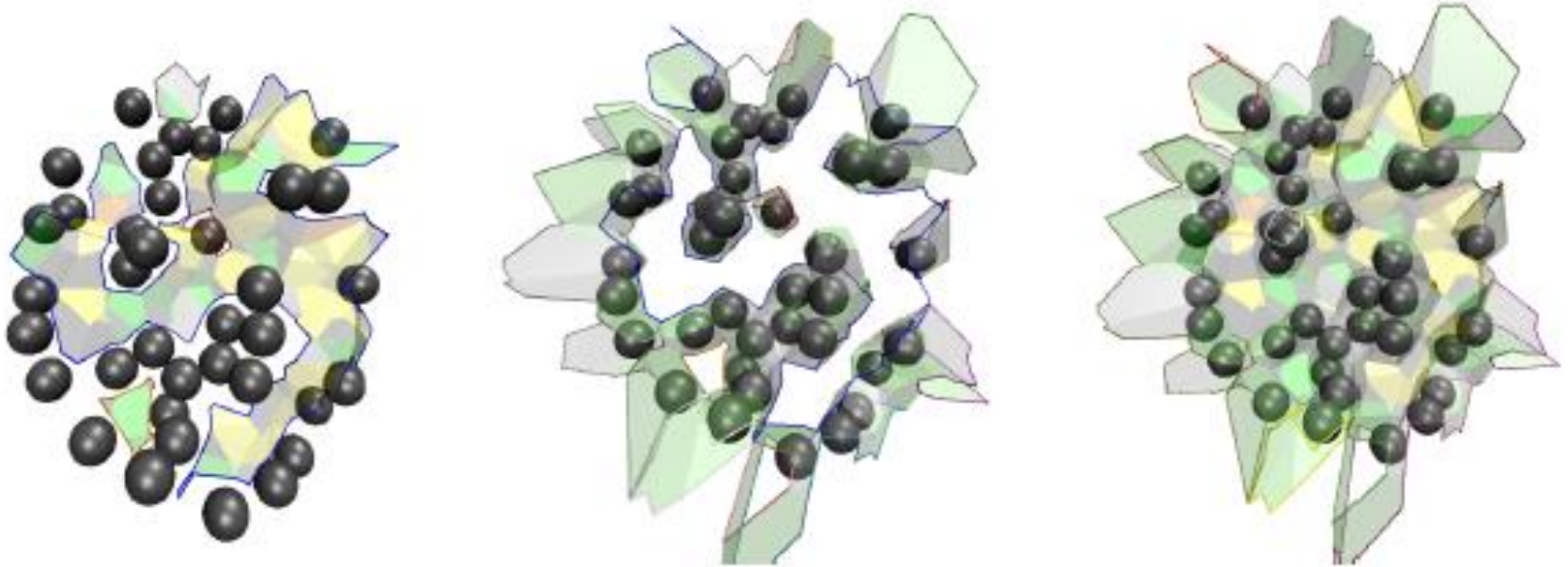
$\{A*W*_*B*W*\}$  interfaces



$\{A^*W^*-*B^*W^*\}$  interfaces



$\{A^*W^*_{-}B^*W^*\}$  interfaces



# Connected Components (CC)

- The transitive pairwise intersections between atoms.
  - For example, a cc of the AB interface corresponds to a collection of A and B atoms such that a restricted atom of type A intersects a restricted atom of type B which intersects a restricted atom of type A and so on

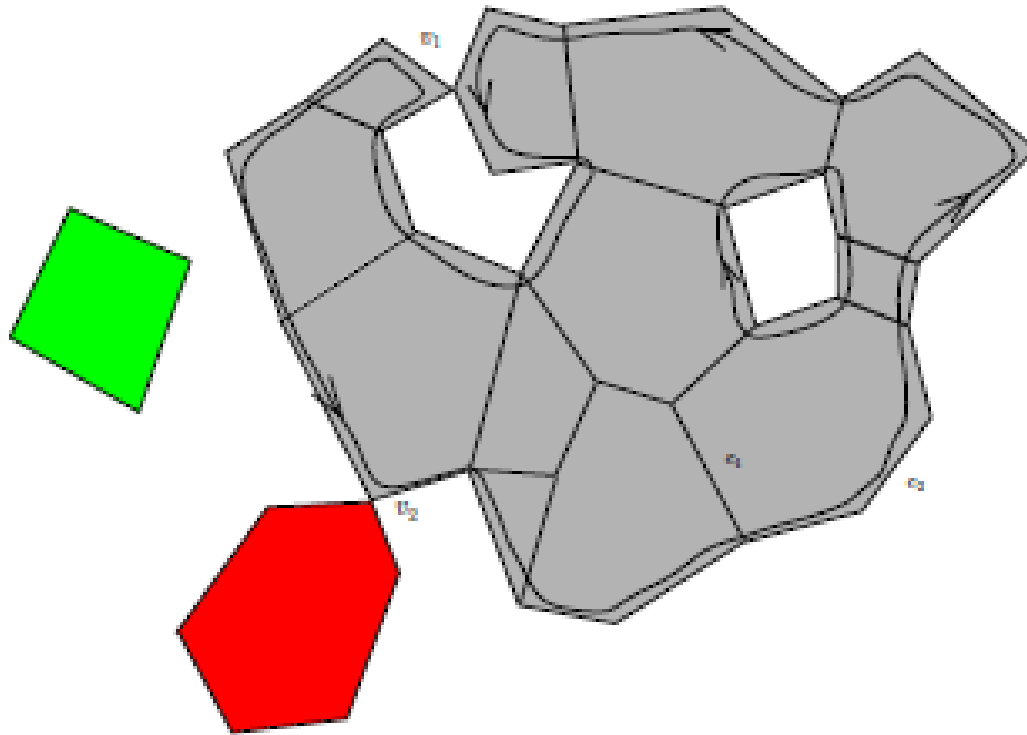


Topological statistics

# CC

## & (SCC)

 Patches



# Usage of Intervor in gathering statistics

- $\#A / \#B / \#W / \#X$ 
  - the number of interface atoms of each of the four species.
- $\#XY$ 
  - the number of interface edges between atoms of types X and Y
- $\#X_{XY}$ 
  - the number of interface atoms of type X involved in the XY interface
  - E.g. AB model :  $\#A_{AB} = \#A$ . ABW model:  $\#A_{AB} < \#A$
- Bur



# Usage of Intervor in gathering statistics

- Multiple ratios and formulas discussed in the referenced paper used for statistics in:
  - Connectivity between interface atoms using biochemical relation senses
  - Geometry of interfaces
  - Topology of interfaces
  - Water role in the interfaces

# Experiments

- 96 proteins (shown in file [proteins.html](#)) taken from 5 families of complexes:
  - Protein – Inhibitor
  - Enzyme - Substrate/Inhibitor
  - Antigen – Antibody
  - Signal Transduction
  - Misc
- Also, 30/96 complexes, at resolution equal or better than 2°A, used for the ABW model

# Experiments

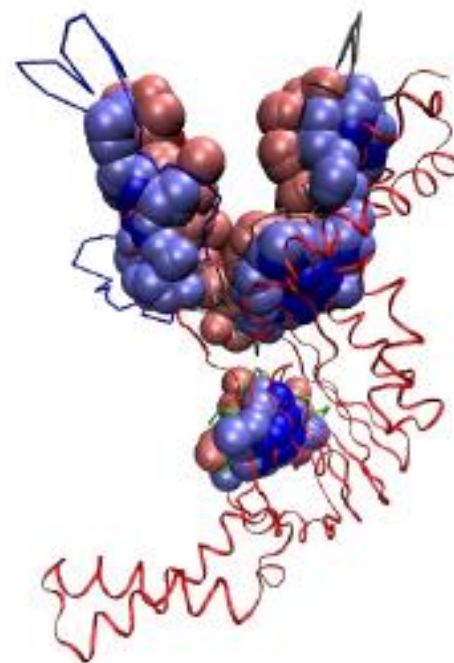
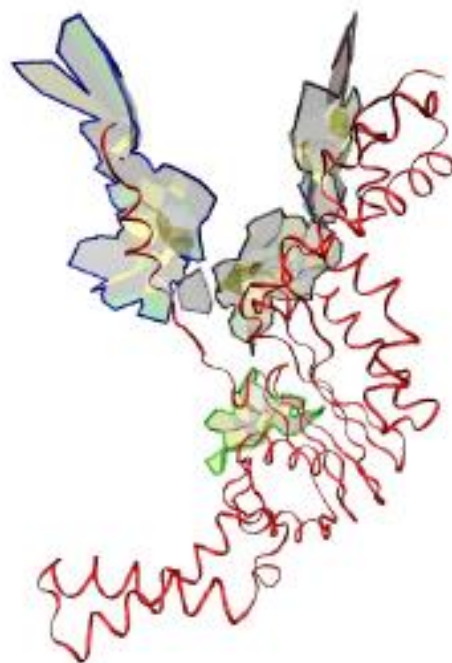
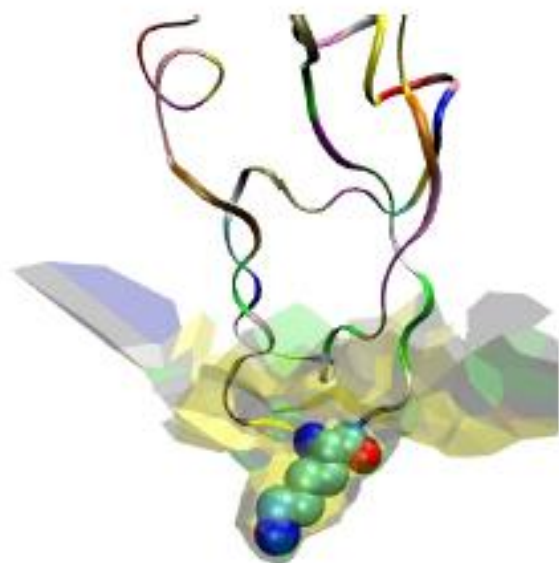
- Interface Atoms (AB model)
  - # interface atoms increases  $\sim 13\%$  due to Buried Surface Area  $> 0$ .
  - Main chain atoms included in 19% of the BSA represent 39% of interface atoms, and represent about  $2/3$  of interface atoms that do not lose solvent accessibility.
  - Main chain atoms important in protein-protein complexes

# Experiments

- Connected components (AB model)
  - Vary in the range 1..6
  - Average CC: 1.9 by complex.
  - Average SCC: 1.21 (threshold of 7.5% of the Voronoi Interface Surface Area).
  - Unique CC for 81/96
  - 2 CCs for 9/96
  - 3 CCs for 6/96
    - 7/15 found in Class of Signal Transduction family.
    - Reason: This family features larger and more fragmented interfaces.

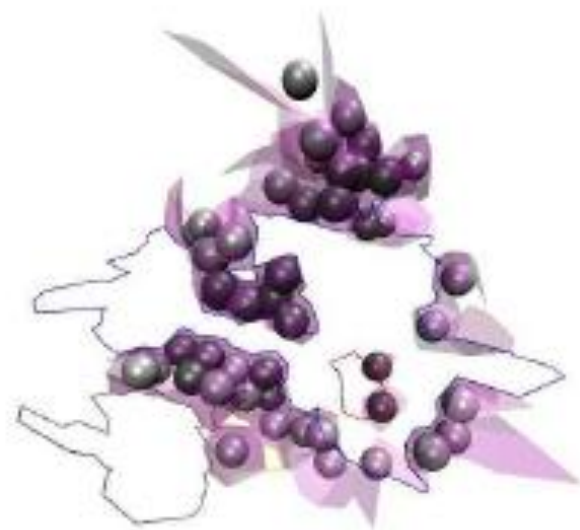
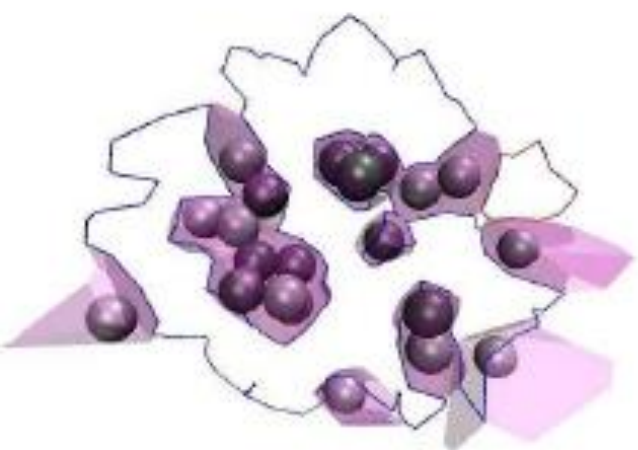
# Experiments

- Curvature in the AB model
  - All families (except Protease-Inhibitor):
    - dihedral angles observed for interior between 12-24 degrees bonded atoms.
  - Protease-Inhibitor family:
    - Larger curvature
    - Cylindrical geometry
    - twice more neighbors than an atom in the concave region (e.g. a protease) (see figure)



# Experiments

- Structural water
  - increase of 45% of interface atoms,
  - ratio of buried atoms shifts from 38% to 68%.
  - ~6,6 CC
  - Water molecules in Antibody-Antigen interface complexes = 2.82 \* water molecules in Protease-Inhibitor complexes (see figure)
- ABW model
  - unique CC, meaning that the CC of the AW–BW reconnect the patches of the AB interface





# The End!

## Thank you!!!

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