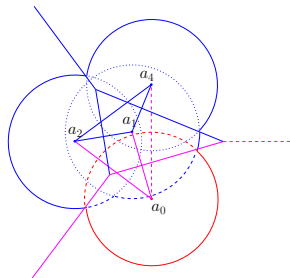
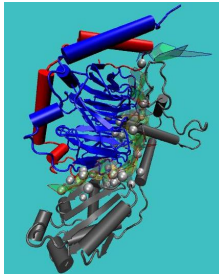
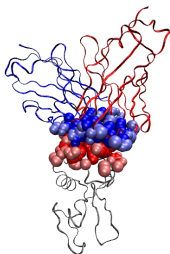


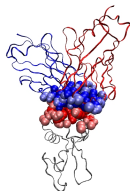
Revisiting the Voronoi Description of Protein-Protein Interfaces: Algorithms

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Modeling the Interface of Macro-molecular Complexes



- ▶ **Key questions:** predicting the ...
stability of interfaces
plasticity of complexes, dynamics of networks
and their **specificity**

- ▶ **Shape - topology:**

- # connected components, holes, voids / cavities [Homology]
- morphology: *fat, skinny, dumbbell-like*

- ▶ **Shape - geometry:**

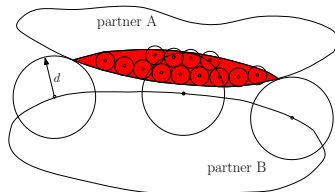
- *privileged* contacts (pairs, triples, quadruples,...)
- packing properties
- accessibility (exposed vs buried atoms)
- curvature information

- ▶ **Correlations with bio-physical quantities**

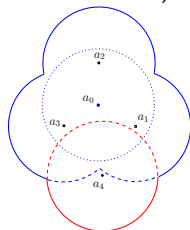
- conservation of amino-acids
- biochemical properties

About Interface Models

- ▷ Distance threshold
(geometric footprint)



- ▷ Loss of solvent accessibility
(cf core and rim models)



- ▷ The Voronoi interface model

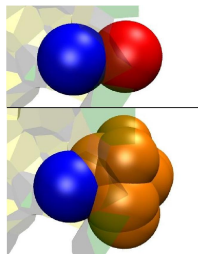
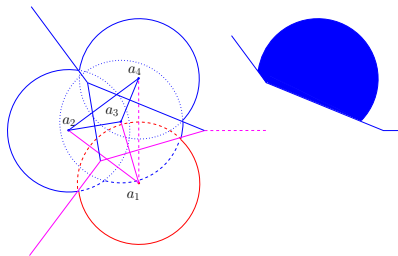
- A parameter free interface model
- Singles out a single layer of atoms
- Is amenable to geometric and topological calculations

- ▷ Applications

- Wet biology: complex analysis and optimization — directed mutagenesis
- Structural modeling: scoring functions for docking
- Systems biology: mining contacts, mating orphan molecules, ...

Voronoi Interface : Definition

(Power Diagram Based Interface Definition)



▷ Interface : bicolor edges in 0-complex

Lemma. Any atom with $\Delta ASA > 0$ is an interface atom.

Attention. Converse is FALSE : cf 13% of interf. atoms missed by previous studies

Importance.

Such atoms are *nearest neighbors* (wrt to the power distance)

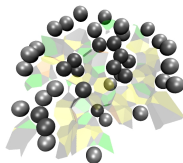
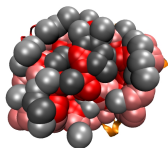
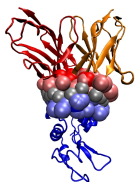
Voronoi interface: balance between geom. footprint and ΔASA

▷Ref: Cazals, Proust, Bahadur, Janin; Protein Science; 2006

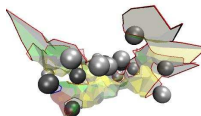
Voronoi Interfaces : Illustrations

(An integrated model from the atomic to the interface scale)

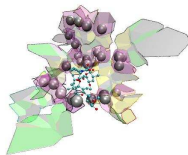
- ▷ Role of structural water –antobody-antigen



- ▷ Curvature –protease-inhibitor



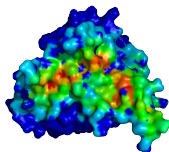
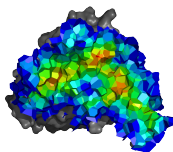
- ▷ Multi-patch structure –signal transduction



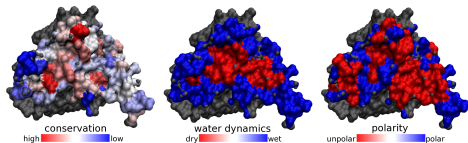
Mining Protein - Protein Interfaces Cont'd (Structural Studies)

▷ Strategy developed: discrete interface parameterization

- Voronoi Shelling Order: interface partitioning into concentric shells
- Integer valued depth of atoms at interface (vs core - rim)
- Statistics (P-values, Fisher meta analysis) for various correlations



▷ Conservation vs dryness vs polarity



▷ Assessment: statements from global → per-complex

- depth and water dynamics: significant **per-complex**
- conservation vs core/rim: **global trend**
- polarity and depth : **global trend**

▷Ref: Cazals, Proust, Bahadur, Janin; Protein Science 15; 2006

▷Ref: Bouvier, Gruenberg, Nilges, Cazals; Proteins 76; 2009

Conclusion

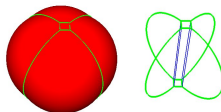
▷ Key properties of the Voronoi interface

- Fully integrated, parameter free interface model
- If speed matters : $< 5s$ per complex
- Improved correlations with biophysical quantities
- Ongoing work – pattern matching:
Interface encoding amenable to comparisons

▷ Soft --- Intervor: interfaces



▷ Soft --- Vorlume: certified surfaces and volumes



<http://cgal.inria.fr/abs/Intervor>

▷Ref: Lorient, Cazals;

Bioinformatics 26(7); 2010

<http://cgal.inria.fr/abs/Vorlume>

▷Ref: Cazals, Lorient;

Under revision; 2010