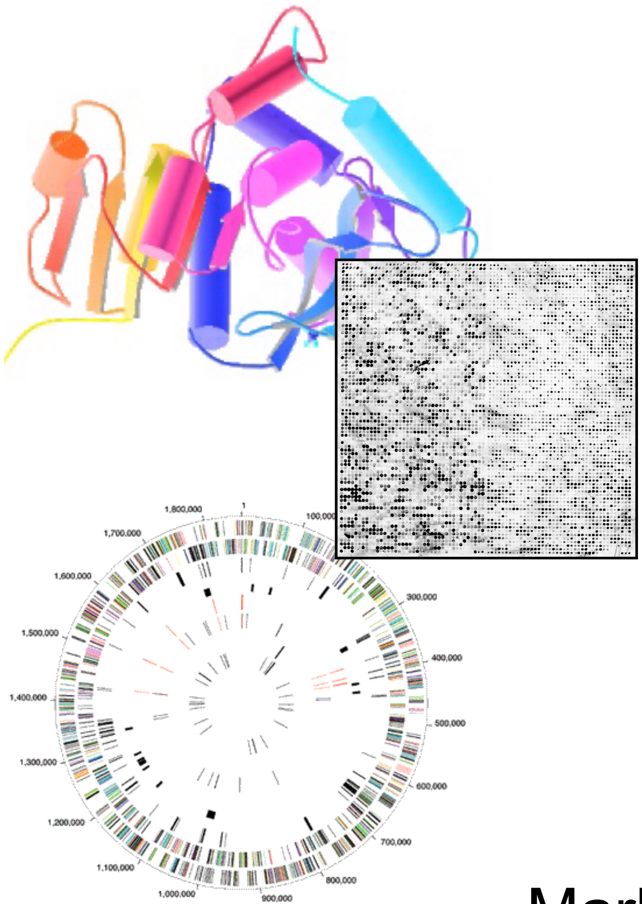
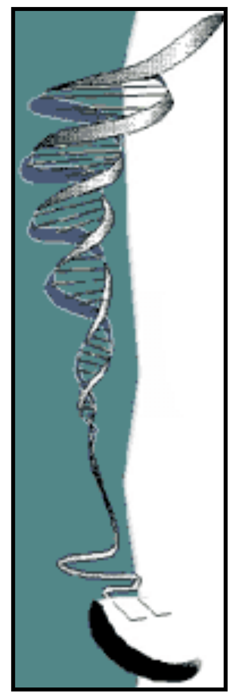
BIOINFORMATICS
Structures #2

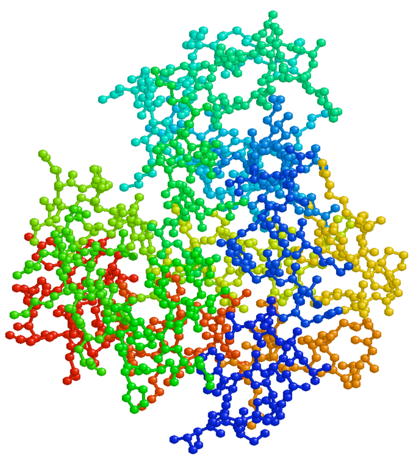




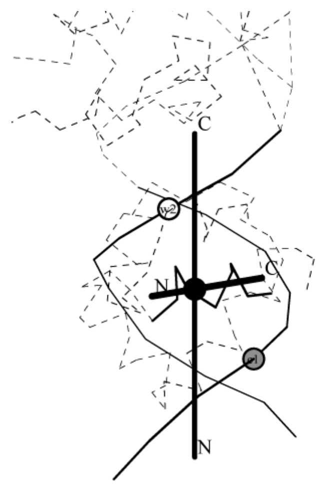
Mark Gerstein, Yale University
gersteinlab.org/courses/452

(last edit in fall '06, includes in-class changes)

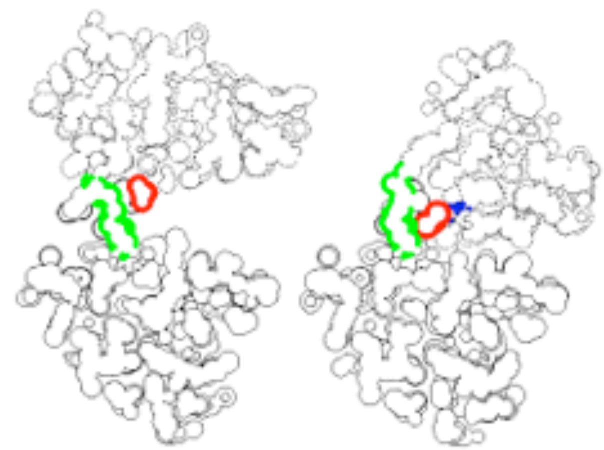
Other Aspects of Structure, Besides just Comparing Atom Positions



Atom
Position,
XYZ triplets



Lines, Axes,
Angles

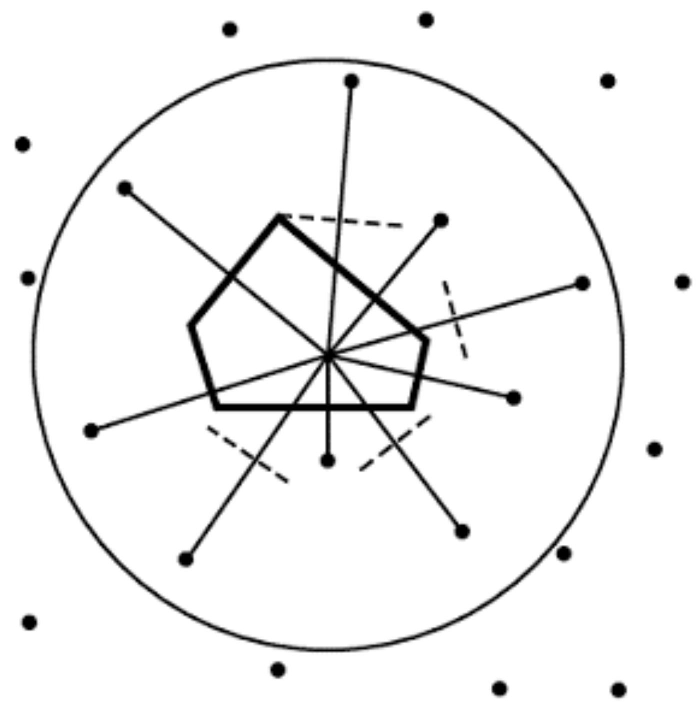


Surfaces, Volumes

Voronoi Volumes

Voronoi Volumes

- Each atom surrounded by a single convex polyhedron and allocated space within it
  - ◊ Allocation of all space (large V implies cavities)
- 2 methods of determination
  - ◊ Find planes separating atoms, intersection of these is polyhedron
  - ◊ Locate vertices, which are equidistant from 4 atoms



Voronoi Volumes, the Natural Way to Measure Packing

Packing Efficiency

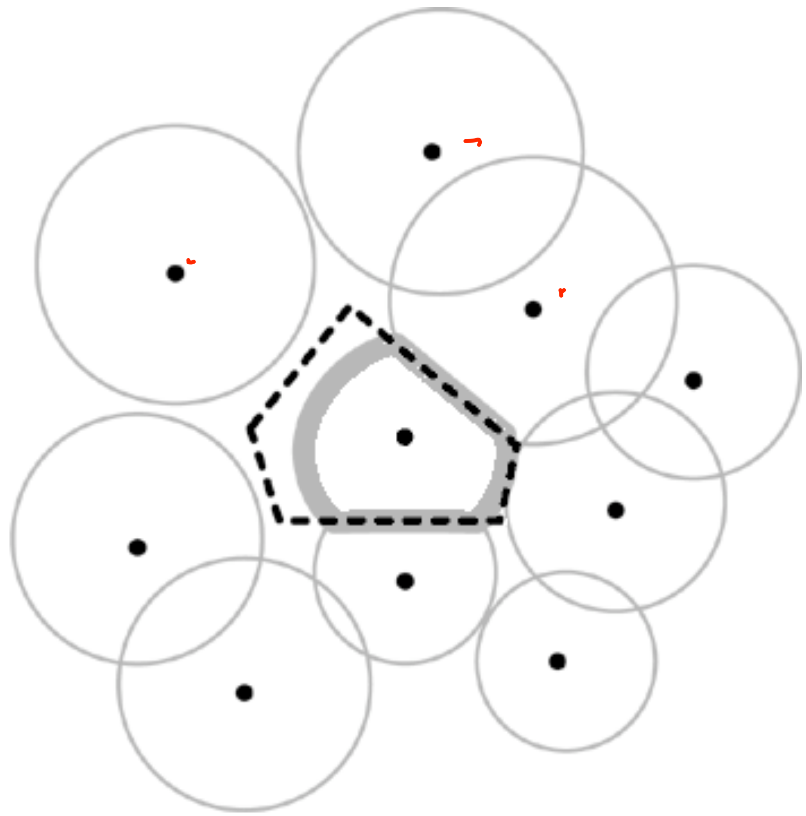
```
= Volume-of-Object
  ----------------
  Space-it-occupies
```

= V(VDW) / V(Voronoi)

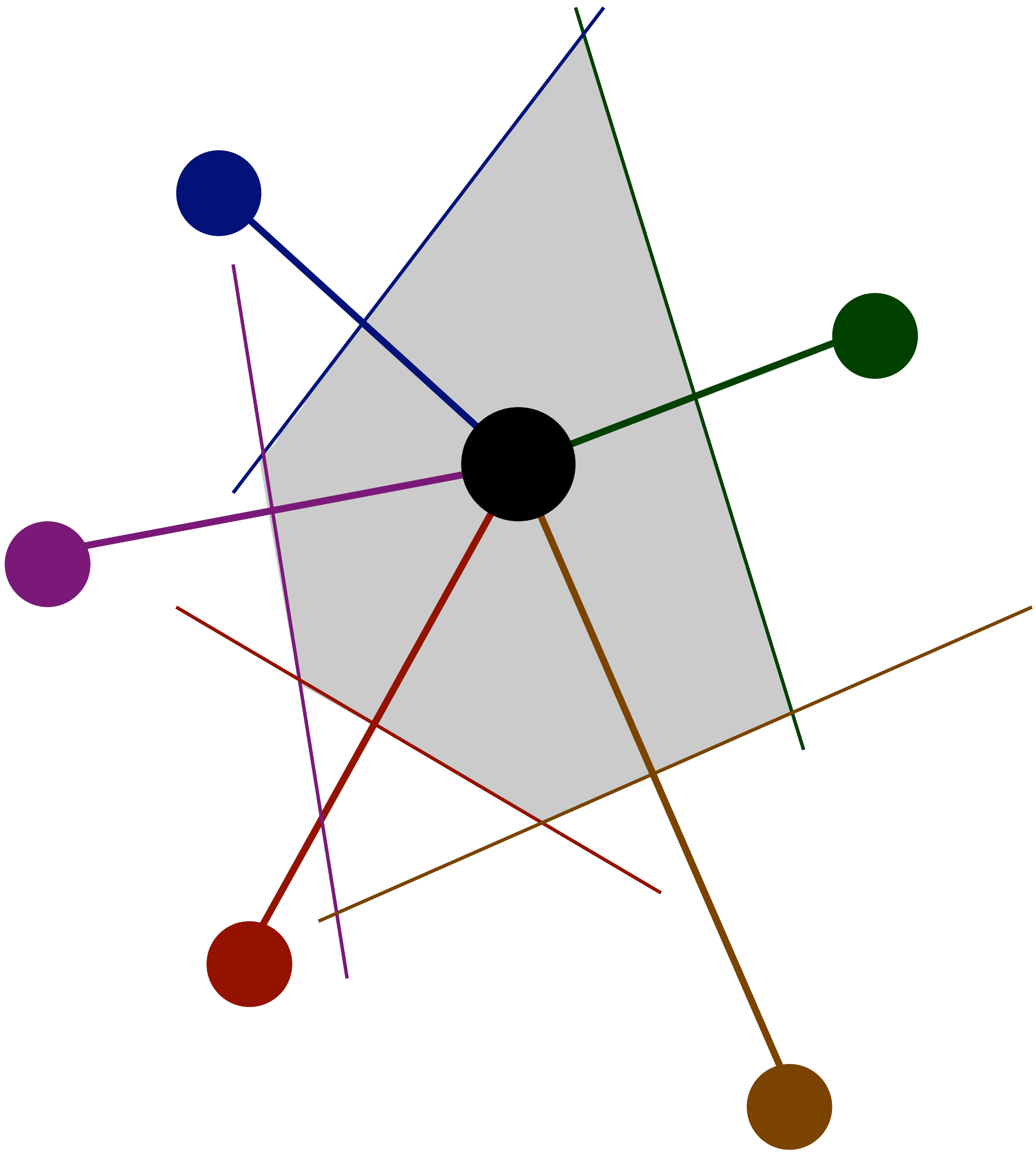
- Absolute v relative eff.

  V1 / V2

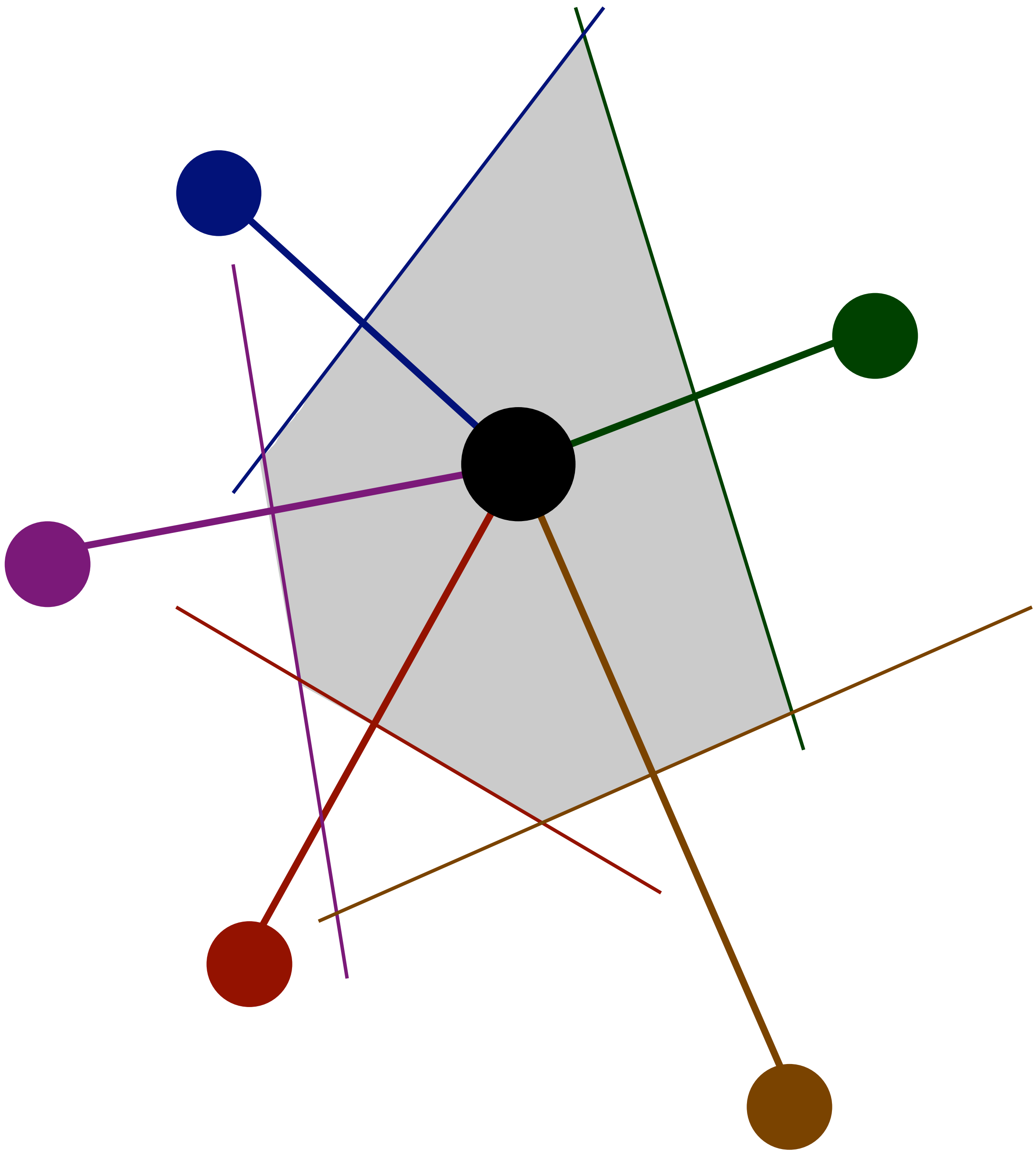
- Other methods
  - ◊ Measure Cavity Volume (grids, constructions, &c)



Voronoi Volumes



Voronoi Volumes



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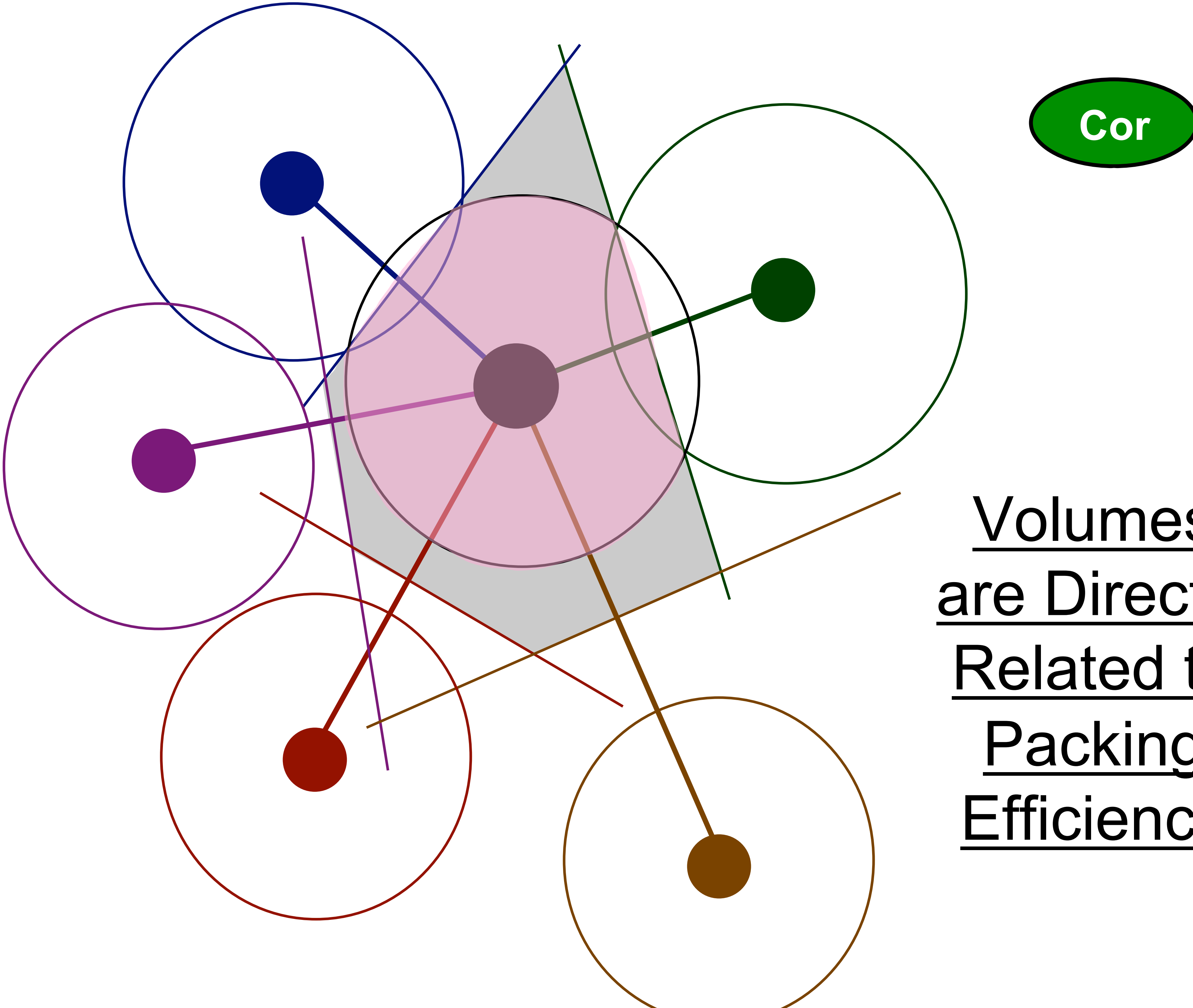
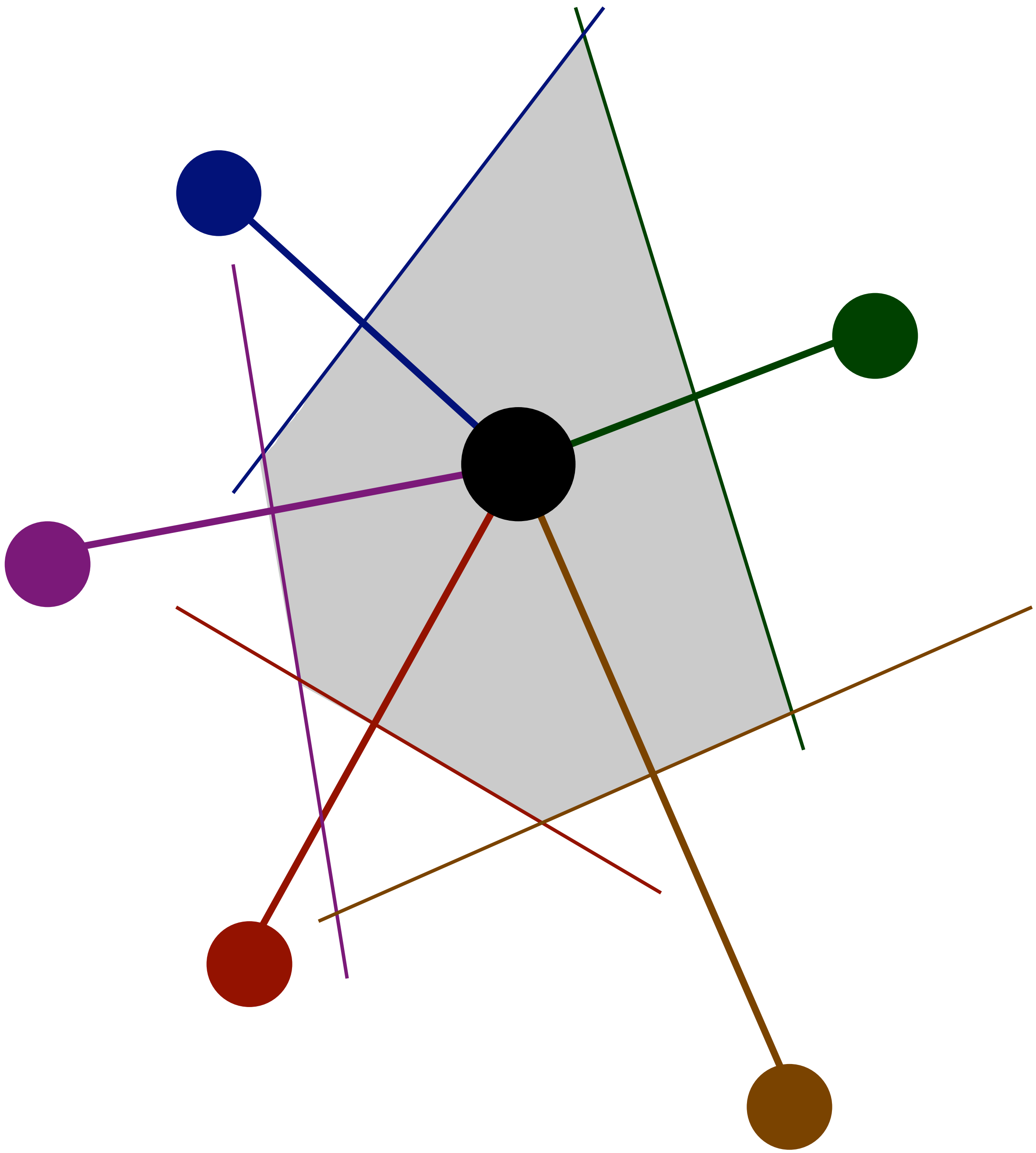


Volumes are Directly Related to Packing Efficiency

Voronoi Volumes



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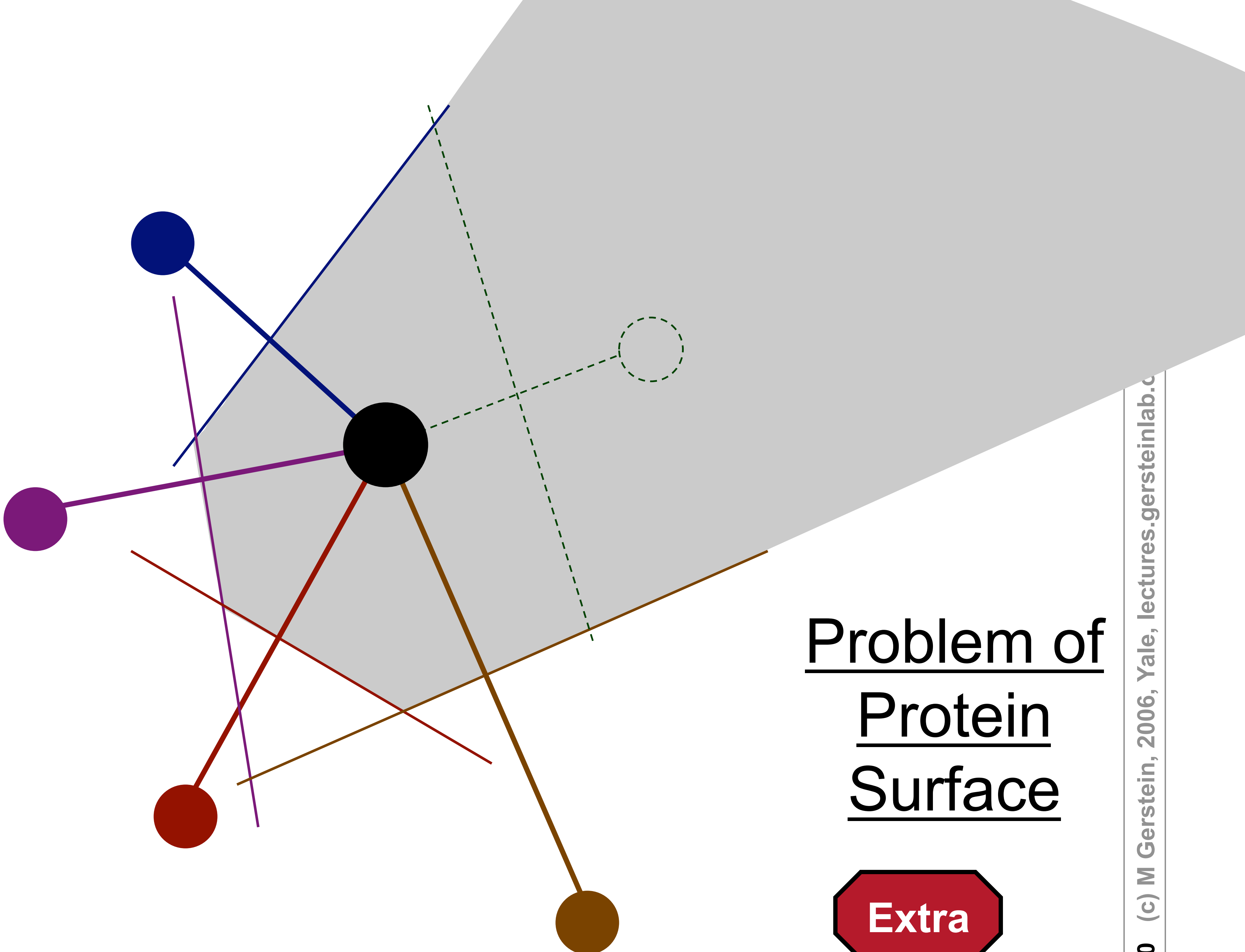
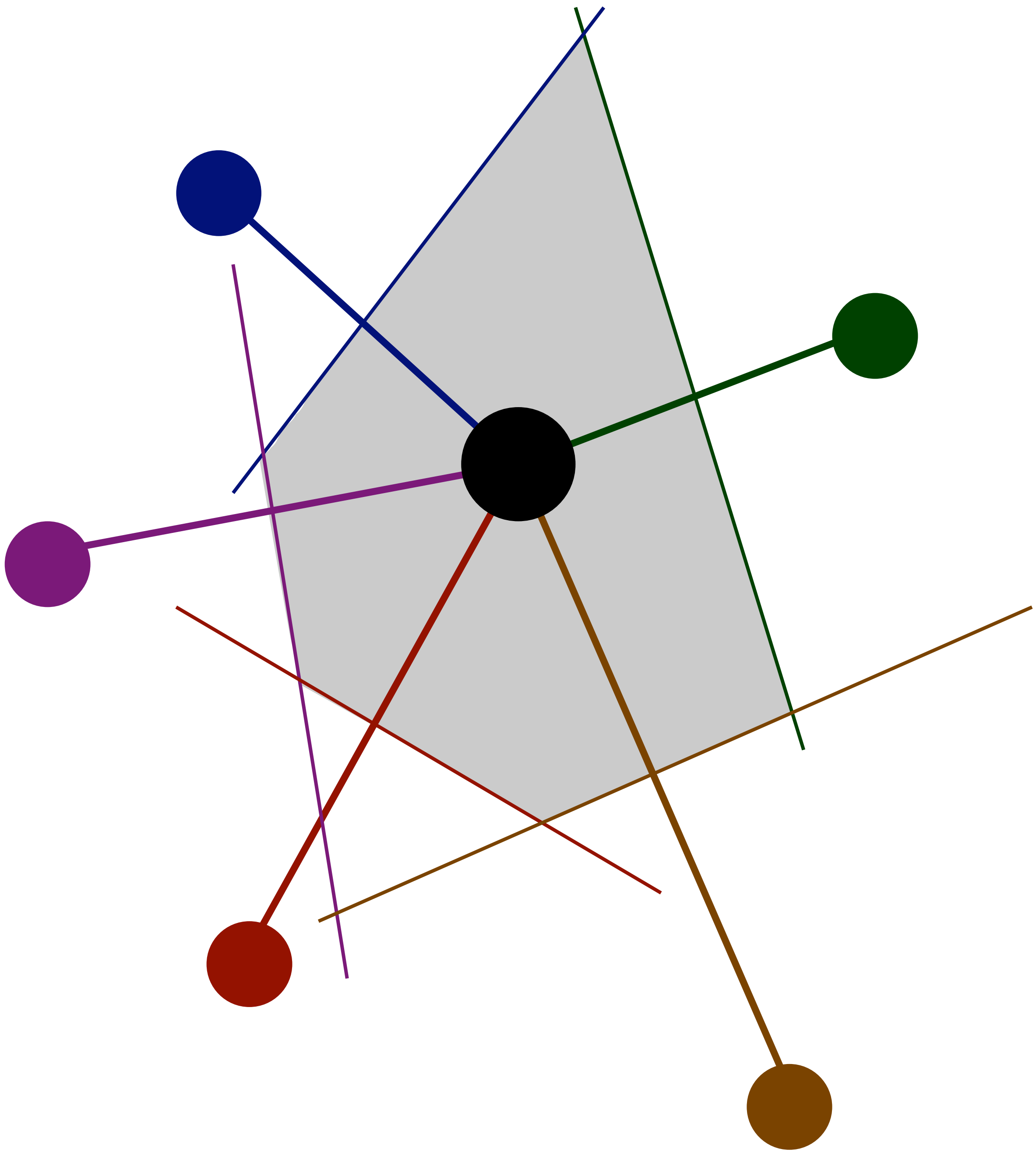


Problem of Protein Surface

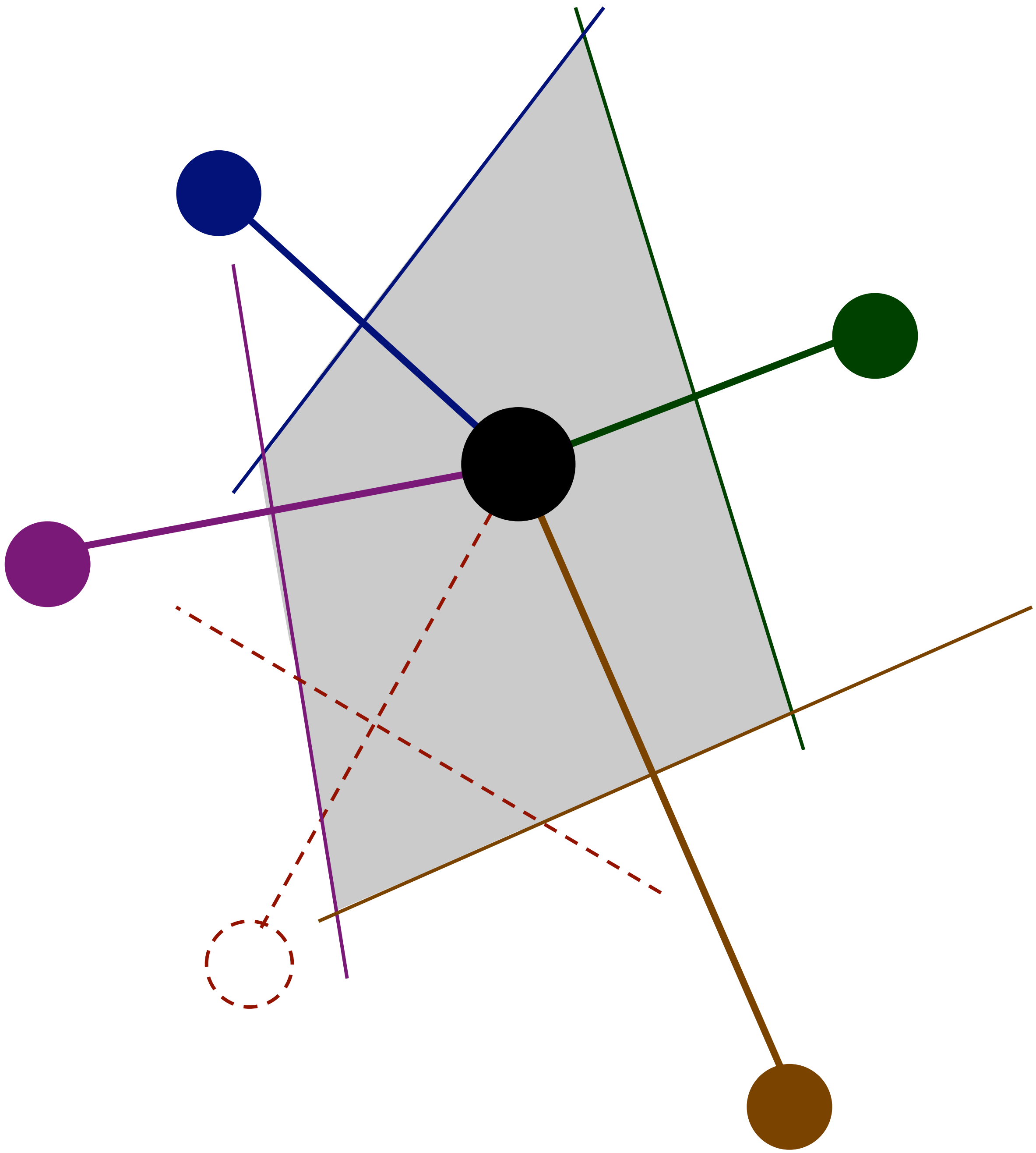
Extra

Voronoi Volumes



Extra

Missing Atoms Give Looser Packing



Extra

Classic Papers

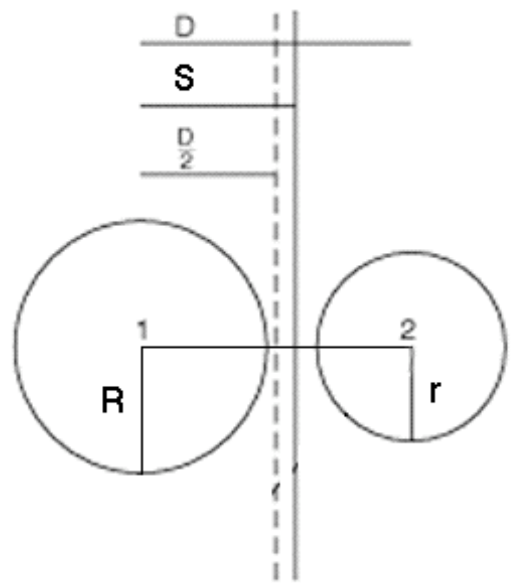
- Lee, B. & Richards, F. M. (1971). “The Interpretation of Protein Structures: Estimation of Static Accessibility,” *J. Mol. Biol*. **55**, 379-400.
- Richards, F. M. (1974). “The Interpretation of Protein Structures: Total Volume, Group Volume Distributions and Packing Density,” *J. Mol. Biol.* **82**, 1-14.
- Richards, F. M. (1977). “Areas, Volumes, Packing, and Protein Structure,” Ann. Rev. Biophys. Bioeng. 6, 151-76.

Voronoi diagrams are generally useful, beyond proteins

- .Nearest neighbor problems. The nearest neighbor of a query point in center of the Voronoi diagram in which it resides
- Largest empty circle in a collection of points has center at a Voronoi vertex
- Voronoi volume of "something" often is a useful weighting factor. This fact can be used, for instance, to weight sequences in alignment to correct for over or under-representation

Atoms have different sizes

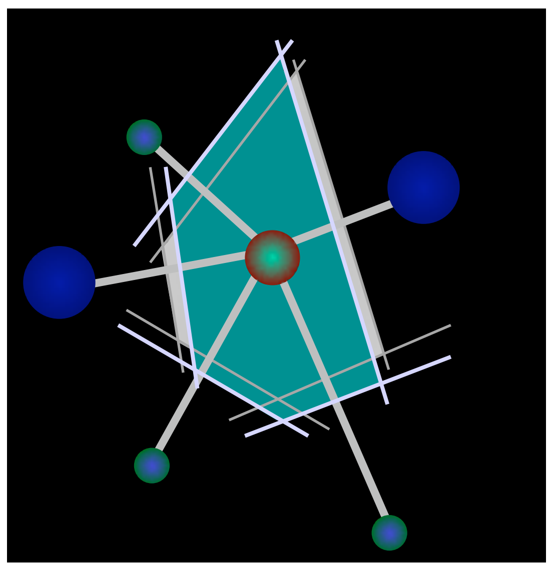
- Difficulty with Voronoi Meth. Not all atoms created equal
- Solutions
  - ◊ Bisection -- plane midway between atoms
  - ◊ Method B (Richards) Positions the dividing plane according to ratio
  - ◊ Radical Plane
- VDW Radii Set



Why Type the Atoms?

- Calculate Average Volumes
- Compare to Protein Atoms of Similar Type
- Allows for Modified Voronoi Volumes: Instead of Equidistant Planes, Use the Ratio of Their Radius

SOLVING SYS OF EQ TO GET VERTICES

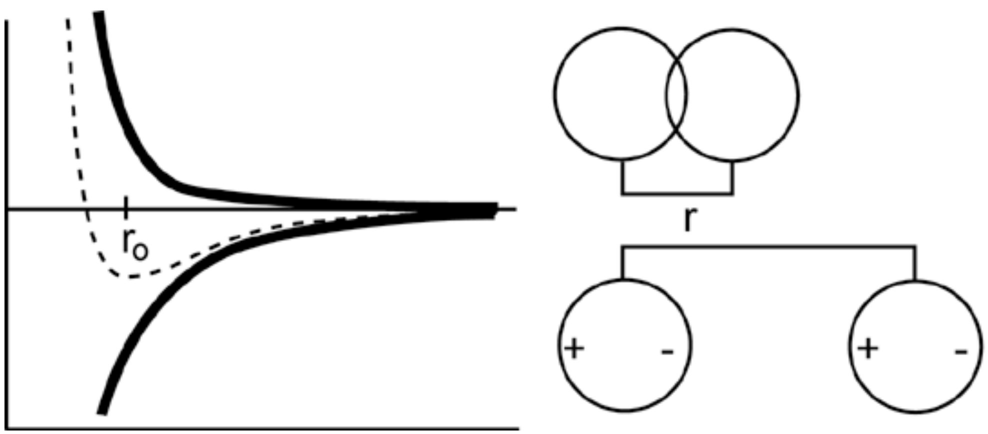


Courtesy of N Voss

Close Packing

Packing ~ VDW force

- Longer-range isotropic attractive tail provides general cohesion
- Shorter-ranged repulsion determines detailed geometry of interaction
- Billiard Ball model, WCA Theory

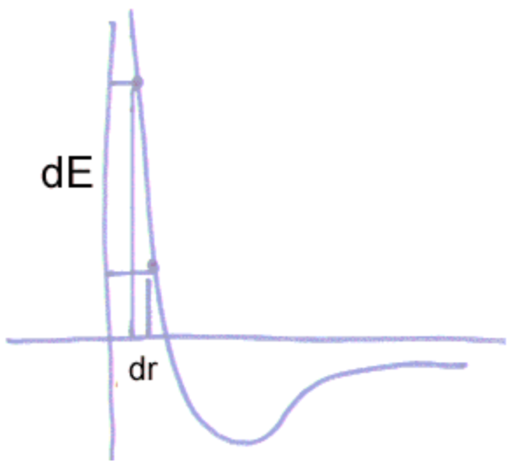


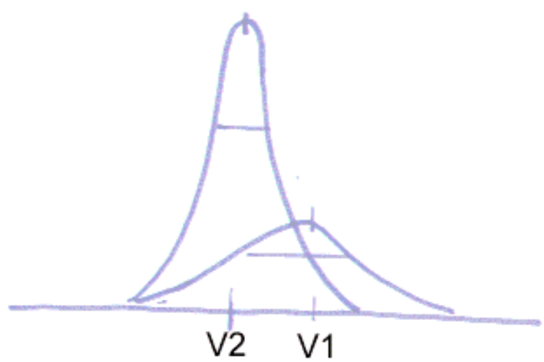
Electron Overlap Replusion $U = \varepsilon \left(\frac{r_0}{r}\right)^{12}$

Dispersion Attraction $U = -4\varepsilon \left(\frac{r_0}{r}\right)^{6}$

Small Packing Changes Significant

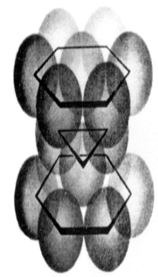
- Exponential dependence
- Bounded within a range of 0.5 (.8 and .3)
- Many observations in standard volumes gives small error about the mean (SD/sqrt(N))

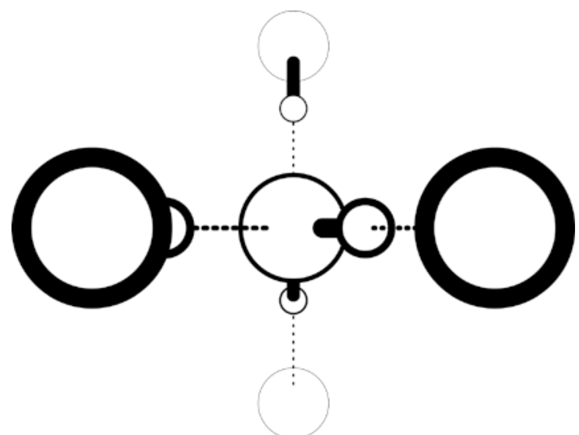




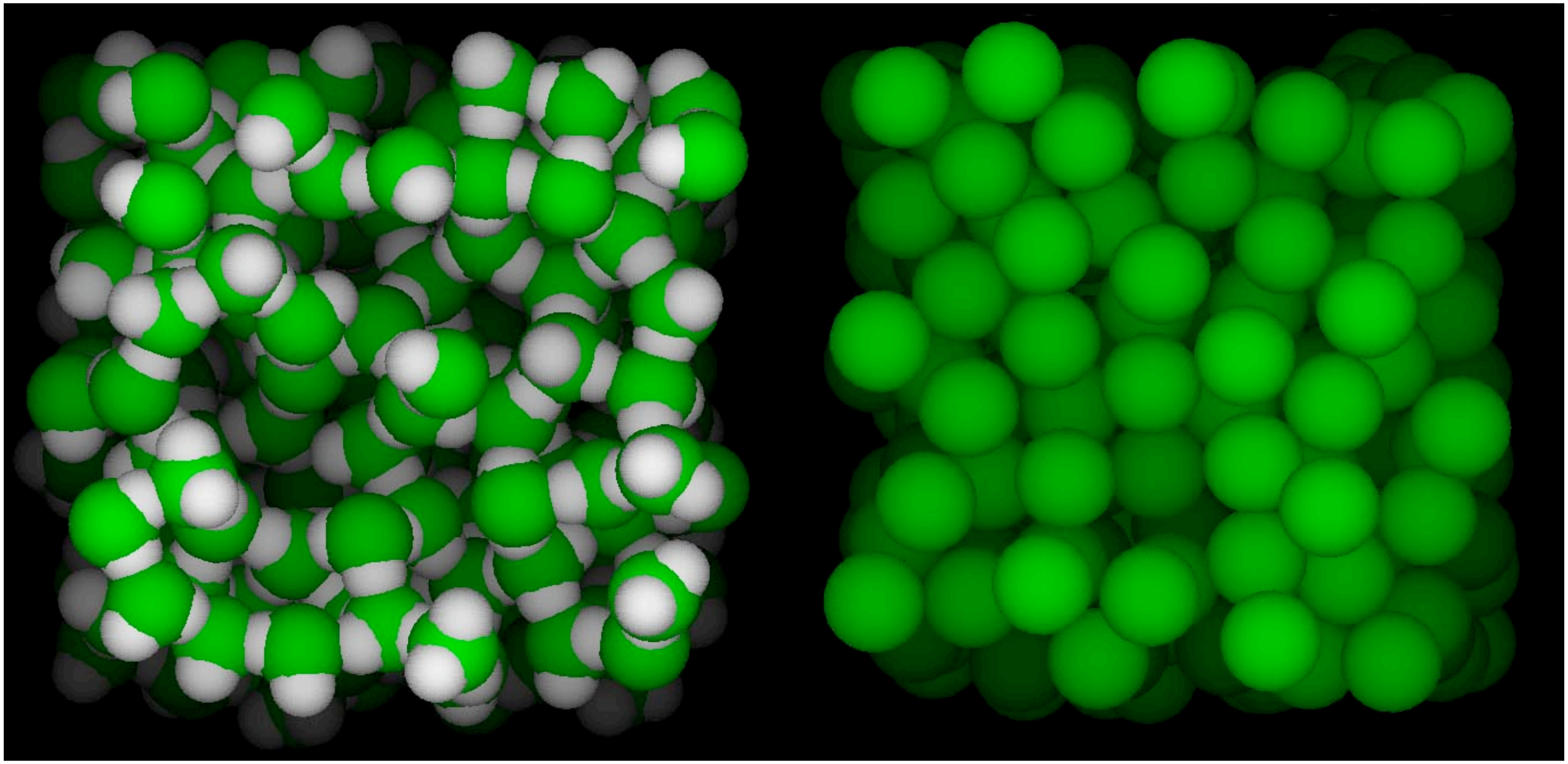
Close-packing is Default

- No tight packing when highly directional interactions (such as H-bonds) need to be satisfied
- Packing spheres (.74), hexagonal
- Water (~.35), “Open” tetrahedral, H-bonds





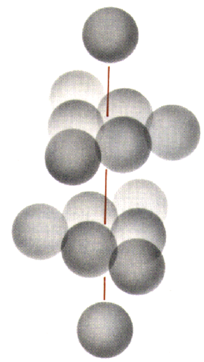
Water v. Argon

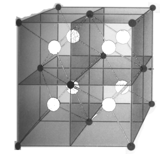


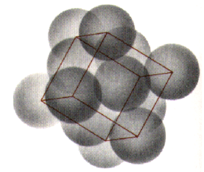
More Complex Systems -- what to do?

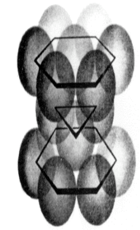
Close-Packing of Spheres

- Efficiency
  - ◊ Volume Spheres / Volume of space
- Close packed spheres
  - ◊ 74% volume filled
  - ◊ Coordination of 12
  - ◊ Two Ways of laying out
- Fcc
  - ◊ cubic close packing
  - ◊ ABC layers
- hcp
  - ◊ Hexagonally close packed
  - ◊ ABABAB









gives rise to face-centred unit cells, and so may also be denoted cubic F (or

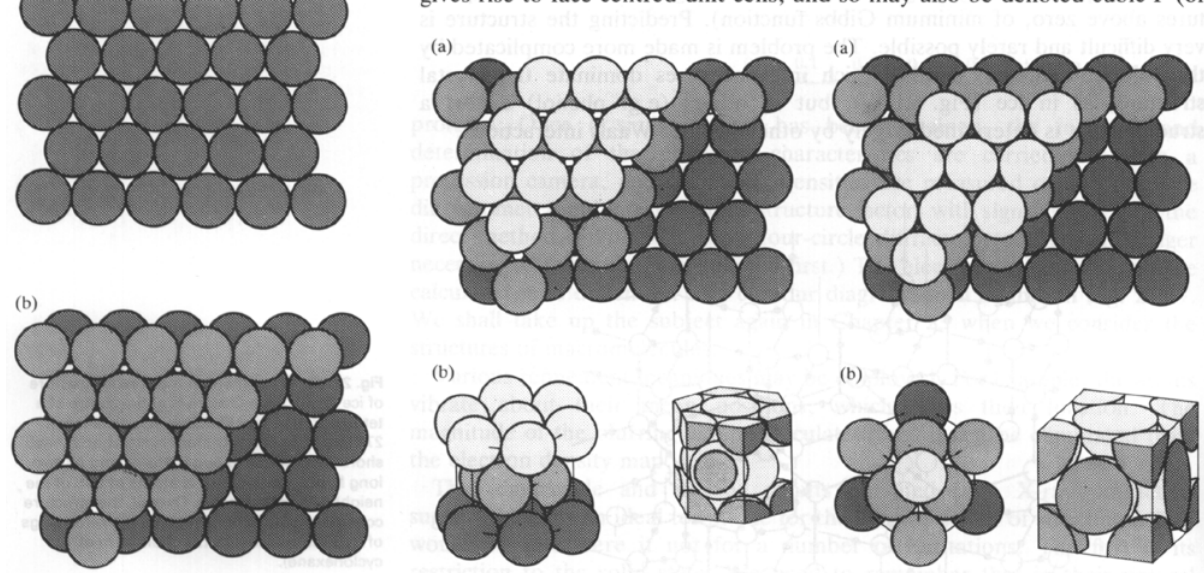


Fig. 21.20 The close-packing of identical spheres. (a) The first layer of close-packed spheres. (b) The second layer of close-packed spheres occupies the dips of the first layer. The two layers are the AB component of the structure.

Fig. 21.21 The third layer of close-packed spheres might occupy the dips lying directly above the spheres in the first layer, resulting in an ABA structure (a) which corresponds to hexagonal close-packing (b). This hcp structure is possessed by the elements Be, Cd, Co, He, Mg, Ti, and Zn.

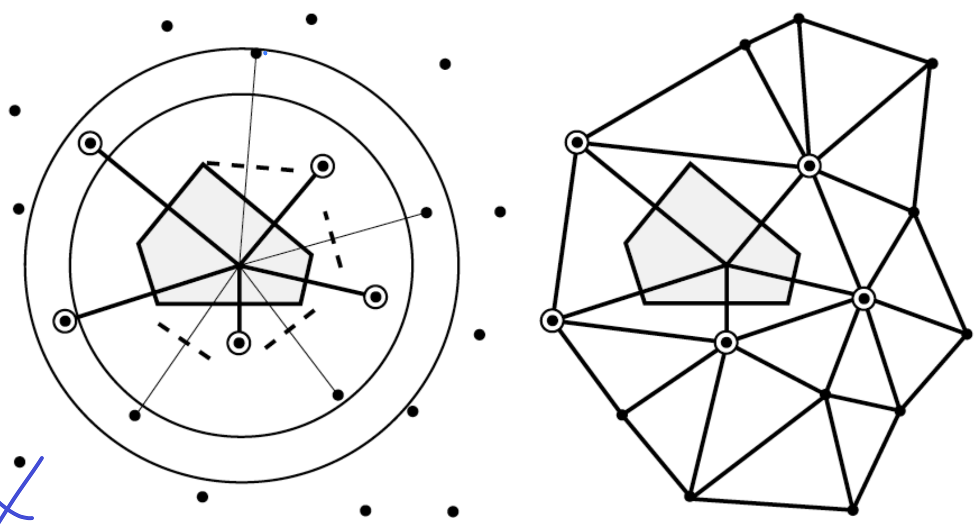
Fig. 21.22 Alternatively, the third layer might lie in the dips that are not above the spheres in the first layer, resulting in an ABC structure (a) which correspond to cubic close-packing (b). This ccp (or fcc) structure is possessed by the elements Ag, Al, Ar, Au, Ca, Cu, Ne, Ni, Pb, Pt, and Xe.

Illustration Credits: Atkins, Pchem, 634

The Protein Surface

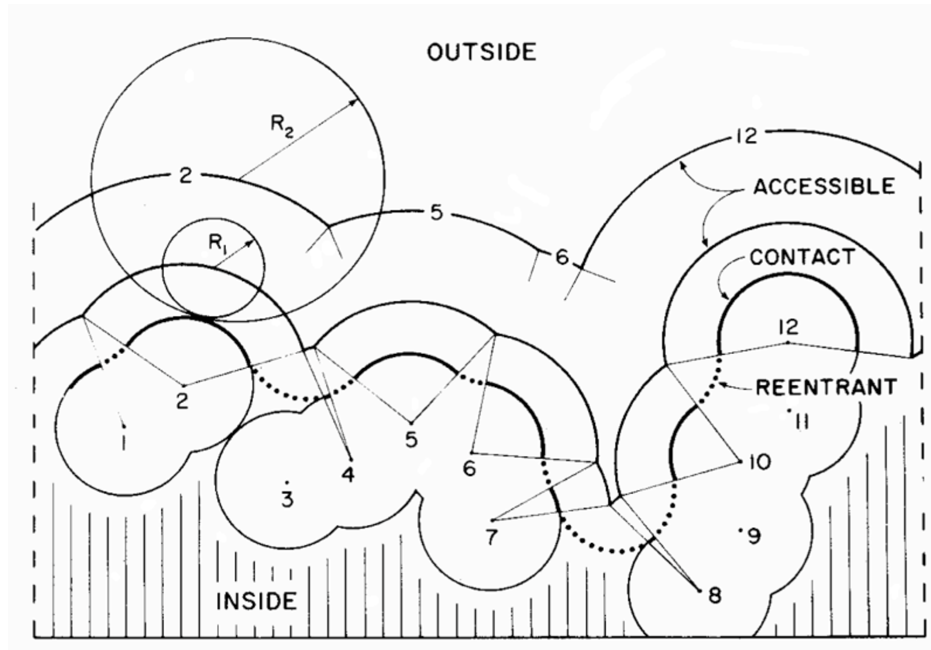
Delauney Triangulation, the Natural Way to Define Packing Neighbors

- Related to Voronoi polyhedra (dual)
- What "coordination number" does an atom have? Doesn't depend on distance
- alpha shape
- threading



CONVEX HULL

Richards' Molecular and Accessible Surfaces



Probe Radius	Part of Probe Sphere	Type of Surface
0	Center (or Tangent)	Van der Waals Surface (vdWS)
1.4 Å	Center	Solvent Accessible Surface (SAS)
""	Tangent (1 atom)	Contact Surface (CS, from parts of atoms)
""	Tangent (2 or 3 atoms)	Reentrant Surface (RS, from parts of Probe)
""	Tangent (1,2, or 3 atoms)	Molecular Surface (MS = CS + RS)
10 Å	Center	A Ligand or Reagent Accessible Surface
∞	Tangent	Minimum limit of MS (related to convex hull)
""	Center	Undefined

Cor

MS

ASA

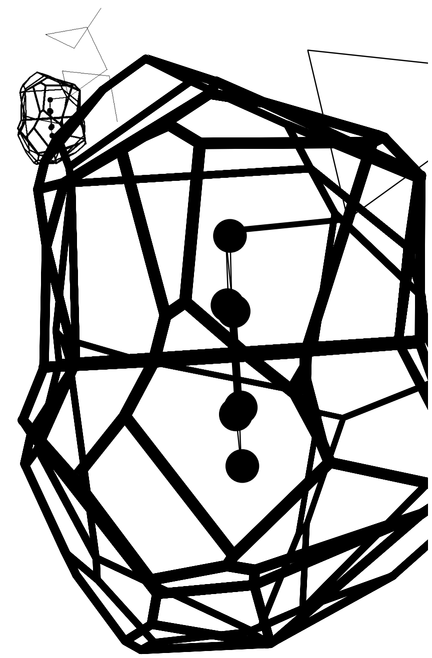
VDW

Packing defines the "Correct Definition" of the Protein Surface

- Voronoi polyhedra are the *Natural* way to study packing!
- How reasonable is a geometric definition of the surface in light of what we know about packing
- The relationship between
  - ◊ accessible surface
  - ◊ molecular surface
  - ◊ Delauney Triangulation (Convex Hull)
  - ◊ polyhedra faces
  - ◊ hydration surface

Properties of Voronoi Polyhedra

- Voronoi volume of an atom is a weighted average of distances to all its neighbors, where the weighting factor is the contact area with the neighbor.

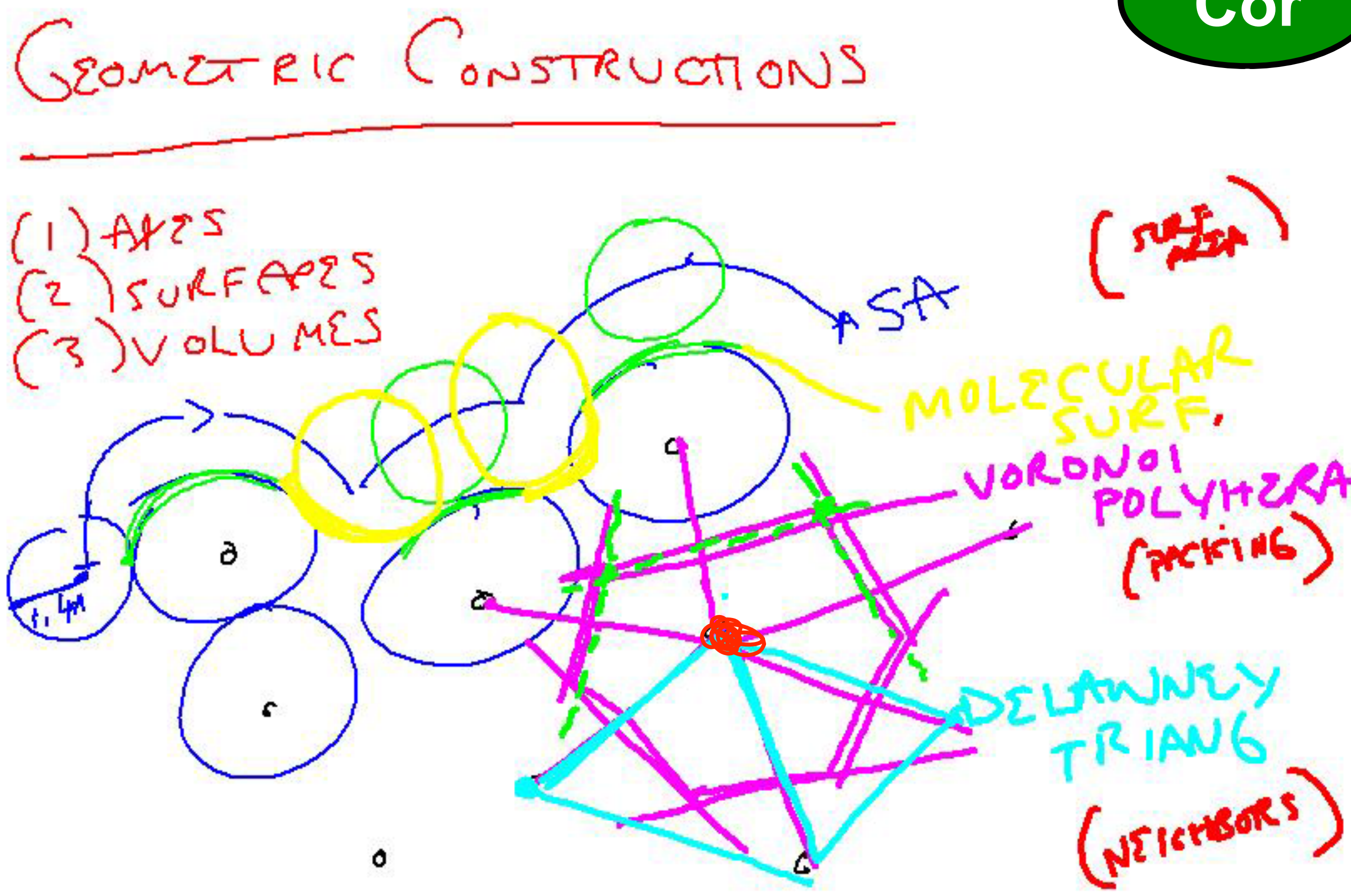


Voronoi diagrams are generally useful, beyond proteins

- Border of D.T. is Convex Hull
- D.T. produces "fatest" possible triangles which makes it convenient for things such as finite element analysis.

Summary of Geometric Constructions

Cor



End of class M7 [2006,11.17]