

Visual Analysis of Biomolecular Surfaces

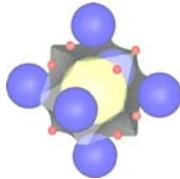
**by Vijay Natarajan¹, Patrice Koehl², Yusu Wang³ and
Bernd Hamann³**

**In: Visualization in Medicine and Life Sciences,
Lars Lisen, Hans Hagen (Eds.), Springer, 2007**

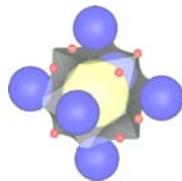
- 1: Indian Institute of Science, India**
- 2: University of California, USA**
- 3: The Ohio State University, USA**

**2008년 7월24일
발표자: 유중현**

Biomolecules and their shapes

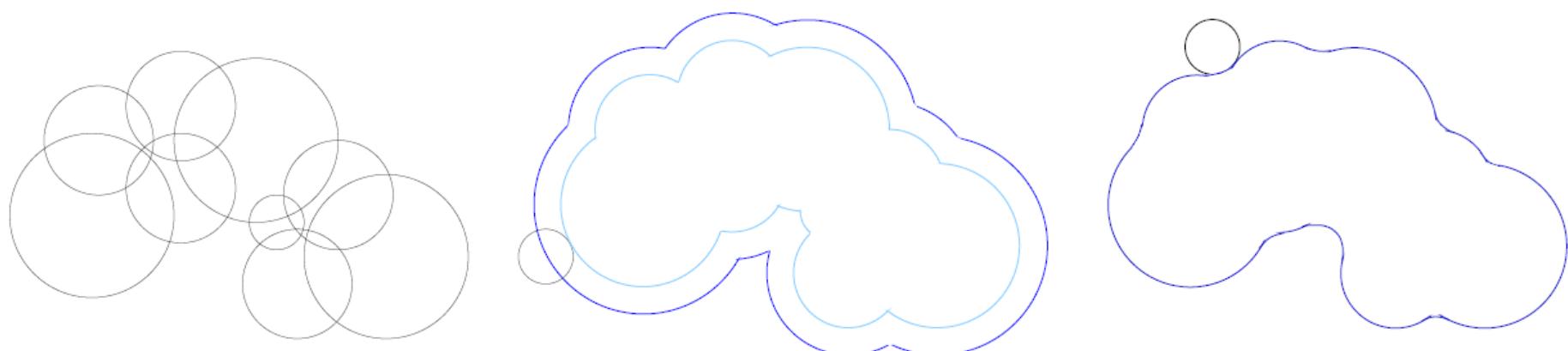


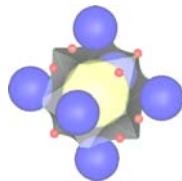
- **Activity of biological macromolecules**
 - DNA, RNA, carbohydrates, lipids and proteins
- **Significance of shape**
 - Protein complex formation
 - Folding rate of small proteins
 - Catalytic activity of enzymes
 - Tolerance to mutation of a protein
- **Topology → geometry or shape**



Biomolecular surface

- Van der Waals surface
- Solvent accessible surface
- Molecular surface (Solvent excluded surface or Connolly surface)

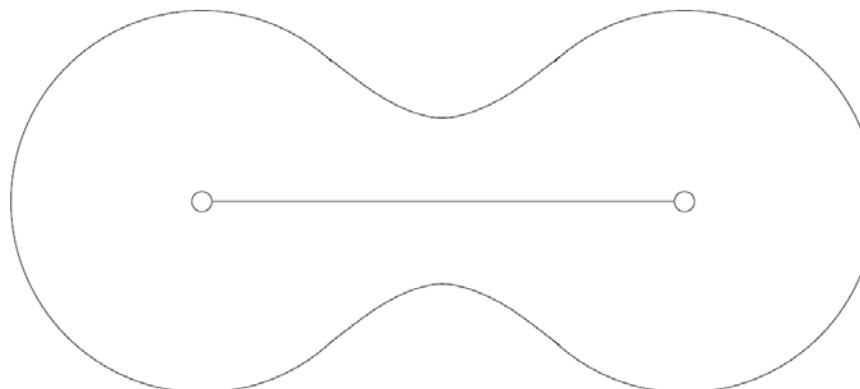
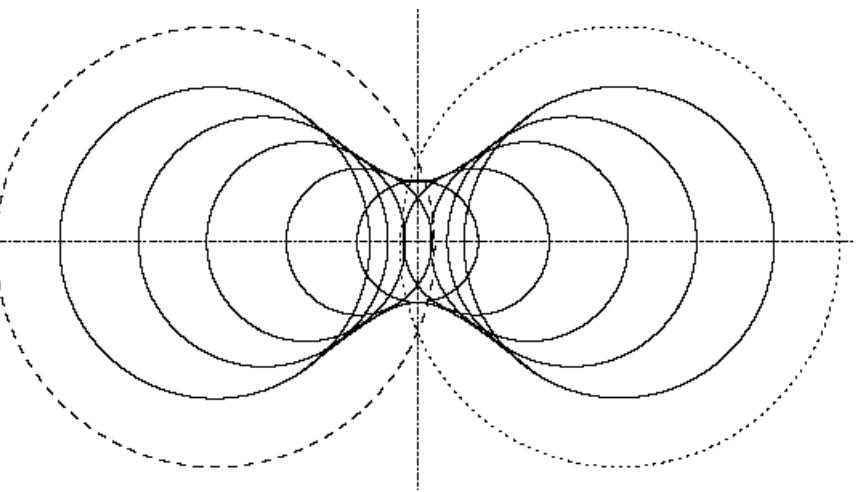
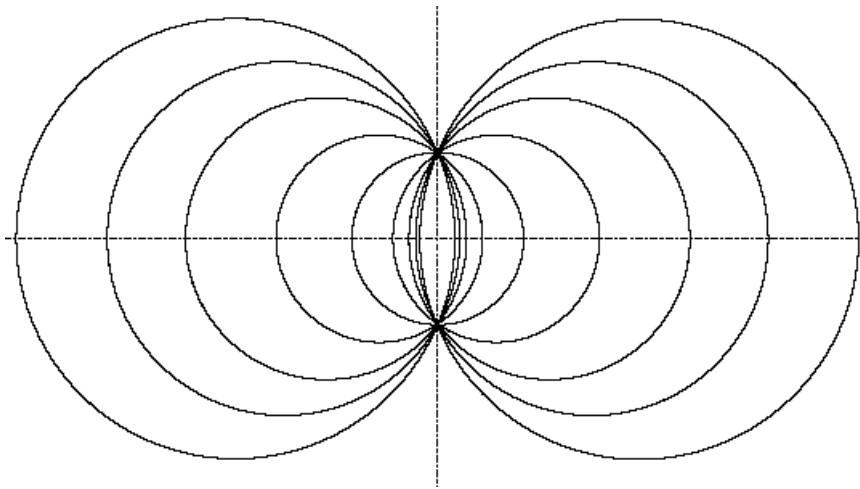




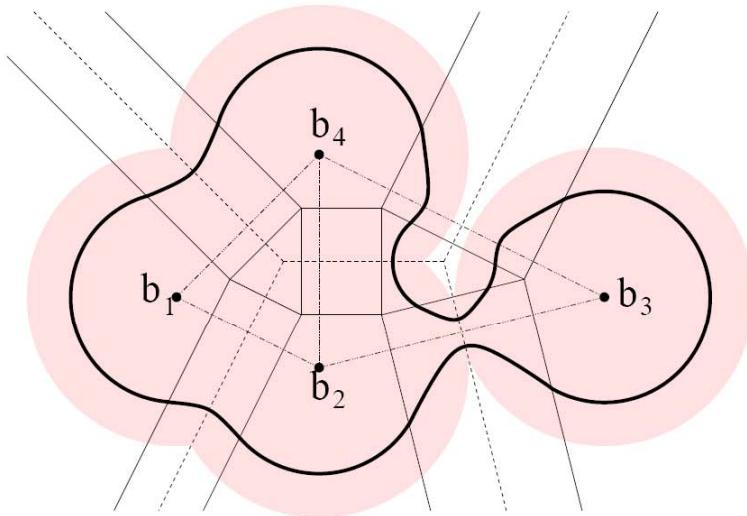
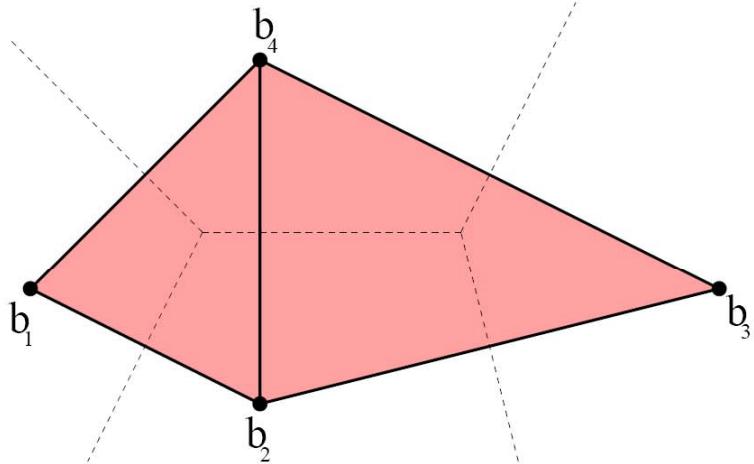
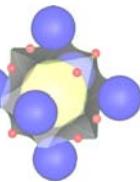
Biomolecular surface

■ Skin

$$\text{skin}(B) = \partial(\bigcup \sqrt{\text{conv}(B)})$$

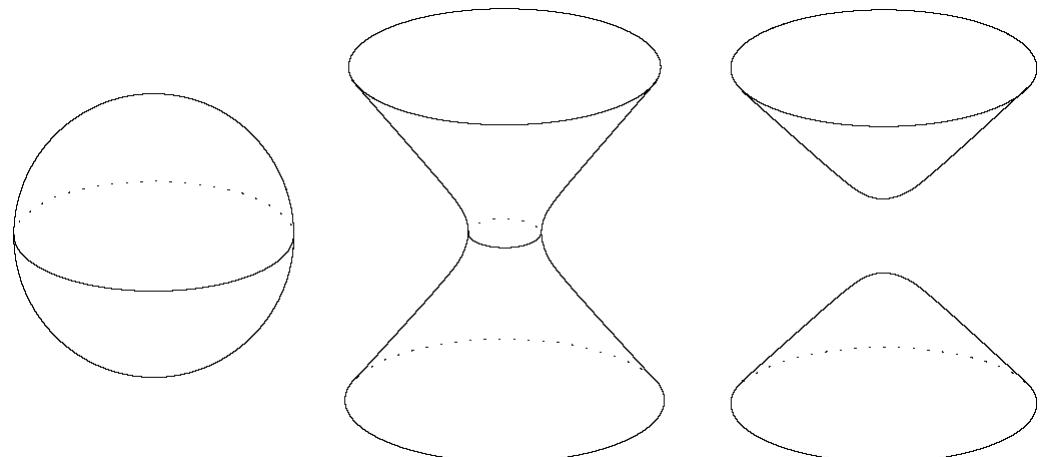


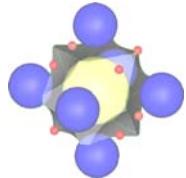
Decomposition by mixed complex



(a) V_0 and D_0 of B_0 .

(b) The skin of B_0 .



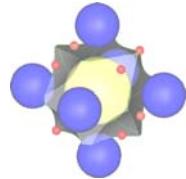


Solvation model

- Solvent molecule is needed
 - Stable conformation in water
 - Molecular dynamics
 - Explicit solvent molecule
- Inefficiency and Inadequacy of the model
- Solvation energy (potential)

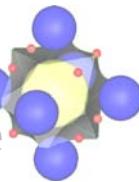
$$W = W_{elec} + W_{np}$$

Solvation model



- W_{elec} : Polar effect (electrostatic polarization)
 - Poisson-Boltzmann eq. : cubic lattice/boundary for dielectric const. → SAS or MS
- W_{np} : Nonpolar effect (hydrophobic effect)
 - $W_{nn} = W_{vdw} + W_{cav}$
 - $W_{np} = \sum_i \alpha_i A_i$
- Area and/or volume of a surface
- Derivative of solvation energy

Visualization for analysis of a molecule



Surface Potential -10.000 -5.000 0.000 5.000 10.000 >-<

$$f_i : M \rightarrow \mathbb{R}$$

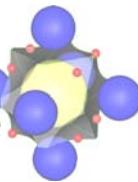
a domain M

scalar functions f_1, \dots, f_k

M : (*Triangular*) mesh

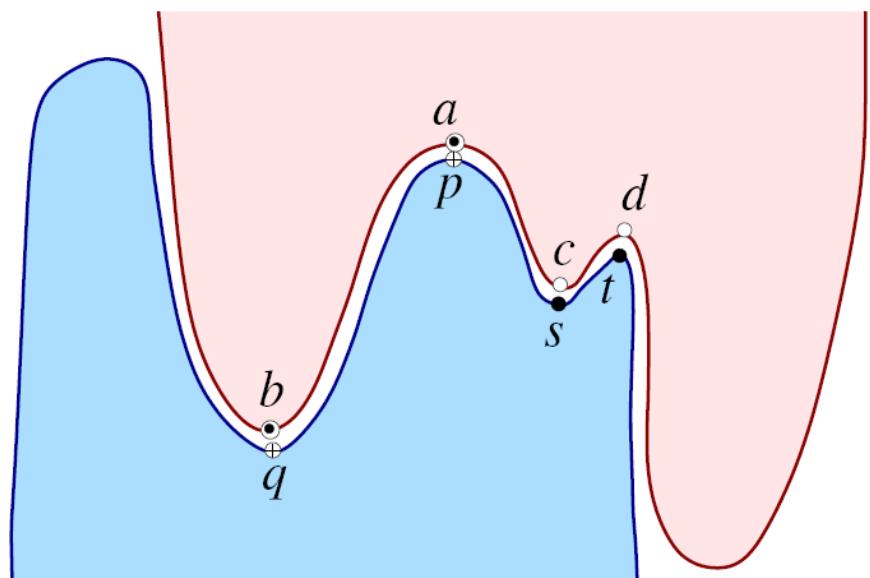
AChE (1ACL.PDB) color coded by electrostatic potential with GRASP.
http://wiki.c2b2.columbia.edu/honiglab_public/index.php/Software:GRASP

Visualization for analysis of a molecule

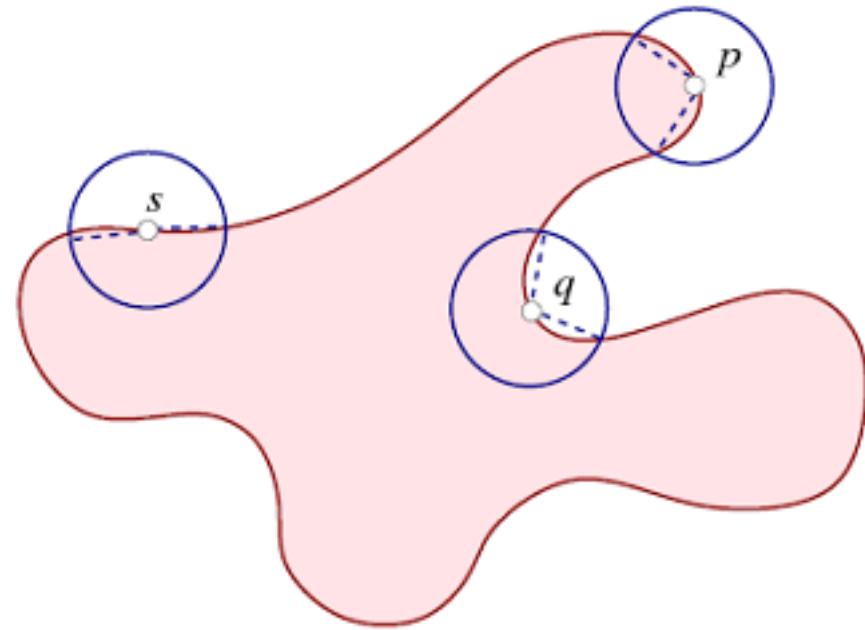
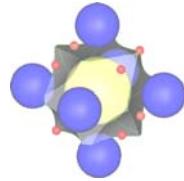


■ Descriptor function

- physicochemical
 - Electrostatic potential
 - Local lipophilicity
 - Hydrogen bond donor/acceptor density
- Geometric (shape)
 - Local/global descriptor



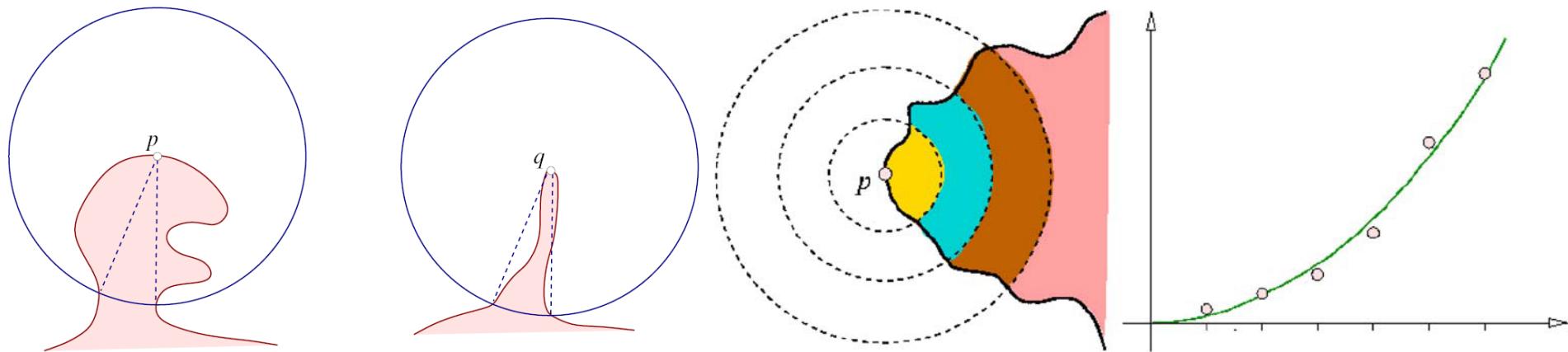
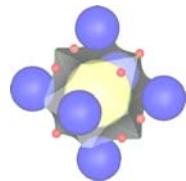
Local descriptor



- Connolly function
 - Solid angle

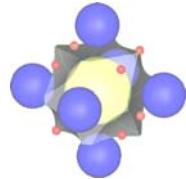
$$f_r(x) = \frac{\text{Area}(S_I)}{r^2}$$

Local descriptor

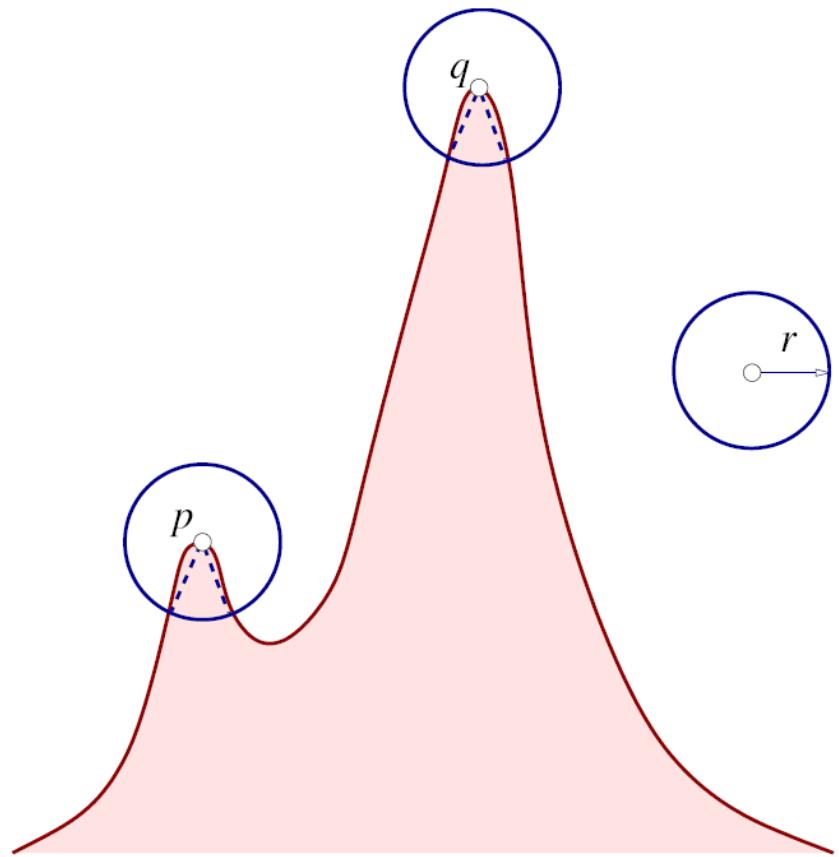


- **Atomic density function**
 - Sequences of Connolly functions

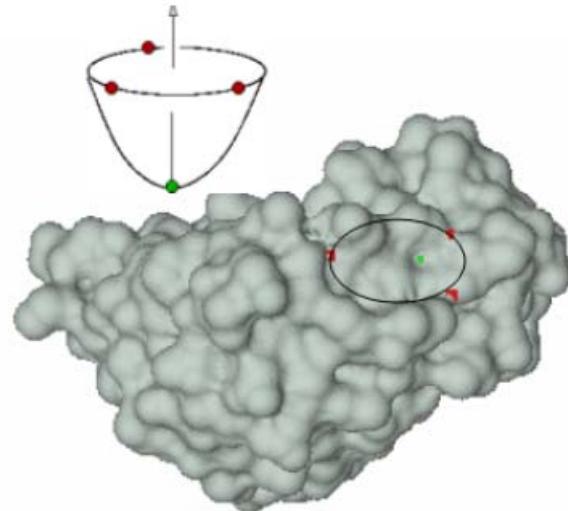
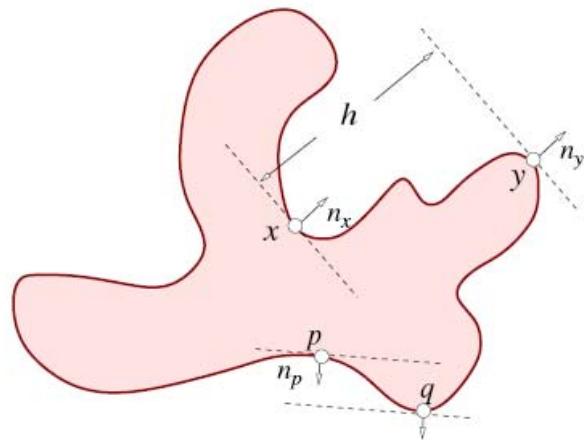
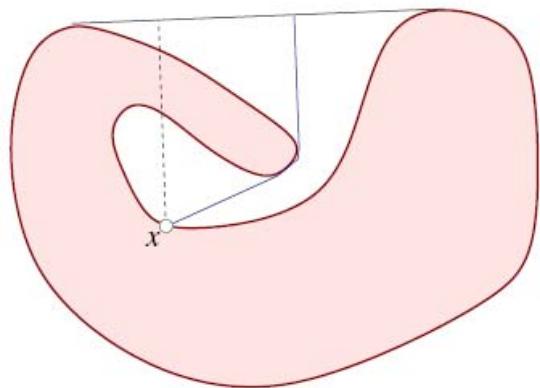
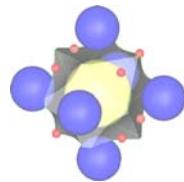
Global descriptor



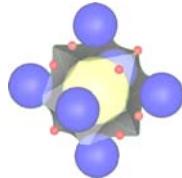
- Demerits of local descriptor
 - Fixed parameter
 - The size of features



Global descriptor

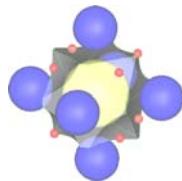


- $f_c(x) = \begin{cases} 0, & \text{if } x \in \text{CH}(\mathbb{M}) \\ d(x, \text{Cover}(\mathbb{M})), & \text{otherwise} \end{cases}$
- **Collision-free shortest path**
- **Elevation function**

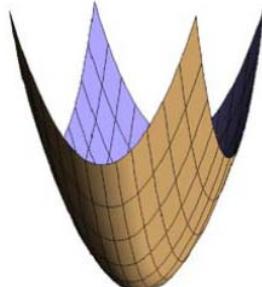
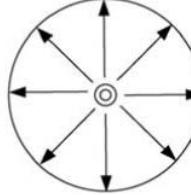
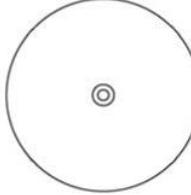
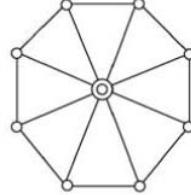
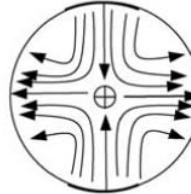
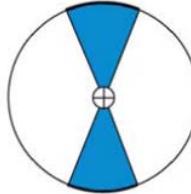
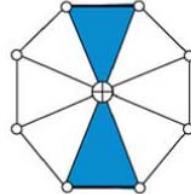
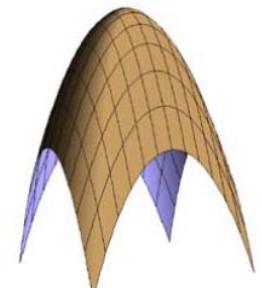
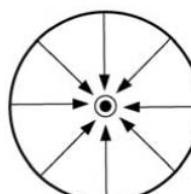
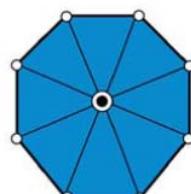


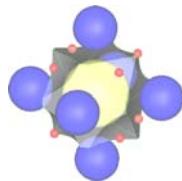
Visualization of descriptors

- **Highlight feature points**
 - Critical points
- **Segment the surface into meaningful regions**
 - Region-growing
 - Seed/Merging/splitting
 - Topological methods
 - Morse theory



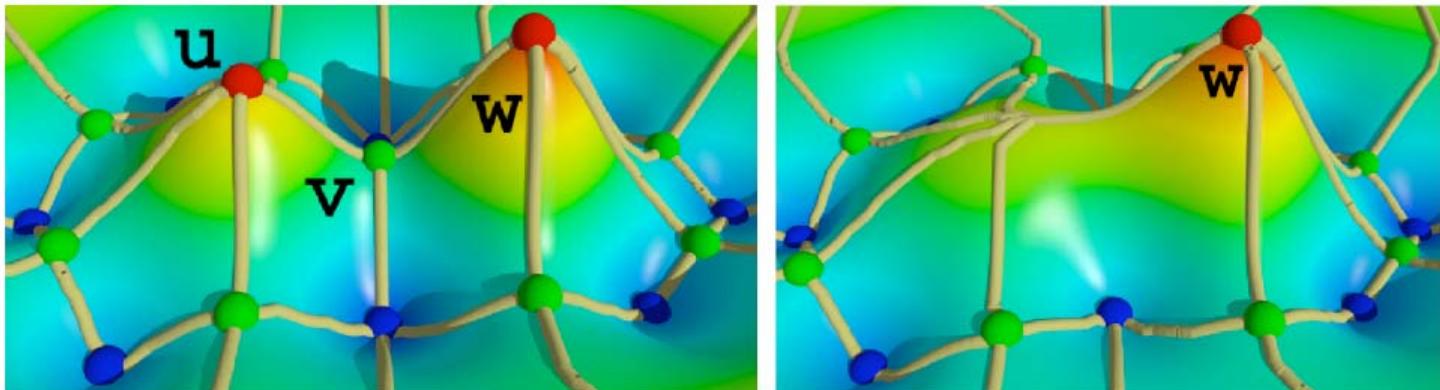
Morse theory

| Local quadric approximation | Gradient flow | ϵ -neighborhood | Lower link |
|---|---|---|---|
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

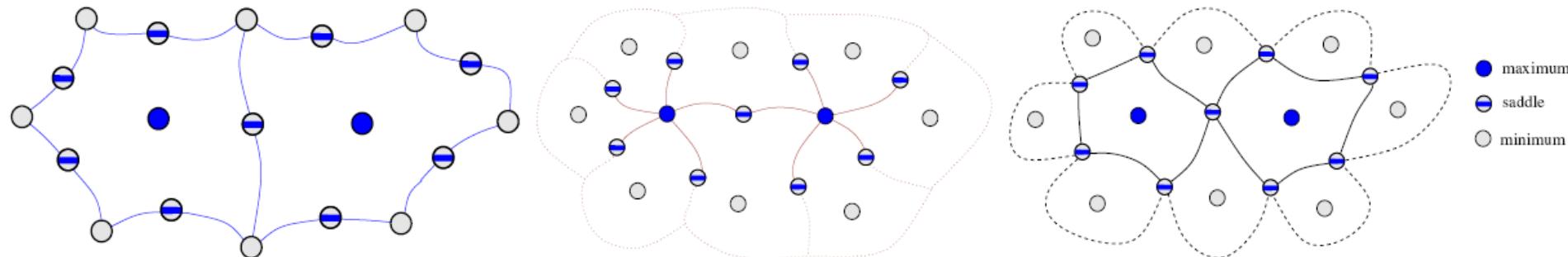


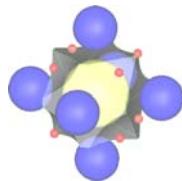
Visualization of descriptors

- Topological methods
 - Morse-Smale complex



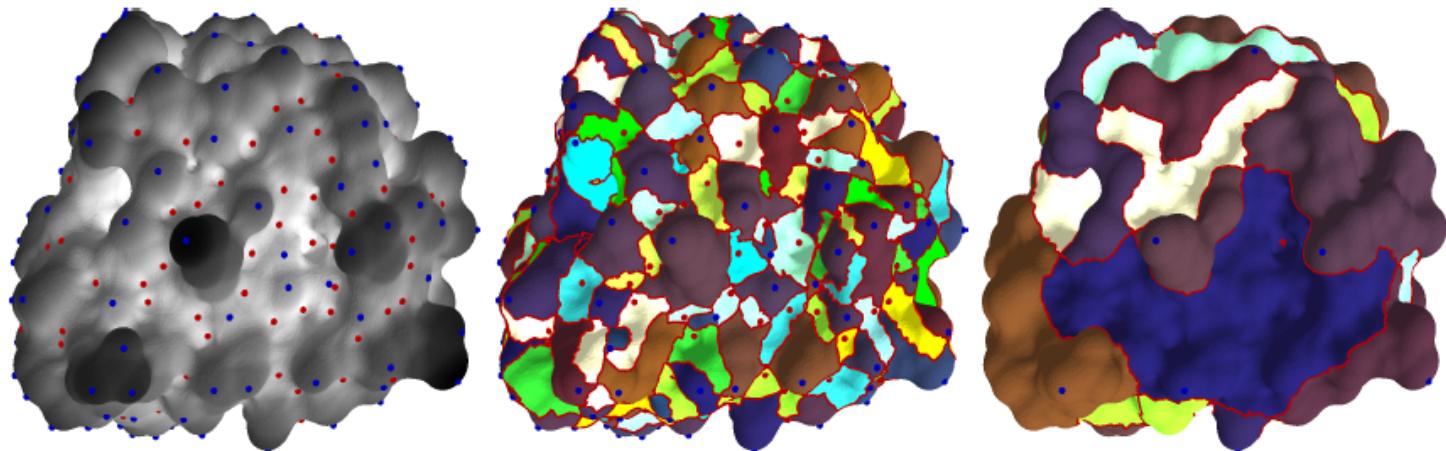
- Morse complex



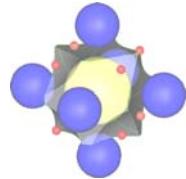


Visualization of descriptors

- Segment the surface at multiple levels of details

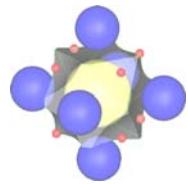


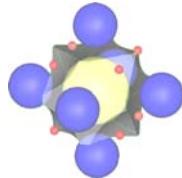
Conclusion



- **Solvation model**
 - Solvation energy
- **No universally good descriptor**
 - Meaningful and easy-to-computable descriptor
- **Visualization of descriptor**
 - Region-growing
 - Topology-based
- **Future direction**
 - Application of the methods to dynamic case

Back-ups





Spheres lifted to points

$$\pi_p(x) = \|x - z_p\|^2 - w_p = 0$$

$$z_p = (\zeta_{p1}, \zeta_{p2}, \zeta_{p3})$$

$$p = (z_p, \sqrt{w_p})$$

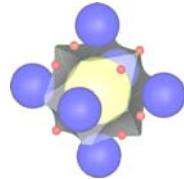
$$\Pi : \mathbf{R}^3 \times \mathbf{R} \rightarrow \mathbf{R}^4$$

$$\Pi(p) = (\zeta_{p1}, \zeta_{p2}, \zeta_{p3}, \|z_p\|^2 - w_p)$$

$$\varpi(x) = ||x||$$

$$\text{where } w_p = 0$$

Operations among spheres



$\Pi(\cdot) \in \mathbf{R}^4$: *vectorspace*

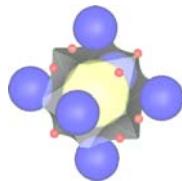
$$\Pi(p) = (\zeta_{p1}, \zeta_{p2}, \zeta_{p3}, \|z_p\|^2 - w_p)$$

$$\Pi(q) = (\zeta_{q1}, \zeta_{q2}, \zeta_{q3}, \|z_q\|^2 - w_q)$$

To define $p + q$ and $\gamma \cdot p$ so that

$$\Pi(p + q) = \Pi(p) + \Pi(q)$$

$$\Pi(\gamma \cdot p) = \gamma \cdot \Pi(p)$$



Sphere algebra

$$p + q = (z_{p+q}, w_{p+q}) \quad (1)$$

$$z_{p+q} = z_p + z_q$$

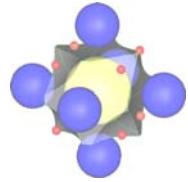
$$w_{p+q} = w_p + w_q + 2 \langle z_p, z_q \rangle$$

$$\gamma \cdot p = (z_{\gamma \cdot p}, w_{\gamma \cdot p}) \quad (2)$$

$$z_{\gamma \cdot p} = \gamma \cdot z_p$$

$$w_{\gamma \cdot p} = \gamma \cdot w_p + (r^2 - r) \cdot \|z_p\|^2$$

Sphere algebra



Linear combination of spheres

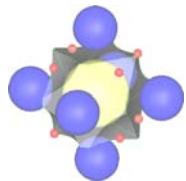
$$PLC = \sum_i \gamma_i \cdot p_i$$

$$\text{where } p_i = (z_{p_i}, \sqrt{w_{p_i}})$$

Change of sphere size

$$p^s = (1 - s) \cdot p' + s \cdot p$$

$$\text{where } p = (z_p, \sqrt{w_p}) \quad p' = (z_p, 0)$$



Sphere algebra

$$p_{LC} = \sum_i \gamma_i \cdot p_i \quad (1)$$

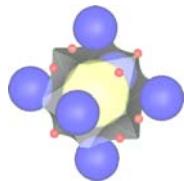
$$z_{p_{LC}} = \sum_i \gamma_i \cdot z_{p_i}$$

$$w_{p_{LC}} = \sum_i \gamma_i \cdot w_{p_i} + \left\| \sum_i \gamma_i \cdot z_{p_i} \right\|^2 - \sum_i \gamma_i \cdot \|z_{p_i}\|^2$$

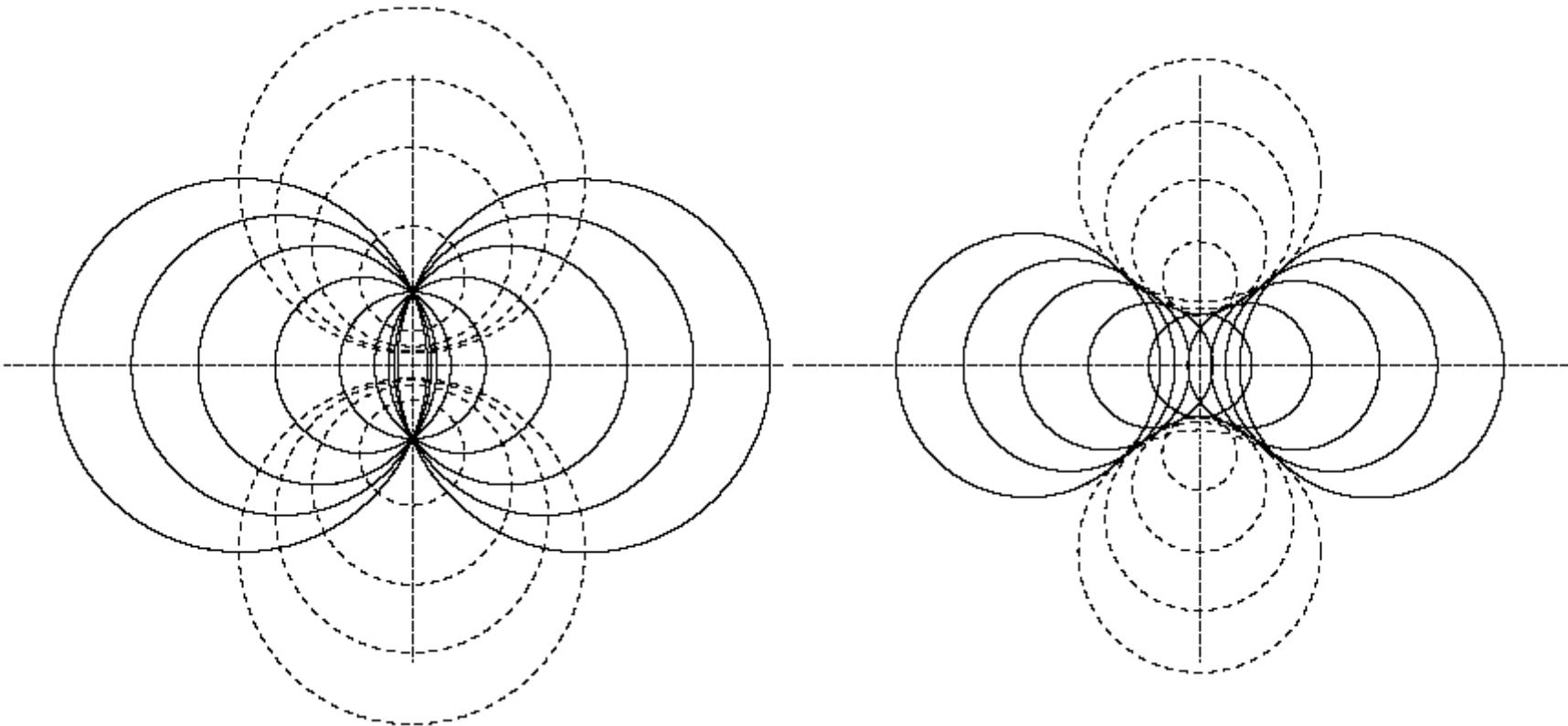
$$p^s = (1 - s) \cdot p' + s \cdot p \quad (2)$$

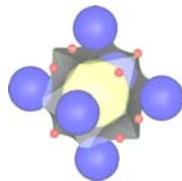
$$z_{p^s} = z_p \quad w_{p^s} = s \cdot w_p$$





Complementarity

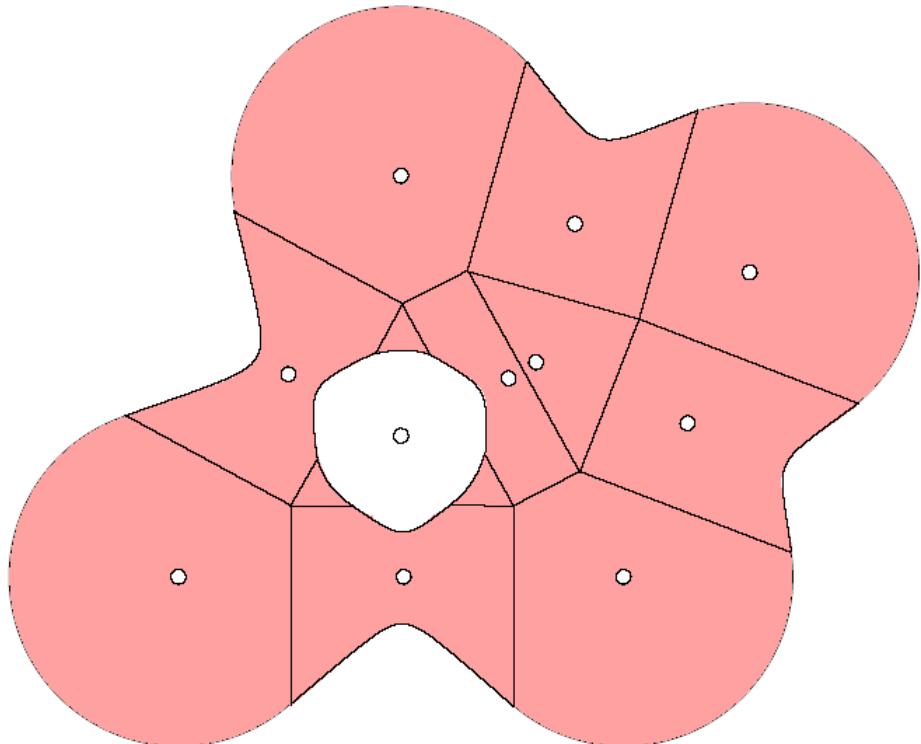
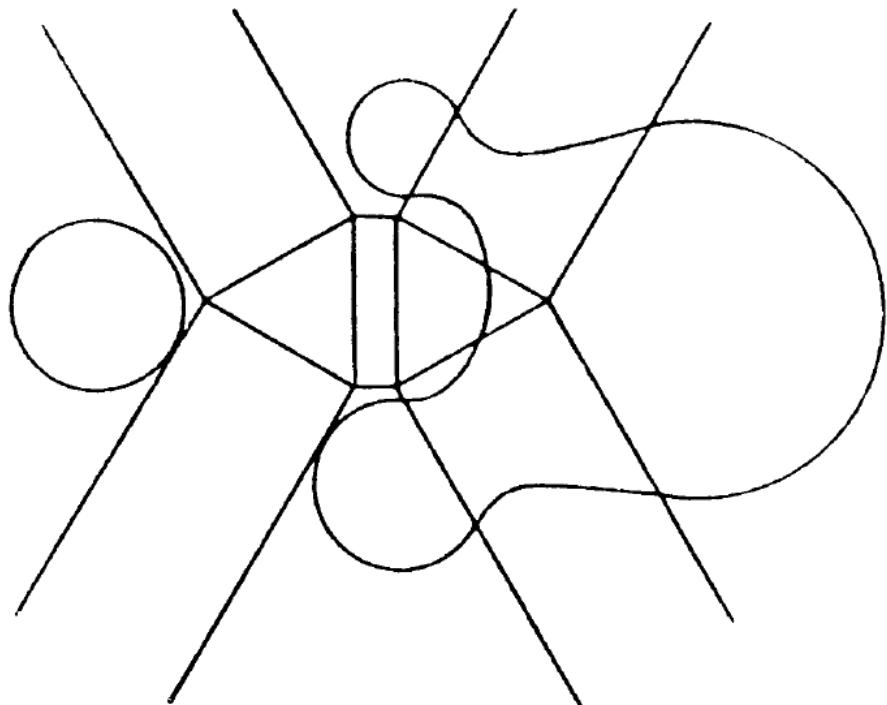




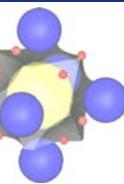
Decomposition of skin

$$\mu_X^s = s \cdot \nu_X + t \cdot \delta_X$$

$$\mu_X^s \cap \text{skn}^s P = \text{env}(\text{aff } X)^s$$

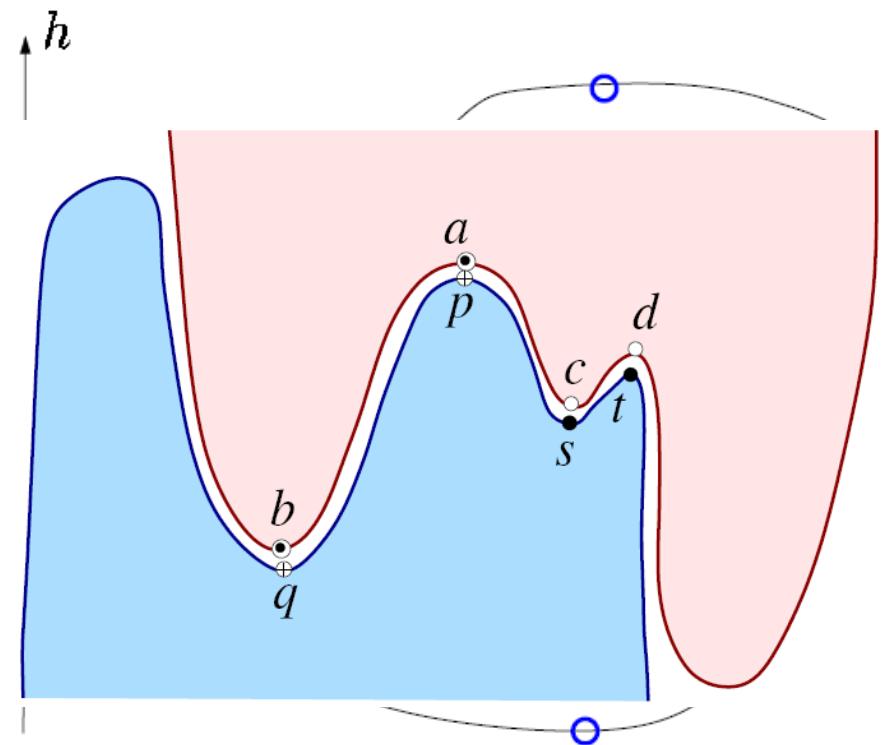


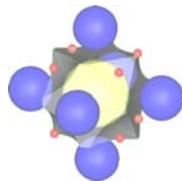
Visualization for analysis of a molecule



■ Descriptor function

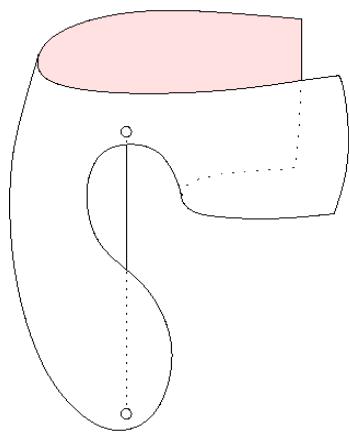
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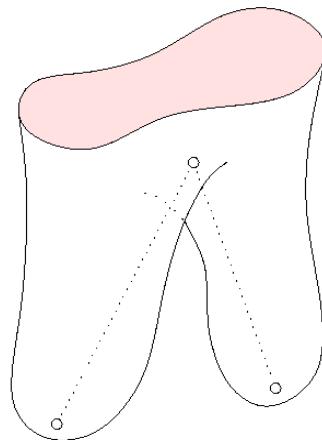


Maxima of elevation function

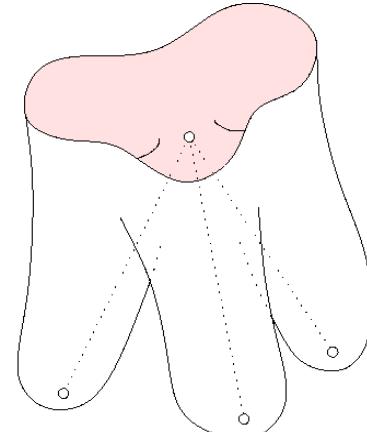
- Extreme Elevation on a 2-Manifold: [P. K. Agarwal et al. SOCG'04]



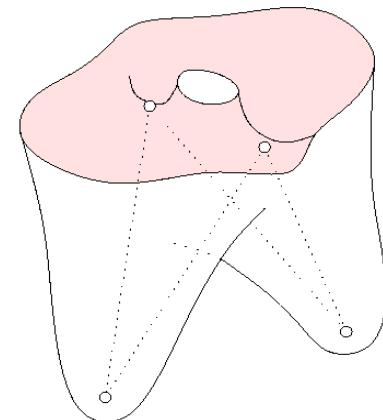
1-legged



2-legged



3-legged



4-legged

Critical points of height function

