Implementing Molecular Hydrophobicity Potential Measurment for the Analysis of Dynamic Biomolecular Interactions

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February 15, 2018

Molecular Hydrophobicity Potential

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Hydrophobicity and log P

Molecular Hydrophobicity Potential

Potential

Force constants

Distance function

Solvent accesible

Evenly distributed points

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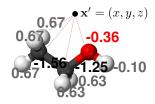
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$$\mathsf{MHP}\left(\mathbf{x}'\right) = \sum_{i=1}^{k} \left[f_i \cdot D\left(\mathbf{x} - \mathbf{x}'_i\right) \right]$$

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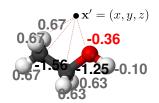
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$$\mathsf{MHP}\left(\mathbf{x}'\right) = \sum_{i=1}^{k} \left[f_i \cdot D\left(\mathbf{x} - \mathbf{x}'_i\right) \right]$$

Summing over all atoms

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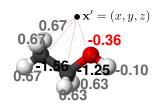
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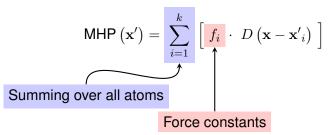
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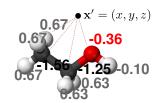
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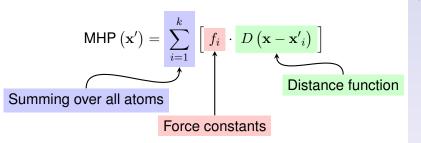
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Force constants

Type	Description	f_i value
	C in:	
3	CHR_3	-0.6681
15	$=CH_2$	-0.7866
36	R-CH-X	-0.2405
	H attached to:	
45	$\mathrm{C}_{\mathrm{sp^3}}$, no X attached to next carbon	0.7341
46	$ m C_{sp^3}, C_{sp^2}$	0.6301
50	Heteroatom	-0.1036
52	$\mathrm{C}_{\mathrm{sp^3}}$, 1 X attached to next carbon	0.6666
	<u>O in</u> :	
56	Alcohol	-0.3567
58	Ketone	-0.0233
62	O ⁻	-0.7941

Source: Arup K. Ghose et al, J. Phys. Chem. A 1998, 102, 3762-3772

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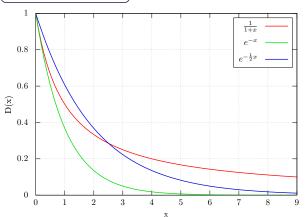
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Audry form

Exponential decay form

$$D\left(x\right) = \frac{1}{1+x}$$

$$D\left(x\right) = e^{-\alpha x}$$



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Solvent accesible surface

 The surface around a molecule accesible to solvent molecules Molecular Hydrophobicity Potential

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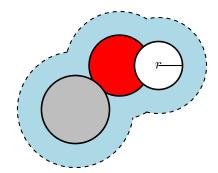
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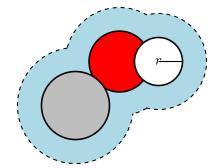
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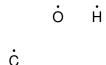
Solvent accesible surface

Evenly distributed points

The surface around a molecule accesible to solvent molecules



For water molecules usually r = 1.4 [Å]



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1. Take all atoms with their vdW-radii

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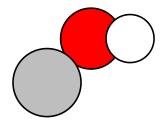
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1. Take all atoms with their vdW-radii

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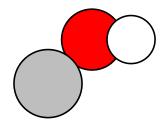
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- 1. Take all atoms with their vdW-radii
- 2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$

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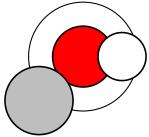
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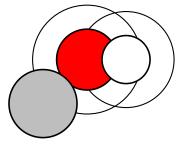
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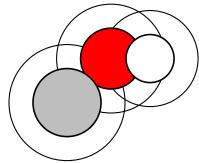


- Take all atoms with their vdW-radii
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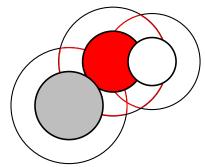
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- 1. Take all atoms with their vdW-radii
- 2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$
- 3. Delete all points that are "burried" in other extended spheres (i.e. $\Delta(p^i, c^j) \leq R^j + R_{\text{probe}}$)

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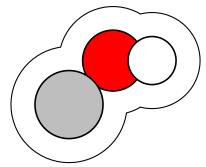
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- 1. Take all atoms with their vdW-radii
- 2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$
- 3. Delete all points that are "burried" in other extended spheres (i.e. $\Delta\left(p^i,c^j\right)\leq R^j+R_{\text{probe}}$)
- The remaining surface is the solvent-accesible surface of the molecule

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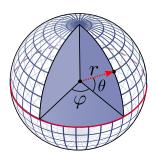
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How to distribute N points on a surface of a sphere?



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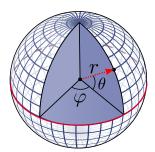
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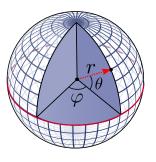
How to distribute N points on a surface of a sphere?



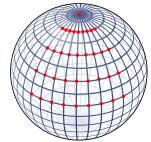
$$\varphi_i = i \cdot \frac{2\pi}{N}$$

$$\theta_j = j \cdot \frac{\pi}{N}$$

How to distribute N points on a surface of a sphere?





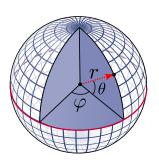


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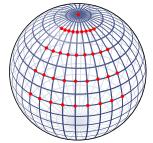
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How to distribute N points on a surface of a sphere?

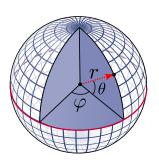




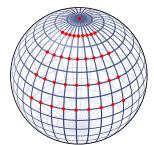


 $\varphi_i = i \cdot \frac{2\pi}{N}$ $\theta_j = j \cdot \frac{\pi}{N}$

Points are not evenly distributed How to distribute N points on a surface of a sphere?







- $\varphi_i = i \cdot \frac{2\pi}{N}$ $\theta_j = j \cdot \frac{\pi}{N}$

- Points are not evenly distributed
- Several points overlap at poles

Solution: Vogel's method

In 2 dimensions:

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Solution: Vogel's method

In 2 dimensions:

▶ Distances:
$$r_i = \sqrt{\frac{i}{N}}$$

• Angle: $\theta_i = \varphi i$ (φ is the golden ratio!) Molecular Hydrophobicity Potential

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In 2 dimensions:

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(φ is the golden ratio!)

In 3 dimensions (cylindrical coordinates):

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In 2 dimensions:

▶ Distances:
$$r_i = \sqrt{\frac{i}{N}}$$

• Angle:
$$\theta_i = \varphi i$$

(φ is the golden ratio!)

In 3 dimensions (cylindrical coordinates):

▶ Distances:
$$z_i = \left(1 - \frac{1}{N}\right) \left(1 - \frac{2i}{N-1}\right)$$

Angles:

$$\theta_i = \varphi i, \ \rho_i = \sqrt{1 - z_i^2}$$

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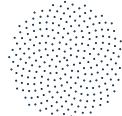
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Solution: Vogel's method

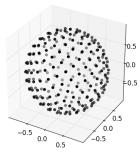
In 2 dimensions:

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Image source: Marmakoide's Blog

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