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

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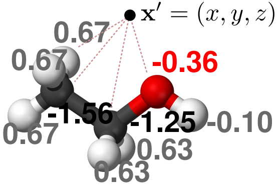
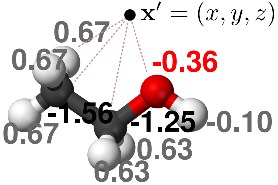
Outline

The MHP Formula



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

The MHP Formula



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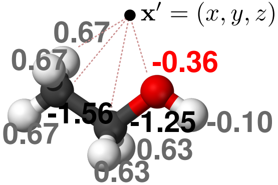
Summing over all atoms

The MHP Formula



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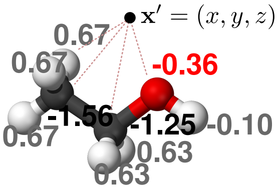
Force constants

The MHP Formula



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Summing over all atoms

Force constants

Distance function

Force constants

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

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

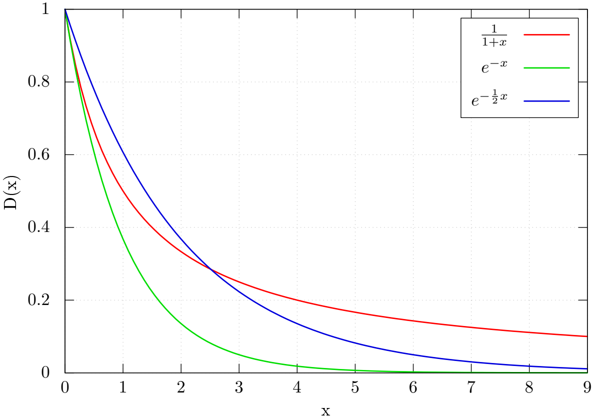
Distance function

Audry form

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

Exponential decay form

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



Solvent accesible surface

- The surface around a molecule accesible to solvent molecules

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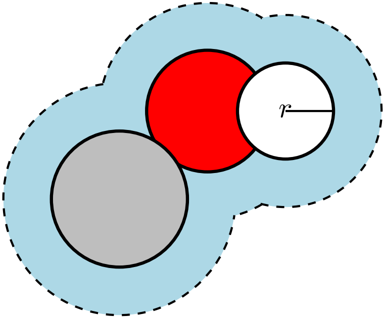
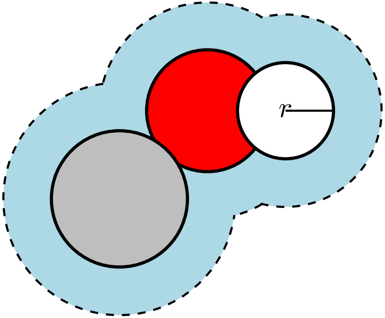


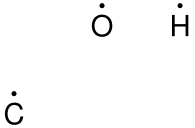
Solvent accesible surface

- The surface around a molecule accesible to solvent molecules



- For water molecules usually $r = 1.4\,[\text{Å}]$

How to Create the Solvent Accesible Surface?



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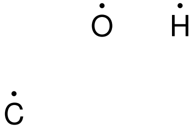

1. Take all atoms with their vdW-radii

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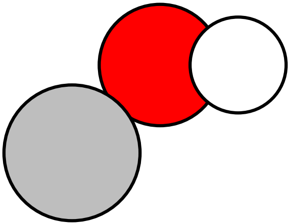

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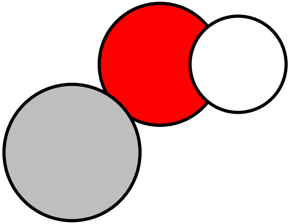

1. Take all atoms with their vdW-radii
2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$

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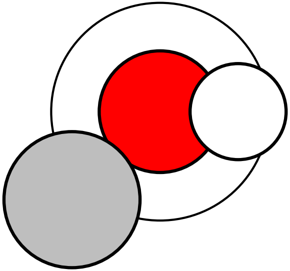

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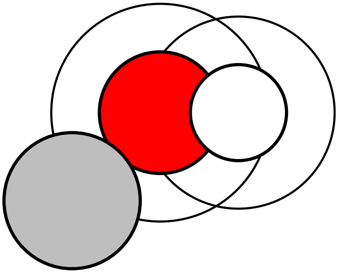

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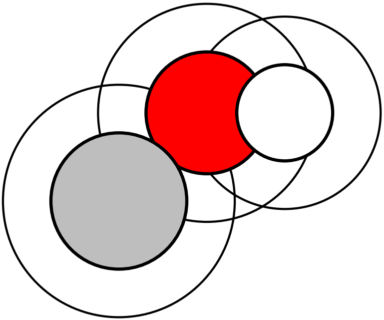

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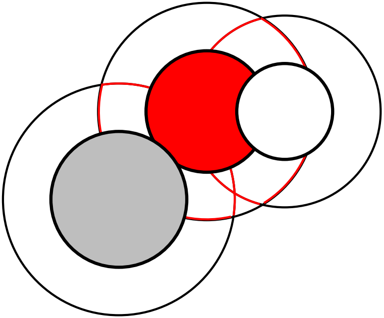

1. Take all atoms with their vdW-radii
2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$
3. Delete all points that are "burried" in other extended spheres (i.e. $\Delta\left(p^i, c^j\right) \leq R^j + R_{\text{probe}}$)

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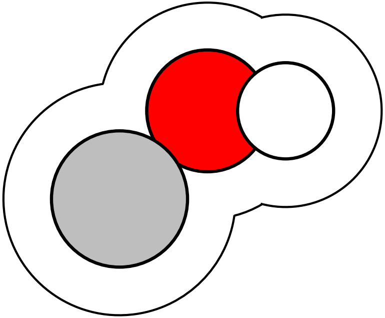
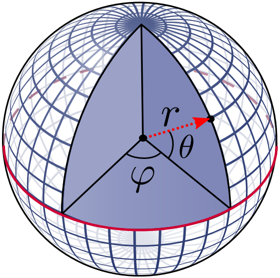


1. Take all atoms with their vdW-radii
2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$
3. Delete all points that are "burried" in other extended spheres (i.e. $\Delta\left(p^i, c^j\right) \leq R^j + R_{\text{probe}}$)
4. The remaining surface is the solvent-accesible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

Evenly distributed points

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



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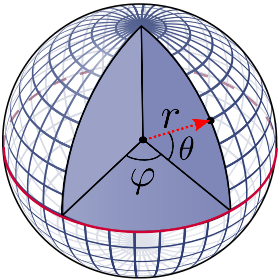

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$$\theta_j = j \cdot \frac{\pi}{N}$$

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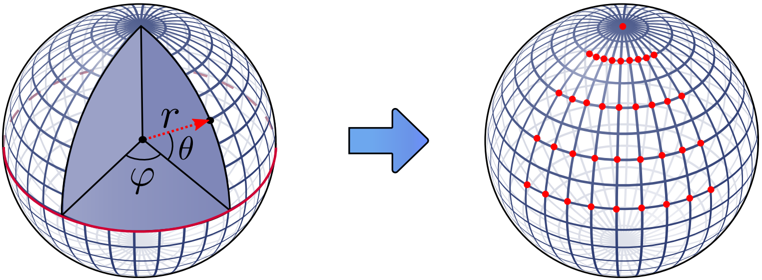

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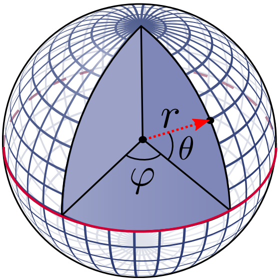

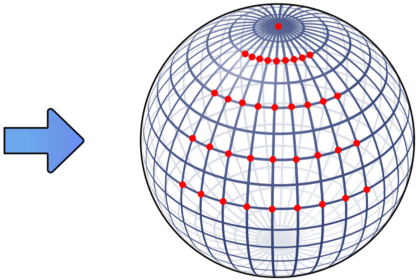

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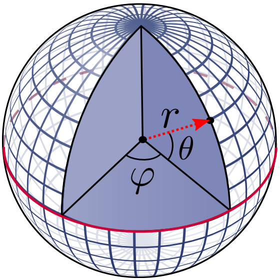

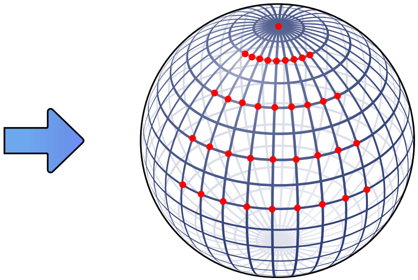

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- Points are not evenly distributed
- Several points overlap at poles

Evenly distributed points

Solution: Vogel's method

In 2 dimensions:

Evenly distributed points

Solution: Vogel's method

In 2 dimensions:

- Distances: $r_i = \sqrt{\frac{i}{N}}$
- Angle: $\theta_i = \varphi i$

  (φ is the golden ratio!)

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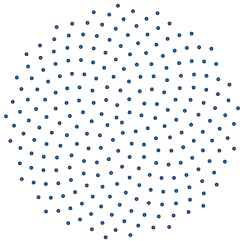

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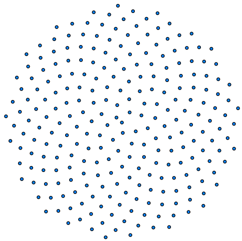

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In 3 dimensions (cylindrical coordinates):

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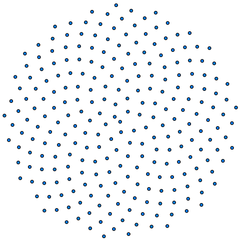

In 3 dimensions (cylindrical coordinates):

- 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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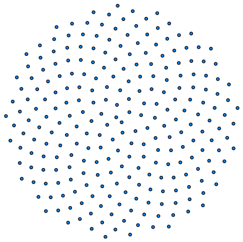

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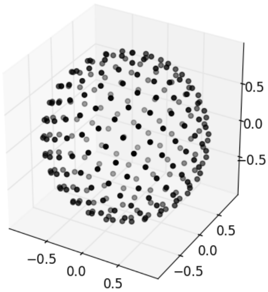

Image source: Marmakoide's Blog

Integration