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

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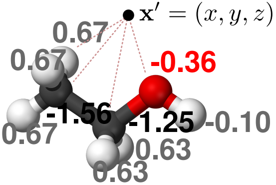
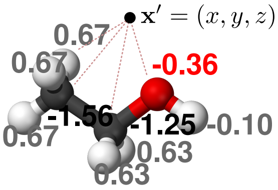
Outline

The MHP Formula



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

The MHP Formula



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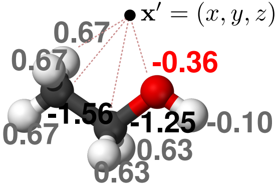
Summing over all atoms

The MHP Formula



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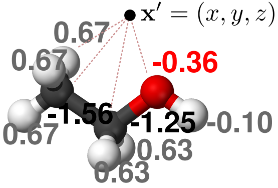
Summing over all atoms

Force constants

The MHP Formula



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Summing over all atoms

Force constants

Distance function

Force Constants

Carbon atom contribution to hydrophobicity[1]

Type	Description	f_i value
	<u>C in:</u>	
1	CH_3R	-1.5603
3	CHR_3	-0.6681
7	CH_2X_2	-1.0305
13	RCX_3	0.7894
17	$=CR_2$	0.0383
24	$R{-}{-}CH{-}{-}R$	-0.3251
25	$R{-}{-}CR{-}{-}R$	0.1492
26	$R{-}{-}CX{-}{-}R$	0.1539

Force Constants

Hydrogen atom contribution to hydrophobicity[1]

Type	Description	f_i value
	H attached to:	
46	C_{sp^3}, no X in α	0.7341
47	C_{sp^2}	0.6301
50	X	-0.1036
52	C_{sp^3}, 1 X in α	0.6666

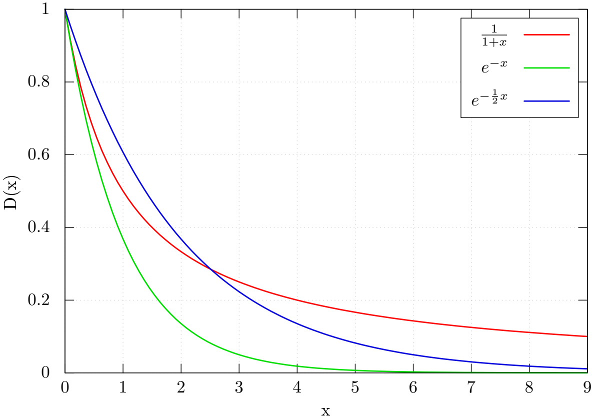
Distance function

Audry form

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

Exponential decay form

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



Solvent accesible surface

- The surface around a molecule accesible to solvent molecules

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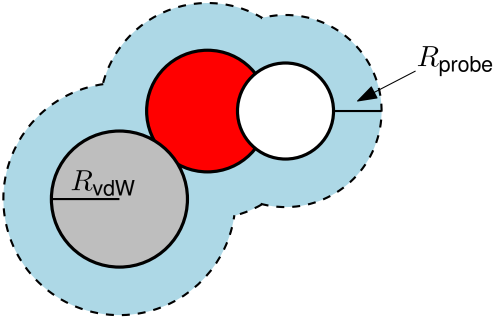

Solvent accesible surface

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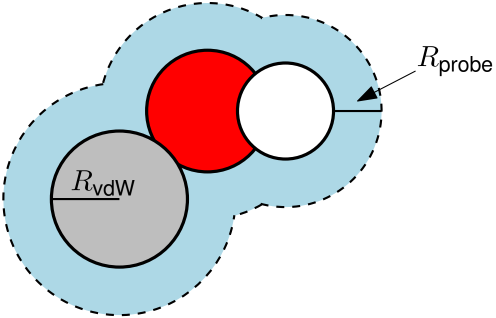
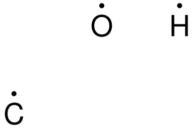


- For water molecules usually $r = 1.4$ [Å]

How to Create the Solvent Accesible Surface?



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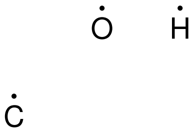

1. Take all atoms with their vdW-radii

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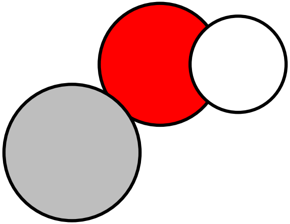

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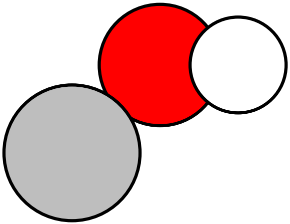

1. Take all atoms with their vdW-radii
2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$

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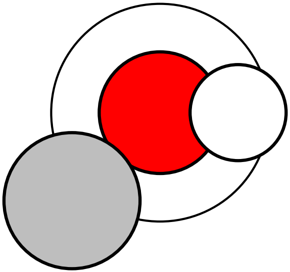

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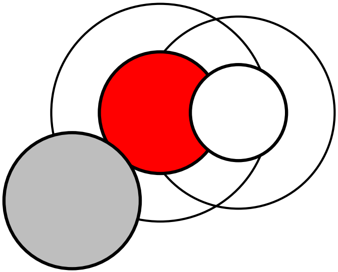

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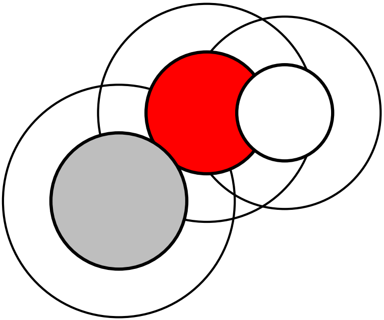

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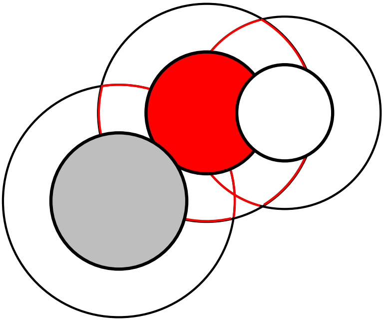

1. Take all atoms with their vdW-radii
2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$
3. Delete all points that are "burried" in other extended spheres (i.e. $\Delta\left(p^i, c^j\right) \leq R^j + R_{\text{probe}}$)

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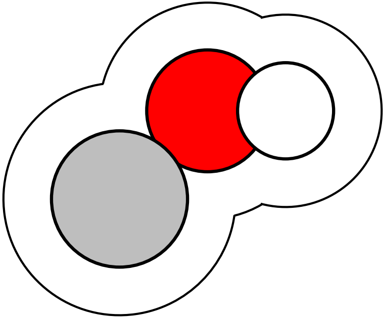
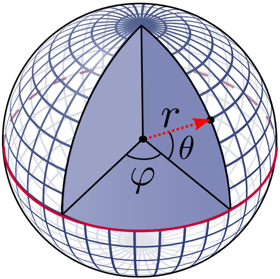


1. Take all atoms with their vdW-radii
2. Create spheres around all atoms with $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$
3. Delete all points that are ”burried” in other extended spheres (i.e. $\Delta\left(p^i, c^j\right) \leq R^j + R_{\text{probe}}$)
4. The remaining surface is the solvent-accesible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

Evenly distributed points

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



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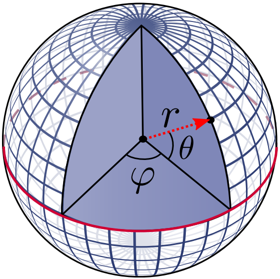

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$$\theta_j = j \cdot \frac{\pi}{N}$$

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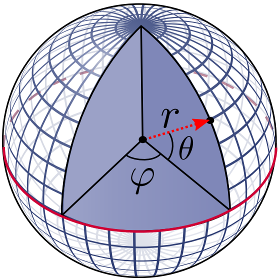

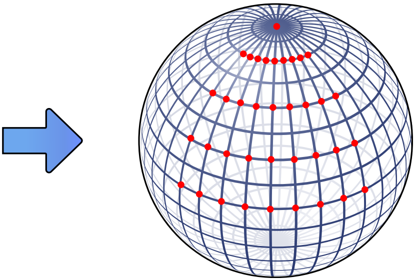

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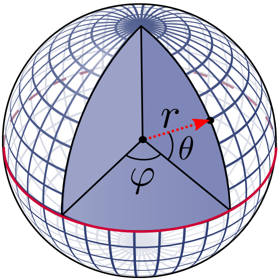

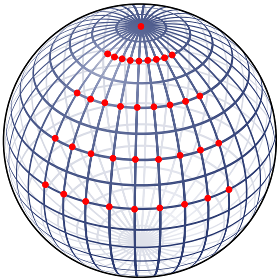

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Evenly distributed points

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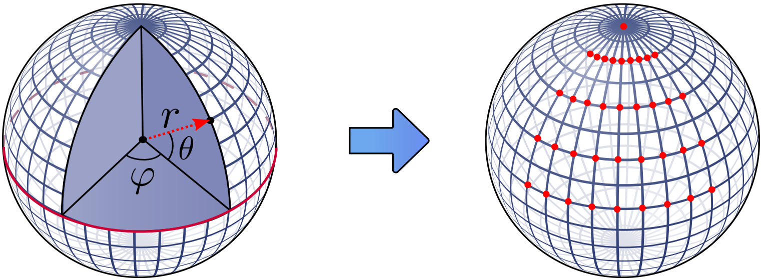

$$\varphi_i = i \cdot \frac{2\pi}{N}$$

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

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

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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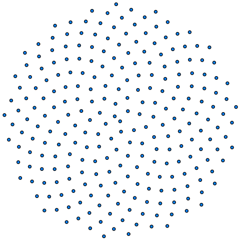

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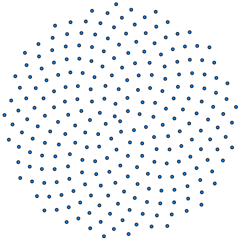

In 3 dimensions (cylindrical coordinates):

Evenly distributed points

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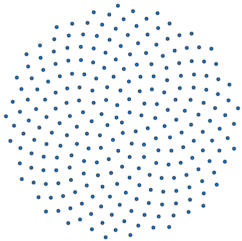

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In 3 dimensions (cylindrical coordinates):

- Distances: $z_i = \left(1 - \frac{1}{N}\right)\left(1 - \frac{2i}{N-1}\right)$
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  $\theta_i = \varphi i, \;\; \rho_i = \sqrt{1 - z_i^2}$

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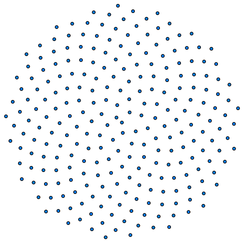

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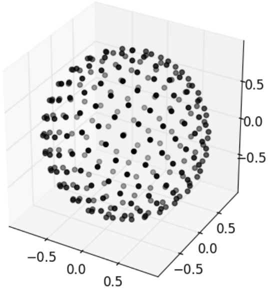

Image source: Marmakoide's Blog

Integration