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

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February 16, 2018

#### Molecular Hydrophobicity Potential

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## **Outline**

## Introduction

Hydrophobicity and log P

## Molecular Hydrophobicity Potential

#### Potential

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#### Surface

Solvent accesible surface

Evenly distributed points

Integration

#### Molecular Hydrophobicity Potential

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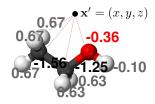
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$$\mathsf{MHP}\left(\mathbf{x}'\right) = \sum_{i=1}^{k} \left[ f_i \cdot D\left(\mathbf{x} - \mathbf{x}'_i\right) \right]$$

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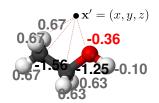
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$$\mathsf{MHP}\left(\mathbf{x}'\right) = \sum_{i=1}^{k} \left[ f_i \cdot D\left(\mathbf{x} - \mathbf{x}'_i\right) \right]$$

Summing over all atoms

#### Molecular Hydrophobicity Potential

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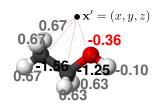
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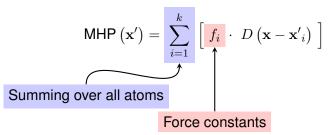
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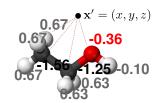
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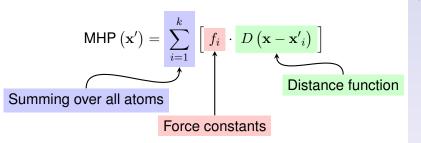
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### **Force Constants**

#### Carbon

atom contribution to hydrophobicity<sup>1</sup>

Type	Description	$f_i$ value
	C in:	
1	$\mathrm{CH_{3}R}$	-1.5603
3	$CHR_3$	-0.6681
7	$CH_2X_2$	-1.0305
13	$RCX_3$	0.7894
17	$=CR_2$	0.0383
24	RCHR	-0.3251
25	RCRR	0.1492
26	RCXR	0.1539

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### **Force Constants**

Hydrogen atom contribution to hydrophobicity<sup>1</sup>

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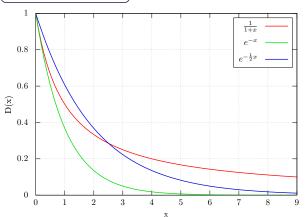
Type	Description	$f_i$ value	
	H attached to:		
46	$\mathrm{C}_{\mathrm{sp^3}}$ , no $\mathrm{X}$ in $lpha$	0.7341	
47	$\mathrm{C_{sp}^2}$	0.6301	
50	X	-0.1036	
52	$C_{sp^3}$ , 1 X in $\alpha$	□ • 0.6666 • • • ■ •	1

## 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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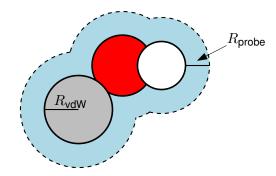
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### Solvent accesible surface

 The surface around a molecule accesible to solvent molecules



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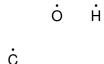
Solvent accesible surface

evenly distributed points

 The surface around a molecule accesible to solvent molecules

 $R_{\text{probe}}$ 

For water molecules usually  $r=1.4~\c|\mbox{\AA}\c|$ 



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1. Take all atoms with their vdW-radii

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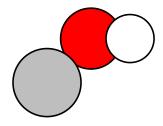
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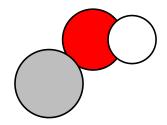
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- 1. Take all atoms with their vdW-radii
- 2. Create spheres around all atoms with  $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$

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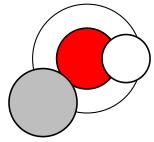
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$$R^i = R^i_{\text{vdw}} + R_{\text{probe}}$$

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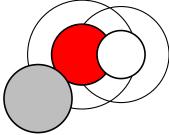
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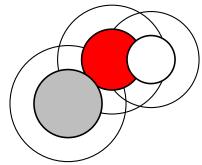
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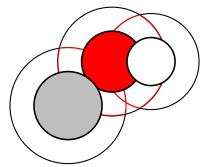
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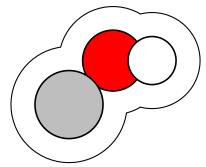


- Take all atoms with their vdW-radii
- Create spheres around all atoms with  $R^i = R^i_{\text{vdw}} + R_{\text{probe}}$
- 3. Delete all points that are "burried" in other extended spheres (i.e.  $\Delta(p^i, c^j) \leq R^j + R_{\text{probe}}$ )

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Solvent accesible surface



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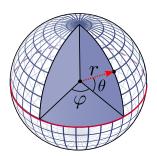
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How to distribute N points on a surface of a sphere?



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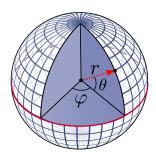
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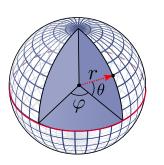
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### How to distribute N points on a surface of a sphere?

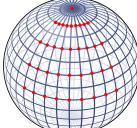


$$\varphi_i = i \cdot \frac{2\pi}{N}$$
 
$$\theta_j = j \cdot \frac{\pi}{N}$$

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



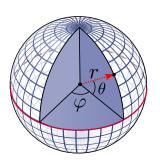




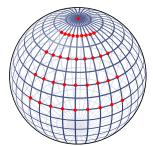
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How to distribute N points on a surface of a sphere?



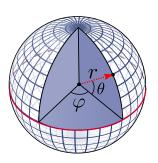




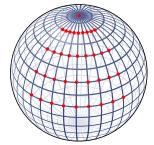
 $\varphi_i = i \cdot \frac{2\pi}{N}$   $\theta_j = j \cdot \frac{\pi}{N}$ 

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:  $\theta_i = \varphi i$ ( $\varphi$  is the golden ratio!)

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#### In 2 dimensions:

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In 3 dimensions (cylindrical coordinates):

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#### In 2 dimensions:

- ▶ Distances:  $r_i = \sqrt{\frac{i}{N}}$
- Angle:  $\theta_i = \varphi i$ ( $\varphi$  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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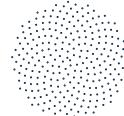
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Solution: Vogel's method

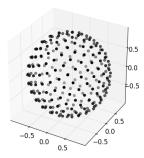
#### In 2 dimensions:

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

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