

Additional File 3: The Physico-Chemical Scoring Function

Similarity between two superimposed interactions $i = (a, b)$ and $i' = (a', b')$ is measured by [1]:

$$S(i, i') = S_{IN}(i) + S_{IN}(i') + S_{PC}(a, a') + S_{PC}(b, b')$$

$$S_{IN}(i) = \begin{cases} 0, & \text{dist}(i) > \text{max_dist}(i) \\ \text{propen}(i) \cdot \begin{cases} (\text{max_dist}(i) - \text{dist}(i)) / (1 + \text{charge_comp}(i)) & \text{chem}(i) = HB \\ (\text{max_dist}(i) - \text{dist}(i)) / (1 + \text{shape_comp}(i)) & \text{chem}(i) = ALI \\ (\text{max_dist}(i) - \text{dist}(i)) / (1 + \text{shape_comp}(i) + n_{PI}(i)) & \text{chem}(i) = PI \end{cases} \end{cases}$$

The similarity between two superimposed pseudocenters is defined by [2]:

$$S_{PC}(a, b) = \begin{cases} 0, & \text{dist}(a, b) > \text{max_dist}(a, b) \text{ or } \text{chem}(a) \neq \text{chem}(b) \\ 0, & \text{shape}(a, b) > 0.2 \text{ or } n_S(a, b) > 0.2 \\ (\text{max_dist}(a, b) - \text{dist}(a, b)) / (1 + \text{charge}(a, b)) & \text{chem}(a) = HB \\ (\text{max_dist}(a, b) - \text{dist}(a, b)) / (1 + \text{shape}(a, b) + n_{PI}(a, b)) & \text{chem}(a) = PI \\ (\text{max_dist}(a, b) - \text{dist}(a, b) + v_{ALI}(a, b)) / (2 + 20 * \text{shape}(a, b)) & \text{chem}(a) = ALI \end{cases}$$

- $\text{dist}(a, b)$ - the distance between a and b after the superimposition. $\text{dist}(i)$ - the distance between

interacting pseudocenters a and b .

- $\text{chem}(a)$, $\text{chem}(i)$ - the physico-chemical property of the point a or interaction i . There are three types of properties: Hydrogen Bonding (HB), Aliphatic Hydrophobic (ALI) and Aromatic (PI).

- $\text{max_dist}(a, b)$ - maximal allowed distance between a pair of pseudocenters, defined by $\varepsilon = 3.0 \text{ \AA}$.

$\text{max_dist}(i)$ - the maximal distance allowed for the specific type of interaction. The default thresholds are

$\gamma = 3.9 \text{ \AA}$ for hydrogen bonds [3] and $\gamma = 8.0 \text{ \AA}$ for hydrophobic aliphatic and aromatic interactions.

bridges.

- $\text{charge}(a)$ - the partial atomic charge of the atom a , which can form hydrogen bonds.

$\text{charge}(a, b) = |\text{charge}(a) - \text{charge}(b)|$ - measures the similarity of charges.

$\text{charge_comp}(i) = |\text{charge}(a) + \text{charge}(b)|$ - measures the complementarity of charges.

- $\text{shape}(a)$ - the average curvature of the surface region created by a . Calculated as an average of the solid angle shape functions [4] with spheres of radius 4, 5, 6 and $7 \text{ \AA}$. The sphere centers are located at projection point of a to the surface. $\text{shape}(a, b) = |\text{shape}(a) - \text{shape}(b)|$ - measures the similarity of shapes.

$\text{shape_comp}(i) = |1 - \text{shape}(a) - \text{shape}(b)|$ - measures the complementarity of shapes which sums to one.

- $n_S(a)$ - normal vector at the projection point of a to the surface, $n_S(a, b) = n_S(a) \cdot n_S(b)$.

- $v_{ALI}(a, b)$ - the overlap of the hydrophobic group bounding spheres of a and b , approximated by the difference between sum of radiuses and the distance between the centers.

- $n_{PI}(a)$ - for aromatic pseudocenters denotes the normal to the plane of the aromatic ring.

$n_{PI}(i) = n_{PI}(a) \cdot n_{PI}(b)$ - represents the angle between two interacting aromatic ring.

• $propen(p)$ - the propensity of the physico-chemical property in the interface compared to the overall protein chain. The propensities of the pseudocenters were calculated by Mintz et al. [5].

$propen(i) = propen(a) \cdot propen(b)$.

References

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