Experimental Benchmark Data Set of Adsorption Free Energy for Synthetic Peptide-Surface Interactions by SPR

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Statement of Purpose

With the increasing interest of synthetic peptide adsorption in different biotechnological fields, including biosensors, biocatalysis, bioseparations, and implant applications, there is growing need for an understanding of the fundamental mechanisms involved in peptide adsorption behavior. However, relatively few groups have attempted to quantitatively characterize peptide adsorption with experimental methods due to the difficulties and complexities involved. To aid the scientific community in the analysis of such data, the objective of this study was therefore to compile a database of experimentally measured standard state adsorption free energy ($\Delta G°_{ads}$) values for a variety of amino acid residue-synthetic surface interactions by surface plasma resonance (SPR) spectroscopy.

Materials and Methods

To quantitatively analyze these types of sub-molecular interactions, a new method was developed by our group [1]. This method was specifically designed for SPR to enable bulk-shift effects to be directly determined and to enable $\Delta G°_{ads}$ to be calculated with minimal influence from peptide-peptide interactions at the adsorbent surface. Alkanethiol self-assembled monolayers (SAMs) on gold with various functionalities were used as our model surfaces. A host-guest peptide was then designed with an amino acid sequence of TGTG-X-GTGT, where G & T are glycine and threonine residues, and X represents a variable residue. In this research work, we applied this method to calculate $\Delta G°_{ads}$ at 25°C and 7.4 pH for a broad range of peptide-SAM surface combinations comprised of nine different SAM surfaces and 12 different types of amino acids, with the -X- residue varied to change the overall characteristics of the peptides. The -X- residue was represented by the amino acids listed below.

-X- residue	Side Chain	Property
Valine (V)	$-CH(CH_3)_2$	Non-polar
Glycine (G)	-H	Non-chiral
Alanine (A)	$-CH_3$	Non-polar
Leucine (L)	$-CH_2-CH-(CH_3)_2$	Non-polar
Phenylalanine (F)	$-CH_2-C_6H_5$	Aromatic
Tryptophan (W)	$-CH_2$-indole ring (C_8H_6N)	Aromatic
Serine (S)	$-CH_2-OH$	Neutral polar
Threonine (T)	$-CH(CH_3)OH$	Neutral polar
Asparagine (N)	$-CH_2-CO-NH_2$	Neutral polar
Aspartic Acid (D)	$-CH_2COO^-$ (pK=3.97)	Negatively charged
Lysine (K)	$-(CH_2)_4-NH_3^+$ (pK=10.78)	Positively charged
Arginine (R)	$-(CH_2)_3-NH-C(NH_2)_2^+$ (pK=12.52)	Positively charged

The SAM surface groups were selected to provide a wide range of functionality, including hydrophobic surfaces (CH_3, OCH_2CF_3, and OC_6H_5), hydrophilic surfaces (OH, EG_3OH, $NHCOCH_3$, and $COOCH_3$), and partially charged surfaces ($COOH/COO^-$ and NH_2/NH_3^+).

Results and Discussion

In this study, we evaluated a total of 108 different molecular systems obtained by the combinations of 12 different guest residues in our host-guest peptide model and 9 types of SAMs with various functionalities. Although there are various characteristics of the guest residues in our peptides models, Figure 1 shows that the nature of the SAM surfaces more strongly influenced the free energy of the adsorbed peptides than the nature of the peptides themselves. Significant differences were also found between different peptides on a given surface.

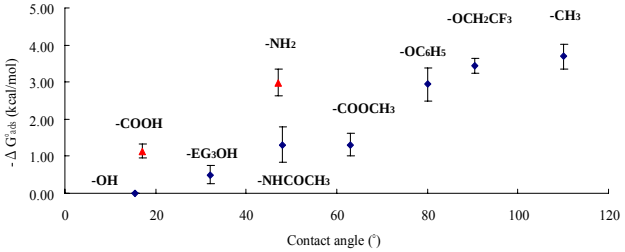

Figure 1. Averaged $-\Delta G°_{ads}$ (kal/mol) vs. water contact angle (°) for the TGTG-X-GTGT peptides on SAM surfaces with various functionalities. (Error bar represents 95% C.I., $N \geq 9$).

To summarize this benchmark data set, several characteristic behaviors were observed based on the chemical nature of the functional groups involved. (1) The hydrophobic SAMs showed the strongest adsorption behavior between these peptides and the SAM surfaces, especially for the guest peptides with non-polar side-groups. (2) The hydrophilic SAMs showed very low-to-moderate adsorption behavior depending on the polarities of the surface functionalities, with the OH-SAM showing essentially no adsorption except when alanine (A) and phenylalanine (F) were used as the guest residue, in which case strong, irreversible adsorption was found. (4) The charged SAMs showed moderately strong adsorption behavior when the net charge of the peptide was opposite to the surface charge. (5) For the residue/surface combination that comprised a mixture of hydrophobic, neutral hydrophilic, and charged systems, a moderate adsorption response was found, which was similar to the moderately hydrophilic SAMs. Overall, while the general strength of peptide adsorption behavior tended to increase with increasing surface hydrophobicity (as characterized by the water contact angle), there were numerous exceptions to this, thus indicating that this in itself does not completely determine adsorption behavior. In addition to this, the specific peptide-surface functional group combinations involved in the adsorption processes are also very important in determining peptide-surface interactions.

Concluding Remarks

This benchmark data set is being used by our molecular simulation group to support force field parameterization for molecular modeling to predict protein-surface interactions. These data will also be beneficial for other applications, such as the design of genetically engineered peptides (GEP) on solid surfaces for applications in nanobiotechnology and peptide/lipid bilayer interactions for cell-signaling research.

Ref: [1] Wei and Latour, Langmuir, 24: 6721-6729 (2008).