Benchmark Experimental Data Set of Adsorption Free Energy for Peptide-Surface Interactions without Peptide-Peptide Effects

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Introduction

● Measurement of energy change for peptide-surface interactions provides fundamental insight into the thermodynamics of protein adsorption and is needed for the validation of empirical force fields for protein adsorption simulations.

● The accuracy of current methods is limited by peptide-peptide interactions, leading to errors in standard state adsorption free energy (ΔG°_{ads}) measurement. To address this deficiency, the objective of this study was to generate a database of experimentally measured ΔG°_{ads} values without peptide-peptide effect for a wide variety of peptide residue-surface interactions using a host-guest peptide and alkanethiol self-assembled monolayers (SAMs) with polymer-like functionality as the model system.

Experimental Method

● **Surface models**: All alkanethiols used in these experiments had a structure of **HS-(CH_2)$_{11}$-R** with the following **R** terminal groups: -OH, -CH_3, -NH_2, -COOH, -$COOCH_3$, -$NHCOCH_3$, -OC_6H_5, -OCH_2CF_3 or -EG_3-OH.

● **Host-guest peptide models**: TGTG-**X**-GTGT,

-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

*Adsorption studies were conducted to measure the adsorption response of each peptide-SAM system by surface plasmon resonance (SPR) spectroscopy in phosphate buffered saline (pH 7.4, 150 mM NaCl at 25°C).

Analytical Model

The peptide adsorption process can be presented by the following equations between the peptide (P) and surface (S):

$$P + S \rightleftharpoons P \cdot S$$

$$SPR = q + mC_b = \frac{QC_b}{C_b + C^o K^{-1}} + mC_b$$

$$\Delta G^o_{ads} = -RT \ln[(C_s)_{C_b \to 0}/C_b] = -RT \ln\left(\frac{QK}{\delta C^o} + 1\right)$$

(By extrapolating SPR vs. C_b behavior towards $C_b \to 0$, ΔG°_{ads} is determined with minimal influence of peptide-peptide interactions)

C_b = [P], mC_b = bulk shift effect, C° = standard state C_b = 1.0 M, δ= thickness of adsorbed layer ≈ 12 Å.

K = effective equilib. const., q = [P·S], Q = q at surface saturation.

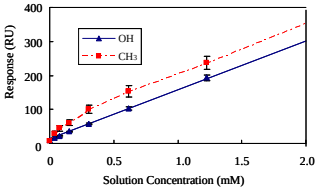

Fig 1. Adsorption isotherm for TGTG-L-GTGT on SAM-OH & SAM-CH_3. (Error bar represents 95% C.I., N = 6.)

Results & Discussions

● We present results from the application of this analytical model to characterize the adsorption behavior of a large series of 108 different peptide-SAM systems.

● These studies indicate that ΔG°_{ads} for each peptide on non-charged surfaces generally correlates linearly with the surface hydrophobicity, with specific interactions between the functional groups of the peptide and the SAM surfaces playing a secondary, but still significant role.

● Peptide adsorption behavior to charged SAMs also followed the same trends, but with electrostatic effects providing additional mechanism to adsorption affinity.

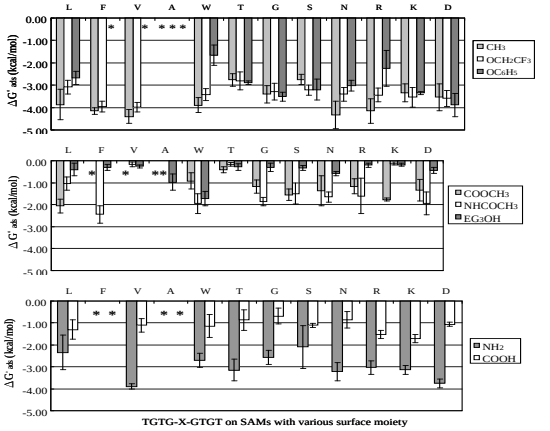

Fig 2. Comparisons of ΔG°_{ads} for each peptide on SAMs with various functionalities. (An asterisks (*) indicates that adsorption was irreversible; the error bar represents the 95% C.I. with N = 6.)

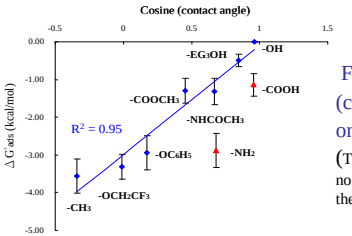

Fig 3. ΔG°_{ads} (kcal/mol) vs. cosine (contact angle) for TGTG-X-GTGT on SAMs with various moieties. (The blue line shows the linear regression for the non-charged SAM surfaces with r^2=0.95; the error bar represents the 95% C.I. with N = 9.)

Conclusions

● This benchmark data set provides fundamental insights into the governing factors that influence protein adsorption behavior; and just as importantly, provides necessary data that is needed for the validation of force field parameters for the molecular simulation methods that can be applied to accurately simulate protein adsorption behavior.

Acknowledgements

We gratefully acknowledge NIH for funding support for this research (NIBIB grant # R01 EB006163).