139a Simulations of Adsorption Properties for Charged Polypeptides on Hydrophobic Chromatography Surfaces

Kosta Makrodimitris, Alexander Freed, Matthew Dalton, Erik Fernandez, and John O'Connell

There is a pressing need for computational design tools to accelerate the development of bioprocess purifications. Our project seeks to fill this need by developing computational methods for predicting adsorption of peptides and proteins on hydrophobic chromatography surfaces. In this work, our previous mesoscopic method (1,2) for successfully obtaining low-coverage adsorption thermodynamics for protected peptides in hydrophobic chromatography, based on a Langevin lattice of dipoles and ions (ALLD), has been extended to systems with charged biochemical solutes. Modifications include appropriate positioning of counterions in the neighborhood of acidic and basic amino acids in pH=7 and pH=2 via geometric and annealing algorithms, as well as obtaining the electrostatic contributions of fully-charged solutes and ions. Parameter determination and successful predictions have been based on new experimental data taken in a strategic manner to minimize the number of molecular variables changed with conditions, substances and surfaces (3). The presentation will describe our extended Langevin dipole methodology, some atomistic simulations of peptides and aprotinin in an aqueous environment with added salt that were used in decisions to set up the mesoscopic systems, and comparisons of the final results with available data. Also to be discussed are effects of conditions on preferential orientations, as well as sensitivity of final results to changes in model assumptions such as lattice dimensions, dipole size, and orientational averaging. References

1. K. Makrodimitris, E. Fernandez, T. Woolf, J. O'Connell, *Analytical Chemistry* 77, 1243 (2005).
2. K. Makrodimitris, E. Fernandez, T. Woolf, J. O'Connell, *Molecular Simulation, in press* (2005).
3. A. Freed, J. O'Connell, E. Fernandez, to be submitted to J. Chem. Eng. Data (2005).

Bibliography

- B. Klein, G. Pack, *Biopolymers* 1983, **22**, 2331.

- K. Sharp, *Biopolymers* 1995, **36**, 227.

- F. Lin,W. Chen, M. Hearn, *J. Mol. Recognit.* 2002, **15**, 55.

- K. Dill, K. A.; S. Bromberg, *Molecular Driving Forces*. ed.; Garland Science, Taylor & Francis: New York, 2003.

- A. Grossfield, J. Sachs, T.B. Woolf, *PROTEINS: Structure, Function, and Genetics* 2001, **41**, 211.

- F. Lee, Z. Chu, A. Warshel, *J. Comp. Chem.* 1993, **14**, 161.

- S. Klatte, T. Beck, *J. Phys. Chem. B* 1996, **100**, 5931.

- C. Roth, A. Lenhoff, *Langmuir* 1995, **11**, 3500.