

Bibliography

1. B. Honig, K. Sharp, and A.-S. Yang. Macroscopic models of aqueous solutions: Biological and chemical applications. *J. Phys. Chem.* **97**: 1101–1109 (1993).
2. B. Honig and A. Nicholls. Classical electrostatics in biology and chemistry. *Science (Washington, D.C.)* **268**: 1144–1149 (1995).
3. J. Novotny and K. Sharp. Electrostatic fields in antibodies and antibody/antigen complexes. *Prog. Biophys. Molec. Biol.* **58**: 203–224 (1992).
4. V. K. Misra, K. A. Sharp, R. A. Friedman, and B. Honig. Salt effects on ligand–DNA binding: Minor groove binding antibiotics. *J. Mol. Biol.* **238**: 245–263 (1994).
5. V. K. Misra, J. L. Hecht, K. A. Sharp, R. A. Friedman, and B. Honig. Salt effects on protein–DNA interactions: The λ CI repressor and EcoRI endonuclease. *J. Mol. Biol.* **238**: 264–280 (1994).
6. K. A. Sharp. Electrostatic interactions in hirudin–thrombin binding. *Biophys. Chem.* **61**: 37–49 (1996).
7. J. Shen and J. Wendoloski. Electrostatic binding energy calculation using the finite difference solution to the linearized Poisson–Boltzmann equation: Assessment of its accuracy. *J. Comput. Chem.* **17**: 350–357 (1996).
8. J. Novotny, R. E. Bruccoleri, M. Davis, and K. A. Sharp. Empirical free energy calculations: A blind test and further improvements to the method. *J. Mol. Biol.* **268**: 401–411 (1997).
9. Z. S. Hendsch and B. Tidor. Do salt bridges stabilize proteins? A continuum electrostatic analysis. *Protein Sci.* **3**: 211–226 (1994).
10. C. Tanford, P. K. De, and V. G. Taggart. The role of the α -helix in the structure of proteins. Optical rotatory dispersion of β -lactoglobulin. *J. Am. Chem. Soc.* **82**: 6028–6034 (1960).
11. C. H. Paul. Building models of globular protein molecules from their amino acid sequences. I. Theory. *J. Mol. Biol.* **155**: 53–62 (1982).
12. C. V. Sindelar, Z. S. Hendsch, and B. Tidor. Effects of salt bridges on protein structure and design. *Protein Sci.* **7**: 1898–1914 (1998).
13. E. K. O’Shea, R. Rutkowski, and P. S. Kim. Mechanism of specificity in the Fos–Jun oncoprotein heterodimer. *Cell* **68**: 699–708 (1992).
14. L.-P. Lee and B. Tidor. Optimization of electrostatic binding free energy. *J. Chem. Phys.* **106**: 8681–8690 (1997).
15. L. T. Chong, S. E. Dempster, Z. S. Hendsch, L.-P. Lee, and B. Tidor. Computation of electrostatic complements to proteins: A case of charge stabilized binding. *Protein Sci.* **7**: 206–210 (1998).
16. S. E. Dempster and B. Tidor. Alternative sub-targeting of enzymatic states: Potential HIV-1 protease inhibitors with distributed physicochemical properties. In preparation.

17. L.-P. Lee and B. Tidor. Barstar is electrostatically optimized for tight-binding to barnase. In preparation.
18. T. L. Hill. *An Introduction to Statistical Thermodynamics*. Dover, New York (1986).
19. R. K. Pathria. *Statistical Mechanics*. Pergamon Press, New York (1972).
20. D. A. McQuarrie. *Statistical Mechanics*. Harper & Row, New York (1976).
21. G. Benedek and F. Villars. *Biological Physics*. To be published by the American Institute of Physics.
22. K. Huang. *Statistical Mechanics*. John Wiley & Sons, New York, second edition (1987).
23. P. R. Bevington and D. K. Robinson. *Data Reduction and Error Analysis For The Physical Sciences*. McGraw-Hill, New York, second edition (1992).
24. B. R. Brooks, R. E. Bruccoleri, B. D. Olafson, D. J. States, S. Swaminathan, and M. Karplus. CHARMM: A program for macromolecular energy, minimization, and dynamics calculations. *J. Comput. Chem.* **4**: 187–217 (1983).
25. W. D. Cornell, P. Cieplak, C. I. Bayly, I. R. Gould, K. M. Merz, Jr., D. M. Ferguson, D. Spellmeyer, T. Fox, J. W. Caldwell, and P. A. Kollman. A second generation force field for the simulation of proteins, nucleic acids, and organic molecules. *J. Am. Chem. Soc.* **117**: 5179–5197 (1995).
26. B. Tidor and M. Karplus. The contribution of vibrational entropy to molecular association. The dimerization of insulin. *J. Mol. Biol.* **238**: 405–414 (1994).
27. M. K. Gilson, J. A. Given, B. L. Bush, and J. A. McCammon. The statistical-thermodynamic basis for computation of binding affinities: A critical review. *Biophys. J.* **72**: 1047–1069 (1997).
28. J.-P. Hansen and I. R. McDonald. *Theory of Simple Liquids*. Academic Press, New York, second edition (1990).
29. S. J. Singer and D. Chandler. Free energy functions in the extended RISM approximation. *Mol. Phys.* **55**: 621–625 (1985).
30. P. H. Lee and G. M. Maggoria. Solvation thermodynamics of polar molecules in aqueous solution by the XRISM method. *J. Phys. Chem.* **97**: 10175–10185 (1993).
31. Y. L. Ha and A. K. Chakraborty. Solvation thermodynamics of simple crown ethers by the XRISM method. *J. Phys. Chem.* **98**: 11193–11203 (1994).
32. D. L. Beveridge and F. M. DiCapua. Free energy via molecular simulation: Applications to chemical and biomolecular systems. *Annu. Rev. Biophys. Biophys. Chem.* **18**: 431–492 (1989).
33. W. L. Jorgensen. Free energy calculations: A breakthrough for modeling organic chemistry in solution. *Acc. Chem. Res.* **22**: 184–189 (1989).
34. P. A. Kollman and K. M. Merz, Jr. Computer modeling of the interactions of complex molecules. *Acc. Chem. Res.* **23**: 246–252 (1990).
35. W. F. van Gunsteren and H. J. C. Berendsen. Computer simulation of molecular dynamics: Methodology, applications, and perspectives in chemistry. *Angew. Chem. Int. Ed. Engl.* **29**: 992–1023 (1990).
36. J. A. McCammon. Free energy from simulations. *Curr. Opin. Struct. Biol.* **1**: 196–200 (1991).
37. C. Jarque and B. Tidor. Simulated annealing on coupled free energy surfaces: Relative solvation energies of small molecules. *J. Phys. Chem. B* **101**: 9362–9374 (1997).
38. T. Simonson and A. T. Brünger. Thermodynamics of protein–peptide interactions in the ribonuclease-S system studied by molecular dynamics and free energy calculations. *Biochemistry* **31**: 8661–8674 (1992).

39. Y.-Y. Shi, A. E. Mark, C.-X. Wang, F. Huang, H. J. C. Berendsen, and W. F. van Gunsteren. Can the stability of protein mutants be predicted by free energy calculations? *Protein Eng.* **6**: 289–295 (1993).
40. J. B. Clarage, T. Romo, B. K. Andrews, B. M. Pettitt, and G. N. Phillips, Jr. A sampling problem in molecular dynamics simulations of macromolecules. *Proc. Natl. Acad. Sci. U.S.A.* **92**: 3288–3292 (1995).
41. M. J. Mitchell and J. A. McCammon. Free energy difference calculations by thermodynamic integration: Difficulties in obtaining a precise value. *J. Comput. Chem.* **12**: 271–275 (1991).
42. C. Chothia and J. Janin. Principles of protein–protein recognition. *Nature (London)* **256**: 705–708 (1975).
43. K. A. Sharp, A. Nicholls, R. F. Fine, and B. Honig. Reconciling the magnitude of the microscopic and macroscopic hydrophobic effects. *Science* **252**: 106–109 (1991).
44. B. Lee and F. M. Richards. The interpretation of protein structures: Estimation of static accessibility. *J. Mol. Biol.* **55**: 379–400 (1971).
45. F. M. Richards. Areas, volumes, packing, and protein structure. *Annu. Rev. Biophys. Bioeng.* **6**: 151–176 (1977).
46. J. D. Jackson. *Classical Electrodynamics*. John Wiley and Sons, New York, third edition (1999).
47. O’M. Bockris and A. K. N. Reddy. *Modern Electrochemistry*. Plenum, New York (1973).
48. M. K. Gilson and B. H. Honig. Calculation of electrostatic potentials in an enzyme active site. *Nature (London)* **330**: 84–86 (1987).
49. K. A. Sharp and B. Honig. Calculating total electrostatic energies with the nonlinear Poisson–Boltzmann equation. *J. Phys. Chem.* **94**: 7684–7692 (1990).
50. E. Kangas and B. Tidor. Charge optimization leads to favorable electrostatic binding free energy. *Phys. Rev. E* **59**: 5958–5961 (1999). (Reproduced in Chapter 6).
51. J. Mathews and R. L. Walker. *Mathematical Methods of Physics*. Addison–Wesley, New York (1970).
52. E. Fredholm. Sur une classe d’équations fonctionnelles. *Acta Math.* **27**: 365–390 (1903).
53. G. F. Carrier, M. Krook, and C. E. Pearson. *Functions of a Complex Variable: Theory and Technique*. Hod Books, Ithaca, NY (1983).
54. O. D. Kellogg. *Foundations of Potential Theory*. Dover, New York (1953).
55. W. R. Smythe. *Static and Dynamic Electricity*. McGraw–Hill, New York, third edition (1968).
56. H. L. Friedman. Image approximation to the reaction field. *Mol. Phys.* **29**: 1533–1543 (1975).
57. P. B. Shaw. Theory of the Poisson Green’s function for discontinuous dielectric media with an application to protein biophysics. *Phys. Rev. A* **32**: 2476–487 (1985).
58. P. B. Shaw. Quasi-images and surface geometry in cavity electrostatics. *Phys. Rev. A* **35**: 2254–2265 (1987).
59. M. K. Gilson and B. Honig. Calculation of the total electrostatic energy of a macromolecular system: Solvation energies, binding energies, and conformational analysis. *Proteins: Struct., Funct., Genet.* **4**: 7–18 (1988).
60. M. K. Gilson, K. A. Sharp, and B. H. Honig. Calculating the electrostatic potential of molecules in solution: Method and error assessment. *J. Comput. Chem.* **9**: 327–335 (1988).
61. K. A. Sharp and B. Honig. Electrostatic interactions in macromolecules: Theory and applications. *Annu. Rev. Biophys. Biophys. Chem.* **19**: 301–332 (1990).

62. G. Strang. *Introduction to Linear Algebra*. Wellesley–Cambridge Press, Wellesley, MA (1993).
63. W. H. Press, S. A. Teukolsky, W. T. Vetterling, and B. P. Flannery. *Numerical Recipes in C: The Art of Scientific Computing*. Cambridge University Press, Cambridge, second edition (1992).
64. W. A. Strauss. *Partial Differential Equations, an Introduction*. John Wiley and Sons, Inc., New York (1992).
65. A.-S. Yang and B. Honig. Free energy determinants of secondary structure formation: I. α -helices. *J. Mol. Biol.* **252**: 351–365 (1995).
66. L. Wang, T. O’Connell, A. Tropsha, and J. Hermans. Energetic decomposition of the α -helix-coil equilibrium of a dynamic model system. *Biopolymers* **39**: 479–489 (1996).
67. C. D. Waldburger, J. F. Schildbach, and R. T. Sauer. Are buried salt bridges important for protein stability and conformational specificity? *Nature Struct. Biol.* **2**: 122–128 (1995).
68. W. C. Wimley, K. Gawrisch, T. P. Creamer, and S. H. White. Direct measurement of salt-bridge solvation energies using a peptide model system: Implications for protein stability. *Proc. Natl. Acad. Sci. U.S.A.* **93**: 2985–2990 (1996).
69. S. A. Allison, G. Ganti, and J. A. McCammon. Simulation of the diffusion-controlled reaction between superoxide and superoxide dismutase. I. Simple models. *Biopolymers* **24**: 1323–1336 (1985).
70. I. Klapper, R. Hagstrom, R. Fine, K. Sharp, and B. Honig. Focusing of electric fields in the active site of Cu-Zn superoxide dismutase: Effects of ionic strength and amino-acid modification. *Proteins: Struct., Funct., Genet.* **1**: 47–59 (1986).
71. S. A. Allison, R. J. Bacquet, and J. A. McCammon. Simulation of the diffusion-controlled reaction between superoxide and superoxide dismutase. II. Detailed models. *Biopolymers* **27**: 251–269 (1988).
72. M. Marquart, J. Walter, J. Deisenhofer, W. Bode, and R. Huber. The geometry of the reactive site and of the peptide groups in trypsin, trypsinogen and its complexes with inhibitors. *Acta Cryst.* **B39**: 480–490 (1983).
73. J. Bajorath, D. H. Kitson, J. Kraut, and A. T. Hagler. The electrostatic potential of Escherichia coli dihydrofolate reductase. *Proteins: Struct., Funct., Genet.* **11**: 1–12 (1991).
74. E. Kangas and B. Tidor. Electrostatic specificity in molecular ligand design. *J. Chem. Phys.* **112** (2000). in press (Reproduced in Chapter 8).
75. J. Janin. Quantifying biological specificity: The statistical mechanics of molecular recognition. *Proteins: Struct., Funct., Genet.* **25**: 438–445 (1996).
76. W. L. Jorgensen and J. Pranata. Importance of secondary interactions in triply hydrogen bonded complexes: Guanine–cytosine vs uracil–2,6-diaminopyridine. *J. Am. Chem. Soc.* **112**: 2008–2010 (1990).
77. T. J. Murray and S. C. Zimmerman. New triply hydrogen bonded complexes with highly variable stabilities. *J. Am. Chem. Soc.* **114**: 4010–4011 (1992).
78. A. D. Hamilton, E. Fan, S. Van Arman, S. J. Geib, and J. Yang. The design of artificial receptors for complexation and controlled aggregation. *Phil. Trans. R. Soc. Lond. A* **345**: 57–66 (1993).
79. J. Pranata, S. G. Wierschke, and W. L. Jorgensen. OPLS potential functions for nucleotide bases. Relative association constants for hydrogen-bonded base pairs in chloroform. *J. Am. Chem. Soc.* **113**: 2810–2819 (1991).
80. B. E. Eaton, L. Gold, and D. A. Zichi. Let’s get specific: The relationship between specificity and affinity. *Chem. & Biol.* **2**: 633–638 (1995).

81. M. L. Connolly. Analytical molecular surface calculation. *J. Appl. Cryst.* **16**: 548–558 (1983).
82. M. K. Gilson and B. H. Honig. Calculation of electrostatic potentials in an enzyme active site. *Nature (London)* **330**: 84–86 (1987).
83. S. L. Sobolev. *Partial Differential Equations of Mathematical Physics*. Dover, New York (1989).
84. F. Fogolari and J. M. Briggs. On the variational approach to Poisson–Boltzmann free energies. *Chem. Phys. Lett.* **281**: 135–139 (1997).
85. E. von Kitzing and D. M. Soumpasis. Electrostatics of a simple membrane model using Green’s functions formalism. *Biophysical J.* **71**: 795–810 (1996).
86. V. A. Parsegian. Ion–membrane interactions as structural forces. *Ann. N. Y. Acad. Sci.* **264**: 161–174 (1975).
87. E. Kangas and B. Tidor. Optimizing electrostatic affinity in ligand–receptor binding: Theory, computation, and ligand properties. *J. Chem. Phys.* **109**: 7522–7545 (1998). (Reproduced in Chapter 3).
88. M. Abramowitz and I. A. Stegun. *Handbook of Mathematical Functions with Formulas, Graphs and Mathematical Tables*. National Bureau of Standards, Washington, D. C. (1964).
89. E. Kangas and B. Tidor. Prediction of improved enzyme inhibitors based on electrostatic affinity optimization: Application to chorismate mutase. In preparation (Reproduced in Chapter 7).
90. L. Greengard. *The Rapid Evaluation of Potential Fields in Particle Systems*. MIT Press, Cambridge, MA (1988).
91. J. G. Kirkwood. Theory of solutions of molecules containing widely separated charges with special application to zwitterions. *J. Chem. Phys.* **2**: 351–361 (1934).
92. G. F. Simmons. *Topology and Modern Analysis*. McGraw–Hill, New York (1963).
93. O. D. Kellogg. *Foundations of Potential Theory*. Dover, New York (1953).
94. P. A. Bartlett and C. R. Johnson. An inhibitor of chorismate mutase resembling the transition-state conformation. *J. Am. Chem. Soc.* **107**: 7792–7793 (1985).
95. E. Haslam. *The Shikimate Pathway*. Wiley, New York (1974).
96. William J. Guilford, Shelly D. Copley, and Jeremy R. Knowles. On the mechanism of the chorismate mutase reaction. *J. Am. Chem. Soc.* **109**: 5013–5019 (1987).
97. Joseph V. Gray, Doron Eren, and Jeremy R. Knowles. Monofunctional chorismate mutase from *bacillus subtilis*: Kinetic and ^{13}C NMR studies on the interaction of the enzyme with its ligands. *Biochemistry* **29**: 8872–8878 (1990).
98. Olaf Wiest and Kendall N. Houk. Stabilization of the transition state of the chorismate–prephenate rearrangement: An ab initio study of enzyme and antibody catalysis. *J. Am. Chem. Soc.* **117**: 11628–11639 (1995).
99. Mark M. Davidson, Ian R. Gould, and Ian H. Hiller. Contribution of transition-state binding to the catalytic activity of *bacillus subtilis* chorismate mutase. *J. Chem. Soc., Chem. Commun.* pages 63–64 (1995).
100. Paul D. Lyne, Adrian J. Mulholland, and W. Graham Richards. Insights into chorismate mutase catalysis from a combined QM/MM simulation of the enzyme reaction. *J. Am. Chem. Soc.* **117**: 11345–11350 (1995).
101. Peter Kast, Jeffery D. Hartgerink, M. Asif-Ullah, and Dolald Hilvert. Electrostatic catalysis of the Claisen rearrangement: Probing the role of Glu78 in *bacillus subtilis* chorismate mutase by genetic selection. *J. Am. Chem. Soc.* **118**: 3069–3070 (1996).

102. Peter Kast, M. Asif-Ullah, Ning Jiang, and Dolald Hilvert. Exploring the active site of chorismate mutase by combinatorial mutagenesis and selection: The importance of electrostatic catalysis. *Proc. Natl. Acad. Sci. USA* **93**: 5043–5048 (1996).
103. Sharon T. Cload, David R. Liu, Richard M. Pastor, and Peter G. Schultz. Mutagenesis study of active site residues in chorismate mutase from *bacillus subtilis*. *J. Am. Chem. Soc.* **118**: 1787–1788 (1996).
104. Peter Kast, Yadu B. Tewari, Olaf Wiest, Donald Hilvert, Kendall N. Houk, and Robert N. Goldberg. Thermodynamics of the conversion of chorismate to prephenate: Experimental results and theoretical predictions. *J. Phys. Chem. B* **101**: 10976–10982 (1997).
105. Darin J. Gustin, Patrizio Mattei, Peter Kast, Olaf Wiest, Lac Lee, W. Wallace Cleland, and Dolald Hilvert. Heavy atom isotope effects reveal a highly polarized transition state for chorismate mutase. *J. Am. Chem. Soc.* **121**: 1756–1757 (1999).
106. Yuh Min Chook, Hengming Ke, and William N. Lipscomb. Crystal structures of the monofunctional chorismate mutase from *bacillus subtilis* and its complex with a transition state analog. *Proc. Natl. Acad. Sci. USA* **90**: 8600–8603 (1993).
107. Yuh Min Chook, Joseph V. Gray, Hengming Ke, and William N. Lipscomb. The monofunctional chorismate mutase from *bacillus subtilis*: Structure determination of chorismate mutase and its complexes with a transition state analog and prephenate, and implications for the mechanism of the enzyme reaction. *J. Mol. Biol.* **240**: 476–500 (1994).
108. B. R. Brooks, R. E. Bruccoleri, B. D. Olafson, D. J. States, S. Swaminathan, and M. Karplus. CHARMM: A program for macromolecular energy, minimization, and dynamics calculations. *J. Comput. Chem.* **4**: 187–217 (1983).
109. A. D. MacKerell, Jr., D. Bashford, M. Bellott, R. L. Dunbrack, Jr., J. D. Evanseck, M. J. Field, S. Fischer, J. Gao, H. Guo, S. Ha, D. Joseph-McCarthy, L. Kuchnir, K. Kuczera, F. T. K. Lau, C. Mattos, S. Michnick, T. Ngo, D. T. Nguyen, B. Prodhom, III W. E. Reiher, B. Roux, M. Schlenkrich, J. C. Smith, R. Stote, J. Straub, M. Watanabe, J. Wiórkiewicz–Kuczera, D. Yin, and M. Karplus. All-atom empirical potential for molecular modeling and dynamics studies of proteins. *J. Phys. Chem.* **102**: 3586–3616 (1998).
110. M. E. Davis and J. A. McCammon. Electrostatics in biomolecular structure and dynamics. *Chem. Rev.* **90**: 509–521 (1990).
111. Z. S. Hendsch and B. Tidor. Electrostatic interactions in the GCN4 leucine zipper: Substantial contributions arise from intramolecular interactions enhanced on binding. *Protein Sci.* **8**: 1381–1392 (1999).
112. D. Sitkoff, K. A. Sharp, and B. Honig. Accurate calculation of hydration free energies using macroscopic solvent models. *J. Phys. Chem.* **98**: 1978–1988 (1994).
113. Schrödinger, Inc., Portland, OR. *Jaguar 3.5*, (1998).
114. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Goll, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, and J. A. Pople. *Gaussian 98 (Revision A.1)*. Gaussian, Inc., Pittsburgh, PA (1998).
115. Christopher I. Bayly, Piotr Cieplak, Wendy D. Cornell, and Peter A. Kollman. A well-behaved electrostatic potential based method using charge restraints for deriving atomic charges: The RESP model. *J. Phys. Chem.* **97**: 10269–10280 (1993).

116. Wendy D. Cornell, Piotr Cieplak, Christopher I. Bayly, and Peter A. Kollman. Application of RESP charges to calculate conformational energies, hydrogen bond energies, and free energies of solvation. *J. Am. Chem. Soc.* **115**: 9620–9631 (1993).
117. S. E. Dempster and B. Tidor. In preparation.
118. E. Kangas and B. Tidor. Electrostatic affinity optimization in ionic solvents. (Reproduced in Chapter 5).
119. W. H. Press, B. P. Flannery, S. A. Teukolsky, and W. T. Vetterling. *Numerical Recipes: The Art of Scientific Computing*. Cambridge University Press, Cambridge (1986).
120. R.J. Vanderbei. An interior-point code for quadratic programming. *Optimization Methods and Software* **12**: 451–454 (1999).
121. R.J. Vanderbei. LOQO user’s manual—version 3.10. *Optimization Methods and Software* **12**: 485–514 (1999).
122. Linus Pauling. Nature of forces between large molecules of biological interest. *Nature* **161**: 707–709 (1948).
123. Ernesto Freire. The propagation of binding interactions to remote sites in proteins: Analysis of the binding of the monoclonal antibody D1.3 to lysozyme. *PNAS* **96**: 10118–10122 (1999).
124. J. M. Gao, S. Qiao, and G. M. Whitesides. Increasing binding constants of ligands to carbonic-anhydrase by using greasy tails. *J. Med. Chem.* **38**: 2292–2301 (1995).
125. Jeffrey B. Doyon and Ahamindra Jain. The pattern of fluorine substitution affects binding affinity in a small library of fluoroaromatic inhibitors for carbonic anhydrase. *Org. Lett.* **1**: 183–186 (1999).
126. Joseph V. Gray, Béatrice Bolinelli-Pimpaneau, and Jeremy R. Knowles. Monofunctional chorismate mutase from *bacillus subtilis*: Purification of the protein, molecular cloning of the gene, and overexpression of the gene product in *escherichia coli*. *Biochemistry* **29**: 376–383 (1990).
127. Z. S. Hendsch, T. Jonsson, R. T. Sauer, and B. Tidor. Protein stabilization by removal of unsatisfied polar groups: Computational approaches and experimental tests. *Biochemistry* **35**: 7621–7625 (1996).
128. S. Spector, M. Wang, S. A. Carp, J. Robblee, Z. S. Hendsch, R. Fairman, B. Tidor, and D. P. Raleigh. Rational modification of protein stability by the mutation of charged surface residues. *Biochemistry*. In press.
129. L. T. Chong, Z. S. Hendsch, and B. Tidor. In preparation.
130. E. Kangas and B. Tidor. Optimizing electrostatic affinity in ligand–receptor binding: Theory, computation, and ligand properties. *J. Chem. Phys.* **109**: 7522–7545 (1998).
131. A. R. Fersht. The hydrogen bond in molecular recognition. *Trends Biochem. Sci.* **12**: 301–304 (1987).
132. Herbert Goldstein. *Classical Mechanics*. Addison–Wesley, Reading, MA (1981).
133. S. K. Stein. *Calculus and Analytic Geometry*. McGraw–Hill, New York, fourth edition (1987).
134. G. Strang. *Introduction to Applied Mathematics*. Wellesley–Cambridge Press, Wellesley, MA (1986).
135. E. Kangas and B. Tidor. Optimization of electrostatic interactions in the presence of aqueous ions. In preparation.
136. A. R. Fersht. *Enzyme Structure and Mechanism*. W. H. Freeman and Company, New York, second edition (1985).

137. A. Husian, C. C. Galopin, S. Zhang, G. Pohnert, and B. Ganem. S-(—)-dinitrobiphenic acid: A selective inhibitor of *escherichia coli* chorismate mutase based on prephenate mimicry. *J. Am. Chem. Soc.* **121**: 2647–2648 (1999).
138. A. Y. Lee, A. Karplus, B. Ganem, and J. Clardy. Atomic structure of the buried catalytic pocket of *escherichia coli* chorismate mutase. *J. Am. Chem. Soc.* **117**: 3627–3628 (1995).
139. A. Lee, J. D. Stewart, J. Clardy, and B. Ganem. New insight into the catalytic mechanism of chorismate mutases from structural studies. *Chem. Biol.* **2**: 195–203 (1995).
140. D. Hilvert, S. H. Carpenter, K. D. Nared, and M.-T. M. Auditor. Catalysis of concerted reactions by antibodies: The Claisen rearrangement. *Proc. Natl. Acad. Sci.* **85**: 4953–4955 (1988).
141. Paul D. Lyne, (1999). Private communication.
142. C. L. Brooks, III and M. Karplus. Solvent effects on protein motion and protein effects on solvent motion: Dynamics of the active site region of lysozyme. *J. Mol. Biol.* **208**: 159–181 (1989).
143. K. Sharp, J. Jean-Charles, and B. Honig. *J. Phys. Chem.* **96**: 3822–3828 (1992).
144. J. Shen and F. A. Quiocho. Calculation of binding energy differences for receptor–ligand systems using the Poisson–Boltzmann method. *J. Comput. Chem.* **16**: 445–448 (1995).
145. J. Theodoor G. Overbeek. The role of energy and entropy in the electrical double layer. *Colloids and Surfaces* **51**: 61–75 (1990).
146. W. K. H. Panofsky and M. Phillips. *Classical Electricity and Magnetism*. Addison–Wesley, Reading, MA, second edition (1962).
147. B. Tidor. Unpublished work.
148. C. T. and J. G. Kirkwood. Theory of protein titration curves. I. General equations for impenetrable spheres. *J. Am. Chem. Soc.* **79**: 5333–5339 (1957).
149. E. Kangas and B. Tidor. Electrostatic solvation and affinity optimization in spheroidal molecular geometries. unpublished work (Reproduced in Chapter 4).
150. A. Nicholls, K. A. Sharp, and B. Honig. Protein folding and association: Insights from the interfacial and thermodynamic properties of hydrocarbons. *Proteins: Struct., Funct., Genet.* **11**: 281–296 (1991).
151. J. G. Kirkwood. *J. Chem. Phys.* **10**: 394 (1942).
152. T. Lazaridis and M. E. Paulaitis. Entropy of hydrophobic hydration: A new statistical mechanical formulation. *J. Phys. Chem.* **96**: 3847–3855 (1992).
153. T. Lazaridis and M. E. Paulaitis. Simulation studies of the hydration of simple, hydrophobic solutes. *J. Phys. Chem.* **98**: 635–642 (1994).
154. L. S. Ornstein and F. Zernike. *Proc. Acad. Sci. (Amsterdam)* **17**: 793 (1914).
155. V. Volterra. *Theory of Functionals and of Integral and Integro-Differential Equations*. Dover, New York (1959).
156. H. C. Anderson and D. Chandler. Optimized cluster expansions for classical fluids. I. General theory and variational formulation of the mean spherical model and hard sphere Percus–Yevick equations. *J. Chem. Phys.* **57**: 1918–1929 (1972).
157. P. J. Rossky and W. D. T. Dale. Generalized recursive solutions to Ornstein–Zernike integral equations. *J. Chem. Phys.* **73**: 2457–2464 (1980).
158. D. Chandler and H. C. Anderson. Optimized cluster expansions for classical fluids. II. Theory of molecular liquids. *J. Chem. Phys.* **57**: 1930–1937 (1972).

159. B. J. Berne, editor. *Statistical Mechanics Part A: Equilibrium Fluids*. Number 5 in Modern Theoretical Chemistry. Plenum Press, New York (1977).
160. J. K. Percus and G. J. Yevick. *Phys. Rev.* **110**: 1 (1958).
161. G. Stell. The Percus–Yevick equation for the radial distribution function of a fluid. *Physica* **29**: 517–534 (1963).
162. D. Beglov and B. Roux. Solvation of complex molecules in a polar liquid: An integral equation theory. *J. Chem. Phys.* **104**: 8678–8689 (1996).
163. D. Beglov and B. Roux. Numerical solution of the hypernetted chain equation for a solute of arbitrary geometry in three dimensions. *J. Chem. Phys.* **103**: 360–364 (1995).
164. M. Ikeguchi and J. Doi. Direct numerical solution of the Ornstein–Zernike integral equation and spatial distribution of water around hydrophobic molecules. *J. Chem. Phys.* **103**: 5011–5017 (1995).
165. P. H. Fries and G. N. Patey. The solution of the Hypernetted-chain approximation for fluids of nonspherical particles. A general method with application to dipolar hard spheres. *J. Chem. Phys.* **82**: 429–440 (1985).
166. G. M. Torrie, P. G. Kusalik, and G. N. Patey. Molecular solvent model for an electrical double layer: Reference Hypernetted-chain (RHNC) results for solvent structure at a charged surface. *J. Chem. Phys.* **88**: 7826–7840 (1988).
167. F. Hirata, M. Pettitt, and P. J. Rossky. Application of an extended RISM equation to dipolar and quadrupolar fluids. *J. Chem. Phys.* **77**: 509–520 (1982).
168. S. J. Singer and D. Chandler. Free energy functions in the extended RISM approximation. *Mol. Phys.* **55**: 621–625 (1985).
169. F. Hirata and P. J. Rossky. An extended RISM equation for molecular polar fluids. *Chem. Phys. Lett.* **83**: 329–334 (1981).
170. J. S. Hoyle and G. Stell. *J. Chem. Phys.* **65**: 18 (1976).
171. D. E. Sullivan and C. G. Gray. *Mol. Phys.* **42**: 443 (1981).
172. H.-A. Yu, B. Roux, and M. Karplus. Solvation thermodynamics: An approach from analytic temperature derivatives. *J. Chem. Phys.* **92**: 5020–5033 (1990).
173. D. Chandler, Y. Singh, and D. M. Richardson. Excess electrons in simple fluids. I. General equilibrium theory for classical hard sphere solvents. *J. Chem. Phys.* **81**: 1975–1982 (1984).
174. T. Ichiye and David Chandler. *J. Chem. Phys.* **92**: 5257 (1988).
175. P. H. Lee and G. M. Maggiora. Solvation thermodynamics of polar molecules in aqueous solution by the XRISM method. *J. Phys. Chem.* **97**: 10175–10185 (1993).
176. E. Kangas and B. Tidor. Unpublished work.
177. F. Lado. Numerical fourier transforms in one, two, and three dimensions for liquid state calculations. *J. Comput. Chem.* **8**: 417–433 (1971).
178. E. Johnson and R. Paul Hazoumé. Application of the RISM theory to Lennard–Jones interaction site molecular fluids. *J. Chem. Phys.* **70**: 1599–1601 (1979).
179. M. J. Gillan. A new method of solving the liquid structure integral equations. *Mol. Phys.* **38**: 1781–1794 (1979).
180. P. A. Monson. Numerical solution of the RISM equations for the site-site 12-6 potential. *Mol. Phys.* **47**: 435–442 (1982).
181. E. Enciso. Numerical solution of the SSOZ equation by extension of Gillan’s method to non-homonuclear molecular fluids. *Mol. Phys.* **56**: 129–140 (1985).