

REFERENCES

1. P. J. Artymiuk, A. R. Poirrette, H. M. Grindley, D.W. Rice, and P. Willett. A graph-theoretic approach to the identification of three-dimensional patterns of amino acid side-chains in protein structure. *J. Mol. Biol.*, 243:327–344, 1994.
2. R.F.W. Bader. *Atoms in Molecules: A Quantum Theory*. The international series of monographs on chemistry, No. 22. Oxford University Press, 1994.
3. Y. Ban, H. Edelsbrunner, and J. Rudolph. Interface surfaces for protein-protein complexes. In *RECOMB*, pages 205–212, 2004.
4. T. A. Binkowski, L. Adamian, and J. Liang. Inferring functional relationship of proteins from local sequence and spatial surface patterns. *J. Mol. Biol.*, 332:505–526, 2003.
5. T.A. Binkowski, P. Freeman, and J. Liang. pvSOAR: Detecting similar surface patterns of pocket and void surfaces of amino acid residues on proteins. *Nucleic Acid Research*, 32:W555–W558, 2004.
6. T.A. Binkowski, A. Joachimiak, and J. Liang. Protein surface analysis for function annotation in high-throughput structural genomics pipeline. *Protein Sci*, 14(12):2972–81, 2005.
7. A. Bondi. VDW volumes and radii. *J. Phys. Chem.*, 68:441–451, 1964.
8. S. Chakravarty, A. Bhinge, and R. Varadarajan. A procedure for detection and quantitation of cavity volumes proteins. Application to measure the strength of the hydrophobic driving force in protein folding. *J Biol Chem*, 277(35):31345–53, 2002.
9. M. L. Connolly. Analytical molecular surface calculation. *J. Appl. Cryst.*, 16:548–558, 1983.
10. G. M. Crippen and T. F. Havel. *Distance Geometry and Molecular Conformation*. J. Wiley & Sons, 1988.

11. J. Dundas, Z. Ouyang, J. Tseng, A. Binkowski, Y. Turpaz, and J. Liang. CASTp: computed atlas of surface topography of proteins with structural and topographical mapping of functionally annotated residues. *Nucleic Acids Res*, 34(Web Server issue):W116–8, 2006.
12. H. Edelsbrunner. The union of balls and its dual shape. *Discrete Comput. Geom.*, 13:415–440, 1995.
13. H. Edelsbrunner. *Geometry and Topology for Mesh Generation*. Cambridge University Press, 2001.
14. H. Edelsbrunner, M. Facello, P. Fu, and J. Liang. Measuring proteins and voids in proteins. In *Proc. 28th Ann. Hawaii Int'l Conf. System Sciences*, volume 5, pages 256–264, Los Alamitos, California, 1995. IEEE Computer Society Press.
15. H. Edelsbrunner and E.P. Mücke. Three-dimensional alpha shapes. *ACM Trans. Graphics*, 13:43–72, 1994.
16. H. Edelsbrunner and N.R. Shah. Incremental topological flipping works for regular triangulations. *Algorithmica*, 15:223–241, 1996.
17. H. Edelsbrunner, M. Facello, and J. Liang. On the definition and the construction of pockets in macromolecules. *Disc. Appl. Math.*, 88:18–29, 1998.
18. J. L. Finney. Volume occupation, environment and accessibility in proteins. The problem of the protein surface. *J. Mol. Biol.*, 96:721–732, 1975.
19. D. Fischer, R. Norel, H. Wolfson, and R. Nussinov. Surface motifs by a computer vision technique: searches, detection, and implications for protein- ligand recognition. *Proteins: Structure, Function and Genetics*, 16:278–292, 1993.
20. B. J. Gellatly and J.L. Finney. Calculation of protein volumes: an alternative to the Voronoi procedure. *J. Mol. Biol.*, 161:305–322, 1982.
21. M. Gerstein and F. M Richards. *Protein Geometry: Distances, Areas, and Volumes*, volume F, chapter 22. International Union of Crystallography, 1999.
22. F. Glaser, T. Pupko, I. Paz, R.E. Bell, D. Shental, E. Martz, and N. Ben-Tal. Consurf: identification of functional regions in proteins by surface-mapping of phylogenetic information. *Bioinformatics*, 19(1):163–4, 2003.
23. A Goede, R Preissner, and C Frömmel. Voronoi cell: New method for allocation of space among atoms: Elimination of avoidable errors in calculation of atomic volume and density. *Journal of computational chemistry*, 18(9):1113–1123, 1997.
24. L. Guibas and J. Stolfi. Primitives for the manipulation of general subdivisions and the computation of Voronoi diagrams. *ACM Transactions on Graphics*, 4:74–123, 1985.
25. Y Harpaz, M Gerstein, and C Chothia. Volume changes on protein folding. *Structure (London, England : 1993)*, 2(7):641–649, 1994.
26. L. Holm and C. Sander. New structure: Novel fold? *Structure*, 5:165–171, 1997.
27. C. Hu, X. Li, and J. Liang. Developing optimal nonlinear scoring function for protein design. *Bioinformatics*, 20:3080–3098, 2004.
28. J. Kleinberg. Efficient algorithms for protein sequence design and the analysis of certain evolutionary fitness landscapes. In *RECOMB*, pages 205–212, 2004.
29. K. W. Kratky. Intersecting disks (and spheres) and statistical mechanics. I. mathematical basis. *J. Stat. Phys.*, 25:619–634, 1981.
30. R. A. Laskowski, N. M. Luscombe, M. B. Swindells, and J. M. Thornton. Protein clefts in molecular recognition and function. *Protein Sci.*, 5:2438–2452, 1996.

31. A. Leaver-Fay, B. Kuhlman, and J. Snoeyink. An adaptive dynamic programming algorithm for the side chain placement problem. In *Pacific Symposium on Biocomputing*, pages 17–28, 2005.
32. B. Lee and F. M. Richards. The interpretation of protein structures: estimation of static accessibility. *J. Mol. Biol.*, 55:379–400, 1971.
33. M. Levitt, M. Gerstein, E. Huang, S. Subbiah, and J. Tsai. Protein folding: the endgame. *Annu Rev Biochem*, 66:549–579, 1997.
34. X. Li, C. Hu, and J. Liang. Simplicial edge representation of protein structures and alpha contact potential with confidence measure. *Proteins*, 53:792–805, 2003.
35. X. Li and J. Liang. Computational design of combinatorial peptide library for modulating protein-protein interactions. *Pac Symp Biocomput*, pages 28–39, 2005.
36. X. Li and J. Liang. Geometric cooperativity and anticooperativity of three-body interactions in native proteins. *Proteins*, 60(1):46–65, 2005.
37. J. Liang and K. A. Dill. Are proteins well-packed? *Biophys. J.*, 81:751–766, 2001.
38. J. Liang, H. Edelsbrunner, P. Fu, P. V. Sudhakar, and S. Subramaniam. Analytical shape computing of macromolecules I: Molecular area and volume through alpha-shape. *Proteins*, 33:1–17, 1998.
39. J. Liang, H. Edelsbrunner, P. Fu, P. V. Sudhakar, and S. Subramaniam. Analytical shape computing of macromolecules II: Identification and computation of inaccessible cavities inside proteins. *Proteins*, 33:18–29, 1998.
40. J. Liang, H. Edelsbrunner, and C. Woodward. Anatomy of protein pockets and cavities: Measurement of binding site geometry and implications for ligand design. *Protein Sci*, 7:1884–1897, 1998.
41. O. Lichtarge, H.R. Bourne, and F.E. Cohen. An evolutionary trace method defines binding surfaces common to protein families. *J Mol Biol*, 257(2):342–58, 1996.
42. A. C. R. Martin, C. A. Orengo, E. G. Hutchinson, A. D. Michie, A. C. Wallace, M. L. Jones, and J. M. Thornton. Protein folds and functions. *Structure*, 6:875–884, 1998.
43. R. Norel, D. Fischer, H. J. Wolfson, and R. Nussinov. Molecular surface recognition by computer vision-based technique. *Protein Eng.*, 7, 1994.
44. C. A. Orengo, A. E. Todd, and J. M. Thornton. From protein structure to function. *Curr. Opinion Structural Biology*, 9(4):374–382, 1999.
45. M. Petitjean. On the analytical calculation of van der waals surfaces and volumes: some numerical aspects. *J. Comput. Chem.*, 15:507–523, 1994.
46. G. Rhodes. *Crystallography Made Crystal Clear: A Guide for Users of Macromolecular Models*. Academic Press, 1999.
47. F. M. Richards. The interpretation of protein structures: total volume, group volume distributions and packing density. *J. Mol. Biol.*, 82:1–14, 1974.
48. F. M. Richards. The interpretation of protein structures: total volume, group volume distributions and packing density. *J. Mol. Biol.*, 82:1–14, 1974.
49. F. M. Richards. Areas, volumes, packing, and protein structures. *Ann. Rev. Biophys. Bioeng.*, 6:151–176, 1977.
50. F. M. Richards. Calculation of molecular volumes and areas for structures of known geometries. *Methods in Enzymology*, 115:440–464, 1985.
51. F. M. Richards and W. A. Lim. An analysis of packing in the protein folding problem. *Q. Rev. Biophys.*, 26:423–498, 1994.

52. T. J. Richmond. Solvent accessible surface area and excluded volume in proteins: analytical equations for overlapping spheres and implications for the hydrophobic effect. *J. Mol. Biol.*, 178:63–89, 1984.
53. W. Rieping, M. Habeck, and M. Nilges. Inferential structure determination. *Science*, 309(5732):303–6, 2005.
54. R. Russell. Detection of protein three-dimensional side-chain patterns: New examples of convergent evolution. *J. Mol. Biol.*, 279:1211–1227, 1998.
55. R. K. Singh, A. Tropsha, and I. I. Vaisman. Delaunay tessellation of proteins: four body nearest-neighbor propensities of amino-acid residues. *J. Comp. Bio.*, 3:213–221, 1996.
56. A. E. Todd, C. A. Orengo, and J. M. Thornton. Evolution of function in protein superfamilies, from a structural perspective. *J. Mol. Biol.*, 307:1113–1143, 2001.
57. J. Tsai, R. Taylor, C. Chothia, and M. Gerstein. The packing density in proteins: standard radii and volumes. *J Mol Biol*, 290(1):253–66, 1999.
58. Y.Y. Tseng and J. Liang. Estimating evolutionary rate of local protein binding surfaces: a bayesian monte carlo approach. *Proceedings of 2005 IEEE-EMBC Conference*, 2005.
59. Y.Y. Tseng and J. Liang. Estimation of amino acid residue substitution rates at local spatial regions and application in protein function inference: A Bayesian Monte Carlo approach. *Mol. Biol. Evol.*, 23(2):421–436, Feb 2006.
60. A. C. Wallace, N. Borkakoti, and J. M. Thornton. TESS: a geometric hashing algorithm for deriving 3d coordinate templates for searching structural databases. Application to enzyme active sites. *Protein Sci.*, 6:2308–2323, 1997.
61. J.M. Word, S.C. Lovell, J.S. Richardson, and D.C. Richardson. Asparagine and glutamine: using hydrogen atom contacts in the choice of side-chain amide orientation. *J Mol Biol*, 285(4):1735–47, 1999.
62. J. Xu. Rapid protein side-chain packing via tree decomposition. In *RECOMB*, pages 423–439, 2005.
63. J. Zhang, R. Chen, C. Tang, and J. Liang. Origin of scaling behavior of protein packing density: A sequential monte carlo study of compact long chain polymers. *J. Chem. Phys.*, 118:6102–6109, 2003.
64. W. Zheng, S. J. Cho, I. I. Vaisman, and A. Tropsha. A new approach to protein fold recognition based on Delaunay tessellation of protein structure. In R.B. Altman, A.K. Dunker, L. Hunter, and T.E. Klein, editors, *Pacific Symposium on Biocomputing'97*, pages 486–497, Singapore, 1997. World Scientific.

EXERCISES

1.1 For two points $\mathbf{x}_1, \mathbf{x}_2 \in \mathbb{R}^d$, the line through \mathbf{x}_1 and \mathbf{x}_2 can be written as: $\{\mathbf{x} | \mathbf{x} = \mathbf{x}_1 + \lambda(\mathbf{x}_2 - \mathbf{x}_1), \lambda \in \mathbb{R}\}$. Equivalently, we can define the line as:

$$\{\mathbf{x} | \mathbf{x} = (1 - \lambda)\mathbf{x}_1 + \lambda\mathbf{x}_2, \lambda \in \mathbb{R}\},$$

or

$$\{\mathbf{x} | \mathbf{x} = p_1\mathbf{x}_1 + p_2\mathbf{x}_2, p_1, p_2 \in \mathbb{R}, p_1 + p_2 = 1\}.$$