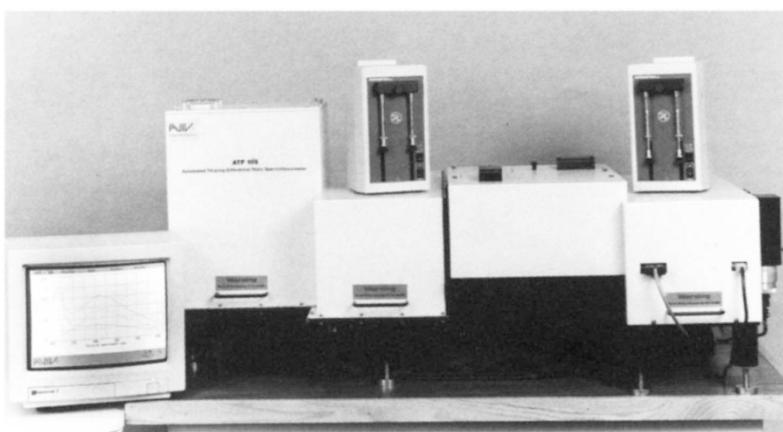


1. Wyman, J. & Gill, S.J. *Binding and Linkage: Functional Chemistry of Biological Macromolecules*. University Science Books, Mill Valley CA (1990).
2. Perutz, M.F. *Mechanisms of cooperativity and allosteric regulation in proteins*. Cambridge University Press, Cambridge England (1990).
3. Bohr, C. *Zentralbl. Physiol.* **17**, 682 (1903).
4. Hill, A.V. The possible effects of aggregation of the molecules of haemoglobin on its dissociation curve. *J. Physiol.* **40**, iv-vii (1910).
5. Antonini, E. & Brunori, M. *Hemoglobin and Myoglobin in Their Reactions With Ligands*. North-Holland Publishing Co., Amsterdam (1971).
6. Imai, K. *Allosteric effects in haemoglobin*. Cambridge University Press, New York (1982).
7. Cullis, A.F., Muirhead, H., Perutz, M.F. & Rossmann, M.G. *Proc. Roy. Soc. A* **265**, 161-187 (1962).
8. Perutz, M.F., Muirhead, H., Cox, J.M. & Goaman L.C.G., Three-dimensional fourier synthesis of horse oxyhaemoglobin at 2.8 Å resolution: the atomic model. *Nature* **219**, 131-139 (1968).
9. Dickerson, R.E. & Geis, I. *Hemoglobin*. The Benjamin/Cummings Publishing Company, Inc., Menlo Park, California (1983).
10. Perutz, M.F. Stereochemistry of cooperative effects in haemoglobin. *Nature* **228**, 726-734 (1970).
11. Perutz, M.F. Hemoglobin Structure and Respiratory Transport. *Sci. Amer.* **239**, 92-125 (1978).
12. Warshel, A. Energy-structure correlation in metalloporphyrins and the control of oxygen binding in hemoglobin. *Proc. Natl. Acad. Sci. USA* **74**, 1789-1793 (1977).
13. Gelin B.R. & Karplus, M. Mechanism of tertiary structural change in hemoglobin. *Proc. Natl. Acad. Sci. USA* **74**, 801-805 (1977).
14. Baldwin, J. & Chothia, C. Hemoglobin: the structural changes related to ligand binding and its allosteric mechanism. *J. Mol. Biol.* **129**, 175-220 (1979).
15. Vuk-Pavlovic, S. Evolution of the haem-haem interaction in vertebrate haemoglobins-a hypothesis. *J. Mol. Evol.* **6**, 209-214 (1975).
16. Barrick, D. Replacement of the proximal ligand of sperm whale myoglobin with free imidazole in the mutant His93→Gly. *Biochemistry* **33**, 6546-6554 (1994).
17. DePillis, G.D., Decatur, S.M., Barrick, D. & Boxer, S.G. Functional cavities in proteins. A general method for proximal ligand substitution in myoglobin. *J. Am. Chem. Soc.* **116**, 6981-6982 (1994).
18. Lu, Y., Casimiro, D.R., Bren, K.L., Richards, J.H. & Gray, H.B. Structurally engineered cytochromes with unusual ligand-binding properties: expression of Saccharomyces cerevisiae Met-80→Ala iso-1-cytochrome c. *Proc. Natl. Acad. Sci. USA* **90**, 11456-11459 (1993).
19. McRee, D.E., Jesen, G.M., Fitzgerald, M.M., Siegel, H.A. & Goodin, D.B. Construction of a bisquo heme enzyme and binding by exogenous ligands. *Proc. Natl. Acad. Sci. USA* **91**, 12847-12851 (1994).
20. Wilks, A., Sun, J., Loehr, T.M. & Ortiz de Montellano, P.R. Heme oxygenase His25Ala mutant: replacement of the proximal histidine iron ligand by exogenous bases restores the catalytic activity. *J. Am. Chem. Soc.* **117**, 2925-2926 (1995).
21. Newmyer, S., Sun, J., Loehr, T.M. & Ortiz de Montellano, P.R. Rescue of the Horseradish Peroxidase His-170→Ala Mutant Activity by Imidazole: Importance of Proximal Ligand Tethering. *Biochemistry* **35**, 12788-12795 (1996).
22. Barrick, D. Depletion and replacement of protein metal ligands. *Curr. Op. Biotechnology* **6**, 411-418 (1995).
23. St. George, R.C.C. & Pauling, L. The combining power of hemoglobin for alkyl isocyanides, and the nature of the heme-heme interactions in hemoglobin. *Science* **114**, 629-634 (1951).
24. Reisberg, P.I. & Olson, J.S. Equilibrium binding of alkyl isocyanides to human hemoglobin. *J. Biol. Chem.* **255**, 4144-4150 (1980).
25. Reisberg, P.I. & Olson, J.S. Kinetic and cooperative mechanisms of ligand binding to hemoglobin. *J. Biol. Chem.* **255**, 4159-4169 (1980).
26. Mims, M.P. et al. Proton nuclear magnetic resonance studies of isonitrile-heme protein complexes. *J. Biol. Chem.* **258**, 6125-6134 (1983).
27. Dahlquist, F.W. The meaning of Scatchard and Hill plots. *Meth. Enzymol.* **48**, 270-299 (1978).
28. Pulsinelli, P.D., Perutz, M.F. & Nagel, R.L. Structure of Hemoglobin M Boston, a Variant with a Five-Coordinated Ferric Heme. *Proc. Acad. Sci. USA* **70**, 3870-3874 (1973).
29. Takahashi, S., Lin, A.K.-L.C. & Ho C. Proton nuclear magnetic resonance studies of hemoglobins M. Boston (α 5E7 His→Tyr) and M Milwaukee (β 67E11 Val→Glu): spectral assignments of hyperfine-shifted proton resonances and of proximal histidine (E7) NH resonances to the α and β chains of normal human adult hemoglobin. *Biochemistry* **19**, 5196-5202 (1980).
30. Monod, J., Wyman, J. & Changeux, J.-P. On the nature of allosteric transitions: a plausible model. *J. Mol. Biol.* **12**, 88-118 (1965).
31. Koshland, D.E. Jr., Nemethy, G. & Filmer, D.L. Comparison of experimental and theoretical models in proteins containing subunits. *Biochemistry* **5**, 365-385 (1966).
32. Wyman, J. Linked functions and reciprocal effects in hemoglobin: a second look. *Adv. Prot. Chem.* **19**, 223-286 (1964).
33. Olson, J.S. & Gibson, Q.H. The functional properties of hemoglobin Bethesda ($\alpha_2\beta_2^{145}\text{His}$). *J. Biol. Chem.* **247**, 3662-3670 (1972).
34. Arnone, A. & Perutz, M.F. Structure of inositol hexaphosphate-human deoxyhaemoglobin complex. *Nature* **249**, 34-36 (1974).
35. Ho, C. Proton NMR studies on hemoglobin: cooperative interactions and partially ligated intermediates. *Adv. Prot. Chem.* **43**, 153-312 (1992).
36. Stryer, L. *Biochemistry 4th ed.*, W.H. Freeman & Co., New York (1995).
37. Voet, D. & Voet, J.G. *Biochemistry 2nd ed.*, John Wiley & Sons, Inc., New York (1995).
38. Rodgers, K.R. & Spiro, T.G. Nanosecond dynamics of the R→T transition in hemoglobin: ultraviolet Raman studies. *Science* **265**, 1697-1698 (1994).
39. Pauling, L. *The nature of the chemical bond*, 3rd ed., Cornell University Press, 1960.
40. Ackers, G.K., Doyle, M.L., Myers, D. & Daugherty, M.A. The molecular code for cooperativity in hemoglobin. *Science* **255**, 54-63 (1992).
41. Paoli, M., Liddington, R., Tame, J., Wilkinson, A. & Dodson, G. Crystal structure of T state haemoglobin with oxygen bound at all four haems. *J. Mol. Biol.* **256**, 775-792 (1996).
42. Viggiani, G. & Ho C. Proton nuclear magnetic resonance investigations of structural changes associated with cooperative oxygenation of human adult hemoglobin. *Proc. Natl. Acad. Sci. USA* **76**, 3673-3677 (1979).
43. Friedman, J.M. Time-resolved resonance Raman spectroscopy as a probe of structure, dynamics, and reactivity in hemoglobin. *Meth. Enzymol.* **232**, 205-231 (1994).
44. Liddington, R. X-ray Crystallography of partially liganded structures. *Meth. Enzymol.* **232**, 15-26 (1994).
45. Kunkel, T.M. Rapid and efficient site-specific mutagenesis without phenotypic selection. *Proc. Natl. Acad. Sci. USA* **82**, 488-492 (1985).
46. Shen, T.-J. et al. Production of unmodified human adult hemoglobin in *Escherichia coli*. *Proc. Natl. Acad. Sci. USA* **90**, 8108-8112 (1993).
47. Hayashi, A., Suzuki, T. & Shin, M. An enzyme reduction system for metmyoglobin and methemoglobin, and its application to functional studies of oxygen carriers. *Biochem. Biophys. Acta* **310**, 309-316 (1973).
48. Johnson M.L. & Frasier, S.G. Nonlinear least-squares analysis. *Meth. Enzymol.* **117**, 301-342 (1985).
49. Plateau, P. & Guérion, M. Exchangeable proton NMR without baseline distortion, using new strong pulse sequences. *J. Amer. Chem. Soc.* **104**, 7310-7311 (1982).

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