Leskovac, V. (1971) *Croat. Chem. Acta 43*, 183–186.
Leskovac, V., & Pfleiderer, G. (1969) *Hoppe-Seyler's Z. Physiol. Chem. 350*, 484–492.
Luzzatti, V. (1952) *Acta Crystallogr. 5*, 808–810.
Matthews, B. W., & Bernhard, S. A. (1973) *Annu. Rev. Biophys. Bioeng. 2*, 257–317.
McLachlan, A. D. (1979) *J. Mol. Biol. 128*, 49–79.
Ploegman, J. H., Drenth, J., Kalk, K. H., & Hol, W. G. J. (1978) *J. Mol. Biol. 123*, 557–594.
Rao, S. T., & Rossmann, M. G. (1973) *J. Mol. Biol. 76*, 241–256.
Remington, S. J., Wiegand, G., & Huber, R. (1982) *J. Mol. Biol. 158*, 111–152.
Richards, F. M. (1974) *J. Mol. Biol. 82*, 1–14.
Richardson, J. S. (1977) *Nature 268*, 495–500.
Richardson, J. S. (1981) *Adv. Protein Chem. 34*, 167–339.
Richmond, T. J., & Richards, F. M. (1978) *J. Mol. Biol. 119*, 537–555.
Roderick, S. L., & Banaszak, L. J. (1986) *J. Biol. Chem. 261*, 9461–9464.
Rossmann, M. G., Liljas, A., Branden, C.-I., & Banaszak, L. J. (1975) *Enzymes (3rd Ed.) 11A*, 61–102.
Rudolph, R., Fuchs, I., & Jaenicke, R. (1986) *Biochemistry 25*, 1662–1669.
Sacchettini, J. C., Gordon, J. I., & Banaszak, L. J. (1988) *J. Biol. Chem. 263*, 5815–5819.
Schirmer, T., Huber, R., Schneider, M., Bode, W., Miller, M., & Hackert, M. L. (1986) *J. Mol. Biol. 188*, 651–676.
Setoyama, C., Joh, T., Tsuzuki, T., & Shimada, K. (1988) *J. Mol. Biol. 202*, 355–364.
Sim, G. A. (1960) *Acta Crystallogr. 12*, 511–512.
Skarzynski, T., Moody, P. C. E., & Wonacott, A. J. (1987) *J. Mol. Biol. 193*, 171–187.
Tronrud, D., TenEyck, L., & Matthews, B. W. (1987) *Acta Crystallogr. 43A*, 489–501.
Wade, M., Tsernoglou, D., Hill, E., Webb, L., & Banaszak, L. J. (1973) *Biochim. Biophys. Acta 322*, 124–132.
Webb, L. E., Hill, E. J., & Banaszak, L. J. (1973) *Biochemistry 12*, 5101–5108.
Weininger, M., Birktoft, J. J., & Banaszak, L. J. (1977) in *Pyridine Nucleotide Dependent Dehydrogenases* (Sund, H., Ed.) pp 87–100, de Gruyter, Berlin.
Zimmerle, C., & Alter, G. (1983) *Biochemistry 22*, 6273–6281.
Zimmerle, C. T., Yung, P. P., & Alter, G. M. (1987) *Biochemistry 26*, 8535–8541.

Geometry of Interaction of Metal Ions with Sulfur-Containing Ligands in Protein Structures†

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ABSTRACT: An analysis of the geometry of binding of metal ions by cysteine and methionine residues in protein structures has been made by using the Protein Data Bank. Metal ions have a distinct mode of binding to each of these residues, and this is independent of the nature of the metal center or the type of protein. Metal ions tend to approach the sulfur of Met roughly 38° from the perpendicular to the plane through atoms C_γ–S_δ–C_ϵ. For Cys, the approach direction is such that the M···S_γ–C_β–C_α torsional angle is about ±90 or 180°. The side-chain conformation of the cysteine residue is affected by the presence of the metal ion; there is a shift from the g^+ conformation toward g^- and mainly t conformations. When two Cys residues at positions $i - 3$ and i bind to the same metal center, there appears to be some restriction on the geometry of metal binding by the residue i; for such a residue χ_1 and M···S_γ–C_β–C_α angles are likely to be around 60° and 270°, respectively. Met and Cys residues coordinating to a metal ion are usually from coil or turn regions of the protein structure.

Many metalloproteins, especially those involved in electron transfer, have one or more sulfur ligands (Cys, Met) bound to metal ions. Many of these proteins have characteristic absorption spectra caused by S → Fe or S → Cu charge transfer. A knowledge of the geometry of the interaction of metal ions with sulfur ligands and their molecular orbitals is essential in understanding electronic structures and oxidation–reduction properties of these metal sites (Gewirth & Solomon, 1988; Noodleman et al., 1985). Although several studies have been carried out on directional preferences of various ligands toward metal ions in small molecule structures (Rosenfield et al., 1977; Chakrabarti & Dunitz, 1982; Einspahr & Bugg, 1981), a comparable analysis with macromolecular structures has not been reported. In this paper we present an analysis of the interaction of metal ions with Cys and Met ligands in protein structures.

Materials and Methods

The analysis is based on atomic coordinates from the Brookhaven Protein Data Bank, (PDB) (Bernstein et al., 1977). All the structures studied had been subjected to some sort of refinement. To compare the results with those of small-molecule structures, the Cambridge Crystallographic Database (CCDB) (Allen et al., 1979) was searched for metal···cysteine interactions where cysteine acts as an unidentate ligand binding metal ions only through the sulfur atom, as in the case of protein structures.

(*a*) *Met.* The relative position of the metal ion was expressed in terms of spherical polar coordinates (Figure 1): the M···S_δ distance; the angle θ between the S_δ···M direction and

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Table I: Geometric Parameters for Metal (M)···Met Interactions

PDB code[a]	protein name[a]	metal[b]	residue[b] no.	M···S_δ distance (Å)	angle[c] (deg)	
					ϕ	θ
2AZA	azurin (ox)	Cu (A)	121 (A)	3.12	150.5	54.0
		Cu (B)	121 (B)	3.10	159.4	65.7
3CYT	cytochrome *c*, tuna (ox)	Fe (A)	80 (A)	2.28	175.6	37.7
		Fe (B)	80 (B)	2.26	176.0	43.3
4CYT	cytochrome *c*, tuna (red.)	Fe	80	2.32	179.7	38.5
1CCR	cytochrome *c*, rice (ox)	Fe	88	2.35	177.4	29.8
2C2C	cytochrome *c*2 (ox)	Fe	91	2.38	170.0	34.8
3C2C	cytochrome *c*2 (red.)	Fe	91	2.43	166.3	27.1
351C	cytochrome *c*551 (ox)	Fe	61	2.36	179.7	39.1
451C	cytochrome *c*551 (red.)	Fe	61	2.35	179.7	40.7
1CC5	cytochrome *c*5 (ox)	Fe	63	2.36	167.8	42.5
1PCY	plastocyanin (ox)	Cu	92	2.90	143.5	40.3
3PCY	plastocyanin (Hg substituted)	Hg	92	3.02	154.6	35.0
1PAZ	pseudoazurin	Cu	86	2.76	153.5	42.6

[a] Ox = oxidized; red. = reduced. 2AZA, Norris et al. (1986). 3CYT, 4CYT, Takano and Dickerson (1980). 1CCR, Ochi et al. (1983). 2C2C, 3C2C, Salemme et al. (1973). 351C, 451C, Matsuura et al. (1982). 1CC5, Carter et al. (1985). 1PCY, Guss et al. (1983). 3PCY, Church et al. (1986). 1PAZ, Petratos et al. (1988). [b] 1,2, or A,B, etc. is used to distinguish different metal atoms or subunits in the same protein molecule. [c] As defined in the text.

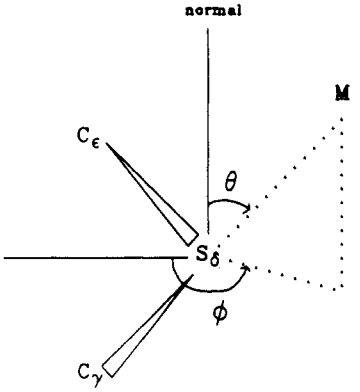

FIGURE 1: Diagrammatic representation of the spherical polar coordinates used to express metal (M)···Met interactions.

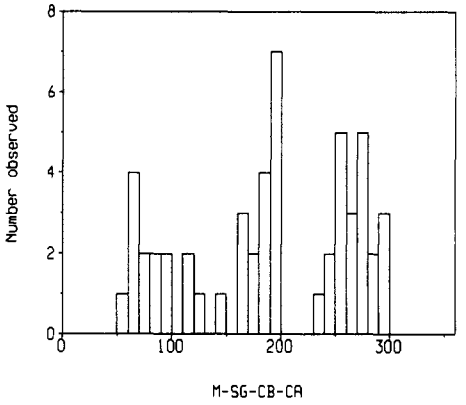

FIGURE 2: Histogram showing the distribution of M···S_γ–C_β–C_α torsional angles (deg) for all data given in Table III.

the normal to the C_γ–S_δ–C_ϵ plane, the colatitude; the angle ϕ between the C_γ–S_δ–C_ϵ angle bisector and the projection of the S_δ···M direction on the C_γ–S_δ–C_ϵ plane, the longitude, taking the angle bisector as the reference angle zero (Rosenfield et al., 1977; Chakrabarti & Dunitz, 1982).

(*b*) *Cys.* The position of the metal ion with respect to Cys side chain was defined in terms of M···S_γ distance, M···S_γ–C_β angle, and M···S_γ–C_β–C_α torsional angle.

Results and Discussion

(*a*) *Met.* All the relevant parameters are given in Table I. The average Fe···S_δ distance in all cytochrome structures is 2.34(5) Å. The direction of S_δ···M relative to C_γ–S_δ–C_ϵ plane is given by the polar and longitudinal angles θ and ϕ, the average values of which from the data (excluding azurin) in Table I are 38(5)° and 169(12)°, respectively. This shows that metal ions lie fairly close to the bisecting plane and make an angle of 38(5)° with the perpendicular to the C_γ–S_δ–C_ϵ plane. The Cu···S_δ distance in azurin is exceptionally long (Norris et al., 1986), and the θ angles for the two independent molecules in the crystal structure are also much larger than the average value. In small-molecule structures, θ was found to be 21(9)°, indicating an interaction of the metal ion with a sulfur lone-pair orbital (Rosenfield et al., 1977). The slightly different θ value found in protein structures may be because of the inaccuracy in the position of the terminal C_ϵ atom of the methionine side chain and the bias in the initial model that has been fitted to the protein electron density map. Three unrefined protein structures, cytochrome *c* from bonito (Tanaka et al., 1975), cytochrome *c*550 (Timkovich & Dickerson, 1976), and cytochrome *b*562 (Lederer et al., 1981), were not considered for this study. These have θ values in the range 67–88°. It is interesting to note that the structures that have been refined show a very similar orientation of the metal ion with respect to the Met ligand, although no geometrical constraint involving the metal ion was imposed during the refinement.

Table I, which includes three pairs of cytochrome structures determined in both oxidized and reduced states, shows that ϕ and θ angles do not change significantly with change of the oxidation state. However, slight variations in these angles may have a role in tuning the redox potential in different proteins.

To find out if Met residues binding to metal ions have any preference to be in any particular secondary structural state, the secondary structure was defined according to the method of Kabsch and Sander (1983) (Table II). As has been observed before (Levitt, 1978), the most dominant secondary structure element for Met is a helix; however, for those residues bound to metal ions, it is a coil.

The position of the metal ion at S_δ with respect to the main-chain atoms depends on the side-chain torsional angles χ_1 and χ_2. The extended conformation (all torsional angles around 180°) is the most common for Met side chain (McGregor et al., 1987). This is also true for Met residues bound to metal ions (however, in azurin, χ_1 is close to −60°, and in cytochrome *c*5, χ_2 is close to 60°).

(*b*) *Cys.* On the basis of the result presented in Table III, the average values for various bond distances are Fe···S_γ 2.3(1), Hg···S_γ 2.39(6), and Zn···S_γ 2.1(2) Å and the M···S_γ–C_β angle

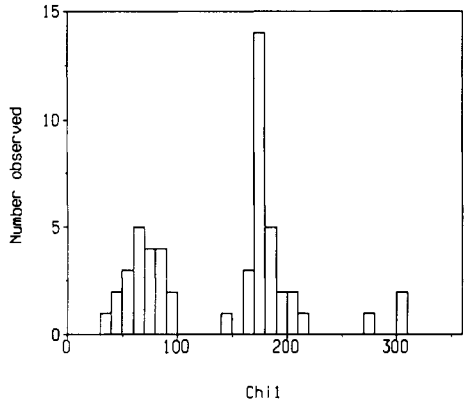

FIGURE 3: Histogram of χ_1 (deg) distribution for all metal-bound Cys residues in Table III.

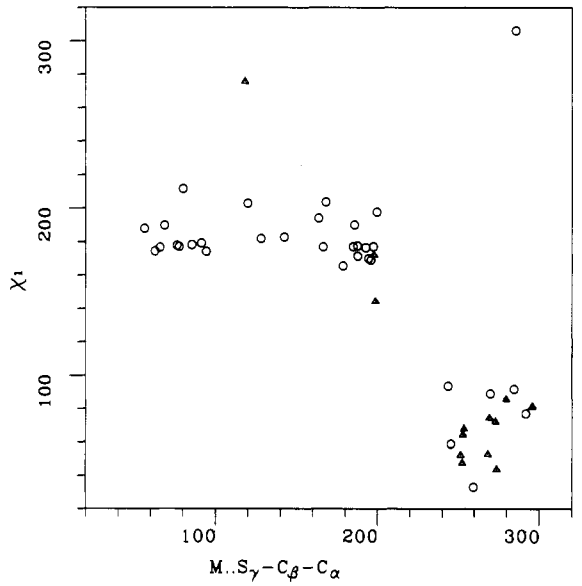

FIGURE 4: Plot of paired values of χ_1 and M···S_γ–C_β–C_α torsional angles (deg) for protein structures given in Table III. Triangles represent those Cys residues i that, along with another Cys at position $i - 3$, bind to the same metal ion or cluster; circles represent the rest.

is 108(10)°. Values observed in protein structures are very similar to those in mercury···cysteine complexes. This indicates that the metal···Cys interaction is not affected by the constraint in protein structure.

The disposition of the metal ion with respect to the Cys ligand, as given by the torsional angle M···S_γ–C_β–C_α, is shown in Figure 2. The distribution is trimodal at about 90°, 190°, and 270°. A recently determined structure of rubredoxin from *Desulfovibrio gigas* (Frey et al., 1987) also shows these torsional angles to be very close to 90° or 180°. The existence of two different values for the dihedral angle provides a basis for differing Fe–S stretching frequencies for the $Fe(S_\gamma)_4$ center (Yachandra et al., 1983). The present study shows that metal···Cys interaction, in general, has a preference for the

Table II: Percentage Distribution of the Secondary Structural States[a] for Free as Well as Metal-Bound Met and Cys Residues in Structures Considered in This Analysis[b]

	Met		Cys	
secondary structure	free	bound	free	bound
α-helix	37.5	0.0	21.1	4.9
extended strand	18.8	0.0	36.8	7.3
isolated β-bridge	0.0	25.0	5.3	2.4
3_{10} helix	6.3	0.0	10.5	7.3
turn	6.3	0.0	10.5	17.1
bend	12.5	12.5	10.5	7.3
coil	18.8	62.5	5.3	53.7
total no.	16	8	19	41

[a] As defined by Kabsch and Sander (1983). [b] For a given protein, the structure in only one subunit or in one oxidation state was considered.

M···S_γ–C_β–C_α torsional angle to be close to ±90° or 180°. The preferred angles in various structures, 90° from each other, may indicate the orientation of the mutually perpendicular p-type lone-pair orbitals on the sulfur atom. The M···S_γ–C_β–C_α angle of 0° is avoided because of the steric interaction between M and C_α atoms. In plastocyanin, with an angle of 194.3°, there has been a suggestion of a strong π interaction between the copper $d_{x^2-y^2}$ and cysteine pπ sulfur orbitals (Gewirth & Solomon, 1988). The geometry of the metal ion with respect to the thiolate sulfur seems to be similar to that found in the interaction of metal ions with the atom X of the C–X (X = Cl, Br, I) group (Ramasubbu et al., 1986).

As in the case of metal-bound Met residues, all Cys residues were analyzed for their secondary structures (Table II). Although Cys residues are most likely to be found in helices or strands, those binding metal ions are predominantly from turn or coil regions. By and large, Cys and Met residues binding to metal ions come from coil or turn regions of protein structure.

To analyze the side-chain conformations of Cys ligands binding to metal ions, a histogram showing χ_1 (torsional angle N–C_α–C_β–S_γ) is given in Figure 3. For amino acids in general, the χ_1 distribution is trimodal, the preferred conformation being around χ_1 = 60° (g^-), 180° (t), and 300° (g^+). However, for Cys residues in non-α/non-β structures, there is a preference for g^+ conformation, and g^- conformation is less favored, especially when the Cys belongs to an α-helix (McGregor et al., 1987). The distribution, however, is quite different in the presence of metal ions—the most preferred conformation is now t, g^- conformation is substantially populated, and a very few structures are found in the g^+ conformation.

To find any correlation between the orientation of the metal ion and the side-chain conformation of the Cys residue, M···S_γ–C_β–C_α and χ_1 torsional angles are plotted in Figure 4. When χ_1 is about 60°, there is a clustering of points around M···S_γ–C_β–C_α of 270°. It is known that in many proteins two Cys residues at positions $i - 3$ and i bind to the same metal ion or cluster (Adman et al., 1975). For the residue i of such pairs the torsional angles are distributed around χ_1 of 60° (g^-)

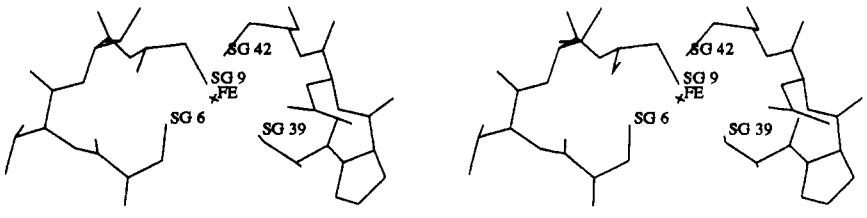

FIGURE 5: Stereoview of residues 6–9 and 39–42 showing the conformation and the mode of binding of Cys residues to Fe atom in rubredoxin.

Table III: Geometric Parameters for Metal (M)···Cys Interactions

PDB code[a]	protein name[a]	metal[b]	residue[b] no.	M···S_γ distance (Å)	M···S_γ–C_β angle (deg)	M···S_γ–C_β–C_α torsion (deg)	χ_1[c] torsion (deg)
4ADH	alcohol dehydrogenase	Zn (1)	46	2.08	112.9	185.6	190.0
			174	2.31	125.8	199.4	197.9
		Zn (2)	97	2.38	107.8	291.7	77.1
			100	2.36	100.7	253.5	68.0
			103	2.29	111.4	118.2	275.7
			111	2.33	106.7	77.9	177.1
7ATC	aspartate carbamyltransferase	Zn (B)	109 (B)	1.99	104.6	166.4	177.0
			114 (B)	2.03	114.8	119.8	202.9
			138 (B)	2.04	103.7	168.0	203.9
			141 (B)	2.02	134.8	268.3	52.7
		Zn (D)	109 (D)	2.04	117.9	163.5	194.1
			114 (D)	2.01	104.5	142.3	182.6
			138 (D)	2.00	98.6	197.5	177.1
			141 (D)	1.98	132.6	273.8	43.8
2AZA	azurin	Cu (A)	112 (A)	2.12	106.7	195.8	169.1
		Cu (B)	112 (B)	2.17	106.7	184.9	177.1
2CPP	cytochrome P450cam	Fe	357	2.20	105.5	91.4	179.2
1FDX	ferredoxin [4Fe-4S]	Fe (1) (A)	8	2.18	110.2	56.3	188.1
		Fe (2) (A)	11	2.28	111.5	295.3	80.9
		Fe (3) (A)	14	2.43	104.7	252.9	64.5
		Fe (4) (A)	45	1.98	123.2	80.1	211.7
		Fe (1) (B)	18	1.98	109.6	94.4	174.2
		Fe (2) (B)	35	2.25	106.6	66.1	176.7
		Fe (3) (B)	38	2.32	121.2	279.6	85.7
		Fe (4) (B)	41	2.46	100.8	252.5	47.6
3FXC	ferredoxin [2Fe-2S]	Fe (1)	41	2.30	99.0	284.7	91.9
			46	2.49	90.8	243.7	93.5
		Fe (2)	49	2.28	83.8	198.7	144.4
			79	2.24	132.1	259.7	33.0
1HIP	high-potential iron protein [4Fe-4S]	Fe (1)	43	2.18	100.2	285.4	306.2
		Fe (2)	46	2.20	102.9	197.8	172.3
		Fe (3)	63	2.26	112.6	128.0	182.0
		Fe (4)	77	2.18	107.0	270.0	89.0
4FD1	ferredoxin [3Fe-4S]	Fe (1)	8	2.28	102.0	85.6	178.2
		Fe (2)	16	2.31	103.1	245.4	59.0
		Fe (3)	49	2.31	107.4	76.5	177.8
	ferredoxin [4Fe-4S]	Fe (1)	20	2.31	107.4	68.7	190.0
		Fe (2)	39	2.32	110.9	62.9	174.5
		Fe (3)	42	2.32	117.8	295.7	81.6
		Fe (4)	45	2.33	108.8	251.5	52.3
1PCY	plastocyanin	Cu	84	2.13	109.7	194.3	170.0
3PCY	plastocyanin (Hg substituted)	Hg	84	2.38	101.6	187.6	171.5
1PAZ	pseudoazurin	Cu	78	2.16	104.8	178.7	165.5
5RXN	rubredoxin	Fe	6	2.33	100.7	192.7	176.5
			9	2.29	109.2	269.3	74.5
			39	2.31	100.0	187.6	177.6
			42	2.25	111.5	273.0	72.3
HGCYSC	Hg–cysteine complex	Hg		2.35	107.5	274.5	72.4
				2.33	108.0	234.9	68.1
HGLCYS	Hg–cysteine complex	Hg		2.49	100.3	173.0	68.3
				2.45	103.9	66.4	68.3
MCYSHG10	Hg–cysteine complex	Hg		2.35	100.1	276.4	301.8

[a] The last three entries are for small molecules and correspond to CCDB code. 4ADH, Colonna-Cesari et al. (1986). 7ATC, Kim et al. (1987). 2AZA, Norris et al. (1986). 2CPP, Poulos et al. (1987). 1FDX, Adman et al. (1976). 3FXC, Tsukihara et al. (1981). 1HIP, Carter et al. (1974). 4FD1, Stout (1988). 1PCY, Guss et al. (1983). 3PCY, Church et al. (1986). 1PAZ, Petratos et al. (1988). 5RXN, Watenpaugh et al. (1980). HGCYSC, HGLCYS, Taylor and Carty (1977). MCYSHG10, Taylor et al. (1975). [b] 1,2 or A,B, etc. is used to distinguish different metal atoms or subunits in the same protein molecule. [c] N–C_α–C_β–C_γ.

and M···S_γ–C_β–C_α of 270°. This is illustrated in Figure 5 by residues 9 and 42 in the rubredoxin structure. For the remaining cases, χ_1 of 180° is strongly preferred and M···S_γ–C_β–C_α has a maximum population around 180°—this conformation is the fully extended one and places the metal ion furthest from the main-chain atoms. Such a conformation is exhibited by residues 6 and 39 in the rubredoxin structure (Figure 5).

In conclusion, this study shows that there is a preferred geometry for the binding of metal ions with Met and Cys residues. This geometry appears to follow the same pattern in various proteins with different functions and is independent of the nature of the metal center.

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Registry No. L-Met, 63-68-3; L-Cys, 52-90-4; S, 7704-34-9; Fe, 7439-89-6; Cu, 7440-50-8; Hg, 7439-97-6; Zn, 7440-66-6.

REFERENCES

Adman, E., Watenpaugh, K. D., & Jensen, L. H. (1975) *Proc. Natl. Acad. Sci. U.S.A. 72*, 4854–4858.

Adman, E. T., Sieker, L. C., & Jensen, L. H. (1976) *J. Biol. Chem. 251*, 3801–3806.

Allen, F. H., Bellard, S., Brice, M. D., Cartwright, B. A.,

Doubleday, A., Higgs, H., Hummelink, T., Hummelink-Peters, B. G., Kennard, O., Motherwell, W. D. S., Rodgers, J. R., & Watson, D. G. (1979) *Acta Crystallogr. B35*, 2331–2339.

Bernstein, F. C., Koetzle, T. F., Williams, G. J. B., Meyer, E. F., Jr., Brice, M. D., Rodgers, J. R., Kennard, O., Shimanouchi, T., & Tasumi, M. (1977) *J. Mol. Biol. 112*, 535–542.

Carter, C. W., Jr., Kraut, J., Freer, S. T., Xuong, N., Alden, R. A., & Bartsch, R. G. (1974) *J. Biol. Chem. 249*, 4212–4225.

Carter, D. C., Melis, K. A., O'Donnell, S. E., Burgess, B. K., Furey, W. F., Jr., Wang, B., & Stout, C. D. (1985) *J. Mol. Biol. 184*, 279–295.

Chakrabarti, P., & Dunitz, J. D. (1982) *Helv. Chim. Acta 65*, 1482–1487.

Church, W. B., Guss, J. M., Potter, J. J., & Freeman, H. C. (1986) *J. Biol. Chem. 261*, 234–237.

Colonna-Cesari, F., Perahia, D., Karplus, M., Eklund, H., Brändén, C. I., & Tapia, O. (1986) *J. Biol. Chem. 261*, 15273–15280.

Einspahr, H., & Bugg, C. E. (1981) *Acta Crystallogr. B37*, 1044–1052.

Frey, M., Sieker, L., Payan, F., Haser, R., Bruschi, M., Pepe, G., & LeGall, J. (1987) *J. Mol. Biol. 197*, 525–541.

Gewirth, A. A., & Solomon, E. I. (1988) *J. Am. Chem. Soc. 110*, 3811–3819.

Guss, J. M., & Freeman, H. C. (1983) *J. Mol. Biol. 169*, 521–563.

Kabsch, W., & Sander, C. (1983) *Biopolymers 22*, 2577–2637.

Kim, K. H., Pan, Z., Honzatko, R. B., Ke, H., & Lipscomb, W. N. (1987) *J. Mol. Biol. 196*, 853–875.

Lederer, F., Glatigny, A., Bethge, P. H., Bellamy, H. D., & Mathews, F. S. (1981) *J. Mol. Biol. 148*, 427–448.

Levitt, M. (1978) *Biochemistry 17*, 4277–4285.

Matsuura, Y., Takano, T., & Dickerson, R. E. (1982) *J. Mol. Biol. 156*, 389–409.

McGregor, M. J., Islam, S. A., & Sternberg, M. J. E. (1987) *J. Mol. Biol. 198*, 295–310.

Noodleman, L., Norman, J. G., Jr., Osborne, J. H., Aizman, A., & Case, D. A. (1985) *J. Am. Chem. Soc. 107*, 3418–3426.

Norris, G. E., Anderson, B. F., & Baker, E. N. (1986) *J. Am. Chem. Soc. 108*, 2784–2785.

Ochi, H., Hata, Y., Tanaka, N., Kakudo, M., Sakurai, T., Aihara, S., & Morita, Y. (1983) *J. Mol. Biol. 166*, 407–418.

Petratos, K., Dauter, Z., & Wilson, K. S. (1988) *Acta Crystallogr. B44*, 628–636.

Poulos, T. L., Finzel, B. C., & Howard, A. J. (1987) *J. Mol. Biol. 195*, 687–700.

Ramasubbu, N., Parthasarathy, R., & Murray-Rust, P. (1986) *J. Am. Chem. Soc. 108*, 4308–4314.

Rosenfield, R. E., Jr., Parthasarthy, R., & Dunitz, J. D. (1977) *J. Am. Chem. Soc. 99*, 4860–4862.

Stout, C. D. (1988) *J. Biol. Chem. 263*, 9256–9260.

Salemme, F. R., Freer, S. T., Xuong, N. H., Alden, R. A., & Kraut, J. (1973) *J. Biol. Chem. 248*, 3910–3921.

Takano, T., & Dickerson, R. E. (1980) *Proc. Natl. Acad. Sci. U.S.A. 77*, 6371–6375.

Tanaka, N., Yamane, T., Tsukihara, T., Ashida, T., & Kakudo, M. (1975) *J. Biochem. (Tokyo) 77*, 147.

Taylor, N. J., & Carty, A. J. (1977) *J. Am. Chem. Soc. 99*, 6143–6145.

Taylor, N. J., Wong, Y. S., Chieh, P. C., & Carty, A. J. (1975) *J. Chem. Soc., Dalton Trans.* 438–442.

Timkovich, R., & Dickerson, R. E. (1976) *J. Biol. Chem. 251*, 4033–4046.

Tsukihara, T., Fukuyama, K., Nakamura, M., Katsube, Y., Tanaka, N., Kakudo, M., Wada, K., Hase, T., & Matsubara, H. (1981) *J. Biochem. (Tokyo) 90*, 1763.

Watenpaugh, K. D., Sieker, L. C., & Jensen, L. H. (1980) *J. Mol. Biol. 138*, 615–633.

Yachandra, V. K., Hare, J., Moura, I., & Spiro, T. G. (1983) *J. Am. Chem. Soc. 105*, 6455–6461.