

Factors Governing the Metal Coordination Number in Metal Complexes from Cambridge Structural Database Analyses

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The metal coordination number (CN) is a key determinant of the structure and properties of metal complexes. It also plays an important role in metal selectivity in certain metalloproteins. Despite its central role, the preferred CN for several metal cations remains ambiguous, and the factors determining the metal CN are not fully understood. Here, we evaluate how the CN depends on (1) the metal's size, charge, and charge-accepting ability for a given set of ligands, and (2) the ligand's size, charge, charge-donating ability, and denticity for a given metal by analyzing the Cambridge Structural Database (CSD) structures of metal ions in the periodic table. The results show that for a given ligand type, the metal's size seems to affect its CN more than its charge, especially if the ligand is neutral, whereas, for a given metal type, the ligand's charge and charge-donating ability appear to affect the metal CN more than the ligand's size. Interestingly, all 98 metal cations surveyed could adopt more than one CN, and most of them show an apparent preference toward even rather than odd CNs. Furthermore, as compared to the preferred metal CNs observed in the CSD, those in protein binding sites generally remain the same. This implies that the protein matrix (excluding amino acid residues in the metal's first and second coordination shell) does not impose severe geometrical restrictions on the bound metal cation.

Introduction

Metal ions are indispensable building blocks in Nature. Currently, about half of all known proteins contain metal cofactors¹ and most ribozymes cannot function without metal ion(s).^{2–6} Despite the growing number of studies elucidating the properties of different metal cations and their complexes, basic properties such as the preferred coordination number (CN) for certain biologically important metal ions is still debatable. Furthermore, the factors determining the metal CN are not fully understood (see below). On the other hand, the Cambridge Structural Database⁷ (CSD) currently contains ~200 000 high-resolution X-ray structures of metal complexes, providing a timely opportunity to study the trends in the metal CN changes. Thus, as a first step to identify the key factors determining the CN of various metal cations in the periodic table, we have carried out statistical analyses of the metal complex structures in the CSD. The results reveal that the size of the metal ion and the charge and charge-donating ability of the ligand play important roles in determining the CN. They also show that most of the metal cations in the periodic table show an apparent preference for even rather than odd CNs.

The metal CN is governed by the properties of both metal cation and ligands and the many-body interactions within the complex.⁸ It is a key characteristic of each metal complex, and it determines its structure and properties to a large extent. It affects the strength of the metal–ligand interactions. Generally, for a given metal cation, the larger the CN, the weaker the

interactions with each individual ligand,^{9–13} which, in turn, affect the ligand–ligand interactions in both the inner and outer coordination shells. Furthermore, the metal CN perturbs the metal–ligand bond distances much more than changes in the environment of the complex.¹⁴ For example, the average Mg²⁺–O(water) distances for 4-coordinated (1.98 Å) and 6-coordinated (2.08 Å) Mg²⁺ from high level *ab initio* calculations differ by 0.10 Å,¹¹ whereas the mean Mg²⁺–O(water) distance from octahedral structures in the crystalline state (2.07 ± 0.03 Å)¹⁵ and in aqueous solution (2.09 ± 0.04 Å)¹⁶ are essentially the same (to within experimental error). The CN is also an important factor in determining the binding mode of polydentate ligands to the metal ion: increasing the CN of a given metal ion favors bidentate, as opposed to monodentate, binding of carboxylate ligands to the metal cation.¹⁷

In some cases, the CN plays a decisive role in selecting a specific metal ion for a given protein; the specific arrangement and directionality of the first-shell ligands in some metal-binding sites, which are optimized to best fit the natural cofactor's coordination requirements, disfavor binding of competing cations with different coordination geometry preferences.^{18–21} For example, the different coordination requirements of Zn²⁺ (the native cofactor) and Cu²⁺, which bind carbonic anhydrase II with a CN of 4 and 5, respectively, have been implicated to play a key role in metal selectivity. Binding of the non-native Cu²⁺ cation to the protein in trigonal bipyramidal, as opposed to tetrahedral, geometry appears to be energetically unfavorable.^{19,20} On the other hand, in low-selectivity binding sites, the “foreign” metal cations often impose their coordination requirements upon binding, thus disrupting the host ligand alignment in the metal-binding site and eventually inactivating the metalloprotein.^{22–24} For example, in certain nonrigid catalytic Zn-binding sites, Hg²⁺ may destroy the native tetra-

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TABLE 1: CNs and Respective % Frequencies for Main Group Metal Cations

IA(1)			IIA(2)			IIIA(13)			IVA(14)			VA(15)		
Li ⁺	4 , 60%	6, 13%	Be ²⁺	4 , 90%	3, 5%	Al ³⁺	4 , 74%	6, 10%	Ge ⁴⁺	4 , 70%	5 = 3 ^a , 10%	Sb ³⁺	4 , 40%	6, 27%
Na ⁺	6 , 51%	4, 20%	Mg ²⁺	6 , 60%	4, 23%	Ga ³⁺	4 , 72%	3, 10%	Sn ⁴⁺	4 , 40%	6, 27%	Bi ³⁺	4 , 26%	5, 22%
K ⁺	4 , 33%	3, 19%	Ca ²⁺	6 , 41%	7, 26%	In ³⁺	4 , 36%	6, 28%	Pb ²⁺	4 , 39%	6, 21%			
			Sr ²⁺	8 , 46%	6, 38%	Tl ³⁺	4 , 34%	3, 22%						
			Ba ²⁺	8 , 30%	7, 25%									

^a These two CNs have the same % frequency.

TABLE 2: CNs and Respective % Frequencies for Group IB-VB Metal Cations

IB(11)			IIB(12)			IIIB(3)			IVB(4)			VB(5)		
Cu ⁺	4 , 62%	3, 25%	Zn ²⁺	4 , 59%	6, 23%	Sc ³⁺	6 , 39%	5, 33%	Ti ²⁺	6 , 41%	4, 22%	V ²⁺	6 , 80%	5, 13%
Cu ²⁺	5 , 41%	4, 34%	Cd ²⁺	4 , 34%	6, 28%	Y ³⁺	7 , 22%	6, 20%	Ti ⁴⁺	6 , 68%	5, 14%	V ³⁺	6 , 58%	4 = 5 ^a , 17%
Ag ⁺	4 , 40%	2, 26%	Hg ²⁺	2 , 53%	4, 31%	La ³⁺	8 , 26%	10, 26%	Zr ⁴⁺	6 , 53%	4, 14%	V ⁴⁺	6 , 55%	5, 35%
Au ⁺	2 , 90%	3, 6%							Hf ⁴⁺	6 , 46%	5 = 8 ^a , 18%	V ⁵⁺	5 , 44%	6, 35%
Au ³⁺	4 , 89%	2, 6%										Nb ⁵⁺	6 , 68%	7, 14%
												Ta ⁵⁺	6 , 43%	5, 33%

^a These two CNs have the same % frequency.

hedral Zn-binding site geometry by adopting a linear or trigonal geometry.²⁴

Insights into the trends of how properties of the metal/ligand affect the CNs of metal ions in the entire periodic table can be obtained from the CSD. Indeed, such statistical analyses have been carried out on relatively small complexes of selected metal ions such as Na⁺, K⁺, Ca²⁺, Mg²⁺, and/or certain first-row transition metal cations that are considered as models of metal-binding sites in proteins. Valuable information has been extracted about their structure (bond lengths, bond angles, dihedral angles, and bond orders) and coordination preferences (CN, type of preferred ligands, and their denticity).^{25–32} In the late 1980s, the CNs for 100 different cations have been obtained by analyzing 14 000 metal complexes retrieved from the Inorganic Crystal Structure Database.³³ The metal's CN was found to be correlated with the following properties of the constituent entities: (i) the Lewis–base strength of the anion, (ii) the Lewis–acid strength of the cation, and (iii) the ion's ionic radius.³⁴ Furthermore, the CNs for a large number of complexes have been successfully predicted using Pauling's ionic radii.³⁴ More recently, the CNs for many metals in the periodic table in different oxidation states have been obtained by analyzing 10 000 metal complexes retrieved from the CSD⁷ and the “Structural Chemistry Data” database.³⁵ The key findings from this empirical survey are that (1) the most common metal CN is 6, followed (in decreasing order) by 4, 5, 7, and 8, and (2) the most common metal oxidation state is +2.³⁶ However, this particular survey³⁶ did not give the criteria used to select the 10 000 structures from which the CNs were derived. Furthermore, to the best of our knowledge, previous statistical analyses have not systematically studied the effect of the metal's or ligand's properties (e.g., size, charge, and charge-accepting/donating ability) on the metal CN, hence, it is not clear which properties of the metal and ligand dictate the observed CN of a given metal.

Despite the plethora of information (from both experiment and theory) about the metal CN(s), the preferred CN is still a matter of controversy for a number of biologically important metal cations; e.g., Cu²⁺ (CN = 4, 5, or 6),^{37,38} Zn²⁺ (CN = 4, 5, or 6),^{11,14} and Ca²⁺ (CN = 6, 7, or 8).^{39–43} Moreover, the factors determining the metal CN are not fully understood (see above). Herein, we evaluate how the metal CN depends on (1) the properties of the metal (its size, charge, and charge-accepting ability) for a given set of ligands, and (2) the properties of the first-shell ligands (their size, charge/charge-donating ability, and denticity) for a given metal cation. We also evaluate if the

preferred CN of a given metal cation that is commonly found in isolated complexes changes in a protein environment, and if so, the significance of the CN change. To reveal the trends in the CN changes, we analyzed the structures of the metal complexes in the CSD as described below.

Methodology

The Cambridge Structural Database, version 5.25⁷ and ConQuest, version 1.6⁴⁴ were used to search for complexes of all the metals in the periodic table. The following structures were excluded in our analyses: (i) structures with R-factor >0.05, (ii) structures that are polymeric or that contain bi- or polynuclear metal-binding sites, and (iii) structures in which the metal ion is forced to assume a given CN by the ligands. The latter are mainly complexes containing polydentate crown ethers that force the metal cation to adopt the CN corresponding to their denticity.

After filtering out the above structures, 28 706 entries (metal complex structures) were left for analyses. The number of entries for each metal found in the CSD is given in Supporting Information (Supplementary Tables 1, 2, and 3). Note that metal cations with insufficient data (<20 entries) were omitted from further statistical analyses. These include Rb, Cs, Po, Pm, Fr, Ra, Ac, Pa, Rh²⁺, and all metals with atomic numbers ≥94. Note that, although there are 256 CSD crystal structures of Rh²⁺ complexes, 237 structures contain bi- or polymetallic Rh²⁺-binding sites, leaving only 19 Rh²⁺ structures. Metals that could adopt more than one oxidation state were distinguished (according to the compound chemical name provided by the authors who deposited the crystal structure into the CSD), resulting in 98 distinct types of metal cations. Their complexes were analyzed for the metal CNs according to the number of atoms that were “connected” to a given metal ion in the PDB coordinate file. Thus, the metal CNs determined herein rely on the “connectivity” provided by the authors of the PDB file. Although the reliability of these results depends on the number of entries for each metal, which varies from 20 to 30 for some lanthanide and actinide metals to a few thousand for some transition metals such as Cu, Ni, Pd, Pt, and Zn, the trend toward certain CNs is evident in most cases.

Results

Tables 1–4 present the metal CNs derived from the CSD survey. For each metal of a given oxidation number, the first number, in bold, is the most common/preferred CN with the

TABLE 3: CNs and Respective % Frequencies for Group VIB–VIII B Metal Cations

VIB(6)			VIIB(7)			VIII B(8)			VIII B(9)			VIII B(10)		
<i>Cr</i> ²⁺	6 , 42%	4, 36%	<i>Mn</i> ⁺	6 , 83%	5, 14%	<i>Fe</i> ²⁺	6 , 74%	4, 18%	<i>Co</i> ⁺	5 , 48%	4, 42%	<i>Ni</i> ²⁺	6 , 48%	4 , 48%
<i>Cr</i> ³⁺	6 , 98%	5, 1%	<i>Mn</i> ²⁺	6 , 83%	4, 13%	<i>Fe</i> ³⁺	6 , 70%	4, 15%	<i>Co</i> ²⁺	6 , 59%	4, 34%	<i>Ni</i> ³⁺	4 , 86%	5, 9%
<i>Mo</i> ²⁺	6 , 50%	7, 47%	<i>Mn</i> ³⁺	6 , 84%	5, 16%	<i>Ru</i> ²⁺	6 , 95%	5, 5%	<i>Co</i> ³⁺	6 , 97%	4 = 5 ^a , 1%	<i>Pd</i> ²⁺	4 , 99%	2, 1%
<i>Mo</i> ³⁺	6 , 95%	4 = 7 ^a , 2%	<i>Tc</i> ³⁺	6 , 74%	5, 16%	<i>Ru</i> ³⁺	6 , 99%	5, 1%	<i>Rh</i> ⁺	4 , 90%	5 = 6 ^a , 5%	<i>Pd</i> ⁴⁺	6 , 88%	4, 8%
<i>Mo</i> ⁴⁺	6 , 45%	5, 34%	<i>Tc</i> ⁵⁺	5 , 60%	6, 40%	<i>Ru</i> ⁴⁺	6 , 67%	4 = 5 ^a , 14%	<i>Rh</i> ³⁺	6 , 87%	5, 10%	<i>Pt</i> ²⁺	4 , 97%	5, 1%
<i>Mo</i> ⁵⁺	6 , 74%	5, 15%	<i>Re</i> ⁺	6 , 97%	4 = 5 ^a , 1%	<i>Os</i> ²⁺	6 , 92%	5, 8%	<i>Ir</i> ⁺	4 , 65%	6, 32%	<i>Pt</i> ⁴⁺	6 , 96%	4, 3%
<i>Mo</i> ⁶⁺	6 , 76%	7, 10%	<i>Re</i> ³⁺	6 , 82%	5, 7%	<i>Os</i> ³⁺	6 , 96%	5, 4%	<i>Ir</i> ³⁺	6 , 79%	4, 13%			
<i>W</i> ²⁺	7 , 55%	6, 40%	<i>Re</i> ⁴⁺	6 , 93%	4, 4%	<i>Os</i> ⁴⁺	6 , 85%	4, 7%						
<i>W</i> ⁴⁺	6 , 79%	5, 10%	<i>Re</i> ⁵⁺	6 , 74%	5, 23%	<i>Os</i> ⁶⁺	6 , 67%	5, 29%						
<i>W</i> ⁶⁺	6 , 78%	5, 12%	<i>Re</i> ⁷⁺	5 , 40%	4 = 6 ^a , 28%									

^a These two CNs have the same % frequency.

TABLE 4: CNs and Respective % Frequencies for Lanthanide and Actinide Metal Cations

lanthanides			actinides		
<i>Ce</i> ³⁺	8 , 39%	5, 23%	<i>Th</i> ³⁺	8 , 48%	6 = 9 = 10 ^a , 10%
<i>Pr</i> ³⁺	9 , 34%	8, 28%	<i>U</i> ⁴⁺	6 , 45%	8, 17%
<i>Nd</i> ³⁺	9 , 40%	8, 21%	<i>U</i> ⁶⁺	7 , 46%	8, 34%
<i>Sm</i> ³⁺	8 , 32%	9, 19%	<i>Np</i> ³⁺	7 = 8 ^a , 30%	2, 22%
<i>Eu</i> ³⁺	8 , 47%	9, 27%			
<i>Gd</i> ³⁺	8 , 38%	9, 32%			
<i>Tb</i> ³⁺	8 , 30%	9, 25%			
<i>Dy</i> ³⁺	8 , 60%	9, 24%			
<i>Ho</i> ³⁺	8 , 44%	9, 33%			
<i>Er</i> ³⁺	8 , 40%	9, 19%			
<i>Tm</i> ³⁺	8 , 39%	9, 26%			
<i>Yb</i> ²⁺	6 , 48%	8, 16%			
<i>Yb</i> ³⁺	8 , 35%	6, 29%			
<i>Lu</i> ³⁺	8 , 40%	9, 32%			

^a These two CNs have the same % frequency.

highest % frequency (the ratio of the number of CSD structures with that CN to the total number of entries for the metal × 100). This is followed by the second most common CN(s) and the corresponding % frequencies.

The Metal CN is Nonunique. All the metal cations surveyed can adopt more than one CN. Three major classes of metal cations can be distinguished according to their CN distribution: Class 1 metal cations (shown in bold in Tables 1–4) show a clear preference for a particular CN (arbitrarily defined as having a frequency ≥ 90%), and seldom adopt other CNs. These include Au⁺, which prefers to be linearly coordinated; Be²⁺, Pd²⁺, Pt²⁺, and Rh⁺, which prefer to be tetraordinated; and Co³⁺, Cr³⁺, Mo³⁺, Pt⁴⁺, Re⁺, Re⁴⁺, Ru²⁺, Ru³⁺, Os²⁺, and Os³⁺, which prefer to be hexacoordinated. In contrast, none of the metal cations in the lanthanide/actinide series strongly prefer a specific CN.

Class 2 metal cations (shown in italic in Tables 1–4) exhibit similar preference for two CNs with the corresponding frequencies differing by ≤ 10%. Cd²⁺, Cr²⁺, In³⁺, and Ni²⁺ show similar preference for CNs 4 and 6, while Bi³⁺, Cu²⁺, and Co⁺ show similar preference for CNs 4 and 5 instead. V⁵⁺, Ta⁵⁺, and Sc³⁺ show similar preference for CNs 5 and 6, whereas Mo²⁺ and Y³⁺ show similar preference for CNs 6 and 7. Sr²⁺ and Ba²⁺ are commonly found octacoordinated as well as hexa and heptacoordinated, respectively. Like Sr²⁺ and Ba²⁺, most of the lanthanide and actinide metal cations are also commonly found octacoordinated, but Pr³⁺, Gd³⁺, Tb³⁺, and Lu³⁺ are as likely to be nonacoordinated, while Yb³⁺, Np³⁺, and La³⁺ are as likely to be hexa, hepta, and decacoordinated, respectively.

Class 3 metal cations (shown in regular font in Tables 1–4) exhibit CN trends intermediate between the class 1 and class 2 metal cations; the frequency of the most common CN is less than 80% but is greater than that of the second most common CN (the difference between the two frequencies is ≤ 60% but

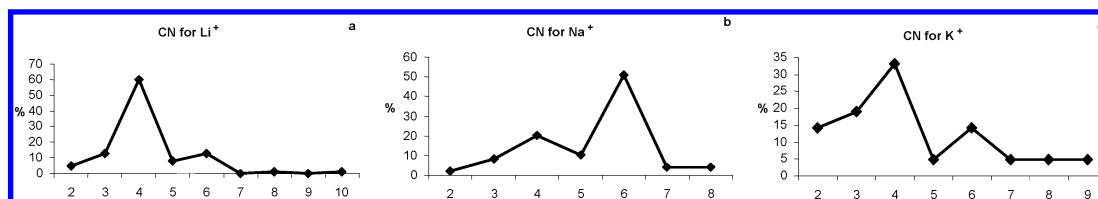
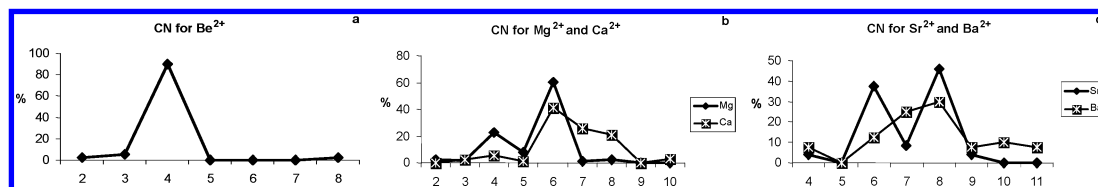
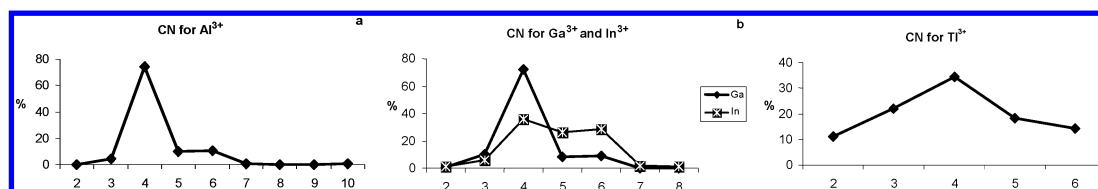
> 10%). These include some of the biologically important metal cations such as Cu⁺ (**4**, 62%; 3, 25%), Mg²⁺ (**6**, 60%; 4, 23%), Ca²⁺ (**6**, 41%; 7, 26%), Zn²⁺ (**4**, 59%; 6, 23%), and Fe²⁺ (**6**, 74%; 4, 18%). They also encompass all the metal cations in group IA, IVA, and IVB in Tables 1–4.

Even CNs are Preferred to Odd CNs. For metal cations in classes 1 and 3 (metals *not* in italic in Tables 1–4), which exhibit a preference for a certain CN, the most common CN of *all* the main group metal cations as well as most of the other metal cations is even (4, 6, or 8). The exceptions all belong to class 3 metals that can exist in variable oxidation states. These are W²⁺ (**7**, 55%), Tc⁵⁺ (**5**, 60%), Re⁷⁺ (**5**, 40%), Nd³⁺ (**9**, 40%), and U⁶⁺ (**7**, 46%).

The preference of a metal ion to adopt an even rather than an odd CN is illustrated in Figures 1, 2, and 3, which show the CN distributions for metal cations in group IA, IIA, and IIIA, respectively. The maxima of each of the CN distribution curves occur at even CNs; 4 or 6 for group IA (Figure 1a–c) and IIIA (Figure 3a–c) metal cations, and 4, 6, 8, or 10 for group IIA metal cations (Figure 2a–c). The odd CNs (5, 7, or 9) are rarer and appear either as shoulders or local minima.

Dependence of the CN on the Metal's Properties. This was determined from the CSD structures of a given metal bound to the same type of ligands, e.g., water molecules. The metal CNs of complexes containing only water molecules in the CSD are shown in Table 5 along with the number of CSD structures for the CN in brackets. The CNs of metal cations with only one aqua complex in the CSD (Sr²⁺, Ba²⁺, Ru²⁺, V³⁺, and Tm³⁺) are probably less certain than those of metal cations with more than 10 aqua complexes with the same CN (e.g., Mg²⁺, Mn²⁺, Co²⁺, Ni²⁺, Zn²⁺, and Al³⁺). For Na⁺, Ca²⁺, Cu²⁺, Y³⁺, Sm³⁺, Dy³⁺, Er³⁺, Yb³⁺, and Lu³⁺, the CN is indeterminate as more than one CN is observed in the CSD aqua-complexes. As an example, for Ca²⁺, there are five aqua complexes with a CN of 7, two with a CN of 6 and one with a CN of 8; the more prevalent CN is listed first in Table 5. Although experimental structures are not available for *all* the metals in the periodic table, some trends in the metal CN changes are evident from Table 5 (see below).

Metal size. The metal size, as reflected by its ionic radius, *R*_{ion}, plays a role in determining the CN. The CN in hydrated complexes often increases with increasing size of the metal. For the group IIA metal hydrates, the CN changes from 4 for Be²⁺ (*R*_{ion} = 0.41 Å), to 6 for Mg²⁺ (*R*_{ion} = 0.86 Å), 6 or 7 for Ca²⁺ (*R*_{ion} = 1.14 Å for CN = 6), 8 for Sr²⁺ (*R*_{ion} = 1.40 Å), and 9 for Ba²⁺ (*R*_{ion} = 1.56 Å). Furthermore, the larger yttrium, bismuth, and lanthanides with ionic radii ≥ 1.12 Å are either octa or nonahydrated, whereas the smaller first-row transition metal cations with ionic radii ranging from 0.69 to 0.92 Å are all hexahydrated.

Figure 1. Distribution of CNs for (a) Li^+ , (b) Na^+ , and (c) K^+ .Figure 2. Distribution of CNs for (a) Be^{2+} , (b) Mg^{2+} and Ca^{2+} , and (c) Sr^{2+} and Ba^{2+} .Figure 3. Distribution of CNs for (a) Al^{3+} , (b) Ga^{3+} and In^{3+} , and (c) Tl^{3+} .TABLE 5: CNs^a of Hydrated Metal Cations in the CSD

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
IA	IIA	IIIB	IVB	VB	VIB	VIIIB	VIIIIB			IB	IIB	IIIA	IVA	VA	VIA
H															
Li^+	Be^{2+}											B	C	N	O
4 (13)	4 (3)														
Na^+	Mg^{2+}											Al^{3+}	Si	P	S
6 (3)	6 (65)											6 (13)			
4 (2)															
K	Ca^{2+}	Sc^{3+}	Ti^{3+}	V^{2+}	Cr^{3+}	Mn^{2+}	Fe^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Ga^{3+}	Ge	As	Se
	7 (5)			6 (2)	6 (8)	6 (24)	6 (9)	6 (66)	6 (36)	6 (17)	6 (18)	6 (2)			
	6 (2)			V^{3+}			Fe^{3+}			4 (2)					
	8 (1)			6 (1)			6 (3)			5 (1)					
Rb	Sr^{2+}	Y^{3+}	Zr	Nb	Mo	Tc	Ru^{2+}	Rh	Pd	Ag^+	Cd^{2+}	In^{3+}	Sn	Sb	Te
	8 (1)	8 (2)					6 (1)				6 (4)	6 (2)			
		9 (1)													
Cs	Ba^{2+}	La^{3+}	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi^{3+}	Po
	9 (1)	9 (5)												9 (2)	
Fr	Ra	Ac	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg					
lanthanides		Ce^{3+}	Pr^{3+}	Nd^{3+}	Pm	Sm^{3+}	Eu^{3+}	Gd^{3+}	Tb^{3+}	Dy^{3+}	Ho^{3+}	Er^{3+}	Tm^{3+}	Yb^{3+}	Lu^{3+}
		9 (3)	9 (3)	9 (6)		9 (3)	9 (3)	9 (3)	9 (2)	9 (2)	9 (2)	9 (1)	9 (1)	9 (3)	8 (3)
						8 (1)				8 (1)		8 (1)		8 (1)	9 (2)
actinides		Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

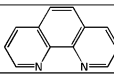

^a For certain metal cations, the CSD does not contain any structures of complexes containing only water molecules, therefore there is no number below these metals. For some metal cations, the aqua complexes show more than one metal CN. The number in bold is the CN while the number in brackets is the number of CSD structures with that CN.

Although the metal size plays a role in determining the CN, it is not the sole determinant, as the CN in hydrated complexes does *not* always increase with increasing size of the metal. The group IIIA metal cations, Al^{3+} , Ga^{3+} , and In^{3+} , are all hexahydrated even though the ionic radius increases from 0.68 Å for Al^{3+} to 0.94 Å for In^{3+} . Likewise, the group IIB metal cations, Zn^{2+} and Cd^{2+} , are both hexahydrated even though the ionic radius increases from 0.88 Å for Zn^{2+} to 1.09 Å for Cd^{2+} . Furthermore, the metal CN is not linearly correlated or proportional to the ionic radius: the group IA metal cations have greater ionic radii, but similar or smaller CNs than their group IIA counterparts. For example, Li^+ and Be^{2+} are both tetrahydrated even though the ionic radius of Li^+ (0.73 Å) is almost twice as large as that of Be^{2+} (0.41 Å).

Metal Charge. The charge of the metal cation, however, does not seem to be a major determinant of the metal CN in complexes containing *neutral* ligands such as water. *Univalent* Na^+ , *divalent* Mg^{2+} , V^{2+} , Mn^{2+} , Fe^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , Ru^{2+} , and Cd^{2+} as well as *trivalent* Al^{3+} , V^{3+} , Cr^{3+} , Fe^{3+} , Ga^{3+} , and In^{3+} are all found to be hexahydrated despite differences in their charges. Along the same vein, *univalent* Co^+ , *divalent* Cu^{2+} , and *trivalent* Bi^{3+} complexes in Tables 1–3 show similar preference for CNs 4 and 5, while the most common CN of Mo, Mn, Ru, and Os complexes in Table 3 is 6, regardless of the metal's oxidation state, which ranges from 1 up to 6.


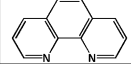
Metal Charge-Accepting Ability. In analogy to the net charge on a metal, the charge-accepting ability of the cation also does not seem to govern the metal CN in complexes

TABLE 6: CNs in Mono or Disubstituted Metal Hydrates^a

No of non-water ligands	Ligand	Chemical Formula	Mg ²⁺	Mn ²⁺	Co ²⁺	Ni ²⁺	Cu ²⁺	Zn ²⁺
1	Phenanthroline		6	6	6	6		6
2	Ammonia	NH ₃				6		
2	Urea	(NH ₂) ₂ CO	(6)		6	6		
2	Tetrahydrofuran		6					
2	Chloride	Cl ⁻				6	4	4
2	Bromide	Br ⁻		(6)	(6)	6	(4)	(4)

^a Numbers in brackets refer to lower-resolution structures (R-factors > 0.05).

TABLE 7: CNs in Uniformly Substituted Metal Complexes^a

Ligand	Chemical Formula	Mg ²⁺	Mn ²⁺	Co ²⁺	Ni ²⁺	Cu ²⁺	Zn ²⁺
Water	H ₂ O	6	6	6	6	6	6
Ammonia	NH ₃		6	6	6	(6)	4 or 6
Dimethyl sulfoxide	(CH ₃) ₂ SO	6	6	6	6	6	
Urea	(NH ₂) ₂ CO	6	(6)	6	6		6
Thiourea	(NH ₂) ₂ CS			4	(6)		(4)
Tetrahydrofuran		6	(6)	(6)			
Phenanthroline			6	6	6	6	6
Chloride	Cl ⁻	(4)	4	4	4	4	4
Bromide	Br ⁻	(4)	4	4	4	4	4
Cyanide	CN ⁻		4	4	4	3	
Oxalate	⁻ OOC-COO ⁻					4	

^a Numbers in brackets refer to lower-resolution structures (R-factors > 0.05).

containing *neutral water* ligands. For example, as compared to Zn²⁺, Mg²⁺ has been shown to be a poorer charge acceptor,¹⁴ whereas Hg²⁺ is a better charge acceptor.²⁴ Yet, Zn²⁺ and Mg²⁺, whose ionic radii differ by only 0.02 Å, are found to be hexahydrated from the CSD structures (see Table 5) and all three metal cations (Mg²⁺, Zn²⁺, and Hg²⁺) are found to be hexacoordinated in aqueous solution.^{16,39} Note, however, that in complexes with *anionic* ligands, which are strong charge donors, the charge-accepting ability of the metal may play a role in determining the metal CN (see below).

Dependence of the CN on the Ligand's Properties. To assess if, and to what extent, the properties of the ligand (its size, charge, charge-donating ability, and denticity) could affect the metal CN, we compared the CNs of the metal hydrates in Table 5 with the respective CNs of a few selected metal cations when one or two metal-bound water molecules are replaced by different ligands of varying size, geometry, denticity, charge, and charge-donating ability (see Table 6). We also determined the CNs of the selected metal cations with different sets of first-shell ligands, which are all of the same type for a given complex, but the ligands in different complexes vary in size, structure, denticity, and charge (see Table 7).

Ligand Size. Unlike the metal size, the ligand size, as reflected by its volume, does not seem to govern the metal CN, which remains the same with increasing size/volume of the neutral/anionic ligands. The preferred CN of hydrated Mg²⁺, Mn²⁺, Co²⁺, Ni²⁺, Cu²⁺, or Zn²⁺ in Table 5 does not change when one water is replaced by the bulky phenanthroline or when

two water molecules are replaced by neutral ligands of increasing size: ammonia, urea, and tetrahydrofuran (see Table 6). It also does not change even when *all* the first-shell water molecules are replaced by other neutral ligands of increasing size (see Table 7). In these cases it seems that the properties of the metal cation rather than those of the ligand dictates its CN.

Ligand Charge and Charge-Donating Ability. In contrast to the ligand's size, its net charge does affect the metal CN. When two water molecules are replaced by other neutral ligands in Table 6, the preferred CN of hydrated Mg²⁺, Mn²⁺, Co²⁺, Ni²⁺, Cu²⁺, or Zn²⁺ remains unchanged. However, when two water molecules are replaced by two negatively charged ligands such as Cl⁻ or Br⁻, the preferred CN is lowered to 4 for Cu²⁺ and Zn²⁺, but remains the same for Mn²⁺, Co²⁺, and Ni²⁺ (Table 6). This indicates that whether the CN changes upon substituting one or more water molecules with anionic ligands depends on the nature of the metal cation, which may have varying degree of flexibility in the first coordination sphere.

In addition to the net charge of the ligand, the charge-donating ability of a ligand also plays a role in determining the metal CN. Negatively charged ligands, which are better charge donors than neutral ligands, affect the metal CN more than neutral ligands. The preferred CNs of the hydrated metal cations in Table 7 decrease by 2 or 3 when negatively charged ligands, such as Cl⁻, Br⁻, CN⁻ or ⁻OOC-COO⁻, replace *all* the first-shell water molecules, but remain the same when neutral ligands such as dimethyl sulfoxide, urea, tetrahydrofuran, and phenanthroline replace all the metal-bound water molecules. Even

neutral ligands may alter the metal CN if they possess sufficiently strong charge-donor atoms, as exemplified by the different CN trends between all-urea and all-thiourea Co^{2+} complexes. In the latter complexes containing strong charge-donating sulfur atoms, Co^{2+} is tetracoordinated, but in the respective all-urea complexes containing the relatively weaker charge-donating oxygen atoms, Co^{2+} is hexacoordinated, as in the aqua complex (Table 7).

Ligand Denticity. Like the ligand size, the denticity of a ligand does not seem to govern the metal CN. For a given metal in Tables 6 and 7, the CN in complexes with neutral bidentate ligands is the same as that in complexes with neutral monodentate ligands (CN = 6). Likewise, for a given metal in Table 7, the CN in complexes with dianionic, bidentate oxalate is the same as that in complexes containing monoanionic, monodentate chloride, bromide, or cyanide (CN = 4).

Discussion

The Preferred CN of Most Metal Cations is Even. The CSD statistical analyses show that the metal CN is nonunique and even CNs are more prevalent than odd CNs. In particular, the CN distributions for group IA, IIA, and IIIA metal cations in Figure 1, 2, and 3, respectively, show a preference of these metal cations toward even CNs. This finding is somewhat unexpected because, for main group metal cations, which lack ligand–field stabilization effects typical of transition metal cations, the CN is expected to increase monotonously with increasing metal size/ionic radii. Indeed, the CSD aqua complexes in Table 5 and gas-phase free energy calculations⁴⁵ show *hydration* numbers of 6 for Mg^{2+} , 6 or 7 for Ca^{2+} , and 7 for Sr^{2+} and Ba^{2+} . Thus, the apparent preference for even CNs depends on both the nature of the ligand and the metal.

Factors Determining the CN. The empirical observations found herein reveal that a factor that could determine the metal CN is the size of the metal, especially in complexes with neutral ligands. Thus, for a given ligand type, metal cations in the top row of the periodic table generally adopt smaller CN than metal cations in the lanthanide/actinide series, whereas metal cations belonging to the same row of the periodic table with similar ionic radii adopt a similar CN (e.g., first-row transition metal cations in Table 5). Relative to a metal with a small ionic radius, a larger metal forms longer and weaker bonds with a given ligand type. This would, in turn, reduce the Pauli repulsion among the first-shell ligands, thus allowing more ligands to be bound to compensate for the weaker metal–ligand interactions.

Another factor that could also affect the metal CN is the charge and the charge-donating ability of the ligand. The CN of a metal bound to strong charge-donor atoms of charged and even neutral ligands (such as thiourea) is lower than that of the same metal bound to weaker charge-donor atoms of neutral ligands (see Tables 6 and 7). Hence, a given metal generally coordinates to more *neutral* ligands than anionic ligands because of the following two reasons. First, a neutral ligand donates less charge to a given metal than a negatively charged ligand, thus the metal charge in complexes containing only neutral ligands is more positive than that in complexes containing the same number of anionic ligands. Second, neutral ligands repel each other much less than the same number of negatively charged ligands. These two factors suggest an upper limit to the number of negatively charged ligands that could coordinate to a given metal. For the divalent cations in Table 7, this number does not exceed four, which is not surprising as a fifth anionic ligand, X^- , would be strongly repelled by a dianionic MX_4^{2-} complex. In the same vein, quantum mechanical calcula-

TABLE 8: Comparison of the Most Common Metal CNs from CSD and PDB Analyses

metal cation	CN from CSD ^a	CN from PDB
Mg^{2+}	6 (4)	6 ^b
Ca^{2+}	6 (7)	7 ^b
Zn^{2+}	4 (6)	4 ^{b,c}
Cu^{2+}	5 (4)	4 ^c
Co^{2+}	6 (4)	6 ^c
Ni^{2+}	6 = 4	6 ^c
Cd^{2+}	4 (6)	4 or 6 ^c
Hg^{2+}	2 (4)	2 ^c

^a From Tables 1–4; the first number is the most common CN, whereas the second number (in parentheses) is second most common CN; the “=” sign means both CNs are equally probable. ^b From Jernigan et al., 1994.⁴⁷ ^c From Rulisek and Vondrtasek, 1998.⁴⁸

tions on the successive binding of negatively charged carboxylate groups to Li^+ , Mg^{2+} , Ca^{2+} , Zn^{2+} , La^{3+} , and Zr^{4+} predict an upper limit of $Z + 2$ carboxylates bound to a metal cation with formal charge, Z .⁴⁶

Aside from the size of the metal and the charge/charge-donating ability of the ligand revealed by the CSD analyses, theoretical calculations are needed to reveal the other factors that also determine the preferred CN of a given metal, as suggested by certain CN trends found herein. For example, the CSD structures of the alkali metal hydrates do *not* exhibit a clear CN increase with increasing metal size: the CN is predominantly 4 for Li^+ ($R_{\text{ion}} = 0.73 \text{ \AA}$) and 4 or 6 for Na^+ ($R_{\text{ion}} = 1.16 \text{ \AA}$). However, infrared photodissociation spectra of hydrated Na^+ clusters show a tetrahedral first hydration shell of Na^+ in the gas phase, indicating no change in the CN in going from the small Li^+ to the larger Na^+ . This is consistent with *ab initio* and density functional calculations of isolated Li^+ , Na^+ , and K^+ water clusters showing a preferred CN of 4 for all three metal hydrates.⁴⁵ These calculations also show that a CN greater than 4 is not favored because, as the hydration number increases beyond 4, more water molecules become immobilized resulting in an unfavorable entropy contribution of such a magnitude that it outweighs the energy gain in the respective metal–water interactions.

Comparison with the CN in Proteins. To see if the CN of a given metal cation, typical of isolated complexes, changes in a protein environment, the metal CNs derived from the CSD structures were compared with the respective numbers obtained from Protein Data Bank (PDB) structures. The results are summarized in Table 8.

For all the metal cations in Table 8 the most common metal CNs observed for small complexes in the CSD generally do not change when the metal binds instead to amino acid ligands in proteins, although the latter are generally bulkier and less flexible than most of the ligands included in the CSD analyses. Thus it appears that the protein matrix does not impose significant geometrical restrictions to the bound metal cation, whose properties and those of the protein ligands dictate the overall coordination geometry of the metal complex. Alternatively, the apparent similarity between the most common metal CNs in small complexes and those in metalloproteins (Table 8) may imply that the metal cations bind preferably to protein sites that are pre-designed to match the specific geometry requirements of the metal ions; rigid protein sites with different geometries may inhibit metal binding.

Conclusion

The present CSD survey has identified the most common CNs of 98 distinct types of metal cations. The results show that the

CN is nonunique for all the metal ions studied. Three major classes of metal cations have been distinguished according to their CN distribution: (i) metal cations with a clear preference for a particular CN, e.g., Be^{2+} ; (ii) metal cations showing similar preference for two CNs, e.g., Cd^{2+} , and (iii) metal cations showing trends intermediate between the previous two groups, e.g., Mg^{2+} . The metal ions surveyed exhibit apparent preference toward even, as opposed to odd, CNs. The results of the survey show that in determining the CN in metal complexes, the metal's size seems to be more important than its charge/charge-accepting ability if the ligand is neutral; however, the metal's ionic radius is not linearly correlated with its CN. On the other hand, the ligand's charge and charge-donating ability appear to be more important than its size. The most common CNs found in small complexes (CSD) and metalloproteins (PDB) appear to be similar.

The results herein also highlight several areas for further experimental and/or theoretical study. For example, it is unclear (1) why some aqua complexes of certain metal groups (e.g., IIIA and IIB) show the same CN with increasing ion size (Table 5), (2) why some metal cations exhibit a strong preference for a specific CN, while others easily adopt multiple CNs, and (3) why most metal cations show a preference toward even rather than odd CNs. Theoretical calculations to provide the physical basis for some of the observed trends found herein are underway in our laboratory.

Knowledge of the factors that affect the coordination geometry of a given metal would be helpful in understanding/predicting the properties of complexes and metal selectivity. It could also be useful in designing compounds with novel/unique properties, for example, complexing agents that can differentiate toxic metal ions such as mercury from harmless ones such as zinc, and thus abstract these unwanted metal cations from the environment.

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Supporting Information Available: The number of entries (complex CSD structures) for each metal found in the CSD.

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