Chapter 1
Bioinorganic Chemistry of the Alkali Metal Ions

Youngsam Kim, Thuy-Tien T. Nguyen, and David G. Churchill

Contents

Abstract The common Group 1 alkali metals are indeed ubiquitous on earth, in the oceans and in biological systems. In this introductory chapter, concepts involving aqueous chemistry and aspects of general coordination chemistry and oxygen atom donor chemistry are introduced. Also, there are nuclear isotopes of importance. A general discussion of Group 1 begins from the prevalence of the ions, and from a comparison of their ionic radii and ionization energies. While oxygen and water molecule binding have the most relevance to biology and in forming a detailed understanding between the elements, there is a wide range of basic chemistry that is potentially important, especially with respect to biological chelation and synthetic multi-dentate ligand design. The elements are widely distributed in life forms, in the terrestrial environment and in the oceans. The details about the workings in animal, as well as plant life are presented in this volume. Important biometallic aspects of human health and medicine are introduced as well. Seeing as the elements are widely present in biology, various particular endogenous molecules and enzymatic

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systems can be studied. Sodium and potassium are by far the most important and central elements for consideration. Aspects of lithium, rubidium, cesium and francium chemistry are also included; they help in making important comparisons related to the coordination chemistry of Na^+ and K^+. Physical methods are also introduced.

Keywords Hydration sphere • Isotopes • Ionic radius • Lithium • Physical methods

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1 Introduction

The alkali metals (Li^+, Na^+, K^+, Rb^+, Cs^+, Fr^+) are ubiquitous in nature and their biological relevance and importance is hard to ignore. These ns^1 ions are centrally important in aspects of life on earth and within biological systems [1–56], from the aspects of the salt water of the oceans, down to miniscule intracellular cellular compartments. In terms of elemental abundances, Li^+, Rb^+, and Cs^+ are far less abundant and important (Figures 1, 2, and 3). Fr, of course, is a radioactive trace element of little current relevance. The ions are commonly involved in osmotic systems, electrolyte balances, ion channels,

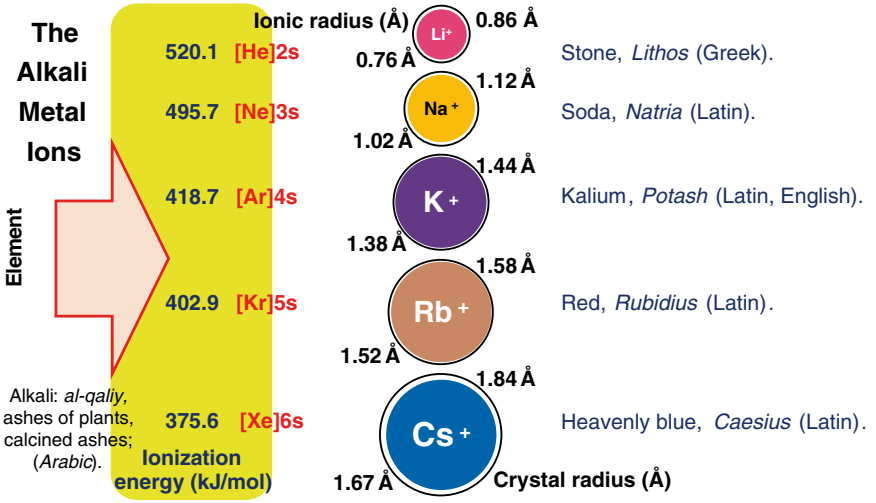

Figure 1 Electronic configurations, ionic radii, and ionization energy of 6-coordinate ions. Origin of the names of the elements. The color of the element is consistent with the color seen in the flame test [2, 11].

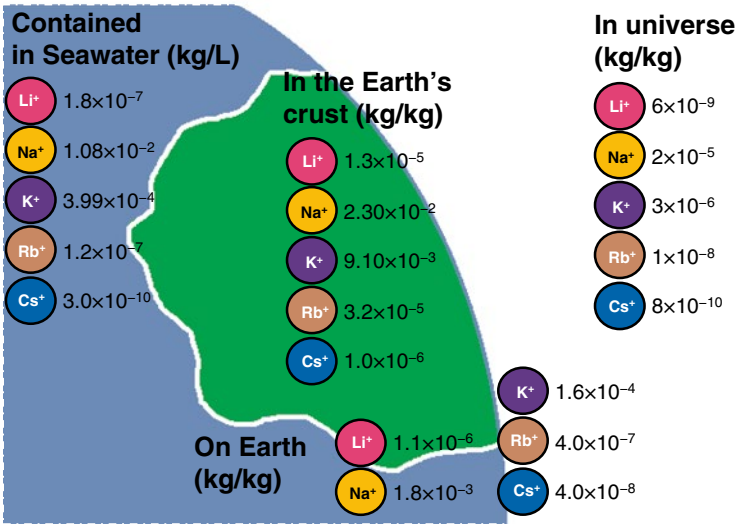

Figure 2 The occurrence of the elements on earth, in the oceans, and in the unverse. In all cases, francium is believed to be a trace element [6–10].

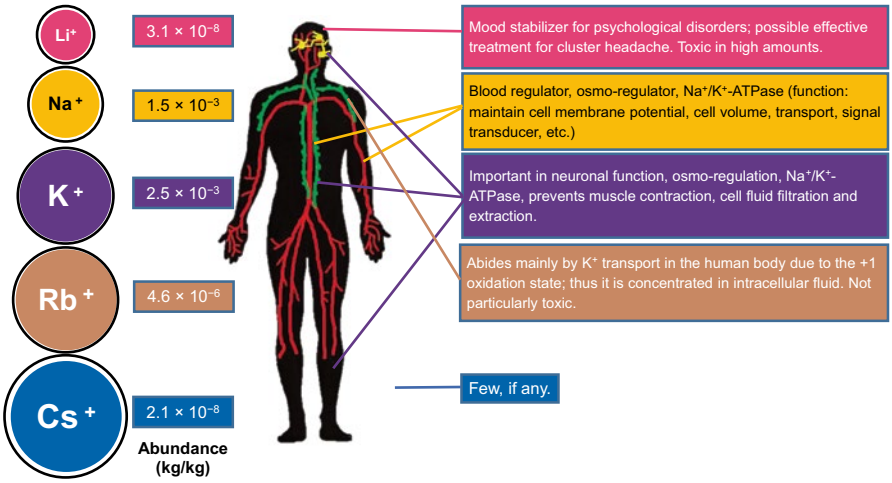

Figure 3 The abundance of alkali metals in the human body and their biological or medicinal roles [3].

and biological systems [1–5]. In the human body, sodium and potassium are by far the most abundant. These ions are often termed "spectator" ions.

This chapter is pertinent to ions in biological media and this inevitably means that fully-hydrated species should be considered. The polarization that the ionic species possess is also important. The inner hydration sphere, defined as the number

of direct metal-oxygen-bound water molecule sites, is affected by cation size; as the cation radius increases (down the group) the number of inner sphere waters increases. The oxophilic nature allows for synthetic ionophore design [16]. Beyond the oxophilic character of the ions, they also have attraction to phosphates, and nitrogen-containing species. Predominant ionic, but also partly covalent bonding exists according to Fajan's rules [42].

Studies of natural and synthetic ligand designs for Group 1 metal ions continue to appear in the literature. These often relate to the biological implications of these metals. The basis for coordination chemistry in polydentate chelate design has often come from motifs also found in amino acids and nucleic acid bases (bioinspired) [2]. Furthermore, biologically there are sugar, vitamin, and hormone complexes that can be formed with the group I metal ions. There are also natural chelators and synthetic chelation motifs involving metal phosphate ligation as well. Ligation aspects are covered in various ways by authors of this volume: Chapter 3 (solid state), Chapter 4 (gas phase and theory) and the solution state (Chapter 5). Below, we will describe some points about the biological relevance of these elements. The basic coordination chemistry can be underscored to support that ionic interactions are predominant but are not the whole story.

2 Spectroscopic Techniques and Other Physical Methods

Various important physical techniques, including spectroscopy and electrochemistry, can be used analytically in the determination of amounts and speciation. Also, means of physical separation are available including ion chromatography and capillary electrophoresis. These techniques can be applied to issues in the chemical laboratory, in understanding biological systems, to issues in human health, within biological building blocks (living cells), and to environmental issues. Spectroscopy has commonly involved atomic absorption spectroscopy (AAS); this has been a powerful method to determine the presence and concentrations of certain elements in samples, especially trace elements in aqueous samples. This technique involves the thermal excitation of the ion through flame absorption spectrophotometry (flame photometry) whereby the species exhibits characteristic absorptions in nanometers

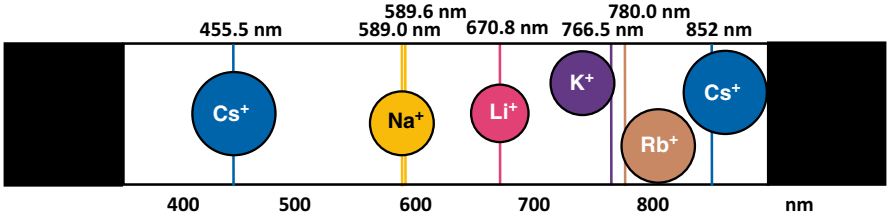

Figure 4 Select wavelengths and observed colors in atomic absorption spectroscopy analysis [15, 17].

[15, 17] (see also Chapter 2). Usually a principal absorption which gives rise to the observed flame color is monitored (Figure 4).

More recent efforts in chemosensing involve quantitative fluorescent methods which can also be used in the detection of metal ions in solution. Well-defined synthetic molecules containing an ionophore can selectively bind to a specific metal ion in solution. This technique is frequently used in biological studies for imaging common endogenous metal ions, such as Na^+ and K^+, within the workings of a single living cell [19, 20]. These cellular methods help probing spectroscopically silent metals [21]. Electrochemistry methods include the development and use of ion-selective electrodes (see also Chapter 2). These can also be used in targeting living cells and the concentrations within a single cell.

3 Lithium

Lithium exists in the lithosphere in various mineralogical forms and as a trace element in biology (Figures 1 and 2). Li^+ concentration is intimately connected to the physiological Na^+/K^+ balance. Thus, the element is important in clinical and pharmacological applications (Figure 3) [33, 34]. The lower bracket of Li^+ concentration in biological systems is not well defined; however, there is distinct Li^+ toxicity in human health often arising from prescription medication above a certain level; Li^+ has a narrow therapeutic index. The attention of lithium in science and society has also involved manufacturing of batteries [18, 22].

3.1 Introduction to the Coordination Chemistry of Li^+

In terms of its aqueous coordination chemistry, Li^+ bears an inner hydration sphere that is primarily tetrahedral. In solution, less ionic mobility is observed with Li^+; increasing ionic mobility is observed going down the group [23]. Li^+ is found "diagonally" (upper-left) to that of Mg^{2+} in the Periodic Table; such a "diagonal relationship" is sometimes helpful in understanding trends and tendencies and also building important relationships between metal ions and elements. When dissolved, Li^+ leads to a solution with very low vapor pressure; a markedly lowered melting point for water is also observed. Hydration sphere considerations can be extended to other solvent systems: the ion can crystallize with diethyl ether, or tetrahydrofuran. Sometimes nitrogen donors such as pyridine are present [1, 2].

In terms of solubility for Li^+, the carbonate and hydroxide are relatively insoluble (sparingly soluble) in water. The element's oxide chemistry contains important insights into the difference between it and heavier group members: upon heating, lithium hydroxide goes to an E_2O compound (Li_2O) analogous to water; MOH species of heavier congeners, however, undergo sublimation with no accompanying chemical change [1, 2]. The evaporation of LiOH gives the monohydrate compound which exists in a tetrahedral environment. Lithium carbonate is sparingly soluble and *anhydrous* as a solid,

unlike LiOH. Lithium nitrate ($LiNO_3$) is hygroscopic, but can be prepared as an anhydrous crystalline sample as well.

3.2 Recent Research Trends Regarding Li^+

There is a wide range of applications for lithium [23–34]. Li^+ has been used reliably for decades to treat manic depressive disorder (see Chapter 15). This application relates to a large drug market. The common medicinal formulation, lithium carbonate ($LiCO_3$), exists commonly in nature. With the pharmacology as such, in recent years, lithium ion has been investigated as a possible treatment for Alzheimer's Disease and in other potentially important applications [23, 24, 34].

Current industrial applications involve extensive battery technology, grease production, metallic lithium alloys, and lithium carbonate glasses and porcelain manufacturing [25–32].

4 Sodium and Potassium

Na^+ and K^+ are grouped here; their chemical properties and abundances are relatively similar. The salts of both metals have various uses in biological as well as industrial processes. Sodium has an abundance of 1.08 % in oceans. It has only one stable isotope (^{23}Na). Sodium nitrate ($NaNO_3$), also known as Chile saltpeter or Peru saltpeter, is found in large deposits in the Atacama Desert of South America. Potassium (0.040 %) is about 30 times less abundant than sodium. Potassium has three naturally abundant isotopes ^{39}K, ^{40}K, and ^{41}K [13]. Particular foods such as bananas contain significant amounts of K^+.

The salts of Na^+ and K^+ were not differentiable until ca. 1807, at which point the method of electrolysis allowed for separation of the two species. Na^+ and K^+ are found in ionic salts in a wide variety of minerals such as halite, and zeolite for Na^+ and orthoclase, granite, and sylvite for K^+. The salts are commonly formed from evaporated portions of seawater in which the less soluble minerals deposit at the bottom. Potassium nitrate (KNO_3, ordinary saltpeter) can be used interchangeably for many purposes. Biologically, there is an interplay between the balance of Na^+ and K^+ and the balance between Mg^{2+} and Ca^{2+}.

4.1 Introduction to the Coordination Chemistry of Na^+ and K^+

Na^+ and K^+ have ionic radii that are small to medium considering the range found for the group I ions (Figure 1). The sodium chloride structure is used as a common model for discussions of unit cells [37]. Na^+ and K^+ are more capable of forming

coordination complexes (multidentate binding) than the heavier alkali elements. Previous experimental and theoretical research suggests that the dominant coordination number for the primary hydration sphere for both K^+ and Na^+ is 6. A coordination number of 7 is also claimed for K^+ [14]. In a separate study, support for a primary coordination sphere of 4 for the metal ions has been made as well [16].

A natural selectivity for Na^+ or K^+ is manifested in biology. In spite of the similarity between Na^+ and K^+ (the Na^+ ion being smaller than K^+), only K^+ will pass along the potassium channels such as KcsA (found in *Streptomyces lividans*) for example, an apparatus in bacterial systems. This transport is due to effective solvation of a K^+ bound to eight peptidic oxygen donor atoms [17]. Artificial channels are discussed in Chapter 15. In terms of oxo chemistry, potassium superoxide (KO_2) is used extensively as a reagent in cell assays and as an analyte for molecular chemosensing.

The relatively small radii of Na^+ and K^+ allow for direct size fitting into ligand hosts. Coordination complex formation with crown ethers and other macrocyclic systems are well known. Primarily, electrostatic interactions exist between the monoatomic ion and the ligand donor atoms [4]. Host–guest chemistry is exemplified through various examples of synthetic supramolecular binding of Na^+ and K^+. The story of synthetic macrocyclic chemistry is fascinating and led to the Nobel Prize in 1987 [43]. Since host–guest chemistry may also include non-metallic cations, it is interesting to note that the K^+ ion has been stated to be similar to the ammonium ion (NH_4^+) [44]. Regarding natural systems, the selectivity in ion channels (K^+ *versus* Na^+) is discussed in Chapter 10.

The ions are also used ubiquitously in industry and in the household. Na^+ and K^+ are involved in processes involving curing meats [45], serve as counter ions in surfactants [46], in bleach, and in innumerable formulations in industry, [47–49, 55, 56], in salt baths, in KI which is used orally as a protectant for radioactive fallout [50], and in salt baths that are used for heat transfer. Azo-dye production also features sodium ion [51].

4.2 Recent Research Trends Regarding Na^+ and K^+

Contemporary research in the life sciences continues to focus on intricate biological pumps, enzymes and related aspects of cellular biology. The most important topics involving Na^+ and K^+ are covered in individual chapters in this volume.

5 Rubidium and Cesium

Rubidium is of more modest abundance (Figure 2) and does not feature prominently in biology. Rubidium has an abundance in seawater of 1.2×10^{-7} kg L^{-1}. It is likely that its primary hydration sphere consists of 6 coordinated water molecules. Rubidium appears with a deep red signal in the flame test (AAS).

Cesium is a relatively rare element with its concentration in seawater being approximately 3.0×10^{-6} kg L^{-1} (Figure 2). It has a golden appearance in the flame

test (AAS). Regarding the Cs^+ ion, found in discussions regarding the cesium chloride unit cell with a coordination number of 8 (for both cesium and chloride), it is likely that the primary coordination sphere under aqueous conditions consists of 6 water molecules. It is the most polarizable of the congeners (excluding Fr^+) and is least disruptive to the aqueous environment. Also, it has the lowest overall *total* hydration number and the greatest ionic mobility in the series. There are some notable deposits in the World such as in Bernic lake (Tanco mine) in Canada. Radioactive forms of cesium (^{137}Cs, half-life = ~30 years) is a main constituent of fallout (or nuclear fission) [52, 53]. Lastly, the element has found practical use in atomic clocks (stable isotope ^{133}Cs).

6 Francium

There is a dearth of studies relating to francium in biology because of its short radioisotopic lifetime (half-life $^{223}_{87}Fr = 21\,min$). Thus, francium is only of trace abundance. It is found in mineral deposits as ^{223}Fr alongside its progenitor isotopes uranium (^{235}U) and thorium (^{231}Th) (see the ^{235}U radioactive decay chain) [54]. As such, it is produced, but is then quickly lost to the formation of astatine (^{219}At), radium (^{223}Ra), and radon (^{219}Rn). While much less has been explored about it compared to the lighter congeners, it stands as an interesting frontier for future endeavors in the biomedical sciences.

7 Conclusions, Outlook, and Further Considerations for Future Studies

The alkali earth metals are a diverse group of elements that are essential for biology and which are found widely in mineral and electrolyte forms in nature – in the oceans, the earth's crust and in the universe (Figure 2). In particular, Na^+ and K^+ species are vital and important ions for life and the ecosystem.

The nuances in size, polarizability, and coordination chemistry among the elements is important to consider. Furthermore, additional donor atom chemistry such as nitrogen chemistry, fluoride chemistry, and phosphate chemistry, while not elaborated upon here, give an additional and fuller perspective of Group 1 ion chemistry in biology and in nature.

There are other singly-charged monoatomic, and even polyatomic species and ions that also behave like alkali metals; these surrogates can and should be studied in their relationship to biology.

A complete treatment of the differences between the Group 1 ions must involve a detailed analysis and expanded discussion of concepts that include ionic strength, ionic mobility, hydration energy, hydration number, hydrated radii, and crystal radii.

Further scientific instrumentation and methods may well focus on emergent spectroscopic techniques that can be more completely exploited, or derived, as well as to better explore issues in the frontiers of the chemical sciences and biomedical sciences. In particular, a thorough understanding of biological compartmentalization and transport of metal ions, it is hoped, can be much better elucidated in years to come.

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