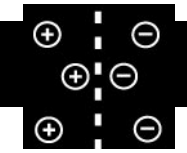
# BIOLOGICAL SYSTEMS: ION EXCHANGE



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There are two very different processes which are described under the heading of ion exchange within biological systems. The first is exchange in an aqueous environment of two different ions, $M_A$ and $M_B$, held by a molecule in free solution, or in a precipitate, or on a membrane surface:

$$M_A^{n+} + M_BX \rightleftarrows M_B^{n+} + M_AX \qquad [1]$$

Here, $M$ is a metal cation and $X$ is an anion, often an organic molecule which can be as large as a protein or DNA. Exchange of anions is also possible, as in the equilibrium:

$$X_A^{n-} + MX_B \rightleftarrows X_B^{n-} + MX_A \qquad [2]$$

Both eqns [1] and [2] have been written for exchanging ions of equal charge type $n$. This is not a necessary condition, so we can also consider:

$$2M_A^{+} + M_BX \rightleftarrows M_B^{2+} + (M_A)_2X \qquad [3]$$

$$2X_A^{-} + MX_B \rightleftarrows X_B^{2-} + M(X_A)_2 \qquad [4]$$

Again, the charge balance shown so far in the equations is not essential, so we must also examine the situation of electrogenic exchange:

$$M_A^{+} + M_BX \rightleftarrows M_B^{2+} + M_AX^{-}$$

$$X_A^{-} + MX_B \rightleftarrows X_B^{2-} + MX_A^{+}$$

where charge distribution is associated with $MX$ changes. Before considering the second way in which ion exchange can occur across a membrane, we give one or two examples of ion exchange to and from a bound condition in a single aqueous solution.

## Exchange of Major Cations and Anions in Cells

The major small cations and anions in cells which undergo ready exchange are shown in **Table 1**. They may associate with one another in rapid exchange or bind to surfaces of proteins, other polymers, precipitates or membranes and exchange rapidly or slowly.

Consider a magnesium protein such as $Mg^{2+}$ parvalbumin, where parvalbumin is a common anionic metal-ion-binding protein in muscle cells. When the protein, which is magnesium bound in the cell, is exposed to calcium, the reaction of exchange occurs: $Ca^{2+}$ parvalbumin is formed and $Mg^{2+}$ is freed. If the initial protein complex had been $Na^{+}$ parvalbumin, then replacement by $Ca^{2+}$ would have been electrogenic, unless of course two $Na^{+}$ ions had been bound originally.

A second example of exchange on the surface of a polymer is provided by polynucleotides such as RNA and DNA. These polymers have anionic phosphate backbones and their negative charges are balanced, not entirely randomly, by exchanging cations, including particularly $K^{+}$, $Mg^{2+}$ and ammonium derivatives. The positive charge, like the negative charge, in an exchanging system can also be carried on a large molecule and in biology there are many polyamines and positively charged proteins, such as histones, which bind DNA. They can bind and exchange anions such as $HPO_4^{2-}$ and $SO_4^{2-}$.

A further example of biological metal ion exchange in one aqueous solution now involving a solid precipitate is the case of bone, which we can write as $(Ca^{2+})_2(OH^{-})PO_4^{3-}$ for simplicity. Bone scavenges many other cations by exchange and contains considerable amounts of $Mg^{2+}$ and even $Al^{3+}$ in place of $Ca^{2+}$. Bone also exchanges $Ca^{2+}$ for protons ($H^{+}$). This mineral is additionally an anion-exchanging solid in which some $OH^{-}$ is replaced by $F^{-}$ (a process used in the protection of teeth). To some extent, a pair of $OH^{-} + PO_4^{3-}$ can be replaced by $2CO_3^{2-}$ anions. Notice that exchange can be electrogenic when charge is left on the surface of the bone mineral.

The last example of this relatively simple exchange is at the surface of membranes. All biological membranes carry negative charge due to covalently bound phosphate or carboxylate groups. Since the charges are quite close-packed, the membranes have a considerable affinity for cations and all membranes have associated $K^{+}$ and $Mg^{2+}$ (mainly internally) and $Na^{+}$ and $Ca^{2+}$ (mainly externally) associated with their surfaces. The outermost coats of cell walls in Gram-negative bacteria are also anionic and are stabilized by exchangeable cation, often $Ca^{2+}$, incorporation.

**Table 1** Major small cations and anions of cells

| *Cation* | *Anion* |
|---|---|
| $Na^+$ largely rejected | $Cl^-$ largely rejected |
| $K^+$ cytoplasmic | $HPO_4^{2-}$ cytoplasmic |
| $Mg^{2+}$ cytoplasmic | $SO_4^{2-}$ cytoplasmic |
| $Ca^{2+}$ rejected (vesicular) | $HCO_3^-$ balanced |
| $RNH_3^+$ cytoplasmic | $RCO_2^-$ cytoplasmic |
| | $ROPO_3^{2-}$ cytoplasmic |

$H^+$(pH 7); $OH^-$(pH 7).

## Exchange of Trace Elements

Major exchange of trace elements (**Table 2**) occurs from many carrier or buffer proteins. For example, iron is carried in the blood stream of higher animals by the protein transferrin in the form of $Fe^{3+}$, in co-association with the carbonate anion, $CO_3^{2-}$. The uptake into the cell involves the transfer of the whole protein to a vesicle, the lysozyme, which is much more acidic than blood. There the protein loses both iron and $CO_3^{2-}$, which are exchanged for bound protons. The iron is processed further into the cell as $Fe^{2+}$, only to be reoxidized in a precipitate inside a protein matrix, ferritin, where it is stored as $Fe(OH)_3$. From this small particle, iron exchanges into the cytoplasm, to give a great variety of compounds (see **Figure 1**) for the case of bacteria.

A second example of cytoplasmic ion exchange of trace elements involves both copper and zinc bound to sulfur-containing proteins. The proteins release copper or zinc ($M$) to the cytoplasm in equilibrium with free hydrogen ions:

$$\mathrm{Pr}.M + \mathrm{H}^+ \rightleftarrows M^+ + \mathrm{PrH}$$

where Pr is a protein such as metallothionein. This equilibration ensures constant levels of $Zn^{2+}$ and $Cu^+$ in the cytoplasm.

Trace anions are also carried in the blood stream by special proteins and are then transported into cells. The proteins which transfer $SO_4^{2-}$, $SeO_4^{2-}$ and $MoO_4^{2-}$ are known to be similar to transferrin.

**Table 2** Trace cations and anions of cells

| *Cation* | *Anion* |
|---|---|
| $Mn^{2+}$ vesicular | $SeO_4^{2-}$ cytoplasmic |
| $Fe^{2+}/Fe^{3+}$ cytoplasmic (precipitate) | $MoO_4^{2-}$ cytoplasmic |
| $Co^{2+}$ cytoplasmic | $I^-$ cytoplasmic |
| $Ni^{2+}$ vesicular | $NO_3^-$ cytoplasmic |
| $Cu^{2+}$ rejected | |
| $Zn^{2+}$ cytoplasmic | |

Many of the ions are held in complexes with organic agents.

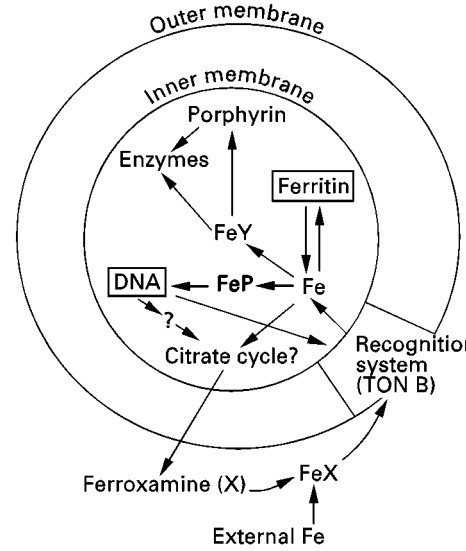


**Figure 1** An outlined scheme of the variety of ion exchange reactions in the uptake of iron. Iron is captured as $Fe^{3+}$ outside the cell by a small organic molecule, ferroxamine (X). FeX is passed through membranes (TON B) using energy, and is then exchanged in a variety of paths. Some involve proteins, P; some enzymes catalyse for example the citrate cell. Some iron is exchanged into new small organic molecules, porphyrins, to make new enzymes. Finally, much is stored in a bound small particle of $Fe(OH)_3$, called ferritin.

## Ion Exchange across Membranes

A different form of ion exchange is that which occurs across a membrane separating two aqueous phases (**Figure 2**). Once again, the simplest exchange is of two ions, cations such as $Na^+/K^+$, $Mg^{2+}/Ca^{2+}$ or of anions such as $OH^-/Cl^-$, where there is equal charge maintenance but change of concentration on both sides of the membrane. There are other possibilities than exchange of equally charged ions, such as the exchange of $2Na^+/Ca^{2+}$ or $2Cl^-/HPO_4^{2-}$, when only concentration changes are again involved on exchange. The further possibility is that the exchange process is electrogenic, when charge differences are built up across a membrane. Simple examples are the exchanges of $H^+/Ca^{2+}$ or $OH^-/HPO_4^{2-}$.

In the case of electrogenic exchange, an electrical potential develops across the membrane. Such potentials exist across most membranes of all cells but to different degrees. The development of such ion exchange potentials has led to the successive evolution from simple cells to nerves and then to the brain. In these cells $Na^+/K^+$ exchange carries the electrolytic current.

Examples of exchange of ions across membranes are numerous in biological systems. One of the best known is the $2Na^+/Ca^{2+}$ exchange in many slow

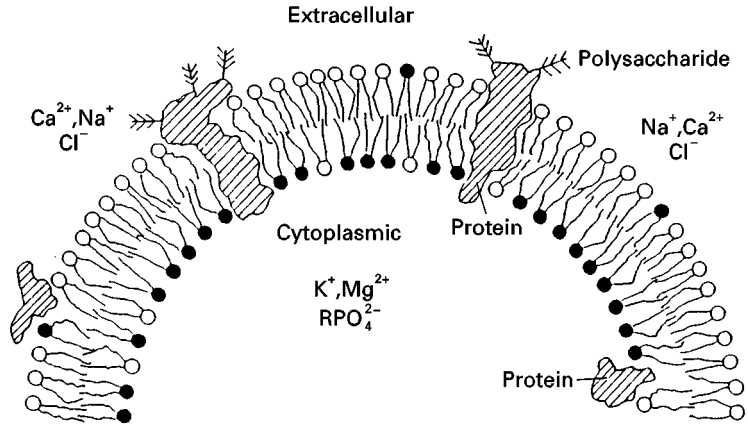


**Figure 2** The distribution of the major anions, $Cl^-$ and $RPO_4^{2-}$ and cations, $Na^+$, $K^+$, $Ca^{2+}$ and $Mg^{2+}$ across a biological cell membrane. Filled circles, charged (negative) phospholipids; open circles, uncharged lipids.

muscle cells. This exchange occurs after muscle action is triggered by the invasion of $Ca^{2+}$ and is used to restore the resting state of a muscle such as that of the heart. An example of electrogenic exchange is found in the nerve when $2K^+$ ions enter the cell in exchange for $3Na^+$, thus creating a membrane potential (**Figure 3**). However, this process costs energy and was a later development in evolution. We turn to the energetics of such exchange processes below.

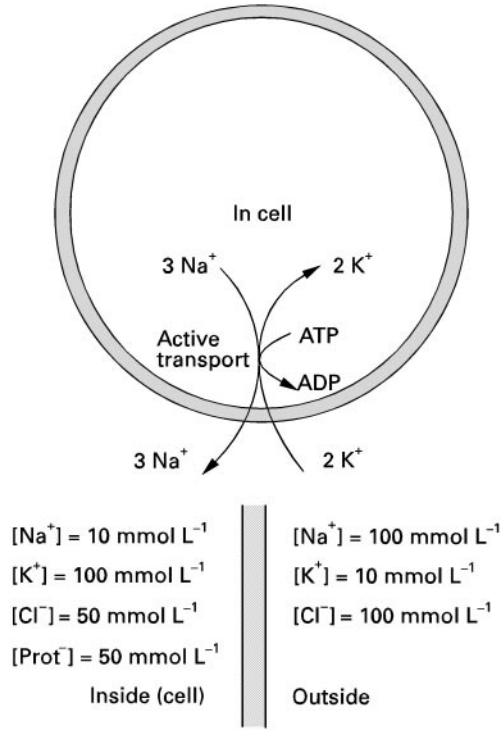


**Figure 3** The adenosine triphosphate (ATP) pump in mammalian cells. It exchanges $3Na^+$ for $2K^+$ and is electrogenic. The concentration of ions inside and outside human cells is shown below.

## The Natural Environment and Ion Exchange

To appreciate the value of ion exchange in biological systems, we must look at the environment of cells and the nature of cellular organic chemicals. The major fluids surrounding cells are the sea, fresh water and artificially maintained body fluids for multicellular species such as humans living in air. All of these fluids are aqueous electrolyte solutions containing elements as ions, as shown in Figure 3. The composition of the sea is given in **Figure 4**. The major feature of the internal cellular solution, that is, the solution protected by the cell's membrane, called the cytoplasm, is that it contains many organic molecules and anions. Both the environmental fluids and the cytoplasm have an osmotic pressure which, unless counter measures are taken to exclude many of the ions of the environment, will be greater for the cytoplasm due to the organic molecules present there. Hence all cells are in danger of bursting through osmotic stress. Due to the anionic nature of the organic molecules in the cell and the fact that the membranes themselves are also anionic due to the phospholipid head groups, they are also in danger of breakdown due to internal electrostatic repulsion between the anions. Various ways of overcoming these problems have been observed in different biological cells and they frequently involve ion-exchange.

Osmotic stress can be overcome by protecting the outer membrane by a cell wall. This wall, built from anionic organic cross-linked polymers, is commonly found in bacteria and plant cells. The anionic wall is exposed to the environment and acts as an ion-exchange resin accepting especially $Ca^{2+}$ and $Mg^{2+}$ ions, which considerably strengthen the wall by cross-linking the organic polymers in it. These cations freely exchange with the environment, so that the wall

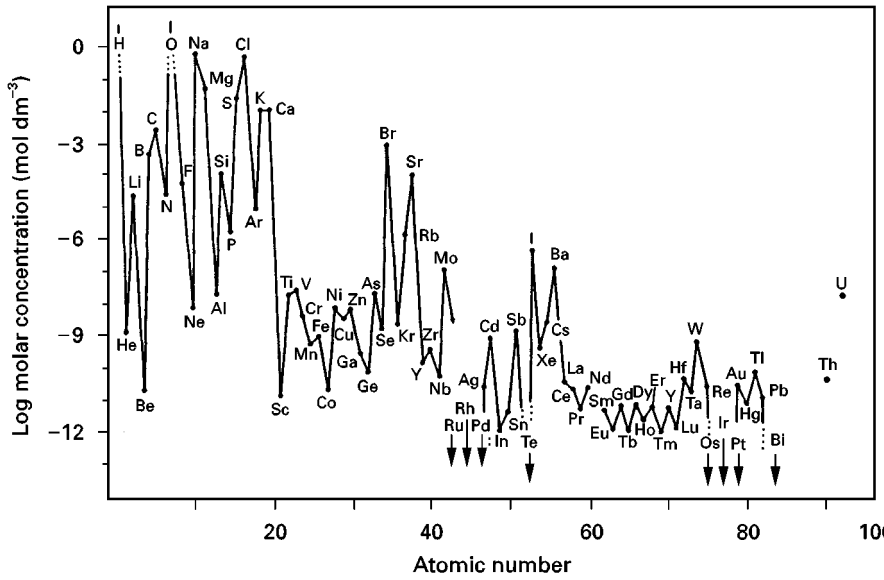


**Figure 4** The concentrations of elements in various ionic forms in the sea. Surfaces of cells exchange ions with all these species but clearly those up to atomic number 20 dominate. However, a biological cell exchanges and picks up more than 20 elements, including molybdate and iodide (from Cox 1995, with permission).

does not have a fixed chemical composition and acts much like an artificial ion exchange resin.

All cells, bacterial, plant and animal, also overcome osmotic stress by the selective admission and rejection of ions of the environment. The major ions of the environment are $Na^+$ and $Cl^-$, and in the case of the sea they are quite highly concentrated. Both must be prevented from equilibrating between the environment and the cytoplasm if the cell is not to burst. However, to maintain approximate electrical neutrality there has to be counterions to the anionic organic constituents of the cell. Hence, all cells admit $K^+$ and $Mg^{2+}$ ions and reject $Na^+$ and $Cl^-$ ions to a greater or lesser degree (**Table 3**). Of course, this arrangement of ions across the cell membrane costs energy, so the forced exchange of ions must use an energy source internal to the cell.

Before describing the modes of employing energy in pumping ions across membranes so as to establish nonequilibrium conditions, we need to observe that cells have to move many substances other than $Na^+$, $K^+$, $Mg^{2+}$ and $Cl^-$ (Table 3). Firstly, they need to exclude $Ca^{2+}$, since at the concentration of the environment these ions would precipitate cell anions such as carboxylates and phosphates. Secondly, the cytoplasmic level of anions such as phosphate is too low and that of sulfate is too high in the environment, especially in the sea, so that their cellular concentrations must be controlled. Thirdly, the cell must be able to take in anions (or cations) useful as food for synthesis of organic molecules and these include nitrate, small organic phosphates and carboxylates and ammonium or small amine cations. Fourthly, there are a variety of trace elements in the environment, all of which are required in selected amounts in the cell; for example, cations such as those of iron and manganese and anions such as selenate and molydate. Finally, we have not mentioned the universal presence

**Table 3** Pumped gradients of metals and their complexes

| *Metal* | *Inward to cytoplasm* | *Outward to* | *Organelle or vesicle* |
|---|---|---|---|
| $Na^+$ | | Free ion | Outside |
| $Mg^{2+}$ | Free ion | | |
| $H^+$ | Free ion and many ligands | Free ion and many ligands | Vesicles, outside |
| $K^+$ | Free ion | | |
| $HPO_4^{2-}$ | Free ion | Several organic phosphates | Mitochondria |
| $Cl^-$ | Free ion | Free ion | Outside |
| $Fe^{3+}$ | Ferroxamines, etc. | | |
| | Transferrin | Citrate | Mitochondria |
| $Co^{2+}$ | Vitamin $B_{12}$ | | |
| $Ca^{2+}$ | | Free ion | Reticula, outside |

of the proton $H^+$ which is in constant exchange with many anionic surfaces. Very much of the energy of biological reactions is expended in ion exchange across membranes.

## Energized Ion Exchange

There are two major sources of energy open to cells. One is a gradient of protons, $H^+$ (a pH gradient), developed from the action of light of from the oxidation of organic molecules (**Figure 5**), while the second comes from the hydrolysis of pyrophosphate bound to nucleotides such as adenosine triphosphate (ATP). The proton gradient can be used in direct ion exchange with other ions, $X$, across the membrane to accumulate them:

$$H^+_{in} + X^-_{out} \rightarrow X^-_{in} + H^+_{out}$$

$$H^+_{in} + M^+_{out} \rightarrow M^+_{in} + H^+_{out}$$

or to develop unfavourable gradients for protection by removing $X$ or $M$ from the cell to the environment:

$$H^+_{in} + X^-_{in} \rightarrow X^-_{out} + H^+_{out}$$

$$H^+_{in} + M^+_{in} \rightarrow M^+_{out} + H^+_{out}$$

The first is termed a symport and the second an antiport. In every case, movement across the membrane can be aided by carriers, $M$ or $X$ in the membrane, or by utilizing channels. Channels are controlled, gated pores through membranes.

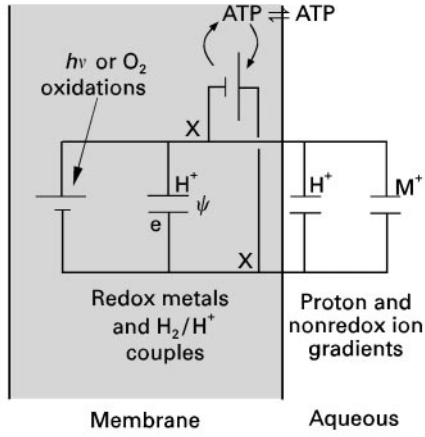


**Figure 5** A simplified picture of the production of a proton gradient and then of ATP by the action of light or oxidation of organic molecules inside a membrane. The gradient or ATP is then connected (X) to aqueous phases when ion ($M$) exchange across membranes can be driven, indicated by $=$ , the symbol for a condenser.

**Table 4** Examples of ATP-driven ion exchange pumps in cell membranes

| *Pump* | *Function* |
|---|---|
| $K^+/Na^+$ | $K^+$ moves in; $Na^+$ moves out. Nerve conduction |
| $H^+/Ca^{2+}$ | $Ca^{2+}$ moves out. Fast (skeletal) muscle recovery |
| $H^+/M$ | Trace element input or rejection |

The use of ATP is that its hydrolysis energy ($-\Delta G$) can pump ions across membranes:

$$ATP \rightarrow ADP + P_i(-\Delta G)$$

$$-\Delta G + X_{in} \rightarrow X_{out}$$

$$-\Delta G + X_{out} \rightarrow X_{in}$$

It is now known that the action of ATP pumps frequently involves ion exchange so that transfer of one cation or anion is coupled to transfer of a second ion in the opposite direction, giving ion exchange while building energized ion gradients. Examples are given in **Table 4**.

## Selectivity of Ion Exchange

The selectivity of ion exchange interactions depends on the relative binding strengths of ions to a site, where the site may be a molecule free in the cytoplasm, a carrier molecule in a membrane, a surface of a membrane or a precipitated phase, or part of a channel or a pump for moving ions across membranes. The affinity for the site can usually be expressed in a very simple form as a binding stability constant, $K$, for the equilibrium:

$$M + X \rightleftarrows MX$$

where $K = [MX]/[M][X]$.

The concentration of $X$ is here treated in mass action equations and takes a similar form for surface sites or sites in free solution. In the case of surface sites, the equation takes the form of a Langmuir isotherm.

Selectivity of binding depends on the size and charge of an ion in the first instance. It would be expected that small highly charged ions of opposite sign would bind together best, but this expectation is not fully borne out in practice, since competition for a site also depends on constraints due to hydration of the ions:

$$M(H_2O)_n + X \rightleftarrows MX + nH_2O$$

Since small, highly charged ions are the most strongly hydrated, making for competition between $H_2O$ and

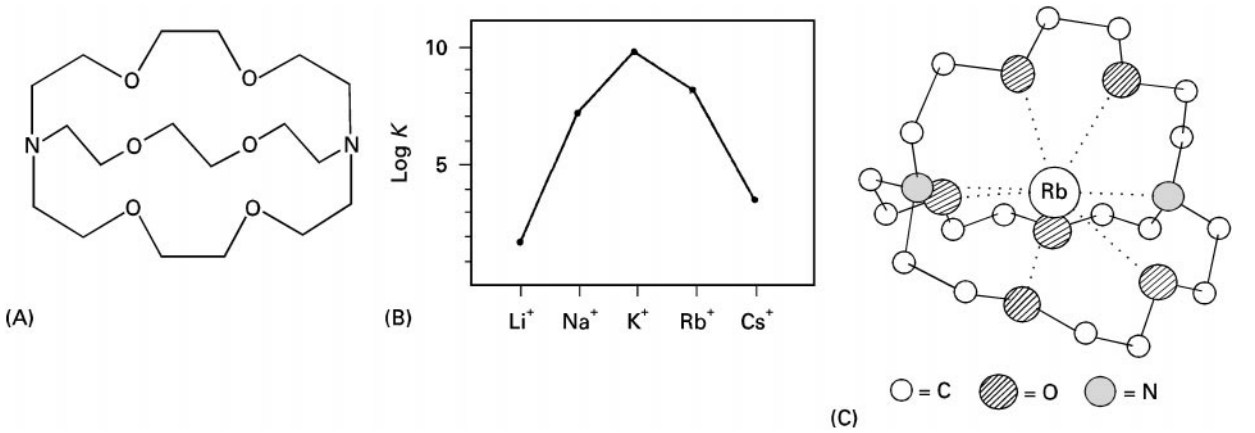


**Figure 6** The molecule shown at (A) can bind the monovalent ions selectively because of how it wraps around them (C). The hole in the middle selects the size of the ion, as shown by the binding constants (B). The best binding is for potassium. Such molecules can pick up cations and transfer them across membranes, exchanging the ion for other ions according to binding strengths and concentrations. Many antibiotics are based on such exchange possibilities.

*X*, there is the possibility of matching ions, *M*, of different charges and sizes with particular kinds of designed exchange site, *X*. Controlling factors now for cations, *M*, are the charge on *X* and the steric restrictions present in *X* or induced in *MX* on binding. Real examples illustrate the point that the binding of cations *M* to sites *X* can be in almost any order. The case of the preferred selection of $K^+$ over the smaller and larger ions $Li^+$, $Na^+$, $Rb^+$ and $Cs^+$ illustrates the point in **Figure 6**. In all cells the $K^+$ channel virtually excludes $Na^+$. Similarly, the $Ca^{2+}$ pump of most cells excludes $Mg^{2+}$. In both bases the larger ion is preferred due to the size of the cavity and the accepting anion, *X*.

For trace element metal ions such as those of iron ($Fe^{2+}$, $Fe^{3+}$), zinc ($Zn^{2+}$) or copper ($Cu^+$, $Cu^{2+}$), facts other than charge and size influence selectivity. They are the ability to form covalent bonds depending on the electron affinity of the cation and stereochemical preferences of the metal ions due to their polarizability. Again, examples illustrate these points.

A very important distinction between the bindings of the major metal ions, $Na^+$, $K^+$, $Mg^{2+}$ and $Ca^{2+}$ and the trace elements, is that the binding units *X* for the former generally employ organic molecules containing oxygen (O) donor centres only, while for the trace elements the group *X* may utilize nitrogen (N) or sulfur (S) donors. Examples are given in **Table 5**, Amongst the trace elements the strength of binding follows the general series of divalent $M^{2+}$ ions:

$$Cu > Ni \geq Zn > Co > Fe > Mn > Mg$$

The additional selectivity factor arises due to the stereochemical preferences of these ions.

We can now consider the cytoplasm of a cell as a solution of ion exchange centres, often proteins, which can all bind *M* but with different affinities. Together with the fact that the amounts of ions, *M*, in the cytoplasm varies from $10^{-1}$ mol $L^{-1}$ ($Na^+$, $K^+$) to $10^{-17}$ mol $L^{-1}$ ($Fe^{3+}$), this chemical selectivity leads to a virtually complete fixation of the *M* distribution on different *X* centres. However, it must not be forgotten that these associations are not permanent and exchange takes place all the time. Many sites will only be occupied preferentially, not specifically, by a given cation. This is particularly important when the environment becomes polluted.

The selective uptake of anions follows similar properties based on size, charge and steric constraints. However, covalent attachment is much less significant than hydrogen bonding. The ability to form hydrogen bonds by anions appears to be related to surface charge density. Thus, $F^-$ and $OH^-$ readily form H bonds when compared with $Cl^-$, $Br^-$ or $SH^-$. Once again, the anions exchange quite rapidly with organic surfaces.

## Ion Exchange and Cell Compartments

The selectivity of binding to carriers, to channels and channel parts of pumps in membranes leads to

**Table 5** Preferred metal/nonmetal ion association

| *Metal* | *Preferred nonmetal association* |
|---|---|
| $Na^+$, $K^+$ | Low association, preference for O-donor |
| $Mg^{2+}$, $Ca^{2+}$ | Moderate association with O-donor anions such as carboxylates and phosphates |
| $Fe^{2+}$, $Co^{2+}$ | Strong association with mixture of N- and O-donors |
| $Cu^{2+}$, $Zn^{2+}$ | Strong association with S-donor such as thiolates |

Exchange is fast for $Na^+$, $K^+$ but progressively slower down the table.

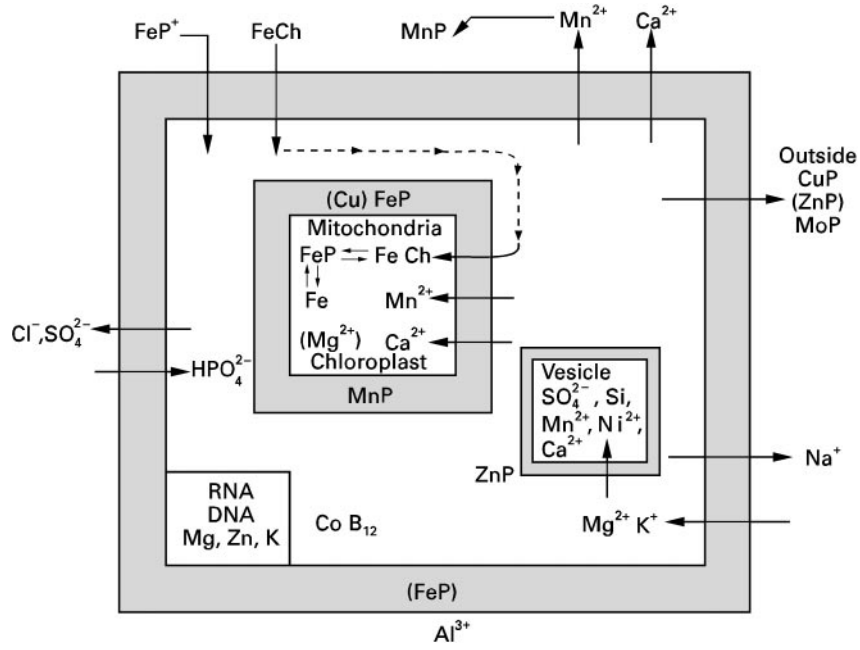


**Figure 7** Some of the distributions of elements in eukaryotic cells. Iron is often in membranes, while $Cl^-$, $Ca^{2+}$ and $Na^+$ are concentrated away from the cytoplasm; $K^+$ and $Mg^{2+}$ concentrate inside cells, $Mn^{2+}$ is to be found in vesicles, but copper is more usual outside cells. Zinc is everywhere and cobalt is rare everywhere. Aluminium may be rejected. P, Protein; Ch, chelating agent. Many movements are due to ion exchange.

separate movement of elements in cells and then positions them in particular zones of vesicles. Within these zones, ion exchange of the selected *M* ions at *X* occurs, so that selectivity of association is manipulated by the input of energy. Some cell compartments and their selective element contents are shown in **Figure 7**.

The setting-up of such ion gradients across membranes has great value, not only in that it allows specific reactions to occur in particular parts of space but also that, under stimulus, the ions can be released from their storage sites into the cytoplasm. There is then ion exchange signal. A particularly important example concerns the storage and subsequent release of calcium ions from vesicles into the cytoplasm, causing manifold changes in metabolism and mechanical structure. Simple examples are muscle contraction and hormone release.

We can look upon a mineral phase as a compartment where minerals such as amorphous silica (often in plants), calcium carbonate and calcium hydroxyphosphate are the obvious examples. These precipitates, by exchanging ions, can buffer solutions holding ions in their neighbouring solutions in fixed amounts.

## Ion Exchange and Organs

As well as the local problems of ion exchange, large-bodied organisms, such as human beings, must control ion levels throughout their whole body. They do this by managing uptake and rejection of ions selectively. Thus it is necessary to ingest sufficient but not too much of many ions such as $Na^+$, $K^+$, $Cl^-$ and $HPO_4^{2-}$. The monitoring and rejection organ is the kidney. The kidney membranes act as complicated ion exchange systems. However, the brain apparently requires special ionic conditions, since cerebrospinal fluids of quite different composition from blood.

## Ion Exchange and Pollution

Many unusual elements enter environmental waters due to mining and industrial processing of minerals. Several of these elements are toxic and we note especially lead and mercury. There is considerable interest today in the removal from cells of poisonous elements such as $Hg^{2+}$, $Pb^{2+}$ and $AsO_4^{3-}$. Once again, even in bacteria, special proteins recognize these ions and either transfer them directly across membranes or release them to specialized pumps for energized movement out of the cell. While bacteria have evolved detoxifying processes, higher animals have not, so humans have to take action to remove the offending elements. The application of a drug may force the offensive element to exchange from the site where it causes damage, becoming bound to the drug when it is excreted.

## Conclusion

While ion exchange appears to be an extremely simple idea, it is used in remarkably complicated ways in living organisms. Of course, we do not know how life began but perhaps the earliest step in the direction of the development of these organized chemical systems was the formation of an ion gradient across a membrane. Once such a gradient had formed, possibly of the proton, ion exchange could be used to move some elements out of cells and others into cells. These ions could be inorganic or organic. The movements became more complicated as more membrane containments developed in evolution. Within each compartment ions could bind to form complexes or precipitates by exchange processes. We know that cells have many different kinds of ion gradient through this exchange: some relate to energy storage and some to messages by release of the gradients. Recently evolved systems are calcium triggering of muscle and sodium/potassium currents in nerves. The restoration of the gradients is very frequently energized by ion exchange across membranes. This leads us to the tantalizing problem of the movement of ions in the brain. Are ion exchange processes deeply involved in storage, memory, and in thinking? We know that the brain is an electrolytic device and hence ion movements are always active. Clearly, we could speculate at length on this topic, but what is really required is more experimental evidence concerning ion exchange in organisms and especially in the brain.

*See also:* **II/Ion Exchange:** Inorganic Ion Exchangers; Theory of Ion Exch]ange.

## Further Reading

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# BIOLOGICALLY ACTIVE COMPOUNDS AND XENOBIOTICS: MAGNETIC AFFINITY SEPARATIONS

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## Introduction

Isolation and separation of specific molecules is used in almost all areas of biosciences and biotechnologies. Separation technology is thus one of the most important areas for further study and development. New separation techniques, capable of treating dilute solutions or solutions containing only minute amounts of target molecules in the presence of vast amounts of accompanying compounds in both small and large-scale processes, even in the presence of particulate matter, are necessary.

In the area of biosciences, isolation of biologically active compounds and xenobiotics is usually performed using a variety of chromatography procedures, affinity chromatography being one of the most important. Affinity ligand techniques currently represent the most powerful tool available for downstream processing both in terms of their selectivity and recovery. The strength of column affinity chromatography has been shown in thousands of successful applications, especially on a laboratory