



Research Paper

## The Biophysical Modeling of the Donnan equilibrium in the Living Systems

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**ABSTRACT:** The transport phenomena mean the variation in time and space of generalized forces when they generate flows for which conservation laws apply. The Donnan equilibrium is a cross-effect, thus is a particular case of the transport phenomena. We studied the distribution of charged particles in compartments separated by a semi-permeable membrane. If one of the compartments on the two sides of membrane contains an impermeable polyelectrolyte, the concentration difference of ions between the two sides at equilibrium and obeying the principle of electroneutrality, is called Donnan equilibrium. Applying, this to the cell membrane, we can see that the Donnan potential is always negative and is the result of immobile, cytoplasmic anions. Donnan potential increases if concentration of the immobile anions increases, and decreases when the extracellular saline concentration increases. When explaining transport phenomena and electric potentials formed across cellular membrane, we not only have to consider the conditions for equilibrium, but also that these states are formed through ion diffusion. The diffusion potential exists only transiently, because in the system described above, concentration differences become balanced sooner or later. Diffusion potential can be stable in systems where compartments having different concentration of permeable ions are separated by selectively permeable membranes. It is known that the permeability of biological membranes is ion-specific.

**Key words:** Nernst equilibrium, Donnan equilibrium, Donnan potential, diffusion potential, transport phenomena

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### I. INTRODUCTION

All living cells show electrical phenomena. A voltage of around 70 mV can be measured between the inner and outer surfaces of resting cells at normal ionic composition. If the potential of the extracellular space is considered zero, then the potential of the intracellular space is negative. [1] This is the so-called resting potential. Table 1. gives the concentrations of the major ions in the extra- and intracellular space of the cells.

**Table 1.** Approximate compositions of extracellular and intracellular fluids

Substance and units	Extracellular fluid	Intracellular fluid
Na <sup>+</sup> (mEq/l)	140	14
K <sup>+</sup> (mEq/l)	4	120
Ca <sup>2+</sup> (mEq/l)	2,5	1x10 <sup>-4</sup>
Cl <sup>-</sup> (mEq/l)	105	10
HCO <sub>3</sub> <sup>-</sup> (mEq/l)	24	10
pH	7,4	7,1
Osmolarity (mOsm/l)	290	290

An important application of the concepts developed is the description of ionic equilibria. The two such equilibria of greatest biological importance are presented below. The first of these is the Nernst equilibrium, which defines the potential difference across a membrane such that an ion, present on both sides, is at equilibrium. [2] This is followed by a description of the Donnan equilibrium, which arises when two phases are in equilibrium and one or more of the charged species in one phase cannot enter the other phase.

### The Nernst Equilibrium

While the current through the external circuit would be carried by electrons, the charges that move across membranes are borne by ions. A general expression for the membrane current is:

$$I = F \sum_i z_i J_i$$

where  $J_i$  is the flux of the  $i^{\text{th}}$  species across the membrane, and  $I$ , the current density. In the present application, only  $P$  can cross the membrane, so  $I=0$  implies  $J_P=0$ . For  $J_P$  be zero, the membrane potential  $\Delta\Psi$  must be equal to the Nernst potential of  $P$ , then  $P$  will be at equilibrium and have no cause rhw membrane. [3, 4] Thus  $\Delta\Psi = E_P$ ;

$$\Delta\Psi = \frac{RT}{z_P F} \ln \frac{a_P^2}{a_P^1}$$

The Nernst equilibrium describes the conditions under which an ion is in equilibrium between two phases. For discussion purposes, we will imagine that the two phases are separated by a membrane. The membrane is permeable to the ion. The equilibrium condition is given by:

$$\mu_i^1 = \mu_i^2$$

In most considerations of ionic equilibria in biological systems, the effect of pressure on the equilibrium state can be shown to be very small, and the system is taken to be isothermal. Under these circumstances, becomes:

$$RT \ln a_i^1 + z_i F \Psi^1 = RT \ln a_i^2 + z_i F \Psi^2$$

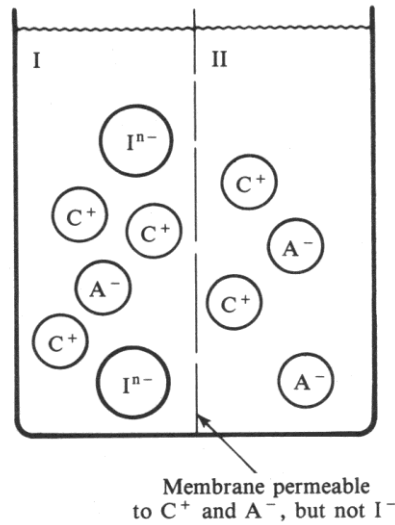
For a nonelectrolyte,  $z_i = 0$ , and the equilibrium condition given above is satisfied only when the activity of the solute is the same in both phases. This is not the case for an ionic species, since interphase differences in activity can be compensated for by a potential difference across the membrane. The required potential difference for ionic equilibrium is found by rearranging:

$$\Delta\Psi = \frac{RT}{z_i F} \ln \frac{a_i^2}{a_i^1}$$

where the  $\Delta$  operator denotes the difference between the values of the operand in the two phases; e.g.,  $\Delta\Psi = \Psi^1 - \Psi^2$ . This equation is the Nernst equation, and the potential difference it defines is the Nernst potential of the  $i^{\text{th}}$  ion,  $E_i$ . [5] Each ion in solution has its own Nernst potential, which is given by this equation and depends on the activity of the ion in each phase.

### Donnan equilibrium for two ions

The Donnan equilibrium defines the conditions that arise when two phases containing electrolyte are in equilibrium, and one or both of the phases contain charged species that cannot exchange between the phases (Fig. 1.). For instance, two solutions, one of which contains a charged protein, might be separated by a membrane through which only small ions can pass. A charged (polyelectrolyte) gel in saline solution generates a Donnan equilibrium; the ions from outside can enter the gel and equilibrate between the gel and the solution, while the longchain charged molecules that make up the gel are covalently linked to one another and cannot enter the saline. [6]



**Fig. 1.** The Donnan equilibrium;  $I^-$  represents a large, multiply charged macromolecule that cannot cross the membrane.

Consider the system represented in Fig. 1. A membrane separates two phases as in earlier figures. Phase II contains only a 1–1 electrolyte,  $CA$ , at a concentration  $c^2 = c_C^2 = c_A^2$ . Both the cation ( $C$ ) and anion ( $A$ ) can cross the membrane, and consequently are present in Phase 1 as well. Phase 1, which could be the interior of a cell bathed by Phase 2, contains charged solutes (e.g., proteins) that cannot cross the membrane; the concentration of charge on these impermeant solutes is  $z_i c_i^1$ . The Gibbs-Donnan equilibrium condition defines the equilibrium state of this system. [7]

As hinted above, the description of the Donnan equilibrium proceeds more simply when concentrations rather than activities are used. Since both  $C$  and  $A$  can cross the membrane, both ions must satisfy the equilibrium condition, for the system as a whole to be at equilibrium. Put another way, their Nernst potentials must each equal the membrane potential,  $\Delta\Psi$ :

$$\Delta\Psi = \frac{RT}{F} \ln \frac{c^2}{c_C^1} = -\frac{RT}{F} \ln \frac{c^2}{c_A^1} \quad *$$

The two expressions on the right yield:

$$\frac{c^2}{c_C^1} = \frac{c^2}{c_A^1} \quad **$$

This ratio, or its reciprocal, is called the Donnan ratio. It is easy to show that when Phase 2 contains multiple monovalent ions, the Donnan ratio is the same for all ions of like charge. Phases 1 and 2 are both electrically neutral; that is, in the  $j^{\text{th}}$  ( $j=1, 2$ ) phase,

$$\sum_i z_i c_i^j = 0$$

Note that this condition is properly written in terms of ionic concentrations, not activities. The electroneutrality condition applied to Phase 2 allowed us to equate the concentrations of  $C$  and  $A$  in that phase; the electroneutrality condition for Phase 1, which contains the charged impermeants, is:

$$c_C^1 - c_A^1 + z_i c_i^1 = 0 \quad ***$$

Equations \*\* and \*\*\* are solved simultaneously for the concentrations of  $C$  and  $A$  in Phase 1. At this point, the simplicity afforded by using concentrations in \*\*, rather than activities, becomes apparent. The solutions are

$$c_c^1 = \frac{-z_i c_i^1 + \sqrt{(c_i^1)^2 + 4(c^2)^2}}{2} \quad \text{****}$$

$$c_A^1 = \frac{z_i c_i^1 + \sqrt{(c_i^1)^2 + 4(c^2)^2}}{2}$$

The Donnan potential,  $\Delta\Psi_D$ , is the membrane potential at equilibrium; substituting \*\*\*\* into \*:

$$\Delta\Psi = \frac{RT}{F} \ln \frac{z_i c_i^1 + \sqrt{(c_i^1)^2 + 4(c^2)^2}}{2c^2}$$

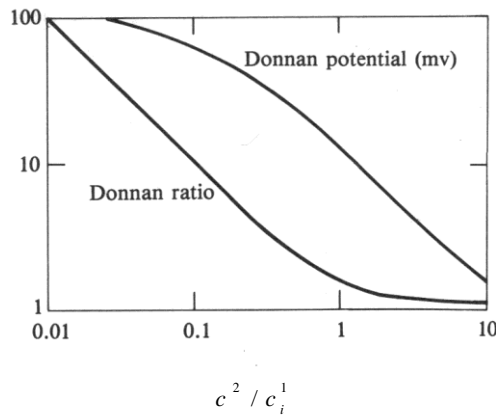


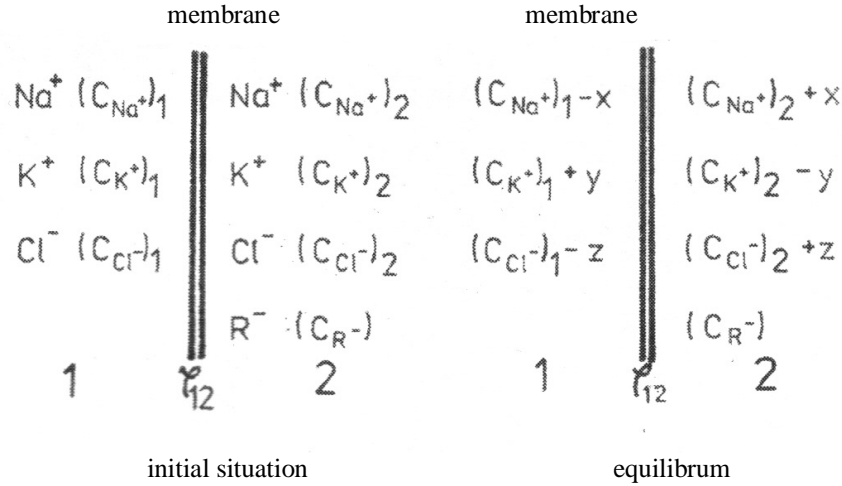
Fig. 2. Donnan ratio and Donnan potential

Figure 2. shows the variation of the Donnan ratio and the Donnan potential with ambient concentration. As  $c^2$  becomes much larger than the concentration of impermeant charge, the Donnan potential approaches zero and the Donnan ratio approaches unity. [8] This phenomenon is referred to as “suppression” of the Donnan effect. The Donnan effect is suppressed in certain analytical and experimental protocols to minimize uncertainties in the result when  $c_i^1$  is unknown or varies widely among preparations.

### Donnan equilibrium for three ions

According to the simplest model of the formation of resting potential in cells, the living cell is considered a Donnan system.

So, phenomena that occur when two electrolyte solutions are separated by a membrane that cannot be penetrated by one ion of the solution are important for several reasons. The equilibria that occur under these circumstances are called Donnan equilibria. [9] Each of the membranes of the living organism has ions of varying concentrations on both sides, and often also attached to macromolecules; in this respect, membranes are generally impermeable, so every condition is given for the Donnan equilibrium to be established. Thus, the Donnan equilibrium is a cross-effect, so as a result of the concentration-gradient, in addition to the transport of matter, it also creates an electric charge transport.



**Figure 3.** Donnan equilibrium for three diffusing and one non-diffusing ion.

To study membrane equilibria, consider the starting position shown in the Figure 3. both compartments contain NaCl and KCl salts, and the K-congo red salt in the second compartment. Separate the two compartments with membranes that are free to be diffused with Na<sup>+</sup>, K<sup>+</sup> and Cl<sup>-</sup> ions, but which do not allow large congo red anions (R<sup>-</sup>) to pass through. By contacting the two solutions with the membrane, the freely diffusing Na<sup>+</sup>, K<sup>+</sup>, and Cl<sup>-</sup> ions diffuse from one solution to another until equilibrium is reached. [10] The membrane potential is indicated by  $\phi_{12}$ . Membrane equilibrium is achieved under general equilibrium conditions when the chemical potential of the free-diffusing electrolyte is the same on both sides of the membrane. We note the chemical potential for each diffusing ion:

$$(\mu_{Na^+})_1 = (\mu_{Na^+})_2 - (\phi_{12}) \quad (1)$$

$$(\mu_{Cl^-})_1 - (\phi_{12}) = (\mu_{Cl^-})_2 \quad (2)$$

$$(\mu_{K^+})_1 = (\mu_{K^+})_2 - (\phi_{12}) \quad (3)$$

The initial condition implies that

$$(c_{Na^+})_1 > (c_{Na^+})_2; (c_{Cl^-})_1 > (c_{Cl^-})_2; (c_{K^+})_1 < (c_{K^+})_2.$$

Adding the first and second equations we get:

$$\begin{aligned} E_{Na^+}^0 + R.T. \ln [Na^+]_1 + E_{Cl^-}^0 + R.T. \ln [Cl^-]_1 - (\phi_{12}) &= \\ = E_{Na^+}^0 + R.T. \ln [Na^+]_2 + E_{Na^+}^0 + R.T. \ln [Cl^-]_2 - (\phi_{12}) \end{aligned}$$

This results the condition of equilibrium:

$$[Na^+]_1 \cdot [Cl^-]_1 = [Na^+]_2 \cdot [Cl^-]_2$$

Similarly, from the second and third equations we obtain that

$$[K^+]_1 \cdot [Cl^-]_1 = [K^+]_2 \cdot [Cl^-]_2$$

Replace the appropriate concentrations:

$$* \quad ((c_{Na^+})_1 - x) \cdot ((c_{Cl^-})_1 - z) = ((c_{Na^+})_2 + x) \cdot ((c_{Cl^-})_2 + z)$$

Under the condition of electron neutrality:

$$** \quad ((c_{K^+})_1 + y) \cdot ((c_{Cl^-})_1 - z) = ((c_{K^+})_2 - y) \cdot ((c_{Cl^-})_2 + z)$$

It follows from the law of flux that  $\mathbf{x} - \mathbf{y} = \mathbf{z}$ , where  $\mathbf{x}$  denotes the amount of diffused  $Na^+$  ions per unit volume, the similar  $K^+$  and  $Cl^-$  parameters of  $\mathbf{y}$ , respectively  $\mathbf{z}$  are indicated the same way. Performing the operations and adding the two equations, then using the flux relation, we get:

$$z = \frac{(c_{Na^+})_1 (c_{Cl^-})_1 + (c_{K^+})_1 (c_{Cl^-})_1 - (c_{Na^+})_2 (c_{Cl^-})_2 - (c_{K^+})_2 (c_{Cl^-})_2}{2 \cdot [(c_{Cl^-})_1 + (c_{Cl^-})_2] + (c_{R^-})}$$

Knowing the value of  $z$ , and replacing it in the equations (\*) and (\*\*), we can determine both  $\mathbf{x}$  and  $\mathbf{y}$ .

Accordingly, the less electrolyte diffuses through the membrane from compartment (1), the higher the concentration of non-diffusing ions. The latter thus inhibits the diffusion of the otherwise free-diffusing electrolyte. If  $(CR^-)$  is big, the non-diffusing ion present in relatively high concentration will almost completely prevent the free diffusing electrolyte from passing through the membrane. [10]

For living systems, the generalized Donnan equilibrium can always be used as a model, because it contains more ions for each of its components. As the membrane equilibrates, an electrical potential difference is created between the two sides of the membrane. [11] The membrane potential of cells is partly explained by the Donnan equilibrium, but this does not answer all the questions that arise.

### The transport phenomena

The Donnan equilibrium is a cross-effect, [12] thus is a particular case of the transport phenomena. The transport phenomena mean the variation in time and space of generalized forces when they generate flows for which conservation laws apply.

This general and strongly scientific definition of the transportation phenomena has two major merits: 1) particular forms of transportation can be deduced from it (mass transport – diffusion; energy transport – thermal conductivity; impulse transport – viscosity; electric charge transport – electric conductivity, crossed effects and other); 2.) it allows a quantitative characterization of the product exchange, which was impossible based on the previous definitions.

If  $\mathbf{W}$  – the amount of the transported parameter, for which the conservation law is valid;  $\mathbf{K}$  – a constant dependent on the type of transportation and the nature of the transported parameter;  $\mathbf{grad a}$  – the generalized force, then the amount of the parameter (flow) transported through the surface  $d\mathbf{S}$  in the  $d\mathbf{t}$  time frame will be given by the relation:

$$W = K \int_{t_1}^{t_2} \iiint_{S(x,y,z)} \mathbf{grad a} \cdot d\mathbf{S} dt$$

If the transportation takes place only after a direction  $\mathbf{x}$ , then we obtain the formula:

$$W = K \int_{t_1}^{t_2} \int_{x_1}^{x_2} \mathbf{grad a}_x dx dt$$

The differential form is the following:

$$\partial W = K \cdot \frac{\partial a}{\partial x} \cdot \Delta S \cdot \Delta t$$

Making the proper replacements in the relation above, we obtain the classical laws which describe particular, simple transportation phenomena. [13]

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