

# Basics: Theory

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## 2.1 Electrical Characteristics of Biological Membranes

The parameters often used in describing electrophysiological phenomena are listed in ■ Table 2.1. These physical constants will be used throughout.

The distribution of particles of potential energy  $U$  is governed by the Boltzmann law:

$$c(U) = c_0 e^{-U/(kT)}.$$

Therefore, the Boltzmann factor  $e^{U/(kT)}$  ( $=e^{\Delta E z F/(RT)}$  with electrical potential gradient  $\Delta E$  and effective valency  $z$ ), which describes the charge distribution in an electrical field, plays an important role in electrophysiological descriptions. It is, therefore, very useful to know the value of  $RT/F$  in mV. At room temperature (293 K) the value is:

$$RT/F = 25 \text{ mV} \quad \text{or} \quad \ln(10)RT/F = 58 \text{ mV}.$$

In electrophysiology, distribution between two orientations is often considered, and the charge distribution  $Q$  is then described by the Fermi equation:

$$Q(\Delta U) = \frac{1}{1 + \exp(\Delta E z F/(RT))}.$$

Other basic physical rules and characteristics are:

- Ohm's law:*  $E = I \cdot R_\Omega$  or  $I = g \cdot E$ ;  $I$  denotes current,  $R_\Omega$  resistance, and the conductance  $g$  is  $R_\Omega^{-1}$ .
- Resistivity ( $r$ ),* which is a measure for the electric resistance. It is defined by  $R_\Omega = r l / F$  with length (e.g. of nerve fibres)  $l$  and sectional area  $F$ .  $r$  is usually given in  $\Omega \text{ cm}$ . Typical values are given in ■ Table 2.2, illustrating again the high electrical resistance of the lipid bilayer compared to electrolyte solution at physiological ion activities.
- Capacitance ( $C = Q/E$ ):* Interestingly, the specific capacitance of a cell membrane hardly depends on the cell type and is close to the capacitance of a pure lipid bilayer (ca.  $0.8 \mu\text{F}/\text{cm}^2$ ). A value of  $1 \mu\text{F}/\text{cm}^2$  is often used to calculate the surface area of a cell from electrical determinations of the capacitance of the total surface area. The capacitance can be obtained from the transient signal of charging or discharging the membrane capacitor.

A simplified model of a membrane (■ Fig. 2.1) consists of the parallel arrangement of a capacitor and a resistor. The capacitor  $C$  represents the capacitance of the lipid bilayer, and the resistor  $R$  combines all conductance pathways across the cell membrane.

A transient signal can be measured under voltage or current clamp, and analyzed in terms of (see ■ Fig. 2.1):

$$I = \frac{dQ}{dt} = C \frac{dE}{dt} \Rightarrow \frac{dE}{dt} = \frac{I}{C} dE = \frac{1}{C} I dt.$$

The charging/discharging of the capacitor follows an exponential time course:

$$E = E_0 e^{-t/\tau} \quad \text{with time constant} \quad \tau = RC.$$

Typical values for a biological membrane with specific membrane resistances of  $10\text{--}10^6 \Omega \text{ cm}^2$  are accordingly in the range of  $10 \mu\text{s}$  to  $1 \text{ s}$ .

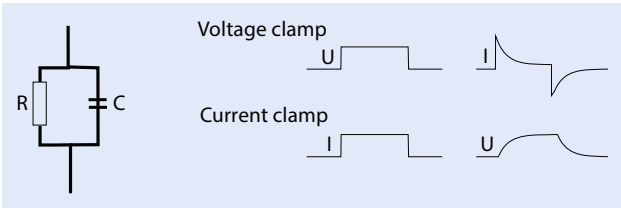
Table 2.1 Often-used physical constants

Constant	Abbreviation	Value	Unit
Avogadro's constant	$N_A$	$6.022 \times 10^{23}$	$\text{mol}^{-1}$
Elementary charge	$e$	$1.602 \times 10^{-19}$	C
Boltzmann's constant	$k$	$1.381 \times 10^{-23}$	$\text{J K}^{-1}$
Universal gas constant	$R$ ( $kN_A$ )	8.314	$\text{J K}^{-1} \text{mol}^{-1}$
Faraday's constant	$F$ ( $eN_A$ )	$9.648 \times 10^4$	$\text{C mol}^{-1}$

Table 2.2 Typical values of resistivity

	Lipid bilayer	Extracellular solution		Seawater
		For mammals	For amphibians	
$r$ ( $\Omega \text{ cm}$ )	$10^{15}$	60	80	20

Fig. 2.1 Simplified electrical diagram of a membrane symbolized by a resistor  $R$  in parallel with a capacitor  $C$ , and responses to voltage ( $U$ )- or current ( $I$ )-clamp pulses, respectively



## 2.2 Ion Distribution at Biological Membranes

All electrical phenomena occurring at a cell membrane are based on asymmetrical ion distributions between cytoplasm and extracellular space, and on ion-selective permeabilities or conductances. Table 2.3 gives an overview of the concentrations of the most relevant inorganic ions outside and inside of cells of three different animal species, which have been used extensively in electrophysiological investigations.

The table also gives rough values for measured resting membrane potentials (by convention: inside–outside potential). The distribution of the ions at cells of different origin shows qualitative similarities. In the cytoplasm we find about ten times less  $\text{Na}^+$  compared to outside, but extracellularly we have more than one order of magnitude lower  $\text{K}^+$ . For  $\text{Ca}^{2+}$  there is also an inwardly directed gradient, and the activities differ by even four orders of magnitude. The extremely low intracellular activity of  $\text{Ca}^{2+}$  in sub- $\mu\text{M}$  range can easily be increased temporarily, either by an influx of extracellular  $\text{Ca}^{2+}$  or by emptying intracellular  $\text{Ca}^{2+}$  stores. Such mechanisms are used by nature to regulate a large variety of cellular functions that depend on  $\text{Ca}^{2+}$ .

The dominating extracellular anion is  $\text{Cl}^-$ . Intracellularly, the negative counter charges are predominantly negative charges on proteins and account for bulk electroneutrality. Electroneutrality is a basic principle that governs all electrophysiological processes. The total activities of ions inside compared to those outside the cell are identical.

■ **Table 2.3** Ion distributions (in mM) out- and inside of cells

	Squid axon		Frog muscle		Mammalian muscle		Ratio
	Outside	Inside	Outside	Inside	Outside	Inside	Outside Inside
Na <sup>+</sup>	460	50	120	9.2	145	12	~ 10
K <sup>+</sup>	10	400	2.5	140	4	155	~ 40 <sup>-1</sup>
Ca <sup>2+</sup>	11	3 × 10 <sup>-4</sup>	1.8	3 × 10 <sup>-4</sup>	1.5	< 10 <sup>-4</sup>	~ 10 <sup>4</sup>
Cl <sup>-</sup>	540	40–100	120	3–4	123	4.2	Variable
E <sub>R</sub> (in mV)	-60		-90		-90		

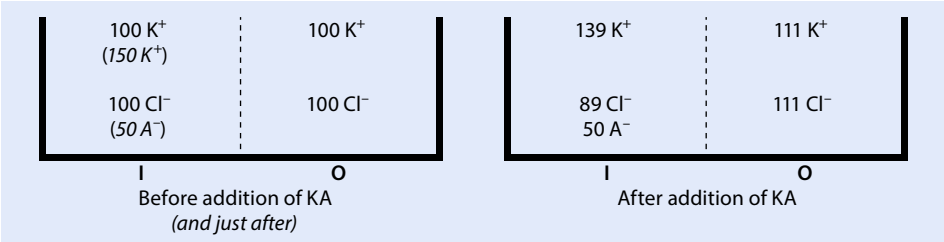
The ion gradients are of physiologically essential importance. The question of the basis of the asymmetry in the gradients of the ion species and its maintenance and that of the functional consequences are of particular interest. In the following section we will consider first the basic electrochemical consequences. For further details, see, e.g. Hille (2001).

2.3 Donnan Distribution and Nernst Equation

Like every thermodynamic system, the cell separated from its surrounding by the membrane approaches steady state, and thermal forces are in equilibrium with other forces. For chemical reactions and transport processes across the cell membrane, this means that forward and backward reactions are identical if there is no additional energy input.

2.3.1 Donnan Distribution

Let us consider two compartments (O and I) separated by a K<sup>+</sup>- and a Cl<sup>-</sup>-permeable membrane with rigid walls (see ■ Fig. 2.2). To one of the water-filled compartments we add KCl. After some time, there will be an equal distribution of the ion activities in the two compartments of, let us say, 100 mM. Via two Ag/AgCl electrodes (see ► Sect. 3.4.1) the electrical potential difference can be measured. Now we add to compartment I 50 mM of a salt KA, where the anion A<sup>-</sup> cannot penetrate the membrane. In analogy to the condition in a living cell, this could represent the nonpermeant protein anions in the cytoplasm.



■ **Fig. 2.2** Illustration of an experiment with K<sup>+</sup> and Cl<sup>-</sup> permeable membranes. The numbers may represent ion activities in mM

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