 doi:10.20944/preprints202106.0475.v1

What membrane capacitance?

Questioning the Hodgkin–Huxley model

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Abstract The most common and taught membrane theory assumes that the membrane behaves as a kind of electrical capacitance that is exposed to an electrical current generated by an ionic flow. If this statement is verifiable, it can be confirmed by the laws of physics, mathematics and in particular electricity. We will demonstrate that this hypothesis is not verified and that it is necessary to modify biophysics according to already established and experimentally verified principles of physics.

Keywords axon · neuron · electric circuit · capacitance · biophysics · HH model

1 Introduction

Bernstein was one of the first to notice that potassium was more abundant inside the cell. By applying certain diffusion principles, a phenomenon based on the thermal agitation of atoms and molecules, he assumed that a certain amount of potassium should come out of the cell, creating a potential difference [1].

This predominant diffusion of potassium is thought to be related to the inability, or even impossibility, of peptide negative charges to cross the plasma

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Table 1 Symbols used in the text

Symbols	Definition
C	Capacitance
Q	electric charge
R	universal gas constant
T	temperature
z	ion valency
F	Faraday constant
E_m	membrane potential
N_A	Avogadro number $= 6.022, 140, 857 \cdot 10^{23}\ mol^{-1}$
r_{wi}	water / salt ratio = number of water molecules per 1 salt molecule
e	elementary charge $= 1.602, 176, 634 \cdot 10^{-19}\ C$

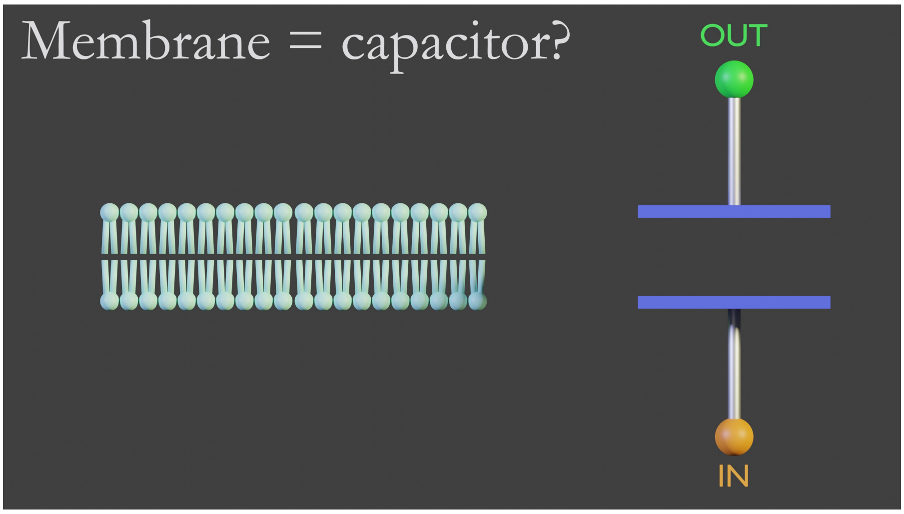

Fig. 1 In the membrane theory, the membrane itself is considered as a capacitance.

membrane. Their size would be too large to cross the plasmic wall. This notion has been known since the beginning of biophysics [6].

The membrane potential theory is based on the fact that this plasma barrier separates the charges between its two sides [3]. Like a capacitor that separates charge imbalances from the intracellular compartment to the external environment [2].

Bernstein thought that this potential also obeyed Nernst's equation, whose work was contemporary with his own [7];

It is true the equation had everything to seduce: a concentration gradient that made it easy to determine a potential. And a concentration gradient was the data available for the diffusion-based model.

$$E_m = \frac{RT}{zF} \ln \frac{[K^+]_{out}}{[K^+]_{in}} \tag{1}$$

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However, this elegant equation has a magical side that seems to have been overlooked by our friend Julius.

2 Capacitance definition

"Capacitance is the ability of a component or circuit to collect and store energy in the form of an electrical charge."

$$C = \frac{Q}{\triangle V} \tag{2}$$

The capacitance is strictly proportional to the charge

$$C \propto Q \tag{3}$$

Whatever the value of C, there is only one and only one value of Q that satisfies the equation 2.

$$\forall\ C\ \exists!\ Q \tag{4}$$

This separation of charge leads to the creation of a positive charge on one side and a negative one on the other. These charges have the same value but are of the opposite sign [8].

$$Q = |Q^+| = |Q^-| \tag{5}$$

3 What contains an electrolyte?

"An electrolyte is a substance that produces an electrically conducting solution when dissolved in a polar solvent, such as water. The dissolved electrolyte separates into cations and anions, which disperse uniformly through the solvent. Electrically, such a solution is neutral."

In the case of the cell the solvent is water and by example, contains some diluted KCl [9].

3.1 A word about dilution

How much salt molecules contains a liter?

1 liter of water contains

$$m_{H_2O} = \frac{1000}{18} = 55,56\ mol \text{ of water molecules}$$

$$m_{H_2O} = 55,56 \cdot N_A$$

A liter of solution of KCl with a concentration of $148 \cdot 10^{-3}\ mol$ contains

$$m_{1KCl} = 148 \cdot 10^{-3} \cdot N_A \text{ KCl molecules}$$

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Thus, we get a water/salt ratio of

$$r_{w1} = \frac{m_{H_2O}}{m_{1KCl}} = \frac{55.56}{148 \cdot 10^{-3}} \approx 375$$

A liter of solution of KCl with a concentration of $4 \cdot 10^{-3}$ *mol* contains

$$m_{2KCl} = 4 \cdot 10^{-3} \cdot N_A \text{ KCl molecules}$$

Thus, we get a water/salt ratio of

$$r_{w2} = \frac{m_{H_2O}}{m_{2KCl}} = \frac{55.56}{4 \cdot 10^{-3}} \approx 13,890$$

Like the capacitor, an electrolyte contains a strictly proportional quantity of charges that is a function of its concentration $[C]$ and volume v. The electrolyte being neutral, there is the same quantity of negative and positive charges.

$$Q_{k^+} + Q_{Cl^-} \propto [KCl] \cdot v \tag{6}$$

One liter of KCL with a concentration of $148 \cdot 10^{-3}$ *mol* contains a positive charge of:

$$Q_{K^+} = 148 \cdot 10^{-3} \cdot N_A \cdot e$$

One liter of KCL with a concentration of $148 \cdot 10^{-3}$ *mol* contains a negative charge of:

$$Q_{Cl^-} = -148 \cdot 10^{-3} \cdot N_A \cdot e$$

Thus,

$$Q_{K^+} = +1.428 \cdot 10^{+4}\ C$$

$$Q_{Cl^-} = -1.428 \cdot 10^{+4}\ C$$

$$|Q_{K^+}| = |Q_{Cl^-}| = 14,280\ C$$

These extraordinary quantities are fortunately without any danger because they aren't separated. We do not find at chemical stores a solution that contains only the positive or negative charges. Such a liter would contain an amount of energy able to produce a lightning strike of around

$$\triangle V \approx 14,280,000,000\ V$$

A potential difference we are unable to produce or observe on Earth.

But if we use the Nernst equation to compute the membrane potential, we are facing some insolvent problems!

It is possible to affirm with equation 1 that E_m is strictly proportional to the ratio of the external and internal concentrations;

$$E_m \propto r_{oi} = \frac{[K^+]_{out}}{[K^+]_{in}} \tag{7}$$

This ratio can be ever written in the form:

With k belonging to the positive real numbers, and with k strictly greater than 0.

$$R_+^* = \{k \in R | k > 0\} \tag{8}$$

Since concentrations are also strictly positive real numbers, it is possible to write them in the form of:

$$C_{out} = \left[K^+\right]_{out} = m \cdot k$$
$$C_{in} = \left[K^+\right]_{in} = n \cdot k$$
$$r_{oi} = \frac{C_{out}}{C_{in}} = \frac{m \cdot k}{n \cdot k} \tag{9}$$

It can be said that whatever k, there is no single value for concentrations. It is also possible to affirm it exists, unfortunately, many solutions that satisfies the same ratio r_{oi} since it exists many real positive values k where

$$\forall\ k\ \nexists!\ C_{out}, \nexists!\ C_{in} \tag{10}$$

since from equations 7 and 9

$$E_m \propto r_{oi} = \frac{C_{out}}{C_{in}} = \frac{m \cdot k}{n \cdot k} \tag{11}$$

It seems then possible to obtain the same membrane potential E_m with many different concentrations implying the contained charges of these solutions satisfy the conditions in eqs. 3 and 4.

It violates the principle of uniqueness of charge for a capacitor and violates the scientific principle of proportionality. That is not a probable situation!

In addition, almost all E_m calculations use the equation 2 where concentration values are not used. There is therefore no mathematical relationship established or considered between the Nernst equation and E_m.

In all means, the Nernst equation is not devoted to diffusion by any kind of relation.

The hypothesis of a membrane capacitance is not mathematically demonstrated neither linked to the Nernst equation.

4 Problem of geometry

We have seen that the negative charges carried by the peptides are located inside the cell and form the negative armature of the capacity considered in the theory.

But this automatically implies, by definition, that the positive external charge has exactly the same quantity but of opposite sign.

The capacitor cannot operate because one of its armatures contains by hypothesis a non-variable negative charge that forces the positive charge to be, likewise, invariant.

It is therefore not possible to find in the situation in figure 2.

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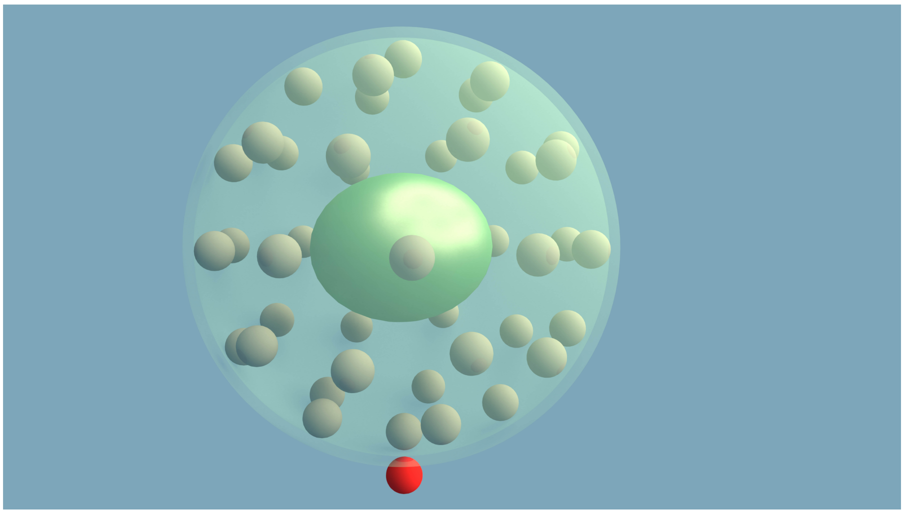

Fig. 2 If negative charges are fixed then the capacitance is made invariable.

5 Invariable phase shift

Goldman's work still provides, if necessary, proof that this capacity has no proven existence [2]. Indeed, he tested his samples in frequency, as we must, as we must do.

The result is implacable: It affirms and measures an almost constant phase shift over the entire frequency range.

This is not possible with a capacitor, the phase always varies with the frequency.

6 Removing capacitance in the HH model

The HH model always includes a capacity in its equations[4, 5].

If the existence of this capacitance is questioned, it becomes possible to assume that the model is only partially valid or even totally inappropriate. Hodgkin and Huxley's model, which emphasizes mathematical simulation, may not be consistent with mathematics or the limitations imposed by physics.

In addition, the absence of capacitance seriously modifies the possible retention of ions by the Coulomb force outside the cell. The behaviour with electrical stimulation must then also find a new explanation.

7 Conclusion

We have demonstrated that the membrane cannot behave as a capacitance: The permanent presence of fixed negative charges, inside the cell, prevents

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any variation of positive ions and we would be in the presence of an invariable capacitor, which is not in accordance with the membrane theory.

The experiments conducted by Goldmann do not confirm a behaviour similar to a capacitor, the frequency phase shift remaining constant. The notion of capacity is, once again, questionable.

If the membrane has some kind of capacity, it is not electrical.

References

1. J. Bernstein and A. Tschermak. Untersuchungen zur Thermodynamik der bioelektrischen Ströme: Zweiter Teil Über die Natur der Kette des elektrischen Organs bei Torpedo. *Pflüger, Archiv für die Gesammte Physiologie des Menschen und der Thiere*, 112(9-10):439–521, June 1906.
2. D. E. Goldman. POTENTIAL, IMPEDANCE, AND RECTIFICATION IN MEMBRANES. *The Journal of General Physiology*, 27(1):37–60, September 1943.
3. Bertil Hille. *Ion channels of excitable membranes.* Sinauer, Sunderland, Mass, 3rd ed edition, 2001.
4. A. L. Hodgkin. Evidence for electrical transmission in nerve: Part I. *The Journal of Physiology*, 90(2):183–210, July 1937.
5. A. L. Hodgkin. Evidence for electrical transmission in nerve: Part II. *The Journal of Physiology*, 90(2):211–232, July 1937.
6. David L. Nelson, Michael M. Cox, and Albert L. Lehninger. *Lehninger principles of biochemistry.* Freeman, New York, NY, 5. ed., 5. print edition, 2008.
7. Walther Nernst. *Begründung der Theoretischen Chemie: Neun Abhandlungen, 1889-1921.* Number Bd. 290 in Ostwalds Klassiker der exakten Wissenschaften. Verlag Harri Deutsch, Frankfurt am Main, 1. aufl edition, 2003. OCLC: ocm52218139.
8. James William Nilsson and Susan A. Riedel. *Electric circuits.* Pearson/Prentice Hall, Upper Saddle River, N.J, 8th ed edition, 2008.
9. Ralph H Petrucci. *General chemistry: principles and modern applications.* Pearson Canada, Toronto, 2017.