

Physics and Biology: Bio-plasma physics

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The purpose of this paper is to show that plasma physics can be useful in the investigation of the physical properties of living cells. Concepts like *charge neutrality*, *Debye length*, and *double layer* are very useful to explain the electrical properties of a cellular membrane. It is hoped that examples of physics applications to biology can be useful in giving students of physics courses new motivations to study physics and to carry out interdisciplinary studies. This paper can be easily understood by students of physics courses with no previous knowledge of plasma physics or biology. © 2000 American Association of Physics Teachers.

I. INTRODUCTION

Hannes Alfvén,¹ the outstanding Swedish astrophysicist, Nobel laureate, in the opening lecture of a symposium on double layers in astrophysics, commenting on the question of science specialization, says that there once was a *Natural Philosophy* (“*reine Naturwissenschaft*”), but that science of today is in danger of losing much of the Natural Philosophy aspect, because science is split up into such an increasing number of small specialties that we lack the global view. He quotes Juan G. Roederer, who points out the conflict between the demand for increased specialization, on the one hand, and the output of an increasingly interdisciplinary approach on the other. Roederer says that scientists tend to resist interdisciplinary inquiries into their own territory.

Usually, textbooks of physics have very few examples of physics applications to medical and biological areas, in spite of the fact that these applications have been continuously increasing. This is comprehensible because it is not possible to present, in a textbook, which necessarily has a limited size, examples of physics applications to every field of human knowledge. However, examples of application of physics to the biological area have, particularly, a didactic interest, because students of physics courses are amazed at such examples. In fact, most of them think that a theoretical intersection between physics and biology can very rarely happen, so distant from each other are the two scientific areas, according to their point of view. Therefore it would be interesting that physics teachers could provide such examples to students of physics courses. It is even possible that many students will find new motivation to study physics. It is interesting to note that many physicists have worked in molecular biology, since its foundation, and physics forms a significant part of the foundation of this most recent advance in science, which represents a new era of modern biology. For example, Francis Crick, one of the founders of molecular biology, was a physicist before becoming a biologist. He collaborated with James D. Watson in the discovery of the molecular structure of DNA, for which they received the Nobel Prize in 1962. Max Delbrück, a theoretical physicist, is a pioneer in the investigation of the molecular basis of heredity.

Biology cannot be reduced to physics. However, physical phenomena do occur in living systems, and physical phenomena obey the laws of physics, even if they occur in living systems, so that physics is important in the investigation of the properties of living systems. Claude Bernard, the great French physician, in his pioneering work on physiology, has already argued that physics and chemistry play a fundamental role in the investigation of biological phenomena. Quoting his own words:² “(...) *les sciences biologiques doivent avoir pour base nécessaire les sciences physico-chimiques auxquelles elles empruntent leurs moyens d’analyse et leurs procédés d’investigation.*”

Examples of the application of physics to biology can be found in biophysics textbooks.³⁻⁵ This journal, also, has already published examples of applications of physics to the medical area.⁶

In the present paper, of pedagogical character, an example of the application of plasma physics to the biological area is provided, in order to show that plasma physics can be useful in the theoretical understanding of the physical properties of living cells. For example, concepts like *charge neutrality*, *Debye length*, and *double layer* are useful for the understanding of the electrical properties of a cellular membrane. There are specialized books on this subject;³⁻⁵ however, the present paper can be easily understood by undergraduate students of physics courses, with no previous knowledge of plasma physics or biology.

Recently, Robert C. Hilborn has stated:⁷ “I firmly believe that it is healthier both for the field of physics and for our students to recognize and indeed to celebrate the wide range of careers that physics majors pursue. We are then obliged to develop flexible curricula that provide students at an early stage in their educational development with this broad vision of what physics is and what a degree in physics can do for them.” The present work is a contribution to provide students with a broad vision of physics.

II. PLASMAS AND BIO-PLASMAS

The term *plasma* was introduced in the study of electrical discharges in gases by Irving Langmuir.^{8,9}

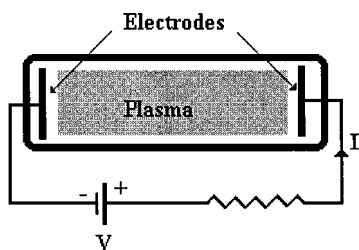


Fig. 1. An electrical gas discharge. V is a power supply and I is the discharge current.

Let us consider a discharge tube, which contains a gas and electrodes connected to an electric power supply, as shown in Fig. 1. If the electric potential difference between the electrodes is higher than a threshold value, named the *breakdown voltage*, the gas becomes partially ionized and conducting. Under suitable conditions, a *glow discharge* develops, in which a beautiful luminous column, uniform along its length, is formed. The luminosity close to the electrodes and the tube wall is much lower than that in the uniform column. The glowing tubes for advertisements provide examples of glow discharges. The partially ionized gas, in the luminous column, consists of ionized molecules and atoms, electrons, neutral molecules and atoms, and photons, and is, macroscopically, electrically neutral. In the darker regions, near the electrodes and the tube wall, there are space charges. To the gas in the region where charge neutrality holds, Langmuir gave the name *plasma*, and to the regions where there are space charges, he gave the name *sheaths*. Alfvén¹ conjectures that the term *plasma* was probably borrowed from medical terminology.

Reitz and Milford give the following definition of plasma:¹⁰ "Equivalently, we may say: an ionized gas which has a sufficiently large number of charged particles to shield itself, electrostatically, in a distance small compared with other lengths of physical interest, is a plasma." On page 272 of their textbook, they give a more precise definition in terms of the shielding distance, after introducing the *Debye length*, which is defined in Sec. V of the present paper.

The cytoplasm, the fluid which fills a cell, is an aqueous solution which contains neutral molecules and ions like K^+ , and large protein anions. The cell is immersed in an aqueous solution which, also, contains ions like Na^+ , Cl^- , etc.^{11,12} Thus the cytoplasm, as well as the environment of the cell, are conducting media, which contain positive and negative ions, but, macroscopically, the condition of charge neutrality is satisfied, as happens in the plasmas of electrical gas discharges, so that we shall call them *bio-plasmas*. The condition of charge neutrality does not hold very close to the boundaries of the bio-plasmas, or near structures like a cell membrane, so that a bio-plasma may contain space charges, whereas, in a gas discharge, the plasma is electrically neutral, and the space charges are contained in the *sheaths*. We shall not give a special name to the regions of a bio-plasma where space charges exist, and which correspond to the sheaths of a gas discharge. The concept of Debye length, which is a typical length for a plasma and is useful to estimate the dimensions of the regions where the condition of charge neutrality does not hold, is explained in Sec. V.

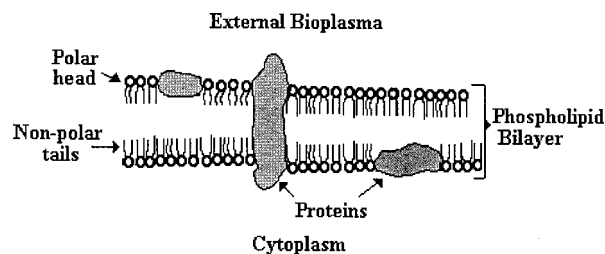


Fig. 2. A cell membrane. Protein molecules may be exposed on either side or may cross the whole thickness of the phospholipid bilayer.

III. THE CELLULAR MEMBRANE AND PLASMA DOUBLE LAYERS

The cellular membrane is not inert but is a living part of the cell. According to the *fluid mosaic model*,^{13,14} a cellular membrane consists of a fluid bilayer of phospholipid molecules in which proteins are embedded or otherwise associated, much like the tiles in a mosaic picture. This mosaic pattern is not static because the proteins constantly move like icebergs in a fluid sea of polar lipids.

Phospholipid molecules are *amphipatic* (*amphi*=both kind of), that is, they have polar heads which are *hydrophilic* ("water loving") and two nonpolar tails that are *hydrophobic* ("water fearing"). In a cellular membrane the polar heads of the lipid molecules are in contact with the bio-plasmas—the heads of the lipid molecules of the external layer are in contact with the external bio-plasma, whereas the heads of the molecules of the internal layer are in contact with the cytoplasm. The nonpolar tails are "hidden" from the bio-plasmas, in the interior of the cellular membrane, as shown is Fig. 2. The lipid molecules are held together by the electrical dipole interaction between them. The lipid molecules can easily move about in the layer at which they belong, but they cannot move to the other layer. Thus the lipid layers behave like a *two-dimensional fluid*.

Ions and neutral molecules are constantly being transported across the cellular membrane which has a selective permeability to the different particles. In a situation of equilibrium there is a difference of the electric potential between the interior and the exterior fluid, called the *resting potential*, whose value can vary from -100 to -10 mV, the potential of the cytoplasm being negative, relative to the external bio-plasma, assumed to be at a null potential.¹¹ Thus, there must exist an excess of negative ions in the inner part of the membrane and an excess of positive ions in the outer part of the membrane. The excess charges are distributed mainly on the membrane surfaces, but there are charges inside the membrane and, also, in the bio-plasmas, as explained below. Therefore, in the region of the membrane there is a *double layer* constituted by the excess of negative ions, inside, and positive ions outside, so that in these regions the condition of charge neutrality does not hold.

Double layers are formed in the boundaries of a plasma, for example, near the cathode of a discharge chamber, or between two plasmas of different physical properties, constituting a transition from one plasma to the other. Let us consider a discharge tube with a variable cross section, as shown in Fig. 3. In this case the electric potential of the plasma is different in regions I and II, and, also, the mean electron energy is different in the two regions. The transition from plasma I to plasma II is made by a double layer.¹

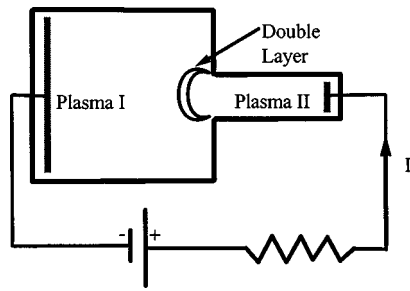


Fig. 3. A discharge in a tube with two different cross sections. Two different plasmas are formed. The transition from one plasma to the other is made through a double layer.

Similarly, in a living cell a double layer makes the transition from the cytoplasm to the external bio-plasma. In this way the double layer protects the cell interior from the external bio-plasma. Figure 4 shows the electric potential $\Phi(x)$, the x component of the electric field $E(x)$, and the charge density $\rho(x)$ through a plasma double layer¹⁵ or, similarly, through a cell membrane, assuming a one-dimensional model, with the x axis perpendicular to the cell membrane. It is interesting to have in mind the relations $E = -d\Phi/dx$, between the electric field and the potential, and

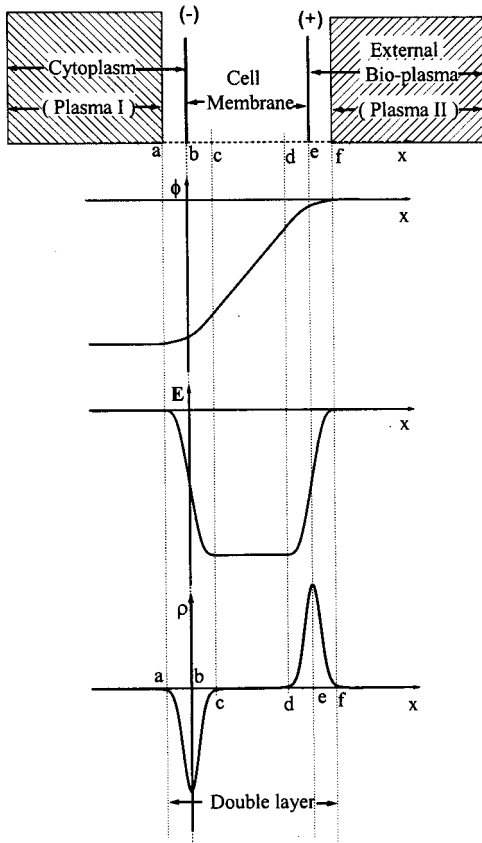


Fig. 4. The electric potential $\Phi(x)$, the electric field $E(x)$, and the charge density $\rho(x)$ through a cell membrane or, similarly, through a plasma double layer. The width of the regions where the charge density is different from zero is exaggerated, in order to show that there are some excess charges in the bio-plasmas. The neutral regions of the cytoplasm and the external bio-plasma correspond, respectively, to plasma I and plasma II.

$\rho = \epsilon dE/dx$, between the charge density and the electric field, ϵ being the electrical permittivity of the cell membrane.

Mathematical models for plasma double layers, which give the results shown in Fig. 4, have already been formulated.¹⁵ A corresponding mathematical model for a cell membrane has not yet been formulated. However, it is reasonable to assume that the electric potential, the electric field, and the charge density in a membrane behave similarly to the corresponding physical quantities in a plasma double layer, because a cell membrane separates two bio-plasmas which can be viewed as liquid plasmas.

It should be noted that, very close to the membrane, at distances of the order of the Debye length, the electric potential in the bio-plasmas is not constant, and there are space charges in these regions. The concept of Debye length, explained in Sec. V, is essential to understanding this point. Thus, in a cell, the double layer, which contains the unbalanced charges, extends itself over a region slightly wider than the cell membrane. In Fig. 4, the regions to the left of $x=a$, and to the right of $x=f$, represent the *neutral regions* of the internal and external bio-plasmas, in the case of the cell, and which correspond, respectively, to plasma I and plasma II of the electric discharge. The double layer extends itself from $x=a$ to $x=f$. The membrane surfaces are at $x=b$ and $x=e$. The width of the regions (ac) and (df) , where the charge density is not zero, is exaggerated in Fig. 4 in order to show that there are some excess charges in the bio-plasma, and that the electric field is continuous, even at the membrane surfaces. The fact that the width of these regions is a small quantity, of the order of the Debye length, justifies the usual approximation in which it is assumed that all the excess charges lay on the membrane surfaces and, consequently, the electric field is discontinuous at the membrane surfaces.

Plasma physicists have a long history of investigation concerning the physical properties of double layers, theoretically as well as experimentally.^{1,8,15-17} Hannes Alfvén in his lecture points out the analogy between double layers that occur in discharge physics and those that occur in membranes of living cells. He says:¹ "Since the time of Langmuir, we know that a double layer is a plasma formation by which a plasma—in the physical meaning of the word—protects itself from the environment. It is analogous to a cell wall by which a plasma—in the biological meaning of this word—protects itself from the environment."

It is amazing that, in spite of so many differences between a cell membrane and a plasma double layer, there are some fundamental similarities between the electrostatic properties of the two structures. These similarities result from the fact that a cell membrane separates two different bio-plasmas, which can be viewed as liquid plasmas.

IV. ION TRANSPORT THROUGH CELLULAR MEMBRANES

The *bio-plasma* can be viewed approximately as an electrolyte constituted of water molecules and N species of ions. The ions are transported across the cellular membrane, due to gradients of concentration and also as a result of the electric field that exists across the cellular membrane. The contribution of the i th ion species to the electric current density is given by¹⁸

$$\mathbf{j}_i = n_i z_i e \mathbf{v}_i, \quad (1)$$

where n_i is the number density of ions, that is, the number of ions per unit volume, $z_i e$ is the ion charge, and \mathbf{v}_i is the mean drift velocity of the ion.

The ion drift can be due to the existence of an electric field or to a concentration gradient of ions. The drift velocity due to an electric field E can be written as¹⁹

$$\mathbf{v}_E = \mu_i \mathbf{E}, \quad (2)$$

where μ_i is the ion mobility.

The mean drift velocity due to the concentration gradient can be written as²⁰

$$\mathbf{v}_D = -(D_i/n_i) \nabla n_i, \quad (3)$$

where D_i is the ion diffusion coefficient. Note that in Reif's formula (12.5.2) J_z is the z component of a vector $\mathbf{J} = n \mathbf{v}_D$, the flux density of particles.

The total mean drift velocity, for ions of species i , is therefore

$$\mathbf{v}_i = \mathbf{v}_E + \mathbf{v}_D = \mu_i \mathbf{E} - (D_i/n_i) \nabla n_i. \quad (4)$$

Equations (1) and (4) yield

$$\mathbf{j}_i = -z_i e [\mu_i n_i \nabla \Phi + D_i \nabla n_i], \quad (5)$$

where $-\nabla \Phi = \mathbf{E}$, Φ being the electric potential.

Assuming that each ionic species is conserved, we can write the continuity equation for charge and electric current densities as

$$\nabla \cdot \mathbf{j}_i + \partial(z_i e n_i) / \partial t = 0. \quad (6)$$

Poisson's equation is

$$\nabla^2 \Phi = -\rho / \epsilon, \quad (7)$$

where ϵ is the electric permittivity of the medium and

$$\rho = \sum_i (z_i e n_i) + \rho_f, \quad (8)$$

the last term being the fixed charge density.

Equations (5)–(8) provide a system of N vector equations and $N+1$ scalar equations for the variables \mathbf{j}_i , n_i , and Φ .

The condition for the *electrodiffusive equilibrium* of the i th species is $\mathbf{j}_i = 0$. This condition and Eq. (5) give for a plane one-dimensional model

$$n_i(x) = n(x_0) \exp\{-\mu_i [\Phi(x) - \Phi(x_0)] / D_i\}$$

which by using Einstein's relation¹⁹ $\mu_i / D_i = z_i e / kT$, where k is Boltzmann's constant and T the absolute temperature, yields

$$n_i(x) = n_i(x_0) \exp\{-z_i e [\Phi(x) - \Phi(x_0)] / kT\}, \quad (9)$$

which gives the number density of particles as a function of the electric potential.

V. THE DEBYE LENGTH

Consider a plate, located at $x=0$ (the x axis being perpendicular to the plate), that contains *fixed* surface charge density σ_f and is bathed by an electrolyte with positive and negative ions whose number densities are, respectively, $n_+(x)$ and $n_-(x)$. Near the plate, ions whose charge is opposite to that of the fixed charges will be attracted, whereas those with the same sign will be repelled. Therefore, near the

plate there will be a region where charge neutrality does not hold. Far from the plate we have $n_+(\infty) = n_-(\infty) = n$, and Eq. (9) yields

$$n_{\pm}(x) = n \exp[-z_{\pm} e \Phi(x) / kT], \quad (10)$$

where we have assumed $\Phi(\infty) = 0$.

Poisson's equation for this case can be written as

$$d^2 \Phi(x) / dx^2 = -\rho / \epsilon = -e(z_+ n_+ + z_- n_-) / \epsilon,$$

which, with Eq. (10), and assuming that $z_- = -z_+ = -z$, gives

$$d^2 \Phi(x) / dx^2 = (2z e n / \epsilon) \sinh[ze \Phi(x) / kT], \quad (11)$$

which reduces to

$$d^2 \Phi(x) / dx^2 = (2z^2 e^2 n / \epsilon kT) \Phi(x), \quad (12)$$

if the condition $ze \Phi(x) \ll kT$ is satisfied. Equation (12) can be written as

$$d^2 \Phi(x) / dx^2 = \Phi(x) / \Lambda_D^2, \quad (13)$$

where

$$\Lambda_D = (\epsilon kT / 2z^2 e^2 n)^{1/2} \quad (14)$$

is the *Debye length*.²¹

Equation (13) has the solution

$$\Phi(x) = \Phi(0) \exp[-x / \Lambda_D]. \quad (15)$$

The boundary condition for the normal component of the electric field²² $-(\partial \Phi / \partial x)_{x=0} = \sigma_f / \epsilon$ and Eq. (11) yield

$$\Phi(x) = (\Lambda_D \sigma_f / \epsilon) \exp[-x / \Lambda_D], \quad (16)$$

so that the charge density is

$$\rho(x) = -\epsilon d^2 \Phi / dx^2 = -(\sigma_f / \Lambda_D) \exp[-x / \Lambda_D], \quad (17)$$

which shows that the space charge region has dimensions of the order of the Debye length.

The concept of Debye length was introduced by Debye and Hückel,²³ in 1923, in their theory of electrolytes, that is, conducting liquids that can be viewed as liquid plasmas.

The concentrations of ions in bio-plasmas, in which living cells are immersed, are different for marine animals and terrestrial animals. In the case of human beings the concentration of Na^+ is about 140 mmol/l and the concentration of Cl^- is about 110 mmol/l, in a sample of venous blood from a normal individual.^{11,12} There are other ions but in much lower concentrations, so that as a first approximation we can assume that there are only the two ions, and that $n_+ \cong n_- \cong 120 \times 10^{-3} \times 6, 02 \times 10^{23}$ ions/ 10^{-3} m³ $\cong 72 \times 10^{24}$ ions/m³. The Debye length corresponding to this ion number density is of the order of 10^{-9} m, assuming $T = 300$ K. Thus, in the case of a human being, the space charge region, around a cell immersed in the blood, has dimensions of the order of 10^{-9} m. Just to compare, it is interesting to remember that a cell membrane has a thickness between 5.0 and 7.5×10^{-9} m. Thus the membrane thickness is several times larger than the Debye length of the external bio-plasma.

The Debye length is a typical length for a plasma which is useful to estimate the dimensions of the regions where charge neutrality does not hold. For example, the thickness of a plasma double layer, a quantity which depends on the potential jump across the double layer, can be considerably larger than the Debye length of the neighboring plasmas.¹⁵ A similar result holds for a cell double layer. In fact, in a cell,

the width of the double layer is slightly larger than the membrane thickness which, by its turn, is several times larger than the Debye length of the external bio-plasma.

VI. THE RESTING POTENTIAL OF A CELLULAR MEMBRANE

The cellular membrane separates two bio-plasmas with different ionic concentrations and is not equally permeable to all the ions that are transported across it. Consequently, a potential gradient is generated across the membrane. This section presents Bernstein's model^{5,24} for the resting electric potential through the cell membrane.

Inside the cell the positive ions are mainly^{11,12} K^+ . In Bernstein's model only the diffusion of ions K^+ is considered, the membrane being assumed impermeable to all other ions. The concentration of K^+ ions inside the cell is higher than outside and they can easily diffuse through the membrane, so they diffuse outwards. However, there are large intracellular anions which cannot diffuse across the membrane, which has a selective permeability. Consequently, an imbalance of charge builds up across the membrane producing a potential difference, the interior of the cell being negative with respect to the external bio-plasma. Thus there is an electric field in the membrane which opposes the further diffusion of K^+ . The equilibrium condition is achieved when the concentration gradient is exactly balanced by the opposing electric field, so that $\mathbf{j}_i=0$, the index i denoting the ion K^+ .

Assuming a plane one-dimensional model, Eq. (5) yields

$$j = -e[\mu nd\Phi/dx + Ddn/dx],$$

where the index i was dropped, z was set equal to 1, and the x axis is perpendicular to the membrane surface. The equilibrium condition for this case gives

$$\mu nd\Phi/dx = -Ddn/dx,$$

which integrated yields

$$\begin{aligned} V_K &= \Phi(\text{inside}) - \Phi(\text{outside}) \\ &= (D/\mu) \log_e[n(\text{out})/n(\text{in})]. \end{aligned}$$

Using Einstein relation¹⁹ $\mu/D = e/kT$, the equilibrium potential for the ion K^+ can be written as

$$V_K = (kT/e) \log_e[n(\text{out})/n(\text{in})]. \quad (18)$$

The concentrations of ions K^+ , in a cardiac cell of human beings, are such that²⁵

$$n(\text{out})/n(\text{in}) \cong 0.027,$$

so that, at $T=300$ K, $V_K \cong -94$ mV, which is close to -90 mV, the value of the resting potential of a ventricular cell.²⁶

For a nerve cell of a giant squid, the relation between the concentrations of K^+ , outside and inside the cell, is²⁷

$$n(\text{out})/n(\text{in}) \cong 5.0 \times 10^{-2},$$

and, consequently, $V_K \cong -78$ mV, which is close to -70 mV, the resting potential of a nerve cell.²⁷

This simple model was proposed by Bernstein²⁴ in 1902 to explain the resting potential of a cellular membrane. Since the cellular membrane is also permeable to other ions, besides K^+ ions, this model must be improved with the inclusion of other ions. Actually, the situation is much more com-

plex than it is presented above, because there are transport mechanisms that drive ions across the membrane *against electric and diffusive forces*. These mechanisms are called *active transport mechanisms* and require energy which is provided by the decomposition of ATP molecules. One of the most important of these mechanisms is the so-called *sodium-potassium pump*.^{28,29} It can be shown that the inclusion of the effects of the active transport mechanisms allows the derivation of stable solutions for the resting potential.³⁰ The effects of these active transport mechanisms are not discussed here for this would lead us far beyond the scope of the present paper.

VII. CONCLUDING REMARKS

It has been shown that plasma physics can be a useful theoretical tool for the investigation of the electrical properties of living cells, because the cells contain and are immersed in bio-plasmas which have many similarities with the plasma of electrical discharges in gases. For example, similarities have been shown between the electrostatic properties of a cell membrane and a plasma double layer. These similarities are consequences of the fact that a cell membrane separates two different bio-plasmas, which can be viewed as liquid plasmas. The concept of Debye length has been shown to be useful in the understanding of the charge distribution in a cell membrane. It is hoped that examples of theoretical applications of physics to biology will motivate many students to study physics. Furthermore, such examples are useful to stimulate physics students to carry out interdisciplinary studies.

ACKNOWLEDGMENT

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EASY TO LEARN, NEARLY IMPOSSIBLE TO DO

Physics may be easy to learn, but it is nearly impossible to do, to create. The weirdness of physics blocks the way. This prevents most of us from making new science, and it is what prevents most novices from understanding the old. Creating science is like creating poetry, of which Proust said: 'If it isn't easy, it is impossible'. To *do* physics, one has to be Bohr, or Curie, or Feynman. But people like me can write about it. And people like you can understand it (probably you're not like Bohr, but secretly I hope that you are).

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