

Some Physical Questions Concerning Signal Generation in Neurons

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Abstract. Some problems related to signal generation at electrically charged membranes of neuron as seen from the view of fundamental physics are discussed. After a short introduction to processes taking place at the synapse, the time reversibility of classical mechanics and quantum mechanics are explained. Some basic ideas for deriving irreversibility from reversible mechanics are introduced, and some typical irreversible processes are illustrated by the use of the master equation. Finally, some speculations are given as to how phenomena in neural systems should be understood based on basic physics.

1. Introduction

This paper is aimed at forming explanations and making speculations on fundamental problems in quantum mechanical and statistical descriptions behind the generation and transmission of signals in neurons. The author is a physicist and not a specialist of biophysics. So, the content of this paper is confined to some basic aspects and ideas, which are expected to be useful for beginners in this field.

In this section a short illustration of phenomena in the generation of neural signals is given. In the following sections some introductory explanations of time reversibility of classical mechanics and quantum mechanics are given, and it will be discussed how irreversibility emerges in many body problems, such as neural signal propagation. Next, mechanisms of sustaining inequilibrium states in open systems are discussed. Since basic properties of open systems are not understood sufficiently, this discussion is partly based on speculations of this author.

Electric signals in neurons are generated and sustained owing to inhomogeneous distribution of ions, Na^+ , K^+ , Cl^- , and an equilibrium electric potential of about -70 mV inside the neural membrane. To be more precise, the equilibrium potential E depends on the ions, because it is related to the ratio of the densities of an ion outside and inside of the membrane by Nernst's formula

$$E = \frac{RT}{2F} \ln K_0 / K_i \quad (1)$$

where R is the gas constant, T is the absolute temperature, F is denotes Faraday's constant and K_0 , K_i are the outside and inside concentrations of ions, respectively.

This inequilibrium state is maintained by differences of permeabilities of ions and by an ion pump, which consumes energy supplied from outside (see Fig. 1). In a quiet state without signal transmission the ratio of permeabilities of these ions, say p_K , p_{Na} and p_{Cl} , for the squid axon is approximately 1:0.03:0.1, so that Na^+ ions with weaker permeability can stay within high potential energy. Since the ion pump is always working the phenomena occurring in neurons are those in so called "open system". Note that the term "equilibrium potential" does not necessarily imply a concept of thermal equilibrium, but simply a stationary value of electric potential under the operation of the ion pump.

The mechanism of signal generation in a neural cell is rather complicated. An important stage is the process taking place at the synapse, a part of a neural cell connected with another neural cell. At this connection the two cells are not directly in contact. The synapse button, a tip of the axon, is located close to another cell but separated by a space of about 10 nm, called a synaptic cleft (see Fig. 2). Molecules, such as acetylcholine or glutamic acid, to mention just two, are extruded from synaptic vesicles entering the synaptic cleft and subsequently bind to receptors at the post-synaptic site. The molecules acting on these receptors located within the post-synaptic membrane lead to the opening of ion channels changing the permeability to Na^+ and K^+ ion flux. The resulting change in membrane potential finally reaches particular membrane locations at the soma of the cell which in turn may trigger a pulse signal, the action potential, that propagates along the postsynaptic axon towards the next synaptic button. The beginning of these processes is marked by an interaction of molecules with receptors, which, if sufficiently resolved, is a quantum chemical process. After the ion channels open or closed state is changed by this interaction, a strong change of ion-permeation creates an electric reponse. Later stages of this process gradually give rise to a macroscopic current, which is described by classical

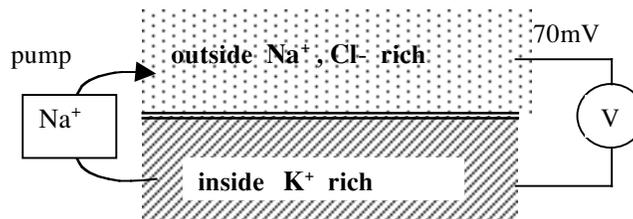


Fig. 1. Stationary state of a neutral cell with respect to the ion distribution and the electric potential.

electrodynamics and thermodynamics. This process is looked upon as an unstable phenomenon with a growing electric current.

It is interesting to remark that a similar phenomenon is seen in the production of a pulse current in the Geiger-Müller counter to measure the quantity of radiation particles. On the counter a quantum mechanical interaction with a particle from radioactive material with atoms in the counter creates several free electrons, which affects successive ionization of atoms, called an avalanche, resulting in a macroscopic current. This process plays an important role in the well known “Gedanken Experiment” of Heisenberg. In this experiment the electric current produced by the quantum mechanical interaction kills a cat, so that the state of the cat is illustrated as a quantum mechanical transition from an alive state to a dead state, which is a mysterious transition for a macroscopic and classical system such as a cat.

It should be noted here that there is an instability process between quantum mechanical and classical states, where an unstable growth of ionization driven by a high electric voltage is working. The application of this high voltage points to a maintenance of an inequilibrium state, and the production of pulse current is possible only in an open system. It is not easy to define an open system from the quantum mechanical point of view. In general, an open system is associated with a maintenance of high energy state as in the Geiger-Müller counter. According to quantum mechanics the higher state should make a transition to a lower state gradually and can not be maintained constantly.

It should also be noted that the instability is an irreversible process with respect to time. It is unknown how the irreversible process results from an initial quantum mechanical process, since the latter has a property of time reversibility as is explained in the next section. Once a signal attains a certain amplitude, it propagates with a fixed wave form, and the mechanism is well described by a model equation (HODGKIN and HUXLEY, 1952a, b). This process is possible only in an open system, because the signal is maintained by the presence of the equilibrium potential.

In the following sections some concepts of basic physics are introduced, which are related to neural signals. However, explanations will not be done deeply, but are confined within the level of basic physics.

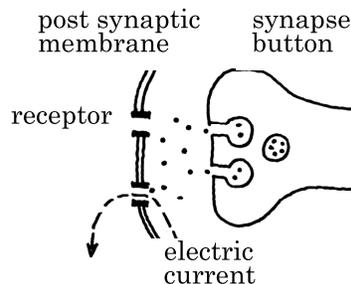


Fig. 2. Synaptic transmission.

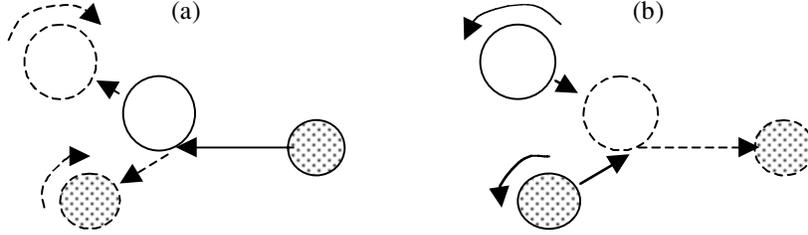


Fig. 3. Collision of a ball with another ball (a) and its reverse process (b). After the collision (drawn with dashed lines) the ball begins to rotate (a) or stop to rotate (b).

2. Time Reversibility of Classical Mechanics and Quantum Mechanics

2.1. Classical mechanics

Phenomena in classical mechanics are governed by the equation of motion,

$$m \frac{d^2 \mathbf{x}}{dt^2} = \mathbf{F}, \quad (2)$$

where m and \mathbf{x} are the mass and the position vector of a particle, and \mathbf{F} is a force acting on it. In most cases the force \mathbf{F} is a function of \mathbf{x} . Reversibility of the classical mechanics is shown by introducing the variable transformation, $t \rightarrow t' = -t$. Then, substituting this transformation into Eq. (2), we have an equation which has the same form as Eq. (2),

$$m \frac{d^2 \mathbf{x}}{dt'^2} = \mathbf{F}. \quad (3)$$

In this way the velocity v of the particle is transformed to $v' = dx/dt' = -v$.

The time reversibility is defined as follows. Phenomena occurring in the world with an opposite direction of time (called a “reverse world” here) are similar to those in our world. To be more precise, phenomena in our world and the reverse world obey the equations of the same form. Therefore, by observing a mechanical phenomenon in the reverse world we can not judge whether it is occurring in our world or in the reverse world. In other words, when we see a movie film of a mechanical phenomenon run inversely, we do not experience the motion in the film as unnatural. An example of this mechanical phenomenon and its reverse process are shown in Fig. 3.

In the process (a) a ball collides with a resting ball, after which the two balls apart while rotating clockwise. In the reverse process (b) two balls rotating anti-clockwise approach each other, and after collision one of them stops and another moves away without rotation. Both of these processes can occur in our world.

Let us consider another example with a charged particle experiencing the Lorentz

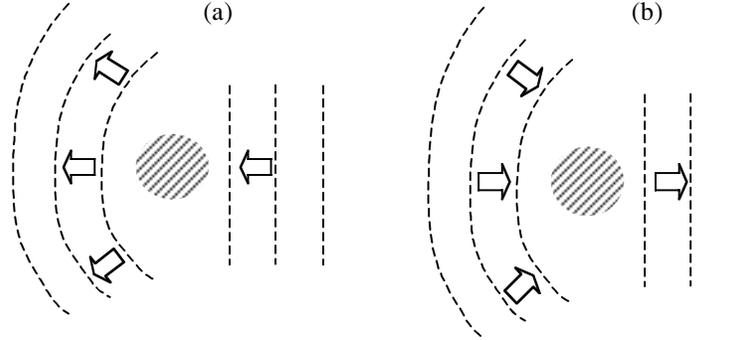


Fig. 4. Scattering of a plane wave by a stationary potential (hatched region) (a), and its reverse process (b). In the reversed process the wave gathers towards the potential region, and after scattering it changes to a plane wave. This process should occur also in our world.

force $\mathbf{F} = e\mathbf{v} \times \mathbf{B}$, where e is the electric charge of the particle, \mathbf{v} is its velocity and \mathbf{B} is a magnetic field. In the reverse world both \mathbf{v} and \mathbf{B} change their directions (note that an electric current that produces \mathbf{B} changes its direction), hence the vector products of these vectors is unchanged by a time reversal and Eqs. (2) and (3) have the same form.

2.2. Quantum mechanics

Phenomena in quantum mechanics are governed by the Schödinger equation:

$$i\hbar \frac{\partial \Psi}{\partial t} = H\Psi, \quad (4)$$

where i is the imaginary unit, $\hbar = h/2\pi$ (h is the Planck constant), Ψ is the wave function and H is the Hamiltonian operator. It is usually assumed that H is Hermitian, i.e. $H = H^\dagger$ (the suffix \dagger denotes Hermitian conjugate) meaning that the two inner products are equal, $\langle \Phi | H\Psi \rangle = \langle H\Phi | \Psi \rangle$, for any pair of wave functions Φ, Ψ .

Following the transformation, $t \rightarrow t' = -t$ and by taking the complex conjugate, Eq. (4) becomes

$$i\hbar \frac{\partial \Psi^*}{\partial t'} = H^\dagger \Psi^* = H\Psi^*, \quad (5)$$

where the suffix $*$ denotes the complex conjugate. By comparing Eqs. (4) and (5) we can see that Ψ^* in the reverse world is governed by the same Hamiltonian H as Ψ is governed in our world. The wave function Ψ^* corresponds to the same probability distribution as Ψ , while the direction of wave propagation is reversed. Therefore, a wave function with reversed propagation direction behaves similar to that in our world. This demonstrates the time reversibility of quantum mechanics.

An example to demonstrate the reversibility of quantum mechanics is a scattering of a particle wave by a stationary potential, as given in Fig. 4. The reverse process with the reversed direction of propagation can occur also in our world because it is governed by the same Hamiltonian.

3. Origin of Irreversibility in Real World

Origin of irreversibility was first treated theoretically in 1872 by L. Boltzmann, who derived the Boltzmann equation and then proved the H -theorem, which is concerned with the irreversibility of phenomena in many body systems. Later, in 1928 W. Pauli derived an equation governing irreversible processes from quantum mechanics, which is called *Pauli's transport equation* and is equivalent to what is known as "*master equation*". Readers are may refer to suitable textbooks for details , for example to REIF (1965), ZUBAREV (1974) and HAKEN (1978). Brief explanations of the Boltzmann equation, the H -theorem and the master equation, etc. will be given here. The aim of this section is to suggest that a cut-off a part of information from variables of many body systems leads to governing equations of irreversible processes.

3.1. Boltzmann equation for a gas of classical molecules

Boltzmann treated a probability density $f(\mathbf{x}, \mathbf{v}, t)$ of a gas of many classical molecules with position \mathbf{x} and velocity \mathbf{v} . In the case without collision of molecules the change of $f(\mathbf{x}, \mathbf{v}, t)$ with time, denoted by Df , is expressed as follows:

$$Df \equiv \frac{\partial f}{\partial t} + \mathbf{v} \frac{\partial f}{\partial \mathbf{x}} + \frac{\mathbf{F}}{m} \frac{\partial f}{\partial \mathbf{v}} = 0, \quad (6)$$

where m is the mass of the molecules and \mathbf{F} is the force exerted on them. In this case the change in distribution with time is looked upon as a deformation of the distribution, while convected in phase space (\mathbf{x}, \mathbf{v}) by the flow within it. This kind of change allows reverse processes, hence Eq. (6) contains no irreversibility. This situation is often explained in an analogy with a mixing of a dye in the water. The dye deforms to a complicated shape through convection by the water flow, but no microscopic mixing occurs. If the water flow is exactly reversed everywhere at a certain instant, the deformed dye comes back to the original shape. It is noted that a generalization of Eq. (6) leads to the *Lieuville equation* in classical and the quantum mechanics.

In the case with collisions between molecules, the right-hand side of Eq. (6) is replaced by $D_c f$, which stands for rapid changes of f via collisions. In general, collisions are characterized by a scattering cross section, denoted by $\sigma(\mathbf{v}_1, \mathbf{v}_2 \rightarrow \mathbf{v}'_1, \mathbf{v}'_2)$, which indicates that the size of a molecule is recognized by each other during the collision process entailing velocity changes $(\mathbf{v}_1, \mathbf{v}_2 \rightarrow \mathbf{v}'_1, \mathbf{v}'_2)$. By assuming that f does not depend on \mathbf{x} , and further that

- i) the gas is sufficiently dilute so that only two body collisions are present,
- ii) the external force \mathbf{F} does not affect collisions,
- iii) $f(\mathbf{x}, \mathbf{v}, t)$ is almost constant during the short collision time,
- iv) velocities of the two molecules before collision have no correlation,

with symmetry properties for each collision process:

$$\sigma(\mathbf{v}_1, \mathbf{v}_2 \rightarrow \mathbf{v}'_1, \mathbf{v}'_2) = \sigma(-\mathbf{v}'_1, -\mathbf{v}'_2 \rightarrow -\mathbf{v}_1, -\mathbf{v}_2) \text{ (time reversibility),}$$

$$\sigma(\mathbf{v}_1, \mathbf{v}_2 \rightarrow \mathbf{v}'_1, \mathbf{v}'_2) = \sigma(-\mathbf{v}_1, -\mathbf{v}_2 \rightarrow -\mathbf{v}'_1, -\mathbf{v}'_2) \text{ (space reversibility),}$$

$D_c f$ is expressed as follows:

$$D_c f = \int_{v_{11}} \int_{v_1'} \int_{v'} \{f(\mathbf{x}, \mathbf{v}', t)f(\mathbf{x}, \mathbf{v}'_1, t) - f(\mathbf{x}, \mathbf{v}, t)f(\mathbf{x}, \mathbf{v}_1, t)\} \mathbf{V} \sigma(\mathbf{v}, \mathbf{v}_1 \rightarrow \mathbf{v}', \mathbf{v}'_1) d\mathbf{v}_1 d\mathbf{v}' d\mathbf{v}'_1, \quad (7)$$

where $\mathbf{V} = \mathbf{v} - \mathbf{v}_1$ is the relative velocity before collision. Then, the Boltzmann equation becomes

$$Df = D_c f, \quad (8)$$

where the left- and the right-hand sides of Eq. (8) are expressed by Eqs. (6) and (7), respectively.

It is proved by the use of Eq. (8) that the H function $H = \int d\mathbf{v} f \ln f$, which was first introduced by J. W. Gibbs, satisfies the H -theorem,

$$\frac{dH}{dt} \leq 0, \quad (9)$$

where the equality corresponds to the case with $f(\mathbf{v}')f(\mathbf{v}'_1) = f(\mathbf{v})f(\mathbf{v}_1)$ for any combination of velocities before collision. This condition is essentially the same as the so-called “detailed balance”, which means, roughly speaking, that the initial and final states of a collision have the same probability densities.

It should be noted that the H theorem claims an irreversibility of the gas state, which approaches an ultimate state (the thermal equilibrium). The H function gives a definition of entropy after adding the factor $-k$ (k is the Boltzmann constant). It should be also noted that the assumption iv) is the most important in deriving the Boltzmann equation. This assumption means a cutoff in information before collision. Note that a mechanism with a complete set of information of molecules is equivalent to classical mechanics, which assures reversibility of processes as mentioned in Sec. 2.

3.2. Master equation for an ensemble of quantum molecules

PAULI (1928) gave a quantum mechanical interpretation of the Boltzmann equation by replacing the classical state of molecules (\mathbf{x}, \mathbf{v}) with a quantum state j with energy ε_j and derived the following equation, called “Pauli’s transport equation”, for the number of molecules N_j :

$$\frac{dN_j}{dt} = \sum_{i, i', j'} \left(A_{ij, i' j'} N_{i'} N_{j'} - A_{i' j', ij} N_i N_j \right), \quad (10)$$

where $A_{ij,i'j'}$ is the transition probability for a pair of states from (i, j) to (i', j') . Note that this transition is limited to that with energy conservation, i.e. $\varepsilon_i + \varepsilon_j = \varepsilon_{i'} + \varepsilon_{j'}$. The H theorem (9) is valid also for a H function $H = \sum N_j \ln N_j$, hence Eq. (10) governs irreversible processes. If a set of molecules with energies $(\varepsilon_1, \varepsilon_2, \dots, \varepsilon_n)$ is denoted by α , Eq. (10) is rewritten into the following equation for a probability P_α :

$$\frac{dP_\alpha}{dt} = \sum_\beta (W_{\alpha\beta} P_\beta - W_{\beta\alpha} P_\alpha), \quad (11)$$

where $W_{\alpha\beta}$ is a transition probability. This equation is called ‘‘master equation’’, and governs irreversible processes of quantum states. The first term of the right-hand side means a gain of the state α by transition from β , while the second term means a loss by transition from α .

It is noted here that the origin of irreversibility in the master equation lies in treating only probabilities, which are defined by absolute values of wave functions $P_\alpha = \langle \Psi_\alpha | \Psi_\alpha \rangle$, and the phase of the wave function is neglected. A more careful treatment of the transition probability reveals that the master equation can be derived if the pair of states α and β have no correlation (in other words they have random relative phase), i.e. a part of information is cut off. The work by VAN HOVE (1955, 1957) is worth noting here. He proved that the master equation is derived, if the random phase approximation is introduced only at the initial time. There is a claim also that the initial randomness is not necessary for derivation of the master equation (JANNER, 1962).

4. General Formula for a Cut-off in Information

Since the origin of irreversibility is associated with the cut-off in information of systems, it will be meaningful to give a general formula to describe effects of this phenomenon. Let a state of classical or quantum system be expressed by a set of variables $q = (q_1, \dots, q_n)$, and a function $f(q_1, \dots, q_n)$ be governed by the following linear equation:

$$\frac{\partial f}{\partial t} = Lf. \quad (12)$$

The Schrödinger equation (4) has this form. Let the variables $q = (q_1, \dots, q_n)$ be composed of two sets $q' = (q_1, \dots, q_m)$ and $q'' = (q_{m+1}, \dots, q_n)$, where the former is a set of variables (observed easily) describing the apparent world and the latter is that for a hidden world (not observed or cut off).

Here a projection operator P is introduced to transform the function f to f' , where the two sets of variables are separated, i.e.

$$f' = Pf = \tilde{f}(q')\varphi(q'') = \int \psi(q'')f(q', q'')dq'' \cdot \varphi(q''), \quad (13)$$

where $\varphi(q'')$ is a function describing the state in the hidden world, and $\psi(q'')$ is an adjoint

function of $\varphi(q'')$, so that

$$\int \psi(q'')\varphi(q'')dq'' = 1. \quad (14)$$

It is easily shown that P satisfies $P^2 = P$, which is a condition for the projection operator. This projection can be understood as picking up apparent variables, while the hidden variables are confined within a properly defined function $\varphi(q'')$. Next, we define a projection P^* of f into a function which contains the neglected information, i.e. $P^*f = f'' = f - Pf$ or $P^* = 1 - P$. P^* is also an projection operator, since it satisfies $(P^*)^2 = P^*$. These operators satisfy $P + P^* = 1$.

When these two projections are operated on Eq. (12), we have the following two sets of equations:

$$\frac{\partial}{\partial t}(Pf) = PLf = PLPf + PLP^*f, \quad \text{or} \quad \frac{\partial f'}{\partial t} = PLf' + PLf'', \quad (14a)$$

$$\frac{\partial}{\partial t}(P^*f) = P^*Lf = P^*LP^*f + P^*LP^*f, \quad \text{or} \quad \frac{\partial f''}{\partial t} = P^*Lf'' + PLf'. \quad (14b)$$

These are simultaneous equations for f' and f'' . By integrating Eq. (14b) formally, we have

$$f''(q', q'', t) = \int_0^t \exp\{(t - \tau)P^*L\} \cdot P^*Lf'(q', q'', \tau) d\tau + \exp(tP^*L)f''(q', q'', 0). \quad (15)$$

The integral term in Eq. (15) shows a continuous effect of the apparent world on the hidden world owing to the dynamics L , and the second term reveals an effect of the initial state.

By substituting Eq. (15) into Eq. (14a) and integrating it, we have a governing equation for the apparent world f' ,

$$\frac{\partial f'}{\partial t} = PLf' + PL \int_0^t \exp\{(t - \tau)P^*L\} \cdot P^*Lf' d\tau + PL \exp(tP^*L) \cdot P^*f''(0). \quad (16)$$

The first term on the right-hand side corresponds to the dynamics described in terms of the apparent variables, the second term is the effect of the dynamics which relates the apparent world to the hidden world and then comes back to the apparent world. Finally, the last term is the effect of the initial hidden world. Equation (16) is an exact equation for f' , when the effect of the hidden world is not neglected (it works through the second and the third terms). Note that the second term is expressed as an integral of the past processes, which means that a neglect of information is associated with an appearance of hysteresis or, in other words, an appearance of non-Markovian nature.

When the effect of past processes decays rapidly, i.e. the second and the third terms are neglected, the system recovers the Markovian nature and f' is governed solely by the dynamics of the apparent world. Note that the dynamics governed by PL are not necessarily

reversible, even if the same process governed by L is reversible.

A good example of recovery of Markovian nature is the derivation of the diffusion equation of molecules. The diffusion is driven by Brownian motions of molecules, which would be governed by the Langevin equation (an equation of motion for each molecule which is receiving a linear frictional force and a random impulsive force). The velocity variables of molecules are looked upon as hidden variables and the macroscopic spatial distribution of molecules is the apparent world. It is possible to write an equation corresponding to Eq. (16), which governs the spatial distribution of molecules. Then, by assuming that the mean free path of molecules is much smaller (at the typical scale of molecular distributions, where the effects of past processes disappear), the (Markovian) diffusion equation of spatial distribution can be recovered.

5. Open Systems—Maintenance of Inequilibrium

5.1. An example of open system

As is noted in Section 1, generation and transmission of neural signals occur as irreversible processes in an open system. However, the basic definition of open systems is not yet enough understood. A typical example of phenomena in open systems would be the Benard convection, which is a convection flow between two horizontal plates with fixed temperatures, as shown in Fig. 5. In order to assure constant temperature of the plates, they are in contact with large heat baths, and a continuous heat flow must be given from the upper plate (lower temperature) to the lower plate (higher temperature). The convection flow in the fluid is assumed to maintain its flow structure through energy consumption from the heat pump. To simplify the situation we will neglect the plates and consider the fluid system to be in contact with two heat baths.

Observing the system shows that thermal convection is initiated when the temperature difference $\Delta T = T' - T''$ becomes larger than a critical value, below which the fluid stays at rest and the heat flow occurs only through thermal conduction.

There is a more complicated situation in the thermal convection, as shown in Fig. 6. When the temperature difference ΔT lays between two specific values (ΔT_1 and ΔT_2),

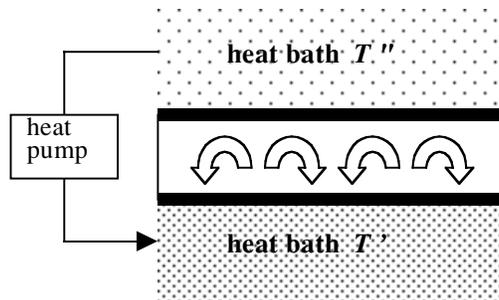


Fig. 5. Total system to create thermal convection. T' should be higher than T'' for onset of convection.

convection grows only if external disturbance of a finite strength is provided: weaker disturbances decay and the system comes back to the static state. This situation is illustrated in Fig. 6 indicated by arrows.

5.2. A system contact with a heat bath

Behaviour of a system in contact with a heat bath can be understood in the framework of quantum mechanics (REIF, 1965). Let a system A be in contact with a heat bath A', as shown in Fig. 7. Let the system $A_0 = A + A'$ be governed by a Hamiltonian

$$H_0 = H (\text{system A}) + H' (\text{heat bath}) + Hi (\text{interaction of A and A'}). \quad (17)$$

States of systems A and A' are characterized by energy eigen values $E_r, E_{r'}$, respectively, which are determined in the absence of the interaction. The probabilities for the systems A and A' to be in states r and r' are denoted by P_r and $P_{r'}$, respectively. Transition of states occurs owing to the interaction Hamiltonian, and the probability from a pair of states (r, r') to (s, s') is denoted by $W_0 (rr' \rightarrow ss')$. Then, from the energy conservation we have $W_0 (rr' \rightarrow ss') = 0$ for $E_0 = E_s + E_{s'} \neq E_r + E_{r'}$. Equality of probabilities of a transition and an opposite transition is assured by quantum mechanics, i.e. $W_0 (rr' \rightarrow ss') = W_0 (ss' \rightarrow rr')$.

In the case where both systems are in thermal equilibrium, we have the canonical distribution

$$P_r = \exp(-\beta E_r), \quad \text{where } \beta = 1/kT. \quad (18)$$

On the other hand, if A and A' are not in equilibrium, the transition probability of the system A, i.e. W_{rs} (from the state r to the state s) is not equal to that from s to r , W_{sr} , for the following reason. Even in the inequilibrium case the heat bath A' is almost in equilibrium, and the canonical distribution applies. Then, both transitions are written as follows:

$$W_{rs} = \sum_{r's'} P_{r'} W_0 (rr' \rightarrow ss') = \text{const} \cdot \sum_{r's'} \exp(-\beta E_{r'}) W_0 (rr' \rightarrow ss'),$$

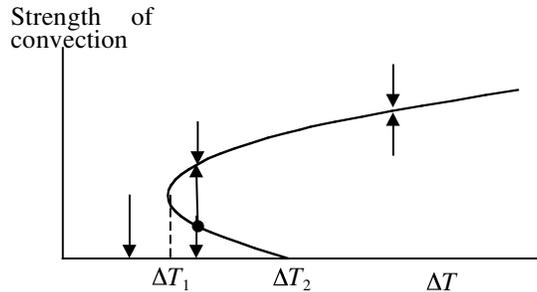


Fig. 6. Growth or decay of thermal convection indicated by arrows. It depends on the temperature difference (abscissa) and the strength of initial disturbance (ordinate).

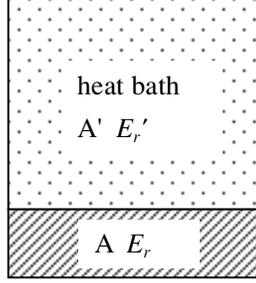


Fig. 7. A system A in contact with a heat bath A'.

$$W_{sr} = \sum_{r's'} P_{s'} W_0(ss' \rightarrow rr') = \text{const} \cdot \sum_{r's'} \exp(-\beta E'_{s'}) W_0(ss' \rightarrow rr').$$

Then, by the use of the conditions $W_0(rr' \rightarrow ss') = W_0(ss' \rightarrow rr')$ (derived by quantum mechanics) and $E'_s - E'_r = E_r - E_s$ (energy conservation), we have a relation between the two transition probabilities,

$$\begin{aligned} W_{sr} &= \exp\{-\beta(E_r - E_s)\} W_{rs}, \\ \text{hence } W_{sr} &= \text{const} \cdot \exp(\beta E_s), \quad W_{rs} = \text{const} \cdot \exp(\beta E_r). \end{aligned} \quad (19)$$

Therefore, the transition probability to higher energy state is smaller than the opposite one. The master equation of the system A in this case is

$$\begin{aligned} \frac{dP_r}{dt} &= \sum_s (P_s W_{sr} - P_r W_{rs}) = \sum_s \text{const} \cdot \{P_s \exp(\beta E_s) - P_r \exp(\beta E_r)\} \\ &\equiv a - b \exp(\beta E_r) P_r, \end{aligned} \quad (20)$$

where a and b are constants. This equation suggests that the state of the system A is not stationary, and P_r approaches to $P_r = a/b \cdot \exp(-\beta E_r)$, i.e. the canonical distribution in equilibrium.

Equation (19) allows another interpretation by introducing a concept of entropy. Entropy increase is defined by a heat input divided by temperature, i.e. $\Delta E/T$. Since the heat bath A' is much larger than the system A, the increase of entropy of the system A₀ in the transition $ss' \rightarrow rr'$ is mainly given by that of A', i.e.

$$\Delta S \cong \frac{E_{r'} - E_{s'}}{T} = k\beta(E_{r'} - E_{s'}) = -k\beta(E_r - E_s). \quad (21)$$

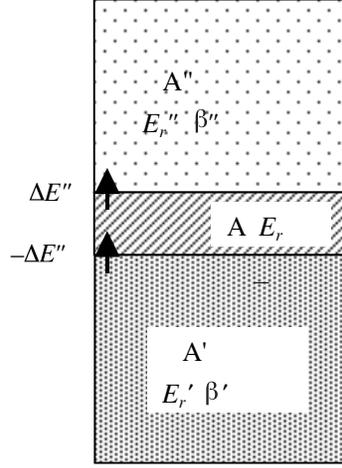


Fig. 8. System of a fluid layer A in contact with heat baths A' and A''.

Then, Eq. (19) can be written as

$$W_{sr} = \exp\left(\frac{\Delta S}{k}\right) W_{rs}. \quad (22)$$

Therefore, W_{sr} is larger than W_{rs} , if the entropy increases with the transition $ss' \rightarrow rr'$, i.e. the transition with increasing entropy occurs more frequently in accordance with the second law of thermodynamics.

5.3. A system contact with two heat baths

For the thermal convection shown in Fig. 5, the total system is composed of at least three parts, system A and two heat baths A' and A'' (the heat pump could be neglected by assuming that the heat baths are almost in equilibrium). The heat baths are assumed to be almost in equilibrium with values β' and β'' for the parameter β , as shown in Fig. 8. Let us assume a higher temperature, i.e. $\beta' < \beta''$. In this case, we can not expect a complete equilibrium state, nor can we introduce a temperature for the system A. In classical fluid dynamics a temperature distribution $T(\mathbf{x}, t)$ is introduced to analyze the convection flow, but it is not a properly defined concept in quantum mechanics.

Let us introduce a Hamiltonian of the total system, H (system A) + H' (heat bath A') + H'' (heat bath A'') + Hi' (interaction of A with A') + Hi'' (interaction of A with A''), and the transition probabilities of the total system, $W_0(rr'r'' \rightarrow ss's'') = W_0(ss's'' \rightarrow rr'r'')$. It should be mentioned that this view is an original suggestion of the present paper, although the possibility remains that similar views have been suggested before. As in the previous subsection, the transition probabilities of the system A, W_{rs} and W_{sr} , are compared, by expressing them as follows:

$$W_{rs} = \sum_{r'r''s's''} P_{r'} P_{r''} W_0(rr'r'' \rightarrow ss's''), \quad W_{sr} = \sum_{r'r''s's''} P_{s'} P_{s''} W_0(ss's'' \rightarrow rr'r''). \quad (23)$$

Since both heat baths are almost in equilibrium, i.e. the canonical distributions are established, and $P_{s'}$ and $P_{s''}$ are expressed as follows:

$$P_{s'} = P_{r'} \exp\{\beta'(E_{r'} - E_{s'})\}, \quad P_{s''} = P_{r''} \exp\{\beta''(E_{r''} - E_{s''})\}. \quad (24)$$

By the use of these relations and the equality of W_0 in both directions, we can rewrite W_{sr} as follows:

$$W_{sr} = \sum_{r'r''s's''} P_{r'} P_{r''} W_0(rr'r'' \rightarrow ss's'') \exp\{\beta'(E_{r'} - E_{s'}) + \beta''(E_{r''} - E_{s''})\}. \quad (25)$$

If entropy increases in the systems A' and A'' the transitions ($ss's'' \rightarrow rr'r''$) are defined by $\Delta S' = k\beta'(E_{r'} - E_{s'})$ and $\Delta S'' = k\beta''(E_{r''} - E_{s''})$, respectively and the exponential factor in Eq. (25) is written as $\exp(\Delta S'/k + \Delta S''/k)$. Therefore, the transition probability W_{sr} is larger than W_{rs} , if the total entropy increases, and the system A moves in this direction.

Next, we denote energy increases of the system A in the transition $s \rightarrow r$ through heat flows from A' and A'' , respectively, by $-\Delta E' = E_{r'} - E_{s'}$ and $-\Delta E'' = E_{r''} - E_{s''}$, and express β' and β'' by an average value and their difference, i.e.

$$\beta' = \bar{\beta} - \frac{1}{2} \Delta\beta, \quad \beta'' = \bar{\beta} + \frac{1}{2} \Delta\beta. \quad (26)$$

Then, the exponential factor in Eq. (25) is rewritten as

$$\exp\{-\bar{\beta}(\Delta E' + \Delta E'')\} \cdot \exp\{-\Delta\beta(\Delta E' - \Delta E'')\}. \quad (27)$$

Since the heat flow occurs in the direction $A' \rightarrow A \rightarrow A''$ (see Fig. 8), we have $\Delta E' > 0$ and $\Delta E'' < 0$, and $\Delta E' - \Delta E''$ indicates the total heat flow. Thus, we can say that the system A makes a transition $s \rightarrow r$ less frequently if it is associated with increasing energy of A, and associated with stronger heat flow. The former condition is analogous to the property of canonical distribution in the equilibrium case, and the latter suggests the principle of minimum entropy production given by I. Prigogine (GLANSDORFF and PRIGOGINE, 1971).

The above analysis is useful to predict that the system A develops towards a certain static state with low energy and a small heat flow. However, in real systems the static state is only possible when $\Delta\beta$ (temperature difference) is small enough, as is mentioned in Subsec. 5.1. There is a critical value of $\Delta\beta$, above which a dynamical thermal convection arises. An analysis predicting this fact may be quite complicated and is not given here. It is, however, suggested that one may be able to proceed further in this question by modifying the assumption of equilibrium regarding the heat baths A' and A'' .

6. Concluding Remarks—Interpretations of Basic Phenomena in Neurons

We have discussed some basic principles in a physical view, employing some aspects of quantum mechanics and statistical physics. Here, I come back to the issue of signal generation and transmission in neurons and will suggest ways on how to involve these physical aspects in the physiological description of neural activities. At this point these suggestions are necessarily rather speculative, but it is hoped that they may still contribute to further development in the neuro-physics of open biological systems.

The initial stage of an electric current generation at the post-synaptic membrane sets out with the interaction of molecules to a sub-domain (or a radical) of a post-synaptic receptor protein. Subsequently, ion channels change their gating state allowing for the passage of ions through the permeation path of the channel. It can be expected that, with increasing chemical resolution, this process should principally be described in terms of quantum chemistry and thus quantum mechanics (BERNROIDER and ROY, 2004).

Channel opening leads to a generation of a current along with a changing electric voltage which was established at the “resting” membrane state. This stage is associated both with quantum mechanics and statistical physics. The membrane resting potential indicates a sustaining, unstable state, which is homologue to the sustaining temperature difference between both boundaries of a thermal convection. However, if the resting potential would be a stable given condition, the initial ion motions are best described by quantum mechanics.

As the number of moving ions increases, an electric current of macroscopic order is established. This process is described by Ohm’s law and belongs to statistical physics. It should be noted here, that although this process, engaging many ions, could in principle be treated by quantum mechanics, it is actually impossible due to its inherited complexity. The most difficult problem at this stage is the recognition of a mechanism of how the complexity increases. Since statistical treatment of complex systems is inevitably associated with a cut-off in information, there may be a possibility that this mechanism may be approximated to a certain degree by applying the formalism using a projection operator as mentioned in Sec. 4. However, actual manipulation of this formalism is still far too complicated and can not be developed here.

After the neural signal is established, the mechanism of signal transmission is very successfully described by the Hodgkin-Huxley model (HODGKIN and HUXLEY, 1952a, b). It is based upon assumptions of relaxations of ion conductions through membranes involving coefficients which are nonlinear functions of the membrane voltage. In my view, this model can be looked upon as a special case of the master equation. The process of signal transmission is essentially a phenomenon taking place in an open system. Moreover, the axon membrane elicits pulse-type Hodgkin-Huxley signals when the membrane potential is raised above a certain threshold value, which seems to be analogous to the onset of convection owing to a disturbance with certain strength.

Finally, I can conclude that the description of neural signal transmission in terms of quantum mechanics could be promising, if the understanding of open system within the context of quantum mechanics and statistical physics further increases.

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REFERENCES

- BERNROIDER, G. and ROY, S. (2004) Quantum-classical correspondence in the brain: Scaling, action distances and predictability behind neural signals, *FORMA*, **19**, this issue, 000–000.
- GLANSDORFF, P. and PRIGOGINE, I. (1971) *Thermodynamic Theory of Structure, Stability and Fluctuations*, Wiley & Sons.
- HAKEN, H. (1978) *Synergetics—An Introduction, Nonlinear Phase Transition and Self-organization in Physics, Chemistry and Biology*, Springer Verlag.
- HODGKIN, A. L. and HUXLEY, A. F. (1952a) *J. Physiol.*, **116**, 449.
- HODGKIN, A. L. and HUXLEY, A. F. (1952b) *J. Physiol.*, **117**, 500.
- JANNER, A (1962) *Helv. Phys. Acta*, **35**, 47.
- PAULI, W. (1928) *Sommerfeld Festschrift*, Leipzig.
- REIF, F. (1965) *Fundamentals of Statistical and Thermal Physics*, McGraw-Hill, Inc.
- VAN HOVE, L. (1955) *Physica*, **21**, 517.
- VAN HOVE, L. (1957) *Physica*, **23**, 411.
- ZUBAREV, D. N. (1974) *Nonlinear Statistical Thermodynamics*, Consultants Bureau, N.Y.