

MITOSIS AND MEIOSIS AS BRANCHES OF A SINGLE KINETIC PROCESS

L. A. Rott

UDC 539.142+576

Two forms of cell division are initiated by a single quantum mechanism in which the number of particles is not an integral of the motion.

As is known, cell division in a living organism occurs in two ways, mitotic and meiotic (see, for example, [1]). However, while in mitosis daughter cells are able to divide further, in cells that appear as a result of meiosis (mature generatives) neither mitotic nor meiotic divisions proceed any more (until fertilization). The processes differ basically in their final results. Here, regulation (selection) of the initial cells induced to divide by mitosis or meiosis (see [2]) is strictly observed.

Both mitosis and meiosis are a continuous kinetic process. Although four individual phases are discerned in mitosis (in a sense, it is an artificial division), there are no time intervals between them. It is assumed that there is a stage of rest between them, but this rest is false. It is precisely in this essentially most active stage that the most mysterious process of chromosome replication (doubling) occurs.

Meiosis consists of two consecutive and more rapid (in time) cell divisions (the first and second meiotic divisions). Four phases are also discerned in each of them. In this case, too, chromosome doubling (replication) still occurs before the beginning of meiosis. This feature is common for both kinetic processes.

The goal of the present work is to show that mitosis and meiosis are basically branches of a single kinetic mechanism predetermined by successive nuclear excitation and decay of a molecule of nucleic acid (DNA), which, in turn, determine the entire behavior of chromosomes.

Although the mechanism of doubling (replication) of a bihelical DNA molecule (Watson–Crick model), which is processes involving nucleic acids (this refers equally to transcription and translation), is coupled with processes involving numerous enzymes added to DNA and the so-called regulatory proteins (see [3]), its initial (basic) aspect is due to specific nuclear transitions. It is these transitions that initially lead to straightening of a DNA molecule and subsequently to replication itself.

The existing concept that after untwisting of the DNA molecule, a daughter molecule, its replica, is synthesized on it as a matrix from proteins due to the environment could hardly be considered satisfactory since it does not contain any indications for construction of a consistent theory. Untwisting and doubling of the molecule comprise a single connected process with strict time regulation. Explanation of all these facts requires a new approach. It is possible that in living nature physics encounters unknown nuclear processes. We consider justification and consequences of this suggestion.

In what follows we will speak about a quantum-mechanical model that is able to explain the process of replication (spontaneous doubling) of a molecule. But, before starting its description, we will make several general conclusions about the genesis of the suggested approach.

It is assumed that we have a set of $3N$ functions divided into triples:

$$\xi_k = f(p_{1k}), \quad \eta_k = f(p_{2k}), \quad \zeta_k = f(p_{3k}), \quad k = 1, 2, \dots, N. \quad (1)$$

Each triple is symbolically denoted by Q_k . If all the variables p_{ik} are the same and have the meaning of time, then the physical relation reflected in this set of functions can be expressed in the form $Q_k[\xi_k(p, p_0, \xi_{k0}, \xi_{k0}), \dots]$ and, accordingly, in the form of a set of integrals of the motion $\Phi(Q_k, \dot{Q}_k) = 0$. Independence from the

initial conditions as a more general relation leads to the existence of differential equations of the second order (classical mechanics).

Now, another possibility is considered: this set of functions is expressed in terms of a more general productive function that has the meaning of a differential-distribution density for a set of N particles $f(q_1, \dots, q_N)$. The latter, in turn, can be the squared modulus of a complex function (a wave function in quantum mechanics). With the aid of f , it is possible to form $N - 1$ new functions that are unary, binary, ternary, etc. distribution functions. The unary function is

$$f_1(q_1) = \int_V \dots \int_V |\psi|^2 dq_2 \dots dq_N, \quad (2)$$

where the position vector of a particle $q(\xi, \eta, \zeta)$ depends on three coordinates. In terms of the unary function, three new functions are formed:

$$f_{1\xi}(\xi_1) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f_1 d\eta d\zeta, \quad f_{1\eta}(\eta_1 | \xi_1) = \frac{1}{f_{1\xi}} f_{1\xi\eta}(\xi_1, \eta_1), \quad (3)$$

where

$$f_{1\xi\eta} = \int_{-\infty}^{\infty} f_1 d\zeta,$$

and

$$f_{1\zeta}(\zeta_1 | \xi_1, \eta_1) = \frac{f_1(\xi_1, \eta_1, \zeta_1)}{f_{1\xi\eta}(\xi_1, \eta_1)}. \quad (4)$$

Functions (3), (4) have the meaning of conditional probability densities. In a similar way, three functions are constructed accordingly from the conditional binary function, etc. With the aid of the differential functions formed, appropriate integral distribution functions that have the meaning of parameters varying in the interval $[0, 1]$ are obtained. The first of these parameters p_{11} is

$$p_{11} = \int_{-\infty}^{\xi_1} f_{1\xi}(\xi) d\xi = \Phi(\xi_1), \quad (5)$$

the second parameter p_{21} is

$$p_{21} = \int_{-\infty}^{\eta_1} f_{1\eta}(\eta | \xi_1) d\eta = \Phi(\eta_1 | \xi_1), \quad (6)$$

and the third of the parameters p_{31} is

$$p_{31} = \int_{-\infty}^{\zeta_1} f_{1\zeta}(\zeta | \xi_1, \eta_1) d\zeta = \Phi(\zeta_1 | \xi_1, \eta_1). \quad (7)$$

From the above functions (5)-(7) it is possible to construct the quasikinematic equations of motion

$$\xi_1 = f(p_{11}), \quad \eta_1 = f(p_{21} | \xi_1(p_{11})), \quad \zeta_1 = f(p_{31} | \xi_1(p_{11}), \eta_1(p_{21})). \quad (8)$$

Similar equations will also be found for the other particles. This is Eqs. (1) in which the first subscript at the parameter p indicates the number of the coordinate and the second subscript is the number of the particle. All the parameters p_{ik} have different initial values. With the lead h added to the parameters, the displacements of all the particles are determined from equations of the type (8). Thus, we speak formally about trajectories of the particle

motions. It is as if the system of particles acquires natural dynamic development. Random (chaotic) motion is mapped onto the space of "ordered motions."

There is a third way to establish physical relations in the space of the chosen $3N$ basic functions. Using them to construct a functional (Lagrangian), we will consider its invariant and group properties.

It seems possible to realize a fourth approach that is used as a basis of the present work. Its essence consists in the following. Having Eqs. (8), it is not difficult to present a situation in which in some "time" interval Δp_k ($p_1 = p_{11}$ is chosen as the leading parameter) two or more "trajectories" can coincide (coalesce), and this is interpreted so that the system is realized physically not as N individual particles but as a smaller number of particles. Then, for the full period $P = 1$ (the system replicates itself completely) the following transformation of the number of particles of the medium occurs:

$$n_1^{(i)} \rightarrow n_2^{(i)} \rightarrow \dots \rightarrow n_M^{(i)}, \quad n_M^{(i)} = n_1^{(i)} \quad (9)$$

with the appropriate "lifetimes" $\Delta p_1^{(i)}, \Delta p_2^{(i)}, \dots, \Delta p_M^{(i)}$, satisfying the condition

$$\sum_{k=1}^M \Delta p_k = 1. \quad (10)$$

Then, for the period P the entire discrete system is characterized by the mean energy

$$\varepsilon_i = \sum_{k=1}^M E_{n_k}^{(i)} \Delta p_k^{(i)}, \quad (11)$$

where Δp_k is the probability of occurrence of the medium in the state with the number n_k . The superscript i indicates the number of the trajectory of development of the system in the sense of Eq. (9).

In what follows an approximate approach will be used. Actually, particles "meet" and "depart" within the finite spatial volume V , but now it is assumed that the mechanism of transformation of the discrete system is added to the Hamiltonian mechanism: subsequently the initial distribution experiences "disappearance" and "restitution" of some of the particles. This compensates for the fact that true knowledge obtained from the interaction is incomplete. The transformation operator can be given a concrete meaning if it is related to the critical closeness of the particles, i.e., if it is determined in the space of quasikinematic equations (1). For example, if the whole volume V is divided into a finite number of cells, the transformation operator excludes filling of each individual cell ΔV ($\Delta V \ll V$) by several particles. Individual "trajectories" will be followed now. In a time interval Δp_k ($p = p_{11}$ is chosen as the leading parameter) two or more particles can occupy individual cells ΔV . The transformation operator leaves one particle in each cell. Their total number in the system is reduced. If during subsequent natural motion, virtual particles, including those that "disappeared," appear again, one in each cell, the system is "restituted."

Having obtained "trajectories" of the motion of the particles, we can speak about their initial distribution over the cells ΔV . Now, the initial distribution is required for which it is the most probable. From the same condition it is possible to select the wave eigenfunction ψ_l that gives the absolute maximum of the integral

$$\int_{\Delta V_i} d\mathbf{q}_1 \dots \int_{\Delta V_k} |\psi_l|^2 d\mathbf{q}_N = \max. \quad (12)$$

Because of this, it is possible to evaluate the initial parameters p_{ik} from the known coordinate functions of the particles (8). Later, condition (12) becomes unnecessary.

According to (12), for a given eigenfunction ψ_l and eigenvalue of the energy of the system E_N , the particle distribution in the volumes ΔV is not unique. Its own family of trajectories with its own character of transformation and average dynamic characteristics corresponds to each possible individual distribution. A new form of quantization of the system takes place.

A single-particle Hamiltonian and, accordingly, hydrogen eigenfunctions in dimensionless variables are chosen. The effective volume of the system is taken as a cube with the linear dimension $RM = 54$, and the linear

dimension of a cell (also in the form of a cube) is $H = 5.4$. Then, the total number of cells is 1000. The origin of the coordinates $\xi\eta\zeta$ is taken to coincide with the center of the cube V , and all the cells are numbered by the triple number ijk ($i, j, k = 1, 2, \dots, 10$, with the numbering started from negative values of the coordinates). For example, the eight central cells are numbered 555, 556, 655, ..., 666. Let the number N be 16. According to (12) the initial particle distribution is found (by exhaustion) for sixteen cells in the corresponding quantum states. As one would expect, this distribution is an example of a degenerate state.

Eight of the sixteen particles occupy the central cells mentioned, being in a quantum state described by the single-particle wave function $\psi_1 = (1/\sqrt{\pi})e^{-r}$. The other eight particles occupy the cells 554, 564, 654, 664, 557, 567, 657, and 667 in the state $\psi_3 = (1/4\sqrt{2\pi})re^{-r/2} \cos \theta$. Then, having found the initial values of p_{11} , p_{21} , and p_{31} from Eqs. (5)-(7) in terms of the known initial coordinates, the initial values are increased by successive leads $h = 0.01$ and the appropriate positions of the particles are found each time [4].

The first transformation of the system takes place after the interval $\Delta p = 0.06$. After another $\Delta p = 0.03$, four particles remain. After $\Delta p = 0.82$ the system consists of twelve particles, and finally, after $\Delta p = 0.07$ the system is restituted completely in the number of particles. Of course, when p reaches the limiting number of unity, the particle returns to the position corresponding to $p = 0$ (actually, the interval Δp at which the particle is outside the volume V can be neglected because of its smallness).

The trajectory of the system A can be written in the form

$$A_{16}^{16} \rightarrow A_8^{16} \rightarrow A_4^{16} \rightarrow A_{12}^{16} \rightarrow A_{16}^{16}, \quad (13)$$

$$\Delta p \cdot 10^2 \quad 6 \quad 3 \quad 73 \quad 7 \quad 11.$$

Previously, natural development of the system was considered as successive changes in all the parameters p_{ij} at the same rate (one-time changes). It seems of interest to extend the theory to the "multitime" mechanism. Now, every function Q_k can have its own period of recurrence P_k in terms of the parameter p . It is evident that the values of P_k cannot be independent. Their mutual dependence follows from the requirement of recurrence of the system as a whole. It follows from this that condition (12) is unnecessary.

Let $p_{11}^{(0)}$ be the initial value of p_{11} . During one cycle $-p_{11}^{(0)} \leq p_{11} \leq 1 + p_{11}^{(0)}$ ($P_1 = 1$) – the functions ξ_1 , η_1 , ζ_1 recur (but this does not refer to all the other functions Q_k). In order that the entire system recur completely, the functions Q_1 have to perform several (s_1) cycles. In the last cycle the parameter p_{11} varies in the range

$$s_1 - 1 + p_{11}^{(0)} \leq p_{11} \leq s_1 + p_{11}^{(0)}. \quad (14)$$

In every individual cycle of changes in the parameter p , the character of transformation of the system is different. The ordinal number of the transformation is again denoted by M , but two subscripts are imparted to each value of it: the number in the cycle (i) and the number of the cycle (j).

Now, the probability that the system occurs in a given state of n_{ij} particles is determined by $p_i^{(j)}/s_1$,

$$\sum_{i,j} \Delta p_i^{(j)} = s_1. \quad (15)$$

During the whole period of restitution the average number of particles in the system is

$$\bar{n} = \frac{1}{s_1} \sum_{i,j} n_{i,j} \Delta p_i^{(j)}. \quad (16)$$

The natural development of the system (transformation of the number of particles in it) can be written in the form (13):

$$A_N^N \rightarrow A_\alpha^N \rightarrow A_\beta^N \rightarrow \dots \rightarrow A_\gamma^N \rightarrow A_N^N. \quad (17)$$

Form (17) indicates the trajectory of the steady-state behavior of the medium. Transition from one trajectory to another is physically observed as absorption (emission) of a particle or a quantum of the field energy. The average mechanical energy (11) of the new trajectory differs from the average energy of the previous trajectory by the energy of the absorbed particle. Absorption can take place with or without changes in the basic number N or without changes in both N and n . In the latter case, similarly to (17), the pumping process that results from irradiation is written as

$$A_{\alpha}^N \rightarrow A_{\alpha}^{\prime N} \rightarrow A_{\beta}^{\prime N} \rightarrow A_{\beta}^{*N} \rightarrow \dots \quad (18)$$

Two or more events of absorption, respectively, are meant here. The prime indicates a new trajectory. Consequently, the average energy changes successively:

$$\bar{E}_{\bar{n}_N}^-(0) + \varepsilon_1 = \bar{E}_{\bar{n}_N}^-(1), \quad \bar{E}_{\bar{n}_N}^-(1) + \varepsilon_2 = \bar{E}_{\bar{n}_N}^-(2), \quad \dots \quad (19)$$

Only such elementary transitions are considered below, which, taken together, are supposed to determine the biological processes. In every elementary event of the transition considered, the energy of the absorbed quantum is much smaller than the energy associated with the other possible transitions (with changes in the basic number N , i.e., when the transition $A_{n_k}^N \rightarrow A_{n_{k+1}}^{N+1}$ occurs, or without changes in N , but again with absorption of particles in the case of $A_{n_k}^N \rightarrow A_{n_{k+1}}^N$).

The case where the excited system is divided into two identical initial (normal) systems is of special interest. The following process of decay (replication) takes place:

$$A_j^{\prime N} \rightarrow A_{2k}^{\prime N} \rightarrow 2A_k^N \quad (20)$$

with, consequently, $i + 2$ events of absorption in

$$\bar{E}_{\bar{n}_N}^-(i+1) + \varepsilon_{i+2} = 2\bar{E}_{\bar{n}_N}^-(0). \quad (21)$$

Now, we consider an example of development of system (13). In the interval when the system was in the state A_8^{16} , the absorbed quantum of energy transferred it to the new excited state

$$A_8^{16} \rightarrow A_{4+4}^{\prime 16}, \quad (22)$$

and now the nucleus consists of two symmetric parts and is divided into two separate nuclei that follow separately the trajectories of the unexcited nuclei (according to Eq. (13)):

$$A_4^{16} \rightarrow A_{12}^{16} \rightarrow A_{16}^{16}. \quad (23)$$

A completely new form of nuclear decay takes place. This approach is a model for description of biophysical problems concerning processes of nuclear division (mitosis and meiosis). In both cases the excited atomic nucleus in the molecule of nucleic acid is divided into two nuclei in the normal state (the electron subsystem of the atom being completed). Excitation of nucleic molecules is accompanied by the appearance of large elastic forces, which, in turn, makes the entire helical structure of DNA straighten out. This also facilitates replication. At very short distances daughter molecules of DNA experience large repulsive intermolecular forces and therefore diverge. As was already mentioned, the metabolic activity of the nucleus in a cell "at rest" between two mitoses is very high and is connected with pumping preceding subsequent replication of the cell.

As regards the theory developed, chromosome replication is none other than replication of the main (nitrogen) nuclei of nucleotides but not their chemical decomposition into separate fragments (thymine, adenine, cytosine, and guanine) followed by restitution due to the environment, as is generally thought. In this case the exceptional accuracy of recombination of the fragments (thymine with adenine and cytosine with guanine) that cannot be explained chemically is striking.

The processes following scheme (20) and (21) due to irradiation by massless particles are only possible for nuclei with a small number of nucleons. That is why nucleic acids where nitrogen plays a leading role constitute the framework of DNA that is responsible for the basic process of life activity.

Of course, the source of internal radiation of energy quanta is of special interest. What is their origin? In general form, the answer to this question can be found from consideration of chemical processes of additional feeding of the organism.

The two ways of development of the cell are determined by different degrees of excitation of, primarily, centrioles. Meiosis is a result of intense excitation of chromosomes. It is this excitation that predetermines the specific part of the cells that is reserved for meiotic reproduction. Excitation of atoms in nucleic acid results ultimately in rupture of the nucleus of the cell (centriole). Intense (strong) excitation leads successively in time to two such ruptures, which takes place in meiotic cell division. Strong excitation of the centriole also predetermines the fact that meiosis occurs in a shorter time in comparison with mitosis.

The double helix of the DNA molecule (chromosome) contains a huge number of nucleotides. It should be noted that the various sections of the helix have, on average, different values of the lead. This is of basic importance in generation of the diversity of functional designation of the structure, which helps to solve the so-called problem of redundancy of DNA [5].

The redundancy is mainly determined by two basic principles. The first is connected with the fact that not all nucleotides are excited to the same degree. Before the start of replication (in the metabolic state of the cell) some of them can remain unexcited and clearly below the critical point of decay of the nucleus of the nitrogen atom. But as a whole, due to the redundancy of the set of nucleotides, the number of excited nucleotides ensures sufficient manifestation of elastic forces, initially, for straightening of the entire helical structure of the DNA molecule, and then, after the critical point of nuclear decay is reached, for replication of the whole chromosome.

Second, the difference in the values of the lead of the helix leads to the fact that the DNA molecule is a set of various segments. Aggregates (saturation) of the corresponding protein are produced, with different connection and density, around every set of nucleotides with the same lead. Different sections of the helix have different energy levels and this affects the character of their pumping under irradiation. Molecular fields change in a different way and, consequently, saturation with proteins is different along the length of the chromosome. The latter fact leads ultimately to redistribution of the cells in their functional designation. Different phases of the cells, both solid and liquid, are formed.

In conclusion it should be stated that the cell acts as a self-reliant object of thermodynamic research. In a sense, it exhibits properties of a thermostat. Maintaining a constant temperature of the organism is an assurance pledge of secure functioning of the kinetic process of replication as well as the other accompanying processes of life activity of the cells (transcription and translation). The cell itself acts as a sustainable system working in a narrow temperature range. As is known, the mean square of temperature fluctuations can be written as

$$\langle(\Delta T)^2\rangle = \frac{kT^2}{c_v}. \quad (24)$$

For a human this value is of the order of ten (actually, the critical value), and under extreme conditions it is still smaller (in aquanauts, at high pressures a temperature of 32.5°C is perceived as terrible heat and 30.5°C is felt as extreme cold (they are shivering)). According to (24), small temperature fluctuations require high specific heats. Calculations show that the lowest estimate of c_v found for a fragment of the DNA molecule (nucleotide) is one or two orders of magnitude higher than the specific heat of well-known organic liquids. But the main point is another matter. The dispersion of entropy fluctuations can be written in the form

$$\langle(\Delta S)^2\rangle = kc_p. \quad (25)$$

In view of the fact that $c_p > c_v$, according to the aforesaid, fluctuations (25) should be high. But it is this fact that gives rise to basic contradictions that are skillfully settled by nature. It only remains to understand how this is done.

Large entropy fluctuations in the DNA structure would inevitably lead to disturbance and even failure of the replication mechanism. This can be seen from the quantum-mechanical model considered. Entropy fluctuations of the molecule (its segments) result in fluctuations of intermolecular interaction, which, in turn, affects the "multitime" mechanism of transformation of the number of individual particles in the atomic (nitrogen) nucleus. Fluctuations of the numbers of cycles (δs) arise, which determine the energy spectrum of the atom as a whole: fluctuations δs lead to fluctuations of the mean values of the energy (11), i.e., deviations $\delta \bar{\epsilon}$ ($\bar{\epsilon} \equiv \langle \epsilon \rangle$) appear.

For stability of replication the necessary condition that the mean value of the square of thermodynamic fluctuations of the energy of the nucleotides in the DNA molecule be much smaller than the mean value of the square of the fluctuations $\delta \bar{\epsilon}$ should be satisfied.

Now, the question arises: how can conditions (24) and (25) be compatible, when large entropy fluctuations and small temperature (energy) fluctuations take place simultaneously in the DNA molecule? It seems probable that thermodynamically the molecule, i.e., the Watson-Crick model, should be considered in combination with regulatory proteins set on it. They function as heat insulators, making a major contribution to large entropy fluctuations due to their structural rearrangement (phase transitions). When the ambient temperature increases, the regulatory proteins largely absorb the heat supplied, and the DNA molecule itself experiences small entropy fluctuations (the double helix imparts great rigidity to its structure).

NOTATION

q , position vector; ξ, η, ζ , coordinates; f , distribution function; N, n , numbers of particles; p , integral distribution functions; E, ϵ , energy; V , volume; ΔV , volume of a cell; ψ , wave function; h , lead; c_v and c_p , specific heats at constant volume and pressure, respectively; T , temperature; S , entropy; s , number of cycles; k , Boltzmann constant.

REFERENCES

1. C. Whillee and V. Dethier, *Biological Principles and Processes*, London (1971).
2. E. Schrödinger, *What Is Life? The Physical Aspect of the Living Cell*, Dublin (1955).
3. Yu. A. Ovchinnikov, *Bioorganic Chemistry* [in Russian], Moscow (1987).
4. L. A. Rott and G. S. Bokun, *Algoritmy i Programmy*, Moscow, No. 1(70), 43 (1986).
5. A. A. Baev, *Vestnik Rossiisk. Akad. Nauk*, 63, No. 2 (1993).