

Motor Activity of Infusoria: Theoretical and Applied Aspects

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Abstract—The article considers morpho-functional organization of cilia—the infusorian locomotion organs—and shows a great complexity of motor behavior of these unicellulars. The problem of control of locomotor activity of infusorian as the single organism is discussed, and the conclusion is made that the system of control of movements is to be multilevel and to include receptor, afferent, central, efferent, and effector links. The role of central integrator and coordinator of motor behavior can be played by the cell nucleus (macronucleus) closely connected with periphery by cytoskeleton dynamic elements. The problem of fight with infusoria parasitizing in the human and animal bodies by impairing motor activity of these unicellulars is also discussed.

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INTRODUCTION

Infusoria belong to the simplest, or unicellular, organisms (Protozoa) and are represented by more than 8000 species. However, the term Protista, if understood literally, little corresponds to reality, as the only cell of these animals, apart from functions of “usual” cells, performs tasks whose solution in multicellular animals is realized with use of complex systems of the whole body.¹

The above-said is particularly true with respect to infusoria that are the most highly organized unicellulars. Thus, infusoria have a differentiated digestion system including oral orifice, pharynx, peculiar digestive vacuoles, and orifice for removal

of non-digested particles. In freshwater infusoria there are complexly arranged systems of osmoregulation and excretion.

In this work, we will consider another, excellently developed infusorian system providing their locomotion. We will discuss general problems associated with motor activity of ciliary infusoria and will describe structure and mechanisms of work of cilia. A particular attention will be paid to mechanisms of control of infusorian movements at the level of the whole organism—the problem that has not yet been solved so far. In conclusion, we will consider some issues of applied significance and will discuss the ways to disturb the motor activity of infusoria-parasites and thereby to make these unicellulars not dangerous to humans and animals.

By the present time, many works have been accumulated on functioning both of individual cilia and of their fields. Even a quick enumeration of all studies in this area is physically impossible. There-

¹ It is to be reminded that “proto” is the first part of complex words and originates from the Greek *πρωτος* that does not mean the simplest, but actually the first, initial, primary.

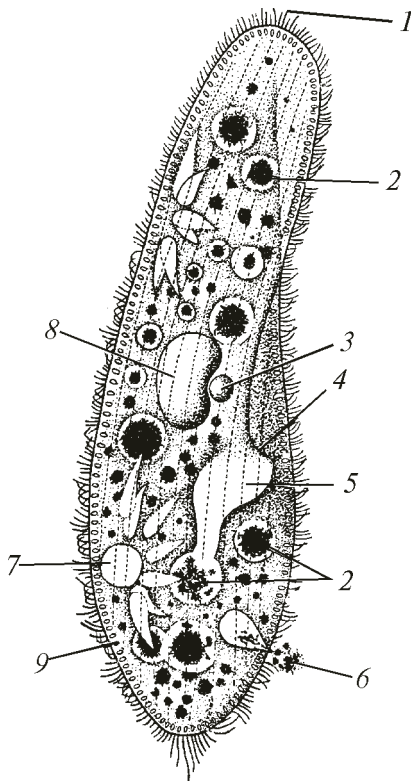


Fig. 1. *Paramecium caudatum*. The total organization *in vivo* ($\times 750$). (1) Cilia, (2) digestive vacuoles, (3) micronucleus, (4) oral orifice, (5) pharynx, (6) the content of anal vacuole, (7) reservoir of contractile vacuole, (8) macronucleus, (9) trypanocysts (from [2]).

fore, in this paper, we will refer mainly to reviews as well as to summarizing articles dealing with the considered topics.

MOTOR ACTIVITY OF FREE-LIVING INFUSORIA

Not all free-living ciliary infusoria have locomotion. There are forms that in the adult state behave the sedentary (fixed to substrate) mode of life. Further we will consider only the infusoria that have locomotion organs—cilia.

GENERAL CHARACTERISTICS

Such infusoria are able (to a degree) to respond to light, temperature gradients, chemical substances, mechanical stimuli, gravitational and electromagnetic fields [1].

Infusoria usually respond to these stimuli by changes of direction and character of their movement. However, in the present works we are mainly interested not in the causes prompting infusoria to perform motor activity, but in the mechanisms supporting this activity.

Paramecia (Paramecium caudatum). These rather large (up to 300 μm and more in length) unicellulars (Fig. 1) have an efficient locomotion system. Their cilia are spread throughout the entire cell surface and form rows (kineties) running along the body at a small angle.

The total number of cilia is very high and reaches 15 000. Frequency of their beats can vary and amounts to 15–30 beats/s. As to the movement rate that is equal to 2–3 mm/s during quiet swimming, it can exceed 10 mm/s under certain conditions. As a result, the paramecium is able to cover distance exceeding its body length 10–15 times, which is considered a rather high parameter in protozoology.

When noting complexity of paramecium motor behavior, researchers usually indicate its ability to move not only forward, but also back and to make turns. But this, as shown by Párducz [3], does not exhaust at all the whole diversity of movement forms in these unicellulars. This author identified in *P. caudatum* 11 (!) movement forms differing by direction, character of the body rotation around the longitudinal or transverse axis, trajectory of movement, and other parameters, although under “usual” conditions, *P. caudatum* prefers moving forward with a left-side rotation of the body around the longitudinal axis. Trajectory of such movement represents a stretched left-wound helix.

Stylonychia (Stylonychium mytilis). Stylonychia are smaller infusoria than paramecia and seldom exceed 200 μm in length (Fig. 2a). Their body is flattened in the dorso-ventral direction; therefore, dorsal and ventral body sides are distinguished in these infusoria.

Unlike other infusoria, stylonychia move by using not cilia, but cirrus located on the abdominal side from sides and below (Fig. 2b). The cirrus are formed by the same cilia densely grouped in bundles. One cirrus can contain from several to more than twenty cilia.

Marginal cirrus are arranged in two rows (each row on the right and on the left). These cirrus

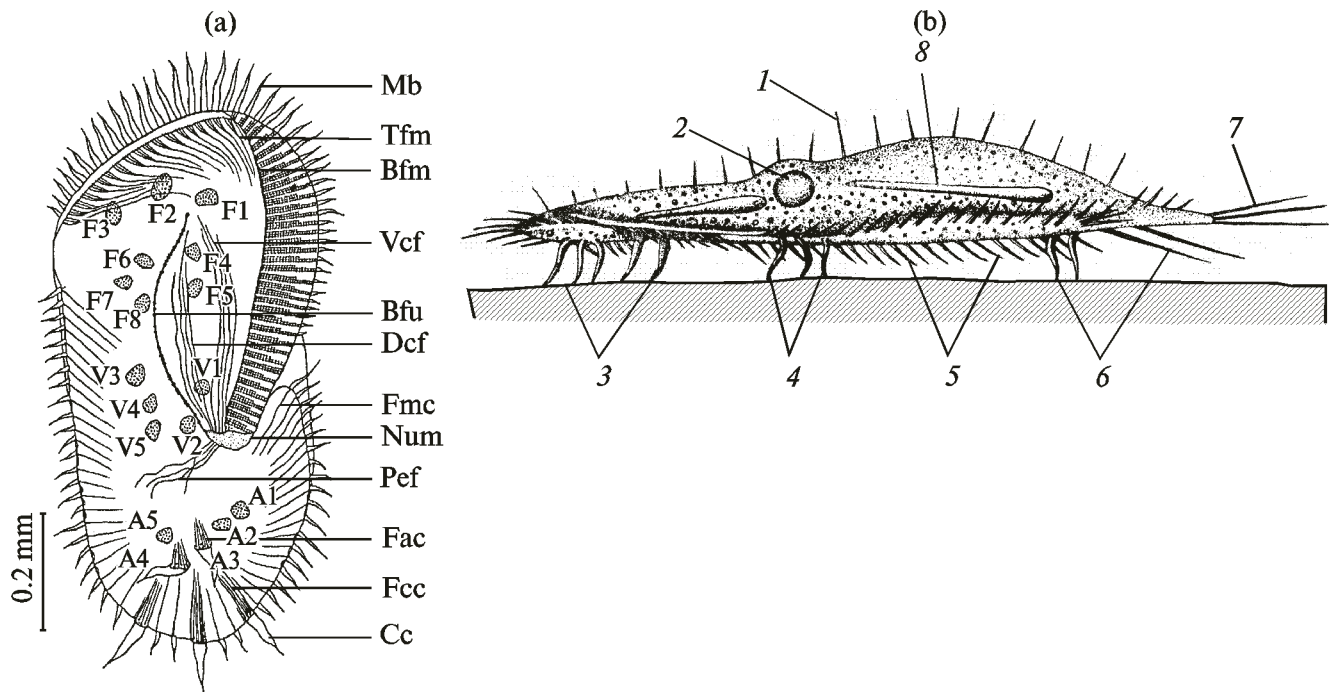


Fig. 2. *Stylonychia mytilis*. (a) View from the abdominal side. A1–A5—Anal cirruses; Bfm—basal fibrils of membranellas; Bfu—basal frontal fibrils of undulating membrane; Cc—caudal cirruses; Dcf—dorsal cytostomal fibrils, F1–F8—frontal cirruses; Fac—fibrils of anal cirruses, Fmc—fibrils of marginal cirruses, Mb—membranellas, Num—neuromotorium, Pef—fibrils located behind peristome, Tfm—terminal filament of membranella; V1–V5—ventral cirruses; Vcf—ventral cytostomal fibrils (from [4]). (b) Movement on substrate (×300). (1) Spinal transversal bristles, (2) reservoir of contractile vacuole; cirruses: (3) frontal, (4) abdominal, (5) marginal, (6) anal, (7) transversal caudal, (8) abducent channel of contractile vacuole (from [5]).

work by the type of cilia; with their help the stylonychia are excellent swimmers. The total number of marginal cirruses varies and can reach 60, but in any case the left body edge contains less cirruses than the right one (approximately 1.3–1.5 times).

Machemer [6] identified 4 types of marginal cirrus movements differing by amplitude, beating frequency, blow angle, duration of working, and return phase. If to take into account that cirruses, like paramecian cilia, are capable for reversion of their movements, it is to be accepted that swimming possibilities of stylonychia, like those of paramecia, are quite diverse.

Of particular interest are the cirruses located from the ventral side below and reminding feet. With their help, stylonychia are able to crawl and “run” on the solid substrate (both forward and back) as well as to climb to small obstacles on their way. Lastly, stylonychia can perform sharp jumps forward.

Several groups of “walking” cirruses are identi-

fied: frontal—8 cirruses (3 + 2 + 3), abdominal—5, transverse—5, and caudal—3 cirruses. Thus, the total number of cirruses of this type in stylonychia amounts to 21, this number being constant.

Participating in walking are frontal, abdominal, and a part of transverse cirruses, whereas jumps are performed by stylonychia with the aid of powerful transverse cirruses. Caudal cirruses, like the marginal ones, are involved in the process of swimming.

It is to be emphasized that the ability of stylonychia, like that of other gastrociliac infusoria, to perform walking is a unique phenomenon in the world of unicellulars.

MECHANISMS PROVIDING MOVEMENT OF CILIA

Whatever locomotion peculiarities the infusoria have, the motor structural unit in these unicellulars is cilium.

Structural-functional organization of cilium appa-

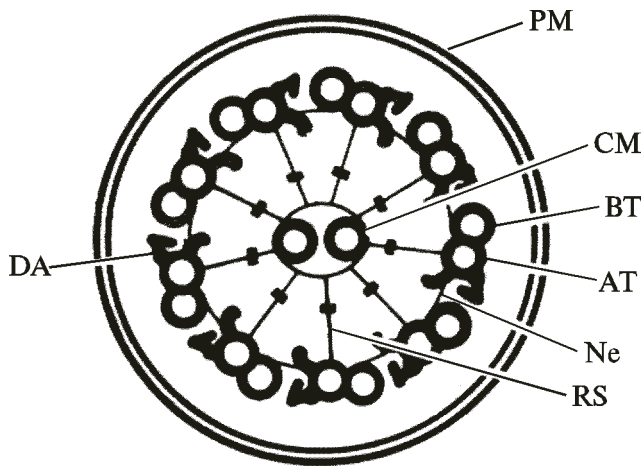


Fig. 3. Cross-section of cilium. AT—A-tubule, BT—B-tubule of peripheral doublet, DA—dinein arms, Ne—nexin bridges, PM—plasma membrane, RS—radial spokes, CM—central membrane (total envelope) around central microtubules of axoneme (from [8]).

ratus. By their internal structure, cilia are identical to flagella from which they are believed to have originated. However, flagella usually are much longer and function in different way than cilia. Each cilium represents an external outgrowth of the cytoplasm and has a cylindrical shape, practically constant diameter (2 μm), and length of 10–15 μm .

The current concept of the structural-functional organization of cilia is based on morphological (mainly electron microscopic) and biochemical methods of studies, while recently also on the electron tomography method [7–10].

The cilium axial skeleton consists of axoneme that includes 9 pairs of microtubules connected with each other and located at the periphery as well as one pair of separated microtubules located in the center (Fig. 3). This system of tubules is designated as $(9 \times 2) + 2$.

Peripheral doublets consist of A- and B-tubules; from A-tubules, the so-called arms as well as radial spokes and bridges go out. The arms are directed to a neighbor doublet, spokes to the envelope surrounding two central microtubules, and bridges connect doublets with each other.

The base of cilia contains basal bodies (kinetosomes). They are not reached by two central microtubules, while peripheral microtubules become triplets (9×3) due to attachment of C-tubules to them. Individual triplets are interconnected with

fibrillary bridges.

Running proximally from kinetosome are roots that, apart from supporting function, also perform some other, still not completely elucidated functions. Interestingly, the root system is especially well developed in large motile infusoria. Thus, in the *Tetrahymena* infusorium the basal body has 3 root elements: the root running towards the anterior end of the infusorian body (kinetodesmal fibril), towards its posterior end (postciliary microtubules), and towards the body side (transversal microtubules) [11]. Axoneme contains more than 250 various proteins, the key role in the ciliary movements being played by two proteins: dinein forming arms and tubulin forming microtubules.

It is considered proven that beating of cilia is realized by dinein arms that interact with ATP (as energy donor) and provide bending of axoneme during slicing of microtubule doublets relative to each other.

Indeed, this concept that initially had been based on analogy with muscle fibers was confirmed in subsequent experiments including computerized modeling of structure and function of cilia [7–9].

True, it has turned out that whereas in muscle contraction the main role is played by actomyosin complex proteins, in ciliary beating this role is played by the above-mentioned proteins: dinein playing the role of myosin, while tubulin—the role of actin. This indicates that in evolution, the contractile systems can independently appear; they can differ biochemically, but act by a similar principle [12].

By continuing the evolutionary issue, it cannot help noticing another, very interesting circumstance. Cilia by their structural-functional organization seemed to have been so fortunate structures that they did not essentially change for million years. Moreover, they are successfully used not only in motor systems of unicellulars, but also in some systems of multicellular invertebrates as well as of vertebrate animals and humans.²

We have already mentioned that the system providing work of cilia in infusoria is able to operate very rapidly (several tens of cycles per 1 s). But even this is not the limit: recently an infusorium was

² Here, however, cilia serve not for cell locomotion, but for translocation of fluid, mucus, various small objects near the cell surface (for instance, in airway epithelium).

studied whose cilia beating rate amounted to 105 ± 10 beatings/s when moving forwards and 160 ± 30 beatings/s when moving backwards [14]. Muscles cannot perform such fast contractions.³

How do individual cilia work during swimming of infusoria? If to characterize their work as a whole, it can be said that cilia act like a miniature paddle rowing water. However, this analogy is true only if to judge “by the final result,” as in the process of rowing the ciliary movement trajectory can be very complex. Two phases of ciliary beatings are identified: effective (working) and passive (reversal). During the working phase, the cilium is straightened and grasps during movement much more water than at the reversal phase when the cilium bends and passes near the water surface. As a result, the ciliary body moves forwards. During the reversal ciliary movement, opposite relation is observed and the infusoria move to the opposite direction.

It is curious that to stop, infusoria do not need any particular ciliary movements, as for such small objects like infusoria, of very great significance is water viscosity, whereas inertia force can be ignored, and infusoria stop at once as soon as their cilia terminate their work.

During swimming all cilia in infusoria work strictly coordinately, meanwhile not synchronously within each row (as paddles were “working” on galleries), but with a phase shift. Therefore, waves of beatings called metachronal ones are running all over the infusorian body. The working blow of each cilium is directed at an angle to the wave.

In the opinion of several researchers, the metachronality is accounted for by purely hydrodynamic (i.e., mechanical) causes. But we will further be interested in more complex coordination mechanisms realized by the infusorian itself; therefore, we will not consider metachronal waves.

MECHANISMS PROVIDING CONTROL OF INFUSORIAN MOVEMENTS

It has been shown that cilia contain all necessary components for efficient functioning. They

³ In this connection, it is to be emphasized that very high frequencies of wing beatings in small insects (hundreds of cycles per 1 s) are achieved by different, non-muscular, mechanisms connected with elastic properties of exoskeleton in these animals [13].

have pronounced automatism and are able to work for some time even outside the infusorian body. This has been convincingly proven, for instance, by experiments carried out on isolated cilia.

However, the cilia “themselves” are not able to respond adequately to changes of the medium surrounding infusoria. The initiation of work of cilia, maintenance of their activity at the level required for a given situation, a change of direction of their movements, and other parameters are provided by mechanisms located outside cilia.

As long ago as in the beginning of the second half of the last century, it was shown that changes in movement of cilia of a swimming infusorian were closely coordinated with electrogenesis in its plasma membrane [15, 16]. It was found, for instance, that the so-called “avoiding reaction” (at which the swimming infusorian when meeting an obstacle is moving backward and then is swimming forwards again, but at an angle to its initial movement) was due to depolarization of the surface membrane; on the contrary, the infusorian “escape reaction” (if to stimulate its body posterior end, it accelerates the movement forwards) was due to hyperpolarization.

Numerous studies were dealing with elucidation of role of various ions (Ca^{2+} , K^+ , etc.) in these processes and with activities of the corresponding ion channels and ion pumps [17–21]. We will not consider in detail all these works, but will merely note a very evolutionarily important circumstance attracting attention of several researchers: the ion mechanisms underlying all electrical phenomena in the infusorian cell have turned out to be principally similar with those in nerve, muscle, and receptor cells of multicellular animals.

For subsequent years, there also was revealed and studied the role of other (apart from Ca^{2+}) second messengers important for functioning of cilia—cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) [22–27].

As a result of these and similar studies, several models explaining the character of ciliary movement were suggested. That is how the corresponding mechanisms are explained, for instance, by Fabczak (Fig. 4) [25].

A more complex model explaining the escape reaction in infusoria was presented by Litvin et al.

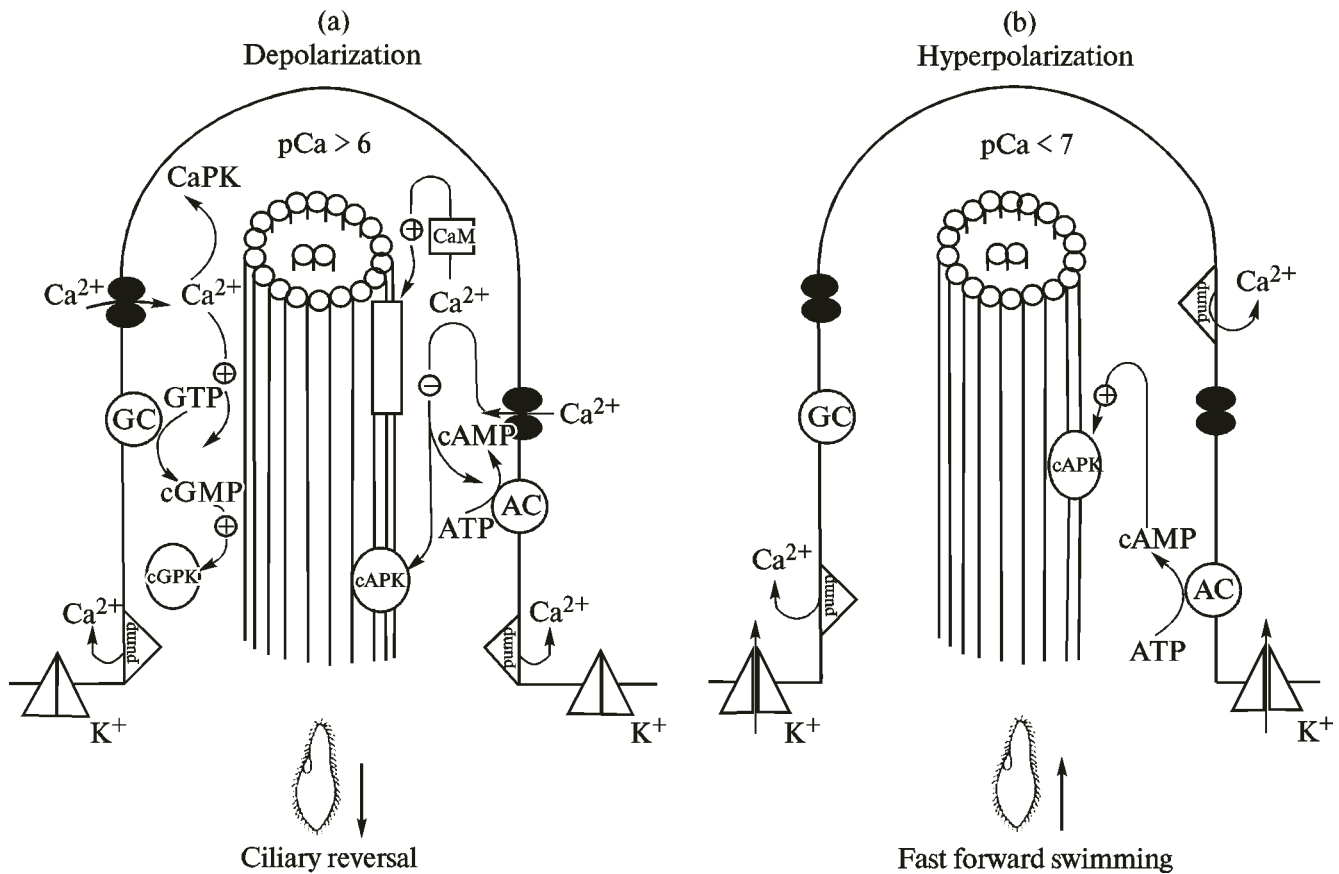


Fig. 4. Diagrams demonstrating response of cilium to depolarization (a) and hyperpolarization (b) of its membrane. (a) Depolarizing stimulus causes opening of potential-dependent Ca^{2+} channels in the ciliary membrane and entrance of extracellular Ca^{2+} into the cilium. An increase of the free Ca^{2+} level in the cilium temporarily changes direction of the ciliary stroke and induces the cell movement back (arrow). An increase of the Ca^{2+} level in axoneme can stimulate activities of Ca^{2+} -dependent protein kinase (CaPK), CaM-dependent protein kinase (CaM), guanylyl cyclase (GC) or cGMP-dependent protein kinase (cGPK). An increase of Ca^{2+} concentration also inhibits activities of adenylyl cyclase (AC) and cAMP-dependent protein kinase (cAPK). (b) Membrane hyperpolarization is accompanied by opening of potential-dependent K^+ -channels in the cell plasma membrane and by activation of adenylyl cyclase (AC) with a subsequent increase of the intraciliary cAMP level. cAMP activates cAPK and in turn produces phosphorylation of axonemal dinein, an increase of ciliary beating rate, and the accelerated forward cell movement (arrow). Removal of Ca^{2+} from cilium is performed by activation of the Ca^{2+} pump located in the ciliary membrane or in plasma as well as in alveolar membranes (from [25]).

[28], while Kotov et al. [29] proposed a system of equations also describing these unicellular motor reactions including the capability for maneuvering. However, let us consider several examples of real motor behavior of infusoria to try making some generalizations.

In experiments by Smith [30], an infusorian was placed into a narrow capillary filled with water, so the infusorian could turn with a difficulty. On reaching meniscus in the end of the capillary, the

infusorian stopped and was moving for some time in the back direction. But it naturally could not round the obstacle and move at an angle. After several unsuccessful attempts the infusorian bent in the U-turn manner, turned, and was swimming to the opposite direction. Here it came across the other meniscus, and all was repeated from the beginning. Interestingly, with time, the infusorian turns took the progressively less time, so instead of the initial 4–5 min it spent only 1–2 s.

We will not consider at all the issue whether the learning occurs in this situation. We think another circumstance is important here: the infusorian is able to turn by 180° in the narrow space by disturbing thereby, due to “difficult circumstances,” the picture of the “classical” escape reaction.

Here is another example. An infusorian is placed into a narrow vessel that has a three-side shape. The infusorian initially stumbles on the side randomly, but soon starts swimming by the “triangle” trajectory. Then the infusorian is transferred into a cylindrical vessel and continues swimming there “by habit” for some time in a “triangular manner.” Here we again are not interested in whether the infusorian has something like memory. We merely consider it important to emphasize that the infusorian is able to perform a rather non-standard coordination of cilia beating. Or let us recall the paramecium ability to change radically the coordination of its movements during different ways of swimming (which were already mentioned to amount to more than 10!).

Lastly, let us consider the swimming stylonychian. We saw that the number of marginal cilia in this infusorian from the right body side was approximately 1.5 times greater than from the left side. Nevertheless, it does not swim by a circle (counterclockwise), but straight on and even can turn to the right. How does it coordinate the work of its cilia in these cases? And the stylonychian also can change the way of locomotion by passing from swimming to walking and back.

It is possible to give very many such examples. Let us mention only the infusorian motor behavior during the combined swimming [31]. And to achieve conjugation, these unicellulars have to “dock” during swimming, very precisely and with particular body parts [32].

Even very general conclusions from such observations make us to think about many things. We see that, on one hand, infusoria are able to perform stereotypic motor reactions that can be repeatedly reproduced without essential changes (for instance, the avoiding reaction). But, on the other hand, infusoria are able to change, modify these reactions as well as to perform very complex acts indicating a high plasticity of its behavior.

So the thoughts inevitably come to mind about the inborn (genetically programmed?) behavior

intrinsic to infusoria and about the behavior induced by the situations in which infusoria can find themselves in the process of their life activity.

If so, what processes can (should) run in the infusorian body, if to consider these processes from the point of view of a physiologist who is used to deal with the integral organism?

When discussing these issues, we will not consider motivations stimulating an infusorian to move (for instance, the “feeling of hunger”). We will focus only on action of external factors on a swimming (“for its own affairs”) infusorian and on the infusorian response to such actions.

Even sufficiently simply organized multicellulars have receptors perceiving external actions, the afferent pathways transmitting signals from receptors to the central nervous system, and this system itself that is able to analyze the obtained signals, to take decisions necessary at the given moment of time, and to convey the corresponding commands along efferent pathways to some particular executive organs (effectors). It is astonishing, but in infusoria there are not (or have not been found?) any analogs of even the most primitive nervous system, although they do have analogs (even structural!) of another most important system for the infusorian life activity—the digestive system. Then how and with the help of which systems the infusorian solves the tasks principally similar with those in other animals during realization of its motor behavior? Let us start with the receptor link.

We have already emphasized that infusoria are able to respond to quite different external actions (light, mechanical, chemical, etc.) [20, 33–40]. And the infusoria perceive such actions differently with differing by size and location receptor fields and individual receptor molecular receptors located in the infusorian plasma membrane.

Thus, in infusoria, the molecules are revealed, in which pigment is close by its composition to rhodopsin of the higher animals [41]. Some chemoreceptors, responses of infusoria on various attractants and repellents have been studied in detail [20, 36, 38]. It is established, for instance, that infusoria are able to respond to sex pheromones if their concentration in the environment is as low as 10^{-12} M! [32]. Many papers deal with studies on mechanisms of perception of gravitation, etc. [42, 43].

If also to take into account that all signals from

the environment come to infusoria not consecutively, but in parallel, by “interrupting” each other, we have to admit that there are no problems with receptor perception in infusoria; it is not by chance that Machemer and de Pyer [17] called the infusorian “the swimming sensory cell.” But the question arises: how and where to is all this sensory information directed for the subsequent analysis? Let us begin with the question “where to.”

Many authors believe that the integrative activity in infusoria is realized by the plasma membrane, particularly that its electrogenesis is exactly coordinated with activity of cilia. Such approach is convenient in that nothing is needed to be sent to anywhere, as the membrane “in one person” both perceives signals and analyzes them, then integrates, and lastly initiates and control the ciliary activity. And although all this reminds the situation with Baron von Münchhausen who managed to pull out himself by hair from a swamp, there are studies indicating that indeed the membrane can perform something like that [20]. But what particularly and under which conditions?

As we saw, stimulation of receptors of the infusorian posterior body end led to the plasma membrane hyperpolarization and as a result—to movement of cilia to the “normal” direction. Can the membrane provide these and similar motor reactions without involvement of extramembranous system? Probably, it can.

But if to recall examples of the very complex infusorian motor behavior, with necessity of controlling the ciliary movement in strictly definite areas (while the cilia can have different locomotion in different areas) and that the coordinational relations can change “on-line” in infusoria and that complex motor acts can be turned on, switched, or turned off, we have to conclude that the membrane itself is unable to manage such tasks. The ideas of necessity of the existence of special mechanisms of regulation of the ciliary activity during the performance by infusoria of complex motor acts were expressed as long ago as in 1967 by Seravin [44], an outstanding researcher of motor behavior of unicellulars, in his monograph. However, for the subsequent years, the issue of “management” has become somewhat less actual on the background of most fine studies of structural-functional organization of the surface membrane, its

electrical properties and properties of ion channels, and ion pumps providing inflow and outflow of various ions important for movement of cilia. These data have moved us quite forwards in understanding the molecular mechanisms providing the ciliary movement, but have not eliminated the question about the general control of movement of the infusorian as an integral organism. Moreover, they forced us again (based on current data) to think that infusoria have to have a movement control system able to regulate the state of the membrane itself at its different sites and located correspondingly outside the membrane—in the cytoplasm.

It is beyond doubts that such candidate for the role of the coordinator-in-chief and of a coordinator of the entire diverse motor activity of the infusorian is of course its nucleus (macronucleus) involved in all processes of the cell life activity except for the function of sexual reproduction (for this, micronucleus exists).⁴

We will not discuss here the possible intranuclear mechanisms responsible for the ability of the nucleus to perceive afferent information, to perform integrative function, and to form the corresponding commands, particularly that participation (or non-participation) of the nucleus in control of ciliary movements still needs to be proven in direct experiments.

But let us accept as a working hypothesis: yes, the nucleus—the “brain” of the cell—is able to solve all these tasks. The nucleus genes store all the information necessary for performance of motor behavior and, depending on situation, it can be transformed into the corresponding locomotion acts.

And now let us try answering (of course, only tentatively so far) the question—how, by what means the afferent signals enter the nucleus and how, by what means the nucleus gives commands to executive organs? Here our attention is involuntarily drawn to cytoskeleton shown by recent studies [45–49] to play an exclusively important

⁴ Micronuclei store (for future generations) the whole genetic information and are capable for mitosis and meiosis, whereas macronuclei contain only the genes necessary for normal “everyday” functioning of the already formed cell.

role in the cell life activity. The tasks of cytoskeleton are not only maintenance and adaptation of the cell shape to external actions, but also performance of other, not yet completely elucidated functions. Thus, cytoskeleton plays an essential role in ecto- and endocytosis, active intracellular transport, cell division, etc.

The cytoskeleton contains protein fibrillary structures: microtubules (20–25 μm in diameter), microfibrils (about 7 μm in diameter), and intermediate filaments (from 8 to 11 μm in diameter). Here we will not deal with the composition and structure of all these elements but will only note that the intermediate filaments are present in unicellulars non-regularly, whereas microtubules playing an important role in the intracellular transport are rather abundant.⁵ It is to be emphasized that they, like tubules of cilia, are composed of tubulin and form the single system with it.

Interestingly, in infusoria, like in other unicellulars, there are often present elements (“periodic fibers,” epiplasma filaments, etc.) that differ from those in “classic” eukaryotic cells. It can be thought that such structures either are directly important for performance of ciliary motor activity or “help” other systems to maintain this activity.⁶

Thus, it is the infusorian cytoskeleton elements that can transmit commands from the nucleus to executive organs—cilia. However, it cannot be ruled out that cytoskeleton is a two-way root and also helps transmission of afferent signals (we do not consider in this work a possible role of other proteins, for instance, of the same second messengers that can not only enhance intracellular signals, but also transmit them further, to the nucleus).

If our considerations are true, the system controlling locomotion in infusoria is multilevel and comparable in principle with analogous systems of multicellular animals.

However, from our idea that without central control the infusorian would be unable to perform all these complex motor acts that it demonstrates does not mean at all that centers control each

movement of cilia. Such control is not required and in fact is simply impossible. This would have been as if the commander-in-chief, instead of solving strategic tasks of control the entire army, had had to control the “motor behavior” of each soldier. So here we are to consider in detail the hierarchy of commanding systems.

Even in the higher vertebrates (with their rich “multicellular” resources), rhythmic movements are known to be realized with the aid of a set of typical programs, the center being not in control of each particular movement of effector. The plasticity of the animal behavior is much determined by that to what degree this program can be modified in particular situations due to sensory influences, involvement of feedback connections, etc. [50]. It is possible that the central programs of such type should also exist in infusoria. But this is, so to say, the central, highest link.

We mentioned automatism inherent in cilia and their ability to work coordinatively for some time, even if they are isolated from the rest of the infusorian body. This coordination is peripheral, due to interconnections of cilia as well as to hydrodynamic forces (in the case of swimming of infusorian body fragments). But such fragments, in our opinion, are in principle incapable for complex behavioral acts (swimming along the “triangle” trajectory, turns in a narrow capillary, etc.).

Interestingly, the coordinated ciliary movements can be retained for some time even in models of infusoria without the plasma membrane. However, from this, it does not follow that the membrane of infusoria at their normal activity is not necessary, nor should it follow that a possibility of realization of some relatively simple motor acts without participation of the nucleus indicates uselessness of the central control of complex behavioral reactions.

Thus, in control of movements in infusoria, like in other animals, hierarchy of systems should exist. The lower links of this system are able to function sufficiently autonomously from control centers, while the centers become involved when the infusorian is to solve more complex tasks than to simply provide the ciliary rhythmic movements: this is both a change-over of programs and realization of complex coordinations in the frame of one program, etc.

⁵ In mammalian nerve cells, for instance, microtubules provide movement of neurotransmitter vesicles along the axon [47].

⁶ The “periodic fibers” have been shown to be closely connected with kinetosomes of cilia [46].

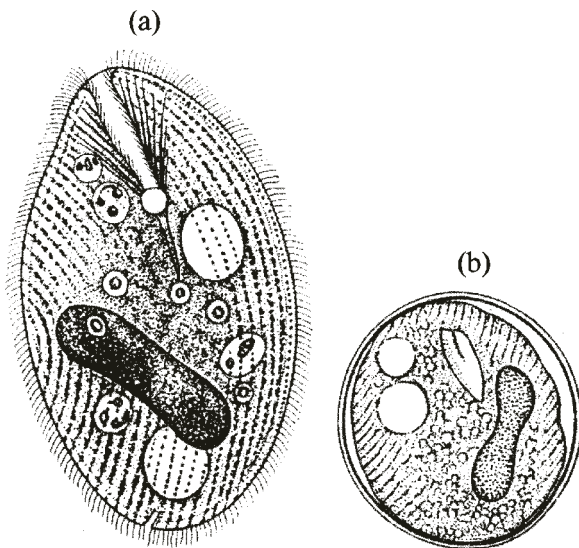


Fig. 5. *Balantidium coli*. (a) Vegetative form, (b) cyst (from [5]).

As to the currently proposed models of the infusorian motor behavior, these models without taking into account the central link can explain only relatively simple ways of behavior of unicellulars, such, for instance, as the escape reaction.

MOTOR ACTIVITY OF PARASITIC INFUSORIA

Infusoria with parasitic mode of life have several advantages over free-living infusoria. These include both constancy of medium in the host body that they inhabit (temperature, humidity, etc.) and practically guaranteed source of nutrition. Lastly, the host (human) also provides infusoria-parasites involuntarily with relative safety of existence (of course, if he will not take into his head a treatment with antiparasitic or some other medications).

But it is necessary to pay for the comfort, and the better the parasites are adapted to life in the host body, the less viable they turn out to become in the environment, outside the host body [51]. Of course, under unfavorable conditions, infusoria acquired a possibility to form cysts, but these are something different than vegetative forms capable for locomotion and performance of other motor function.

In the process of adaptation to life in the body of their host, endoparasites undergo morphophysio-

logical regress of organs and systems whose function turns out to be non-demanded. This can also involve the locomotor organs. Thus, intracellular forms of leishmania and trypanosomes lose their cilia. Nothing similar occurs with locomotion organs (flagella) in balantidia that will be considered below. This indicates importance of locomotion apparatus of these infusoria for their normal life activity in the host body.

Balantidium coli. Balantidia are even smaller than the above-considered free-living infusoria; their body has an egg-like shape, its length seldom reaches 200 μm and usually does not exceed 50–80 μm (Fig. 5). However, these infusoria are the largest among the unicellulars parasitizing in the human and animal intestine. Apart from human intestine, balantidia parasitize in intestine of pigs, horses, monkeys, rodents, fish, reptilians, birds, crustaceans, and annelids [51]. These are most often various species of balantidia, only one species—*E. coli*—being pathogenic for humans. Balantidia of this species are also known to damage pigs and monkeys, although some authors add here rats as well as such domestic animals as horses, sheep, and dogs. The cilia serving to balantidia for movement are smaller than cilia in other infusoria, their length amounting to 4–6 μm . They are arranged in parallel rows and act quite efficiently. At any rate, with their help, balantidia not only can find a necessary place in intestine (and this is the large intestine), but are able to invade its mucosa. Unfortunately, it is not known how *E. coli* behaves in human body by producing ulceration of intestine. However, it has been established in direct experiments that balantidia invade the fish intestinal mucosa with the aid of rotating body movements by acting like a corkscrew [54]. Balantidium facilitates its work on penetration into the intestinal wall by releasing hyaluronidase that is believed to break connections between cells and thereby to “loosen” the mucosa.

Outside the host body the motile balantidian forms live rather briefly—as few as several hours. In the liquid medium they are able to move sufficiently rapidly with aid of cilia by rotating around the longitudinal body axis.

Meanwhile in the human and animal intestine, *B. coli* can behave in a dual manner: either as commensals by consuming bacteria, fungi, starch

grains, and remnants of the host food (without causing a marked harm to the host) or as tissue parasites by invading intestine tissues and starting consumption with erythrocytes, leukocytes, and host tissues (by producing ulcerative lesions of the host intestine). What causes transition from one form of balantidian nutrition to the other—is not exactly known. Probably, the main role here is played by the state of the immune system. Anyway, if the intestine lesion does take place, it can acquire very severe forms. The state that then appears is called balantidiasis (in animals—balantidiosis) and is characterized, apart from ulcerative lesion of large intestine, by the total body intoxication and tendency for long-term and chronic course. When etiotropic treatment is started late, lethal outcomes are possible (up to 20% in severe cases).

According to WHO data, more than 100 mln people in the world suffer from protozoan diseases (including balantidiasis). The current opinion that balantidiasis is spread in hot climate countries does not have sufficient grounds. It is present at all latitudes, especially in regions with intensive pig-breeding.⁷ Therefore, fight with balantidiasis is a quite actual task. To eliminate *E. coli* that entered the human intestine various strong-acting antiparasitic agents have been used: medications of tetracycline group, monomycin, ampicillin, metronidazol. For the recent years, oxytetracycline and metronidazole have been recognized to be the most efficient agents [51].

Unfortunately, these compounds, alongside with a pronounced positive effect, have quite a few counterindications for their use (apart from an increased sensitivity, these are some diseases of blood, liver, brain, the state of pregnancy) and, what is the most important, they produce severe side effects by affecting the state of the gastrointestinal tract, blood system, central nervous system, etc. During treatment with tetracycline group agents, for instance, the patient should be especially cautious during car driving and operating with

other potentially dangerous mechanisms [56, 57].

It is not by chance that a dream of any physician is to find agents deprived of all these unnecessary effects often dangerous for health. But do such agents exist at all?

And here in a physiologist, an absurd, at first glance, but perhaps sensible thought appears—is it necessary to try eliminating completely the infusoria-parasites by using strong and in many aspects toxic substances? Maybe is it better to try at least to “slightly” disturb their motor behavior, as it is very important, as we have seen, for the balantidian life activity and actually determines their pathogenicity?

But then, not antibiotics, but quite different agents are to be used—desirably maximally safe for humans. Such approach has important advantages: it allows using for treatment of balantidiasis relatively non-expensive compounds and at low concentrations (doses); a possibility of avoiding in this connection a harmful effect on the human body of strongly acting medications as well as of the disintegration products themselves of the eliminated parasites; lastly, this makes it possible not to allow conversion of cysts in the human body into mobile and accordingly pathogenic forms.

Attempts in this direction have already been made, with preliminary results being promising. Thus, it has been established that among studied compounds the most promising from the point of view of the above-indicated criteria are solutions containing concentrations of electrolytically obtained silver ions.

It can be recalled that studies on a possibility of using silver ions for water disinfection began as long ago as in the 1930s [59]. It was found the same time that the electrolytically obtained ions of this metal can help in treatment of skin and mucosa disease if these solutions (at concentrations of 10–30 mg/l) are used as lotions, gargles, and lavages.

The silver ion solutions were also tried for the peroral use (10–20 mg/l) to treat diseases caused by bacteria and viruses. For the reasons that we are not aware of, all these ways of treatment had not been introduced into everyday practice.

At present the food industry manufactures widely the so-called “Silver water” allowed for drinking (its silver ion concentration reaches 3 mg/l).

As to motor activity of ciliate infusoria, it can be

⁷ Pigs are one of the main sources of infestation. The pigs themselves (especially piglets) suffer from balantidiosis rather severely: loss of these animals and their forced slaughter can reach 50% of the amount of the sick animals, while the young animals that got this disease, but survived, have an essential delay in growth and development.

disturbed by solutions containing silver ions at concentrations not exceeding 0.05 mg/l (unfortunately, so far only in experiments *in vitro*). These studies continue.

INSTEAD OF CONCLUSION

In our work we tried to show that the so-called primitive organisms are not such at all, and motor behavior of the most highly organized of them—infusoria—turns out to be astonishingly complex. We considered in sufficient detail all links of the infusorian motor system to lead the reader to the conclusion that the system of control of movements in these unicellulars also should be complex and multilevel, including receptor, central, efferent, and effector links.

The possibility of performance of the simplest motor reactions in an infusorian controlled by its plasma membrane does not rule out, in our opinion, the necessity of the “extramembranous” central control when dealing with very complex motor acts requiring their coordination at the level of the whole infusorian organism (turn on, turn off, the complete change of motor programs).

As such candidate for the role of the commander-in-chief of the infusorian complex motor behavior, we propose its nucleus—macronucleus closely connected with cell periphery with the aid of very dynamic cytoskeleton structures.

Of course, the reader in a skeptic mood can reproach us with a rich fantasy (which is not that bad from our point of view) as well as with that we merely put forward a suggestion without actual proving anything. And here the reader will be quite right. No, we do not prove (so far) that it is the nucleus that can serve as such “motor brain.” But we prove (almost) that such “brain” cannot be the plasma membrane that, besides, has sufficiently many of its own, purely membranous things. And this is already something.

In the end of this work we are putting forward an idea that knowledge of peculiarities of motor behavior of infusoria-parasites to whom the motor activity is necessary for invasion into the intestinal mucosa allows a new approach to the problem of fight with these unicellulars. We believe that it is possible to try not to kill infusoria with the help of agents strongly acting and toxic for humans, but

merely to disturb the infusorian motor activity and thereby to make them non-pathogenic to humans. The work in this direction continues.

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