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CHAOTIC BIOLOGICAL SYSTEMS

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Abstract

At first glance, the movement of amino acids and proteins (peptides) in the cell appears chaotic. How is a clear temporal order maintained, with strict sequential processes following one after another, creating the impression that someone accurately guides them? How does DNA replication occur? On one hand, the model of this replication, using a special protein, DNA polymerase, has been established for a long time. On the other hand, there are still more questions than answers in this process. Due to limitations in measurement tools, cellular biologists cannot answer all questions. In this article, we will attempt to address some of these questions using a systemic approach. The study will also help answer questions about the content and interactions of other proteins in the cell. These answers can then be verified using established biological methods.

Keywords:

Introduction

The DNA model was presented by Watson and Crick in 1953. The model of DNA replication was proposed five years later by Meselson and Franklin (Crick, 1954; Meselson, 1958).

According to Watson and Crick, nitrogenous bases (adenine, guanine, thymine, or cytosine) on each level of one strand are connected by hydrogen bonds to the base at the same level of the other strand. Structural requirements permit only adenine-thymine and guanine-cytosine base pairs, resulting in the complementarity of the two strands.

In this article, we delve into the question of the availability of a sufficient number of nucleotide molecules and proteins for DNA replication and the mechanism of their incorporation into daughter chains. It should be noted that all processes – DNA-DNA replication, DNA transcription to RNA, RNA translation to protein, and reverse transcription from DNA to RNA – operate on the same principle of complementary nucleotide interactions.

Text

Let us review the DNA replication mechanism:

- Unwinding of the double-stranded DNA is carried out by Helicase, at a speed of approximately 100,000 base pairs per minute in prokaryotes, and approximately 500 base pairs per minute in eukaryotes;

- Primase synthesizes the initial segment, the primer, after which the secondary DNA chain will be built;
- DNA polymerase synthesizes DNA by initially binding to the primer, using freely floating nitrogenous bases (adenine, guanine, thymine, or cytosine) in the cell plasma;
- Ligase "stitches" DNA fragments into a single chain after ribonuclease removes unnecessary fragments (primers, etc.) from the chain.

We have omitted many mechanisms that are specific to different organisms or too complex for the purposes of this article and do not affect its conclusions. The accuracy of replication is ensured by the precise matching of complementary pairs of bases and the activity of DNA polymerase, which recognizes and corrects errors. The human genome contains approximately 3 billion pairs of nucleotides, approximately 1.5 billion units of the nitrogenous bases. During the replication of the entire DNA chain (for example, before cell division), the same number of nucleotides must be extracted from the cell's plasma. Nucleotides also play various roles within the cell, including functioning as coenzymes, providing energy, regulating cellular activities, and transporting sulfate and methyl groups. Additionally, they supply the cell with remnants of phosphoric acid. In some cases, RNA can serve as a nucleator.

Many researchers are convinced that DNA not only encodes proteins but also the sequence of various processes. However, this is not actually the case. The processes themselves, their sequence, and the initiation and termination of protein work occur randomly, "chaotically," or more precisely, due to self-organization. In particular, it has been proven that Cooley bodies can form starting from any protein. There is no strictly defined assembly sequence, only self-organization. However, there are structures, such as paraspeckles, that cannot form randomly.

The majority of processes in the cell are controlled by proteins. The proteome inside the cell is very dynamic and depends on many factors, such as the cellular environment, cellular stresses, etc. In turn, the concentration of proteins directly influences the functions carried out within the cell (Brandon, 2017). Researchers have estimated the number of proteins in a yeast cell to be approximately 7.9*10^7 (with a median number of 4.2*10^7). The entire proteome of a yeast cell is estimated to consist of 5858 proteins. Approximately two-thirds of cells contain between 1000 and 10.000 protein molecules, with low-molecular-weight proteins being, on average, five orders of magnitude less abundant than high-molecular-weight proteins. In living cells, organic substances are represented by proteins (10–20%), lipids (1–5%), carbohydrates (0.2–2.0%), and nucleic acids (0.1–0.5%). Thus, the number of nucleic acids in a yeast cell is generally estimated to be between 10^5–10^6 (Овсепян, 2014).

The composition of proteins constantly changes depending on their production from mRNA, participation in processes like replication, and degradation of used proteins (Laurent, 2010), mRNA contains both translated and untranslated regions that play an important role, for example, acting as a timer in protein production. When a ribosome "skips" a stop codon, it gets stuck on the mRNA, preventing the ribosomes following it from continuing to read and produce incorrect proteins from the triplets following the stop codon. This process also appears to be random. However, if it were entirely random, no regular processes could occur in the cell.

Let's provide several definitions that are necessary for further discussions:

Natural system – a model constructed by the subject who investigates the object (elements, relationships, purpose), having integration potential, emergence, and integral properties.

Chaotic system – a biological system in which the sequence of processes is unpredictable, the interaction of elements is random, and the result of its work can be anything.

Ordered system – a stable dynamic biological system that adequately responds to external influences.

In the context of biological systems, there is no difference between chaos and order. Moreover, we assert that order does not arise from chaos (Prigogine, 1984), as chaos itself does not exist. Let's explore this using simple examples.

Consider a closed Thermodynamic system consisting of two hydrogen molecules. Knowing the initial state at time T and the

particles' momentum, we can easily calculate their subsequent movements and interactions. If we increase the number of molecules to 5, using a more powerful computer, we can also calculate the system's state at time T + ΔT. However, if we increase the number of molecules to 100, we would exceed the computational capacity available to humanity to perform such calculations. In this context, chaos is the order that we are unable to calculate, so we are forced to use statistics and probability theory.

Another example: A good hostess has all the necessary tools for cooking, consuming food, and storing it always in the right places on shelves, in cabinets, and in refrigerators. Food ingredients are also always located in the same places. During cooking or eating, people always know where and what to take to perform the necessary functions. The second scenario is "chaos," where all the tools and ingredients are scattered around the kitchen in random order, and the hostess has to search for the necessary tools each time to perform any tasks.

It's impossible to perform processes in a timely and correct manner in such a "chaotic" kitchen. However, if we imagine a kitchen of the future, perhaps all the tools and food ingredients will be flying through the air in a random order and very quickly, so with correct timing the hostess will be able to simply grab the necessary items from the "flying" ingredients to facilitate the cooking (or consumption) process. Perhaps the speed of these processes will be even faster than a scenario in which all the ingredients are in their places, and the hostess has to move around the kitchen to retrieve them from their storage locations. However, in a biological cell, such "chaos" is always organized. How does the cell perform its functions? In a cell, there is no "hostess" who knows what ingredients are needed at what time. Here, chemistry and physics are at work, whose laws are the same on interstellar scales as they are on the cellular level. Specifically, the necessary molecules are preassembled in the appropriate areas of the cell (for example, in the nucleus and nucleoli,) where they move about in a chaotic manner. Past the DNA polymerase, the required nitrogenous bases are constantly "flying through," from which it constructs the DNA's duplicating chain. If this process were carried out exclusively by transport proteins, bacterial cells wouldn't be able to divide every half hour, and eukaryotic cells wouldn't be able to duplicate within the framework of mitosis at the necessary speed.

As a result, the chaotic movement of molecules in specific areas of the cell allows necessary reactions to occur orders of magnitude faster than if they were to occur using transport proteins, which move relatively slowly. An individual molecule can reach any area of the cell within a few minutes. Stable structures are formed from highly dynamic molecules for the duration necessary for interaction (Misteli, 2001). Microtubules aid in the self-organization of cell structures. They randomly assemble and disassemble, creating random structures (networks, whirls, asterisks.) Like all self-organizing systems, structures arise abruptly, not gradually, and different initial arrangements of molecules occasionally lead to the same results. This is due to autocatalysis, autoinhibition, and cross-catalysis (where the concentration of certain molecules can lead to a sharp increase in the production of the same molecules, a decrease in production, or a mixed effect of various molecules.) Biologists know that there is a glycolytic cycle. The fluctuations in the concentration of ADP and ATP are determined by processes that activate ADP and inhibit ATP.

Often, we assume that a biological cell is homogeneous because molecules within it move freely. However, we forget that just as there are waves in space, matter, and energy, there are also waves in the concentration of certain molecules in the cell. It is entirely possible that during DNA replication, local concentrations of the required amino acids arise near DNA polymerase. It is also possible that the concentration of amino acids serves as a driver for DNA replication. The activity of specific proteins during their binding occurs very rapidly, within milliseconds, at most, a few seconds. Upon release, they can remain at the reaction site for a significant amount of time, thanks to these concentration waves. It is important to remember that these are not two-dimensional waves but three-dimensional, volumetric ones. Such states are referred to as "strange attractors" (Prigogine, 1984).

When a cell requires symmetry, it is forced to contend with spatial waves (for example, when pulling chromosomes to the poles before cell division.) To achieve this, the cell uses microtubules, which, in turn, also form and disassemble in a wave-like manner. Thus, the seemingly random movement of molecules, due to self-organization, symmetry disruption, and spatial waves, begins to adhere to strict biological laws. This is how most processes in a living cell occur.

A striking example is the assembly and disassembly of nucleoli depending on the phase of cell division. During the M-phase, the nucleolus is repressed, and its constituent proteins participate in other processes. During telophase, rDNA transcription resumes, and the nucleolus reassembles.

Research on molecular movement inside living cells demonstrates the fundamental possibility of organizing directed movement based on random motions. Stochastic mobility of molecules contributes to the creation of macroscopic order (Misteli, 2001; Арифулин, 20180.

Let's consider another simple example from everyday life. Ask a specific person to imagine a dog. Then ask another person to do the same. The images of the "dog" will almost never exactly coincide between two different people. Why? The cause-effect relationship is straightforward: they were asked to imagine an object, and they imagined an object. However, in reality, the initial conditions for two different people are absolutely distinct. Each person's experience is unique. These questions were extensively discussed by Prigogine in the context of fractal attractors in examples of chemical reactions. The main idea here is that with even the smallest change in initial data, the system ends up in a completely different state, an attractor, and predicting this state seems impossible (Misteli, 2001).

Conclusions

We assert that chaotic motion enables life processes within the cell to occur orders of magnitude faster than in a stable state where cell content remains motionless. DNA polymerase, for instance, cannot swim through the cell nucleus in search of necessary components; it is tethered to the DNA strand itself. Hence, these components must "search" for the precise location where they are needed.

Ultimately, chaotic molecular motion within the cell, along with their concentration, is influenced by both global processes (such as external temperature and illumination,) and minor fluctuations in concentration, spatial arrangement, attraction force, external molecule concentration, molecular movement speed within the cell, concentration auto-oscillations, and so forth. It is crucial to understand that in non-equilibrium states, even a very slight disturbance can serve as a trigger for new processes (cell division, protein production, etc.).

Many significant processes are known to biologists, but we still lack understanding of which "noise" effects affect the cell and how they can act as triggers. When studying processes in living cells, it is necessary to build models that account for all known periodic and non-periodic disturbances of the system. We cannot construct a model in the common variant where the researcher disregards insignificant processes. It is not always possible to suffice with a simple dynamic model.

The main conclusion we reach is that all living things cannot be considered systems because there is no predefined goal and it is impossible to define absolutely all elements and processes, as well as their interactions. On the other hand, when modeling, it is impossible to exclude insignificant processes, elements, external influences, and even quantum processes within living organisms. This paradox cannot be resolved with existing research technologies, but it is possible to significantly expand the model using modern computational power capable of analyzing hundreds and thousands of elements, interactions, external and internal factors.

The second conclusion arising from the systems approach is that the model, which is studied as a system, must constantly change. That is, its structure, connections, external and internal influences must change. This new dimension adds immense complexity to the study of future systems.

Questions for discussion

In practice, it turns out that some proteins or amino acids may appear where they theoretically shouldn't be. Experiments con-

ducted using GFP (Green fluorescent protein) have shown that proteins needed only in nucleoli can not only appear but also accumulate outside nucleoli. Such situations are usually dismissed by researchers as they are experimental errors. However, upon closer examination, it becomes clear that due to "chaotic" movement, these proteins first end up in areas of the cell where they are not used, and then accumulate to perform functions in the cell that researchers are not yet aware of. This is essentially a new area of cellular biology that requires a lot of work from interested researchers.

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