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Short Communication

The Problem of Time at the Molecular Level

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Abstract

According to recent experiments into stem and tumor cells, the asymmetry of time could be an important factor in the cellular world. In this paper an alternative idea is proposed to explain some mechanisms that are not well understood today.

Keywords: Time asymmetry; Cells; Molecular level

Description

Thermodynamics is the branch of physics that studies the effects of temperature, pressure and volume of physical systems on a macroscopic level. The amount of entropy of any thermodynamically isolated system tends to increase over time, which would indicate that time has a direction, that there is a temporal asymmetry.

Ilya Prigogine [1,2] proposed that irreversibility and entropy differ from those of traditional physics. He argued that, at the macroscopic level, the universe of non-equilibrium is coherent. Everything seems clear at the macroscopic level; however, on a microscopic scale, since the amount of energy involved in the processes is so small, it is more difficult to say that entropy is increasing and that, as a consequence, time is moving forward.

Lately, important breakthroughs were made in cellular biology, precisely on the subject of molecular mechanisms that determine the cellular arrow of time. Cells function and split thanks to proteins. The instructions to produce proteins are coded in DNA, they are the so-called genes. But not all proteins are produced at the same time. There are highly specialized proteins that are only produced in neurons, while others are produced in blood cells. Some proteins are expressed everywhere, while others are not produced in specific "places", but in specific "moments".

The RNA molecule plays a central role in molecular biology, performing essential tasks in the transcription, translation and replication processes. Recent experiments based on single molecule manipulation generated important information that could have not been produced otherwise. A popular single molecule manipulation technique is optical tweezers microscopy. With this technique, the mechanical properties of the molecule can be analyzed to obtain information about the structure, stability and interactions during the formation of such structure. In these experiments, called stretching experiments, a mechanical force is applied at both ends of an RNA molecule. Basically, the value of the force applied grows linearly until the molecule unfolds. If the process is reversed, relaxing the tension applied on the system, the molecule folds back again. The information obtained from these experiments is force as a function of distance from end to end of the system. Temporal asymmetry is described more accurately than a simple measurement of average entropy, since average entropy is affected by abnormal events.

The entangled RNA unfolds really slowly; the process is essentially of temporal asymmetry. It was proven that this process generates a great average dissipation or entropy increase, and a small temporal asymmetry, as it would be intuitively expected due to slow traction. Could this be the key to the longevity of tumoral cells and stem cells? This is still uncertain, but there have been many breakthroughs on these topics, as we can see, and an interesting space for ideas emerged.

The high sensitivity of the so-called optical tweezers allows sub-nanometric movements and rotations [3]. This has opened the door to a lot of research on biochemical and biophysical processes, on the mechanical properties of nucleic acids and proteins, and on the behaviour of different molecular nanomachines and nanomotors that work within the cells. Optical tweezers have been used, for instance, to measure the force needed to stretch, compress or untangle single or double DNA and RNA strands, and to perform a controlled hybridization or dehybridization of both strands of a DNA double helix.

Feng and Crooks [4] created a method to accurately measure the time asymmetry at the microscopic level. Using a new measurement and testing method, they sought to prove that time moves forward even when entropy decreases. On a microscopic scale and for some intervals, entropy can actually decrease. To this aim, they employed experimental methods [4,5] to analyze how an RNA molecule folds and unfolds when held by its ends. They discovered that, at certain intervals, entropy can actually decrease, while the general entropy increases on average.

They started researching the increase of energy dissipation in several distributions and proved that, at certain intervals, entropy actually decreased, so that while time moves forward in the macroscopic world, the direction of time becomes confusing at the scale of a single molecule. They analyzed temporal asymmetry in an experiment with a single RNA molecule. They defined temporal asymmetry as the Jensen-Shannon divergence between probability distributions of the trajectory of an experiment [5].

Continuing with the previous calculations [6,7], but consistent with low temperatures, we can see that the equations are reduced almost naturally to zero entropy, and this could eventually lead to

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an inversion in the arrow of time, opening the possibility for this to be an alternative explanation for why some cells could become hypothetically immortal.

If, on a molecular and cellular level, the arrow of time raises these questions, many of the current controversies and doubts that arise when interpreting certain characteristics of cells could be explained otherwise; for stem cells and tumor cells, this would be very important, since with current knowledge it is practically impossible to do so.

The fact that many times RNA is seen to stretch and compress without the influence of external forces such as those applied on experiments leads to suspect that the inversion of the arrow of time could be playing an important part. This could have an influence on stem cells and prevent the wear and tear produced by the evolution of time. The question is if the arrow of time is related with tumor cells and stem cells, and if this relationship could provide an alternative explanation to their mysteries.

There is a whole body of research assuming that stem cells are involved with cancer, based on the similar behaviour of stem cells and tumor cells. They both show an unlimited capacity to split, are very sensitive to the cellular medium where they grow and many of the genes activated on stem cells are also activated on tumor cells.

The abnormal behaviour of tumor cells is due, in large part, to genetic alterations and dysfunctional functioning. The stretching and compression caused by the arrow of time could be the cause of the dysfunctional operation. There is still no convincing explanation for cancer as the result of a gradual loss of cellular self-control. We pose the idea that the change in entropy at the local level could influence this observable disorder, for example in tumour cells. It is important to remember that the decrease in entropy is at the molecular level. This paper does not challenge the widely accepted notion that cancer cells have increased entropy, this is accepted by all [8,9].

Conclusion

Concluding, on a microscopic scale, since the amount of energy involved in the processes is very small, it is very difficult to say that the entropy is always increasing. The above-mentioned experiments determined that, for some brief intervals, entropy may decrease, even if global entropy increases, and this is important because it might explain some strange behaviour. As time does not have a clear direction in these cases, this could be an alternative explanation, for lack of a definitive one. In general, time goes inexorably in one direction [10], since in the history of the universe and in complex systems, the temporal evolution is associated with the increase of entropy. In other words, with the passage of time, disorder always grows from a more orderly initial situation. However, it is also clear that the temporal direction becomes confusing at the molecular level.

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