Evolutionary role of the nucleus

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Communication is of great importance in cells: it is matter of survival. Cells communicate each other in many ways. Inside the cell the information proceeds through the form of signal transduction pathways. We consider a possible role of the nucleus in the regulation of the flow of information at the last step of signal transduction pathways. In particular, we evaluate the importance of clarity for the report about the environmental conditions and the relative response of cells using over-estimating and under-estimating probabilities concepts.

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Introduction

Signal transduction occurs when an extracellular signaling molecule activates a specific receptor on the membrane or inside the cell. The signal is now amplified by a series of kinase at every step. This cascade is finally able to regulate the activation of transcription factors (TF). This allows TF to (enter into the nucleus in the case of eukariyota and) bind specific regions of DNA and exert their action: namely to induce or inhibit gene transcription. Protein levels as well as mRNA levels are matter of investigation in many biological laboratories every day, however the interpretation of the all process remains to be elucidated. For example, bacteria need to receipt environmental conditions as nutrients to be able to adapt their enzymatic apparatus as a consequence. The response mechanisms had sensibly evolved in eukaryotic cells, in fact they developed a nucleus and react as a tissue.

Background

The nucleus is enclosed by the nuclear envelope contiguous with the endoplasmic reticulum. The channel for bidirectional trafficking is the nuclear pore complex, a mechanism of mechanical support (lamins) and of chromosomal positioning and segregation (Devos, Graf et al. 2014). Many models have been offered for nuclear origins and the events underlying the acquisition of an endomembrane system (Devos, Dokudovskaya et al. 2004, Embley and Martin 2006, Field, Sali et al. 2011, Hoelz, Debler et al. 2011, Wilson and Dawson 2011, Koumandou, Wickstead et al. 2013, Field, Koreny et al. 2014). Moreover, signal transduction pathways evolved to use all the strategies to ensure the receipt of the signal. Imagine that you and your friends have to decide who will receive a gift (of course everyone would like to). Everyone will write his name on the paper and there will be an extraction. Which strategies can you adopt in order to maximize the probability to be the selected winner? First you can write your name on a piece of paper bigger than the others. Another option can be to put in the ballet box more than one note with your name. Cells adopt similar strategies to optimize signal transduction pathways. Some proteins as mTOR complexes are big, contemporary, the number of activated kinases increments. But

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then the information flow have to reach the nucleus, however TFs encounter a barrier: the nuclear envelope (with only nuclear pores through which they can enter).

Many researchers during the years tried to create models to describe signal transduction pathways. Hormoz (Hormoz 2013) shows that cross talk and interference enhance information capacity of a signaling pathway. In particular, he suggests that overlapping sites on DNA, where transcription factors (TFs) bind to, interact and synergistically control transcription of a target gene. Using concepts from information theory, he demonstrates that this maximizes information flow in a noisy network. In fact, gene expression is an inherently noisy process due to thermal fluctuations and the small number of molecules involved. A consequence of multiple TF interacting at overlapping binding sites is that their binding noise becomes correlated. Wilson (Wilson and Dawson 2011) suggests that the evolution of nuclear structure was tightly coupled to genome partitioning during mitosis.

The first eukaryotic common ancestor (FECA) had no nuclear structure and have given rise to a cell with fully functional nucleus (LECA - last eukaryotic common ancestor) (Neumann, Lundin et al. 2010). The evolution of nuclear structure followed different pathways as seen in the six living eukaryotic supergroups (Hampl, Hug et al. 2009). The proteins that require to be imported into the nucleus present a specific sequence called NLS (nuclear localization sequence) recognized by importins. The import process requires a GTPase, so the process requires energy.

Studies of human reaction to low probability (rare) events reveal an interesting difference between judgment and decision-making in repeated settings (Barron and Yechiam 2009). Judgments (probability estimations) appear to reflect over-sensitivity to rare events (Erev, Wallsten et al. 1994). On the other hand, decision-making from experience tends to reflect underweighting of (insensitivity to) rare events (Barron and Erev 2003, Hertwig, Barron et al. 2004, Weber, Shafir et al. 2004).

Results

Here we consider an alternative explanation for the creation of the nucleus taking into account the estimation probability. Imagine a ballot box with 10 black and 2 white balls. However you ignore what it contains (except for an idea of the total number of the balls), the aim is to guess it with the higher confidence in the shorter time interval. It could be reasonable to plan to extract about 1/4 of the balls (3 in our case). At the first extraction you will obtain a black ball with an higher probability (10/12). At the second attempt it will happen the same: you will have a black with a probability greater or equal to 9/11. If this happens the probability of getting a black at the third extraction will be greater or equal to 8/10. The nucleus does the same: the aim is to establish which TFs have been activated (the better approximation the more fast than possible).

It is known the role of nuclear cytoplasmic ratio as a diagnostic indicator. In particular the nuclear cytoplasmic ratios (N/C) and the nuclear volume densities (VvN) are calculated from the following equations:

$$N/C = \frac{Anuc}{Acell - Anuc} \qquad Vv_N = \frac{Anuc}{Acell}$$

These parameters varies from a cell type to another and towards cells life and differentiation. However the mean value is of about 1/4, as the number of balls that have been extracted from the ballot box in our example.

In this way the cell (knowing nothing about the TF that have been activated) tends to overestimate the number of the more abundant TF and to underestimate the minority groups. In fact, if I had to guess the ballot box content I would say that there are probably only black balls inside.

Conclusions

These considerations lead us to suggest that cells react to one stimulus a time, this delays the shift from a condition to another, but ensure a more precise response. For example, this mechanism permits to avoid the contemporary transcription of genes that cause to opposite effects: if the blood becomes rich of nutritive substances, a muscle cell accelerates its metabolism (inducing the transcription of genes related to metabolism) and not autophagy nor protein degradation (phenomena occurring when other tissue needs nutrients and muscle cells sacrifice themselves). On the other hand a near cell can concentrate its response on autophagy. In other words, eukaryotic cells have a more focused reaction, although a tissue present an heterogeneous answer, while bacteria must react contemporary to all the stimuli to survive.

With this perspective the nucleus could represent a physical barrier for TF, so for the signals to determine a response. The more abundant activated TF would be able to determine a response, instead in prokaryots their relative abundance causes a response proportional to the different stimuli. This mechanism can be an evolutionary strategy to optimize the cellular response to the environment.

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