The information isn’t lost in gene expression

Massimo Fioranelli*, Maria Grazia Roccia

Department of Nuclear, Sub-nuclear and Radiation Physics, Guglielmo Marconi University, Via Plinio, 44-00193, Rome, Italy

ARTICLE INFO

Keywords:
Gene expression
Information loss
DNA
RNA
Protein

ABSTRACT

The present question is the possibility of information loss in gene expression? Information loss in the gene expression disrupts the cellular dynamics and can lead to serious defects, including cancer. Using Gottesman and Preskill method for calculating information loss in black holes, a mechanism for calculating the amount of information transformation in gene expression is proposed. In this proposal, there are three different Hilbert spaces that belong to degrees of freedom of DNA, RNA, and protein. The genetic sequence of the DNA is transcribed into protein at two stages. At first stage it is shown that the internal stationary state of the cell can be represented by a maximally entangled two-mode squeezed state of DNA and mRNA. At second stage, the state of the cell is described by a maximally entangled two-mode squeezed state of mRNA and protein. The amount of information transformation can be obtained by projecting the state at first stage on the state at second stage. Evidently for all finite values of the transcription factor concentration y, binding energy E and free energy F of the transcription factor, the information isn’t lost in gene expression.

1. Introduction

The information necessary for the functioning of a given organism is encoded in its DNA [1,2]. Gene expression is a process by which this information is extracted from the DNA in order to synthesize proteins that carry out specific functions in the cell. The expression of genes in cells is controlled mainly by binding and unbinding of regulatory proteins, called transcription factors (TFs), to specific short DNA sequences, called binding sites [3–6]. These regulatory proteins can act either as activators, which means they increase the rate of expression of the genes, or as repressors that decrease the rate of expression of the regulated genes. The genetic sequence of the DNA is transcribed into mRNA by a holoenzyme called RNA polymerase. Activators often act by recruiting the polymerase, whereas repressors often act by sterically blocking the polymerase from binding. Ribosomes translate mRNA strands into proteins [6].

The present question is the possibility of information loss in gene expression? Information loss in the gene expression disrupts the cellular dynamics and can lead to serious defects, including cancer. Using Gottesman and Preskill method [7] we suggest a mechanism to calculate the amount of information transformation in gene expression. In this proposal, there are three different Hilbert spaces that belong to degrees of freedom of DNA, RNA, and protein. We define annihilation and creation operators for information in each space and obtain the relation between these operators during transcribing genetic sequence of the DNA into mRNA and then transcribing information of the mRNA into protein. We derive the entangled state on DNA and mRNA spaces at first stage and the entangled state on mRNA and protein spaces at second stage. The amount of information loss is obtained by projection the first state onto the second state.

The outline of the paper is as follows. In section II we obtain the entangled two-mode squeezed states on DNA and mRNA Hilbert spaces of cells. Then we study the entangled two-mode squeezed states on mRNA and protein Hilbert spaces of the cells in section III. Finally we calculate the information transformation from DNA to protein in section IV. The last section is devoted to summary and conclusion.

2. The entangled two-mode squeezed states on DNA and mRNA Hilbert spaces of cells

The primary step in the production of a protein is the transcription of a gene from the DNA template to a mRNA molecule by activating RNA-polymerase by transcription factors. Transcription factors are proteins which bind to specific sites on DNA. These binding sites are located in the so-called regulatory region of a gene, which for yeast typically extends over several hundred nucleotides before the starting point of transcription. A fully assembled set of transcription factors will attract and activate the machinery (called RNA-polymerase) which transcribes the DNA template to an mRNA molecule. When one site is occupied by transcription factors, the regulated gene will get

* Corresponding author.
E-mail address: massimo.fioranelli@gmail.com (M. Fioranelli).

https://doi.org/10.1016/j.bbrep.2020.100749
Received 16 December 2019; Received in revised form 24 January 2020; Accepted 25 February 2020
2405-5808/ © 2020 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).
transcribed into mRNA. Thus the probability of this transcribing is equal to the probability for a site to be occupied.

Assuming that a transcription factor may either be bound at a binding site, or be suspended in solution or bound non-specifically elsewhere on DNA, the probability of a given site being occupied is given by elementary statistical mechanics \([5,6]\) as

\[ n_{\text{occupied}}(y) = \frac{ye^{\mu E}}{ye^{\mu E} + e^{-\mu F}} \]

(1)

and depends on the transcription factor concentration \(y\), binding energy \(E\) and a free energy \(F\) of the transcription factor in solution or bound elsewhere.

Now we want to consider the transcribing information of DNA into mRNA. To this end we construct two Hilbert spaces with a set of operators of creation/annihilation that have the same commutation properties. The total Hilbert space of cell at this stage is the tensor product of the two spaces \(H_{\text{cell}} = H_{\text{DNA}} \otimes H_{\text{mRNA}}\), where in this case \(H_{\text{cell}}\), \(H_{\text{DNA}}\) and \(H_{\text{mRNA}}\) denote the physical quantum states spaces of cell, DNA and mRNA respectively.

The commutation relations satisfied by the various operators in these spaces are:

\[
\begin{align*}
[\alpha^{\dagger}_{\text{DNA},E,F,Y}, \alpha_{\text{DNA},E,F,Y}] &= 0, \\
[\alpha^{\dagger}_{\text{DNA},E,F,Y}, \alpha^*_{\text{DNA},E',F',Y'}] &= 0, \\
[\alpha^*_{\text{DNA},E,F,Y}, \alpha_{\text{DNA},E',F',Y'}] &= 0, \\
[\alpha^{\dagger}_{\text{mRNA},E,F,Y}, \alpha_{\text{mRNA},E,F,Y}] &= 0, \\
[\alpha^{\dagger}_{\text{mRNA},E,F,Y}, \alpha^*_{\text{mRNA},E',F',Y'}] &= 0, \\
[\alpha^*_{\text{mRNA},E,F,Y}, \alpha_{\text{mRNA},E',F',Y'}] &= 0
\end{align*}
\]

Where \(\alpha^{\dagger}_{\text{DNA},E,F,Y}\) and \(\alpha_{\text{DNA},E,F,Y}\) are annihilation and creation operators that act on DNA space of cells respectively. Also \(\alpha^{\dagger}_{\text{mRNA},E,F,Y}\), \(\alpha^*_{\text{mRNA},E,F,Y}\) are annihilation and creation operators that act on mRNA space of cells respectively. The indices \(E,F,Y\) are binding energy, free energy and concentration of transcription factor respectively. The Bogoliubov transformation between these operators can be written as following:

\[
\alpha^{\dagger}_{E,F,Y} = c^{\dagger}_{E,F,Y} \alpha^{\dagger}_{\text{DNA},E,F,Y} + \sinh(r_{E,F,Y}) \alpha_{\text{mRNA},E,F,Y}
\]

where \(c^{\dagger}_{E,F,Y}\) is annihilation operator that acts on the Hilbert space of cell. By using the Bogoliubov transformation, the condition

\[
\alpha^{\dagger}_{E,F,Y} |\text{cell}\rangle_{\text{DNA} \otimes \text{mRNA}} = 0
\]

(4)

give rise to the so called thermal state conditions:

\[
\cosh(r_{E,F,Y}) \alpha^{\dagger}_{\text{DNA},E,F,Y} + \sinh(r_{E,F,Y}) \alpha_{\text{mRNA},E,F,Y} = |\text{cell}\rangle_{\text{DNA} \otimes \text{mRNA}}
\]

(5)

or equivalently

\[
\alpha^{\dagger}_{\text{DNA},E,F,Y} + \tanh(r_{E,F,Y}) \alpha_{\text{mRNA},E,F,Y} = |\text{cell}\rangle_{\text{DNA} \otimes \text{mRNA}} = 0
\]

(6)

Now, we assume that when information is transcribed of DNA into mRNA, the cell state \(|\text{cell}\rangle_{\text{DNA} \otimes \text{mRNA}}\) is related to the cell vacuum \(|0\rangle\) by

\[
|\text{cell}\rangle_{\text{DNA} \otimes \text{mRNA}} = F(\alpha^{\dagger}_{\text{DNA},E,F,Y}, \alpha_{\text{mRNA},E,F,Y}) |0\rangle
\]

(7)

where \(F\) is some function to be determined later.

From \([\alpha^{\dagger}_{\text{DNA},E,F,Y}, \alpha_{\text{DNA},E,F,Y}] = 1\), we obtain \([\alpha^{\dagger}_{\text{DNA},E,F,Y}, (\alpha^*_{\text{mRNA},E,F,Y})^m] = 1\). Then using equations (6) and (7), we get the following differential equation for \(F\):

\[
\frac{\partial F}{\partial \alpha^{\dagger}_{\text{DNA},E,F,Y}} - \tanh(r_{E,F,Y}) \alpha_{\text{mRNA},E,F,Y} = 0
\]

(8)

and the solution is given by

\[
F = \exp(tanh(r_{E,F,Y}) \alpha^{\dagger}_{\text{DNA},E,F,Y})
\]

(9)

By substituting (9) into (7) and by properly normalizing the state vector, we get

\[
|\text{cell}\rangle_{\text{DNA} \otimes \text{mRNA}} = e^{\exp(tanh(r_{E,F,Y}) \alpha^{\dagger}_{\text{DNA},E,F,Y})} |0\rangle
\]

\[
= \frac{1}{\cosh(r_{E,F,Y})} \sum_m \tanh^m(r_{E,F,Y}) \alpha_{\text{mRNA},E,F,Y}^m |\text{m}(E,F,y)\rangle_{\text{DNA}} \otimes |\text{m}(E,F,y)\rangle_{\text{mRNA}}
\]

(10)

where \(|\text{m}(E,F,y)\rangle_{\text{DNA}}\) and \(|\text{m}(E,F,y)\rangle_{\text{mRNA}}\) are orthonormal bases (normal mode solutions) for \(H_{\text{DNA}}\) and \(H_{\text{mRNA}}\) respectively. Now we intend to determine \(\tanh(r_{E,F,Y})\) by calculating the probability for transcribing information into mRNA and comparing it with equation (1). We can calculate this probability as the following:

\[
n_{\text{mRNA}} = n_{\text{occupied}} \Rightarrow \sinh^2(r_{E,F,Y}) = \frac{ye^{\mu E}}{ye^{\mu E} + e^{-\mu F}} \Rightarrow \tanh(r_{E,F,Y}) = \sqrt{1 - \frac{1 - ye^{\mu E}}{1 + ye^{\mu E} + e^{-\mu F}}}
\]

(12)

As mention before when one site of DNA is occupied, it’s information will get transcribed into mRNA. Thus the probability of transcribing information into mRNA is equal to the probability for a site to be occupied.

\[
n_{\text{mRNA}} = n_{\text{occupied}} \Rightarrow \sinh^2(r_{E,F,Y}) = \frac{ye^{\mu E}}{ye^{\mu E} + e^{-\mu F}} \Rightarrow \tanh(r_{E,F,Y}) = \frac{1}{\sqrt{1 - \frac{1 - ye^{\mu E}}{1 + ye^{\mu E} + e^{-\mu F}}}}
\]

(12)

Equation (10) shows that the internal stationary state of the cell can be represented by a maximally entangled two-mode squeezed state of DNA and mRNA. The entanglement between these molecules depends on binding energy, free energy and concentration of transcription factor.

3. The entangled two-mode squeezed states on mRNA and protein Hilbert spaces of cell

Now we consider the second step in extracting information from the DNA in order to synthesize proteins. At this stage, the mRNA molecule will be translated to a protein. The proposed reaction scheme for this translation is shown in Fig. 1 [8]. Before protein production, mRNA molecules may bind to form a complex with rate \(\alpha\), the dissociation rate for this complex is \(\beta\). The probability for translating one protein from a...
single mRNA before it decays can be obtained as [8]:

$$n_{\text{protein}} = \frac{k_p(\mu_c + \beta) + k_p \alpha}{\mu_m(\mu_c + \beta) + \mu_c}$$  \hspace{1cm} (13)$$

In this scheme, the parameters $k_p$ and $k_{p2}$ are the rates of protein production from the mRNA in free and bound states and $\mu_m$ and $\mu_c$ are the corresponding decay rates.

Now we discuss the transcribing information of mRNA into protein. For this purpose we construct two Hilbert spaces with a set of operators of creation/annihilation that have the same commutation properties. The total Hilbert space of cell at this stage is the tensor product of the production from the mRNA in free and bound states and $H_{\text{protein}}$ denote the physical quantum states spaces of protein and mRNA respectively.

The commutation relations satisfied by the various operators in these spaces are:

$$\alpha_{\text{protein}}^{\dagger}\alpha_{\text{mRNA}} + \alpha_{\text{mRNA}}^{\dagger}\alpha_{\text{protein}} = 0,$$  \hspace{1cm} (14)

$$\alpha_{\text{protein}}^{\dagger}\alpha_{\text{mRNA}} = \delta_{\alpha\alpha}^{\dagger}\delta_{\alpha\alpha},$$  \hspace{1cm} (15)

$$\alpha_{\text{mRNA}}^{\dagger}\alpha_{\text{protein}} = \delta_{\alpha\alpha}^{\dagger}\delta_{\alpha\alpha},$$  \hspace{1cm} (16)

where $\alpha_{\text{protein}}^{\dagger}$ and $\alpha_{\text{mRNA}}^{\dagger}$ are annihilation and creation operators that act on protein space of cells respectively. Also $\alpha_{\text{protein}}^{\dagger}$ and $\alpha_{\text{mRNA}}^{\dagger}$ are annihilation and creation operators that act on mRNA space of cells respectively. The Bogoliubov transformation between these operators can be written as follows:

$$\alpha_{\text{cell}}^{\dagger}\alpha_{\text{mRNA}} + \alpha_{\text{mRNA}}^{\dagger}\alpha_{\text{cell}} = \begin{cases} \cosh(n_{p1,k_{p2},p_{2},p_{2},p_{2}}) \alpha_{\text{mRNA}}^{\dagger}\alpha_{\text{protein}} + \sinh(n_{p1,k_{p2},p_{2},p_{2},p_{2}}) \alpha_{\text{protein}}^{\dagger}\alpha_{\text{mRNA}} & \text{if } n_{p1,k_{p2},p_{2},p_{2},p_{2}} > 0 \\ \cosh(n_{p1,k_{p2},p_{2},p_{2},p_{2}}) \alpha_{\text{mRNA}}^{\dagger}\alpha_{\text{protein}} - \sinh(n_{p1,k_{p2},p_{2},p_{2},p_{2}}) \alpha_{\text{protein}}^{\dagger}\alpha_{\text{mRNA}} & \text{if } n_{p1,k_{p2},p_{2},p_{2},p_{2}} < 0 \end{cases}$$  \hspace{1cm} (17)

where $\alpha_{\text{cell}}^{\dagger}\alpha_{\text{mRNA}}$ is annihilation operator that acts on the Hilbert space of cell. By using the Bogoliubov transformation, the condition

$$\alpha_{\text{cell}}^{\dagger}\alpha_{\text{mRNA}} |\text{cell}\rangle_{\text{mRNA}+\text{protein}} = 0$$  \hspace{1cm} (18)

Gives rise to the so called thermal state conditions:

$$\cosh(n_{p1,k_{p2},p_{2},p_{2},p_{2}}) \alpha_{\text{mRNA}}^{\dagger}\alpha_{\text{protein}} + \sinh(n_{p1,k_{p2},p_{2},p_{2},p_{2}}) \alpha_{\text{protein}}^{\dagger}\alpha_{\text{mRNA}} = 0$$  \hspace{1cm} (19)

or equivalently

$$\alpha_{\text{mRNA}}^{\dagger}\alpha_{\text{protein}} + \tanh(n_{p1,k_{p2},p_{2},p_{2},p_{2}}) \alpha_{\text{protein}}^{\dagger}\alpha_{\text{mRNA}} = 0$$  \hspace{1cm} (20)

With similar calculations for the first stage we calculate the stationary state of cell at second stage which is a maximally entangled two-mode state on mRNA and protein Hilbert spaces as:

$$|\text{cell}\rangle_{\text{mRNA}+\text{protein}} = e^{\frac{n_{\text{protein}}}{n_{p1,k_{p2},p_{2},p_{2},p_{2},p_{2}}}} \sum_{p_{2},p_{2},p_{2}} \tanh(n_{p1,k_{p2},p_{2},p_{2},p_{2},p_{2}}) |m(k_{p1},k_{p2},p_{2},p_{2},p_{2},p_{2})\rangle_{\text{mRNA}} \otimes |m(k_{p1},k_{p2},p_{2},p_{2},p_{2},p_{2})\rangle_{\text{protein}}$$  \hspace{1cm} (21)

where $|m(k_{p1},k_{p2},p_{2},p_{2},p_{2},p_{2})\rangle_{\text{mRNA}}$ and $|m(k_{p1},k_{p2},p_{2},p_{2},p_{2},p_{2})\rangle_{\text{protein}}$ are orthonormal bases (normal mode solutions) for $H_{\text{mRNA}}$ and $H_{\text{protein}}$ respectively. We can obtain $\tanh(n_{p1,k_{p2},p_{2},p_{2},p_{2},p_{2}})$ by calculating the probability for transcribing information to protein and comparing it with equation (13). We can obtain this probability as following:

$$n_{\text{protein}} = \text{probability of protein} \otimes |\text{cell}\rangle_{\text{mRNA}+\text{protein}}$$

4. The information loss for DNA in cells

Now we can calculate the resulting information transformation from DNA to protein. At first stage, there is an entanglement between the DNA and mRNA spaces of cell. At second stage, we can describe the state of the cell as an entangled state of both mRNA and protein spaces of cell.

Using Horowitz and Maldacena mechanism for black holes, we describe the unknown effect of transcribing genetic sequences of DNA by an additional unitary transformation $S$ [9]. Also by using Gottesman and Preskill idea we introduce a unitary transformation $U$ [7] to describe interactions between DNA and mRNA molecules.

$$|\text{DNA}+\text{mRNA}\rangle|\text{cell}\rangle = (|\text{DNA}+\text{mRNA}\rangle|\text{cell}\rangle |S \otimes I)U$$  \hspace{1cm} (22)

By extending Gottesman and Preskill method to gene expression, we calculate the information transformation from DNA to protein.

$$T_{\text{gene}} = \langle \text{cell} | |\text{cell}\rangle_{\text{DNA}+\text{mRNA}} \otimes |\text{DNA}+\text{mRNA}\rangle |\text{cell}\rangle_{\text{DNA}+\text{mRNA}}$$

$$= \langle \text{cell} | \text{DNA}+\text{mRNA} \otimes |\text{DNA}+\text{mRNA}\rangle |\text{cell}\rangle_{\text{DNA}+\text{mRNA}}$$

$$= \sum_{\text{cell} \text{DNA}+\text{mRNA} \text{protein}} \text{tanh}(n_{p2,k_{p2},p_{2},p_{2},p_{2},p_{2}})$$
If information transformation from the collapsing matter to the state of outgoing Hawking radiation be complete, the value of $f$ should be one. Evidently for all finite values of the transcription factor concentration $y$, binding energy $E$ and free energy $F$ of the transcription factor, the value of $f$ is unity and so information isn’t lost in gene expression.

5. Summary and conclusion

In this manuscript, we extend the Gottesman and Preskill method for calculating information loss in black holes to gene expression. We calculate the amount of information transformation from DNA to protein in cells. To this end, we introduce three Hilbert spaces that belong to degrees of freedom of DNA, RNA, and protein. At first stage we show that the internal stationary state of the cell can be represented by a maximally entangled two-mode squeezed state of DNA and mRNA. At second stage, the state of the cell can be described by a maximally entangled two-mode squeezed state of mRNA and protein. The amount of information transformation can be obtain by projecting the state at first stage on the state at second stage. We observe that information isn’t lost in gene expression.

Information loss has many effects on the activity of cells and gene expression within the nucleus. For example, if during replication, some errors occur in genetic sequences or choosing base pairs, some new DNAs are emerged which are different respect to original ones. This causes that number of binding sites for polymerase, RNAs and proteins increases or decreases and the velocity of transcription, translation and replication grows or decreases. Consequently, the velocity of producing new cells grows or decreases and some diseases like the cancers are emerged. For melanocytes, information loss causes to some destructions in the structure of produced DNAs during replication. These destructions may be similar to those seen in exposed cells to ultraviolet ray and cause to melanoma.

Author statement

This is a paper regarding new mechanism for exchanging information between genes. There is no conflict of interest.

Declaration of competing interest

There is no conflict of interest.

References

[1] J.R. Broach, Cell 119 (2004) 583.
[2] R.G. Roeder, Nat. Med. 9 (2003) 1239 Lewin. ,B Genes IX (2007), Jones and Bartlett Publishers, Boston, MA.
[3] T.I. Lee, et al., Science 298 (2002) 799 Harbison C. T. et al., Nature , 431 (2004) 99.
[4] G.D. Stormo, DNA binding sites: representation and discovery, Bioinformatics 16 (2000) 16–23 Hertz G., G. Stormo, Bioinformatics , 15 (1999)563.
[5] Jose M.G. Vilar, Leonor Saiz, Phys. Rev. Lett. 96 (2006) 238103.
[6] Berg, Johannes Revised Version to Appear in Europhys. Lett.) arXiv: 0712. 3791) . Tkacik Gasper, Aleksandra M. Walczak, arXiv:1101.4240.
[7] D. Gottesman, J. Preskill, J. High Energy Phys. 3 (2004) arXiv:hep-th/0310281v2.