Symmetry and Dynamics in living organisms: The self-similarity principle governs gene expression dynamics

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Abstract

The ambitious and ultimate research purpose in Systems Biology is the understanding and modelling of the cell’s system. Although a vast number of models have been developed in order to extract biological knowledge from complex systems composed of basic elements as proteins, genes and chemical compounds, a need remains for improving our understanding of dynamical features of the systems (i.e., temporal-dependence).

In this article, we analyze the gene expression dynamics (i.e., how the genes expression fluctuates in time) by using a new constructive approach. This approach is based on only two fundamental ingredients: symmetry and the Markov property of dynamics. First, by using experimental data of human and yeast gene expression time series, we

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found a symmetry in short-time transition probability from time $t$ to time $t+1$. We call it self-similarity symmetry (i.e., surprisingly, the gene expression short-time fluctuations contain a repeating pattern of smaller and smaller parts that are like the whole, but different in size). Secondly, the Markov property of dynamics reflects that the short-time fluctuation governs the full-time behaviour of the system. Here, we succeed in reconstructing naturally the global behavior of the observed distribution of gene expression (i.e., scaling-law) and the local behaviour of the power-law tail of this distribution, by using only these two ingredients: symmetry and the Markov property of dynamics. This approach may represent a step forward toward an integrated image of the basic elements of the whole cell.

1 Introduction

The final goal in Systems Biology is the understanding and modelling of the cell’s system. In the cell, the expression level of genes plays a key role, since gene expression is a complex transcriptional process where mRNA molecules are translated into proteins, which control most of the cell functions. Recently, gene expression profiles for different types of cells of several organisms have been measured, and some experiments have also provided data about the fluctuation of expression level of thousands genes in time. Here, we propose a stochastic approach to gain insight into gene expression time series data, in order to uncover fundamental principles that govern the gene dynamics.

Although many complex systems may be governed by non-stochastic processes, in the gene expression problem the random variation is reasonable, plays a relevant role in cellular process, and furthermore stochastic noise (e.g., intrinsic and extrinsic) have recently been measured and studied theoretically [1, 2, 3, 4, 6]. For example, the expression level of thousands genes is very low, which creates intrinsic uncertainties in the number of expressed genes in the cells [7]. Furthermore, the number of molecules which are involved in signal transduction pathways fluctuates from $10^2$ to $10^4$. Therefore, the randomness connected with elementary molecular interactions and their amplification in the signaling cascade generates significant spatio-temporal noise. Therefore, the stochastic approach seems more plausible than the deterministic approach. Finally, we also note that the current experimental techniques also generate an additional source of fluctuation, which come from
the ubiquitous instrumental noise (which may be around 30% or more) from chip to chip with the current GeneChips technologies.

Currently, DNA microarray/GeneChips [8, 9] (like the pendulum clock of Hyugens used by Newton to uncover the dynamical laws written in his famous *Principia Mathematica*) offers the ability to monitor in time changes in expression level of large subsets of genes from a variety of organisms on a scale unattainable by other methods. In particular, experiments done on time series of absolute value of gene expression level studying the yeast mitotic cell cycle [10] and transcriptional regulation during human cell cycle [11] have provided a huge wealth of data to uncover general principles of gene expression dynamics.

In this article, by using these experimental data [10, 11], we have found the following interesting phenomena: 1) "Mean-Reverting" and "Extremely Value Jumps-More" mechanisms. These mechanisms are present in short-time fluctuation (i.e., how the gene expression level changes from time-step $t$ to time-step $t+1$). Surprisingly, these two mechanisms are governed by a symmetry: Self-similarity (see Fig. 2 and Fig. 3). By inserting this information (i.e., two mechanisms and the self-similarity symmetry) into the general stochastic partial differential equation (SPDE) which spontaneously emerges from Markov property, we found the fundamental equation for gene expression dynamics. This equation has a high predictive power. Here, we enumerate a couple of results. For example, the distribution solution of this equation $\rho^m(x)$ gives the distribution of expression level $x$ of genes which fluctuate around $m$ (i.e., their average expression is in the vicinity of the value $m$). This solution agrees with the experimental data shown later in Fig. 4 (for more details see Figs. 10, 11, and 12). Furthermore, we rebuild the observed global behaviour of gene expression distribution, which is characterized by the following relation $\rho^{cm}(x) = \frac{1}{c}\rho^m(x/c)$ (or as the more symmetric form $\rho^{cm}(x)dx = \rho^m(x/c)d(x/c)$). We call it scaling-law formula. This formula indicates that distribution of gene expression level also has the self-similarity structure (We can observe a repeating pattern of smaller and smaller parts that are like the whole, but different in size in Figs. 4, 10, 11, and 12), which is a direct consequence of the self-similarity symmetry in short-time transition probability (Fig. 2 and Fig. 3). In a sense, the self-similarity governs all the dynamical structure of gene expression phenomena, by means of Markov property. On the other hand, our model can predict sensitive aspects of gene expression systems. More precisely, our constructive model predicts that the tail of the distribution has a power-law tail $\rho^m(x) \propto x^{-4}$
(when $x \to \infty$), which is observed in experimental data (see Fig. 5).

2 Databases

**Databases.** We used experimental data from two well-known experiments on Yeast [10] and Human [11] organisms. The first experiment analysed cell cycle of the budding yeast *S. Cerevisiae*, where around 6220 genes were monitored. Data of absolute value of gene expression fluctuations were collected at 17 time points every 10 min intervals. Data was obtained from WWW site [http://genomics.standford.edu](http://genomics.standford.edu).

The second experiment identifies cell-cycle-regulated transcripts in human cells using high-density oligonucleotide arrays. Data are collected every 2 hours for 24 hours, what is equivalent to almost 2 full cell cycles. The number of genes monitored was around 35000, and data for absolute value of gene expression fluctuations was obtained from WWW site [http://www.salk.edu/docs/labs/chipdata](http://www.salk.edu/docs/labs/chipdata).

**Subgroups of Genes.** In order to explain in more detail our findings, let us observe Fig. 1. We see that gene expression time series for genes fluctuates around some mean value. Therefore, it seems natural to classify all the genes of human and yeast organisms into subgroups according to the time-averaged expression value of each gene denoted by $m$. We cluster the data of genes by using the mean value $m$. We made a group of genes composed by all the genes within 1% of the following values of $m$: 500, 1000, 1500, 2000. Furthermore, all the genes which are within 1% of the previous values of $m$ are called subgroups of genes. We also make more groups and subgroups of genes. We detail them as follows: within 2% of the values of $(m=2500, 3000)$, within 3% of the values of $(m=3500, 4000, 4500)$, within 4% of the values of $(m=5000, 5500, 6000)$ and within 5% of the values of $(m=7000, 8000, 9000)$.

3 Methods

Let $\{X(t), 0 \leq t < \infty\}$ be a stochastic process. For $(s > t)$, the conditional probability density function $p(y, s|x, t) = p(X(s) = y|X(t) = x)$ is defined as usual manner. For the matter of convenience, we often write $p(y, s)$ for $p(y, s|x, t)$.
Ito Stochastic Process. By observing Fig. 1, we see that the gene expression time series fluctuate around their own mean value, which is denoted by $m$. Therefore, we characterized the gene expression time series data by the mean value $m$. For each set of genes which fluctuates around the mean value $m$, we use the most general Stochastic Partial Differential Equation (SPDE) (see [12, 13, 14, 15, 16] for more details). More precisely, we respectively use the following general SPDE for each gene which fluctuates around mean value $m$ (gene whose average expression level is $m$):

$$dX^m(t) = \alpha^m(X^m(t))dt + \beta^m(X^m(t))dW(t),$$

(1)

where stochastic variable $X^m(t)$ denotes the gene expression level which has mean value $m$ and $W(t)$ denotes the Wiener process. Here $\alpha^m(x)$ denotes the drift (i.e., by starting with expression level $x$ at time $t$, it means the average change of expression level $x$ at time $t + \epsilon$) defined by

$$\alpha^m(x) = \lim_{\epsilon \to 0} \frac{1}{\epsilon} \int_{-\infty}^{\infty} (y - x)T^m_\epsilon(y, x)dy,$$

(2)

$\beta^m(x)$ denotes the diffusion (i.e., by starting with the expression level $x$ at time $t$, it means the average jumping size of expression level $x$ at time $t + \epsilon$) defined by

$$\beta^m(x) = \left( \lim_{\epsilon \to 0} \frac{1}{\epsilon} \int (y - x)^2 T^m_\epsilon(y, x)dy \right)^{\frac{1}{2}}.$$

(3)

Here, $T^m_\epsilon(y, x)$ is the short-time transition probability of genes fluctuating around $m$ defined by $T^m_\epsilon(y, x) = p^m(y, t + \epsilon|x, t)$ for sufficient small $\epsilon$. Details of the proof can be found in [12, 13, 14, 15, 16]. This equation allows us to predict long-time behaviour of gene expression dynamics, by using the short-time transition probability as follows.

How to use the SPDE Eq. (1). We can obtain the dynamical information of gene expression from experimental data of the short-time transition probability $T^m_\epsilon(y, x)$ ($\epsilon$ is sufficiently small and fixed), by the following procedure:

(i) Given the experimental data of the short-time transition probability, we obtain the drift $\alpha^m(x)$ and the diffusion $\beta^m(x)$ by using Eq. (2) and (3) respectively.
(ii) By inserting the drift $\alpha^m(x)$ and the diffusion $\beta^m(x)$ obtained in previous step into the most general SPDE (1), we obtain the specific equation for gene expression dynamics.

(iii) Solving this specific equation obtained in step two, we can obtain the dynamical information of gene expression.

4 Self-Similarity Symmetry

Next, for each set of genes which fluctuates around the mean value $m$, we compute the two most important quantities to characterize the gene expression fluctuations: 1) the drift $\alpha^m(x)$ and 2) the diffusion $\beta^m(x)$ from the experimental data [10, 11].

**Input data: Short-time transition probability.** From the experimental data [10, 11], we compute $T^m_r(y, x)$ for each set of genes which has mean value $m$. Next, from $T^m_r(y, x)$, we evaluate the drift $\alpha^m(x)$ and the diffusion $\beta^m(x)$ by using Eqs. (2) and (3). We show the results of the drift $\alpha^m(x)$ and the diffusion $\beta^m(x)$ in Fig. 2 and Fig. 3 respectively. (More precisely, see Fig. 6, 7, 8, 9). By observing these figures, we see that the drift $\alpha^m(x)$ and the diffusion $\beta^m(x)$ can be fitted by the following analytical expressions:

$$\alpha^m(x) = \mu(m - x) \quad (4)$$

$$\beta^m(x) = m((x/m - 1)^2 + b) \quad (5)$$

where $\mu = 1$ (resp. $\mu = 0.8$) and $b = 0.2 \sim 0.3$ (resp. $b = 0.2 \sim 0.3$) for human (resp. yeast) organism.

These results obtained by using experimental data are interesting, since expression level of genes follows the same tendency independently of the scale $m$ of gene expression (self-similar symmetry in the drift $\alpha^m(x)$ and the diffusion $\beta^m(x)$). In other words, the drift $\alpha^m(x)$ and the diffusion $\beta^m(x)$ in Fig. 2 and Fig. 3 and Figs. 6, 7, 8, 9 contain a repeating pattern of smaller and smaller parts that are like the whole, but different in size. In addition, same feature has been found in simple organism as Yeast and in complex one as Human. Therefore, this tendency probably represents a universal property of gene expression dynamics in all living organisms.
Mean-Reverting mechanism  For the drift $\alpha^m(x)$ (Eq. (4)) computed by Eq. (2), we observe the ”Mean-Reverting” mechanism in short-time fluctuation for Human organism in Fig. 2 (see Figs. 6, 7 for more details). In other words, genes with higher expression level than the mean value $m$ at time-step $t$ (i.e., $m < x$) tend to decrease their expression level at time-step $t+1$ (i.e., $\alpha^m(x) < 0$), while genes with lower expression level than the mean value $m$ (i.e., $x < m$) have tendency to increase their expression level (i.e., $\alpha^m(x) > 0$). Interestingly, the parameter ($\mu = 1$) in Eq. (4) is conserved for all the values $m$ in human organism (i.e., constant for all the subgroups of genes). Surprisingly, a value in the vicinity of one ($\mu = 0.8$) is also observed for yeast organism (see Fig. 7). Futhermore, this value is conserved for all the values $m$ in yeast organism.

Extreme-Value-Jumps-More mechanism  For the diffusion $\beta^m(x)$ (Eq. (5)) computed by Eq. (3), we observe the ”Extreme-Value-Jumps-More” mechanism in short-time fluctuation for Human organism in Fig. 3 (see Figs. 8, 9 for more details). This mechanism means that values far from the mean value $m$ change more. Remarkably, the parameter $b = 0.2 \sim 0.3$ in Eq. 5 is conserved among organisms (same for yeast and human) and among all the subgroups of genes of each organism. (see Figs. 8, 9)

Self-Similarity Symmetry  The most important fact on short-time transition probability analysis is that both $\alpha^m(x)$ and $\beta^m(x)$ show the same pattern for all values of ”$m$” (i.e., even although the system is re-scaled by different ”$m$” ). We call this phenomena self-similarity symmetry of gene expression system. Namely, the gene expression short-time fluctuations contain a repeating pattern of smaller and smaller parts that are like the whole, but different in size (See Fig. 2, 3 and Fig. 13). In an equation level, we can see this phenomena as

$$\alpha^{cm}(x) = c\alpha^m(x/c) \quad (6)$$

$$\beta^{cm}(x) = c\beta^m(x/c) \quad (7)$$

for arbitrary real number $c$. We remark that the self-similarity structure exists in both human and yeast organism. Probably, this symmetry is conserved among all the organism. It is also important to remark that this symmetry has been revealed by analyzing only experimental data of yeast and human time series.
5 The fundamental equation for gene expression dynamics

The fundamental equation for gene expression dynamics By substituting these expressions Eqs. (4) and (5) into Eq. (1), we obtain:

\[ dX_m(t) = \mu(m - X_m(t))dt + m((X_m(t)/m - 1)^2 + b)dW(t), \]

This equation describes how gene expression level changes in time. We believe that it is the fundamental equation for gene expression dynamics. By looking at this equation, we can see that it contains a relevant symmetry. Namely, when we take different \( m' \), we can recover the original equation by substituting \( X_m(t) \rightarrow X_m(t)m'/m \). This symmetry is a consequence of the self-similarity symmetry of \( \alpha^m(x) \) and \( \beta^m(x) \) in Eqs. (6) and (7).

The solution of the SPDE This dynamical equation (8) has a powerful prediction capability as follows. First, although we can solve it by obtaining a time-dependent solution, we focus our attention on the stationary solution. The stationary distribution solution of Eq. (8) is given by the following equation:

\[ \rho^m(x) = K \frac{1}{m((x/m - 1)^2 + b)^2} \exp\left(\frac{\mu}{(x/m - 1)^2 + b}\right) \]

where \( K \) is the normalization constant. This distribution solution (9) gives us the probability distribution that genes fluctuating around \( m \) (i.e., its average expression value is \( m \)) have expression level \( x \). Comparing with the experimental results, the solution of our model Eq. (9) shows a good agreement with experimental data shown in Fig. 4 (For more details see Figs. 10, 11 and 12).

6 Other Results

Scaling-law. Secondly, by direct computation, we can easily see that the distribution function of Eq. (9) has the scaling law:

\[ \rho^{cm}(x) = \frac{1}{c}\rho^m(x/c) \]

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(More symmetric form: $\rho^m(x)dx = \rho^m(x/c)dx(x/c)$) for arbitrary real number $c$. This formula is a consequence of the self-similarity symmetry of $\alpha^m(x)$ and $\beta^m(x)$ in Eqs. 6 and 7. We see in Fig. 4 (For more details see Figs. 10, 11 and 12) that the experimental data follows this scaling-law Eq. 10. The scaling law Eq. 10 indicates that the peak of each distribution is decreased by $1/m$ (see Fig. 14) and the distribution of gene expression level also has self-similarity structure (i.e. a repeating pattern of smaller and smaller parts that are like the whole, but different in size. See Figs. 10, 11 and 12). Roughly speaking, the self-similarity structure exists in both short-time transition data (i.e., $\alpha^m(x)$ and $\beta^m(x)$) and the probability distribution (i.e., $\rho^m(x)$). They are connected with each other by means of Markov property of dynamics. Therefore, in a sense, the self-similarity governs all the dynamical structure of gene expression phenomena, by means of Markov property (i.e., all the dynamical information is scaled by the mean value $m$).

**Power-law tail.** Our model can reproduce precise aspects of the gene expression system. In particular, we remark that the tail of the distribution solution of our model Eq. (9) follows the power law tail $\rho^m(x) \propto x^{-4}$ (when $x \to \infty$), which is also observed in the distribution of experimental data (see Fig. 5). This indicates that the experimental distribution can not be fitted by a normal distribution, although normal distribution seems to be similar to the experimental distribution in linear-linear scale. The main difference is that the tail of the distribution of experimental data obeys a power-law distribution, while the tail of the normal distribution quickly decays as an exponential function. Interestingly, the experimental data indicates that the tail of distribution decays as a power-law, and not exponentially (see Fig. 5). This illustrates the powerful prediction capability of our approach because it reflects very sensitive aspects of the gene expression distribution.

**The peak of distribution of yeast and human.** We found that the average increasing (decreasing) tendency parameter $\mu$ in Eq. (11) is directly related to the maximum value of stationary distribution by means of an exponential function $\rho^m(m) \propto \exp(\mu/b)$ due to Eq. (9). By following this equation, we see that if $\mu$ increases, the maximum value of the stationary distribution $\rho^m(m)$ also increases. Interestingly, this predicted behaviour by our model is also observed in experimental data. As we see in Figs. 10, 11 and 12 the strength of the peak of yeast distribution ($\rho^m(m)$ for yeast) is
lower than the peak of human distribution (i.e., \( \rho^m(m) \) for human) because \( \mu \) (yeast) \(< \mu \) (human).

7 Formal analogy to Quantum Mechanics Framework

It is worth noticing that our approach exhibits formal analogies to the Quantum Mechanics framework. However, it is also important to remark that the following analogies are contrained to the formal level and there is no relationship between the features of the analyzed biological system and the properties of the quantum mechanical system. But, we believe that this formal analogy will help the reader to understand more clearly the present work.

There is one to one correspondence between our approach and the Schrodinger equation and the Hamiltonian of the system as follows:

\( (i) \) The assumption of a stochastic process with Markov property in our approach can be understood as the assumption of the Schrodinger Equation in physics.

\( (ii) \) In our approach, by using the experimental short-time transition probability, we characterize the dynamical equation for gene expression. This procedure corresponds to identify the Hamiltonian of the system (system-dependent feature) in physics.

\( (iii) \) Furthermore, and interestingly, the self-similarity symmetry found in short-time transition probability of gene expression can be understood as a symmetry of the Hamiltonian in physics.

However, we remark again that despite of some formal analogies between the Schrodinger equation and classical stochastic equations, it is also worth noticing that the difference is still crucial because quantum coherence and superposition principles are absent in our approach.

8 Summary

In this article, by using the experimental data of Yeast and Human organisms [10][11], we have found the following interesting phenomena: 1) ”Mean-
Reverting” and ”Extreme Value- Jumps-More” mechanisms. These mechanisms are present in short-time fluctuation (i.e., how the gene expression level changes from time-step $t$ to time-step $t + 1$). Surprisingly, these two mechanisms are governed by a symmetry: Self-similarity (see Figs. 2 and Fig. 3).

By inserting this information (i.e., two mechanisms and the self-similarity symmetry) into the most general partial differential equation Eq. (1) which spontaneously emerges from Markov property, we found the fundamental equation for gene expression dynamics Eq. (8). The stationary distribution solution Eq. (9) for this fundamental equation re-builds the observed distribution $\rho_m(x)$. Finally, we succeed in naturally reconstructing the global behaviour of the observed distribution of gene expression (i.e., scaling-law $\rho_m(x) = \frac{1}{c} \rho_m(x/c)$) and the precise behaviour of the power-law tail of this distribution $\rho_m(x) \propto x^{-4}$ (when $x \to \infty$), by using only these two ingredients: Self-similarity symmetry in short-time transition probability and the assumption of Markovian feature of dynamics.

The crucial point of our approach is that we can spontaneously recover both global behaviour of gene expression distribution (scaling-law formula) and the local behaviour of gene expression distribution (power-law tail), by using only two principles: Markov property of dynamics and self-similarity symmetry exhibited by the short-time transition probability.

In a sense, the self-similarity governs all the dynamical structure of gene expression phenomena, by means of Markov property. All the dynamical information is scaled by the mean value $m$. We believe that this mechanism also happens in many other systems of Nature.

Furthermore, it is worth noticing that this self-similar symmetry may help to understand other properties found in complex systems. For example, preliminary results shown in a companion work [18] indicate that the universal property of fluctuation (i.e., coupling between the average flux and dispersion follows a scaling-law with exponent one) reported in [17] can be re-built by using the self-similar symmetry explained in this work.

Although we have solved the fundamental equation Eq. (8) in a stationary way, we may solve the same equation by searching for a time-dependent solution. This solution could predict the dynamical behaviour of the cells elements under some specific conditions, for example an external stimulus (shock) on the cell. Theoretical studies and future experiments on this topic are expected to yield interesting dynamical biological knowledge.

Finally, although our analysis focuses on a single gene expression dynamics, our framework has a flexible capability to deal with multi-degree of
freedom as it is shown in [13]. Similarly, the flexibility of our model allows us to extend it to other elements in cells as chemical compounds. Therefore, complementary time series experiments aimed to study the reaction fluxes and the concentrations of chemical compounds (metabolic pathways) are encouraged in order to obtain an integrated image of the whole cell system.

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Figure 1: As an example, we show the gene expression time series data of a few genes which belong to human organism [11]. We see that the gene expression value fluctuates around the mean value $m = 6000$ and $m = 1000$. Therefore, we group all these genes into two subgroups (one group consists of all genes fluctuating around $m = 6000$ and the other group consists of all genes fluctuating around $m = 1000$) according to the mean value $m$. 
Figure 2: We show the "Mean-Reverting" mechanisms. Horizontal axis denotes the gene expression level $x$. Vertical axis denotes the drift $\alpha^m(x)$ of genes which fluctuate around mean value $m$ (i.e., genes whose average expression level is $m$). Orange: genes with fluctuations around expression value of $m=4000$ (resp., Green: 2000. Red: 1000. Blue: 500. ) Here, we remark that the experimental data of this figure is fitted by $\alpha^m(x) = \mu(m - x)$. This mechanism indicates that gene expression dynamics is a robust system. It means that each gene tends to recover its average value $m$. We also see that the system exhibits a self-similar symmetry (see Fig. 13) because a repeating pattern of smaller and smaller parts that are like the whole, but different in size is found with respect to $m$ in this figure. (We remark that the slope $\mu$ is invariant under all $m = 4000, 2000, 1000, 500$.) This figure is constructed from selected figures with $m=500, 1000, 2000$ and 4000 in Fig
Figure 3: We show "Extreme-Value-Jumps-More" mechanisms. Horizontal axis denotes the gene expression level $x$. Vertical axis denotes the diffusion $\beta^m(x)$ of genes which fluctuate around mean value $m$. Orange: genes with fluctuations around expression value of $m=4000$ (resp., Green: 2000. Red: 1000. Blue: 500. ) Here, we remark that the experimental data of this figure is fitted by $\beta^m(x) = m((x/m - 1)^2 + b)$. This mechanism indicates that values far from the mean value $m$ change more. We also see that the system exhibits a self-similar symmetry because a repeating pattern of smaller and smaller parts that are like the whole, but different in size is found with respect to $m$ in this figure. (We remark that the parameter $b$ is invariant under all $m = 4000, 2000, 1000, 500$.) This figure is constructed from selected figures with $m=500, 1000, 2000$ and 4000 in Fig 8.
Figure 4: We show the distribution $\rho^m(x)$. It shows the distribution of expression level $x$ of genes with average expression level $m$. Horizontal axis denotes the gene expression level $x$. Vertical axis denotes the distribution $\rho^m(x)$ of genes which fluctuate around mean value $m$. Continuous line shows the prediction of our model by using the probability distribution (Eq. (9)). Dots show experimental data of Human organism from [11]. Orange: genes with fluctuations around expression value of $m=4000$ (resp., Green: 2000. Red: 1000. Blue: 500.) This figure shows the scaling law: $\rho^m(x) = \frac{1}{c} \rho^{m}(x/c)$ (More symmetric form: $\rho^{m}(x)dx = \rho^{m}(x/c)d(x/c)$) for arbitrary real number $c$. This figure is constructed from selected figures with $m = 500, 1000, 2000$ and $4000$ in Fig 10, 11.
Figure 5: We show the distribution $\rho^m(x)$ of expression level $x$ of genes with average expression value $m = 500$ in log-log scale. Horizontal axis denotes the gene expression level $x$. Vertical axis denotes the distribution $\rho^m(x)$ of genes which fluctuate around mean value $m = 500$. Dots: Experimental data of Human genes around mean value of $m = 500$. Blue line: Normal distribution. Green line: The stationary distribution solution of our model Eq. (9). Here, we remark that the tail of distribution of experimental data obeys the power law $\rho^m(x) \propto x^{-4}$ (when $x \to \infty$), not the exponential function, as suggested by the model prediction in Eq. (9). This indicates that the experimental data cannot fitted by normal distribution and our model is sensitive to crucial aspects of real system.
HUMAN GENE TIME SERIES ANALYSIS

Figure 6: This figure is a more detailed version of Fig. 2. For the drift $\alpha_m(x)$, we observe the "Mean-Reverting" mechanism in short-time fluctuation of gene expression for Human organism from $m = 500$ to $m = 9000$. For each figure, the vertical axis represents the drift $\alpha_m(x)$ of genes which fluctuate around mean value $m$. Horizontal axis denotes the gene expression level $x$. This mechanism indicates that genes with high expression level at time-step $t$ tend to decrease their expression level at time-step $t + 1$ (i.e., $\alpha_m(x) < 0$), while genes with low expression level have tendency to increase their expression level (i.e., $\alpha_m(x) > 0$). This behaviour can be represented by the expression $\alpha_m(x) = \mu(m - x)$ (continuous line). Interestingly, the parameter $\mu \simeq 1$ is conserved for all the values $m$ in human organism (i.e., constant for all the subgroups of genes). Fig. 2 is constructed from selected figures with $m = 500, 1000, 2000$ and $4000$. 
Figure 7: (Same as Fig. [but this organism is Yeast]. A value in the vicinity of one $\mu \simeq 0.8$ is also observed for yeast organism.
Figure 8: This figure is a more detailed version of Fig. 3. For the diffusion $\beta^m(x)$, we observe the "Extreme-Value-Jumps-More" mechanism in short-time fluctuation for human organism from $m = 500$ to $m = 9000$. Horizontal axis denotes the gene expression level $x$ and vertical axis denotes the diffusion $\beta^m(x)$ of genes which fluctuate around mean value $m$. It means that values far from the mean value $m$ change more. This phenomena can be parameterized by the following expression $\beta^m(x) = m((x/m - 1)^2 + b)$. Remarkably, this value $b = 0.2 \sim 0.3$ is conserved under the all mean value $m$. Fig. 8 is constructed from selected figures with $m = 500, 1000, 2000$ and $4000$. 
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Figure 9: Same as Fig. 8 but for yeast organism.
Figure 10: This figure is a more detailed version of Fig. [4]. We show the distribution $\rho^m(x)$. It shows the distribution of expression level $x$ of genes with average expression level $m$. Horizontal axis denotes the gene expression level $x$. Vertical axis denotes the distribution $\rho^m(x)$ of genes which fluctuate around mean value $m$. Green circles represent experimental data [11] and solid line represents theoretical prediction in Eq. [9]. This theoretical solution (solid line) agrees with the experimental results human organism [11] (green circles).
Figure 11: Same as Fig. 10 but we show genes which fluctuate around different mean value \( m \).
Figure 12: Same as Fig. 10 but we show the results for yeast organism.
Figure 13: A figure (or system) has self-similarity if it contains a repeating pattern of smaller and smaller parts that are like the whole, but different in size. We show three examples of self-similar property. The self-similarity property was found in gene fluctuations and it was illustrated in Figs. 2, 3, 4 which have the same pattern to these figures. Colours have the same meaning as in Figs. 2, 3, 4.
Figure 14: This figure is the same as Fig. 9 but in log-log scale. It is possible to observe that the convolution of the peak of distributions follows a power-law $x^{-1}$. 