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Turnover of messenger RNA: Polysome statistics beyond the steady state

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Abstract – The interplay between turnover or degradation and ribosome loading of messenger RNA (mRNA) is studied theoretically using a stochastic model that is motivated by recent experimental results. Random mRNA degradation affects the statistics of polysomes, *i.e.*, the statistics of the number of ribosomes per mRNA as extracted from cells. Since ribosome loading of newly created mRNA chains requires some time to reach steady state, a fraction of the extracted mRNA/ribosome complexes does not represent steady state conditions. As a consequence, the mean ribosome density obtained from the extracted complexes is found to be inversely proportional to the mRNA length. On the other hand, the ribosome density profile shows an exponential decrease along the mRNA for prokaryotes and becomes uniform in eukaryotic cells.

Introduction. – In all living cells, the genetic information encoded in the DNA is first transcribed into mRNA and then translated into proteins. The translation process from mRNA to protein is performed by ribosomes and involves several subprocesses known as initiation, elongation, and termination.

The translating machines of the cell, the ribosomes, consist of two subunits that assemble on the mRNA at the position of initiation. After a complete ribosome has passed the start codon, it translates the information encoded in the nucleotide sequence into a polypeptide chain. When the ribosome reaches the end of the mRNA chain, it dissociates from this chain and releases a new protein into the cell. In the case of premature termination of translation, the ribosome drops off prematurely from the mRNA chain, thereby releasing an incomplete polypeptide chain, which is then degraded [1,2].

The number of ribosomes on the mRNA chains, called the polysome size, is a stochastic variable that varies from chain to chain, and over time for the same chain. The statistics of the polysome size, the spatial distribution of ribosomes along the mRNA chains, and the ribosome flux along the mRNAs are key features of protein production and of regulation at the translational level.

Degradation of mRNA plays also an important role in the regulation of translation. This process starts when a mRNA encounters a RNA-degrading protein [3] and can occur at any stage of the mRNA life cycle [3–6], irrespective of the time for mRNA synthesis and initiation of the translation [7]. Thus, degradation leads to a turnover of the mRNA and to the coexistence of young and old mRNAs.

From a theoretical point of view, modeling of translation is mostly performed using a class of non-equilibrium models called exclusion processes. This approach was introduced several decades ago [8] and has recently been applied to address several aspects of ribosome traffic under steady state conditions [9–12]. A slightly different approach was taken in [13], where the interplay between degradation and the efficiency of translation is discussed.

From the experimental point of view, newly developed techniques provide high-quality data that are likely to revolutionize our view of mRNA translation in the next years [14–19]. These techniques provide accurate measurements of the polysome statistics that still lack a general mechanistic explanation.

In this letter, we introduce and study a model that contributes to a better understanding of the role of mRNA degradation on the statistics of polysomes. The key observation behind our model is that the number of

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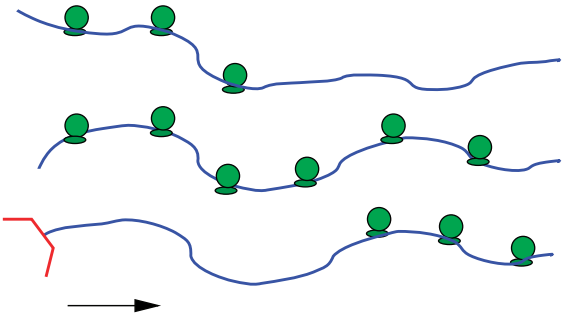

Fig. 1: (Colour on-line) Young (top) and old (middle) mRNA chains of the same length, both with ribosomes moving from left to right. The young chain is loaded with only a few ribosomes close to the initiation region at the left end of the chain. The old chain is uniformly loaded with ribosomes and has reached its steady state. The average number of ribosomes computed from these two chains is smaller than the steady state value. The bottom mRNA chain corresponds to a decapped chain as found in eukaryotes.

ribosomes on a given mRNA varies with time and depends on the age of this mRNA. This behavior is illustrated in fig. 1. If one extracts the mRNA/ribosome complexes or polysomes from a cell, one implicitly performs an average over the age distribution of the mRNAs.

Thus, our strategy is to derive the mean density and the density profile of ribosomes by taking into account the age effect produced by degradation. We first assume that degradation stops any translation, as described in *E. coli* [20]. Later we include the possibility that translocating ribosomes are allowed to complete translation after the start of degradation, as observed in eukaryotic cells [21].

Transient and stationary polysome size. – Let us consider a mRNA molecule in the cytosol, surrounded by diffusing ribosomes and by diffusing RNA-degrading proteins. Translation is initiated with the constant on-rate $\omega_{\rm on}$, ribosomes drop-off prematurely from the mRNA with rate $\omega_{\rm off}$, and the turnover time of the mRNA is governed by the constant degradation rate $\omega_{\rm de}$. We take all of these rates to be independent of the length and of the mRNA sequence. In addition, we assume that the ribosome density is sufficiently low and that the termination rate is sufficiently large to avoid traffic jams. These assumptions are compatible with several *in vivo* measurements [14–16,18].

The length of a mRNA will be expressed here in terms of footprints, fp, which is 10 codons [22]. Each footprint is the size covered by a ribosome when it translates the mRNA. The typical time scale is of the order of minutes and the velocity v of a ribosome is expressed in units of fp/min. For simplicity, we will focus on the coding region and consider the initiation region as a source of ribosomes.

Let $N(t)$ be the random number of ribosomes on a chain of length L and age t. The state space of N is given by $\{0,1,2,\ldots,L\}$. The quantity

$$P_n(t) = \Pr\{N(t) = n | N(0) = 0\}, \tag{1}$$

is the probability that the number of ribosomes is n at age t, with $n = 0,1,2\ldots,L$, given that it was 0 at age $t = 0$. The probabilities $P_n(t)$ are solutions of the Master equation

$$\frac{{\rm d}P_n}{{\rm d}t} = \omega_{\rm on} P_{n-1} + \omega_{\rm off}(n+1)P_{n+1} - (\omega_{\rm on} + \omega_{\rm off} n)P_n, \tag{2}$$

for $t \leqslant t_L \equiv L/v$, where t_L is the time needed by the first ribosome to reach the end of the chain. Obvious modifications are needed for $n = 0$, L and the initial condition is $P_0(0) = 1$. For $t > t_L$ instead, the solution is given by

$$P_n(t > t_L) = P_n(t_L), \tag{3}$$

where $P_n(t_L)$ is given by the solution of eq. (2) at time t_L. The expectation value of $N(t)$, denoted here with $M(t)$, gives the average polysome size over an ensemble of mRNA of length L and age t. $M(t)$ evolves with time t according to

$$\frac{{\rm d}M}{{\rm d}t} = \omega_{\rm on} - \omega_{\rm off} M, \qquad \text{for } t < t_L. \tag{4}$$

For $t > t_L$, we have $M(t) = M(t_L) \equiv M_L$, where M_L is the stationary polysome size on a chain of length L.

The solution of (4), with initial condition $M(0) = 0$ is now given by

$$M(t) = \frac{\omega_{\rm on}}{\omega_{\rm off}} \left(1 - \exp(-\omega_{\rm off} t)\right), \tag{5}$$

for $t \leqslant t_L$ and by the steady state value

$$M(t) = M_L \equiv \frac{\omega_{\rm on}}{\omega_{\rm off}} \left(1 - \exp(-\omega_{\rm off} L/v)\right). \tag{6}$$

for $t > t_L$. The average ribosome density as a function of the length L and of the age t of the mRNA chain is then given by $M(t)/L$.

Mean ribosome density and mean density profile. – In order to find the mean ribosome density over a large population of mRNA chains of different ages, we need to determine their age distribution. The age distribution is determined by the turnover time distribution.

The turnover time U of any mRNA molecule is a random number distributed according to the probability density $\phi_U(t)$. For a fixed degradation rate $\omega_{\rm de}$, the turnover probability density is given by

$$\phi_U(t) = \omega_{\rm de} \exp\left(-\omega_{\rm de} t\right), \tag{7}$$

where the value of $\omega_{\rm de}$ can be computed from the mean turnover time of mRNA in the cytosol.

The probability density $\phi_A(t)$ of the age of the mRNA chains can be determined assuming that the total number

of such chains is constant. This problem is equivalent to a renewal process, the age distribution of which was derived in [23]. The general solution is

$$\phi_A(t) = \int_t^\infty \mathrm{d}u \, \frac{\phi_U(u)}{\mathrm{E}[U]}, \tag{8}$$

for $t \geqslant 0$, where $\mathrm{E}[U]$ is the average turnover time of a chain. By using (7) in (8) we obtain

$$\phi_A(t) = \omega_{\mathrm{de}} \exp\left(-\omega_{\mathrm{de}} t\right), \tag{9}$$

i.e., $\phi_A(t) = \phi_U(t)$ that reflects the memoryless property of the exponential distribution.

Finally, on chains of length L, the mean polysome size is given by a convolution of $M(t)$ with the probability density $\phi_A(t)$, *i.e.*, by

$$\langle M \rangle = \int_0^\infty \mathrm{d}t \, M(t) \phi_A(t). \tag{10}$$

It now follows from (5), (6), (9) that the mean ribosome density is

$$\frac{\langle M \rangle}{L} = \frac{\omega_{\mathrm{on}}}{(\omega_{\mathrm{de}} + \omega_{\mathrm{off}})L} \left[1 - \exp\left(-(\omega_{\mathrm{de}} + \omega_{\mathrm{off}})\frac{L}{v}\right)\right]. \tag{11}$$

This expression implies that the mean density decreases monotonically with increasing L and decays as $1/L$ for large L. It is important to note that this behavior is achieved even in the limit of vanishing drop-off rate ω_{off}.

Using parameter values from *E. coli*, we plot (11) in fig. 2(a). The length distribution of mRNAs varies from 10 to 2000 codons corresponding to 1 to 200 footprints. The typical life time of a mRNA chain is between 2 and 5 minutes [24]. We can thus assume that the mean turnover time is 3.5 minutes, corresponding to the degradation rate $\omega_{\mathrm{de}} = 1/3.5\,\mathrm{min}^{-1}$. The velocity of a ribosome depends on the environmental conditions. Under conditions of slow population growth, the velocity of ribosomes is estimated to be about 10 codons per second and thus $v = 60\,\mathrm{fp/min}$ [25]. The rate ω_{off} of premature drop-off of the ribosome from a mRNA has been estimated in [26] to be of the order of $4 \cdot 10^{-4}$ per codon and, taking into account the velocity of the ribosomes, $\omega_{\mathrm{off}} = 0.24\,\mathrm{min}^{-1}$. Finally, the average initiation rate is estimated to be one ribosome every four seconds [27] but translational attenuation in the initiation region [28] may lower this rate. We thus have set it to one ribosome every six seconds, which leads to an initiation rate of $\omega_{\mathrm{on}} = 10\,\mathrm{rb/min}$. A comparison between curves with and without a premature ribosome drop-off, see black and red lines in fig. 2, respectively, shows that the effect of age is more visible when the drop-off rate is small. In addition, the steady state lines lie above the turnover lines indicating that the turnover has a strong influence on the polysome statistics.

Next, we look at the density profile of an ensemble of chains of fixed length L. This profile corresponds to the mean number of ribosomes $\langle m(z) \rangle$ per unit length at

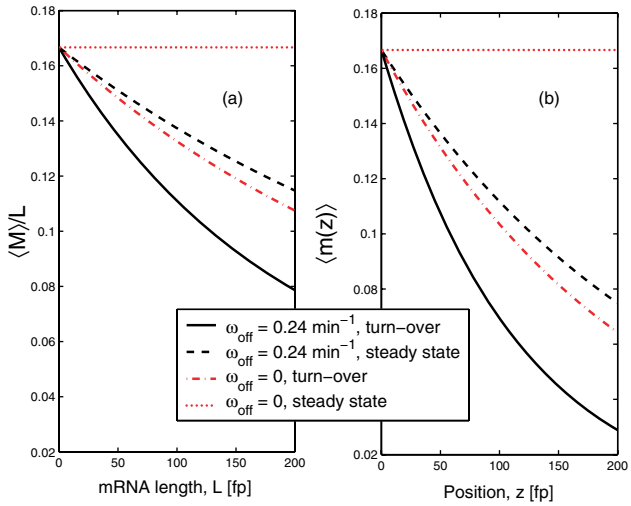

Fig. 2: (Colour on-line) Ribosome densities: (a) Mean density $\langle M \rangle / L$ of ribosomes as a function of the chain length L as given by (11); (b) mean density profile as a function of the position along a mRNA of length $L = 200\,\mathrm{fp}$, from (13). The four cases displayed both in (a) and in (b) correspond to different values of the drop-off rate ω_{off} as explained in the inset. The steady state curves are obtained in the limit of zero ω_{de}.

position z along a mRNA chain of length L taking into account the age distribution of the mRNA chains. The profile $\langle m(z) \rangle$ determines the mean polysome size $\langle M \rangle$ via

$$\langle M \rangle = \int_0^L \mathrm{d}z \, \langle m(z) \rangle, \tag{12}$$

where the lhs is (11) multiplied by L. After substituting (11) into (12), the profile $\langle m(z) \rangle$ is obtained by taking the derivative of both sides of (12) with respect to L and setting $L = z$. This leads to

$$\langle m(z) \rangle = \frac{\omega_{\mathrm{on}}}{v} \exp\left(-(\omega_{\mathrm{off}} + \omega_{\mathrm{de}})\frac{z}{v}\right), \tag{13}$$

which decays exponentially with z even if the drop-off rate ω_{off} is vanishingly small. Expression (13) is plotted in fig. 2(b). Note that for $\omega_{\mathrm{off}} = 0$, the distribution of the ribosomes on a chain is uniform at steady state conditions. On the other hand, taking into account the different ages of the chain, the resulting mean profile density decays exponentially. This indicates that the mean profile density measured on mRNA chains loaded with many ribosomes may show a uniform distribution if the drop-off rate is negligible.

Polysome size distribution. – The experimental determination of the polysome statistics allows measurements of the distribution of the number of ribosomes for a population of mRNA with a fixed sequence. The mRNA turnover should affect this distribution.

In order to find the distribution of ribosomes, we define the probability Π_n that a chain of length L and any age has n ribosomes on it. These probabilities are obtained by

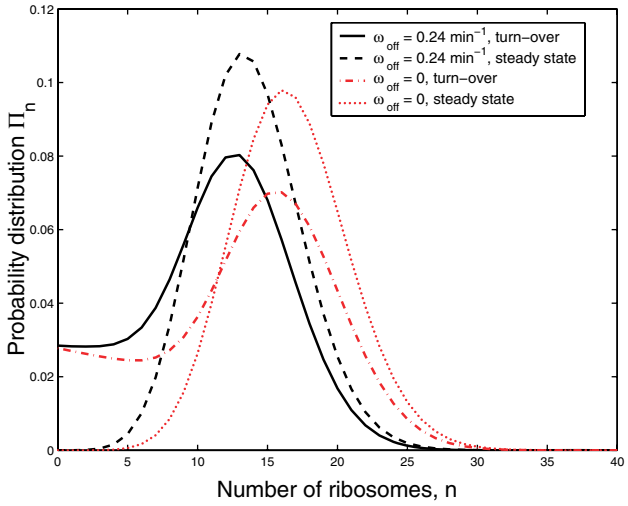

Fig. 3: (Colour on-line) Probability distribution of the number n of ribosomes on mRNA chains of length 100 fp with drop-off rate of $\omega_{\rm off} = 0.24\,{\rm min}^{-1}$ (black lines) and $\omega_{\rm off} = 0$ (red lines). The four cases displayed here are identical to those in fig. 2.

averaging $P_n(t)$, which is the solution of (2) and (3), over the age distribution $\phi_A(t)$ as in (9) thus giving

$$\Pi_n = \langle P_n(t)\rangle = \int_0^\infty {\rm d}t\, P_n(t)\phi_A(t). \tag{14}$$

It can be readily seen that $\sum_n \Pi_n = 1$. The probability distribution Π_n is plotted in fig. 3 for different rate parameters. One can make a comparison between the steady state distribution $P_n(t_L)$ (black dashed line) and the distribution Π_n that takes the age into account (black full line). The latter distribution shows a remarkable plateau at small ribosome number. To understand the nature of this plateau we can analyze the system when $\omega_{\rm off} = 0$ because it can be solved analytically. In fact, for $\omega_{\rm off} = 0$ the process can be approximated by a Poisson process if $P_L(t_L) \ll 1$ (this is ensured if $\omega_{\rm on}$ is sufficiently small). In this case, the probabilities are given by

$$P_n(t) = \frac{(\omega_{\rm on}t)^n \exp(-\omega_{\rm on}t)}{n!}, \tag{15}$$

for $t \leqslant t_L$ and for any $n = 0, 1, 2, \ldots$. For $t > t_L$, $P_n(t > t_L) = P_n(t_L)$. Plugging this into eq. (14), we can obtain the distribution of the number of ribosomes for $\omega_{\rm off} = 0$. For $n = 0$ the resulting expression reads

$$\Pi_0 = \frac{\omega_{\rm de}}{\omega_{\rm on}+\omega_{\rm de}} + \frac{\omega_{\rm on}}{\omega_{\rm on}+\omega_{\rm de}} \exp(-(\omega_{\rm on}+\omega_{\rm de})t_L), \tag{16}$$

where we see that for large chains the plateau is small for either small degradation rate $\omega_{\rm de}$ and/or large initiation rate $\omega_{\rm on}$. A comparison of the distribution Π_n and the steady state distribution for $\omega_{\rm off} = 0$ is also shown in fig. 3. Inspection of this plot shows that Π_0 as in (16) is identical to the Π_0 computed from (14). Therefore, measurements of Π_n under controlled conditions close to $\omega_{\rm off} = 0$ provide an estimate of the degradation rate of mRNA.

The effect of translation after decapping. – In the previous sections we have assumed that the degraded mRNA disappears immediately from the cell. This scenario may be correct for prokaryotes but in eukaryotes the process of degradation is more complex [21]. Indeed, in eukaryotes the mRNA is first "decapped" in order to suppress loading of new ribosomes, and then the remaining ribosomes complete translation before the mRNA chain is completely degraded. A cartoon about this part of the translation process is shown in fig. 1.

We should first notice that the contribution to the polysome statistics arising from undecapped mRNA chains is the same as computed above. For the sake of clarity, we will now slightly change the notation in order to distinguish between ribosome numbers M_u on undecapped chains, and ribosome numbers on decapped chains, M_d. Thus, what was previously called M becomes now M_u. Now, we just need to consider those chains that have already been decapped. The time at which decapping takes place will be denoted with τ_d. This time is measured after the release of the mRNA in the cytosol and is distributed according to the probability density ϕ_U. In order to determine how many ribosomes are on the chain at the decapping time, we should distinguish between chains that have reached the steady state before decapping and chains that are not yet at the steady state at the time of decapping. This information is provided by the random variable t_d, whose probability distribution $\Phi_D(t) \equiv \Pr\{t_d \leqslant t\}$ is related to the decapping time τ_d through

$$\begin{aligned} \Pr\{t_d \leqslant t < t_L\} &= \Pr\{\tau_d \leqslant t < t_L\} = \int_0^t {\rm d}\tau\, \phi_U(\tau), \\ \Pr\{t_d = t_L\} &= \Pr\{\tau_d \geqslant t_L\} = \int_{t_L}^\infty {\rm d}\tau\, \phi_U(\tau), \end{aligned} \tag{17}$$

so that when $t_d < t_L$ the mRNA has been decapped before reaching the steady state and for $t_d = t_L$ the mRNA has been decapped after having reached the steady state.

Therefore, we have

$$\begin{aligned} \Phi_D(t_d) &= \phi_U(t_d), && \text{for } t_d < t_L, \\ \Phi_D(t_L) &= \int_{t_L}^\infty {\rm d}\tau\, \phi_U(\tau), && \text{for } t_d = t_L, \end{aligned} \tag{18}$$

where $\Phi_D(t_L)$ is a probability. We start by considering an ensemble of chains all having the same length L and the same t_d. At the decapping time τ_d, the chains will be loaded with a certain number of ribosomes $\overline{M}_d = M(\tau_d)$ given as the solution of (5) and (6) for $t = \tau_d$. During the subsequent time, no more ribosomes will initiate translation but ribosomes will leave the chain either because they reach the end of the chain or because of premature drop-off. The average number of ribosomes at any time $t_a \geqslant 0$ after decapping, denoted here with $M_d(t_a)$,

is the solution of the following equation:

$$\frac{\mathrm{d}M_d(t_a)}{\mathrm{d}t_a} = -\frac{\Theta\left(t_a - t_0\right) M_d(t_a)}{t_L - t} - \omega_{\mathrm{off}} M_d(t_a), \qquad (19)$$

with boundary condition $M_d(0) = \overline{M}_d$, where $\Theta(x) = 1$ for $x > 0$ and is zero otherwise, and

$$t_0 \equiv t_L - t_d. \qquad (20)$$

The first term on the rhs of (19) indicates that the more advanced ribosome needs a time t_0 to terminate translation. The solution of (19) reads

$$M_d(t_a) = \begin{cases} M(t_d)\exp(-\omega_{\mathrm{off}} t_a), & 0 \leqslant t_a < t_0, \\ M(t_d)\dfrac{t_L - t_a}{t_L - t_0}\exp(-\omega_{\mathrm{off}} t_a), & t_0 \leqslant t_a \leqslant t_L, \end{cases} \qquad (21)$$

with t_0 given in (20). The time variable t_a is the age after decapping of the decapped chain. Since the life time of decapped mRNAs of length L is given by t_L, the age distribution is uniform between 0 and t_L. Thus, taking this age distribution into account the mean number of ribosomes is given by

$$\langle M_d \rangle_{t_d} = \int_0^{t_L} \mathrm{d}t_a \, \frac{M_d(t_a)}{t_L}, \qquad (22)$$

where the subscript on the lhs reminds us that we are still conditioning in t_d. Considering now the solution given in (21) we have

$$\langle M_d \rangle_{t_d} = \frac{\overline{M}_d}{\omega_{\mathrm{off}} t_L}\left[1 + \frac{\mathrm{e}^{-\omega_{\mathrm{off}} t_L} - \mathrm{e}^{-\omega_{\mathrm{off}} t_0}}{\omega_{\mathrm{off}}(t_L - t_0)}\right], \qquad (23)$$

where the dependence on t_d is both in t_0 and in $\overline{M}_d$. Thus, the mean number of ribosomes on decapped chains is given by the convolution of (23) and the probability distribution of the t_d defined in (18). This leads to

$$\langle M_d \rangle = \int \mathrm{d}t_d \, \langle M_d \rangle_{t_d} \phi_U(t_d) \, + \, \langle M_d \rangle_{t_L} \int_{t_L}^{\infty} \mathrm{d}\tau \, \phi_U(\tau) \, , \qquad (24)$$

which is made of an integral for $t_d < t_L$ plus a contribution for $t_d = t_L$.

In order to keep the model simple and analytically tractable, we make the assumption that the turnover time distribution is still given by (7) and that the premature drop-off rate is zero. We set thus hereafter $\omega_{\mathrm{off}} = 0$. Under this assumption, (23) becomes

$$\langle M_d \rangle_{t_d} = \frac{\omega_{\mathrm{on}} t_d}{2}\frac{2t_L - t_d}{t_L} \qquad (25)$$

and inserting this expression in (24) we obtain

$$\langle M_d \rangle = \frac{\omega_{\mathrm{on}}}{\omega_{\mathrm{de}}}\left(\frac{\omega_{\mathrm{de}} t_L - 1 + \mathrm{e}^{-\omega_{\mathrm{de}} t_L}}{\omega_{\mathrm{de}} t_L}\right), \qquad (26)$$

which has the intuitive property of becoming a constant for large L, which implies a $1/L$ behavior of the mean density for large L.

Now that the mean number of ribosomes after decapping has been found, we need to bring together the contribution from undecapped mRNAs given in (11) and that from decapped chains given in (26). To do this, we need to find the weights that have to be applied in the sum of the two contributions. We make the natural assumption that these weights are proportional to the life times before decapping and after decapping, respectively. Thus, the proportion p_d of decapped chains of a given length L is given by

$$p_d = \frac{t_L}{t_L + \omega_{\mathrm{de}}^{-1}} = \frac{\omega_{\mathrm{de}} L}{\omega_{\mathrm{de}} L + v} \, , \qquad (27)$$

while $p_u = 1 - p_d$ is the proportion of undecapped mRNA. This gives the final mean ribosome number

$$\langle M \rangle = p_u \langle M_u \rangle + p_d \langle M_d \rangle, \qquad (28)$$

where M_u is given by (11) and leads to

$$\frac{\langle M \rangle}{L} = \frac{\omega_{\mathrm{on}}}{\omega_{\mathrm{de}} L + v}, \qquad (29)$$

which behaves as $1/L$ for large chain length L and shows that the continuation of translation after decapping does not change the qualitative behavior of the mean density as obtained in (11).

Concerning the profile density $m_d(z)$, we start by considering a chain of given length L, conditioned on t_d and on the age t after decapping, $m_d(z|t, t_d)$. The local density of positions covered with ribosomes is given by $\overline{m}_d = \omega_{\mathrm{on}}/v$ and the length of the polysome is given by $L_d = v t_d$. We can then write

$$m_d(z|t, t_d) = \begin{cases} \overline{m}_d, & \max\left(0, \dfrac{z - L_d}{v}\right) \leqslant t \leqslant \dfrac{z}{v}, \\ 0, & \text{otherwise}, \end{cases} \qquad (30)$$

for $0 \leqslant z \leqslant L$. This equation shows that the density is non-zero only over a piece of the chain and that this piece moves with time until $t = t_L$. After taking the convolution with the uniform age distribution of the decapped chains and then taking the convolution with the distribution $\Phi_D(t_d)$, we finally obtain

$$\langle m_d(z) \rangle = \frac{\omega_{\mathrm{on}}}{\omega_{\mathrm{de}}}\frac{1 - \exp(-\omega_{\mathrm{de}} z/v)}{L} \qquad (31)$$

which, contrary to the result for the undecapped chains given in (13), indicates a monotonous *increase* of the density along the chain. Finally, the whole profile density is given by a weighted sum of decapped and undecapped chains

$$\langle m(z) \rangle = p_u \langle m_u(z) \rangle + p_d \langle m_d(z) \rangle \, , \qquad (32)$$

where $\langle m_u(z)\rangle$ is given by (13). Using (27) and setting $\omega_{\rm off}=0$ in (13) leads to

$$\langle m(z)\rangle = \frac{\omega_{\rm on}}{\omega_{\rm de}L+v}\,, \tag{33}$$

which means that in the absence of premature drop-off, the profile along the mRNA is constant, independent of z. Taking into account that $\langle m_u(z)\rangle$ is a decreasing function of z and that $\langle m_d(z)\rangle$ is increasing in z, the constant behavior in (33) is due to the choice of p_d made in (32).

Conclusions. – In this study, we have taken the effect of mRNA degradation on the statistics of polysomes into account.

The model makes a distinction between the polysome statistics for undecapped and decapped mRNA. When only undecapped mRNA is considered, the model is relevant for prokaryotic cells such as *E. coli*. In *E. coli* it is also known that the time scale of translation is close to the mRNA life time [29,30] and thus the effect of degradation should be strong. In this case, the mean density decays as $1/L$ for large chain length L even in the limit of vanishing drop-off rate. We have also shown that the profile density has an exponential decay along the mRNA chain and that such an exponential decay applies also to the case in which the drop-off rate is zero.

For eukaryotic cells, we have also taken the recent observation into account that translation may continue after decapping until the last translocating ribosome has finished [21]. In addition, we have assumed that premature drop-off has a negligible effect. Under these conditions, the mean ribosome density behaves again as $1/L$ as a function of the chain length L. This pattern is qualitatively similar to the one found in [14] for yeast cells and in [16] for *Drosophila* and, thus, indicates that mRNA degradation may be a possible mechanism underlying these experimental findings. The profile density, on the other hand, is a weighted sum of a decreasing profile density from undecapped sequences and an increasing one from decapped sequences. These two contribution cancel each other and lead to a constant. This result is in agreement with the profile density measurements presented in [15] but disagrees with those presented in [18]. Thus, further experiments are required to disentangle these two findings and verify the predictions of the model.

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REFERENCES

[1] Buchan J. R. and Stansfield I., *Biol. Cell*, **99** (2007) 475.
[2] Wolin S. L. and Walter P., *EMBO J.*, **7** (1988) 3559.
[3] Houseley J. and Tollervey D., *Cell*, **136** (2009) 763.
[4] Kushner S. R., *IUBMB Life*, **56** (2004) 585.
[5] Deutscher M. P., *Prog. Mol. Biol. Transl. Sci.*, **85** (2009) 369.
[6] Kaberdin V. R. and Bläsi U., *Microbiol. Rev.*, **30** (2006) 967.
[7] Cannistraro V. J. and Kennell D., *J. Bacteriol.*, **161** (1985) 820.
[8] MacDonald C. T., Gibbs J. H. and Pipkin A. C., *Biopolymers*, **6** (1968) 1.
[9] Romano C. M., Thiel M., Stansfield I. and Grebogi C., *Phys. Rev. Lett.*, **102** (2009) 198104.
[10] Shaw L. B., Zia R. K. P. and Lee K. H., *Phys. Rev. E*, **68** (2003) 021910.
[11] Dong J. J., Schmittmann B. and Zia R. K. P., *Phys. Rev. E*, **76** (2007) 051113.
[12] Chou T., *Biophys. J.*, **85** (2003) 755.
[13] Mitarai N., Sneppen K. and Pedersen S., *J. Mol. Biol.*, **382** (2008) 236.
[14] Arava Y., Wang Y., Storey J. D., Long Liu C., Brown P. O. and Herschlag D., *Proc. Natl. Acad. Sci. U.S.A.*, **100** (2003) 3889.
[15] Arava Y., Boas F. E., Brown P. O. and Herschlag D., *Nucleic Acids Res.*, **33** (2005) 2421.
[16] Qin X., Ahn S., Speed T. P. and Rubin G. M., *Gen. Biol.*, **8** (2007) R63.
[17] Eldad N. and Arava Y., *Methods in Molecular Biology*, edited by Wilusz J., Vol. **419** (Humana Press, Totowa, NJ) 2007.
[18] Ingolia N. T., Ghaemmaghami S., Newman J. R. S. and Weissman J. S., *Science*, **324** (2009) 218.
[19] Morris D. R., *Genome Biol.*, **10** (2009) 215.
[20] Richards J., Sundermeier T., Svetlanov A. and Karzai A. W., *Biochim. Biophys. Acta*, **1779** (2008) 574.
[21] Hu W., Sweet T. J., Chamnongpol S., Baker C. E. and Coller J., *Nature*, **461** (2009) 225.
[22] Steitz J. A., *Nature*, **224** (1969) 957.
[23] Cox D. R., *Renewal Theory*, edited by Bartlett M. S. F. R. S. (Methuen & Co. LTD, Science Paperbacks), 1970.
[24] Bernstein J. A., Khodursky A. B., Lin P., Lin-Chao S. and Cohen S. N., *Proc. Natl. Acad. Sci. U.S.A.*, **99** (2002) 9697.
[25] Bremer H. and Dennis P. P., *Escherichia coli and Salmonella typhimurium: Cellular and Molecular Biology*, edited by Neidhardt F. C. *et al.*, 2nd edition (American Society for Microbiology), 1987, Chapt. 97, table 3, pp. 1559.
[26] Kurland G. C., *Annu. Rev. Genet.*, **26** (1992) 29.
[27] Jacques N. and Dreyfus M., *Mol. Biol.*, **4** (1990) 1063.
[28] Zhang D. and Ignatova Z., *PLoS ONE*, **4** (2009) e5036.
[29] Grunberg-Manago M., *Annu. Rev. Genet.*, **33** (1999) 193.
[30] Johansson M., Lovmar M. and Ehrenberg M., *Curr. Opin. Microbiol.*, **11** (2008) 141.