Single-cell transcription dynamics

In experiments on single cells Golding and Co. measured the number of RNAs produced from a single gene:

![Graphs showing RNA production over time](image)

Are these observations consistent with the simple model of RNA production, where RNA is produced at rate \( r \)? In this experiment RNA is not degraded. Given that the rate of production is \( r \), how many RNAs are produced in a generation time \( T_g \) (\( T_g = 70 \text{ min} \) in Jodo's experiment)

\[
0 \quad at \quad 2r \quad at \quad 3r \quad at \quad 4r \quad \quad (N) \quad at \quad T_g = N = T_g / \Delta t : \# \text{ of time intervals}
\]

\( \frac{r}{\Delta t} \quad \frac{r}{\Delta t} \quad \frac{r}{\Delta t} \quad \frac{r}{\Delta t} \quad \text{probability that an RNA is produced} \)

To produce a single cell trajectory, for every time interval pick a random number between 0 and 1. If this number is less than \( r \), add one RNA. → Write Python code and visually compose trajectories...
To compose our model of RNA production to Jolo's experiments, we expect the probability distribution of $m$, the number of RNAs produced in time $T_g$.

\[ p(m) = \frac{N!}{m!(N-m)!} \left( \frac{rT_g}{N} \right)^m \left( 1 - \frac{rT_g}{N} \right)^{N-m} \]

For $rT_g \ll 1$, $N = \frac{t}{rT_g} \gg m$, since $m$ is of order $rT_g$ (≈ 10 in Jolo's experiment), and these limits the Binomial distribution becomes (it works too!!) Poisson.

\[ p(m) = \frac{(rT_g)^m}{m!} e^{-rT_g} \]

\[ \langle m \rangle \approx \frac{N}{rT_g} \]

\[ \langle m \rangle = e^{-\mu} \sum_{m=1}^{\infty} \frac{\mu^m}{(m-1)!} \]

To compare to Jolo's data we can compute the mean and variance which he measures. (Could also compare the distributions directly as they do in the Zenzkleine et al. paper).
\[
\langle m \rangle = e^{-\mu} \sum_{m=0}^{\infty} \frac{\mu^m}{m!} \left\{ m = m+1; \text{ change of variables} \right. \\
\langle m \rangle = e^{-\mu} \sum_{m=1}^{\infty} \frac{\mu^m}{m!-1} = \mu \\
\]

Mean of the Poisson distribution \( P(m) = \frac{\mu^m}{m!} e^{-\mu} \) is \( \mu \).

**Variance**

\[
\text{Var } m = \langle m^2 \rangle - \langle m \rangle^2 \\
\langle m^2 \rangle = \sum_{m=0}^{\infty} m^2 \frac{\mu^m}{m!} e^{-\mu} \\
= \sum_{m=0}^{\infty} m^2 \left( m+1 \right) \frac{\mu^{m+1}}{(m+1)!} e^{-\mu} \\
= \sum_{m=0}^{\infty} m^2 \left( m+1 \right) \frac{\mu^{m+1}}{m!} e^{-\mu} \\
= \mu \left( \sum_{m=0}^{\infty} m^2 \frac{\mu^m}{m!} e^{-\mu} + \sum_{m=0}^{\infty} \frac{\mu^m}{m!} e^{-\mu} \right) \\
= \mu \left( \text{from the Mean calculation} \right) \\
\langle m^2 \rangle = \mu (\mu+1) \\
\]

With this result \( m \) hand we compute the variance.

\[
\text{Var } m = \langle m^2 \rangle - \langle m \rangle^2 = \mu (\mu+1) - \mu^2 = \mu! \\
\]

Variance is equal to the mean! This is a key feature of the Poisson distribution.

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Odo varies the mean by using different levels of monochin and finds \( \text{Var } m = 4.1 \langle m \rangle \) which disagrees with the prediction of the model. Therefore, transcription is not described as production of RNA at a constant rate. It is bursty!