Matched Asymptotic Analysis of the Luria–Delbrück Distribution in a Reversible Fluctuation Assay

Matfyz Connections, 26.11.2025

Anna Hlubinová [1], Pavol Bokes [1], Abhyudai Singh [2]

[1] Department of Applied Mathematics and Statistics, Comenius University, Slovakia
[2] Department of Electrical and Computer Engineering, University of Delaware, USA

Table of contents

Motivation

Motivation

"Do mutations in bacteria arise **randomly**, or are they **induced by the environment**?"

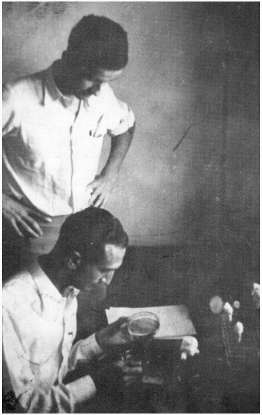


Fig. 1: Max Delbrück and Salvador Luria in the laboratory. Source: *https://profiles.nlm.nih.gov/101584611X127*

Fluctuation test

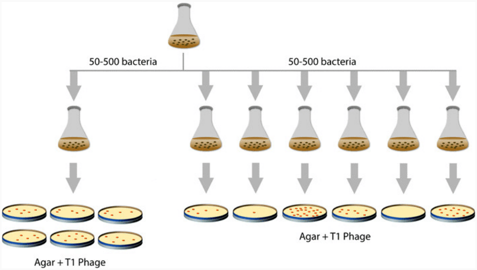


Fig. 2: Luria-Delbrück experiment.
Source: *https://link.springer.com/article/10.1007/s00018-016-2371-2/figures/1*

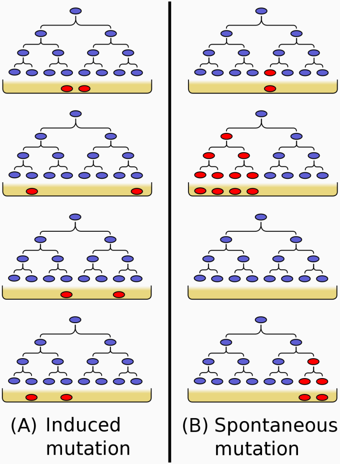
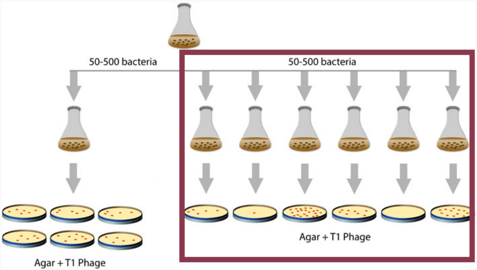
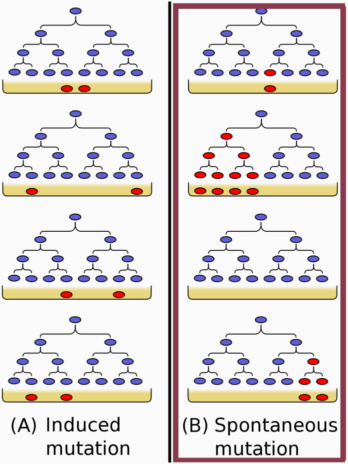


Fig. 3: Fluctuation test. Source: *https://en.m.wikipedia.org/wiki/File:Luria-delbruck_diagram.svg#filehistory*

Fluctuation test



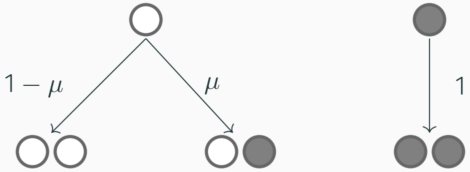


Genetic mutations occur **without the presence of external stimuli**.

Model

Original Model

Classical Luria–Delbrück test assumes **irreversible resistance** [1] :

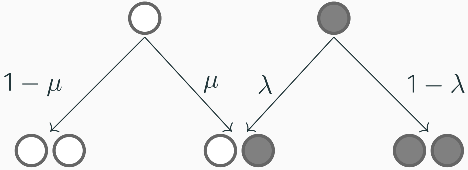


- white ball = **sensitive** cell (”non-mutant”)
- black ball = **tolerant** cell (”mutant”)
- sensitive mother cell has a tolerant daughter cell with probability μ

[1] D. A. Kessler and H. Levine, “Large population solution of the stochastic Luria–Delbrück evolution model,” *Proceedings of the National Academy of Sciences*, vol. 110, no. 29, pp. 11682–11687, 2013.

Our generalization

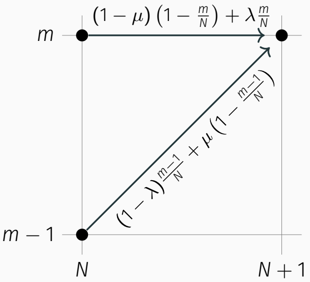
Our approach, motivated by recent research on **drug resistance in cancer and microbial cells**, generalizes the classical framework by incorporating **reversible transitions**:



- tolerant mother cell has a sensitive daughter cell with probability λ

We study the **probability distribution** $P_N(m)$ **of the number** m **of resistant cells** in the structurally symmetric fully stochastic Luria–Delbrück model with a population of size N.

Master equation



The probability $P_N(m)$, that there are exactly m resistant cells in a population of size N, where $1 \leq m \leq N$, satisfies the equation:

$$P_{N+1}(m) = \frac{1}{N}\Big\{P_N(m-1)\Big[\mu(N-(m-1)) + (1-\lambda)(m-1)\Big] + P_N(m)\Big[(1-\mu)(N-m) + \lambda m\Big]\Big\}.$$

Results

Overview

Assume: One sensitive cell as the **initial condition:** $\boxed{N_0 = 1, m_0 = 0}$.
(Other cases discussed in [2] .)

We examine the **asymptotic behavior of** $P_N(m)$ as $\boxed{\mu, \lambda \to 0}$ across different regimes:

	$m = O(1)$	$m = O(N) = N - m$	$N - m = O(1)$
$N = O(1/\mu)$	left	regular coarse-grained	right

[2] P. Bokes, A. Hlubinová, and A. Singh, "Reversible transitions in a fluctuation assay modify the tail of Luria–Delbrück distribution," *Axioms*, vol. 12, no. 3, p. 249, 2023.

Regular coarse-grained solution

	$m = O(1)$	$m = O(N) = N - m$	$N - m = O(1)$
$N = O(1/\mu)$	left	regular coarse-grained	right

- Regular coarse-grained solution: $P_N(m) \sim \frac{\mu N}{m^2}$.

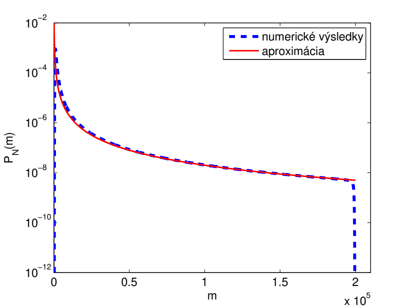


Fig. 4: Initial condition: $N_0 = 1, m_0 = 0$. Final population size: $N = 2 \times 10^5$. Perturbation parameters: $\mu = \lambda = 10^{-3}$.

Left boundary-layer solution

	$m = O(1)$	$m = O(N) = N - m$	$N - m = O(1)$
$N = O(1/\mu)$	left	regular coarse-grained	right

- **Left boundary-layer solution:** $P_N(m) \sim \frac{1}{\mu N} f_{\text{Landau}}\left(\frac{m}{\mu N} - \ln(\mu N)\right)$

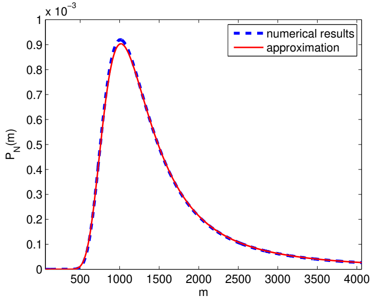


Fig. 5: Initial condition: $N_0 = 1, m_0 = 0$. Final population size: $N = 2 \times 10^5$. Perturbation parameters: $\mu = \lambda = 10^{-3}$.

Right boundary-layer solution

	$m = O(1)$	$m = O(N) = N - m$	$N - m = O(1)$
$N = O(1/\mu)$	left	regular coarse-grained	right

- **Right boundary-layer solution:** $P_N(m) \sim \frac{\mu}{N} F_{\text{Landau}}\left(\frac{N-m}{\lambda N} - \ln(\lambda N)\right)$

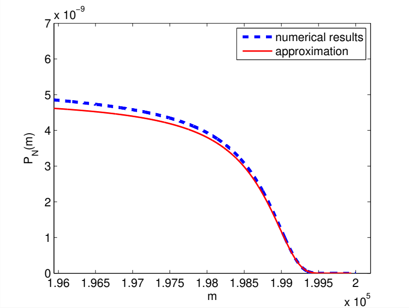


Fig. 6: Initial condition: $N_0 = 1$, $m_0 = 0$. Final population size: $N = 2 \times 10^5$. Perturbation parameters: $\mu = \lambda = 10^{-3}$.

Log-composite solution

	$m = O(1)$	$m = O(N) = N - m$	$N - m = O(1)$
$N = O(1/\mu)$	left	regular coarse-grained	right

- **Composite solution:** $P_N(m) \sim \frac{1}{\mu N} f_{\text{Landau}}\left(\frac{m}{\mu N} - \ln \mu N\right) F_{\text{Landau}}\left(\frac{N-m}{\lambda N} - \ln \lambda N\right).$

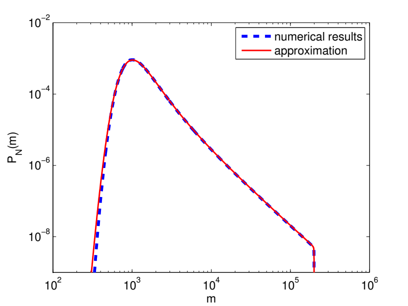
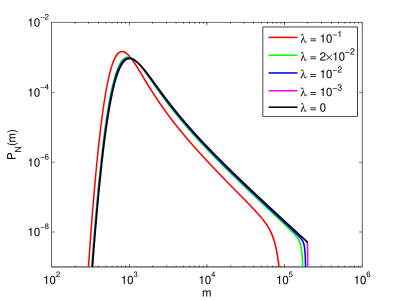


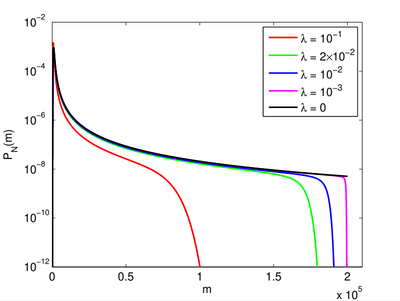
Fig. 7: Initial condition: $N_0 = 1$, $m_0 = 0$. Final population size: $N = 2 \times 10^5$. Perturbation parameters: $\mu = \lambda = 10^{-3}$.

Main effect of λ

Reversible resistance introduces a boundary layer at the right tail of the distribution, which is described by the **Landau CDF**.



(a) Logarithmic scale for m



(b) Linear scale for m

Fig. 8: Comparison of $P_N(m)$ for different values of λ. Initial condition: $N_0 = 1, m_0 = 0$. Final population size: $N = 2 \times 10^5$. Perturbation parameter: $\mu = 10^{-3}$.

Thank you for your attention!

References i

- D. A. Kessler and H. Levine, “Large population solution of the stochastic luria–delbrück evolution model,” *Proceedings of the National Academy of Sciences*, vol. 110, no. 29, pp. 11682–11687, 2013.
- P. Bokes, A. Hlubinová, and A. Singh, “Reversible transitions in a fluctuation assay modify the tail of luria–delbrück distribution,” *Axioms*, vol. 12, no. 3, p. 249, 2023.