

# Virus Transmission Bottleneck Size Estimation Using Patterns of Clonal Passenger Mutations

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## Introduction

- Transmission bottleneck** is defined as the number of viral particles transmitted from one host to establish an infection in another.<sup>1</sup>
- Accurate determination of the size of the bottleneck is important, especially for fast-mutating viruses like influenza, since narrow bottlenecks restrict the transfer of viral genetic diversity, potentially leading to a lower rate of viral adaptation.<sup>2</sup>
- Estimating **clonal passenger mutations** can reveal important insights into viral transmission dynamics.
- Here, we present a method for estimating transmission bottleneck sizes based on patterns of clonal passenger mutations observed in transmission pairs.

### Question to be addressed:

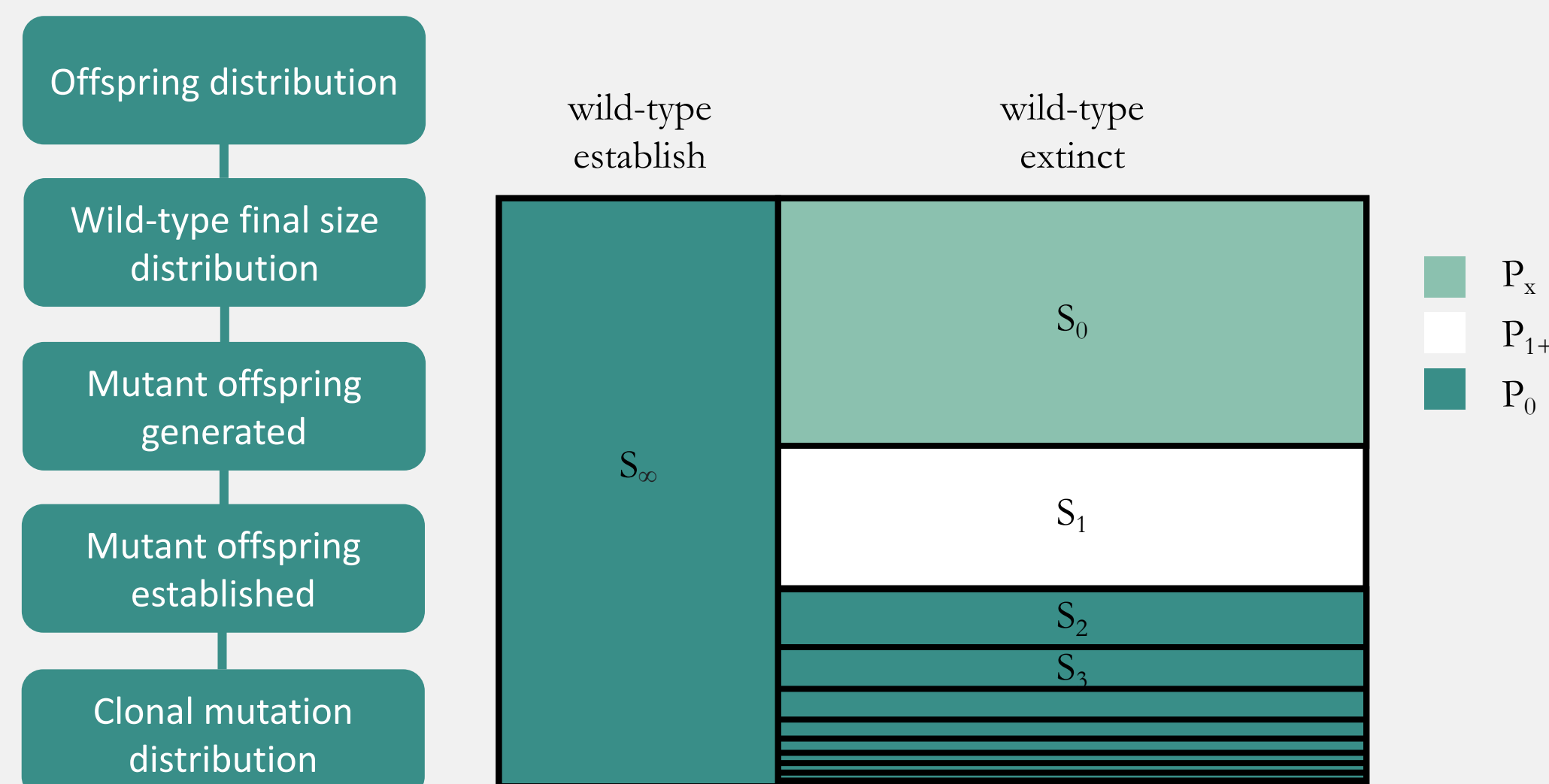
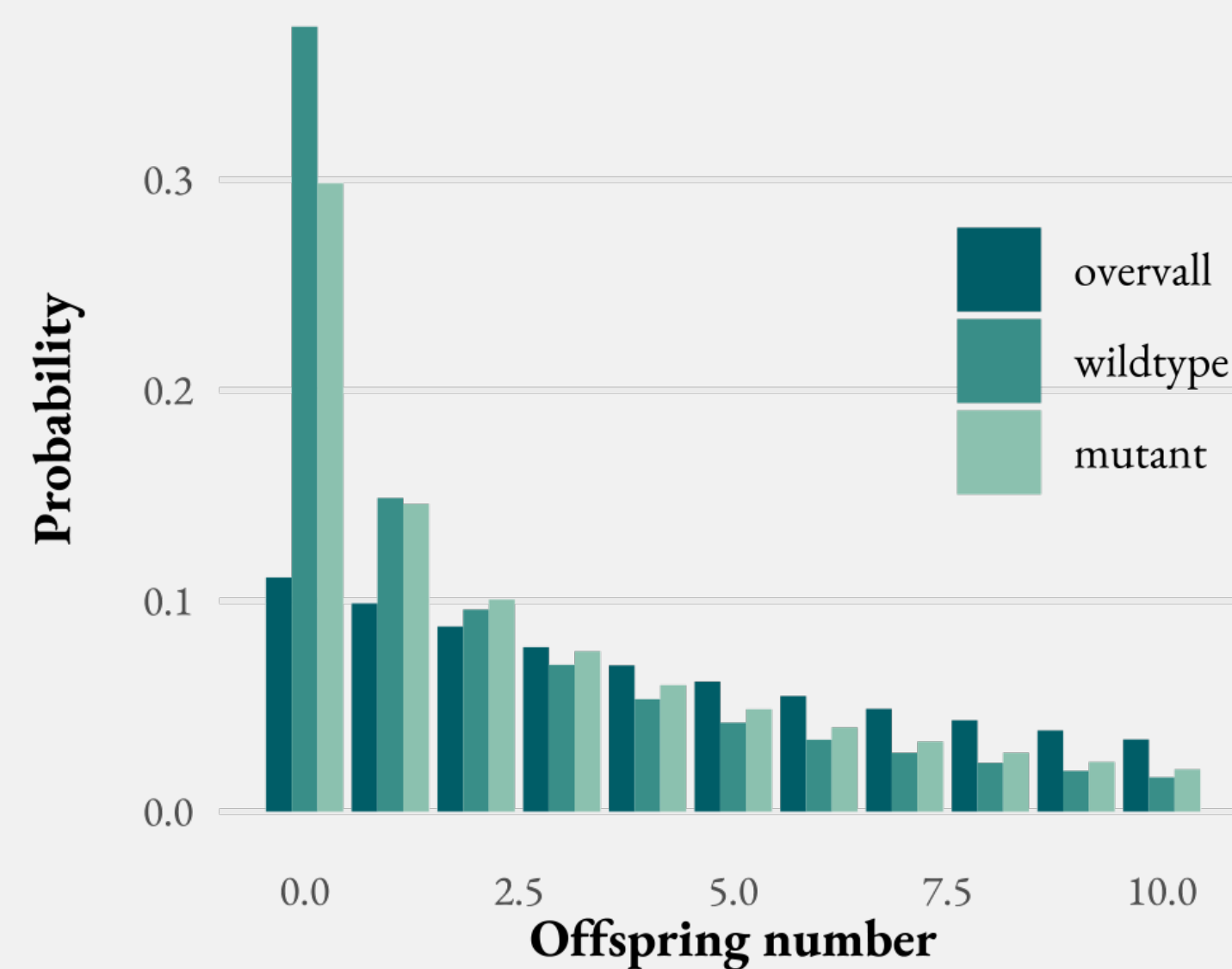
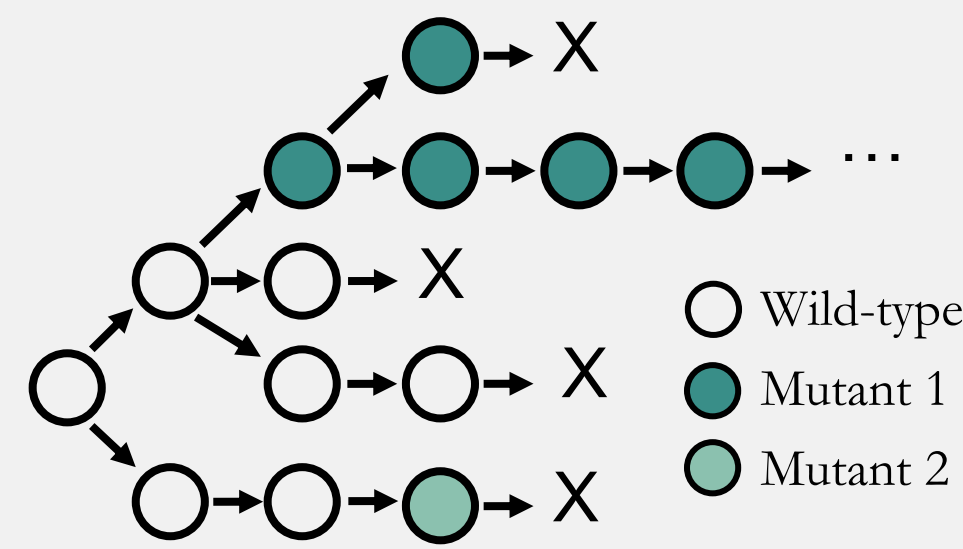
What is the probability distribution of the number of clonal passenger mutations observed in a viral population? We will use this expression to calculate the viral transmission bottleneck size from empirical data

## Approaches

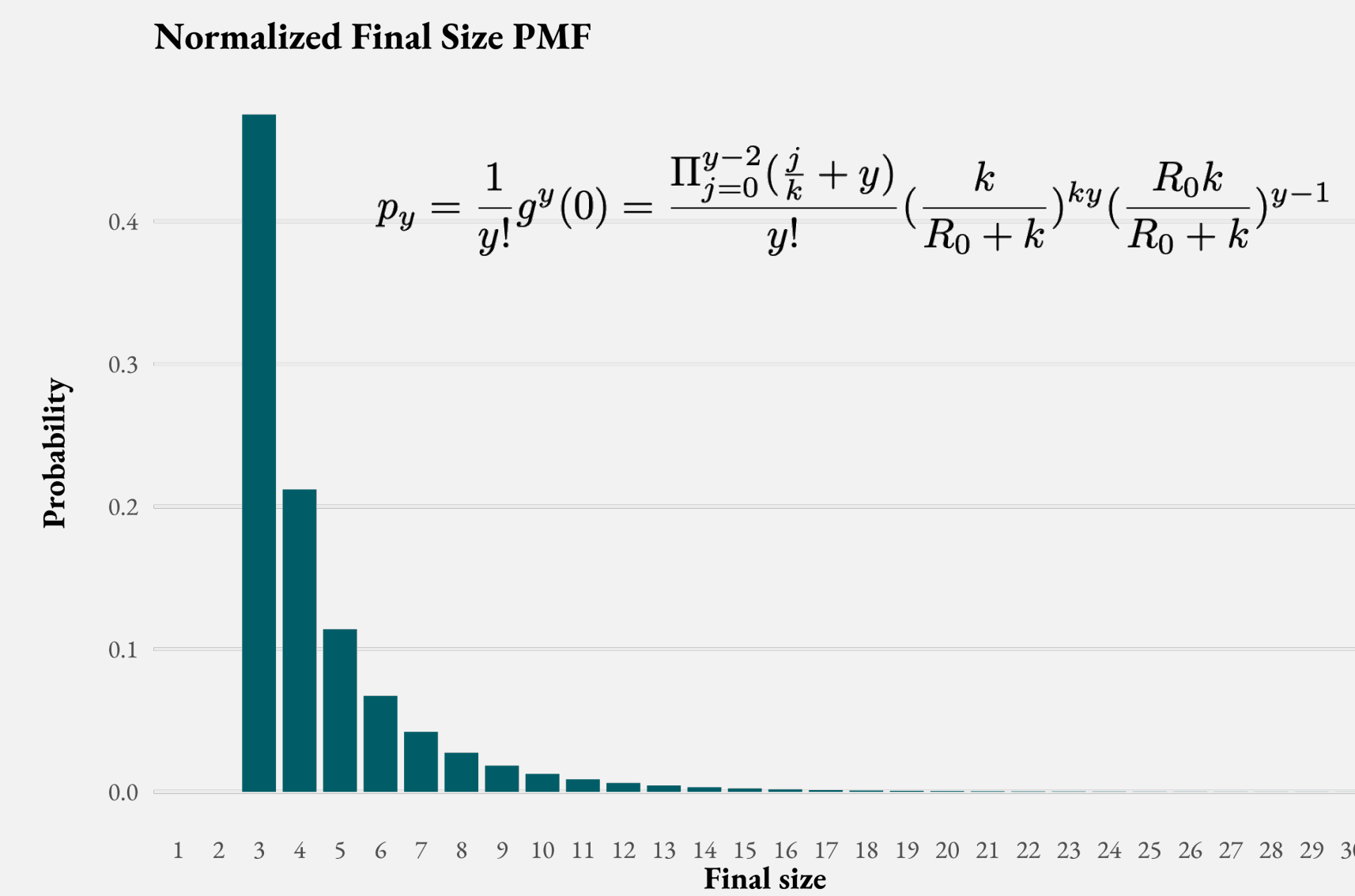
- We model the possible mutations generated by a single viral particle using **Poisson distribution** with mean  $\mu$ .

$$P(\text{mutation} = k) = \frac{\mu^k e^{-\mu}}{k!}$$

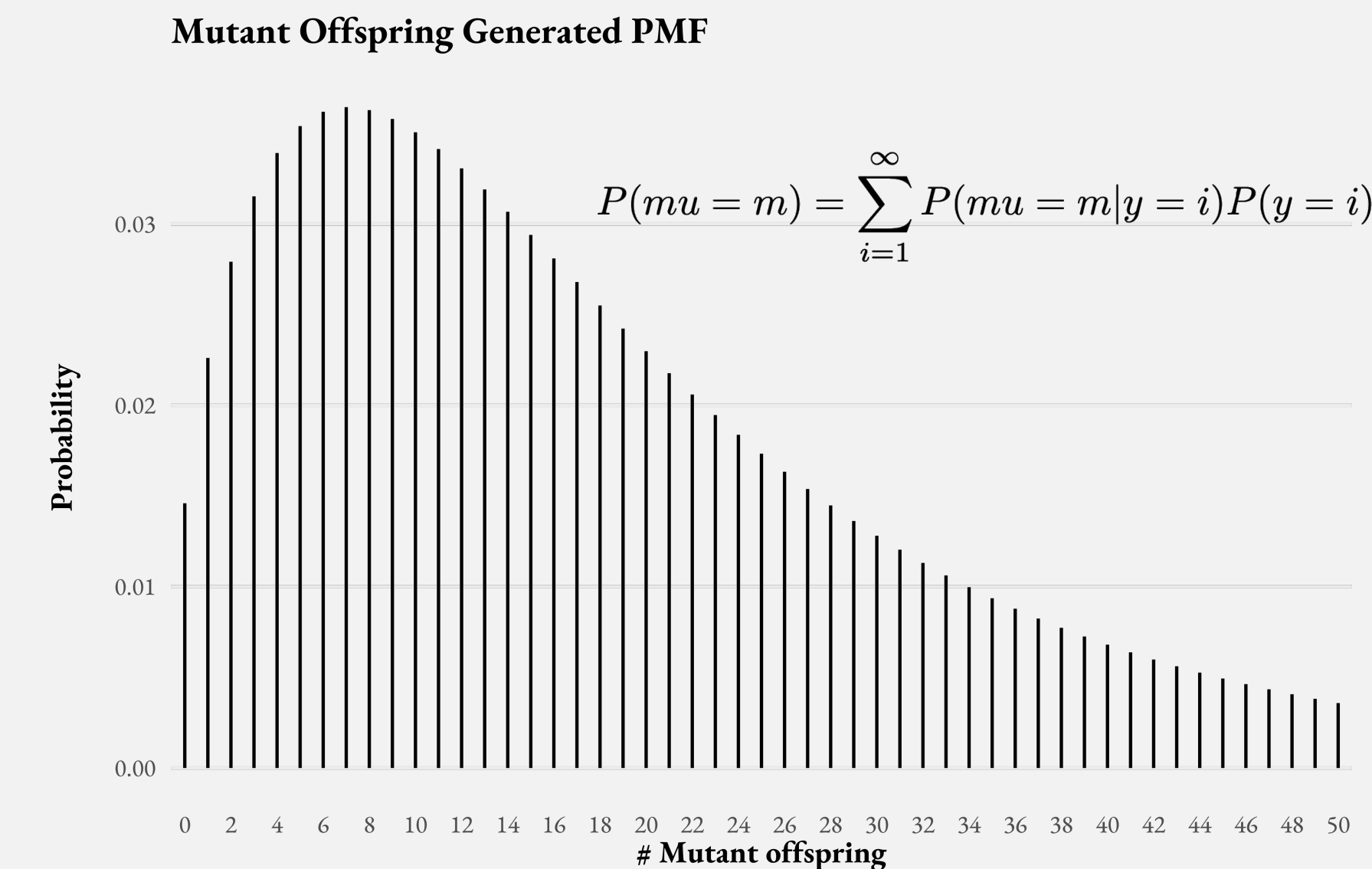
- We model the offspring distribution of viral particles using a **negative binomial distribution**.



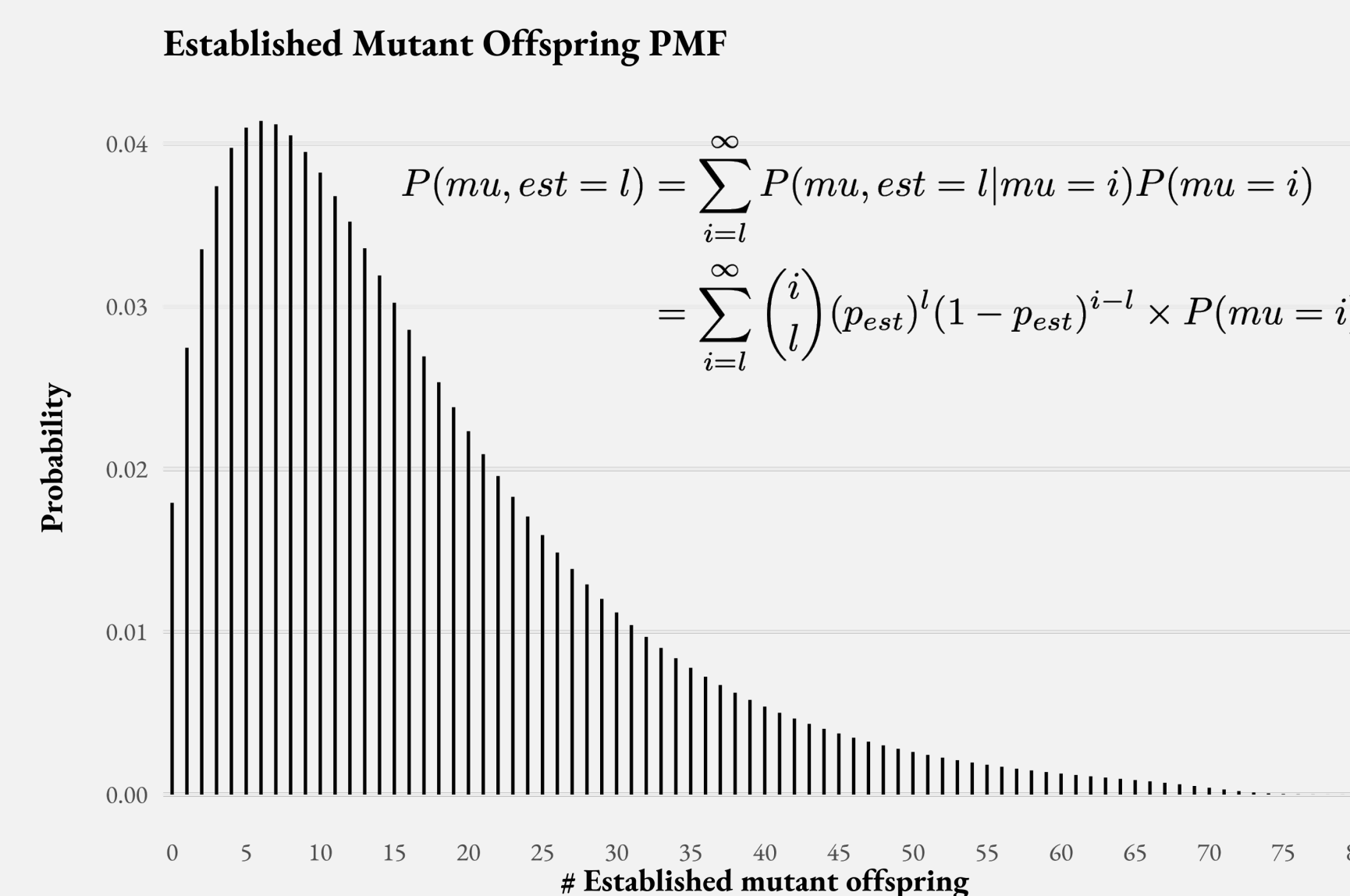
## Results



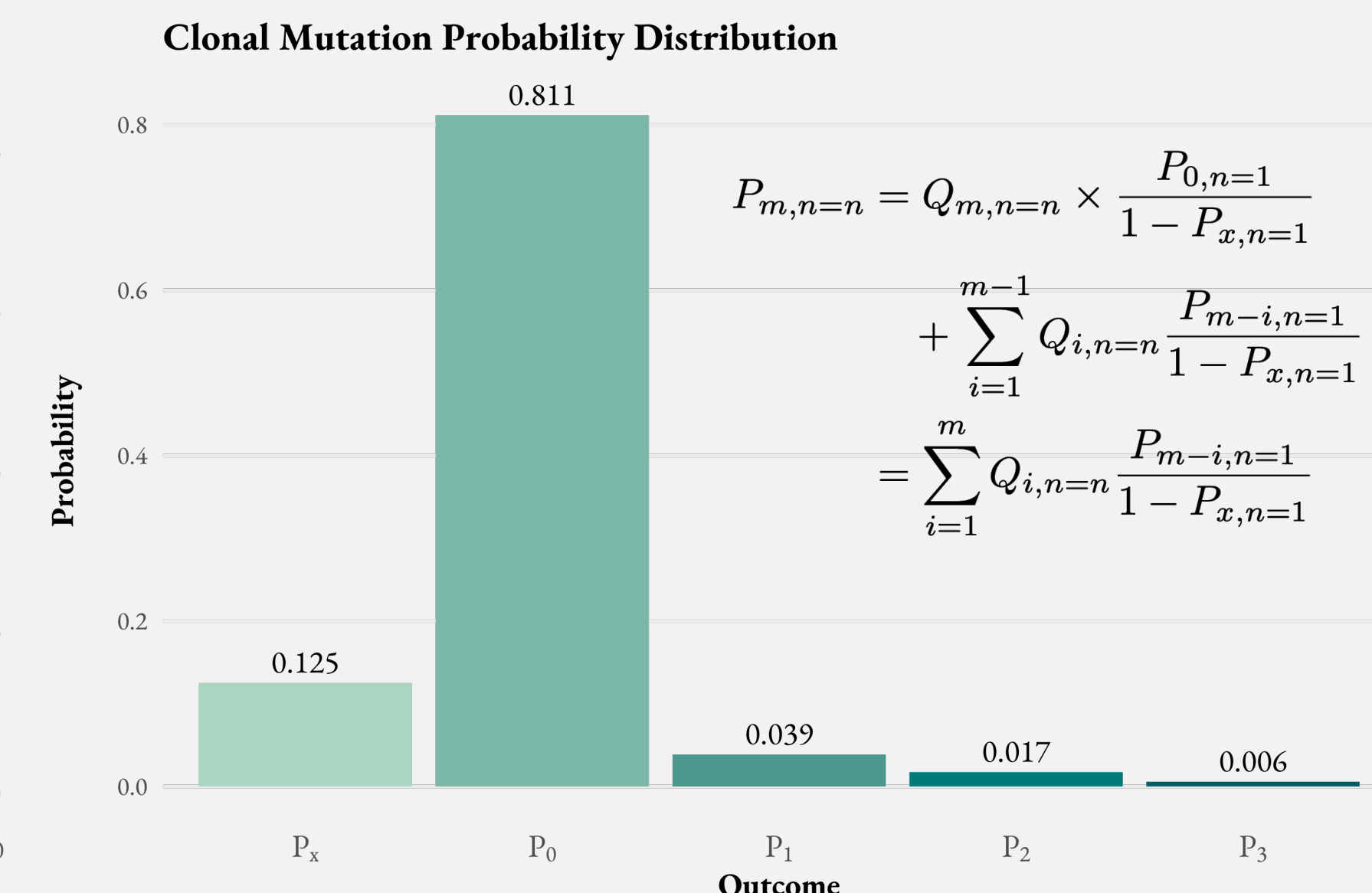
**Figure 1. Normalized wild-type final size probability distribution.<sup>3</sup>**  
A sample distribution with  $n_{\text{initial}} = 3$ , within-host  $R_0 = 8$ ,  $\mu = 0.8$



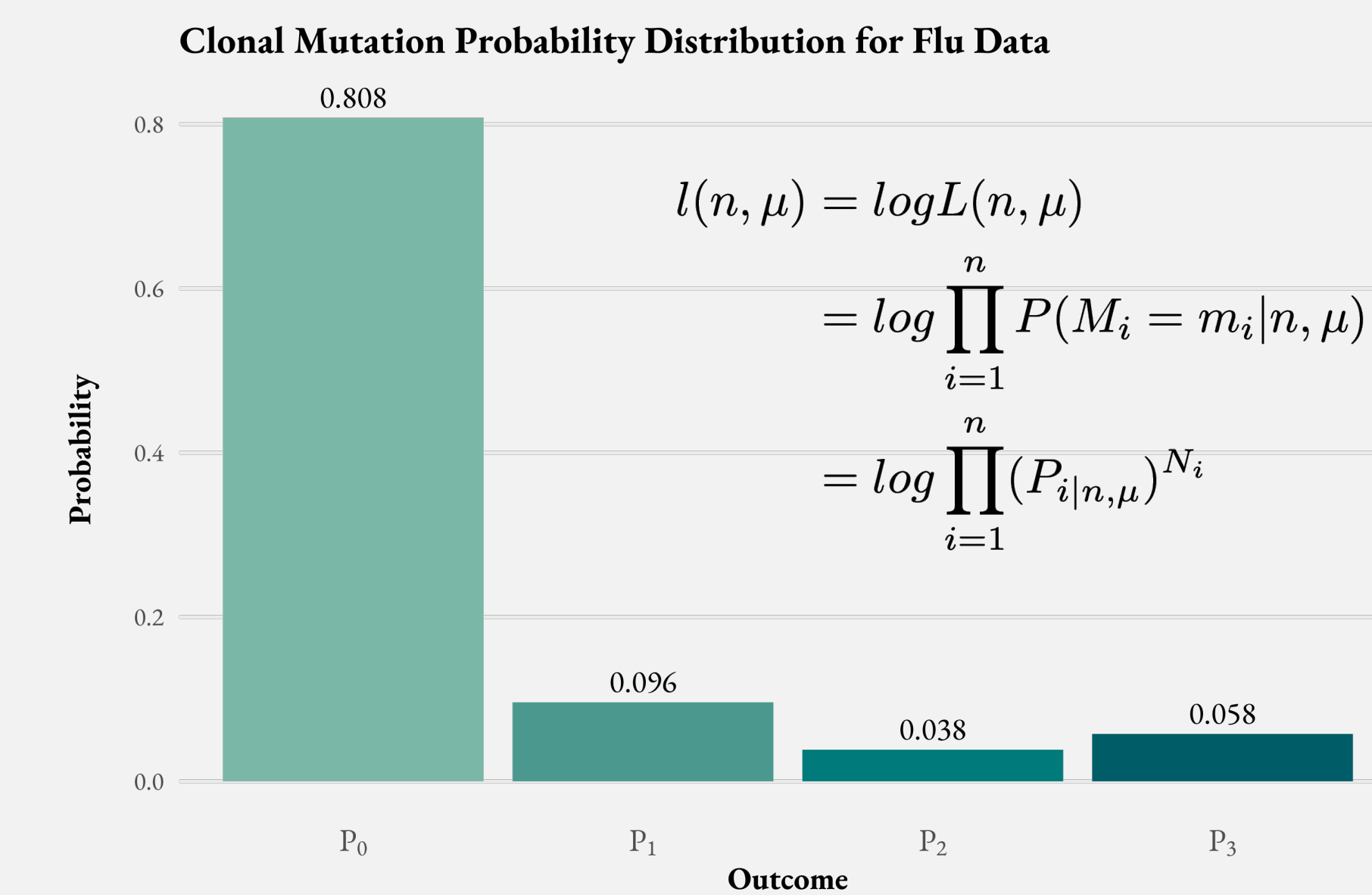
**Figure 2. Mutant offspring generated probability distribution.**  
A sample distribution with  $n_{\text{initial}} = 3$ , within-host  $R_0 = 8$ ,  $\mu = 0.8$



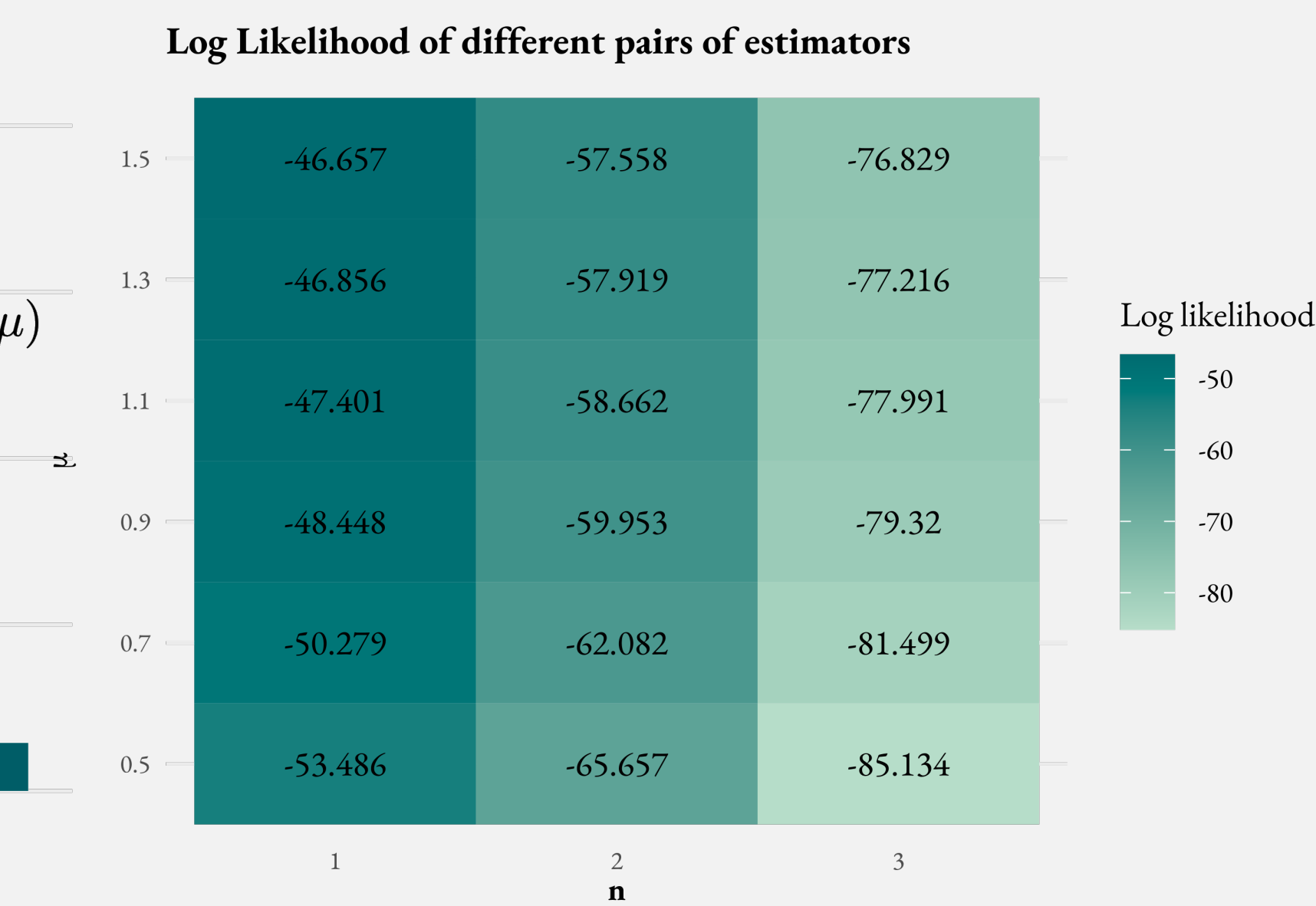
**Figure 3. Established mutant offspring probability distribution.**  
A sample distribution with  $n_{\text{initial}} = 3$ , within-host  $R_0 = 8$ ,  $\mu = 0.8$



**Figure 4. Clonal passenger mutation probability distribution.**  
A sample distribution with  $n_{\text{initial}} = 1$ , within-host  $R_0 = 8$ ,  $\mu = 0.8$



**Figure 5. Clonal mutation probability distribution from a sample flu data.**



**Figure 6. Log-likelihood heat map to estimate the expected mutation rate and initial population size.**

We use the maximum likelihood estimation (MLE) method to plot the log likelihood heat map for a sample of flu data with known within-host  $R_0 = 11.1$ .<sup>4</sup>

## Conclusions

- The probability distribution of clonal passenger mutations can be used to estimate the expected mutation number  $\mu$  present on a viral particle and initial viral population size  $n$ .
- The expected initial viral population size can be used to estimate the transmission bottleneck.
- The application to flu data support that this model can faithfully predict the mean mutation number  $\mu$  and initial viral population size  $n$ .
- The relatively small transmission bottleneck of flu underlines the effect of genetic drift in the process of flu transmission.

## Future Directions

- Using the estimated initial viral population size  $n$ , generate the Poisson distribution of initial size among the sample.
- Apply the establishment probability to the expected initial viral population size  $n$  and estimate for the transmission bottleneck.

## Acknowledgements

Thanks to Dr. Koelle for unwavering support and guidance throughout the project. Thanks to Nancy Chen, my generous roommate, for providing me with possible ideas for the development of methods. Thanks to Kurumi and Mochi, two little kitten giving me emotional support whenever I needed.

## References

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