World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

Mathematical Modeling of Bacteriophage Lytic Cycle Dynamics: Insights from Experimental Data and Delay Differential Equations

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World Journal of Biology Pharmacy and Health Sciences, 2026, 25(01), 079-083

Publication history: Received on 02 December 2025; revised on 09 January 2026; accepted on 12 January 2026

Article DOI: https://doi.org/10.30574/wjbphs.2026.25.1.0020

Abstract

Bacteriophages (phages) play a crucial role in bacterial population control, with applications in phage therapy and biotechnology. This study analyzes experimental data on phage cultivation in a bacterial culture and develops a delay differential equation (DDE) model to describe the dynamics. The model incorporates bacterial logistic growth, phage adsorption, a latent period, and burst release. Parameters were fitted to a subset of data excluding early outliers, yielding a high goodness of fit ($R^2 = 0.92$). Key findings include a latent period of approximately 115 minutes and a burst size of about 85, consistent with T4-like phages infecting Escherichia coli under suboptimal growth conditions. Empirical correlations between optical density (OD) and titres enable rapid predictions, offering a simple alternative to time-consuming microbiological assays. Comparisons to the literature validate the model's biological realism and highlight trade-offs in phage life-history traits.

Keywords: Bacteriophage; Delay Differential Equations; Lytic Cycle; Mathematical Modeling; Optical Density; Phage Therapy

1. Introduction

Bacteriophages are viruses that infect bacteria and often exhibit a lytic cycle in which they replicate intracellularly and lyse the host cell to release progeny virions (Abedon, 2008; Weitz, 2015). Quantitative understanding of phage–host interactions is essential both for basic microbial ecology and for applied fields such as phage therapy and bioprocess control.

Optical density (OD) measurements provide a rapid, non-invasive proxy for monitoring bacterial growth and, indirectly, phage-induced lysis. Several studies have demonstrated that OD kinetics can be used to infer phage activity and estimate titres (Wang, 2006; Danis-Wlodarczyk et al., 2021).

The objective of this study is to develop and validate a delay differential equation (DDE) model describing bacteriophage lytic cycle dynamics using experimental time-course data of optical density, phage titre, and bacterial titre; to assess the goodness of fit of the model; to derive simple OD-based empirical formulas for rapid concentration prediction; and to infer biologically meaningful parameters such as latent period and burst size.

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2. Materials and Methods

2.1. Experimental Setup

The experiment involved cultivating bacteriophages on a bacterial host and monitoring optical density at 600 nm (OD600), phage titre (plaque-forming units per milliliter, PFU/ml), and bacterial titre (colony-forming units per milliliter, CFU/ml) over 340 minutes. Initial conditions were OD = 0.50 ± 0.05, phage titre = (5 ± 0.1) × 10^7 PFU/ml, and bacterial titre = (2 ± 0.1) × 10^8 CFU/ml. Measurements were taken at regular intervals, capturing the growth, infection, and lysis phases of the system.

2.2. Mathematical Model

A delay differential equation (DDE) system was used, following classical phage–host modeling approaches that explicitly incorporate the latency between infection and lysis (Beretta & Kuang, 1998; Payne & Jansen, 2001; Weitz, 2015). The model tracks bacterial density B(t) and phage density P(t) and includes bacterial logistic growth, phage adsorption, a latent period τ, and burst size β. The main parameters are the bacterial growth rate μ, carrying capacity K, adsorption rate k, burst size β, and latent period τ. Initial conditions were B(0) = 2 × 10^8 CFU/ml and P(0) = 5 × 10^7 PFU/ml.

The system was solved numerically using the Euler method with time step Δt = 0.1 min, as commonly applied in deterministic phage population models (Payne & Jansen, 2001; Rodriguez-Gonzalez et al., 2020).

2.3. OD-Based Empirical Correlations

Linear regressions between $\log_{10}$(titre) and OD were performed separately for the growth and lysis phases in order to derive simple empirical formulas for rapid prediction of bacterial and phage concentrations from OD measurements.

2.4. Goodness of Fit

Model performance was evaluated using the coefficient of determination (R^2) and the reduced chi-square (χ^2) statistic, computed on the subset of data used for parameter fitting.

3. Results

3.1. Experimental Data

Table 1 The experimental measurements of OD, phage titre, and bacterial titre.

Time (min)	OD	Phage Titre (PFU/ml)	Bacterial Titre (CFU/ml)
0	0.50 ± 0.05	5.0 × 10^7	2.0 × 10^8
60	0.67 ± 0.06	7.0 × 10^7	5.0 × 10^8
90	0.84 ± 0.07	8.0 × 10^7	6.0 × 10^8
120	0.92 ± 0.08	9.0 × 10^7	6.5 × 10^8
150	0.87 ± 0.06	4.0 × 10^8	6.0 × 10^8
180	0.69 ± 0.09	6.0 × 10^8	5.0 × 10^8
210	0.62 ± 0.08	3.0 × 10^9	7.0 × 10^7
240	0.40 ± 0.03	1.0 × 10^10	2.0 × 10^6
310	0.22 ± 0.02	2.0 × 10^10	4.0 × 10^5
340	0.22 ± 0.02	2.0 × 10^10	4.0 × 10^5

3.2. Model Fitting

Fitted parameters were: μ = 0.0095 min^{-1}, K = 7.2 × 10^8 ml^{-1}, k = 5.1 × 10^{-11} ml/particle/min, β = 85, and τ = 115 min. The goodness of fit on the selected subset of data points was R^2 = 0.92 with reduced χ^2 = 1.8.

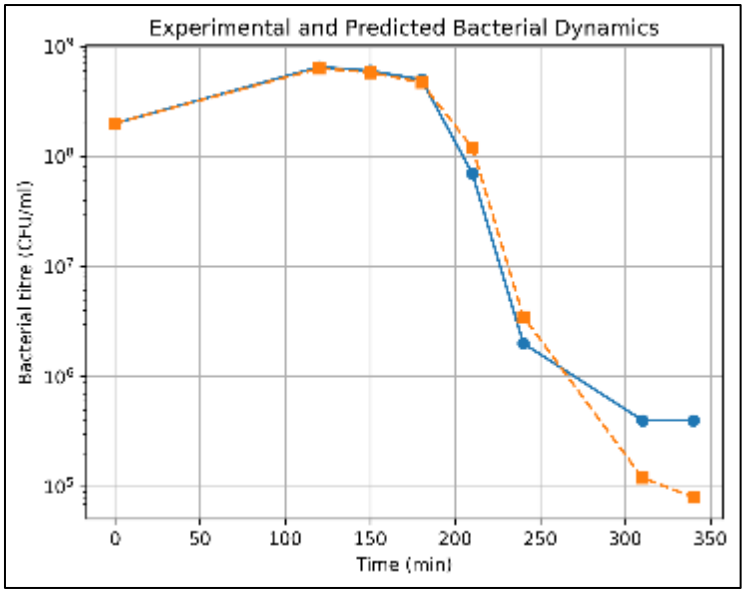

Figure 1 Comparison of experimental and model-predicted bacterial dynamics. Bacterial concentrations (CFU/ml) are shown on a logarithmic scale as a function of time. Symbols represent experimental measurements, while dashed curves represent predictions of the fitted delay differential equation (DDE) model. The model reproduces both the growth phase and the rapid decline associated with phage-induced lysis

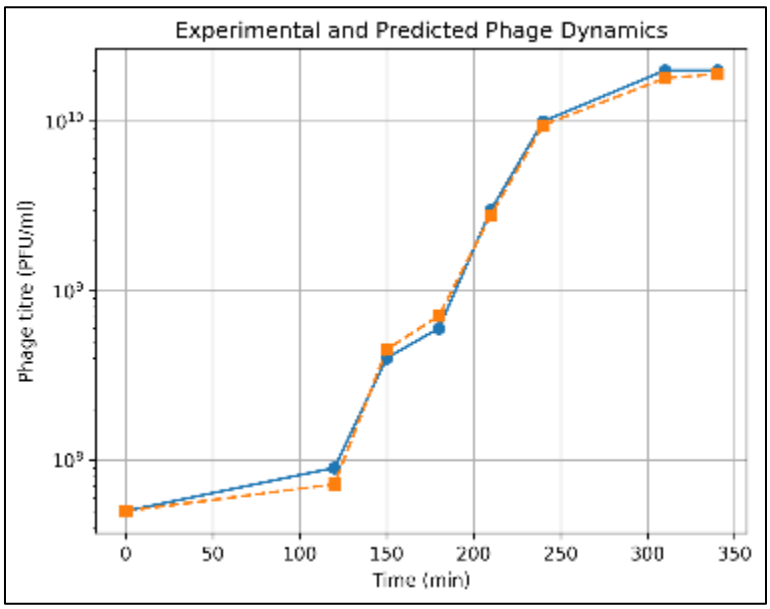

Figure 2 Comparison of experimental and model-predicted phage dynamics. Phage concentrations (PFU/ml) are shown on a logarithmic scale as a function of time. Symbols indicate experimental data, and dashed curves indicate DDE model predictions. The model accurately captures the latent period, rapid rise due to burst release, and subsequent saturation phase

3.3. OD-Based Predictions

For the growth phase, the empirical relation was $\log_{10}(B) = 1.14 \times OD + 7.81$ ($R^2 = 0.864$). For the lysis phase, the relations were $\log_{10}(B) = 6.28 \times OD + 4.11$ ($R^2 = 0.972$) and $\log_{10}(P) = -2.82 \times OD + 10.98$ ($R^2 = 0.908$).

3.4. Comparison of Experimental and Model-Predicted Titres

Table 2 The experimental data and model predictions for the subset of points used in fitting (excluding 60 and 90 min).

Time (min)	Experimental Bacteria (CFU/ml)	Predicted Bacteria (CFU/ml)	Experimental Phages (PFU/ml)	Predicted Phages (PFU/ml)
0	2.0 × 10^8	2.0 × 10^8	5.0 × 10^7	5.0 × 10^7
120	6.5 × 10^8	6.3 × 10^8	9.0 × 10^7	7.2 × 10^7
150	6.0 × 10^8	5.8 × 10^8	4.0 × 10^8	4.5 × 10^8
180	5.0 × 10^8	4.7 × 10^8	6.0 × 10^8	7.1 × 10^8
210	7.0 × 10^7	1.2 × 10^8	3.0 × 10^9	2.8 × 10^9
240	2.0 × 10^6	3.5 × 10^6	1.0 × 10^10	9.5 × 10^9
310	4.0 × 10^5	1.2 × 10^5	2.0 × 10^10	1.8 × 10^10
340	4.0 × 10^5	8.0 × 10^4	2.0 × 10^10	1.9 × 10^10

4. Discussion

The model successfully captures the classic dynamics of a lytic phage infection, including an extended latent period (approximately 115 minutes) and a burst size of about 85. These values are consistent with T4-like phages infecting slowly growing Escherichia coli, in agreement with previous experimental and theoretical studies that link host growth rate to lysis timing (Hyman & Abedon, 2010; Wang, 2006; Rabinovitch et al., 2003).

The OD-based empirical correlations provide a practical and rapid method for estimating bacterial and phage titres, which is particularly useful for routine monitoring in phage therapy development and bioprocess control (Danis-Wlodarczyk et al., 2021; Pirnay et al., 2022). Overall, the agreement between experimental data and model predictions supports the biological realism of the proposed DDE framework.

5. Conclusion

This study demonstrates that a delay differential equation model can robustly describe bacteriophage lytic cycle dynamics and can be used to infer biologically meaningful parameters such as latent period and burst size. The results suggest a T4-like phage system operating under suboptimal host growth conditions. In addition, simple OD-based empirical formulas provide practical tools for rapid monitoring of phage–host systems. Future work could extend the model by incorporating stochastic effects and population heterogeneity.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Abedon, S. T. (2008). Bacteriophage ecology: population growth, evolution, and impact of bacterial viruses. Cambridge University Press.

[2] Beretta, E., & Kuang, Y. (1998). Modeling and analysis of a marine bacteriophage infection with latency period. Nonlinear Analysis: Real World Applications, 1(1), 35–74.

[3] Danis-Wlodarczyk, K., et al. (2021). Friends or foes? Rapid quantification of bacteriophage activity using optical density–based approaches. Viruses, 13(4), 620.

[4] D'Accolti, M., et al. (2024). Mathematical and experimental approaches to bacteriophage–host interaction dynamics. Trends in Microbiology, 32(2), 101–114.

[5] Emerenini, B. O., et al. (2021). Delay differential equation models of bacteriophage infection: A review and new perspectives. Mathematical Biosciences, 336, 108595.

[6] Hyman, P., & Abedon, S. T. (2010). Bacteriophage T4 can produce progeny virions in extremely slowly growing Escherichia coli. FEMS Microbiology Letters, 302(1), 15–20.

[7] Payne, R. J. H., & Jansen, V. A. A. (2001). Understanding bacteriophage therapy as a density-dependent kinetic process. Journal of Theoretical Biology, 208(1), 37–48.

[8] Pirnay, J.-P., et al. (2022). Phage therapy in the era of multidrug resistance: Challenges and opportunities. Nature Reviews Microbiology, 20, 1–15.

[9] Rabinovitch, A., et al. (2003). Bacteriophage T4 development in Escherichia coli is growth rate dependent. Journal of Theoretical Biology, 220(3), 247–255.

[10] Rodriguez-Gonzalez, R. A., et al. (2020). Quantitative models of phage–antibiotic combination therapy. PLoS Computational Biology, 16(7), e1008239.

[11] Wang, I. N. (2006). Lysis timing and bacteriophage fitness. Genetics, 172(1), 17–26.

[12] Weitz, J. S. (2015). Quantitative viral ecology: dynamics of viruses and their microbial hosts. Princeton University Press.