

Article

Nonlinear Responses and Population-Level Coupling of Growth and MC-LR Production in *Microcystis aeruginosa* Under Multifactorial Conditions

Melina Celeste Crettaz-Minaglia ^{1,2,*} , Sandro Goñi ^{2,3} and Leda Giannuzzi ^{1,2,3,†} 

¹ Área de Toxicología, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP), La Plata 1900, Argentina

² Consejo Nacional de Investigaciones Científicas y Técnicas, San Lorenzo 2290, Argentina; sandro.goni@ing.unlp.edu.ar

³ Centro de Investigación y Desarrollo en Criotecología de Alimentos (CIDCA) CONICET-UNLP, La Plata 1900, Argentina

* Correspondence: crettaz.melina@uader.edu.ar

† Deceased. Prof. Leda Giannuzzi passed away before the submission of this manuscript.

Abstract: *Microcystis aeruginosa* is a cyanobacterium frequently associated with toxic blooms in eutrophic freshwater systems. Certain strains produce microcystins (MCs), a group of hepatotoxins with significant ecological and public health implications. In this study, we examined the quantitative response of a temperate native *M. aeruginosa* strain to combinations of temperature (26, 30, and 36 °C), light intensity (30, 50, and 70 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$), and N:P ratio (10, 100, 150), using a full-factorial experimental design. Growth parameters (μ , lag phase duration, and maximum cell density), chlorophyll-a production, and MC-LR synthesis were modeled using Gompertz, linear, and dynamic approaches. High temperature and irradiance increased the specific growth rate but decreased final biomass, while elevated N:P ratios shortened the lag phase. MC-LR production peaked under low temperature, low irradiance, and low N:P ratio. Although MC-LR synthesis did not correlate positively with growth rate, and the environmental conditions maximizing growth differed from those enhancing toxin production, a population-level coupling between both processes was observed using the Long model. These findings suggest that MC-LR synthesis in *M. aeruginosa* is not merely a metabolic by-product of growth, but a context-dependent trait with potential adaptive significance.

Keywords: cyanobacterial blooms; growth modeling; multifactorial design; toxin production; environmental drivers



Received: 30 April 2025

Revised: 12 June 2025

Accepted: 13 June 2025

Published: 18 June 2025

Citation: Crettaz-Minaglia, M.C.; Goñi, S.; Giannuzzi, L. Nonlinear Responses and Population-Level Coupling of Growth and MC-LR Production in *Microcystis aeruginosa* Under Multifactorial Conditions.

Phycology **2025**, *5*, 26. <https://doi.org/10.3390/phycology5020026>

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1. Introduction

Cyanobacterial blooms are a growing global concern due to their ecological impacts and health risks associated with toxin production. Among bloom-forming genera, *Microcystis* is one of the most prevalent and widely distributed in freshwater ecosystems, with numerous strains capable of producing microcystins (MCs), a group of hepatotoxins with demonstrated toxicity to aquatic organisms and humans [1,2]. These blooms can disrupt ecosystem structure and function, reduce biodiversity, and impair water use for drinking, recreation, agriculture, and aquaculture [3,4].

Environmental factors such as light intensity, temperature, and nutrient availability shape both the growth dynamics and toxin synthesis of *M. aeruginosa*. While the individual effects of these drivers have been extensively studied, there is growing evidence that their

interactions can lead to nonlinear and context-dependent responses [5,6]. Understanding these interactions is essential for improving predictions of bloom dynamics under future climate and eutrophication scenarios. Several laboratory studies have explored how temperature, irradiance, or N:P ratio influence either growth or MC production (e.g., [7–9]), often revealing that conditions optimizing growth do not necessarily maximize microcystin synthesis. However, the relationship between *M. aeruginosa* growth and toxin production remains ambiguous, with some studies reporting positive coupling [10] and others suggesting inverse or nonlinear associations [8,11]. To clarify these patterns, experimental designs that integrate multiple environmental drivers are essential. Multifactorial approaches allow for the detection of interactive effects that would otherwise remain hidden in single-factor analyses [12]. Moreover, applying mathematical models to the full growth curve provides robust kinetic parameters, enabling more precise comparisons across conditions and taxa [13,14].

Given the growing interest in forecasting harmful cyanobacterial blooms under climate change scenarios, laboratory-based studies remain essential to provide reliable growth and toxin parameters. These data are increasingly used to inform predictive frameworks that integrate climate variables, nutrient loads, and microbial interactions [15–17].

Recent advances in modeling *Microcystis* dynamics have applied approaches ranging from multiple regression [18] and kinetic models for toxin release [19] to mechanistic simulations incorporating photosynthetic activity and environmental variables [20]. Our study complements these efforts by using a full-factorial experimental design combined with Gompertz and dynamic models to derive quantitative growth and toxin production parameters under controlled conditions.

In this study, we applied a $3 \times 3 \times 3$ factorial design to investigate how temperature, irradiance, and N:P ratio jointly affect the growth, chlorophyll-a (Chl-a) production, and MC-LR synthesis of a temperate native *M. aeruginosa* strain under controlled conditions. We modeled growth using the Gompertz equation and applied both linear and dynamic modeling approaches to describe Chl-a and MC-LR production over time. We hypothesized that (a) microcystin production is coupled to cellular growth rate and (b) the optimal environmental conditions for growth differ from those that maximize MC-LR synthesis.

2. Materials and Methods

2.1. Experimental Design and Culture Conditions

A temperate, native, non-axenic *Microcystis aeruginosa* strain (CAAT2005–3), previously characterized as a [D-Leu1] MC-LR producer [14], was used in this study. The strain is maintained in our laboratory collection at the Área de Toxicología, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP), Argentina. Cultures were grown in sterile 500 mL Erlenmeyer flasks under controlled laboratory conditions. The base medium was BG11o, supplemented with $0.15 \text{ g} \cdot \text{L}^{-1}$ of sodium nitrate (NaNO_3) and $0.04 \text{ g} \cdot \text{L}^{-1}$ of dipotassium hydrogen phosphate trihydrate ($\text{K}_2\text{HPO}_4 \cdot 3\text{H}_2\text{O}$), corresponding to a molar N:P ratio of approximately 10:1 (1.76 mM nitrate-N and 0.175 mM phosphate-P). Pre-cultures were maintained at 26°C under a 10:14 h light–dark cycle, with continuous aeration and a light intensity of $30 \mu\text{mol photons m}^{-2} \text{ s}^{-1}$, until reaching the exponential phase.

A full-factorial design with three environmental variables, temperature (26, 30, and 36°C), irradiance (30 , 50 , and $70 \mu\text{mol photons m}^{-2} \text{ s}^{-1}$), and N:P ratio (10, 100, and 150), was applied, resulting in 27 experimental conditions. The N:P ratios of 100 and 150 were obtained by proportionally adjusting the concentrations of nitrate and phosphate in the base medium. Each condition was tested in triplicate using a growth chamber with precise environmental control. Samples were collected over 15–20 days to measure cell density, chlorophyll-a concentration, and [D-Leu1] MC-LR content.

Cell density was determined by direct counts using an optical microscope and a Neubauer chamber. Chlorophyll-a was quantified spectrophotometrically after methanol extraction, following [21]. Finally, MC-LR concentrations were measured by HPLC-MS, as previously described by [14].

2.2. Growth Curve Modeling

The modified Gompertz equation [13] was applied to model *M. aeruginosa* growth over time. The following kinetic parameters were derived from the fitted curves: specific growth rate (μ), lag phase duration (LPD), and maximum population density (MPD). Parameter calculations followed the approach described in [14], with μ calculated as the slope at the inflection point, LPD as the time-axis intercept of the tangent, and MPD as the asymptotic maximum of the curve.

2.3. Modeling of Chlorophyll-A and Microcystin-LR Production

Chlorophyll-a production was modeled using a first-order kinetic equation, from which the rate constant (k_0) and mean doubling time ($dt_{\text{Chl-a}}$) were calculated.

Microcystin production was described using a dynamic model in which the toxin concentration is a function of cell division rate, incorporating a production coefficient (p) and a depletion rate (dM). The model assumes that toxin accumulation is proportional to growth and is balanced by degradation or release. Additionally, the model proposed by [10] was applied to assess the net MC-LR production rate (RMC) as a function of specific growth rate and intracellular toxin quota (QMC).

2.4. Statistical Analyses

Data were analyzed using SigmaPlot 12.0. A multifactorial analysis of variance (ANOVA) with post hoc Tukey's test ($p < 0.05$ and 0.001) was performed to assess the effects of temperature, irradiance, and N:P ratio, and their interactions, on each measured and modeled parameter. The assumptions of normality and homoscedasticity were checked before ANOVA. Model performance was evaluated through R^2 and root mean square error (RMSE), and correlations between variables were assessed using linear regression.

3. Results

3.1. Growth Kinetics

Growth parameters derived from the Gompertz model (Figure 1) exhibited strong variation across treatments, as summarized in Table 1. The model showed a good fit between the experimental and predictive values for cell density (Figure 2).

The specific growth rate (μ) ranged from 0.17 to 0.46 d^{-1} , with the highest values occurring at 30°C under high irradiance and low to intermediate N:P ratios. In contrast, the lag phase duration (LPD) ranged from 0.18 to 3.55 days and displayed an inverse pattern, with the shortest LPDs under similar conditions. Maximum population density (MPD) showed less variability and no consistent environmental pattern.

Statistical analysis confirmed significant effects of temperature and irradiance on both μ and LPD (ANOVA, $p < 0.01$), with an interaction effect between these two factors influencing LPD. The N:P ratio exerted a milder effect, primarily on LPD under high nutrient imbalance. Collectively, these results indicate that growth rate and adaptation time are highly sensitive to temperature and light but less so to nutrient stoichiometry.

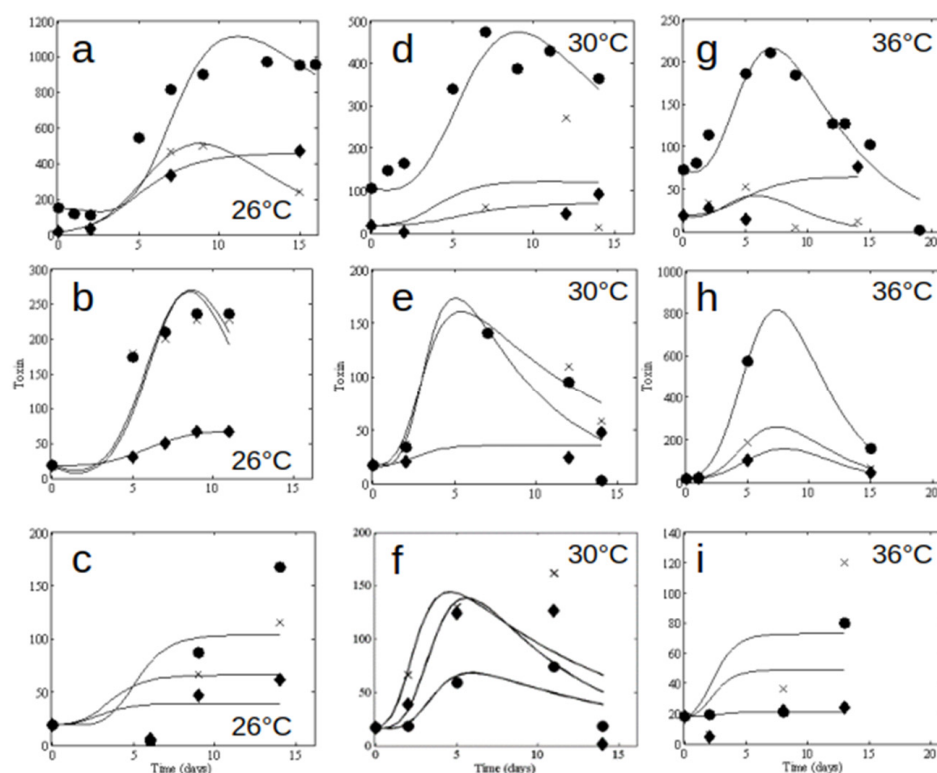


Figure 1. Modeling of *M. aeruginosa* growth ($\text{cells} \cdot \text{mL}^{-1}$) in culture media. Solid lines represent Gompertz model fits to experimental data at 26 °C (a–c), 30 °C (d–f), and 36 °C (g–i), under different light intensities: 30 $\mu\text{mol photons} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$ (a,d,g), 50 $\mu\text{mol photons} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$ (b,e,h), and 70 $\mu\text{mol photons} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$ (c,f,i). Symbols represent N:P ratios: ● = 10, × = 100, ◆ = 150.

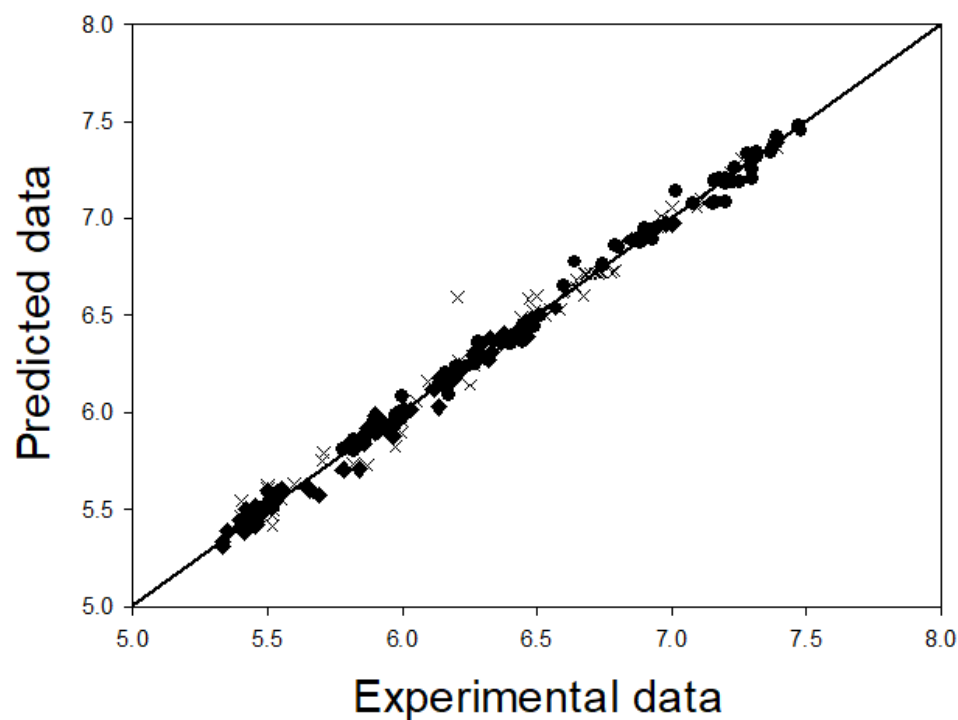


Figure 2. Correlation between experimental and predicted values of *M. aeruginosa* cell density ($\text{cells} \cdot \text{mL}^{-1}$) based on RMSE values. Symbols represent temperatures: ● = 26 °C, × = 30 °C, ◆ = 36 °C. The diagonal line indicates the line of equivalence.

Table 1. Application of the Gompertz model to the experimental data. Parameters a, b, c, and m correspond to the model coefficients; μ (d^{-1}) is the specific growth rate; LPD (d) is the lag phase duration; and MPD ($\text{cells}\cdot\text{mL}^{-1}$) is the maximum population density. The table also shows the coefficient of determination (R^2) and root mean square error (RMSE).

RMSE	R^2	MPD ($\text{cells}\cdot\text{mL}^{-1}$)	LPD (d)	μ (d^{-1})	m	c	b	a	26 °C	
0.082	0.99	7.28 ± 0.02^a	3.55 ± 0.07^a	0.20 ± 0.05^a	5.39 ± 0.06	0.54 ± 0.02	0.99 ± 0.01	6.29 ± 0.01	N:P 10	30 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.030	0.99	7.49 ± 0.03^a	0.65 ± 0.26^b	0.21 ± 0.05^a	3.15 ± 0.07	0.40 ± 0.01	1.39 ± 0.02	6.10 ± 0.01	N:P 100	
0.033	0.99	7.37 ± 0.05^a	0.18 ± 0.40^b	0.24 ± 0.07^a	2.22 ± 0.09	0.49 ± 0.02	1.32 ± 0.03	6.06 ± 0.02	N:P 150	
0.059	0.99	7.19 ± 0.03^b	2.28 ± 0.36^a	0.24 ± 0.07^a	4.42 ± 0.05	0.47 ± 0.02	1.39 ± 0.02	5.80 ± 0.01	N:P 10	50 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.085	0.99	7.44 ± 0.03^b	2.24 ± 0.38^b	0.27 ± 0.06^a	4.45 ± 0.06	0.45 ± 0.01	1.64 ± 0.02	5.80 ± 0.01	N:P 100	
0.055	0.99	7.33 ± 0.05^b	0.88 ± 0.43^b	0.29 ± 0.08^a	3.01 ± 0.09	0.47 ± 0.01	1.66 ± 0.03	5.67 ± 0.02	N:C:\N:\PP 150	
0.040	0.99	7.35 ± 0.03^b	2.54 ± 0.16^a	0.35 ± 0.05^b	3.71 ± 0.01	0.85 ± 0.01	1.11 ± 0.00	6.23 ± 0.00	N:P 10	70 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.075	0.99	7.22 ± 0.03^b	0.72 ± 0.32^b	0.38 ± 0.09^b	1.94 ± 0.05	0.82 ± 0.03	1.27 ± 0.02	5.95 ± 0.02	N:P 100	
0.021	0.99	7.05 ± 0.03^b	0.56 ± 0.34^b	0.36 ± 0.10^b	1.66 ± 0.06	0.91 ± 0.07	1.09 ± 0.02	5.96 ± 0.01	N:P 150	
RMSE	R^2	MPD ($\text{cells}\cdot\text{mL}^{-1}$)	LPD (d)	μ (d^{-1})	m	c	b	a	30 °C	
0.033	0.99	$7.39 \pm 0.06^{a,c}$	0.94 ± 0.27^a	0.22 ± 0.08^a	3.10 ± 0.14	0.46 ± 0.02	1.31 ± 0.03	6.08 ± 0.03	N:C:\N:\PP 10	30 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.073	0.99	$6.75 \pm 0.07^{a,d}$	0.68 ± 0.46^a	0.30 ± 0.12^a	2.18 ± 0.10	0.66 ± 0.06	1.25 ± 0.04	5.50 ± 0.03	N:P 100	
0.026	0.99	6.74 ± 0.09^a	0.94 ± 0.62^a	0.22 ± 0.11^a	3.01 ± 0.18	0.48 ± 0.05	1.24 ± 0.05	5.49 ± 0.04	N:P 150	
0.134	0.99	$6.72 \pm 0.06^{b,c}$	1.04 ± 0.25^a	0.46 ± 0.14^b	2.03 ± 0.06	1.01 ± 0.08	1.22 ± 0.03	5.49 ± 0.03	N:P 10	50 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.090	0.99	$6.58 \pm 0.06^{b,d}$	0.75 ± 0.38^a	0.40 ± 0.12^b	1.81 ± 0.08	0.95 ± 0.07	1.14 ± 0.03	5.44 ± 0.03	N:P 100	
0.020	0.99	6.62 ± 0.08^b	0.54 ± 0.38^a	0.43 ± 0.15^b	1.55 ± 0.07	1.00 ± 0.08	1.17 ± 0.04	5.45 ± 0.04	N:P 150	
0.018	0.99	$7.19 \pm 0.06^{a,c}$	1.09 ± 0.44^a	0.43 ± 0.08^b	2.15 ± 0.11	0.94 ± 0.02	1.24 ± 0.03	5.95 ± 0.03	N:P 10	70 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.067	0.99	$7.06 \pm 0.02^{a,d}$	0.35 ± 0.23^a	0.44 ± 0.08^b	1.27 ± 0.03	1.08 ± 0.03	1.10 ± 0.01	5.96 ± 0.01	N:P 100	
0.055	0.99	7.13 ± 0.06^a	0.91 ± 0.61^a	0.38 ± 0.06^b	2.06 ± 0.16	0.87 ± 0.02	1.19 ± 0.04	5.94 ± 0.02	N:P 150	
RMSE	R^2	MPD ($\text{cells}\cdot\text{mL}^{-1}$)	LPD (d)	μ (d^{-1})	m	c	b	a	36 °C	
0.055	0.99	6.44 ± 0.07^a	1.28 ± 0.60^a	0.19 ± 0.04^a	2.56 ± 0.19	0.50 ± 0.04	1.05 ± 0.04	5.39 ± 0.03	N:C:\N:\PP 10	30 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.070	0.99	6.41 ± 0.08^a	0.90 ± 0.55^a	0.18 ± 0.07^a	2.02 ± 0.18	0.45 ± 0.02	1.09 ± 0.04	5.33 ± 0.04	N:P 100	
0.576	0.99	6.46 ± 0.04^a	1.25 ± 0.43^a	0.19 ± 0.06^a	2.62 ± 0.10	0.48 ± 0.02	1.07 ± 0.02	5.39 ± 0.02	N:P 150	
0.058	0.99	6.46 ± 0.02^a	1.21 ± 0.29^a	0.20 ± 0.04^a	3.32 ± 0.04	0.47 ± 0.01	1.14 ± 0.01	5.32 ± 0.01	N:C:\N:\PP 10	50 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.028	0.99	6.33 ± 0.06^a	1.05 ± 0.51^a	0.21 ± 0.08^a	3.07 ± 0.13	0.49 ± 0.03	1.15 ± 0.03	5.32 ± 0.03	N:C:\N:\PP 100	
0.030	0.99	6.50 ± 0.05^a	0.78 ± 0.49^a	0.17 ± 0.06^a	3.37 ± 0.12	0.39 ± 0.02	1.21 ± 0.03	5.28 ± 0.03	N:C:\N:\PP 150	
0.026	0.99	6.20 ± 0.03^b	0.42 ± 0.31^b	0.31 ± 0.08^b	1.40 ± 0.05	1.01 ± 0.05	0.82 ± 0.01	5.38 ± 0.01	N:C:\N:\PP 10	70 μmol photon $\text{m}^{-2}\cdot\text{s}^{-1}$
0.026	0.99	6.13 ± 0.02^b	0.29 ± 1.10^b	0.26 ± 0.06^b	1.37 ± 0.04	0.93 ± 0.03	0.75 ± 0.01	5.38 ± 0.01	N:P 100	
0.071	0.99	6.27 ± 0.04^b	0.51 ± 0.36^b	0.31 ± 0.09^b	1.55 ± 0.07	0.96 ± 0.06	0.89 ± 0.02	5.39 ± 0.02	N:P 150	

Different letters are significant differences ($p < 0.05$).

3.2. Chlorophyll-A Production

The chlorophyll-a production rate (k_0), derived from first-order kinetic modeling (Figure 3, Table 2), exhibited a relatively narrow range of variation across treatments. Although some differences were statistically significant (ANOVA, $p < 0.05$), no clear or consistent patterns emerged in response to temperature, irradiance, or N:P ratio. The highest k_0 values were observed under intermediate light and temperature conditions, but these trends were not systematic across treatments.

Overall, this parameter showed limited sensitivity to the tested environmental factors, suggesting a constrained discriminative capacity under the conditions of this experiment.

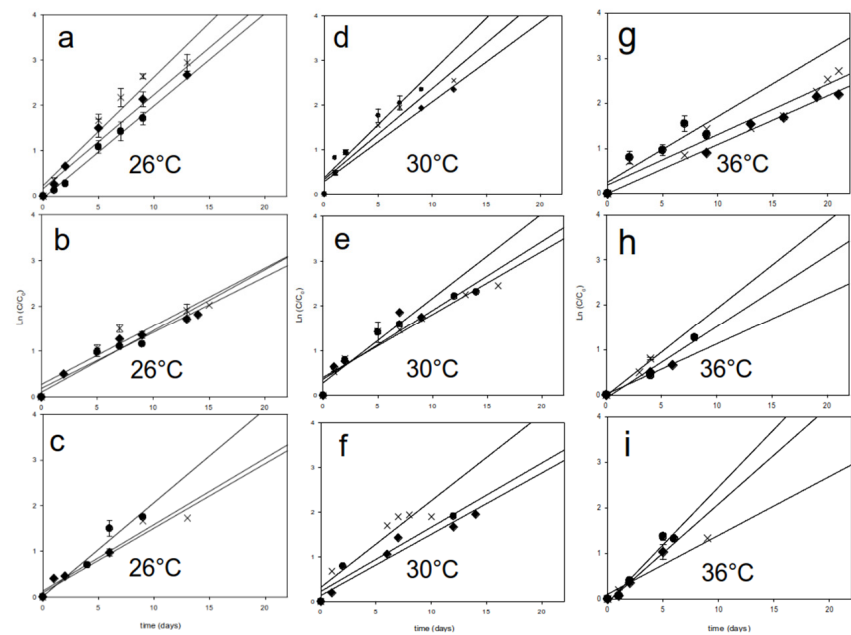


Figure 3. Chlorophyll-a levels expressed as $\ln(C/C_0)$ as a function of time (days). Experimental data shown for 26 °C (a–c), 30 °C (d–f), and 36 °C (g–i) under different light intensities: 30 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ (a,d,g), 50 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ (b,e,h), and 70 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ (c,f,i). Symbols represent N:P ratios: ● = 10, ✕ = 100, ◆ = 150. Error bars denote standard deviation (SD).

Table 2. Chlorophyll-a parameters obtained from the first-order kinetic model. k_0 (d^{-1}) is the specific rate constant; $\text{dt}_{\text{Chl-a}}$ (d) is the chlorophyll-a doubling time; and R^2 is the coefficient of determination.

R ²	dt _{clo-a} (d)	k ₀ (d ⁻¹)	26 °C	
0.99	3.46 ± 0.05 ^a	0.20 ± 0.07 ^a	N:C:\N:\PP 10	30 μmol photon m ⁻² .s ⁻¹
0.94	2.88 ± 0.05 ^a	0.24 ± 0.08 ^a	N:P 100	
0.97	3.30 ± 0.06 ^a	0.21 ± 0.09 ^a	N:P 150	
0.91	5.33 ± 0.06 ^b	0.13 ± 0.09 ^a	N:P 10	50 μmol photon m ⁻² .s ⁻¹
0.91	5.33 ± 0.04 ^b	0.13 ± 0.06 ^a	N:P 100	
0.96	5.77 ± 0.06 ^b	0.12 ± 0.09 ^a	N:P 150	
0.95	3.30 ± 0.03 ^b	0.21 ± 0.04 ^a	N:P 10	70 μmol photon m ⁻² .s ⁻¹
0.93	4.95 ± 0.05 ^b	0.14 ± 0.08 ^a	N:P 100	
0.93	4.62 ± 0.05 ^b	0.15 ± 0.07 ^a	N:P 150	
R ²	dt _{clo-a} (d)	k ₀ (d ⁻¹)	30 °C	
0.93	2.88 ± 0.06 ^a	0.24 ± 0.09 ^a	N:C:\N:\PP 10	30 μmol photonm ⁻² .s ⁻¹
0.94	3.46 ± 0.05 ^a	0.20 ± 0.08 ^a	N:P 100	
0.95	3.85 ± 0.06 ^a	0.18 ± 0.09 ^a	N:P 150	
0.93	4.62 ± 0.06 ^a	0.15 ± 0.09 ^a	N:P 10	50 μmol photon m ⁻² .s ⁻¹
0.93	4.95 ± 0.06 ^a	0.14 ± 0.09 ^a	N:P 100	
0.91	3.64 ± 0.05 ^a	0.19 ± 0.08 ^a	N:P 150	
0.93	4.95 ± 0.05 ^b	0.14 ± 0.07 ^a	N:P 10	70 μmol photon m ⁻² .s ⁻¹
0.95	3.64 ± 0.05 ^b	0.19 ± 0.07 ^a	N:P 100	
0.95	4.95 ± 0.05 ^b	0.14 ± 0.08 ^a	N:P 150	

Table 2. Cont.

R^2	$dt_{\text{clo-a}}$ (d)	k_0 (d^{-1})	26 °C	
R^2	$dt_{\text{clo-a}}$ (d)	k_0 (d^{-1})	36 °C	
0.93	4.95 ± 0.07^a	0.14 ± 0.10^b	N:C:\N:\PP 10	30 $\mu\text{mol photon m}^{-2}\cdot\text{s}^{-1}$
0.95	6.30 ± 0.06^a	0.11 ± 0.09^b	N:P 100	
0.99	6.30 ± 0.05^a	0.11 ± 0.08^b	N:P 150	
0.97	4.33 ± 0.06^a	0.16 ± 0.09^b	N:C:\N:\PP 10	50 $\mu\text{mol photon m}^{-2}\cdot\text{s}^{-1}$
0.98	3.64 ± 0.07^a	0.19 ± 0.10^b	N:C:\N:\PP 100	
0.99	6.30 ± 0.05^a	0.11 ± 0.08^b	N:P 150	
0.96	2.77 ± 0.06^a	0.25 ± 0.09^b	N:P 10	70 $\mu\text{mol photon m}^{-2}\cdot\text{s}^{-1}$
0.99	4.62 ± 0.05^a	0.15 ± 0.08^b	N:C:\N:\PP 100	
0.98	3.30 ± 0.07^a	0.21 ± 0.10^b	N:C:\N:\PP 150	

Different letters are significant differences ($p < 0.05$).

3.3. Microcystin-LR Production

Microcystin production was modeled using a dynamic growth-dependent equation, from which the toxin synthesis (p) and loss (dM) coefficients were estimated (Figure 4, Table 3). The synthesis parameter p displayed high variability among treatments, spanning nearly two orders of magnitude. The highest values were observed under moderate temperature (26–30 °C), medium irradiance, and intermediate N:P ratios, although the response pattern was not uniform.

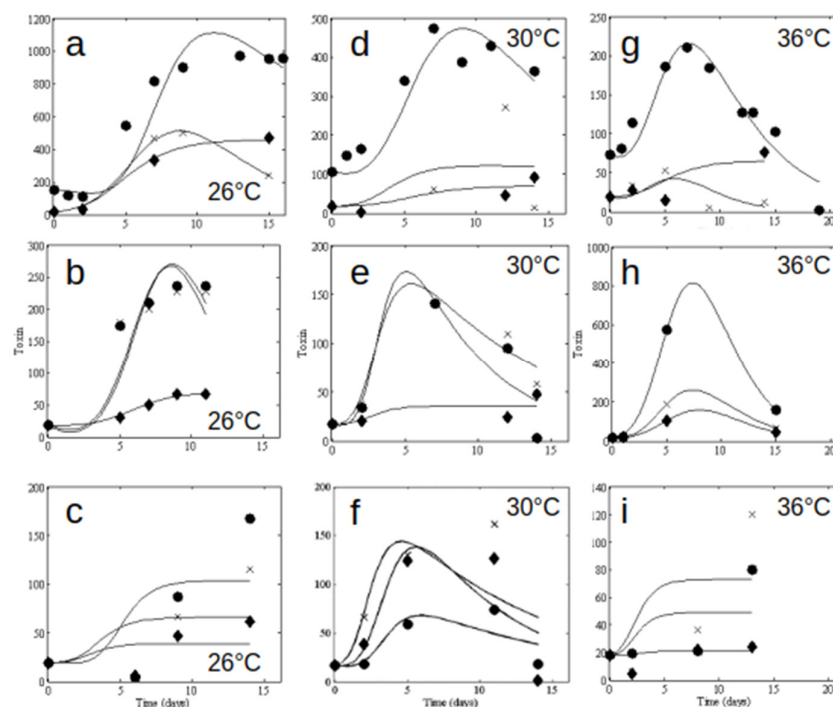


Figure 4. Modeling of [D-Leu¹] MC-LR production ($\mu\text{mol}\cdot\text{L}^{-1}$) in culture media. Solid lines represent model fits to experimental data at 26 °C (a–c), 30 °C (d–f), and 36 °C (g–i) under different light intensities: 30 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ (a,d,g), 50 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ (b,e,h), and 70 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ (c,f,i). Symbols represent N:P ratios: ● = 10, × = 100, ◆ = 150. Error bars omitted for clarity.

Table 3. Application of the dynamic model equation. p ($\text{fg}\cdot\text{cell}^{-1}$) and dM (d^{-1}) are the model coefficients.

R ²	d _M (day ⁻¹)	p (fg.cell ⁻¹)	N:P	Irradiation (μmol.photon m ⁻² .s ⁻¹)	Temperature
0.97	6.36 × 10 ⁻² ± 4.04 × 10 ⁻²	2.27 × 10 ⁻⁵ ± 6.17 × 10 ⁻⁶	10	30	26 °C
0.98	1.77 × 10 ⁻¹ ± 1.50 × 10 ⁻¹	1.63 × 10 ⁻⁵ ± 9.24 × 10 ⁻⁶	100		
0.99	1.00 × 10 ⁻⁶ ± 6.54 × 10 ⁻²	6.94 × 10 ⁻⁶ ± 3.53 × 10 ⁻⁶	150		
0.91	1.31 × 10 ⁻¹ ± 2.45 × 10 ⁻¹	1.19 × 10 ⁻⁵ ± 9.83.10 ⁻⁶	10	50	
0.80	1.34 × 10 ⁻¹ ± 3.89 × 10 ⁻¹	5.83 × 10 ⁻⁶ ± 7.34 × 10 ⁻⁶	100		
0.94	1.00 × 10 ⁻⁶ ± 1.33 × 10 ⁻¹	7.43 × 10 ⁻⁷ ± 7.99 × 10 ⁻⁷	150		
0.91	1.00 × 10 ⁻⁶ ± 3.68 × 10 ⁻¹	8.09 × 10 ⁻⁷ ± 1.62 × 10 ⁻⁶	10	70	
0.87	1.00 × 10 ⁻⁶ ± 4.46 × 10 ⁻¹	5.87 × 10 ⁻⁷ ± 1.07 × 10 ⁻⁶	100		
0.77	1.00 × 10 ⁻⁶ ± 3.70 × 10 ⁻¹	4.11 × 10 ⁻⁷ ± 1.43 × 10 ⁻⁶	150		
0.96	7.86 × 10 ⁻² ± 4.72 × 10 ⁻²	1.03 × 10 ⁻⁵ ± 2.97 × 10 ⁻⁶	10	30	30 °C
0.18	4.17 × 10 ⁻⁴ ± 1.18 × 10 ⁻⁰	5.35 × 10 ⁻⁶ ± 6.32.10 ⁻⁵	100		
0.94	1.01 × 10 ⁻⁶ ± 8.76 × 10 ⁻¹	3.64 × 10 ⁻⁶ ± 1.74 × 10 ⁻⁵	150		
0.77	1.85 × 10 ⁻¹ ± 3.07 × 10 ⁻¹	8.02 × 10 ⁻⁶ ± 1.39 × 10 ⁻⁵	10	50	
0.77	5.71.10 ⁻² ± 3.46 × 10 ⁻¹	6.35 × 10 ⁻⁶ ± 2.27 × 10 ⁻⁵	100		
0.99	1.00 × 10 ⁻⁶ ± 1.75 × 10 ⁻¹	7.21 × 10 ⁻⁷ ± 6.30 × 10 ⁻⁷	150		
0.58	6.80 × 10 ⁻² ± 2.15.10 ⁻¹	7.00 × 10 ⁻⁷ ± 1.23 × 10 ⁻⁶	10	70	
0.40	7.49 × 10 ⁻² ± 3.02 × 10 ⁻¹	2.10 × 10 ⁻⁶ ± 4.30 × 10 ⁻⁶	100		
0.59	1.34 × 10 ⁻¹ ± 3.17 × 10 ⁻¹	2.48 × 10 ⁻⁶ ± 4.73 × 10 ⁻⁶	150		
0.81	2.30 × 10 ⁻¹ ± 1.46 × 10 ⁻¹	6.28 × 10 ⁻⁵ ± 3.79 × 10 ⁻⁵	10	30	36 °C
0.88	4.91 × 10 ⁻¹ ± 3.98 × 10 ⁰	2.69 × 10 ⁻⁵ ± 2.13 × 10 ⁻⁴	100		
0.99	1.00 × 10 ⁻⁶ ± 5.34 × 10 ⁻¹	5.16 × 10 ⁻⁶ ± 1.70 × 10 ⁻⁵	150		
0.99	4.56 × 10 ⁻¹ ± 6.39 × 10 ⁻¹	2.96 × 10 ⁻⁴ ± 2.73 × 10 ⁻⁴	10	50	
0.99	3.11 × 10 ⁻¹ ± 1.94 × 10 ⁻¹	7.15 × 10 ⁻⁵ ± 2.95 × 10 ⁻⁵	100		
0.99	3.73 × 10 ⁻¹ ± 2.15 × 10 ⁻¹	6.05 × 10 ⁻⁵ ± 2.65 × 10 ⁻⁵	150		
0.99	1.00 × 10 ⁻⁶ ± 1.61 × 10 ⁻¹	4.71 × 10 ⁻⁶ ± 2.77 × 10 ⁻⁶	10	70	
0.99	1.00 × 10 ⁻⁶ ± 2.28 × 10 ⁻¹	1.04 × 10 ⁻⁵ ± 6.56 × 10 ⁻⁶	100		
0.40	1.00 × 10 ⁻⁶ ± 6.84 × 10 ⁻¹	3.43 × 10 ⁻⁷ ± 1.35 × 10 ⁻⁶	150		

No statistically significant differences were found.

In contrast, the degradation/loss coefficient dM showed lower variability and lacked a clear association with any single environmental factor. Statistical analysis confirmed significant effects of temperature and N:P ratio on p (ANOVA, $p < 0.01$), while dM was not significantly influenced.

A significant negative correlation was found between p and the specific growth rate μ (Pearson $r = -0.48$, $p = 0.012$), suggesting a trade-off between cellular proliferation and toxin synthesis capacity under varying environmental conditions.

3.4. Long Model: Net Toxin Production and Growth Coupling

To evaluate the relationship between cellular growth and net toxin production, the Long model was applied using empirical estimates of intracellular toxin quota (QMC) and the specific growth rate (μ). The resulting net microcystin production rate ($\text{RMC} = \text{QMC} \times \mu$) showed a significant positive linear correlation with μ (Figure 5), in-

dicating that higher growth rates were associated with increased overall toxin output per time unit.

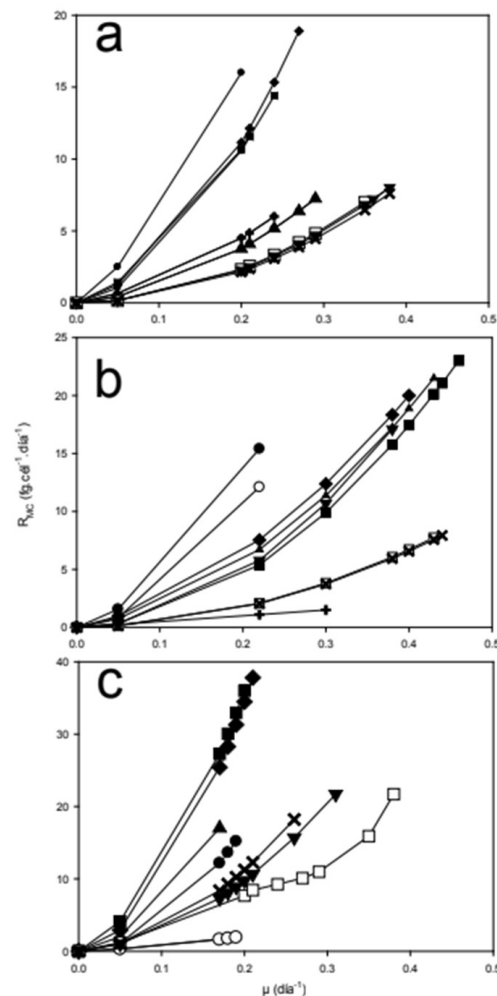


Figure 5. Application of the Long model [10] to experimental data on growth and MC-LR production. Panels correspond to 26 °C (a), 30 °C (b), and 36 °C (c). Symbols represent N:P ratios under different light intensities:—At 30 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$: $\bullet$ = N:P 10, $+$ = N:P 100, $\circ$ = N:P 150;—At 50 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$: $\blacksquare$ = N:P 10, $\blacklozenge$ = N:P 100, $\blacktriangle$ = N:P 150;—At 70 $\mu\text{mol photons}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$: $\square$ = N:P 10, $\times$ = N:P 100, $\blacktriangledown$ = N:P 150.

This finding contrasts with the inverse relationship observed between μ and the synthesis parameter p derived from the dynamic model, suggesting that different modeling approaches capture distinct aspects of the toxin production process. While p reflects the capacity for synthesis under varying physiological states, RMC integrates both growth and intracellular toxin content, providing a population-level view of total microcystin output.

4. Discussion

This study modeled the growth, chlorophyll-a production, and microcystin synthesis of a temperate *Microcystis aeruginosa* strain under multifactorial environmental conditions. The results revealed distinct responses of growth dynamics and toxin production to temperature, irradiance, and nutrient ratios, highlighting complex regulatory patterns that have both physiological and ecological significance.

The specific growth rate (μ) was primarily driven by temperature and irradiance, with optimal values observed at 30 °C and under moderate to high light conditions. These findings align with previous studies showing that *M. aeruginosa* tends to accelerate growth

with increasing temperature and irradiance up to a physiological threshold [22,23]. In our experiment, irradiance stimulated growth, especially at 26 °C and 30 °C, but showed signs of inhibition or photolimitation at 36 °C likely due to thermal stress and loss of colony structure, which could reduce photoprotection [24,25]. The lag phase duration (LPD) decreased with increasing temperature and nitrogen availability, reflecting faster adaptation to favorable conditions—a pattern consistent with microbial physiological theory and some cyanobacterial studies [26–28].

Chlorophyll-a production (k_0) did not show consistent trends across treatments, echoing the complexity noted in the literature regarding its regulation in *M. aeruginosa* [29,30]. Given its dual role as a pigment and as a proxy for biomass, its variability may reflect physiological adjustments not strictly tied to growth rate.

Microcystin production, modeled through dynamic growth-dependent equations, revealed a synthesis parameter (p) that was highly variable across treatments and negatively correlated with μ . This indicates a functional decoupling between proliferation and toxin synthesis, suggesting that toxin production is not a passive by-product of growth but a regulated trait potentially modulated by environmental stress, nutrient availability, or interspecific interactions [31–33]. High toxin synthesis occurred under low temperatures and higher phosphorus availability, a combination that has been associated with stress-related toxin induction in other studies [34,35].

Despite this apparent decoupling, the application of the Long model ($RMC = QMC \times \mu$) revealed a positive relationship between growth rate and net toxin output, indicating that biomass accumulation remains a key driver of bloom toxicity. This coexistence of coupled and uncoupled mechanisms highlights the importance of considering both cellular regulation and population dynamics when interpreting toxin production patterns.

From an ecological perspective, these findings support the hypothesis that microcystins may act as adaptive molecules under suboptimal conditions, potentially enhancing survival or competitive advantage. Conversely, the association between fast growth and increased net toxin output under high phosphorus availability suggests that active metabolism can also support toxin synthesis during bloom expansion. Although this study was conducted under controlled laboratory conditions using a monoculture, it is important to consider that in natural environments, *M. aeruginosa* interacts with a variety of organisms, including other phytoplankton and macrophytes, which may compete for resources. Such biotic interactions can trigger chemical signaling or resource competition that influences the regulation of microcystin production. Several studies have proposed that under certain conditions, microcystins may act as allelochemicals—that is, compounds involved in interspecific chemical interference—modulating competitive dynamics within the community [36,37]. Incorporating this ecological perspective reinforces the interpretation of microcystins as adaptive molecules whose expression may be shaped not only by abiotic stressors but also by complex ecological signals.

In the context of global environmental change, these regulatory patterns acquire further relevance. Thermal adaptation may enable toxigenic strains of *M. aeruginosa* to shift their geographic distribution and bloom dynamics, potentially altering the balance between growth and toxicity. Predictive models must, therefore, integrate both physiological responses and environmental drivers to accurately assess bloom risk and toxin production under future climate scenarios [15–17].

5. Conclusions

This study demonstrated that microcystin production in *M. aeruginosa* responds to both coupled and uncoupled dynamics relative to cellular growth. While the synthesis parameter (p) decreased as the specific growth rate (μ) increased, indicating a trade-off

at the cellular level, the net toxin production rate (RMC), derived from the Long model, increased with growth due to biomass accumulation.

These findings suggest that microcystin production is not a passive consequence of cell proliferation but a regulated physiological trait with potentially adaptive value. One possible interpretation is that microcystins serve a protective or competitive function under suboptimal thermal conditions or nutrient imbalance, enhancing survival in stressful environments. Conversely, the association between rapid growth and increased total toxin output highlights the role of active cellular metabolism in supporting toxin synthesis, particularly when phosphorus is available.

Such dual regulation underscores the complexity of cyanobacterial responses to environmental change. From an ecological perspective, it implies that *M. aeruginosa* may shift its growth–toxicity strategy depending on the context, with possible consequences for competition, bloom persistence, and ecosystem impacts. In light of ongoing climate change, these adaptive patterns may influence strain distribution, bloom dynamics, and risk scenarios in freshwater systems. Therefore, predictive models should integrate both physiological traits and environmental drivers to better anticipate the severity and toxicity of cyanobacterial blooms.

Author Contributions: M.C.C.-M. participated in the experimental design, sample analysis, data collection, data analysis and modeling, original draft, writing, review, and editing. S.G. participated in the data analysis and modeling, original draft, writing, review, and editing. L.G. participated in experimental design, modeling, funding acquisition, project administration, data analysis, original draft, writing, review, and editing. All authors have read and agreed to the published version of the manuscript.

Funding: This study was financially supported by the National University of La Plata (UNLP X526), the National Agency of Scientific and Technical Research (PICT 0861-2013), and CONICET (PIP 0959). Moreover, it was funded through the doctoral fellowship given by the National Agency of Scientific and Technical Research to the first author.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Acknowledgments: This work is dedicated to the memory of Leda Giannuzzi, who served as thesis advisor to the first author and whose guidance and commitment were fundamental to the development of this research. We are also grateful to the members of the Laboratory of Toxicology (FCE-UNL) for their valuable collaboration in fine-tuning the techniques applied in this study.

Conflicts of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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