Received X XX XXXX; | Revised X XX XXXX; | Accepted X XX XXXX

DOI: xxx/xxxx

ARTICLE TYPE

Diauxic behaviour for biological processes at various timescales

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Summary

In the present paper we provide the conditions guaranteeing the generalization of so-called *diauxic* behaviour of solutions of ODEs. This behaviour was described by Monod in 1949 in the context of bacterial growth. Then a similar behaviour was observed and described referring to dynamic of CDK1 protein during cell cycle.[1] The diauxic behaviour is described in terms of inflection points.

KEYWORDS:
diauxic behaviour, inflection point

1 | INTRODUCTION

Monod described bacterial growth in a batch culture containing a mixture of two carbon sources.[2] This growth, called *diauxic* (or rarely *diauxie*) growth, is characterized by the appearance of two seperated logistic growth phases. This phenomenon is caused by sequentially metabolizing two sugars present on a culture growth media. Consumption of the first one is followed by lag phase, while the cellular machinery starts to metabolize the second sugar. The typical example of diauxic growth is growth of *Escherichia coli* on a mixture of glucose and lactose. The order in which carbon sources are metabolized is controlled by carbon catabolite repression (CCR).

A number of mathematical models have been proposed to describe and understand diauxic growth. For instance, some have used ordinary differential equation to model the process of the growth of bacteria.[3,4,5] Some authors considered the model of gene regulation in diauxic growth.[6] Kremling et al. described many variants of models: flux balance models, kinetic models with growth dilution, kinetic models with regulation and resource allocation models, all showing diauxic behaviour of the solution.[7] Authors understood and defined diauxic growth in the intuitive sense i.e. as two seperated growth phases.

In regression modeling the double logistic curve or double sigmoid curve has diauxic behaviour. Logistic functions are used in many applied research like nonlinear regressions, neural networking.[8,9] There are problems for which describing by a double sigmoid function is more adequate. For instance, such function were considered in describing enzyme kinetics[10], fatigue profiling[11] and score normalization[12] in biometrics systems.

In the previous work, we observed that the dynamic of CDK1 protein during cell cycle has diauxic behaviour.[1] This type of growth is caused by inhibitor protein CDC6. We proposed a mathematical model which provides a possible explanation for the experimental data. Consideration the protein CDC6 as inhibitor of CDK1 was the first attempt in the literature to explain double growth CDK1 activation curve.

In mathematical terms, we define the diauxic behaviour of the function as the existence of more than one inflection points of the function. Proposed definition is generalization of diauxic behaviour described by Monod, because of lack of upper limitation on number of inflection points. For instance, the number of inflection points on the curve described by Monod is three[2] and the number of inflection points on curve defining the dynamics of CDK1 is three or four depending on initial data[1]. The latter paper was the first approach proposing the description of diauxic growth in terms of number of inflection points.

The appearance of diauxic behaviour in various biological systems inspired our subsequent research on the conditions guaranteeing the diauxic behaviour of the solution of the ordinary differential equations.

The present paper, to the knowledge of the author, is the first approach giving a general mathematical basis for description of diauxic phenomena. In contrast to[1] we refer here to the biological phenomena at two different time scales.[13]

The structure of the paper is as follows. In Section 2 we provide the conditions in the autonomic system of one dimensional equation to obtain the diauxic behaviour of the solutions. In section 3 we introduce the small parameter in the system of two differential equation and then using the Tikhonov and Vasil'eva theorem we compare the solution to solution of one dimensional case.[13]. Section 4 provides conclusions and directions for further research.

2 | ONE–DIMENSIONAL CASE

Let $f : [0,1] \to \mathbb{R}$ be a continuous function such that

$$f(0) = f(1) = 0\,, \tag{1}$$

and

$$f(x) > 0 \qquad \forall\, x \in (0,1)\,, \tag{2}$$

and

$$\forall\, a, b :\ 0 \leqslant a < b \leqslant 1 \qquad f(x) \neq \text{const on } (a,b) \tag{3}$$

Additionally we assume that $f \in C^2\big([0,1]\big)$ with the meaning that $f'(0)$, $f'(1)$, $f''(0)$, $f''(1)$ are one–sided derivatives. Analogously we undestand $C^k\big([0,1]\big)$, for any $k \in \mathbb{N}$.

We consider the following Cauchy Problem

$$\begin{aligned} \dot{x} &= f(x), \\ x(0) &= \ x_0, \end{aligned} \tag{4}$$

where $\dot{x} = \frac{\mathrm{d}x}{\mathrm{d}t}$ and $x_0 \in (0,1)$.

We refer here only to global (time) solution of the Cauchy Problem, but the generalization to finite time intervals is obvious. We propose the following definition of diauxic behaviour.

Definition 1. We say that a solution of the Cauchy Problem Eq. (4) has the diauxic behaviour, if the solution, for $t > 0$, is non-decreasing and has n inflection points, where $n > 1$.

Let

$$\mathbb{W}_1 = \{x \in [0,1] :\ f'(x) = 0\},$$

where $f' = \frac{\mathrm{d}f}{\mathrm{d}x}$.

Assumption 1. The function f is such that $|f'(x)| + |f''(x)| > 0$ for any $x \in [0,1]$.

Proposition 1. Let Assumption 1 be satisfied. Then $|\mathbb{W}_1|$ is finite, where $|\cdot|$ denotes the number of elements.

Proof. Assume that $|\mathbb{W}_1|$ is infinite. Because $\mathbb{W}_1$ is compact, there exists a convergent sequence $(a_{n_k})_{k\in\mathbb{N}}$ and a corresponding limit point a_∞ in $\mathbb{W}_1$. By $f \in C^2\big([0,1]\big)$ we can calculate

$$f''(a_\infty) = \lim_{k\to\infty} \frac{f'(a_{n_k}) - f'(a_\infty)}{a_{n_k} - a_\infty} = \lim_{k\to\infty} \frac{0}{a_{n_k} - a_\infty} = 0.$$

By Assumption 1 this contradicts $f'(a_\infty) = 0$ and $a_\infty \in \mathbb{W}_1$. It means that $\mathbb{W}_1$ is a finite set. □

Let

$$\mathbb{W} = \{x \in (0,1) :\ \exists\, \varepsilon > 0\ \ \forall \eta_1, \eta_2 \in (0,\varepsilon) \quad f'(x - \eta_1) \cdot f'(x + \eta_2) < 0\}.$$

An obvious observation is that $\mathbb{W} \subseteq \mathbb{W}_1$ and from Proposition 1 we obtain that $|\mathbb{W}|$ is finite.

The set $\mathbb{W}$ containts the points belonging to $(0,1)$, in which the derivative of function f changes sign. We denote

$$\mathbb{W} = \{x_1, x_2, \ldots, x_n\}, \tag{5}$$

where $0 < x_1 \leqslant x_2 \leqslant \ldots \leqslant x_n < 1$.

Proposition 2. Assume that Assumption 1 is satisfied. Then n, define above, is an odd number.

Proof. From Eqs. (1) and (2) we obtain that there exists $\varepsilon > 0$ such that $f'(x) > 0$ for $x \in (0, \varepsilon)$ and $f'(x) < 0$ for $x \in (1-\varepsilon, 1)$. It means that there exist $x^* \in (0, 1)$ such that $f'(x^*) = 0$. It means that set $\mathbb{W}$ is nonempty. Assume that $n = 2m$, where $m \in \mathbb{N}$. Then $f'(x) > 0$ for $x \in (0, x_1) \cup (x_2, x_3) \cup \ldots \cup (x_{2m}, 1)$ and $f'(x) < 0$ for $x \in (x_1, x_2) \cup (x_3, x_4) \cup \ldots \cup (x_{2m-1}, x_{2m})$. Therefore $f'(x) > 0$ for $x \in (x_{2m}, 1)$. This contradicts $f'(x) < 0$ for $x \in (1 - \varepsilon, 1)$. It means that n is an odd number. □

Corollary 1. The number of inflection points of the solution $x = x(t)$ of Eq. (4) is equal

- n if $x_0 \in (0, x_1)$,
- $n - k$ if $x_0 \in [x_k, x_{k+1})$, where $k \in \{1, \ldots, n - 1\}$,
- 0 if $x_0 \in [x_n, 1)$.

Proof. From Eqs. (1) and (2) the unique solution $x = x(t)$ is an increasing function for $t \geqslant 0$, such that $\lim_{t\to\infty} x(t) = 1$. We obtain

- if $x_0 \in (0, x_1)$, then there exists $t_l > 0$ such that $x(t_l) = x_l$ for any $l \in \{1, 2, \ldots, n\}$,
- if $x_0 \in [x_k, x_{k+1})$, where $k \in \{1, 2, \ldots, n-1\}$, then there exists $t_l > t_0$ such that $x(t_l) = x_l$ for any $l \in \{k+1, k+2, \ldots, n\}$,
- if $x_0 \in [x_n, 1)$, then $\forall\ x \in (x_n, 1)\ \ f'(x) < 0$.

□

From Corollary 1 we obtain the following remark.

Remark 1. The following two cases are possible:

- $x(t)$ is convex in the neighbourhood of $t = 0$ if $x_0 \in (0, x_1) \cup (x_2, x_3) \cup \ldots \cup (x_{2m}, x_{2m+1})$ — see Figure 1 ,
- $x(t)$ is concave in the neighbourhood of $t = 0$ if $x_0 \in (x_1, x_2) \cup (x_3, x_4) \cup \ldots \cup (x_{2m+1}, 1)$ — see Figure 2 .

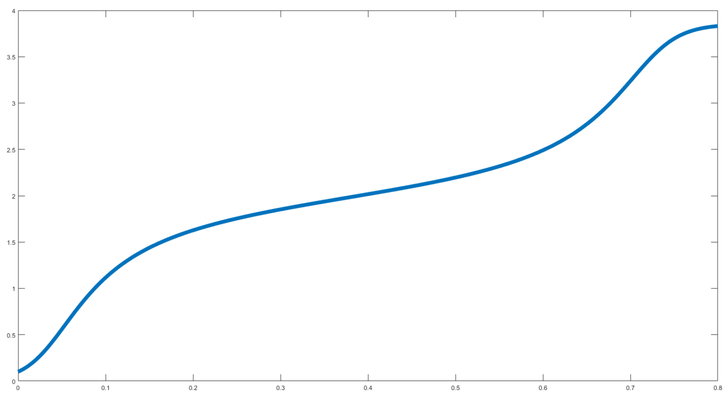

FIGURE 1 Convex function $x(t)$ in the neighbourhood of $t = 0$.

Example 1. Consider $f(x) = x(1 - x)((x - \alpha)^2 + \omega)$, where $\alpha \in (0, 1)$ and $0 < \omega \ll 1$. Then solution $x = x(t)$ of Eq. (4) with initial data $x(0) \in (0, x_1)$ has three inflection points — see Figure 3 .

Example 2. Consider $f(x) = x(1 - x)((x - \alpha)^2(x - \beta)^2 + \omega)$, where $0 < \alpha < \beta < 1$ and $0 < \omega \ll 1$. Then solution $x = x(t)$ of Eq. (4) with initial data $x(0) \in (0, x_1)$ has five inflection points — see Figure 4 .

Examples 1 and 2 are particular cases of the replicator equations for the multiplayer games. Example 1 is the replicator equation for the three players game, and Example 2 – five players game.[14]

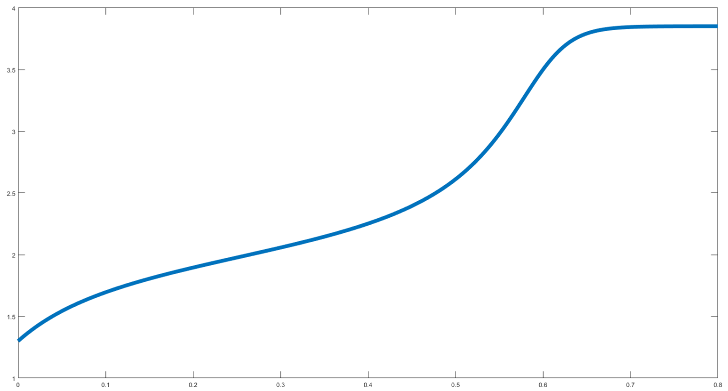

FIGURE 2 Concave function $x(t)$ in the neighbourhood of $t = 0$.

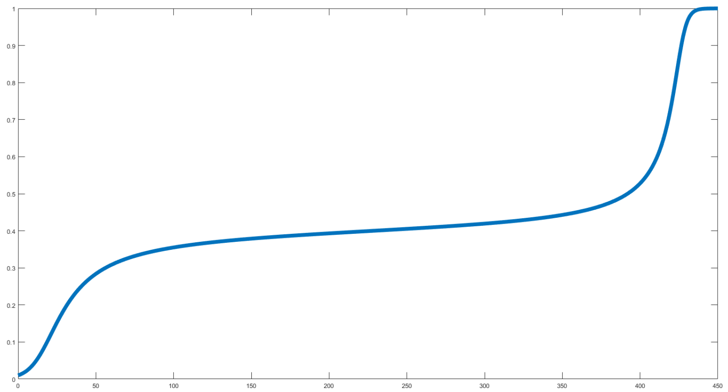

FIGURE 3 Function $x(t)$ with three inflection points.

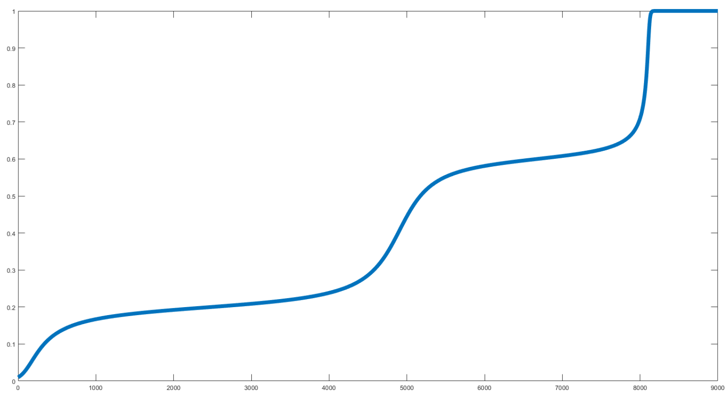

FIGURE 4 Function $x(t)$ with five inflection points.

3 | TWO–DIMENSIONAL CASE

Consider the following systems of ODEs

$$\begin{aligned} \dot{x} &= f(x,y), \quad x(0)=x_0, \\ \dot{y} &= g(x,y), \quad y(0)=y_0, \end{aligned} \tag{6}$$

where

$$f(0,0) = g(0,0) = 0\,. \tag{7}$$

Following the Definition 1 we propose the definition of diauxic behavior for two-dimensional case.

Definition 2. We say that a solution $(x,y) = (x(t), y(t))$ of the Cauchy Problem Eq. (6) has the diauxic behaviour with respect to the first variable x, if $x = x(t)$, for $t > 0$, is non-decreasing and has n inflection points, where $n > 1$.

In the sequel, for simplicity, we omit "with respect to the first variable" assuming it everywhere.

Assumption 2. Assume that functions f and g:

$$f : \mathcal{U} \times \mathcal{V} \to \mathbb{R}$$
$$g : \mathcal{U} \times \mathcal{V} \to \mathbb{R}$$

are

- continuous with respect to all variables,
- three times continuously differentiable with respect to the variables $x,\ y$ in $\mathcal{U} \times \mathcal{V}$, $k \geqslant 1$,

where $\mathcal{U}$ is a compact set in $\mathbb{R}$ and $\mathcal{V}$ is a bounded open set in $\mathbb{R}$.

We consider two dimensional system with two different time scales. [13] We are interested in diauxic behaviour of the variable with time scale $O(1)$. We may apply the method of small parameter [13] and consider the following system

$$\begin{aligned} \dot{x} &= f(x,y)\,, \\ \dot{y} &= \tfrac{1}{\varepsilon} g(x,y)\,, \end{aligned} \tag{8}$$

where ε is a (small) positive number.

We consider the corresponding *degenerate* system of the system Eq. (8)

$$\begin{aligned} \dot{\bar{x}} &= f(\bar{x},\bar{y}), \quad \bar{x}(0)=x_0, \\ 0 &= g(\bar{x},\bar{y}). \end{aligned} \tag{9}$$

Assumption 3. Assume that there exists a solution $\bar{y} = \phi(\bar{x}) \in \mathcal{V}$ of the second equation of the system Eq. (9), for $\bar{x} \in \mathcal{U}$. The solution is continuous in $\mathcal{U}$ and there exists $\delta > 0$ such that

$$g(x,y) \neq 0 \quad \text{for} \quad 0 < |y - \phi(x)| < \delta, \quad x \in \mathcal{U}.$$

The system Eq. (9) leads to the following *reduced* equation

$$\dot{\bar{x}} = f(\bar{x}, \phi(\bar{x}))\,, \quad \bar{x}(0) = x_0. \tag{10}$$

Assumption 4. Assume that function $\bar{x} \to f(\bar{x}, \phi(\bar{x}))$ satisfies the Lipschitz condition with respect to $\bar{x}$ in $\mathcal{U}$ for $t \in [0,T]$. Assume moreover that there exists a unique solution $\bar{x}(t)$ of Eq. (10) on $[0,T]$ such that

$$\bar{x}(t) \in \operatorname{Int}\mathcal{U}, \quad \forall t \in (0,T).$$

According to theory of small parameter [13], we consider the following equation

$$\frac{\mathrm{d}\hat{y}}{\mathrm{d}\tau} = g(x_0, \hat{y}), \quad \hat{y}(0) = y_0. \tag{11}$$

Assumption 5. Assume that the solution $\hat{y} = \hat{y}(\tau)$ of Eq. (11) satisfies

$$\lim_{\tau\to\infty} \hat{y}(\tau) = \phi(x_0),$$

and $\hat{y}(\tau) \in \mathcal{V}$ for all $\tau \geq 0$.

Assumption 6. Assume that $\frac{\partial g}{\partial y}(x, \phi(x)) < 0$, for $x \in \mathcal{U}$.

We are interested in the diauxic growth (say to Eqs. (1) and (2)), so we assume additionally

Assumption 7. Assume that $f(1,\phi(1)) = 0$ and $f(x,\phi(x)) > 0$ for $x \in (0,1)$.

We want to compare number of inflection points of each of two solutions: solution $x = x(t)$ of the system Eq. (8) and solution $x = x(t)$ of the equation Eq. (4). We compare the second derivatives and provide the following theorem

Theorem 3. Let Assumptions 2, 3, 4, 5, 6 be satisfied. There exists $\varepsilon_0 > 0$ and a positive constant c such that for any $\varepsilon \in (0,\varepsilon_0]$ there exists a unique solution $(x(t), y(t))$ of the system Eq. (8) on $[0,T]$ and

$$|\ddot{x}(t) - \ddot{\bar{x}}(t)| < c\varepsilon \quad \text{for} \quad t \in [\alpha, T],\ \alpha > 0.$$

Proof. Under Assumptions 2, 3, 4, 5, 6 the Tikhonov–Vasil'eva theorem holds.[13] It follows that there exists $\varepsilon_0 > 0$ and a constant d such that for any $\varepsilon \in (0,\varepsilon_0]$ there exists a unique solution $(x(t), y(t))$ of the system Eq. (8) on $[0,T]$ and

$$\begin{aligned} |x(t) - \bar{x}(t) - \varepsilon\bar{x}_1(t)| &\leqslant d\varepsilon^2, \\ |y(t) - \bar{y}(t) - \varepsilon\bar{y}_1(t)| &\leqslant d\varepsilon^2, \end{aligned} \tag{12}$$

for all $t \in [\alpha, T]$, $\alpha > 0$, where $(\bar{x}(t), \bar{y}(t))$ is a solution of the degenerate system Eq. (9) and $(\bar{x}_1(t), \bar{y}_1(t))$ satisfies the following equations

$$\begin{aligned} \dot{\bar{x}}_1 &= \bar{x}_1 f_x(\bar{x},\bar{y}) + \bar{y}_1 f_y(\bar{x},\bar{y}), \\ \dot{\bar{y}} &= \bar{x}_1 g_x(\bar{x},\bar{y}) + \bar{y}_1 g_y(\bar{x},\bar{y}). \end{aligned} \tag{13}$$

We want to estimate $|\ddot{x}(t) - \ddot{\bar{x}}(t)|$. We have

$$\begin{aligned} |\ddot{x}(t) - \ddot{\bar{x}}(t)| &= |f_x(x,y)\dot{x}(t) + f_y(x,y)\dot{y}(t) - f_x(\bar{x},\bar{y})\dot{\bar{x}}(t) - f_y(\bar{x},\bar{y})\dot{\bar{y}}(t)| \leqslant \\ &\leqslant \underbrace{\Big|f_x(x,y)f(x,y) - f_x(\bar{x},\bar{y})f(\bar{x},\bar{y})\Big|}_{:=\mathfrak{J}_1} + \underbrace{\Big|\frac{1}{\varepsilon}f_y(x,y)g(x,y) - f_y(\bar{x},\bar{y})\dot{\bar{y}}(t)\Big|}_{:=\mathfrak{J}_2} \end{aligned}$$

Now we estimate $\mathfrak{J}_1$ and $\mathfrak{J}_2$ separately. We begin with $\mathfrak{J}_1$.

$$\begin{aligned} \mathfrak{J}_1 &= |f_x(x,y)f(x,y) - f_x(x,y)f(\bar{x},\bar{y}) + f_x(x,y)f(\bar{x},\bar{y}) - f_x(\bar{x},\bar{y})f(\bar{x},\bar{y})| \leqslant \\ &\leqslant |f_x(x,y)| \cdot |f(x,y) - f(\bar{x},\bar{y})| + |f(\bar{x},\bar{y})| \cdot |f_x(x,y) - f_x(\bar{x},\bar{y})| \end{aligned}$$

Under Assumption 2 we obtain that $|f_x(x,y)| \leqslant M_1$, $|f(\bar{x},\bar{y})| \leqslant M_2$, $|f(x,y) - f(\bar{x},\bar{y})| \leqslant L_1(|x-\bar{x}| + |y-\bar{y}|)$ and $|f_x(x,y) - f_x(\bar{x},\bar{y})| \leqslant L_2(|x-\bar{x}| + |y-\bar{y}|)$ where M_1, M_2 are positive constants and L_1, L_2 are Lipschitz constants. We have

$$\mathfrak{J}_1 \leqslant (M_1L_1 + M_2L_2)(|x-\bar{x}| + |y-\bar{y}|)$$

By Eq. (12) it follows that

$$\begin{aligned} x(t) &= \bar{x}(t) + \varepsilon\bar{x}_1(t) + \varepsilon^2 r_1(t,\varepsilon), \\ y(t) &= \bar{y}(t) + \varepsilon\bar{y}_1(t) + \varepsilon^2 r_2(t,\varepsilon), \end{aligned} \tag{14}$$

where $r_1(t,\varepsilon)$, $r_2(t,\varepsilon)$ are bounded functions for any $t \in [\alpha, T]$ and $\varepsilon \in (0,\varepsilon_0]$. Thus, there exist positive constats N_1, N_2 such that $|r_1(t,\varepsilon)| \leqslant N_1$ and $|r_2(t,\varepsilon)| \leqslant N_2$ or any $t \in [\alpha, T]$ and $\varepsilon \in (0,\varepsilon_0]$. Then we have

$$\begin{aligned} |x(t) - \bar{x}(t)| &= |\varepsilon\bar{x}_1(t) + \varepsilon^2 r_1(t,\varepsilon)| \leqslant K_1\varepsilon, \\ |y(t) - \bar{y}(t)| &= |\varepsilon\bar{y}_1(t) + \varepsilon^2 r_2(t,\varepsilon)| \leqslant K_2\varepsilon, \end{aligned}$$

where K_1 and K_2 are positive constants. Finally, we estimate $\mathfrak{J}_1$

$$\mathfrak{J}_1 \leqslant (M_1L_1 + M_2L_2)(K_1 + K_2)\varepsilon$$

Now we estimate $\mathfrak{J}_2$.

$$\begin{aligned} \mathfrak{J}_2 &= \Big|\frac{1}{\varepsilon}f_y(x,y) - f_y(x,y)\dot{\bar{y}}(t) + f_y(x,y)\dot{\bar{y}}(t) - f_y(\bar{x},\bar{y})\dot{\bar{y}}(t)\Big| \leqslant \\ &\leqslant |f_y(x,y)| \cdot \Big|\frac{1}{\varepsilon}g(x,y) - \dot{\bar{y}}(t)\Big| + |\dot{\bar{y}}(t)| \cdot |f_y(x,y) - f_y(\bar{x},\bar{y})| \end{aligned}$$

By Assumption (6), there exists $\lambda > 0$ such that $g_y(\bar{x}, \bar{y}) < -\lambda$ for $\bar{y} = \phi(\bar{x})$ and $\bar{x} \in \mathcal{U}$. Using this and chain rule applied to second equation of degenerate system Eq. (9) it follow that

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{d}t} g(\bar{x}, \bar{y}) = 0,\\
&g_x(\bar{x}, \bar{y}) \cdot \dot{\bar{x}}(t) + g_y(\bar{x}, \bar{y})\dot{\bar{y}}(t) = 0,\\
&\dot{\bar{y}} = -\frac{g_x(\bar{x}, \bar{y}) f(\bar{x}, \bar{y})}{g_y(\bar{x}, \bar{y})},\\
&|\dot{\bar{y}}(t)| \leqslant \frac{|g_x(\bar{x}, \bar{y})||f(\bar{x}, \bar{y})|}{\lambda}, \quad \text{for} \quad t \in [\alpha, T].
\end{aligned}$$

By Assumption (2) we obtain that $|f_y(\bar{x}, \bar{y})| \leqslant M_3$, $|g_x(\bar{x}, \bar{y})| \leqslant M_4$, $|g_y(\bar{x}, \bar{y})| \leqslant M_5$ and $|f_y(x, y) - f_y(\bar{x}, \bar{y})| \leqslant L_3(|x - \bar{x}| + |y - \bar{y}|)$, where $M_3,\ M_4,\ M_5$ are positive constant and L_3 is Lipschitz constant. We have

$$\mathcal{J}_2 \leqslant M_3 \left| \frac{1}{\varepsilon} g(x, y) - \dot{\bar{y}}(t) \right| + \frac{M_4 M_2 L_3}{\lambda} (|x - \bar{x}| + |y - \bar{y}|)$$

By Assumption (2) and Eq. (14) we provide the following Taylor series for $g(x, y)$ at $(\bar{x}, \bar{y})$

$$\begin{aligned}
g(x, y) &= g(\bar{x} + \varepsilon \bar{x}_1 + \varepsilon^2 r_1(t, \varepsilon), \bar{y} + \varepsilon \bar{y}_1 + \varepsilon^2 r_2(t, \varepsilon)) =\\
&= g(\bar{x}, \bar{y}) + (\varepsilon \bar{x}_1 + \varepsilon^2 r_1(t, \varepsilon)) g_x(\bar{x}, \bar{y}) + (\varepsilon \bar{y}_1 + \varepsilon^2 r_2(t, \varepsilon)) g_y(\bar{x}, \bar{y}) + R(t, \varepsilon) =\\
&= \varepsilon(\bar{x}_1 g_x(\bar{x}, \bar{y}) + \bar{y}_1 g_y(\bar{x}, \bar{y})) + \varepsilon^2 (r_1(t, \varepsilon) g_x(\bar{x}, \bar{y}) + r_2(t, \varepsilon) g_y(\bar{x}, \bar{y})) + R(t, \varepsilon).
\end{aligned}$$

where $|R(t, \varepsilon)| \leqslant K\varepsilon^2$, $K > 0$. Then, using the second equation of Eq. (13)

$$\begin{aligned}
\left| \frac{1}{\varepsilon} g(x, y) - \dot{\bar{y}}(t) \right| &= \left| \bar{x}_1 g_x(\bar{x}, \bar{y}) + \bar{y}_1 g_y(\bar{x}, \bar{y}) + \varepsilon (r_1(t, \varepsilon) g_x(\bar{x}, \bar{y}) + r_2(t, \varepsilon) g_y(\bar{x}, \bar{y})) + \frac{R(t, \varepsilon)}{\varepsilon} - \dot{\bar{y}}(t) \right| \leqslant\\
&\leqslant \varepsilon \big(|r_1(t, \varepsilon)||g_x(\bar{x}, \bar{y})| + |r_2(t, \varepsilon)||g_y(\bar{x}, \bar{y})| \big) + K\varepsilon \leqslant \varepsilon (N_1 M_4 + N_2 M_5 + K).
\end{aligned}$$

Finally, we get the following inequality

$$\mathfrak{J}_2 \leqslant M_3 (N_1 M_4 + N_2 M_5 + K)\varepsilon + \frac{M_4 M_2}{\lambda} L_3 (K_1 + K_2)\varepsilon.$$

We conclude that

$$|\ddot{x}(t) - \ddot{\bar{x}}(t)| \leqslant \mathcal{J}_1 + \mathcal{J}_2 \leqslant \varepsilon \Big((M_1 L_1 + M_2 L_2)(K_1 + K_2) + M_3 (N_1 M_4 + N_2 M_5 + K + \frac{M_4 M_2}{\lambda} L_3 (K_1 + K_2) \Big) = c\varepsilon$$

valid for $t \in [\alpha, T]$.

□

By Theorem 3 we obtain the diauxic behaviour of the first variable $x = x(t)$ of the system Eq. (8) provided the corresponding reduced equation Eq. (10) leads to the solution that behaves in diauxic way. In fact

Corollary 2. Under assumptions of Theorem 3 and Assumption 7, if $\bar{x} = \bar{x}(t)$ is a solution of Eq. (10) and the corresponding number of inflection points $n > 1$, for $t > 0$, then the solution (x, y) of the system Eq. (8) has diauxic behaviour provided ε is sufficiently small.

4 | CONCLUSIONS

In the present paper we provided the conditions ensuring the diauxic behaviour at various time scales. We considered one-dimensional ordinary differential equation and system of two ordinary differential equations. In the latter system we introduced the small parameter and we compared the solution of reduced equation Eq. (10) with the first variable of solution of Eq. (8). The interesting novelty of the present paper is in the precise mathematical description of diauxic behaviour. The interesting generalization of diauxic growth for description at microscopic and macroscopic level is still an open problem. Consideration multiple timescales is also an open problem. The interesting possibilities of description of diauxic-type behaviour come from recent result by Banasiak, who provided a new proof of the Tikhonov theorem for the infinite time interval.[15] We intend to study it in the future.

ACKNOWLEDGMENTS

Financial disclosure

None reported.

Conflict of interest

The author declare no potential conflict of interests.

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How to cite this article: Dębowski, M., (2020), Diauxic behaviour for biological processes at various time scales., *Math Method Appl Sci.*, .