Received 4 June 2021; revised 17 November 2021; accepted 19 November 2021. Date of publication 23 November 2021; date of current version 8 December 2021. The review of this paper was arranged by Associate Editor Ichiro Yamashita.

Digital Object Identifier 10.1109/OJNANO.2021.3130043

Analysis of Periodic Solution of DNA Catalytic Reaction Model With Random Disturbance

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This work was supported in part by the National Key R&D Program of China under Grant 2018YFC0910500, in part by the National Natural Science Foundation of China under Grants 61425002, 61751203, 61772100, 61972266, and 61802040, in part by the Natural Science Foundation of Liaoning Province under Grants 2020-KF-14-05 and 2021-KF-11-03, in part by the High-level Talent Innovation Support Program of Dalian City under Grant 2018RQ75, in part by the State Key Laboratory of Light Alloy Casting Technology for High-end Equipment under Grant LACT-006, in part by the Innovation and Entrepreneurship Team of Dalian University under Grant XQN202008, and in part by Liaoning Revitalization Talents Program under Grant XLYC2008017.

ABSTRACT The realization of molecular logic circuit is inseparable from the design and analysis of catalytic reaction chain, and the DNA catalytic gate plays an important role in it. Discuss the nature of the solution to DNA catalytic reaction system, using Khasminskii's periodicity and Lyapunov analysis methods to obtain the existence of non-trivial positive periodic solutions of the system, and the solution is globally attractive. The existence of the solution indicates that according to the mathematical model established by the DNA catalytic reaction system, the system may reach the expected concentration value of an ideal state and obtain better reaction data, which provides a theoretical basis for the realization of the DNA catalytic gate function. Numerical simulation results show that under the influence of random disturbance and periodic parameters, the solution to the random DNA catalytic reaction system exists and is globally attractive, which also reflects that the DNA catalytic reaction system can reach an ideal reaction state. The solution to the DNA catalytic system with random disturbance will converge on a certain value and oscillate periodically between the solution to the deterministic system.

INDEX TERMS DNA catalyzed reaction, periodic solution, global attractivity, stochastic perturbation.

I. INTRODUCTION

At present, it has been proved that nucleic acid is a multifunctional construction material for engineering molecular structures and devices. Due to the outstanding recognition characteristics of Watson-Crick base pairing, DNA is programmed and assembled in a predictable manner [1]–[5]. In addition to data storage functions and flexible design, DNA molecular logic gates also play a pivotal role. Catalysis and logic control elements and circuits [6]–[18] realize the functions of DNA molecules. Among them, the DNA catalytic gate driven by entropy is faster and more obvious modularity [19]. The realization of DNA catalytic gate not only needs to adjust the base, but also needs to analyze the kinetic behavior of the reaction process. The analysis of the dynamic characteristics of the DNA catalytic gate is inseparable from the complete nonlinear system model. However, there are few kinetic analyses on the catalytic gate of DNA molecules at home and abroad. Santovito, Elisa and others have proposed a new type of DNA-based biosensor with high sensitivity and selectivity for the detection of ochratoxin A (OTA)[20]; Keijzer, Jordi F and others proposed that the complex between heme and G-quadruplex DNA effectively catalyzes the modification of proteins by N-methylluminol derivatives and is applied to different organisms. Proteins with medical functions [21]. Among them, most of the research results are about the realization of logical operations and arithmetic operations in DNA circuits, and few involve the dynamics of the reaction system. In this case, this article mainly constructs a nonlinear mathematical model for the DNA catalytic gate reaction processes to simplify certain steps of the DNA catalytic reaction, random interference factors are considered, and the reaction process is analyzed from the perspective of kinetics

[22]–[25]. In addition, considering that the DNA catalytic gate in this article can be regarded as a periodic process, periodic parameters are added to the modeling to quantitatively analyze the properties of DNA catalytic reactions. The nature of the DNA catalytic model solution also verifies the periodicity of the reaction process.

In fact, the establishment of a DNA catalytic gate model under random disturbance can accurately describe the actual reaction process, and random noise is an inevitable influence factor in nature. At the same time, when analyzing the dynamics of the system, considering the influence of random disturbances has become increasingly important to domestic and foreign research [26]–[31]. Actually, the rate of DNA reaction is closely related to the size of activation energy. The lower the activation energy is, the faster the reaction rate is. In reality, chemical reactions occur as discrete events as a result of molecular collisions which are impossible to predict with certainty [32]. Furthermore, while in many cases a deterministic approach can be implemented to a satisfactory degree of accuracy, for many important intracellular processes, populations of molecules can be small and stochastic effects become important [33]. In the process to establish the mathematical model of DNA reactions, the reaction rate is closely related with the temperature and pressure when the reaction is proceeding. In addition, the reaction rate is also affected by such as the catalyst, condition of concentration, solvent and other factors. It is apparently that DNA reaction models are inevitably affected by environmental white noise which is an important component in realism, because it can provide an additional degree of realism in compared to their deterministic counterparts [34], [35]. Therefore, it is a well-established way of introducing stochastic environmental noise into realistic DNA reaction dynamic models. When analyzing the kinetic properties of the DNA catalytic gate, taking random disturbances into consideration can more clearly describe the reaction process of the DNA system. The random perturbation here mainly considers a standard white noise, that is, Gaussian white noise represented by Brownian motion [36]–[38]. The purpose is to construct and analyze the nature to the solution of the DNA catalytic gate system, and deeply understand and analyze the DNA system. The dynamic behavior of the model has important theoretical significance and practical application value.

The DNA catalytic gate is the circuit basis of amplifying nucleic acid signals, and the analysis of its dynamics law is beneficial to the combination of robust amplifying circuit components. The dynamic behavior analysis of the system requires the establishment of corresponding mathematical model. Because the DNA catalytic gate has periodic and random disturbances during the reaction, these influencing factors will be added to the system during the modeling process. In this paper, based on the DNA catalytic gate reaction process, and taking into account the influence of random disturbance factors, a stochastic differential system is established. The random disturbance here is the environmental white noise, and the nature to the solution of the DNA catalytic reaction under the influence of white noise and periodic parameters is explored. Moreover, the Lyapunov analysis method is used to prove that the system has a nontrivial positive periodic solution, which verifies that the random DNA catalytic gate system model with periodic function constructed in this paper is in accordance with practical significance. Secondly, by analyzing the dynamic behavior of the DNA catalytic gate system, it is concluded that even with a small noise intensity, the random DNA catalytic gate model with periodic function fluctuates in the small neighborhood of the periodic orbit. In other words, under the influence of periodic functions and random disturbances, the DNA catalytic gate has a positive periodic solution with overall attractiveness, which provides a basic guarantee for the realization of the catalytic gate. Finally, the results of numerical simulation verify the conclusions of this paper.

II. PREPARATION

In this paper, the kinetic behavior analysis of the catalytic part in the reaction process is based on the construction of the secondary cascade feedback circuit (Engineering Entropy-Driven Reactions and Networks Catalyzed by DNA) proposed in the reference [39], this paper simplifies the reaction process, establishes a mathematical model of random perturbation, and analyzes and discusses the properties of the catalytic reaction solution in the reaction process. Among them, A is the substrate, C is the catalyst, B is the product and the reactant, and F is the fuel chain. The catalytic reaction process is simplified to

$$
\begin{aligned}
&A + C \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \\
&B + F \xrightarrow{k_2} E \\
&E \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} C
\end{aligned}
\tag{1}
$$

The change in the concentration of the substances involved in the reaction is expressed by a differential equation, and the following system model is established

$$
\begin{cases}
\dot{A}(t) = k_{-1}B(t) - k_1A(t)C(t) \\
\dot{C}(t) = k_{-1}B(t) - k_1A(t)C(t) + k_3E(t) - k_{-3}C(t) \\
\dot{B}(t) = k_1A(t)C(t) - k_{-1}B(t) - k_2B(t)F(t) \\
\dot{F}(t) = -k_2B(t)F(t) \\
\dot{E}(t) = k_2B(t)F(t) - k_3E(t) + k_{-3}C(t)
\end{cases}
\tag{2}
$$

Remark 1: The rate constant of each reaction process is represented by $k_1, k_{-1}, k_2, k_3, k_{-3}$, which is an important reference factor for measuring the kinetic properties of biochemical reactions. The value directly reflects the speed of the reaction. The rate values of different biochemical reaction processes are different, which are related to the reactants, catalysts, temperature and so on. It can often be measured before and after the reaction concentration value.

Considering the principle of conservation of mass, the initial concentration of the reactant is expressed as the sum of the remaining concentration of the reactant and the product concentration. A_0, C_0, F_0 is the initial concentration, available

$$\begin{cases} C_0 = C(t) + B(t) + E(t) \\ B(t) = B_0 - A(t) - E(t) \end{cases} \tag{3}$$

Substitute (3) into (2), the following formula is obtained

$$\begin{cases} \dot{A}(t) = & a_1 - k_{-1}A(t) - k_{-1}E(t) - b_1A(t) - k_1A^2(t) \\ \dot{F}(t) = & -b_2F(t) + k_2A(t)F(t) + k_2E(t)F(t) \\ \dot{E}(t) = & b_2F(t) - k_2A(t)F(t) - k_2E(t)F(t) - k_3E(t) \\ & + k_{-3}A(t) + a_2 \end{cases} \tag{4}$$

here $a_1 = k_{-1}B_0, b_1 = k_1(C_0 - B_0), a_2 = k_{-3}(C_0 - B_0), b_2 = k_2B_0$.

Remark 2: In view of the fact that the calculation process is more complicated and the amount of calculation is large when solving the system equilibrium point and analyzing the system characteristics. Using the law of conservation of chemical reaction mass, the dimensionality of the system equation is reduced, which not only simplifies the DNA system, but also reduces the difficulty of calculation.

Taking into account the continuous progress of the DNA catalytic reaction and keeping the concentration of the product B at a constant value, assuming that the fuel substance F is added in a periodic function, the system (4) can be expressed as

$$\begin{cases} \dot{A}(t) = & a_1 - k_{-1}A(t) - k_{-1}E(t) \\ & -b_1A(t) - k_1A^2(t) \\ \dot{F}(t) = & Q(t)(F_0 - F(t)) - b_2F(t) \\ & + k_2A(t)F(t) + k_2E(t)F(t) \\ \dot{E}(t) = & b_2F(t) - k_2A(t)F(t) \\ & - k_2E(t)F(t) - k_3E(t) + k_{-3}A(t) + a_2 \end{cases} \tag{5}$$

where $Q(t)$ represents the concentration change function caused by the influx of reactive substances, and $F_0 - F(t)$ denotes the consumption of fuel chain.

In addition to periodic parameter changes, the biochemical reaction system is also disturbed by random environmental white noise. Even though the experimental results observed under controlled laboratory conditions are in good agreement with the theoretical behavior of ODE, we cannot ignore what may happen under operating conditions. difference. So, randomness is another important effect to consider. The random disturbance considered in this paper is a standard white noise, namely Gaussian white noise represented by Brownian motion. The following stochastic system model is defined

$$\begin{cases} \dot{A}(t) = & a_1 - k_{-1}A(t) - k_{-1}E(t) - b_1A(t) - k_1A^2(t) \\ & + \sigma_1(t)A(t)dB_1(t) \\ \dot{F}(t) = & Q(t)(F_0 - F(t)) - b_2F(t) + k_2A(t)F(t) \\ & + k_2E(t)F(t) + \sigma_2(t)F(t)dB_2(t) \\ \dot{E}(t) = & b_2F(t) - k_2A(t)F(t) - k_2E(t)F(t) - k_3E(t) \\ & + k_{-3}A(t) + a_2 + \sigma_3(t)E(t)dB_3(t) \end{cases} \tag{6}$$

where $B_1(t), B_2(t)$ and $B_3(t)$ are Brownian motions and $Q(t), \sigma_1(t), \sigma_2(t)$ and $\sigma_3(t)$ are continuous $\theta-$ periodic functions and $Q(t) > 0$. Thus $\sigma_1^2 > 0, \sigma_2^2 > 0, \sigma_3^2 > 0$ represent the intensities of white noise. Let complete probability space $(\Omega, F, \{F_t\}_{t\geq 0}, P)$ with filtration $\{F_t\}_{t\geq 0}$ approving the usual conditions, that is, it is correctly continuous, and unless otherwise stated, F_0 contains all P-empty sets. Denote

$$\mathbb{R}_+^l = \{x \in \mathbb{R}^l : x_i > 0 \text{ for all } 1 \leq i \leq l\}.$$

Throughout this paper, unless otherwise specified, hfit denotes the mean value of function $f(t)$ on $[0, \infty)$, i.e., $\langle f \rangle_t$is an integrable function defined on $[0, \infty)$ and $f(t)$ is recorded as the average value of the function, namely $\langle f \rangle_t = \frac{1}{t}\int_0^t f(s)ds$. In addition,

$$f^u = \sup_{t\in[0,\infty)} f(t), f^l = \inf_{t\in[0,\infty)} f(t).$$

Definition 1: For a random process $X(t, \omega)$ (where ω is a sampling point in Ω), the values of $\mathbb{R}^l$ is defined as $t \geq 0$ on a probability space (Ω, F, P) , is regarded as a Markov process if for all A $\in$ B (B is the Borel σ-algebra), $0 \leq$ k $<$ t,

$$P\{X(t, \omega) \in \mathrm{A}\,|\mathcal{N}_k\} = P\{X(t, \omega) \in \alpha\,|X(k, \omega)\}, \text{ a.s .}$$

where $\mathcal{N}_k$ is the σ-algebra of events generated by all events of the form

$$\{X(u, \omega) \in \mathrm{A}\} \quad (u \leq k, \mathrm{A} \in \mathrm{B}).$$

Remark 3: It can be demonstrated that there exists a function $P(k, l, t, \mathrm{A})$ defined as $0 \leq k \leq t$, $l \in \mathbb{R}^l$, A $\in$ B, it is the Bcan be measured in $l$for each fixed k, t, A , which constitutes a measure as a function of the set A, fulfilling the condition

$$P\{X(t, \omega) \in \mathrm{A}\,|X(k, \omega)\} = P\{k, X(t, \omega), t, \mathrm{A}\}\text{a.s.}$$

In addition, it can be proved that for all l, except those that may come from the set N such that $P\{X(t, \omega) \in N\} = 0$, the Chapman-Kolmogorov equation holds

$$P\{k, l, t, \mathrm{A}\} = \int_{\mathbb{R}^l} P(k, l, u, dy)P(u, y, t, \mathrm{A}). \tag{7}$$

The function $P(k, l, t, \mathrm{A})$ is considered as the transition probability function of Markov process.

Definition 2: If for each finite sequence of numbers $t_1, t_2, \ldots t_n$, the random process $X(t)(-\infty < t < +\infty)$is regarded as the period θ, the joint distribution of random variables $X(t_1 + h), \ldots X(t_n + h)$ is independent of h, where $h = k\theta(k = \pm1, \pm2, \ldots)$.

Remark 4: According to the theorem proposed by Khasminskii, when the transition probability function is $\theta-$periodic and the function $P_0(t, A) = P\{X(t) \in \alpha\}$ satisfies the equation, and define the Markov process $X(t)$ is $\theta-$ periodic

$$P_0(k, A) = \int_{\mathbb{R}^l} P_0(k, dl)P(k, l, k + \theta, \mathrm{A}) \equiv P_0(k + \theta, \mathrm{A})$$

for every A $\in$ B.

The following equation holds

$$X(t) = X(t_0) + \int_{t_0}^t b(k, X(k))dk + \sum_{r=1}^n \int_{t_0}^t \sigma_r(k, X(k))\,dB_r(k), \quad X \in \mathbb{R}^l. \tag{8}$$

The vectors $b(k, X), \sigma_1(k, X), \dots \sigma_n(k, X)$ are continuous functions of (k, X) and meets the following conditions:

$$\begin{cases} |b(k,l) - b(k,y)| + \sum_{r=1}^{n} |\sigma_r(k,l) - \sigma_r(k,y)| \\ \leq M|l - y|, \\ |b(k,l)| + \sum_{r=1}^{k} |\sigma_r(k,l)| \leq M(1 + |l|), \end{cases} \tag{9}$$

where M is a constant. Let U be the given open set in $\mathbb{R}^l$ and $\bar{E} = I \times \mathbb{R}^l$. The function C^2 is given as the function on $\bar{E}$, they are differentiable twice consecutively with respect to $x_1, \dots x_n$ and continuously differentiable with respect to t.

Lemma 1 Define the differential operator L

$$L = \frac{\partial}{\partial t} + \sum f_i(A,t)\frac{\partial}{\partial A_i} + \frac{1}{2}\sum [g^T(A,t)g(A,t)]_{ij}\frac{\partial^2}{\partial A_i A_j} \tag{10}$$

Define $V \in C^{2,1}(\mathbb{R}^n \times \bar{\mathbb{R}}_+; \bar{\mathbb{R}}_+)$, the following formula is obtained

$$LV(A,t) = V_t(A,t) + V_A(A,t)f(A,t) + \frac{1}{2}\text{trace}\left[g^T(A,t)V_{AA}(A,t)g(A,t)\right]. \tag{11}$$

where $V_t = \frac{\partial V}{\partial t}$, $V_A = (\frac{\partial V}{\partial A_1}, \dots, \frac{\partial V}{\partial A_d})$ and $V_{AA} = (\frac{\partial^2 V}{\partial A_i \partial A_j})_{d\times d}$.

Assume that the coefficient of (8) is the θ period in t, and the condition (9) is satisfied in each cylinder $I \times U$. There is a function $V(t, x) \in C^2$ in $\bar{E}$ which is guessed, it is the θ period in t, and satisfies the following conditions:

$$outside\ some\ tight\ set,$$

$$\inf_{|l|>\boldsymbol{R}} V(t,l) \to \infty, \text{ as } R \to \infty, \text{ and } LV(t,l) \leq -1, \tag{12}$$

Then the DNA system (6) has a solution, and it is a periodic Markov process.

III. THE EXISTENCE OF NONTRIVIAL POSITIVE PERIODIC SOLUTIONS

Unlike linear periodic stochastic differential systems that can get exact solutions, nonlinear stochastic differential systems are difficult to get exact solutions under normal circumstances, and the existence of solutions can only be obtained in the process of theoretical proof. Since the DNA-catalyzed reaction to periodic random disturbances is a nonlinear system, the periodic solution has no explicit representation. According to Lemma 1, a sufficient condition for the existence of a positive periodic solution is obtained. The existence of periodic solutions shows that the DNA catalytic reaction models has practical significance for research.

Theorem 1. If condition $\langle\lambda\rangle_\theta > 0$holds, then system (6) has a unique positive periodic solution.

Proof: For any initial value $(A(0), E(0), F(0)) \in \mathbb{R}^3_+$, there is a unique global positive solution for system (5), so $\mathbb{R}^3_+$ is regarded as the whole space. It is easy to verify that the coefficient of the system (5) satisfies the condition (9). According to Lemma 1, in order to prove Theorem 1, it successfully found a C^2 function $V(t, A, F, E)$ and a closed set $U \in \mathbb{R}^3_+$ which makes condition (12) hold.

Let $\lambda = m - \langle Q + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2\rangle_\theta$ and $\alpha \in (0, 1)$ satisfy the following conditions

$$\text{(H1)} \begin{array}{l} k_{-1} + b_1 + \frac{k_{-1}\alpha}{\alpha+1} - \frac{\alpha}{2}\sigma_1^2 > 0, \\ \frac{Q^l + b_2}{A_0} + \frac{b_2}{A_0} - 2k_2 - \frac{\alpha\sigma_2^2}{2A_0} > 0 \end{array}$$

$$\text{(H2)}\ M\left(-\lambda + \frac{1}{2}\langle\sigma_1^2\rangle_\theta\right) + g^u + h^u \leq -2,$$

where $m = a_1$ and the function $g(F), h(E)$ are given later (H3), $-\lambda + \frac{1}{2}\langle\sigma_1^2\rangle_\theta < 0$ and M is a large enough normal number.

Define a C^2-function $V(A, F, E)$: $\mathbb{R}^3_+ \to \bar{\mathbb{R}}_+$ by

$$V(t,A,F,E) = \frac{1}{\alpha+1}A^{\alpha+1} + \frac{1}{A_0(\alpha+1)}F^{\alpha+1} + M(E - \ln A - \ln F - \ln E) + w(t),$$

this moment, $w(t)$ is a function defined on $[0, +\infty)$, satisfying

$$\dot{w}(t) = \langle R_0\rangle_\theta - R_0, w(0) = 0.$$

where $R_0(t) = Q(t) + \frac{1}{2}\sigma_1^2$. It is not difficult to find that $w(t)$ is the $\theta-$ periodic function of $[0, +\infty)$, and $V(t, A, F, E)$ is the $\theta-$period in t and satisfies the condition (12).

For the convenience of calculation, $Q(t)$ is expressed as Q, and the other parameter functions are the same. Through direct calculation, the following results are obtained

$$\begin{aligned} LV &= A^\alpha[a_1 - k_{-1}A - k_{-1}E - b_1A - k_1A^2] \\ &+ \frac{1}{A_0}F^\alpha[Q(F_0 - F) - b_2F + k_2AF + k_2EF] \\ &- M\frac{1}{A}(a_1 - k_{-1}A - k_{-1}E - bA - k_1A^2) \\ &- M\frac{1}{F}[Q(F_0 - F) - b_2F + k_2AF + k_2EF \\ &- \frac{M}{E}(b_2F - k_2AF - k_2EF - k_3E + k_{-3}A + a_2) \\ &+ (b_2F - k_2AF - k_2EF - k_3E + k_{-3}A + a_2)M \\ &+ \dot{w}(t) \\ &\leq a_1A^\alpha - \left(k_{-1} + b_1 + \frac{k_{-1}\alpha}{\alpha+1} - \frac{\alpha}{2}\sigma_1^2\right)A^{\alpha+1} \\ &- \frac{k_{-1}}{\alpha+1}E^{\alpha+1} \\ &- \left(\frac{Q^l + b_2}{A_0} + \frac{b_2}{A_0} - 2k_2 - \frac{\alpha\sigma_2^2}{2A_0}\right)F^{\alpha+1} + \frac{Q^uF_0}{A_0}F^\alpha \\ &+ M\left[(k_1 - k_2)A - \lambda + \frac{1}{2}\langle\sigma_1^2\rangle_\theta\right] + c^* \\ &+ M\left[k_2F - \frac{Q^lF_0}{F} + (k_{-1} - k_2 - k_3)E - \frac{a_2}{E}\right] \end{aligned} \tag{13}$$

This $c^* = M(k_1 + b_2 + b_1 + a_2 + k_3)$. The above equation can be expressed as

$$LV \le f(A) + g(F) + h(E)$$

where

$$\text{(H3)}\begin{cases} f(A) = a_1A^\alpha - (k_{-1} + b_1 + \frac{k_{-1}\alpha}{\alpha+1} - \frac{\alpha}{2}\sigma_1^2)A^{\alpha+1} \\ + M\left[(k_1 - k_2)A - \lambda + \frac{1}{2}\langle\sigma_1^2\rangle_\theta\right] \\ g(F) = -(\frac{Q^l+b_2}{A_0} + \frac{b_2}{A_0} - 2k_2 - \frac{\alpha\sigma_2^2}{2A_0})F^{\alpha+1} \\ + \frac{Q^uF_0}{A_0}F^\alpha + Mk_2F - \frac{Q^lF_0M}{F} \\ h(E) = -\frac{k_{-1}}{\alpha+1}E^{\alpha+1} + (k_{-1} - k_2 - k_3)EM - \frac{Ma_2}{E} \end{cases}$$

According to the (H1) condition, the following formula is obtained

$$\begin{gathered} f(A) + g^u + h^u \to -\infty, asA \to +\infty, \\ f^u + g(F) + h^u \to -\infty, asF \to +\infty, \\ f^u + g^u + h(E) \to -\infty, asE \to +\infty, \\ f^u + g(F) + h^u \to -\infty, asE \to 0^+, \\ f^u + g^u + h(E) \to -\infty, asF \to 0^+, \end{gathered}$$

$LV < -1$ can be derived from the above situations, respectively. Recall condition (H2), as $A \to 0^+$, the conclusion $M(\lambda - \frac{1}{2}\langle\sigma_1^2\rangle_\theta) + g^u + h^u \le -2$ is clearly obtained.

Take ε small enough, and let $U = [\varepsilon, \frac{1}{\varepsilon}] \times [\varepsilon, \frac{1}{\varepsilon}] \times [\varepsilon, \frac{1}{\varepsilon}]$. It follows that $LV < -1$, $(A, F, E) \in \mathbb{R}^3_+$. This completes the proof.

Remark 5: On the basis of Lemma 1, it is obtained that the stochastic system (6) has a non-trivial periodic solution. The function $V(t, A, F, E)$ established by the *Itô* formula is analyzed, and $LV < -1$, $(A, F, E) \in \mathbb{R}^3_+ \backslash U$. The proof of the existence of the solution provides basic conditions for analyzing the global attraction properties of the solution, and understanding the dynamics of the DNA subtraction gate model has important theoretical significance and practical application value.

IV. EXISTENCE AND GLOBAL ATTRACTIVITY OF BOUNDARY PERIODIC SOLUTION

This part mainly discusses the global attractivity of solution of stochastic DNA catalytic system (6). When certain conditions are met, the system has a unique periodic solution, which lays the foundation for attractiveness analysis. The DNA catalytic reaction model is carried out periodically, and the periodic solution of the reaction process is obtained through quantitative analysis. To further prove the global attractiveness of the solution.

Lemma 2: Assume that $Z^*(t)$ is the solution of a one-dimensional linear random differential equation

$$\begin{aligned} dZ(t) = [Q(t)(F_0 - Z(t)) - b_2Z(t)]dt \\ + \sigma_2(t)Z(t)dB_2(t) \end{aligned} \tag{14}$$

with initial value $Z(0) = F(0)$,where $Q(t) and \sigma_2(t)$are $\theta-$periodic functions defined on $[0, +\infty)$. Moreover, $Z^*(t)$ is globally attractive, i.e., Attract all other positive solutions of stochastic differential equation (15).

Proof**.** Define the C^2-function $V(t, Z)$ as follows

$$V(t, Z) = Z - 1 - \ln Z + \dot{w}_0(t)$$

Here $\dot{w}_0(t)$ is the θ periodic function defined on $[0, +\infty)$ satisfying the following equation

$$\dot{w}_0(t) = \left\langle(F_0 + 1)Q + \frac{1}{2}\sigma_2^2\right\rangle_\theta - (F_0 + 1)Q(t) - \frac{1}{2}\sigma_2^2(t),$$

$$w_0(0) = 0.$$

Calculated by Ito's formula

$$\begin{aligned} LV(t, Z) &= Q(F_0 - Z) - \frac{QF_0}{Z}(F_0 - Z) \\ &+ b_2 - b_2Z + \frac{1}{2}\sigma_2^2(t) + \dot{w}_0(t) \\ &\le -Q^lZ - \frac{Q^lF_0}{Z} - b_2Z + b_2 + \left\langle(F_0 + 1)Q + \frac{1}{2}\sigma_2^2\right\rangle_\theta \\ &\triangleq \varphi(Z) \end{aligned} \tag{15}$$

Obviously easy to see,

$$\varphi(Z) \to -\infty, \text{as } Z \to 0^+; \ \varphi(Z) \to -\infty, \ \text{ as } Z \to +\infty.$$

Take ε as a small enough value and $U = [\varepsilon, \frac{1}{\varepsilon}]$to make $LV < -1, Z \in \mathbb{R}_+ \backslash U$ hold. It can be concluded that equation (15) has a positive periodic solution $Z^*(t)$.

Remark 6: Analyze the one-dimensional stochastic linear differential equation, construct the Lyapunov function and use the Khasminskii-type theorem to prove and obtain $LV < -1$, so that the system has a periodic solution $Z^*(t)$. The DNA catalytic system model has a solution, and its solution is periodic, which also lays the foundation for proving the global attractiveness of the solution.

Next, it will be proved that the solution $Z^*(t)$ is globally attractive. Knowing that $Z^*(t)$ satisfies equation (15), the equation is processed as follows

$$\begin{aligned} d(Z(t) - Z^*(t)) = -Q(t)\left(Z(t) - Z^*(t)\right) \\ - b_2\left(Z(t) - Z^*(t)\right)dt \\ + \sigma_2(t)\left(Z(t) - Z^*(t)\right)dB_2(t) \end{aligned}$$

Therefore

$$Z(t) - Z^*(t) = (Z(0) - Z^*(0))e^{-\int_0^t(Q(r)+b_2+\frac{1}{2}\sigma_2^2(t))dr+M_0(t)}$$

After further processing the above formula,

$$\begin{aligned} \log|Z(t) - Z^*(t)| = \log|(Z(0) - Z^*(0))| \\ - \int_0^t\Big(Q(r) + b_2 \\ + \frac{1}{2}\sigma_2^2(t)\Big)dr + M_0(t), \end{aligned} \tag{16}$$

$M_0(t)$ is assigned to $M_0(t) = \int_0^t\sigma_2(r)dB_2(r)$ and $M_0(t)$ is a local martingale whose quadratic variation is $\langle M_0(t), M_0(t)\rangle = \int_0^t\sigma_2^2(s)ds \le (\sigma_2^u)^2t$. According to the strong law of large numbers for local martingales [40], the following formula is obtained

$$\lim_{t\to+\infty}\frac{M_0(t)}{t}=0a.s. \tag{17}$$

Therefore,

$$\frac{\log\left|Z(t)-Z^*(t)\right|}{t}=\frac{\log\left|Z(0)-Z^*(0)\right|}{t} -\frac{1}{t}\int_0^t\left(Q(r)+\frac{1}{2}\sigma_2^2(r)dr\right)+\frac{M_0(t)}{t}. \tag{18}$$

According to the principle of equation (18), the result of seeking the limit of equation (19) is

$$\lim_{t\to+\infty}\frac{\log\left|Z(t)-Z^*(t)\right|}{t}=-\left\langle Q+b_2+\frac{1}{2}\sigma_2^2\right\rangle_\theta<0$$

It indicates that $Z(t)-Z^*(t)\to 0$ a.s. Now, it can be concluded that the periodic solution $Z^*(t)$ of equation (15) is globally attractive. This completes the proof.

Remark 7: By calculating the linear differential function with Ito's formula, on the basis of the existence of positive periodic solutions of random systems, the periodic solutions of the system are globally attractive based on the strong theorem of local martingales. Under the condition that the periodic solution of the system is satisfied, the DNA catalytic system can obtain the expected value of the real reaction process.

Remark 8: The periodical oscillation can be understood as a example of stochastic resonance. Stochastic resonance is a nonlinear effect whereby a system is able to improve, via noise addition, the detectability of a signal in noise. In this paper, when the periodic signal is applied to the nonlinear system with white noise, periodic stochastic resonance occurs.

By Lyapunov analysis method, the existence solution of the random perturbed DNA catalytic system with periodicity is obtained, and it has a nontrivial positive periodic solution. According to the strong number theorem of the local martingale, it is proved that the nontrivial positive periodic solution is globally attractive, which is of great practical significance for the theoretical study of DNA catalytic gates. Numerical simulation is used to present the DNA catalytic reaction process, and the simulation results will be used to verify the nature of the solution of the random DNA catalytic system.

V. NUMERICAL SIMULATIONS AND INVESTIGATIONS

In order to verify the theoretical results obtained in this paper, a numerical simulation of a stochastic system is given. Since the nonlinear stochastic differential system is too complex to be solved accurately, it is necessary to give parameter values to find an approximate solution.

Example 1: According to the condition to satisfy Theorem 1, take the initial value $(A(0), F(0), E(0)) = (1.2, 0.19, 0.12)$ and assume that the constant parameter is set to $k_{-1} = 0.4, k_1 = 0.6,\ k_2 = 0.9, k_3 = 1.2,\ k_{-3} = 0.3,\ A_0 = 3,\ C_0 = 3.1, F_0 = 1.9$. Observing to the following image changes, it is observed that the data at this time is that when the DNA catalytic system reaches the ideal state, the system (6) has a non-trivial positive periodic solution. Now, the solution of the corresponding deterministic system also shows periodic changes. The numerical simulation in Figure 1 clearly proves this point. Under the action of low noise intensity, the Markov process $A(t), F(t), E(t)$ oscillates back and forth in the domain of the periodic solution of the deterministic system. Through the change curve of the image, the side reflects the periodicity of the reactants in the DNA catalytic reaction model. The periodic nature of the solution of the random perturbation system shows that the material utilization rate of the DNA catalytic system can be improved.

Example 2: Compared with the above example, increase the $Q(t)$value, and other data remain unchanged. It is clearly observed from Figure 2 that the value does not reach the most suitable ideal state, but still satisfies the nature of the solution, and the DNA catalytic gate reaction still proceeds smoothly. The change of image amplitude can significantly show that the deterministic system still satisfies the global attractiveness of the periodic solution.

Even if the noise intensity does not change, with the change of $Q(t)$, the oscillation amplitude of the $A(t), F(t), E(t)$image is significantly increased. Obviously, the periodic amplitudes of DNA catalytic model changed significantly.

Example 3: Keep the period of $Q(t)$unchanged, and increase or decrease the noise intensity. Through the change of the image curve, the stochastic system still satisfies the condition of the existence of a positive periodic solution, which indicates that for any positive initial value, the solution of the deterministic model will enter a periodic orbit after a period of time. When the intensity increases, it is obvious that the oscillation amplitude of the random perturbed DNA catalytic system with periodic function is greatly enhanced, and the solution of the random system is still a non-trivial positive periodic solution, but the periodic nature is not as obvious as the above example.

Conversely, when the intensity decreases, although the model of the random process (6) fluctuates near a smaller orbit. And the solution of the random disturbance system is almost close to the solution of the deterministic system. No matter how the intensity changes, the stochastic system is realized under ideal conditions if Theorem 1 are fulfilled. As shown in Figs. 3 and 4.

From the above simulation results, it can be clearly concluded that when the noise intensity is within a certain range and meets certain conditions, the random DNA catalytic periodic system can find a non-trivial positive periodic solution. In an ideal state, the DNA catalytic reaction models uses cycles as the unit, and the concentration of substances change periodically. In addition, when the noise intensity is too small, the solution of the random periodic DNA catalytic system may be close to the solution of the deterministic system. Finally, the combination of theoretical analysis and simulation results clearly shows that the periodic model of the stochastic DNA catalytic system has a positive periodic solution, which satisfies the global attractive force. These theoretical results also

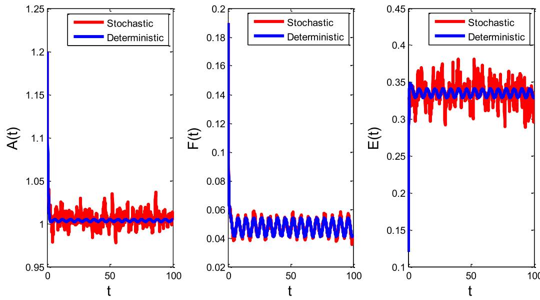

FIGURE 1. **When the DNA catalytic reaction system is in an ideal state, the sample orbitals of the nontrivial positive periodic solutions of the random system and the deterministic system. Here, $Q(t) = 0.1 + 0.1\sin(t)$, and define $\sigma_1 = \sigma_2 = \sigma_3 = 0.2 + 0.1\sin(t)$.**

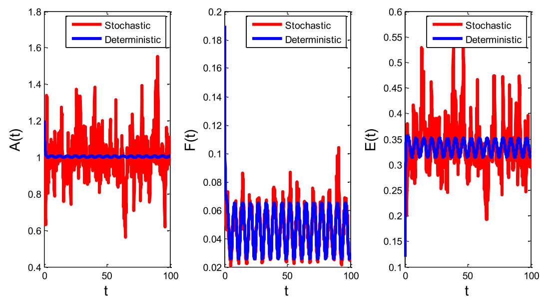

FIGURE 2. **A Sample orbits of nontrivial positive periodic solutions for stochastic systems and deterministic systems. Where $Q(t) = 0.5 + 0.3\sin(t)$ $\sigma_1 = \sigma_2 = \sigma_3 = 0.2 + 0.1\sin(t)$.**

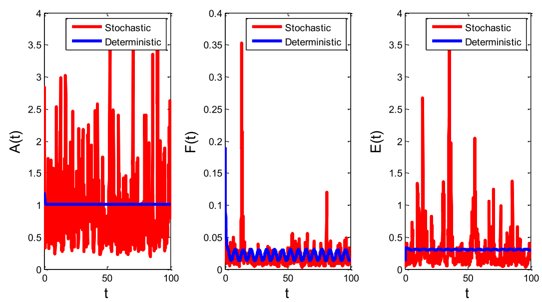

FIGURE 3. **Sample orbits of nontrivial positive periodic solutions for stochastic systems and deterministic systems. Where $Q(t) = 0.2 + 0.1\sin(t)$, $\sigma_1 = \sigma_2 = \sigma_3 = 1.2 + 0.2\sin(t)$.**

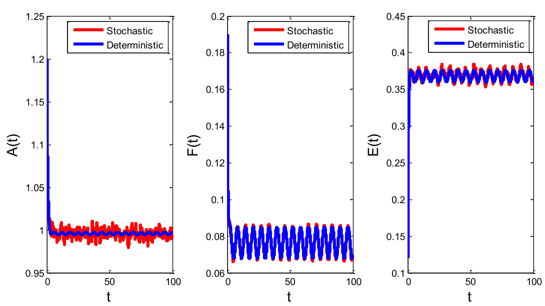

FIGURE 4. **Sample orbits of nontrivial positive periodic solutions for stochastic systems and deterministic systems. Here $Q(t) = 0.1\sin(t)$ and Noise intensity parameter $\sigma_1 = \sigma_2 = \sigma_3 = 0.1\sin(t)$.**

imply that the DNA catalytic system can achieve the expected reaction effect on ideal experimental conditions.

VI. CONCLUSION

In this paper, the properties of the solution of DNA catalytic gate with periodic random disturbances is studied. The DNA catalytic reaction system is analyzed for solution, and it is assumed that the reaction material is added regularly to keep the reaction continuing. Considering that the reaction will be affected by random interference, here is mainly white noise, so adding random interference to the DNA catalytic system is more in line with the actual reaction of the system. Firstly, the nature of the periodic solution of DNA catalytic reaction with random disturbances is analyzed, and the sufficient conditions for the existence of nontrivial positive periodic solutions are proposed, and the periodic solutions are obtained. The existence of the solution indicates that it is of practical significance to study the dynamic behavior of DNA catalytic gate. Secondly, the strong number theorem of local martingale proves that the periodic solution of DNA catalytic reaction models under random disturbance has global attractiveness. Finally, a numerical simulation of DNA catalytic reaction system with random perturbations and cycles is carried out using Milstein's high-order method. Numerical simulation results show that it is very meaningful that nonlinear equations with random disturbance and periodicity can be used to describe the kinetic characteristics of DNA catalytic reactions. At the same time, the DNA catalytic reaction models can predict the reaction process of ideal conditions.

ACKNOWLEDGMENT

H. Lv and H. W. Li collected data, constructed a model for dynamic behavior analysis, and drafted a manuscript. Both H. Lv and Q. Zhang modified manuscript and they are the corresponding authors. All authors read and corrected the manuscript.

REFERENCES

[1] A. J. Genot *et al.*, "Reversible logic circuits made of DNA," *J. Amer. Chem. Soc.*, vol. 133, no. 50, pp. 20080–20083, 2011.
[2] J. Zhu *et al.*, "Four-way junction-driven DNA strand displacement and its application in building majority logic circuit," *ACS Nano*, vol. 7, no. 11, pp. 10211–10217, 2013.
[3] J. Elbaz *et al.*, "DNA computing circuits using libraries of DNAzyme subunits," *Nature Nanotechnol.*, vol. 5, no. 6, pp. 417–422, 2010.
[4] Y.-J. Chen *et al.*, "Programmable chemical controllers made from DNA," *Nature Nanotechnol.*, vol. 8, no. 10, pp. 755–762, 2013.
[5] C. Xing *et al.*, "Light-controlled, toehold-mediated logic circuit for assembly of DNA tiles," *ACS Appl. Mater. Interfaces*, vol. 12, no. 5, pp. 6336–6342, 2020.
[6] W. E. Arter *et al.*, "Digital sensing and molecular computation by an enzyme-free DNA circuit," *ACS Nano*, vol. 14, no. 5, pp. 5763–5771, 2020.
[7] X. Zheng *et al.*, "Allosteric DNAzyme-based DNA logic circuit: Operations and dynamic analysis," *Nucleic Acids Res.*, vol. 47, no. 3, pp. 1097–1109, 2019.
[8] F. Wang *et al.*, "Implementing digital computing with DNA-based switching circuits," *Nature Commun.*, vol. 11, no. 1, pp. 1–8, 2020.
[9] S. Kogikoski Jr. *et al.*, "Electrochemical sensing based on DNA nanotechnology," *TrAC Trends Anal. Chem.*, vol. 118, pp. 597–605, 2019.

[10] A. R. Chandrasekaran *et al.*, "DNA nanotechnology approaches for microRNA detection and diagnosis," *Nucleic Acids Res.*, vol. 47, no. 20, pp. 10489–10505, 2019.
[11] Y. Liu *et al.*, "Modelling and analysis of haemoglobin catalytic reaction kinetic system," *Math. Comput. Model. Dyn. Syst.*, vol. 26, no. 4, pp. 306–321, 2020.
[12] Z. T. Sandhie, F. U. Ahmed, and M. H. Chowdhury, "Design of ternary logic and arithmetic circuits using GNRFET," *IEEE Open J. Nanotechnol.*, vol. 1, pp. 77–87, 2020.
[13] H. Wang *et al.*, "Compact graphene-based spiking neural network with unsupervised learning capabilities," *IEEE Open J. Nanotechnol.*, vol. 1, pp. 135–144, 2020.
[14] N. Soheili *et al.*, "Design and evaluation of biological gate circuits and their therapeutic applications in a model of multidrug resistant cancers," *Biotechnol. Lett.*, vol.42, no.8, pp. 1419–1429.
[15] M. Lv *et al.*, "Illuminating diverse concomitant DNA logic gates and concatenated circuits with hairpin DNA-templated silver nanoclusters as universal dual-output generators," *Adv. Mater.*, vol. 32, no. 17, 2020, Art. no. 1908480.
[16] T. Song *et al.*, "Fast and compact DNA logic circuits based on single-stranded gates using strand-displacing polymerase," *Nature Nanotechnol.*, vol. 14, no. 11, pp. 1075–1081, 2019.
[17] D. Wang *et al.*, "Precise regulation of enzyme cascade catalytic efficiency with DNA tetrahedron as scaffold for ultrasensitive electrochemical detection of DNA," *Anal. Chem.*, vol. 91, no. 5, pp. 3561–3566, 2019.
[18] Y. Yuan, H. Lv, and Q. Zhang, "DNA strand displacement reactions to accomplish a two-degree-of-freedom PID controller and its application in subtraction gate," *IEEE Trans. Nanobiosci.*, vol. 20, no. 4, pp. 554–564, Oct. 2021.
[19] D. Y. Zhang *et al.*, "Engineering entropy-driven reactions and networks catalyzed by DNA," *Science*, vol. 318, no. 5853, pp. 1121–1125, 2007.
[20] E. Santovito *et al.*, "Development of a DNA-based biosensor for the fast and sensitive detection of ochratoxin a in urine," *Analytica Chimica Acta*, vol. 1133, pp. 20–29, 2020.
[21] J. F. Keijzer *et al.*, "Site-specific and trigger-activated modification of proteins by means of catalytic hemin/g-quadruplex DNAzyme nanostructures," *Bioconjugate Chem.*, vol. 31, no. 10, pp. 2283–2287, 2020.
[22] J. Nilsson *et al.*, "Stochastic analysis and control of real-time systems with random time delays," *Automatica*, vol. 34, no. 1, pp. 57–64, 1998.
[23] L. W. Gelhar *et al.*, "Three-dimensional stochastic analysis of macrodispersion in aquifers," *Water Resour. Res.*, vol. 19, no. 1, pp. 161–180, 1983.
[24] L. W. Gelhar *et al.*, "Stochastic analysis of macrodispersion in a stratified aquifer," *Water Resour. Res.*, vol. 15, no. 6, pp. 1387–1397, 1979.
[25] B. Pei *et al.*, "Averaging principles for SPDEs driven by fractional brownian motions with random delays modulated by two-time-scale markov switching processes," *Stochastics Dyn.*, vol. 18, no. 4, 2018, Art. no. 1850023.
[26] M. Bandyopadhyay *et al.*, "Deterministic and stochastic analysis of a nonlinear prey-predator system," *J. Biol. Syst.*, vol. 11, no. 2, pp. 161–172, 2003.
[27] V. E. Saouma *et al.*, "Stochastic analysis of concrete dams with alkali aggregate reaction," *Cement Concrete Res.*, vol. 132, 2020, Art. no. 106032.
[28] A. Maiti *et al.*, "Deterministic and stochastic analysis of a prey-dependent predator–prey system," *Int. J. Math. Educ. Sci. Technol.*, vol. 36, no. 1, pp. 65–83, 2005.
[29] C. Ji *et al.*, "Dynamics of a stochastic density dependent predator–prey system with Beddington–Deangelis functional response," *J. Math. Anal. Appl.*, vol. 381, no. 1, pp. 441–453, 2011.
[30] E. J. Chichilnisky, "A simple white noise analysis of neuronal light responses," *Netw.: Comput. Neural Syst.*, vol. 12, no. 2, pp. 199–213, 2001.
[31] Z. Wu *et al.*, "A study of the characteristics of white noise using the empirical mode decomposition method," in *Proc. Roy. Soc. London. Ser. A: Math. Phys. Eng. Sci.*, 2004, vol. 460, no. 2046, pp. 1597–1611.
[32] D. T. Gillespie, "Exact stochastic simulation of coupled chemical reactions," *J. Phys. Chem.*, vol. 81, pp. 2340–2361, 1977.
[33] H. H. McAdams *et al.*, "It's a noisy business! Genetic regulation at the nanomolar scale," *Trends Genet.*, vol. 15, pp. 65–69, 1999.
[34] A. Golightly *et al.*, "Bayesian inference for stochastic kinetic models using a diffusion approximation," *Biometrics*, vol. 61, pp. 781–788, 2005.
[35] Y. Ying *et al.*, "The dynamics of the stochastic multi-molecule biochemical reaction model," *J. Math. Chem.*, vol. 52, pp. 1477–1495, 2014.
[36] L. Cao *et al.*, "Tuned tandem mass dampers-inerters with broadband high effectiveness for structures under white noise base excitations," *Struct. Control Health Monit.*, vol. 26, no. 4, 2019, Art. no. e2319.
[37] Y. Wang *et al.*, "The electrical activity of neurons subject to electromagnetic induction and gaussian white noise," *Int. J. Bifurcation Chaos*, vol. 27, no. 2, 2017, Art. no. 1750030.
[38] J. Z. Ma *et al.*, "Slowing down critical transitions via gaussian white noise and periodic force," *Sci. China Technological Sci.*, vol. 62, no. 12, pp. 2144–2152, 2019.
[39] D. Y. Zhang *et al.*, "Engineering entropy-driven reactions and networks catalyzed by DNA," *Science*, vol. 318, no. 5853, pp. 1121–1125, 2007.
[40] X. Mao *et al.*, *Stochastic differential equations with Markovian switching*, London, U.K.: Imperial College Press, 2006.