Synthesizing a Clock Signal with Reactions—
Part I: Duty Cycle Implementation Based on Gears

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Abstract—Timing is of fundamental importance in biology and our life. Borrowing ideas from mechanism, we map our clock signals onto a gear system, in pursuit of better depiction of a clock signal implemented with chemical reaction networks (CRNs). On a chassis of gear theory, more quantitative descriptions are offered for our method. Inspired by gears, our work to synthesize a tunable clock signal could be divided into two parts. Part I, this paper, mainly focuses on the implementation of clock signals with three types of duty cycles, namely 1/2, 1/N (N > 2), and M/N. Part II devotes itself in addressing frequency alteration issues of clock signals. The experimental chassis can be taken care of by DNA strand displacement reactions, which lay a solid foundation for the physical implementation of nearly arbitrary CRNs.

Index Terms—Clock signal, chemical reaction networks (CRNs), gears systems, duty cycle.

I. INTRODUCTION

Harnessing engineering principles to design biological components opens a new era of synthetic biology [1]. Indeed, since synthetic biology gained its more modern usage in 1974, a significant quantity of achievements have been initialized—synthetic DNA [2–5], designed proteins [6, 7], bio-information storage [8–10], biosensors [11–13], and even synthetic life [14–16]. To date, exciting and novel ideas show this nascent field’s amazing vigorousness and endless potential. However, to coordinate tasks more properly, both biology and engineering call for clock signals of synthetic biology. Though systematic methods for designing an electrical clock signal can be used for both hardware and software, it becomes inapplicable in synthetic biology due to implementation differences.

Actually, a plenty of literature devote themselves in synthesizing biochemical time. In [17], Franco used a synthetic biochemical oscillator proposed by Kim and Winfree [18], which consists of two DNA transcription templates and two output RNA species. Power analysis was carried out to make this oscillator capable of driving a given load. Although it does not offer a method to synthesize a biochemical clock signal, it provides a reference to study the driving strength of a biochemical oscillator. In [19], a method to implement a biological oscillator with positive feedback transitions was proposed. Unfortunately, those aforementioned literature did not offer a systematic method to synthesize a biological clock signal with CRNs. Though our previous work [20] proposed a synthesis methodology for a clock signal regarding duty cycle, it lacks systematic modeling, fundamental analysis, and generalization on both generation and operation. By far, for a more vivid depiction and a better understanding, it is required to find a physical analogy and formal design methodology for synthesizing a clock signal.

Amazingly, from a common sense—time is invisible but could be heard with the sound of “tick-tack” from a mechanical watch in our daily life. Thus gear systems turn out to be a candidate to offer a general clock design methodology. Apart from this intuition, there are another three reasons to focus on gear systems. First, purely observing or studying the CRNs may be too abstract, and the design steps remain unrevealed. Second, the existence of a wide range of literature on gear systems [21–23] makes the theory and implementation of gear systems quite mature. Third, various resemblances between a gear system and a clock tree enables such literature good references for bio-clock signal design. Specifically, both gear systems and clock tree aim at efficient energy transmission in a designed regularity. Therefore, with a fundamental model of gear system, a clock tree in CRNs could be better understood. All those understandings offer us guidance and feasibility to generalize the methodology for further and wider applications. Thus, our study is initially motivated to better depict our previous work in [20] based on a newly proposed gear model, and is dedicated itself to implement a tunable CRN clock signal in terms of duty cycle and frequency. Part I offers a systematic method to implement nearly arbitrary duty cycle on a chassis of gear systems. Part II contemplates to handle frequency alteration. This paper mainly covers the first part.

The remainder of this paper is organized as follows. Section II briefly reviews the prerequisite preliminaries. Section III illustrates inspirations from a gear system to a CRN clock tree. Case studies are also given in this section. Section IV presents the design methodology for a clock signal with tunable duty cycle. A description of clock tree is also given in this section. Finally, Section V concludes the entire paper.

II. PRELIMINARIES

Before proceeding to substantive parts of this paper, some preliminaries are given in this section for a better explanation of our contributions.

A. Rationale of Pure CRN Design

Essentially, a mathematical foundation guarantees the safety of our pure CRN design and an RGB(Y) mechanism ensures...
the oscillation of our clock signal. That is, in 2011, Soloveichik and Winfree proposed in [24] that DNA as a universal substrate for chemical kinetics, mathematically confirms that nearly all arbitrary chemical reaction networks (CRNs) could be “translated” into DNA strand displacement reactions [25–28], which lays a solid foundation for physical implementation of our proposal. Hence, we are safe in purely designing arbitrary CRNs of target functionality. Moreover, based on the RGB(Y) oscillator, which is first proposed by Jiang Hua in [29, 30], clock signals of nearly arbitrary duty cycle could be successfully obtained in a general way via our previous work in [20], with an extended method for 1/N and novel solutions for both 1/2 and N/M.

To better understand what we do, a design flow is illustrated in Fig. 1. Feasibilities of the CRNs are guaranteed by numerical results based on the corresponding ODEs, which are obtained via mass-actions [32, 33]. With the aid of tools such as Visual DSD [34] and NUPACK [35], one could finally translate the designed CRNs into DNA strand displacement reactions with desired clock signal. We view the design of CRNs as “front end”, whereas view the DNA implementations as “back end”.

B. Simulation Model

With the help of ODEs, a simulation model, various dynamic behaviors of certain CRNs could be properly emulated. This ODE-based approach is convenient and can perfectly imitate the time-varying evolution of chemical kinetics. The details of extracting ODEs from a CRN are well-described in [36]. Key factors are reactants, rate constants, and products. It is worth noting that although [24] requires each chemical reaction has no more than two reactants, in the rest part of this paper, this constraint is ignored for design convenience. Because we can always decompose reactions with more than two reactants into cascaded bimolecular or unimolecular ones. For example, use “A + B ⇔ C” and “C + D → E + F” to realize “A + B + D → E + F”. Also, there are some CRN-to-DNA translation schemes like [28] that can directly handle higher order reactions. Moreover, as pointed out in [24], the scaled system of lower rate constants and concentrations maintains the same, albeit scaled, behavior. Thus, both the simulated concentration and time are unitless. What’s more, for an experimental setup, these systems would be scaled in an appropriate way. For more details, please refer to [24, 37].

C. A Quick Review of Our Previous Work

A (circle-map)-aided (C-map) method was proposed in our previous work [20], briefly illustrated in Algorithm 1. We use an N-phase oscillator to realize a 1/N (N > 2) clock signal. This totally requires 4N chemical reactions. However, a 1/2 clock signal is a different case. Its implementation method differs from that of 1/N (N > 2) and 12 chemical reactions are in demand. While for an arbitrary M/N clock signal, we need to combine the aforementioned two methods. This M/N clock signal calls for in total (12 + 4N) chemical reactions with a little changes in 4 reactions.

Algorithm 1 Implementation of 1/N (N > 2), 1/2, and M/N.

Require: A system of oscillators and a circle-map (C-map).
1: if Synthesize 1/N (N > 2) duty cycle clock signal then
2: An N-phase oscillator is in demand.
3: Due to the given C-map, especially for its arrows, map all the four-type reactions: “absence”, “phase signal”, “threshold” and “main power” reactions.
4: Extending the RGB oscillation mechanism, this implementation calls for 4N chemical reactions.
5: else if Engineer a 1/2 clock signal with a modified C-map then
6: To trigger a transference between two phase signals.
7: Molecule $t_{10}$ and $t_{01}$ are introduced to instruct the transference between $clk_1$ and $clk_0$.
8: Require 12 chemical reactions.
9: end if
10: if Construct an M/N clock signal then
11: Combine both 1/N (N > 2) and 1/2 clock signal implementation. Only 4 reactions need a little fine-tuning.
12: Use different two phase signals of an N-phase oscillator to control the transference of 1/2 clock signal.
13: Call for (12 + 4N) reactions.
14: end if

1) Chemical Reactions for RGB Oscillation: In our previous proposal, totally four-type reactions are required for RGB oscillation mechanism, named after their functionality: “absence indicators”, “phase signals”, “threshold reactions” and “main power reactions”. Concrete chemical reactions are given in Table VI in Appendix A. Note that an absence indicator is logically complementary to a phase signal, which means in a system, if there exists an absence indicator, then there is no its corresponding phase signal and vice versa.

2) Chemical Reactions for 1/2 Duty Cycle: Employing the aforementioned four-type reactions, the implementation of 1/2 duty cycle calls for 12 reactions. Introducing two instructors, $t_{10}$ and $t_{01}$, the oscillation mechanism hence could be successfully established between $clk_0$ and $clk_1$. Concrete chemical reactions are given in Table VI in Appendix A.

All the C-maps of those three-type implementation methods are shown in Fig. 2 as well as the corresponding simulation results. For more details, please refer to [20].

III. CLOCK DESIGN INSPIRATIONS FROM GEARS

In this section, after announcing our goal is to design a tunable clock signal, several bijective concepts between gear systems and clock signals are provided. Through analyzing the operating mechanism of gears, several useful instructions are accumulated.
A Tunable Clock Signal

To put it simple, our goal is to design a tunable clock signal in a CRN level. In synthetic biology, a good tunable clock signal means parameters, including frequency, period and duty cycle as well as amplitude, could be freely tweaked for various special uses. Since different amplitudes could be easily realized by employing distinctive values of molecule concentrations, our study does not cover more about this simple issue. This paper mainly focuses on the duty cycle implementation. For frequency alteration implementation, please refer to Part II.

Remark 1: It is interesting to note that amplitude nearly takes no place for clock signals in traditional electronics, people only focus on its comparing results with the reference level, hence this kind of comparison will produce a high or low voltage. However, concentrations actually matter a lot in synthetic biology. And in our proposal, the amplitude owns a close relationship with concentration. Therefore, we care about the amplitude of a clock signal.

B. Analogy between Gear Systems and Clock Trees

Interestingly, C-maps are found to look like a gear. Different phase nodes look like gear teeth. What’s more, the process of a clock signal finishes a time period, just like a gear rotates a cycle at a uniform speed. Thus, an analogy between C-maps, or rather CRNs, and a gear system is direct.

1) Main Parameters: For a single gear, parameters in Table 1 should be paid attention to. Among all the parameters, the top three are related to the size of a gear. While the bottom four are in relation to its rotation. Note that modem m must be the same for all gears, otherwise they would not mesh.

| Parameter | Meaning                        |
|-----------|--------------------------------|
| D         | Number of teeth on the gear    |
| m         | modem = D/t                   |
| ω         | Angular velocity              |
| v         | Linear velocity on the circle  |
| Rev       | Rotational speed (unit: rev/s) |
| α         | rotation direction             |

2) Bijective Concepts: Table II offers a straight bijective concepts between a gear system and a clock tree. We assume the value of torque to drive a gear, is equal to that of transmission energy in a clock tree. The number of gear teeth has a strong linear relationship with that of phase nodes. So does the relationship between diameter of a gear and length of a clock period, or rather D ∝ T. What’s more, the angular velocity of a gear remains the same relationship in physics with a clock time period T.

Remark 2: As shown in the bottom of Table II a certain gear could also map with a clock signal in at least three aspects. Since the rotation period of a gear is exactly the time period of a clock signal, the amplitude could be directly reflected from the dedendum of a gear, which means the height of gear teeth is exactly the amplitude of a signal. When it comes to duty cycle of a clock signal, it could be tweaked via different painted schemes of a certain pinion “translated” into the connected rack.
3) **Length of a Clock Time Period:** First, we offer a basic idea to define a clock time period of the synthesized chemical clock signal. Both technical measurements and definitions are included. Then, data analysis is conducted to verify the correctness of our clock implementation and definition.

**a) Basic Idea:** Extract data from Mathematica, regenerate the curve with Matlab, and confirm the specific value of the peak of turning-up and bottom of turning-down. More specifically, use Case in [38] or Flatten to extract data in Mathematica, then regenerate them in Matlab. Finally, utilize the datatip in Matlab to confirm the wanted value.

![Fig. 3. Simple model for measuring \( T_{1/N} \) and \( \tau_{1/N} \).](image)

Besides, recall that our previous work mainly presented three approaches to construct a clock signal, essentially the approach of 1/2 differs from that of 1/N \((N > 2)\), while the clock signal of \( M/N \) has the same clock period of 1/N. Therefore, considering different implementation methods of a clock signal may result in various magnitudes in the length of a clock period, we mainly measure the length of clock time period for 1/2 and 1/N.

**Definition 1:** As shown in Fig. 3 the length of a clock period is defined as the distance of two neighboring points in the same location of a period signal, top or bottom, denoted \( T_{1/N} \) (colored blue or orange). While the existing time of a phase signal indicates how long a phase signal exists in a cycle of \( T_{1/N} \), or when its concentration is the highest level. Hence \( \tau_{1/N} \) is the distance of two neighboring points that a bottom value minus a previous peak one (colored red). Indeed, \( \tau_{1/N} \) is the evaluated existing time of a phase signal, with a definition of \( T_{1/N}/N \). All of them contribute to build a better understanding about the gear size in what follows.

**Remark 3:** Theoretically, different implementation methods lead to different lengths of a clock period, hence we mainly measure the clock period of 1/2 and 1/N \((N > 2)\). Due to the implementation method of 1/N, different phase signals should theoretically have the same existing time, namely \( \tau_{1/N} \). For convenience, clock signals of 1/3, 1/5, 1/15, and 1/2 are measured.

**b) Data Analysis:** Processing the data shown in Fig. 4 all the parameters we care most are listed in Table III. Carefully observe a single phase existing time of 1/2 and 1/N duty cycle, \( \tau_{1/2} \) is really different from others. While \( \tau_{1/3}, \tau_{1/5}, \) and \( \tau_{1/15} \) are nearly the same. This result proves that various implementation methods lead to different \( \tau_{1/N} \). Due to the high value of \( T_{1/2} \) and the rule of \( t \propto D \propto T \), the diameter of a gear representing 1/2 duty cycle is much bigger than that of 1/3, 1/5, and 1/15 duty cycle.

![Table II: Mapping from a Gear System to a Clock Tree](image)

![Table III: Measurements of 1/2, 1/3, 1/5, and 1/15](image)

**Remark 4:** In Table III the data extracted from Fig. 4 are coherent to our design goal, which means our previous design method could really realize 1/2 and 1/N duty cycle. Because \( \tau_{1/N} \) times \( N \) approximately equals to \( T_{1/N} \) we measure. Take 1/3 duty cycle as an example, the product of \( \tau_{1/3} \) and \( N = 3 \) equals to 0.27501, which is approaching to \( T_{1/3} = 0.275 \). Hence Fig. 4(a) is really simulated the clock duty cycle. So are the other clock signals implemented with our methods.

4) **Size of a Gear:** Seizing upon the rule of \( t \propto D \propto T \), we denote “Ratio” in Table III as “\( T_{1/N}/T_{1/3} \)”. The last column of Table III shows the gear size ratio comparing with the 1/3 clock signal. Therefore, we use the gear of 1/3 duty cycle as the standard one, with \( D = 1 \) (unitless). Take a gear of 1/5 as an example, its diameter \( D = 1.64109 \) and so on.

**C. Fundamental Paradigms from Gears to Clock Signals**

Totally four types of gears could be utilized to synthesize chemical clock signals.

1) **Simple Gear Train:** Fig. 5 typically shows spur gears. Imagine that rotation is from Gear A then B and finally C, whereas the direction of this rotation is reversed from one gear to another. Gear B, also named an idler gear, has no effect on the gear ratio but merely plays a role in changing the direction of rotation. To mesh with each other, the teeth of all gears must be the same size; hence \( m \) for all gears should be identical.

Velocity is transferred through the implementation shown in Fig. 5. All the linear velocity \( v \) must be the same. Gears comply with the rules of Eq. 1

\[
\begin{align*}
\frac{\omega_A D_A}{2} &= \frac{\omega_B D_B}{2} = \frac{\omega_C D_C}{2} \\
\implies \omega_A D_A &= \omega_B D_B = \omega_C D_C \\
\implies \omega_A m t_A &= \omega_B m t_B = \omega_C m t_C \\
\implies \omega_A t_A &= \omega_B t_B = \omega_C t_C.
\end{align*}
\]

For a simple gear train, there exist a lot of physical properties hidden in the following theorems, from which several instructions to model our clock signal of CRNs could be gradually accumulated.
Theorem 1: A larger-size gear must rotate slower in order to achieve the same \( \omega \).

Proof: According to \( v = \omega D \) in physics, angular velocity \( \omega \) must be larger on condition that the diameter of the gear \( D \) is relatively small, hence all the gear share the same linear velocity. Note that rotational speed \( \text{Rev} \) is physically equal to \( \omega \) divided by \( 2\pi \), namely \( \text{Rev} = \omega/2\pi \), therefore \( \omega \) is proportional to \( \text{Rev} \) and smaller gear runs faster.

Corollary 1: If a large gear turns a small gear, the speed increases, and vice versa.

Proof: Under the circumstances of identical \( v \), Theorem 1 indicates that a smaller gear runs faster than another one between the neighboring two gears. Suppose energy is transferred from a large gear to a smaller one—viewed as an input and an output, respectively—it is obvious that the input gear has a slower \( \omega \) while the output faster. Thus, the speed from input to output increases in the aspect of angular velocity.

**Theorem 2:** For a simple gear train, the relationship among \( D, t, \) and \( T \) could be well expressed as \( t \propto D \propto T \).

Proof: A good mesh calls for the same modem \( m \). Because \( m = D/t \), therefore \( t \propto D \) could be easily obtained. Recall that \( v = \omega D \) and \( \omega = 2\pi/T \), consequently \( D \propto T \) when all \( v \) are the same.

**Design Inspirations:** In practical, we often use a simple gear train to make the time period of a 1/2 duty cycle clock signal identical with its meshed gear signal. For different gear sizes, although the implementation like Fig. 5 indicates the same linear velocity but various time periods, we can still change the time period or frequency through an appropriate CRN synthesis. To exemplify this frequency alteration, two meshed gears shown in Fig. 5 are taken into consideration. We assume that Gear A is a 1/6 duty cycle clock signal while Gear B represents 1/2 duty cycle. The simulation of standard 1/6 and 1/2 duty cycle are the red and blue curve shown in Fig. 6 and their parameters are in accordance with Table V. We use the first phase of 1/6 duty cycle clock signal to control the existing time of one phase of 1/2 clock signal, and the last phase of 1/6 signal to manipulate the existing time of another phase of 1/2. The corresponding result is the black curve shown in Fig. 6. This changed 1/2 duty cycle has the
same time period of the standard $1/6$, which differs from its initial time period. One thing should be emphasized is that, the final output is usually meaningless when we use this method to unitize the time period between other kinds of clock signals. Therefore, a simple gear train is often used to unify the time period of a $1/2$ duty cycle clock signal with that of another arbitrary duty cycle. Other kinds of frequency or time period alteration should employ other different gear models.

2) Compound Gears: Compound gears are widely used in many mechanical devices like engines and workshop machines. As Fig. 7 indicates, compound gears are actually two gears attached to each other and they rotate around the same center. Sometimes compound gears are employed, thus the final gear in a gear train could rotate at a target speed. One of the most important properties for compound gears is illustrated in Theorem 3.

**Theorem 3:** Compound gears always have the same time period $T$.

**Proof:** Rotating around the same center, compound gears share the same angular velocity $\omega$. Based on the physical rule of $\omega = 2\pi / T$, they also have an identical $T$ but different $\nu$ for different $D$.

**Design Inspirations:** This compound gear model is usually used for frequency alteration in terms of CRN synthesis. Two ways are motivated to unitize the time period of two gears through this implementation in Fig. 7. Assume Gear $A$ is a three-phase signal, while Gear $B$ a six-phase one. (1) Purely change the rate constants of the respective CRNs, especially those constants of threshold and main power reactions. When both Gear $A$ and $B$ take the standard parameters as in Table V, the corresponding results are the top two waves shown in Fig. 8. Note that their time periods are different. For Gear $B$, adopt 1.55 as the rate constant of threshold reactions and 500 as that of main power reactions. The changed clock signal colored purple is still $1/6$ duty cycle, but has the same time period as the standard $1/3$ duty cycle of Gear $A$. Similarly, the changed $1/3$ duty cycle clock signal could own the identical time period of the standard $1/6$ one when it adopts 0.5 as the threshold reactions’ rate constant and 26 as the main power reactions’. The changed two clock signals are shown in the bottom of Fig. 8 (2). Segment a phase signal into pieces and still adopt appropriate rate adjustments. This means we use a phase of an oscillator to control the threshold and main power reactions of another oscillator. The bottom curve of Fig. 9 is the simulation when we use one phase of the standard $1/6$ duty cycle clock signal to control the aforementioned two-type reactions of a $1/3$ one. This blue curve is actually the output of the three-phase oscillator, but has the same time period of the standard $1/6$ duty cycle clock signal. Since this CRN synthesis is essentially to segment one phase of $1/6$ into three pieces, the final output is actually a $1/18$ duty cycle. Therefore, this kind of frequency alteration also changes the final duty cycle. A purple curve in Fig. 9 is the result of segmenting one phase of $1/3$ duty cycle into six pieces, and it is also a $1/18$ duty cycle. Interestingly, although both the bottom two curves are $1/18$ duty cycle clock signal, their time period are different. Therefore, our further CRN synthesis of frequency alteration in Part II is based on compound gear model. More detailed discussion will also be offered.

3) Compound Gear Train: A compound gear train is an upgraded version of compound gears. As shown in Fig. 10, suppose that energy is transferred from left to right one by one, both $\{\text{Gear } A, \text{ Gear } C\}$ and $\{\text{Gear } B, \text{ Gear } D\}$ compose a pair of simple gear train with the same $\nu$, respectively. While $\{\text{Gear } A, \text{ Gear } B\}$ implements a compound gear with the property of identical $\omega$.

**Design Inspirations:** A compound gear train is usually employed to model a clock tree. Because this implementation is composed of compound gears and a simple gear train, thus the time period of a clock signal could be controlled through
is to say the “rotary motion” is changed to be a “linear one”.

Moreover, if the pinion rotates in a round, the rack will move the pinion gear only if their respective teeth could mesh well. Actually, the pinion is a normal round gear while the rack is a straight one with teeth. Therefore, the rack could move gears, this rack and pinion gear system looks quite unusual.

Fig. 11. Simple model for a rack and pinion gear system.

According to Fig. 11, although it is still composed of two gears, this rack and pinion gear system looks quite unusual. Actually, the pinion is a normal round gear while the rack is a straight one with teeth. Therefore, the rack could move the pinion gear only if their respective teeth could mesh well. Moreover, if the pinion rotates in a round, the rack will move in a straight line—another way of describing this phenomenon is to say the “rotary motion” is changed to be a “linear one”.

**Design Inspirations:** Since a “rotary motion” could be altered into a linear one, a visual clock signal could be obtained via the implementation of a rack and pinion gear system. Moreover, to reflect the specific duty cycle, the pinion should be colored with two colors. Thus, the rack could well display the duty cycle in a line that we are familiar with.

IV. GEAR MODELS FOR CLOCKS WITH DUTY CYCLE

This section proposes different operating mechanisms for three-type clock signals, including duty cycles of 1/2, 1/N (N > 2), and M/N. Moreover, the operation of a clock tree is also elaborated in this section.

A. Operating Mechanism

On a chassis of analogy mentioned above, we propose an operating mechanism of our previous clock implementations as follows.

1) **For a Single 1/2 Clock Signal:** In our proposal, a clock signal of 1/2 duty cycle is denoted by a gear with nearly 227 (6 \times 37.8182) teeth if the standard gear of 1/3 duty cycle has 6 teeth. Meshed with other relatively tiny gears of 1/N (N > 2), the drawn gear of 1/2 in Fig. 12(a) only has 45 teeth, but actually represents 227 teeth. It is interesting to note that this yellow gear looks like the C-map shown in Fig. 2(b).

2) **For a Single 1/N Clock Signal:** Each 1/N (N > 2) clock signal works as a single rotated gear as shown in Fig. 12(b). Although the 1/2 duty cycle clock signal is also functionally equal to a single rotated gear, its effective diameter is distinctively different because it uses another implementation method. More specifically, the gear size of 1/N duty cycle equals to that of 1/2 only when N = 117, therefore the gear size of 1/N is usually smaller than that of 1/2 duty cycle if N \ll 117. Similarly, this blue gear quite looks like the C-map shown in Fig. 2(a).

3) **For a Clock Signal of M/N Duty Cycle:** In fact, the operating mechanism of M/N duty cycle that we propose works like what Fig. 12(c) shows. Both G_1 and G_2 are required to implement a clock signal with M/N duty cycle, representing 1/2 and 1/N (N > 2) duty cycle, respectively. While G_3, painted with two colors, is used to “segment” the denominator N.

**Remark 5:** From a standpoint of CRNs, after the implementation of CRNs for both 1/2 and 1/N duty cycle clock signal, an interaction of these two CRNs should be established; thereby two phase signals of N oscillator controlling the transference of 1/2 clock signal, especially the procedure of its “threshold” and “main power” reaction.

To be specific, based on Remark 5, the operating mechanism is proposed as follows: G_2 and G_3 compose the compound gears as shown in Section II.C2, sharing the same gear size and velocity. While G_1 and G_3 constitute a simple gear chain, transferring the painting for M/N. After that, the final M/N duty cycle clock signal is obtained via the implementation of a rock and pinion, translating the “rotary motion” into a linear one. Note that G_3 is colored by two different colors, one is pink for M sections, and another is grey for N – M sections.
The final time period is the same as $G_2$, but differs from that of the initial $G_1$.

**Remark 6:** When it comes to $M/N$ duty cycle clock signal, the implementation of $G_1$ and $G_3$ looks like the corresponding C-map in Fig. 12(c) Note that there is no essential distinction between $G_2$ and $G_3$, because $G_3$ is introduced for the convenience of painting. These 3-type gear models are summarized in Algorithm 2.

**Algorithm 2** Gear models of $1/2, 1/N$ ($N > 2$), and $M/N$.

**Require:** Three-type gears.

1. **if** Implement a clock signal of $1/2$ duty cycle. **then**
2. **else if** Implement a clock signal of $1/N$ duty cycle. **then**
3. **end if**

**Remark 7:** Based on the analysis in Section III.B, we know the diameter of $G_1$ is usually larger than $G_2$, hence there are a large number of planets could be engaged with $G_1$. Most clock signals could be produced through this mechanism.

**Example.** Take a $2/3$ duty cycle clock signal as an example. After the implementation of a rock and pinion as Fig. 15(a) the time has been recorded in the rock just as the simulation results shown in Fig. 15(b).

Actually, a skew is found in Fig. 15(b) at the very beginning of simulation time. This skew can be attributed to the first touch or mesh between $G_1$ and $G_3$. After that, they mesh well with each other and nearly no skew would be produced.

**V. DISCUSSION AND CONCLUSION**

To our best knowledge, we are the first to borrow ideas from gears to synthesize a tunable clock signal with CRNs. In this paper, inspired by a gear system, we could better understand the operating mechanism of a clock signal with different duty cycles in CRNs. In our previous work [20], nearly no quantitative description of the results was offered, however. This paper semi-quantitatively reproduces all the simulation data with a set of physically reasonable parameters. On a chassis of our gear model, a good understanding of a clock tree in CRNs could be obtained from the standpoint of signal generation, information transport as well as the unwanted clock skew. The proposed clock synthesis methodology based on gear systems can helps designers conveniently derive the

![Gears and clock tree](image-url)
Fig. 13. Gear model of a clock tree.

Fig. 14. Side view of the gear model for a clock tree. The biggest gear colored yellow is the sun gear, and others are the planet ones. All the planet gears rotate around the sun gear, transmitting the clock information.

required clock signals. Experimental works with DNA strand displacement reactions will be shown in our future work.

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APPENDIX A
CONCRETE CHEMICAL REACTIONS
A. Reactions for RGB Oscillators
Concrete chemical reactions are shown in Table IV with totally 12 reactions. Attention should be paid to the different rate constants of reactions with various functionalities.

B. Reactions for 1/2 Duty Cycle Clock Signal
Concrete chemical reactions are shown in Table V with wholly 12 chemical reactions. Note the reactions of instructor production and annihilation, especially the rate constant of main power reactions.

C. Reactions for Frequency Division 1/15
Concrete chemical reactions are shown in Eq. 2 with wholly 72 chemical reactions, rate constant of which remains the same with reactions in Tables IV and V.

\[
\begin{align*}
\varphi & \rightarrow r_5, & \varphi & \rightarrow r_{10}, \\
\varphi & \rightarrow r_6, & \varphi & \rightarrow r_{11}, \\
\varphi & \rightarrow r_7, & \varphi & \rightarrow r_{12}, \\
\varphi & \rightarrow r_{13}, & \varphi & \rightarrow r_{14}.
\end{align*}
\]
### Table IV
Reactions for the RGB oscillators

| Clock | Absence | Phase signal | Threshold | Main power |
|------|---------|--------------|-----------|------------|
| Rate | $k = 1$ | $k = 100$ | $k = 1$ | $k = 100$ |
| RGB | $\phi \rightarrow r$ | $R + r \rightarrow R$ | $R + b \rightarrow G + b$ | $R + 2G \rightarrow 3G$ |
|     | $\phi \rightarrow g$ | $G + g \rightarrow G$ | $G + r \rightarrow B + r$ | $G + 2B \rightarrow 3B$ |
|     | $\phi \rightarrow b$ | $B + b \rightarrow B$ | $B + r \rightarrow R + 0$ | $B + 2R \rightarrow 3R$ |

### Table V
Reactions for 1/2 duty cycle clock

| State | Rate | Cycle |
|------|------|-------|
| Absence | $k = 1$ | $\phi \rightarrow in_0$ |
| Phase signal | $k = 1$ | $clk_1 + in_0 \rightarrow clk_1$ |
| Instructors | $k = 1$ | $clk_1 + in_0 \rightarrow clk_1 + t_{10}$ |
| Threshold | $k = 1$ | $R_{14} + t_{01} + clk_0 \rightarrow R_{14} +clk_1 + t_{01}$ |
| Main power | $k = 1000$ | $t_{10} + 2clk_0 + clkl = 3clk_0 + t_{10}$ |
| Annihilation | $k = 1$ | $t_{10} \rightarrow \phi$ |

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