Synthesizing a Clock Signal with Reactions—
Part II: Frequency Alteration Based on Gears

Chuan Zhang, Member, IEEE, Lulu Ge, Student Member, IEEE, Xiaohu You, Fellow, IEEE

Abstract—On a chassis of gear model, we have offered a quantitative description for our method to synthesize a chemical clock signal with various duty cycles in Part I. As Part II of the study, this paper devotes itself in proposing a design methodology to handle frequency alteration issues for the chemical clock, including both frequency division and frequency multiplication. Several interesting examples are provided for a better explanation of our contribution. All the simulation results verify and validate the correctness and efficiency of our proposal.

Index Terms—Clock signal, chemical reaction networks (CRNs), gear systems, frequency alteration.

I. INTRODUCTION

CLOCK signal is essentially an artificial measurement of time, which is of great significance to our life. Under the instruction of clock signals, rhythms abound in biological systems decide the cellular behaviors—cells make decisions and operate assignments from seconds to hours, people work and sleep in a day of 24 hours, plants blossom and bear fruits in a period of years—underlying those various timing processes, all the rhythms are well-orchestrated. This is the same truth for electrical systems to coordinate tasks. All in all, clock signals undeniably play an important role in both synthetic biology [1–3] and electrical systems [5–6].

In Part I of our study, which synthesizes a tunable clock signal in CRN level, we have presented an appropriate gear model to offer: 1) physical analogy for CRN clock design methodology, and 2) a quantitative description of duty-cycle modulation. In other words, with gear models proposed in Part I, our methods to synthesize a chemical clock signal conform to a physical intuition. Unlike Part I, Part II focuses on the frequency alteration instead of duty-cycle modulation. In this paper, by further exploiting the compound gear model, we offer a formal frequency alteration methodology for a clock signal with fixed duty cycle: generating a new clock whose frequency is \( L/J \) times of the input clock. Although there exists a limitation on \( L \) (being a factor of \( N \)), the proposed methodology enables us to change the frequency of chemical clock to some extent and makes the frequency processing of CRNs possible. The work shown in Part II is put forward based on the gear theory illustrated in Part I, thus being considered as a continuation of Part I.

In this paper, under the accumulated instructions derived from Part I, we attempt to address the frequency alteration in two steps: 1) frequency division by \( J \), and 2) frequency multiplication by \( L \). Our proposed approaches are validated via numerical simulations of the chemical kinetics based on ordinary differential equations (ODEs). It is noted that, the chemical reactions here are all formal chemical reactions, which could be translated into DNA strand displacement reactions if properly designed [9]. Therefore, our work owns its physical implementation, namely DNA reactions, although it looks like just pure CRN design.

The rest of this paper is organized as follows. With the definition of fundamental frequency with fixed duty cycle, Section II proposes a method to realize the frequency division by \( J \). On a chassis of Part I, a detailed gear model analysis is given in Section III for frequency multiplication by \( L \). Different gear combinations for frequency multiplication are taken into consideration in the same section. Concrete examples are offered for a better understanding. Finally, Section IV concludes the entire paper.

II. FREQUENCY DIVISION

This section focuses on the frequency division for CRN clocks. Frequency alteration is meaningful only after the fundamental frequency (input clock) is defined. More specifically, when it comes to frequency alteration, the compared two clock signals must have the same duty cycle but different frequencies or clock cycles. Theoretically, frequency division implementation tends to address a problem described as follows:

**Question Forming 1:** For a clock of fundamental frequency \( f_{in} \) and a given duty cycle \( M/N \), frequency division aims to output a new clock with \( f_{in}/J \) frequency and unchanged duty cycle. The main elements for this question are listed in Table 1, from which, only two clock signals are concerned: the fundamental (input) clock signal and the output signal with divided frequency.

### Table 1

| Input               | Output               |
|---------------------|----------------------|
| Fundamental frequency \( f_{in} \) | Divided frequency \( f_{in}/J \) |
| References          | Unchanged parameter  |
| \( N \) and \( J/N \)-phase gears* | \( M/N \) duty cycle   |

*Note: \( J \) is an integer.

A. Fundamental Frequency

Frequency alteration is given based on an implementation of fundamental frequency. For better explanation, here the fixed duty cycle is set as \( 1/N \). Other duty cycles can be processed in the same fashion. To synthesize a clock signal with CRNs,
$\tilde{T}_{1/N}$ would be 0.091 when we adopt the rate constant scheme in Appendix of Part I. Therefore, the whole time period of $1/N$ depends on the number of phases the oscillator has, and the exact value of $T_{1/N}$ is $N \times \tilde{T}_{1/N}$, namely 0.091$N$. Therefore, in our proposal for a $1/N$ ($N>2$) duty cycle clock signal, the fundamental frequency is defined with our previous method.

Fundamental frequencies of $1/3$, $1/4$, and $1/5$ duty cycle clocks are shown in Fig. 1. These results show that they have different time period $T_{1/N}$ but the same phase existing time $\tilde{T}_{1/N}$. One thing should be emphasized is that, the fundamental frequencies might have a clock skew at the first beginning. And the reason for this phenomenon is the first touch between two meshed gears. After this first “uncomfortable” touch, everything will be okay, including the oscillation and the produced clock signals.

![Fig. 1. Simulation results of $1/3$, $1/4$, and $1/5$ fundamental frequencies.](image)

Hence in our proposal, the fundamental frequency is defined as those clock signals implemented with our previous method for $1/N$ ($N > 2$) duty cycle, or rather the time period measured by $\tilde{T}_{1/N}$. The corresponding gear model is the implementation of $1/N$ duty cycle illustrated in Section VI of Part I. Owing to this fundamental frequency, frequency alteration could be further conducted. Additionally, frequency division could be easily understood as it has a longer time period while frequency multiplication has a shorter one.

B. Rationale of Frequency Division

In traditional electronics, for a given fundamental frequency $f_{in}$, the realization of $f_{in}/J$ indicates frequency division, where $J$ is an integer. In our proposal for CRNs, $J$ multiple for both numerator and denominator of $f_{in}$ gives frequency division, where the fundamental frequency is defined based on the standard implementation of $1/N$ duty cycle clock signal. For instance, on a chassis of a $1/N$ duty cycle clock, frequency division could be realized through the construction of $2/2N$, $3/3N$, ..., and $n/nN$.

C. Case Study for Frequency Division

Take a $1/3$ duty cycle clock signal as an example. As shown in Fig. 2 the fundamental frequency of $1/3$ duty cycle is the top red curve, which is synthesized with our method illustrated in Part I. Its frequency division could be realized by implementing clock signals with duty cycles of $2/6$, $3/9$, and so on. The other two curves in Fig. 2 representing $2/6$ and $3/9$ respectively, realize the wanted frequency divisions. Both $2/6$ and $3/9$ duty cycle clock signals are constructed according to the implementation methodology of $M/N$ duty cycle clock signal in Part I. Each phase signal is colored brown by a dashed line in this figure.

![Fig. 2. Simulation of $1/3$ fundamental frequency and frequency division.](image)

Hence, the clock signal synthesized with $1/N$ ($N > 2$) duty cycle in Part I would be viewed as a fundamental frequency. Frequency division would be realized through the implementation of $M/N$ duty cycle, which has its physical meaning of longer time period than the fundamental one. The corresponding gear models can also be found in Part I.

III. FREQUENCY MULTIPLICATION

Based on the related work in Part I for compound gears, this section focuses on the frequency multiplication issue. Two methods are given in this section. Frequency multiplication of CRN clock aims to address the following problem:

**Question Forming 2:** For a clock of fundamental frequency $f_{in}$ and a given duty cycle $M/N$, frequency multiplication aims to output a new clock with $Lf_{in}$ frequency and unchanged duty cycle. The main elements for this question are listed in Table II from which, only two clock signals are concerned: the fundamental (input) clock signal and the output signal with divided frequency.

| TABLE II |
|-----------|
| Question forming for frequency multiplication |
| Input | Output |
| Fundamental frequency $f_{in}$ | Multiplied frequency $Lf_{in}$ |
| Reference signal | Unchanged parameter |
| $K$ and $L$-phase gears* | $1/N$ duty cycle |

*Note: $N = K \times L$.

A. Rationale of Frequency Multiplication

Our frequency multiplication is actually based on the compound gears illustrated in Part I. The more specific design inspiration is derived from Part I by segmenting a phase signal into pieces and adopting an appropriate rate constant adjustment. For a better explanation of our proposal, a detailed illustration is given as follows.
First of all, a compound gear model is shown as Fig. 3. Assume $G_A$ is a $K$-phase oscillator, and $G_B$ is an $N$-phase one. Additionally, if one tooth of $G_A$ denotes a phase signal of the $K$-phase oscillator, the enlarged colorful painting scheme is actually to equally divide this phase signal’s existing time into $L$ pieces, and each piece corresponds to a phase signal of $G_B$. Moreover, this segmentation essentially realizes a $1/N$ duty cycle, that is $G_B$, where $N = K \times L$. The corresponding clock signals for both $G_A$ and $G_B$ are shown in Fig. 4.

From Fig. 4, the input clock signal of the design target in Section I is the top one, which is a fundamental frequency of $1/N$ duty cycle. The remained two signals are the results of our compound gear model shown in Fig. 3. The $1/K$ duty cycle signal (denoted by $G_A$) has the same pulse width with the fundamental frequency $1/N$ one, their difference is the teeth number. Additionally, this $1/K$ duty cycle signal owns the same time period of the produced $1/N$ one (represented by $G_B$), which has shorter time period of its fundamental frequency. Thus, this operation based on the compound gear model does really realize frequency multiplication. The target clock signal for frequency multiplication, represented by $G_B$, could be obtained via three steps summarized in Algorithm 1. Note that the number of these chemical reactions is less than that of reactions realizing the same duty cycle clock signal with our method in Part I.

**Remark 1:** The property of this frequency multiplication could be realized by “phase signal controlling”. It means only one phase signal of $K$-phase oscillator controls the transference of $L$-phase oscillator, especially the process of threshold and main power reactions. Meanwhile, two phase signals of $L$-phase oscillator are used to control the whole transference of $1/2$ duty cycle clock signal.

**Algorithm 1** CRNs to implement $G_B$.

**Require:** CRNs for $1/K$, $1/L$ and $1/2$ duty cycle.

1. Construct a $K$ and $L$-phase oscillator with CRNs, respectively, where $K, L \geq 3$.
2. Implement a $1/2$ duty cycle with 12 chemical reactions.
3. Use one phase signal of $K$-phase oscillator to control the transference of $L$-phase one.
4. Use two phase signals of $L$-phase oscillator to control the transference of $1/2$ duty cycle.
5. Detect one phase of $1/2$ clock signal, the duty cycle of final clock signal could range from $1/(K \times L)$, $2/(K \times L)$, $3/(K \times L)$, $\ldots$, $1/K$.

**Remark 2:** Implementing in Algorithm 1 requires a total of $(4K + 4L + 12)$ chemical reactions. Whereas in our previous work, the same duty cycle calls for $(4N + 12)$ reactions, where $K, L \geq 3$. Hence, the method in Fig. 3 could not only realize the frequency multiplication, but also reduce chemical reactions because $KL \gg (K + L)$.

**B. Different Conditions for Frequency Multiplication**

Since the aforementioned phase signal controlling is given by segmenting one phase of $K$-phase oscillator into $L$ pieces, conditions are categorized for: $K \neq L$ and $K = L$. For $K \neq L$, two methods are proposed.

1) **Frequency Multiplication When $K \neq L > 2$**

On the premise of $K \neq L$, two methods are proposed to address $K > L$ and $L < K$ issues, named Method 1 and Method 2, respectively. Both conditions segment one phase signal of $K$-phase oscillator into $L$ pieces. Method 1 and Method 2 do not only differ in terms of the values of $K$ and $L$, but also the time period of output clock signals, as well as the rate constant adjustment schemes they require. The corresponding gear models are shown in Fig. 3.

- **Method 1 for $K > L$**

Three gears are required in our gear model, namely $G_{A1}$, $G_B$, and $G_1$, representing oscillators of $1/K$, $1/N$ and $1/2$ duty cycle, respectively. The rationale for $G_{A1}$ and $G_B$ has been illustrated in Fig. 3. More specifically, to realize this target $1/N$ duty cycle, we harness one phase signal of CRNs for $1/K$ duty cycle to control the whole transference of CRNs for $1/L$ duty cycle. In practice, we often use one phase of the $K$-phase oscillator to manipulate the threshold and main power reactions of the CRNs for the $L$-phase oscillator. If CRNs of the $K$-phase oscillator adopt the standard rate constant scheme, one thing should be emphasized is that, the rate constant of main power reactions for $L$-phase oscillator should be slowed down. Otherwise, an unwanted oscillation will occur.

**Example.** An example of frequency multiplication with $1/15$ duty cycle is given for our proposal. Since $15 = 3 \times 5$ and $K > L$, we have $K = 5$ and $L = 3$ in Method 1. Synthesized with the methods in Part I and introduced the phase signal controlling procedure, the final clock signal is shown as the bottom red curve in Fig. 6 if no rate constant adjustment has been taken. Note that the red curve in Fig. 6(b) is an enlarged version of the red one in Fig. 6(a). From Fig. 6, an unwanted oscillation occurs since all the CRNs for oscillators.
Method 1: $K > L$

$$\frac{1}{N} \text{ duty cycle}$$

Method 2: $K < L$

$$\frac{1}{N} \text{ duty cycle}$$

Fig. 5. Gear model for frequency multiplication with Method 1 and Method 2 when $K \neq L$.

(a) Fundamental frequency and frequency multiplication.

(b) Output of $K$ oscillator and frequency multiplication.

Fig. 6. Simulation results for Method 1 without rate constant adjustment.

Fig. 7. Simulation results for Method 1 with rate constant adjustment.

Results and Analysis. Verified by Figs. 6 and 7 our $K$-phase oscillator, or rather the five-phase oscillator, operates well and produces the standard fundamental frequency of $1/5$ duty cycle in a black curve colored gray. However, chaos occurs when no appropriate rate constant adjustment is adopted in the CRNs of $L$-phase oscillator. The main reason for this chaos in Fig. 6 is the too rapid transference of $L$-phase oscillator. Because the standard fundamental frequency of $1/3$ duty cycle has shorter time period than that of $1/5$ one, which means the transference rate of 3-phase oscillator is much faster. Seize this key point, the rate constant of main power reactions for 3-phase oscillator, under the control of one phase signal
of 5-phase oscillator, should be slowed down. Validated by Fig. 7, the final frequency multiplication of 1/15 duty cycle colored red in Fig. 7(b) works well, since it has a shorter time period than its blue-colored fundamental one in Fig. 7(a).

**Method 2 for** $K < L$: Similar to Method 1, the gear model for this method still requires three gears shown in Fig. 5. They are $G_A$, $G_B$, and $G_1$, representing oscillators of 1/$K$, 1/$N$, and 1/2 duty cycles, respectively. The only difference between Method 2 and Method 1 is that the rate constant of main power reactions for $L$-phase oscillator should be a little faster. In other words, it should be greater than 100.

**Example.** Still take the 1/15 duty cycle frequency multiplication as an example. This time $K = 3$ and $L = 5$. Similar to Method 1, a rate constant adjustment should be adopted in this method. The corresponding results are shown in Fig. 8 when the rate constant of main power reactions for $L$-phase oscillator is set as 104.

![simulation results for frequency multiplication when $K = L = 3$](image)

**Results and Analysis.** As shown in Fig. 8(a), the red-colored final clock signal of 1/15 duty cycle synthesized with Method 2 owns shorter time period than its blue-colored fundamental frequency. From Fig. 8(b), the $K$-phase oscillator, namely the 3-phase one, produces a fundamental frequency of 1/3 duty cycle. As an enlarged version of the red curve in Fig. 8(a), the bottom red curve in Fig. 8(b) really segments one phase signal of 3-phase oscillator into 5 pieces. Thus the final clock signal colored red realizes the frequency multiplication of 1/15 duty cycle.

2) **Frequency Multiplication When $K = L$:** Conditions of “$K = L > 2$” and “$K = L = 2$” are taken into consideration as follows.

a) **For $K = L > 2$:** Two methods are merged into one. We still employ the gear model in Fig. 5 and slow down the rate constant of main power reactions for the controlled $L$-phase oscillation.

**Example.** Take a frequency multiplication of 1/9 duty cycle as an example. The two oscillators are identical. The rate constant of main power reactions for $L$-phase oscillator is set to be 25.5. Simulation results are shown in Fig. 9. Finally, a nice frequency multiplication of 1/9 duty cycle with only 36 (3×4×2+12=36) reactions is well implemented in this way.

![simulation results for frequency multiplication when $K = L = 3$](image)
Example. Take a $1/6$ duty cycle for an example. The corresponding gear models are still employed those shown in Fig. 5. Before conducting the frequency multiplication of $1/6$ duty cycle, fundamental frequencies for both $1/2$ and $1/3$ are given in Fig. 11 from which the fundamental frequency of $1/2$ duty cycle has a bigger time period than that of $1/3$ one. This too fast transference of fundamental frequency makes CRNs for $1/3$ duty cycle have a longer time period in Method 1, while CRNs for $1/2$ duty cycle have a shorter one.

a) For $K = 2$: Adopted Method 1, $G_{A1}$ in Fig. 5 represents $1/2$ duty cycle. Employing the rate constant adjustment scheme that only rate constants for $1/3$ duty cycle oscillator are changed (threshold: $0.0002$, main power: $0.7$) while others still adopt the standard parameters in Part I, simulations are shown in Fig. 12. From Fig. 12(a) the final frequency multiplication of $1/6$ duty cycle seems to be good enough, but its enlarged version reveals that the segmentation of the second orange curve is not as precise as before. And the final red-colored frequency multiplication of $1/6$ duty cycle is a little bigger than the curve colored purple, although theoretically they should be the same size, as well as the same time period. To some extent, this error could be omitted.

One thing should be emphasized is that, although this Method 1 seems to successfully construct a $1/6$ duty cycle clock signal, it is essentially a frequency division of the fundamental frequency, rather than frequency multiplication. This can be figured out when carefully comparing the “wanted” bottom red curve of Fig. 12 and the top blue curve of fundamental frequency. Thus in this sense, we roughly think Method 1 for the case of $K = 2$ is feasible for frequency division, but invalid for frequency multiplication.

b) For $L = 2$: Adopted Method 2, then $G_{A2}$ in Fig. 5 represents $1/3$ duty cycle. To shorten the time period of $1/2$ duty cycle, the rate constant for main power reactions of $G_{A2}$ should be smaller than before. When it is set to be $0.08$, although the time period of $1/2$ duty cycle clock signal is really slowed down, it is not short enough to segment a single phase of a fundamental frequency for $1/3$ duty cycle. Moreover, this rate constant adjustment scheme produces a non-square wave of $1/2$ duty cycle clock signal. Therefore, revealed by Fig. 13 the final frequency multiplication of $1/6$ duty cycle makes nonsense of Method 2.
successfully implemented. Additionally, an appropriate rate constant adjustment should be adopted for a better final result. The basic idea to realize frequency multiplication of \(1/N\) is illustrated in Algorithm 2.

Note that, the mentioned methods in Algorithm 2 could not only implement a \(1/N\) duty cycle clock signal with fewer reactions, but also construct an \(M/N\) one, with a restriction that \(M\) must be less (greater) than \(L/N\) \((1 - L/N)\) in Method 1 or less (greater) than \(K/N\) \((1 - K/N)\) in Method 2. This is because we use one phase of an oscillator to control the rotation of another one, only \(1/K\) \((1/L)\) time period of the former clock signal could be segmented into \(L\) \((K)\) pieces, and duty cycle of \(1/N, 2/N, ..., 1/L\) \((1/K)\) could be realized. The corresponding dual clock signals, namely duty cycle of \((N - L)/N, (N - K)/N, ..., (N - 1)/N\) could also be implemented.

Take a \(M/15\) duty cycle as an example, the other simulation results of \(M/15\) duty cycle clock signals are shown in Fig. 14. That means, the model as shown in Fig. 5 could only be utilized to realize 1/15, 2/15 duty cycle clock signal with Method 1, and their dual ones, namely 14/15, 13/15. Moreover, simulation results for 1/15, 2/15, 3/15, 4/15 as well as their dual ones of 14/15, 13/15, 12/15, 11/15 with Method 2 are also shown at the bottom of Fig. 14. One thing should be emphasized is that the corresponding CRNs only requires \(4 \times (3 + 5) + 12 = 44\) chemical reactions. All of these prove that our gear model is meaningful to instruct us in further study and future applications of a clock tree in CRN level.
Algorithm 2 Methods for frequency multiplication of $1/N$.

Require: A compound gear model of three oscillators.
1: if $N = K \times L$ is a composite number ($K, L \neq 1$) then
2:   The three oscillators are $1/2$, $1/K$ and $1/L$ duty cycle.
3: end if
4: if $K \neq L > 2$ then
5:   Use a phase signal of $K$-phase oscillator to control the whole transferece of $L$-phase one.
6: Two phase signals of $L$-phase oscillator are used to control $1/2$ duty cycle.
7: end if
8: (Method 1.) For $K > L$, slow down the rate constant of main power reactions of the controlled $L$-phase oscillator.
9: (Method 2.) For $K < L$, speed up the rate constant of main power reactions of controlled $L$-phase oscillator.
10: else if $K = L$ then
11:   Two methods are merged into a single method.
12:   if $K = L > 3$ then
13:     This situation is similar to Method 1.
14:     else if $K = L = 2$ then
15:       Our methods are inefficient.
16:     end if
17:     end if
18: else if $K$ or $L = 2$ then
19:   Invalid methods.
20: end if

IV. DISCUSSION AND CONCLUSION

In this paper, by exploiting the compound gear model in Part I, we could realize the frequency alteration by $L/J$, with frequency division and frequency multiplication. Another benefit is, with the accumulated instructions, we successfully use fewer chemical reactions to implement a clock signal with $M/N$ duty cycle, where $M$ may be very large. One thing should be emphasized is that, here $M$ does not range from 1 to $N$, but has different ranges for Method 1 and Method 2. More conditions are also taken into considerations in our proposal, which has been summarized in Algorithm 2. With a bit slower or faster fine-tunings of rate constant, frequency multiplication could be well implemented based on our gear model, with fewer chemical reactions. In our previous work of [10], nearly no quantitative description of the results was offered, however. Our simple model semi-quantitatively reproduces all the simulation data with a set of physically reasonable parameters.

Another Inspiration. Motivated by the idea illustrated in Section III.A, if we use more than three oscillators to realize the frequency multiplication, a clock jitter would be produced. Although this operation to some extent could work, the final clock signal might be a little bias, which uncovers another problem of coupling efficiency. Take a $1/60$ as an example. Since $60 = 3 \times 4 \times 5$, four oscillators are required, representing the duty cycle of $1/2$, $1/3$, $1/4$, and $1/5$, respectively. As illustrated in Fig. 15 with the approach similar to Method 1, a single phase signal of $1/5$ duty cycle controls the whole transference of $1/4$ duty cycle. Then this controlling stream is towards $1/3$ and finally to $1/2$. Two phase signals are in demand of $1/3$ duty cycle to manipulate the rotation of $G_1$, which represents $1/2$ duty cycle.

Rate Constant Adjustment Scheme. Adapting the methods similar to Algorithm 2, no change exists in the rate constant of CRNs for the $5$-phase oscillator of $G_{AB}$. The rotation speed of $1/4$ duty cycle should be slowed down for its whole physical transferring period is shorter than $1/5$, and the rate constant of $1/3$ should be much faster than before. With the changed rate constant of main power reactions (duty cycle of $1/4$: $57$, $1/3$: $1100$), the corresponding simulation results are shown in Fig. 16.

Analysis. From Fig. 16, simulation results, especially the top three curves, show the gears of $1/3$, $1/4$, and $1/5$ operate well. However in practical operations, gears shown in Fig. 15 might produce a flawed final frequency multiplication in the long run. This gear really works well as shown in the enlarged version of the first figure. If observe carefully, we can find that a blue-colored single phase of fundamental frequency for $1/5$ duty cycle is divided into four pieces. And this gray-colored single phase of $1/4$ duty cycle is segmented into three pieces. The bottom red curve is the final frequency multiplication of $1/60$ duty cycle, which is produced through a mesh between $G_{B2}$ and $G_1$. Note that this bottom red curve is actually a little bigger than the above purple one, and this kind of clock skew can be explained by the too long stage of meshing or coupling, since the standard single phase existing time is segmented again and again. Therefore, coupling efficiency in our gear model is also a problem worthy of more attention. Roughly, this tiny error of a little extended frequency multiplication for $1/60$ duty cycle might be omitted if the requirement is not strict. To our knowledge, we cannot completely solve the issue resulting from too many segmentations of $\tilde{\tau}_{1/N}$ at this time. In our future work, we would like to handle this problem, as well as offer more quantitative analysis of our gear model in the aspect of information transport and clock skew. More experimental works with real DNA strand displacement reactions will also be offered.

ACKNOWLEDGMENT

First, we would like to thank Dr. David Soloveichik for his kind help. We also would like to thank Editor-in-Chief, the associate editor, and the reviewers for their time and efforts to review this paper.

REFERENCES

[1] Wikipedia. [Online]. Available: [https://en.wikipedia.org/wiki/Synthetic biology]
Fig. 16. Results for frequency multiplication of $\frac{1}{60}$ with more gears.

(a) The produced signals for all gears.

(b) An enlarged version of all signals.

[2] E. Andrianantoandro, S. Basu, D. K. Karig, and R. Weiss, “Synthetic biology: New engineering rules for an emerging discipline,” Molecular Systems Biology, vol. 2, no. 1, 2006.

[3] S. A. Benner and A. M. Sismour, “Synthetic biology,” Nature Reviews Genetics, vol. 6, no. 7, pp. 533–543, 2005.

[4] K. Brenner, L. You, and F. H. Arnold, “Engineering microbial consortia: a new frontier in synthetic biology,” Trends in Biotechnology, vol. 26, no. 9, pp. 483–489, 2008.

[5] L. L. Sheets, “Electrical system having variable-frequency clock,” Jun. 2 1987, US Patent 4,670,837.

[6] J. G. Kassakian, “Automotive electrical systems—the power electronics market of the future,” in Proc. IEEE Applied Power Electronics Conference and Exposition, vol. 1, 2000, pp. 3–9.

[7] E. Friedman, Clock distribution networks in VLSI circuits and systems. IEEE, 1995.

[8] D. M. Russell, “Random clock generating circuit and method for control of electrical systems thereof,” Jun. 25 1996, US Patent 5,530,390.

[9] D. Soloveichik, G. Seelig, and E. Winfree, “DNA as a universal substrate for chemical kinetics,” Proceedings of the National Academy of Sciences (PNAS), vol. 107, no. 12, pp. 5393–5398, 2010.

[10] L. Ge, C. Zhang, Z. Zhong, and X. You, “A formal design methodology for synthesizing a clock signal with an arbitrary duty cycle of M/N,” in Proc. IEEE Workshop on Signal Processing Systems (SiPS), 2015, pp. 1–6.