Compare Behavior of Dual-time Switch under Different Logic Gates

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Abstract

The regulatory networks in biological systems often incorporate logic gate structures to achieve specific functions. This study investigates the behavior of dual-time switches under AND and OR logic gates in systems with two coupled positive feedback loops. Using deterministic and stochastic models, we compare the response dynamics of these gates under various kinetic conditions. Our results demonstrate that AND gates exhibit slower response times and better noise resistance compared to OR gates, which are more sensitive and respond faster. These findings highlight the distinct roles of AND and OR gates in biological regulatory networks, offering insights into their potential physiological implications. AND gates may be suited for processes requiring cautious, resource-conserving responses, while OR gates could be advantageous in scenarios demanding rapid and sustained activation. Future research should explore other logic gates and more complex network structures to further understand regulatory dynamics in biological systems.

Introduction

The regulatory networks in biological systems are highly complex, with some components capable of forming logical gate structures to achieve specific regulatory functions for specific processes, such as AND gate, NOT gate, OR gate, NOR gate, etc. The inputs and outputs of logical gates can take different forms, such as RNA synthesis, protein degradation, external temperature changes, light exposure, etc.[1]. Literature has reported many logical gates in natural or artificially synthesized biological systems, including fluorescent probes activated by certain conditions[2]-[5], and the lactose operon in prokaryotes (a middleman between and gate and or gate logic functions)[6],[7]-[9]; in fact, simple logical gate structures shape most transcriptional regulatory circuits[6].

However, unlike computer or electronic systems, we need to specify the “0” and “1” values of inputs and outputs. In building models, it is often convenient to define a higher value state as “1” and a lower value state as “0”[6]. The multi-input logic gate structure includes AND gate, NOR gate, OR gate, and XOR gate. A simple observation shows that for continuous changes in input values, the and gate has a more sensitive response to the input transitioning from low to high than the or gate, while the or gate has a more sensitive response to the input transitioning from high to low, i.e., the or gate opens slowly and closes quickly, while the and gate opens quickly and closes slowly (Figure 1). In this article, the behavior of the two most basic logic gates, and gate and or gate, is explored in a system that is coupled by two positive feedback loops.

Many biological systems have multiple positive feedback loops coupled in loops, such as polarization in budding yeast[10],[11] and regulation of p53 activity[12]. There is literature that shows that a slow-fast positive feedback loop coupled with an OR gate can achieve a fast response and long-term maintenance of a high output state, thereby driving reliable cellular decision-making[13]. This article will compare the different behaviors of the system under AND gate and OR gate and perform dynamic simulations using deterministic and stochastic models.

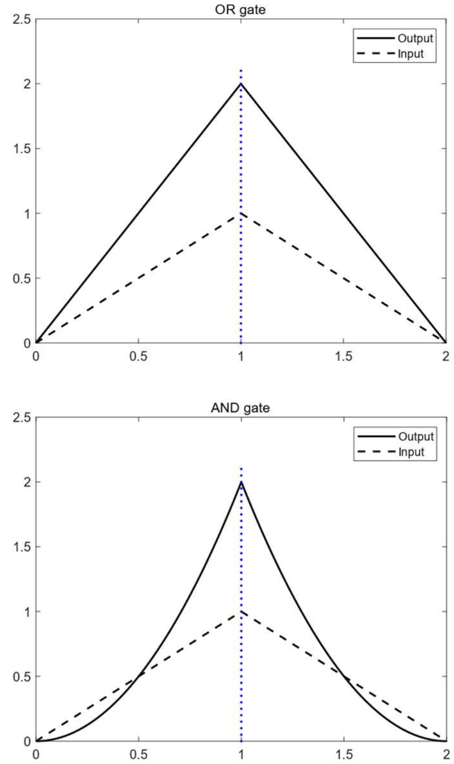


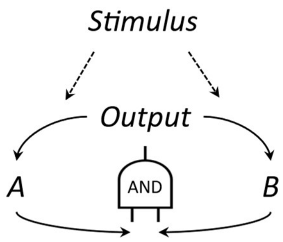
Figure 1: Output on continuous change of Input through OR gate(top) or AND gate(bottom). For OR gate, Output = 2*Input; For AND gate, Output = 2*Input^2

Models and Methods

Models

For the dual-loop model constructed, we assumed either fast kinetics for both the A and B loops, slow kinetics for both loops, or fast kinetics for the A loop and slow for the B loop (see model below). Each model responded to a noise-free stimulus (deterministic model) and a noisy stimulus (stochastic model).

1) AND gate

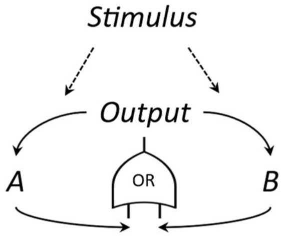


$$\frac{\mathrm{d}OUT}{\mathrm{d}t} = k_{\text{out\_on}} * (A + B) * (1 - OUT) - k_{\text{out\_off}} * OUT + k_{\text{out\_min}}$$

$$\frac{\mathrm{d}A}{\mathrm{d}t} = \left[stimulus * \frac{OUT^n}{OUT^n + ec_{50}^n} * (1 - A) - A + k_{\min} \right] * \tau_A$$

$$\frac{\mathrm{d}B}{\mathrm{d}t} = \left[stimulus * \frac{OUT^n}{OUT^n + ec_{50}^n} * (1 - B) - B + k_{\min} \right] * \tau_B$$

2) OR gate



$$\frac{\mathrm{d}OUT}{\mathrm{d}t} = k_{\text{out\_on}} * (2 * A * B) * (1 - OUT) - k_{\text{out\_off}} * OUT + k_{\text{out\_min}}$$

$$\frac{\mathrm{d}A}{\mathrm{d}t} = \left[stimulus * \frac{OUT^n}{OUT^n + ec_{50}^n} * (1 - A) - A + k_{\min} \right] * \tau_A$$

$$\frac{\mathrm{d}B}{\mathrm{d}t} = \left[stimulus * \frac{OUT^n}{OUT^n + ec_{50}^n} * (1 - B) - B + k_{\min} \right] * \tau_B$$

Parameters for all models: $k_{\text{out\_on}} = 2, k_{\text{out\_off}} = 0.1, k_{\text{out\_min}} = 0.01, k_{\min} = 0.01, n = 3, ec50 = 0.35$. For fast loop, $tau = 0.5$. For slow loop, $tau = 0.008$. Set simulation start at $t = 0$, then stimulus begins and stops at $t = 200$ and $t = 600$. Simulation ends at $t = 1200$. All quantities are dimensionless.

Methods

All analyses were done using MATLAB R2023a. Function “ode45” were used when solving ordinary differential equations.

Results

Deterministic Model and Results

We compared the behavior of three systems under the AND gate and OR gate conditions: two coupled fast loops, two coupled slow loops, and two loops with dual time (a coupled fast loop and a slow loop) (Figure 2). For the two coupled fast loops, there is no essential difference between the behavior of the AND gate and the OR gate. However, the AND gate responds (i.e., rises to a high state) slightly slower than the OR gate, which may be due to the OR gate being more sensitive to continuously increasing input compared to the AND gate (Figure 1). The behavior of both logic gates is almost identical after the stimulus is removed.

For the two coupled slow loops, the AND gate exhibits a much longer process for the output to rise from a low state to a high state compared to the OR gate, and it shows clear ultrasensitivity. After the stimulus is removed, the AND gate returns to the low state faster than the OR gate, overall presenting a slow-on, fast-off pattern.

Literature suggests that for two loops with dual time, the behavior of the AND gate is a mirror image of the OR gate behavior[13]. Specifically, the OR gate can respond quickly to stimulus and maintain a high state for an extended period, whereas the AND gate responds more slowly to stimulus and quickly returns to a low state after the stimulus is removed. Our simulation results are consistent with this observation (Figure 3).

Deterministic model simulation indicates that systems composed of AND gates exhibit more cautious and conservative behavior compared to those composed of OR gates. In biological systems, this characteristic may have important physiological significance in terms of resource conservation and response to certain long-term external stimulus.

Stochastic Model and results

Stochastic model simulation demonstrated features broadly similar to those of the deterministic model simulation (Figure 3). However, in the stochastic model, the AND gate exhibited resistance to noise. Due to the noisy nature of the stimulus, sporadic stimulus still appeared outside the stimulus duration ($t < 200$ or $t > 600$). For these sporadic stimulus, the OR gate systems were quite sensitive, quickly pushing the output to a high state (we observed significant fluctuations even in the two coupled slow loops system). After the stimulus disappeared, the output quickly returned to a lower state (Figure 3, A gray box).

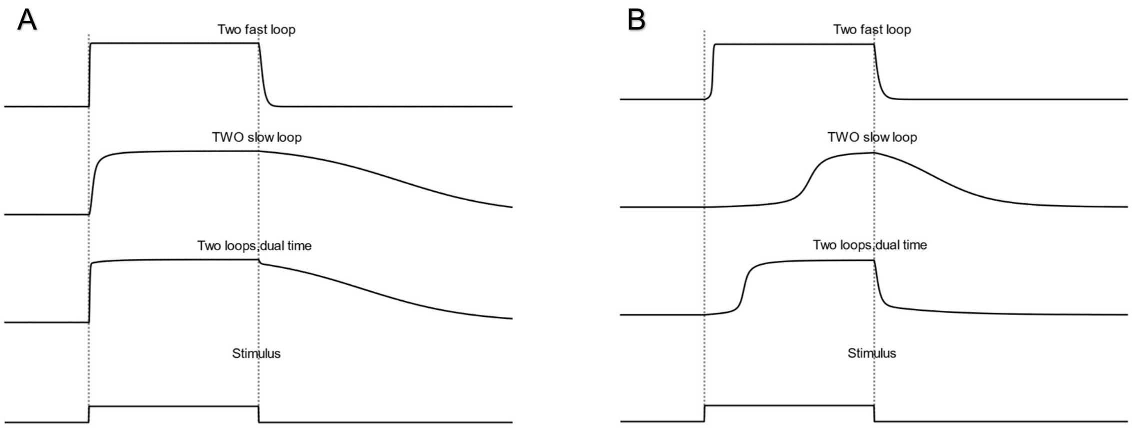


Figure 2: Deterministic model simulations of dual-loop switch. A. through OR gate; B. through AND gate. From top to bottom : two fast loops, two slow loops, two loops dual time (coupled fast loop and slow loop), stimulus signal.

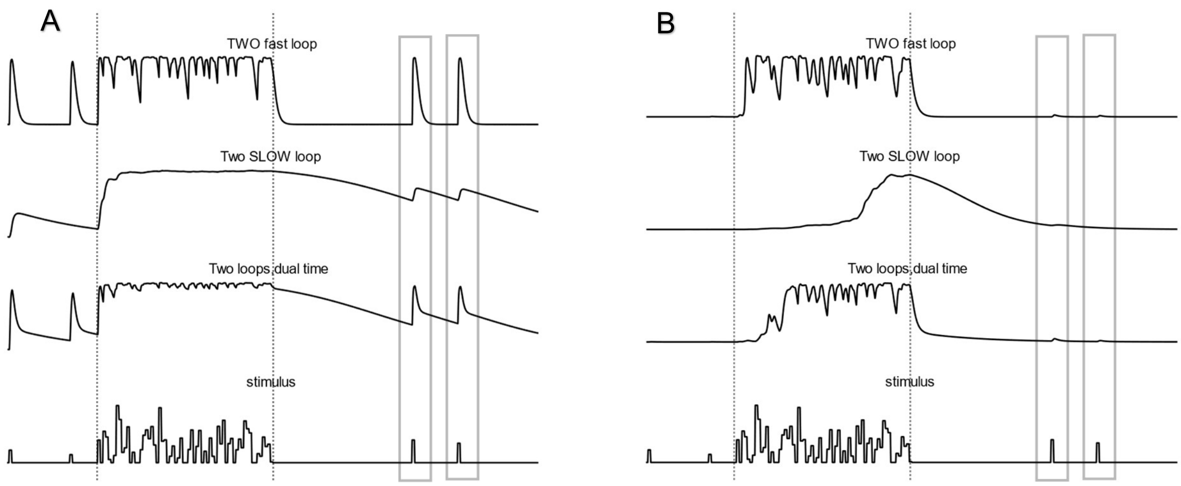


Figure 3: Stochastic model simulations of dual-loop switch. A. through OR gate; B. through AND gate. From top to bottom : two fast loops, two slow loops, two loops dual time (coupled fast loop and slow loop), stimulus signal.

In contrast, the AND gate systems showed excellent resistance to these sporadic stimulus. In the same positions (Figure 3, B gray box), the output hardly responded to them.

The good resistance of the AND gate to noise has important physiological significance in biological systems. It can prevent unnecessary waste of resources by the organism, albeit at the expense of sensitivity to external stimulus.

Discussion

The comparison between the behaviors of dual-time switches under different logic gates reveals significant insights into the dynamics of biological regulatory networks. Our study primarily focused on the AND gate and the OR gate, two fundamental logic gates that are often found in both natural and synthetic biological systems. The results from our deterministic and stochastic models underscore the distinct characteristics and potential physiological implications of these gates.

The deterministic model simulations highlight how the AND and OR gates influence the response times and sensitivity of the system. The OR gate's ability to quickly respond and maintain a high state aligns with its potential role in processes requiring rapid and persistent activation. Conversely, the AND gate's conservative approach, characterized by a slower response and quicker return to a low state, suggests its use in scenarios where avoiding premature or unnecessary activation is essential. Specifically, for two coupled fast loops, both the AND and OR gates showed similar behavior, with the OR gate being slightly faster in transitioning to a high state. This suggests that in rapidly responding systems, the choice of gate might not drastically alter the overall behavior, although the OR gate's quicker response could be beneficial in scenarios where speed is critical. For two coupled slow loops the AND gate demonstrated a much slower rise to a high state compared to the OR gate, along with clear ultrasensitivity. This slow-on, fast-off pattern implies that AND gates can act as stringent filters, ensuring that only strong and sustained stimuli result in a response. This could be crucial in processes where precision and avoidance of false positives are necessary. For Dual-Time Loops, the behavior of the AND gate contrasted sharply with that of the OR gate, mirroring the findings in previous literature. The OR gate's ability to quickly respond and maintain a high state aligns with its potential role in processes requiring rapid and persistent activation. Conversely, the AND gate's conservative approach, characterized by a slower response and quicker return to a low state, suggests its use in scenarios where avoiding premature or unnecessary activation is essential.

The stochastic model simulations provided further depth to our understanding, especially in the context of noise resistance. The AND gate systems exhibited remarkable resistance to sporadic stimuli outside the designated stimulus duration. This resistance indicates that AND gates could play a crucial role in maintaining stability and preventing resource wastage in noisy environments. On the other hand, the high sensitivity of OR gates to sporadic stimuli, leading to significant output fluctuations, underscores their potential use in environments where rapid detection of transient signals is advantageous.

The distinct behaviors of AND and OR gates have profound physiological implications. Cautious and conservative nature of AND gates makes them suitable for processes where resource conservation and precise response to long-term stimuli are vital. In biological systems, this could translate to mechanisms that require stringent control, such as cell cycle regulation or stress responses, where premature activation could be detrimental.

For OR Gates, their rapid response and sensitivity to increasing inputs suggest their utility in scenarios requiring quick decision-making and sustained activation. This could include processes like immune responses or signaling pathways that need to be activated swiftly and maintained robustly once initiated.

Future studies could explore the behavior of other logic gates, such as NOR and XOR gates, in dual-time switch systems. Additionally, investigating the impact of varying kinetic parameters and incorporating more complex network structures could provide a more comprehensive understanding of the regulatory dynamics in biological systems.

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