Influence of update schemes on boolean networks

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Abstract—Boolean networks are a widely used framework for modeling the qualitative dynamics of biological regulatory systems. A central modeling decision is the choice of update scheme, which determines how and when individual nodes are evaluated at each time step and directly shapes the resulting dynamics. This paper introduces and compares four commonly used update schemes: synchronous, sequential, probabilistic, and asynchronous. We analyze how each scheme affects attractor structure, reachability, and network robustness, and discuss their practical implications for the modeling of gene regulatory networks. A central finding is that the same network can exhibit fundamentally different attractors depending on which scheme is used, demonstrating that the choice of update scheme is not a neutral implementation detail but a direct factor that influences the dynamical behavior of the model and the biological conclusions that can be drawn from it.

1 Introduction

Boolean networks were first introduced by Stuart Kauffman in the late 1960s as a simplified model of biochemical systems [1]. In this framework, genes or regulatory components are represented as binary variables, each taking a value of either 0 (inactive) or 1 (active), whose states evolve according to logical update functions encoding regulatory interactions. Despite their simplicity, boolean networks have proven useful in capturing qualitative dynamical behavior in complex biochemical systems, and have since become a standard tool of modeling in systems biology [2].

A key abstraction in boolean network modeling is the concept of attractors. Since a boolean network with n nodes has exactly 2^n possible states and the dynamics are deterministic, the system must eventually revisit a state it has already visited, by the pigeonhole principle [3]. The resulting recurring patterns, either fixed-points or limit cycles, are called attractors and are often interpreted as stable cellular or functional states [1]. In the context of gene regulatory networks (GRNs), attractors have been proposed to correspond to distinct cell types or phenotypic states [2].

Gene regulatory networks describe the interactions between genes, transcription factors, and other molecular entities that together control gene expression. Modeling GRNs as boolean networks provides a simplified view: instead of tracking continuous concentration levels of molecular species, each gene is treated as either expressed or silenced. This allows for qualitative insight into questions such as how different cell types arise from the same genetic blueprint, or how mutations affect the stable states of the system [2, 4].

When it comes to modeling a system as a boolean network, the choice of update scheme plays an important role, as it defines how and when individual nodes are updated at each time step. This choice is not merely a technical detail, since it affects which attractors exist, which states are reachable from a given initial condition, and how robustly the network responds to perturbations [4, 5]. The most commonly used schemes include the synchronous scheme, where all nodes update simultaneously; the sequential scheme, where nodes are updated one after another in a fixed order; the probabilistic scheme, which introduces randomness into the update process; and the asynchronous scheme, where only one node is updated per time step.

The question of which update scheme best reflects biological reality has been an active area of research. Asynchronous schemes have often been considered more biologically plausible, since biochemical processes in living cells rarely occur simultaneously across all genes. However, as recent studies have shown, synchronous and asynchronous schemes can lead to the same meaningful behavior under the right conditions, and the practical choice of scheme often comes down to available biological knowledge and computational feasibility [4].

In the following, we will introduce the formal model of boolean networks in section 2, followed by a comparison of the different update schemes in section 3. Finally, in section 4, we will discuss the implications of these schemes for the modeling of gene regulatory networks.

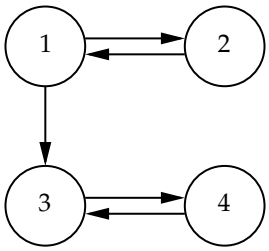
2 Boolean networks

A boolean network consists of nodes $x_i(t)$ that have a boolean state, either 0 or 1, at a point in time t. Each node has a corresponding update function

$$f_i(x_1(t), x_2(t), \ldots, x_n(t)) = x_i(t+1), \tag{1}$$

expressing the new state of $x_i(t+1)$, where f_i takes as input the states of all nodes connected to node i by an incoming edge. The state of the boolean network can be described as a binary string $x(t) = x_1 x_2 \ldots x_n$ where each node is replaced with the corresponding state 0 or 1.

Consider the boolean network shown in fig. 1. For example, if the state is $x(t) = 0011$ at time t, it means



$$
\begin{aligned}
f_1 &= \neg x_2 \\
f_2 &= x_1 \\
f_3 &= x_1 \oplus x_4 \\
f_4 &= x_3
\end{aligned} \tag{2}
$$

Fig. 1. Example of a boolean network with four nodes. Each vertex indicates that a node is part of the update function of the other node. For instance x_1 is part of f_2 and f_3. Note that $\neg$ means the logical NOT and $\oplus$ means the logical XOR function.

that x_1, x_2 are 0 and x_3, x_4 are 1. After applying the synchronous update, the next state $x(t+1)$ is 1011. Updating the network multiple times creates a trajectory, which is the sequence of the states starting from the initial state. Continuing with the example from fig. 1, the trajectory is $0011 \rightarrow 1011 \rightarrow 1101 \rightarrow 0100 \rightarrow \ldots$. Each trajectory in a boolean network eventually reaches one of two scenarios: either it falls into a fixed-point attractor, which is a state that loops back into itself upon update; or it falls into a periodic cycle of states called limit cycle.

A *state graph* is a directed graph that shows all the possible states of the boolean network along the corresponding trajectories that can be navigated by starting at any state and following the direction of the edges. For example, the state graph in fig. 3 shows the trajectories from the boolean network in fig. 1. These state graphs help visualize the fixed-point and limit cycles, e.g. 2 cycles of length 8.

In boolean networks, *robustness* refers to the stability of the behavior with regard to perturbations, e.g. a single node state change. A boolean network with poor robustness means that a simple flip of a node can change the resulting attractor or cycle for that trajectory. With regard to our example from fig. 3, if either x_3 or x_4 (not both at once) is flipped, the cycle switches. A strong robustness however would mean that even with such perturbations, the resulting attractor or cycle does not change.

The set of all states that eventually lead to a particular attractor is called its *basin of attraction*. In the state graph in fig. 3, the two cycles each have a basin of eight states, meaning that starting from any state in a basin, the network will always converge to the corresponding attractor. Larger basins generally indicate more dominant or robust attractors. In biological terms, a large basin could, for example, represent a cell state that is easily reached and hard to escape from, which shows that they are ideal to model stable functional states.

Not every state in a boolean network is reachable from another state through the dynamics. States that have no predecessor in the state graph are called *garden-of-Eden states*: they can only appear as initial conditions and are never produced by any update step. Their presence reduces

$x(t)$	$x(t+1)$
0000	1000
0001	1010
0010	1001
0011	1011
0100	0000
0101	0010
0110	0001
0111	0011
1000	1110
1001	1100
1010	1111
1011	1101
1100	0110
1101	0100
1110	0111
1111	0101

Fig. 2. State transitions for all states of the boolean network from fig. 1 using synchronous update scheme once.

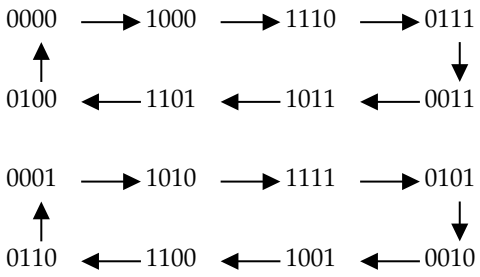


Fig. 3. State graph of the boolean network shown in fig. 1 using synchronous update scheme showing two separate limit cycles of length 8.

the effective state space that the network can explore during normal operation. In the synchronous state graph of fig. 3, no garden-of-Eden states are present, since every state is reachable from at least one other state within the two cycles.

The structure of the state graph, including the number and size of attractors, the shape of their basins and the presence of garden-of-Eden states, depends critically on both the network topology and the choice of update scheme. The following section illustrates how changing the update scheme while keeping the network and its update functions fixed can produce a completely different state graph, with different attractors, different basins and different reachability properties.

3 Update Schemes

The dynamics of a boolean network depend not only on its topology and update functions, but also on the choice of update scheme, which defines how and when nodes are updated at each time step. Different schemes can lead to a notably different behavior, including different attractor structures, reachability properties and robustness characteristics [4, 5]. In general, update schemes can be divided into deterministic schemes, where the sequence of updates is fixed, and stochastic schemes, where randomness plays a role. In the following subsections, we introduce four

commonly used update schemes and depict their effects on the boolean network from fig. 1.

3.1 Synchronous scheme

In section 2, we have used the *synchronous update scheme* to introduce the general dynamics of boolean networks. This scheme assumes that each update function takes the exact same amount of time and executes at the same time, which means that regardless of the outcome of the first function, any subsequent function will have the same result. Updating the network with this method is quite simple, always leads to a deterministic output, and does not require a lot of computing power in order to simulate larger networks, as each state of the network results in exactly one updated state. With regard to gene regulatory networks however, this is an oversimplification as biological GRNs never execute fully synchronously. Furthermore, the change of one node has no direct effect on any other function, whereas larger biochemical systems often show dependencies between regulatory functions [1, 4].

Despite this biological limitation, the synchronous scheme has important structural properties that make it the most widely used scheme in practice. Since every global state maps to exactly one successor state, the state space forms a functional graph in which every node has exactly one outgoing edge, which, as we previously covered, will converge to either a fixed-point attractor or a limit cycle. Hence, the full attractor landscape is completely determined by the update functions alone [1]. As a direct consequence, all attractors can be found by exhaustively simulating every possible initial state, which requires at most 2^n simulations of bounded length. For networks of moderate size this is computationally feasible, making synchronous update well suited for systematic attractor analysis. For very large networks, however, this exhaustive approach quickly becomes infeasible due to the exponential growth of the number of states.

The synchronous scheme was also the original formulation used by Kauffman when he introduced random boolean networks as a model of gene regulation [1]. In his analysis of networks, where update functions are assigned randomly, Kauffman found that the average number and length of attractors depends strongly on the average node connectivity K. At low connectivity the network settles quickly into a small number of short attractors; at high connectivity the dynamics become chaotic with very long cycle lengths. At a critical connectivity of around $K = 2$ the network is poised between these two regimes, a property that has been proposed as a signature of real biological regulatory networks [2]. This critical behavior and the tools used to study it are defined with respect to the synchronous scheme, which illustrates why the synchronous update remains central to the theoretical analysis of boolean networks even when other schemes may be more biologically appropriate.

3.2 Sequential scheme

In the *sequential update scheme*, nodes are updated one after another in a fixed order within each time step, which allows for side effects: the updated value of an earlier node in the sequence can influence the outcome of later ones. For example, take the sequence (x_1, x_2, x_3, x_4). Updating the state 0000 means first using f_1 which results in an intermediate state 1000, then using f_2, then f_3, and lastly f_4. This will lead to $0000 \to 1111$, a different state from that produced when using the synchronous update scheme. In fact, the whole state graph changes depending on the update scheme used, namely every initial state will fall into a single 4-state cycle: $0000 \to 1111 \to 0011 \to 1100 \to 0000$ (see fig. 4).

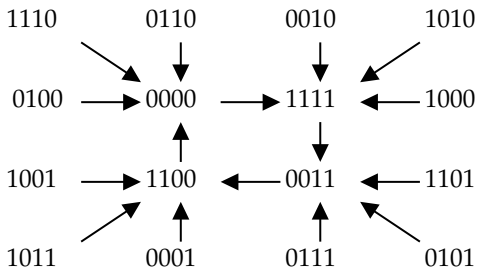


Fig. 4. State graph of the boolean network shown in fig. 1 using the sequential update with the sequence (x_1, x_2, x_3, x_4), leading to a limit cycle of length 4.

While the sequential update scheme produces different dynamics than those of the synchronous one (see fig. 3), it is always possible to derive an equivalent synchronous function set that produces identical state transitions. The key observation is that when a node x_i is evaluated in a sequential update, all nodes x_j that appear earlier in the sequence have already been updated to their new values. The synchronous equivalent f_i' is therefore obtained from f_i (see eq. (1)) by substituting, for each input variable x_j that precedes x_i in the sequence, the already-derived new function f_j' in place of x_j.

For the boolean network from fig. 1 with sequence (x_1, x_2, x_3, x_4), the conversion proceeds as follows. Since x_1 is first in the sequence, its function is unchanged. For x_2, the original function $f_2 = x_1$ depends on x_1, which has already been updated; substituting $x_1 \mapsto f_1'$ gives $f_2' = f_1'$. For x_3, the function $f_3 = x_1 \oplus x_4$ depends on x_1 (already updated) but not x_2; substituting $x_1 \mapsto f_1'$ gives $f_3' = f_1' \oplus x_4$. Finally, $f_4 = x_3$ depends on x_3, which has already been updated; substituting $x_3 \mapsto f_3'$ gives $f_4' = f_3'$. Expanding these yields the synchronous functions

$$\begin{aligned} f_1' &= \neg x_2, \\ f_2' &= f_1' = \neg x_2, \\ f_3' &= f_1' \oplus x_4 = \neg x_2 \oplus x_4, \\ f_4' &= f_3' = \neg x_2 \oplus x_4. \end{aligned} \tag{3}$$

This means that a sequential scheme can always be expressed as an equivalent synchronous scheme with a different set of update functions, as shown in eq. (3). Furthermore, if the side-effects from the sequential scheme are desired, the resulting synchronous function set is generally larger and more complex.

An extension of the sequential scheme is the *block-sequential scheme*. This allows the modeler to divide the nodes into groups, called blocks, that run synchronously, while the blocks execute in sequence. This allows for further fine-tuning of the behavior and can simplify the modeling

of realistic systems. The block-sequential scheme can also be converted to a synchronous scheme, thus producing the same behavior as previously described [6].

An important practical consideration is that for a network with n nodes, there are $n!$ possible sequential orderings, and different orderings can produce different state graphs and attractors. This makes the choice of sequence both a useful modeling tool and a potential source of ambiguity, since the biologically correct ordering is often not known in advance [6]. The block-sequential scheme partially addresses this by only requiring a partition of nodes into blocks and an ordering of those blocks, rather than a complete linear ordering over all nodes. This reduction in the number of free parameters for the sequence makes it more tractable to systematically explore how update ordering affects the dynamics, while still capturing meaningful temporal structure between different groups of regulatory events [4, 6].

3.3 Probabilistic scheme

The *probabilistic scheme* introduces a qualitatively different kind of update rule. Instead of a single deterministic update function per node, each node is assigned a set of possible update functions, each with an associated probability. Upon updating a node, one function from this set is selected at random according to a predefined distribution, making the dynamics of the network stochastic rather than deterministic. This is in contrast to the synchronous, sequential, and asynchronous deterministic schemes, where the outcome of each update step is fully determined by the current state of the network.

$$\begin{aligned} f_1 &= \neg x_2 \\ f_2 &= x_1 \\ f_3 &= x_1 \oplus x_4 \\ f_4 &= x_3 \quad (p = 0.5) \\ f_{4,\text{switch}} &= \neg x_3 \quad (p = 0.5) \end{aligned} \tag{4}$$

Fig. 5. Update functions of the boolean network from fig. 1, extended with the probabilistic alternative $f_{4,\text{switch}}$ for node x_4. Both functions for x_4 are selected with equal probability at every update step.

An example of how this can drastically change the outcome is shown in fig. 5, where a second function is added to node x_4 from the network in fig. 1. Let $f_{4,\text{switch}} = \neg f_4 = \neg x_3$ with an equal probability distribution. This simple addition means that, on average, every second update the state switches from one cycle to the other. Thus there are no longer two individual cycles. Any initial state will eventually reach all possible states and will never fall into a repeating pattern.

More formally, a probabilistic boolean network assigns to each node x_i a set of update functions $\{f_i^{(1)}, \ldots, f_i^{(k_i)}\}$ with corresponding probabilities $\{p_i^{(1)}, \ldots, p_i^{(k_i)}\}$ that sum to 1. At each step, one function per node is selected at random according to these probabilities. The resulting dynamics can be analyzed as a Markov chain over the 2^n possible states, where the long-term behavior is described by a stationary distribution over states rather than a single fixed attractor [4]. In other words, once sufficient noise is introduced, the system can escape what would otherwise be deterministic attractors, and over time it explores a much broader region of the state space than any single deterministic trajectory would cover.

This connection to GRN modeling is particularly relevant for oscillatory networks, such as the Repressilator, discussed in detail in section 4. Under deterministic update schemes, the Repressilator produces a clean periodic oscillation. In real biological cells, however, gene expression is inherently noisy: a gene that should be repressed may occasionally still produce a small amount of transcript due to stochastic effects, such as transcriptional bursting or low molecule counts. By introducing a small probability for an alternative update function, this noise can be captured in the model. The result is an irregular oscillation whose period varies from cycle to cycle, which is considerably closer to the gene expression dynamics observed in living cells than the perfectly regular output of a deterministic scheme [4].

3.4 Asynchronous scheme

While synchronous, sequential and probabilistic schemes update all the nodes in one time step, the *asynchronous scheme* only updates one node per time step. There are two main variants. In asynchronous deterministic update, a fixed predetermined sequence specifies which single node is updated at each time step. This differs from the sequential scheme in a fundamental way: in the sequential scheme, the entire sequence is executed within one time step, updating all nodes once; in asynchronous deterministic update, each element of the sequence constitutes a separate time step that updates exactly one node. The same node can therefore appear at multiple positions across successive time steps, giving it a higher effective update frequency and allowing the modeler to encode that certain regulatory processes occur faster than others. In asynchronous random update, the node to be updated at each step is chosen randomly, with the simplest case being a uniform selection over all nodes. While the probabilistic scheme introduced stochasticity at the level of function selection, asynchronous random update introduces stochasticity at the level of node selection: there is no predetermined order, and from any given state, multiple different transitions are possible depending on which node happens to be selected.

During early stages of boolean network research, it was believed that the asynchronous update would lead to more realistic models of biochemical systems [4]. However, as some studies have shown, asynchronous and synchronous schemes can lead to the same meaningful behavior for certain networks, and the choice between them often comes down to practical considerations. A concrete limitation of the asynchronous approach is its computational cost: since each time step updates only one node, a single full round over all n nodes requires n sequential steps. Assuming each step takes seconds to minutes, this could add up to several days for large networks [4].

The intuition behind the belief that asynchronous update is more realistic is that biological processes rarely occur simultaneously: genes are transcribed and translated on

different timescales, and regulatory events in one part of the network need not coincide with those elsewhere. Despite this motivation, studies have shown that for many practical GRN models the attractors that correspond to meaningful biological states tend to be preserved across update schemes. This suggests that the coarse-grained behavior of a network is often robust to the specific update schedule, provided the biological logic encoded in the update functions is correct [4].

A key structural consequence of the random asynchronous variant is that, as in the probabilistic scheme, it introduces non-determinism into the state graph. Since the node to update is chosen at random, from any given state there are in general multiple possible successor states rather than a single deterministic one. This makes identifying attractors more complex than in the synchronous or sequential case, since a state can lead to different trajectories on different runs [4].

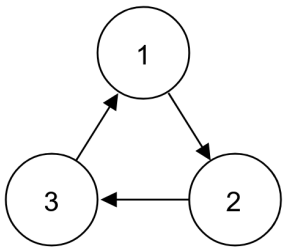
More generally, cyclic attractors that arise in synchronous networks due to the simultaneous evaluation of all update functions are often absent under asynchronous dynamics. Because only one node is updated at a time, the global symmetry that produces such artificial cycles is broken, and the system instead settles into attractors that more faithfully reflect the underlying regulatory logic [2]. The practical consequence of this is discussed in detail using the repressilator as a case study in section 4.

Furthermore, the random asynchronous scheme is closely related to the probabilistic scheme. Rather than randomizing which update function is applied to each node, it randomizes which node is updated at each step, while keeping the update functions themselves fixed.

4 Relevance for Gene Regulatory Networks

A gene regulatory network (GRN) is a system of interactions between genes, transcription factors and other regulatory molecules that together control gene expression in a cell. Since each gene can be treated as either active (expressed) or inactive (silenced), boolean networks are a natural fit for modeling GRNs. They have been applied to a variety of well-known GRNs, such as the cell-cycle network of *Saccharomyces cerevisiae* or the segment polarity network of *Drosophila melanogaster* [1, 2]. In these models, the attractors of the boolean network are interpreted as stable gene expression patterns corresponding to distinct cell types or functional states. A cell that has committed to a specific developmental fate, for example, would correspond to a fixed-point attractor in the GRN model, while transient oscillations in gene expression would appear as limit cycles.

A particularly instructive example for studying the effect of update schemes on GRN models is the *repressilator*: a synthetic regulatory circuit in which three genes each repress the next in a cyclic fashion [2]. As shown in fig. 6, the network has update functions of the form $f_i = \neg x_{i-1}$ (indices modulo 3). Despite having only three nodes and eight possible states, the Repressilator shows a strikingly different attractor structure depending on which update scheme is used.



$$f_1 = \neg x_3$$
$$f_2 = \neg x_1$$
$$f_3 = \neg x_2$$

$x(t)$	$x(t+1)$
000	111
001	011
010	110
011	010
100	101
101	001
110	100
111	000

Fig. 6. The GRN Repressilator modeled as a boolean network and the update table using the synchronous scheme.

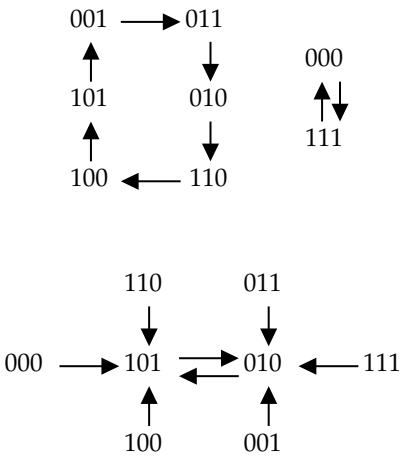
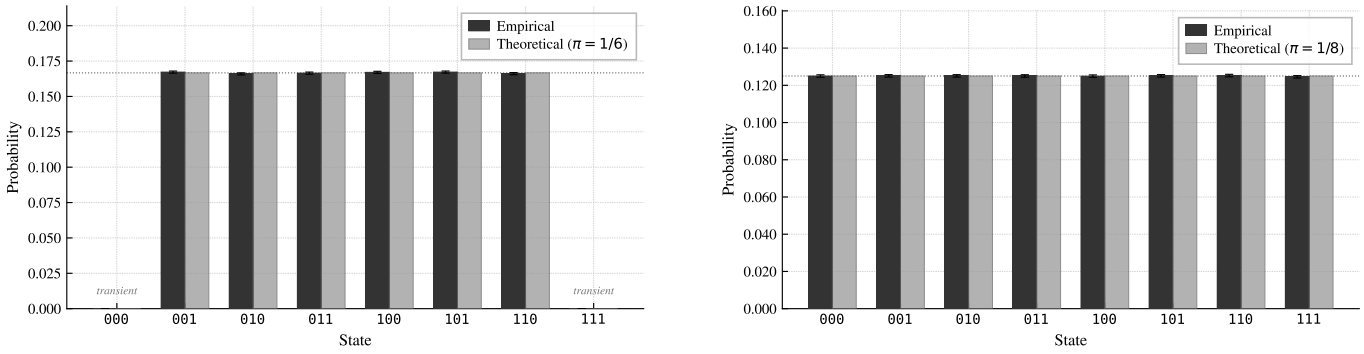


Fig. 7. State graphs of the repressilator as boolean network: The upper two cycles are the result of the use of synchronous scheme; the lower graph is the result of sequential scheme with sequence (x_1, x_2, x_3).

Under the synchronous scheme, the network has two attractors, shown in the upper part of fig. 7. The first is a period-6 oscillation cycle through the states $100 \to 101 \to 001 \to 011 \to 010 \to 110 \to 100$, which corresponds to the alternating gene expression observed in experimental implementations of the repressilator. The second is an artificial period-2 cycle alternating between 000 (all genes off) and 111 (all genes on). This second attractor has no biological basis: it arises purely because updating all three repressors simultaneously maps 000 to 111 and back, a dynamic that would not occur if the genes were updated at slightly different times.

Under random asynchronous update, the picture changes. From state 000, any node selected for updating will have $f_i = \neg 0 = 1$, meaning the network is immediately pushed into one of the oscillatory states regardless of which node is chosen. The same applies to 111. Neither state can sustain itself, so they become transient states and the artificial 2-cycle disappears entirely. Only the biologically meaningful oscillation remains as an attractor. This confirms that the period-2 cycle in the synchronous case was indeed an artifact of simultaneous updating [2], and it illustrates



(a) Asynchronous update scheme

(b) Probabilistic update scheme

Fig. 8. Comparison between theoretical stationary probability distribution and empirical data from a test run using asynchronous random (fig. 8a) and probabilistic (fig. 8b) with one million simulated time steps, both starting from initial state $x = 000$.

why asynchronous update is often considered more biologically faithful for oscillatory GRN models.

Under a sequential scheme with sequence (x_1, x_2, x_3), the attractor structure changes even more dramatically, as shown in the lower part of fig. 7. Tracing through the state transitions reveals that the only attractor is now a period-2 cycle between states 010 and 101, a subset of the states from the synchronous 6-cycle. The synchronous 6-cycle itself no longer exists as an attractor, and all eight states converge to this single 2-cycle. This is a clear example that even among deterministic schemes, changing the update order can completely alter the attractor landscape.

Under a probabilistic scheme, the clean periodic oscillation gives way to an irregular, noisy one. Introducing a small probability for an alternative update function on any of the three genes, modeling the stochastic fluctuations that occur in real gene expression, means the network occasionally deviates from the regular cycle. The long-term behavior is no longer a fixed attractor but a stationary distribution over states, reflecting how much time the system spends in each expression configuration on average [4]. This type of model is particularly useful for understanding phenotypic variability within a population of genetically identical cells.

The repressilator example illustrates a key point for GRN modeling in general: the choice of update scheme is not a neutral decision. It directly affects which attractors exist, which states are biologically accessible, and how realistically the model captures the noise and timing characteristics of the underlying system. For large-scale GRNs where the biological timing of regulatory events is not known, synchronous update remains the practical standard due to its computational simplicity and the ease of attractor analysis. Sequential or block-sequential update is appropriate when relative timing information is available. Asynchronous update is biologically motivated but becomes slow for large networks, and probabilistic update is the method of choice when transcriptional noise is a central modeling goal.

The long-term behavior of stochastic update schemes can be analyzed formally through the theory of Markov chains. A *Markov chain* is a stochastic process over a finite set of states with the memoryless property: the probability of moving to the next state depends only on the current state, not on any earlier history. Both the random asynchronous and the probabilistic synchronous schemes satisfy this property, since the update rule at each step is determined entirely by the current network state. The dynamics are fully captured by a *transition matrix* $P \in [0,1]^{2^n \times 2^n}$, where each entry P_{ij} gives the probability of moving from state i to state j in one time step. Since the network must always transition to some state, every row of P sums to one.

States in a Markov chain fall into two categories. A state is *transient* if the network will eventually leave it and never return; it is visited only a finite amount of times. A state is *recurrent* if the network returns to it infinitely often. Groups of recurrent states that can all reach each other and have no outgoing transitions to other groups form *recurrent classes*. A Markov chain with a single recurrent class is called *irreducible*.

The *stationary distribution* π is a probability vector over all states, where $\pi(x) \in [0,1]$, denotes the probability of the network being in state x. It satisfies

$$\pi P = \pi, \tag{5}$$

meaning π is a fixed point of the dynamics: if at some point in time the state of the network is drawn from π, then after one update step its state is still distributed according to π. In practice, $\pi(x)$ corresponds to the long-run fraction of time the system spends in state x, regardless of the initial state. Transient states receive $\pi(x) = 0$, since they are eventually abandoned, while recurrent states have $\pi(x) > 0$. For any finite irreducible Markov chain, a unique π satisfying eq. (5) always exists. Comparing π against empirical visit frequencies from a long simulation then provides a practical validation of the model.

Under random asynchronous update of the repressilator, the states 000 and 111 are transient: from either state, every possible node selection immediately moves the network away, so once left they are never revisited, giving $\pi(000) = \pi(111) = 0$. The remaining six oscillatory states $\{100, 101, 001, 011, 010, 110\}$ form a single recurrent class. Since the repressilator's cyclic repression structure treats each gene symmetrically and the update rule selects each of the three nodes with equal probability $\frac{1}{3}$, no oscillatory state is inherently preferred over any other. The unique solution to eq. (5) is therefore the uniform distribution $\pi(x) = \frac{1}{6}$ for

each of the six states. Figure 8a shows that a long simulation run closely matches this theoretical result.

Under the probabilistic synchronous scheme, the analysis differs. When a per-node bit-flip probability $p \neq 0$ is introduced alongside the standard repression function, the resulting transition matrix P is *doubly stochastic*: not only does every row sum up to one, but every column does as well. For any doubly stochastic matrix over a finite irreducible Markov chain, the uniform distribution is the unique solution to eq. (5), giving $\pi(x) = \frac{1}{8}$ for all eight states in the long run, including 000 and 111, which carry zero probability under the asynchronous scheme. Figure 8b confirms this result empirically, illustrating how the two stochastic schemes produce qualitatively different long-term behavior despite both introducing randomness.

5 Conclusion

This paper gave an overview of four update schemes for boolean networks and analyzed how they affect the dynamics of a model. The synchronous scheme, where all nodes update simultaneously, produces fully deterministic and easily enumerable dynamics, making it the most widely used approach in practice despite its biological simplifications. Sequential and block-sequential schemes allow for a more realistic encoding of temporal ordering between regulatory events while retaining determinism. The probabilistic scheme introduces stochastic variation at the level of the update functions, capturing noise and fluctuations in the system. The asynchronous scheme updates one node at a time and, in its random variant, introduces non-determinism at the level of node selection rather than function selection.

The repressilator example from section 4 makes the practical stakes of this choice concrete. Even in a network with only three nodes, as illustrated in fig. 7, the synchronous scheme produces a spurious 2-cycle between 000 and 111 alongside the biologically relevant 6-cycle. The asynchronous scheme eliminates this artifact. The sequential scheme with sequence (x_1, x_2, x_3) replaces the 6-cycle with an entirely different 2-cycle through $010 \leftrightarrow 101$. The probabilistic scheme turns the regular oscillation into a noisy, variable one. The update scheme is therefore not just a computational choice; it determines which attractors the model has and what biological conclusions can be drawn from them.

The question of which scheme best captures the biology of a given system remains an active area of research. A notable recent contribution is the introduction of Most Permissive Boolean Networks [7], a new update semantics that generalizes both synchronous and asynchronous approaches and carries a formal guarantee that no behavior achievable by a compatible quantitative model is missed. Unlike standard asynchronous update, the most permissive semantics also avoids the state-space explosion that makes large-scale asynchronous analysis intractable, enabling attractor analysis of genome-scale regulatory networks. On the tooling side, software packages such as BoolNet [8] and GINsim [9] bring multiple update schemes and attractor analysis algorithms to a broader research community.

Open questions include how to choose a biologically grounded update scheme when experimental timing data is sparse [4, 5], how to parameterize probabilistic models from single-cell RNA sequencing data [4], and how to efficiently compute attractor landscapes in asynchronous networks with thousands of nodes [7]. Boolean networks, despite their simplicity, remain a powerful framework for understanding the dynamical logic of gene regulation, and the choice of update scheme is central to using them well.

References

[1] Tomas Helikar, Naomi Kochi, John Konvalina, and Jim A Rogers. Boolean modeling of biochemical networks. *The Open Bioinformatics Journal*, 5(1), 2011.

[2] Stefan Bornholdt. Boolean network models of cellular regulation: prospects and limitations. *Journal of the Royal Society interface*, 5(suppl_1):S85–S94, 2008.

[3] Kenneth H. Rosen. *Discrete Mathematics and Its Applications*. McGraw-Hill Education, 8th edition, 2019.

[4] Julian D Schwab, Silke D Kühlwein, Nensi Ikonomi, Michael Kühl, and Hans A Kestler. Concepts in boolean network modeling: What do they all mean? *Computational and structural biotechnology journal*, 18:571–582, 2020.

[5] Julio Aracena, Eric Goles, Andrés Moreira, and Luis Salinas. On the robustness of update schedules in boolean networks. *Biosystems*, 97(1):1–8, 2009.

[6] Eric Goles and Mathilde Noual. Block-sequential update schedules and boolean automata circuits. *Discrete Mathematics & Theoretical Computer Science*, (Proceedings), 2010.

[7] Loïc Paulevé, Juri Kolčák, Thomas Chatain, and Stefan Haar. Reconciling qualitative, abstract, and scalable modeling of biological networks. *Nature communications*, 11(1):4256, 2020.

[8] Christoph Müssel, Martin Hopfensitz, and Hans A Kestler. Boolnet—an r package for generation, reconstruction and analysis of boolean networks. *Bioinformatics*, 26(10):1378–1380, 2010.

[9] Aurélien Naldi, Céline Hernandez, Nicolas Levy, Gautier Stoll, Pedro T Monteiro, Claudine Chaouiya, Tomáš Helikar, Andrei Zinovyev, Laurence Calzone, Sarah Cohen-Boulakia, et al. The colomoto interactive notebook: accessible and reproducible computational analyses for qualitative biological networks. *Frontiers in physiology*, 9:680, 2018.