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## Cellular automata models and their applications in biology and biomedicine

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### Abstract

Besides being the basis for modern computers, Alan Turing's conceptual automaton, also known as the "Turing machine", provides a useful way of viewing organisms. For instance, an organism (automaton) is affected by the outside world (inputs) and it behaves (outputs) according to its habits or condition (state) and nature (program). The "cellular automaton" extends this analogy to provide a way of viewing whole populations of interacting "cells". By creating appropriate rules into a cellular automaton, one can simulate many kinds of complex behavior. A cellular automaton is an array of identically programmed automata that can interact with one another. With the invention of parallel computing, the "cellular automaton" has become central to computation. The crucial difference between cellular automata and sets of independent automata is that the cells interact with each other. These interactions can completely change the overall behavior of a set of objects. Hence, we need to consider cellular automata as whole systems, rather than as many individuals. Despite their simplicity, cellular automata are capable of an astonishing variety of Behaviors. An important property is that they tend to be "self-organizing". Starting from complex and random cell configurations, to simple and conceptual automata behavior. Many natural phenomena can be modelled as cellular automata. For instance, linear automata provide good models of pattern formation on mollusk shells and the growth of crystals, such as snowflakes, are modelled as hexagonal automata growing from a seed. The state of each cell depends on the number of living neighbors it has: with Less than 2 living neighbor cells they die from isolation, but with more than 3 they die from overcrowding, and with exactly 3 living neighbors, a birth occurs in a dead cell. As with linear automata, these rules tend to produce order from arbitrary initial configurations. Ultimately, most configurations either disappear or break up into isolated pieces of pattern. Countless more applications of cellular automata will be discussed in detail in the research paper. Cellular automata provide global representations for processes that require context and involve discrete state changes in interacting populations of separate automata. The usual arrangement of cells is a rectangular grid, but different or flexible structures are appropriate for some processes, such as growth. Therefore, in understanding biological processes and in developing modern day medicine, the study of cellular automata can prove to be extremely useful.

**Keywords:** Automata models, Turing machine, Alan Turing's

### 1. Introduction

Mathematically speaking, the theory of computation (TOC) is "the study of algorithms and the computational processes used in science, mathematics, engineering, and other fields." The subfield of TOC surveyed by this article mainly focuses on computing techniques. Most famously, TOC is associated with Turing's theoretical model of a Universal Turing machine. But more recent developments have started to break through barriers which have been erected around human computational abilities since early 20th century. The focus is on a human-like capacity to deal with problems of a computational nature.

#### 1.1 Recent concerns

Recently, concern about the ethical and ethical issues of TOC has spread, particularly in relation to computing techniques involving humans, e.g., in applied mathematics, economics and informatics. Specialists have been warning about the dangers of algorithms. In addition to these concerns, there is a large body of theoretical research on modeling various aspects of computation in biology and medicine. Much work has been done on formalizing theoretical models for biological processes that can be modeled by Turing machines (computational mechanisms in biology). The example discussed in this article demonstrates a new direction: theoretical models in biology and medicine based on computation instead of Turing's model.

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## 1.2 Automata

“Automaton” is a technical term used in computer science and mathematics, for a theoretical machine that changes its internal state based on inputs and its previous state. The state set is usually defined as finite and discrete, which often causes nonlinearity in the system’s dynamics. Besides being the basis for modern computers, Alan Turing’s conceptual automaton, also known as the “Turing machine”, provides a useful way of viewing organisms. For instance, an organism (automaton) is affected by the outside world (inputs) and it behaves (outputs) according to its habits or condition (state) and nature (program). The “cellular automaton” extends this analogy to provide a way of viewing whole populations of interacting “cells”. By creating appropriate rules into a cellular automaton, one can simulate many kinds of complex behavior<sup>[1, 2]</sup>.

Similar to CAs, most of the multicellular organisms begin their life as single cells and grow until they become highly complex anatomies. This process is called morphogenesis and it consists of how cells communicate with their neighbors to decide the shape and position of the organs. Or, even more impressive, when to stop. Interestingly, patterns of some seashells, such as *Conus* and *Cymbiola*, are generated by natural cellular automata. For these seashells, the pigment cells reside in a narrow band along the shell’s lip. Each cell secretes pigments according to the activating and inhibiting activity of its neighbor pigment cells, obeying a natural version of a mathematical rule. The cell band leaves the colored pattern on the shell as it grows slowly.

## 2. Cellular Automata

Cellular Automata (or CA) are a set of such automata arranged along a regular spatial grid, whose states are simultaneously updated by a uniformly applied state-transition function that refers to the states of their neighbors. The original idea of CA was invented in the 1940s and 1950s by John von Neumann and Stanisław Ulam. They invented this modeling framework, which was among the very first to model complex systems, in order to describe self-reproductive and evolvable behavior of living systems. A cellular automaton can be described as an array of identically programmed automata that can interact with one another. With the invention of parallel computing, CA has become central to computation. The crucial difference between cellular automata and sets of independent automata is that the cells interact with each other. These interactions can completely change the overall behavior of a set of objects. Cellular automata can also be one-dimensional, two-dimensional (like the board game “Game of Life”) or 3-dimensional. Game of Life may be defined on any (usually a large) grid. Each grid cell exists in one of two possible states, alive or dead. The neighborhood of a given grid cell is made up of the eight next-nearest neighbors which are orthogonally adjacent and diagonally adjacent to that cell (This is sometimes called a Moore neighborhood). Each grid cell will be updated synchronously every time step according to the following rules:

- If a living cell has less than 2 living neighbors it dies (as if by loneliness).
- If a living cell has more than 3 living neighbors it dies (as if by overcrowding).
- If a dead cell has exactly 3 living neighbors it becomes alive.

To begin, each cell in the grid is initialized with either the state living or dead. Some of the initial configurations which

give rise to some of the more interesting patterns have been given names, such as ‘glider’, ‘small exploder’, and ‘lightweight spaceship’. This example shows how some of these interesting patterns repeat themselves on successive time steps. Hence, we need to consider cellular automata as whole systems, rather than as many individuals. Despite their simplicity, cellular automata are capable of an astonishing variety of behaviors. An important property is that they tend to be “self-organizing”. Starting from complex and random cell configurations, to simple and conceptual automata behavior.

## 2.1 History of Cellular Automata

Cellular automata trace their beginning to the Los Alamos Laboratory in the 1940s, where mathematician John von Neumann was studying the concept of self-replicating robots. His idea was that moons or asteroids would be most efficiently mined by such automata, due to the exponential growth of their population. The cost of experimenting with such robots, however, was prohibitive. Stanislaw Ulam, also at Los Alamos, was working on the problem of crystal growth using a lattice model<sup>[3, 4]</sup>. At his suggestion von Neumann applied a lattice grid model also to the problem of self-reproducing automata. This model became what is now known as cellular automata.

What von Neumann invented with pen and paper was later popularized by the automaton known as the Game of Life, which is described above. Invented in the 1970s by John Conway, this model displays a wide variety of complex patterns despite its very simple rules for whether a given cell should ‘live’ or ‘die’. This simple CA caught the attention of researchers in a wide variety of fields including computer science, physics, biology, economics, and mathematics.

In the 1980s Stephen Wolfram published a number of papers detailing his study of the universality of cellular automata and the complexity of their patterns. In 2002, after having studied cellular automata for decades, Stephen Wolfram published a twelve-hundred-word text on the subject of their simple rules and complex patterns. This fact, that cellular automata can display complex patterns despite having simple rules, is a reason that they are considered to be such a useful model type. At the University of Siegen, Duchting and Vogelsaenger did some of the earliest research in the area of using cellular automata to model tumor growth. Their 1984 paper describes a three-dimensional simulation of tumor growth and describes what its application to tumor treatment might be.

## 2.2 Mathematical theory

Although CA follow simple rules, mathematical analysis of a CA may not be straightforward. First of all, there is the problem of classifying cellular automata. Stephen Wolfram’s set of four CA classes is probably the most popular method of CA classification. It is, however, strictly qualitative and suffers from a degree of subjectivity. According to this classification, all cellular automata may be categorized as being in one of the four Wolfram classes:

- Class I: these CA have the simplest behavior; almost all initial conditions result in the same uniform final state.
- Class II: different initial conditions yield different final patterns, but these different patterns consist of an arrangement of a certain set of structures, which stays the same forever or repeats itself within a few steps

- Class III: behavior is more complicated and appears random, but some repeated patterns are usually present (often in the form of triangles)
- Class IV: in some respects, these are the most complicated class; these behave in a manner somewhere in between Class II and III, exhibiting sections both of predictable patterns and of randomness in their pattern formation

All cellular automata fit into one of these four categories, however it is not always clear which category a CA ought to be placed in.

### 3. Application in Biological Systems

Many natural phenomena can be modelled as cellular automata. For instance, linear automata provide good models of pattern formation on mollusk shells and the growth of crystals, such as snowflakes, are modelled as hexagonal automata growing from a seed. The state of each cell depends on the number of living neighbors it has: with less than 2 living neighbor cells they die from isolation, but with more than 3 they die from overcrowding, and with exactly 3 living neighbors, a birth occurs in a dead cell. As with linear automata, these rules tend to produce order from arbitrary initial configurations. Ultimately, most configurations either disappear or break up into isolated pieces of pattern<sup>[5]</sup>. Here are some examples of CA models which could make them more useful and applicable to real-world phenomena -

- **Stochastic cellular automata:** CA that can be a computational process which produces the output probabilistically. This plays an important role in mathematical modeling of various biological, social, and physical phenomena. For example - epidemiological processes where infection of a disease takes place stochastically (being well described by a random probability distribution).
- **Multi-layer cellular automata:** States of cells don't have to be scalar. Instead, each spatial location can be associated with several variables (or vectors). Multi-layer CA models are useful when multiple biological or chemical species are interacting with each other in a space-time. For example - in reaction-diffusion systems.
- **Asynchronous cellular automata:** There are several asynchronous updating mechanisms possible, such as random updating, sequential updating (predetermined sequential order of updating), state-triggered updating (certain states trigger updating of nearby cells), etc. It is often argued that synchronous updating in conventional CA models is too artificial and fragile against slight perturbations in updating orders, and in this sense, the behaviors of a synchronous CA models are deemed more robust and applicable to real-world problems.

Nearly all biological phenomena involve some kind of spatial extension, such as excitation patterns on neural or muscular tissue, cellular arrangements in an individual organism's body, and population distribution at ecological levels<sup>[15, 16, and 17]</sup>. If a system has a spatial extension, nonlinear local interactions among its components may cause spontaneous pattern formation, i.e., self-organization of static or dynamic spatial patterns from initially uniform

conditions. Such self-organizing dynamics are quite counter-intuitive, yet they play essential roles in the structure and function of biological systems.

- **Turing patterns -** Animal skin patterns are a beautiful example of pattern formation in biological systems. To provide a theoretical basis of this intriguing phenomenon, Alan Turing (who is best known for his fundamental work in theoretical computer science) developed a family of models of spatial and temporal dynamics of chemical reaction and diffusion processes. His original model was first written in a set of coupled ordinary differential equations on compartmentalized cellular structures, and then it was extended to partial differential equations in a continuous space. Assume a two-dimensional space made of cells where each cell can take either a passive (0) or active (1) state. A cell becomes activated if there are a sufficient number of active cells within its local neighborhood. However, other active cells outside this neighborhood try to suppress the activation of the focal cell with relatively weaker influences than those from the active cells in its close vicinity. These dynamics are called short-range activation and long-range inhibition.
- **Waves in excitable media -** Neural and muscle tissues made of animal cells can generate and propagate electrophysiological signals. These cells can get excited in response to external stimuli coming from nearby cells, and they can generate action potential across their cell membranes that will be transmitted as a stimulus to other nearby cells. Once excited, the cell goes through a refractory period during which it doesn't respond to any further stimuli. This causes the directionality of signal propagation and the formation of "traveling waves" on tissues. This kind of spatial dynamics, driven by propagation of states between adjacent cells that are physically touching each other, are called contact processes. This model and the following two are all examples of contact processes.
- **Host-pathogen model -** A spatially extended host-pathogen model, studied in theoretical biology and epidemiology demonstrates the subtle relationship between these two antagonistic players. This model can also be viewed as a spatially extended version of the "predator-prey" model, where each cell at a particular location represents either an empty space or an individual organism, instead of population densities that the variables in the "predator-prey" model represented. Assume a two-dimensional space filled with empty sites in which a small number of host organisms are initially populated. Some of them are "infected" by pathogens. A healthy host without pathogens will grow into nearby empty sites stochastically. A healthy host may get infected by pathogens with a probability determined by a function of the number of infected hosts in its neighborhood. An infected host will die immediately. The spatial patterns formed in this model are quite different from those in the previously discussed models. Turing patterns and waves in excitable media have clear characteristic length scales (like the size of spots or width of waves), but the dynamic patterns formed in the host-pathogen model lacks such characteristic length scales. You will see a number of dynamically forming patches of various sizes, from tiny ones to very large continents.



- Epidemic/forest fire model-The final example, the epidemic model, is also about contact processes similar to the previous two examples. One difference is that this model focuses more on static spatial distributions of organisms and their influence on the propagation of an infectious disease within a single epidemic event. This model is also known as the “forest fire” model. Assume there is a square-shaped geographical area, represented as a CA space, in which trees are distributed with some given probability. Then, you set fire to one of the trees in this forest to see if the fire you started eventually destroys the entire forest. A tree will catch fire if there is at least one tree burning in its neighborhood, and the burning tree will be charred completely after one time step. This model doesn't have cyclic local dynamics. Possible state transitions are always one way from a tree, to a burning tree, then to being charred, which is different from the previous two examples. The whole system eventually falls into a static final configuration with no further changes possible <sup>[6]</sup>. But the total area burned in the final configuration greatly depends on the density of trees.

Near critical values of probability, the system is very sensitive to minor perturbations (uneasiness), and a number of intriguing phenomena (such as the formation of self-similar fractal patterns) are found to take place at or near this transition point, which are called critical behaviors. Many complex systems, including biological and social ones, are considered to be utilizing such critical behaviors for their self-organizing and information processing purposes. For example, there is a speculation that animal brains tend to dynamically maintain critical states in their neural dynamics in order to maximize their information processing capabilities. Such self-organized criticality in natural systems has been a fundamental research topic in complex systems science.

In the last, researchers are suggested to refer articles <sup>[7-15]</sup> to know about popular and serious concerns in this smart era. Such concerns are interested with respect to healthcare sector and require efficient solutions from the scientific community.

#### 4. Conclusion

There are a variety of reasons why cellular automata and cellular automata-like models attract researchers who want to model biological phenomena. They are simple models with complex behaviors that lend themselves well to modeling the behaviors of some sort of population. It should come as no surprise that a model that was invented to simulate a population of artificial self-reproducing individuals can also model populations of living self-reproducing individuals, such as cells. Cells are the building blocks of life, maybe then they also be the building blocks of life models. There are many reasons that a CA may be chosen to perform this task. There is much ongoing research in this field. These models continue to be improved, especially by means of combining successful models together in a hybrid model. There is much research to be done in developing useful analysis for these models. Cellular automata provide global representations for processes that require context and involve discrete state changes in *interacting* populations of separate automata. The usual arrangement of cells is a rectangular grid, but

different or flexible structures are appropriate for some processes, such as growth. Therefore, in understanding biological processes and in developing modern day medicine, the study of cellular automata can prove to be extremely useful.

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