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Programmable Living Nanorobots

Programlanabilir Yaşayan Nanorobotlar

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ABSTRACT

There are many different nanorobots in the literature, but the nanorobots that we will talk about in this review is a unique robot and the first of their kind because it is made entirely from the heart and skin cells of a frog, which means only living cells without any artificial materials. This type of robot has been programmed and studied using the silico system, in which the heart and skin cells will be arranged before being applied in vivo have been designed. On the other hand, this robot has many negatives, like anything in our world has disadvantages and advantages, so we will mention them and discuss them in this review by mentioning the aspirations and future directions of this unique robot.

Key Words

Xenobots, nanorobots, nanotechnology, reconfigurable organisms, *Xenopus laevis*.

ÖZ

Literatürde pek çok farklı nanorobot var ama bu derlemede bahsedeceğimiz nanorobot, tamamen bir kurbağanın kalp ve deri hücrelerinden yani sadece canlı hücrelerden oluşması nedeniyle benzersiz bir robot ve türünün ilk örneği. herhangi bir yapay malzeme olmadan. Bu tip robotlar, in vivo uygulanmadan önce kalp ve cilt hücrelerinin düzenleneceği silico sistemi kullanılarak programlanmış ve çalışılmıştır. Öte yandan, bu robotun birçok olumsuzluğu var, tıpkı dünyamızdaki her şeyin dezavantajları ve avantajları olduğu gibi, bu yüzden bu eşsiz robotun özlemlerinden ve gelecekteki yönlerinden bahsederek bu incelemede onlardan bahsedeceğiz ve tartışacağız.

Anahtar Kelimeler

Ksenobotlar, nanorobotlar, nanoteknoloji, yeniden yapılandırılabilir organizmalar, *Xenopus laevis.*

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INTRODUCTION

What are Living Organisms Reconfigurable? Or Living robots "novel living machines" [1,2]? It was the title of a paper published in mid-2020. Several years ago, and until now, steel, concrete, chemicals, and polymers were used in most technologies, which degrade over time and it has negative environmental and health consequences [1,2]. Including the problems of treating difficult diseases such as malignant tumors, tracking cancer cells, or the presence of plaques in the arterial wall, as well as environmental problems, including oil leakage and the presence of plastic waste in ocean waters [3].

Therefore, researchers and scientists have tried to focus on better ways to improve technology, through the use of Biocompatible materials and self-renewable, hence the title of the research because reconfigurable organisms are the best candidate for solving these problems and replacing harmful manufactured materials. But there are many difficulties to inventing or discovering such a thing; firstly because of our lack of full understanding of the system of living organisms, and secondly, because of the difficulty of obtaining resources [4,5], and it raises many ethical and behavioral problems as described by some scientists that research and modification in this field like trying to play the role of God [6].

However, a group of scientists carried out some laboratory and theoretical research to solve and discover a way to avoid these problems, and this research led to the discovery of the first and most important living robot called xenobots, which is a living robot, which means that it has not been programmed or used any type of metal, plastic or any other materials for its manufacture, only a live cell that comes from the stem cells of the embryos of a type of African frog named(Xenopus laevis) [1]. One co-author of the paper [1] that recently presented xenobots said, "They are neither a traditional robot nor a known type of animal". Another one says "They are a new class of artifacts: a programmable organism" [2]. Also, Michael Levin said, "These are entirely new lifeforms. They have never before existed on Earth,", but some scientists say that These "reconfigurable beings" have already raised many philosophical and ethical questions [6].

What are xenobots

Xenobot is a dissident robot from among the nanorobots, but it is unique because it is the first robot that is a living organism designed with nanotechnology, but where was the beginning of this idea? The first time a fully alive robot was mentioned was in a play by the Czech writer Karel R.U.R in 1921, and it was mentioned as Čapek, which is a Czech word meaning laborer. It was fleshy and autonomous, he was inspired by an emerging technology of in vivo tissue culture that ignored and blurred the boundaries between engineering and biotechnology to a degree beyond the techniques of the time, but the findings of some reports in our century changed knowledge and the limits of technology these days, though, this discovery seems a bit troubling because they described a "reconfigurable living organism" that is a xenobot [1,7]

Xenobots are a type of living robot that is less than 1 mm in size and consists of 500-1000 embryonic stem cells. This name comes from the African clawed frog Xenopus laevis. The cell that we use to build this robot is harvested from embryos at the blastula stage [8], most of these cells retain their ability to grow in any type of body tissue if the right atmosphere is provided, but also most of them depend on its internal energy to live at its maximum for seven days [7]. But inside the liquid solution, it can last for several days or weeks, even without any additional recources or human intervention.

It has been called a reconfigurable living organism because that is reshaped in proportion to being able to renew itself even if it is cut almost in half, as that is reconstituted and self-renewing without any external interventions, but the most important question is how this manufactured body can move and how it was called a robot since it is made of cells only. The reason is this organism will move not by its own decision, Its movement will be related to the design chosen for it so here we can not call it an organism or robot, but we can get both names organism and robot and make a new name which is living robot. About the cell used to make this robot is the lower cell of the heart (which is the precursor of the heart muscle) and the skin. In other words, the skin cell is used as scaffolding or stents, and the heart cells are responsible for movement because they can contract through electrical activity [9].

Synthesis of xenobot

In our time, many 3D printing and computational research techniques have been developed until they have reached a point where we can design and build machines or robots in a process called in silico evolution to create and test different designs of what we try to make robots or machines by using computer simulations to predict how they would move and behave[10], after which physical models can be manufactured according to the best design that's the computer shows and the behavior that we need unlike the traditional methods used. This technology allows the development of machines more quickly and efficiently [11,12].

Here we explain how the synthesis of xenobot:

As we know that the xenobot is made up of frog stem cells, but how we can know the best shape of the xenobot that we want for a specific application? the answer is what we mention above in the silico process. The designs were chosen and developed using evolutionary and complicated algorithms in silico, to predict their movement and behavior. Initially, for detecting the best design 100 independent experiments were conducted in silico for different groups for specific applications in different physics-based virtual environments in this stage the low-performance bots were deleted, and in the end, the process keep going until 100 different designs of xenobots have good stability in a different environments were shown in silico as we can see in the figure (1), but not all of them are high-performance designs or they can do the predicted work in vivo this process was only to know the best stable design in the environments without any other effects on them. Then to get the best high-performance designs that are stable and undisturbed some extra experiments were done in the silico [13,1].

in the next stage, the developers used a robustness filter. Where the robustness filter used in the design process for xenobots takes into account the differences between the simulated and targeted physical environments. Only designs that can maintain their desired behavior in the presence of noise are allowed to pass through the filter. This is based on the understanding that noise resistance in simulation is a good predictor of whether a design will maintain its behavior when it is physically instantiated. This helps to ensure that the xenobots will be able to function effectively in vivo. At the end of this process, the data of designs that pass the filter stage will back to the silico system to eliminate other designs and continue the other process to get the perfect design. Figure (1B-1G) shows the whole process and the successful designs in 1st stage from 100 [1].

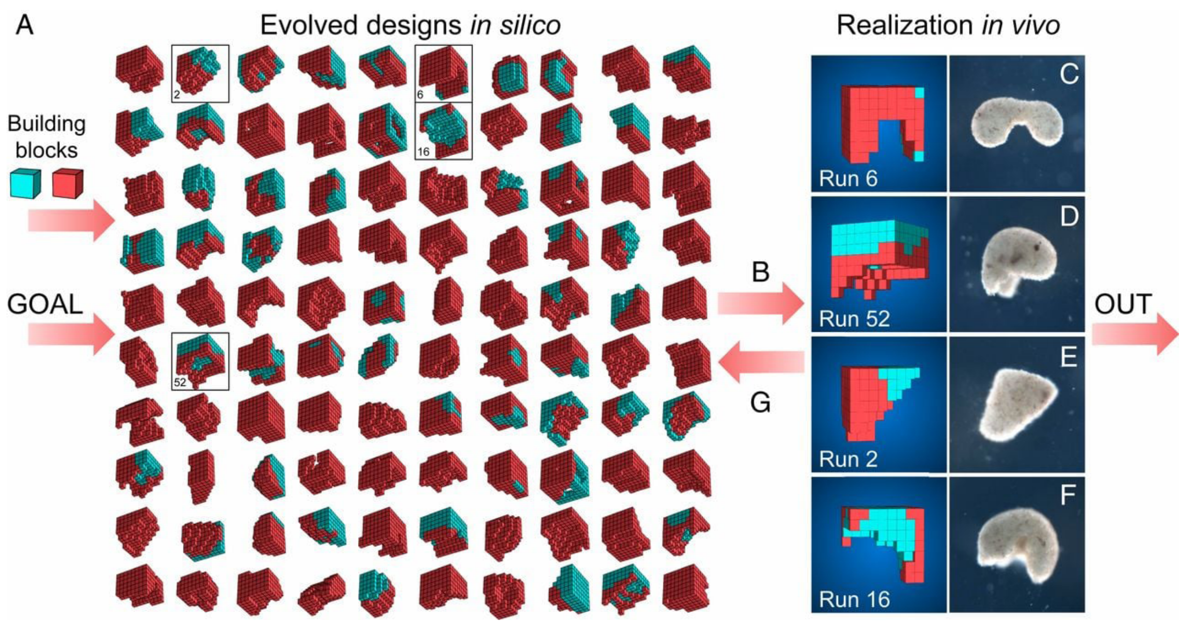

Figure 1. (A) shows an example of the first 100 samples selected in silico, (B) Shows the robustness filter, (C-F) the design that passes the robustness filter stage in vivo view, and (G) is the last thing after completing the first stage which is inserted the information into the silica with a different type of behavior that we will mention later [1].

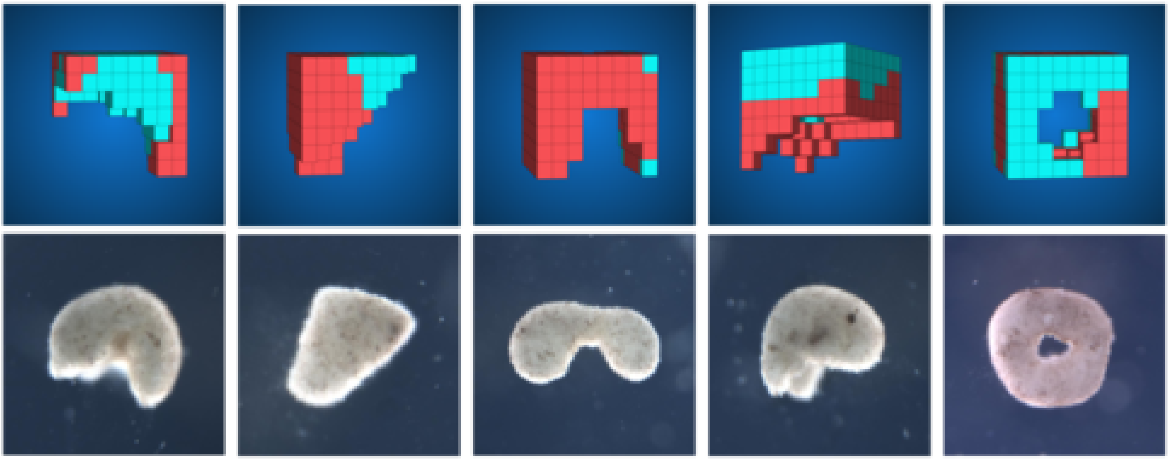

Figure 2. Shows how the samples were installed in silico and their final shape in vivo [1].

Successful designs from the previous process are then passed through a construction filter which is used to remove designs that are unsuitable for the current construction method or are not likely to be suitable for more complex processes. The success measures of this design depend on the ability of the design to reduce the minimum size of the concavity that tends to be blocked by the stem cell due to its behavior in mass engineering. The design also depends on the percentage of negative tissue (skin cells) that provides space for future organ systems or payloads.

The designs that successfully pass through the constructed filter are then built and used in vivo, but first, to build a xenobot with a specific design, stem cells are harvested from frog embryos at the blastula stage and they are separated for each cell separately, and then assembled according to the design taken from in silico using microscopic tweezers and a cautery electrode with a 13 µm wire tip, then we get a biological robot close to a simulated design. The end product of this is a live 3D approximation of the cutting-edge design as shown in figure (2). Where we can see the silico successful designs at the top and how they will be in vivo under it, which can autonomously navigate and explore an aquatic environment for days or weeks without additional feeders. These organisms are then propagated into their physical environment; the resulting behavior is observed, and the behaviors are then compared with those predicted by their mimic counterparts to determine if the behaviors are transmitted from in silico to in vivo [1,14].

Properties

As for the characteristics of the xenobot, it depends on the way it is assembled in the silico system, as we discussed previously. We can understand from this that each design we obtain has different or similar characteristics in some cases [1]. However, some properties are the same for all xenobot forms, such as self-healing as Figure (3) shows, where 2 different design of xenobot cutted from the middle and after 10 minute they almost back as they was, and there is also the regulation of microplastics and chemical communication with pheromones [15]. One of the most important of these similar properties is that they can enter the human body without exposure to the immune system because they are living cells [1,15] and the other one, according to Bongard. "The negative side of living tissues is that they are weak and degrade." That's why we use steel [2]. But these robots can work for seven days depending on their internal energy; and when they lose all their energy, they only die and collapse without damage. He says they finished their work after seven days; they are just dead skin cells [1].

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On the other hand, some xenobots will have other characteristics that depend on their shapes, for example, a "legged xenobot" with contractile cells in the lower half was able to show non-random directional movement on a surface. Some designs gather and move in a circular motion around a specific object or push it and make a circle around it, that is its center we will discuss its usefulness later. Wherefore some researchers (D. Blackiston, et al) tested the ability of "xenobots" without specifying a spe-

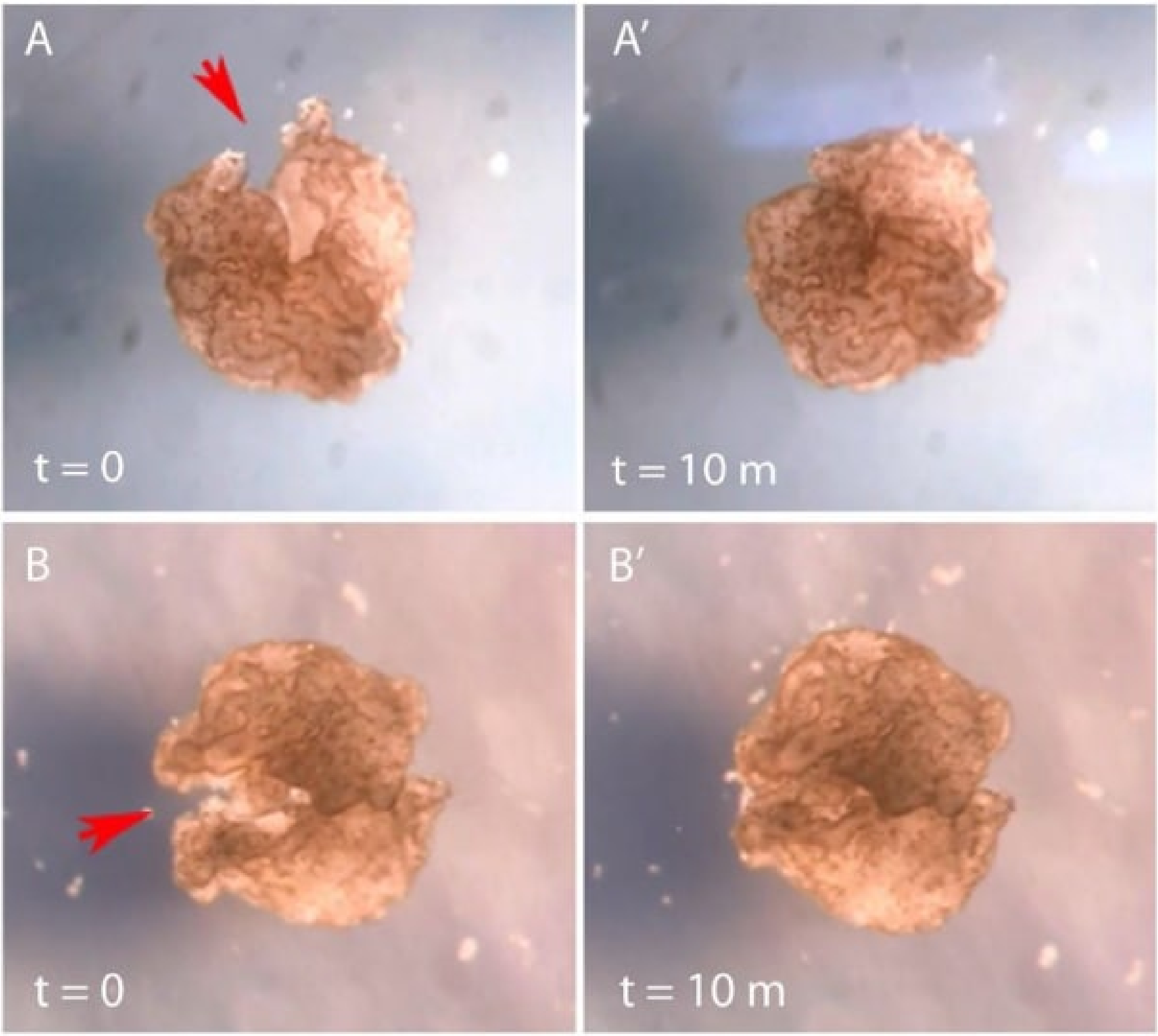

Figure 3. Shows the self-healing ability of Xenobot after cutting it by 10 minutes [1].

cific shape and design, the experiment was conducted to study the movement of the Xenobot to navigate through different environments. They constructed arenas with varying dimensions, including open fields, mazes, and narrow capillary tubes. The xenobots were able to move through these spaces, although some had difficulty in the narrower passages. In an open field with a debris field, the xenobots showed a combination of linear and circular movement. When placed in a narrow maze, they moved along the center of the channel and sometimes changed direction. When placed in an even narrower maze, they often circled one wall. In a capillary tube, 42% of the xenobots were able to traverse the entire length of the tube, even if they did not show movement in the open field test. These results show that xenobots can navigate through a range of environments without being specifically designed for a specific scenario, which is a useful ability for xenobot [2,9].

In some versions, the xenobot was designed with a hole in the center to reduce dynamic drag, and this enabled scientists to use the hole as a bag to carry things "It's a step toward using computer-designed organisms to intelligently deliver drugs," as Bongard says about the latest design [2,16].

Application

The observed tasks that have been published so far are numerous due to their unique properties, including the regulation of microplastics, self-healing, and chemical communication with pheromones. Therefore, one of the most important uses of Xenobot is related to the human body inside and outside it with the possibility of increasing the areas of application of Xenobot in the future with a full understanding of it.

Therefore, we will first address its many uses inside the body, including the precise sculpting of nervous tissues. It can be a treatment for some neurological and chronic diseases such as peripheral neuropathy and diabetes [3]. Also scraping the deposits of unwanted substances (for example, in arthritic joints) or control events in locations of disease. Can also inactivate cancer cells in the lymph nodes. We can add also they are used if equipped to express signaling circuits and proteins for enzymatic and sensory (receptors) and mechanically distorted functions to search for, clean up, or digest toxins [17] and due to their non-toxicity and self-limiting lifespan, they can serve as a new vehicle for intelligent drug delivery by specific design [18] or internal surgery [19], and it can be used by injecting Xenobot into the traumatized area to degrade the myelin sheath to prevent the condition from deteriorating into nerve damage [20] with all these uses of Xenobot inside the human of course here it should note that all these applications inside the human can be used after (made Xenobot from the patient's cells) [17].

There are also some uses outside the human body but related to it, would be used to monitor virus concentrations in a specific area because of their ability to introduce and assay read/write circuitry in living xenobots, allowing for a record of their experiences to be retrieved. These xenobots would be equipped with a virus stimulus and a fluorescent light indication system. When xenobots come into contact with viruses, they gradually change the color of the light they emit in response to the presence or absence of the virus. This color change could be used to determine how long a particular virus has been present in an area, which could be useful for contact tracing and understanding the spread of the virus. The xenobots would be sensitive to viruses through the use of horizontal gene integration and synthetic RNA and DNA origami mechanisms. The half-life of the fluorescence emitted by the xenobots in response to the presence of a virus could be modeled by a differential equation. It is worth noting that this proposed application for xenobots is currently in the conceptual stage and has not yet been tested or implemented in practice [15,21,9].

In addation, there are also some uses away from the human body that is available for a specific type of design that has been discovered, and this type is the one that rotates around an object and surrounds it like a circle then it disperses after sticking to it, which leads to the scattering of this target into small pieces, making its decomposition easier and not affecting the environment. Also, it can be used in the oceans to collect microscopic plastic pieces by piling them in a specific place, then driving them to recycling centers or to places where humans can easily collect them, unlike the traditional methods that are used, as they do not negatively affect the environment first because of their non-toxicity and secondly because they depend on energy and it completely decomposes when its energy runs out or when it dies.

Additionally, Xenobot can be used as a scientific tool to study how cells cooperate to build complex bodies during formation. This use is based on the unique properties of Xenobot, such as its biocompatibility and ability to be programmed with specific behaviors, which make it well-suited for studying cellular and developmental biology. On the other hand, Xenobot could serve as a basic reference to understand the evolution of multicellularity, exobiology, artificial life, basal cognition, and regenerative medicine, also this type of robot may help to improve the possibility of establishing intelligence in living and non-living organisms by equipping them with electrically active cells that have been selected for cognitive or computational functions. In the end, it is worth mentioning that most of these uses were suggested and speculated but without practical application [1,9].

Problems may encounter in progressing xenobot evolution:

As previously discussed, the xenobot has many uses and uses and the results of this new living robot were smooth and excellent. However, this type of biological robot has many restrictions and ethical and behavioral questions around it. In another hand, not all the limitations of the Xenobot and how it behaves in the environments in which it is intended to be used were not understood. It may have collateral damage as much as its benefits. Therefore, this type of research is dealt with slowly and greatly to study it.

The development of the equipment used to create this type of robot is also something necessary to understand its limitations more. There are also ethical restrictions, as many scientists object to this type of research because the development of research in the biological field (living organisms) is considered tampering with the ecosystem.

After all, scientists did not reach the degree of full understanding of these things [8], for example, a xenobot can be considered a living robot, but it cannot be considered a complete living being because, for example, living organisms can reproduce, but the xenobot does not have this ability, although it may have a simple sensory perception, but in the future, it may develop into a special intelligence and reach the level of awareness with the development of artificial intelligence technology that's used to develop this kind of robots to a degree that enables it to reach a certain level that makes it superior to the ability of humans to control it [1,22]. Although these assumptions can be challenged, they cannot be ignored, especially when dealing with a system that we do not fully understand [23].

We can also add that some scientists have said that tampering with living organisms and trying to develop them is like playing the role of God [6]. This may be weak to the previously mentioned issues of risk and the essential ethical situation. however, concerns about "playing God" may be similar to the criticism that engineering life "from the ground up" represents or promotes disrespect for life [24,25] but this criticism has been challenged by Douglas in his paper [26].

One can add the possibility that the xenobot may not perform its specific function since it is made of a stem cell that has its agenda and whose fate is governed by signals from the surrounding [7]. In addition to all of this, one of the obstacles to the development of this robot is the possibility of using it in wars and assassinations by using it to transport harmful materials due to its ability to completely decompose after a certain period, so it is difficult to detect it in such a field if it is used [25].

All of these are hypotheses and theories, and this does not prevent us from looking at the positive aspects of biological robots such as serving as a unique model system that facilitates work in multicellular evolution, exogenous biology, artificial life, basic cognition, and regenerative medicine. If equipped with electrically active cells and selected for cognitive or computational functions [17]. Here we can conclude that the development of biological robots first needs to consider ethical and behavioral values, also wait until get a full understanding of this field to avoid unexpected problems to determine the direction and course of action of bio robotics technology.

Thus, from the last 2 sections, we can summarize the advantages and disadvantages of xenobot which are:
Xenobots have several advantages that make them appealing for various applications. For example, they can regulate microplastics, which could be useful for cleaning up pollution in the oceans. They also have self-healing properties, allowing them to repair themselves if they are damaged. Xenobots can also communicate with each other through chemical pheromones, which could potentially be used for various purposes such as detecting and monitoring virus concentrations. In addition, xenobots are non-toxic and have a self-limiting lifespan, making them safer to use in certain applications than traditional robots. They also have the potential to be used as a scientific tool for understanding how cells cooperate to build complex bodies, which could have various applications.

On the other hand, the use of xenobots raises a number of ethical and behavioral questions, such as whether they should be considered living organisms and whether they have rights. Additionally, there is potential for collateral damage as it is not yet clear how xenobots will behave in certain environments and there is a lack of understanding of their limitations. There is also a risk of unintended consequences if xenobots are not fully understood and controlled, and a concern that they may evolve and become more complex over time, leading to unforeseen problems.

Conclusion:
Xenobot is considered a revolution in the world of robotics away from its disadvantages and advantages. Also, away from robots, it is considered a revolution in many fields, the most important of which is the beginning to understand and develop the science of living organisms to be able to benefit from them in many fields due to its consideration of the basis of the ecosystem in contrast to foreign materials such as materials made of metals, plastics, and chemicals. Which harms all living organisms, whether animals, humans, or plants, but knowing its damage, a human cannot live without it so if he can understand and develop the science of living organisms to a level where he can compensate for some uses, it will be great technological progress and a great achievement

So, we can say that Xenobot is the beginning of the implementation of this technology. As we have seen, only one type of biological robot can be used in many fields to the extent that most kinds of medicines can be dispensed with to treat some hard diseases that the human cannot cure 100% until now, which is considered a great help to save the ecosystem facing humans at present time difficulty in maintaining and this is because of the chemical waste that is used in the manufacture of medicines for diseases that Xenobot will treat instead of these medicines.

It is not limited to This is on medicines due to their various uses in different fields. Therefore, in the end, we can see how important these vital robots can make in our lives and they will make a big jump in the future in different fields because this kind of robot as we say will make everything different and easy especially in the medical field which is the most important thing.

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