Investigation and Fabrication of Micromotors for Biomedical Applications

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Abstract: The research of micromotors have received extensive attention in recent years, and their iconic feature is the ability to utilize external energy to achieve autonomous motion then carry out various tasks. Micromotor for biological applications is a common type of micromotors, this specific type of micromotor is capable to be applied to drug delivery system and transportation of cells. The content of this article is to introduce examples, potential, and current problems of micromotors based on hydrogels or other kind of environment-friendly materials for cell culture and drug delivery, and to further explore the effects of hydrogels and micromotors on cells and drugs. In addition, methods and steps of the preparation of a four-sided, dual-power Sodium Alginate (SA) hydrogel micromotor is demonstrated and explicitized, the micromotor's ability to achieve independent movement and its potential applications are also explored.
Keywords: Micromotor; Bioengineering; Tissue Engineering; Hydrogel

Introduction

Inspired and influenced by natural biological motors, artificial micromotors, which can convert external energy into motion are considered as a new type of intelligent biomimetic materials. Because its function is similar to the motor in daily life, it is often referred to as micromotor by researchers. Micromotors have received extensive attention due to their wide range of applications. Since researchers first reported millimeter-scale chemically actuated motors in 2002, more and more researchers have proposed various types of novel micromotors with autonomous motion capabilities are developing rapidly. Due to the unique self-transforming ability of micromotors, they may revolutionize bioapplication fields, including active drug delivery, biological surgery, environmental remediation, and micro/nanoengineering.

However, due to the complexity and particularity of diseases in different parts of the human body, although the capability of active movement of micromotors can bring benefits and revolutionary changes to traditional disease treatments, the realization of many advantages of micromotors in disease treatment is still in its infancy and the actual micromotor-based drug delivery system for disease treatment *in vivo* is still far from clinical application. There are still many problems and limitations in the application and research of micromotors. At present, many major diseases (such as cancer, cardiovascular diseases, organ fibrosis, etc.) have limited therapeutic drugs and poor therapeutic effects due to their complex pathogenesis and environment of diseased tissue, thus the need for innovative therapeutics involving micro and nanotechnology is imminent.

Literature Review

In previous literature, a series of micromotors fabricated by different materials and different methods can successfully accomplish a large number of direct medical and biological tasks, such as biosensing, in vivo imaging, cancer therapy, diagnostic analysis, etc., among which drug delivery and cell encapsulation It is the relatively common and main application of micromotors. (Figure 1).

Figure 1

Micromotor Based on Pine Pollen for Drug Delivery[1]

Taking a micromotor based on pollen as an example, the author developed a pollen based micromotor (PPBM) using natural pine pollen as material. After remove the lipid on the outer wall to improve its permeability, Fe_3O_4 magnetic nanoparticles (MNPs) and drugs are filled into the two cavities by vacuum loading. The resulting micromotor can realize the rolling, tumbling and spinning under the manipulation of the external magnetic filed (MF) (Figure 2), which has a great potential as a carrier applies to targeted drug delivery.

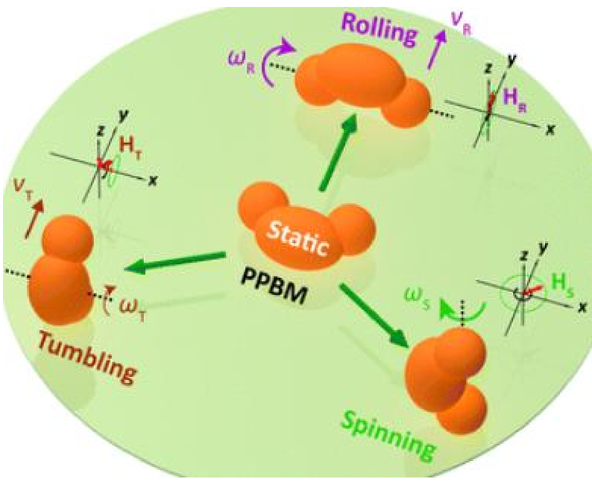

Figure 2

Micromotors for Pickup and Transportation of Circulating Tumor Cells (CTCs)[2]

In this article, The authors prepared a hollow tubular micromotor called microrocket and use H_2O_2 and catalase as a power source to provide traction to transport large cells, for example, CTCs. Antibodies were also attached to the surface of the micromotor, so that the microrocket is able to identify, grab, and transport CTCs (Figure 3) , thus could be applied to extract tumor cell samples for the early detection of cancer and to prevent its recurrence, and to reduce the chances of cancer metastases and recurrence. It can be a solution to efficiently separate cancer cells, diagnose cancer, and prevent cancer recurrence.

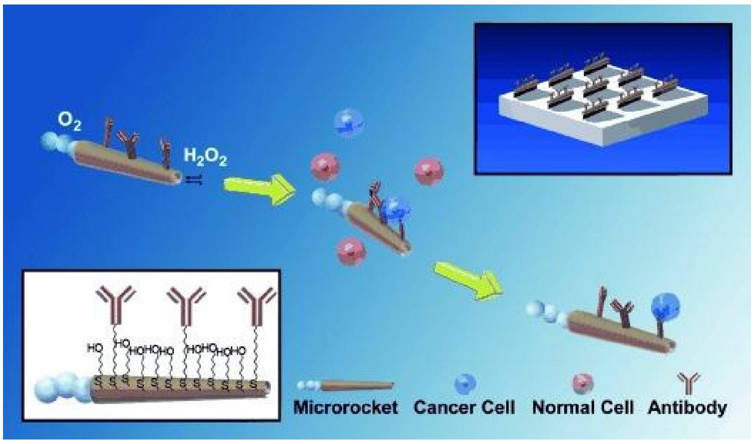

Figure 3

Bio-inspired Helical Micromotors as Cell Carriers[3]

The researchers who wrote this article, developed a SA hydrogel based spiral micromotor, and used as a dynamic cell microcarrier (Figure 4) , and then by further encapsulating MNPs in its raw materials, make the micromotor has high manipulation in the external moving MF, and can achieve rotation and linear movement. At the same time, because SA hydrogel is an environmental-friendly material with good biocompatibility, the micromotor prepared by this material has great potential as a cell carrier, and can be applied into the application of cell inoculation and cell planting. Because of this, the spiral micromotor can be further embedded into other natural structures, stacked together with each other to form cell blocks, which can be used in cell culture.

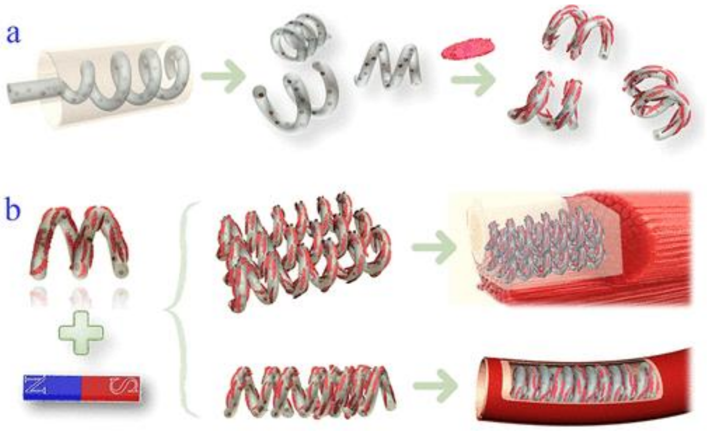

Figure 4

Eight-sided Dual-power Micromotors Fabricated via a Biocompatible Gas-shearing Strategy[4]

In this article, the authors propose an environmentally friendly method for manufacturing multifaceted micromotors with dual power sources, with no organic reagents required for the whole preparation process. The raw material that the author chooses is the biocompatible SA hydrogel, the power source is the Fe_3O_4 MNPs or catalase mixed into the raw material, and then the spherical micromotor is prepared through a specially customized eight-chamber needle. The resulting micromotor can carry out movements under the action of the magnetic field, including rotational motion, linear motion, curve motion and circular motion.

Experimentation

Inspired by the above article, we decided to design and develop a spherical micromotor, with SA hydrogel as raw material, a special custom needle containing four smaller diameter needles for output mixed power source SA raw materials or pure SA hydrogel, and a slightly larger channel for gas to connect high pressure gas, adjust the size and size of micromotor production a solution containing $CaCl_2$ is placed below to help condense the SA hydrogel into a glue. The power source we designed for the micromotor is the Fe_3O_4 MNPs, equipped with MNPs micromotor can rotate on the magnetic stirrer and can be guided to perform other forms of motion; the another power source is the catalase. When the early micromotor and its related movement mode is explored, the cells will be add into part of pre-gel solution, make two of the four surfaces of magnetic motor has cells, and then let the micromotor move for a period of time, then study the cell migration during the period and explore the cell encapsulation of micromotor. (Figure 5).

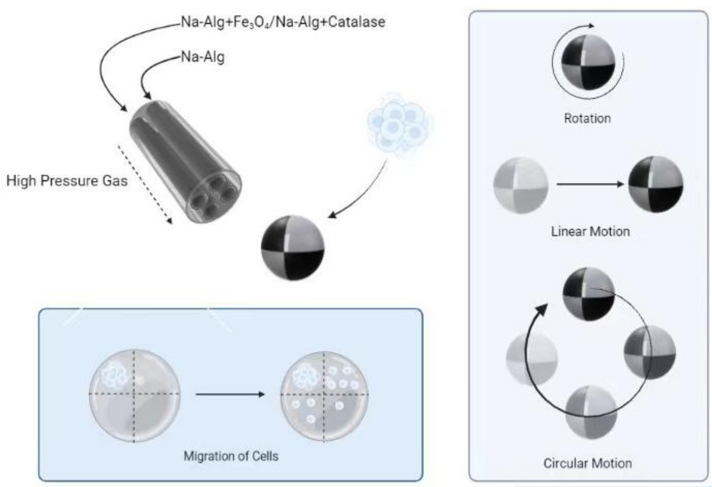

Figure 5

The experiment is divided into two parts. In the first stage (Figure 6) , we will first prepare micromotors equipped with MNPs or catalase, to explore the relationship between air flow and particle size, and to study their movement mode under different conditions. In the second stage(Figure 7) , the cells will be added to the raw material, and the cell migration in the micromotors will be further investigated and explored.

Figure 6

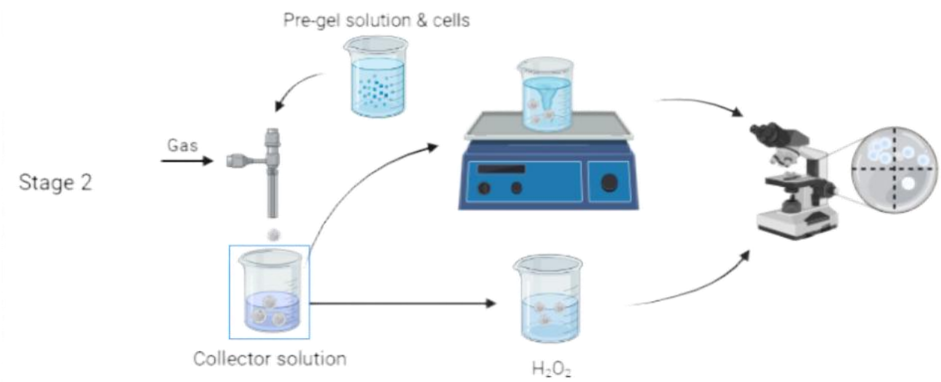

Figure 7

Result and Discussion

Through the experiments, We have successfully prepared bidynamic micromotors with a particle size of around 1mm, It can perform linear motion, rotation and circular motion under magnet guidance or on a magnetic agitator, Flow velocity reduces the particle size of the magnetic motor to some extent, However, if the air flow velocity exceeds a certain threshold value, The regional distribution of the magnetic motor is disrupted by the airflow, Since size is a key factor influencing micromotors in medical applications, The next step we hope is that by regulating the concentration and viscosity of the pre-gel solution, And regulating the viscosity of MNPs to avoid fine internal divisions of micromotors disrupted by airflow, Thus further reducing the diameter of the micromotors, If the particle size of the micromotor reaches a certain size requirement, The cell experiments will be performed very soon.

Conclusion

This research report introduces the inspiration of micro motor, development history and the current problems and the future development direction, in-depth study related to biological application of two categories of micro motor mechanism, use and preparation process, and prepared a double-powered micro motor, ready to further study its performance indicators, provide new ideas for micro motor research, increase its potential in biological applications.

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