Review on Bio-inspired Materials with Nanotechnology Applications in Medical Devices

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Abstract. Nano-biomimetic material is a multidisciplinary field emerging gradually with the development of micro-nano technology, which covers many fields such as materials science, nanotechnology, biology, artificial intelligence, medicine. The existence of micro-nano technology has led to major breakthroughs in many aspects of these fields, giving people possible opportunity to design and modify new drugs, organ-on-chips and so on at the micron or nanometer scale. At present, nano-biomimetic materials have played an important role in drug development and toxicity testing, self-healing of biomedical materials and flexible nanorobots. For example, hydrogels performance has been improved by the addition of some specific nanomaterials. The future research direction of nanoscale-hydrogel binding materials is still under search now. Another new product--Organ-on-chip is also highly dependent on nanotechnology. Three kinds of representative organ-on-chip, heart-on-chip, kidney-on-chip and lung-on-chip are now been supported by microfluidic technology. Their applications and prospect in medicines are hot topics at present. Furthermore, the principle of how nanomaterials improved (Ion-exchange polymer-metal composite) IPMC’s characters and its application in capsule robot field and artificial muscle field are under discussion. But to people’s expectation, IPMC still has a good prospect. This research looks forward to the application of biological nanotechnology in more fields.

1. Introduction

Biomimetics, also known as bionics, biognosis, or biomimicry, is the use and implementation of concepts and principles from nature to creating new materials, devices and systems. This adaptation of methods and systems found in nature into synthetic constructs is desirable because evolutionary pressure typically forces natural systems to become highly optimized and efficient. Nature provides a database of several solutions that already work and thus serve as models of inspiration for synthetic paradigms. Most of the applications developed in the past have been created on the macromolecular level. Only recently has biomimetics begun to approach the micro and sub-micro molecular level of matter. At the turn of the century, however, the interests of scientists and researchers have shifted towards thinking of the matter at the atomic level hence the field of nanotechnology. Products derived from bio-inspired nanotechnology have a high demand in today's healthcare field [1]. Three sorts of products derived from biomimetics nanotechnology are involved in this paper, polymer hydrogels, organ-in-a-chip and ion-exchange polymer-metal composite (IPMC).

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1.1. Polymer Hydrogel
Polymer hydrogel has biomimetic properties, biocompatibility and flexible structures, thus sensitive to external stimuli such as pH, strength, light and temperature [2, 3]. Recently, several flexible hydrogels have been developed and assembled into different wearable sensors to monitor human motion, possessing properties close to human skin [4-6]. To optimize users’ experience and stabilize the performance, there is a great motivation to integrate more functions into the hydrogel [7, 8]. Severe limitations, however, still exist in the traditional hydrogels with chemically crosslinked polymer networks such as low strength and toughness. Nano-biomimetics plays a significant role in enhancing the properties of hydrogels. In this paper, nanoparticle–hydrogel structures based on biomimicry are illustrated through few examples like mussels, lotus and sundew. The mechanism of their working principles is demonstrated via referring to current research.

1.2. Organ-in-a-chip
Organ-on-chip is a new research direction derived from the development of micro-nano technology and microfluidic technology in recent years. The processing and manufacturing of organ-on-chips are highly dependent on nanotechnology, whose main function is to model and test the toxicity and metabolism of novel drugs in vitro. The main function of the heart chip is to use microfluidic technology to create an in vitro heart model that can monitor drugs and determine drug toxicity by recording and analyzing the information after using the drugs. Magnetic nanoparticles can be used here to convert the information of drug action on the chip into mechanical information, which is easy observed and recorded. The kidney-on-chip is mainly used for the toxicity detection and testing of renal drugs, as well as attempt to replace the function of the kidney. The key point of kidney-on-chip is silicon nanotechnology chip, which has the same process as those used in the computer microelectronics industry. Those organ-on-chips are not expensive, but they are sophisticated enough to act as an ideal filter. lung-on-chip works similar to other organ-on-chips and can be used as an ideal model for drug toxicity testing as well.

1.3. IPMC
IPMC, mimic to bristles of gecko's toes, has the characteristics of good electric field response, strong biological compatibility, etc. As for its mechanism, the theory of hydrated cationic motion has now been widely accepted. The preparation of IPMC is mainly divided into four steps: pretreatment of Nafion membrane, roughening of the membrane, preparation of anode and cathode, as well as ion exchange. Although the Nafion membrane has the advantages of its great stability, its output torque is a little bit small, which causes IPMC just its own short life. Therefore, a large number of scholars try to improve the performance of IPMC by adding some new materials. For instance, carbon nanotubes, graphite, nanoparticles, etc. Because of great elasticity and low driving voltage, researchers at Nanjing University of Aeronautics and Astronautics have designed a capsule robot powered by IPMC.

2. Polymer Hydrogel
Hydrogels are a kind of highly hydrophilic, three-dimensional (3D) polymeric network, capable of absorbing large quantities of water and biological fluids [9]. High water content and biocompatibility of hydrogels allow them to be explored for use in many biological and biomedical applications, such as wound dressings [10], surface coatings and tissue engineering [11].

2.1. Features
Cross-linking plays a significant role in hydrogel functions. Depending on the type of cross-linking, hydrogels can be divided into two categories: (i) chemically cross-linked hydrogels, which are formed by covalent bonding networks [12]. (ii) physically cross-linked hydrogels, which are formed through dynamic cross-linking based on physical entanglements [13].

Polymer hydrogel has biomimetic properties, biocompatibility and flexible structures, thus sensitive to external stimuli such as pH, strength, light and temperature. Recently, several flexible hydrogels have been developed and assembled into different wearable sensors to monitor human motion, possessing
properties close to human skin [12, 13]. To optimize users’ experience and stabilize the performance, there is a great motivation to integrate more functions into the hydrogel [14].

It is an ongoing task to pursue recoverable and highly stretchable hydrogel with desired electrical properties. Although wearable devices developed in recent years have possessed flexibility, their extensibility and recoverability are usually lacked, which are extremely brittle after full swelling [15]. Therefore, applications in the human joint movement are seriously limited [14]. Self-healing is an ability to repair inner or surface damages spontaneously [16, 17]. The main strategies for self-healable hydrogels are to use the dynamic covalent bonds or supramolecular interactions such as hydrogen bonding, electrostatic interaction, host-guest recognition, hydrophobic association, and π−π stacking [18]. Therefore, the hydrogel can be easily reshaped and reused, which greatly reduces the robustness and service lifespan of hydrogel devices.

Self-adhesiveness is another ideal attribute of multifunctional hydrogels. When attached to the skin, a normal hydrogel with poor adhesiveness causes unwanted interface delamination between the electronic devices and the human body. One solution is to use adhesive tapes to facilitate adhesion with the human body, involving tedious operation processes in practical applications [18]. Adhesive hydrogel is able to attach to biological tissues strongly, minimizing the device size and enhancing the users’ experience, which provides a vital property for biomedical devices applications. Conductive hydrogel is typically prepared by incorporating conductive nanomaterials or inherently conductive polymers into a hydrogel matrix. Human motion is transformed into electrical signals like capacitance and current through conductivity [19].

Ideal hydrogel sensors are supposed to combine the four significant features, self-adhesiveness, self-healing, high conductivity, high strength and toughness. However, it is difficult to achieve in practice. Song et al. used flexible, stretchable and transparent ionic conductive hydrogel in conductive fiber to improve the conductivity, however, spinnability, freeze temperature and mechanical properties decreased. The perfect combination of functions has been attracting a tremendous amount of attention recently [20]. Moreover, in up-to-date researches, the bio-inspired hydrogel is a hot spot to achieve this. Xu et al. [21] synthesized a zwitterionic natural polymeric conductive hydrogel with high stretchability, self-healing shape and good conductivity by sacrificing adhesiveness.

2.2. Nanotechnology and Hydrogel

However, severe limitations dictated by traditional hydrogels composed of chemically crosslinked polymer networks, such as low strength and toughness have hindered the applications [2]. Nanotechnology plays a significant role in enhancing the properties of hydrogels. Nanoparticle–hydrogel superstructures represent an emerging category of nanomaterial and are generally composed of hydrated, crosslinked polymeric networks incorporated with nanoparticles. Significant advances have been made in both nanoparticle and hydrogel platforms in recent studies. For example, the incorporation of inorganic nanoparticles (NPs) has been proved to reinforce the hydrogel matrix, resulting in stronger and tougher nanocomposite gels. Even though specific interactions with the hydrogel polymer chains, nanoparticles can effectively contribute to the polymer network elasticity and increase the mechanical strength of the hydrogels as a result [3]. Besides, if the polymer–particle interfacial cross-links are mechanically reversible, which may involve electrostatic interactions or hydrogen bonds, dynamic hydrogels with intrinsic self-healing capabilities can result [4]. Plus, nanoparticles can introduce a variety of inorganic materials’ functions into the hydrogel system, such as electronic conductivity and magnetic response, which may lead to stimuli-responsive hydrogel applications [5].
2.3. Bio-inspired Hydrogels with Nanotechnology

2.3.1. Mussel-inspired Hydrogels

2.3.1.1. Principles
Mussels adhere their byssal threads onto a variety of solid surfaces underwater, and research has revealed that the adhesive protein of mussels shows high adhesiveness to many surfaces by forming coordination bonds with transition metal ions in the bulk thread [6]. This mussel-inspired mechanism provides new approaches for integrating biosensor adhesiveness and multifunctional conductive hydrogels design [6].

2.3.1.2. Nanocomposite Hydrogels via Metal Coordination
Inspired by the mussel, catechol-containing adhesives have now been developed for multiple surfaces, [7] and catechol-modified polymer side groups are extensively applied in nanomaterials surface engineering [8]. In addition, since the metal coordination bonds are mechanically reversible, they have been demonstrated to function as dynamic cohesive cross-links in bulk self-healing of polymer materials [22].

Li et al. [23] incorporated iron oxide nanoparticles (Fe3O4 NPs) with a catechol-modified polymer network to obtain hydrogels cross-linked via reversible metal-coordination bonds at Fe3O4 NP surfaces. Unique material mechanics result from the supramolecular cross-link structure dynamics in the gels. In contrast to the previously reported fluid-like dynamics of transient catechol–Fe3+ cross-links, the catechol–Fe3O4 NP structures provide solid-like yet reversible hydrogel mechanics. This mechanism also indicates how to develop hydrogels with remote-controlled self-healing dynamics.

2.3.1.3. Dopamine-tale-PAM (DTPAM) Hydrogel for Sensing Applications
With structural similarity with adhesive protein of mussels containing amine and catechol groups, polydopamine (PDA) has been extensively investigated to improve the adhesiveness of hydrogels [24]. During the dopamine self-polymerization process, excellent biocompatibility and cell affinity are also shown. Additionally, between PDA chains, there exist cation π interaction, hydrogen bonding and other noncovalent interactions existing due to the presence of catechol groups [25], which could provide the self-heal ability for hydrogels. PDA also has a powerful ability for binding with nanoparticles, leading to a new nanocomposite hydrogel through promoting nanomaterials’ uniform distribution in the network. Jing et al. [6] reported a multifunctional hydrogel, capable of integrating special functions are induced in light, motivated by the mussel adhesive mechanism. It was found that tale induced partial dopamine oxidation, and polydopamine-modified tale particles achieved uniform dispersion in the PAM hydrogel, resulting in significantly high stretchability, self-healing, self-adhesion, conductivity and biocompatibility. The developed dopamine-tale-PAM (DTPAM) hydrogel incorporates desirable features, highly suitable for wearable sensors for detecting human motion.

2.3.2. Other Bio-inspired Hydrogels

2.3.2.1. Sundew-inspired Hydrogels for Wound Healing
Adhesive hydrogels secreted from the leaves of sundew (Drosera) have long attracted interests due to their excellent physical, chemical, and biological properties [26]. Previous studies demonstrated that sundew’s unique adhesive architecture consists of an intricate network of nanofibers and nanoparticles [26]. The linear arrangement of nanoparticle-derived nanofibers makes sundew adhesive hydrogel an excellent accelerator for wound healing [27].

However, the advancement of sundew-derived wound-healing therapeutics still faces the limitation of low yield from the plant [28]. It is possible to synthesize sundew-inspired adhesive hydrogels with wound-healing functions with the structural traits and morphological characteristics known.

Sun et al. [29] reported a sundew-inspired adhesive hydrogel overcoming the drawbacks of natural sundew hydrogels and can be used in combination with stem-cell-based therapy to enhance wound-
healing therapeutics. They synthesized adhesive hydrogels comprised of sodium alginate, gum arabic, and calcium ions to mimic the properties of the natural sundew-derived adhesive hydrogels. The sundew-inspired hydrogels are proved to have the capability of wound-healing through superior adhesive strength, nanostructure, and shearing resistance when compared to other hydrogels in vitro.

2.3.2.2. Lotus-inspired Spiral Hydrogels

Compared to those of some load-bearing tissues (such as ligaments and tendons), the limited mechanical properties of hydrogels (low strength and toughness) have hindered the applications of hydrogel materials, particularly hydrogel fibers as structural biomedical materials [30].

Lotus (Nelumbo nucifera Gaertn) is an aquatic perennial plant widely cultivated throughout Asia. A famous Chinese say is “the lotus roots may break, but the fiber remains joined”, which indicates the unique structure and mechanical properties of the fiber. This outstanding toughness of lotus fibers is vital for the lotus to resist lodging and breaking off and is relevant to its regular spiral microstructure [31]. Therefore, it is possible to find an ultrastrong and ultratough hydrogel fiber with a lotus-fiber-mimetic structure. Guan et al. [32] reported a biomimetic hydrogel fiber with the lotus-fiber-mimetic spiral structure providing unique characteristics, such as superstretchability and good energy dissipation, resulting in high toughness and strength. This biomimetic hydrogel fiber has a 3D cellulose nanofiber network produced by bacteria. Unlike hydrogels formed by covalently bonded cross-linked polymer molecules, this hydrogels are formed by a reversible hydrogen bond between cellulose nanofibers. This 3D cellulose nanofiber network provides BC hydrogels with good plasticity, which is different from molecule-based hydrogels and results in outstanding properties, such as high strength, high hydrophilicity, porous structure, and excellent biocompatibility, which make it a promising hydrogel fiber for biomedicine.

3. Organs-on-a-chip

3.1. History of drug testing

With the high incidence of various diseases in modern times, researchers and professionals in the medical fields are actively seeking new ways to understand the mechanism and treatment of diseases. In order to screen for useful drugs and study pathogenesis effectively, establish an in vitro model is necessary, it has an important indicating function for finding the final treatment. In the early days, animal models were the most common in vitro disease models that people used. However, due to the differences between animal and human body structure and physiological mechanism of action, the final results obtained in the experiments of the animal model cannot rely completely on a basis in clinical practice. Another widely used technique, in vitro cell culture, is also one of the mainstream traditional methods of in vitro model construction. Usually, researchers would choose human cells or animal cells that need to be studied, such as tumor cells, to observe the conditions of the cells in petri dishes by controlling the physical and chemical conditions. But with the development of society and the ascend of people's cognition, the discussion about the ethical issues of animal experiments gradually appeared in the public view. The animal model establishment has to face not only the cost problems but also the long experimental circle problem, and those make it has many certain limits [33]. Furthermore, though the in vitro cell culture technology is low in price and easy to operate, it cannot create an effective simulation of the real physical and chemical environment, as well as let cells remain consistent with the shape in the body. Therefore, such two methods at present of building disease model are able to reach the experiment goal accurately.

3.2. Development of organ-on-chip

In this context, with the development of nanotechnology and the emergence of microfluidic technology, organ-on-chip has been created and gradually becomes a new choice for in vitro disease model construction and drug toxicity test [34]. Organ-on-chip’s size is generally maintained at the micron level, it is through the nano machining technology and microfluidic technology, using organic glass, hydrogel
[35] and so on as the material base, cultivate the corresponding cell on the surface, so as to build the smallest basic unit of one or many organs, such as glomerular, alveolar and hepatic lobule [36]. The invention of the organ chip enables the three-dimensional culture of cells in vitro and largely reproduces the real activity level of important tissues and organs in vitro. At the moment, the types of organ-on-chip that under research are including liver-on-chip, heart-on-chip, kidney-on-chip, lung-on-chip, intestinal-on-chip, etc. These chips are still in the laboratory research stage. How to achieve mass production of organ-on-chip and how to solve the flux and nondestructive testing problems of chip still need further research.

3.3. Three types of organ-on-a-chip

3.3.1. Heart-on-a-chip
In recent days, the increased risk of heart disease has attracted people’s attention about developing relative drugs as well as searching for better ways to test them. However, as one of the most important and accurate organs in the human body, its working environment is changeable and complex, which means is a hard job for researchers to build such a reliable testing platform in vitro. Furthermore, for widely use, the material and processing technology should be cheap as well.

3.3.1.1. Drug Testing
In the 1970s, "Cardiotoxicity" was raised to describe the cardiac complication caused by adriacin doxorubicin and so on. It was also one of the main reason that led to the failure of the drug’s clinical test. Xi Zhang and his workmates [37] has mentioned that drug preclinical assessments are necessary before putting the drug into clinical use. They used high-speed impedance detection technology to evaluate how efficient the drug is on the heart-on-chip. Therefore, it was possible to measure the contraction and relaxation of cardiomyocytes in real-time. When the heart beating is in a stable frequency and amplitude, the toxicity of the drug can be easily known by observing the change of the signals coming out. To simulate and evaluate drug toxicity with more accurate fluid flow, Kamei [38] and his team developed a new heart-on-chip. This chip mimics a more realistic circulation loop by growing tissue cells from different organs in chambers. Cells from different tissues were cultured in three sets of artificial blood circulation circuits in one device, which provided accurate fluid manipulation through pneumatic valves and pumps to simulate drug-induced reactions. In addition, soft lithography technical has been modified by numerical optimization simulation. Soft lithography, as a basic technology applied in microfabrication, makes it possible to fabricate nanoscale 3D structures [20]. The combination of microfluidic technology and soft lithography allows for a high degree of integration of pneumatic valves and pumps on a chip of limited size and enables monitoring of precise flow control at the micron and nanometer scales. To build a testing heart-on-chip is a high reliance on these micronano techniques. Except for using electronic signals to observe the condition changing, mechanical signals can be used as well. Zhao [21] and his team is the first to use a microfluidic spinning approach for the design of microfibers. It can produce a series of microfibers with different morphology and structure. Nanometer magnetic particle has also been used to create a magnetic responsive helical fiber micromotor. Magnetic nanoparticles can also be added to the Na-alginate solution, and the mixtures were pumped into the microfluidic devices to fabricate helical microfibers with different function [39]. By combing the microfiber with the structure to cultivate cells, the beating of myocardia cells would bring measurable mechanical changes. Therefore, the influence of the drug on the heart cell is able to know. The toxic effects of drugs on the heart that tested would inevitably be affected by other organs as well as blood circulation in the body. Therefore, the difference between toxicity monitoring and the real situation still cannot be ignored by using the heat-on-chip independently. Building a multi-organ circulatory system on a chip is still under exploration, so the heart-on-chip technology still needs to be improved.
3.3.2. Kidney-on-a-chip
The irregular work and rest of modern people’s life lead to a lot of kidney diseases such as proteinuria, chronic nephritis, uremia and so on. Kidney-specific drug development and toxicity testing are urgently needed. However, the proportion of renal drug toxicity in clinical drug toxicity is quite high [40]. Renal drug monitoring highly relies on a simulated three-dimensional in vitro drug detection model. Therefore, kidney-on-chip is mainly relying on simulating the basic unit of kidney construction ---the glomerulus and its proximal segment structure to test the real situation of the kidney under the effect of the renal drug.

3.3.2.1. Make kidney patients get rid of dialysis completely
Dialysis is an important way to maintain life for patients with severely impaired kidney function. It is used to expel metabolic wastes from the body. However, dialysis is not only expensive but also has a great impact on the of patients’ life quality. Nissenson A.R [41] and his team has used chip and nanostructure polyethersulfone (PES) membrane to create a micro-scale dialyser. However, this kind of chip only has the function of filter the wastes, it’s not able to stimulate the function of glomerular. William H. Fissell IV and Amanda Barker [42] from Vanderbilt University has tried to create a kind of organ-on-chip that containing living kidney cells and nano-silicon filter membrane, in order to completely replace the function of the kidney. The key point is to make the silicon nanotechnology chip, the scale of the chip should be as small as possible but still with high flux. Zhu [43] and his team was aimed to find create a multi-functional kidney-on-chip. They wanted to combine glomerular function and tubular function in the same microdialysis device to prepare an artificial kidney microchip dialysis device with multiple functions. This research will pave the way for future portable or implantable artificial kidney dialysis systems.

3.3.2.2. Kidney-on-a-chip in drug development and drug toxicity test
Kidney-on-chip models can be used to test drug nephrotoxicity, in vitro biomarker analysis and in vivo microenvironment simulation. Weber et al.[44] reconstructed the physiological function of human proximal renal tubules in vitro by combining the single-channel micro-physiological system (MPS) with proximal renal tubular epithelial cells (PTECs). This kidney-on-chip can safely detect polynynixin by recording and analyzing the strength of damage signals related to miRNAs and so on. It could help in the future with drug development in the areas of toxicity analysis and toxicological testing of compounds. Qu et al. [45] has designed a multilayer kidney-on-chip that includes glomeruli, Bowman capsules, proximal renal tubules, and capillary tubules. The co-existence of these structures can simulate a more realistic nephron working condition. They added the drug doxorubicin and cis-platinum to the bloodstream of an imitation kidney blood made of bovine serum albumin and so on. Fluorescence imaging is used to record and analyze the effects of the drug on the kidneys. The results show that the renal cells in the kidney-on-chip designed by Qu are more sensitive to external drug changes, which demonstrates the influence of the microenvironment on drug toxicity testing. And this also plays an indicator role for the detection of drug nephrotoxicity in the future.

3.3.3. Lung-on-a-chip
Air pollution is a constant problem that threatens the lives and health of modern people. Polluting gas emissions and haze make more and more people suffer from lung diseases. Common symptoms include pulmonary edema, pneumonia, etc. At the same time, smoking as a recreational activity also brings a lot of health risks to the lungs, and a lot more cases of lung cancer have been reported. Today, with the development of micro-nano technology, it is possible to construct a simulated alveolar model in vitro. Just like other kinds of organ-on-chips, lung-on-chip is mainly used to estimate the toxicity of relative drugs. Other applications like assessing the air pollutant PM2.5’s influence on the lung is also known now.
3.3.3.1. Multi-sensor lung cancer-on-chip platform

In clinical practice, real-time monitoring of the physiological state can not only help determine the state of micro-physiological systems but also provide information to evaluate their response to different external stimuli. Muhammad Asadullah Khalid et al. [45] aimed to use a transepithelial electrical (TEER) impedance sensor to monitor the toxicity of doxorubicin (DOX) and docetaxel. They used an elastomeric microfluidic channel to print on the lower side of the top glass of a glass-based microfluidic chip and the chip has equipped with TEER impedance sensing electrodes inside. A highly sensitive non-invasive optical pH sensor, TEER impedance sensor, and a 3D-printed dedicated digital fluorescence type microscope were used for real-time monitoring on the NCI-H1437 lung cancer cell in this research and its result has good reference value. Therefore, toxicology studies and future personalized drug designs may be able to rely on this multi-sensor lung cancer-on-chip in the future.

3.3.3.2. PDMS Membrane Based Lung-on-chip and Nanofiber Supported PLGA Membrane Based Lung-on-chip

Polyethylene terephthalate (PET), Polymethylsiloxane (PDMS), etc can be used to establish the monolayer reticulated porous membrane. The artificial membrane can be used to build the structure of alveolar, in order to stimulate the barrier effect. Huh et al. [46, 47] built the chip's two-layer structure and the micro-nano porous structure in between using PDMS as the material. PDMS has a certain flexibility, which can be deformed under the vacuum conditions brought by the air pump. This can bring cell deformation, restoring the breathing state of the human body. By using air pumps on either side of the chip, they simulated the actual periodic operation of cells above and at the bottom of the membrane (cultured epithelial cells on the upper side and endothelial cells on the bottom side) to reconstruct the alveolar operation during respiration. Yang et al. [48] use poly(lactic-co-glycolic acid) (PLGA) electrospinning nanofiber as the cell scaffold developed a new kind of lung-on-chip, which stimulate the microenvironment of alveolar. This new chip not only highly stimulate the environment in vitro (by creating a 3D environment for culturing cells) but also use PLGA as a more suitable material to stimulate the alveolar respiratory membrane. With the combination of electrospinning with microfluidic chip technology, PLGA nanofiber membrane was able to be created as the scaffold material for 3D cell culture. These two kinds of lung-on-chip mentioned above can both provide reliable data in lung drug toxicity testing, speed up the development of new drugs and the research process of drug toxicology.

4. IPMC

IPMC (Ion-exchange polymer-metal composite), mimic to bristles of gecko's toes, is a new nano-scaled intelligent material in the 21st century. IPMC uses Nafion membrane as substrate material. Both sides of the film are coated with precious metal electrodes, Pt electrodes are mainly chosen. Due to its outstanding character and multipurpose features, it has arisen the interests of scientists from different fields and its forming methods are under research as well. In recent years, scholars, research institutions and universities were work in cooperation in order to optimize the preparation methods of IPMC for meeting the needs of developing future related cutting-edge products.

4.1. Features

It has the features of good electric field response, strong biological compatibility, strong mechanical and electrical coupling. Except for the given characters above, another property which is also the most significant one is that IPMC can bend a lot under low voltage and that’s also one of the reasons why IPMC is an excellent flexible driving material for soft robots.

4.2. Mechanism

At present, the energy change inside IPMC is very complex, including the calculation of the mutual conversion of mechanical energy, electric energy, internal energy and the energy of the material itself. Therefore, people have not agreed on the driving mechanism of IPMC. However, among a variety of mechanisms, involving the theory of hydration cationic motion, the theory of ion electrostatic action and
the theory of Coulomb force action, the first theory mentioned above is the one that been widely accepted by people nowadays. As shown in figure 1, cations in the IPMC proton exchange base membrane combine with water molecules. Under the driving voltage, these hydrated cations then swim through tiny pores, making the cathode more and more water molecules. Gradually, the water molecules will be less in the anode. This series of actions ultimately lead the water molecules to become unevenly distributed, making the IPMC bend toward the anode.

4.3. Modification Research
The preparation of IPMC is mainly divided into four steps: pretreatment of Nafion membrane, roughening of the membrane, preparation of anode and cathode, as well as ion exchange. Although the Nafion membrane has the advantages of its great stability, its output torque is a little bit small, which causes IPMC just its own short life. Therefore, a large number of scholars try to improve the performance of IPMC by adding some new materials. For instance, nanoparticles, carbon nanotubes, graphite, etc. In this way, the last two steps of the whole IPMC preparation can be modified.

4.3.1. IPMC modification with nanoparticles

4.3.1.1. Using silver nanoparticles
Tan, etc have combined silver nanoparticles with carbon materials, in order to modify electrodes [51]. Silver nanoparticles inherit strong electrical conductivity and photomagnetic characteristics. At the same time, silver nanoparticles also have a bigger surface area as well as excellent catalytic performance, thus choosing them can enlarge the surface area of electrodes and speed up the rate of electron transfer. However, with high absorbability, silver nanoparticles cannot disperse evenly on the surface. Therefore, the researchers have combined silver nanoparticles with other materials, such as carbon nanotubes or graphite. In this way, the modified electrode has better catalytic performance and stability.

4.3.1.2. Using copper nanoparticles
Instead of Pt electrodes, Yang, etc have replaced platinum ions with copper nano-scaled ions [52]. In order to prepare copper type ionic polymer-metal composites, The researchers have used the method of electroless plating. The data of the experiment has shown that the voltage of Cu-IPMC can be achieved at 10V, which is much higher than Pt-IPMC. At the same time, the power output of it could reach 17mN, the biggest displacement of this Cu-IPMC is up to 30mm. The result tells us that the traditional Pt-IPMC can be replaced by the Cu-IPMC because of its great power put out as well as its cheap price.

4.3.2. IPMC modification with nanotubes
Sui, etc modify multi-walled carbon nanotubes (MWCND) by electrophoresis deposition [53]. through this operation, the MWCND will then grow on Ag-IPMC surfaces, acting as electrodes. The researchers have chosen to use poly dimethyl diallyl ammonium chloride(PDDA) to modify multi-walled carbon nanotube (MWCN) by the method of electrophoresis deposition. Therefore, MCNT then has grown on IPMC surfaces.

4.3.3. IPMC modification with graphenes
Xv et al. use polydiene dimethyl ammonium chloride to do charged modification on graphenes in the methanol electrolyte [54]. So the productivity of the IPMC actuator will be better.

4.4. Main Application
Because of the great elasticity and low driving voltage, IPMC has the characters resemble muscles. In the medical field, researchers at Nanjing University of Aeronautics and Astronautics have designed a capsule robot powered by IPMC [55]. Through capsule endoscope in the robot, our diseases about intestinal tracts can be well detected [56]. Nowadays, this kind of capsule robot has been studying and hopefully, it can be more powerful.
5. Conclusion
To conclude, hydrogel, organ-on-a-chip and IPMC are all of the great nano-sized biomimetic materials. Each of them plays an important role in different fields of medical science. For polymer hydrogel, biomimicry and nanotechnology play a significant role in improving its functions, such as strength and toughness, self-healing and self-adhesive ability. Ideal hydrogel for sensing is expected to combine the four critical functions, self-adhesiveness, self-healing, high conductivity and strength. Therefore, in the future, it's promising to develop such a multifunctional hydrogel inspired by biotechnology with the aid of nanotechnology, which will be highly useful for sensing applications. For organ-on-a-chip, the toxic effects of drugs in the body are highly dependent on the circulation construction of the organ, which means that the accuracy of drug testing on a single organ chip still have shortcomings. In the future, it is necessary to continue to study the joint culture of multiple organ cells on a single organ chip. For IPMC, future research should not only pay attention to the modification but also is supposed to develop the performance of the water.

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