

A Theoretical Research on the Biological Applications of Nanofluids / Ferrofluids due to the Amazing Properties of Nanofluids / Ferrofluids

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Abstract

Nanofluids are suspensions of nanoparticles in fluids. They show substantial augmentation of their properties at modest nanoparticle concentrations. They have also shown many interesting properties, and the distinctive features offer unprecedented potential for many applications. Most of the publications on nanofluids are about understanding their behavior so that they can be utilized where straight enhancement of nanofluids is paramount as in many industrial applications, nuclear reactors, transportation, electronics as well as biomedicine and food. My paper focuses on presenting the wide range of biological applications that involve nanofluids, prominence to their improved properties that are controllable and the specific characteristics that these nanofluids possess that make them suitable for such applications. Nanofluid as a smart fluid, where the properties like heat transfer, thermal properties and so on, will be used in many biological applications, has also been reported.

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Nanoparticles -

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magnetic properties of, 75.75.Fk

optical properties of, 78.67.Bf

phonons in, 63.22.-m

structure of, 61.46.Df

thermal properties of, 65.80.-g, 82.60.Qr

Sensors - biosensors, 87.85.fk

ZnO films (dielectric films), 77.55.hf

Introduction

Nanofluids are a new class of fluids engineered by dispersing nanometer-sized materials (nanoparticles, nanofibers, nano-

tubes, nanowires, nanorods, nanosheet, or droplets) in base fluids. In other words, nanofluids are nanoscale colloidal sus

pensions containing condensed nanomaterials. They are two-phase systems with one phase (solid phase) in another (liquid phase).

Nanofluids have been found to possess enhanced thermo-physical properties such as thermal conductivity, thermal diffusivity, viscosity and convective heat transfer coefficients compared to those of base fluids like oil or water. It has demonstrated great potential applications in many fields. In this paper we will review the biological applications of nanofluids due to their important characteristics and advantages of their properties.

In recent years, nanofluids have attracted more and more attention. The main driving force for nanofluids research lies in a wide range of applications. Although some review articles involving the progress of nanofluid investigation were published in the past several years [1-6], most of the reviews are concerned on the experimental and theoretical studies of the thermophysical properties or the convective heat transfer of nanofluids.

The purpose of this paper will focus on the applications of nanofluids based on biology, especially the new application trends for nanofluids in addition to the heat transfer properties, i.e., thermal properties of nanofluids. We will try to find some challenging issues that need to be solved for future research based on the review on these aspects of nanofluids. My only aim is to expose the applications due to amazing properties of nanofluids.

This paper involves three sections: First section includes the applications of nanofluids in biomedical side. In the second section, we have shown how used a new initiative which takes advantage of several properties of certain nanofluids, in cancer imaging and drug delivery. Third section discusses the use of Nanocryosurgery. In the fourth section, we have shown how nanofluids use in medicine.

Theory

• Biomedical application

Some special kinds of nanoparticles have antibacterial activities or drug delivery properties, so the nanofluids containing these nanoparticles will exhibit some relevant properties.

1) Bacteriostatic activity against

Organic antibacterial materials are often less stable particularly at high temperatures or pressures. As a consequence, inorganic materials such as metal and metal oxides have attracted lots of attention over the past decade due to their ability to withstand harsh process conditions. The antibacterial behaviour of ZnO nanofluids shows that the ZnO nanofluids have bacteriostatic activity against [7].

Electrochemical measurements suggest some direct interaction between ZnO nanoparticles and the bacteria membrane at high ZnO concentrations. Jalal et al. prepared ZnO nanoparticles via a green method. The antibacterial activity of suspensions of ZnO nanoparticles against *Escherichia coli* (*E. coli*) has been evaluated by estimating the reduction ratio of the

bacteria treated with ZnO. Survival ratio of bacteria decreases with increasing the concentrations of ZnO nanofluids and time [8].

Further investigations have clearly demonstrated that ZnO nanoparticles have a wide range of antibacterial effects on a number of other microorganisms. The antibacterial activity of ZnO may be dependent on the size and the presence of normal visible light [9].

Recent research showed that ZnO nanoparticles exhibited impressive antibacterial properties against an important food-borne pathogen, *E. coli* O₁₅₇:H₇, and the inhibitory effects increased as the concentrations of ZnO nanoparticles increased. ZnO nanoparticles changed the cell membrane components including lipids and proteins. ZnO nanoparticles could distort bacterial cell membrane, leading to loss of intracellular components, and ultimately the death of cells, considered as an effective antibacterial agent for protecting agricultural and food safety [10].

The antibacterial activity research of CuO nanoparticles showed that they possessed antibacterial activity against four bacterial strains. The size of nanoparticles was less than that of the pore size in the bacteria and thus they had a unique property of crossing the cell membrane without any hindrance. It could be hypothesized that these nanoparticles formed stable complexes with vital enzymes inside cells which hampered cellular functioning resulting in their death [11]. Bulk equivalents of these products showed no inhibitory activity, indicating that particle size was determinant in activity [12].

Lee et al. reported the antibacterial efficacy of nanosized silver colloidal solution on the cellulosic and synthetic fabrics [13]. The antibacterial treatment of the textile fabrics was easily achieved by padding them with nanosized silver colloidal solution. The antibacterial efficacy of the fabrics was maintained after many times laundering. Silver colloid is an efficient antibacterial agent.

The silver colloid prepared by a one-step synthesis showed high antimicrobial and bactericidal activity against Gram-positive and Gram-negative bacteria, including highly multi-resistant strains such as methicillin-resistant *Staphylococcus aureus*. The antibacterial activity of silver nanoparticles was found to be dependent on the size of silver particles.

A very low concentration of silver gave antibacterial performance [14]. The aqueous suspensions of fullerenes and nano-TiO₂ can produce reactive oxygen species (ROS). Bacterial (*E. coli*) toxicity tests suggested that, unlike nano-TiO₂ which

was exclusively phototoxic, the antibacterial activity of fullerene suspensions was linked to ROS production. Nano-TiO₂ may be more efficient for water treatment involving UV or solar energy, to enhance contaminant oxidation and perhaps for disinfection.

However, fullerol and PVP/C₆₀ may be useful as water treatment agents targeting specific pollutants or microorganisms

that are more sensitive to either superoxide or singlet oxygen [15].

Lyon et al. proposed that C₆₀ suspensions exerted ROS- independent oxidative stress in bacteria, with evidence of protein oxidation, changes in cell membrane potential, and interruption of cellular respiration. This mechanism requires direct contact between the nanoparticle and the bacterial cell and differs from previously reported nanomaterial antibacterial mechanisms that involve ROS generation (metal oxides) or leaching of toxic elements (nanosilver) [16].

2) Nanodrug delivery

Over the last few decades, colloidal drug delivery systems have been developed in order to improve the efficiency and the specificity of drug action [17]. The small size, customized surface, improved solubility, and multi-functionality of nanoparticles open many doors and create new biomedical applications. The novel properties of nanoparticles offer the ability to interact with complex cellular functions in new ways [18].

Gold nanoparticles provide non-toxic carriers for drug and gene delivery applications.

With these systems, the gold core imparts stability to the assembly, while the monolayer allows tuning of surface properties such as charge and hydrophobicity. Another attractive feature of gold nanoparticles is their interaction with thiols, providing an effective and selective means of controlled intracellular release [19].

Nakano et al. proposed the drug delivery system using nanomagnetic fluid [20], which targeted and concentrated drugs using a ferrofluid cluster composed of magnetic nanoparticles. The potential of magnetic nanoparticles stems from the intrinsic properties of their magnetic cores combined with their drug loading capability and the biochemical properties that can be bestowed on them by means of a suitable coating. CNT has emerged as a new alternative and efficient tool for transporting and translocating therapeutic molecules.

CNT can be functionalised with bioactive peptides, proteins, nucleic acids and drugs, and used to deliver their cargos to cells and organs. Because functionalised CNT display low toxicity and are not immunogenic, such systems hold great potential in the field of nanobiotechnology and nanomedicine [21, 22].

Pastorin et al. have developed a novel strategy for the functionalisation of CNTs with two different molecules using the 1,3-dipolar cycloaddition of azomethine ylides [23]. The attachment of molecules that will target specific receptors on tumour cells will help improve the response to anticancer agents.

Liu et al. have found that prefunctionalized CNTs can adsorb widely used aromatic molecules by simple mixing, forming

“forest-scrub”-like assemblies on CNTs with PEG extending into water to impart solubility and aromatic molecules densely populating CNT sidewalls. The work establishes a novel, easy-to-make formulation of a SWNT-doxorubicin complex with extremely high drug loading efficiency [24].

In recent years, graphene based drug delivery systems have attracted more and more attention. In 2008, Sun et al. firstly reported the application of nano-graphene oxide (NGO) for cellular imaging and drug delivery [25]. They have developed functionalization chemistry in order to impart solubility and compatibility of NGO in biological environments. Simple physisorption via π -stacking can be used for loading doxorubicin, a widely used cancer drug onto NGO functionalized with antibody for selective killing of cancer cells in vitro.

Functional nanoscale graphene oxide is found to be a novel nanocarrier for the loading and targeted delivery of anticancer drugs [26]. Controlled loading of two anticancer drugs onto the folic acid-conjugated NGO via π - π stacking and hydrophobic interactions demonstrated that NGO loaded with the two anticancer drugs showed specific targeting to MCF-7 cells (human breast cancer cells with folic acid receptors), and remarkably high cytotoxicity compared to NGO loaded with either doxorubicin or camptothecin only.

The PEGylated (PEG: polyethylene glycol) nanographene oxide could be used for the delivery of water-insoluble cancer drugs [27]. PEGylated NGO readily complexes with a water insoluble aromatic molecule SN₃₈, a camptothecin analogue, via noncovalent van der Waals interaction. The NGO-PEG-SN₃₈ complex exhibits excellent aqueous solubility and retains the high potency of free SN₃₈ dissolved in organic solvents.

Yang et al. found GO-Fe₃O₄ hybrid could be loaded with anticancer drug doxorubicin hydrochloride with a high loading capacity [28]. This GO-Fe₃O₄ hybrid showed superparamagnetic property and could congregate under acidic conditions and be redispersed reversibly under basic conditions. This pH-triggered controlled magnetic behavior makes this material a promising candidate for controlled targeted drug delivery.

More on Biomedical Applications

Nanoparticles of iron(III) oxide are biocompatible, non-toxic, are chemically active on their surface, and are paramagnetic at particle sizes above a critical limit of about 5 nanometers. They find wide use in biomedical applications. Can be used as con-

trast agents in magnetic resonance imaging, in labeling of cancerous tissues, magnetically controlled transport of pharmaceuticals, localized thermotherapy (where the tissue is labeled by iron oxide nanoparticles, then heated by application of AC field to particles), and preparation of ferrofluids.

Ayse et al presented a simple microfluidic platform that uses biocompatible ferrofluids for the controlled manipulation and rapid separation of both microparticles and live cells. This low-cost platform exploits differences in particle size, shape,

and elasticity to achieve rapid and efficient separation. Using microspheres, we demonstrate size-based separation with 99% separation efficiency and sub-10- μm resolution in <45 s. It also shows continuous manipulation and shape-based separation of live red blood cells from sickle cells and bacteria. These initial demonstrations reveal the potential of ferromicrofluidics in significantly reducing incubation times and increasing diagnostic sensitivity in cellular assays through rapid separation and delivery of target cells to sensor arrays.[29]

- **Cancer Therapeutics**

A new initiative, which takes advantage of several properties of certain nanofluids to use in cancer imaging and drug delivery is there. This involves the use of iron-based nanoparticles as delivery vehicles for drugs or radiation in cancer patients. Magnetic nanofluids are to be used to guide the particles up the bloodstream to a tumor with magnets. It will allow doctors to deliver high local doses of drugs or radiation without damaging nearby healthy tissue, which is a significant side effect of traditional cancer treatment methods. In addition, magnetic nanoparticles are more adhesive to tumor cells than non-malignant cells and they absorb much more power than microparticles in alternating current magnetic fields tolerable in humans; they make excellent candidates for cancer therapy.

Magnetic nanoparticles are used because as compared to other metal-type nanoparticles, these provide a characteristic for handling and manipulation of the nanofluid by magnetic force [29]. This combination of targeted delivery and controlled release will also decrease the likelihood of systemic toxicity since the drug is encapsulated and biologically unavailable during transit in systemic circulation. The nanofluid containing magnetic nanoparticles also acts as a super-paramagnetic fluid which in an alternating electromagnetic field absorbs energy producing a controllable hyperthermia. By enhancing the chemotherapeutic efficacy, the hyperthermia is able to produce a preferential radiation effect on malignant cells [30].

There are numerous biomedical applications that involve nanofluids such as magnetic cell separation, drug delivery, hyperthermia, and contrast enhancement in magnetic resonance imaging. Depending on the specific application, there are different chemical syntheses developed for various types of magnetic nanofluids that allow for the careful tailoring of their properties for different requirements in applications. Surface coating of nanoparticles and the colloidal stability of biocompatible water-based magnetic fluids are the two particu-

larly important factors that affect successful application [31,32].

Nanofluids could be applied to almost any disease treatment techniques by reengineering the nanoparticles' properties. In their study, the nanoparticles were laced with the drug docetaxel to be dissolved in the cells' internal fluids, releasing the anticancer drug at a predetermined rate.

The nanoparticles contain targeting molecules called aptamers which recognize the surface molecules on cancer cells preventing the nanoparticles from attacking other cells. In order to prevent the nanoparticles from being destroyed by macro

phages—cells that guard against foreign substances entering our bodies—the nanoparticles also have polyethylene glycol molecules. The nanoparticles are excellent drug-delivery vehicles because they are so small that living cells absorb them when they arrive at the cells' surface.

For most biomedical uses the magnetic nanoparticles should be below 15 nm in size and stably dispersed in water. A potential magnetic nanofluid that could be used for biomedical applications is one composed of FePt nanoparticles. This FePt nanofluid possesses an intrinsic chemical stability and a higher saturation magnetization making it ideal for biomedical applications. However, before magnetic nanofluids can be used as drug delivery systems, more research must be conducted on the nanoparticles containing the actual drugs and the release mechanism.

- **Nanocryosurgery**

Cryosurgery is a procedure that uses freezing to destroy undesired tissues. This therapy is becoming popular because of its important clinical advantages. Although it still cannot be regarded as a routine method of cancer treatment, cryosurgery is quickly becoming as an alternative to traditional therapies.

Simulations were performed by Yan and Liu [32] on the combined phase change bioheat transfer problems in a single cell level and its surrounding tissues, to explicate the difference of transient temperature response between conventional cryosurgery and nanocryosurgery.

According to theoretical interpretation and existing experimental measurements, intentional loading of nanoparticles with high thermal conductivity into the target tissues can reduce the final temperature, increase the maximum freezing rate, and enlarge the ice volume obtained in the absence of nanoparticles.

Additionally, introduction of nanoparticle enhanced freezing could also make conventional cryosurgery more flexible in many aspects such as artificially interfering in the size, shape, image and direction of iceball formation. The concepts of nanocryosurgery may offer new opportunities for future tumor treatment.

With respect to the choice of particle for enhancing freezing, magnetite (Fe₃O₄) and diamond are perhaps the most popular and appropriate because of their good biological compatibility. Particle sizes less than 10 μm are sufficiently small to start permitting effective delivery to the site of the tumor, either via encapsulation in a larger moiety or suspension in a carrier fluid. Introduction of nanoparticles into the target via a nanofluid would effectively increase the nucleation rate at a high temperature threshold.

Nanofluids are important because they can be used in numerous applications involving heat transfer, and other applications such as in detergency. Colloids which are also nanofluids have been used in the biomedical field for a long time, and

their use will continue to grow. Nanofluids have also been demonstrated for use as smart fluids. Problems of nanoparticle agglomeration, settling, and erosion potential all need to be examined in detail in the applications.

Nanofluids employed in experimental research have to be well characterized with respect to particle size, size distribution, shape and clustering so as to render the results most widely applicable.

Once the science and engineering of nanofluids are fully understood and their full potential researched, they can be reproduced on a large scale and used in many applications. Colloids which are also nanofluids will see an increase in use in biomedical engineering and the biosciences.

- **Medicine**

In medicine, ferrofluids are used as contrast agents for magnetic resonance imaging and can be used for cancer detection. The ferrofluids are in this case composed of iron oxide nanoparticles and called SPION, for "Superparamagnetic Iron Oxide Nanoparticles"

There is also much experimentation with the use of ferrofluids in an experimental cancer treatment called magnetic hyperthermia. It is based on the fact that a ferrofluid placed in an alternating magnetic field releases heat.

Most common applications of ferrofluids in biomedicine involve highly dilute colloidal suspensions of magnetic nanoparticles. Their widest commercial use is as MRI contrast agents. When properly coated with targeting antibodies, they can also be used in hyperthermia therapy for cancer or as sensors to detect pathogens.

Latest research on cancer is partly focused on localized delivery of cancer medicine to the affected part of the body. To achieve the same the medicine is bound to magnetic particles (e.g. ferrofluids) which are biologically compatible. For targeting the same permanent magnets can be used by positioning them at suitable locations of the external body.

To study the interaction between the magnetic fluid particles passing through the blood with the external magnetic field, magnetohydrodynamic equations and finite element analysis are used. Thus the efficacy of such treatments can be estimated.

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Using highly concentrated ferrofluids with live cells has traditionally proven to be a challenge, because it requires a carefully engineered colloidal system. The ferrofluid parameters

that are most relevant to sustaining live cells include pH, ionic strength, and nanoparticle-surfactant combination, together with their overall and relative concentrations.

Finding the right nanoparticle-surfactant combination is crucial in this regard: the ferrofluid needs to be stable at a pH of 7.4, and colloidal stability has to be maintained up to an ionic strength that can sustain live cells. One also needs to pay special attention to the size distribution of the nanoparticles within the ferrofluid. If there exist nanoparticles only a few nanometers in diameter, they could pass through the cell membrane and cause direct cytotoxicity (35).

Finally, there is much hope for future biomedical applications of ferrofluids. For example, researchers are attempting to design ferrofluids that can carry medications to specific locations in the body through the use of applied magnetic fields. Other ongoing work is investigating the use of ferrofluids as contrast agents for magnetic resonance imaging (MRI).

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