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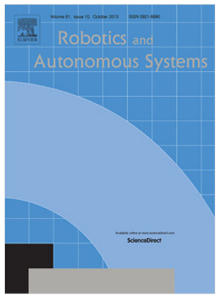

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Macro-micro manipulation platform for inner ear drug delivery

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Abstract

This paper describes the pulling and steering of magnetic therapeutic microparticles for drug delivery based on a macro-micro manipulator system. The macromanipulation system is composed of a 6 Degree Of Freedom (6 DOF) serial manipulator while a linear permanent-based actuator (1 DOF) is equipped at the end-effector as a micropart to precisely steer and pull magnetic microparticles. Using the classical mathematical tools of robotics, we developed the global kinematic model of the robot-device assembly, thus defining a reference trajectory to propel the microparticles. A novel actuator-based permanent magnet has been designed and realized as a robot micro end-effector to control the trajectory of a microparticle along a millimeter-sized workspace. Simulations and experiments were conducted to show the ability of the macro-micro manipulator system to steer particles on a viscous fluid simulating a biological media.

Keywords: Inner ear, drug delivery, Serial manipulator, Microrobots, Permanent magnets

1. Introduction

Robotic agents controlled within the human body allow minimal invasive interventions for the improved treatment and diagnosis of disease, while reducing the risk of complications and allowing for faster recovery. To this end, the magnetic actuation solution has proven to be effective for remote navigation devices or small particles to reach deeper areas in the human body [1], [2]. By using magnetic fields and gradients, pushing and pulling forces can be applied on magnetic microparticles functionalized with drug molecules. As example, recent medical applications demonstrate the difficulty for drug delivery to reach the human ear due to its complex structure [3].

As shown in Fig.1, the ear is a complex and important organ of the living being. It is responsible of two senses which are balance and hearing sense. The first one is given by the three semicircular channels which define the orientation of the head according to the 3 dimensions of the space with respect to the gravitational axis [4], [5]. The second one is related to the anatomy of the cochlea. It allows to treat the sound waves going from 20 to 20.000 Hz and contains a liquid called perilymph [6], through which the sound waves are transmitted to the different regions of the cochlea. Access to the inner ear is limited by the presence of a blood-cochlear barrier, which is anatomically and functionally similar to the blood-brain barrier [7], [8]. As depicted in Fig.1, the inner ear provides a unique opportunity for local drug delivery through the round window membrane (RWM) [9]. Due to tight junctions between cells, substances in systemic circulation encounter substantial physical barriers to entry, preventing many substances with potentially therapeutic effect from gaining access to their inner ear targets. Additionally, the cochlea is a closed space, and cochlear function is sensitive to small changes in fluid volume. Therefore, delicate approaches are required to avoid possible damage from the delivery method itself.

Usually, three conventional medical techniques are used to drug delivery into the human cochlea. The first one is the intratympanic injection [10], [11] where drugs are placed in the tympanic cav-

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