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Stigmergic cooperation of nanoparticles for swarm fuzzy control of low-density lipoprotein concentration in the arterial wall

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ABSTRACT

This paper proposes the use of stigmergic cooperation between two swarms of Fuzzy Nanoparticles (FNPs) and Auxiliary Nanoparticles (ANPs) for intelligent control of Low-Density Lipoprotein (LDL) concentration in the arterial wall, as a novel non-invasive method for prevention of atherosclerosis. Given any desired fuzzy controller, a swarm of FNPs in the aqueous environment of a living tissue can collectively realize an accurate approximation of this controller, which is called swarm fuzzy controller. In this study, the task of the swarm fuzzy controller is to manipulate the pheromone level of the environment as output according to the sensed value of LDL concentration as input. Pheromone is a chemical substance that is used for stigmergic communication between two swarms of FNPs and ANPs. An ANP consists of a drug reservoir connected to a nanoscale valve which is controllable by pheromone concentration. The level of pheromone in the local environment of an ANP determines how much drug should be released by it. The hardware complexity of the proposed approach is lower than nanorobotics to facilitate its manufacturing. Simulation results on a well-known mathematical model demonstrate that this method can successfully reduce the LDL level to a desired value in the arterial wall of a patient with very high LDL level, while its performance is much better in contrast to the previous work of authors. Also, the mass of the released drug in a healthy wall is 16 times lesser than its corresponding value in an unhealthy wall.

1. Introduction

Medical investigations have shown that an abnormally high accumulation of LDL (low-density lipoprotein) macromolecules, ~22 nm in diameter, within the arterial wall plays a significant role in initiation and development of atherosclerosis (or hardening of the arteries) that is one of the major causes of death in humans [1]. Recent advances in nanomedicine lead to manufacturing of nano-meter-sized agents such as drug-encapsulated nanoparticles (DENPs) that can selectively and locally deliver drugs to a specific organ or tissue which can considerably reduce unwanted side effects and thus increase the variety in choosing the type and dosage of drug. In contrast to the existing methods such as global drug delivery, angioplasty, and open surgery, local drug delivery by nanoscale agents have recently received significant attention as a promising non-invasive approach to prevent and treat atherosclerosis. Some of the previous works in this context have been reviewed by authors in their prior research [2].

Authors, in their previous paper [2], proposed the notion of proportional DENP (PDENP) that utilizes a simple piecewise-proportional controller to realize swarm feedback control of LDL concentration within the arterial wall in computer simulation. The hardware complexity of PDENP is much lower than most of the nanorobots in order to be more reasonably realized technologically. But PDENP has a very simple piecewise-proportional controller unit which limits its flexibility and generality. Since the environment of a living tissue is usually uncertain, nonlinear and complex, nanoscale agents need intelligent controller units. But the structure of an intelligent controller unit is usually too complex to be implemented on a single nanoscale agent.

A single nano-meter-sized agent has very limited capabilities either due to the inherent and physical limitations of nanoscale world or due to a need for further technological advancements. In other words, the hardware complexity of any realizable nano-meter-sized agent should remain as low as possible to facilitate its manufacturing within the existing bounds of technologies. Fortunately, nanomedicine has access to large swarms of nanoscale agents in even small volumes of the environment. The central question here is: can we exploit a swarm of very simple nanometer-sized agents to realize intelligent controller unit in a distributed manner

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at nanoscale? As one of the most important methods of intelligent control, this paper aims to focus on fuzzy control [3].

There exist some works in the literature that have applied swarm computing to solve nanoscale problems. Hogg [4] proposed a multi-agent paradigm for distributed control of microscopic robots under Brownian motion to solve a specific locating problem in an aqueous environment thorough simulation. Hla et al. [5] considered each nanorobot as a particle and used particle swarm optimization (PSO) for collective movement and obstacle avoidance of a swarm of nanorobots in simulation environment. Chandrasekaran et al. [6] discussed the application of quorum sensing to realize swarm intelligence in a swarm of bio-nanorobots. Brickner [7] considered the populating problem in groups of nanorobots. Solomon [8] proposed a systematic method for the organization and self-assembly of the collectives of evolvable nanorobots and microrobots. Martel et al. [9] discussed a micro-assembly process and considered it on several thousand flagellated bacteria acting as micro-workers. Moreover, they described the problems of communication and cooperation in the swarms of sensotaxis-based bacterial microrobots [10]. Martel [11] also compared the aggregates of synthetic microscale nanorobots with the swarms of computer-controlled flagellated bacterial robots for target therapies through the human vascular network. Hirabayashi et al. [12] discussed the self-assembly of phage-like nanorobots. Al-Hudhud [13] proposed a communication model for a swarm of nanorobots performing a sweeping task to find cholesterol plaques and starts to swarm around the plaque. In [14,15], scientists demonstrated that a system of nanoparticles and engineered proteins can exploit one of the body's own communication pathways to communicate with one another to raise the concentration of systemically administered drugs at the site of a tumor. In comparison with this paper, most of these previous works are problem-specific and do not propose a general technique for realizing intelligent control at nanoscale.

As a general method for realization of fuzzy control at nanoscale, this paper aims to propose a swarm fuzzy approach for control of Low-Density Lipoprotein (LDL) concentration in the arterial wall. The proposed idea is based on stigmergic cooperation between two swarms of Fuzzy Nanoparticles (FNPs) and Auxiliary Nanoparticles (ANPs). Given any desired fuzzy controller, a swarm of FNPs in the aqueous environment of a living tissue can collectively realize an accurate approximation of the desired fuzzy controller that is called swarm fuzzy controller. Since fuzzy controller has universal function approximation property [3], the new scheme can be considered as a powerful method for realizing intelligent nonlinear control at nanoscale. In order to facilitate its manufacturing, the hardware complexity of the proposed approach is lower than nanorobotics [16–20], while the performance is maintained by the synergism in the swarm architecture.

The rest of the paper is organized as follows. In Section 2, mathematical modeling of the arterial wall including the LDL, FNP, pheromone, ANP, and drug transport is briefly reviewed. The proposed control approach is explained in Section 3. The notion of swarm fuzzy control, the details of the desired fuzzy controller of this study, the structures of FNP and ANP, and the concept of the stigmergic cooperation between two swarms of FNPs and ANPs are explained in this section. Simulation results on a well-known mathematical model of the arterial wall are illustrated in Section 4 for two distinguishing cases of unhealthy and healthy arterial walls and the performance of the proposed approach is compared with PDENP [2]. Finally, Section 5 concludes the paper.

2. Mathematical modeling

The anatomical structure of arterial wall is schematically illustrated in Fig. 1 [1]. The important layers that play critical role in atherosclerosis are endothelium, intima, IEL (internal elastic

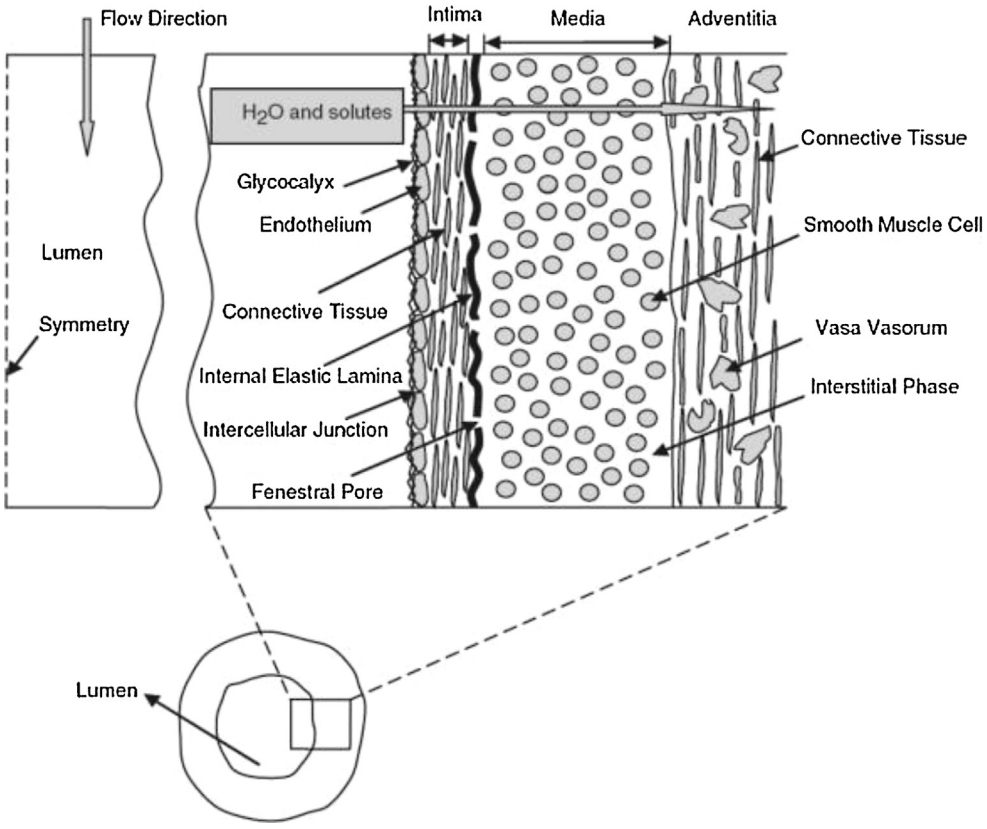

Fig. 1. Transverse section of the arterial wall [1].