

NANOROBOTIC CHALLENGES IN BIOMEDICAL APPLICATIONS, DESIGN AND CONTROL

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ABSTRACT

Ongoing developments in molecular fabrication, computation, sensors and motors will enable the manufacturing of nanorobots - nanoscale biomolecular machine systems. The present work constitutes a novel simulation approach, intended to be a platform for the design and research of nanorobots control. The simulation approach involves a combined and multi-scale view of the scenario. Fluid dynamics numerical simulation is used to construct the nanorobotic environment, and an additional simulation models nanorobot sensing, control and behavior. We discuss some of the most promising possibilities for nanorobotics applications in biomedical problems, paying a special attention to a stenosed coronary artery case.

Keywords: Biomedical computing, control systems, coronary stenosis, mobile robots, nanomedicine, nanorobots,nanotechnology.

1. INTRODUCTION

This paper describes a study for developing nanorobotics control design to deal with many of the challenging problems in biomedical applications. The problem we

consider here is mainly focused on nanomedicine [10], where the biomedical interventions and manipulations are automatically performed by nanorobots. While these nanorobots cannot be fabricated yet, theoretical and simulation studies defining design strategies, capabilities and limitations, will supply better comprehension of nanorobots behavior and the nanoworld [4][5].

In recent years, the potential of a new interdisciplinary field of science has motivated many governments to devote significant resources to nanotechnology [16][22]. The U.S. National Science Foundation has launched a program in “Scientific Visualization” [15], in part to harness supercomputers in picturing the nanoworld. A 1 trillion US\$ market consisting of devices and systems with some embedded nanotechnology is projected by 2015 [8]. The research firm DisplaySearch predicts rapid market growth of organic light emitting diodes, from 84 million US\$ in 2002 to 1.6 billion US\$ in 2007 [14]. A first series of commercial nanoproducts is foreseeable by 2007 [11]. In order to build electronics at nanoscales, firms are collaborating to produce new nanoproducts. Such companies include IBM, PARC,

Hewlett Packard, Bell Laboratories, and Intel Corp., to name a few [14].

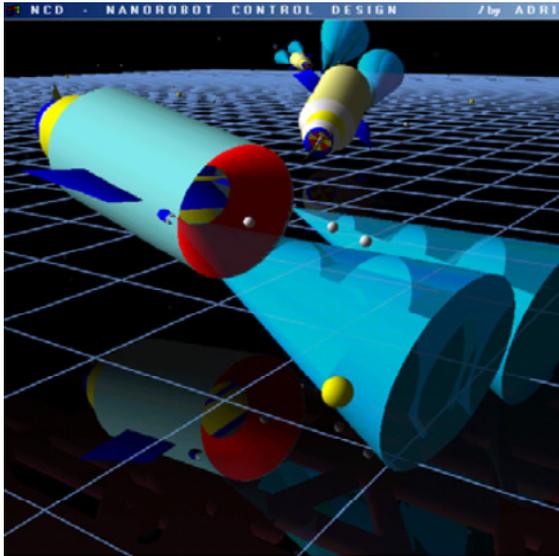


Figure 1: Schematic view of molecular identification by chemical signals through nanorobot sensors.

Recent developments in the field of biomolecular computing [1] have demonstrated positively the feasibility of processing logic tasks by bio-computers [12], which is a promising first step to enable future nanoprocessors with increased complexity. Studies targeted at building biosensors [21] and nanokinetic devices [20], required to enable nanorobotics operation and locomotion, have been advancing recently as well. A first generation of nanorobots is likely to emerge within the next five to ten years [17].

2. MEDICAL NANOROBOTIC APPLICATIONS

Applications of nanorobots are expected to provide remarkable possibilities. An interesting utilization of nanorobots may be their attachment to transmigrating inflammatory cells or white blood cells, to reach inflamed tissues and assist in their healing process [3]. Nanorobots will be applied in chemotherapy to combat cancer through precise chemical dosage administration, and a similar approach could be taken to enable nanorobots to deliver anti-HIV drugs. Such drug-delivery nanorobots have been termed “pharmacytes” by Freitas [10].

Nanorobots could be used to process specific chemical reactions in the human body as ancillary devices for injured organs. Monitoring and controlling nutrient concentrations in the human body [5], including glucose levels in diabetic patients will be a possible application of medical nanorobots. Nanorobots might be used to seek and break kidney stones. Another important possible feature of medical nanorobots will be the capability to locate atherosclerotic lesions in stenosed blood vessels, particularly in the coronary circulation, and treat them either mechanically, chemically or pharmacologically [10]. The coronary arteries are one of the most common sites for the localization of atherosclerotic plaques, although they could be found in other regions as well.

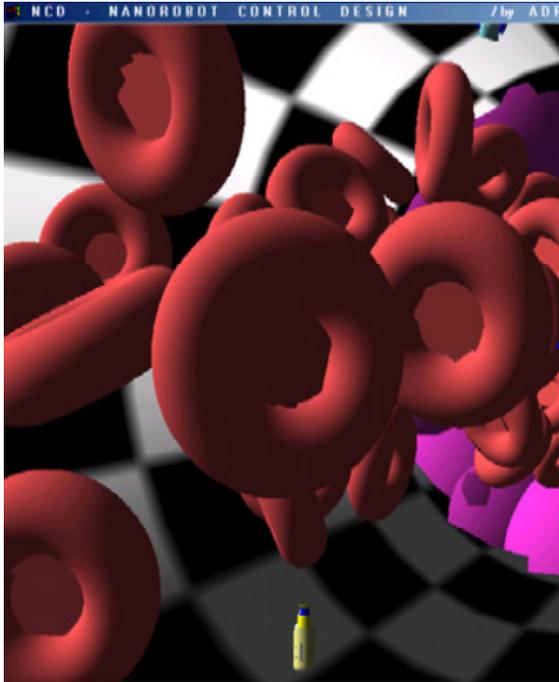


Figure 2: View of the NCD simulator workspace showing the vessel wall ,red blood cells nanorobots.

The eradication of disease involves three sub-goals:

- 1) Using nano-robots [7], nano-machines or other methods at the molecular level to search and destroy disease causing cells.
- 2) Same as above for the purposes of repairing damaged cells.
- 3) Using pumps or similar technology at the molecular scale as a means of drug delivery.

Nanotechnology involves the creation and use of materials and devices at the level of molecules and atoms. As life itself creates and uses molecular materials and devices, Nanoscience will provide great insights in life science concepts,

such as how molecular materials self-assemble, self-regulate, and self-destroy. NanoMedicine eventually will infiltrate virtually every field of medicine, if not every realm of human endeavor. NanoMedicine may be defined as the monitoring, repair, construction and control of human biological systems at the molecular level, using engineered Nano devices and nanostructures.

A sample list of areas covered by and converged with NanoMedicine include: Biotechnology, Genomics, Genetic Engineering, Cell Biology, Stem Cells, Cloning, Prosthetics, Cybernetics, Neural Medicine, Dentistry, Cryonics, Veterinary Medicine, Biosensors, Biological Warfare, Cellular Reprogramming, Diagnostics, Drug Delivery, Gene Therapy, Human Enhancement, Imaging Techniques, Skin Care, Anti-Aging.

3. PROPOSED DESIGN

Nanorobot manufacturing will undoubtedly require development of breakthrough technologies in fabrication, computation, sensing and manipulation. Researching the requirements, anticipated behavior and performance, and design of control strategies will require simulation tools which will both model foreseeable nanoscale technologies, and in turn influence the development of the same technologies. The simulation approach presented in this paper consists of adopting a multi-scale view of the scenario, which is

comprised of: macroscale physical morphology and physiological flow patterns, and on the nanoscale, the nanorobot fluid dynamics, orientation and drive mechanisms, sensing and control. Two simulations are used to achieve the most faithful modeling of nanorobots behavior in a real physical context. These simulations (NCD for the micro level, CFD for the macro level) are described in the next paragraphs, starting with assumptions made for the nanorobot simulation.

The nanorobot design is comprised of components such as *molecular sorting rotors* and a robot arm (*telescoping manipulator*) [7], derived from biological models. The nanorobot exterior shape consists of a diamondoid material, to which may be attached an artificial glycocalyx surface that minimizes fibrinogen (and other blood proteins) adsorption and bioactivity, ensuring sufficient biocompatibility to avoid immune system attack [10]. Different molecule types are distinguished by a series of chemotactic sensors (Fig. 1) whose binding sites have a different affinity for each kind of molecule [10]. These sensors also detect obstacles which might require a new trajectory planning.

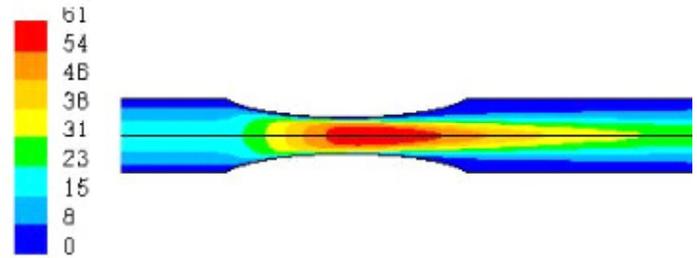


Figure 3: Blood velocity profile in the systolic phase of a 50% diameter stenotic segment of the left anterior descending coronary artery model (blood flows from left to right).

Some concepts provided from underwater robotics [23] were applied for nanorobot locomotion. The nanorobot kinematics can be predicted using state equations, positional constraints, inverse kinematics and dynamics, while some individual directional component performance can be simulated using control system models of transient and steady-state response [6]. Plane surfaces and bi-directional propellers provide navigation, while two simultaneously counter-rotating screw drives provide the propulsion [5], enabling motion with six degrees of freedom. Then nanorobots may use a macrotransponder navigational system for their positioning, which will allow high positional accuracy, independent of nanorobot orientation [10]. Such a system could involve externally generated signals from beacons placed at fixed positions outside the skin. The nanorobots satisfy their energy requirements via the chemical reaction of oxygen and glucose [10],

both of which are plentiful in the human body.

We developed the Nanorobot Control Design (NCD) simulator, and used it for the 3D investigation of a stenosed left anterior descending (LAD) coronary artery, in which we optimize the activating trigger for medical nanorobots. This trigger will turn the nanomachine “on”, switching it from “seek mode” to “repair mode”. It may also cause other close nanorobots switch to a “higher awareness mode”. Once we have previous knowledge about the general localization of the stenosis (in large, small or microvessels), we may inject the appropriate nanorobot type, which is pre-programmed to be activated only at the pre-specified target region.

The NCD simulator consists of several modules that simulate the physical conditions, run the nanorobot control programs determining their actions, provide a visual display of the environment in 3D, and record the history of nanorobot behaviors for later analysis. The NCD simulation enables the nanorobot control programs to be tested using various strategies, e.g. based on neural network control, motion with low energy consumption, or any different predefined motion strategy. The virtual environment in the NCD simulator is inhabited by plasma, red blood cells, nanorobots, different molecules whose concentrations are being monitored, and the blood vessel (Fig. 2).

Using FLUENT, a finite-volume based Computational Fluid Dynamics (CFD) package [9], we simulated the pulsatile blood flow in stenosed LAD coronary artery models, differing in the degree of stenosis severity. By solving the flow governing equations we computed blood velocity profiles (Fig. 3).

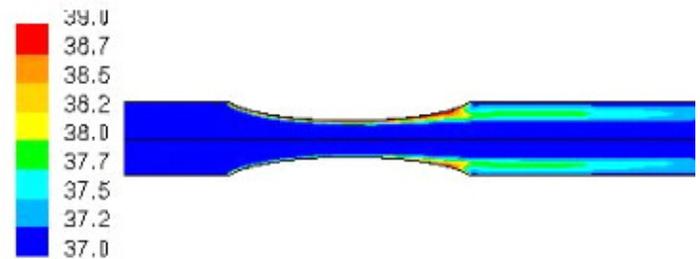


Figure 4: Blood temperature distribution in the systolic phase of a 50% diameter stenotic segment of the LAD coronary artery model (blood flows from left to right). Wall temperature at the stenosis region is set to 39°C.

We also defined and calculated various signaling functions, known to be indicative of stenosis, caused by an atherosclerotic plaque. Such parameters include time-averaged wall shear stress, wall shear stress gradients and oscillatory shear index [2]. It is well documented [19] that there is significant temperature heterogeneity over plaque surfaces, as inflamed plaques are hotter. The temperature difference at the site of the lesion from the core temperature can reach up to ~2°C [18]. Hence, in order to simulate various levels of inflammation, we used different wall temperatures in the atherosclerotic plaque region, and calculated the

temperature distribution in the stenosed coronary artery (Fig. 4). Significant temperature gradients were found in the recirculation zone, following the stenosis (Fig. 5).

As the transcatheter concentration gradient of some soluble adhesion molecules has been recently found to be correlative with the progression of coronary

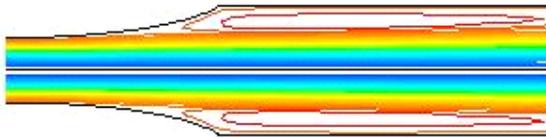


Figure 5: Flow streamlines, showing the recirculation zone after the stenosis predefined motion strategy.

atherosclerosis [24], we also monitor their concentration in the blood vessel (using uniform distribution release from the plaque). In a similar manner, we monitor the concentrations of some specific pro-inflammatory cytokines, whose elevated concentrations are known as an evidence of formation of atherosclerotic lesions [13].

The parameters generated from the CFD simulation, namely velocities, temperature, signaling functions values, pro-inflammatory cytokines and soluble adhesion molecules concentrations, are transferred to the NCD simulator to serve as the nanorobots operating environment. As the nanorobot should perform a pre-defined task in a specific target area, the trigger must be activated when the nanorobot is as close as possible to the target. Taking advantage of the fact that the

nanorobots flow mostly in a near-wall region [10][25], where the blood flow velocity profile dictates significantly lower velocities, such rapid activation could result in lower demand of energy (Fig. 6). Optimization of control algorithms and activating triggers is the key for rapid behavior response in minimal energy cost.

Thus, approaches for trigger strategies include analyzing time-gradients of the former mentioned nanorobot measurable parameters, as they change during nanorobot locomotion, and particularly in the neighborhood of a lesion. By running the nanorobots control programs we determine the optimal trigger values, with respect to the stenosed artery models being investigated.

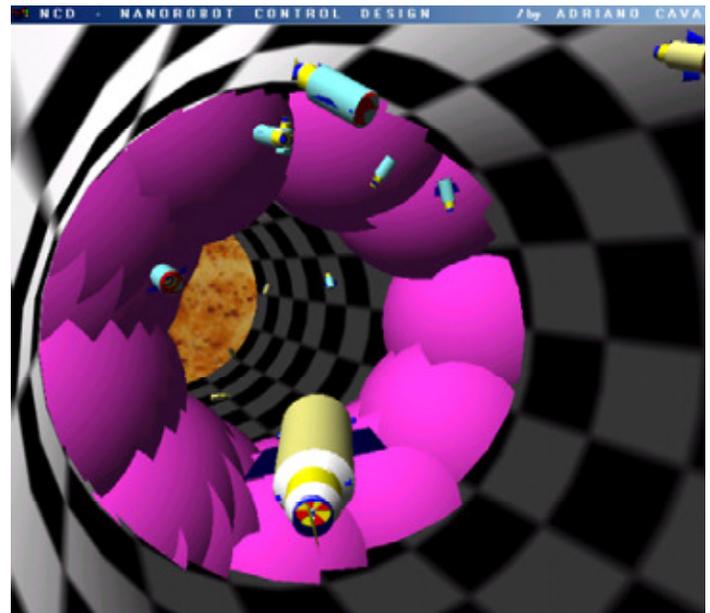


Figure 6: Vein inside view without the red blood cells. The target plaque is represented by the pink spheres surrounding the vessel

wall. The nanorobots swim in a near-wall region searching for the atherosclerotic lesion.

4.SURGICAL SYSTEM

Robotic surgical systems are being developed to provide surgeons with unprecedented control over precision instruments. This is particularly useful for minimally invasive surgery. Instead of manipulating surgical instruments, surgeons use their thumbs and fingers to move joystick handles on a control console to maneuver two robot arms containing miniature instruments that are inserted into ports in the patient.

The surgeon's movements transform large motions on the remote controls into micro-movements on the robot arms to greatly improve mechanical precision and safety. A third robot arm holds a miniature camera, which is inserted through a small opening into the patient. The camera projects highly magnified 3-D images on a console to give a broad view of the interior surgical site. The surgeon controlling the robot is seated at an ergonomically designed console with less physical stress than traditional operating room conditions.



Figure7:Nano Robotic arm

5. CONCLUSIONS

The approach presented in this paper, of combining a precise physical simulation to establish the environment in which nanorobots would inhabit, with a nanorobot control design simulator capable of modeling behavior and used for optimizing performance, has been shown to be of an extreme potential for exploration of techniques, strategies, and nanorobot mobility considerations. The work is intended to serve as a practical framework for investigating designs and models of medical nanorobots, with an application to the case of establishing a trigger and control criteria for the treatment of stenosed blood vessels having been successfully demonstrated. Future work may include addition of a statistical and operational research envelope for evaluating large-scale performance, simulations of new environments and nanorobot designs. We strongly believe that the merging of the new technologies into operational nanomachines will

go hand in hand with progressing simulation fidelity.

6. ACKNOWLEDGEMENTS

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