Medical Nanorobot Architecture Based on Nanobioelectronics

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Received: December 8, 2006; Accepted: December 14, 2006; Revised: December 15, 2006

Abstract: This work describes an innovative medical nanorobot architecture based on important discoveries in nanotechnology, integrated circuit patents, and some publications, directly or indirectly related to one of the most challenging new fields of science: molecular machines. Thus, the architecture described in this paper reflects, and is supported by, some remarkable recent achievements and patents in nanoelectronics, wireless communication and power transmission techniques, nanotubes, lithography, biomedical instrumentation, genetics, and photonics. We also describe how medicine can benefit from the joint development of nanodevices which are derived, and which integrate techniques, from artificial intelligence, nanotechnology, and embedded smart sensors. Teleoperated surgical procedures, early disease diagnosis, and pervasive patient monitoring are some possible applications of nanorobots, reflecting progress along a roadmap for the gradual and practical development of nanorobots. To illustrate the described nanorobot architecture, a computational 3D approach with the application of nanorobots for diabetes is simulated using clinical data. Theoretical and practical analysis of system integration modeling is one important aspect for supporting the rapid development in the emerging field of nanotechnology. This provides useful directions for further research and development of medical nanorobotics and suggests a time frame in which nanorobots may be expected to be available for common utilization in therapeutic and medical procedures.

Keywords: Biomedical instrumentation, CMOS, diabetes, DNA molecular machine, equipment design, lithography, medical nanorobotics, nanoelectronics, nanomanufacturing design, nanomechatronics, nanomedicine, nanorobot architecture, nanotubes, photonics, remote inductive powering.

INTRODUCTION

This paper presents a nanorobot architecture for biomedical applications in nanomedicine [1]. The advent of biomolecular science and new manufacturing techniques is helping to advance the miniaturization of devices from micro to nanoelectronics. A first series of nanotechnology prototypes for molecular machines are being investigated in different ways [2-5], and some interesting device propulsion and sensing approaches have been presented [6-8]. More complex molecular machines, or nanorobots, having embedded nanoscopic features may provide new tools for medical procedures [1,2,9]. Sensors for biomedical applications are advancing through tele-operated surgery and pervasive medicine [10,11].

The use of microdevices in surgery and medical treatments is a reality which has brought many improvements in clinical procedures in recent years. For example, catheterization has been used as an important methodology for many cardiology procedures [12] and aneurysm surgery [13]. In the same way as the development of microtechnology in the 1980s has led to new tools for surgery, emerging nanotechnologies will similarly permit further advances providing better diagnosis and new devices for medicine through the manufacturing of nanoelectronics based on new CMOS technologies [14]. Nanorobots may be considered a new possibility for medical instrumentation to solve many problems in health care [15-17], including cardiology interventions, medical analysis, cancer early diagnosis, diabetes monitoring, and minimally invasive brain surgery.

For effective manufacturing progress we consider a nanorobot architecture design using embedded devices with nanoelectronic circuits [18] based on RF CMOS transducers [19,20], to integrate the sensing, communication, energy transfer, and actuation for the nanorobots as the most effective way to accomplish the work to advance molecular machines. Devices based on CMOS are achieving 45nm sizes, with functional sensors and actuators being produced with sizes equal and smaller than 500nm [21-23]. The correct architecture for medical nanorobots may include the minimal number of embedded devices for its effective application [1], having embedded sensors and actuators for specified tasks. It is important to define actual capabilities to enable Nano-Build Hardware Integrated Systems [24], establishing how to enable pathways to help on research and development of nanorobots based on the present stages of nanotechnology development. Nanoelectronics integrated circuits using nanowires, nanotubes and photonics are leading to smaller sizes on complex devices [14,25]. Allied with this fact, the mobile phone as a widely used device in everyday life could be applied as a source of coupling energy and data transmission for communication, control, and energy supply for the operation of a nanorobot inside a human body.

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1872-2105/07 $100.00+.00

The feasibility of advancing techniques for control [26] and manufacturing molecular machines should be understood as emergent results from actual and upcoming stages of nanotechnology, based on nanoelectronics [27] and new materials [24,28]. New possibilities are coming from these developments which will enable new medical procedures [1,9,15-17,28].

PATENT REVIEW

Current developments and patents in nanoelectronics and nanobiotechnology may provide feasible technology development pathways to enable molecular machine manufacturing, including embedded and integrated devices which may comprise the main sensing, actuation, data transmission, remote control uploading, and coupling power supply subsystems providing the basics for operation of medical nanorobots.

For example, surgical robots and other telepresence systems employ enhanced grip actuation for manipulating tissues and objects having extremely small sizes [10]. An actuator with biologically-based components has also been proposed [29]. This actuator has a mobile member that moves substantially linearly as a result of a biomolecular interaction between biologically-based components within the actuator. Such actuators can be utilized in nanoscale mechanical devices to pump fluids, open and close valves, or to provide translational movement [29].

A power supply implanted behind a tissue barrier in a human body and operating a medical device and incorporating a high frequency power receiver antenna coil [30] demonstrates the use of remote energy powering for implanted medical devices. A similar approach could supply exogenous energy to a molecular machine system possessing embedded nanoelectronics. To help control nanorobot position, a system for tracking an object in space may comprise a transponder device connectable to the object [31]. The transponder device has one or several transponder antennas through which a transponder circuit can receive an RF signal. The transponder device adds a known delay to the RF signal thereby producing an RF response for transmitting through the transponder antenna [31]. A series of several transmitters and antennas allow a position calculator associated with the transmitters and receivers to calculate the position of the object as a function of the known delay and the time period between the emission of the RF signal and the reception of the RF response from the first, second and third antennas [31].

Monitoring devices coupled to a transceiver and a memory component for remote patient monitoring are currently in use, and provide a central monitoring system platform for monitoring a large number of physiological parameters [11]. For example, methods of monitoring patients and evaluating the status of a tumor in a patient undergoing treatment includes monitoring *in vivo* at least one physiological parameter associated with a tumor, transmitting data from an *in situ* sensor to a receiver external to the subject, analyzing the transmitted data, repeating the monitoring and transmitting steps at sequential points in time, and then re-evaluating the treatment strategy [32]. This method can also include identifying in a substantially real time manner when conditions are favorable for treatment, and it can be used to verify or quantify how much of a known drug dose or radiation dose was actually received at the tumor. This method can include remote transmission from a non-clinical site to allow oversight of the tumor's condition even during non-active treatment periods (in between active treatments) [32]. The disclosure also includes monitoring systems with *in situ in vivo* biocompatible sensors and telemetry based operations and related computer program products. The RF telemetry antenna comprises an LC tank circuit including an RF head telemetry coil and a tuning capacitor and has a predetermined antenna Q. A transmit telemetry pulse is generated for establishing a pulse width of the telemetry RF pulse [33]. Upon termination of the telemetry transmit pulse, antenna Q is reduced from the predetermined antenna Q and the declining amplitude oscillations are thereby attenuated [33]. The sensor can receive data transmitted from an external device and can also transmit data to an external device [19]. A tuning circuit comprising capacitors and/or varactors is used, thus creating a sufficiently large effective signal aperture.

For diabetes application, the most important use of nanorobots is monitoring daily the patient's glucose levels, if possible without interfering in their way of life. Thus, one mobile phone is enough for data transferring and monitoring purposes. Whether the doctor wants to track the nanorobots current positions due some medical reason, it can be done clinically or at home with at least two additional transmitters, which may comprise other ancillary preprogrammed cellular phones or transponder devices.

Nanotechnology is moving fast towards nanoelectronics fabrication. Chemically assembled electronic nanotechnology provides an alternative to using Complementary Metal Oxide Semiconductor (CMOS) for constructing circuits with feature sizes in the tens of nanometers [23]. Such structures can be operated both as a transistor and as a memory. The thin active silicon channel and the thin front oxide provide dual function of the device, using two voltage ranges. At small voltages the structure operates as a normal transistor, and at higher voltages the structure operates as a memory device [34]. A CMOS component can be configured in a semiconductor substrate as part of the circuit assembly [14]. An insulating layer is configured on the semiconductor substrate, which covers the CMOS component. A nanoelectronic component is configured above the insulating layer. If several nanoelectronic components are provided, they are preferably grouped in nanocircuit blocks [14]. Three-dimensional (3D) integration schemes of fabricating a 3D integrated circuit in which the nFETs are located on an optimal crystallographic surface for that type of device can also be applied [35]. Semiconductor devices are pre-built on a semiconductor surface of a first silicon-on-insulator (SOI) substrate and second semiconductor devices are pre-built on a semiconductor surface of a second SOI substrate [35].

A method of fabricating a nano SOI wafer having an excellent thickness evenness without performing a chemical mechanical polishing and a wafer fabricated by the same have been announced [36]. The provided method includes preparing a bond wafer and a base wafer, and forming a dielectric on at least one surface of the bond wafer.

Thereafter, an impurity ion implantation unit is formed by implanting impurity ions into the bond wafer to a predetermined depth from the surface of the bond wafer at a low voltage. The dielectric of the bond wafer and the base wafer contact each other in order to be bonded. Next, a thermal process of low temperature is performed to cleave the impurity ion implantation unit of the bond wafer. Finally, the cleaved surface of the bond wafer bonded to the base wafer is etched to form a nanoscale device region. Here, the cleaved surface may be etched by performing a hydrogen surface process and a wet etching [36].

Nanotube/nanofiber electrodes are integrated with electronic devices to form a single-chip nano-bio-sensor [37]. The single-chip nano-bio-sensor which uses nano-meter scale electronic devices, includes sensing transistors in close proximity to nano-tube/nano-fiber electrodes, and provides an arrangement of the nano-tube/nano-fiber electrodes into high density clusters and groups so that sensitive, low noise detection of the activities of small cells, large cells and a network of cells is possible. The integrated, single-chip approach provides that differential signal extraction is possible. The single-chip nano-bio-sensor includes small feature size transistors [37]. New methods allow the fabrication of novel gated field emission structures that include aligned nanowire electron emitters localized in central regions within gate apertures [38], and novel devices using nanoscale emitters for microwave amplifiers, electron-beam lithography, field emission displays and X-ray sources.

For lithographic processes, an optical device can include an array of heterogeneous optical waveguides. The elements to be excited are selected for each line by intensities of light rays in the first optical waveguides functioning as horizontal waveguides; light rays in the second waveguides functioning as vertical waveguides are modulated in intensity on the basis of data signals, and the data signal light rays whose intensities have been modulated are extracted to the outside via the selected elements to be excited [25]. The alignment material orients the subsequently deposited photoactive material such that the photoactive material interacts with or emits light preferentially along a selected polarization axis [39]. Additional layers and sublayers optimize and tune the optical and electronic responses of the device. An integrated circuit package includes a chip having a number of chip pads adapted to receive a variety of signals from, or to output the same to, an external circuit, with nanoceramic materials in thermal communication with the chip employed for efficient heat removal from the chip [18].

Nanosensors are a related area of rapidly progressing research and development. For example, coating nanomagnets with biological molecules produces ultra-small, highly sensitive and robust biomagnetic devices which combine molecular electronics and spin electronics. When these nanosensors are integrated into microfluidic channels, highly efficient single-molecule detection chips for rapid diagnosis and analysis of biological agents are constructed [27]. A magnetic sensor device formed using SOI CMOS techniques includes a substrate, a silicon oxide layer and in some cases a variety of gated regions [40]. Electromagnetic field sensors can employ the motion of a mechanical oscillator caused by electromagnetic interaction, such as a magnetic polarization with a magnetic field or an electric polarization with an electric field [41]. For monitoring patients with diabetes, methods are described for a novel chemosensor that involves the modulation of hSGLT3 protein glucosensor activity [42]. This natural glucose sensor molecule is expressed in cholinergic neurons that regulate muscle activity, and in tissues including the brain and pancreas [42].

Biosensors may incorporate living components including tissues or cells which are electrically excitable or are capable of differentiating into electrically excitable cells, and which can be used to monitor the presence or level of a molecule in a physiological fluid [43]. Nanotubes and DNA are recent candidates for new forms of nanoelectronics [44]. These may be combined to create new genetically programmed self-assembling materials for facilitating the selective placement of nanotubes on a substrate by functionalizing nanotubes with DNA. Through recombinant DNA technology, targets labeled with distinct detectable biomarkers can be defined, such as fluorescent labels, enzyme labels, and radioactive patterns, and employed in suitable biomolecular transducers [45]. Such biosensors can be used to detect labels selected from among those known in the art, including, but not limited to, radioactive labels, enzymes, specific binding pair components, colloidal dye substances, fluorochromes, reducing substances, latexes, digoxigenin, metals, particulates, dansyl lysine, antibodies, protein A, protein G, electron dense materials, and chromophores [45].

Finally, current developments in implant biocompatibility have demonstrated suitable composites that could permit a nanorobot to operate continously inside the human body. For example, surfactant polymers which are useful for changing the surface properties of biomaterials have been presented [46]. Such surfactant polymers comprise a polymeric backbone of repeating monomeric units having functional groups for coupling to side chains, with separate hydrophobic and hydrophilic side chains linked to said backbone via the functional groups. The hydrophobic side chains comprise an alkyl group (CH_3 (CH_2 -)n) possessing from about 2 to 18 methylene groups [46]. This "artificial

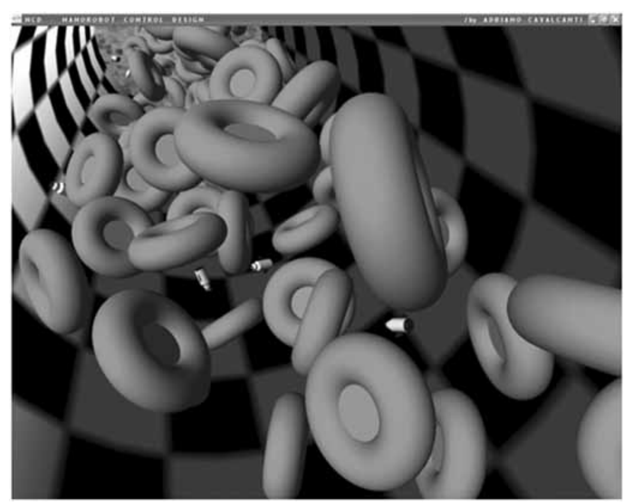

Fig. (1). Medical complications can arise due to diabetes problems. Nanorobots use sensors to detect glucose levels in bloodstream.

glycocalyx,” currently intended for use on biomedical implants, could also provide biocompatibility for nanorobots to operate inside the human body while remaining largely invisible to the immune system.

NANOROBOT MEDICAL APPLICATIONS

The use of nanorobots may advance biomedical intervention with minimally invasive surgeries [1,16,47], help patients who need constant body function monitoring, and improve treatment efficiency through early diagnosis of possibly serious diseases [48,49]. Implantable devices in medicine have been used for continuous patient data acquisition. Patient monitoring can help in preparing for neurosurgery [50], early stage diagnostic reports to fight cancer [51], and blood pressure control for cardiology problems [52]. The same approach is quite useful in monitoring patients with diabetes [53,54].

To visualize how stages of the actual technologies can be used to medicine, based on current discoveries, publications, and patents, we implemented a system simulation of nanorobots monitoring blood glucose levels (Fig. **1**). Actual advances in wireless technologies, nanoelectronics devices, and their use in the implementation of nanorobots applied to diabetes can illustrate what upcoming technologies can enable in terms of medicine applications. The software implemented from our group is used as a practical tool for control and manufacturing design analyses.

As an example, patients with diabetes must take small blood samples many times a day to control glucose levels. Such procedures are uncomfortable and extremely inconvenient. Serious problems may affect the blood vessels if the correct target levels of glucose in the blood are not controlled appropriately. Improper glucose control may result in a large range of consequences for the nervous system, kidney, eyes, exacerbate heart problems, and can even lead to stroke [55].

The level of sugar in the body can be observed via constant glucose monitoring using medical nanorobotics. This important data may help doctors and specialists to supervise and improve the patient medication and diary diet. The glycemic levels and parameters for an adult with diabetes stay inside the desired ranges, the patients must try to keep their glucose between 90-130 mg/dl (5.0-7.2 mmol/l) before refection, and <180 mg/dl (<10.0 mmol/l) after refection, here including 2 hours concluded it. Upon waking the expected blood pressures should be <130/80 mmHg. The glycated hemoglobin (A1C) time series results must stay <7.0% [55], as a result of good blood sugar levels [54, 56]. A red blood cell lifespan is 120 days. Thus the A1C reflects the blood sugar levels correlation for this time length. Notoriously, each person may have some particularities that may require a different prescription given by his doctor.

NANOROBOT ARCHITECTURE

The main parameters used for the medical nanorobot architecture and its control activation, as well as the required technology background that may lead to manufacturing hardware for molecular machines, are described next.

Manufacturing Technology

The ability to manufacture nanorobots may result from current trends and new methodologies in fabrication, computation, transducers and manipulation. The hardware architecture for a medical nanorobot must include the necessary devices for monitoring the most important aspects of its operational workspace: the human body. Depending on the case, different gradients on temperature, concentration of chemicals in the bloodstream, and electromagnetic signature are some of relevant parameters when monitoring patients. Teams of nanorobots may cooperate to perform predefined complex tasks in medical procedures. To reach this aim, data processing, energy supply, and data transmission capabilities can be addressed through embedded integrated circuits, using advances in technologies derived from nanotechnology and VLSI design [57]. CMOS VLSI design using deep ultraviolet lithography provides high precision and a commercial way for manufacturing early nanodevices and nanoelectronics systems [41]. The CMOS industry may successfully drive the pathway for the assembly processes needed to manufacture nanorobots, where the joint use of nanophotonic and nanotubes may even accelerate further the actual levels of resolution ranging from 248nm to 157nm devices [22]. To validate designs and to achieve a successful implementation, the use of VHDL has become the most common methodology utilized in the integrated circuit manufacturing industry [58].

Chemical Sensor

Manufacturing silicon-based chemical- and motion-sensor arrays using a two-level system architecture hierarchy has been successfully conducted in the last 15 years [59]. Applications range from automotive and chemical industry with detection of air to water element pattern recognition through embedded software programming, and biomedical uses. Through the use of nanowires, existing significant costs of energy demand for data transfer and circuit operation can be decreased by up to 60% [60]. CMOS-based sensors using nanowires as material for circuit assembly can achieve maximal efficiency for applications regarding chemical changes, enabling new medical applications [17,61].

Sensors with suspended arrays of nanowires assembled into silicon circuits can drastically decrease self-heating and thermal coupling for CMOS functionality [62]. Factors like low energy consumption and high-sensitivity are among some of the advantages of nanosensors. Nanosensor manufacturing array processes can use electrofluidic alignment to achieve integrated CMOS circuit assembly as multi-element systems [60]. Passive and buried electrodes can be used to enable cross-section drive transistors for signal processing circuitry readout. The passive and buried aligned electrodes must be electrically isolated to avoid loss of processed signals.

Some limitations to improving BiCMOS, CMOS and MOSFET methodologies include quantum-mechanical tunneling for operation of thin oxide gates, and subthreshold slope [63]. Surpassing expectations, the semiconductor branch nevertheless has moved forward to keep circuit capabilities advancing. Smaller channel length and lower voltage circuitry for higher performance are being achieved with new materials aimed to attend the growing demand for high complex VLSIs. New materials such as strained channel with relaxed SiGe layer can reduce self-heating and improve performance [21]. Recent developments in 3D circuits and FinFETs double-gates have achieved astonishing results and according to the semiconductor roadmap should improve even more. To further advance manufacturing techniques, Silicon-On-Insulator (SOI) technology has been used to assemble high-performance logic sub 90nm circuits [40,64]. Circuit design approaches to solve problems with bipolar effect and hysteretic variations based on SOI structures has been demonstrated successfully [21]. Thus, already-feasible 90nm and 45nm CMOS devices represent breakthrough technology devices that are already being utilized in products.

Energy Supply

The most effective way to keep the nanorobot operating continuously is to establish the use of a continuous available source of power. The energy may be available and delivered to the nanorobot while it is performing predefined tasks in the operational environment. For a medical nanorobot, this means that the device must keep working inside the human body, sometimes for long periods, and must have easy access to clean and controllable energy to maintain efficient operation.

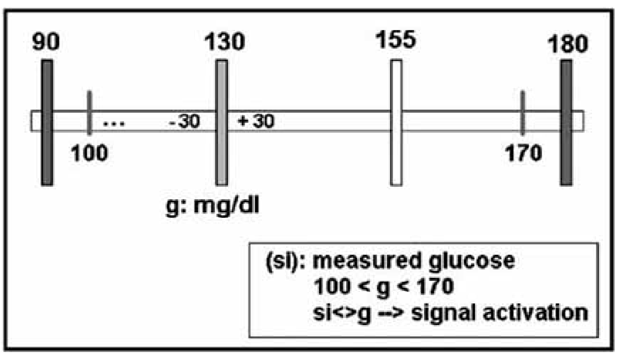

Fig. (2). Accepted levels of glucose. The nanorobot sends a signal to the mobile phone at every observed critical level.

Some possibilities to power the nanorobot can be provided from ambient energy [1]. Temperature displacements could likewise generate useful voltage differentials. Cold and hot fields from conductors connected in series may also produce energy using the well-established Seebeck effect. Electromagnetic radiation from light is an option for energy generation in determined open workspaces [65] but not for *in vivo* medical nanorobotics, especially since lighting conditions in different kinds of workspaces could sharply change depending on the application. Kinetic energy can be generated from the bloodstream due to motion interaction with designed devices embedded with the nanorobot [66], but this kinetic process would demand costly room within the nanorobot architecture.

Most recently, remote inductive powering has been used both for RFID and biomedical implanted devices to supply power on the order of milliwatts [67-69]. To operate nanorobots, a low frequency energy source may be enough. This functional approach presents the possibility of supplying energy in a wireless manner [70] in order to operate sensors and actuators necessary for the controlled operation of nanorobots inside the human body.

The use of CMOS for active telemetry and power supply is the most effective and secure way to ensure energy as long as necessary to keep the nanorobot in operation. The same technique is also appropriate for other purposes like digital bit encoded data transfer from inside a human body [71]. Thus nanocircuits with resonant electric properties can operate as a chip providing electromagnetic energy supplying 1.7 mAat 3.3V for power, allowing the operation of many tasks with few or no significant losses during transmission [50]. RF-based telemetry procedures have demonstrated good results in patient monitoring and power transmission with the use of inductive coupling [32,67,72,73], using well established techniques already widely used in commercial applications of RFID [74]. The energy received can be also saved in ranges of ~1μW while the nanorobot stays in inactive modes, just becoming active when signal patterns require it to do so. Some typical nanorobotic tasks may require the device only to spend low power amounts, once it has been strategically activated. For communication, sending RF signals ~1mW is required. Allied with the power source devices, the nanorobots need to perform precisely defined actions in the workspace using available energy resources as efficiently as possible.

A practical way to achieve easy implementation of this architecture will obtain both energy and data transfer capabilities for nanorobots by employing mobile phone in such process [75]. The mobile phone should be uploaded with the control software that includes the communication and energy transfer protocols.

Data Transmission

The application of devices and sensors implanted inside the human body to transmit data about the health of patients can provide great advantages in continuous medical monitoring [54,76]. Most recently, the use of RFID for *in vivo* data collecting and transmission was successfully tested for electroencephalograms [50]. For communication in liquid workspaces, depending on the application, acoustic, light, RF, and chemical signals may be considered as possible choices for communication and data transmission [2]. Chemical signaling is quite useful for nearby communication among nanorobots for some teamwork coordination [51]. Acoustic communication is more appropriate for longer distance communication and detection with low energy consumption as compared to light communication approaches [77]. Although, optical communication permits faster rates of data transmission, its energy demand makes it not ideal for nanorobots [1].

Work with RFID (Radio Frequency Identification Device) has been developed as an integrated circuit device for medicine [69,74,78]. Using integrated sensors for data transfer is the better answer to read and write data in implanted devices. Teams of nanorobots may be equipped with single-chip RFID CMOS based sensors [79]. CMOS with submicron SoC design could be used for extremely low power consumption with nanorobots communicating collectively for longer distances through acoustic sensors [80]. For the nanorobot active sonar communication frequencies may reach up to 20μW@8Hz at resonance rates with 3V supply [77].

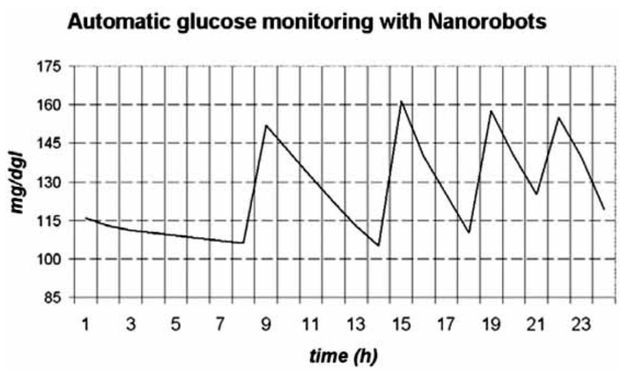

Fig. (3). In the proposed model, the nanorobots monitor the BGL. A patient with diabetes can benefit from monitoring the metabolism uninterruptedly. The same architecture can also serve to early stages of diagnosis of different health problems.

More widely accepted and usual than an RF CMOS transponder, mobile phones can be extremely practical and useful as sensors for acquiring wireless data transmission from medical nanorobots implanted inside the patient's body. Such phones can be a good choice for monitoring predefined patterns in various biomedical applications, such as helping in the treatment of diabetes, and likewise for many other health problems. To accomplish that, chemical nanosensors may be embedded in the nanorobot to monitor glucose levels. The nanorobot will emit signals to send an alarm in case the patient urgently needs medications prescribed by his doctor. In our nanorobotic system architecture, the mobile phone is applied [50,75,81]. It uses electromagnetic radio waves to command and detect the current status of nanorobots inside the patient. This occurs as a transponder device emits magnetic signature to the passive CMOS sensors embedded in the nanorobot, which enables sending and receiving data through electromagnetic fields [72]. The nanorobots monitoring data convert the wave propagation generated by the emitting signal through a well defined protocol. From the last set of events recorded in pattern arrays, information can be reflected back by wave resonance [81]. For nanorobot passive data transferring ~4.5 kHz frequency with approximate 22 μs delays are possible ranges for data communication.

Frequencies ranging from 1 to 20MHz can be successfully used for biomedical applications without any damage [78]. To avoid possibly loss of information in monitoring the patient's glucose levels it is used a team of nanorobots. It serves to solve some signal noise interference. A small loop planer antenna working as an electromagnetic pick-up with a good matching to the Low Noise Amplifier is used with the nanorobot.

SYSTEM IMPLEMENTATION

Real time 3D prototyping tools and simulation are important aids in nanotechnology development. Such tools have significantly helped the semiconductor industry to achieve faster VLSI development [57]. It may have similarly direct impact on the implementation of nanomanufacturing techniques and also on nanoelectronics progress [82]. Simulation can anticipate performance and help in new device design and manufacturing [83,84], nanomechatronics control design and hardware implementation [36,85].

The nanorobot design includes integrated nanoelectronics [60,64]. The nanorobot architecture involves the use of mobile phones for, e.g., the controlled measurement of glucose levels in diabetes monitoring [74,75]. The nanorobot uses a RFID CMOS transponder system for *in vivo* positioning [1,74], using well established communication protocols which allow track information about the nanorobot position [75]. The simulation consists of adopting a multi-scale view of the scenario. It incorporates the physical morphology of the biological environment along with physiological fluid flow patterns, and this is allied with the nanorobot systems for orientation, drive mechanisms, sensing and control. Thus, these simulations are used to achieve high-fidelity control modeling. The simulation includes the NCD (Nanorobot Control Design) software for nanorobot sensing and actuation.

The nanorobot exterior shape consists of a diamondoid material [86-88], to which may be attached an artificial glycocalyx surface [46], that minimizes fibrinogen (and other blood proteins) adsorption and bioactivity, ensuring sufficient biocompatibility to avoid immune system attack [45,89]. Different molecule types are distinguished by a series of chemotactic sensors whose binding sites have a different affinity for each kind of molecule [1,37]. These sensors can also detect obstacles which might require new trajectory planning [26]. We simulate the nanorobot with sensory capabilities allowing it to detect and identify the nearby possible obstacles in its environment, as well as the biomedical target for its task, such as glucose molecules in the case of diabetic monitoring. A variety of sensors are possible [43,59,62]. For instance, chemical detection can be very selective, e.g., for identifying various types of cells by markers [1]. Acoustic sensing is another possibility, using different frequencies to have wavelengths comparable to the object sizes of interest [77,79].

SYSTEM SIMULATION

The use of microdevices in surgery and medical treatments is a reality which brought many improvements for clinical procedures in the last years [19]. In the same way as the development of microtechnology has lead on the 1980s to new tools for surgery [90], now nanotechnology will equally permit further advances providing better diagnosis, and new devices for medicine through the manufacturing of nanoelectronics [14,44,31,82]. As a result from the advances on nanoelectronics, nanorobots may be considered a promising new technology to help with new treatments for medicine [16,17], here including improvement to assist patients who suffer from diabetes.

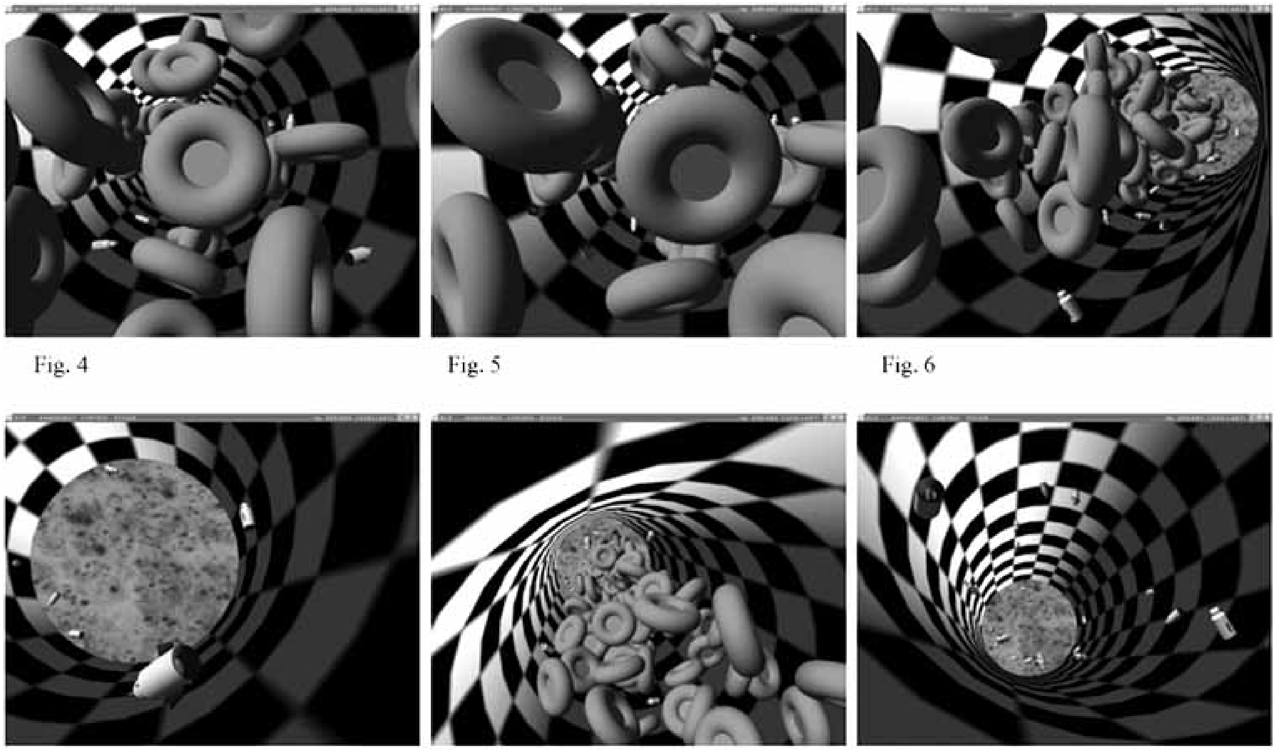

Fig. 4 Fig. 5 Fig. 6

Fig. 7 Fig. 8 Fig. 9

Figs. (4-9). Set of different camera views in the simulator. The nanorobots are inside the vessel (with grid texture); they can be either observed in 3D real time with or without the visualization of red blood cells.

The bloodstream keeps the human body alive. The plasma represents 55% of the blood volume which is 8% of the body weight; the size of red blood cells is about 7.5 μm in diameter; for the vessels geometry, the lumen diameters ranges from the Vena Cava with ~3cm in the heart, to ~10μm of capillary vessels. Glucose carried through the blood stream is important to maintain the human metabolism working healthfully, and its correct level is a key issue in the diagnosis and treatment of diabetes. Intrinsically related to the glucose molecules, the protein hSGLT3 has an important influence in maintaining proper gastrointestinal cholinergic nerve and skeletal muscle function activities, regulating extracellular glucose concentration [42]. The hSGLT3 also regulates the gradient of membrane potential. But for our study interest, the hSGLT3 molecule can serve to define the glucose levels for diabetes patients. The hSGLT3 protein was classified through genome analyses being identified in chromosome 22, encoding the structural RNAs [56]. The most interesting aspect of this protein is the fact that it serves as a sensor to identify glucose [42]. Through its onboard chemical sensor, the nanorobot can thus effectively determine if the patient needs to inject insulin or take any further action, such as any medication clinically prescribed.

The simulated nanorobot prototype model has embedded CMOS nanobioelectronics. It features a size of ~2 micron-meter, which permits it to operate freely inside the body. The nanorobot computation is performed through embedded nanosensor; for pervasive computing, performance requires low energy consumption as described on page 5. Whether the nanorobot is invisible or visible for the immune reactions, it has no interference for detecting glucose levels in blood-stream. For the glucose monitoring the nanorobot uses embedded chemosensor that involves the modulation of hSGLT3 protein glucosensor activity [56]. Even with the immune system reaction inside the body, the nanorobot is not attacked by the white blood cells due biocompatibility [46].

The image of the NCD simulator workspace shows the inside view of a venule blood vessel with grid texture, red blood cells (RBCs) and nanorobots (Fig. **1**). They flow with the RBCs through the bloodstream detecting the glucose levels. At a typical glucose concentration, the nanorobots try to keep the glucose levels ranging around 130 mg/dl as a target for the Blood Glucose Levels (BGLs). A variation of 30mg/dl was adopted as a displacement range (Fig. **2**), though this can be changed based on medical prescriptions - glucose levels were detailed on page 4. At any time, if the glucose achieves critical levels, the nanorobot emits an alarm through the mobile phone. In the simulation, the nanorobot is programmed also to emit a signal based on specified lunch times, and to measure the glucose levels in desired intervals of time. In the medical nanorobot architecture, the significant measured data can be then transferred automatically to the mobile phone.

The nanorobot can be programmed to activate sensors and measure regularly the BGLs early in the morning, before the expected breakfast time. Levels are measured again each 2 hours after the planned lunch time. The same procedures can be programmed for other meals through the day times.

Occasionally, if the doctor asked for shorter intervals of time for measurement, such information can be sent to reprogram the nanorobot to perform the tasks on different schedules. As a matter of standard for measurements, the nanorobot is programmed in our work to measure BGLs at intervals of 2 hours throughout the day. Thus, every two hours the nanorobot keeps the sensor activated 2 minutes and transmits the BGL measurements directly to the mobile phone (Fig. **3**). Different programs and commands can easily be sent to the nanorobot, and it may also serve for the nanorobot to communicate with the patient or with the medical specialists. This approach to *in vivo* chemical concentrations control can also be useful for monitoring other diseases [71,78]. In order to simulate various levels of glucose, we used a time series of events based on clinical data where a patient with diabetes is monitored 24 hours a day for 30 days. Significant concentrations of hSGLT3 will determine the glucose gradients. Each time the glucose achieves critical levels (Fig. **2**), the nanorobot sends a signal of alert. Beyond that, all the historical BGLs can be transferred every two hours to the mobile phone which records the information for later clinical analyses.

Deployment of large numbers of independent nanorobots can offer many other advantages over the use of a single blood-contacting implant having similar function (Figs. **4-9**). A multiplicity of blood borne nanorobots will allow glucose monitoring not just at a single site but in many different locations simultaneously throughout the body, thus permitting the physician to assemble a whole-body map of serum glucose concentrations. Examination of time series data from many locations allows precise measurement of the rate of change of glucose concentration in the blood that is passing through specific organs, tissues, capillary beds, and specific vessels. This will have diagnostic utility in detecting anomalous glucose uptake rates which may assist in determining which tissues may have suffered diabetes-related damage, and to what extent. Other onboard sensors can measure and report diagnostically relevant observations such as patient blood pressure, early signs of tissue gangrene, or changes in local metabolism that might be associated with early-stage cancer. Whole-body time series data collected during various patient activities levels (e.g., resting, exercising, postprandial, etc.) could have additional diagnostic value in assessing the course and extent of disease. Data reporting rates could be increased from 2-hour intervals up to continuous sampling if necessary to obtain sufficiently high resolution temporal discrimination.

CURRENT & FUTURE DEVELOPMENTS

A nanorobot architecture for data transmission, manufacturing approach, and telemetric control was presented, building from advances represented in several recent patents. This paper also described how mobile phones can play an important role to bring the application of medical nanorobot therapies into people's lives. Meanwhile, manufacturing methodologies may advance progressively, and the use of computational nanomechatronics and virtual reality may also help in the process of creating transducers and actuators relevant to nanorobotic equipment design, along with RFID and advances in nanobiotechnology applied to medical nanorobotics. This paper has outlined a pathway toward effective ways to advance nanotechnology as a diagnostic and treatment tool for patients with diabetes, and showed at the same time how actual developments in new manufacturing technologies are enabling innovative works and patents which may help in constructing and employing nanorobots most effectively for biomedical problems.

The implemented 3D simulator is a practical tool for exploring new techniques, nanomanufacturing strategies, and nanorobot mobility considerations including actuation and data transmission, helping designers to define the appropriate molecular machine architecture. The joint use of nanophotonic and nanotube-based technologies may further accelerate the actual levels of CMOS resolution ranging down to 45nm devices.

ACKNOWLEDGMENT

The authors thank Lior Rosen, Tad Hogg, and Warren W. Wood, for their helpful comments. This project was partially supported by the Australian Research Council (ARC).

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