Sensor based Autonomous Medical Nanorobots A cure to Demyelination

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***Abstract*— Nowadays medical science is more and more improving with the blessings of new scientific discoveries. Nanotechnology is such a field which is changing vision of medical science. New automated procedures are being discovered with new aspects of self guided nanorobots. Nanorobot is an excellent tool for future medicine. We can envision a day when you could inject billions of these nanorobots that would float around in your body. Nanorobots could carry and deliver drugs into defected cells. These nanorobots will be able to repair tissues, clean blood vessels and airways, transform our physiological capabilities, and even potentially counteract the aging process [1]. Many scientist working on this bright field of nanorobotics specially on Alzheimer disease and cancer treatments [2]. The researchers are also working on nanomanipulation, nanopositioning and also on the nano-level control systems [3]. In this paper we are going to address a disease called dymyelination and propose a nanorobotic control system for the cure. Demyelination is a disease of the nervous system where the protecting layer of neurons called myelin sheath is damaged. This disease hampers the conduction of signals in the affected nerves, causing impairment in sensation, movement, cognition, or other functions depending on which nerves are involved. This paper describes an innovative approach for the development of nanorobots that use neural network for identifying and repairing the damaged, demyelinated neurons. Firstly, the disease it self will be addressed to understand the later work easily, then a control system for automated nanorobots to cure dymyelination will be described. In later portion the proposed control system will be simulated to show the stability and usefulness of proposed design. The nanorobots operate in a virtual environment with nerve signals carrying nerve impulses. This paper also presents the control and the simulation of nerve-borne nanorobots to find and repair the affected nerves.**

***Index Terms*— demyelination, control system, nanorobots, neural nanotechnology.**

I. INTRODUCTION

NANOROBOTS are expected to enable significant new methodologies in diagnosis, medical therapies, and minimally invasive surgery [4-8]. The nanorobots hardware feasibility may be observed as the result of most recent advances in a broad range of manufacturing techniques [9]. A first series of nanotechnology prototypes for molecular machines are being investigated in different ways [6, 10-15], and some interesting device propulsion and sensing approaches have been presented [16-19]. Some work has been done in 2D on cellular automata with the examination of collective behaviors of large numbers of robots to locate specific types of tissue [20]. More complex molecular machines, or nanorobots, having embedded nanoscopic features may provide broad advances on health care sector [21-26].

Most researches on Nanorobots have been done for different type of automated and accurate medical target identification. [4] For example- Chemical signals can be used for identifying medical target in cerebral treatment. The amyloid-β protein deposits show changes on gradients as a symptom of Alzheimer disease [28, 29]. This information serves for the early diagnosis of Alzheimer disease and to guide possible immunotherapy treatments, with more efficient neurotransmitters delivery, like dopamine and amino acids such as g-aminobutyrate (GABA), with better medical administration. Nanorobots can use such signals to delivery genomic improved myelin basic protein [30].

Considering the ability of the nanorobots to be able to navigate over the myelin sheath of a nerve, they can help in better diagnosis and improved treatment procedures for diseases in relation to nerve signal disorders. A very promising application of nerve-borne nanorbots is the efficient delivery of genomic improved myelin basic protein. Here a nanorobot can be made to detect leakage of charge and thereby detecting demyelinated portion of a nerve. And then Synthetic myelin, carried by nanorobots, can then be effectively delivered to these affected portions. In our work we point out this possible application of using nanorobots on nerves and demonstrate a control system based on classical approach where nanorobots repair a damaged (demyielinated) nerve.

II. BACKGROUND OF MEDICAL NANOROBOTICS

Recent developments in nano-electronics and nano-biotechnology is providing feasible development pathways to enable molecular machine manufacturing, including embedded and integrated devices which can comprise the main sensing, actuation, data transmission, remote control uploading, and coupling power supply subsystems addressing the basics for operation of medical nanorobots [4].

The application of new materials has demonstrated a large range of possibilities for use in manufacturing better sensors and actuators with nano-scale sizes [4]. Manufacturing silicon-based chemical and motion sensor arrays using a two-level system architecture hierarchy has been successfully conducted in the last 15 years [32]. Tunneling current sensor for a long-range nano-positioning device has been developed and demonstrated few days back [33]. A recent actuator with biologically-based components has been proposed [35]. Such actuators can be utilized in nano-scale mechanical devices to pump fluids, open and close valves, or to provide translational movement. Different other kinds of nano-sized actuators, such as electromagnetic, piezoelectric, electrostatic, electro-thermal are also being researched and demonstrated now-a-days [34].

Nanotechnology is moving fast towards nano-electronics fabrication. Chemically assembled electronic nanotechnology provides an alternative to using a Complementary Metal Oxide Semiconductor (CMOS) for constructing circuits with feature sizes in the tens of nanometers [36]. The feasibility of advancing techniques for control [31] and manufacturing molecular machines should be understood as emergent results from actual and upcoming stages of nanotechnology based on nano-electronics, new materials and genomics research. New possibilities are coming from these developments which will enable new medical procedures. As a result of these researches CNTs (carbon nano-tubes) and DNA (Deoxyribo-Nucleic acid) are now being considered as recent candidates for new forms of nano-electronics [37]. And lastly recent developments in bio-molecular computing have demonstrated the feasibility of bio-computers [27], a very promising and much needed first step toward future nano-processors.

III. Nerve Impulse & Demyelination

A. Neuron

The nervous system is an organ system containing a network of specialized cells called neurons that coordinate the actions of an animal and transmit signals between different parts of its body. The protecting layer of neurons is called Myelin. It is a dielectric (electrically insulating) material that forms a layer, the myelin sheath, usually around only the axon of a neuron. It is essential layer for the proper functioning of the nervous system.

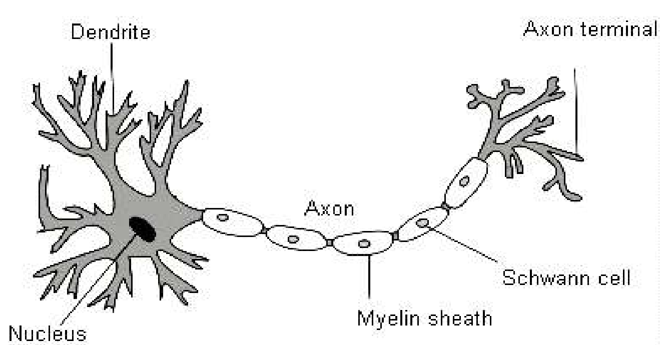

Figure 1: Structure of Neuron

B. Nerve Impulse Propagation

Neurons send signals to other cells as electrochemical waves travelling along thin fibers called axons, which cause chemicals called neurotransmitters to be released at junctions called synapses. A cell that receives a synaptic signal may be excited, inhibited, or otherwise modulated.

Neurones and muscle cells are electrically excitable cells, which mean that they can transmit electrical nerve impulses. These impulses are due to events in the cell membrane. The resting potential tells us about what happens when a neuron is at rest. An action potential occurs when a neuron sends information down an axon. This involves an explosion of electrical activity, where the nerve and muscle cells resting membrane potential changes. In nerve and muscle cells the membranes are electrically excitable, this means they can change their membrane potential, and this is the basis of the nerve impulse. The neurotransmitters i.e. sodium and potassium channels in these cells are voltage-gated, which means that they can open and close depending on the voltage across the membrane. The normal membrane potential inside the axon of nerve cells is –70mV, and since this potential can change in nerve cells it is called the resting potential. When a stimulus is applied a brief reversal of the membrane potential, lasting about a millisecond, occurs. This brief reversal is called the action potential.

Once an action potential has started it is moved (propagated) along an axon automatically. The local reversal of the membrane potential is detected by the surrounding voltage-gated ion channels, which open when the potential changes enough.

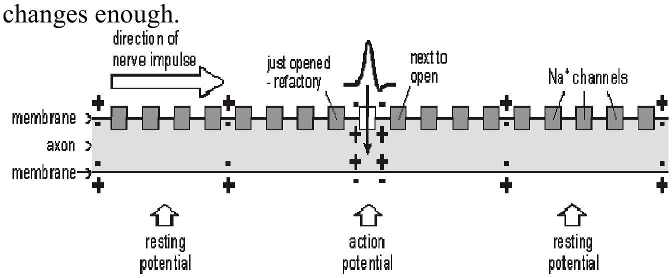

Figure 2: Nerve Impulse Propagation

C. Demyelination

Demyelination is the loss of the myelin sheath insulating the nerves, and is the hallmark of some neurodegenerative autoimmune diseases, including multiple sclerosis, acute disseminated encephalomyelitis, transverse myelitis, chronic demyelinating polyneuropathy, Guillain-Barré Syndrome, central pontine myelinosis etc. When myelin degrades, conduction of signals along the nerve can be impaired or lost and the nerve eventually withers.

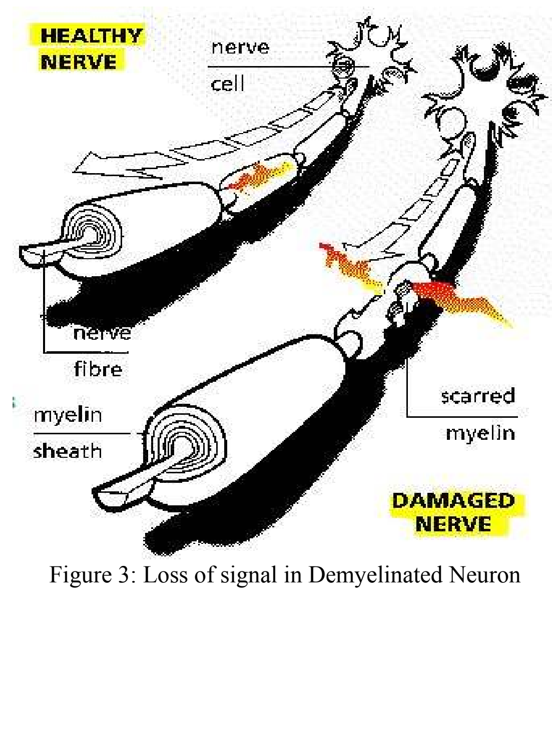

Figure 3: Loss of signal in Demyelinated Neuron

Demyelination can results in thousand complexities starting from loss of balance, optical illusions to short term memory loss and loss of concentration, judgment or reasoning. Each year thousands of people around the world suffer from this disease. And most of the people have to live with it because the expensive conventional surgery method is very complex, almost inaccessible and do not cure perfectly.

IV. Proposed Nanorobots

Nanorobot being placed on nerves, it can detect electrical signals i.e nerve impulses and takes decision on which path it will take. We address this procedure by illustrating a nanorobot whose sole aim is to find demyelinated area and to deliver synthetic myelin sheath on it. A team of this nanorobot can deliver us an autonomous, accurate and minimum invasive surgical procedure to cure demyelination.

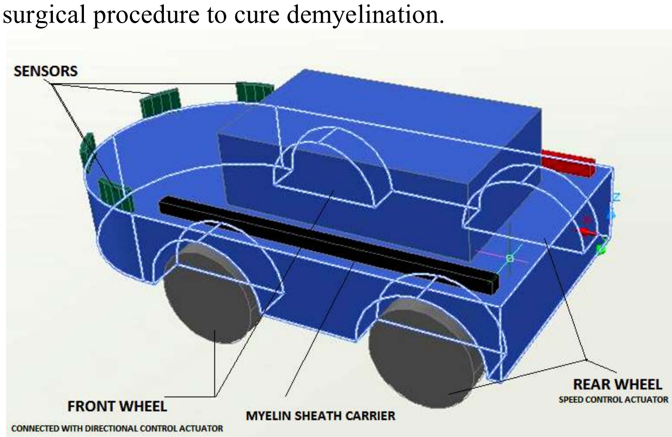

Figure 4: Hypothetical model of Proposed Nanorobot

A. Actuator

There are different kinds of actuators, such as electromagnetic, piezoelectric, electrostatic, electrothermal, where they should be utilized depending on the aim and the workspaces where they will be applied. A flagella motor has been quoted quite frequently as an example for a kind of biologically inspired actuator for molecular machine propulsion. Adenosine triphosphate, also known in short as ATP, is equally used as an alternative for nanomotors [7]. DNA and RNA (ribonucleic acid) prototypes were also proposed for designing different types of devices. A set of fullerene structures were presented for nanoactuators. The use of CNTs as conductive structures permits electrostatically driven motions providing the forces necessary for nano-manipulation [4]. For ours purpose, the use of CMOS as an actuator based on biological patterns and CNTs is considered a natural choice.

B. Directional Control

While nerve impulses in unmyelinated neurons have a maximum speed of around 1 m/s, in myelinated neurons they travel at 100 m/s. electrical voltage is to be detected and passed over low pass filter to get the sensor voltages V_{xi}.

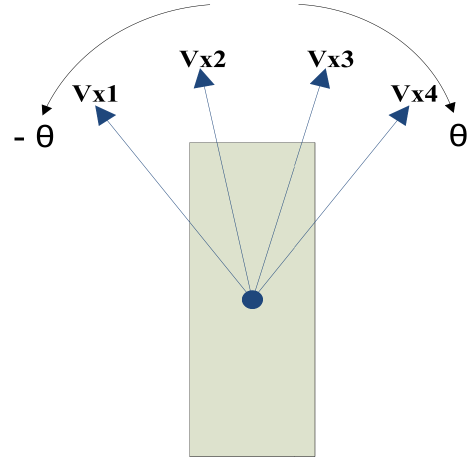

Figure 5: Sensor positions and angel of rotation

$$V_{effective} = 2V_{x1} + V_{x2} - 2V_{x4} - V_{x3}$$

The outputs of four sensors are fed into a summing circuit with consideration to their weights. The resulting *Veffective* is input for an actuator which is connected to the front wheels.

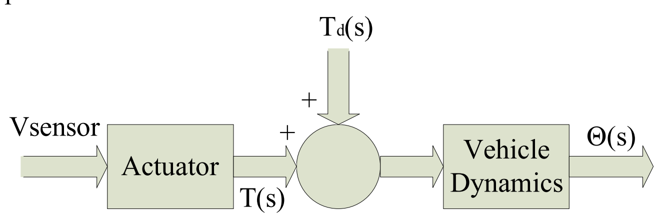

Figure 6: Block diagram of Directional Control

Vehicle dynamics is considered to be of the form

$$\theta(s) = \frac{1}{J * s^2 + B * s + k} T(s)$$

C. Speed Control:

The back wheels are for speed control. Stability in speed and rejection of disturbances like Brownian motion is crucial for positive performance of the nanorobots. A lead lag controller is used and stability and performance of the system is studied by using hypothetical actuator model.

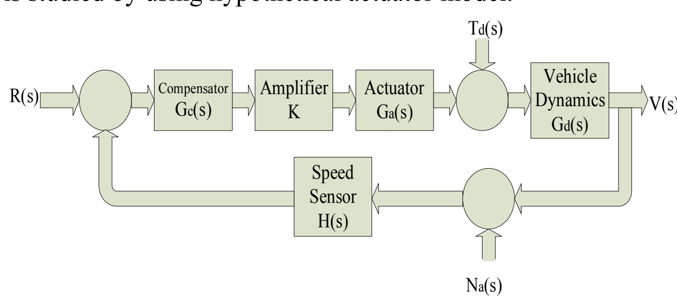

Figure 7: Block Diagram of Speed Control System

Now here $E(s) = R(s) - Y(s)$; for unity feedback

$$E(s) = \frac{1}{1+L(s)} R(s) - \frac{Gd(s)}{1+L(s)} Td(s) + \frac{L(s)}{1+L(s)} Na(s);$$

Where $L(s) = k\, G_c(s)\, Ga(s)$.

$T_d(s)$ is dominant in low frequency. We want Sensitivity function [1/{1+L(s)}] to be small for $T_d(s)$ at low frequency, and Complementary Sensitivity function [L(s)/{1+L(s)}] to be low at high frequency.

So we want loop gain L(s) to be large at low frequency and small at high frequency. To meet this lead lag controller is used.

$$G_c(s) = \frac{s+a}{s+b}$$

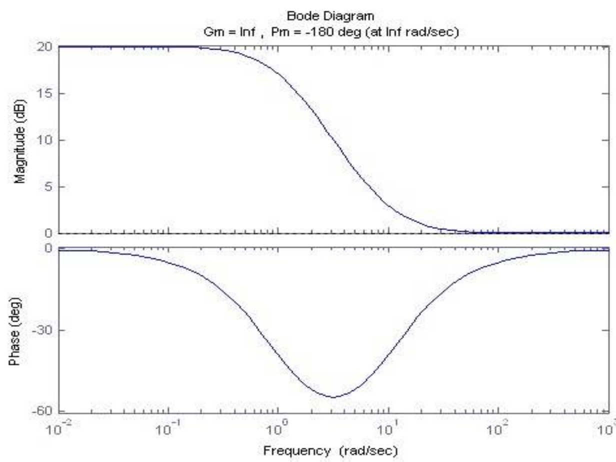

Figure 8: Lead Lag controller with a=10, b=1

D. Weight Control

A very significant design requirement is that the nanorobots always stay nerve-borne. To do this we simply propose to use the concept of attractive force between two current carrying conductors- one being the nerve and the other being current carrying nanowire on the nanorobot.

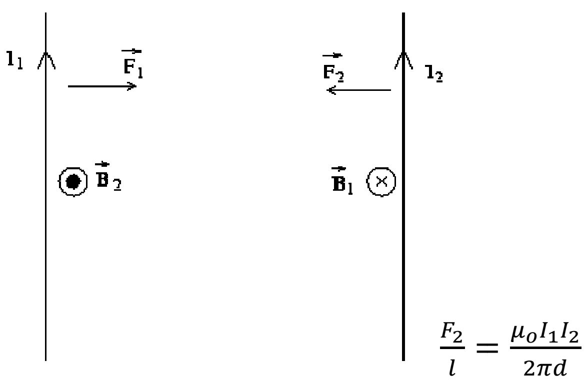

Figure 9: Simple illustration of forces between nano-wires

E. Energy Supply

The most effective way to keep the nanorobot operating successfully is to establish the use of a continuous available source of power. The energy must 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 has to keep working inside the human body, sometimes for long periods, and requires easy access to clean and controllable energy to maintain efficient operation.

Some possibilities to power the nanorobot can be provided from ambient energy. Temperature displacements could likewise generate useful voltage differentials. Electromagnetic radiation from light is another option for energy generation in determined open environments [39] but not for in vivo medical nanorobotics. Most recently, remote inductive powering has been used both for RFID (radio frequency identification device) and biomedical implanted devices to supply power on the order of milliwatts. A low frequency energy source can be sufficient to operate nanorobots. This functional approach presents the possibility of supplying energy in a wireless manner [4]. Thus, it enables one to operate sensors and actuators necessary for the controlled operation of nanorobots inside the human body.

V. Simulations and Results

A. Simulation for Directional Control

Transfer function of directional control can be found from the block diagram of Figure 7.

$$\theta(s) = Vehicle\ Dynamics * Direction\ Control\ Actuator, T(s)$$

Assuming $T_d(s) = 0$ (i.e. no disturbances) it can be written as-

$$\theta(s) = \frac{1}{2.26 * 10^{-21}s^2 + 9.04 * 10^{-22}s + 10^{-22}} * \frac{10^{-20}}{(s+1)(s+2)(s+7)}$$

Values used in the equations are hypothetical and calculated based on practical speculations by taking mass and volume in nano-scale. The actuator transfer function is taken similar to a macro-level actuator but in nano-range.

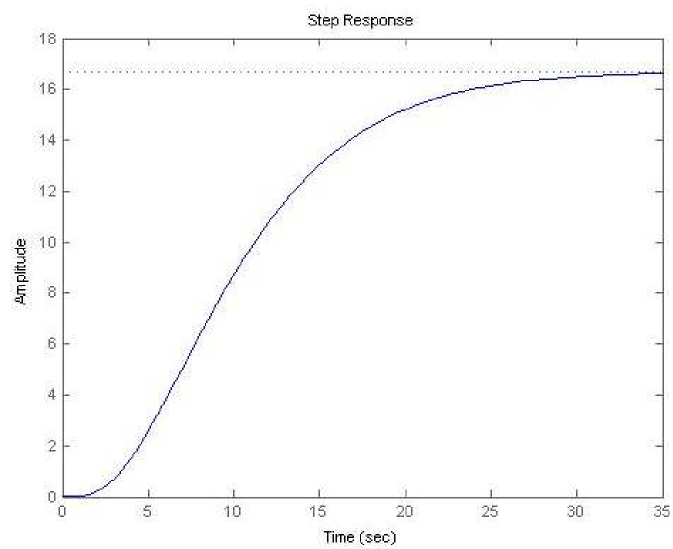

Figure 10: Step response of Directional Control

Step response of the open loop directional control indicates that even a small $V_{effective}$ can rotate the direction of movement. This sensitive control ensures that nanorobot moves toward the damaged area only.

B. Simulation for Speed Control

The speed control transfer function for speed control can be written as-

$$G(s) = K * Compensator, G_c(s) * Actuator, G_a(s) * Vehicle\ dynamics, G_d(s)$$

As stated before we will use a lead lag controller as a compensator with a pole at –b and zero at –a; actuator model will be same as direction control actuator and vehicle dynamics as used before. So above mentioned equation can be re-written as-

$$G(s) = \frac{s+a}{s+b} * \frac{10^{-20}}{(s+1)(s+2)(s+7)} * \frac{k}{2.26 * 10^{-21}s^2 + 9.04 * 10^{-22}s}$$

Now to find out appropriate range of values of “a”, “b” and “k” we have applied classical approach of stability analysis, Routh Criterion.

Table 1: Routh Table

s^5	235.04	524.32 + 610.2p=C	126.5p+k
s^4	610.2+235.04p=B	126.5 + 524.32p = D	kz
s^3	E	$\frac{(126.5p+k)D - Ckz}{D}$	
s^2	M		
s^1			
s^0			

From the table it is eminent that to have a stable system-

$$\frac{E * D - \frac{B}{D}(126.5pD + kD - Ckz)}{E} > 0$$

$$Or$$

$$k > \frac{126.5pD - \frac{ED^2}{B}}{Cz - D}$$

So we have found valid range of “a”, “b” and “k” which can also be demonstrated in 3D plot.

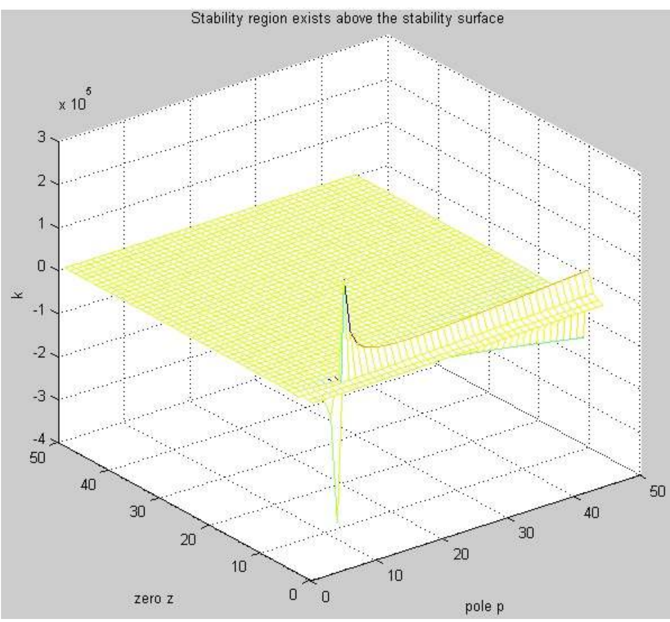

Figure 11: Three dimensional plot of stability region

The stability region exists above the stability surface. So we can choose a=10 and b=1. So Compensator transfer function

$$G_c(s) = \frac{s+10}{s+1}$$

Root locus and step response of the compensated system now can be plotted to show the stability.

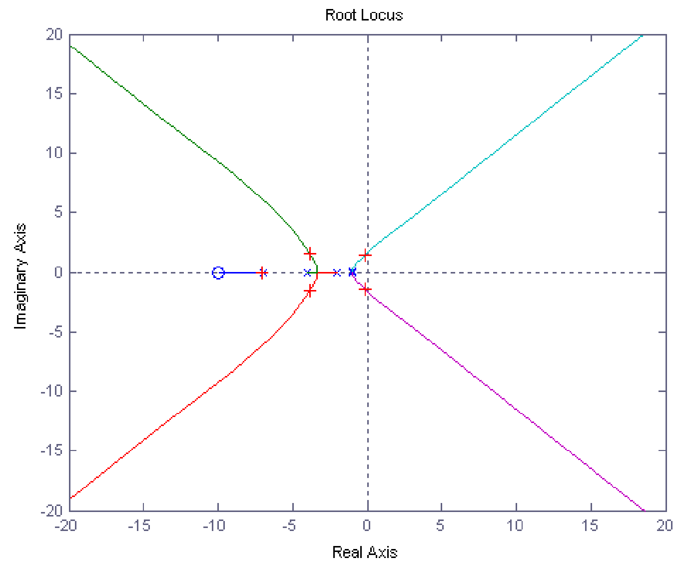

Figure 12: Root Locus Plot of Proposed System

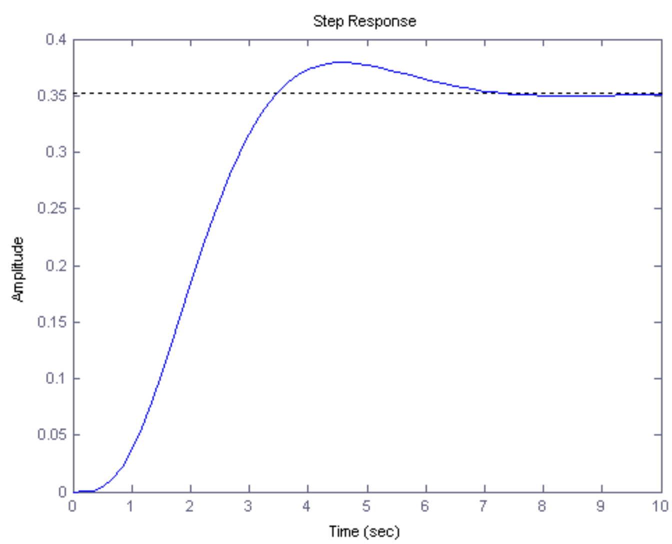

Figure 13: Step response of proposed System

So the compensated system is stable. Nanorobot with this control system can successfully move on the nerve to find demyelinated neurons. State space representation of this system have been found using MATLAB and rank of system was 6, same as the order of the system which means the system is both controllable and observable.

VI. Further Developments

Although the direction, speed and energy supply system was discussed but we are still working on the payload delivery system, where it is necessary to sense where exactly the delivery of myelin sheath should be made.

Here in this paper we have presented a theoretical development of a stable nanorobotic system that can be used to cure demyelinated neurons, but practically manufacturing of such nanorobots is not yet possible due to several practical limitations in the process. However technologies are developing so fast and time will come when producing nanorobots like this one will not be difficult. With the appropriate technologies in hand we can even think of improving the system for further complex operations.

The perspective that the same manufacturing technologies required to assemble this nanorobot could also be applied to a broad range of fields. The research and development of nanorobots can also provide new technologies and devices for enhanced industrial automation. As a result of such development, more effective and safe operations are expected for manufacturing processes, as well as better electronics, featuring higher performance and lower requirements.

The application of nanorobots with embedded sensor devices for drug and diagnosos is an interesting subjcet, which can enable significant improvements as a big precission device for medical treatments [5]. Thus all the possibilities needs to be considered to have better utilisation nanorobots in future medical applications.

VII. Conclusion

This paper has proposed a new concept of using nerve-borne sensor based nanorobots for medical applications. Nerve-borne nanorobots should help, through sensing nerve impulse singnals, to provide better understanding of correlation of nerve signals and disease. They should also be able to help give early diagnosis and provide new therapeutic procedures. Again even they can help us to invastigate the nervous system from close point of vies. Here classical control systems analysis was adopted to illustrate one specific application: to find the demyelinated neuron automatically and to deliver synthetic myelin sheath to demyelinated portion of nerve.

Stability of the nanorobots and disturbance rejection, like brownian motion and electrical noise, are crucial to the performance of the nanorobots. They define the limitations of the nanorobots, and thus limit the applications where they can be used. Therefore, collecting data and adapting to the new situation with better control methods is paramount to the future success of the use of nanorobots in medicine.

Although this nanorobot is not a reality today but with the advancement of technology this proposed nanorobot can cure thousands of demyelination disease victims with very low cost and accurate minimal invasive surgery.

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