بسم الله الرحمن الرحيم

Sudan University of Science and Technology

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Graduate Studies

Department of Biomedical Engineering

Design of an embedded system of spinal cord stimulator

تصميم منظومه مدمجه لتحفيز الحبل الشوكي

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Dedication

I *dedicate this work to my parents, all of my family members, my friends and professors in Sudan University Especially Biomedical engineering college and departments, special thanks to my guidance Supervisor who inspire me the knowledge and all information and he didn't let me down during this research ...Doctor\Fragoon my letters has not enough meaning to express my gratitude and thanks for your kindness and guidance ...*

Acknowledgement

Pursuing master study thesis project is a both painful and enjoyable experience. It is just like climbing a high peak; gradually, accompanied with bitterness, hardness, frustration, encouragement and trust, and with so many people's kind help, when I found myself at the top enjoying the beautiful sincerely. I realized that it was in fact team work that got me there, so it will not be enough to express my gratitude in words to all those people who helped me, I would still like to give my many may thanks to all these people.

First of all, my supervisor Dr\Fragoon, who surrounding me by his patentees and for guiding me to the end of the road safely and for his kindness and faithfulness to his work and to my project as a part of it.

Lastly, words could never express my gratitude to all of staff of Sudan University, Collage of Graduate study and special thanks for Biomedical Department section.

Doaa Arabi Ali Karrar

المستخلص

تحفيز الحبل الشوكي (SCS) هو عباره عن علاج للألم عن طريق استخدام تيار كهربي خفيف لمنع النبضات العصبيه في العمود الفقري. تستخدم تقنيه العلاج بالتحفيز بعد الفشل في محاولات المعالجه عن طريق استخدام الادويه وممارسه التمارين الرياضيه.

هناك ايضا بعض الانشطه في الحبل الشوكي ليست لها علاقه بالمخ لذلك توجد خلايا عصبيه تعمل علي التوصيل بين الخلايا الحسيه والحركيه في كل اجزاء الحبل الشوكيز ينقسم الحبل الشوكي الي جزئين متساويين الجزء الامامي والجزء الخلفي.

صمم هذا العمل كموديل لجهاز تحفيز الحبل الشوكي الذي يقوم بقراءه الترددات وحساب النبضات المراد اخراجهامن خلال المتحكم حيث يستفاد من خاصيه توليد الترددات الموجوده داخل المتحكم لاخراج النبضات المطلوبه. يستخدم لبرمجه المتحكم لغه BASCOB واستخدم برنامج المحاكاةPRUTOUS لبرمجه المتحكم وعرض النتائج.

تعتمد النتائج في جهاز التحفيز علي حاله المريض ودرجه الألم فعندما نقوم بضبط قيمه معينه لمتغيرات الجهاز تظهر القيمه المطلوبه علي شكل موجه مربعه عند توصيل جهز التحفيز بجهاز راسم الاشاره.

يعتبر هذا العمل معد ليقدم نسخه جديده من جهاز تحفيز الحبل الشوكي ومن مميزاته انه سهل الاستخدام حيث يمكن استخدامه في المنزل ويعتبر قليل التكلفه مقارنه بباقي الاجهزه. جوده الرسم البياني المعروض يمكن تطويرها وتحسينها.

Abstract

Spinal cord stimulation is a treatment for pain that uses a mild electric current to block nerve impulses in the spine. SCS is used after you have tried other treatments such as medication and exercise and they have not worked.

Some activities of the spinal cord are independent of the brain, i.e. spinal reflexes. To facilitate these there are extensive neuron connections between sensory and motor neurons at the same or different levels in the cord. The spinal cord incompletely divided into two equal parts, anteriorly by a short, shallow median fissure and posteriorly by a deep narrow septum, the posterior median septum.

This work we designed module of the job of a spinal cord impulse simulator, which reads the vibration through a PIN-B1 and the provisional rules of procedure runs to calculate the pulse counter in a given time. Moreover, the program condition counts per cycle and amplitude in a given time. In addition, the program condition involves output pulses that uses PWM technique, impulses and frequency duty emerging count of impulses input .Finally, this work carried out using BASCOM and PRUTOUS software to stimulate the circuit work and display the results.

The results of the stimulator depending on the state of patient when we adjusted the values of the parameters that we need in specific patient state of problem the signal appears as square waveform in the oscilloscope.

This research intended to produce new version of spinal cord stimulator, this design will make home usage possible, cheap compared with the other types of stimulators. This stimulator design intended to be flexible and medical experts could adjust to the need and requirement of the patients. The quality of graphic display used and improved.

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List of nomenclature

CNS	Central nervous system.
SCS	Spinal cord stimulator.
C	Cervical Nerves.
T	Thoracic Nerves.
L	Lumbar Nerves.
CRPS	Complex regional pain syndrome.
HZ	Hertz.
V	Volt.
ms	Mille second.
RF	Radiofrequency.
IPG	Implantable pulse generator.
FBSS	Failed back surgery syndrome.
CSF	Cerebrospinal fluid.
MRI	Magnetic resonance imaging.
PT	Physical therapy.
CMM	Conventional medical management.
LCD	Liquid crystal display.
AC	Alternative current.

DC	Direct current.
°C	Degree centigrade.
IC	Integrated circuit.
LED	Light emitting diode.
ADC	Analog to digital converter.
f	Frequency.
R1,R2	Resistors.
Ω	Ohm.
MΩ	Milli ohm.
kΩ	Killo ohm.
F	Farad
µF	Micro farad
S	Second.
kHz	Kilohertz.
I/O	Input/output.
CPU	Central processing unit.
RISC	Reduced Instruction Set Computing

Terminologies

- **Grey matter** (or **gray matter**) is a major component of the central nervous system, consisting of neuronalcell bodies, neuropil (dendrites and myelinated as well as unmyelinatedaxons), glial cells (astroglia and oligodendrocytes), synapses, and capillaries. Grey matter is distinguished from white matter, in that it contains numerous cell bodies and relatively few myelinated axons, while white matter contains relatively very few cell bodies and is composed chiefly of long-range myelinated axon tracts [7070].
- **White matter** is composed of bundles of myelinated nerve cell projections (or axons), which connect various gray **matter** areas (the locations of nerve cell bodies) of the brain to each other, and carry nerve impulses between neurons. myelinated axons), glial cells (astroglia and oligodendrocytes), synapses, and capillaries [7171]
- **Brain** is the central trunk of the mammalian brain, consisting of the medulla oblongata, pons, and midbrain, and continuing downward to form the spinal cord.
- Stimulus is a thing or event that evokes a specific functional reaction in an organ or tissue
- **Spinal cord** is the cylindrical bundle of nerve fibres and associated tissue that is enclosed in the spine and connects nearly all parts of the body to the brain, with which it forms the central nervous system.
- **Nerve cord** is the major cord of nerve fibres running the length of an animal's body, especially a ventral cord in invertebrates that connects segmental nerve ganglia

- **Embedded system** is a computer system with a dedicated function within a larger mechanical or electrical system, often with real-time computing constraints [72] [73]. It is embedded as part of a complete device often including hardware and mechanical parts. It controls many devices in common use today [74].

Chapter 1 INTRODUCTION

1.1 Introduction

The spinal cord is a long, thin, tubular bundle of nervous tissue and support cell that extends from the medulla oblongata in the brainstem, the brain and spinal cord together make up the central nervous system (CNS) [**Error! Reference source not found.**1]. It is suspended in vertebral canal surrounded by the meninges and cerebrospinal fluid [1].

The spinal cord is approximately 45cm long in an adult Caucasian male, 43cm in female and is about the thickness of the little finger. Except for the cranial nerves, the spinal cord is the nervous tissue link between the brain and the rest of the body [1].

The spinal cord is the main pathway for information connecting the brain and peripheral nervous system, its length is much shorter than the length of vertebral column [**Error! Reference source not found.**1]. It is composed of many nerve fibres that run from the base of the brain to the small of the back. It is the most important way for the brain to communicate with the rest of the body [3].

Some activities of the spinal cord are independent of the brain, i.e. spinal reflexes. To facilitate these there are extensive neuron connections between sensory and motor neurons at the same or different levels in the cord. The spinal cord is incompletely divided into two equal parts, anteriorly by a short, shallow median fissure and posteriorly by a deep narrow septum, the posterior median septum [1].

The spinal cord has a core of grey matter containing nerve cell bodies, dendrites, and supporting cells. Surrounding the grey matter is white matter containing columns of nerve fibres that carry signals to and from the brain along the length of the spinal cord [4].

1.2 Problem statement

Stimulation in general refers to how organisms perceive incoming stimuli. As such it is part of the stimulus-response mechanism. Simple organisms broadly react in three ways to

stimulation, too little stimulation causes them to stagnate, too much to die from stress or inability to adapt, and a medium amount causes them to adaptand grow as they overcome it. Similar categories or effects are noted with psychological stress with people. Thus, stimulation may be described as how external events provoke a response by an individual in the attempt to cope [6666].

Spinal cord stimulation is a treatment for pain that uses a mild electric current to block nerve impulses in the spine.SCS is used after you have tried other treatments such as medication and exercise and they have not worked [5]. This treatment is used the spinal cord stimulator which is the electrical therapy for pain management. A spinal cord stimulator (SCS), also known as a dorsal column stimulator, is a device surgically placed under your skin or outside the body and connected by a sensor to the spinal cord (as the device that used in this research) to send a mild electric current to your spinal cord. A small wire carries the current from a pulse generator to the nerve fibres of the spinal cord. When turned on, the stimulation feels like a mild tingling in the area where pain is felt. Your pain is reduced because the electrical current interrupts the pain signal from reaching your brain [6].

1.3 Objectives

- The mainaim off this researchis proposing a modify stimulator to block the pain of the spinal cord.
- Identifies the system components which have the ability to output signals same as natural signals of the body.

- Programmed the circuit by using simple machine language. This code is used to program the microcontroller of the embedded system.
- Test the system after the adjusting of the variables used to restrict the range that used to give signal for specific problem. This step confirms the system accuracy.

1.4 Research plan

The organization of thesis is a follow; in the following chapter has two part, the first part is the background of the spinal cord mainly focus in the anatomy and physiology of the spinal cord in details, the second part is the stimulation definition and why we used stimulation for the spinal cord then mention technique used to stimulate the spinal cord. The literature review in chapter 3, system design reviews all the software and hardware in details and operation of the system in chapter 4, the result of the system is explained in chapter 5, chapter 6 is the conclusion of the research and the future work and recommendation for this research.

Chapter 2 THEORATICAL BACKGROUND

2.1 Part one - Anatomy and physiology

2.1.1 Introduction

The central nervous system (CNS) is the part of the nervous system consisting of the brain and spinal cord. The central nervous system is so named because it integrates information it receives from, and coordinates and influences the activity of, all parts of the bodies of bilaterally symmetric animals — that is, all multicellular animals except sponges and radially symmetric animals such as jellyfish — and it contains the majority of the nervous system. Arguably, many consider the retina [77] and the optic nerve (2nd cranial nerve) [8][9], as well as the olfactory nerves (1st) and olfactory epithelium [10] as parts of the CNS, synapsing directly on brain tissue without intermediate ganglia. Following this classification the olfactory epithelium is the only central nervous tissue in direct contact with the environment, which opens up for therapeutic treatments [10]. The CNS is contained within the dorsal body cavity, with the brain housed in the cranial cavity and the spinal cord in the spinal canal. In vertebrates, the brain is protected by the skull, while the spinal cord is protected by the vertebrae, both enclosed in the meninges [11].

The central nervous system (CNS) controls most functions of the body and mind. The brain is the center of our thoughts, the interpreter of our external environment, and the origin of control over body movement. Like a central computer, it interprets information from our eyes (sight), ears (sound), nose (smell), tongue (taste), and skin (touch), as well as from internal organs such as the stomach [**Error! Reference source not found.**].

The brain plays a central role in the control of most bodily functions, including awareness, movements, sensations, thoughts, speech, and memory. Some reflex movements can occur via spinal cord pathways without the participation of brain structures [12].

The spinal cord is the highway for communication between the body and the brain. When the spinal cord is injured, the exchange of information between the brain and other parts of the body is disrupted [**Error! Reference source not found.**].

The spinal cord is connected to a section of the brain called the brainstem and runs through the spinal canal. Cranial nerves exit the brainstem. Nerve roots exit the spinal cord to both sides of the body. The spinal cord carries signals (messages) back and forth between the brain and the peripheral nerves [12].

2.1.2 The Spinal cord

The spinal cord is the elongated, almost cylindrical part of the central nervous system, which is suspended in the vertebral canal surrounded by the meninges and cerebrospinal fluid (Figure 2-1). It is continuous above with the medulla oblongata and extends from the upper border of the atlas to the lower border of the 1st lumbar vertebra (Figure 2-2). It is approximately 45 cm long in an adult Caucasian male, and is about the thickness of the little finger. When a specimen of cerebrospinal fluid is required, it is taken from a point below the end of the cord, i.e. below the level of the 2nd lumbar vertebra. This procedure is called lumbar puncture [**Error! Reference source not found.**].

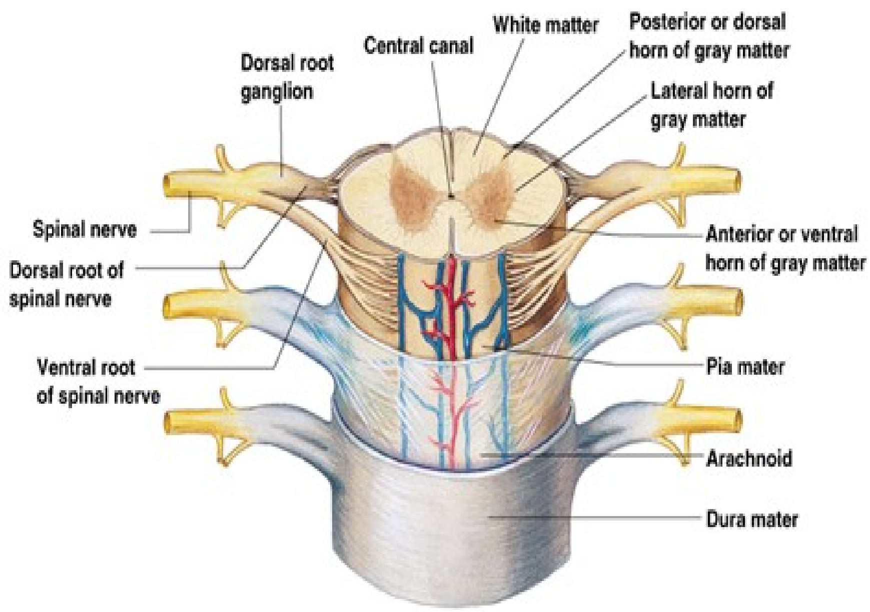


Figure 2-1: The meninges covering the spinal Cord. Each cut away to show the Underlying layers [13].

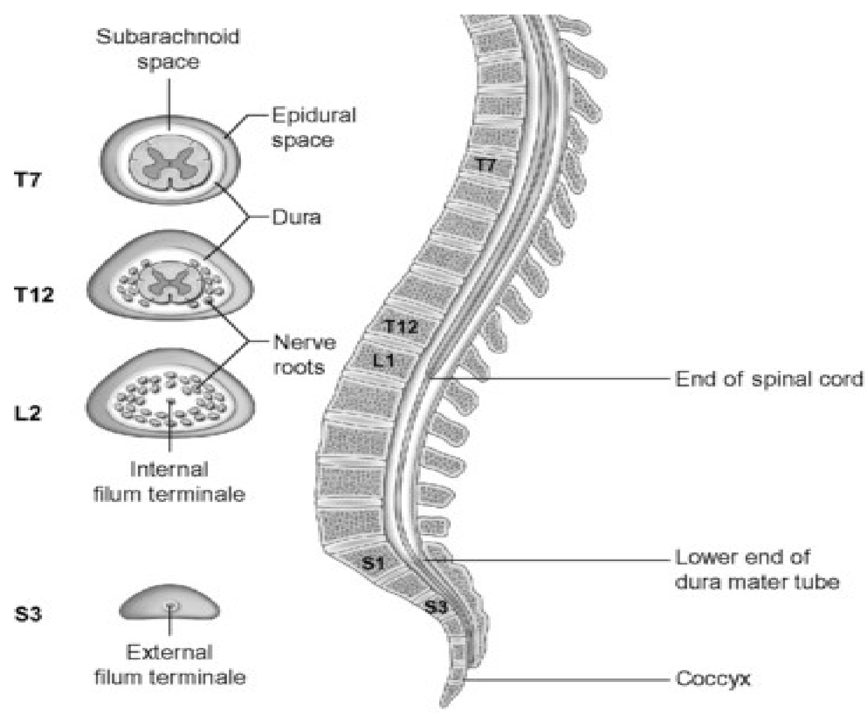


Figure 2-2: Section of the distal end of the vertebral canal [13].

Except for the cranial nerves, the spinal cord is the nervous tissue link between the brain and the rest of the body (**Error! Reference source not found.**). Nerves conveying impulses from the brain to the various organs and tissues descend through the spinal cord. At the appropriate level, they leave the cord and pass to the structure they supply. Similarly, sensory nerves from organs and tissues enter and pass upwards in the spinal cord to the brain [13].

Some activities of the spinal cord are independent of the brain, i.e. spinal reflexes. To facilitate these there are extensive neurone connections between sensory and motor neurones at the same or different levels in the cord. The spinal cord is incompletely divided into two equal parts, anteriorly by a short, shallow median fissure and posteriorly by a deep narrow septum, the posterior median septum [13].

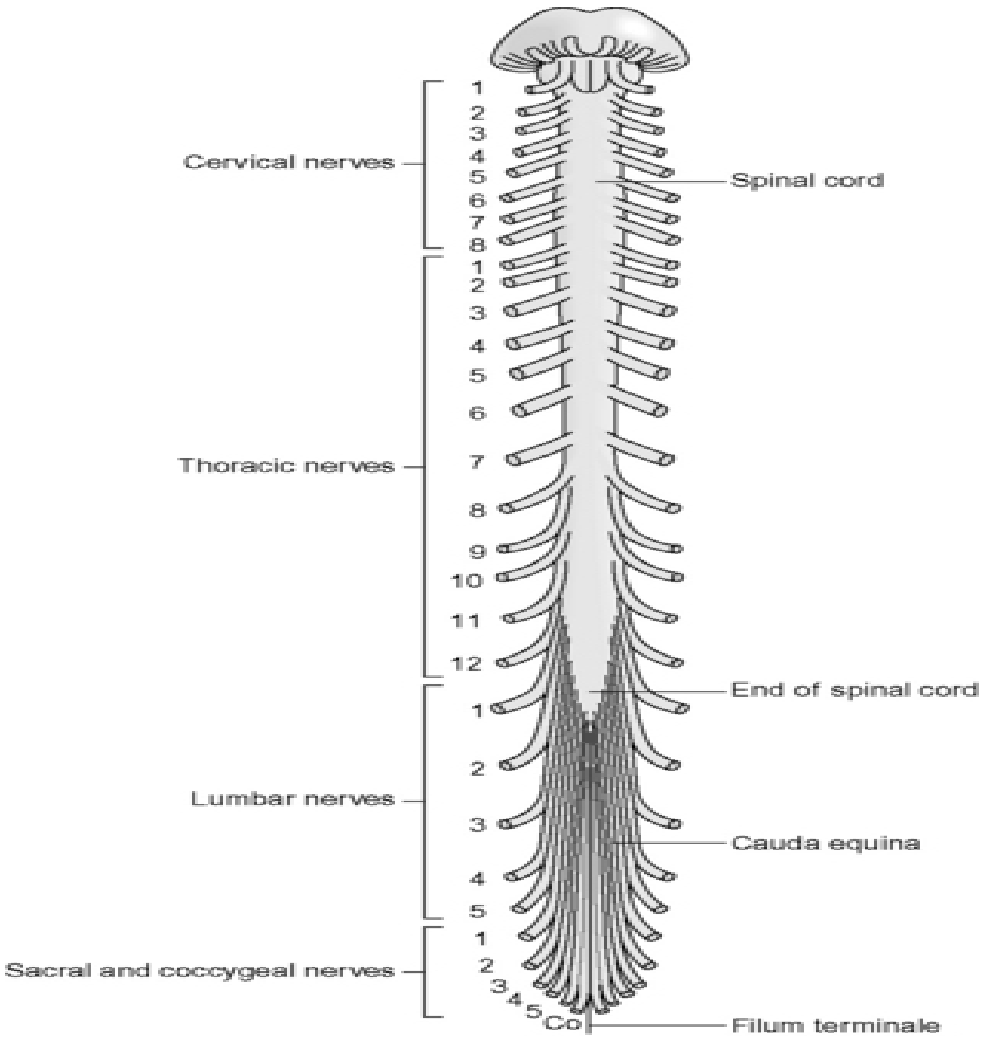


Figure 2-3: The spinal cord and spinal nerves [**Error! Reference source not found.**].

2.1.3 The anatomy and physiology of the spinal cord

The spinal cord is located at the center of the vertebral column and extends from the foramen magnum of the skull to the first or second lumbar vertebra, it is made up of:

- Vertebrae, sacrum and coccyx – bony sections that house and protect the spinal cord (commonly called the spine)
- The vertebral body is the biggest part of a vertebra. It is the front part of the vertebra, which means it faces into the body.

- Spinal cord – a column of nerves inside the protective vertebrae that runs from the brain to the bottom of the spine
- Disc – a layer of cartilage between each vertebra that cushions and protects the vertebrae and spinal cord [16].

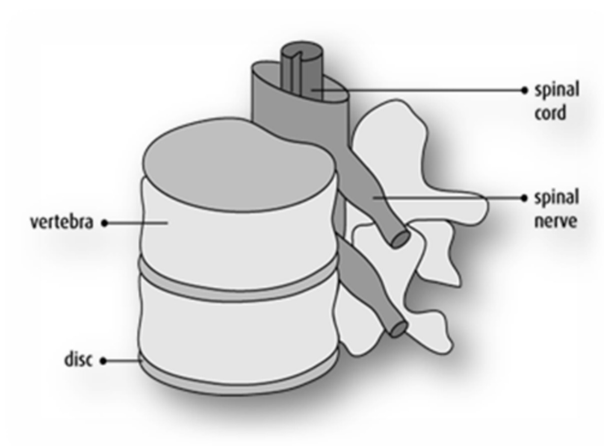


Figure 2-4: The spine [16].

The anatomy of the spinal cord itself consists of millions of nerve fibres, which transmit electrical information to and from the limbs, trunk and organs of the body, back to and from the brain. The nerves which exit the spinal cord in the upper section, the neck, control breathing and the arms. The nerves, which exit the spinal cord in the mid and lower section of the back, control the trunk and legs, as well as bladder, bowel and sexual function.

The nerves, which carry information from the brain to muscles, are called Motor Neurones and the nerves, which carry information from the body back to the brain, are called Sensory Neurones. Sensory Neurones carry information to the brain about skin temperature, touch, pain and joint position.

The brain and spinal cord are referred to as the Central Nervous System, whilst the nerves connecting the spinal cord to the body are referred to as the Peripheral Nervous System.

Its primary functions are to relay messages between the brain and the rest of the body and to serve as a reflex center. Within the vertebral column, the spinal cord is surrounded by an epidural space containing fat, ligaments, and blood supply and three meninges: the dura mater, arachnoid, and pia mater. Below the dura mater, cerebrospinal fluid, which is a clear, nutrient-rich fluid, circulates around and through the spinal cord. When viewed transversely, the posterior median sulcus and anterior median fissure partially divide the spinal cord into two halves [15].

The spine is divided into 5 sections:

- Cervical – the vertebrae from the base of the skull to the lowest part of the neck
- Thoracic – the vertebrae from the shoulders to mid-back
- Lumbar – the vertebrae from mid-back to the hips
- Sacrum – the vertebrae at the base of the spine.
    - the vertebrae in this section are fused and do not flex
- Coccyx – the “tail bone” at the end of the spine.
    - The vertebrae in this section are fused and do not flex [16].

The cross section of the spinal cord shows that it is composed of grey matter in the center surrounded by white matter.

2.1.3.1 Grey matter

Grey matter or gray matter is a major component of the central nervous system, consisting of neuronal cell bodies, neuropil(dendrites and myelinated as well as unmyelinated axons),glial cell(astroglia and oligodendrocytes) , synapses, and capillaries. Grey matter is distinguished from white matter, in that grey matter contains numerous cell bodies and relatively few myelinated axons, while white matter is composed chiefly of long-range myelinated axon tracts and contains relatively very few cell bodies [19]. The color difference arises mainly from the whiteness of myelin. In living tissue, grey matter actually has a very light grey color with yellowish or pinkish hues, which come from capillary blood vessels and neuronal cell bodies [21].

The arrangement of grey matter in the spinal cord resembles the shape of the letter H, having two posterior, two anterior and two lateral columns. The area of grey matter lying transversely is the transverse commissure and it is pierced by the central canal, an extension from the fourthventricle, containing cerebrospinal fluid. The cell bodies may be:

- Sensory cells, which receive impulses from the periphery of the body
- Lower motor neurones, which transmit impulses to the skeletal muscles
- Connector neurones, linking sensory and motor neurones, at the same or different levels, which form spinal reflex arcs.

At each point where nerve impulses are passed from one neurone to another there is a synaptic cleft and a neurotransmitter.

2.1.3.1.1 Posterior columns of grey matter:

These are composed of cell bodies which are stimulated by sensory impulses from the periphery of the body. The nerve fibers of these cells contribute to the formation of the white matter of the cord and transmit the sensory impulses upwards to the brain [13].

The posterior grey column contains the points where sensory neurons synapse. These receive sensory information from the body, including fine touch, proprioception, and vibration. This information is sent from receptors of the skin, bones, and joints through sensory neurons whose cell bodies lie in the dorsal root ganglion. This information is then transmitted in axons up the spinal cord in spinal tracts, including the dorsal column-medial lemniscus tract and the spinothalamic tract [22].

2.1.3.1.2 Anterior columns of grey matter:

These are composed of the cell bodies of the lower motor neurones which are stimulated by the axons of the upper motor neurones or by the cell bodies of connector neurons linking the anterior and posterior columns to form reflex arcs [13].

The anterior grey column contains motor neurons. These synapse with interneurons and the axons of cells that have travelled down the pyramidal tract. These cells are responsible for the movement of muscles [22].

The posterior root (spinal) ganglia are composed of cell bodies, which lie just outside the spinal cord on the pathway of the sensory nerves. All sensory nerve fibres pass through these ganglia. The only function of the cells is to promote the onward movement of nerve impulses [13].

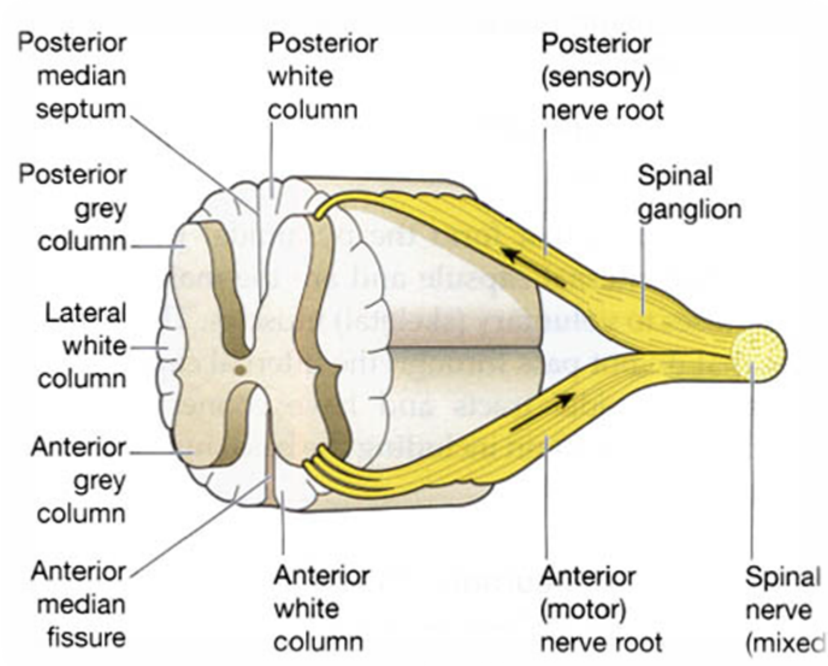


Figure 2-5: A section of the spinal cord showing nerve roots on one side [13].

2.1.3.2 White matter

White matter is a component of the central nervous system, in the brain and superficial spinal cord, and consists mostly of glial cells and myelinated axons thattransmit signals from oneregion of the cerebrum to another and between the cerebrum and lower brain centers.

White matter tissue of the freshly cut brain appears pinkish white to the naked eye because myelin is composed largely of lipid tissue veined with capillaries. Its white color in prepared specimens is due to its usual preservation in formaldehyde.

White matter, long thought to be passive tissue, actively affects how the brain learns and functions. While grey matter is primarily associated with processing and cognition, white matter modulates the distribution of action potentials, acting as a relay and coordinating communication between different brain regions [23].

The white matter of the spinal cord is arranged in three columns or tracts; anterior, posterior and lateral. These tracts are formed by sensory nerve fibres ascending to the brain, motor nerve fibres descending from the brain and fibres of connector neurones. Tracts are often named according to their points of origin and destination, e.g. spinothalamic, corticospinal [13].

2.1.3.3 Ascending and Descending Spinal Tracts

The nerves within the spinal cord are grouped together in different bundles called Ascending and Descending tracts.

Ascending tracts within the spinal cord carry sensory information from the body, upwards to the brain, such as touch, skin temperature, pain and joint position. The ascending pathways are formed by the central axons of dorsal root ganglion cells entering the spinal cord via the dorsal roots. They either enter an ascending fiber tract (dorsal column pathways) or terminate in the spinal grey matter [17] [18].

Descending tracts within the spinal cord carry information from the brain downwards to initiate movement and control body functions. The corticospinal tract is most developed in higher primates and species differences are most pronounced for this tract. The cells of origin are located in the motor cortex and their axons form the pyramidal tract. In most mammals, fibers from neurones in the postcentral gyrus also contribute to this tract [19] [20].

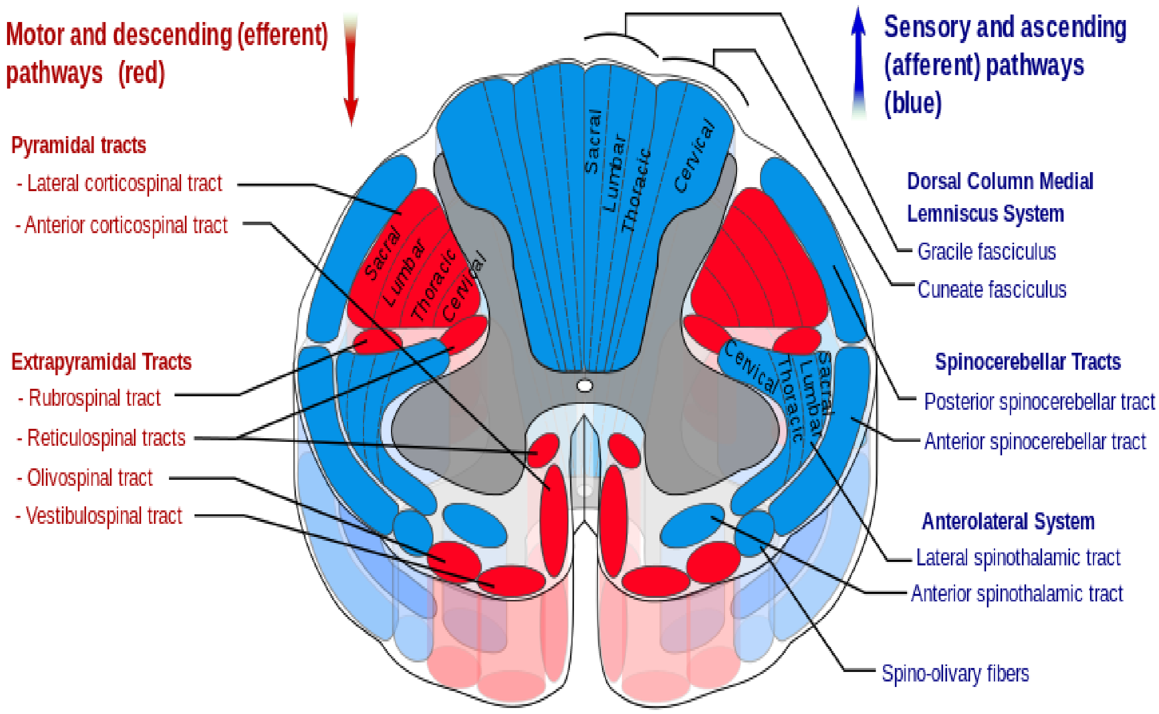


Figure 2-6: Major ascending and descending tracts of the spinal cord [68].

2.1.3.4 Spinal Nerves

Nerves called the spinal nerves or nerve roots branch off the spinal cord and pass out through a hole in each of the vertebrae called the Foramen. These nerves carry information from the spinal cord to the rest of the body and from the body back up to the brain.

There are four main groups of spinal nerves, which exit different levels of the spinal cord. These are in descending order down the vertebral column:

- Cervical Nerves "C": (nerves in the neck) supply movement and feeling to the arms, neck and upper trunk. Also, control breathing.
- Thoracic Nerves "T": (nerves in the upper back) supply the trunk and abdomen.
- Lumbar Nerves "L" and Sacral Nerves "S": (nerves in the lower back) supply the legs, the bladder, bowel and sexual organs.

2.1.3.5 Spinal Cord Level Numbering System

Emerging from the spinal cord between the vertebrae are 31 pairs of spinal nerves. Each nerve emerges in two short branches (roots):

- One at the front (motor or anterior root) of the spinal cord
- One at the back (sensory or posterior root) of the spinal cord [24].

Nerves called the spinal nerves or nerve roots branch off the spinal cord and pass out through a hole in each of the vertebrae called the foramen. These nerves carry information from the spinal cord to the rest of the body and from the body back up to the brain [15].

The spinal nerves carry information to and from different levels (segments) in the spinal cord. Both the nerves and the segments in the spinal cord are numbered in a similar way to the vertebrae. The point at which the spinal cord ends is called the conus medullaris, and is the terminal end of the spinal cord. It occurs near lumbar nerves L1 and L2. After the spinalcord terminates, the spinal nerves continue as a bundle of nerves called the cauda equina. The upper end of the conus medullaris is usually not well defined.

There are 31 pairs of spinal nerves which branch off from the spinal cord. In the cervical region of the spinal cord, the spinal nerves exit above the vertebrae. A change occurs with the C7 vertebra however, where the C8 spinal nerve exits the vertebra below the C7 vertebra. Therefore, there is an 8th cervical spinal nerve even though there is no 8th cervical vertebra. From the 1st thoracic vertebra downwards, all spinal nerves exit below their equivalent numbered vertebrae.

The spinal nerves which leave the spinal cord are numbered according to the vertebra at which they exit the spinal column. So, the spinal nerve T4, exits the spinal column through the foramen in the 4th thoracic vertebra. The spinal nerve L5 leaves the spinal cord from the conus medullaris, and travels along the cauda equina until it exits the 5th lumbar vertebra.

The level of the spinal cord segments does not relate exactly to the level of the vertebral bodies i.e. damage to the bone at a particular level e.g. L5 vertebrae does not necessarily mean damage to the spinal cord at the same spinal nerve level [34].

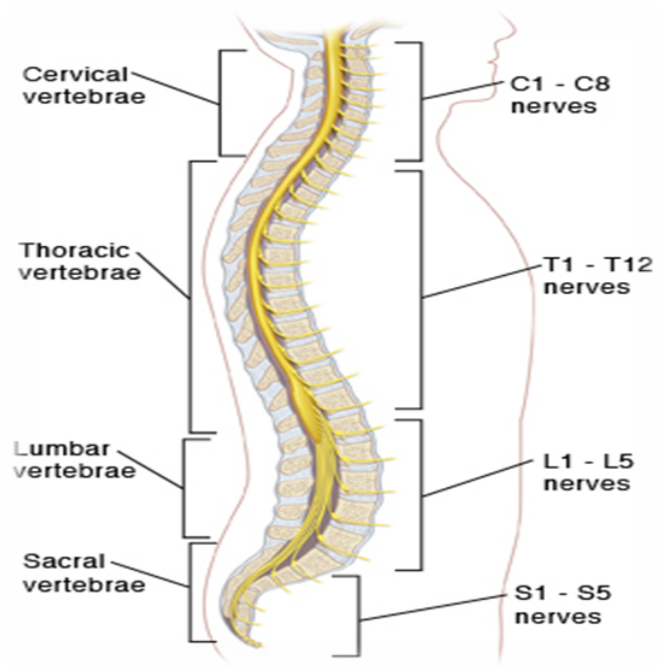


Figure 2-7: Spinal cord nerves [1818].

2.2 Part two - The stimulation

2.2.1 Introduction

Generally stimulation or excitation is the action of various agents (stimuli) on nerves, muscles, or a sensory end organ, by which activity is evoked; especially, the nervous impulse produced by various agents on nerves, or a sensory end organ, by which the part connected with the nerve is thrown into a state of activity, whether everyday general physical activity or sexual stimulation. Stimulation is often connected with psychological stimulation, which concerns how a stimulus affects a person's thinking process.

The word is also often used metaphorically. For example, an interesting or fun activity can be described as "stimulating", regardless of its physical effects on nerves. Stimulate means to act as a stimulus to; stimulus means things that rouse to activity [26].

Stimulation in general refers to how organisms perceive incoming stimuli. As such it is part of the stimulus-response mechanism. Simple organisms broadly react in three ways to stimulation: too little stimulation causes them to stagnate, too much to die from stress or inability to adapt, and a medium amount causes them to adapt and grow as they overcome it. Similar categories or effects are noted with psychological stress with people. Thus, stimulation may be described as how external events provoke a response by an individual in the attempt to cope [26].

2.2.2 Differences between model and stimulation

A model is a product (physical or digital) that represents a system of interest. A model is similar to but simpler than the system it represents, while approximating most of the same salient features of the real system as close as possible. A good model is a judicious tradeoff between realism and simplicity. A key feature of a model is manipulability. A model can be a physical model (for example a physical architectural house scale model, a model aircraft, a fashion mannequin, or a model organism in biology research); or a conceptual model (for example a computer model, a statistical or mathematical model, a business model, so the modeling is the act of building a model.

A simulation is the process of using a model to study the behavior and performance of an actual or theoretical system. In a simulation, models can be used to study existing or proposed characteristics of a system. The purpose of a simulation is to study the characteristics of a real-life or fictional system by manipulating variables that cannot be controlled in a real system. Simulations allow evaluating a model to optimize system performance or to make predictions about a real system. Simulations are useful to study properties of a model of a real-life system that would otherwise be too complex, too large/small, too fast/slow, not accessible, too dangerous or unacceptable to engage. While a model aims to be true to the system it represents, a simulation can use a model to explore states that would not be possible in the original system.

so the simulating is the act of using a model for a simulation [51].

2.2.3 Spinal cord stimulation

Spinal cord stimulation (SCS) is an advanced therapy and method of pain management for certain types of chronic pain [**Error! Reference source not found.**]. Also it isan innovative technology that addresses some of the most difficult pain problems experienced. Identified as an effective treatment option for many chronic sufferers, SCS is most often used for neuropathic pain, including diabetic neuropathy, post-laminectomy syndrome (residual pain after back surgery), and complex regional pain syndrome (CRPS) [25].

If you suffer from chronic neuropathic pain, spinal cord stimulation (SCS) may enable you to control and relieve your pain. Our board-certified pain specialists can determine if this is an option for you and help stop pain from interfering with your life [25].

Spinal cord stimulation uses low voltage stimulation of the spinal nerves to block the feeling of pain. It helps you to better manage your pain and potentially decrease the amount of pain medication. It may be an option if you have long-term (chronic) leg or arm pain, and have not found relief through traditional methods. A small battery-powered generator implanted in the body transmits an electrical current to your spinal cord. The result is a tingling sensation instead of pain. By interrupting pain signals, the procedure has shown success in returning some people to a more active lifestyle [1].

SCS uses electrodes (sometimes called channels) placed in the thoracic or cervical region of the spine to stimulate both afferent and inhibiting nerve fibers related to the sensation of pain. The stimulation results in a feeling called paresthesia, where the pain is replaced by a tingling effect similar to that of the vibration from an electric massager. The typical stimulation frequency range is 33 Hz to 80 Hz [27], the typical voltage is between 5V and 12V, and the typical pulse width is 210 ms [15].

2.2.3.1 Mechanisms of Spinal Cord Stimulation

Although SCS has been used as a method for reducing pain in the clinical setting for more than 30 years, its exact mechanisms remain unknown [15]. The following steps explain why SCS does not cause a conduction block in spinothalamic fibers as follows:

1. The thin, high-threshold spinothalamic fibers that carry the pain messages to the brain are not stimulated in the clinical setting.
2. Equally, the pain-inhibiting pathways in the dorsilateral funiculus are not stimulated.
3. Perception of acute nociceptive or experimental pain is still a present.

4. The depressive effect of SCS lasts long after the stimulation is an applied.

5. Low frequencies (f o 5 Hz) are sufficient for reducing pain [26].

2.2.3.2 SCS Implantation

If the SCS trial provides adequate pain relief, then a permanent system may be implanted. SCS is a reversible therapy, so even though it is called permanent, treatment can be discontinued at any time and the implanted parts turned off or removed.

Prior to the procedure, the patient is lightly sedated. Trial leads, if present, are removed. If leads are to be placed under the skin, a local anesthetic will be administered while the leads are placed, then the patient will be given a general anesthesia prior to the rest of the system being implanted. If surgical leads are used, the patient will likely be under general anesthesia the entire time. The leads are inserted in the epidural space above the spinal cord using a small needle or through a small incision. The exact location of the lead or leads depends on the specificity of the patient's pain. The generator is usually implanted in the abdominal or buttock region, but the physician/patient may determine other comfortable areas in which to place it [38].

Once the leads and generator are in place, connected and working, the incision will be closed, a dressing applied, and the patient will be taken to recovery, where he or she will be slowly withdrawn from the anesthesia. Most patients go home the same day, but some physicians will request an overnight stay in the hospital. Before being released from the hospital, the patient will receive instructions on caring for the incision area and how to program and regulate the SCS device [38].

Following implantation, lifting, bending, stretching, and twisting should be avoided. However, light exercise, such as walking can be helpful to build strength and relieve pain.

Although there may be some discomfort while the surgical incision heals, most patients say that they cannot feel the presence of the device under the skin after healing takes place [38].

2.2.4 Spinal cord stimulator

Electrotherapy of pain by neurostimulation began shortly after Melzack and Wall proposed the gate control theory in 1965 [28]. This theory proposed that nerves carrying painful peripheral stimuli and nerves carrying touch and vibratory sensation both terminate in the dorsal horn (the gate) of spinal cord. It was hypothesized that input to the latter could be manipulated to "close the gate" to the former. As an application of the gate control theory, Shealy et al. implanted the first spinal cord stimulator device directly on the dorsal column for the treatment of chronic pain [2929], and in 1971, Shimogi and colleagues first reported the analgesic properties of epidural spinal cord stimulation [30]. Since then this technique has undergone numerous technical and clinical developments [313131].

At this time, neurostimulation for the treatment of pain is used with nerve stimulation, spinal cord stimulation, deep brain stimulation, and motor cortex stimulation.

A spinal cord stimulator is a device used to exert pulsed electrical signals to the spinal cord to control chronic pain. Further applications are in motor disorders. The lumbar spinal cord is a preferred target for the control of spinal spasticity [32][3333]or augmentation of standing and stepping capabilities [3434][3535][36][3737]. Spinal cord stimulation (SCS), in the simplest form, consists of stimulating electrodes, implanted in the epidural space, an electrical pulse generator, implanted in the lower abdominal area or gluteal region, conducting wires connecting the electrodes to the generator, and the generator remote control . SCS has notable analgesic properties and, at the present, is used mostly in the treatment of failed back surgery syndrome, complex regional pain syndrome and refractory pain due to ischemia.

A spinal cord stimulator is a specialized device that stimulates the spinal cord and spinal nerves by tiny electrical impulses via a small electrical wire placed behind and just outside the spinal cord in the epidural space. The electrical wire or lead contains a series of four to eight evenly spaced electrodes that can be programmed to generate an electrical field.

Chronic pain is longstanding pain that persists beyond the usual recovery period or that accompanies a chronic health condition. Because this pain is not protective and is not a result of an ongoing injury, it is referred to as "pathological" and is therefore treated as a condition, not as a symptom. Chronic pain may prevent people from working, eating properly, participating in physical activity, or enjoying life [38].

Spinal cord stimulation (SCS) is a pain relief technique that delivers a low-voltage electrical current continuously to the spinal cord to block the sensation of pain. SCS is the most commonly used implantable neurostimulation technology for management of pain syndromes. As many as 50,000 neurostimulators are implanted worldwide every year. SCS is a widely accepted FDA-approved medical treatment for chronic pain of the trunk and limbs (back, legs and arms) [38].

There are three SCS device types:

2.2.4.1 Conventional systems

Require little effort on the patient's part for maintenance. However, a minor surgical procedure is required to replace the power source when it runs out.

2.2.4.2 Radiofrequency systems

These are designed to sustain therapy over long periods at the highest output level. Because of its high power capabilities, the RF system is suitable for the most challenging cases in which there is complex, multi-extremity pain. With this type of system, the patient must wear an external power source to activate stimulation.

2.2.4.3 Rechargeable systems

These are the newest types of SCS device. The patient is responsible for recharging the power source when it runs low. A rechargeable system typically lasts longer than a conventional system. Eventually a minor surgical procedure may be required to replace the power source if the time between recharges becomes impractical [38].

2.2.4.4 Selection of Stimulation Parameters

Four parameters in the SCS system can be adjusted for the best results. They are frequency, pulse width, pulse amplitude, and mode. The first purpose of adjusting the parameters is to superimpose the stimulation pattern over the patient's pain pattern. The second purpose is to prolonm battery life. Figure 6 shows the stimulation waveform in SCS. Amplitude is a measure of the strength of the stimulation [15].

It is measured in volts, and it can be set from 0V to12V, depending on needs. Pulse width, measured in microseconds (ms), is the duration of an electrical pulse. Thewider the electricalpulse width, the stronger the sensation of paresthesia. The pulse width is set at about 210 ms. Frequency is the number of times per second that an electrical pulse is generated. The frequency in an SCS system is typically set between 33 Hz and 80 Hz [15].

Two stimulation modes can be selected. Continuous mode is the mode that switches ON the generator all the time. This mode can help the patient become used to sensation of stimulation. After the implantation of the stimulator, cycling mode should be selected as soon as possible to save power. The pattern of cycling mode is ON for several minutes and OFF for several minutes [15].

Spinal cord stimulators consist of:

2.2.4.4.1 Equipment

SCS, in simplest form, consists of a pulse generator with its remote controls, implanted stimulating electrodes and conducting wires connecting the electrodes to the generator [39].

2.2.4.4.2 Generator

The generator, implanted subcutaneously, could be a complete pulse generator module with its own battery or only a radio frequency (RF) receiver. The former case, usually called implantable pulse generator or IPG, has a battery of its own and could come with rechargeable battery, which can be charged externally via a wireless power charger so that it does not need to be replaced surgically when it loses charge.

The RF receiver on the other hand is externally driven by a transmitter from which it gets its power and pulses. This external transmitter has a battery, which can be easily replaced. RF receivers have traditionally been used for patients who require high power settings that would quickly deplete a primary cell IPG [39]. The patient is also provided with a remote control to turn on and off the stimulator, and depending on the device and the surgeon's preference, can change the programming of the stimulation patterns. The surgeon has a programming device that could be used to modify a wide range of stimulation settings of the RF generator [39].

Various current, voltage and waveforms configurations are possible. SC stimulators come in constant current, variable voltage or constant voltage, variable current [39].

2.2.4.4.3 Electrodes

The electrodes, which consist of an array of leads, could be percutaneous type or paddle type. Percutaneous electrodes are easier to insert in comparison with paddle type, which are inserted via incision over spinal cord and laminectomy [313131].

Figure 2-8: Spinal cord stimulator leads [31].

2.2.4.5 Insertion procedures and techniques

SCS procedure involves careful placement of electrodes in the epidural space, a trial period (which takes between 5–7 days), and, if the results of pain relieving was satisfactory in the trial period, anchoring the electrodes to the interspinal ligaments, positioning and implantation of the pulse generator, tunneling and connection of the connecting wires, programming the system for the special pattern of stimulation and performing required postoperative cares [39].

2.2.4.6 Selecting the level of stimulation

The representation of the dermatomal level in the dorsal columns of the spinal cord is much higher than the corresponding vertebral level. For instance, the sweet spot for sciatic pain (dermatomal level L5/S1) is around T10 nerve [39].

2.2.4.6.1 Electrodes selection

For the SCS to be effective, the area of paresthesia must overlap the area of pain. Selection of leads depends on which arrangement will give the best paresthesia coverage to the painful area.

2.2.4.6.2 Generator implant

The IPG or the RF unit is usually implanted in the lower abdominal area or in the posterior superior gluteal region. It should be in a location that patients can access with their dominant hand for adjustment of their settings with the patient-held remote control. The decision to use a fully implantable IPG or an RF unit depends on several considerations. If the patient's pain pattern requires the use of many electrodes with high power settings, an RF unit should be used. The IPG battery life will largely depend on the power settings utilized, but the newer IPG units will generally last several years at average power settings [39].

Figure 2-9: Implanted pulse generator [39].

2.2.4.6.3 Programming

Programming involves selecting the electrode stimulating configuration, adjusting the amplitude, width and frequency of electrical pulses. Amplitude indicates the intensity of stimulation. This is delivered in milliamperes or volts depending on the system used. Lower voltage or current is chosen for peripheral nerves and paddle leads. Pulse width usually varies from 100 to 400 us. Widening the pulse width will also broaden the area of paraesthesia. Frequency of pulse wave is usually between 20 and 120 hertz. It is an individual preference: some patients choose low frequency beating sensation whereas others prefer high frequency buzzing [39].

Selection of lowest possible setting on all parameters is important in conserving battery life in non-rechargeable models of SCS. Cycling of stimulation is also employed to save battery life. Changing of stimulator program may have to be undertaken during the course of therapy and follow-up [39].

2.2.4.6.4 Patient selection

Appropriate patients for neurostimulation implants must meet the following criteria: the patient has a diagnosis amenable to this therapy, the patient has failed conservative therapy, significant psychological issues have been ruled out, and a trial has demonstrated pain relief. A trial period of stimulation over a period of 5–7 days should follow the psychiatric evaluation to demonstrate its effectiveness. This part of the protocol is important because of the cost of the equipment and the invasive nature of the procedure. The trial is considered successful if the patient achieves more than a 50% reduction in pain [31].

2.2.4.6.5 Indications

The most common use of SCS is failed back surgery syndrome (FBSS) in the United States and peripheral ischemic pain in Europe.

FBSS, classified as mixed pain syndrome (neuropathic and nociceptive), is the persistent or recurrent pain, mainly involving the lower back and/or legs after successful spinal surgery. It affects about 40% of patients who undergo spinal surgeries. Several studies showed overall efficacy of the SCS for FBSS [41][42][43][44][45].

SCS is also indicated in the treatment of inoperable ischemic limb pain.[46] Furthermore, this technique is studied in various applications. For instance, it has been shown to modulate the function of sympathetic nervous system and increase norepinephrine release in refractory angina pectoris[47], decreasing the probability of angina attack. SCS units have been used to treat patients with frequent migraines. The electrodes are implanted in the bilateral suboccipital region [48].

2.2.4.6.6 Complications

Complications with SCS range from simple easily correctable problems to devastating paralysis, nerve injury and death. However, in a 7-year follow-up, the overall complication rate was 5-18%. The most common complications include lead migration, lead breakage, and infection. Other complications include haematomas (subcutaneous or epidural),cerebrospinal fluid (CSF) leak, post dural puncture headache, discomfort at pulse generator site, seroma and transient paraplegia. Hardware-related complications such as electrode migration, fractured electrodes, and rotation of pulse generator are also reported [50]. They examined 104 patients with failed back surgery syndrome. Of the 104 patients, 60 were implanted with a spinal cord stimulator. Both groups were monitored over a period of five years. The stimulation group annual cost was $29,000 versus $38,000 in the other group. 15% returned to work in the stimulation group versus 0% in the other group. The higher costs in the nonstimulator group were in the categories of medications, emergency center visits, x-rays, and ongoing physician visits [50].

2.3 Advantages and disadvantages

SCS is analgesia on demand. It is a useful option when other forms of therapy fail. It reduces pain medication and side effects. It is effective in about 50–70% cases. It is an invasive procedure, so it can have associated complications such as infection, bleeding, and dural puncture. It has the risk of disconnection or equipment failure [39].

SCS interaction with diathermy, pacemakers, MRI and therapeutic ultrasound can result in unexpected changes in stimulation, serious patient injury or death. It can also lead to failure of the device [39].

Chapter 3 LITERATURE REVIEW

3.1 Introduction

This chapter concentrated on the literature reviews of the spinal cord stimulation using different ways of stimulation to treat the pain of the spinal cord.

These reviews are the results of many researches using many ways trying to reach to the best treatment to the spinal problems, by using electrical stimulation, easily implemented techniques and….

The following lines show the literature reviews in details:

3.1.1 The electrical spinal cord stimulation

In 1995, John Hopkins, Electrical stimulation of the spinal cord for the relief of pain was first reported in 1967. Since that time there have been marked improvements in patient selection criteria, hardware, technology, and methods for implantation, which have resulted in substantial improvement in the overall results achieved with spinal cord stimulation [52].

Richard B. North, over 25 years ago, electrical stimulation of the spinal cord using implanted electrodes was introduced as a reversible technique for the management of chronic, intractable pain.

- As a reversible alternative to ablative procedures, this prototypical "neuroaugmentative" procedure was appealing; but the indications for neurosurgical intervention for chronic, benign pain were not widely understood at that time.
- As the behavioral and psychological issues in pain management have become more widely appreciated, and as programs specializing in chronic pain have proliferated, the process of patient selection has been refined considerably. At the same time, there

have been major improvements in implantable spinal cord stimulation devices, which have significantly enhanced clinical results [53].

3.1.2 Single and multi-channel devices of Scs

In February1991, Richard B Northet al. Spinal cord stimulation has evolved over the past 20 years into an easily implemented technique, with low morbidity, for the treatment of intractable, chronic pain in properly selected patients. We report our experience with a series of 62 patients implanted between 1983 and 1987, with percutaneous and laminectomy electrodes, and with single- and "multi-channel" (programmable, multi-contact) devices. Fifty had chronic, intractable low back and leg pain ("failed back surgery syndrome," lumbar arachnoid fibrosis), five had spinal cord injuries, and seven "peripheral" pathology or stump pain. Statistical analysis of these and other patient characteristics and technical factors was undertaken to identify predictors of outcome.

All patients were interviewed by a disinterested third party at a mean of 2.14 years following implantation. A majority of patients reported at least 50% sustained relief of pain and indicated that they would go through the procedure again for the same result. There was corresponding improvement in ability to perform various everyday activities, and decrease in use of analgesics. Ten of 40 failed back patients who were disabled before the procedure returned to work postoperatively.

Superposition of stimulation paresthesias upon a patient's topography of pain was found to be a statistically significant predictor of successful relief of pain, by linear regression methods. Univariate and multivariate analysis of patient characteristics and technical factors as predictors of outcome demonstrated significant advantages for female patients, and for patients implanted with "multi-channel" devices. With these devices, electrode geometries with central cathode(s) flanked by rostral and caudal anode(s) were favored disproportionately.

Technical improvements in implanted spinal cord stimulation devices, in particular the development of multi-contact percutaneous electrode arrays and supporting programmable electronics, have significantly improved clinical results [53].

In March 1993, North, Richard et al. over the past two decades, spinal cord stimulation devices and techniques have evolved from single-channel systems, with electrodes requiring laminectomy, into programmable "multichannel" systems with electrodes that may be placed percutaneously. We have reviewed our experience in 320 consecutive patients treated with these devices at our institution between 1972 and 1990. Technical details of treatment as well as patient characteristics have been assessed as predictors of clinical outcome and of hardware reliability by univariate and multivariate statistical methods. Current follow-up has been obtained at intervals from 2 to 20 years (mean, 7.1 yr) postoperatively on 205 patients. All clinical outcome measures have been based on disinterested third-party interview data--standard analog pain ratings, employment status, activities of daily living, and use of analgesics. At 7-year mean follow-up, 52% of the 171 patients who received permanent implants reported at least 50% continued pain relief. A majority had maintained improvements in activities of daily living and analgesic use. Analysis of hardware reliability for 298 permanent implants revealed significantly fewer clinical failures ($P < 0.001$) and technical failures (in particular, electrode migration and malposition, $P = 0.025$) as single-channel implants have evolved into programmable, multichannel devices. Our analysis of technical and clinical prognostic factors may be useful to the clinician in selecting patients for this procedure [56].

3.1.3 Systemic review of effectiveness and complications of Scs

In March 2004, Judith A Turnera et al.We conducted a systematic review of the literature on the effectiveness of spinal cord stimulation (SCS) in relieving pain and improving functioning for patients with failed back surgery syndrome and complex regional pain syndrome (CRPS). We also reviewed SCS complications. Literature searches yielded 583 articles, of which seven met the inclusion criteria for the review of SCS effectiveness, and 15 others met the criteria only for the review of SCS complications. Two authors independently extracted data from each article, and then resolved discrepancies by discussion. We identified only one randomized trial, which found that physical therapy (PT) plus SCS, compared with PT alone, had a statistically significant but clinically modest effect at 6 and 12 months in relieving pain among patients with CRPS. Similarly, six other studies of much lower methodological quality suggest mild to moderate improvement in pain with SCS. Pain relief with SCS appears to decrease over time. The one randomized trial suggested no benefits of SCS in improving patient functioning. Although life-threatening complications with SCS are rare, other adverse events are frequent. On average, 34% of patients who received a stimulator had an adverse occurrence. We conclude with suggestions for methodologically stronger studies to provide more definitive data regarding the effectiveness of SCS in relieving pain and improving functioning, short- and long-term, among patients with chronic pain syndromes [54].

In May1997, Gregory K. Bell et al.This article presents an analysis of the medical costs of spinal cord stimulation (SCS) therapy in the treatment of patients with failed back surgery syndrome (FBSS). We compared the medical costs of SCS therapy with an alternative regimen of surgeries and other interventions. Externally powered (external) and fully internalized (internal) SCS systems were considered separately. Clinical management models of each of the therapy alternatives were derived from the clinical literature, retrospective data sets, expert opinion, and published diagnostic and therapy protocols. No value was placed on pain relief or improvements in the quality of life that successful SCS therapy can generate. We found that by reducing the demand for medical care by FBSS patients, SCS therapy could lower medical costs. On average, given current screening and efficacy rates, SCS therapy pays for itself within 5.5 years. For those patients for whom SCS therapy is clinically efficacious, the therapy pays for itself within 2.1 years [50].

3.1.4 Different procedures using for spinal cord pain

In November 2007, Krishna Kumara et al.A multicentrerandomised controlled trial in patients with failed back surgery syndrome" Patients with neuropathic pain secondary to failed back surgery syndrome (FBSS) typically experience persistent pain, disability, and reduced quality of life. We hypothesised that spinal cord stimulation (SCS) is an effective therapy in addition to conventional medical management (CMM) in this patient population. We randomised 100 FBSS patients with predominant leg pain of neuropathic radicular origin to receive spinal cord stimulation plus conventional medical management (SCS group) or conventional medical management alone (CMM group) for at least 6 months. The primary outcome was the proportion of patients achieving 50% or more pain relief in the legs. Secondary outcomes were improvement in back and leg pain, health-related quality of life, functional capacity, use of pain medication and non-drug pain treatment, level of patient satisfaction, and incidence of complications and adverse effects. Crossover after the 6-months visit was permitted, and all patients were followed up to 1 year. In the intention-to-treat analysis at 6 months, 24 SCS patients (48%) and 4 CMM patients (9%) ($p < 0.001$) achieved the primary outcome. Compared with the CMM group, the SCS group experienced improved leg and back pain relief, quality of life, and functional capacity, as well as greater treatment satisfaction ($p \leqslant 0.05$ for all comparisons). Between 6 and 12 months, 5 SCS patients crossed to CMM, and 32 CMM patients crossed to SCS. At 12 months, 27 SCS patients (32%) had experienced device-related complications. In selected patients with FBSS, SCS provides better pain relief and improves health-related quality of life and functional capacity compared with CMM alone [55].

In December 1995, Turner, Judith A. Ph.D. et al. A systemic literature synthesis was performed to analyze the long-term risks and benefits of spinal cord stimulation for patients with failed back surgery syndrome. Relevant articles were identified through a MEDLINE search (January 1966-June 1994), bibliography reviews, searches of personal files, and literature supplied by a stimulator manufacturer. Two investigators independently reviewed each article to determine whether it met the following study inclusion criteria: 1) original data on return to work, pain, medication use, reoperations, functional disability, or stimulator use after permanent implantation of spinal cord stimulators in patients with chronic low back or leg pain despite previous back surgery; and 2) follow-up ≥30 days for all patients. Articles were excluded if data from patients with other diagnoses were mixed with (and could not be separated from) data from patients with chronic low back or leg pain, or if their data were redundant with those reported in an included article. Articles written in languages other than English or French were excluded. Thirty-nine studies, all case studies, were analyzed. At follow-up (mean, 16 mo; range, 1–45 mo), an average of 59% of patients had ≥50% pain relief (range, 15–100% of patients). Complications occurred in 42% of patients but were generally minor. It seems that approximately 50 to 60% of patients with failed back surgery syndrome report >50% pain relief with the use of spinal cord stimulation at follow-up; the lack of randomized trials precludes conclusions concerning the effectiveness of spinal cord stimulation relative to other treatments, placebo, or no treatment [57].

In 2000, Barolat G, Sharan AD.Spinal cord stimulation (SCS) has been available for about 30 years, but only in the past five years has it met with widespread acceptance and recognition by the medical community. Traditionally performed by neurosurgeons, SCS is being increasingly utilized by anesthesiologists, orthopedic surgeons and physiatrists. Pain management continues to be the most widespread application of SCS. More sophisticated technology has allowed the implanters to successfully address more complex pain syndromes such as widespread reflex sympathetic dystrophy and the failed back syndrome. Other applications are being developed, combining the ability to stimulate the spinal cord, the nerve roots and the peripheral nerves. Examples include angina pectoris, urinary incontinence and occipital neuralgia. Computer-interactive programming is gaining popularity, especially due to the extreme complexity of the implanted stimulation devices. The ability to stimulate independently multiple channels as well as multiple arrays of electrodes is today a reality. This has increased greatly the efficacy, safety and reliability of the modality. In the future, SCS will undoubtedly move several steps up in the treatment ladder of chronic pain conditions, while new applications will be discovered. The future of neural implantable technologies is bright, with an increasingly important role in the medical management of chronic conditions affecting the nervous system [58].

In1989, Sánchez-Ledesma M.J et al. Spinal cord stimulation (SCS) was used in 49 cases to control resistant deafferentation pain resulting from causalgia, phantom limb, plexus and nerve root avulsion, postherpetic neuralgia, reflex sympathetic dystrophy and amputation. In all cases, one or two Standard percutaneous leads were introduced into the epidural space and manipulated until the spinal segment at which external stimulation provoked paresthesic sensation in the painful area. Two weeks of external stimulation trial was used to determine the efficiency of the system. Pulse width of 0.1–0.2 ms, a rate of 80–120 cps and amplitude to low paresthesia threshold were programed as electric parameters.

In 36 out of the 49 tested cases showing a positive response to percutaneous SCS, the device was permanently implanted. After a mean follow-up of 5.5 years, 57% of patients had satisfactory pain relief (over 75 %). Side effects were limited to dislodgement of the electrode in 1 case and wire extrusion in another, both requiring replacement of the stimulator [59].

Chapter 4 The system design

4.1 Introduction

This chapter explained the system design that used to stimulate the spinal cord, this technique is used electrical stimulation to cause the nerve cells or muscle fibers got induced The stimulator designed to control, managed or reduced the pain and the effects of the spinal cord problems.

The human brain is able to receive annoying stimulus which detected by pain receptors developed within the body as urgent signals. Then the signal is carried to the spinal cord as impulses and then transferred to the brain for evaluation and interrupting.

The system is consisting of hardware part which is operates by programming the software part. This chapter described the system design in expansion. The component of the hardware circuit and the method of work then explained the code that used in the operation of the circuit.

The hardware designed to stimuli the spinal cord problem by sending the signals to the spinal cord to release or stop the chronic pain or the specific problem which the stimulator could solve it. The parameters in the stimulator adjust for specific problems, which the patients suffer from. The instrument is designed in two types; bedside or portable depending on the case of patient.

The design of the hardware consists of the555 timer, microcontroller, the output that displays in LCD, the power supply circuit; all these parts will explain in more details in this chapter.

The software is the language of the microcontroller, which is, controlled the value of output; the language which is used is the Bascom also will explain in more details in this chapter.

4.2 Stimulator hardware design

The stimulator consists firstly from the microcontroller (Atmega 16) which is programmed to control the stimulation operation, the LCD display that displaying the parameters (amplitude, frequency and duty cycle) which operating with the 555 timer (simulation of the spinal cord), the variable resistor connected with the 555 timer to manage the changing of the 555 timer values. In addition, the circuit of the power supply to convert the input volt from AC to DC.

The following paragraphs explain of the components of the hardware system:

4.2.1 The 555 timer (A stable)

The 555 timer used in this circuit type is the NE555; its parts were commercial temperature range, 0 °C to +70 °C [60].

The 555 timer IC is an integrated circuit (chip) used in a variety of timer, pulse generation, and oscillator applications. It can be used to provide time delays, as an oscillator, and as a flip-flop element. Derivatives provide up to four timing circuits in one package [61].

The figure below shows the 555 timer pins:

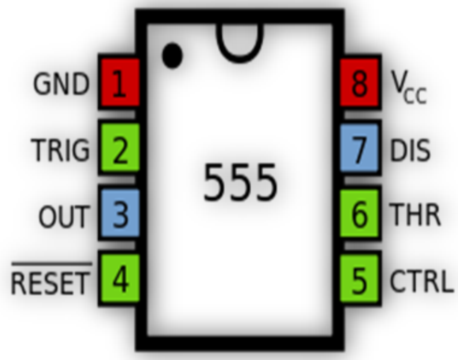


Figure 4-1: The 555 timer pins [61].

The 555 timer is capable of being used in astable and monostable circuits. In an astable circuit, the output voltage alternates between VCC and 0 volts on a continual basis.

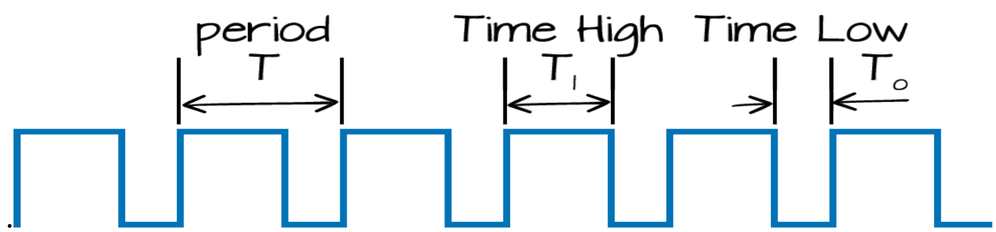


Figure 4-2: The waveform of the 555 timer [**Error! Reference source not found.**].

By selecting values for R1, R2 and C we can determine the period/frequency and the duty cycle.

The period is the length of time it takes for the on/off cycle to repeat itself; whilst the duty cycle is the percentage of time, the output is on, i.e. T1/T. In this type of circuit, the duty cycle can never be 50% or lower.

At this state, we considered that:

- Increasing C will increase the cycle time (and hence, reduce the frequency).
- Increasing R1 will increase Time High (T1), but will leave Time Low (T0) unaffected.
- Increasing R2 will increase Time High (T1), increase Time Low (T0) and decrease the duty cycle (down to a minimum of 50%.

Astable (free-running) mode – the 555 can operate as an electronic oscillator. Uses include LED and lamp flashers, pulse generation, logic clocks, tone generation, security alarms, pulse position modulation and so on. The 555 can be used as a simple ADC, converting an analog value to a pulse length (e.g., selecting a thermistor as timing resistor allows the use of the 555 in a temperature sensor and the period of the output pulse is determined by the temperature). The use of a microprocessor-based circuit can then convert the pulse period to temperature, linearize it and even provide calibration means.

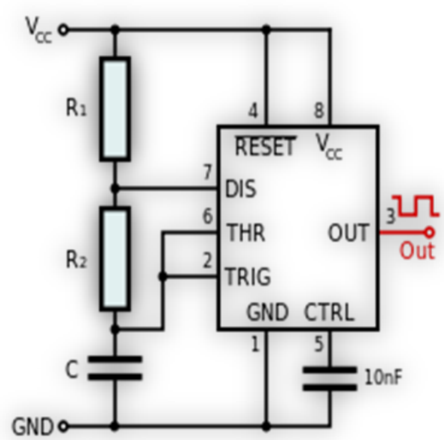


Figure 4-3: Schematic of a stable mode [**Error! Reference source not found.**].

The frequency, or repetition rate, of the output pulses is determined by the values of two resistors, R1 and R2 and by the timing capacitor, C [62].

The design formula for the frequency of the pulses is:

$$f = \frac{1.44}{(R1 + 2R2) \times C}$$

The period, t, of the pulses is given by:

$$t = \frac{1}{f} = 0.69(R1 + 2R2) \times C$$

The HIGH and LOW times of each pulse can be calculated from:

$$\text{HIGH time} = 0.69(R1 + R2) \times C \quad \text{LOW time} = 0.69(R2 \times C)$$

The duty cycle of the waveform, usually expressed as a percentage, is given by:

$$\text{duty cycle} = \frac{\text{HIGH time}}{\text{pulse period time}}$$

An alternative measurement of HIGH and LOW times is the mark space ratio:

$$\text{mark space ratio} = \frac{\text{HIGH time}}{\text{LOW time}}$$

Before calculating a frequency, you should know that it is usual to make R1=1 kΩ because this helps to give the output pulses a duty cycles close to 50%, that is, the HIGH and LOW times of the pulses are approximately equal [62].

Remember that design formulae work in fundamental units. However, it is often more convenient to work with other combinations of units:

Table 4-1: The fundamental units used in the design of the system:

resistance	Capacitance	Period	Frequency
Ω	F	S	Hz
MΩ	Mf	S	Hz
kΩ	Mf	Ms	kHz

With R values in MΩ and C values in μF, the frequency will be in Hz. Alternatively, with R values in kΩ and C values in μF, frequencies will be in kHz [62].

Example:

Suppose you want to design a circuit to produce a frequency of approximately 1 kHz for an alarm application. What values of R1, R2 and C should you use? [62] [**Error! Reference source not found.**]

Solution:

R1 should be 1kΩ, as already explained. This leaves you with the task of selecting values for R2 and C. The best thing to do is to rearrange the design formula so that the R values are on the right hand side:

$$R1 + 2R2 = \frac{1.44}{f \times C}$$

Now substitute for R1 and f:

$$1 + 2R2 = \frac{1.44}{1 \times C}$$

You are using R values in kΩ and f values in kHz, so C values will be in μF.

To make further progress, you must choose a value for C. At the same time, it is important to remember that practical values for R2 are between 1 kΩ and 1MΩ. Suppose you choose C = 10 nF = 0.01 μF:

$$1 + 2R2 = \frac{1.44}{0.01} = 144$$

That is:

$$2R2 = 144 - 1 = 143$$

And:

$$R2 = 71.5\ \text{k}\Omega$$

This is within the range of practical values and you can choose values from the E12 range of 68 kΩ or 82 kΩ. (The E12 range tells you which values of resistor are manufactured and easily available from suppliers) [62][**Error! Reference source not found.**].

4.2.2 The variable resistance

It is a resistor of which the ohmic resistance value can be adjusted. Either mechanically (potentiometer, rheostat) or electronically (digital potentiometer).It is an electronic component. It is applied in an electronic circuit for adjusting circuit resistance to control voltage or current of that circuit or part of that circuit. The electrical resistance is varied by sliding a wiper contact along a resistance track. Sometimes the resistance is adjusted at present value as required at the time of circuit building by adjusting screw attached to it and sometimes resistance can be adjusted as when required by controlling knob connected to it. The active resistance value of the variable resistor depends upon the position of the slider contact on the resistance track [63].

It mainly consists of a resistance track and a wiper contact. The wiper contact moves along the resistance track when adjustable component is adjusted. There are mainly three different types of resistance track used in this resistor they are carbon track, cermet (ceramic and metal mixture) track and wire wound track. Carbon track and cermet track are used for high resistance application whereas wire wound track is used for low resistance variable resistor. The resistance tracks generally are of circular shape but straight track is also used in many cases.

A variable resistor is a resistor of which the electric resistance value can be adjusted. A variable resistor is in essence an electro-mechanical transducer and normally works by sliding a contact (wiper) over a resistive element. When a variable resistor is used as a potential divider by using 3 terminals it is called a potentiometer. When only two terminals are used, it functions as a variable resistance and is called a rheostat. Electronically controlled variable resistors exist, which can be controlled electronically instead of by mechanical action. These resistors are called digital potentiometers.

A variable resistance is useful when we don't know in advance what resistor value will be required in a circuit. By using pots as an adjustable resistor we can set theright value once the circuit is working. Controls like this are often called 'presets' because they are set by the manufacturer before the circuit is sent to the customer. They're usually hidden away inside the case of the equipment, away from the fingers of the users [63].

Figure 4-4: The potentiometer [69].

4.2.3 Microcontroller (atmega16)

Microcontrollers are single-chip computers consisting of CPU (central processing unit), data and program memory, serial and parallel I/O (input/output), timers, external and internal interrupts, all integrated into a single chip are cheap for users. They areintelligent electronic devices used to control and monitor devices in the real world.

Microcontrollers are programmed devices. A program is a sequence of instructions that tell the microcontroller what to do. Microcontrollers have traditionally been programmed using the low levelassembly language of the target processor.

A microcontroller can be considered a self-contained system with a processor, memory and peripherals and can be used as an embedded system [64]. The majority of microcontrollers in use today are embedded in other machinery, such as automobiles, telephones, appliances, and peripherals for computer systems.

While some embedded systems are very sophisticated, many have minimal requirements for memory and program length, with no operating system, and low software complexity. Typical input and output devices include switches, relays, solenoids, LEDs, small or custom liquid-crystal displays, radio frequency devices, and sensors for data such as temperature, humidity, light level etc. Embedded systems usually have no keyboard, screen, disks, printers, or other recognizable I/O devices of a personal computer, and may lack human interaction devices of any kind.

The microcontroller used in this stimulation circuit is atmega 16; it is an 8-bit high performance microcontroller of Atmel's Mega AVR family with low power consumption. Atmega16 is based on enhanced RISC (Reduced Instruction Set Computing, Know more about RISC and CISC Architecture) architecture with 131powerful instructions. Most of the instructions execute in one machine cycle. Atmega16 can work on a maximum frequency of 16MHz.

ATmega16 has 16 KB programmable flash memory, static RAM of 1 KB and EEPROM of 512 Bytes. The endurance cycle of flash memory and EEPROM is 10,000 and 100,000, respectively. In addition, it is a 40 pin microcontroller. There are 32 I/O (input/output) lines which are divided into four 8-bit ports designated as PORTA, PORTB, PORTC and PORTD. It has various in-built peripherals like USART, ADC, Analog Comparator, SPI, JTAG etc. Each I/O pin has an alternative task related to in-built peripherals. The following table shows the pin description of ATmega16.

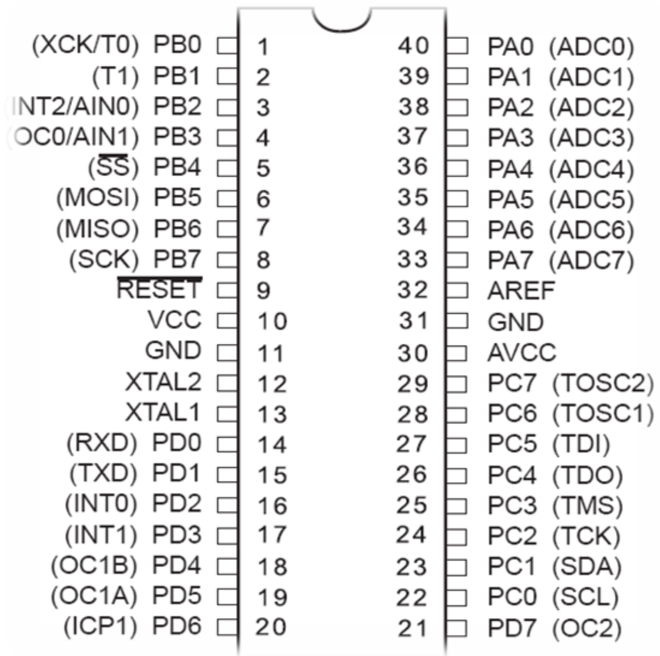


Figure 4-5: Atmega 16 pin layout [65].

The advantage of using Atmega 16:

- To support different design requirements and reduce cost, the Atmel

  AVR family has many microcontrollers: ATmega8515, ATmega16, etc.

- Microcontrollers in the 8-bit AVR family share a similar instruction setand architecture.

- The ATmega16 has components that are useful for typical

- microcontroller applications, such as:

   Analog-to-digital converter,

   Pulse-width-modulator [65].

4.2.4 LCD 16x2

LCD (Liquid Crystal Display) screen is an electronic display module and find a wide range of applications. A 16x2 LCD display is very basic module and is very commonly used in various devices and circuits. These modules are preferred over seven segments and other multi segment LEDs. The reasons being: LCDs are economical; easily programmable; have no limitation of displaying special & even custom characters (unlike in seven segments), animations and so on [**Error! Reference source not found.**].

A 16x2 LCD means it can display 16 characters per line and there are 2 such lines. In this LCD each character is displayed in 5x7 pixel matrix. This LCD has two registers, namely, Command and Data.

The command register stores the command instructions given to the LCD. A command is an instruction given to LCD to do a predefined task like initializing it, clearing its screen, setting the cursor position, controlling display etc. The data register stores the data to be displayed on the LCD. The data is the ASCII value of the character to be displayed on the LCD. Click to learn more about internal structure of a LCD [**Error! Reference source not found.**].

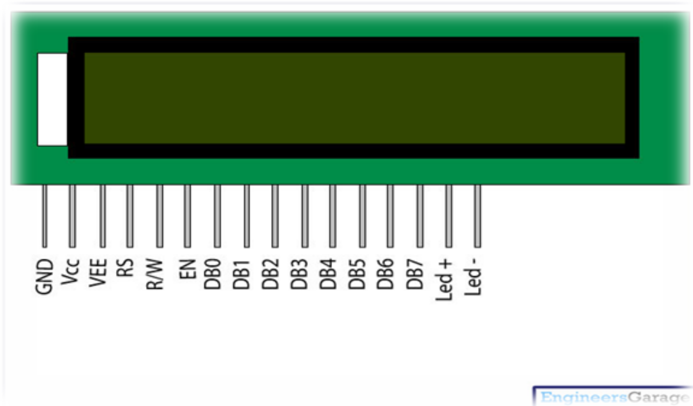


Figure 4-6: LCD pin diagram [**Error! Reference source not found.**].

4.2.5 The power supply circuit

The power supply circuit is used to convert the AC volt to Dc which needs in digital circuit. It consists of transformer the firstly convert the 220 V DC to 12 V DC, but the circuit needs 5V DC, by adding a rectifier consisting of four diodes connected as bridge to convert the 12V AC to12V DC also we need to smooth the signal by connecting the capacitor to the rectifier and lastly the voltage regulator 7805 produced 5V DC that required in the circuit.

The system was designed to stimulate the spinal cord by blocking the pain. This system depends on three variables; duty cycle, pulse period and amplitude the table below show the hardware capabilities of the spinal cord stimulator designed, developed and tested.

The purpose of a power supply is to provide power for an electronic circuit. For a given amount of power, there is an inverse relationship between voltage and current. Whenever current increases, voltage must decrease, and whenever current decreases, voltage must increase. This simple fact, unfortunately, has an adverse effect on power supply circuits.

When you connect a voltmeter to the output terminals of a power supply, the meter itself draws an almost insignificant amount of current, so the meter reads very close to the voltage you expect to obtain from the power supply [75]

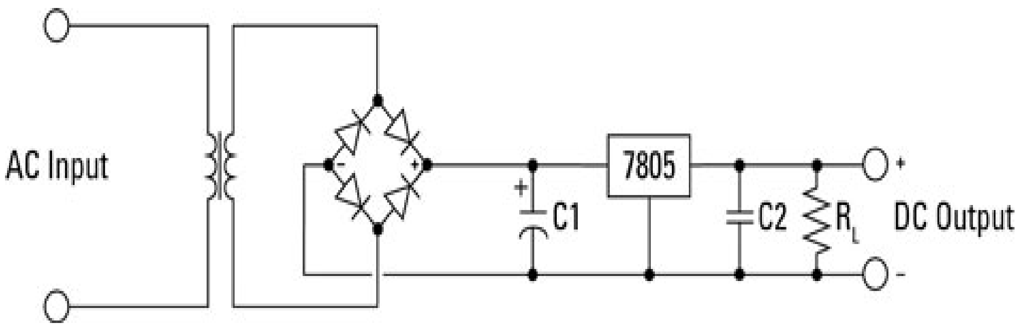


Figure 4-7: Power supply circuit [75].

4.2.5.1 Transformer

A transformer is an electrical device that transfers electrical energy between two or more circuits through electromagnetic induction. Electromagnetic induction produces an electromotive force within a conductor, which is exposed to time varying magnetic fields. Transformers are used to increase or decrease the alternating voltages in electric power applications. Since the invention of the first constant potential transformer in 1885, transformers have become essential for the transmission, distribution, and utilization of alternating current electrical energy [**Error! Reference source not found.**76].

4.2.5.2 The rectifier

A rectifier is an electrical device that converts alternating current (AC), which periodically reverses direction, to direct current (DC), which flows in only one direction. The process is known as rectification.

A full-wave rectifier converts the whole of the input waveform to one of constant polarity (positive or negative) at its output. Full-wave rectification converts both polarities of the input waveform to pulsating DC (direct current), and yields a higher average output voltage. Two diodes and a center tapped transformer, or four diodes in a bridge configuration and any AC source (including a transformer without center tap), are needed [77].

4.2.5.3 The capacitor

A capacitor is a passivetwo-terminalelectrical component that stores electrical energy in an electric field[78]. The effect of a capacitor is known as capacitance. While capacitance exists between any two electrical conductors of a circuit in sufficiently close proximity, a capacitor is specifically designed to provide and enhance this effect for a variety of practical applications by consideration of size, shape, and positioning of closely spaced conductors, and the intervening dielectric material. A capacitor was therefore historically first known as an electric condenser.

4.2.5.4 The voltage regulator

IC 7805 is a 5V Voltage Regulator that restricts the voltage output to 5V and draws 5V regulated power supply. It comes with provision to add heatsink.

A voltage regulator is designed to automatically maintain a constant voltage level. A voltage regulator may be a simple "feed-forward" design or may include negative feedbackcontrol loops. It may use an electromechanical mechanism, or electronic components. Depending on the design, it may be used to regulate one or more AC or DC voltages.

Table 4-2: Comparison between the hardware parameters of three types of spinal cord stimulators

One-time implantable spinal cord stimulation system prototype	**Medtronic Itrel**	**Embedded spinal cord stimulation**	**Stimulation parameters**
4	1	3	number of independent channels
impulse	impulse	-sine wave. -square wave. -triangle wave.	Signal types
6 ms- 500 ms	60 ms- 450 ms	50 ms -1000 ms	Pulse period
0 V-10.5 V	0 V -10.5 V	0 V -5 V	Amplitude
0% -100%	100%	0%-100%	Duty cycle
Implantable	Implantable	Bedside-portable	Stimulator type
No	No	Yes	User defined waveforms/patient specific waveform
No	No	Yes	Modular structure-extendable design

4.3 Final circuit design

The spinal cord embedded system design Module as a simulator of work for the spinal cord impulse stimulation which is connected to the electronic circuit of 5 DC volts, is controlled by rheostat (POTENTIMETER) connected with oscillators circuit (555 TIMER) that run on PULSE generator signals (PULSES) passers-to (MICROCONTROLLER) which works to read the vibrations through in (PIN B1) and the provisional rules of procedure run to calculate pulse s counter in time and through the program conditions as count per cycle and amplitude in time and through the program conditions which involved are output pulses using PWM technique is variation in impulses and frequency duty cycle emerging count of impulses input, was all this work using software (BASCOM) and PRUTOUS software simulation program to simulate the circuit work and display the result. The figures below illustrated the (555 timer) the (microcontroller) and the final circuit in the simulation program (Figure 4-8), (Figure 4-9) and Figure 4-10.

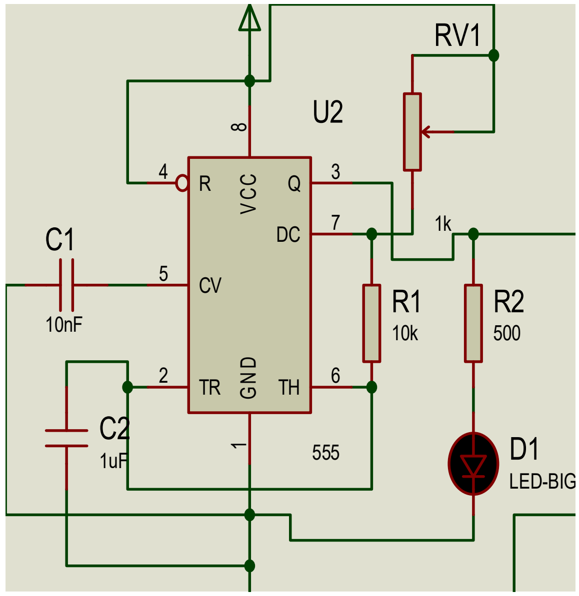


Figure 4-8:555 timer circuit.

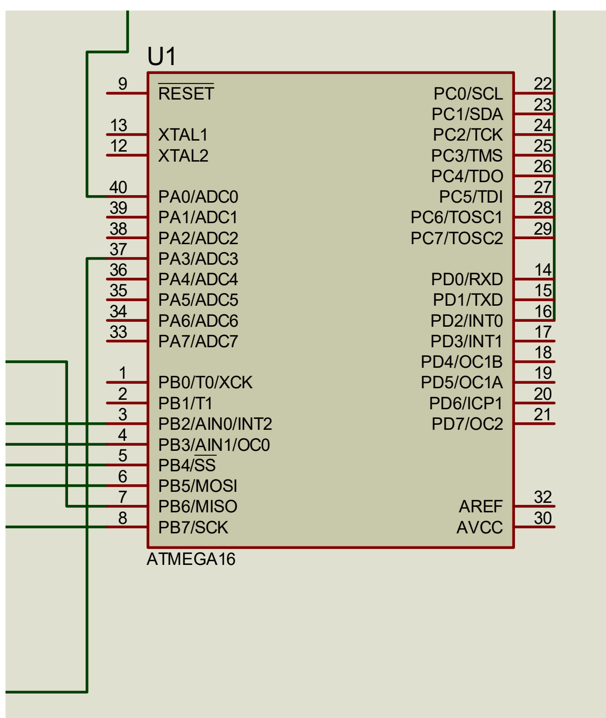


Figure 4-9: Microcontroller circuit.

The spinal cord stimulation required different pulses with variable widths. These pulses generated using microcontroller (Atmega 16) which contain DAC and an operational amplifier. The design of the spinal cord stimulator with multiple outputs makes the system quite complicated in all these realizations.

The figure below shows the embedded spinal cord stimulator:

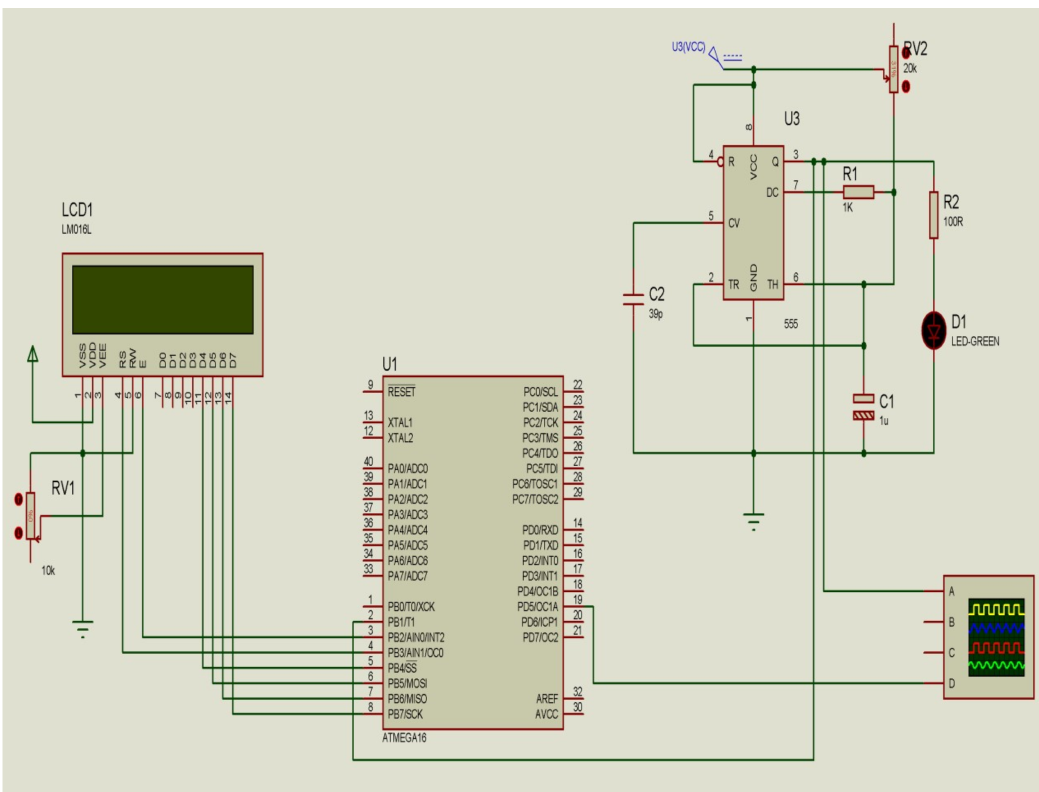


Figure 4-10: View of SCS channel board design.

4.4 The stimulator software design

The system software design consists of programming the microcontroller by using Bascom language that developed and implements on the following features: the stimulus applied for three different subject simultaneously; amplitude, duty cycle and frequency which is programmable and change for different patients. The adjusted variables are appearing in the LCD screen and the output of the nerve stimulus is appearing as a waveform.

Before the software program has been started, the medical experts define parameters of the stimulation signals taking into account the requirement of the patient. Having chosen the input parameters (frequency, amplitude and duty cycle) and their usable limits set with numeric by the potentiometer then transmitted to the LCD. The lines below illustrate the microcontroller program and flow chart:

4.4.1 System code

The code used to program the microcontroller used bascom language as shown below:

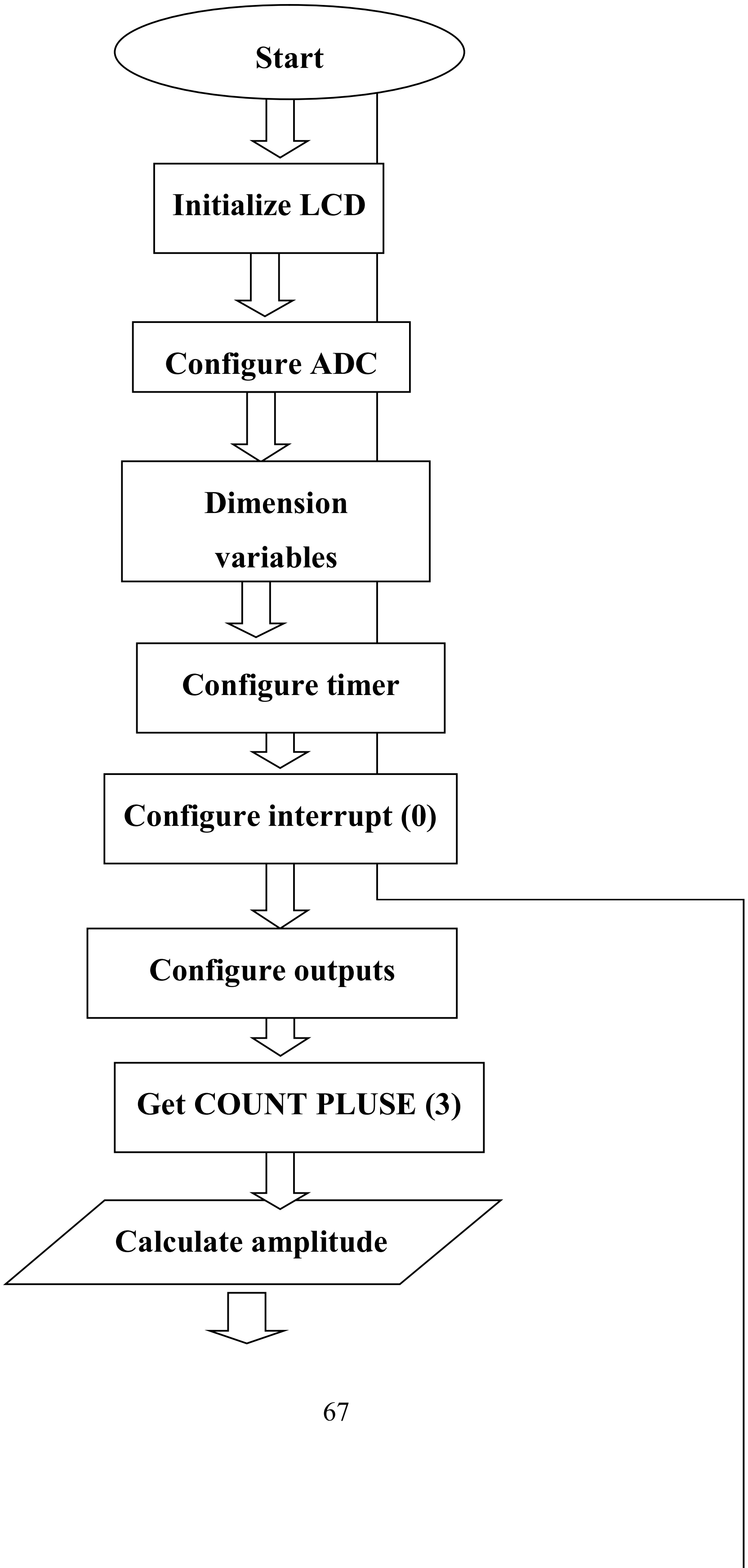
```
$regfile = "m16def.dat"

$crystal = 8000000

ConfigLcd = 16 * 2

ConfigLcdpin = Pin , Db4 = Portb.4 , Db5 = Portb.5 , Db6 = Portb.6 , Db7 = Portb.7 , E =
Portb.2 , Rs = Portb.3

Config Pinb.1 = Input

Config Pind.5 = Output

Cls

Locate 1 , 1

Lcd"  spinal cord   "

Locate 2 , 1

Lcd "   simulator     "

Dim Count As Integer

Dim Aa As Integer

Dim S As Integer

Dim I As Integer

Dim D As Integer

Dim L As Integer

Config Timer1 = Counter , Edge = Rising

Config Timer0 = Timer ,Prescale = 1024

On Ovf0 Displays

Start Timer0

 Enable Interrupts

Enable Timer0
```

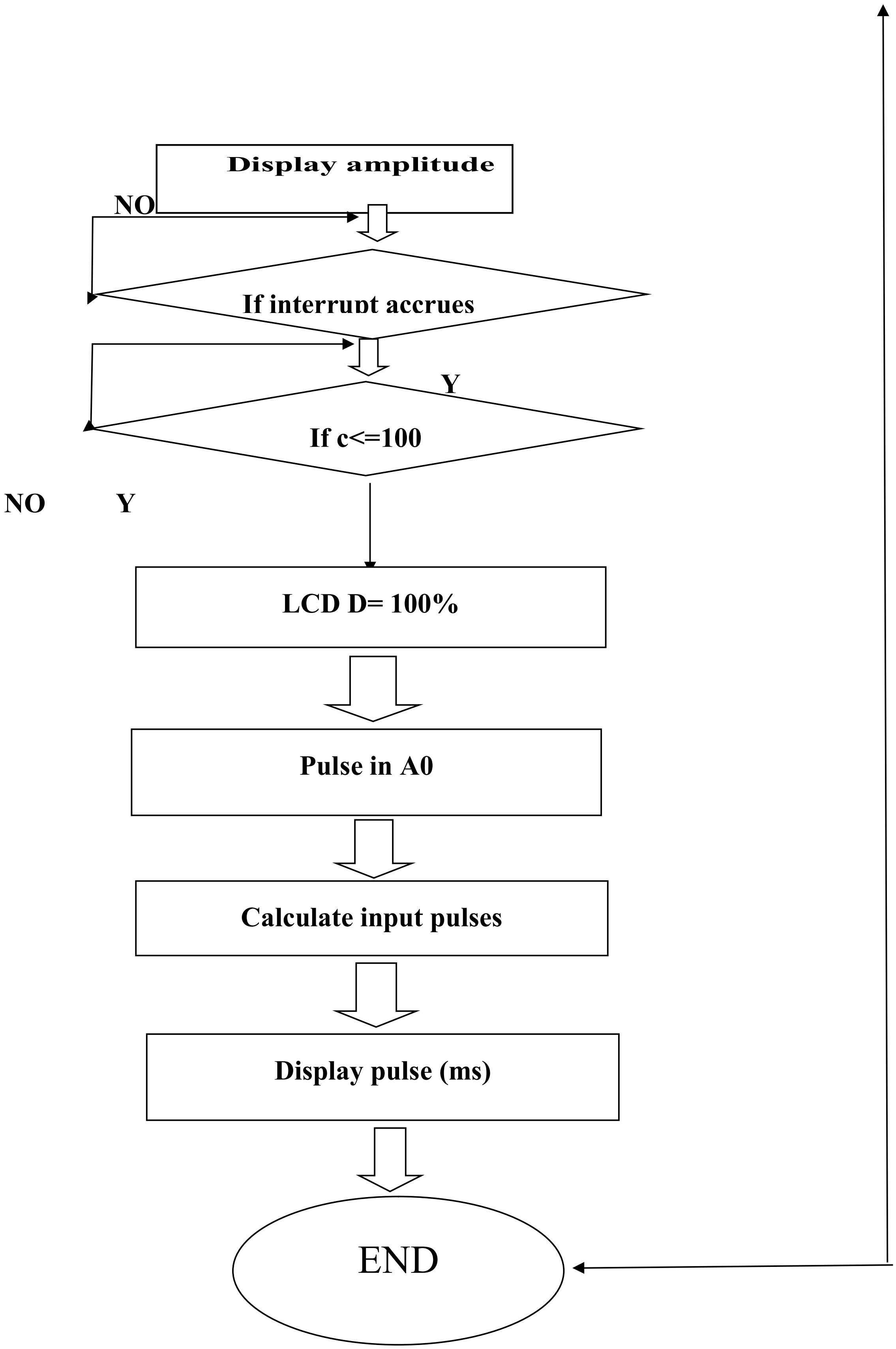
```
Enable Timer1

Start Timer1

On Int0 Label2

Do

Cls

Locate 1 , 1

Lcd "s = " ; S ; " ls= " ; L;

Locate 2 , 1

Lcd " b = " ; D ;

Waitms 100

If L >= 0 And L <= 50 Then

For I = 1 To 10

Portd.5 = 1

Waitms 50

Portd.5 = 0

Waitms 50

Next I

End If

If L >= 51 And L <= 100 Then

For I = 1 To 10

Portd.5 = 1

Waitms 100

Portd.5 = 0

Waitms 100

Next I

End If
```

```
If L >= 101 And L <= 150 Then
For I = 1 To 10
Portd.5 = 1
Waitms 150
Portd.5 = 0
Waitms 150
Next I
End If
If L >= 151 And L <= 200 Then
For I = 1 To 10
Portd.5 = 1
Waitus 200
Portd.5 = 0
Waitus 200
Next I
End If
If L >= 201 And L <= 250 Then
For I = 1 To 10
Portd.5 = 1
Waitus 250
Portd.5 = 0
Waitus 250
Next I
End If
If L >= 250 Then
For I = 1 To 10
```

```
Portd.5 = 1
Waitus 300
Portd.5 = 0
Waitus 300
Next I
End If
 Loop
 Label2:
Incr Count
Return
Displays:
Incr Aa
If Aa = 30 Then
Incr S
Waitms 100
If S = 2 Then
S = 0
Timer1 = 0
 L = D
End If
D = Timer1
Aa = 0
End If
Return
```

4.4.2 System flow chart:




Display amplitude
NO
If interrupt accrues
Y
If c<=100
NO
Y
LCD D= 100%
Pulse in A0
Calculate input pulses
Display pulse (ms)
END

Chapter 5 THE RESULTS

5.1 Practical results of spinal cord stimulator

In this chapter, the main aim is to show the operation of the circuit and the results by connecting the circuit with the oscilloscope to show the signals we needed.

Stimulation is one effort used when human body functions improperly, the body make natural repair. However, sometimes the body cannot do this work so it needs external stimulation. This research is prepared to develop the spinal cord stimulation in electronic circuit.

The system discussed in details in chapter 4. This chapter test and result values of the stimulation. The more important values are the variables values in range as shown below:

- Frequency (50-1000ms).
- Amplitude (0-5V).
- Duty cycle (0-100%).

When we adjusted the values that we need in specific patient state of problem the signal appears as waveform in the oscilloscope. The waveform is appearing in the oscilloscope in the system design. The LCD below shows the adjusted three variables in LCD:

The variable appears in LCD before the stimulation.

The figures below show the practical work of the circuit to find the results:

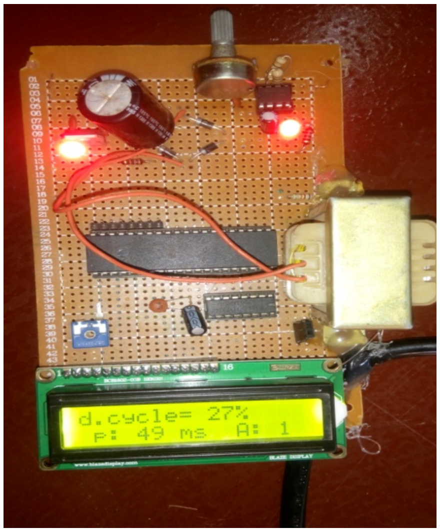


Figure 5-1: The circuit LCD output when duty cycle =27% and pulse: 49 ms when amplitude of 1.

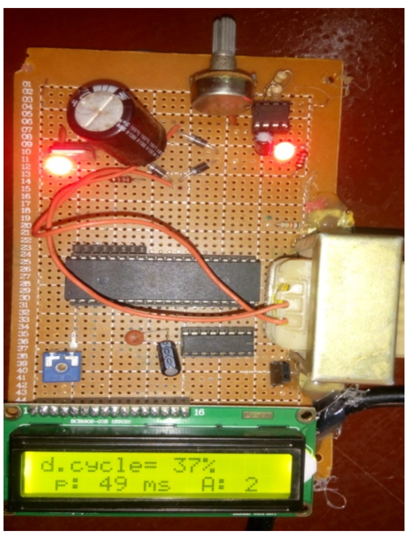


Figure 5-2: The circuit LCD output when duty cycle =37% and pulse: 49 ms when amplitude of 1.

Figure 5-3: The signals in oscilloscope refer to the above parameters measured.

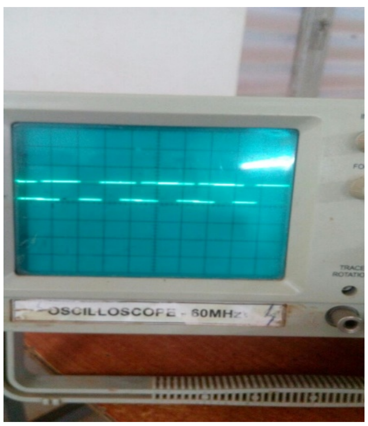


Figure 5-4: The signals appears in oscilloscope refer to the above parameters measured.

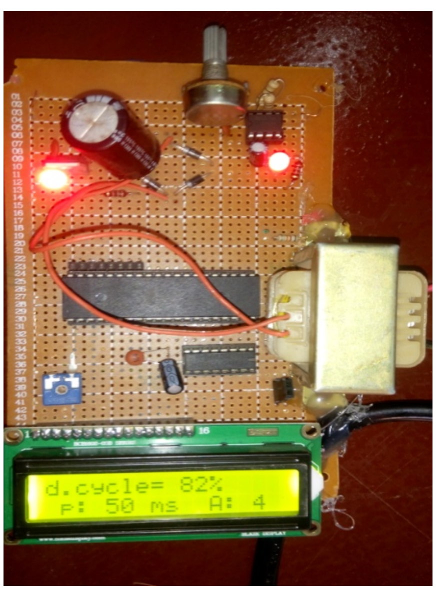


Figure 5-5: Circuit LCD output when duty cycle =82% and pulse: 50 ms when amplitude of 4.

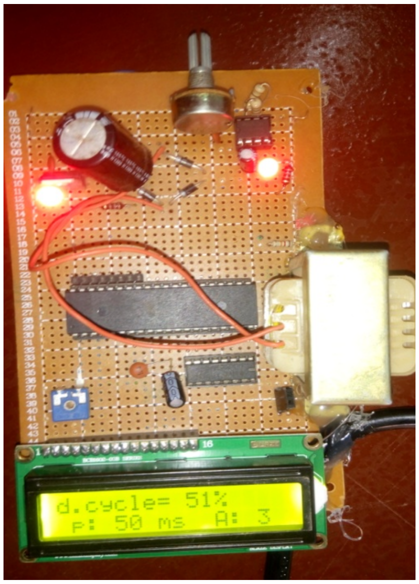


Figure 5-6: Circuit LCD output when duty cycle =82% and pulse: 50 ms when amplitude of 3.

Figure 5-7: The signals in oscilloscope refer to the above parameters measured.

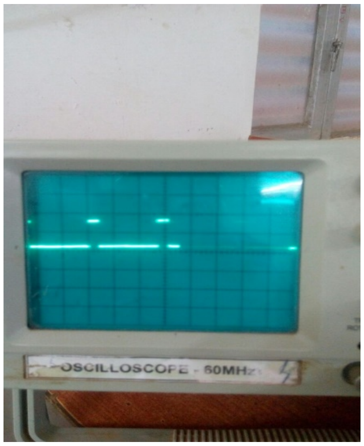


Figure 5-8: The signals in oscilloscope refer to the above parameters measured.

Table (): the results of the stimulator measured by oscilloscope

Chapter 6 CONCLOUSION AND FUTURE WORK

6.1 Conclusion

The conventional types of spinal cord stimulators used are the PC based stimulators, which are heavy, expensive and have a limited number of features; these types are used in hospitals or medical centers.

Another type is the implantable version which needs the microelectronics in an ASIC integrated circuit(IC) customized for a particular use rather than intended for general-purpose use chip mode. The implantable versions of SCSs need medical operation and high technology used also very high accuracy and sensitivity.

This research intended to produce new version of spinal cord stimulator, this design will make home usage possible, cheap compared with the other types of stimulators. This stimulator design intended to be flexible and medical experts could adjust to the need and requirement of the patients. The quality of graphic display used and improved.

The conventional SCS systems main difficulty is the general use without take in consideration the patient specific requirement. This research stimulator is able to produce patient specific requirement.

6.2 The future work:

The future work of this research will focus into modifying the system to be less and more practically in clinical critical states to help and consultation of medical experts. Also as future work is developed the embedded system to integrate with two more features and used keyboard instead of the potentiometer. The simplicity and the smaller is the target of the future working in this stimulator.

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