ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE ENGINEERING AND TECHNOLOGY

COMMUNICATION PROTOCOLS FOR NEURAL NANONETWORKS IN CASE OF NEURON SPECIFIC FAULTS

Ph.D. THESIS

Hakan TEZCAN

Department of Computer Engineering

Computer Engineering Programme

JANUARY 2016

ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE ENGINEERING AND TECHNOLOGY

COMMUNICATION PROTOCOLS FOR NEURAL NANONETWORKS IN CASE OF NEURON SPECIFIC FAULTS

Ph.D. THESIS

Hakan TEZCAN
(504072503)

Department of Computer Engineering

Computer Engineering Programme

Thesis Advisor: Prof. Dr. Sema F. OKTUĞ
Thesis Co-advisor: Assoc. Prof. Dr. Fatma N. KÖK

JANUARY 2016

İSTANBUL TEKNİK ÜNİVERSİTESİ ★ FEN BİLİMLERİ ENSTİTÜSÜ

SİNİR HÜCRELERİNE ÖZGÜ HATA DURUMLARINDA SİNİR NANOAĞLAR İÇİN HABERLEŞME PROTOKOLLERİ

DOKTORA TEZİ

Hakan TEZCAN
(504072503)

Bilgisayar Mühendisliği Anabilim Dalı

Bilgisayar Mühendisliği Programı

Tez Danışmanı: Prof. Dr. Sema F. OKTUĞ
Tez Eşdanışmanı: Doç. Dr. Fatma N. KÖK

OCAK 2016

Hakan TEZCAN, a Ph.D. student of ITU Graduate School of Science Engineering and Technology 504072503, successfully defended the thesis entitled **"COMMUNICATION PROTOCOLS FOR NEURAL NANONETWORKS IN CASE OF NEURON SPECIFIC FAULTS"**, which he/she prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below.

Thesis Advisor :	**Prof. Dr. Sema F. OKTUĞ** İstanbul Technical University	....
Co-advisor :	**Assoc. Prof. Dr. Fatma N. KÖK** İstanbul Technical University	....
Jury Members :	**Prof. Dr. A. Emre HARMANCI** İstanbul Technical University	....
	Prof. Dr. Seyhun SOLAKOĞLU İstanbul University	....
	Prof. Dr. Zeynep Petek ÇAKAR İstanbul Technical University	....
	Prof.Dr. Özgür Barış AKAN Koç University	....
	Assoc. Prof. Dr. Şima E.UYAR İstanbul Technical University	....

Date of Submission : 06 November 2015
Date of Defense : 13 January 2016

To my spouse and sons,

FOREWORD

There had been many late nights and early mornings, and after all the work, it is a great pleasure to conclude that the thesis is over. I am really honored to be writing these lines.

Through the rough road of this thesis, I have been personally blessed with family, friends, mentors, and colleagues, who had so generously given their times as well as intellectual, spiritual, and emotional support. There are many people to whom I am eternally grateful.

First and foremost, I would like to express my deepest gratitude to my advisor, Prof. Dr. Sema F. OKTUĞ. You have been supportive since the first day I began. You not only guided my research, but also encouraged me to keep on studying. Thank you very much for your useful critiques, enthusiastic encouragement, and patient guidance. I am really honored and lucky to know you and work with you.

I would like to offer my special thanks to Assoc. Prof. Dr. Fatma N. KÖK, my co-advisor for her support, motivation and creative ideas in my research field that I know very little at the beginning.

I would like to thank my committee members who were more than generous with their expertise and precious time. Thanks Prof. Dr. A. Emre HARMANCI, Prof. Dr. Seyhun SOLAKOĞLU, and Assoc. Prof. Dr. Şima E. UYAR for your supportive and improving discussions, encouraging, and guidance. I am also thankful to Prof. Dr. Zeynep Petek ÇAKAR and Prof.Dr. Özgür Barış AKAN for agreeing to be on my thesis jury and their valuable suggestions and comments.

I would like to thank Asst. Prof. Dr. Devrim Y. AKSIN for the directive discussions on nanoelectronics.

I also would like to thank my colleagues at Turkish Navy Research Center Command: İldeniz Duman, Hakan Savaşan, Sinan Tümen and Kadir Alpaslan Demir.

I am also grateful to my friends and colleagues at Computer Networks Research Lab at Istanbul Technical University, for their collaboration and friendship.

Last but not least, I would like to thank my family. Thank you for being indulgent when I spend time studying, which I should have spent with you. My beloved wife, Biray, thank you for supporting me, and at times, being a single-parent to our children. Be sure that I could not have done this without your support and motivation.

January 2016 Hakan TEZCAN

TABLE OF CONTENTS

Page

ABBREVIATIONS

ARP : Absolute Refractory Period
CNS : Central Nervous System
CNTs : Carbon Nano Tubes
EqNN : Equivalent Neuron-Nanomachine
FDL : Fiber Delay Lines
FIFO : First-In First-Out
ICT : Information and Communication Technologies
MC : Molecular Communication
MEAs : Multielectrode Arrays
ms : Milisecond
mV : Milivolt
NDB : Neural Delay Box
NEST : Neural Simulation Tool
NW FETs : Nano Wire Field Effect Transistor Arrays
PMNS : Peripheral Motor Nervous System
PNS : Peripheral Nervous System
PSNS : Peripheral Sensory Nervous System
RN : Receptor Neuron
SBMP : Switch Based Multiplexing Protocol
SM : Statistical Multiplexing
SnM : Synaptic Nanomachine
SNR : Signal to Noise Ratio
TDM : Time Division Multiplexing
TDMA : Time Division Multiple Access
VACNFs : Vertically Aligned Carbon Nano Fibers

LIST OF TABLES

Page

LIST OF FIGURES

Page

COMMUNICTION PROTOCOLS FOR NEURAL NANONETWORKS IN CASE OF NEURON SPECIFIC FAULTS

SUMMARY

Recent developments in nanotechnology and biology allow engineering of nano scale biocompatible machines capable of communicating with the existing biological systems at molecular level. The development of this innovative technology will enable to build nanomachines that can be considered as the most basic functional units at nanoscale. Either artificially created or naturally occurring bio-nanomachines are functional nanoscale units that can perform very simple tasks. The limited capabilities of nanomachines can be expanded by interconnecting them to cooperate and share information. Resulting networks of nanomachines, namely nanonetworks can be referred as the interconnection of nanomachines that work in a collaborative manner to carry out a common complex objective by communicating with each other. Although nanonetworking is in its infancy, wide range of appealing application areas of nanonetworks especially in human healthcare field draw the attention of the scientific communities from various disciplines. Nanonetworks cannot be considered as a simple extension of the conventional communication networks. The differences between nanonetworks and traditional communication networks come in view in message encoding, propagation speed, noise factors and energy consumption.

Communication processes of nanonetworks are mostly inspired by the existing biological systems. Although various means such as nanomechanical, acoustic, electromagnetic methods are introduced to maintain the communication between the nanomachines, molecular communication (MC) glitters as the most promising approach among the others and therefore attracted the attention of many researchers in recent years. MC is inspired by the communication mechanisms that naturally occur among living cells and it is based on the use of molecules to encode information. MC has some advantages over nano or micro scale components because of the natural size of molecules and biological cells. Biocompatibility property of the MC is the most distinctive advantage that enables the integration to medical applications. Another important characteristic of MC is the efficiency in energy consumption. With these appealing features of MC, it is possible to have more direct interaction with the medical applications such as health monitoring, immune system support, bio-hybrid implants, and drug delivery systems. One of the techniques which is proposed for MC is the use of neural networks. This technique is inspired by the nervous system that spreads throughout the human body to control somatic and autonomic behaviors.

In this thesis, we study the somatosensory system that is a subnetwork of the nervous system in detail and explore the analogies between this intra-body nanonetwork and the conventional communication networks. The somatosensory system processes information about the somatic perceptions that include four major sensations:

discriminative touch, proprioception, nociception, and temperature. For the somatosensory system, perceived stimulus converted into spike trains by the receptor neurons (RNs) and conveyed to the somatosensory cortex via second and higher order neurons. Brain, as the main processing unit, has a precise map for perceived information to preserve the spatial relation of the RNs. Therefore, the location of the sensed stimulus is determined by the pathway that transports the spikes, not by the spike itself. This feature resembles the circuit switching in traditional communication networks. Sensory data is coded with following three properties, the number of spikes generated, the inter-spike intervals, and the pathway that the spikes are carried through. During our researches, we recognized that many neurodegenerative diseases such as Multiple Sclerosis, Alzheimer and Paralysis are caused by the interruption of spike propagation due to the malfunctioning neurons in the pathway where the signal is carried through. Even if the RNs function properly, a faulty relaying neuron (inter-neuron) in the signaling pathway hinders the spikes to be delivered to the somatosensory cortex. Thus, a fault in the pathway results in a loss of sense in the relevant part of the human body. These irreversible impairments remind the same problem in the transmission lines of the conventional communication networks. In communication networks, multiplexing methods that combine more than one signal over a shared medium are employed to solve this problem.

In this thesis, we propose three neuron specific techniques for conveying the spike trains of RNs that have faulty pathways over a functional neighboring pathway by using the above-mentioned analogy. For the techniques we propose, our aim is twofold. Firstly, conveying the spikes of an RN that has faulty pathway through a shared functional pathway. The latter is to minimize the number of spikes that can be lost while multiplexing the spikes of RNs in order to feel the correct sensation. The proposed techniques require the spikes of RNs to be converted to electronic domain. This conversion can be done with neural interfaces that can detect an incoming spike and stimulate the generation of a new spike. Therefore, we also reviewed the competitive methods in the literature for interfacing neurons and proposed the use of neural interfaces in our techniques. For the evaluation of a realistic performance analysis of our studies, we employed Neural Simulation Tool in order to reflect the electrical and chemical aspects of the neuro-spike communication channel.

Among the proposed techniques in this thesis, we firstly propose a neuron specific Time Division Multiple Access (TDMA) based protocol for ensuring the RNs that have the faulty pathway to communicate with the somatosensory system. For sharing the functional pathway between the RNs, we develop a novel multiplexing and buffering mechanism employing the Neural Delay Box (NDB) scheme that is composed of a relay unit and a buffering unit. The relay unit can be realized as a nanoelectronic device. The buffering unit can be implemented either by using neural delay lines as employed in optical switching systems or by using nano scale delay flip flops. The spikes received at the assigned time slot of RNs are directly conveyed to the shared neural pathway by using NDBs. The spikes transmitted at the unassigned time slots are buffered and transmitted at the next assigned time slot. Thus, the spikes are carried through a functional pathway and they can be easily demultiplexed according to the assigned time slots of RNs, thereafter are delivered to corresponding destination. Furthermore, we evaluate the performance of the proposed method under various scenarios via simulations. The results demonstrate that significant performance improvement on the successively delivered number of spikes is achievable when the delay lines are employed as neural buffers in NDBs.

Secondly, we propose a neuron specific statistical multiplexing (SM) based technique to establish the communication between an RN and somatosensory cortex in case of an intermediate neuron failure in its own sensory pathway. The proposed technique utilizes the multiplexer and the demultiplexer units that can be realized as nanoelectronic devices and an addressing scheme. As we consider the traditional packet switching networks, every packet have a header part to identify the source and the destination addresses. Nevertheless, spikes neither have any information about which RN generated them nor the arrival address. To employ statistical multiplexing, the spikes of each transmitting RN must be distinguished at the demultiplexer unit before conveying them to the related part of the somatosensory cortex. Hence, we introduce an addressing scheme to identify the transmitting RNs by using the spikes themselves. Actually, we establish a packet switching neural nanonetwork by employing this addressing scheme. Furthermore, we show that a priority mechanism can be developed for the proposed technique. We present the performance of the proposed technique is in terms of the percentage of the spikes transmitted under various scenarios. We also compare the performance of the SM based sensory nanonetwork with the previously proposed TDMA based sensory nanonetwork. Despite that the performance achieved by SM based sensory nanonetwork is lower than the TDMA based sensory nanonetwork, the proposed SM based sensory nanonetwork has implementation simplicity. We also examine the similarity between the input spike generation times (spike times of the RNs) and the output spike generation times (spike times at the demultiplexer unit). Test results demonstrate that the input and output spike patterns have similar properties.

Finally, we propose the Switch Based Multiplexing Protocol (SBMP) to substitute a faulty sensory neural pathway with a functional neighboring neural pathway. The proposed multiplexing protocol depends on the multiplexer and the demultiplexer units that can be realized as nanoelectronic devices. The spiking activity between these units is regulated by the SBMP. The SBMP is developed to set the pathway i.e. route where the spikes are carried through. The SBMP uses some control packets that exploits spikes themselves to manage the spike traffic. Via the control packets of the SBMP, the sensory pathway is alternated according to the owner of the spike to deliver the spike to the corresponding part of the somatosensory cortex. Besides, we also show that a priority mechanism can be developed for the proposed technique. We evaluate the performance of the proposed protocol by simulations under various scenarios. We also examine the similarity between the input and the output spike firing patterns either the RNs have equal priority or different priorities. The test results demonstrate that the input and output spike patterns have similar properties. We assured that both the input spike generation times of the RNs and the output spike generation times (at the demultiplexer unit) are from the same distribution. Furthermore, we compare the input inter-spike interval distribution (inter-spike interval times of the RNs) and output inter-spike interval distribution (inter-spike interval times at the demultiplexer unit) when equal or various priorities are assigned to the RNs. As the priority value assigned to the RN is increased, the output inter-spike interval distribution of the related RN converges to the input inter-spike distribution of the RN as expected. We also compare the obtained results with the previously proposed multiplexing techniques. SNMP, exhibits significant performance enhancement over the statistical multiplexing based technique and TDMA without delay lines technique. Although a better performance is achievable with TDMA with delay lines technique via its buffering capability, the SBMP has lower implementation complexity.

SİNİR HÜCRELERİNE ÖZGÜ HATA DURUMLARINDA SİNİR NANOAĞLAR İÇİN HABERLEŞME PROTOKOLLERİ

ÖZET

Son yıllarda nanoteknoloji ve biyoloji alanında yaşanan gelişmeler, moleküler seviyedeki mevcut biyolojik sistemlerle haberleşebilen nano ölçekli biyo-uyumlu makinelerin tasarlanmasını mümkün kılmıştır. Bu yenilikçi teknolojideki gelişmeler nano seviyedeki en temel işlevsel birim olarak kabul edilen nanomakinaların üretilmesine olanak sağlayacaktır. Hem yapay olarak üretilen hem de doğada mevcut olan biyo-nanomakinalar, yalnızca basit görevleri yerine getirebilen nano ölçekli işlevsel birimlerdir. Nanomakinaların kısıtlı yetenekleri, birlikte çalışabilmeleri ve bilgiyi paylaşmaları maksadıyla birbirleriyle haberleşmeleri sağlanarak artırılabilir. Sonuçta ortaya çıkan ve nanoağlar olarak bilen bu ağlar, birbirleriyle haberleşerek işbirliği içinde çalışan, ortak ve karmaşık bir görevi yerine getirmek üzere nanomakinaların oluşturduğu ağlar olarak tanımlanabilir. Nanoağlar gelişimin başlangıç evrelerinde olmasına rağmen, nanoağların özellikle insan sağlığı alanındaki uygulama alanları farklı disiplinlerde çalışan araştırmacıların ilgisini çekmektedir. Nanoağlar geleneksel haberleşme ağlarının basit bir uzantısı olarak düşünülmemelidir. Nanoağlar ve geleneksel haberleşme ağları arasındaki farklar verinin kodlanması, propagasyon hızı, gürültü faktörleri ve enerji tüketiminde ortaya çıkmaktadır.

Nanoağların haberleşme yöntemleri büyük ölçüde mevcut biyolojik sistemlerden esinlenmiştir. Nanomakinalar arasında haberleşmeyi sağlamak üzere nanomekanik, akustik ve elektromanyetik yöntemler gibi çeşitli metotlar önerilmesine rağmen moleküler haberleşme diğer yöntemler arasında en çok umut vadeden yaklaşım olarak öne çıkmakta ve bu nedenle de birçok araştırmacının dikkatini çekmektedir. Moleküler haberleşme doğada mevcut hücrelerde gerçekleşen haberleşme süreçlerinden esinlenmiştir ve bilginin kodlanması maksadıyla moleküllerin kullanımına dayanmaktadır. Sistem bileşenlerinin moleküler sevideki kontrolü ile biyo-uyumlu ve kararlı nanoağlar tasarlanabilir. Moleküler haberleşmenin moleküllerin ve biyolojik hücrelerin doğal büyüklükleri nedeni ile nano ve mikro ölçekli bileşenlere göre birtakım avantajları bulunmaktadır. Moleküler haberleşmenin biyo-uyumluluk özelliği bu yöntemin en ayırt edici özelliğidir ve bu sayede tıp uygulamaları için kullanılabilmesine olanak sağlamaktadır. Diğer önemli bir karakteristik özelliği ise enerji tüketimindeki verimliliktir. Bu dikkat çekici özellikleri sayesinde moleküler haberleşme sağlık izleme, bağışıklık sistemi desteği, biyo-melez implantlar ve ilaç dağıtım sistemleri gibi tıp uygulamalarıyla doğrudan etkileşimi mümkün kılmaktadır. Moleküler haberleşme yöntemi olarak haberleşen nanomakinaların arasındaki mesafeyi dikkate alan çeşitli yöntemler önerilmiştir. Önerilen metotlardan birisi de nanomakinaların haberleşmesi için sinir hücrelerinin kullanılmasıdır. Bu yöntem, somatik ve otomatik davranışlarımızı kontrol etmek üzere insan vücuduna yayılmış olan sinir sisteminden esinlenmiştir.

Bu tez çalışmasında, sinir sistemimizin bir alt ağı olan bedensel-duyusal (somatosensoriyel) ağ üzerinde detaylı araştırmalar yapılmış ve söz konusu vücut içi nanoağ ile geleneksel haberleşme ağları arasındaki benzerlikler belirlenmiştir. Bedensel-duyusal sistem, ayırt edilebilir dokunma hissi (nesnelerin büyüklüğü, şekli, yapısı ve deri üzerindeki hareketinin ayırt edilmesi), vücut kısımlarının (kas, eklem vb.) hareketleri ve pozisyonları, doku hasarı veya kimyasal tahriş kaynaklı ağrı/acı ve ısı (sıcaklık ve soğukluk) olarak bilinen dört temel duyuyu içeren bedensel algılara yönelik bilgiyi işler. Bedensel-duyusal sistemde hissedilen uyarı, algılayıcı sinir hücreleri tarafından uyarı katarına dönüştürülür ve bu uyarı katarı ikinci ve daha büyük dereceli ara sinir hücrelerinin oluşturduğu yollar kullanılarak beyindeki bedensel-duyusal kabuğa iletilir. Beyin ana işlem birimi olarak algılanan hissin ilgili algılayıcı sinir hücresiyle ilişkilendirilebilmesi için kusursuz bir eşleştirme haritasına sahiptir. Bu nedenle, algılanan uyarının yeri uyarı katarı ile değil uyarı katarını beyne ileten yol ile belirlenir. Bu özellik geleneksel haberleşme ağlarındaki devre anahtarlama kavramına benzemektedir. Algılanan his, üretilen uyarı sayısı, uyarılar arasındaki süre ve uyarının beyne iletildiği yol ile kodlanmaktadır. Çoklu skleroz, Alzheimer ve felç gibi birçok sinir hastalığı, uyarının iletildiği yolları oluşturan ara sinir hücrelerindeki fonksiyonel bozukluklardan dolayı uyarı iletiminin kesintiye uğramasından kaynaklanmaktadır. Algılayıcı sinir hücreleri düzgün çalışsa bile, uyarının taşındığı yol üzerinde bulunan hatalı bir ara sinir hücresi uyarının bedensel-duyusal kabuğa iletilmesine engel olmaktadır. Bu nedenle, uyarı yolu üzerindeki bir hata vücudun ilgili bölgesinde bir his kaybı olarak sonuçlanmaktadır. Uyarının taşındığı yol üzerindeki bozukluklar geleneksel haberleşme ağlarının iletim hatlarındaki benzer problemleri andırmaktadır. Haberleşme ağlarında, bu tip problemler birden çok sinyalin paylaşılan bir hat üzerinden taşınmasını sağlayan çoklama metotlarıyla çözülebilmektedir.

Bu tez çalışmasında, hatalı bir uyarı yoluna sahip bir algılayıcı sinir hücresi tarafından oluşturulan uyarı katarlarını, fonksiyonel komşu bir uyarı yolu kullanarak iletmek maksadıyla, yukarıda belirtilen benzerlik yaklaşımı kullanılarak sinir hücrelerine özgü üç farklı teknik önerilmiştir. Önerilen tekniklerdeki amacımız iki yönlüdür. Birinci amacımız, hatalı bir uyarı yoluna sahip bir algılayıcı sinir hücresi tarafından oluşturulan uyarı katarlarını paylaşılan bir uyarı yolu kullanarak iletmektir. İkinci amacımız ise, algılanan gerçek duyunun hissedilebilmesi için çoklama aşamasındaki uyarı kaybını asgari seviyeye indirmektir. Önerdiğimiz teknikler algılayıcı sinir hücreleri tarafından oluşturulan uyarıların elektronik ortama çevrilmesine ihtiyaç duymaktadır. Söz konusu çevrim, gelen bir uyarıyı tespit edebilen ve yeni bir uyarının oluşturulmasını sağlayabilen sinir arayüzleri ile gerçeklenebilmektedir. Bu nedenle, literatürde birbiriyle yarışan sinir arayüz metotları araştırılarak önerilen tekniklerde bu metotların kullanımı öngörülmüştür. Ayrıca, önerdiğimiz tekniklerin gerçekçi başarım analizlerini yapabilmek ve sinir-uyarı haberleşme kanalındaki kimyasal ve elektriksel özelliklerin başarım üzerindeki etkisini de yansıtabilmek amacıyla Sinir Benzetim Aracı (Neural Simulation Tool) kullanılmıştır.

Bu tez çalışmasında önerilen teknikler arasında ilk olarak, hatalı uyarı yollarına sahip algılayıcı sinir hücrelerine ait uyarıların duyusal-bedensel kabuğa iletilmesini sağlamak amacıyla sinir hücrelerine özgü Zaman Bölümlemeli Çoklu Erişim (TDMA) tabanlı bir yöntem önerilmiştir. Fonksiyonel uyarı yolunun birden çok algılayıcı sinir hücresi tarafından paylaşılabilmesi maksadıyla, aktarma birimi ve tampon biriminden oluşan Sinir Geciktirme Kutusu (NDB)'nu kullanan yeni bir çoklama ve tamponlama mekanizması geliştirilmiştir. Aktarma birimi nano elektronik bir aygıt olarak gerçekleştirilebilir. Tampon birimi ise optik anahtarlama ağlarında kullanılan optik geciktirme hatlarına benzer şekilde tasarladığımız gerçek sinir hücrelerinden oluşan sinir geciktirme hatları ya da nano ölçekli kapanlar (flip-flop) kullanarak gerçekleştirilebilir. Algılayıcı sinir hücreleri tarafından kendilerine atanmış zaman diliminde üretilen uyarılar, NDB tarafından doğrudan paylaşılan iletim ortamına aktarılır. Algılayıcı sinir hücrelerinin kendilerine atanmış zaman dilimleri haricinde oluşturdukları uyarılar ise NDB'nin tampon birimi kullanılarak algılayıcı sinir hücrelerine atanmış bir sonraki zaman diliminde gönderilmek üzere geciktirilir. Böylelikle, uyarılar paylaşılan iletim ortamı kullanılarak taşınır ve algılayıcı sinir hücrelerine ait atanmış zaman dilimi bilgisi kullanılarak çoklama çözücü birim (demultiplexer) tarafından kolayca çözülerek bedensel-duyusal kabuktaki ilgi varışa iletilir. Önerdiğimiz tekniğin başarım analizleri benzetim yöntemiyle birçok senaryo kullanılarak değerlendirilmiştir. Deneylerimizden elde edilin sonuçlar, geciktirme hatlarının NDB'de tampon olarak kullanıldığı durumda bedensel-duyusal kabuğa iletilen uyarı sayısında önemli bir artışın başarılabildiğini göstermektedir.

Tez çalışmamızda ikinci olarak, algılayıcı sinir hücrelerinin uyarılarını taşıyan yol üzerindeki ara sinir hücrelerinde bir hata olduğu durumda, algılayıcı sinir hücreleri ile bedensel-duyusal kabuk arasındaki haberleşmenin sağlanması amacıyla sinir hücrelerine özgü bir istatistiksel çoklama tekniği önerilmiştir. Önerdiğimiz teknik, nano elektronik bir aygıt olarak geliştirilebilecek bir çoklama ve çoklama çözme birimi ile bir adresleme yapısına dayanmaktadır. Geleneksel paket anahtarlamalı haberleşme ağları göz önüne alındığında, her bir paketin gönderici ve alıcı istasyon bilgisini içeren bir başlık kısmına sahip olduğu görülmektedir. Sinir hücreleri tarafından üretilen uyarılar ise ne hangi hücre tarafından üretildiği ne de hangi varış hücresine teslim edileceğine ilişkin bir bilgi barındırmaktadır. İstatistiksel çoklama yönteminin kullanılabilmesi için, her bir algılayıcı sinir hücresine ait uyarının çoklama çözme birimi tarafından bedensel-duyusal kabuktaki ilgili kısma iletilmesi öncesinde ayırt edilmesi gerekmektedir. Bu nedenle, uyarıların kendisinin kullanıldığı bir adresleme yöntemiyle uyarıları oluşturan algılayıcı sinir hücrelerinin tanımlamasını sağlayan bir adresleme yöntemi geliştirilmiştir. Aslında, bu yöntem ile devre anahtarlamalı haberleşme ağlarına benzeyen duyusal sinir ağı, paket anahtarlamalı bir ağ yapısına dönüştürülmektedir. Ayrıca, çalışmamızda önerdiğimiz teknik için algılayıcı sinir hücreleri arasında bir önceliklendirme yapısının da geliştirilebileceği gösterilmiştir. Önerdiğimiz yapının başarımı, çeşitli senaryolar kullanarak benzetim yöntemiyle değerlendirilmiştir. Önerilen istatistiksel çoklama tekniği ile ilk olarak önerdiğimiz TDMA tabanlı tekniğin başarımı da karşılaştırılmıştır. Önerdiğimiz istatistiksel çoklama tabanlı tekniğin başarımı, TDMA tabanlı tekniğin başarımından daha düşük olmasına rağmen, istatistiksel çoklama tabanlı tekniğin uygulama karmaşıklığının daha az olduğu görülmektedir. Buna ek olarak, algılayıcı sinir hücreleri tarafından üretilen uyarıların oluşturulma zamanları (giriş) ile çoklayıcı çözme birimindeki uyarı oluşturma zamanları (çıkış) arasındaki benzerlik de incelenmiştir. Test sonuçları giriş ve çıkış uyarı zamanlarının benzer özellikler sergilediğini göstermektedir.

Bu tez çalışmasında son olarak, bedensel-duyusal kabuğa uyarı iletiminin, hatalı uyarı yolunun yerine paylaşılan bir uyarı yolu ile sağlanması maksadıyla Anahtar Tabanlı Çoklama Protokolü (SBMP) önerilmiştir. Önerilen çoklama protokolü, nano elektronik aygıt olarak geliştirilebilecek bir çoklama birimi ve çoklama çözme birimine dayanmaktadır. Bu iki aygıt arasında gerçekleşen uyarı aktivitesi uyarıların taşınacağı yolun belirlenmesi amacıyla geliştirilen SBMP ile düzenlenmektedir. SBMP, uyarı trafiğini yönetmek maksadıyla uyarıların kendisinden oluşturulan kontrol paketlerini kullanır. Uyarının bedensel-duyusal kabuktaki ilgili kısma ulaştırılması için, uyarının taşındığı yol, kontrol paketleri kullanılarak uyarıyı oluşturan algılayıcı sinir hücresinin kimliğine göre değiştirilir. Ayrıca, önerilen teknik için algılayıcı sinir hücrelerine yönelik bir önceliklendirme yapısının da geliştirilebileceği gösterilmiştir. Önerilen tekniğin başarımı benzetim metodu ile değişik senaryolar kullanılarak değerlendirilmiştir. Algılayıcı sinir hücrelerin aynı ya da farklı önceliklendirmeye tabi tutulduğu durumlarda, giriş ve çıkışta oluşan uyarı örüntülerinin benzerliği de incelenmiştir. Test sonuçları giriş ve çıkıştaki uyarı örüntülerinin benzer özellikler taşıdığını göstermiştir. Algılayıcı sinir hücreleri tarafından üretilen uyarıların oluşturulma zamanları (giriş) ile çoklayıcı çözme birimindeki uyarı oluşturulma zamanlarının (çıkış) aynı dağılımdan geldiği ispatlanmıştır. Algılayıcı sinir hücrelerine atanan önceliklendirme değeri arttırıldığında, çıkıştaki uyarılar arasındaki zaman dağılımının girişteki uyarılar arasındaki zaman dağılımına yakınsadığı görülmektedir. Bu nedenle, algılayıcı sinir hücresi önceliklendirme değeri SBMP için bir servis kalitesi parametresi olarak kullanılabilir. Ayrıca, SBMP'nin başarımı, önerdiğimiz diğer iki tekniğin başarımı ile karşılaştırılmıştır. SBMP, istatistiksel çoklama ve geciktirme hatlarının kullanılmadığı TDMA tabanlı tekniğe nazaran daha üstün sonuçlar vermektedir. Sahip olduğu tamponlama yeteneğiyle geciktirme hatlarının kullanıldığı TDMA tabanlı teknik daha iyi bir başarım sergilemekte olmasına rağmen, SBMP tekniği uygulama açısından daha az bir karmaşıklığa sahiptir.

1. INTRODUCTION

1.1 Motivation

Although nanonetworking is in its infancy, wide range of appealing application areas, especially in human healthcare field, draw the attention of scientific community from diverse disciplines. Drug delivery systems, monitoring human body, neural treatment via implantable engineered devices can be the envisaged future application areas of nanonetworking.

Human body intrinsically houses different kinds of intra-body nanonetworks such as nervous nanonetwork, cardiovascular nanonetwork and endocrine nanonetwork [1]. In this thesis, we focus on the somatosensory system that is an important branch of sensory nervous nanonetwork and explore the analogies between the traditional communication networks. The somatic perception includes four major sensations; discriminative touch, proprioception, nociception and temperature [2]. For the somatosensory system, perceived stimulus converted into spike trains by receptor neurons (RNs) and conveyed to the somatosensory cortex via second and higher order neurons. Sensory data is coded with following three properties: the number of spikes generated, the inter-spike intervals, and the pathway that the spikes are carried through.

Communication problems due to the interruption of spike propagation in this nanonetwork emerge as neurodegenerative diseases such as Multiple Sclerosis, Alzheimer and Paralysis. Even though the RNs function properly, a faulty relaying neuron (inter-neuron) in the sensory pathway hinders the spikes to be delivered to the somatosensory cortex. Thus, a fault in the pathway results in a loss of sense in the relevant part of the human body.

Neural impairments at the sensory pathways resemble the same problem in the transmission lines of communication networks. Therefore, in our studies, we focus on ensuring the continuity of spike propagation in case of neuron specific faults in the signaling pathway. In communication networks, multiplexing methods that combine more than one signal over a shared medium are employed to solve this problem. By using this analogy, we devise different neuron specific techniques to convey the spike trains over a functional neighboring pathway. Our objective is to preserve the spike firing patterns generated by the RNs and deliver the spikes to the corresponding part of the somatosensory cortex in order to achieve the generation of correct sensation across the perceived information.

ICT inspired techniques like the proposed techniques in this thesis, ultimately pave the way for developing novel treatment strategies for neural diseases. One of the major neural diseases, peripheral neuropathy is caused by the lack of communication between the neurons in the sensory pathway. The proposed techniques that bring the communication capability between the RNs and somatosensory cortex may be applied to treat this kind of irreversible neural impairments in near future.

1.2 Work Done

In this thesis, we propose three techniques for conveying the spike trains of RNs those have faulty pathways over a functional neighboring pathway by using the multiplexing approaches in conventional communication networks. Due to the characteristics of the somatosensory system, proposed techniques employ neuron specific methods. For the techniques we propose, our aim is twofold. Firstly, conveying the spikes of an RN that has faulty pathway through a shared functional pathway. The latter is minimizing the number of spikes that can be lost while multiplexing the spikes of RNs in order to feel the correct sensation.

In the thesis period, we firstly proposed a TDMA based neural nanonetwork with some sources connected to a shared medium to reach a common destination. We introduced the concept of using neurons to form the underlying communication network infrastructure among the nanomachines. The spikes generated by these source nanomachines are multiplexed and carried over a shared medium to be delivered to a single destination nanomachine. In this system, the spikes generated by a source nanomachine are transmitted at the time slot assigned to it. In order to prevent the loss of the spikes which arrive at the unassigned time slots, we introduced a novel multiplexing and buffering mechanism via neural delay lines as used in optical switching systems [3,4]. We presented this work [5] in IEEE International Conference on Communications (ICC'12).

Afterwards, we studied the somatosensory system in detail. We improved our work [5] and proposed a neuron specific TDMA based protocol for ensuring the communication of RNs of the somatosensory system. For the proposed neural nanonetwork, the spikes of an RN are conveyed through a functional pathway in case of a path fault exists in its own pathway. For sharing the functional path between the RNs, we developed a multiplexing mechanism employing the Neural Delay Box (NDB) technique. An NDB is composed of a relay unit and a buffering unit. The relay unit can be realized as a nano electronic device. Buffering unit can be implemented either by using neural delay lines as employed in optical switching systems or by using nano scale delay flip flops. Both of these devices require the spikes be converted to electronic domain. This conversion can be done with neural interfaces that can detect an incoming spike and stimulate the generation of a new spike. We reviewed the competitive methods in the literature for interfacing neurons and proposed the use of neural interfaces in the NDBs and the demultiplexer unit. Our study [6] is published in IEEE Transactions on NanoBioscience (SCIE).

Thereafter, we proposed a neuron specific statistical multiplexing scheme to establish the communication between an RN and somatosensory cortex in case of intermediate neuron failure in its sensory pathway. For sharing the functional sensory pathway, we developed an addressing scheme that exploits spikes themselves to identify the owner of the spikes. Furthermore, we showed that a priority mechanism can be developed for the proposed technique. We presented this work [7] in IEEE International Congress on Ultra Modern Telecommunications and Control Systems (ICUMT'14).

Subsequently, we proposed the Switch Based Multiplexing Protocol (SBMP) to substitute a faulty sensory neural pathway with a functional neighboring pathway. The SBMP is developed to set the pathway i.e. route where the spikes are carried through. The SBMP employs some control packets that utilize the spikes themselves. Via the control packets of the SBMP, sensory pathways are alternated according to sender RNs and the spikes are delivered to the corresponding part of the somatosensory cortex. The proposed multiplexing protocol depends on the multiplexer and the demultiplexer units that can be realized as nanoelectronic devices. The spiking activity between these units is regulated by SBMP. The spike firing patterns at the input and the output are analyzed also. We also showed that a priority mechanism can be developed for the proposed technique and the priority values assigned to the RNs can be used as a quality of service parameter for SBMP. This work [8] is submitted for publication in IET Nanobiotechnology (SCIE).

1.3 Structure Of The Thesis

The outline of this thesis is as follows: Chapter 2 gives brief information about the nanonetworks, molecular communication, neurons, the somatosensory system and the multiplexing methods used in our techniques. In Chapter 3, we present the proposed neuron specific TDMA protocol for the neural nanonetworks. The proposed statistical multiplexing based technique for the neural nanonetworks is explained in Chapter 4. The Switch Based Multiplexing Protocol is discussed in Chapter 5. Finally, Chapter 6 concludes the thesis by giving future directions and summarizes our main contributions.

2. BACKGROUND INFORMATION

2.1 Nanonetworks

Many biological structures found in nature can be considered as nanomachines that are the most basic functional units of nanonetworks [9]. Nanobiosensors, nanoactuators, biological data storing components and control units which are found in cells are the examples of these existing biological nanomachines [9,10]. Engineered biological nanomachines can be developed by using these existing nanomachines or integrating them for creating more complicated systems such as nano-robots [9], synthetic protocells [11], and implantable neuron devices [12]. Either those found in biological systems or artificially created, nanomachines are capable of performing only very simple tasks such as computation, sensing, data storing or actuation [13]. Hence, it is not possible for a nanomachine to complete a macro-scale objective because of its limited size and complexity. As we consider the limited abilities of a single nanomachine, the most important property of these tiny components is the communication capability. Resulting networks of nanomachines, namely nanonetworks can be referred as the interconnection of nanomachines that work in a collaborative manner to carry out a common complex objective by communicating with each other. Nanonetworks cannot be considered as a simple extension of the conventional communication networks [9]. Communication processes of this paradigm are mostly inspired by the existing biological systems. The differences between nanonetworks and traditional communication networks can be summarized as below [9];

- In nanonetworks, the message is represented by using molecules instead of encoding the message in electromagnetic, acoustic or optical signals.

- The propagation speed of signals (molecules) in nanonetworks is much slower than the propagation speed of conventional signal forms.

- In traditional communication networks, noise can be described as undesired overlapped energy that degrades the quality of signals. In nanonetworks, noise occurs when unwanted reaction happens between the information molecules themselves or with the other molecules in environment.

- Multimedia data are usually encoded and transmitted over traditional communication networks. However, transmitted information represents a phenomena, chemical states and processes in nanonetworks.

- Nanonetworks generally have chemically driven processes resulting efficiency in energy consumption and perform more computation with less energy dissipation than existing electrical components of traditional communication networks [14].

Biomedical, environmental, industrial and military applications can be considered as the potential application areas of nanonetworks [9]. By controlling, the system components at the molecular level, biocompatible and biostable nanonetworks can be designed. With these promising features of nanonetworks, it is possible to have more direct interaction with medical applications such as health monitoring, immune system support, bio-hybrid implants and drug delivery systems and genetic engineering [9]. As an example of the envisaged medical applications, body area networks and in-body nanonetworks can be integrated and parameters from inside and from outside the body can be combined and analyzed in one information system and automatic reactions will become possible according to the analysis results [15,16].

2.2 Molecular Communication

Although various techniques are proposed to maintain the communication between the nanomachines, molecular communication (MC) glitters as the most promising approach among the others and therefore attracted the attention of many researchers in recent years [9,17]. MC is inspired by the communication mechanisms that naturally occur among living cells and it is based on the use of molecules to encode information [13,18]. A general molecular nanonetwork system consists of three main functional components that are transmitter, channel and receiver [1]. The transmitter nanomachine generates a signal by encoding the information onto molecules and releases these molecules to the communication medium. Propagation process provides the transportation of information molecules to the receiver nanomachine. The receiver nanomachine collects incoming molecules to decode the molecular message and generates intended response. General molecular nanonetwork with two nanomachines is illustrated in Figure 2.1 [1].

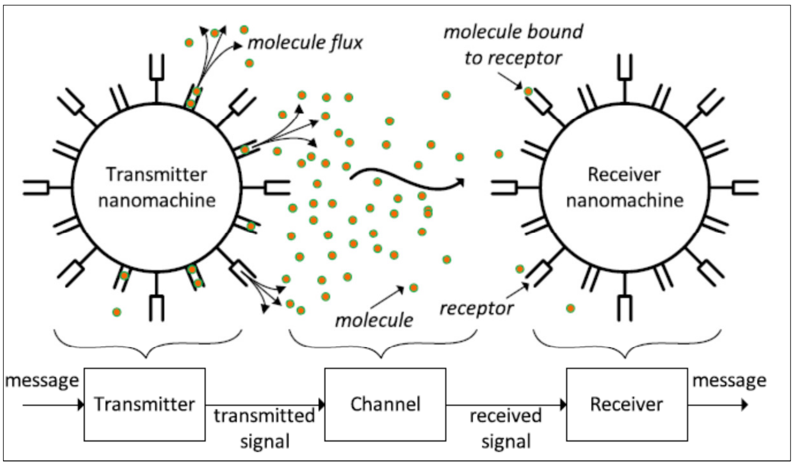

Figure 2.1 : General molecular communication system with two nodes [1].

MC has some advantages over nano or micro scale components because of the natural size of molecules and biological cells. Biocompatibility property of the MC is the most distinctive advantage that enables the integration to medical applications. Another important characteristics of MC is the efficiency in energy consumption. Communications in nature is a very energy-efficient process, much less than the bounds achieved by electrical signaling [14,19]. A single molecular reaction representing multiple computations consumes 10,000 times less energy less than a microelectronic transistor [13].

In literature, several means are proposed for biological and artificially created nanomachines to communicate over short [20,21] medium [22-25] and long [19] distances. The classification of these methods according to the transmission distances is illustrated in Figure 2.2.

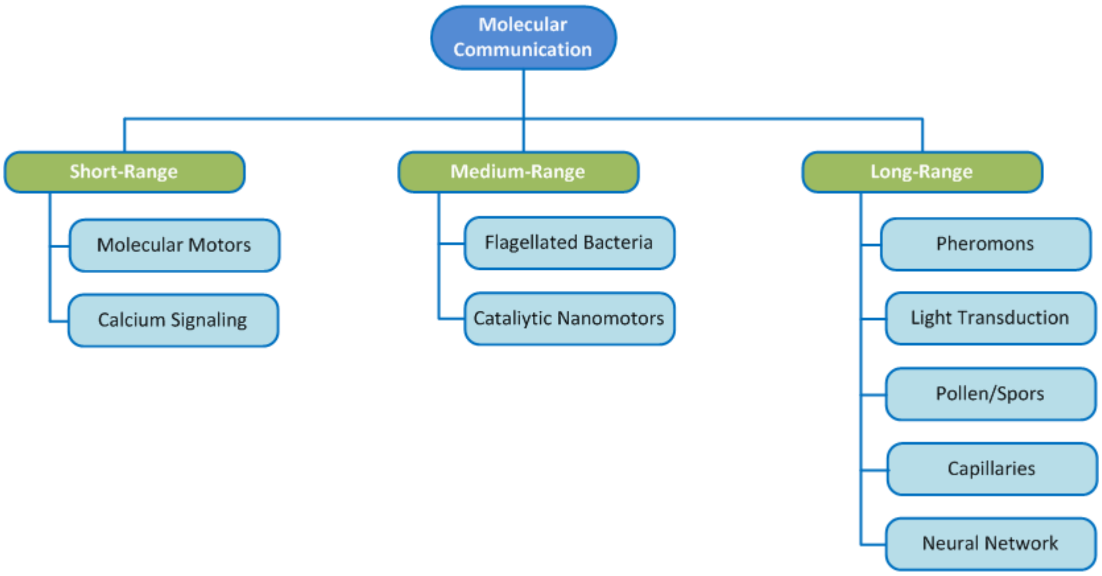

Figure 2.2 : Means for molecular communication.

One of the techniques which is proposed for long range MC is the use of neural networks. This technique is inspired by the nervous system that spreads throughout the human body to control somatic and autonomic behaviors [19]. In this thesis, we used nerve cells, i.e., neurons as the building blocks of the underlying communication network infrastructure. Hence, a brief information about neurons is given in the following subsection.

2.3 Neurons

Among the other intra-body molecular communication nanonetworks, the nervous system is the most complex and advanced system [1]. The nervous system, formed by billions of neurons, coordinates the somatic and autonomic behaviors of human body. A typical neuron is composed of dendrites, soma (cell body), axon and axon terminals. Perceived information is transduced into pulse packets, i.e. spikes by neurons. The spikes generated by a neuron propagate along the neurons (neural medium) in two different forms, namely electrical and chemical [26]. Stimulated dendrites trigger an electrical discharge that leads generation of an electrical pulse called as action potential [27]. The spike propagates along the axon part of a neuron in the form of electrical pulse. Spikes are stereotyped events and are generated according to the all-or-none principle that states that if a stimulus is sufficiently strong then the spike is generated at the maximum strength. Before the spike transferred to the next neuron, it is converted to chemical form that is known as synaptic transduction [28]. When the axon terminal is stimulated by the action potential, vesicles that contain neurotransmitter chemicals are released to the intercellular region. Neurotransmitter chemicals then bind to the receptors located in the membrane of the next neuron to activate the generation of spike. However, in order to fire the subsequent action potential, a neuron has to wait a time period (typically just a few milliseconds) which is called as Absolute Refractory Period (ARP) [29]. The structure of a neuron and the propagation forms of spikes are illustrated in Figure 2.3.

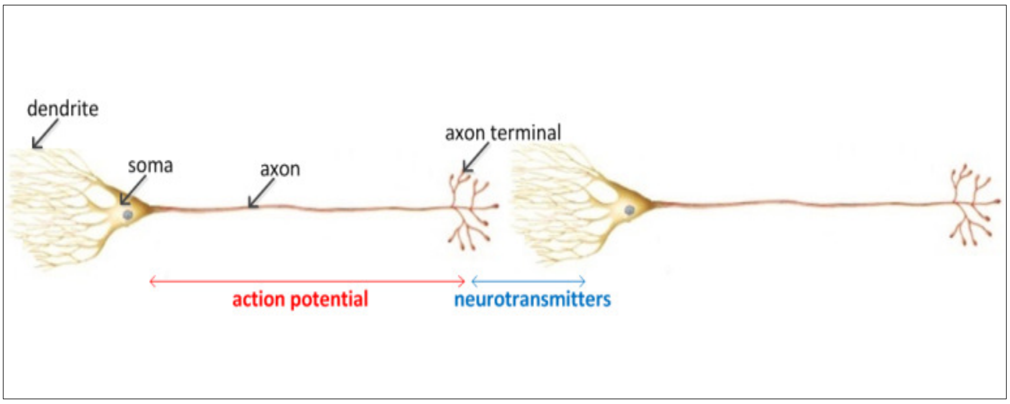

Figure 2.3 : Neuron structure and propagation forms of spikes.

Since neural communication is a suitable option for long-range communication in nanonetworks [19], there is a growing interest in the nanonetworking research community to explore neurons [30,31]. In [32], the electrical properties of neurons such as preferred frequencies, resonance occurrence and the effects of different excitation signals are analyzed by simulations. A conceptual nanoscale stimulator device called synaptic nanomachine (SnM) and an equivalent neuron-nanomachine model (EqNN) are introduced in [33] and the interactions between SnM and EqNN are investigated by statistical methods. In [34], the RF-induced effects on the neural activity are described and the potential strategies for the treatment of neurodegenerative diseases based on RF exposure are presented. In [35], a theoretical physical channel model is introduced for the communication between an input and an output neuron and this model is analyzed based on the error probability and delay. Besides, Galluccio et al. [29] defined the phases of the communication between the neurons as sequences of blocks and each of the phases are characterized by the transfer functions, gain and delay while considering the operational frequency of neurons. Despite the fact that the main purpose of the neurotransmitter chemicals is to fire an action potential at the next neuron, some neurotransmitter chemicals are inhibitory which suppress neural firing. By using excitatory and inhibitory neurotransmitter chemicals, Balasubramaniam et al. provided an interface to initiate and suppress the spikes in a neural nanonetwork in order to realize the communication between nanomachines [26]. In [36], a Moore machine which reflects the complete biological cycle of neuro-spike communication channel is developed and a basic nano computer model is devised to perform communication between two neurons based on the proposed Moore machine.

2.4 Somatosensory System

The nervous system can be categorized into two main parts, the central nervous system (CNS), and the peripheral nervous system (PNS). All the behaviors of our body are mediated by the CNS that includes the brain and the spinal cord. According to the way of the spike transmission, PNS can be classified as peripheral sensory nervous system (PSNS) and peripheral motor nervous system (PMNS). The information perceived by the receptor neurons (RNs) is carried to CNS by the PSNS. Received information is processed by the CNS and generated signals are delivered to the corresponding body parts by the PMNS to take appropriate actions.

In this thesis, we focused on the somatosensory system that is a subnetwork of the PSNS. The somatosensory system processes information about four major somatic sensations:

1. discriminative touch (recognizing the size, shape, and texture of objects and their movement across the skin),
2. proprioception (the position and movement of our body parts),
3. nociception (pain or itch caused by tissue damage or chemical irritation) and,
4. temperature (warmth and cold).

Despite the diversity of sensations, sensory information is coded with four common attributes, modality, intensity, duration, and location [2]. Sensations happen when an RN is stimulated by the external events. Somatosensory system has different classes of receptors such as photoreceptor, mechanoreceptor, thermoreceptor, and chemoreceptor. The modality of the sensation is perceived by the receptor types. Each receptor class holds various receptor types that react to a limited range of stimulus energies. For the somatosensory system, touch sense is determined via mechanoreceptor class which includes Meissner corpuscle, Merkel cells, Pacinian corpuscle, and Ruffini endings [2,38]. The sensed stimulus is converted into spike trains by these receptors. Intensity of the stimulus is pertinent to the amplitude of the energy received by the receptors. Duration of the stimulus is expressed as the beginning and end time of the stimulus and the variation in the sensed energy level. Hence, RNs code the intensity and the time course of the stimulus by the spike firing patterns. RNs are distributed topographically throughout our body and the resolution of this distribution varies relevant to the part of the body. The RN is the first node in the somatosensory system. Perceived sensory information is conveyed via second and higher order neurons in the spinal cord to the somatosensory cortex. Brain, as the main processing unit has a precise map for perceived information to preserve the spatial relation of the receptors. Therefore, the location of the sensed stimulus is determined by the pathway that transports the spikes, not by the spike itself.

The ICT literature has very few studies about the somatosensory system. In [37], a communication channel model of somatosensory system with special interest in body discriminative touch and proprioception information is presented and an equivalent Moore machine is developed to represent the internal working principles of this channel. Authors also present a linear algorithm that depicts all the processes happening in the signaling pathway and an automaton-based nanomachine is designed.

Each receptor class of the somatosensory system includes various receptor types that generate different spike patterns according to the received stimulus energies. In literature, Poisson distribution is frequently used to model the spike trains generated by neurons [38]. It well captures the statistical properties of the real neural spike trains. As an example, when probes of different diameters are pressed upon the human skin with constant force, the firing rate of individual Merkel disk receptors signals the probe diameter. The firing rate increases as the probe diameter decreases and Merkel disk receptors exhibit spike firing rates similar to spike traffic patterns generated by Poisson distribution [2]. However, it is important to note that the ARP of real neurons causes the inter-spike interval distribution to diverge from an exponential distribution for small intervals. Besides that, some of the spike trains generated by the mechanoreceptors show bursty traffic patterns. For example, pressure on a receptor neuron with the tip of a needle that punctures the skin and pinching the skin with serrated forceps produces bursty spike traffic [2,40]. Pareto distribution which exhibits the burstiness property is one of the most commonly used distribution in modeling self-similar network traffic and related behavior.

For the above-mentioned reasons, in our studies, we used different distributions such as Bernoulli, Poisson, and Pareto distributions to model the generation of spike firing patterns. We also employed Neural Simulation Tool (NEST) [40] to reflect the electrical and chemical aspects of the neuro-spike communication channel and to evaluate the performance analysis of our studies in a realistic manner [31]. We also applied Gaussian noise factor to simulation environment to model the axonal and synaptic noise in the neuro-spike communication channel.

2.5 Neural Interfaces

The proposed techniques in this thesis utilizes some nanoelectronic devises (the neural delay box, the multiplexer and the demultiplexer unit). These devices require the received spikes to be converted to the electronic domain. This conversion can be done with neural interfaces that can detect an incoming spike and stimulate the generation of a new spike. In this subsection, we briefly reviewed the competitive methods in literature for interfacing neurons.

In order to overcome the defects of neural functions, neural interfaces are used to enable communication links between the nervous system and the man-made modules via detecting and/or triggering the generation of spikes in living organisms [41]. Over the past several decades, many technologies based on micropipette electrodes, multielectrode arrays (MEAs), nano wire field effect transistor arrays (NW FETs), carbon nano fibers (CNFs), and carbon nano tubes (CNTs) are used to develop the neural interfaces. The brief information of these techniques is given below.

2.5.1 Micropipette electrodes

Micropipette electrode is the conventional method for measuring the action potential activity of a neuron. By the help of micropipette electrodes, intracellular and extracellular potentials can be recorded and the generation of a spike can be triggered. This method has relatively good spatial resolution, about 100μm per pipette and inter-electrode spacing is about 10 μm but difficult to multiplex [42,43].

2.5.2 Multielectrode arrays

MEAs are micro scale fabricated structures that connect neurons to electronic circuitry. Neurons of planar network systems can be recorded and stimulated simultaneously using MEAs [44]. Despite the fact that they allow recording up to several months, this technique prohibits single cell level detection and stimulation due to its large intra electrode spacing (100-500μm), and exhibits low spatial resolution [45].

2.5.3 Nano wire field effect transistor arrays

Semiconductor NW FET arrays that have been developed in past decade became prominent with the unique chemical and electronic properties among the other techniques [46]. By integrating the arrays of NW FET with the axons and the dendrites of neurons, it is possible to detect, stimulate and/or inhibit the neural signals with high spatial and temporal resolution [42]. Using NW FET arrays, many research groups achieve successful results via in vitro experiments [42,47].

2.5.4 Carbon nano fibers

The distinguished characteristics of CNFs such as bio-compability, bio-stability, robustness and small size makes them promising candidates for electrical and chemical neural interface development [48]. Vertically aligned carbon nano fibers (VACNFs) are used by many researchers for electrical stimulation and recording the electrical potential simultaneously [49,50]. VACNFs are also used as neural-chemical interfaces for bidirectional communication [51]. Besides, single carbon fiber microelectrodes can be used for detecting the neural signals in chemical form in a single site [51,52].

2.5.5 Carbon nano tubes

CNTs, another novel product of nanotechnology, have received great attention by the researchers for interfacing neurons. As well as their salient chemical and electrical properties, neural growth can also be directed over CNTs [53]. Mazzatenta et al. developed an interface with single walled nanotubes (SWNTs) and showed that neural signaling can be triggered over healthy hippocampal neurons with electrical stimulation via these interfaces [54].

Using the information given in the above references, we composed Table 2.1 to compare the characteristics of the neural interface methods. When sensitivity, signal to noise ratio (SNR), spatial and temporal resolution are taken into consideration, NW FET arrays, CNTs, and CNFs are the most appropriate methods that can be used to implement the neural interfaces in the proposed techniques.

Table 2.1 : Characteristics of neural interfaces.

Methods	Sensitivity	SNR	Spatial Resolution	Temporal Resolution
Micropipette	Medium	Medium	High	Low
MEAs	Low	Bad	Low	Low
NW FET Arrays	Very High	Good	High	High
CNTs	Very High	Good	High	High
CNFs	Very High	Good	High	High

2.6 Multiplexing In Communication Networks

In this thesis, we draw an analogy between the transmission medium in communication networks and the signaling pathways of somatosensory system. This analogy is related to the multiplexing concept in communication networks. For the both local and wide area communication networks, the capacity of the transmission medium is actually over the capacity needed for the transmission of one signal. The transmission medium that is an expensive resource can be shared by combining multiple signals into one signal. This process is referred as multiplexing [55]. The capacity of the communication medium is separated into several logical communication channels via multiplexing techniques.

Figure 2.4 [56] depicts the multiplexing function in its basic form. In Figure 2.4.a three stations inefficiently use the dedicated transmission medium. To the contrary, an efficient and inexpensive use of transmission medium is illustrated in Figure 2.4.b. The signals from tree stations are combined by a multiplexer. Demultiplexer accepts the multiplexed signal and separates the signal according to the channel, and delivers them to the appropriate stations [56].

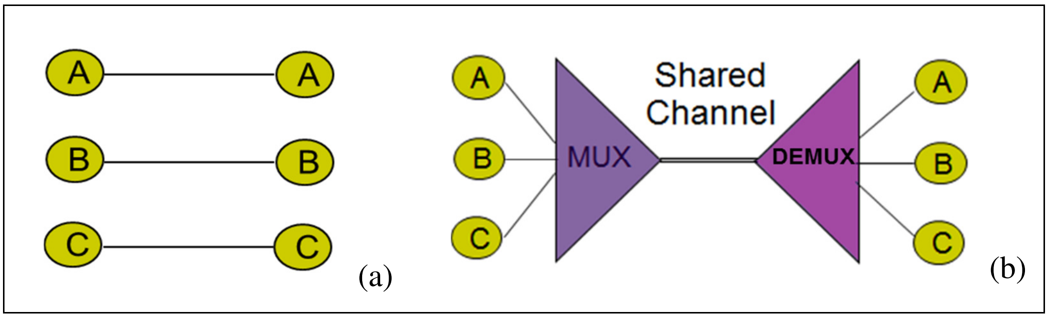

Figure 2.4 : Multiplexing [56] : (a) Users have dedicated and more costly resources (b) Users share a single transmission medium via multiplexing.

Besides, the multiplexing is an efficient way of connecting stations. It is also compulsory when only a single connection is available between two stations. By this approach, we adapted the multiplexing techniques of the conventional communication networks in the following subsections for neural signaling and employed them to overcome the failures in the sensory neural pathways.

2.6.1 Time division multiplexing

In Time Division Multiplexing (TDM), the multiplexed connections share the transmission medium by means of a time period. Each station periodically gain control of the full capacity of the shared transmission medium for a short instance of time i.e. time slot. Multiplexer and demultiplexer devices works synchronously and both of them switch to next channel simultaneously. For example, in Figure 2.5.a each stations generates a signal that produces one unit of data in every *3T* seconds. Generally, transmitted information separated into frames that in turn are divided into equal sized slots. On the other hand, in Figure 2.5.b transmission medium is three times faster and can transmit one unit of data in in every *T* seconds. Please note that, the frame structure of the combined signal consists of three time slots for each station [56]. The combined signal is demultiplexed quite easily with respect to time slots assignment information.

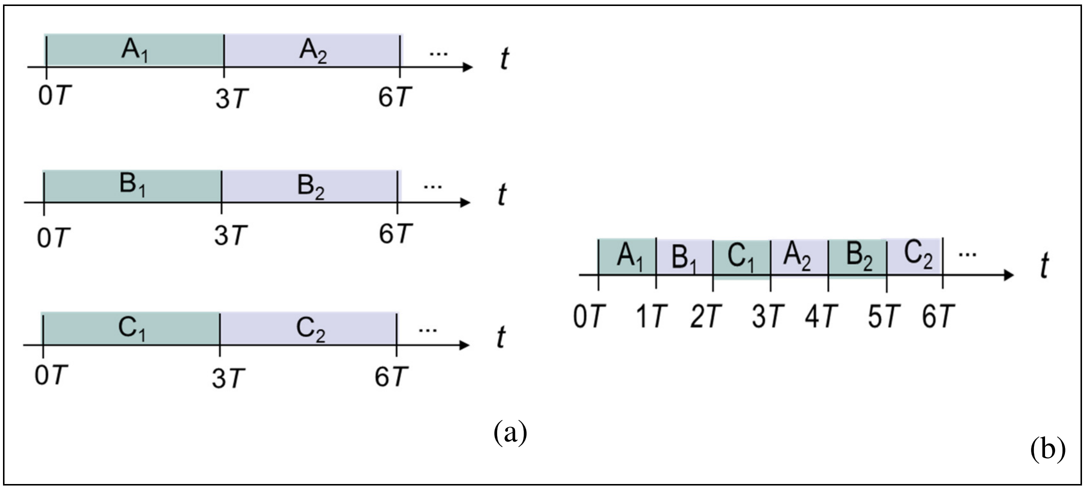

Figure 2.5 : Time Division Multiplexing [56] (a) Each signal generates 1 unit of information in every 3T seconds. (b) Combined signal transmit 1 unit of information in every T seconds.

2.6.2 Statistical multiplexing

Current communication networks support various applications that generate traffic in highly bursty fashion. Bursty traffic mostly has long idle periods and this makes statistical multiplexing (SM) is a good method for cost-effective resource sharing [56]. In the packet switching networks, information is formatted into packets that are variable in size. The packets have a header to identify the source and the destination stations and the data payload (information). SM dynamically allocates transmission medium to each stations on an as-needed basis. This is in contrast to TDM techniques, in which stations that have no information to send also waste a time slot. Statistical multiplexing allocates bandwidth only to the stations that are currently transmitting. Overlapping packet generation times of stations necessity a buffering mechanism for the SM. When simultaneous packets are received, the multiplexer buffers and delays some of the packets while serving the one. Typically, received packets are sent according to first in first out (FIFO) fashion. However, priority mechanism and scheduling of various types are used in multiplexers nowadays. At the other end, demultiplexing is done according to the destination address information in the header of the packet. The concept of SM of data is illustrated in Figure 2.6 [56].

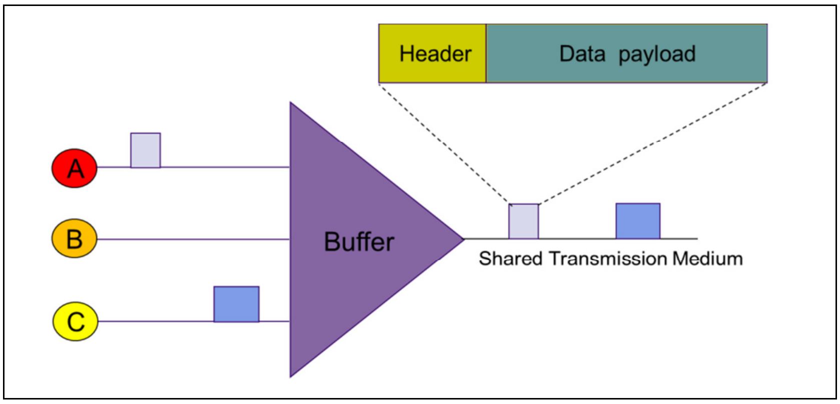

Figure 2.6 : Statistical Multiplexing of data, adapted from [56].

3. EMPLOYING TDMA PROTOCOL IN NEURAL NANONETWORKS IN CASE OF NEURON SPECIFIC FAULTS

Peripheral neuropathy arises from the malfunctioning neurons in the pathway where the signal is carried. In this chapter, we propose neuron specific Time Division Multiple Access (TDMA)/multiplexing and demultiplexing mechanisms to convey the spikes of a receptor neuron (RN) over a neighboring path in case of an irreversible path fault existing in its original path. The multiplexing mechanism depends on Neural Delay Box (NDB) that is composed of a relay unit and a buffering unit. The relay unit can be realized as a nanoelectronic device. The buffering unit can be implemented either via neural delay lines as employed in optical switching systems or via nanoelectronic delay lines i.e. delay flip flops. Demultiplexing is realized by a demultiplexer unit according to the time slot assignment information. Besides, we propose the use of neural interfaces in the NDBs and the demultiplexer unit for detecting and stimulating the generation of spikes. The objective of the proposed mechanisms is to substitute a malfunctioning path, increase the number of spikes delivered and correctly deliver the spikes to the intended part of the somatosensory cortex. We evaluate the performance of the proposed method under various scenarios via simulations. The results demonstrate that significant performance improvement on the successively delivered number of spikes is achievable when the delay lines are employed as neural buffers in NDBs.

The preliminary results of this study are presented in IEEE International Workshop on Molecular and Nanoscale Communications, International Conference on Communications (ICC’12) [5]. The extended version of this work is published in IEEE Transactions on NanoBioscience (SCIE) [6].

3.1 The Proposed TDMA Based Neural Nanonetwork

The interruption of spike propagation in the nervous system due to the malfunctioning neurons in the signaling pathway causes many functional disorders such as multiple sclerosis, Alzheimer and paralysis. The RNs of the somatosensory system perceive the stimulus, convert it into spike trains and convey to the somatosensory cortex via second and higher order neurons in the sensory pathway. Even if the RN senses the stimulus and generates the spike trains, a faulty relaying neuron (inter-neuron) in the signaling pathway interrupts the communication between the RNs and the somatosensory cortex. Thus, a fault in the pathway results in a loss of sense in the relevant part of the human body. We propose that these irreversible impairments can be coped with by conveying the spike trains over a functional neighboring pathway. Our aim is to form a neuron specific TDMA based neural nanonetwork in order to convey the spikes of an RN over a neighboring path in case of an irreversible path fault exists in its original path. The spikes generated by the RNs are multiplexed and carried through a functional path and demultiplexed according to the assigned time slots of the RNs. After demultiplexing, spikes are delivered to the corresponding part of the somatosensory cortex. Under the light of the information given in Chapter 2.4, sensory data is coded with following three properties, the number of spikes generated, the inter-spike intervals, and the pathway that the spikes are carried through. As a consequence, spike patterns and the pathway that the spike travels defines the meaning of the perceived sensory information. Accordingly, if we can convey the spike trains of RN via an alternative path and deliver the spikes to the intended destination in the somatosensory cortex, we can achieve to generate correct sensation. By using this approach, we propose a neuron specific TDMA protocol to share the functional neural pathway between more than one RN. We devised NDB and the demultiplexer unit to implement the proposed mechanism. Both of these devices use neural interfaces. As explained in Chapter 2.5, neural interfaces can record an incoming spike and have the capability to stimulate the generation of a new spike. NDBs are used for the multiplexing the sensory information of RNs. An NDB is composed of a relay unit and a buffering unit. Here, the spikes are transmitted at the time slots assigned to them. Buffering is required to resolve the contention when successive packets destined to the same outlet are received. In order to prevent the loss of the spikes that arrive at the unassigned time slots, we propose two delay based buffering mechanisms to be employed in NDBs. We followed two approaches to realize the buffering unit in an NDB. The first approach is based on the *neural delay lines* concept which is inspired by the use of delay lines in the optical switching systems and the latter utilizes nano electronic delay lines for buffering. In the first option, ordinary neurons are used to form neural delay lines analogous to the fiber delay lines (FDLs) in optical domain. Since the capability of storing packets has not been realized for optical switching systems, FDL is the only way to delay the colliding optical packets for the required time slots [3,4]. Advances in nanotechnology enable the development of nanoelectronic devices in many application domains such as medical diagnosis, nanocomputers and nanosensors. After the spikes are converted to electronic domain via neural interfaces, they can be easily delayed for the required time slots by using nanoshift registers made of nano delay flip-flops. Both of the buffering approaches also need neural interfaces for the transfer of a spike to an NDB. Demultiplexer unit is used just before the signal delivered to the somatosensory cortex in order to convey the spikes to the correct destinations.

The scenario of alternating two faulty sensory pathways to a functional path is illustrated in Figure 3.1. This scenario is based on the dorsal column-medial lemniscal pathway where tactile sensation and limb proprioception are conveyed to somatosensory cortex [2,38]. The malfunctioning sensory pathways are represented as dashed red lines and continuous blue line symbolizes the functional sensory pathway. As it can be seen in Figure 3.1, the TDMA based multiplexing is done after the spikes are generated by RNs. The multiplexed spikes are conveyed through the functional pathway and demultiplexing is carried out just before the spikes conveyed to the relevant part of the somatosensory cortex. Following subsections give the detailed information about the proposed protocol.

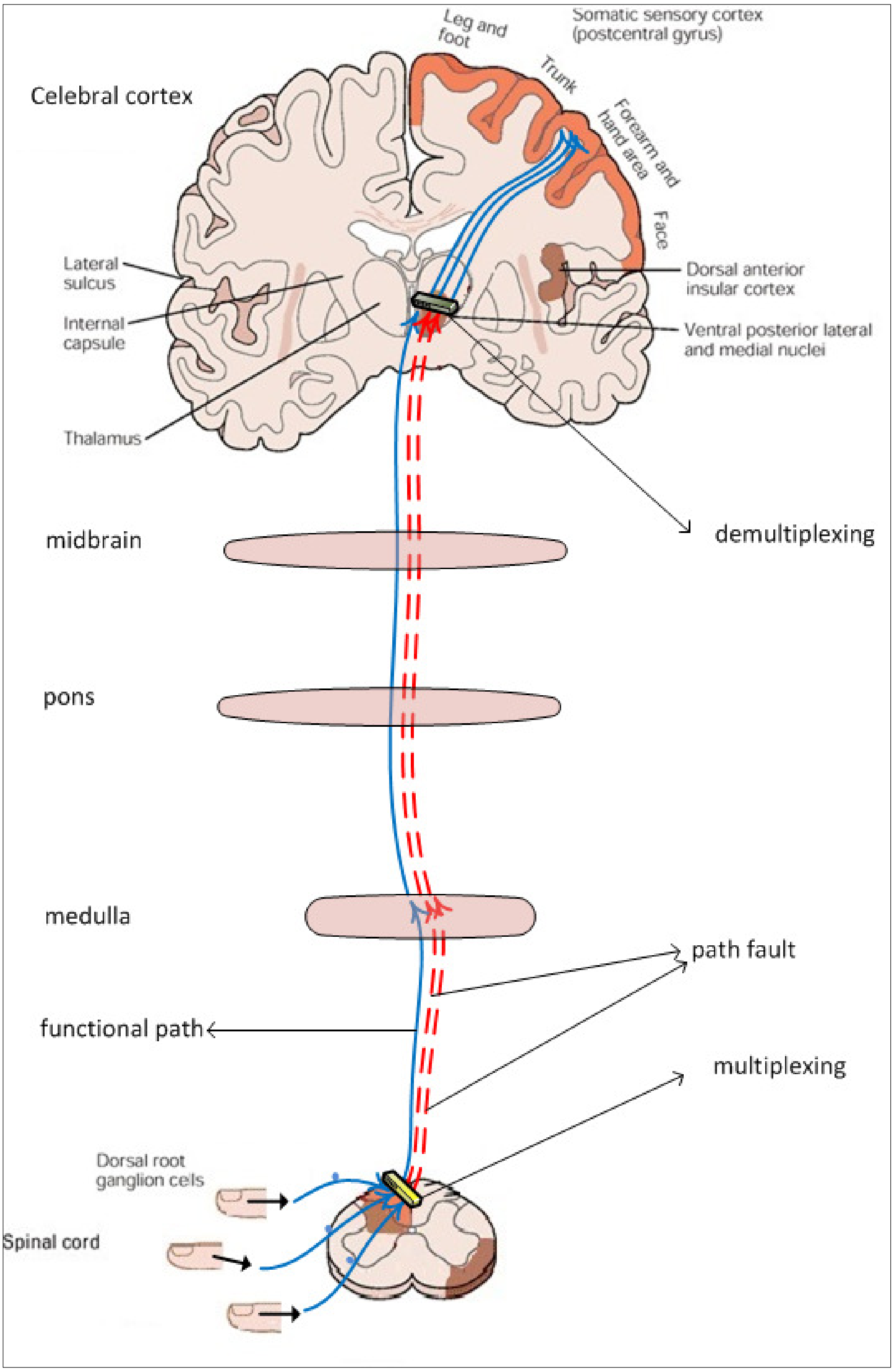

Figure 3.1 : Sensory pathway alternation, adapted from [2].

3.2 Multiplexing

Consider a neural nanonetwork that is composed of three RNs that share a common medium in order to transmit their spikes to the corresponding part of the somatosensory cortex. When any of the RNs stimulated, it generates spikes. Such a neural nanonetwork system is shown in Figure 3.2. This system which enables the use of a common medium cannot be used because of the destination address of spikes cannot be determined. However, when multiple spikes are generated simultaneously by the multiple RNs, only one spike is transferred through the shared neurons. Hence, the other spikes will be lost and the perceived sensation cannot be processed at the somatosensory cortex.

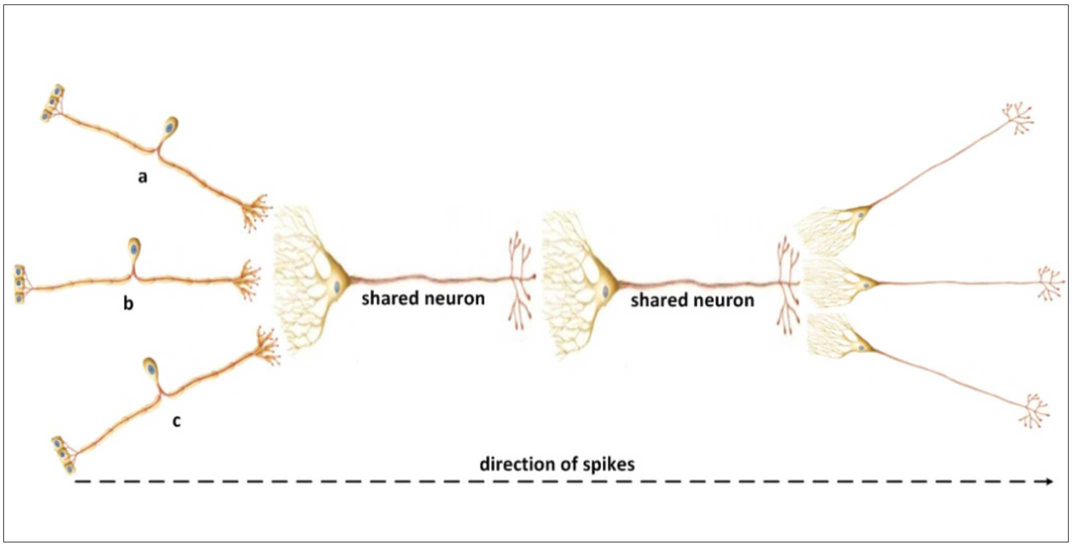

Figure 3.2 : Neural nanonetwork system using a common transmission medium.

In order to achieve a better performance by using a common transmission medium, a TDMA based approach could be employed. When such a system is used the RNs shown in Figure 3.3, will have assigned time slots on the shared medium. As stated in Chapter 2.3, it is impossible to fire a subsequent spike before ARP is completed. Therefore, for the successful generation of received spikes the time slot duration is taken greater than the ARP of the RNs. Hence, the transmitting RNs which are active (have spikes to transfer) in their assigned time slots will transmit all spikes successfully. As illustrated in Figure 3.3, the proposed TDMA based neural nanonetwork system can be realized by the use of NDBs connecting transmitting RNs to the shared medium.

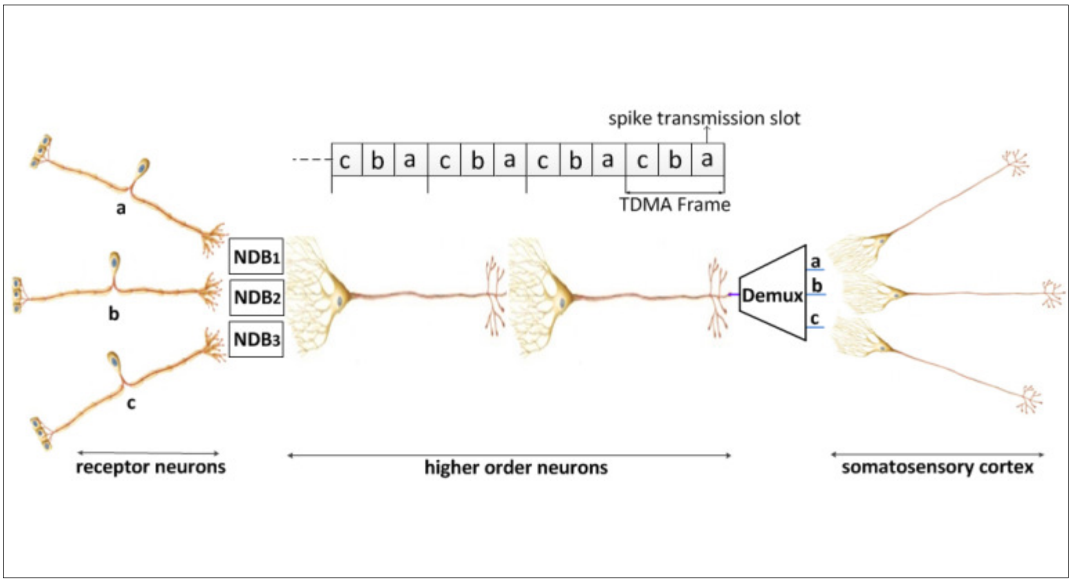

Figure 3.3 : Proposed TDMA based neural nanonetwork.

We assume that all the neurons that form the network have the same transmission capacity. Neurons which have the same properties such as axonal length can be grown in vitro to assure same transmission capacity. Cell culture medium conditions, in which the cells are incubated, could be tailored to control the neuron growth. Guided neural growth can be achieved by using different patterning techniques such as polylysine patterning [42]. However, we assume that the transmitting neurons are not active all the time. Here, we also assume that an RN generates spikes covering 1/3 of the total transmission capacity of a neuron. If the number of RNs is n then each source RN generates the $1/n$ of the total transmission capacity of the system. Otherwise, losing some of the spikes at the multiplexing stage will be inevitable which is still possible. For the network topology shown in Figure 3.3, the RNs a, b, and c are assigned to the specific time slots to transmit their spikes. If multiple spikes arrive simultaneously, contention occurs. Moreover, when a transmitting neuron is active in a time slot which is not assigned to it, the spike will not be transferred. Hence, we observe that a time slot assignment for each single transmitter RN in the system is not sufficient.

As stated before, the proposed TDMA based neural nanonetwork system could be realized by the use of NDBs. An NDB consists of a relay unit and a buffering unit. The spikes that arrive at the unassigned time slots will be forwarded to buffering unit by the relay unit. The relay unit can be thought as a switch and can be realized as a nanoelectronic device. Synchronization of the NDBs can be easily maintained by the relay units using a common clock signal. As a nanoelectronic device, the assigned time slot of the transmitter RN can be set to its relay node. The relay unit detects the incoming spike via neural interface in the inlet compartment. Then, it forwards the spike directly to the shared medium if it is arrived at the assigned time slot. If not, the relay unit relays the spike to the proper buffer and the spike is delayed until the next assigned time slot. Afterward, the spike is generated in the shared medium via the neural interface in the corresponding outlet. For the implementation of the buffering unit, we propose two buffering mechanisms which utilizes neural delay lines as in optical switching systems [3,4] and nanoelectronic delay lines which exploits nano delay flip flops. The following two subsections explain these mechanisms, respectively.

3.3 Buffering With Neural Delay Lines

Internal structure of an NDB that utilizes neural delay lines for buffering is illustrated in Figure 3.4. Neural delay lines are composed of the same type of neurons in the network. An NDB for three-source RNs system has one inlet and three outlets. The inlet is connected to the transmitting neuron of the corresponding RNs. The outlets are connected to the shared medium, one-neural-delay-line, and two-neural-delay-line, respectively, since a spike either arrives at the assigned slot or at one of the unassigned slots. The inlet and outlet connections are realized by the use of neural interfaces. An incoming spike is detected as a change in the electrical potential by the neural interface and forwarded to the inlet compartment of the relay unit. If this variation in the electrical potential is above a predetermined threshold, the relay unit figures out that a spike is received. Thereafter, the relay unit triggers the corresponding neural interface for the generation of the spike according to the time slot information of the received signal.

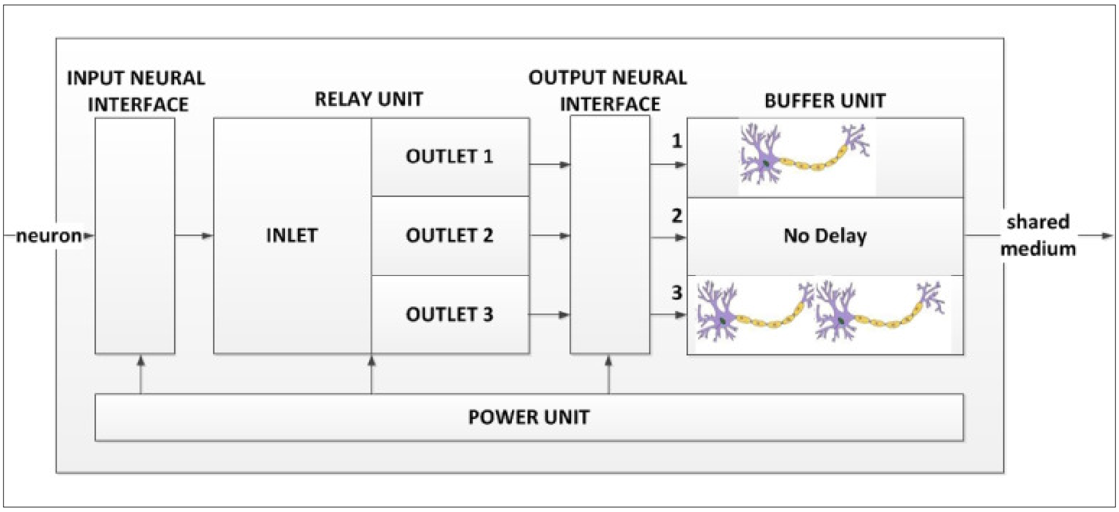

Figure 3.4 : Internal structure of NDB with neural delay lines.

Let's show the implementation of the proposed technique having three source RNs. Spikes are relayed to the appropriate neural delay lines according to the slots that they arrive. If a spike arrives at the assigned slot, the relay unit transmits it directly to the shared medium. If a spike is one slot late, it is transmitted to the two-neural-delay-line. Otherwise, (meaning that the spike arrives two slots later) it is transmitted to the one-neural-delay-line. For *n* sources RNs network, there will be *n-1* neural delay lines in the NDBs. The working logic of this mechanism is shown as a flow chart in Figure 3.5.

Researches on the transmission speed of the neuron signaling demonstrate that speed of the spikes varies according to the density of the myelin sheath which is the dielectric material around the axon of a neuron. The transmission speed of a spike can reach up to 120 m/s in a densely myelinated axon whereas the transmission speed remains only 1 m/s in a poorly myelinated axon [57]. This property of neurons can be used to obtain required delay time. Instead of using multiple similar neurons to form a neural delay line, a single hop neural delay line can be formed by only one neuron with a corresponding myelin sheath density needed to maintain appropriate delay.

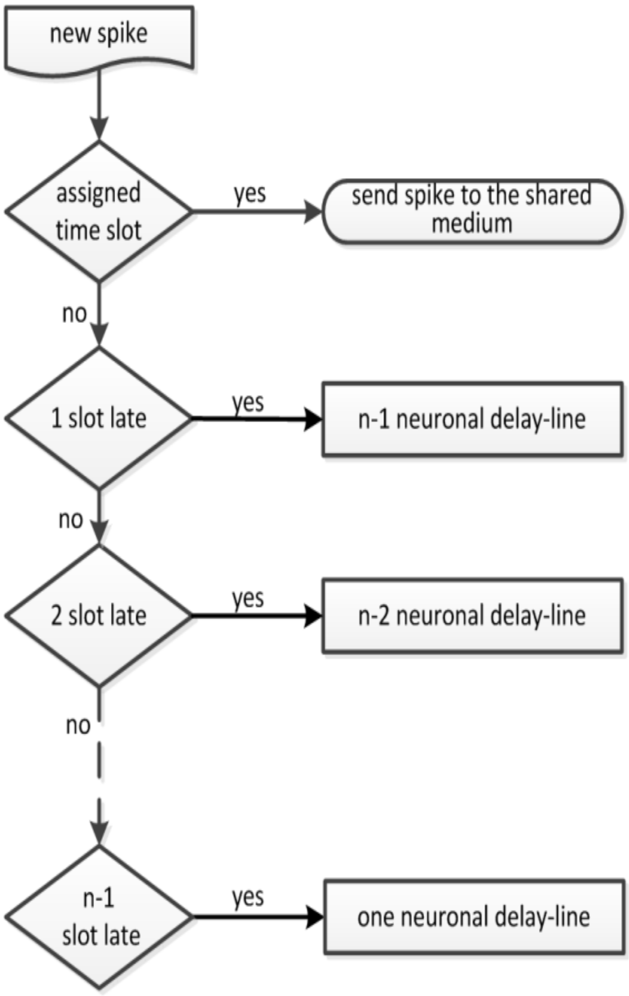

Figure 3.5 : Flow chart employed by the relay unit.

3.4 Buffering With Nanoelectronic Delay Lines

After the conversion of the spike into the electrical domain via neural interface, buffering can easily be implemented via nanoelectronic circuits [58]. Nano scale shift registers made up of delay flip flops can be viewed as memory or a delay line. An NDB that utilizes nano scale shift registers for a three source RNs system is illustrated in Figure 3.6. The relay unit fulfills the same task as stated in the previous buffering mechanism. Shifting the spikes in the time domain is maintained by the nanoelectronic delay lines. The relay unit detects the spikes via neural interface. When a spike detected at the assigned time slot of the RN, the relay unit forwards it directly to the shared medium. If the spike arrives at the unassigned time slots, it will be forwarded to appropriate nano shift registers by the relay unit in NDBs. When the spike is delayed until the next assigned time slot, the shared medium is stimulated via output neural interface for the spike generation. Thus, the potentially colliding spikes are aligned in the time domain and more spikes are delivered to the somatosensory cortex.

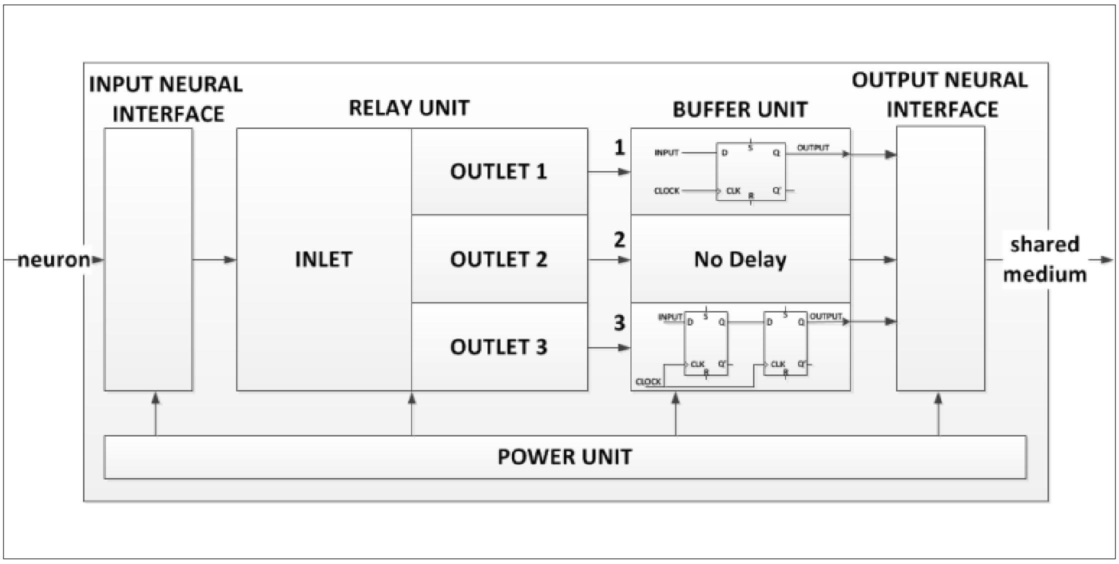

Figure 3.6 : Internal structure of NDB with delay flips flops.

In accordance with the above-mentioned information, conceptual diagram of an NDB for a generic source RN system is illustrated in Figure 3.7.

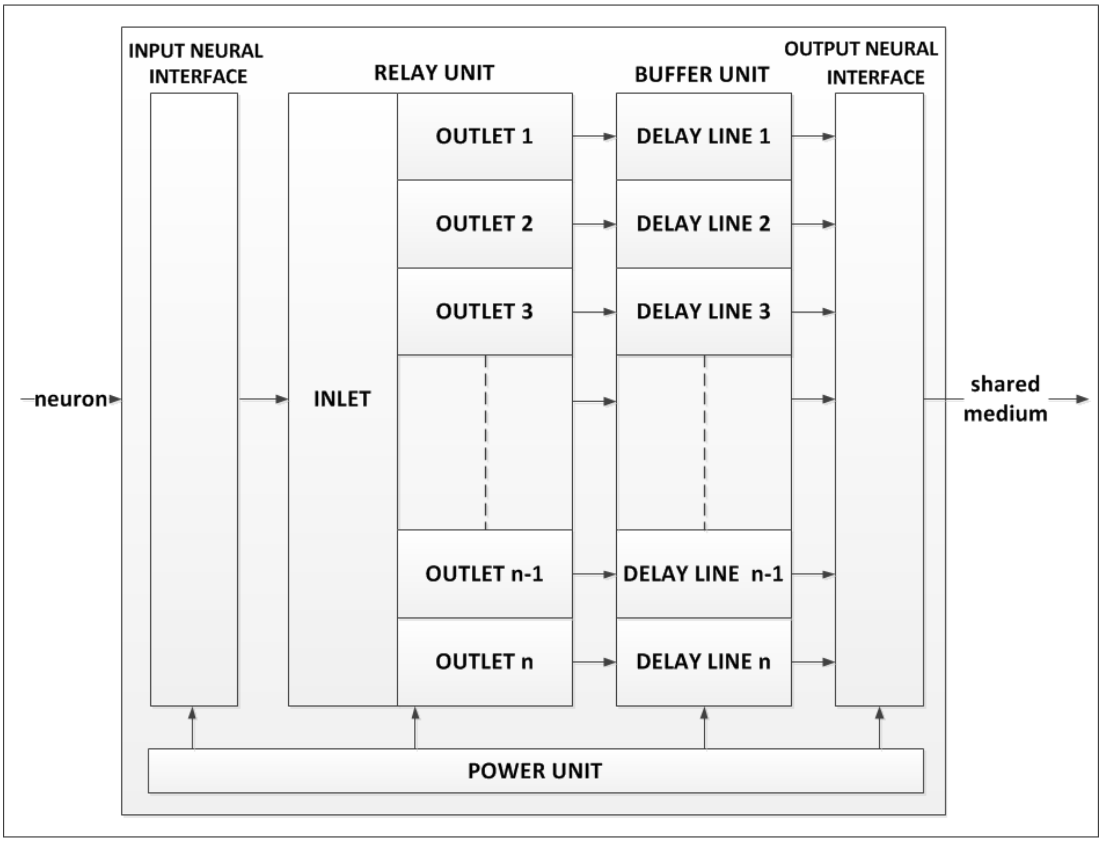

Figure 3.7 : Conceptual diagram of an NDB.

3.5 DeMultiplexing

After the spikes of RNs are multiplexed and carried through a functional neighboring pathway, they should be demultiplexed before delivered to the somatosensory cortex. The demultiplexer unit that is a nanoelectronic device does this process. The demultiplexer unit also uses neural interfaces at the input and at the output for the conversion of the spikes into electronic domain and vise versa. The inlet of the demultiplexer unit is connected to the shared medium. The outlets of the demultiplexer unit are connected to the inter-neurons of the sensory pathway that ends in the somatosensory cortex. Here, the spikes of RNs are already aligned to their assigned time slots by delay lines. Hence, demultiplexing can be done quite easily with respect to their time slots. After demultiplexing, spikes are delivered to the corresponding part of the somatosensory cortex. If the spike firing patterns generated by the RNs can be preserved and delivered to the corresponding part of the somatosensory cortex, the correct sensation can be sensed across the perceived information.

3.6 Performance Analysis

The performance of the proposed multiplexing mechanism is mainly based on the generation of spikes in the unused assigned time slots. If a spike of an RN is detected in an unassigned time slot by the NDBs, the spike is delayed until the next assigned time slot of the related RN. Therefore, we analytically modeled the performance of an outgoing slot $P(S)$ as follows:

$$P(S) = 1 - \left(P(\bar{X})\right)^n \tag{3.1}$$

where $P(\bar{X})$ is the probability of an incoming slot being idle and n is the number of time slots (also the number of the RNs). We used Bernoulli distribution to model the generation of spike traffic and repeated our experiment according with various success rates in order to compare with the results of analytical studies. The analytical results and the simulation results are consistent with each other and they are given in Table 3.1.

Table 3.1 : Performance of the TDMA based multiplexing technique under Bernoulli traffic.

Arrival Rate / RN	*3-RNs System*	*4-RNs System*	*5-RNs System*
0.20	0.49	0.59	0.67
0.25	0.58	0.68	0.76
0.30	0.66	0.76	0.83
0.33	0.71	0.80	0.87

In our studies, we employ Neural Simulation Tool (NEST) [40] in order to reflect the electrical and chemical aspects of the neural communication channel. For the evaluation of a realistic performance analysis of the proposed system, we also applied Gaussian noise factor to simulation environment to model the axonal and synaptic noise in the neuro-spike communication channel. The simulation setup is presented in Appendix A. Except stated otherwise; spikes are generated by source RNs according to the Poisson distribution with various mean arrival rates. We evaluate the percentage of the successfully transmitted spikes for the total of 3000 incoming spikes. In the related literature, the upper limit on the firing rate of neurons is defined about 1200 spikes/s [2]. Therefore, the capacity of the proposed system is assumed as 1200 spikes/s.

In the proposed scheme, delay lines are used for buffering. We compare the results of this method with a TDMA based multiplexing method without buffering ability that is called as "TDMA without delay lines". The TDMA without delay lines method can only relay the spikes that are generated in the assigned time slots of the RNs to the shared functional pathway, otherwise spikes are dropped.

Figure 3.8 illustrates the performance of the system under the best and the worst cases for the various mean arrival rates when the number of source RNs in the network is equal to three. For the best-case analysis, every spike is generated at the assigned time slots of the transmitting RN. In this case, 94% of all spikes are successfully transmitted to the intended destination. As shown in Figure 3.8, neural channel dynamics and the Gaussian noise applied to simulation environment affects successful delivery of all the spikes. For the worst-case analysis, all of the spikes generated by a specific source RN arrive continuously in the consecutive time slots (in the assigned and unassigned ones). Under the best and the worst-case scenarios, unfortunately delay lines do not have any effect on the performance of the system.

However, if the spikes arrive randomly at the assigned/unassigned time slots, we observe the effect of delay lines. The performance of the multiplexed system with/without delay lines for arrival rate λ=200, λ=300 and λ=400 spikes/s are also given in Figure 3.8. The decrease in λ values results in the increase in the inter-arrival times of the spikes. When the inter-arrival times of the spikes are sparse, it is more probable for a spike that is generated in an unassigned time slot to find the shared medium idle in the next assigned time slot. Hence, the spike arrives at the unassigned time slot successively shifted to the next assigned time slot by using buffering capability of the NDBs. For the TDMA without delay lines method, only the spikes that are generated in the assigned time slots can be relayed and this causes nearly fixed performance independent from the variation in the arrival rates. It can easily be seen in Figure 3.8, the performance of the proposed scheme is enhanced significantly as the inter-arrival times of the spikes get longer.

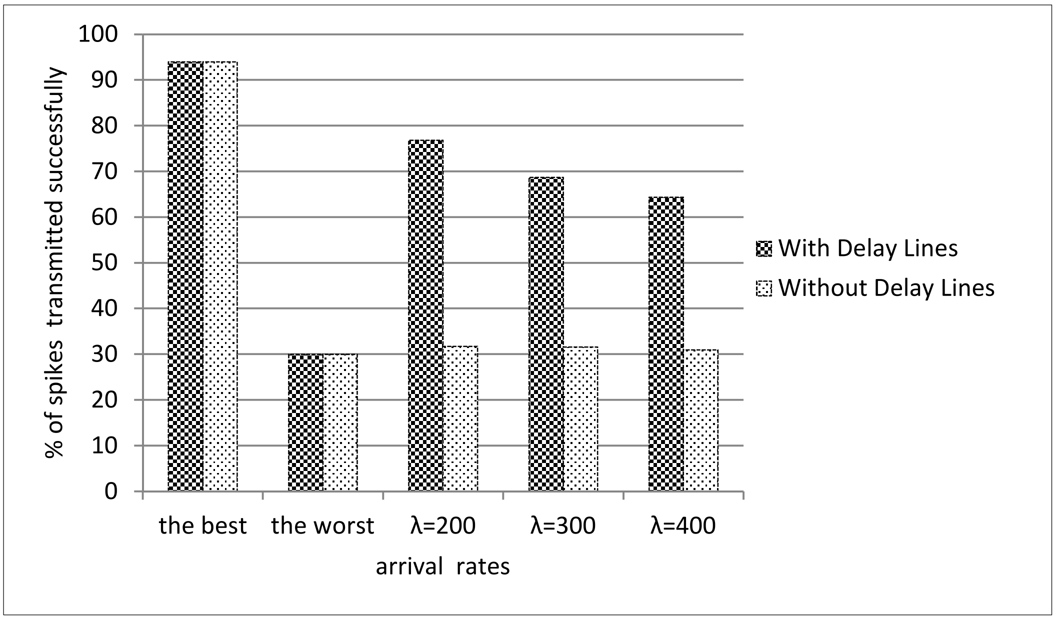

Figure 3.8 : Performance of the TDMA based multiplexing technique with/without neural delay lines for n=3.

In Figure 3.9, we show the effects of variation in the number of source RNs on the performance of the proposed scheme. As we assumed the capacity of the system 1200 spikes/s, the results are given for the mean arrival rates of λ=400, λ=300 and λ=240 spikes/s, and the number of source RNs in the network is equal to 3, 4 and 5, respectively. Although the total arrival rate is the same for all three networks, the proposed scheme exhibits a better performance for the small sized source RN networks. For the greater number of source RNs, the probability of a spike of a source RN to be generated in an assigned time slot gets lower. Therefore, small sized source RN networks exhibit a better performance than the greater number of source RNs networks.

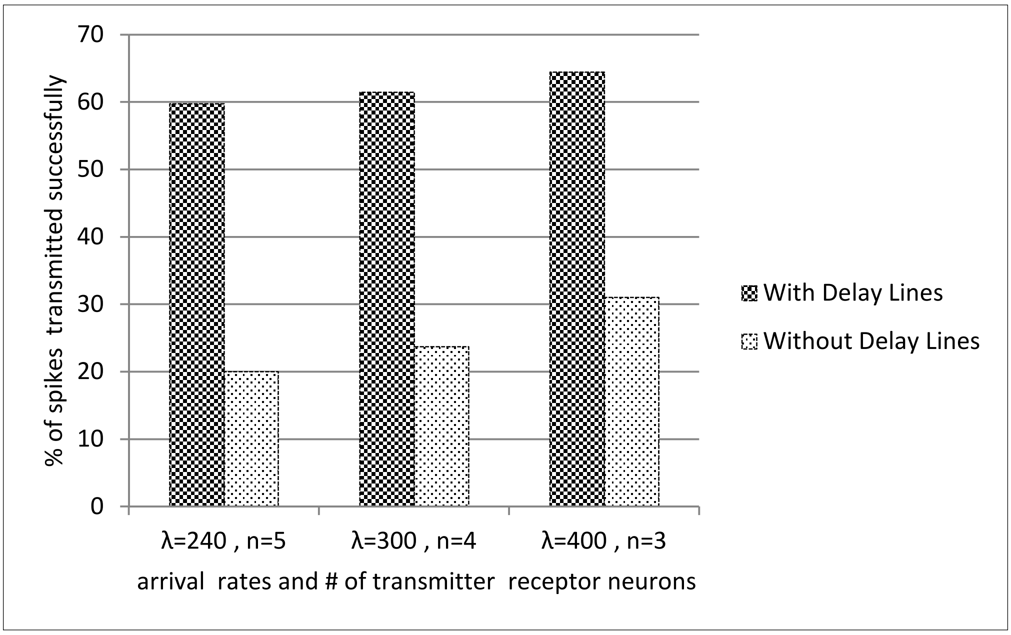

Figure 3.9 : Performance of the TDMA based multiplexing technique with/without delay lines for various RNs and various Poisson arrival rates (λ) are employed.

For the system given in Figure 3.3, the response of the neuron just after the NDBs during the first 350 ms of the simulated time is shown in Figure 3.10. Whenever the membrane potential of the neuron reaches the firing threshold potential at -55 mV, because of the incoming Poisson spike trains, the neuron spikes and the membrane potential is reset to -70 mV that is the reset potential.

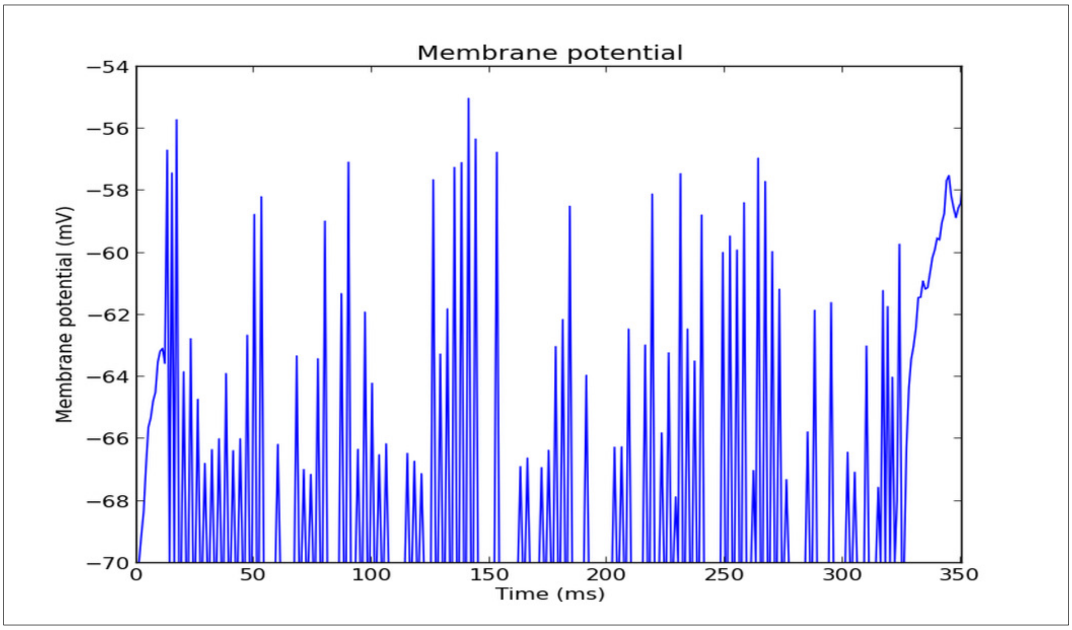

Figure 3.10 : Membrane potential of the RN in response to spike events.

We also study the performance of the proposed technique under the Pareto distribution considering the spike arrival pattern which is similar to the spike generation patterns of mechanoreceptors [2,40]. As we know, Pareto distribution is employed to generate self-similar sequences [59]. Figure 3.11 illustrates the performance of the two systems when various shape parameters (α) are employed. When the shape parameter value increases, inter-arrival times of the spikes decreases. This decrease results in generation of bursty spike traffic. As it can be seen in the Figure 3.11, when low α values are employed, the performance of the proposed system becomes significantly better than the system without delay lines. However, as the higher values of α are employed, the spike traffic becomes bursty and the multiple spikes arriving at the consecutive unassigned time slots cannot be shifted to the next assigned time slot and lost. Hence, delay lines do not have any impact on the performance of the system and the performance of proposed system converges to the worst-case performance.

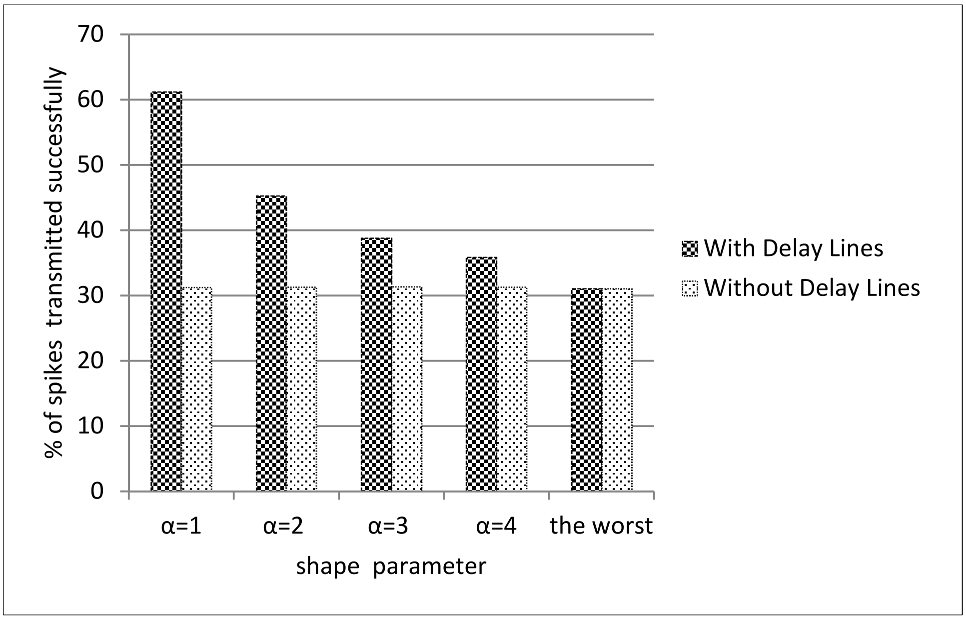

Figure 3.11 : The impact of the shape parameter, Pareto Distribution, to the performance of the TDMA based multiplexing technique with/without neural delay lines for n=3.

We also observe the effect of number of transmitter RNs on the performance of the proposed system when Pareto distribution is used to generate spikes. Figure 3.12 shows the performance when the number of transmitting RNs is equal to 3, 4, and 5 while keeping $\alpha = 1$. For all three networks, each RN generates the same amount of spike traffic. As the number of transmitting RNs increases, total amount of spike traffic over the shared medium is also increases. As a result, the number of spikes which are generated in unassigned time slots are increased. For the proposed system, only one spike that is received in one of the unassigned time slots can be shifted to next assigned time slot. Therefore, when we increase the number of transmitting RNs that generate bursty spike traffic, the performance of the proposed system is decreased as expected.

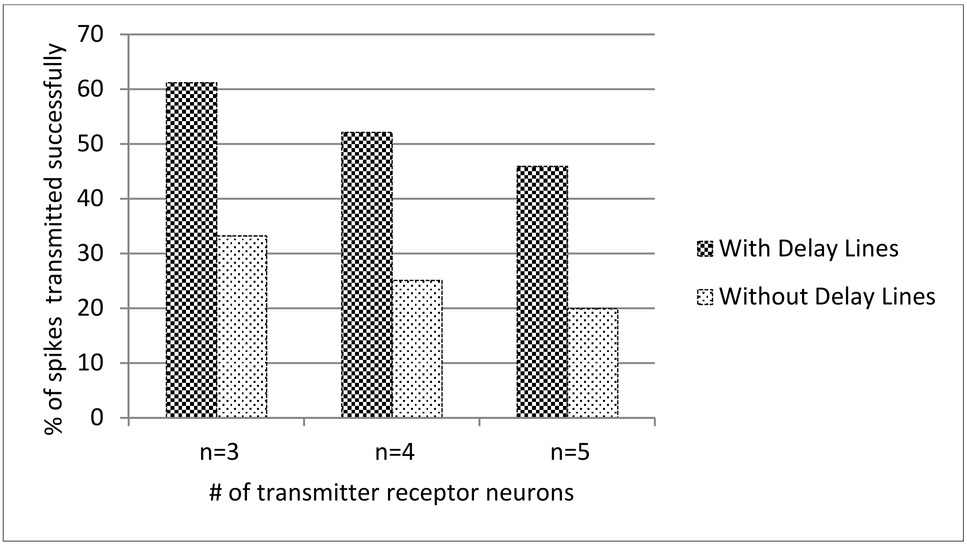

Figure 3.12 : Performance of the TDMA based multiplexing technique with/without delay lines for various RNs ($\alpha = 1$).

In Figure 3.13, the effect of the variation of ARP is shown when the number of source RNs in the network is equal to 3 and the spikes are generated by RNs according to the Poisson distribution with the mean arrival rate λ=300 spikes/s. As stated in Chapter 2.3, when a neuron is in this period, it is impossible to trigger a subsequent spike. When ARP value is increased, neurons could not generate a spike before this period is finished. Therefore, for the bigger values of ARP the number of transmitted spikes decreases and this result in a performance decrease of the proposed scheme.

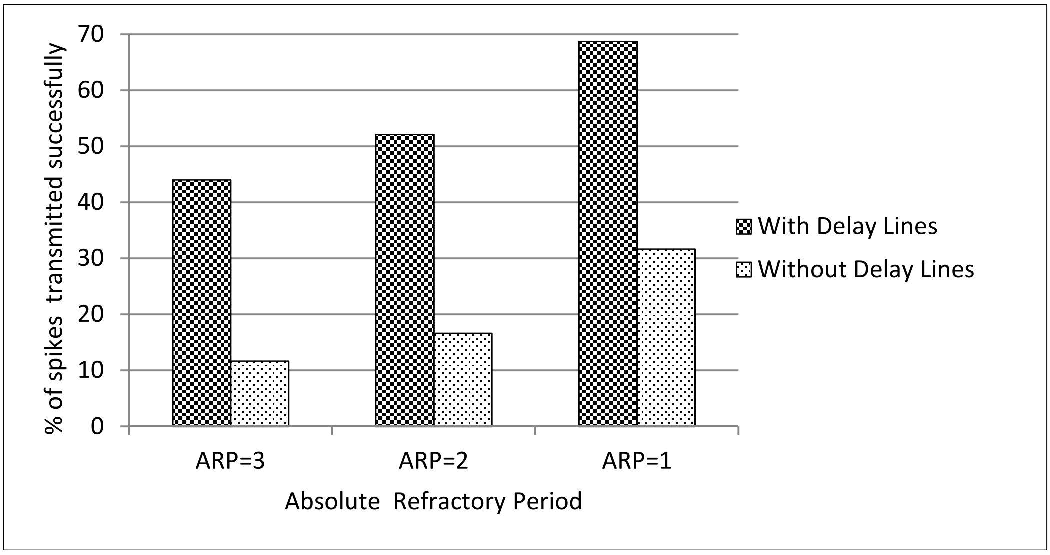

Figure 3.13 : The effect of ARPs to the performance of the TDMA based multiplexing technique with/without neural delay lines.

3.7 Conclusion

In this chapter, we proposed a neuron specific TDMA based protocol for ensuring the communication in neural nanonetworks. For the proposed protocol, the spikes of an RN are conveyed through a functional pathway in case of a path fault exists in its own pathway. For sharing the functional pathway between the RNs, we developed a multiplexing mechanism employing the NDB technique. An NDB is composed of a relay unit and a buffering unit. The relay unit can be realized as a nanoelectronic device. Buffering unit can be implemented either by using neural delay lines as employed in optical switching systems or by using nano scale delay flip flops. We also proposed the use of neural interfaces in the NDBs and the demultiplexer unit for detecting and triggering the generation of the spikes. By using NDBs, the spikes that are transmitted at the unassigned time slots are buffered and transmitted at the consecutive assigned time slot. Thus, the spikes are carried through a functional pathway and they can be easily demultiplexed according to the assigned time slots of RNs, thereafter are delivered to corresponding destination.

The objective of the proposed protocol is twofold. Firstly, conveying the spikes of an RN that has faulty pathway, through a shared functional pathway. The latter is to minimize the number of spikes that can be lost while multiplexing the spikes of RNs in order to feel the correct sensation. Although the proposed technique enables RNs that have faulty pathways to send their spikes to the somatosensory cortex, it also introduces some delay for the spikes that are generated in unassigned time slots due to the buffering phase in NDBs. Since the spikes are already generated by RNs, they are not affected by this delay while they are moving along the sensory pathway. The delay period gains importance in decoding the spikes. Apart from the single RN based sensations, some stimuli i.e. touching the texture of an object activate combination of RNs. In this chapter, we focused on single RN based sensations and the impact of the delay to coordinated sensory information is beyond the scope of this study.

We evaluated the performance of the proposed technique by using spike patterns generated according to Bernoulli, Poisson, and Pareto distributions. Simulation results show that significant improvement on the successively delivered number of spikes is achievable when delay lines are employed as neural buffers in NDBs. We also analytically modeled the performance of an outgoing slot and compared the analytical results with the simulation results. We observed that both results are consistent with each other.

ICT inspired techniques ultimately pave the way for developing promising curing strategies for neural diseases [31]. One of the major neural diseases, peripheral neuropathy is caused by the lack of communication between the neurons in the sensory pathway. The proposed technique that brings the communication capability between the RN and somatosensory cortex may be applied to treat this kind of irreversible neural impairments in near future.

4. STATISTICAL MULTIPLEXING FOR NEURAL NANONETWORKS IN CASE OF NEURON SPECIFIC FAULTS

In this chapter, we propose a neuron specific statistical multiplexing (SM) scheme to substitute a faulty sensory neural pathway with a neighboring functional one. The proposed technique depends on the multiplexer and the demultiplexer units that can be realized as nanoelectronic devices and an addressing scheme. Since the spikes are stereotyped events and they have no addressing information, we developed an addressing scheme utilizing the spikes themselves. A functional neural pathway is shared with the both of the RNs of the two pathways i.e. functional and faulty pathways. The objective of the proposed mechanism is to utilize a functional pathway instead of a malfunctioning pathway, increase the number of spikes delivered while preserving the spike firing patterns and correctly deliver the spikes to the intended part of the sensory cortex. We evaluate the performance of the proposed technique is in terms of the percentage of the spikes transmitted under various scenarios. We also compared the performance of the SM based sensory nanonetwork with the TDMA based sensory nanonetworks proposed in the previous chapter. Despite that the performance achieved by SM based sensory nanonetwork is lower than the TDMA based sensory nanonetwork, proposed SM based sensory nanonetwork has implementation simplicity. Additionally, we evaluated the performance of the proposed technique when a priority mechanism is employed.

We presented this work [7] in IEEE International Congress on Ultra Modern Telecommunications and Control Systems (ICUMT'14).

4.1 Proposed Statistical Multiplexing Based Neural Nanonetwork

Under the light of the information given in Chapter 2.4, our objective is to convey the sensory information, namely, spike trains to the somatosensory cortex via functional neighboring pathway in case that a path fault exists. To overcome this deficiency, we propose a neuron specific SM protocol to share the functional neural pathway between more than one RN. The proposed SM based neural nanonetwork system can be realized by the use of multiplexer and demultiplexer units as illustrated in Figure 4.1.

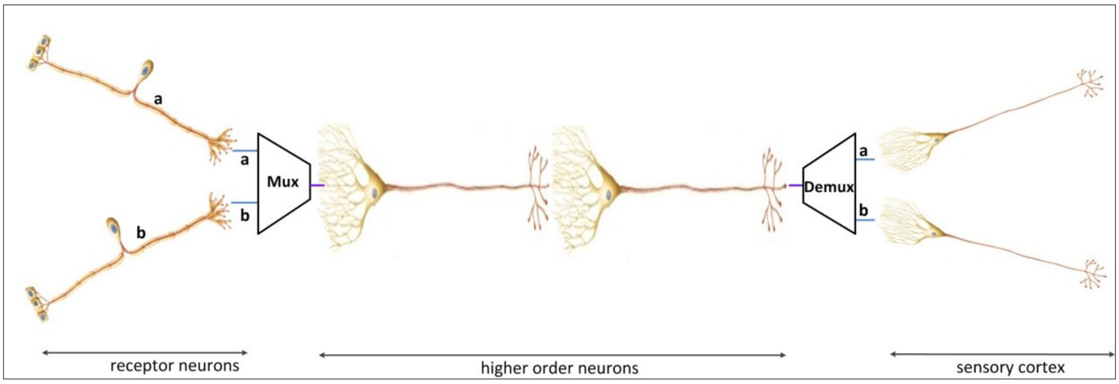

Figure 4.1 : Proposed SM based neural nanonetwork.

As we consider the traditional packet switching networks, every packet has a header part to identify the source and the destination addresses. On the contrary, spikes neither have any information about which RN generated them nor the arrival address. To employ statistical multiplexing, the spikes of each transmitting RNs must be distinguished at the demultiplexer unit before conveying them to the related part of the somatosensory cortex. Hence, we introduce an addressing scheme to identify the transmitting RNs by using the spikes themselves. Actually, we establish a packet switching neural nanonetwork by employing this addressing scheme.

We assume that the transmitting neurons are not active all the time. For the topology given in Figure 4.1, we also assume that an RN generates spikes covering 1/2 of the total transmission capacity of shared neurons. If the number of RNs is n then each source RN generates the $1/n$ of the total transmission capacity of the system shown in Figure 4.1. Otherwise, losing some of the spikes at the multiplexing stage will be inevitable which is still possible.

Both of the multiplexer and the demultiplexer units utilize neural interfaces for the spikes to be converted to the electronic domain. As explained in Chapter 2.5, the communication links between the nervous system and the nanoelectronic devices can be established via neural interfaces that can detect and/or trigger the generation of spikes. By using the neural interfaces, multiplexing or demultiplexing logic can be easily performed by nanoelectronic multiplexing and demultiplexing circuitry [58]. The following subsections give details about the components of the proposed SM based neural nanonetwork system.

4.2 Spike Based Addressing Scheme

Consider a neural nanonetwork that is composed of two RNs that share a common medium in order to transmit their spikes to the relevant part of the somatosensory cortex. When any of the RNs is stimulated, it generates spikes. We can assume the spiking activity between two neurons as binary communication [12]. Two different cases that are bit "1" and bit "0" can be expressed by the presence or absence of a spike, respectively. We use this approach to develop the addressing scheme. Spikes are used to encode the identities (Ids) of the transmitting RNs. For the given topology in Figure 4.1, two spikes are used to denote the Id of an RN. Therefore, one spike is expressed with two spikes in this scheme. $(2^n - 1)$ number of RNs can be addressed with n spikes. In Table 4.1, the coding information of the proposed addressing scheme is given when the number of RNs is 2.

Table 4.1 : Coding information of the SM based addressing scheme.

Spike Code	Meaning
00	No spike
01	RN A
10	RN B
11	Reserved

According to the inlet of the multiplexer unit where the spike is received, two spike periods are used to express the Id of the source RN. An incoming spike from RN "A" is expressed with the spike sequence "*01*" which consists of an empty spike slot "*0*" and a spike event "*1*". Similarly, an incoming spike from RN "B" is encoded with the spike sequence "*10*" which consists of a spike event "*1*" and an empty spike slot "*0*". In Figure 4.2, an example spike stream and its meaning are given as the output of the proposed addressing scheme.

output spike stream	0	1	0	0	0	1	1	0	1	0
meaning	RN B		No Spike		RN B		RN A		RN A	

Figure 4.2 : Example output of the spike based addressing scheme.

4.3 Multiplexing

Multiplexer unit concentrates spike traffic from multiple RNs onto a shared neural pathway. It is a simple nanoelectronic device and has no buffer space to arrange the spikes arrived. Therefore, when simultaneous packets are received, one of these spikes is dropped. According to the inlet where the spike is received, multiplexer unit employs the addressing scheme introduced above. Since the spikes are generated in a bursty fashion, it is possible to combine spike trains onto a shared neural pathway. Multiplexer unit transmits the spikes in first-in, first-out (FIFO) basis. By using the proposed addressing scheme, a priority mechanism can also be employed. According to the priority values assigned to the RNs, multiplexer unit can yield precedence to the spikes of the prioritized RN when simultaneous spikes arrived. The conceptual diagram of multiplexer unit is illustrated in Figure 4.3.

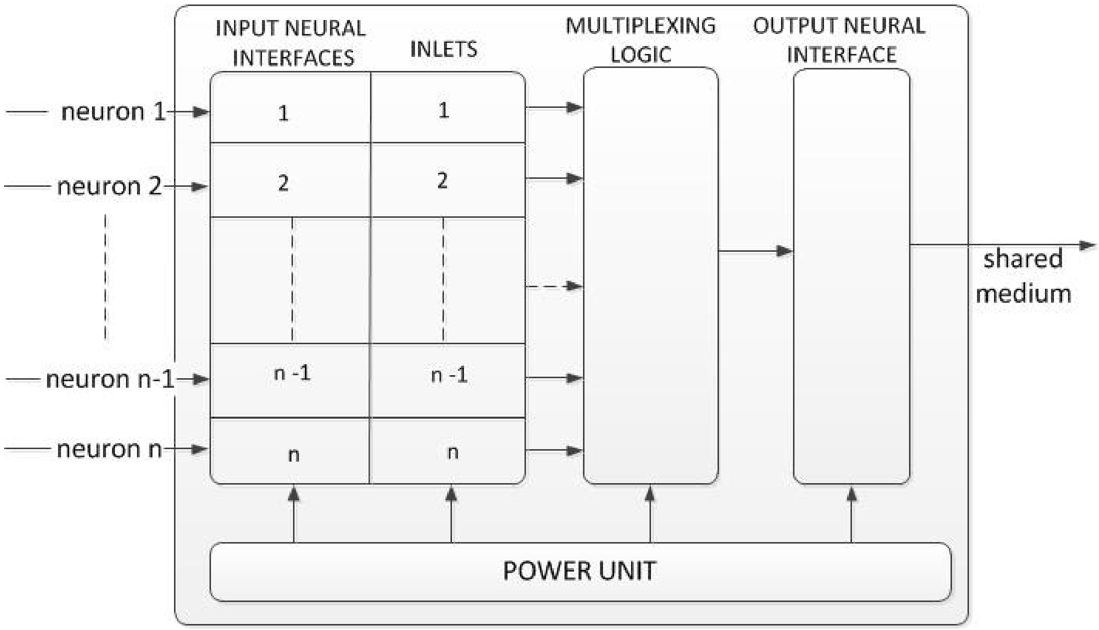

Figure 4.3 : Conceptual diagram of the multiplexer unit for a generic source RN system.

4.4 Demultiplexing

Demultiplexer unit can be realized as nanoelectronic device. It separates the spike traffic by decoding spike trains via employing the introduced addressing scheme. After the source of the spike is determined by the demultiplexer unit, spikes are conveyed to the intended part of the somatosensory cortex by relaying the spike to the proper outlet. The conceptual diagram of demultiplexer unit is shown in Figure 4.4.

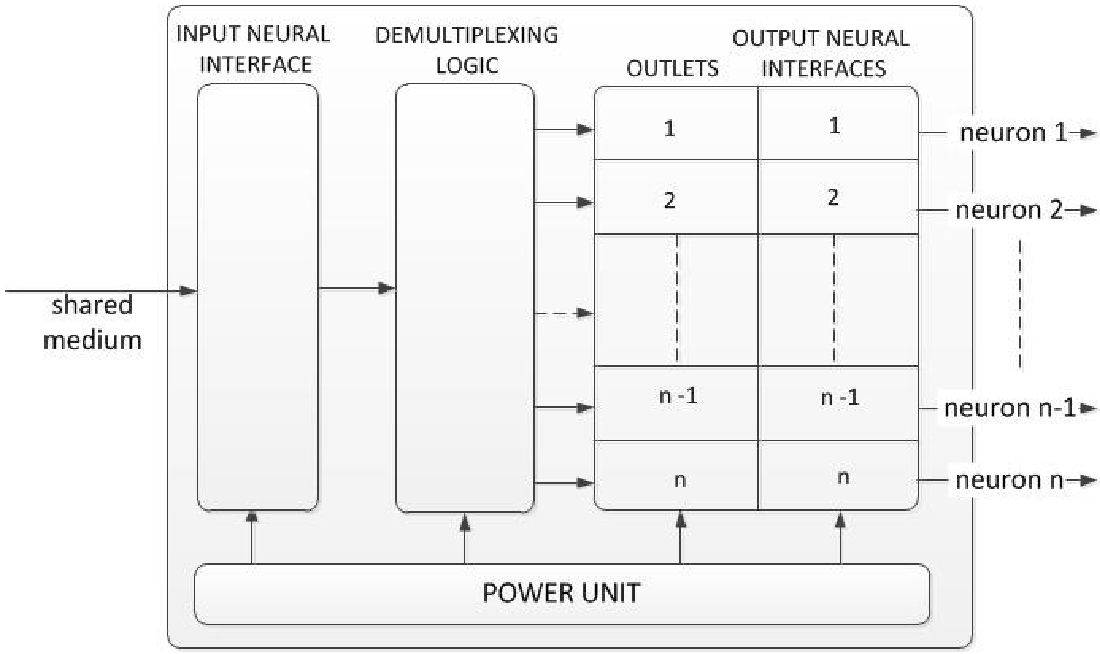

Figure 4.4 : Conceptual diagram of the demultiplexer unit for a generic source RN system.

If the spike firing patterns generated by the RNs can be preserved and delivered to the relevant part of the somatosensory cortex, the correct sensation can be achieved across the perceived information.

4.5 Performance Analysis

The performance of the proposed multiplexing mechanism is mainly based on the utilization of idle time of the shared medium i.e. signaling pathway. Contrary to the traditional statistical multiplexers, the proposed multiplexer unit has no capability to buffer and arrange the simultaneous spikes of different RNs. Thus, if more than one spike arrives at the multiplexer unit at the same time, only one of them is conveyed to the shared medium and the others are dropped.

In our studies, we employ Neural Simulation Tool (NEST) [40] in order to reflect the electrical and chemical aspects of the neural communication channel. We use the two-source RNs topology that is given in Figure 4.1 and the source RNs are named as the Primary RN and the Secondary RN, respectively. The Primary RN has the functional signaling pathway and shares its pathway with the Secondary RN that has the malfunctioning signaling pathway. The spikes are generated by the source RNs according to the Poisson distribution with various mean arrival rates. Since it is impossible to for an RN to fire a subsequent spike in the ARP, we adapted the spike generation times for an RN to exhibit this characteristics. We evaluate the percentage of the successfully transmitted spikes for the total of 1000 incoming spikes of each RNs. The setup we used in our simulations is given in Appendix A.

In Figure 4.5, the behavior of the SM based neural nanonetwork is given for various Poisson arrival rates (λ=200, λ=400 and λ=600 spikes/s). The decrease in λ values results in the increase in the inter-arrival times of the spikes. Hence, it is more probable for a spike to find the shared medium idle. It can easily be seen from Figure 4.5, the performance of the proposed technique is enhanced significantly when the inter-arrival times of the spikes are sparse.

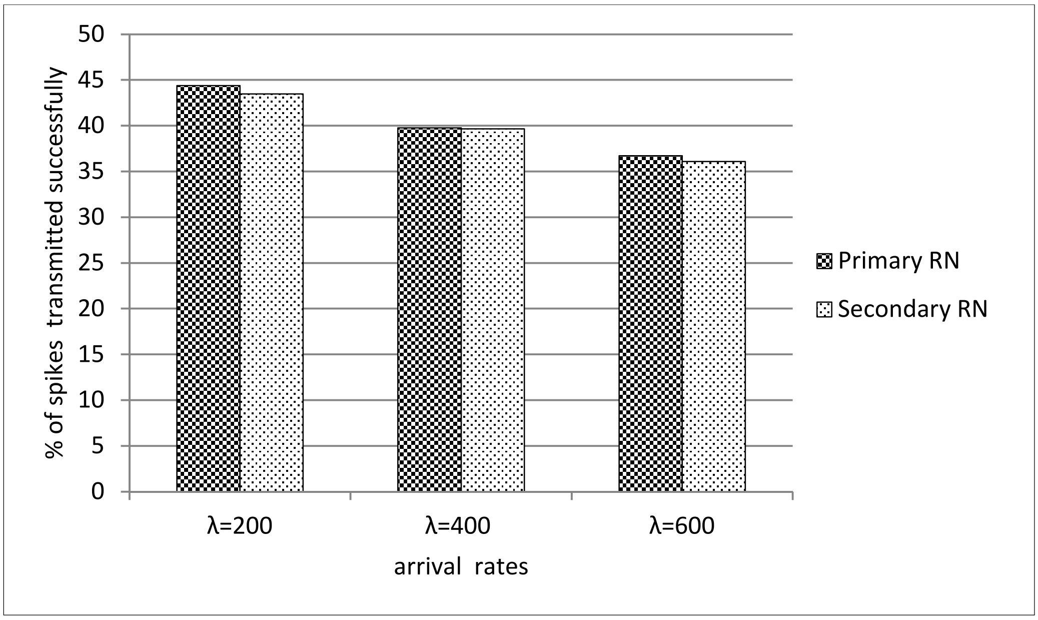

Figure 4.5 : Performance of the SM based multiplexing technique when Poisson distribution with various arrival rates (λ) are employed.

In Chapter 3, we introduced two TDMA based techniques (TDMA with delay lines and TDMA without delay lines) for neural nanonetworks [6]. Briefly, TDMA with delay lines based multiplexing scheme utilizes neural delay lines for buffering the spikes that are received in unassigned time slots. The TDMA without delay lines based multiplexing scheme does not have buffering capability. According to this scheme, only the spikes received at the assigned time slots can be transmitted, other spikes are dropped. The performance of the proposed SM based neural nanonetwork and the previously proposed TDMA based techniques are compared in Figure 4.6 for various Poisson arrival rates (λ=200, λ=400 and λ=600 spikes/s). Since the SM based technique does not have the buffering capability, only one of the incoming spikes is conveyed to the shared medium among the simultaneous spikes of the both transmitting RNs. Despite that, the increase in the inter-arrival times of the spikes improves the performance of the three schemes; TDMA with delay lines based technique outperforms the other techniques via its buffering ability. Please remember that, TDMA based techniques always reserve a time slot for each RNs even if an RN has no spike to transmit, and causes poor utilization of shared medium. For such cases, SM based technique outperforms the others since it employs the FIFO logic. Besides, SM based technique has lower implementation complexity than both of the TDMA based techniques.

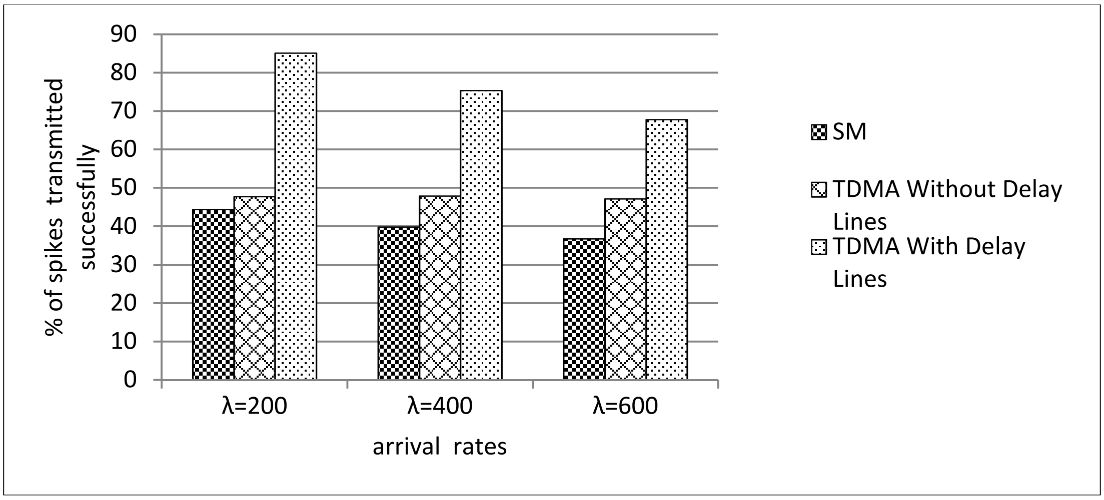

Figure 4.6 : Performance comparison of the SM and TDMA based multiplexing techniques when Poisson distribution with various arrival rates (λ) are employed.

A priority mechanism can be developed for the introduced SM based neural nanonetwork. In Figure 4.7, we evaluated the performance of the proposed SM based technique for various priority values of the Primary RN when the arrival rate is 400 spikes/s. As it can be seen in Figure 4.7, when the priority value of the selected RN i.e. the Primary RN is increased, the blocking probability of the selected RN decreases. Hence, the increase in the priority value results in the performance improvement of the prioritized RN. When the highest priority value (*priority=1*) is given to the Primary RN, the multiplexer units generates spikes for the Secondary RN if and only if there is no spike transmitted by the Primary RN. Pease note that, even the highest priority value (*priority=1*) is given the Primary RN, about 30% of the spikes of the Secondary RN is transmitted successfully.

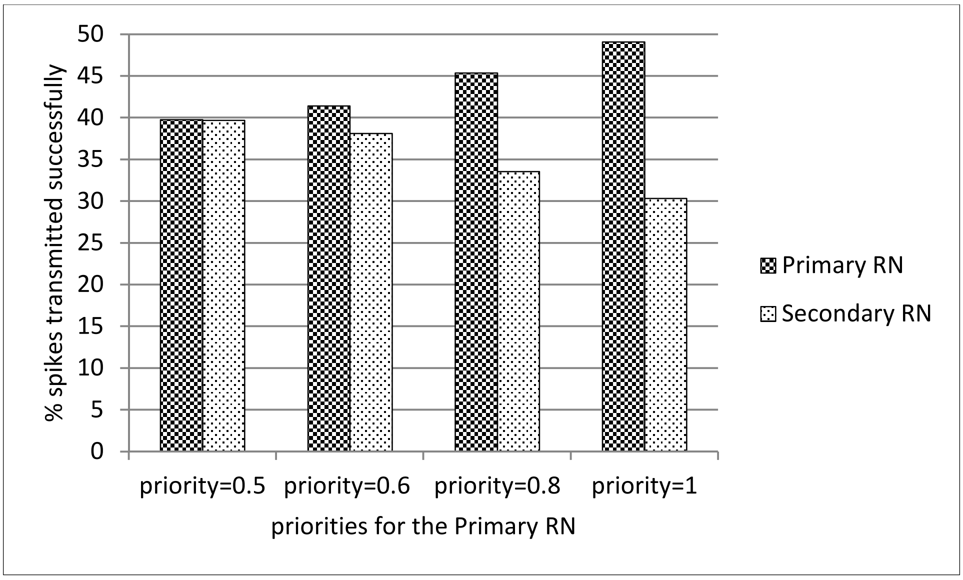

Figure 4.7 : Performance of the priority mechanism of the SM based neural nanonetwork.

In Figure 4.8, the performance of the priority mechanism is evaluated under various Poisson arrival rates when the highest priority value (*priority=1*) is given to the Primary RN. Whenever the Primary RN has a spike to send, it is transmitted directly to the shared medium, the simultaneous spikes of the Secondary RN are dropped. The decrease in the traffic load increases the probability of the shared medium being idle and gives an opportunity to the multiplexer unit to transmit the spikes of the Secondary RN. As it can be seen in Figure 4.8, as the λ values decreases the performance of the Secondary RN increases.

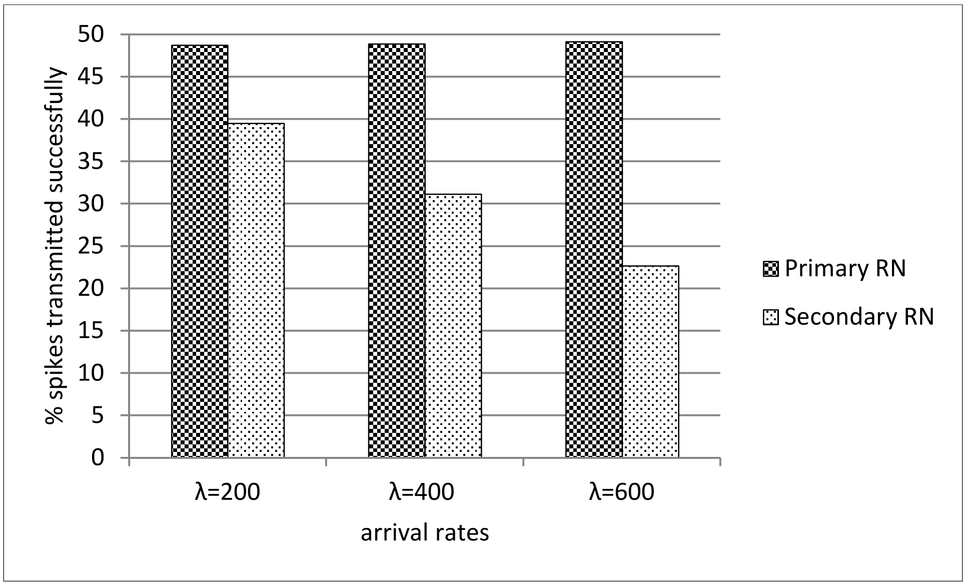

Figure 4.8 : Performance of the priority mechanism of the SM based neural nanonetwork when priority=1 for the Primary RN.

We also examine the similarity between the input spike generation times (spike times of the RNs) and the output spike generation times (spike times at the demultiplexer unit) when the Primary and the Secondary RN has the same priority. The Two Sample Kolmogorov-Smirnov test is one of the most useful and general nonparametric method to test whether two samples come from the same distribution [60]. This statistic quantifies a distance between the empirical distribution functions of two samples. The null distribution of this statistic is calculated under the null hypothesis that the samples are drawn from the same distribution. The Two Sample Kolmogorov-Smirnov is sensitive to differences in both location and shape of the empirical cumulative distribution functions of the two samples. This statistic test reports an *asymptotic p value* by calculating the differences between the two cumulative distributions. If the *asymptotic p value* is small, the test concludes that the two groups are sampled from populations with different distributions. If the *asymptotic p value* is bigger than 0.05, the null hypothesis stating that both samples come from a population with the same distribution is accepted. In this case, the test result reveals that there is no significant difference between the distributions of the two samples. Therefore, we employ the Two Sample Kolmogorov-Smirnov test to measure the similarity between the input and the output spike generation times under various Poisson mean arrival rates. The test results are given in Table 4.2. For all the mean arrival rates, the *asymptotic p values* are over 0.97 and it shows that both of the input and output spike generation times of the Primary and the Secondary RNs are from the same distribution. Hence, we can assume that the input and output spike patterns have similar properties. Since the spike generation times are random and follow a Poisson distribution, the inter-arrival times are also random and follow a negative-exponential distribution. However, the input spike generation times are adapted to exhibit the ARP characteristics as denoted at the beginning of this section. The mean input and the mean output inter-arrival times of spikes are also shown in Table 4.2. Although, the input and output inter-arrival times of spikes are from the same distribution for the both RNs, the mean output inter-arrival times differs from the corresponding mean input inter-arrival times due to sharing the functional sensory pathway between two RNs and the protocol overhead of SM.

Table 4.2 : Two Sample Kolmogorov-Smirnov test results of the SM based multiplexing technique.

Arrival Rates (spikes/s)	Asymptotic p-values		Input/Output Mean Inter-Arrival Times (ms)		I/O from same distribution?	
	Primary RN	Secondary RN	Primary RN	Secondary RN	Primary RN	Secondary RN
200	0.9811	0.9891	5.328/11.66	5.328/11.66	Yes	Yes
400	0.9929	0.9979	2.477/6.141	2.477/6.141	Yes	Yes
600	0.9799	0.9896	1.923/5.294	1.923/5.294	Yes	Yes

4.6 Conclusion

Many neurodegenerative diseases are eventuated when the spike propagation is interrupted due to a failure in the signaling pathway. In this chapter, we proposed a neuron specific SM technique to establish the communication between an RN and somatosensory cortex in case of intermediate neuron failure in the sensory pathway.

Our aim is to share a functional pathway between the RN of the faulty pathway and the owner RN of the functional pathway. To this purpose, we devised two nanoelectronic devices namely the multiplexer and the demultiplexer units and developed an addressing scheme to distinguish the owner of the spikes that exploits spikes themselves.

We evaluated the performance of the proposed technique by simulations. We also compared the obtained results with the TDMA based multiplexing protocol introduced in Chapter 3. The proposed SM based technique has lower implementation complexity than the previously introduced TDMA based techniques.

We also showed that a priority mechanism can be applied for the proposed technique.

Besides, we examined the similarity of the input and the output spike patterns and the test results demonstrated that the input and the output spike patterns have similar properties.

The obtained results reveal new opportunities in neural communication and may pave the way to the advancement of the real healthcare applications of neural nanonetworking in the near future.

5. SWITCH BASED MULTIPLEXING PROTOCOL FOR NEURAL NANONETWORKS IN CASE OF NEURON SPECIFIC FAULTS

In this chapter, we propose the Switch Based Multiplexing Protocol (SBMP) to substitute a faulty sensory neural pathway with a functional neighboring pathway. The SBMP employs some control packets that utilize the spikes themselves. The proposed multiplexing protocol depends on the multiplexer and the demultiplexer units that can be realized as nanoelectronic devices. The spiking activity between these units is regulated by SBMP. Thus, a functional neural pathway is shared with the both of the RNs of the two pathways i.e. functional and faulty pathways. The objective of the proposed SBMP is twofold. Firstly, conveying the spikes of an RN that has faulty pathway through a shared functional pathway. The latter is to minimize the number of spikes that can be lost while multiplexing the spikes of RNs in order to feel the correct sensation. The performance achieved by SBMP is evaluated by simulations and obtained results are also compared with the techniques that we proposed in Chapter 3 and Chapter 4. Since the SBMP employs smarter algorithms than the SM based neural nanonetwork, the results demonstrate significant improvements on the successively delivered number of spikes is achievable when SBMP is employed. Despite that, the performance achieved by SBMP is lower than the TDMA based neural nanonetwork, the proposed SBMP has implementation simplicity. Furthermore, we evaluated the performance of SBMP when a priority mechanism is employed. Besides, we analyzed the similarity between the input inter-spike interval distribution (inter-spike interval times of the RNs) and output inter-spike interval distribution (inter-spike interval times at the demultiplexer unit) when the various priority values are assigned to the RNs.

After we concluded this study, we submitted for publication in IET Nanobiotechnology (SCIE).

5.1 The Proposed Switch Based Multiplexing Protocol

The SBMP is developed to set the pathway i.e. route where the spikes are carried through. The scenario of alternating a faulty sensory pathway to a functional pathway is illustrated in Figure 5.1. This scenario is based on the dorsal column-medial lemniscal pathway where tactile sensation and limb proprioception are conveyed to somatosensory cortex [38]. The malfunctioning sensory pathway is represented as the dashed red line and the continuous blue line symbolizes the functional sensory pathway. As it can be seen in Figure 5.1, the multiplexing is done after the spikes are generated by RNs. The multiplexed spikes are conveyed through the functional pathway and demultiplexing is carried out just before the spikes are conveyed to the corresponding part of the somatosensory cortex. Please note that, we utilize the functional pathway as it is, but just adding the multiplexing unit and the demultiplexing unit for sharing it.

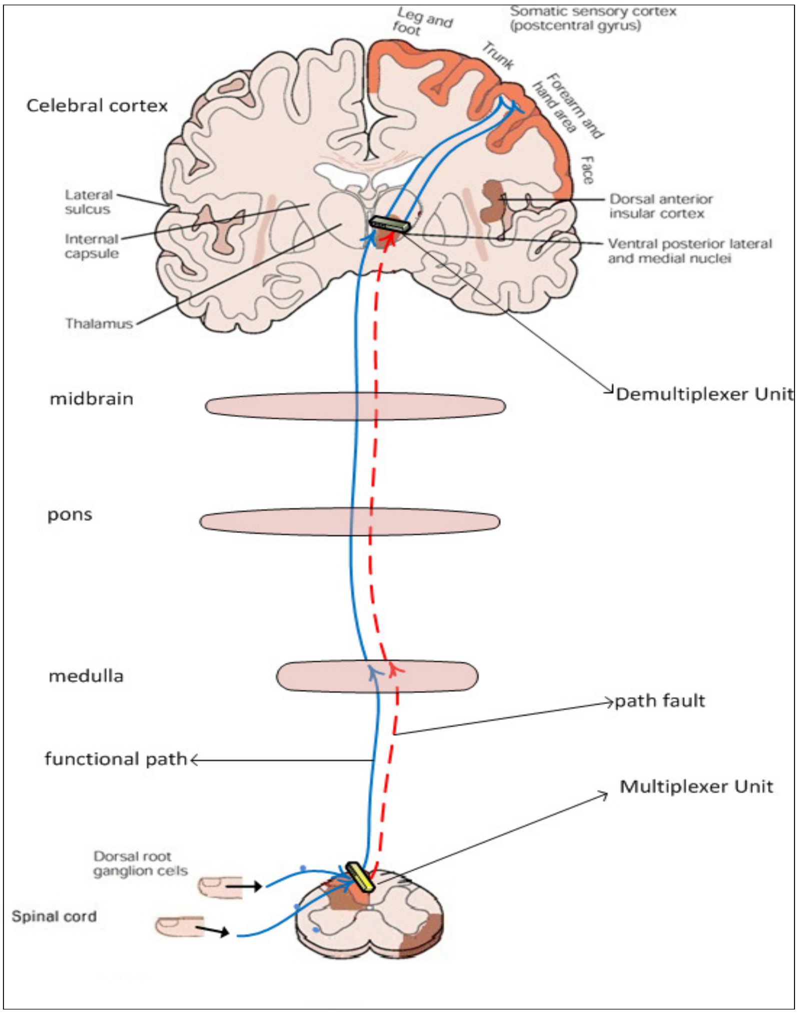

Figure 5.1 : Sensory pathway alternation, adapted from [2].

Under the light of the information given in Chapter 2.4, our objective is to share the functional neighboring pathway for conveying the spikes of more than one RN and maintain the communication of the RN that has the faulty pathway with the somatosensory cortex. The SBMP is proposed to overcome this deficiency. The proposed neural nanonetwork system can be realized by the use of the multiplexer and the demultiplexer units as illustrated in Figure 5.2.

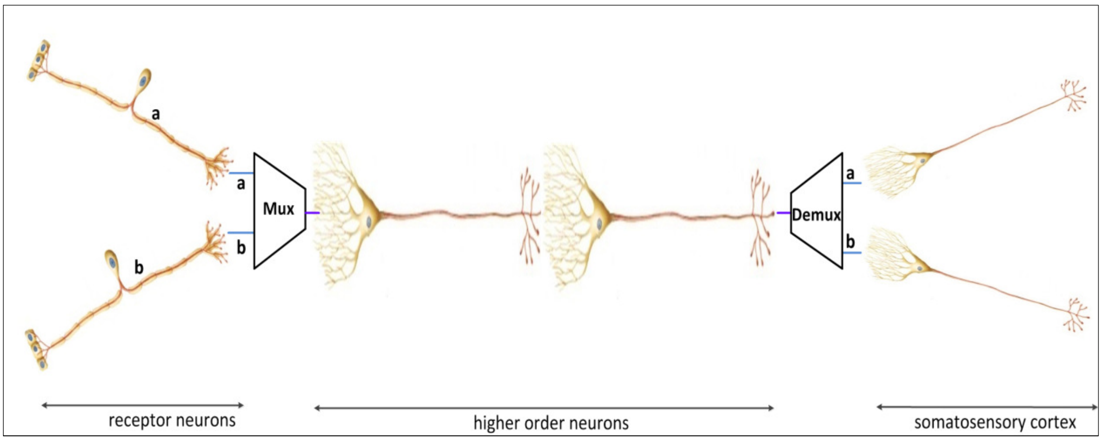

Figure 5.2 : The proposed SBMP based neural nanonetwork.

As stated in Chapter 2.3, spikes are identical events and they do not include any information about the sender or receiver. To employ a multiplexing scheme, the spikes of each transmitting neuron must be determined at the demultiplexer unit before conveying them to the corresponding part of the somatosensory cortex. Hence, we introduce a switch based communication mechanism to regulate the spiking activity between the multiplexer and demultiplexer units. Consider the neural nanonetwork in Figure 5.2, the RNs shares the common medium in order to transmit their spikes to the corresponding part of the somatosensory cortex. When any of the RNs is stimulated, it generates spikes. The spiking activity between two neurons can be assumed as binary communication [12]. As stated in Chapter 4.1, two different cases which are bit “1” and bit “0” can be expressed by the presence or absence of a spike, respectively. The SBMP is developed by using this approach. The proposed protocol is based on the control packets that utilize the spikes themselves.

We assume that the transmitting neurons i.e. RNs are not active all the time. For the system given in Figure 5.2, we also assume that an RN generates spikes covering 1/2 of the total transmission capacity of the shared neuron. In the related literature, the upper limit on the firing rate of neurons is defined about 1200 spikes/s [2].

Therefore, the capacity of the proposed system is assumed as 1200 spikes/s. If the number of the RNs is *n* then each source RN generates the *1/n* of the total transmission capacity of the system shown in Figure 5.2. Otherwise, losing some of the spikes at the multiplexing stage will be inevitable which is still possible.

Firstly, an inlet of the multiplexer unit and the relevant outlet of the demultiplexer unit are set as the default inlet and outlet. The multiplexer unit sends the proper control packets that are shown in Figure 5.3 to the demultiplexer unit to encode the spiking activity and the source RN of the incoming spikes. The multiplexer unit keeps on silence unless it receives a spike. Whenever the multiplexer unit receives spikes from the default source RN (the default inlet), it simply generates a spike to be carried through the default pathway. When the other source RN generates a spike, the multiplexer unit transmits the change outlet control packet "*01*" to denote the source of the spike traffic is changed. When the demultiplexer unit receives the change outlet control packet, it switches to the other outlet. From now on, the spikes are routed to the other pathway. Actually, the outlets of demultiplexer units are altered via the change outlet packets. Changing the outlet of the demultiplexer unit determines which of the inter-neurons that ends in the somatosensory cortex is used. The following subsections give details about the components of the proposed SBMP based neural nanonetwork system.

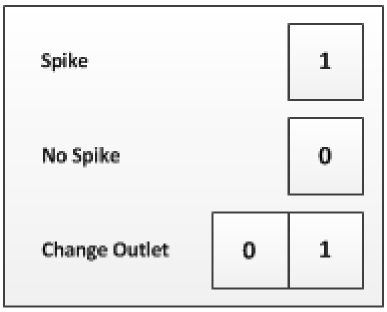

Figure 5.3 : The control packets of the SBMP.

5.2 Multiplexing

The spike traffic from multiple RNs is multiplexed onto a shared neural pathway via the multiplexer unit that is a simple nanoelectronic device. Contrary to conventional multiplexers, the multiplexer unit has no buffer capability to arrange the spikes arrived. Therefore, when simultaneous spikes are received, one of these spikes is dropped. The conceptual diagram of the multiplexer unit is illustrated in Figure 5.4.

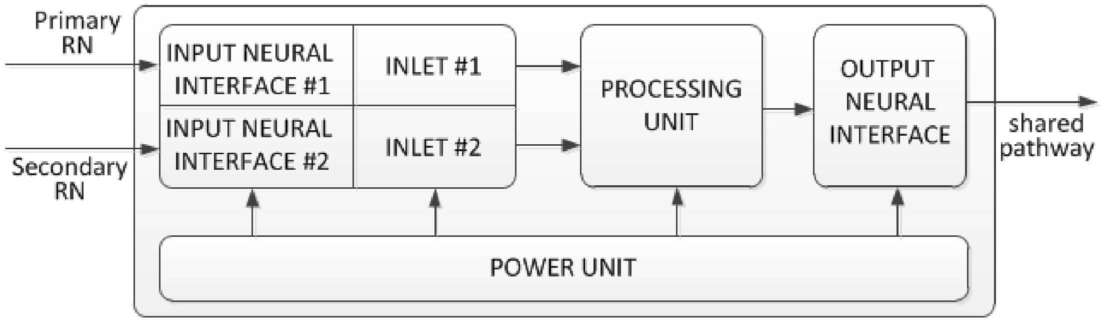

Figure 5.4 : The conceptual diagram of the multiplexer unit.

The input and output connections of the multiplexer unit are realized by the use of neural interfaces explained in Chapter 2.5. Neural interfaces detect and convert incoming spikes to electronic domain. After the spikes are converted to the electronic domain, the processing unit can easily employ the multiplexing logic. Thereafter, the spikes are generated onto the shared pathway via the output neural interface.

The processing unit employs the working logic of SBMP that is shown as a flow chart in Figure 5.5. The processing unit has a one-bit counter. Every spike cycle this counter is incremented. Hence, the even or odd cycle information is known by the processing unit. For the demultiplexer unit, the change outlet control packet (a spike following an idle spike period) means the alternation of the outlet. Therefore, the idle periods are important for SBMP. If no spikes arrives in an even cycle, a register (*C*) is set as "*1*" by the processing unit. While the register value is "*1*", an incoming spike is discarded to prevent to mislead the demultiplexer unit to change the outlet.

Whenever an incoming spike is received via the default inlet of the multiplexer unit and the register value is "*0*", the multiplexer unit generates a spike onto the shared medium. If the incoming spike is received via the other inlet and the register value is "*0*", change outlet control packet "*01*" is generated by the multiplexer unit. Besides, this inlet is set as the default inlet of the multiplexer unit. Unless the multiplexer unit receives any spike, it does not initiate a spiking activity.

Since the spikes are generated in a bursty fashion, it is possible to combine spike trains into a shared neural pathway. The multiplexer unit generates the spikes in FIFO basis. With the proposed protocol, the functional neural pathway is shared with an RN that has a malfunctioning pathway. Therefore, a priority mechanism can also be employed between the owner RN and the RN which shares the functional pathway.

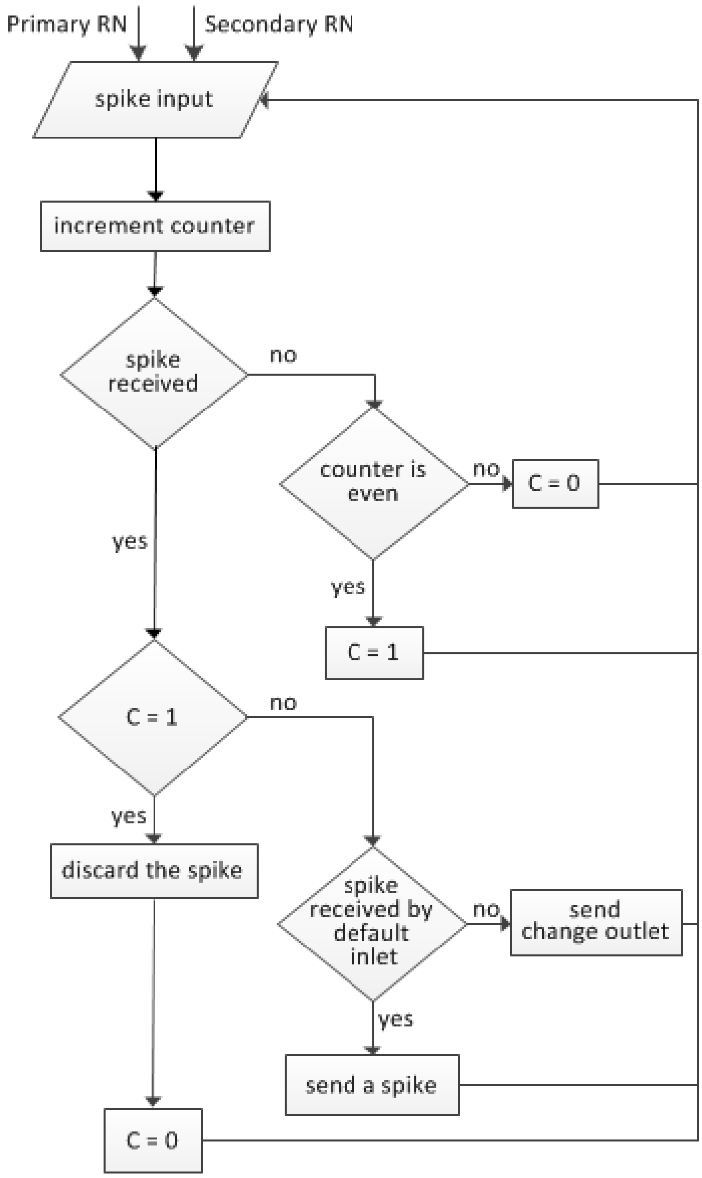

Figure 5.5 : The flow chart employed by the multiplexer unit.

5.3 Demultiplexing

The demultiplexer unit can also be realized as nanoelectronic device. The objective of this unit is to separate the spike traffic according to the control packets given in Figure 5.3. Similar to the multiplexer unit, neural interfaces are used to realize the input and output connections of the demultiplexer unit. After the spikes are converted to the electronic domain by the input neural interface, the processing unit employs the demultiplexing logic. The conceptual diagram of the demultiplexer unit is shown in Figure 5.6.

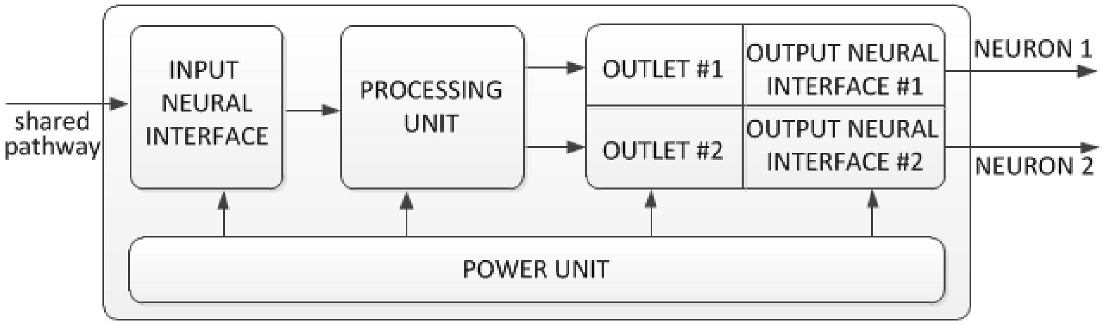

Figure 5.6 : The conceptual diagram of the demultiplexer unit.

As it is in the multiplexer unit, the processing unit of the demultiplexer has a one-bit counter also. Every spike cycle, this counter is incremented. If no spike is received in an even cycle, the register *(C)* is set as “1”. Otherwise, the register *(C)* is set as “0”. Whenever the demultiplexer unit receives a spike while the register value *(C)* is “0”, a spike is generated onto the inter-neuron via the default outlet. The register value gets importance for changing the default outlet. If a spike is received and the register value *(C)* is “1”, the processing unit detects that it received a change outlet control packet. Afterward, it switches to the other outlet i.e. disables the current outlet and enables the other outlet. Then, a spike is generated onto the corresponding inter-neuron via output neural interface. Actually, the change outlet control packet determines the source RN of the spiking activity. After the source of the spikes is identified, they are conveyed to the corresponding part of the somatosensory cortex by relaying the spikes to the proper outlet. The working principles of the demultiplexer unit are given as a flowchart in Figure 5.7.

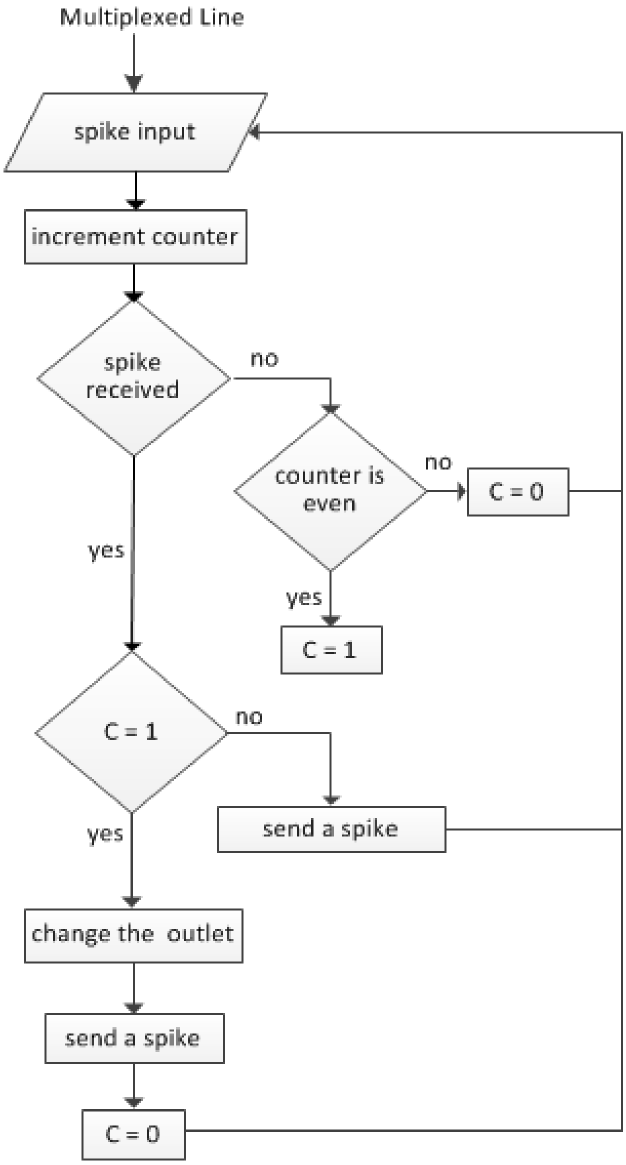

Figure 5.7 : The flow chart employed by the demultiplexer unit.

Let us explain the working logic of the multiplexer unit by using an example spike train given in Figure 5.8. Firstly, we assume that the inlet for the Primary RN set as the default inlet of the multiplexer unit and the corresponding outlet for the Primary RN set as the default outlet of the demultiplexer unit, respectively. We assume that both of the RNs have equal priority. The register value of the multiplexer unit and the demultiplexer unit is set as "*1*" according to the absence of a spike in an even spike cycle of the one-bit counter.

Time	0	1	2	3	4	5	6	7	8	9
Default Inlet	P	P	P	S	S	S	S	S	S	P
Primary RN	1	1	0	0	0	0	0	1	1	0
Secondary RN	0	1	1	1	1	0	0	0	0	1
Output	1	1	0	1	1	0	0	0	0	1
Meaning P (Primary) S (Secondary) N (No Spike)	P	P	Change Outlet		S	N	N	N	Change Outlet	

Figure 5.8 : Explanation of the working logic of the multiplexer unit by using an example input spike train.

- At time 0, only the Primary RN generates a spike. Since the spike is received from the default inlet of the multiplexer unit, the multiplexer unit generates a spike onto the shared medium.

- At time 1, both of the RNs generate a spike. Because of the each RN has the same priority and the multiplexer unit has no buffer capability, one of the incoming spike is dropped. For this case, let's assume that the spike of the Primary RN is conveyed to the shared medium.

- At time 2, only the Secondary RN generates a spike. For this case, the multiplexer unit receives a spike from the other inlet not from the default inlet. Since the register value is not set as "*1*", the multiplexer unit generates a change outlet control packet and set this inlet as the default inlet.

- At time 3, the Secondary RN generates a spike again. Since the change outlet control packet "*01*", consumes two spike periods, the multiplexer unit discards this spike. This case can be considered as the protocol overhead of the SBMP and denoted as red filled box in Figure 5.8.

- At time 4, only the Secondary RN generates a spike. Since the spike is received from the new default inlet of the multiplexer unit, the multiplexer unit generates a spike onto the shared medium.

- At time 5, neither the Primary RN nor the Secondary RN generates a spike. This is an example case of silence period. Since it is and odd period, the register value is not set as "*1*". Consequently, the multiplexer unit does not generate a spike.

- At time 6, neither the Primary RN nor the Secondary RN generates a spike again. Apart from the above case, this is an even cycle, so the register values of the multiplexer unit and the demultiplexer unit are set as "*1*". Thereafter, the multiplexer unit keeps silence, no spike is generated by the multiplexer unit.

- At time 7, only the Secondary RN generates a spike. Since the register value of the multiplexer unit was set as "*1*". This spike is discarded in order not to mislead the demultiplexer unit. In this manner, the demultiplexer unit is prevented from changing its the default outlet erroneously. This case can be thought as the protocol overhead also, and denoted as red filled box in Figure 5.8. Consequently, no spike is generated by the multiplexer unit.

- At time 8, only the Primary RN generates a spike. For this case, the multiplexer unit receives the spike from the other inlet, not from the default inlet. Since the register value is set as "*0*", the multiplexer unit generates a change outlet control packet and set this inlet as the default inlet. Consequently, no spike is generated by the multiplexer unit.

At time 9, the Secondary RN generates a spike. Since the change outlet control packet "*01*" consumes two spike periods, this spike is not taken into consideration and discarded by the multiplexer unit. This spike period is used for the change outlet control packet and the multiplexer unit generates a spike in order to transmit the *change control* packet. This is a similar case with the case at time 3, and can be considered as the protocol overhead of the SBMP and denoted as red filled box in Figure 5.8.

Similarly, let us explain the working logic of the demultiplexer unit by using the example spike train generated by the multiplexer unit that is given in Figure 5.9. As stated before, we assume that the inlet for the Primary RN set as the default inlet of the multiplexer unit and the corresponding outlet for the Primary RN set as the default outlet of the demultiplexer unit, respectively. We also assume that both of the RNs have equal priority. The multiplexer unit processes the incoming spike train two by two. The explanation of the working logic of the demultiplexer unit is given according the time steps that is shown in Figure 5.9.

Time	0	1	2	3	4	5	6	7	8	9
Default Outlet	P	P	0	S	S	N	N	N	N	P
Input	1	1	0	1	1	0	0	0	0	1
Ouput	1	1	0	1	1	0	0	0	0	1
Meaning P (Primary) S (Secondary) N (No Spike)	P	P	N	S	S	N	N	N	N	P

Figure 5.9 : Explanation of the working logic of the demultiplexer unit by using an example input spike train from shared medium.

- At time 0 and 1, the demultiplexer unit receives consecutive two spikes "11". The demultiplexer unit generates two sequential spikes and conveys these spikes to the default outlet. Consequently, the spikes are delivered to the corresponding destination address for the Primary RN in the somatosensory cortex.

- At time 2 and 3, the demultiplexer unit receives "01" spike stream which is a change outlet control packet. When the demultiplexer unit receives this control packet, it switches the other outlet i.e. the outlet for the Secondary RN and set this outlet as the new default outlet. As shown in Figure 5.9, it generates and conveys a spike onto this outlet at time 3. Consequently, the spike is delivered to the corresponding destination address for the Secondary RN in the somatosensory cortex.

- At time 4 and 5, the demultiplexer unit receives "10" spike stream. When the demultiplexer unit receives the spike, it generates a spike and conveys the spike to the default outlet at time 4. Consequently, the spike is delivered to the corresponding destination address for the Secondary RN in the somatosensory cortex. Since no spike is received at time 5, the demultiplexer unit does not generate a spike.

- At time 6 and 7, the demultiplexer unit receives no spike. This is an example case of silence period. Consequently, the demultiplexer unit does not generate a spike.

- At time 8 and 9, the demultiplexer unit receives "01" spike stream which is a change outlet control packet. When the demultiplexer unit receives this control packet, it switches the other outlet i.e. the outlet for the Primary RN and set this outlet as the default outlet. As shown in Figure 5.9, it generates and conveys a spike onto this outlet at time 9. Consequently, the spike is delivered to the corresponding destination address for the Primary RN in the somatosensory cortex.

If the spike firing patterns generated by the RNs can be preserved and delivered to the corresponding part of the somatosensory cortex, the correct sensation can be sensed across the perceived information.

5.4 Performance Analysis

The performance of the proposed multiplexing mechanism is based on the utilization of idle time of the shared medium i.e. signaling pathway. Contrary to the traditional multiplexers, the proposed multiplexer unit has no capability to buffer and arrange the simultaneous spikes of different RNs. Thus, if more than one spike arrives at the multiplexer unit at the same time, only one of them is conveyed to the shared medium and the others are dropped.

In order to evaluate the performance of the proposed protocol, we employ Neural Simulation Tool (NEST) [40] to reflect the electrical and chemical aspects of the neural communication channel. For the evaluation a realistic performance analysis of the proposed system, we also applied Gaussian noise factor to the simulation environment to model the axonal and synaptic noise in the neuro-spike communication channel. The details about the simulation setup are given in Appendix A.

We use the two-source RNs topology which is given in Figure 5.2 and the source RNs are named as the Primary RN and the Secondary RN, respectively. The Primary RN has the functional signaling pathway and shares its pathway with the Secondary RN that has the malfunctioning signaling pathway. Spikes are generated by source RNs according to the Poisson distribution with various mean arrival rates. Since it is impossible for an RN to fire a subsequent spike in the ARP, we adapted the spike generation times for an RN to exhibit this characteristics. We evaluate the percentage of the successfully delivered spikes for the total of 1000 incoming spikes of each RN.

In Figure 5.10, the behavior of the proposed neural nanonetwork is given for various Poisson arrival rates (λ=200, λ=400 and λ=600 spikes/s). The decrease in λ values results in the increase in the inter-arrival times of the spikes. Hence, it is more probable for a spike to find the shared medium idle. In consequence of equal priority values are given to the RNs, the results do not vary for both of the RNs. It can easily be seen from Figure 5.10, the performance of the proposed scheme is enhanced significantly as the inter-arrival times of the spikes get longer.

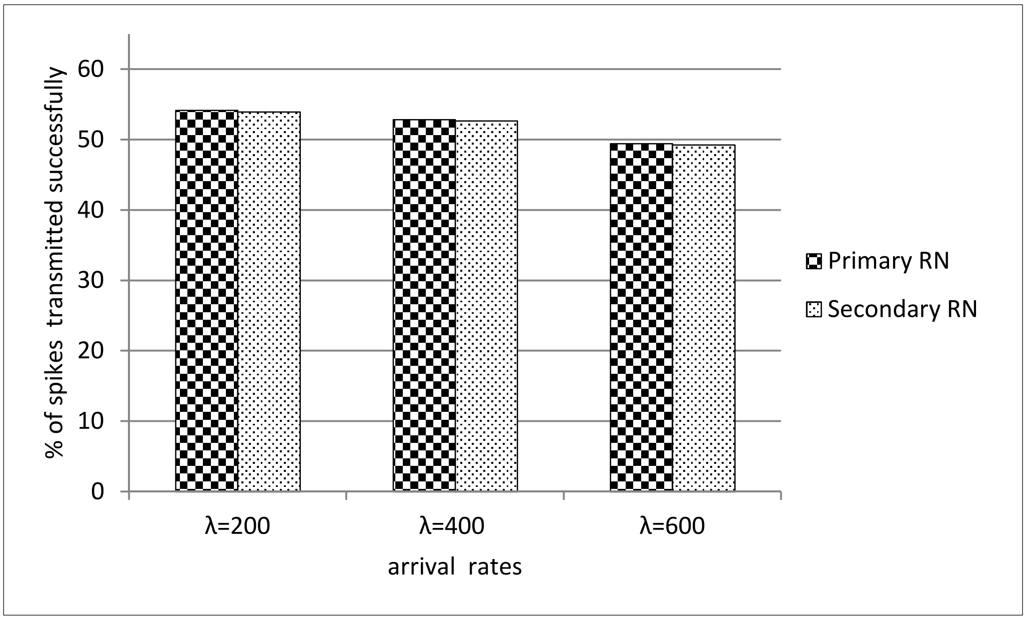

Figure 5.10 : Performance of the SBMP when Poisson distribution with various arrival rates (λ) are employed.

The performance of the proposed SBMP based neural nanonetwork and the other proposed techniques which are introduced in Chapter 3 and Chapter 4 are compared in Figure 5.11 for various Poisson arrival rates (λ=200, λ=400 and λ=600 spikes/s). For this analysis, equal priority values (*priority=0.5*) are given to the Primary and the Secondary RN. Since the results do not change for the Primary and the Secondary RN when the same priority values are applied, the results illustrated in Figure 5.11 are valid for the both of the RNs. For a brief reminding, we proposed two TDMA based techniques (TDMA with delay lines and TDMA without delay lines) for neural nanonetworks in Chapter 3. The TDMA with delay lines based multiplexing scheme utilizes neural delay lines for buffering the spikes that are received in unassigned time slots. The TDMA without delay lines based multiplexing scheme does not have a buffering capability. According to this scheme, only the spikes that are generated in the assigned time slots of the RNs can be relayed to the functional path, otherwise the spikes are dropped. The SM scheme introduced in Chapter 4, encodes a spike as two spikes to denote the identity of the source RN. Please note that, the SBMP and the SM based techniques do not have a buffering capability, only one of the incoming spikes is conveyed to the shared medium among the simultaneous spikes of the transmitting RNs. SBMP does not encodes a single spike with two spikes for every spike generated. Only a spike period is consumed for an idle time or a spike generation. Furthermore, SBMP utilizes change outlet control packet for encoding the destination addresses. Therefore, significant performance improvement on the successively delivered number of spikes is achievable when SBMP is used. As shown in Figure 5.11, the TDMA with delay lines based technique outperforms the other techniques via its buffering ability. Please remember that, the TDMA based techniques always reserve a time slot for each RNs even if an RN has no spike to transmit and causes poor utilization of shared medium. For such cases, the SBMP outperforms the TDMA with delay lines technique due to the FIFO logic it employs. Besides, the SBMP has lower implementation complexity than the TDMA based techniques.

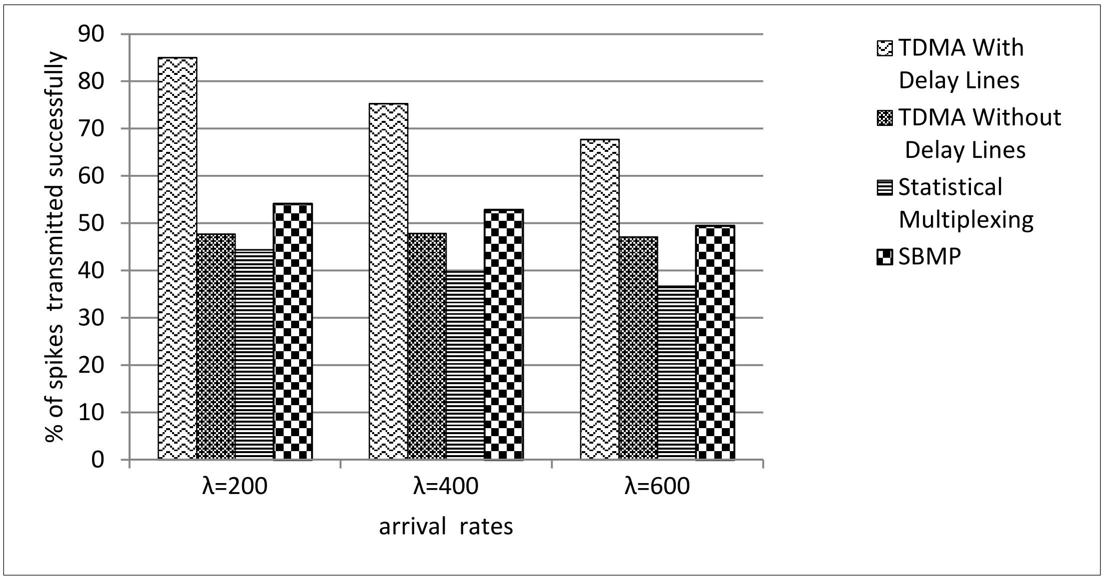

Figure 5.11 : Performance comparison of the SBMP and the other proposed techniques when Poisson distribution with various arrival rates (λ) are employed.

We also compare the performance of the proposed SBMP based neural nanonetwork and the other proposed techniques which are introduced in Chapter 3 and Chapter 4 when spikes are generated according to the Pareto distribution with various shape parameters (α) are employed. When the shape parameter (α) value decreases, inter-arrival times of the spikes increase. As it can be seen in the Figure 5.12, when low shape parameters (α) values are employed, the performance of the proposed techniques becomes significantly better. As the higher shape parameter (α) values are employed, inter-arrival times of the spikes decrease and the performance of the proposed techniques decreases due to the bursty spike traffic. For the TDMA with delay lines technique, when the inter-arrival times of the spikes decreases it is less probable for a spike received at the unassigned time slots to find the shared medium idle in the next assigned time slot. Hence, the spikes arrives at the unassigned time slots cannot be shifted to the next assigned time slot by using buffering capability of the NDBs. For the TDMA without delay lines method, only the spikes that are generated in the assigned time slots can be conveyed to the shared medium and this causes nearly fixed performance independent from the variation in the inter-arrival times of the spikes. For the SBMP, the performance degrades due to protocol overhead caused by the change outlet control packets and the discarded spikes that are generated in odd spike slots following a no spike event in an even slot. As the inter-arrival times of the spikes decreases SM based technique exhibits the worst performance due to the protocol overhead caused by encoding every single spike with two spikes.

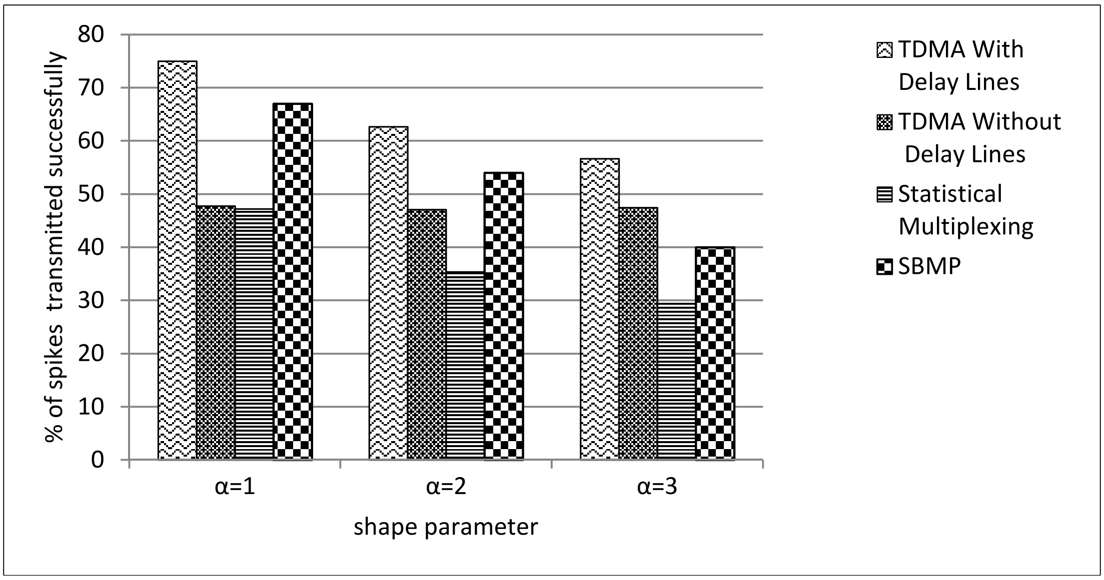

Figure 5.12 : Performance comparison of the SBMP and the other proposed techniques when Pareto distribution with various shape parameters (α) are employed.

A priority mechanism can easily be developed for the introduced SBMP based neural nanonetwork. In Figure 5.13, we evaluate the performance of the proposed protocol for various priority values of the Primary RN when the arrival rate is 400 spikes/s. As it can be seen in Figure 5.13, when the priority value of the selected RN i.e. the Primary RN is increased the blocking probability of the selected RN decreases. Hence, the increase in the priority value results in the performance improvement of the prioritized RN. When the highest priority value (*priority=1*) is given to one of the RNs, the spikes of the other RN are relayed by the multiplexer unit unless the prioritized RN does not transmits a spike. Pease note that, even the highest priority value (*priority=1*) is given to one of the RNs, about 40% of the spikes of the other RN is delivered successfully.

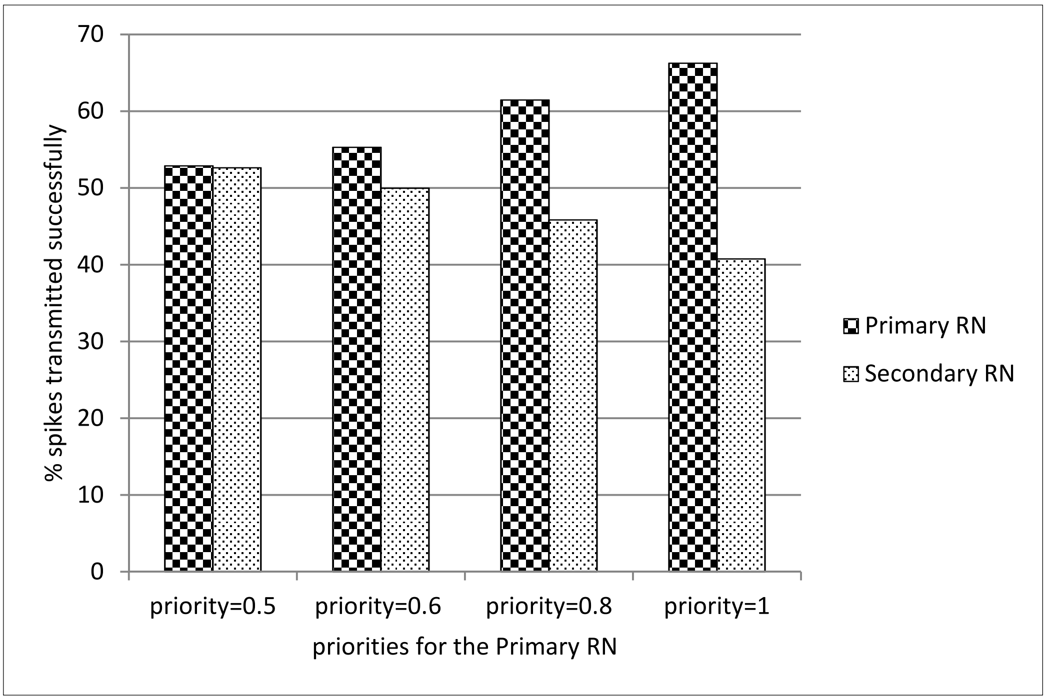

Figure 5.13 : The performance of the priority mechanism of the SBMP.

In Figure 5.14, the performance of the priority mechanism is evaluated under various Poisson arrival rates (λ=200, λ=400 and λ=600 spikes/s) when the highest priority value (*priority=1*) is given to the Primary RN. As the arrival rate of the prioritized RN increases, the overhead of the proposed protocol caused by the change outlet control packet decreases. Whenever the Primary RN has a spike to send, it is transmitted directly to the shared medium, simultaneous spikes of the Secondary RN are dropped. The decrease in the traffic load increases the probability of the shared medium being idle and gives an opportunity to the Secondary RN to transmit its spikes. As it can be seen in Figure 5.14, as the λ values decreases, the performance of the Secondary RN increases.

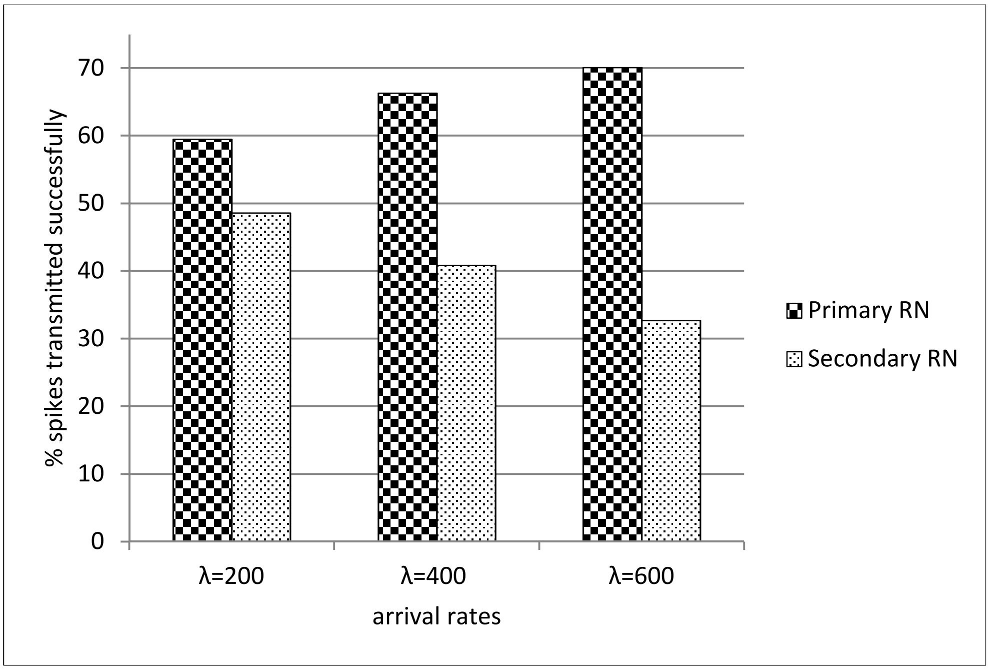

Figure 5.14 : The performance of the priority mechanism of the SBMP when priority=1 for the Primary RN.

We also examine the similarity between the input spike generation times (spike times of the RNs) and the output spike generation times (spike times at the demultiplexer unit) when the Primary and the Secondary RN has the same priority (*priority=0.5)*. As explained in Chapter 4.5, Two-Sample Kolmogorov-Smirnov test is employed to measure the similarity between input and output spike generation times under various Poisson mean arrival rates. This statistic is one of the most useful and general nonparametric method to test whether two samples come from the same distribution [60]. The test results given in Table 5.1 shows that both input and output spike generation times of the Primary and Secondary RNs are from the same distribution and the asymptotic p-values of the test results are over 0.98. Hence, we can assume that the input and output spike patterns have similar properties. Since the spike generation times are random and follow a Poisson distribution, the inter-arrival times are also random and follow a negative-exponential distribution. However, the input spike generation times are adapted to exhibit the ARP characteristics as denoted at the beginning of this section. The mean input and the mean output inter-arrival times of spikes are also shown in Table 5.1. Although, the input and output inter-arrival times of spikes are from the same distribution for the both RNs, the mean output inter-arrival times differs from the corresponding mean input inter-arrival times due to sharing the functional sensory pathway between two RNs and the protocol overhead of SBMP.

Table 5.1 : Two Sample Kolmogorov-Smirnov test results of the SBMP when equal priority value (0.5) is assigned to the RNs.

Arrival Rates (spikes/s)	Asymptotic p-values		Input/Output Mean Inter-Arrival Times (ms)		I/O from Same Distribution?	
	Primary RN	Secondary RN	Primary RN	Secondary RN	Primary RN	Secondary RN
200	0.9981	0.9951	5.082/9.059	4.936/8.83	Yes	Yes
400	0.9987	0.9919	2.635/4.972	2.613/4.968	Yes	Yes
600	0.9881	0.9804	1.89/4.049	1.937/3.806	Yes	Yes

After ensuring that both the input and the output spike generation times of the Primary and the Secondary RNs are from the same distribution, in Figure 5.15 and Figure 5.16 we analyzed the spike generation patterns of the Primary RN and the Secondary RN, respectively. For this purpose, we used the probability plot analysis for assessing whether or not the input and output inter-spike interval times follows a given distribution [61]. The input and output inter-spike interval times are plotted against a theoretical distribution in such a way that the points should form approximately a straight line. Since the spike generation (arrival) rate is random and follows a Poisson distribution, then the inter-arrival time is also random and follows a negative-exponential distribution. As we denoted at the beginning of this section, we adapted the spike generation times which are drawn from the Poisson distribution to exhibit the ARP characteristics. Therefore, the input inter-spike interval distribution slightly departure the theoretical input exponential distribution. When the equal priority is assigned to the RNs and the input arrival rate is 400 spikes/s, Figure 5.15 and Figure 5.16 compares the input inter-spike interval distribution (inter-spike interval times of the RNs) and output inter-spike interval distribution (inter-spike interval times at the demultiplexer unit) for the Primary and Secondary RN, respectively. For the both Figure 5.15 and Figure 5.16, the solid lines denote the theoretical exponential distribution curves for the corresponding inter-spike interval data (circles). As shown in the Figures 5.15 and Figure 5.16, the output inter-spike interval distribution differs from the corresponding input inter-spike interval distribution and the arrival rate is about 202 spikes/s for the both of the RNs. Since the functional pathway is shared between two RNs with equal priorities, the spike generation rates at the output decreases nearly half of the input spike generation rates for both of the RNs. Although, the all of spikes of the Primary RN could not delivered, the RN which has a faulty pathway successfully sends its spikes to the corresponding destination according to the same distribution with the half of the original spike generation rate via the proposed protocol.

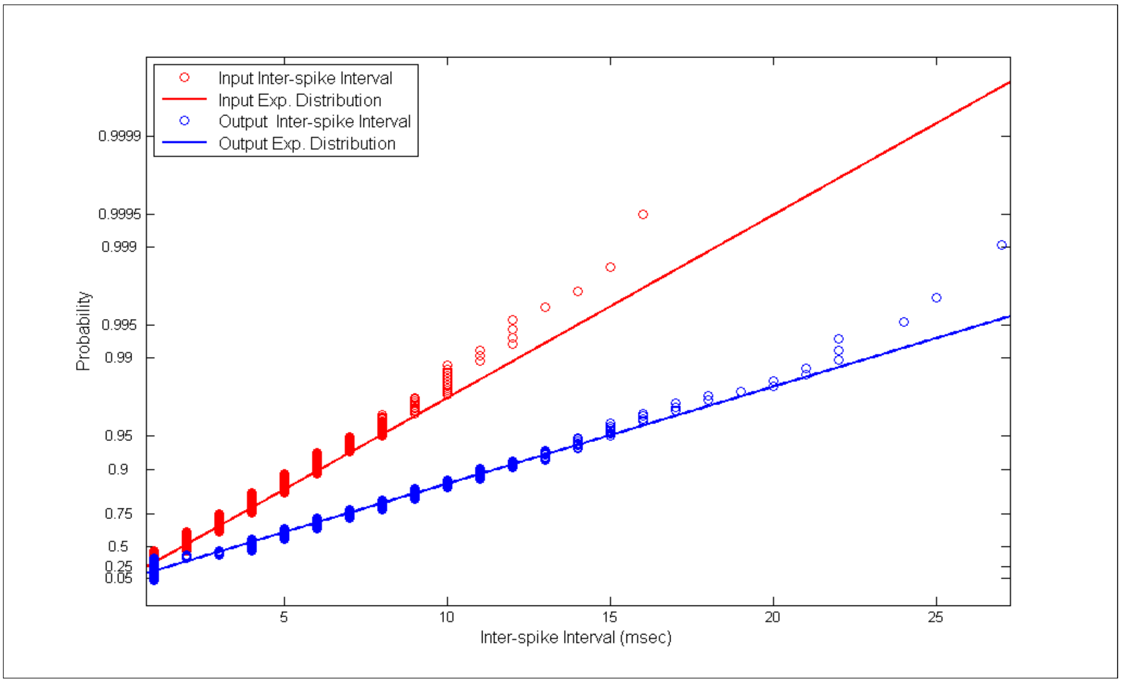

Figure 5.15 : Probability plot analysis of the input and output inter-spike intervals of the Primary RN.

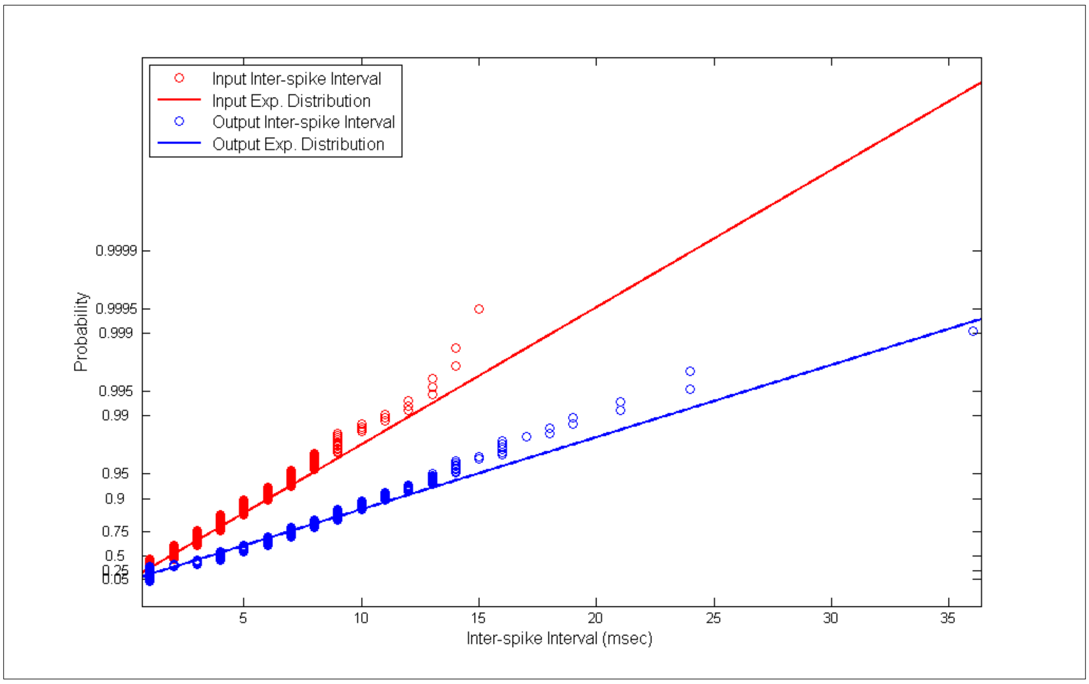

Figure 5.16 : Probability plot analysis of the input and output inter-spike intervals of the Secondary RN.

When the equal priority is assigned to the RNs and the input arrival rate is 400 spikes/s for the both RNs, histogram plots of input and output spike times of the Primary and the Secondary RNs are given in Figure 5.17 and Figure 5.18, respectively. These plots visually compare the number of spikes generated by the RNs with the number of the spikes generated at the output (at the demultiplexer unit). Since the equal priority value (*priority=0.5*) is given to both of the RNs, the number of the spikes generated at the demultiplexer unit for both of the RNs shows similar trends.

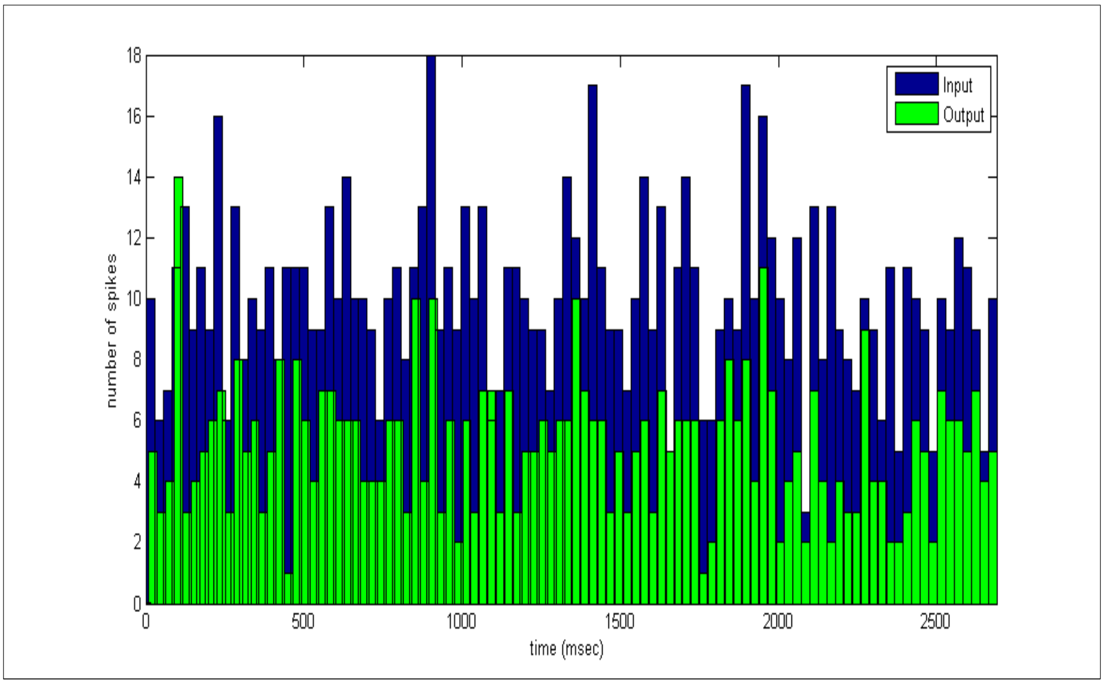

Figure 5.17 : Histogram plot of the spike times of the Primary RN.

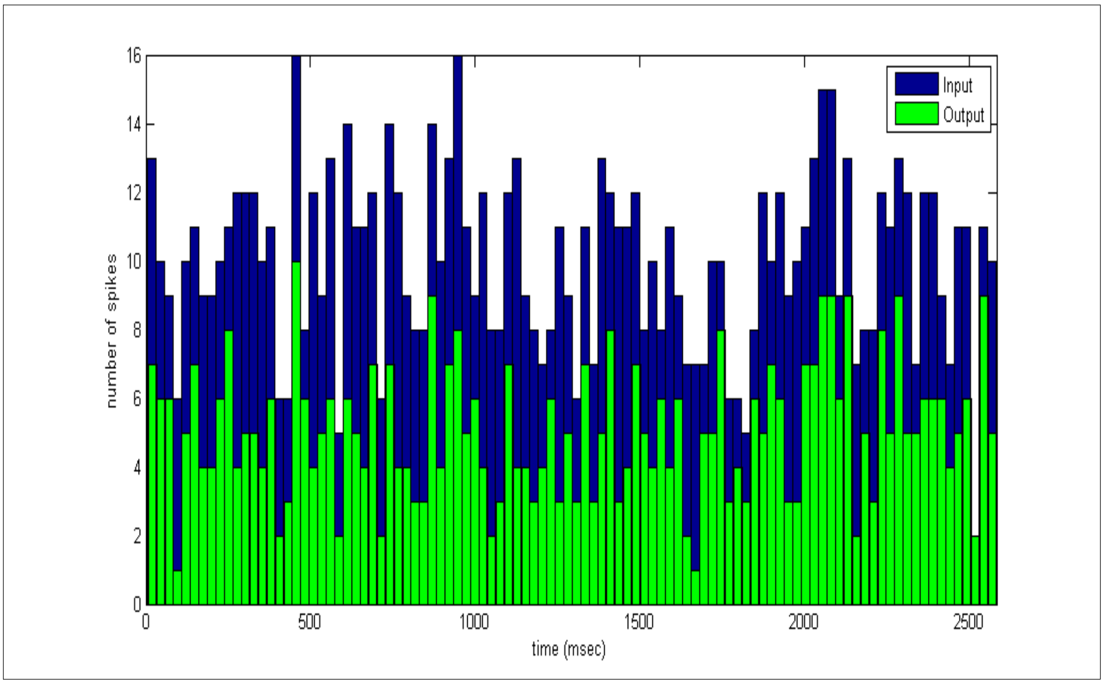

Figure 5.18 : Histogram plot of the spike times of the Secondary RN.

In Figure 5.19 and Figure 5.20, we analyzed the effect of the priority values assigned to the RNs to the output inter-spike interval distribution of the Primary and the Secondary RN, respectively when the input arrival rate is 400 spikes/s. We used the probability plot analysis as well to compare the variation of the inter-spike interval times at the demultiplexer unit. For the both Figure 5.19 and Figure 5.20, solid lines denote the theoretical exponential distribution curves for the corresponding inter-spike interval data (circles). As the priority value assigned to the Primary RN is increased, the output inter-spike interval distribution of the Primary RN converges to the input inter-spike interval distribution of the Primary RN, as shown in Figure 5.19. When the highest priority value (*priority=1*) is given to the Primary RN, output spike arrival rate at the demultiplexer unit approaches 243 spike/s. On the other hand, Figure 5.20 illustrates the effect of the priority values assigned to the Primary RN to the output inter-spike interval distribution of the Secondary RN at the demultiplexer unit. As the priority values for the Secondary RN are decreased, the output inter-spike interval distribution divergences from the input inter-spike interval distribution of the Secondary RN. Even though, the lowest priority value (*priority=0*) is given to the Secondary RN i.e. spikes of the Secondary RN are not transmitted unless the shared pathway is idle, the output spike arrival rate at the demultiplexer unit is approaches 156 spike/s by employing the proposed protocol.

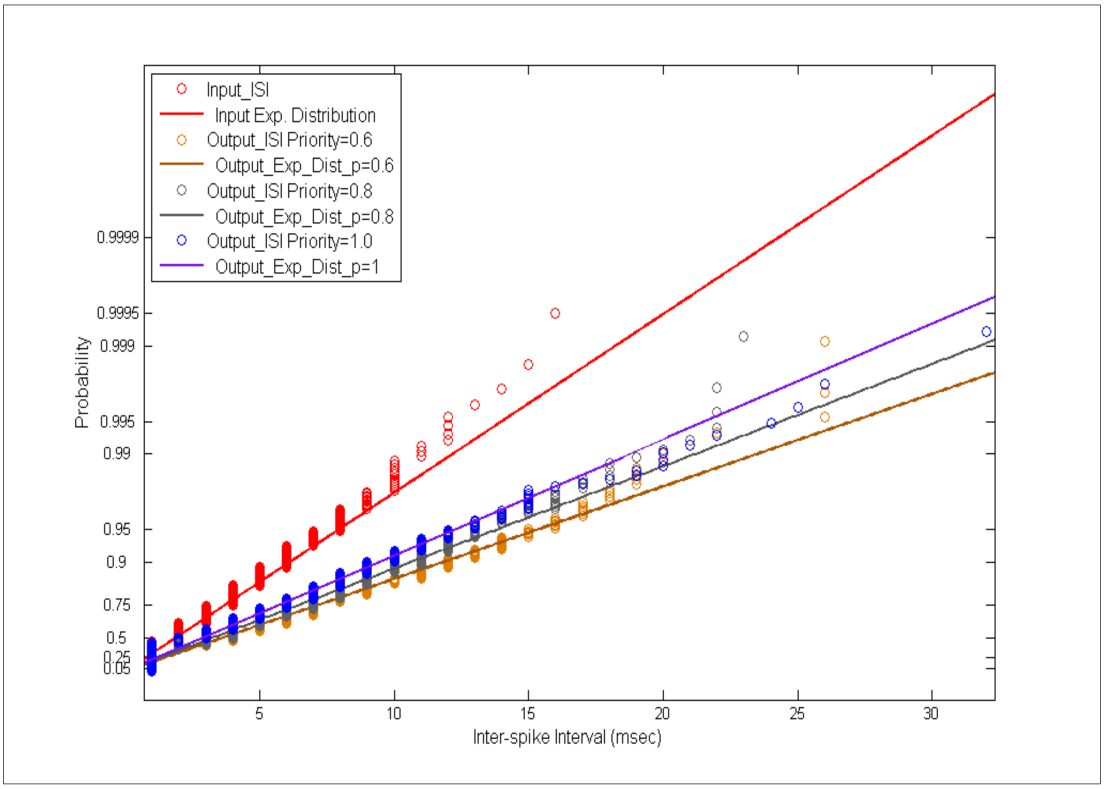

Figure 5.19 : The effect of the priority values to the input and output inter-spike intervals of the Primary RN.

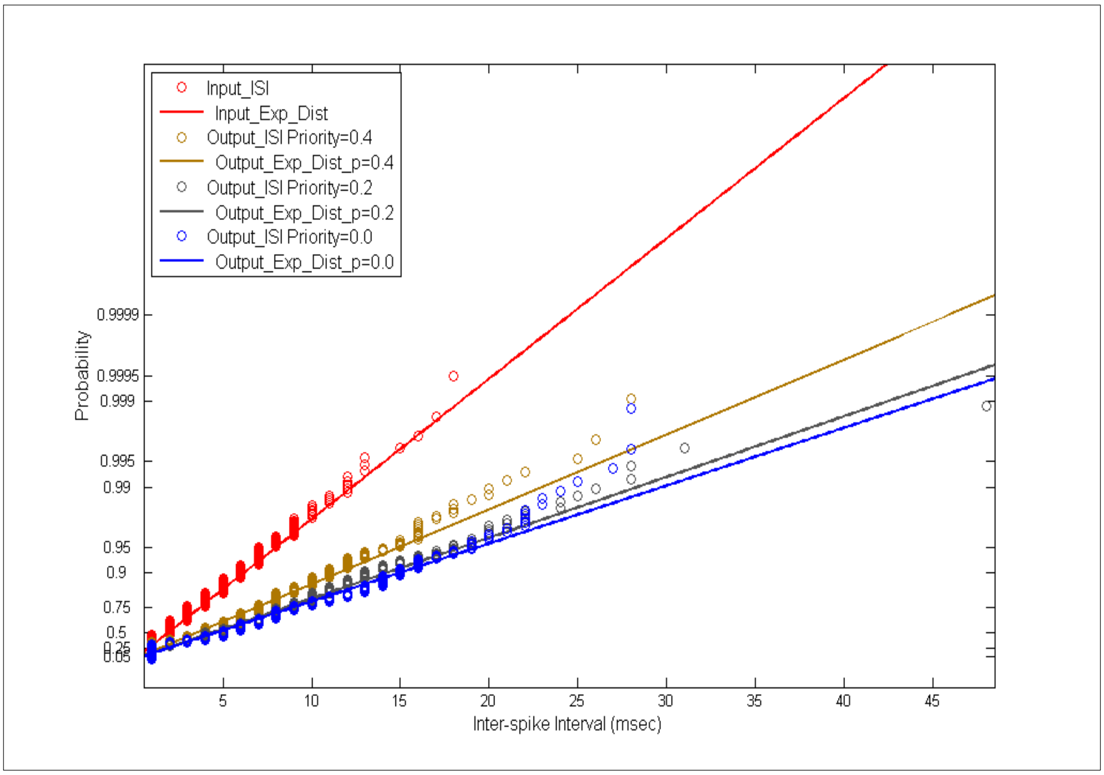

Figure 5.20 : The effect of the priority values to the input and output inter-spike intervals of the Secondary RN.

We also examine the similarity between the input spike generation times (spike times of the RNs) and the output spike generation times (spike times at the demultiplexer unit) when various priority values are assigned to the Primary and the Secondary RN. We employed Two-Sample Kolmogorov-Smirnov test as well to evaluate the similarity between the input and output spike generation times when the input arrival rate is 400 spikes/s. The test results are given in Table 5.2 and the results show that the both input and output spike generation times of the Primary and the Secondary RNs are from the same distribution. However, the priority values affect the similarity between the input and the output inter-spike interval distributions of the RNs. As it can be figured out from the variation of the asymptotic p-values of the test results, as the assigned priorities get higher the similarity between the input and output inter-spike interval distributions of the prioritized RN gets better. We also show the mean input and the mean output inter-arrival times of spikes in Table 5.2. Similarly, as the priority given to the RN is increased, the mean output inter-arrival times of spikes convergences to the corresponding input inter-arrival times of spikes. Hence, we can assume that the priority mechanism can be used as a quality of service parameter for the proposed protocol.

Table 5.2 : Two Sample Kolmogorov-Smirnov test results of the SBMP when various priority values assigned to the RNs.

Priority values		Asymptotic p-values		Input/Output Mean Inter-Arrival Times (ms)		I/O from Same Distribution?	
Primary RN	Secondary RN	Primary RN	Secondary RN	Primary RN	Secondary RN	Primary RN	Secondary RN
0.5	0.5	0.9987	0.9919	2.635/4.972	2.639/4.968	Yes	Yes
0.6	0.4	0.9899	0.9709	2.635/4.793	2.639/4.976	Yes	Yes
0.8	0.2	0.9999	0.8982	2.635/4.598	2.639/6.138	Yes	Yes
1.0	0.0	1.0	0.8216	2.635/4.069	2.639/6.443	Yes	Yes

5.5 Conclusion

In this chapter, we proposed a neuron specific SBMP to establish the communication between an RN and somatosensory cortex in case of intermediate neuron failure in the its sensory pathway. Actually, our aim is twofold. Firstly, conveying the spikes of an RN that has the faulty pathway by sharing a functional neighboring pathway. The letter is minimizing the number of spikes that can be lost while employing proposed protocol to obtain the correct sensation.

The SBMP which exploits spikes themselves is developed to set the pathway i.e. route where the spikes are carried through. Via the control packets of the SBMP, the sensory pathway is alternated according to the owner of the spikes. Besides, we also showed that a priority mechanism can be developed for the proposed technique.

We evaluated the performance of the proposed protocol by simulations under various scenarios. We also examined the similarity between the input and the output spike firing patterns either the RNs have the equal priority or different priorities are given to the RNs. The test results indicate that the input and output spike patterns have similar properties. Furthermore, we compared the input inter-spike interval distribution (inter-spike interval times of the RNs) and output inter-spike interval distribution (inter-spike interval times at the demultiplexer unit) when the various priority values are assigned to the RNs. As the priority value assigned to the RN is increased, the output inter-spike interval distribution of the related RN converges to the input inter-spike interval distribution of the RN. Hence, the priority value can be used as a quality of service parameter for SBMP.

We also compared the performance of SBMP with the performance of proposed techniques introduced in Chapter 3 and Chapter 4. As well as the significant performance improvement of SBMP, it has lower implementation complexity than the previously introduced techniques.

ICT inspired techniques like the SBMP, reveal new opportunities in neural communication and may pave the way for the advancement of treatment techniques for neural diseases.

6. CONCLUSIONS AND RECOMMENDATIONS

Although nanonetworking is in its infancy, wide range of appealing application areas especially in human healthcare field draw the attention of the scientific communities from various disciplines. Human body intrinsically houses different kinds of intra-body nanonetworks. We perceive the external world by the somatosensory system that is an important branch of sensory nervous nanonetwork. In this study, we investigate the somatosensory system in detail and explore the analogies between the conventional communication networks. By this in-body nanonetwork, perceived stimulus is converted into spike trains via the receptor neurons (RNs) distributed topographically throughout our body and conveyed to the somatosensory cortex. The somatosensory system has below three characteristics:

1. The information flow in this nanonetwork is one-way, from the RNs to the somatosensory cortex in the brain

2. There exist dedicated neural pathways between the RNs and the somatosensory cortex.

3. The spikes generated by RNs are identical events and they do not include source and destination addressing information.

With these major features, the somatosensory system resembles the circuit switching networks. Communication problems such as interruption of spike propagation in this nanonetwork emerge as neurodegenerative diseases in human body. Even though the RNs function properly, a faulty relaying neuron in the sensory pathway hinders the spikes to be delivered to the somatosensory cortex. Therefore, in our studies, we focus on ensuring the continuity of spike propagation in case of neuron specific faults in the signaling pathway. These impairments remind the same problem in the transmission lines of the conventional communication networks. In communication networks, multiplexing methods that combine more than one signal over a shared medium are employed to solve this problem.

In this thesis, we propose three techniques for conveying the spike trains of RNs those have faulty pathways over a functional neighboring pathway by using the above-mentioned analogy. Due to the characteristics of the somatosensory system, our techniques employ neuron specific methods.

For the techniques we propose, our aim is twofold:

- Conveying the spikes of an RN that has faulty pathway through a shared functional pathway.
- Minimizing the number of spikes that can be lost while multiplexing the spikes of RNs in order to feel the correct sensation.

We evaluated the performance of the proposed techniques by simulations under various scenarios. For the evaluation a realistic performance analysis of the proposed system, we employed Neural Simulation Tool (NEST) in order to reflect the electrical and chemical aspects of the neural communication channel. We also compared the obtained results of the proposed techniques with each other.

6.1 Unique Contributions

The proposed techniques in this thesis bring the communication capability between the RNs that have malfunctioning pathways and the somatosensory cortex. In literature, there is no study analogous to our work yet. This thesis may lead to new studies on ICT inspired techniques for the nervous nanonetworks. The obtained results show that the techniques proposed in this thesis may reveal new opportunities in neural communication and may pave the way for the advancement of novel treatment techniques for the neural diseases. Following sections describes our contributions.

- We proposed a neuron specific TDMA based protocol for ensuring the RNs that have the faulty pathway to communicate with the somatosensory system. For sharing the functional pathway between the RNs, we developed a novel multiplexing and buffering mechanism employing the Neural Delay Box (NDB) scheme that is composed of a relay unit and a buffering unit. The relay unit can be realized as a nanoelectronic device. The buffering unit can be implemented either by using neural delay lines as employed in optical switching systems or by using nano scale delay flip flops. The spikes received at the assigned time slot of RNs are directly conveyed to the shared neural pathway by using NDBs. The spikes transmitted at the unassigned time slots are buffered and transmitted at the consecutive assigned time slot. Thus, the spikes are carried through a functional pathway and they can be easily demultiplexed according to the assigned time slots of RNs, thereafter are delivered to corresponding destination in the somatosensory system.

- We introduced a neuron specific statistical multiplexing based technique to establish the communication between an RN and somatosensory cortex in case of intermediate neuron failure in its own sensory pathway. The proposed technique utilizes the multiplexer and the demultiplexer units that can be realized as nanoelectronic devices and an addressing scheme. To employ statistical multiplexing, the spikes of each transmitting RNs must be distinguished at the demultiplexer unit before conveying them to the related part of the somatosensory cortex. Hence, we introduced an addressing scheme to identify the transmitting RNs by using the spikes themselves. Actually, we established a packet switching neural nanonetwork by employing this addressing scheme. Furthermore, we showed that a priority mechanism can be developed for the proposed technique. We also examined the similarity between the input spike generation times (spike times of the RNs) and the output spike generation times (spike times at the demultiplexer unit). Test results demonstrate that the input and output spike patterns have similar properties.

- We proposed the Switch Based Multiplexing Protocol (SBMP) to substitute a faulty sensory neural pathway with a functional neighboring pathway. The proposed multiplexing protocol depends on the multiplexer and demultiplexer units that can be realized as nanoelectronic devices. The spiking activity between these units is regulated by the SBMP. The SBMP is developed to set the pathway i.e. route where the spikes are carried through. The SBMP uses some control packets that exploits spikes themselves to manage the spike traffic. Via the control packets of the SBMP, the sensory pathway is alternated according to the owner of the spike to deliver the spike to the corresponding part of the somatosensory cortex. Besides, we also showed that a priority mechanism can be developed for the proposed technique. We also examined the similarity between the input and the output spike firing patterns when the RNs have either the equal priority or different priorities. The test results demonstrate that the input and output spike patterns have similar properties. Furthermore, we compared the input inter-spike interval distribution (inter-spike interval times of the RNs) and output inter-spike interval distribution (inter-spike interval times at the demultiplexer unit) when the equal or various priorities are assigned to the RNs. We observed that as the priority value assigned to the RN is increased, the output inter-spike interval distribution of the related RN converges to the input inter-spike distribution of the RN. Therefore, the priority value can be used as a quality of service parameter for the SBMP.

6.2 Future Work

As the future work, we plan to study on following topics in our research field.

- In this thesis, we focused on single RN based somatic sensations. Apart from the single RN based sensations, some stimuli i.e. touching the texture of an object activate combination of RNs. The performance of the proposed techniques can be examined over the coordinated sensory information of the multiple RNs that have malfunctioning pathways. The proposed techniques can be improved or new communication techniques can be developed to feel the correct sensation across the perceptions via combinations of RNs.

- In literature, Poisson and Pareto distribution is frequently used to model the spike trains generated by neurons [38]. Although, they well captures the statistical properties of the real neural spike trains, there is no information for the real somatic sensations including the spike trains with inter-spike interval data. If the real spike firing patterns (spike trains with inter-spike intervals) for the exact somatic sensations such as itch, pain, warmth and cold can be determined via in vivo experiments, the performance of the proposed techniques can be examined in detail by using these real spike firing patterns.

- By using the above-mentioned real spike firing patterns, a database for somatic sensations can be formed. This database can be loaded to the multiplexer and the demultiplexer units. Instead of transferring as many as possible spikes between these nanoelectronic devises, smarter coding strategies can be designed. For instance, when the multiplexer unit receives a spike train that fits a somatic sensation in the database, it encodes this perception in a smarter way i.e. encoding it with lower number of spikes. The demultiplexer decodes this code by using the database, generates the same spike train for the encoded stimulus, and relays it to the somatosensory cortex. By using the somatic database, according to the type of the perceptions novel priority mechanisms can also be devised.

REFERENCES

[1] **Malak, D., and Akan, O. B.** (2012). Molecular communication nanonetworks inside human body, *Elsevier Nano Communication Networks, 3*(1), 19-35.

[2] **Kandel, E. R., Schwartz, J. H., and Jessell, T. M.** (2012). *Principles of neural science,* New York : McGraw-Hill.

[3] **Xiaomin, L., and Mark, B.L.** (2004). Performance modeling of optical-burst switching with fiber delay lines, *IEEE Transactions on Communications, 52*(12), 2175–2183.

[4] **Li, L., Scott, S.D., and Deogun, J.S.** (2003). A novel fiber delay line buffering architecture for optical packet switching. In *GLOBECOM'03. Proceedings of the IEEE Global Telecommunications Conference*, (pp. 2809-2813). USA : San Francisco, December 1-5.

[5] **Tezcan, H., Oktug, S., and Kok, F. N.** (2012). Neural delay lines for TDMA based molecular communication in neural networks. In *ICC. Proceedings of the IEEE International Conference on Communications*, (pp. 6209-6213). Canada : Ottawa, June 10-15.

[6] **Tezcan, H., Oktug, S., and Kok, F. N.** (2015). Employing TDMA protocol in neural nanonetworks in case of neuron specific faults, *IEEE Transactions on NanoBioscience, 14*(6), 572-580.

[7] **Tezcan, H., Oktug, S., and Kok, F. N.** (2014). Statistical multiplexing for neural nanonetworks in case of neuron specific faults. In *ICUMT. Proceedings of the IEEE 6th International Congress on Ultra Modern Telecommunications and Control Systems and Workshops,* (pp. 254-259). Russia : Petersburg, October 6-8.

[8] **Tezcan, H., Oktug, S., and Kok, F. N.** (2015). Switch based multiplexing protocol for neural nanonetworks in case of neuron specific faults, *IET Nanobiotechnology*, submitted for publication.

[9] **Akyildiz, I. F., Brunetti, F., and Blazquez, C.** (2008). Nanonetworks: a new communication paradigm, *Elsevier Computer Networks, 52*(12), 2260–2279.

[10] **Eric, D. K., Peterson, C., and Pergamit, G.** (2003). *Unbounding the future: the nanotechnology revolution*. New York : Quill Books.

[11] **Sole, R. V, Munteanu, A., Rodriguez-Caso, C. and Macía, J.** (2007). Synthetic protocell biology: from reproduction to computation, *Philosophical Transactions of the Royal Society B: Biological Sciences, 362*(1486), 1727-1739.

[12] **Galluccio L.,** et al. (2013). Characterization of molecular communications among implantable biomedical neuro-inspired nanodevices, *Elsevier Nano Communication Networks, 4*(2), 53-64.

[13] **Suda, T., Moore, M., Nakano, T., Egashira, R. and Enomoto, A.** (2005). Exploratory research on molecular communication between nano-machines. In *GECCO*. *Proceedings of the Genetic and Evolutionary Computation Conference*, (p.25). USA : Washington, D.C., June 25-29.

[14] **Alfano, G. and Miorandi, D.** (2006). On Information Transmission among Nanomachines. In *Nano-Net'06*. *Proceedings of the 1st International Conference on Nano-Networks and Workshops,* (pp. 1-5). Switzerland : Lausanne, September 14-16.

[15] **Piro, G., Boggia, G., and Grieco, L. A.** (2015). On the design of an energy-harvesting protocol stack for Body Area Nano-NETworks, *Elsevier Nano Communication Networks, 6*(2), 74-84.

[16] **Dressler, F., and Fischer, S.** (2015). Connecting in-body nano communication with body area networks: Challenges and opportunities of the Internet of Nano Things, *Elsevier Nano Communication Networks, 6*(2), 29-38.

[17] **Nakano, T., Eckford, W. A. and Haraguchi, T.** (2013). *Molecular communication.* United Kingdom : Cambridge University Press.

[18] **Nakano, T., and Liu, J. Q.** (2009). Information transfer through calcium signaling, Lecture Notes of the Institute for Computer Sciences, In *Social Informatics and Telecommunications Engineering* (Vol. 20, Chapter 4, pp. 29-33). Springer, Berlin Heidelberg.

[19] **Parcerisa, L. and Akyildiz, I. F.** (2009). Molecular communication options for long range nanonetworks, *Elsevier Computer Networks, 53*(16), 2753-2766.

[20] **Moore, M.,** et al. (2006). A design of a molecular communication system for nanomachines using molecular motors. In *PerCom Workshops*. *Proceedings of the Annual IEEE International Conference on Pervasive Computing and Communications Workshops*, (pp. 559-564). Italy : Pisa, March 13-17.

[21] **Nakano T.,** et al. (2005). Molecular communication for nanomachines using intercellular calcium signaling. In *Nanotechnology. Proceedings of the 5th IEEE Conference on Nanotechnology*, (pp. 478 - 481). Japan : Nagoya, July 11-15.

[22] **Gregori, M. and Akyildiz, I. F.** (2010). A new nanonetwork architecture using flagellated bacteria and catalytic nanomotors, *IEEE Journal on Selected Areas in Communications, 28*(4), 612-619.

[23] **Abadal, S. and Akyildiz, I. F.** (2011). Automata modeling of quorum sensing for nanocommunication networks, *Elsevier Nano Communication Networks, 2*(1), 74-83.

[24] **Lio, P. and Balasubramaniam, S.** (2012). Opportunistic routing through conjugation in bacteria communication nanonetwork, *Elsevier Nano Communication Networks, 3*(1), 36-45.

[25] **Bai, C., Leeson, M. S., and Higgins, M. D.** (2015). Performance of SW-ARQ in bacterial quorum communications, *Elsevier Nano Communication Networks, 6*(1), 3-14.

[26] **Balasubramaniam, S.,** et al. (2011). Development of artificial neuronal networks for molecular communication, *Elsevier Nano Communication Networks, 2*(2-3), 150-160.

[27] **Url-27** http://hyperphysics.phy-astr.gsu.edu/hbase/biology/nervecell.html, date retrieved 12.01.2014.

[28] **Kandel, E. R.** et al. (2000). *The Neural Basis of Cognition, in Principles of Neural Science* (4th ed., pp. 412-428). New York: McGraw-Hill.

[29] **Galluccio, L., Palazzo, S., and Santagati, G. E.** (2011). Modeling signal propagation in nanomachine-to-neuron communications, *Elsevier Nano Communication Networks, 2*(4), 213-222.

[30] **Malak, D., Kocaoglu, M. and Akan, O. B.** (2013). Communication theoretic analysis of the synaptic channel for cortical neurons, *Elsevier Nano Communication Networks, 4*(3),131-141.

[31] **Malak, D., and Akan, O. B.** (2014). Communication theoretical understanding of intra-body nervous nanonetworks, *IEEE Communications Magazine, 52*(4),129-135.

[32] **Veletic, M., Balasingham, I. and Babic, Z.** (2013). On spectrum analysis for nanomachine-to-neuron communications. In *BlackSeaCom. Proceedings of the IEEE First International Black Sea Conference on Networking,* (pp. 64-68). Georgia : Batumi, July 3-5.

[33] **Mesiti, F. and Balasingham, I.** (2013).Nanomachine-to-neuron communication interfaces for neuronal stimulation at nanoscale. *IEEE Journal on Selected Areas in Communications, 31*(12), 695-704.

[34] **Mesiti, F., Floorb, P. A., Kim, A. N. and Balasingham, I.** (2012). On the modeling and analysis of the RF exposure on biological systems: a potential treatment strategy for neurodegenerative diseases, *Elsevier Computer Networks, 3*(2), 103-115.

[35] **Balevi, E. and Akan, O. B.** (2013). A physical channel model for nanoscale neuro-spike communications, *IEEE Transactions on Communications, 61*(3), 1178-1187.

[36] **Ray, P. P.** (2012). Nano computer design based on intra body nanoscale neuro-spike communication: a nanonetwork paradigm. In *CODIS. Proceedings of the IEEE International Conference on Communications, Devices and Intelligent Systems,* (pp. 306-309). India : Kolkata, December 28-29.

[37] **Ray, P. P.** (2013). Channel modeling of human somatosensory nanonetwork: body discriminative touch and proprioception perspective, *International Journal on Comptuter Science and Engineering, 5*(10), 874-884.

[38] **Wallisch, P., Lusignan, M. E., Benayoun, M. D., Baker, T. I., Dickey, A. S., and Hatsopoulos, N. G.** (2014). *MATLAB for neuroscientists: an introduction to scientific computing in MATLAB.* San Diego, CA. : Academic Press.

[39] **Perl, E. R.** (1968). Myelinated afferent fibres innervating the primate skin and their response to noxious stimuli, *The Journal of Physiology, 197*(3), 593-615.

[40] **Gewaltig M. O. and Diesmann M.** (2007). NEST (Neural Simulation Tool), *Scholarpedia, 2*(4), 1430.

[41] **Hatsopoulos, N. G., and Donoghue, J. P.** (2009). The science of neural interface systems, *Annual review of neuroscience, 32,* 249-266.

[42] **Patolsky, F.,** et al. (2006). Detection, stimulation, and inhibition of neuronal signals with high-density nanowire transistor arrays, *Science, 313*(5790), 1100-1104.

[43] **Windhorst U. and Johansson H.** (1999). Electrical activity of individual neurons in situ: extra and intracellular, In *Modern Techniques in Neuroscience Research* (pp. 127-172). Springer, Berlin Heidelberg.

[44] **Taketani, M. and Baudr, M.** (2006). *Advances in network electrophysiology using multi-electrode array*s. Springer, New York.

[45] **Berdondini L.**, et al. (2001). High-density microelectrode arrays for electrophysiological activity imaging of neuronal networks. In *ICECS. Proceedings of the 8th IEEE International Conference on Electronics, Circuits and Systems,* (pp. 1239-1242). Malta, September 02-05.

[46] **Cohen-Karni, T., Timko, B. P., Weiss, L. E., and Lieber, C. M.** (2009). Flexible electrical recording from cells using nanowire transistor arrays, *The National Academy of Sciences, 106*(18), 7309-7313.

[47] **Qing, Q., Pal, S. K., Tian, B., Duan, X., Timko, B. P., Cohen-Karni, T.,and Lieber, C. M.** (2010). Nanowire transistor arrays for mapping neural circuits in acute brain slices, *The National Academy of Sciences, 107*(5), 1882-1887.

[48] **Zhang, H., Yu, M., Xie, L., Jin, L., and Yu, Z.** (2012). Carbon-nanofibers-based micro-/nanodevices for neural-electrical and neural-chemical interfaces, *Journal of Nanomaterials, 2012*(6).

[49] **Edward Jr, D.,** et al. (2009). High efficient electrical stimulation of hippocampal slices with vertically aligned carbon nanofiber microbrush array, *Biomedical microdevices, 11*(4), 801-808.

[50] **Yu, Z.,** et al. (2010). Vertically aligned carbon nanofibre neural chip for interfacing with neurological system. In *NANOMED. Proceedings of the IEEE 4th International Conference on Nano/Molecular Medicine and Engineering,* (pp. 188-191). Hong Kong : Macau, December 5-9.

[51] **Koehne, J. E.,** et al. (2011). Carbon nanofiber electrode array for electrochemical detection of dopamine using fast scan cyclic voltammetry, *Analyst, 136*(9), 1802–1805.

[52] **Zhao X.,** et al. (2010). A single carbon fiber microelectrode with branching carbon nanotubes for bioelectrochemical processes, *Biosensors and Bioelectronics, 25*(10), 2343–2350.

[53] **Lovat, V.**, et al. (2005). Carbon nanotube substrates boost neuronal electrical signaling, *Nano Letters, 5*(6), 1107–1110.

[54] **Mazzatenta, A.,** et al. (2007). Interfacing neurons with carbon nanotubes: electrical signal transfer and synaptic stimulation in cultured brain circuits, *Journal of Neuroscience, 27*(26), 6931-6936.

[55] **Stallings, W.** (2002). *Wireless communications and networks*. New Jersey : Prentice Hall.

[56] **Leon-Garcia, A., and Widjaja, I.** (2000). *Communication networks: fundamental concepts and key architectures.* New York : Mc GrawHill.

[57] **Dayan, P., and Abbott, L. F.** (2001). *Theoretical Neuroscience Computational and Mathematical Modeling of Neural Systems.* Massachusetts : MIT Press.

[58] **Mitin, V. V., Kochelap,V. A., and Stroscio, M. A.** (2008). *Introduction to nanoelectronics: science, nanotechnology, engineering, and applications.* New York : Cambridge University Press.

[59] **Gordon, J.** (1995). Pareto process as a model of self-similar packet traffic. In *GLOBECOM'95. Proceedings of the IEEE Global Telecommunications Conference,* (pp. 2232-2236). Singapore, November 14-16.

[60] **Url-60** <https://en.wikipedia.org/wiki/Kolmogorov%E2%80%93Smirnov_test>, date retrieved 12.06.2015.

[61] **Url-61** <http://www.itl.nist.gov/div898/handbook/eda/section3/probplot.htm>, date retrieved 02.02.2015.

[62] **Burkitt, A. N.**, (2006). A review of the integrate-and-fire neuron model: I. homogeneous synaptic input, *Biological Cybernetics, 95*(1), 1-19.

[63] **Vogels T.,** et al. (2005). Neural network dynamics, *Annual Reviews Neuroscience, 28*(1), 357-376.

APPENDICES

APPENDIX A: Simulation Setup

APPENDIX A : Simulation Setup

In our studies, we employ Neural Simulation Tool (NEST) [40] in order to reflect the electrical and chemical aspects of the neuro-spike communication channel. NEST is a simulator for spiking neural network models that focuses on the dynamics, size and structure of neural systems.

Different neuron models are provided in NEST. In our experiments, we used integrate-and-fire neuron model which can be used for the simulation of somatosensory system [62,63]. The neuron that we have simulated has generic parameters. Whenever the membrane potential of the neuron reaches the firing threshold potential at -55mV, the neuron spikes and the membrane potential is reset to -70mV that is the reset potential. Thereafter, the membrane potential is then clamped to the resting value for 1 ms, the ARP of the neuron. After the ARP, the membrane continues to depolarize due to the continuing input stimulation.

For the evaluation of a realistic performance analysis of the proposed system, we also applied Gaussian noise factor to simulation environment to model the axonal and synaptic noise in the neuro-spike communication channel.

The simulation setup is given in Table A.1.

Table A.1 : Simulation setup.

Type	**Description**
Neuron Model	Integrate-and-fire, fixed voltage threshold, fixed ARP
Synapse model	Static Synapse
Refractory period t_{rp}	1 ms
Firing threshold V_{th}	-55 mV
Membrane capacitance C_m	250 pF
Resting potential V_E	-70 mV
Reset potential V_{reset}	-70 mV
Synaptic delay D	1.0 ms
Noise	Gaussian (mean 300 pA standard deviation 150 pA)

CURRICULUM VITAE

Name Surname: Hakan Tezcan

Place and Date of Birth: Artvin 1975

E-Mail: tezcanha@itu.edu.tr

EDUCATION:

B.Sc.: Control Systems Engineering, Turkish Naval Academy

M.Sc.: Computer Science, Naval Science and Engineering Institute of Turkish Naval Academy

PROFESSIONAL EXPERIENCE AND REWARDS:

- Network/System Engineer in Aksaz Naval Base
- System Support and Execution Officer in Atatürk Wargaming and Simulation Center
- Software engineer, Turkish Navy Research Command
- Software engineer, R&D Division, Technical Directorate of Turkish Navy HQ.

PUBLICATIONS, PRESENTATIONS AND PATENTS ON THE THESIS:

▪ **Tezcan H.**, Oktug S., and Kok F.N. (2012). Neural delay lines for TDMA based molecular communication in neural networks. In *ICC. Proceedings of the IEEE International Conference on Communications*, (pp. 6209-6213). Canada : Ottawa, June 10-15.

▪ **Tezcan H.**, Oktug S., and Kok F.N. (2014). Statistical multiplexing for neural nanonetworks in case of neuron specific faults. In *ICUMT*. *Proceedings of the IEEE 6th International Congress on Ultra Modern Telecommunications and Control Systems and Workshops,* (pp. 254-259). Russia : Petersburg, October 6-8.

▪ **Tezcan H.**, Oktug S., and Kok F.N. (2015). Employing TDMA protocol in neural nanonetworks in case of neuron specific faults, *IEEE Transactions on NanoBioscience, 14*(6), 572-580.

▪ **Tezcan H.**, Oktug S., and Kok F.N. (2015). Switch based multiplexing protocol for neural nanonetworks in case of neuron specific faults, *IET Nanobiotechnology*, submitted for publication.

▪ **Tezcan H.,** Oktug S., and Kok F.N. (2013). Nano Ağlar: Nanorobotlar birbirleriyle nasıl konuşur?, *İTÜ Vakfı Dergisi*, *61*, 14-16.

OTHER PUBLICATIONS, PRESENTATIONS AND PATENTS :

- **Tezcan H.**, Cayirci E., and Coskun V. (2004). A distributed scheme for 3D space coverage in tactical underwater sensor networks. In *MILCOM'04. Proceedings of the IEEE Military Communications Conference,* (pp. 697-703). US : Monterey, CA., 31 October -3 November.

- Cayirci E., **Tezcan H**., Dogan Y., and Coskun V. (2006). Wireless sensor networks for underwater surveillance systems. *Elsevier Ad Hoc Networks*, *4*(4), 431-446.

- Oktug S., Khalilov A., and **Tezcan H.** (2008). 3D coverage analysis under heterogeneous deployment strategies in wireless sensor networks. In *AICT'08. Proceedings of the Fourth Advanced International Conference on Telecommunications*, (pp. 199-204). Greece : Athens, June 8-13.

- Oktug S., Khalilov A., and **Tezcan H.** (2008). The effects of terrain types on 3D coverage under heterogeneous deployment strategies in Wireless Sensor Networks. In *ISCIS'08. Proceedings of the 23rd International Symposium on Computer and Information Sciences,* (pp. 1-6). Turkey : Istanbul, October 27-29.