Identification and Significance of the Problem or Opportunity

CroftSoft Inc proposes to develop software to train military persons with upper or lower extremity limb loss to use peripheral nerve signals to control a prosthetic limb. This effort will be in collaboration with the University of Texas at Dallas (UTD) to provide a software interface to their novel wireless peripheral nerve interface hardware technology including the peripheral interface nerve guide (PING) and the neuro-micro-transponder (NeμT). The software will provide real-time visual and auditory biofeedback to persons learning to control a prosthetic using the PING implants. Customization features will permit the simulation of existing prosthetic limbs as well as virtual precursors with fine control of the individual digits of a hand.

Brain-Machine Interfaces

In 1982, Georgopoulos and his colleagues (see Krakauer 2000) first demonstrated the correlation between the direction of arm movements and the simultaneously recorded spiking activity in the primary motor cortex (MI) of monkeys. Chapin and his colleagues (Chapin 1999) built upon this discovery by demonstrating that spike signals recorded simultaneously from many MI neurons in rats could be processed in real-time such that rats could directly move a robotic arm using brain activity alone. Several investigators have subsequently demonstrated the feasibility of using MI cortical brain activity for the real-time control robotic arms or computer cursors moving in three dimensions in monkeys (Taylor 2002, 2003; Tillery 2003) and even human subjects.

Peripheral Nerve Interfaces

As a member of the NeuroEngineering Laboratory headed by Dr. Lawrence J. Cauller, the Principal Investigator is interested in the long-term objective of contributing to and commercializing research related to the recently awarded grant "Neuro-micro-Transponders: Wireless Neural Control of Artificial Arms and Hands". This research differs from previous efforts in that spike activity from peripheral nerves, rather than intracranial cortical neurons, will be used as the input to the control system. The ultimate objective is to enable amputees to control prosthetic arms and hands using signals from the peripheral nerves that remain in the stumps of amputated arms. By all accounts, a peripheral control system is far more medically acceptable than the intracranial systems described above and may even provide a superior neuroprosthesis for spinal cord patients, the major application proposed for the intracranial systems. If it becomes possible to obtain these peripheral neural control signals without damaging the nerves, additional applications abound, including physical enhancement or human/robot integration (Dhillon 2004).

While the use of peripheral nerve may be more medically acceptable, this new technology faces significant challenges before peripheral nerve signals may be harnessed for such a control system. This project will tackle one of these challenges. Cortical brain signals correlate with high level features of movement related to the subject's intention such as which way to move or which object to grasp. In contrast, peripheral nerve spikes are bottom level signals for the control of individual muscle units. This requires a new approach to the design of a control system which must transform the temporal sequence of spike impulses from a variety of fibers into a set of analog signals for the control of the actuators or motors that move the limb.

Each approach to a neuromotor prosthetic (NMP) device requires an integrated system (Serruya 2004). The Neuroprosthetic Training Software will provide a crucial component of the PING system.

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Phase I Technical Objectives

The Phase I technical objectives include developing a software interface to the PING hardware and developing auditory and visual biofeedback training software.

Hardware Interface Library

The first technical objective is to create a software interface to the PING hardware. Dr. Cauller, the research institution point of contact, has developed custom hardware and software processes to extract and record the signal from the PINGs. Mr. Croft, the principal investigator, will work with Dr. Cauller to develop a reusable real-time PING hardware interface software library so that the signals can be used in a variety of applications, including the auditory and visual biofeedback training software.

Auditory Biofeedback Software

Once the real-time hardware interface library is developed, the second technical objective will be to develop biofeedback training software. As Dr. Cauller has successfully demonstrated recording signals from an amputated peripheral nerve in the leg of a rat, the first iteration will focus on generating a mode of real-time feedback that this species can reliably detect. For this purpose we propose to test auditory feedback in the form of tones with the pitch proportional to the PING spike frequency.

The experimental methods are divided into two phases. The first phase is the initial training protocol in which the rats learn to control the audio speaker manually. The second phase, the closed-loop control training, begins with the implantation of the PING recording electrodes and ends with the direct peripheral nerve control of the audio speakers.

Initial Training Protocol

A rat will be placed in a cage with a water dispenser, an exercise wheel, a food pellet dispenser, an audio speaker, and a manipulandum such as an analog slider switch or a spring-loaded lever (Figure 1). The rat will have unlimited access to the water dispenser and the exercise wheel. A computer will control the release of food pellets from the food pellet dispenser. The computer will also control the audio speaker and monitor the position of the manipulandum.

The computer will be programmed to play a target tone on the speaker at periodic feeding times. As rats are nocturnal, these feeding times will be scheduled during the night.

At the beginning of each feeding time, the frequency of the target tone will be randomly selected from a fixed frequency range. The fixed frequency range will be selected to fall within the overlap of the normal hearing range of both rats and humans. The frequency of the target tone, once randomly selected, will be held constant during play.

The duration of this initial target tone will be three seconds (3 s). For a five minute (5 min.) period immediately following the target tone, any movement of the manipulandum will initiate play of a new controlled tone. Unlike the target tone, the frequency of the controlled tone may be varied during play and will be determined by the current position of the manipulandum.

If at any time the frequency of the controlled tone falls within a frequency window centered about the target tone frequency, the controlled tone will terminate and a food pellet will be dispensed immediately. This will reward the rat for adjusting the frequency of the controlled tone to match the frequency of the target tone by moving the manipulandum.

Initially the frequency window will be broad so that any movement of the manipulandum whatsoever will result in a food pellet reward. The frequency window will be gradually reduced so that the rat must deliberately adjust the control frequency to approach the target frequency.

If the rat fails to adjust the control frequency to match the target frequency within the five minute period following the play of the target tone, the control tone will terminate automatically and a food pellet will be dispensed to prevent starvation. Rats that learn to use the manipulandum will be able to receive their food pellet up to five minutes sooner than untrained rats.

Rats will be manually weighed and visually inspected on a daily basis. The recorded weights will be logged and plotted over time to ensure that the rats are receiving adequate nutrition. Any behavioral anomalies will be noted and investigated.

Maintenance of the cages will be performed daily. The levels of water and food pellets in the dispensers will be monitored to ensure that they falling at the expected rates. Failure of the levels to fall as predicted may indicate an obstruction or an automated control problem.

Closed-loop Control Training

Closed-loop control training begins with the chronic installation of PING implants on a peripheral nerve of the rat. The PING electrodes will record the spikes based on the voltage fluctuations in the extracellular space corresponding to the firing of individual neurons. Each electrode, although spaced at reasonable distances from its neighboring electrodes, will record many of the same spiking events nearly simultaneously (Takahashi 2003). The situation is analogous to two or more microphones placed in a room full of individuals speaking over each other. The challenge is to distinguish the voice of a single speaker as recorded from multiple microphones with varying delays. Independent Component Analysis (ICA), a relatively new data analysis technique, solves this problem by exploiting the statistical independence of the signals from the individual speakers (Hyvarinen 2001). ICA will be used to isolate individual neuron spiking events from the mixed signal recorded by the multichannel electrodes.

The firing frequencies of the individual neurons will be measured and correlated with the tone frequency played by the audio speaker. In an offline analysis, a simple artificial neural network (ANN), a single-layer perceptron (Hertz 1991), will be trained to predict the audio speaker frequency based on the current firing frequencies of the recorded neurons. Except for a non-linearity in the final stage of processing, using a single-layer perceptron is roughly equivalent to a mathematical operation variously described as the dot product, inner product, projection, or vector angle cosine (Taylor 2002).

The input to the perceptron will be the firing frequencies of the neurons as converted to z-scores (Triola 1998) where the means will be set to the baseline firing frequency of each neuron. After successful offline training of the perceptron, the synaptic weights will be fixed.

Thereafter, control of the auditory tone will be divided between the manipulandum position and the output of the perceptron as driven by the real-time signal from the multichannel electrodes. Initially, the manipulandum position will receive the majority of the control weighting. The weighting of the perceptron will be gradually increased at a rate that is slow enough for the rat to adapt. Eventually control will be based solely on the cortical-driven perceptron with no input from the manipulandum.

Visual Biofeedback Software

The next mode of feedback will be visual for use in monkeys and humans. In previous work, Mr. Croft has developed a 2D visual training task using simulated PING input, as described below in the section on “Related Work”. Other researchers in the field of brain-machine interface (BMI) technology have used 3D cursors for training monkeys. We will develop a 3D virtual prosthetic limb with joints controlled in real-time from signals coming from the PINGs. The simulation will be validated against the operation of a non-virtual robotic arm. We will also examine using a combination of both auditory and visual feedback.

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- Triola MF (1998) Elementary Statistics, 7th Ed., p92. Reading, Massachusetts: Addison Wesley Longman.

Phase I Work Plan

As the principal investigator, Mr. Croft will focus on software development. Dr. Cauller will assist Mr. Croft in creating an interface to the PING hardware. Additionally, a 3D animator will be employed to create realistic 3D models of prosthetic limbs with simulated joints that can be controlled by the biofeedback software.

The first two months of the six-month project will be dedicated to creating the real-time hardware interface library. The third month will focus on the auditory feedback system and the last three months will focus on the visual (Figure 1). Mr. Croft and Dr. Cauller will be employed on the project for all six months and the 3D animator will begin in the fourth month.

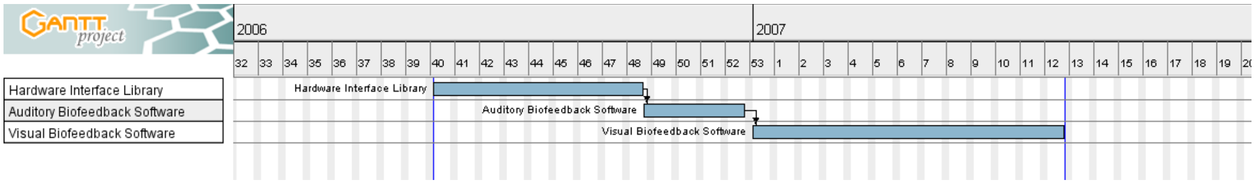

Figure 1. Work Plan

In the event of a schedule slip, the Visual Biofeedback Software and the hiring of the 3D animator will be postponed to Phase II.

Related Work

Dr. Cauller and Mr. Croft are actively engaged in related work on the development of the peripheral interface nerve guide (PING) hardware and software for training and assessment in virtual environments.

PING Hardware

Dr. Cauller is an inventor of the patent pending peripheral interface nerve guide (PING)[1]. He is a Co-Principal Investigator of the grant "Neuro-micro-Transponders: Wireless Neural Control of Artificial Arms and Hands", originally part of the DARPA Defense Sciences Office (DSO) Human-Assisted Neural Devices (HAND) Program[2]. This grant is being phased into the DARPA Defense Sciences Office (DSO) Revolutionizing Prosthetics Program[3]. The approach of the research of Dr. Cauller is unique within the overall program in that it is wireless, records from peripheral nerves, and guides nerves to grow into contact with the electrodes. In contrast, other approaches use wired electrodes which are inserted into cortex and extend through an opening in the skull.

Training and Assessment Software

As a doctoral student in Dr. Cauller's NeuroEngineering Lab, Mr. Croft developed a real-time software simulation of peripheral nerve spiking activity, CroftSoft Newt Cyborg (Figure 2). The task to be learned by the user was to use a joystick to generate simulated spiking activity in order to move a cursor to a target and hold it on the target for three seconds. The software and documentation is available for download[4].

Spike signals from individual axons may lack the information content, or be too noisy for adequate limb control. The CroftSoft Newt Cyborg project addressed the problem with simulation software that transformed artificial spike signals generated under the control of a joystick into movement commands that controlled the position of a virtual limb. User control of the joystick in this simulation corresponds to the amputee's intended movements, and the artificial spike signals correspond to those which would be transmitted through peripheral nerves in the amputated stump where they are detected and transformed into limb movements. By providing immediate feedback, the accuracy and responsiveness of the control system was be evaluated with respect to a range of spike signal properties. In addition, the project provided a testing platform for alternative transform algorithms. This software served as an initial prototype of a training simulator to prepare amputees for artificial limb control.

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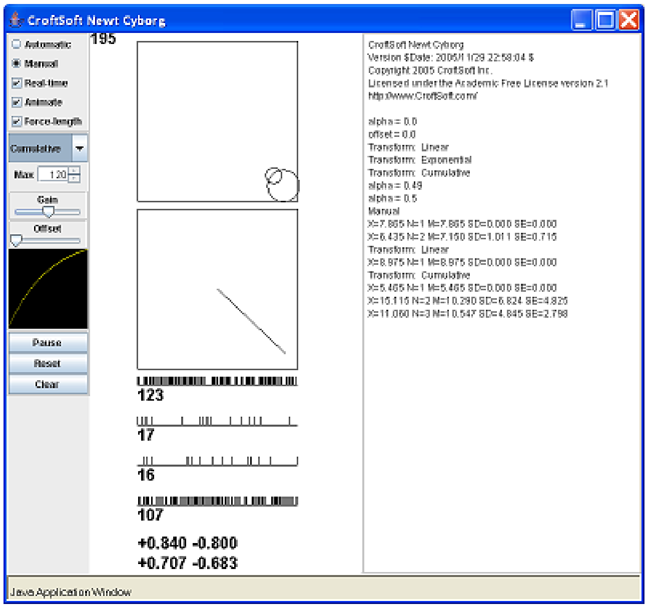
[1] U.S. Patent Application 20050137652, http://www.utdallas.edu/~lcauller/NElabs/NEindex.html

[2] http://www.darpa.mil/dso/thrust/biosci/hand.htm

[3] http://www.darpa.mil/dso/thrust/biosci/revprost.htm

[4] http://www.CroftSoft.com/library/software/newt/



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CroftSoft Newt Cyborg
Version $Date: 2005/11/29 22:58:04 $
Copyright 2005 CroftSoft Inc.
Licensed under the Academic Free License version 2.1
http://www.CroftSoft.com/

alpha = 0.0
offset = 0.0
Transform:  Linear
Transform:  Exponential
Transform:  Cumulative
alpha = 0.49
alpha = 0.5
Manual
X=7.885 N=1 M=7.885 SD=0.000 SE=0.000
X=6.435 N=2 M=7.160 SD=1.011 SE=0.715
Transform:  Linear
X=8.975 N=1 M=8.975 SD=0.000 SE=0.000
Transform:  Cumulative
X=5.465 N=1 M=5.465 SD=0.000 SE=0.000
X=15.115 N=2 M=10.290 SD=6.824 SE=4.825
X=11.060 N=3 M=10.547 SD=4.845 SE=2.798
```

Figure 2: CroftSoft Newt Cyborg

Mr. Croft is also the lead Software Developer on the National Institute of Standards and Technology (NIST) Advanced Technologies Program (ATP) grant "Peer-to-Peer Virtual Reality Learning Environments"[5]. As part of this effort to provide teachers and students with zero-cost, royalty-free software for creating immersive training simulations, Mr. Croft has authored Whoola Cyberspace, a virtual reality web browser with fly-through hyperlinks (Figure 3)[6]. The 3D scene graph can be updated using network messages to initiate and terminate animation. This Open Source application is based on non-proprietary and open standards such as COLLADA, HTTP, Java, OpenGL, and XML.

An earlier prototype, Whoola Dock, demonstrates the use of automated assessment in a virtual training environment (Figure 4). Event messages generated by movements controlled by the students in the virtual space are monitored by a software agent. The agent assesses the performance of the student in a given task or progress toward a goal. It provides text and verbal feedback using an Open Source text-to-speech (TTS) engine.

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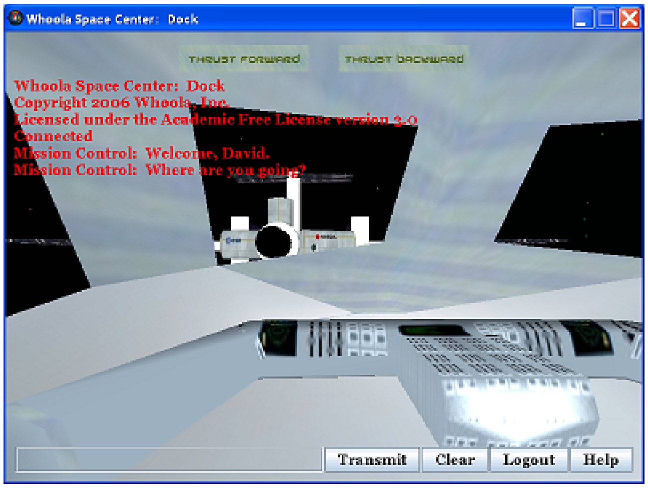
[5] http://jazz.nist.gov/atpcf/prjbriefs/prjbrief.cfm?ProjectNumber=00-00-5541

[6] http://earth.whoola.com:8080/space/

Figure 3: Whoola Cyberspace



```
Whoola Space Center:  Dock
Copyright 2006 Whoola, Inc.
Licensed under the Academic Free License version 3.0
Connected
Mission Control:  Welcome, David.
Mission Control:  Where are you going?
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Figure 4: Whoola Dock

The proposed neuroprosthetic training software would combine the technologies and reuse the Open Source software libraries developed as part of both CroftSoft Newt Cyborg and Whoola Cyberspace. This would include the quantification of learning as demonstrated in the statistical analysis provided by CroftSoft Newt Cyborg as well as the bot-based assessment and feedback demonstrated in Whoola Dock. Mr. Croft, as the lead Software Developer of these products, would bring his expertise on this related work to the Neuroprosthetic Training Software project.

Relationship with Future Research or Research and Development

If the project is successful, the anticipated results of the proposed approach is the development of a real-time PING hardware interface software library and audio-visual biofeedback training software. The software will be used to train amputees to successfully control the joints of virtual and robotic prosthetic limbs using peripheral nerves signals detected by implanted PINGs.

Commercialization Strategy

CroftSoft Inc will commercialize through publishing, licensing, training, and consulting.

Publishing

CroftSoft derives the majority of its revenue from ad banners embedded in webpages containing online content such as technical tutorials. This content also includes documentation for Open Source code libraries. CroftSoft uses an Open Source development methodology in which software is distributed online via a public repository as it is developed[7]. Third-party software developers are encouraged to reuse the source code under the terms of a highly flexible "academic" Open Source license which permits integration with commercial products. In 2004, Mr. Croft published a book documenting the CroftSoft source code library. In the future, CroftSoft plans to publish tutorials and documentation on the Neuroprosthetic Training Software both online and in print to maximize revenue income.

Licensing

In conjunction with the University of Texas at Dallas (UTD), CroftSoft will pursue patents on training and assessment methodologies in the use peripheral nerve neuroprosthetics. CroftSoft will seek to license these patents to third-party developers.

Training

Once the Neuroprosthetic Training Software is shown to be effective, CroftSoft will train and certify prosthetic therapists in the use of the software. The training courses will certify that the therapists are qualified to introduce patients to the software and initial adjustment period. In-house therapists will be employed by CroftSoft to provide the training to the third-party therapists as well as to work with the patients themselves.

Consulting

CroftSoft will contract with organizations to develop specific enhancements to its software. CroftSoft will also provide expertise on as-needed basis on research related to its patents, software, and the technology in general.

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[7] http://www.croftsoft.com/library/code/

Key Personnel

The key personnel are Mr. David W. Croft, President of CroftSoft Inc, and Dr. Lawrence J. Cauller, Associate Professor at UT Dallas.

David Wallace Croft, M.Sc.

David Wallace Croft is the principal investigator of the proposed experiment and the President of CroftSoft, Inc, the prime contractor. His full résumé is available on the Web[8].

Education

Mr. Croft is pursuing a doctorate in Cognition and Neuroscience within the School of Behavioral and Brain Sciences (BBS) at the University of Texas at Dallas (UTD). He is a student in the NeuroEngineering Laboratory led by Dr. Cauller.

Degrees

- M.Sc. Applied Cognition and Neuroscience (2005), University of Texas at Dallas (UTD)
- M.Sc. Electrical Engineering (1995), California Institute of Technology (Caltech)
- B.Sc. Electrical Engineering (1990), United States Air Force Academy (USAFA)

Honors and Awards

Academic

- 1986 Congressional appointment to United States Air Force Academy (USAFA)
- 1989 Scored perfect 800 on quantitative section of GRE
- 1990 Dean's Honor List, all 8 semesters, USAFA
- 1990 Graduated with Academic Distinction, Top 5%, USAFA
- 1993 Virginia Steele Scott Fellowship, California Institute of Technology (Caltech)

Military

- 1991 National Defense Service Medal
- 1993 Air Force Commendation Medal
- 1997 Promotion to Captain, USAF Inactive Ready Reserve

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[8] http://www.CroftSoft.com/people/david/resume/

Publications

- Mel, B.W., Niebur, E., & Croft, D.W., "When neurons crave regularity and shun cooperativity in their synaptic input stream". In Proc. of the 3rd Joint Symposium on Neural Computation, Caltech and UCSD, 1996.
- Mel, B.W., Niebur, E., & Croft, D.W., "How neurons may respond to temporal structure in their inputs." Proceedings of CNS*96, Computational Neuroscience Meeting, Boston, MA, 1996. In: *Computational Neuroscience: Trends in Research*, 1997, edited by J.M. Bower. New York: Plenum Press, 1997, p. 135-140.
- Croft, David Wallace, *Advanced Java Game Programming*, 558 pages, Apress, 2004.

Professional Talks

- 1995, "An Analog VLSI Depolarizing-Hyperpolarizing Neuron", presented at the kickoff of the NSF Center for Neuromorphic Systems Engineering at the California Institute of Technology.
- 2006, “Real-time Simulation and Processing of Peripheral Nerve Spike Activity”, Dallas Area Neuroscience Group.

Teaching

- 2003 Spring and Fall, Lecturer I, “Computer Game Development”, UTD
- 2004 Spring, Teaching Assistant, “Research Design and Analysis”, UTD

Associations

- American Association for Artificial Intelligence (AAAI), Member
- Society for Neuroscience (SfN), Member

Relevant Employment Experience

In addition to the following government and military research projects, Mr. Croft has years of experience in industry as a Software Developer.

- 1990 Jun - 1993 Oct, Computer Systems Engineer, USAF
  B-2 Combined Test Force, Operational Test and Evaluation
  31st Test and Evaluation Squadron, Edwards A.F.B.
- 1995 Jun - 1996 Jul, Systems Engineer, Tanner Research Inc.
  “Silicon Neural Network Compiler” and “Silicon Cochlea”
  Granting agency: United States Air Force (USAF)
- 1997 May - 1999 Jun, Senior Intelligent Systems Engineer, Analytic Services Inc.
  “Technologies for Identifying Missing Children”

Granting agency: National Institute of Justice (NIJ)

- 2004 May – Present, Software Developer, Whoola Inc.
  "Peer-to-Peer Virtual Reality Learning Environments"
  Granting agency: National Institute of Standards and Technology (NIST)

Research Summary

Mr. Croft's doctoral research within Dr. Cauller's NeuroEngineering Lab is focused on neuroprosthetics. His particular role is the development of the real-time software to convert the signals from the implanted PINGs to the control of the robotic prosthetics. This grant proposal is aligned with his doctoral research thesis.

In addition to his academic studies, Mr. Croft is currently employed by Whoola, Inc. as the lead Software Developer on a research grant to develop peer-to-peer (P2P) virtual reality learning environments with computer-assisted assessment. Whoola Cyberspace, described previously, is a spin-off product of this effort.

Mr. Croft's previous related research by topic includes biologically-plausible learning rules for neuronal networks, computational neuroscience modeling, neuromorphic and artificial neural network (ANN) VLSI chip design, intelligent software agents (ISA), P2P networks, and graphics programming.

Lawrence J. Cauller, Ph.D.

Lawrence J. Cauller is an Associate Professor in the Neuroscience Program at the University of Texas at Dallas (UTD). He obtained a B.S. in Psychology from the University of Utah in 1980, a M.A. in Psychology and Neuroscience from Dalhousie University in 1981 and the Ph.D. in Biological Sciences from the Northeastern Ohio Universities College of Medicine in 1988.

Dr. Cauller is the head of the NeuroEngineering Laboratory at UTD and co-inventor of the peripheral interface nerve guide (PING), patent pending. His resume and further descriptions of his inventions and research are available online[9].

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[9] http://www.utdallas.edu/~lcauller/

Facilities/Equipment

The facilities where the proposed work will be performed meet environmental laws and regulations of federal, state (Texas), and local Governments for, but not limited to, the following groupings: airborne emissions, waterborne effluents, external radiation levels, outdoor noise, solid and bulk waste disposal practices, and handling and storage of toxic and hazardous materials.

The facilities include the office of CroftSoft Inc and the NeuroEngineering Laboratory at UTD. Equipment includes high performance personal computers, a robotic arm, a Skinner box, animal care facilities, and recording equipment, including the following:

- Two (2) Dell Precision 650 computers (3.2 GHz, 3.5 GB RAM)
- MathWorks MatLab
- Nex Technologies NeuroExplorer
- Plexon Data Analysis Software Offline Sorter
- Plexon MAP Control Software Rasputin
- National Instruments (NI) BNC-2090
- NI PCI-MIO-16E-4 DAQ
- LabView 6.1

Subcontractors/Consultants

The University of Texas at Dallas (UTD) is the research institution partner and subcontractor.

Prior, Current, or Pending Support of Similar Proposals or Awards

No prior, current, or pending support for proposed work.