SECTION C – DESCRIPTION/SPECIFICATION/WORK STATEMENT

ARTICLE C.1. INTRODUCTION

Long-term simultaneous recording of single unit activity from large numbers of neurons in the central nervous system (CNS) is one of the key techniques used by neural prosthesis researchers to collect executive neuronal signals for prosthetic control. Neurophysiologists also utilize the technique for studying neuronal interactions, plasticity, and learning in intact and chronic preparations. The NINDS Neural Prosthesis Program supports the development of a chronic, multichannel microelectrode recording array capable of recording single-unit neuronal activities 3-dimensionally over wide cortical areas and across deep cortical layers with at least 50 recording sites. These arrays can also be further assembled into a 3-dimensional array structure to provide hundreds of recording sites.

In past research and development, multiple microelectrode recording sites have been fabricated on shanks as small as 60 microns wide and 15 microns thick. Circuits integrated into the silicon microelectrodes have been successfully implemented to amplify and buffer signals from extracellular action potentials corresponding to single and multiple neurons or units. Additional electronic circuitry that provides selection of multiple recording channels and multiplexing of signals from multiple recording sites has also been integrated into the array. Acute recordings have demonstrated the functionality of this multiplexed system. After implantation in guinea pig auditory cortex, excellent biocompatibility of these microeletrodes has been demonstrated with healthy appearing neurons within 10 microns of the microelectrode recording site. A series of polymide cables have been fabricated allowing high-density two-dimensional interconnections to active recording probes *in vivo*.

In moving towards the long-term goal of developing an integrated microelectrode system that permits recording of extracellular neural activity from many neurons over decades of use in humans, this research and development project will build on previous results with an emphasis on chronic implant applications. In addition to the microelectrode array, the implantable system should incorporate a wireless means of power transmission and a telemetry system for transmission of the signals from an implanted array to an extracorporal receiver. Any cabling comprising this system should be designed to be compatible with human implantation and not transmit mechanical force to the microelectrode array that would cause displacement within the neural tissue. Interface circuitry will be designed to provide on-chip amplification, filtering, time-division multiplexing, and in vivo real-time signal processing. Although no human studies are required at this stage, the system should be tested rigorously both in vitro *and* in vivo, especially on any chronic applications in non-human primates with a goal of eventually developing a probe system capable of providing chronic neural recordings from human cortex. The focus of this project will be on the function and reliability of this system in recording quality signals over a period of no less than 1 month, and on its safety and effectiveness in overall design.

ARTICLE C.2. STATEMENT OF WORK

The overall objective of this contract is the development and demonstration of an implantable probe technology capable of chronic recording in mammalian cortex. Over the duration of the 25-month period of the project, the following specific tasks with associated performance specifications shall be completed:

A. System fabrication: Independently and not as an agent of the Government, the contractor shall design, fabricate, and test multiple-site, intracortical recording microelectrode probe system. Probe systems shall consist of multiple-site microelectrode recording array, a telemetered interface, and an extra-corporal transceiver. Connection between the microelectrode recording array and the telemetered interface may incorporate a flexible cable and percutaneous connector. Specifically, the system to be developed and delivered shall build on the existing technologies and shall meet or exceed the following minimum characteristics:

1. The probe shall have at least 50 recording sites distributed across a three-dimensional array.

2. The sites shall have characteristics suitable for, and be capable of, recording extracellular single-unit neural activity with signal to noise ratios exceeding 3:1 over a bandwidth of 500 Hz to 6 kHz.

3. The input referred noise level should be less than 20 microvolts root mean square for a source impedance of 2 megohms.

4. The probe system should allow rapid switching (<1000 ms) through external control to allow selection of any of the probe recording sites for direct monitoring of at least one recording site.

5. Cross-talk signals from non-selected recording sites shall have a magnitude of at least 40 db less than signals from selected recording sites.

6. For microelectrode array should be fabricated to have sufficient strength to penetrate the pia-arachnoid and cortex in primates without probe breakage.

7. The probe electronics shall be covered with a biocompatible coating that will maintain the above stated characteristics and permit stable operation of the probe in a 0.9% NaCl bath for at least 1 year.

8. If a cable is required to connect the microelectrode array to the telemetered interface for power, data transmission and control, the flexibility of the at least 4 mm of this cable closest to the probe shall be at least as flexible as that for an 100 micron diameter gold wire. The cable and any percutaneous connector, if required, shall be comprised of biocompatible materials.

9. The telemetry component of the system shall provide power to operate at least the probe with minimal adverse thermal effect on the surrounding structure, and shall have telemetering capacity to control and receive a data stream representing action potential activity from at least 50 recording sites and at least one user-selected recording site at high temporal resolution. Action potential activity across at least 50 recording sites can be encoded as time stamps based on amplitude crossing a threshold based on the input referred noise level. At least one recording site should be able to be selected from the recording sites for output at least 30 kilo-samples/second.

10. All components of the implanted system shall be capable of sustaining sterilization with steam or ethylene oxide (either is adequate for this requirement) without changes in operating characteristics.

B. Testing and validation of probe system: Specifically, the contractor shall test, evaluate and validate the probe system developed in section A, both in vitro and in vivo, of a mammalian cortex (excluding chimpanzees and humans). Test and validation shall be comprised of the following:

1. The probe system shall be designed to eventually be capable of providing chronic neural recordings from human cortex, but shall be tested, in this contract, in mammalian cortex in vivo. Chronic in vivo recording refers to being capable of continuous collecting neural signals over a period of no less than 1 month after one implantation of the system in a live animal.

2. Test the assemblies in vitro in a simulation of the conditions to be expected in vivo. In vitro testing shall include soak testing (0.9% NaCl solution) of all implanted components, testing of the connect-disconnect function of the percutaneous connector (if such a component comprises the system), testing of the transmission reliability of the telemetry, and testing of the mechanical shock resistance of the complete system.

3. Report all findings from testing and validation of the system to the NINDS Project Officer and Contracting Officer. This report should not only include the stability data recorded with the microelectrode arrays, but also any problems identified during the test and validation phase.

4. Provide a plan for the continued development of the technology initiated under this contract to be included in the Final Report.

C. Structure of the contract:

The project shall consist of a 25-month performance period. The specific milestones, deliverables, and accomplishments for lifetime of the project are hereby attached to the contract as Attachment No. 6 with amendment according to Attachment No. 7.

During this project, the contractor will hire personnel, buy equipment and supplies, and secure fabrication services sufficient to enable comprehensive characterization and reporting of probe performance and technical demonstration to the NINDS Project Officer and Contracting Officer of their probe system. It is the intent of the government to encourage the collection of supplementary data that supports the overall goal of this project for a robust implantable microelectrode array technology capable of chronic recording in mammalian cortex. Any additional results that are indicative of the potential of the probe system providing an optimal solution for chronic recording problem are encouraged.

Deliverables:

Quarterly Reports – same as before

Interim Report: During the first 18 months of this project**,** the contractor is expected to have designed, fabricated, and characterized the performance of the prototype system with respect to the specifications outlined above in section A which include input referred noise, data transmission bandwidth and fidelity, thermal effects, and number of recording channels. The contractor shall prepare and deliver to the NINDS Project Officer and Contracting Officer an interim performance report, no later than 16 months of the performance period, documenting and detailing how the system meets or exceeds the minimal performance specifications required herein. Additional results that are indicative of the potential of the probe system to perform chronic recording in the mammalian brain are encouraged but not required.

Final Report: same language as before with the addition: The Final Report shall also contain a plan for the continued development of the technology initiated under this contract. This plan shall be developed with input from the NINDS Project Officer during months 20-24 of the project.