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 three months 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 chronic applications in non-human primates with a goal of eventually developing a system capable of providing chronic neural recordings from human cortex. The focus will be on the reliability of the system in recording quality signals over a period of no less than 6 months, 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 a robust implantable microelectrode array technology capable of chronic recording in mammalian cortex. The contract will consist of a base contract period of 18 months followed by three possible consecutive option periods of 12 months, 12 months, and 6 months duration, respectively. Over the duration of the 48-month period (if all options are exercised) 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 systems developed in section A, both in vitro and in vivo of a mammalian cortex (excluding chimpanzees and humans). In addition, the contractor shall seek independent testing and validation of the system with proposed criteria from at least two external organizations. 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 rigorously, in this contract, in non-human primates in vivo. Long-term chronic in vivo recording refers to being capable of continuous collecting neural signals over a period of no less than 6 months 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. Demonstrate effective and stable chronic single-unit recording though in vivo primate experiments over periods of at least 6 months using the recording probe array systems. Modify the system design as needed in response to any problems revealed from the long-term chronic recordings to ensure that the system can perform in a safe, effective, and reliable manner.

4. Report all findings, which include, from independent testing and validation by external organizations 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.

5. Provide a translation plan for the technology that has been developed under this contract.

C. Structure of the contract:

1. **The Base Contract Period** shall consist of an 18-month performance period. During the base contract period the Contractor shall design, fabricate, and characterize a fully functional prototype of the proposed probe system planned for chronic recording. This prototype system must at a minimum meet, but preferably exceed, the functional performance specifications and requirements outlined in Section A of the Statement of Work. To demonstrate that the prototype system meets the minimum performance specifications and requirements, the contractor will demonstrate the capability of this system to perform continuous long-term recording for a period of no less than 1 month. During this base contract period, the contractor will hire personnel, buy equipment and supplies, and secure fabrication services sufficient to enable comprehensive characterization and reporting of prototype performance and technical demonstration to the NINDS Project Officer and Contracting Officer of their prototype system. Specifically, the contractor is expected to:

   a. fully characterize 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.

   b. prepare and deliver to the NINDS Project Officer and Contracting Officer a performance report, no later than 60 days prior to the end of the base contract period, documenting and detailing how the system meets or exceeds the minimal performance specifications required herein.

   It is the intent of the government to encourage the collection of supplementary data that supports the likely success for meeting and exceeding 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 prototype system providing an optimal solution for chronic recording problem are encouraged. These supplementary data may include in vivo results in mammalian brain showing feasibility use in chronic recording for durations exceeding the minimum period of 1 month.

2. **Option Periods**: Based on the Contractor's performance during the base contract period, the Government may unilaterally extend the period of this contract for up

to 3 consecutive option periods, two (2) twelve-month periods and one (1) six-month period for a possible total of 30 months. The desired milestones and deliverables for the base contract period are outlined above and the final option period must demonstrate the full capability for chronic recording with the probe system with robust recordings for no less than 6 months. The desired milestones and deliverables for the Option periods along with accomplishments for lifetime of the project are hereby attached to the contract as Attachment No. 6.

Exercise of options 1, 2, and 3 will be contingent upon: 1) the level and degree of performance by the Contractor in meeting deliverables, milestones, and accomplishments according to the timeline in Attachment No. 6 to this contract; 2) any findings from organizations providing independent test and evaluation; 3) Government's continuing need for development of the system; and 4) availability of funds.

The decision of the Government to exercise any future option will depend on the quality of the data generated and supplementary data provided by the Contractor that demonstrates the increased likelihood for success in demonstrating chronic recording capability; compelling arguments for likely success would include preliminary data collected in vivo.

The contractor is aware and understands that the NINDS may award multiple contracts for a base contract period of 18-months. It is the intent of the Government during this base contract period to assess the likelihood of success for one or more contractors during progression into later option periods where the chronic recording capability of the system will be more fully developed and demonstrated.