Neural Engineering System Design
Proposed Team Activities

DARPA's Neural Engineering System Design (NESD) program aims to develop a portable neural interface system capable of providing precise communication between the brain and the digital world at a scale far greater than is currently possible. The program's primary goals are to generate foundational knowledge relevant to the development of improved neural interface capabilities and to create functional technologies potentially applicable to sensory restoration. Four of the six teams selected by DARPA will focus on vision and two teams will focus on aspects of hearing and speech.

The teams' approaches mix fundamental research and applied science and engineering. In addition to overcoming engineering challenges relating to hardware, biocompatibility, and information processing, the teams will also have to significantly advance current understanding of how the brain processes sensory inputs and develop new mathematical and neuro-computation techniques to decode and encode neural data and compress those troves of information so they are tractable within the limits of available bandwidth and power.

Brown University

Principal Investigator: Dr. Arto Nurmikko
Location: Providence, R.I.
Sensory Focus: Auditory perception of speech

- **Engineering Objectives and Challenges:** The team led by Brown University will attempt to develop an interface system composed of networks of up to 100,000 untethered, submillimeter-sized "neurograin" sensors. The grains—envisioned to be no larger than 150 micrometers square in their final form, or about the size of a grain of table salt—would each incorporate an electrode to sense discrete neural signals and deliver stimulation, a radio frequency (RF) antenna to communicate neural activity and receive data, and a charge pump that converts RF waves into electrical energy. A separate RF unit worn on or under the scalp as a flexible electronic patch would passively power the neurograins and serve as the hub for relaying data to and from an external command center that transcodes and processes neural and digital signals. One of the greatest challenges the team will face in implementing the system is similar to one faced by cellular providers. Each neurograin will be akin to a wireless device in a vast mobile network. The team must develop a strategy for multiplexing communication between the neurograins and the base station that allows for coordinated transmission from individual nodes at near-real-time speeds.

- **Fundamental Research Objectives and Challenges:** The team aims to decode neural processing of speech, focusing on the tone and vocalization aspects of auditory perception. In addition, the team will study movement, touch, and proprioception, seeking to assemble a library of neural codes that can be generalized and used in the future to help speed processing of information within the neurograin system. For example, during animal testing, researchers will compare sensor data on an animal's gait to readouts from microelectrode arrays implanted in the animal's brain to identify the neuronal firing patterns involved with specific ambulatory movements.

Columbia University

Principal Investigator: Dr. Ken Shepard
Location: New York, N.Y.
Sensory Focus: Vision

- **Engineering Objectives and Challenges:** The team led by Columbia University will attempt to develop a non-penetrating bioelectric interface with the visual cortex. To minimize the volume of the device, the team envisions layering over the cortex a single, flexible complementary metal-oxide semiconductor (CMOS) integrated circuit with integrated high-density electrodes. A relay station transceiver worn on the head would wirelessly power and communicate with the implanted device. The Columbia team aims to build from proven commercial and prototyped technologies, improving their precision and scale. To enable simultaneous recording and stimulation of neurons, the team will have to overcome the challenge posed by electrical stimulation artifacts that sensors can misinterpret as neuronal activity.

- **Fundamental Research Objectives and Challenges:** The team aims to develop strategies for "listening" to neurons beneath the surface of the visual cortex and delivering specific stimuli to those neurons. When reading neuronal activity, the researchers will need to infer activity taking place deep within the brain from activity recorded in the surface layers of the cortex. Surface recording electrodes have already demonstrated the ability to detect action potentials at depths of up to 200 micrometers and recording from lower layers may be possible. When providing inputs, the team will attempt to use dense arrays of electrodes to steer current to stimulate specific neurons located up to 400 micrometers deep, delivering patterns of stimuli into the visual cortex. To do so, the team needs to build mathematical models that encode images as stimulation patterns and assemble a library of such patterns for transmission.

Fondation Voir et Entendre (The Seeing and Hearing Foundation)

Principal Investigators: Dr. Jose-Alain Sahel and Dr. Serge Picaud
Location: Paris Vision Institute, Paris, France
Sensory Focus: Vision

- **Engineering Objectives and Challenges:** The team led by Fondation Voir et Entendre (FVE) aims to apply techniques from the field of optogenetics to enable communication between neurons of the visual cortex and a camera-based, high-definition artificial retina worn over the eyes, facilitated by a system of implanted electronics and optical technology. To overcome the challenge of processing the vast amount of information collected by the retina, FVE plans to develop a neuromorphic, event-based camera system to capture only contextually relevant content from dynamic scenes—that is, only the elements of the scene that change substantially from frame to frame. In FVE's model, this information would be sent from the camera to an external device worn on the head and responsible for transforming the images into stimulation patterns that are wirelessly communicated to a high-density micro-LED stimulator array for the visual cortex. For recording cortical neuronal activity, the team will attempt to develop an *in vivo* miniature microscope.

- **Fundamental Research Objectives and Challenges:** Optogenetics involves making neurons respond to specific wavelengths of light. To achieve this, FVE will draw from its existing library of vectors and from discovered promoters to determine which of them are appropriate for targeting specific neurons in the visual cortex. The FVE team will also attempt to map how the eye and brain work together to process vision. The team intends to work in animal models to demonstrate the feasibility of optogenetically activating neurons in the visual cortex while recording activity with an *in vivo* miniature microscope.

John B. Pierce Laboratory

Principal Investigator: Dr. Vincent Pieribone
Location: New Haven, Conn.
Sensory Focus: Vision

- **Engineering Objectives and Challenges:** The team led by the John B. Pierce Laboratory will pursue an interface system in which modified neurons capable of bioluminescence and responsive to optogenetic stimulation communicate with an all-optical prosthesis for the visual cortex. The team aims to configure the prosthesis with a lensless microscopy single-photon avalanche diode array "read" module that obtains maximal light efficiency for neural imaging. Inputs would be enabled by a directional micro-LED array for scalable and precise stimulation of neurons.

- **Fundamental Research Objectives and Challenges:** To facilitate recording of neural activity, the team will attempt to develop genetically encoded bioluminescent reporters that endogenously express luciferin, a small molecule involved in the production of light in fireflies and other bioluminescent systems. These reporters would create bursts of light when neurons activate.

Paradromics, Inc.

Principal Investigator: Dr. Matthew Angle
Location: San Jose, Calif.
Sensory Focus: Speech and hearing

- **Engineering Objectives and Challenges:** The team led by Paradromics, Inc., aims to create a high-data-rate cortical interface using large arrays of penetrating microwire electrodes for high-resolution recording and stimulation of neurons. The implantable device, which Paradromics calls the "Neural Input-Output Bus" (NIOB), would exploit the reliability of traditional wire electrodes, but at a much greater density and scale than current technology allows. As envisioned, it will be composed of multiple 1 cm x 1 cm modules, each bonded to an array containing tens of thousands of microwire electrodes. Each microwire would be bonded to an individual pixel of a specially designed, low-power CMOS circuit on one end. On the other end, the wires would extend into the cortex, where they would record and stimulate clusters of neurons. Paradromics will work to streamline production of the NIOB to facilitate manufacturing of the devices at scale.

- **Fundamental Research Objectives and Challenges:** The team aims to demonstrate the improved safety of microwires with highly reduced cross-sections relative to traditional electrodes, as an approach to minimizing immunological reactivity as well as potential vascular and tissue damage when deployed in large numbers.

University of California, Berkeley

Principal Investigator: Dr. Ehud Isacoff
Location: Berkeley, Calif.
Sensory Focus: Vision

- **Engineering Objectives and Challenges:** The team led by the University of California, Berkeley, aims to develop a novel miniaturized microscope that can detect and modulate the activity of up to a million neurons at a time in the cerebral cortex. Detection would be achieved by a "light field" microscope that uses image compression and reconstruction technologies to measure flashes of light that occur in active neurons and identify each neuron in a field of a million. As envisioned, three-dimensional, computer-generated holography would point light at these cells and stimulate them optogenetically, rapidly switching natural or synthetic patterns.

- **Fundamental Research Objectives and Challenges:** The million-neuron read-write optical interface is intended for the visual and somatosensory cortices. The Berkeley team will attempt to build quantitative encoding models that predict the responses of single neurons and neural populations to arbitrary visual and tactile stimuli, and these predictions will be used to structure photo-stimulation patterns to elicit percepts. Applications in the visual cortex include as a prosthesis for blindness, and in the somatosensory cortex as a critical sensory input for closed-loop control of an artificial limb. In both brain regions, the ability to detect and modulate activity on such a massive scale would greatly advance understanding of how the brain operates.