P-21: Biophysics

Neuromagnetic Mapping of Multiple Visual Areas in Humans

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This NIH (National Institutes of Health) project includes a series of experiments aimed at identifying and characterizing multiple visual areas in the human brain. These studies employ stimulus manipulations that have been shown in nonhuman primates to differentially activate specific cortical regions (e.g., regions with color or motion processing). Magnetoencephalography (MEG), in conjunction with magnetic resonance imaging (MRI), is used to determine the locations and arrangement of multiple visual areas in the human cortex and to probe their functional significance. In addition to suggesting human parallels to the nonhuman primate results, the proposed experiments provide an opportunity to discover new properties of the human visual system that may not exactly parallel those in nonhuman primates or expectations from other data in humans. For example, results obtained during the preceding project period on the retinotopic organization (point-to-point projection of the visual field onto areas of the brain) of the human visual cortex suggest that although the functional anatomy of the human occipital cortex corresponds in general terms to the "cruciform model" derived from lesion and human event-related potential (ERP) data, there are important differences revealed by the combination of magnetic measurements and anatomical MRI (Aine et al., "Unexpected Features of Retinotopic Organization in Human Visual Cortex Revealed by Neuromagnetic Mapping," in "Physics Division Progress Report, January 1, 1994–December 31, 1994," G. Y. Hollen and G. T. Schappert, Eds., Los Alamos National Laboratory report LA-13048-PR [November 1995], p. 36). We have also made a new and unexpected finding: the cingulate cortex in the central/frontal regions is not only responsive to visual stimulation but also appears to have some crude retinotopy. Because this region shows evidence of retinotopy, it should be classified as a visual area. This result has not been shown in invasive monkey studies because this region is too difficult to access in monkeys.

Identification of Two Streams of Visual Processing Using Magnetoencephalography, Functional Magnetic Resonance Imaging, and Positron Emission Tomography

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Recent studies in nonhuman primates and noninvasive functional imaging studies in humans suggest the existence of two streams of processing visual information, labeled the “dorsal” and “ventral” streams, that represent two different paths of activation along the cortex. The dorsal stream progresses from the occipital to the superior parietal cortex and is associated with processing spatial location and motion. The ventral stream (arrayed along the inferior occipital and temporal cortex) is associated with the processing of color and form. Anatomical and physiological studies indicate that these two streams differ in terms of their sensitivities to stimulus parameters such as luminance, spatial frequency, temporal frequency, and chromatic cues. In collaboration with the German National Laboratory in Juelich, we acquired positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and magnetoencephalographic (MEG) data in the same six subjects in order to separate the streams of processing in the visual cortex. Responses to a stimulus containing a combination of features that preferentially excite the dorsal stream are being compared with responses to a stimulus containing features that should preferentially excite the ventral stream. Two different stimuli (circular with radially symmetric sinusoidal variation in either color contrast or luminance, using a black background and the highest possible contrast) were presented in the lower right visual field. The stimulus designed to activate the ventral stream was 3.5-deg in diameter, isoluminant, placed foveally, with a spatial frequency of 4.5 cycles/deg, and alternated at 2 Hz. The luminance of the red and green bands was adjusted to be equal for each subject. The larger (7.3-deg-diameter) isochromatic stimulus with luminance cues was placed as peripherally as possible, within the limitations of the hardware. The spatial frequency of the yellow bands was 3.5 cycles/deg, and alternated at 4 Hz. In all subjects, the activation evident in the primary visual cortex, for both fMRI and MEG measures, was found to be more anterior when the stimulus was presented more peripherally. Activations evoked when the stimulus was located more foveally were more posterior. This result reveals retinotopic organization. As predicted, more regions of activation were evident in the ventral slices for the foveal stimulus (of isoluminant color) than for the more peripheral stimulus containing luminance cues. Activity associated with the more peripheral stimulus was more medial and dorsal, in general.

Ultrasensitive Genetic Analysis

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Our research group focuses on the development of laser-based techniques for the ultrasensitive detection and analysis of biological molecules and the application of these techniques to molecular biology and medical diagnosis. We have recently developed a procedure for the rapid, direct detection of specific nucleic-acid sequences in biological samples. This method is based on a two-color, single-fluorescent-molecule detection technique. The basis of our approach is to monitor for the presence of a specific nucleic-acid sequence of bacterial, human, plant, or other origin. The nucleic-acid sequence may be a DNA or RNA sequence and may be characteristic of a specific taxonomic group, a specific physiological function, or a specific genetic trait. The detection scheme involves the use of two nucleic-acid probes that have sequences that are complementary to the nucleic-acid target. The two probes are labeled with two different fluorescent dyes. If the target is present when the probes are mixed in the sample under investigation, both probes bind to the target. The sample is then analyzed by a laser-based ultrasensitive fluorescence system capable of simultaneously detecting single fluorescent molecules at two different wavelengths. Since the probes bind to the same nucleic-acid target fragment, their signals will appear at the same time. Thus, the simultaneous detection of the two probes signifies the presence of a target molecule. When there is no target present, the probes will emit signals after illumination that are not coincident in time.

Studies of the Human Visual System Using m-Sequences and Sparse-Stimulation Techniques

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The m-sequence pseudorandom signal has shown itself to be a more effective probing signal for studying nonlinear biological systems using cross-correlation techniques than the traditional Gaussian white noise. However, anomalies occurring in the measurements of second- and higher-order cross-correlations become obstacles to the m-sequence being more widely used in studying nonlinear systems. In these studies, a new approach using a short m-sequence as a probing signal together with the "padded sparse-stimulation" method is proposed. Simulation results showed that when using the sparse-stimulation method the estimation errors caused by anomalies will be greatly alleviated even for a short m-sequence. Another advantage of the padded sparse-stimulation method is that it can obtain all the information of the second- and higher-order kernels, whereas the traditional "inserted sparse-stimulation" method could not obtain all of the information of a nonlinear system. The new approach has been applied to neuromagnetic studies of the human brain. The weak neuromagnetic responses were stimulated by light modulated by short m-sequences

(1023 in length for binary and 728 in length for ternary) and measured by highly sensitive SQUID (superconducting quantum interference device) sensors located on the scalp of the human head. Cross-correlations with high signal-to-noise ratios were obtained, which show that the proposed methods in these studies are well applicable to the study of practical systems. These methods will be useful for both basic research and clinical applications.

Automatic Source Localization Procedures for MEG

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Cortical brain activity encountered in magnetoencephalography (MEG) studies can usually be modeled as electric current dipoles, if the regions of activation are relatively focused. The dipole location, orientation, and moment parameters are determined by fitting the measured data with a nonlinear minimization procedure. Due to the existence of many local minima and the properties of various minimization techniques, such minimization in a high-dimensional search space is usually very sensitive to the initial guesses when the number of modeled dipoles is greater than one. Manually selecting initial guesses is a time-consuming procedure, and if the initial guesses are not close enough to the global minimum, the calculation may fail to find the global minimum and become trapped in the local minima. Therefore, it is necessary to find an automated procedure to effectively handle the multiplicity of local minima. In this project, the performance of a number of global-minimization techniques applied to MEG is studied. These techniques include: (1) Multi-Start Downhill Simplex, (2) Genetic Algorithm, and (3) Simulated Annealing. These algorithms are tested for different simulated noise conditions (different noise levels and white noise versus color noise) and head models (a spherical head model and a real-shape head model). In addition to the simulated conditions, we will examine the algorithms using empirical MEG data collected with 122 channels from the whole-head Neuromag system.

Spatio-Temporal Magnetoencephalography and Electroencephalography Source Estimation

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MEG and electroencephalography (EEG) provide unique views of the dynamic behavior of the human brain because they are able to follow changes in neural activity on a millisecond time scale. There is a clear need both for the development of new algorithms that exploit the most recent advances in sensor design, signal processing theory, and other functional and anatomical imaging modalities, and for a detailed study of the limitations of these and existing inverse procedures. LANL is a subcontractor to the University of Southern California on a three-year National Institute of Mental Health grant to develop such algorithms and to distribute the software and phantom data generated by this research. In addition to providing a suite of thoroughly tested inverse procedures, we anticipate that this work will provide insight into the fundamental limitations of EEG- and MEG-based source estimation.

Nuclear Magnetic Resonance Imaging with Hyperpolarized Noble Gases

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Several novel aspects of nuclear magnetic resonance (NMR) or MRI with hyperpolarized noble gases have recently been demonstrated, including the ability to easily image gas-filled spaces and to transfer part of the polarization to other nuclei. Using these new techniques, we have been investigating diffusion. We hyperpolarized ^{3}He by applying laser-optical pumping in the presence of rubidium molecules. We obtained one-dimensional images of ^{3}He gas diffusing in a slice that was tagged by inverting its magnetization, a technique previously used for observing the diffusion of thermally polarized ^{129}Xe gas. Also, a one-dimensional diffusion image of the gas was made with and without a temperature gradient present. Our results show that temperature changes can be monitored by diffusion images of ^{3}He gas.

Biomorphic Walking Machines for Unattended UXO (Unexploded Ordinance) Detection

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The purpose of this project was to demonstrate the feasibility of building an automatic system for locating and, eventually, destroying UXO on military test ranges. The system would consist of three parts: sensors, legged robot platforms to carry the sensors, and an interface to connect the sensors and robots to implement a search strategy. In this first year, it was decided to concentrate on the development of robots capable of surviving harsh (Yuma desert) environments while carrying minimal sensor payloads. The robots are distinguished by the nervous-net (Nv) analog design, which is very inexpensive and is based on biological organism control. This design avoids the complexity and cost of computer-based systems and allows the use of inexpensive, off-the-shelf components. In September 1996 the most successful of the legged-walker prototypes was tested on a Yuma range, and, using a prototype Nv magnetic gradiometer sensor, found its footing, True North, and a mock magnetic mine during repeated trials. It was the first such device in the history of the range to perform these actions with complete autonomy and under full desert conditions (ground temperature ≅ 140°F). Work is proceeding now on a solar-powered version with a weeks-long survival potential and on more sophisticated magnetic sensors for true UXO detection.

Biomorphic Control of Autonomous Spacecraft

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The objective of this project is to define a mission to continuously monitor the characteristics of a major portion of the terrestrial magnetopause. This would be accomplished using one hundred or more biomorphically controlled, autonomous microsatellites with simple sensors. The mission would capitalize on highly innovative and radically smaller and cheaper satellite and sensor technologies that are currently under development by NASA, the Department of Defense (DoD), and DOE. This is a first step toward defining a useful, minimal microsatellite design for the future and is relevant to all areas that use spacecraft platforms. Toward this, we presented an application of a technology that seems, in experiment, to overcome most of the problems normally present in space missions: complexity, reliability, redundancy, and cost. Although the nervous-net (Nv) control method could be adapted to most types of machine control, we have applied it to autonomous satellite control because of the difficulty that conventional control systems have in solving the seemingly simple task of negotiating complex magnetic gradients. Over a dozen "nanosat" magnetic gradiometer prototypes were built and studied in a range of magnetic fields; analyses were performed, papers published, and a prototype presented at NASA and JPL workshops. The conclusions are that Nv systems could trivialize the cost of small-scale (20-g) satellite systems, and work is progressing toward a larger (200-g) prototype to assess payload control and handling requirements for commercial platforms.

Nonlinear Analysis of Nervous-Net (Nv) Designs

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Three years of studying experimental Nv control devices has resulted in various successes and several amusing failures that have implied some general principles on the nature of capable control systems for autonomous machines and, perhaps, biological organisms. These systems are minimal, elegant, and, depending upon their implementation in a "creature" structure, astonishingly robust. Their only problem seems to be that since they are collections of nonlinear asynchronous elements, only a very complex analysis can adequately extract and explain the emergent competency of their operation. The implications are that so long as Nv nonlinear topologies can retain some measure of subcritically coupled planar stability, the Piexito theorem will guarantee a form of plastic mode-locking necessary for broad-behavior competency. Further experimental evidence also suggests that if Nv topologies are kept in subchaotically stable regimes, they can be implemented at any scale and still automatically fall into effective survival strategies in unstructured environments. The conclusion is that Nv controllers have the power to scale, both physically and dimensionally, into any range of tasks that would otherwise require sophisticated programming. Research continues into understanding how such devices can converge their skills to evolve retentive abilities similar to neural-net structures, resulting in capable learning machines that have a trivial setup cost.

Autonomous Self-Assembling Robotic Mechanisms

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This research is aimed at the study, development, and integration of minimal nervous-net (Nv) artificial agents and the principles that allow for their elegant design, operation, organization, and self-assembly. Previous work along these lines (by Hasslacher and Tilden) has hinted that the field of nonlinear dynamics may provide important, broad principles with which we can promote the survival of active, robust devices in unstructured environments. Advances in this area will allow for the design of devices that are "smart enough" for a task without the usual cost-intense complexity that accompanies traditional robotic construction. Since the start of the project, 18 self-contained "assembler bots" have been built and studied in our robot "Jurassic Park." New control systems have been devised to allow these devices to power-mine their environment—exploiting the available light-energy sources—without having to resort to internal batteries. Future work will examine and promote the development of these mobile machine components so that they may act as coordinating organs in sophisticated robots for application-specific tasks, creating a form of "living Lego" with inherent self-repair and self-optimization characteristics.