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# Proceedings of the Third International Workshop on Advances in Electrocorticography

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## Abstract

The Third International Workshop on Advances in Electrocorticography (ECoG) was convened in Washington, DC, on November 10-11, 2011. As in prior meetings, a true multidisciplinary fusion of clinicians, scientists, and engineers from many disciplines gathered to summarize contemporary experiences in brain surface recordings. The proceedings of this meeting serve as evidence of a very robust and transformative field, but will yet again require revision for the advances that the following year will surely bring.

### Keywords

electrocorticography; brain-computer interface; high-frequency oscillations; brain mapping; seizure detection; gamma-frequency electroencephalography; neuroprosthetics; subdural grid

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## 1. Introduction

A. Ritaccio

Swiftly the brain becomes an enchanted loom, where millions of flashing shuttles weave a dissolving pattern, always a meaningful pattern though never an abiding one.

—Charles Sherrington

The Third International Workshop on Advances in Electrocorticography (ECoG) convened in Washington, DC, in November 2011 to discuss advances and consolidate shared experiences in the rapidly evolving science of recording and decoding brain surface electrical activity. This time, beyond advances in recording techniques and material engineering, we heard about the emerging promise of ECoG as a potent tool in deciphering complex human behaviors like attention and saw evidence for interregional communication in the brain evidenced by phase coupling. Summaries of ongoing work in ECoG-based functional mapping and ECoG-driven brain-computer interface were given. The search for a pragmatic role for pathologic high-frequency oscillations in the presurgical assessment of intractable epilepsy was elegantly summarized. All in all, it was a highly successful annual gathering of the state of the art, summarized in the content below.

## 2. Basics of ECoG Recordings

P. Brunner, J. Williams, J. Viventi

Ever since the 1950s, when Wilder Penfield and Herbert Jasper used a mechanical stylus and paper system to pioneer the recording of electrocorticographic (ECoG) activity in humans [1], researchers and clinicians have continued to explorer better techniques to acquire and analyze brain signals.

In the past, the lack of computational resources has limited the analysis of brain signals to visually accessible features. The advent of the digital age has lifted this restriction and has sparked the interest of clinicians and researchers in ECoG features beyond those that are visually accessible, for example, task-related gamma band (i.e., 40-180 Hz) power augmentations that are informative of cortical function [2]. However, this interest quickly revealed that contemporary clinical instrumentation is built to acquire ECoG signals at a fidelity that is more suitable for post hoc visual inspection (e.g., 0.1-50 Hz, sampled at 256 Hz) than it is for computerized analysis of ECoG features beyond those that are visually accessible. The increasing interest in observing and interacting with distributed cortical brain function at high temporal resolution [3] eventually lead to commercially available instrumentation that uses conventional technology to provide access to ECoG activity in real time (e.g., g.tec g.USBamp, 0-5 kHz, sampled at 38 kHz). In conjunction with now contemporary computational resources, this allowed the full exploration of ECoG signals and the development of novel clinical applications (e.g., mapping of cortical function) [4]. The ability to observe and interact with cortical processes in real time with high temporal fidelity led to an interest in higher spatial fidelity, e.g., by increasing the number of ECoG electrodes beyond one hundred. While this increase in spatial fidelity could initially be met

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with conventional technology by miniaturizing grids, connectors, head stages and bio-signal amplifiers, it became clear that further increases in the number of electrodes challenges four limitations of conventional technology:

1. Conventional subdural implantation technology requires the penetration of the skull and the outer meningeal covering, which increases the risk of bacterial infection and adverse tissue response. Increasing electrode density and coverage may further increase morbidity beyond what could be justified by the clinical benefit.
2. Conventional grid technology uses platinum electrodes sandwiched between Silastic sheets. Increasing electrode density makes these grids stiff and unable to conform to and make contact with the cortical curvature.
3. Conventional connector technology uses one dedicated wire per electrode that is typically bundled with a set of other electrodes and tunneled through the incision in the dura, to exit the scalp distant from the incision. Further miniaturization of the wires is limited by mechanical stability requirements. Consequently, increasing the number of electrodes results in more and thicker bundled wires that further increase the risk of infection beyond what could be justified by clinical benefit.
4. Conventional signal acquisition technology amplifies and digitizes the signal distant from the electrode. Increasing electrode density results in smaller electrodes with higher impedance that are more susceptible to noise. Consequently, increasing electrode density severely limits ECoG signal quality.

To overcome these four limitations, researchers and clinicians have pursued four innovative approaches:

1. Minimally invasive epidural implantation techniques minimize the risk of bacterial infection and adverse tissue response by using functional magnetic resonance imaging (fMRI) to localize specific and cortical areas [e.g., M1 motor cortex for brain-computer interface (BCI) applications] [5] and intraoperative computed tomography (CT) that guide the implantation of an expanding grid through a small borehole [6]. This technology is currently undergoing testing in non-human primates and human cadavers that must be completed before it can be made available for clinical applications.
2. Ultra-thin grid technology uses biocompatible thin-film polymeric substrates that allow for high spatial resolution (e.g., electrode distance of 500 μm) combined with mechanical flexibility (e.g., ultra-thin 10 μm) and excellent electrode adhesion based on surface tension [7]. In combination with minimally invasive epidural implantation techniques, thin-film polymeric grid technology is currently undergoing testing in non-human primates and requires longitudinal biocompatibility studies before it can be made available for clinical applications.
3. Integrated connector technology directly interfaces the connector with the thin-film polymeric grid. Additional electronics in the connector may also multiplex and preamplify the ECoG signals to reduce the number of wires. This technology is currently employed for studies with non-human primates and has seen limited translation into human studies to date.

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4. Integrated signal acquisition technology uses flexible silicon electronics to directly amplify and multiplex signals on the grid. A demonstration of this technology required only 39 wires to acquire ECoG at 10 kHz with the use of 360 electrodes that were spaced 500 μm apart and covered 10 × 9 mm of cat cortex (Figure 1) [8]. While further studies are needed to investigate biocompatibility of the substrate and the dissipated heat, this technology allows for simultaneous high spatial fidelity and large cortical coverage.

In summary, ECoG instrumentation is evolving from the use of conventional technology that requires invasive implantation of individually wired passive electrodes to advanced technology that merely requires minimally invasive implantation of integrated ultra-thin active grids. This advanced ECoG technology will enable researchers and clinicians to observe and interact with distributed cortical processes at high spatial and temporal fidelity in real time. This will lead to a better understanding of distributed cortical processes and to the development of novel clinical applications that use ECoG signals to augment, substitute or rehabilitate function.

## 3. Current Understanding of ECoG Physiology

### 3.1 Mesoscale Cortical Electrophysiology

R. Knight, B. Voytek

Penfield's seminal work in the 1950s highlighted the power of ECoG performed on neurosurgical patients to understand human behavior [1]. The last decade has witnessed an explosion of cortical recording in both neurosurgical patients and animal models. These neurophysiological data obtained with intracranial recordings (ECoG) have provided a wealth of evidence on the role of cortical oscillations in human behavior. This research has documented that distributed neural networks support many behaviors including language, perception, attention motor control, and executive function [9-22]. Importantly, oscillation-dependent networks are increasingly linked to neurological and psychiatric disorders [23-26; de Hemptinne C et al., unpublished observations].

Low-frequency gamma coherence (30-60 Hz) has been reported in many tasks and is proposed to be key for feature binding in local cortical regions [27-32]. Research over the last decade in animals and humans has found that high-frequency gamma oscillations (high gamma, HG; 60-200 Hz) are ubiquitous in the cortex and hippocampus, robustly track behavior across large regions of cortex [33-42], and drive the blood oxygen level-dependent (BOLD) signal [43-45]. Importantly, optogenetic and single-unit recording studies have shown that HG is generated by recurrent inhibitory neuronal activity linked to increased single-unit activity, supporting the notion that HG indexes local cortical activation [46, 47]. These findings in animals and humans provide a unique opportunity for bridging human physiology with the wealth of animal single-unit and local field potential data. Network interactions are increasingly studied using coherence or information flow analysis. Many models of interregional neocortical interaction, including fMRI blood oxygen level-dependent (BOLD) correlations and electrophysiological phase coherence alike, assume that low-frequency statistical coherence between regions reflects communication or interaction, yet the mechanism for such communication remains unclear.

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Recent evidence supports the argument that local neuronal population activity—as indexed via broadband gamma amplitude shifts—is co-modulated with the phase of multiple overlapping lower frequencies [13, 48, 49]. Such phase/amplitude cross-frequency coupling (PAC) is usually assessed within a single electrode; however, PAC may provide a tool for indexing modulation of neural population spiking activity as a function of interregional coherence, as shown in Figure 2. Such a model is attractive because it provides a framework constructed of testable hypotheses to bridge basic neurophysiology with higher level cognition.

Under the proposed model, regions co-involved in cognitive or behavioral tasks demonstrating statistical coherence should also show increased PAC; that is, regions involved in a task-related phase-coherent network should show transient increases in PAC compared with regions not involved in the task. Furthermore, a single region involved in multiple simultaneous processes may show multiplexed PAC across a variety of low-frequency bands. For example, gamma amplitude in visual cortical regions appears to couple more strongly with the alpha (8-12 Hz) as opposed to theta (4-8 Hz) phase [49], whereas over motor cortex, coupling between beta (12-24 Hz) and gamma phases is most dominant. Interestingly, patients with unilateral prefrontal cortex (PFC) lesions have abnormally high alpha power in the visual cortex of the lesioned hemisphere [50], suggesting an important role of long-range interregional communication in modulating low-frequency activity.

Human and animal neuroscientists are now increasingly exploring ECoG to explain how the human brain enables behavior in both health and disease. This exciting cross-species effort promises new insights into human cognition with critical implications for understanding the neural basis of human behavior.

### 3.2 Relationship of ECoG and fMRI

N. Ramsey

One of the most challenging goals today is to understand the functional meaning of ECoG signal features. The richness of ECoG signal can provide a powerful tool for investigating the neuronal representation of human brain function, but interpretation of the signals is not straightforward and requires a deeper understanding of where they originate and what they represent. Some insights may be obtained by bridging the ECoG research to noninvasive functional neuroimaging given the large body of work done with fMRI in recent years. The fMRI signal, generally called the blood oxygen level-dependent (BOLD) signal, is predominantly affected by changes in blood oxygenation in microvasculature near neuronal tissue and is closely coupled to neuronal activity. Although EEG and MEG may also contribute to understanding ECoG, one of the problems is the scale at which the signals are generated. For both ECoG and fMRI, signals can be reliably detected at a scale of a few millimeters, and adjacent sources can be discriminated at the same scale (spatial resolution). EEG and MEG, sensitive as they may be for even small regions, are not capable of resolving at millimeter scale.

Direct comparison of ECoG and fMRI signals is not possible, because implanted electrode grids preclude fMRI scans due to the risk of heating the electrodes. The same cognitive

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experiment can, however, be conducted presurgically in the MRI and after implantation with ECoG measurements. Matching those signals first requires accurate co-localization of electrodes and brain tissue [51]. We have shown that for a simple motor task, the spatial pattern of BOLD activity correlates well with increases in power in the higher frequency band (HFB) as measured with ECoG (65-95 Hz and higher) within primary sensorimotor cortex [52]. Lower frequencies do not correlate well within this region. However, when all exposed cortex is included, BOLD activity also correlates with decreases in lower frequencies (8-30 Hz), even when corrections are made for the typical (anti)correlation between those and HFB power. Similar correlations between BOLD and ECoG signal have been found for the language system, but here the theta frequency (4-7 Hz) is the prevailing lower frequency. In general, HFB correlates best with BOLD signal (see also Lachaux et al. [53]), with a close spatial match, but interactions with lower frequencies (which may be specific for specific brain functions) also impact on BOLD signal, indicating a functional significance for such interactions.

With the advent of ultra-high MRI scanners, the spatial detail obtainable with fMRI approaches (sub)millimeter levels, at which point one can address questions at cortical laminar layers and column levels [54]. One of the issues that then becomes relevant is the intrinsic spatial resolution of human cortex for the various cortical domains; in other words, what is the size of a neuronal population with a shared functionality? Ocular dominance columns are reportedly in the order of 600 μm, but little is known about existence and/or size of columns in other regions. To address this issue, the size of ECoG electrodes matters in that a diameter of <600 μm is required to investigate functions in columns. Larger diameters will capture signal from multiple columns, obscuring the true representation of human brain functions. Research with 7 Tesla (T) scanners has successfully discriminated columns in humans. Also, detailed imaging of hand function has shown a highly detailed functional organization at the millimeter level [55]. Moreover, separate fingers are represented in primary motor cortex at a similar scale, as shown with both 7T (1-mm resolution) and high-density ECoG (3-mm pitch) in the same patients.

In summary, fMRI (especially at 7T and higher) and ECoG can complement each other in many ways, and measurements in the same patients are likely to further our understanding of the neuronal underpinnings of human brain functions.

## 4. Contemporary Clinical ECoG

### 4.1 Chronic and Intraoperative ECoG

J. Ojemann

ECoG has been recorded in people with epilepsy for many decades. Epilepsy can be caused by genetic, structural/metabolic, or unknown mechanisms. For surgical cases, structural categories are sought and others to be avoided as the concept of a surgical-remediable disease requires a limited zone of brain that is generating seizures. This could be as broad as one side of the brain in cases requiring hemispherectomy, or as focal as a tumor in lesion-associated epilepsy. The majority of epilepsy is from idiopathic or stroke and does not

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evolve to surgical treatment. In those patients who do have EEG and/or MRI evidence of a focus, they may proceed to surgery if they have failed medical management.

The surgical approach to epilepsy is not standardized. Intraoperative recording from the brain surface, or ECoG, may augment resection of lesions and does appear to improve outcome when added to removal of the hippocampus [56] or cavernous malformations [57]. ECoG can be performed through a grid electrode array or from placement of individual electrodes at targeted locations. Intraoperative ECoG is also useful for determining any afterdischarges during cortical stimulation mapping [58] and has been proposed for immediate identification of functional cortex during awake cranial surgeries [59]. Endogenous variations in ECoG may be evident quickly enough to be used intraoperatively, as well [60].

Intraoperative ECoG can only document the physiology over a limited time period and is often confounded by anesthesiology and interictal spikes. Therefore, when seizure localization needs more precise definition, long-term (typically 4-10 days) ECoG can be used. This can be in the setting of bitemporal monitoring, typically with subdural strip electrode arrays, or neocortical foci (often combined with medial temporal monitoring), using larger subdural grid electrode arrays. The arrays used most often have 4-mm-diameter electrodes and 1-cm inter-electrode distance and are imbedded in a silicon array. There is no set limit to the number of electrodes implanted, but overall mass effect on the brain and the channel capacity of clinical setups pose challenges as electrode numbers increase. The complications of these arrays can result from brain injury or swelling, infection, cerebrospinal fluid leak, or general surgical and anesthetic complications [61]. Medial cortical coverage can be achieved, but access can be limited by bridging veins, especially over the frontoparietal region.

A second surgery is necessary to remove the arrays, and the resection can be done at the time of electrode removal or at a later point if desired. Mapping of speech and motor function can be done during the extraoperative monitoring session, using stimulation mapping or perhaps electrocorticographic mapping [62], well away from the acute effects of anesthesia.

Both intraoperative and chronic ECoG recordings are a well-accepted and well-tolerated aspect of surgical management of epilepsy and offer a wealth of opportunity to study brain dynamics at this scale.

### 4.2 Pathological (Ictal) Recordings in Epilepsy

B. Litt

Recent work by our group and others has identified interictal biomarkers of epileptic networks that have great promise to improve outcome from epilepsy surgery [63-65]. These biomarkers appear to be generated by submillimeter microdomains in brain whose activity may be initiated and propagated by synaptic noise and pathological changes associated with epilepsy, including sprouting of aberrant connectivity, loss of interneuron subtypes, and changes in gap junctions [66, 67]. The challenge then is to develop technologies that allow sampling of high-resolution, submillimeter ECoG and depth EEG from small electrodes that

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can cover clinically relevant regions, perhaps up to 100 $cm^2$ at a time. We present a technological platform to record this activity from electrode contacts spanning from 300-100 μm on a side, spaced from 250-500 μm apart [8, 68]. Electrodes are incorporated onto flexible, active electronics, and each has its own transistor circuitry realizing amplification and multiplexing beneath it. In recent work, we presented data from a 360-channel array spanning ~1.0 $cm^2$. We first demonstrated that sleep spindles, under anesthesia, are manifested on the cortical surface by small, variably sized, circular microdomains that fire synchronously but do not propagate. We next demonstrated recordings of visual evoked potentials (VEPs) on V1 cortex in the cat, demonstrating retinotopic organization of V1 and V2 regions, and showed that VEPs recorded using this device look similar to voltage-sensitive dye recordings obtained in the same region. Finally, we demonstrated that picrotoxin-induced seizures are manifested as spiral waves on the cortical surface when viewed in two dimensions from the electrode array.

We present these findings as an application of a high-resolution microECoG platform with significant potential utility in brain-computer interfacing. The non-penetrating nature of these electrodes allows great potential for long-term biocompatibility (studies in progress) and stable long-term recordings of ECoG. The active electronics platform also allows for incorporation of a number of different sensor and effector types that can be coupled to it, including optical, pressure, temperature, strain, heat, and other sensors as well as electrical stimulation, light emitting, and other stimuli that can be generated by the platform [69]. This versatile platform also allows for fabrication of different forms of penetrating electrode contacts, through similar fabrication processes. We expect increasing research and clinical applications for these devices as we begin to make them available to other groups, we hope in the near future, for experimental use. We currently are using them in experiments outside of epilepsy to explore use in auditory, visual, and motor prostheses.

## 5. ECoG Cognitive Neuroscience

M. Beauchamp, C. A. Bosman, E. Chang, A. Gunduz, D. Gupta, J. Parvizi

ECoG opens unparalleled avenues for human brain research and facilitates studies of higher level cognitive functions, such as visual perception, selective visual and auditory attention, and language and auditory processing. Studying these cognitive mechanisms with ECoG enables the investigation of the underlying distributed networks with very high temporal resolution.

ECoG also allows for the simultaneous stimulation of brain areas and recording of evoked activity in distant sites. In a recent study, Beauchamp et al. [70] observed a burst of high-frequency gamma activity in the temporoparietal junction (TPJ) with the electrical stimulation of occipital electrodes. This high-frequency activity was evoked only when the stimulation current was high enough to induce bright spots in the subject's visual field (i.e., induce perception of phosphenes). This observation of visual perception-related gamma activity in the TPJ is striking, because converging evidence suggests that the TPJ is critical for detecting behaviorally relevant stimuli, particularly if salient or unexpected. In particular, damage to the TPJ has been implicated in spatial neglect. Hence, it is possible to suggest a parallel with the Beauchamp [70] study: when electrical stimulation does not

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produce a phosphene, it does not evoke TPJ activity, and hence it is “neglected.” In contrast, when neural activity at the stimulation site does propagate to the TPJ, the activity probes “visual perception.”

Another essential mechanism for visual processing is selective attention, which lends a competitive bias to behaviorally relevant stimuli at the expense of irrelevant distractors. Gunduz et al. [71, 72] showed that ECoG could identify cortical areas and time periods that hold the most information about covert attentional shifts. ECoG was recorded when subjects covertly attended to a spatial location and responded to contrast changes in the presence of distractors in a cueing task. ECoG amplitudes in the alpha, beta, and gamma bands identified neural changes associated with covert attention and motor response in the different stages of the task. The results suggest a transient distributed frontoparietal mechanism for orienting of attention that is represented by different physiological processes. This neural mechanism encodes not only whether or not a subject shifts their attention to a location, but also the locus of attention.

As wide subdural coverage over the visual cortex is not clinically practical in humans, Schoffelen et al. [73] obtained chronic ECoG recordings from two macaque monkeys spanning visual areas V1 through V4, as well as parietal and central regions up to the frontal eye fields, during performance of an attentional change detection paradigm. They found that a visual area could be linked to both local and distant areas of interest through synchronization in distinct frequency bands. Beta-band synchronizations were observed to mediate top-down attention, whereas gamma-band synchronizations mediated bottom-up influences. The strength of these influences was enhanced dynamically when attention was directed toward the contralateral side of space. Moreover, the power of a parietal beta network (V4-7a) was reduced during attentional shifts, preceding a local V1–V4 gamma power enhancement. In contrast, during sustained attention, the parietal beta network was enhanced. These findings support the hypothesis that cortical beta-band activity is related to the maintenance of the current sensorimotor or cognitive state.

Attentional networks can also be studied in auditory systems. Mesgarani and Chang [74] investigated how the human auditory system manages to extract intelligible speech under acoustically complex and adverse listening conditions. Using ECoG recordings from subjects engaged in a dichotic listening task, they demonstrated that population responses in non-primary auditory cortex faithfully encode critical features of attended speech: speech spectrograms reconstructed on the basis of cortical responses to the mixture of speakers revealed salient spectral and temporal features of the attended speaker, as if listening to that speaker alone. A simple classifier trained solely on examples of single speakers was able to decode both attended words and speaker identity. In addition, task performance was well predicted by a rapid increase in attention-modulated neural selectivity across both local single-electrode and population-level cortical responses. These findings demonstrate that the cortical representation of speech does not merely reflect the external acoustic environment, but instead gives rise to the perceptual aspects relevant for the listener's intended goal.

In a related study, Potes et al. [75] showed that human ECoG activity in the high gamma band recorded from the posterior superior temporal gyrus (pSTG) was highly correlated with

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the intensity of complex continuous music ($r = 0.5$, $p < 0.01$). In addition, they observed that the gamma activity in pSTG was highly correlated with the gamma activity in pre-central gyrus (pCG), with the pSTG activity leading pCG by 110 msec. These results not only confirm the role of human auditory cortices in auditory processing but also support the motor theory of auditory perception. Gupta et al. [76] further investigated the perceptual filling-in of temporary absences in ongoing complex auditory stimuli. They derived the spatiotemporal patterns of ECoG high gamma activation in response to 1-sec silent gaps in popular music. It was observed that pSTG showed reduced correlation with the sound intensity with the onset of silence, and at about 300-600 msec after the beginning of the gap, ECoG gamma at middle temporal gyrus (mTG) showed significant correlation (ranging between 0.2-0.4, $p < 0.05$) with the sound intensity of the music that would have been played at this time. These findings of "anticipatory perception" are the first of their kind and could lead to further exploration of the detailed dynamics of short- or long-term recall, implicit musicality, auditory imagery, and semantic predictability.

Finally, ECoG recordings can even facilitate the study of controversial topics such as default-mode networks (DMN). Dastjerdi et al. [77] have found electrophysiological evidence that the posteromedial cortex (PMC) has increased broadband gamma power during short (5 sec) and extended (5 min) periods of rest using ECoG. In contrast, they found that PMC broadband gamma power was suppressed by externally guided attention demanding tasks, such as arithmetic processing. ECoG recordings have also proven to be useful in distinguishing the signature of electrophysiological oscillatory activity of the PMC in contrast to their neighboring regions [78]. Whereas alpha-band (8-12 Hz) activity was observed to be the main modulating rhythm in the nearby visual cortex, theta band (4-7 Hz) was the dominant oscillatory activity within the PMC and the chief phase-modulating frequency of its broadband gamma power. Furthermore, the magnitude of theta-modulated broadband gamma power within the PMC fluctuated at slow timescales (~0.1 Hz), which closely matched signals of correlated resting state networks like the DMN.

In conclusion, the method of ECoG is a feasible and unique opportunity to probe the function of human brain regions with an unmatched spatial and temporal resolution.

## 6. Clinical Utility of Functional Brain Mapping with ECoG

Nathan E. Crone

To date, ECoG has been used with greatest success as a tool for cognitive neurophysiological research, but its potential clinical use in preoperative functional mapping has always motivated its development by neurologists and neurosurgeons caring for the patients in whom these recordings are necessary. Although electrocortical stimulation mapping (ESM) is still the *de facto* gold standard for predicting postresection neurological impairments, ECoG has important practical advantages over ESM that make it attractive in clinical settings [79]. These include the avoidance of seizures and pain triggered by electrical stimulation, and the ability to assess the function of all recording electrodes simultaneously, potentially reducing the time needed for comprehensive brain mapping. Despite these advantages, however, ECoG has not been widely used for clinical purposes. One reason has been a lack of consensus about which components of ECoG signals serve as

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the best index of task-related cortical activation. Although cognitive neurophysiologists studying human brain function have successfully used phase-locked (e.g. event-related potentials) and non-phase-locked signal components in a variety of frequency bands, most recent studies have focused on task-related power modulations in high gamma (~60-200 Hz) frequencies [80].

Perhaps the most important reason why ECoG has not been adopted for clinical use is the level of technical difficulty and the lack of immediacy in its implementation. Of the several commercial systems in routine clinical use for presurgical epilepsy monitoring, none have integrated systems for ECoG functional mapping. Furthermore, until recently, analyses of task-related ECoG signal changes were performed off-line, after the completion of testing, lacking the immediate feedback to which clinicians are accustomed during ESM. Recent technological advances, however, have made it possible to get online functional mapping results during ECoG recordings. In particular, SIGnal modeling For Real-time Identification and Event Detection (SIGFRIED) is an extension of the widely used BCI2000 software system that leverages its real-time streaming and signal analysis engine to provide online visual feedback about task-related functional brain activation [4, 59]. This system compares the level of ECoG high gamma activity during periods of task performance vs. periods of rest and detects statistically significant task-related changes in this activity. When SIGFRIED was tested against ESM in motor cortex for tongue and hand in the same patients, there were no false negatives and negligible false positives. The immediate visualization of task-related ECoG activation is provided by SIGFRIED on a brain map showing all of the ECoG electrodes that were tested simultaneously. In contrast, another system for real-time ECoG mapping, called Brain TV, has focused on changes in high gamma activity at single recording sites during single trials [81]. Using a strategy analogous to receptive field mapping in single-unit recordings, Lachaux and colleagues [81] have used this system to test the behavioral variables that account for functional responses at individual recording sites, and they have allowed patients to use visual feedback of their brain responses to discover functional responses that might otherwise have been missed during formal testing.

To date, studies of the clinical utility of ECoG for preoperative functional mapping have been promising [82], but clinical decisions about surgical resections continue to rely on ESM. More studies are needed to assess the relative abilities of ECoG and ESM to predict postresection neurological impairments. Such studies will be greatly facilitated, however, by implementation of emerging ECoG mapping systems providing real-time online feedback to clinicians so that ESM can then be used to confirm ECoG-based brain maps.

## 7. Brain-Computer Interfaces

### 7.1 ECoG-Based Brain-Computer Interfaces in Monkeys

D. Moran

In natural able-bodied movements, a limb's contralateral motor cortex plays a much larger role in controlling the limb than the corresponding ipsilateral motor cortex. This laterality is well documented in stroke studies where, for instance, damage in hand area of the right

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motor cortex leads to significant weakness in the left hand's grip. The primary reason is that 90% of the axons in the corticospinal track cross over, while only 10% project ipsilaterally. It is unfortunate for the stroke patient that the healthy ipsilateral cortex cannot be rerouted to control the affected hand.

In BCI studies, one is not limited by hardwired corticospinal connections. By implanting bilateral, epidural microECoG grids, we can give each cortex the same amount of control over a device. In our latest studies, we implanted 64 electrodes (32 per hemisphere) into non-human primates previously trained to perform a two-dimensional (2D) center-out task with a joystick. Power estimations in the mu, beta, and three separate gamma bands were performed in real time, providing 320 control features. Using simple regressing techniques to adapt the 320 feature weights during closed-loop BCI control of a 2D cursor, a naive subject was able to gain accurate control in 20 minutes. Using similar techniques and after being presented with a 3D brain control task (note: the subject had never seen a 3D center-out task prior to the closed-loop experiments), the subject gained very fast and accurate control in a manner of weeks. Finally, the subject was presented with a 4D task [83] where it had to control both the 3D translation and 1D rotation of a computer cursor. In a little over a month, the subject gained accurate control over a 4D cursor. In post hoc analysis of the data, both hemispheres were significantly involved in the control of the cursor. The control did not naturally lateralize to one hemisphere, but rather the two hemispheres worked in concert to control the multidimensional cursor.

### 7.2 Motor Representation of Human Brain by ECoG

J. Rieger

ECoG offers a unique spatiotemporal window to investigate the nature of motor representations in the human brain. To date, the vast majority of studies of the human motor system employed noninvasive recording techniques that trade-off spatial vs. temporal resolution. One advantage of noninvasive methods is their wide spatial coverage, which allows for simultaneous recordings of different components of the motor system [84]. Electrophysiological recordings in animal preparations, on the other hand, are mostly confined to small patches of cortex that are sampled with high temporal resolution and high signal-to-noise ratio [85]. ECoG-recordings provide a wide spatial coverage, dense spatial sampling, an excellent signal bandwidth, and high signal-to-noise ratio. These properties, together with the relative insensitivity to movements, make ECoG an excellent method to study motor representations in human cortex by using an information based approach that can inform brain-machine interfacing (BMI).

Our BMI-research has revealed that different information appears to be coded in different dynamic ranges of the ECoG signal. In one study, we found that direction invariant information about movement, derived from the high gamma-range (HG) neural activity in motor cortex, can be used to significantly improve the reconstruction of the directional arm kinematics decoded from slow neural activation variations. In another study, we found adaptive changes in the interaction between theta and HG during skill learning in a cortical network involved in movement control. In addition, the topological adaptive changes in this network differed between theta and HG. Our current working hypothesis is that slow

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variations of neural activation may support the coordination of distributed neural modules during movement planning and execution, whereas high-frequency oscillations appear to represent local processing in specialized modules [86].

A second finding of importance for motor BMI research pertains to the relationship between motor-related neural activity in ipsi- and contralateral cortex. This is of particular importance for BMI applications targeting paresis caused by motor cortex damage, e.g., in stroke. Using a single-trial classification approach, we extended results from previous studies indicating that arm movement kinematics can be reconstructed from ipsilateral cortex [85, 87, 88]. We investigated the relationship between contra- and ipsilateral activity and found that, in some areas, ipsi- and contralateral movement representations are similar enough that classifiers trained on contralateral activations transfer to ipsilateral activations, and vice versa. This supports the notion that ipsi- and contralateral movement representations substantially overlap in the feature space offered by ECoG. This opens the possibility that ipsilateral motor representations may offer a signal space for BMI control even after contralateral cortical damage.

In conclusion, we find that ECoG provides a fine-grained spatial and a wide temporal signal space plus high signal-to-noise ratio, making it an excellent approach for single-trial information-based studies of the human cortical motor system.

### 7.3 ECoG-Based Brain-Computer Interfaces in Humans

E. Leuthardt

ECoG is generating substantial interest for its potential to support basic neuroscientific investigations and powerful and clinically practical BCI systems. This is driven by several advantageous characteristics of ECoG recordings, as well as by the growing recognition of the limitations of existing noninvasive and invasive signal modalities. ECoG has greater amplitude, higher topographical resolution, and a much broader frequency range than scalp-recorded EEG and is also less susceptible to artifacts. At the same time, ECoG is likely to have, and will likely continue to have, greater long-term stability than intracortically recorded signals. Additionally, the technical requirements for ECoG-based systems are much lower than those for intracortical systems; thus, they should be more amenable to chronic implantation.

ECoG detects a number of physiological phenomena that are represented in different time- or frequency-domain components and their interactions. This includes activity in the mu and beta bands, which are related to general aspects of movements or cognition, and can also be detected in scalp-recorded EEG. Presumably more important for BCI function, it also detects gamma activity at higher frequencies, which show much greater functional and anatomical specificity than signals in the mu and beta bands and also cannot readily be detected by EEG. In 2004, Leuthardt et al.[89] demonstrated the first use of ECoG in closed-loop control in a 1D cursor-control task with minimal training requirements (under 30 minutes). To date, 2D control has been achieved, and additional experiments have demonstrated that distinct frequency alterations encode very specific information about motor, speech and attentional and higher cognitive-related operations [72, 90-93].

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To date, ECoG-based BCI studies have been largely limited to people that were temporarily implanted with ECoG recording arrays prior to surgery. Despite the many practical difficulties of such studies, the results are promising. They suggest that ECoG-based BCIs might provide control comparable or even superior to that reported for EEG-based BCIs. These results, combined with the likely practical and robustness advantages of ECoG, are encouraging further efforts to develop ECoG-based BCI systems. Scientific issues of particular importance include the determination of the best cortical systems (motor, sensory, language, attention, etc.), the best recording methods (epidural vs. subdural, cortical location, and electrode spacing), the optimal ECoG features (mu, beta, gamma, local motor potential), and the most effective algorithm designs.

Ultimately, ECoG-based BCI systems suitable for chronic use must be wholly implantable and capable of performing reliably for many years. While such systems have not yet been developed, the individual components that would comprise them do exist or are under development. The extensive work needed to develop the complete systems and to validate them first in animals and then in humans has just begun. Its successful completion, combined with resolution of the other issues summarized above, could lead to ECoG-based BCI systems of great value to people with disabilities.

## 8. Perspectives on ECoG Research and Applications

G. Schalk

Electrocorticography is the technique of interrogating the brain using electrodes that are placed subdurally or epidurally. ECoG has been used for decades for select clinical purposes —most commonly to identify functional and epileptic brain areas in people with epilepsy— and on occasion for research. The important role of ECoG for basic research and its potential to create a new range of clinical applications has long been greatly underappreciated. Research over the past several years, including the work summarized in this article, has begun to change this view. Basic research suggests that ECoG can elucidate brain function in ways that cannot be readily achieved using other imaging modalities, and translational research is producing exciting new ECoG-based applications that will soon be available in the clinic. These exciting results also suggest the great potential for continuing improvements in signal acquisition, signal analysis, and interpretation of ECoG signals. These improvements should continue to serve to establish ECoG as an important technique for characterizing normal and abnormal brain function.

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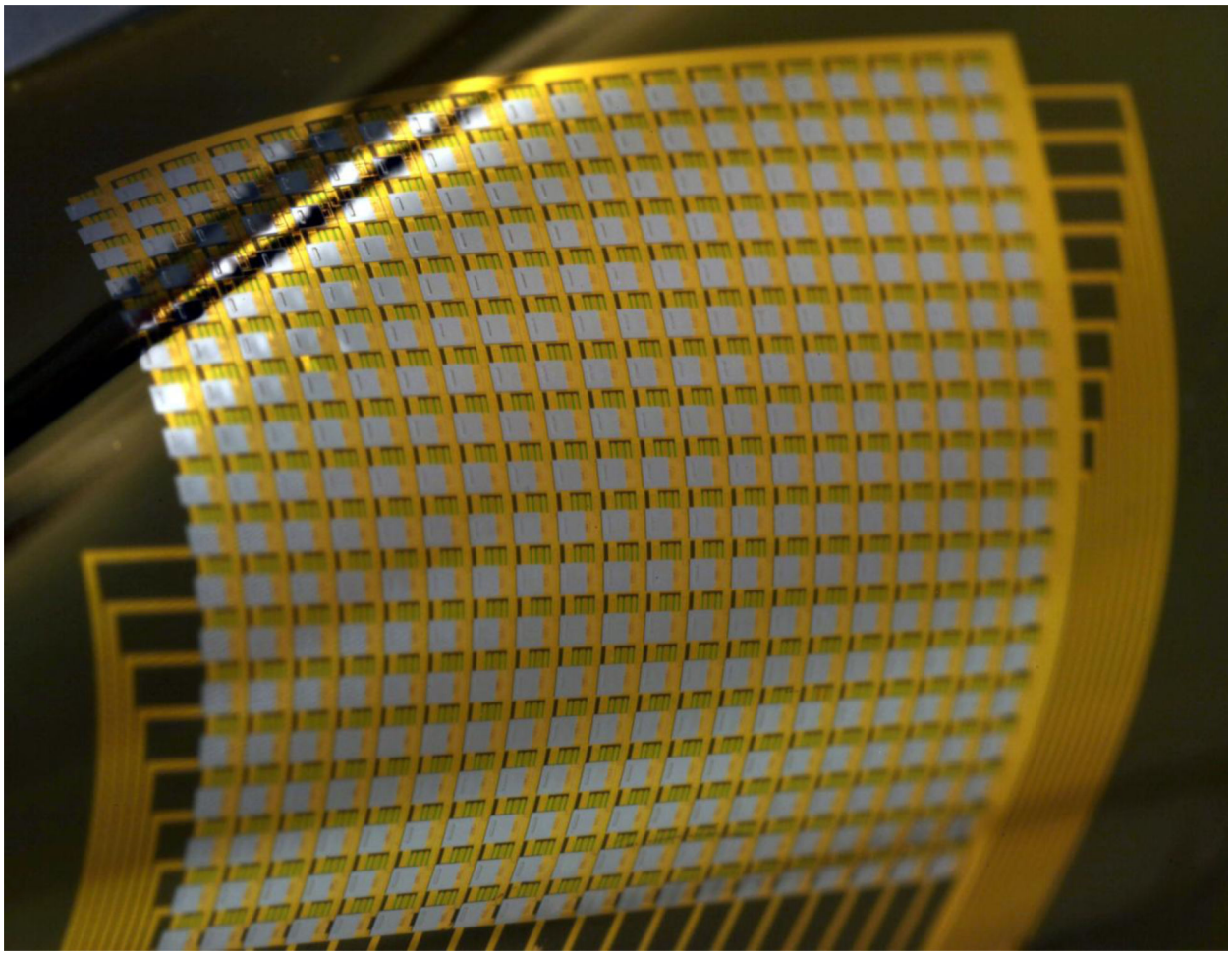

**Figure 1.**
Flexible, high-resolution multiplexed electrode array. This photograph shows a high-density active electrode array with 360 electrodes that cover 10 × 9 mm. Each electrode is sized 300 × 300 μm, and electrodes are spaced 500 μm apart.

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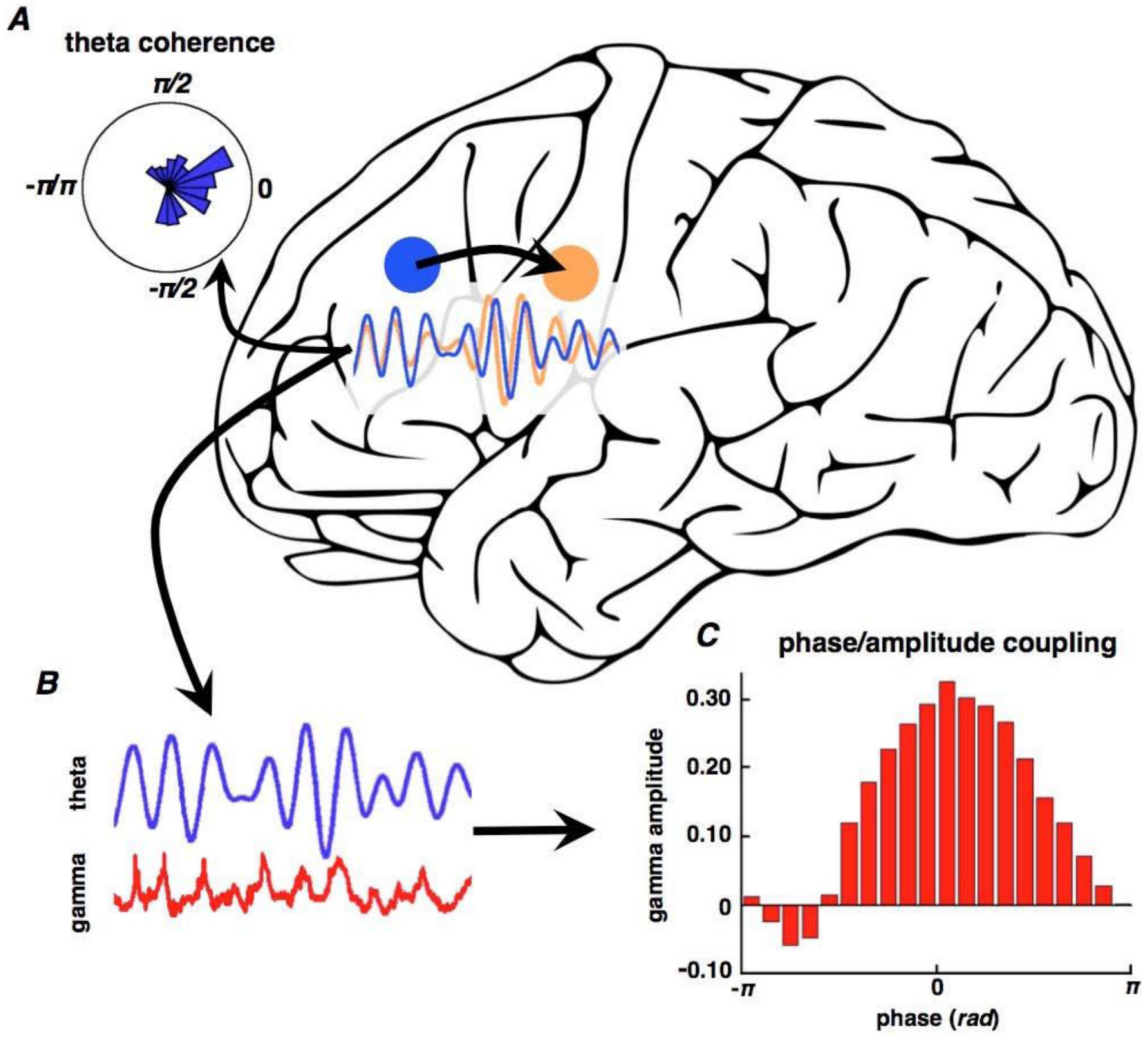


**Figure 2.**

Model for mesoscale neocortical oscillatory interactions. (**A**) Interactions between two neocortical brain regions (represented by blue and orange circles) can be statistically assessed via long-range low-frequency coherence (e.g., 4-8 Hz theta coherence). (**B**) Concurrently, within a region, theta phase is co-modulated with broadband gamma amplitude, which reflects the integrated local neuronal population firing rate. (**C**) Such phase/amplitude coupling is statistically assessed as a non-uniformity in the distribution of the amplitude of one frequency by the phase of another. We propose that when two coherent brain regions are synchronized, they communicate via low-frequency phase-dependent modulations of broadband gamma amplitude.